Total Synthesis of (-)-Fumiquinazolines A, B, C, E, H, and I.**Approaches to the Synthesis of Fiscalin A**

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Deprotection of 30a. To a solution of **30a** (210 mg, 0.35 mmol) in acetic acid (1.0 mL) was added zinc dust (800 mg). The mixture was stirred at rt for 30 min. The mixture was diluted with EtOAc (10 mL), and the zinc dust was filtered off. The filtrate was washed with saturated NaHCO₃ (3 × 10 mL) and brine (10 mL), dried (Na₂SO₄), and concentrated to give 135 mg (92%) of the amine as a white solid: ¹H NMR 7.89 (d, 1, *J* = 7.9), 7.48 (d, 1, *J* = 7.9), 7.46-7.35 (m, 5), 7.29 (ddd, 1, *J* = 7.9, 7.9, 1.2), 7.25 (ddd, 1, *J* = 7.9, 7.9, 1.2), 5.34 (s, 2), 4.79 (q, 1, *J* = 6.7), 3.78 (m, 1), 3.63 (s, 3), 3.45 (m, 1), 3.28 (m, 1), 1.70 (d, 3, *J* = 6.7).

Aniline 31. To a mixture of the crude amine (126 mg, 0.30 mmol) and EDAC (130 mg, 0.66 mmol) in MeCN (1 mL) was added anthranilic acid (77 mg, 0.56 mmol) in several portions over 60 min at rt with stirring. The reaction mixture was stirred for an additional 20 min, and concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL), saturated NaHCO₃ (3 × 10 mL) and brine (10 mL), and dried over Na₂SO₄ and concentrated. Flash chromatography on silica gel (20:1 CH₂Cl₂/EtOAc) gave 166 mg (88%) of **31** as a white solid: mp 101-105 °C; ¹H NMR 7.89 (d, 1, *J* = 7.9), 7.58 (d, 1, *J* = 7.9), 7.45-7.37 (m, 6, Cbz plus one doublet), 7.33 (dd, 1, *J* = 7.9, 7.9), 7.27 (dd, 1, *J* = 7.9, 7.9), 7.21 (br, 1), 7.15 (dd, 1, *J* = 7.9), 6.61 (d, 1, *J* = 7.9), 6.47 (dd, 1, *J* = 7.9, 7.9), 5.48 (br, 2, NH₂), 5.33 (br, 2, CH₂ of Cbz), 4.85 (ddd, 1, *J* = 8.5, 4.2, 2.4), 4.76 (br, 1, NH), 4.74 (q, 1, *J* = 6.7), 3.91-3.78 (m, 1), 3.74 (s, 3), 3.37 (dd, 1, 14.6, 2.4), 1.53 (d, 3, *J* = 6.7); ¹³C NMR 172.5, 169.0, 165.5, 149.0 (2 C), 144.9, 135.7, 134.5, 132.4, 129.0, 128.9 (2 C), 128.7 (3 C), 127.2, 126.9, 125.1, 123.8, 118.7, 117.2, 116.1, 113.2, 95.8, 69.0, 62.5, 52.6, 52.4, 26.1, 17.1.

Diamide 32. To a solution of **31** (108 mg, 0.2 mmol) and EDAC (84 mg, 0.44 mmol) in MeCN (1 mL) was added *N*-Fmoc-L-alanine (124 mg, 0.40 mmol). The resulting mixture was stirred at rt for 1.5 h and concentrated. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL), saturated NaHCO₃ (3 × 10 mL) and brine, dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel gave 156 mg (96%) of **32** as a white solid: mp 128-132 °C; ¹H NMR 8.58

(d, 1, $J = 7.9$), 7.90 (d, 1, $J = 7.9$), 7.81-7.75 (m, 2), 7.66-7.56 (m, 2), 7.54 (d, 1, $J = 7.9$), 7.48-7.25 (m, 14, including 1 NH), 6.90 (dd, 1, $J = 7.9, 7.9$), 5.46 (d, 1, $J = 6.7$, NH), 5.35 (d, 1, $J = 11.2$), 5.29 (d, 1, $J = 11.2$), 4.84-4.70 (m, 2), 4.46-4.26 (m, 3), 4.25-4.17 (m, 1), 4.15 (br, 1, NH), 3.80 (m, 1), 3.70 (s, 3), 3.37 (dd, 1, $J = 14.6, 3.2$), 1.54 (d, 3, $J = 6.7$), 1.47 (d, 3, $J = 6.7$); ^{13}C NMR 171.9, 171.1 (2 C), 168.9, 157.1, 155.5, 143.8 (2 C), 141.2 (2 C), 139.4, 136.5, 135.5, 134.4, 132.7, 129.1 (2 C), 128.9 (2 C), 128.7, 127.6 (2 C), 127.0 (2 C), 126.6, 125.2 (2 C), 125.1, 124.8, 123.9, 122.7, 121.4, 120.0, 119.9 (2 C), 118.6, 113.3, 95.4, 69.2, 67.0, 62.4, 52.9, 52.5, 51.7, 47.1, 25.7, 19.2, 17.2.

Iminobenzoxazine 33. To a solution of Ph_3P (78 mg, 0.3 mmol, 2.0 eq) in dry CH_2Cl_2 (5 mL) was added a Br_2 solution in CH_2Cl_2 (1.0 M, 0.29 mmol, 1.95 eq) under N_2 . The resulting solution was stirred at rt for 15 min, and Et_3N (0.10 mL, 3 eq) and **32** (122 mg, 0.15 mmol) were added. The resulting mixture was stirred at rt for 15 min and concentrated. The dark residue was shaken with anhydrous benzene (5 mL) and the triethylamine hydrobromide was filtered off. The filtrate was concentrated to give a dark red residue. Flash chromatography on silica gel (20:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 96 mg (81%) of **33** as a light red solid: mp 125-128 °C; ^1H NMR 7.97 (d, 1, $J = 7.9$), 7.83 (d, 1, $J = 7.9$), 7.77 (d, 2, $J = 8.0$), 7.65 (d, 1, $J = 8.0$), 7.62 (d, 1, $J = 8.0$), 7.59 (d, 1, $J = 7.9$), 7.51 (dd, 1, $J = 7.9, 7.9$), 7.46-7.22 (m, 12), 7.20 (dd, 1, $J = 7.9, 7.9$), 5.52 (br, 1, NH), 5.36 (br, 2), 4.84 (m, 1), 4.75 (q, 1, $J = 6.7$), 4.48-4.34 (m, 2), 4.30 (br, 1), 4.24 (t, 1, $J = 6.7$), 3.72 (m, 1), 3.66 (s, 3), 3.50 (m, 1), 1.45 (d, 3, $J = 6.7$), 1.34 (d, 3, $J = 6.7$); ^{13}C NMR 172.5, 165.9, 159.4, 155.4, 150.9, 149.7, 147.5, 144.0, 143.7, 141.3, 140.9, 136.5, 136.2, 135.3, 133.3, 128.7 (4 C), 128.6, 128.2, 127.7 (2 C), 127.0 (2 C), 126.9, 126.4, 126.1, 125.1, 125.0, 125.6, 124.3, 119.9 (2 C), 119.5, 119.1, 113.0, 97.2, 68.6, 66.8, 62.8, 59.6, 52.1, 48.8, 47.2, 27.9, 19.4, 18.2.

Quinazolinone 35. To a solution **33** (82 mg, 0.10 mmol) in EtOAc (1 mL), was added pyrrolidine (0.02 mL, 0.20 mmol). The resulting mixture was stirred at rt for 30 min, and concentrated to give crude amidine **34**. A solution of crude **34** in CH_3CN (5 mL) was refluxed for 2 h. The reaction mixture was cooled down and concentrated. Flash chromatography on silica gel (1:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 42

mg (67%) of **35** as a sticky oil: ^1H NMR (two rotamers, major rotamer) 9.85 (s, 1, NH), 8.35 (d, 1, $J = 7.9$), 7.86 (d, 1, $J = 7.9$), 7.73 (m, 2), 7.35-7.26 (m, 5), 7.19 (dd, 1, $J = 7.9, 7.9$), 7.13 (dd, 1, $J = 7.9, 7.9$), 7.00 (m, 2), 5.65 (br, 1, NH), 5.60 (m, 1, H-14), 4.66 (q, 1, $J = 6.7$), 4.34 (d, 1, $J = 12.2$), 3.75 (m, 2), 3.66 (q, 1, $J = 6.7$), 3.39 (d, 1, $J = 12.2$), 3.21 (m, 2), 3.14 (m, 1), 2.96 (m, 1), 1.70 (m, 2), 1.45 (m, 2), 1.39 (d, 3, $J = 6.7$), 0.82 (d, 3, $J = 6.7$); ^1H NMR (minor rotamer, partial) 10.29 (s, 1, NH), 8.32 (d, 1, $J = 7.9$), 2.03 (m, 2), 1.10 (d, 3, $J = 6.7$).

Methyl (2S,9S,9aS, α R)-9-hydroxy- α -[[[(2,2,2-trichloroethoxy)carbonyl]amino]-2-methyl-3-oxo-1-[(phenylmethoxy)carbonyl]-2,3,9,9a-tetrahydro-1H-imidazo(1,2-a)indole-9-propanoate (39a**). To 4 mL of acetic acid in an ice water bath was added NaBH_4 (570 mg, 15 mmol) in several portions. The NaBH_4 solution in acetic acid was warmed to 25 °C and added to a solution of **38a** (322 mg, 0.5 mmol) in acetic acid (2 mL). The resulting mixture was stirred at 25 °C for 2 h, then diluted with CH_2Cl_2 (10 mL) and washed with water (3×10 mL), saturated NaHCO_3 solution and brine, dried (Na_2SO_4) and evaporated to give a crude mixture of **39a** and **37a**. Rapid flash chromatography on silica (15:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 26 mg (9%) of **37a** followed by 240 mg (78%) of a 14:1 mixture of **39a** and **37a** as a white solid. Hydroxy ester **39a** lactonized to **37a** very readily.**

Data for **39a** were determined from the mixture: mp 79-82 °C; $[\alpha]_D -33.0$ (c 0.46, CHCl_3); ^1H NMR 7.51 (d, 1, $J = 7.9$), 7.45-7.36 (m, 6), 7.34 (t, 1, $J = 7.9$), 7.21 (t, 1, $J = 7.9$), 5.65 (s, 1), 5.63 (br s, 1, NH), 5.32-5.21 (m, 2), 4.72 (d, 1, $J = 12.2$), 4.65 (d, 1, $J = 12.2$), 4.62-4.44 (m, 2), 3.89 (br s, 1, OH), 3.62 (s, 3), 2.26-2.13 (m, 1), 1.91-1.79 (m, 1), 1.57 (br, d, 3, $J = 6.7$); ^{13}C NMR 172.2, 166.8, 156.2, 153.8, 135.4, 131.3, 130.1, 128.8 (br, 3 C), 128.4 (2 C), 127.0, 126.2, 125.8, 116.5, 95.2, 86.9, 79.8, 74.7, 68.9, 59.6, 52.7, 50.1, 37.1, 17.9; IR (KBr) 3420, 1734 (br), 1609, 1540.

