SUPPORTING INFORMATION

Model Studies to Access the [6,7,5,5]-Core of Ineleganolide Using Tandem Translactonization-Cope or Cyclopropanation-Cope Rearrangements as Key Steps

Jennifer L. Roizen, Amanda C. Jones, Russell C. Smith, Scott C. Virgil, and Brian M. Stoltz*

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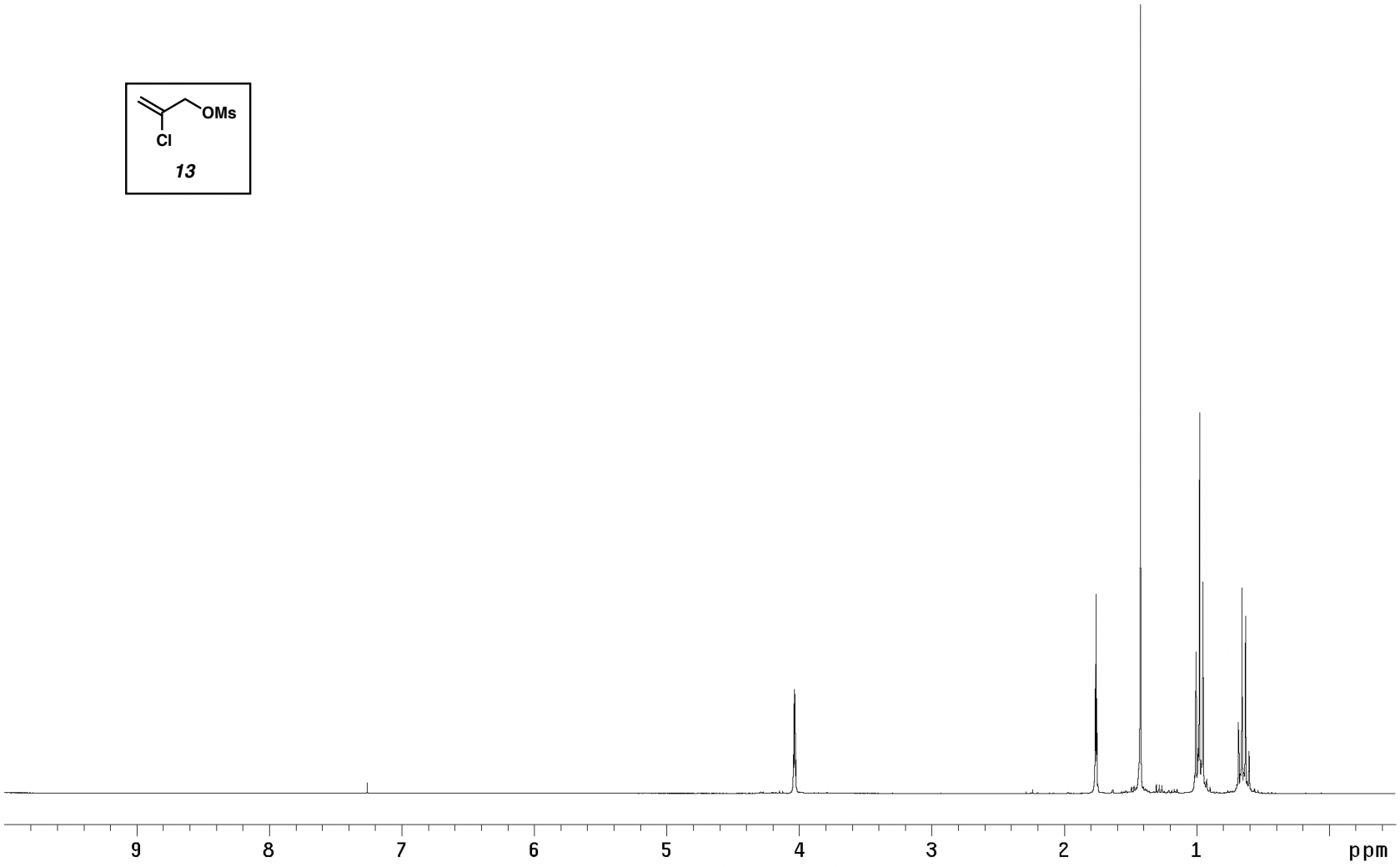


