SUPPORTING INFORMATION

# Towards an Asymmetric β-Selective Addition of Azlactones to Allenoates

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## Table of Contents

# 1. General Information

$^{1}$H-,$^{13}$C- spectra were recorded on a Bruker Avance III 300 MHz spectrometer with a broad band observe probe. All NMR spectra were referenced on the solvent residual peak ($CDCl_3$: δ 7.26 ppm for $^{1}$H NMR and δ 77.16 ppm for $^{13}$C NMR). NMR data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet), coupling constants (Hz).

High resolution mass spectra were obtained using a Thermo Fisher Scientific LTQ Orbitrap XL with an Ion Max API Source and analyses were made in the positive ionization mode if not otherwise stated.

HPLC was performed using a Shimadzu Prominence system with a diode array detector with a CHIRALPAK AD-H, CHIRAL ART Amylose-SA, (250 × 4.6 mm, 5 μm) chiral stationary phase. Optical rotations were recorded on a Schmidt + Haensch Polarimeter Model UniPol L1000 at 589 nm ([α]D values are listed in deg/(dm(g/cm$^3$)); concentration c is given in g/100 mL).

Unless otherwise stated, all chemicals were purchased from commercial suppliers and used without further purification.

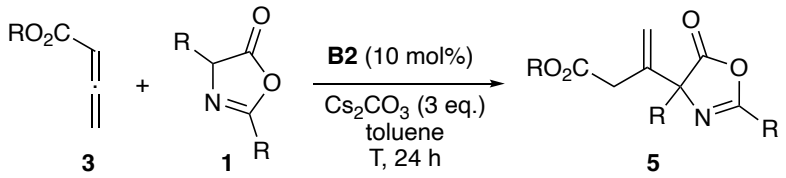
Azlactones[1] and allenoates[2] were synthesized according to known procedures.

Dry solvents were obtained from an MBraun-SPS-800 solvent purification system. All reactions were carried out under argon atmosphere unless stated otherwise.

1) a) Macovei, C.; Vicennati, P.; Quinton, J.; Nevers, M.-C.; Volland, H.; Créminon, C.; Taran, F. *Chem. Commun*. **2012**, *48*, 4411-4413; b) de Mello, A. C.; Momo, P. B.; Burtoloso, A. C. B.; Amarante, G. W. *J. Org. Chem*. **2018**, *83*, 11399-11406; c) Žabka, M.; Kocian, A.; Bilka, S.; Andrejčák, S.; Šebesta, R. *Eur. J. Org. Chem*. **2019**, 6077-6087.
2) Zebrowski, P.; Röser, K.; Chrenko, D.; Pospíšil, J.; Waser, M. *Synthesis* **2023**, *55*, 1706-1713.

## 2. Asymmetric Protocol

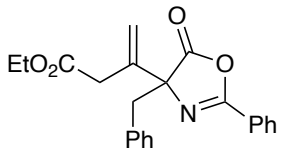
### General Procedure




3 1 5

An oven-dried Schlenk tube equipped with a stirring bar was charged with the azlactone **1** (0.05 – 0.1 mmol), catalyst **B2** (10 mol% related to **1**), and $Cs_2CO_3$ (3 eq.). Then the respective allenoate **3** (2 eq.) and toluene (0.05 M with respect to **1**) were added and the mixture was stirred at room temperature for 24 h (Ar atmosphere). The crude product was passed through a short column of silicagel (rinsed with DCM and EtOAc), concentrated under reduced pressure, and subsequently purified by preparative TLC (silica gel, heptanes/EtOAc = 4/1) to obtain the products **2** in the given yields and enantiopurities.

### Characterization of the Products




**5a**

**Compound 5a:** Obtained as a colorless oil in 61% yield with *e.r.* = 81:19.

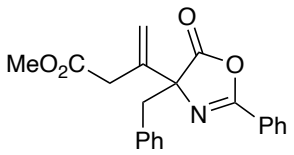
$[\alpha]_D^{22}$ (c = 1.1, $CHCl_3$) = - 11.4°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.85 (2H, dd, *J*=8.6, 1.4 Hz), 7.54 (1H, t, *J*=7.4 Hz), 7.43 (2H, t, J=7.53 Hz), 7.11-7.24 (5H, m), 5.79 (1H, s), 5.37 (1H, s), 3.90-4.14 (2H, m), 3.16-3.52 (4H, m), 1.15 (3H, t, *J*=7.1 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.4, 171.0, 160.3, 139.1, 133.8, 132.6, 130.5, 128.6, 128.0, 127.8, 127.3, 125.6, 118.1, 75.9, 60.9, 44.9, 39.3, 13.9.

HRMS for $C_{22}H_{21}NO_4$ [M+H]+: m/z calcd: 364.1543, found: 364.1554.

HPLC (Chiralpak SA, eluent: n-hexane:*i*-PrOH = 100/2, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 16.15 min , $t_{minor}$ = 17.00 min.




**5b**

**Compound 5b:** Obtained as a colorless oil in 67% yield with e.r =80:20

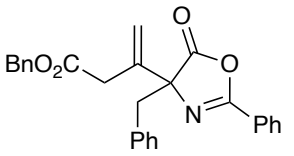
$[\alpha]_D^{22}$ (c = 0.93 $CHCl_3$) -13.8°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.81-7.88 (2H, m), 7.49-7.58 (1H, m), 7.38-7.48 (2H, m), 7.13-7.23 (5H, m), 5.78 (1H, s), 5.36 (1H, s), 3.56 (3H, s), 3.20-3.48 (4H, m).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.4, 171.4, 160.3 138.9, 133.7, 132.6, 130.4, 128.6, 128.0, 127.8, 127.3, 125.5, 118.2, 75.9, 51.9, 44.8, 39.1.

HRMS for $C_{21}H_{19}NO_4$[M+H]+: m/z calcd: 350.1387, found: 350.1377.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/1, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 52.66 min, $t_{minor}$= 56.59 min.




**5c**

**Compound 5c:** Obtained as a colorless oil in 47% yield with *e.r* =82:18

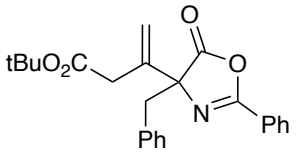
$[\alpha]_D^{22}$ (c = 1.05 $CHCl_3$) -21.4°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.76-7.83 (2H, m), 7.49-7.57 (1H, m), 7.35-7.45 (2H, m), 7.23-7.35 (5H, m), 7.12-7.21(5H, m), 5.79 (1H, s), 5.37 (1H, s), 5.01 (1H, d, *J*=0.57 Hz), 3.26-3.51 (4H, m).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.4, 170.9, 160.3, 138.9, 135.5, 133.7, 132.6, 130.4, 128.6, 128.5, 128.5, 128.3, 128.0, 127.8, 127.3, 125.5, 118.3, 75.9, 66.6, 44.9, 39.2.

HRMS for $C_{27}H_{23}NO_4$ [M+H]+: m/z calcd: 426.1700, found: 426.1690.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 37.04 min, $t_{minor}$ = 41.42 min.




**5d**

**Compound 5d:** Obtained as a colorless oil in 56% yield with *e.r.* = 67:33.

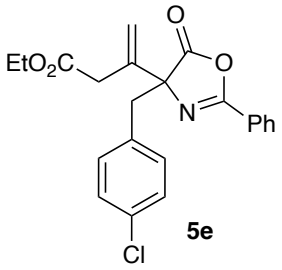
$[\alpha]_D^{22}$ (c = 1.1, $CHCl_3$) + 7.9°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.82-7.88 (2H, m), 7.49-7.56 (1H, m), 7.38-7.46 (2H), 7.10-7.24 (5H, m), 5.76 (1H, s), 5.34 (1H, s), 3.14-3.42 (4H, m), 1.35 (9H, s).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.5, 170.3, 160.1, 139.5, 132.5, 130.4, 128.5, 128.0, 127.2, 125.7, 117.8, 81.0, 76.0, 44.9, 40.3, 27.8.

HRMS for $C_{24}H_{25}NO_4$ [M+H]+: m/z calcd: 392.1856, found: 392.1860.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 13.73 min, $t_{minor}$ = 14.74 min.




**5e**

**Compound 5e:** Obtained as a yellow oil in 65% yield with *e.r* = 77:23

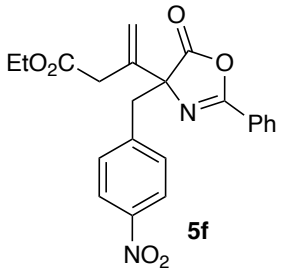
$[\alpha]_D^{22}$ (c = 0.97 $CHCl_3$) -20.1°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 8.06 (2H, d, *J*=8.76 Hz), 7.82-7.90 (1H, m), 7.52-7.60 (2H, m), 7.35-7.50 (4H, m), 5.79 (1H, s), 5.37 (1H, s), 5.01 (1H, d, *J*=0.57 Hz), 3.98-4.22 (2H, m), 3.26-3.51 (4H, m), 1.15 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.2, 170.9, 160.5, 138.9, 133.3, 132.8, 132.3, 131.7, 128.7, 128.2, 127.8, 125.4, 118.3, 75.6, 61.0, 44.1, 39.3, 13.9.

HRMS for $C_{22}H_{20}ClNO_4$ [M+H]+: m/z calcd: 398.1154, found: 398.1149.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 150/1, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{minor}$= 39.63 min, $t_{major}$ = 41.52 min.




**5f**

**Compound 5f:** Obtained as a yellow oil in 49% yield with *e.r* = 79:21

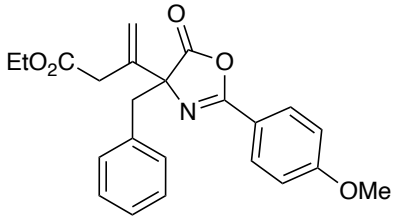
$[\alpha]_D^{22}$ (c = 0.98 $CHCl_3$) -13.7°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 8.06 (2H, d, J=8.76 Hz), 7.82-7.90 (2H, m), 7.53-7.61 (1H, m), 7.35-7.50 (4H, m), 5.78 (1H, s), 5.39 (1H, s), 3.93-4.09 (2H, m), 3.18-3.56 (4H, m), 1.15 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 176.9, 170.8, 160.8, 147.3, 141.5, 138.6, 133.1, 131.4, 128.8, 127.8, 125.0, 123.2, 118.7, 75.2, 61.0, 44.3, 39.2, 13.9.

HRMS for $C_{22}H_{20}N_2O_6$[M+H]+: m/z calcd: 409.1394, found: 409.1398.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{minor}$= 52.67 min, $t_{major}$ = 55.12 min.




**5g**

**Compound 5g:** Obtained as a colorless oil in 51% yield with *e.r.* = 82:18.

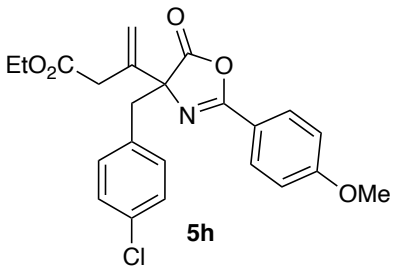
$[\alpha]_D^{22}$ (c = 1.00 $CHCl_3$) = - 36.9°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.79 (2H, d, *J*=8.9 Hz), 7.13-7.22 (5H, m), 6.92 (2H, d, *J*=8.9 Hz), 5.77 (1H, s), 5.35 (1H, s), 4.01 (2H, m), 3.86 (3H, s), 3.18-3.45 (4H, m), 1.15 (3H, t, *J*=7.1 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.6, 171.0, 163.0, 159.9, 139.3, 133.9, 130.4, 129.7, 128.0, 127.2, 117.9, 117.9, 114.0, 75.8, 60.8, 55.4, 44.9, 39.4, 13.9.

HRMS for $C_{23}H_{23}NO_5$ [M+H]+: m/z calcd: 394.1649, found: 394.1665.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 38.93 min,$t_{minor}$ = 48.14 min.




**5h**

**Compound 5h:** Obtained as a colorless oil in 80% yield with *e.r.* = 81:19.

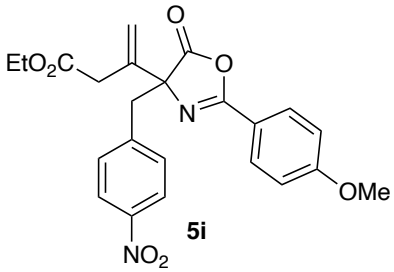
$[\alpha]_D^{22}$ (c = 0.90, $CHCl_3$) = - 73°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.81 (2H, d, J=8.9 Hz), 7.09-7.19 (4H, m), 6.94 (2H, d, J=8.9 Hz), 5.35 (1H, s), 5.75 (1H, s), 3.91-4.10 (2H, m), 3.87 (3H, s), 3.15-3.44 (4H, m), 1.16 (3H, t, J=7.1 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.4, 170.9, 163.2, 160.2, 139.2, 133.2, 132.5, 131.8, 129.7, 128.2, 118.1, 117.7, 114.1, 75.5, 60.9, 55.4, 44.1, 39.3, 13.9.

HRMS for $C_{23}H_{22}ClNO_5$ [M+H]+: m/z calcd: 428.1259, found: 428.1275.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 40.07 min, $t_{minor}$ = 42.30 min.




**5i**

**Compound 5i:** obtained as a pale-yellow oil in 80% yield with e.r. = 78:22.

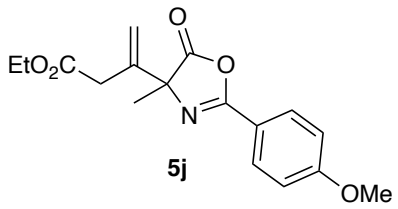
$[\alpha]_D^{22}$ (c = 1.1, $CHCl_3$) = -22°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 8.06 (2H, d, *J*=8.76 Hz), 7.80 (2H, d, *J*=8.97 Hz), 7.39 (2H, d, *J*=8.76 Hz), 6.93 (2H, d, *J*=8.97 Hz), 5.77 (1H, s), 5.38 (1H, s), 3.95-4.07 (2H, m), 3.88 (3H, s), 3.18-3.52 (4H, m), 1.16 (3H, t, *J*=7.1 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.1, 170.8, 163.4, 160.5, 147.2, 141.7, 138.9, 131.4, 129.7, 123.1, 118.5, 117.3, 114.2, 75.1, 61.0, 55.4, 44.3, 39.3, 13.9.

HRMS for $C_{23}H_{22}N_2O_7$ [M+H]+: m/z calcd: 439.1500., found: 439.1496.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.8 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 55.99 min, $t_{minor}$ = 59.93 min.




**5j**

**Compound 5j:** Obtained as a colorless oil in 67% yield with *e.r.* = 78:22.

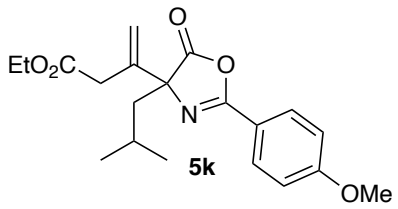
$[\alpha]_D^{22}$ (c = 0.97, $CHCl_3$) +19.7°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.96 (2H, d, *J*=8.9 Hz), 7.01 (2H, d, *J*=9.0 Hz), 5.60 (1H, s), 5.29 (1H, s), 3.97-4.10 (2H, m), 3.90 (3H, s), 3.37 (1H, dd, *J*=16.2, 0.9 Hz), 3.17 (1H, dd, *J*=16.2, 0.8 Hz), 1.17 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.7, 170.9, 163.3, 160.3, 139.9, 129.9, 118.0, 117.5, 114.2, 71.0, 60.9, 55.5, 38.8, 25.2, 13.9.

HRMS for $C_{17}H_{19}NO_5$ [M+H]+: m/z calcd: 288.1230, found: 288.1238.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 31.90 min, $t_{minor}$= 45.37 min.




**5k**

**Compound 5k:** Obtained as a colorless oil in 46% yield with e.r = 83:17

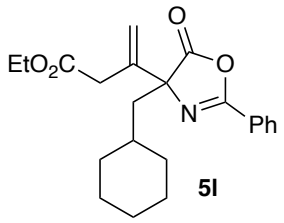
$[\alpha]_D^{22}$ (c = 0.91 $CHCl_3$) +5.4°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.95 (2H, d, *J*=8.9 Hz), 6.97 (2H, d, *J*=8.9 Hz), 5.57 (1H, s), 5.21 (1H, s), 3.90-4.09 (2H, m), 3.87 (3H, s), 3.35 (1H, d, *J*= 16.4 Hz), 3.16 (1H, d, *J*= 16.2 Hz), 2.08 (1H, dd, *J*= 13.8, 5.1 Hz), 1.83 (1H, dd, *J*= 13.8, 7.4 Hz), 1.58-1.73 (1H, m), 1.13 (3H, t, *J*=7.1 Hz), 0.82-0.91 (6H, m).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.9, 171.0, 163.2, 159.8, 140.1, 129.8, 118.2, 117.1, 114.1, 74.4, 60.8, 55.5, 47.3, 39.0, 24.9, 24.2, 23.0, 13.9.

HRMS for $C_{20}H_{25}NO_5$ [M+H]+: m/z calcd: 360.1805, found: 360.1806.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 23.55 min, $t_{minor}$= 31.88 min.




**5l**

**Compound 5l:** Obtained as a colorless oil 65% yield with e.r = 81:19

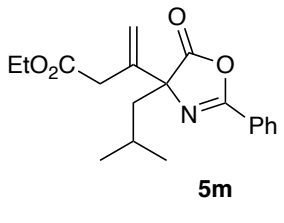
$[\alpha]_D^{22}$ (c = 0.94 $CHCl_3$) +6.9°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.89-7.98 (2H, m), 7.47-7.54 (1H, m), 7.37-7.46 (2H, m), 5.51 (1H, s), 5.16 (1H, s), 3.81-4.01 (2H, m), 2.96-3.35 (2H, m), 1.99 (1H, dd, *J*=14.2, 4.8 Hz), 1.76 (1H, dd, *J*=7.0, 14 Hz), 1.38-1.71 (13H, m), 1.05 (1H, t, *J*= 7.1 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.7, 171.0, 160.1, 139.7, 132.7, 128.7, 127.9, 125.9, 117.3, 74.4, 60.8, 46.0, 39.0, 34.6, 34.1, 33.6, 26.1, 26.1, 26.0, 13.9.

HRMS for $C_{23}H_{27}NO_4$ [M+H]+: m/z calcd: 370.2013, found: 370.2014.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· $min^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{minor}$ = 13.73 min, $t_{major}$ = 15.60 min.




**5m**

**Compound 5m:** Obtained as a colorless oil in 70% yield with *e.r.* =79:21.

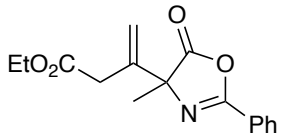
$[\alpha]_D^{22}$ (c = 0.95, $CHCl_3$) + 19.7°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): (2H, m), 7.56-764 (1H, m), 7.46-7.55 (2H, m), 5.62 (1H, s), 5.26 (1H, s), 3.90-4.06 (2H, m), 3.38 (1H, dd, *J*=16.4, 0.9 Hz), 3.20 (1H, d, *J*=16.3 ), 2.13 (1H, dd, *J*= 13.9, 5.0 Hz), 1.87 (1H, dd, J= 13.9, 7.4 Hz), 1.61-1.77 (1H, m), 1.15 (3H, t, *J*=7.14 Hz), 0.81-0.94 (6H, m).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.7, 170.9, 160.1, 139.8, 132.7, 128.7, 128.4, 127.9, 117.3, 74.5, 60.8, 47.3, 38.9, 24.9, 24.2, 22.5.

HRMS for $C_{19}H_{23}NO_4$ [M+H]+: m/z calcd: 330.1700, found: 330.1707.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 12.38 min, $t_{minor}$ = 14.14 min.




**5n**

**Compound 5n:** Obtained as a colorless oil in 71% yield with *e.r.* = 75:25.

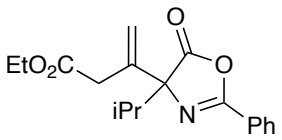
$[\alpha]_D^{22}$ (c = 0.98, $CHCl_3$) +19.7°.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.93 (2H, dd, *J*= 8.6, 1.4 Hz), 7.51 (1H, t, *J*=7.5 Hz), 7.42 (2H, t, *J*=7.4 Hz), 5.52 (1H, s), 5.21 (1H, s), 3.86-4.04 (2H, m), 3.09 (1H, d, *J*=16.3 Hz), 3.29 (1H, d, *J*= 16.3 Hz), 1.61 (3H, s), 1.07 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.55, 170.90, 160.62, 139.65, 132.86, 129.20, 128.78, 128.50, 127.99, 119.06, 117.67, 71.17, 60.94, 38.84, 25.18, 13.95.

HRMS for $C_{16}H_{17}NO_4$ [M+H]+: m/z calcd: 288.1230, found: 288.1238.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL·min-1, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 16.47 min, $t_{minor}$ = 19.96 min.




**5o**

**Compound 5o:** Obtained as a colorless oil in 81% yield with e.r = 75:25

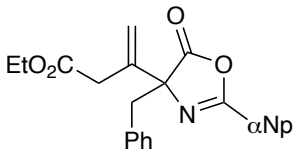
$[\alpha]_D^{22}$ (c = 0.97 $CHCl_3$) +25.7.

$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.99-8.08 (2H, m), 7.55-7.63 (1H, m), 7.45-7.50 (2H, m), 5.64 (1H, s), 5.31 (1H, s), 3.87-4.03 (2H, m), 3.38 (1H, dd, *J*=16.3, 1.0 Hz), 3.22 (1H, dd, *J*=16.3, 0.6 Hz), 2.50-2.45 (1H, m), 1.14 (3H, t, *J*=7.1 Hz), 1.07 (3H, d, *J*=6.7 Hz), 0.89 (3H, d, *J*=6.7 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 178.3, 171.0, 160.5, 138.9, 132.7, 128.7, 128.0, 125.8, 117.7, 78.3, 60.8, 39.3, 36.5, 16.7, 16.7, 13.9.

HRMS for $C_{18}H_{21}NO_4$ [M+H]+: m/z calcd: 316.1543, found: 316.1558.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 12.21 min, $t_{minor}$= 16.53 min.




**5p**

**Compound 5p:** Obtained as a colorless oil 91% yield with e.r = 73:27

$[\alpha]_D^{22}$ (c = 1.00 $CHCl_3$) -35.2°.

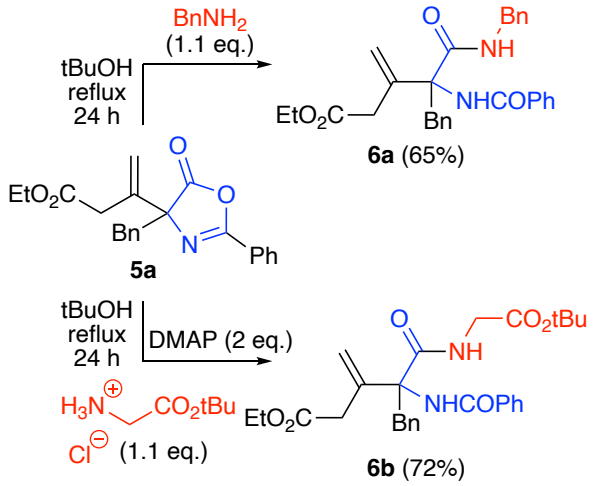
$^1$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 8.19 (1H, s), 7.89 (1H, dd, *J*=8.6, 1.6 Hz), 7.75-7.83 (3H, m), 7.40-7.51 (2H, m), 7.00-7.16 (5H, m), 5.73 (1H, s), 5.30 (1H, s), 3.81-4.00 (2H, m), 3.11-3.43 (4H, m), 1.05 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 177.4, 171.0, 160.4, 139.2, 135.3, 133.8, 132.4, 130.4, 129.2, 129.1, 128.6, 128.3, 128.1, 127.9, 127.3, 126.9, 123.4, 122.8, 118.1, 76.1, 60.9, 45.0, 39.4, 13.9.

HRMS for $C_{26}H_{23}NO_4$ [M+H]+: m/z calcd: 414.1700, found: 414.1712.

HPLC (Chiralpak AD-H, eluent: n-hexane:*i*-PrOH = 100/3, 0.5 mL· min$^{-1}$, 20 °C, λ = 254 nm) retention times: $t_{major}$ = 30.22 min, $t_{minor}$= 33.44 min.

## 3. Ring Opening Reactions




**Compound 6a:**

In a flame-dried Schlenk tube under Ar atmosphere at room temperature, 0.08 mmol of compound **5a** in 0.5 mL tert-butyl alcohol and 0.09 mmol of benzylamine (1.1 equivalent), were added. This mixture was refluxed for 24 hours in a preheated oil bath. After cooling to room temperature and evaporation of solvent under vacuum, the crude reaction mixture was purified through PTLC silica gel chromatography, using 33% ethyl acetate in heptane as eluent, yielding 65 % of the pure product (0.024 g).

$^{1}$H NMR (300 MHz, δ, $CDCl_3$, 298 K): 7.96 (1H, s), 7.66-7.78 (3H, m), 7.46-7.54 (1H, m), 7.30-7.45 (7H, m), 7.06-7.22 (3H, m), 6.87-6.94 (2H, m), 5.54 (1H, s), 5.43 (1H, s), 4.42-4.60 (2H, m), 4.16 (2H, q, *J*=7.1 Hz), 4.03 (1H, d, *J*=12.9 Hz), 3.71 (1H, d, *J*= 17.3 Hz), 3.27 (1H, d, *J*=17.4 Hz), 3.13 (1H, d, *J*=12.9 Hz), 1.27 (3H, t, *J*=7.14 Hz).

$^{13}$C NMR (75 MHz, δ, $CDCl_3$, 298 K): 173.4, 171.3, 165.9, 143.5, 137.7, 135.3, 134.6, 131.5, 130.0, 128.7, 128.5, 128.1, 128.0, 127.6, 127.0, 126.9, 119.6, 65.9, 61.3, 44.3, 39.1, 38.4, 14.1.

HRMS for $C_{29}H_{30}N_2O_4$ [M+H]+: m/z calcd. 471.2278, found: 471.2283.

**Compound 6b:**

In a flame-dried Schlenk tube under argon atmosphere 0.08 mmol of compound **5a** in 0.5 mL tert-butyl alcohol were combined with 0.16 mmol DMAP (2 eq) and 0.09 mmol of glycine t-butyl ester hydrochloride (1.1 equivalent). This mixture was refluxed for 24 hours in a preheated oil bath. After cooling to room temperature and evaporation of solvent under vacuum, the crude reaction mixture was

purified through PTLC silica gel chromatography using 33% ethyl acetate in heptane as eluent, yielding 72 % of the pure product (0.028 g).

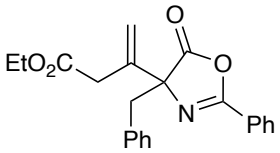
1H NMR (300 MHz, δ, CDCl3, 298 K): 7.80 (1H, s), 7.65-7.74 (2H, m), 7.45-7.57 (2H, m), 7.36-7.45 (2H), 7.12-7.23 (3H, m), 7.03-7.11 (2H, m), 5.66 (1H, s), 5.52 (1H, s), 3.88-4.20 (5H, m), 3.60 (1H, d, *J*=17.0 Hz), 3.20-3.31 (2H, m), 1.53 (9H, s), 1.25 (3H, t, *J*=7.1 Hz).

13C NMR (75 MHz, δ, CDCl3, 298 K): 172.9, 171.2, 168.3, 166.0, 143.0, 135.4, 134.6, 131.5, 130.1, 128.5, 128.0, 127.0, 119.6, 82.4, 66.2, 61.2, 42.5, 39.1, 38.6, 28.0, 14.0. HRMS for $C_{28}H_{34}N_2O_6$ [M+H]+: m/z calcd. 495.2489, found: 495.248.