Methyl (2S,9R,9aR, α R)-9-hydroxy- α -[[[(2,2,2-trichloroethoxy)carbonyl]amino]-2-methyl-3-oxo-1-[(phenylmethoxy)carbonyl]-2,3,9,9a-tetrahydro-1H-imidazo(1,2-a)indole-9-propanoate (41a**). To 2 mL of acetic acid in an ice water bath was added NaBH_4 (220 mg, 6 mmol) in several portions. The NaBH_4 solution in acetic acid was warmed to 25 °C and added to a solution of **40a** (120 mg, 0.19**

mmol) in acetic acid (1 mL). The resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with water (3 × 10 mL), saturated NaHCO₃ solution and brine, dried (Na₂SO₄) and evaporated under reduced pressure. Rapid flash chromatography on silica (40:1 CH₂Cl₂/EtOAc) gave 6 mg (5%) of **43a** followed by 94 mg (81%) of **41a** as a white solid: mp 83-85 °C; [α]_D +70.3 (*c* 0.57, CHCl₃); ¹H NMR (6:1 mixture of rotamers), 7.53 (d, 1, *J* = 8.0), 7.47 (d, 1, *J* = 8.0), 7.44-7.36 (m, 6), 7.24 (t, 1, *J* = 8.0), 6.41 (br d, 1, *J* = 5.5, NH), 5.72 (s, 1), 5.32 (d, 1, *J* = 12.2), 5.24 (d, 1, *J* = 12.2), 4.81 (d, 1, *J* = 12.2), 4.74 (d, 1, *J* = 12.2), 4.47 (q, 1, *J* = 6.7), 4.42 (s, 1, OH), 4.47-4.41 (m, 1), 3.66 (s, 3), 1.92 (dd, 1, *J* = 14.4, 11.0), 1.85 (dd, 1, *J* = 14.4, 4.0), 1.62 (d, 3, *J* = 6.7); ¹H NMR (minor rotamer, partial), 7.56 (d, 1, *J* = 8.0), 6.24 (br, 1, NH), 5.68 (s, 1), 3.63 (s, 3), 1.71 (d, 3, *J* = 6.7); ¹³C NMR (major rotamer), 171.8, 167.2, 155.1, 154.0, 135.3, 134.9, 134.6, 130.2, 128.8 (3 C), 128.2 (2 C), 126.6, 125.3, 116.9, 95.4, 86.32, 8.52, 74.6, 68.7, 60.1, 52.5, 51.0, 34.2, 17.2; ¹³C NMR (minor rotamer, partial) 129.9, 129.6, 129.4, 50.3, 34.7, 16.2; IR (KBr) 3372, 2953, 1728 (br), 1609, 1546, 1512. On longer reaction times or slower chromatography, **41a** cyclized to **43a**.

Aniline Precursor to 61a. To a solution of **43a** (475 mg, 0.82 mmol) in acetic acid (3.0 mL) was added zinc dust (1.2 g). The mixture was stirred at rt for 30 min. The zinc dust was filtered off and the filtrate was concentrated. The residue was dissolved in EtOAc (10 mL), which was washed with saturated NaHCO₃ (3 × 10 mL) and brine (10 mL), dried over Na₂SO₄, and concentrated to give the crude amine.

To a mixture of the crude amine and EDAC (350 mg, 1.82 mmol) in MeCN (2 mL) was added anthranilic acid (200 mg, 1.46 mmol) in several portions over 60 min at rt with stirring. The reaction mixture was stirred for an additional 20 min, and concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10 mL). The resultant solution was washed with water (5 mL), saturated NaHCO₃ (3 × 10 mL) and brine (10 mL), dried over Na₂SO₄ and concentrated. Flash chromatography on silica gel (10:1 CH₂Cl₂/EtOAc) gave 312 mg (85%) of the aniline as a white solid: mp 118-120 °C; ¹H NMR (4:1 mixture of rotamers, major rotamer) 7.88 (d, 1, *J* = 7.9), 7.49 (d, 1, *J* = 7.9), 7.43-7.32 (m, 6), 7.29

(d, 1, $J = 7.9$), 7.25 (dd, 1, $J = 7.9, 7.9$), 7.16 (dd, 1, $J = 7.9, 7.9$), 6.77 (br d, 1, $J = 3.7$, NH), 6.64-6.52 (m, 2), 5.94 (s, 1), 5.57 (br s, 2, NH₂), 5.23 (d, 1, $J = 11.6$), 5.19 (d, 1, $J = 11.6$), 4.43 (q, 1, $J = 6.7$), 4.15 (ddd, 1, $J = 10.4, 9.2, 3.7$), 2.75 (dd, 1, $J = 14.0, 10.4$), 2.28 (dd, 1, $J = 14.0, 9.2$), 1.65 (d, 3, $J = 6.7$); ¹H NMR (minor rotamer, partial) 7.89 (d, 1, $J = 7.9$), 7.44 (d, 1, $J = 7.9$), 5.31 (d, 1, $J = 11.6$), 5.08 (d, 1, $J = 11.6$), 3.97 (br, 1), 2.82 (dd, 1, $J = 12.2, 11.0$), 1.68 (d, 3, $J = 6.7$); ¹³C NMR (major rotamer) 174.6, 169.3, 168.9, 154.2, 149.2, 136.0, 135.9, 135.6, 132.9, 130.6, 128.7 (3 C), 128.4 (2 C), 127.4, 127.2, 126.1, 117.4, 116.4, 116.0, 113.7, 89.6, 83.4, 68.3, 59.5, 51.2, 34.9, 17.5; ¹³C NMR (minor rotamer, partial) 129.4, 125.5, 68.1, 60.0, 50.8, 34.6, 16.5.

Diamide Precursor to 61a. To a solution of the aniline (240 mg, 0.45 mmol) and EDAC (1400 mg, 0.736 mmol, 1.6 eq) in MeCN (3 mL) was added *N*-Fmoc-phenylselenenyl-L-alanine (318 mg, 0.68 mmol, 1.5 eq). The resulting mixture was stirred at rt for 1 h and concentrated. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL) and saturated NaHCO₃ (3 × 10 mL), dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel gave 420 mg (93%) of the diamide as a white solid: mp 158-160 °C; [α]_D + 88 (*c* 0.50 in CHCl₃); ¹H NMR (3.5:1 mixture of rotamers, major rotamer) 11.30 (s, 1, NH), 8.32 (br d, 1, $J = 8.0$), 8.05 (d, 1, $J = 7.3$, NH), 7.76-7.68 (m, 2), 7.66-7.58 (m, 2), 7.49 (d, 1, $J = 8.0$), 7.49-7.39 (m, 4), 7.40-7.30 (m, 8), 7.30-7.20 (m, 4), 7.09-6.99 (m, 3), 6.99 (dd, 1, $J = 8.0$), 5.99 (br d, 1, $J = 7.3$, NH), 5.91 (br s, 1), 5.26-5.15 (m, 2), 4.50 (br, 1), 4.39 (q, 1, $J = 6.7$), 4.39-4.22 (m, 3), 4.17 (t, 1, $J = 6.7$), 3.54-3.34 (m, 2), 2.74 (dd, 1, $J = 13.6, 10.6$), 2.29 (dd, 1, $J = 13.6, 9.2$), 1.58 (d, 3, $J = 6.7$); ¹H NMR (minor rotamer, partial) 11.12 (br s, 1, NH), 8.36 (br d, 1, $J = 7.9$), 7.92 (d, 1, $J = 8.0$), 5.89 (br d, 1, $J = 7.1$, NH), 5.84 (br s, 1), 5.33 (d, 1, $J = 12.1$), 5.00 (d, 1, $J = 12.1$), 4.56-4.48 (m, 1), 2.95-2.83 (m, 1), 2.47-2.36 (m, 1), 1.53 (br d, 3, $J = 6.6$); ¹³C NMR (major rotamer) 174.8, 169.2, 168.8, 168.4, 155.9, 154.3, 143.9, 143.6 (2 C), 141.2, 141.1, 138.7, 136.0, 135.6, 135.5, 133.3 (3 C), 133.1, 130.9, 129.0 (2 C), 128.7 (2 C), 128.5, 128.4 (2 C), 127.6 (2 C), 127.2, 127.05, 126.95, 126.7, 126.0, 125.4, 125.0 (2 C), 123.3, 121.7, 119.8 (2 C), 116.1, 90.0, 83.4, 68.3, 67.4, 59.5, 55.9, 51.6, 46.9, 34.5, 30.5, 17.4; ¹³C NMR (minor rotamer, partial) 168.8, 135.1, 134.9,

134.5, 131.0, 129.3, 129.0, 127.4, 127.2, 118.9, 116.4, 89.8, 84.1, 68.5, 68.1, 60.1, 51.3, 34.8, 16.4; IR (KBr) 3408 (br), 1790, 1728, 1692, 1645, 1603, 1587, 1519. Anal. Calcd for C₅₃H₄₅N₅O₉Se: C, 65.29; H, 4.65; N, 7.18. Found: C, 65.56; H, 4.91; N, 6.78.

Diamide Precursor to 61b. To a solution of aniline **51** (320 mg, 0.56 mmol) and EDAC (200 mg, 1.04 mmol, 1.85 eq) in MeCN (3 mL) was added *N*-Fmoc-phenylselenenyl-L-alanine (420 mg, 0.90 mmol, 1.6 eq). The resulting mixture was stirred at rt for 1 h and concentrated. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL) and saturated NaHCO₃ (3 × 10 mL), dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel gave 560 mg (98%) of the diamide as a white solid: mp 137-139 °C; [α]_D +95.5 (*c* 0.32 in CHCl₃); ¹H NMR (5:1 mixture of rotamers, major rotamer) 11.20 (s, 1, NH), 8.35 (br d, 1, *J* = 7.9), 8.03 (d, 1, *J* = 6.7, NH), 7.73 (br, 2), 7.65-7.58 (m, 1), 7.53-7.30 (m, 14), 7.30-7.18 (m, 3), 7.10-7.00 (m, 5), 5.99 (br d, 1, *J* = 7.6, NH), 5.91 (br s, 1), 5.25 (d, 1, *J* = 12.2), 5.17 (d, 1, *J* = 12.2), 4.76 (br, 1), 4.45-4.35 (m, 1), 4.40-4.20 (m, 3), 4.16 (t, 1, *J* = 6.7), 3.54-3.35 (m, 2), 2.75 (dd, 1, *J* = 13.8, 11.7), 2.29 (dd, 1, *J* = 13.8, 9.4), 1.96-1.75 (m, 3), 0.92 (d, 3, *J* = 5.5), 0.84 (d, 3, *J* = 6.1); ¹H NMR (minor rotamer, partial) 11.07 (br s, 1, NH), 8.40 (br d, 1, *J* = 7.9), 7.92 (d, 1, *J* = 8.0), 5.84 (br d, 1, *J* = 7.1, NH), 5.73 (br s, 1), 5.33 (d, 1, *J* = 12.2), 5.07 (d, 1, *J* = 12.2), 4.49 (m, 1), 0.96 (br d, 3, *J* = 6.0); ¹³C NMR (major) 174.4, 168.8, 168.7, 168.5, 156.0, 154.2, 144.0, 143.6 (2 C), 141.2, 141.1, 138.6 (br), 136.1, 135.6, 135.5, 133.4 (3 C), 133.1, 130.9, 129.0 (2 C), 128.7 (2 C), 128.64 (2 C), 128.59, 128.5, 127.6 (2 C), 127.05, 126.98, 126.7, 126.0, 125.4, 125.1 (2 C), 123.4, 121.8, 119.9 (2 C), 116.2, 90.1, 83.6, 68.3, 67.4, 62.2, 55.9, 51.7, 46.9, 39.9, 34.7, 30.5, 24.1, 23.5, 22.0; ¹³C NMR (minor rotamer, partial) 129.4, 128.9, 127.3, 127.2, 125.7, 119.3, 94.3; IR (KBr) 3396 (br), 3297 (br), 1795, 1723, 1713, 1643, 1602, 1588, 1520, 1504.

