Supporting Information

Intramolecular Diels–Alder and Tandem Intramolecular Diels–Alder/1,3-Dipolar Cycloaddition Reactions of 1,3,4-Oxadiazoles

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***N*¹-Methyl-*N*-carbonylimidazole tryptamine (S1).** Distilled *N*¹-methyl tryptamine (15.0 g, 86.2 mmol) in CH₂Cl₂ (500 mL) was added dropwise to a stirring solution of 1,1-carbonyldiimidazole (20.95 g, 129.0 mmol) in THF (100 mL) under Ar cooled to 0 °C. The reaction mixture was allowed to stir and equilibrate to 23 °C overnight before the solvent was removed under reduced pressure. Flash chromatography (SiO₂, 6 × 30 cm, 5% MeOH/CHCl₃) provided **S1** (20.0 g, 74.9 mmol) in 86% yield as a pale yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 8.04 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.12 (t, *J* = 7.0 Hz, 1H), 7.02 (s, 1H), 6.92 (s, 1H), 5.90 (s, 1H), 3.76 (s, 3H), 3.72 (t, *J* = 6.5 Hz, 2H), 3.09 (t, *J* = 6.5 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 148.3, 137.1, 135.6, 128.9, 127.6, 127.0, 122.0, 119.2, 118.6, 116.3, 110.7, 109.5, 41.8, 32.7, 24.9; IR (film) ν_{max} 1727, 1603, 1528, 1511, 1471, 1415 cm⁻¹; FABHRMS (NBA/NaI) *m/z* 269.1410 (C₁₅H₁₆N₄O + H⁺ requires 269.1402).

Tryptamine semicarbazide S2. Methyl oxalylhydrazide^{S1} (3.11 g, 26.4 mmol) was added to a solution of **S1** (7.10 g, 26.4 mmol) and AcOH (1.8 mL, 26.4 mmol) in THF (200 mL) under Ar and the reaction mixture was warmed at 40 °C for 16 h. The reaction mixture was concentrated under reduced pressure and flash chromatography (SiO₂, 6 × 15 cm, 2.5% MeOH/22.5% acetone/75% CHCl₃) provided **S2** (5.40 g) in 65% yield as a white solid: mp 102–104 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.94 (bs, 1H), 7.52 (d, *J* = 6.2 Hz, 1H), 7.24 (d, *J* = 5.7 Hz, 1H), 7.17 (t, *J* = 5.7 Hz, 1H), 7.07 (t, *J* = 6.2 Hz, 1H), 6.81 (s, 1H), 5.79 (bs, 1H), 3.77 (s, 3H), 3.65 (s, 3H), 3.41 (m, 2H), 2.87 (t, *J* = 5.3 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 159.2, 157.1, 154.7, 137.0, 127.7, 127.0, 121.6, 118.8, 118.7, 111.1, 109.2, 53.6, 40.6, 32.5, 25.4; IR (film) $\nu_{\max}$ 3394, 1769, 1728, 1707, 1523, 1420 cm⁻¹; MALDIFTMS (DHB) *m/z* 341.1220 (C₁₅H₁₈N₄O₄ + Na⁺ requires 341.1233).

Methyl 5-[(2-(1-methyl-1H-indol-3-yl)ethyl)amino]-1,3,4-oxadiazole-2-carboxylate (S3). Et₃N (19.5 mL, 140 mmol) was added to a stirring solution of semicarbazide **S2** (17.9 g, 56.0 mmol) and TsCl (10.75 g, 56.0 mmol) in CH₂Cl₂ (500 mL) under Ar at 23 °C. The reaction mixture was stirred for 16 h before the solvent was removed under reduced pressure. Flash chromatography (SiO₂, 6 × 15 cm, 50% EtOAc/hexane) provided **S3** (10.9 g, 36.4 mmol) in 65% yield as white crystals: mp 144–146 °C (MeOH); ¹H NMR (CDCl₃, 500 MHz) δ 7.58 (d, *J* = 8.1 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.24 (m, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.90 (s, 1H), 5.63 (s, 1H), 3.95 (s, 3H), 3.74 (s, 3H), 3.73 (m, 2H), 3.10 (t, *J* = 6.6 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 164.4, 154.8, 150.9, 137.2, 127.4, 127.3, 121.9, 119.1, 118.6, 110.0, 109.4, 53.2, 43.6, 32.7, 25.1; IR (film) $\nu_{\max}$ 3421, 1743, 1619, 1537, 1473, 1155, 1068 cm⁻¹; MALDIFTMS (DHB) *m/z* 301.1284 (C₁₅H₁₆N₄O₃ + H⁺ requires 301.1295).

Methyl 5-{{2-(1-methyl-1*H*-indol-3-yl)ethyl}-(pent-4-enoyl)amino}-1,3,4-oxadiazole-2-carboxylate (1a**).** A solution of pent-4-enoic acid (0.05 mL, 0.5 mmol) in 5 mL of anhydrous CH₂Cl₂ was treated with EDCI (98 mg, 0.5 mmol) followed by DMAP (2 mg, 0.02 mmol). Oxadiazole **S3** was added (50 mg, 0.17 mmol) and the reaction mixture was allowed to stir at 23 °C for 16 h. The reaction mixture was concentrated in vacuo to 1 mL then diluted with 30 mL of EtOAc and 10 mL of 1 N aqueous HCl. The organic layer was separated and washed with 10 mL of saturated aqueous NaHCO₃ and 10 mL of saturated aqueous NaCl. The organic layer was dried over Na₂SO₄, filtered, and concentrated. PTLC (SiO₂, 50% EtOAc/hexanes) provided **1a** (49 mg, 75%) as a white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.21 (dd, *J* = 7.0, 7.9 Hz, 1H), 7.12 (dd, *J* = 7.0, 7.5 Hz, 1H), 6.86 (s, 1H), 5.87–5.77 (m, 1H), 5.09–4.98 (m, 2H), 4.24 (t, *J* = 7.5 Hz, 2H), 4.06 (s, 3H), 3.72 (s, 3H), 3.12 (dd, *J* = 7.9, 8.5 Hz, 2H), 2.92 (dd, *J* = 7.9, 8.5 Hz, 2H), 2.45 (dt, *J* = 7.0, 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz) δ 171.9, 162.3, 154.2, 153.5, 137.2, 136.7, 127.8, 127.6, 121.9, 119.3, 119.1, 116.1, 110.1, 109.4, 53.9, 48.0, 35.8, 32.8, 28.9, 24.5; IR (film) $\nu_{\max}$ 2923, 1749, 1702, 1567, 1442, 1328, 1153, 813, 743 cm⁻¹; MALDIFTMS (DHB) *m/z* 405.1536 (C₂₀H₂₂N₄O₄ + Na⁺ requires 405.1533).

Solid curved lines represent nOe's observed
in 1D ¹H–¹H GOESY (CDCl₃, 600 MHz)

Compound 1b (microwave). A solution of **1a** (5.0 mg, 0.013 mmol) in 2.5 mL of anhydrous, degassed 1,2-dichlorobenzene was placed in a capped, silated microwave safe tube under Ar and irradiated for 30 min in a microwave (Personal Chemistry) at 250 °C. The cooled reaction mixture was loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO₂, 55% EtOAc/hexanes) providing **1b** (3.2 mg, 70%) as a white solid.

Compound 1b (thermal). A solution of **1a** (15.0 mg, 0.039 mmol) in 10 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 178 °C for 3 h. The cooled reaction mixture was loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO₂, 55% EtOAc/hexanes) providing **1b** (12 mg, 87%) as a white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.09 (dt, *J* = 1.3, 7.9 Hz, 1H), 6.70 (dd, *J* = 0.9, 7.5 Hz, 1H), 6.58 (dt, *J* = 1.3, 7.9 Hz, 1H), 6.42 (d, *J* = 7.9 Hz, 1H), 4.02 (d, *J* = 1.3 Hz, 1H), 3.98 (dt, *J* = 9.2, 12.2 Hz, 1H), 3.76 (s, 3H), 3.75–3.70 (m, 2H), 2.86 (s, 3H), 2.35–2.27 (m, 2H), 2.23 (ddd, *J* = 2.2, 6.6, 8.8 Hz, 1H), 2.13 (ddd, *J* = 5.7, 6.1, 12.7 Hz, 1H), 1.74 (apparent dq, *J* = 5.2, 12.7 Hz, 1H), 1.62–1.57 (m, 1H), 1.49–1.45 (m, 1H), 1.38 (ddd, *J* = 3.1, 3.1, 12.7 Hz, 1H); ¹³C NMR (CDCl₃, 150 MHz) δ 171.6, 170.5, 153.2, 129.7, 129.0, 123.2, 118.1, 107.1, 105.8, 87.4, 81.9, 65.2, 52.9, 47.1, 36.4, 34.93, 34.91, 33.9, 32.2, 26.7; IR (film) $\nu_{\max}$ 2949, 1735, 1667, 1606, 1493, 1384, 1119 cm⁻¹; MALDIFTMS (DHB) *m/z* 355.1656 (C₂₀H₂₂N₂O₄ + H⁺ requires 355.1652).

Methyl 5-{(E)-hex-4-enoyl-[2-(1-methyl-1H-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (2a). DMAP (107 mg, 0.88 mmol) was added to a solution of *trans*-4-hexenoic acid^{S2} (100 mg, 0.88 mmol), **S3** (106 mg, 0.35 mmol), and EDCI (168 mg, 0.88 mmol) in CH₂Cl₂ (40 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 13 h. The reaction mixture was concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 2.5 × 20 cm, 30–50% EtOAc/hexanes gradient elution) providing **2a** (110 mg, 80%) as an amorphous white solid: ¹H NMR (CDCl₃, 500 MHz) δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.89 (s, 1H), 5.56–5.43 (m, 2H), 4.27 (t, *J* = 7.3 Hz, 2H), 4.03 (s, 3H), 3.74 (s, 3H), 3.15 (t, *J* = 7.3 Hz, 2H), 2.91 (t, *J* = 7.3 Hz, 2H), 2.41 (dt, *J* = 6.6, 7.0 Hz, 2H), 1.67 (d, *J* = 5.9 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.8, 162.0, 154.0, 153.2, 136.9, 128.9, 127.5, 127.3, 126.5, 121.6, 119.0, 118.8, 109.8, 109.2, 53.6, 47.7, 36.2, 32.5, 27.7, 24.2, 17.9; IR (film) $\nu_{\max}$ 2954, 1748, 1704, 1587, 1441, 1152 cm⁻¹; MALDIFTMS (DHB) *m/z* 419.1691 (C₂₁H₂₄N₄O₄ + Na⁺ requires 419.1690).

Solid curved lines represent nOe's observed
in 2D ^1H - ^1H ROESY (CD_2Cl_2 , 400 MHz)

Compound 2b. A solution of **2a** (10 mg, 0.025 mmol) in 5 mL of anhydrous degassed 1,2-dichlorobenzene was warmed under Ar at 178 °C for 24 h. The cooled reaction mixture was loaded directly onto SiO_2 (1.5×10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO_2 , 55% EtOAc/hexanes) providing **2b** (6 mg, 65%) as a white solid: ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.10 (dt, $J = 1.2, 7.9$ Hz, 1H), 6.69 (dd, $J = 0.8, 7.2$ Hz, 1H), 6.56 (dt, $J = 0.8, 7.2$ Hz, 1H), 6.30 (d, $J = 7.9$ Hz, 1H), 4.14 (d, $J = 1.6$ Hz, 1H), 4.04 (dt, $J = 3.0, 11.7$ Hz, 1H), 3.76 (s, 3H), 3.68 (dt, $J = 2.8, 10$ Hz, 1H), 2.86 (s, 3H), 2.38–2.22 (m, 3H), 2.08 (ddd, $J = 5.6, 6.0, 7.8$ Hz, 1H), 1.97–1.93 (m, 1H), 1.72–1.65 (m, 2H), 1.25 (dt, $J = 5.2, 12.0$ Hz, 1H), 1.04 (d, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.1, 170.4, 152.4, 129.5, 128.5, 122.8, 117.3, 106.0, 105.1, 88.3, 81.4, 65.0, 52.5, 48.3, 46.4, 41.6, 37.0, 33.9, 31.7, 26.6, 12.6; IR (film) ν_{max} 2950, 1734, 1669, 1497, 1437, 1382, 1118 cm^{-1} ; MALDIFTMS (DHB) m/z 369.1802 ($\text{C}_{21}\text{H}_{24}\text{N}_4\text{O}_4 + \text{H}^+$ requires 369.1809).

Methyl 5-[[6-*tert*-butyldimethylsilyloxy)hex-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate ((*E*)-3a**).** Oxadiazole **S3** (121 mg, 0.403 mmol) was added in one portion to a solution of (*E*)-6-(*tert*-butyldimethylsilyloxy)hex-4-enoic acid^{S3} (295 mg, 1.21 mmol) in anhydrous CH₂Cl₂ (5 mL) at 25 °C under Ar. The mixture was cooled to 0 °C and EDCI (232 mg, 1.21 mmol) was added. The resulting mixture was stirred for 5 min, before the addition of DMAP (147 mg, 1.21 mmol). The reaction mixture was stirred overnight at 23 °C before the solvent was removed in vacuo. Flash chromatography (SiO₂, 2 × 16 cm, 30% EtOAc/hexane) afforded (*E*)-**3a** (150 mg, 71%) as an off-white solid: ¹H NMR (CDCl₃, 500 MHz) δ 7.66 (d, *J* = 8.1 Hz, 1H), 7.24–7.08 (m, 3H), 6.84 (s, 1H), 5.97–5.50 (m, 2H), 4.20 (t, *J* = 7.3 Hz, 2H), 4.09–4.10 (m, 2H), 3.98 (s, 3H), 3.69 (s, 3H), 3.08 (t, *J* = 7.7 Hz, 2H), 2.88 (t, *J* = 7.3 Hz, 2H), 2.40 (dd, *J* = 7.0, 13.9 Hz, 2H), 0.88 (s, 9H), 0.04 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.6, 161.9, 154.0, 153.2, 136.9, 130.7, 128.5, 127.5, 127.3, 121.6, 119.0, 118.8, 109.8, 109.2, 63.6, 53.6, 47.7, 35.9, 32.5, 27.2, 25.9 (3C), 24.2, 18.4, –5.2 (2C); IR (film) $\nu_{\max}$ 2954, 2855, 1749, 1707, 1567, 1442, 1252, 1152, 836 cm^{–1}; MALDIFTMS (DHB) *m/z* 549.2490 (C₂₇H₃₈N₄O₅Si + Na⁺ requires 549.2504).

Compound 3b. A solution of (*E*)-**3a** (16.5 mg, 0.0313 mmol) in 1,2-dichlorobenzene (6.3 mL, 0.0052 M, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) was warmed to a gentle reflux in the absence of light for 16–24 h, at which time the solvent was removed in vacuo. Flash chromatography (SiO₂, 2 × 9 cm, 50% EtOAc/hexane) afforded **3b** (13.5 mg, 86%) as a yellow oil: *R_f* = 0.25 (50% EtOAc/hexane); ¹H NMR (CDCl₃, 500 MHz) δ 7.17 (t, *J* = 7.7 Hz, 1H), 6.74 (d, *J* = 7.0 Hz, 1H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 8.1 Hz, 1H), 4.15–4.06 (m, 2H), 3.85 (s, 3H), 3.82–3.61 (m, 4H), 2.98 (s, 3H), 2.25–2.16 (m, 6H), 1.88 (t, *J* = 2.9 Hz, 2H), 1.50–1.45 (m, 1H), 0.78 (s, 9H), –0.15 (s, 3H), –0.17 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 170.8, 170.6, 152.2, 129.6, 128.0, 122.7, 118.1, 106.7, 105.8, 88.3, 81.1, 64.9, 61.8, 56.5, 52.7, 46.3, 39.6, 36.7, 34.4, 31.5, 27.4, 25.8 (3C), 18.2, –5.5 (2C); IR (film) $\nu_{\max}$ 2952, 2855, 1738, 1674, 1607, 1495, 1385, 1258, 1117, 1072, 1023, 837, 740 cm^{–1}; MALDIFTMS (DHB) *m/z* 521.2454 (C₂₇H₃₈N₂O₅Si + Na⁺ requires 521.2442).

