

SUPPORTING INFORMATION

Polymer-supported Synthesis of *N*-substituted Anthranilates as the Building Blocks for Preparation of *N*-Arylated 3-Hydroxyquinolin-4(1*H*)-ones

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General information

All reagents were of reagent grade and used without further purification. Solvents and chemicals were purchased from Sigma-Aldrich (US), Acros Organics (Belgium) or Fluorochem (UK). Anhydrous solvents were dried over 4 Å molecular sieves or stored as received from commercial suppliers. Reactions were performed in plastic reaction vessels (syringes, each equipped with a porous disk) using a manually operated synthesizer (Torviq, US) or in ace-pressure tubes, unless stated otherwise. The volume of wash solvent was 10 mL per 1 g of resin. For washing, resin slurry was shaken with the fresh solvent for at least 1 min before changing the solvent. Resin-bound intermediates were dried under a stream of nitrogen for prolonged storage and/or quantitative analysis. For the UHPLC-MS analysis a sample of resin (~5 mg) was treated with CH₂Cl₂/TFA (1:1, 1 mL, v/v), the cleavage cocktail was evaporated under a stream of nitrogen, and cleaved compounds extracted into CH₃CN (1 mL). Yields of final compounds were calculated from loading of commercially available Rink amide resin (0.6 mmol/g).

Cyclization reactions to corresponding 3-hydroxyquinolin-4(1*H*)-ones were monitored by UHPLC-MS analysis or by thin-layer chromatography (TLC) using aluminum plates pre-coated with silica gel (silica gel 60 F₂₅₄, Merck, US) impregnated with a fluorescent indicator. TLC plates were visualized by exposure to ultraviolet light ($\lambda = 254$ nm). Column chromatography was performed using silica gel (60 Å, 230–400 mesh, Sigma-Aldrich). Prior to HPLC separation (column Phenomenex Gemini, 50 × 2.00 mm, 3 μm particles, C¹⁸), the samples were injected by direct infusion into the mass spectrometer using autosampler. Mobile phase was isocratic 80% CH₃CN and 20% 0.01 M ammonium acetate in H₂O or 95% methanol + 5% H₂O + 0.1% formic acid and flow 0.3 mL/min.

Instrumentation

UHPLC-MS analyses were carried out on UHPLC-MS system consisting of UHPLC chromatograph Acquity with photodiode array detector and single quadrupole mass spectrometer (Waters, US), using X-Select C¹⁸ column at 30 °C and flow rate of 0.6 mL/min. Mobile phase was (A) 0.01 M ammonium acetate in H₂O, and (B) CH₃CN, linearly programmed from 10% A to 80% B over 2.5 min, kept for 1.5 min. The column was re-equilibrated with 10% of solution B for 1 min. The ESI source operated at discharge current of 5 μA, vaporizer temperature of 350 °C and capillary temperature of 200 °C. HPLC purification was carried out on C¹⁸ reverse phase column (YMC Pack ODS-A, 20 × 100 mm, 5 μm particles), gradient was formed from CH₃CN and 0.01 M ammonium acetate in H₂O, flow rate 15 mL/min. For lyophilization of residual solvents at -110 °C the ScanVac Coolsafe 110-4 was used.

HRMS analyses were performed using LC chromatograph (Dionex Ultimate 3000, Thermo Fischer Scientific, US) and Exactive Plus Orbitrap high-resolution mass spectrometer (Thermo Fischer Scientific, US) operating at positive full scan mode (120 000 FWHM) in the range of 100-1000 m/z. The settings for electrospray ionization were as follows: oven temperature of 150 °C and source voltage of 3.6 kV. The acquired data were internally calibrated with phthalate as a contaminant in methanol (m/z 297.15909). Samples were diluted to a final concentration of 0.1 mg/mL in CH₃CN/H₂O (90:10, v/v).

NMR spectra were recorded on JEOL ECX500 spectrometer at magnetic field strengths of 11.75 T with operating frequencies 500.16 MHz (for ¹H) and 125.77 MHz (for ¹³C) at 27°C. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). The ¹H and ¹³C NMR chemical shifts (δ in ppm) were referenced to the residual signals of DMSO-*d*₆ [2.50 (¹H) and 39.52 (¹³C)]. The residual signal of acetic acid (from column chromatography) exhibited signals at 171.9 and 21.0 ppm (¹³C), ammonium acetate (from HPLC purification) exhibited signals at 1.90 ppm (¹H), at 21.3 ppm and 172.0 ppm (¹³C) and DMSO exhibited signals at 2.54 ppm (¹H) and 40.45 ppm (¹³C).

Abbreviations in NMR spectra: app – apparent, br s – broad singlet, d – doublet, dd – doublet of doublets, m – multiplet, s – singlet.

Experimental procedures

3-Iodo-4-(methoxycarbonyl)benzoic acid

Compound was prepared according to the published procedure. The characterization data are in accordance with literature^[1].

Procedure for arylation of Rink amide resin

Rink amide AM resin **1** (1 g, loading 0.6 mmol/g) was swollen in CH₂Cl₂ (10 mL) for 30 min and then washed with CH₂Cl₂ (3 x 10 mL). Solution of DBU/CH₂Cl₂ (1:1, 10 mL, v/v) was added to the resin and the reaction slurry was shaken for additional 10 minutes and then again washed with CH₂Cl₂ (3 x 10 mL) and DMF (3 x 10 mL).

For **2**: 3-amino-4-(methoxycarbonyl)benzoic acid (390 mg, 2 mmol) and HOBt (288 mg, 2 mmol) were dissolved in DMF (10 mL) and DIC (315 μ L, 2 mmol) was added. The resulting solution was added to polypropylene fritted syringe with Rink amide resin. The reaction slurry was shaken at ambient temperature for 2 h, followed by wash with DMF (5 x 10 mL) and CH₂Cl₂ (3 x 10 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to arylated product.

For **3**: 3-iodo-4-(methoxycarbonyl)benzoic acid (612 mg, 2 mmol) and HOBt (288 mg, 2 mmol) were dissolved in DMF (10 mL) and DIC (315 μ L, 2 mmol) was added. The resulting solution was added to polypropylene fritted syringe with Rink amide resin. The reaction slurry was shaken at ambient temperature for 2 h, followed by wash with DMF (5 x 10 mL) and CH₂Cl₂ (3 x 10 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to arylated product.

General procedure A for Buchwald-Hartwig amination

Resin **3** (250 mg) was swollen in CH₂Cl₂ (5 mL) for 30 min and then washed with CH₂Cl₂ (3 x 5 mL). The solution of corresponding aniline (0.2M), XPhos Pd G2 (70 mg, 0.09 mmol) and K₃PO₄ (318 mg, 1.5 mmol) in properly nitrogen-flushed mixture of toluene/DMF (4:1, 3 mL, v/v) was added to the ace-pressure tube with resin **3**. The reaction slurry was stirred at 90°C for 18 h, followed by washing with DMF (5 x 5 mL), H₂O (5 x 5 mL), DMF (5 x 5 mL) and CH₂Cl₂ (5 x 5 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to products **4 – 17**.

General procedure B for ester hydrolysis

Resins **4 – 17** (250 mg) or **2** (250 mg) were swollen in CH₂Cl₂ (5 mL) for 30 min and then washed with CH₂Cl₂ (3 x 5 mL) and DMF (3 x 5 mL). The solution of TMSOK (128 mg, 1 mmol) in DMF (2.5 mL) was added to the polypropylene fritted syringes with **4 – 17** or **2**. The reaction slurry was shaken at ambient temperature for 16 h, followed by wash with DMF (5 x 5 mL) and CH₂Cl₂ (3 x 5 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to hydrolyzed products.

General procedure C for acylation with 2-bromoacetophenone

Resins-bounded products **18 – 29** (250 mg) or hydrolyzed **2** (250 mg) were swollen in CH₂Cl₂ (5 mL) for 30 min and then washed with CH₂Cl₂ (3 x 5 mL) and DMF (3 x 5 mL). The solution of 2-bromoacetophenone (149 mg, 0.75 mmol) and triethylamine (96 μ L, 0.75 mmol) in DMF (2.5 mL) was added to the polypropylene fritted syringes with starting material. The reaction slurry was shaken

at ambient temperature for 16 h, followed by wash with DMF (5 x 5 mL) and CH₂Cl₂ (3 x 5 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to acylated products **30 – 41, 46**.

General procedure D for reductive amination

Resin **46** (250 mg) was swollen in CH₂Cl₂ (5 mL) for 30 min and then washed with CH₂Cl₂ (3 x 5 mL) and THF (3 x 5 mL). The corresponding benzylamine or aliphatic amine (0.4M) in anhydrous THF (4 mL) was added to the ace-pressure tube with resin **46**, followed by addition of Bu₂SnCl₂ (36 mg, 0.12 mmol). The reaction slurry was stirred at ambient temperature for 10 minutes. Phenylsilane (197 µL, 1.6 mmol) was added subsequently and the reaction mixture was stirred at reflux for 18 h, followed by wash with DMF (5 x 5 mL), THF (5 x 5 mL) and CH₂Cl₂ (5 x 5 mL). Subsequent cleavage from the resin and UHPLC-MS analysis confirmed the full conversion to products **47 – 49**.

General procedure E for cleavage and cyclization to 3-hydroxyquinolin-4(1H)-ones

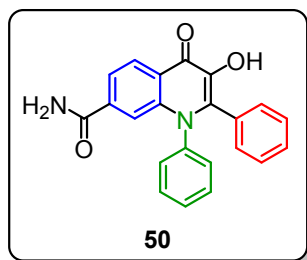
Cleavage of all intermediates from resin in analytical scale (~5 mg) prior to analysis was carried out in CH₂Cl₂/TFA (1:1, 1 mL, v/v) for 30 min according to the General Information.

Cleavage of the intermediates **30, 32, 33, 36 – 38, 40, 41** from resin followed by final cyclization in preparative scale: The corresponding resin (200 mg) was swollen in CH₂Cl₂ (3 mL) for 30 min and then washed with CH₂Cl₂ (3 x 5 mL). Solution of CH₂Cl₂/TFA (1:1, 4 mL, v/v) was added, the reaction slurry was shaken at ambient temperature for 2 h and then washed with CH₂Cl₂/TFA (1:1, 3 x 4 mL, v/v) and CH₂Cl₂ (3 x 4 mL). The cleavage cocktail and washes were combined, evaporated under a stream of nitrogen, the crude product was then again dissolved in neat TFA (10 mL) and refluxed from 24 h to 5 days obtain full conversion. The cyclized final compounds were cooled down to ambient temperature, residual TFA was evaporated under stream of nitrogen and crude products were purified as follows:

- **50, 56 – 58**: purified by semipreparative HPLC
- **52, 53, 60, 61**: treated with aqueous NaHCO₃ (30 mL) and extracted with EtOAc (3 x 50 mL). Organic extracts were combined, dried over MgSO₄, filtered and evaporated under reduced pressure. The residual material was purified by column chromatography (gradient elution with CH₂Cl₂/methanol from 10:1 to CH₂Cl₂/methanol/acetic acid 5:1:0.1, v/v).

Analytical data

3-hydroxy-4-oxo-1,2-diphenyl-1,4-dihydroquinoline-7-carboxamide 50



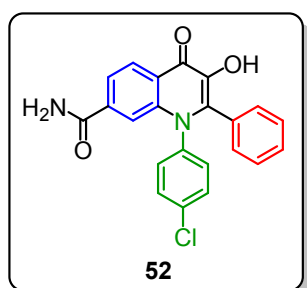
Cyclized for 24 h. Pale brown solid (23 mg, 80% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.37 – 8.36 (m, 1H), 7.80 – 7.78 (m, 1H), 7.48 – 7.34 (m, 6H), 7.26 – 7.21 (m, 7H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 169.5, 167.0, 139.3, 138.7, 137.2, 136.2, 130.3, 130.2, 129.3, 128.8, 128.0, 127.4, 125.1, 120.8, 118.4, 118.2, 116.0, 113.6 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{17}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+ = 357.1234$, found $[\text{M}+\text{H}]^+ = 357.1232$.