Iminobenzoxazine Precursor to 61a. To a solution of Ph₃P (210 mg, 0.78 mmol, 2 eq) in dry CH₂Cl₂ (5 mL) was added a Br₂ solution in CH₂Cl₂ (1.0 M, 0.77 mmol, 1.95 eq) under N₂. The resulting solution was stirred at rt for 5 min, and (*i*-Pr)₂NEt (0.28 mL, 4 eq) and 380 mg (0.39 mmol) of the diamide were added. The resulting mixture was stirred at rt for 5 min, quenched with saturated

NaHCO₃ (5 mL), washed with brine (5 mL), dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel (20:1 CH₂Cl₂/EtOAc) gave 302 mg (81%) of the iminobenzoxazine as a light-yellow solid: mp 121-123 °C; [α]_D +54.6 (*c* 0.30 in CHCl₃); ¹H NMR (3:1 mixture of rotamers, major rotamer) 8.00 (d, 1, *J* = 7.9), 7.75 (d, 2, *J* = 7.3), 7.63 (d, 2, *J* = 7.3), 7.60-7.48 (m, 4), 7.49-7.42 (m, 1), 7.44-7.25 (m, 14), 7.08-6.93 (m, 2), 6.10 (d, 1, *J* = 7.9, NH), 6.05 (s, 1), 5.39 (d, 1, *J* = 12.2), 5.24 (d, 1, *J* = 12.2), 4.98-4.84 (m, 2), 4.52 (q, 1, *J* = 6.1), 4.40-4.28 (m, 2), 4.22 (t, 1, *J* = 7.3), 3.60 (dd, 1, *J* = 13.0, 4.3), 3.45 (dd, 1, *J* = 13.0, 5.8), 2.97 (dd, 1, *J* = 13.4, 9.8), 2.16 (dd, 1, *J* = 13.0, 7.3), 1.63 (br d, 3, *J* = 6.1); ¹H NMR (minor rotamer, partial) 7.97 (d, 1, *J* = 8.0), 6.12 (d, 1, *J* = 7.9, NH), 6.00 (s, 1), 5.40 (d, 1, *J* = 11.6), 5.18 (d, 1, *J* = 11.6), 4.64 (q, 1, *J* = 6.1), 4.60-4.53 (m, 2), 4.44-4.37 (m, 1), 3.62-3.53 (m, 1), 3.45-3.35 (m, 1), 2.81 (dd, 1, *J* = 13.2, 9.1), 2.02 (dd, 1, *J* = 13.2, 6.1), 1.72 (br d, 3, *J* = 6.1); ¹³C NMR (major rotamer) 174.2, 169.2, 156.5, 155.5, 154.4, 149.2, 143.7 (2 C), 141.2 (2 C), 140.7, 136.1 (2 C), 135.2, 133.5, 133.3 (3 C), 130.6, 129.0 (2 C), 128.7 (2 C), 128.5 (2 C), 128.4, 128.2, 127.6 (2 C), 127.1, 127.0 (2 C), 126.9, 126.5, 126.0, 125.2 (2 C), 124.9, 119.9 (2 C), 118.8, 116.4, 90.0, 83.2, 68.3, 67.2, 59.8, 55.3, 53.0, 47.0, 37.8, 30.4, 17.6; ¹³C NMR (minor rotamer, partial), 173.7, 169.2, 152.6, 149.4, 143.5, 140.7, 135.9, 135.2, 134.5, 130.8, 129.2, 128.8, 128.0, 126.6, 125.0, 90.7, 82.7, 68.4, 68.0, 59.4, 60.1, 54.7, 37.2, 30.4, 16.5; IR (KBr) 3413 (br), 2957, 1793, 1725, 1717, 1676, 1654, 1607, 1522, 1507

Iminobenzoxazine Precursor to 61b. To a solution of Ph₃P (262 mg, 1.0 mmol, 2 eq) in dry CH₂Cl₂ (10 mL) was added a Br₂ solution in CH₂Cl₂ (1.0 M, 97 mmol, 1.95 eq) under N₂. The resulting solution was stirred at rt for 5 min, and (i-Pr)₂NEt (0.35 mL, 4 eq) and the diamide (508 mg, 0.50 mmol) were added. The resulting mixture was stirred at rt for 5 min, quenched with saturated NaHCO₃ (5 mL), washed brine (5 mL), dried over Na₂SO₄ and concentrated. Flash chromatography on silica gel (20:1 CH₂Cl₂/EtOAc) gave 460 mg (92%) of the iminobenzoxazine as a light-yellow solid: mp 114-116 °C; [α]_D +33.2 (*c* 0.30 in CHCl₃); ¹H NMR (3:1 mixture of rotamers, major rotamer) 8.00 (d, 1, *J* = 7.9), 7.76 (d, 2, *J* = 7.3), 7.63 (d, 2, *J* = 7.3), 7.60-7.47 (m, 4), 7.49-7.42 (m, 1), 7.44-7.25 (m, 14), 7.10-6.93

(m, 2), 6.10 (d, 1, $J = 7.9$, NH), 6.04 (s, 1), 5.43 (d, 1, $J = 12.2$), 5.19 (d, 1, $J = 12.2$), 4.98-4.84 (m, 2), 4.55-4.45 (m, 1), 4.42-4.30 (m, 2), 4.27-4.19 (m, 1), 3.61 (dd, 1, $J = 13.0$, 4.3), 3.46 (dd, 1, $J = 13.0$, 5.8), 2.97 (dd, 1, $J = 13.4$, 9.8), 2.16 (dd, 1, $J = 13.0$, 7.3), 2.09-1.78 (m, 3), 0.91 (br d, 3, $J = 6.1$), 0.83 (br d, 3, $J = 6.1$); ^1H NMR (minor rotamer, partial) 7.97 (d, 1, $J = 8.0$), 6.14 (d, 1, $J = 7.9$, NH), 5.16 (d, 1, $J = 11.2$), 4.62-4.55 (m, 1), 4.48-4.41 (m, 1), 3.65-3.53 (m, 1), 3.45-3.36 (m, 1), 2.85-2.75 (m, 1), 2.18-2.07 (m, 1), 1.01 (br d, 3, $J = 6.1$), 0.87 (br, d, 3, $J = 6.1$); ^{13}C NMR (major rotamer) 174.3, 168.9, 156.5, 155.5, 154.2, 149.2, 143.7 (2 C), 141.2 (2 C), 140.7, 136.1, 136.0, 135.1, 133.6, 133.4 (3 C), 130.6, 129.0 (2 C), 128.7 (3 C), 128.5 (2 C), 128.2, 127.7 (2 C), 127.1, 127.0 (2 C), 126.9, 126.5, 126.0, 125.2 (2 C), 124.9, 119.9 (2 C), 118.8, 116.5, 90.1, 83.5, 68.3, 67.2, 62.5, 55.4, 53.0, 47.0, 39.9, 37.9, 30.4, 24.1, 23.5, 21.9; ^{13}C NMR (minor rotamer, partial), 174.3, 156.2, 155.4, 149.4, 143.8, 140.7, 135.9, 135.4, 135.3, 133.7, 133.5, 129.2, 128.8, 128.6, 127.3, 126.7, 90.9, 83.0, 68.0, 62.8, 54.8, 38.1, 37.2, 22.3; IR (KBr) 3417 (br), 1792, 1679, 1654, 1607, 1505.

***N*-19-Cbz-Dehydrofumiquinazoline I Analogue 61a.** To a solution of the iminobenzoxazine (550 mg, 0.57 mmol) in dry EtOAc (0.5 mL) was added dry piperidine (0.1 mL, 10 eq). The resulting mixture was stirred at rt for 10 min, diluted with hexane (3 mL) and concentrated under reduced pressure to give the crude amidine, which was dissolved in dry MeCN (4 mL), and AcOH (0.1 mL) was added. The solution was refluxed for 1.5 h, cooled, and concentrated to give a light-red residue. Flash chromatography on silica gel (5:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 16 mg (5%) of **64a** as white solid followed by 185 mg (56%) of **61a** as a white solid: mp 161-164 °C; $[\alpha]_{\text{D}} -53.8$ (c 0.30 in CHCl_3); ^1H NMR (2:1 mixture of rotamers, major rotamer) 8.96 (s, 1, NH), 8.17 (d, 1, $J = 8.2$), 8.00 (d, 1, $J = 7.3$), 7.83-7.68 (m, 2), 7.54 (d, 1, $J = 7.9$), 7.50-7.25 (m, 7), 7.13 (dd, 1, $J = 7.9$, 7.9), 6.02 (s, 1), 5.67 (d, 1, $J = 1.2$), 5.55 (dd, 1, $J = 10.7$, 3.7), 5.22-5.16 (m, 2), 4.56 (q, 1, $J = 6.7$), 4.40 (d, 1, 1.2), 4.25 (s, 1, OH), 2.24 (dd, 1, $J = 13.4$, 10.7), 1.96 (dd, 1, $J = 13.4$, 3.7), 1.60 (d, 3, $J = 6.7$); ^1H NMR (minor rotamer, partial) 8.77, (s, 1), 8.14 (d, 1, $J = 7.9$), 6.81 (t, 1, $J = 7.9$), 6.06 (s, 1), 5.75 (d, 1, $J = 1.2$), 5.25 (d, 1, $J = 12.2$), 5.15 (d, 1, $J = 12.2$), 4.47 (d, 1, $J = 1.2$), 4.41-4.35 (m, 1), 4.15 (s, 1, OH), 2.49-2.37 (m, 1), 1.57 (d, 3, J

= 6.7); ^{13}C NMR (major rotamer) 167.6, 166.7, 159.6, 155.1, 146.9, 143.5, 136.5, 135.7, 135.2, 134.9, 133.6, 130.1, 128.6 (3 C), 128.5 (2 C), 128.2, 127.6, 127.5, 127.0, 126.3, 120.5, 116.3, 103.2, 86.4, 80.8, 68.2, 60.0, 52.2, 36.4, 17.3; ^{13}C NMR (minor rotamer, partial) 160.5, 147.0, 143.5, 120.4, 116.6, 102.5, 87.1, 80.6, 68.4, 60.0, 51.4, 38.0, 17.4; IR (KBr) 3460 (br), 3285 (br), 2957, 1701, 1686, 1654, 1607, 1578, 1568, 1507.

