Highly Efficient Enantioselective Three-Component Synthesis of 2-Amino-4*H*-Chromenes Catalysed by Chiral Tertiary Amine-Thioureas

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Content

General information. All the enantioselective three-component reactions of salicylaldehyde, malononitrile/cyanoacetate with nitromethane were carried out with flame-dried Schlenk-type glassware. The chiral tertiary amino-thiourea catalysts derived from (1R, 2R)-cyclohexane-1,2-diamine were synthesized according to reference.[1] The catalyst derived from cinchona alkaloids was synthesized according to reference.[2] All the other reagents were purchased from commercial suppliers and purified by standard techniques. Flash column chromatography was performed using silica gel (200–400 mesh). For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded at 300 MHz NMR spectrometer in $CDCl_3$ or DMSO-d_6. All chemical shifts (δ) are given in ppm relative to TMS (δ = 0 ppm) as internal standard. Data are reported as follows: chemical shift, multiplicity, coupling constants and integration. Melting points were uncorrected. IR spectra were reported in frequency of absorption (cm^{-1}). High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI.

References

[1] T. Okino, Y. Hoashi and Y. Takemoto, *J. Am. Chem. Soc.,* 2003, **125**, 12672.
[2] N. Zhu, B.-C. Ma, Y. Zhang and W. Wang, *Adv. Synth. Catal.,* 2010, **352**, 1291.

X-ray crystallographic analysis

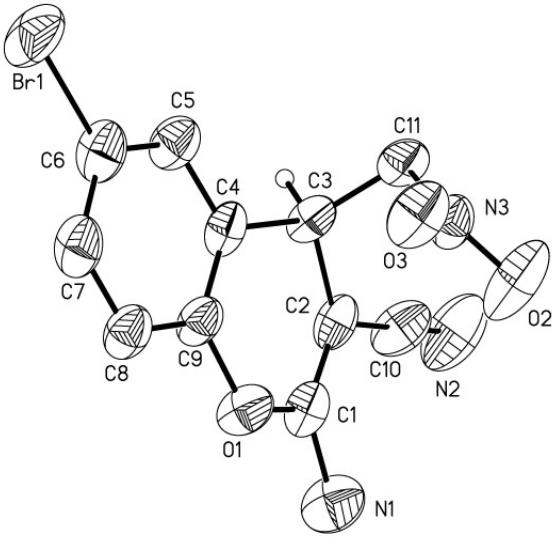
The single crystals of the products **4b**, **5b** and the intermediate **Ia** suitable for X-ray crystallographic analysis were obtained by recrystallization from dichloromethane/isopropanol, dichloromethane/n-hexane, and dichloromethane respectively. The single crystal X-ray diffraction data for the three compounds were collected on a diffractometer with graphite

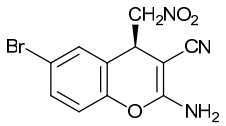
monchromated Mo K_α radiation (λ = 0.71073 Å) at room temperature. Saint program and SADABS program carried out the data integration. The structure was solved by a direct method and refined on F^2 using SHELXTL suite of program. All non-hydrogen atoms were anisotropically refined by full-matrix least squares methods. All hydrogen atoms were geometrically generated and isotropically refined using a riding model. The details of the X-ray data collection, structure solution and structure refinements are given in Table S1.

Table S1 Crystallographic data and structural refinement details for compound **4b**, **5b** and **Ia**.

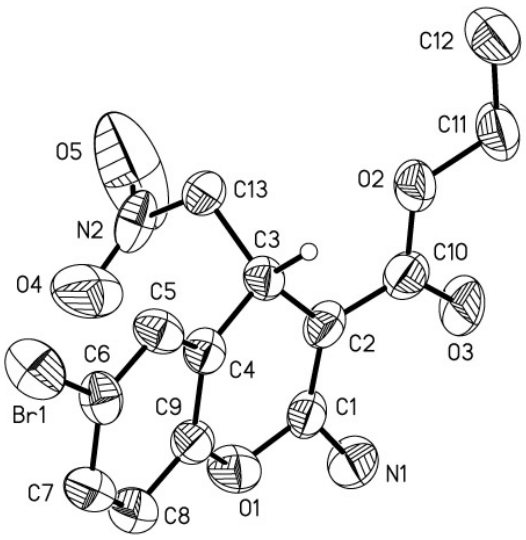
Compound	**4b**	**5b**	**Ia**
Formula	$C_{11}H_8BrN_3O_3$	$C_{13}H_{13}BrN_2O_5$	$C_{10}H_6N_2O$
Formula weight	310.10	357.15	170.17
Temperature/K	293(2)	293(2)	293(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	P21	P21	P21/c
a/Å	9.397(6)	5.413(2)	11.833(4)
b/Å	5.142(3)	17.675(7)	9.268(3)
c/Å	12.852(8)	7.539(3)	7.280(2)
β/°	109.6(7)	96.083(5)	95.8(4)
V/Å ^{3}	584.9(6)	717.2(5)	794.2(4)
Z	2	2	4
μ(Mo Ka), mm^{-1}	3.518	2.889	0.096
θ range for data collection, deg	1.7 to 27.7	2.3 to 27.5	1.7 to 27.6
Reflections collected	4955	5934	6600
Unique reflections/R_{int}	2349 / R(int) = 0.105	2951 / R(int) = 0.056	1835 / R(int) = 0.021
Goodness-of-fit on F^2	0.89	0.99	0.98
R, R_w [I > 2σ(I)]	0.0811, 0.2211	0.0547, 0.1541	0.0530, 0.1773
Residual ρ/(e·Å $^{-3}$)	1.33, –0.73	1.08, –0.50	0.39, –0.42
Flack χ	0.03(3)	0.016(17)	/
CCDC No.	860045	860044	860046

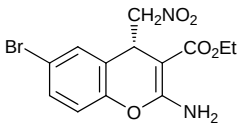
Figure S1 X-ray structure (50 % probability ellipsoids) of **4b**, **5b** and **Ia**.



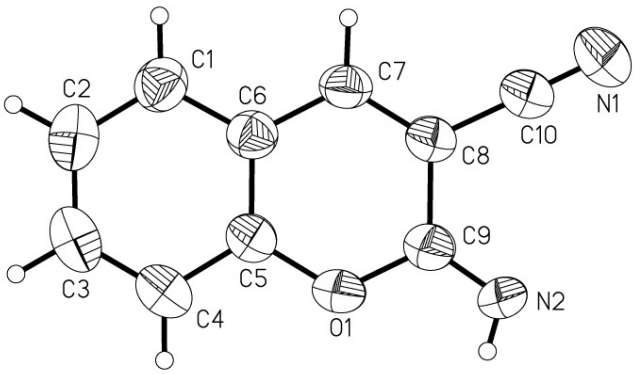


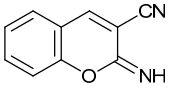
4b





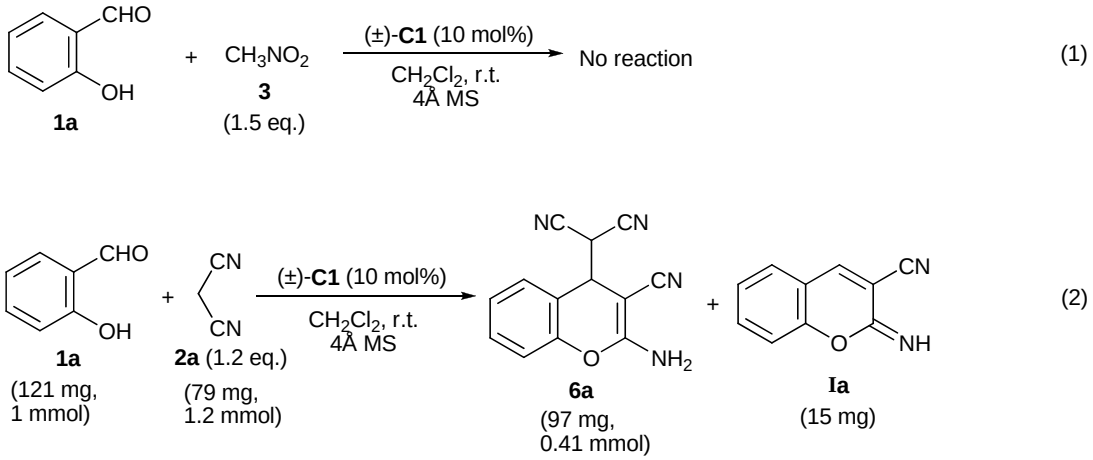
5b





Ia

Scheme S1 Control experiments for mechanistic study.



General procedure for the enantioselective three-component reaction: To a solution of salicylaldehyde **1** (0.3 mmol, 1.0 equiv), malononitrile/ethyl cyanoacetate **2** (0.36 mmol, 1.2 equiv), nitromethane **3** (0.45 mmol, 1.5 equiv) and 50 mg of 4Å MS in CH_2Cl_2 (1.5 mL) at room temperature, was added catalyst **C3** (0.03 mmol) in one portion. The resulting reaction mixture was stirred at room temperature and monitored by TLC. Upon completion, the solvent was removed under vacuum and the residue was purified by flash chromatography to afford the desired product.

(*R*)-2-Amino-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4a): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a yellow solid in 88% yield and 84% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (3/2 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_{major} = 25.8 min, t_{minor} = 19.9 min). $[\alpha]^{20}_D$ = –66.3 (c = 0.51, EtOAc). Mp: 139–140 °C. **IR** (KBr): ν = 3451, 3337, 2191, 1655, 1612, 1584, 1537, 1491, 1460, 1379, 1275, 1227 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 1H), 7.21–7.13 (m, 2H), 7.04 (d, *J* = 8.2 Hz, 1H), 4.85 (s, 2H), 4.62 (dd, *J* = 12.1, 4.7 Hz, 1H), 4.50 (dd, *J* = 12.1, 7.1 Hz, 1H), 4.37 (dd, *J* = 7.1, 4.7 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 161.7, 149.3, 129.6, 127.9, 125.7, 118.6, 116.9, 80.2, 54.2, 34.8 ppm. **HRMS** (ESI): calcd for $C_{11}H_{10}N_3O_3$ $[M+H]^+$ 232.0722; found 232.0711.

(*R*)-2-Amino-6-bromo-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4b): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a white solid in 92% yield and 87% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (3/2 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 34.9 (major), 21.7 (minor) min). $[\alpha]_D^{20}$ = –15.7 (c = 0.61, EtOAc). Mp: 177–178 °C. IR (KBr): ν = 3456, 3308, 2205, 1653, 1637, 1601, 1574, 1530, 1481, 1423, 1375, 1271, 1225 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.63 (s, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.23 (s, 2H), 6.99 (d, *J* = 8.7 Hz, 1H), 4.87 (dd, *J* = 12.8, 4.8 Hz, 1H), 4.69 (dd, *J* = 12.8, 4.8 Hz, 1H), 4.33 (t, *J* = 4.8 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 162.3, 149.2, 132.2, 131.3, 122.4, 119.9, 118.8, 116.6, 80.8, 50.2, 34.7 ppm. **HRMS** (ESI): calcd for $C_{11}H_9BrN_3O_3$ $[M+H]^+$ 309.9827; found 309.9816.

(*R*)-2-Amino-6-chloro-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4c): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a white solid in 85% yield and 82% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (3/2 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 33.5 (major), 18.1 (minor) min). $[\alpha]_D^{20}$ = –24.7 (c = 0.59, EtOAc). Mp: 165–166 °C. **IR**

(KBr): ν = 3460, 3308, 2205, 1655, 1636, 1601, 1576, 1530, 1483, 1427, 1377, 1271, 1227 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.51 (d, J = 2.5 Hz, 1H), 7.37 (dd, J = 8.7, 2.5 Hz, 1H), 7.21 (s, 2H), 7.06 (d, J = 8.7 Hz, 1H), 4.87 (dd, J = 12.6, 5.0 Hz, 1H), 4.70 (dd, J = 12.6, 4.8 Hz, 1H), 4.33 (t, J = 4.8 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 162.3, 148.8, 129.4, 128.7, 128.4, 122.0, 119.9, 118.5, 80.8, 50.2, 34.8 ppm. **HRMS** (ESI): calcd for $C_{11}H_9ClN_3O_3$ $[M+H]^+$ 266.0332; found 266.0320.

(*R*)-2-Amino-6-nitro-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4d): Purified by column chromatography (petroleum ether/ethyl acetate = 2/1) to afford a yellow solid in 80% yield and 81% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (1/3 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 30.0 (major), 19.3 (minor) min). $[\alpha]_D^{20}$= +26.5 (c = 0.46, EtOAc). Mp: 171–172°C. **IR** (KBr): ν = 3449, 3362, 2191, 1651, 1582, 1416, 1348, 1306, 1264 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 8.41 (d, J = 2.7 Hz, 1H), 8.19 (dd, J = 9.0, 2.7 Hz, 1H), 7.38 (s, 2H), 7.27(d, J = 9.0 Hz, 1H), 4.99 (dd, J = 12.9, 4.5 Hz, 1H), 4.76 (dd, J = 12.9, 4.5 Hz, 1H), 4.48 (t, J = 4.5 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 161.8, 154.4, 144.2, 125.2, 125.1, 121.6, 119.5, 118.0, 80.7, 50.3, 34.5 ppm. **HRMS** (ESI): calcd for $C_{11}H_8N_4O_5Na$ $[M+Na]^+$ 299.0392; found 299.0387.

(*R*)-2-Amino-6,8-dibromo-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4e): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a white solid in 78% yield and 96% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (1/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 28.9 (major), 20.0 (minor) min). $[\alpha]_D^{20}$= 33.8 (c = 0.55, EtOAc). Mp: 211–212°C. **IR** (KBr): ν = 3431, 3316, 2207, 1659, 1614, 1541, 1458, 1418, 1377, 1246, 1196 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.88 (s, 1H), 7.66 (s, 1H), 7.38 (s, 2H), 4.90 (dd, J = 12.8, 4.7 Hz, 1H), 4.72 (dd, J = 12.8, 4.7 Hz, 1H), 4.38 (t, J = 4.7 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 161.4, 145.9, 134.3, 130.4, 123.5, 118.9, 116.2, 110.5, 80.1, 50.1, 34.6 ppm. **HRMS** (ESI): calcd for $C_{11}H_7Br_2N_3O_3Na$ $[M+Na]^+$ 409.8752; found

409.8751.

(*R*)-2-Amino-6,8-dichloro-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4f): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a yellow solid in 75% yield and 80% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (1/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 30.6 (major), 17.0 (minor) min). Mp: 208–209°C. **IR** (KBr): ν = 3428, 3318, 2210, 1661, 1616, 1572, 1541, 1464, 1423, 1381, 1248, 1200 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.67 (d, J = 2.4 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H), 7.39 (s, 2H), 4.91 (dd, J = 12.9, 4.8 Hz, 1H), 4.72 (dd, J = 12.9, 4.8 Hz, 1H), 4.38 (t, J = 4.8 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 161.3, 144.5, 128.9, 128.2, 127.0, 123.2, 121.2, 119.0, 80.1, 49.9, 34.5 ppm. **HRMS** (ESI): calcd for $C_{11}H_8Cl_2N_3O_3$ $[M+H]^+$ 299.9942; found 299.9936.

(*R*)-2-Amino-5-methoxy-4-(nitromethyl)-4*H*-chromene-3-carbonitrile (4g): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a yellow solid in 64% yield and 83% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (1/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 20.7 (major), 16.1 (minor) min). $[\alpha]_D^{20}$ = –29.2 (c = 0.52, EtOAc). Mp: 139–140°C. **IR** (KBr): ν = 3445, 3331, 2191, 1651, 1635, 1618, 1599, 1487, 1472, 1423, 1253, 1090 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.30 (t, J = 8.3 Hz, 1H), 7.16 (s, 2H), 6.85 (d, J = 8.3 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 4.67–4.56 (m, 2H), 4.24 (t, J = 4.7 Hz, 1H), 3.83 (s, 3H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 162.5, 156.7, 150.7, 130.0, 120.2, 108.9, 108.2, 107.3, 79.6, 56.6, 50.7, 31.7 ppm. **HRMS** (ESI): calcd for $C_{12}H_{12}N_3O_4$ $[M+H]^+$ 262.0828; found 262.0820.

2-Amino-4-(1-nitroethyl)-4*H*-chromene-3-carbonitrile (4h): Purified by column chromatography (petroleum ether/ethyl acetate = 3/1) to afford a white solid in 88% yield, 43/57 dr and 58% ee_1, 75% ee_2. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (9/1 hexane/*i*-PrOH; flow rate 1.0

mL/min; λ = 254 nm; t_R = 65.4 (major$_1$), 74.8 (minor$_1$), 100.0 (major$_2$), 84.2 (minor$_2$) min). $[\alpha]_D^{20}$= –35.9 (c = 1.03, EtOAc). Mp: 138–139°C. **IR** (KBr): v = 3319, 3269, 2197, 1638, 1605, 1578, 1541, 1487, 1456, 1420, 1389, 1362 cm^{-1}. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.39–7.13 (m, 5H), 7.10–7.01 (m, 1H), 4.87–4.71 (m, 1H), 4.29–4.18 (m, 1H), 1.38–1.26 (m, 3H) ppm. **^{13}C NMR** (75.5 MHz, DMSO-d_6): δ = 163.2, 163.0, 149.9, 149.8, 129.1, 128.5, 128.3, 124.8, 120.2, 119.81, 119.79, 119.4, 116.1, 115.9, 87.3, 86.9, 49.2, 48.4, 14.1, 13.5 ppm. **HRMS** (ESI): calcd for $C_{12}H_{12}N_3O_3$ $[M + H]^+$ 246.0878; found 246.0870.

(*S*)-Ethyl 2-amino-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5a): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 76% yield and 87% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column (3/2 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 20.7 (major), 13.8 (minor) min). $[\alpha]_D^{20}$= 87.7 (c = 0.9, EtOAc). Mp: 109–110℃. **IR** (KBr): v = 3451, 3316, 1672, 1630, 1537, 1512, 1485, 1456, 1410, 1381, 1300 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.31–7.24 (m, 1H), 7.21–7.09 (m, 2H), 7.05–6.99 (m, 1H), 6.82–5.88 (br s, 2H), 4.65 (dd, J = 8.0, 4.4 Hz, 1H), 4.54 (dd, J = 11.2, 4.4 Hz, 1H), 4.39 (dd, J = 11.2, 8.0 Hz, 1H), 4.30–4.19 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 168.3, 162.0, 149.8, 128.9, 128.2, 125.0, 121.8, 116.3, 81.2, 73.0, 59.9, 34.3, 14.5 ppm. **HRMS** (ESI): calcd for $C_{13}H_{15}N_2O_5$ $[M+H]^+$ 279.0981; found 279.0969.

(*S*)-Ethyl 2-amino-6-bromo-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5b): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 83% yield and 91% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column/OJ-H column (8/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 111.2 (major), 127.1 (minor) min). $[\alpha]_D^{20}$= 35.9 (c = 1.38, EtOAc). Mp: 128–129°C. **IR** (KBr): v = 3462, 3306, 1676, 1616, 1541, 1477, 1410, 1379, 1315, 1290, 1221 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.38 (dd, J = 8.7, 2.4 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 8.7 Hz, 1H), 6.80–5.88 (br s, 2H), 4.59 (dd, J = 7.5, 4.2 Hz, 1H), 4.50 (dd, J = 11.7, 4.2 Hz, 1H), 4.43 (dd, J = 11.7, 7.5 Hz,

1H), 4.30–4.18 (m, 2H), 1.33 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.9, 161.5, 148.9, 131.7, 130.8, 123.8, 117.8, 117.2, 80.6, 72.4, 59.9, 33.8, 14.3 ppm. **HRMS** (ESI): calcd for $C_{13}H_{14}BrN_2O_5$ $[M+H]^+$ 357.0086; found 357.0074.

(*S*)-Ethyl 2-amino-6-chloro-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5c): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 76% yield and 84% ee. The ee was determined by HPLC analysis using a Chiralcel AS-H column (11/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 23.7 (major), 27.1 (minor) min). $[\alpha]_D^{20}$= 29.1 (c = 1.05, EtOAc). Mp: 141–142°C. **IR** (KBr): ν = 3474, 3312, 2982, 1678, 1620, 1541, 1518, 1483, 1418, 1377, 1317, 1292, 1221 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.24 (dd, J = 8.7, 2.4 Hz, 1H), 7.19 (d, J = 2.4 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 6.82–5.95 (br s, 2H), 4.59 (dd, J = 7.5, 4.2 Hz, 1H), 4.52 (dd, J = 11.6, 4.2 Hz, 1H), 4.43 (dd, J = 11.6, 7.5 Hz, 1H), 4.30–4.18 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.9, 161.5, 148.3, 129.8, 128.8, 127.8, 123.3, 117.5, 80.6, 72.3, 59.9, 33.9, 14.3 ppm. **HRMS** (ESI): calcd for $C_{13}H_{14}ClN_2O_5$ $[M+H]^+$ 313.0591; found 313.0578.

(*S*)-Ethyl 2-amino-6,8-dibromo-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5d): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 78% yield and 89% ee. The ee was determined by HPLC analysis using a Chiralpak AS-H column/AS-H column (16/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 69.6 (major), 80.2 (minor) min). $[\alpha]_D^{20}$= 14.3 (c = 0.88, EtOAc). Mp: 187–188°C. **IR** (KBr): ν = 3458, 3318, 1678, 1614, 1572, 1541, 1520, 1454, 1400, 1385, 1344, 1315, 1279, 1248 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 2.1 Hz, 1H), 7.29 (d, J = 2.1 Hz, 1H), 6.97–5.79 (br s, 2H), 4.62 (dd, J = 7.8, 4.2 Hz, 1H), 4.51 (dd, J = 11.8, 4.3 Hz, 1H), 4.41 (dd, J = 11.8, 7.9 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.7, 161.3, 146.2, 135.0, 130.1, 125.2, 117.4, 111.2, 80.5, 72.7, 60.2, 34.4, 14.4 ppm. **HRMS** (ESI): calcd for $C_{13}H_{13}Br_2N_2O_5$ $[M+H]^+$

434.9191; found 434.9182.

(*S*)-Ethyl 2-amino-6,8-dichloro-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5e): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 81% yield and 77% ee. The ee was determined by HPLC analysis using a Chiralpak AS-H column/AS-H column (30/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 115.5 (major), 132.3 (minor) min). $[\alpha]_D^{20}$= 30.7 (c = 1.08, EtOAc). Mp: 148–149°C. **IR** (KBr): ν = 3468, 3316, 1678, 1616, 1582, 1541, 1460, 1404, 1387, 1317, 1279, 1252 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.35 (d, J = 2.4 Hz, 1H), 7.10 (d, J = 2.4 Hz, 1H), 6.96–5.72 (br s, 2H), 4.62 (dd, J = 7.8, 4.2 Hz, 1H), 4.52 (dd, J = 11.8, 4.2 Hz, 1H), 4.41 (dd, J = 11.8, 7.9 Hz, 1H), 4.31–4.20 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.7, 161.3, 144.7, 129.8, 129.4, 126.5, 124.9, 122.5, 80.5, 72.5, 60.2, 34.4, 14.4 ppm. **HRMS** (ESI): calcd for $C_{13}H_{13}Cl_2N_2O_5$ $[M+H]^+$ 347.0201; found 347.0190.

(*S*)-Ethyl 2-amino-6-methoxy-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5f): Purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to afford a white solid in 86% yield and 77% ee. The ee was determined by HPLC analysis using a Chiralcel OJ-H column/OJ-H column (2/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 45.4 (major), 55.7 (minor) min). $[\alpha]_D^{20}$= 63.9 (c = 0.97, EtOAc). Mp: 109–110°C. **IR** (KBr): ν = 3422, 3292, 2982, 1674, 1620, 1597, 1547, 1491, 1414, 1379, 1344, 1292, 1271, 1221 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 6.94 (d, J = 9.0 Hz, 1H), 6.80 (dd, J = 9.0, 3.0 Hz, 1H), 6.68 (d, J = 3.0 Hz, 1H), 6.62–5.99 (br s, 2H), 4.62 (dd, J = 8.0, 4.4 Hz, 1H), 4.53 (dd, J = 11.4, 4.4 Hz, 1H), 4.39 (dd, J = 11.3, 8.0 Hz, 1H), 4.29–4.18 (m, 2H), 3.76 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 168.2, 162.1, 156.3, 143.6, 122.3, 116.9, 114.7, 112.0, 80.9, 72.3, 59.7, 55.5, 34.5, 14.3 ppm. **HRMS** (ESI): calcd for $C_{14}H_{17}N_2O_6$ $[M+H]^+$ 309.1086; found 309.1080.

(*S*)-Ethyl 2-amino-5,7-dichloro-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5g): Purified by column

chromatography (petroleum ether/ethyl acetate = 4/1) to afford a white solid in 76% yield and 87% ee. The ee was determined by HPLC analysis using a Chiralcel AS-H column (40/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 24.9 (major), 21.1 (minor) min). $[\alpha]_D^{20}$= 73.5 (c = 0.49, EtOAc). Mp: 105–106°C. **IR** (KBr): ν = 3443, 3312, 2982, 1682, 1633, 1603, 1550, 1520, 1462, 1408, 1379, 1301, 1261, 1219 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 2.0 Hz, 1H), 6.99 (d, J = 2.0 Hz, 1H), 6.80–5.90 (br s, 2H), 4.73–4.63 (m, 2H), 4.42–4.18 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 167.8, 161.2, 151.6, 134.4, 133.4, 125.6, 118.9, 115.8, 78.3, 72.6, 60.2, 32.8, 14.5 ppm. **HRMS** (ESI): calcd for $C_{13}H_{13}N_2O_5Cl_2$ $[M+H]^+$ 347.0201; found 347.0196.

(*S*)-Ethyl 2-amino-5-methoxy-4-(nitromethyl)-4*H*-chromene-3-carboxylate (5h): Purified by column chromatography (petroleum ether/ethyl acetate = 6/1) to afford a yellow solid in 41% yield and 61% ee. The ee was determined by HPLC analysis using a Chiralcel AS-H column (16/1 hexane/*i*-PrOH; flow rate 1.0 mL/min; λ = 254 nm; t_R = 54.8 (major), 43.2 (minor) min). $[\alpha]_D^{20}$= 35.9 (c = 0.58, EtOAc). Mp: 104–105°C. **IR** (KBr): ν = 3441, 3308, 2982, 1682, 1643, 1545, 1524, 1470, 1439, 1283, 1223, 1202, 1097, 1070 cm^{-1}. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.22 (t, J = 8.3 Hz, 1H), 6.67 (d, J = 8.3 Hz, 1H), 6.63 (d, J = 8.3 Hz, 1H), 4.68–4.58 (m, 3H), 4.32–4.15 (m, 2H), 3.88 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 168.6, 161.8, 156.6, 151.0, 128.9, 110.3, 108.7, 106.0, 79.2, 73.1, 59.8, 55.7, 30.3, 14.5 ppm. **HRMS** (ESI): calcd for $C_{14}H_{17}N_2O_6$ $[M+H]^+$ 309.1086; found 309.1084.

2-(2-Amino-3-cyano-4H-chromen-4-yl)malononitrile (6a): ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.50 (s, 2H), 7.47–7.40 (m, 2H), 7.33–7.23 (m, 1H), 7.17–7.10 (m, 1H), 5.06 (d, J = 3.9 Hz, 1H), 4.59 (d, J = 3.9 Hz, 1H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 163.9, 150.2, 130.7, 129.4, 125.5, 119.8, 118.5, 116.9, 113.6, 113.4, 49.4, 37.6, 32.9 ppm.

Ethyl 2-amino-4-(1-cyano-2-ethoxy-2-oxoethyl)-4*H*-chromene-3-carboxylate (6b): ^{1}H NMR (300 MHz,

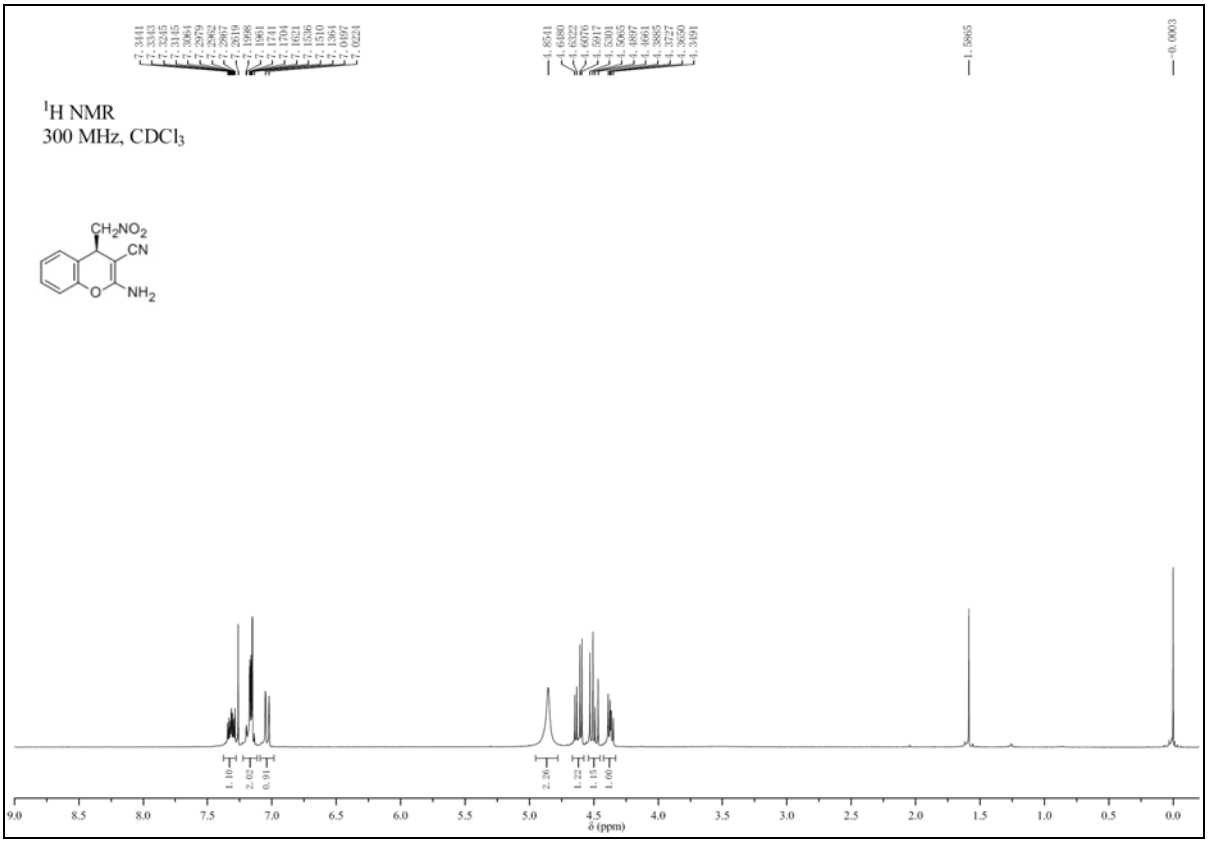
$CDCl_3$): δ = 7.31–7.27 (m, 1H), 7.12–7.05 (m, 3H), 6.81–5.90 (br s, 2H), 4.72 (d, J = 3.0 Hz, 1H), 4.30–4.22 (m, 4H), 3.98 (d, J = 3.0 Hz, 1H), 1.35 (t, J = 7.2 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 168.1, 165.2, 162.6, 150.6, 129.4, 128.3, 124.8, 120.3, 116.7, 115.6, 73.6, 62.8, 60.0, 46.8, 37.0, 14.6, 14.1 ppm.

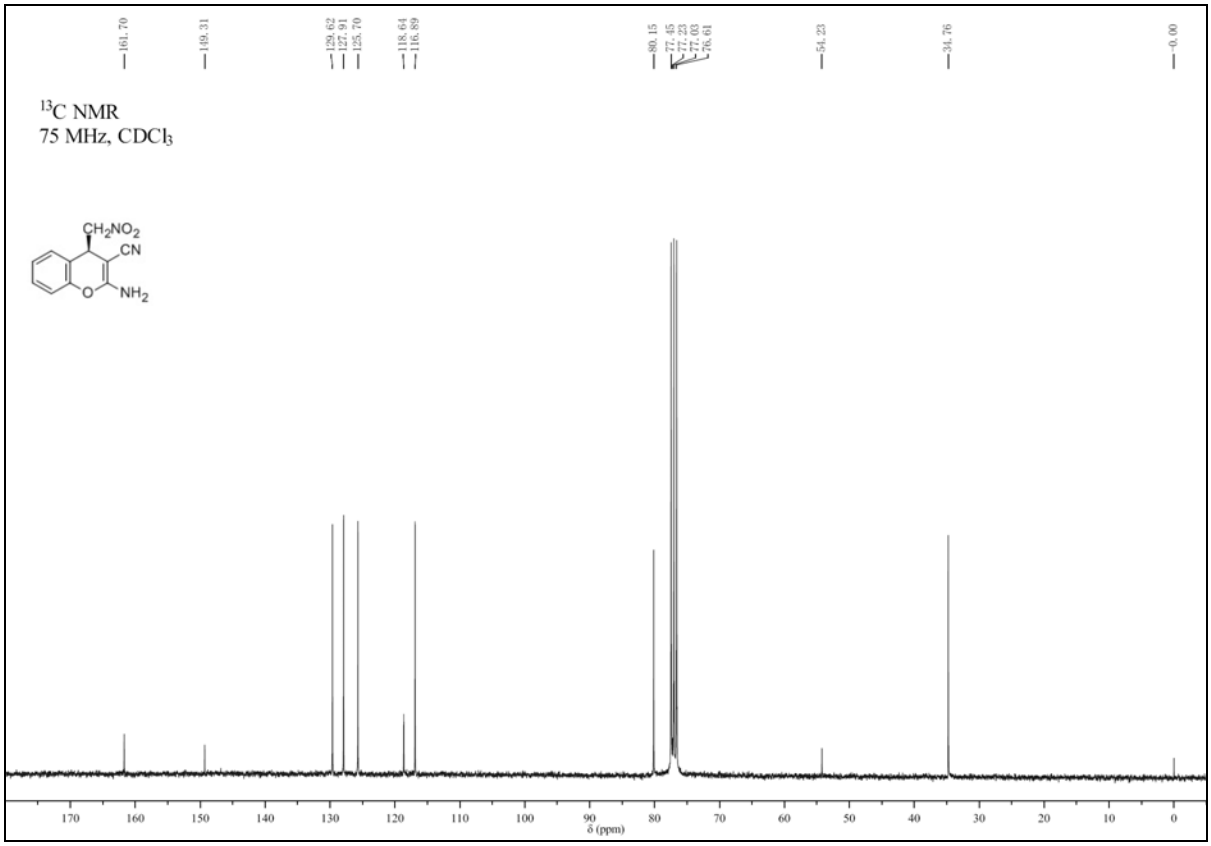
2-Imino-2*H*-chromene-3-carbonitrile (Ia): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.29 (s, 1H), 7.77–7.71 (m, 1H), 7.65–7.60 (m, 1H), 7.46–7.39 (m, 2H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 156.4, 154.6, 151.8, 135.6, 129.3, 125.7, 117.5, 117.1, 113.5, 103.4 ppm.

