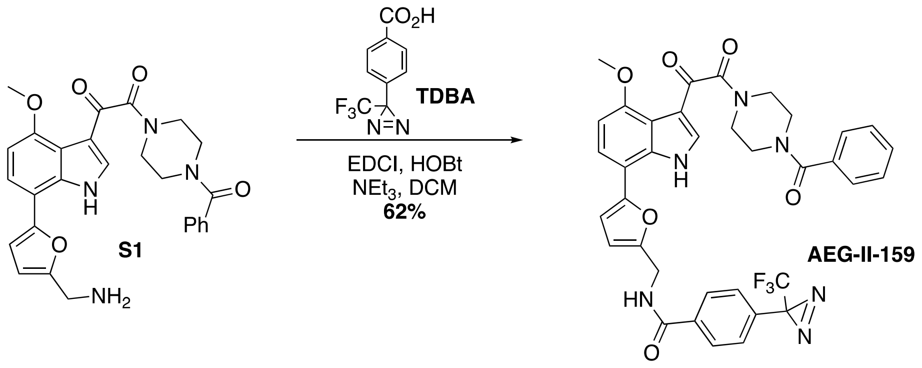
SUPPLEMENTAL MATERIAL

Synthetic Chemistry

All reagents were purchased from commercially available sources and used as received. Reactions were magnetically stirred under a nitrogen atmosphere, unless otherwise noted and reactions were monitored by either thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates or liquid chromatography mass spectrometry (LCMS). Proton (^{1} H) and carbon (^{13} C) NMR spectra were recorded on a Bruker Avance III 500-MHz spectrometer or on a Bruker DRX500 500-MHz spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to chloroform (δ 7.26) for 1 H NMR, and (δ 77.0) for 13C NMR. Infrared spectra were recorded using a JASCO 480-Plus FT-IR spectrometer, or a Perkin-Elmer Spectrum Two FT-IR spectrometer. Accurate mass measurement data were acquired on Waters Instruments. Waters software calibrates and reports by use of neutral atomic masses. The mass of the electron is not included. Preparative scale HPLC was pre-formed with a Gilson 333/334 preparative pump system equipped with a 5 mL injection loop, Sunfire C18 OBD column (5 µm packing material, 19 x 100 mm column dimensions) equipped with a UV-Vis dual wavelength (210 and 254 nm) detector and 215 liquid handling module. Solvent systems were comprised of H_2O containing 0.1% trifluoroacetic acid, and acetonitrile containing 0.1% trifluoroacetic acid. Lyophilization was performed in a Labconco FreeZone 12 Plus lyophilizer (0.035 mbar). The purity of new compounds was judged by NMR.

Synthesis of AEG-II-159



To a solution of **S1** (0.074 g, 0.15 mmol) (58), TDBA (0.052 g, 0.23 mmol, 1.5 eq.), EDCI•HCl (0.071 g, 0.46 mmol, 3 eq.), and HOBt•H_2O (0.070 g, 0.46 mmol, 3 eq.) in CH_2Cl_2 (6.8 mL) in a round bottom flask shielded from light under N_2 was added NEt_3 (0.11 mL, 0.76 mmol, 5 eq.). After 90 min, no starting material was observed by TLC. The crude reaction mixture was purified by flash column chromatography (SiO_2, 50-100% EtOAc/Hexanes) to afford **AEG-II-159** as a (0.066 g, 62%) yellow solid.

