A facile synthesis of β-amino carbonyl compounds through an aza-Michael addition reaction under solvent-free conditions

Chao Huang,*[ab] Yanqing Yin,[a] Jiahui Guo,[a] Jiong Wang,[ab] Baomin Fan,[ab] Lijuan Yang*[ab]

[a]*Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission & Ministry of Education, Yunnan University of Nationalities, Kunming, 650500, China*

[b]*Engineering Research Center of Biopolymer Functional Materials of Yunnan, Yunnan University of Nationalities, Kunming, 650500, China*

*Corresponding author. Tel.: +86 871 65910017; fax: +86 871 65910017.

E-mail: huang.chao@hotmail.com (C. Huang)

Supporting Information

Table of Contents

General Method

All compounds were fully characterized by spectroscopic techniques. The NMR spectra were recorded on a Bruker-Avance 400 MHz spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz) with tetramethylsilane (TMS) as the internal standard (δ 0.0 ppm), chemical shifts (δ) are expressed in ppm, and J values are given in Hz. Deuterated $CDCl_3$ was used as a solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using neutral alumina. The melting points were determined on an XT-4A melting point apparatus and are uncorrected. HRMS was performed on an Agilent LC-MSD TOF instrument.

All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on neutral alumina.

Preparatiotion of diethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate 1.

Diethyl acetylenedicarboxylate 12 mmol and furan 60 mmol were placed in a sealed tube, which was heated at 100 ^{o}C for 20 hours. The reaction mixture was distilled under vacuum. The endoxide was obtained as a light yellow oil.[1]

General Procedure for the Synthesis of oxanorbornene β-amino esters 3.

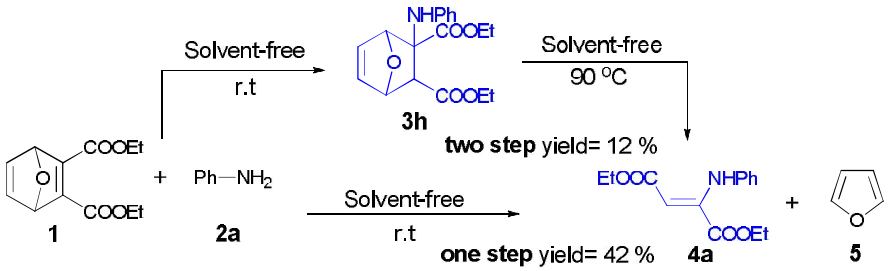
A schlenk was charged with **1** (0.4 mmol, 95.3 mg), amine **2** (0.8 mmol), and the solution was stirred for 1 minute to 6 days at room temperature until the **1** was completely consumed. The mixture was purified by flash column chromatography. The desired compounds (**3a**–**3j**) were formed from **1** in yields: 54-97%.

General Procedure for the Synthesis of β-enamine esters 4.

A Schlenk was charged with diethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate **1** (0.4 mmol, 95.3 mg), amine **2** (0.8 mmol), and the solution was stirred for 1 minute to 6 days at 90 ^{o}C until **1** was completely consumed. The mixture was purified by flash column chromatography. The desired compounds **4** were formed from **1** in yields 42-77%.

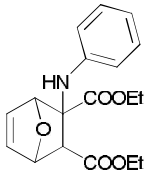
Synthesis of β-amino carbonyl compounds 3h and 4a

The β-amino carbonyl compound **4a** was prepared during the formation of β-amino carbonyl compound **3h.** According to experimental results (scheme 1), **4a** and **5** can be obtained directly with 42% yield from oxabornene **1** and aniline **2a** under room temperature without reagent and catalyst. Also, compound **4a** and **5** were obtained from thermal degradation of **3h** at 90 ^{o}C, identified by spectroscopy.



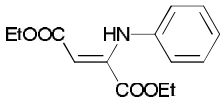
Scheme 1. Synthesis of β-amino carbonyl compounds **3h** and **4a**

Diethyl 2-(phenylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3h):



Yield 62%; White solid; mp: 107-108 ^{o}C; IR (KBr) (ν_{max}, cm^{-1}) 3385, 2974, 2331, 1735, 1604, 1511, 1449, 1377, 1321, 1254, 1062, 1011, 859, 749, 689, 551 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.16 (2H, m), 6.84-6.80 (4H, m), 6.47-6.46 (1H, dd, J = 5.8, 1.9 Hz), 5.15-5.14 (1H, m), 5.06-5.05 (1H, m), 4.41 (1H, s), 4.20-4.09 (4H, m), 3.19 (1H, d, J = 4.4Hz), 1.30 (3H, t, J = 7.2 Hz), 1.15 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 169.8, 144.9, 138.3, 132.3, 129.1, 119.5, 115.8, 86.5, 80.6, 72.4, 61.9, 61.2, 58.2, 14.1, 14.0. HRMS (TOF ES^{+}): *m/z* calcd for $C_{18}H_{22}NO_5^{+}$ [(M+H)$^{+}$], 332.1492; found, 332.1483.

Diethyl 2-(phenylamino)maleate (4a):



Yield 77%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3279, 2984, 2344, 1735, 1668, 1607, 1498, 1382, 1274, 1208, 1137, 1039, 861, 755, 693, 553 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (1H, s), 7.30-7.25 (2H, m), 7.11-7.07 (1H, m), 6.92 (2H, d, J = 7.7 Hz), 5.38 (1H, s), 4.22-4,13 (4H, m), 1.30 (3H, t, J = 7.1 Hz), 1.09 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 164.5, 148.5, 140.5, 129.2, 124.3, 121.1, 93.9, 62.2, 60.1, 14.5, 13.7. HRMS (TOF ES^{+}): m/z calcd for $C_{14}H_{17}NO_4Na^{+}$ [(M+Na)$^{+}$], 286.1050; found, 286.1055.