Ethyl 2-imino-2H-chromene-3-carboxylate (Ib): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.53 (s, 1H), 7.70–7.60 (m, 2H), 7.40–7.28 (m, 2H), 4.42 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 163.1, 156.7, 155.2, 148.5, 134.3, 129.5, 124.8, 118.4, 117.9, 116.8, 62.0, 14.2 ppm.

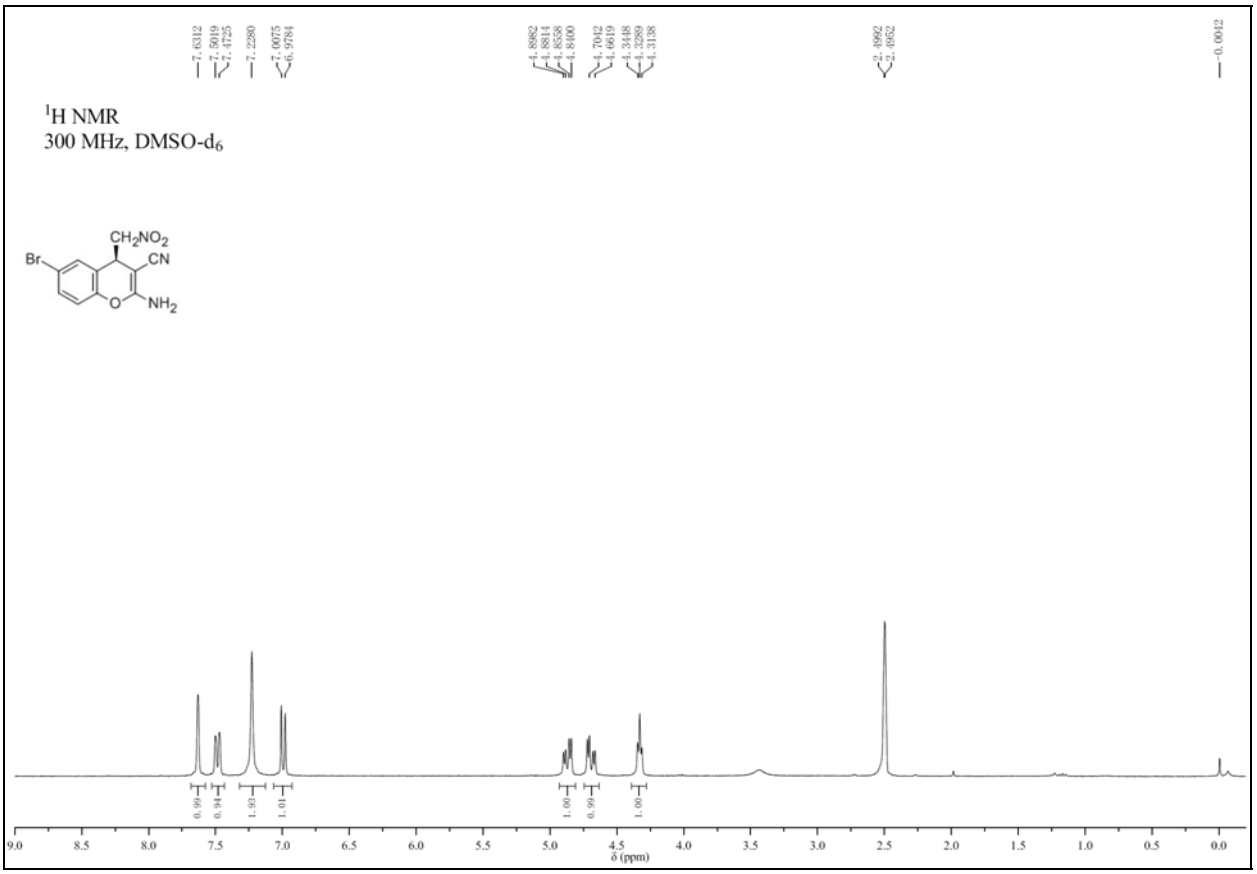
^{1}H, ^{13}C NMR Spectra

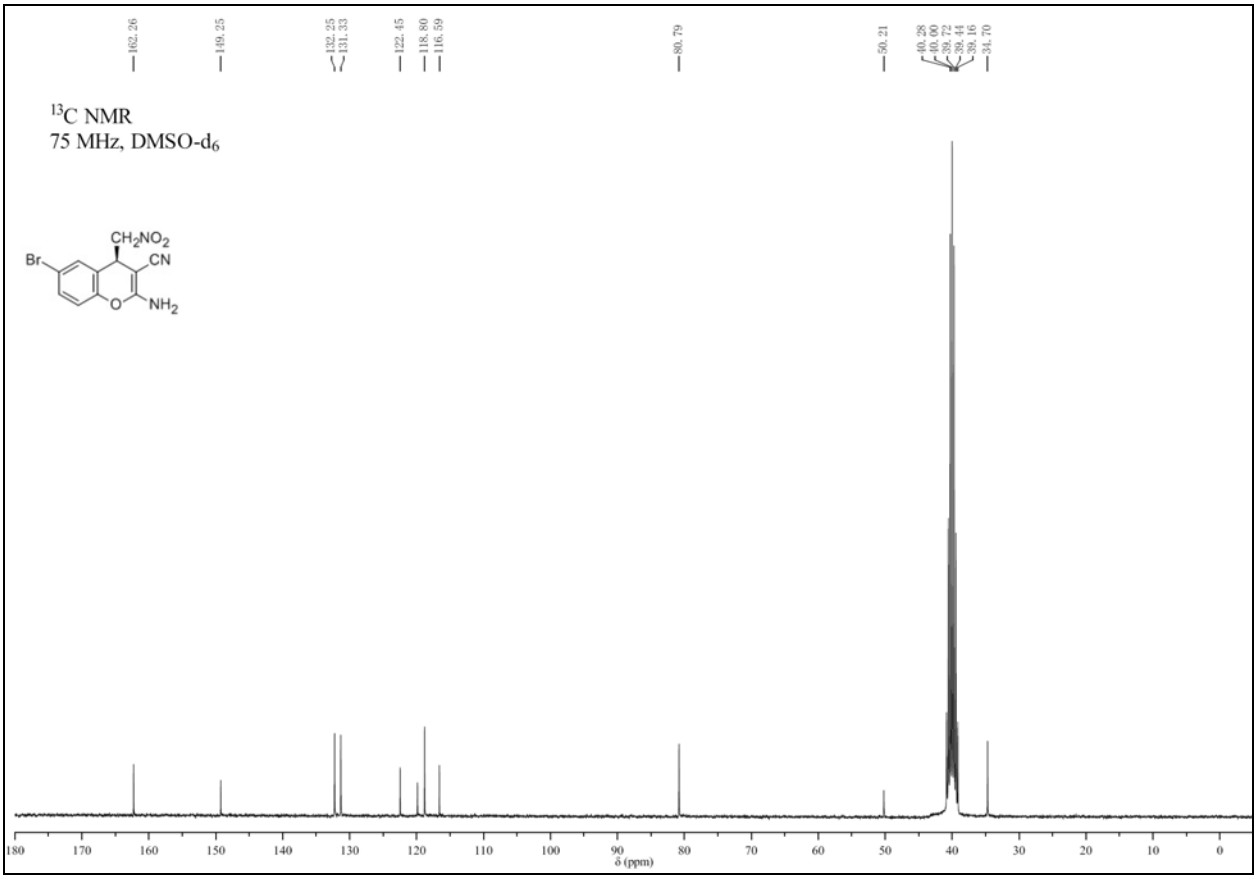
Compound **4a**



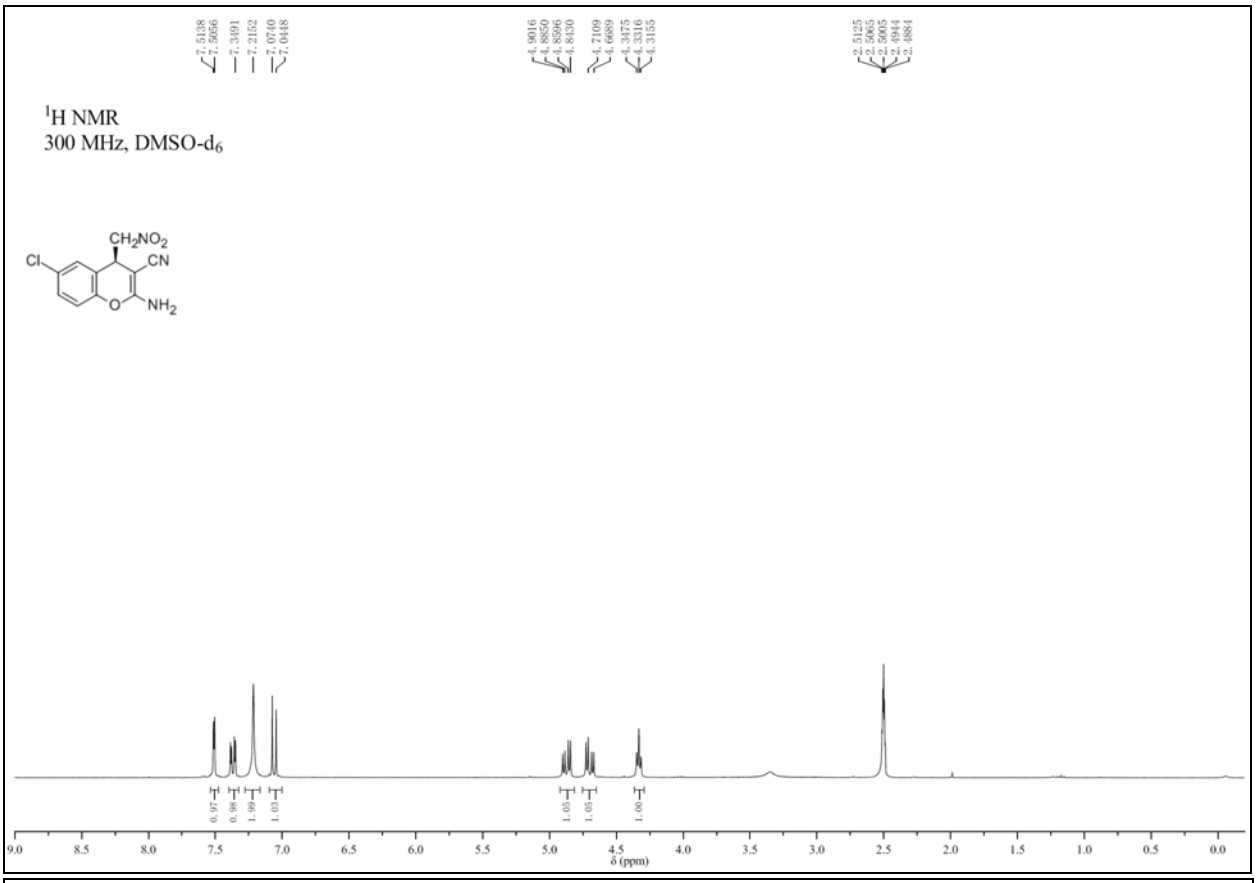


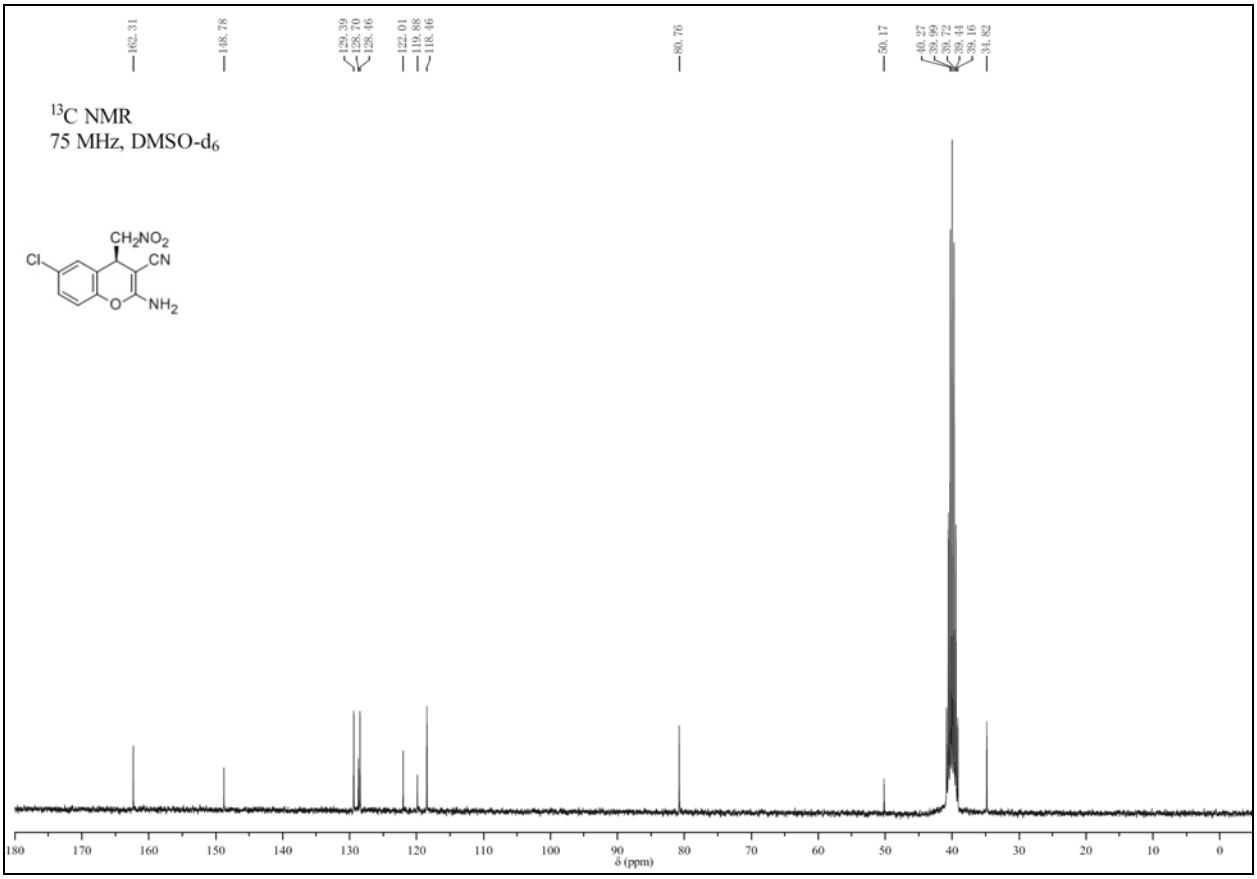
Compound **4b**


7.6312
7.5019
7.4725
7.2280
7.0075
6.9784
4.8862
4.8814
4.8538
4.8490
4.7042
4.6619
4.3448
4.3289
4.3138
2.6962
2.6952
0.0042
^{1}H NMR
300 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Br
NH$_2$
O
0.99
0.94
1.93
1.01
1.00
0.99
1.00
δ (ppm)

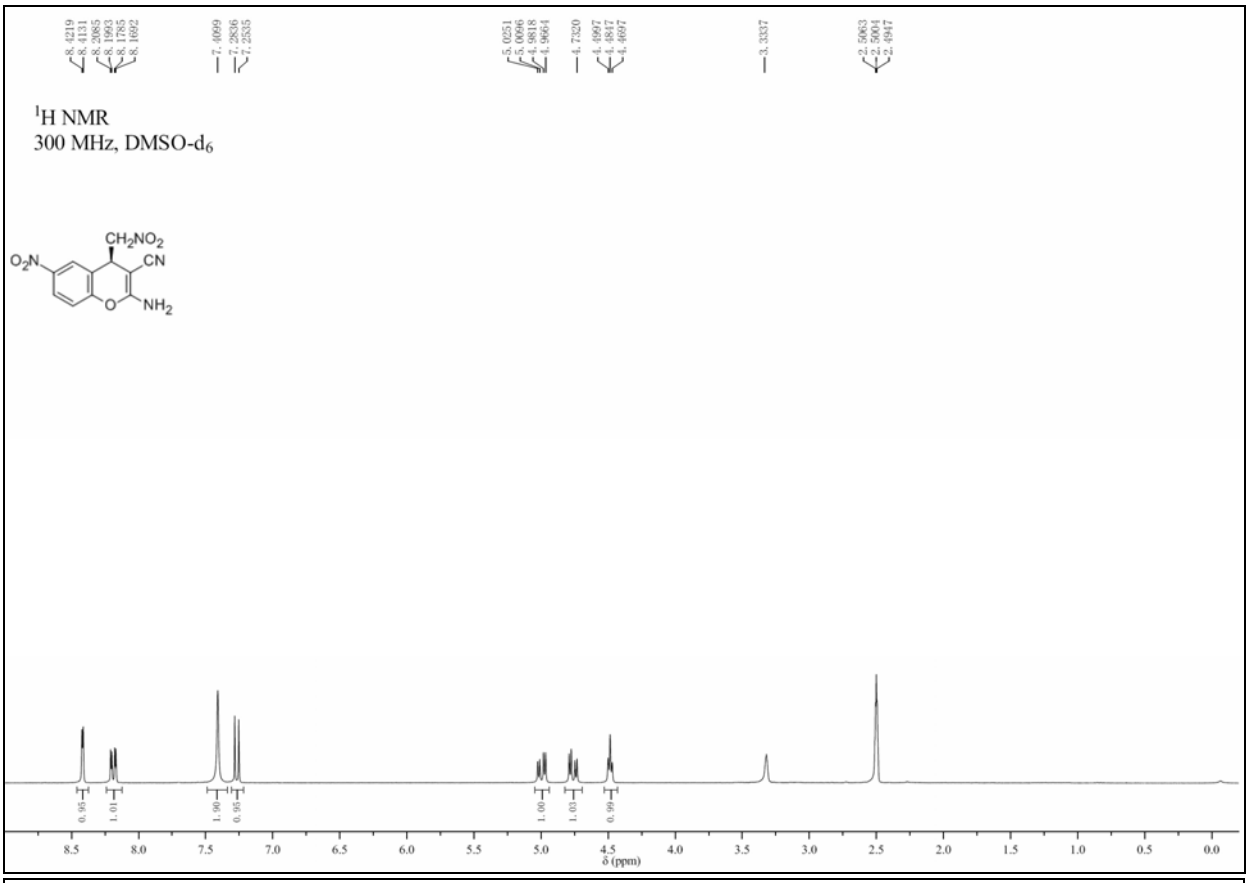

162.26
149.25
132.25
131.33
122.45
118.80
116.59
80.79
50.21
40.28
40.06
39.72
39.44
39.16
34.70
^{13}C NMR
75 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Br
NH$_2$
O
δ (ppm)

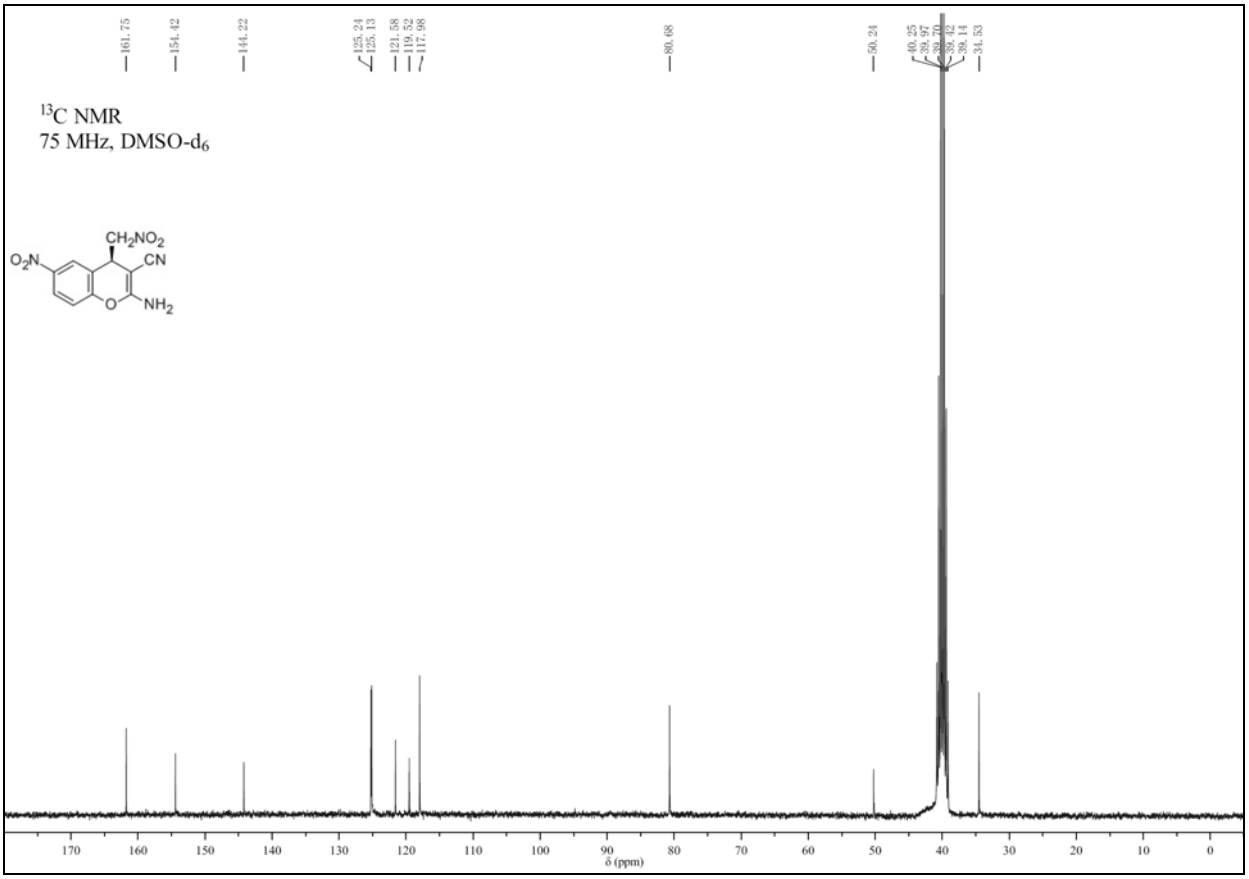
Compound **4c**


7.5138
7.5056
7.3491
7.2152
7.0740
7.0448
6.9016
6.8850
6.8596
6.8430
6.7109
6.6889
6.3475
6.3316
6.3155
2.5125
2.5065
2.5005
2.4944
2.4884
^{1}H NMR
300 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Cl
NH$_2$
O
0.97
0.98
1.99
1.03
1.05
1.05
1.00
δ (ppm)

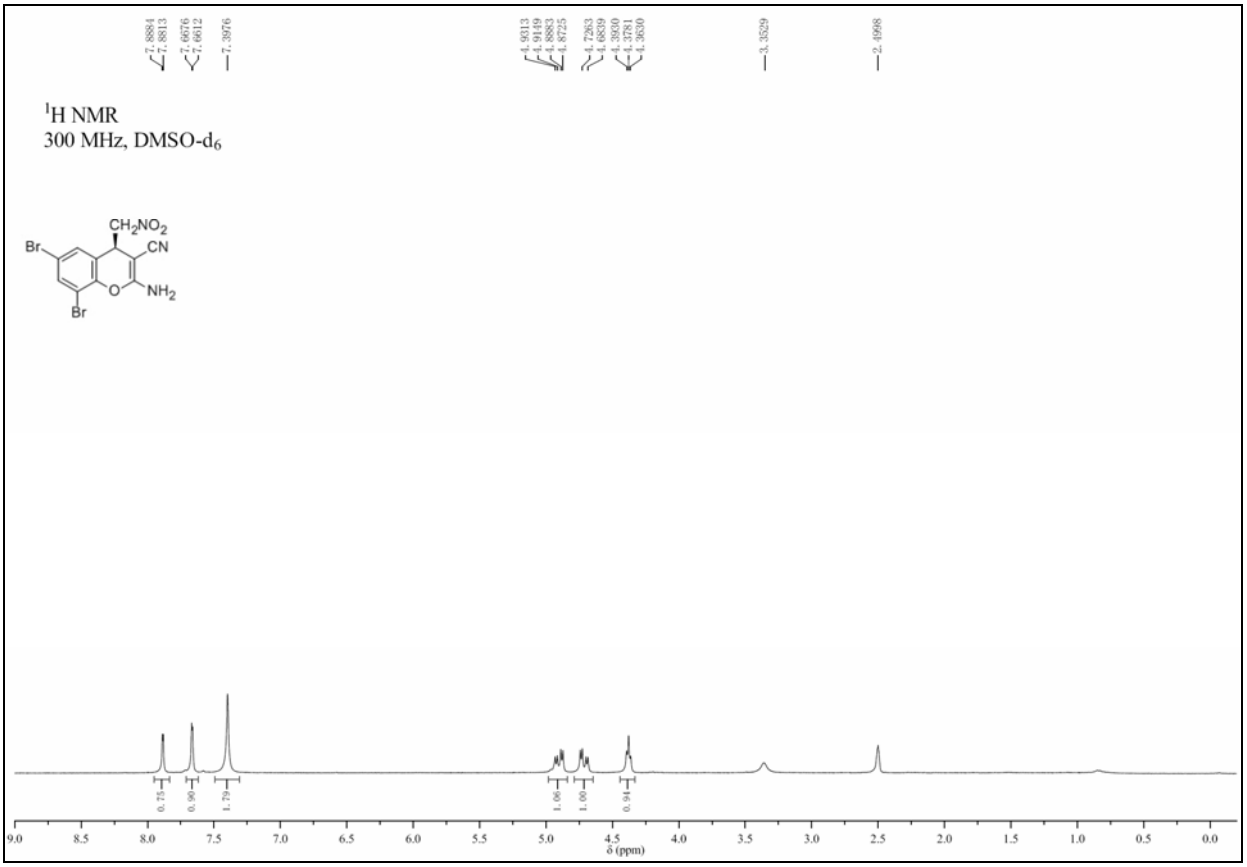

162.31
148.78
129.39
128.70
128.46
122.01
119.88
118.46
80.76
50.17
40.27
39.99
39.72
39.44
39.16
34.82
^{13}C NMR
75 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Cl
NH$_2$
O
δ (ppm)

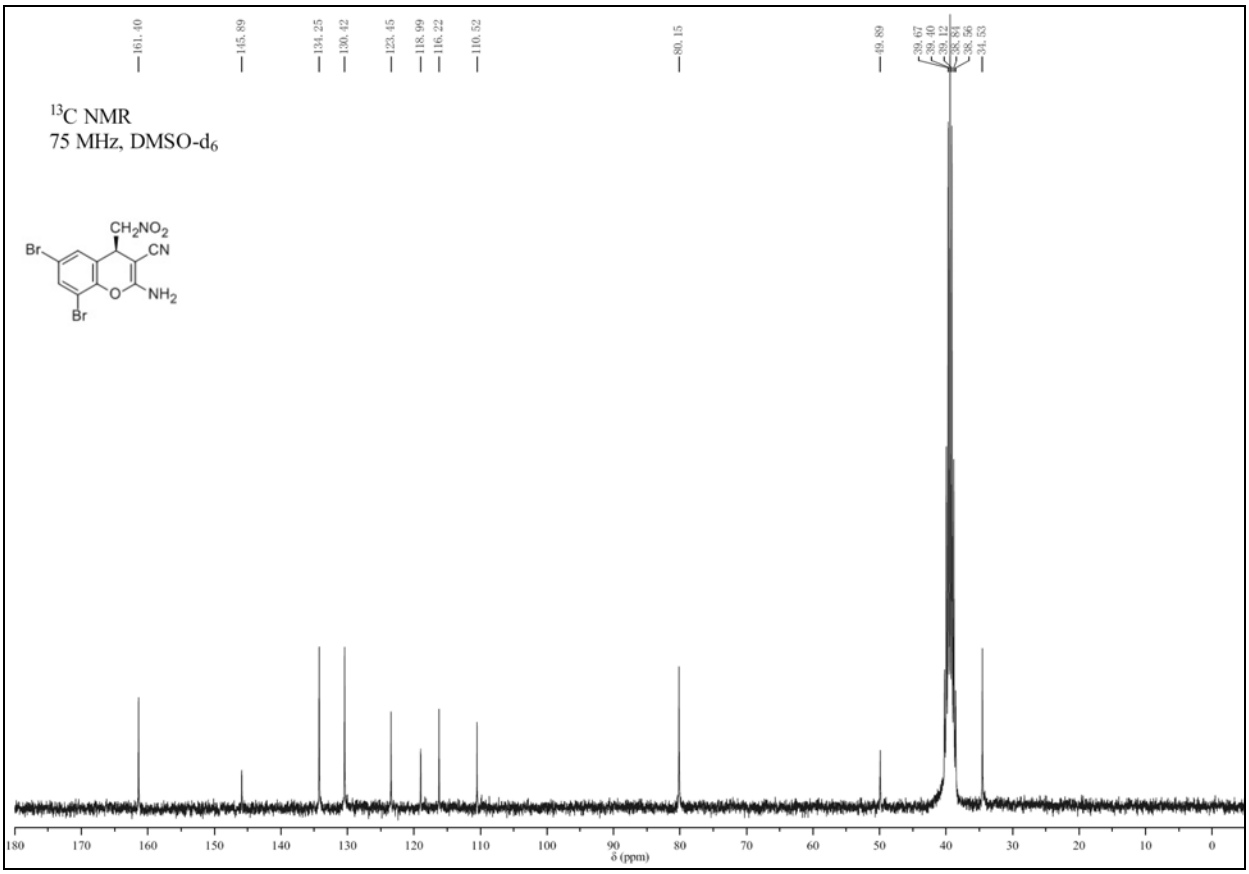
Compound **4d**


^{1}H NMR
300 MHz, DMSO-d$_6$
CH_2NO_2
CN
O_2N
NH_2
O
δ (ppm)

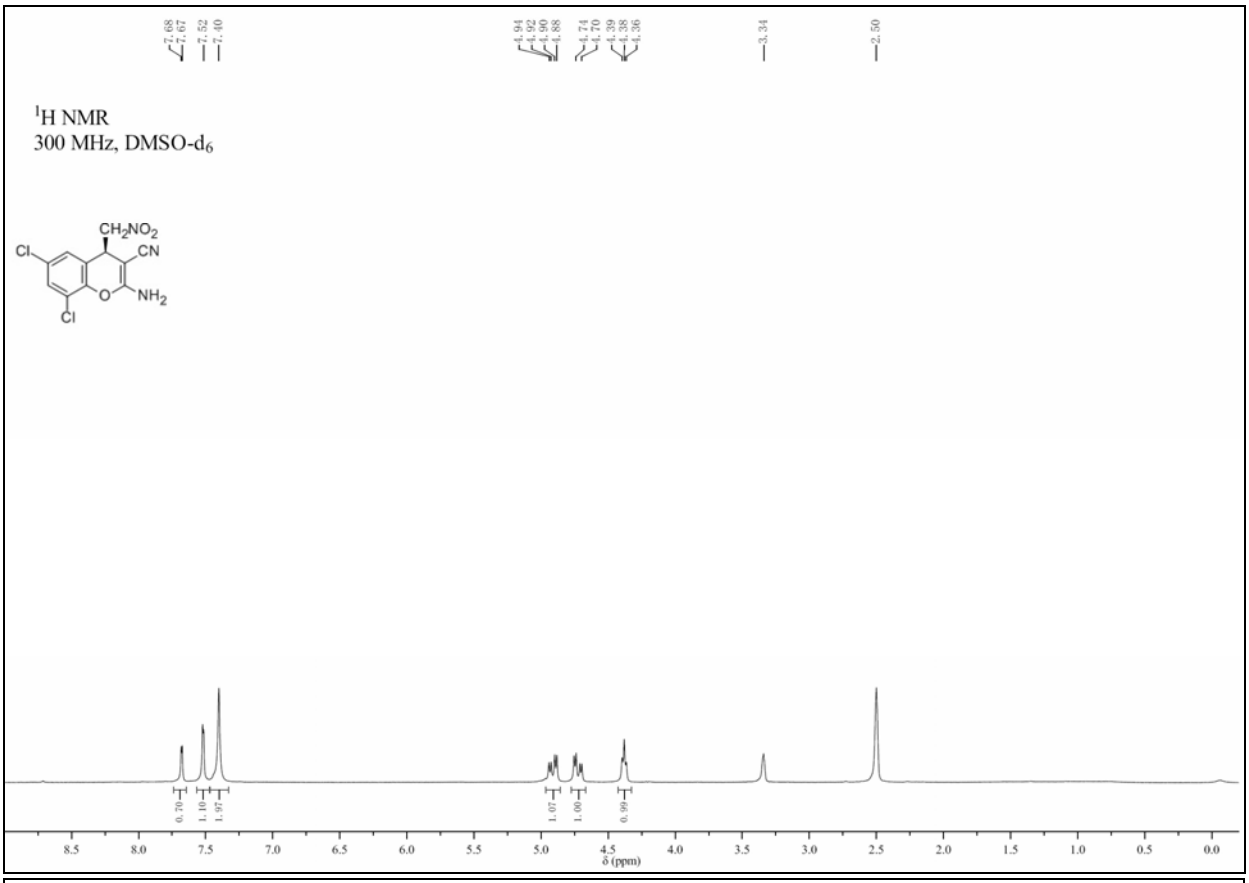

^{13}C NMR
75 MHz, DMSO-d$_6$
CH_2NO_2
CN
O_2N
NH_2
O
δ (ppm)

