SUPPORTING INFORMATION

FOR

Towards the Total Synthesis of Alpkinidine: Michael Addition to Isoquinolinetrione CE Ring-System Synthons

Marco Buccini,[a]+ Francis Dhoro,[a]+ Louisa Tham,[a] Brian W. Skelton,[a] Craig M. Williams,[b] and Matthew J. Piggott[a]*

[a] *Dr M. Buccini, Dr F. Dhoro, Ms L. Tham, Dr B. Skelton, Assoc. Prof. M. J. Piggott, Chemistry, School of Molecular Sciences, University of Western Australia, Perth, Australia.*
E-mail: matthew.piggott@uwa.edu.au

[b] *Prof. C. Williams, School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, Queensland, Australia*

+ These authors contributed equally.

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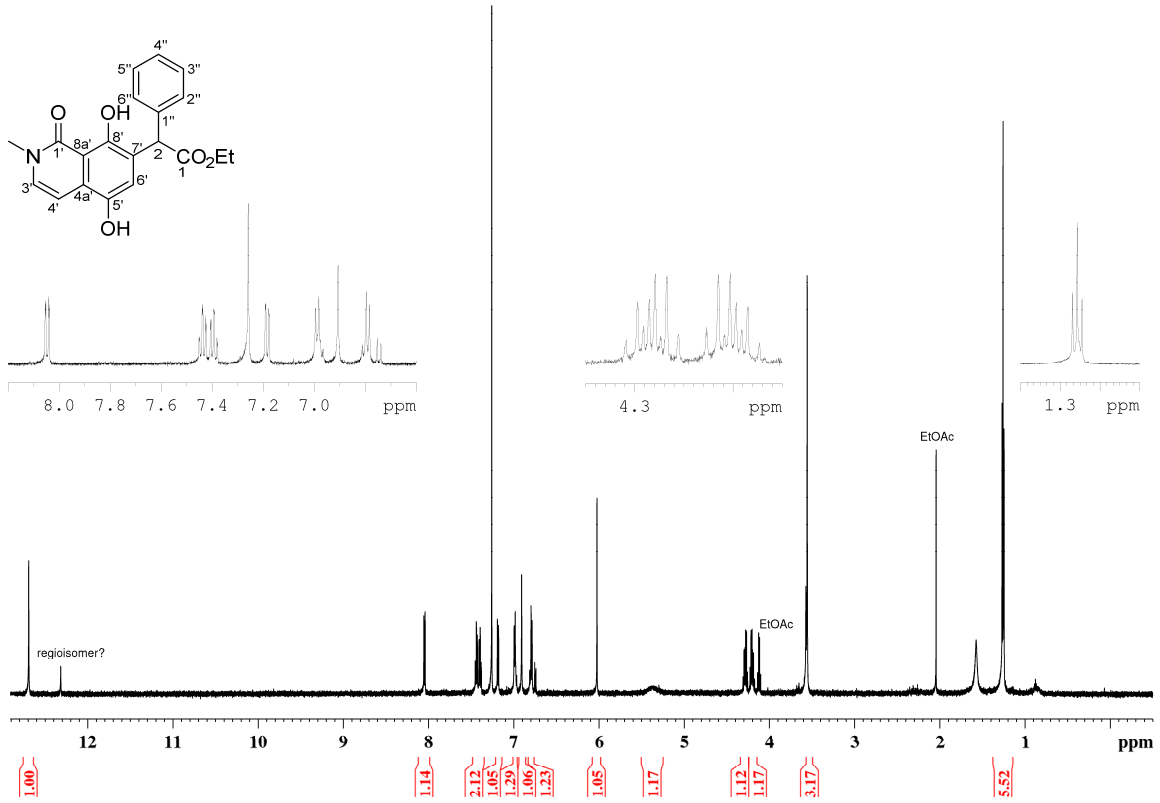
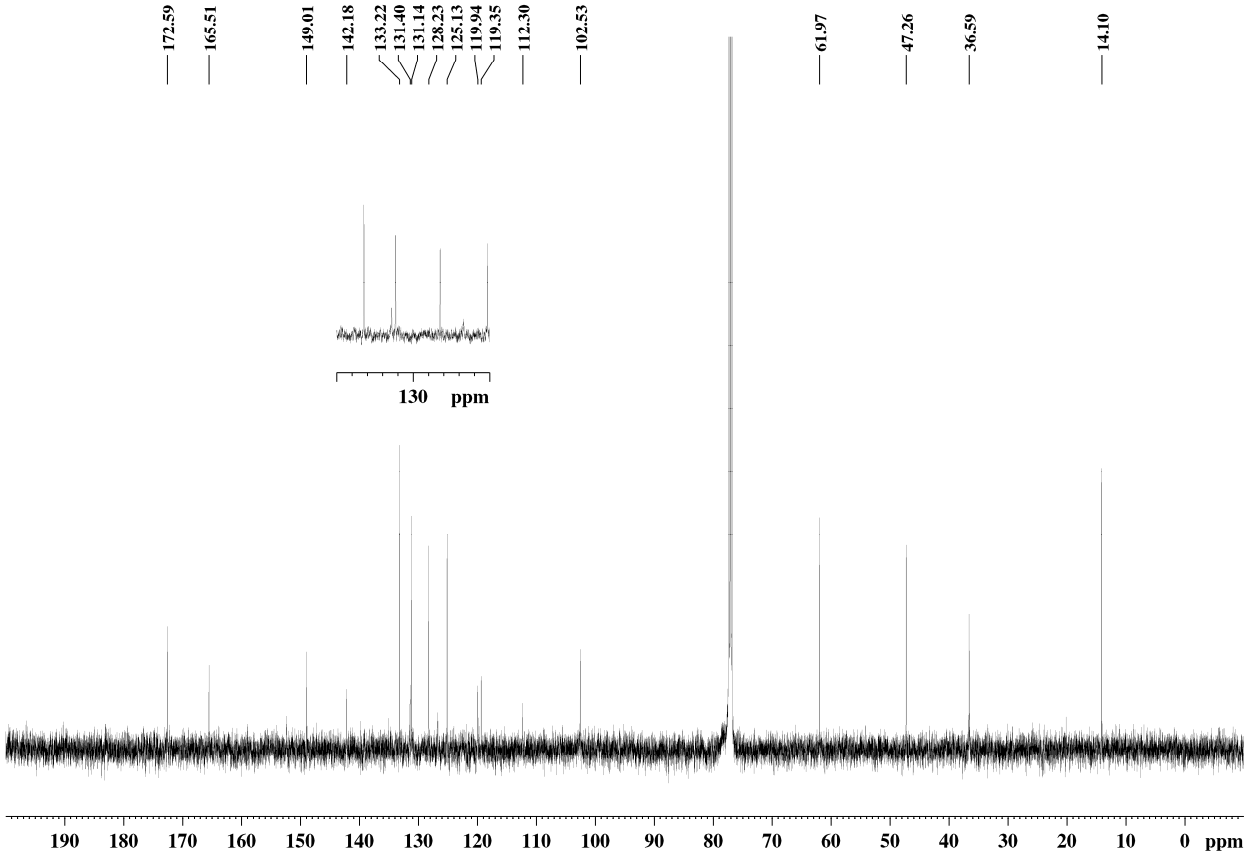
I. NMR SPECTRA

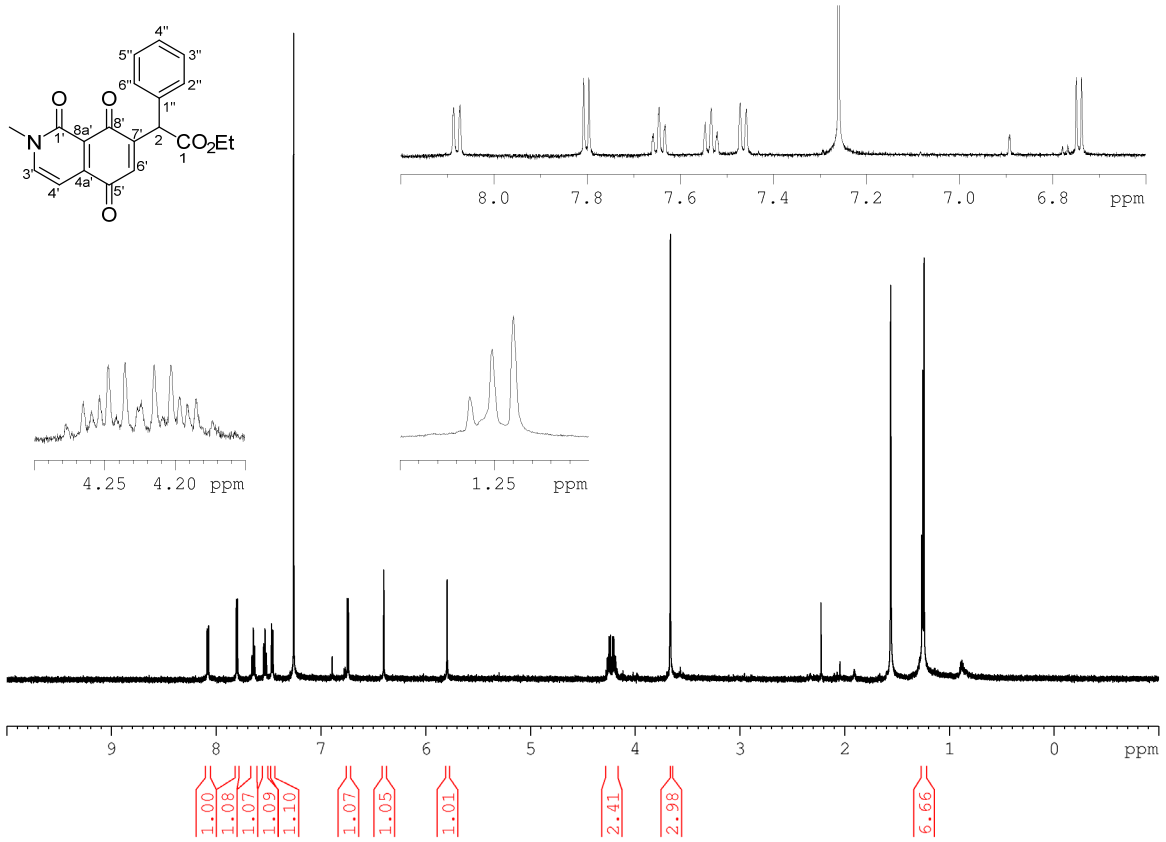
600 MHz ^{1}H NMR spectrum of **16** in $CDCl_3$



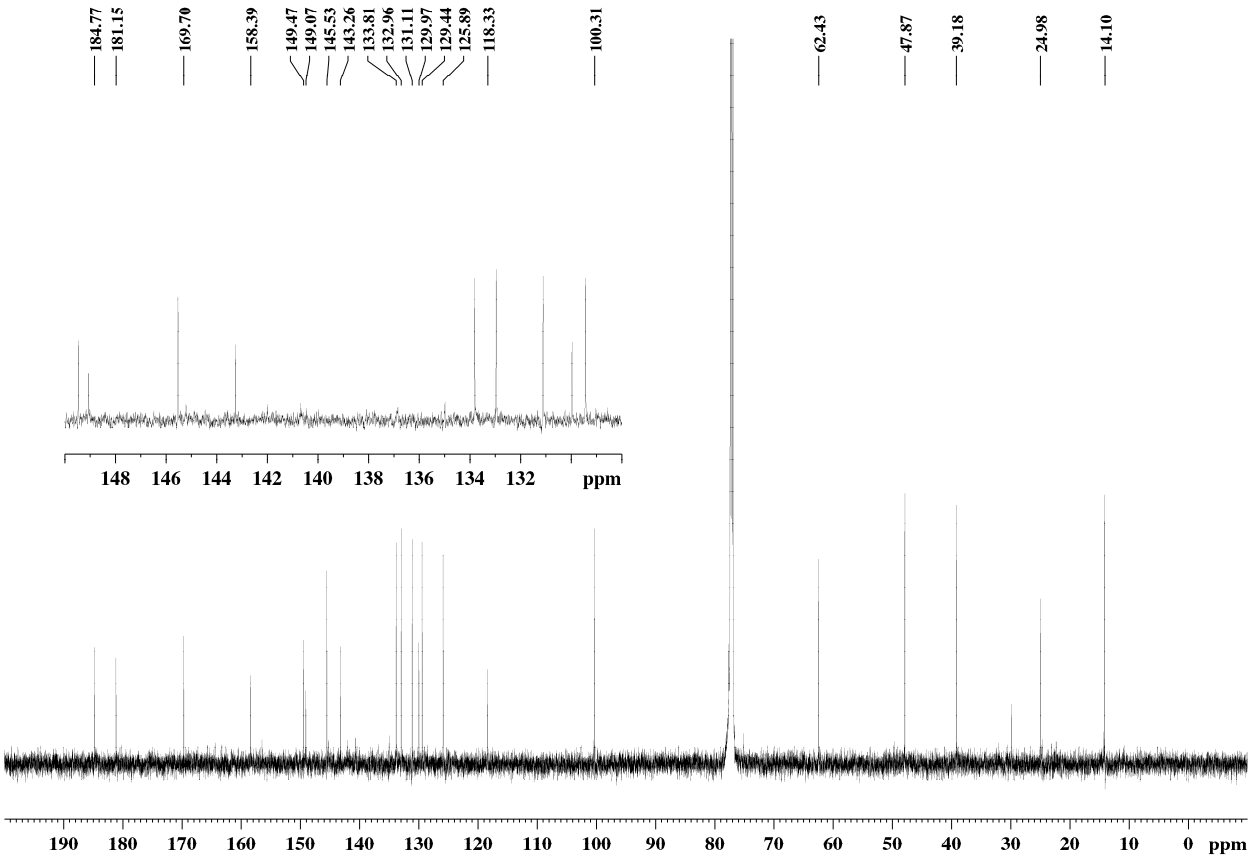
150 MHz ^{13}C NMR spectrum of **16** in $CDCl_3$



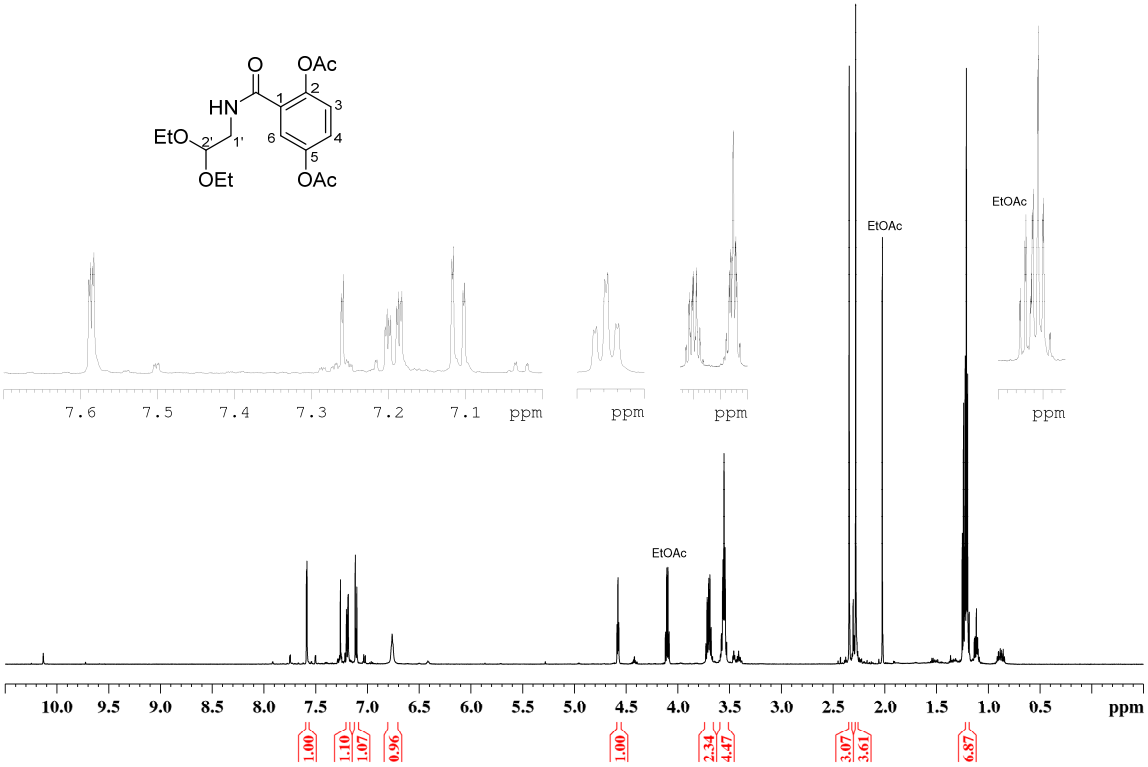
600 MHz ^{1}H NMR spectrum of **17** in $CDCl_3$



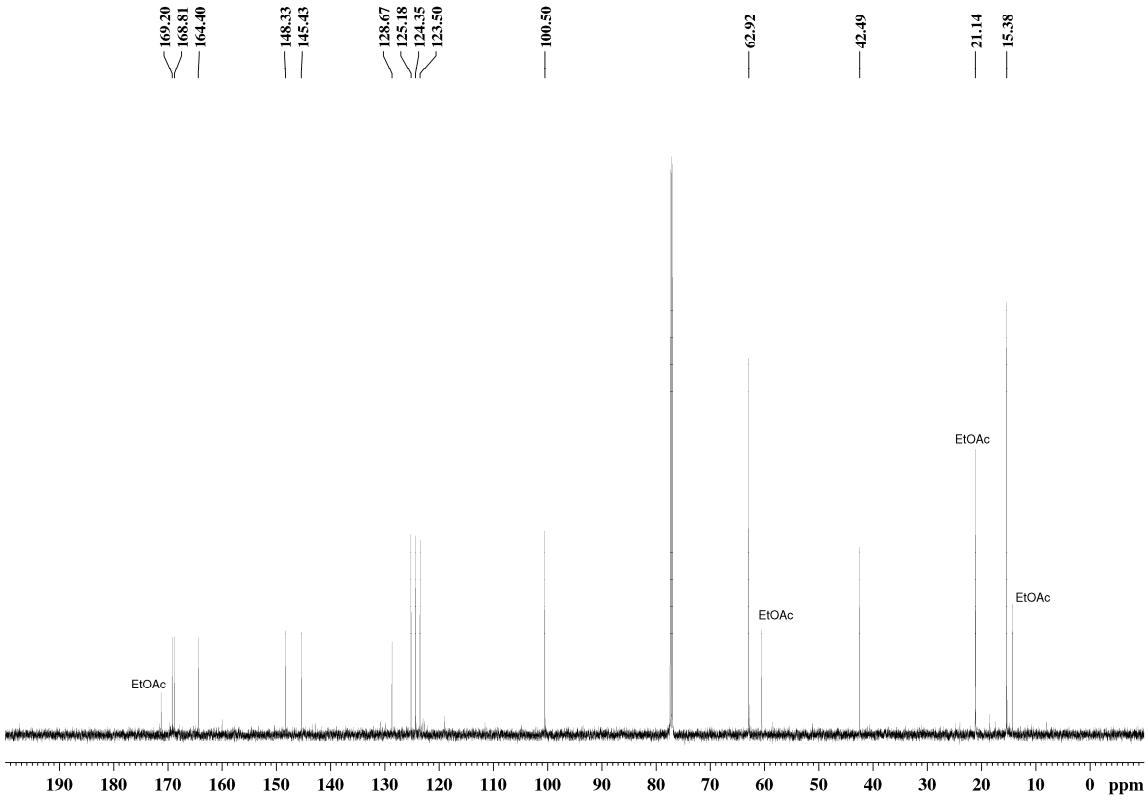
150 MHz ^{13}C NMR spectrum of **17** in $CDCl_3$



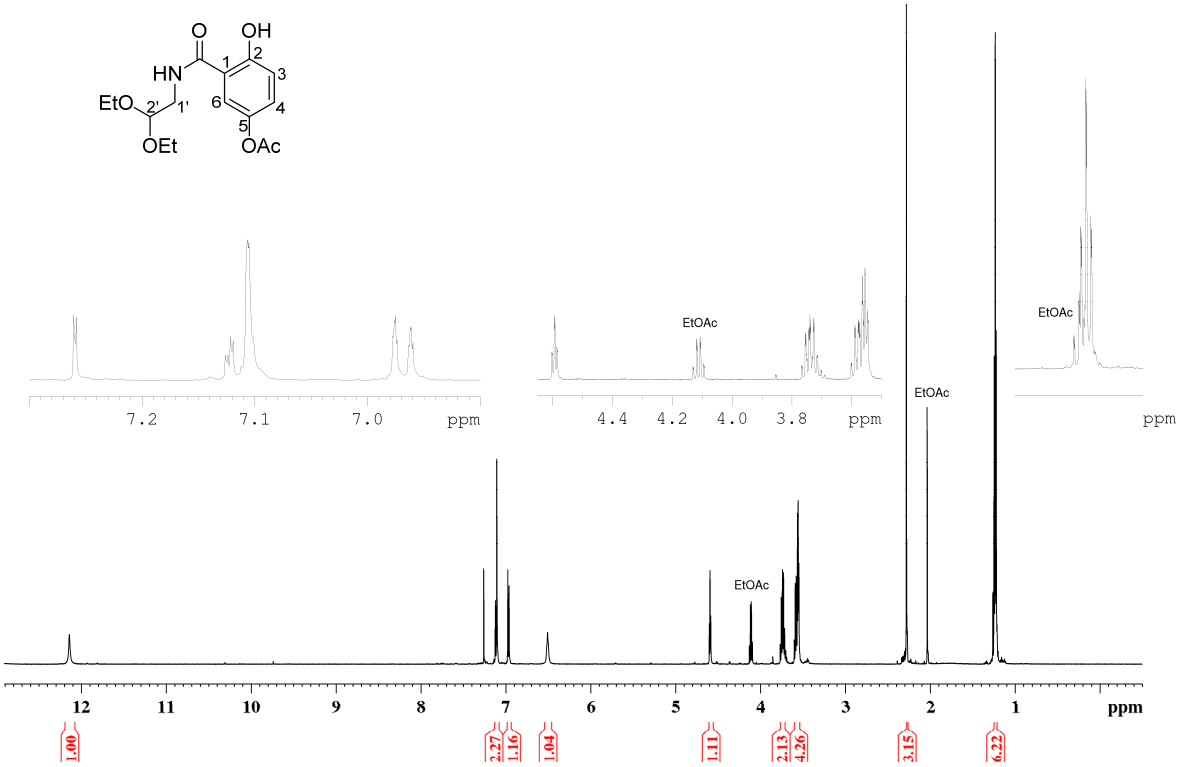
600 MHz ^{1}H NMR spectrum of **22** in $CDCl_3$



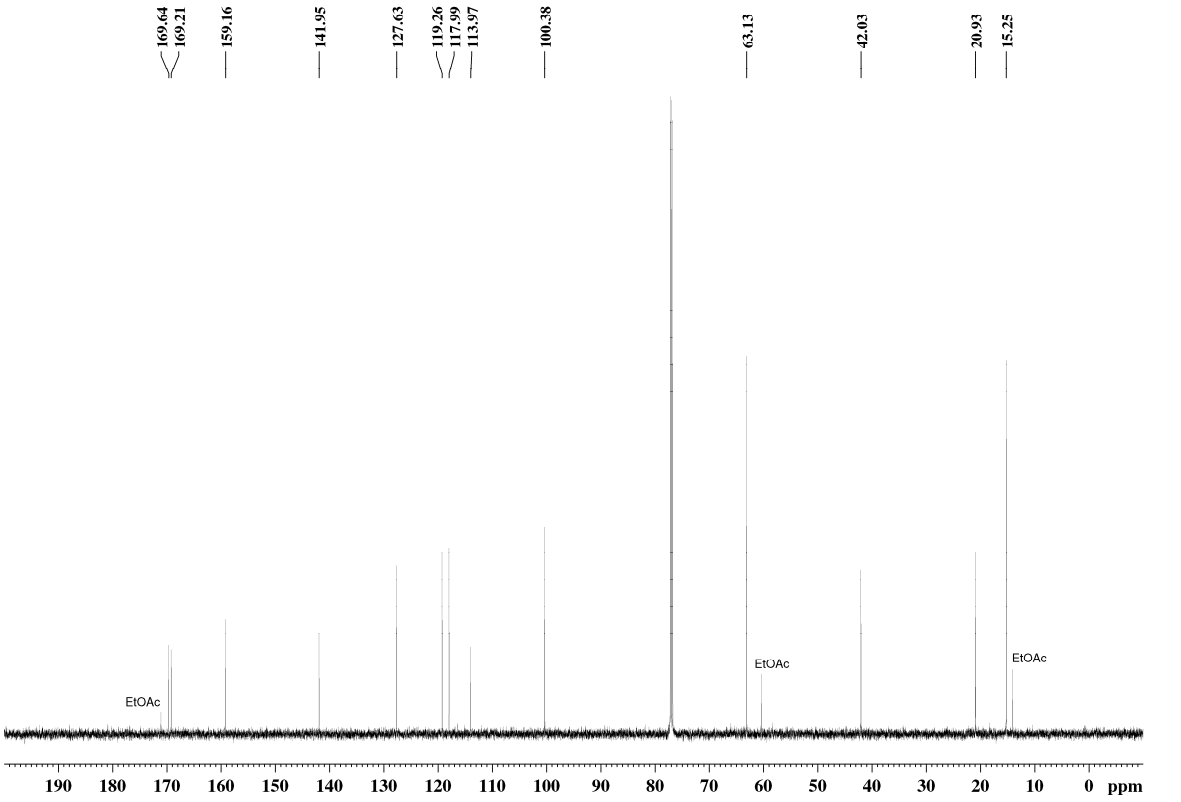
150 MHz ^{13}C NMR spectrum of **22** in $CDCl_3$