^{1}H and ^{13}C NMR Spectra of Compounds 3a-3k, 4a-4f

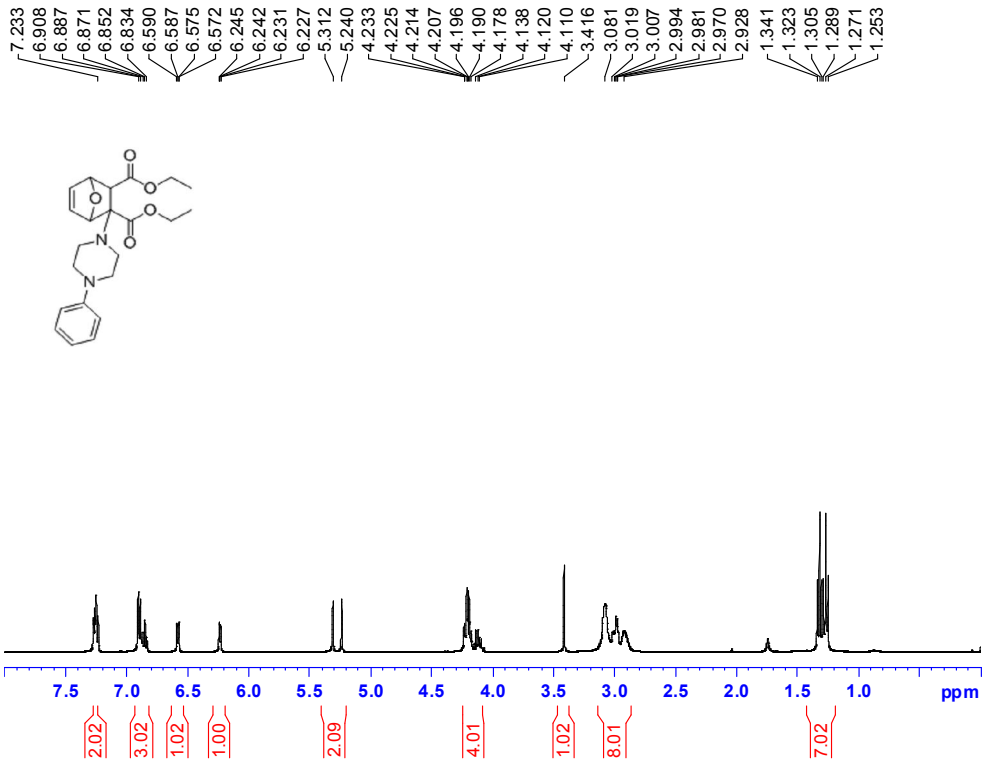


Figure 1 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3a**

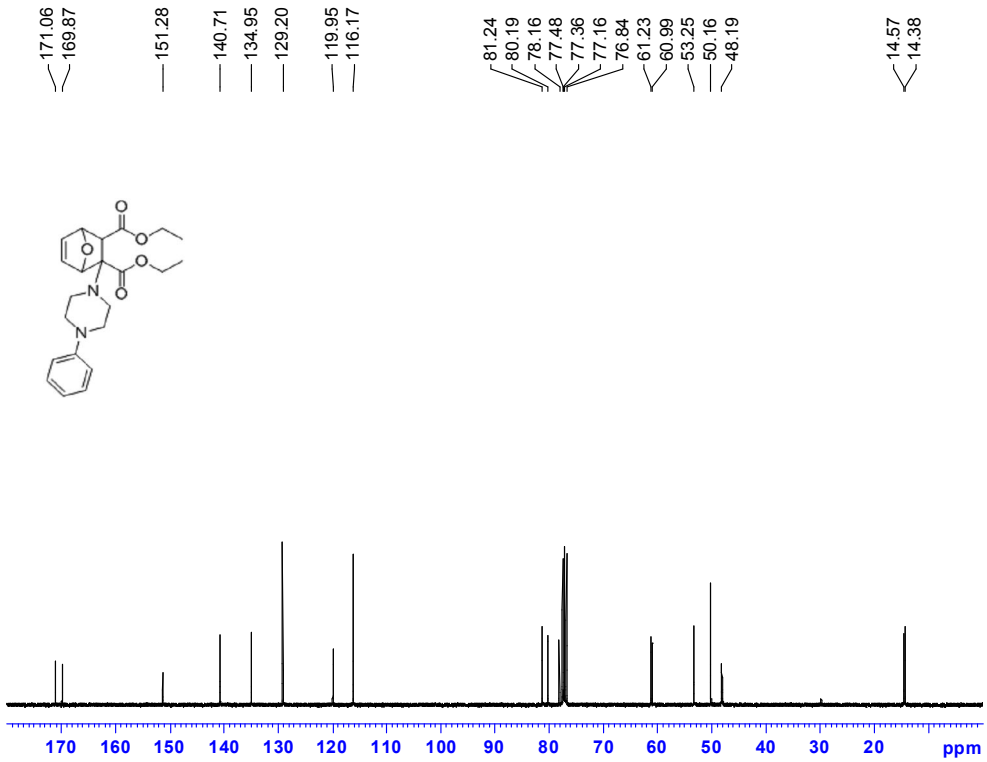


Figure 2 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3a**

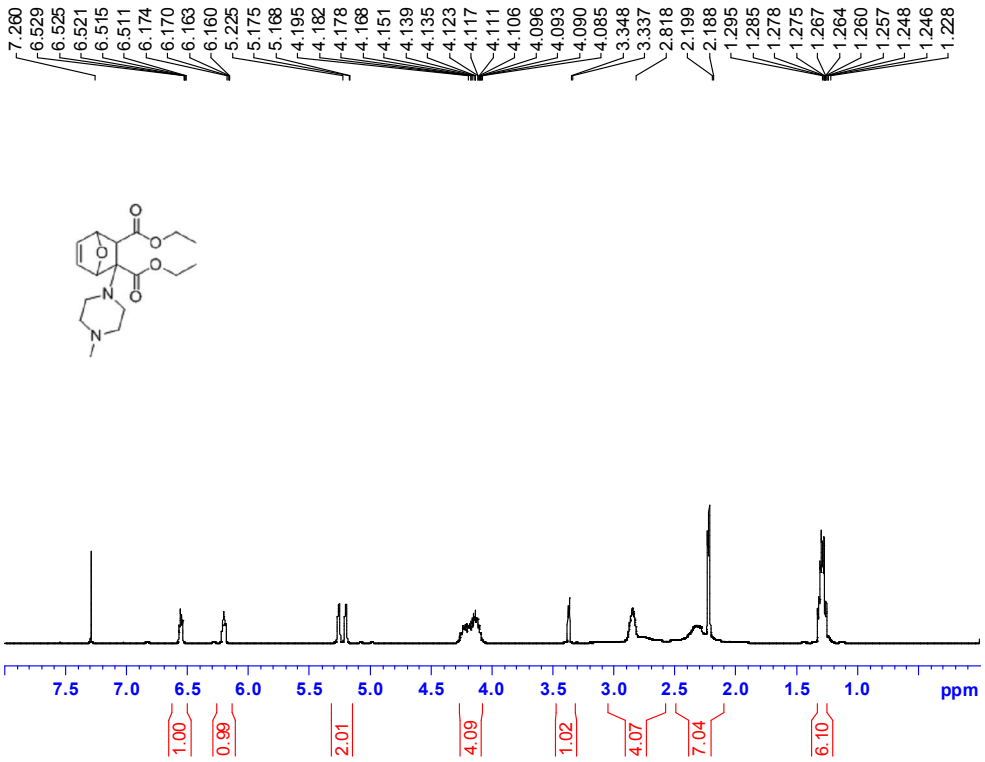


Figure 3 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3b**

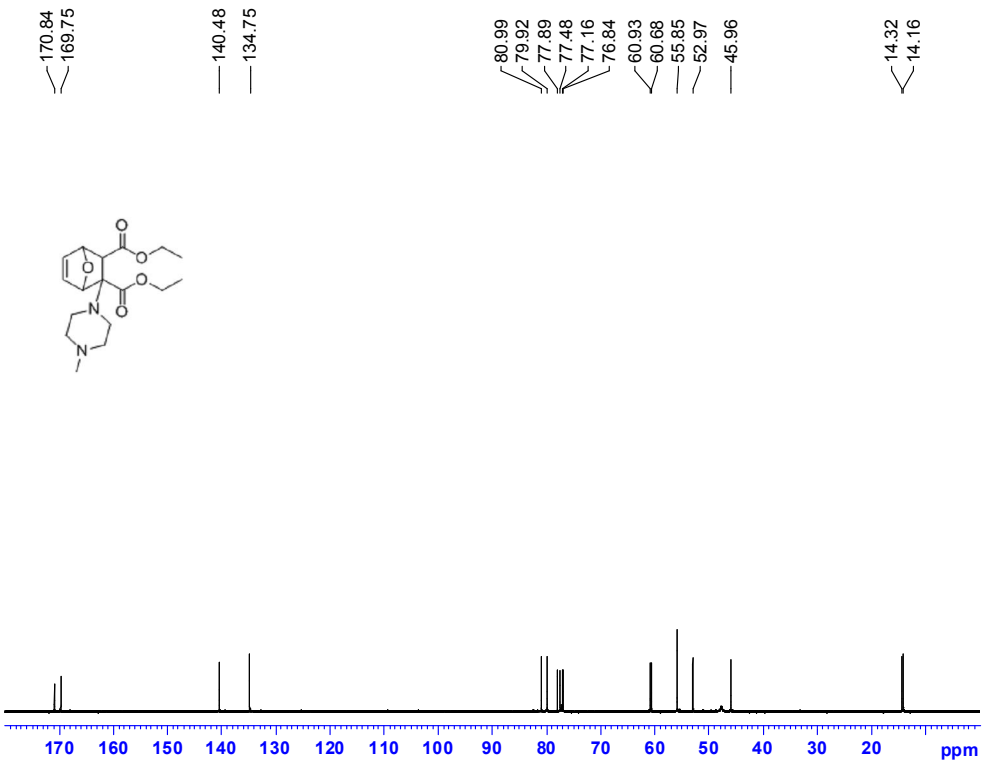


Figure 4 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3b**