1-(4-chlorophenyl)-3-hydroxy-4-oxo-2-phenyl-1,4-dihydroquinoline-7-carboxamide 52



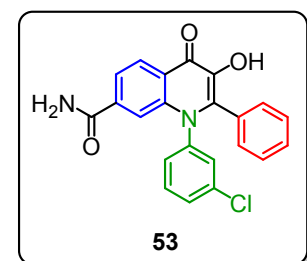
Cyclized for 3 days. Brown solid (6.5 mg, 14% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.50 (br s, 1H), 8.37 (d, $J = 8.4$ Hz, 1H), 8.13 (d, $J = 3.9$ Hz, 1H), 7.82 – 7.80 (m, 1H), 7.54 – 7.51 (m, 1H), 7.46 – 7.41 (m, 4H), 7.35 – 7.34 (m, 1H), 7.28 – 7.20 (m, 5H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 169.7, 166.9, 139.4, 139.2, 137.7, 137.0, 136.3, 133.3, 132.1, 131.8, 130.3, 129.4, 128.2, 127.6, 125.2, 124.0, 120.5, 117.8 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{16}\text{ClN}_2\text{O}_3$ $[\text{M}+\text{H}]^+ = 391.0844$, found $[\text{M}+\text{H}]^+ = 391.0841$.

1-(3-chlorophenyl)-3-hydroxy-4-oxo-2-phenyl-1,4-dihydroquinoline-7-carboxamide 53



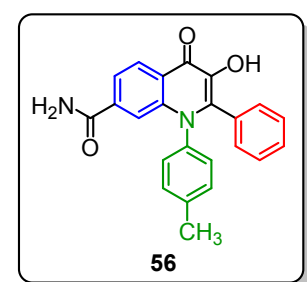
Cyclized for 3 days. Dark brown solid (11.5 mg, 24% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.34 (d, $J = 8.3$ Hz, 1H), 8.12 – 8.11 (m, 1H), 7.80 – 7.78 (m, 1H), 7.57 – 7.56 (m, 1H), 7.51 – 7.50 (m, 1H), 7.42 – 7.37 (m, 4H), 7.27 – 7.18 (m, 6H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 167.0, 133.4, 130.7, 130.6, 130.3, 129.1, 129.0, 127.4, 126.3, 125.0, 117.9 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{16}\text{ClN}_2\text{O}_3$ $[\text{M}+\text{H}]^+ = 391.0844$, found $[\text{M}+\text{H}]^+ = 391.0841$.

3-hydroxy-4-oxo-2-phenyl-1-(*p*-tolyl)-1,4-dihydroquinoline-7-carboxamide 56



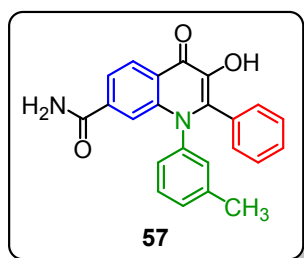
Cyclized for 2 days. Pale brown solid (4 mg, 8% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.36 (d, $J = 8.4$ Hz, 1H), 8.05 – 8.01 (m, 1H), 7.78 – 7.76 (m, 1H), 7.51 – 7.50 (m, 1H), 7.37 (s, 1H), 7.27 – 7.15 (m, 10H), 2.28 (s, 3H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 169.4, 167.0, 139.4, 139.3, 138.1, 137.3, 136.2, 132.0, 130.3, 129.8, 129.2, 128.9, 128.0, 127.9, 127.8, 127.4, 125.1, 123.9, 120.2, 118.2, 20.6 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+ = 371.1390$, found $[\text{M}+\text{H}]^+ = 371.1388$.

3-hydroxy-4-oxo-2-phenyl-1-(*m*-tolyl)-1,4-dihydroquinoline-7-carboxamide 57



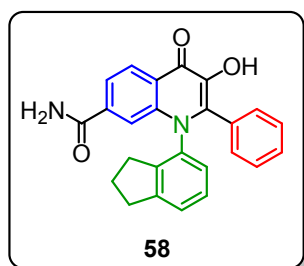
Cyclized for 3 days. Pale brown solid (6 mg, 14% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.36 (d, J = 8.5 Hz, 1H), 8.05 – 8.01 (m, 1H), 7.78 – 7.76 (m, 1H), 7.51 – 7.50 (m, 1H), 7.39 (d, J = 1.4 Hz, 1H), 7.28 – 7.12 (m, 10H), 2.21 (s, 3H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 169.5, 167.0, 139.3, 138.8, 138.5, 137.2, 136.2, 131.9, 130.5, 130.3, 129.4, 129.2, 129.0, 128.0, 127.9, 127.4, 125.1, 123.9, 120.3, 118.2, 20.6 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ = 371.1390, found $[\text{M}+\text{H}]^+$ = 371.1390.

1-(2,3-dihydro-1*H*-inden-4-yl)-3-hydroxy-4-oxo-2-phenyl-1,4-dihydroquinoline-7-carboxamide 58



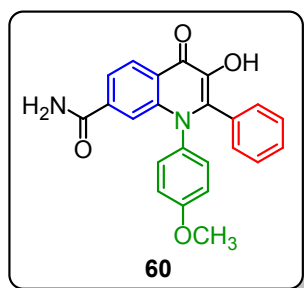
Cyclized for 4 days. Brown solid (4 mg, 8% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.36 (d, J = 8.4 Hz, 1H), 8.04 – 8.02 (m, 1H), 7.97 – 7.91 (m, 1H), 7.78 – 7.74 (m, 1H), 7.72 – 7.65 (m, 1H), 7.62 – 7.52 (m, 3H), 7.41 – 7.40 (m, 1H), 7.23 – 7.17 (m, 5H), 2.86 – 2.79 (m, 3H), 2.70 – 2.64 (m, 1H), 2.01 – 1.97 (m, 2H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 168.4, 167.7, 145.5, 144.8, 140.1, 137.4, 137.3, 134.1, 130.9, 129.5, 129.4, 128.4, 128.3, 127.9, 126.4, 125.2, 122.4, 120.8, 118.9, 32.6, 32.4, 25.3 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ = 397.1547, found $[\text{M}+\text{H}]^+$ = 397.1546.

3-hydroxy-1-(4-methoxyphenyl)-4-oxo-2-phenyl-1,4-dihydroquinoline-7-carboxamide 60



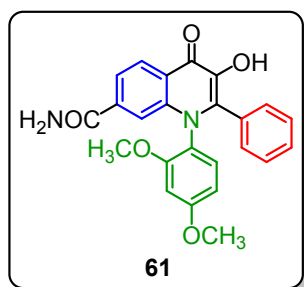
Cyclized for 3 days. Dark brown solid (20 mg, 42% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.35 (d, J = 7.5 Hz, 1H), 8.17 – 8.00 (m, 2H), 7.82 – 7.80 (m, 1H), 7.53 – 7.50 (m, 1H), 7.42 – 7.41 (m, 1H), 7.27 – 7.20 (m, 6H), 6.90 – 6.89 (m, 2H), 3.73 (s, 3H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 167.6, 159.3, 138.1, 136.4, 132.8, 132.0, 131.7, 130.9, 128.4, 128.3, 128.0, 125.6, 120.8, 119.4, 118.8, 114.8, 55.8 ppm.

HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ = 387.1339, found $[\text{M}+\text{H}]^+$ = 387.1337.

1-(2,4-dimethoxyphenyl)-3-hydroxy-4-oxo-2-phenyl-1,4-dihydroquinoline-7-carboxamide 61



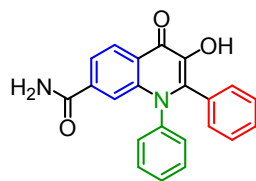
Cyclized for 5 days. Dark brown solid (55 mg, 88% yield).

^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.34 (d, J = 8.3 Hz, 1H), 8.17 – 8.15 (m, 1H), 8.03 – 8.01 (m, 1H), 7.93 – 7.92 (m, 1H), 7.80 – 7.81 (m, 1H), 7.57 – 7.50 (m, 5H), 7.39 (s, 1H), 6.54 – 6.51 (m, 1H), 6.50 – 6.48 (m, 1H), 3.74 (s, 3H), 3.61 (s, 3H) ppm.

^{13}C NMR (126 MHz, $\text{DMSO-}d_6$): δ 166.6, 164.7, 142.2, 139.3, 138.0, 137.15, 136.3, 133.9, 131.7, 130.6, 129.7, 128.8, 128.2, 127.7, 127.3, 126.7, 120.3, 119.9, 55.6, 55.4 ppm.

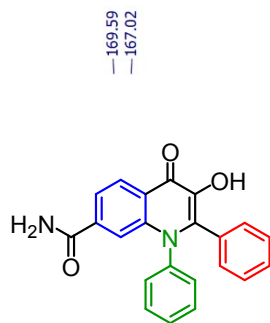
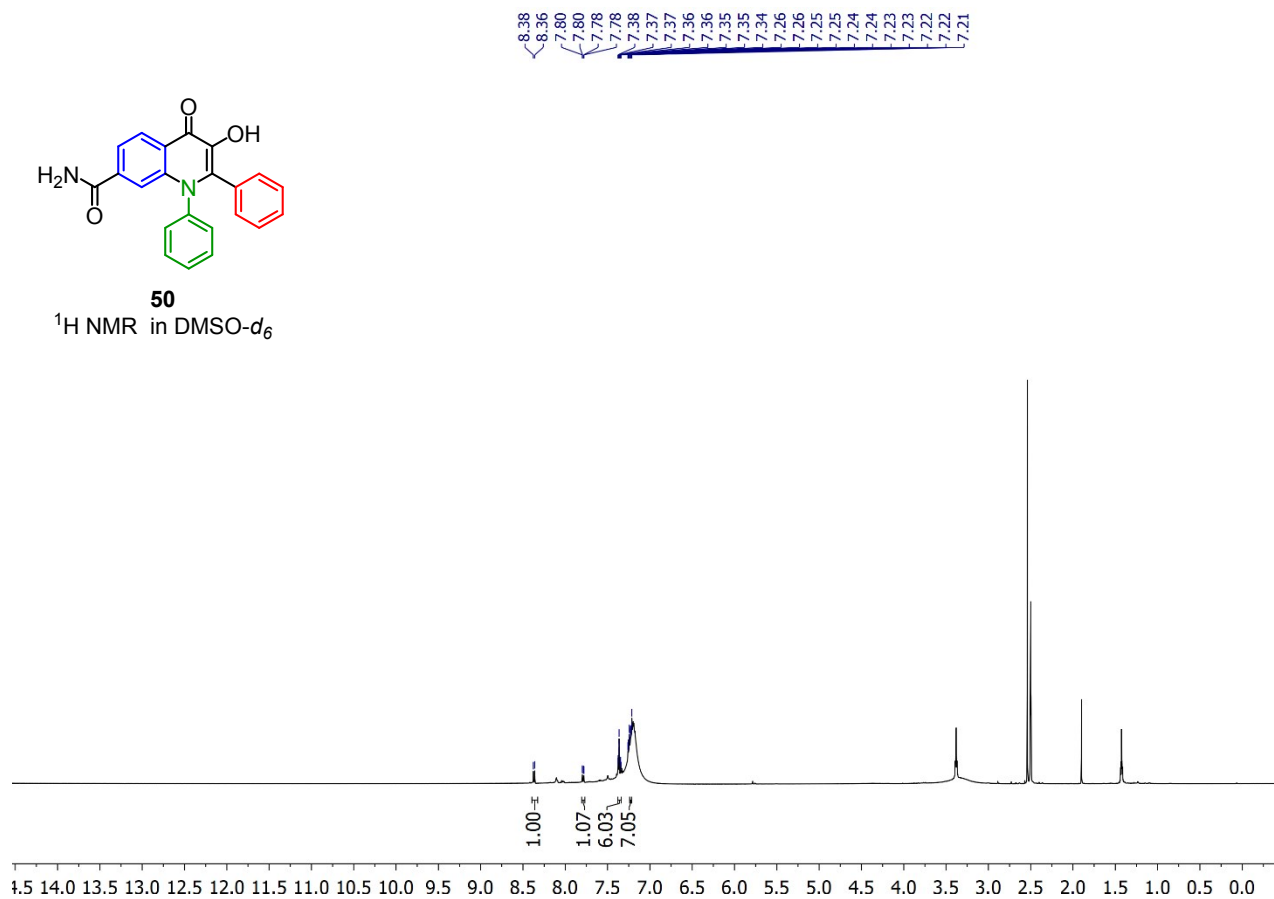
HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$ = 417.1445, found $[\text{M}+\text{H}]^+$ = 417.1448.