600 MHz ^{1}H NMR spectrum of **23** in $CDCl_3$



150 MHz ^{13}C NMR spectrum of **23** in $CDCl_3$



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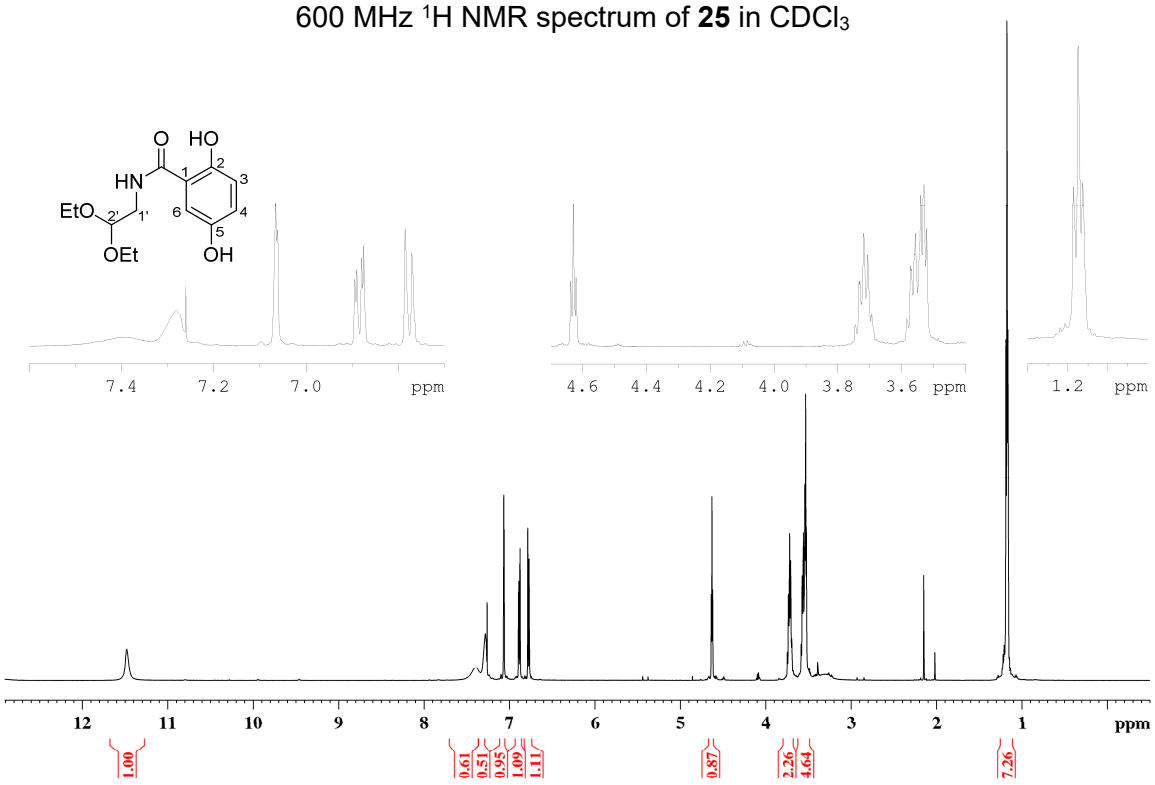
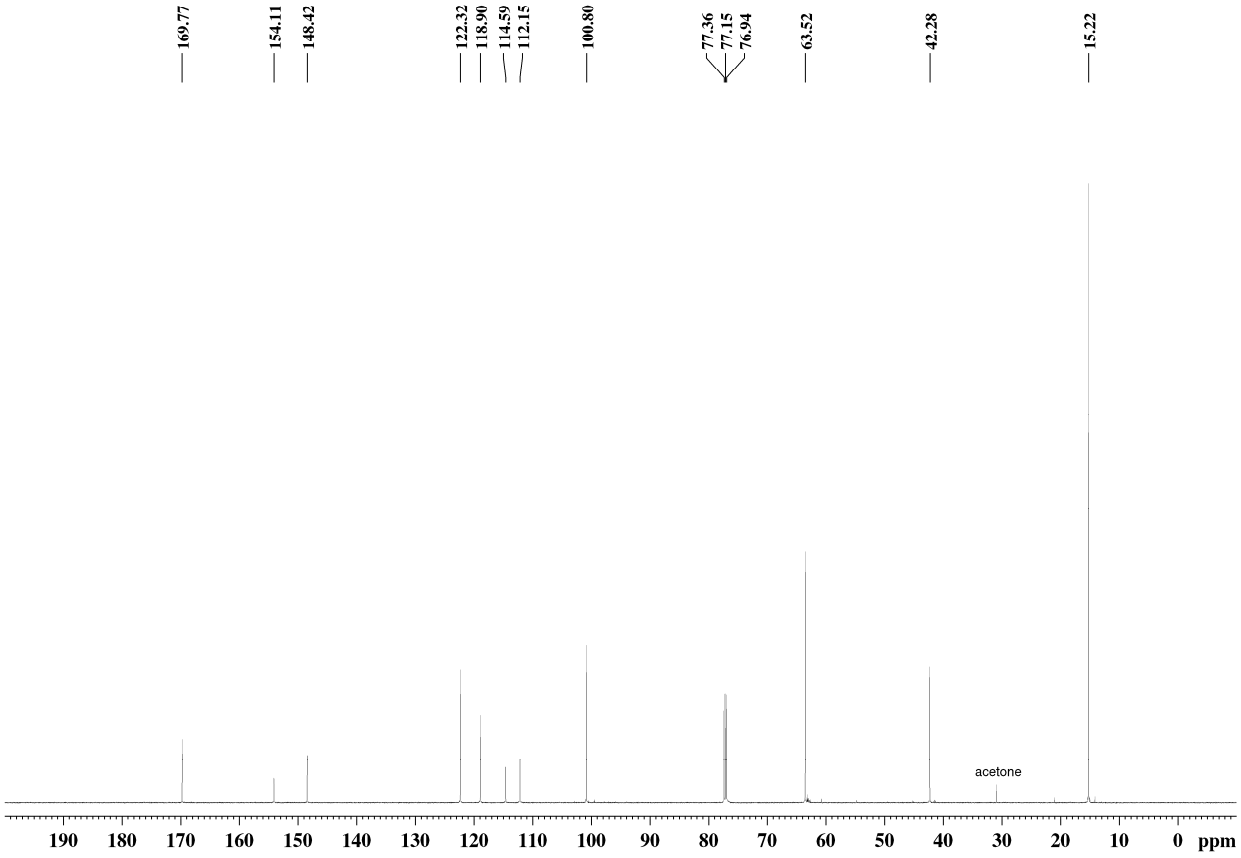
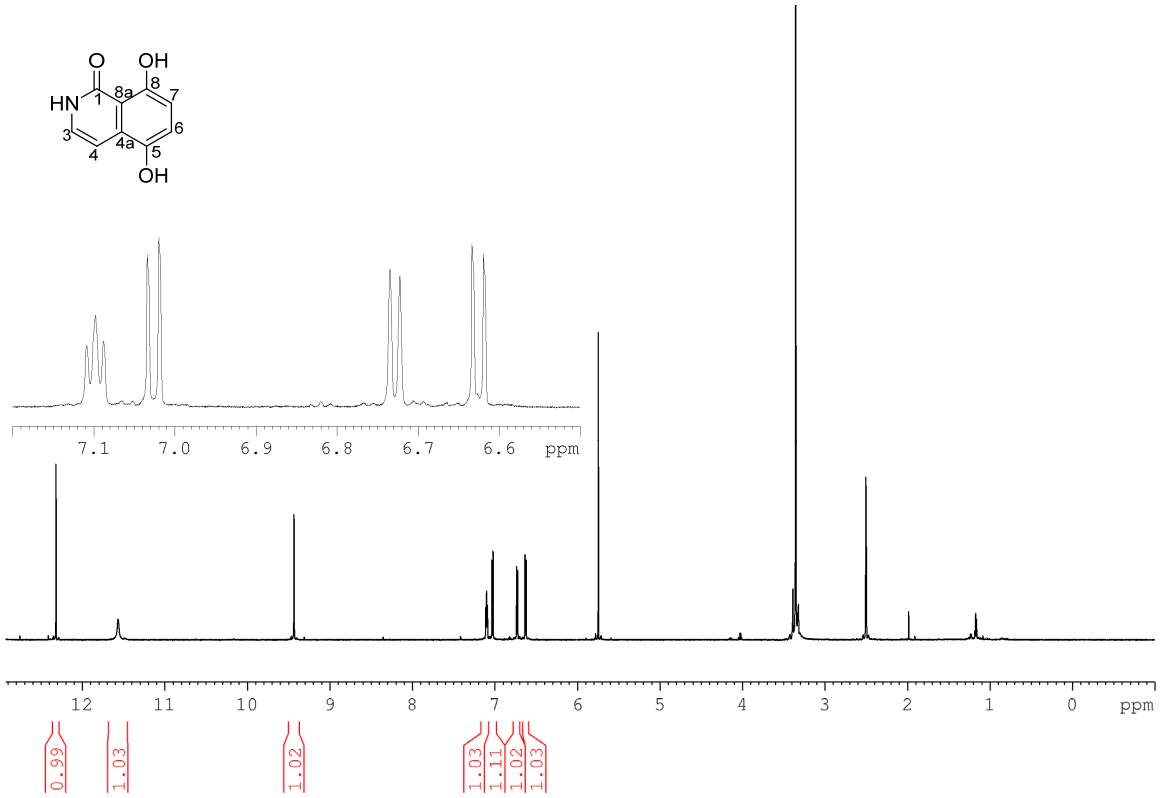


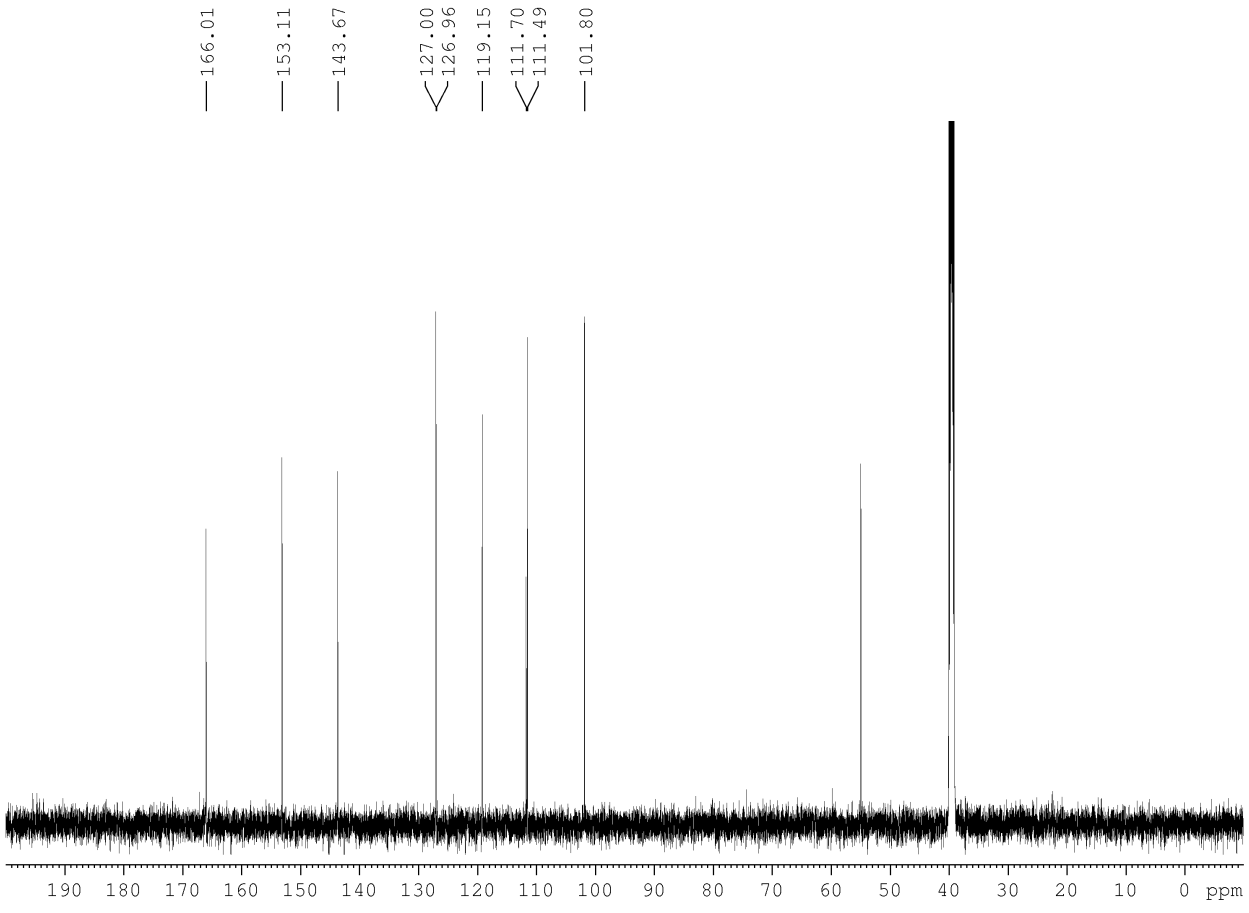
150 MHz ^{13}C NMR spectrum of **25** in $CDCl_3$



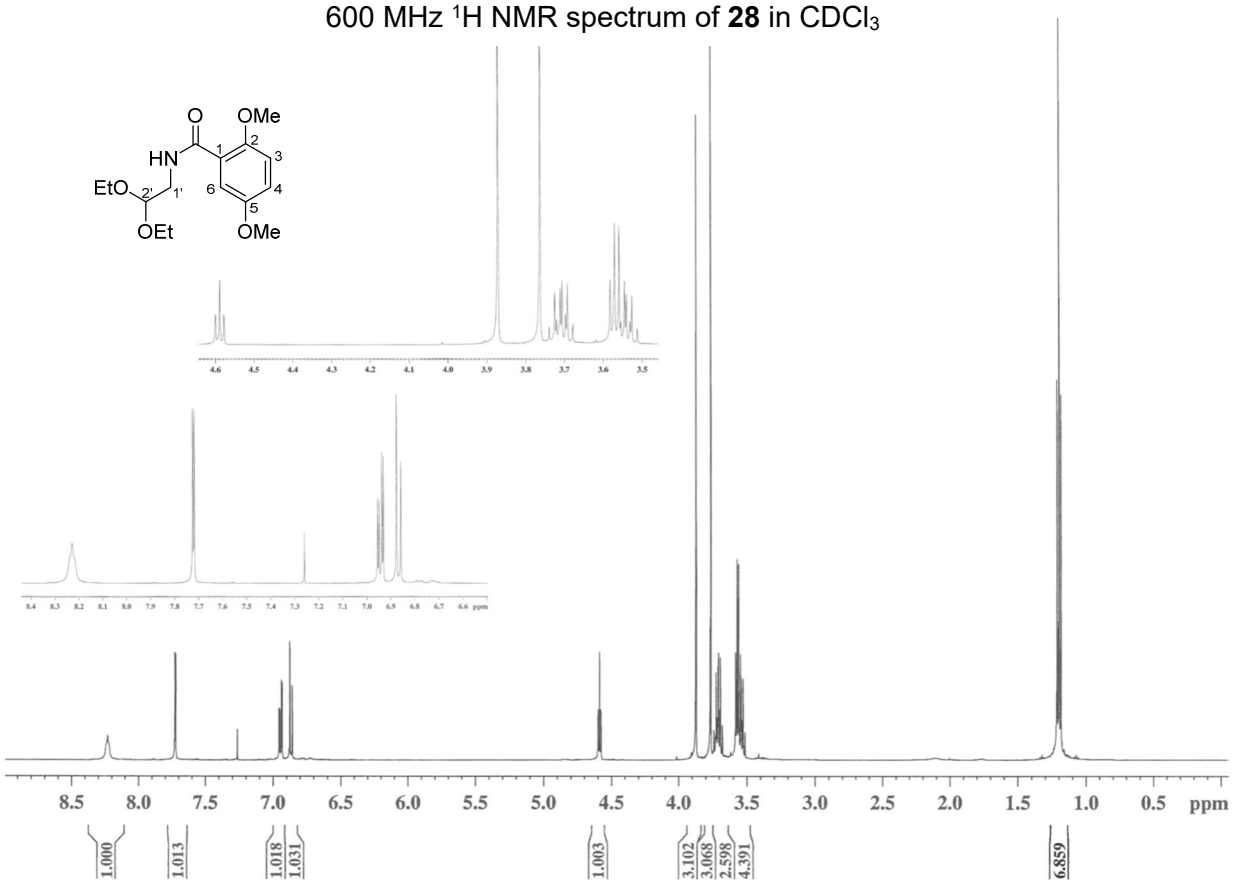
600 MHz ^{1}H NMR spectrum of **26** in d_6-DMSO



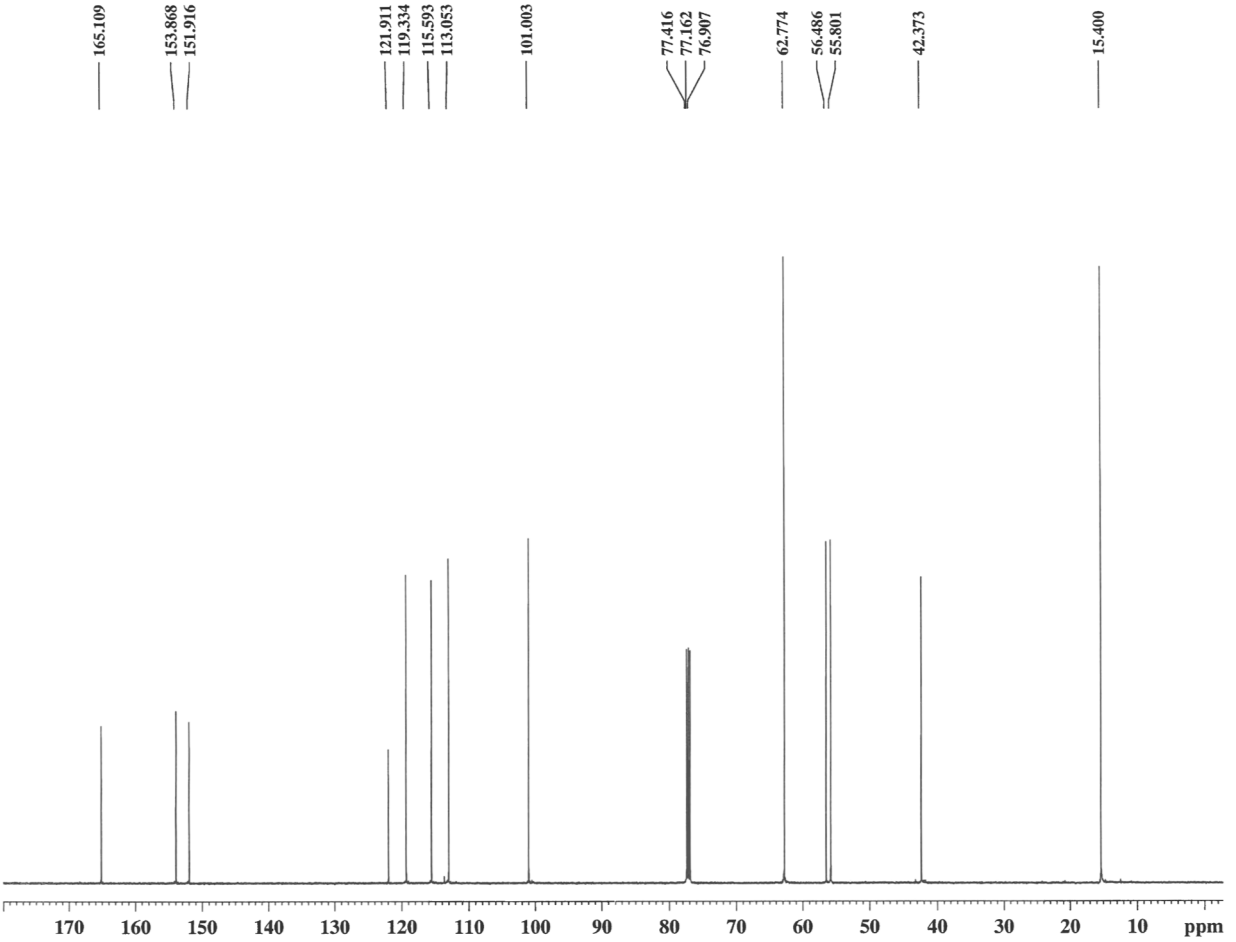
150 MHz ^{13}C NMR spectrum of **26** in d_6-DMSO



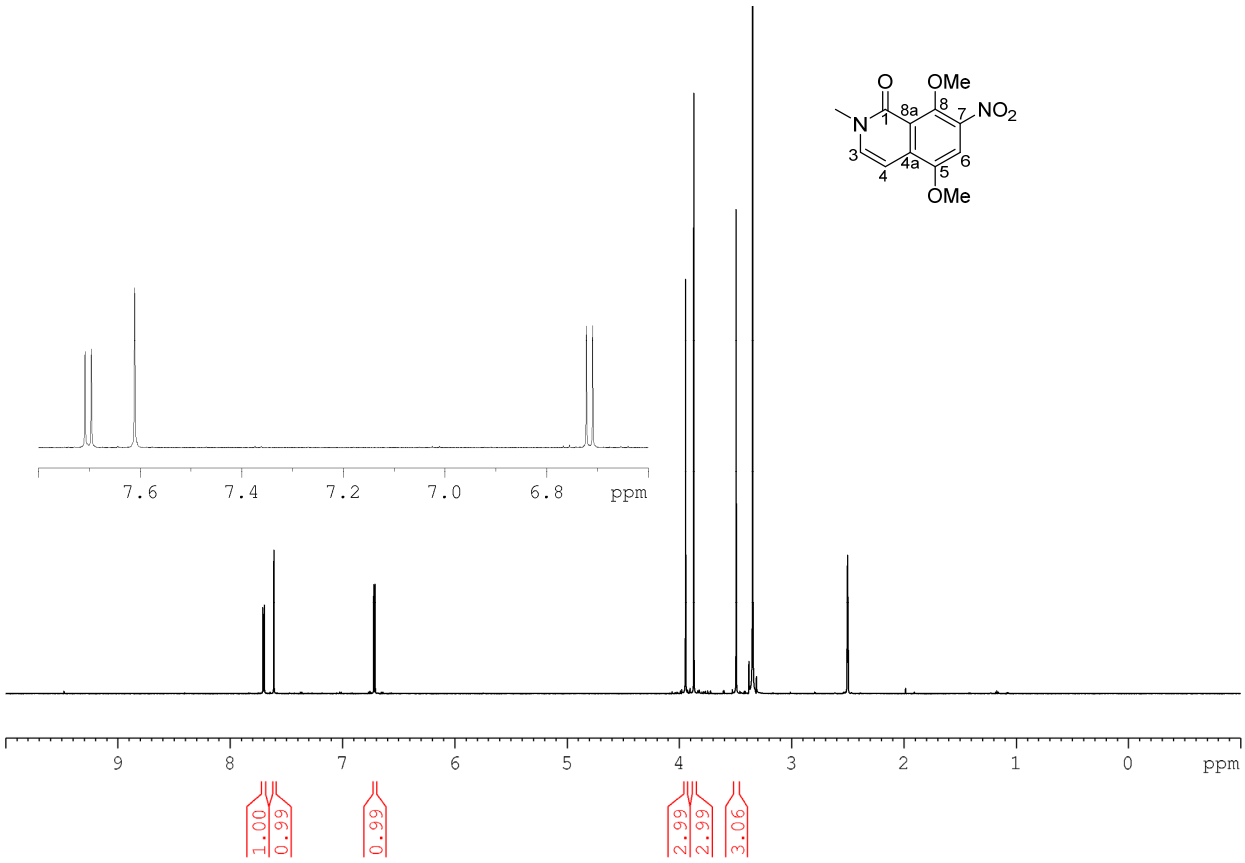
600 MHz ^{1}H NMR spectrum of **28** in $CDCl_3$



