

Enantioselective Tandem Reaction of Chromone-Derived Morita-Baylis-Hillman Carbonates with Benzylamines catalyzed by a Trifunctional Organocatalyst: The Synthesis of Chiral 3-aminomethylene-Flavanones

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Supplementary Information

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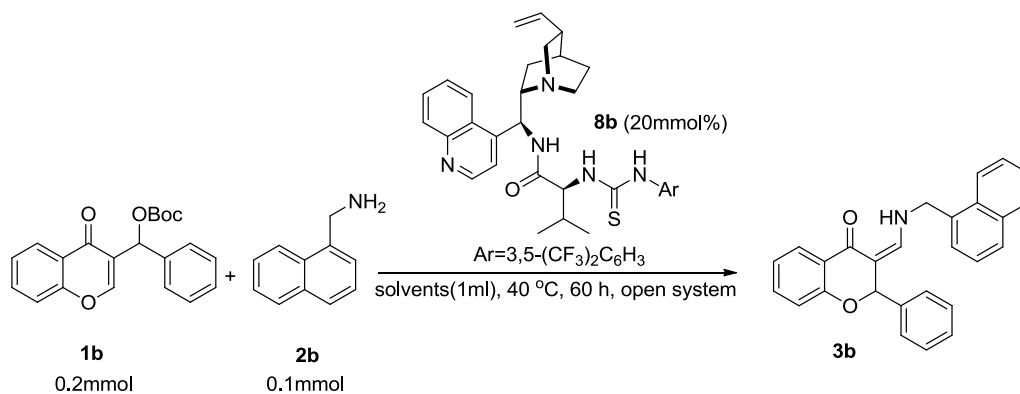
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1. General methods

Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. Cinchona alkaloid based catalysts **4-6**,^[1] **7**^[2], **8-9**^[3] and all the substrates^[4,5] were prepared according to original or modified literature procedures. All reactions were carried out directly in air atmosphere, unless otherwise noted. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s= singlet, d= doublet, t= triplet, q= quartet, h= heptet, m= multiplet, br= broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). IR spectra were recorded on a Bruker tensor 27 infrared spectrometer. Melting points were measured on Beijing Tech X-4 apparatus without correction. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. Optical rotations were measured using a 1 mL cell with a 1 dm path length and are reported as follows: $[\alpha]_D^{25}$ (c in g per 100 mL of solvent). HPLC analysis was performed using ChiralPak columns purchased. Column chromatography was performed using silica gel (200-300 mesh). TLC was performed on glass-backed silica plates.

2. Experimental section

2.1 Solvent Screening for the Reaction of **1b** and **2b**



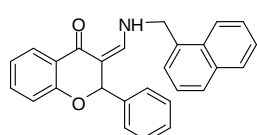
Entry	Solvents	Product	Yield ^a (%)	Ee ^b (%)
1	xylene	3b	--	63
2	EtOAc	3b	32	57
3	THF	3b	17	45
4	DCE	3b	30	59

^aIsolated yield. ^b Determined by chiral HPLC analysis.

2.2. General procedure for the reaction of Morita-Baylis-Hillman Carbonate **1** with amine **2**.

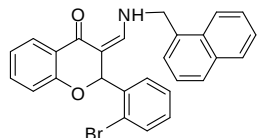
To the mixture of Morita-Baylis-Hillman Carbonate (0.2mmol) and amine **2** (0.1 mmol) in 1.0 mL toluene, catalyst **8d** (0.02 mmol, 11.3 mg) was added. Then, the reaction system was stirred for about 60h at 40°C in open system. The column chromatography on silica gel was flashed by petroleum ether and triethylamine with 20:1 first, then the crude reaction mixture was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate,10-16:1) to afford the desired products.

(Z)-3-((naphthalen-1-ylmethylamino)methylene)-2-phenylchroman-4-one (**3b**)



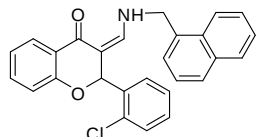
yellow solid. yield 75%, ee 82%. $[\alpha]_D^{20}$ -33.9 (*c* 0.56, CHCl₃). m.p. 164-166°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.51-10.47 (t, *J*=5.7Hz, 1H), 7.91-7.56 (m, 4H), 7.56-7.49 (m, 2H), 7.44-7.30 (m, 8H), 7.03-6.98 (t, *J*=7.2Hz, 1H), 6.94-6.91 (d, *J* = 8.1Hz, 1H), 6.42-6.37 (d, *J*=12.6Hz, 1H), 5.96 (s, 1H), 4.80-4.78 (d, *J* = 5.7Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ : 182.3, 158.7, 151.4, 139.4, 134.0, 133.8, 132.7, 130.7, 129.0, 128.7, 128.5, 128.5, 127.8, 126.7, 126.4, 126.1, 125.5, 125.5, 124.0, 122.6, 121.5, 117.6, 102.6, 81.2, 50.51. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1642, 1601, 1509, 1217, 767. HRMS (ESI): calcd for C₂₇H₂₁NO₂ [M+H]⁺ 392.1645, found: 392.1639. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 0.7 mL·min⁻¹, *t_R* = 28.7 min (minor), 49.6 min (major)].

(Z)-2-(2-bromophenyl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (**3c**)



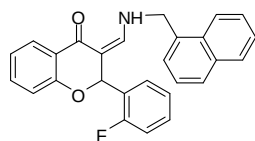
white solid. yield 64%, ee 86%. $[\alpha]_D^{20}$ -146.0 (*c* 0.36, CHCl₃). m.p. 158-160°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.51-10.47 (t, *J*=6.0Hz, 1H), 7.95-7.94 (d, *J*=1.8Hz, 1H), 7.92-7.78 (m, 3H), 7.65-7.62 (dd, *J*=1.5Hz, *J*=7.8Hz, 1H), 7.53-7.49 (m, 3H), 7.43-7.31 (m, 4H), 7.21-7.18 (dd, *J*=1.5Hz, *J*=7.5Hz, 1H), 7.08-7.03 (t, *J*=7.5Hz 1H), 6.95-6.92 (d, *J*=3.6Hz, 1H), 6.32 (s, 1H), 6.23-6.19 (d, *J*=12.6Hz, 1H), 4.78-4.76 (d, *J*=5.7Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ : 182.5, 158.9, 151.2, 138.3, 133.9, 133.8, 132.6, 132.5, 130.8, 129.8, 129.5, 128.9, 128.7, 127.9, 126.7, 126.5, 126.0, 125.6, 125.4, 124.0, 123.1, 122.6, 121.7, 117.4, 101.0, 80.0, 50.5. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1643, 1602, 1463, 1217, 769. HRMS (ESI): calcd for C₂₇H₂₀BrNO₂ [M+H]⁺ 470.0750, found: 470.0743. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.2 mL·min⁻¹, *t_R* = 17.0 min (minor), 38.5 min (major)].

(Z)-2-(2-chlorophenyl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (**3d**)



white solid. yield 65%, ee 84%. $[\alpha]_D^{20}$ -97.2 (*c* 0.37, CHCl₃). m.p. 135-137°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.50-10.48 (t, *J*=5.4Hz, 1H), 7.95-7.92 (d, *J*=7.5Hz, 1H), 7.88-7.85 (t, 1H), 7.80-7.78 (d, 2H), 7.63-7.61 (d, *J*=6.3Hz, 1H), 7.52-7.49 (t, 2H), 7.43-7.32 (m, 4H), 7.28-7.25 (t, 2H), 7.07-7.02 (t, *J*=7.5Hz, 1H), 6.94-6.91 (d, *J*=8.1Hz, 1H), 6.37 (s, 1H), 6.25-6.21 (d, *J*=12.6Hz, 1H), 4.77-4.76 (d, *J*=5.4Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ : 182.5, 158.9, 151.1, 136.7, 133.9, 133.7, 133.0, 132.5, 130.8, 129.5, 129.3, 129.2, 128.9, 128.7, 127.3, 126.7, 126.5, 126.0, 125.6, 125.4, 124.0, 122.6, 121.7, 117.4, 101.0, 77.7, 50.5. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1648, 1607, 1464, 1202, 756. HRMS (ESI): calcd for C₂₇H₂₀ClNO₂ [M+H]⁺ 426.1255, found: 426.1250. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.0 mL·min⁻¹, *t_R* = 20.0 min (minor), 44.6 min (major)].

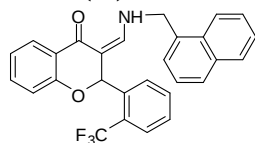
(Z)-2-(2-fluorophenyl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (3e)



yellow solid. yield 64%, ee 79%. $[\alpha]_D^{20}$ -27.8 (c 0.18, CHCl₃). m.p. 172-174°C. ¹H NMR (300 MHz, CDCl₃) δ: 10.52-10.48 (t, *J*=6.0Hz, 1H), 7.93-7.78 (m, 4H), 7.53-7.43 (m, 3H), 7.41-7.33 (m, 3H), 7.30-7.27 (m, 1H), 7.12-7.00 (m, 3H), 6.92-6.89 (d, *J*=8.1Hz, 1H), 6.46-6.42 (d, *J*=12.6Hz, 1H), 6.32 (s, 1H), 4.80-4.78 (d, *J*=5.7Hz, 2H).

¹³C NMR (75 MHz, CDCl₃) δ: 182.2, 160.2 (d, ¹*J*_{CF}=246.7Hz), 158.7, 151.0, 134.0, 133.7, 132.6, 130.7, 130.1 (d, ²*J*_{CF}=8.3Hz), 129.2 (d, ³*J*_{CF}=3.4Hz), 129.0, 128.7, 126.7, 126.6, 126.5, 126.1, 125.5, 125.5, 124.4 (d, ³*J*_{CF}=3.5Hz), 123.8, 122.5, 121.7, 117.4, 115.4 (d, ²*J*_{CF}=21.4Hz), 101.1, 74.7 (d, ³*J*_{CF}=3.6Hz), 50.5. IR ν_{max} (KBr, film, cm⁻¹): 1644, 1603, 1462, 1218, 761. HRMS (ESI): calcd for C₂₇H₂₀FNO₂ [M+H]⁺ 410.1551; found: 410.1543. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.0 mL·min⁻¹, t_R = 22.1 min (minor), 43.7 min (major)].

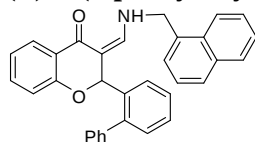
(Z)-3-((naphthalen-1-ylmethylamino)methylene)-2-(2-(trifluoromethyl)phenyl)chroman-4-one (3f)



yellow solid. yield 80%, ee 85%. $[\alpha]_D^{20}$ -41.0 (c 0.49, CHCl₃). m.p. 149-151°C. ¹H NMR (300 MHz, CDCl₃) δ: 10.47-10.43 (t, *J*=6.3Hz, 1H), 7.88-7.87 (d, *J*=1.2Hz, 1H), 7.85-7.67 (m, 4H), 7.57-7.54 (d, *J*=7.8Hz, 1H), 7.45-7.41 (m, 3H), 7.37-7.24 (m, 3H), 7.22-7.18 (d, *J*=11.7Hz, 1H), 7.00-6.96 (t, *J*=7.2Hz, 1H), 6.85-6.82 (d, *J*=5.4Hz, 1H), 6.31 (s, 1H), 6.97-6.93 (d, *J*=12.6Hz, 1H), 4.67-4.65 (d, *J*=5.7Hz, 2H).

¹³C NMR (75 MHz, CDCl₃) δ: 182.1, 158.8, 151.6, 137.7, 137.7 134.0, 133.7, 132.4, 132.3, 130.7, 129.9, 128.9, 128.8, 128.6, 128.2, 126.7, 126.5, 126.1, 125.6, 125.4(q, ²*J*_{CF} =6.5Hz), 125.4, 124.0(), 124.0(q, ¹*J*_{CF} =271.5Hz), 122.5, 121.8, 117.4, 102.9, 50.5. IR ν_{max} (KBr, film, cm⁻¹): 1644, 1603, 1464, 1294, 1122, 765. HRMS (ESI): calcd for C₂₈H₂₀F₃NO₂ [M+H]⁺ 460.1519, found:460.1513. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.3 mL·min⁻¹, t_R = 10.8 min (minor),34.6 min (major)].

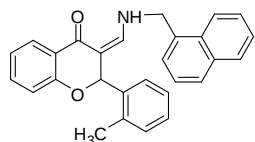
(Z)-2-(biphenyl-2-yl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (3g)



yellow solid. yield 84%, ee 89%. $[\alpha]_D^{20}$ -109.0 (c 0.19, CHCl₃). m.p. 155-157°C. ¹H NMR (300 MHz, CDCl₃) δ: 10.47-10.43 (t, *J*=6.0Hz, 1H), 7.88-7.83 (t, 2H), 7.81-7.76 (t, 2H), 7.72-7.69 (t, 1H), 7.51-7.48 (t, 2H), 7.41-7.36 (m, 3H), 7.32-6.7.20 (m, 6H), 7.13 (s, 1H), 7.12 (s, 1H), 6.99-6.94 (t, *J*=5.4Hz, 1H), 6.87-6.84 (d, *J*=5.4Hz, 1H), 6.27-6.23 (d, *J*=12.6Hz, 1H), 6.02 (s, 1H) 4.79-4.64 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ: 182.7, 159.3, 151.6, 141.8, 140.1, 135.9, 133.9, 133.8, 132.8, 130.0, 129.0, 128.8, 128.8, 128.8, 128.5, 128.3, 128.2, 128.0 127.5, 126.8, 126.5, 126.1, 125.8, 125.4, 124.0, 122.7, 121.5, 117.4, 103.6, 78.4, 50.4. IR ν_{max} (KBr, film, cm⁻¹): 1647, 1605, 1463, 1276, 755. HRMS (ESI): calcd for C₃₃H₂₅NO₂ [M+H]⁺ 468.1958, found:468.1952. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.3 mL·min⁻¹, t_R = 15.8 min (minor), 49.5 min (major)].

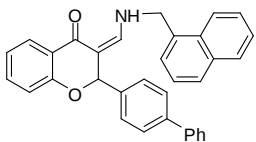
(Z)-3-((naphthalen-1-ylmethylamino)methylene)-2-o-tolylchroman-4-one (3h)



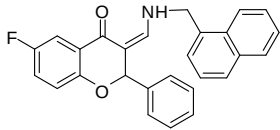
yellow solid. yield 72%, ee 89%. $[\alpha]_D^{20}$ -35.0 (c 0.29, CHCl₃). m.p. 138-140°C. ¹H NMR (300 MHz, CDCl₃) δ: 10.44-10.40 (t, *J*=6Hz, 1H), 7.95-7.92 (d, *J*=7.5Hz, 1H), 7.87-7.84 (t, 1H), 7.79-7.77 (d, 2H),

7.51-7.45 (m, 3H), 7.41-7.30 (m, 3H), 7.24-7.20 (m, 2H), 7.12-7.10 (t, 1H), 7.05-7.00 (t, $J=7.5\text{Hz}$, 1H), 6.93-6.90 (d, $J=8.4\text{Hz}$, 1H), 6.18-6.13 (d, 2H), 4.72-4.70 (d, $J=5.4\text{Hz}$, 2H), 2.24 (s, 3H), ^{13}C NMR (75 MHz, CDCl_3) δ : 182.9, 159.3, 150.8, 136.6, 136.1, 133.9, 133.8, 132.7, 130.7, 130.6, 129.0, 128.7, 128.3, 128.0, 126.7, 126.5, 126.3, 126.0, 125.6, 125.4, 124.1, 122.6, 121.5, 117.5, 101.8, 79.1, 50.4, 19.2. IR ν_{max} (KBr, film, cm^{-1}): 1641, 1604, 1462, 1218, 757. HRMS (ESI): calcd for $\text{C}_{28}\text{H}_{23}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 406.1802, found: 406.1795. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C , $1.0\text{ mL}\cdot\text{min}^{-1}$, t_{R} = 16.5 min (minor), 32.3 min (major)].

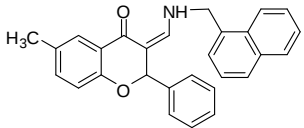
(Z)-2-(biphenyl-4-yl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (3i)

 yellow solid. yield 78%, ee 80%. $[\alpha]_{\text{D}}^{20}$ -47.9 (c 0.32, CHCl_3). m.p. 121-123 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 10.54-10.50 (t, $J=6.0\text{Hz}$, 1H), 7.92-7.90 (d, $J=7.5\text{Hz}$, 1H), 7.86 (s, 1H), 7.83 (s, 1H), 7.78-7.61 (d, $J=6.9\text{Hz}$, 1H), 7.59-7.35 (m, 14H), 7.04-6.99 (t, $J=7.5\text{Hz}$, 1H), 6.95-6.93 (d, $J=5.4\text{Hz}$, 1H), 6.47-6.43 (d, $J=12.6\text{Hz}$, 1H), 6.00 (s, 1H), 4.82-4.80 (d, $J=5.4\text{Hz}$, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ : 182.3, 158.7, 151.3, 141.3, 140.6, 138.4, 134.0, 133.8, 132.6, 130.8, 129.0, 128.8, 128.8, 128.2, 127.5, 127.2, 127.1, 126.7, 126.5, 126.1, 125.6, 125.4, 124.0, 122.6, 121.6, 117.6, 102.5, 81.0, 50.5. IR ν_{max} (KBr, film, cm^{-1}): 1644, 1605, 1465, 1217, 762. HRMS (ESI): calcd for $\text{C}_{33}\text{H}_{25}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 468.1958, found: 468.1952. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C , $0.8\text{ mL}\cdot\text{min}^{-1}$, t_{R} = 44.2 min (minor), 53.1 min (major)].

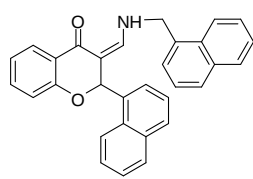
(Z)-6-fluoro-3-((naphthalen-1-ylmethylamino)methylene)-2-phenylchroman-4-one (3j)

 yellow solid. yield 61%, ee 82%. $[\alpha]_{\text{D}}^{20}$ -32.8 (c 0.32, CHCl_3). m.p. 147-149 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 10.53-10.49 (t, $J=6.0\text{Hz}$, 1H), 7.89-7.79 (m, 3H), 7.56-7.50 (m, 3H), 7.44-7.31 (m, 7H), 7.08-7.01 (m, 1H), 6.89-6.85 (dd, $J=4.2\text{Hz}$, $J=8.7\text{Hz}$, 1H), 6.43-6.39 (d, $J=12.9\text{Hz}$, 1H), 5.91 (s, 1H), 4.79-4.77 (d, $J=5.7\text{Hz}$, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ : 181.2 (d, $^4J_{\text{CF}}=1.65\text{Hz}$), 157.6 (d, $^1J_{\text{CF}}=238.8\text{Hz}$), 154.7 (d, $^3J_{\text{CF}}=1.58\text{Hz}$), 151.8, 139.2, 133.8, 132.6, 130.7, 129.0, 128.8, 128.6, 127.8, 126.8, 126.1, 125.6, 125.5, 124.8 (d, $^3J_{\text{CF}}=6.5\text{Hz}$), 122.6, 120.9 (d, $^2J_{\text{CF}}=24\text{Hz}$), 119.0, 118.9, 111.8 (d, $^2J_{\text{CF}}=23.4\text{Hz}$), 102.3, 81.3, 50.5. IR ν_{max} (KBr, film, cm^{-1}): 1644, 1562, 1450, 1239, 786. HRMS (ESI): calcd for $\text{C}_{27}\text{H}_{20}\text{FNO}_2$ $[\text{M}+\text{H}]^+$ 410.1556, found: 410.1544. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C , $1.0\text{ mL}\cdot\text{min}^{-1}$, t_{R} = 17.1 min (minor), 24.8 min (major)].