Figure SI.1 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **13**

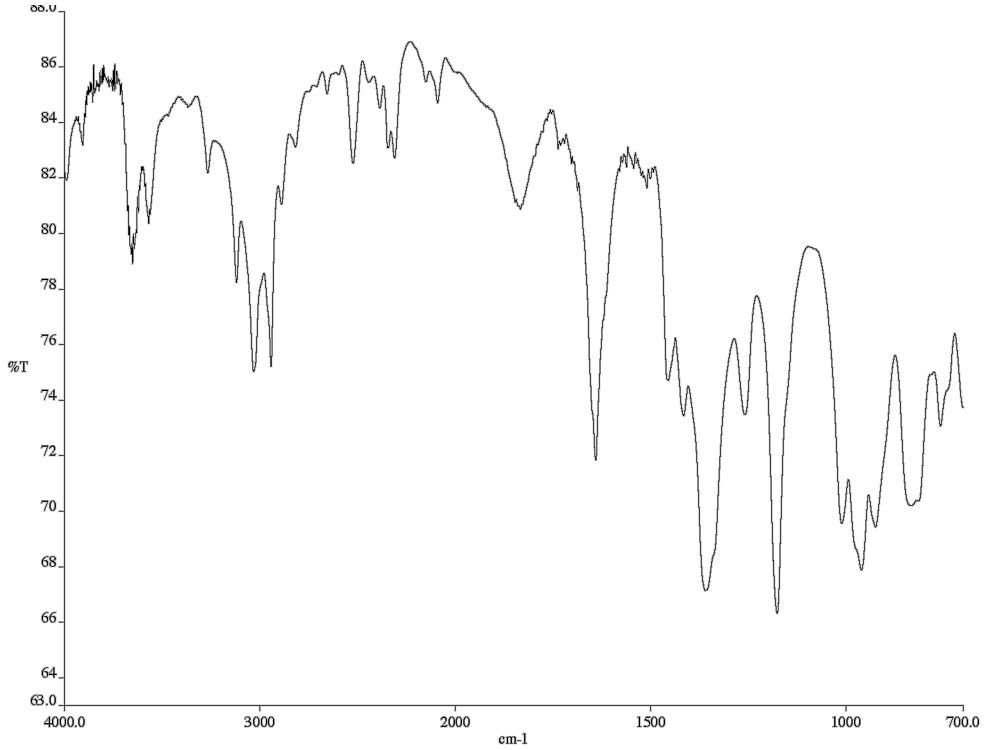


Figure SI.2 Infrared spectrum (thin film/NaCl) of compound **13**

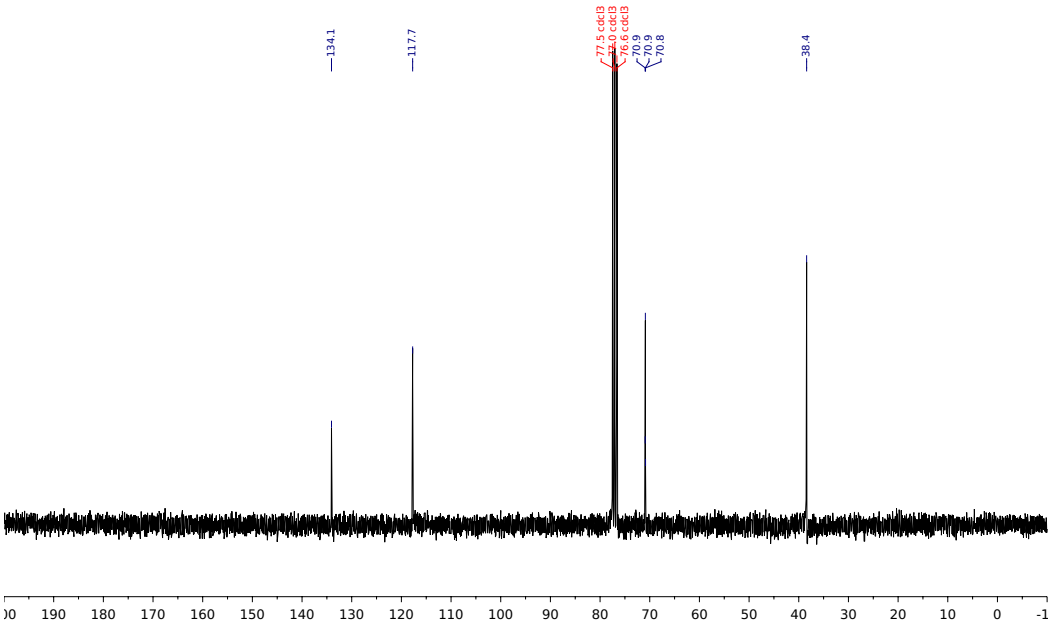


Figure SI.3 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **13**

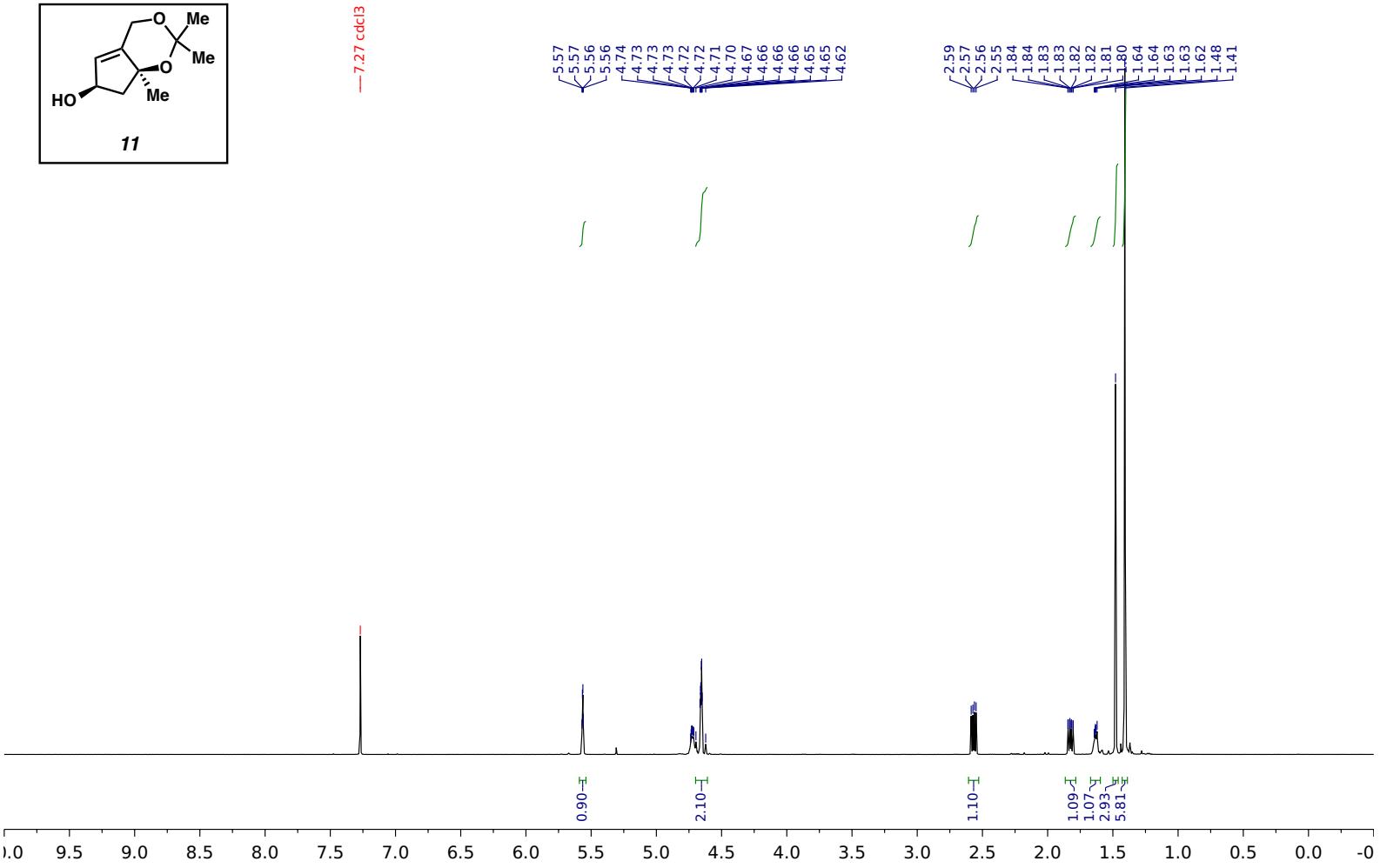


Figure SI.4 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **11**

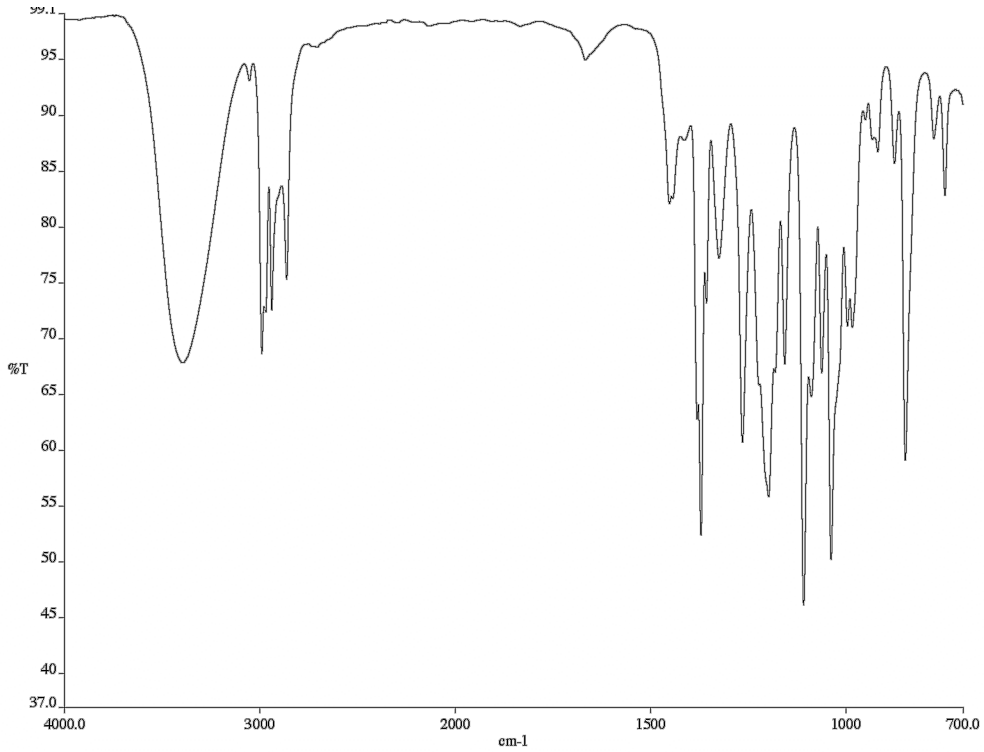


Figure SI.5 Infrared spectrum (thin film/NaCl) of alcohol **11**

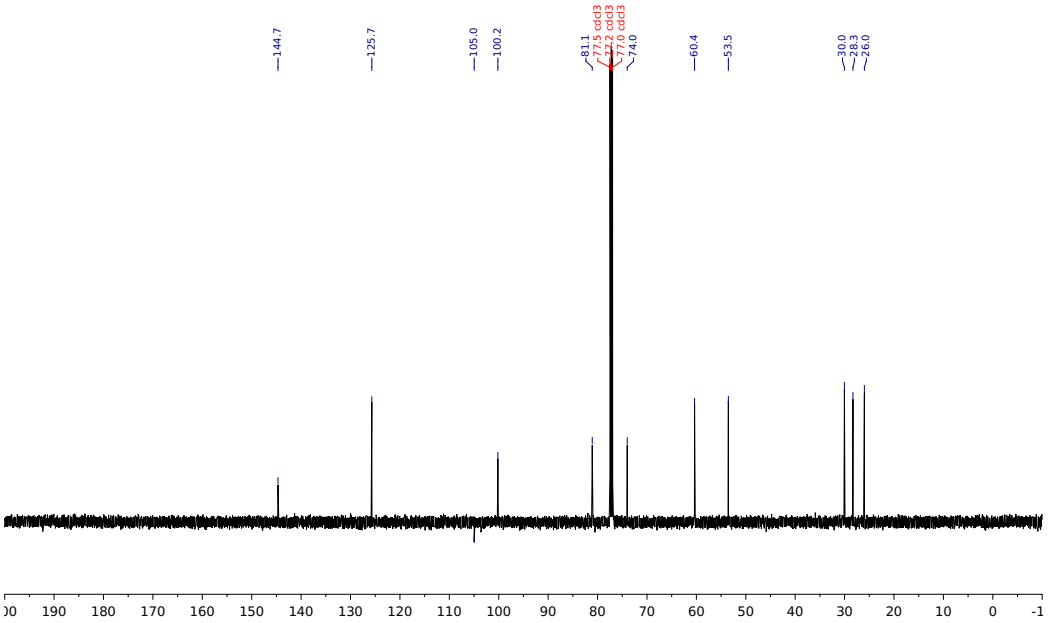


Figure SI.6 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **11**

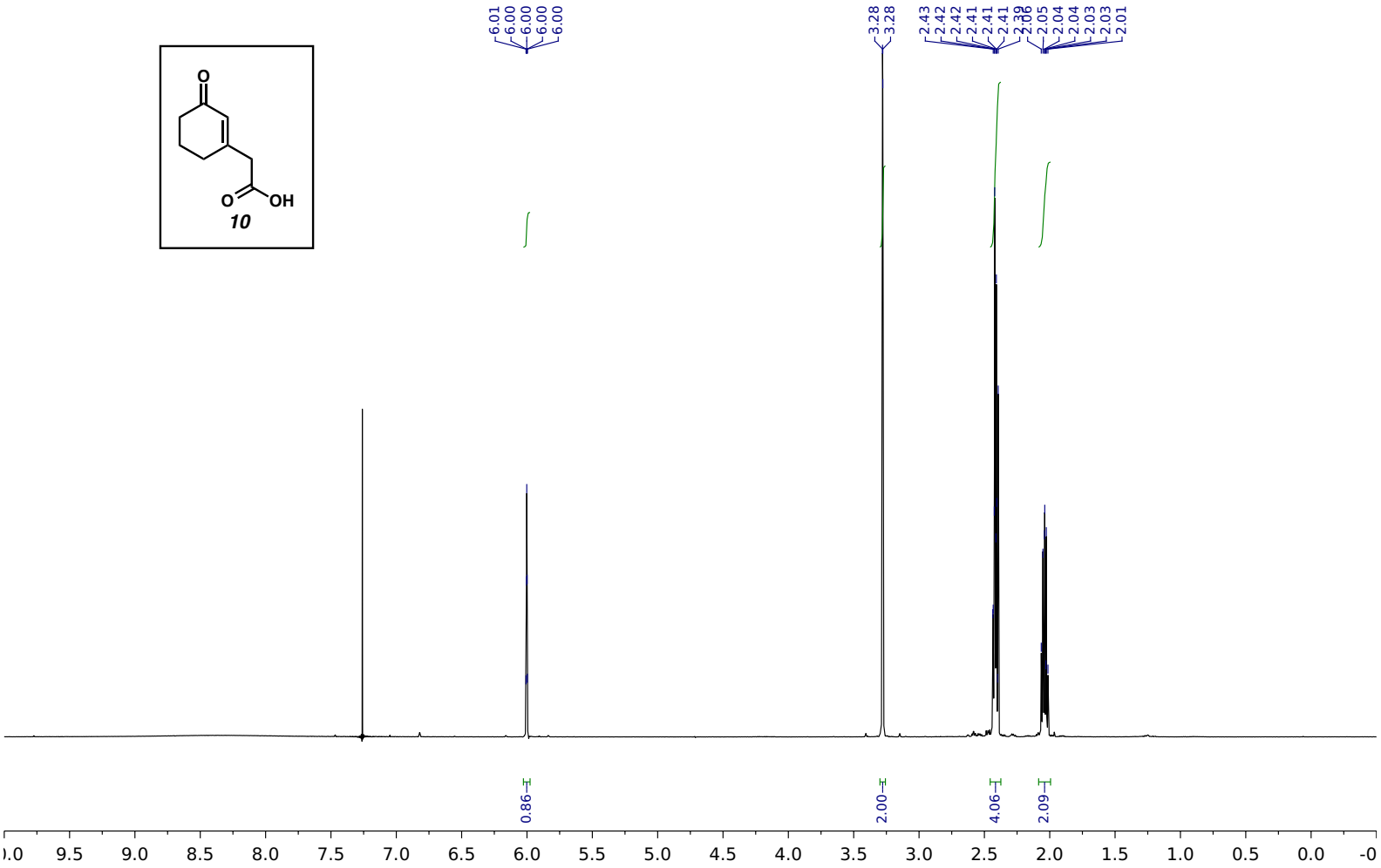


Figure SI.7 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **10**

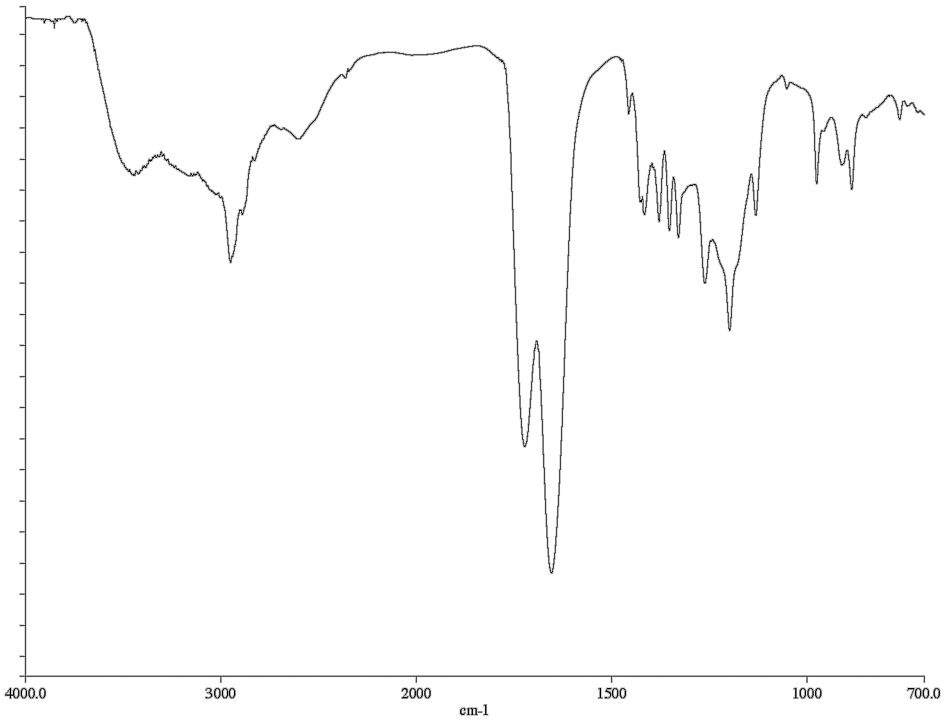


Figure SI.8 Infrared spectrum (thin film/NaCl) of compound **10**

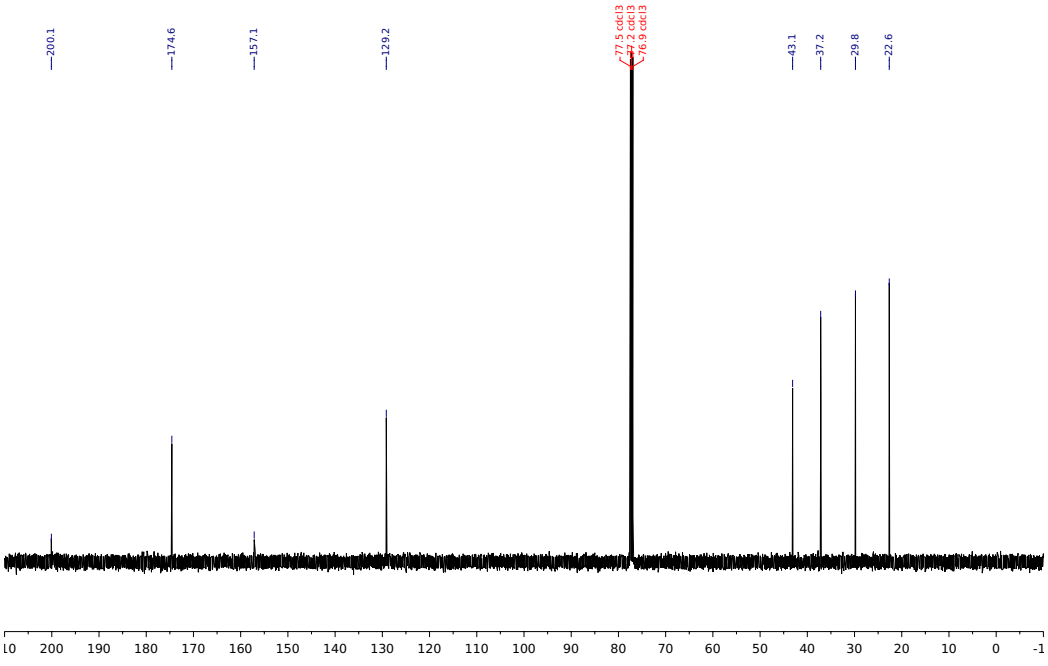


Figure SI.9 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **10**

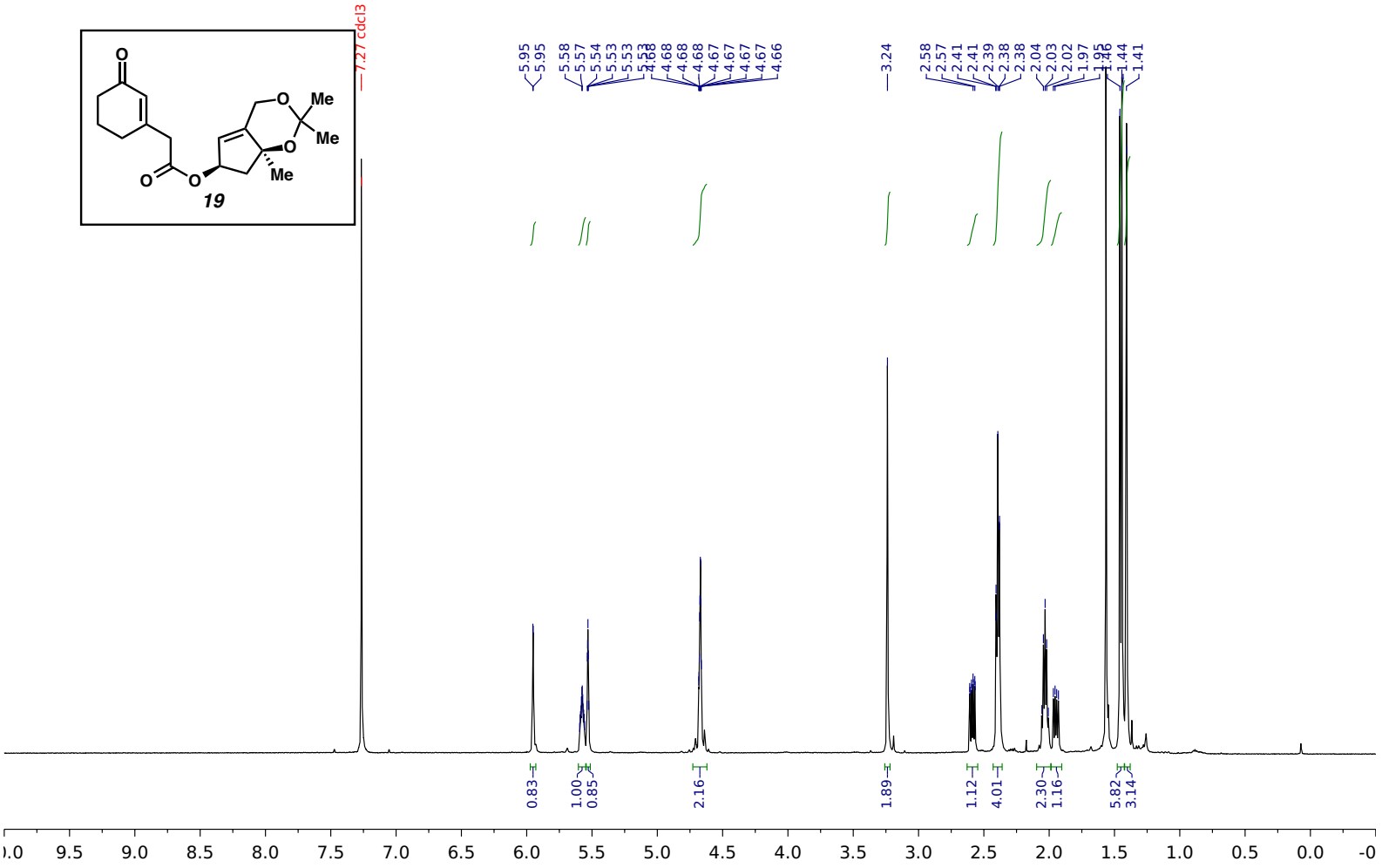


Figure SI.10 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **19**

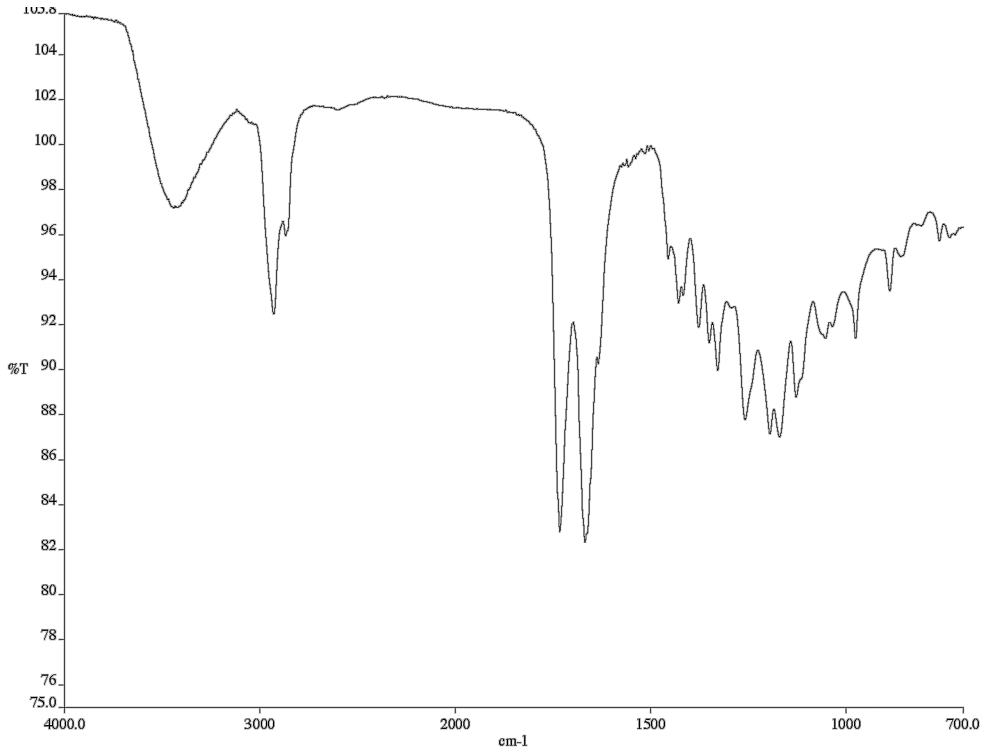


Figure SI.11 Infrared spectrum (thin film/NaCl) of compound **19**

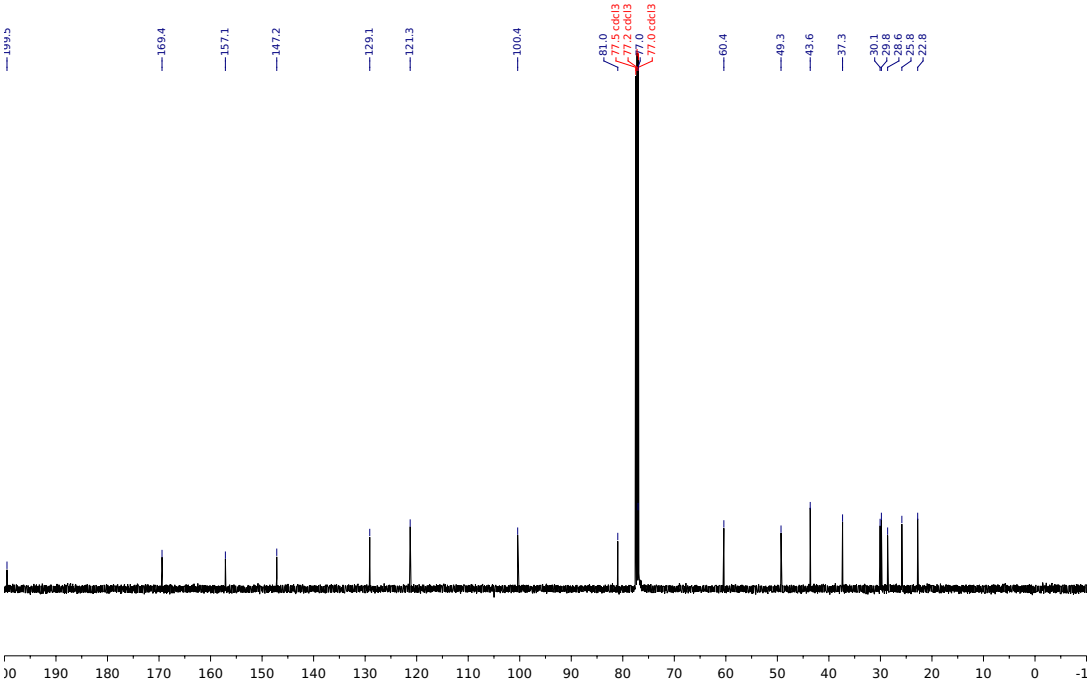


Figure SI.12 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **19**

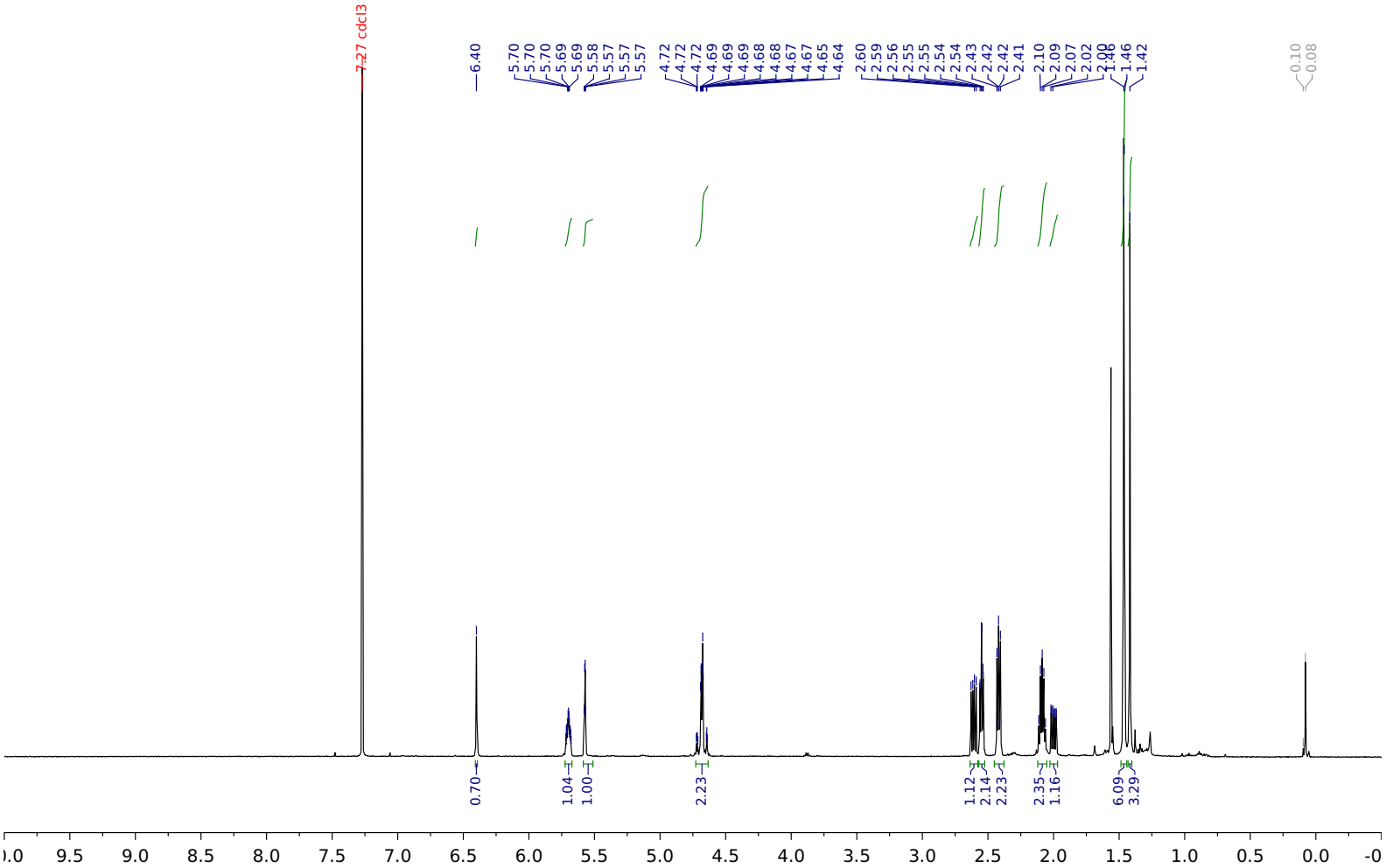


Figure SI.13 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **9**

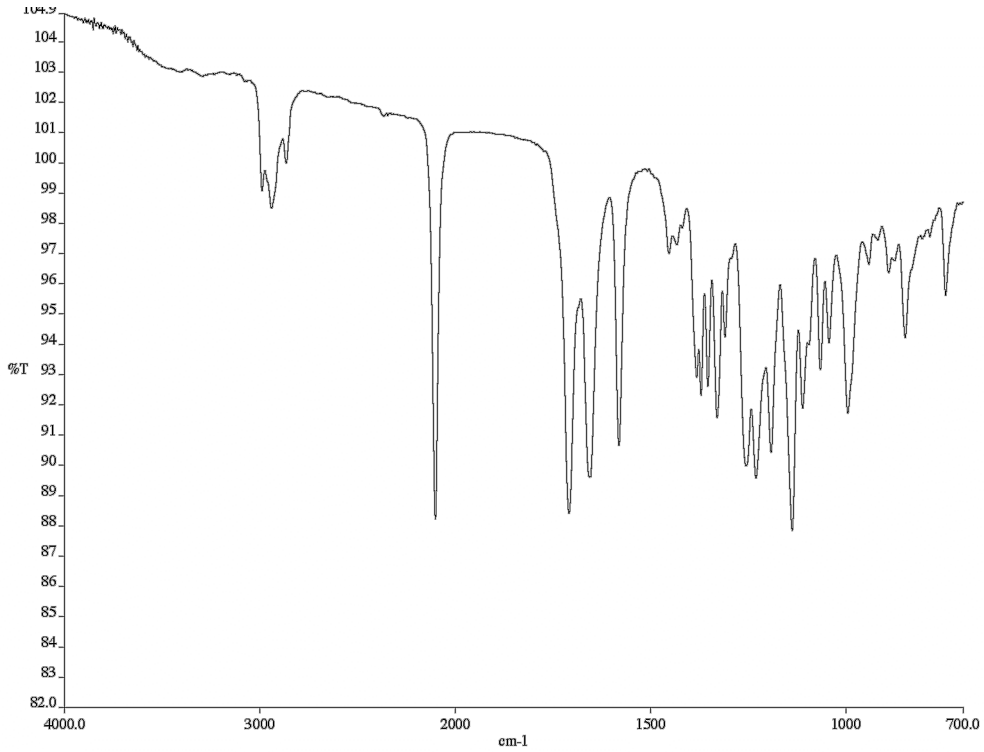


Figure SI.14 Infrared spectrum (thin film/NaCl) of compound **9**

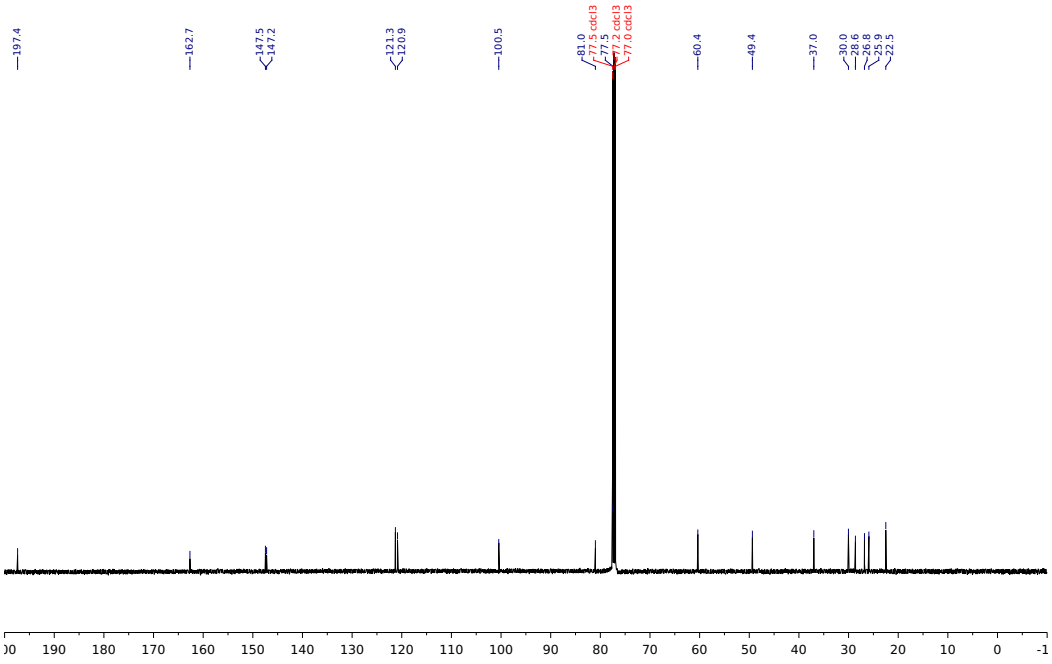


Figure SI.15 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **9**

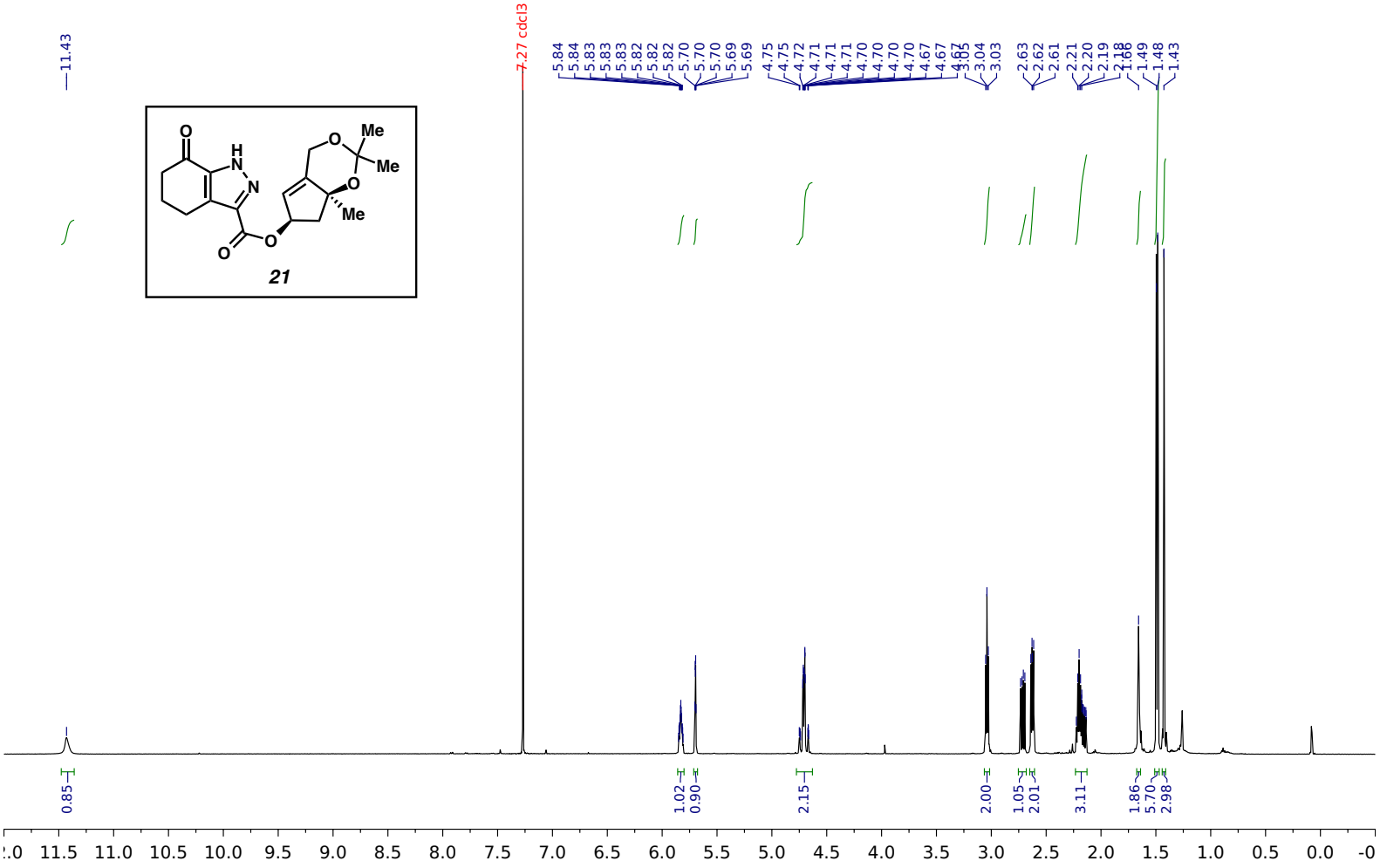


Figure SI.16 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **21**

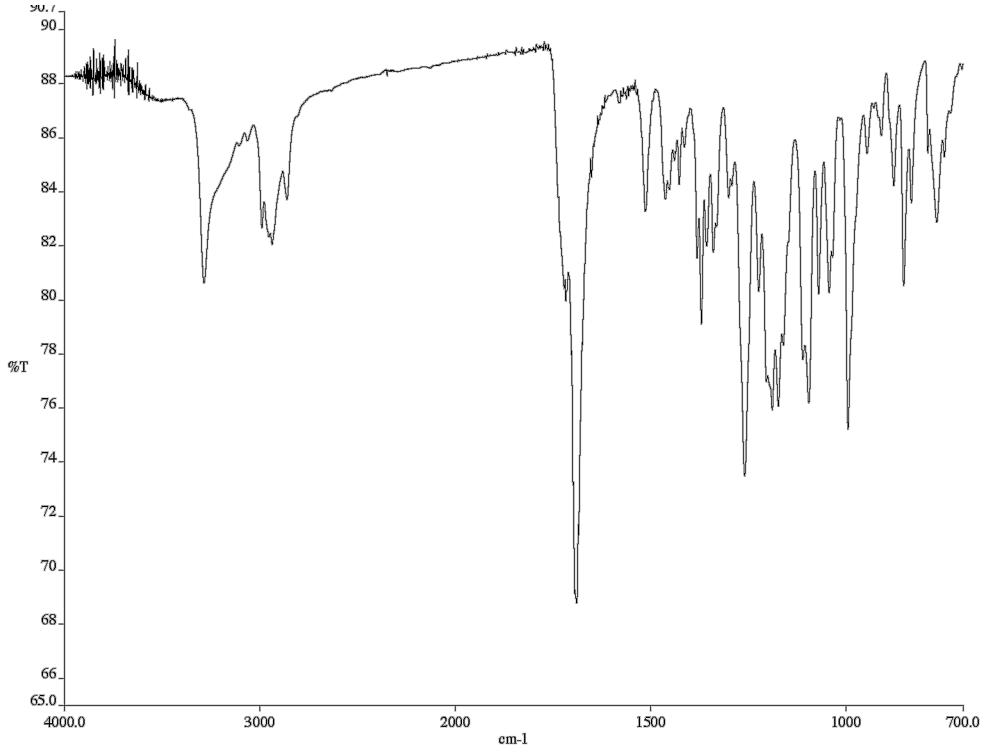


Figure SI.17 Infrared spectrum (thin film/NaCl) of compound **21**

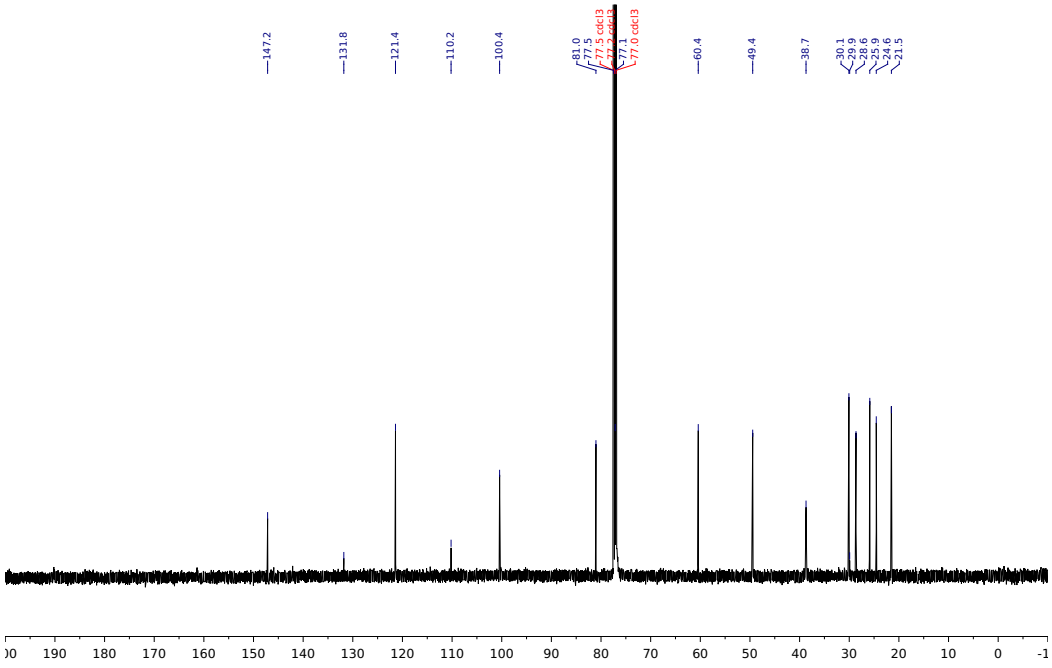


Figure SI.18 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **21**

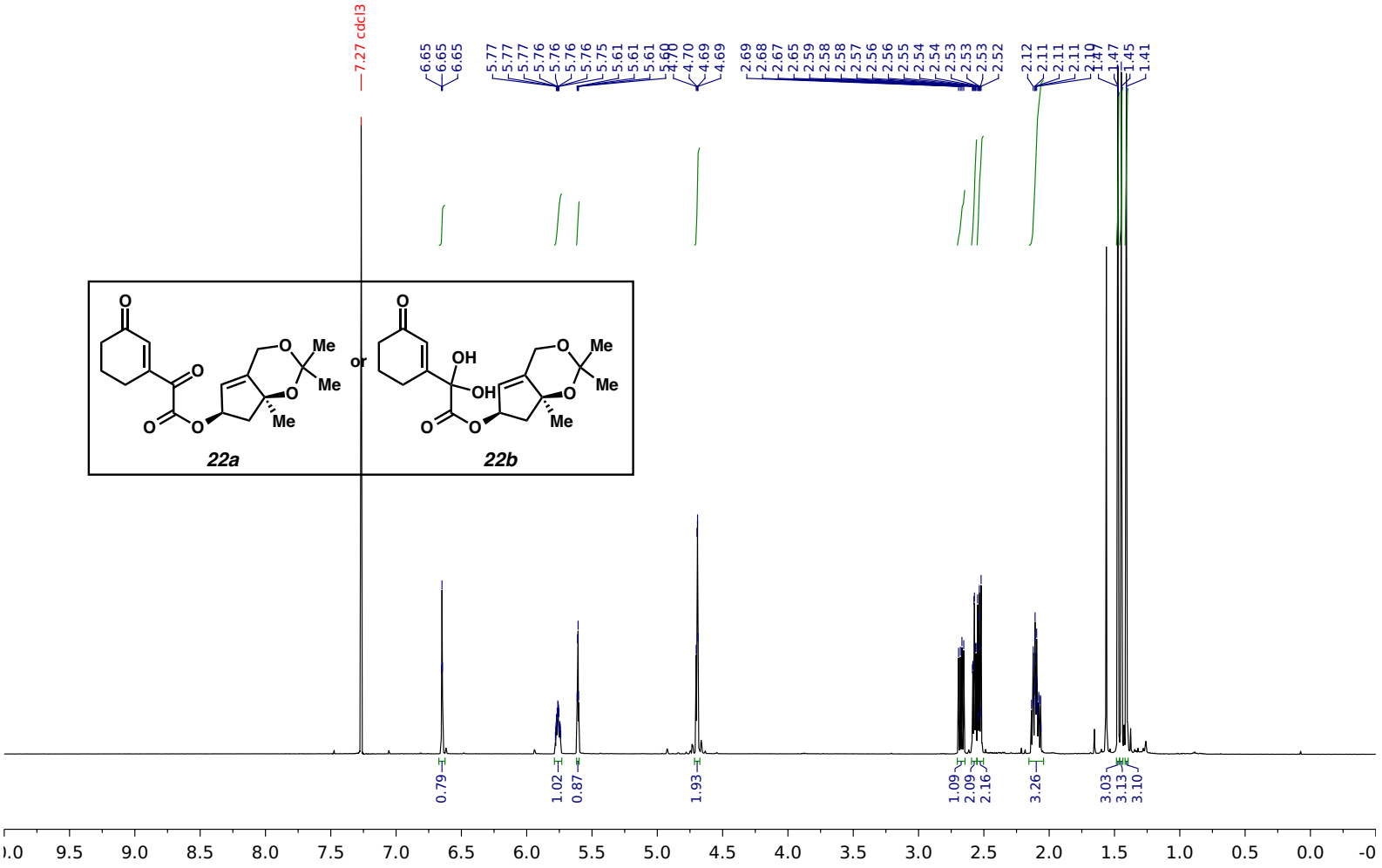


Figure SI.19 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **22**

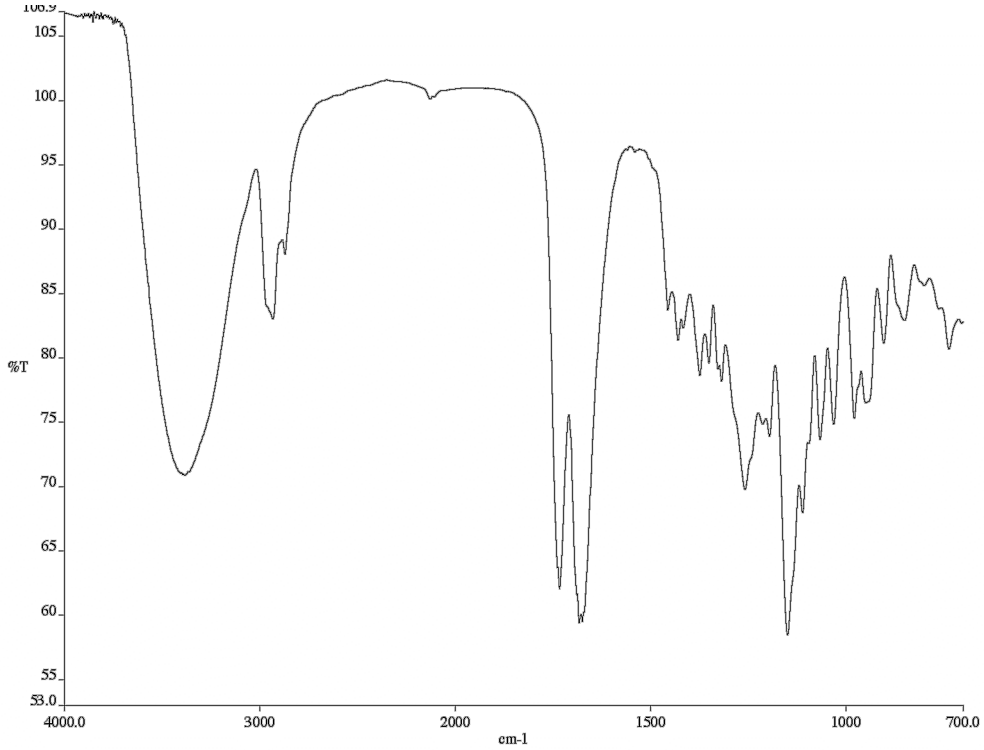


Figure SI.20 Infrared spectrum (thin film/NaCl) of compound **22**

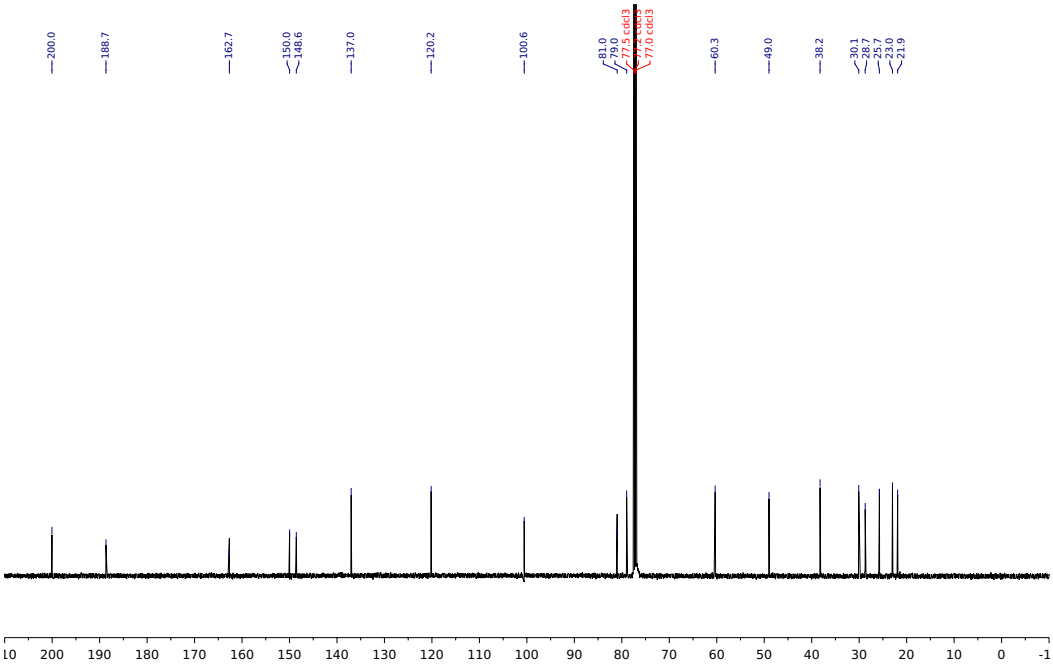


Figure SI.21 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **22**

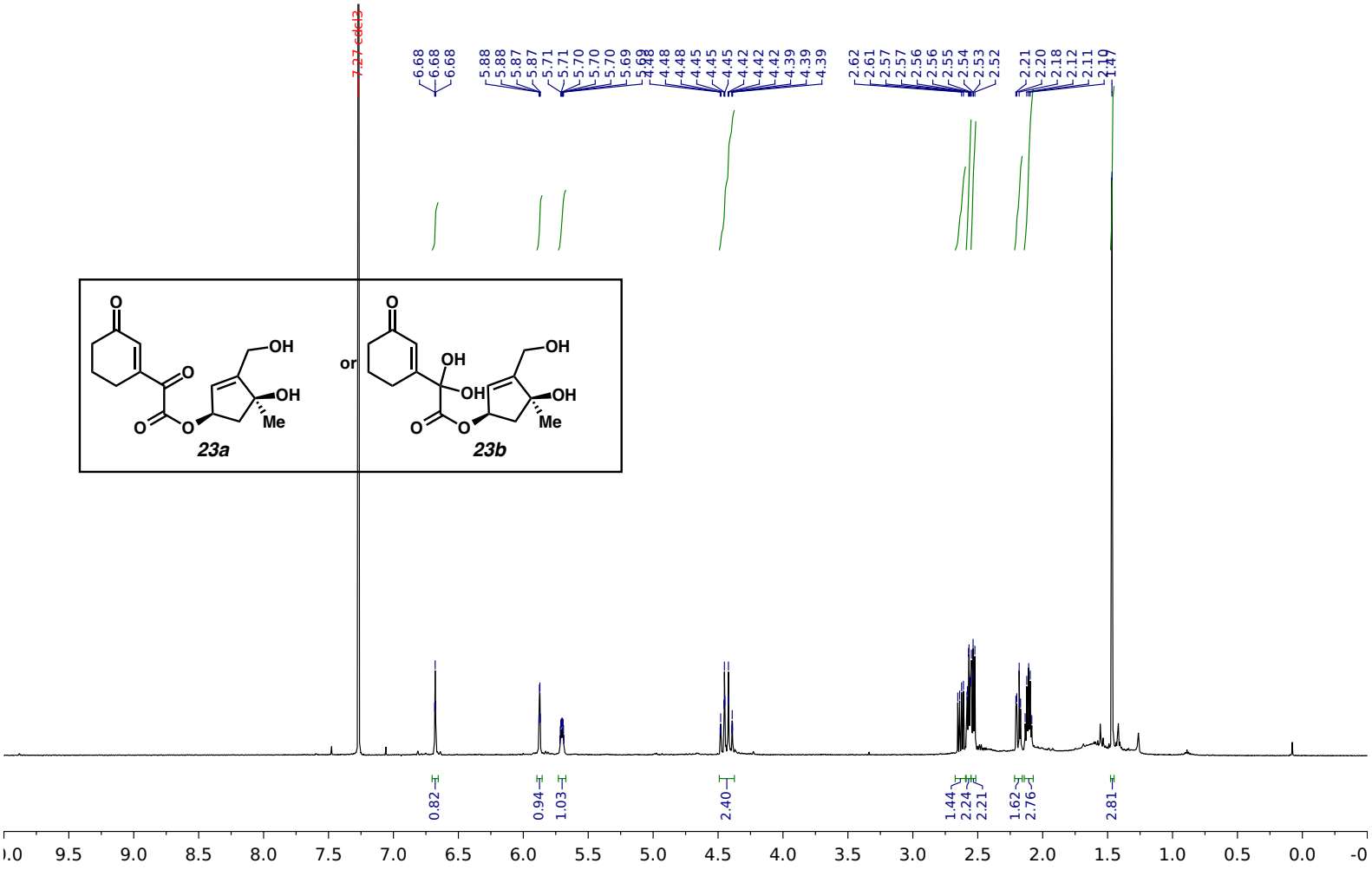


Figure SI.22 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **23**

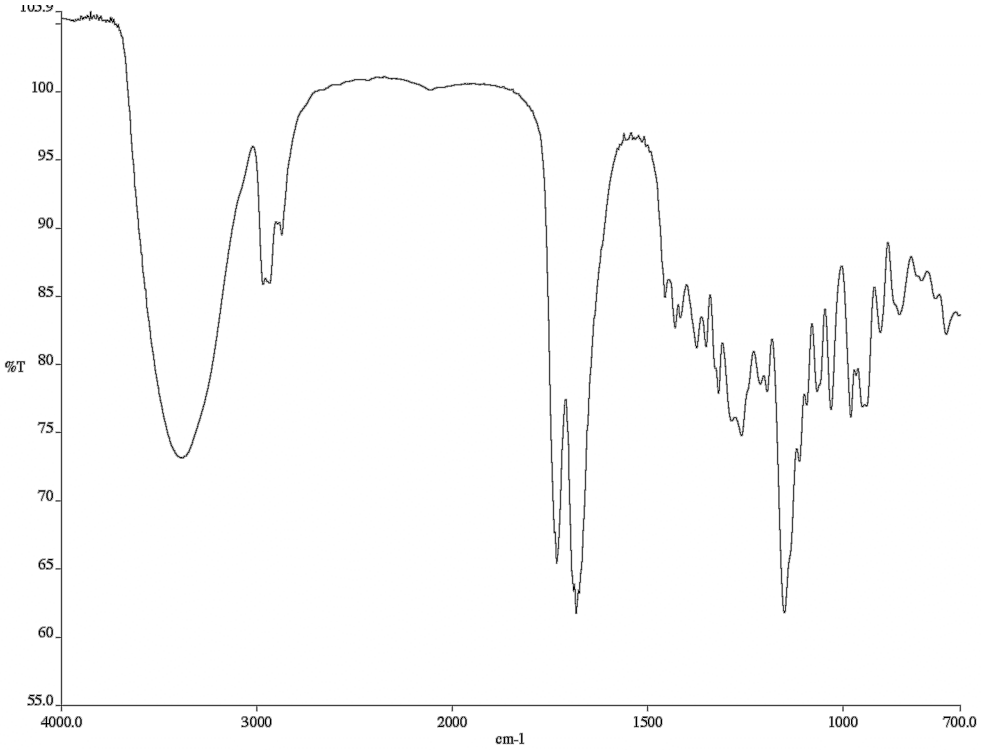


Figure SI.23 Infrared spectrum (thin film/NaCl) of compound **23**