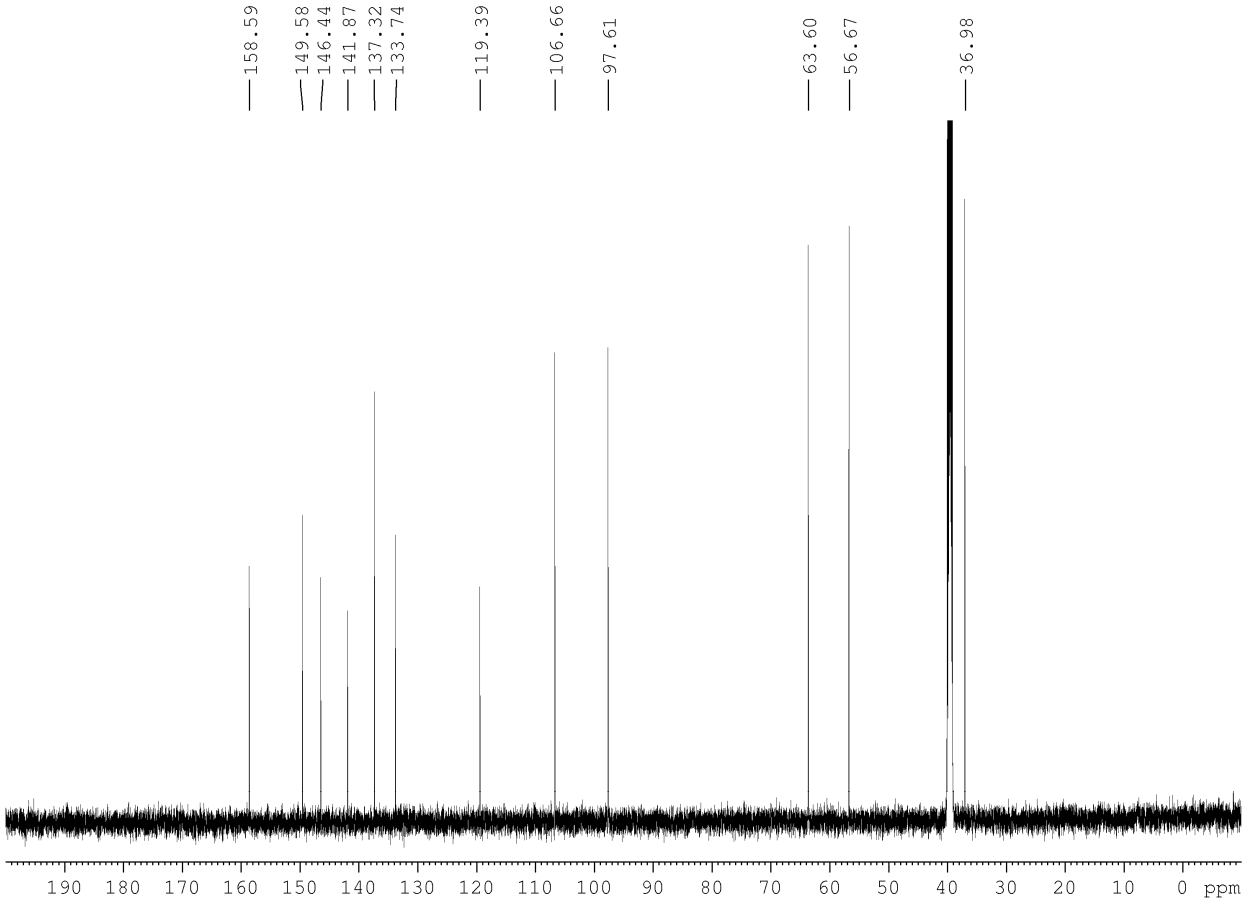
125 MHz ^{13}C NMR spectrum of **28** in $CDCl_3$



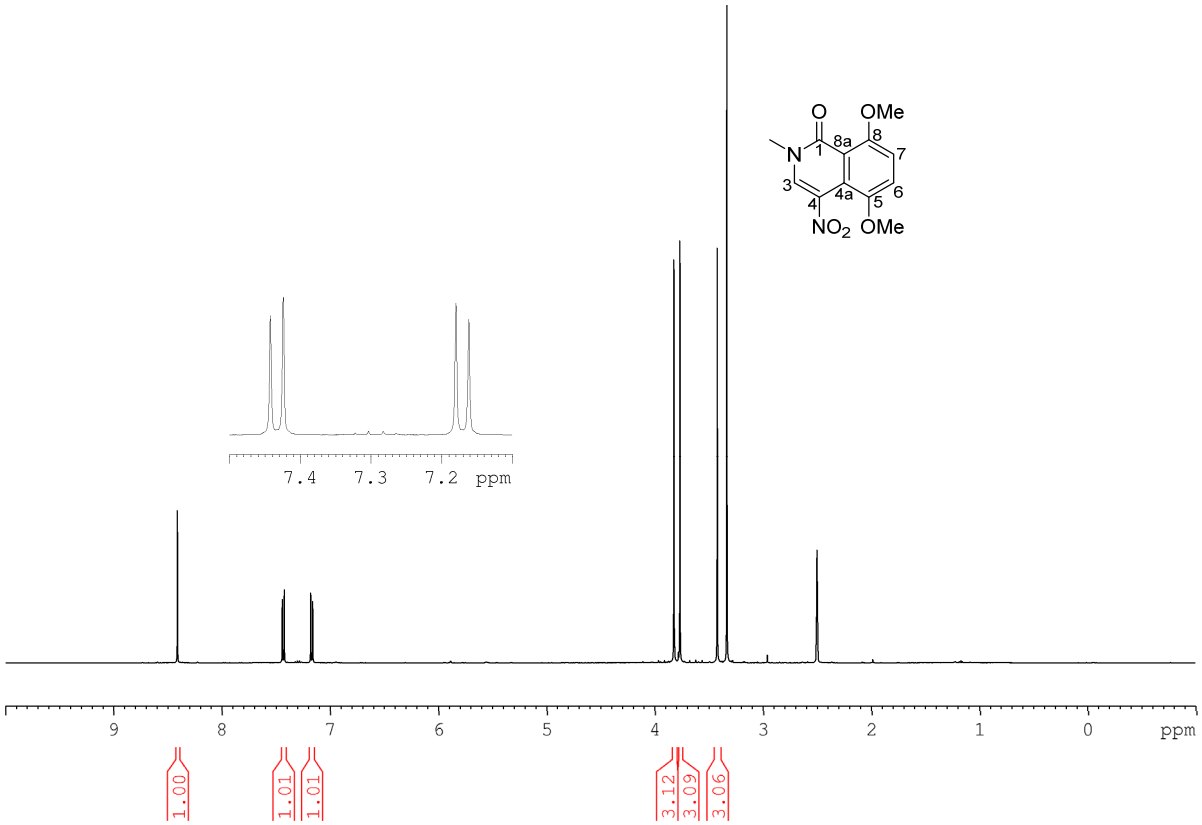
600 MHz ^{1}H NMR spectrum of **36** in d_6-DMSO



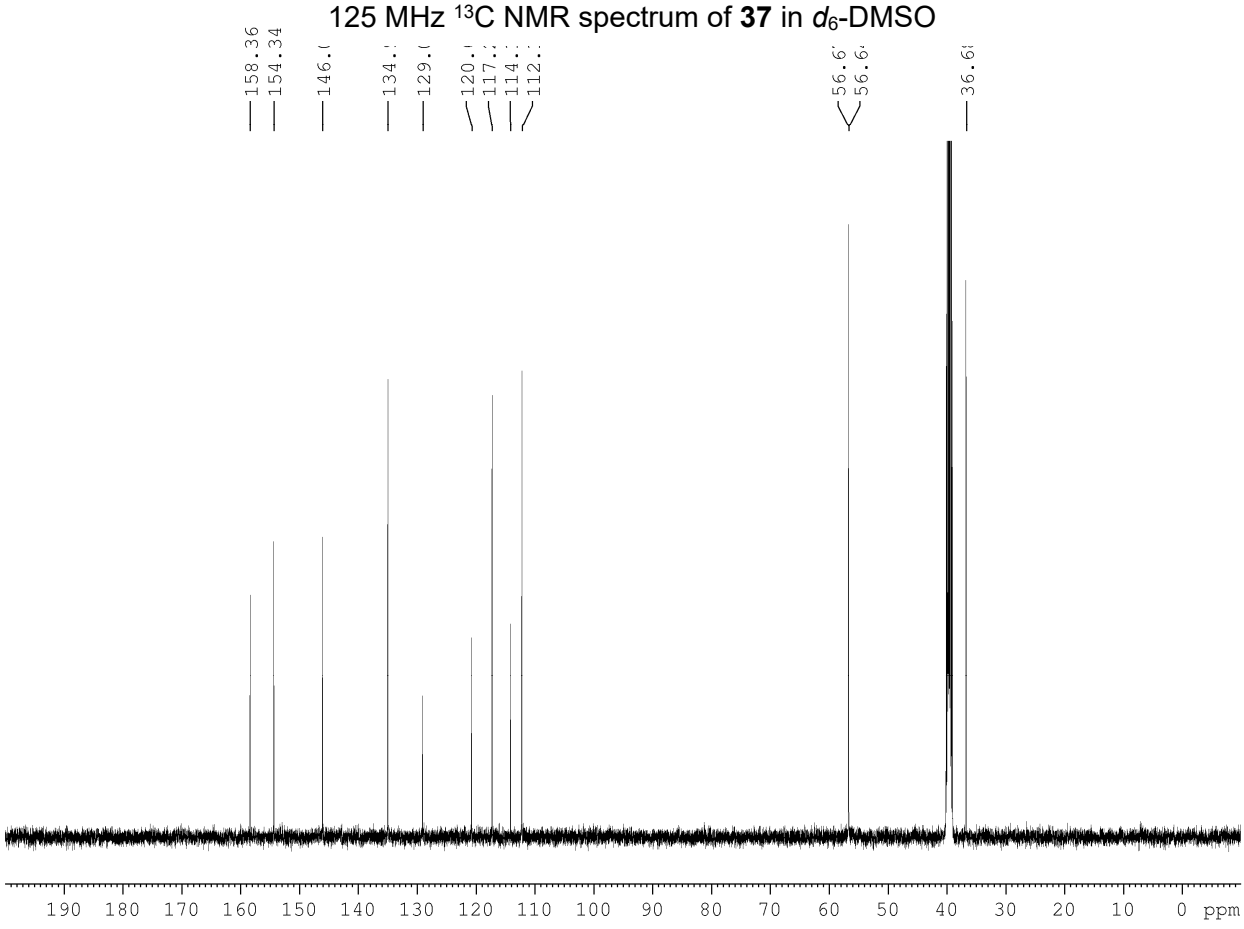
150 MHz ^{13}C NMR spectrum of **36** in d_6-DMSO



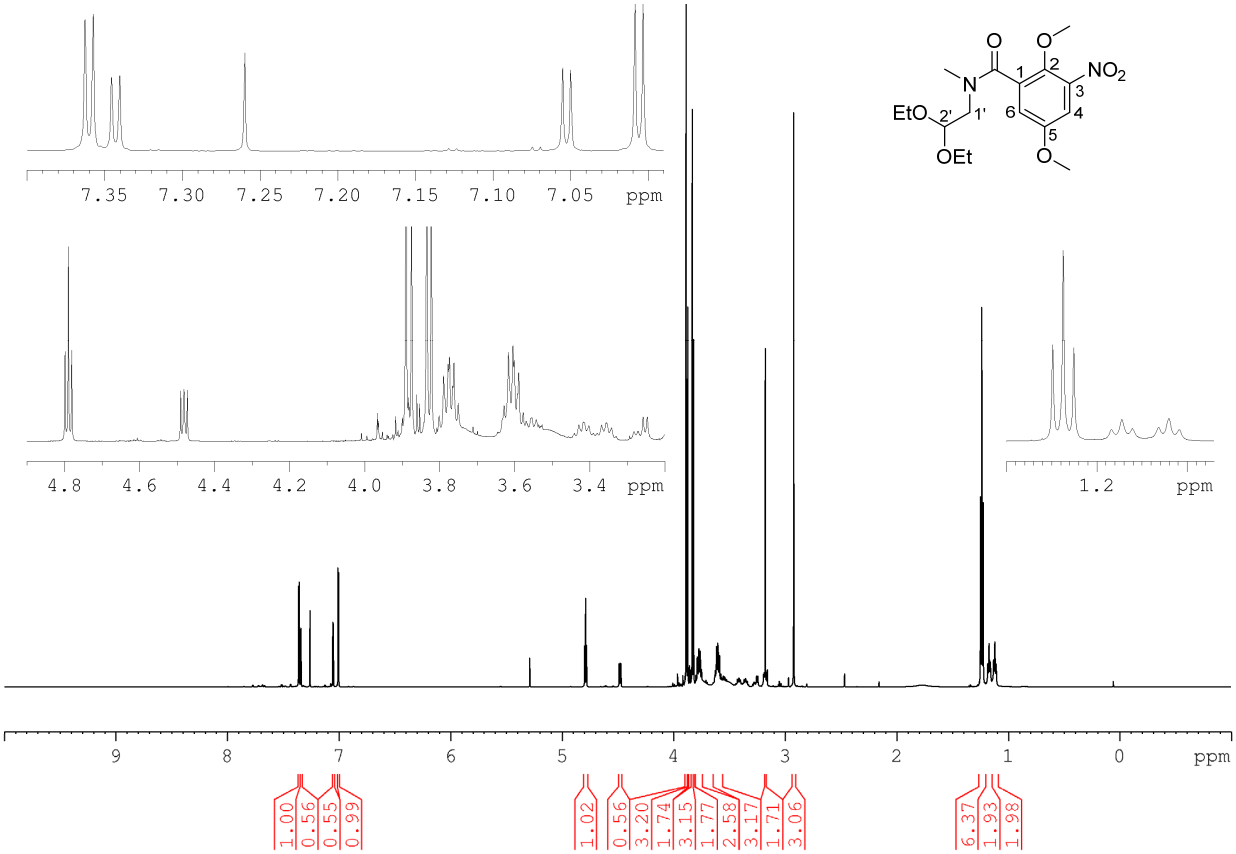
500 MHz ^{1}H NMR spectrum of **37** in d_6-DMSO



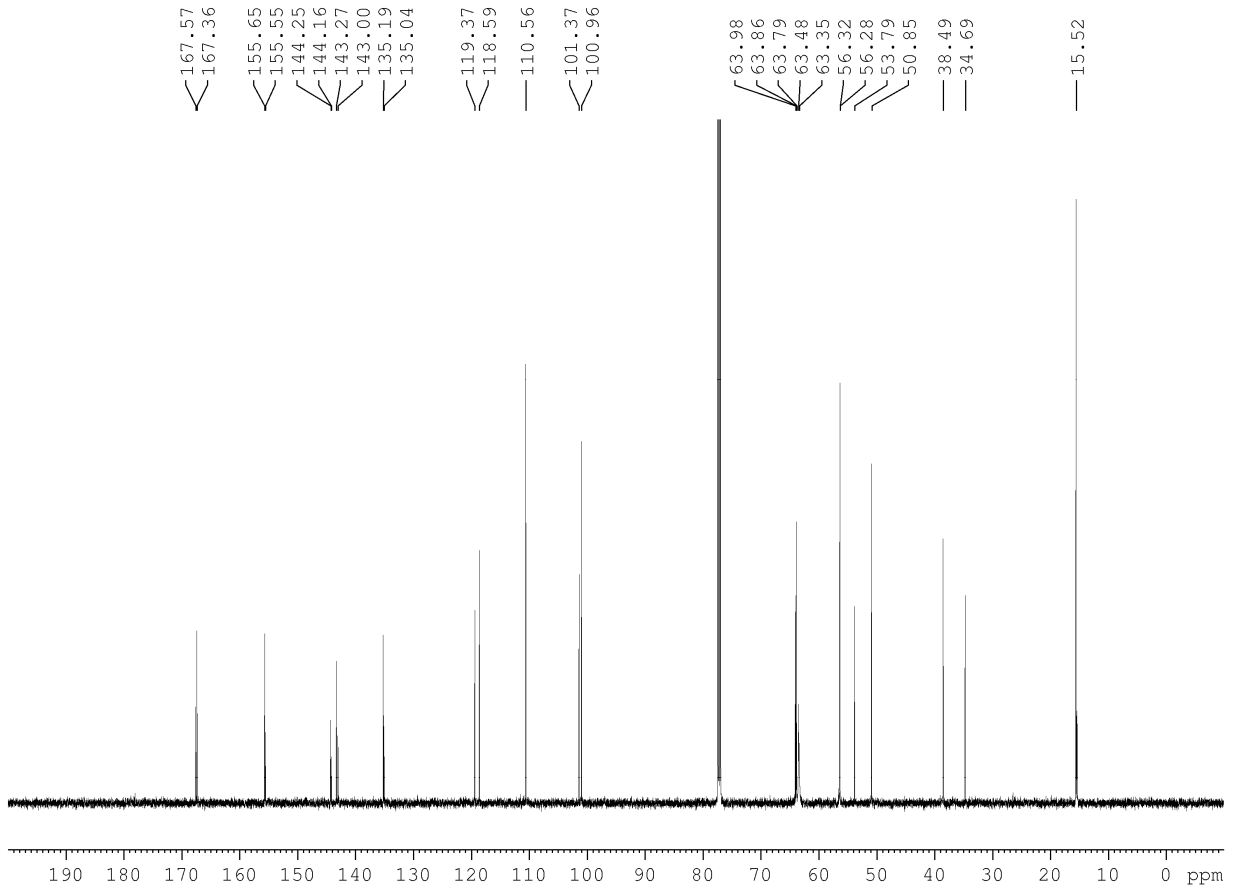
125 MHz ^{13}C NMR spectrum of **37** in d_6-DMSO



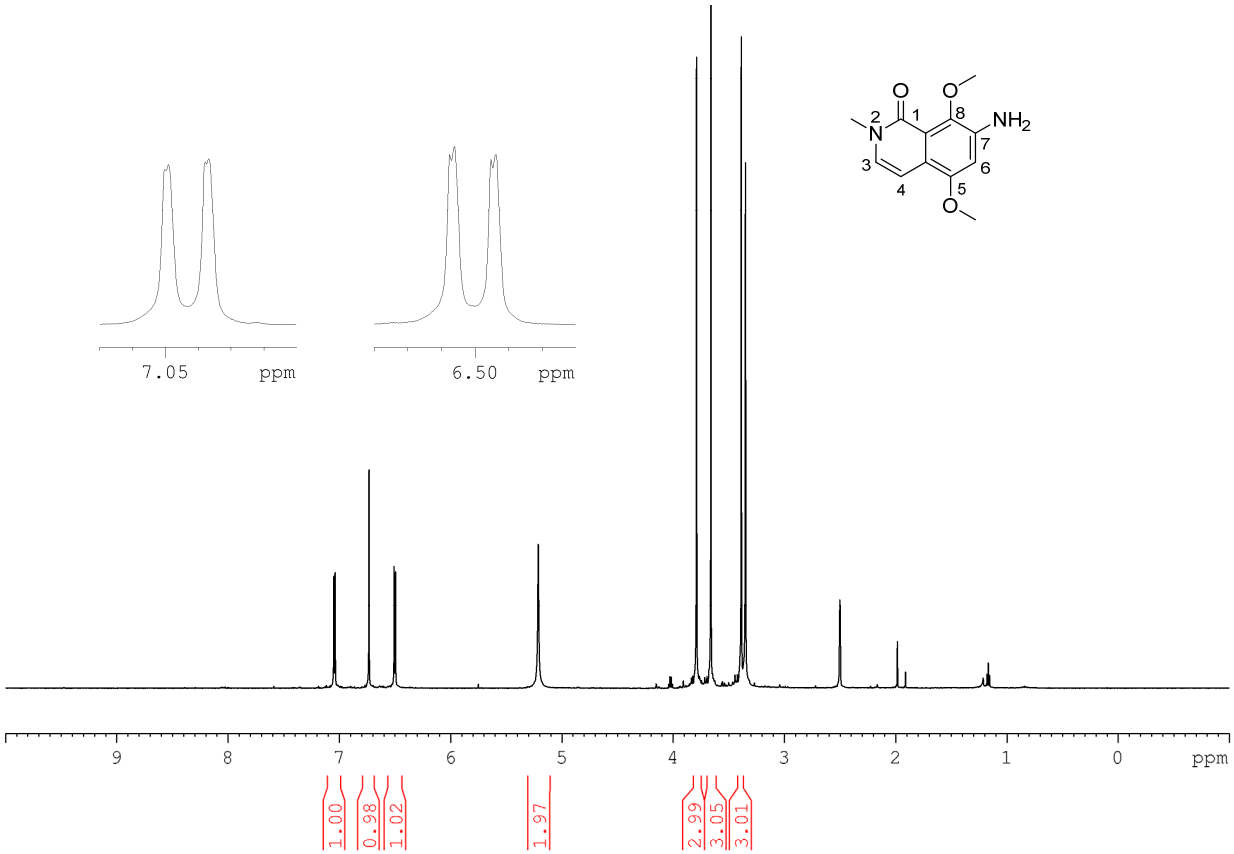
500 MHz ^{1}H NMR spectrum of **44** in $CDCl_3$



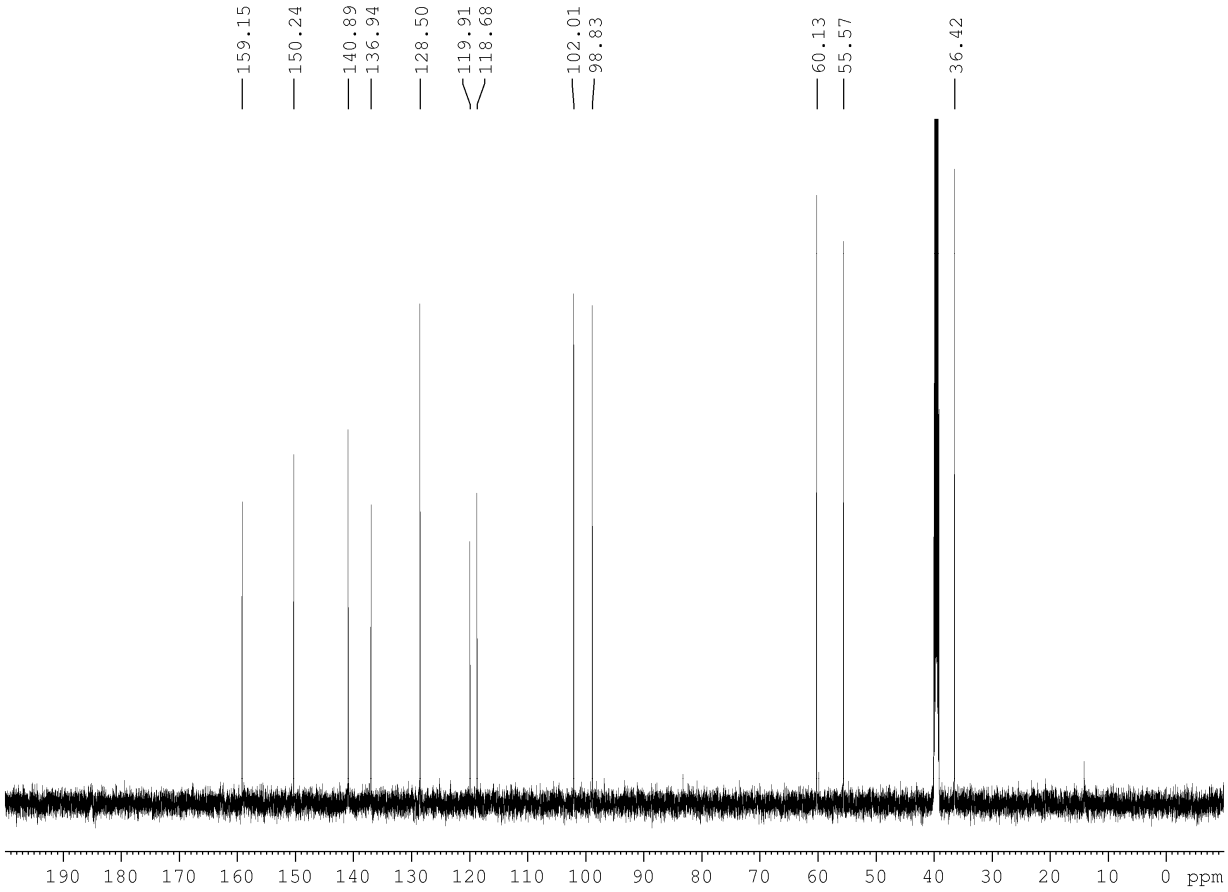
125 MHz ^{13}C NMR spectrum of **44** in $CDCl_3$