Methyl 5-{[2-(1-methyl-1*H*-indol-3-yl)ethyl]-((*E*)-5-phenylpent-4-enoyl)amino}-1,3,4-oxadiazole-2-carboxylate (4a). DMAP (34 mg, 0.28 mmol) was added to a solution of *trans*-5-phenylpent-4-enoic acid^{S4} (50 mg, 0.28 mmol), **S3** (34 mg, 0.11 mmol), and EDCI (53 mg, 0.28 mmol) in CH₂Cl₂ (5 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 13 h. The mixture was concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 2.5 × 15 cm, 30–50% EtOAc/hexanes gradient elution) providing **4a** (110 mg, 90%) as an amorphous white solid: ¹H NMR (CDCl₃, 500 MHz) δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.26–7.10 (m, 7H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.75 (s, 1H), 6.37 (d, *J* = 15.8 Hz, 1H), 6.16 (dt, *J* = 7.0, 15.8 Hz, 1H), 4.18 (t, *J* = 7.3 Hz, 2H), 3.90 (s, 3H), 3.60 (s, 3H), 3.05 (t, *J* = 7.7 Hz, 2H), 2.93 (t, *J* = 7.4 Hz, 2H), 2.54 (q, *J* = 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.6, 162.0, 154.0, 153.2, 137.2, 136.9, 131.2, 128.5 (2C), 128.2, 127.5, 127.3, 127.1, 126.0 (2C), 121.6, 119.0, 118.8, 109.8, 109.2, 53.6, 47.7, 36.0, 32.5, 28.2, 24.2; IR (film) ν_{max} 2953, 1747, 1703, 1564, 1440, 1409, 1327, 1150 cm⁻¹; MALDIFTMS (DHB) *m/z* 481.1840 (C₂₆H₂₆N₄O₄ + Na⁺ requires 481.1846).

Solid curved lines represent nOe's observed in 2D ¹H–¹H ROESY (CD₂Cl₂, 400 MHz)

Compound 4b. A solution of **4a** (9 mg, 0.019 mmol) in 3.8 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 178 °C for 14 h. The cooled reaction mixture was loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO₂, 55% EtOAc/hexanes) providing **4b** (5 mg, 61%) as a white solid: ¹H NMR (CD₂Cl₂, 500 MHz) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.47–7.33 (m, 6H), 7.28 (dt, *J* = 1.1, 7.3 Hz, 1H), 7.11 (t, *J* = 7.0 Hz, 1H), 4.90 (d, *J* = 7.7 Hz, 1H), 4.71 (dd, *J* = 4.4, 8.1 Hz, 1H), 4.01 (dd, *J* = 3.0, 8.1 Hz, 1H), 3.93 (s, 3H), 3.71 (s, 3H), 3.57–3.51 (m, 2H), 3.00 (ddd, *J* = 5.1, 7.3, 8.5 Hz, 1H), 2.70–2.62 (m, 2H), 2.42–2.38 (m, 1H), 1.70–1.67 (m, 2H); ¹³C NMR (CD₂Cl₂, 100 MHz) δ 172.0, 169.0, 139.4, 138.2, 129.5 (2C), 128.0, 127.8 (2C), 127.5, 126.3, 123.2, 119.6, 119.0, 116.3, 109.6, 95.5, 82.2, 52.5, 49.5, 48.6, 37.8, 32.6, 27.3, 21.5, 17.4; IR (film) ν_{max} 2951, 2925, 1733, 1656, 1454, 1389, 1272, 1164 cm⁻¹; MALDIFTMS (DHB) *m/z* 431.1978 (C₂₆H₂₆N₂O₄ + H⁺ requires 431.1965).

Methyl 5-{[(*E*)-5-(benzyloxy)pent-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (5a**).** DMAP (94 mg, 0.80 mmol) was added to a solution of *trans*-5-(benzyloxy)pent-4-enoic acid (165 mg, 0.80 mmol), oxadiazole **S3** (96 mg, 0.32 mmol), and EDCI (153 mg, 0.80 mmol) in CH₂Cl₂ (40 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 13 h. Saturated aqueous NH₄Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated. Chromatography (SiO₂, 2.5 × 20 cm, 30–50% EtOAc/hexanes gradient elution) afforded **5a** (122 mg, 78%) as an amorphous solid: ¹H NMR (CD₂Cl₂, 600 MHz) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.36–7.24 (m, 6H), 7.18 (t, *J* = 7.9 Hz, 1H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.88 (s, 1H), 6.40 (d, *J* = 12.3 Hz, 1H), 4.87 (dt, *J* = 12.3, 7.5 Hz, 1H), 4.69 (s, 2H), 4.19 (t, *J* = 7.5 Hz, 2H), 3.98 (s, 3H), 3.70 (s, 3H), 3.09 (t, *J* = 7.5 Hz, 2H), 2.83 (t, *J* = 7.0 Hz, 2H), 2.29 (dt, *J* = 7.0, 7.5 Hz, 2H); ¹³C NMR (CD₂Cl₂, 150 MHz) δ 171.9, 162.4, 154.6, 153.7, 147.5, 137.7, 137.4, 128.8, 128.8 (2C), 128.7 (2C), 128.1, 127.9, 127.8 (2C), 121.9, 119.2, 119.1, 110.3, 109.6, 103.0, 71.4, 48.0, 37.8, 32.8, 24.5, 23.6; IR (film) ν_{max} 2955, 2914, 1744, 1703, 1559, 1436, 1410, 1149 cm⁻¹; MALDIFTMS (DHB) *m/z* 489.2138 (C₂₇H₂₈N₄O₅ + H⁺ requires 489.2132).

Compound 5b. A solution of **5a** (23 mg, 0.047 mmol) in 1,3,5-triisopropylbenzene (5.90 mL) was warmed at 230 °C for 19 h. After cooling to 25 °C, the solution was poured onto a plug of SiO₂ (2 × 8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and concentrated. PTLC (SiO₂, 50% EtOAc/hexanes) afforded **5b** (19 mg, 88%) as an amorphous solid: ¹H NMR (C₆D₆, 500 MHz) δ 7.15–7.02 (m, 6H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 7.4 Hz, 1H), 6.19 (d, *J* = 8.0 Hz, 1H), 4.39 (s, 1H), 4.10 (dt, *J* = 9.2, 12.1 Hz, 1H), 4.07 (d, *J* = 11.6 Hz, 1H), 4.00 (d, *J* = 11.6 Hz, 1H), 3.81 (t, *J* = 2.2 Hz, 1H), 3.67 (dt, *J* = 2.4, 12.2 Hz, 1H), 3.34 (s, 3H), 2.78 (s, 3H), 2.25–2.18 (m, 1H), 2.02 (dt, *J* = 12.8, 9.9 Hz, 1H), 1.92–1.82 (m, 2H), 1.59–1.49 (m, 2H), 1.15–1.10 (m, 1H); ¹³C NMR (C₆D₆, 125 MHz) δ 170.8, 169.3, 152.8, 138.4, 129.8, 128.8, 128.7 (2C), 128.5, 128.3, 122.8, 116.9, 107.5, 105.6, 88.0, 86.4, 80.2, 73.9, 64.8, 53.7, 52.4, 47.1, 41.0, 36.7, 32.5, 31.9, 23.2; IR (film) ν_{max} 2954, 2892, 1733, 1667, 1605, 1497, 1385, 1262, 1113, 1204 cm⁻¹; MALDIFTMS (DHB) *m/z* 461.2068 (C₂₇H₂₈N₂O₅ + H⁺ requires 461.2071).

Methyl 5-[(Z)-5-(benzyloxy)pent-4-enoyl]-[2-(1-methyl-1H-indol-3-yl)ethyl]amino-1,3,4-oxadiazole-2-carboxylate (6a). DMAP (197 mg, 1.70 mmol) was added to a solution of a 1:1 mixture of *trans*- and *cis*-5-(benzyloxy)pent-4-enoic acid (250 mg, 1.2 mmol), oxadiazole **S3** (181 mg, 0.60 mmol), and EDCI (301 mg, 1.50 mmol) in CH₂Cl₂ (24 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 16 h. Saturated aqueous NH₄Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated. Chromatography (SiO₂, 2.5 × 25 cm, 30–50% EtOAc/hexanes gradient elution) afforded a mixture of **5a** and **6a** (246 mg, 83%) as an amorphous solid. The isomers were separated by PTLC with multiple elutions (SiO₂, 50% EtOAc/hexanes) providing a sample of pure **6a** as an amorphous white solid: ¹H NMR (CD₂Cl₂, 500 MHz) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.37–7.24 (m, 6H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.89 (s, 1H), 6.07 (d, *J* = 6.2 Hz, 1H), 4.78 (s, 2H), 4.43 (dt, *J* = 6.9, 6.2 Hz, 1H), 4.19 (t, *J* = 7.3 Hz, 2H), 3.99 (s, 3H), 3.70 (s, 3H), 3.08 (t, *J* = 7.7 Hz, 2H), 2.86 (t, *J* = 7.3 Hz, 2H), 2.45 (ddt, *J* = 1.5, 7.3, 7.3 Hz, 2H); ¹³C NMR (CD₂Cl₂, 125 MHz) δ 172.2, 162.5, 154.6, 153.7, 146.0, 138.1, 137.4, 128.8 (2C), 128.7, 128.2, 128.1, 127.9, 127.8 (2C), 121.9, 119.2, 119.1, 110.4, 109.5, 105.3, 74.1, 48.0, 36.6, 32.8, 24.5, 19.9; IR (film) $\nu_{\max}$ 3029, 2935, 1747, 1700, 1563, 1149 cm⁻¹; MALDIFTMS (DHB) *m/z* 489.2138 (C₂₇H₂₈N₄O₅ + H⁺ requires 489.2132).

Solid curved lines represent nOe's observed in 2D ¹H–¹H ROESY (C₆D₆, 400 MHz)

Compound 6b. A solution of **6a** (9.3 mg, 0.019 mmol) in 1,3,5-triisopropylbenzene (2.80 mL) was warmed at 230 °C for 38 h. After cooling to 25 °C, the solution was poured onto a plug of SiO₂ (2 × 8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and concentrated. PTLC (SiO₂, 60% EtOAc/hexanes) afforded **6b** and an impurity that was further separated by PTLC (SiO₂, 2.5% MeOH/CH₂Cl₂) to give **6b** (3.6 mg, 41%) as an amorphous solid: ¹H NMR (C₆D₆, 600 MHz) δ 7.15–7.02 (m, 6H), 6.62 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 7.5 Hz, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 4.26 (d, *J* = 7.0 Hz, 1H), 4.14 (d, *J* = 11.4 Hz, 1H), 4.06 (dt, *J* = 9.2, 12.3 Hz, 1H), 3.98 (d, *J* = 11.4 Hz, 1H), 3.76 (t, *J* = 10.5 Hz, 1H), 3.66 (s, 1H), 3.40 (s, 3H), 2.77 (s, 3H), 2.32 (dd, *J* = 4.4, 13.6 Hz, 1H), 2.14 (ddt, *J* = 5.3, 13.1, 13.1 Hz, 1H), 1.95 (dt, *J* = 9.6, 12.7 Hz, 1H), 1.85 (ddd, *J* = 5.7, 7.9, 13.6 Hz, 1H), 1.72 (dd, *J* = 9.8, 10.1 Hz, 1H), 1.57 (m, 1H), 0.99 (dt, *J* = 7.0, 13.6 Hz, 1H); ¹³C NMR (C₆D₆, 150 MHz) δ 170.0, 169.4, 153.0, 138.6, 129.6, 129.1, 128.6, 128.5, 128.1, 127.7, 127.6, 123.1, 118.8, 107.3, 104.3, 91.8, 80.6, 80.4, 74.3, 64.7, 51.7, 47.3, 41.1, 36.1, 35.2, 31.5, 19.0; IR (film) $\nu_{\max}$ 2936, 2847, 1762, 1734, 1669, 1399, 1117 cm⁻¹; MALDIFTMS (DHB) *m/z* 461.2076 (C₂₇H₂₈N₂O₅ + H⁺ requires 461.2071).

Methyl 5-[(*E*)-5-(methoxycarbonyl)pent-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino-1,3,4-oxadiazole-2-carboxylate (7a**).** EDCI (146 mg, 0.76 mmol) was added to a 1:1 solution of *trans*- and *cis*-hex-2-endioic acid 1-methyl ester^{S5} (100 mg, 0.63 mmol), oxadiazole **S3** (95 mg, 0.38 mmol), and DMAP (88 mg, 0.76 mmol) in CH₂Cl₂ (6.3 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 11 h. Saturated aqueous NH₄Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated. Chromatography (SiO₂, 2.5 × 20 cm, 30–50% EtOAc/hexanes gradient elution) afforded a mixture of **7a** and **8a** (121 mg, 83%) as a white solid. The isomers could be separated by PTLC with multiple elutions (SiO₂, 50% EtOAc/hexanes) providing a pure sample of **7a**: ¹H NMR (CDCl₃, 600 MHz) δ 7.65 (d, *J* = 6.9 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 7.10 (t, *J* = 7.0 Hz, 1H), 6.95 (dt, *J* = 15.8, 6.6 Hz, 1H), 6.85 (s, 1H), 5.87 (d, *J* = 15.8 Hz, 1H), 4.23 (t, *J* = 7.4 Hz, 2H), 3.99 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.10 (t, *J* = 7.4 Hz, 2H), 2.98 (t, *J* = 7.5 Hz, 2H), 2.58 (m, 2H); ¹³C NMR (CD₂Cl₂, 150 MHz) δ 170.9, 166.7, 161.8, 153.9, 153.2, 146.8, 136.9, 127.6, 127.3, 122.1, 121.7, 119.1, 118.8, 109.7, 109.3, 53.7, 51.5, 47.7, 34.7, 32.6, 27.0, 24.2; IR (film) $\nu_{\max}$ 2943, 2902, 1743, 1707, 1701, 1562, 1436, 1149 cm⁻¹; MALDIFTMS (DHB) *m/z* 463.1582 (C₂₂H₂₄N₄O₆ + Na⁺ requires 463.1588).

Solid curved lines represent nOe's observed
in 2D ^1H - ^1H ROESY (CD_2Cl_2 , 400 MHz)

Compound 7b. A solution of **7a** (13 mg, 0.03 mmol) in 1,3,5-triisopropylbenzene (3.7 mL) was warmed at 230 °C for 46 h. After cooling to 25 °C, the solution was poured onto a plug of SiO_2 (2×8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and concentrated. PTLC (SiO_2 , 60% EtOAc/hexanes) afforded **7b** (8.6 mg, 71%) as a white solid: ^1H NMR (CD_2Cl_2 , 500 MHz) δ 7.19 (t, $J = 7.5$ Hz, 1H), 6.78 (d, $J = 7.4$ Hz, 1H), 6.72 (t, $J = 7.3$ Hz, 1H), 6.43 (d, $J = 7.9$ Hz, 1H), 4.39 (s, 1H), 4.08 (dt, $J = 12.2$, 8.8 Hz, 1H), 3.89 (s, 3H), 3.72 (dt, $J = 12.2$, 2.4 Hz, 1H), 3.59 (s, 3H), 3.02 (d, $J = 4.9$ Hz, 1H), 2.78 (s, 3H), 2.47–2.36 (m, 2H), 2.32 (ddd, $J = 2.4$, 9.2, 15.8 Hz, 1H), 2.21 (ddd, $J = 5.5$, 12.8, 15.8 Hz, 1H), 2.09 (dt, $J = 12.2$, 4.9 Hz, 1H), 1.92–1.86 (m, 1H), 1.81 (ddt, $J = 5.5$, 7.9, 13.4 Hz, 1H); ^{13}C NMR (CD_2Cl_2 , 150 MHz) δ 170.1, 169.4, 168.8, 154.0, 129.6, 128.9, 122.8, 119.3, 108.8, 107.0, 89.3, 80.6, 65.0, 56.1, 53.8, 53.3, 51.9, 46.6, 36.1, 35.6, 31.8, 26.8; IR (film) ν_{max} 2943, 2912, 1739, 1662, 1487, 1384 cm^{-1} ; MALDIFTMS (DHB) m/z 413.1699 ($\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_6 + \text{H}^+$ requires 413.1707).

Methyl 5-[(Z)-5-(methoxycarbonyl)pent-4-enoyl]-[2-(1-methyl-1H-indol-3-yl)ethyl]amino-1,3,4-oxadiazole-2-carboxylate (8a). DMAP (67 mg, 0.57 mmol) was added to a solution of *cis*-hex-2-endioic acid 1-methyl ester^{S5} (75 mg, 0.47 mmol), oxadiazole **S3** (71 mg, 0.24 mmol), and EDCI (109 mg, 0.57 mmol) in CH_2Cl_2 (23 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 12 h. Saturated aqueous NH_4Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Chromatography (SiO_2 , 2.5×20 cm, 30–50% EtOAc/hexanes gradient elution) afforded **8a** (88 mg, 85%) as a white solid: ^1H NMR (CDCl_3 , 500 MHz) δ 7.66 (d, $J = 7.7$ Hz, 1H), 7.24 (d, $J = 8.4$ Hz, 1H), 7.19 (t, $J = 8.4$ Hz, 1H), 7.10 (t, $J = 7.0$ Hz, 1H), 6.85 (s, 1H), 6.22 (dt, $J = 7.3$, 11.4 Hz, 1H), 5.80 (d, $J = 11.4$ Hz, 1H), 4.22 (t, $J = 7.3$ Hz, 2H), 3.99 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 3.09 (t, $J = 7.3$ Hz, 2H), 3.05–2.96 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.2, 166.4, 161.8, 154.0, 153.1, 147.8, 136.8, 127.5, 127.3, 121.6, 120.5, 119.0, 118.8, 109.7, 109.2, 53.6, 51.1, 47.6, 35.5, 32.5, 24.2, 24.1; IR (film) ν_{max} 2944, 2913, 1744, 1713, 1564, 1441, 1410, 1194, 1153 cm^{-1} ; MALDIFTMS (DHB) m/z 463.1602 ($\text{C}_{22}\text{H}_{24}\text{N}_4\text{O}_6 + \text{Na}^+$ requires 463.1588).