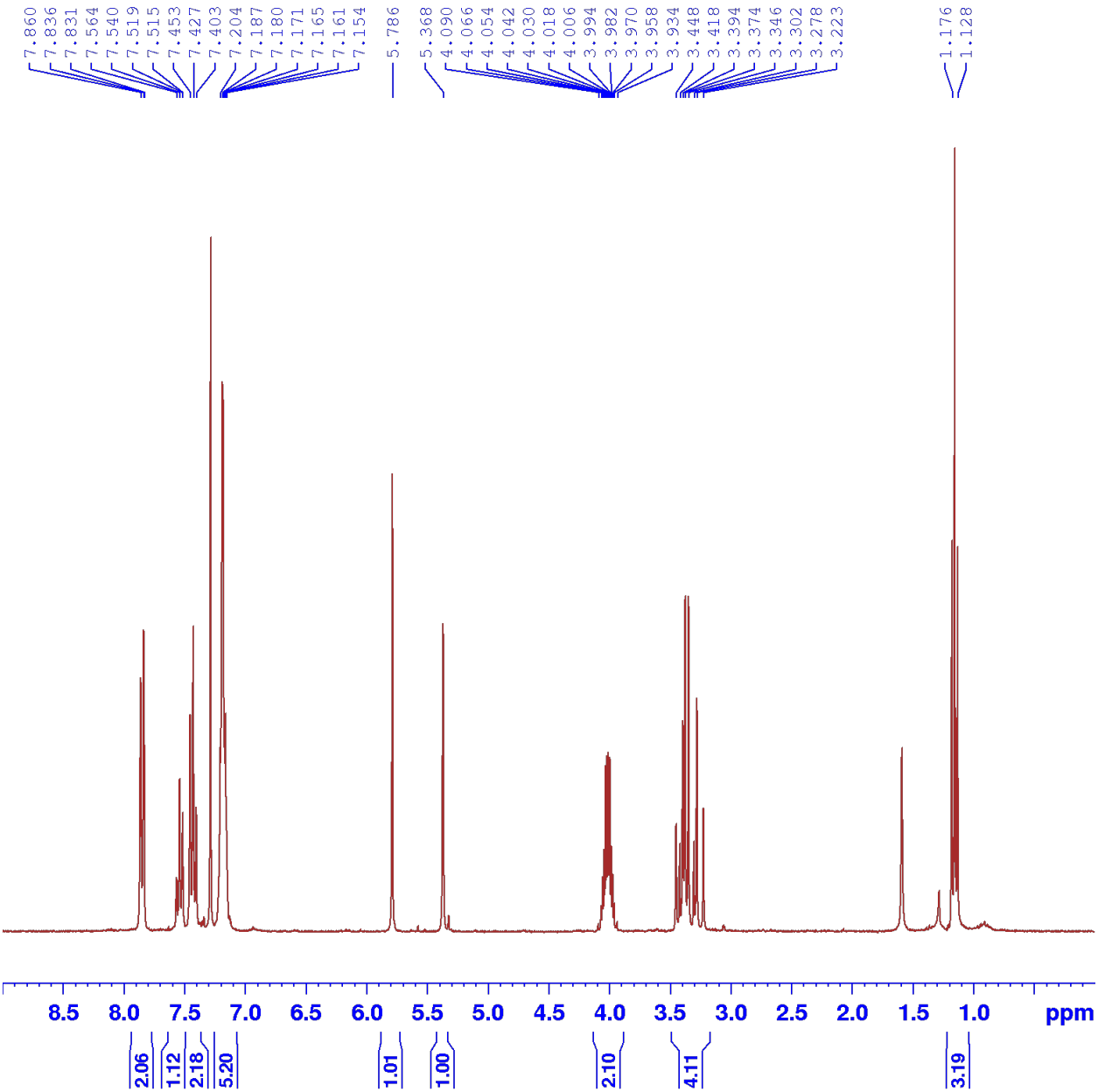
# 4. NMR Spectra

## NMR spectra of compound 5a

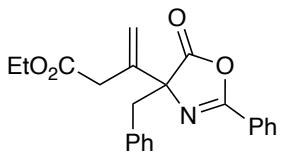
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



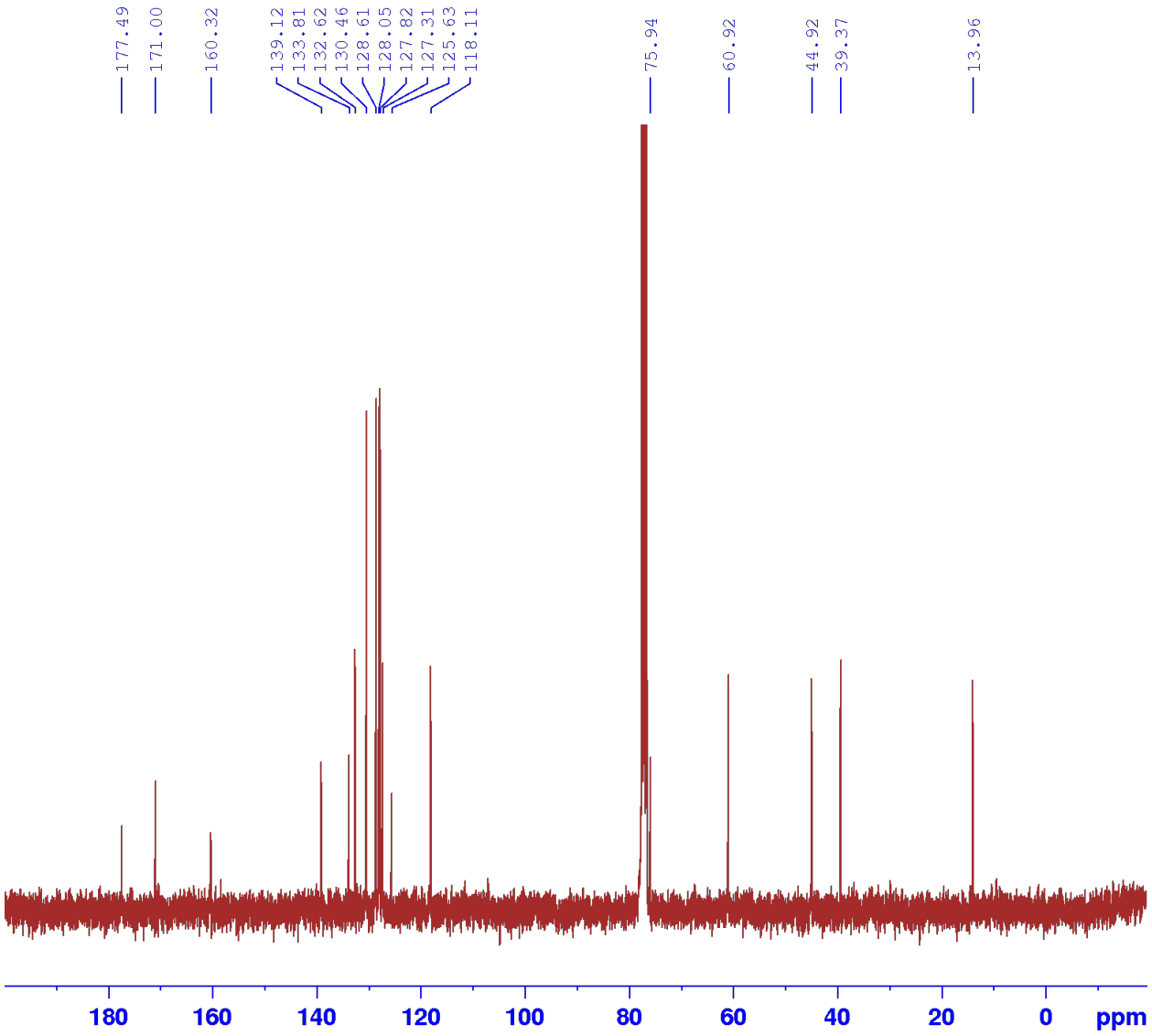

**5a**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

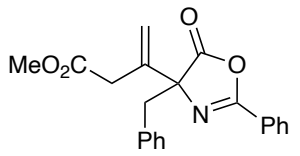



**5a**

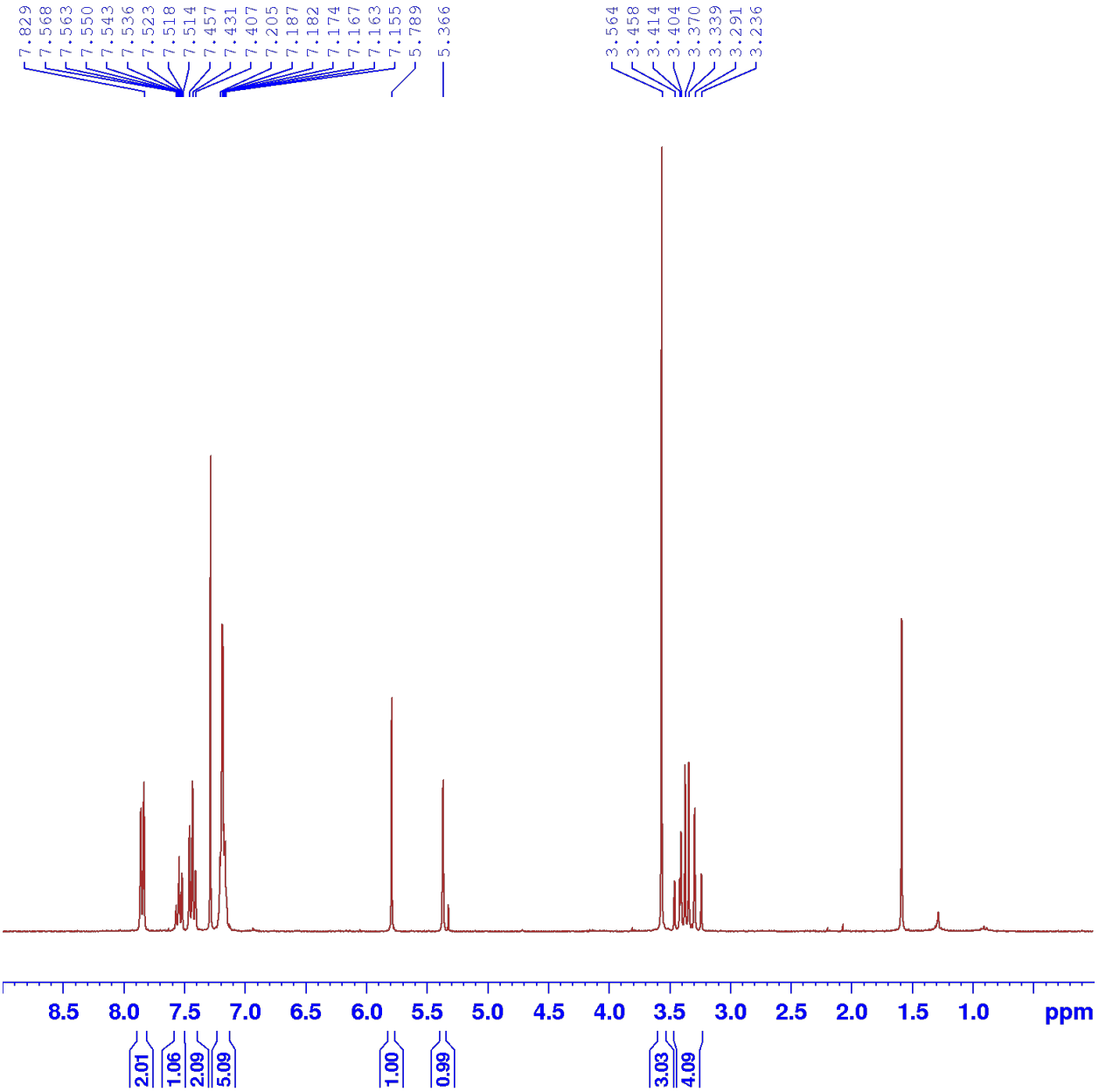


## NMR spectra of compound 5b

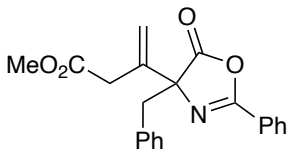
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



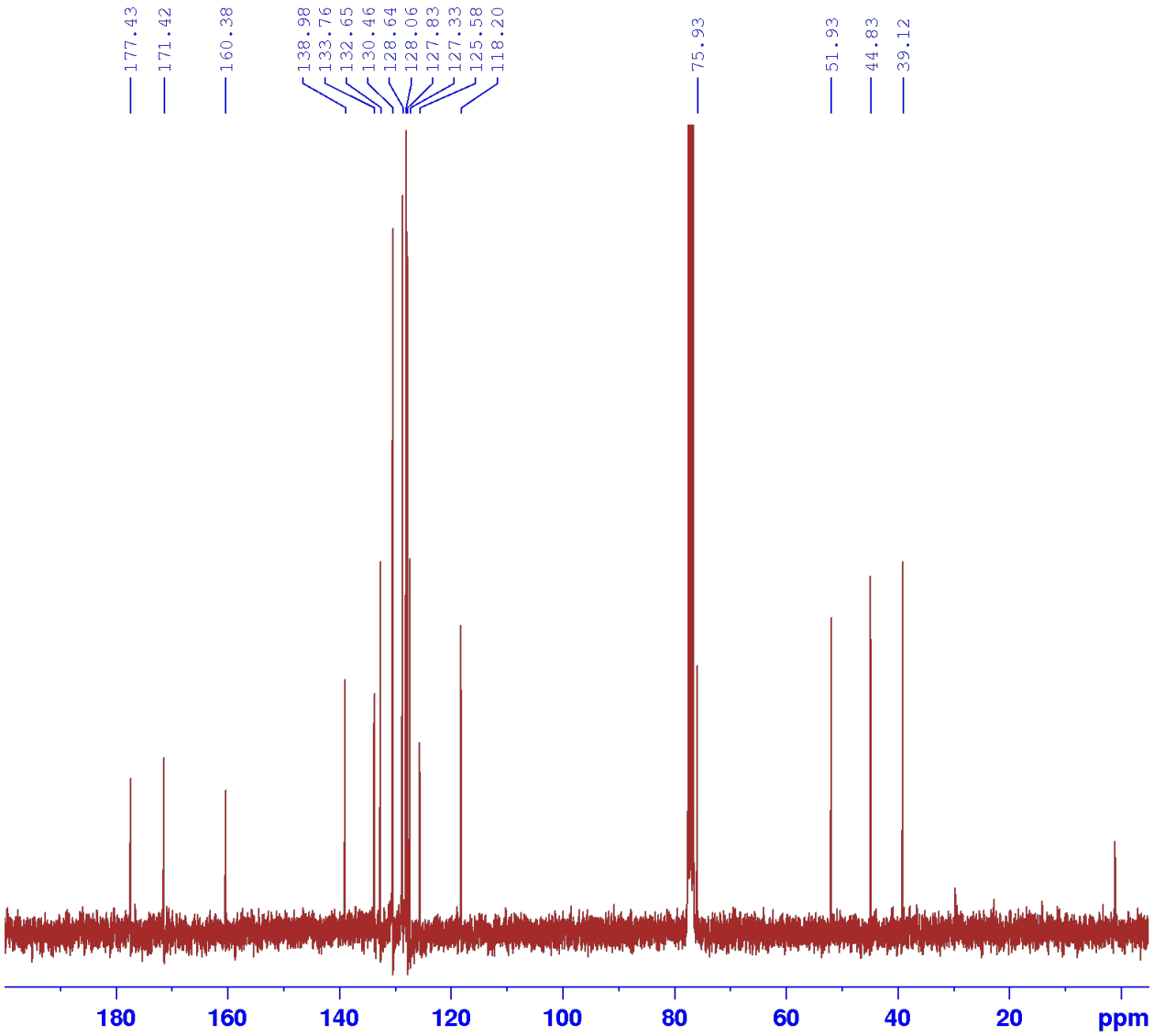

**5b**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

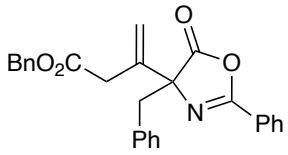



**5b**

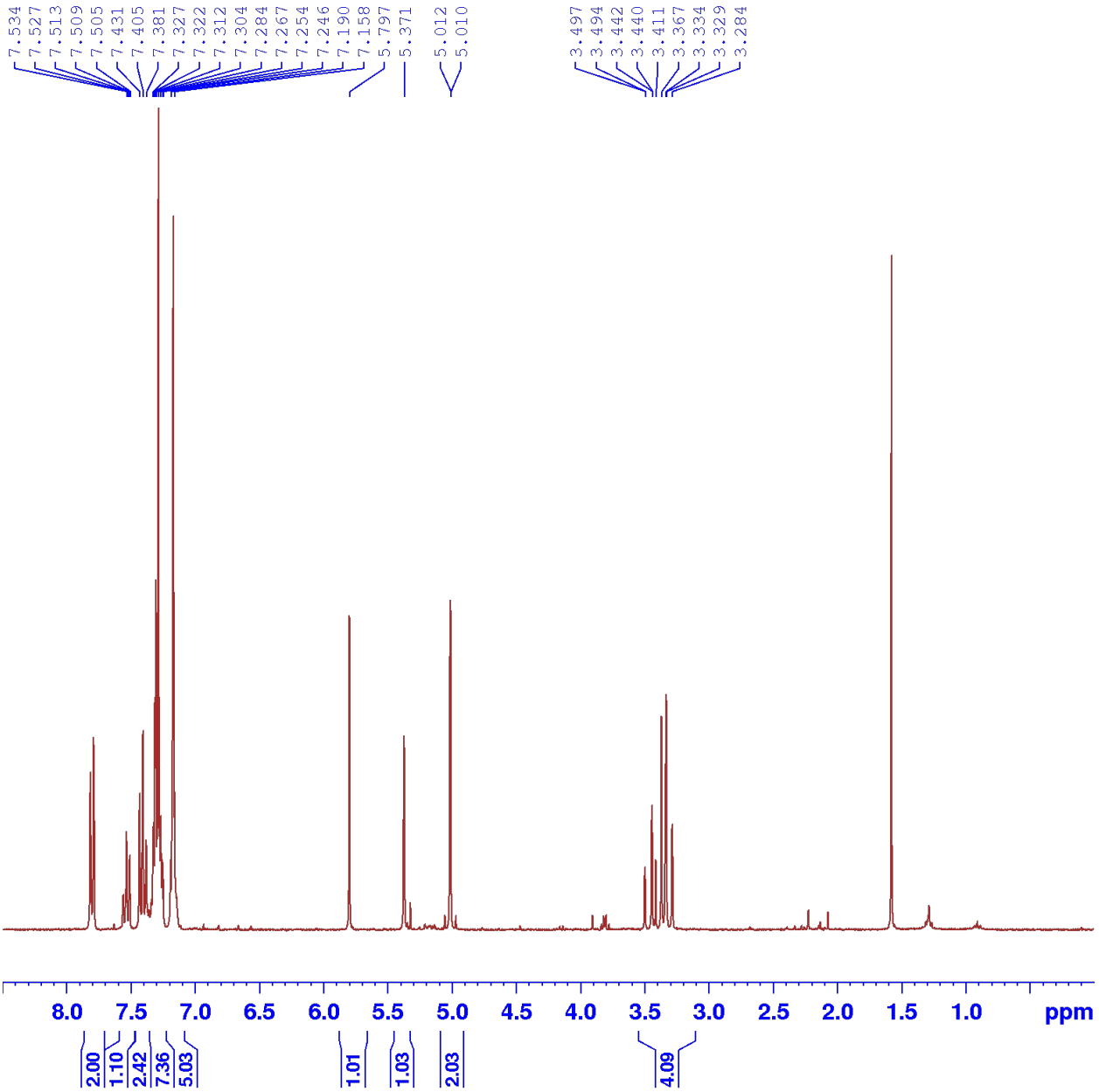


## NMR spectra of compound 5c

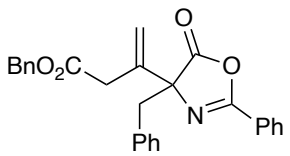
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



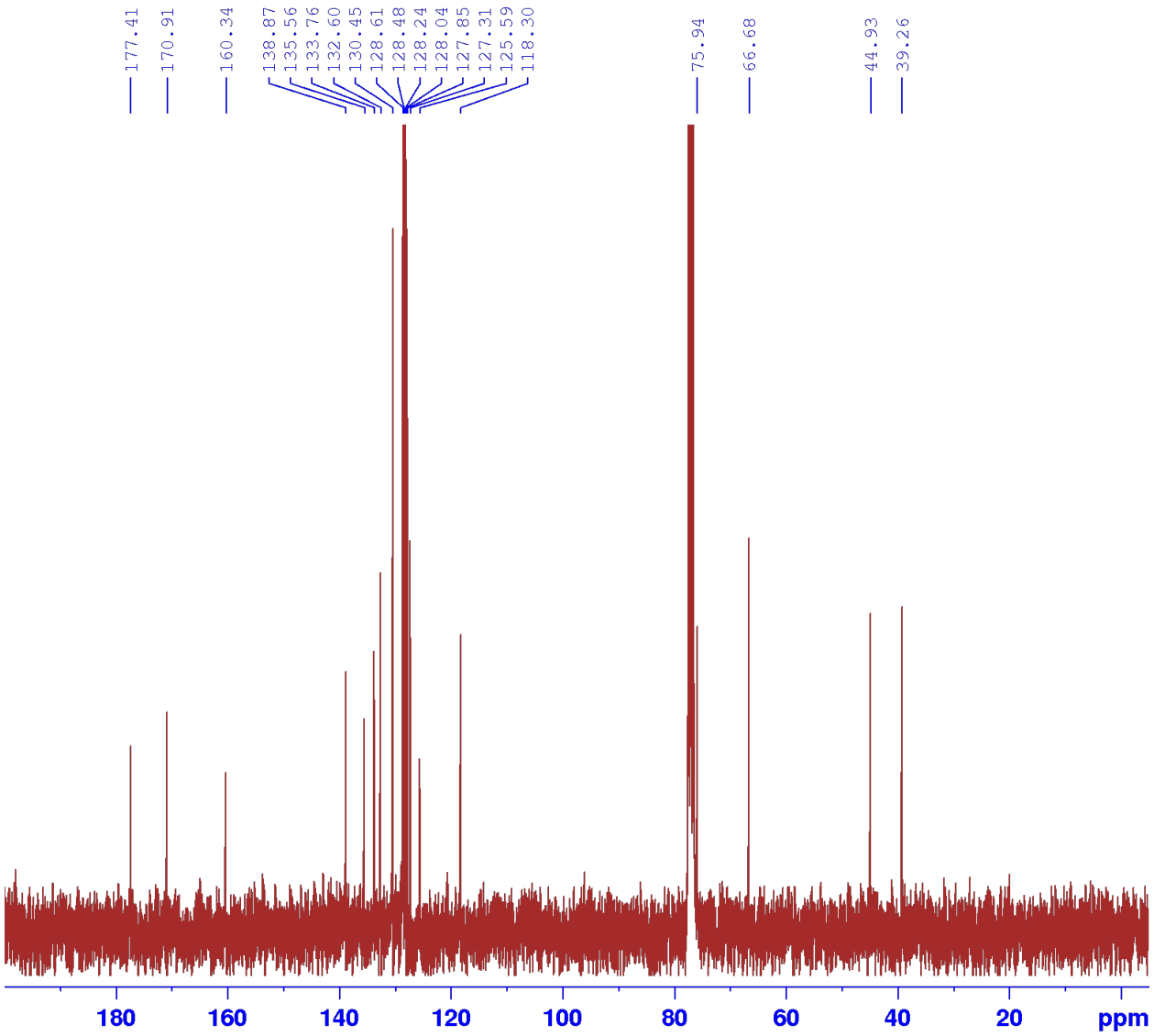

**5c**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

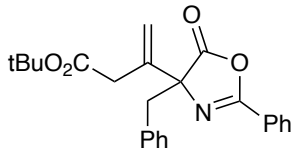



**5c**

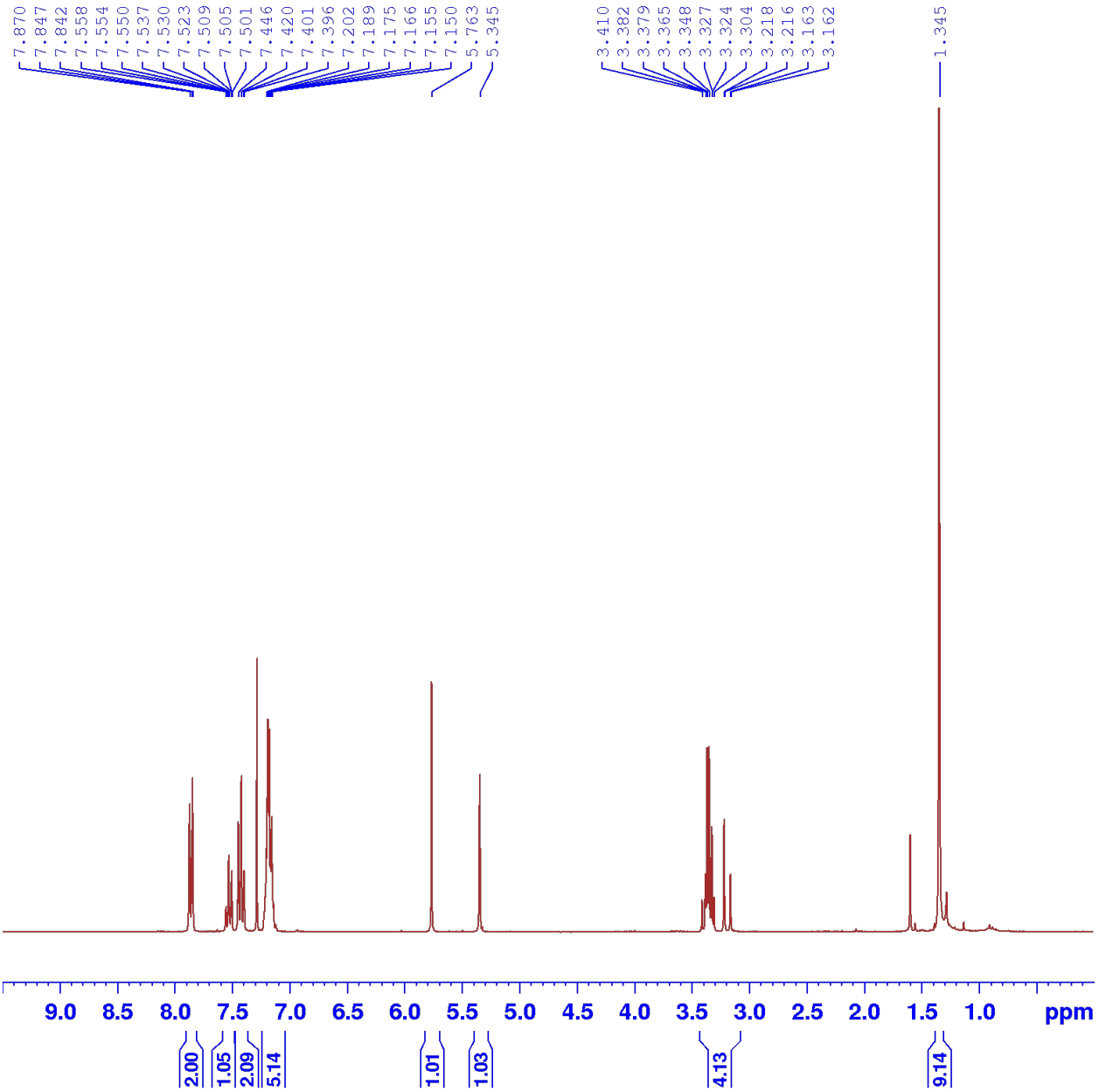


## NMR spectra of compound 5d

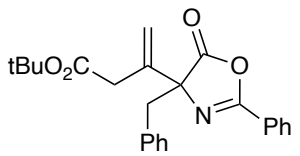
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