Spectral data of the final compounds and intermediates



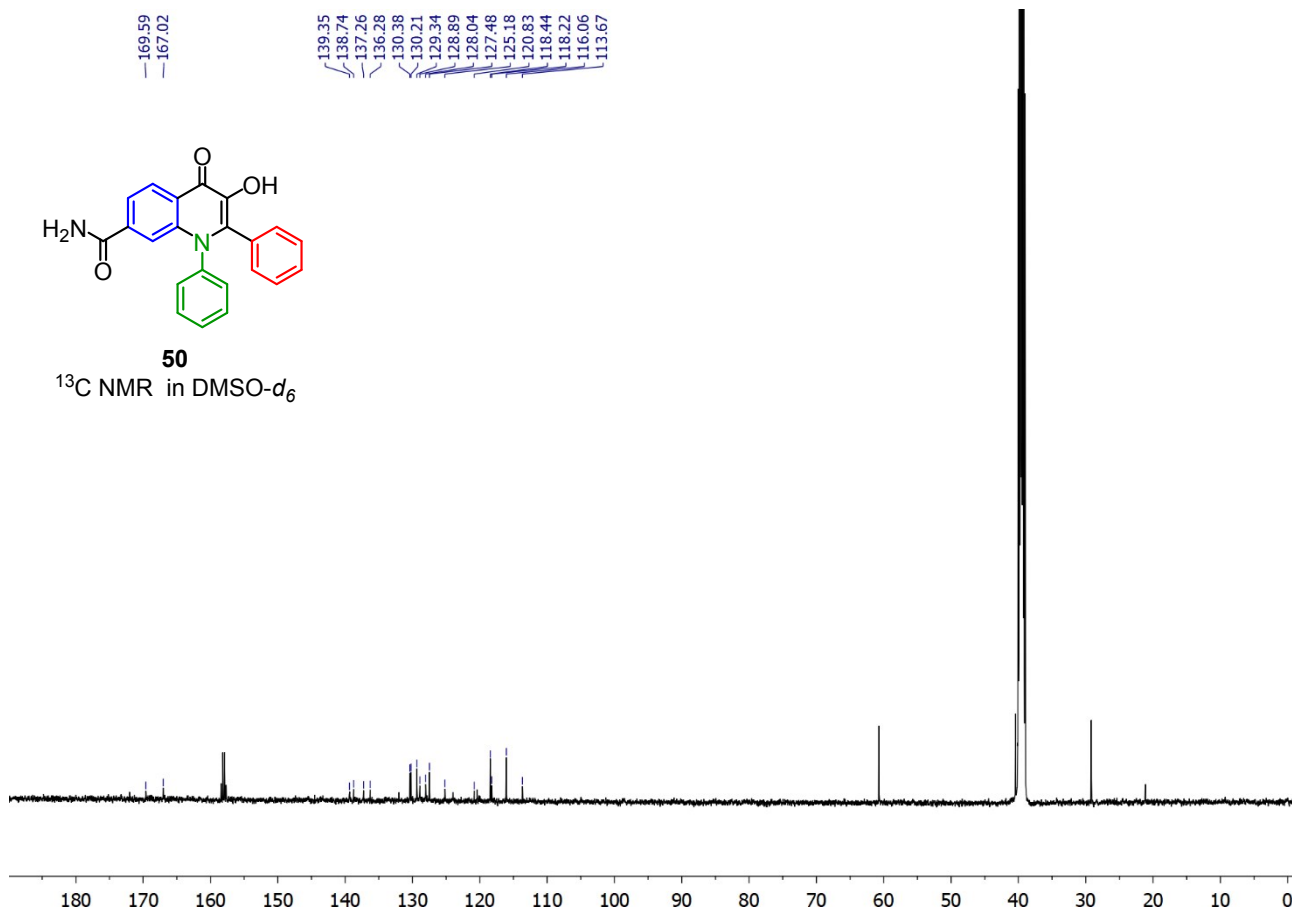
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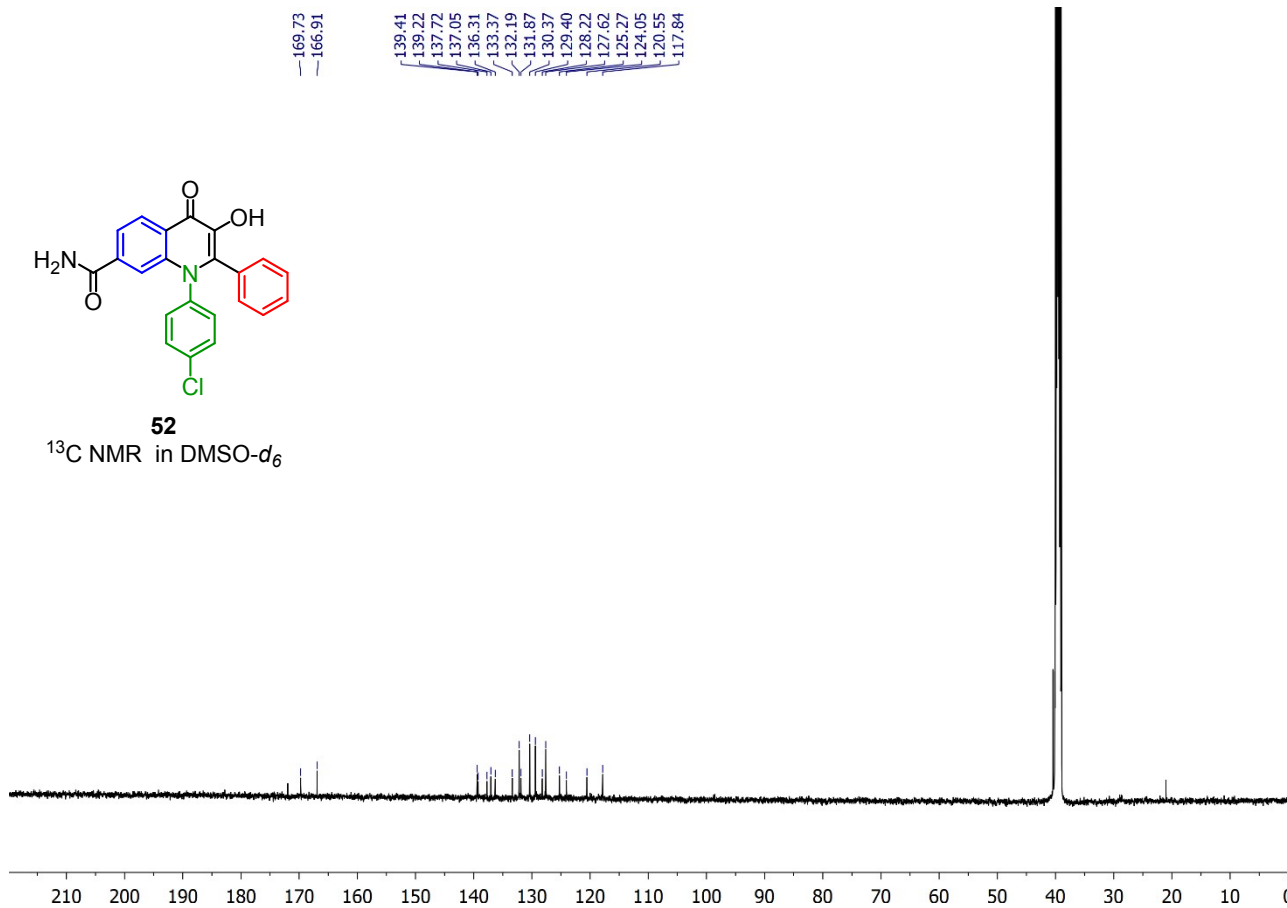
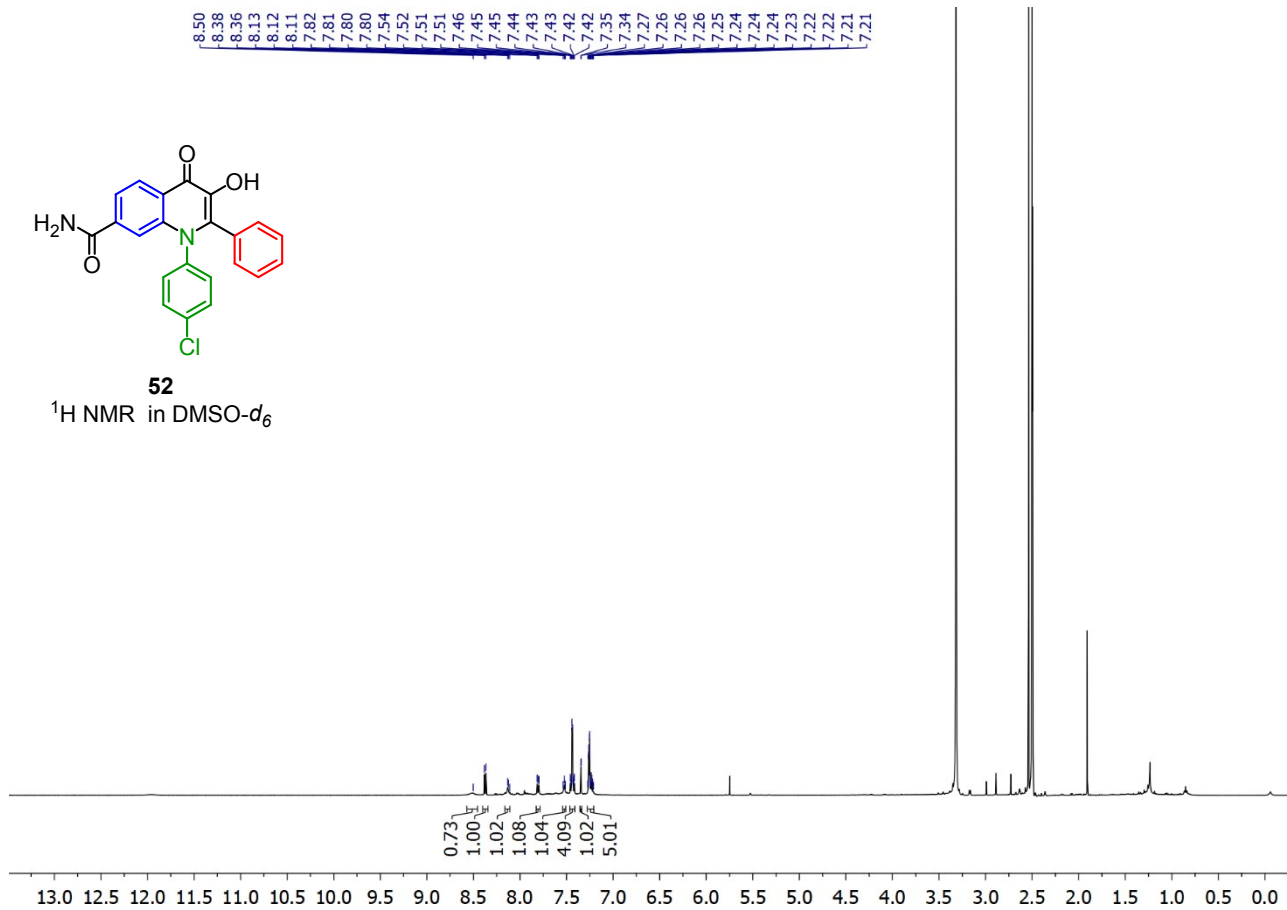
^1H NMR in $\text{DMSO-}d_6$