(Z)-6-methyl-3-((naphthalen-1-ylmethylamino)methylene)-2-phenylchroman-4-one (3k)

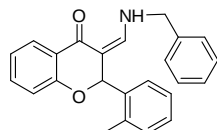
 white solid. yield 60%, ee 77%. $[\alpha]_{\text{D}}^{20}$ -38.0 (c 0.44, CHCl_3). m.p. 135-137 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 10.50-10.46 (t, $J=6.0\text{Hz}$, 1H), 7.89-7.81 (m, 3H), 7.78 (s, 1H), 7.68-7.48 (m, 2H), 7.44-7.30 (m, 7H), 7.18-7.14 (dd, $J=1.8\text{Hz}$, $J=8.4\text{Hz}$, 1H), 6.84-6.81 (d, $J=8.1\text{Hz}$, 1H), 6.41-6.37 (d, $J=12.6\text{Hz}$, 1H), 5.91 (s, 1H), 4.79-4.77 (d, $J=5.7\text{Hz}$, 2H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ : 182.6, 156.6, 151.3, 139.5, 134.9, 133.8, 132.8, 130.8, 130.7, 129.0, 128.7, 128.5, 128.4, 127.8, 126.7, 126.3, 126.1, 125.5, 125.4, 123.6, 122.6, 117.3, 102.8, 81.1, 50.5, 20.6. IR ν_{max} (KBr, film, cm^{-1}): 1645, 1616, 1443, 1225, 773. HRMS (ESI): calcd for $\text{C}_{28}\text{H}_{23}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 406.1802, found: 406.1795. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C , $1.0\text{ mL}\cdot\text{min}^{-1}$, t_{R} = 19.6 min (minor), 26.8 min (major)].

(Z)-2-(naphthalen-1-yl)-3-((naphthalen-1-ylmethylamino)methylene)chroman-4-one (3l)



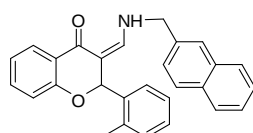
yellow solid. yield 87%, ee 85%. $[\alpha]_D^{20}$ -9.1 (c 0.22, CHCl₃). m.p. 190-193°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.52-10.48 (t, J =6.0Hz, 1H), 8.21-8.18 (d, J =8.1Hz, 1H), 7.98-7.95 (d, J =7.5Hz, 1H), 7.86-7.80 (t, 3H), 7.73-7.70 (d, J =8.1Hz, 1H), 7.66-7.61 (t, 2H), 7.49-7.39 (m, 5H), 7.35-7.28 (m, 2H), 7.23-7.18 (t, d, J =7.2Hz, 1H), 7.05-7.00 (t, d, J =7.5Hz, 1H), 6.90-6.87 (d, J =8.1Hz, 1H), 6.59 (s, 1H), 6.25-6.20 (d, J =12.6Hz, 1H), 4.59-4.57 (d, J =5.7Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ : 182.7, 159.0, 151.6, 134.4, 133.9, 133.7, 132.6, 131.0, 130.7, 129.4, 128.9, 128.8, 128.7, 126.9, 126.6, 126.5, 126.3, 126.0, 125.9, 125.5, 125.3, 125.2, 124.9, 124.1, 122.5, 121.6, 117.6, 102.0, 79.8, 50.4. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1647, 1605, 1463, 1199, 779. HRMS (ESI): calcd for C₃₀H₂₃NO₂ [M+H]⁺ 442.1802, found: 442.1796. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 0.7 mL·min⁻¹, t_R = 36.6 min (minor), 55.2 min (major)].

(Z)-3-((benzylamino)methylene)-2-o-tolylchroman-4-one (3m)



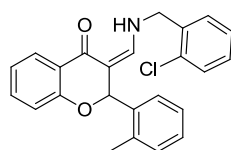
white solid. yield 60%, ee 76%. $[\alpha]_D^{20}$ +40.1 (c 0.18, CHCl₃). m.p. 108-110°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.36-10.32 (t, J =5.7Hz, 1H), 7.96-7.92 (dd, J =1.5Hz, J =7.8Hz, 1H), 7.53-7.50 (t, J =4.5Hz, 1H), 7.40-7.25 (m, 6), 7.24-7.15 (m, 3H), 7.06-7.01 (t, J =7.2Hz, 1H), 6.94-6.91 (d, J =8.4, 1H), 6.20-6.17 (d, 2H), 4.29-4.27 (d, J =6.0Hz, 2H), 2.35 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ : 182.9, 159.3, 151.0, 137.5, 136.7, 136.2, 133.9, 130.6, 128.8, 128.4, 128.1, 127.8, 127.1, 126.5, 126.4, 124.0, 121.5, 117.4, 101.6, 79.1, 52.8, 19.3. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1650, 1606, 1463, 1222, 748. HRMS (ESI): calcd for C₂₄H₂₁NO₂ [M+H]⁺ 356.1645; found: 356.1641. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.0 mL·min⁻¹, t_R = 13.4 min (minor), 27.2 min (major)].

(Z)-3-((naphthalen-2-ylmethylamino)methylene)-2-o-tolylchroman-4-one (3n)



yellow solid. yield 50%, ee 84%. $[\alpha]_D^{20}$ +95.6 (c 0.36, CHCl₃). m.p. 128-130°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.43-10.39 (t, J =6.0Hz, 1H), 7.97-7.96 (d, J =1.5Hz, 1H), 7.94-7.84 (m, 3H), 7.59 (s, 1H), 7.53-7.46 (m, 3H), 7.40-7.34 (m, 1H), 7.26-7.19 (m, 3H), 7.14-7.11 (t, J =4.2Hz, 1H), 7.06-7.01 (t, J =7.2Hz, 1H), 6.94-6.92 (d, J =8.1Hz, 1H), 6.23-6.19 (d, J =12.9Hz, 1H), 6.17 (s, 1H), 4.43-4.41 (d, J =6.0Hz, 2H), 2.33 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ : 183.0, 159.3, 151.0, 136.6, 136.2, 134.9, 133.9, 133.3, 132.8, 130.6, 128.8, 128.4, 128.1, 127.8, 127.7, 126.6, 126.4, 126.3, 126.2, 125.9, 125.0, 124.1, 121.5, 117.5, 101.7, 79.1, 52.9, 19.3. IR $\nu_{\max}$ (KBr, film, cm⁻¹): 1649, 1606, 1464, 1286, 750. HRMS (ESI): calcd for C₂₈H₂₃NO₂ [M+H]⁺ 406.1802; found: 406.1794. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15°C, 1.0 mL·min⁻¹, t_R = 18.0 min (minor), 36.8 min (major)].

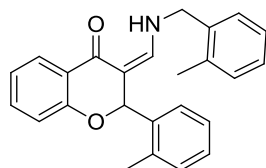
(Z)-3-(((2-chlorobenzyl)amino)methylene)-2-(o-tolyl)chroman-4-one (3o)



yellow solid. yield 70 %, ee 80%. $[\alpha]_D^{20}$ +66.5 (c 0.2, CHCl₃). m.p. 71-73°C. ¹H NMR (300 MHz, CDCl₃) δ : 10.32-10.28 (t, J =5.8Hz, 1H), 7.95-7.93 (d, J =3.8Hz, 1H), 7.53-7.50 (t, 1H), 7.39-7.31 (m, 2H), 7.27-7.21 (m, 6H), 7.06-7.01 (t, J =7.5Hz, 1H), 6.94-6.91 (d, J =8.2Hz, 1H), 6.20-6.16 (d, 2H), 4.34-4.32 (d, J =6.2Hz, 2H), 2.34 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ : 183.1, 159.4, 151.2, 136.5, 136.2, 135.3, 134.0, 133.3, 130.6, 129.7, 129.2, 128.9, 128.5, 128.1, 127.3, 126.6, 126.4, 124.0, 121.5, 117.5, 101.9, 79.1, 50.8, 19.3. IR $\nu_{\max}$ (KBr, film, cm⁻¹):

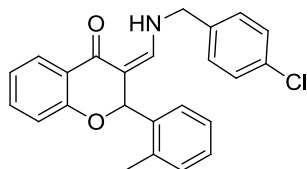
1647, 1607, 1465, 1276, 758 HRMS (ESI): calcd for $C_{28}H_{23}NO_2$ $[M+Na]^+$ 412.1074, found: 412.1063. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15 °C, 1.0 mL·min⁻¹, t_R = 12.0 min (minor), 25.3min (major)].

(Z)-3-(((2-methylbenzyl)amino)methylene)-2-(o-tolyl)chroman-4-one (3p)



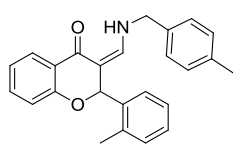
yellow solid. yield 75%, ee 65%. $[\alpha]_D^{20} +74.2$ (c 0.6, $CHCl_3$). m.p. 124-126 °C. ¹H NMR (300 MHz, $CDCl_3$) δ : 10.31-10.27 (t, $J=6.0$ Hz, 1H), 7.95-7.93 (d, $J=7.7$ Hz, 1H), 7.51-7.48 (t, 1H), 7.38-7.33 (m, 1H), 7.25-7.22 (t, 2H), 7.21-7.12 (m, 5H), 7.05-7.00 (t, $J=7.4$ Hz, 1H) 6.93-6.90 (d, $J=8.2$, 1H), 6.14-6.10 (d, 2H), 4.24-4.22 (d, $J=5.7$ Hz, 2H), 2.31 (s, 3H) 2.20(s, 3H). ¹³C NMR (75 MHz, $CDCl_3$) δ : 182.8, 159.3, 151.0, 136.7, 136.1, 135.8, 135.3, 133.9, 130.6, 130.6, 128.4, 128.1, 128.0, 127.8, 126.5, 126.4, 124.1, 121.5, 117.5, 101.5, 79.1, 50.9, 19.3, 19.0. IR ν_{max} (KBr, film, cm⁻¹): 1647, 1605, 1463, 1271, 758. HRMS (ESI): calcd for $C_{24}H_{21}NO_2$ $[M+Na]^+$ 392.1611, found: 392.1621. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15 °C, 1.0 mL·min⁻¹, t_R = 10.7 min (minor), 21.2 min (major)].

(Z)-3-(((4-chlorobenzyl)amino)methylene)-2-(o-tolyl)chroman-4-one (3q)



yellow solid. yield 66%, ee 80%. $[\alpha]_D^{20} +72.2$ (c 0.2, $CHCl_3$). m.p. 89-91 °C. ¹H NMR (300 MHz, $CDCl_3$) δ : 10.31-10.27 (t, $J=6.0$ Hz, 1H), 7.95-7.92 (d, $J=7.6$ Hz, 1H), 7.51-7.48 (t, 1H), 7.39-7.34 (t, 1H), 7.27-7.24 (d, 4H), 7.20-7.17 (t, 1H), 7.08-7.00 (m, 2H) 6.93-6.91 (d, $J=8.2$ Hz, 1H), 6.15-6.10 (d, 2H), 4.23-4.20 (d, $J=6.0$ Hz, 2H), 2.34 (s, 3H). ¹³C NMR (75 MHz, $CDCl_3$) δ : 183.1, 159.3, 150.7, 136.6, 136.2, 136.1, 134.0, 133.6, 130.7, 129.0, 128.5, 128.4, 128.1, 126.6, 126.4, 124.0, 121.6, 117.5, 101.9, 79.0, 52.0, 19.4. IR ν_{max} (KBr, film, cm⁻¹): 1648, 1607, 1585, 1465, 1222. HRMS (ESI): calcd for $C_{24}H_{21}NO_2$ $[M+Na]^+$ 412.1074; found: 412.1064. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15 °C, 1.0 mL·min⁻¹, t_R = 14.6 min (minor), 29.0 min (major)].

(Z)-3-(((4-methylbenzyl)amino)methylene)-2-(o-tolyl)chroman-4-one (3r)

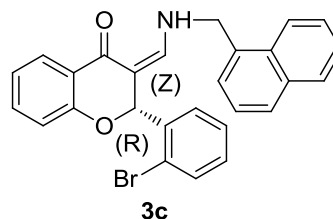
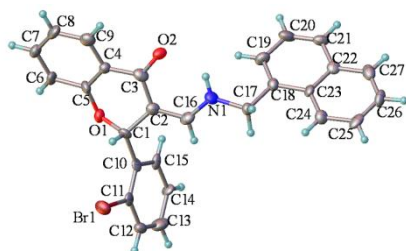


yellow solid. yield 80%, ee 71%. $[\alpha]_D^{20} +85.3$ (c 0.6, $CHCl_3$). m.p. 104-106 °C. ¹H NMR (300 MHz, $CDCl_3$) δ : 10.33-10.29 (t, $J=6.0$ Hz, 1H), 7.95-7.92 (dd, $J=1.3$ Hz, $J=7.7$ Hz, 1H), 7.53-7.50 (t, 1H), 7.38-7.32 (q, 1H), 7.26-7.23 (t, 2H), 7.21-7.16 (m, 1H), 7.11-7.09 (d, 2H) 7.04-7.00 (t, 3H) 6.93-6.90 (d, $J=8.2$, 1H) 6.19-6.15 (d, 2H), 4.22-4.20 (d, $J=6.0$ Hz, 2H), 2.34 (s, 3H) 2.31(s, 3H). ¹³C NMR (75 MHz, $CDCl_3$) δ : 182.8, 159.2, 151.0, 137.5, 136.7, 136.2, 134.5, 133.8, 130.6, 129.5, 128.4, 128.1, 127.1, 126.5, 126.4, 124.1, 121.5, 117.4, 101.4, 79.1, 52.6, 21.1, 19.4. IR ν_{max} (KBr, film, cm⁻¹): 1647, 1607, 1465, 1296, 748. HRMS (ESI): calcd for $C_{24}H_{21}NO_2$ $[M+Na]^+$ 392.1621; found: 392.1611. HPLC analysis [Chiralcel IA, n-hexane/ i-propanol (90:10), 15, 1.0 mL·min⁻¹, t_R = 11.0 min (minor), 22.6 min (major)].

References:

- [1] (a) T. Y. Liu, J. Long, B. J. Li, L. Jiang, R. Li, Y. Wu, L. S. Ding, Y. C. Chen, *Org. Biomol. Chem.*, **2006**, *11*, 2097;
(b) J. Ye, D. J. Dixon, P. S. Hynes, *Chem. Commun.*, **2005**, *35*, 4481;
(c) B. Vakulya, S. Varga, A. Csampai, T. Sóos, *Org. Lett.*, **2005**, *7*, 1967.
- [2] C. J. Wang, Z. H. Zhang, X. Q. Dong, X. J. Wu, *Chem. Commun.*, **2008**, *12*, 1431.
- [3] Q. Zhu, Y. X. Lu, *Angew. Chem. Int. Ed.* **2010**, *49*, 7753.
- [4] (a) S. Luo, P. G. Wang, J. P. Cheng, *J. Org. Chem.* **2004**, *69*, 555;
(b) S. Luo, X. Mi, P. G. Wang, J. P. Cheng, *J. Org. Chem.* **2004**, *69*, 8413.
- [5] R. Zhou, J. F. Wang, H. B. Song, Z. J. He, *Org. Lett.*, **2011**, *13*, 580.

3. Single-crystal information of **3c**



ORTEP plot of enantiomerically pure **3c** drawn with ellipsoids at 30% probability

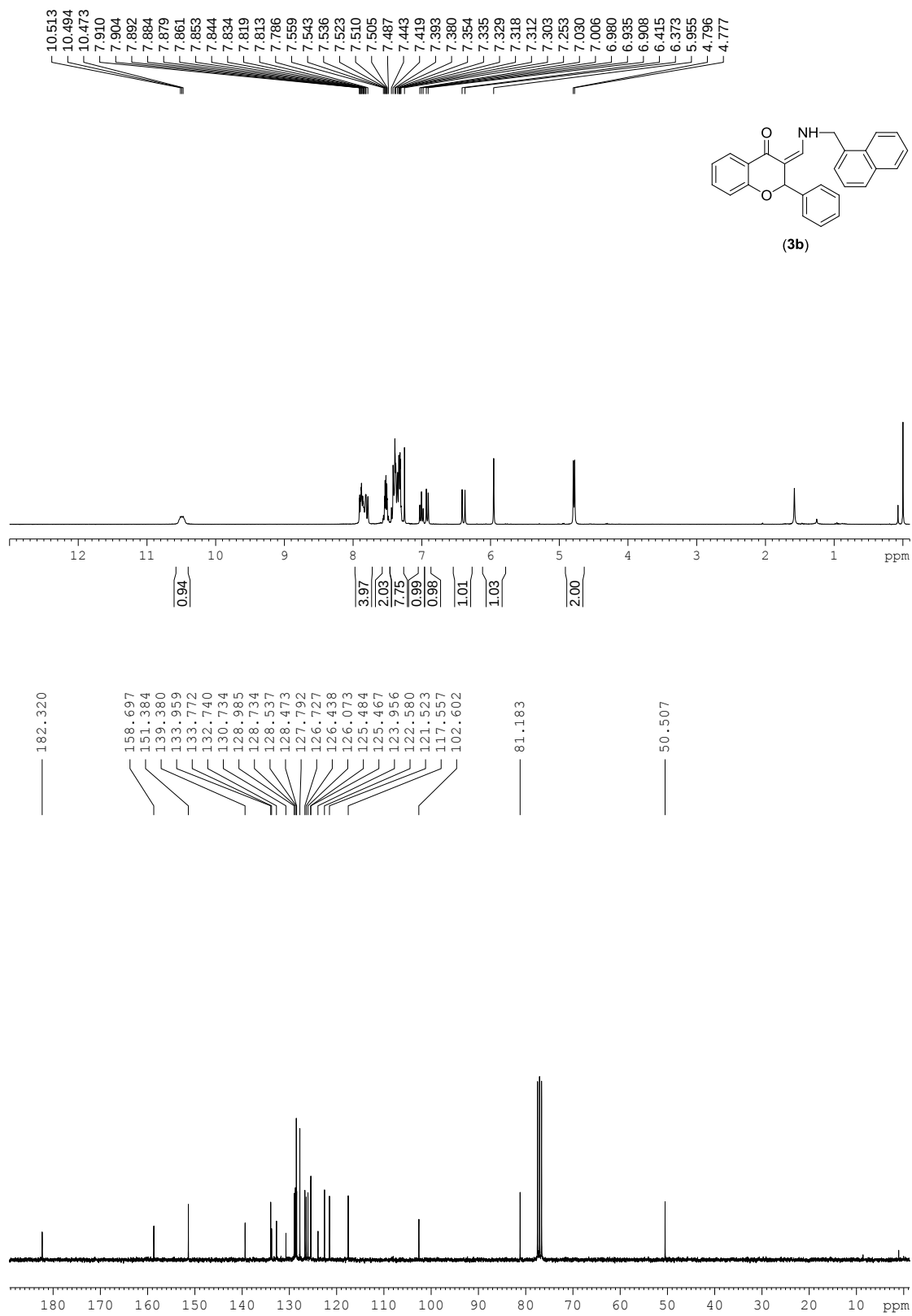
Crystal data and structure refinement for mx1973.