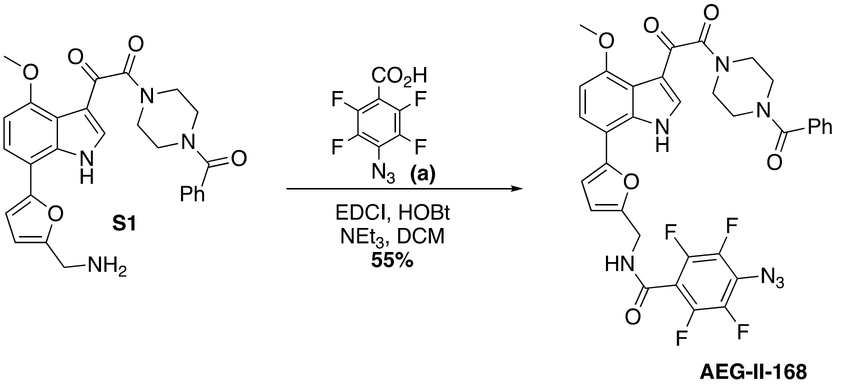
^{1}H NMR (500 MHz, $CDCl_3$) δ11.26 (s, 1 H), 8.15 (d, 1 H, *J* = 3.3 Hz), 7.82 (app. d, 1 H, *J* = 6.6 Hz), 7.42 (br. s, 5 H), 7.38 (d, 1 H, *J* = 8.3 Hz), 7.20 (d, 2 H, *J* = 8.2 Hz), 7.07 (t, 1 H, *J* = 6.2 Hz), 6.66 (d, 1 H, *J* = 8.3 Hz), 6.52 (d, 1 H, *J* = 3.3 Hz), 6.33 (d, 1 H, *J* =3.3 Hz), 4.66 (d, 2 H, *J* = 6.1 Hz), 3.91 (s, 3 H), 3.97-3.38 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 170.9, 167.9, 167.8, 153.8, 152.9, 149.6, 135.7, 135.2, 134.9, 134.4, 133.0, 130.3, 128.8, 127.7, 127.2, 126.8, 120.9, 120.3, 115.6, 115.1, 109.5, 109.4, 103.9, 77.4, 56.1, 37.4, 29.9, 28.6, 28.3.

IR υ_{max} 3849, 3404, 2917, 2849, 2359, 1629, 1577, 1541, 1511, 1467, 1432, 1284, 1155

HRMS (ESI) *m/z* 699.2180 [calcd for (M+H)$^+$ 699.2179]

Synthesis of AEG-II-168



To a solution of **S1** (0.100 g, 0.206 mmol), **(a)** (0.073 g, 0.31 mmol, 1.5 eq.), EDCI•HCl (0.096 g, 0.62 mmol, 3 eq.), and HOBt•H_2O (0.095 g, 0.62 mmol, 3 eq.) in CH_2Cl_2 (6.8 mL) in a round bottom flask shielded from light under N_2 was added NEt_3 (0.14 mL, 1.03 mmol, 5 eq.). The reaction was allowed to proceed overnight. The crude reaction mixture was concentrated, and purified by flash column chromatography (SiO_2, 60-100% EtOAc/Hexanes) to afford **AEG-II-168** (0.080 g, 55%) as a viscous orange oil.

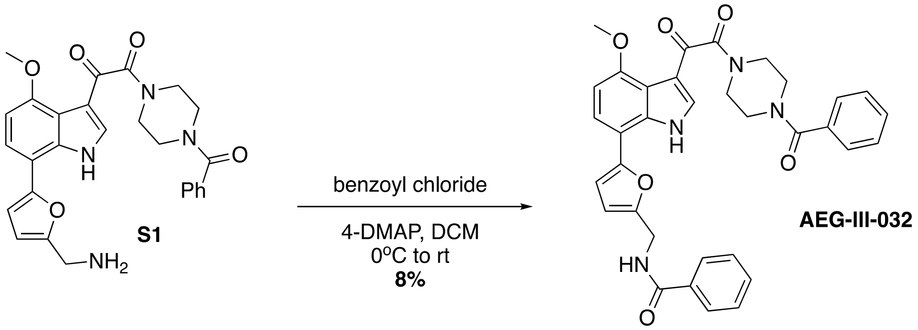
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.95 (s, 1 H), 8.06 (app. s, 1 H), 7.43 (m, 5 H), 7.20 (m, 1 H), 6.68 (d, 1 H, *J* = 8.3 Hz), 6.56 (d, 1 H, *J* = 3.3 Hz), 6.37 (d, 1 H, *J* = 3.3 Hz), 4.68 (d, 2 H, *J* = 6.1 Hz), 3.90 (s, 3 H), 3.97-3.30 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 185.8, 170.8, 167.6, 159.3, 153.7, 152.9, 148.9, 145.3, 139.4, 139.3, 136.1, 134.9, 139.3, 136.1, 134.9, 134.2, 130.2, 128.7, 127.1, 122.3, 120.5, 115.3, 114.8, 110.6, 110.4, 110.3, 109.7, 109.2, 109.1, 108.9, 104.1, 103.9, 55.9, 41.6, 37.3, 29.7