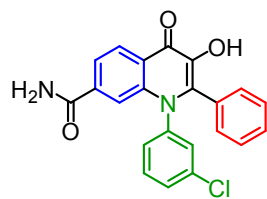


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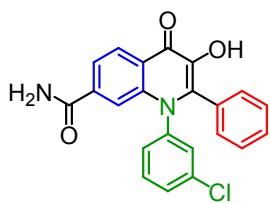
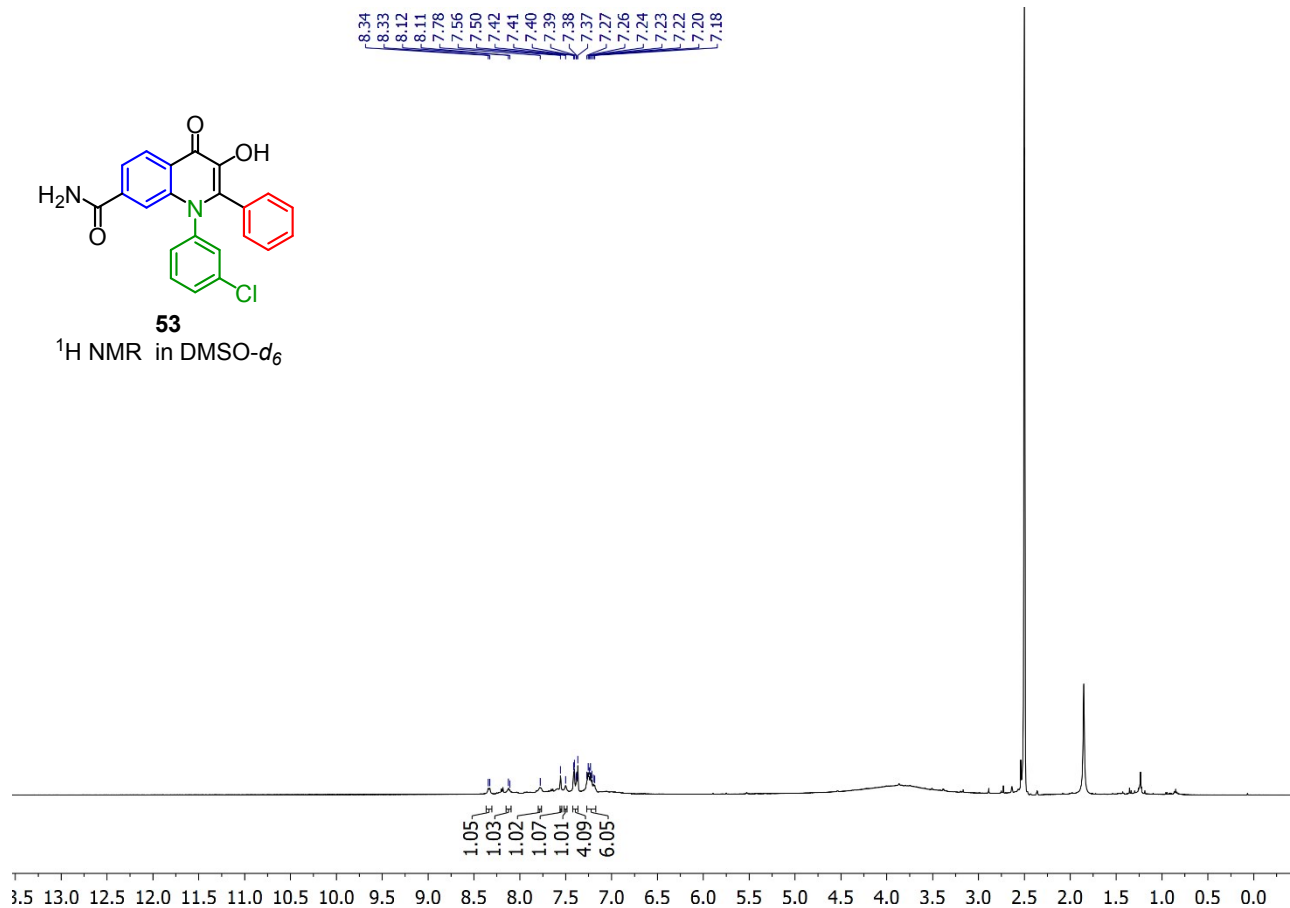
^{13}C NMR in $\text{DMSO-}d_6$