Solid curved lines represent nOe's observed
in 2D ^1H - ^1H ROESY (CD_2Cl_2 , 400 MHz)

Compound 8b. A solution of **8a** (17 mg, 0.039 mmol) in 1,3,5-triisopropylbenzene (4.8 mL) was warmed at 230 °C for 60 h. After cooling to 25 °C, the solution was poured onto a plug of SiO_2 (2×8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and concentrated. PTLC (SiO_2 , 50% EtOAc/hexanes) afforded **8b** (9.9 mg, 62%) as a white solid: ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.18 (t, J = 8.0 Hz, 1H), 6.77 (d, J = 7.2 Hz, 1H), 6.70 (t, J = 7.2 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 4.04 (dt, J = 12.4, 9.2 Hz, 1H), 3.97 (s, 1H), 3.80 (dt, J = 2.4, 12.0 Hz, 1H), 3.79 (s, 3H), 3.62 (d, J = 8.8 Hz, 1H), 3.59 (s, 3H), 2.90 (s, 3H), 2.45–2.35 (m, 2H), 2.29 (ddd, J = 2.4, 9.2, 12.8 Hz, 1H), 2.15 (ddd, J = 6.0, 9.2, 13.2 Hz, 1H), 1.97 (ddd, J = 4.4, 8.8, 13.2 Hz, 1H), 1.79 (ddt, J = 5.0, 5.2, 13.2 Hz, 1H), 1.50–1.42 (m, 1H); ^{13}C NMR (CD_2Cl_2 , 100 MHz) δ 170.6, 170.2, 169.5, 152.8, 129.6, 128.3, 122.9, 118.6, 107.7, 104.2, 87.8, 82.7, 64.9, 52.3, 51.8, 47.8, 46.8, 38.5, 36.4, 35.4, 31.1, 21.2; IR (film) ν_{max} 2943, 2892, 1764, 1733, 1666, 1487, 1431, 1385, 1194, 1113 cm^{-1} ; MALDIFTMS (DHB) m/z 413.1710 ($\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_6 + \text{H}^+$ requires 413.1707).

Methyl 5-((5-cyanopent-4-enoyl)-[2-(1-methyl-1H-indol-3-yl)ethyl]amino)-1,3,4-oxadiazole-2-carboxylate (9a and 10a). DMAP (47 mg, 0.40 mmol) was added to a solution of a 1:1 mixture of *cis*- and *trans*-5-cyanopent-4-enoic acid (50 mg, 0.40 mmol), oxadiazole **S3** (40 mg, 0.13 mmol), and EDCI (77 mg, 0.40 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The reaction mixture was stirred for 14 h and gradually warmed to 25 °C. Saturated aqueous NH_4Cl (10 mL) was added and the organic layer was removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Chromatography (SiO_2 , 2.5×20 cm, 30–50% EtOAc/hexanes gradient elution) afforded a mixture of **9a** and **10a** (51 mg, 94%) as a white solid. The isomers could be separated by PTLC with multiple elutions (SiO_2 , 50% EtOAc/hexanes).

9a. (*E*)-Isomer: ^1H NMR (CD_2Cl_2 , 600 MHz) δ 7.62 (d, $J = 7.9$ Hz, 1H), 7.28 (d, $J = 7.9$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 6.89 (s, 1H), 6.68 (dt, $J = 7.0, 16.2$ Hz, 1H), 5.38 (d, $J = 16.2$ Hz, 1H), 4.22 (t, $J = 8.0$ Hz, 2H), 4.0 (s, 3H), 3.71 (s, 3H), 3.10 (t, $J = 7.5$ Hz, 2H), 2.96 (t, $J = 7.0$ Hz, 2H), 2.57 (q, $J = 7.0$ Hz, 2H); ^{13}C NMR (CD_2Cl_2 , 150 MHz) δ 171.3, 162.6, 155.0, 154.5, 154.2, 137.9, 128.4, 128.3, 122.4, 119.8, 119.4, 118.1, 110.6, 110.2, 101.8, 54.5, 48.5, 35.2, 33.3, 28.9, 24.9; IR (film) ν_{max} 2933, 2851, 2226, 1749, 1702, 1564, 1441, 1410, 1136 cm^{-1} ; MALDIFTMS (DHB) m/z 430.1478 ($\text{C}_{21}\text{H}_{21}\text{N}_5\text{O}_4 + \text{Na}^+$ requires 430.1486).

10a. (*Z*)-Isomer: ^1H NMR (CDCl_3 , 600 MHz) δ 7.64 (d, $J = 7.9$ Hz, 1H), 7.24 (d, $J = 7.9$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 6.85 (s, 1H), 6.46 (dt, $J = 7.5, 11.0$ Hz, 1H), 5.35 (d, $J = 11.0$ Hz, 1H), 4.25 (t, $J = 7.5$ Hz, 2H), 4.00 (s, 3H), 3.71 (s, 3H), 3.11 (t, $J = 7.5$ Hz, 2H), 3.01 (t, $J = 7.0$ Hz, 2H), 2.78 (q, $J = 7.0$ Hz, 2H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 170.5, 161.7, 153.9, 153.2, 152.6, 136.9, 127.6, 127.3, 121.7, 119.1, 118.7, 115.6, 109.6, 109.3, 100.9, 53.7, 47.7, 34.9, 32.6, 26.8, 24.2; IR (film) ν_{max} 3046, 2933, 2205, 1744, 1703, 1564, 1441, 1419, 1149 cm^{-1} ; MALDIFTMS (DHB) m/z 430.1476 ($\text{C}_{21}\text{H}_{21}\text{N}_5\text{O}_4 + \text{Na}^+$ requires 430.1486).

Solid curved lines represent nOe's observed
in 2D ^1H - ^1H ROESY (CD_2Cl_2 , 400 MHz)

Compound 9b. A solution of **9a** (13 mg, 0.032 mmol) in 1,3,5-triisopropylbenzene (4.0 mL) was warmed at 230 °C for 22 h. After cooling to 25 °C, the solution was poured onto a plug of SiO₂ (2 × 8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and the eluent was concentrated. PTLC (SiO₂, 60% EtOAc/hexanes) afforded **9b** (9.6 mg, 79%) as a white solid: ¹H NMR (CD₂Cl₂, 600 MHz) δ 7.22 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 7.0 Hz, 1H), 6.71 (t, *J* = 7.0 Hz, 1H), 6.52 (d, *J* = 7.9 Hz, 1H), 4.38 (s, 1H), 4.11 (dt, *J* = 9.2, 12.3 Hz, 1H), 3.92 (s, 3H), 3.79 (ddd, *J* = 2.6, 7.0, 9.6 Hz, 1H), 2.93 (s, 3H), 2.85 (d, *J* = 4.4 Hz, 1H), 2.50–2.38 (m, 3H), 2.18 (ddd, *J* = 5.7, 4.3, 12.2 Hz, 1H), 2.03–1.97 (m, 1H), 1.91 (dt, *J* = 4.8, 12.3 Hz, 1H), 1.80 (ddd, *J* = 4.8, 7.9, 12.3 Hz, 1H); ¹³C NMR (CDCl₃, 150 MHz) δ 169.4, 168.8, 152.3, 130.3, 127.3, 122.7, 118.5, 117.1, 107.5, 106.7, 87.3, 81.3, 65.0, 53.6, 46.9, 39.9, 37.8, 35.7, 34.6, 31.4, 26.5; IR (film) *v*_{max} 2954, 2902, 2236, 1738, 1667, 1605, 1487, 1436, 1385, 1113 cm⁻¹; MALDIFTMS (DHB) *m/z* 380.1598 (C₂₁H₂₁N₃O₄ + H⁺ requires 380.1605).

Solid curved lines represent nOe's observed in 2D ¹H–¹H ROESY (CD₂Cl₂, 400 MHz)

Compound 10b. A solution of **10a** (11.4 mg, 0.028 mmol) in 1,3,5-triisopropylbenzene (3.5 mL) was warmed at 230 °C for 22 h. After cooling to 25 °C, the solution was poured onto a plug of SiO₂ (2 × 8 cm) and the solvent was eluted with hexanes (25 mL). The product was eluted with EtOAc (25 mL) and concentrated. PTLC (SiO₂, 60% EtOAc/hexanes) afforded **10b** (7.9 mg, 74%) as a white solid: ¹H NMR (CD₂Cl₂, 600 MHz) δ 7.22 (t, *J* = 7.0 Hz, 1H), 6.79 (d, *J* = 6.4 Hz, 1H), 6.73 (t, *J* = 7.0 Hz, 1H), 6.59 (d, *J* = 7.9 Hz, 1H), 4.10 (s, 1H), 4.07 (dt, *J* = 9.2, 11.8 Hz, 1H), 3.93 (s, 3H), 3.83 (d, *J* = 7.8 Hz, 1H), 3.83 (t, *J* = 11.8 Hz, 1H), 2.98 (s, 3H), 2.59–2.52 (m, 1H), 2.42 (dt, *J* = 9.7, 13.2 Hz, 1H), 2.34 (ddd, *J* = 2.2, 4.4, 8.8 Hz, 1H), 2.23 (ddd, *J* = 5.7, 7.5, 13.2 Hz, 1H), 2.04 (ddt, *J* = 4.8, 9.2, 13.6 Hz, 1H), 1.89–1.83 (m, 2H); ¹³C NMR (CD₂Cl₂, 150 MHz) δ 169.4, 168.4, 152.9, 130.1, 127.8, 123.1, 119.5, 116.8, 108.6, 105.1, 89.4, 82.1, 64.9, 53.3, 47.0, 37.2, 36.2, 36.1, 35.7, 31.3, 23.6; IR (film) *v*_{max} 2954, 2902, 2236, 1759, 1733, 1667, 1487, 1390, 1118 cm⁻¹; MALDIFTMS (DHB) *m/z* 380.1599 (C₂₁H₂₁N₃O₄ + H⁺ requires 380.1605).

Methyl 5-[(*E*)-5-(toluene-4-sulfonyl)pent-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (11a**).** A stirring solution of oxadiazole **S3** (31 mg, 0.10 mmol), (*E*)-5-tosyl-4-pentenoic acid^{S10} (39 mg, 0.15 mmol), and EDCI (78 mg, 0.41 mmol) in CH₂Cl₂ (1.4 mL) under Ar at 25 °C was treated with DMAP (25 mg, 0.20 mmol). The mixture was stirred at 25 °C for 16 h before the reaction mixture was concentrated. Chromatography (SiO₂, 2 × 8 cm, 5% EtOAc/CH₂Cl₂) provided **11a** (40.7 mg, 74%) as a white solid: mp 184–185 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.99–6.92 (m, 1H), 6.85 (s, 1H), 6.37 (d, *J* = 15.0 Hz, 1H), 4.21 (t, *J* = 7.3 Hz, 2H), 4.01 (s, 3H), 3.72 (s, 3H), 3.07 (t, *J* = 7.6 Hz, 2H), 3.00 (t, *J* = 7.0 Hz, 2H), 2.62 (m, 2H), 2.39 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 170.7, 161.9, 154.1, 153.4, 144.6, 144.0, 137.6, 137.1, 132.1, 130.1 (2C), 127.9 (2C), 127.8, 127.5, 121.9, 119.3, 119.0, 109.8, 109.5, 53.9, 47.9, 34.5, 32.8, 26.6, 24.4, 21.8; IR (film) $\nu_{\max}$ 1744, 1703, 1559, 1441, 1410, 1313, 1287, 1144 cm⁻¹; MALDIFTMS (DHB) *m/z* 559.1627 (C₂₇H₂₈N₄O₆S + Na⁺ requires 559.1622).

Methyl 5-[(4-ethylpent-4-enoyl)-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (12a**).** Oxadiazole **S3** (515 mg, 1.72 mmol) was added in one portion to a solution of 4-ethylpent-4-enoic acid^{S6} (654 mg, 5.15 mmol) in anhydrous CH₂Cl₂ (40 mL) at 25 °C under Ar. The mixture was cooled to 0 °C and EDCI (988 mg, 5.15 mmol) was added. The resulting mixture was stirred for 5 min, before the addition of DMAP (628 mg, 5.15 mmol). The reaction mixture was stirred overnight at 23 °C, before the solvent was removed in vacuo. Flash chromatography (SiO₂, 3 × 19.5 cm, 50% EtOAc/hexane) afforded **12a** (536 mg, 76%) as a yellow oil: ¹H NMR (CDCl₃, 500 MHz) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.24–7.06 (m, 3H), 6.84 (s, 1H), 4.74 (s, 1H), 4.68 (s, 1H), 4.25–4.18 (m, 2H), 3.98 (s, 3H), 3.70 (s, 3H), 3.09 (t, *J* = 8.0 Hz, 2H), 2.94 (t, *J* = 7.3 Hz, 2H), 2.39 (t, *J* = 7.7 Hz, 2H), 2.01 (dd, *J* = 7.3, 14.6 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 172.0, 162.0, 154.0, 153.2, 149.4, 136.9, 127.5, 127.4, 121.6, 119.0, 118.9, 109.8, 109.2, 108.3, 53.6, 47.8, 34.7, 32.6, 30.9, 28.9, 24.3, 12.3; IR (film) $\nu_{\max}$ 2963, 1749, 1705, 1567, 1441, 1409, 1328, 1152, 742 cm⁻¹; MALDIFTMS (DHB) *m/z* 433.1860 (C₂₂H₂₆N₄O₄ + Na⁺ requires 433.1846).

Compound 12b. A solution of **12a** (500 mg, 1.22 mmol) in 1,2-dichlorobenzene (40 mL) was added to refluxing 1,2-dichlorobenzene (80 mL, 0.010 M final concentration, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) via syringe pump over 6.5 h and the resulting mixture was warmed at a gentle reflux in the absence of light for a total of 24 h, at which time the solvent was removed in vacuo. Flash chromatography (SiO₂, 2.5 × 15 cm, 20% Et₂O/CH₂Cl₂) afforded **12b** (346 mg, 74%) as a white foam: *R_f* = 0.28 (20% Et₂O/CH₂Cl₂); ¹H NMR (CDCl₃, 500 MHz) δ 7.14 (t, *J* = 7.9 Hz, 1H), 6.83 (d, *J* = 7.4 Hz, 1H), 6.61 (t, *J* = 7.5 Hz, 1H), 6.46 (d, *J* = 8.3 Hz, 1H), 4.07 (s, 1H), 3.98–3.89 (m, 2H), 3.84 (s, 3H), 2.92 (s, 3H), 2.43 (m, 1H), 2.35 (dd, *J* = 4.8, 18.0 Hz, 1H), 2.27–2.13 (m, 4H), 1.72–1.68 (m, 2H), 0.91–0.84 (m, 1H), 0.58 (t, *J* = 7.4 Hz, 3H), 0.41–0.36 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.5, 170.3, 153.1, 129.3, 128.5, 123.4, 118.0, 107.4, 106.3, 85.8, 82.4, 64.9, 52.6, 46.8, 43.6, 39.1, 37.5, 35.1, 29.1, 27.8, 22.4, 9.6; IR (film) *v*_{max} 2954, 1737, 1667, 1606, 1493, 1440, 1397, 1270, 1120, 734 cm⁻¹; MALDIFTMS (DHB) *m/z* 383.1965 (C₂₂H₂₆N₂O₄ + H⁺ requires 383.1965).

Methyl 5-[[*(E)*-6-(*tert*-butyldimethylsilyloxy)-4-ethylhex-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate ((E)**-13a).** DMAP (87 mg, 0.75 mmol) was added to a solution of *trans*-6-(*tert*-butyldimethylsilyloxy)-4-ethylhex-4-enoic acid (193 mg, 0.75 mmol), oxadiazole **S3** (112 mg, 0.38 mmol), and EDCI (144 mg, 0.75 mmol) in CH₂Cl₂ (50 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 13 h. Saturated aqueous NH₄Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated. Chromatography (SiO₂, 2.5 × 20 cm, 20% EtOAc/hexanes) afforded **13a** (141 mg, 70%) as a white solid: ¹H NMR (CD₂Cl₂, 400 MHz) δ 7.69 (d, *J* = 7.9 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.85 (s, 1H), 5.36 (t, *J* = 6.2 Hz, 1H), 4.23 (d, *J* = 6.2 Hz, 2H), 4.22 (t, *J* = 7.0 Hz, 2H), 4.00 (s, 3H), 3.71 (s, 3H), 3.12 (t, *J* = 7.6 Hz, 2H), 2.87 (t, *J* = 7.6 Hz, 2H), 2.44 (t, *J* = 7.6 Hz, 2H), 2.02 (q, *J* = 7.4 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.8, 161.9, 153.9, 153.1, 140.5, 136.8, 127.4, 127.2, 124.9, 121.6, 119.0, 118.7, 109.7, 109.1, 59.8, 53.5, 47.6, 35.1, 32.5, 28.9, 25.9 (3C), 25.9, 24.2, 18.3, 12.3, -5.14 (2C); IR (film) *v*_{max} 2944, 2851, 1749, 1703, 1564, 1441, 1410, 1154, 1082 cm⁻¹; MALDIFTMS (DHB) *m/z* 577.2809 (C₂₉H₄₂N₄O₅Si + Na⁺ requires 577.2817).