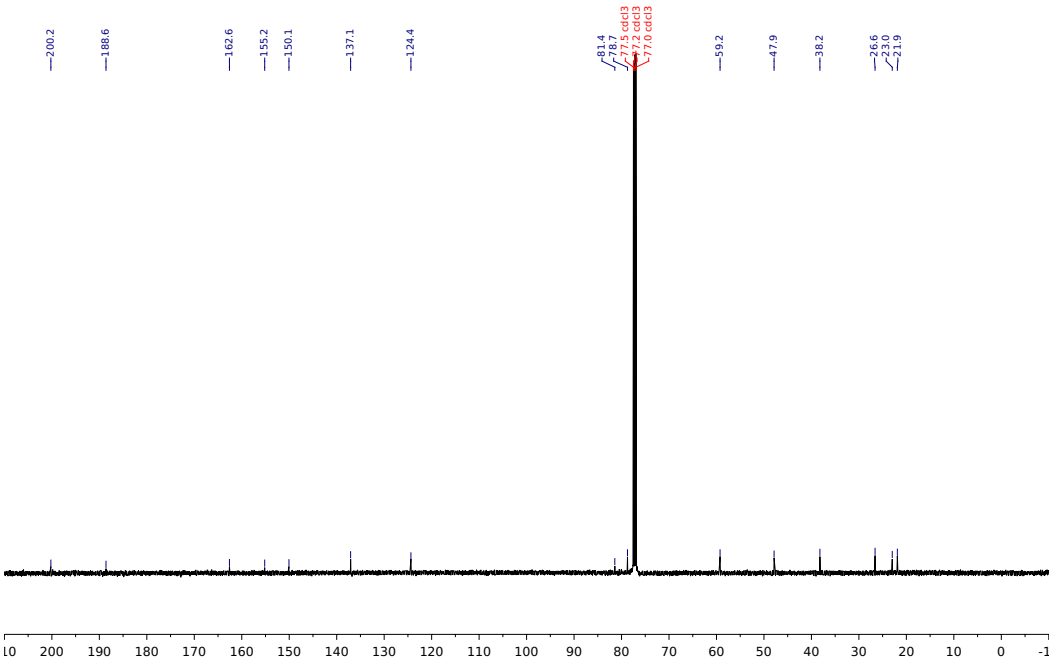


Figure SI.24 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **23**

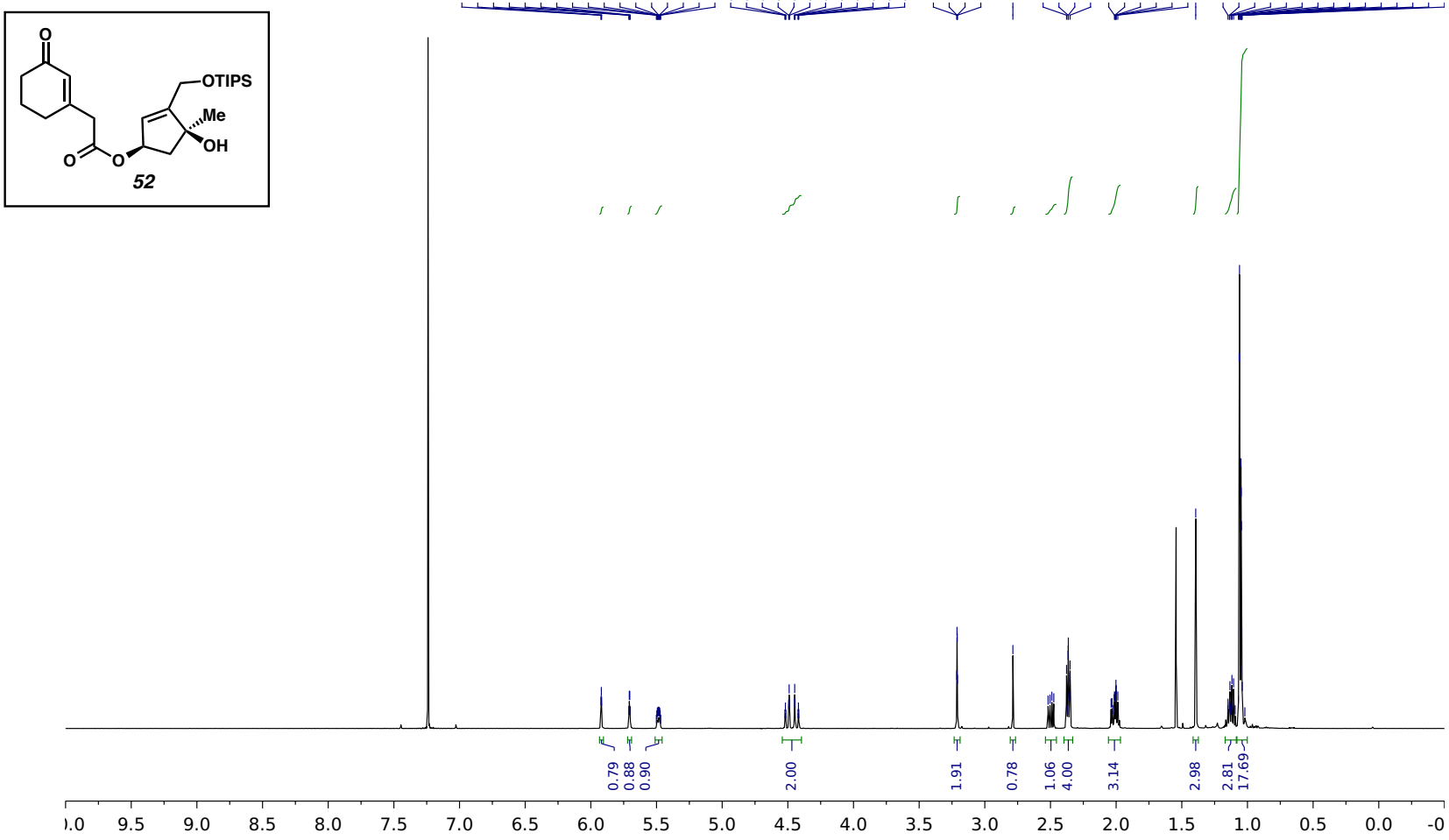


Figure SI.25 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **52**

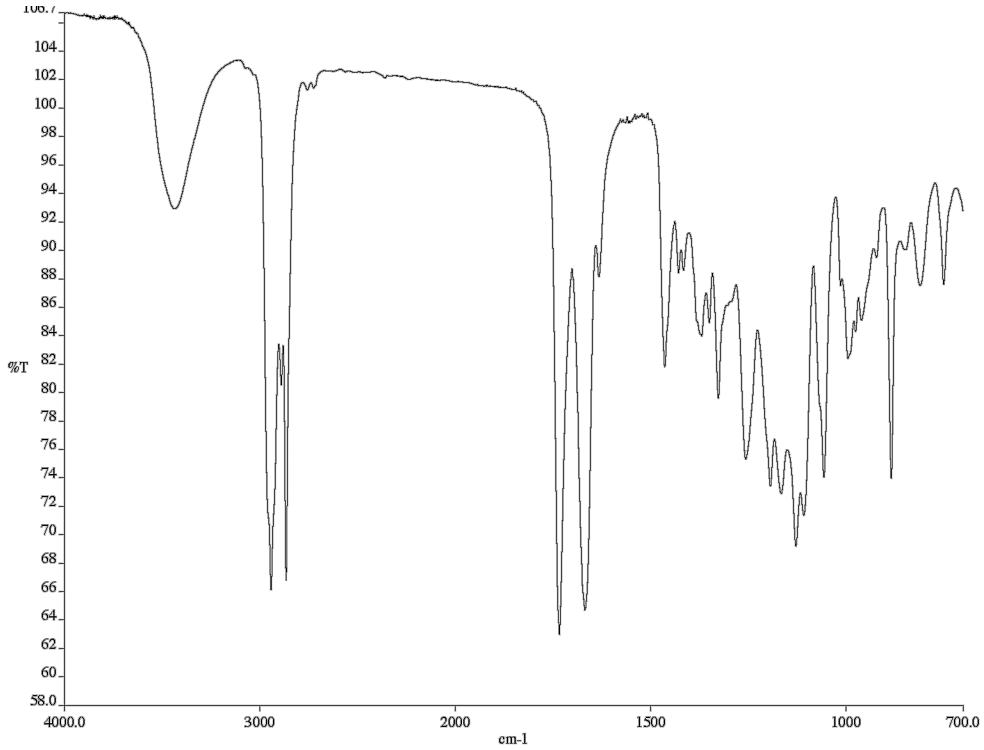


Figure SI.26 Infrared spectrum (thin film/NaCl) of compound **52**

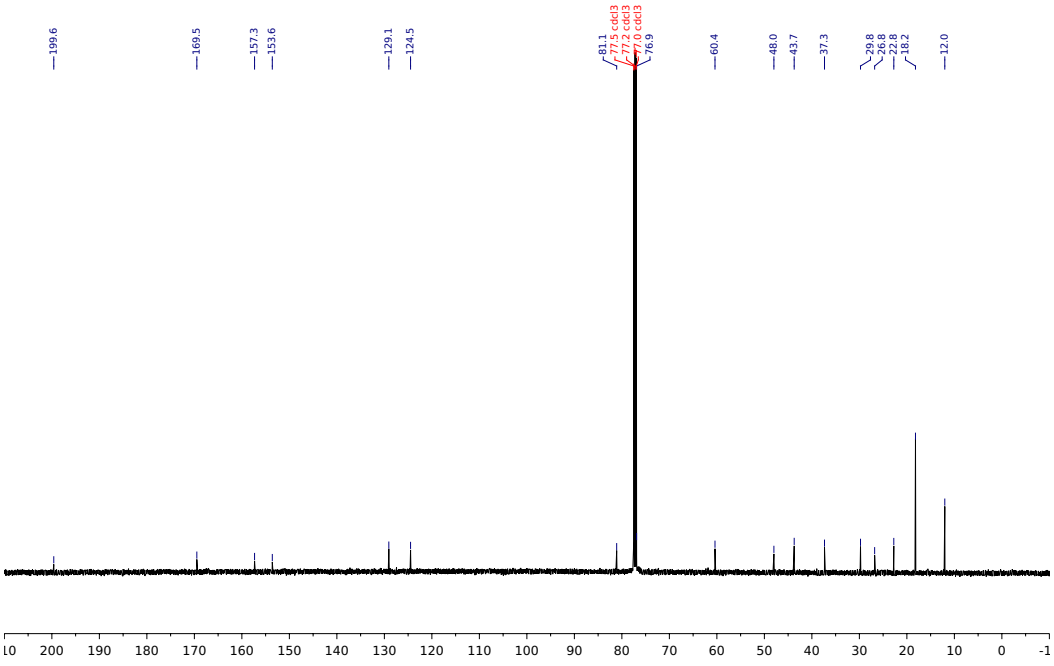


Figure SI.27 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **52**

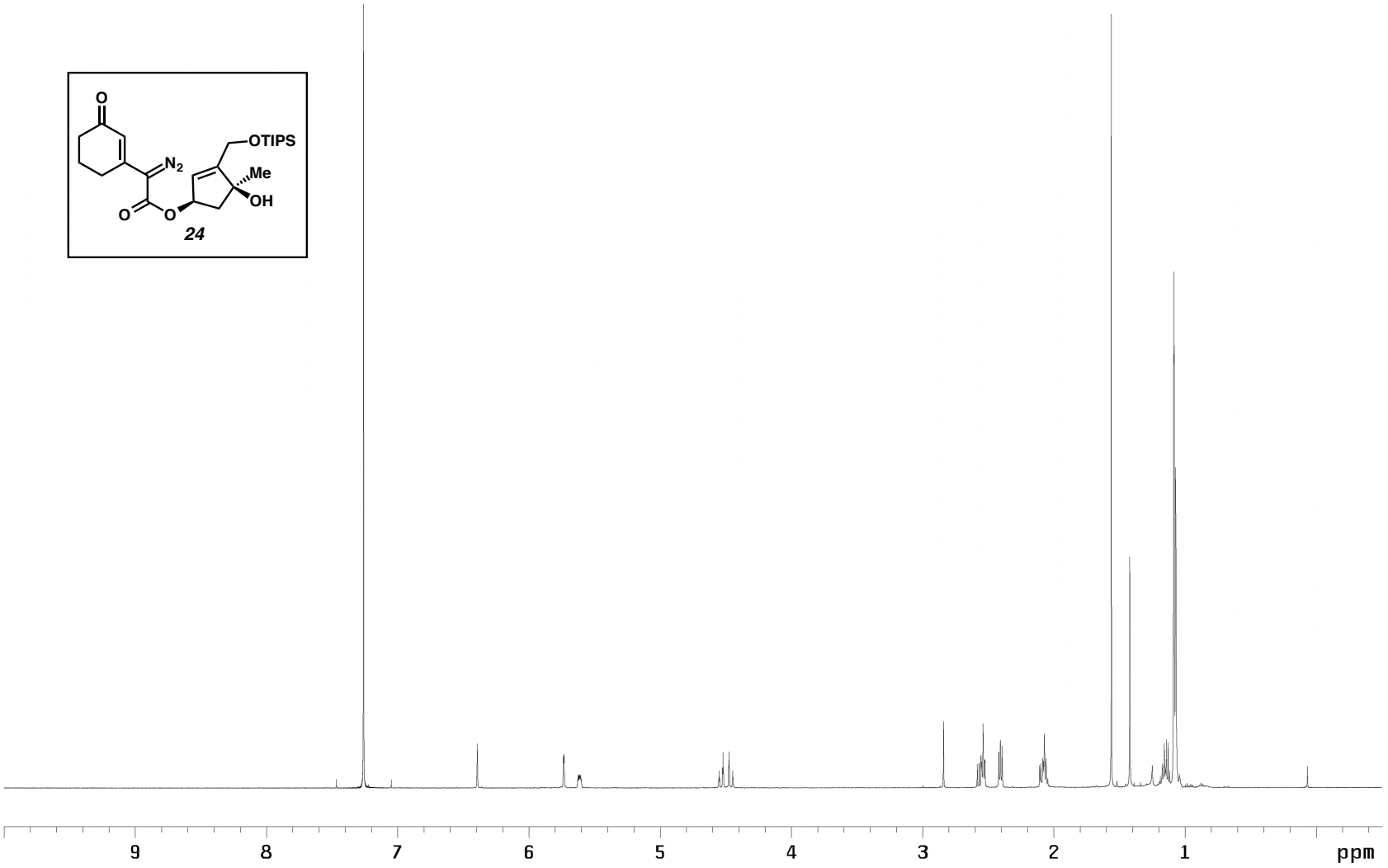


Figure SI.28 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **24**

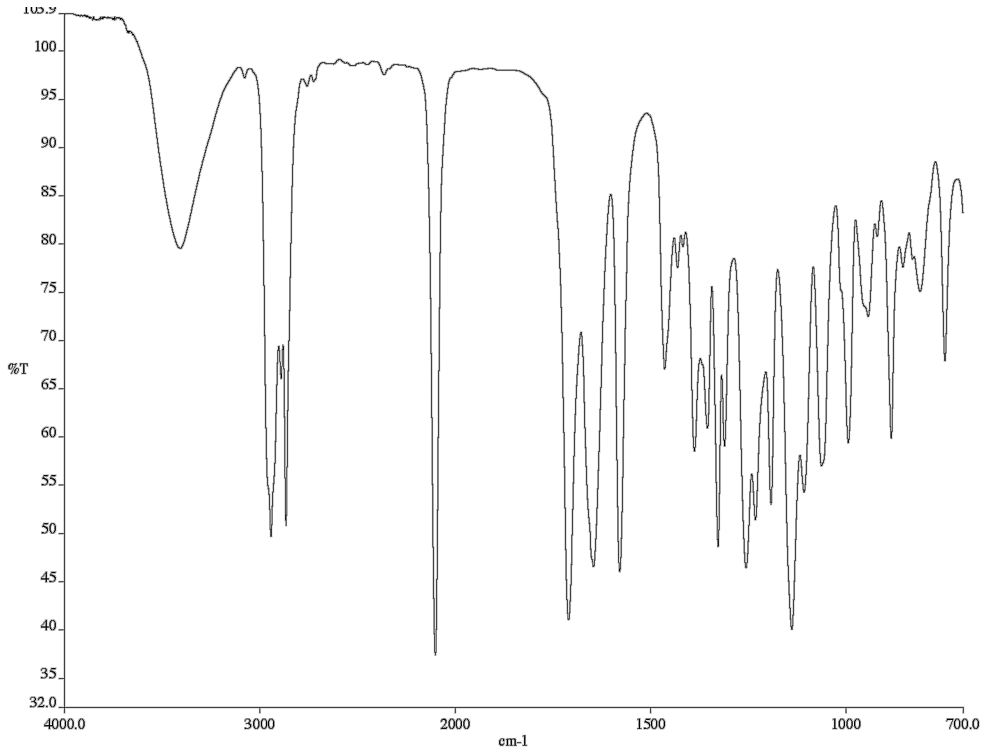


Figure SI.29 Infrared spectrum (thin film/NaCl) of compound **24**

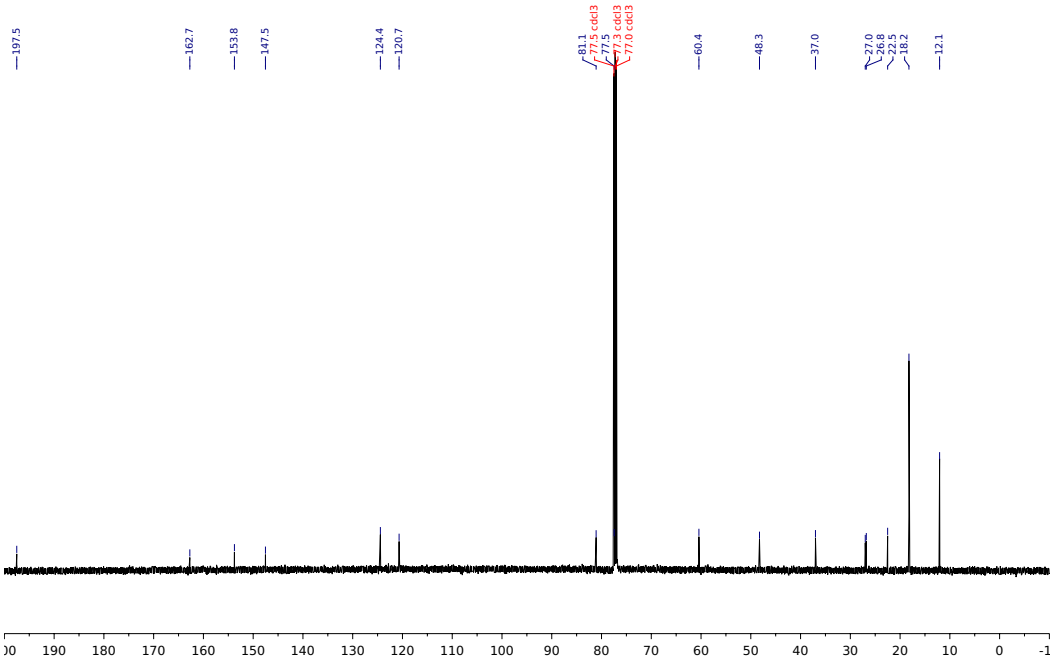


Figure SI.30 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **24**

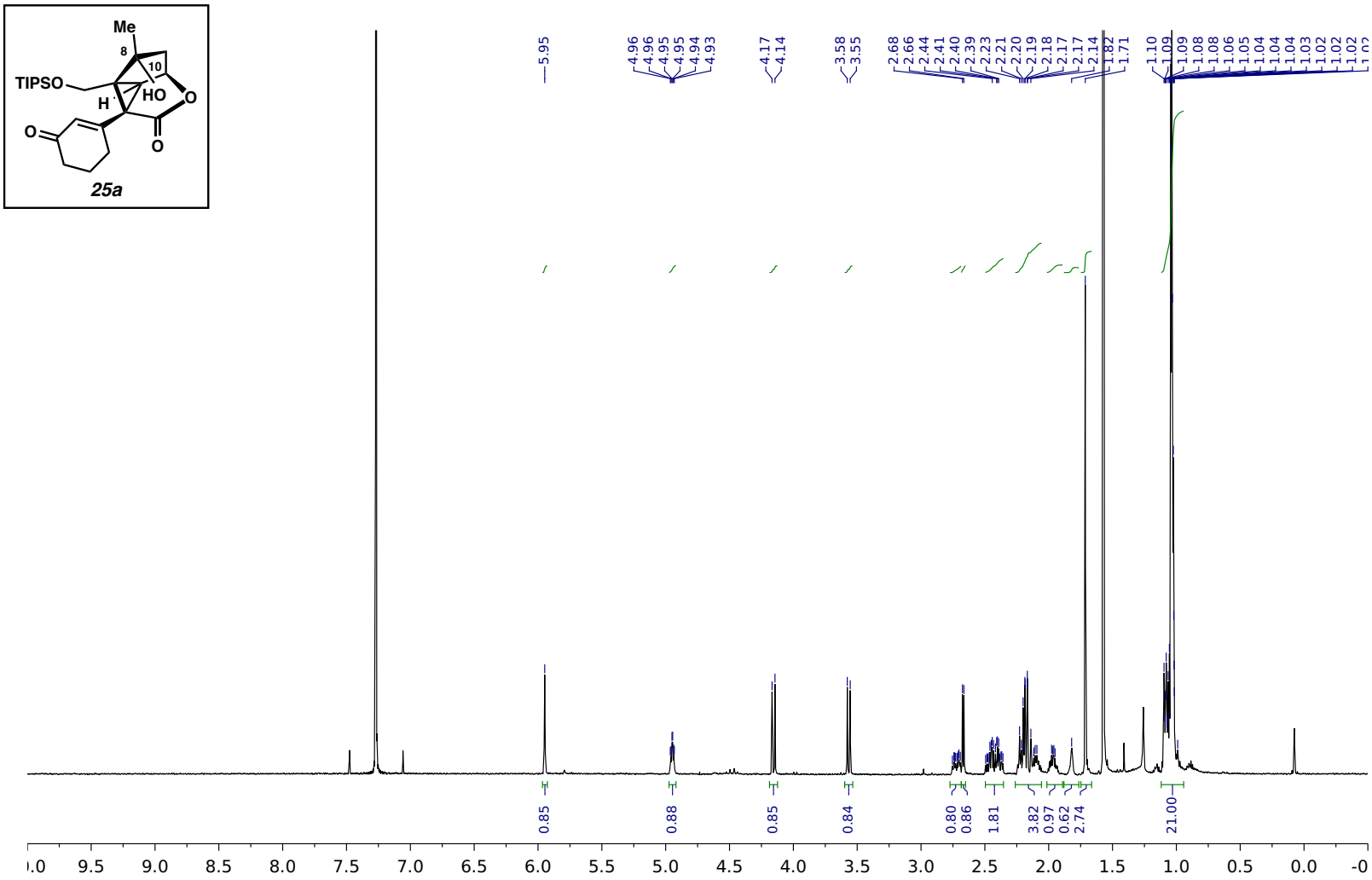


Figure SI.31 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **25a**

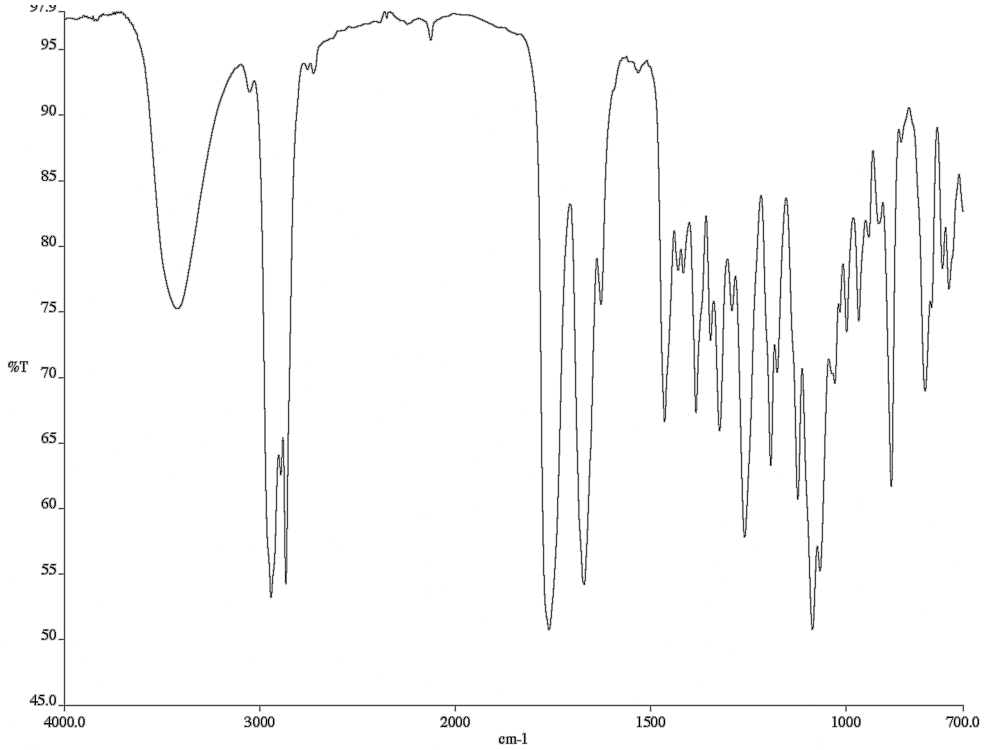


Figure SI.32 Infrared spectrum (thin film/NaCl) of compound **25a**

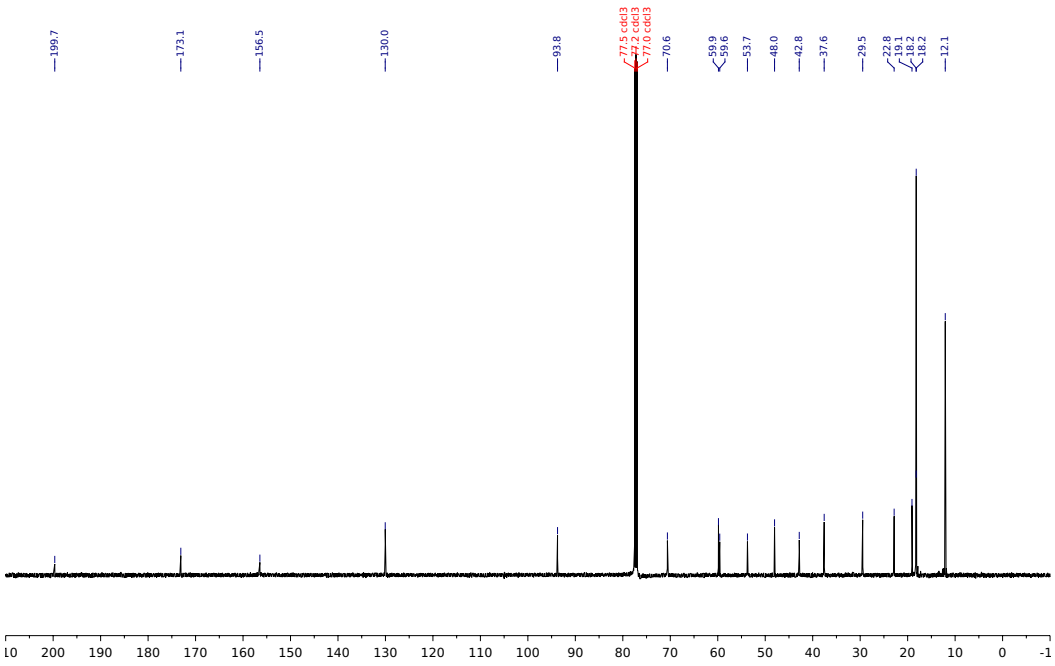


Figure SI.33 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **25a**

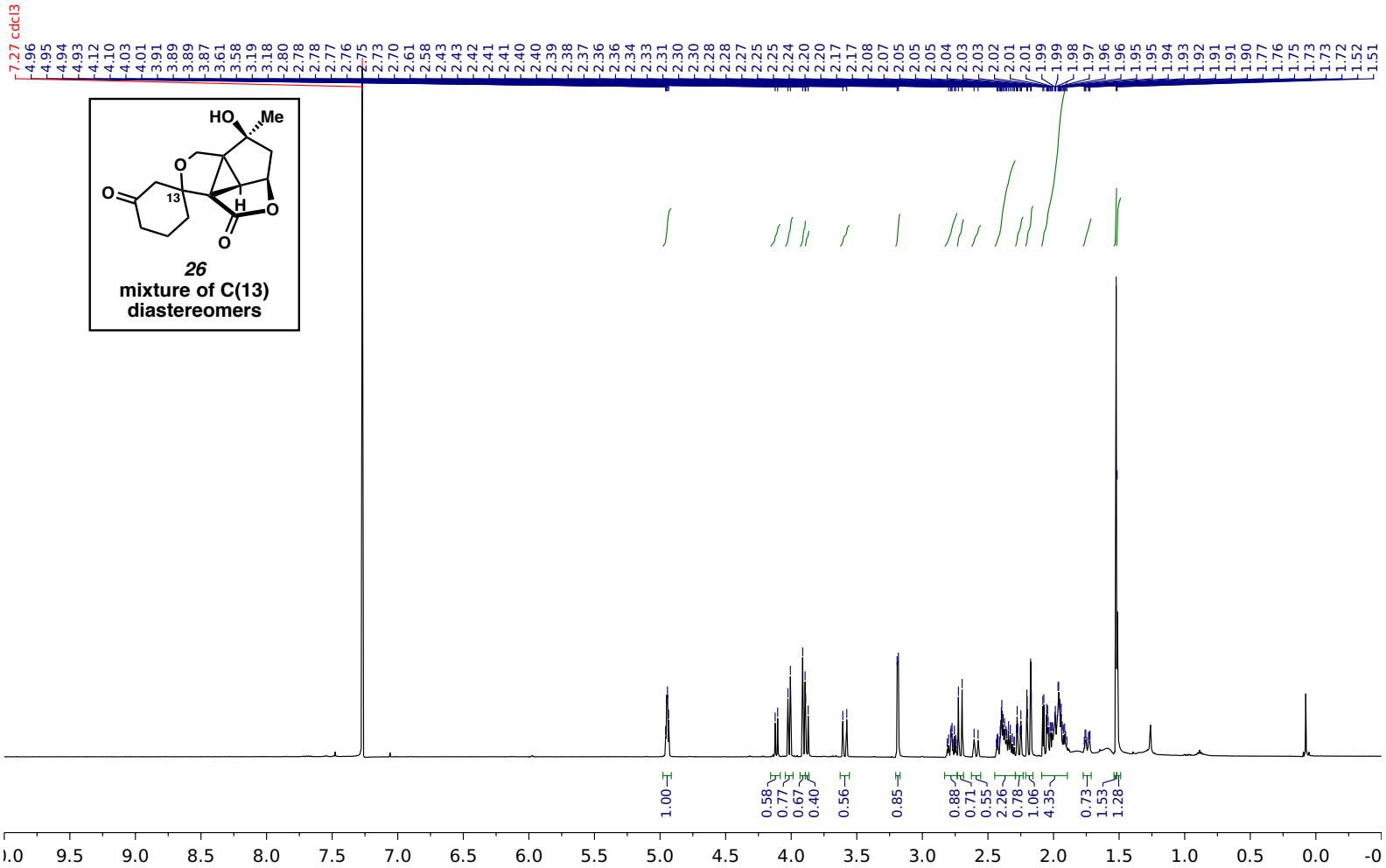


Figure SI.34 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **26**

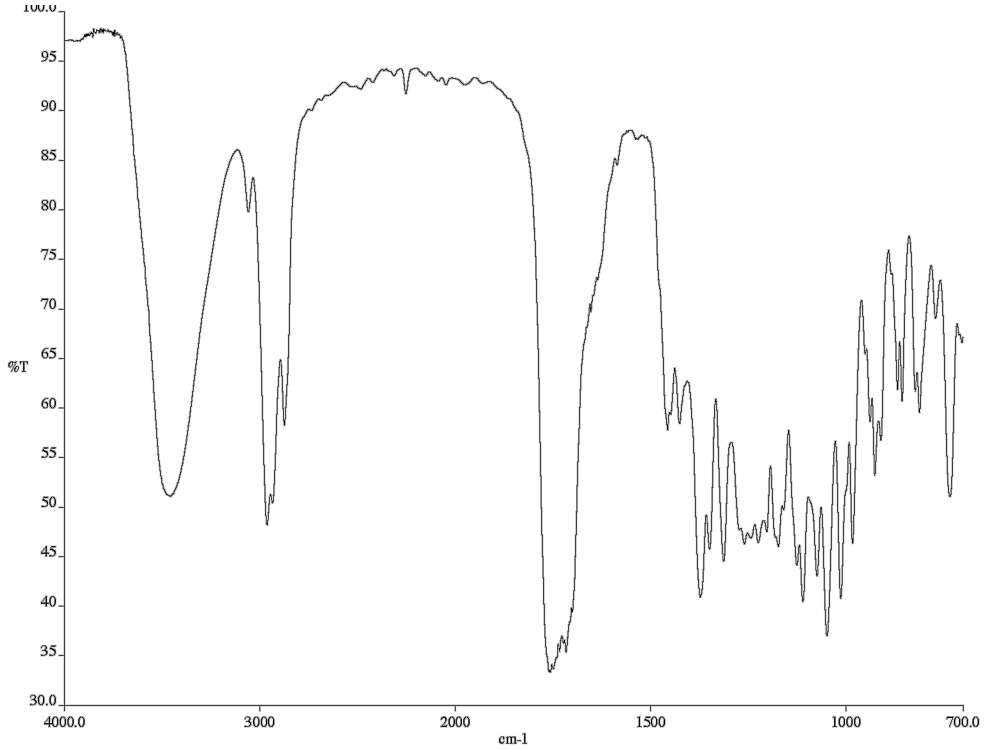


Figure SI.35 Infrared spectrum (thin film/NaCl) of compound **26**

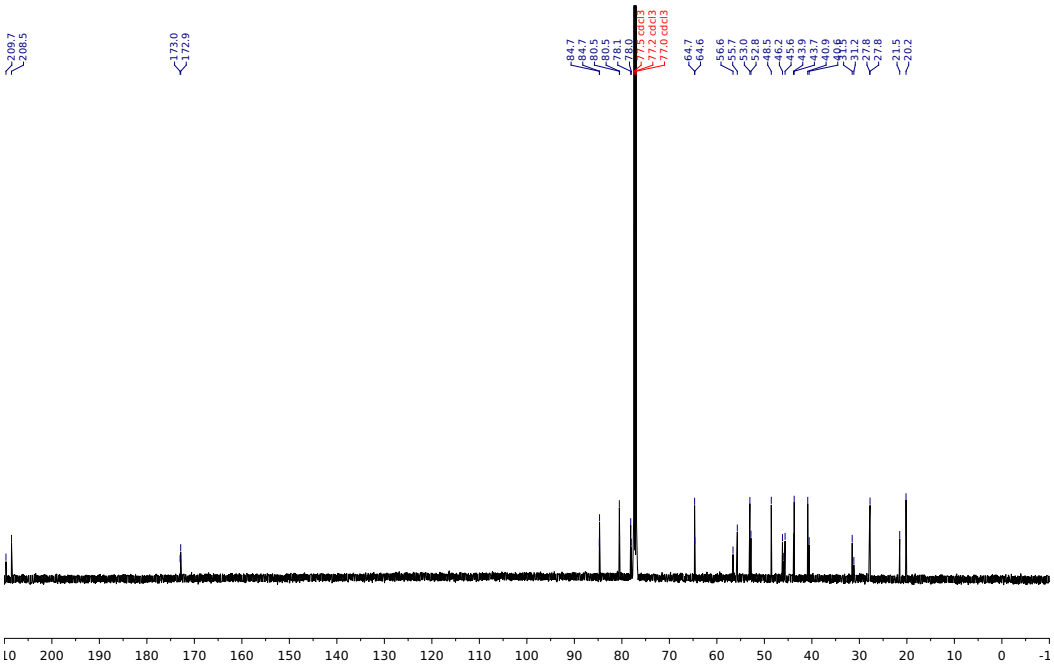


Figure SI.36 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **26**

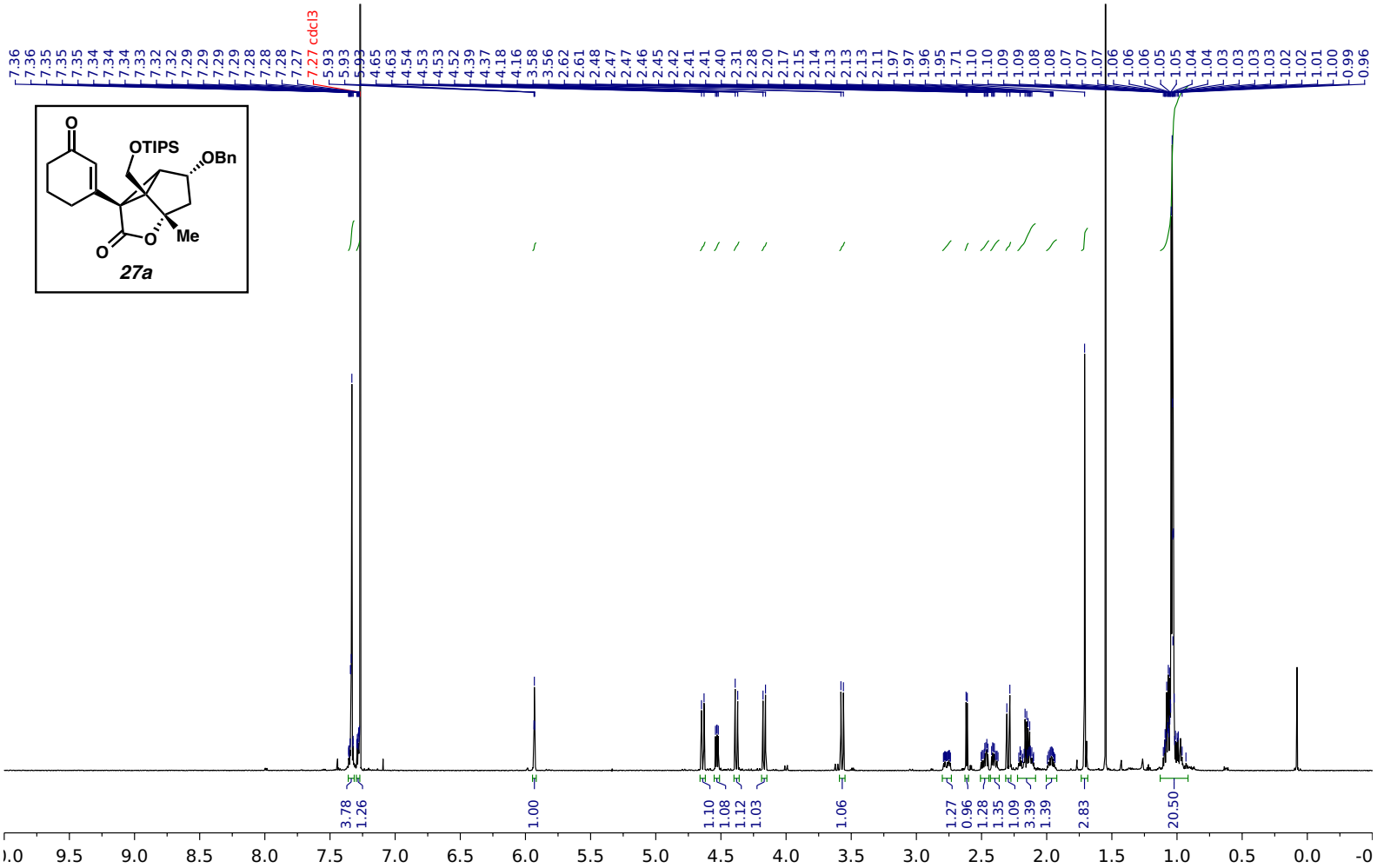


Figure SI.37 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **27a**

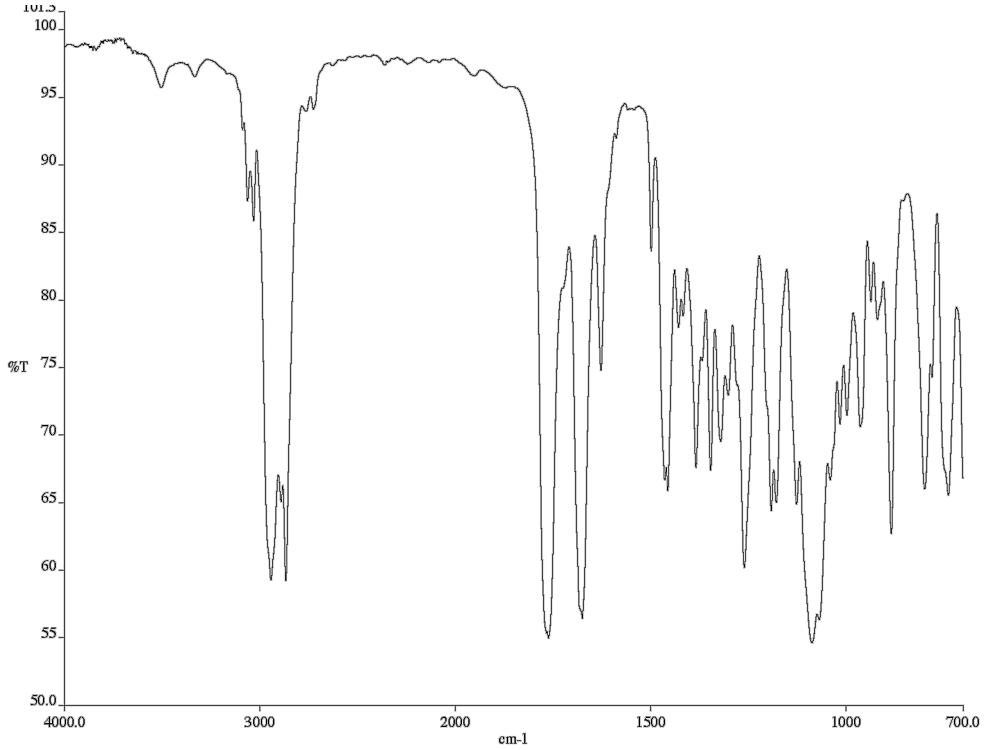


Figure SI.38 Infrared spectrum (thin film/NaCl) of compound **27a**

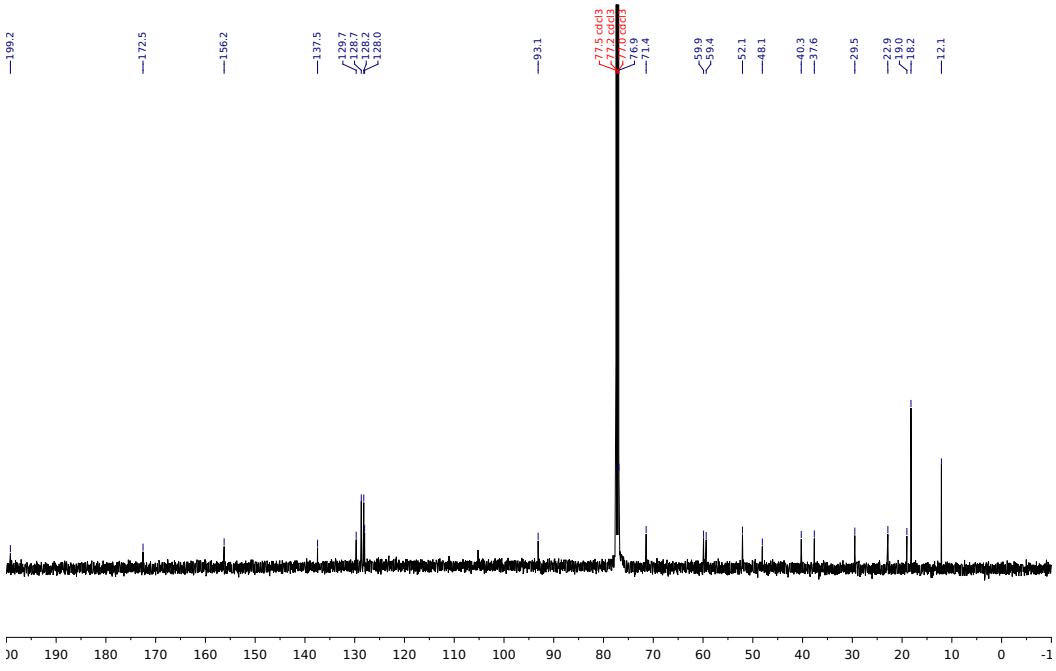


Figure SI.39 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **27a**

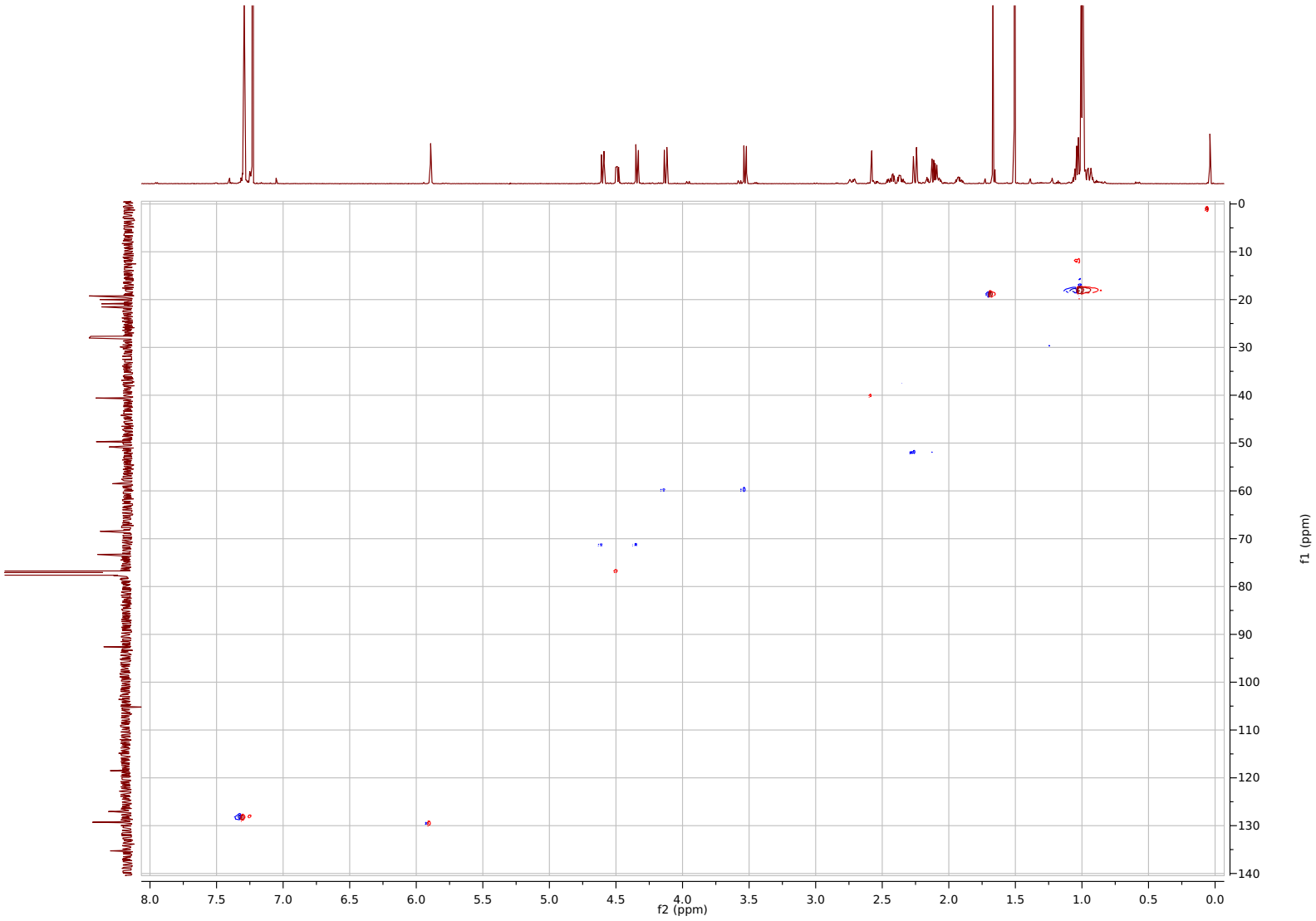


Figure SI.40 gHSQCAD (500 MHz, $CDCl_3$) of compound **27a**

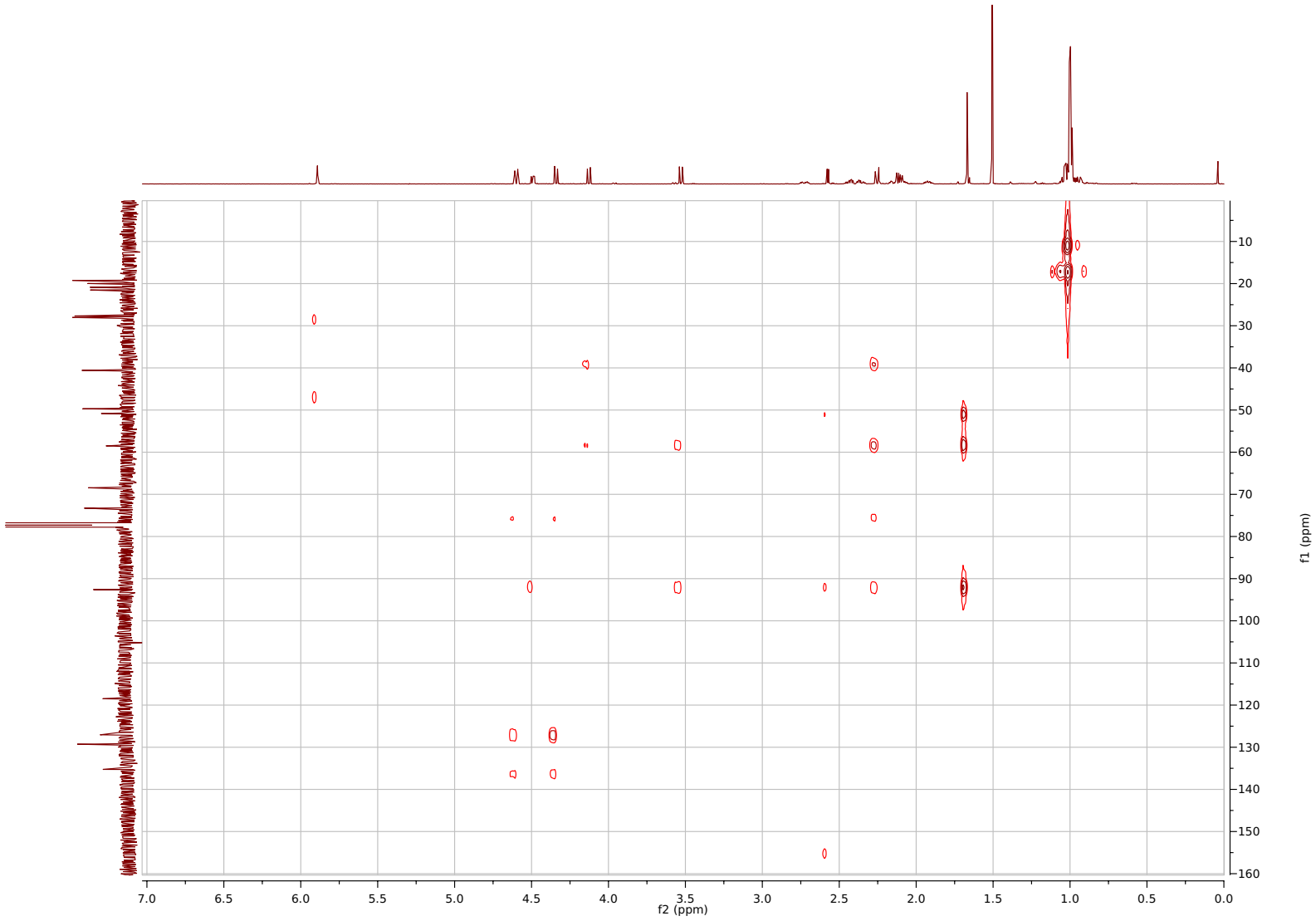


Figure SI.41 gHMBC (500 MHz, $CDCl_3$) of compound **27a**

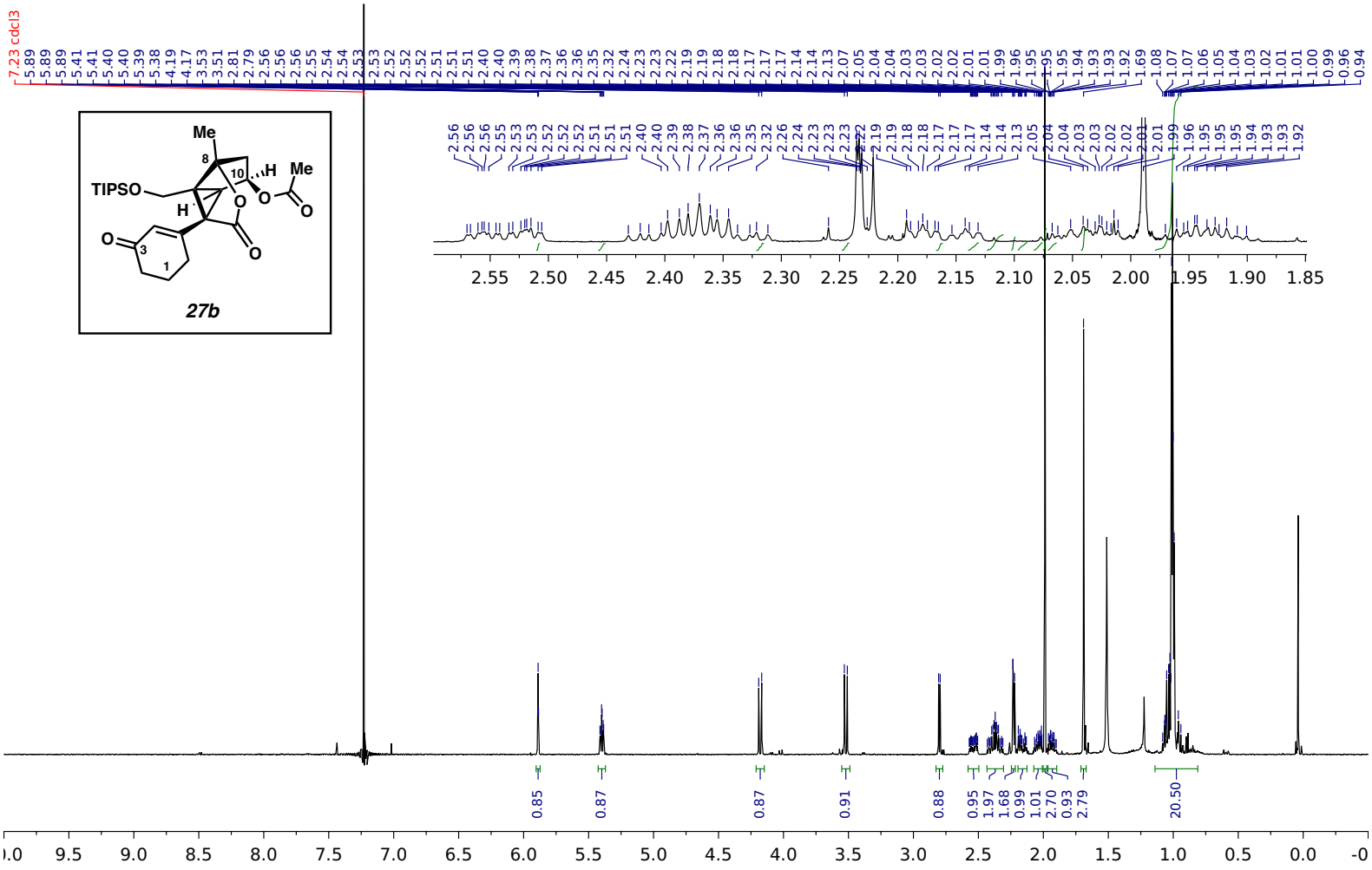


Figure SI.42 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **27b**

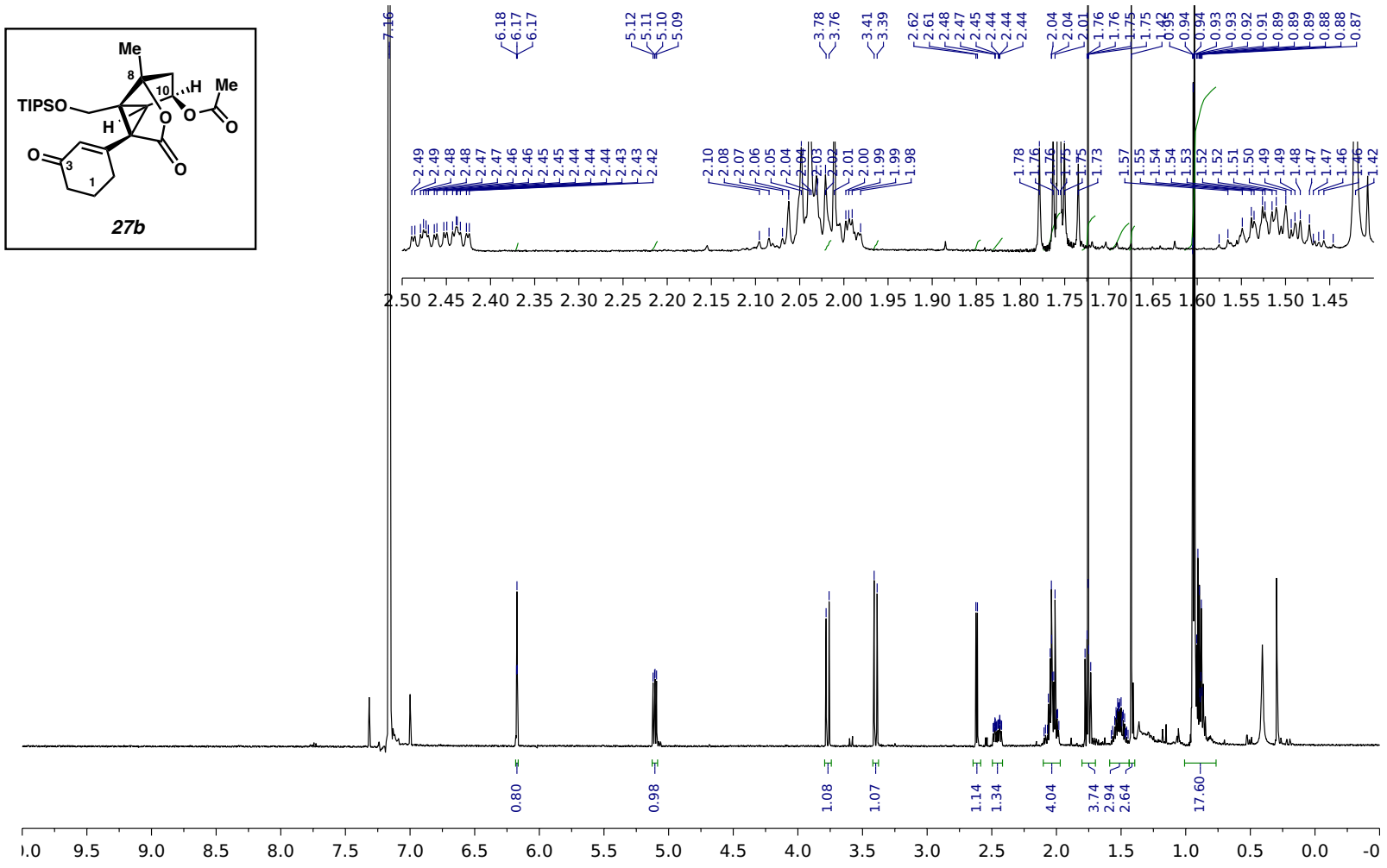


Figure SI.43 ^{1}H NMR (500 MHz, C_6D_6) of compound **27b**

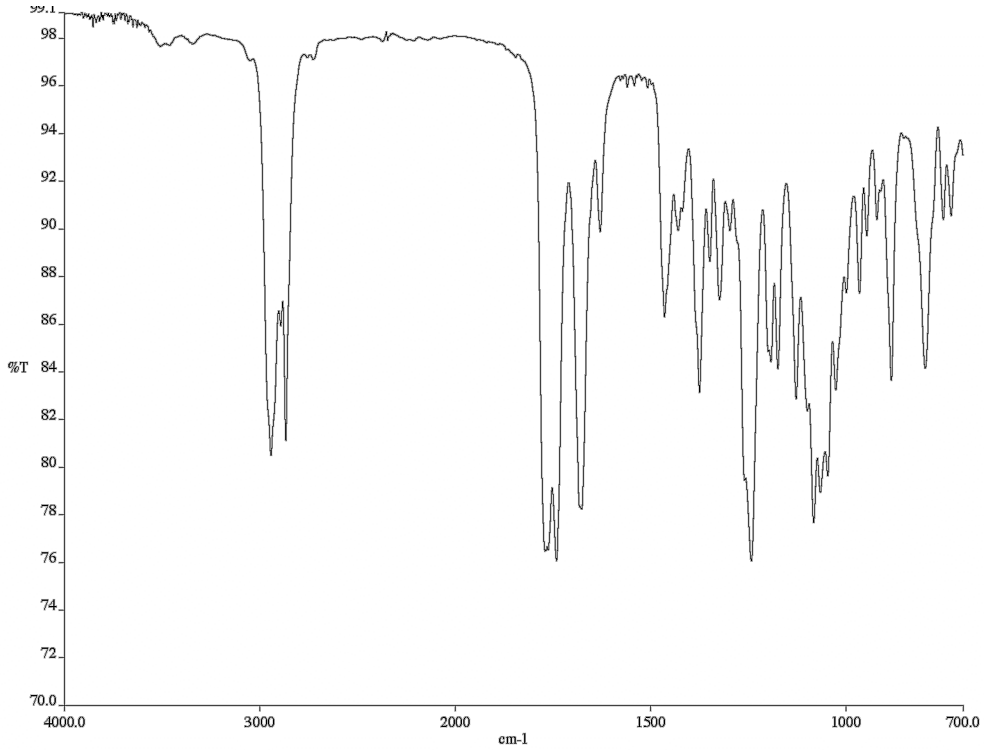


Figure SI.44 Infrared spectrum (thin film/NaCl) of compound **27b**

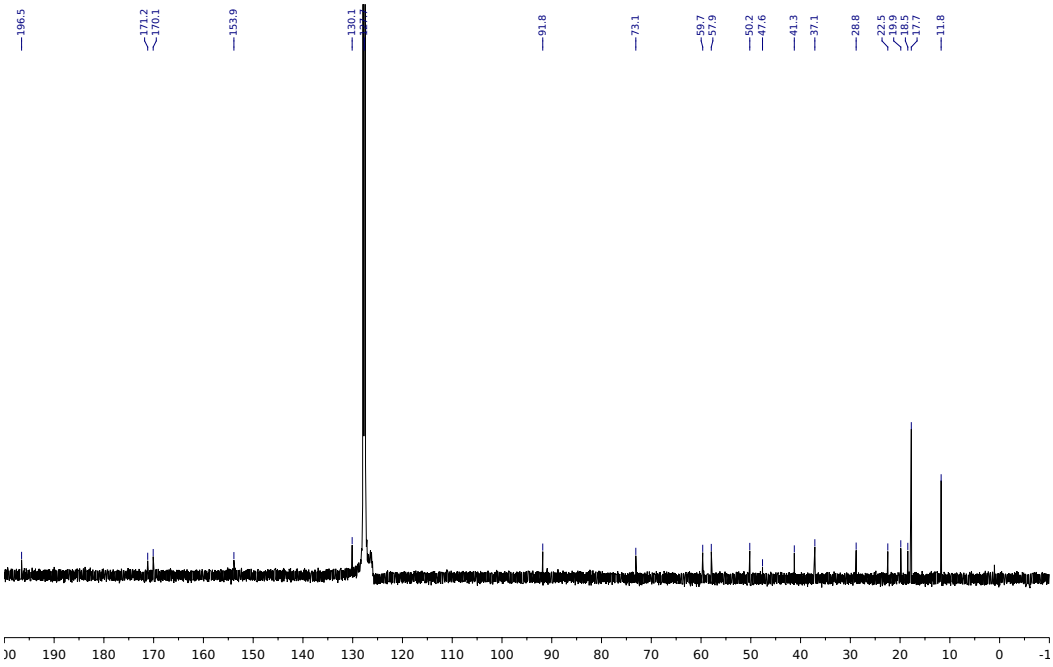


Figure SI.45 ^{13}C NMR (125 MHz, C_6D_6) of compound **27b**

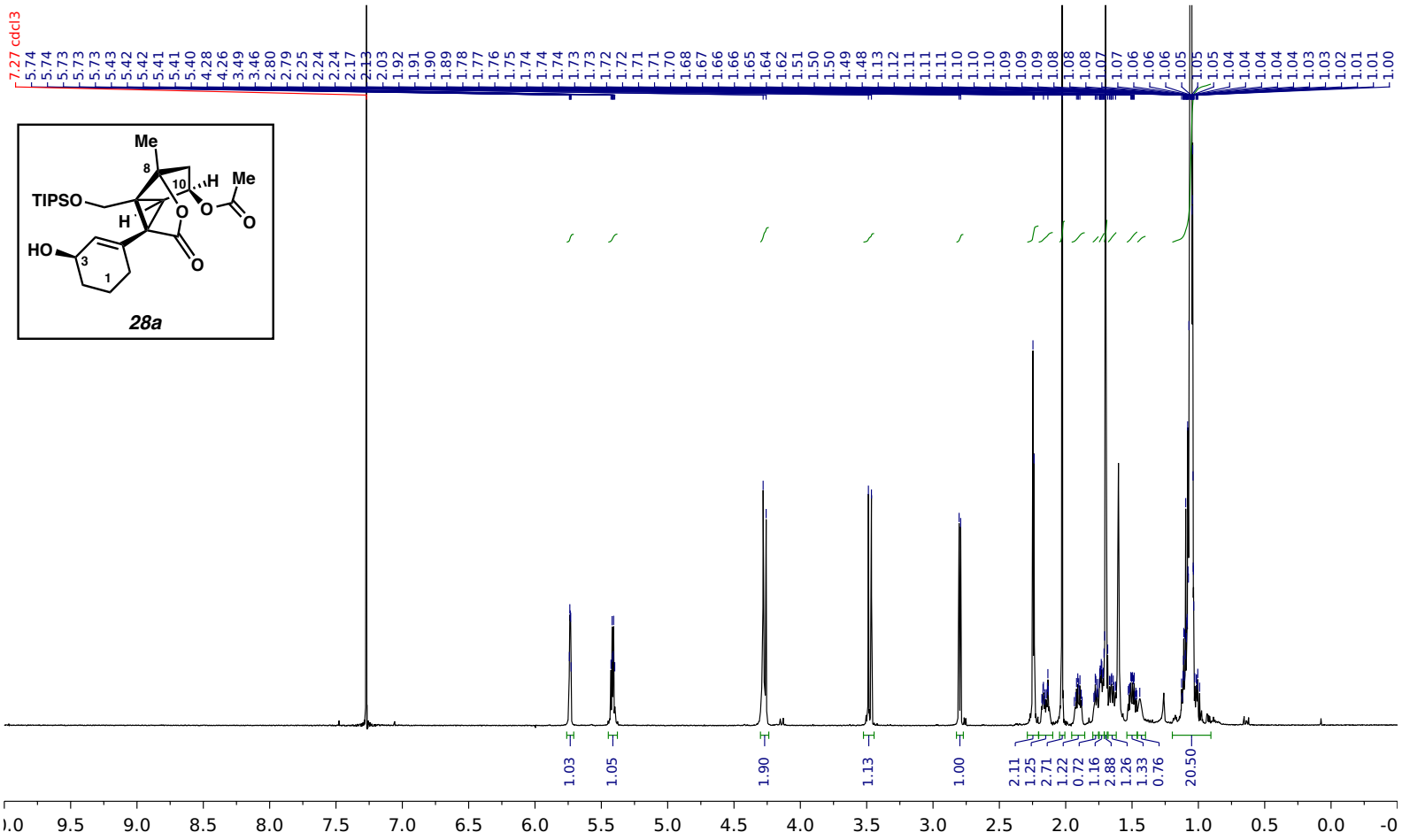


Figure SI.46 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **28a**