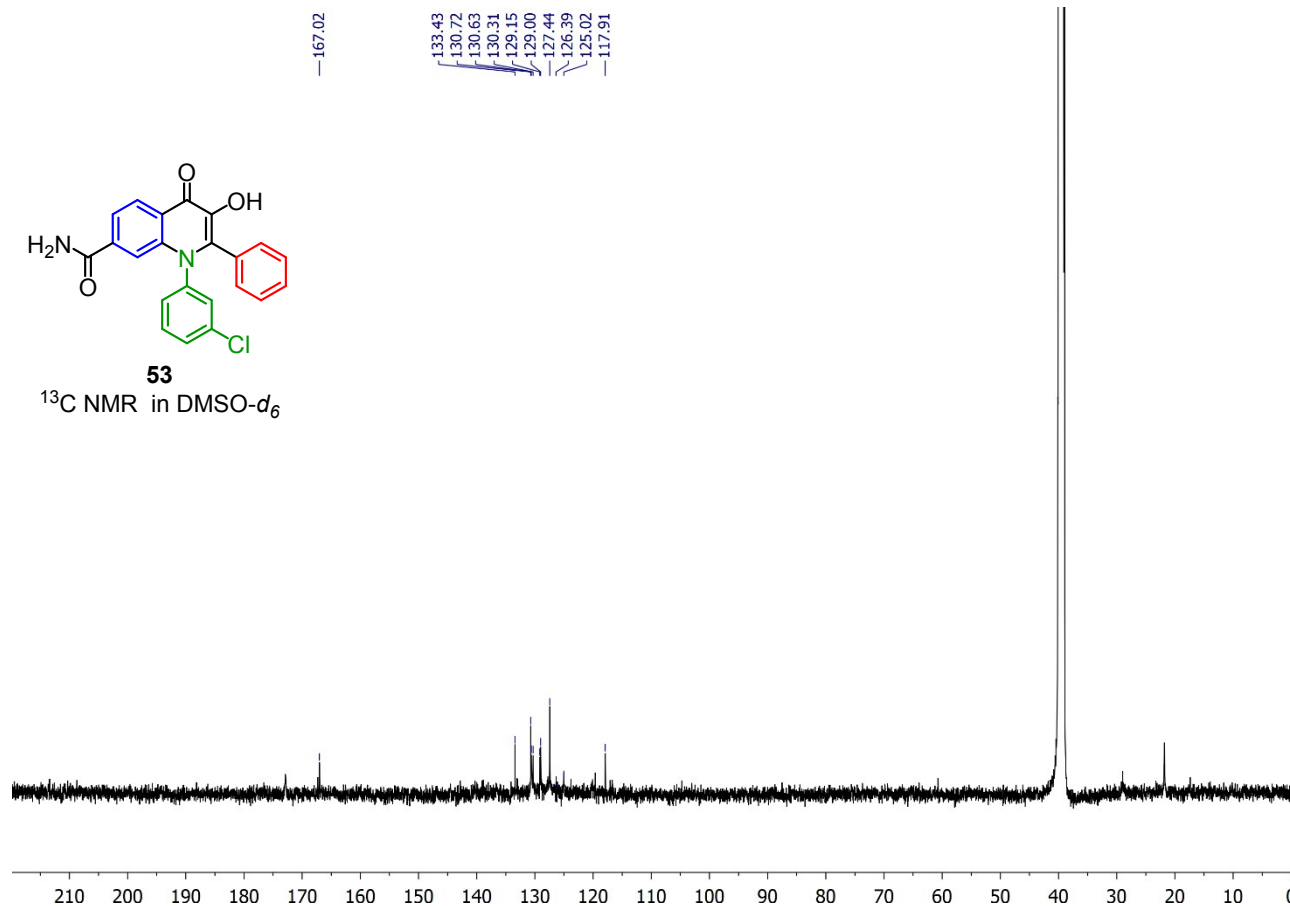


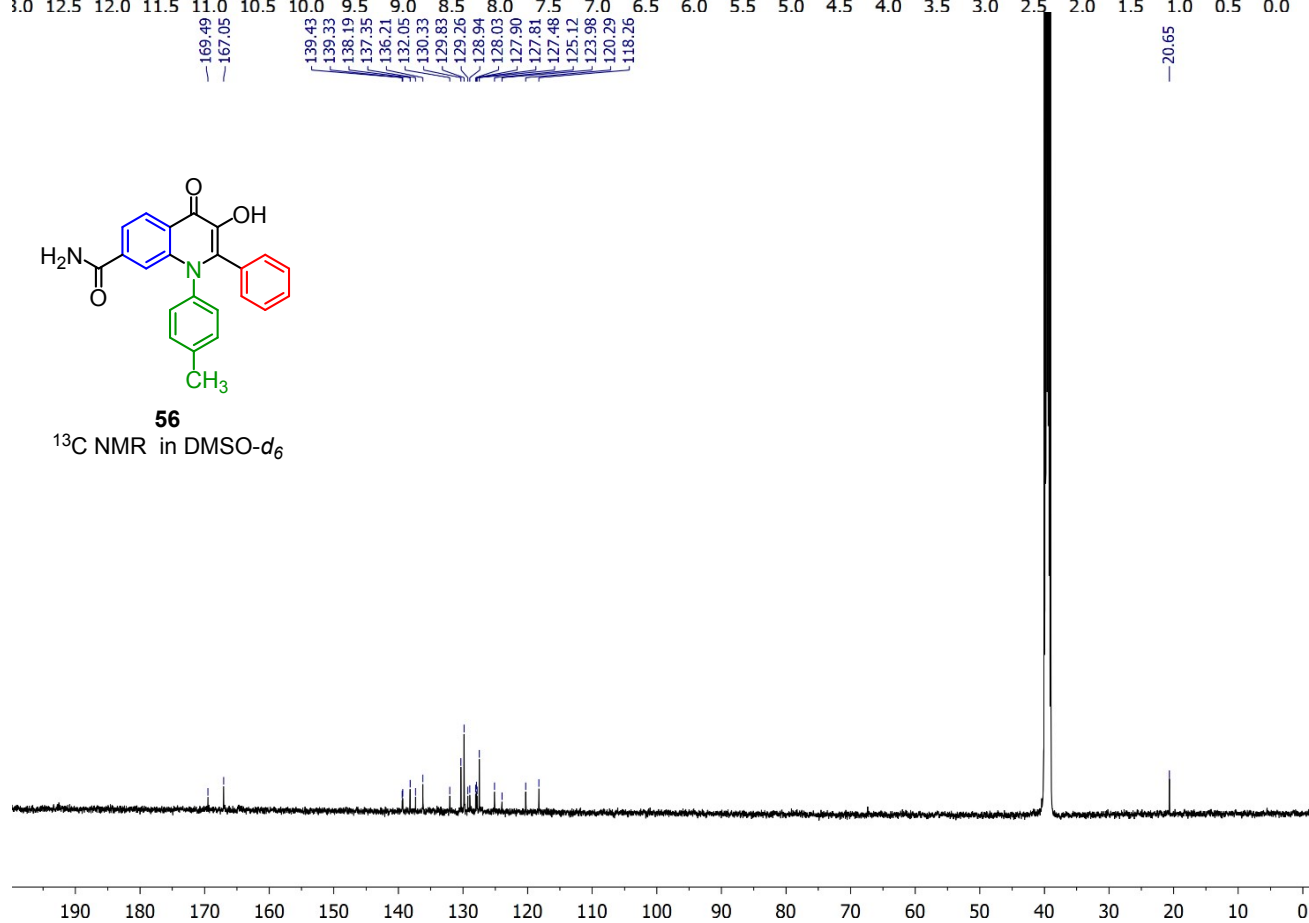
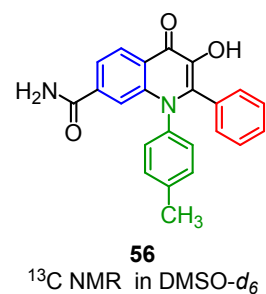
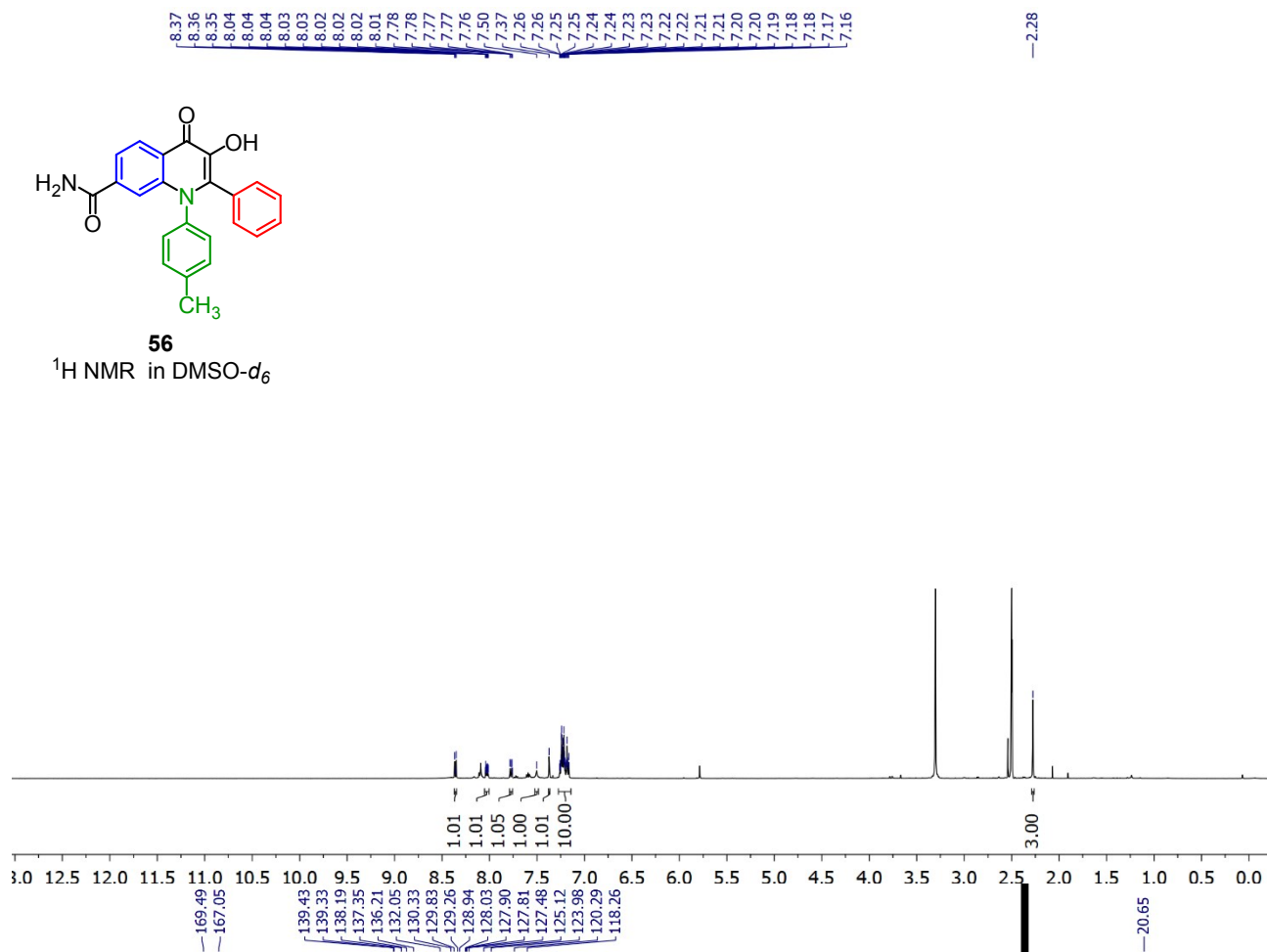
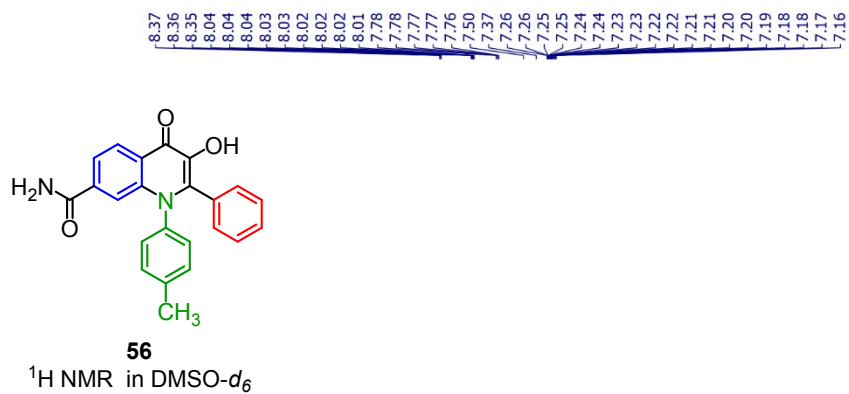


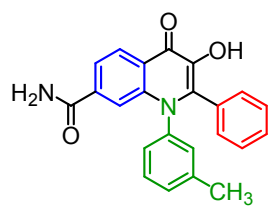
53
 $^1\text{H NMR}$ in $\text{DMSO-}d_6$



53
 $^{13}\text{C NMR}$ in $\text{DMSO-}d_6$





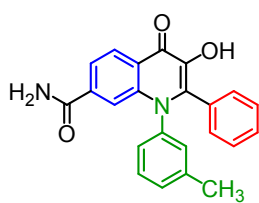
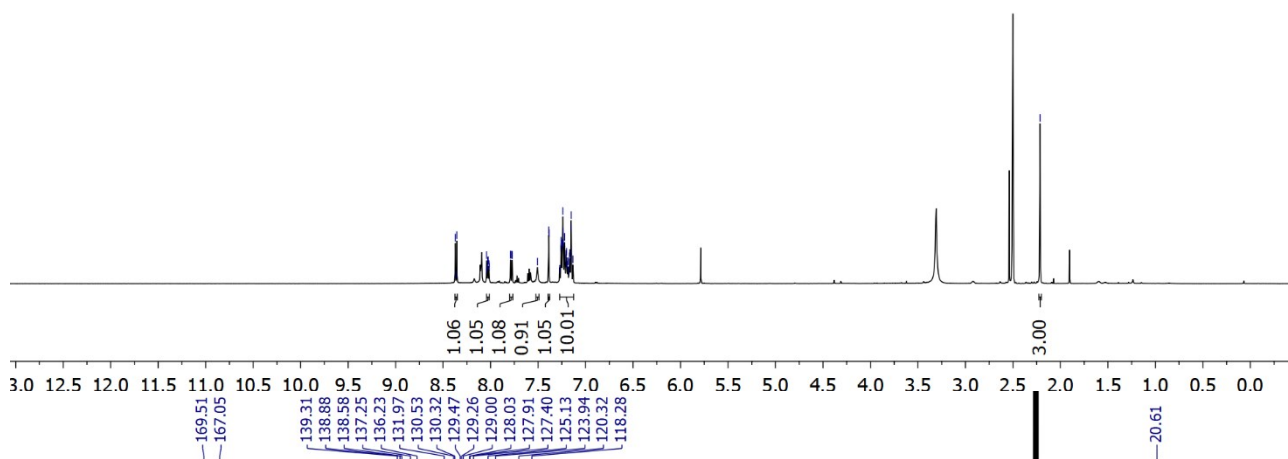


57

¹H NMR in DMSO-*d*₆

8.37
8.36
8.36
8.04
8.04
8.03
8.03
8.03
8.02
8.01
7.79
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7.77
7.77
7.51
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7.15

-2.21

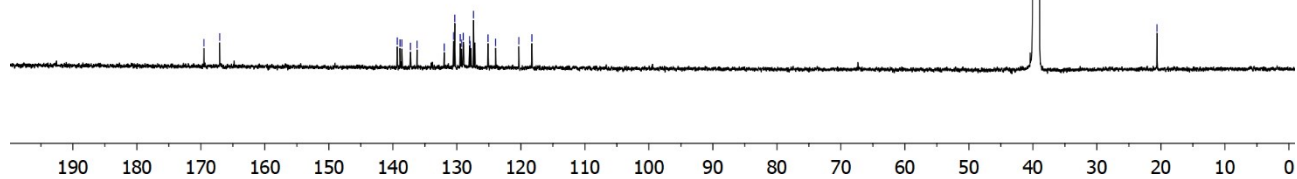


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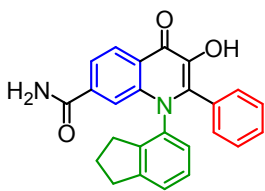
¹³C NMR in DMSO-*d*₆

169.51
167.05
139.31
138.88
138.58
137.25
136.23
131.97
130.53
130.32
129.47
129.26
129.00
128.03
127.91
127.40
125.13
123.94
120.32
118.28

-20.61

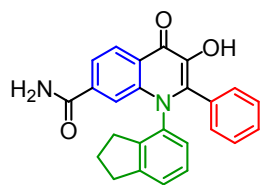
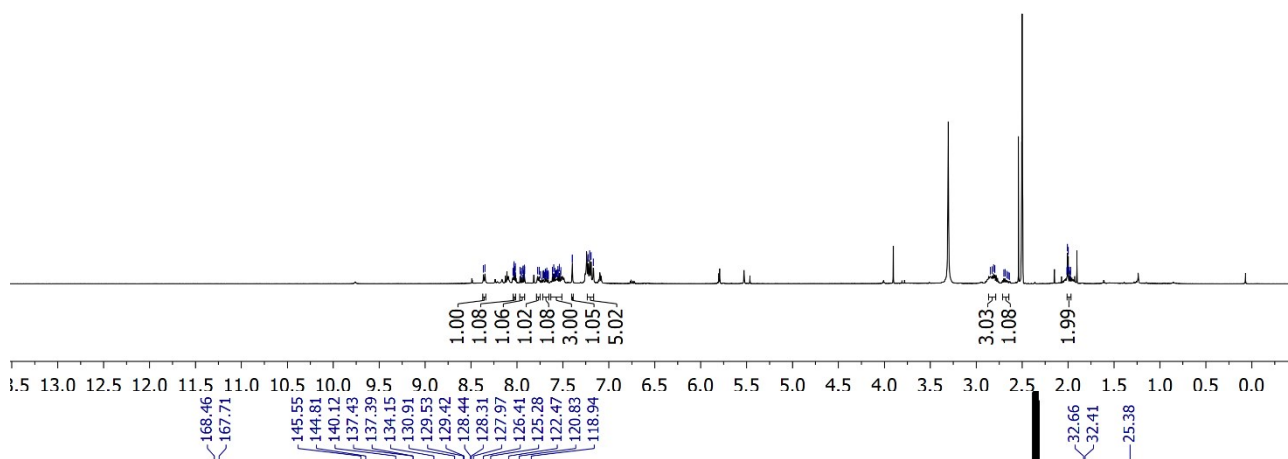