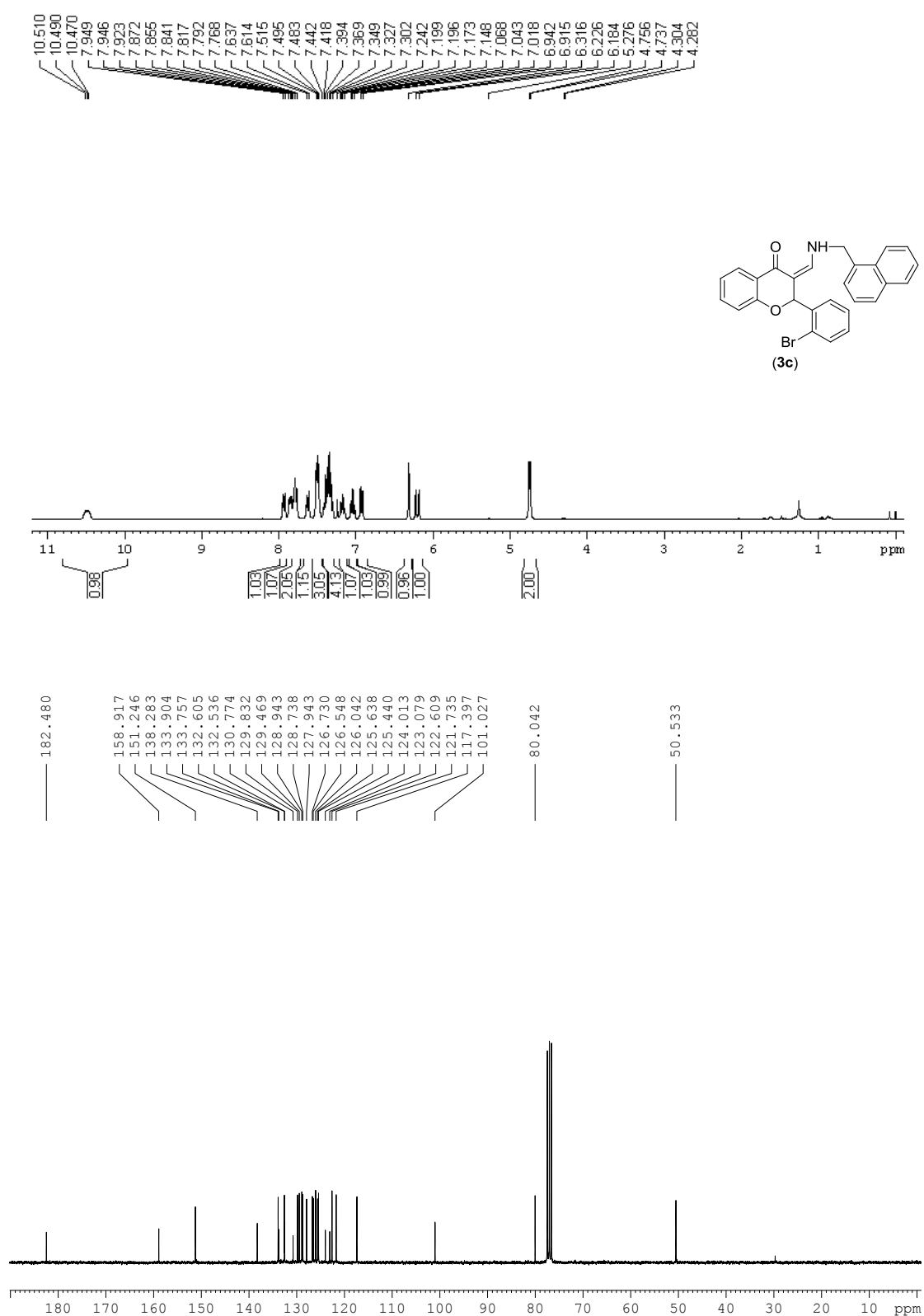
Identification code	mx1973
CCDC number	915036
Empirical formula	C ₂₇ H ₂₀ Br N O ₂
Formula weight	470.35
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 7.419(3) Å α = 90 deg. b = 32.757(7) Å β = 99.572(4) deg. c = 8.541(3) Å γ = 90 deg.
Volume	2046.8(12) Å ³
Z, Calculated density	4, 1.526 Mg/m ³
Absorption coefficient	2.034 mm ⁻¹
F(000)	960
Crystal size	0.17 mm x 0.15 mm x 0.14 mm
Theta range for data collection	2.42 to 25.00 deg.
Limiting indices	-8 ≤ h ≤ 8, -35 ≤ k ≤ 38, -10 ≤ l ≤ 10
Reflections collected / unique	14144 / 7029 [R(int) = 0.0688]
Completeness to theta = 25.00	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7638 and 0.7237
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7029 / 1 / 512
Goodness-of-fit on F ²	1.049
Final R indices [I > 2σ(I)]	R1 = 0.0951, wR2 = 0.2130
R indices (all data)	R1 = 0.1085, wR2 = 0.2251
Absolute structure parameter	0.078(17)