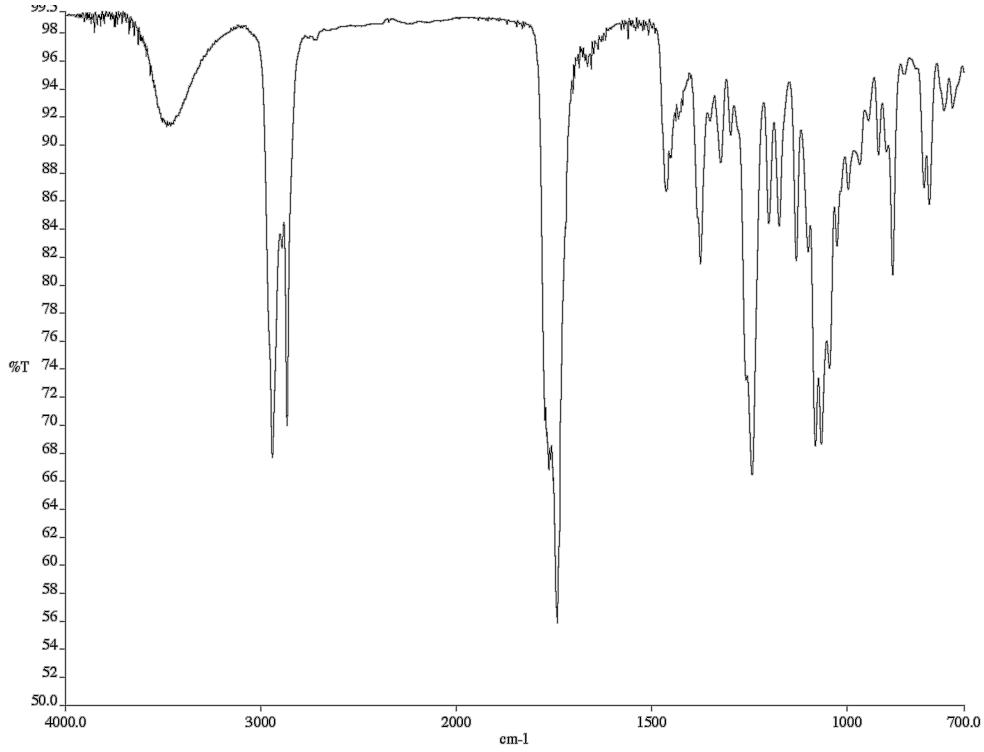


Figure SI.47 Infrared spectrum (thin film/NaCl) of compound **28a**

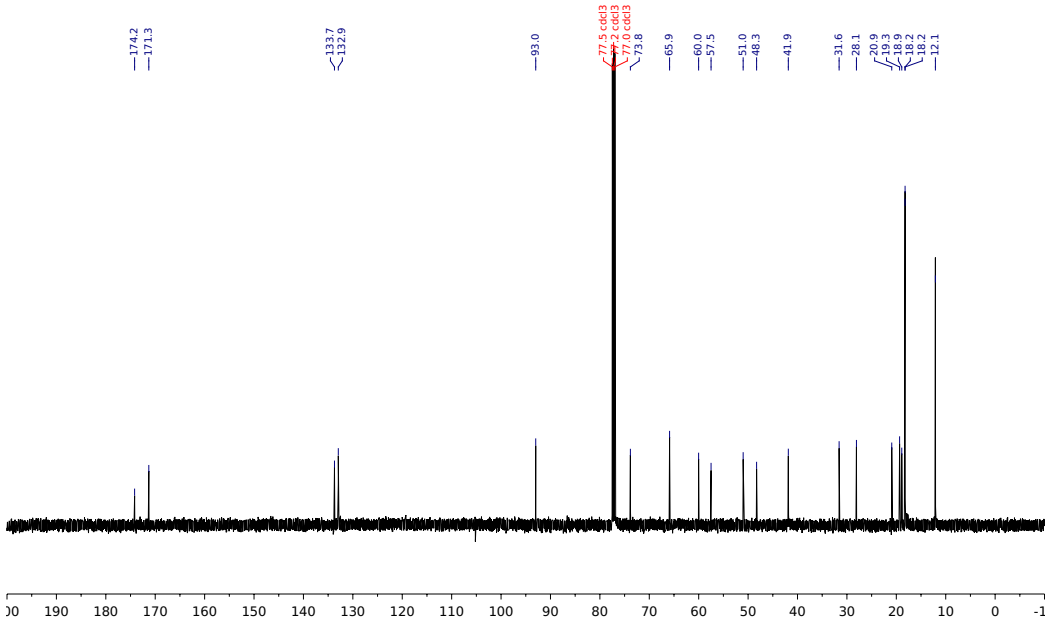


Figure SI.48 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **28a**

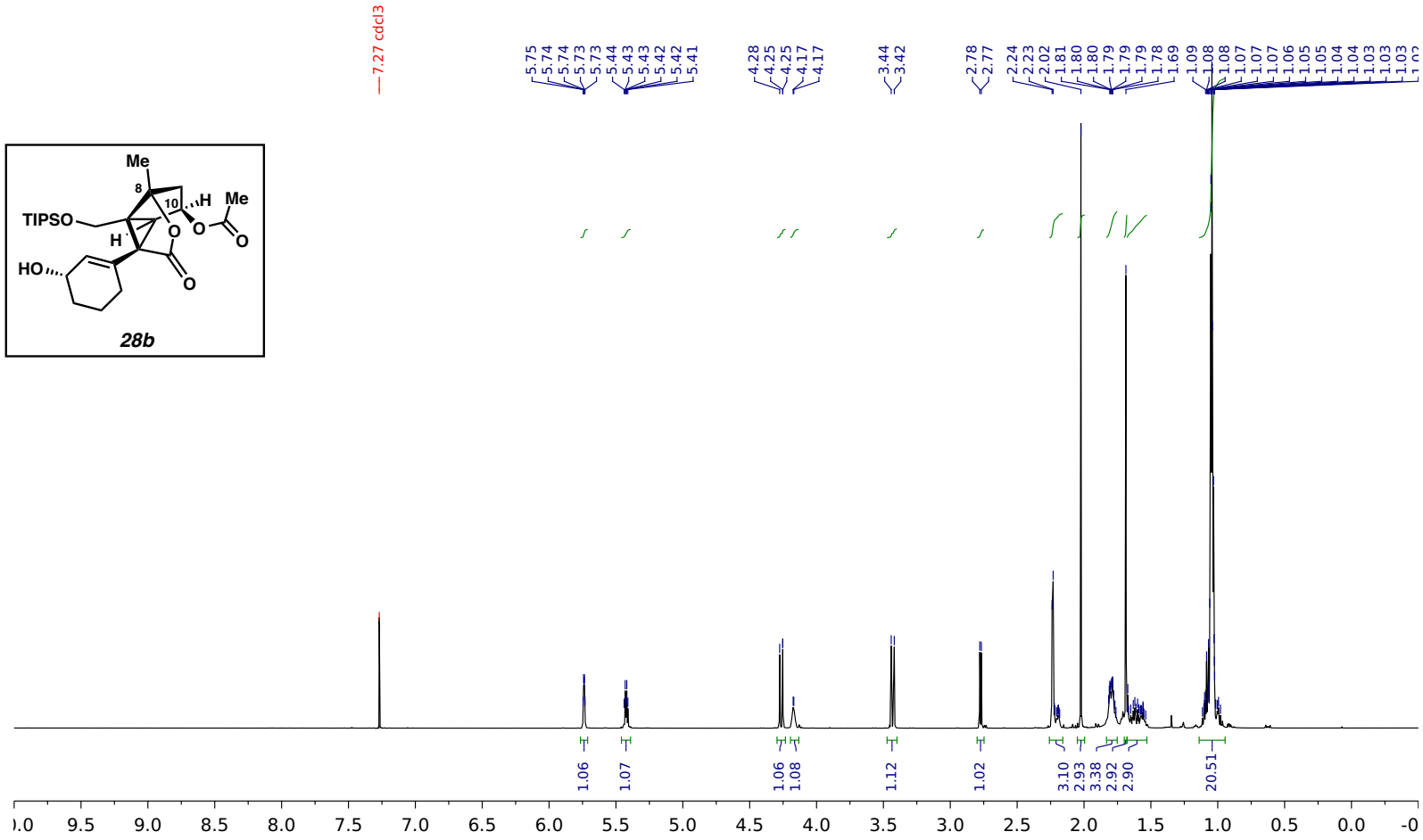


Figure SI.49 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **28b**

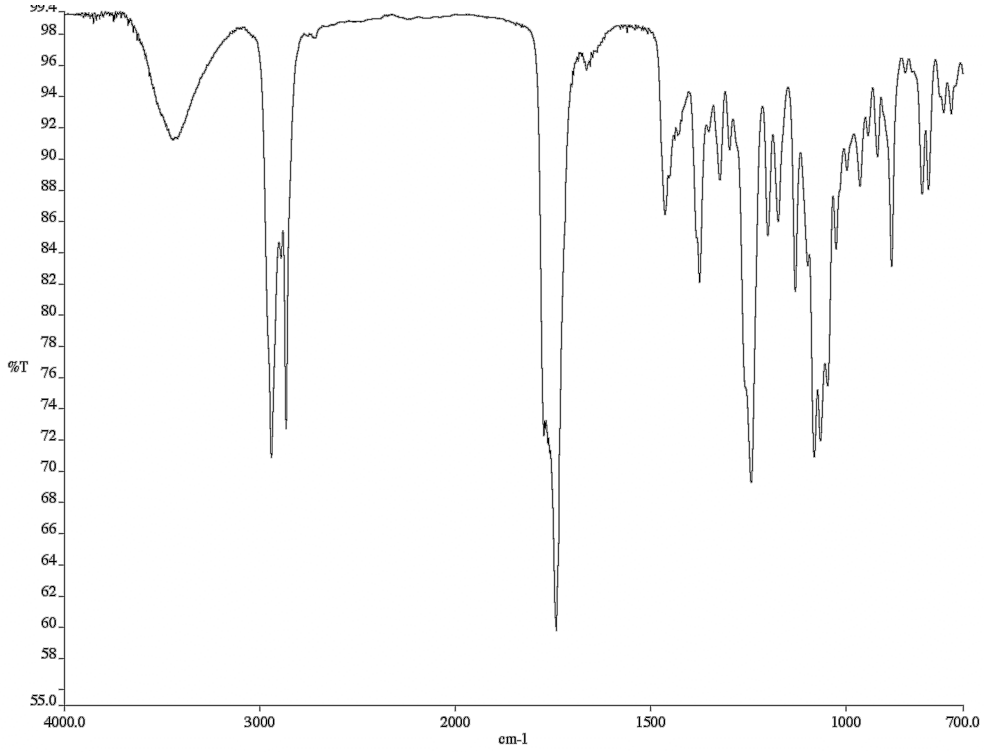


Figure SI.50 Infrared spectrum (thin film/NaCl) of compound **28b**

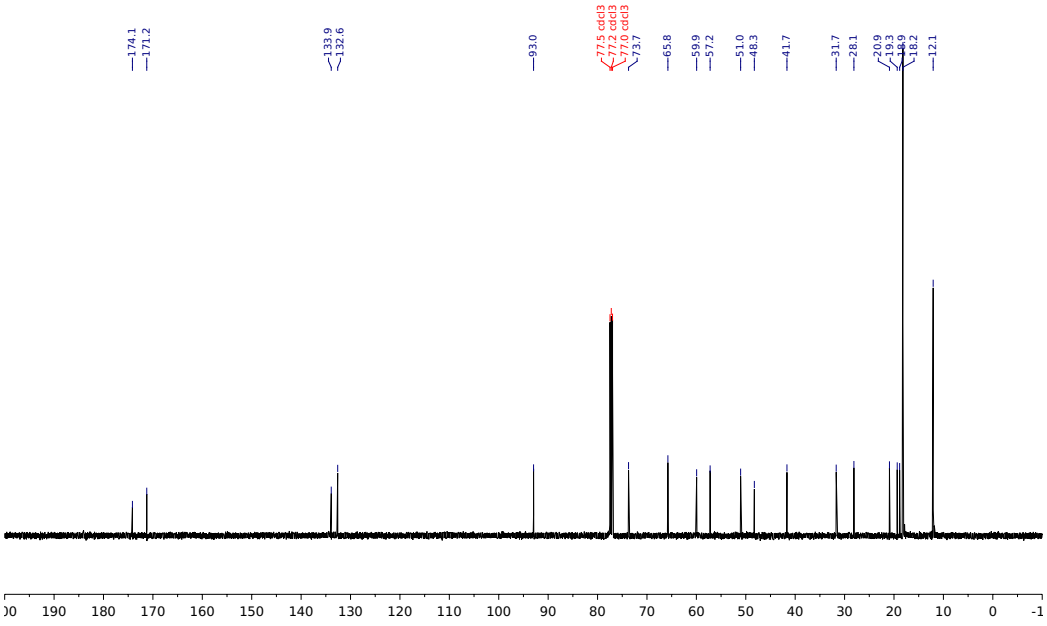


Figure SI.51 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **28b**

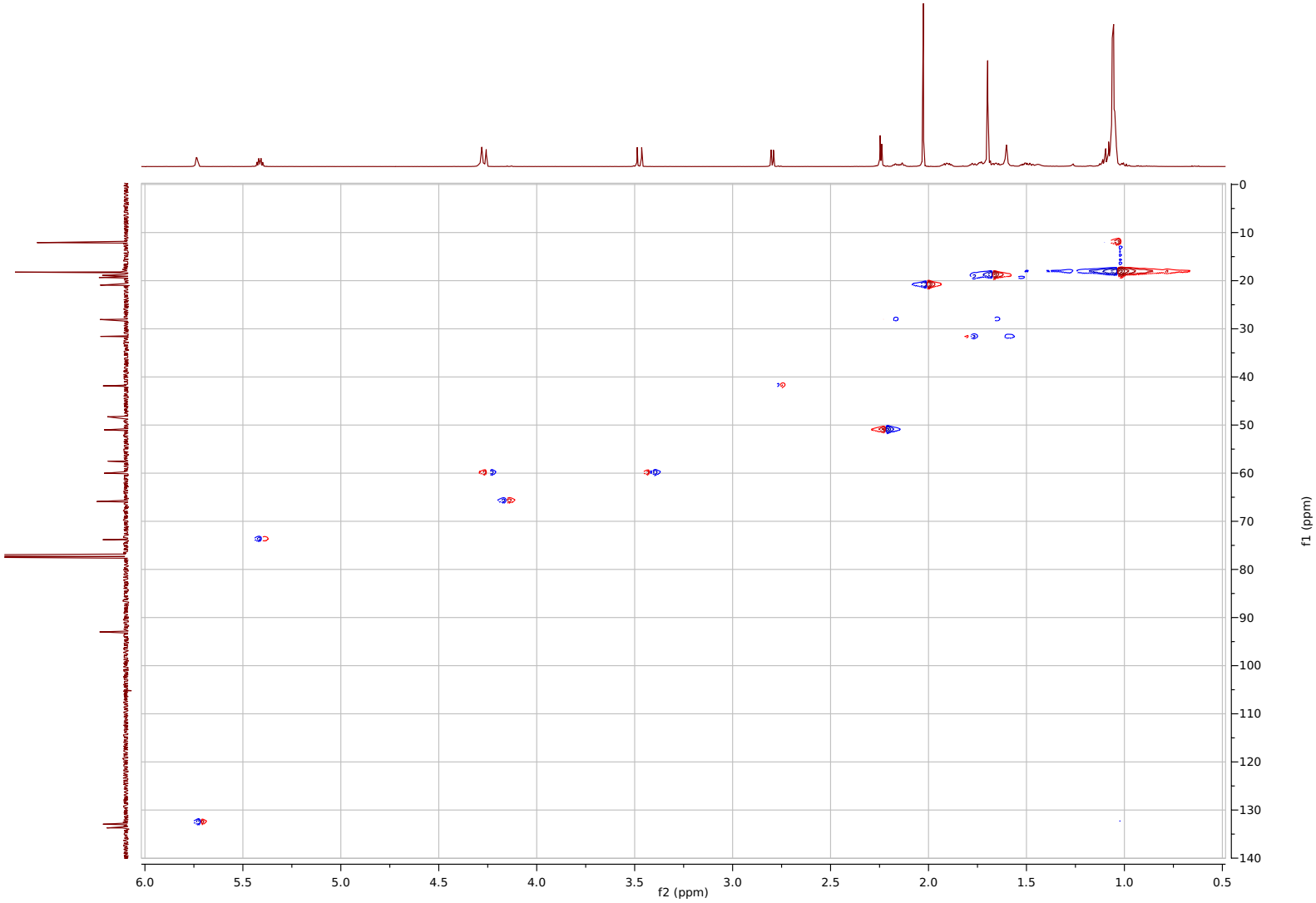


Figure SI.52 gHSQCAD (500 MHz, $CDCl_3$) of compound **28b**

Figure SI.53 gHMBC (500 MHz, $CDCl_3$) of compound **28b**

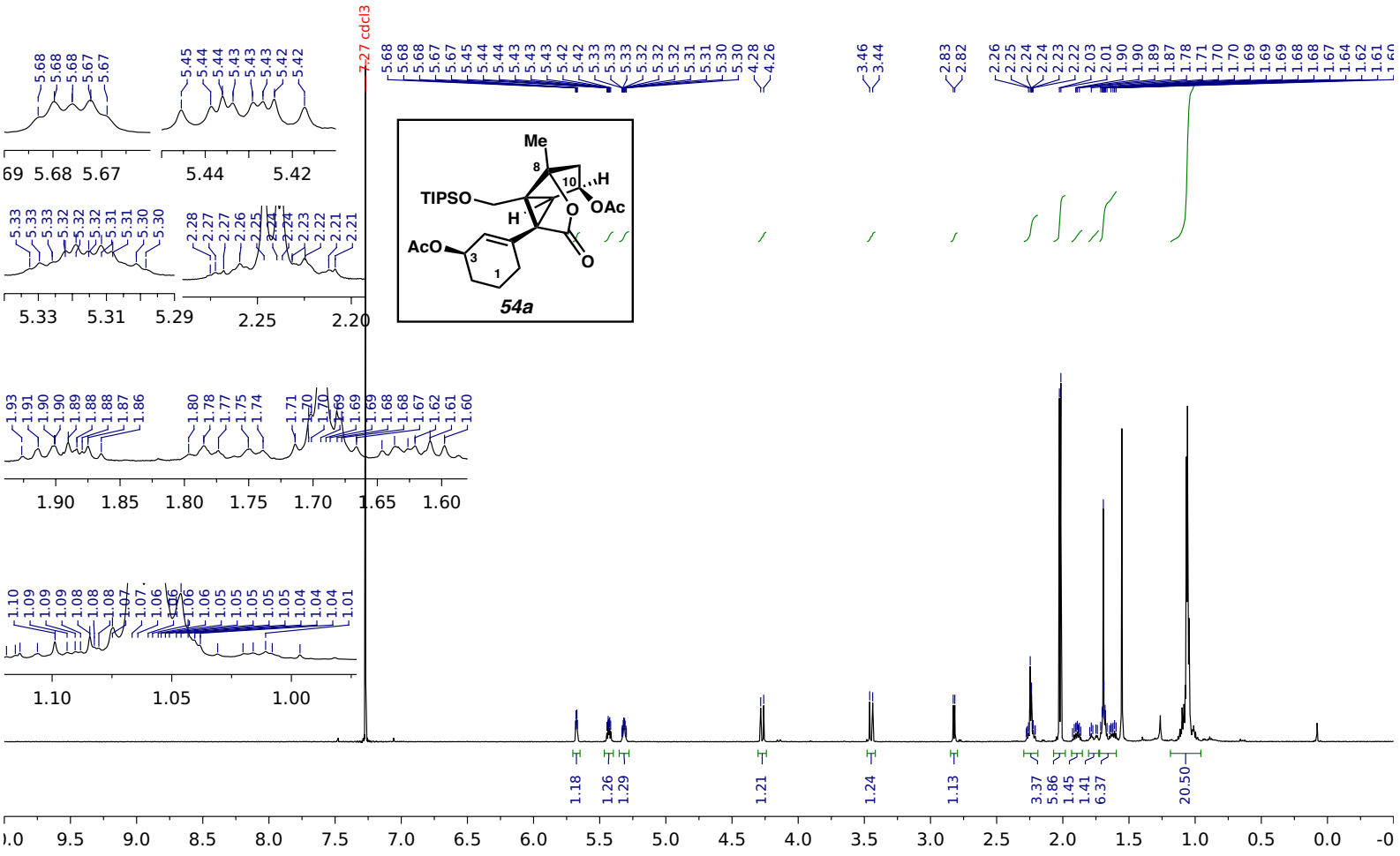


Figure SI.54 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **54a**

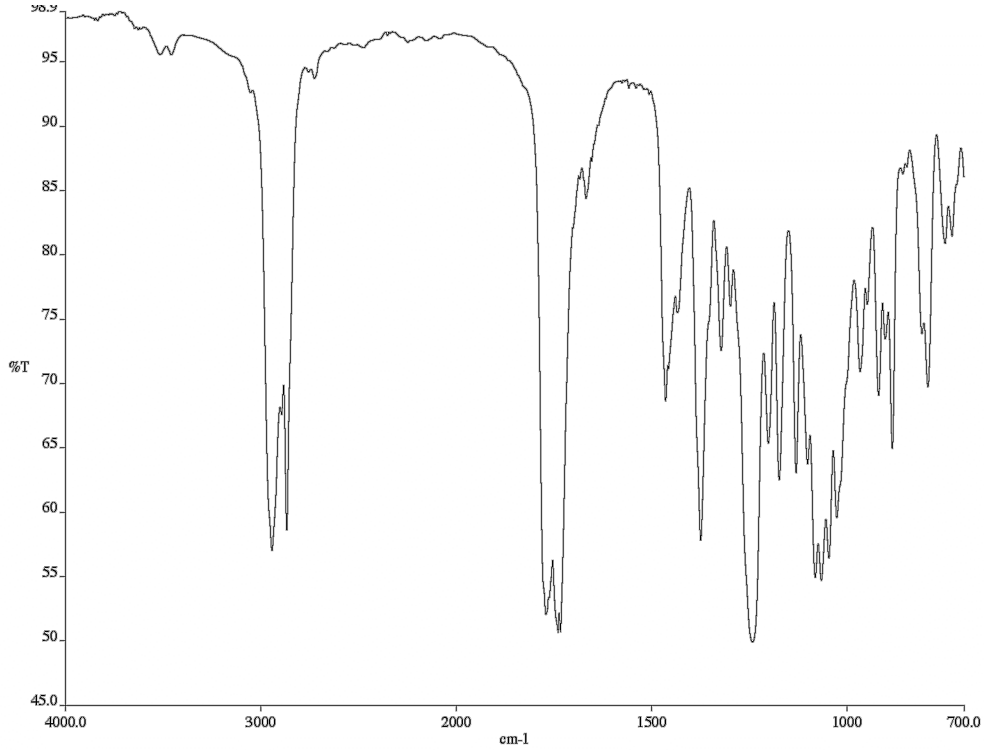


Figure SI.55 Infrared spectrum (thin film/NaCl) of compound **54a**

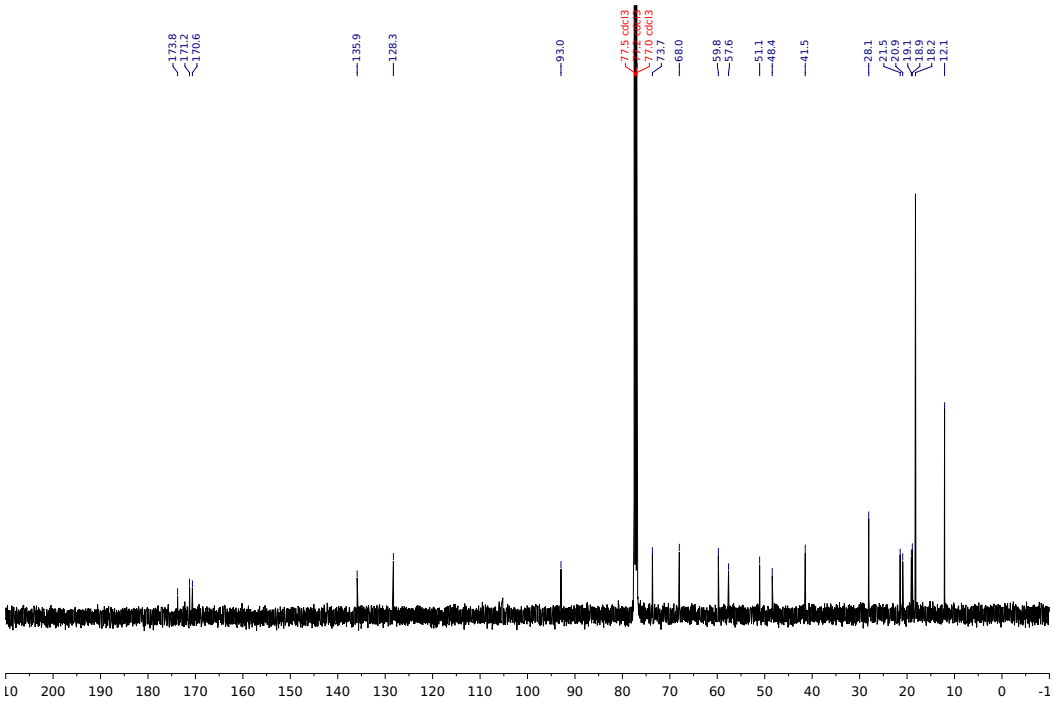


Figure SI.56 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **54a**

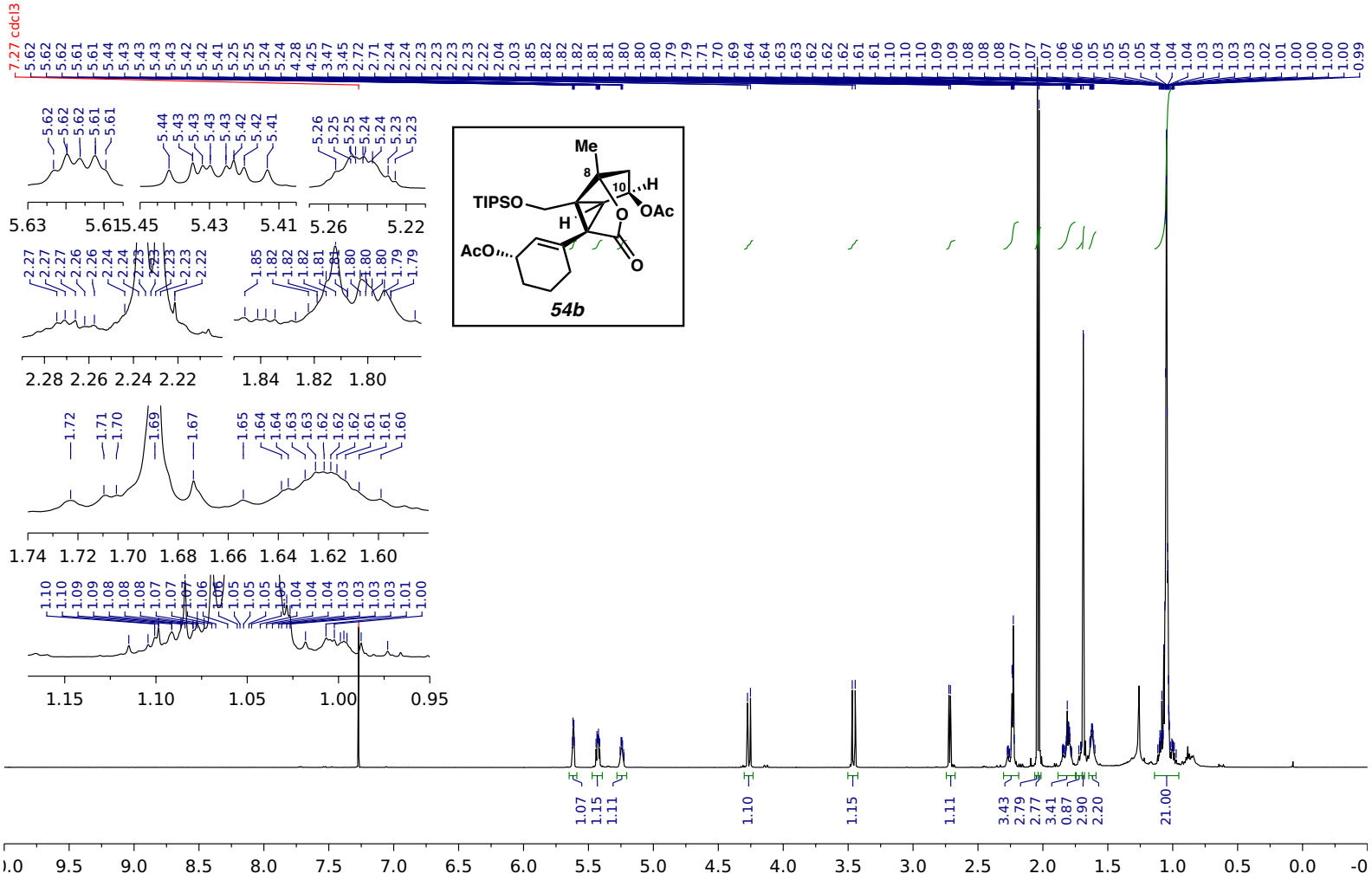


Figure SI.57 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **54b**

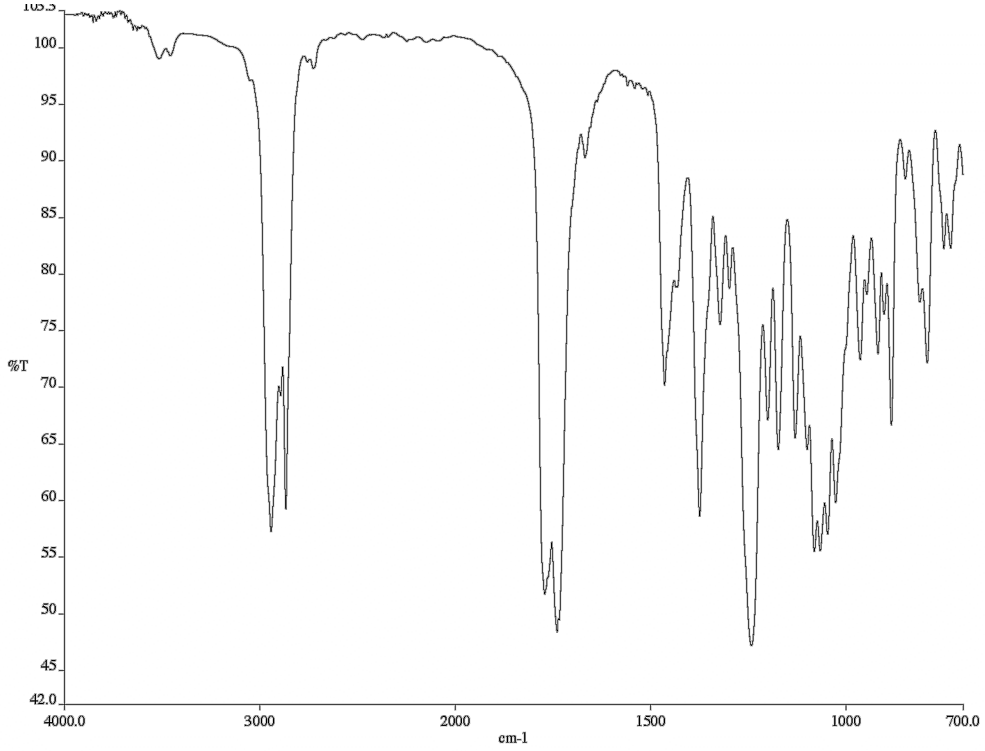


Figure SI.58 Infrared spectrum (thin film/NaCl) of compound **54b**

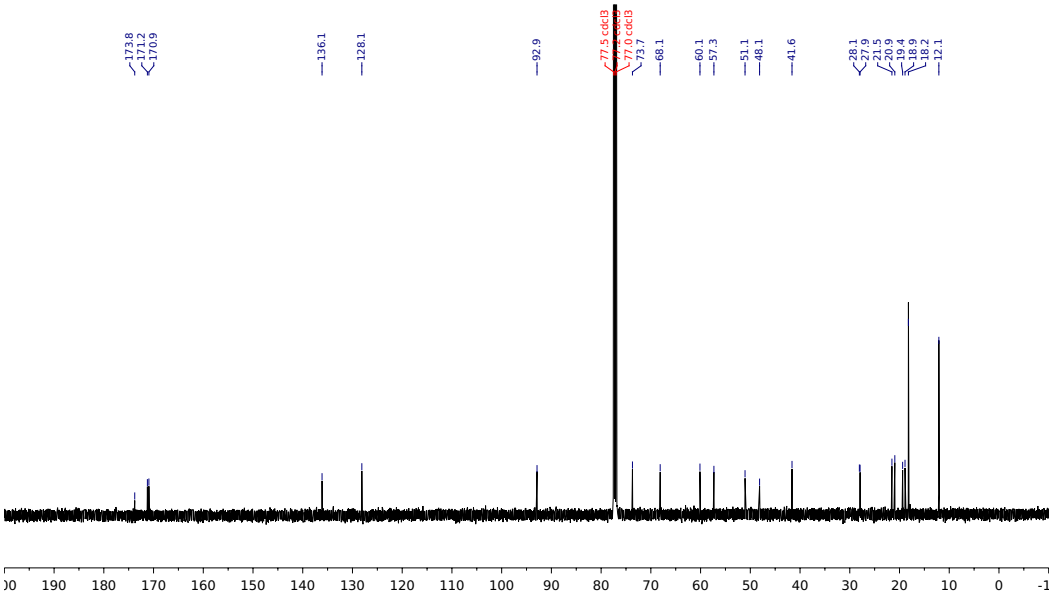


Figure SI.59 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **54b**

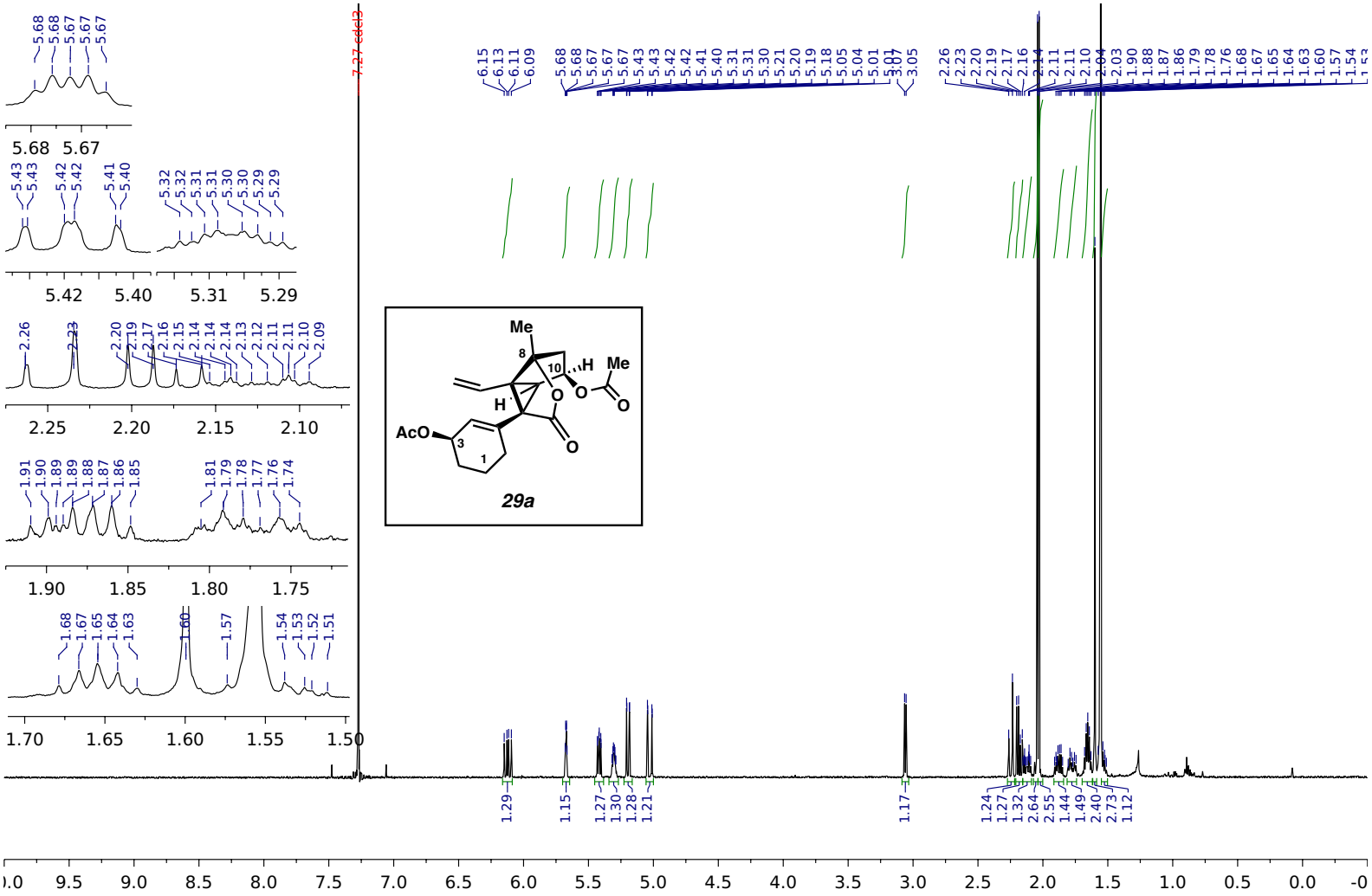


Figure SI.60 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **29a**

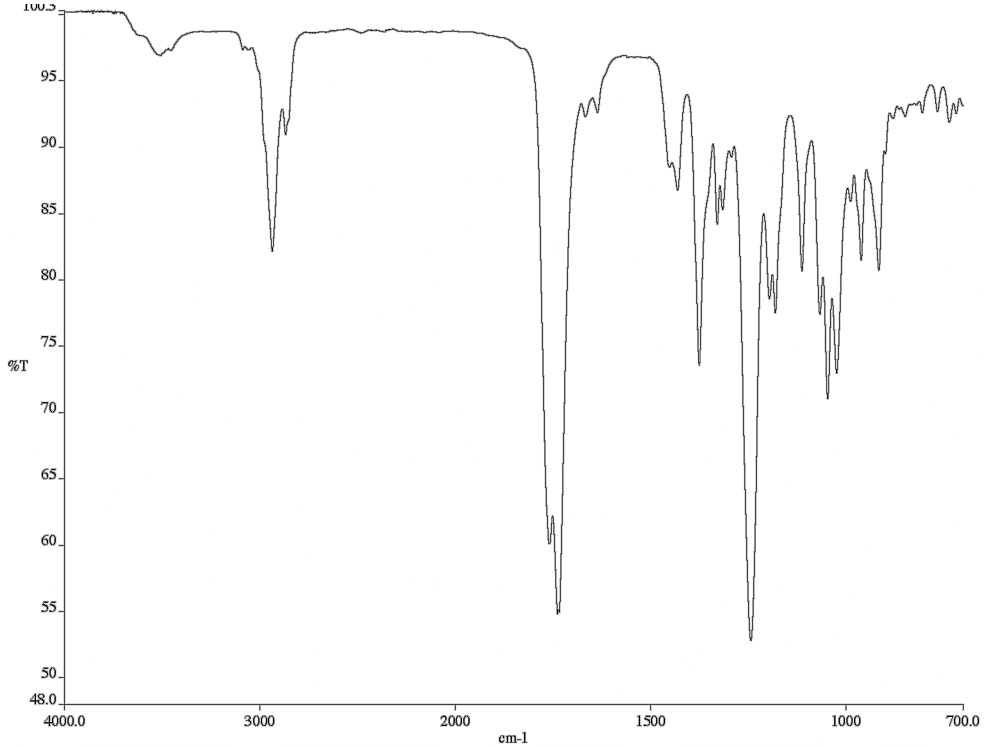


Figure SI.61 Infrared spectrum (thin film/NaCl) of compound **29a**

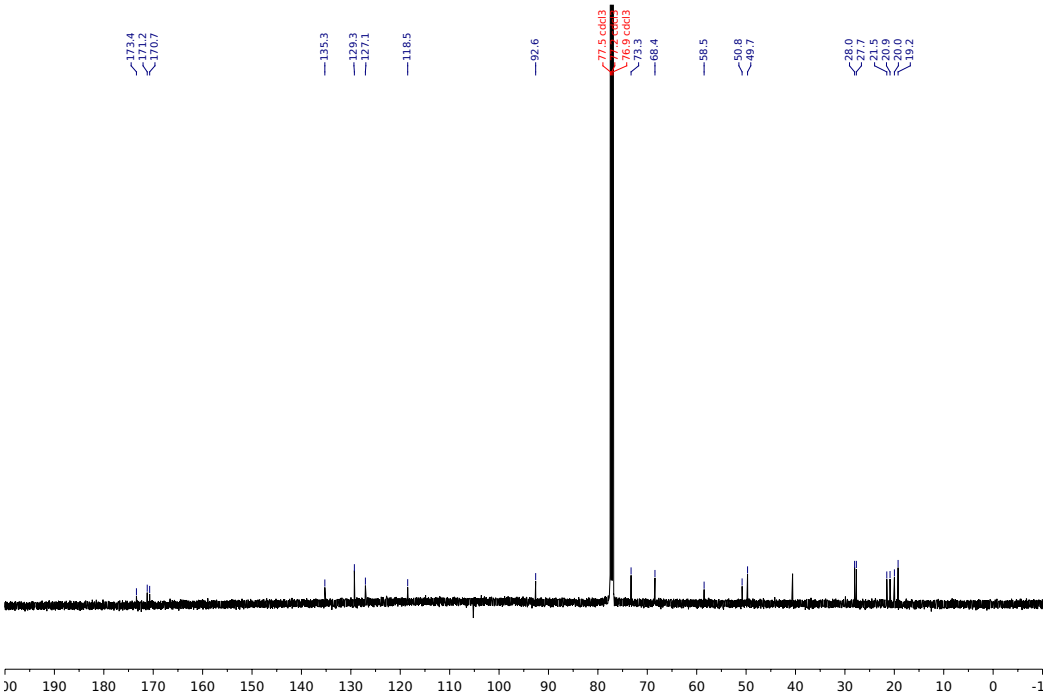


Figure SI.62 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **29a**

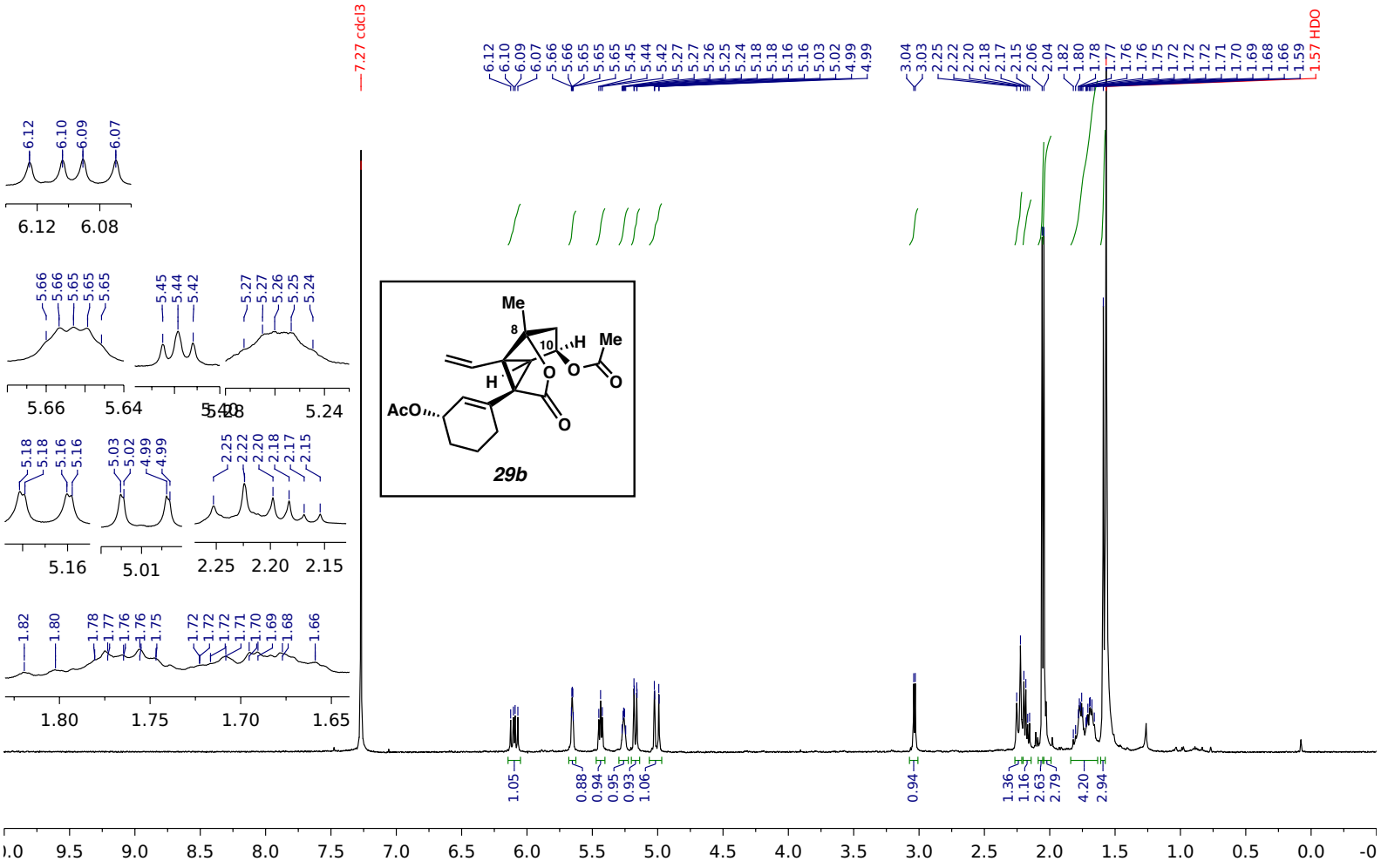


Figure SI.63 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **29b**

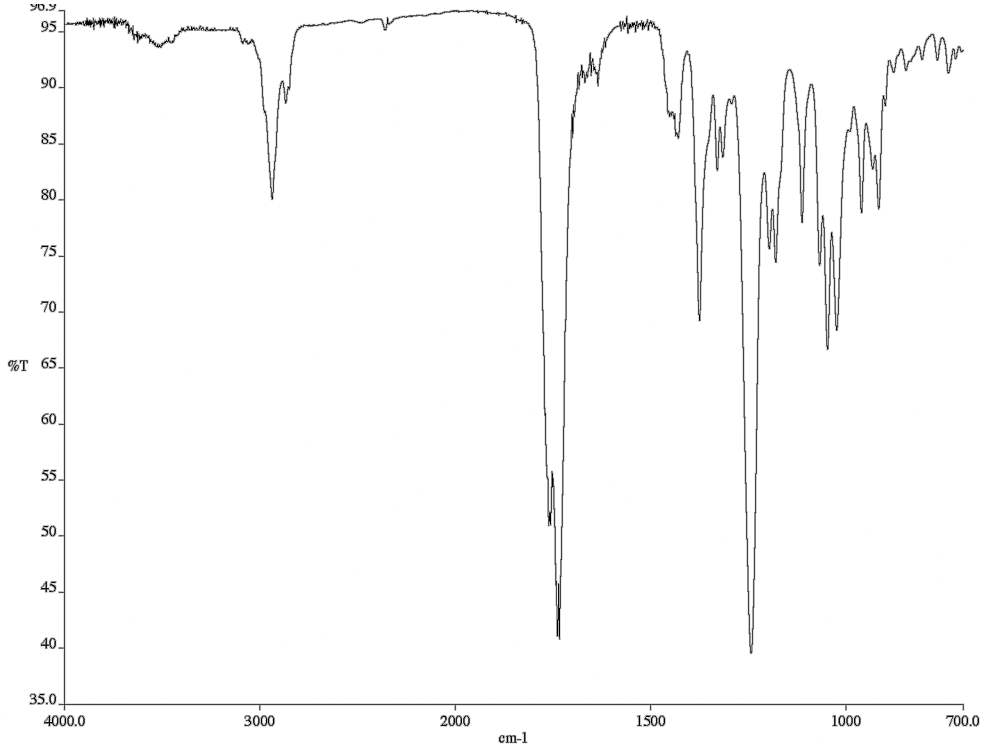


Figure SI.64 Infrared spectrum (thin film/NaCl) of compound **29b**

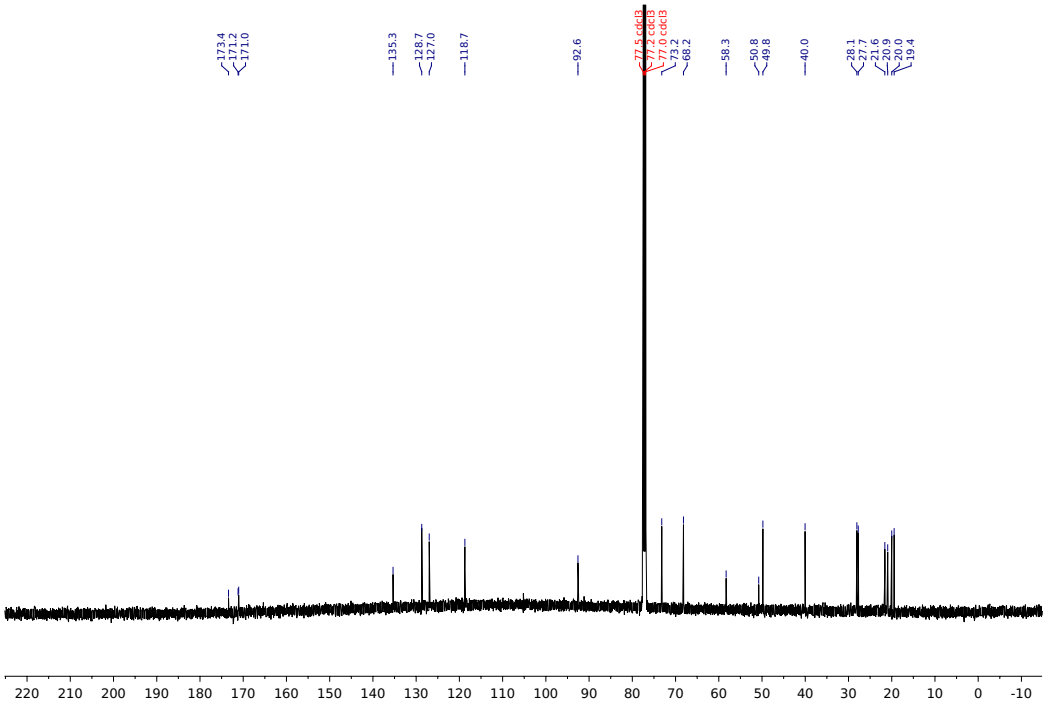


Figure SI.65 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **29b**

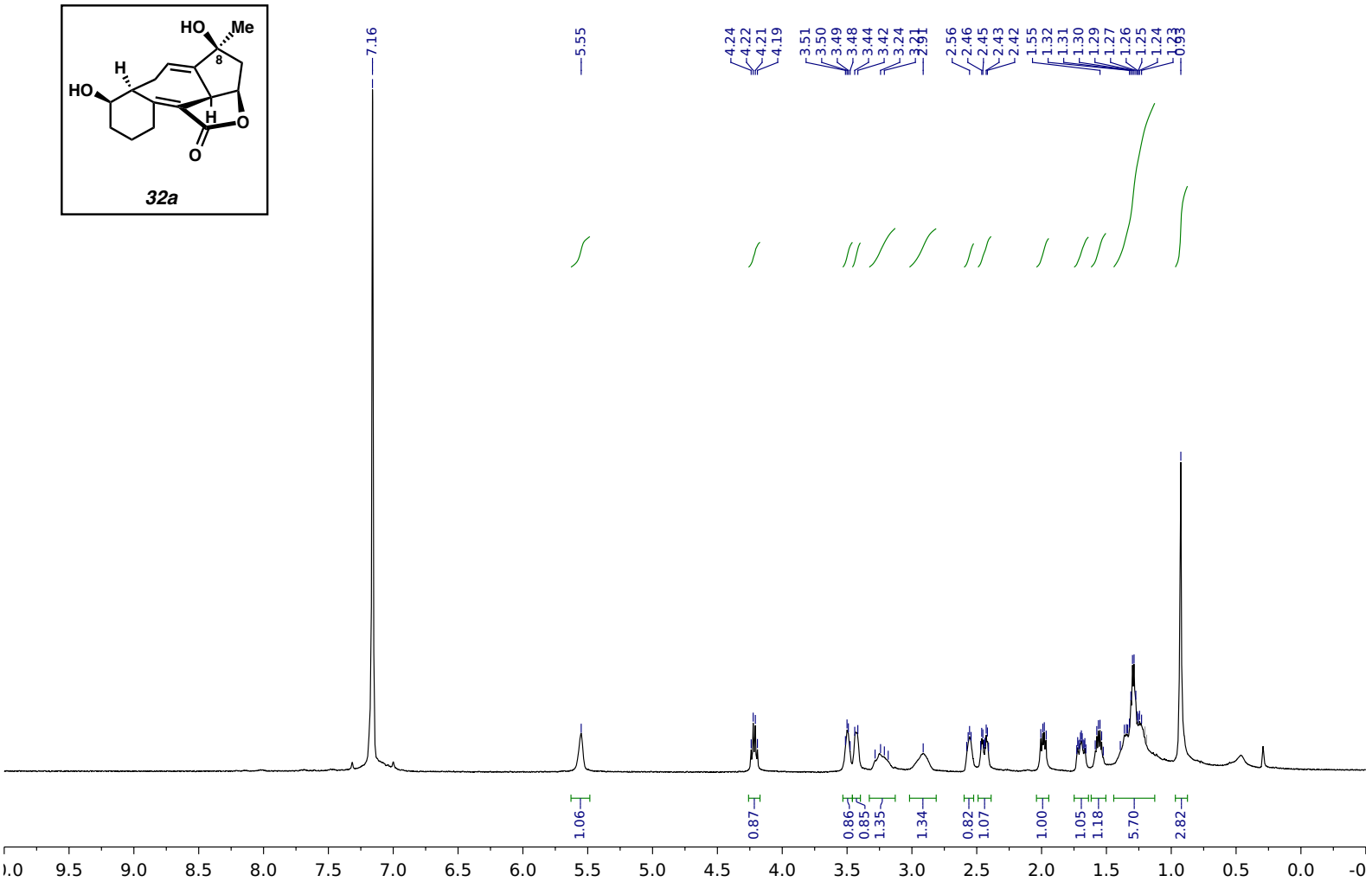


Figure SI.66 ^{1}H NMR (500 MHz, C_6D_6) of compound **32a**

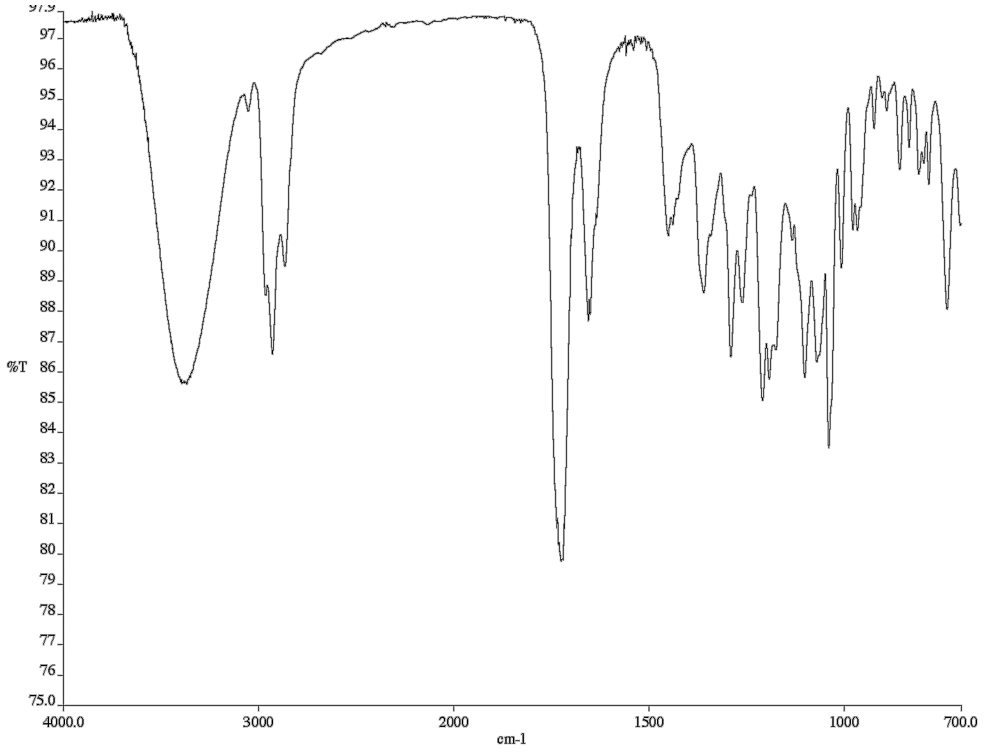


Figure SI.67 Infrared spectrum (thin film/NaCl) of compound **32a**

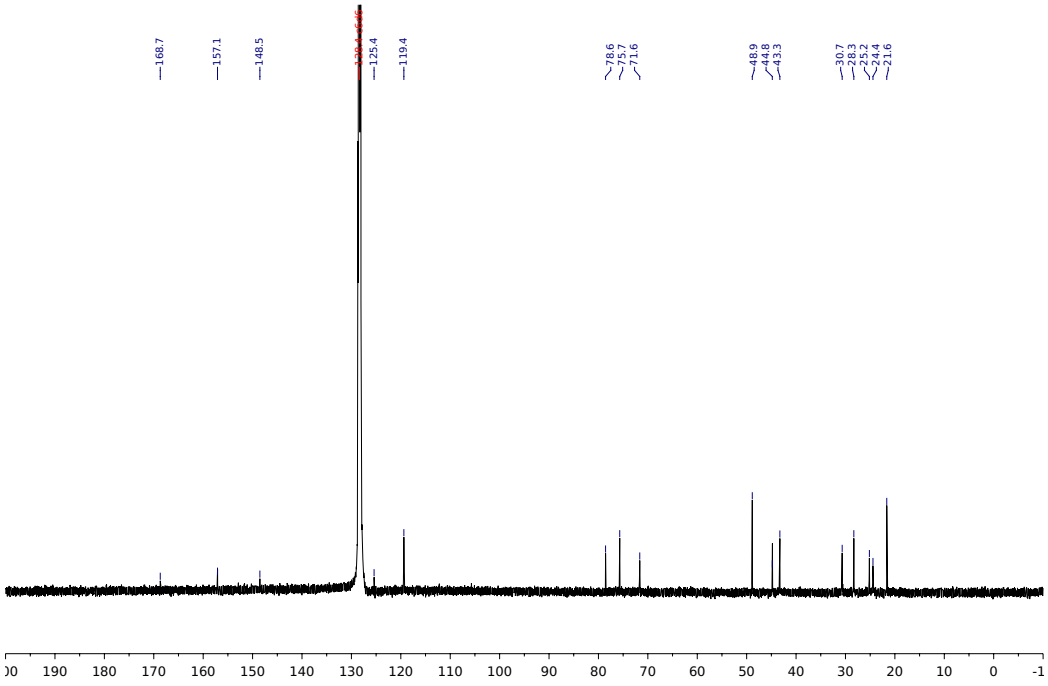


Figure SI.68 ^{13}C NMR (125 MHz, C_6D_6) of compound **32a**

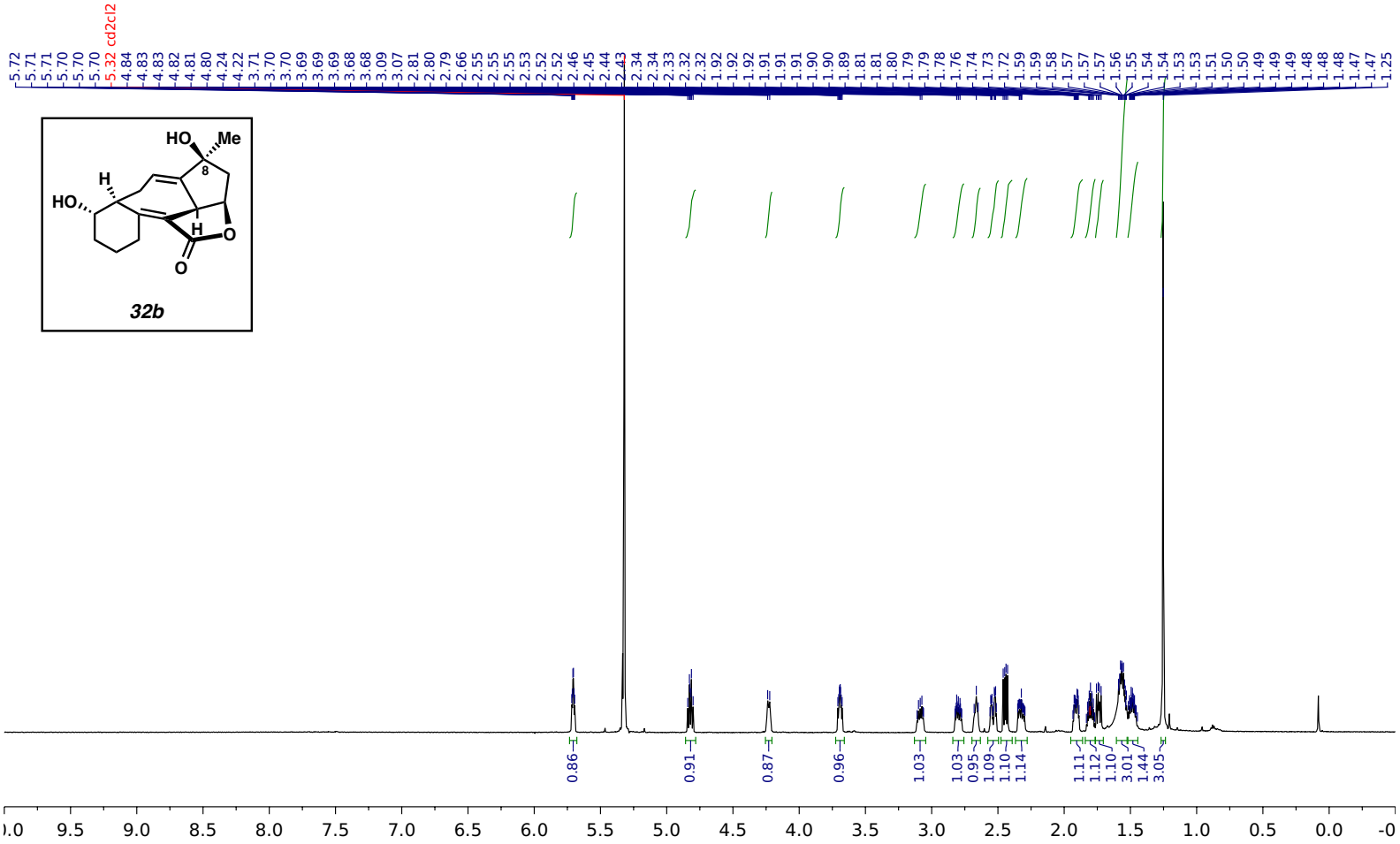


Figure SI.69 ^{1}H NMR (500 MHz, CD_2Cl_2) of compound **32b**

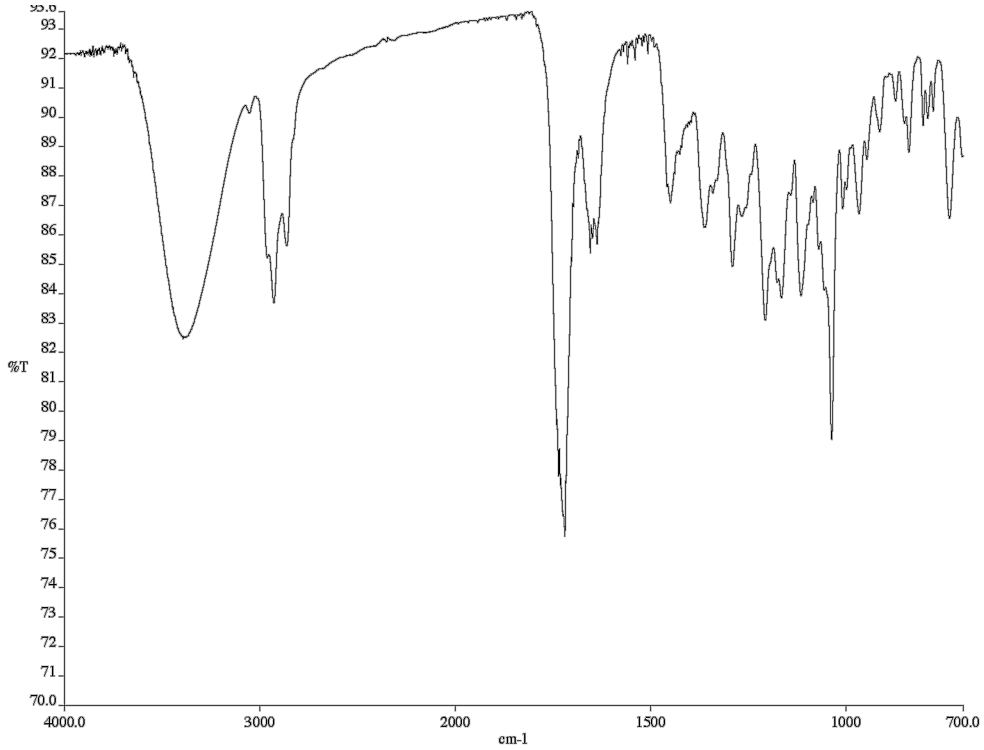