***N*-19-Cbz-Dehydrofumiquinazoline I (61b).** To a solution of the iminobenzoxazine (340 mg, 0.34 mmol) in dry EtOAc (0.5 mL) was added dry piperidine (0.1 mL, 3 eq). The resulting mixture was stirred at rt for 10 min, diluted with hexane (3 mL) and concentrated under reduced pressure to give the crude amidine, which was dissolved in dry MeCN (4 mL), and AcOH (0.1 mL) was added. The solution was refluxed for 1.5 h, cooled down, and concentrated to give a light-red residue. Flash chromatography on silica gel (5:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 15 mg (7%) of **64b** as white solid followed by 125 mg (60%) of **61b** as a white solid: mp 154-156 °C; $[\alpha]_{\text{D}}^{25} +94.3$ (*c* 0.32 in CHCl_3); ^1H NMR (2:1 mixture of rotamers, major rotamer) 9.58 (s, 1, NH), 8.16 (d, 1, $J = 8.2$), 8.00 (d, 1, $J = 7.3$), 7.83-7.65 (m, 2), 7.54 (d, 1, $J = 7.9$), 7.50-7.25 (m, 7), 7.12 (dd, 1, $J = 7.9, 7.9$), 6.02 (s, 1), 5.73 (d, 1, $J = 1.2$), 5.54 (dd, 1, $J = 10.7, 3.4$), 5.21 (d, 1, $J = 11.6$), 5.15 (s, 1, OH), 5.13 (d, 1, $J = 11.6$), 4.41 (d, 1, $J = 1.2$), 4.40-4.35 (m, 1), 2.24 (dd, 1, $J = 13.4, 10.4$), 1.96-1.72 (m, 4), 0.87 (d, 3, $J = 6.1$), 0.81 (d, 3, $J = 6.1$); ^1H NMR (minor rotamer, partial) 8.47, (s, 1), 8.14 (d, 1, $J = 7.9$), 6.78 (dd, 1, $J = 7.9$), 6.12 (s, 1), 5.63 (d, 1, $J = 1.2$), 5.31 (d, 1, $J = 12.2$), 5.15 (d, 1, $J = 12.2$), 5.05 (d, 1, $J = 1.2$), 4.56-4.48 (m, 1), 4.22 (s, 1, OH), 2.41-2.29 (m, 1), 0.89 (d, 3, $J = 6.1$), 0.83 (d, 3, $J = 6.1$); ^{13}C NMR (major rotamer) 167.2, 166.7, 159.6, 154.7, 147.0, 144.0, 135.8, 135.5, 134.8, 134.7, 133.8, 130.1, 128.6 (5 C), 128.4, 127.7, 127.1, 126.3, 125.6, 120.3, 116.4, 103.2, 86.7, 80.9, 68.2, 62.7, 51.4, 39.9, 37.8, 24.1, 23.5, 22.0; ^{13}C NMR (minor rotamer, partial) 160.5, 146.9, 116.4, 80.7, 68.5, 62.8, 52.2, 37.8; IR (KBr) 3460 (br), 1716, 1685, 1654, 1612.

Analogue 64a. To a solution of **61a** (37 mg, 0.064 mmol) in MeCN (4 mL) was added AcOH (0.01 mL). The solution was refluxed for 12h, cooled and concentrated. Flash chromatography on silica gel

(10:1 CH₂Cl₂/EtOAc) gave 8 mg (27%) of a 2:1 mixture of **64a** and the enantiomer of **60** as a white solid followed by 12 mg (33%) of recovered **61a**.

Data for **64a** were determined from the mixture: ¹H NMR 8.30 (d, 1, *J* = 7.9), 7.86 (d, 1, *J* = 7.9), 7.80 (ddd, 1, *J* = 7.9, 7.9, 1.2), 7.71 (s, 1, NH), 7.58 (d, 1, *J* = 7.9), 7.55 (d, 1, *J* = 7.9), 7.50 (dd, 1, *J* = 7.9, 7.9), 7.35 (dd, 1, *J* = 7.9, 7.9), 7.30-7.26 (m, 4), 7.25 (dd, 1, *J* = 7.9, 7.9), 6.98-6.92 (m, 1), 5.77 (s, 1), 5.74-5.67 (m, 1), 4.39 (d, 1, *J* = 12.2), 4.34 (d, 1, *J* = 12.2), 4.31 (q, 1, *J* = 6.7), 2.62 (dd, 1, *J* = 15.6, 3.6), 2.29 (dd, 1, *J* = 15.6, 4.3), 2.14 (s, 3), 1.45 (d, 3, *J* = 6.7); ¹³C NMR 169.2, 168.9, 160.4, 153.2, 150.4, 147.6, 140.4, 135.0, 134.4, 129.8, 128.5 (2 C), 128.4 (3 C), 128.3 (2 C), 127.5, 127.4, 126.3, 124.3, 121.6, 116.8, 86.5, 85.3, 83.6, 67.7, 59.6, 51.8, 30.9, 24.4, 17.4; IR (KBr) 3261 (br), 1721, 1690, 1607, 1603, 1571, 1547, 1512.

Analogue 65a. To a solution of the 2:1 mixture of **64a** and the enantiomer of **60** (3 mg, 0.005 mmol) in EtOH (1 mL) was added Pd (5%) on carbon (3 mg). The suspension was stirred at rt under H₂ (60 PSI) for 24 h. The catalyst was filtered off and the filtrate was evaporated to give crude product. Flash chromatography on silica gel (1:1 CH₂Cl₂/EtOAc) gave 1.5 mg (68%) of a 2:1 mixture of **65a** and the enantiomer of **7** as a light yellow solid.

Data for **65a** were determined from the mixture: ¹H NMR (CDCl₃) 8.37 (dd, 1, *J* = 7.9, 1.2), 7.85 (dd, 1, *J* = 7.9, 7.9), 7.81 (d, 1, *J* = 7.9), 7.62 (dd, 1, *J* = 7.9, 7.9), 7.43 (d, 1, *J* = 7.9), 7.35 (d, 1, *J* = 7.9), 7.34 (dd, 1, *J* = 7.9, 7.9), 7.21 (td, 1, *J* = 7.9, 1.2), 6.72 (s, 1, NH), 5.72 (d, 1, 7.3), 5.36 (dd, 1, *J* = 8.2, 1.2), 3.56 (qdd, 1, *J* = 6.7, 4.6, 1.2), 2.81 (dd, 1, *J* = 15.2, 7.3), 2.19 (d, 1, *J* = 15.2), 2.06 (s, 3), 0.91 (d, 3, *J* = 6.7), 0.70 (dd, 1, *J* = 8.2, 4.6, NH); ¹H NMR (acetone-d₆) 8.83 (s, 1, NH), 8.27 (dd, 1, *J* = 7.9, 1.2), 7.89 (dd, 1, *J* = 7.9, 7.9), 7.77 (d, 1, *J* = 7.9), 7.63 (dd, 1, *J* = 7.9, 7.9), 7.39 (d, 1, *J* = 7.9), 7.34 (d, 1, *J* = 7.9), 7.33 (dd, 1, *J* = 7.9, 7.9), 7.23 (td, 1, *J* = 7.9, 1.2), 5.48 (d, 1, 7.3), 5.29 (dd, 1, *J* = 8.2), 3.43 (qdd, 1, *J* = 6.7, 7.3), 2.83 (dd, 1, *J* = 15.2, 7.3), 2.19 (d, 1, *J* = 15.2), 2.02 (s, 3), 1.96 (d, 1, 7.3, NH), 0.82 (d, 3, *J* = 6.7).

Analogue 64b. To a solution of **61b** (37 mg, 0.06 mmol) in MeCN (4 mL) was added AcOH (0.01 mL). The solution was refluxed for 12h, cooled and concentrated. Flash chromatography on silica gel (10:1 CH₂Cl₂/EtOAc) gave 12 mg (33%) of **61b** as white solid preceded by 10 mg (22%) of **64b** as a white solid: mp 166-168 °C; [α]_D +83.9 (*c* 0.06 in CHCl₃); ¹H NMR 8.31 (d, 1, *J* = 8.0, H-10), 7.88 (d, 1, *J* = 7.9, H-7), 7.81 (ddd, 1, *J* = 7.9, 7.9, 1.2, H-8), 7.56 (d, 1, *J* = 7.9, H-24), 7.53 (d, 1, *J* = 7.9, H-27), 7.50 (dd, 1, *J* = 7.9, 7.9, H-9), 7.36 (dd, 1, *J* = 7.9, 7.9, H-26), 7.24 (s, 1, NH, H-2), 7.30-7.26 (m, 4, H-36, H-37), 7.25 (dd, 1, *J* = 7.9, 7.9, H-25), 6.96 (dd, 1, *J* = 6.4, 3.2, H-38), 5.77 (s, 1, H-18), 5.68 (dd, 1, *J* = 4.0, 3.5, H-14), 4.39 (d, 1, *J* = 11.6, H-34a), 4.32 (d, 1, *J* = 11.6, H-34b), 4.31-4.25 (m, 1, H-20), 2.57 (dd, 1, *J* = 15.3, 3.5, H-15a), 2.26 (dd, 1, *J* = 15.3, 4.0, H-15b), 2.14 (s, 3, H-16), 1.82-1.60 (m, 3, H-29, H-30), 0.79 (d, 3, *J* = 6.7, H-31), 0.73 (d, 3, *J* = 6.7, H-32); ¹³C NMR 168.9, 168.4, 160.4, 152.9, 150.4, 147.6, 140.4, 135.1, 134.8, 134.4, 129.8, 128.6 (2 C), 128.52, 128.48 (2 C), 128.4, 127.4, 127.3, 126.3, 124.2, 121.5, 116.9, 86.8, 85.5, 83.5, 67.7, 62.1, 51.8, 40.0, 30.9, 24.5, 23.9, 23.6, 21.8; a ROESY experiment showed cross peaks between H-2 and H-16, H-2 and H-27, H-20 and H-29, H-20 and H-31, H-24 and H-25, H-26 and H-27, H-14 and H-15a, H-14 and H-15b, H-18 and H-16, H-18 and H-29, H-18 and H-31, H-34 and H-36, H-9 and H-10; IR (KBr) 3261 (br), 1721, 1690, 1607, 1603, 1571, 1547, 1512.

Analogue (65b). To a solution of **64b** (13 mg, 0.02 mmol) in EtOH (1 mL) was added Pd (10%) on carbon (13 mg). The suspension was stirred at rt under H₂ (60 PSI) for 24 h. The catalyst was filtered off and the filtrate was evaporated to give crude **65b**. Flash chromatography on silica gel (1:1 CH₂Cl₂/EtOAc) gave 1.6 mg (17%) of **65b** as a light yellow solid: ¹H NMR (in CDCl₃) 8.35 (dd, 1, *J* = 7.9), 7.85 (dd, 1, *J* = 7.9, 7.9), 7.81 (d, 1, *J* = 7.9), 7.60 (dd, 1, *J* = 7.9, 7.9), 7.43 (d, 1, *J* = 7.4), 7.35 (d, 1, *J* = 7.9), 7.33 (td, 1, *J* = 7.9, 1.2), 7.22 (td, 1, *J* = 7.9, 1.2), 6.86 (s, 1, NH), 5.74 (d, 1, 6.1), 5.37 (d, 1, *J* = 6.7), 3.55-3.47 (m, 1), 2.88 (dd, 1, *J* = 15.2, 7.3), 2.18 (d, 1, *J* = 15.2), 2.06 (s, 3), 1.20-0.79 (m, 3), 0.59 (d, 3, *J* = 6.7), 0.57 (d, 3, *J* = 6.7), 0.74 (dd, 1, *J* = 6.7, 6.1, NH).