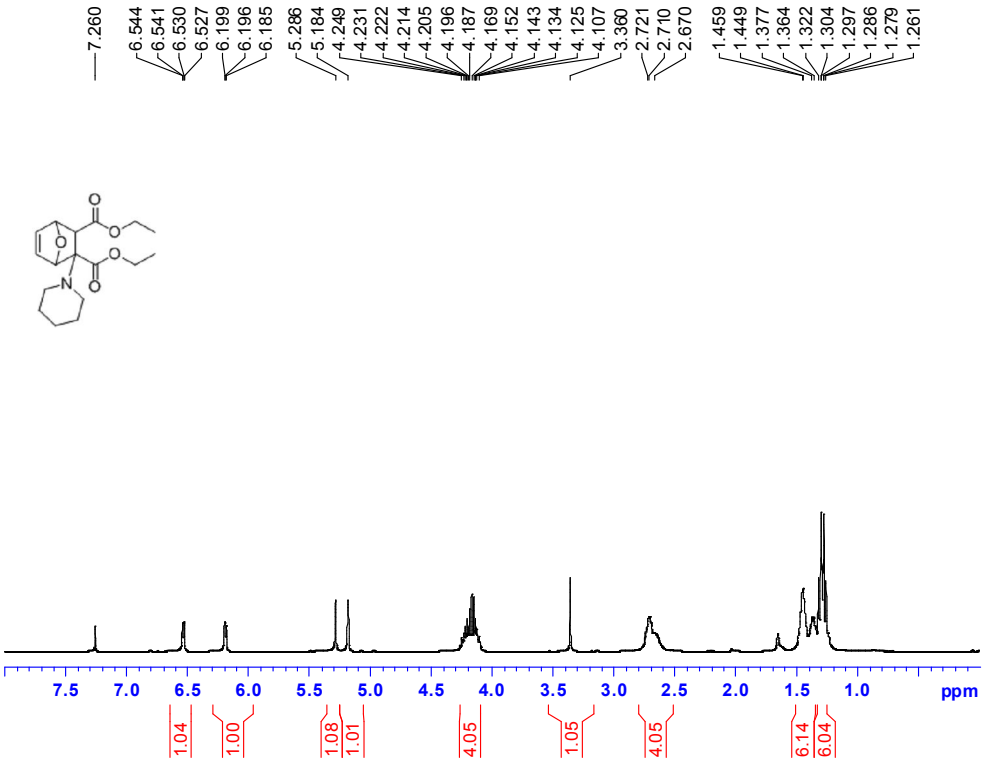


Figure 5 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3c**

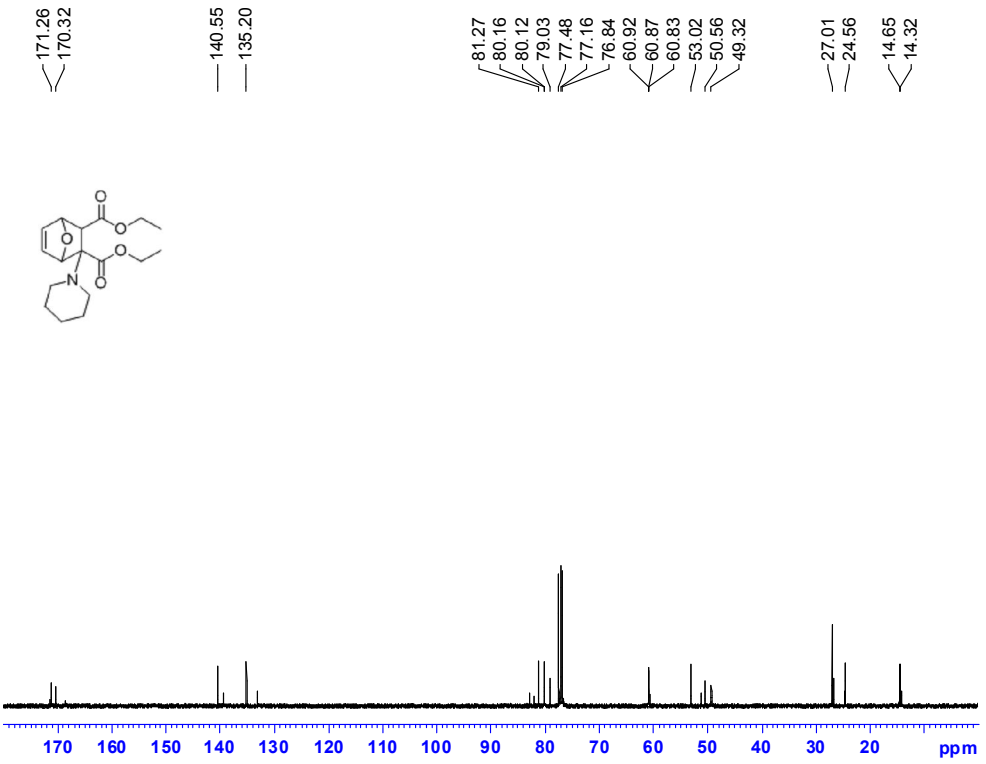


Figure 6 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3c**

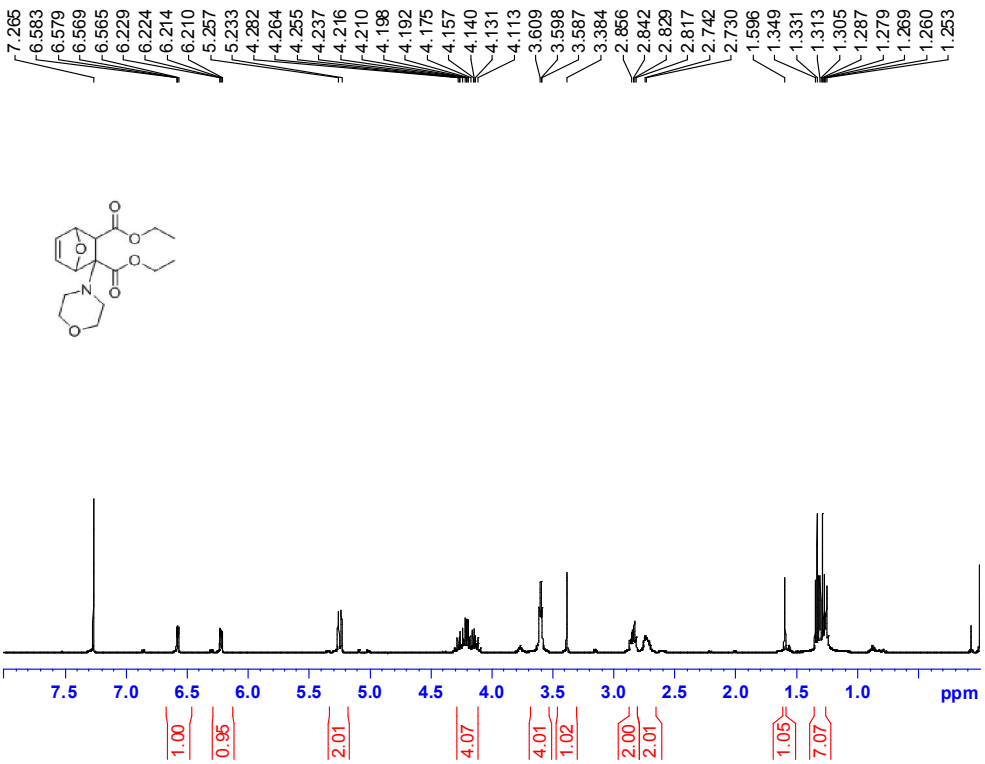


Figure 7 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3d**

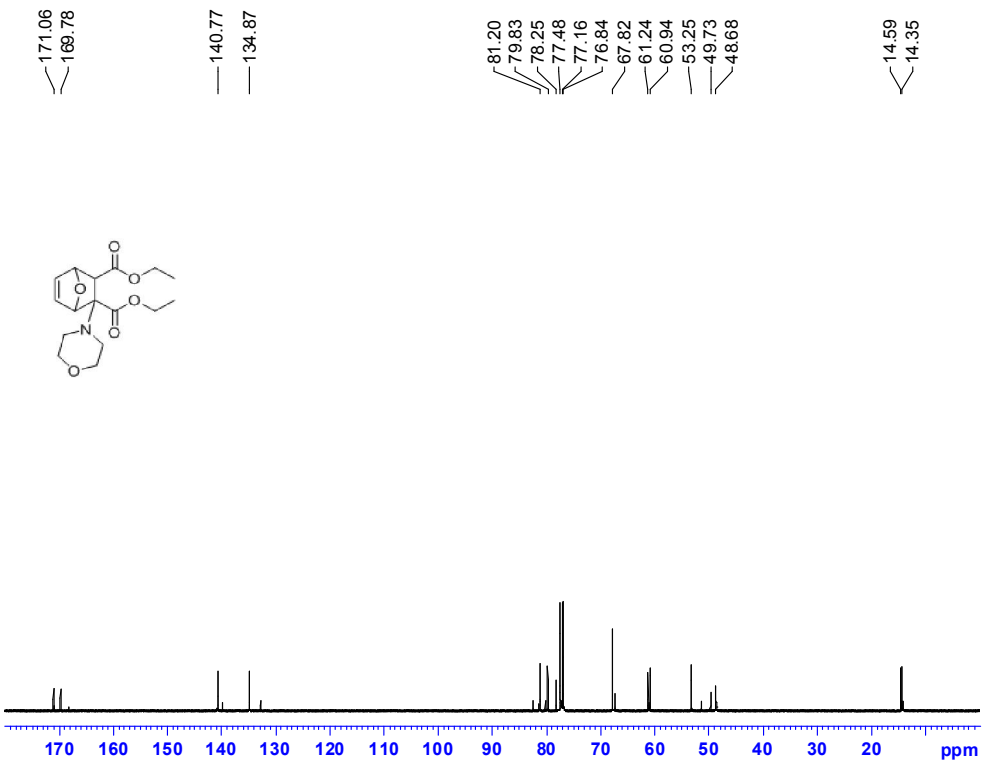


Figure 8 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3d**

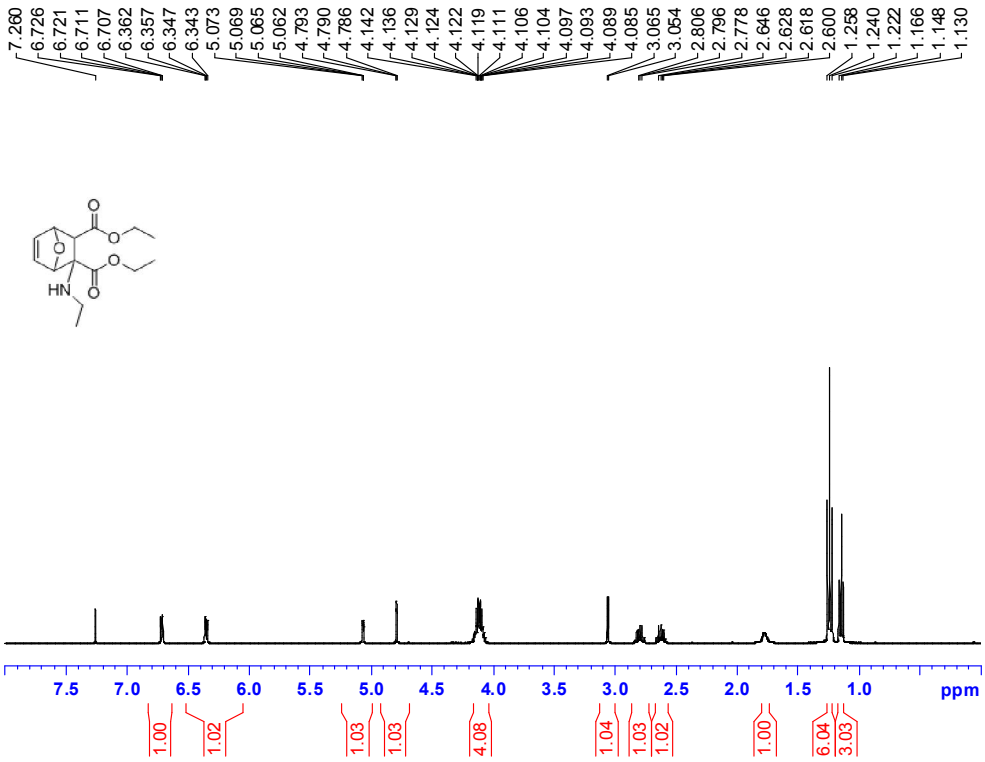