IR υ_{max} 3299, 2918, 2849, 2360, 2341, 2128, 1631, 1545, 1510, 1486, 1429, 1401, 1364, 1271, 1131

HRMS (ESI) *m/z* 704.1859 [calcd for $C_{34}H_{25}F_4N_7O_6$ $(M+H)^+$ 704.1881]

Synthesis of AEG-III-032



To a solution of **S1** (0.039 g, 0.081 mmol) in CH_2Cl_2 (2 mL) under N_2 at 0°C was added 4-DMAP (0.020 g, 0.16 mmol, 2 eq.). After 10 min, benzoyl chloride was added (0.023 g, 0.16 mmol, 2 eq.) and the reaction was allowed to gradually warm to room temperature overnight. The crude reaction mixture was concentrated and subjected to flash column chromatography (SiO_2, 50% EtOAc/Hexanes – 20% MeOH/EtOAc), concentrated, dissolved in 1.5 mL ACN + 0.8 mL water, and further purified by reverse phase HPLC (15 mL/min 45-80% ACN/H_2O + 0.1% TFA, 6 min) to afford **AEG-III-032** (0.004 g, 8%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.31 (s, 1 H), 8.21 (s, 1 H), 7.80 (d, 1 H, *J* = 7.3 Hz), 7.52 (t, 1 H, *J* = 7.5 Hz), 7.43 (m, 8 H), 6.99 (t, 1 H, *J* = 6.4 Hz), 6.69 (d, 1 H, *J* = 8.3 Hz), 6.53

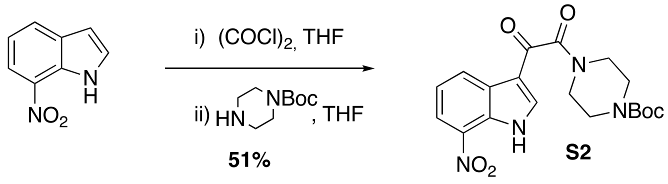
(d, 1 H, *J* = 3.3 Hz), 6.34 (d, 1 H, *J* = 3.3 Hz), 4.69 (d, 1 H, *J* = 6.1 Hz), 3.93 (s, 3 H), 3.99-3.39 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 171.5, 169.6, 167.9, 158.6, 158.3, 153.9, 152.9, 149.7, 136.1, 134.5, 133.7, 132.4, 130.6, 129.0, 128.9, 127.2, 127.2, 120.4, 116.0, 115.7, 115.0, 113.7, 109.6, 109.4, 104.1, 103.9, 56.1, 37.4

IR υ_{max} 3434, 2360, 2095, 1645, 1517, 1432, 1272, 1206, 1147, 916

HRMS (ESI) *m/z* 591.2265 [calcd for $C_{34}H_{30}N_4O_6$ $(M+H)^+$ 591.2244]

Synthesis of S4



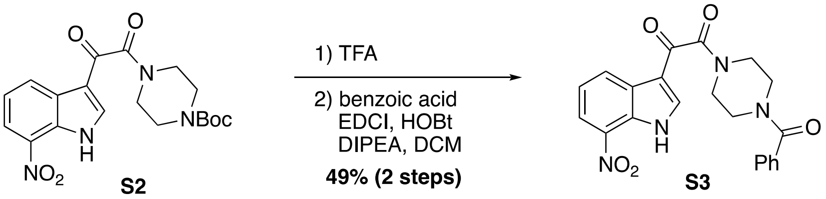
To 7-nitroindole (0.50 g, 3.1 mmol) in THF (8 mL) under N_2 at room temperature was added oxalyl chloride (1.4 mL, 15.4 mmol, 5 eq.). After 23 hours the crude reaction mixture was concentrated and redissolved in THF under N_2. To this solution was added 1-boc-piperazine (0.69 g, 3.7 mmol, 1.2 eq.) then NEt_3 (1.2 mL, 6.16 mmol, 2 eq.). The reaction was allowed to proceed for 24 h. The crude reaction mixture was diluted with CH_2Cl_2 and washed with $NaHCO_3$. The organic layer was dried with $MgSO_4$, decanted, and concentrated. The crude reaction mixture was purified using flash column chromatography (SiO_2, 0-100% EtOAc/Hexanes) to afford **S2** as a (0.626 g, 51%) yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1 H), 8.76 (d, 1 H, *J* = 7.9 Hz), 8.28 (d, 1 H, *J* = 8.1 Hz), 8.21 (d, 1 H, *J* = 3.1 Hz), 7.47 (app. t, 1 H, *J* = 8.0 Hz), 3.75 (m, 2 H), 3.58 (m, 2 H), 3.55-3.47 (m, 4 H).