Figure SI.70 Infrared spectrum (thin film/NaCl) of compound **32b**

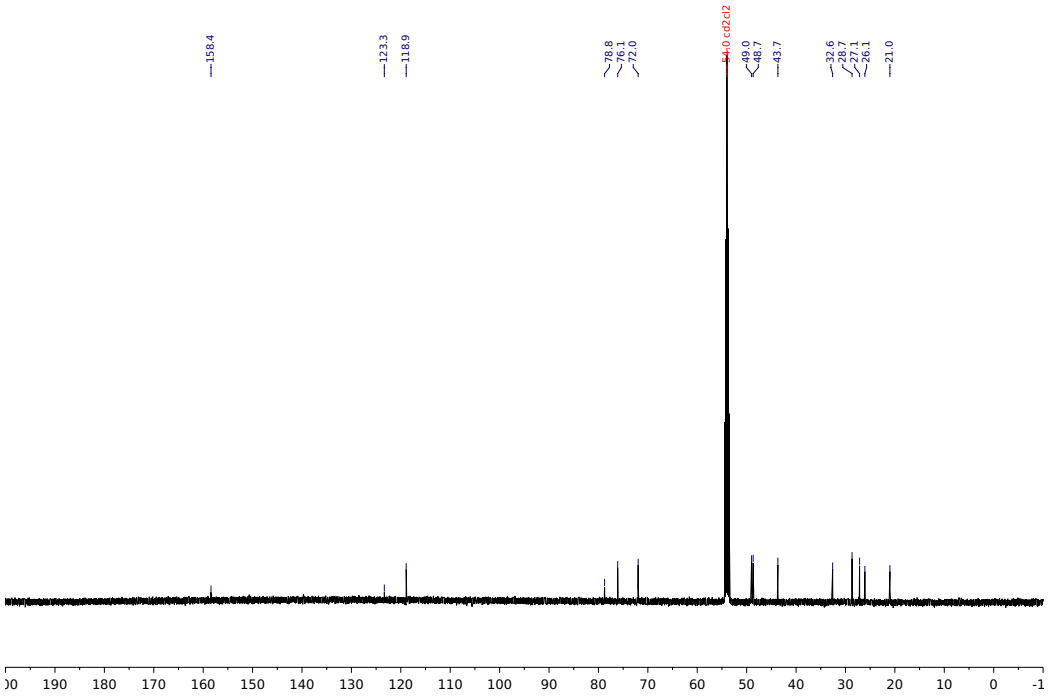


Figure SI.71 ^{13}C NMR (125 MHz, CD_2Cl_2) of compound **32b**

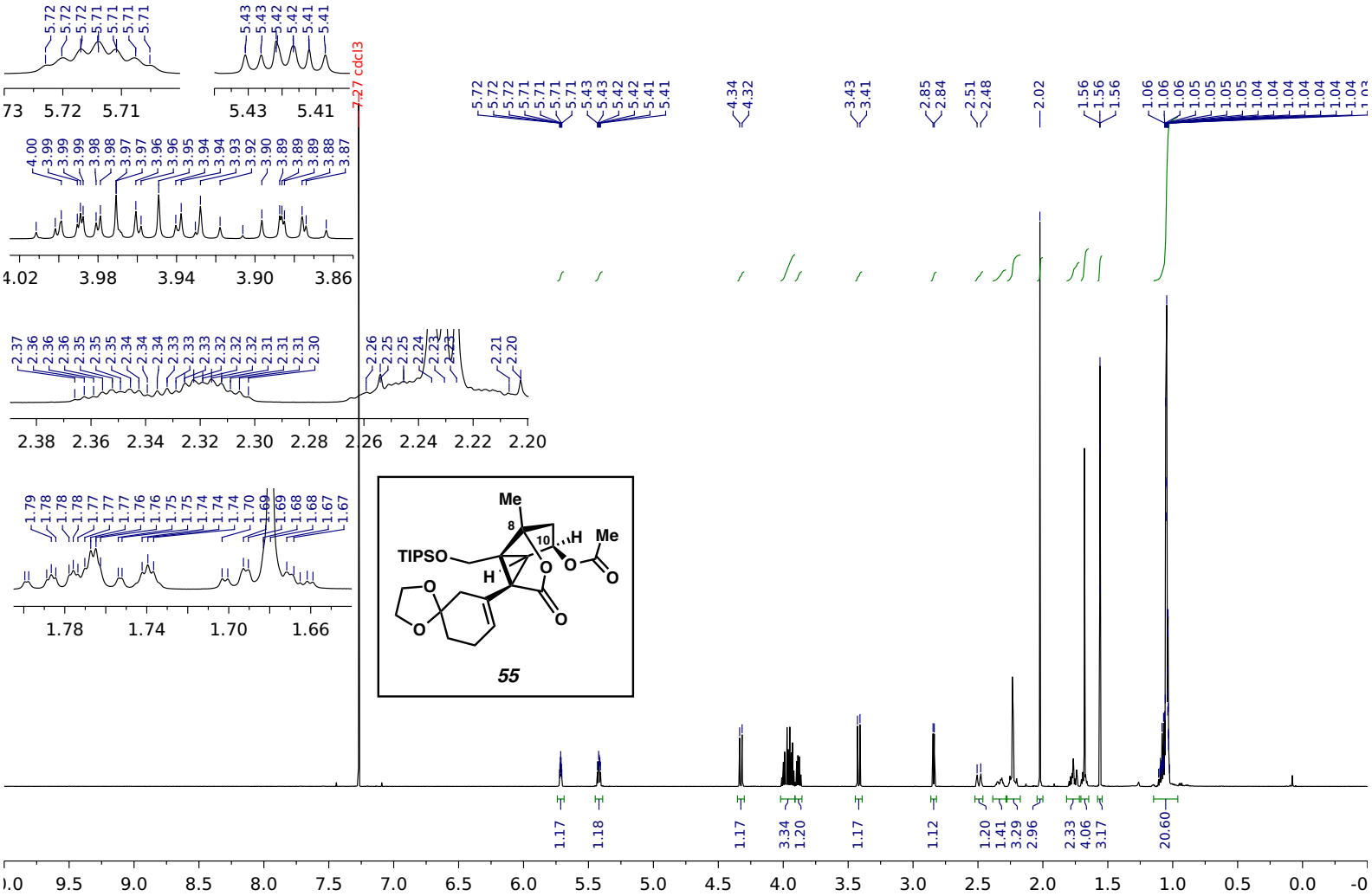


Figure SI.72 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **55**

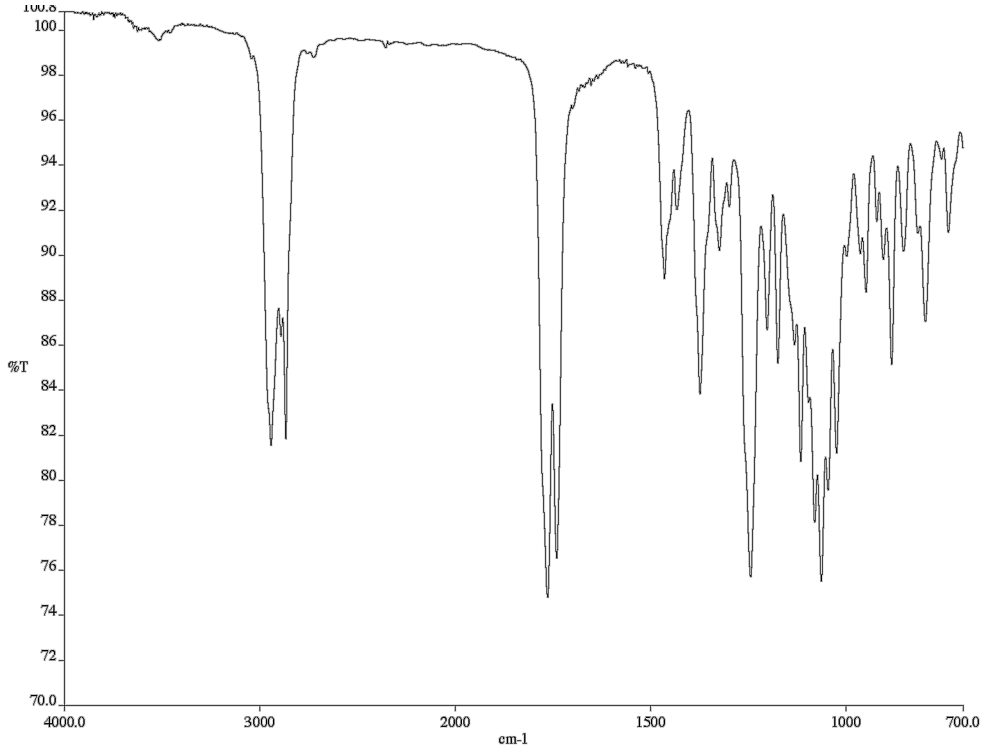


Figure SI.73 Infrared spectrum (thin film/NaCl) of compound **55**

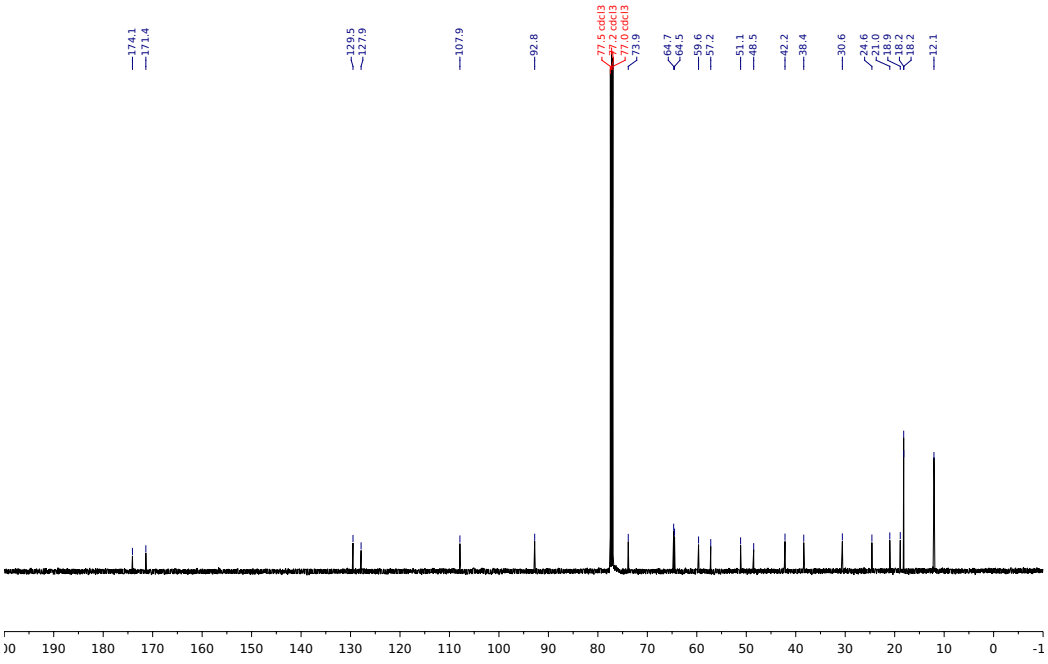


Figure SI.74 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **55**

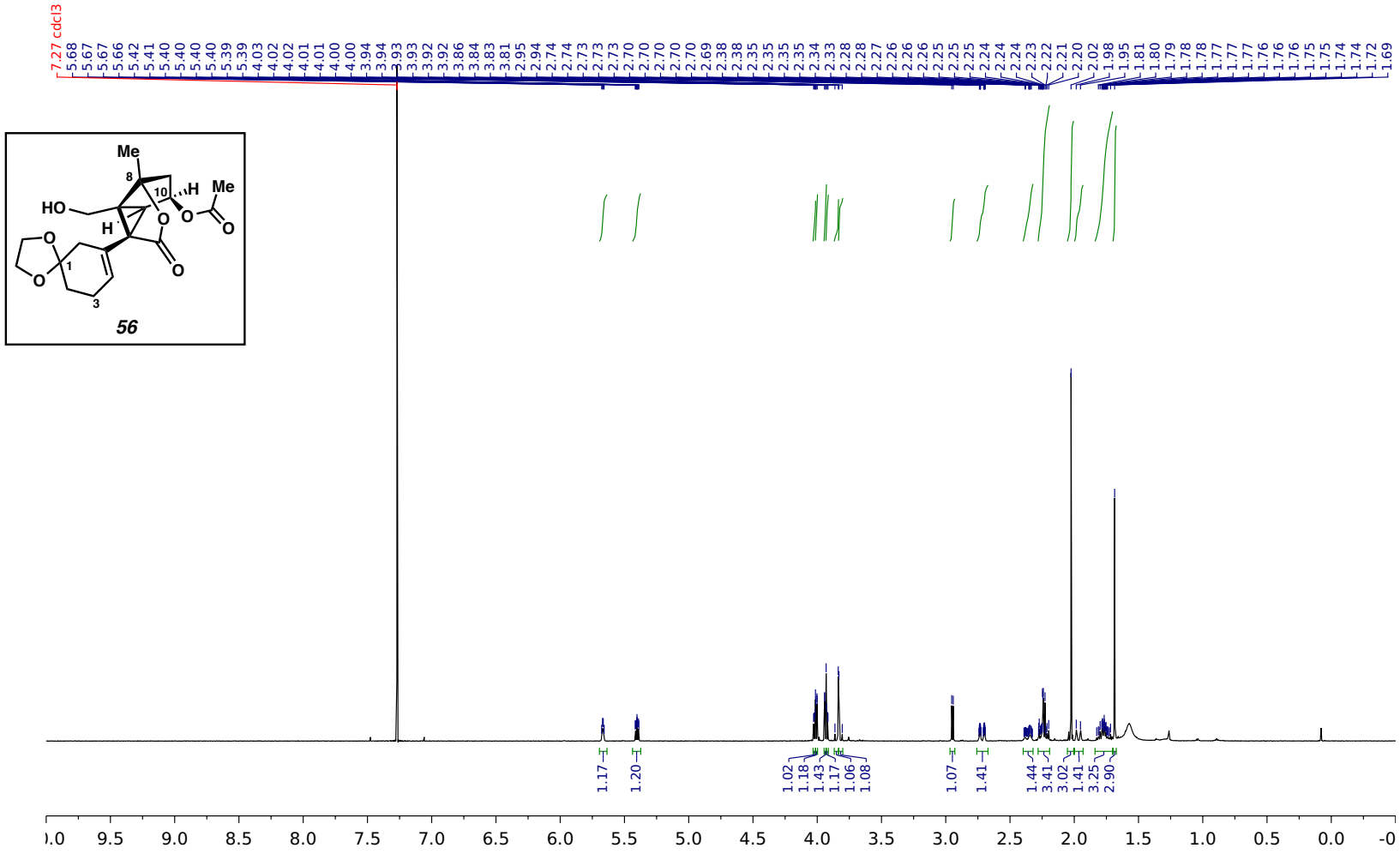


Figure SI.75 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **56**

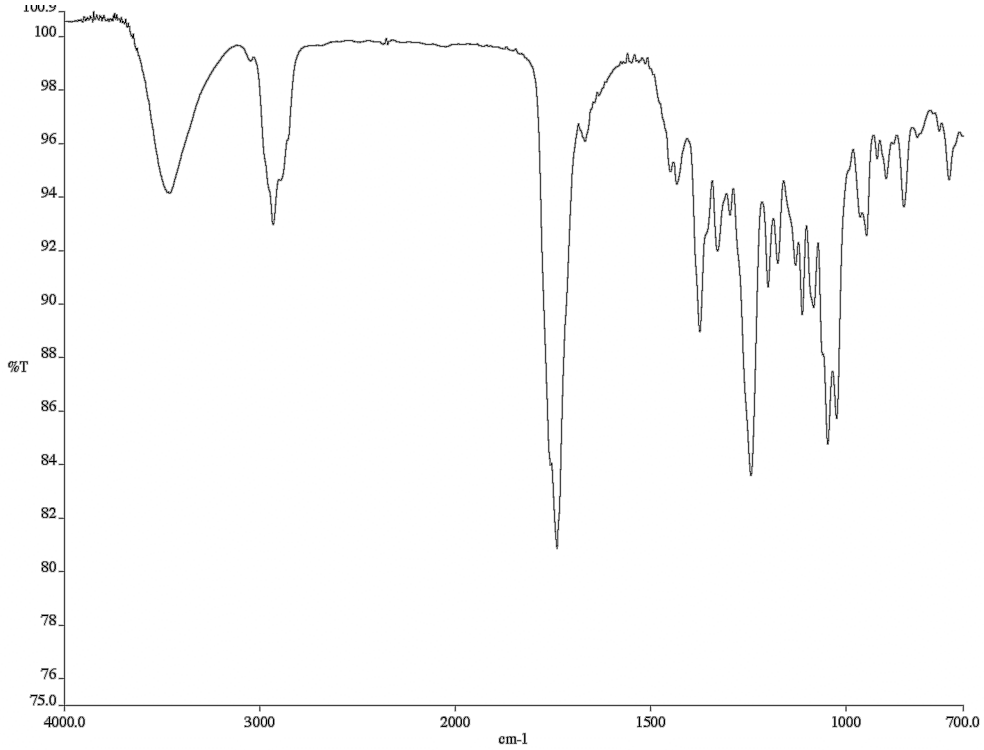


Figure SI.76 Infrared spectrum (thin film/NaCl) of compound **56**

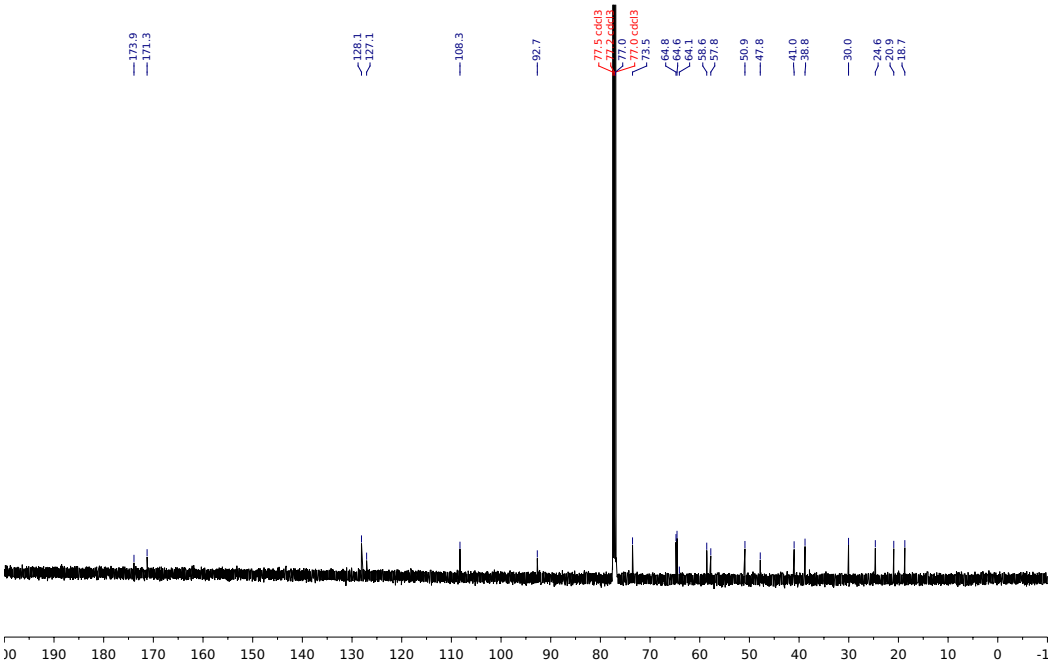


Figure SI.77 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **56**

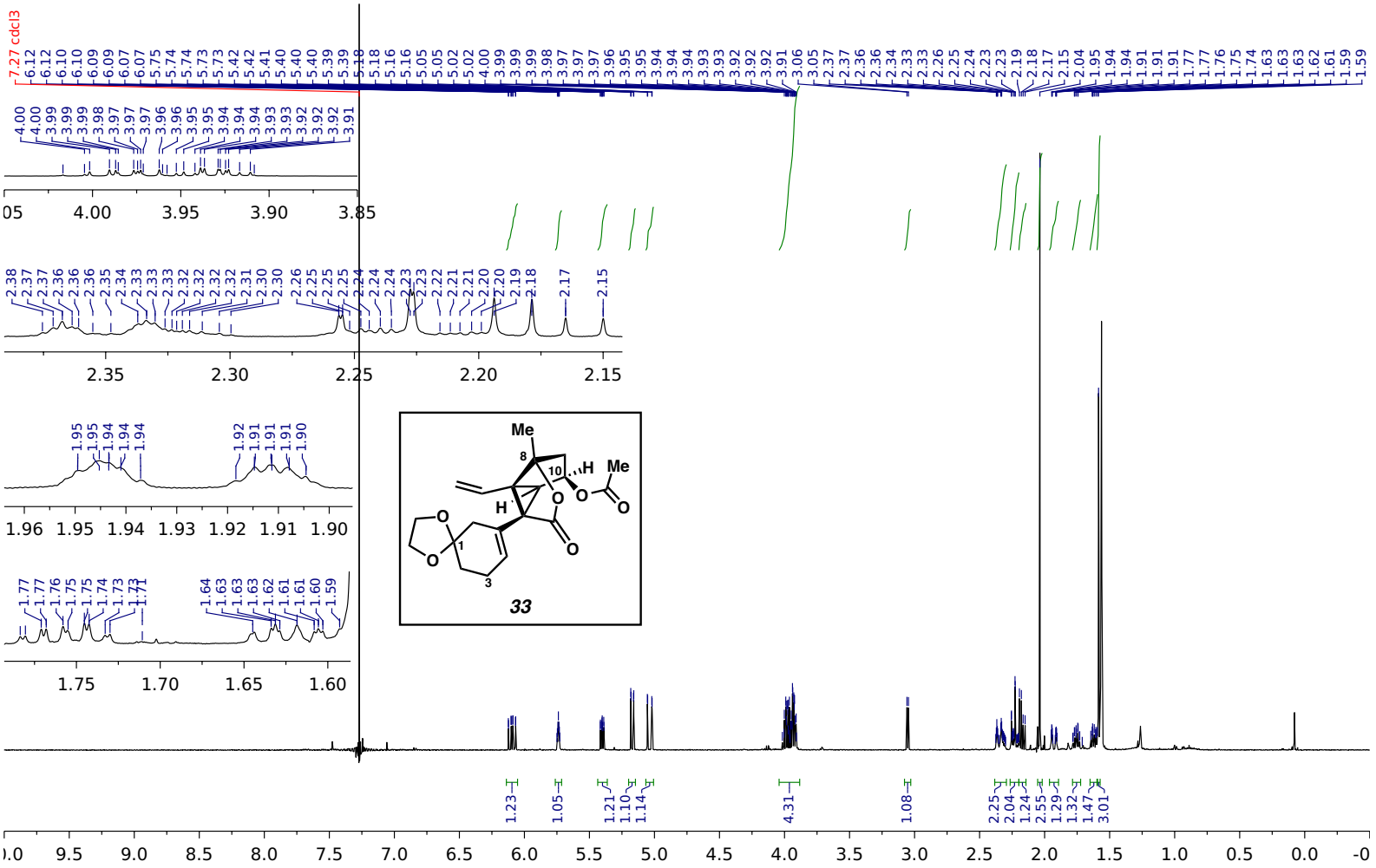


Figure SI.78 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **33**

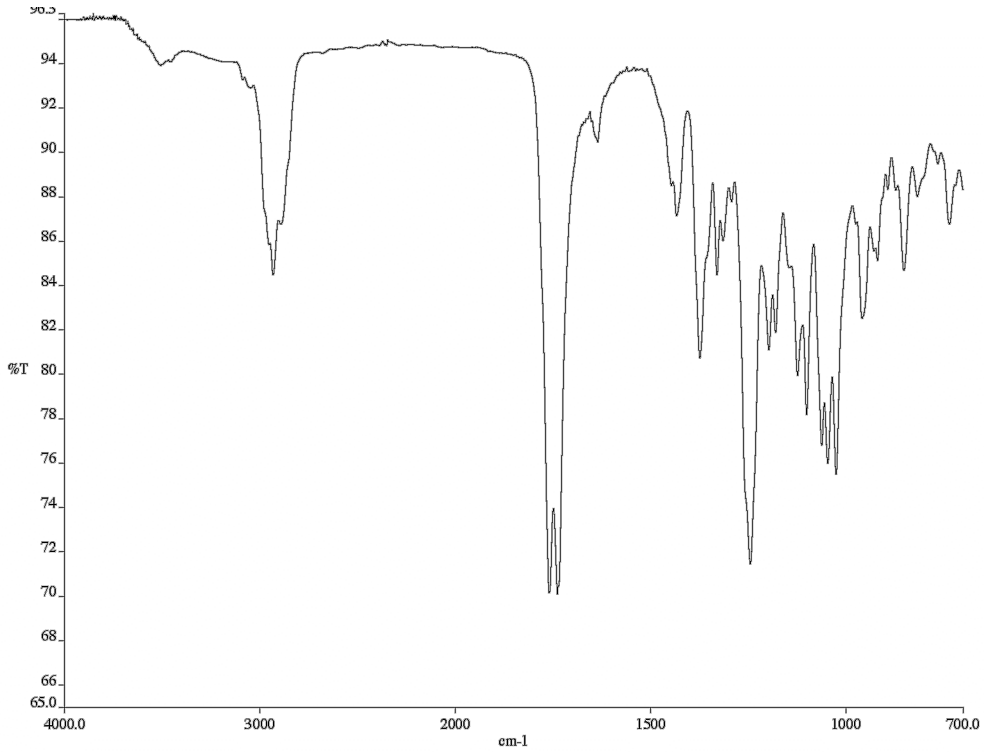


Figure SI.79 Infrared spectrum (thin film/NaCl) of compound **33**

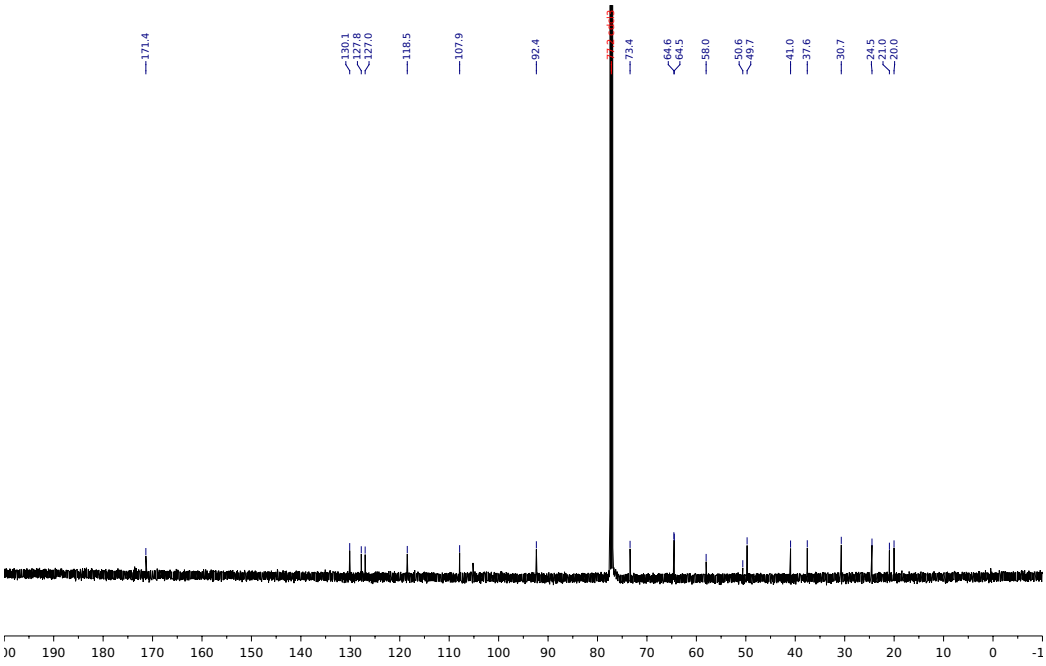


Figure SI.80 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **33**

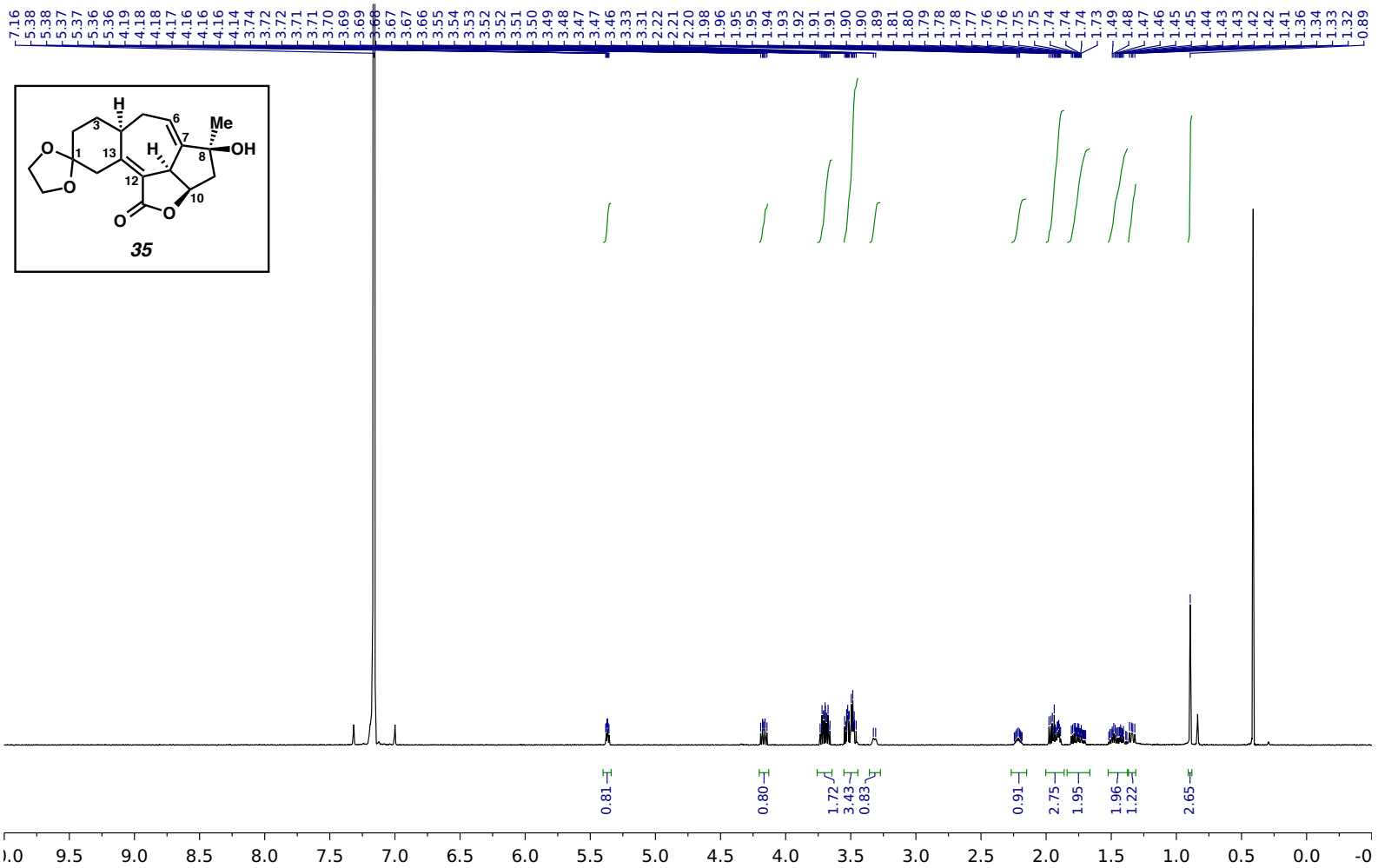


Figure SI.81 ^{1}H NMR (600 MHz, C_6D_6) of compound **35**

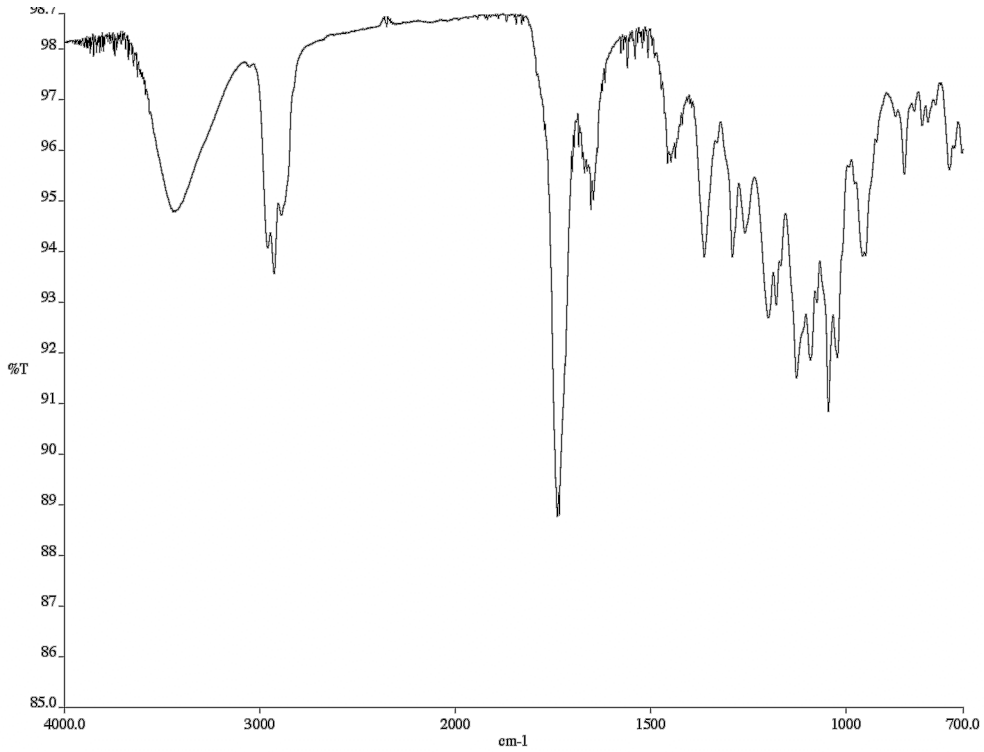


Figure SI.82 Infrared spectrum (thin film/NaCl) of compound **35**

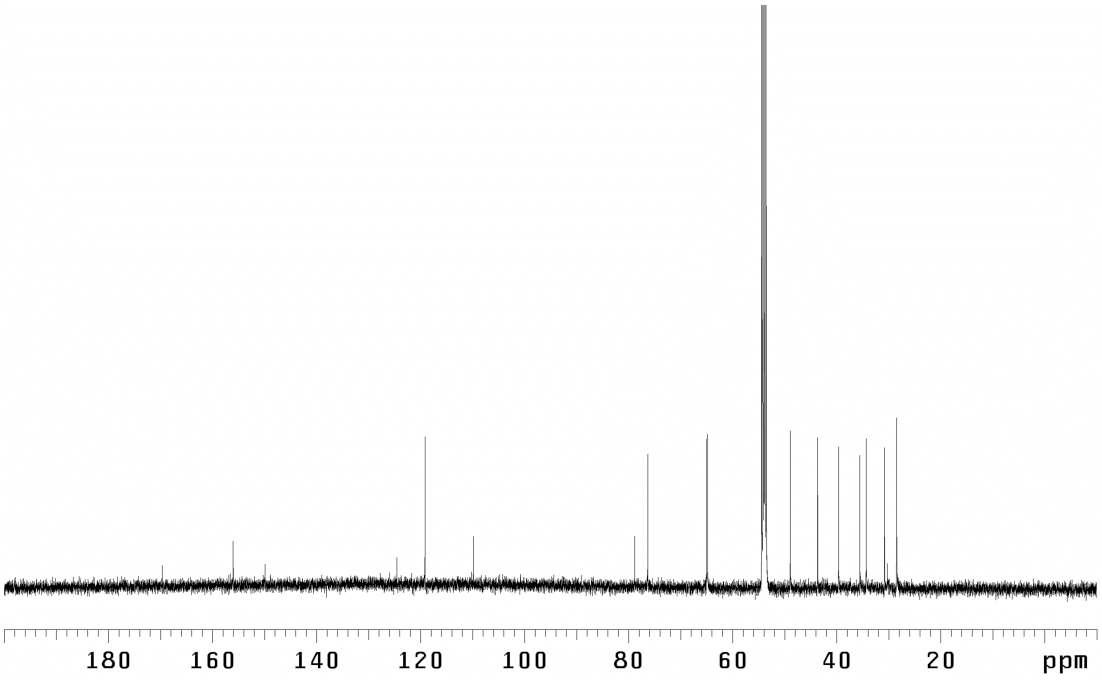


Figure SI.83 ^{13}C NMR (125 MHz, CD_2Cl_2) of compound **35**

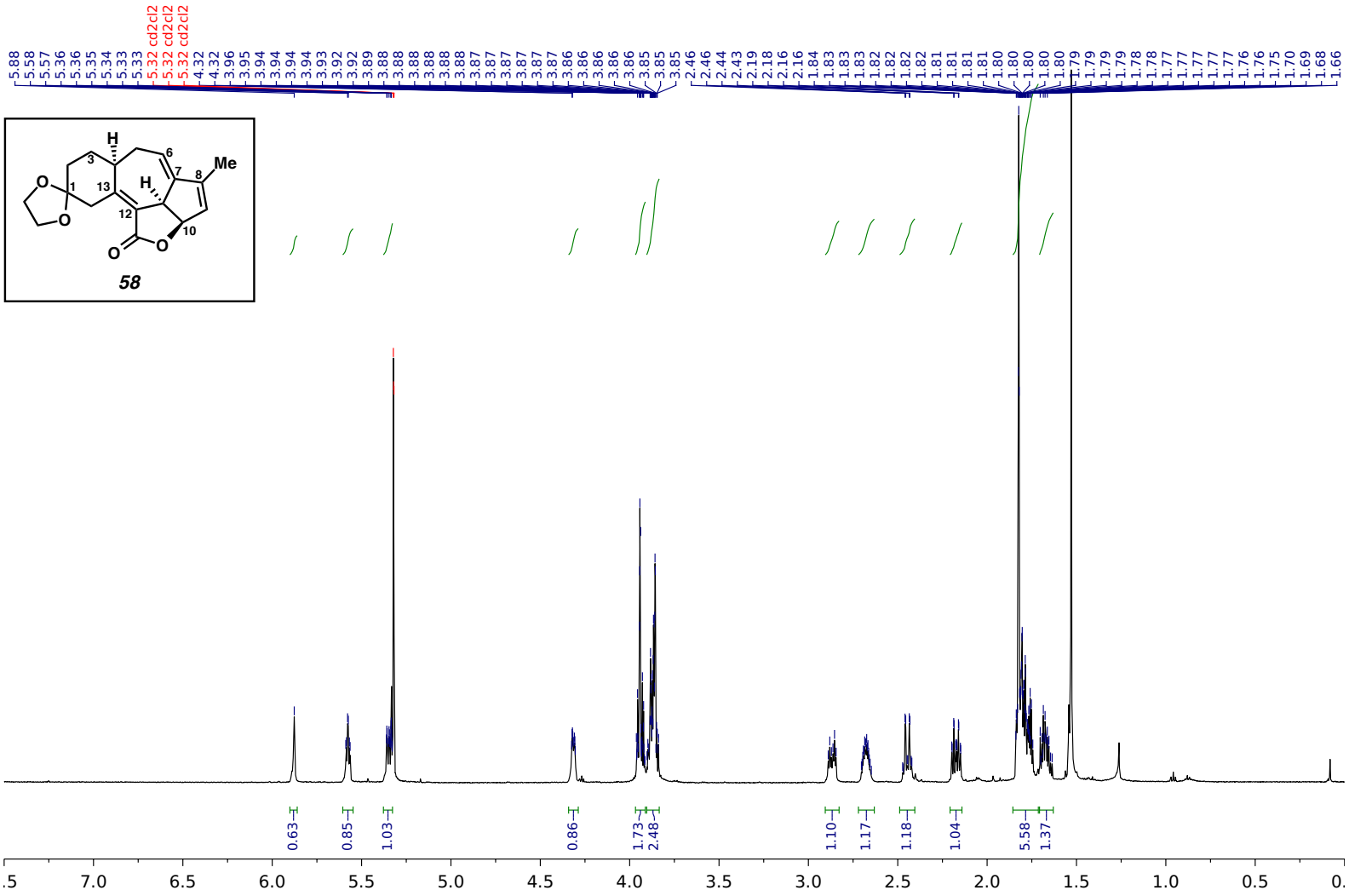


Figure SI.84 ^{1}H NMR (600 MHz, CD_2Cl_2) of compound **58**

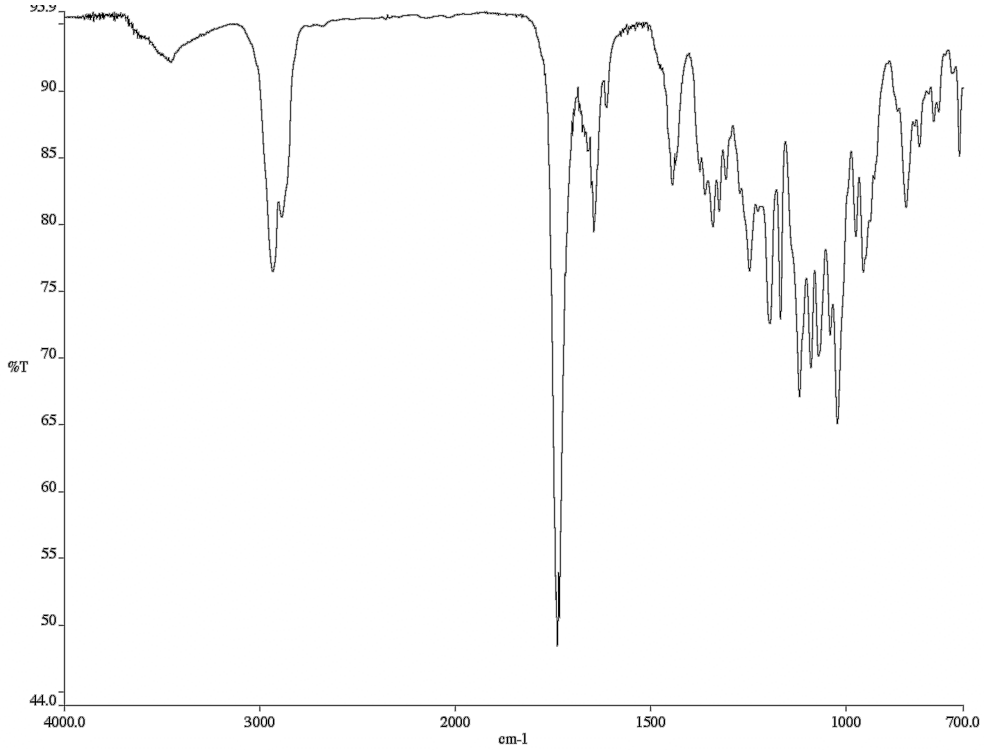


Figure SI.85 Infrared spectrum (thin film/NaCl) of compound **58**

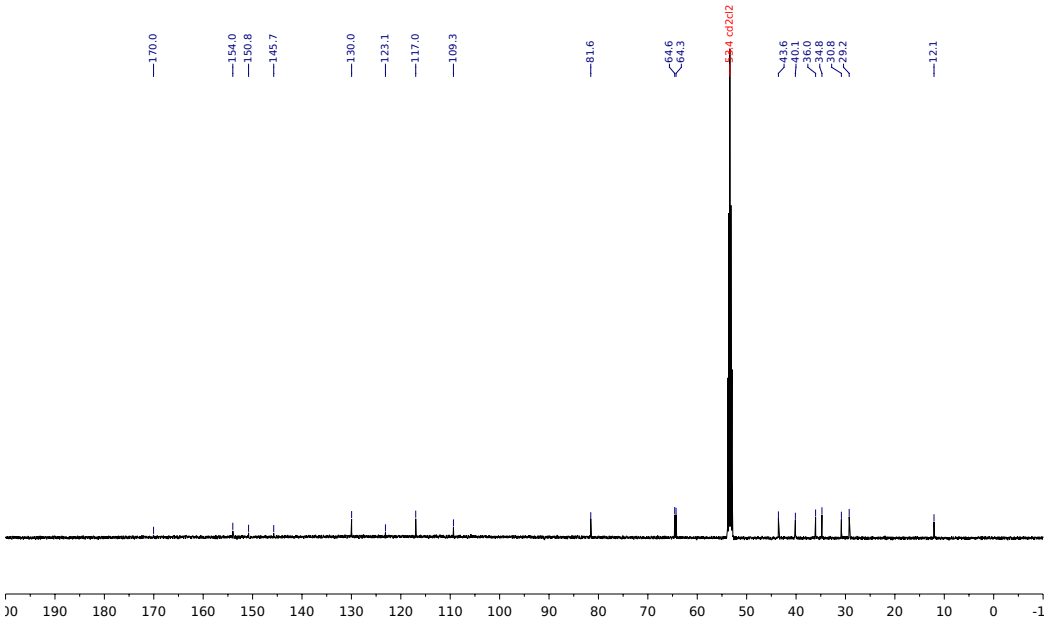


Figure SI.86 ^{13}C NMR (125 MHz, CD_2Cl_2) of compound **58**

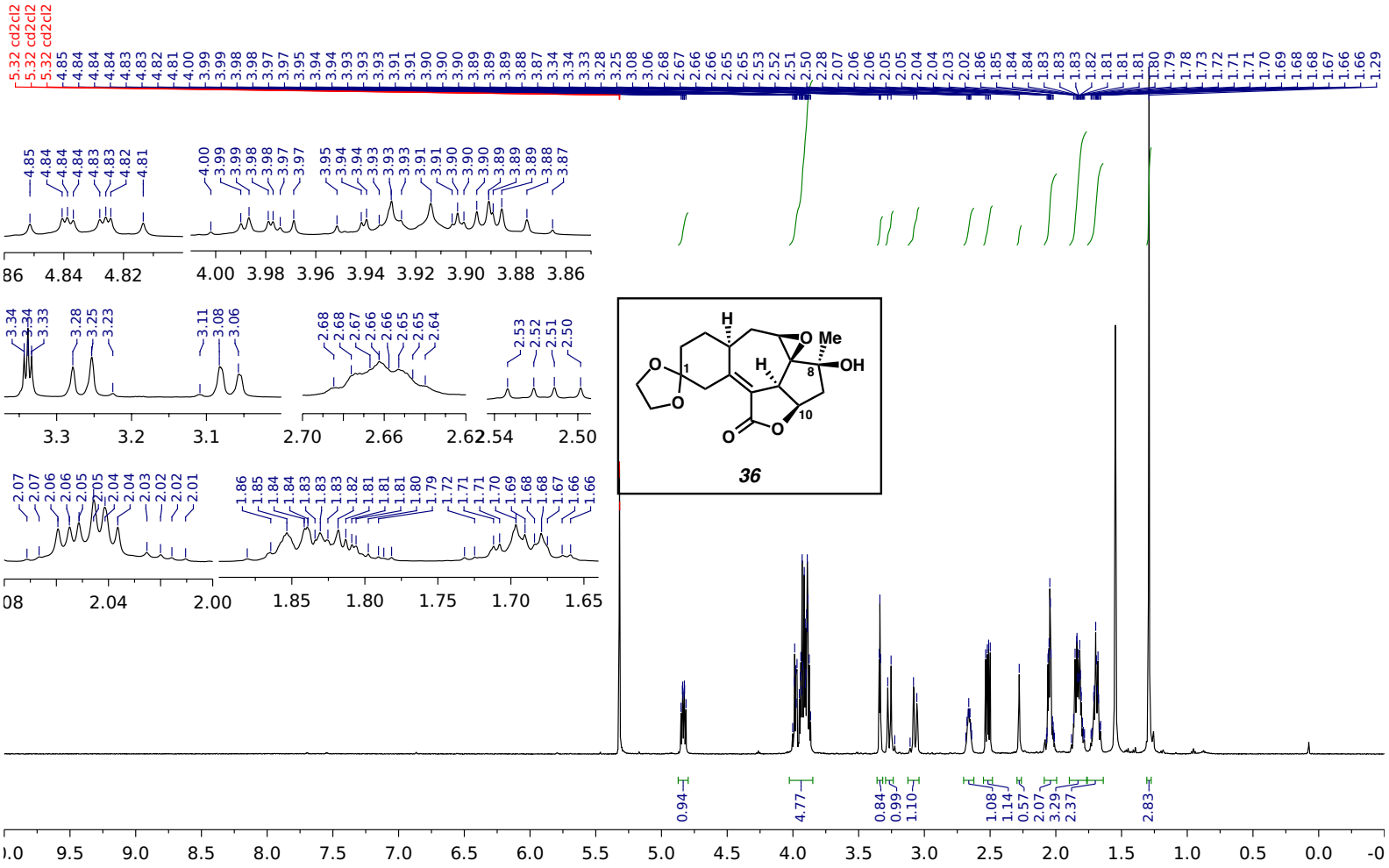


Figure SI.87 ^{1}H NMR (500 MHz, CD_2Cl_2) of compound **36**

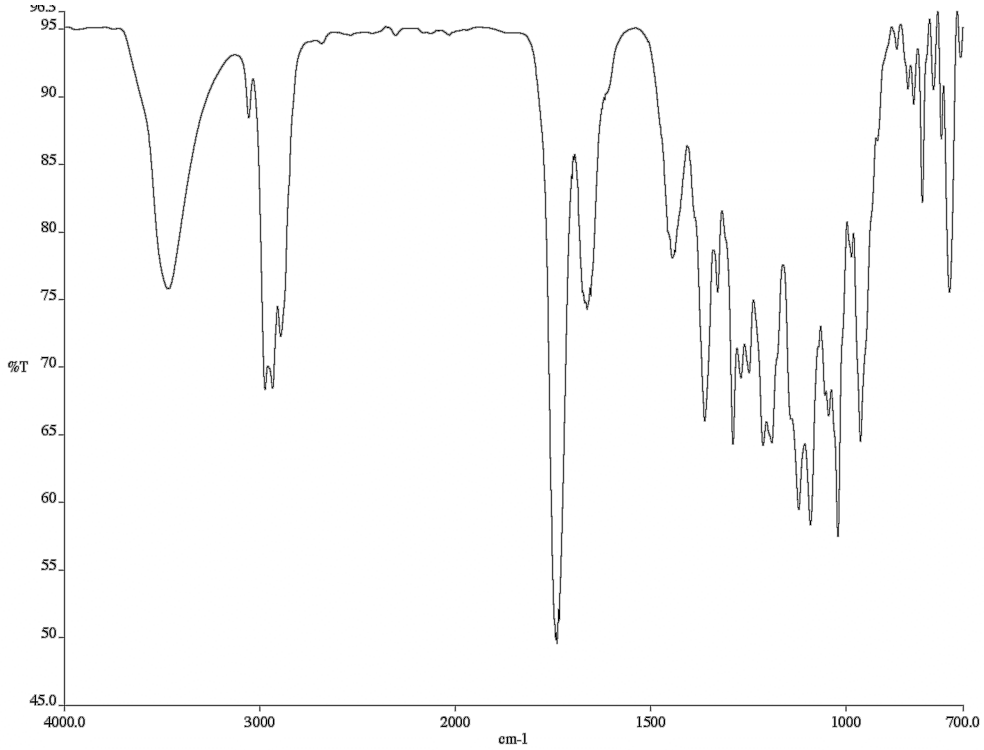


Figure SI.88 Infrared spectrum (thin film/NaCl) of compound **36**

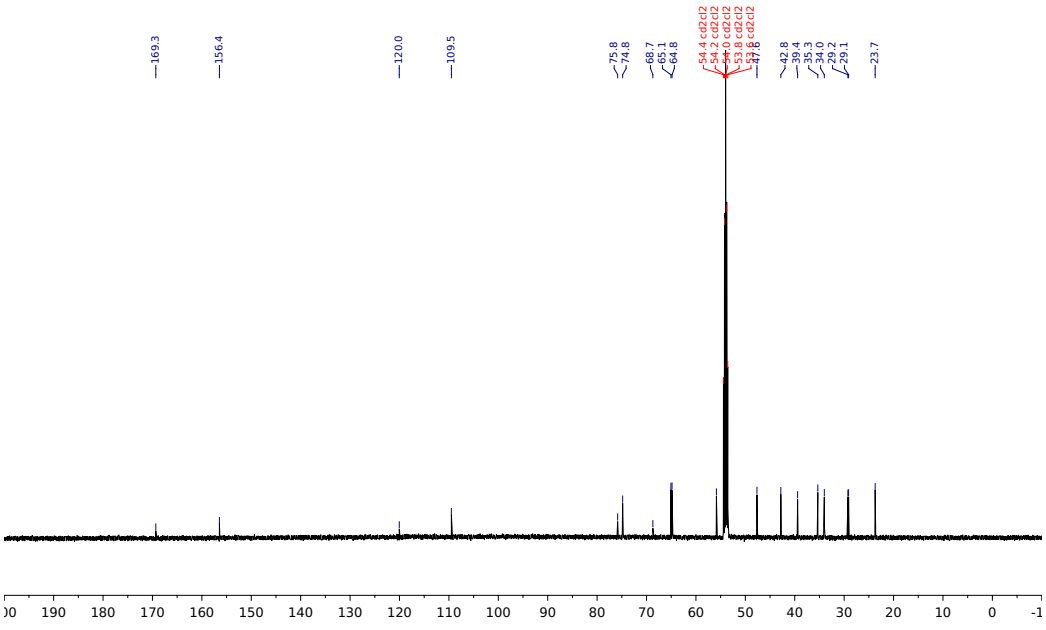


Figure SI.89 ^{13}C NMR (125 MHz, CD_2Cl_2) of compound **36**

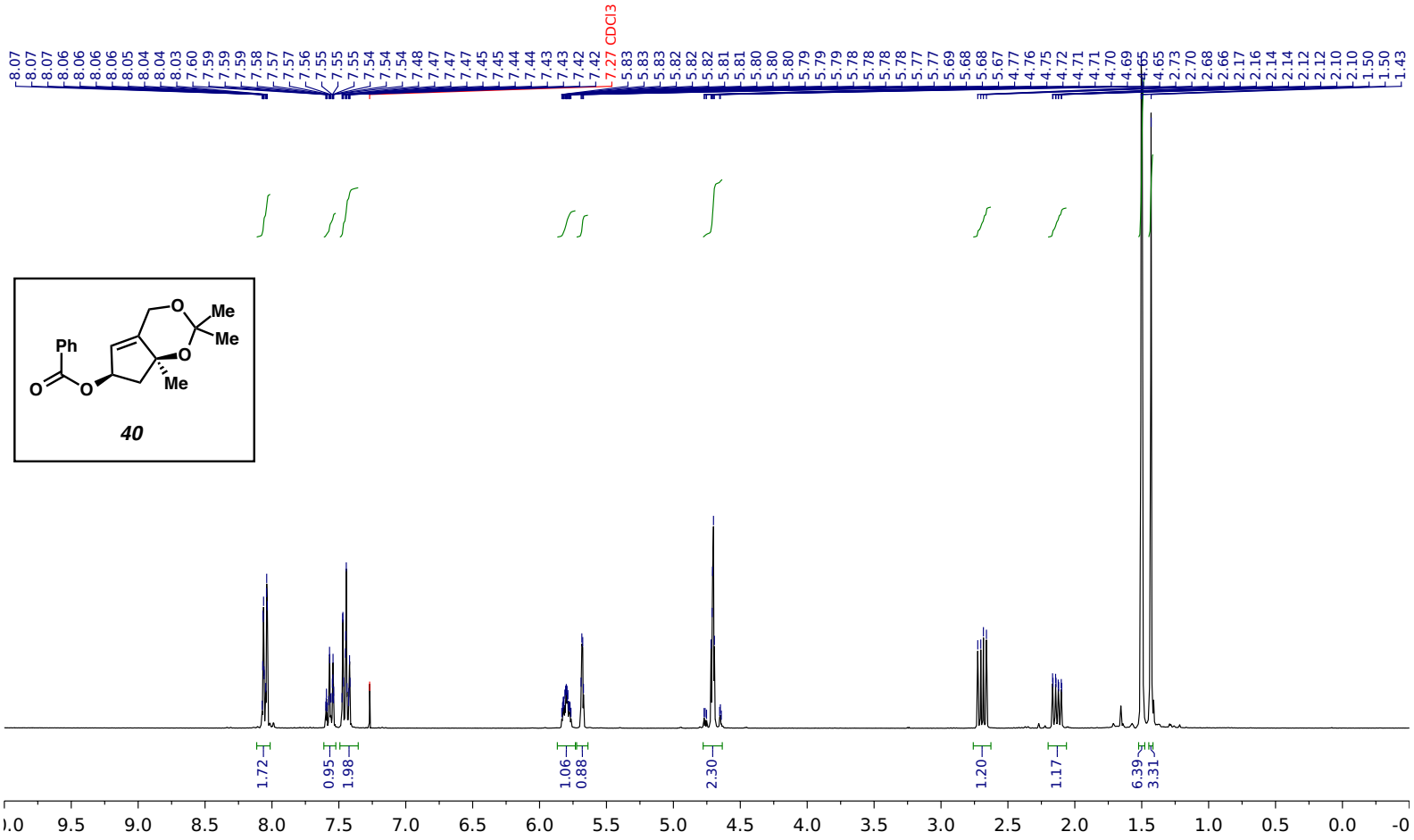


Figure SI.90 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **40**

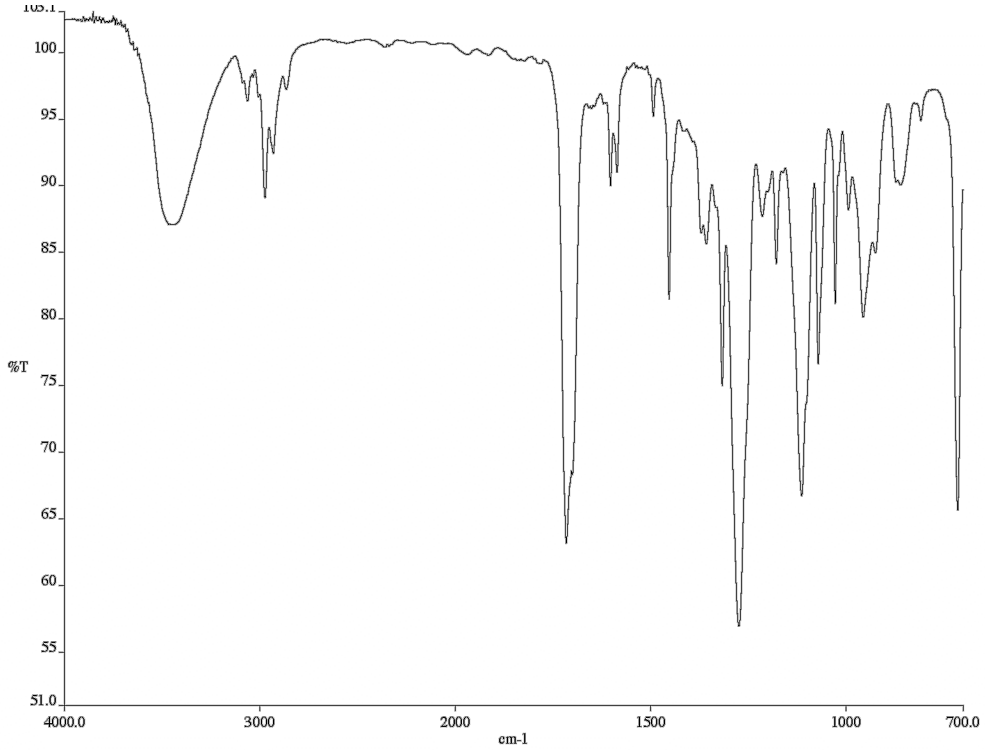


Figure SI.91 Infrared spectrum (thin film/NaCl) of compound **40**

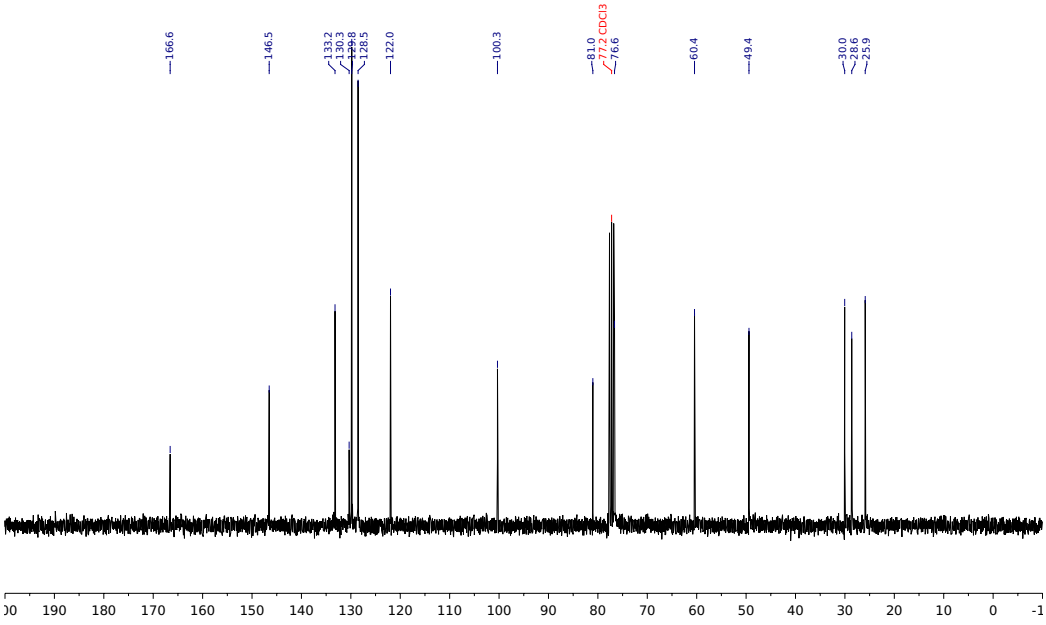


Figure SI.92 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **40**

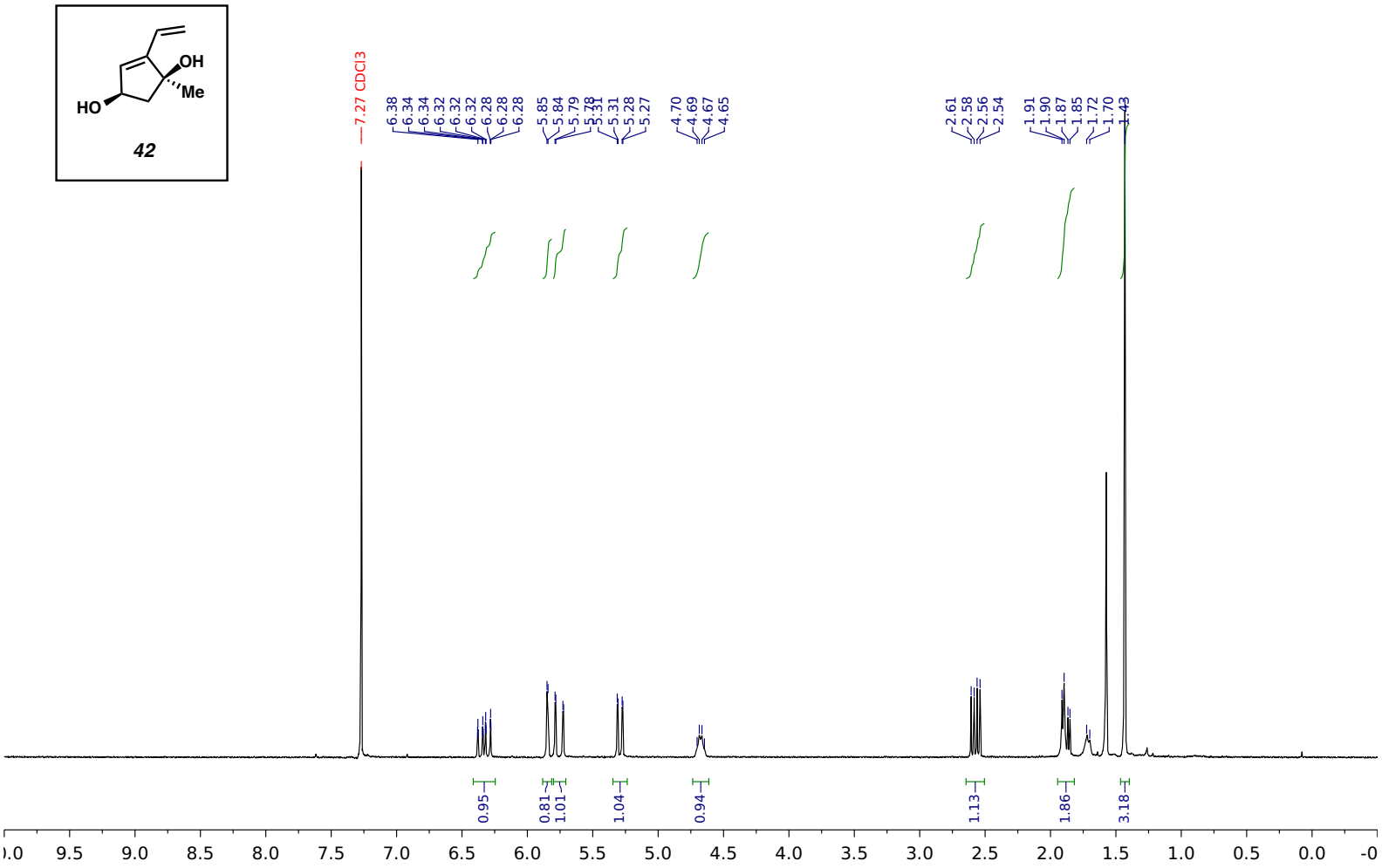