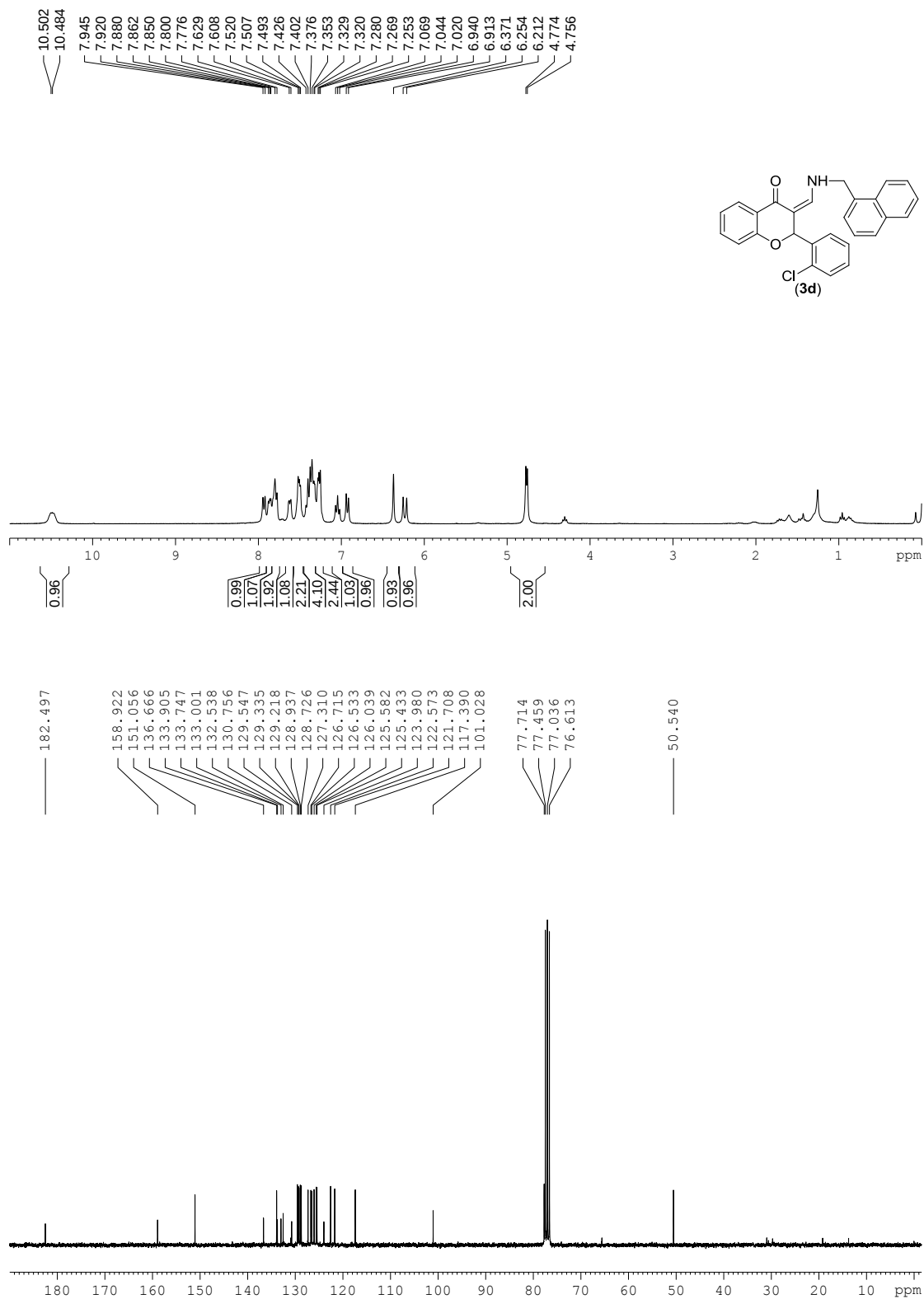
Largest diff. peak and hole

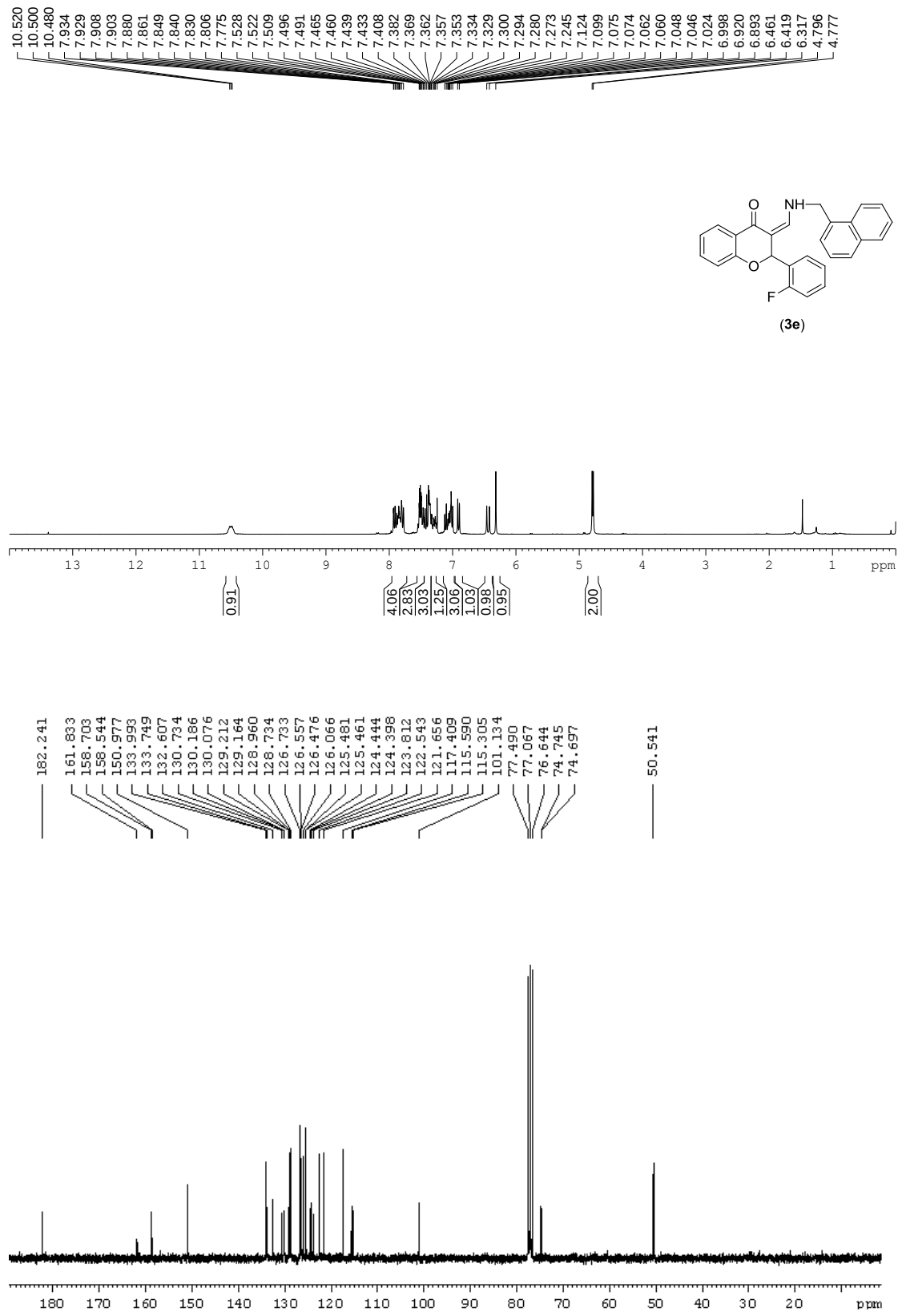
2.567 and -0.698 e.A⁻³

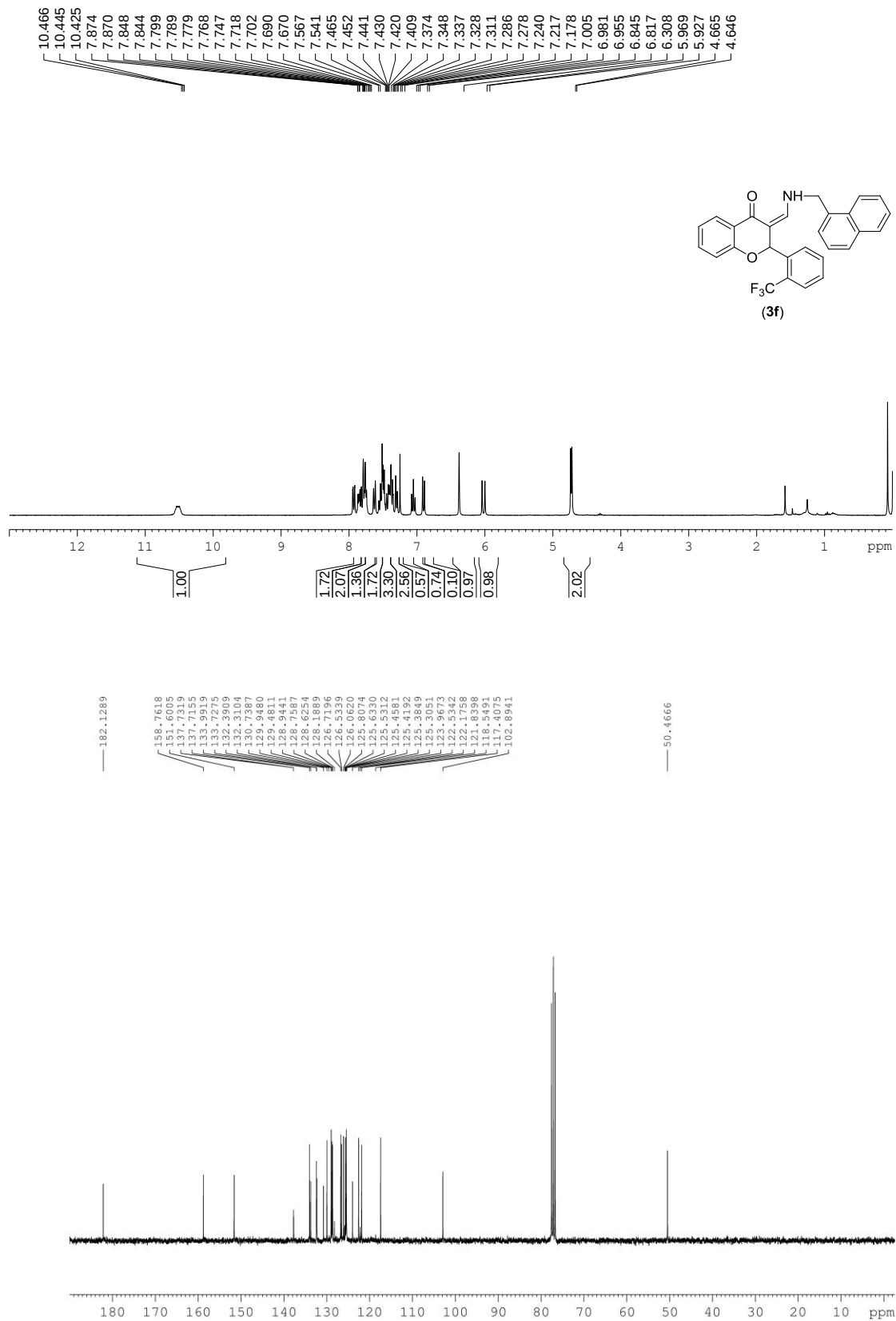
4. HPLC tracks and NMR spectra

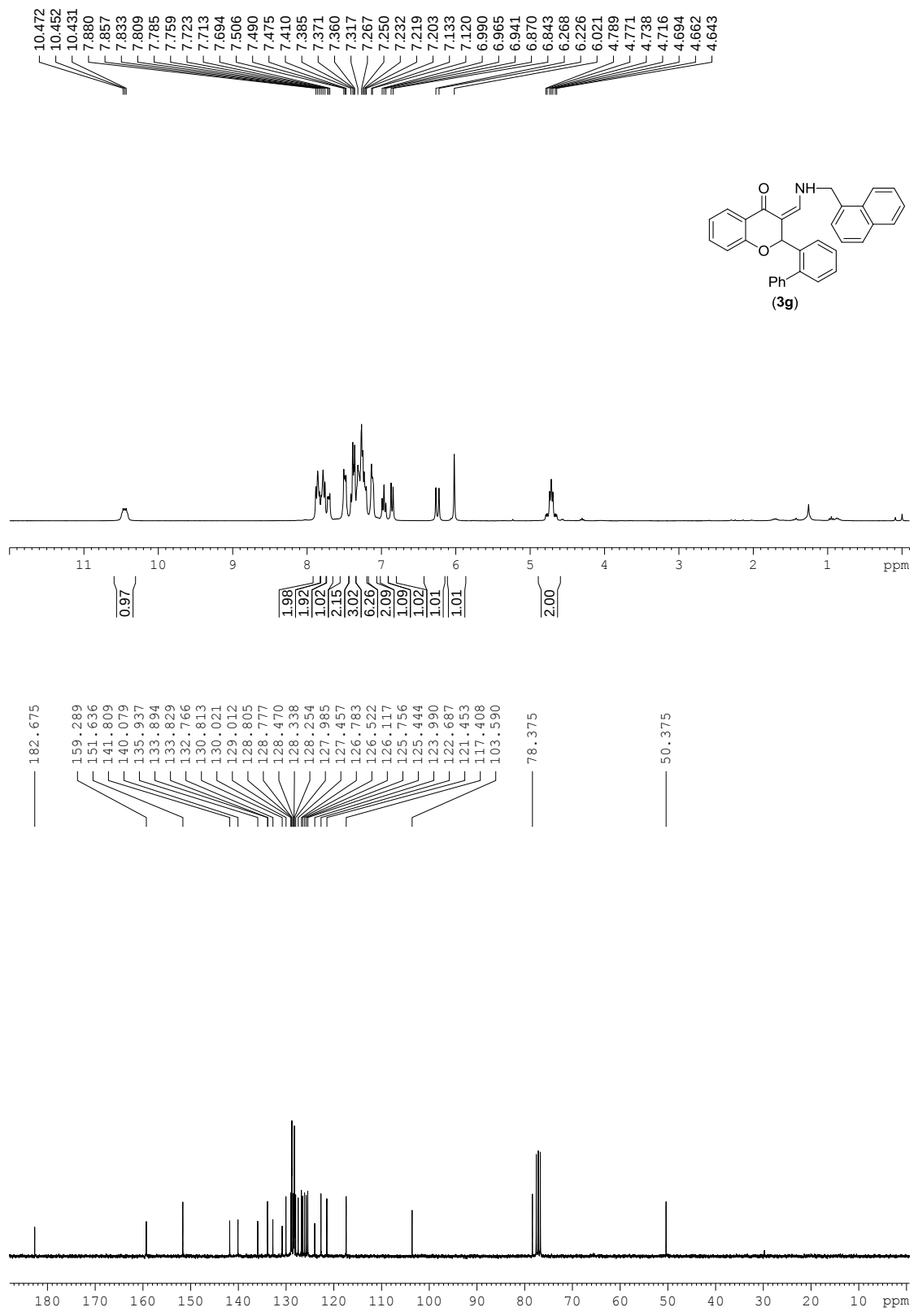


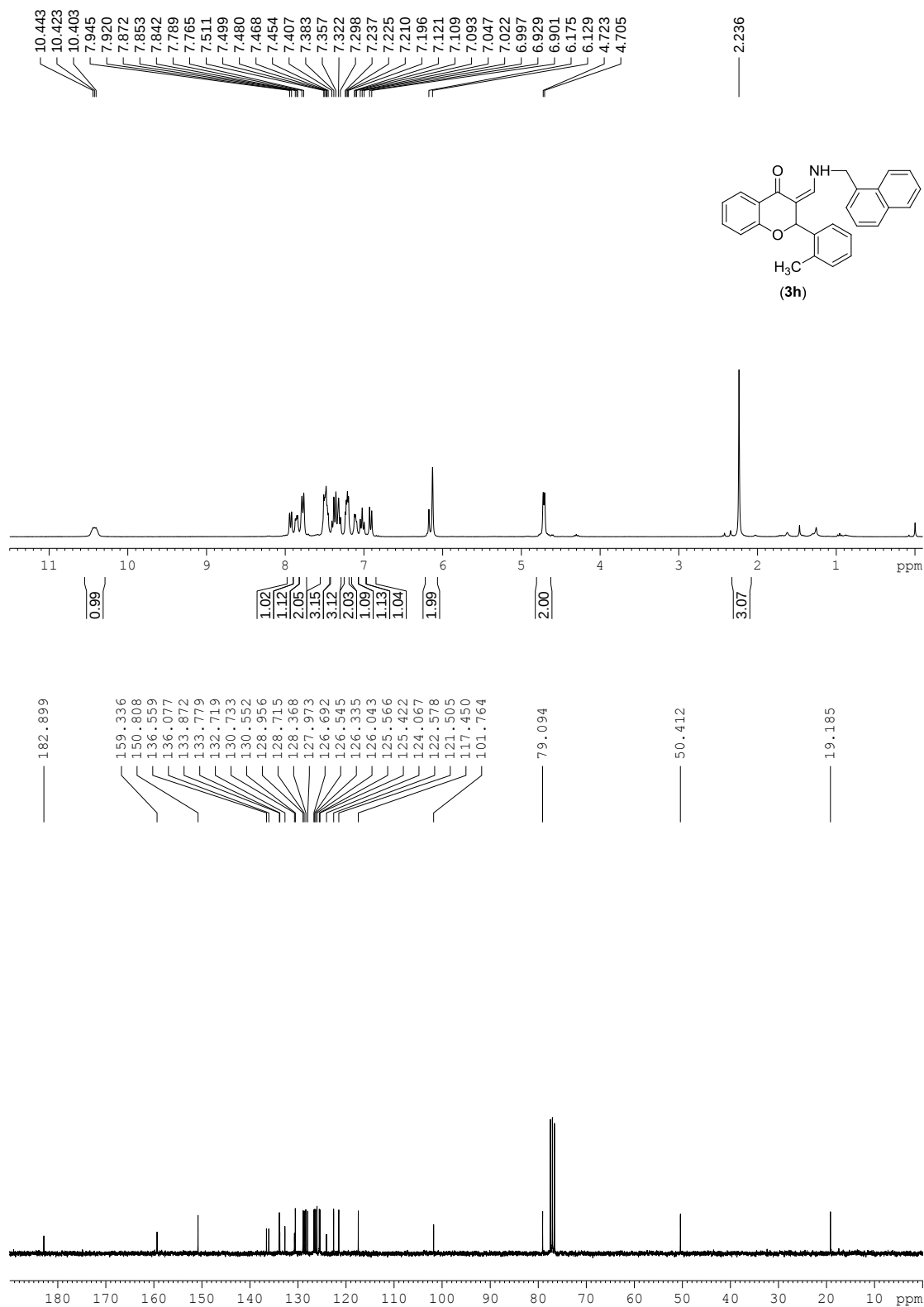


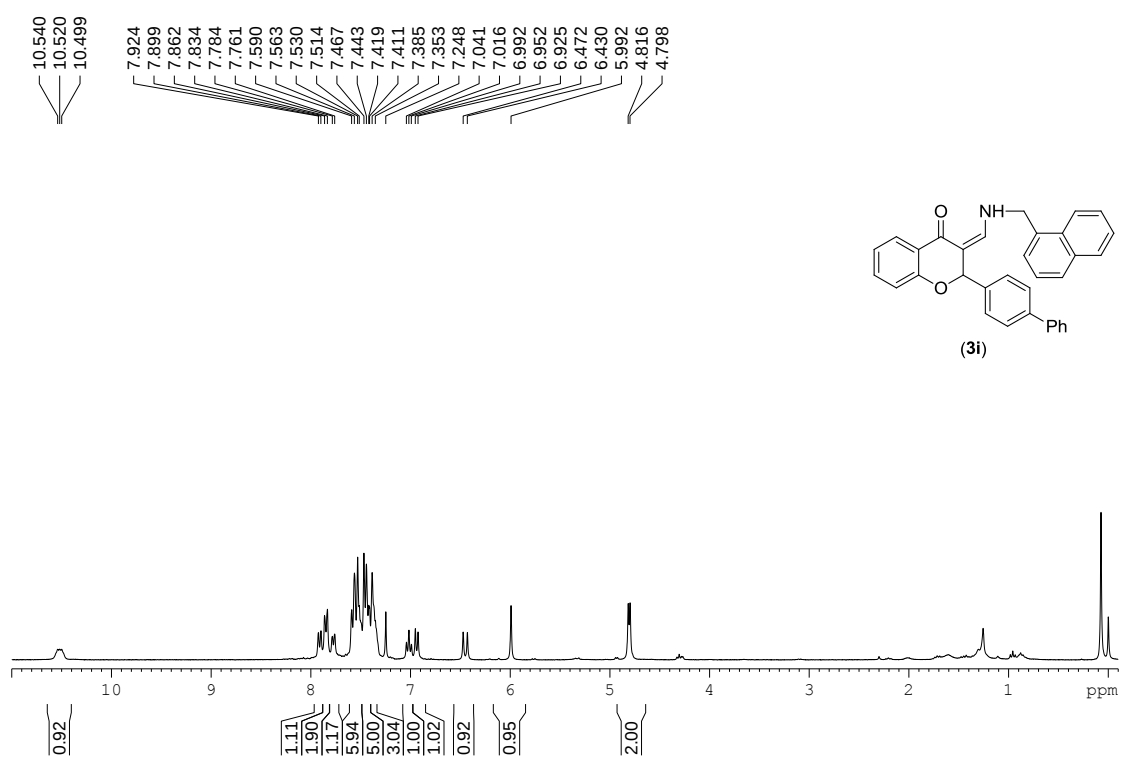


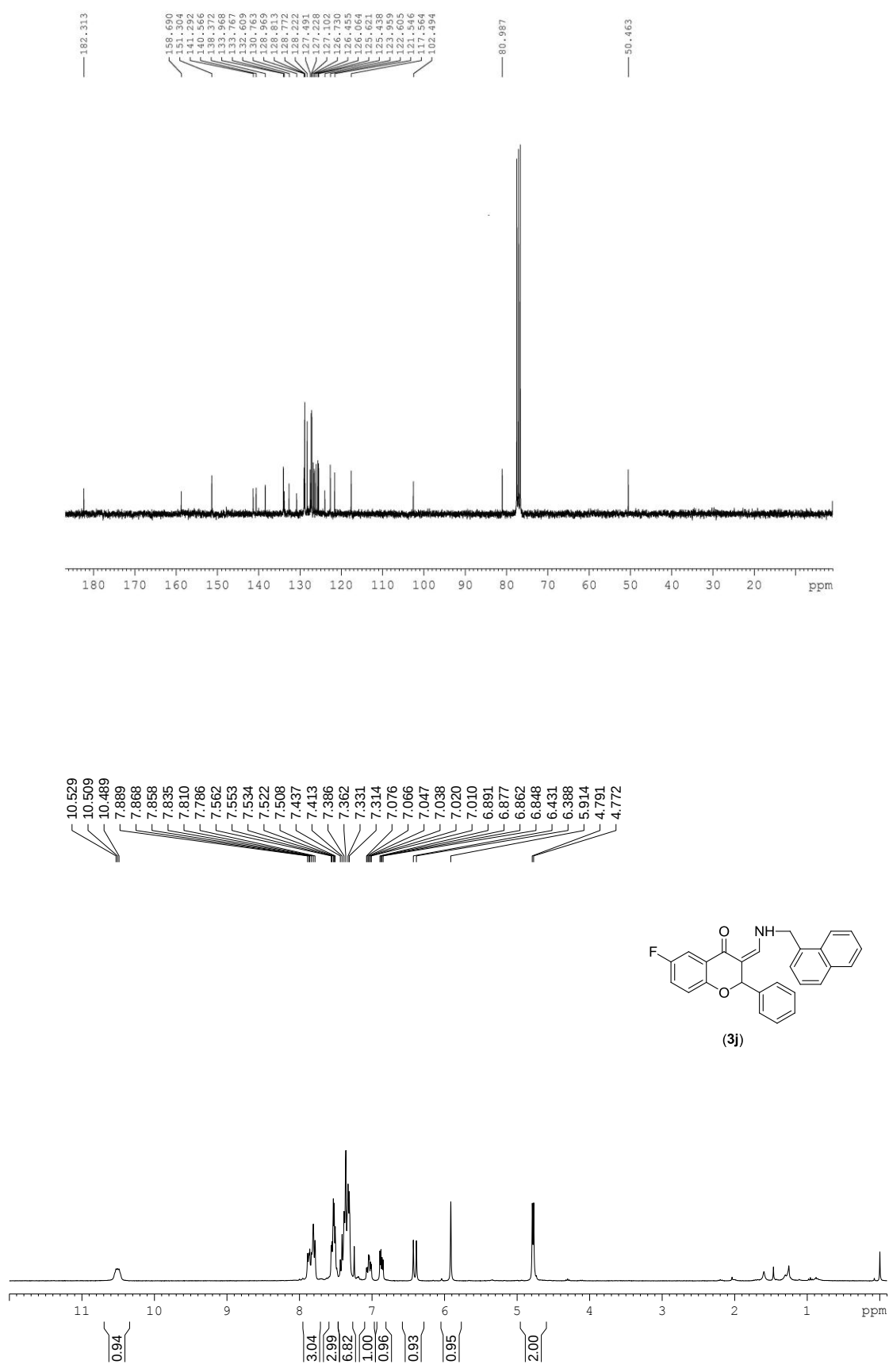


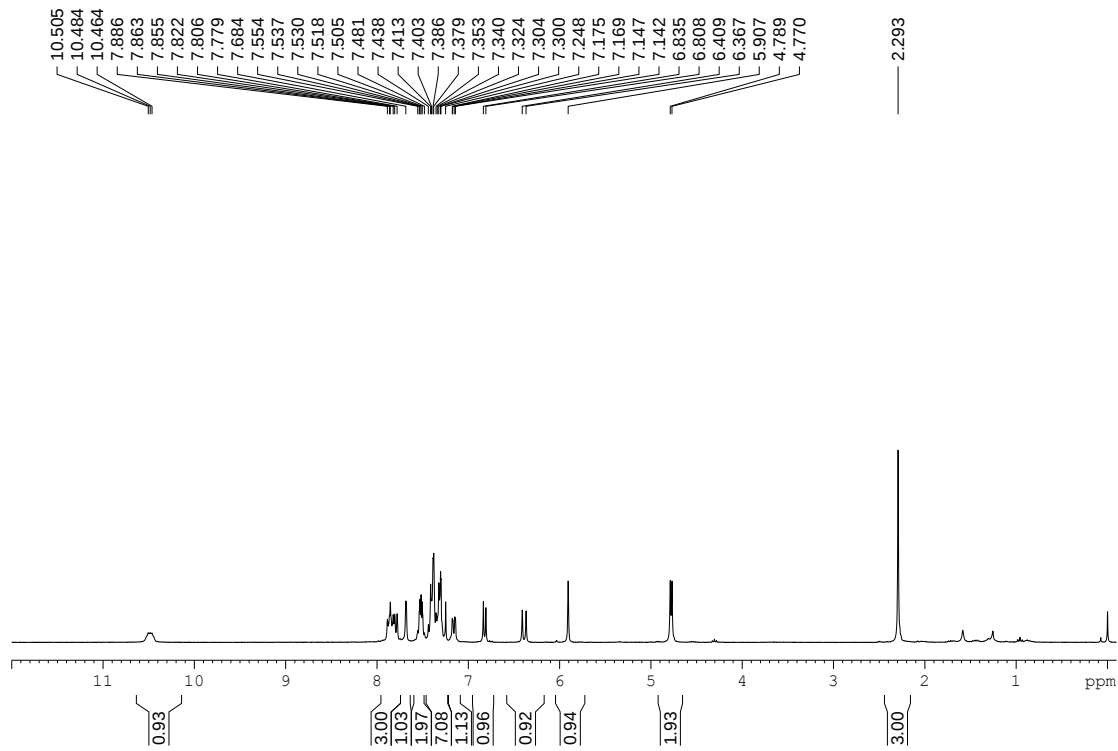
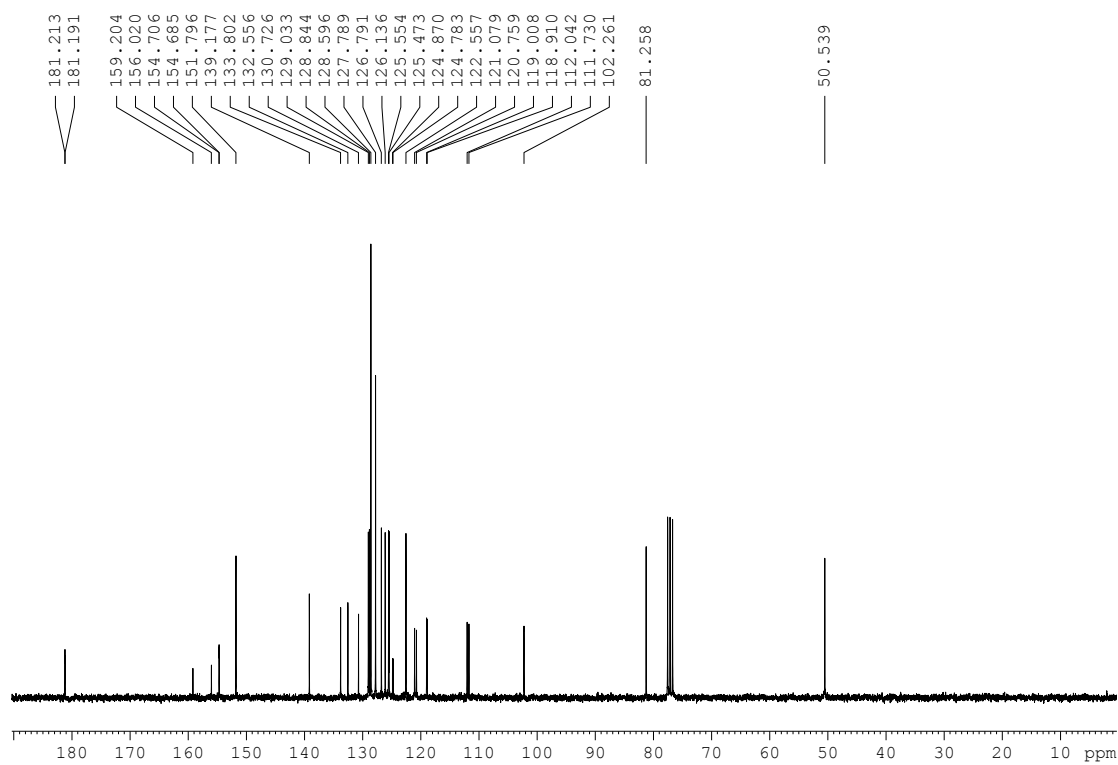


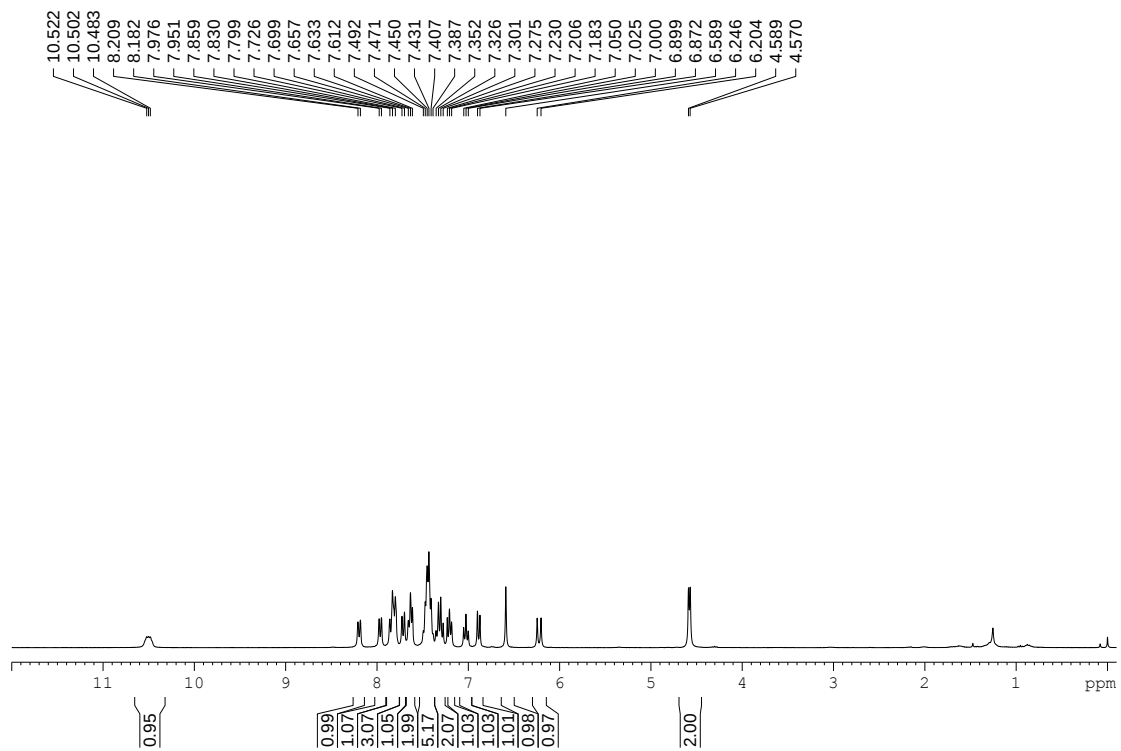
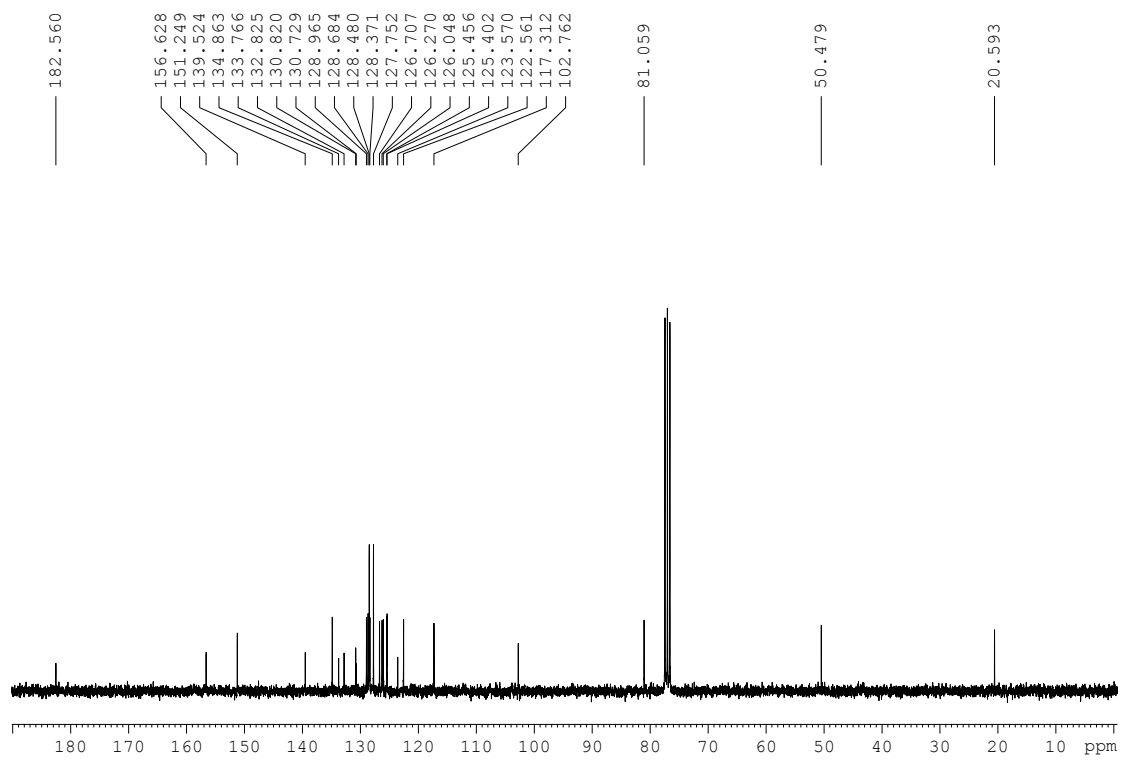