^{13}C NMR (500 MHz, $CDCl_3$): 185.3, 165.3, 154.6, 137.0, 133.6, 130.5, 129.8, 128.8, 123.1, 121.2, 115.7, 80.8, 46.2, 41.8, 28.5

IR υ_{max} 3273, 2976, 1699, 1634, 1532, 1485, 1412, 1364, 1332, 1302, 1286, 1249, 1166, 1125, 1063, 1035, 995, 974, 928, 863, 810, 795, 772, 734, 659

HRMS (ESI) *m/z* 425.1255 [calcd for $C_{19}H_{22}N_4O_6$ (M+Na) 425.1437]



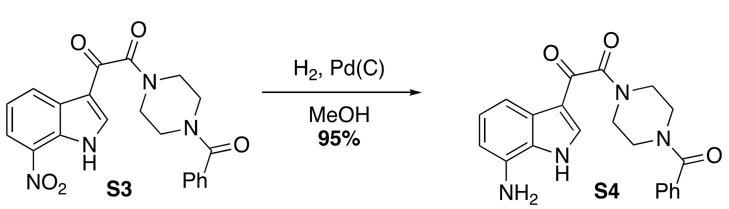
To a solution of **S2** (0.386 g, 0.959 mmol) in CH_2Cl_2 (6.5 mL) was added TFA (1.5 mL, 1.5 mL / mmol). After four hours, no starting material was observed by LC/MS. The reaction mixture was concentrated repeatedly with CH_2Cl_2. The crude product was then put under N_2 atmosphere and dissolved in CH_2Cl_2 (10 mL). To this solution was added benzoic acid (0.129 g, 1.05 mmol, 1.1 eq.), EDCI•HCl (0.203 g, 1.05 mmol, 1.1 eq.), and HOBt•H_2O (0.142 g, 1.05 mmol, 1.1 eq). After 25 minutes NEt_3 was added and to the reaction mixture, and the reaction was allowed to proceed overnight. The crude reaction mixture was washed with $NaHCO_3$ then NH_4Cl. The organic layer was dried with $MgSO_4$, decanted, and concentrated. The crude reaction mixture was purified using flash column chromatography (SiO_2, 50% EtOAc/Hexanes – 10% MeOH/EtOAc) to afford **S3** as a (186 mg, 49%) yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.58 (s, 1 H), 8.74 (s, 1 H), 8.27 (d, 1 H, *J* = 8.1 Hz), 8.23 (d, 1 H, *J* = 2.9 Hz), 7.45 (m, 6 H), 4.08-3.41 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 185.0, 170.9, 165.2, 137.2, 135.0, 133.6, 130.4, 129.8, 128.9, 128.8, 127.2, 123.2, 121.3, 115.6, 42.1, 29.9

IR υ_{max} 3449, 2925, 2854, 1741, 1631, 1532, 1438, 1369, 1333, 1251, 1116, 1050, 975, 792, 736, 440, 425, 410

HRMS (ESI) *m/z* 407.1341 [calcd for $C_{21}H_{18}N_4O_5$ (M+H) 407.1355]



To a solution of **S3** (0.186 g, 0.458 mmol) in methanol (10 mL) under N_2 was added Pd/C (0.010 g). H_2 gas was then bubbled into the solution and the reaction was allowed to stir overnight. The crude reaction mixture was filtered through sand and concentrated to afford **S4** (163 mg, 95%) as an olive green solid.