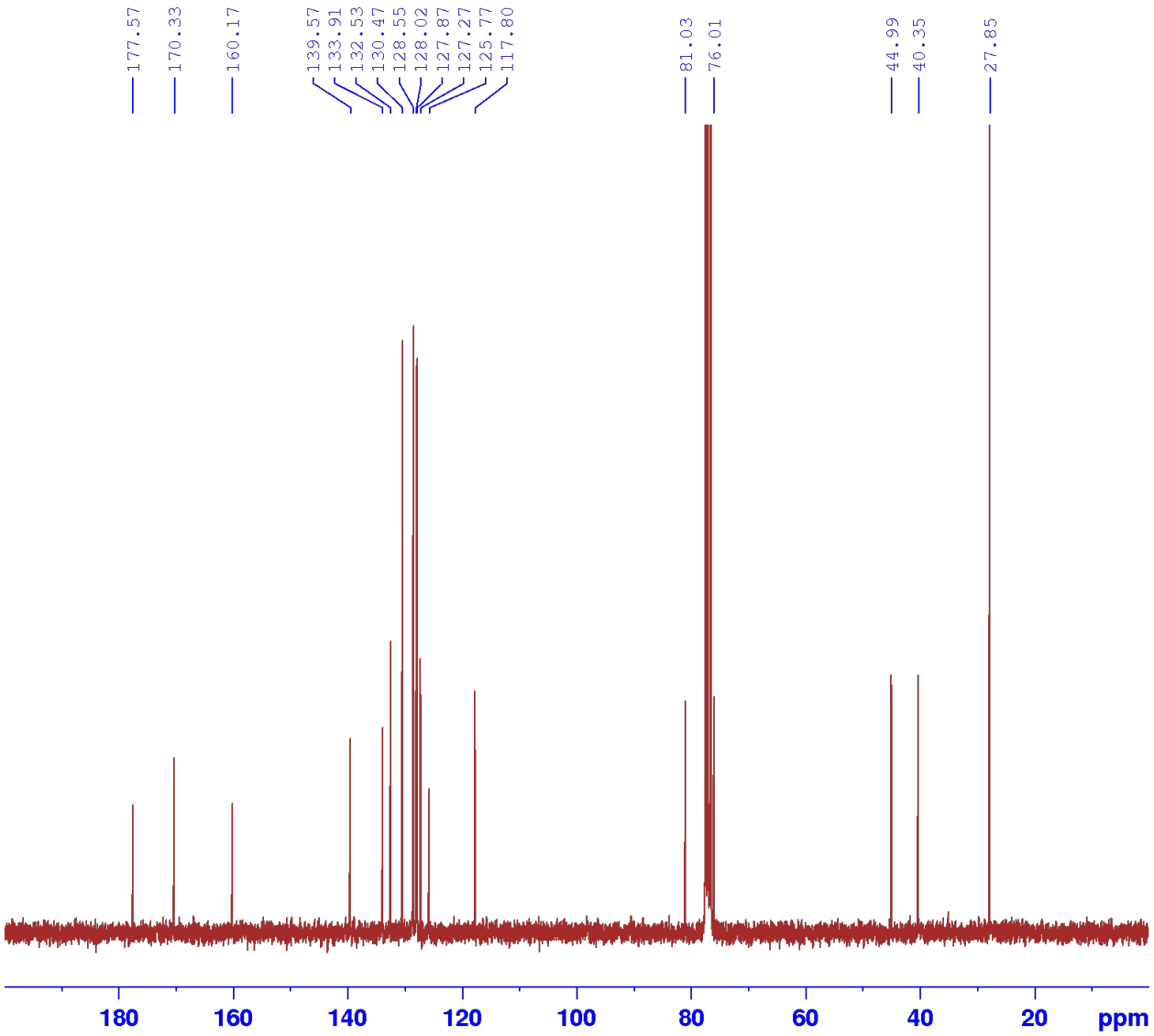

**5d**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

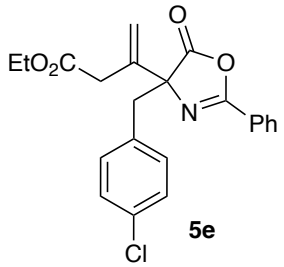



**5d**

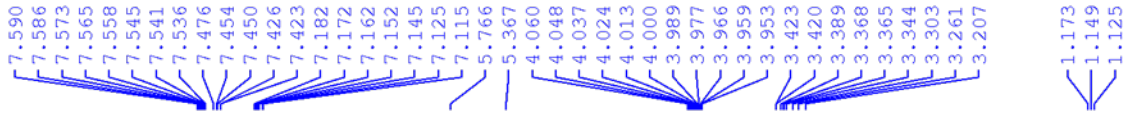


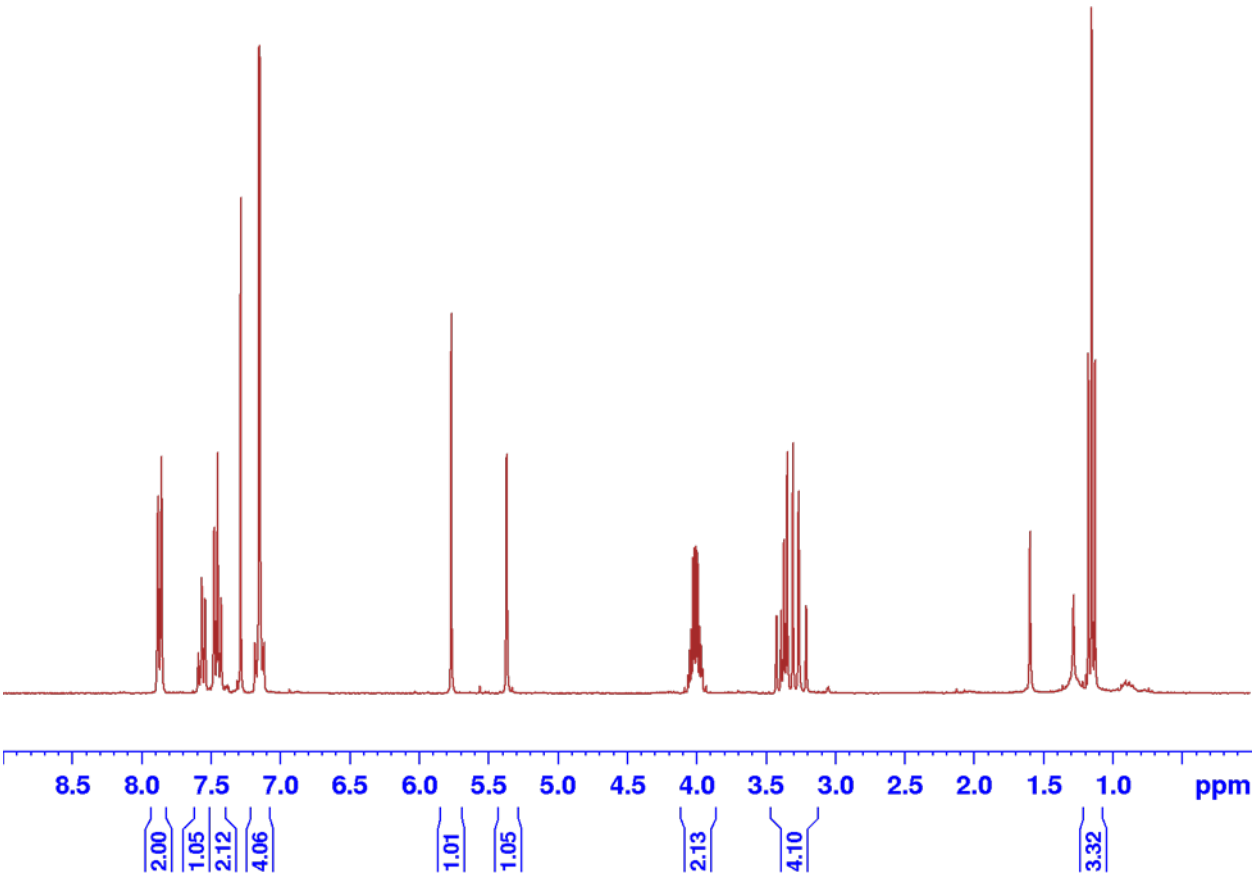
## NMR spectra of compound 5e

**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)

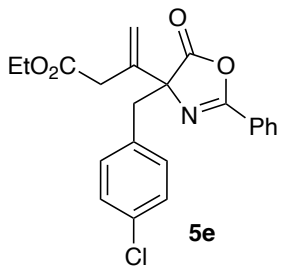



**5e**

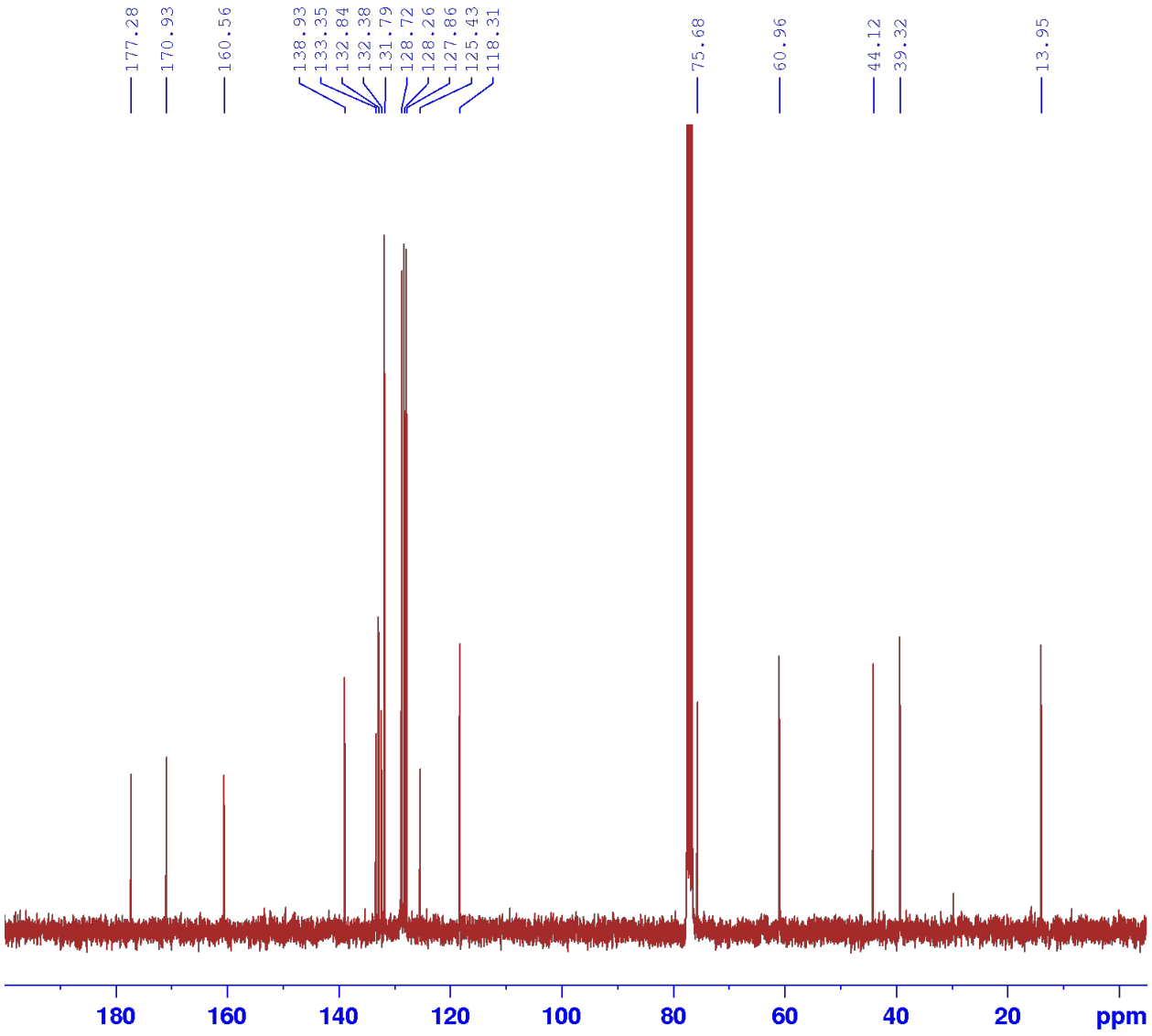


**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

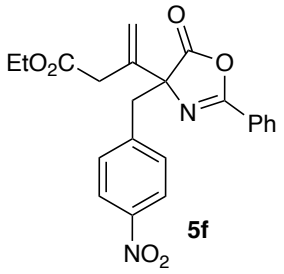



**5e**

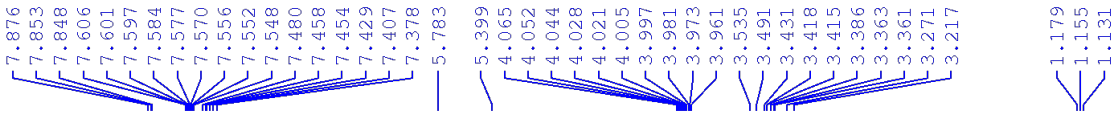


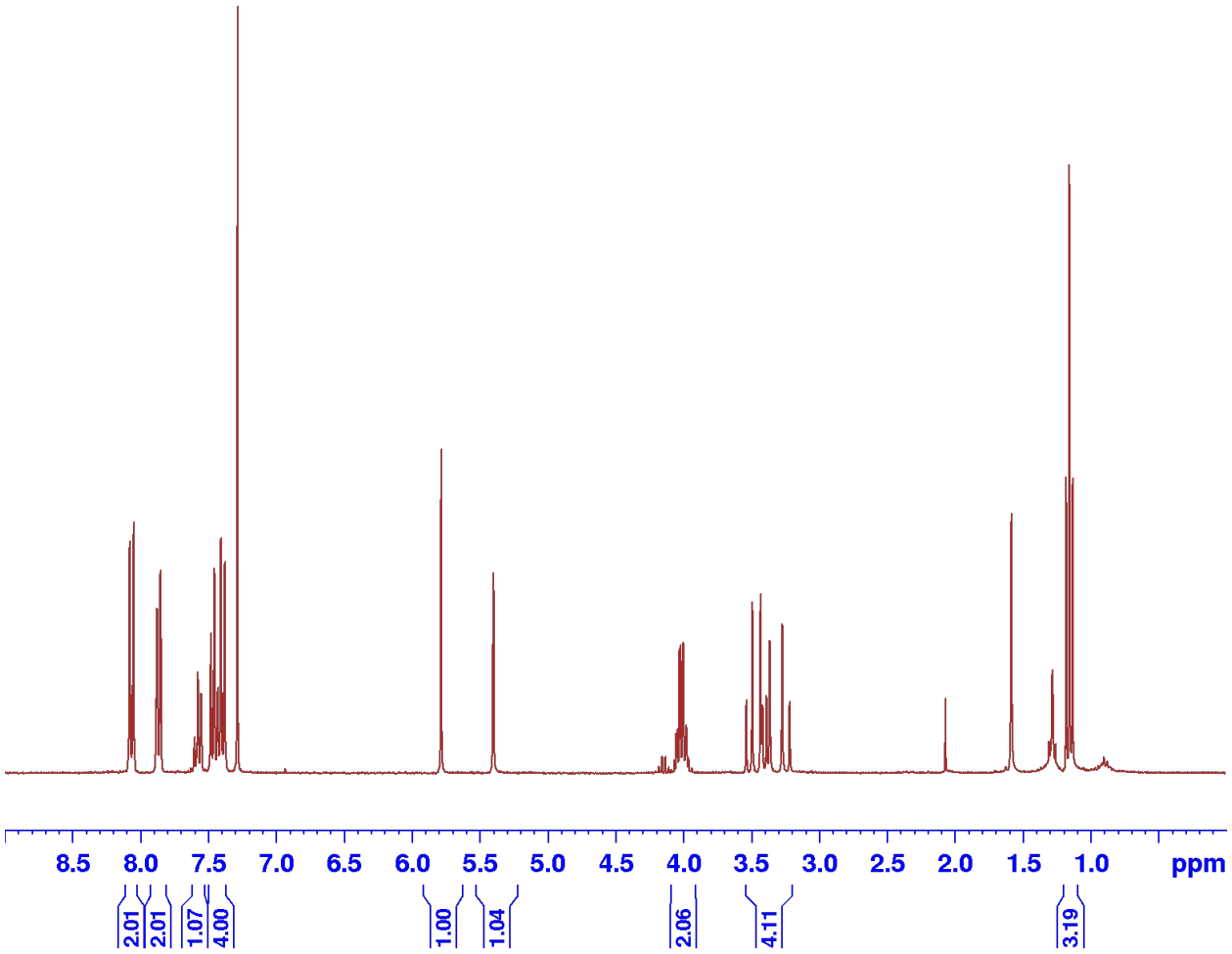
## NMR spectra of compound 5f

**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)

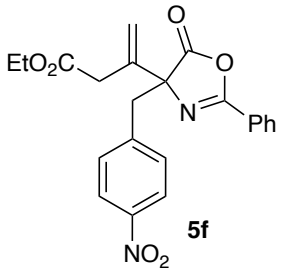



**5f**

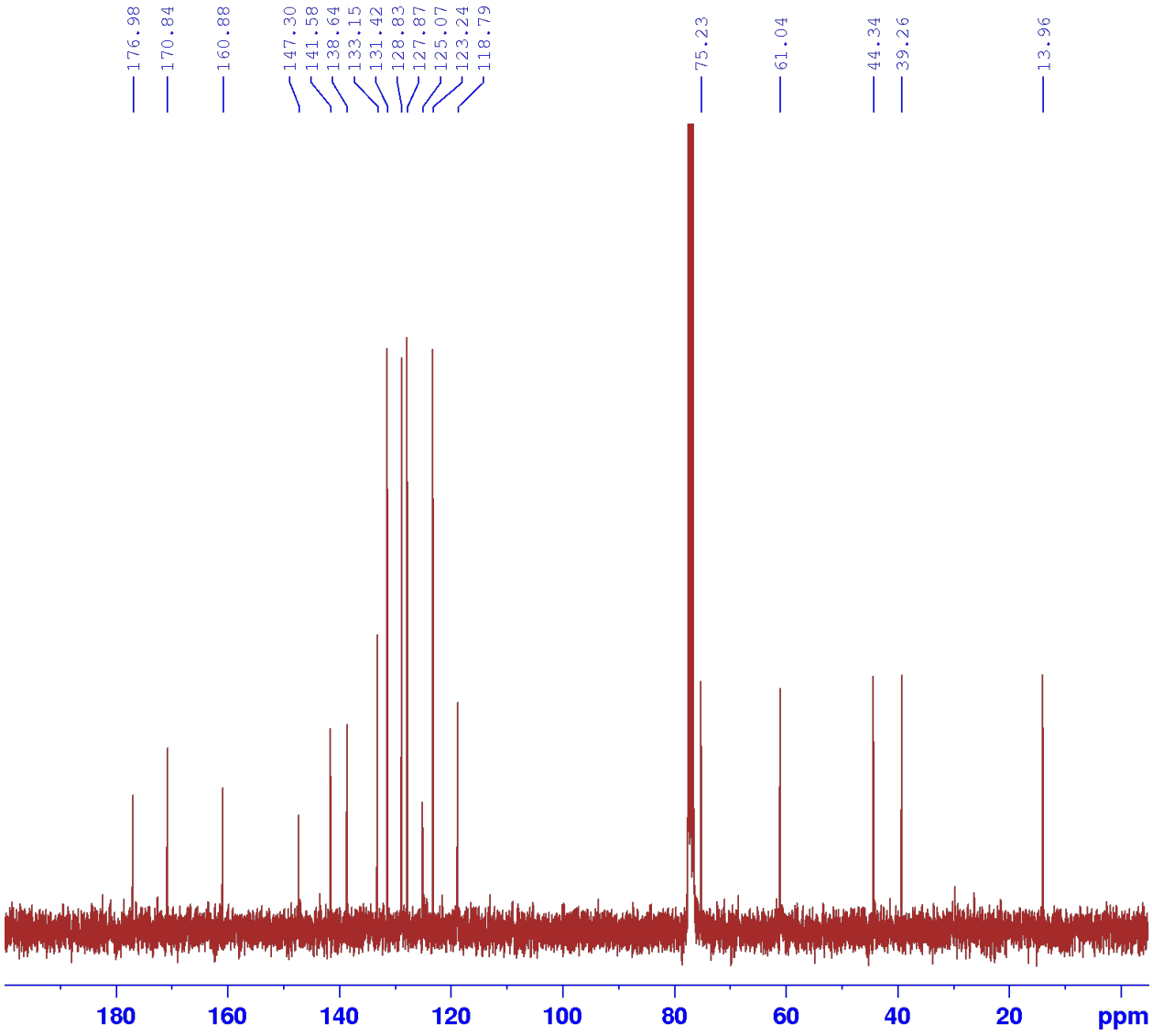


**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

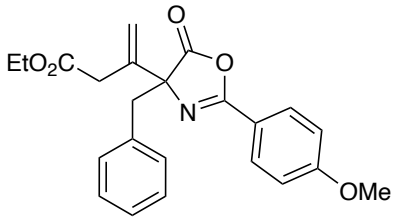



**5f**

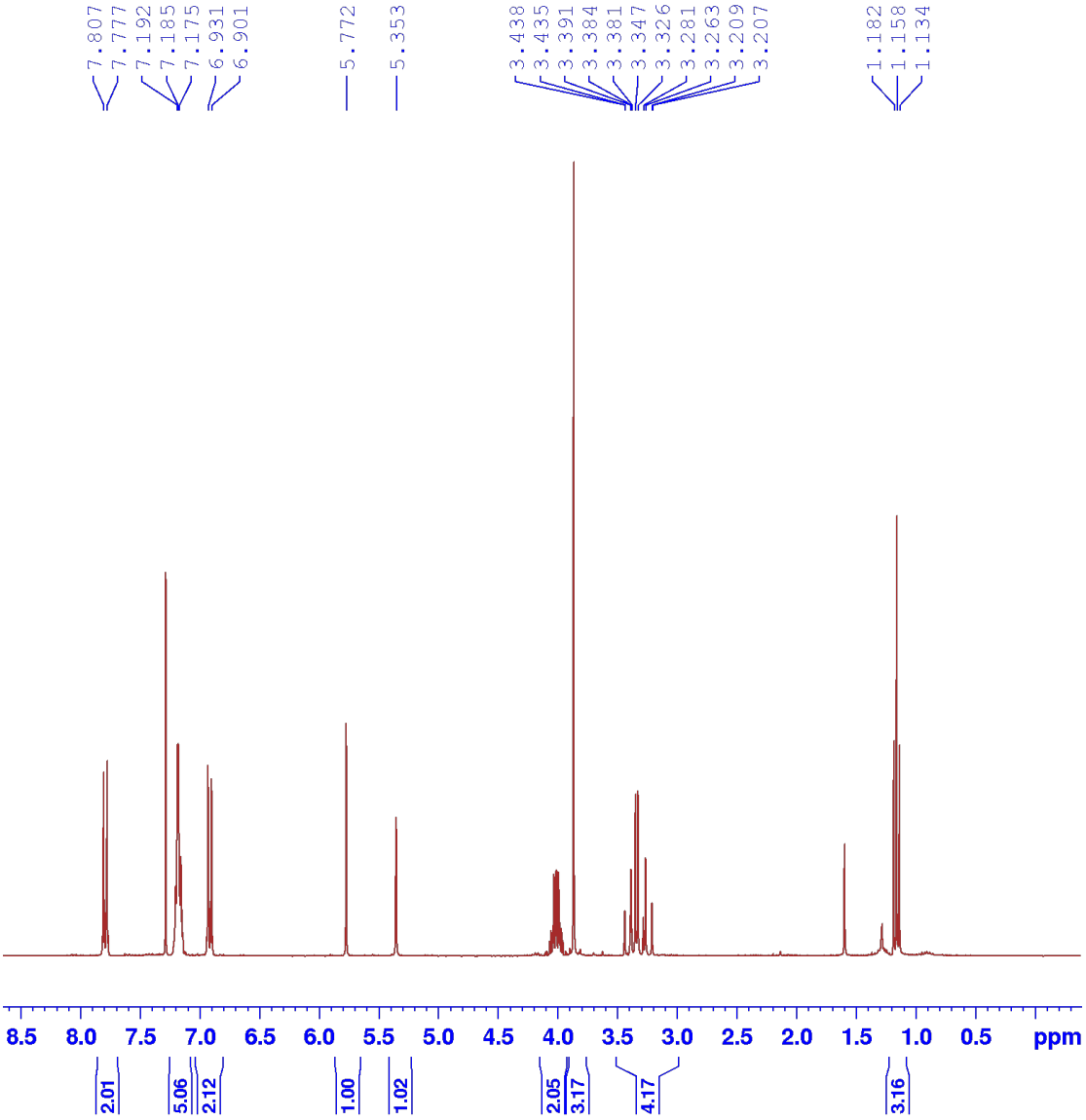


## NMR spectra of compound 5g

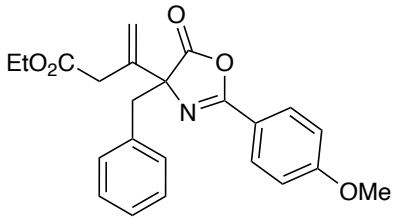
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



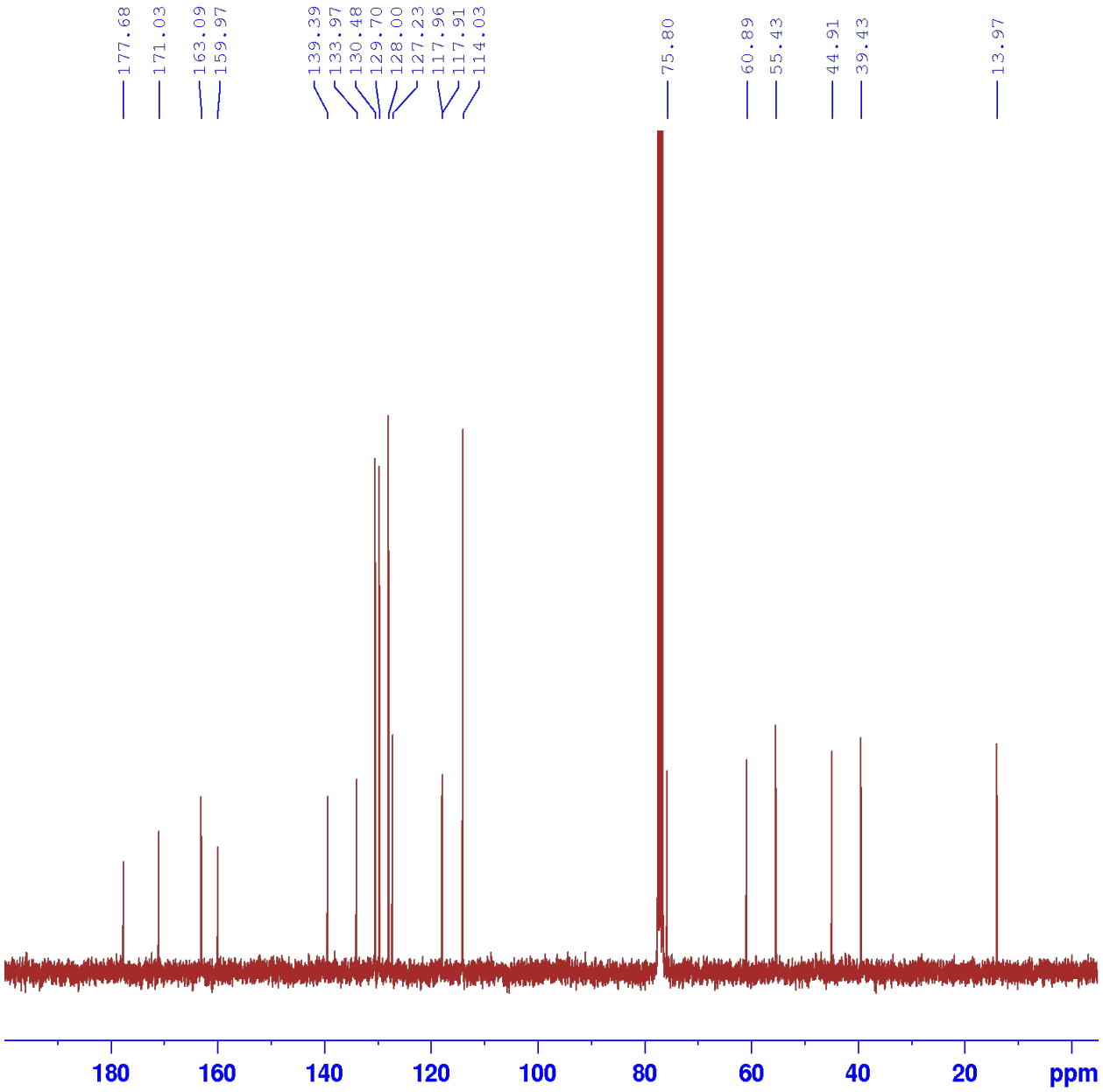

**5g**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

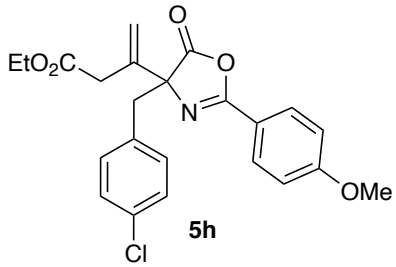



**5g**

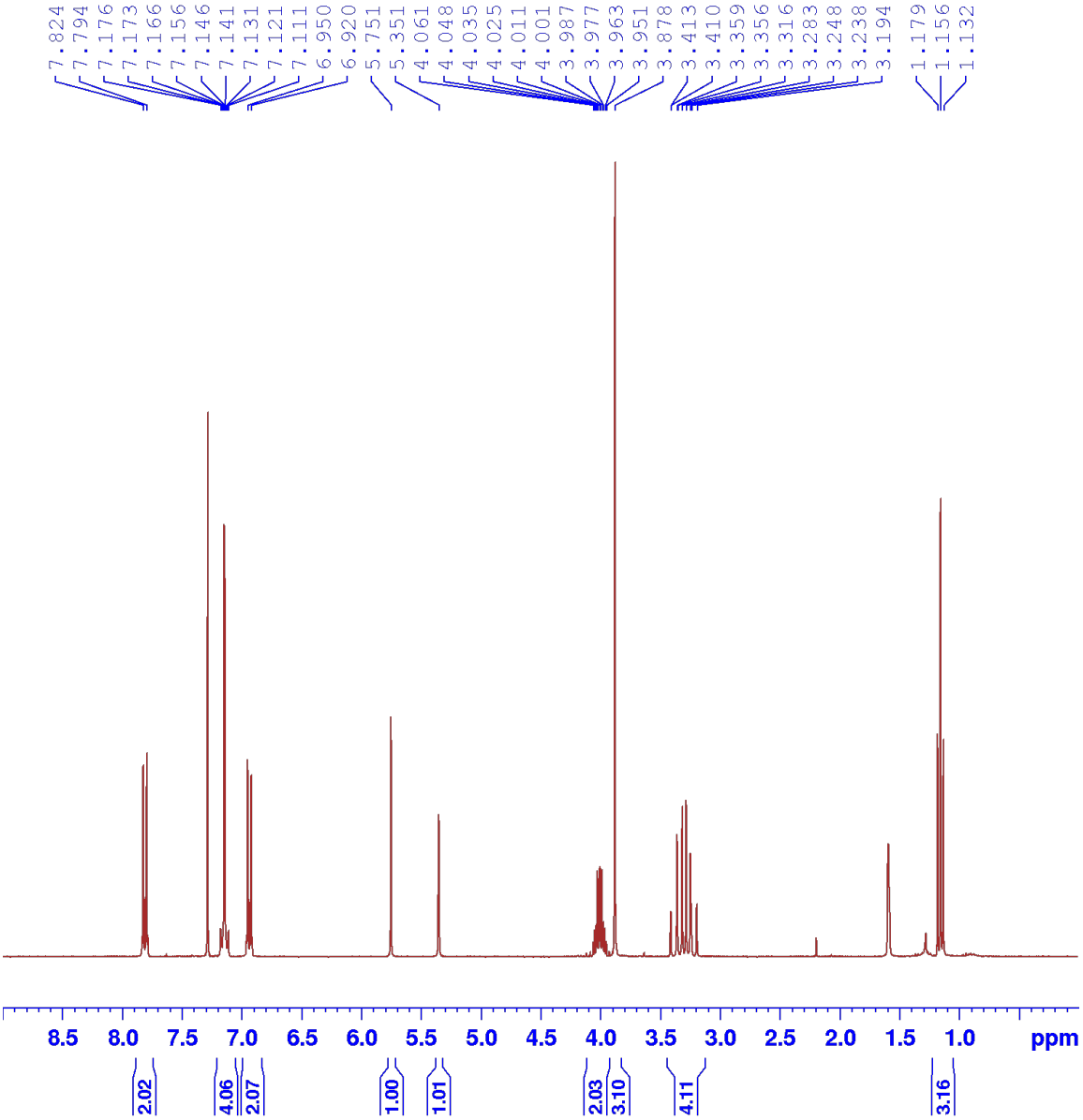


## NMR spectra of compound 5h

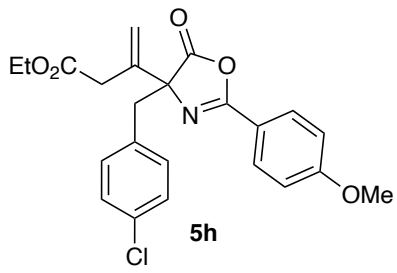
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