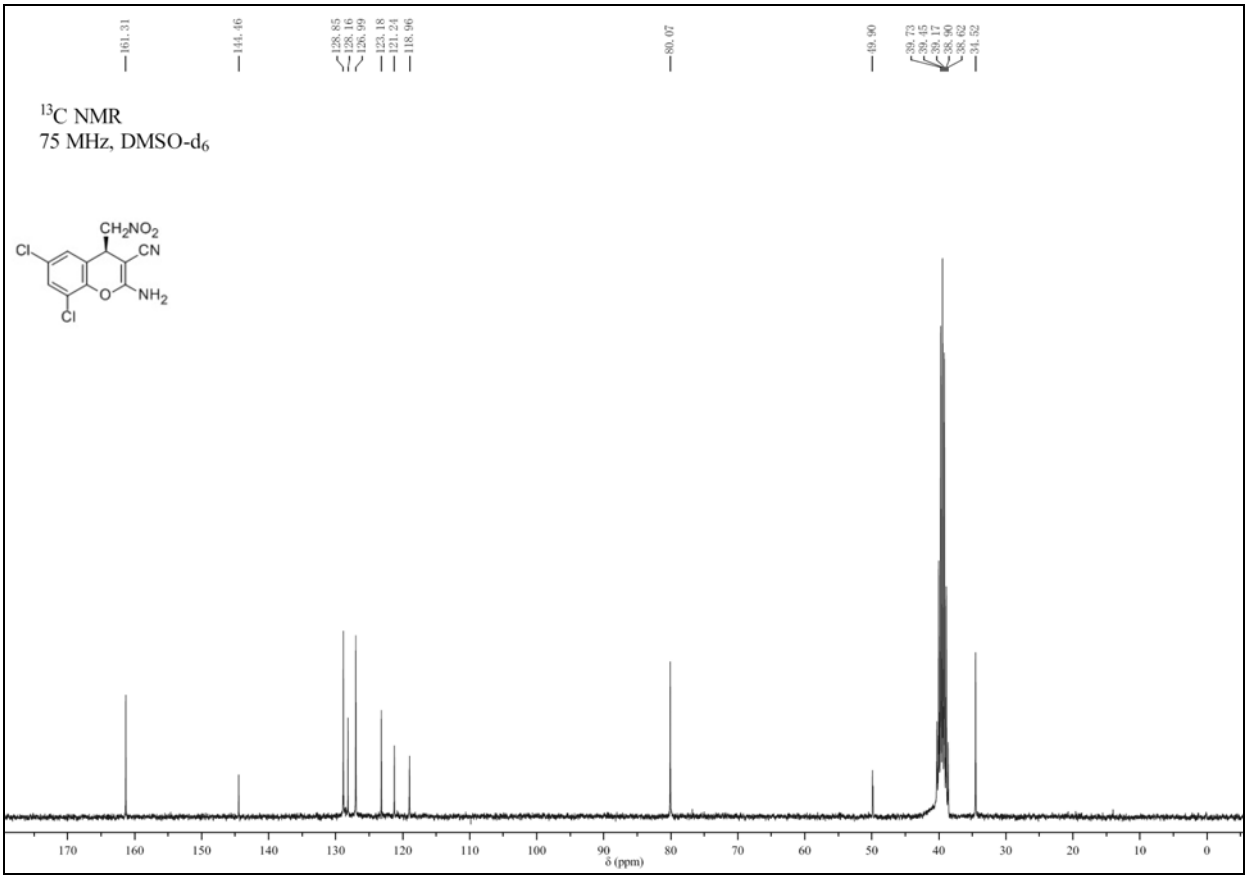
Compound **4e**


7.8884
7.8813
7.6676
7.6612
7.3976
4.9313
4.9149
4.8883
4.8725
4.7263
4.6839
4.3930
4.3781
4.3630
3.3529
2.4998
^{1}H NMR
300 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Br
NH$_2$
Br
0.75
0.99
1.79
1.06
1.69
0.94
δ (ppm)

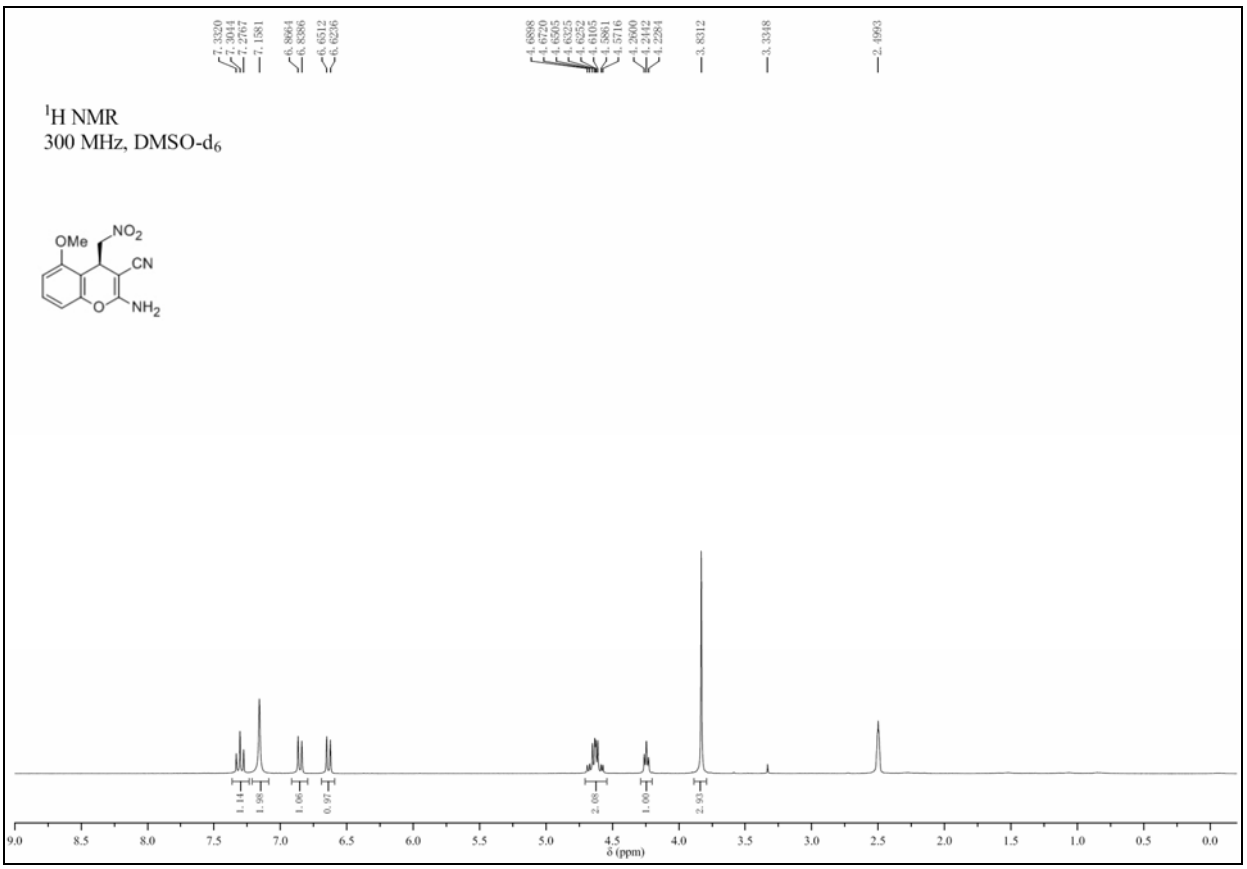

161.40
145.89
134.25
130.42
123.45
118.99
116.22
110.52
80.15
69.89
39.67
39.40
39.12
38.84
38.56
34.53
^{13}C NMR
75 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Br
NH$_2$
Br
δ (ppm)

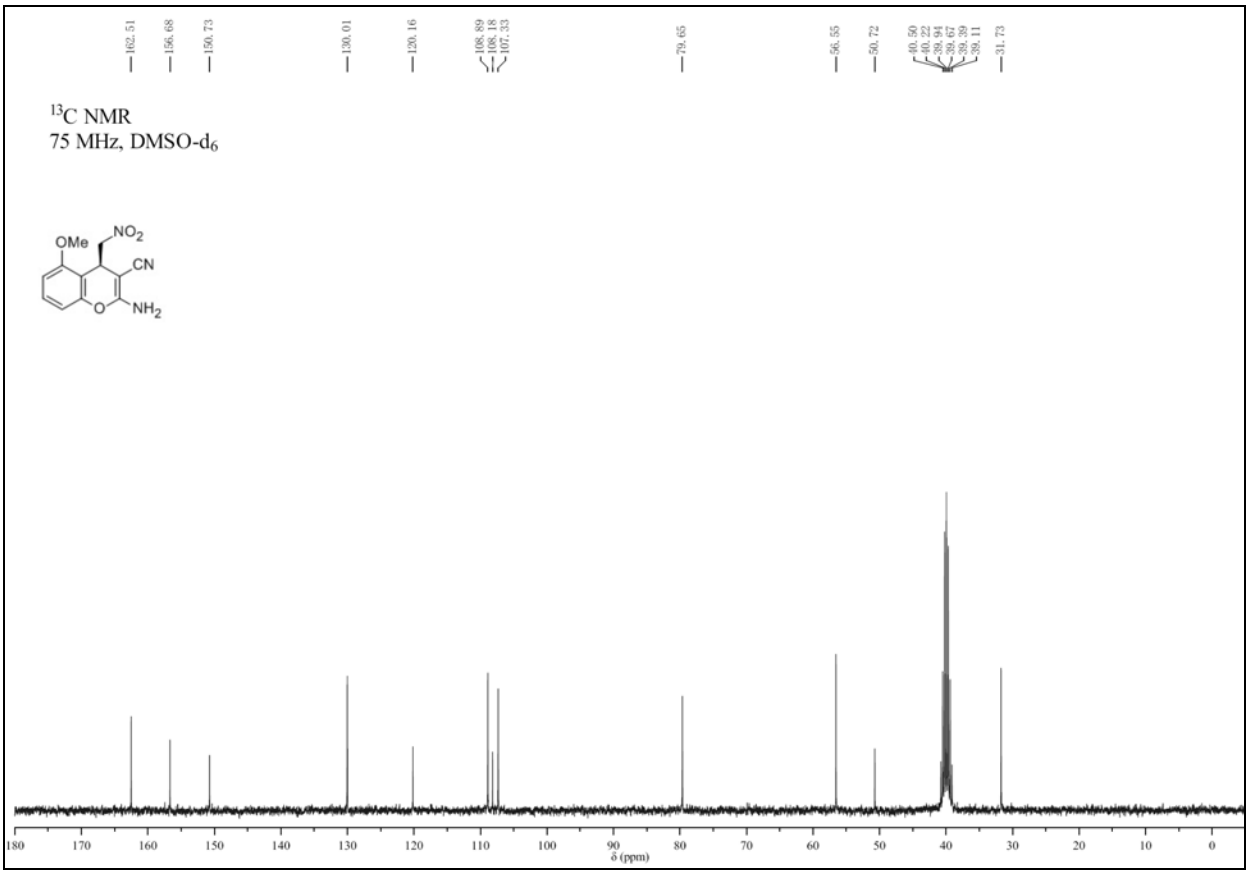
Compound **4f**


7.68
7.67
7.52
7.40
4.94
4.92
4.90
4.88
4.74
4.70
4.39
4.38
4.36
3.34
2.50
^{1}H NMR
300 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Cl
NH$_2$
Cl
0.70
1.10
1.97
1.07
1.00
0.99
δ (ppm)

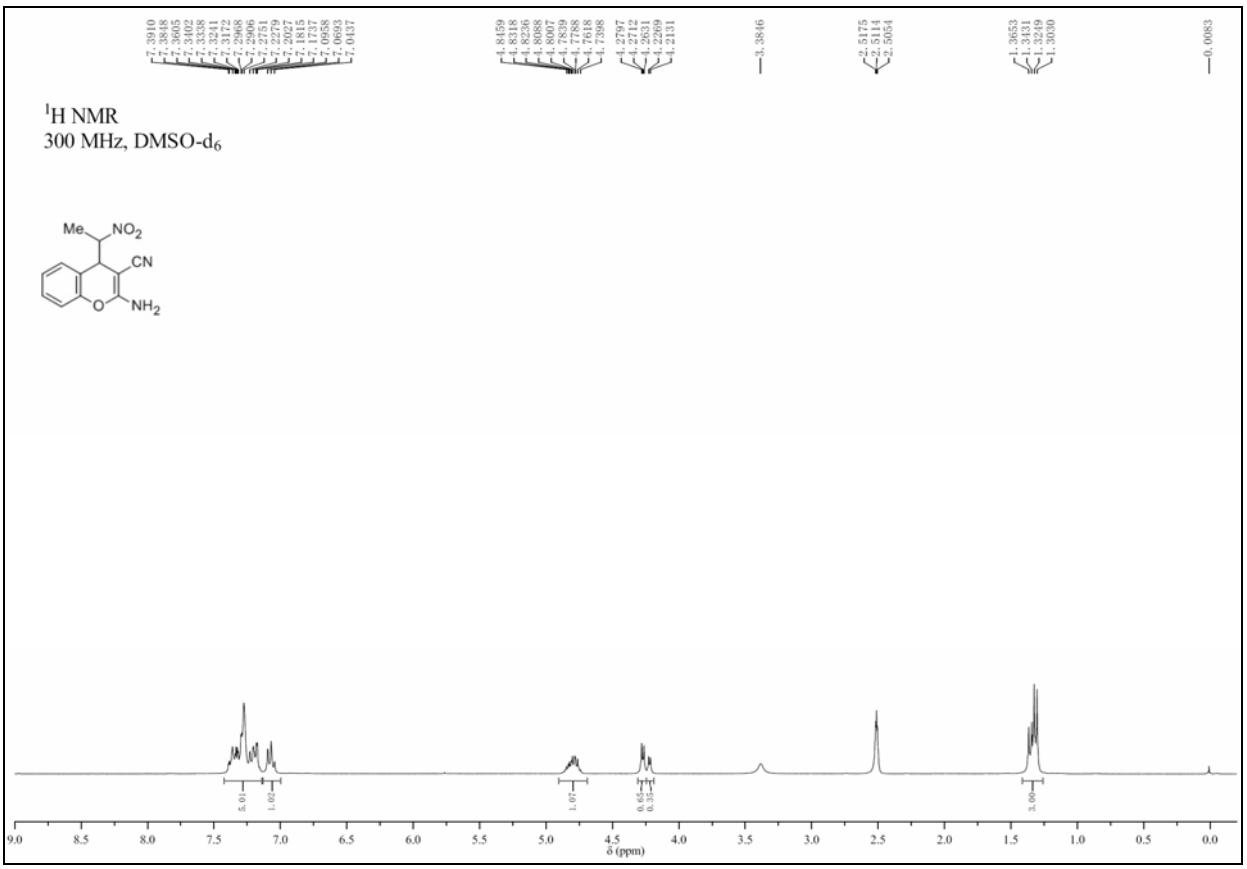

161.31
144.46
128.85
128.16
126.99
123.18
121.24
118.96
80.07
69.90
39.73
39.45
39.17
38.90
38.62
34.52
^{13}C NMR
75 MHz, DMSO-d$_6$
CH$_2$NO$_2$
CN
Cl
NH$_2$
Cl
δ (ppm)

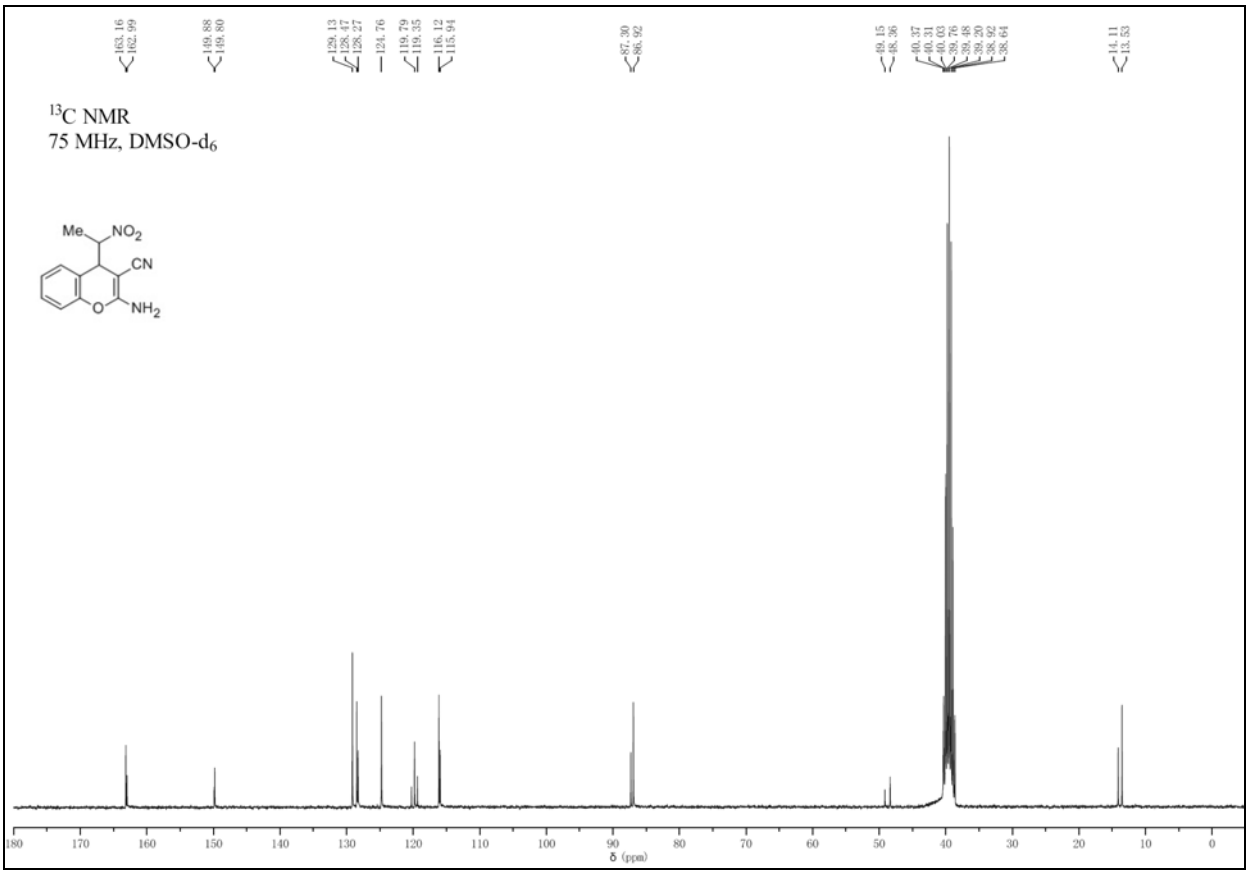
Compound **4g**


7.3329
7.3044
7.2767
7.1381
6.8664
6.8386
6.6512
6.6256
4.6898
4.6720
4.6545
4.6325
4.6252
4.6105
4.5981
4.5716
4.2600
4.2442
4.2284
3.8312
3.3348
2.4993
1H NMR
300 MHz, DMSO-d6
OMe
NO2
CN
NH2
1.14
1.00
1.98
1.06
0.97
2.08
1.00
2.93
δ (ppm)

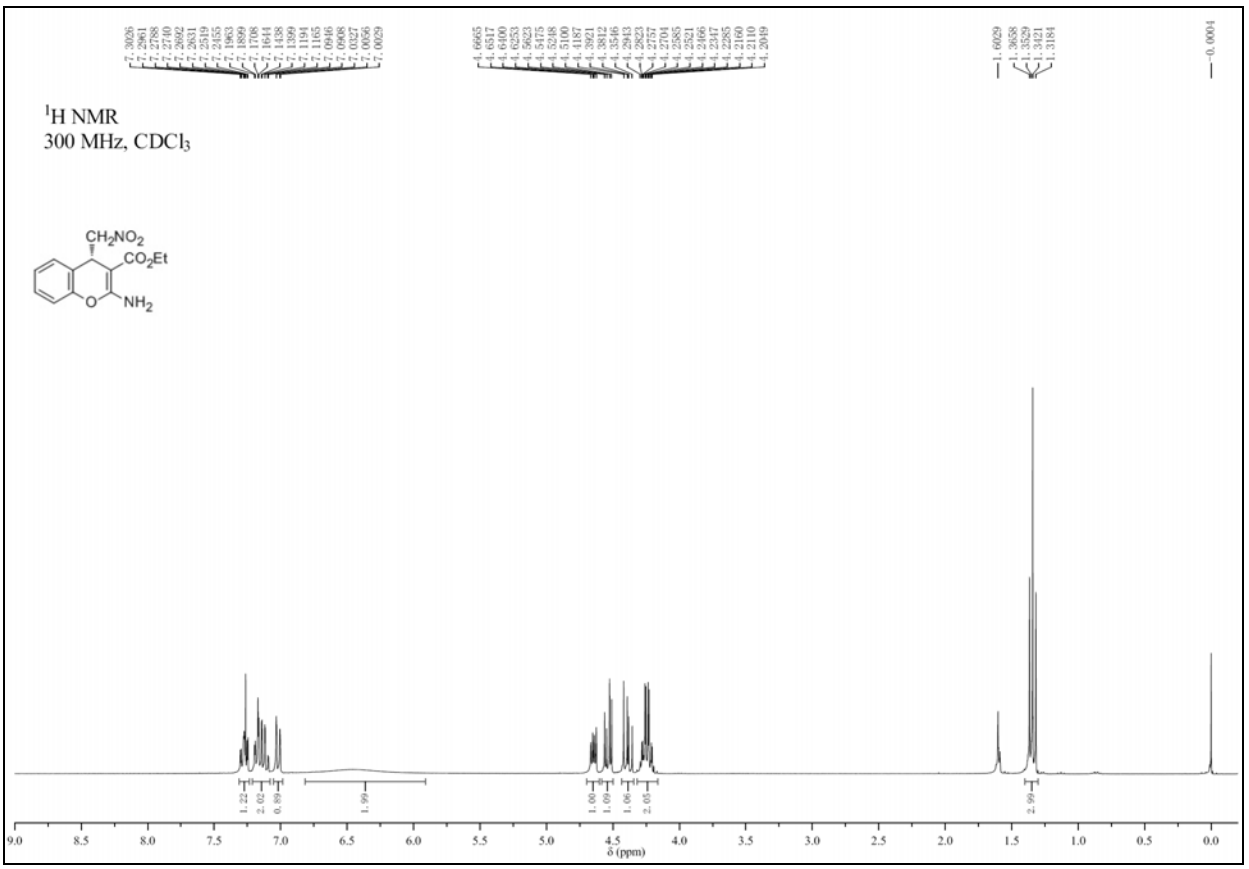

162.51
156.68
150.73
130.01
120.16
108.89
108.18
107.33
79.65
56.55
50.72
40.50
40.22
39.94
39.67
39.39
38.11
31.73
13C NMR
75 MHz, DMSO-d6
OMe
NO2
CN
NH2
δ (ppm)

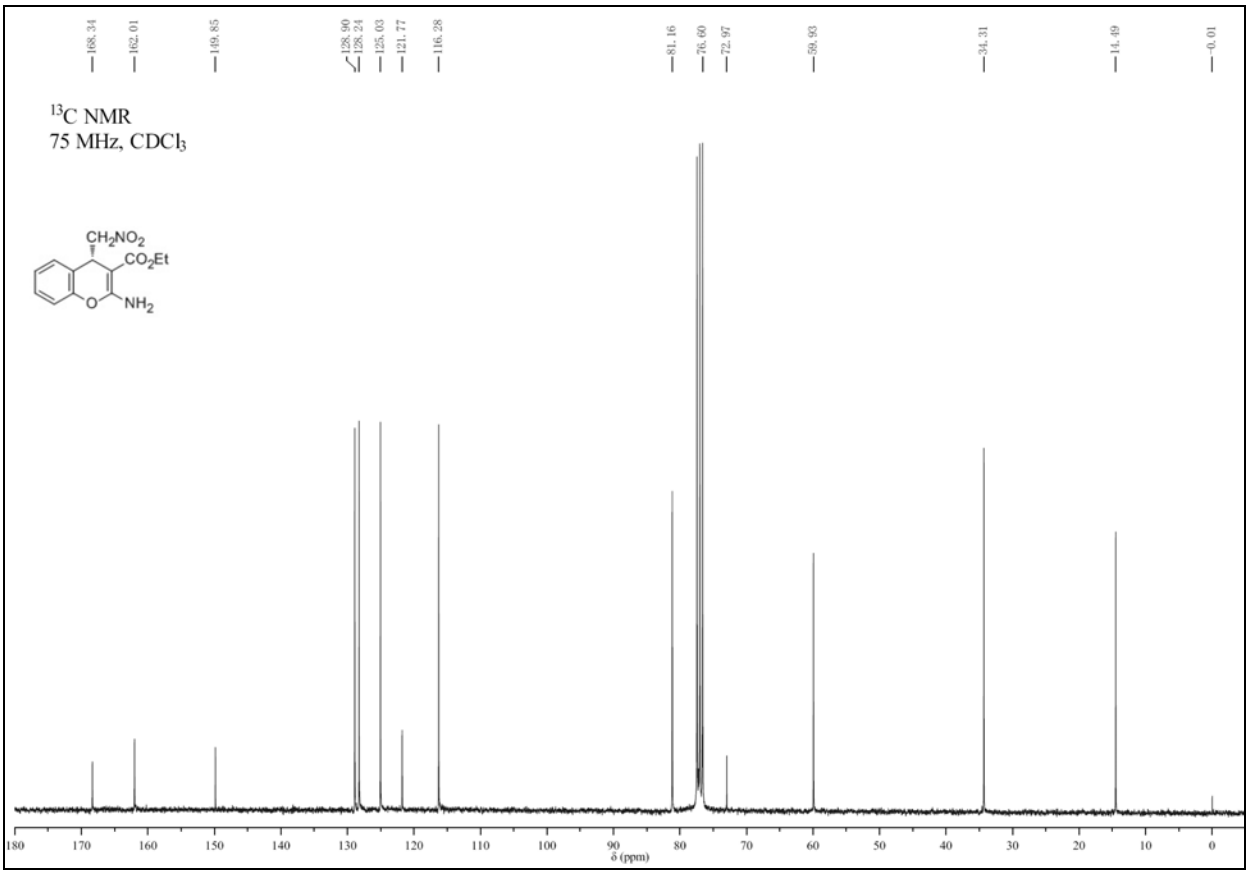
Compound **4h**


7.3910
7.3848
7.3605
7.3402
7.3338
7.3241
7.3172
7.2968
7.2906
7.2771
7.2579
7.2027
7.1815
7.1737
7.0958
7.0693
7.0437
4.8459
4.8318
4.8236
4.8088
4.8007
4.7839
4.7788
4.7618
4.7398
4.2797
4.2712
4.2631
4.2269
4.2131
3.3846
2.5175
2.5114
2.5054
1.3653
1.3431
1.3249
1.3030
0.0083
^{1}H NMR
300 MHz, DMSO-d$_6$
Me
NO$_2$
CN
NH$_2$
δ (ppm)

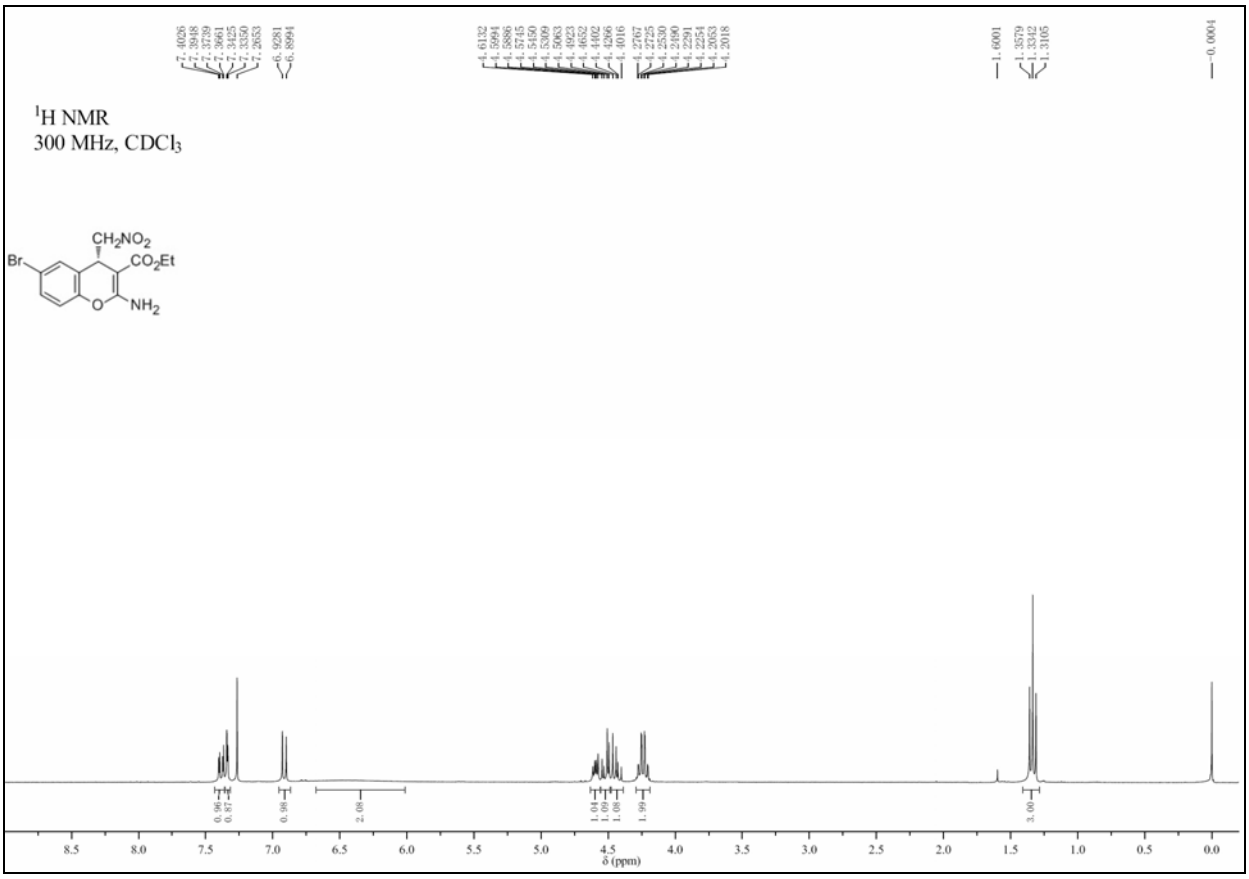

163.16
162.99
149.88
149.80
128.13
128.47
128.27
124.76
119.79
119.35
116.12
115.94
87.30
86.92
69.15
68.96
40.37
40.31
40.03
39.76
39.48
39.20
38.92
38.64
14.11
13.53
^{13}C NMR
75 MHz, DMSO-d$_6$
Me
NO$_2$
CN
NH$_2$
δ (ppm)