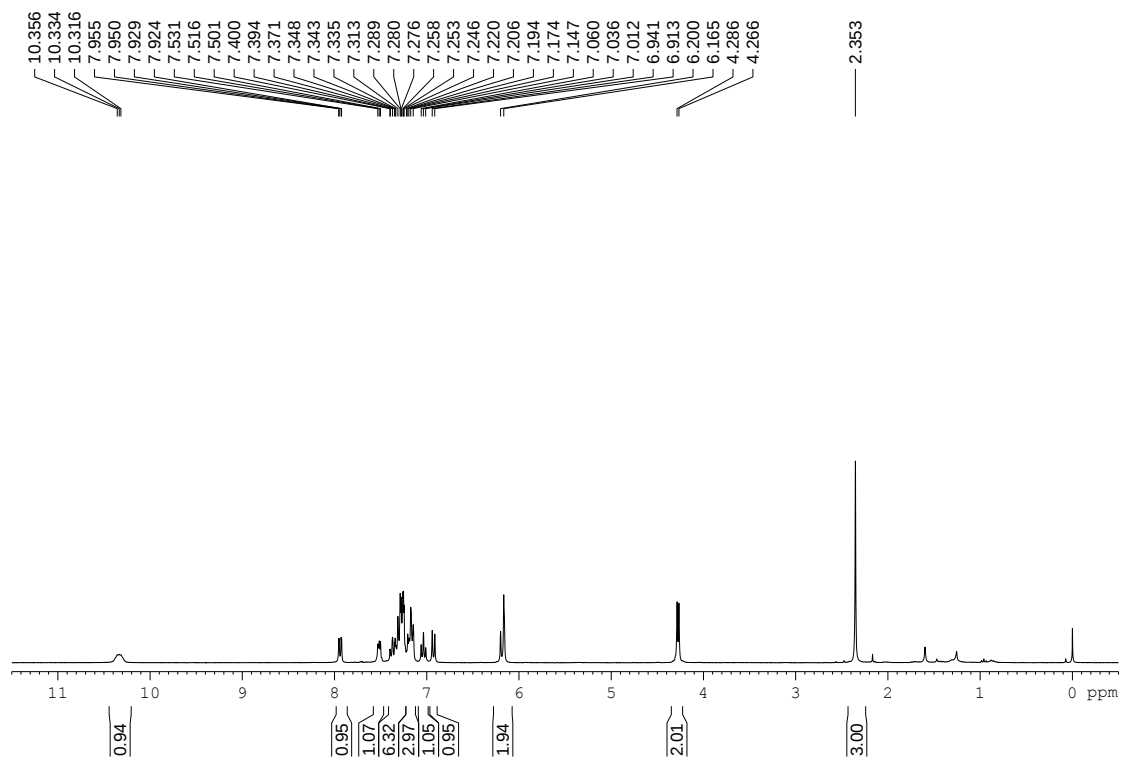
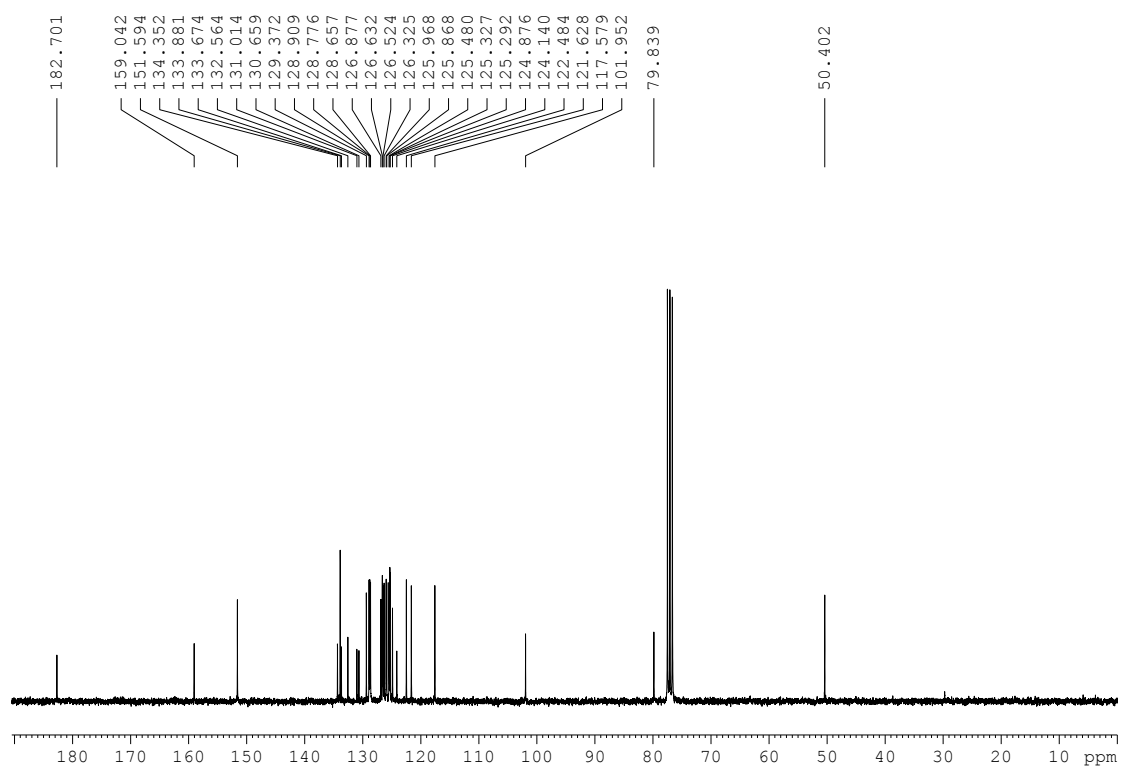


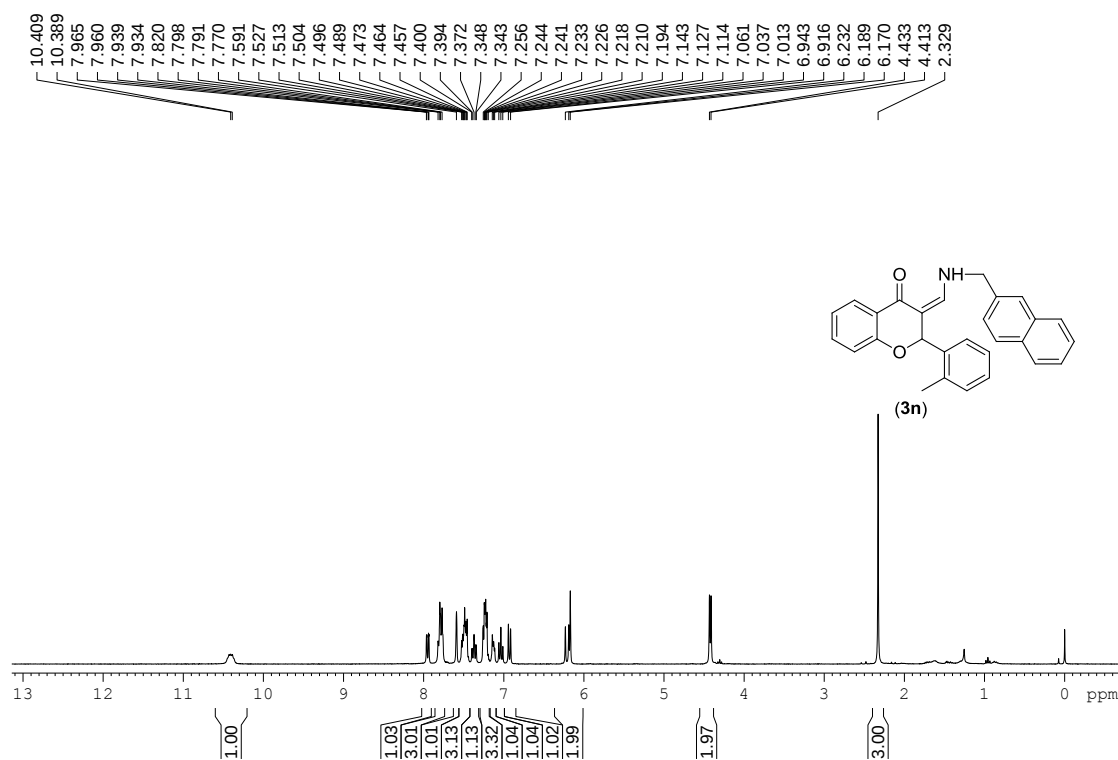
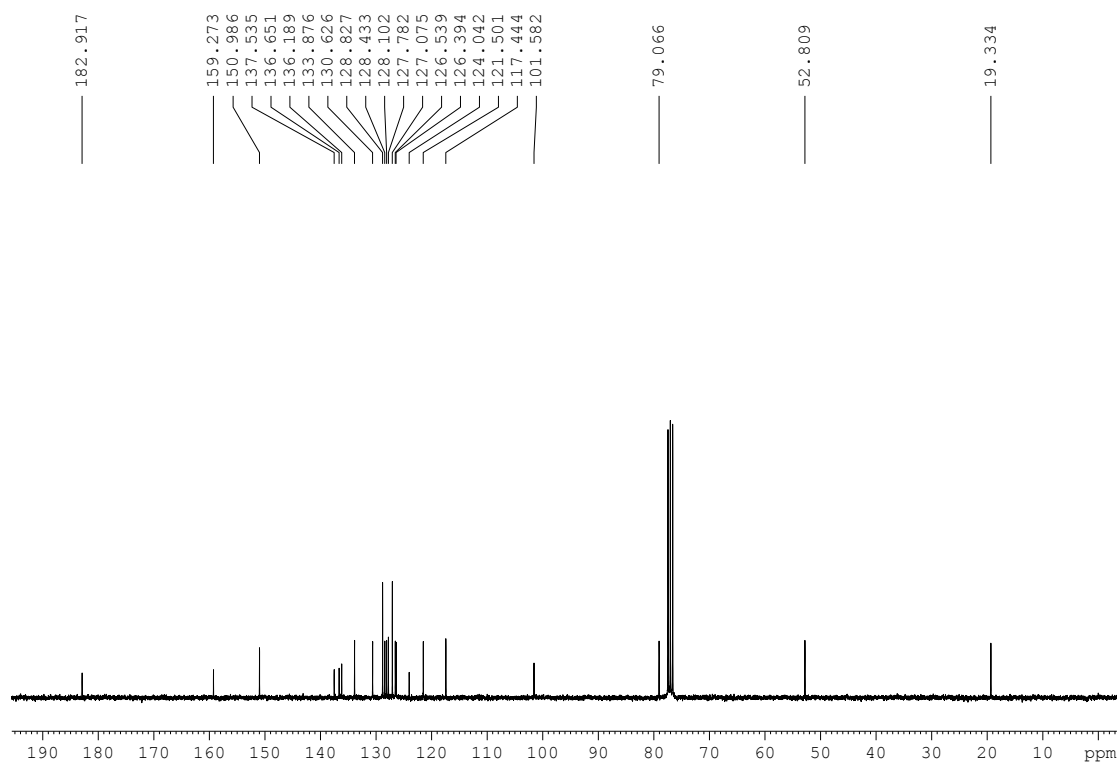


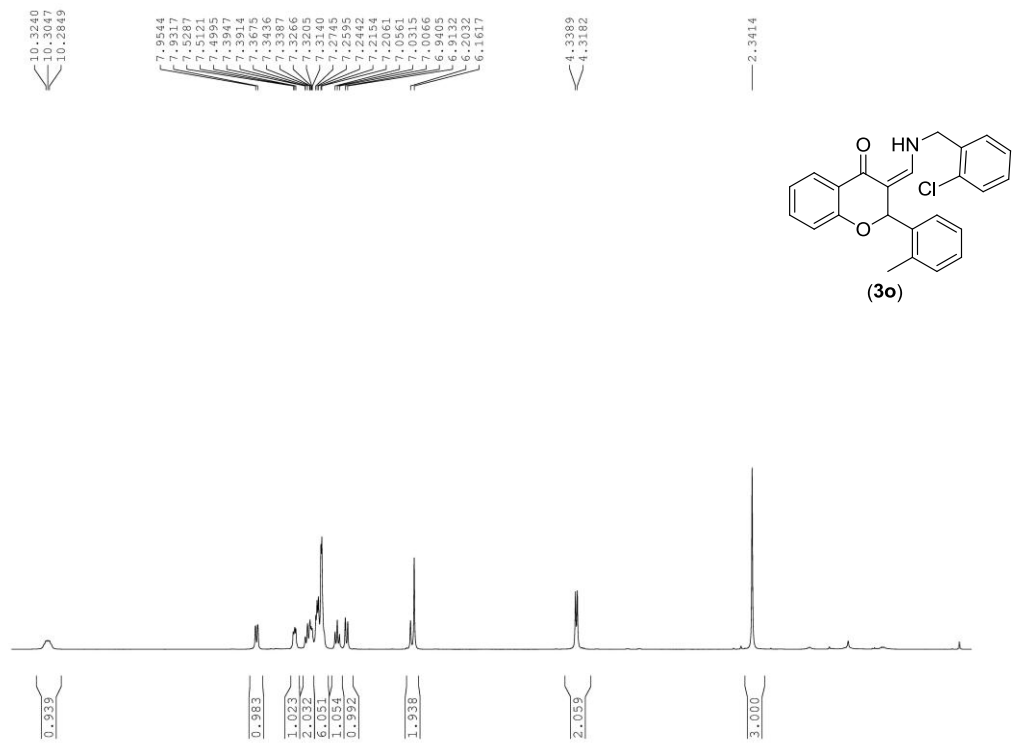
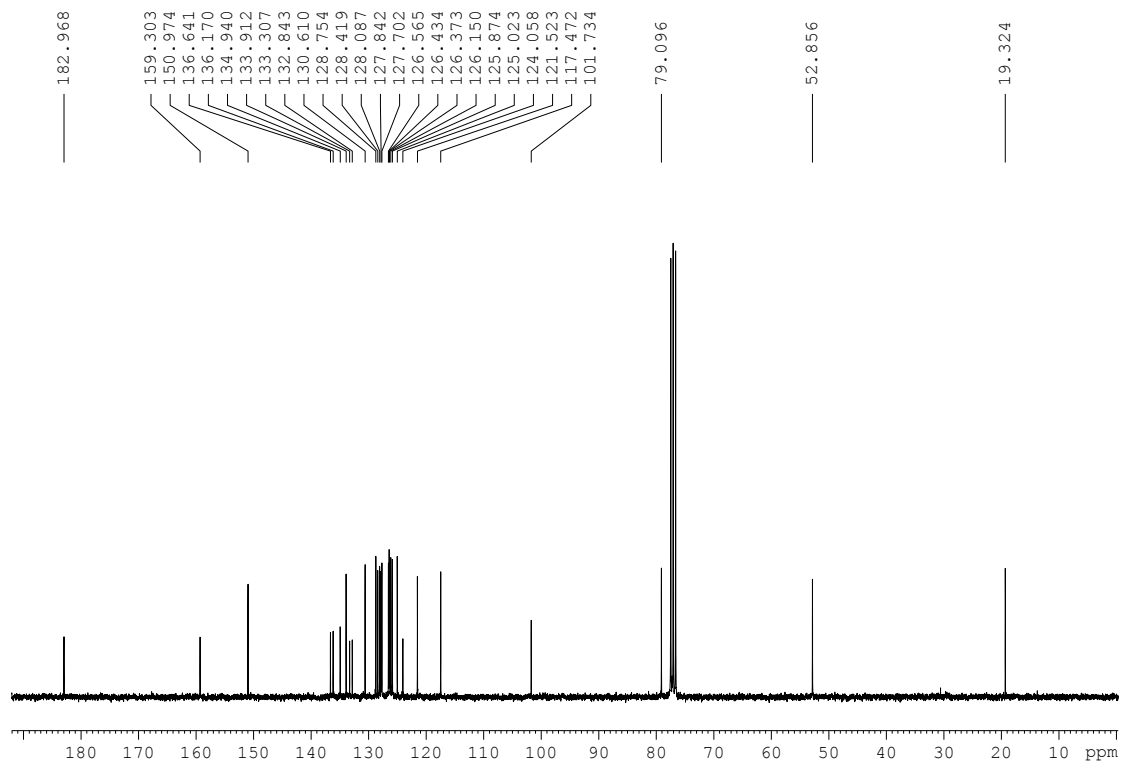