Figure 9 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3e**

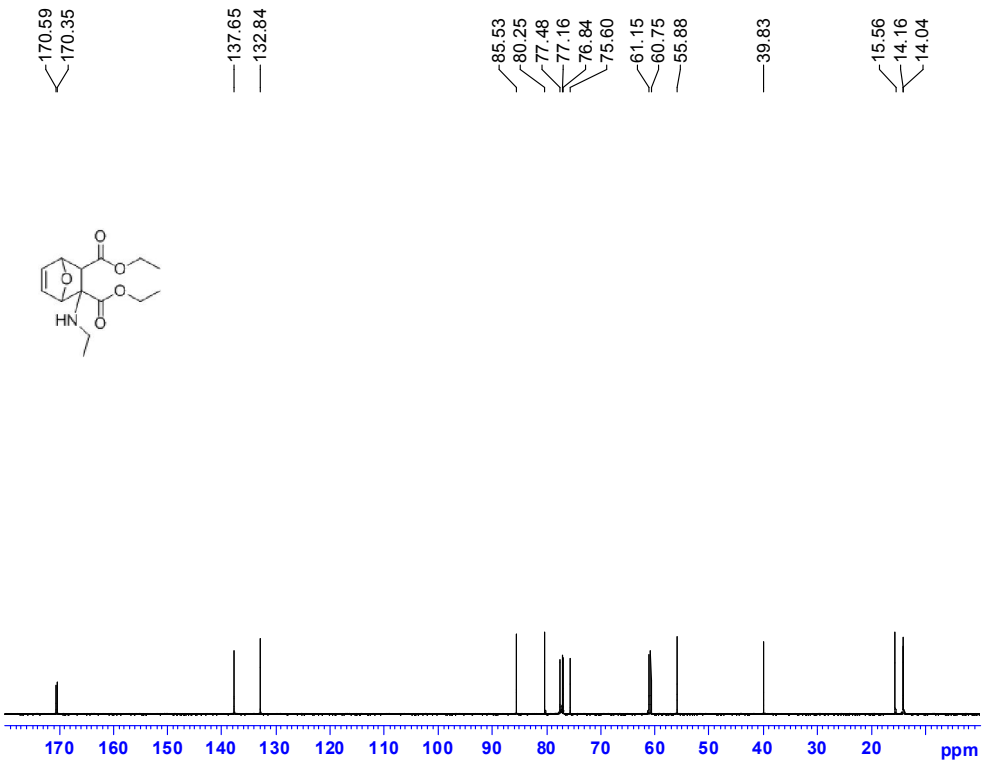


Figure 10 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3e**

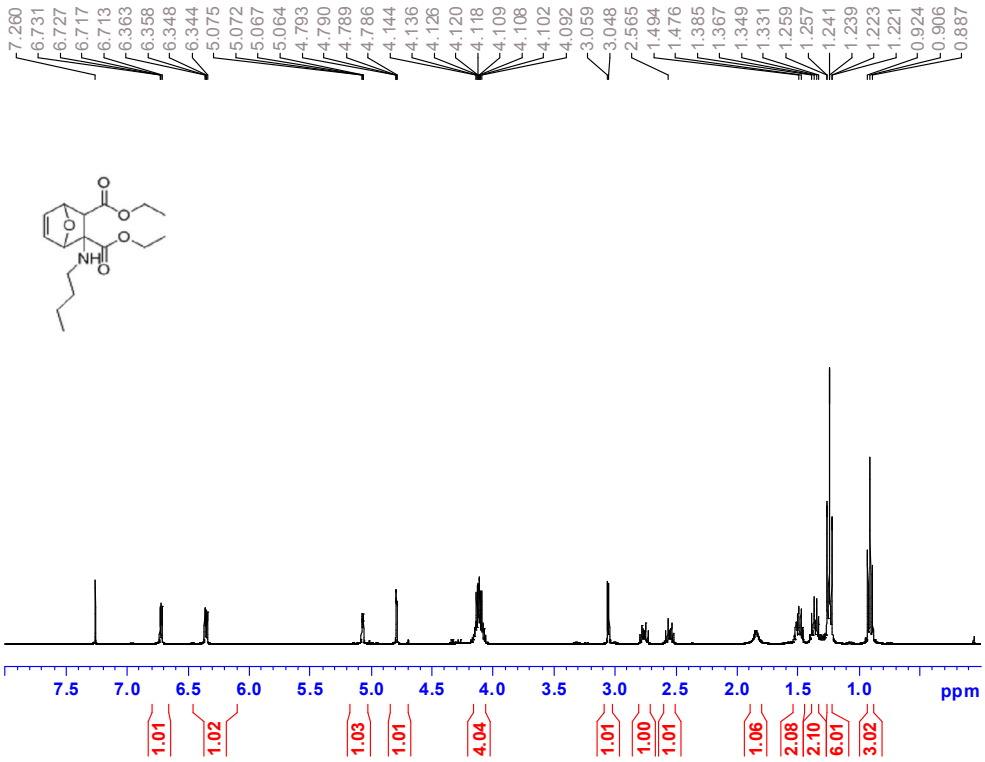


Figure 11 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3f**

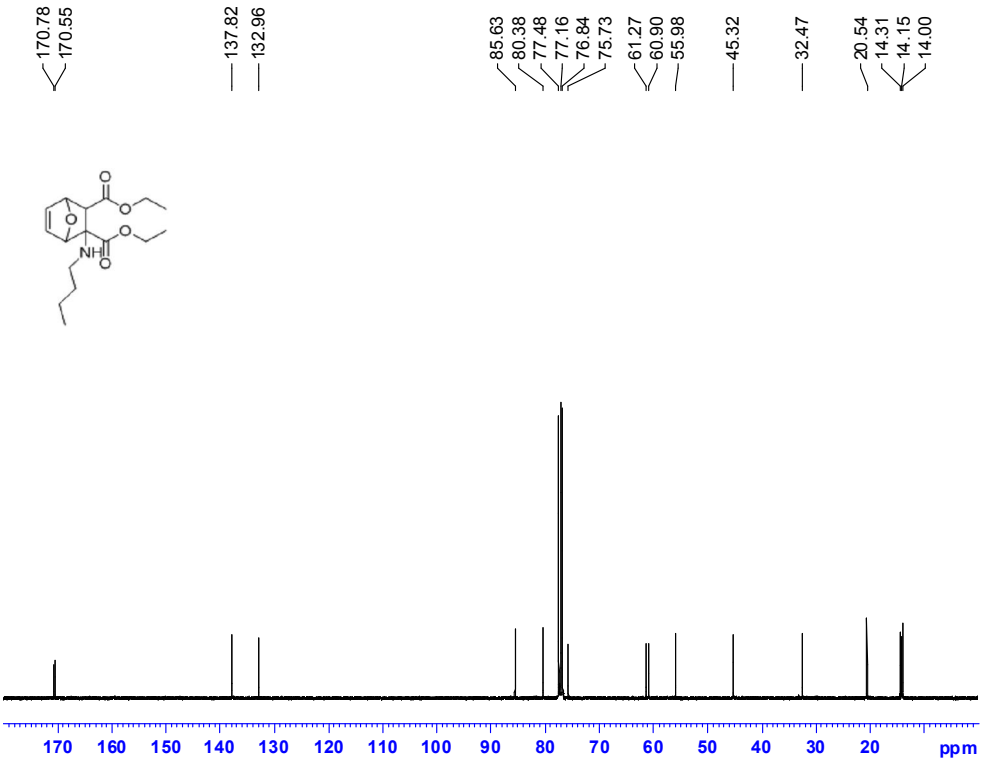


Figure 12 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3f**

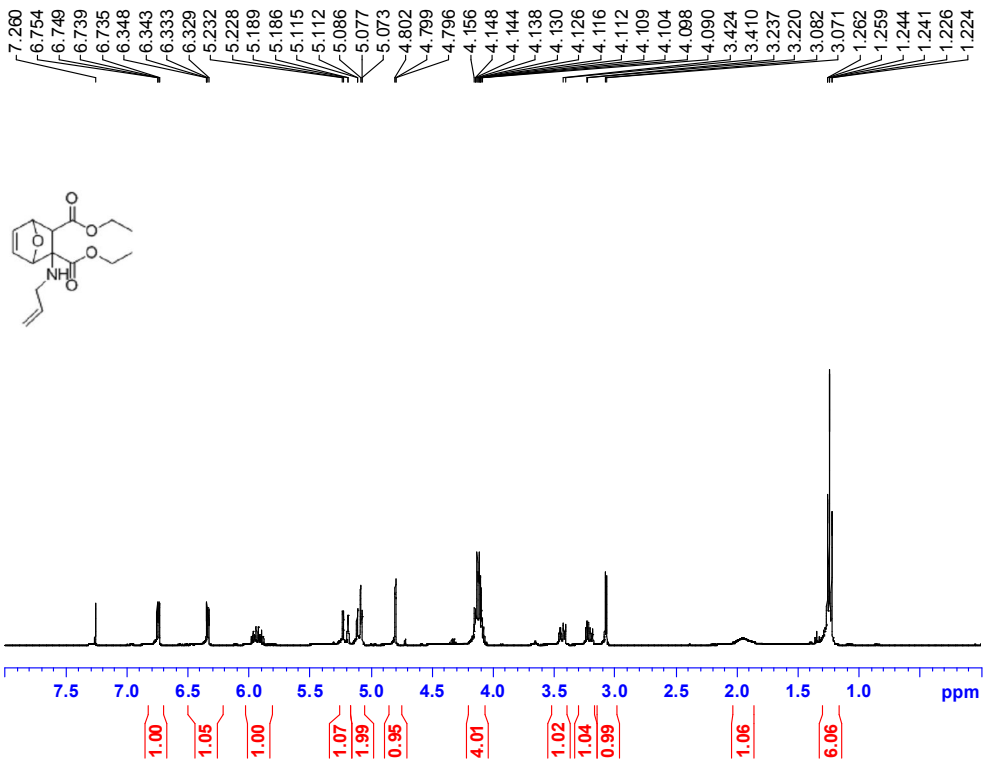


Figure 13 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3g**