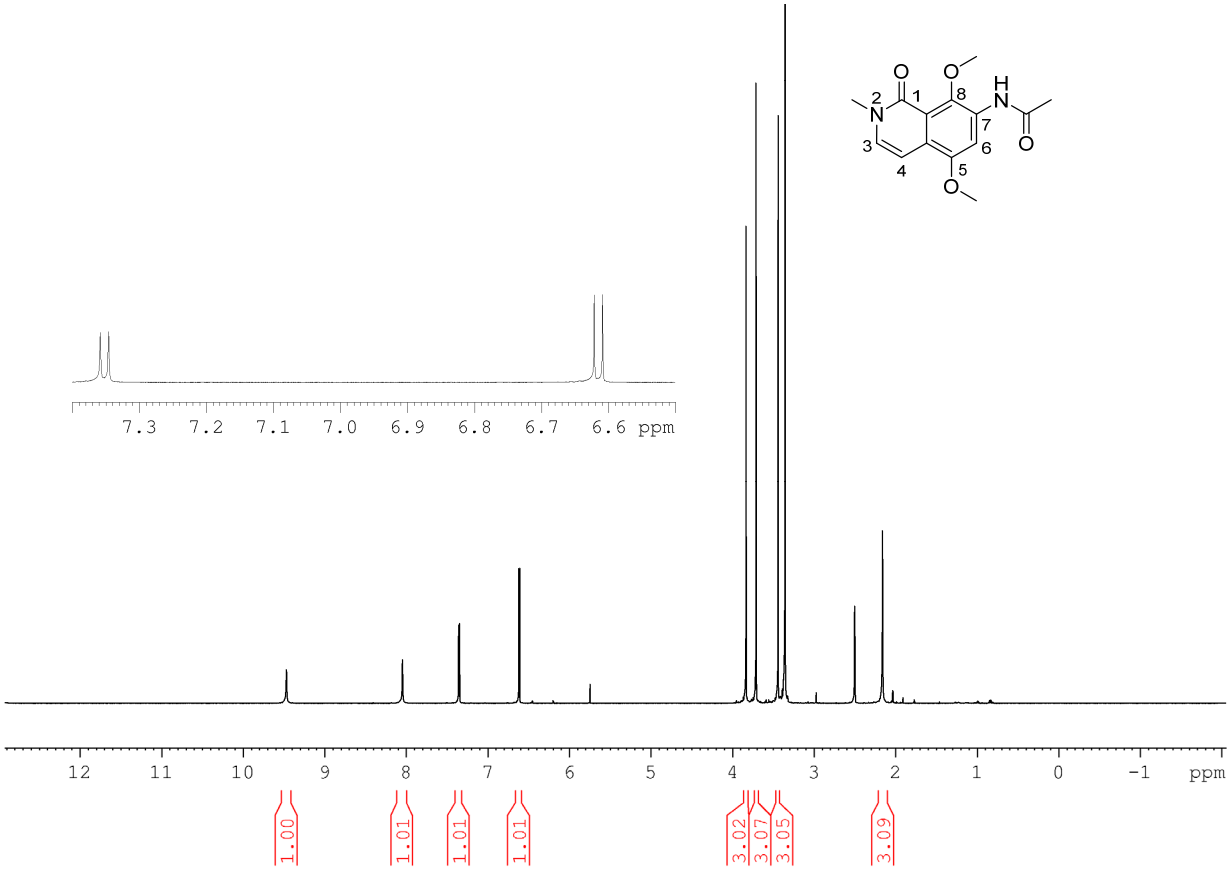
600 MHz ^{1}H NMR spectrum of **45** in d_6-DMSO



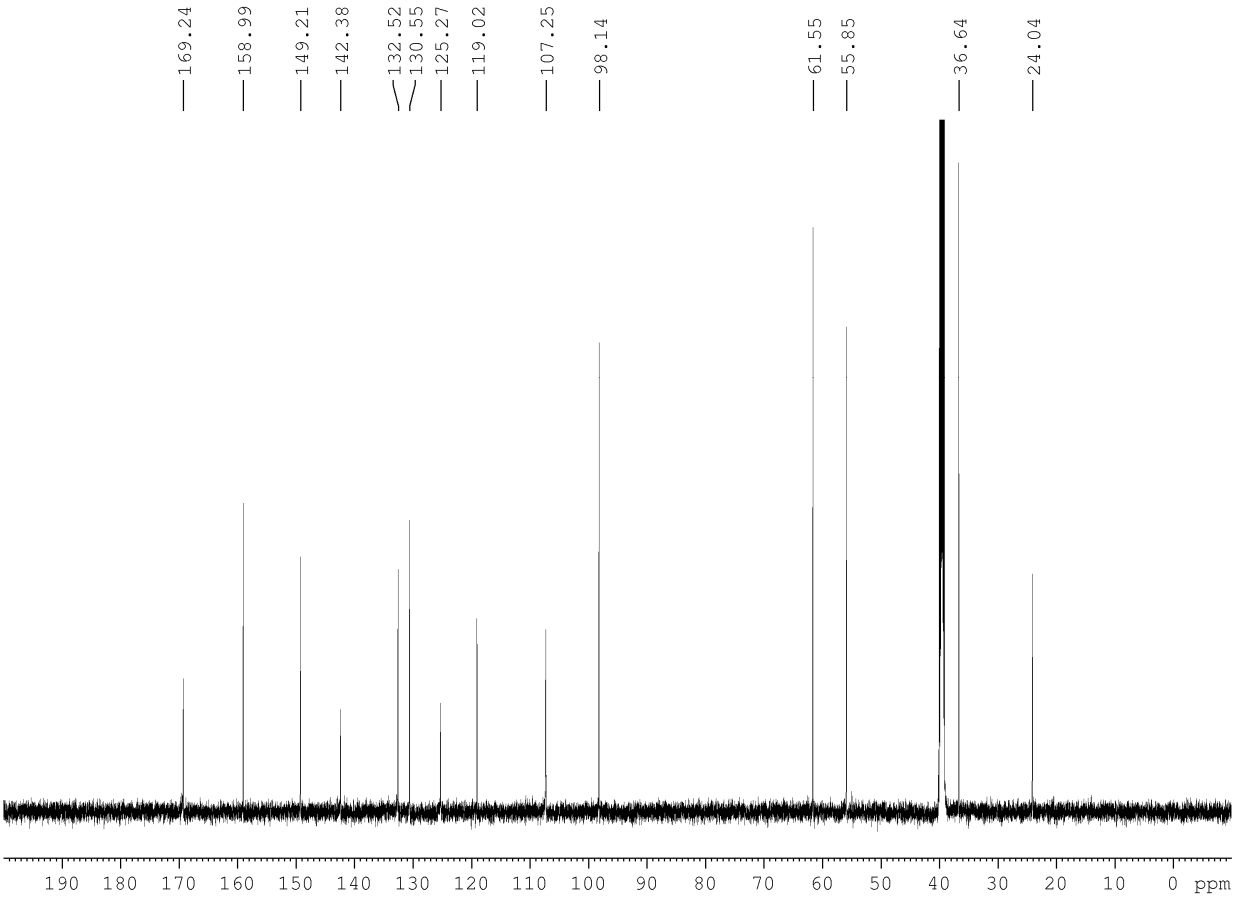
150 MHz ^{13}C NMR spectrum of **45** in d_6-DMSO



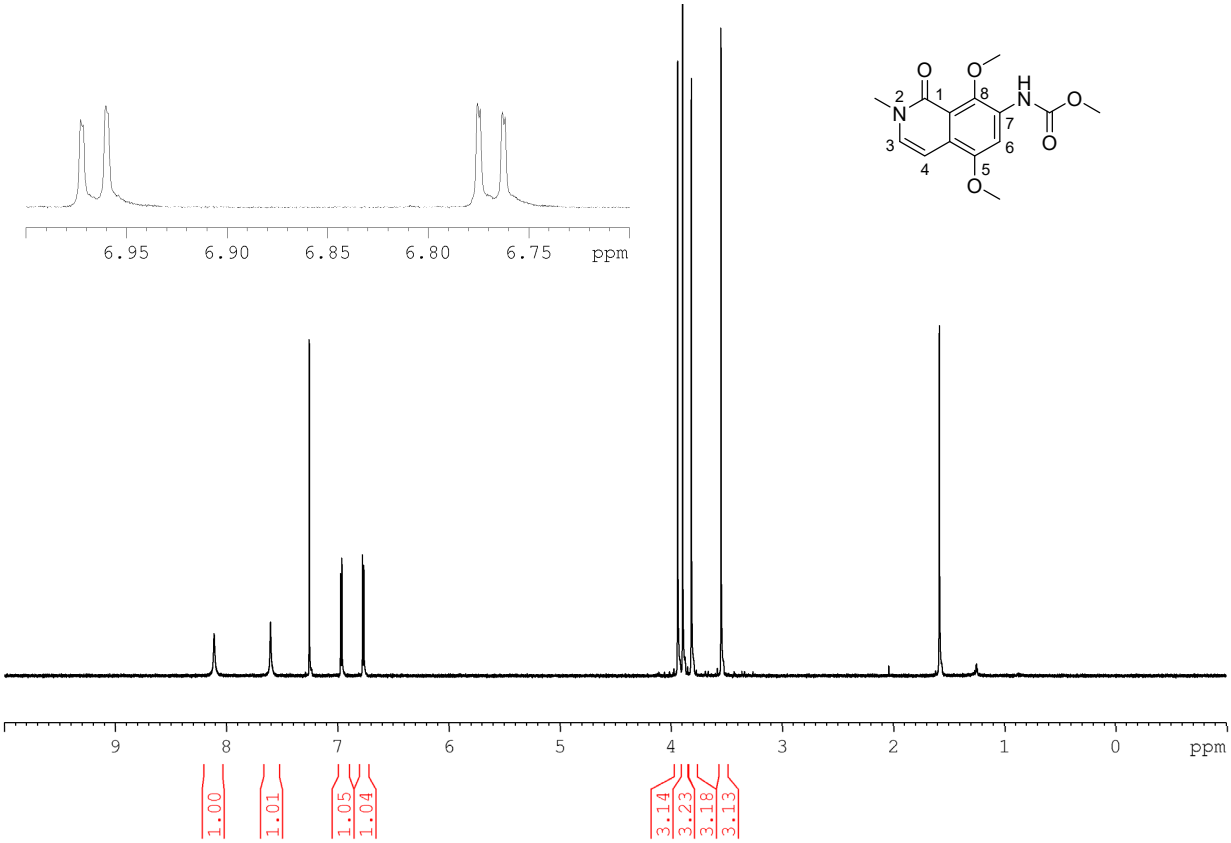
600 MHz ^{1}H NMR spectrum of **46** in d_6-DMSO



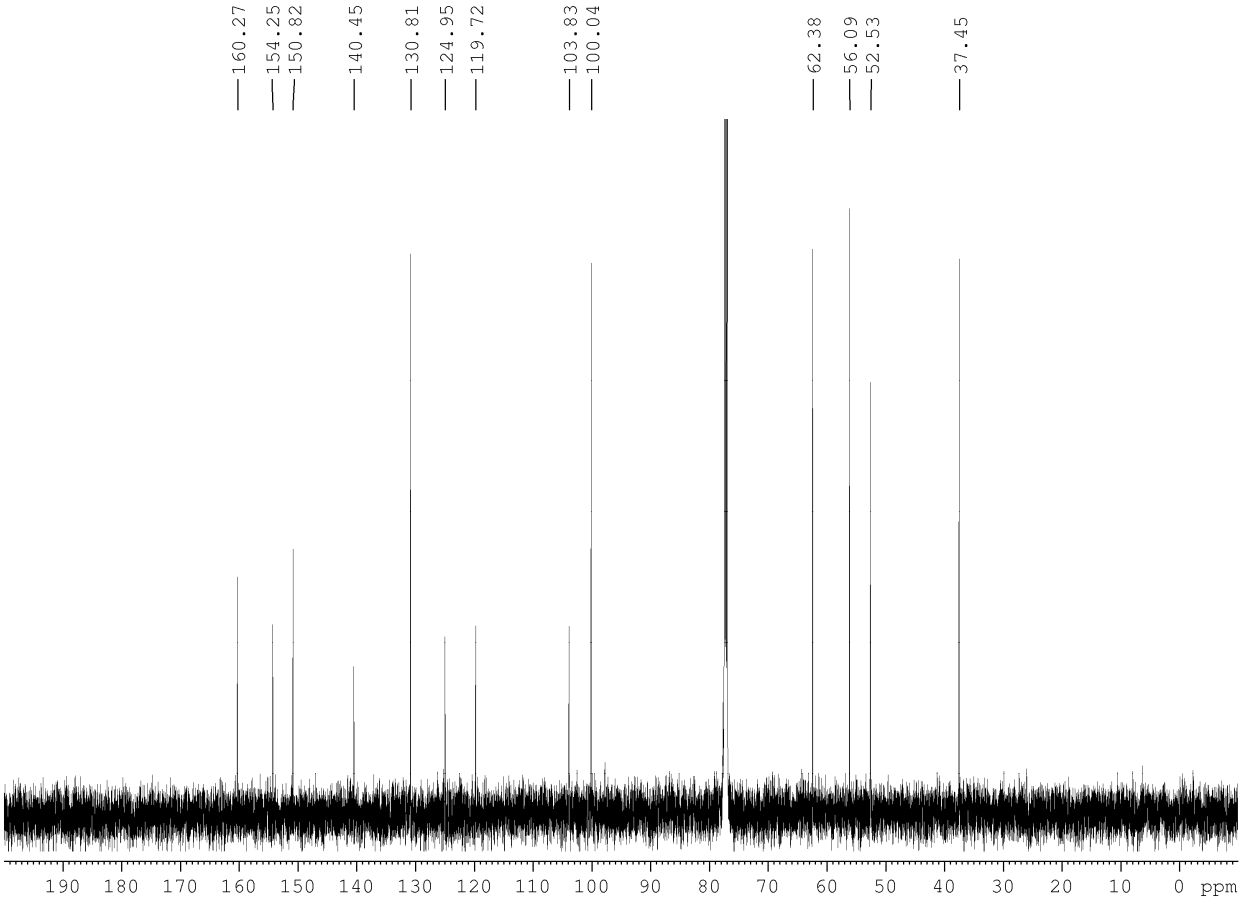
150 MHz ^{13}C NMR spectrum of **46** in d_6-DMSO



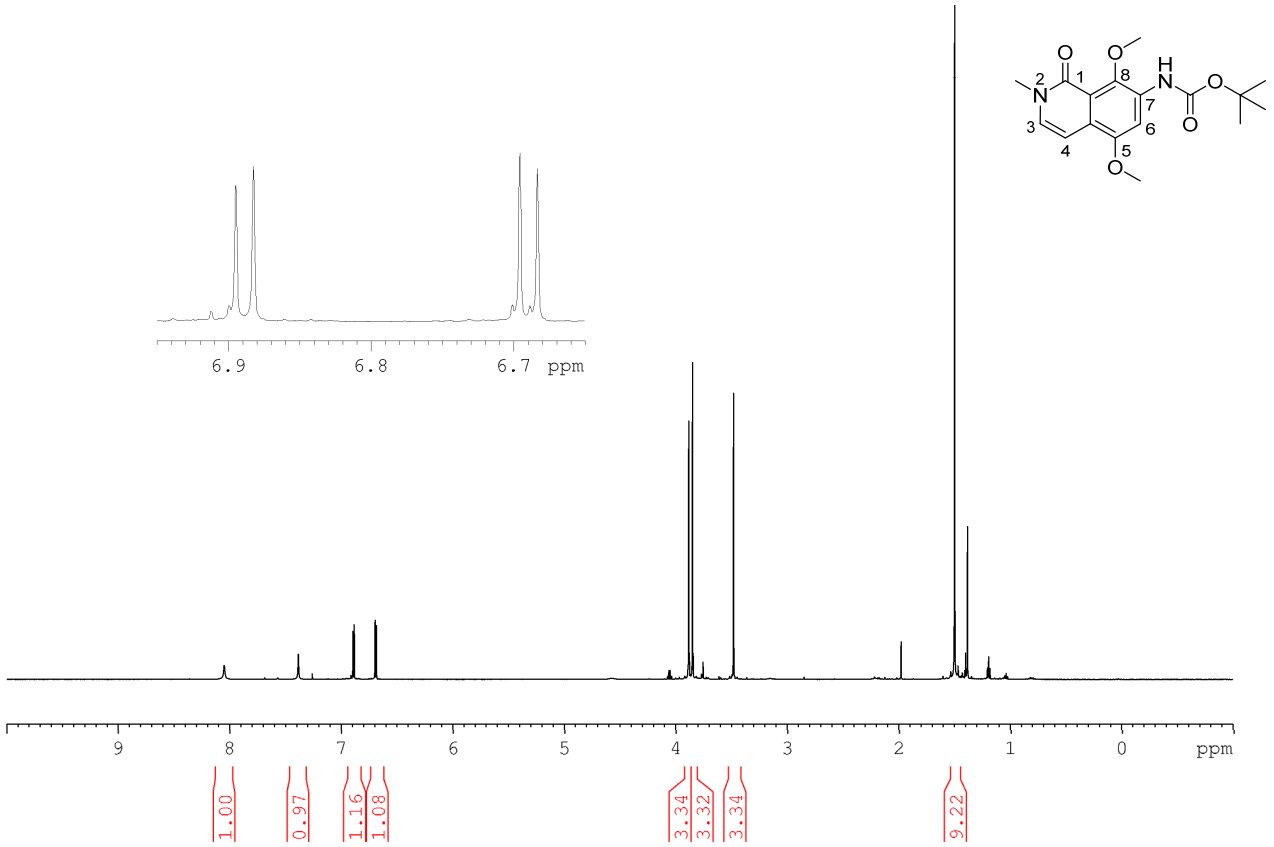
600 MHz ^{1}H NMR spectrum of **47** in $CDCl_3$



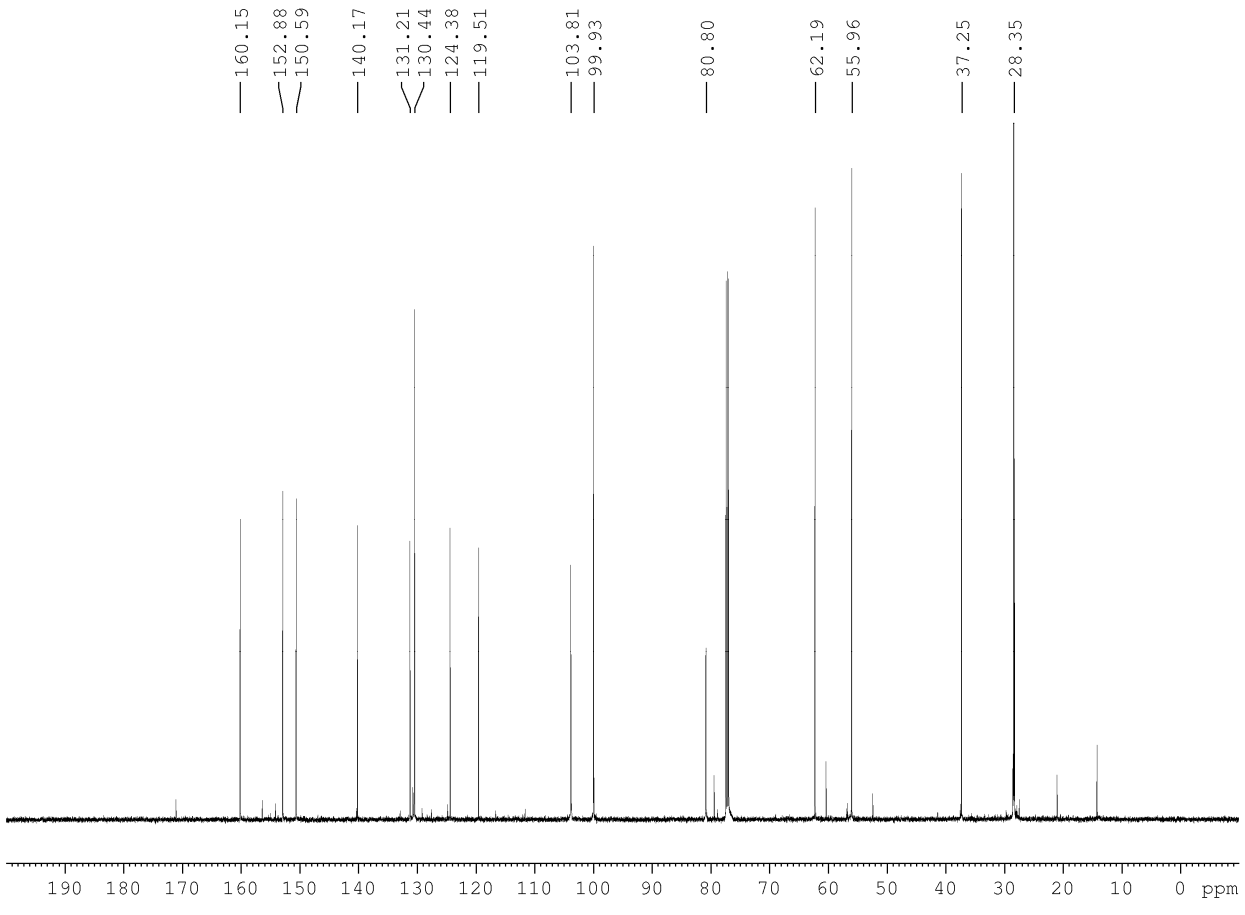
150 MHz ^{13}C NMR spectrum of **47** in $CDCl_3$



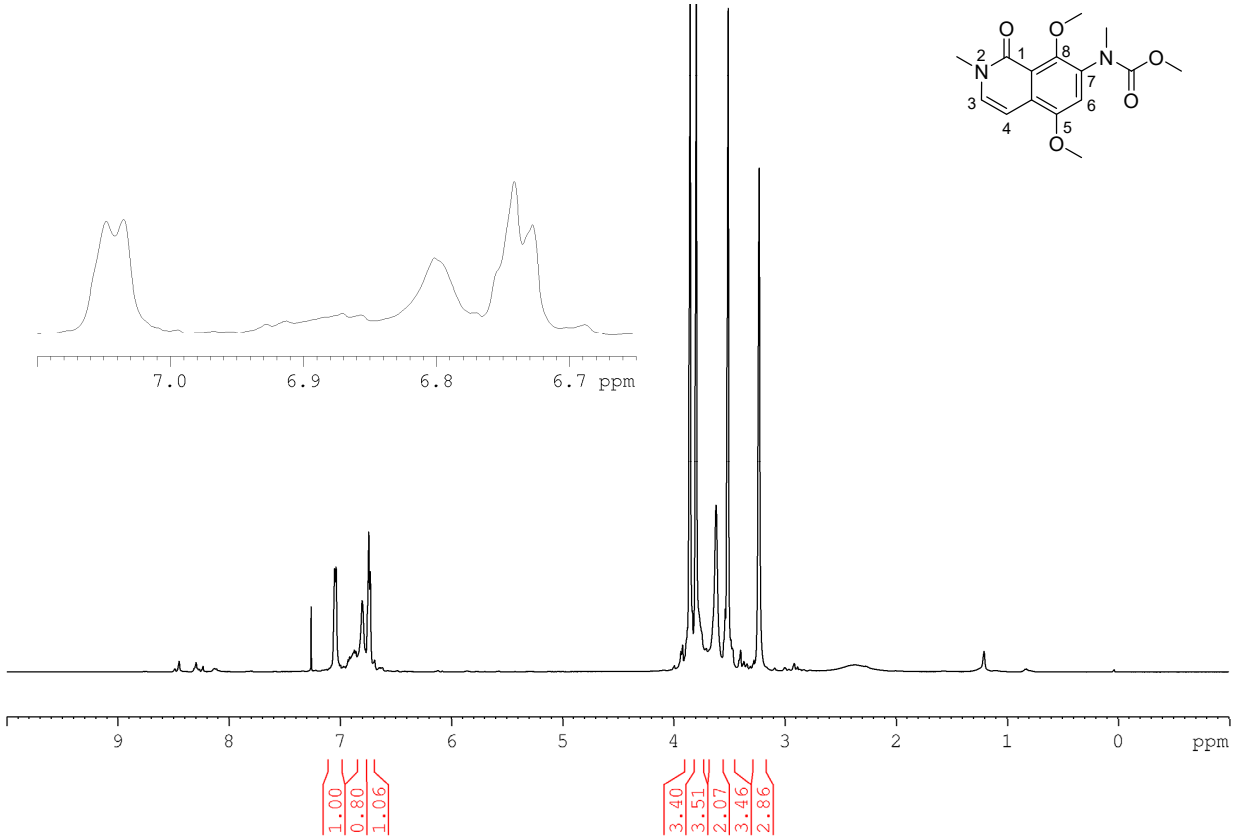
400 MHz ^{1}H NMR spectrum of **48** in $CDCl_3$