Fmoc Tetracyclic lactone 66a. To a solution of the free lactone amine **42a** (108 mg, 0.25 mmol) in CH_2Cl_2 (1 mL) was added FmocCl (140 mg, 2.2 eq) and (*i*-Pr)₂NEt (0.1 mL, 2e q). The reaction mixture was stirred at rt for 12 h, and quenched with saturated NaHCO_3 . The organic layer was washed with brine, dried, and concentrated. Flash chromatography on silica gel (50:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 155 mg (94%) of the **66a** as a white solid: mp 138-140 °C; $[\alpha]_D +39.6$ (*c* 0.25 in CHCl_3); ^1H NMR (5:1 mixture of rotamers, major rotamer) 7.79 (d, 2, $J = 7.3$), 7.77 (d, 1, $J = 8.0$), 7.57 (d, 2, $J = 7.3$), 7.48 (d, 1, $J = 8.0$), 7.44 (d, 1, $J = 7.3$), 7.40 (d, 1, $J = 7.3$), 7.38-7.30 (m, 3), 7.27 (t, 1, $J = 8.0$), 5.82 (s, 1), 5.62 (br d, 1, $J = 7.4$, NH), 4.84-4.75 (m, 1), 4.81 (d, 1, $J = 11.6$), 4.75-4.68 (m, 1), 4.72 (d, 1, $J = 11.6$), 4.39-4.23 (m, 1), 4.18 (dd, 1, $J = 10.8, 9.2$), 4.05 (q, 1, $J = 6.7$), 2.69 (dd, 1, $J = 13.7, 10.8$), 2.23 (dd, 1, $J = 13.7, 9.2$), 1.63 (br d, 3, $J = 6.7$); ^1H NMR (minor rotamer, partial) 7.62 (d, 1, $J = 7.3$), 5.75 (br d, 1, $J = 6.1$, NH), 5.57 (s, 1), 4.41-4.32 (m, 1), 2.92-2.84 (m, 1), 2.35-2.28 (m, 1), 1.40 (d, 3, $J = 6.7$); ^{13}C NMR (major rotamer) 173.7, 169.0, 154.2, 153.8, 143.3, 143.1, 141.5, 141.4, 135.8, 135.7, 130.7, 127.95, 127.92, 127.2 (2 C), 125.7, 124.7, 124.5, 124.4, 120.20, 120.17, 116.0, 95.1, 89.3, 83.1, 74.7, 67.3, 59.5, 51.8, 47.1, 34.8, 16.8; ^{13}C NMR (minor rotamer, partial) 144.3, 127.5, 127.1, 127.0, 120.0, 65.0, 50.3; IR 3436, 1795, 1734, 1701, 1601, 1509.

Aniline precursor to 67a. To a solution of **66a** (131 mg, 0.2 mmol) in acetic acid (2.0 mL) was added zinc dust (600 mg). The mixture was stirred at rt for 30 min and diluted with EtOAc (10 mL). The zinc dust was filtered off and the filtrate washed with saturated NaHCO_3 (3 $\times$ 10 mL) and brine (10 mL), dried over Na_2SO_4 , and evaporated under reduced pressure to give the crude amine.

To a mixture of the crude amine and EDAC (87 mg, 0.44 mmol) in MeCN (1 mL) was added anthranilic acid (55 mg, 0.4 mmol) in several portions over 60 min at rt with stirring. The reaction mixture was stirred for an additional 20 min, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL), which was washed with water (5 mL) and saturated NaHCO_3 (3 $\times$ 10 mL), dried over Na_2SO_4 and concentrated. Flash chromatography on silica gel (10:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 101 mg (84%) of the aniline as a white solid: mp 153-155 °C; $[\alpha]_D +123.3$ (*c* 0.25 in CHCl_3); ^1H NMR

(10:1 mixture of rotamers, major) 8.03 (d, 1, $J = 7.9$), 7.75 (d, 1, $J = 7.3$), 7.73 (d, 1, $J = 7.3$), 7.57 (d, 1, $J = 7.3$), 7.53 (d, 1, $J = 7.3$), 7.45 (d, 1, $J = 7.9$), 7.42-7.26 (m, 6), 7.22 (dd, 1, $J = 7.9, 7.9$), 7.11 (dd, 1, $J = 7.9, 7.9$), 7.09 (d, 1, $J = 6.7$, NH), 6.60-6.53 (m, 2), 5.78 (s, 1), 5.54 (br, 2, NH), 4.82 (dd, 1, $J = 10.7, 5.2$), 4.76 (dd, 1, $J = 10.7, 5.2$), 4.25 (ddd, 1, $J = 10.4, 9.2, 6.7$), 4.24-4.15 (m, 1), 4.00 (q, 1, $J = 6.7$), 2.55 (dd, 1, $J = 13.4, 10.4$), 2.22 (dd, 1, $J = 13.4, 9.2$), 1.22 (d, 3, $J = 6.7$); ^1H NMR (minor rotamer, partial) 7.83 (d, 1, $J = 7.9$), 7.68 (d, 1, $J = 7.9$), 5.67 (s, 1), 4.79 (m, 1), 4.40-4.32 (m, 1), 2.80 (dd, 1, $J = 13.4, 10.4$), 2.32 (dd, 1, $J = 13.4, 9.2$), 1.41 (d, 3, $J = 6.7$); ^{13}C NMR 175.0, 169.2, 168.9, 154.0, 149.2, 143.4, 143.2, 141.43, 141.37, 136.0, 135.8, 132.8, 130.5, 127.84, 127.78, 127.5, 127.2 (2 C), 127.1, 126.2, 124.50, 124.46, 120.14, 120.08, 117.4, 116.4, 115.8, 113.6, 89.6, 83.3, 67.2, 59.5, 51.3, 47.2, 34.7, 16.8; IR (KBr) 3422, 1790, 1732, 1696, 1643, 1513.

Diamide precursor to 67a. To a solution of the aniline (72 mg, 0.12 mmol) and EDAC (46 mg, 2 eq) in MeCN (3 mL) was added *N*-Fmoc-phenylselenenyl-L-alanine (84 mg, 0.18 mmol 1.5 eq). The resulting mixture was stirred at rt for 1 h and concentrated. The residue was dissolved in CH_2Cl_2 (5 mL), which was washed with water (2.5 mL) and saturated NaHCO_3 (3×5 mL), dried over Na_2SO_4 , and concentrated. Flash chromatography on silica gel gave 115 mg (91%) of the diamide as a white solid: mp 161-164 °C; $[\alpha]_{\text{D}} + 86.5$ (c 1.20 in CHCl_3); ^1H NMR 11.2 (s, 1, NH), 8.36 (br d, 1, $J = 8.0$), 8.04 (d, 1, $J = 7.3$, NH), 7.80-7.69 (m, 4), 7.65-7.52 (m, 3), 7.50-7.20 (m, 18), 7.08 (dd, 1, $J = 8.0, 8.0$), 7.08-7.03 (m, 2), 5.96 (br d, 1, $J = 8.1$, NH), 5.77 (s, 1), 4.91 (dd, 1, $J = 10.8, 5.3$), 4.80-4.70 (m, 1), 4.64-4.54 (m, 1), 4.39-4.20 (m, 4), 4.16 (t, 1, $J = 7.3$), 4.00 (q, 1, $J = 6.7$), 3.54-3.34 (m, 2), 2.56 (dd, 1, $J = 13.6, 10.6$), 2.25 (dd, 1, $J = 13.6, 8.8$), 1.26 (d, 3, $J = 6.7$); ^{13}C NMR 175.5, 169.2, 168.6, 168.2, 155.9, 153.9, 144.0, 143.6, 143.4 (2 C), 143.3, 141.5, 141.3, 141.2, 141.1, 139.0, 135.9, 135.6, 133.3 (3 C), 133.1, 130.9, 129.0 (2 C), 127.8 (2 C), 127.6 (2 C), 127.4, 127.1, 127.07, 127.02, 126.96, 126.8, 126.2, 125.1 (2 C), 124.4, 124.2, 123.2, 121.6, 120.3, 120.2, 119.9 (2 C), 118.3, 116.0, 90.2, 83.1, 67.3 (2 C), 59.5, 55.8, 51.8, 47.3, 46.9, 34.2, 30.4, 16.9; IR (KBr) 3425 (br), 1796, 1730, 1696, 1655, 1602, 1502.

Iminobenzoxazine 67a. To a solution of Ph_3P (52 mg, 0.2 mmol, 2 eq) in dry CH_2Cl_2 (2 mL) was added a Br_2 solution in CH_2Cl_2 (1.0 M, 0.19 mmol, 1.9 eq) under N_2 . The resulting solution was stirred at rt for 5 min, and $(i\text{-Pr})_2\text{NEt}$ (0.08 mL, 4 eq) and the diamide (105 mg, 0.10 mmol) were added. The resulting mixture was stirred at rt for 5 min and concentrated. The residue was washed with saturated NaHCO_3 (5 mL), brine (5 mL), dried over Na_2SO_4 and concentrated. Flash chromatography on silica gel (20:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 302 mg (81%) of **67a** as a light-yellow solid: mp 138-141 °C; $[\alpha]_D^{25} +19.0$ (c 0.10 in CHCl_3); ^1H NMR (6:1 mixture of rotamers, major rotamer) 7.99 (d, 1, $J = 7.9$), 7.78-7.69 (m, 4), 7.66-7.61 (m, 1), 7.58-7.48 (m, 7), 7.43-7.24 (m, 14), 7.06-6.93 (m, 2), 6.10 (d, 1, $J = 7.9$, NH), 5.91 (s, 1), 4.92-4.82 (m, 3), 4.79 (dd, 1, $J = 10.7$, 5.2), 4.33 (d, 2, $J = 7.3$), 4.31-4.20 (m, 2), 4.10 (q, 1, $J = 6.1$), 3.54 (dd, 1, $J = 13.4$, 4.9), 3.38 (dd, 1, $J = 13.4$, 7.1), 2.79 (dd, 1, $J = 14.1$, 8.2), 2.15 (dd, 1, $J = 14.1$, 7.6), 1.19 (d, 3, $J = 6.1$); ^1H NMR (minor rotamer, partial) 7.97 (d, 1, $J = 8.0$), 6.14 (d, 1, $J = 7.9$, NH), 5.79 (s, 1), 5.01-4.93 (m, 1), 4.72-4.63 (m, 1), 3.53-3.46 (m, 1), 3.30-3.23 (m, 1), 2.32-3.23 (m, 1), 1.51 (d, 3, $J = 6.1$); ^{13}C NMR (major rotamer) 174.1, 169.1, 156.5, 155.4, 154.2, 149.3, 143.7 (2 C), 143.4, 143.0, 141.4 (2 C), 141.2 (2 C), 140.8, 136.0, 135.8, 133.5, 133.3 (3 C), 130.6, 129.0 (2 C), 128.4, 127.94, 127.88, 127.6 (2 C), 127.2, 127.02 (4 C), 126.96, 126.6, 126.0, 125.3 (3 C), 124.9, 124.5, 124.3, 120.1 (2 C), 119.9 (2 C), 116.3, 89.9, 83.1, 67.4, 67.2, 59.7, 55.4, 53.2, 47.1, 47.0, 37.9, 30.2, 16.8; ^{13}C NMR (minor rotamer, partial) 169.9, 135.2, 133.8, 128.7, 128.2, 118.9, 90.2, 82.6, 67.8, 59.4, 60.1, 54.4, 16.5; IR (KBr) 3407 (br), 1792, 1729, 1678, 1649, 1602, 1506.