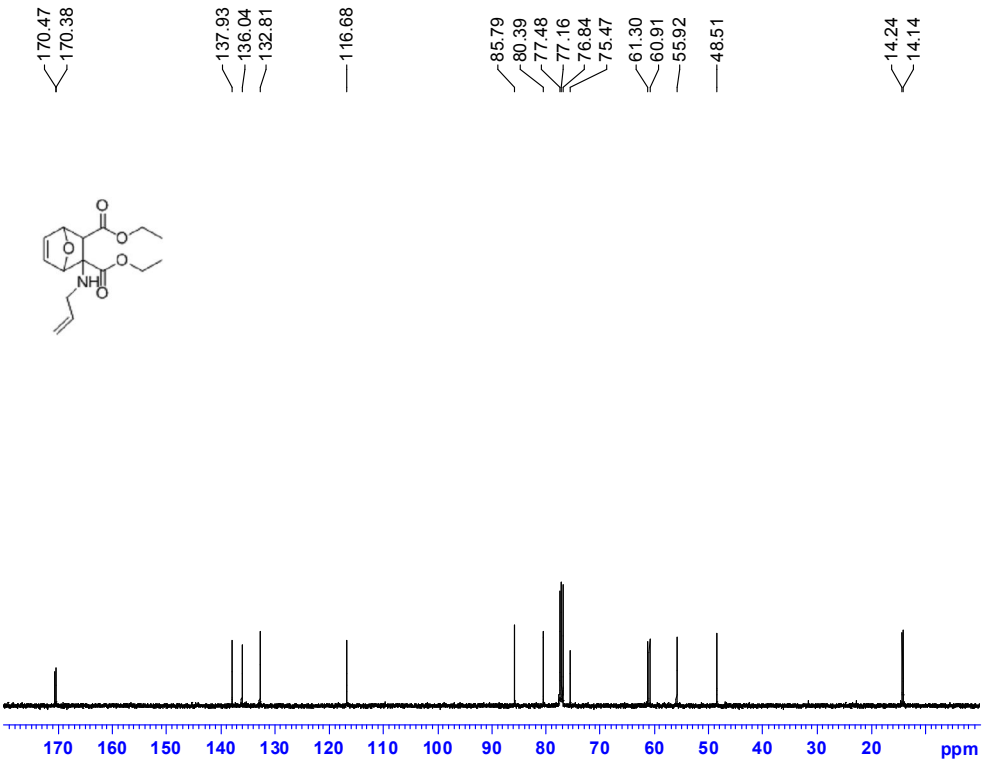


Figure 14 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3g**

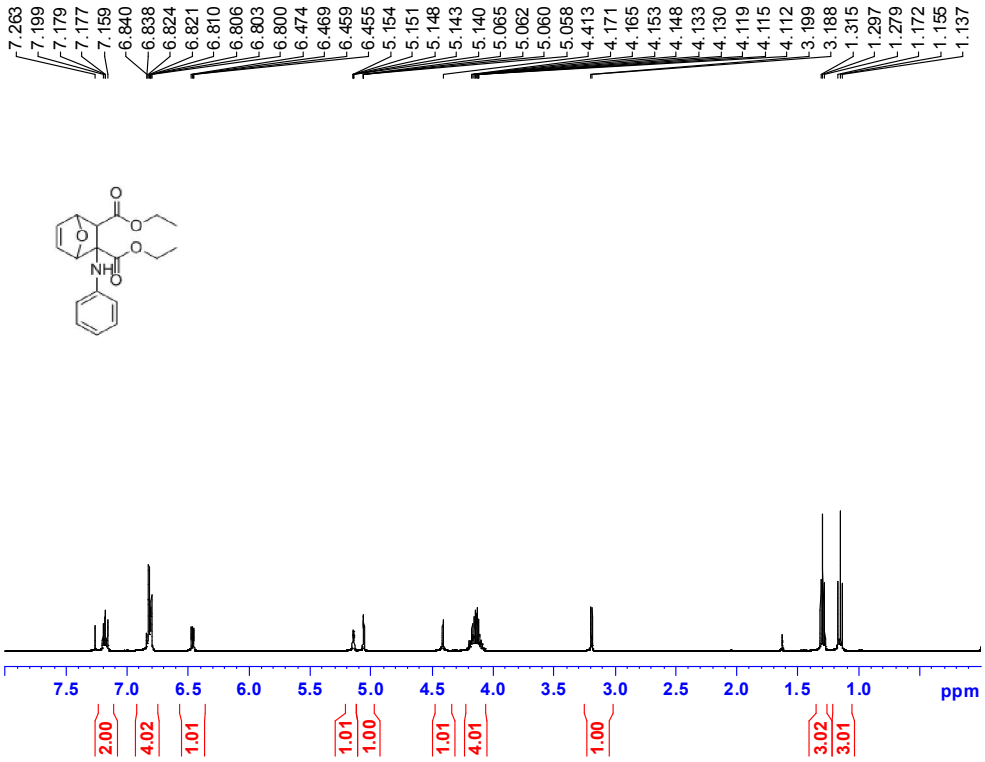


Figure 15 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3h**

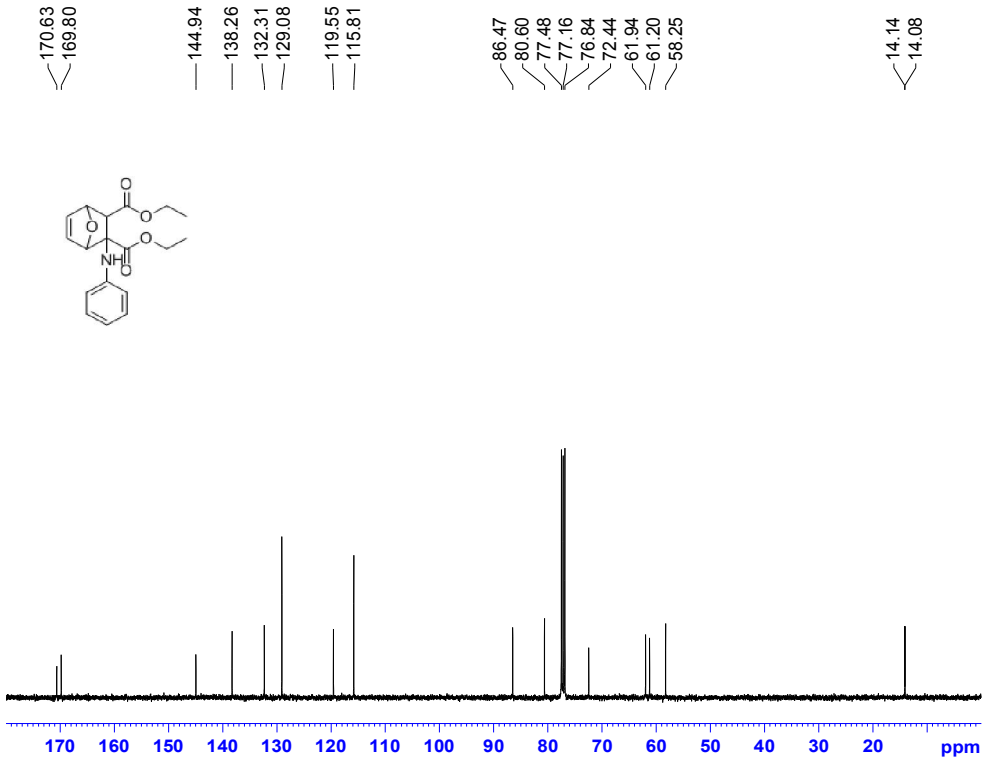


Figure 16 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3h**

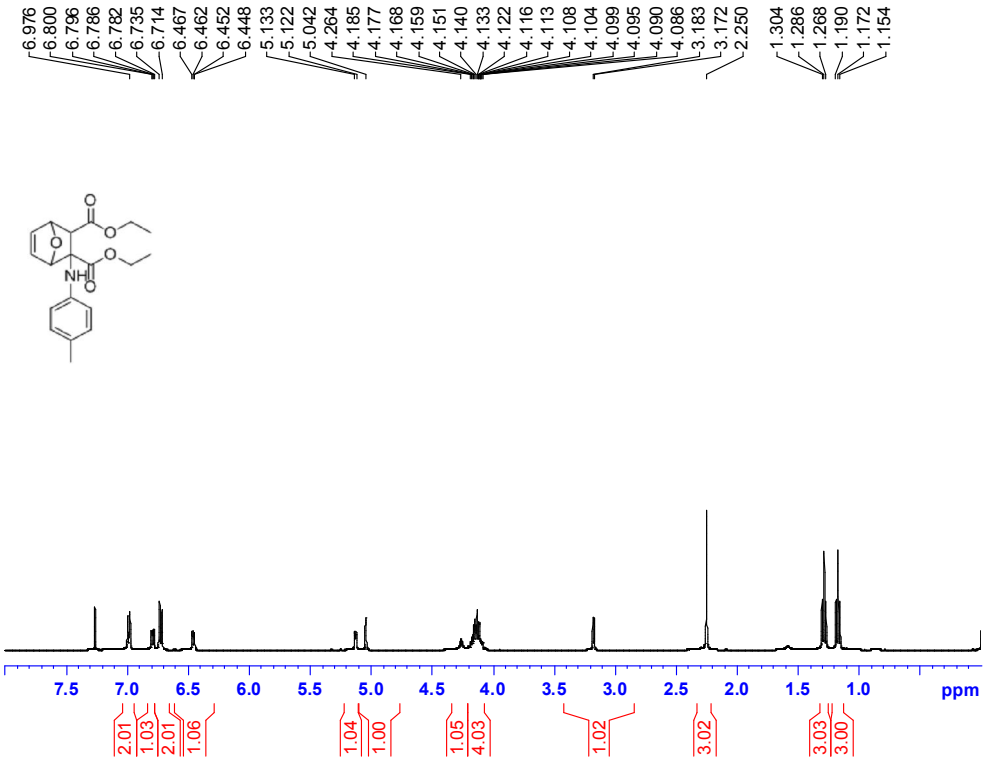


Figure 17 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3i**

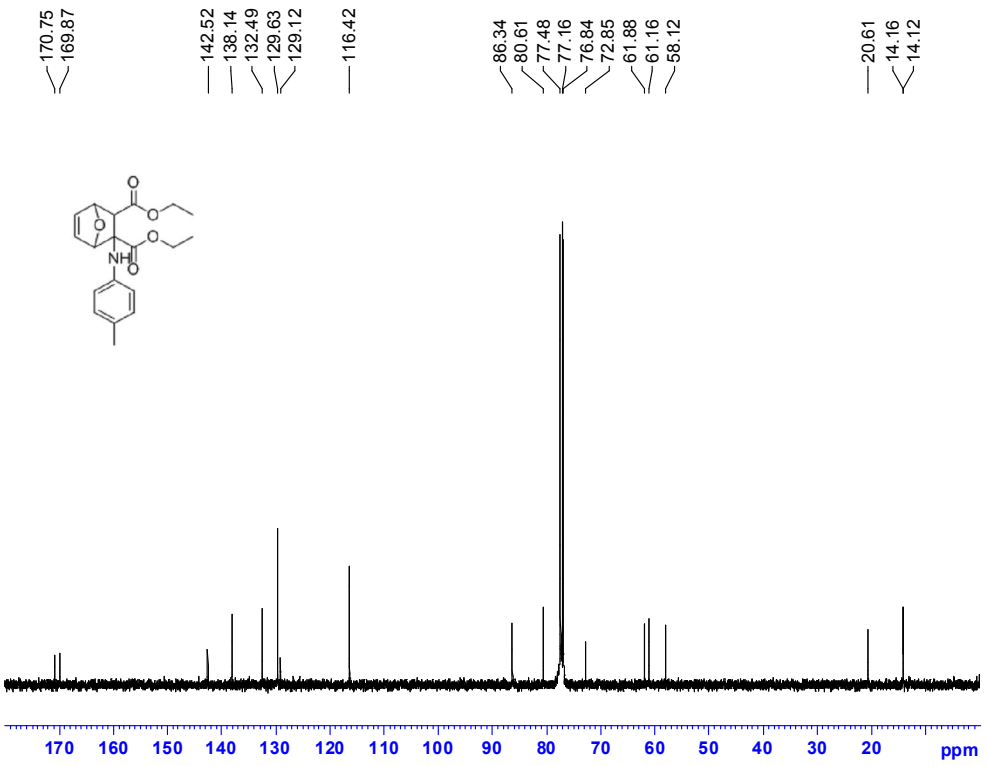