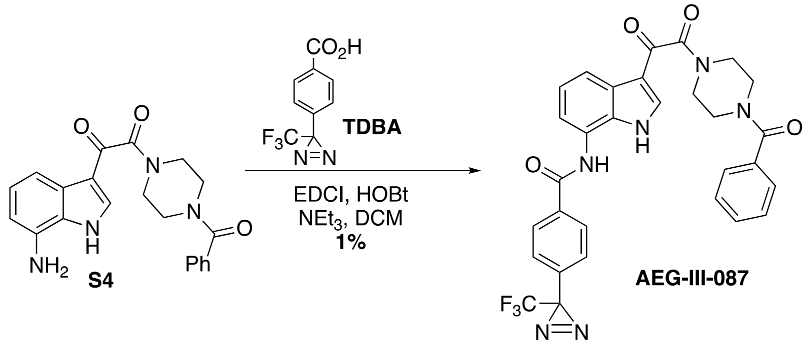
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.89 (s, 1 H), 7.64 (app. s, 1 H), 7.40 (m, 6 H), 7.07 (t, 1 H, *J* = 7.7 Hz), 6.56 (d, 1 H, *J* = 7.6 Hz), 3.49 (s, 2 H), 3.94-3.32 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 185.0, 171.0, 167.2, 135.2, 134.8, 132.8, 130.5, 129.8, 128.9, 127.2, 127.0, 126.3, 124.7, 114.6, 112.1, 110.2, 51.0, 46.3, 41.7

IR υ_{max} 3583, 3366, 3237, 2914, 1717, 1621, 1522, 1434, 1251, 1158, 1003, 427

HRMS (ESI) *m/z* 377.1600 [calcd for $C_{21}H_{20}N_4O_3(M+H)^+$ 377.1614]

Synthesis of AEG-III-087



To a solution of **S4** (0.156 g, 0.414 mmol), TDBA (0.143 g, 0.622 mmol, 1.5 eq.), EDCI•HCl (0.119 g, 0.622 mmol, 1.5 eq.), and HOBt•H_2O (0.095 g, 0.622 mmol, 1.5 eq.)

in CH_2Cl_2 (18.4 mL) in a round bottom flask shielded from light under N_2 was added NEt_3 (0.11 mL, 0.828 mmol, 2 eq.). After 18 h, the crude reaction material was concentrated, dissolved in 1:1 ACN/H_2O and purified using reverse phase HPLC (15 mL/min 20-95% ACN/H_2O + 0.1% TFA, 15 min) to afford **AEG-III-087** as a green-yellow solid (3.4 mg, 1.4%).

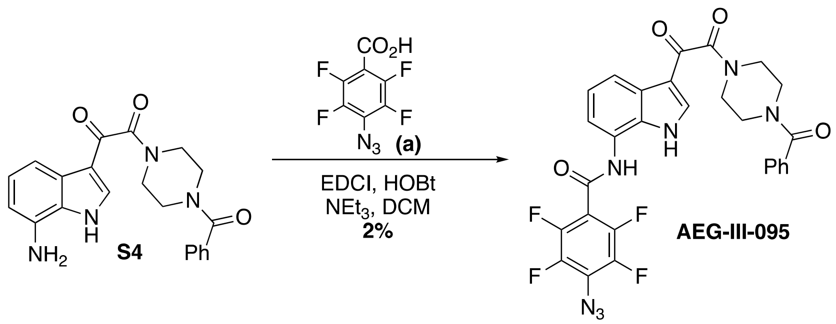
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1 H), 8.10 (s, 1 H), 8.00(d, 2 H, *J* = 8.1 Hz), 7.64 (s, 1 H), 7.43 (m, 5 H), 7.30 (d, 2 H, *J* = 8.1 Hz), 7.20 (m, 1 H), 7.01 (d, 1 H, *J* = 7.6 Hz), 4.02-3.33 (m, 8 H)

^{13}C NMR (500 MHz, $CDCl_3$): 184.9, 171.3, 166.7, 165.2, 135.6, 134.7, 134.5, 133.5, 130.6, 130.5, 128.9, 128.7, 128.2, 127.7, 127.2, 126.9, 126.5, 123.6, 123.1, 122.9, 120.9, 119.9, 116.8, 114.2, 41.8, 29.9, 28.7, 28.4, 28.0