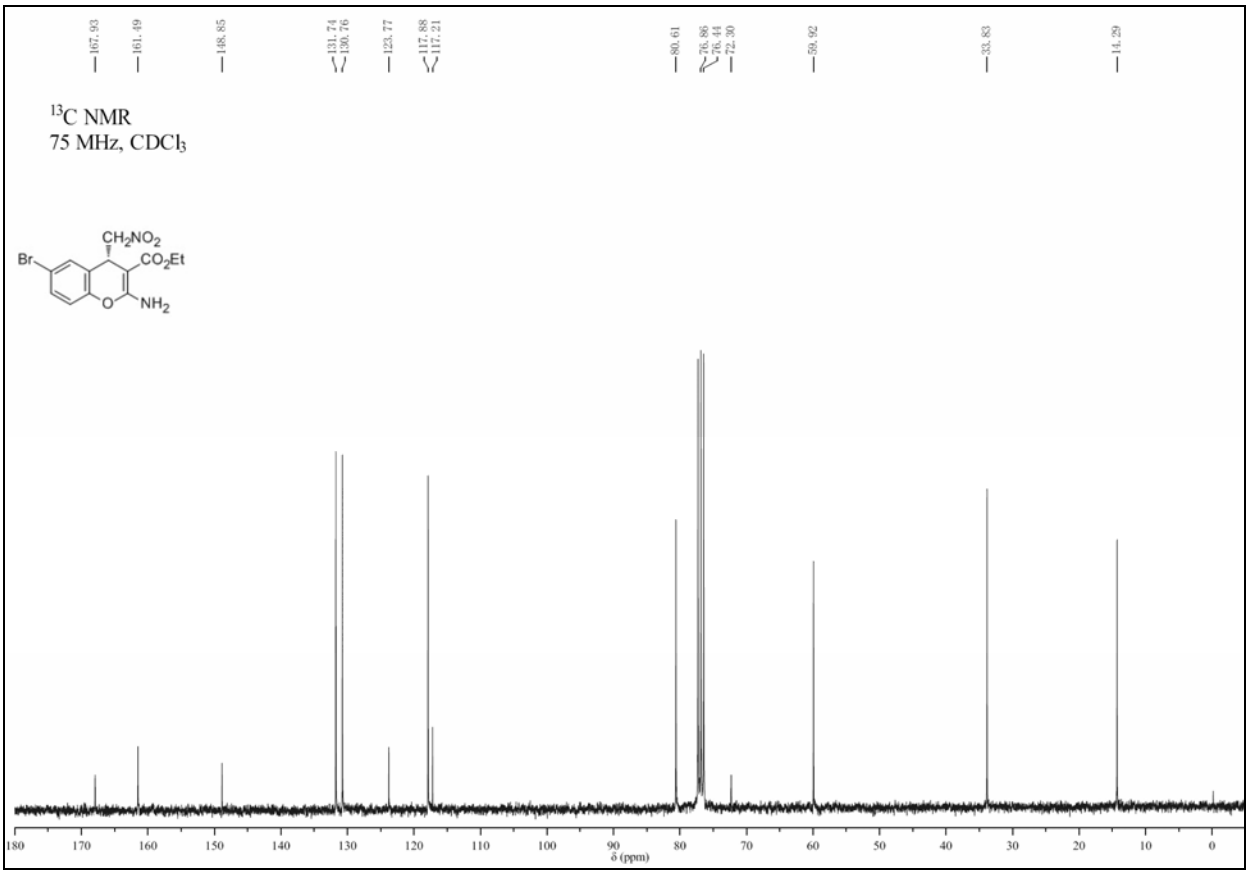
Compound **5a**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
NH_2
δ (ppm)

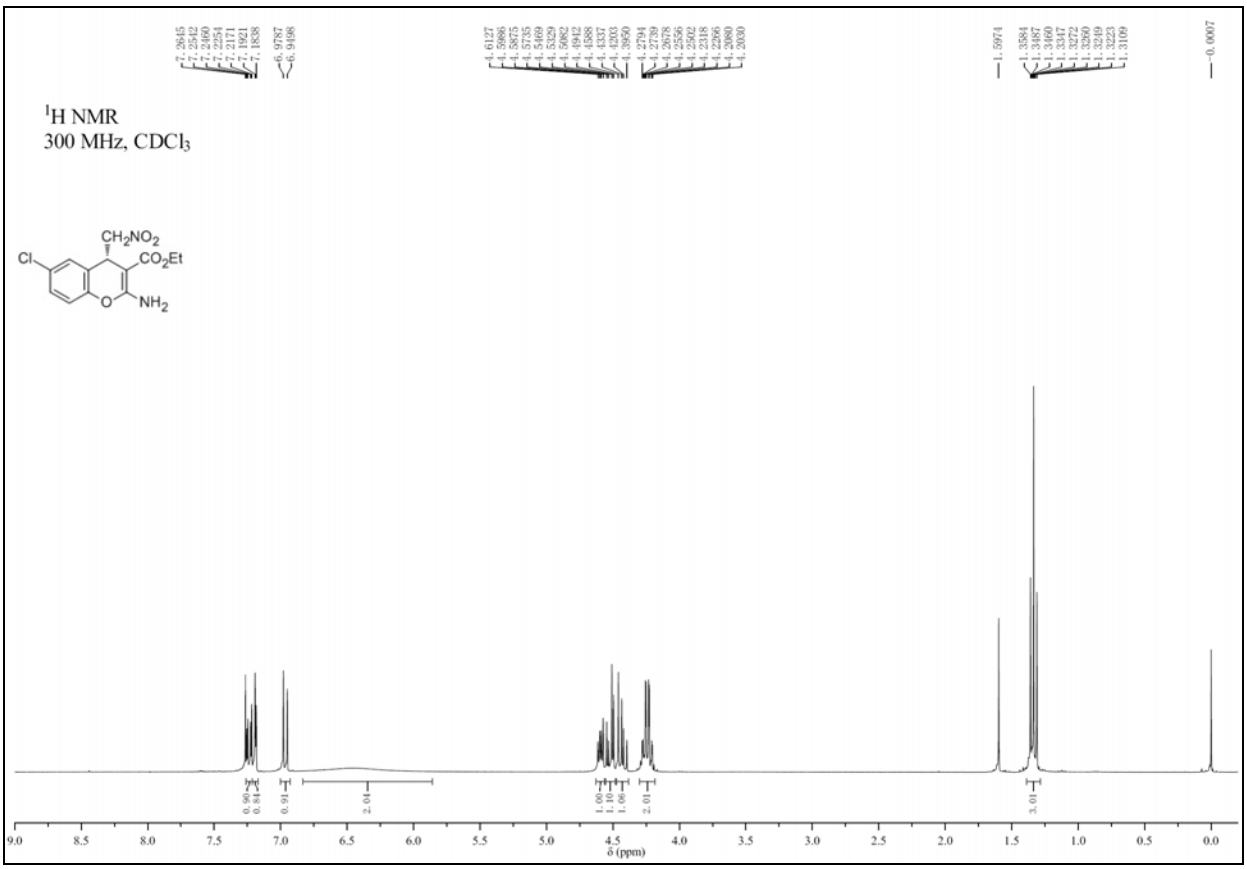

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
NH_2
δ (ppm)

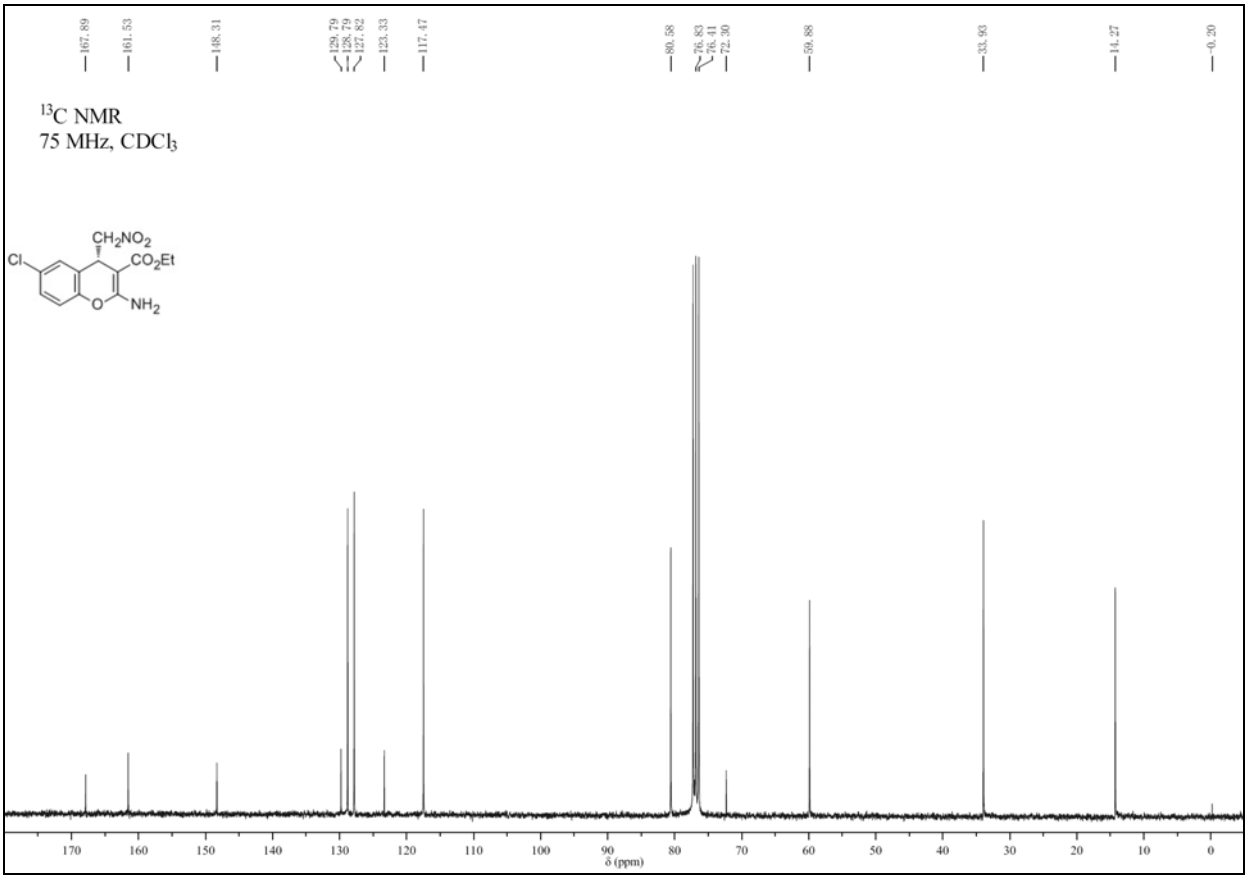
Compound **5b**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
Br
CO_2Et
NH_2
δ (ppm)

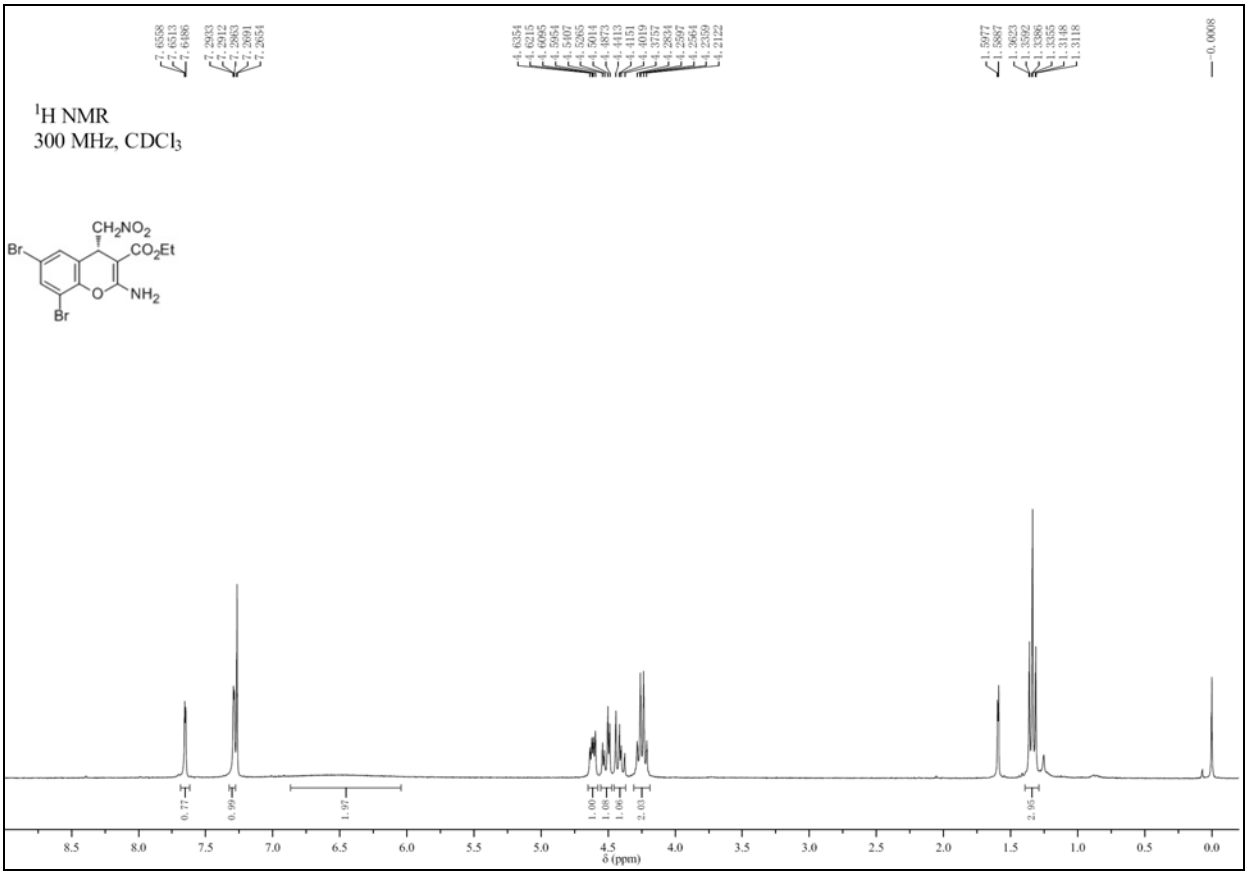

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
Br
CO_2Et
NH_2
δ (ppm)

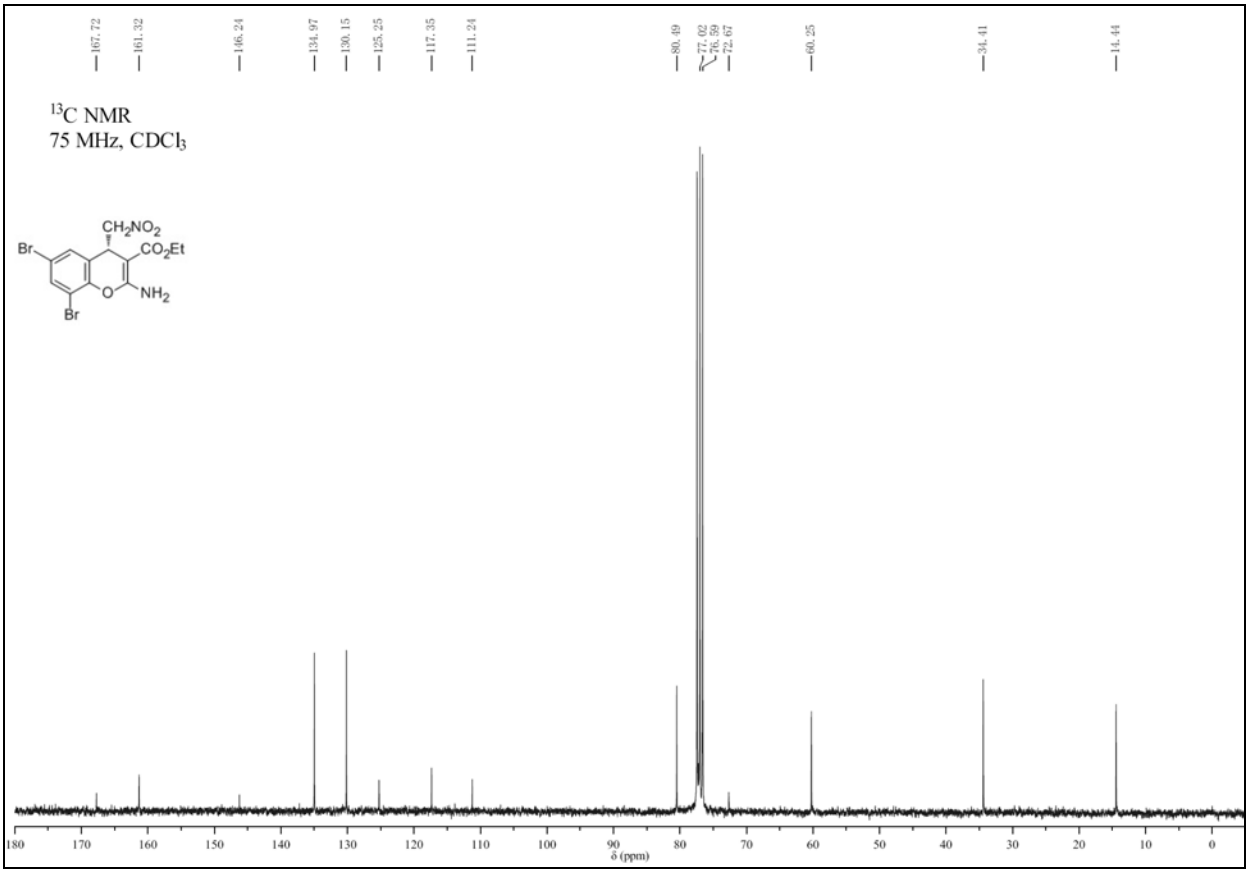
Compound **5c**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Cl
NH_2
O
δ (ppm)

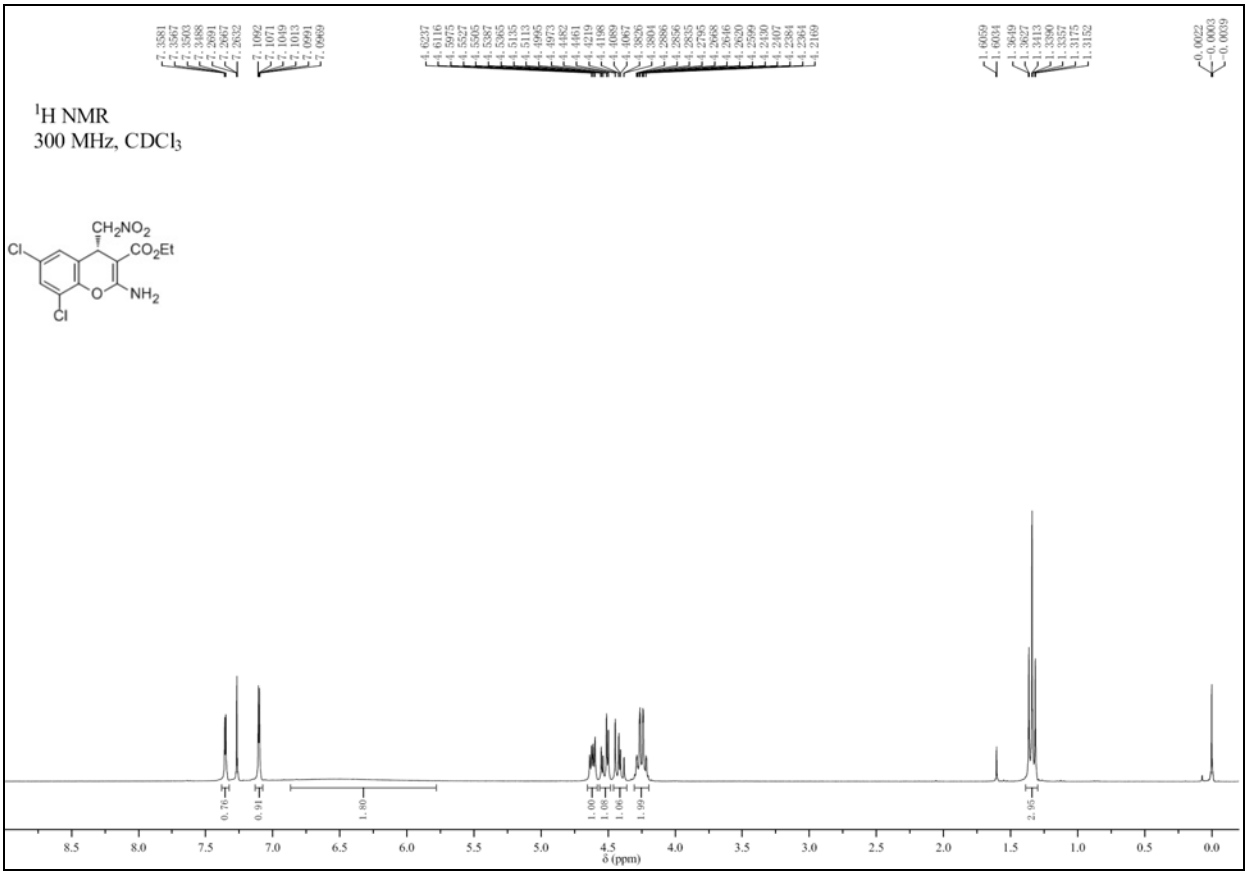

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Cl
NH_2
O
δ (ppm)

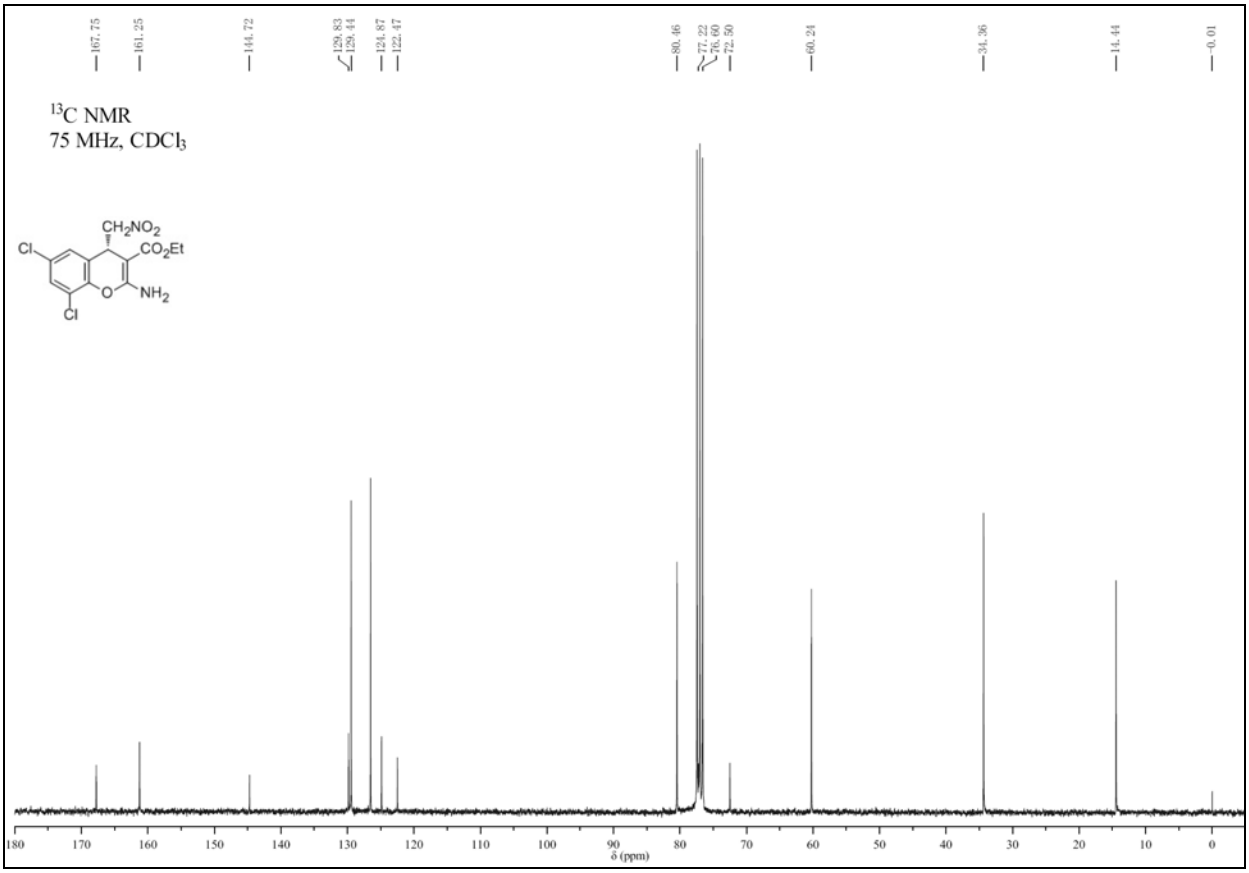
Compound **5d**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Br
Br
NH_2
δ (ppm)

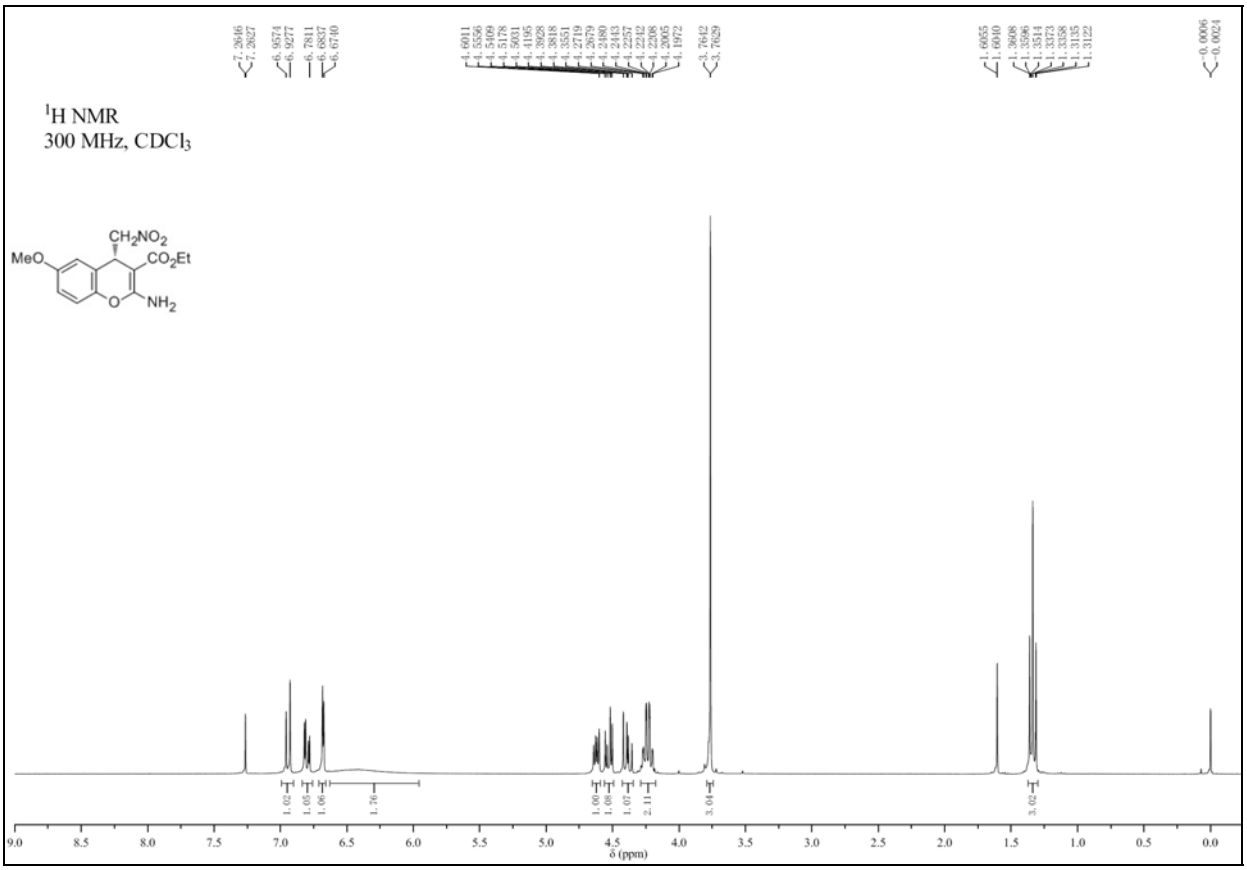

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Br
Br
NH_2
δ (ppm)

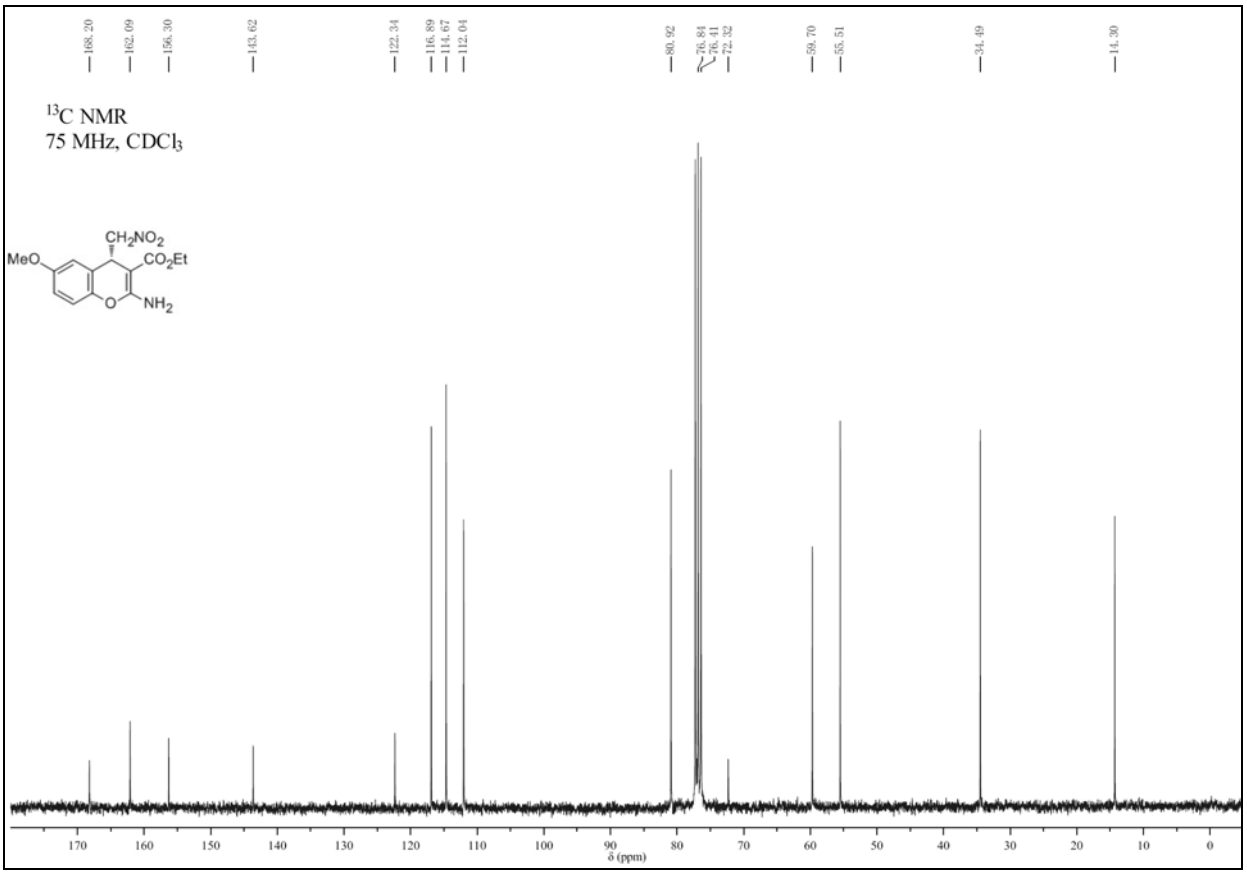
Compound **5e**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Cl
NH_2
Cl
δ (ppm)

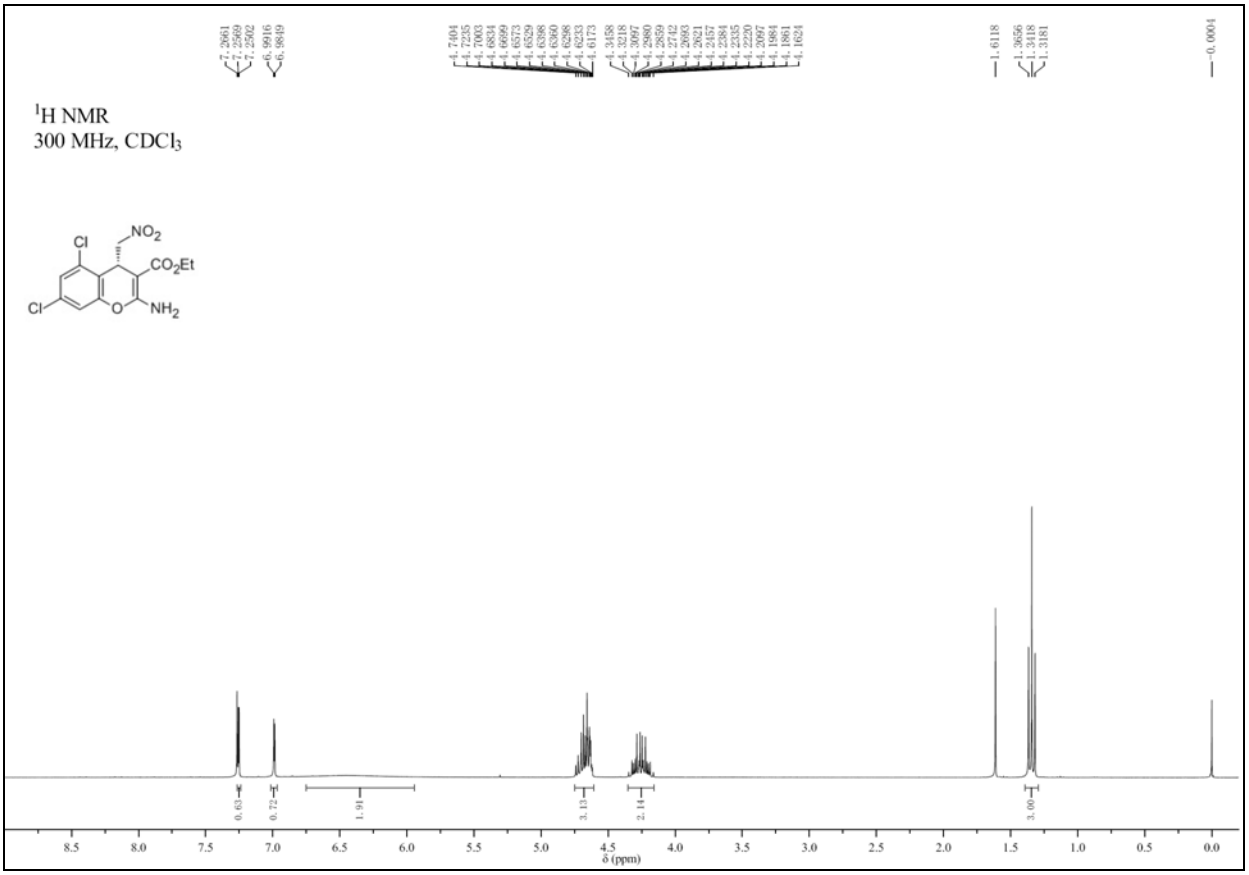

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
Cl
NH_2
Cl
δ (ppm)