Figure 18 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **3i**

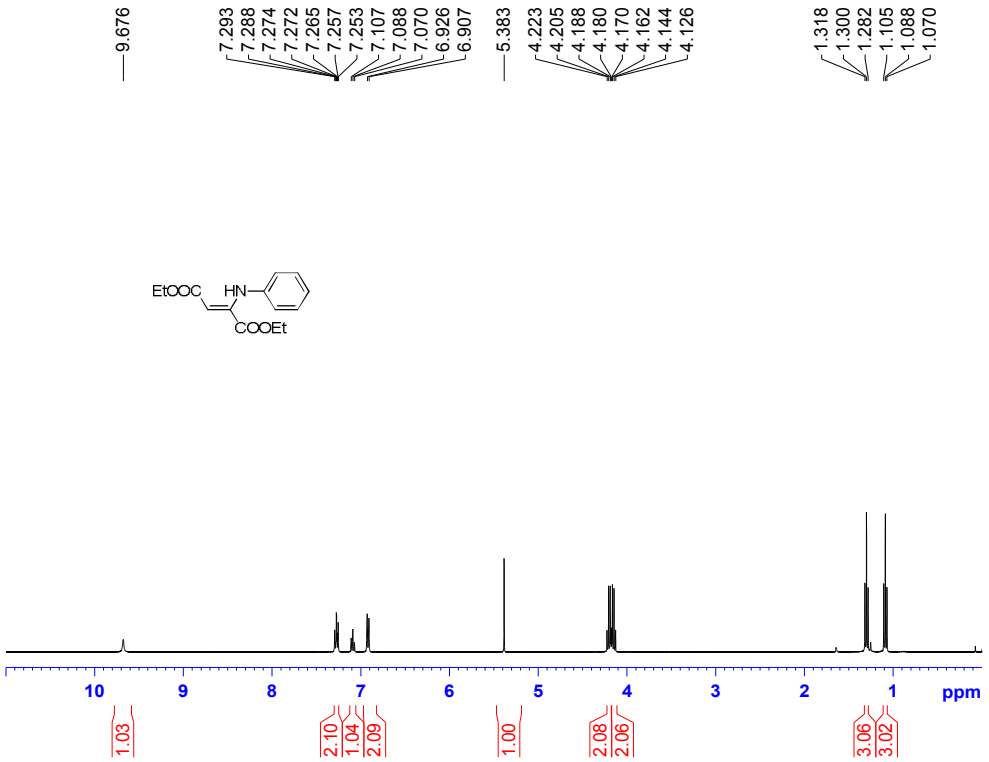


Figure 19 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4a**

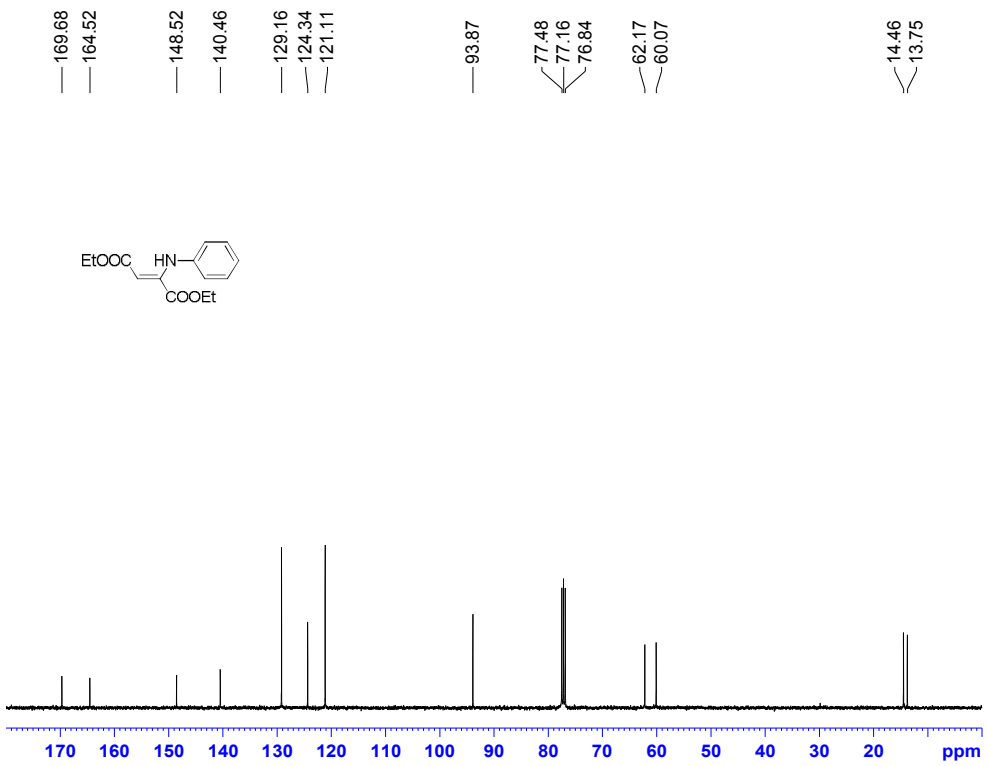


Figure 20 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound 4**a**

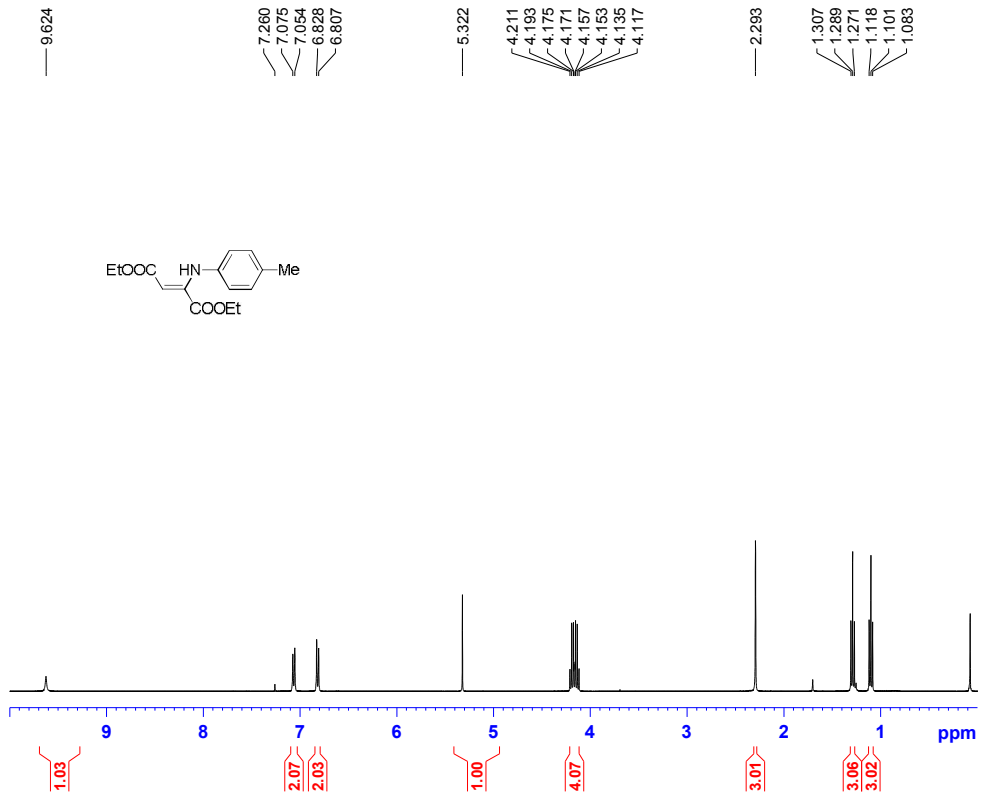


Figure 21 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4b**

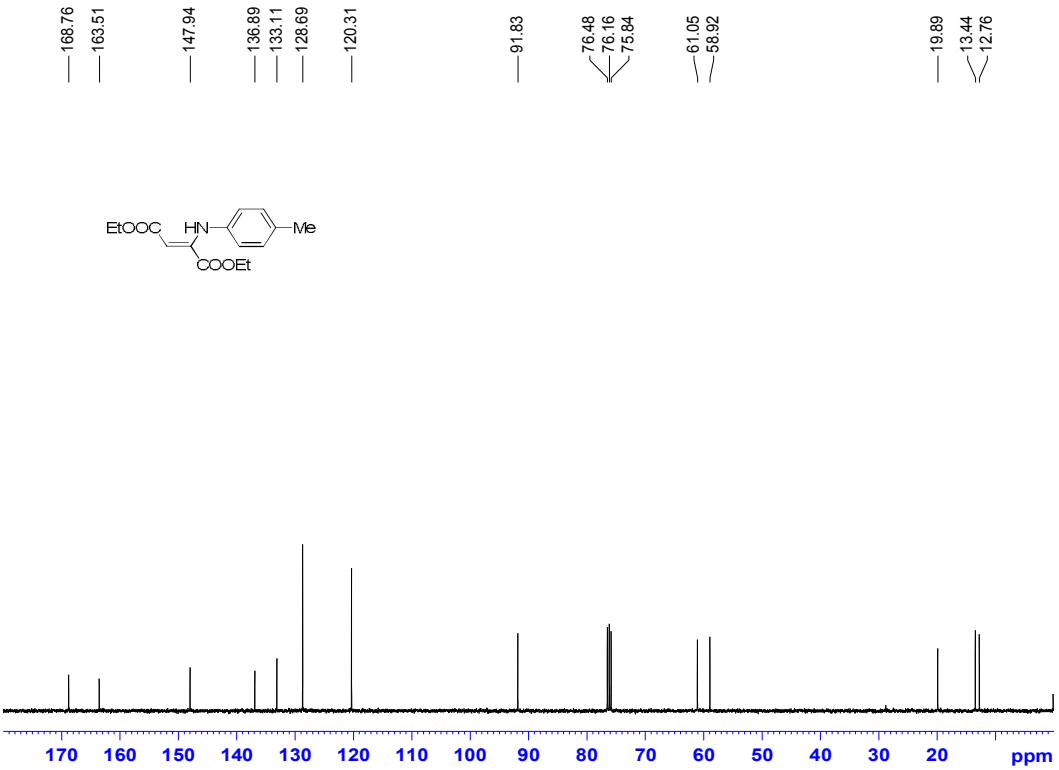


Figure 22 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **4b**