Methyl 5-[[*(Z)*-6-(*tert*-butyldimethylsilyloxy)-4-ethylhex-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate ((*Z*)-13a**).** DMAP (76 mg, 0.65 mmol) was added to a solution of *cis*-6-(*tert*-butyldimethylsilyloxy)-4-ethylhex-4-enoic acid (167 mg, 0.65 mmol), oxadiazole **S3** (97 mg, 0.33 mmol), and EDCI (125 mg, 0.65 mmol) in CH₂Cl₂ (40 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 13 h. Saturated aqueous NH₄Cl was added and the organic layer removed. The aqueous layer was washed with EtOAc and the combined organic layers were dried (Na₂SO₄), filtered, and concentrated. Chromatography (SiO₂, 2.5 × 20 cm, 20% EtOAc/hexanes) afforded **13a** (136 mg, 78%) as a white solid: ¹H NMR (CDCl₃, 400 MHz) δ 7.69 (d, *J* = 7.9 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 5.28 (t, *J* = 6.2 Hz, 1H), 4.25 (m, 4H), 4.00 (s, 3H), 3.71 (s, 3H), 3.11 (t, *J* = 7.6 Hz, 2H), 2.93 (t, *J* = 7.9 Hz, 2H), 2.41 (t, *J* = 7.6 Hz, 2H), 2.05 (q, *J* = 7.6 Hz, 2H), 0.99 (t, *J* = 7.6 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.9, 161.9, 153.9, 153.1, 140.9, 136.8, 127.4, 127.3, 124.8, 121.5, 118.9, 118.8, 109.7, 109.1, 59.7, 53.5, 47.7, 34.8, 32.5, 31.0, 25.9 (3C), 24.2, 23.6, 18.3, 13.2, -5.2 (2C); IR (film) $\nu_{\max}$ 2944, 2862, 1749, 1703, 1564, 1441, 1410, 1154, 1062 cm⁻¹; MALDIFTMS (DHB) *m/z* 577.2807 (C₂₉H₄₂N₄O₅Si + Na⁺ requires 577.2817).

Methyl 5-[(4-ethyl-5-methoxypent-4-enoyl)-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (14a**).** Oxadiazole **S3** (291 mg, 0.969 mmol) was added in one portion to a solution of 4-ethyl-5-methoxypent-4-enoic acid (459 mg, 2.91 mmol) in anhydrous CH₂Cl₂ (10 mL) at 25 °C under Ar. The mixture was cooled to 0 °C and EDCI (557 mg, 2.91 mmol) was added. The resulting mixture was stirred for 5 min, before the addition of DMAP (352 mg, 2.91 mmol). The reaction mixture was stirred at ambient temperature overnight, before the solvent was removed in vacuo. Flash chromatography (SiO₂, 3 × 15 cm, 30% EtOAc/hexane) afforded **14a** (300 mg, 70%) as a yellow solid in a mixture of (*E*)- and (*Z*)-stereoisomers: ¹H NMR (CDCl₃, 500 MHz; mixture, (*Z*)-**14a**) δ 7.72 (d, *J* = 8.1 Hz, 1H), 7.28–7.20 (m, 2H), 7.15–7.11 (m, 1H), 6.88 (s, 1H), 5.77 (s, 1H), 4.26–4.22 (m, 2H), 4.02 (s, 3H), 3.73 (s, 3H), 3.51 (s, 3H), 3.13 (t, *J* = 7.5 Hz, 2H), 2.93 (t, *J* = 7.7 Hz, 2H), 2.43 (t, *J* = 7.8 Hz, 2H), 1.92 (q, *J* = 7.3 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H); ¹H NMR (CDCl₃, 500 MHz; mixture, (*E*)-**14a**, partial data) δ 6.88 (s, 1H), 5.81 (s, 1H), 3.55 (s, 1H), 3.08 (t, *J* = 7.3 Hz, 2H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.06 (q, *J* = 7.7 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz; mixture, (*Z*)-**14a**) δ 172.3, 162.1, 154.0, 153.3, 142.5, 136.9, 127.5, 127.4, 121.6, 119.0, 118.9, 117.5, 109.9, 109.1, 59.2, 53.5, 47.8, 34.6, 32.5, 24.8, 24.2, 22.8, 13.1; IR (film) $\nu_{\max}$ 2958, 2927, 1747, 1700, 1562, 1436, 1409, 1326, 1200, 1153, 1129, 1070 cm⁻¹; FABHRMS (NBA/NaI) *m/z* 441.2126 (C₂₃H₂₈N₄O₅ + H⁺ requires 441.2138).

Solid curved lines represent nOe's observed
in 1D ^1H - ^1H GOESY (CDCl_3 , 600 MHz)

Compound 14b. A solution of enriched (*E*)-**14a** (20 mg, 0.045 mmol) in 1,2-dichlorobenzene (9 mL, 0.005 M, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) was warmed to a gentle reflux in the absence of light for 9 h (not optimized). The reaction mixture was cooled to 25 °C, and the solvent was removed in vacuo. Flash chromatography (SiO_2 , 3×15 cm, 20% $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$) afforded **14b** (14 mg, 70%) as a single diastereomer as a pale yellow oil which solidified upon standing: ^1H NMR (C_6D_6 , 600 MHz) δ 7.10 (t, J = 6.5 Hz, 1H), 6.60 (d, J = 6.5 Hz, 1H), 6.53 (t, J = 7.2 Hz, 1H), 6.18 (d, J = 7.9 Hz, 1H), 4.28 (s, 1H), 3.95–3.82 (m, 2H), 3.49 (s, 1H), 3.37 (s, 3H), 3.10 (s, 3H), 2.79 (s, 3H), 2.23 (ddd, J = 1.3, 5.3, 12.7 Hz, 1H), 2.15–1.99 (m, 3H), 1.78 (ddd, J = 1.3, 7.9, 12.3 Hz, 1H), 1.45 (ddd, J = 1.8, 5.7, 12.7 Hz, 1H), 0.92–0.86 (m, 1H), 0.69–0.62 (m, 1H), 0.37 (t, J = 7.4 Hz, 3H); IR (film) ν_{max} 1738, 1623, 1153, 897 cm^{-1} ; FABHRMS (NBA/NaI) m/z 413.2087 ($\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_5 + \text{H}^+$ requires 413.2076).

C4 Diastereomer of 14b. A solution of enriched (*Z*)-**14a** (46.7 mg, 0.106 mmol) in 1,2-dichlorobenzene (20 mL, 0.0052 M, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) was warmed to a gentle reflux in the absence of light for 20.5 h (not optimized). The reaction mixture was cooled to 25 °C, and loaded directly onto SiO_2 (2×16 cm) equilibrated in hexanes. The 1,2-dichlorobenzene solvent was eluted with hexanes, and then the column was eluted with 30–60% EtOAc /hexane gradient elution to afford the C4 diastereomer of **14b** (18.5 mg, 42%) as a white amorphous solid: R_f 0.23 (60% EtOAc /hexane); ^1H NMR (C_6D_6 , 600 MHz) δ 7.06–7.02 (m, 1H), 6.59–6.55 (m, 2H), 6.23 (d, J = 8.3 Hz, 1H), 3.98 (s, 1H), 3.89 (dd, J = 4.4, 10.1 Hz, 2H), 3.71 (s, 1H), 3.45 (s, 3H), 3.10 (s, 3H), 2.82 (s, 3H), 2.51 (ddd, J = 5.7, 14.0, 19.7 Hz, 1H), 2.29 (dd, J = 5.7, 18.4 Hz, 1H), 2.10–2.02 (m, 2H), 1.67–1.63 (m, 1H), 1.41 (dd, J = 5.7, 14.5 Hz, 1H), 0.87–0.79 (m, 1H), 0.49–0.43 (m, 1H), 0.37 (t, J = 7.5 Hz, 3H); ^{13}C NMR (C_6D_6 , 600 MHz) δ 170.2, 169.1, 153.5, 129.4, 129.3, 123.9, 118.7, 107.9, 104.9, 91.2, 89.0, 81.7, 64.8, 59.9, 51.5, 50.0, 47.2, 37.8, 35.6, 28.6, 22.5, 21.1, 9.8.

Methyl 5-([4-(2-methoxyethoxymethylene)hexanoyl]-[2-(1-methyl-1H-indol-3-yl)ethyl]amino)-1,3,4-oxadiazole-2-carboxylate (15a). Oxadiazole **S3** (189 mg, 0.630 mmol) was added in one portion to a solution of 4-(2-methoxyethoxymethylene)hexanoic acid (382 mg, 1.89 mmol) in anhydrous CH₂Cl₂ (10 mL) at 25 °C under Ar. The mixture was cooled to 0 °C and EDCI (362 mg, 1.89 mmol) was added. The resulting mixture was stirred for 5 min, before the addition of DMAP (230 mg, 1.89 mmol). The reaction mixture was stirred at ambient temperature overnight, before the solvent was removed in vacuo. Flash chromatography (SiO₂, 4 × 15 cm, 30% EtOAc/hexane) afforded **15a** (229 mg, 75%) as a white foam as a *E:Z* mixture of isomers: ¹H NMR (CDCl₃, 500 MHz, 1:1 mixture) δ 7.71 (app t, *J* = 8.4 Hz, 2H), 7.29–7.20 (m, 4H), 7.13 (app t, *J* = 7.3 Hz, 2H), 6.89 (d, *J* = 5.1 Hz, 2H), 5.90 (s, 1H), 5.87 (s, 1H), 4.26–4.22 (m, 4H), 4.02 (s, 6H), 3.84 (t, *J* = 4.9 Hz, 2H), 3.79 (t, *J* = 4.8 Hz, 2H), 3.73 (s, 6H), 3.57 (t, *J* = 4.8 Hz, 2H), 3.53 (t, *J* = 4.8 Hz, 2H), 3.40 (s, 3H), 3.35 (s, 3H), 3.14 (app t, *J* = 7.5 Hz, 4H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.88 (t, *J* = 7.7 Hz, 2H), 2.45 (t, *J* = 7.7 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.10 (q, *J* = 7.3 Hz, 2H), 1.93 (q, *J* = 7.3 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.99 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 600 MHz) δ 172.3, 172.0, 162.0, 161.9, 154.0, 153.9, 153.2 (2C), 141.2 (2C), 136.8, 127.4 (2C), 127.3 (2C), 121.5 (2C), 118.9 (2C), 118.8, 118.7, 118.4, 118.1, 109.9, 109.7, 109.1 (2C), 71.5 (2C), 71.0 (2C), 59.0, 58.9, 53.5, 53.4, 47.7 (2C), 35.4, 34.5, 32.4, 26.5, 24.7, 24.2, 22.8, 19.8, 13.0, 12.5; IR (film) ν_{max} 2958, 2927, 2872, 1749, 1704, 1566, 1442, 1409, 1378, 1300, 1251, 1200, 1151, 1124, 1073 cm⁻¹.

Compound 15b. A solution of 3:1 (*E*):(*Z*) **15a** (33 mg, 0.069 mmol) in 1,2-dichlorobenzene (9 mL, 0.001 M, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) was warmed to a gentle reflux in the absence of light for 24 h. The reaction mixture was cooled to 25 °C, and the solvent was removed in vacuo. Flash chromatography (SiO₂, 1 × 6 cm, 50% EtOAc/hexane) afforded **15b** (20.5 mg, 64%) from which the major diastereomer (3:1) above could be isolated pure as white solid: *R_f* 0.40 (50% EtOAc/hexane); ¹H NMR (C₆D₆, 600 MHz) major isomer δ 6.89 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.66 (t, *J* = 7.4 Hz, 1H), 6.25 (d, *J* = 7.3 Hz, 1H), 4.09 (m, 1H), 4.02 (s, 1H), 3.64 (t, *J* = 10.9 Hz, 1H), 3.48 (ddt, *J* = 2.7, 4.6, 3.7 Hz, 1H), 3.39 (s, 3H), 3.34 (ddt, *J* = 2.7, 4.6, 3.7 Hz, 1H), 3.09–3.06 (m, 1H), 2.95–2.89 (m, 1H), 2.95 (s, 3H), 2.82 (s, 3H), 2.29 (ddd, *J* = 11.0, 2.8, 1.8 Hz, 1H), 2.10 (ddt, *J* = 4.6, 9.2, 4.6 Hz, 1H), 1.73 (dt, *J* = 4.6, 9.2 Hz, 1H), 1.37–1.34 (m, 2H), 1.21 (dd, *J* = 6.4, 3.7 Hz, 1H), 0.85–0.76 (m, 2H), 0.58 (dq, *J* = 7.3, 7.4 Hz, 1H), 0.30 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) major isomer δ 171.5, 167.8, 142.0, 131.5, 130.3, 127.8, 124.1, 123.4, 108.9, 106.3, 103.7, 86.1, 72.2, 71.5, 60.3, 58.2, 52.7, 51.3, 42.3, 33.7, 28.3, 26.5, 25.0, 20.6, 8.9.

S4
>95% pure *E*

S5
>95% pure *Z*

(*E*)- and (*Z*)-5-Benzyloxy-4-ethylpent-4-enoic acid (S4 and S5): direct Wittig reaction. A solution of (benzyloxymethyl)triphenylphosphonium bromide (5.00 g, 11.9 mmol) in anhydrous THF (52 mL) was cooled to –78 °C and treated dropwise with *t*-BuLi (5.9 mL, 10.0 mmol, 1.7 M solution in pentane). The reaction mixture was stirred for 5 min at –78 °C before warming to –40 °C where the solution was stirred for 30–40 min (mixture turns a deep red color), and then recooled to –78 °C. A solution of 4-ketohexanoic acid^{S7} (260 mg, 2.0 mmol) in THF (3 mL) was added slowly via a cannula and the resulting mixture was stirred overnight while slowly warming to 25 °C. The reaction mixture was quenched by careful addition of 1 N aqueous NaH₂PO₄ (52 mL), extracted with Et₂O (3 × 75 mL), and the combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude material (ca. 85:15 ratio of isomers by GC) thus obtained was purified by flash chromatography (SiO₂, 5 × 16 cm, 10–100% EtOAc/hexane gradient elution) to afford a yellow oil (262 mg, 56%) which was found to be almost exclusively one enol isomer. Analysis of a similarly prepared sample was found to afford >94% pure (*E*)-enol ether by GC and ¹H NMR (NOE) after chromatography. Continued purification can furnish >95% pure (*E*)- as well as >95% (*Z*)-enol ether as separate fractions, as determined by the respective GC traces of the individual fractions.

Major isomer (*E*-enol ether S6): ^1H NMR (CDCl_3 , 600 MHz) δ 7.35–7.30 (m, 5H), 5.90 (s, 1H), 4.73 (s, 2H), 3.61 (s, 3H), 2.36 (t, $J = 7.9$ Hz, 2H), 2.21 (t, $J = 7.9$ Hz, 2H), 2.12 (q, $J = 7.4$ Hz, 2H), 0.97 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 173.7, 140.7, 137.8, 128.3 (2C), 127.7, 127.2 (2C), 118.9, 73.4, 51.4, 33.3, 26.7, 20.0, 12.5; MALDIFTMS (DHB) m/z 271.1308 ($\text{C}_{15}\text{H}_{20}\text{O}_3 + \text{Na}^+$ requires 271.1305).

Minor isomer (*Z*-enol ether S7): ^1H NMR (CDCl_3 , 500 MHz) δ 7.38–7.27 (m, 5H), 4.74 (s, 2H), 5.92 (s, 1H), 3.64 (s, 3H), 2.47–2.36 (m, 4H), 1.90 (q, $J = 7.4$ Hz, 2H), 0.96 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 174.1, 140.7, 137.8, 128.4 (2C), 127.7, 127.3 (2C), 118.8, 73.4, 51.4, 32.6, 24.8, 23.0, 13.1.