8.36
8.35
8.04
8.04
8.03
8.03
8.03
8.02
8.02
8.02
7.97
7.95
7.95
7.93
7.93
7.93
7.92
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7.92
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7.78
7.74
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7.67
7.66
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7.62
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7.19
7.19
7.17
2.85
2.83
2.81
2.80
2.70
2.68
2.67
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2.01
2.00
2.00
1.99
1.98
1.98
1.97



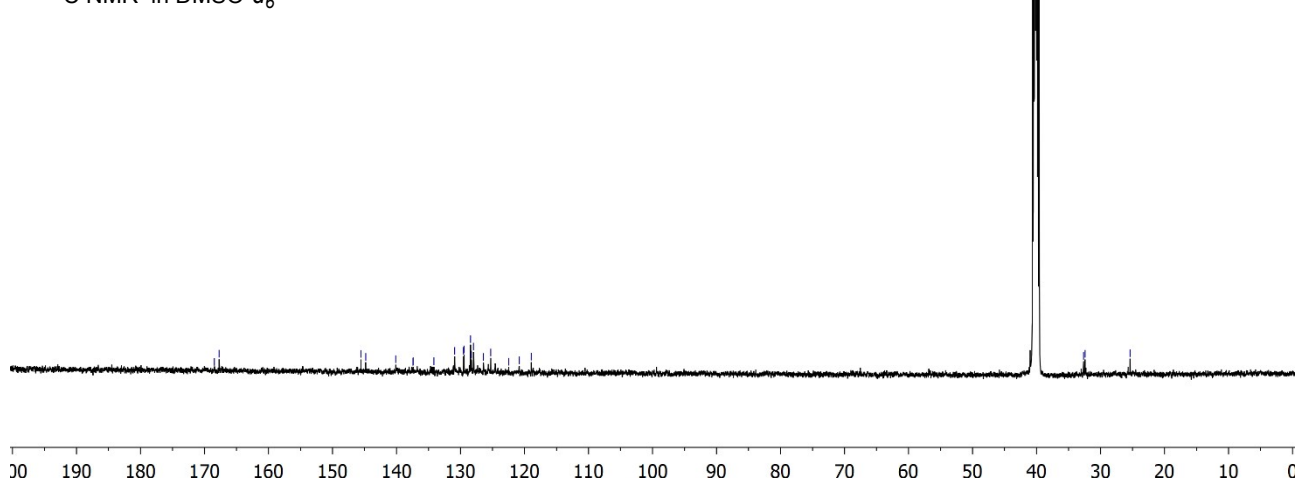
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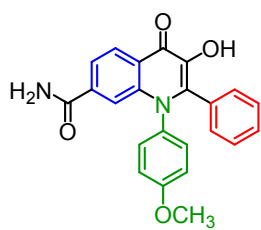
$^1\text{H NMR}$ in $\text{DMSO-}d_6$



58

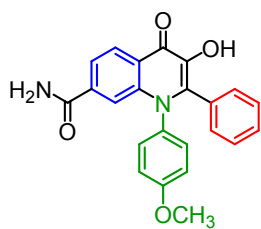
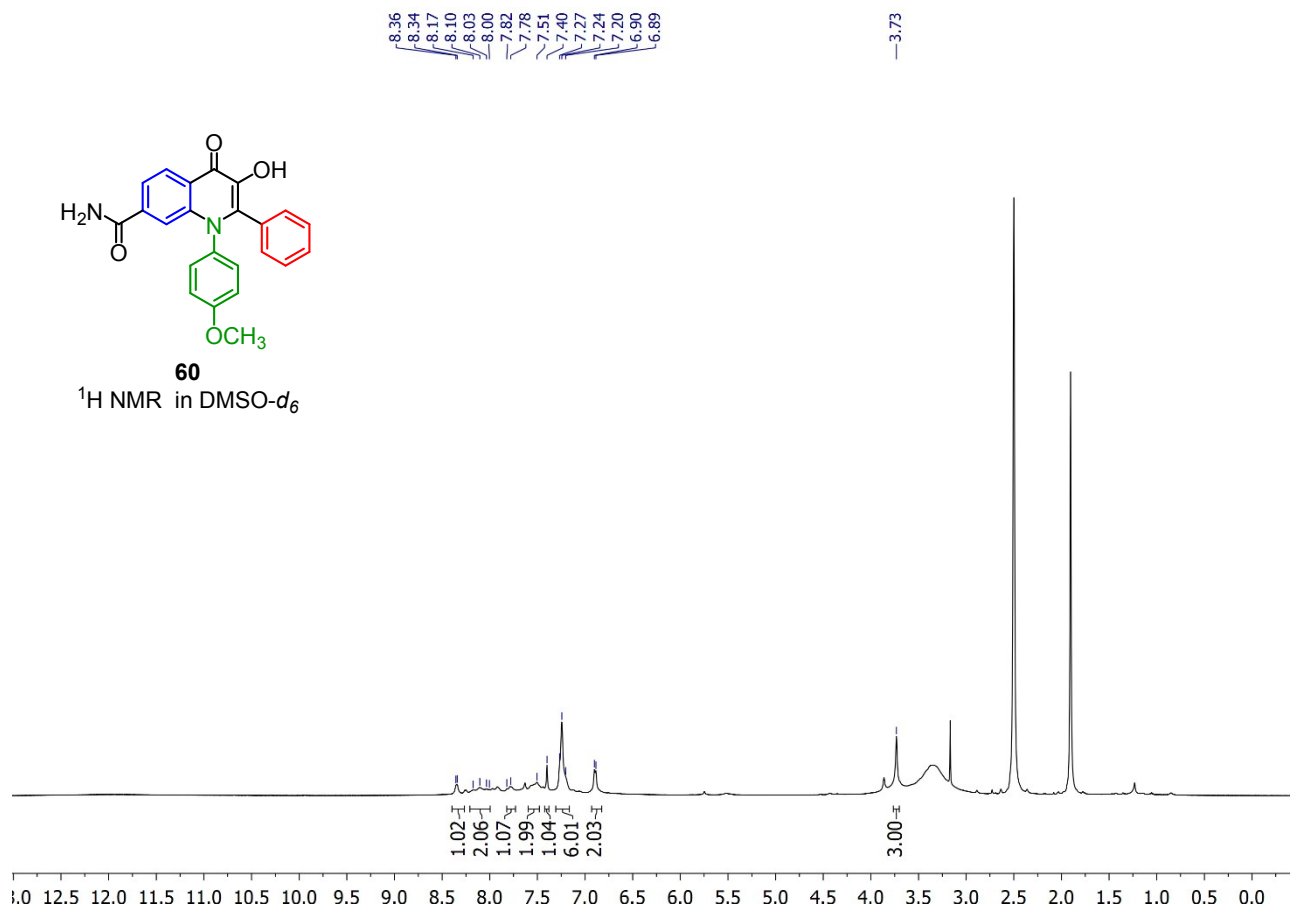
$^{13}\text{C NMR}$ in $\text{DMSO-}d_6$





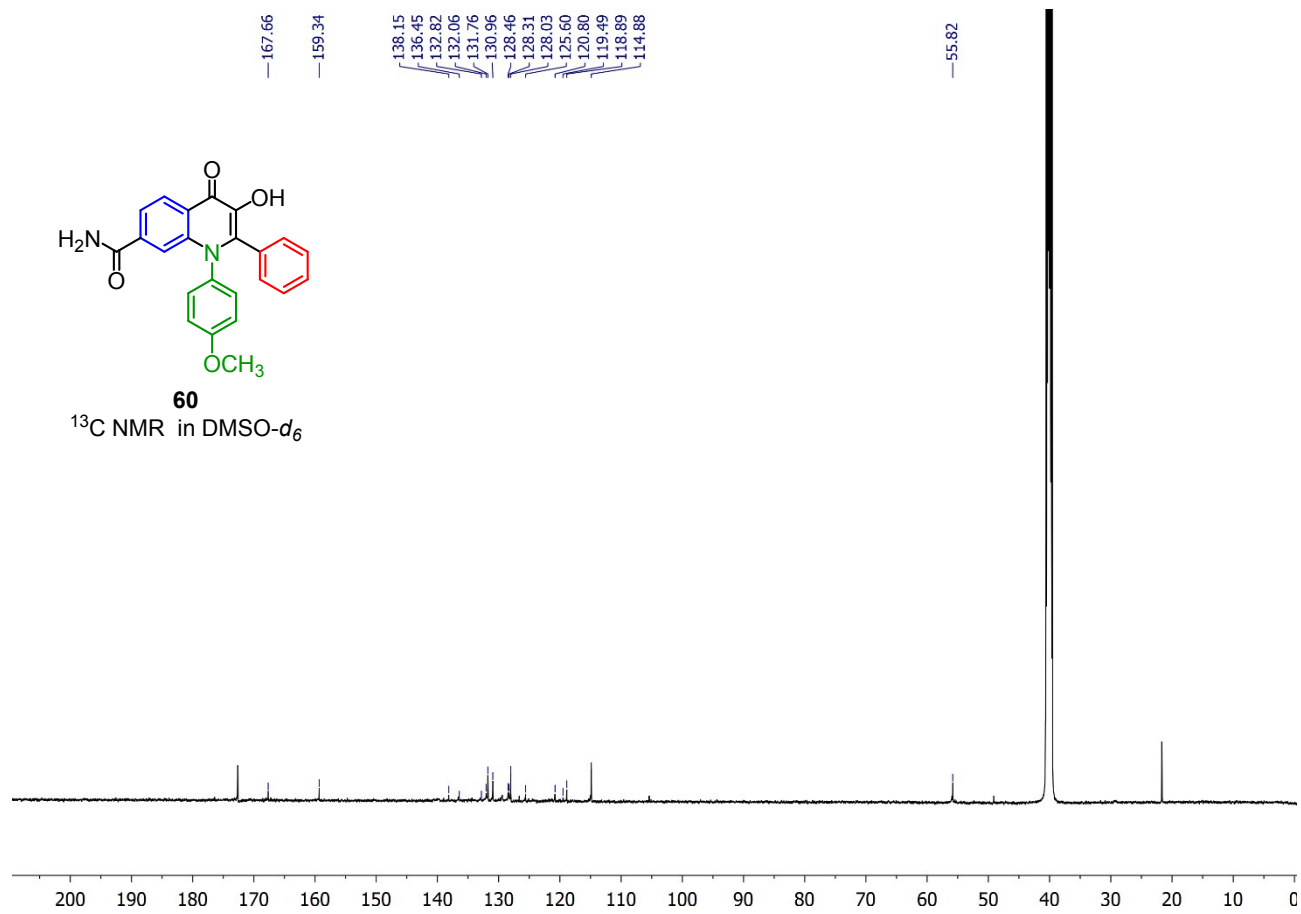
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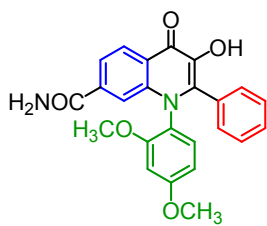
¹H NMR in DMSO-*d*₆