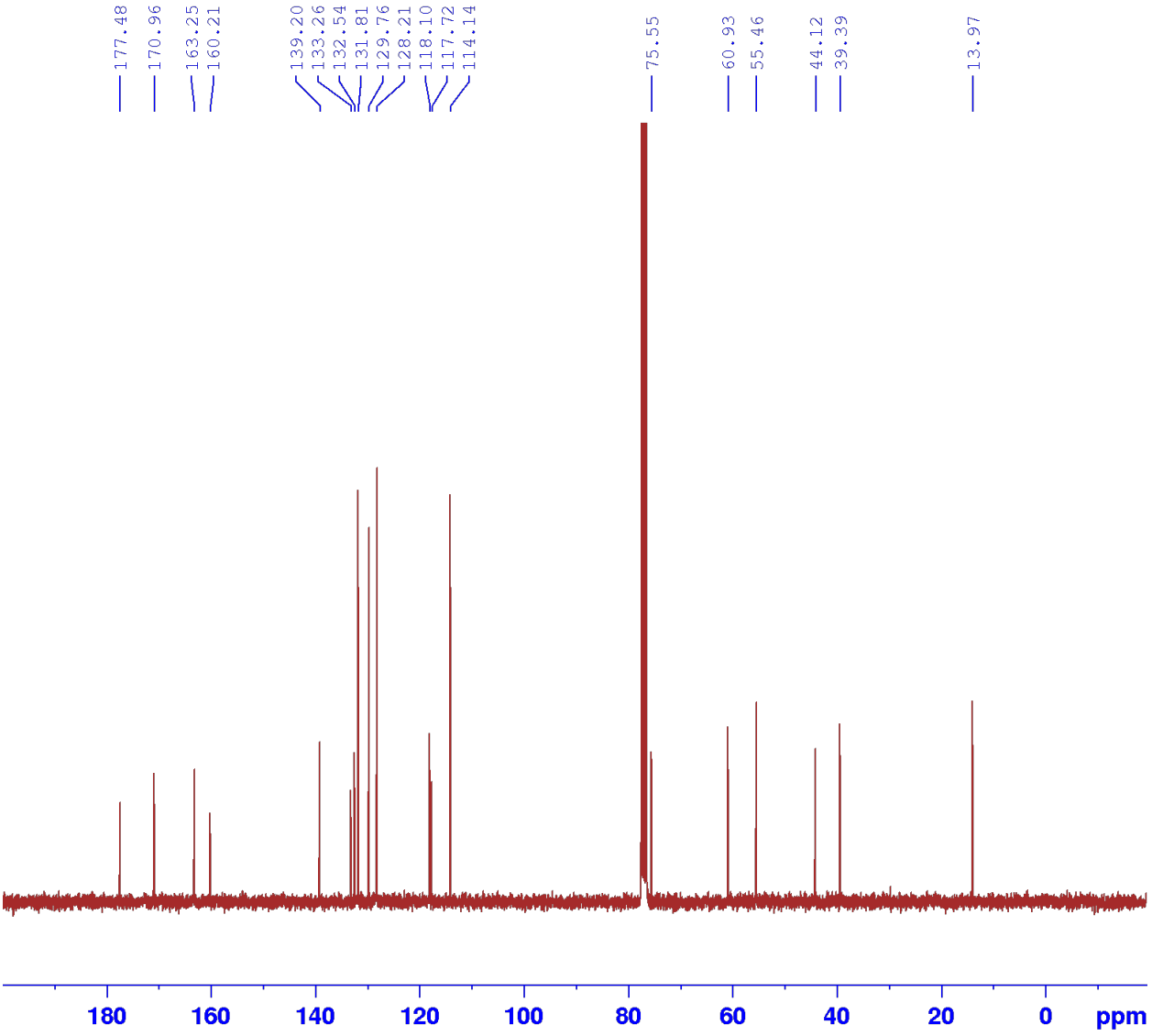

**5h**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

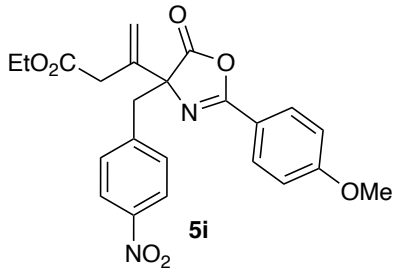



**5h**

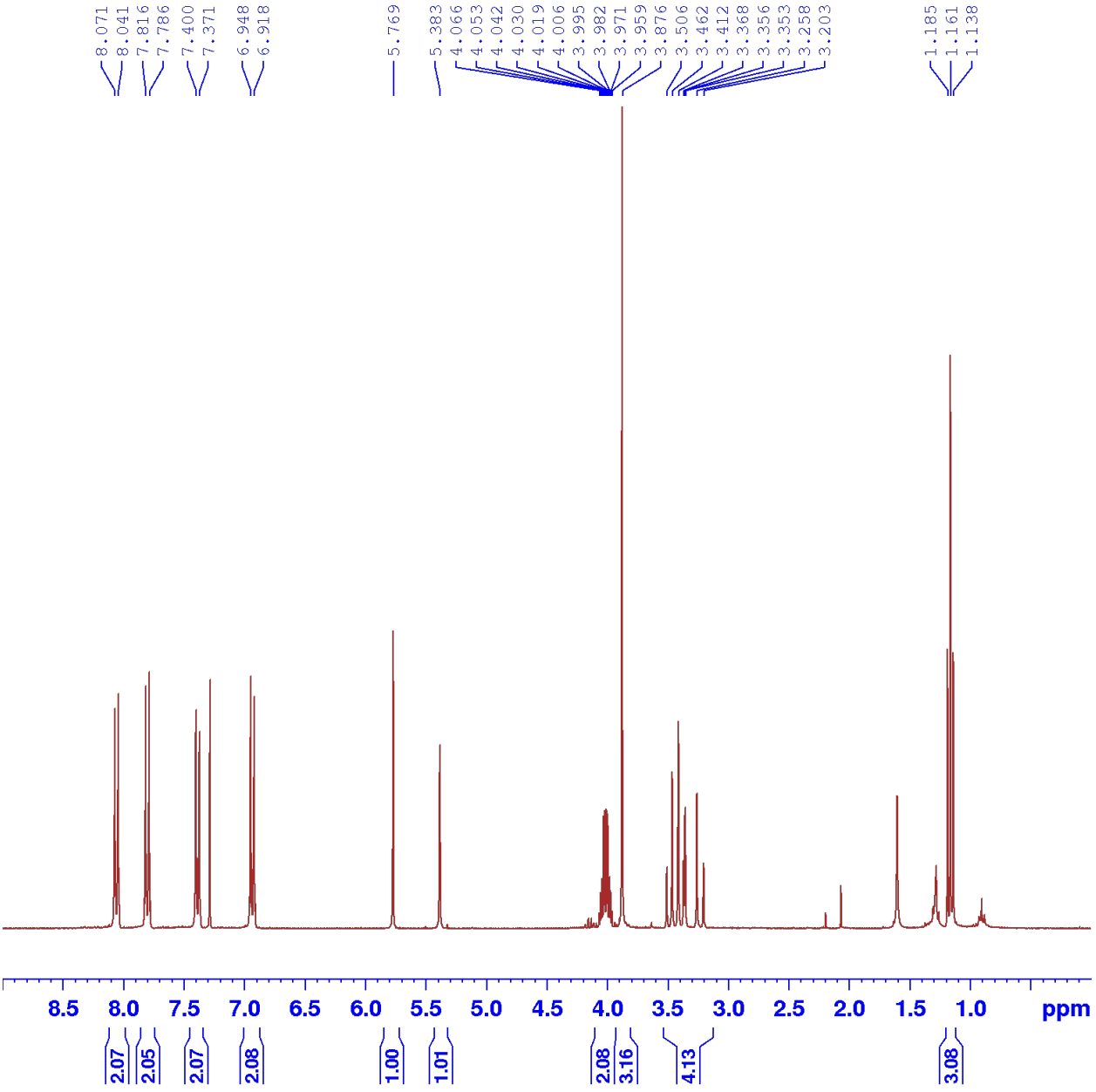


## NMR spectra of compound 5i

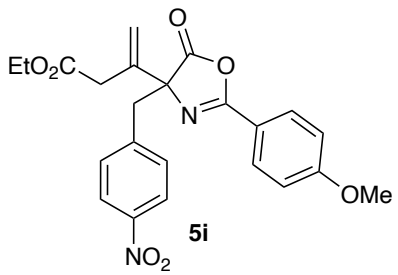
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



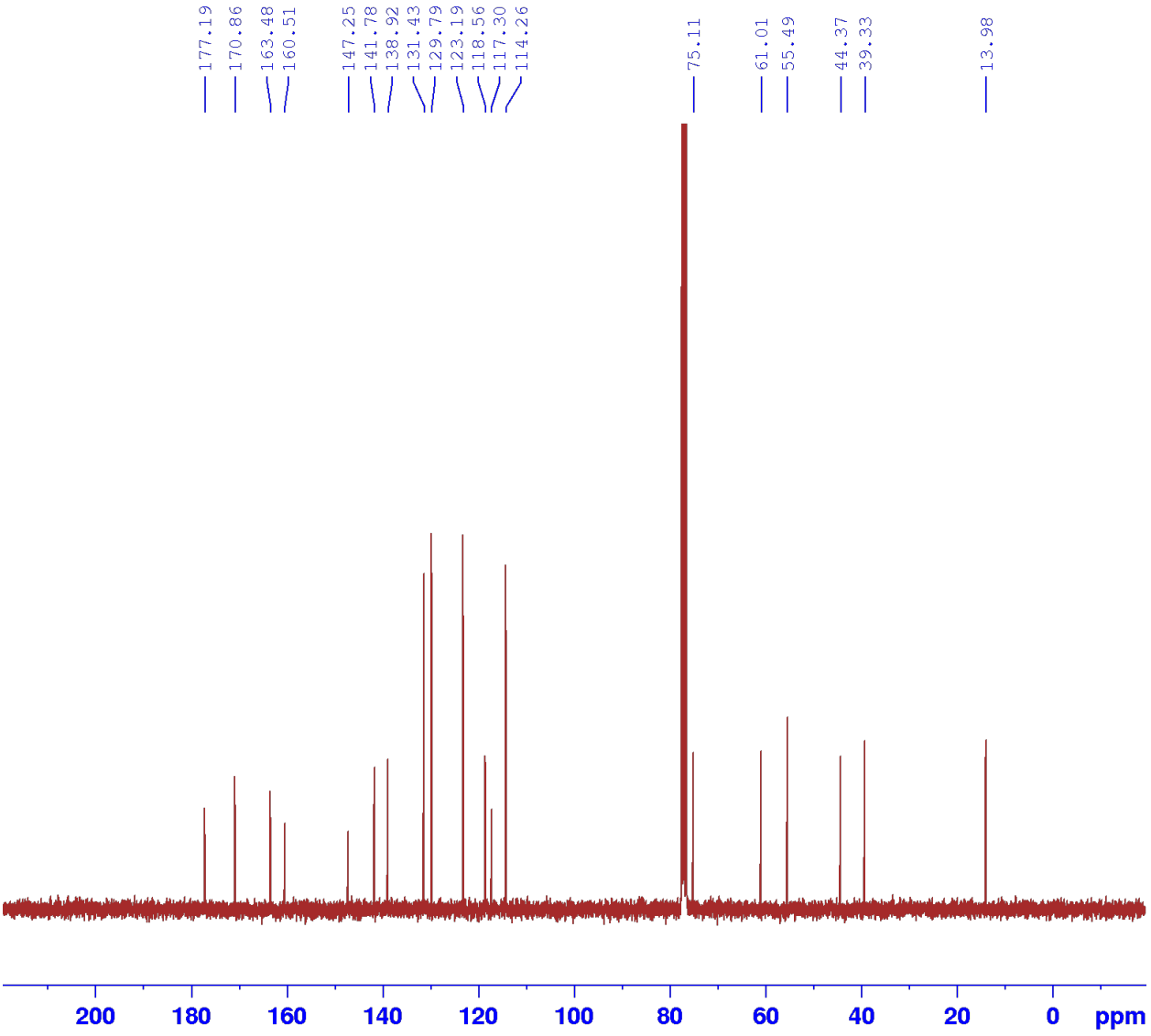

**5i**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

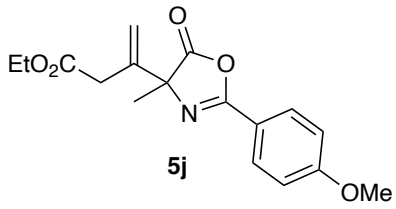



**5i**

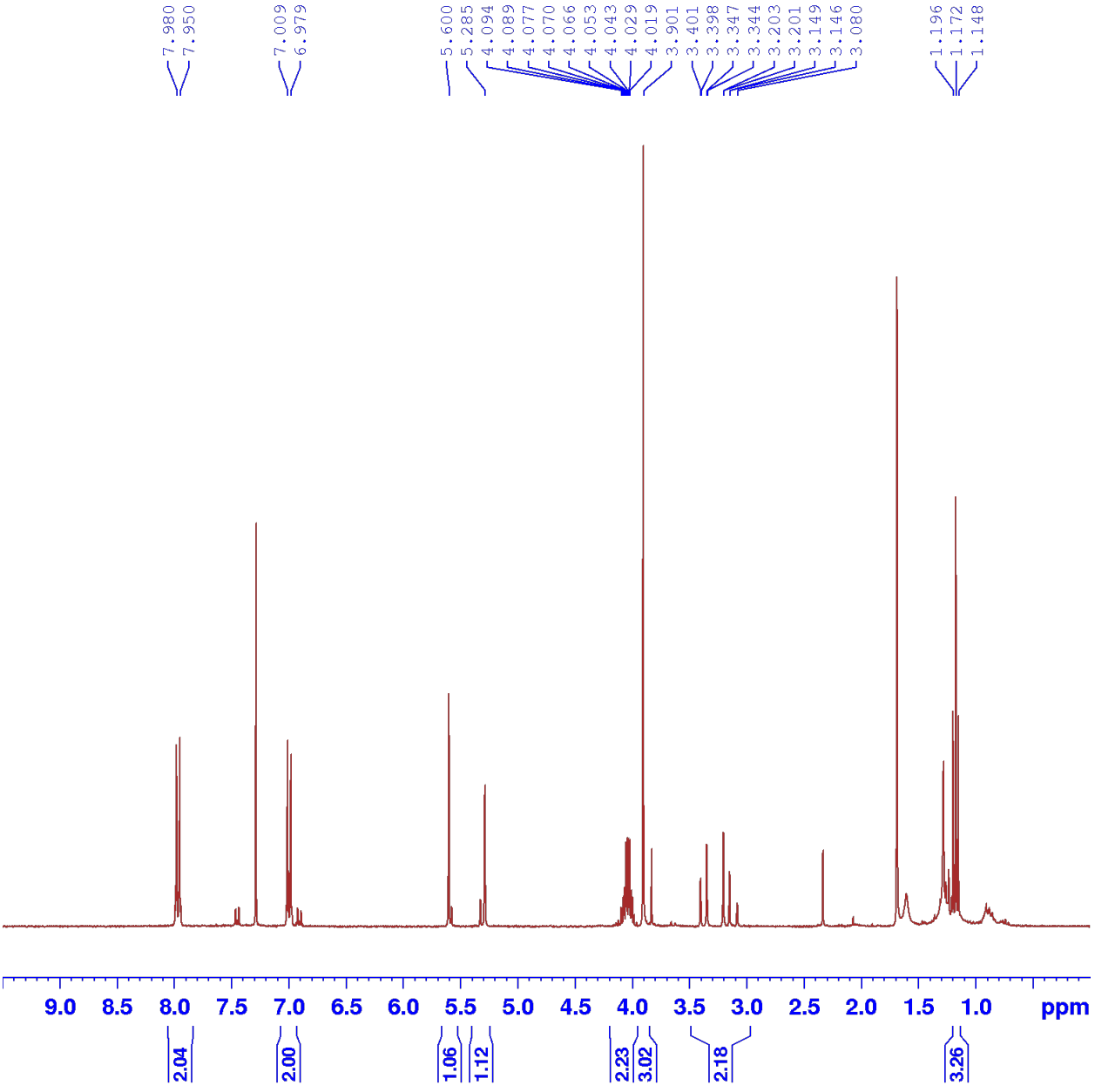


**NMR spectra of compound 5j** (*containing traces of ring-opened product*)

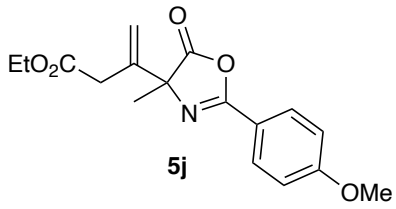
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



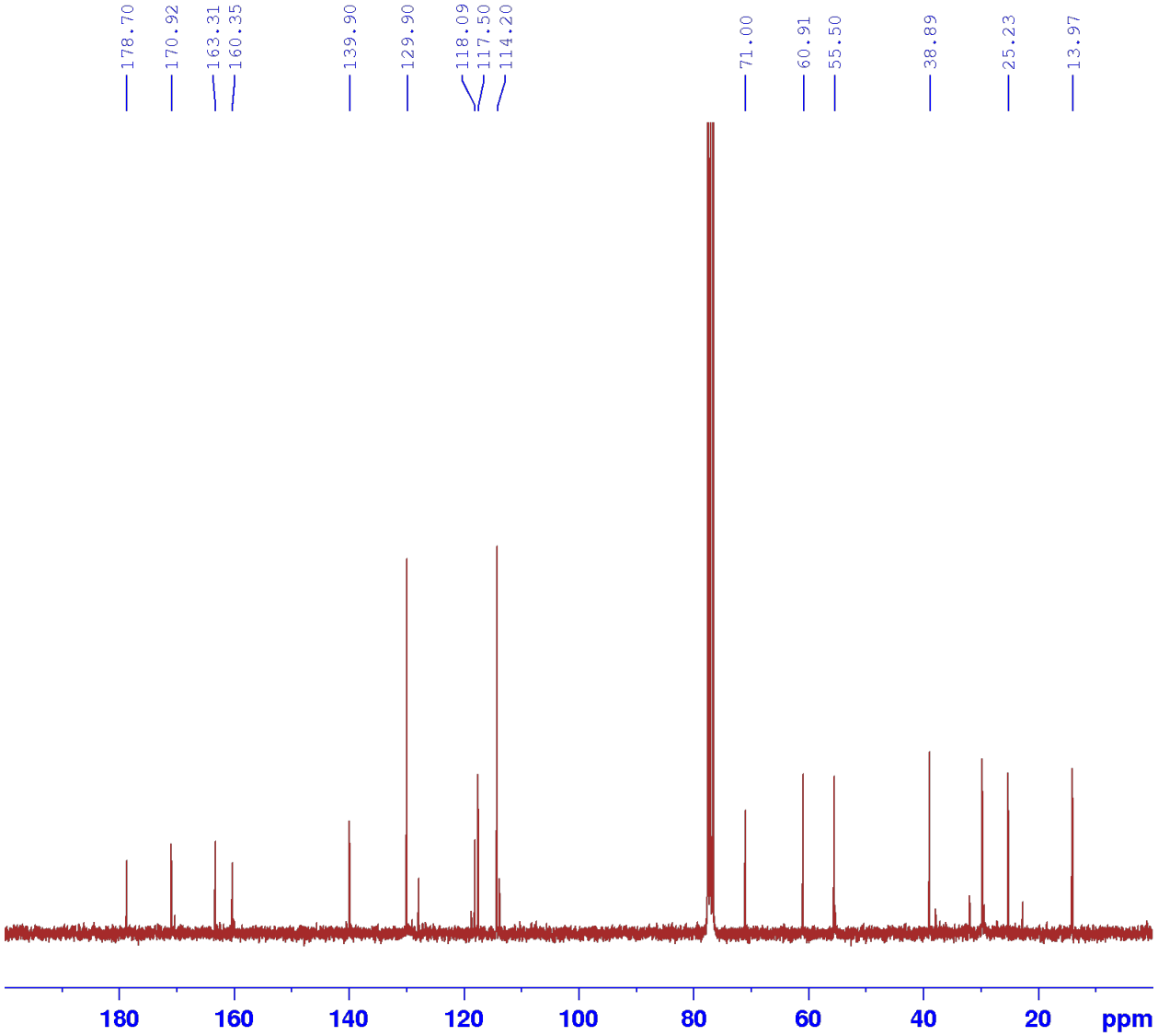

**5j**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

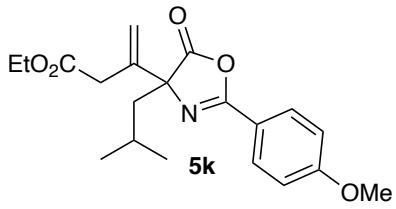



**5j**

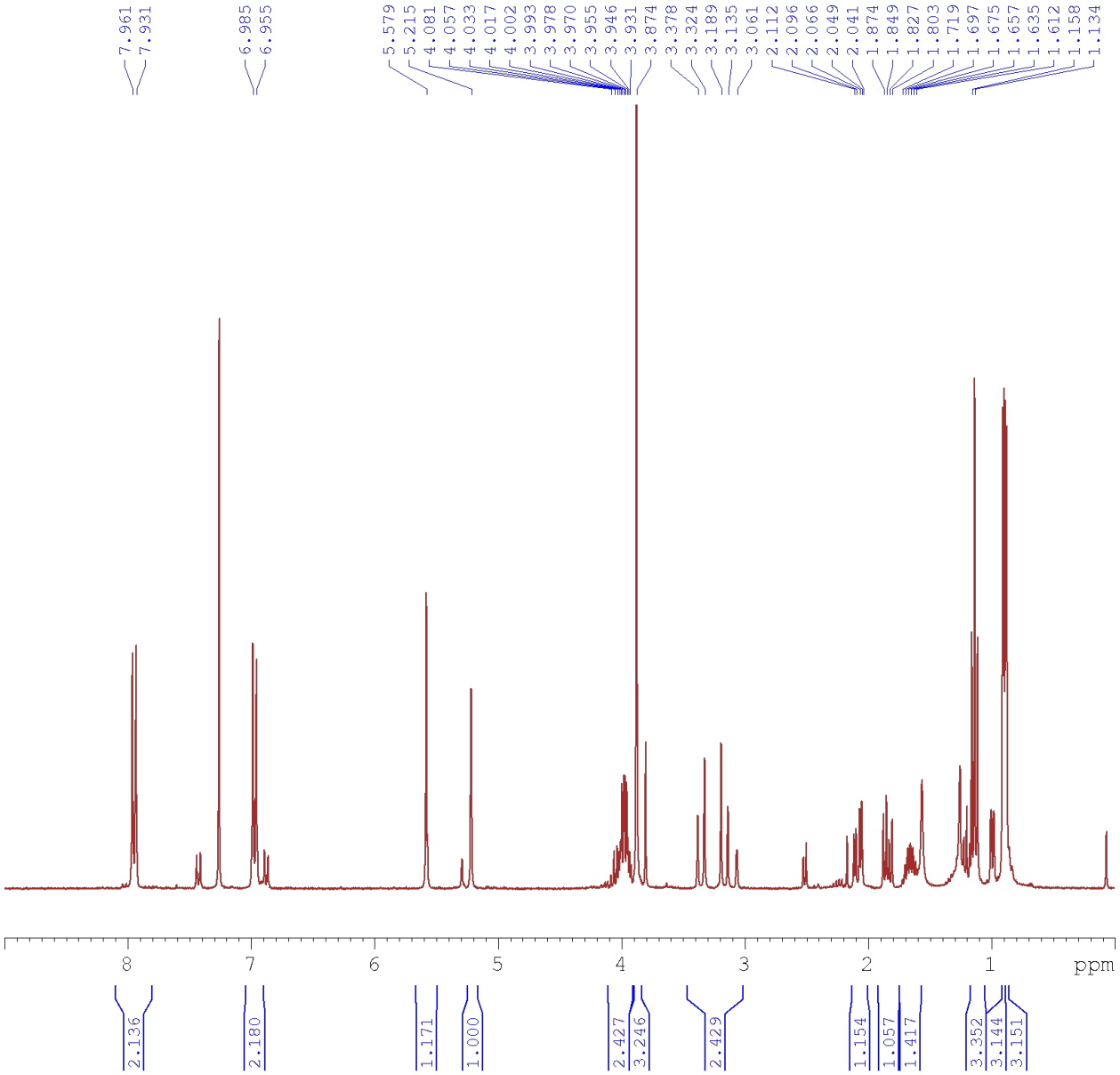


**NMR spectra of compound 5k** (*containing traces of ring-opened product*)

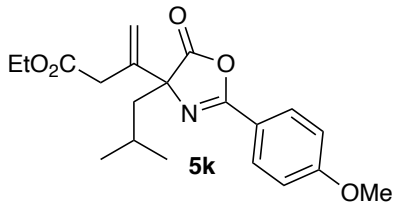
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