IR υ_{max} 3281, 2923, 2861, 1784, 1717, 1627, 1429, 1250, 1156, 999, 939, 440, 425, 409

HRMS (ESI) *m/z* 589.1798 [calcd for $C_{30}H_{23}F_3N_6O_4$ $(M+H)^+$ 589.1811]

<u>Synthesis of AEG-III-095</u>



To a solution of **(a)** (0.024 g, 0.10 mmol, 1.5 eq.) in CH_2Cl_2 (4 mL) in a round bottom flask shielded from light under N_2 at 0°C was added EDCI•HCl (0.016 g, 0.010 mmol, 1.5 eq.), HOBt•H_2O (0.015 g, 0.10 mmol, 1.5 eq.), NEt_3 (0.02 mL, 0.13 mmol, 2 eq.), then **S4** (0.025 g, 0.066 mmol). The reaction mixture was allowed to gradually warm to room temperature overnight. The crude reaction mixture was concentrated, dissolved in 1:1 ACN/H_2O, and purified using reverse phase HPLC (15 mL/min 20-95% ACN/H_2O + 0.1% TFA, 15 min) to afford **AEG-III-095** as a green-yellow solid (0.68 mg, 2%).

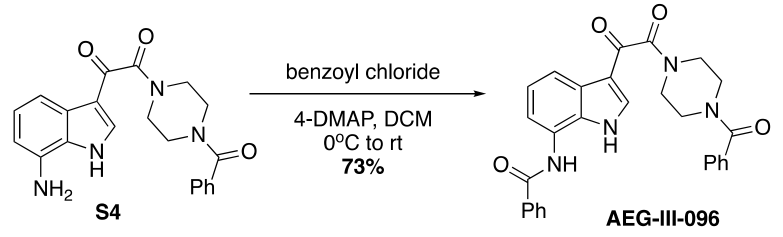
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1 H), 8.80 (s, 1 H), 8.24 (s, 1 H), 7.81 (s, 1 H), 7.45 (m, 5 H), 6.96 (d, 1 H, *J* = 7.6 Hz), 4.03-3.40 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 184.7, 171.0, 166.4, 156.3, 135.5, 134.5, 130.4, 128.8, 128.1, 127.8, 127,1, 123.5, 121.8, 120.5, 116.4, 114.3, 29.7

IR υ_{max} 3265, 2359, 2127, 1634, 1486, 1422, 1257, 1157, 999, 912, 731, 668

HRMS (ESI) *m/z* 594.1520 [calcd for $C_{28}H_{19}F_4N_7O_4$ $(M+H)^+$ 594.1513]

Synthesis of AEG-III-096



To a solution of **S4** (0.044 g, 0.12 mmol) in CH_2Cl_2 (2.5 mL) under N_2 at 0°C was added benzoyl chloride (0.049 g, 0.35 mmol, 3 eq.), then 4-DMAP (0.043 g, 0.35 mmol, 3 eq.). The reaction mixture was allowed to gradually warm to room temperature overnight. After 15 h, the crude reaction mixture was purified using flash column chromatography (SiO_2, 0-100% EtOAc/Hex) to afford **AEG-III-096** (0.041 g, 73%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.07 (s, 1 H), 8.95 (s, 1 H), 8.10 (s, 1 H), 7.96 (d, 1 H, *J* = 7.6 Hz), 7.70 (s, 1 H), 7.58 (t, 1 H, *J* = 7.5 Hz), 7.40 (m, 5 H), 7.18 (app. s, 1 H), 7.06 (d, 1 H), *J* = 7.51 Hz), 3.93-3.29 (m, 8 H).

^{13}C NMR (500 MHz, $CDCl_3$): 185.1, 170.9, 166.6, 166.4, 135.6, 135.0, 133.8, 132.5, 130.4, 129.0, 128.9, 128.8, 127.7, 127.2, 123.5, 123.4, 119.5, 116.6, 114.4, 29.9

IR υ_{max} 3283, 1629, 1528, 1425, 1251, 1157, 998, 710, 427

HRMS (ESI) *m/z* 481.1876 [calcd for $C_{28}H_{24}N_4O_4$ $(M+H)^+$ 481.1876]