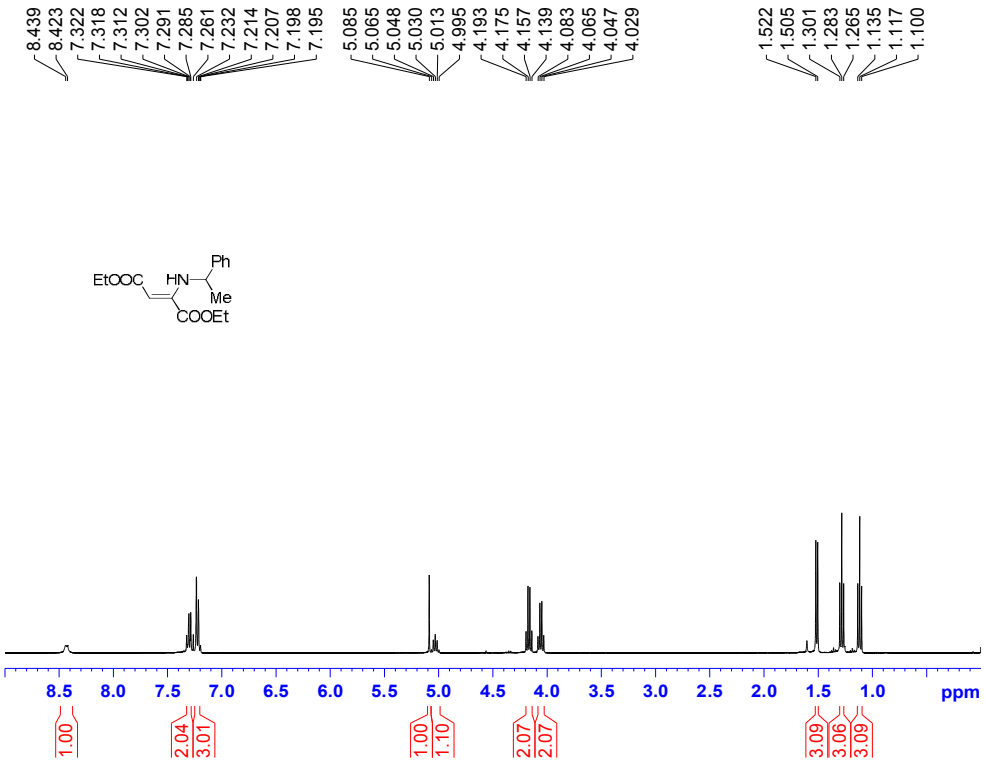


Figure 23 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4c**

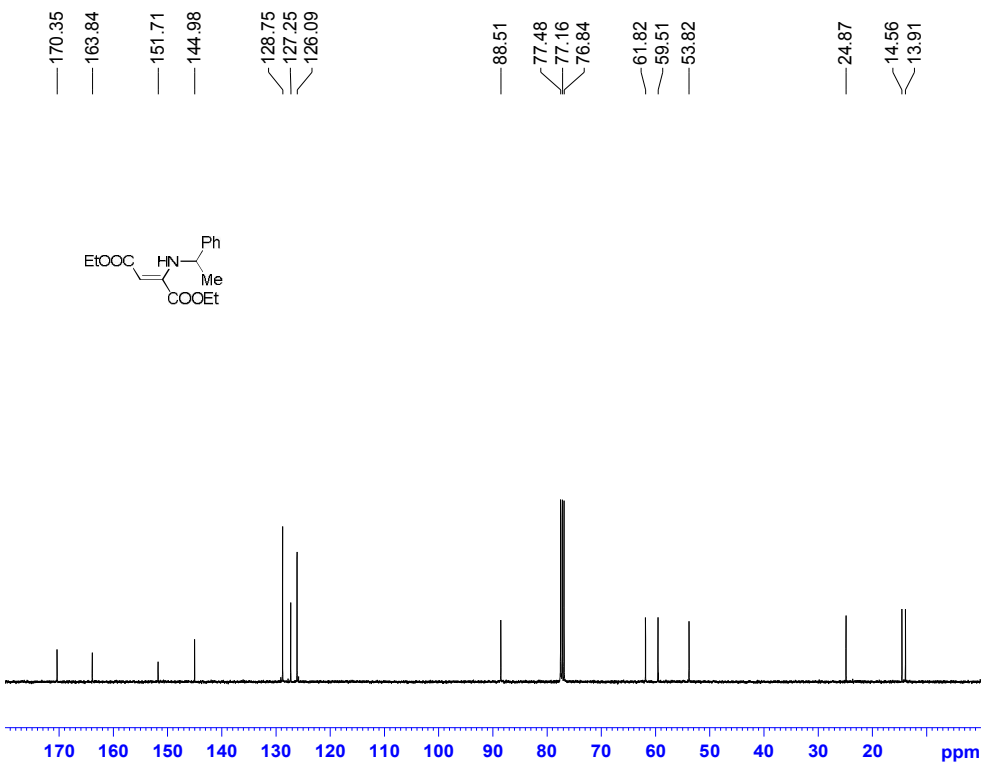


Figure 24 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **4c**

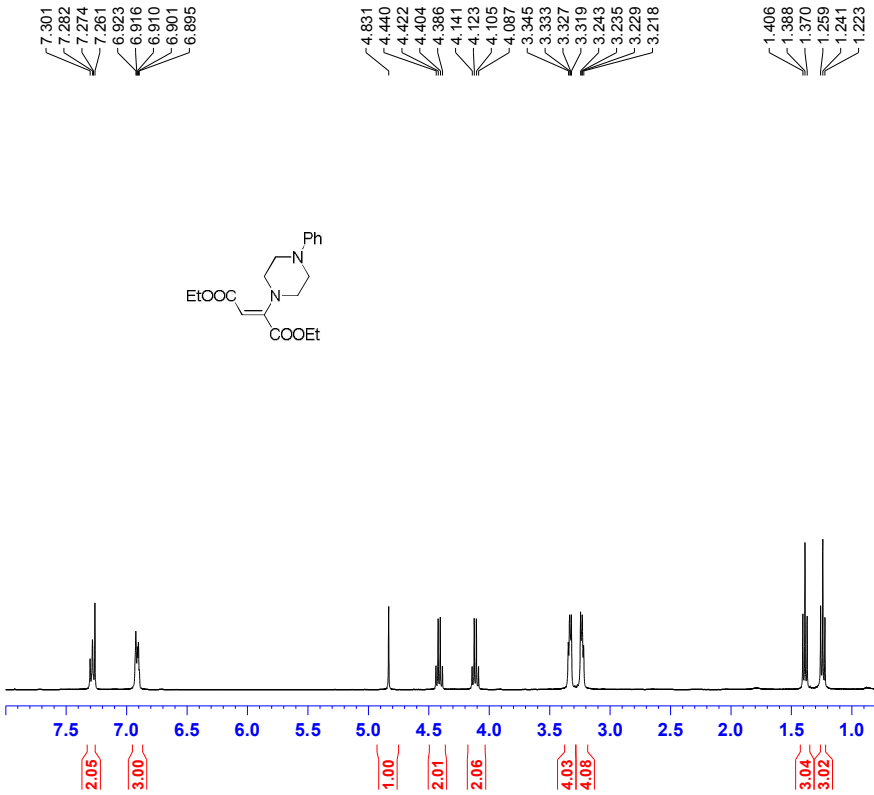


Figure 25 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4d**

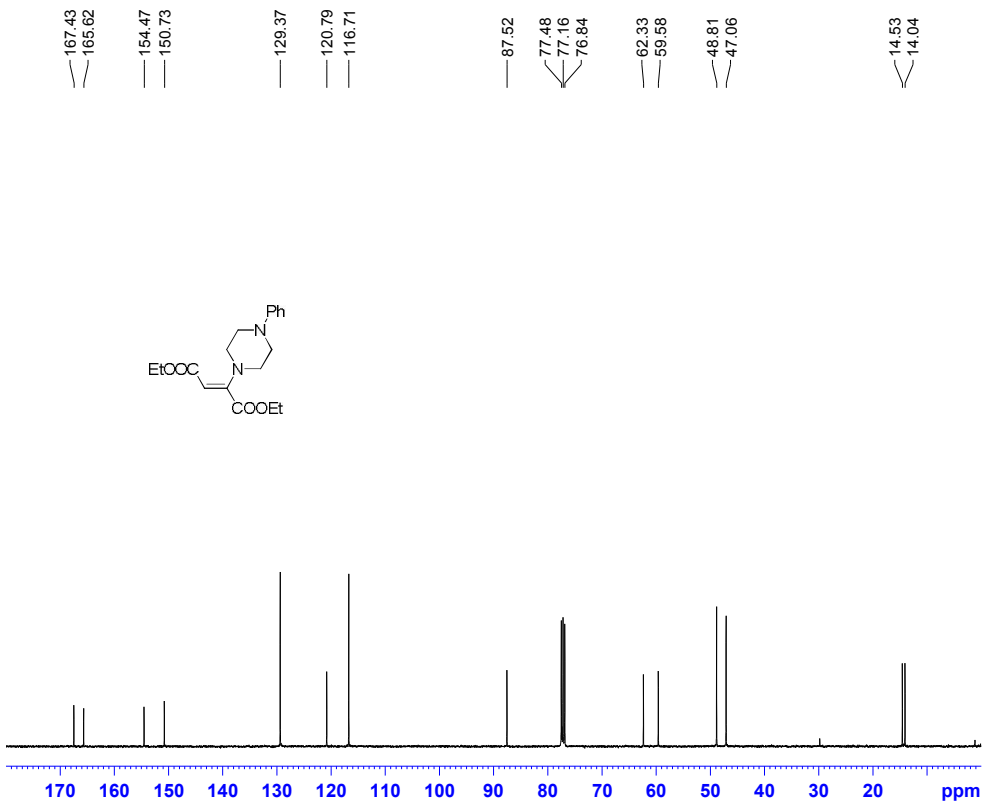


Figure 26 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **4d**

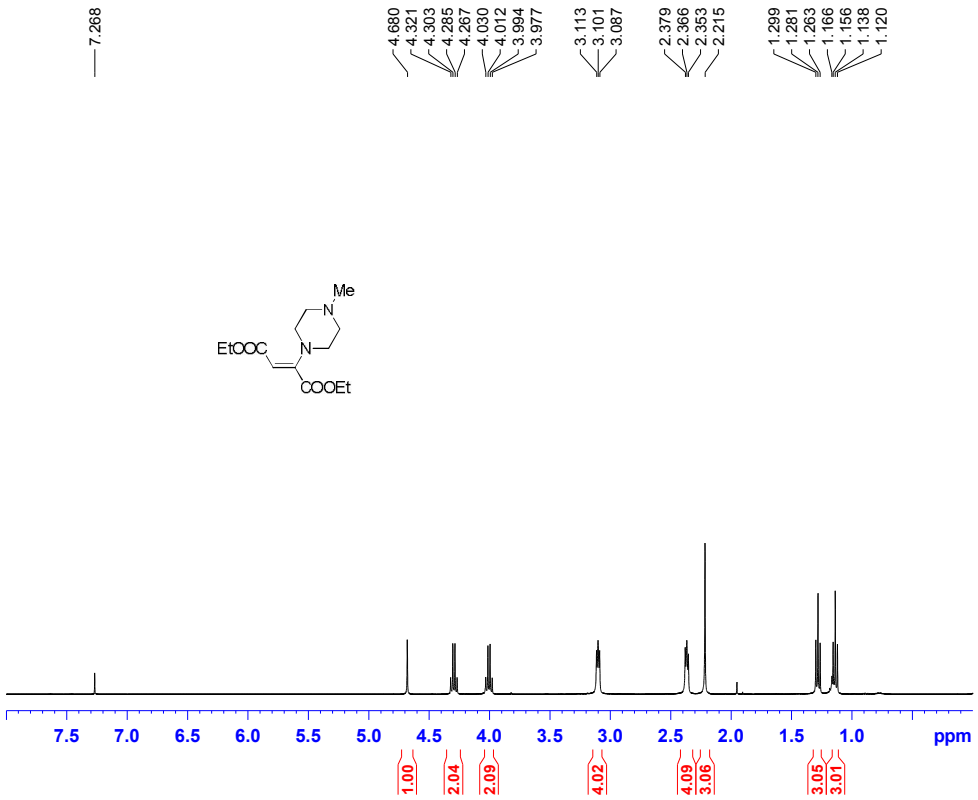