Figure SI.93 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **42**

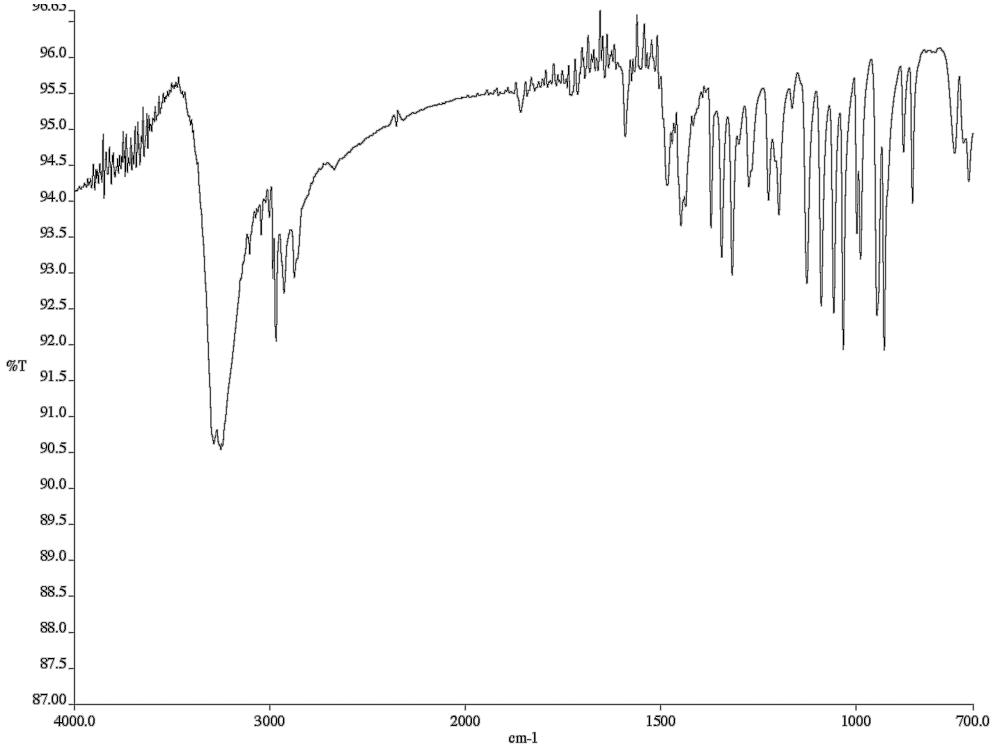


Figure SI.94 Infrared spectrum (thin film/NaCl) of ketone **42**

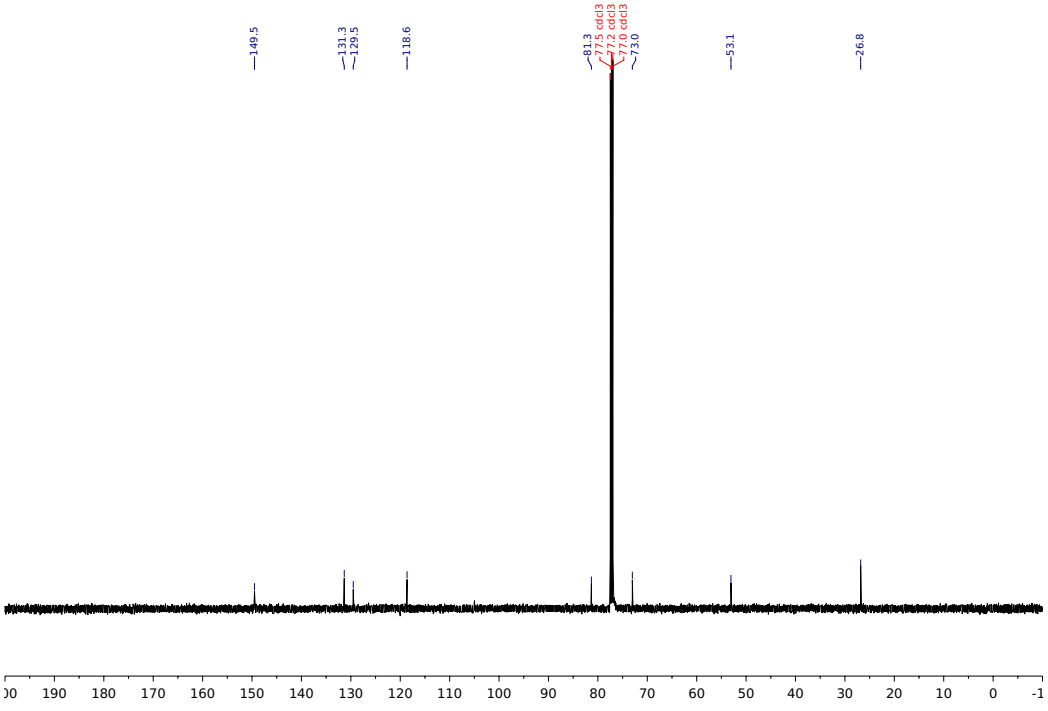


Figure SI.95 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **42**

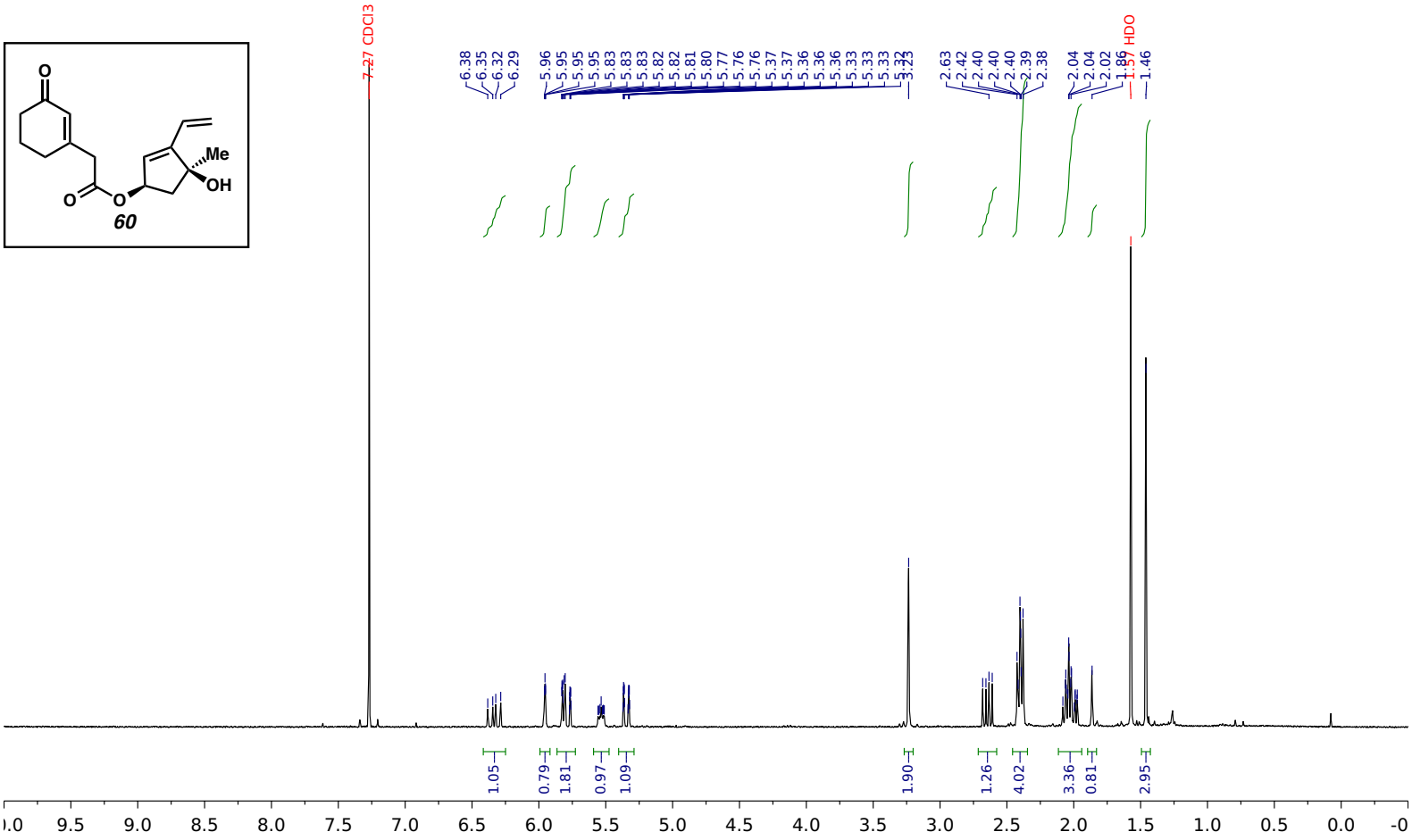


Figure SI.96 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **60**

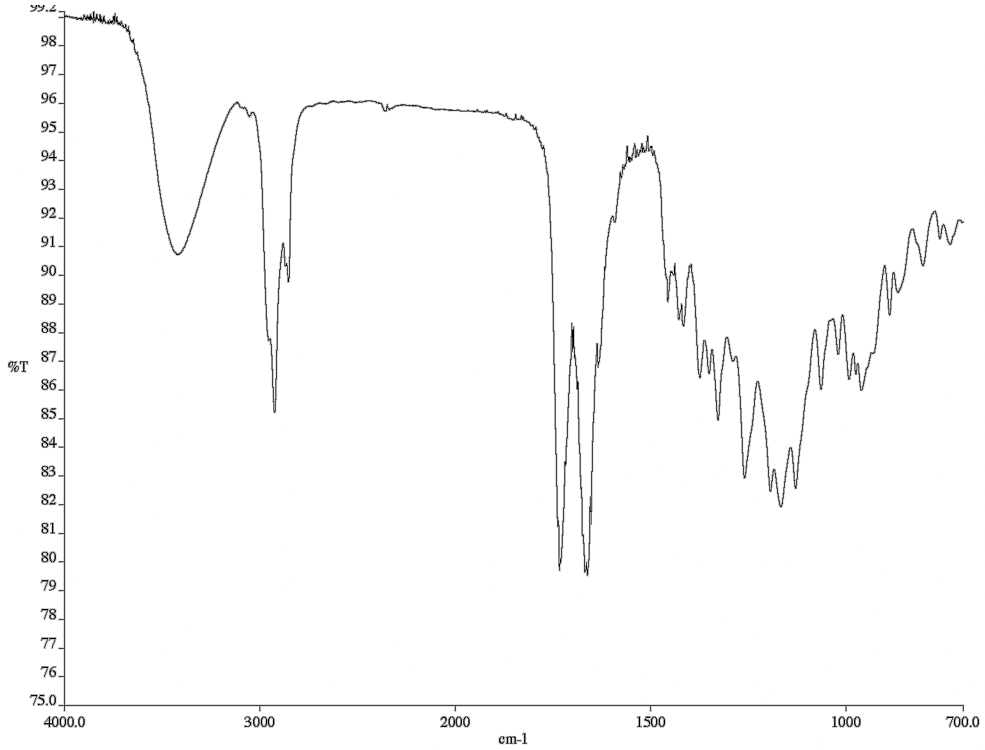


Figure SI.97 Infrared spectrum (thin film/NaCl) of compound **60**

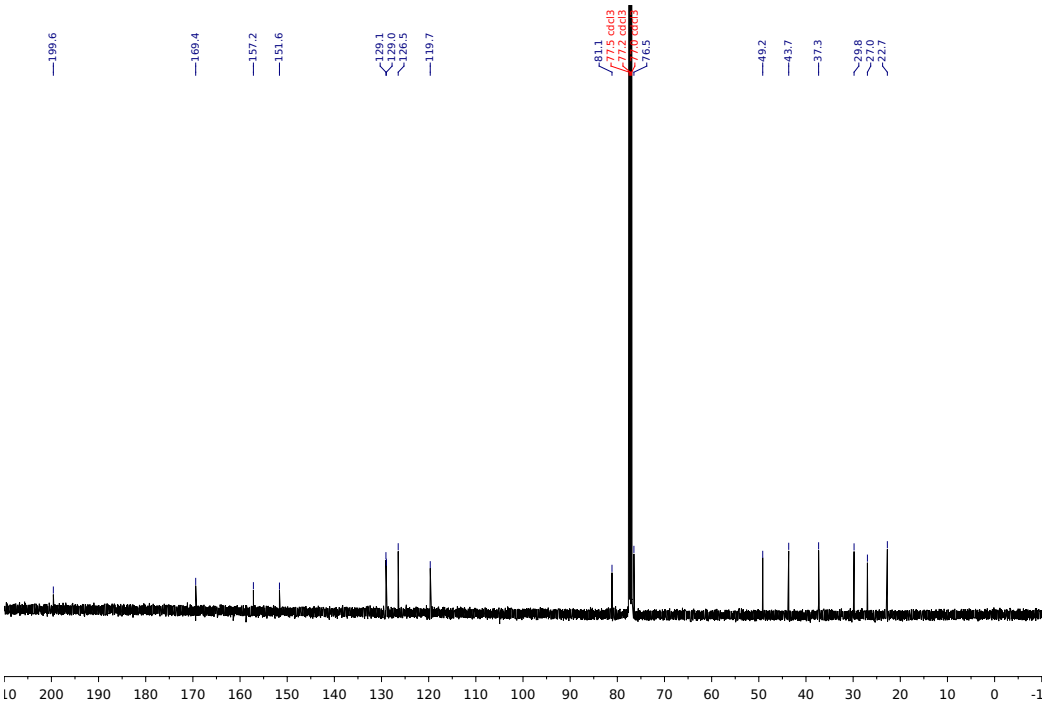


Figure SI.98 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **60**

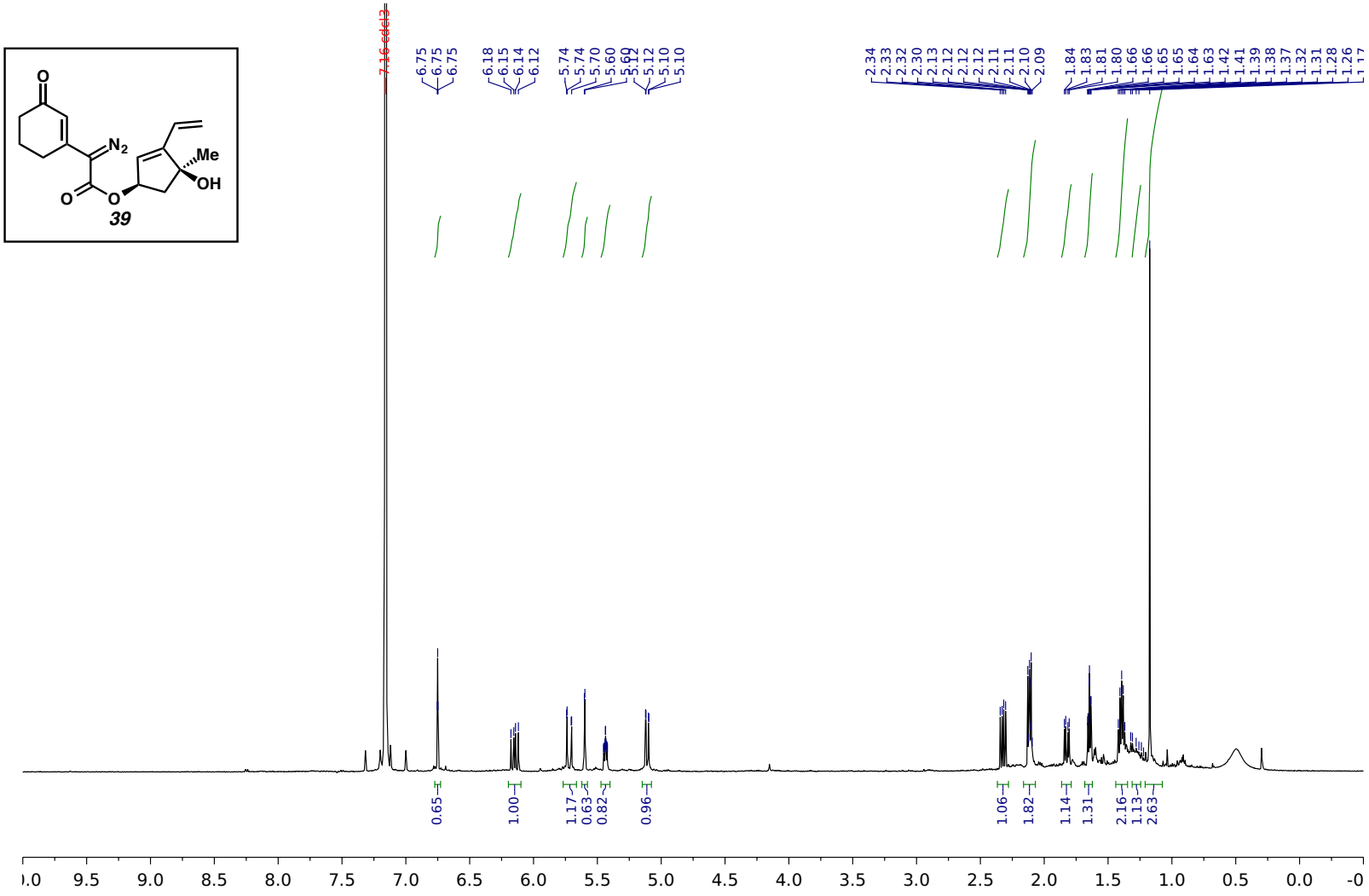


Figure SI.99 ^{1}H NMR (500 MHz, C_6D_6) of compound **39**

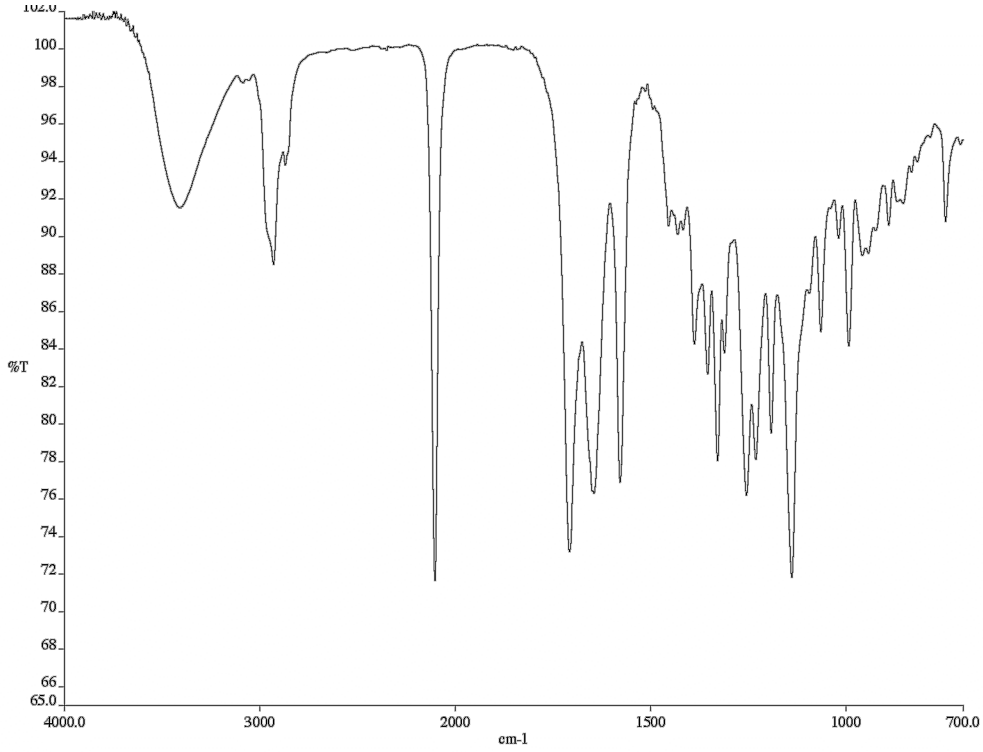


Figure SI.100 Infrared spectrum (thin film/NaCl) of compound **39**

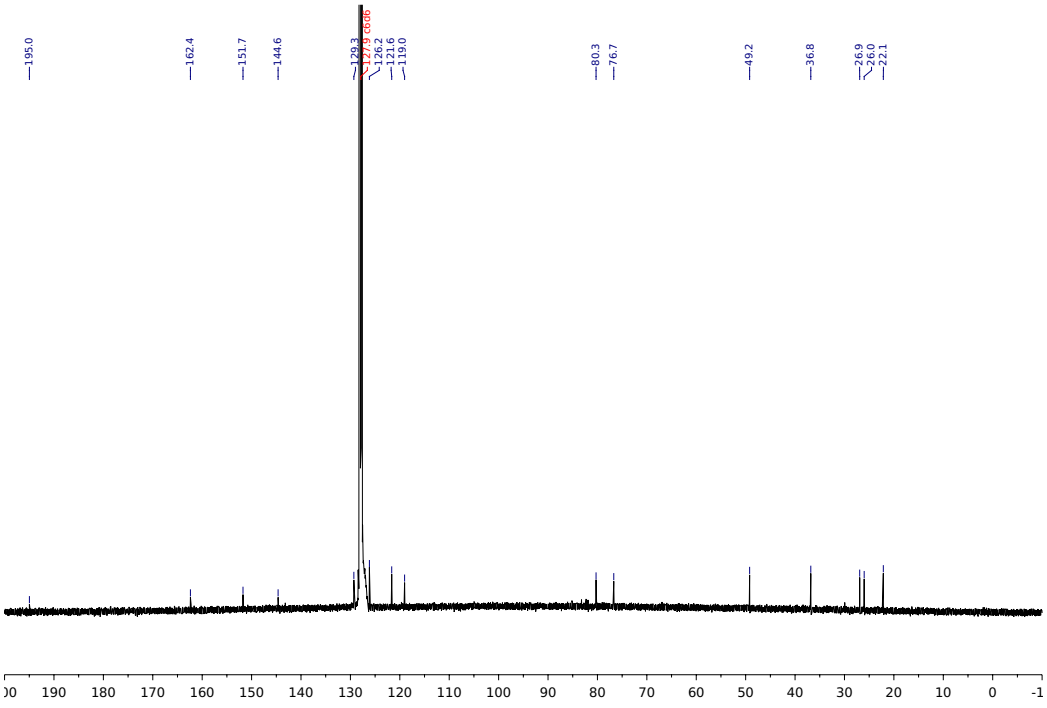


Figure SI.101 ^{13}C NMR (125 MHz, C_6D_6) of compound **39**

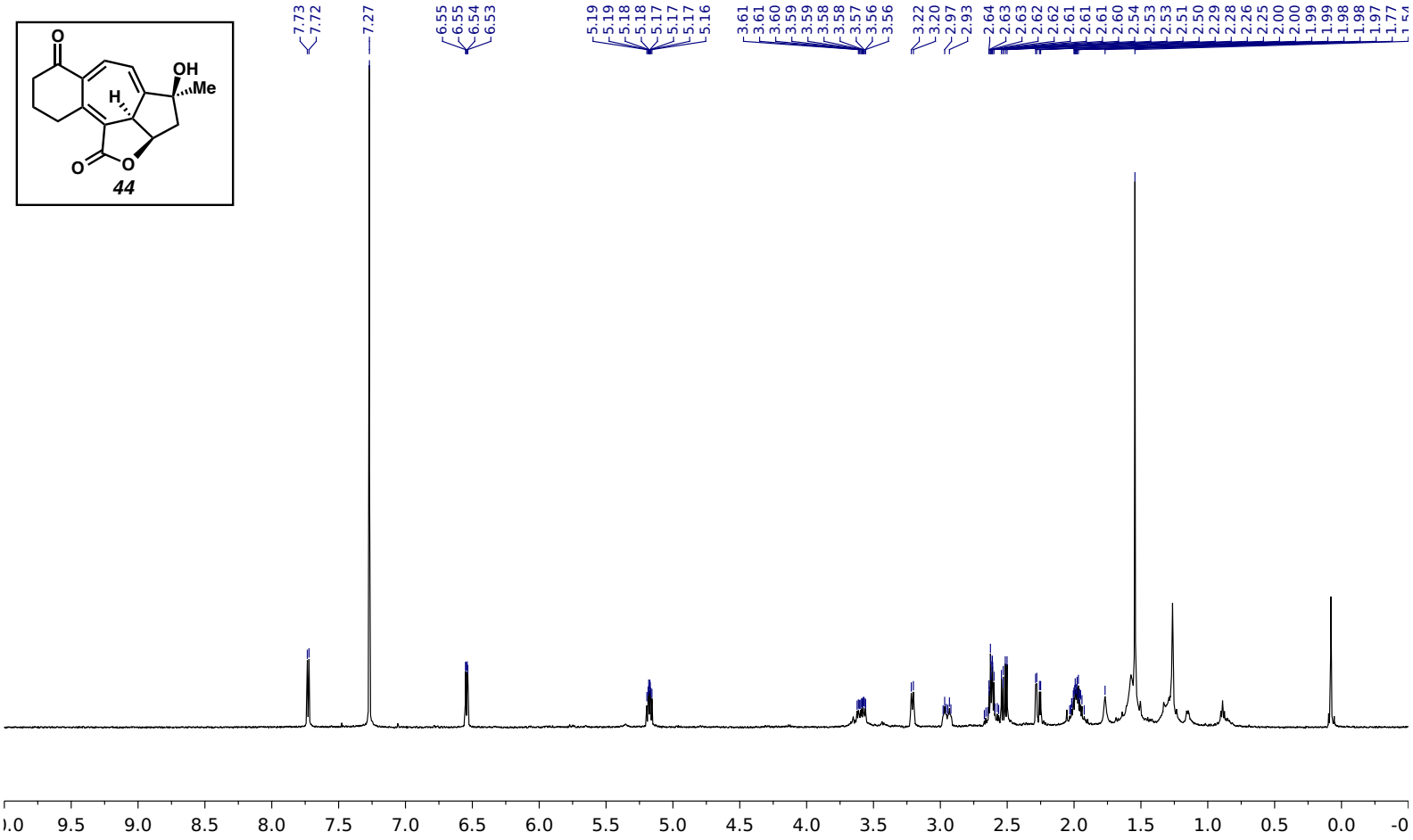


Figure SI.102 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **44**

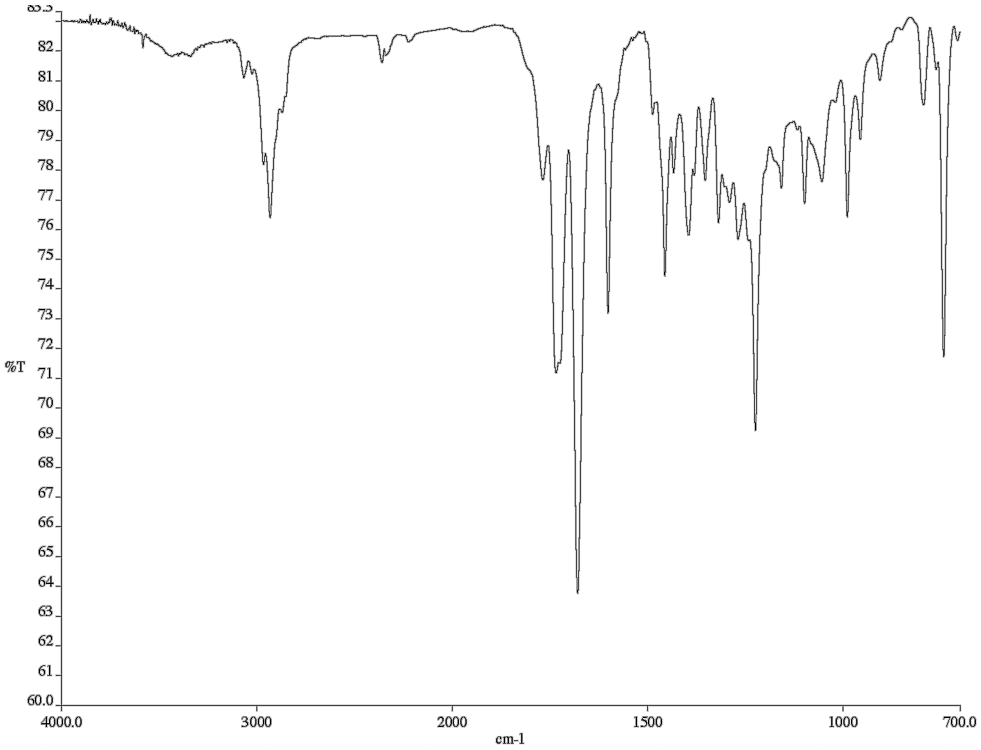


Figure SI.103 Infrared spectrum (thin film/NaCl) of compound **44**

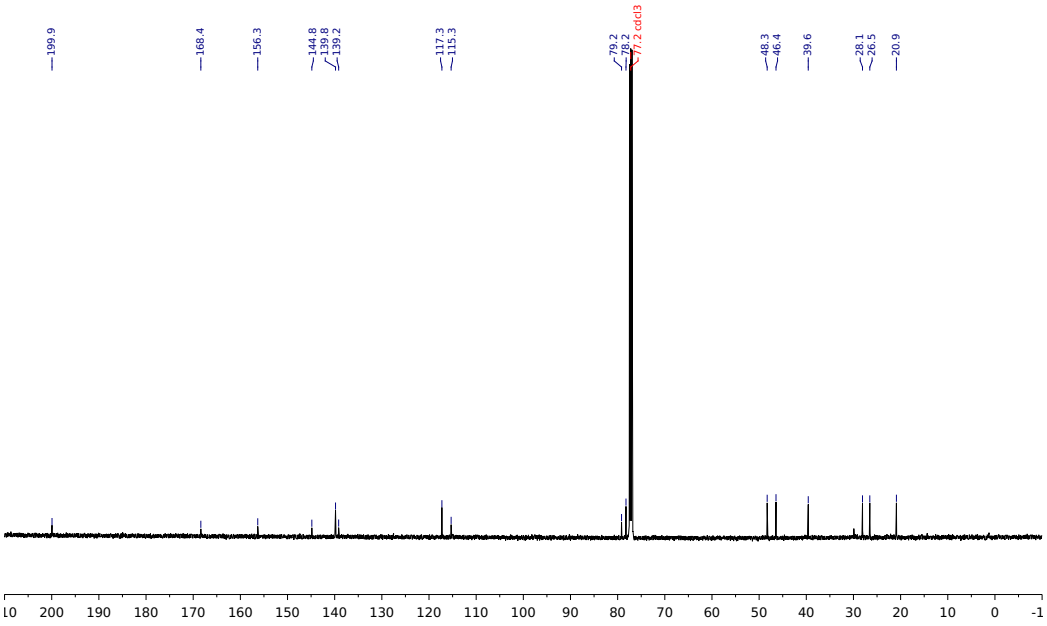


Figure SI.104 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **44**

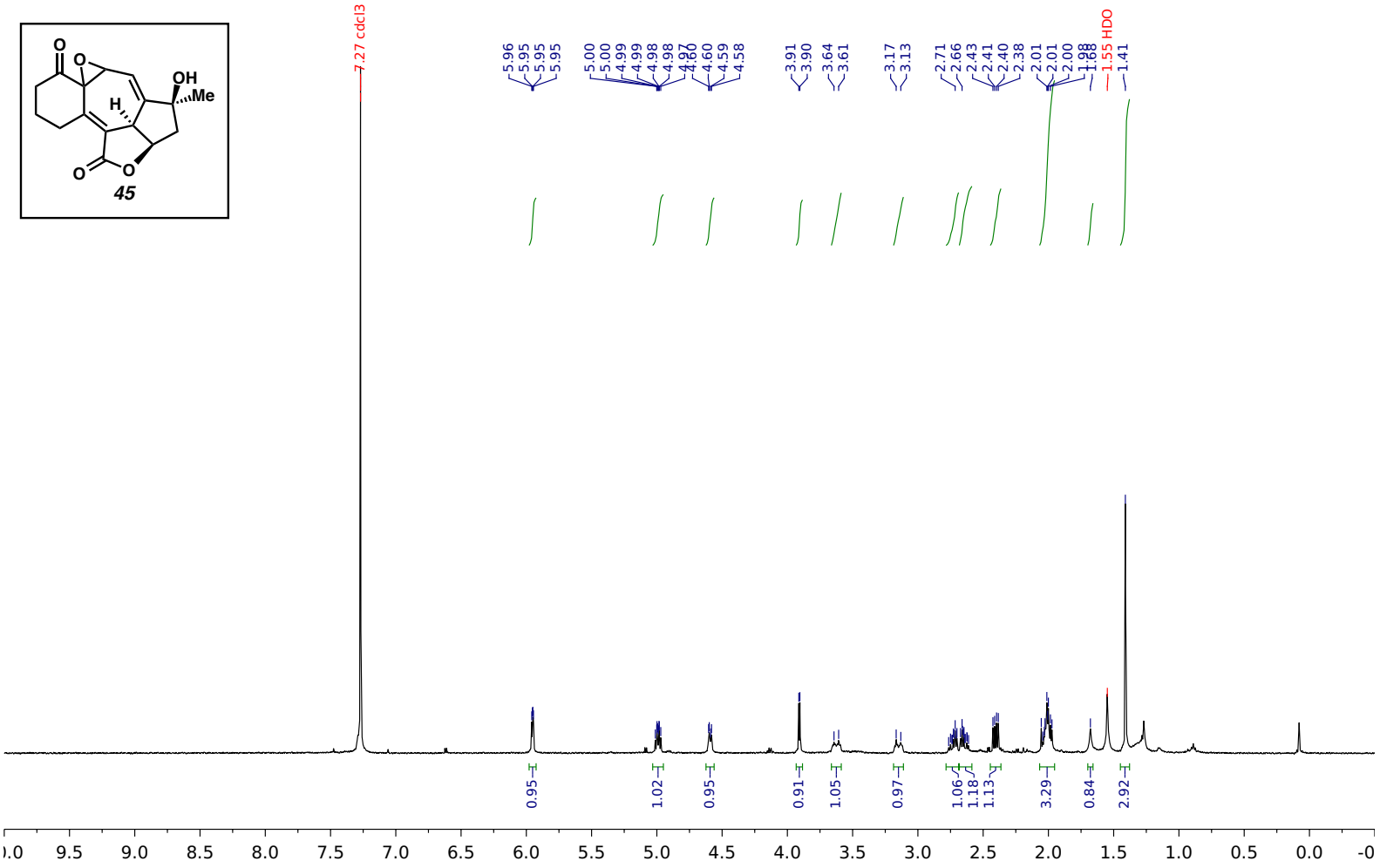


Figure SI.105 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **45**

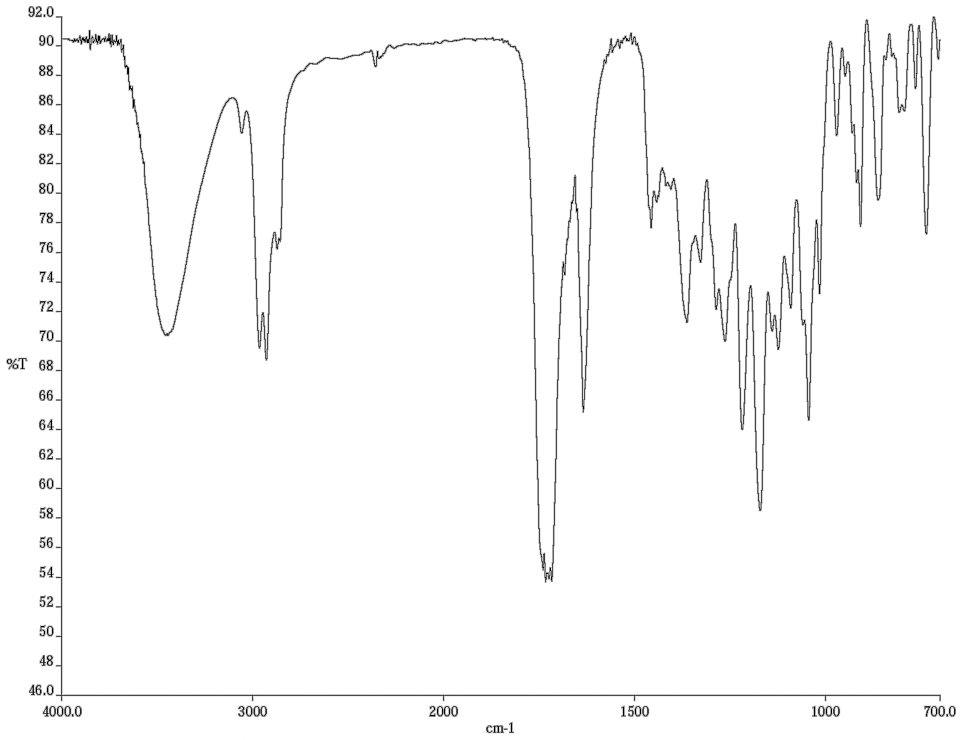


Figure SI.106 Infrared spectrum (thin film/NaCl) of compound **45**

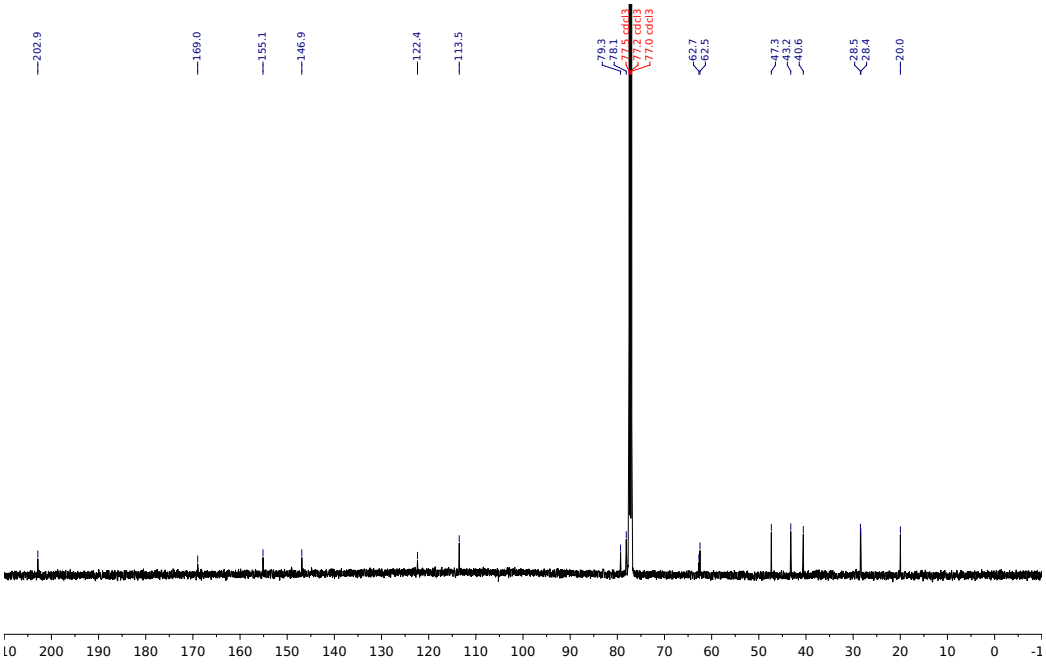


Figure SI.107 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **45**

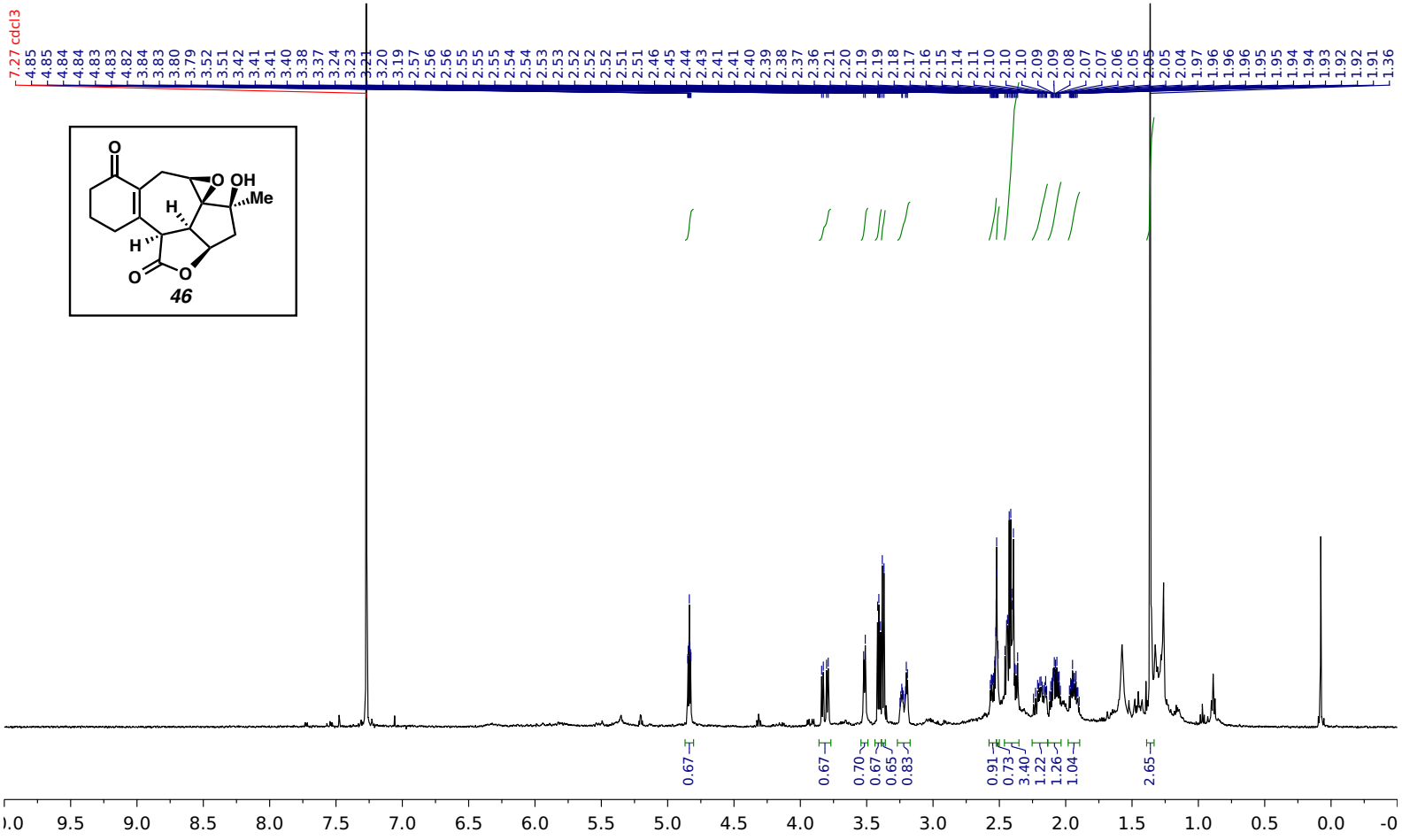


Figure SI.108 ^{1}H NMR (600 MHz, $CDCl_3$) of compound **46**

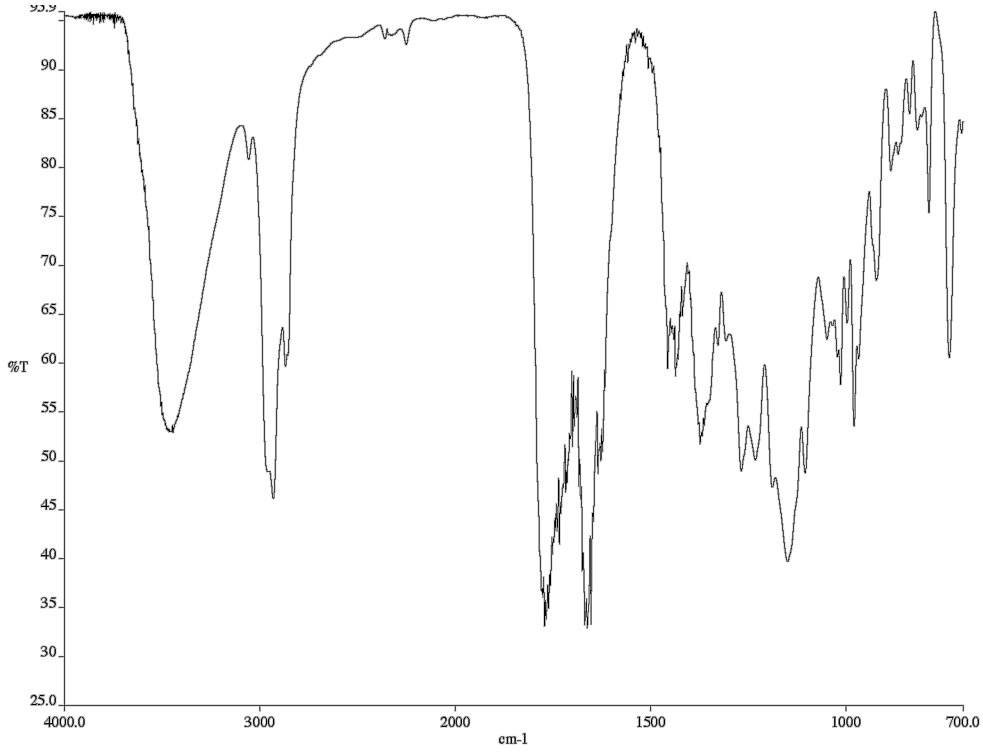


Figure SI.109 Infrared spectrum (thin film/NaCl) of compound **46**

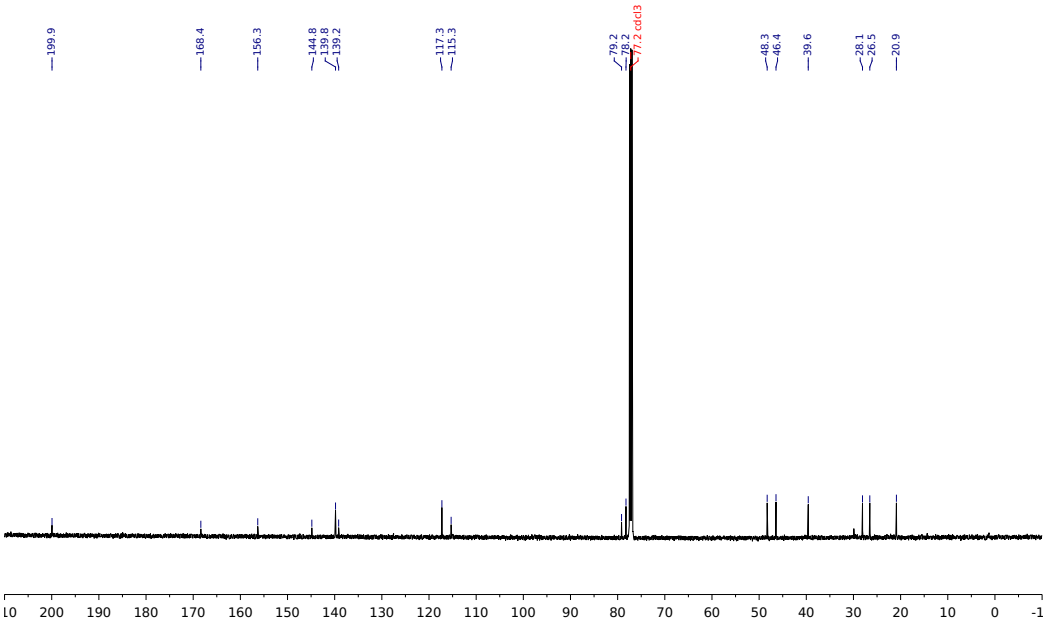


Figure SI.110 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **46**

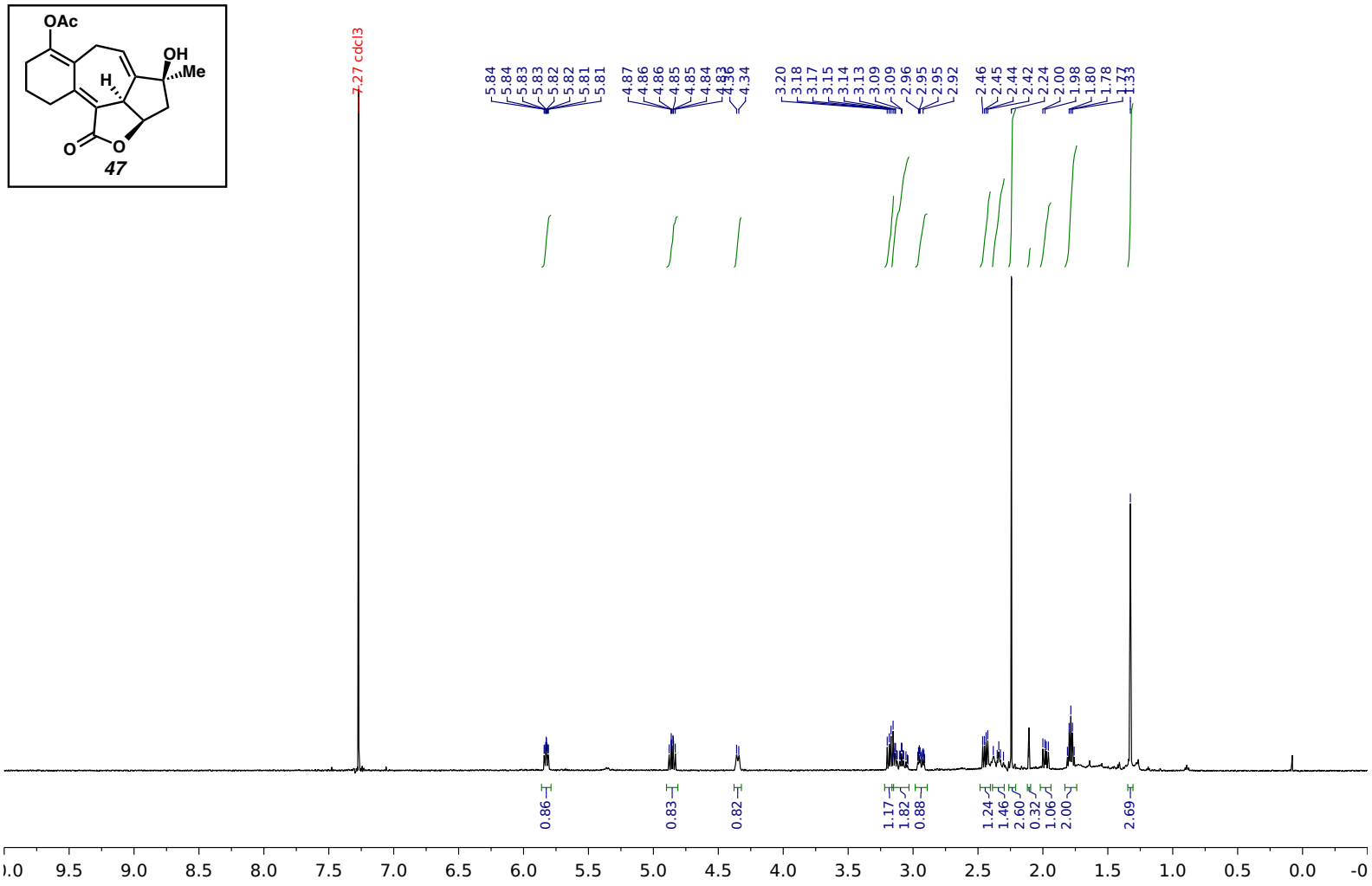


Figure SI.111 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **47**

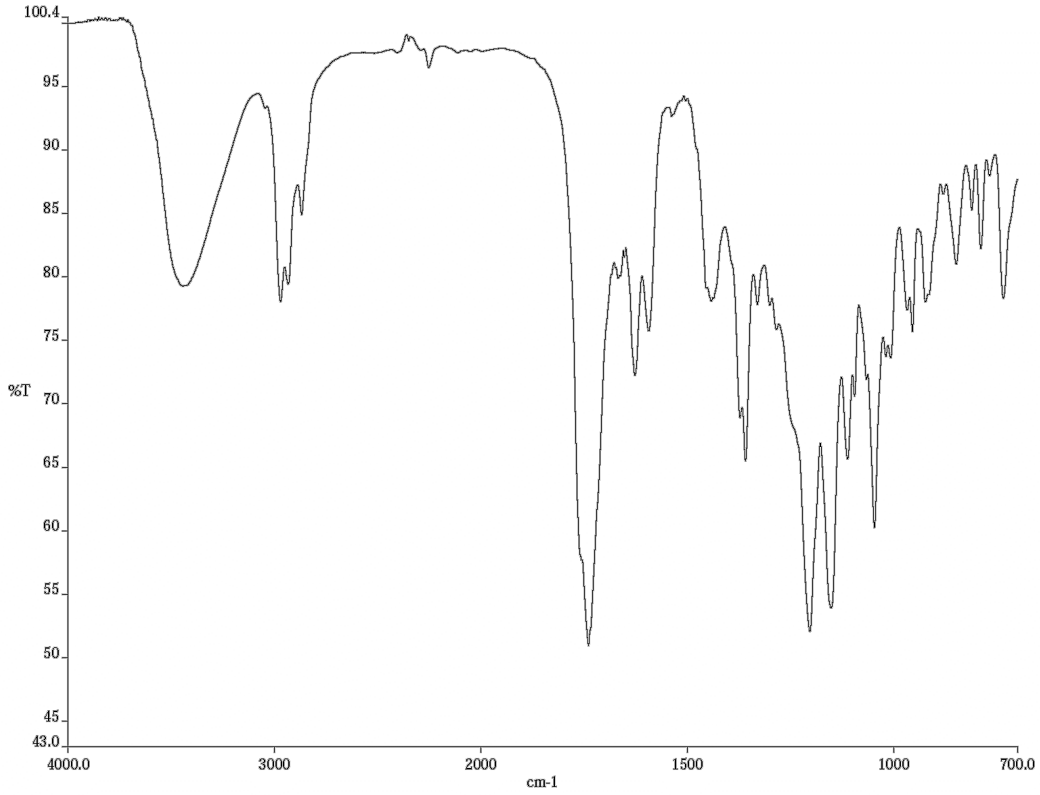


Figure SI.112 Infrared spectrum (thin film/NaCl) of compound **47**

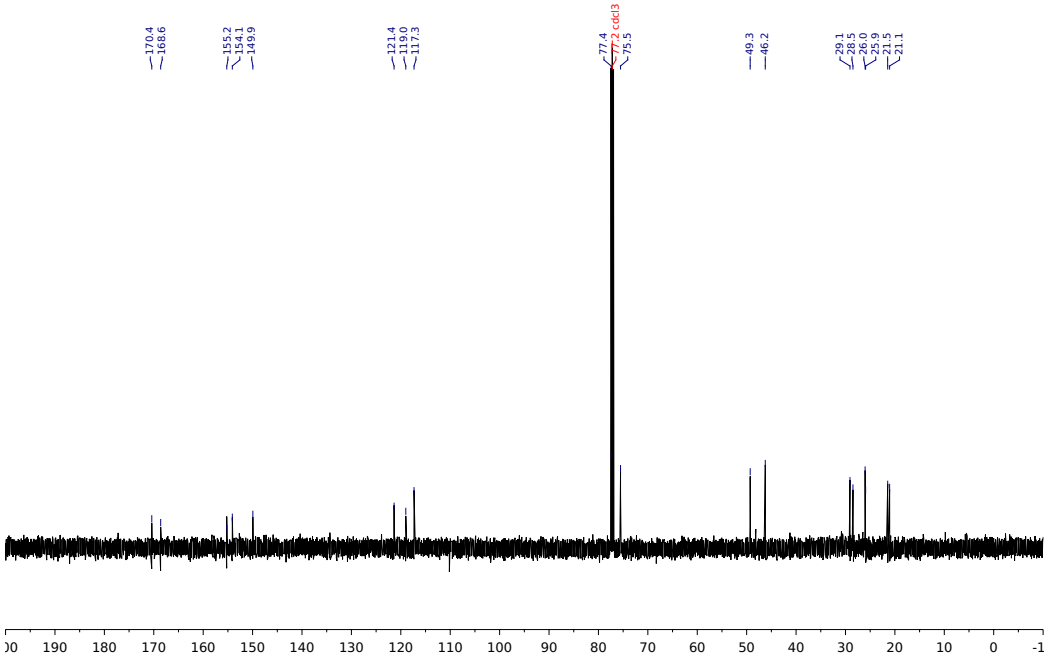


Figure SI.113 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **47**

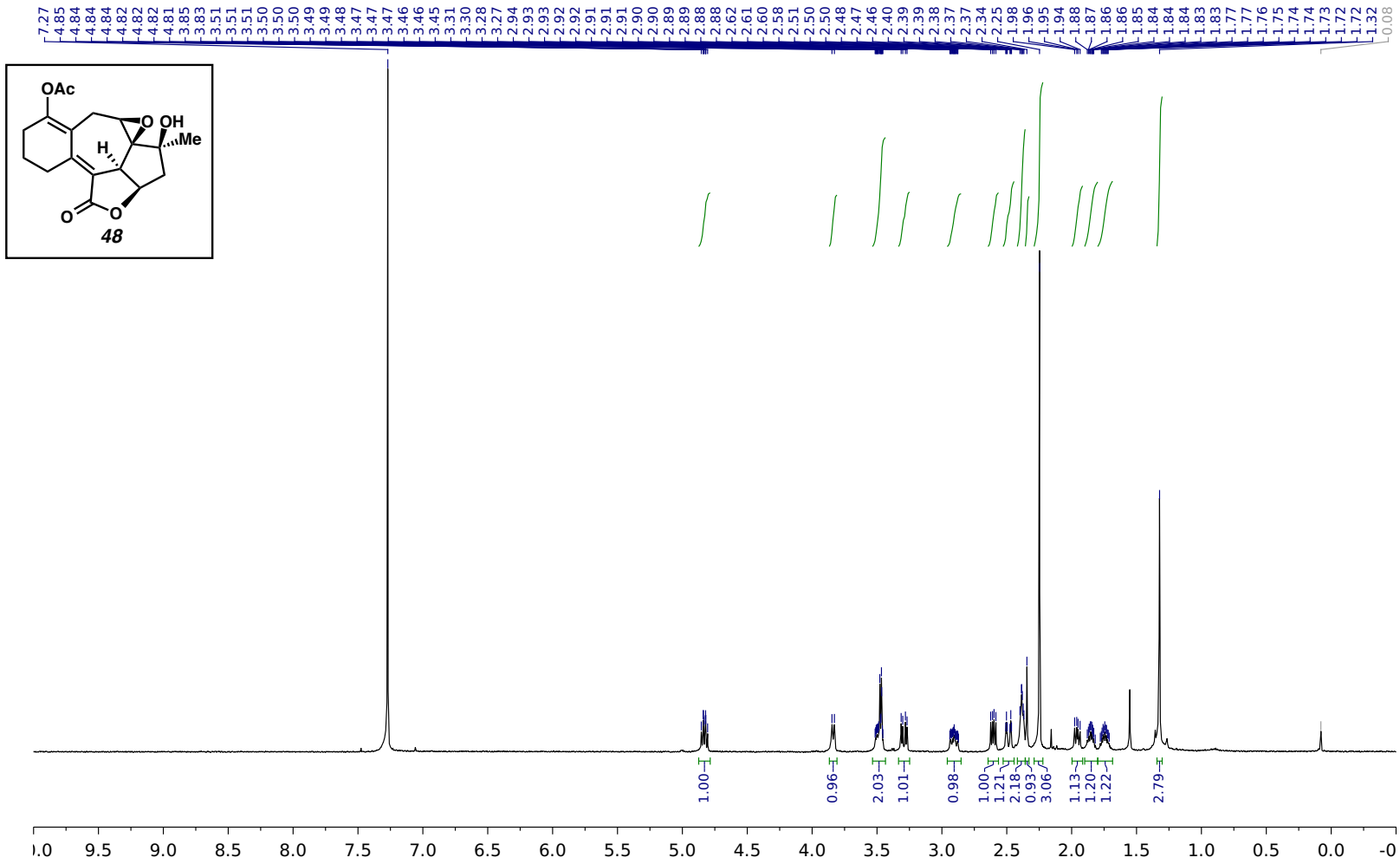


Figure SI.114 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **48**

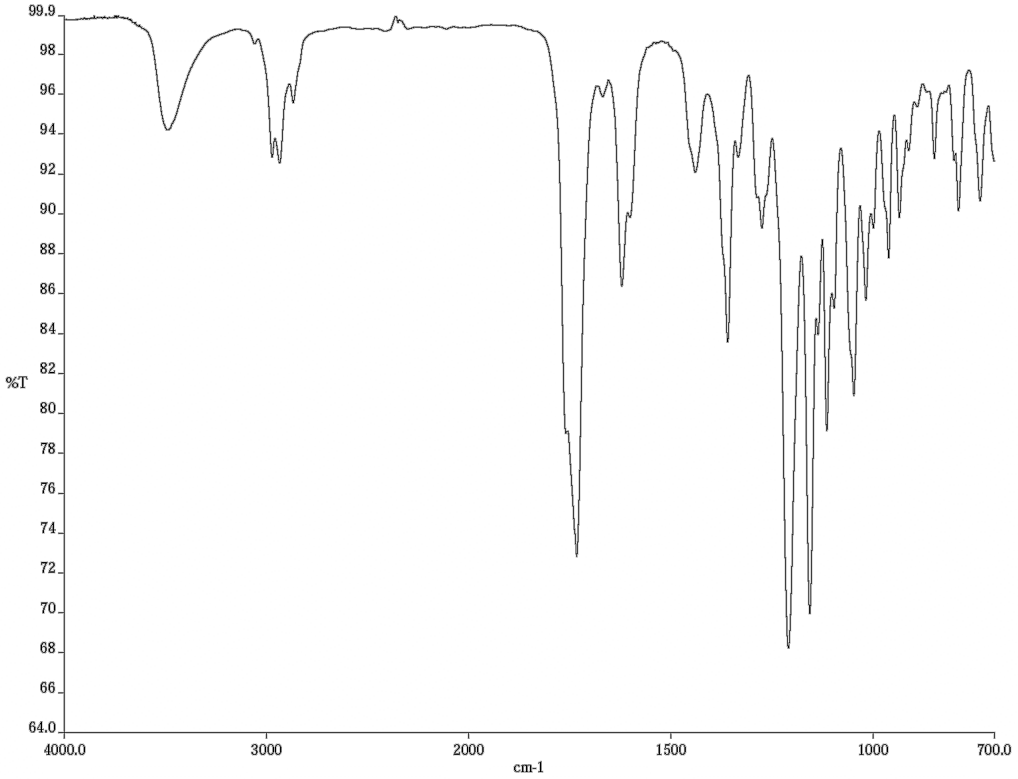


Figure SI.115 Infrared spectrum (thin film/NaCl) of compound **48**

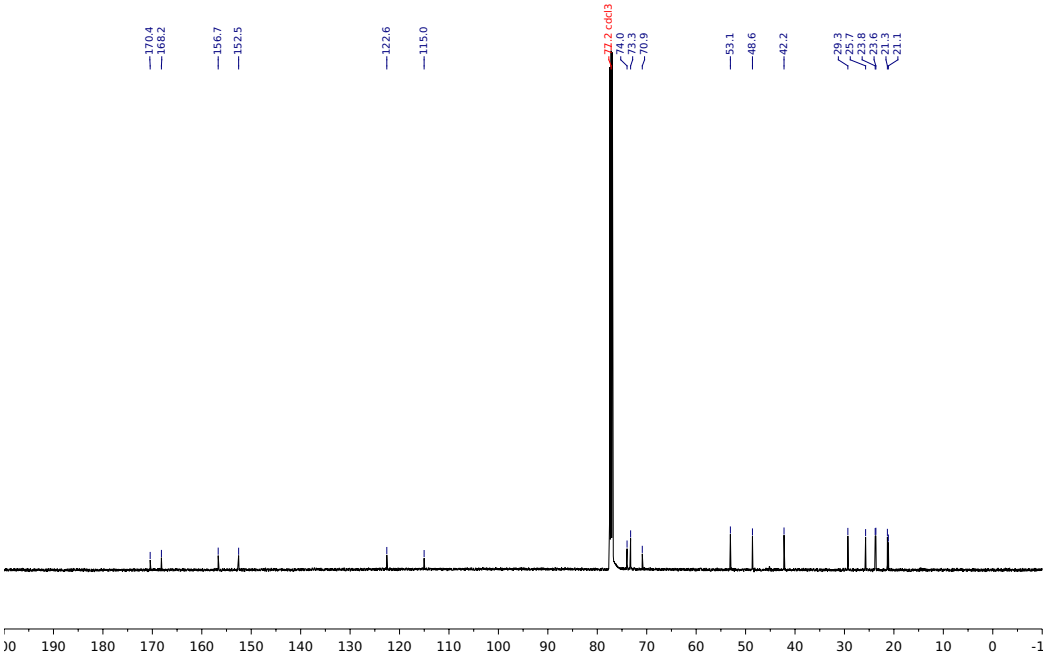