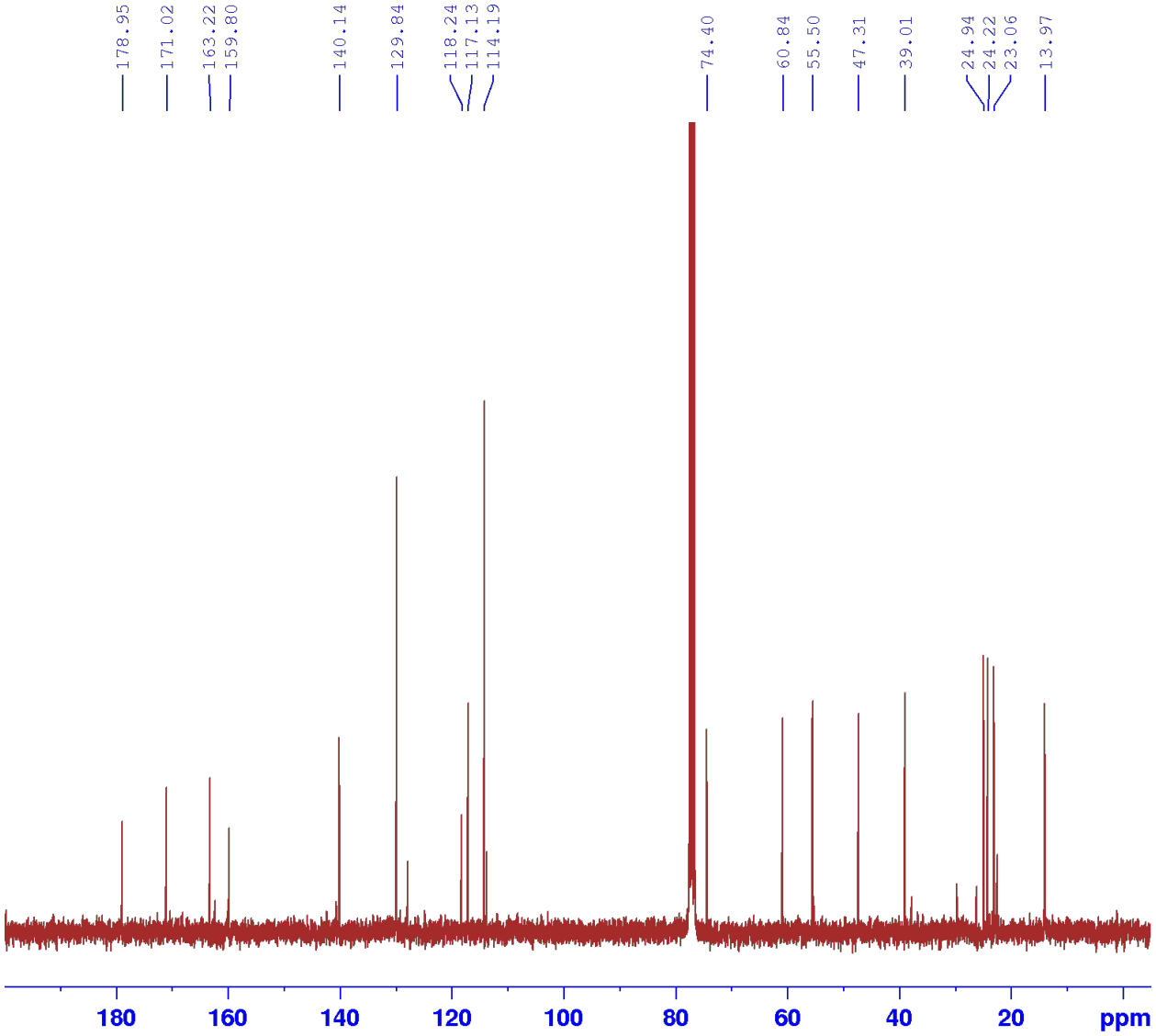

**5k**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

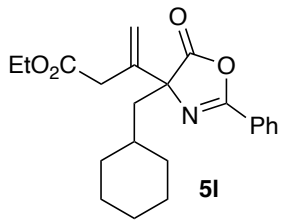



**5k**

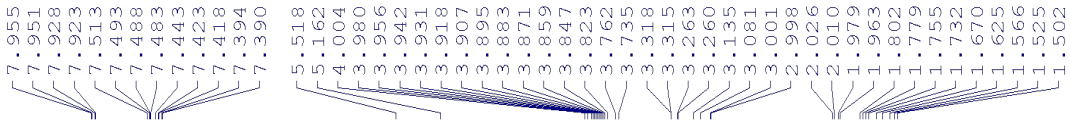


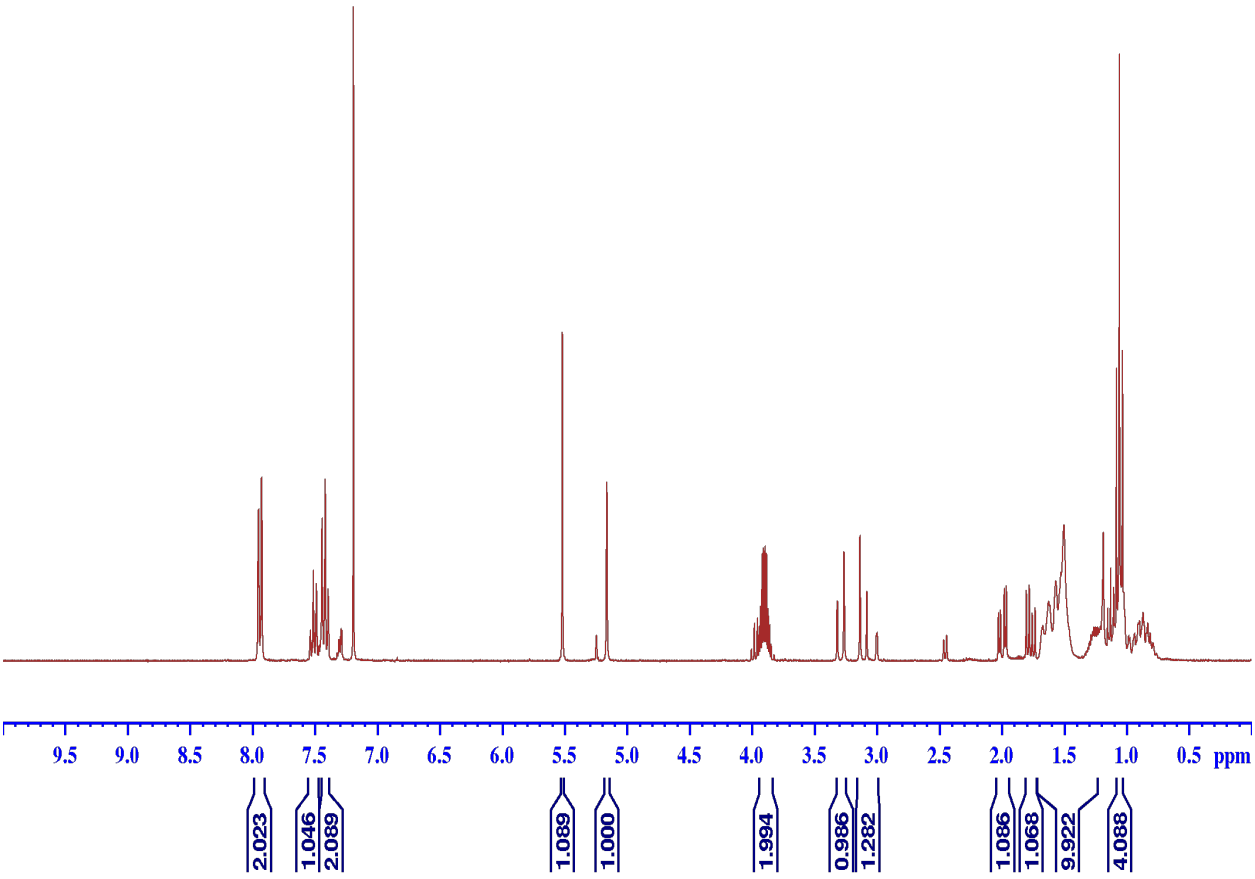
## NMR spectra of compound 5l

**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)

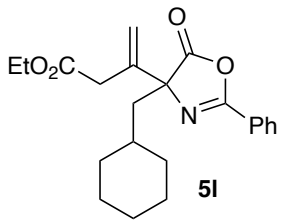



**5l**

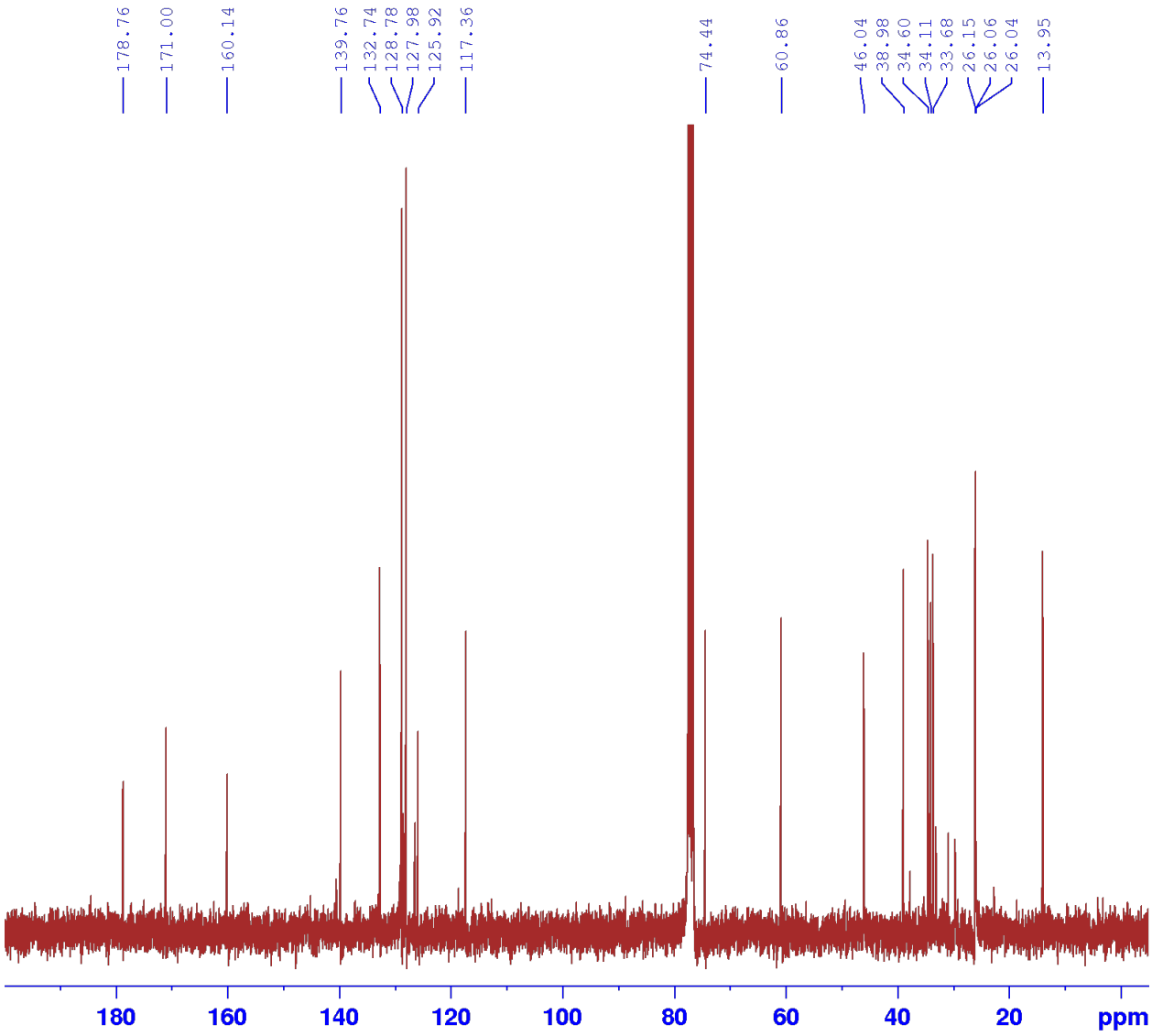


**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

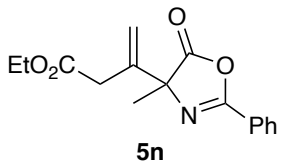



**5l**

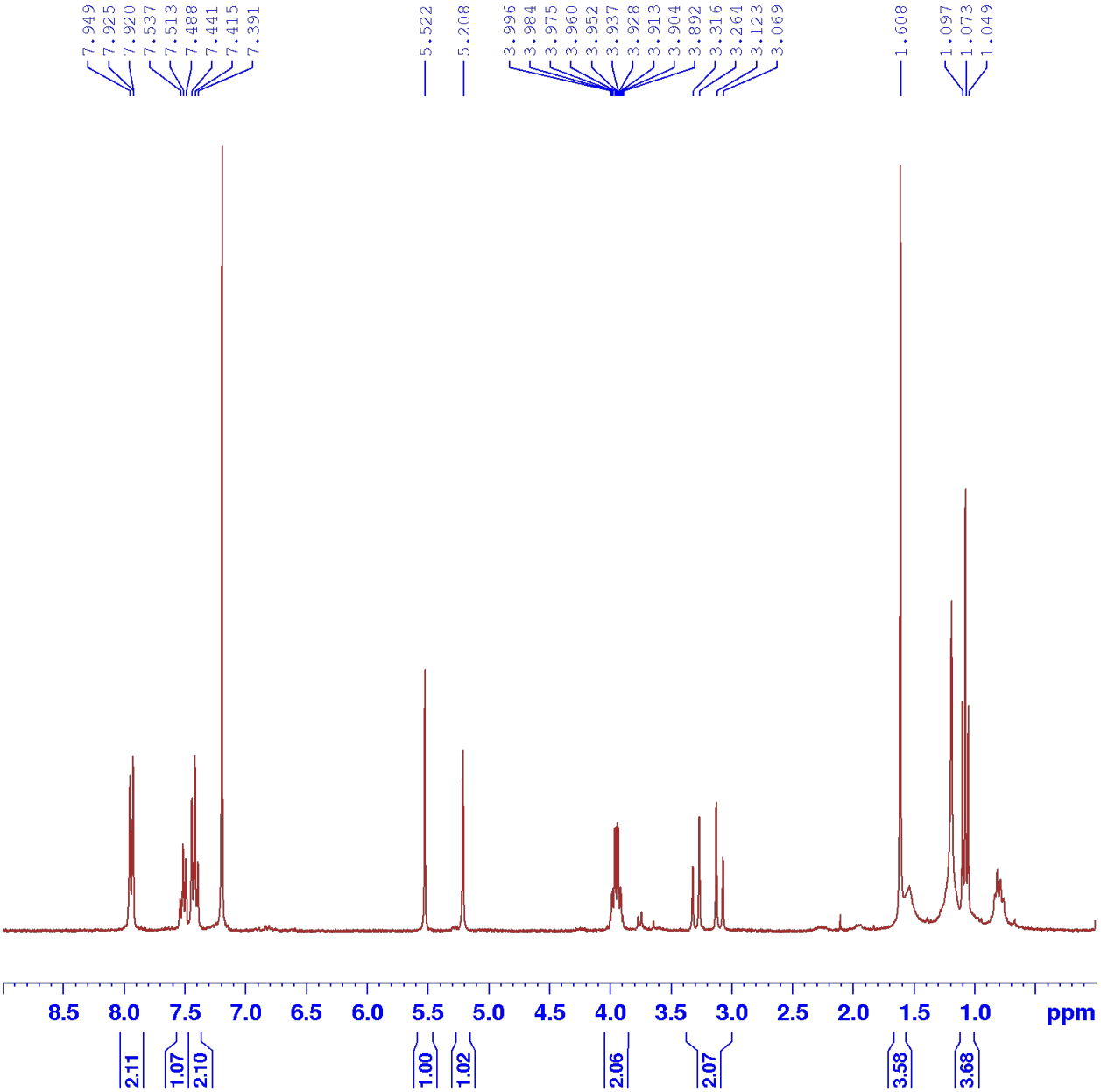


## NMR spectra of compound 5n

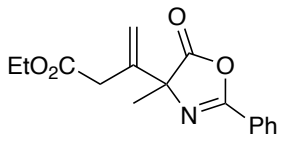
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



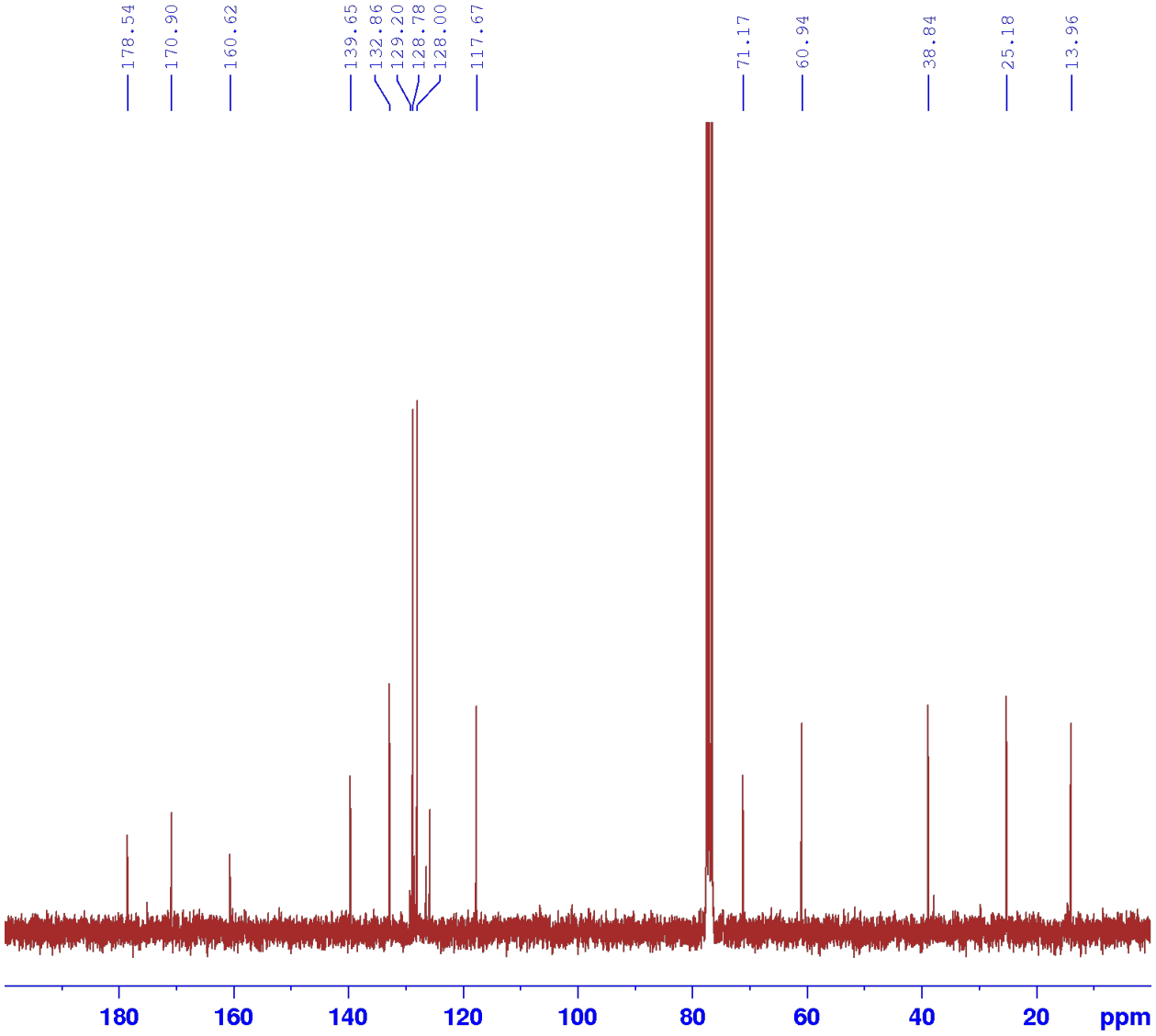

**5n**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

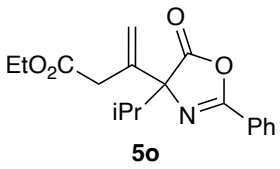



**5n**

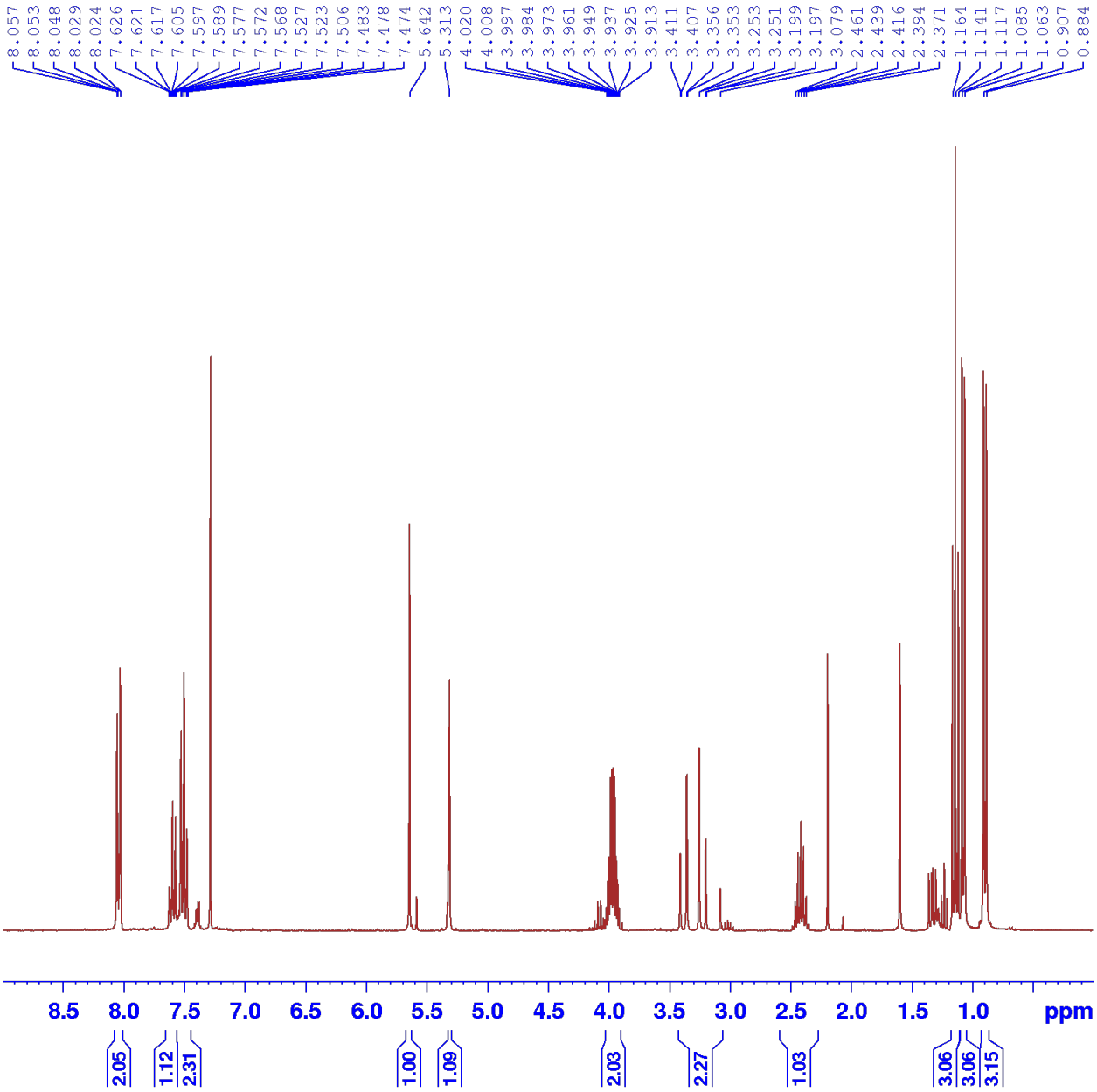


**NMR spectra of compound 5o** (*containing traces of ring-opened product*)

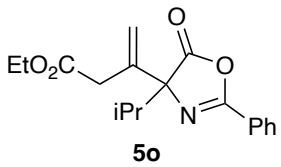
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



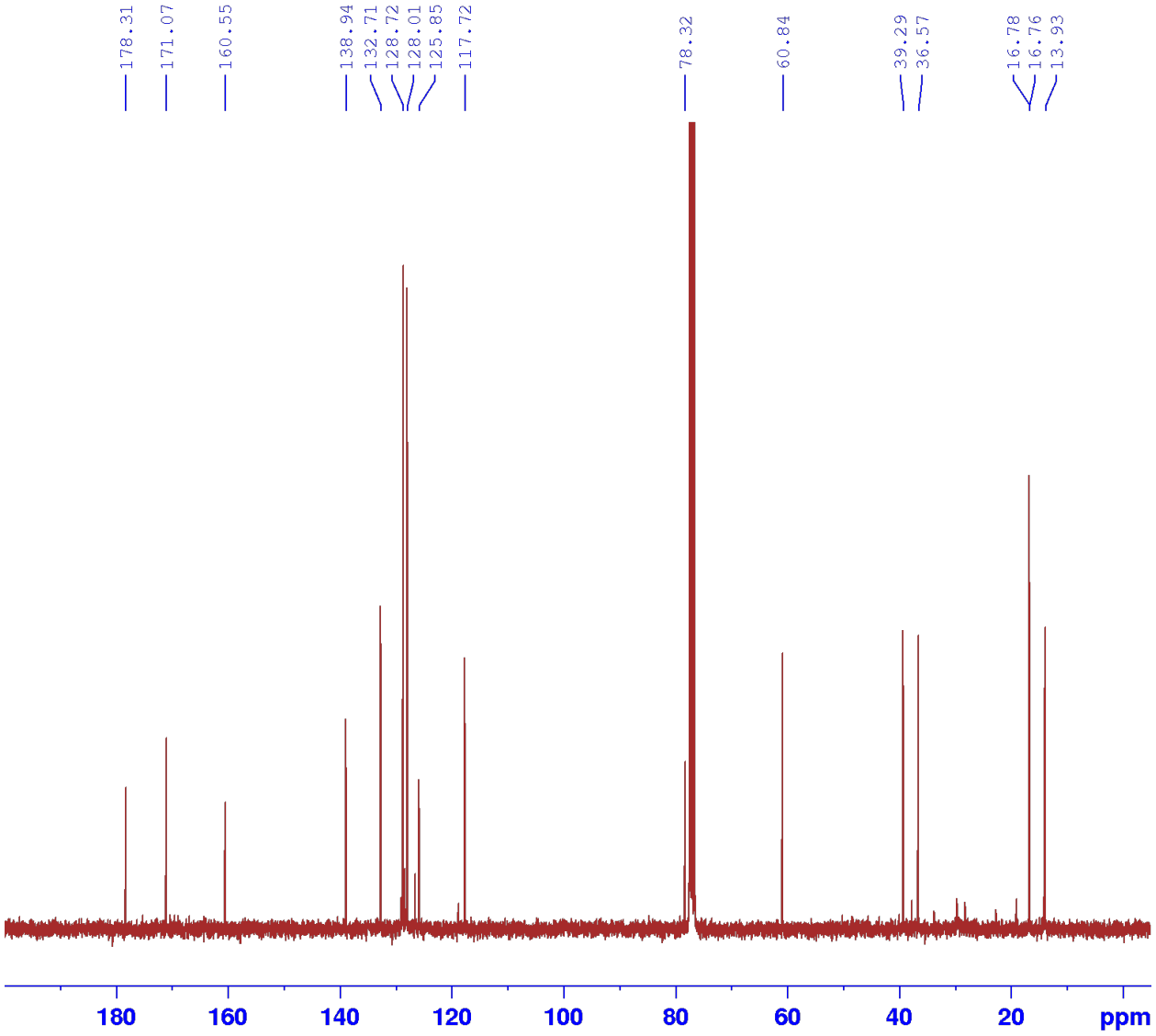

**5o**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

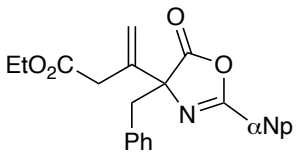



**5o**

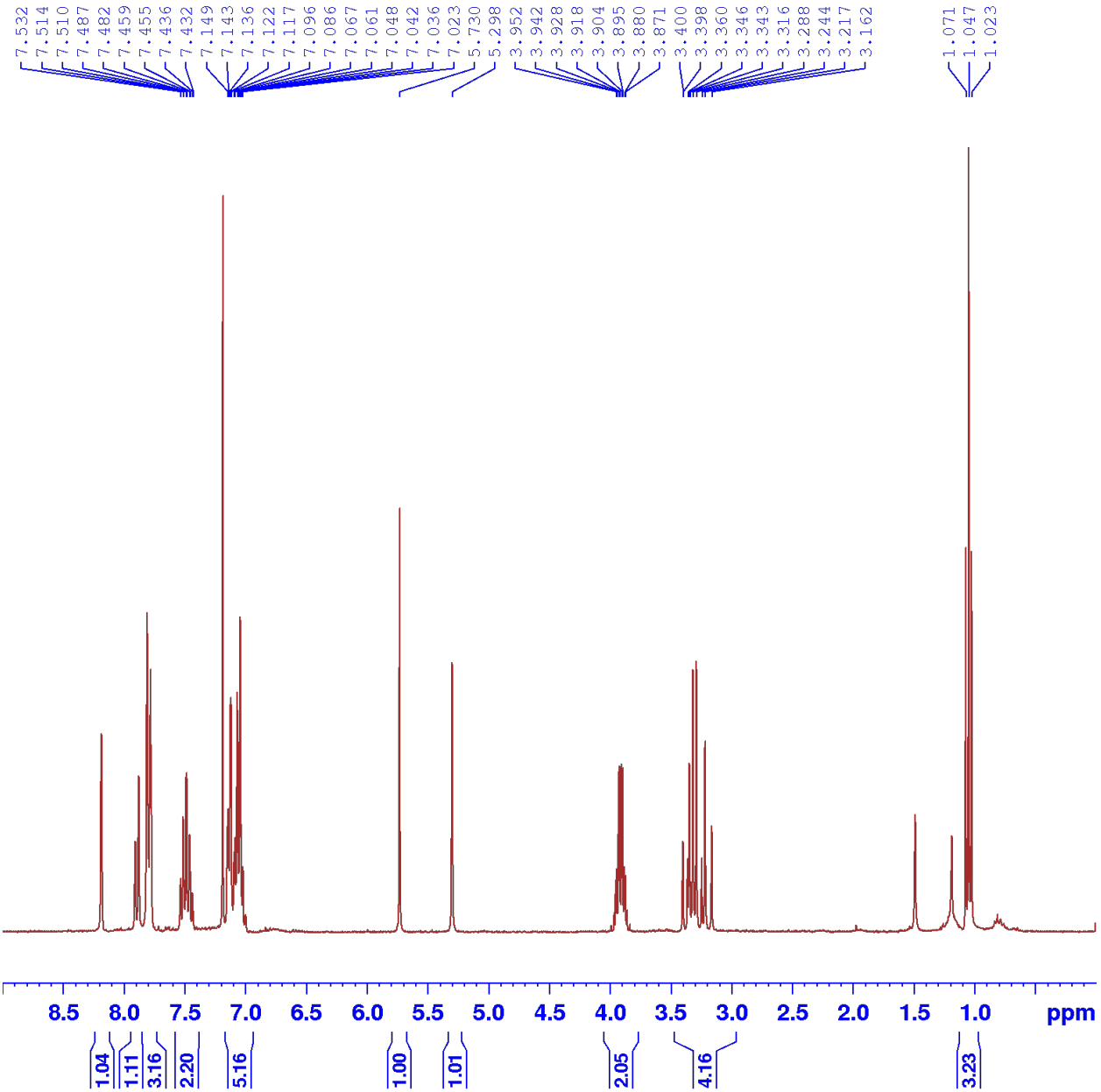


## NMR spectra of compound 5p

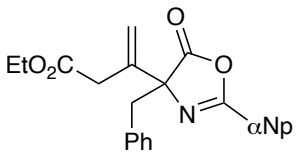
**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