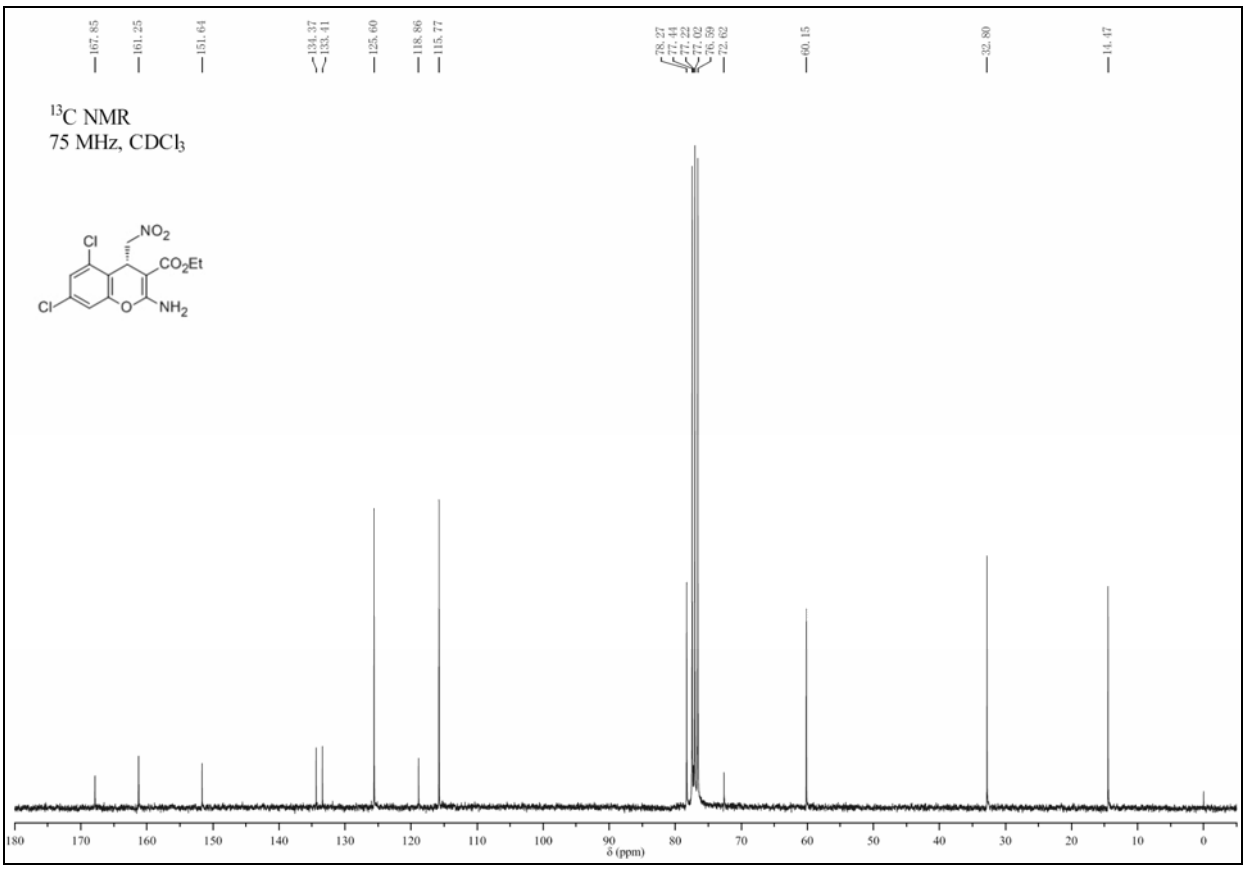
Compound **5f**


^{1}H NMR
300 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
MeO
NH_2
δ (ppm)

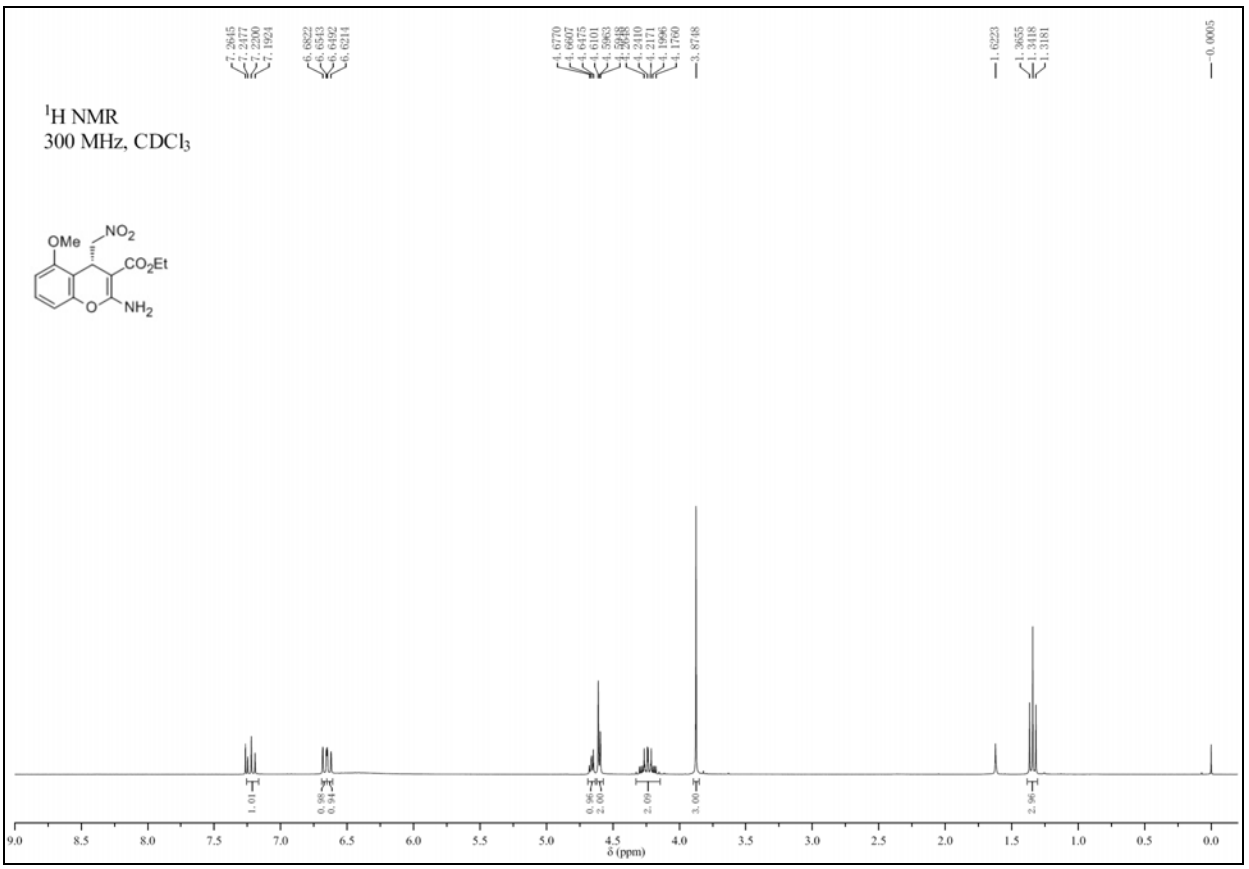

^{13}C NMR
75 MHz, $CDCl_3$
CH_2NO_2
CO_2Et
MeO
NH_2
δ (ppm)

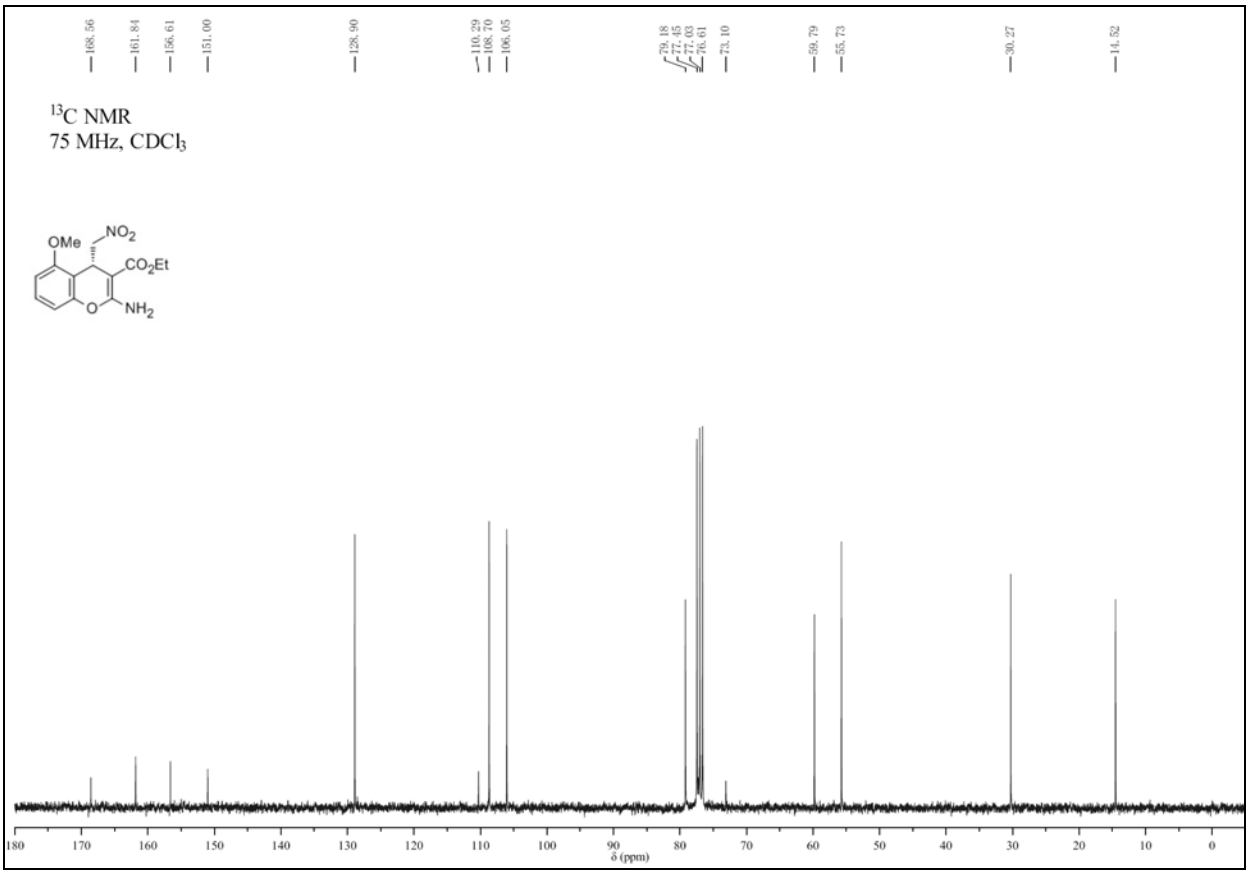
Compound **5g**


^{1}H NMR
300 MHz, $CDCl_3$
Cl
NO_2
CO_2Et
Cl
O
NH_2
δ (ppm)

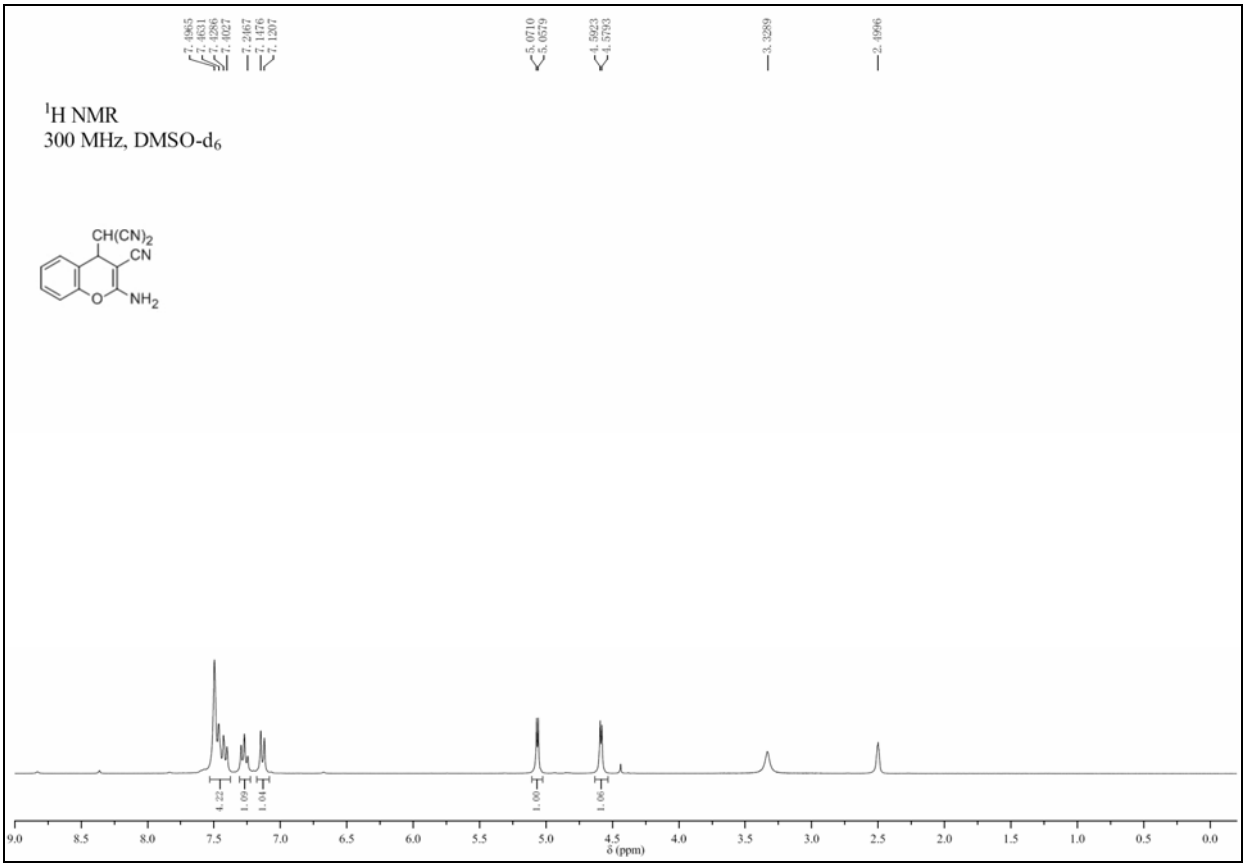

^{13}C NMR
75 MHz, $CDCl_3$
Cl
NO_2
CO_2Et
Cl
O
NH_2
δ (ppm)

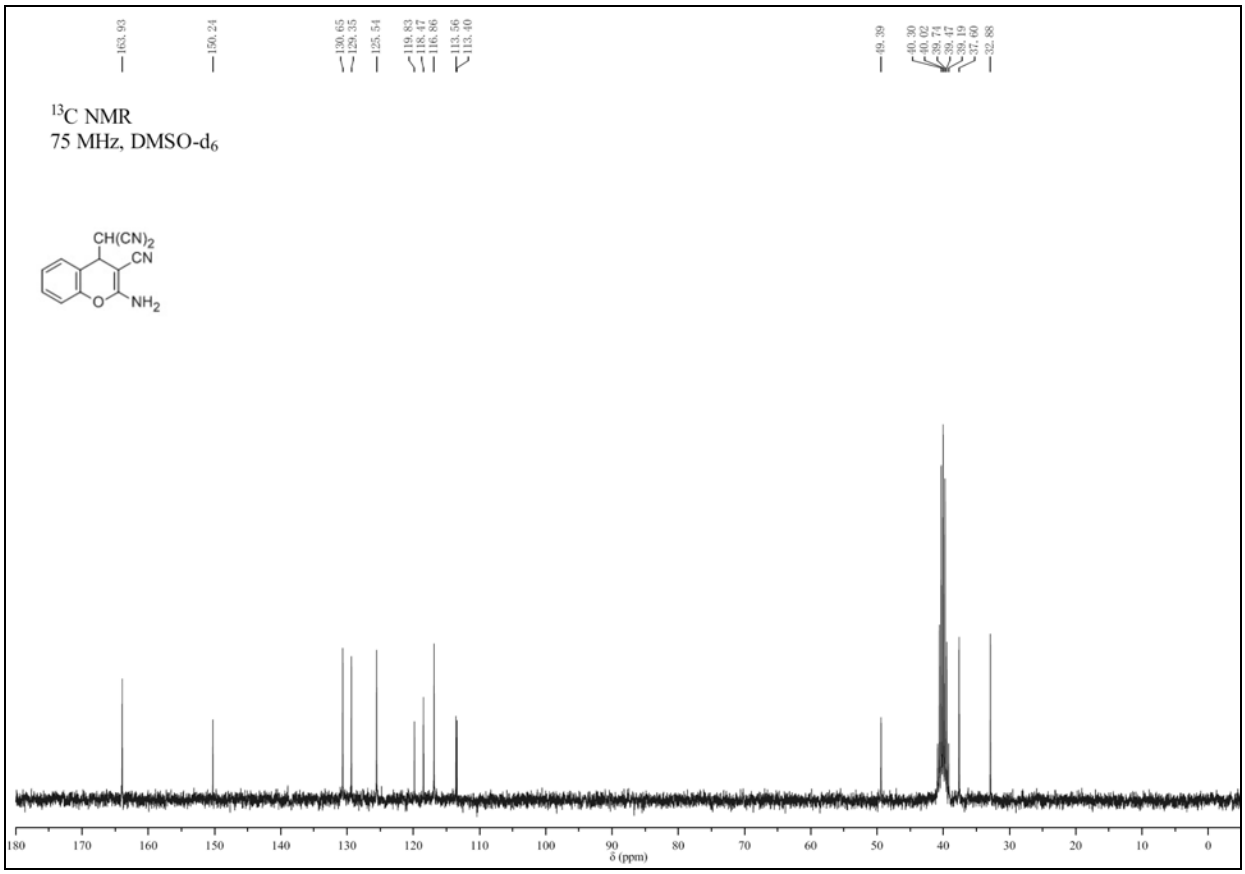
Compound **5h**


^{1}H NMR
300 MHz, CDCl$_3$
OMe
NO$_2$
CO$_2$Et
NH$_2$
δ (ppm)

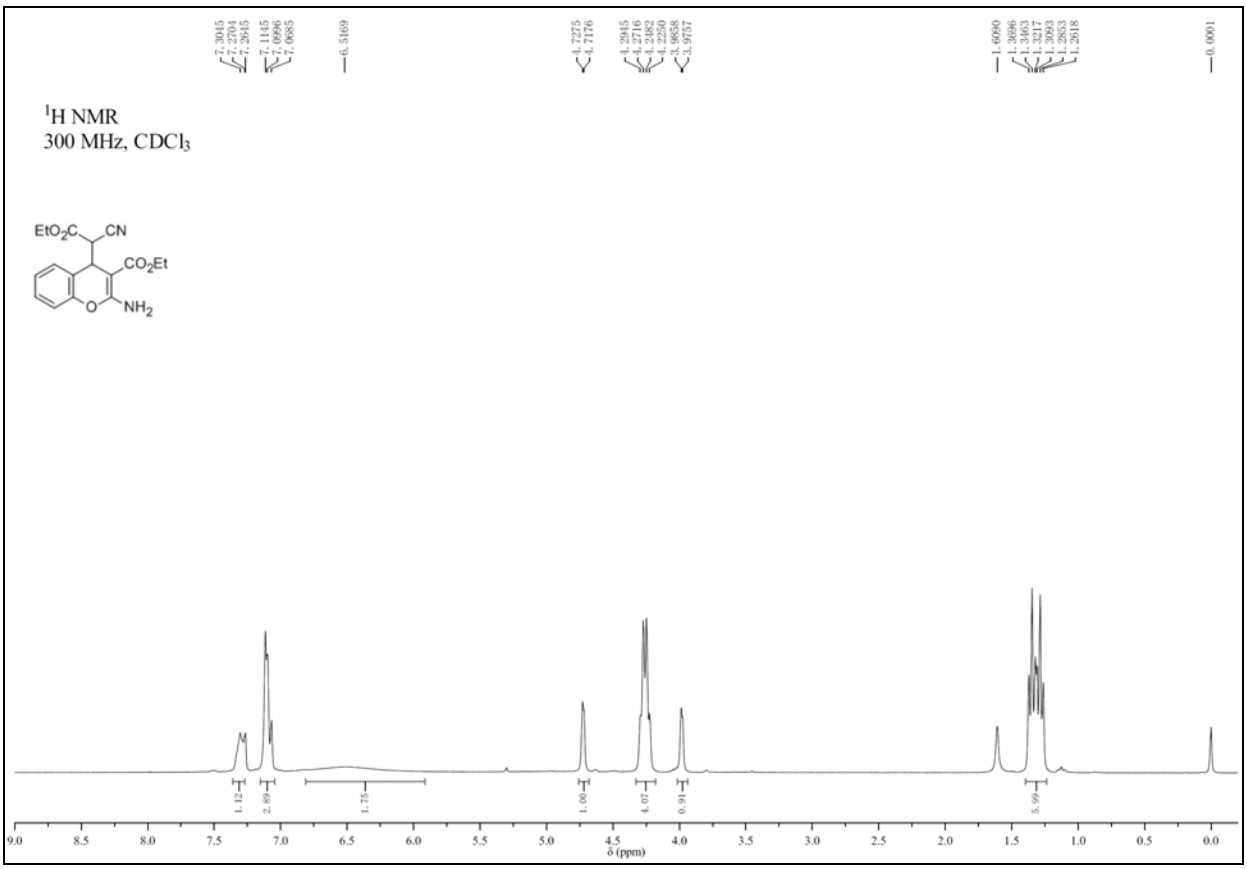

^{13}C NMR
75 MHz, CDCl$_3$
OMe
NO$_2$
CO$_2$Et
NH$_2$
δ (ppm)

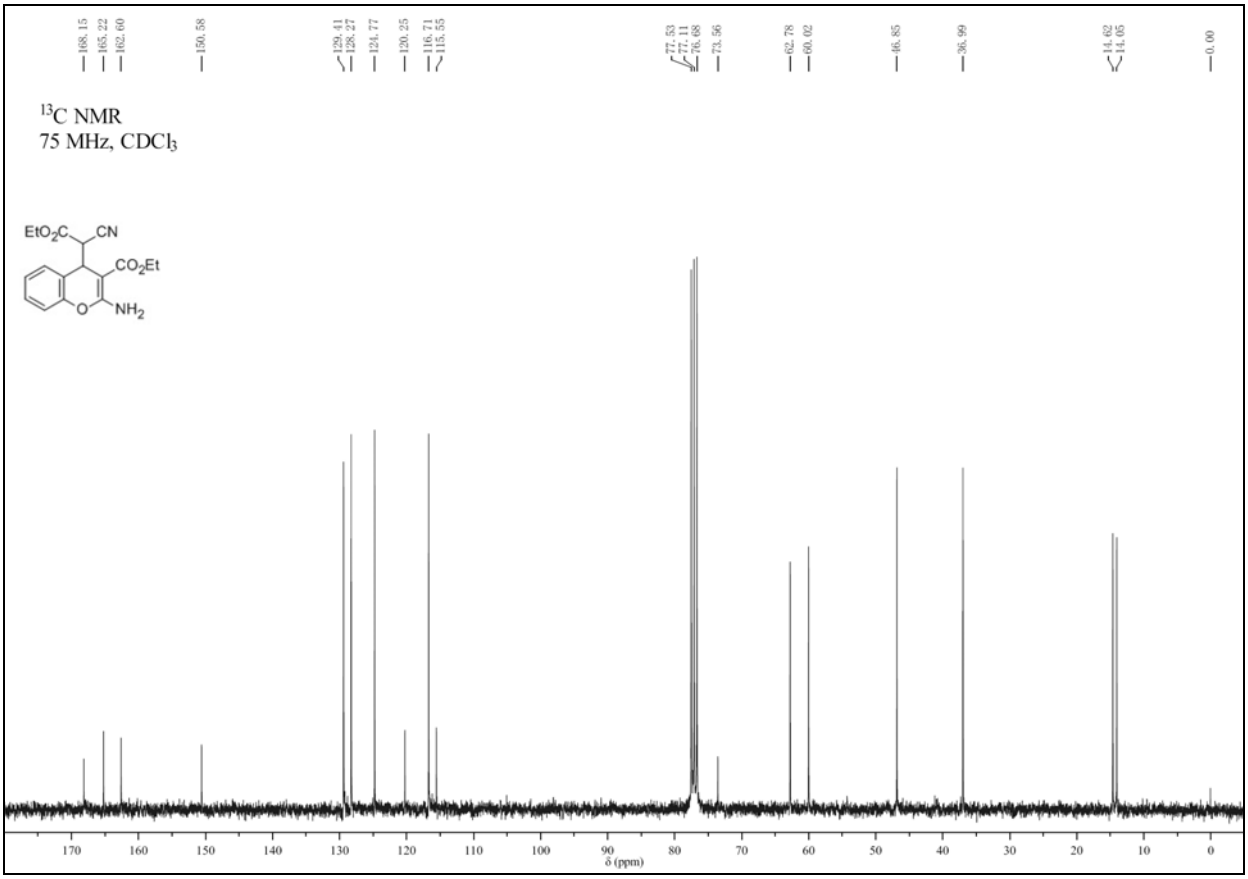
Compound **6a**


7.4965
7.4631
7.4286
7.4027
7.2467
7.1476
7.1207
5.6710
5.6579
4.5923
4.5793
3.3289
2.4996
^{1}H NMR
300 MHz, DMSO-d$_6$
CH(CN)$_2$
CN
NH$_2$
O
4.22
1.69
1.04
1.00
1.06
δ (ppm)

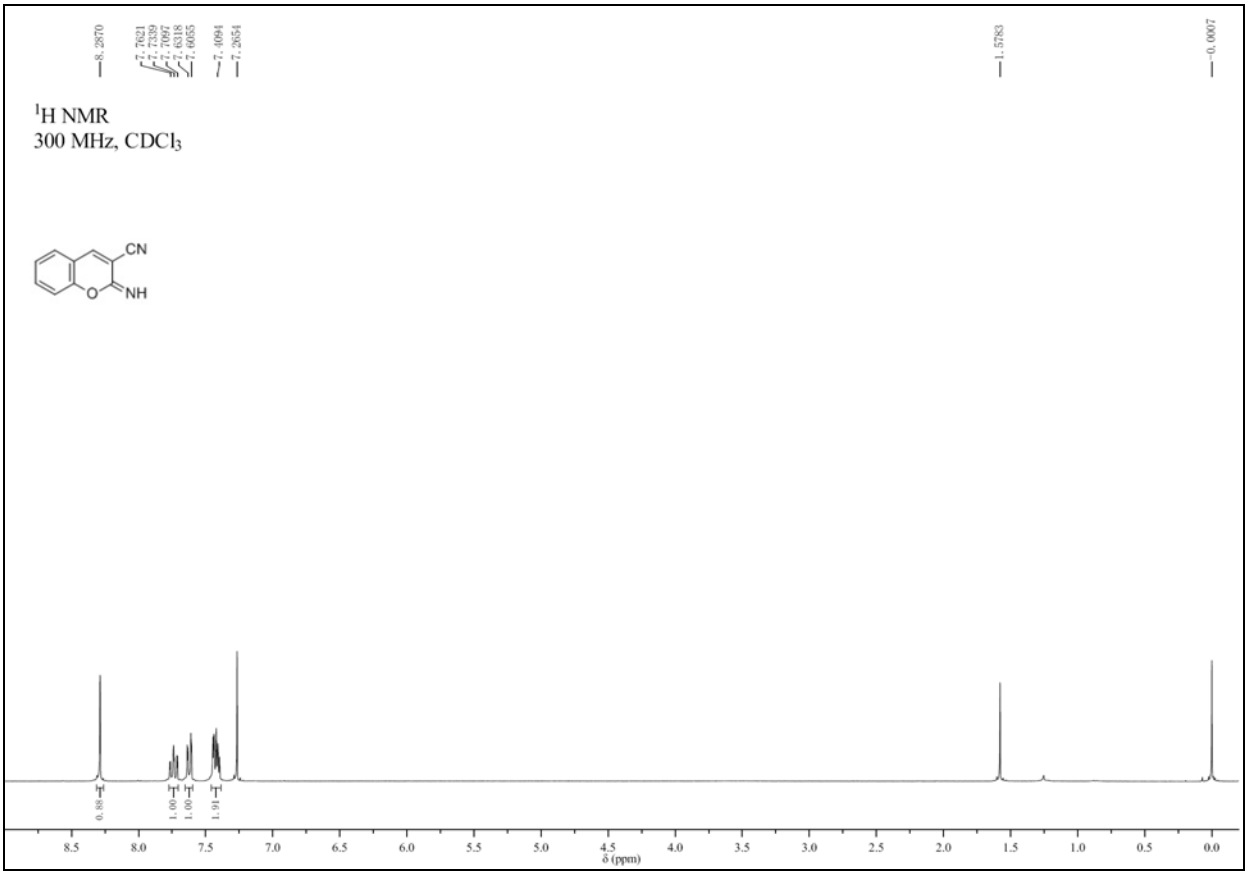

163.93
150.24
130.65
129.35
125.54
119.83
118.47
116.86
113.56
113.40
69.39
40.30
40.02
39.74
39.47
39.19
37.60
32.88
^{13}C NMR
75 MHz, DMSO-d$_6$
CH(CN)$_2$
CN
NH$_2$
O
δ (ppm)

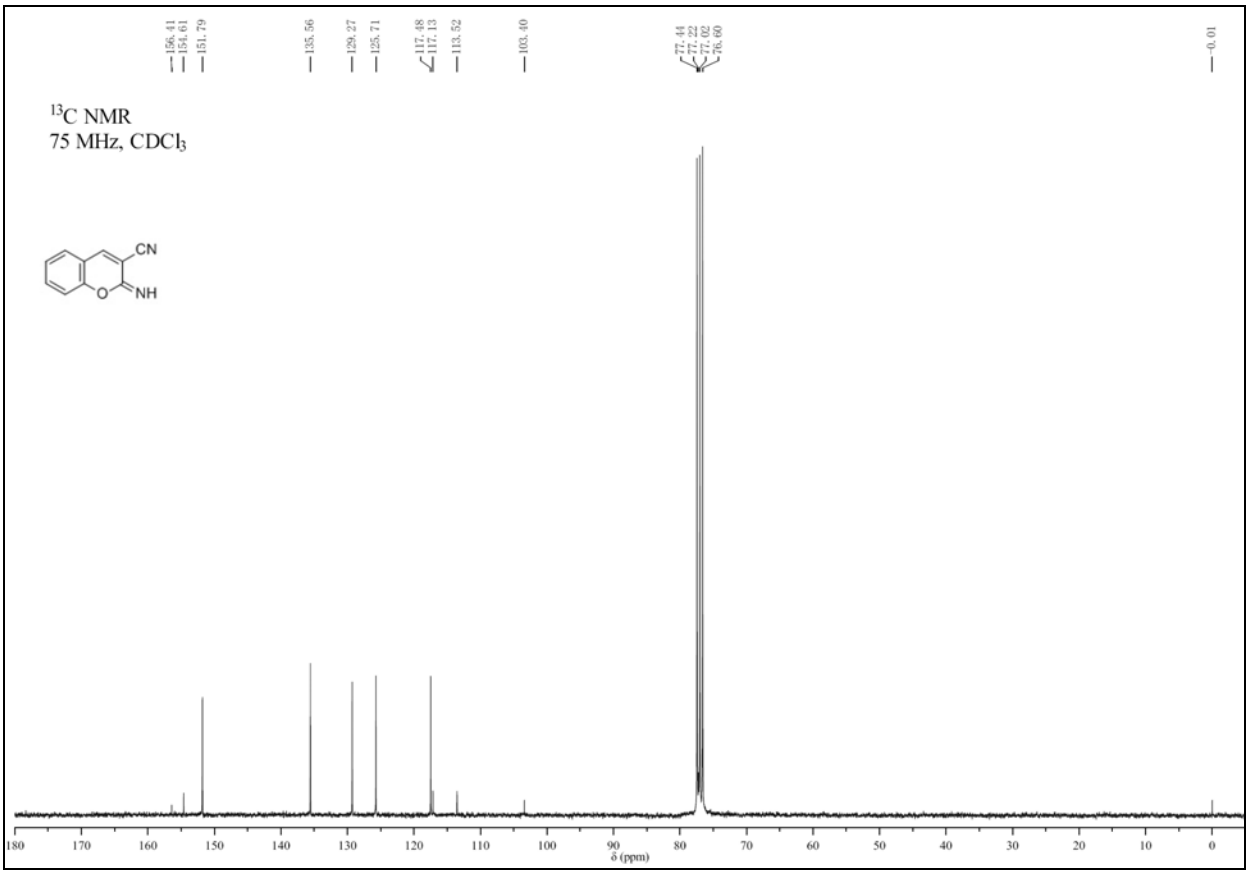
Compound **6b**


7.3045
7.2704
7.2645
7.1445
7.0846
7.0685
6.5169
4.7275
4.7176
4.2945
4.2716
4.2482
4.2250
3.9658
3.9757
1.6090
1.3696
1.3463
1.3217
1.3093
1.2853
1.2618
0.0001
^{1}H NMR
300 MHz, CDCl$_3$
EtO$_2$C
CN
CO$_2$Et
NH$_2$
1.12
2.89
1.75
1.60
4.07
0.94
5.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