Figure SI.116 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **48**

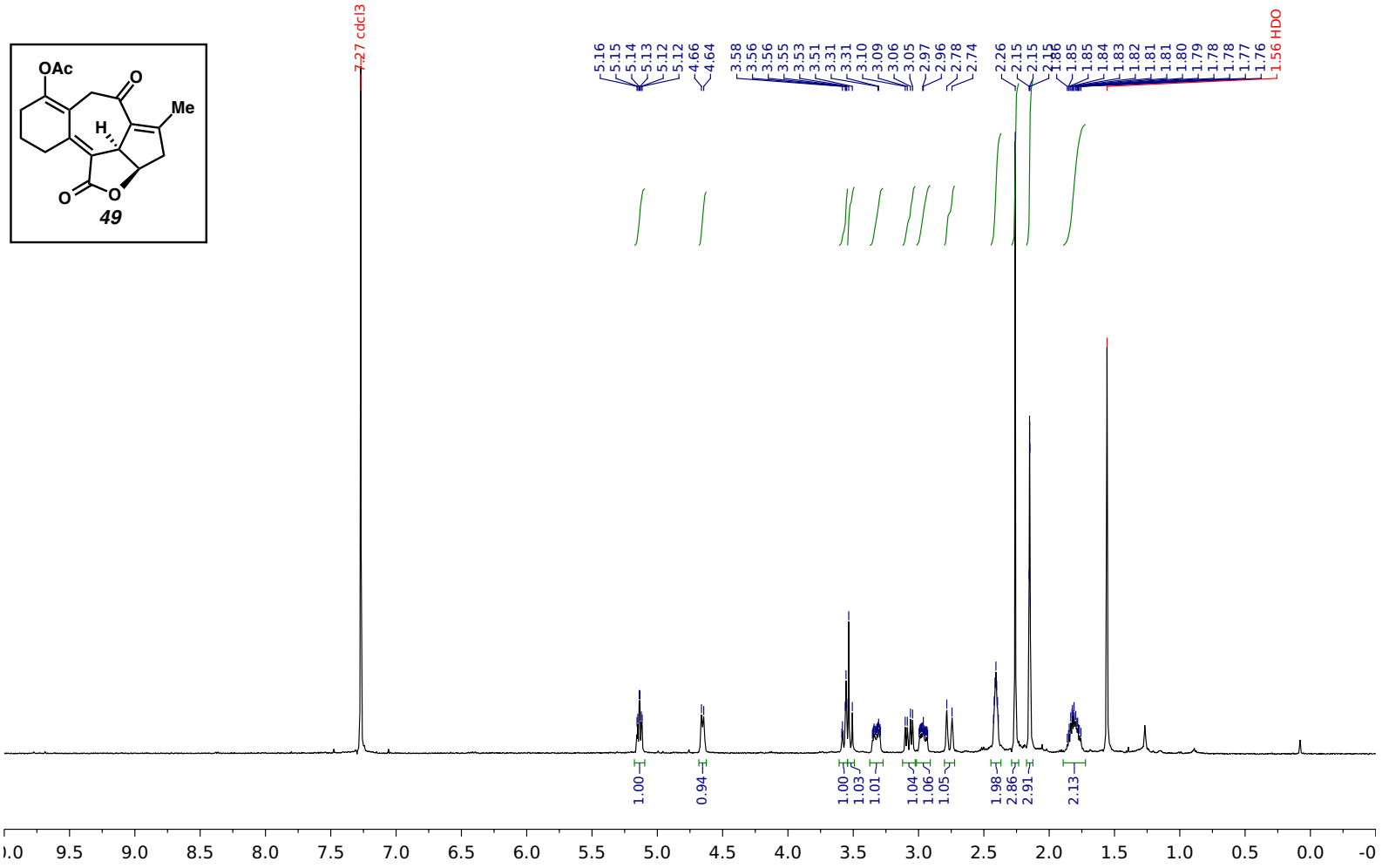


Figure SI.117 ^{1}H NMR (500 MHz, $CDCl_3$) of compound **49**

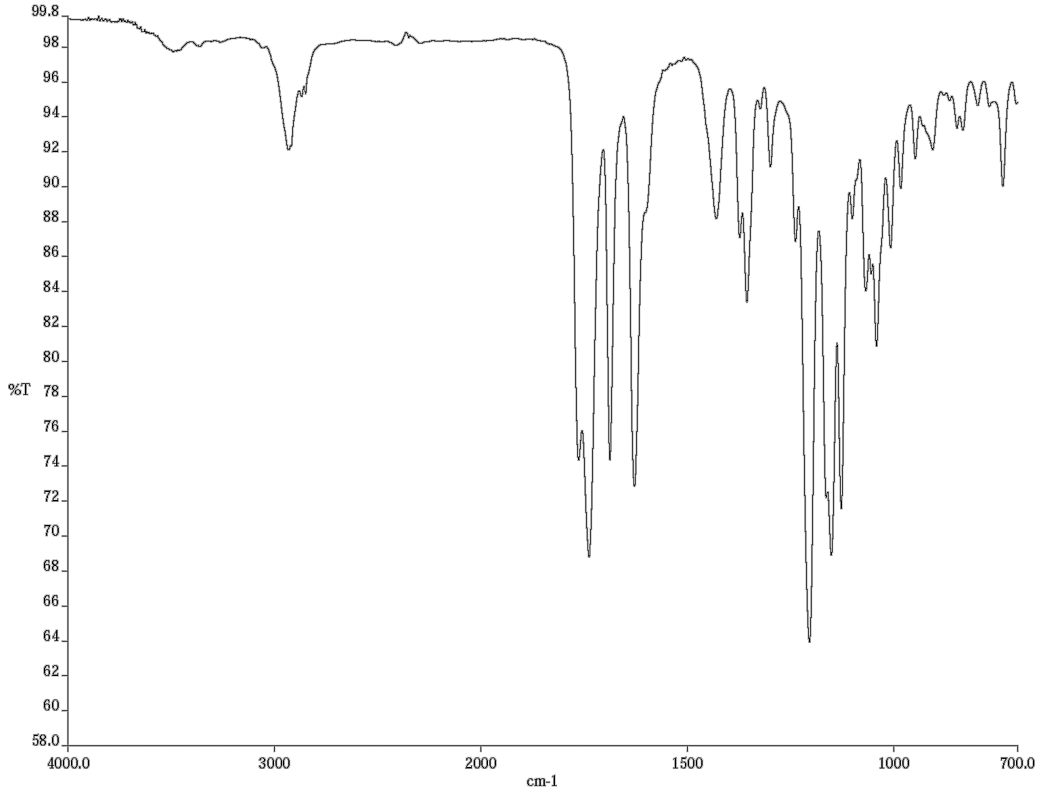


Figure SI.118 Infrared spectrum (thin film/NaCl) of compound **49**

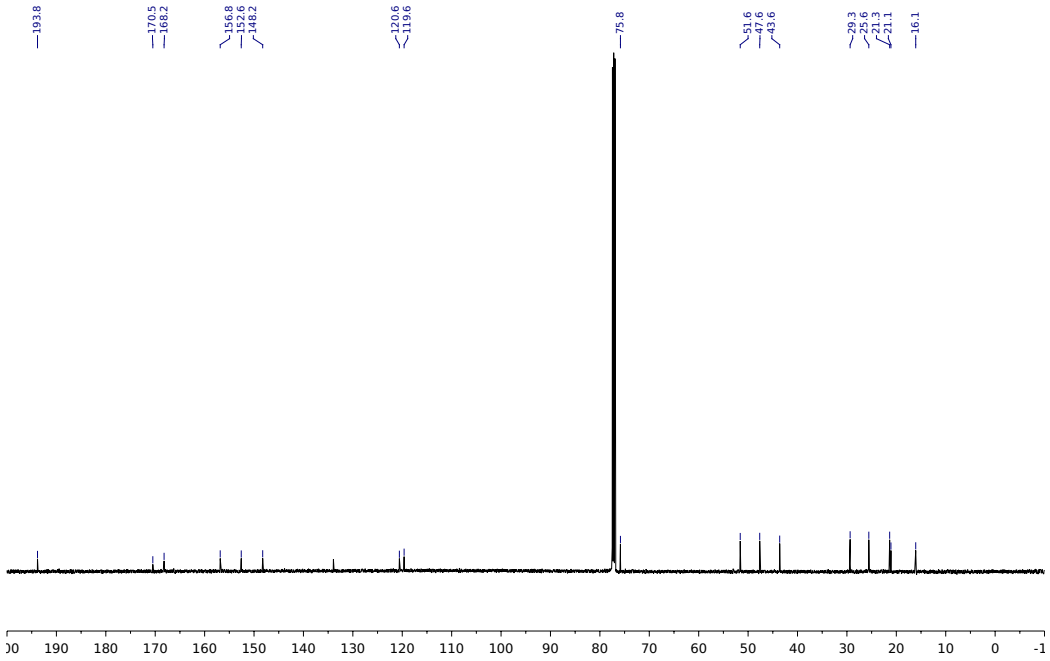
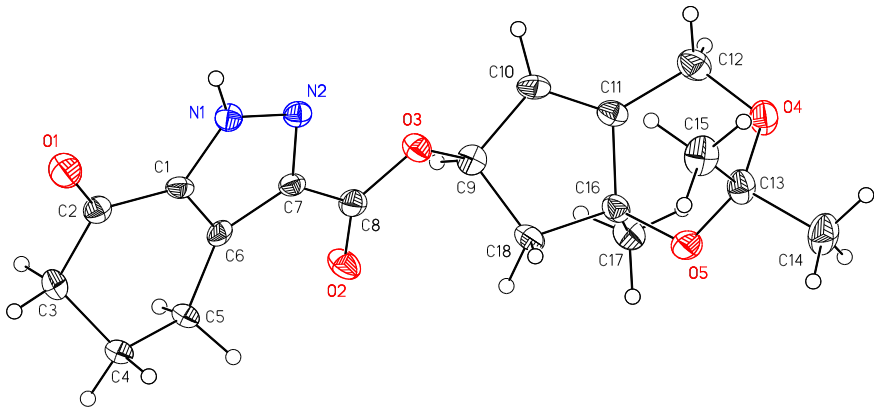


Figure SI.119 ^{13}C NMR (125 MHz, $CDCl_3$) of compound **49**

Crystal Structure Analysis of Pyrazole 21



Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 656609.

Crystal data for pyrazole **21** (CCDC 656609)

Empirical formula	$C_{18}H_{22}N_2O_5$
Formula weight	346.38
Crystallization Solvent	Not given
Crystal Habit	Column
Crystal size	0.41 x 0.28 x 0.19 mm^3
Crystal color	Colorless

Data collection for pyrazole **21** (CCDC 656609)

Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
θ range for 5408 reflections used in lattice determination	2.38 to 32.03°
Unit cell dimensions	a = 6.970(2) Å b = 7.005(2) Å c = 34.186(11) Å
Volume	1669.1(9) $Å^3$
Z	4
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Density (calculated)	1.378 mg/m^3
F(000)	736
Data collection program	Bruker SMART v5.630
θ range for data collection	2.38 to 36.11°
Completeness to θ = 36.11°	76.6 %
Index ranges	$-8 \le h \le 10, -10 \le k \le 9, -45 \le l \le 54$
Data collection scan type	ω scans at 4 ϕ settings
Data reduction program	Bruker SAINT v6.45A
Reflections collected	15494
Independent reflections	5579 [R_{int}= 0.1208]
Absorption coefficient	0.101 mm^{-1}
Absorption correction	None
Max. and min. transmission	0.9810 and 0.9597

Structure solution and refinement for pyrazole **21** (CCDC 656609)

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	5579 / 0 / 229
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.298
Final R indices [I>2σ(I), 3654 reflections]	R1 = 0.0694, *w*R2 = 0.1073
R indices (all data)	R1 = 0.1046, *w*R2 = 0.1141
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.001
Average shift/error	0.000
Absolute structure determination	Not able to reliably determine absolute conformation
Absolute structure parameter	0.2(12)
Largest diff. peak and hole	0.422 and -0.342 e.Å^{-3}

Spectral Refinement Details for Pyrazole 21

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt), etc., and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account

individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for pyrazole **21** (CCDC 656609). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	8129(2)	6441(3)	6756(1)	29(1)
O(2)	527(2)	6007(2)	7862(1)	26(1)
O(3)	2492(2)	6164(2)	8378(1)	21(1)