Methyl 5-[[*E*]-4-benzyloxy-4-ethylpent-4-enoyl]-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino-1,3,4-oxadiazole-2-carboxylate (16a). Oxadiazole **S3** (290 mg, 0.966 mmol) was added in one portion to a solution of (*E*)-5-benzyloxy-4-ethylpent-4-enoic acid (**S4**, 565 mg, 2.41 mmol) in anhydrous CH_2Cl_2 (10 mL) at 25 °C under Ar. The mixture was cooled to 0 °C and EDCI (463 mg, 2.41 mmol) was added. The resulting mixture was stirred for 5 min, before the addition of DMAP (295 mg, 2.41 mmol). The reaction mixture was stirred at ambient temperature for 5 h, before the solvent was removed in vacuo. Flash chromatography (SiO_2 , 4×14 cm, 30% EtOAc/hexane) afforded **16a** (376 mg, 75%) as an oil, which solidified on standing to a white solid: ^1H NMR (CDCl_3 , 400 MHz) δ 7.70 (d, $J = 7.6$ Hz, 1H), 7.35–7.25 (m, 6H), 7.23 (t, $J = 6.8$ Hz, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 6.86 (s, 1H), 5.95 (s, 1H), 4.75 (s, 2H), 4.23 (t, $J = 6.7$ Hz, 2H), 4.01 (s, 3H), 3.72 (s, 3H), 3.12 (t, $J = 7.4$ Hz, 2H), 2.88 (t, $J = 7.3$ Hz, 2H), 2.32 (t, $J = 6.7$ Hz, 2H), 2.13 (q, $J = 7.6$ Hz, 2H), 0.98 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 172.0, 162.0, 154.0, 153.2, 141.0, 137.9, 136.9, 128.3 (2C), 128.2, 127.6, 127.5, 127.3 (2C), 121.6, 119.0, 118.8, 118.6, 109.8, 109.1, 73.4, 53.6, 47.7, 35.5, 32.5, 26.6, 24.3, 20.0, 12.6; IR (film) ν_{max} 2961, 1748, 1703, 1564, 1441, 1407, 1151, 813, 742, 699 cm^{-1} ; MALDIFTMS (DHB) m/z 517.2430 ($\text{C}_{29}\text{H}_{32}\text{N}_4\text{O}_5 + \text{H}^+$ requires 517.2430).

Compound 16b. A solution of **16a** (40 mg, 0.077 mmol) in 1,2-dichlorobenzene (15 mL, 0.0052 M, passed through a column of basic alumina, degassed with Ar for 1 h while protected from the light) was warmed to a gentle reflux in the absence of light for 24 h. The reaction mixture was cooled to 25 °C, and the solvent was removed in vacuo. Flash chromatography (SiO₂, 1.5 × 22 cm, 60% EtOAc/hexane) afforded **16b** (29.7 mg, 79%) as a white solid: R_f = 0.22 (60% EtOAc/hexane); ¹H NMR (CDCl₃, 500 MHz) δ 7.31–7.25 (m, 3H), 7.27–7.11 (m, 3H), 6.82 (d, J = 7.3 Hz, 1H), 6.55 (t, J = 7.3 Hz, 1H), 6.19 (d, J = 8.1 Hz, 1H), 4.79 (d, J = 11.4 Hz, 1H), 4.46 (d, J = 11.4 Hz, 1H), 4.45 (s, 1H), 4.02–3.90 (m, 2H), 3.88 (s, 3H), 3.86 (s, 1H), 2.78 (s, 3H), 2.43–2.26 (m, 4H), 2.15 (td, J = 13.9, 5.5 Hz, 1H), 1.89 (dd, J = 5.5, 13.6 Hz, 1H), 0.97–0.91 (m, 1H), 0.79–0.73 (m, 1H), 0.57 (t, J = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.6, 170.2, 152.6, 137.8, 129.3, 128.1 (2C), 127.6, 127.3 (2C), 126.7, 123.4, 115.9, 107.6, 105.7, 87.4, 85.8, 81.8, 74.1, 64.5, 52.9, 46.7, 46.0, 38.1, 33.1, 29.2, 28.9, 18.5, 9.5; IR (film) ν_{max} 3029, 2954, 1732, 1667, 1607, 1504, 1455, 1393, 1120, 1025, 911, 735 cm⁻¹; MALDIFTMS (DHB) m/z 489.2401 (C₂₉H₃₂N₂O₅ + H⁺ requires 489.2389).

Methyl 5-{[(Z)-5-benzyloxy-4-ethylpent-4-enoyl]-[2-(1-methyl-1H-indol-3-yl)ethyl]amino}-1,3,4-oxadiazole-2-carboxylate (17a). DMAP (83 mg, 0.68 mmol) was added to a solution of (Z)-5-benzyloxy-4-ethylpent-4-enoic acid (**S5**, 170 mg, 0.68 mmol), **S3** (81 mg, 0.27 mmol), and EDCI (130 mg, 0.68 mmol) in CH₂Cl₂ (25 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C and stirred for 3 days. The organic layer was concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 2.5 × 20 cm, 30% EtOAc/hexanes gradient elution) providing **17a** (100 mg, 69%) as a clear oil: ¹H NMR (CDCl₃, 500 MHz) δ 7.69 (d, J = 6.6 Hz, 1H), 7.32–7.23 (m, 6H), 7.21 (t, J = 6.3 Hz, 1H), 7.12 (t, J = 6.6 Hz, 1H), 6.84 (s, 1H), 5.91 (s, 1H), 4.70 (s, 2H), 4.20 (t, J = 6.2 Hz, 2H), 3.98 (s, 3H), 3.70 (s, 3H), 3.10 (t, J = 6.2 Hz, 2H), 2.93 (t, J = 6.3 Hz, 2H), 2.47 (t, J = 6.3 Hz, 2H), 1.92 (q, J = 6.3 Hz, 2H), 0.97 (t, J = 6.2 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 172.4, 162.1, 154.4, 153.2, 140.9, 137.7, 136.9, 128.4 (2C), 128.3, 127.7, 127.5, 127.4, 127.3 (2C), 121.6, 118.9, 118.5, 110.0, 109.2, 73.4, 53.5, 47.7, 34.6, 32.5, 24.9, 24.3, 23.0, 13.1; IR (film) ν_{max} 2960, 1748, 1704, 1565, 1442, 1409, 1327, 1151 cm⁻¹; MALDIFTMS (DHB) m/z 539.2274 (C₂₉H₃₂N₄O₅ + Na⁺ requires 539.2265).

Solid curved lines represent nOe's observed
in 2D ^1H - ^1H ROESY (C_6D_6 , 400 MHz)

Compound 17b. A solution of **17a** (11 mg, 0.021 mmol) in 4 mL of anhydrous degassed 1,3,5-triisopropylbenzene was warmed under Ar at 230 °C for 32 h. The cooled reaction mixture was loaded directly onto SiO_2 (1.5×10 cm) equilibrated in hexanes. The 1,3,5-triisopropylbenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO_2 , 55% EtOAc/hexanes) providing **17b** (7.3 mg, 72%) as a white solid: ^1H NMR (CD_2Cl_2 , 400 MHz) δ 7.26–7.17 (m, 5H), 7.11 (t, J = 8.0 Hz, 1H), 6.82 (d, J = 6.0 Hz, 1H), 6.59 (t, J = 7.2 Hz, 1H), 6.47 (d, J = 8.0 Hz, 1H), 4.43 (s, 2H), 4.18 (s, 1H), 3.94 (s, 1H), 3.89–3.78 (m, 2H), 3.67 (s, 3H), 2.97 (s, 3H), 2.83–2.80 (m, 1H), 2.34–2.11 (m, 3H), 1.68–1.65 (m, 2H), 0.90–0.84 (m, 1H), 0.58 (t, J = 7.6 Hz, 3H), 0.41–0.39 (m, 1H); ^1H NMR (C_6D_6 , 400 MHz) δ 7.21–7.11 (m, 6H), 6.60–6.58 (m, 2H), 6.28 (d, J = 8.1 Hz, 1H), 4.50 (d, J = 11.0 Hz, 1H), 4.29 (s, 1H), 4.27 (d, J = 11.0 Hz, 1H), 3.93 (dd, J = 4.4, 10.3 Hz, 2H), 3.74 (s, 1H), 3.38 (s, 3H), 2.86 (s, 3H), 2.60 (ddd, J = 5.9, 5.5, 7.5 Hz, 1H), 2.32 (dd, J = 5.5, 12.5 Hz, 1H), 2.11–2.05 (m, 2H), 1.70 (dt, J = 12.5, 4.8 Hz, 1H), 1.47 (dd, J = 5.5, 8.5 Hz, 1H), 0.89 (m, 2H), 0.37 (t, J = 7.3 Hz, 3H); ^{13}C NMR (C_6D_6 , 100 MHz) δ 170.3, 169.1, 153.4, 138.5, 129.9, 129.2 (2C), 128.3, 127.6, 127.4 (2C), 123.8, 118.6, 107.8, 104.9, 91.2, 87.2, 81.6, 74.2, 64.8, 51.4, 50.0, 47.1, 37.7, 35.5, 28.5, 22.5, 21.3, 9.7; IR (film) ν_{max} 2958, 1758, 1666, 1650, 1454, 1120, 743 cm^{-1} ; MALDIFTMS (DHB) m/z 489.2398 ($\text{C}_{29}\text{H}_{32}\text{N}_2\text{O}_5 + \text{H}^+$ requires 489.2389).

Imidazole-1-carboxylic acid pent-4-en-1-ylamide (S8). 5-Amino-1-pentene hydrochloride^{S8} (4.80 g, 35.0 mmol) was suspended in anhydrous CH_2Cl_2 (500 mL) under Ar. Carbonyldiimidazole (8.10 g, 50.0 mmol) was added in one portion followed by Et_3N (4.60 mL, 33.0 mmol). The reaction mixture was stirred for 16 h at 23 °C before solvent was removed under reduced pressure. Flash chromatography (SiO_2 , 5×30 cm, 5% MeOH/ CHCl_3) provided **S8** (5.50 g, 89%) as a pale yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.16 (s, 1H), 7.90 (s, 1H), 7.40 (s, 1H), 7.07 (s, 1H), 5.78 (m, 1H), 5.10 (m, 2H), 3.41 (m, 2H), 2.13 (ddd, J = 7.6, 7.0, 6.8 Hz, 2H), 1.72 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.0, 137.4, 135.9, 129.5, 116.5, 115.5, 40.6, 31.0, 28.4; IR (film) ν_{max} 3448, 1727, 1528, 1510, 1477, 1315, 1275, 1057, 911 cm^{-1} ; MALDIFTMS (DHB) m/z 180.1129 ($\text{C}_9\text{H}_{13}\text{N}_3\text{O} + \text{H}^+$ requires 180.1131).

***N*-(Pent-4-en-1-yl)-2-(methyl-oxo-acetate) hydrazine carboxylate (S9).** A solution of **S8** (5.50 g, 31.0 mmol) in THF (300 mL) and AcOH (3.6 mL, 64.0 mmol) under Ar was treated with methyl oxalylhydrazide^{S1} (2.50 g, 31.0 mmol) and the reaction mixture was warmed at 40 °C for 16 h. The solvent was removed under reduced pressure and flash chromatography (SiO₂, 3 × 30 cm, 2.5% MeOH/22.5% acetone/75% CHCl₃) provided **S9** (3.10 g, 42%) as a yellow solid: mp 97–98 °C; ¹H NMR (CDCl₃, 400 MHz) δ 9.42 (s, 1H), 8.05 (bs, 1H), 5.75 (m, 2H), 4.98 (m, 2H), 3.90 (s, 3H), 3.20 (dd, *J* = 4.8, 5.6 Hz, 2H), 2.06 (q, *J* = 5.6 Hz, 2H), 1.36 (m, 2H); ¹³C NMR (CD₃OD, 100 MHz) δ 161.1, 160.5, 159.1, 139.4, 115.5, 53.9, 40.6, 32.2, 30.5; IR (film) ν_{max} 3374, 3282, 1730, 1697, 1543, 1435, 1292, 1230, 1143 cm⁻¹; MALDIFTMS (DHB) *m/z* 252.0960 C₉H₁₅N₃O₄ + Na⁺ requires 252.0955).

Methyl 5-(pent-3-en-1-yl)amino-1,3,4-oxadiazole-2-carboxylate (S10). TsCl (2.50 g, 13.0 mmol) was added to a solution of **S9** (3.00 g, 13.0 mmol) in anhydrous CH₂Cl₂ (160 mL) immediately followed by Et₃N (4.6 mL, 33.0 mmol). The reaction mixture was allowed to stir at 25 °C for 16 h before being concentrated in vacuo to 30 mL. The crude solution was diluted with EtOAc (150 mL) and the organic layer was washed with 1 N aqueous HCl (30 mL), saturated aqueous NaHCO₃ (30 mL), and saturated aqueous NaCl (30 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated. Chromatography (SiO₂, 5% MeOH/CH₂Cl₂) provided **S10** (2.50 g, 91%) as a white solid: mp 92–93 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 500 MHz) δ 6.50 (s, 1H), 5.85–5.71 (m, 1H), 5.08–4.95 (m, 2H), 3.98 (s, 3H), 3.43 (dt, *J* = 6.6, 7.0 Hz, 2H), 2.14 (dt, *J* = 8.3, 7.0 Hz, 2H), 1.79–1.72 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 165.0, 155.1, 150.9, 137.4, 115.9, 53.5, 43.2, 30.9, 28.8; IR (film) ν_{max} 1738, 1634, 1549, 1444, 1365, 1266, 1205, 1167, 1060 cm⁻¹; MALDIFTMS (DHB) *m/z* 212.103 (C₉H₁₃N₃O₃ + H⁺ requires 212.1029).

Methyl 5-{{2-(1-methyl-1*H*-indol-3-yl)acetyl}-(pent-4-en-1-yl)amino}-1,3,4-oxadiazole-2-carboxylate (18a**).** A solution of 2-(1-methyl-1*H*-indol-3-yl)acetic acid (75 mg, 0.50 mmol) in 5 mL of anhydrous CH₂Cl₂ was treated with EDCI (98 mg, 0.50 mmol) followed by DMAP (2 mg, 0.02 mmol). Oxadiazole **S10** was added (103 mg, 0.50 mmol) and the reaction mixture was allowed to stir at 23 °C for 24 h. The reaction mixture was concentrated in vacuo to 1 mL then diluted with 30 mL of EtOAc and 10 mL of 1 N aqueous HCl. The organic layer was separated and washed with 10 mL of saturated aqueous NaHCO₃ and 10 mL of saturated aqueous NaCl. The organic layer was dried over Na₂SO₄, filtered, and concentrated. PTLC (50% EtOAc/hexanes) provided **18a** (108 mg, 57%) as a yellow oil: ¹H NMR (CDCl₃, 500 MHz) δ 7.54 (d, *J* = 8.1 Hz, 1H), 7.23–7.15 (m, 2H), 7.09 (d, *J* = 7.0 Hz, 1H), 6.90 (s, 1H), 5.75–5.69 (m, 1H), 4.97–4.91 (m, 2H), 4.32 (s, 2H), 4.03 (s, 3H), 3.91 (t, *J* = 7.7, 7.3 Hz, 2H), 3.71 (s, 3H), 2.06–2.00 (m, 2H), 1.70 (dd, *J* = 7.7, 7.3 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 170.8, 162.0, 154.3, 153.7, 137.0, 136.8, 128.0, 127.4, 121.9, 119.34, 119.30, 115.4, 109.3, 60.6, 53.8, 47.2, 33.3, 32.7, 30.5, 27.0; IR (film) $\nu_{\max}$ 2932, 1749, 1703, 1567, 1442, 1159 cm⁻¹; FABHRMS (NBA/NaI) *m/z* 383.1711 (C₂₀H₂₂N₄O₄ + H⁺ requires 383.1719).

Solid curved lines represent nOe's observed in 1D ¹H–¹H GOESY (CDCl₃, 600 MHz)

Compound 18b. A solution of **18a** (11 mg, 0.03 mmol) in 1.5 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 160 °C for 6 h. The solution was concentrated under a stream of N₂ and the crude material was purified by PTLC (SiO₂, 40% EtOAc/CH₂Cl₂) providing **18b** (6.2 mg, 61%) as a yellow solid: ¹H NMR (CDCl₃, 500 MHz) δ 7.18 (dd, *J* = 7.3, 7.7 Hz, 1H), 6.86 (d, *J* = 7.3 Hz, 1H), 6.67 (dd, *J* = 7.7, 7.3 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 4.15 (s, 1H), 3.93 (dd, *J* = 12.8, 4.0 Hz, 1H), 3.87 (s, 3H), 3.03 (dd, *J* = 13.2, 9.5 Hz, 1H), 2.96 (s, 3H), 2.94 (d, *J* = 13.5 Hz, 1H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.30 (dd, *J* = 7.7, 4.7 Hz, 1H), 1.75 (d, *J* = 11.0 Hz, 1H), 1.69 (dd, *J* = 8.0, 4.3 Hz, 1H), 1.49 (m, 2H), 1.41 (dd, *J* = 11.1, 11.0 Hz, 1H), 1.28 (dd, *J* = 8.0, 4.2 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ 174.7, 169.2, 152.1, 130.9, 129.5, 128.3, 122.6, 117.8, 106.7, 103.9, 86.1, 80.4, 59.4, 52.6, 45.1, 38.3, 34.6, 33.9, 28.0, 23.0; IR (film) $\nu_{\max}$ 1707, 1584, 1420, 1343, 1164, 1092 cm⁻¹; FABHRMS (NBA/NaI) *m/z* 355.1652 (C₂₀H₂₂N₂O₄ + H⁺ requires 355.1658).