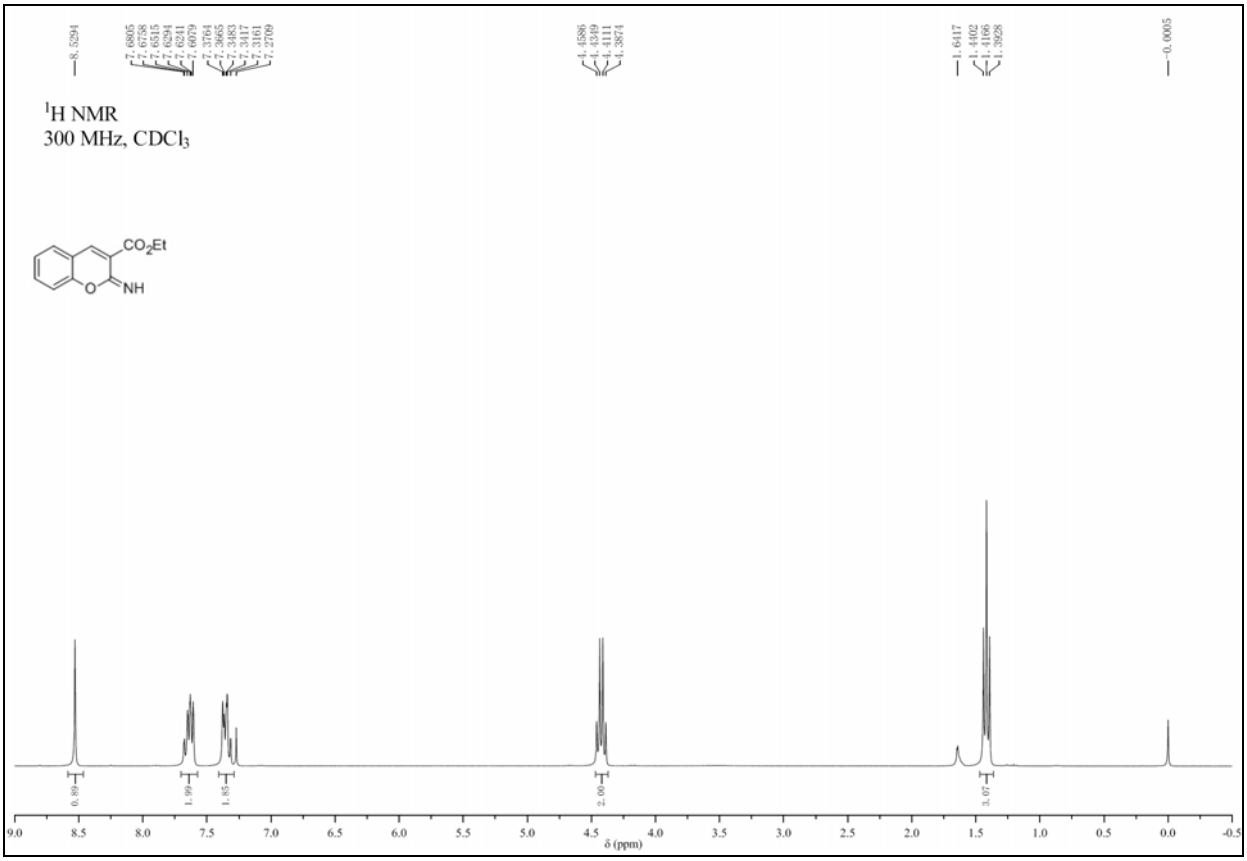

168.15
165.22
162.60
150.58
129.41
128.27
124.77
120.25
116.71
115.55
77.53
77.11
76.68
73.56
62.78
60.02
46.85
36.99
14.62
14.05
0.00
^{13}C NMR
75 MHz, CDCl$_3$
EtO$_2$C
CN
CO$_2$Et
NH$_2$
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

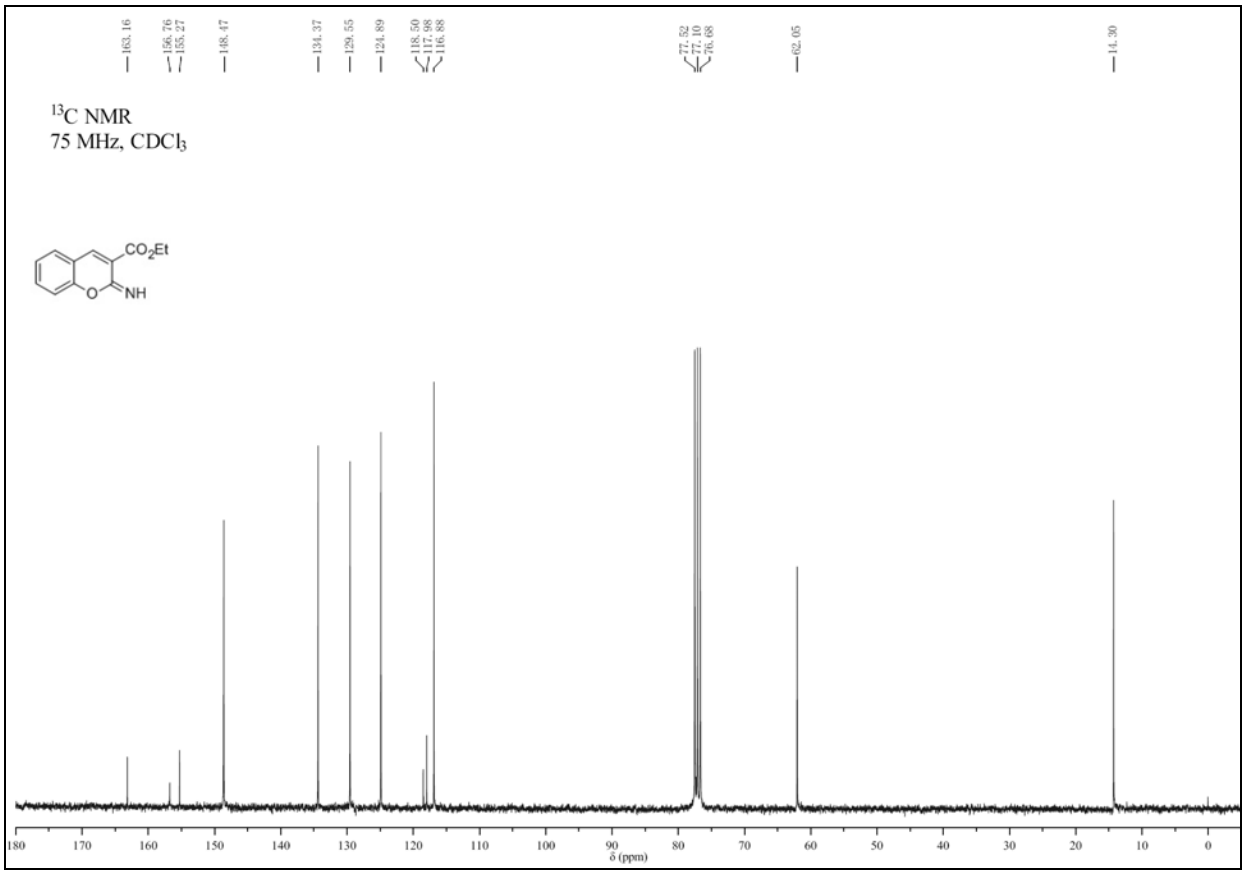
Compound **Ia**


8.2870
7.7021
7.7339
7.7097
7.6518
7.6055
7.4094
7.2654
1.5783
0.0007
^{1}H NMR
300 MHz, $CDCl_3$
CN
NH
0.88
1.00
1.00
1.91
δ (ppm)


156.41
154.61
151.79
135.56
129.27
125.71
117.48
117.13
113.52
103.40
77.44
77.22
77.02
76.60
0.01
^{13}C NMR
75 MHz, $CDCl_3$
CN
NH
δ (ppm)

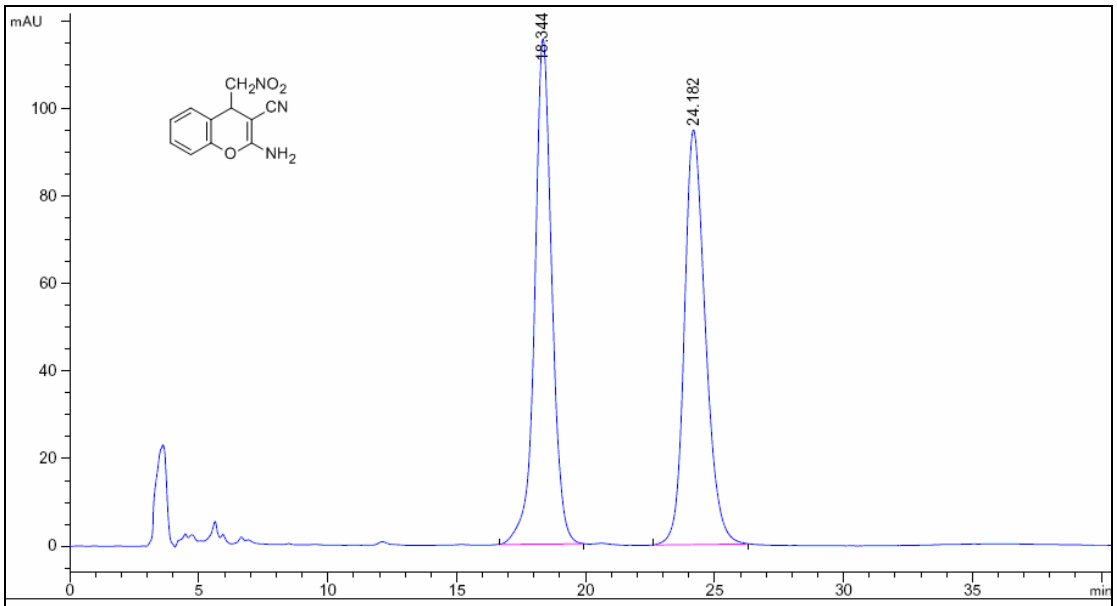
Compound **Ib**


8.5294
7.6805
7.6758
7.6515
7.6294
7.6241
7.6079
7.3764
7.3665
7.3483
7.3417
7.3161
7.2709
4.4586
4.4349
4.4111
4.3874
1.6417
1.4402
1.4166
1.3928
0.0005
^{1}H NMR
300 MHz, $CDCl_3$
CO_2Et
NH
0.89
1.99
1.85
2.00
3.07
δ (ppm)


163.16
156.76
155.27
148.47
134.37
129.55
124.89
118.50
117.98
116.88
77.52
77.10
76.68
62.05
14.30
^{13}C NMR
75 MHz, $CDCl_3$
CO_2Et
NH
δ (ppm)

HPLC Profile

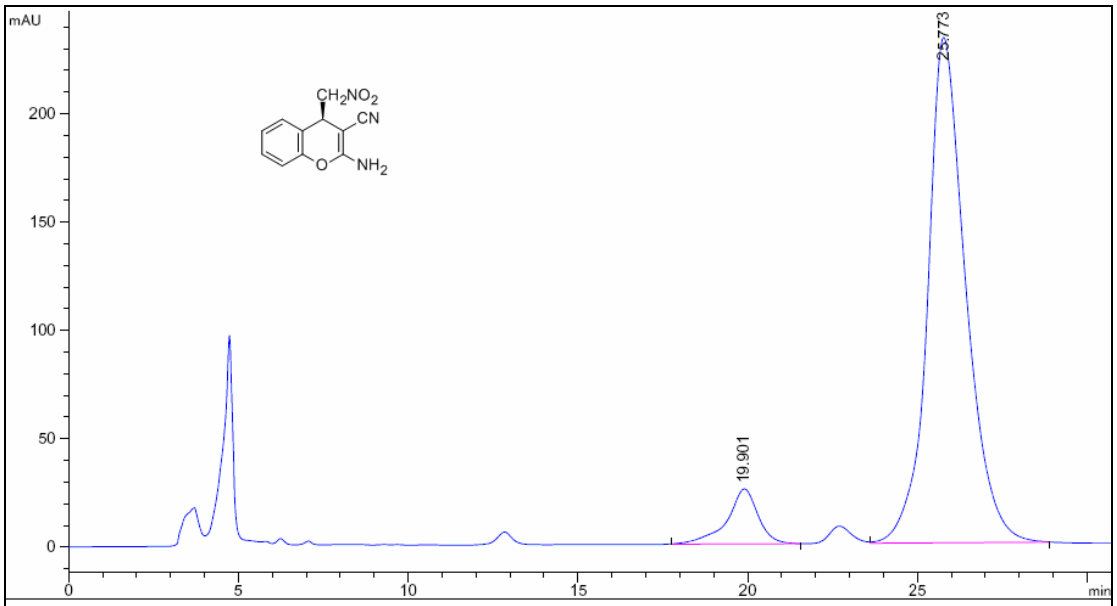
Racemic **4a**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	18.344	BB	0.6938	5346.73926	115.63126	49.8619
2	24.182	BB	0.8666	5376.34717	94.85082	50.1381
Totale :				1.07231e4	210.48208	

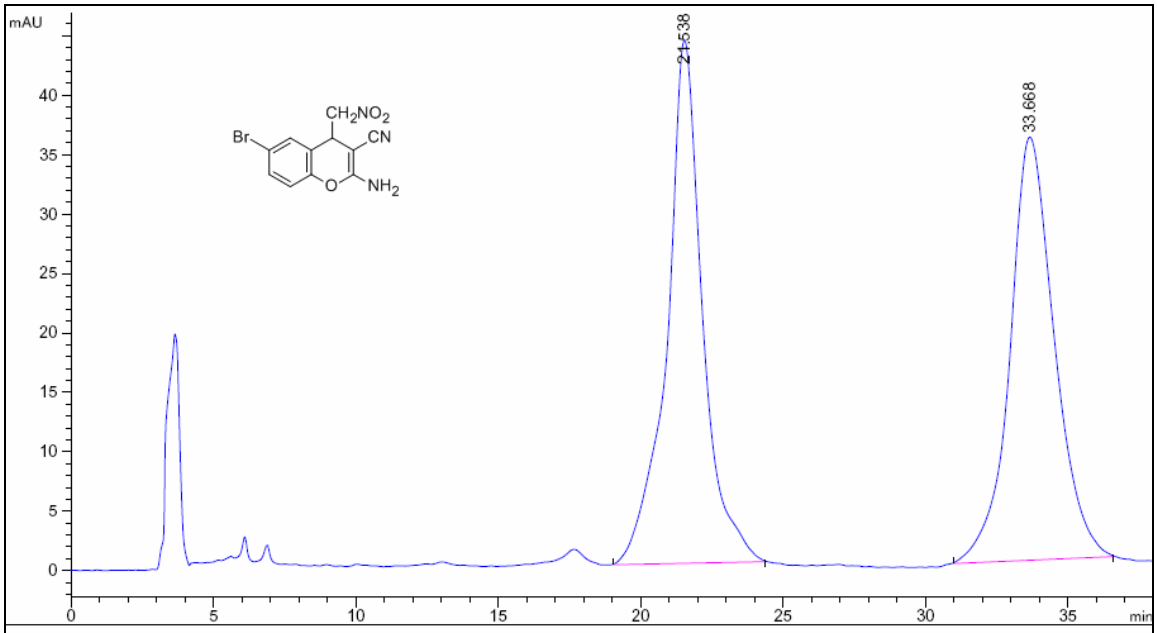
Enantiomeric enriched **4a**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	19.901	BB	0.9148	1618.57446	25.36471	8.1578
2	25.773	VB	1.1530	1.82221e4	233.27843	91.8422
Totale :				1.98407e4	258.64314	

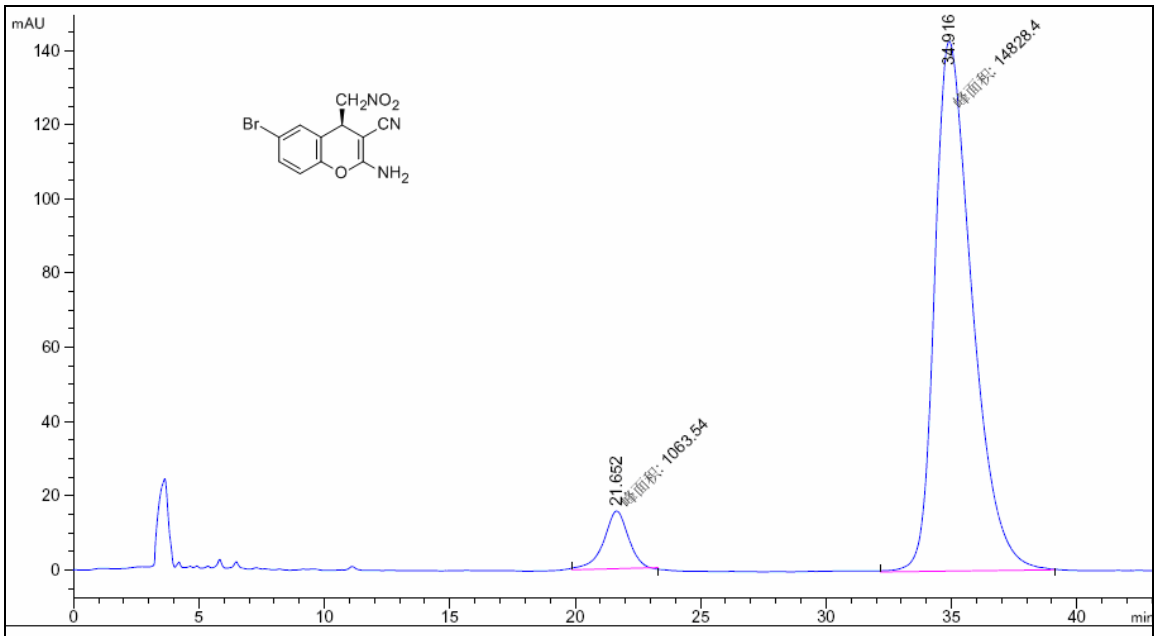
Racemic **4b**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	21.538	BB	1.2275	3816.86475	44.00229	49.7242
2	33.668	BB	1.5609	3859.20117	35.58274	50.2758
Totale :				7676.06592	79.58503	

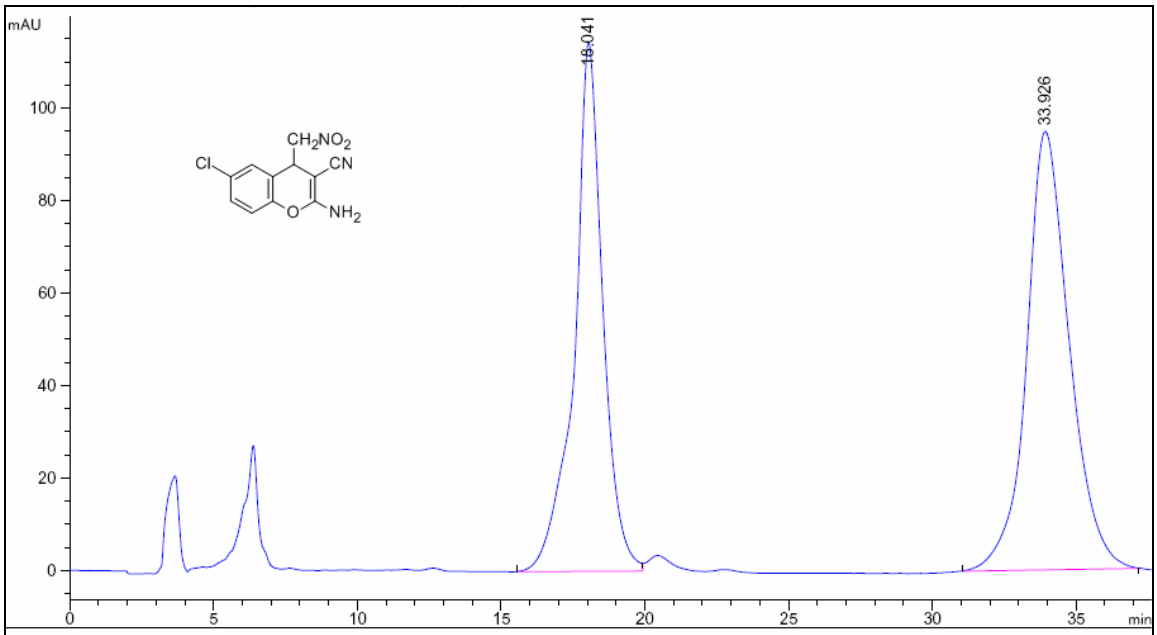
Enantiomeric enriched **4b**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	21.652	MM	1.1416	1063.54395	15.52757	6.6923
2	34.916	MM	1.7309	1.48284e4	142.77995	93.3077
Totale :				1.58919e4	158.30753	

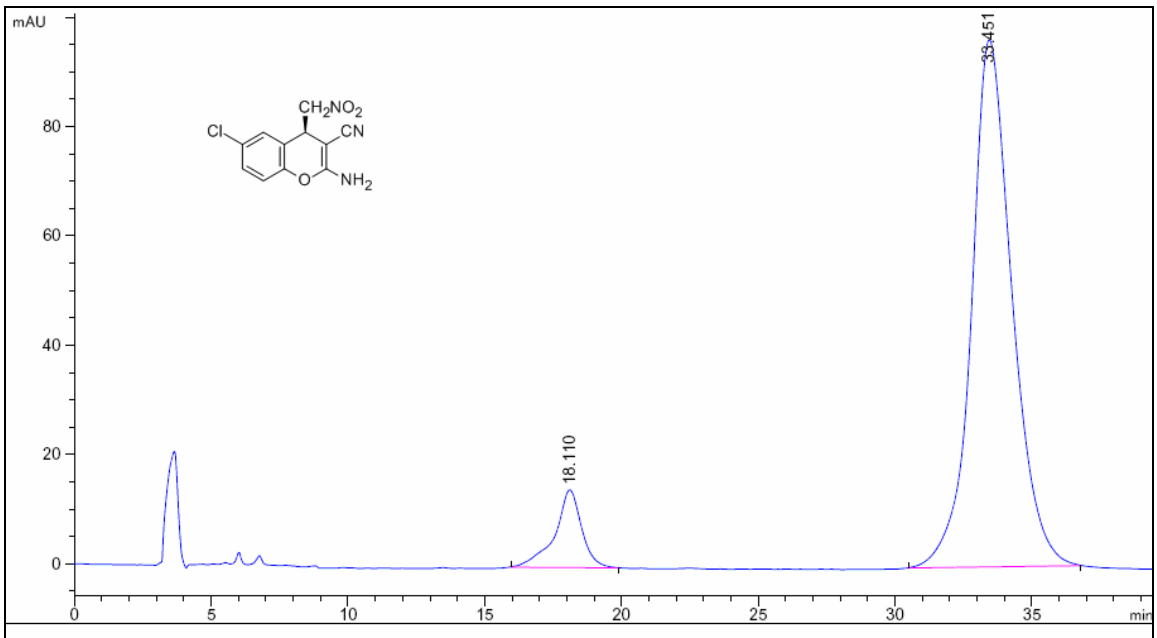
Racemic **4c**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	18.041	BB	0.9854	7886.70801	114.32209	44.6584
2	33.926	BB	1.5420	9773.38184	94.79971	55.3416
Totale :				1.76601e4	209.12180	

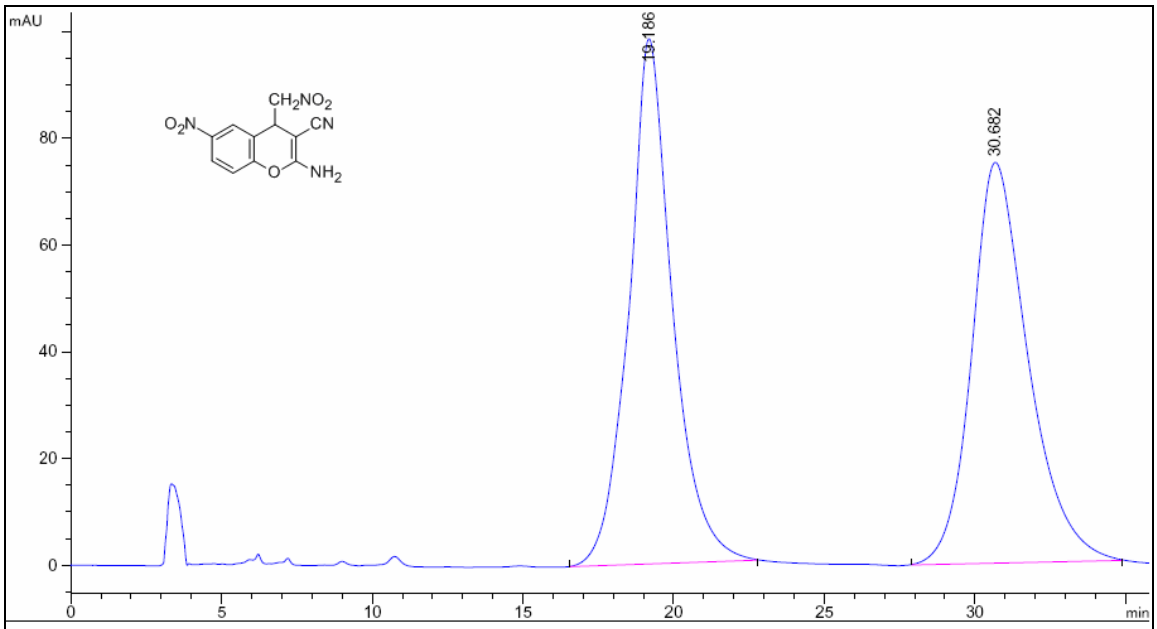
Enantiomeric enriched **4c**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	18.110	BB	0.9697	972.05835	14.21289	8.9028
2	33.451	BB	1.5249	9946.52441	96.45229	91.0972
Totale :				1.09186e4	110.66518	

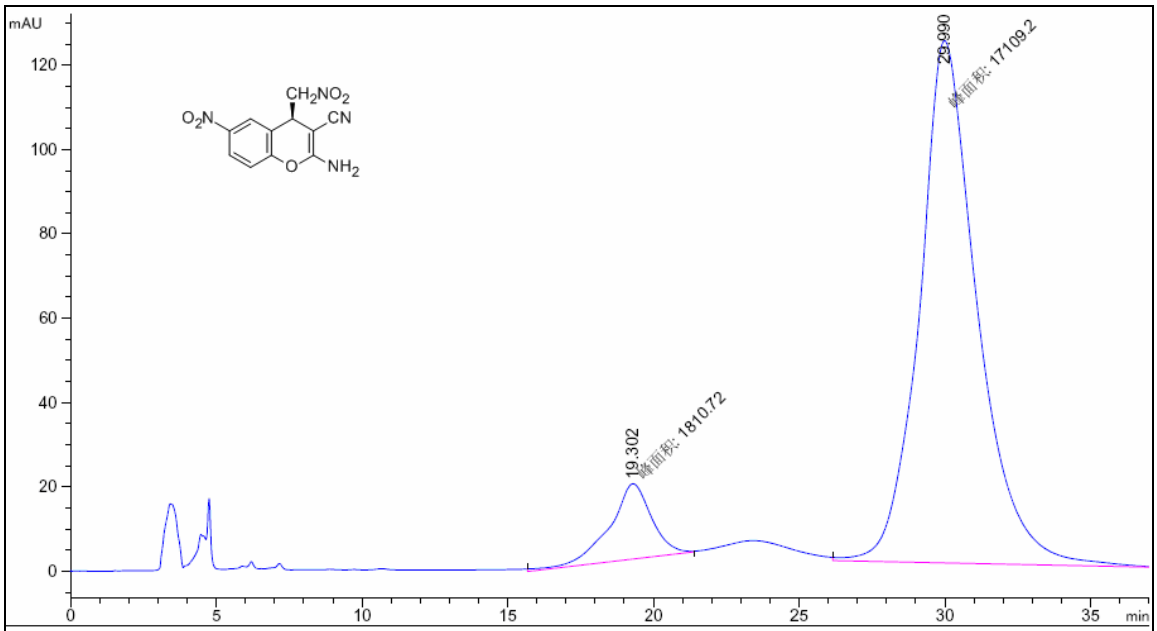
Racemic **4d**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	19.186	BB	1.4205	9910.91797	98.45699	50.2394
2	30.682	BB	1.9137	9816.45508	75.09951	49.7606
Totale :				1.97274e4	173.55650	

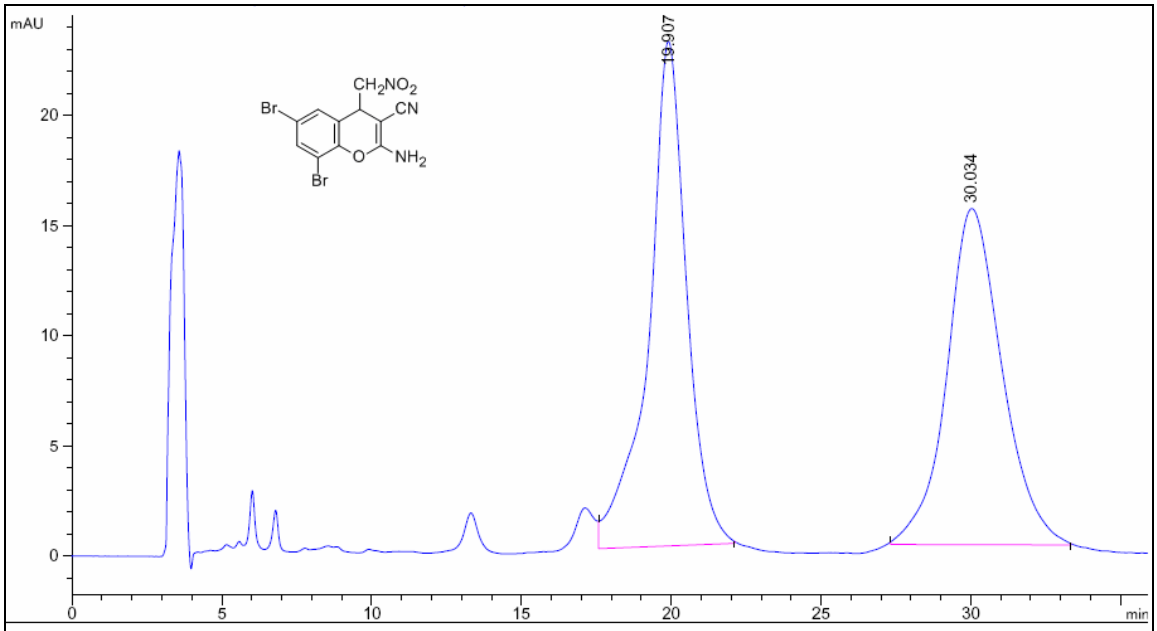
Enantiomeric enriched **4d**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	19.302	MM	1.6884	1810.72302	17.87382	9.5704
2	29.990	MM	2.3024	1.71092e4	123.85033	90.4296
Totale :				1.89199e4	141.72415	

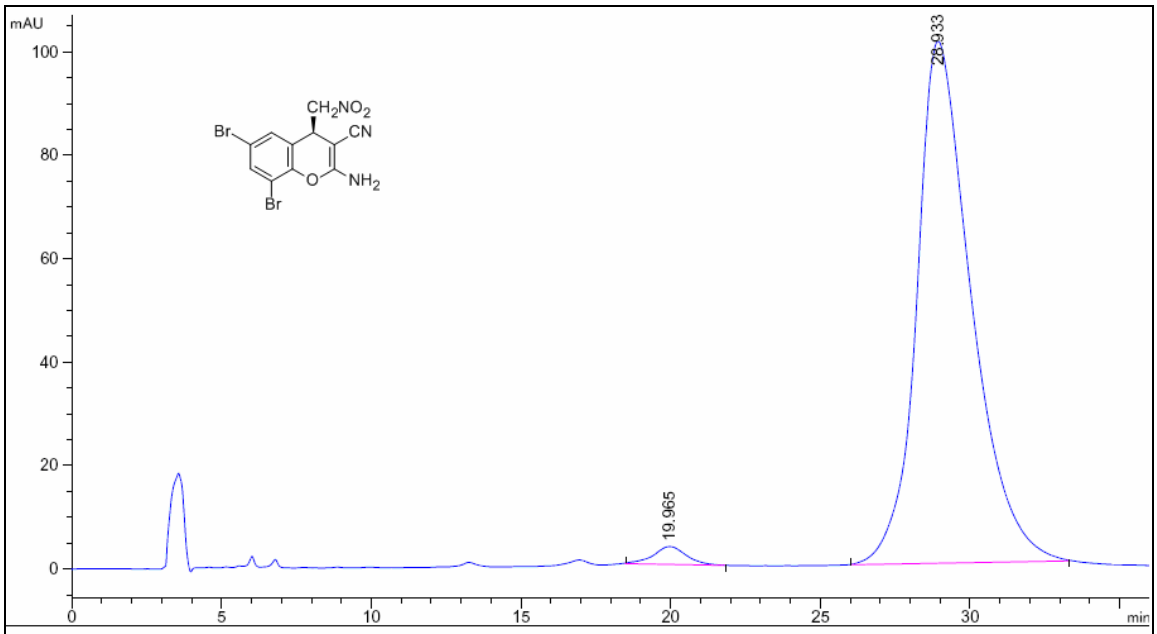
Racemic **4e**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	19.907	VB	1.2750	2025.31860	22.89971	50.7950
2	30.034	BB	1.7843	1961.92065	15.25537	49.2050
Totale :				3987.23926	38.15508	