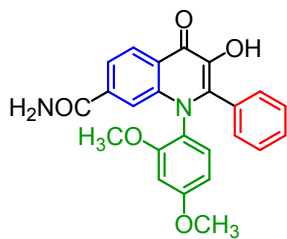
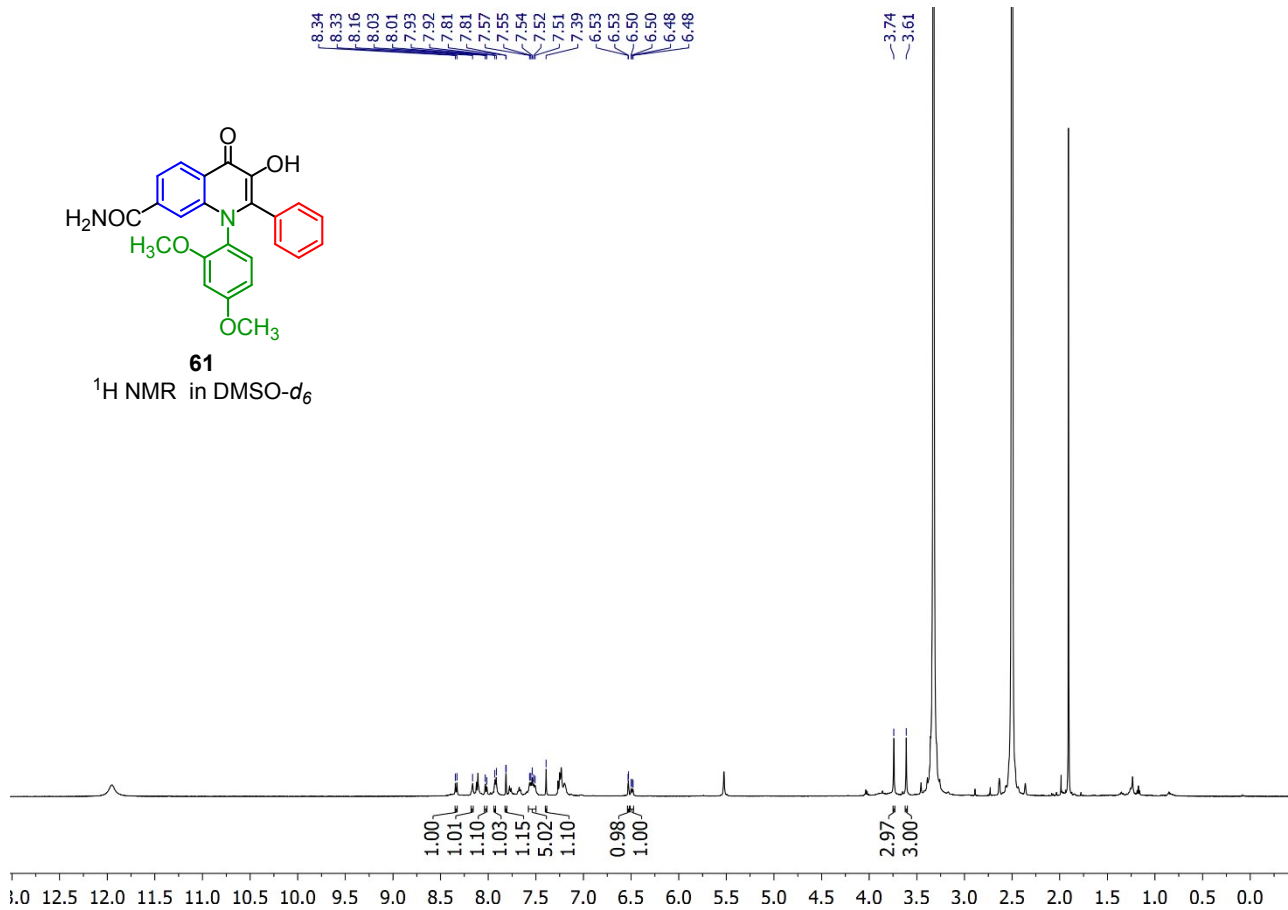
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¹³C NMR in DMSO-*d*₆

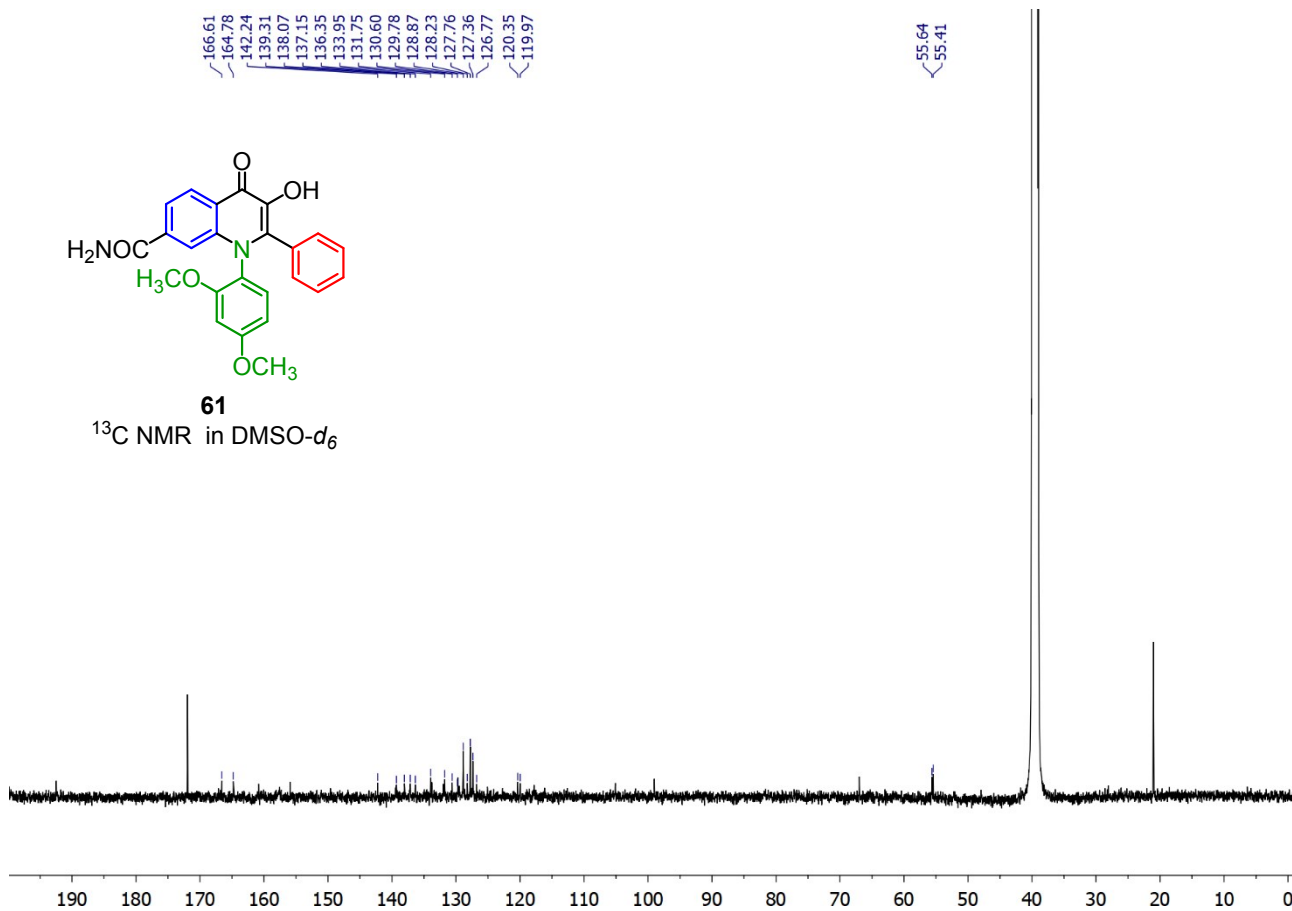




61
 ^1H NMR in $\text{DMSO-}d_6$



61
 ^{13}C NMR in $\text{DMSO-}d_6$



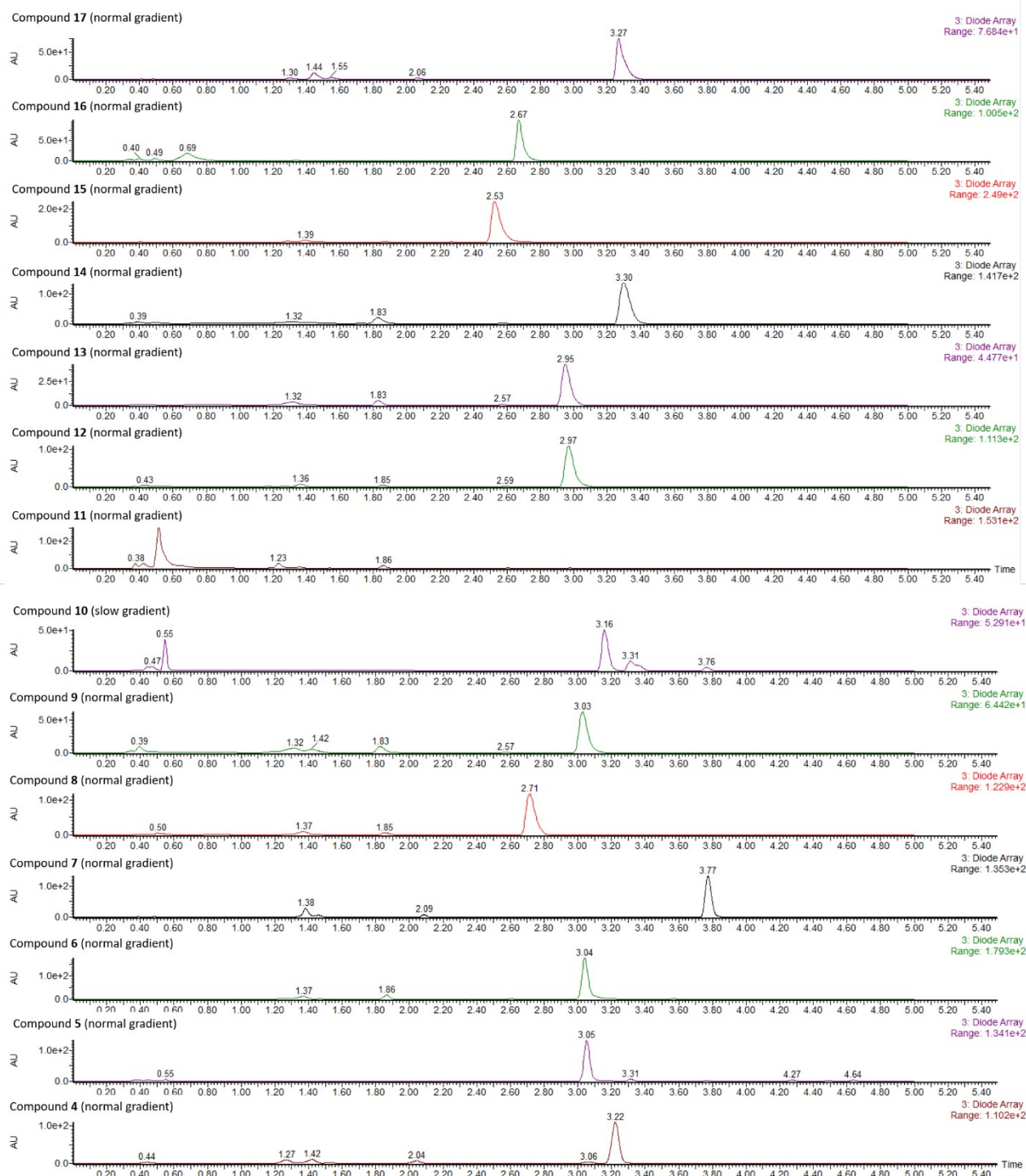


Figure S-1. UHPLC-UV chromatograms of intermediates 4–17 after Buchwald-Hartwig amination. (4, ESI+ = 271; 5, ESI+ = 361; 6, ESI+ = 304; 7, ESI+ = 304; 8, ESI+ = 289; 9, ESI+ = 339; 10, ESI+ = 315; 11, ESI+ = 315; 12, ESI+ = 285; 13, ESI+ = 285; 14, ESI+ = 311; 15, ESI+ = 356; 16, ESI+ = 301; 17, ESI+ = 331)