Imidazole-1-carboxylic acid but-3-en-1-ylamide (S11). 4-Amino-1-butene hydrochloride^{S8} (5.10 g, 35.0 mmol) was suspended in anhydrous CH₂Cl₂ (500 mL) under Ar. Carbonyldiimidazole (8.50 g, 53.0 mmol) was added in one portion followed by Et₃N (4.90 mL, 35.0 mmol). The reaction mixture was stirred for 16 h at 23 °C before solvent was removed under reduced pressure. Flash chromatography (SiO₂, 5 × 30 cm, 5% MeOH/CHCl₃) provided **S11** (5.30 g, 91%) as a pale yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 8.16 (s, 1H), 7.90 (s, 1H), 7.41 (s, 1H), 7.03 (s, 1H), 5.76 (m, 1H), 5.10 (m, 2H), 3.46 (dt, *J* = 7.0, 5.7 Hz, 2H), 2.37 (dt, *J* = 6.7, 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.3, 136.3, 135.1, 130.3, 118.2, 116.7, 40.4, 33.9; IR (film) $\nu_{\max}$ 3448, 1729, 1528, 1510, 1477, 1099, 909 cm⁻¹; MALDIFTMS (DHB) *m/z* 166.0975 (C₈H₁₁N₃O + H⁺ requires 166.0975).

***N*-(But-3-en-1-yl)-2-(methyl-oxo-acetate) hydrazine carboxylate (S12).** A solution of **S11** (5.30 g, 32.0 mmol) in THF (300 mL) and AcOH (3.6 mL, 64.0 mmol) under Ar was treated with methyl oxalylhydrazide^{S1} (2.70 g, 32.0 mmol) and the reaction mixture was warmed at 40 °C for 16 h. The solvent was removed under reduced pressure and flash chromatography (SiO₂, 3 × 30 cm, 2.5% MeOH/22.5% acetone/75% CHCl₃) provided **S12** (3.50 g, 46%; 46–64%) as a white solid: mp 110–112 °C; ¹H NMR (DMSO-*d*₆, 500 MHz) δ 10.45 (s, 1H), 7.99 (s, 1H), 6.50 (s, 1H), 5.81–5.75 (m, 1H), 5.03–4.99 (m, 2H), 3.79 (s, 3H), 3.05 (dt, *J* = 6.3, 7.0 Hz, 2H), 2.13 (dt, *J* = 7.0, 7.0 Hz, 2H); ¹³C NMR (DMSO-*d*₆, 125 MHz) δ 161.1, 158.1, 157.6, 137.0, 117.1, 53.7, 39.6, 35.0; IR (film) $\nu_{\max}$ 3374, 1728, 1707, 1528, 1482, 917 cm⁻¹; FABHRMS (NBA/NaI) *m/z* 216.0986 (C₈H₁₃N₃O₄ + H⁺ requires 216.0984).

Methyl 5-(but-3-en-1-yl)amino-1,3,4-oxadiazole-2-carboxylate (S13). TsCl (3.10 g, 16 mmol) was added to a solution of **S12** (3.50 g, 16.0 mmol) in anhydrous CH₂Cl₂ (160 mL) immediately followed by Et₃N (5.6 mL, 41.0 mmol). The reaction mixture was allowed to stir at 25 °C for 16 h before being concentrated in vacuo to 30 mL. The crude solution was diluted with EtOAc (150 mL) and the organic layer was washed with 1 N aqueous HCl (30 mL), saturated aqueous NaHCO₃ (30 mL), and saturated aqueous NaCl (30 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated. Chromatography (SiO₂, 5% MeOH/CH₂Cl₂) provided **S13** (2.80 g, 89%) as a white solid: mp 92–93 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 500 MHz) δ 6.26 (s, 1H), 5.83–5.70 (m, 1H), 5.17–5.07 (m, 2H), 3.97 (s, 3H), 3.51 (dd, *J* = 6.2, 5.2 Hz, 2H), 2.41 (dt, *J* = 6.7, 6.7 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 164.8, 155.0, 151.0, 134.3, 118.4, 53.5, 42.6, 33.8; IR (film) $\nu_{\max}$ 1738, 1633, 1551, 1445, 1358, 1282, 1205, 1167, 1052 cm⁻¹; MALDIFTMS (DHB) *m/z* 198.0873 (C₈H₁₁N₃O₃ + H⁺ requires 198.0872).

Methyl 5-((but-3-en-1-yl)-[3-(1H-indol-3-yl)propionyl]amino)-1,3,4-oxadiazole-2-carboxylate (19a). A solution of 3-(indol-3-yl)propionic acid (95 mg, 0.5 mmol) in 5 mL of anhydrous CH₂Cl₂ was treated with EDCI (98 mg, 0.5 mmol) followed by DMAP (2 mg, 0.02 mmol). Oxadiazole **S13** was added (33 mg, 1.7 mmol) and the reaction mixture was allowed to stir at 23 °C for 16 h. The reaction mixture was concentrated in vacuo to 1 mL and diluted with 30 mL of EtOAc and 10 mL of 1 N aqueous HCl. The organic layer was separated and washed with 10 mL of saturated aqueous NaHCO₃ and 10 mL of saturated aqueous NaCl. The organic layer was dried over Na₂SO₄, filtered, and concentrated. PTLC (SiO₂, 50% EtOAc/hexanes) provided **19a** (46 mg, 74%) as a white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.98 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.04 (s, 1H), 5.76–5.66 (m, 1H), 5.04–4.99 (m, 2H), 4.04 (s, 3H), 3.99 (dt, *J* = 7.5, 7.0 Hz, 2H), 3.24 (dd, *J* = 7.5, 7.0 Hz, 2H), 3.17 (dd, *J* = 7.0, 7.5 Hz, 2H), 2.37 (dt, *J* = 7.0, 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz) δ 172.3, 162.0, 154.5, 153.6, 136.4, 133.9, 127.2, 122.3, 122.1, 119.6, 118.9, 118.2, 111.3, 99.8, 53.9, 46.5, 36.9, 32.8, 21.0; IR (film) *v*_{max} 2944, 1749, 1702, 1588, 1441, 1410, 1162, 923, 814 cm⁻¹; MALDIFTMS (DHB) *m/z* 369.1559 (C₁₉H₂₀N₄O₄ + H⁺ requires 369.1557).

Solid curved lines represent nOe's observed in 1D ¹H–¹H GOESY (C₆D₆, 600 MHz)

Compound 19b. A solution of **19a** (14.1 mg, 0.04 mmol) in 4 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 165 °C for 3 h. The solution was concentrated under a stream of N₂ and the crude material was purified by PTLC (SiO₂, 40% EtOAc/CH₂Cl₂) providing compound **19b** (8.3 mg, 64%) as a yellow solid: ¹H NMR (C₆D₆, 600 MHz) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.71 (s, 1H), 7.08 (dd, *J* = 7.5, 7.9 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 4.06 (dd, *J* = 6.1, 7.3 Hz, 1H), 3.99 (dt, *J* = 2.6, 8.8 Hz, 1H), 3.33 (ddd, *J* = 10.0, 7.0, 2.6 Hz, 1H), 3.28 (s, 3H), 2.66–2.60 (m, 1H), 2.51 (dd, *J* = 7.9, 7.2 Hz, 1H), 2.45–2.38 (m, 1H), 1.62 (dt, *J* = 13.6, 8.8 Hz, 1H), 1.51 (dt, *J* = 13.2, 6.1 Hz, 1H), 1.32–1.27 (m, 1H), 0.86–0.78 (m, 2H), 0.87–0.70 (m, 1H); ¹³C NMR (C₆D₆, 150 MHz) δ 175.2, 171.9, 168.2, 157.3, 139.1, 126.9, 123.7, 122.6, 104.6, 77.6, 64.0, 52.1, 45.2, 44.6, 36.2, 29.0, 28.7, 28.0, 23.1; IR (film) *v*_{max} 1752, 1449, 1403, 1216, 1154, 1087, 1053, 1021, 913 cm⁻¹; MALDIFTMS (DHB) *m/z* 341.1493 (C₁₉H₂₀N₂O₄ + H⁺ requires 341.1493).

Methyl 5-((but-3-en-1-yl)-[3-(1-methyl-1H-indol-3-yl)propionyl]amino)-1,3,4-oxadiazole-2-carboxylate (20a). A solution of 3-(1-methyl-1H-indol-3-yl)propionic acid (93 mg, 0.46 mmol) in 5 mL of anhydrous CH₂Cl₂ was treated with EDCI (88 mg, 0.46 mmol) followed by DMAP (5.6 mg, 0.05 mmol). Oxadiazole **S13** was added (30 mg, 0.15 mmol) and the reaction mixture was allowed to stir at 23 °C for 9 h. The reaction was concentrated in vacuo to 1 mL and diluted with 30 mL of EtOAc and 10 mL of 1 N aqueous HCl. The organic layer was separated and washed with 10 mL of saturated aqueous NaHCO₃ and 10 mL of saturated aqueous NaCl. The organic layer was dried over Na₂SO₄, filtered, and concentrated. PTLC (SiO₂, 50% EtOAc/hexanes) provided **20a** (47 mg, 82%) as a white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.56 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.22 (dd, *J* = 7.0, 7.9 Hz, 1H), 7.10 (dd, *J* = 7.9, 7.0 Hz, 1H), 6.90 (s, 1H), 5.74–5.66 (m, 1H), 5.05–4.98 (m, 2H), 4.05 (s, 3H), 4.01 (t, *J* = 7.0 Hz, 2H), 3.99 (s, 3H), 3.24 (dd, *J* = 7.9, 7.0 Hz, 2H), 3.77 (t, *J* = 7.0 Hz, 2H), 2.39 (dt, *J* = 7.1, 6.6 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz) δ 172.3, 162.0, 154.3, 153.6, 137.0, 133.8, 127.4, 126.8, 121.7, 118.9, 118.8, 118.0, 112.8, 109.3, 53.8, 46.4, 37.0, 32.8, 32.7, 20.9; IR (film) ν_{max} 2944, 1749, 1703, 1564, 1441, 1149 cm⁻¹; MALDIFTMS (DHB) *m/z* 383.1725 (C₂₀H₂₂N₄O₄ + H⁺ requires 383.1714).

Solid curved lines represent nOe's observed in 1D ¹H–¹H GOESY (C₆D₆, 600 MHz)

Compound 20b. A solution of **20a** (10 mg, 0.026 mmol) in 2.6 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 165 °C for 2 h. The solution was concentrated under a stream of N₂ and the crude material was purified by PTLC (SiO₂, 40% EtOAc/CH₂Cl₂) providing **20b** (6.6 mg, 72%) as a yellow solid: ¹H NMR (C₆D₆, 600 MHz) δ 7.09 (ddd, *J* = 7.9, 7.5, 1.3 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.56 (dd, *J* = 7.5, 7.9 Hz, 1H), 6.25 (d, *J* = 7.9 Hz, 1H), 3.69 (t, *J* = 10.1 Hz, 1H), 3.64 (d, *J* = 0.9 Hz, 1H), 3.52 (dt, *J* = 7.9, 10.5 Hz, 1H), 3.35 (s, 3H), 2.70–2.65 (m, 1H), 2.64 (s, 3H), 2.46 (ddd, *J* = 11.8, 7.0, 1.3 Hz, 1H), 2.22 (dd, *J* = 7.9, 11.8 Hz, 1H), 2.16 (dt, *J* = 7.5, 13.2 Hz, 1H), 1.69–1.63 (m, 1H), 1.55 (ddd, *J* = 1.8, 7.0, 11.8 Hz, 1H), 1.50 (dd, *J* = 13.2, 1.8 Hz, 1H), 1.36–1.28 (m, 1H), 1.27–1.21 (m, 1H); ¹³C NMR (C₆D₆, 150 MHz) δ 171.6, 169.1, 163.9, 153.7, 129.9, 124.2, 118.4, 107.5, 105.6, 87.4, 81.2, 54.4, 52.1, 48.5, 43.3, 35.8, 34.5, 32.3, 30.4, 29.0; IR (film) $\nu_{\max}$ 2952, 1735, 1666, 1603, 1493, 1441, 1124, 1071 cm⁻¹; MALDIFTMS (DHB) *m/z* 355.1651 (C₂₀H₂₂N₂O₄ + H⁺ requires 355.1651).

Methyl 5-((4-(*p*-toluenesulfonyl)but-3-enyl)amino)-1,3,4-oxadiazole-2-carboxylate (S14). According to the method of Nájera et al.^{S10} a solution of sodium *p*-toluenesulfinate hydrate (141 mg, 0.76 mmol) in 7.6 mL of H₂O was treated with a solution of I₂ (193 mg, 0.76 mmol) in 3 mL of EtOH. The resulting brown–yellow suspension was immediately added to a solution of **S13** (150 mg, 0.76 mmol) in 4.5 mL of CH₂Cl₂, and the reaction mixture was stirred vigorously for 22 h. The reaction was quenched with the addition of 2 M aqueous Na₂SO₃ (1 mL) and extracted with CH₂Cl₂ (3 × 2.5 mL). The combined organic extracts were dried (Na₂SO₄), concentrated under reduced pressure, dissolved in 9 mL CH₂Cl₂, cooled to 0 °C, and treated with Et₃N (212 μL, 1.52 mmol). After warming to 25 °C and stirring an additional 2 h, the reaction was quenched with the addition of 1 M aqueous HCl (30 mL). The organic extract was washed with saturated aqueous NaHCO₃ (30 mL), dried (Na₂SO₄), concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 3.5 × 12 cm, 0–2% MeOH/CH₂Cl₂ gradient elution) to provide **S14** (114 mg, 43%) as a white solid: mp 166–167 °C (EtOH); ¹H NMR (DMSO-*d*₆, 500 MHz) δ 8.41 (t, *J* = 5.9 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 6.84 (dt, *J* = 6.4, 15.1 Hz, 1H), 6.78 (d, *J* = 15.1 Hz, 1H), 3.86 (s, 3H), 3.38 (dt, *J* = 6.2, 6.2 Hz, 2H), 2.48 (m, 2H), 2.37 (s, 3H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 164.9, 155.1, 151.0, 144.7, 144.0, 138.2, 132.9, 130.6 (2C), 127.8 (2C), 53.6, 41.3, 31.2, 21.7; IR (film) $\nu_{\max}$ 3326, 1741, 1625, 1144 cm⁻¹; MALDIFTMS (DHB) *m/z* 352.0960 (C₁₅H₁₇N₃O₅S + H⁺ requires 352.0962).

Methyl 5-([4-(*p*-toluenesulfonyl)but-3-en-1-yl]-(6-vinylbenzo[1,3]dioxole-5-carbonyl)amino)-1,3,4-oxadiazole-2-carboxylate (21a). A solution of **S14** (7.5 mg, 0.021 mmol) and 6-vinylbenzo[1,3]dioxole-5-carboxylic acid^{S11} (4.5 mg, 0.021 mmol) in 0.6 mL of anhydrous CH₂Cl₂ was treated with EDCI (41 mg, 0.21 mmol) and DMAP (2.5 mg, 0.021 mmol) and stirred at 25 °C for 18 h. The reaction mixture was quenched with the addition of H₂O (1.5 mL) and extracted with CH₂Cl₂ (3 × 1.5 mL). The combined organic extracts were dried (Na₂SO₄), concentrated under reduced pressure, and purified by PTLC (SiO₂, 50% EtOAc/hexanes) to provide **21a** (7.5 mg, 72%) as a colorless oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.73 (d, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 6.91 (s, 1H), 6.88 (dt, *J* = 7.0, 15.4 Hz, 1H), 6.59 (s, 1H), 6.58 (dd, *J* = 10.9, 16.0 Hz, 1H), 6.42 (d, *J* = 14.9 Hz, 1H), 6.00 (s, 2H), 5.46 (d, *J* = 17.1 Hz, 1H), 5.18 (d, *J* = 11.0 Hz, 1H), 4.20 (t, *J* = 7.0 Hz, 2H), 3.93 (s, 3H), 2.72 (dt, *J* = 7.0, 7.0 Hz, 2H), 2.41 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.4, 154.1, 154.0, 150.5, 147.6, 144.7, 140.7, 137.1, 134.0, 132.6, 131.8, 130.1 (2C), 128.7, 128.1, 126.2 (2C), 117.0, 107.4, 106.0, 102.1, 54.0, 46.5, 30.4, 21.8; IR (film) $\nu_{\max}$ 3726, 2961, 1749, 1694, 1565, 1256, 1144 cm⁻¹; MALDIFTMS (DHB) *m/z* 548.1105 (C₂₅H₂₃N₃O₈S + Na⁺ requires 548.1098).