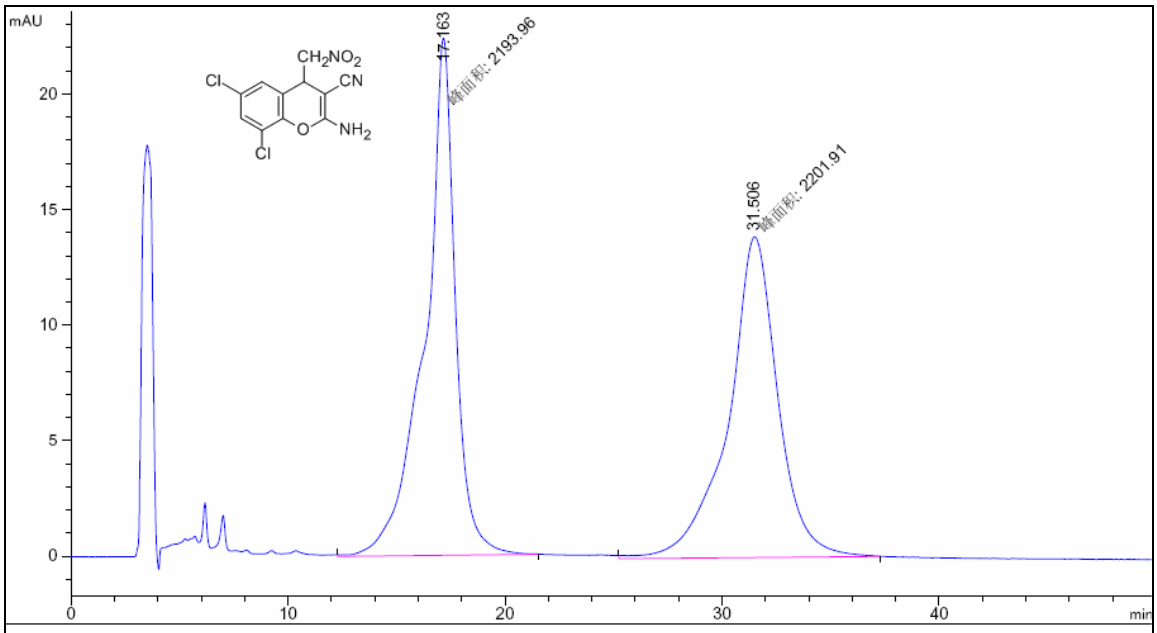
Enantiomeric enriched **4e**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	19.965	BB	0.9305	266.11240	3.45557	2.0379
2	28.933	BB	1.8537	1.27918e4	100.97070	97.9621
Totale :				1.30579e4	104.42626	

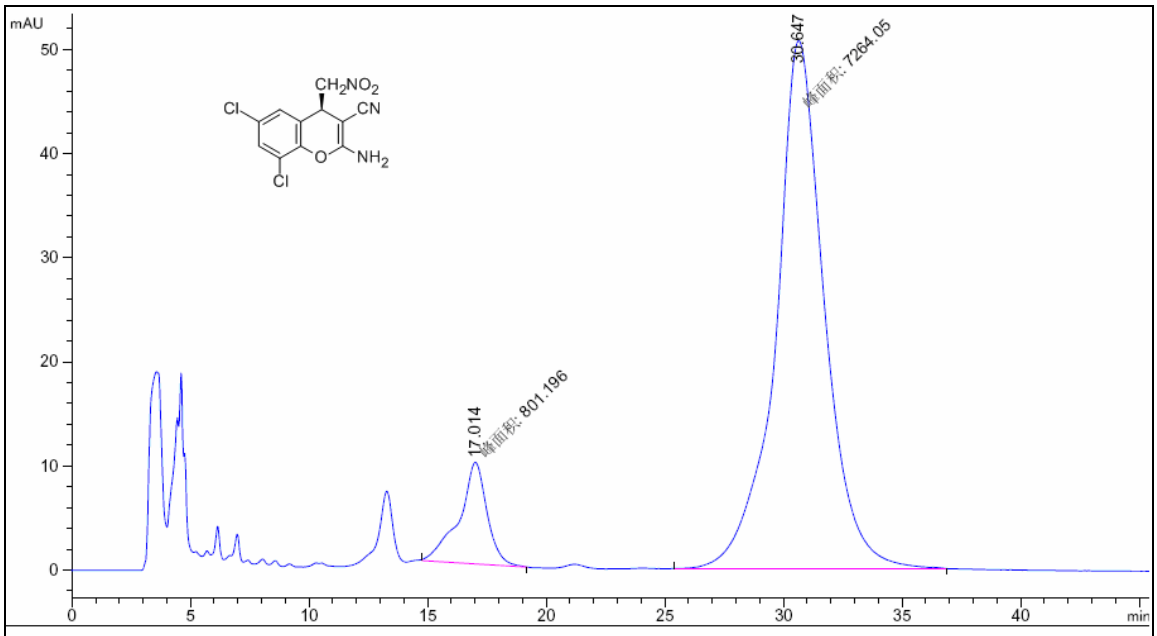
Racemic **4f**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	17.163	MM	1.6350	2193.96411	22.36448	49.9096
2	31.506	MM	2.6457	2201.90918	13.87091	50.0904
Totale :				4395.87329	36.23540	

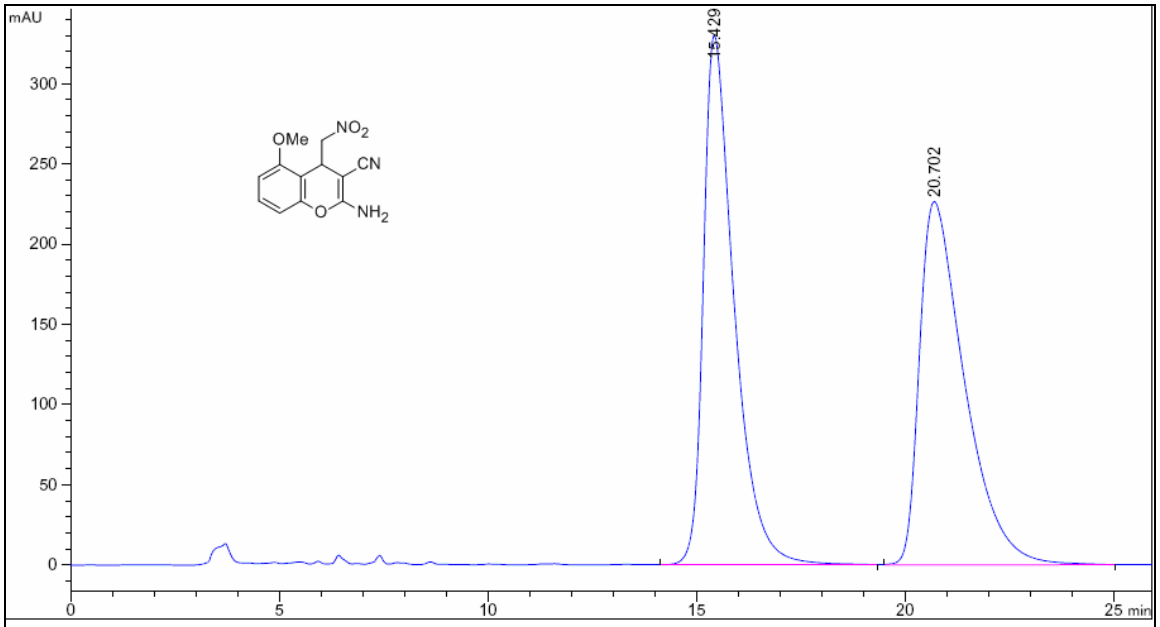
Enantiomeric enriched **4f**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	17.014	MM	1.3678	801.19562	9.76251	9.9339
2	30.647	MM	2.3849	7264.05469	50.76444	90.0661
Totale :				8065.25031	60.52695	

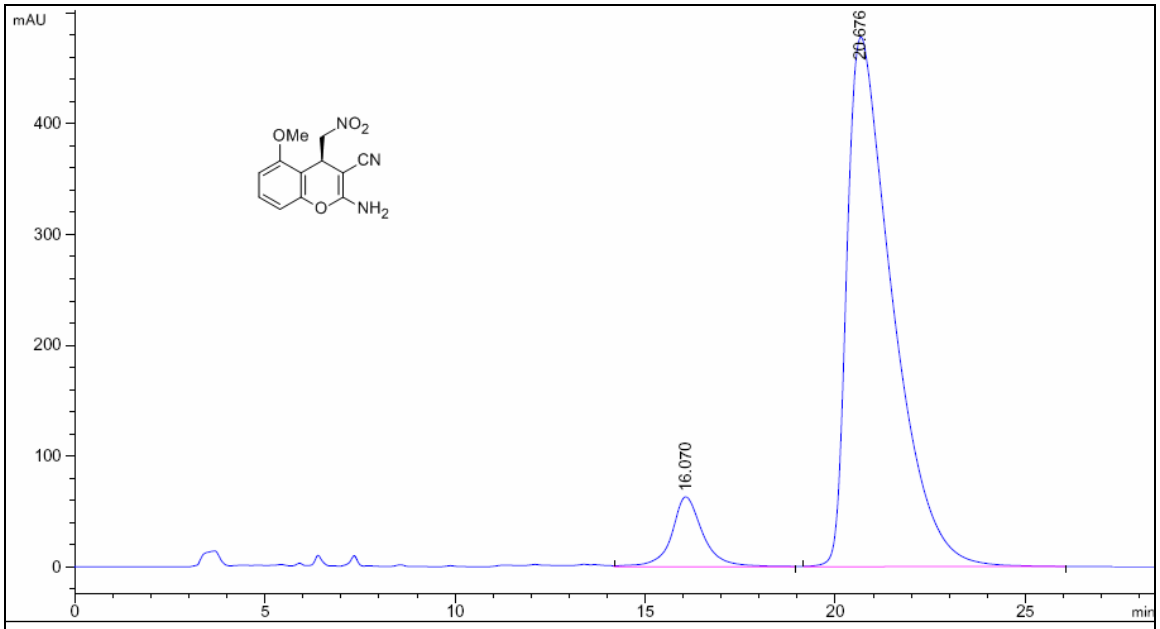
Racemic **4g**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	15.429	VB	0.7625	1.69560e4	330.01517	49.9748
2	20.702	BB	1.1256	1.69731e4	226.26030	50.0252
Totale :				3.39292e4	556.27547	

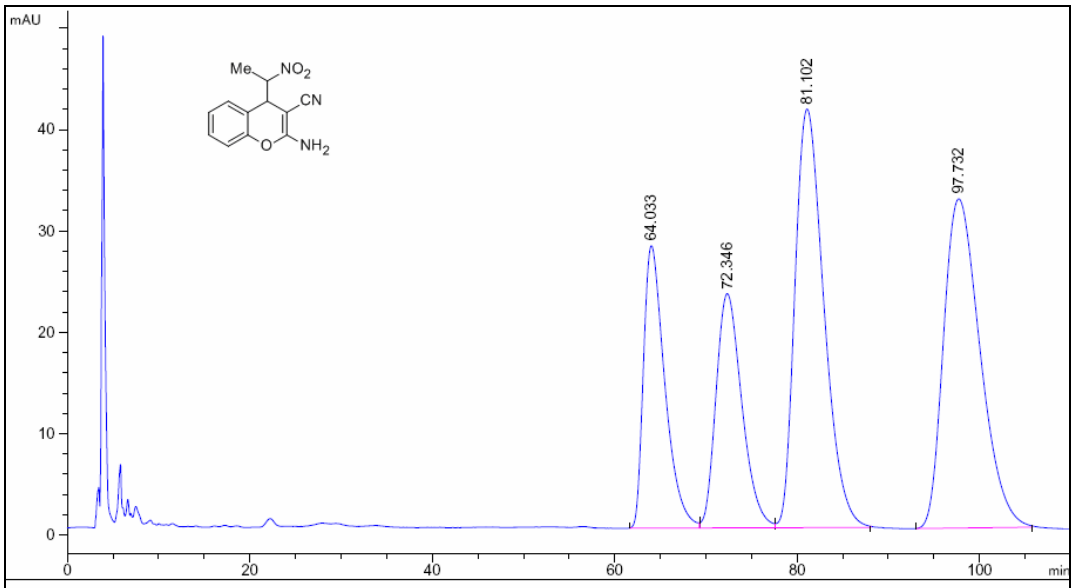
Enantiomeric enriched **4g**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	16.070	VB	0.8384	3619.78418	63.07911	8.3640
2	20.676	BB	1.2301	3.96585e4	477.98624	91.6360
Totale :				4.32783e4	541.06535	

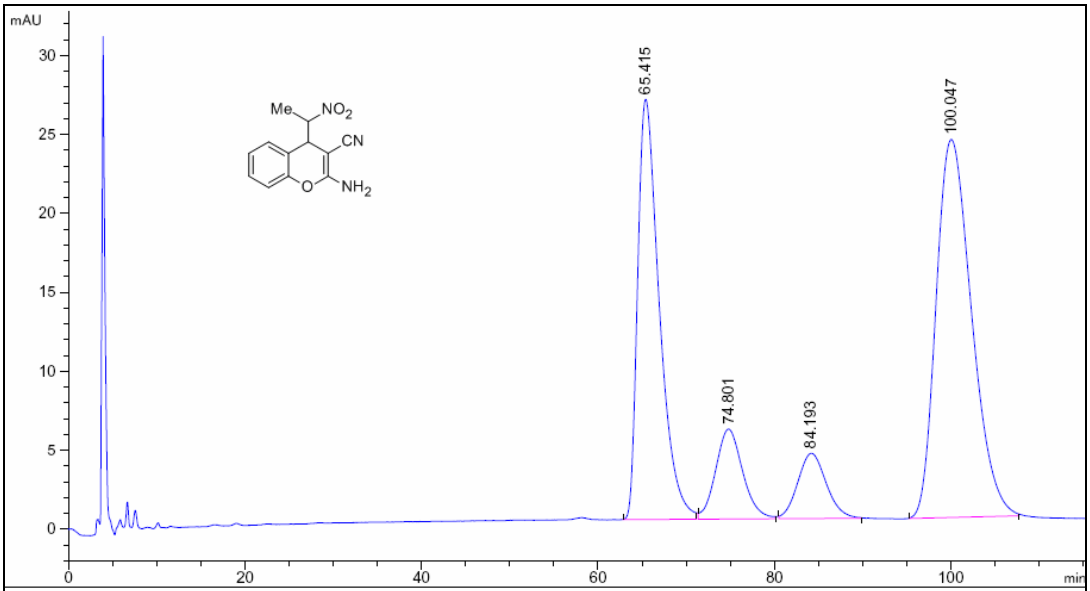
Racemic **4h**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	64.033	BB	2.4689	4534.87256	27.87222	16.6601
2	72.346	BV	3.0589	4560.58105	23.11514	16.7546
3	81.102	VB	3.4120	9087.97949	41.29465	33.3872
4	97.732	BB	4.2706	9036.51465	32.48269	33.1981
Totale :				2.72199e4	124.76469	

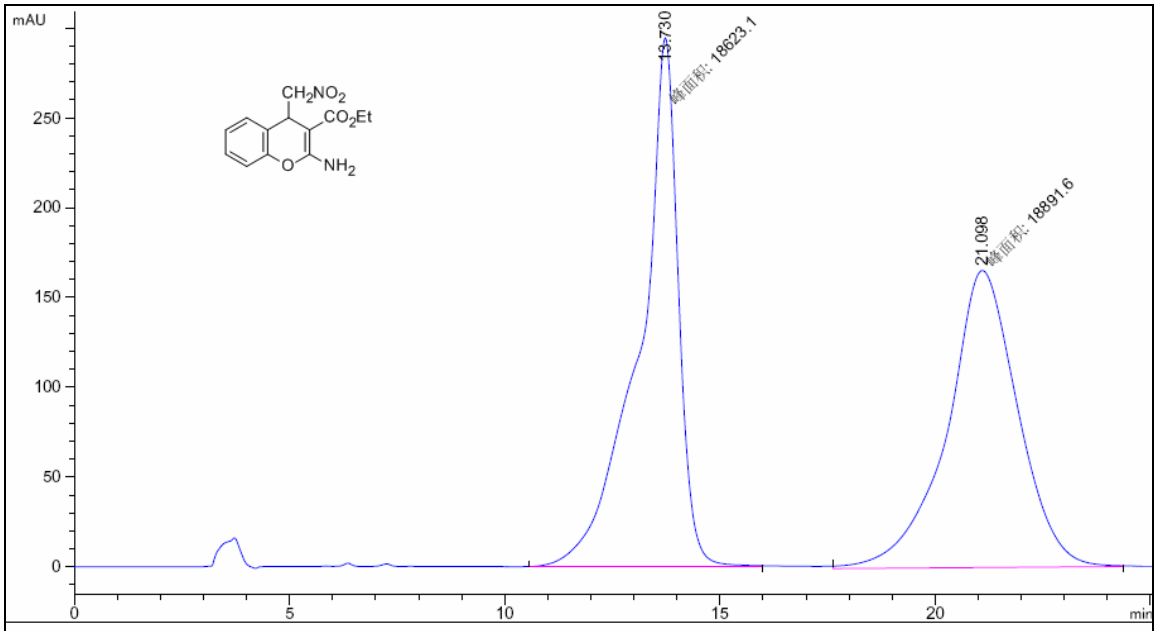
Enantiomeric enriched **4h**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	65.415	BB	2.5457	4531.35059	26.61077	33.9242
2	74.801	BB	3.1314	1211.80090	5.70262	9.0722
3	84.193	BB	2.9291	929.72028	4.13006	6.9604
4	100.047	BB	4.2712	6684.40186	23.93775	50.0432
Totale :				1.33573e4	60.38121	

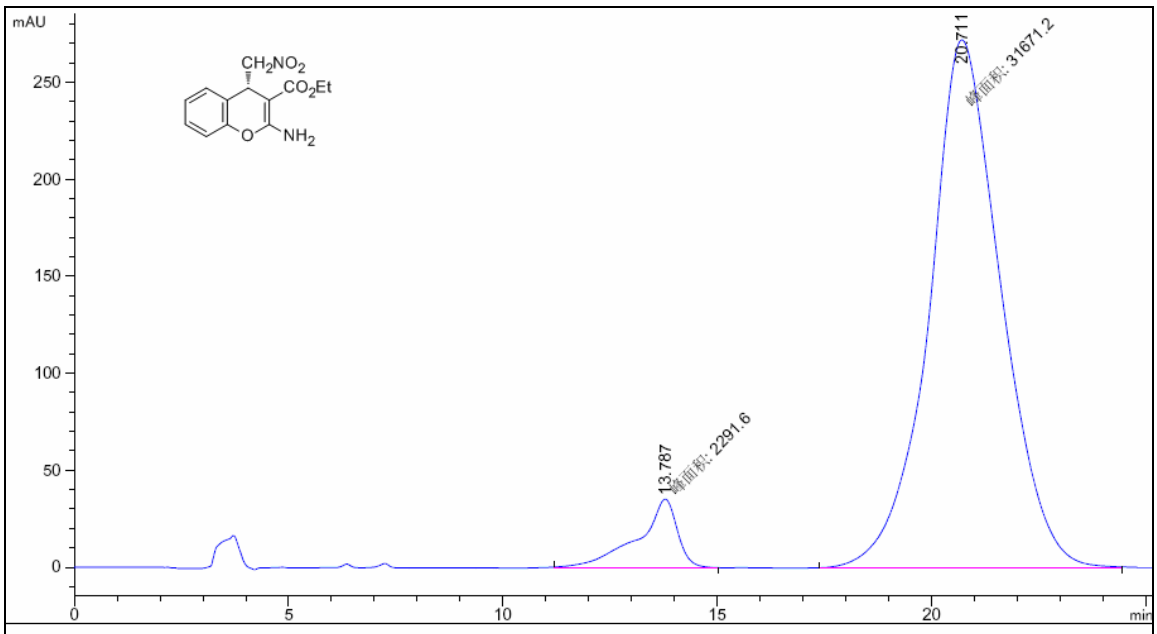
Racemic **5a**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	13.730	MM	1.0541	1.86231e4	294.46802	49.6422
2	21.098	MM	1.9033	1.88916e4	165.42921	50.3578
Totale :				3.75147e4	459.89723	

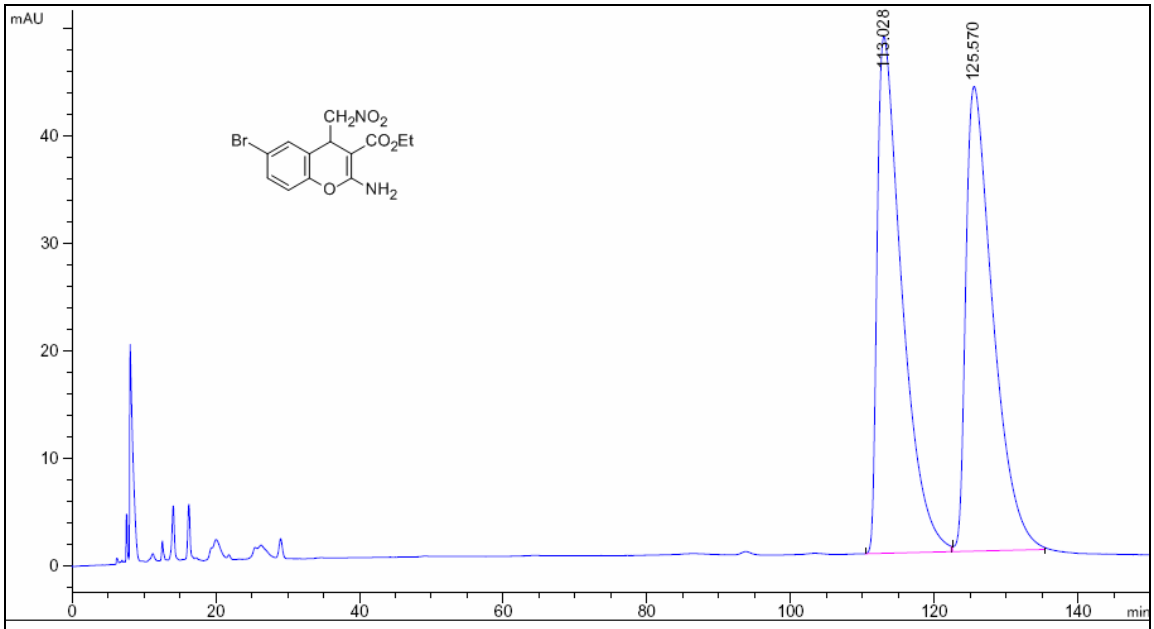
Enantiomeric enriched **5a**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	13.787	MM	1.0780	2291.60083	35.42891	6.7474
2	20.711	MM	1.9391	3.16712e4	272.21429	93.2526
Totale :				3.39628e4	307.64321	

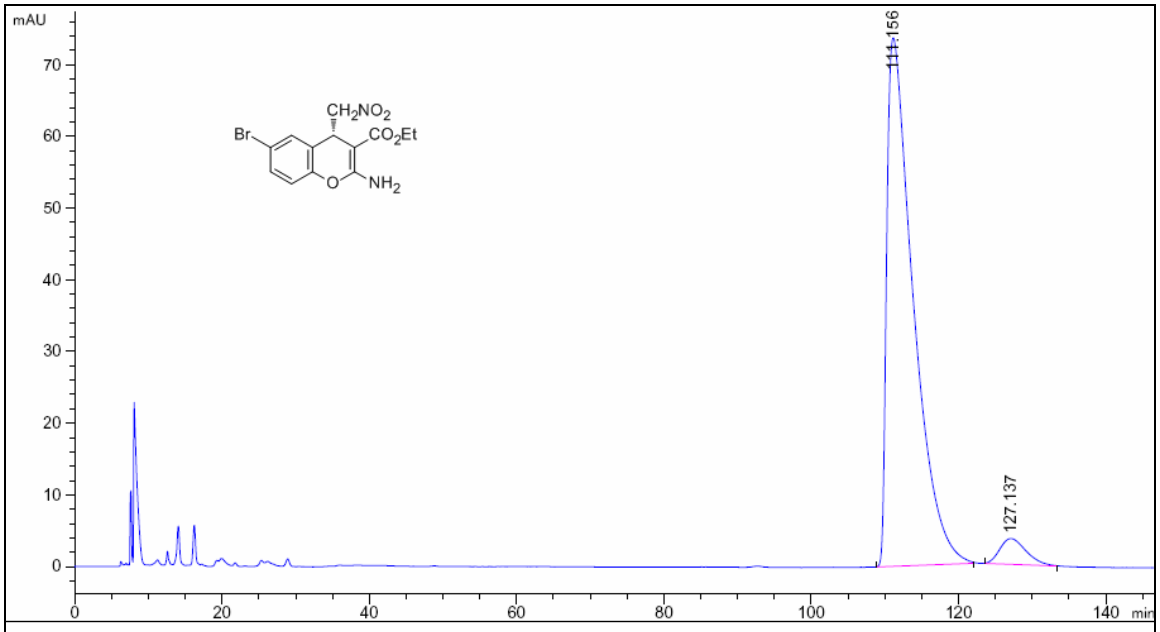
Racemic **5b**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	113.028	BB	3.4950	1.15267e4	47.99526	50.4654
2	125.570	BB	3.8619	1.13141e4	43.16154	49.5346
Totale :				2.28408e4	91.15680	

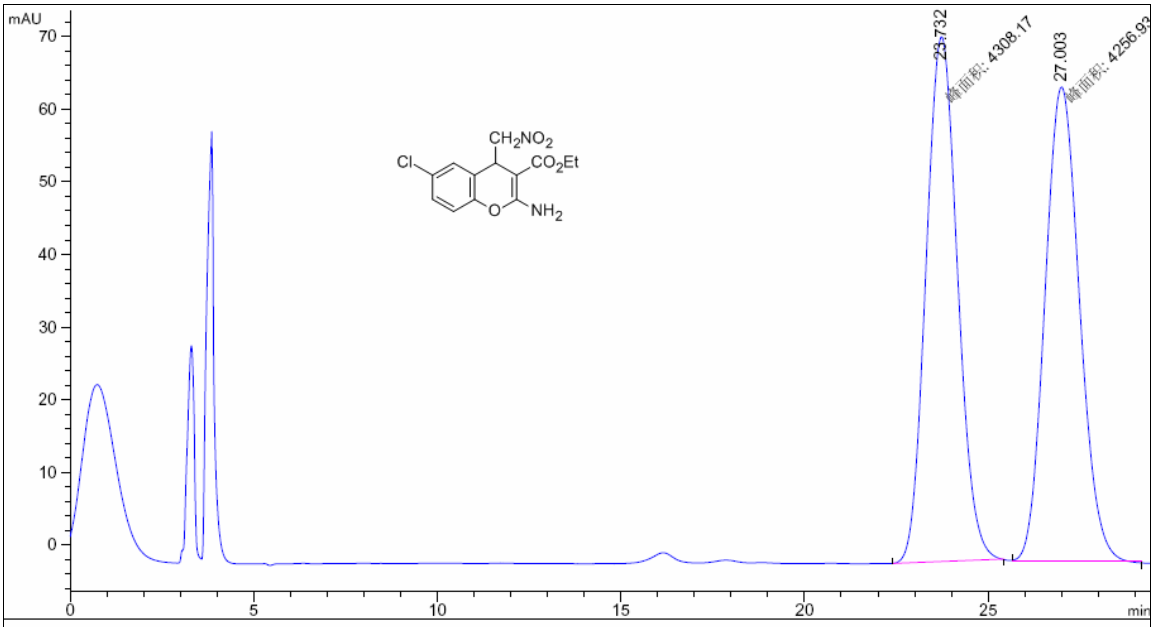
Enantiomeric enriched **5b**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	111.156	BB	3.5177	1.83197e4	73.68957	95.3402
2	127.137	BB	2.9240	895.38690	3.59401	4.6598
Totale :				1.92150e4	77.28358	

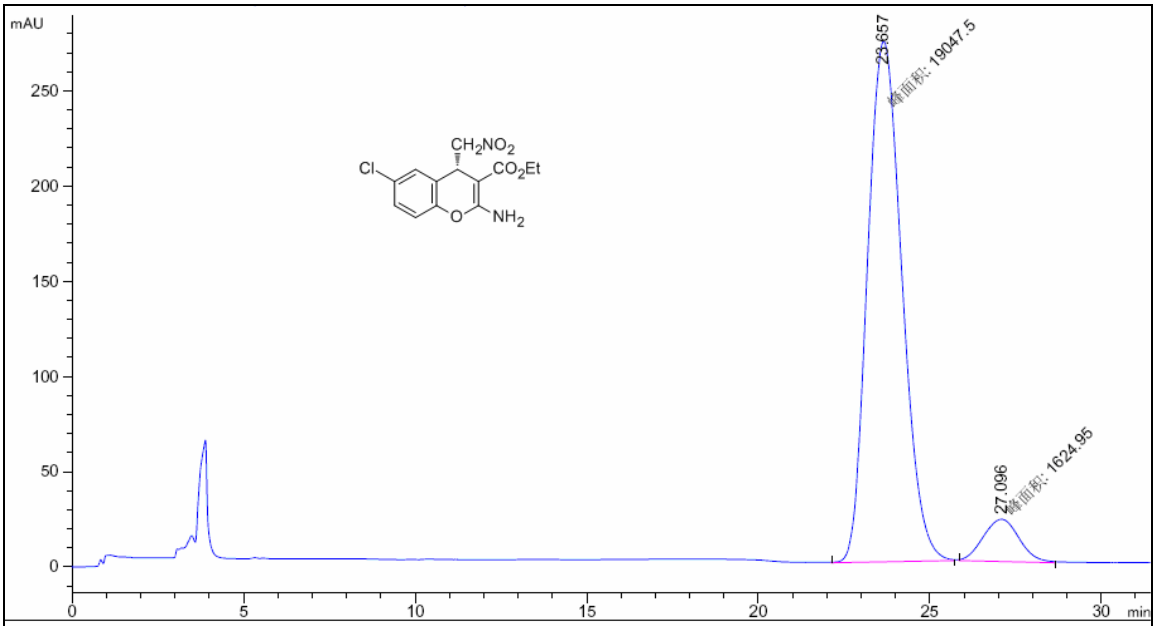
Racemic **5c**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	23.732	MM	0.9940	4308.17090	72.23798	50.2991
2	27.003	MM	1.0867	4256.92871	65.28969	49.7009
Totale :				8565.09961	137.52767	

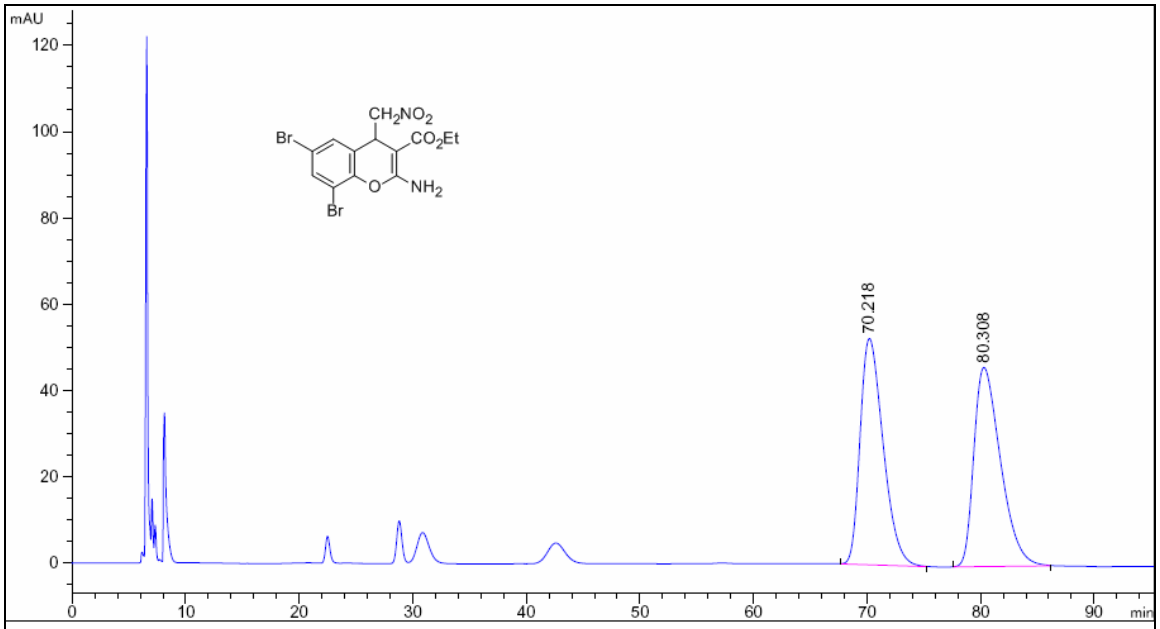
Enantiomeric enriched **5c**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	23.657	MM	1.1613	1.90475e4	273.36624	92.1395
2	27.096	MM	1.2202	1624.95020	22.19533	7.8605
Totale :				2.06725e4	295.56157	