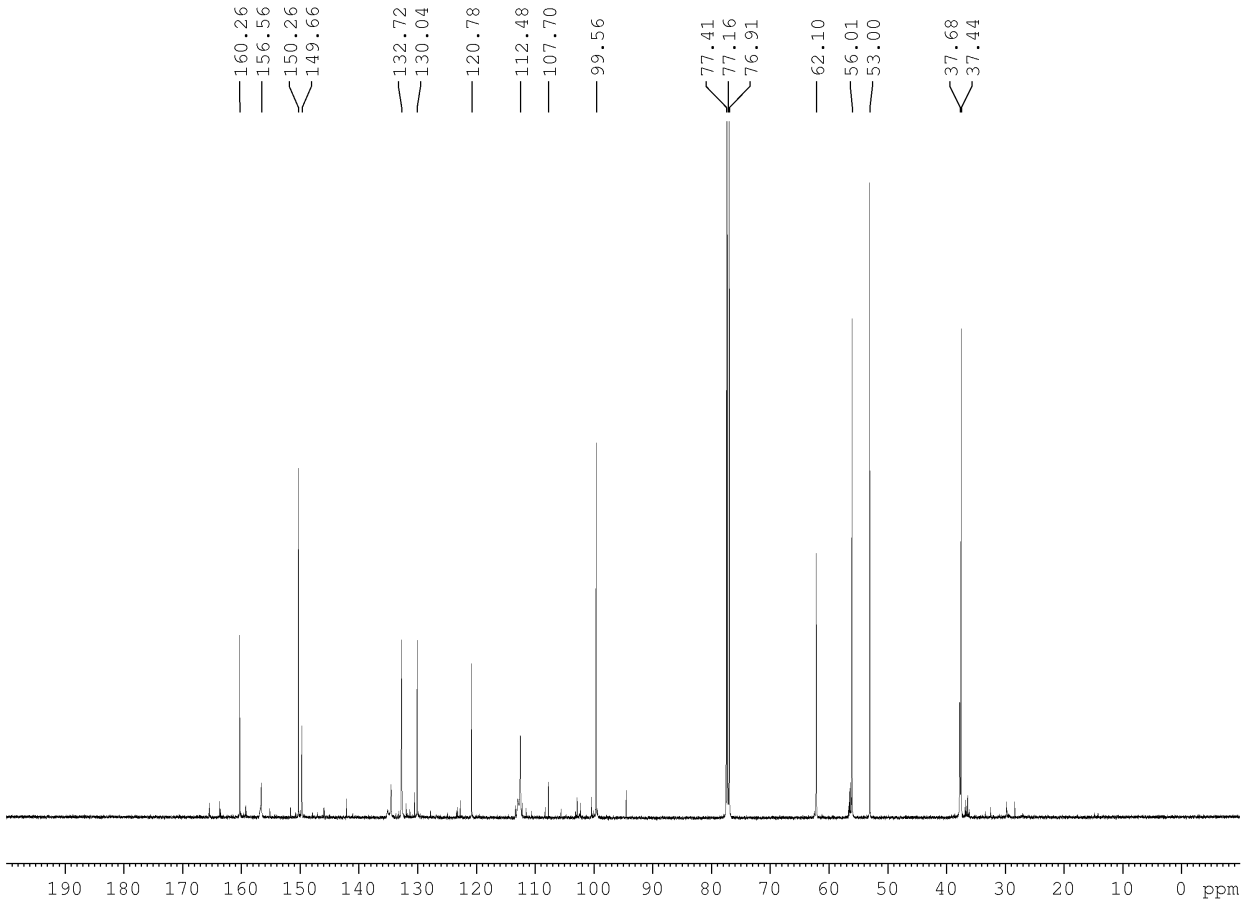
100 MHz ^{13}C NMR spectrum of **48** in $CDCl_3$



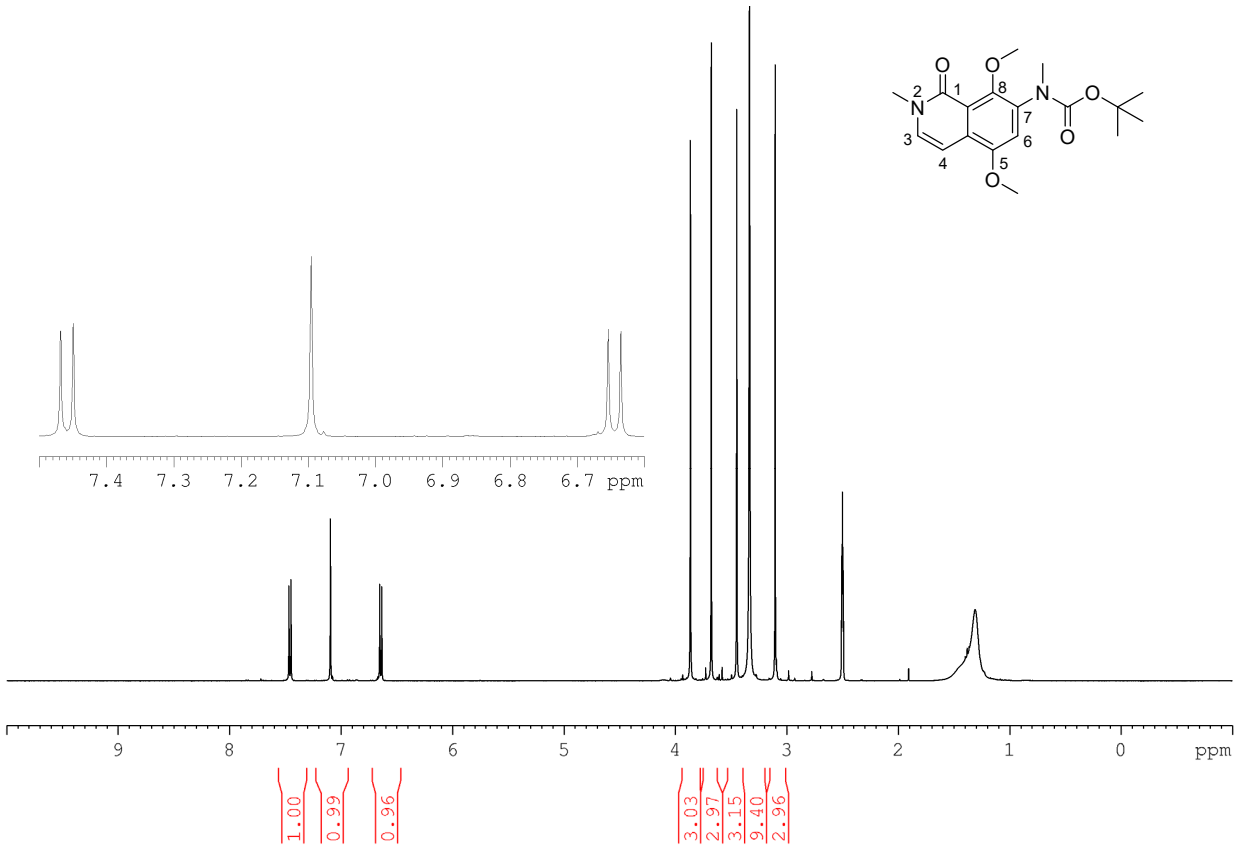
500 MHz ^{1}H NMR spectrum of **49** in $CDCl_3$



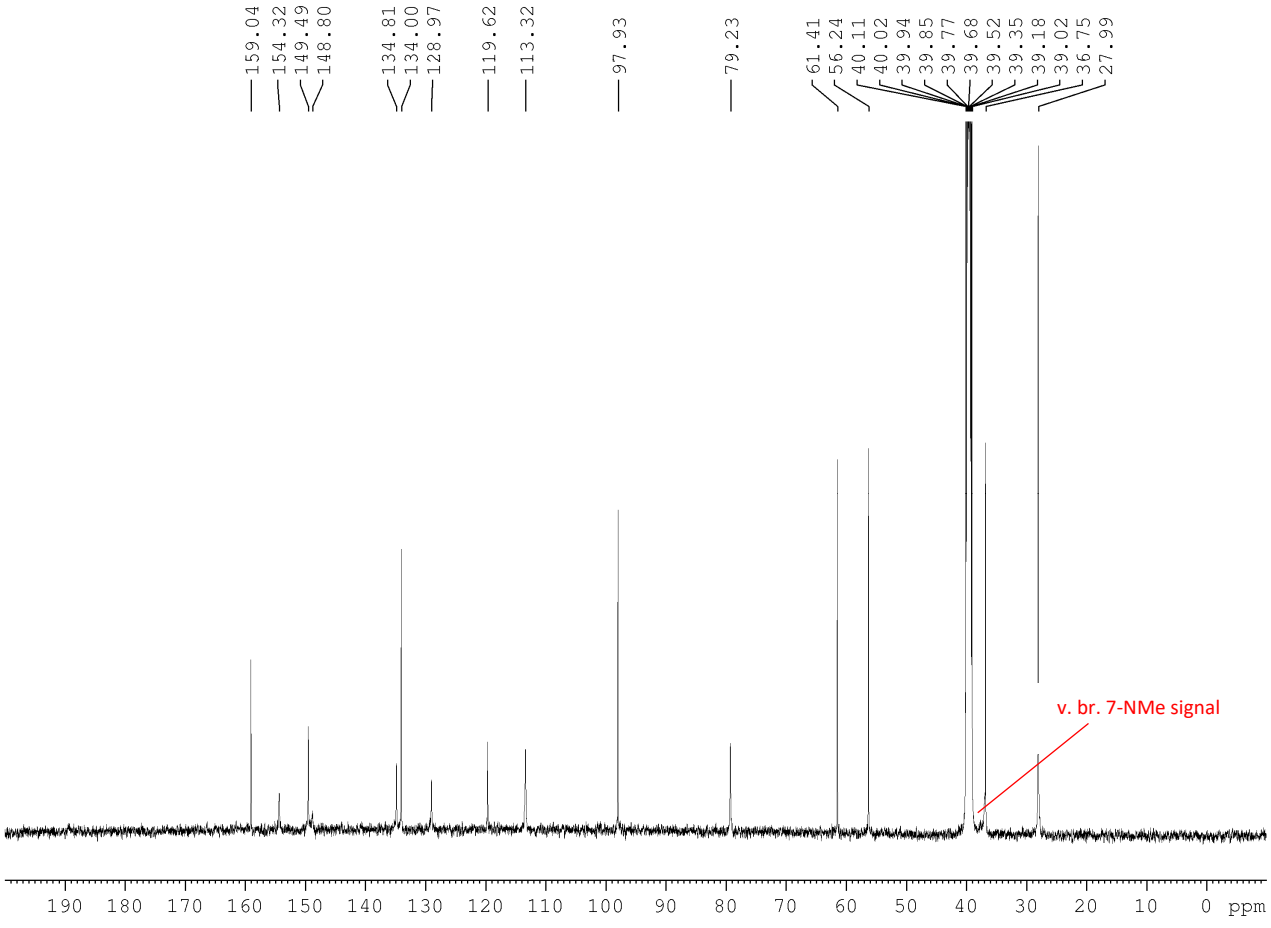
125 MHz ^{13}C NMR spectrum of **49** in $CDCl_3$



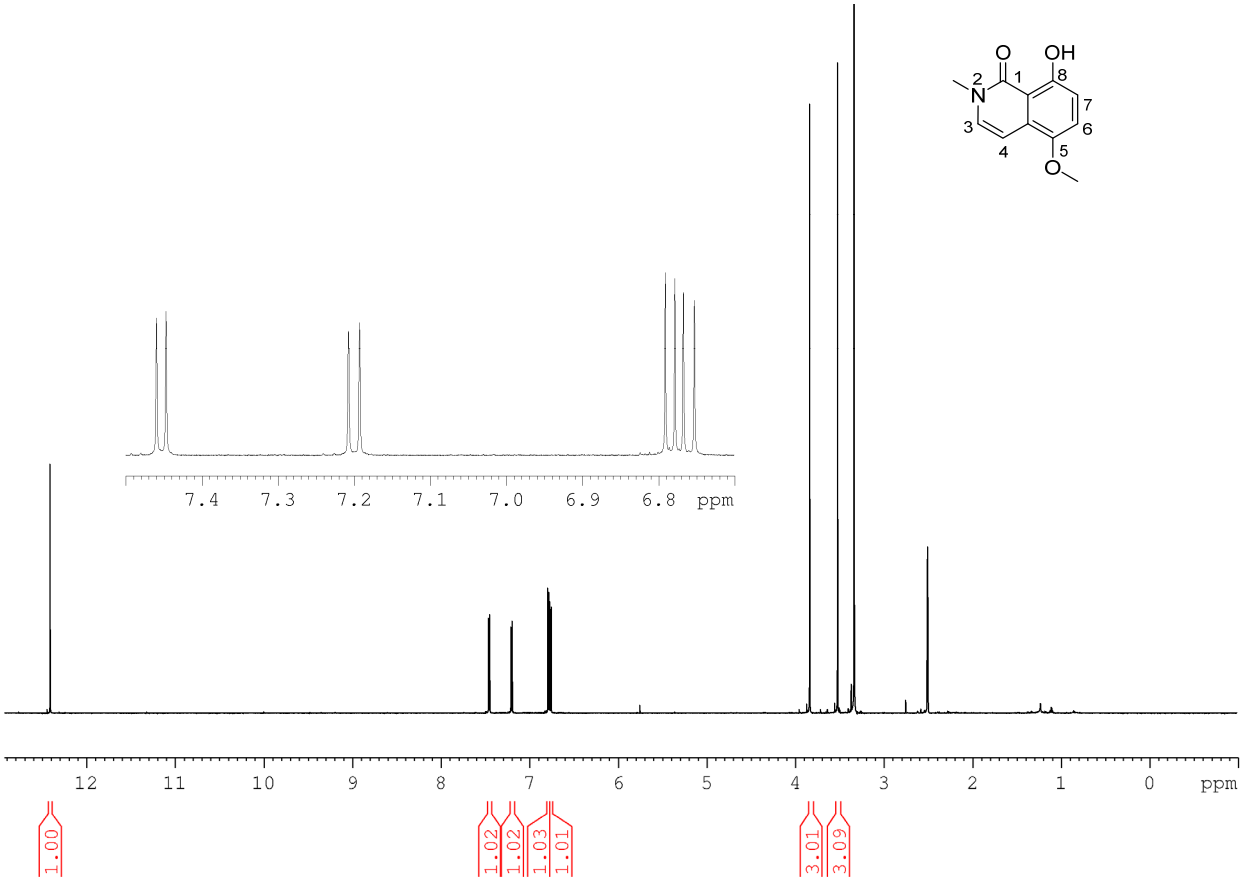
400 MHz ^{1}H NMR spectrum of **50** in d_6-DMSO



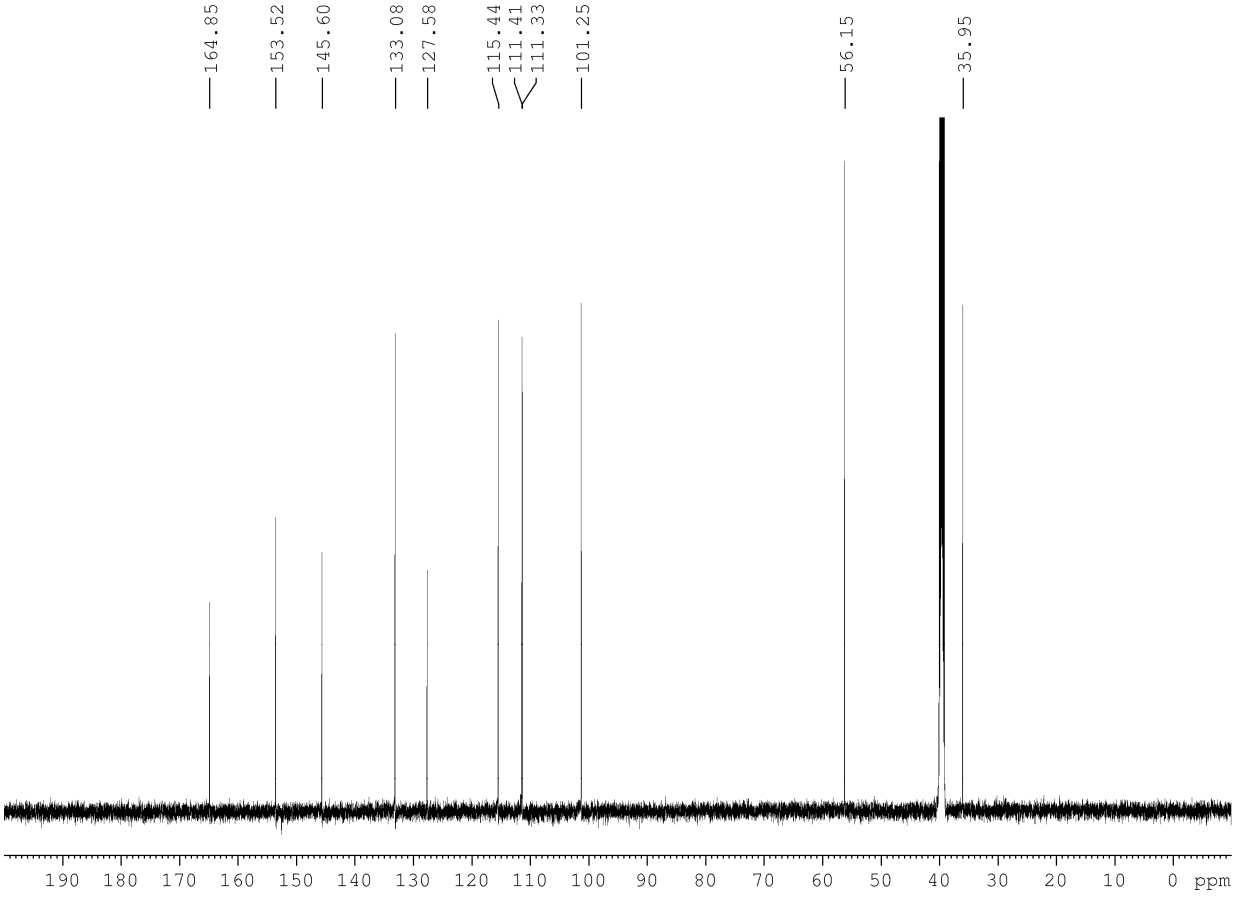
125 MHz ^{13}C NMR spectrum of **50** in d_6-DMSO



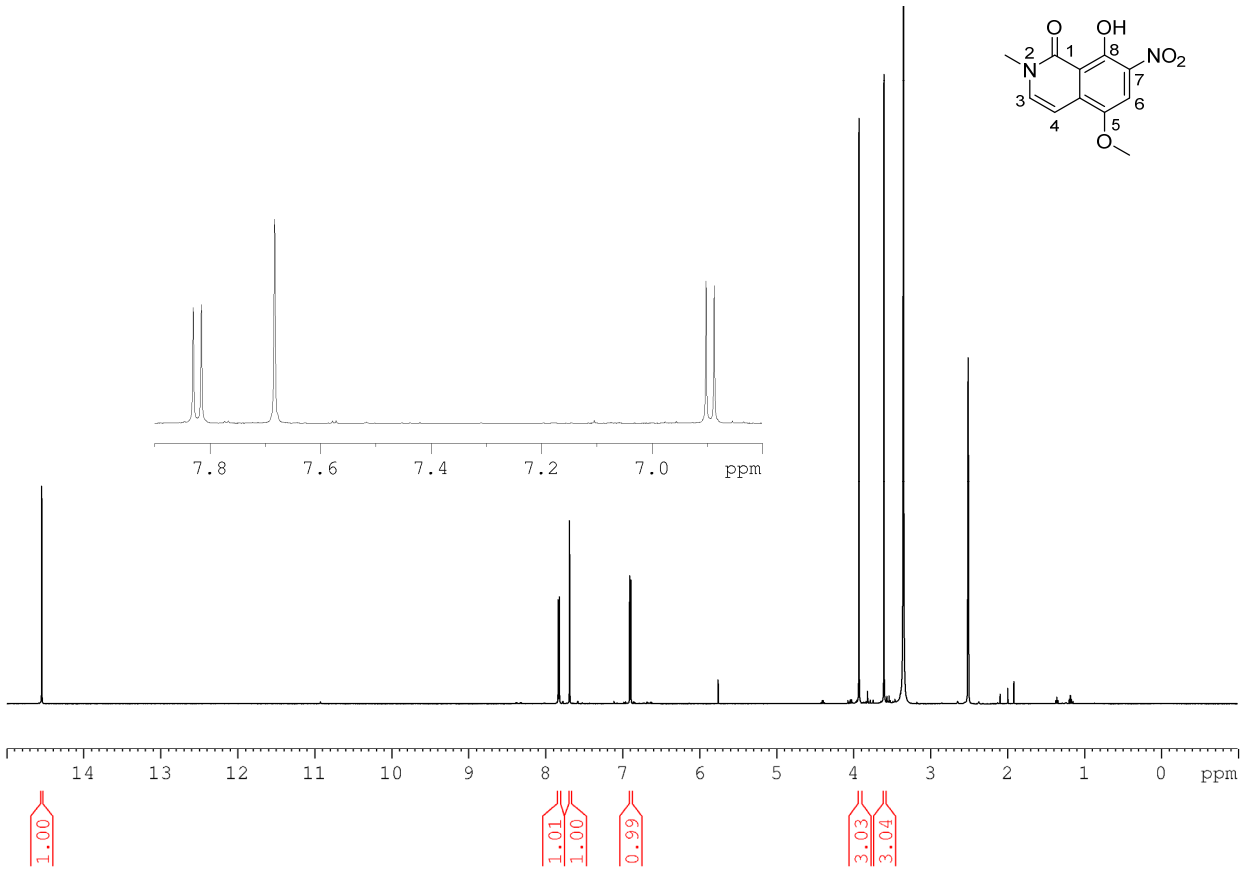
400 MHz ^{1}H NMR spectrum of **51** in $CDCl_3$