Methyl 2-hydroxy-7-oxo-3-(*p*-toluenesulfonyl)-1,2,3a,4,5,7-hexahydro-3H-[1,3]dioxolo[4,5-j]pyrrolo[3,2,1-de]phenanthridine-2-carboxylate (21b). A solution of **21a** (7.5 mg, 0.014) in 1.5 mL of anhydrous, degassed 1,2-dichlorobenzene was heated under Ar at 165–170 °C for 1 h. The reaction mixture was cooled and loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in CH₂Cl₂. The 1,2-dichlorobenzene was eluted with CH₂Cl₂, and the column was then eluted with 2% MeOH/CH₂Cl₂ to provide **21b** (5.0 mg, 72%) as a white solid: mp 166–167 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 500 MHz) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.78 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 6.63 (s, 1H), 5.96 (s, 2H), 4.38 (s, 1H), 4.36 (dd, *J* = 8.5, 12.5 Hz, 1H), 4.13–4.08 (m, 1H), 4.92–3.86 (m, 1H), 3.88 (s, 3H), 3.68 (d, *J* = 11.7 Hz, 1H), 3.22 (d, *J* = 17.3 Hz, 1H), 2.86 (dd, *J* = 2.6, 16.9 Hz, 1H), 2.74 (apparent p, *J* = 6.3 Hz, 1H), 2.37 (s, 3H), 1.71 (m, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 173.7, 159.8, 152.3, 147.6, 145.7, 138.3, 137.4, 133.4, 130.2 (2C), 128.4 (2C), 121.4, 106.4, 103.3, 102.1, 100.2, 75.1, 72.0, 54.0, 47.6, 39.7, 37.9, 31.7, 21.9; IR (film) $\nu_{\max}$ 3479, 2921, 1732, 1615, 1486, 1246 cm⁻¹; MALDIFTMS (DHB) *m/z* 498.1212 (C₂₅H₂₃NO₈S + H⁺ requires 498.1217).

The relative stereochemistry of **21b** was determined by single crystal X-ray diffraction analysis.

Methyl 5-{[2-(1-methyl-1*H*-indol-3-yl)ethyl]-(pent-4-en-1-yl)amino}-1,3,4-oxadiazole-2-carboxylate (22a**).** Oxadiazole **S3** (100 mg, 0.33 mmol) was dissolved in 2 mL of anhydrous DMF. The solution was cooled to 0 °C and CsCO₃ (119 mg, 0.37 mmol) was added. After 30 min, 5-bromo-1-pentene (0.1 mL, 0.74 mmol) was added. The reaction mixture was allowed to warm to 23 °C and was stirred for 16 h. The mixture was diluted with 20 mL of Et₂O and the organic layer was washed with saturated aqueous NaCl (2 × 5 mL). The organic layer was dried over Na₂SO₄ filtered, and concentrated in vacuo. PTLC (SiO₂, 60% EtOAc/hexanes) provided **22a** (26 mg, 21%) as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.24 (dd, *J* = 8.2, 7.0 Hz, 1H), 7.14 (dd, *J* = 7.9, 7.0 Hz, 1H), 6.89 (s, 1H), 5.79–5.71 (m, 1H), 5.04–4.96 (m, 2H), 3.98 (s, 3H), 3.77–3.73 (m, 2H), 3.73 (s, 3H), 3.44 (t, *J* = 7.5 Hz, 2H), 3.11 (dd, *J* = 7.9, 7.5 Hz, 2H), 2.06 (dt, *J* = 7.5, 7.0 Hz, 2H), 1.72 (dt, *J* = 7.5, 7.9 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz) δ 165.2, 163.3, 155.2, 137.4, 137.3, 127.8, 127.2, 122.0, 119.3, 118.9, 115.7, 110.7, 109.6, 53.3, 50.3, 49.4, 32.9, 30.8, 27.0, 23.9; IR (film) $\nu_{\max}$ 2933, 1739, 1615, 1436, 1328, 1150, 1067, 741 cm⁻¹; MALDIFTMS (DHB) *m/z* 369.1921 (C₂₀H₂₄N₄O₃ + H⁺ requires 369.1921).

3-(2-Isothiocyantoethyl)-1-methylindole (S15**).**^{S12} A solution of CS₂ (0.7 mL, 11.6 mmol) in pyridine (0.3 mL) under Ar at -10 °C was treated with Et₃N (190 μL, 1.38 mmol). A solution of *N*¹-methyl tryptamine (241 mg, 1.38 mmol) in pyridine (0.7 mL) was added dropwise to the reaction over 30 min and the mixture was stirred at -10 °C for 1 h. A solution of DCC (285 mg, 1.38 mmol) in pyridine (0.7 mL) was added dropwise over 5 min and stirring was continued at -10 °C for 1 h, then warmed to 25 °C for 1 h. The reaction mixture was concentrated to dryness in vacuo, dissolved in Et₂O, and the precipitated thiourea was removed by filtration. The filtrate was concentrated and chromatography (SiO₂, 2.5 × 7 cm, 25% EtOAc/CH₂Cl₂) yielded **S15** (154 mg, 51%) as a white solid: mp 34–35 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.37 (ddd, *J* = 0.9, 8.2, 8.2 Hz, 1H), 7.27 (ddd, *J* = 1.2, 7.9, 7.9 Hz, 1H), 7.02 (s, 1H), 3.81 (s, 3H), 3.79 (t, *J* = 6.7 Hz, 2H), 3.21 (t, *J* = 6.8 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 137.0, 130.3, 127.7, 127.2, 121.8, 119.1, 118.4, 109.6, 109.5, 45.8, 32.7, 26.4; IR (film) $\nu_{\max}$ 2919, 2179, 2097, 1472, 1373, 1337, 738 cm⁻¹; MALDIFTMS (DHB) *m/z* 217.0794 (C₁₂H₁₂N₂S + H⁺ requires 217.0794).

1-Methoxalyl-4-[(1-methyl-1*H*-indol-3-yl)ethyl]thiosemicarbazide (S16). A solution of **S15** (155 mg, 0.72 mmol) in MeOH (5 mL) under Ar at 25 °C was treated with methyl oxalylhydrazide^{S1} (85 mg, 0.72 mmol). The reaction mixture was warmed to 60 °C for 42 h before the solvent was removed in vacuo. Chromatography (SiO₂, 2.5 × 5 cm, 0.6% MeOH/6% acetone/CHCl₃) afforded **S16** (87 mg, 36%) as a light yellow solid: mp 145–147 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 500 MHz) δ 10.34 (bs, 1H), 9.58 (bs, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.90 (s, 1H), 3.90 (m, 2H), 3.79 (s, 3H), 3.72 (s, 3H), 3.08 (t, *J* = 7.0 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 179.6, 158.5, 151.4 (br), 137.2, 127.9, 127.2, 121.9, 119.1, 118.9, 111.1, 109.5, 54.0, 45.6, 32.8, 24.6; IR (film) ν_{max} 3302, 3052, 2934, 1759, 1714, 1552, 1472, 1161 cm⁻¹; MALDIFTMS (DHB) *m/z* 357.0988 (C₁₅H₁₈N₄O₃S + Na⁺ requires 357.0992).

Methyl 5-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino-1,3,4-thiadiazole-2-carboxylate (S17). Substrate **S16** (90.2 mg, 0.27 mmol) was dissolved in conc. H₂SO₄ (0.8 mL)^{S13} at 0 °C, then warmed to 25 °C for 2 h. The reaction mixture was slowly pipetted into 50 g ice water, and neutralized with saturated aqueous NaHCO₃. The aqueous layer was extracted with CH₂Cl₂, dried over Na₂SO₄, and concentrated in vacuo. Chromatography (SiO₂, 2 × 8 cm, 20% EtOAc/CH₂Cl₂) afforded **S17** (43.3 mg, 51%) as a white solid: mp 146–148 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.0 Hz, 1H), 6.94 (s, 1H), 6.69 (bs, 1H), 3.97 (s, 3H), 3.75 (s, 3H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.16 (t, *J* = 6.4 Hz, 2H); ¹³C NMR (10% CD₃OD–CDCl₃, 100 MHz) δ 159.6, 137.1, 127.5, 127.3, 127.2, 121.9, 119.1, 118.5, 110.3, 109.5, 53.3, 47.8, 32.6, 24.5; IR (film) ν_{max} 3272, 1739, 1713, 1544, 1446, 1318, 1277, 1097 cm⁻¹; MALDIFTMS (DHB) *m/z* 339.0883 (C₁₅H₁₆N₄O₂S + Na⁺ requires 339.0886).

Methyl 5-{pent-4-enoyl-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-thiadiazole-2-carboxylate (23a**).** A stirring solution of thiadiazole **S17** (48 mg, 0.15 mmol) and EDCI (115 mg, 0.60 mmol) in CH₂Cl₂ (2 mL) under Ar at 25 °C was treated with 4-pentenoic acid (31 μL, 0.30 mmol) and DMAP (37 mg, 0.30 mmol). The mixture was stirred at 25 °C for 16 h before the reaction was concentrated. Chromatography (SiO₂, 2 × 8 cm, 5% EtOAc/CH₂Cl₂) afforded **23a** (59 mg, 99%) as a white solid: mp 119–121 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.65 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.24 (ddd, *J* = 0.9, 7.5, 7.5 Hz, 1H), 7.14 (ddd, *J* = 0.9, 7.2, 7.2 Hz, 1H), 6.82 (s, 1H), 5.58 (m, 1H), 4.93 (d, *J* = 12.3 Hz, 1H), 4.89 (d, *J* = 17.5 Hz, 1H), 4.53 (t, *J* = 7.0 Hz, 2H), 4.04 (s, 3H), 3.73 (s, 3H), 3.28 (t, *J* = 7.4 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 2.24 (q, *J* = 6.8 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 172.2, 162.4, 160.4, 156.0, 137.2, 136.2, 127.7, 127.4, 122.2, 119.6, 118.8, 116.1, 110.2, 109.6, 53.4, 49.0, 33.0, 32.8, 28.3, 23.9; IR (film) $\nu_{\max}$ 2954, 2923, 2851, 1744, 1718, 1677, 1456, 1421, 1272 cm⁻¹; MALDIFTMS (DHB) *m/z* 421.1301 (C₂₀H₂₂N₄O₃S + Na⁺ requires 421.1305).

Methyl 5-{(4-ethylpent-4-enoyl)-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino}-1,3,4-thiadiazole-2-carboxylate (24a**).** A stirring solution of thiadiazole **S17** (87 mg, 0.28 mmol), 4-ethylpent-4-enoic acid^{S6} (35 mg, 0.28 mmol), and EDCI (105 mg, 0.55 mmol) in CH₂Cl₂ (5 mL) was treated with DMAP (34 mg, 0.28 mmol). The mixture was stirred at 25 °C for 16 h before the reaction was concentrated. Chromatography (SiO₂, 2 × 13 cm, 2% MeOH/CHCl₃) afforded **24a** (87 mg, 75%) as a white solid: mp 109–111 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 400 MHz) δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.0 Hz, 1H), 6.82 (s, 1H), 4.68 (s, 1H), 4.56 (t, *J* = 7.0 Hz, 2H), 4.45 (s, 1H), 4.05 (s, 3H), 3.73 (s, 3H), 3.31 (t, *J* = 7.0 Hz, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.21 (t, *J* = 8.2 Hz, 2H), 1.84 (q, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 172.6, 162.4, 160.4, 156.0, 149.3, 137.2, 127.7, 127.4, 122.2, 119.6, 118.8, 110.2, 109.6, 108.4, 53.5, 49.1, 32.8, 32.3, 30.5, 29.0, 23.9, 12.4; IR (film) $\nu_{\max}$ 2962, 1746, 1721, 1673, 1455, 1422, 1269 cm⁻¹; MALDIFTMS (DHB) *m/z* 427.1799 (C₂₂H₂₆N₄O₃S + H⁺ requires 427.1798).

Methyl 5-{[2-(1-methyl-1*H*-indol-3-yl)ethyl]-[3-(1-methyl-1*H*-indol-3-yl)propionyl]amino}-1,3,4-oxadiazole-2-carboxylate (25a**).** A solution of 3-(1-methyl-1*H*-indol-3-yl)propionic acid (203 mg, 1.00 mmol) in 10 mL of anhydrous CH₂Cl₂ was treated with EDCI (191 mg, 1.00 mmol) and DMAP (12.2 mg, 0.10 mmol). Oxadiazole **S3** was added (100 mg, 0.30 mmol) and the reaction mixture was allowed to stir at 23 °C for 24 h. The reaction mixture was concentrated in vacuo to 2 mL and diluted with 50 mL of EtOAc and 10 mL of 1 N aqueous HCl. The organic layer was separated and washed with 10 mL of saturated aqueous NaHCO₃ and 10 mL saturated aqueous NaCl. The organic layer was dried over Na₂SO₄, filtered, and concentrated. PTLC (SiO₂, 50% EtOAc/hexanes) provided **25a** (93 mg, 64%) as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.66 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.26–7.24 (m, 2H), 7.21–7.18 (m, 2H), 7.12–7.06 (m, 2H), 6.87 (s, 1H), 6.79 (s, 1H), 4.18 (dd, *J* = 7.3, 7.5 Hz, 2H), 3.98 (s, 3H), 3.72 (s, 3H), 3.69 (s, 3H), 3.21 (dd, *J* = 7.0, 6.6 Hz, 2H), 3.15 (dd, *J* = 6.6, 8.5 Hz, 2H), 3.07 (dd, *J* = 7.9, 7.5 Hz, 2H); ¹³C NMR (CDCl₃, 150 MHz) δ 172.5, 162.2, 154.2, 153.3, 137.1, 128.5, 127.8, 127.6, 127.5, 127.0, 121.9, 121.8, 119.3, 119.1, 119.0, 118.9, 113.0, 110.1, 109.5, 109.4, 53.7, 48.0, 37.1, 32.8, 37.7, 24.5, 21.0; IR (film) $\nu_{\max}$ 2933, 1749, 1697, 1583, 1441, 1323, 1151 cm⁻¹; MALDIFTMS (DHB) *m/z* 508.1955 (C₂₇H₂₇N₅O₄ + Na⁺ requires 508.1952).

Ethyl 5-(pent-4-ynoyl)amino-1,3,4-oxadiazole-2-carboxylate (26a**).** A solution of ethyl 5-amino-1,3,4-oxadiazole-2-carboxylate^{S14} (50 mg, 0.32 mmol), EDCI (151 mg, 0.79 mmol) and pent-4-ynoic acid (78 mg, 0.79 mmol) was stirred at 25 °C for 18 h. The solvent was concentrated under reduced pressure, and the residue was subjected to flash chromatography (SiO₂, 2.5 cm × 20 cm, 30% EtOAc/hexanes) providing **26a** (53 mg, 70%) as mixture of rotamers: ¹H NMR (CDCl₃, 500 MHz) δ 8.01 (bs, 1H), 5.41 (bs, 1H), 4.48 (q, *J* = 8.8 Hz, 4H), 3.14 (t, *J* = 8.8 Hz, 2H), 2.76 (t, *J* = 8.8 Hz, 2H), 2.66 (dt, *J* = 3.3, 9.2 Hz, 2H), 2.58 (dt, *J* = 3.3, 9.2 Hz, 2H), 2.02 (t, *J* = 3.3 Hz, 2H), 1.46 (t, *J* = 8.8 Hz, 6H); MALDIFTMS (DHB) *m/z* 260.0642 (C₁₀H₁₁N₃O₄ + Na⁺ requires 260.0649)

Methyl 5-[(pent-4-ynoyl)methylamino]-1,3,4-oxadiazole-2-carboxylate (27a). DMAP (96 mg, 0.79 mmol) was added to a solution of pent-4-ynoic acid (78 mg, 0.79 mmol), methyl 5-methylamino-1,3,4-oxadiazole-2-carboxylate^{S14} (50 mg, 0.32 mmol), and EDCI (151 mg, 0.79 mmol) in CH₂Cl₂ (25 mL) at 0 °C. The reaction mixture was gradually warmed to 25 °C overnight (13 h). The solvent was concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 2.5 × 20 cm, 30% EtOAc/hexanes) providing **27a** (66 mg, 88%) as a clear oil: ¹H NMR (CDCl₃, 500 MHz, δ 4.06 (s, 3H), 3.51 (s, 3H), 3.19 (t, J = 7.0 Hz, 2H), 2.62 (dt, J = 2.5, 7.0 Hz, 2H), 1.97 (t, J = 2.5 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 170.7, 162.0, 154.2, 153.4, 82.4, 69.1, 53.8, 35.7, 33.4, 14.1; IR (film) $\nu_{\max}$ 3281, 1748, 1705, 1575, 1443, 1339, 1210, 1147 cm⁻¹; MALDIFTMS (DHB) m/z 238.0823 (C₁₀H₁₁N₃O₄ + H⁺ requires 238.0822).