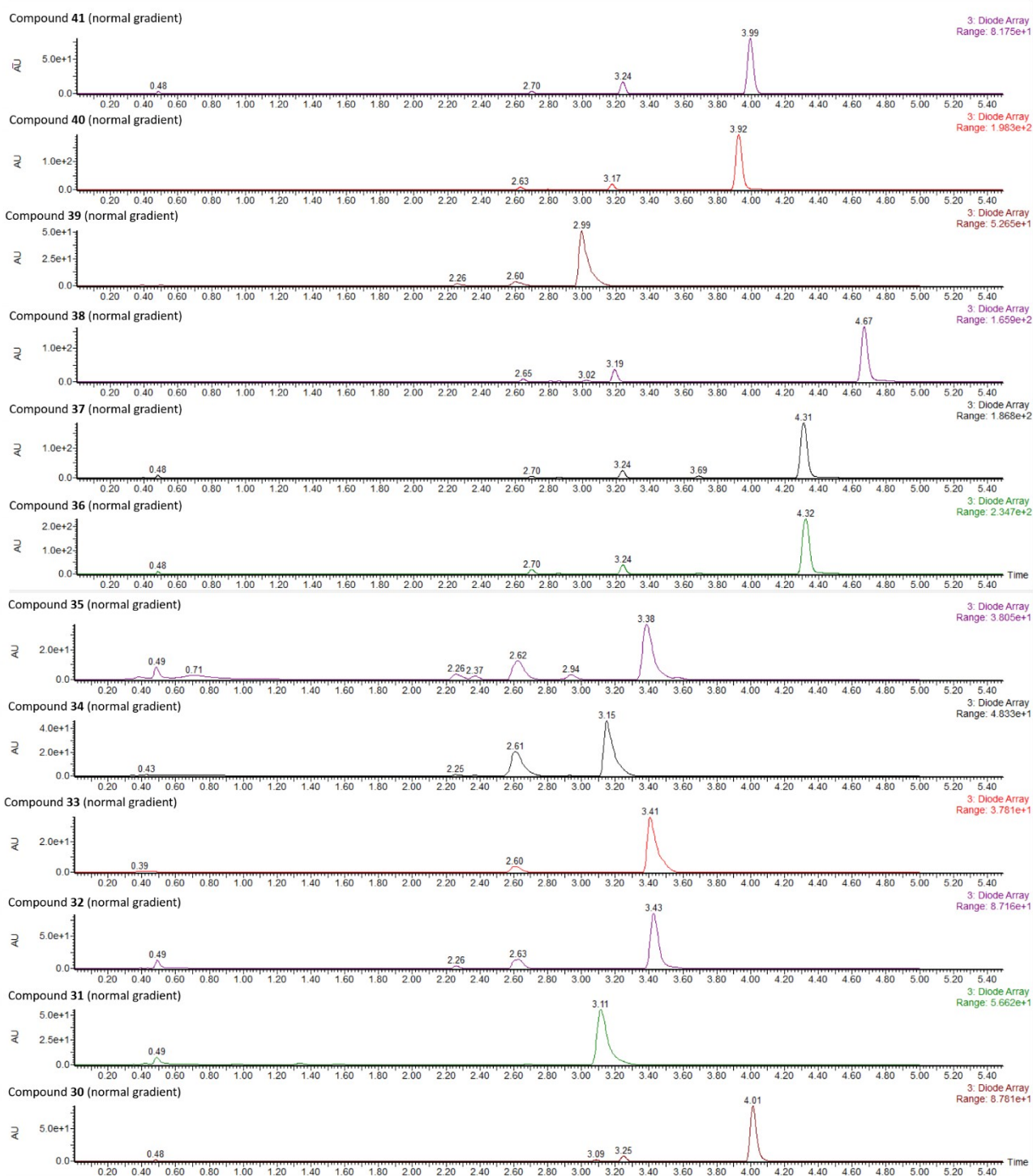


Figure S-2. UHPLC-UV chromatograms of intermediates **30–41** after alkylation to phenacyl esters. (**30**, ESI+ = 375; **31**, ESI+ = 465; **32**, ESI+ = 409; **33**, ESI+ = 409; **34**, ESI+ = 394; **35**, ESI+ = 443; **36**, ESI+ = 389; **37**, ESI+ = 389; **38**, ESI+ = 415; **39**, ESI+ = 460; **40**, ESI+ = 405; **41**, ESI+ = 435)

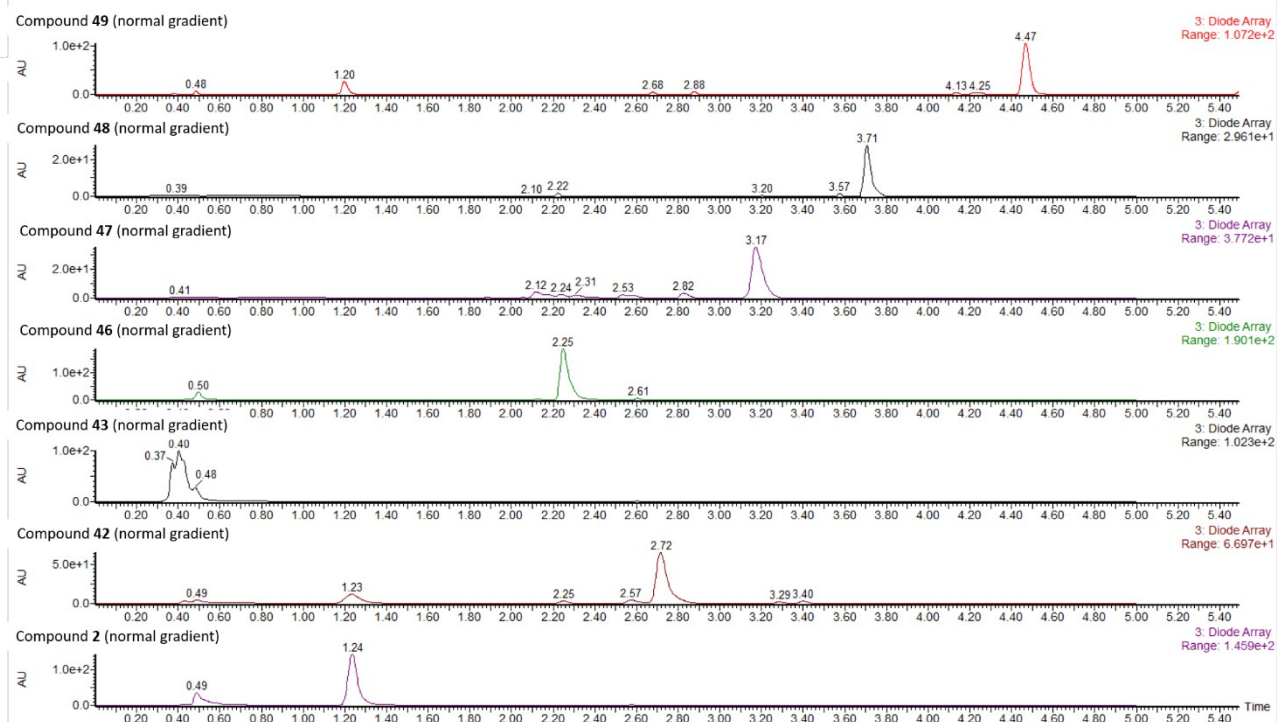


Figure S-3. UHPLC-UV chromatograms of intermediates **2**, **42**, **43**, **46–49** after reductive amination. (**2**, ESI+ = 196; **42**, ESI+ = 285; **43**, ESI+ = 271; **46**, ESI+ = 299; **47**, ESI+ = 389; **48**, ESI+ = 395; **49**, ESI+ = 369).

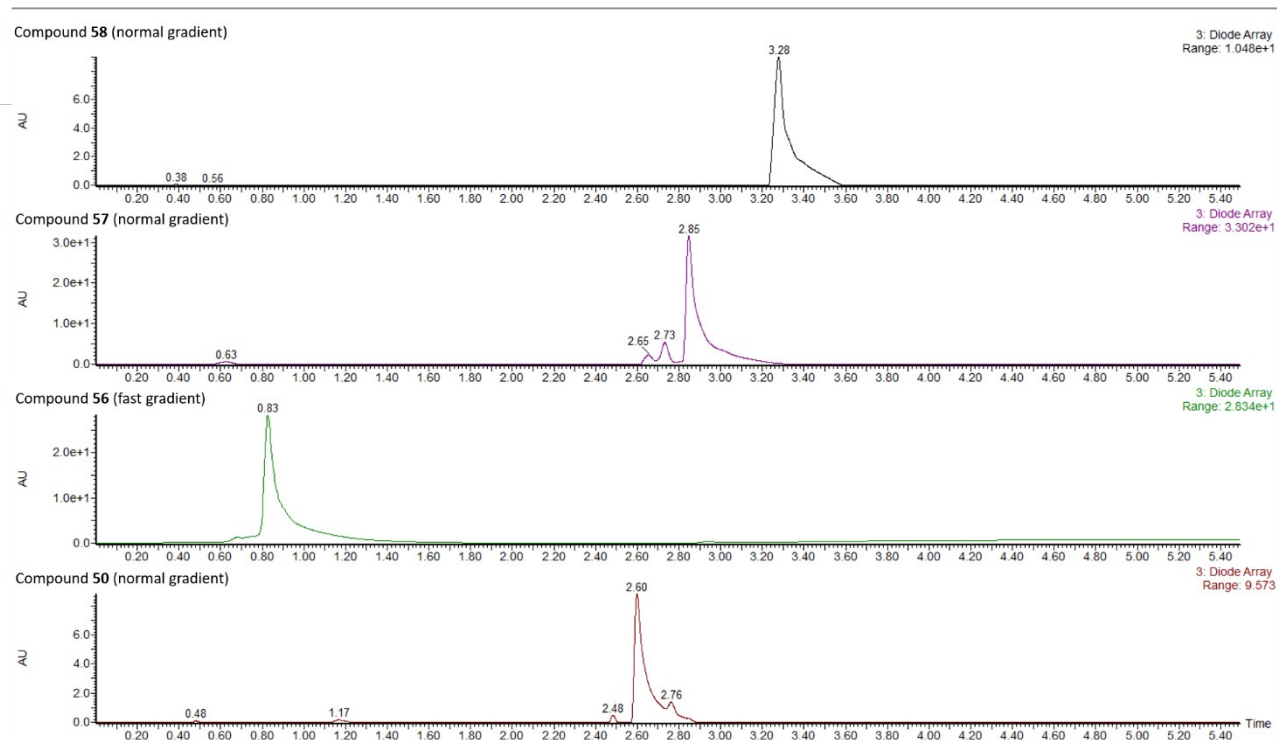


Figure S-4. UHPLC-UV chromatograms of final compounds **50**, **56–58**.

References

- [1.] P. Gobbo, P. Gunawardene, W. Luo, M. S. Workentin, *Synlett*, **2015**, *26*, 1169-1174.