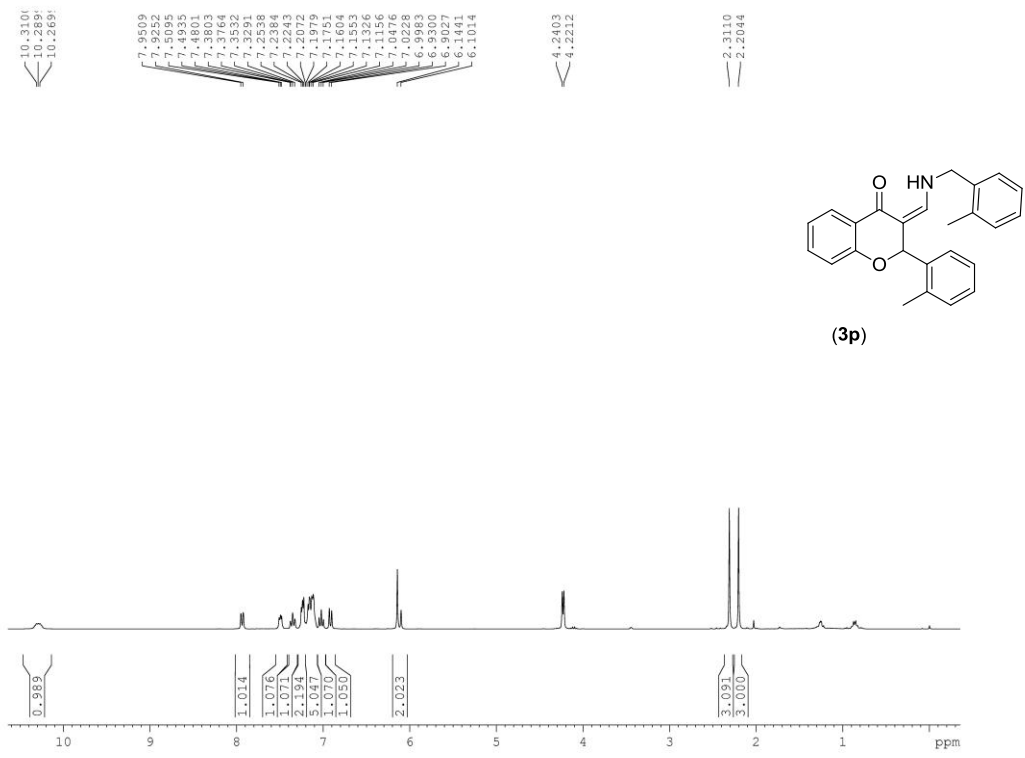
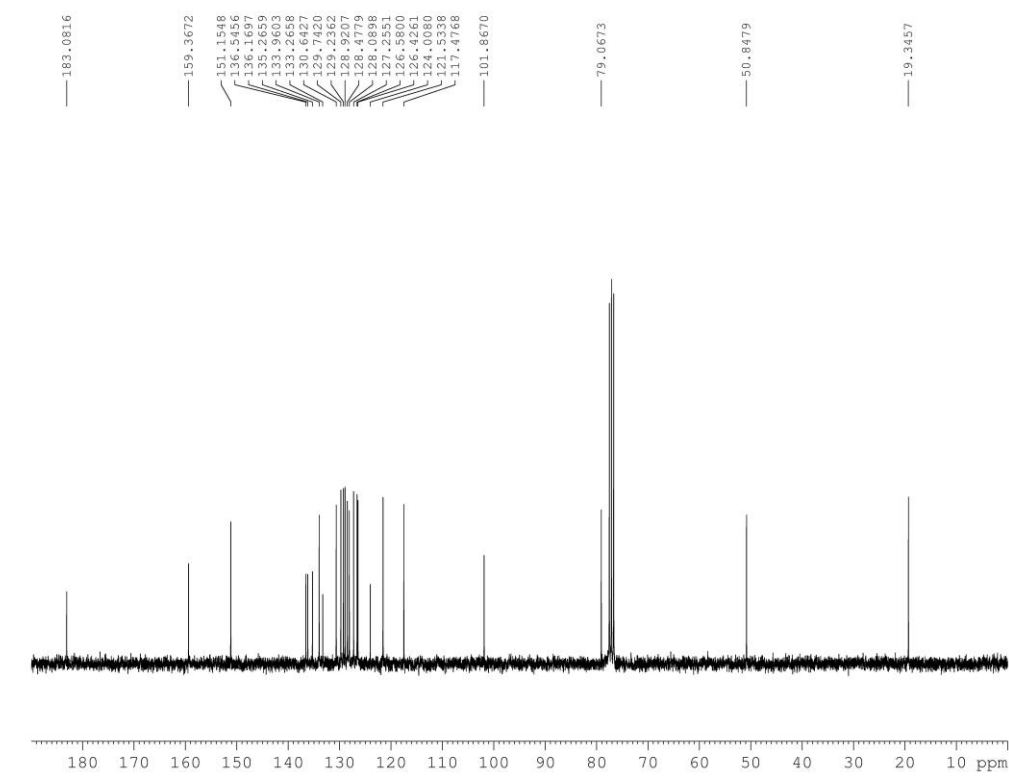


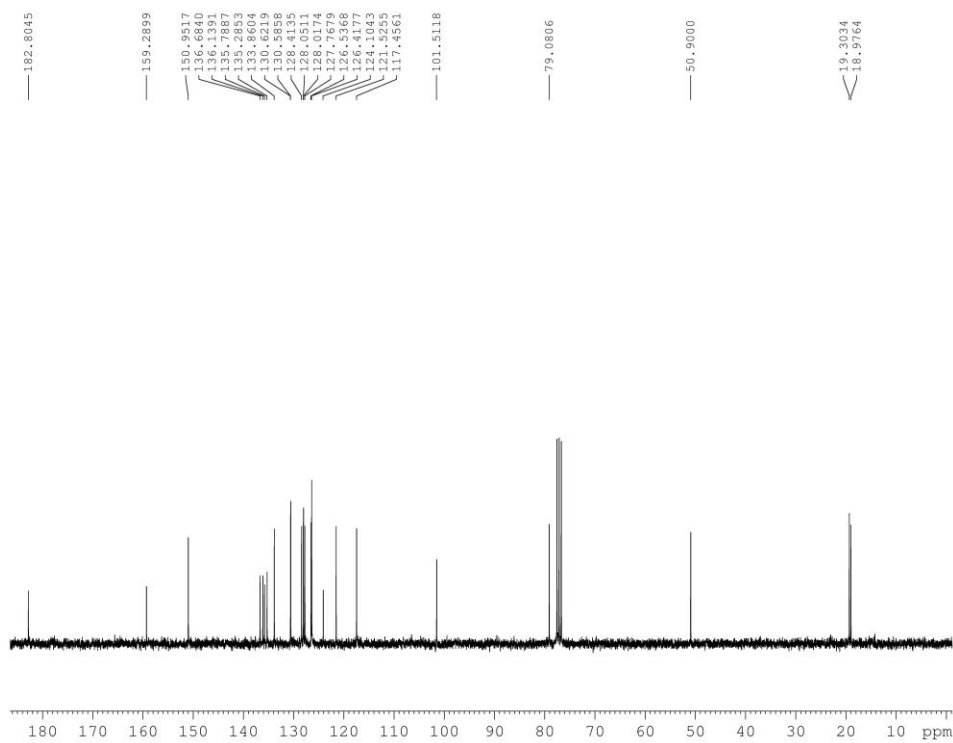


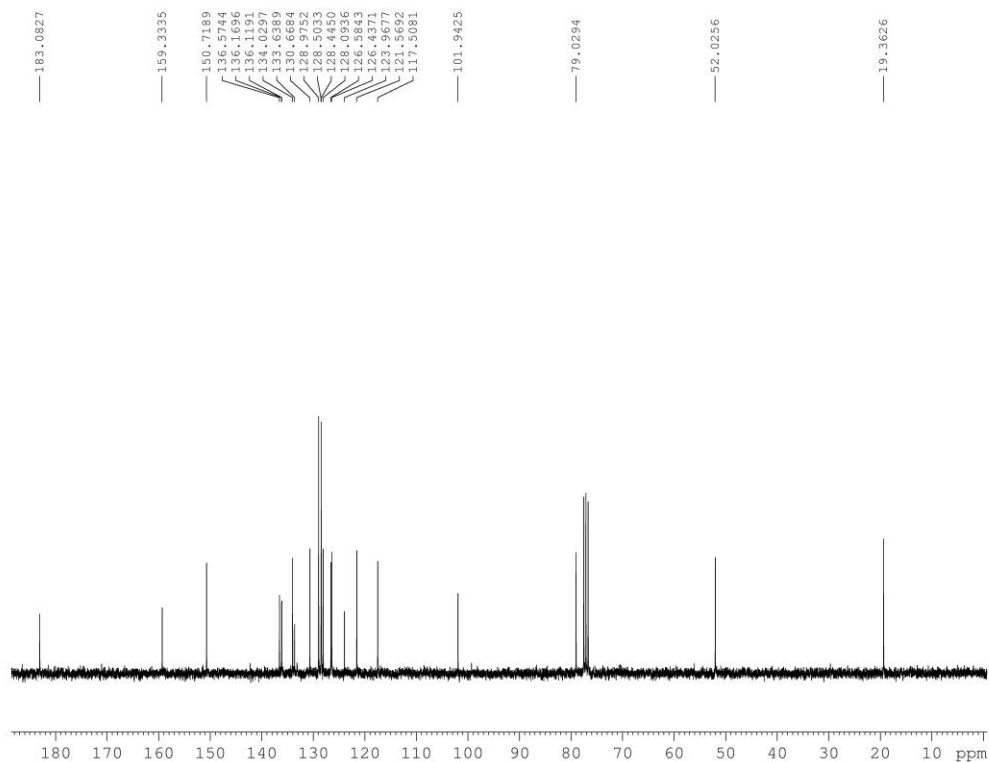


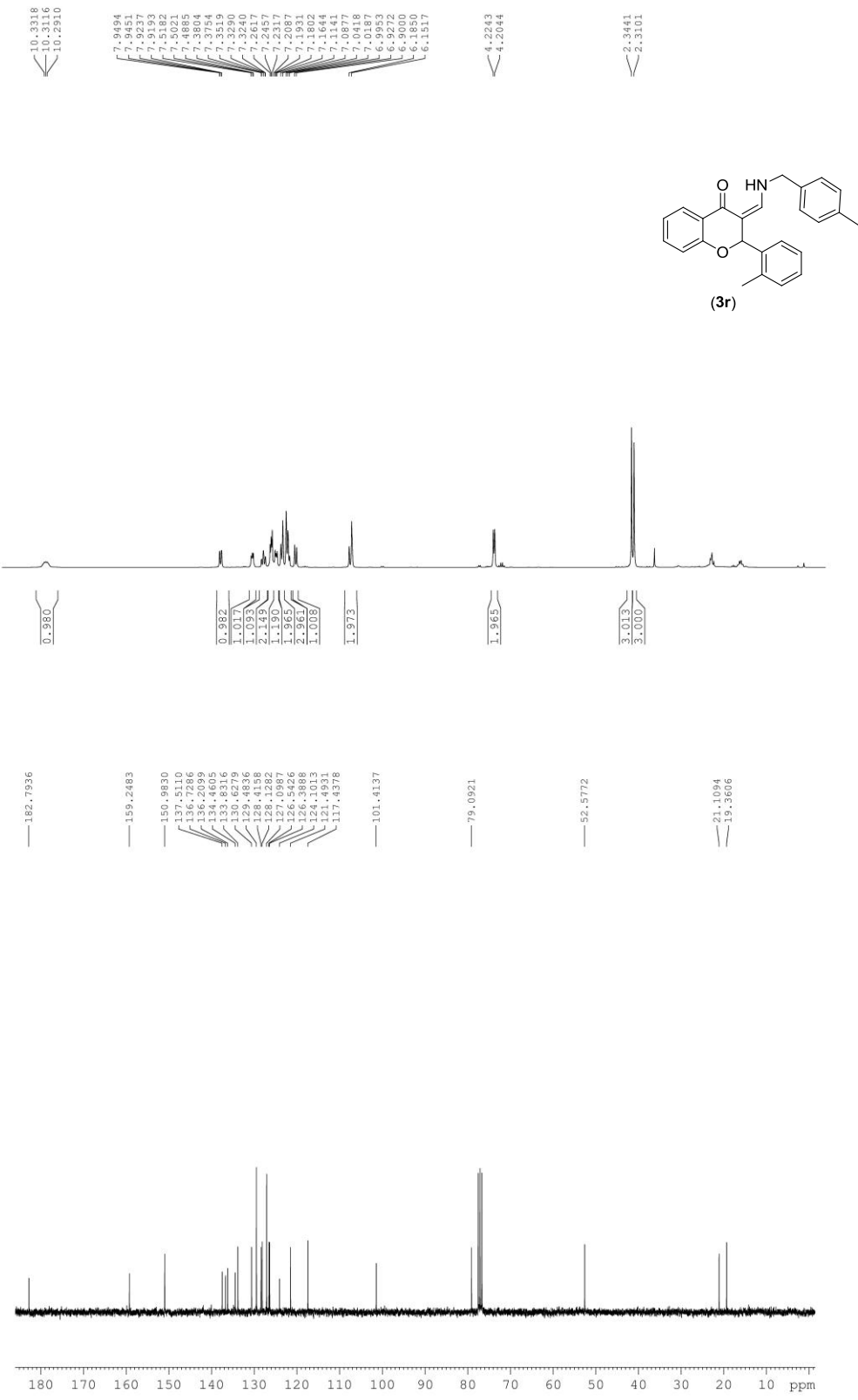


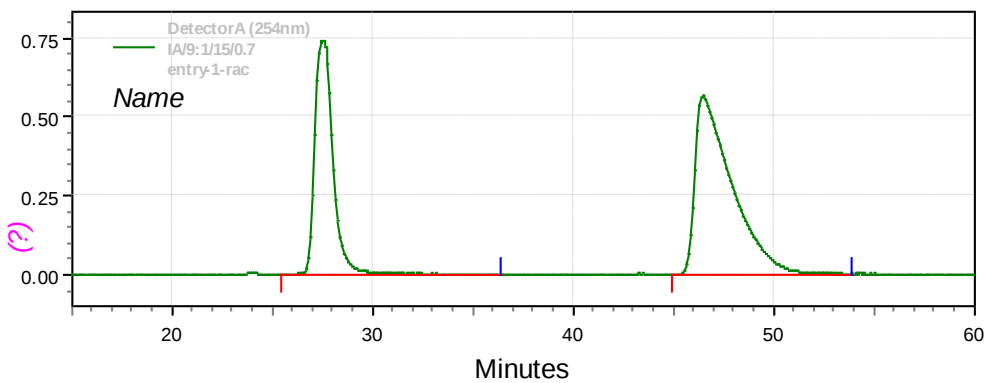
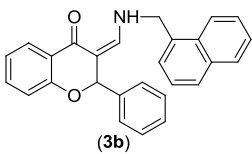




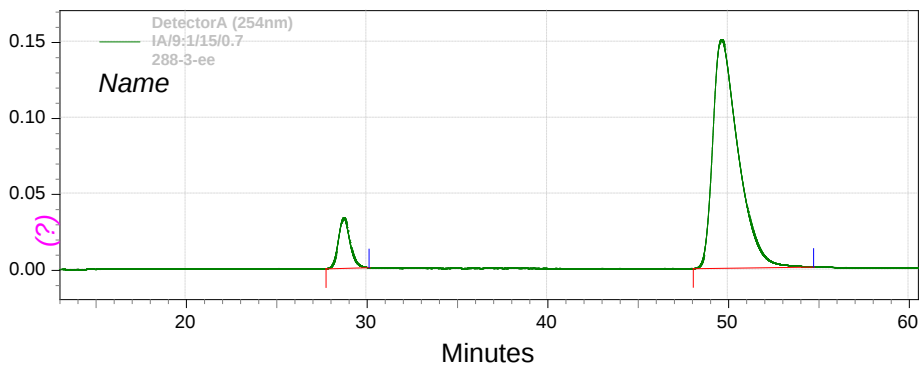




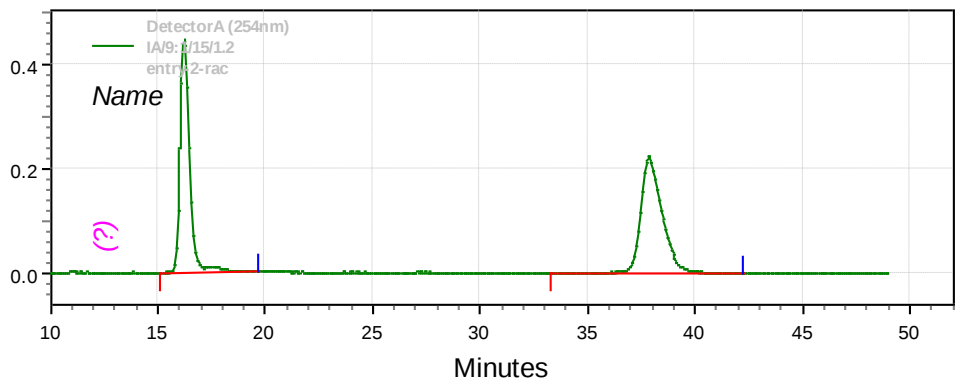
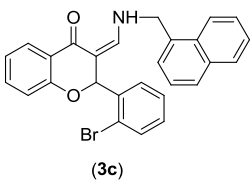




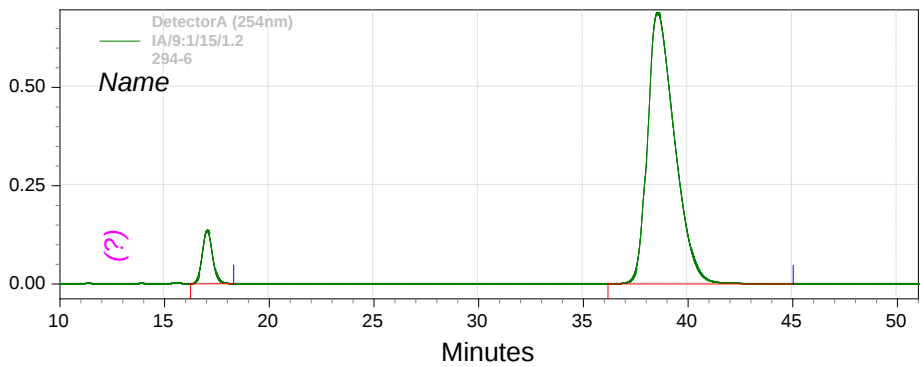
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2	46.523	71295215	58.229



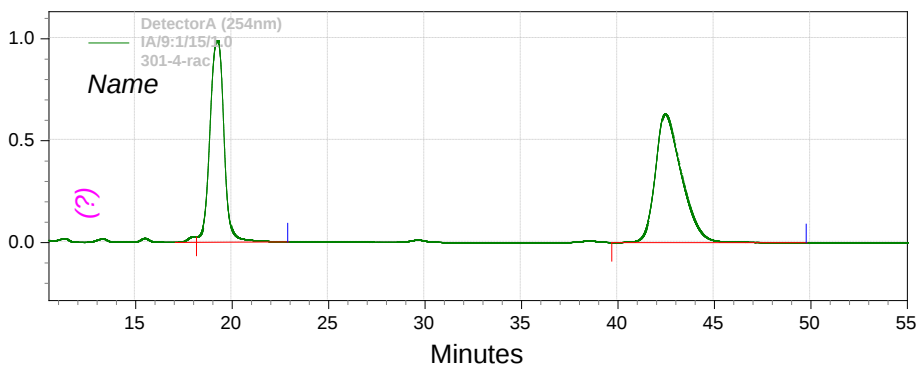
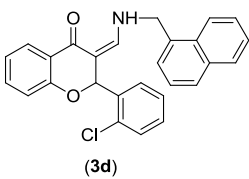
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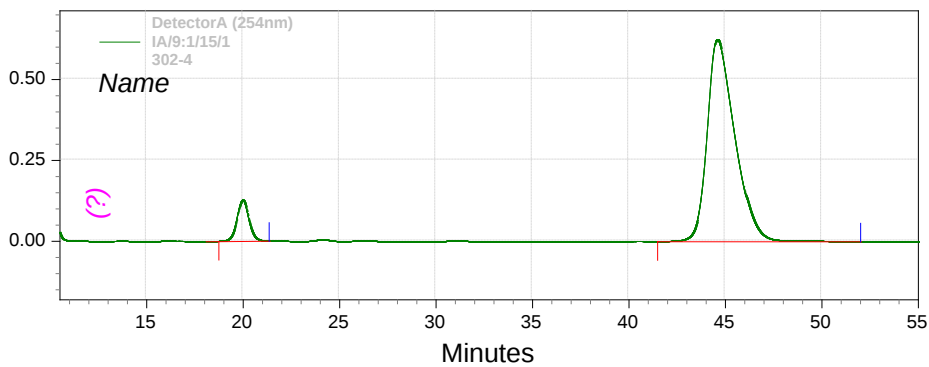
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1	16.248	14395355	47.747
2	37.882	15754160	52.253