Methyl 7-methyl-6-oxo-4,5,6,7-tetrahydrofuro[2,3-*b*]pyridine-2-carboxylate (27b). A solution of **27a** (10 mg, 0.04 mmol) in 8 mL of anhydrous degassed 1,2-dichlorobenzene was warmed under Ar at 178 °C for 22 h. The cooled reaction mixture was loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with distilled hexanes (20 mL) and then the column was flushed with distilled EtOAc (25 mL). The EtOAc was concentrated and the residue was purified by PTLC (SiO₂, 55% EtOAc/hexanes) providing **27b** (5 mg, 57%) as a white solid: ¹H NMR (CDCl₃, 500 MHz) δ 7.09 (s, 1H), 3.87 (s, 3H), 3.35 (s, 3H), 2.78–2.68 (m, 4H); ¹³C NMR (CDCl₃, 125 MHz) δ 168.9, 158.9, 151.8, 138.0, 120.0, 99.5, 51.6, 32.0, 27.7, 16.6; IR (film) $\nu_{\max}$ 2954, 1714, 1694, 1630, 1537, 1439, 1332, 1319, 1165 cm⁻¹; MALDIFTMS (DHB) m/z 210.0765 (C₁₀H₁₁NO₄ + H⁺ requires 210.0761).

Methyl 5-((pent-4-ynoyl)-[2-(1-methyl-1*H*-indol-3-yl)ethyl]amino)-1,3,4-oxadiazole-2-carboxylate (28a). A solution of oxadiazole **S3** (15.0 mg, 0.05 mmol), 4-pentynoic acid (9.81 mg, 0.10 mmol), and EDCI (38.2 mg, 0.20 mmol) in CH₂Cl₂ (1.5 mL) under Ar at 25 °C was treated with DMAP (12.2 mg, 0.10 mmol). The mixture was stirred at 25 °C for 18 h before the white slurry was concentrated. Chromatography (SiO₂, 1.5 × 5 cm, 2.5% MeOH/CH₂Cl₂) provided **28a** (18.2 mg, 96%) as a white solid: mp 185–186 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 400 MHz) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 6.8 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 4.26 (t, *J* = 7.3 Hz, 2H), 4.01 (s, 3H), 3.72 (s, 3H), 3.11 (m, 4H), 2.60 (dt, *J* = 2.6, 7.0 Hz, 2H), 1.97 (t, *J* = 2.4 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 170.7, 162.0, 154.2, 153.5, 137.2, 127.8, 127.6, 121.9, 119.3, 119.1, 110.0, 109.5, 82.6, 69.3, 53.9, 48.0, 35.7, 32.8, 24.5, 14.4; IR (film) $\nu_{\max}$ 3260, 1739, 1714, 1573, 1438, 1414, 1179, 1149 cm⁻¹; MALDIFTMS (DHB) *m/z* 403.1381 (C₂₀H₂₀N₄O₄ + Na⁺ requires 403.1377).

Methyl 7-[2-(1-methyl-1*H*-indol-3-yl)ethyl]-6-oxo-4,5,6,7-tetrahydrofuro[2,3-*b*]pyridine-2-carboxylate (28b). A solution of **28a** (7.0 mg, 0.02 mmol) in 1,2-dichlorobenzene (1.8 mL) was heated in a sealed tube at 175 °C for 53 h. The solvent was removed by SiO₂ chromatography (hexanes) and the crude reaction mixture was eluted with EtOAc. Chromatography (SiO₂, 1.5 × 4 cm, 3.5% EtOAc/CH₂Cl₂) afforded **28b** (4.0 mg, 63%) as an off-white solid: mp 114–116 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 7.7 Hz, 1H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.04 (s, 1H), 6.95 (s, 1H), 4.13 (t, *J* = 7.6 Hz, 2H), 3.89 (s, 3H), 3.73 (s, 3H), 3.11 (t, *J* = 7.9 Hz, 2H), 2.72 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.3 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.8, 159.1, 151.8, 138.1, 137.1, 128.2, 127.2, 121.8, 120.0, 119.3, 119.1, 110.9, 109.3, 100.0, 51.8, 42.5, 32.8, 32.4, 24.4, 16.9; IR (film) $\nu_{\max}$ 1718, 1682, 1631, 1533, 1472, 1431, 1323, 1190, 1154 cm⁻¹; MALDIFTMS (DHB) *m/z* 353.1488 (C₂₀H₂₀N₂O₄ + H⁺ requires 353.1496).

Methyl 5-(3-butyn-1-yl)amino-1,3,4-oxadiazole-2-carboxylate (29a). Prepared according to the procedure of **S13** and isolated as a white solid (41% over 3 steps): mp 151–154 °C; ¹H NMR (CDCl₃, 500 MHz) δ 5.91 (bs, 1H), 3.98 (s, 3H), 3.61 (dt, *J* = 6.3, 6.3 Hz, 2H), 2.57 (dt, *J* = 2.6, 6.3 Hz, 2H), 2.04 (t, *J* = 2.6 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 164.6, 155.2, 151.6, 80.6, 71.4, 53.7, 42.4, 19.8; IR (film) $\nu_{\max}$ 3234, 1741, 1626, 1549, 1442, 1205, 1159 cm⁻¹; MALDIFTMS (DHB) *m/z* 218.0535 (C₈H₉N₃O₃ + Na⁺ requires 218.0536).

Methyl 5-(*N*-acetyl-(but-3-yn-1-yl)amino)-1,3,4-oxadiazole-2-carboxylate (30a). A solution of **29a** (20 mg, 0.10 mmol) in 2 mL of acetic anhydride was treated with DMAP (6 mg, 0.051 mmol) and stirred at 25 °C for 18 h. The reaction mixture was concentrated under reduced pressure and subjected to flash chromatography (SiO₂, 1.0 × 8 cm, 2% MeOH/CH₂Cl₂) to provide **30a** (20 mg, 84%) as a white solid: mp 85–86 °C (CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 4.15 (t, *J* = 7.0 Hz, 2H), 4.04 (s, 3H), 2.59 (dt, *J* = 2.6, 6.8 Hz, 2H), 2.55 (s, 3H), 1.91 (t, *J* = 2.6 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 169.6, 162.3, 154.7, 154.0, 80.0, 71.1, 54.2, 45.7, 24.9, 18.5; IR (film) $\nu_{\max}$ 3285, 2959, 1747, 1713, 1568, 1445, 1163, 814 cm⁻¹; MALDIFTMS (DHB) *m/z* 238.0819 (C₁₀H₁₁N₃O₄ + H⁺ requires 238.0822).

Methyl *N*-trifluoroacetyl-5,6-dihydro-4*H*-furo[2,3-*b*]pyrrole-2-carboxylate (31b). A solution of **29a** (16.2 mg, 0.083 mmol) in 0.7 mL of trifluoroacetic anhydride was stirred at 25 °C for 20 h. The reaction mixture was concentrated under reduced pressure to afford the unstable trifluoroacetamide **31a** which was used immediately in subsequent reactions: ¹H NMR (1,2-Cl₂C₆D₄, 400 MHz) δ 4.04 (t, *J* = 6.8 Hz, 2H), 3.83 (s, 3H), 2.56 (dt, *J* = 2.6, 6.8 Hz, 2H), 1.90 (t, *J* = 2.6 Hz, 1H). A solution of **31a** in 0.5 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 165–170 °C for 18 h. The reaction mixture was cooled and loaded directly onto SiO₂ (1 × 8 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with hexanes, and the column was then eluted with 1% MeOH/CH₂Cl₂ to provide **31b** (8.9 mg, 71%) as a 2:1 mixture of trifluoroacetamide rotomers: mp 148–150 °C; ¹H NMR (CDCl₃, 400 MHz) major rotomer δ 7.10 (s, 1H), 4.56 (t, *J* = 7.6 Hz, 2H), 3.85 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H); minor rotomer δ 7.13 (s, 1H), 4.65 (t, *J* = 7.4 Hz, 2H), 3.85 (s, 3H), 3.05 (t, *J* = 7.6 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) major rotomer δ 158.7, 155.8, 152.6, 144.6, 117.6, 117.1, 113.0, 55.5, 52.4, 21.0; minor rotomer δ 158.9, 155.9, 152.6, 144.5, 117.6, 117.0, 113.0, 54.5, 52.4, 22.4; IR (film) $\nu_{\max}$ 2954, 1726, 1690, 1140 cm⁻¹; MALDIFTMS (DHB) *m/z* 286.0291 (C₁₀H₈NO₄F₃ + Na⁺ requires 286.0298).

2,3-Butadienyl-(5-phenyl-1,3,4-oxadiazol-2-yl)amine (S18). A solution of 2-methanesulfonyl-5-phenyl-1,3,4-oxadiazole^{S15} (150 mg, 0.67 mmol) and the hydrochloride salt of 1-amino-2,3-butadiene^{S16} (143 mg, 1.35 mmol) in 6 mL of anhydrous THF was treated with Et₃N (376 μ L, 2.70 mmol) and stirred under N₂ at 50 °C for 23 h. The reaction mixture was cooled, concentrated under reduced pressure, diluted with H₂O (15 mL), and extracted with CH₂Cl₂ (3 $\times$ 15 mL). The combined organic extracts were dried (Na₂SO₄), concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 3 $\times$ 15 cm, 30–40% EtOAc/hexanes gradient elution) to provide **S18** (92 mg, 64%) as a white solid: mp 104–106 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.91–7.89 (m, 2H), 7.45–7.44 (m, 3H), 5.37 (apparent p, *J* = 5.8 Hz, 1H), 5.26 (bs, 1H), 4.93–4.90 (m, 2H), 4.05 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 208.6, 163.6, 159.5, 131.0, 129.3 (2C), 126.2 (2C), 124.8, 88.0, 78.5, 42.0; IR (film) ν_{max} 3200, 3006, 1652, 1621, 1449, 1242 cm⁻¹; MALDIFTMS (DHB) *m/z* 214.0976 (C₁₂H₁₁N₃O + H⁺ requires 214.0975).

N-Acetyl-2,3-butadienyl-(5-phenyl-1,3,4-oxadiazol-2-yl)amine (32a). A solution of **S18** (20 mg, 0.094 mmol) in 1 mL of acetic anhydride was treated with DMAP (34 mg, 0.28 mmol) and stirred at 25 °C for 18 h. The reaction mixture was concentrated under reduced pressure, diluted with H₂O (2 mL), and extracted with EtOAc (3 $\times$ 2 mL). The combined organic extracts were dried (Na₂SO₄), concentrated under reduced pressure, and subjected to flash chromatography (SiO₂, 1.5 $\times$ 10 cm, 25% EtOAc/hexanes) to provide **32a** (22 mg, 90%) as a white solid: mp 72–74 °C; ¹H NMR (CDCl₃, 500 MHz) δ 8.01–7.99 (m, 2H), 7.55–7.49 (m, 3H), 5.28 (apparent p, *J* = 6.6 Hz, 1H), 4.80–4.78 (m, 2H), 4.53–4.51 (m, 2H), 2.47 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 209.8, 169.8, 163.1, 160.7, 132.3, 129.6 (2C), 126.9 (2C), 123.9, 86.2, 77.8, 45.6, 24.4; IR (film) ν_{max} 2964, 1953, 1703, 1575, 1548, 1229 cm⁻¹; MALDIFTMS (DHB) *m/z* 278.0905 (C₁₄H₁₃N₃O₂ + Na⁺ requires 278.0900).

2-(*N*-Acetyl-pyrrol-3-yl)-1-phenylethanone (32b). A solution of **32a** (9.8 mg, 0.038 mmol) in 2 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 165–170 °C for 25 min. The reaction mixture was cooled and loaded directly onto SiO₂ (1.5 × 10 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with hexanes, and the column was then eluted with 20% EtOAc/hexanes to provide **32b** (5.6 mg, 65%) as a white solid: mp 63–65 °C (EtOAc/hexanes); ¹H NMR (CDCl₃, 500 MHz) δ 8.07 (m, 2H), 7.62 (m, 1H), 7.51 (t, *J* = 8.1 Hz, 2H), 7.34 (bs, 1H), 7.31 (dd, *J* = 2.8, 3.3 Hz, 1H), 6.25 (dd, *J* = 1.9, 3.1 Hz, 1H), 4.19 (s, 2H), 2.52 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 206.2, 196.9, 133.5, 129.0 (2C), 128.5 (2C), 122.0, 119.8, 119.3, 118.6, 114.3, 37.0, 21.9; IR (film) $\nu_{\max}$ 3142, 1713, 1682, 1371, 1328, 1220 cm⁻¹; MALDIFTMS (DHB) *m/z* 228.1018 (C₁₄H₁₃NO₂ + H⁺ requires 228.1014).

Methyl 5-((but-3-en-1-yl)-[6-(2-methoxyvinyl)benzo[1,3]dioxole-5-carbonyl]amino)-1,3,4-oxadiazole-2-carboxylate (33a). A solution of **S13** (6.0 mg, 0.030 mmol) and 6-(2-methoxyvinyl)benzo[1,3]dioxole-5-carboxylic acid^{S17} (14 mg, 0.060 mmol) in 0.3 mL of DMF was treated with NaHCO₃ (7.5 mg, 0.090 mmol), EDCI (12 mg, 0.060 mmol), and DMAP (11 mg, 0.090 mmol) and stirred under Ar at 25 °C for 18 h. The reaction mixture was diluted with EtOAc (5 mL) and washed with H₂O (3 × 5 mL). The organic extract was dried (Na₂SO₄) and concentrated under reduced pressure before being subjected to flash chromatography (SiO₂, 1 × 5 cm, 25% EtOAc/hexanes) to provide **33a** (8.5 mg, 72%) as a colorless oil: ¹H NMR (acetone-*d*₆, 500 MHz) δ 6.90 (d, *J* = 12.9 Hz, 1H), 6.88 (s, 1H), 6.82 (s, 1H), 6.02 (s, 2H), 5.88–5.80 (m, 1H), 5.83 (d, *J* = 12.9 Hz, 1H), 5.13–5.10 (m, 1H), 5.06–5.03 (m, 1H), 4.13 (dd, *J* = 7.0, 7.4 Hz, 2H), 3.92 (s, 3H), 3.62 (s, 3H), 2.55 (dt, *J* = 7.0, 7.4 Hz, 2H); ¹³C NMR (acetone-*d*₆, 125 MHz) δ 168.8, 162.2, 154.6, 154.5, 150.9, 150.3, 146.3, 135.0, 130.3, 126.2, 117.3, 108.0, 105.3, 102.2, 101.8, 56.5, 53.2, 47.5, 32.8; IR (film) $\nu_{\max}$ 2963, 1748, 1564, 1258, 1036, 800 cm⁻¹; MALDIFTMS (DHB) *m/z* 402.1299 (C₁₉H₁₉N₃O₇ + H⁺ requires 402.1301).

Methyl 4-(but-3-enyl)-5-oxo-4,5-dihydro-3,7,9-trioxa-4-azadicyclopenta[*a,g*]naphthalene-2-carboxylate (33b). A solution of **33a** (7.1 mg, 0.018 mmol) in 1.5 mL of anhydrous, degassed 1,2-dichlorobenzene was warmed under Ar at 165–170 °C for 30 min. The reaction mixture was cooled and loaded directly onto SiO₂ (1 × 6 cm) equilibrated in hexanes. The 1,2-dichlorobenzene was eluted with hexanes, and the column was then eluted with 25% EtOAc/hexanes to provide **33b** (4.8 mg, 78%) as a white solid: mp 182–184 °C (EtOAc/hexanes); ¹H NMR (acetone-*d*₆, 500 MHz) δ 7.96 (s, 1H), 7.65 (s, 1H), 7.48 (s, 1H), 6.20 (s, 2H), 5.93–5.85 (m, 1H), 5.04–5.00 (m, 1H), 4.98–4.95 (m, 1H), 4.35 (dd, *J* = 7.0, 7.3 Hz, 2H), 3.89 (s, 3H), 2.60 (dt, *J* = 7.0, 7.0 Hz, 2H); ¹³C NMR (acetone-*d*₆, 125 MHz) δ 160.1, 158.8, 153.2, 150.8, 147.8, 147.6, 139.4, 135.1, 128.8, 118.9, 117.1, 115.3, 106.9, 102.8, 101.6, 51.6, 41.8, 32.7; IR (film) $\nu_{\max}$ 2913, 1712, 1649, 1587, 1563, 1469, 1302, 1233, 1202, 1036 cm⁻¹; MALDIFTMS (DHB) *m/z* 342.0966 (C₁₈H₁₅NO₆ + H⁺ requires 342.0978).

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