O(4)	-159(2)	8678(2)	9815(1)	27(1)
O(5)	-1479(2)	9411(2)	9205(1)	26(1)
N(1)	6724(3)	6421(3)	7577(1)	19(1)
N(2)	5613(3)	6387(3)	7891(1)	18(1)
C(1)	5703(3)	6412(3)	7239(1)	17(1)
C(2)	6436(3)	6325(3)	6839(1)	19(1)
C(3)	4890(3)	6008(3)	6539(1)	24(1)
C(4)	3014(3)	7014(3)	6646(1)	21(1)
C(5)	2241(3)	6406(3)	7042(1)	20(1)
C(6)	3815(3)	6393(3)	7337(1)	17(1)
C(7)	3819(3)	6357(3)	7746(1)	17(1)
C(8)	2126(3)	6165(3)	7997(1)	20(1)
C(9)	832(3)	5747(3)	8627(1)	20(1)
C(10)	1545(3)	5599(3)	9039(1)	21(1)
C(11)	450(3)	6555(3)	9284(1)	20(1)
C(12)	645(4)	6878(3)	9711(1)	27(1)
C(13)	-263(4)	10052(3)	9509(1)	24(1)
C(14)	-1250(4)	11746(3)	9686(1)	34(1)
C(15)	1716(4)	10556(4)	9355(1)	31(1)
C(16)	-1210(3)	7474(3)	9076(1)	21(1)
C(17)	-3087(3)	6460(4)	9153(1)	26(1)
C(18)	-603(3)	7381(3)	8646(1)	22(1)

Bond lengths [Å] and angles [°] for pyrazole **21** (CCDC 656609)

O(1)-C(2)	1.216(3)	O(1)-C(2)-C(1)	123.74(19)
O(2)-C(8)	1.211(2)	O(1)-C(2)-C(3)	123.06(19)
O(3)-C(8)	1.327(2)	C(1)-C(2)-C(3)	113.17(18)
O(3)-C(9)	1.467(2)	C(2)-C(3)-C(4)	112.45(17)
O(4)-C(13)	1.423(3)	C(5)-C(4)-C(3)	112.74(18)
O(4)-C(12)	1.425(3)	C(6)-C(5)-C(4)	110.20(18)
O(5)-C(13)	1.415(3)	C(1)-C(6)-C(7)	104.29(17)
O(5)-C(16)	1.439(3)	C(1)-C(6)-C(5)	122.95(18)
N(1)-N(2)	1.323(2)	C(7)-C(6)-C(5)	132.8(2)
N(1)-C(1)	1.358(2)	N(2)-C(7)-C(6)	111.65(18)
N(2)-C(7)	1.345(3)	N(2)-C(7)-C(8)	122.42(17)
C(1)-C(6)	1.359(3)	C(6)-C(7)-C(8)	125.78(19)
C(1)-C(2)	1.459(3)	O(2)-C(8)-O(3)	123.5(2)
C(2)-C(3)	1.504(3)	O(2)-C(8)-C(7)	121.78(18)
C(3)-C(4)	1.529(3)	O(3)-C(8)-C(7)	114.76(19)
C(4)-C(5)	1.519(3)	O(3)-C(9)-C(10)	107.39(17)
C(5)-C(6)	1.491(3)	O(3)-C(9)-C(18)	113.16(17)
C(6)-C(7)	1.398(3)	C(10)-C(9)-C(18)	103.33(17)
C(7)-C(8)	1.464(3)	C(11)-C(10)-C(9)	111.7(2)
C(9)-C(10)	1.495(3)	C(10)-C(11)-C(12)	130.6(2)
C(9)-C(18)	1.521(3)	C(10)-C(11)-C(16)	111.37(18)
C(10)-C(11)	1.316(3)	C(12)-C(11)-C(16)	118.0(2)
C(11)-C(12)	1.484(3)	O(4)-C(12)-C(11)	110.19(17)
C(11)-C(16)	1.502(3)	O(5)-C(13)-O(4)	110.81(18)
C(13)-C(14)	1.499(3)	O(5)-C(13)-C(14)	105.85(19)
C(13)-C(15)	1.518(3)	O(4)-C(13)-C(14)	105.18(18)
C(16)-C(17)	1.512(3)	O(5)-C(13)-C(15)	111.29(18)
C(16)-C(18)	1.531(3)	O(4)-C(13)-C(15)	111.50(19)
		C(14)-C(13)-C(15)	111.9(2)
C(8)-O(3)-C(9)	114.78(16)	O(5)-C(16)-C(11)	111.12(18)
C(13)-O(4)-C(12)	115.78(16)	O(5)-C(16)-C(17)	106.05(19)
C(13)-O(5)-C(16)	116.51(17)	C(11)-C(16)-C(17)	112.52(18)
N(2)-N(1)-C(1)	112.58(17)	O(5)-C(16)-C(18)	111.75(18)
N(1)-N(2)-C(7)	104.28(15)	C(11)-C(16)-C(18)	102.84(19)
N(1)-C(1)-C(6)	107.18(17)	C(17)-C(16)-C(18)	112.72(18)
N(1)-C(1)-C(2)	127.87(19)	C(9)-C(18)-C(16)	104.75(17)
C(6)-C(1)-C(2)	124.86(19)		