Figure 27 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4e**

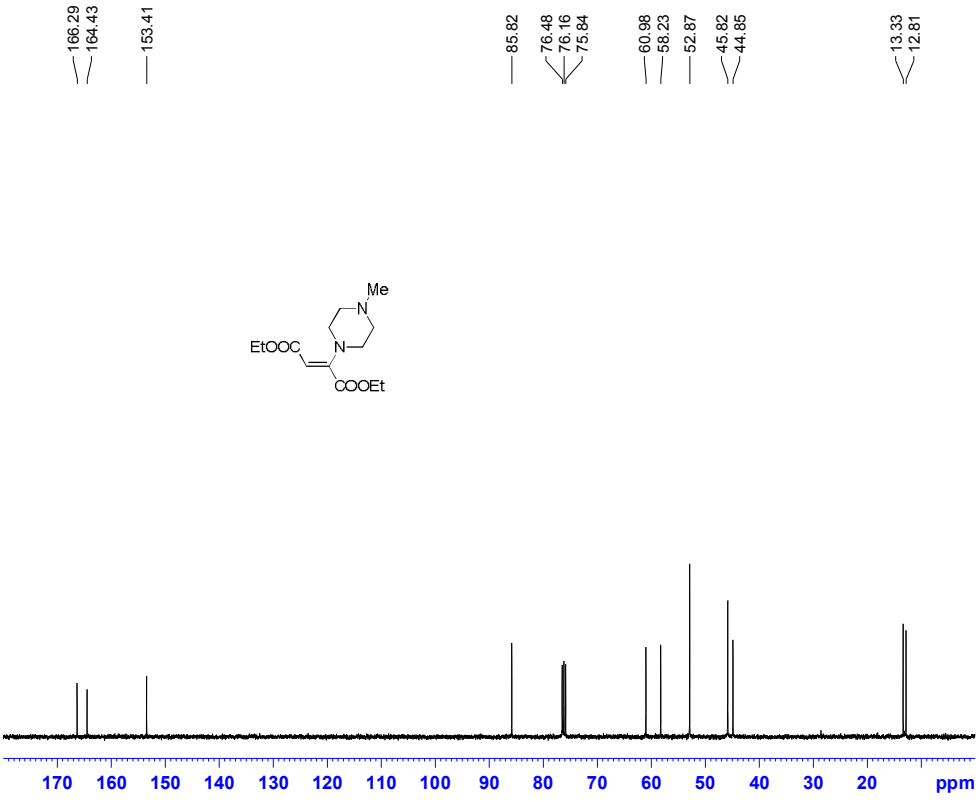


Figure 28 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **4e**

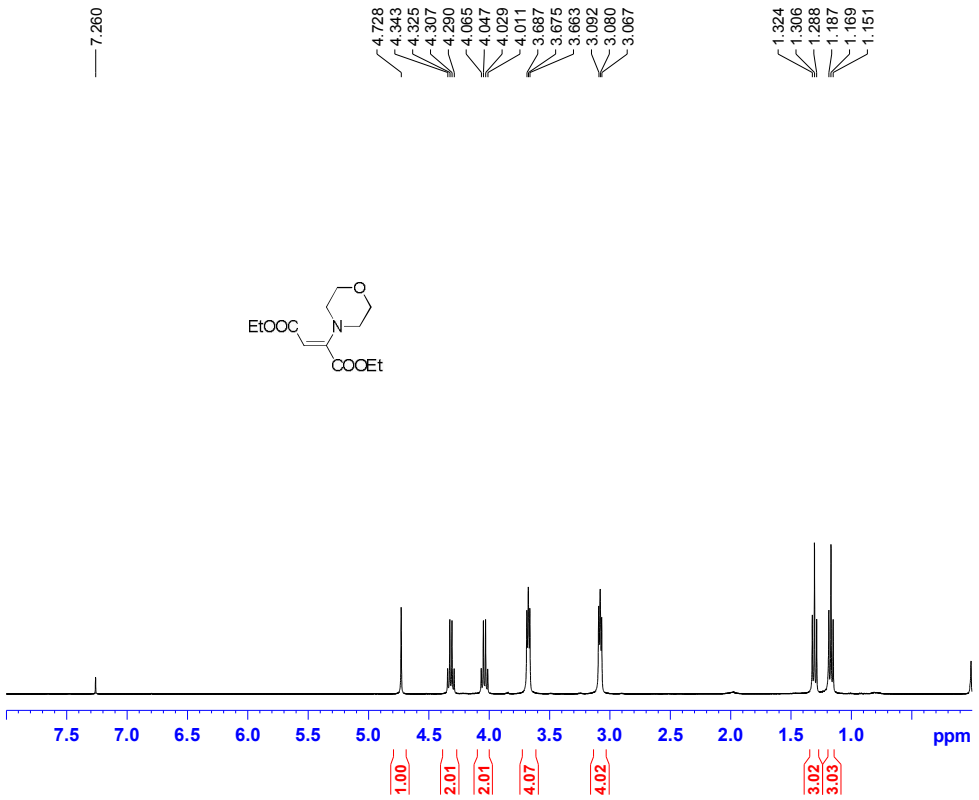


Figure 29 ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **4f**

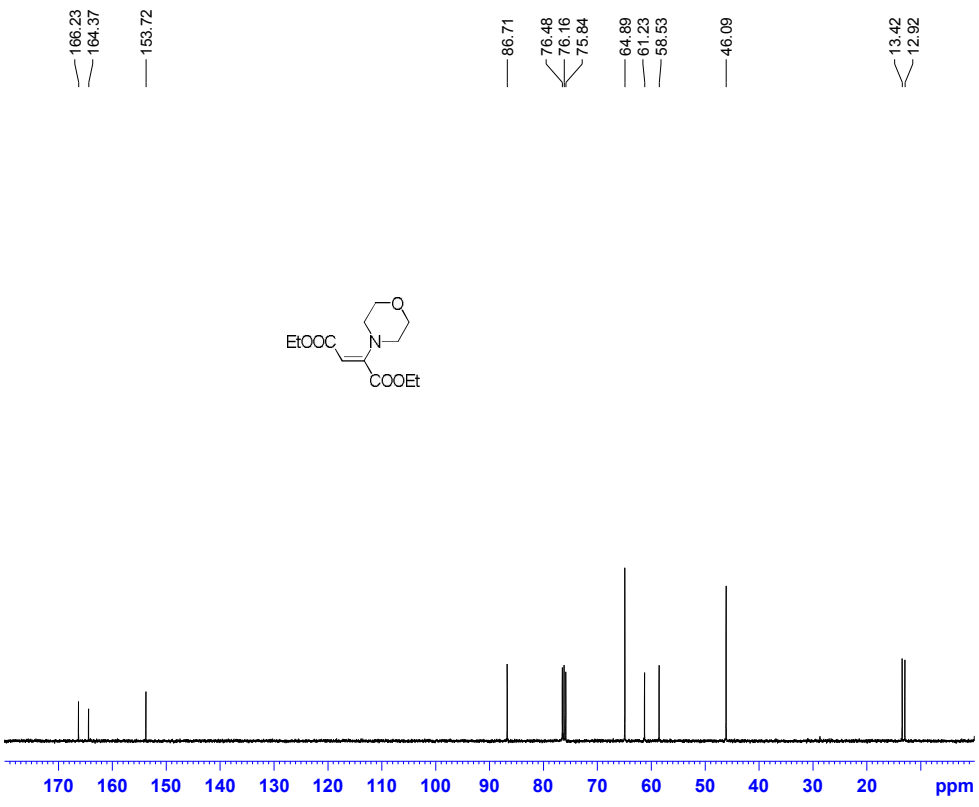


Figure 30 ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **4f**

References

1. N. E. Leadbeater, S. J. Pillsbury, E. Shanahan, V. A. Williams, *Tetrahedron,* 2005**,** **61**, 3565.