Fumiquinazoline H Analogue (70). To a solution of **67a** (22 mg, 0.02 mmol) in dry EtOAc (0.10 mL) was added dry piperidine (0.01 mL, 10 eq). The resulting mixture was stirred at rt for 10 min, diluted with hexane (3 mL) and concentrated under reduced pressure to give the crude amidine **68a** as a solid, which was dissolved in dry MeCN (4 mL). The solution was refluxed for 1 h, cooled, and concentrated to give a light-red residue. Flash chromatography on silica gel (1.5:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 4.2 mg (41%) of **70** as a white solid: 179-181 °C; $[\alpha]_D^{25} -191.2$ (c 0.15 in CHCl_3); ^1H NMR (CDCl_3) 8.32 (d, 1, $J = 7.9$, H-10), 7.83 (ddd, 1, $J = 7.9$, 7.9, 1.2, H-8), 7.78 (d, 1, $J = 7.9$, H-7), 7.58 (ddd, 1, $J =$

7.9, 7.9, 1.2, H-9), 7.52 (d, 1, $J = 7.9$, H-24), 7.30 (ddd, 1, $J = 7.9$, 7.9, 1.8, H-25), 7.08-7.00 (m, 2, H-26, H-27), 6.79 (br, 1, NH, H-2), 5.83 (dd, 1, $J = 6.1$, 1.8, H-18), 5.79-5.73 (m, 1, H-14), 4.01 (q, 1, $J = 6.7$, H-20), 3.14 (dd, 1, $J = 15.2$, 5.5, H-15a), 2.08 (s, 3, H-16), 2.05 (d, 1, $J = 6.1$, NH, H-19), 1.94 (dd, 1, $J = 15.2$, 1.8, H-15b), 1.53 (d, 3, $J = 6.7$, H-29); ^1H NMR (acetone- d_6) 8.63 (br, 1, NH), 8.21 (d, 1, $J = 7.9$), 7.86 (ddd, 1, $J = 7.9$, 7.9, 1.2), 7.74 (d, 1, $J = 7.9$), 7.59 (dd, 1, $J = 7.9$, 7.9), 7.42 (d, 1, $J = 7.9$), 7.29 (dd, 1, $J = 7.9$, 7.9), 7.23 (d, 1, $J = 7.9$), 7.03 (dd, 1, $J = 7.9$, 7.9), 5.94 (d, 1, $J = 5.5$), 5.55-5.49 (m, 1), 3.84 (q, 1, $J = 6.7$), 3.14 (dd, 1, $J = 15.2$, 5.5), 2.43 (d, 1, $J = 5.5$, NH), 2.05 (d, 1, $J = 15.2$), 2.02 (s, 3), 1.44 (d, 3, $J = 7.3$); ^{13}C NMR (CDCl_3) 172.5, 169.2, 159.4, 150.9, 146.9, 137.4, 136.4, 134.9, 130.4, 128.3, 128.0, 127.1, 125.8, 125.2, 120.7, 115.3, 87.9, 87.2, 84.5, 60.2, 52.9, 34.8, 24.7, 19.3; ^{13}C NMR (acetone- d_6) 173.4, 169.4, 160.0, 152.8, 148.2, 138.9, 138.0, 135.4, 130.6, 128.9, 128.3, 127.5, 126.9, 126.0, 122.0, 115.3, 88.6, 87.8, 85.6, 60.7, 54.0, 35.2, 24.5, 18.9; a ROESY (CDCl_3) experiment showed cross peaks between H-2 and H-18, H-2 and H-16, H-27 and H-15b, H-14 and H-15a, H-14 and H-15b, H-18 and H-19, H-18 and H-29, H-20 and H-19, H-20 and H-29, H-15a and H-15b; IR (KBr) 3440 (br), 1715, 1611.

Fmoc Tetracyclic lactone 71. To a solution of the free-amine lactone **36a** (110 mg, 0.25 mmol) in CH_2Cl_2 (3 mL) was added FmocCl (140 mg, 2.2 eq), $i\text{-Pr}_2\text{NEt}$ (0.1 mL, 2eq). The reaction mixture was stirred at rt for 12 h, and quenched with saturated NaHCO_3 . The organic layer was washed with brine, dried, and concentrated. Flash chromatography on silica gel (50:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 165 mg (98%) of **71** as a white solid: mp 172-175 $^\circ\text{C}$; ^1H NMR 7.76 (d, 2, $J = 7.3$), 7.56 (d, 2, $J = 7.3$), 7.54 (d, 1, $J = 7.9$), 7.44-7.35 (m, 3), 7.36-7.27 (m, 3), 7.24 (t, 1, $J = 7.9$), 5.80 (d, 1, $J = 6.7$, NH), 5.73 (br s, 1), 5.07-4.92 (m, 1), 4.81 (d, 1, $J = 12.2$), 4.80-4.68 (m, 2), 4.68 (d, 1, $J = 12.2$), 4.27 (br s, 1), 4.10 (q, 1, $J = 6.7$), 2.55 (dd, 1, $J = 14.0$, 11), 2.33-2.20 (m, 1), 1.04 (br d, 3); ^{13}C NMR 172.9, 168.8, 155.8, 154.4, 143.1 (2 C), 141.5 (2 C), 136.9, 133.8, 131.1, 128.0 (2 C), 127.3, 127.2, 127.0 (2 C), 124.4, 124.2, 120.2, 120.1, 116.4, 95.1, 89.5, 83.6, 74.9, 68.1, 58.7, 50.1, 46.9, 35.7, 17.6; IR (KBr) 3344, 1796, 1727, 1710, 1678, 1606, 1529.

Aniline Precursor to 72. To a solution of **71** (164 mg, 0.24 mmol) in acetic acid (3.0 mL) was added zinc dust (600 mg). The mixture was stirred at rt for 30 min and diluted with EtOAc (10 mL). The zinc dust was filtered off and the filtrate was washed with saturated NaHCO₃ (3 × 10 mL), brine (10 mL), dried over Na₂SO₄ and evaporated under reduced pressure to give the crude amine.

To a mixture of the crude amine and EDAC (110 mg, 0.54 mmol, 2.2eq) in MeCN (1 mL) was added anthranilic acid (65 mg, 0.5 mmol, 2 eq) in several portions over 60 min at rt with stirring. The reaction mixture was stirred for an additional 20 min, and concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL) and saturated NaHCO₃ (3 × 10 mL), dried (Na₂SO₄) and concentrated. Flash chromatography on silica gel (10:1 CH₂Cl₂/EtOAc) gave 134 mg (85%) of the aniline as a white solid: mp 115-118 °C; ¹H NMR 7.72 (d, 2, *J* = 7.3), 7.52 (d, 1, *J* = 7.3), 7.49-7.16 (m, 11), 7.10 (br, 1, NH), 6.67 (d, 1, *J* = 7.9), 6.59 (dd, 1, *J* = 7.9), 5.75 (br s, 1), 5.61 (br, 2, NH), 5.43-5.29 (m, 1), 4.67 (dd, 1, *J* = 10.4, 4.9), 4.55-4.43 (m, 1), 4.21-4.10 (m, 1), 4.10 (q, 1, *J* = 6.7), 2.66 (dd, 1, *J* = 13.4, 11.6), 2.37-2.24 (m, 1), 1.05 (br d, 3, *J* = 6.7); ¹³C NMR 174.1, 168.8 (2 C), 155.8, 149.2, 143.0, 142.8, 141.3, 136.9, 134.0, 132.9, 130.9, 127.9 (2 C), 127.4, 127.2, 127.1 (2 C), 127.0 (2 C), 124.3 (br, 2 C), 120.1, 120.0, 117.4, 116.5, 116.2, 114.2, 89.8, 83.9, 68.1, 58.7, 48.1, 46.7, 36.3, 17.6; IR (KBr) 3361, 1795, 1726, 1642, 1612, 1586, 1513;

Diamide Precursor to 72. To a solution of the aniline (92 mg, 0.15 mmol) and EDAC (60 mg, 0.31mmol, 2.2 eq) in MeCN (3 mL) was added *N*-Fmoc-phenylselenenyl-L-alanine (110 mg, 0.24 mmol, 1.6 eq). The resulting mixture was stirred at 35°C for 1 h and concentrated. The residue was dissolved in CH₂Cl₂ (10 mL), which was washed with water (5 mL) and saturated NaHCO₃ (3 × 10 mL), dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel gave 135 mg (86%) of the diamide as a white solid: mp 137-140 °C; ¹H NMR 11.8 (br, 1, NH), 8.52 (br d, 1, *J* = 7.9), 7.73-7.66 (m, 4), 7.64-7.57 (m, 2), 7.53 (d, 4, *J* = 7.7), 9.49 (d, 1, *J* = 8.0), 7.43 (dd, 1, *J* = 8.0), 7.42-7.10 (m, 15), 7.08 (br d, 1, *J* = 7.3, NH), 6.95 (dd, 1, *J* = 7.9), 5.83 (br d, 1, *J* = 6.2, NH), 5.68 (br s, 1), 5.26-5.15 (m, 1), 4.73-4.78 (m, 2), 4.47-4.33 (m, 2), 4.30-4.10 (m, 4), 3.46 (br, 2), 2.40 (dd, 1, *J* = 13.9, 12.7), 2.32 (dd, 1,

$J = 13.9, 6.5$), 1.10 (br, 3); ^{13}C NMR 173.4, 168.7, 168.6, 168.2, 168.5, 156.0, 155.7, 143.9, 143.6 (2 C), 142.8, 142.7, 141.4, 141.3, 141.1 (2 C), 139.5, 136.4, 133.7 (2 C), 133.3, 133.2, 131.1, 129.2 (2 C), 128.8, 128.1 (2 C), 127.7, 127.6, 127.4, 127.3, 127.15, 127.06, 126.9 (2 C), 126.5, 125.3, 125.2, 124.3, 124.1, 123.1, 121.6, 120.2, 119.9 (2 C), 118.8, 116.2, 89.8, 84.0, 68.4, 67.3, 58.8, 56.0, 48.1, 47.1, 46.7, 35.7, 30.3, 17.7; IR (KBr) 3424 (br), 1794, 1721, 1685, 1657, 1603, 1586, 1546, 1514.

Iminobenzoxazine 72. To a solution of Ph_3P (52 mg, 0.19 mmol, 2.1 eq) in dry CH_2Cl_2 (2 mL) was added a Br_2 solution in CH_2Cl_2 (1.0 M, 0.18 mmol, 2 eq) under N_2 . The resulting solution was stirred at rt for 5 min, and (*i*-Pr) $_2\text{NEt}$ (0.086 mL, 4 eq) and the diamide (94 mg, 0.09 mmol) were added. The resulting mixture was stirred at rt for 5 min and quenched with saturated NaHCO_3 (5 mL), washed with brine (5 mL), dried over Na_2SO_4 and concentrated. Flash chromatography on silica gel (20:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 87 mg (93%) of **72** as a light-yellow solid: mp 125-127 °C; ^1H NMR 8.00 (br, 1), 7.80-7.70 (m, 4), 7.65-7.53 (m, 4), 7.51-7.23 (m, 18), 7.10-6.80 (m, 2), 6.24 (br, 1), 5.98 (br, 1, NH), 5.16 (br, 1), 4.97-4.88 (m, 1), 4.68 (br, 1), 4.48 (br, 1), 4.40-4.27 (m, 4), 4.20 (br, 1), 3.51 (dd, 1, $J = 12.8, 4.9$), 3.43 (dd, 1, $J = 12.8, 5.5$), 2.91 (br, 1), 2.45 (br, 1), 1.65 (br, 3); ^{13}C NMR 173.1, 169.4, 167.7, 156.7, 155.6, 149.8, 143.7 (2 C), 143.6 (2 C), 141.3 (2 C), 141.2 (2 C), 140.7, 136.5, 134.7, 133.7, 133.2 (3 C), 130.8, 129.0 (2 C), 128.5, 128.4, 127.8 (2 C), 127.6 (2 C), 127.1 (2 C), 127.0 (4 C), 126.5, 126.1, 125.1 (2 C), 124.7 (2 C), 123.8, 119.9 (br, 4 C), 118.6, 117.0, 90.2, 82.8, 69.3, 63.1, 59.3, 53.6, 52.8, 50.9, 47.0, 46.5, 37.1, 30.6, 18.0 (br); IR (KBr) 3420 (br), 1790, 1728, 1681, 1652, 16086, 1504, 1499.