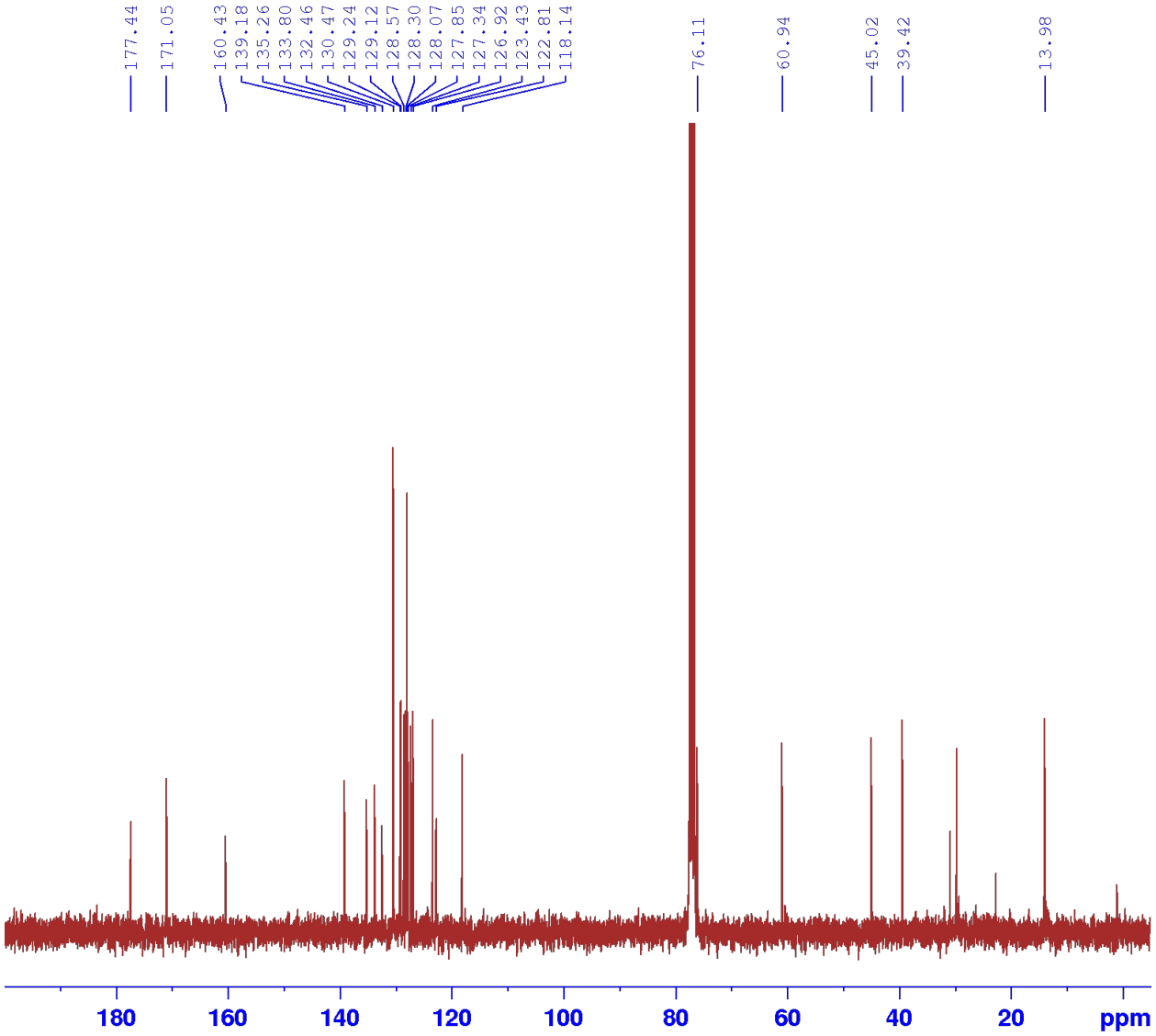

**5p**



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

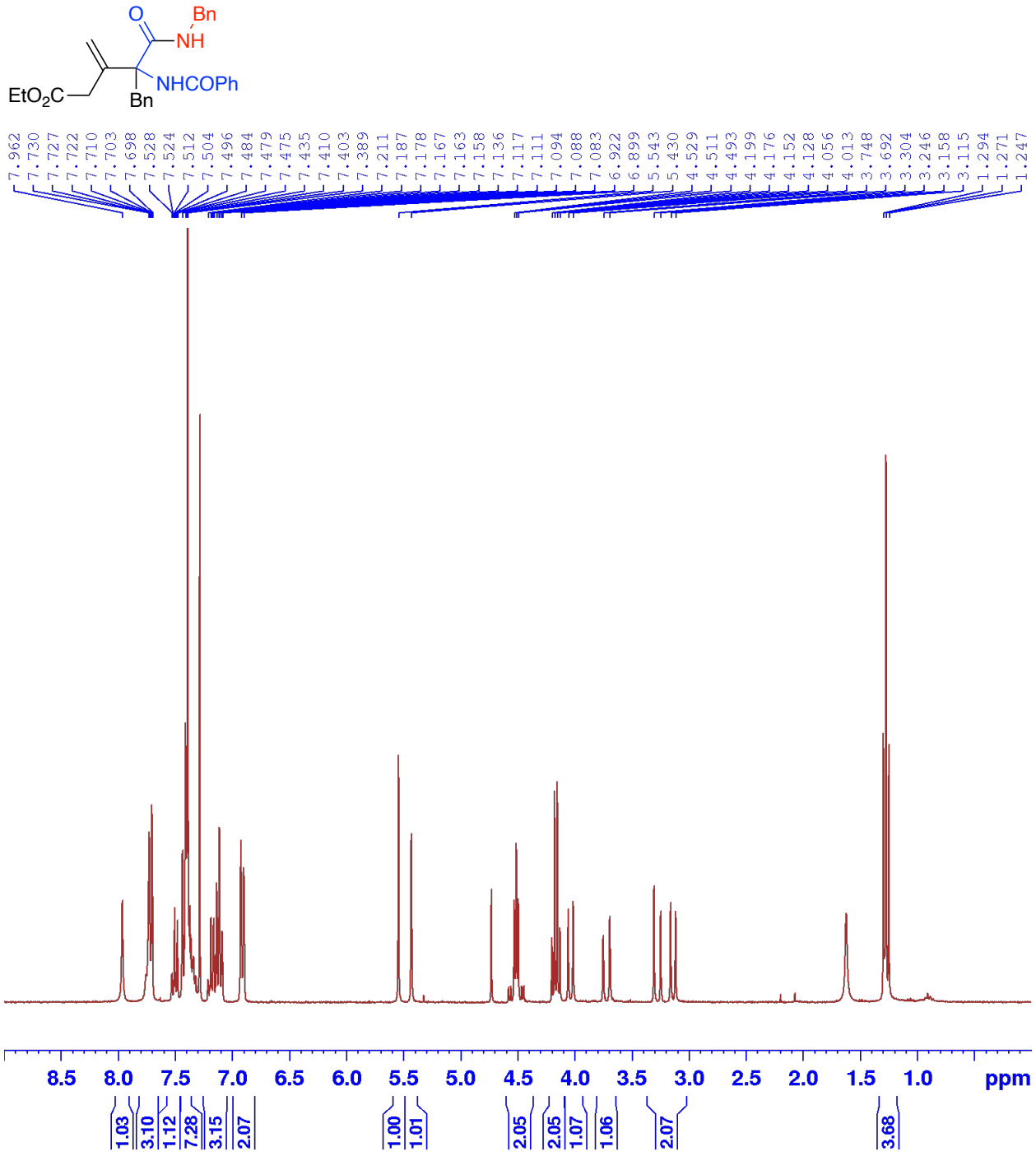



**5p**

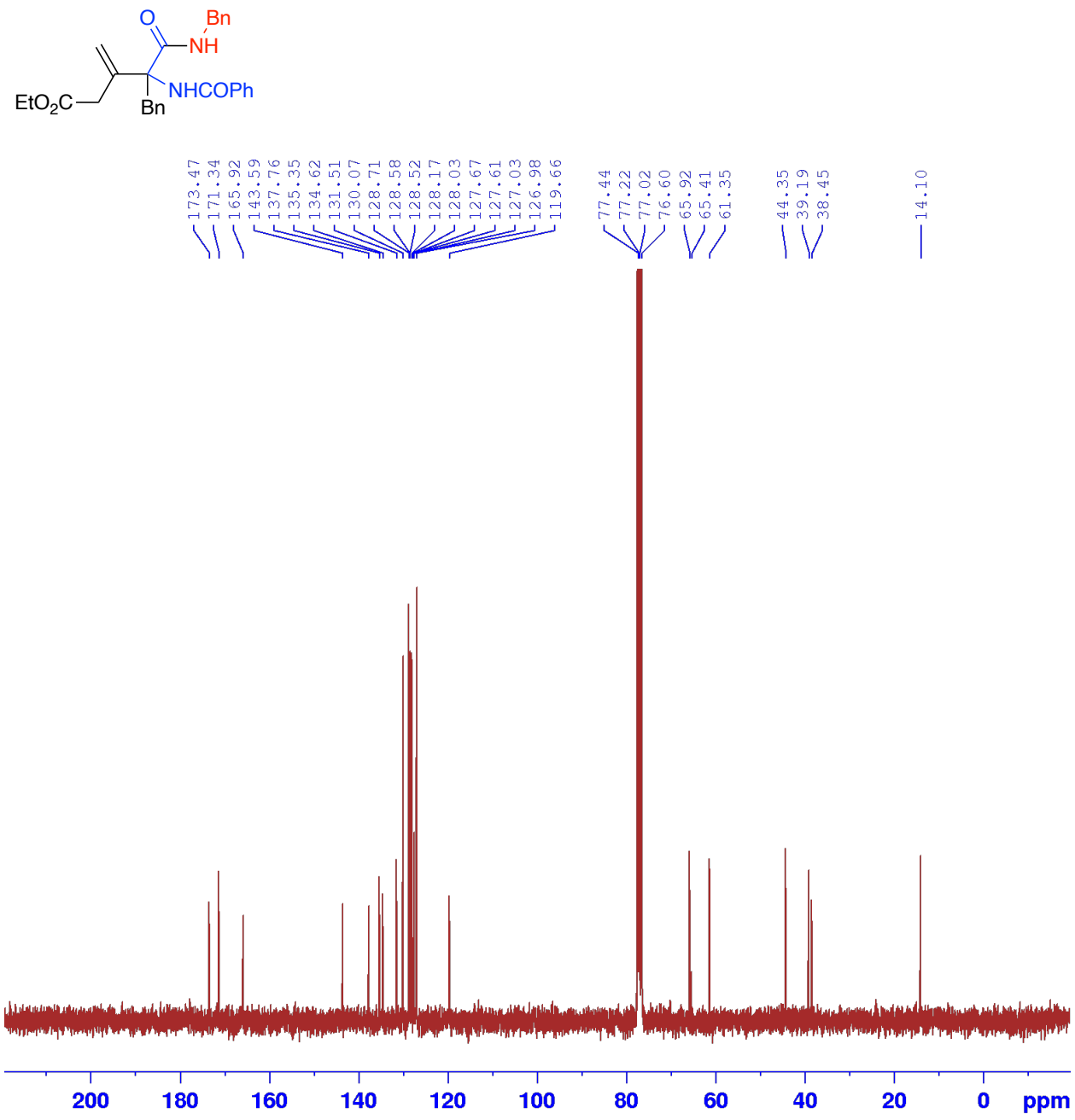


## NMR spectra of compound 6a

**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)

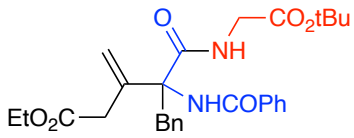


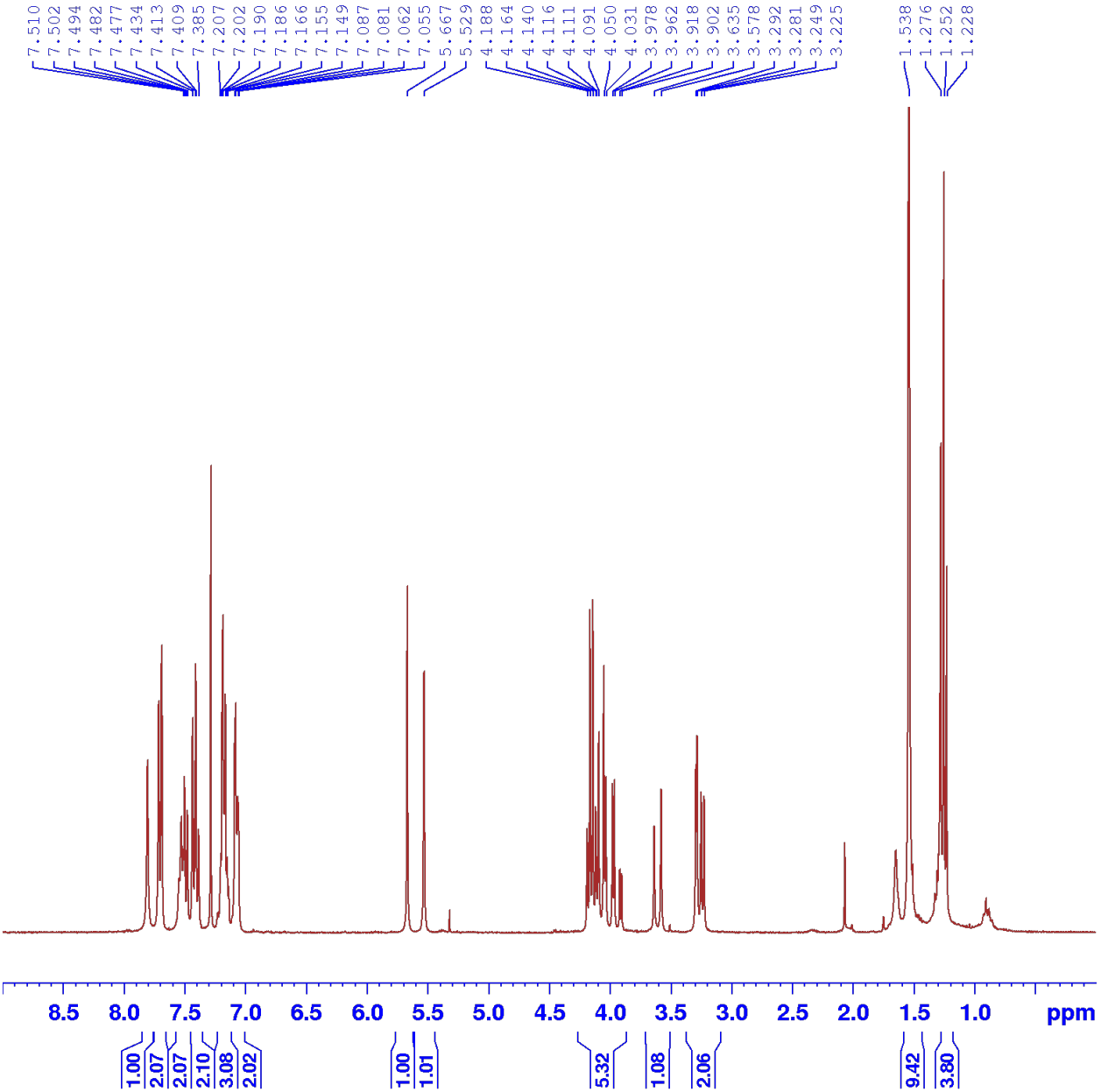
**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)



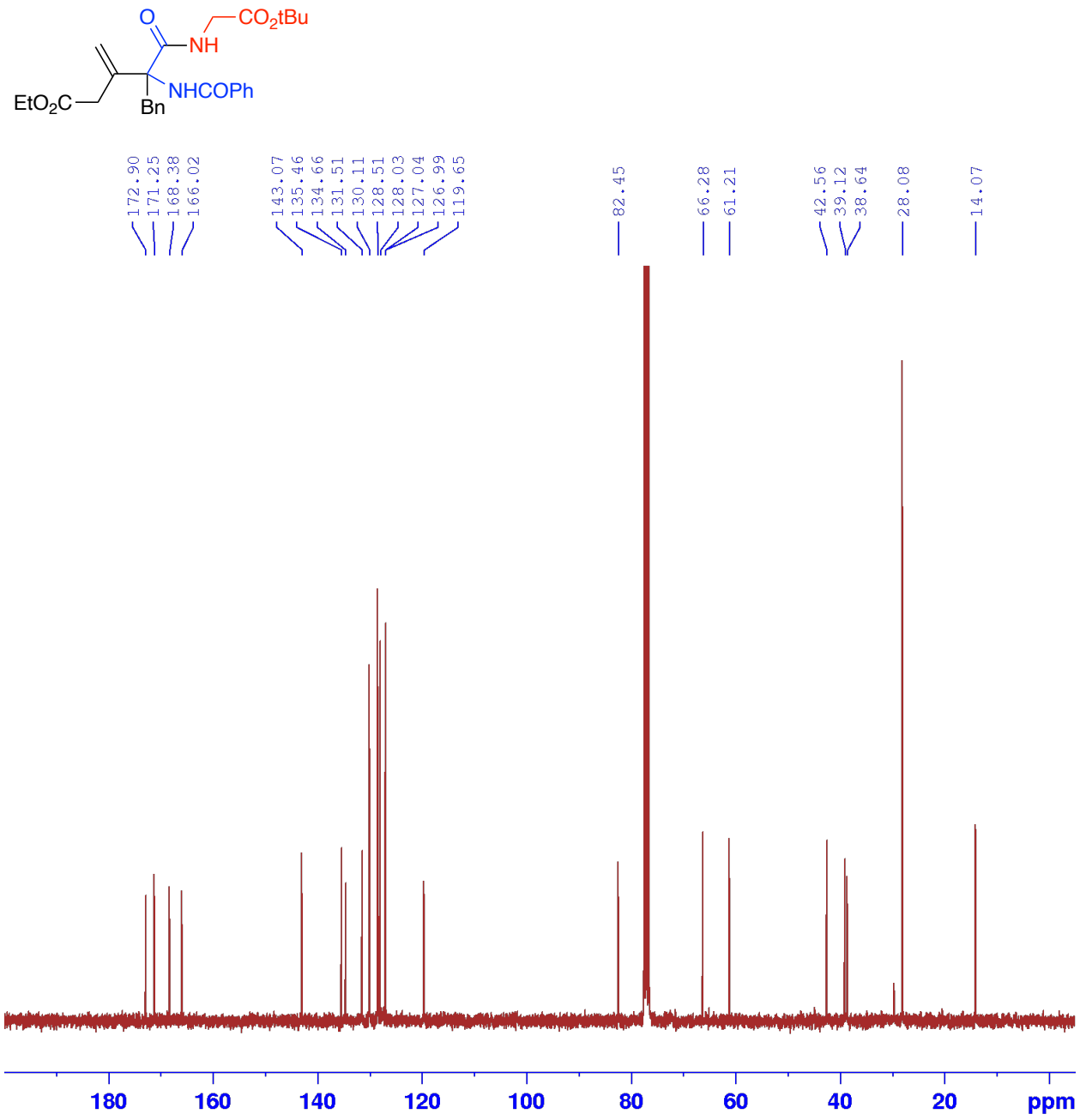
## NMR spectra of compound 6b

**$^1$H NMR** (300 MHz, $CDCl_3$, 298 K)



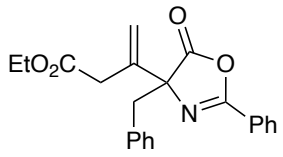



**$^{13}$C NMR** (75 MHz, $CDCl_3$, 298 K)

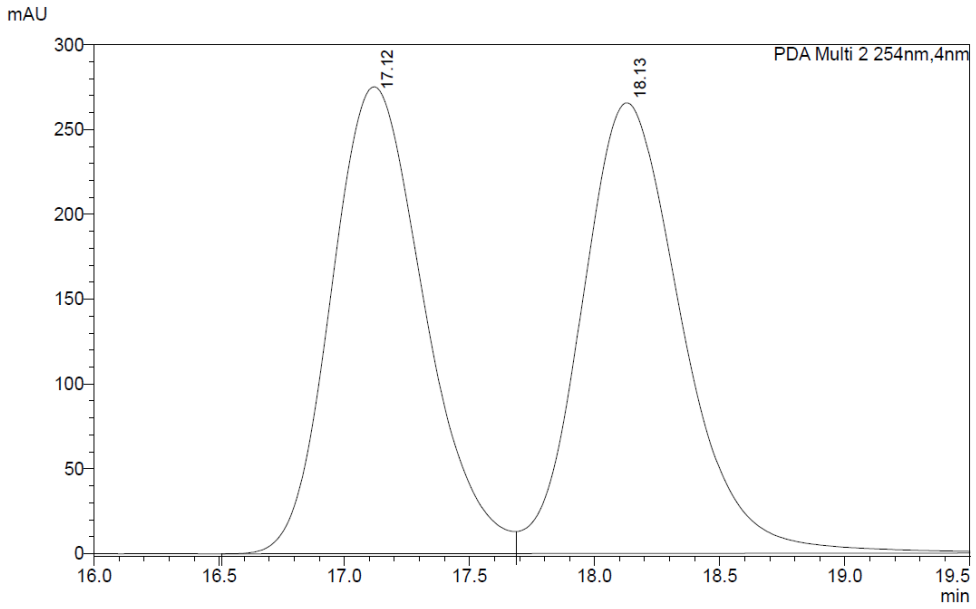


# 5. HPLC Chromatograms

## HPLC traces of compound 5a



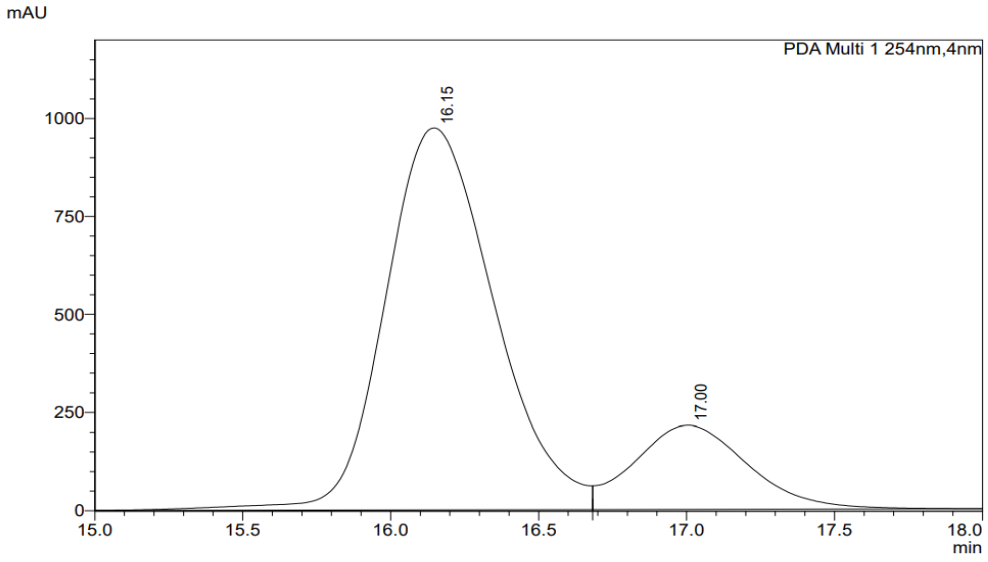

**5a**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 17.12 | 7090681 | 48.98 |
| 2 | 18.13 | 7387342 | 51.02 |
| Total | | 14478023 | 100.00 |

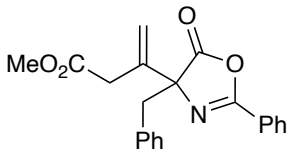



Peak Table

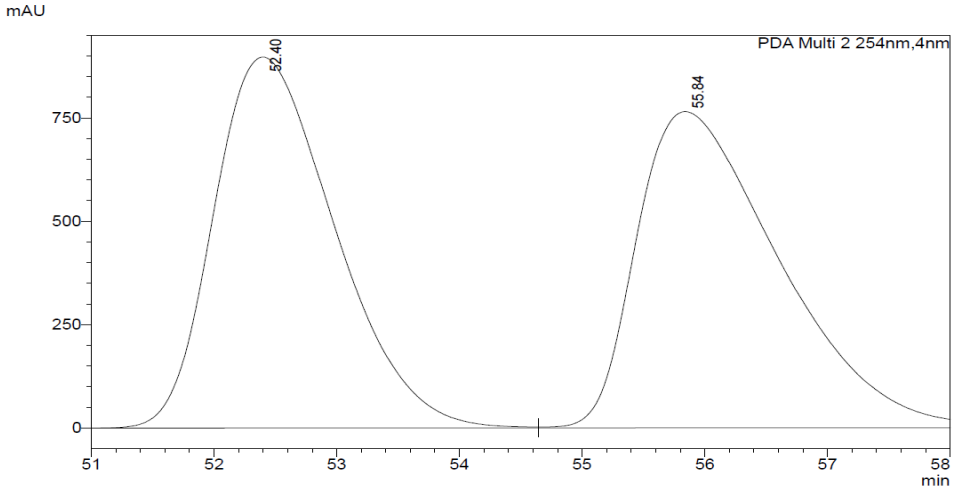
PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 16.15 | 24915611 | 81.41 |
| 2 | 17.00 | 5689961 | 18.59 |
| Total | | 30605572 | 100.00 |

## HPLC traces of compound 5b



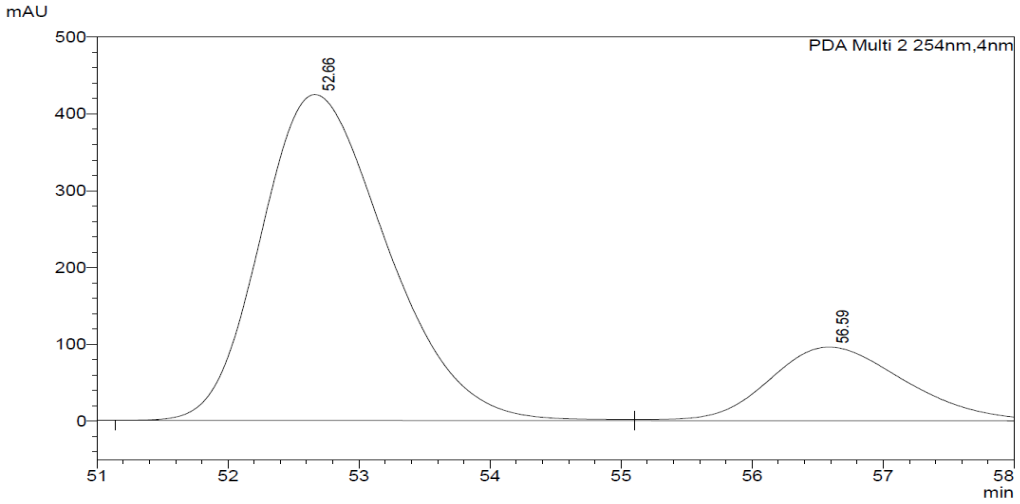

**5b**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 52.40 | 61451526 | 49.72 |
| 2 | 55.84 | 62152914 | 50.28 |
| Total | | 123604440 | 100.00 |

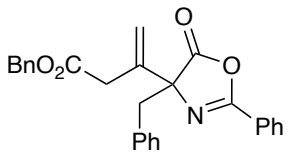



Peak Table

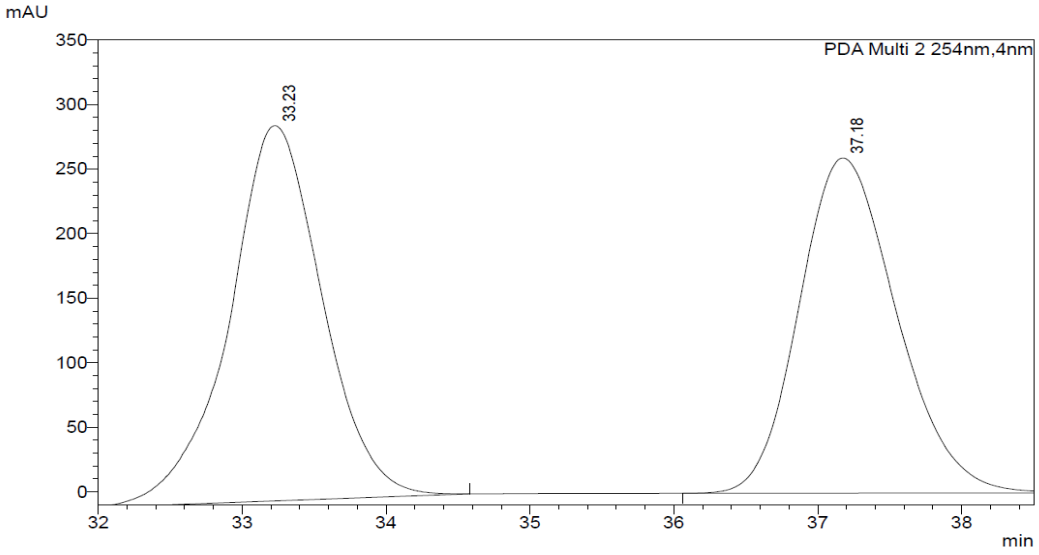
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 52.66 | 28371001 | 80.41 |
| 2 | 56.59 | 6913381 | 19.59 |
| Total | | 35284382 | 100.00 |