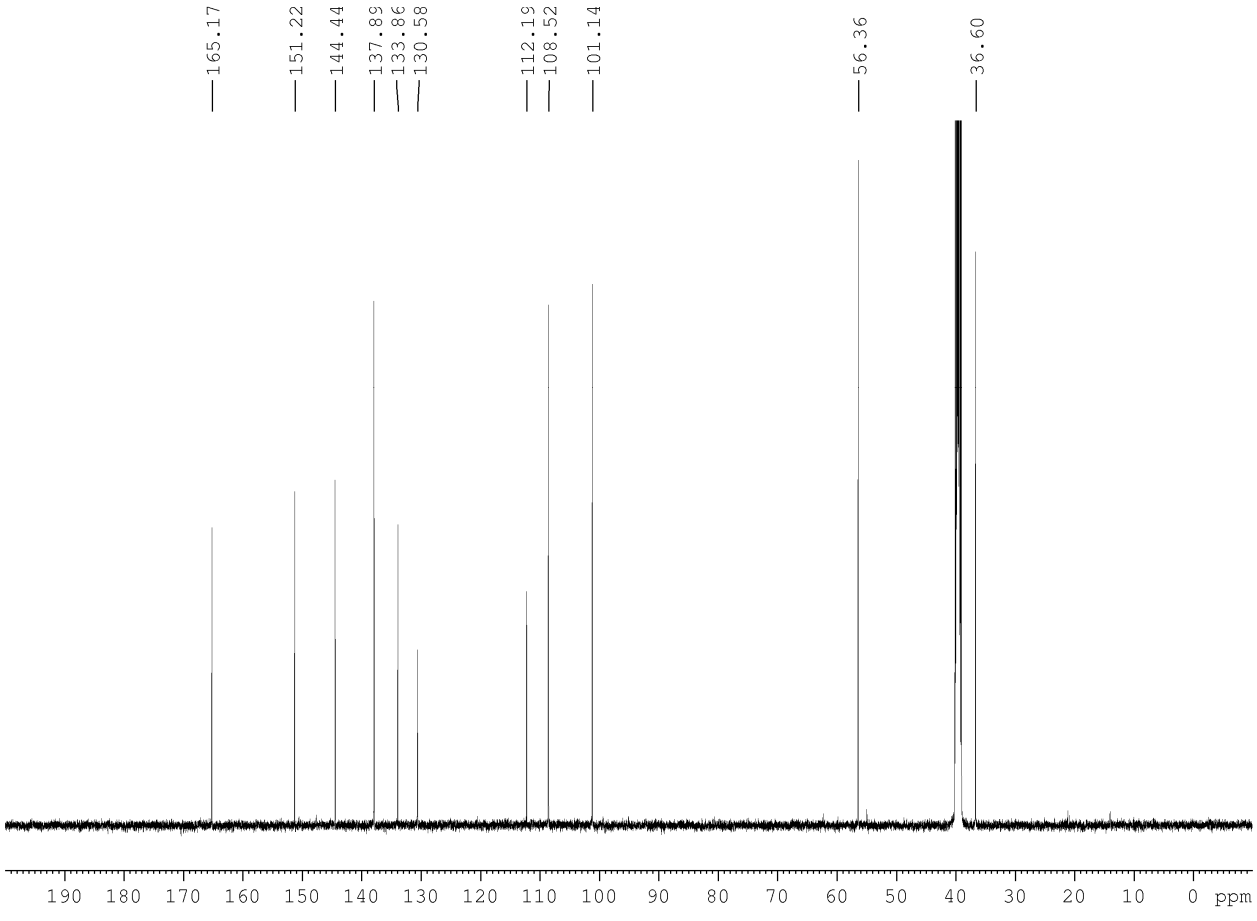
100 MHz ^{13}C NMR spectrum of **51** in $CDCl_3$



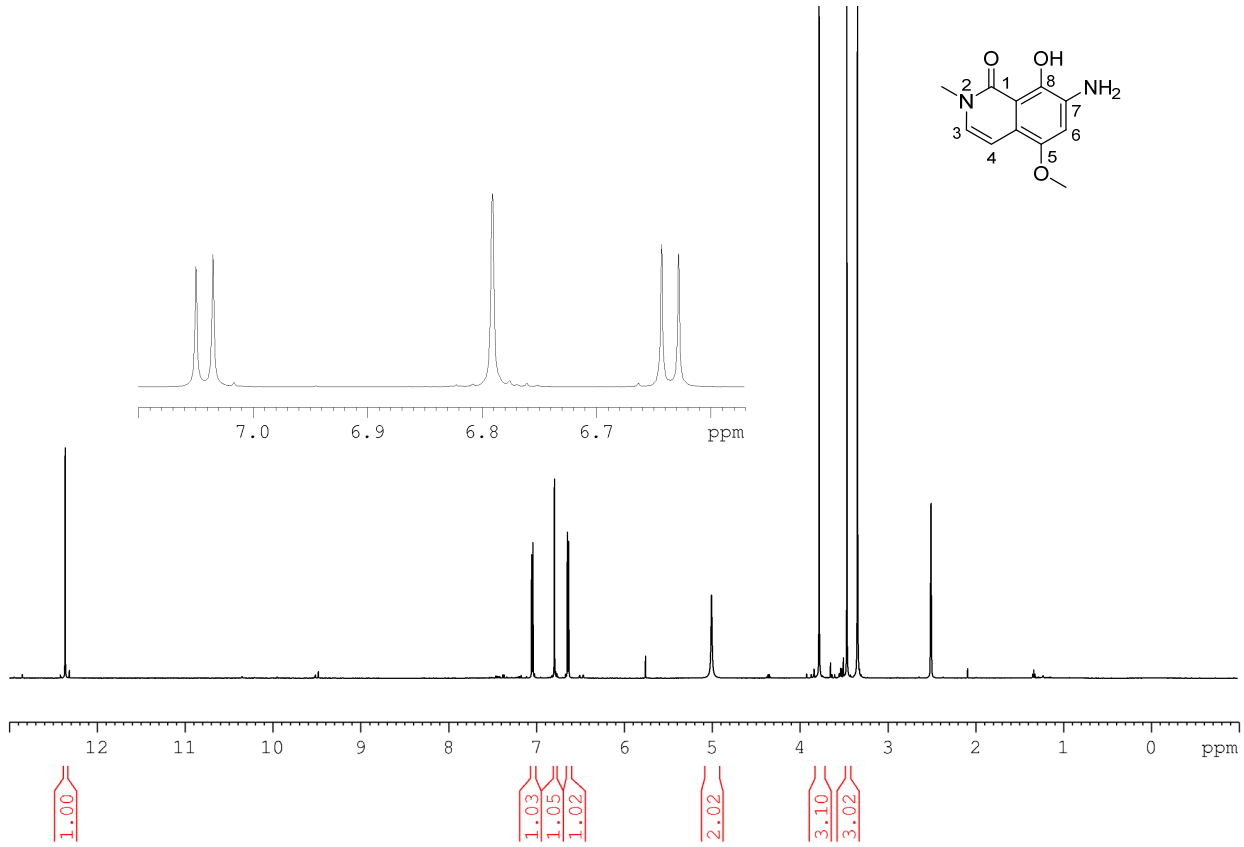
500 MHz ^{1}H NMR spectrum of **52** in d_6-DMSO



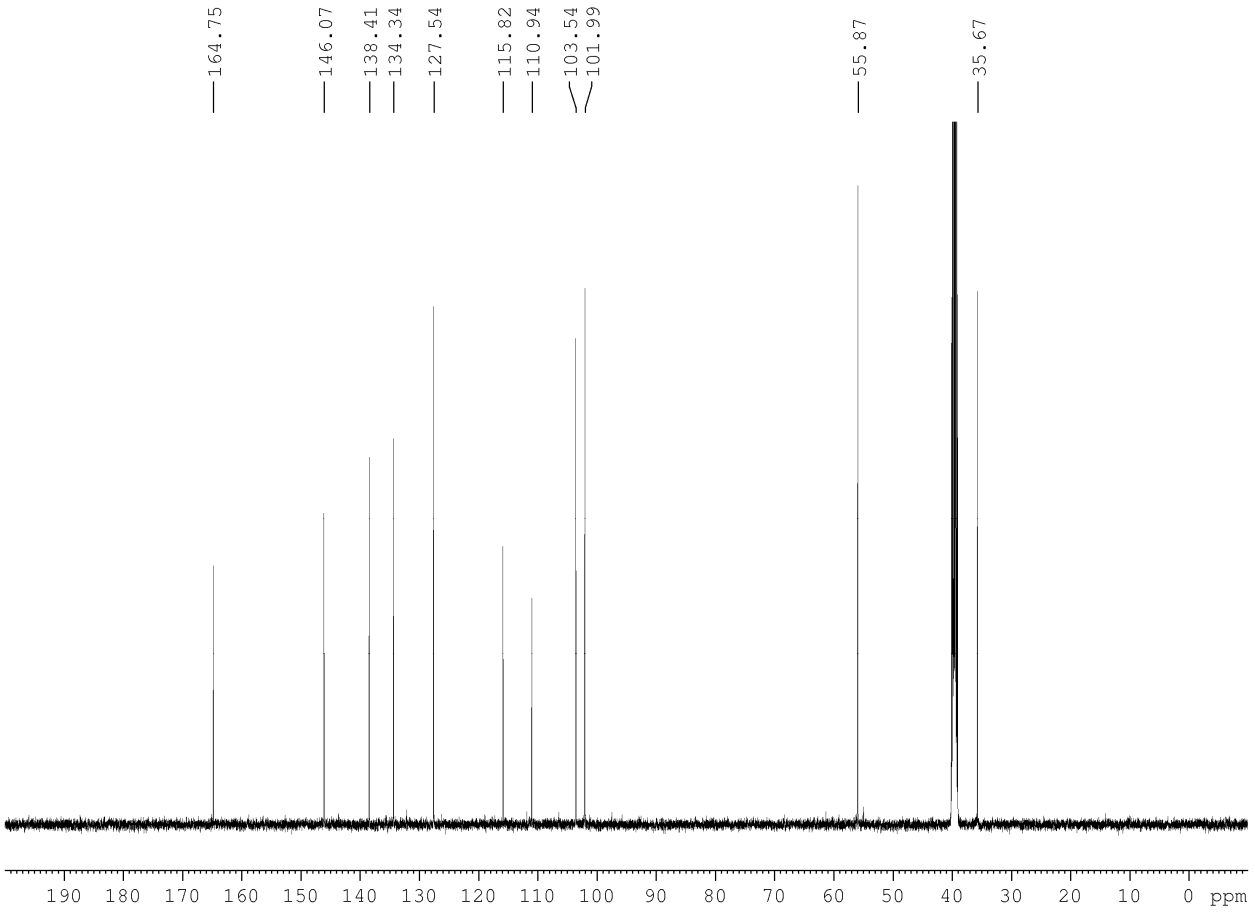
125 MHz ^{13}C NMR spectrum of **52** in d_6-DMSO



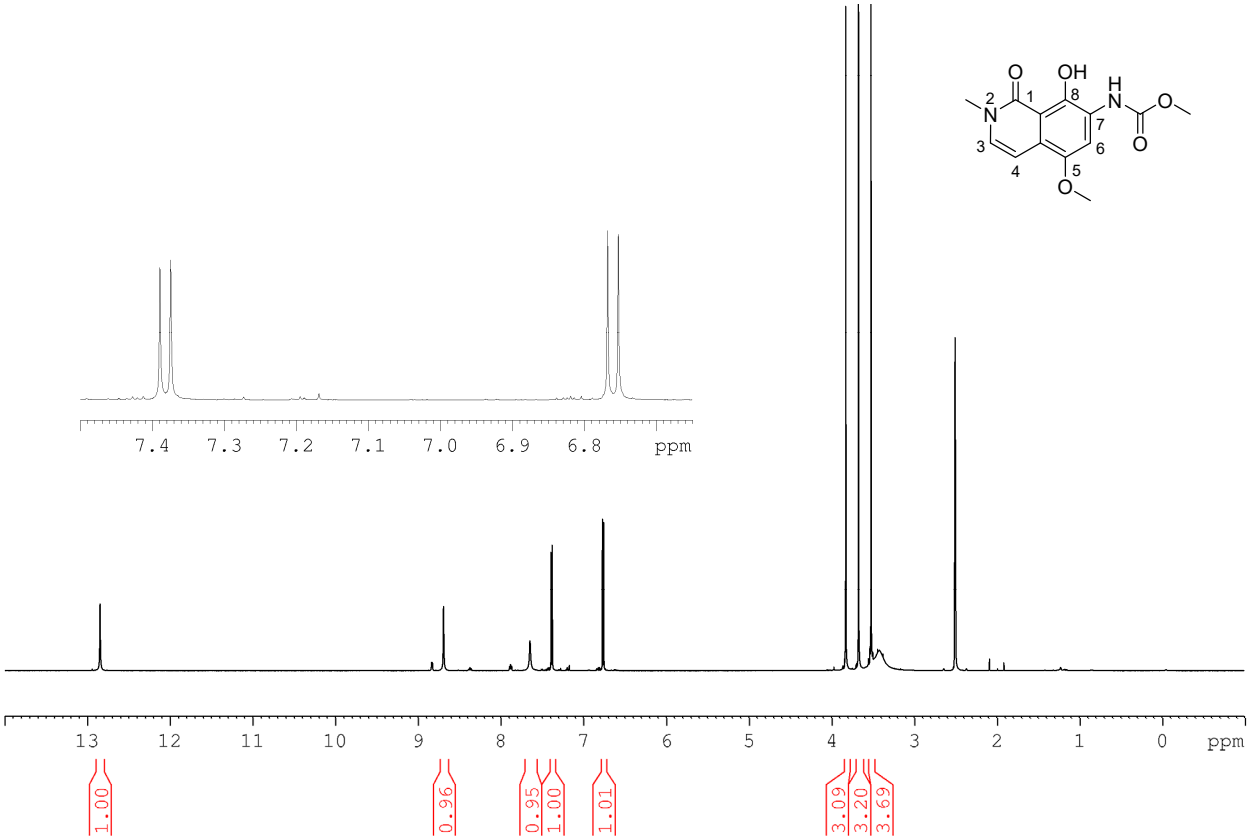
500 MHz ^{1}H NMR spectrum of **53** in d_6-DMSO



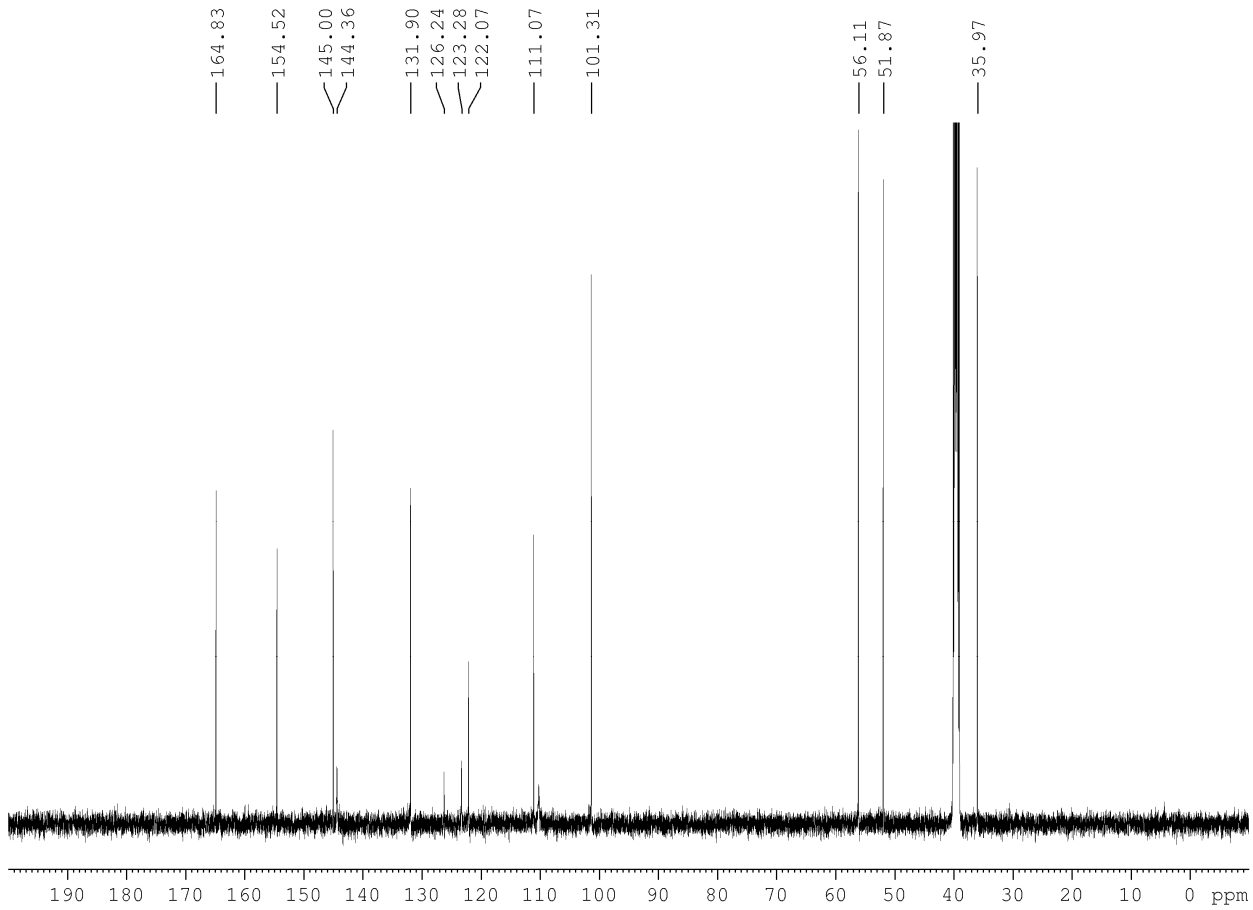
125 MHz ^{13}C NMR spectrum of **53** in d_6-DMSO



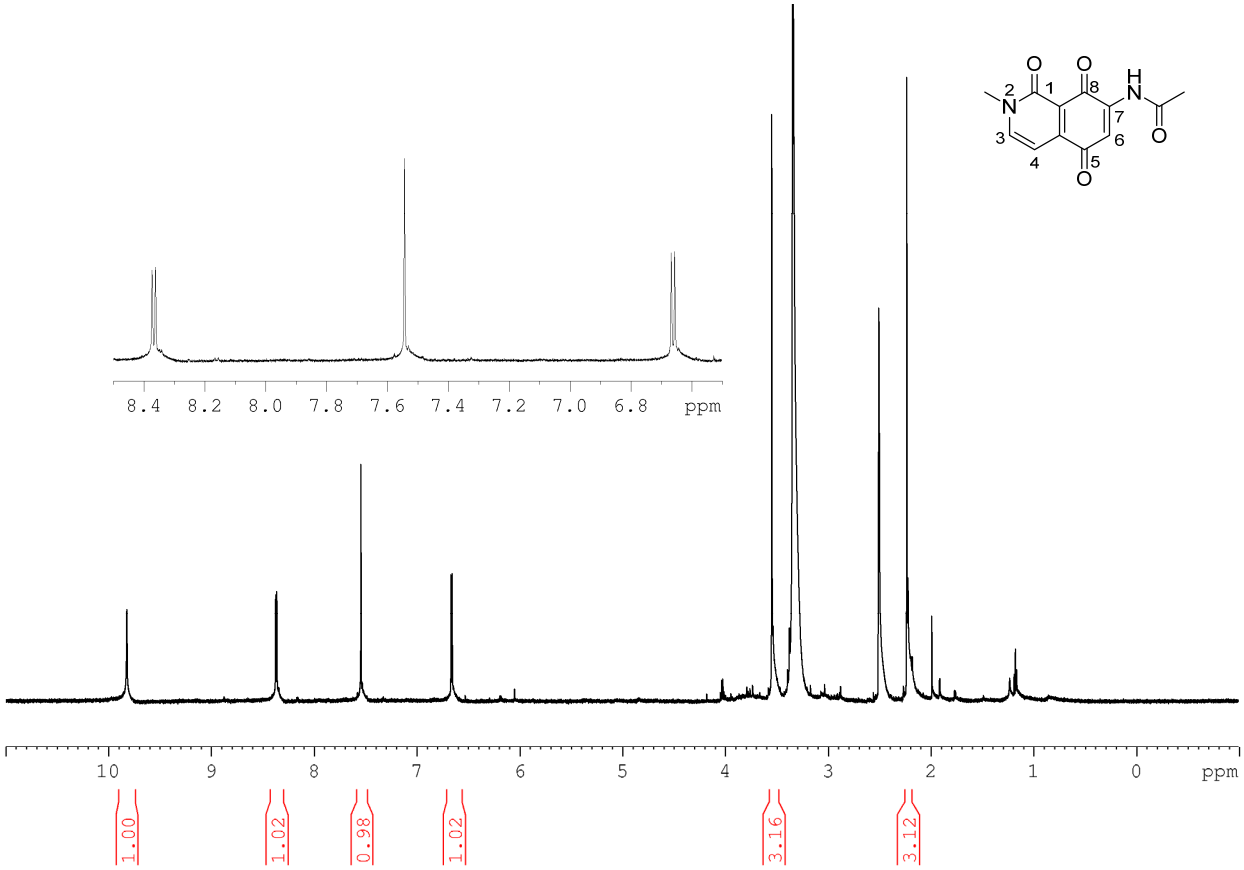
500 MHz ^{1}H NMR spectrum of **54** in d_6-DMSO



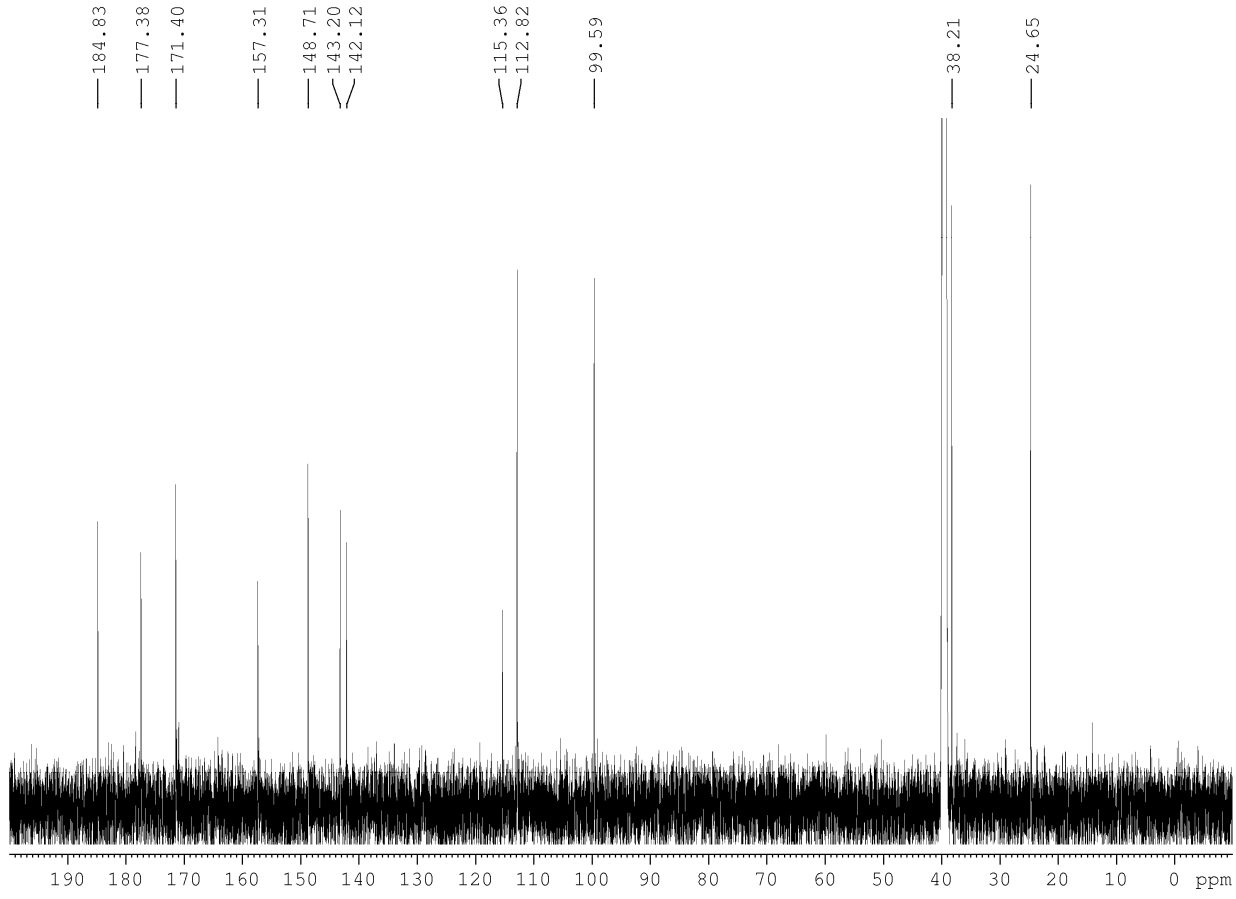
125 MHz ^{13}C NMR spectrum of **54** in d_6-DMSO