Fumiquinazoline C (7). To a solution of **72** (52 mg, 0.05 mmol) in dry EtOAc (1.0 mL) was added dry piperidine (0.05 mL, 10 eq). The resulting mixture was stirred at rt for 10 min, diluted with hexane (3 mL) and concentrated under reduced pressure to give the crude amidine as yellow solid, which was dissolved in dry MeCN (4 mL). The solution was refluxed for 1.5 h, cooled, and concentrated to give a light-red residue. Flash chromatography on silica gel (3:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 8.8 mg (40%) of **7** as white solid (no fumiquinazoline D (**73**) was obtained).

α -Methoxy Lactone 75 and Triamide 74. To a solution of **38a** (150 mg, 0.23 mmol) in CH₂Cl₂ (5 mL) was added silica gel (4.5 g). The mixture was stirred at rt for 24 h, and diluted with EtOAc (15 mL). The silica gel was filtered off and the filtrate was concentrated. Flash chromatography on silica gel (20:1 CH₂Cl₂/EtOAc) gave 85 mg (65%) of **75** as a white solid followed by 37 mg (29%) of **74** as a white solid.

Data for **75**: mp 102-104 °C; ¹H NMR (2:1 mixture of rotamers, major rotamer) 7.60 (d, 1, *J* = 7.9), 7.54-7.35 (m, 6), 7.33-7.19 (m, 2), 5.65 (d, 1, *J* = 11.6), 4.88 (d, 1, *J* = 11.6), 4.87 (m, 1), 4.68 (q, 1, *J* = 6.7), 4.70 (s, 2), 4.69 (br, 1, NH), 3.21 (s, 3, OMe), 2.43 (dd, 1, *J* = 12.0, 9.6), 2.20 (12.0, 11.0), 1.61 (d, 3, *J* = 6.7); ¹H NMR (minor rotamer, partial) 7.60 (d, 1, *J* = 7.9), 7.54-7.35 (m, 6), 7.33-7.19 (m, 2), 5.82 (br, 1, NH), 5.29 (s, 2), 3.29 (s, 3, OMe), 2.64 (dd, 1, *J* = 12.0, 11.6), 2.43 (dd, *J* = 12.0, 10.5), 1.55 (d, 3, *J* = 6.7); ¹³C NMR (major rotamer) 171.8, 167.0, 154.1, 152.4, 135.5, 134.8, 133.8, 130.7, 129.8 (2 C), 129.0 (3 C), 126.7, 122.8, 117.0, 95.2, 87.6, 75.0, 68.0, 60.6, 49.4, 37.9, 31.5, 22.6, 14.1; ¹³C NMR (minor rotamer, partial) 171.8, 166.9, 154.1, 152.4, 129.6, 128.6, 127.2, 123.3, 116.5, 68.9, 60.0, 49.8, 38.4, 17.9, 16.9.

Data for **74**: mp 108-111 °C; ¹H NMR 7.60 (d, 1, *J* = 7.9), 7.49 (d, 1, *J* = 7.9), 7.44 (dd, 1, *J* = 7.9, 7.9), 7.43-7.33 (m, 5), 7.29 (dd, 1, *J* = 7.9), 5.31 (d, 1, *J* = 12.2), 5.22 (d, 1, *J* = 12.2), 4.68 (d, 1, *J* = 12.2), 4.63 (d, 1, *J* = 12.2), 4.46 (q, 1, *J* = 6.7), 4.53 (dd, 1, 11.0, 9.5), 3.74 (s, 3), 3.18 (s, 1, OH), 3.16 (dd, 1, *J* = 13.2, 11.0), 3.07 (dd, 1, *J* = 13.2, 9.5), 1.85 (d, 3, *J* = 6.7); ¹³C NMR 170.4, 170.3, 154.2, 150.7, 137.4, 135.3, 133.2, 131.3, 128.7 (3 C), 128.4, 127.7, 126.3, 124.7, 116.6, 100.5, 94.5, 85.4, 75.0, 68.1, 60.3, 57.7, 52.6, 38.3, 16.1; HRMS (FAB, DCM/NBA/PPG) calcd for C₂₆H₂₄Cl₃N₃O₈Na⁺ (MNa⁺) 634.0527, found 634.0544.

β -Methoxy Lactone 76 and β -Hydroxy Lactone Analogue. To a solution of **75** (122 mg, 0.20 mmol) in CH₂Cl₂ (1 mL) was added TFA (0.05 mL). The solution was stirred at rt for 12 h, and neutralized with NaHCO₃. The organic layer was washed with brine and dried over Na₂SO₄ and

concentrated. Flash chromatography on silica gel (20:1 CH₂Cl₂/EtOAc) gave 107 mg (88%) of **76** as white solid followed by 10 mg (8%) of the β-hydroxy lactone as a white solid.

Data for **76**: mp 103-105 °C, ¹H NMR 7.58 (d, 1, *J* = 7.9), 7.49 (dd, 1, *J* = 7.9, 7.9), 7.44-7.33 (m, 6), 7.33 (dd, 1, *J* = 7.9), 5.96 (d, 1, *J* = 9.2, NH), 5.22 (d, 1, *J* = 12.2), 5.12 (d, 1, *J* = 12.2), 5.09 (ddd, 1, *J* = 11.6, 9.2, 8.5), 4.89 (d, 1, *J* = 11.6), 4.70 (d, 1, *J* = 11.6), 4.53 (q, 1, *J* = 6.7), 3.48 (dd, 1, *J* = 14.7, 8.5), 3.34 (s, 3), 3.04 (dd, 1, *J* = 14.7, 11.6), 1.67 (d, 3, *J* = 6.7); ¹³C NMR 173.0, 169.4, 154.8, 154.0, 137.5, 134.8, 134.2, 131.7, 128.8 (2 C), 128.7, 128.2 (2 C), 127.0, 124.3, 117.7, 108.9, 94.4, 87.0, 75.0, 68.8, 59.6, 50.4 (2 C, C-20 & OMe), 32.2, 17.6, IR (KBr) 3419 (br), 1798, 1740, 1714, 1651, 1517; HRMS (FAB, DCM/NBA/PPG) calcd for C₂₆H₂₄Cl₃N₃O₈Na⁺ (MNa⁺) 634.0527, found 634.0555.

Data for the β-hydroxy lactone: ¹H NMR 7.59 (d, 1, *J* = 7.9), 7.49 (dd, 1, *J* = 7.9, 7.9), 7.44-7.33 (m, 6), 7.33 (dd, 1, *J* = 7.9, 7.9), 6.01 (d, 1, *J* = 9.8, NH), 5.26 (d, 1, *J* = 11.6), 5.16 (d, 1, *J* = 11.6), 5.15 (ddd, 1, *J* = 11.6, 9.8, 8.5), 4.92 (d, 1, *J* = 11.6), 4.75 (d, 1, *J* = 11.6), 4.54 (q, 1, *J* = 6.7), 3.50 (s, 1, OH), 3.47 (dd, 1, *J* = 14.7, 8.5), 3.13 (dd, 1, *J* = 14.7, 11.6), 1.71 (d, 3, *J* = 6.7); ¹³C NMR 172.7, 168.64, 154.8, 153.7, 137.5, 134.8, 134.4, 131.9, 128.8 (3 C), 128.3 (2 C), 127.0, 124.6, 117.2, 105.0, 95.2, 86.5, 75.0, 68.8, 59.9, 50.5, 32.3, 19.4.

Imine 80. To a solution of **78** (110 mg, 0.30 mmol) in EtOAc (3 mL) was added Pd (10%) on carbon (40 mg). The suspension was stirred at rt under H₂ (1 atm) for 2 h. The catalyst was filtered off and the filtrate was washed with saturated Na₂CO₃ and brine, dried over Na₂SO₄, and concentrated to give crude **80**. Flash chromatography on silica gel (EtOAc) gave 52 mg of pure **80** (86%) as a white solid: mp 68-70 °C; ¹H NMR 7.57 (d, 1, *J* = 7.9), 7.50 (d, 1, *J* = 7.9), 7.39 (dd, 1, *J* = 7.9, 7.9), 7.25 (dd, 1, *J* = 7.9, 7.9), 5.98 (br, 1, OH), 4.54 (s, 2), 1.80 (s, 3); ¹³C NMR 175.2, 173.2, 137.2, 134.2, 130.1, 126.0, 124.4, 112.8, 71.5, 65.4, 25.8.

Alcohol 81. To a solution of **80** (20 mg, 0.10 mmol) in MeOH (1 mL) was added Pd (10%) on carbon (10 mg). The suspension was stirred at rt under H₂ (4 atm) for 48 h. The catalyst was filtered off and the filtrate was washed with saturated NaHCO₃ and brine, dried over Na₂SO₄. Flash chromatography on

silica gel (EtOAc) gave 18 mg (90%) of **81** as a white solid: mp 141-143 °C; ^1H NMR 7.52 (d, 1, $J = 7.9$), 7.37 (d, 1, $J = 7.9$), 7.33 (dd, 1, $J = 7.9, 7.9$), 7.18 (dd, 1, $J = 7.9, 7.9$), 5.46 (s, 1), 4.08 (d, 1, $J = 15.3$), 3.75 (d, 1, $J = 15.3$), 2.48 (s, 1, OH), 2.30 (br, 1, NH), 1.41 (s, 3); ^{13}C NMR 170.2, 139.6, 136.5, 129.5, 125.7, 123.5, 115.6, 88.9, 80.4, 53.9, 23.2; IR (KBr) 3453, 3414, 3326, 1685, 1606.

Triethylsilylation of 78. To a solution of **78** (100 mg, 0.27 mmol) in CH_2Cl_2 (2.0 mL) under N_2 was added 2,6-lutidine (0.16 mL, 5 eq) and TESOTf (0.18 mL, 3 eq). The mixture was stirred at rt for 12 h, and concentrated. Flash chromatography on silica gel (50:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 8 mg of recovered **78** (8%) preceded by 110 mg of the TES ether (85%) as a sticky oil: ^1H NMR (2:1 isomer mixture, major isomer) 7.47 (d, 1, $J = 7.9$), 7.41-7.32 (m, 6), 7.30 (dd, 1, $J = 7.9, 7.9$), 7.20 (dd, 1, $J = 7.9, 7.9$), 5.44 (d, 1, $J = 11.6$), 5.14 (d, 1, $J = 11.6$), 4.47 (d, 1, $J = 16.5$), 4.28 (d, 1, $J = 16.5$), 3.27 (s, 3, OMe), 1.23 (s, 3), 0.95-0.83 (m, 9), 0.57-0.43 (m, 6); ^1H NMR (minor isomer) 7.50 (d, 1, $J = 7.9$), 7.41 (d, 1, $J = 7.9$), 7.41-7.32 (m, 5), 7.29 (dd, 1, $J = 7.9, 7.9$), 7.19 (dd, 1, $J = 7.9, 7.9$), 5.24 (br, 2), 4.47 (d, 1, $J = 16.5$), 4.28 (d, 1, $J = 16.5$), 3.27 (s, 3, OMe), 1.38 (s, 3), 0.97-0.85 (m, 9), 0.70-0.53 (m, 6); ^{13}C NMR (major isomer) 165.4, 153.1, 140.7, 135.8, 134.0, 128.8, 128.4 (2 C), 128.1, 126.2, 124.8, 123.7 (2 C), 116.5 (2 C), 84.4, 67.8, 53.6, 49.0, 27.4, 7.4 (3C), 6.8 (3 C).