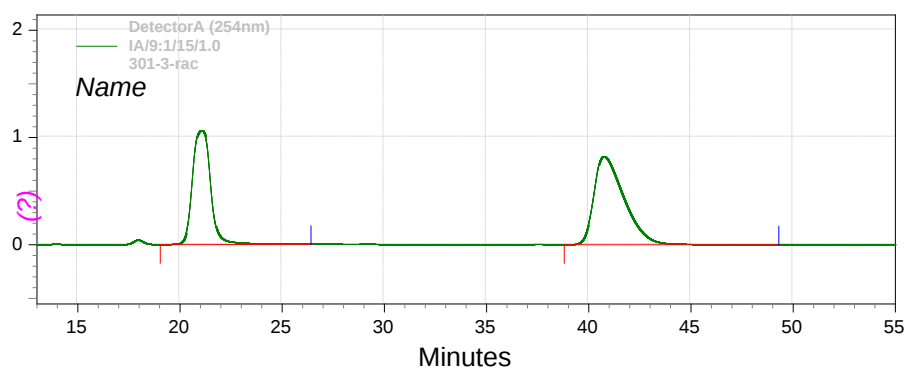
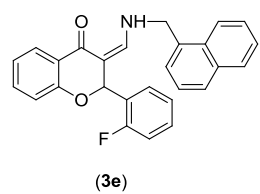
Pk #	Retention Time	Area	Area %
1	17.032	4626613	6.949
2	38.548	61952185	93.051



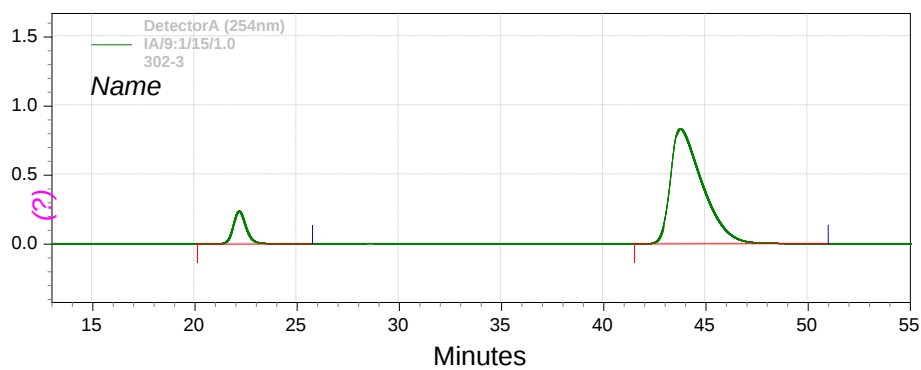
Pk #	Retention Time	Area	Area %
1	19.230	50084673	45.818
2	42.443	59227583	54.182



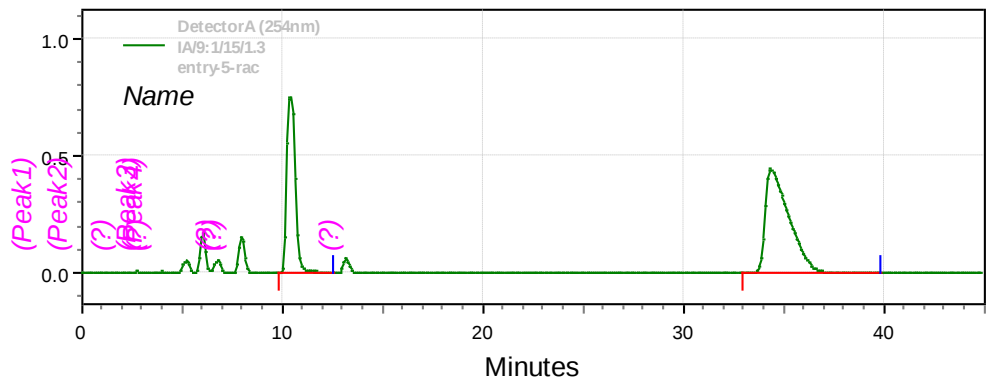
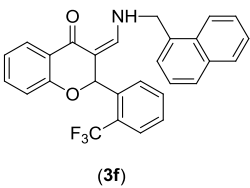
Pk #	Retention Time	Area	Area %
1	19.979	5558127	8.171
2	44.588	62460446	91.829



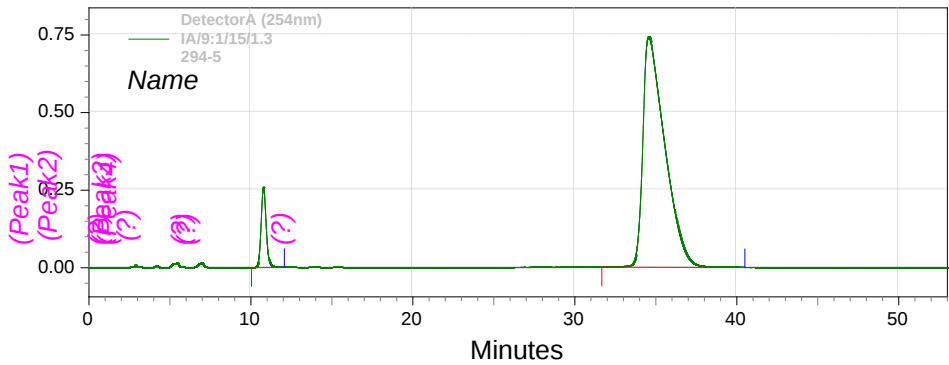
Pk #	Retention Time	Area	Area %
1	21.047	65434664	43.875
2	40.740	83705749	56.125



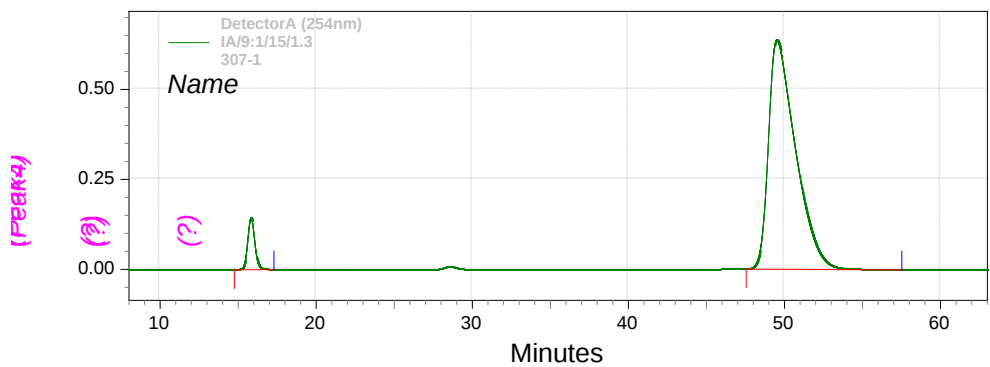
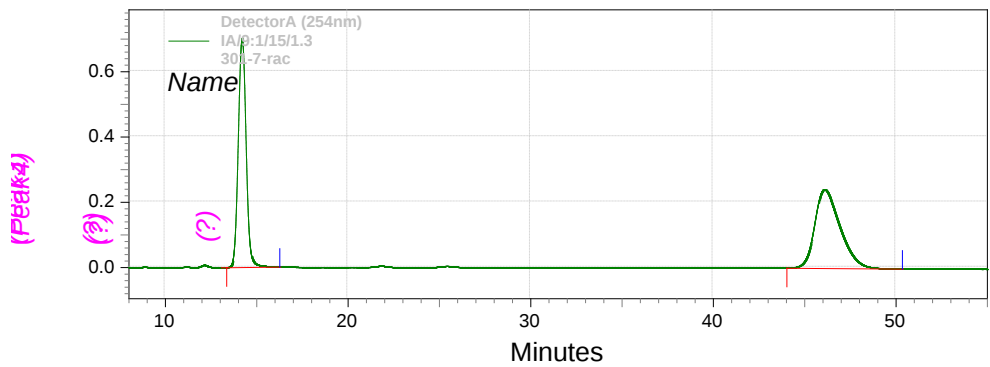
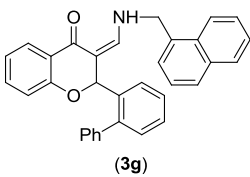
Pk #	Retention Time	Area	Area %
1	22.144	10565644	10.542
2	43.734	89654259	89.458

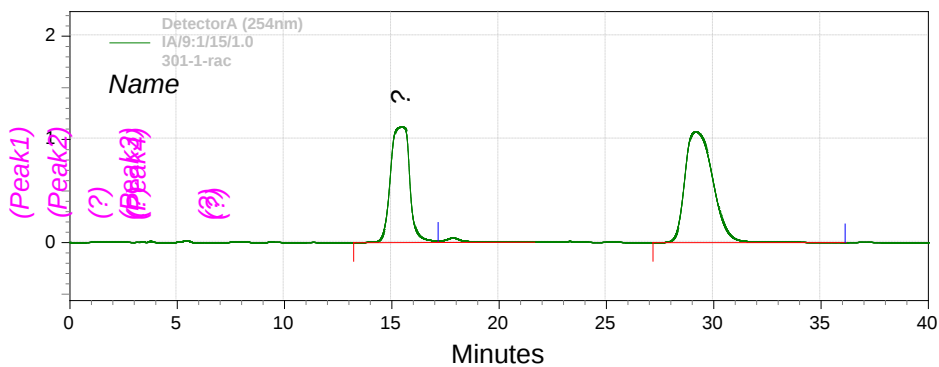
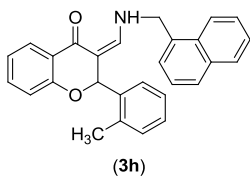


Pk #	Retention Time	Area	Area %
1	10.401	22474298	38.130
2	34.464	36466391	61.870

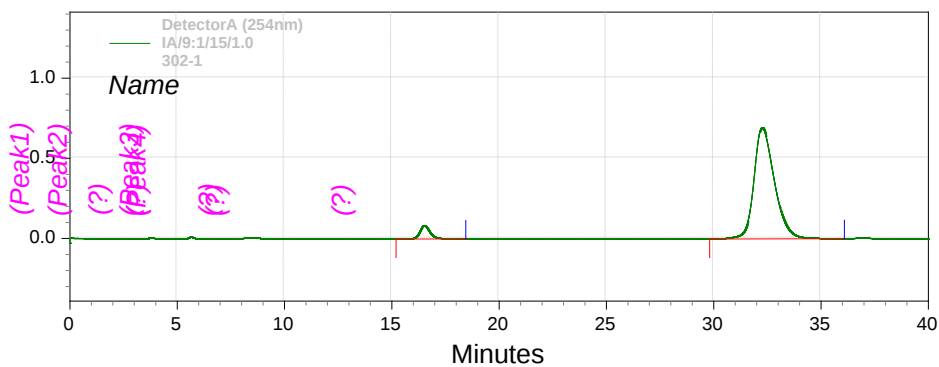


Pk #	Retention Time	Area	Area %
1	10.780	5667841	7.513
2	34.568	69777337	92.487

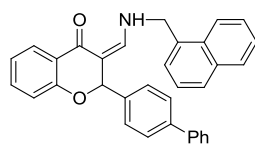




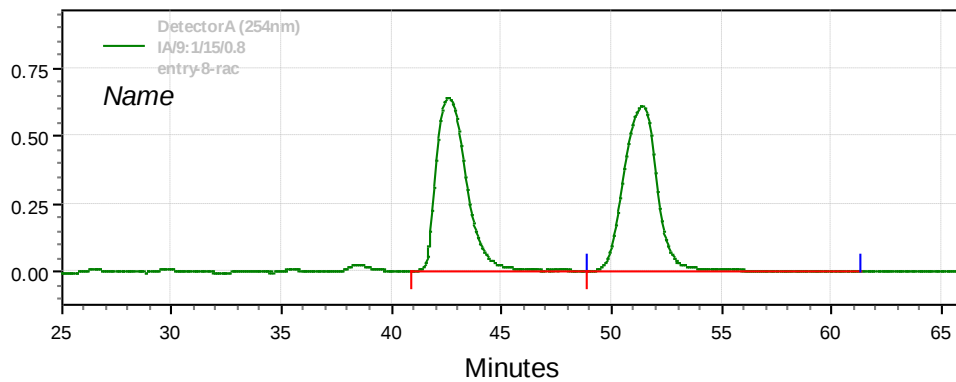
Pk #	Retention Time	Area	Area %
1	15.459	69379175	41.785
2	29.152	96659788	58.215



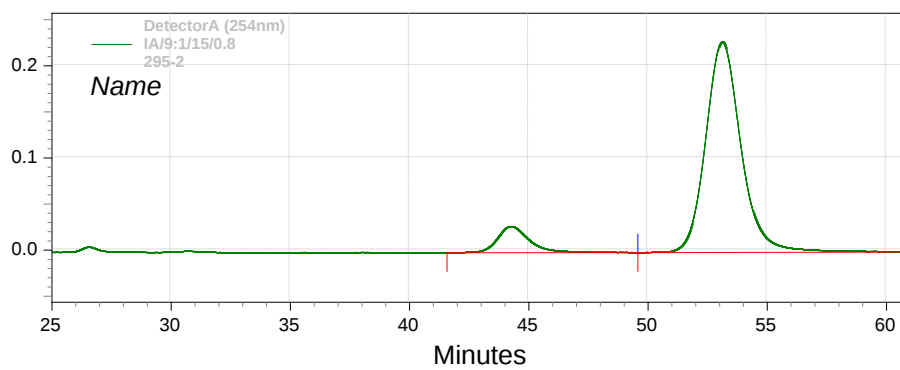
Pk #	Retention Time	Area	Area %
1	16.508	2750813	5.634
2	32.264	46072601	94.366



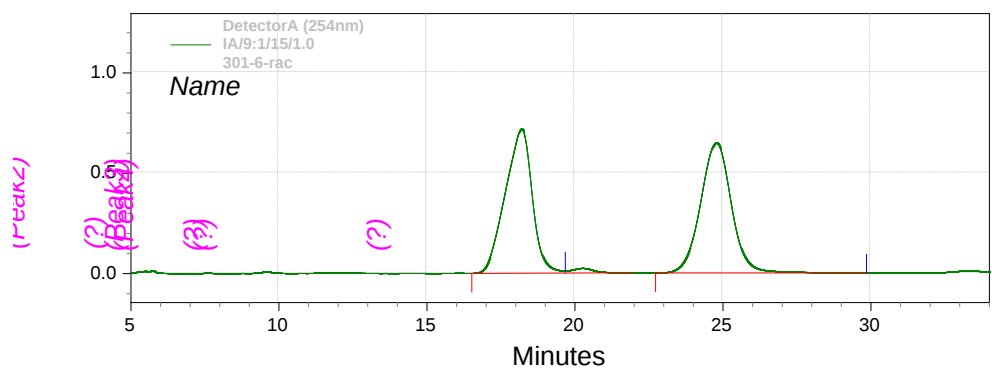
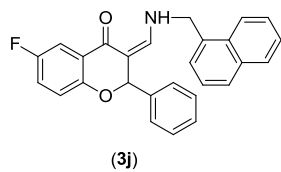
(3i)



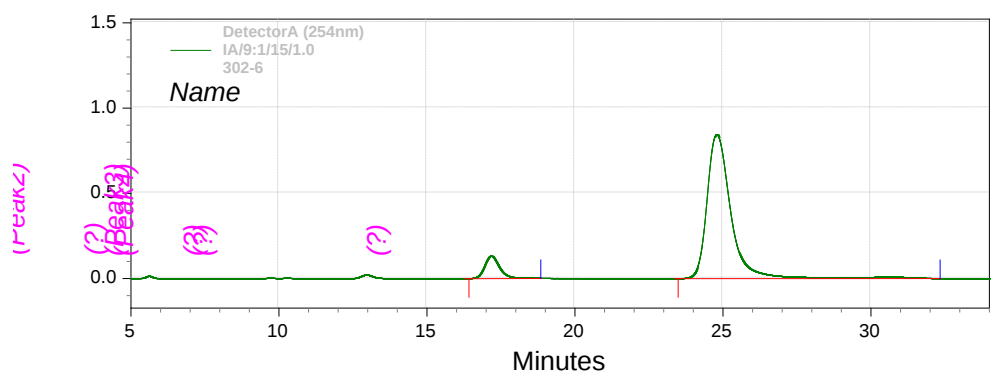
Pk #	Retention Time	Area	Area %
1	42.633	60572611	48.848
2	51.336	63430278	51.152



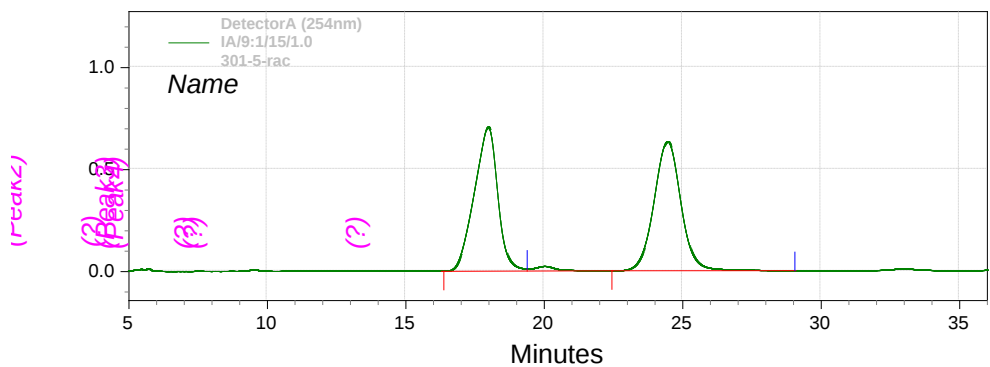
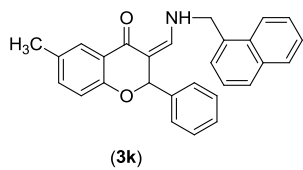
Pk #	Retention Time	Area	Area %
1	44.242	2667817	10.135
2	53.113	23655199	89.865



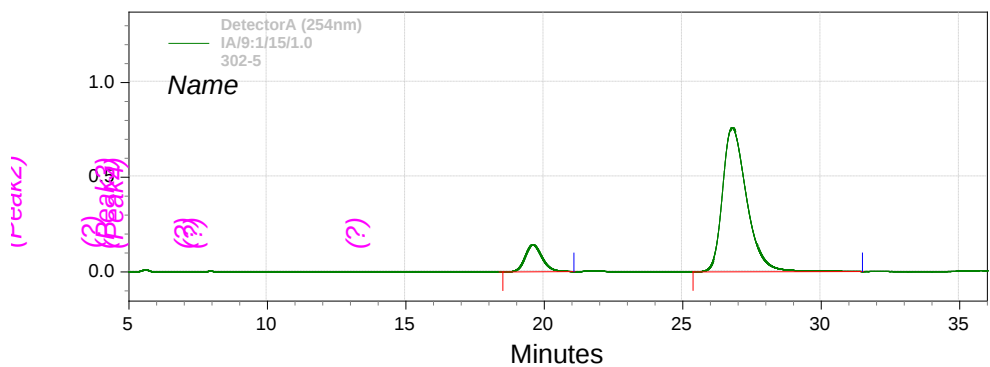
Pk #	Retention Time	Area	Area %
1	18.198	45504792	49.277
2	24.777	46839195	50.723



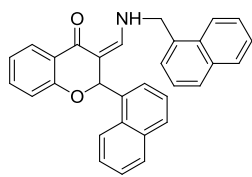
Pk #	Retention Time	Area	Area %
1	17.166	4628656	8.928
2	24.788	47213226	91.072



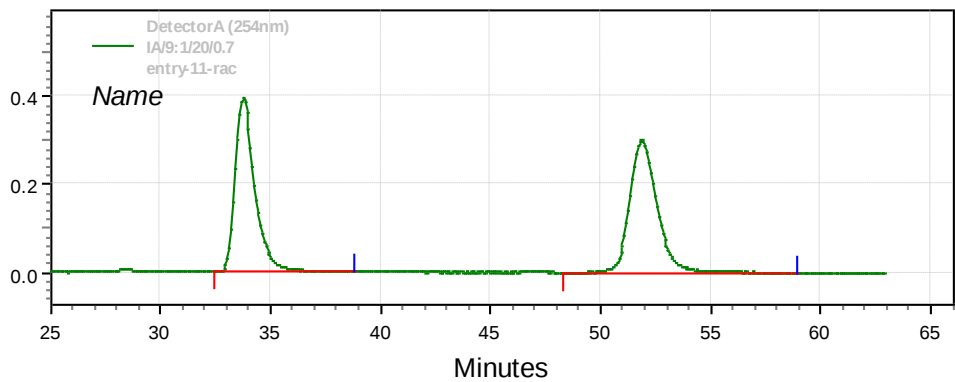
Pk #	Retention Time	Area	Area %
1	17.975	41578164	49.298
2	24.451	42761720	50.702