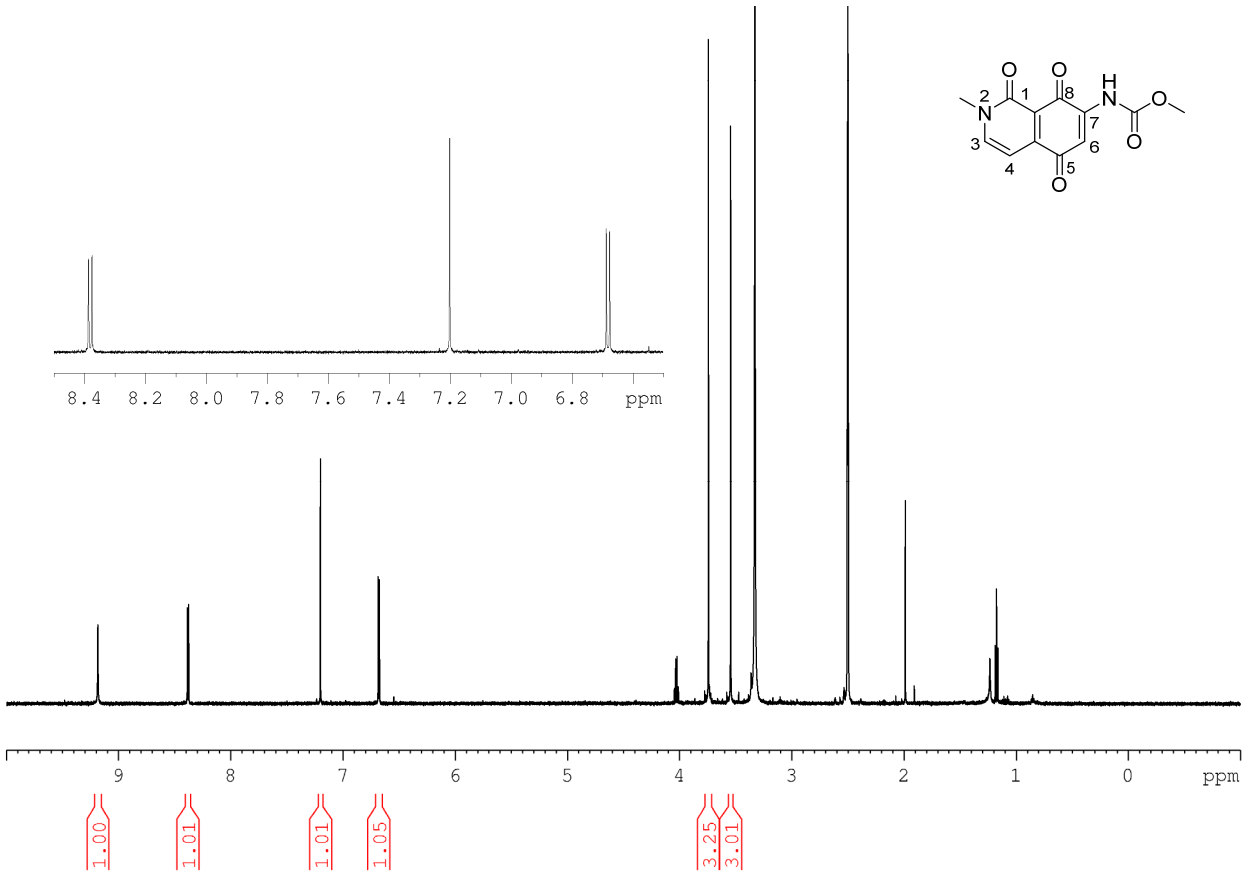
600 MHz ^{1}H NMR spectrum of **56** in d_6-DMSO



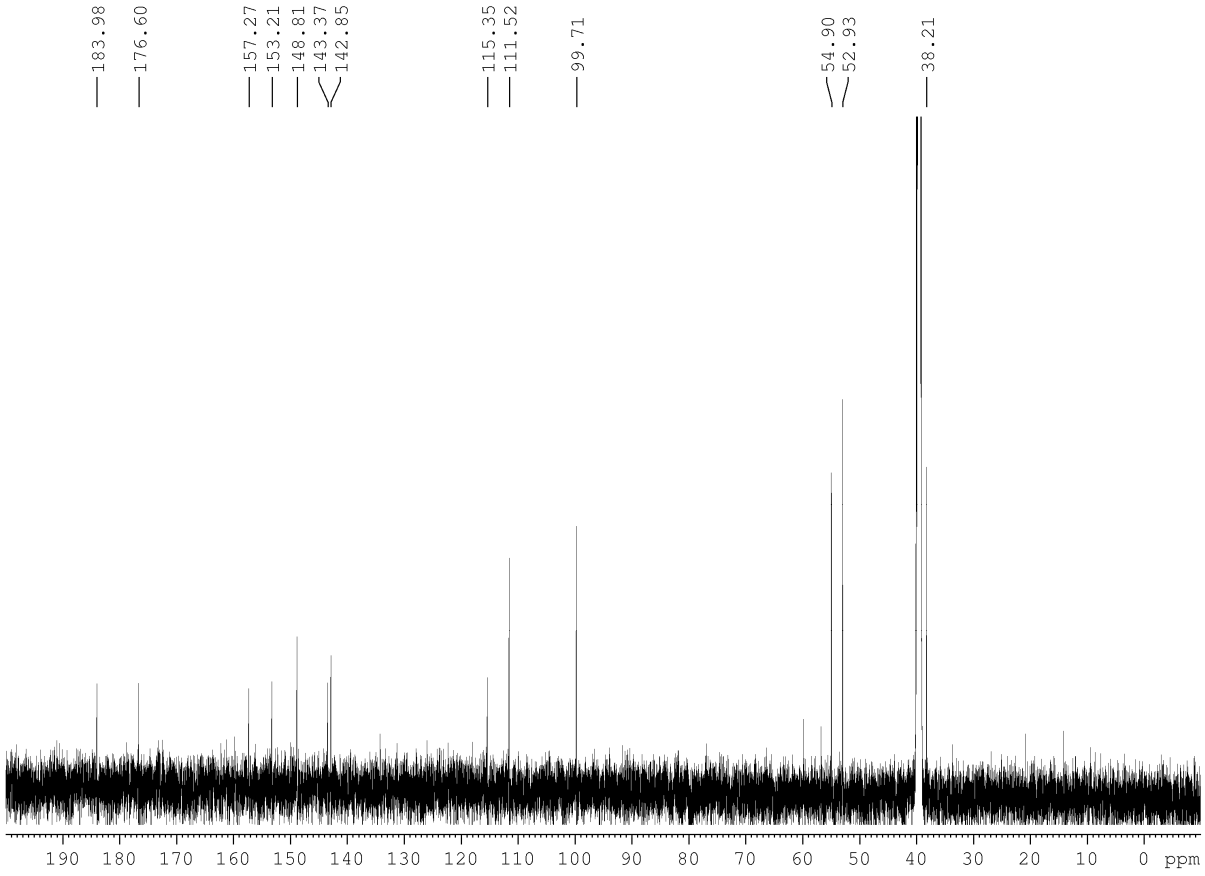
150 MHz ^{13}C NMR spectrum of **56** in d_6-DMSO



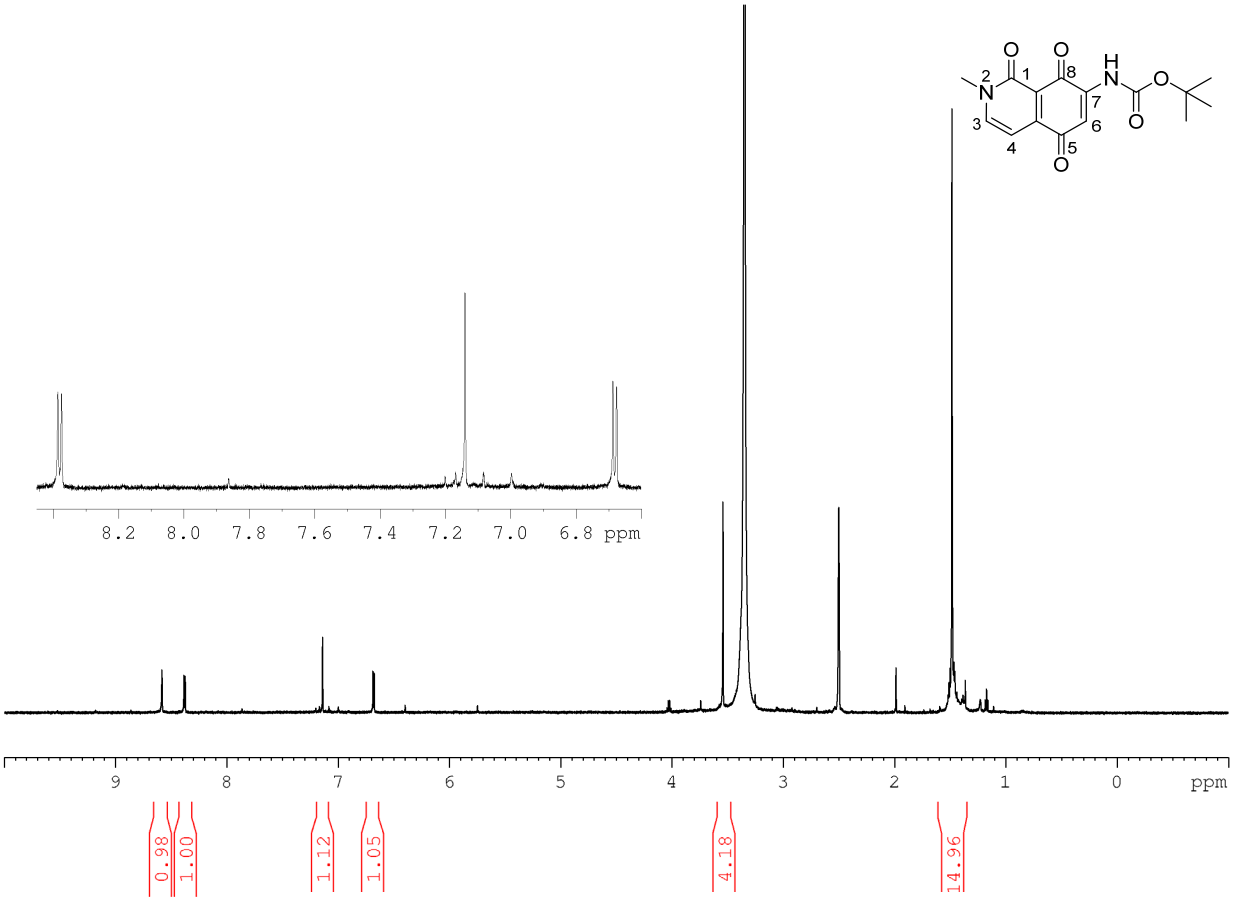
600 MHz ^{1}H NMR spectrum of **57** in d_6-DMSO



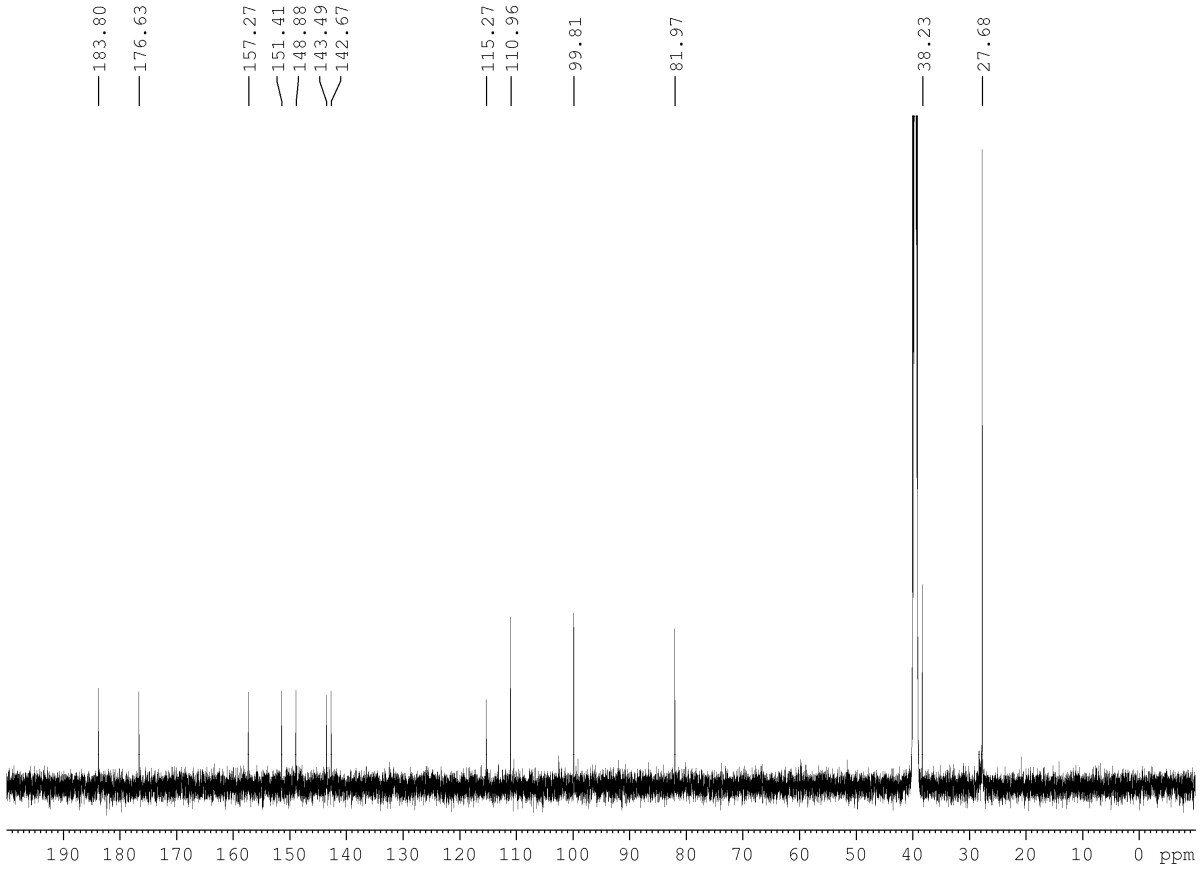
150 MHz ^{13}C NMR spectrum of **57** in d_6-DMSO



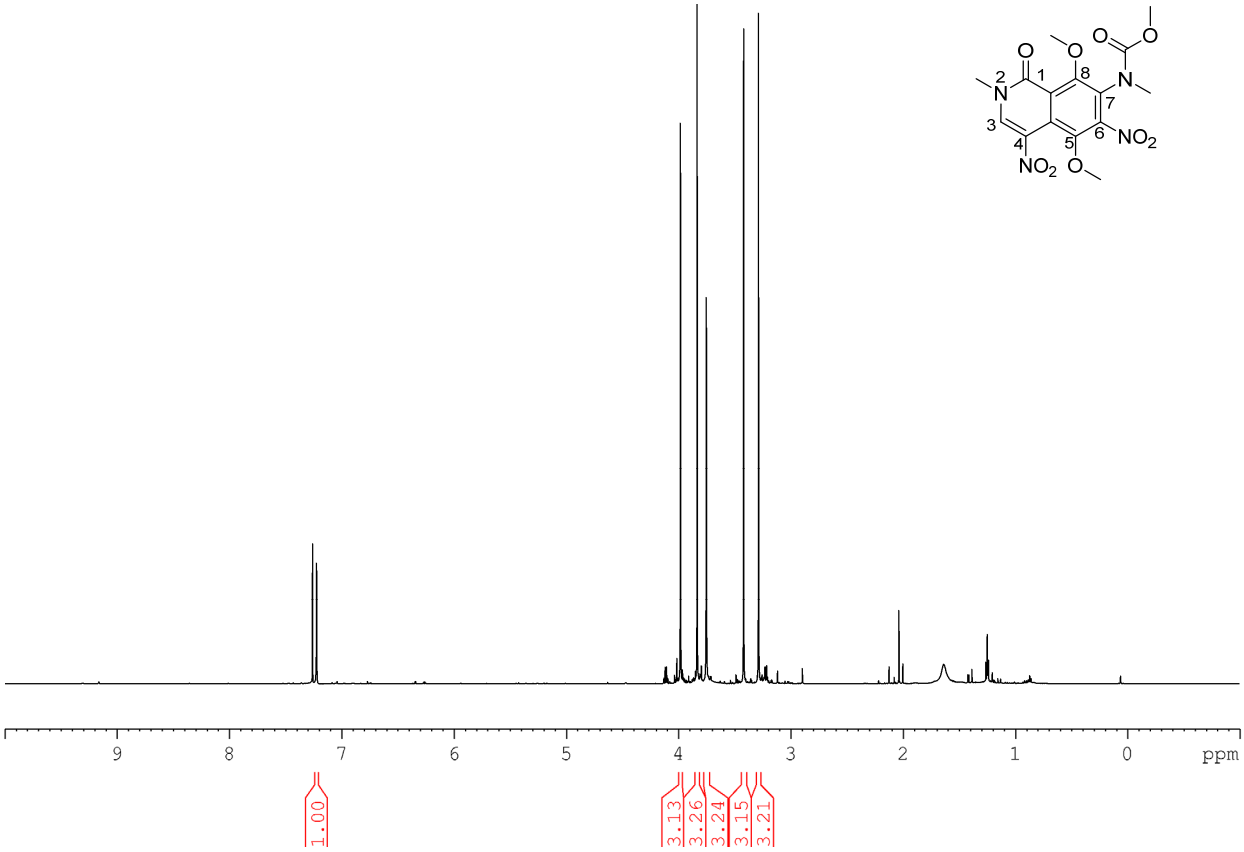
600 MHz ^{1}H NMR spectrum of **58** in d_6-DMSO



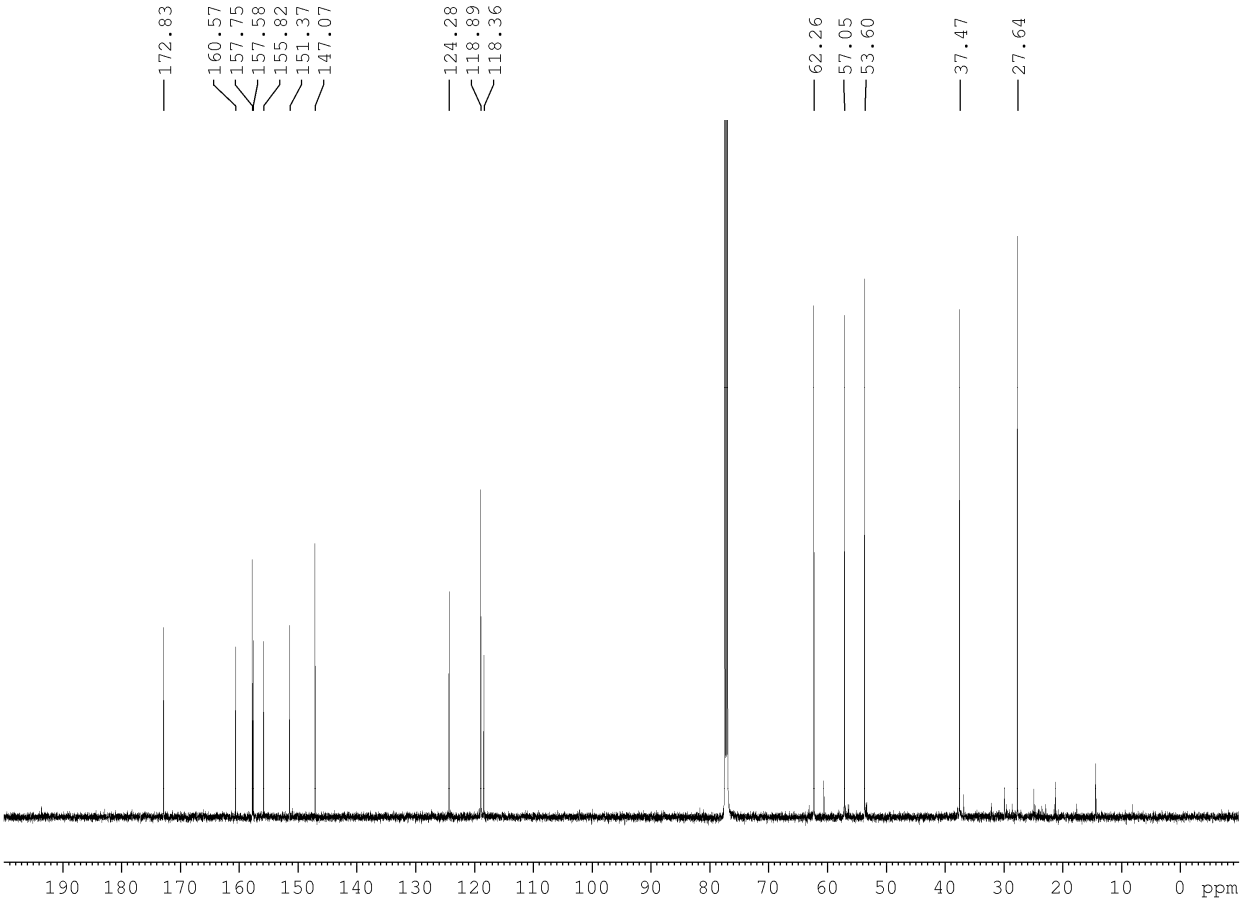
150 MHz ^{13}C NMR spectrum of **58** in d_6-DMSO



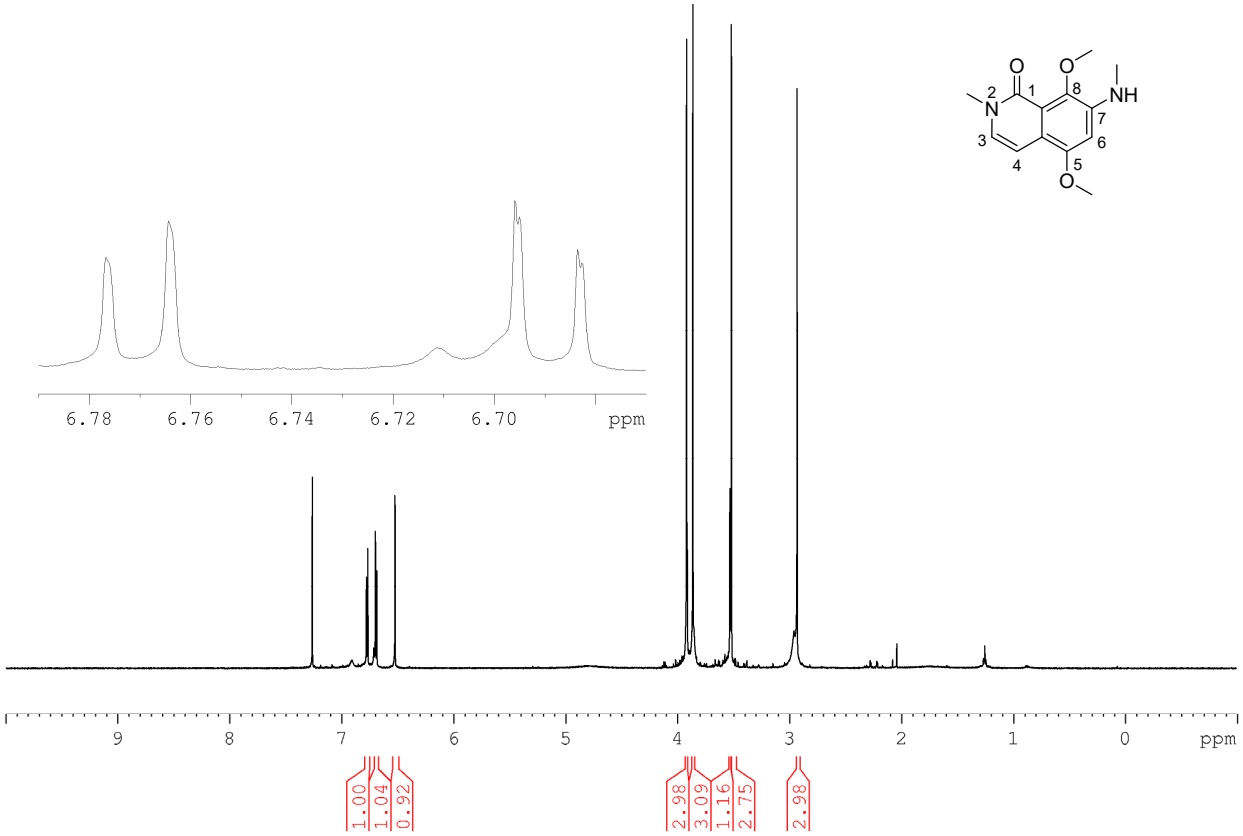
600 MHz ^{1}H NMR spectrum of **61** in $CDCl_3$