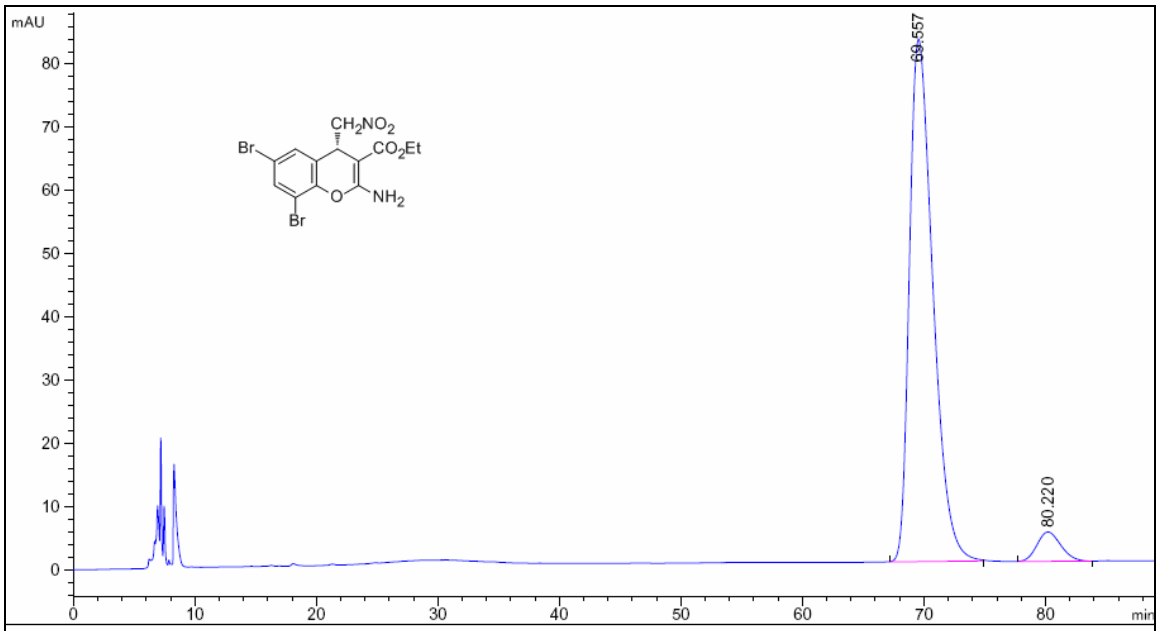
Racemic **5d**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	70.218	BB	2.1909	7386.23633	52.43292	49.4734
2	80.308	BB	2.5191	7543.48730	46.13674	50.5266
Totale :				1.49297e4	98.56966	

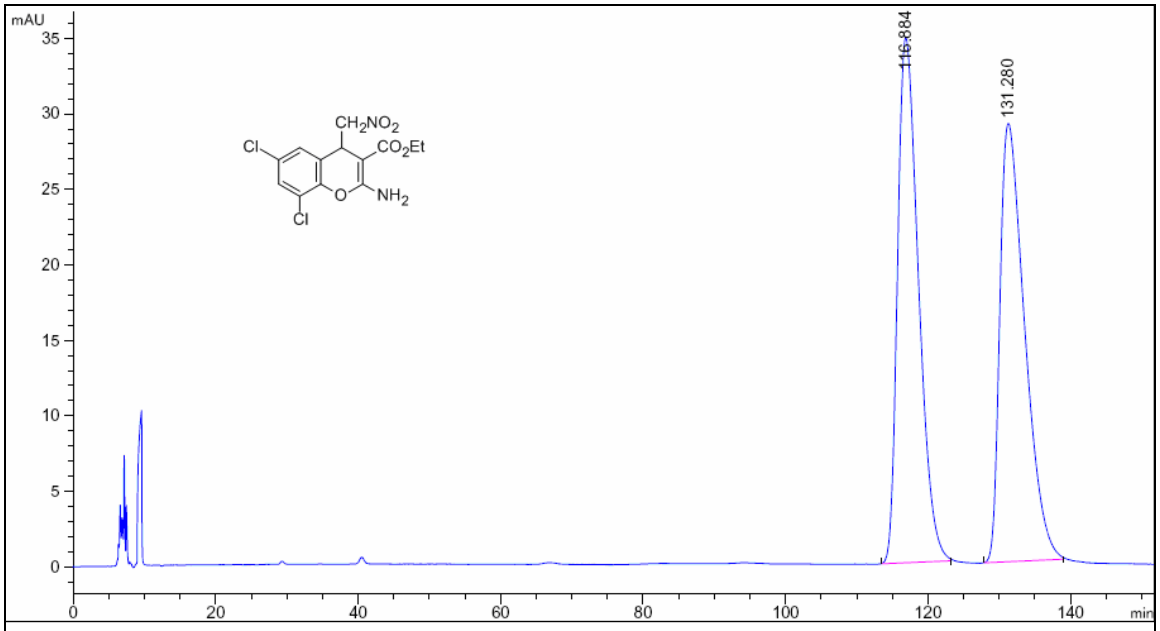
Enantiomeric enriched **5d**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	69.557	BB	2.0713	1.10824e4	82.63819	94.5688
2	80.220	BB	1.8824	636.47284	4.64950	5.4312
Totale :				1.17189e4	87.28769	

Racemic **5e**

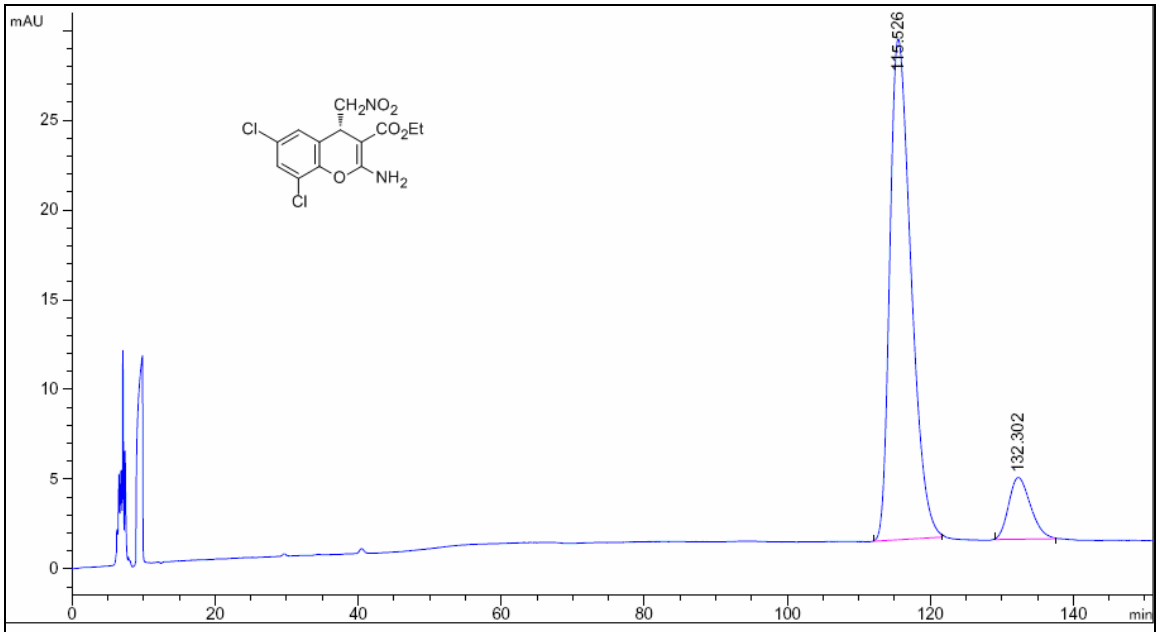


Area Percent Report

15 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	116.884	BB	3.0857	7078.70264	34.76939	50.2055
2	131.280	BB	3.3983	7020.76123	29.02812	49.7945
Totale :				1.40995e4	63.79751	

Enantiomeric enriched **5e**

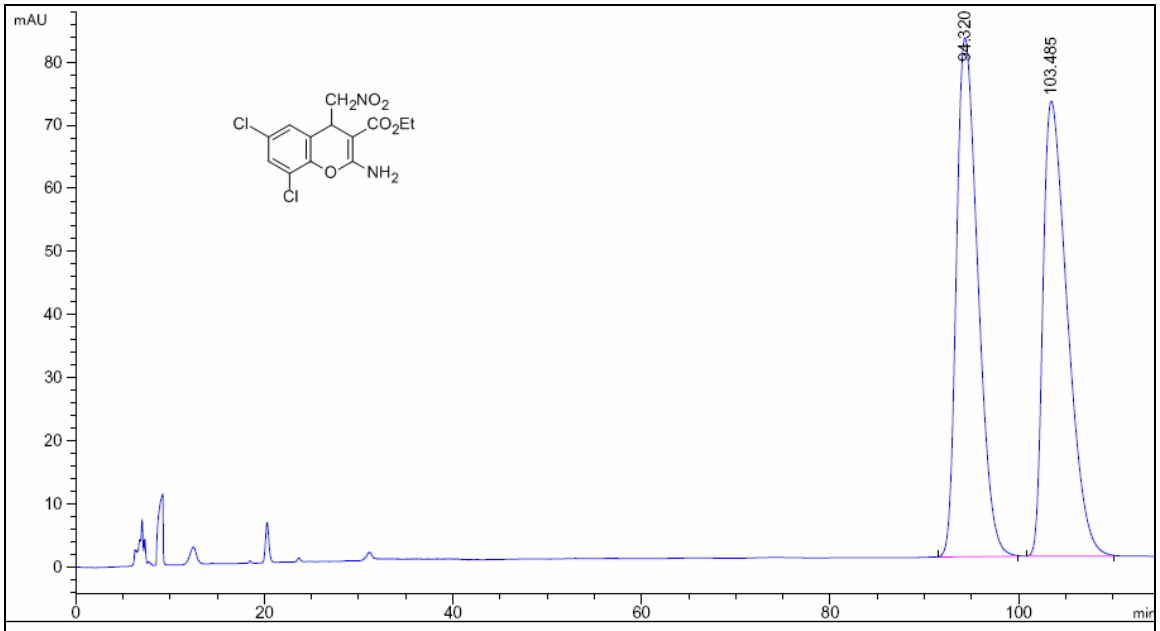


Area Percent Report

15 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	115.526	BB	3.0865	5735.95410	27.89116	88.7035
2	132.302	BB	2.5125	730.48431	3.43975	11.2965
Totale :				6466.43842	31.33091	

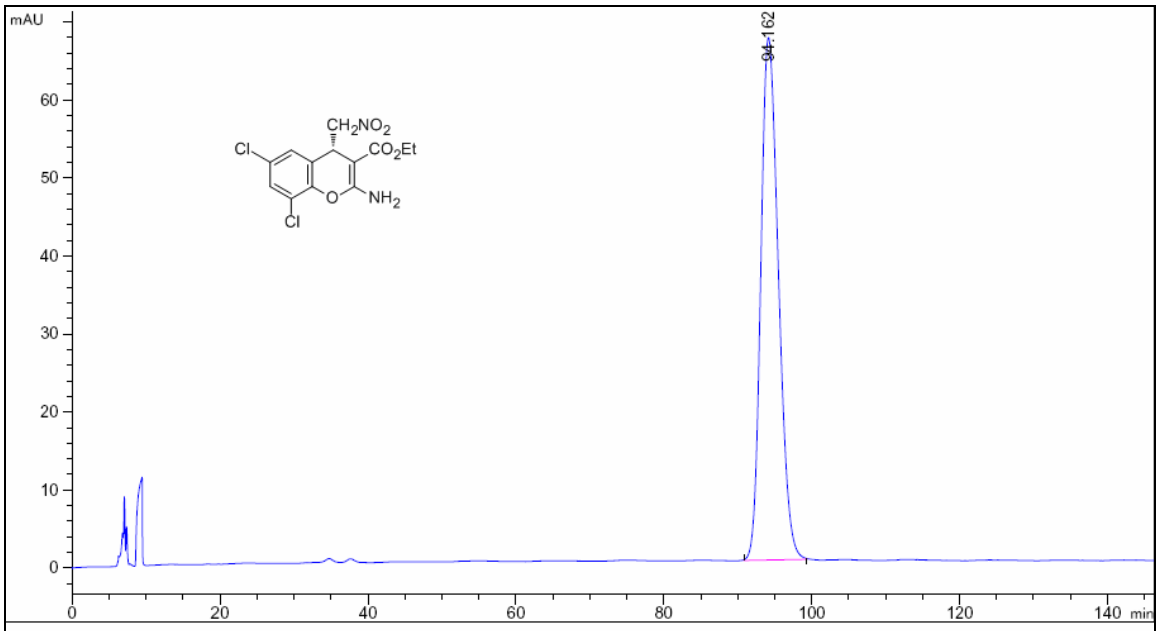
Racemic **5e**



Area Percent Report — 20 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	94.320	BB	2.4637	1.29663e4	82.19175	50.0676
2	103.485	BB	2.7458	1.29313e4	72.06460	49.9324
Totale :				2.58977e4	154.25635	

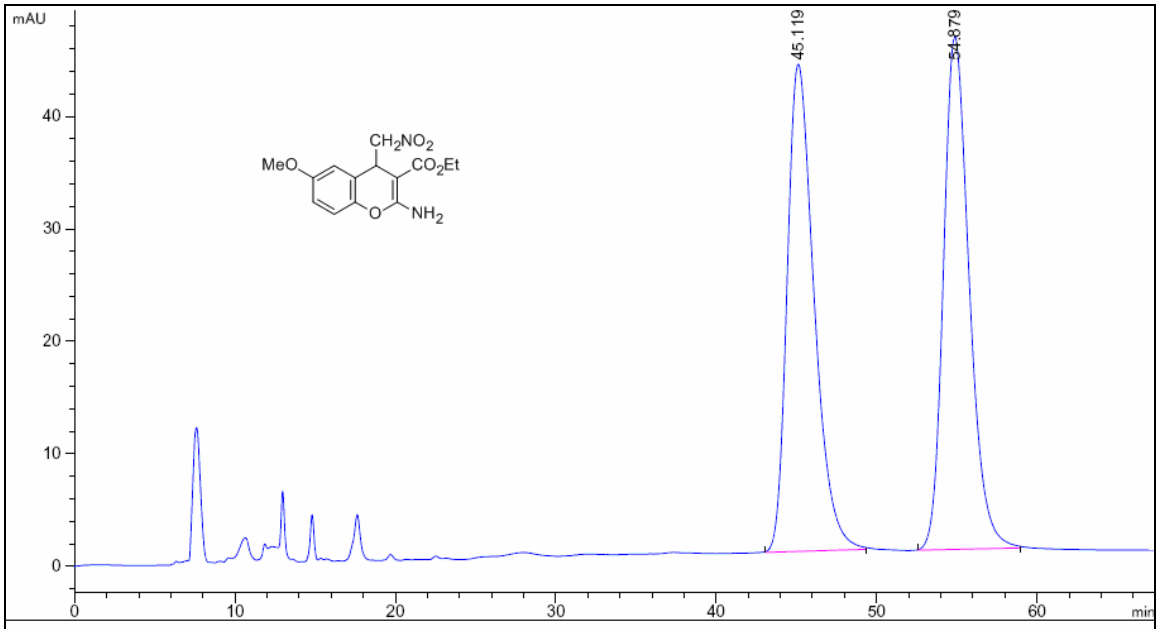
Enantiomeric enriched **5e** (After recrystallization from dichloromethane/n-hexane)



Area Percent Report — 20 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	94.162	BB	2.5666	1.10950e4	67.00609	100.0000
Totale :				1.10950e4	67.00609	

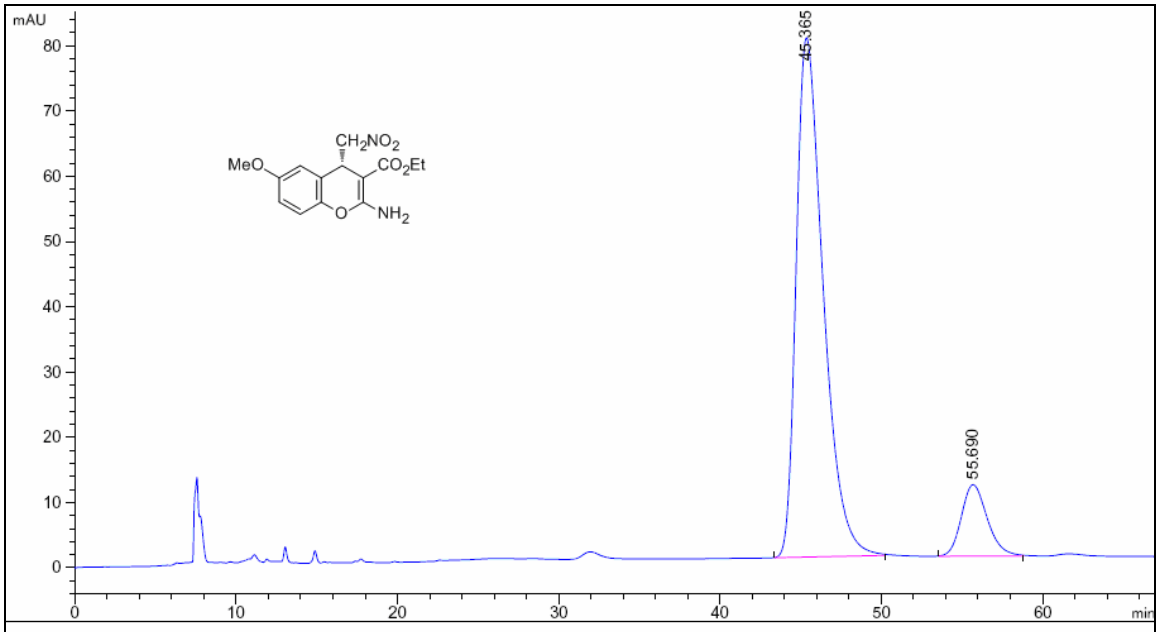
Racemic **5f**



Area Percent Report — 15 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	45.119	BB	1.7780	5044.25977	43.31394	49.8161
2	54.879	BB	1.7140	5081.49805	45.58627	50.1839
Totale :				1.01258e4	88.90021	

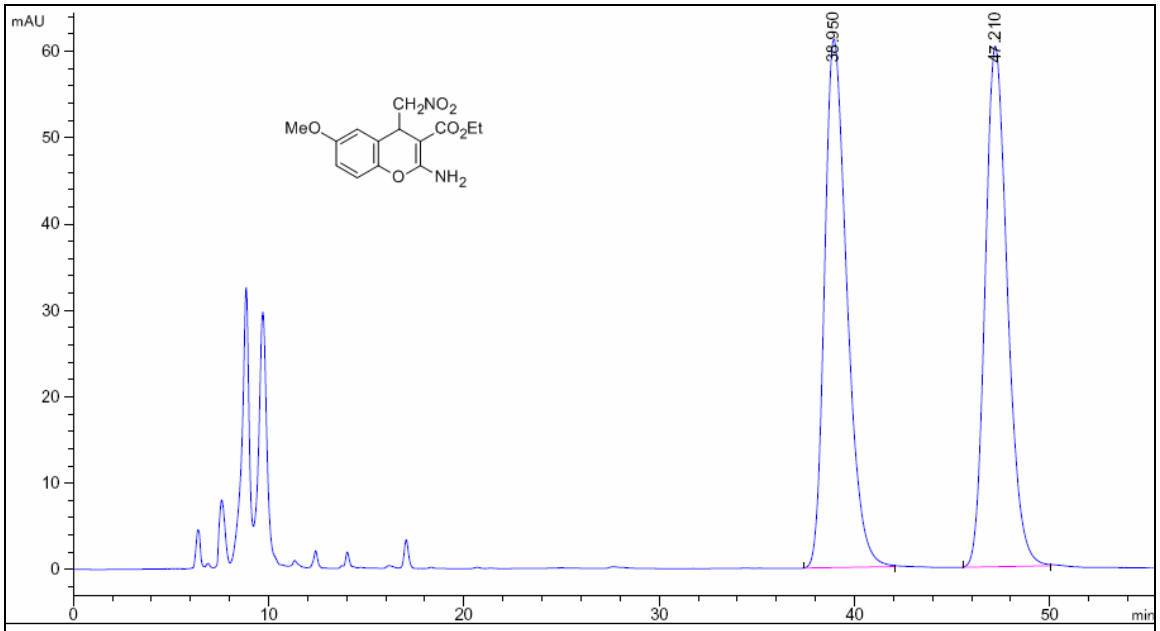
Enantiomeric enriched **5f**



Area Percent Report — 15 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	45.365	BB	1.7720	9267.18359	79.58627	88.3570
2	55.690	BB	1.6801	1221.15662	10.94603	11.6430
Totale :				1.04883e4	90.53230	

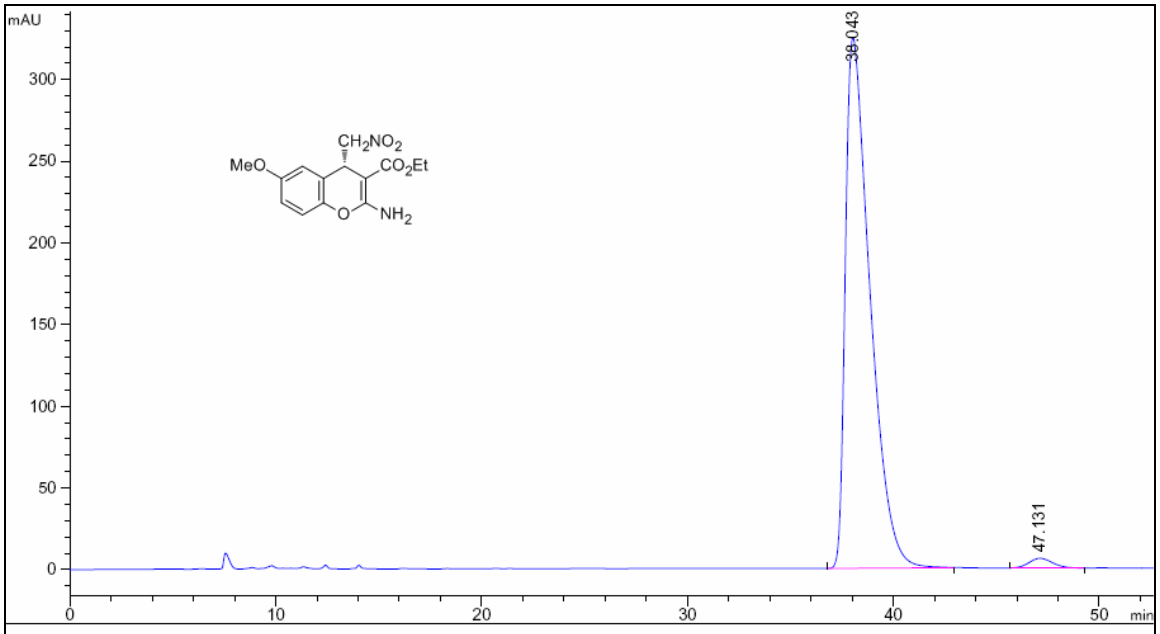
Racemic **5f**



Area Percent Report — 20 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	38.950	BB	1.2255	4870.00977	61.19575	50.4442
2	47.210	BB	1.2289	4784.24219	60.27367	49.5558
Totale :				9654.25195	121.46942	

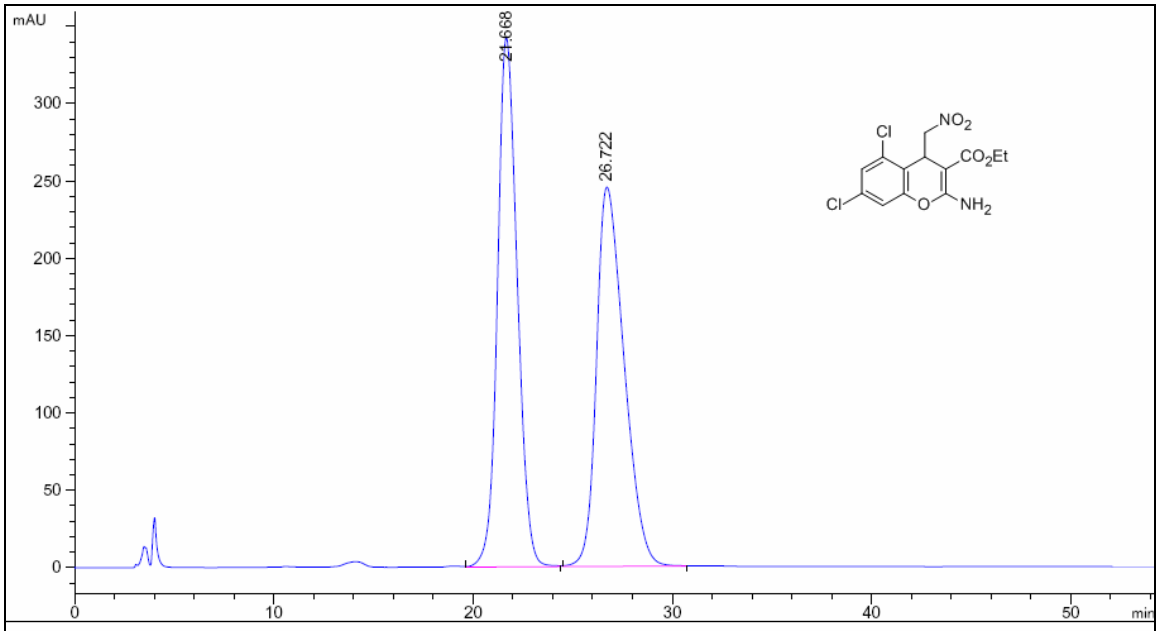
Enantiomeric enriched **5f** (After recrystallization from dichloromethane/n-hexane)



Area Percent Report — 20 °C

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	38.043	BB	1.2501	2.70109e4	324.70013	98.2872
2	47.131	BB	1.1946	470.71582	5.92591	1.7128
Totale :				2.74816e4	330.62605	

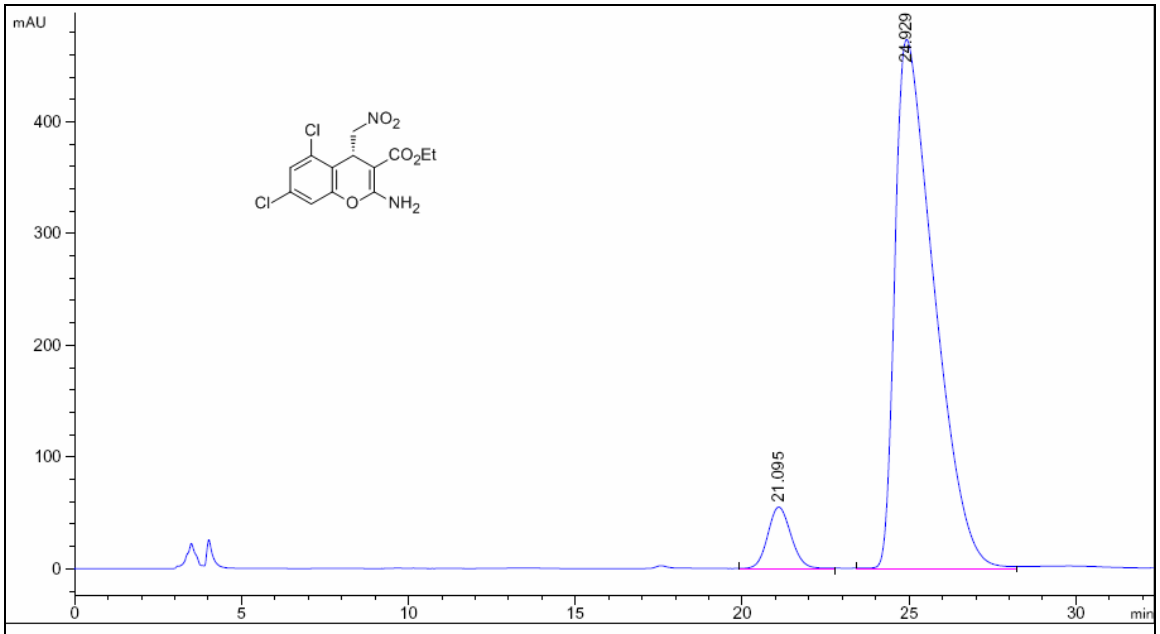
Racemic **5g**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	21.668	VB	1.0678	2.36225e4	342.03036	49.9965
2	26.722	BB	1.4794	2.36258e4	245.18695	50.0035
Totale :				4.72483e4	587.21732	

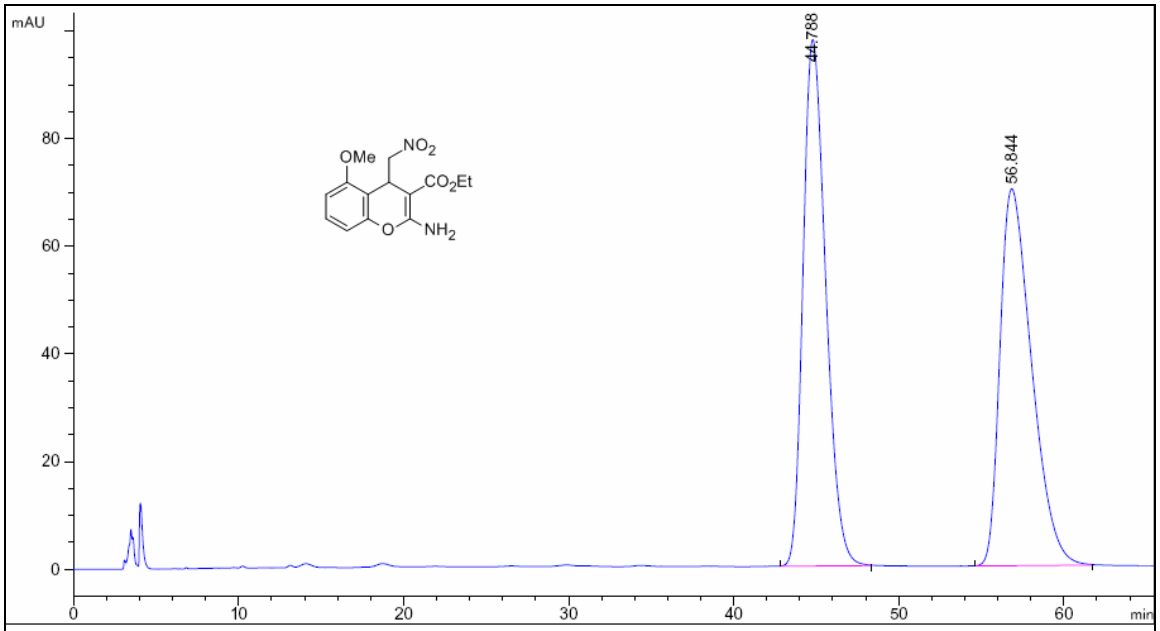
Enantiomeric enriched **5g**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	21.095	BB	0.7502	2654.35327	54.91907	6.4515
2	24.929	BV	1.2344	3.84890e4	473.14310	93.5485
Totale :				4.11434e4	528.06216	

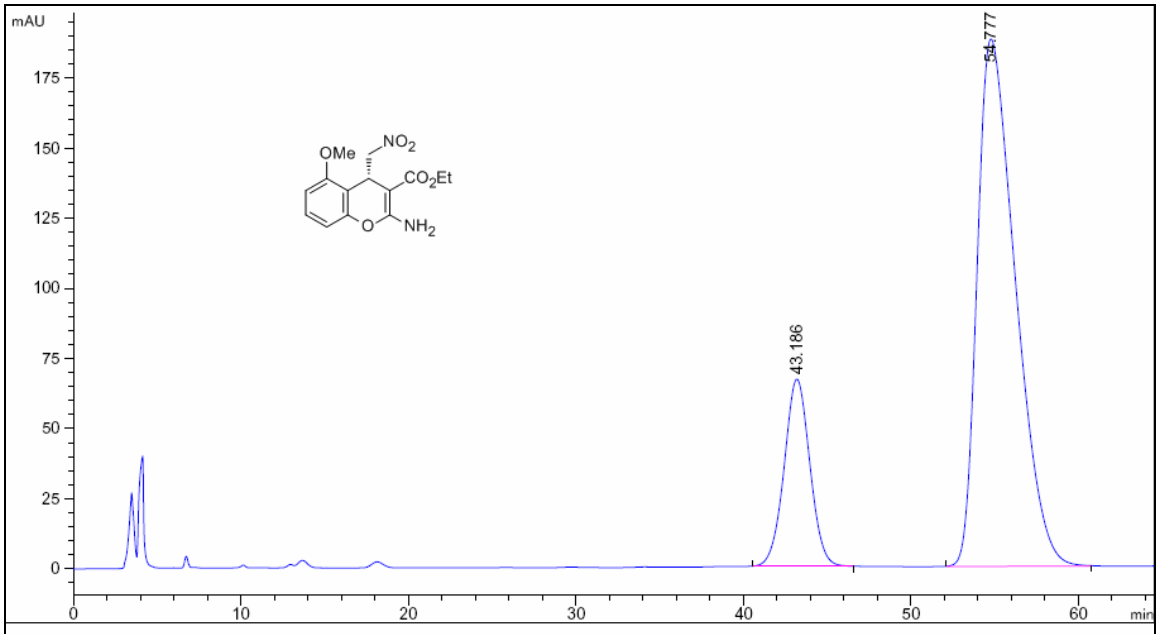
Racemic **5h**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	44.788	BB	1.4865	9333.76465	97.77242	50.0180
2	56.844	BB	2.0144	9327.05664	70.00844	49.9820
Totale :				1.86608e4	167.78085	

Enantiomeric enriched **5h**



Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	High [mAU]	Area %
1	43.186	BB	1.6420	7128.91455	66.74977	19.3185
2	54.777	BB	2.4242	2.97731e4	187.99904	80.6815
Totale :				3.69020e4	254.74881	