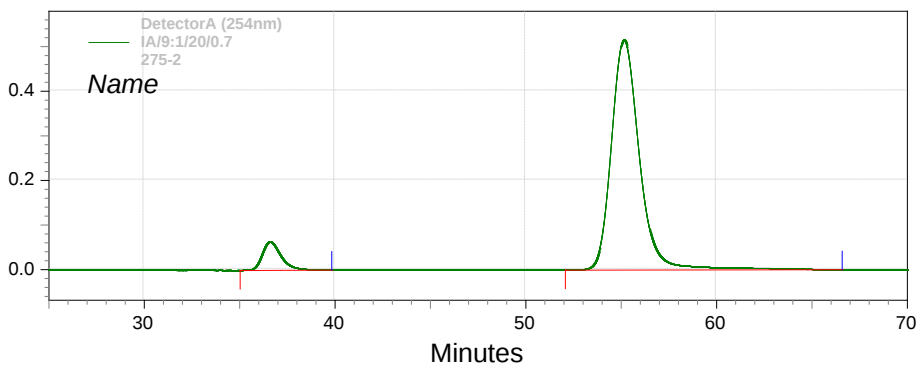
Pk #	Retention Time	Area	Area %
1	19.572	6092707	11.694
2	26.782	46008936	88.306



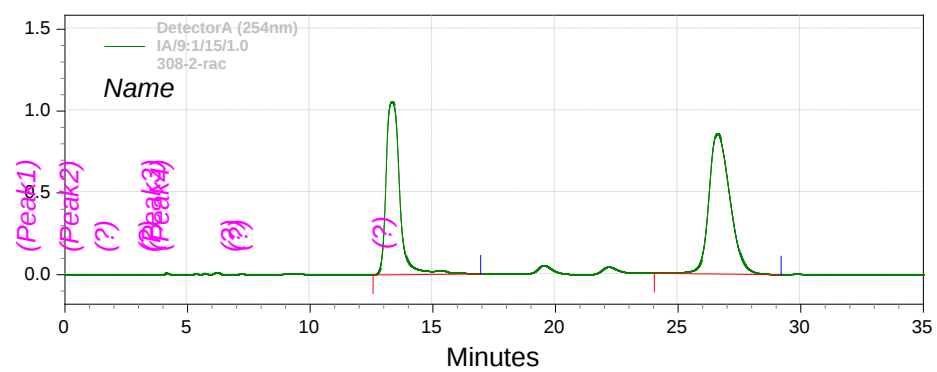
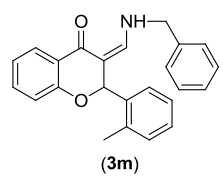
(3l)



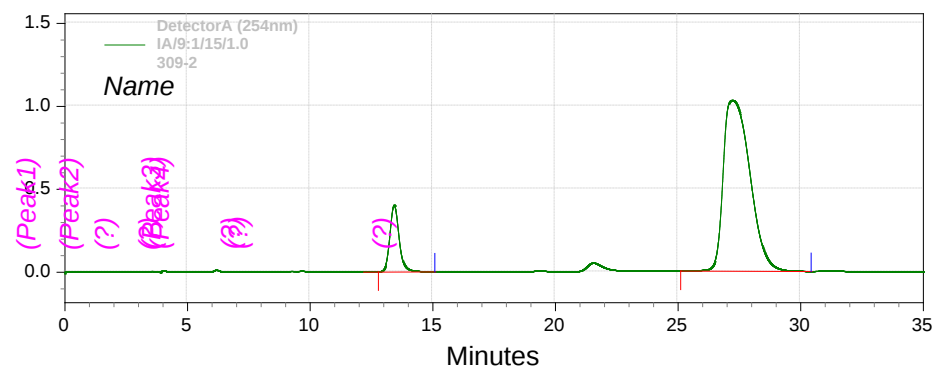
Pk #	Retention Time	Area	Area %
1	33.756	24665769	48.261
2	51.875	26443366	51.739



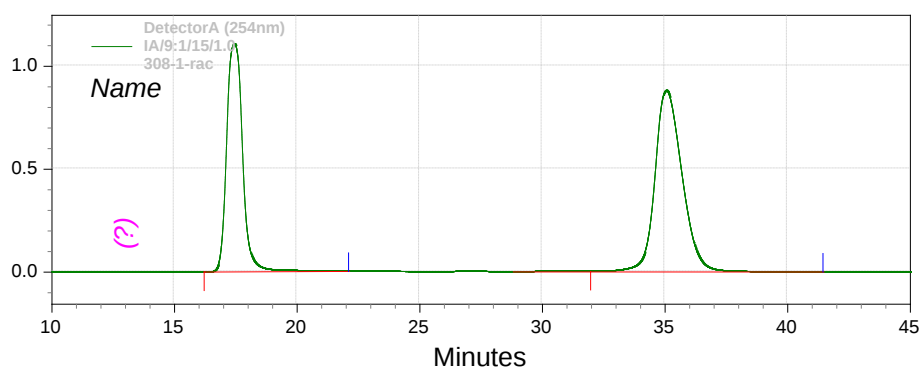
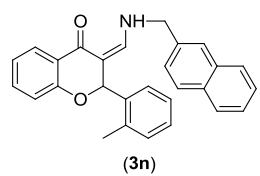
Pk #	Retention Time	Area	Area %
1	36.584	4358978	7.616
2	55.150	52878777	92.384



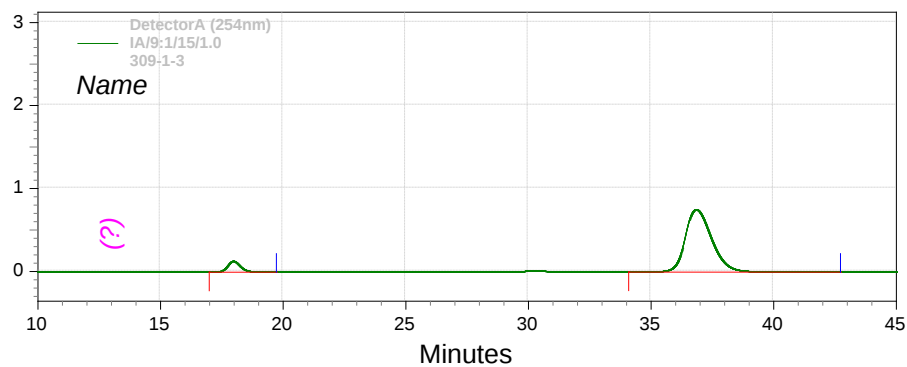
Pk #	Retention Time	Area	Area %
1	13.335	40839659	44.469
2	26.607	50998530	55.531



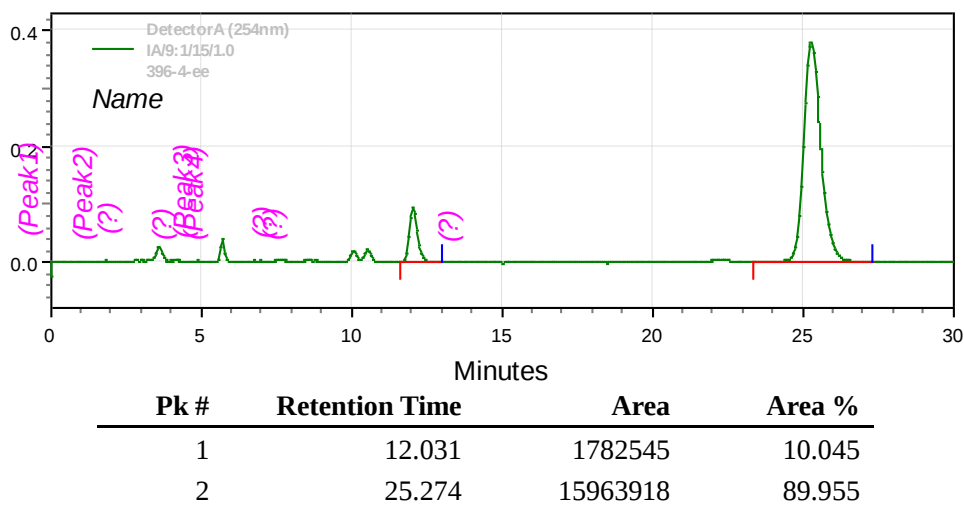
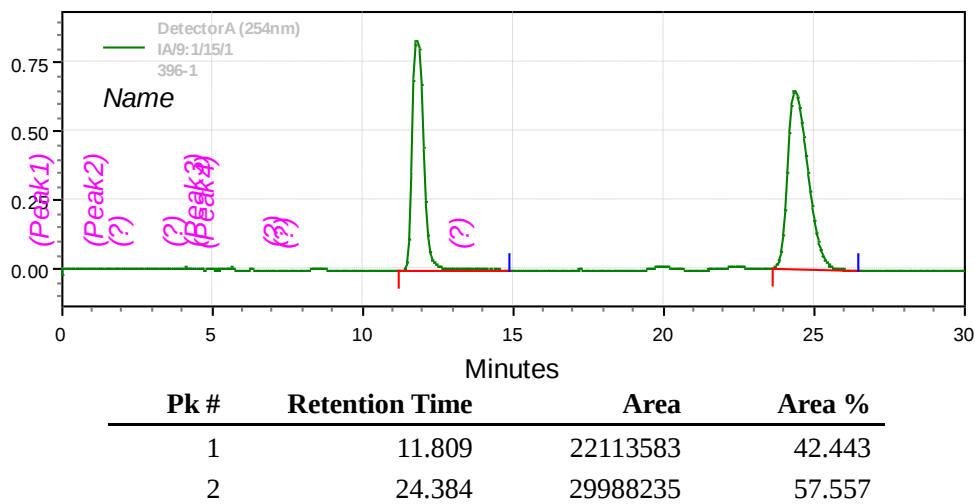
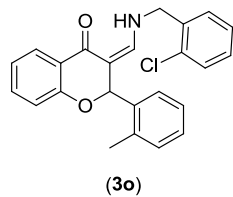
Pk #	Retention Time	Area	Area %
1	13.425	10694026	12.097
2	27.202	77708885	87.903

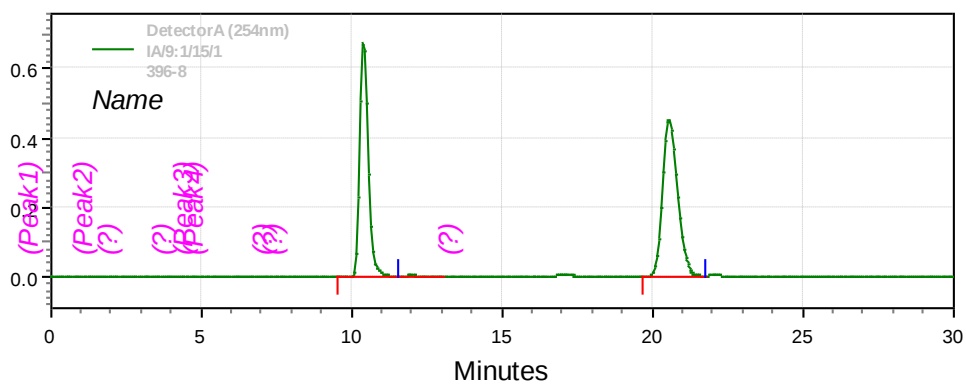
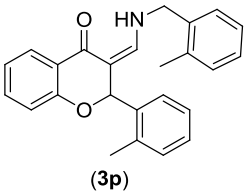


Pk #	Retention Time	Area	Area %
1	17.439	50157922	42.361
2	35.056	68248654	57.639

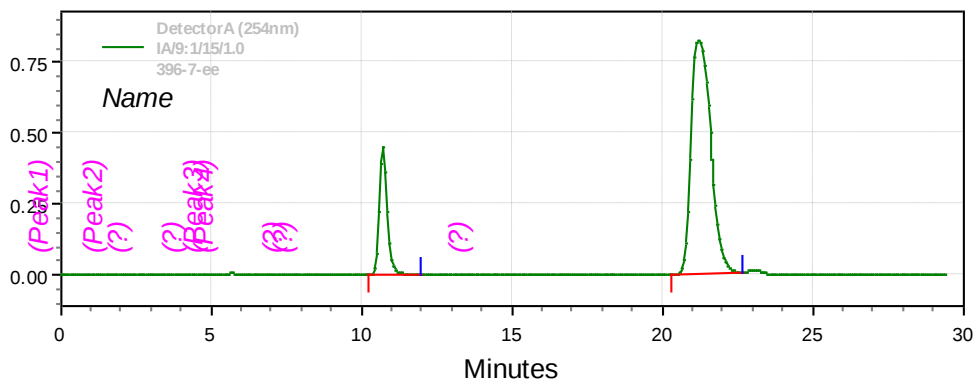


Pk #	Retention Time	Area	Area %
1	17.962	4809210	7.888
2	36.835	56159434	92.112

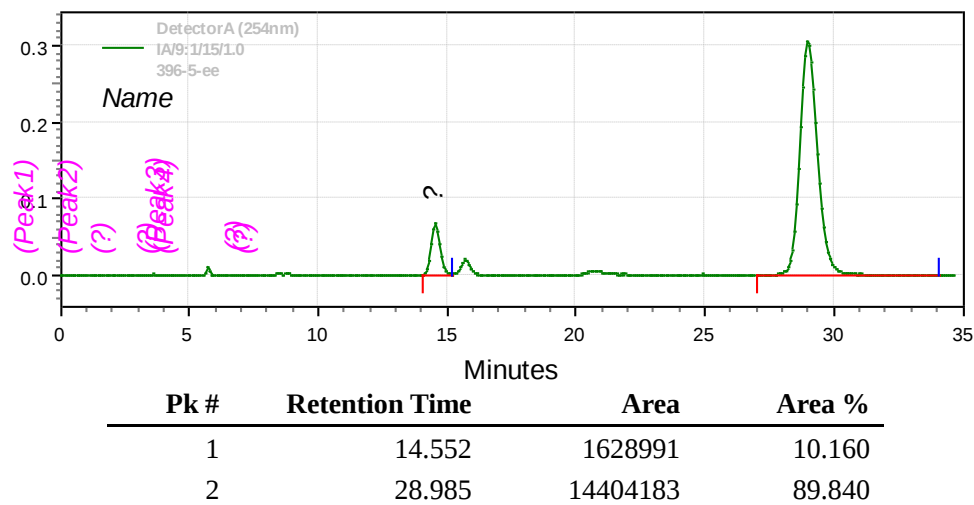
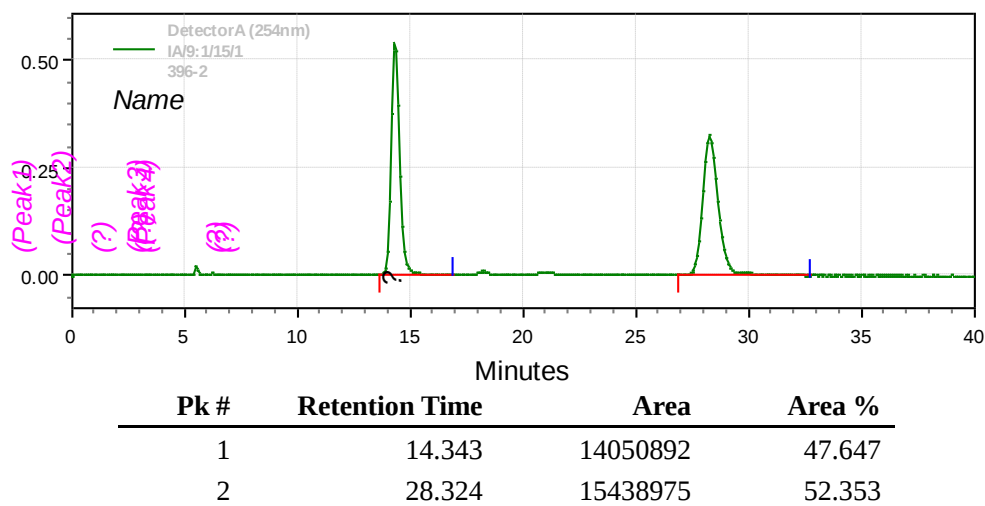
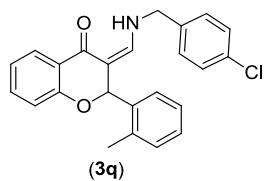


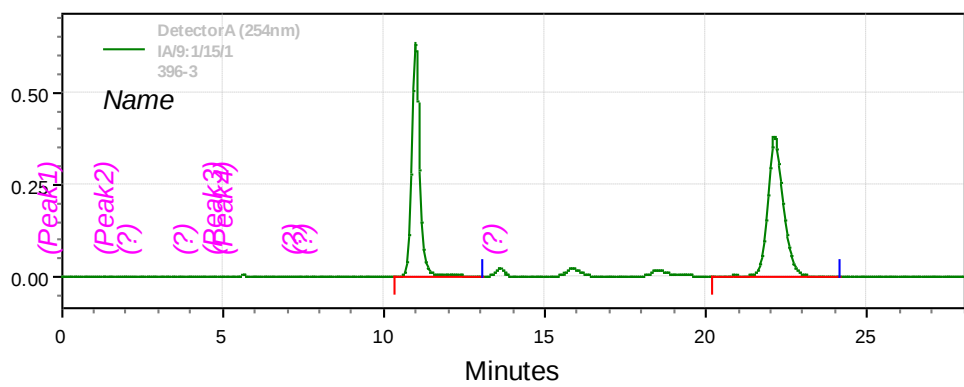
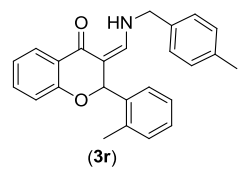


Pk #	Retention Time	Area	Area %
1	10.414	13494439	46.396
2	20.550	15590866	53.604

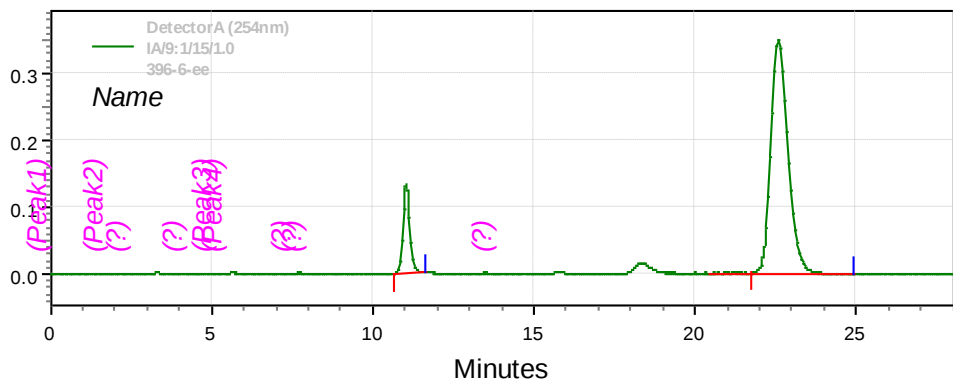


Pk #	Retention Time	Area	Area %
1	10.724	7990223	17.479
2	21.216	37721818	82.521





Pk #	Retention Time	Area	Area %
1	10.978	12554376	47.847
2	22.131	13684188	52.153



Pk #	Retention Time	Area	Area %
1	11.038	2233892	14.777
2	22.611	12883626	85.223