## HPLC traces of compound 5c



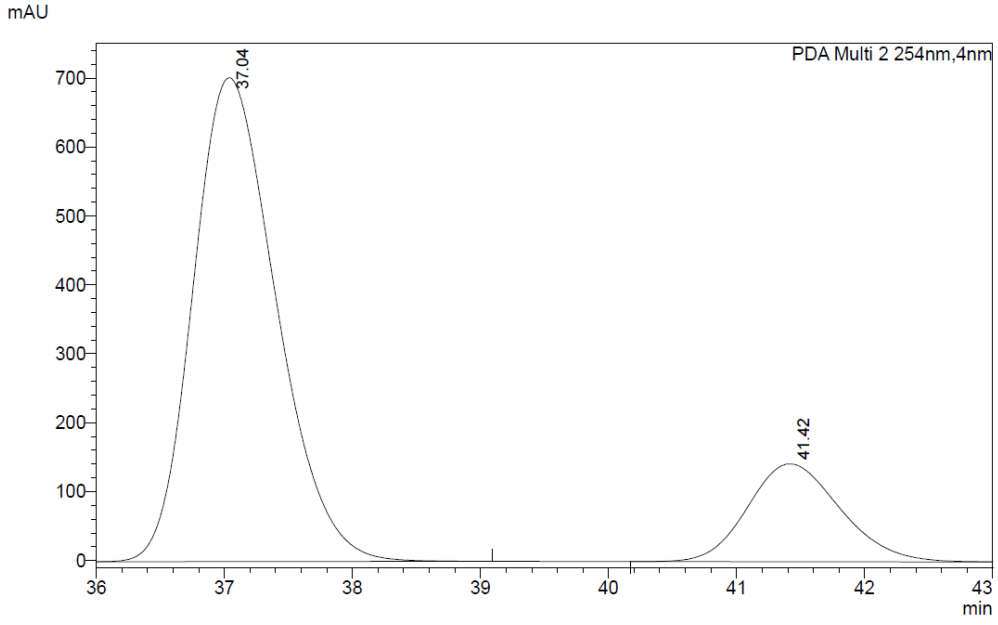

**5c**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 33.23 | 13050646 | 51.61 |
| 2 | 37.18 | 12234954 | 48.39 |
| Total | | 25285600 | 100.00 |

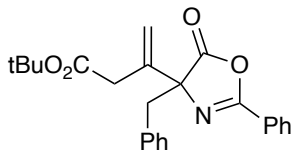



Peak Table

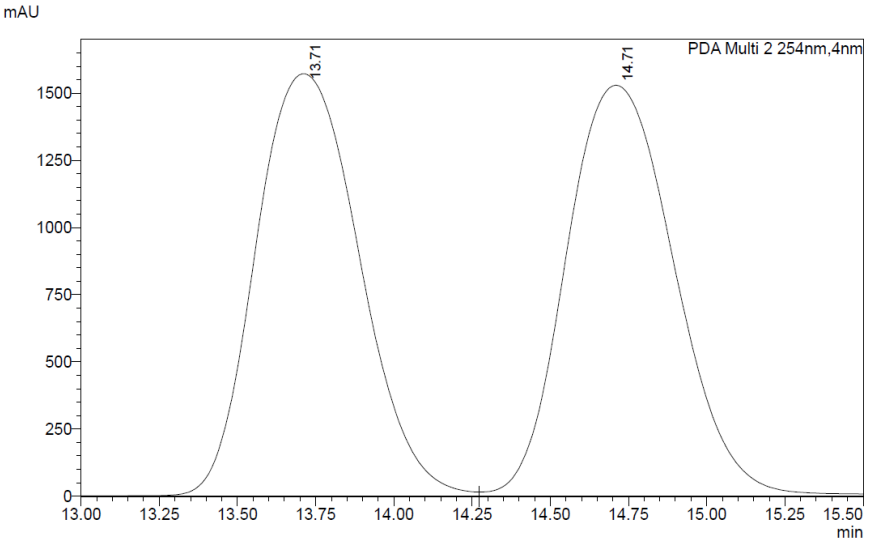
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 37.04 | 31666267 | 81.58 |
| 2 | 41.42 | 7149212 | 18.42 |
| Total | | 38815479 | 100.00 |

## HPLC traces of compound 5d



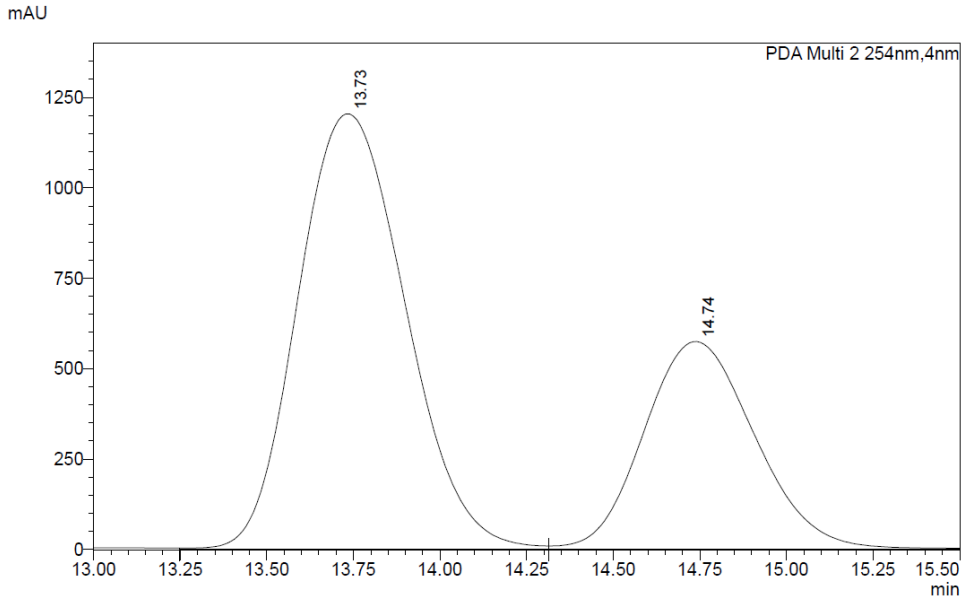

**5d**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 13.71 | 36239310 | 49.23 |
| 2 | 14.71 | 37369328 | 50.77 |
| Total | | 73608638 | 100.00 |

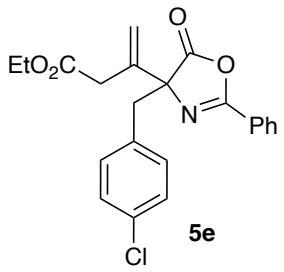



Peak Table

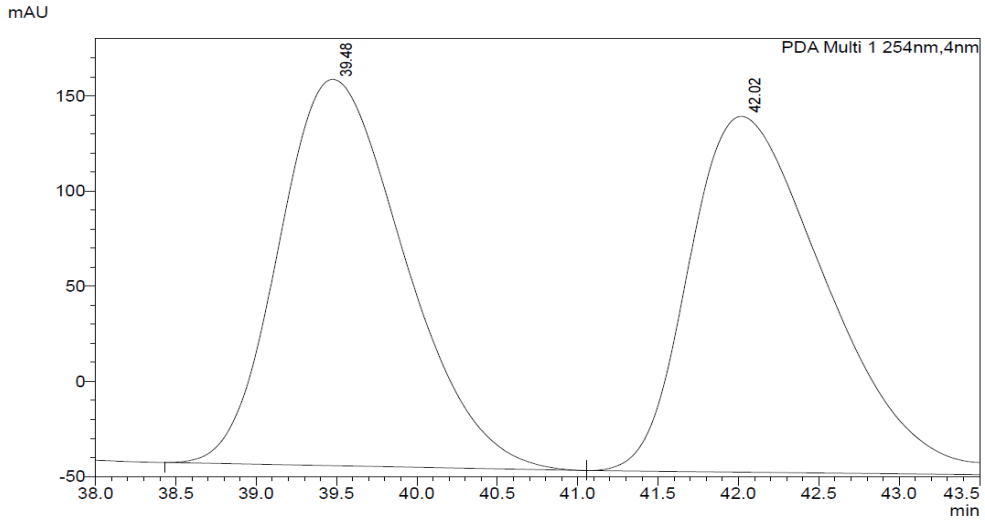
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 13.73 | 26022533 | 66.86 |
| 2 | 14.74 | 12898901 | 33.14 |
| Total | | 38921434 | 100.00 |

## HPLC traces of compound 5e



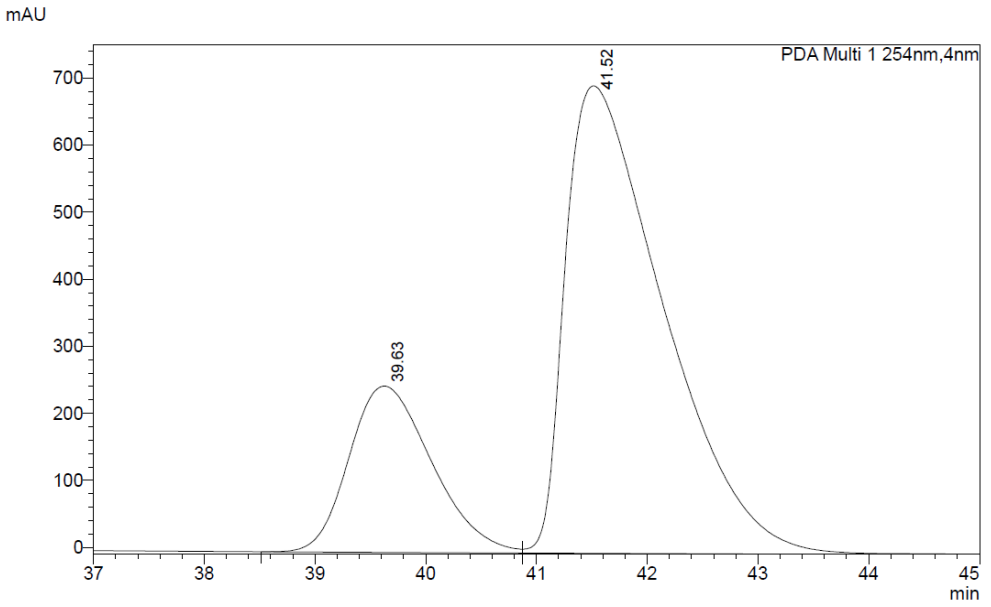

**5e**




Peak Table

PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 39.48 | 11003087 | 49.96 |
| 2 | 42.02 | 11022192 | 50.04 |
| Total | | 22025279 | 100.00 |

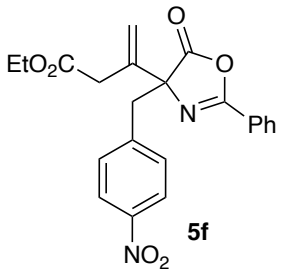



Peak Table

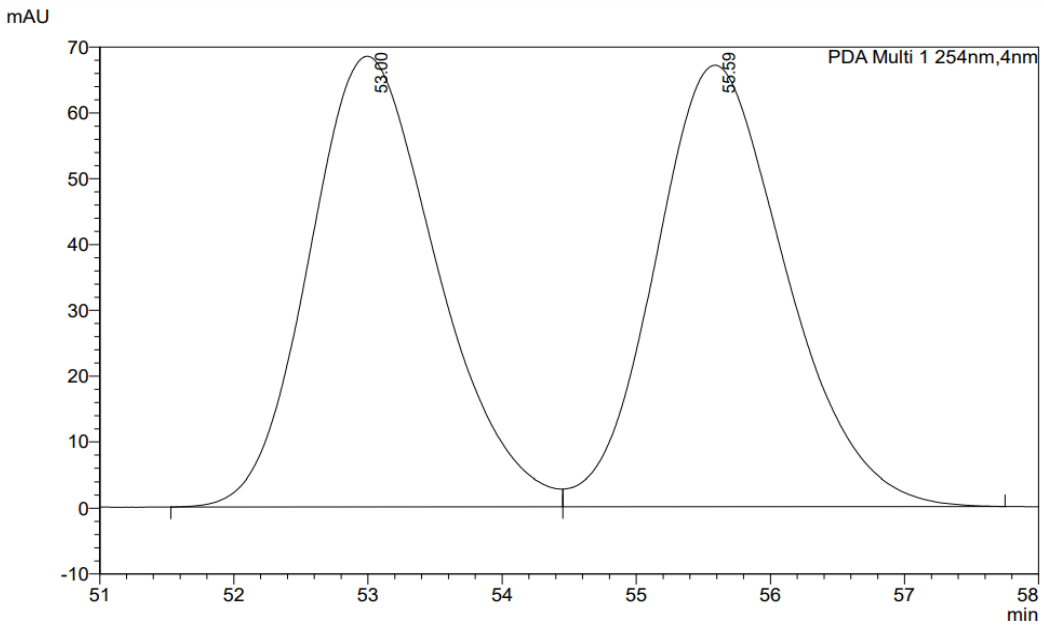
PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 39.63 | 12888472 | 23.05 |
| 2 | 41.52 | 43032898 | 76.95 |
| Total | | 55921370 | 100.00 |

## HPLC traces of compound 5f



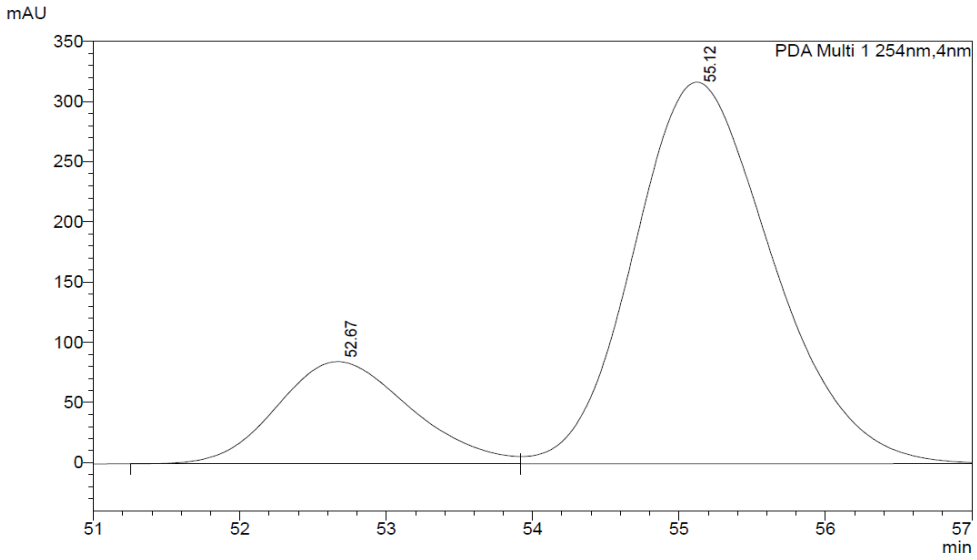

**5f**




Peak Table

PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 53.00 | 4512895 | 49.85 |
| 2 | 55.59 | 4539681 | 50.15 |
| Total | | 9052576 | 100.00 |

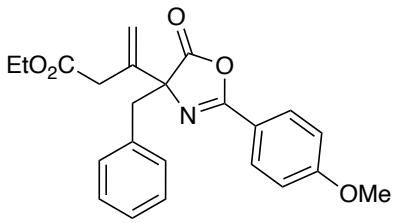



Peak Table

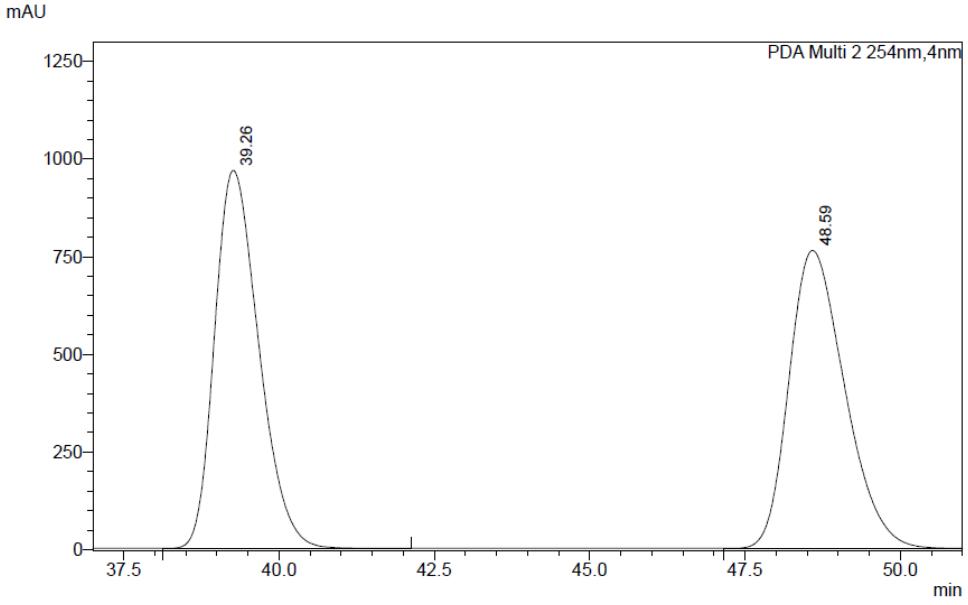
PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 52.67 | 5420086 | 20.54 |
| 2 | 55.12 | 20967253 | 79.46 |
| Total | | 26387339 | 100.00 |

## HPLC traces of compound 5g



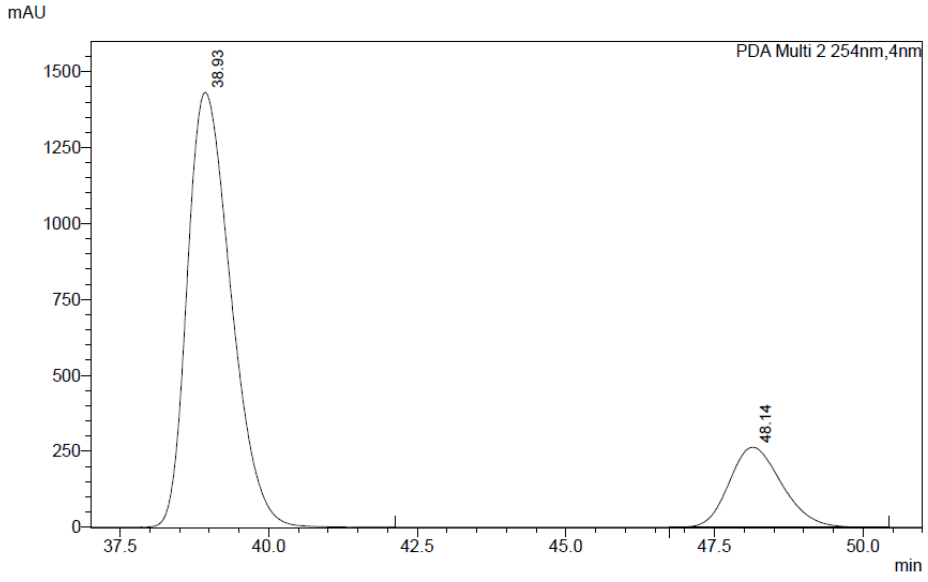

**5g**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 39.26 | 47885898 | 50.13 |
| 2 | 48.59 | 47646696 | 49.87 |
| Total | | 95532594 | 100.00 |

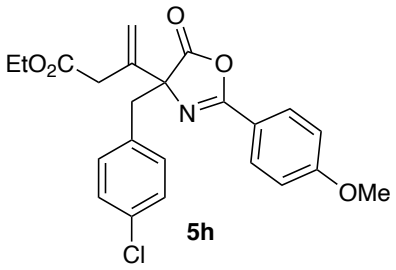



Peak Table

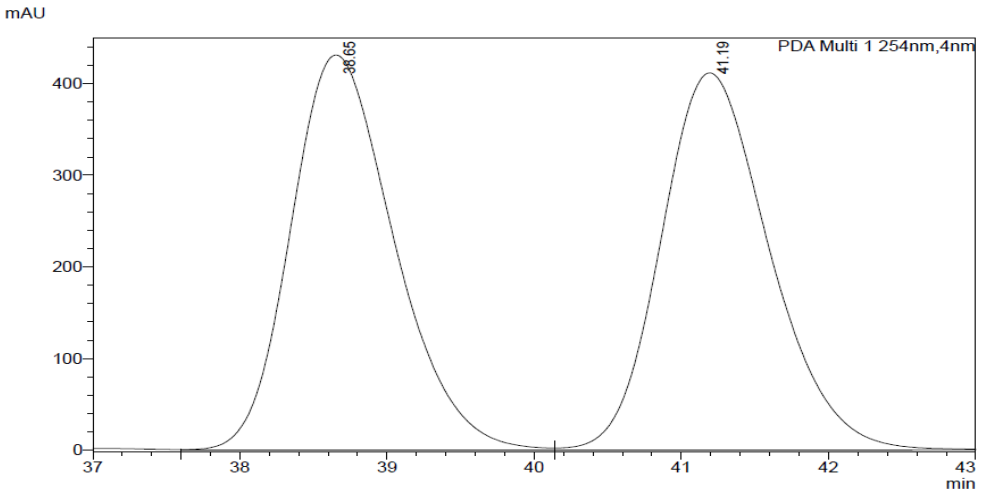
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 38.93 | 73851534 | 81.96 |
| 2 | 48.14 | 16253845 | 18.04 |
| Total | | 90105379 | 100.00 |

## HPLC traces of compound 5h



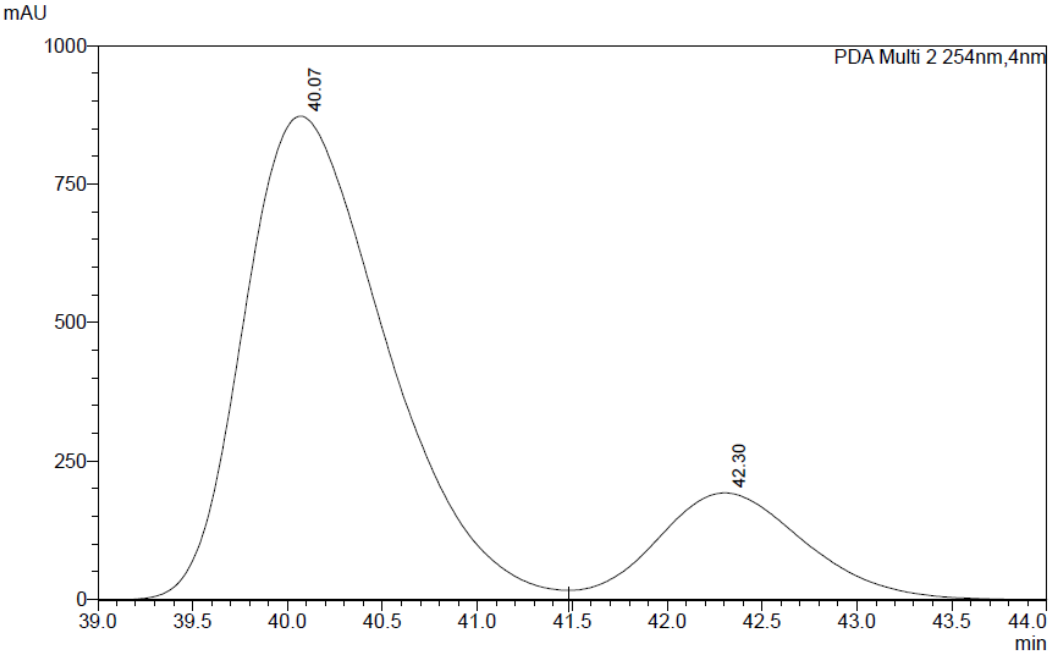

**5h**




Peak Table

PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 38.65 | 21021081 | 49.93 |
| 2 | 41.19 | 21081792 | 50.07 |
| Total | | 42102873 | 100.00 |

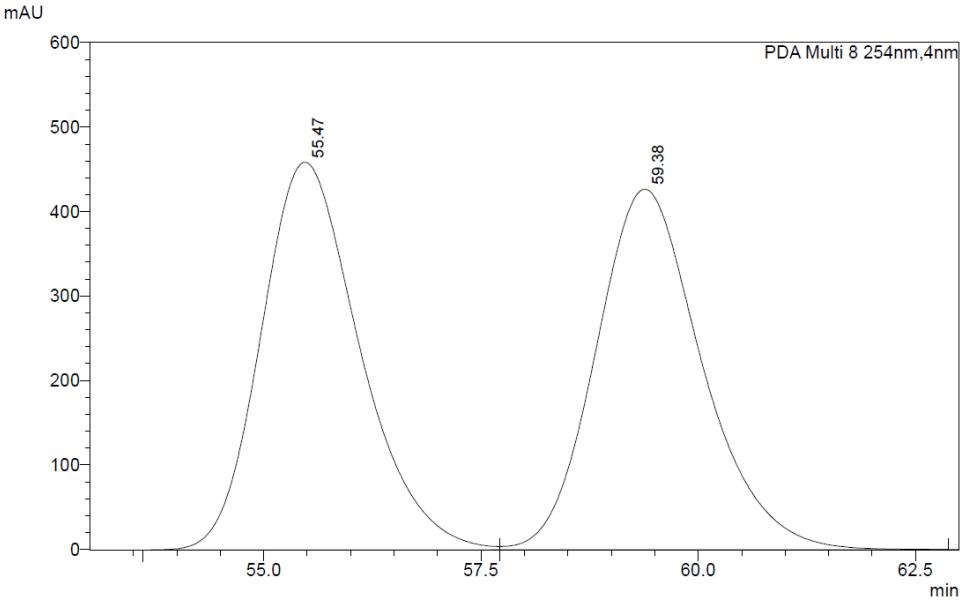



Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 40.07 | 45563752 | 81.18 |
| 2 | 42.30 | 10559991 | 18.82 |
| Total | | 56123743 | 100.00 |

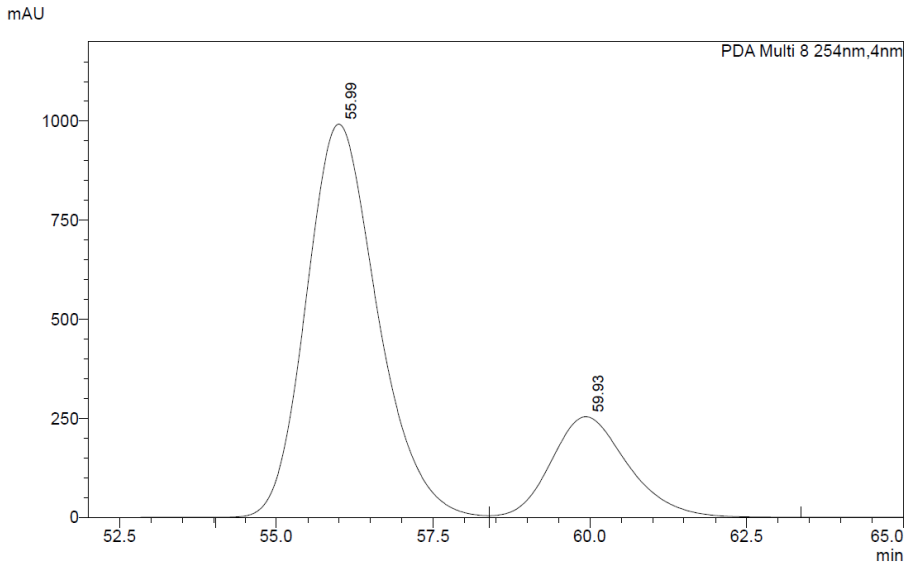
## HPLC traces of compound 5i




Peak Table

PDA Ch8 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 55.47 | 36122440 | 49.97 |
| 2 | 59.38 | 36164191 | 50.03 |
| Total | | 72286631 | 100.00 |

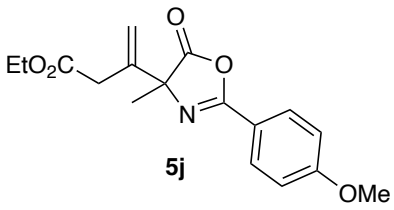



Peak Table

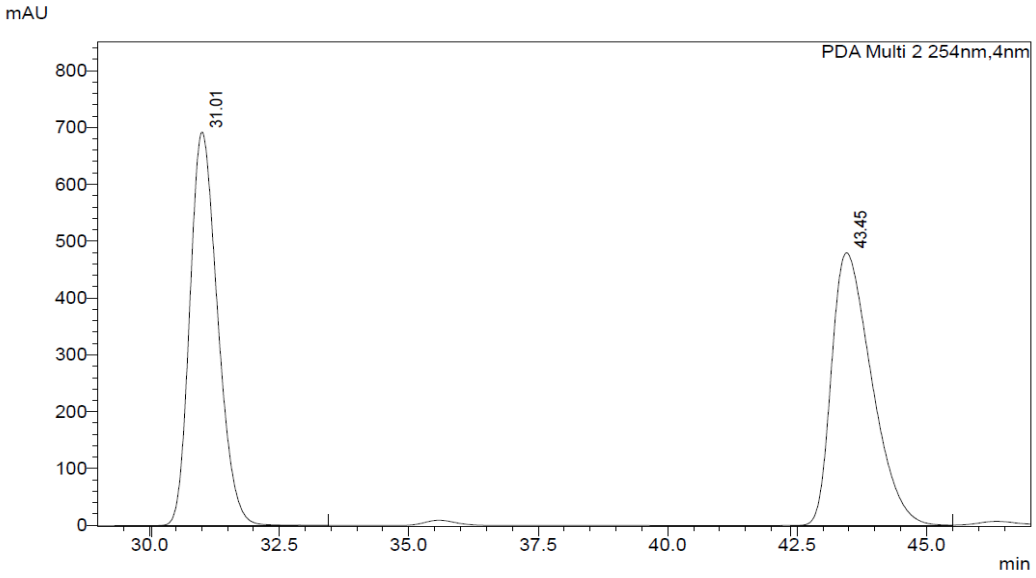
PDA Ch8 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 55.99 | 78354208 | 78.33 |
| 2 | 59.93 | 21670718 | 21.67 |
| Total | | 100024926 | 100.00 |