Triethylsilyloxy Imine Precursor to 82. To a solution of the triethylsilyl ether (100 mg, 0.21 mmol) in EtOAc (2 mL) was added Pd (10%) on carbon (30 mg). The suspension was stirred at rt under H_2 (1 atm) for 2 h. The catalyst was filtered off and the filtrate was washed with saturated Na_2CO_3 and brine, dried over Na_2SO_4 , and concentrated. Flash chromatography on silica gel (20:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 57 mg (86%) of the triethylsilyloxy imine: ^1H NMR 7.60 (d, 1, $J = 7.9$), 7.45 (d, 1, $J = 7.9$), 7.39 (dd, 1, $J = 7.9, 7.9$), 7.24 (dd, 1, $J = 7.9, 7.9$), 4.61 (s, 2), 1.76 (s, 3), 0.83 (t, 9, $J = 7.9$), 0.50-0.32 (m, 6); ^{13}C NMR 174.0, 173.1, 138.2, 133.9, 130.0, 125.6, 124.4, 112.7, 72.7, 66.3, 27.7, 6.6 (3 C), 5.5 (3 C); HRMS (DCI/ NH_3) calcd for $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_2\text{Si}^+$ (MH^+) 317.1685, found 317.1686.

Triethylsilyl ether of 82. To a solution of the imine (32 mg, 0.10 mmol) in MeOH (1 mL) was added PtO_2 (12 mg, 0.40 eq). The suspension was stirred at rt under H_2 (1 atm) for 4 h. The catalyst was

filtered off and the filtrate was washed with saturated NaHCO_3 and brine, dried over Na_2SO_4 , and concentrated. Flash chromatography on silica gel (5:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 26 mg (81%) of the triethylsilyl ether of **82** as a sticky oil: ^1H NMR 7.55 (d, 1, 7.9), 7.41-7.35 (m, 2), 7.15 (d, 1, $J = 7.9$), 5.04 (s, 1), 3.92 (d, 1, $J = 16.5$), 3.80 (d, 1, $J = 16.5$), 2.98 (br, 1, NH), 1.72 (s, 3), 0.79 (t, 9, $J = 7.9$), 0.43-0.25 (m, 6); ^{13}C NMR 170.7, 137.9, 137.6, 130.7, 124.7, 124.6, 116.0, 87.8, 76.1, 56.0, 24.0, 7.0 (3 C), 6.0 (3 C).

Alcohol 82. The triethylsilyl ether of **82** (16 mg, 0.10 mmol) was added to a solution of TBAF in THF (1.0 M, 1.0 mL). The mixture was stirred at rt for 10 min, and concentrated. Flash chromatography on silica gel (EtOAc) gave 9.6 mg of free alcohol amine **82** (94%) as a white solid: ^1H NMR 7.54 (d, 1, $J = 7.9$), 7.43 (d, 1, $J = 7.9$), 7.37 (ddd, 1, $J = 7.9, 7.9, 1.2$), 7.19 (ddd, 1, $J = 7.9, 7.9, 1.2$), 5.22 (s, 1), 4.09 (d, 1, $J = 15.3$), 3.71 (d, 1, $J = 15.3$), 3.70 (s, 1, OH), 2.62 (br, 1, NH), 1.64 (s, 3); ^{13}C NMR 170.6, 138.3, 137.5, 130.0, 125.6, 124.0, 115.9, 85.4, 73.5, 54.2, 23.4; HRMS (EI) calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2^+ (\text{M}^+)$ 204.0899, found 204.0893.

Triethylsilylation of 83. To a solution of an inseparable 2.3:1 mixture of the isomers of **83** (127 mg, 0.33 mmol) in CH_2Cl_2 (2.0 mL) was added 2,6-lutidine (0.10 mL, 0.83 mmol), and then TESOTf (0.12 mL, 0.50 mmol). The mixture was stirred at rt for 1 h. The solution was washed with water and brine, dried over Na_2SO_4 , and concentrated. Flash chromatography on silica gel (50:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 153 mg (93%) of a 2.3:1 mixture of triethylsilyl ethers as a sticky oil.

Triethylsilyloxy Imines 84 and 85. To a solution of triethylsilyl ethers (150 mg, 0.31 mmol) in EtOAc (4 mL) was added Pd (10%) on carbon (50 mg). The suspension was stirred at rt under H_2 (1 atm) for 1 h. The catalyst was filtered off and the filtrate was washed with saturated NaHCO_3 and brine, dried over Na_2SO_4 , and concentrated to give 88 mg (87%) of a crude 2.1:1 mixture of **84** and **85**, which epimerize rapidly. For NMR spectral analysis, a fast column gave a trace of purer **84** (8:1 mixture with **85**) in the first fraction, and purer **85** (20:1 mixture with **84**) in the final fraction.

Data for **84** were determined from the mixture: ^1H NMR 7.59 (d, 1, $J = 7.9$), 7.45 (d, 1, $J = 7.9$), 7.39 (dd, 1, $J = 7.9, 7.9$), 7.23 (dd, 1, $J = 7.9, 7.9$), 4.60 (q, 1, $J = 7.9$), 1.76 (s, 3), 1.57 (d, 3, $J = 7.9$), 0.82 (t, 9, $J = 7.9$), 0.48-0.30 (m, 6).

Data for **85** were determined from the mixture: ^1H NMR 7.59 (d, 1, $J = 7.9$), 7.45 (d, 1, $J = 7.9$), 7.39 (dd, 1, $J = 7.9, 7.9$), 7.23 (dd, 1, $J = 7.9, 7.9$), 4.60 (q, 1, $J = 7.9$), 1.75 (s, 3), 1.59 (d, 3, $J = 7.9$), 0.81 (t, 9, $J = 7.9$), 0.50-0.32 (m, 6).

To a solution of the crude imine mixture (64 mg, 0.20 mmol) in MeOH (1 mL) was added PtO_2 (32 mg, 0.80 eq). The suspension was stirred at rt under H_2 (1 atm) for 2 h. The catalyst was filtered off and the filtrate was diluted with EtOAc (10 mL), washed with saturated NaHCO_3 and brine, dried over Na_2SO_4 , and concentrated to give the crude triethylsilyl ethers of **86** and **87**. Flash chromatography on silica gel (5:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$) gave 35 mg (53%) of the triethylsilyl ether of **86** as a sticky oil followed by 18 mg (28%) of the triethylsilyl ether of **87** as a sticky oil.

Data for the triethylsilyl ether of **86**: ^1H NMR 7.53 (d, 1, $J = 7.9$), 7.41-7.36 (m, 2), 7.15 (dd, 1, $J = 7.9, 7.9$), 5.07 (s, 1, H-18), 3.96 (q, 1, $J = 7.3$), 3.21 (br, 1, NH), 1.72 (s, 3, H-15), 1.51 (d, 3, $J = 7.3$, H-29), 0.78 (t, 9, $J = 7.9$), 0.42-0.25 (m, 6); ^{13}C NMR 173.7, 137.8, 137.6, 130.5, 124.5, 124.3, 116.0, 85.7, 76.2, 62.2, 23.6, 18.3, 6.7 (3 C), 5.8 (3 C). A 2D NOESY experiment showed cross peaks between H-15 and H-18, and H-18 and H-29.

Data for the triethylsilyl ether of **87**: ^1H NMR 7.55 (d, 1, 7.9), 7.41-7.35 (m, 2), 7.13 (dd, 1, $J = 7.9, 7.9$), 4.95 (s, 1, H-18), 4.0 (q, 1, $J = 7.3$), 2.62 (br, 1, NH), 1.73 (s, 3, H-15), 1.44 (d, 3, $J = 7.3$, H-29), 0.79 (t, 9, $J = 7.9$), 0.44-0.24 (m, 6); ^{13}C NMR 172.4, 137.5 (2 C), 130.5, 124.3, 124.2, 115.7, 84.7, 75.6, 61.5, 23.9, 15.9, 6.8 (3 C), 5.8 (3 C); A 2D NOESY experiment showed cross peaks between H-15 and H-18, and H-18 and H-20; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_2\text{Si}^+$ (M^+) 332.1920, found 332.1907.

Alcohol 86. To a solution of the triethylsilyl ether of **86** (17 mg, 0.08 mmol) in THF (0.1 mL) was added TBAF (1.0 M, 0.1 mL). The solution was stirred at 0 °C for 15 min and triturated with 3:1 $\text{Et}_2\text{O}/\text{EtOAc}$ (5 mL). The solution was washed with H_2O (5 ml $\times$ 2) and brine, dried over Na_2SO_4 , and

concentrated. Flash chromatography on silica gel (1:1 Et₂O/EtOAc) gave 9 mg (85%) of **86** as a white solid: ¹H NMR 7.53 (d, 1, *J* = 7.9), 7.43 (d, 1, *J* = 7.9), 7.37 (ddd, 1, *J* = 7.9, 7.9, 1.2), 7.19 (ddd, 1, *J* = 7.9, 7.9, 1.2), 5.25 (s, 1, H-18), 3.96 (q, 1, *J* = 6.7), 3.56 (s, 1, OH), 2.40 (br, 1, NH), 1.62 (s, 3, H-15), 1.57 (d, 3, *J* = 6.7, H-29); ¹³C NMR 173.6, 138.1, 137.7, 129.9, 125.6, 123.9, 116.2, 83.6, 73.6, 60.96, 23.2, 19.29. A 2D NOESY experiment showed cross peaks between H-15 and H-18, and H-18 and H-29; HRMS (EI) calcd for C₁₂H₁₄N₂O₂⁺ (M⁺) 218.1055, found 218.1057.

Alcohol 87. To a solution of the triethylsilyl ether of **87** (26 mg, 0.08 mmol) in THF (0.1 mL) was added TBAF (1.0 M, 0.1 mL). The solution was stirred at 0 °C for 15 min and diluted with EtOAc (5 mL). The solution was washed with H₂O (5 ml × 2), Brine, dried over Na₂SO₄, and concentrated. Flash chromatography on silica gel (1:1 Et₂O/EtOAc) gave 19 mg (88%) of **87** as a white solid: ¹H NMR 7.55 (d, 1, *J* = 7.9), 7.42 (d, 1, *J* = 7.9), 7.35 (ddd, 1, *J* = 7.9, 7.9, 1.2), 7.16 (ddd, 1, *J* = 7.9, 7.9, 1.2), 5.14 (s, 1, H-18), 4.28 (q, 1, *J* = 6.7, H-20), 3.80 (s, 1, OH), 2.72 (br, 1, NH), 1.63 (s, 3, H-15), 1.40 (d, 3, *J* = 6.7); ¹³C NMR 171.9, 138.3, 137.7, 129.9, 125.4, 123.9, 115.8, 82.2, 72.8, 59.6, 23.6, 17.9; a 2D NOESY experiment showed cross peaks between H-15 and H-18, H-18 and H-20; HRMS (EI) calcd for C₁₂H₁₄N₂O₂⁺ (M⁺) 218.1055, found 218.1056.