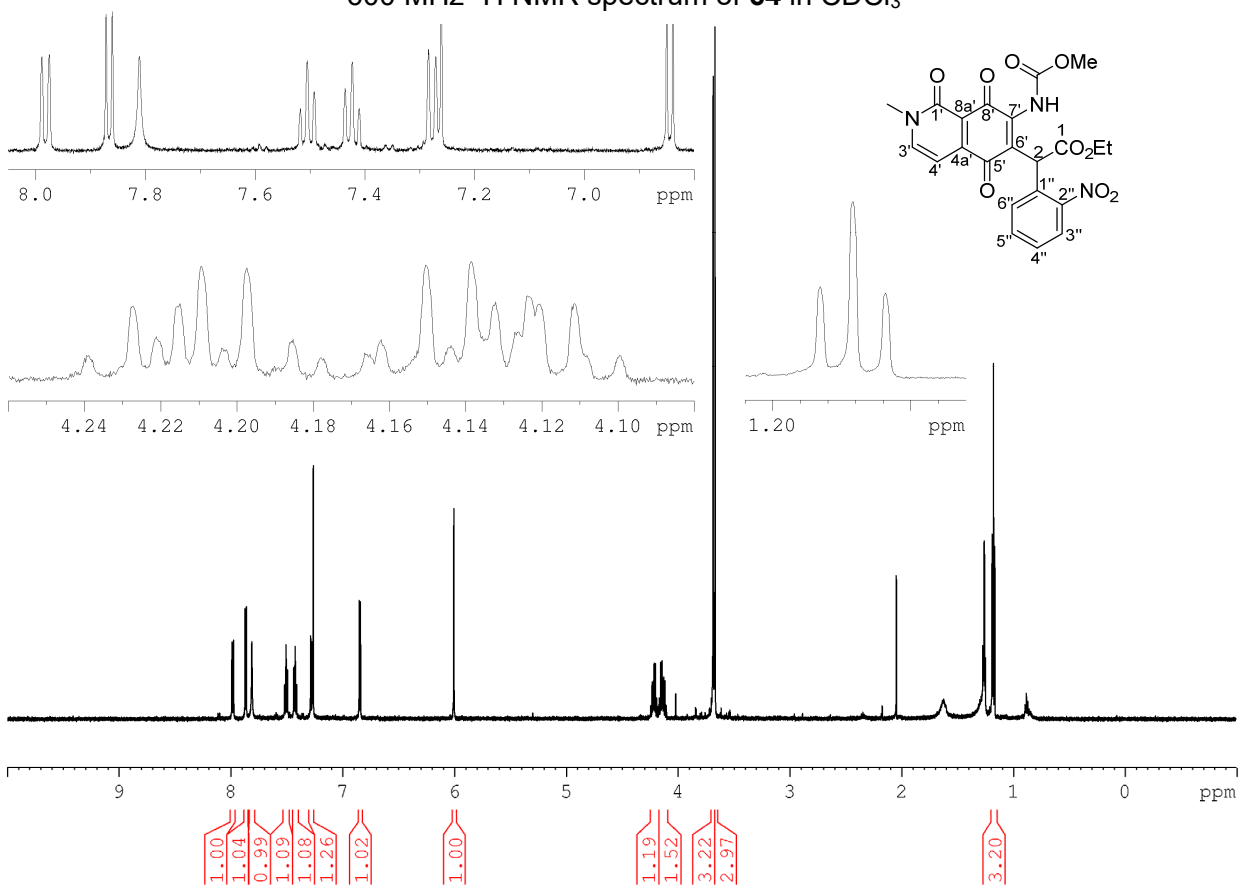
150 MHz ^{13}C NMR spectrum of **61** in $CDCl_3$



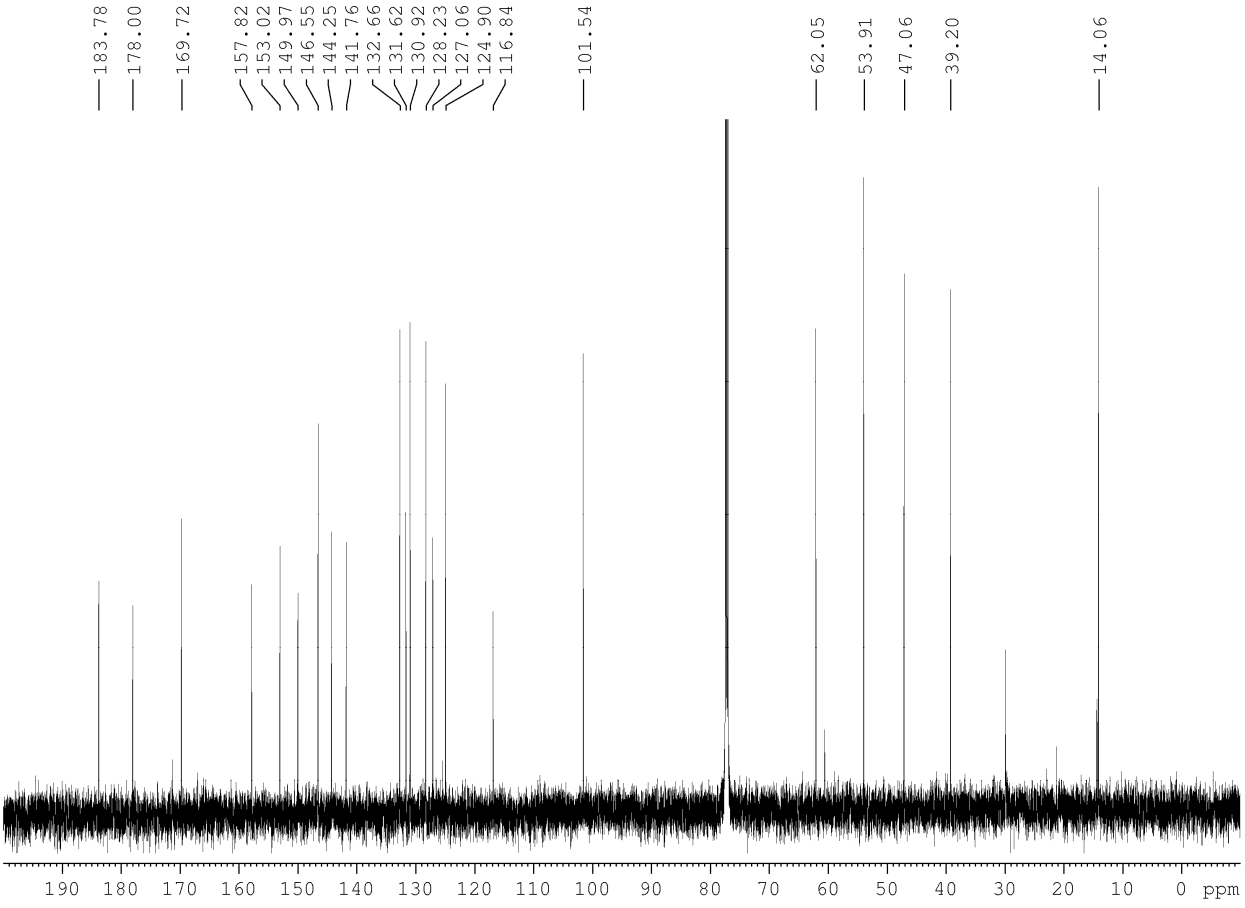
600 MHz ^{1}H NMR spectrum of **62** in $CDCl_3$



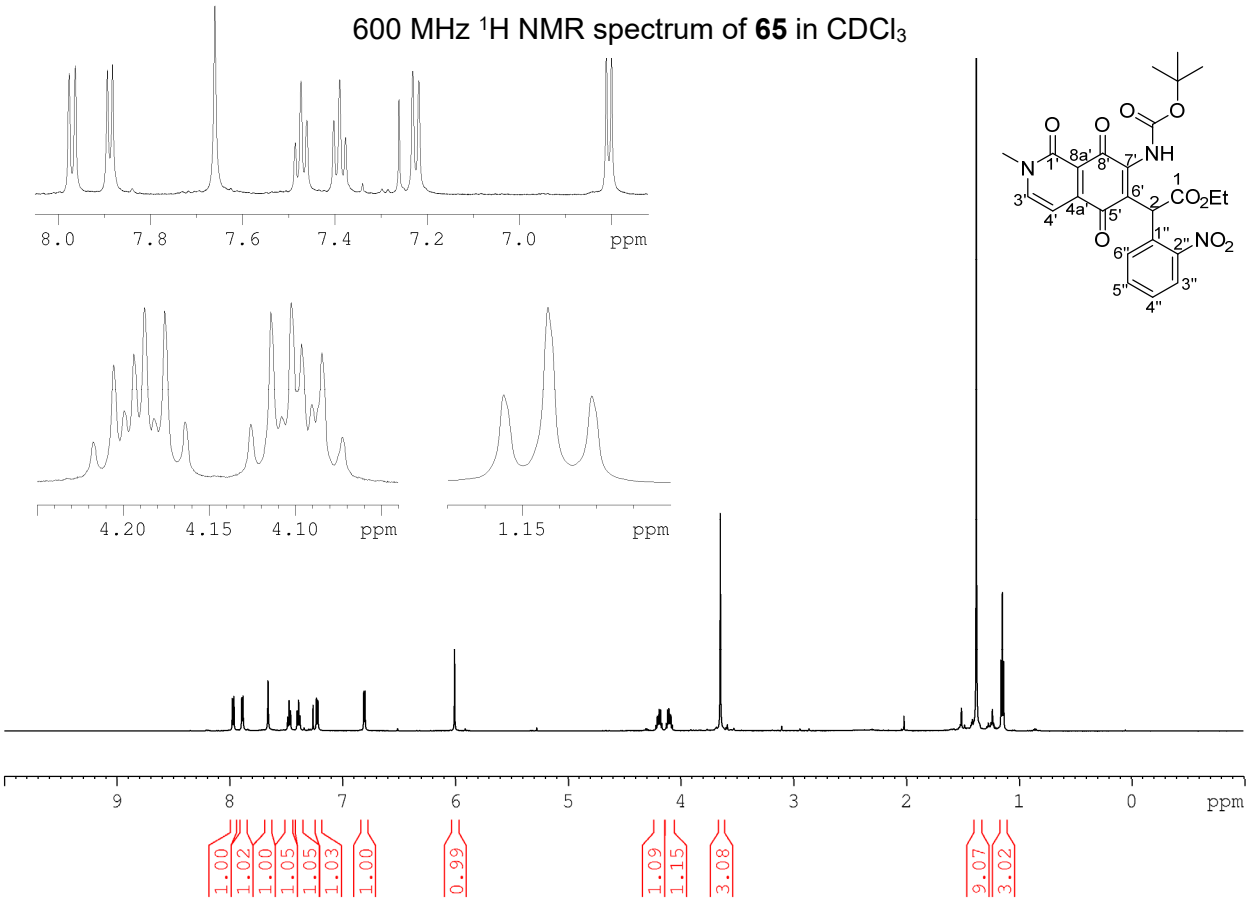
600 MHz ^{1}H NMR spectrum of **64** in $CDCl_3$



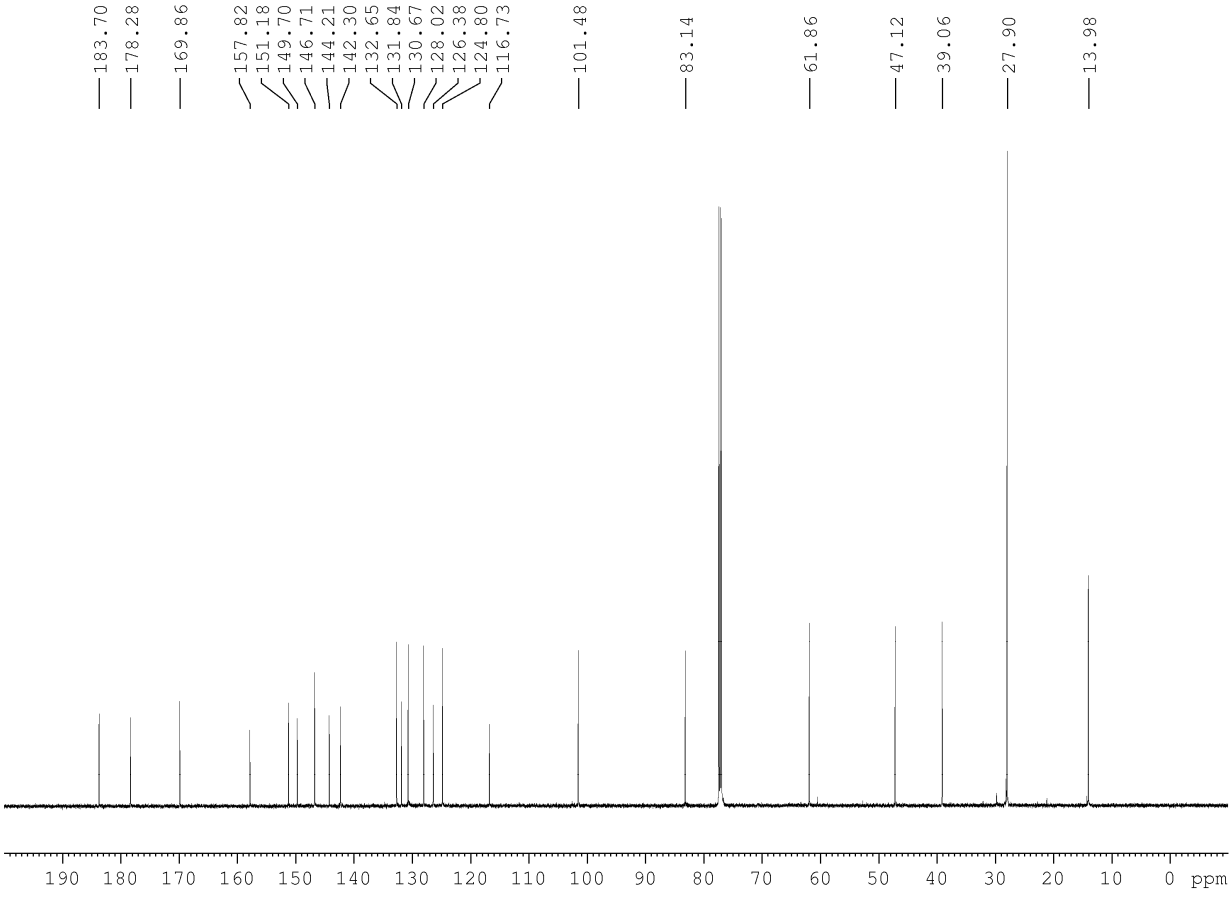
150 MHz ^{13}C NMR spectrum of **64** in $CDCl_3$



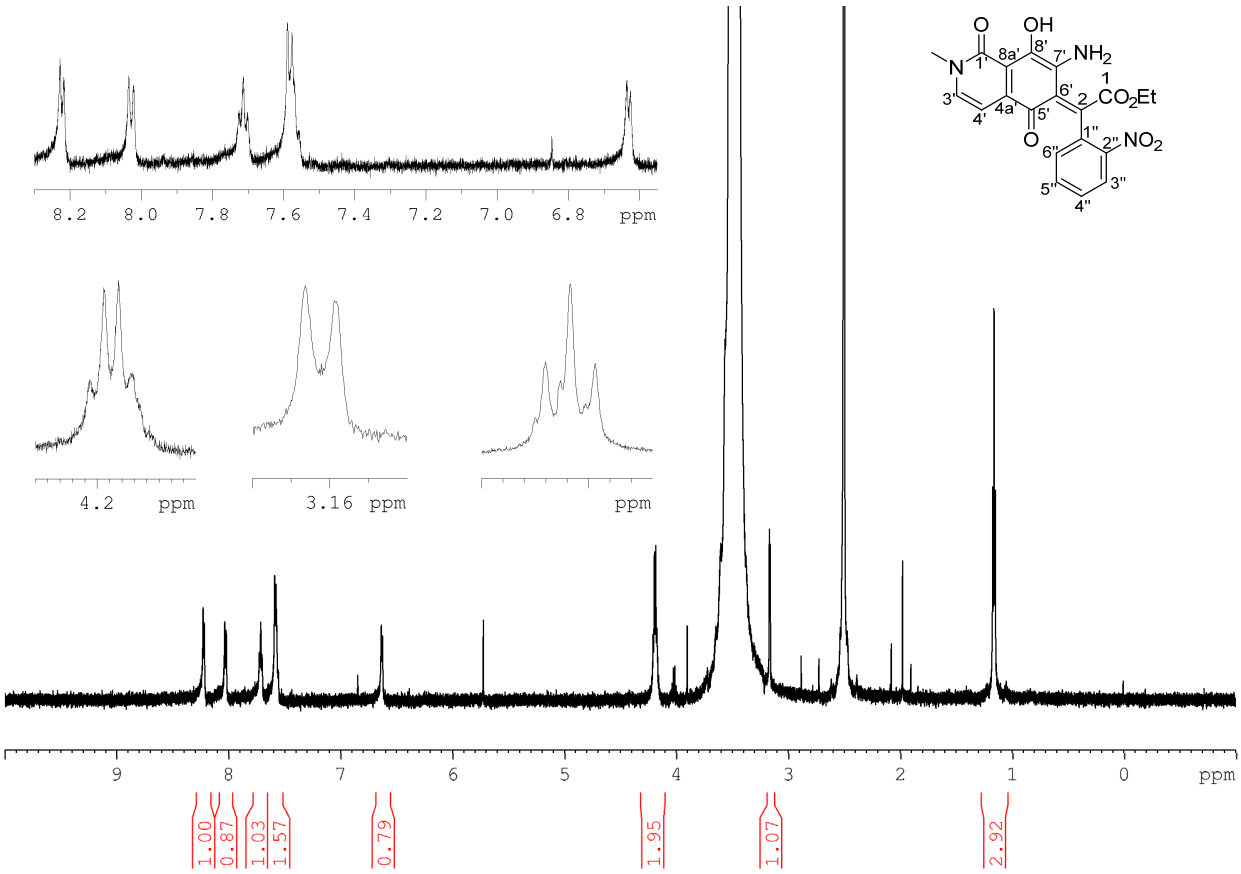
600 MHz ^{1}H NMR spectrum of **65** in $CDCl_3$



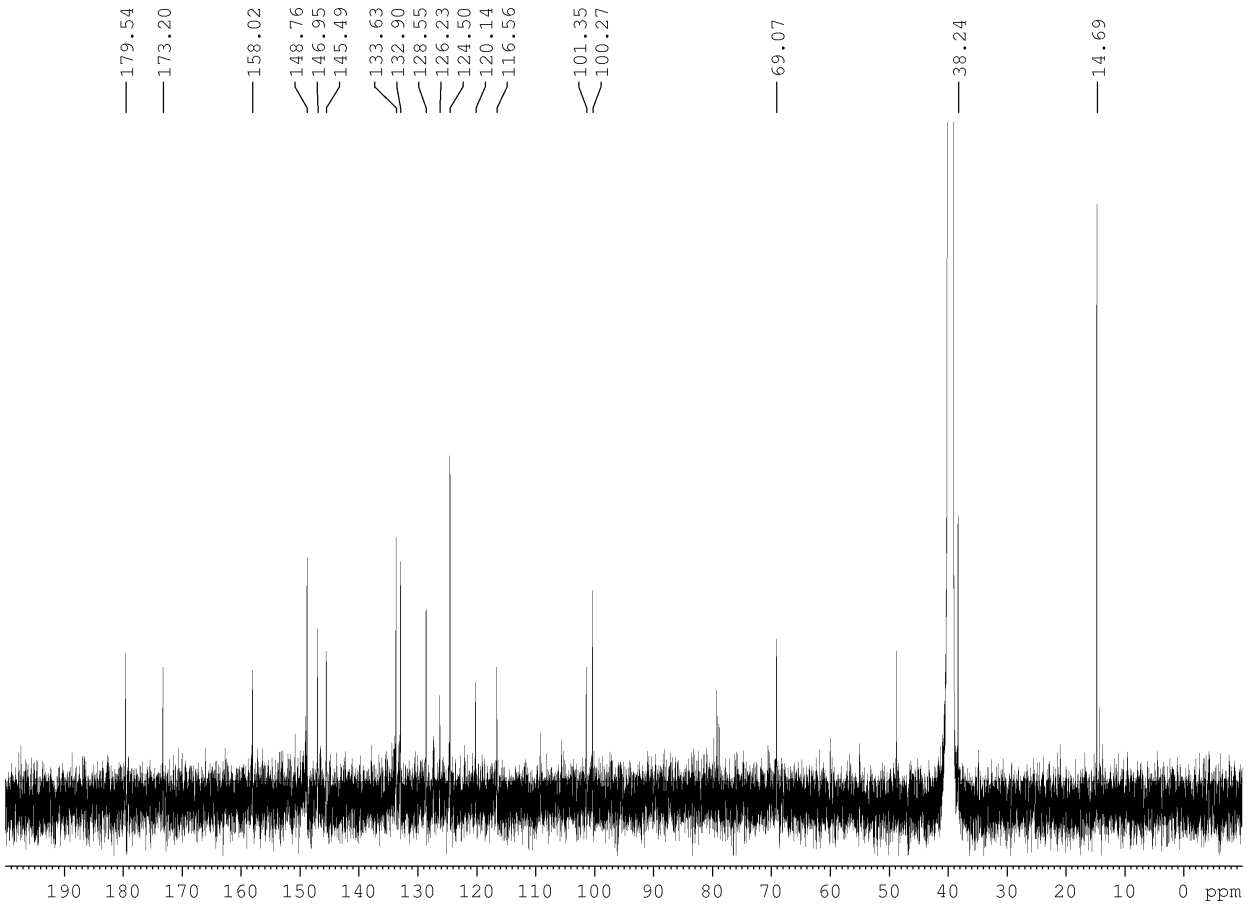
150 MHz ^{13}C NMR spectrum of **65** in $CDCl_3$



600 MHz ^{1}H NMR spectrum of **66** in d_6-DMSO



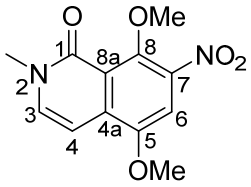
150 MHz ^{13}C NMR spectrum of **66** in d_6-DMSO



II. X-RAY CRYSTALLOGRAPHIC DATA

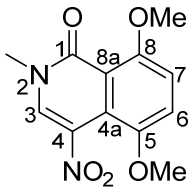
Crystallographic data were collected at 100(2) K on an Oxford Diffraction Xcalibur diffractometer using Mo Kα radiation (λ = 0.71073 Å). Following multi-scan absorption corrections and solution by direct methods, the structures were refined against F^2 with full-matrix least-squares using the program SHELXL-2017. All hydrogen atoms were added at calculated positions and refined by use of a riding model with isotropic displacement parameters based on those of the parent atoms. Anisotropic displacement parameters were employed for the non-hydrogen atoms.

Table S1. Crystallographic data for 5,8-dimethoxy-2-methyl-7-nitroisoquinolin-1(2*H*)-one (**36**)



Empirical formula	$C_{12}H_{12}N_2O_5$
Formula weight	264.24
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 15.7383(9) Å
	b = 10.5862(4) Å
	c = 7.0845(4) Å
	β = 90.023(5)°
Volume	1180.34(10) $Å^3$
Z	4
Density (calculated)	1.487 Mg/m^3
μ	0.118 mm^{-1}
Crystal size	0.34 x 0.17 x 0.02 mm^3
θ range for data collection	2.88 to 28.99°.
Index ranges	–19<=h<=21, –14<=k<=13, –9<=l<=9
Reflections collected	10397
Independent reflections	3090 [R(int) = 0.0412]
Completeness to θ = 28.75°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max./min transmission	1.00/0.892
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3090 / 0 / 176
Goodness-of-fit on F^2	1.179
Final R indices [I>2σ(I)]	R1 = 0.0687, wR2 = 0.1186
R indices (all data)	R1 = 0.0851, wR2 = 0.1242
Largest diff. peak and hole	0.307 and –0.314 e.$Å^{-3}$
CCCDC	1825607

Table S2. Crystallographic data for 5,8-dimethoxy-2-methyl-4-nitroisoquinolin-1(2*H*)-one (**37**)



Empirical formula	$C_{12}H_{12}N_2O_5$
Formula weight	264.24
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 9.8063(3) Å
	b = 15.7583(3) Å
	c = 7.4795(2) Å
	β = 102.000(3)°
Volume	1130.55(5) $Å^3$
Z	4
Density (calculated)	1.552 Mg/m^3
Absorption coefficient	0.123 mm^{-1}
Crystal size	0.40 x 0.10 x 0.08 mm^3
θ range for data collection	3.07 to 31.00°.
Index ranges	–14<=h<=14, –22<=k<=22, –10<=l<=7
Reflections collected	12815
Independent reflections	3559 [R(int) = 0.0328]
Completeness to θ = 28.75°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max./min transmission	1.00/0.963
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3559 / 0 / 175
Goodness-of-fit on F^2	1.107
Final R indices [I>2σ(I)]	$R1$ = 0.0482, $wR2$ = 0.1162
R indices (all data)	$R1$ = 0.0580, $wR2$ = 0.1212
Largest diff. peak and hole	0.492 and –0.244 e.$Å^{-3}$
CCDC	1825618