## HPLC traces of compound 5j



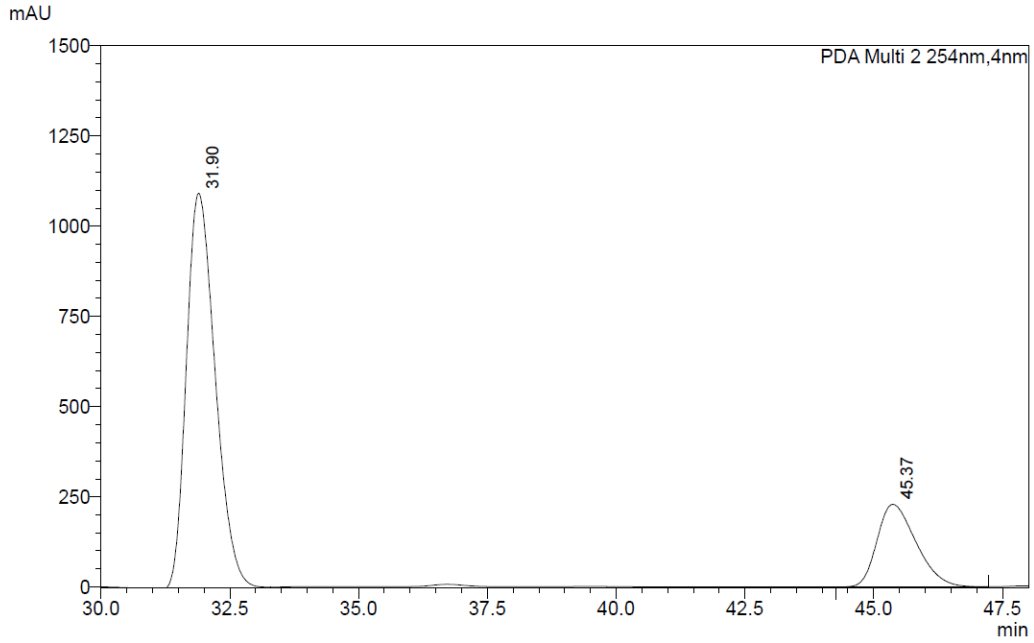

**5j**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 31.01 | 25809245 | 49.95 |
| 2 | 43.45 | 25859036 | 50.05 |
| Total | | 51668281 | 100.00 |

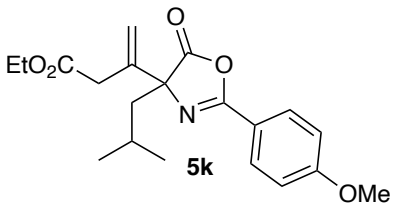



Peak Table

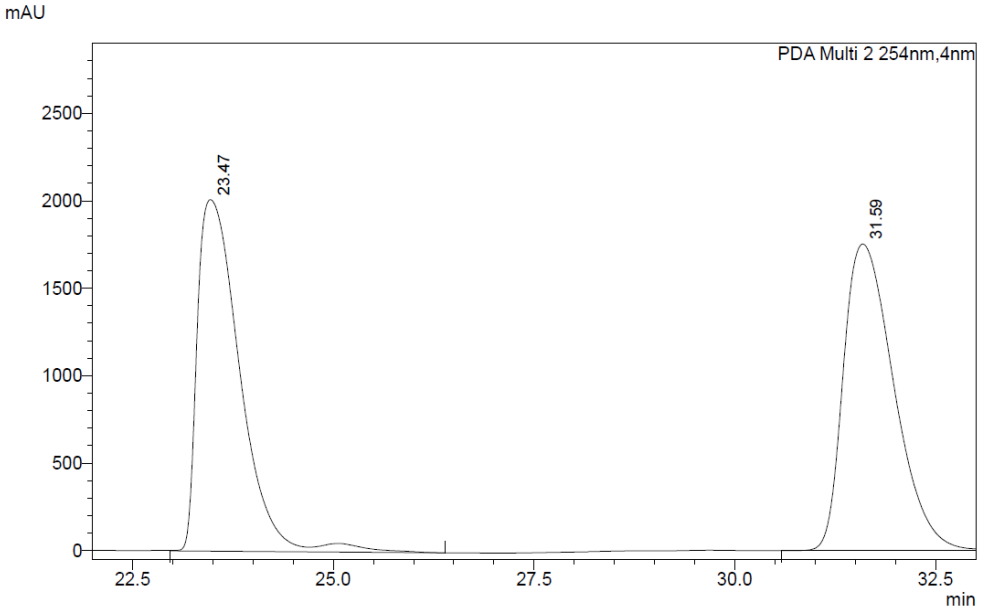
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 31.90 | 43027961 | 78.00 |
| 2 | 45.37 | 12135252 | 22.00 |
| Total | | 55163214 | 100.00 |

## HPLC traces of compound 5k



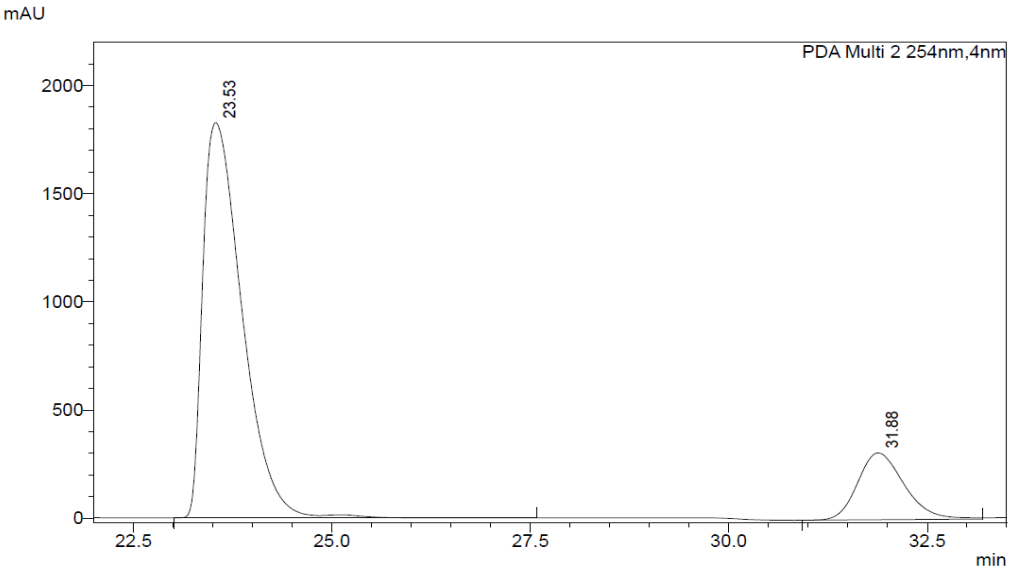

**5k**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 23.47 | 74530914 | 49.30 |
| 2 | 31.59 | 76659495 | 50.70 |
| Total | | 151190409 | 100.00 |

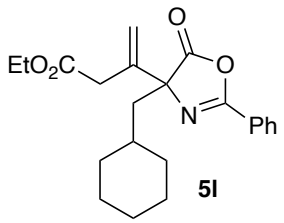



Peak Table

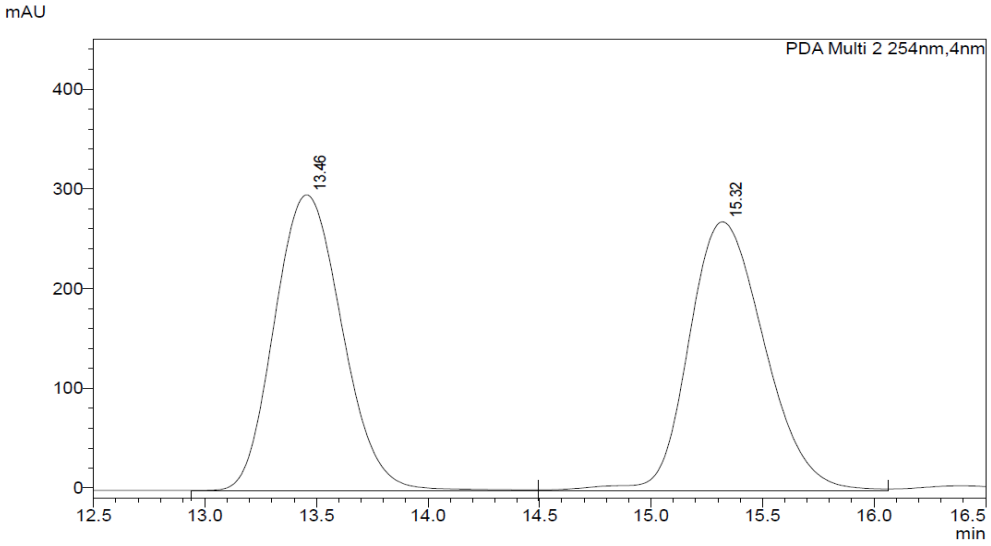
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 23.53 | 63048120 | 83.36 |
| 2 | 31.88 | 12583478 | 16.64 |
| Total | | 75631598 | 100.00 |

## HPLC traces of compound 5l



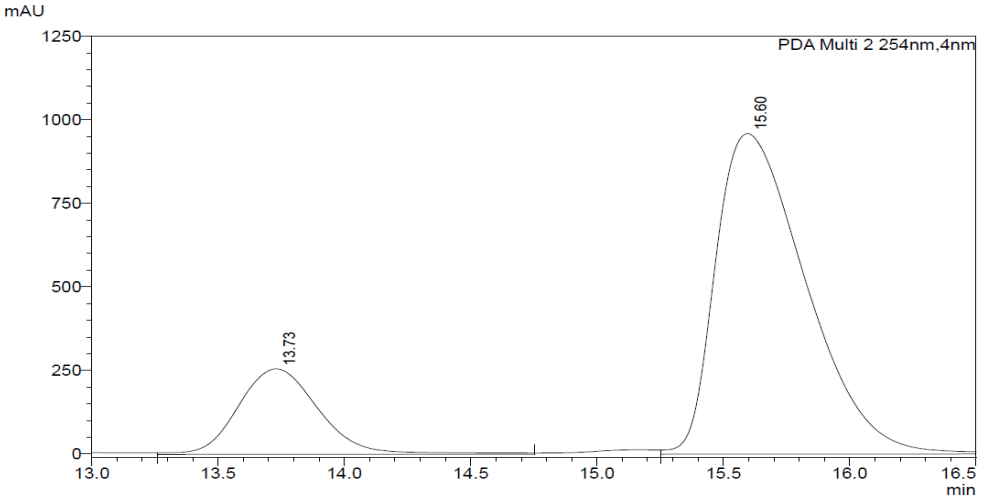

**5l**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 13.46 | 6258547 | 49.59 |
| 2 | 15.32 | 6362149 | 50.41 |
| Total | | 12620696 | 100.00 |

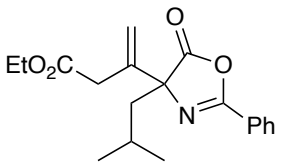



Peak Table

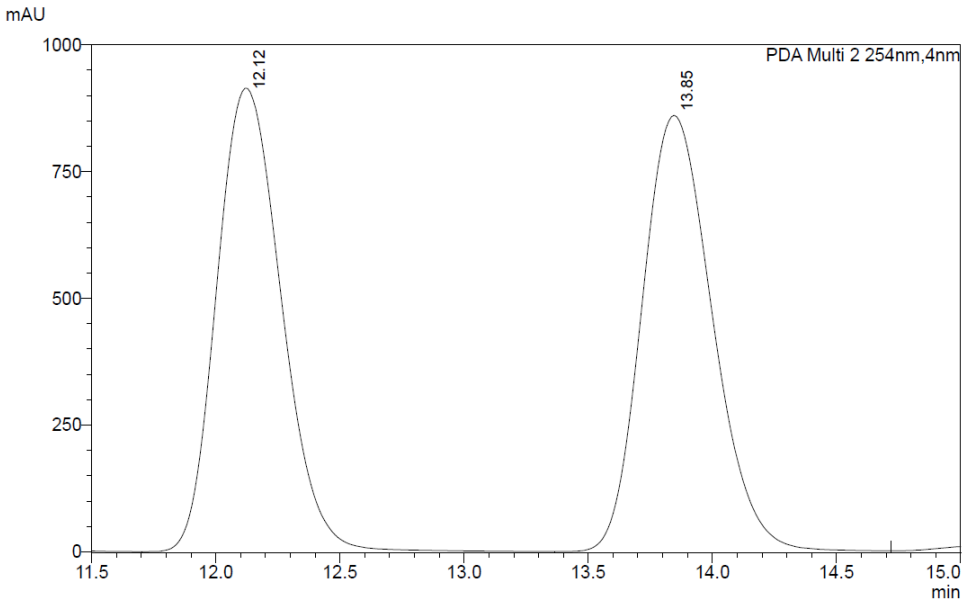
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 13.73 | 5681974 | 19.09 |
| 2 | 15.60 | 24075662 | 80.91 |
| Total | | 29757636 | 100.00 |

## HPLC traces of compound 5m



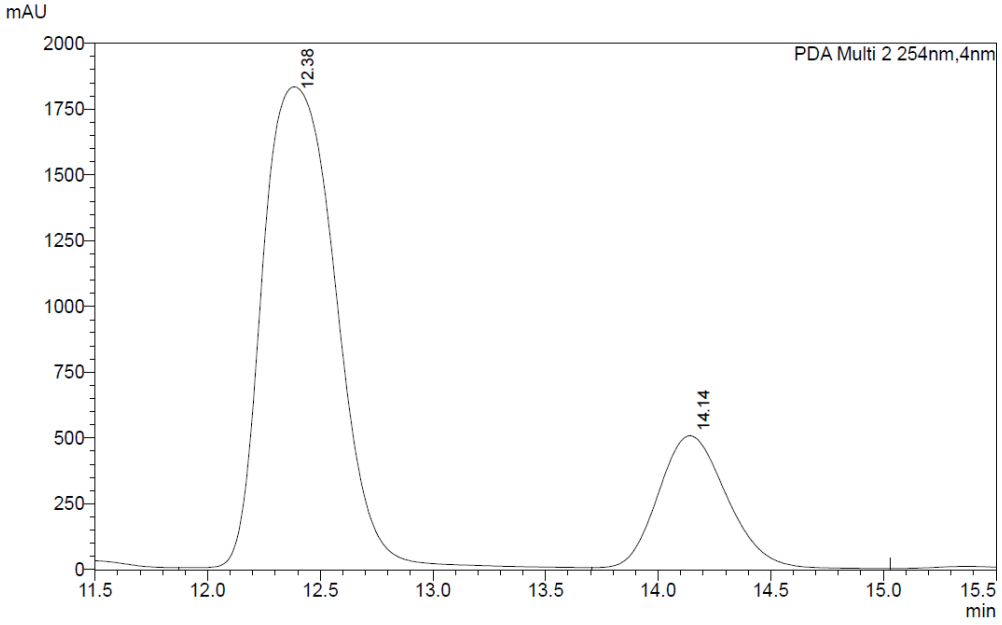

**5m**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 12.12 | 16858574 | 49.63 |
| 2 | 13.85 | 17106534 | 50.37 |
| Total | | 33965107 | 100.00 |

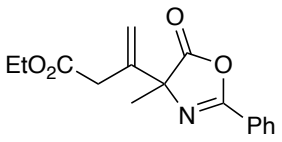



Peak Table

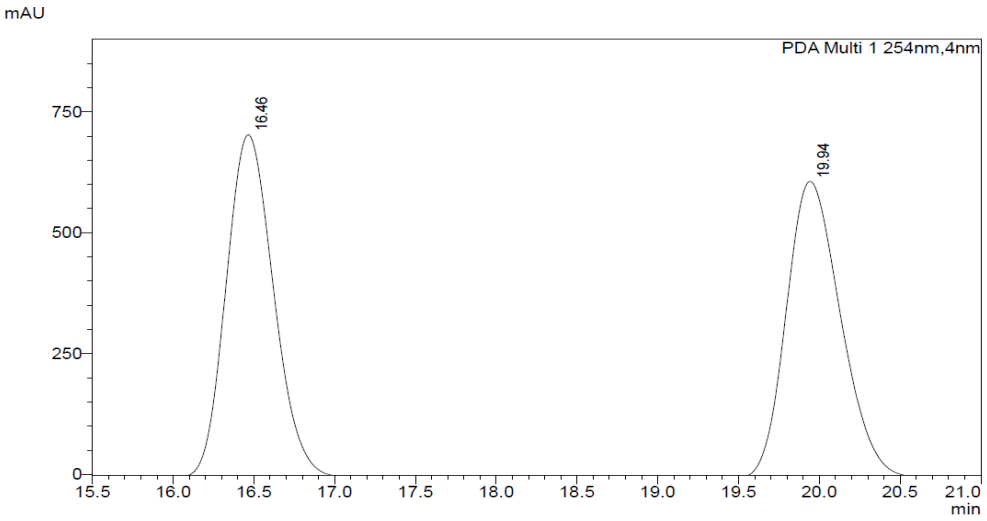
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 12.38 | 42338909 | 79.09 |
| 2 | 14.14 | 11193623 | 20.91 |
| Total | | 53532533 | 100.00 |

## HPLC traces of compound 5n



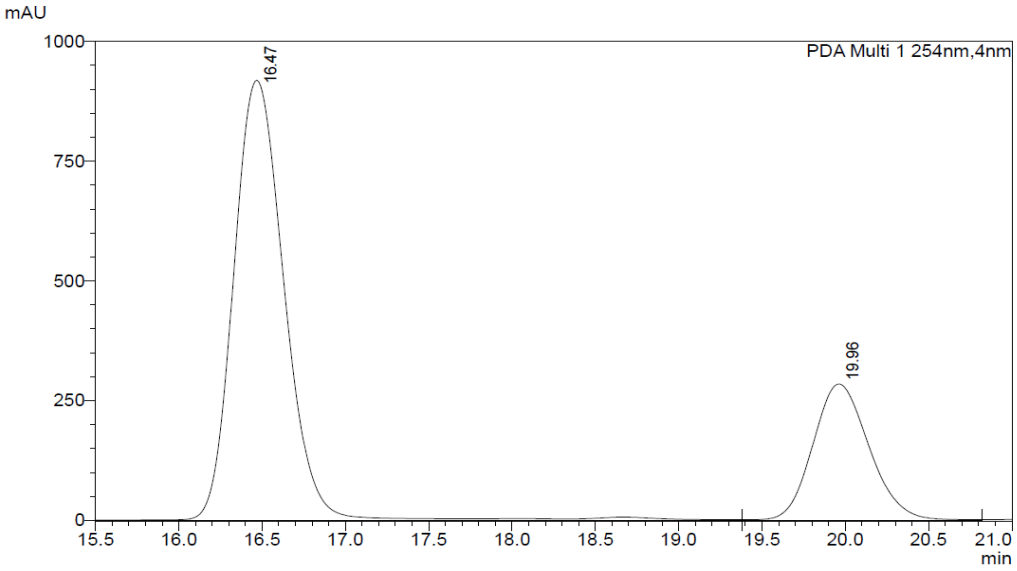

**5n**




Peak Table

PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 16.46 | 14552051 | 49.75 |
| 2 | 19.94 | 14698394 | 50.25 |
| Total | | 29250445 | 100.00 |

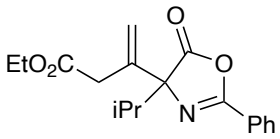



Peak Table

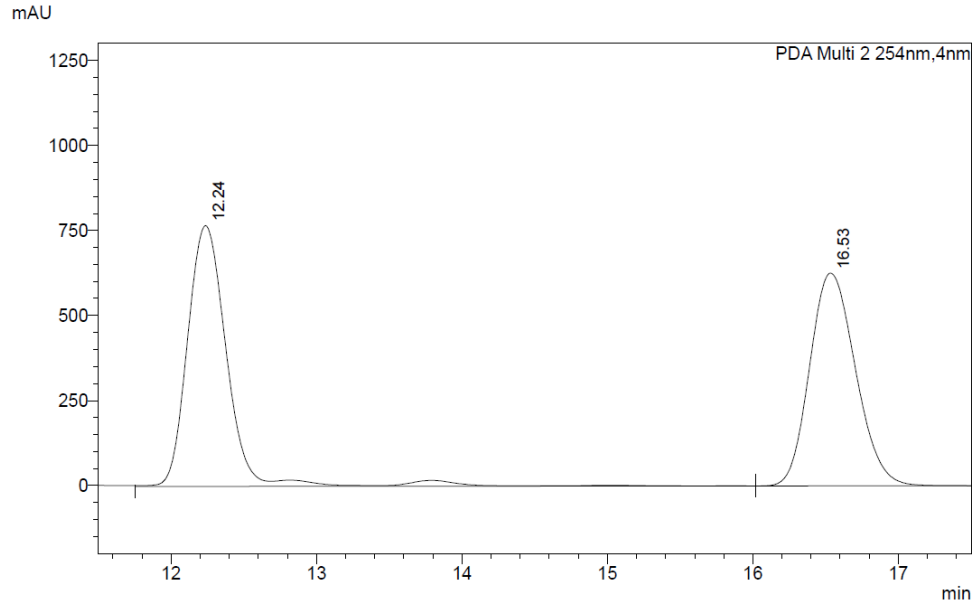
PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 16.47 | 19567857 | 74.55 |
| 2 | 19.96 | 6678516 | 25.45 |
| Total | | 26246373 | 100.00 |

## HPLC traces of compound 5o



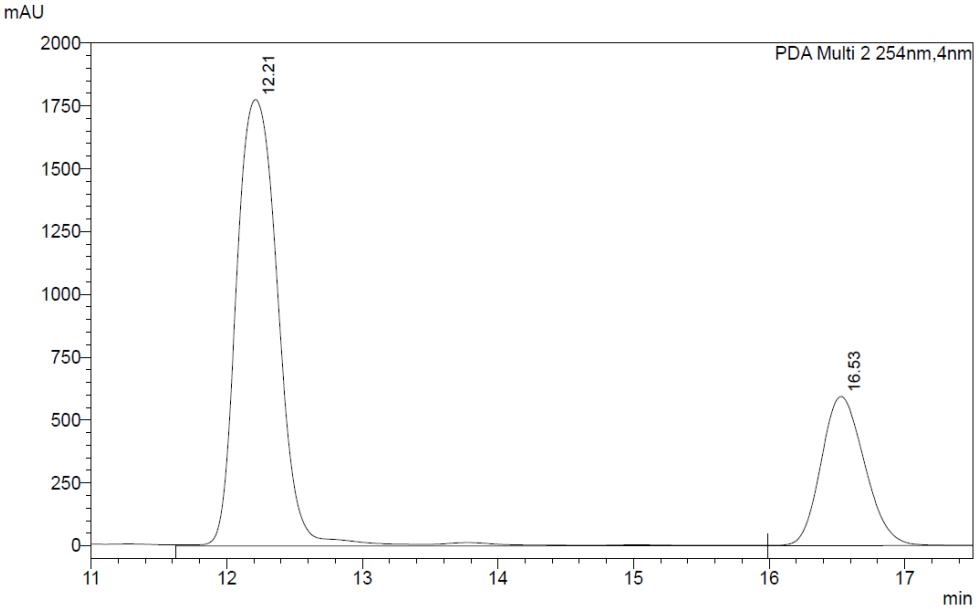

**5o**




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 12.24 | 14733960 | 51.77 |
| 2 | 16.53 | 13726796 | 48.23 |
| Total | | 28460757 | 100.00 |

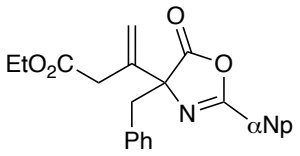



Peak Table

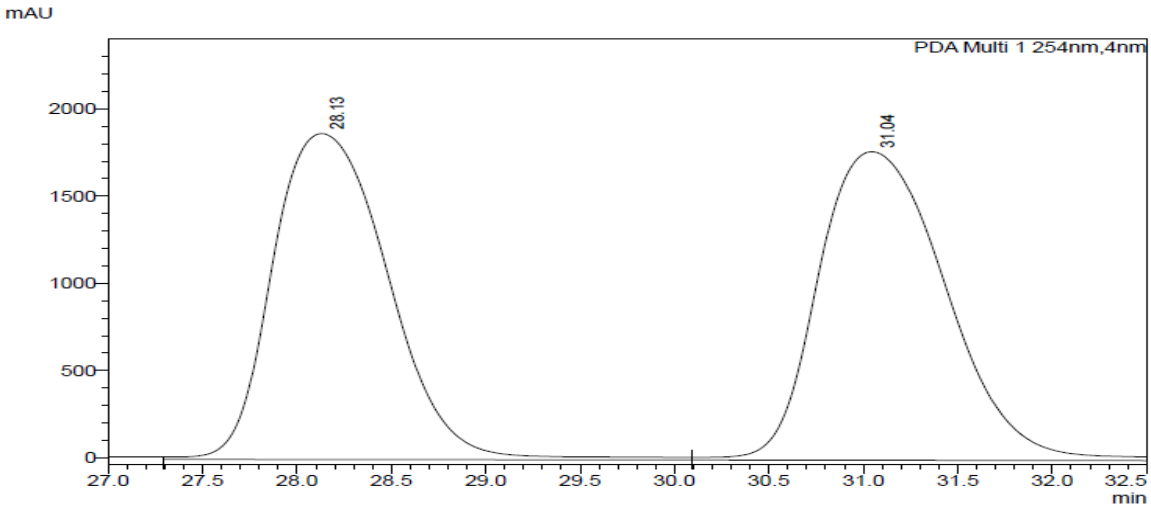
PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 12.21 | 38245981 | 74.18 |
| 2 | 16.53 | 13315363 | 25.82 |
| Total | | 51561344 | 100.00 |

## HPLC traces of compound 5p



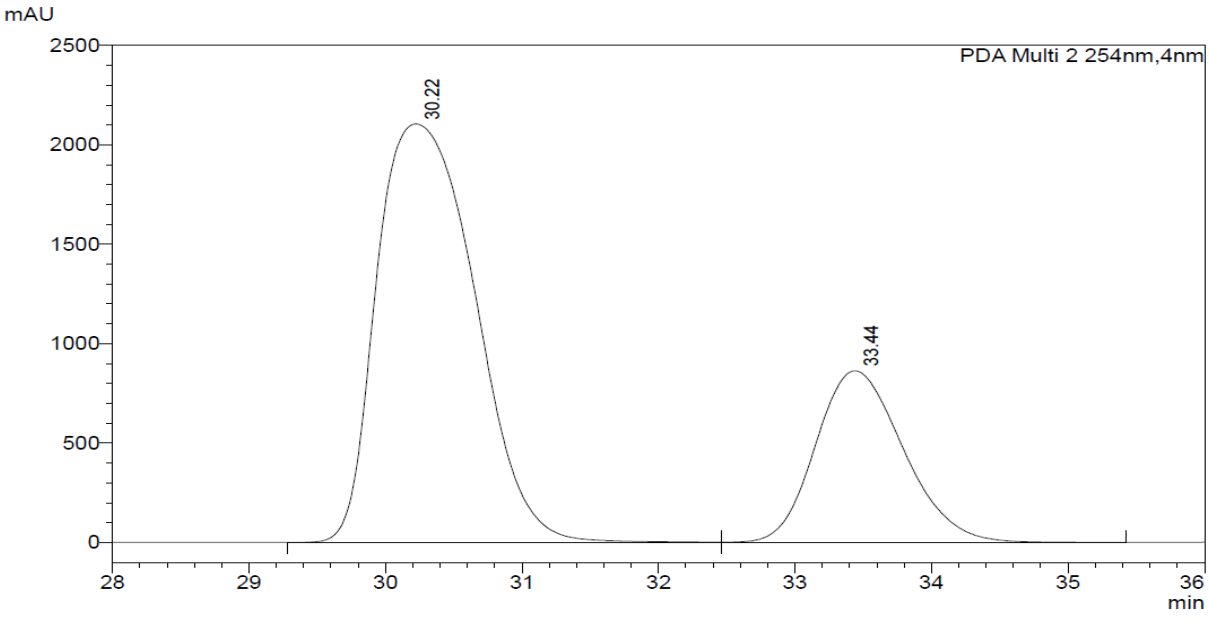

**5p**




Peak Table

PDA Ch1 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 28.13 | 79700929 | 46.66 |
| 2 | 31.04 | 91121437 | 53.34 |
| Total | | 170822366 | 100.00 |




Peak Table

PDA Ch2 254nm

| Peak# | Ret. Time | Area | Area% |
|---|---|---|---|
| 1 | 30.22 | 105150834 | 73.15 |
| 2 | 33.44 | 38586996 | 26.85 |
| Total | | 143737830 | 100.00 |