

Supporting Information

Total Synthesis of Cananginone C and Structural Revision of Debilisone A

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- 1. General Experimental Procedure: S2**
- 2. X-ray Structure Determination of Compound 22: S(3- 4)**
- 3. NMR Comparison Tables: S(5-7)**
- 4. Copies of Spectra: S(8-43)**

General Experimental Procedures:

All moisture sensitive reactions were performed in oven or flame-dried glassware with Teflon coated magnetic stirring bar under argon atmosphere using dry, freshly distilled solvents, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via a gastight syringe and a stainless-steel needle. Reactions were monitored by thin layer chromatography (TLC, Silica gel 60 F₂₅₄) plates with UV light, ethanolic anisaldehyde (with 1% AcOH and 3.3% conc. H₂SO₄)-heat and aqueous KMnO₄ (with K₂CO₃ and 10% aqueous NaOH solution) as developing agents. All workup and purification procedures were carried out with reagent-grade solvents under ambient atmosphere unless otherwise stated. Column chromatography was performed using silica gel 60-120 mesh, 100-200 mesh and 230-400 mesh. Yields mentioned as chromatographically and spectroscopically homogeneous materials unless otherwise stated. Optical rotations were measured using sodium (589, D line) lamp and are reported as follows: $[\alpha]^{25}_D$ (c = mg/100 ml, solvent). Melting points of solids were measured in melting point apparatus. IR spectra were recorded as thin films (for liquids) or KBr matrix (for solids). HRMS were taken using Quadruple TOF (Q-TOF) micro MS system using electrospray ionisation (ESI) technique. ¹H NMR spectra were recorded on 300, 400 and 500 MHz spectrometers in appropriate solvents and calibrated using residual undeuterated solvent as an internal reference (taken CDCl₃ as δ 7.26), and the chemical shifts are shown in δ ppm scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved lines) etc. ¹³C and 2D NMR spectra were recorded on 75, 100 and 125 MHz spectrometers.

X-ray structure determination of Compound 22.

Diffraction-quality crystals of compound **22** were obtained from toluene-dichloromethane mixture. A single crystal, coated with Parabar oil, was mounted under cold nitrogen stream (150 K). Data were collected on a Bruker SMART APEX-II diffractometer that uses a graphite-monochromated Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$). The operations were controlled by the APEX 2 (v. 2010.1–2) software package. Raw data was integrated and corrected for Lorentz and polarization effects using the Bruker APEX II program suite.¹ Absorption correction was performed using SADABS. Space group was assigned using XPREP by analysis of metric symmetry and systematic absences. The structure was solved by direct method and refined against all data in the reported 2θ ranges by full-matrix least squares on F2 with the SHELXL program suite.² Hydrogen atoms at idealized positions were included in final refinements. The OLEX 2³ interface was used for structure visualization and drawing ORTEP^{4, 5} plots. Crystallographic data and final agreement factors for compound **22** are provided in Table 1.

Table 1. X-ray crystallographic data for compound **22** at 150 K^a

compound	22
formula	C ₁₇ H ₂₈ O ₃
formula weight	280.39
crystal system	orthorhombic
space group	P2 ₁ 2 ₁ 2 ₁
a, Å	4.672(4)
b, Å	5.359(4)
c, Å	67.02(5)
V, Å ³	1678(2)
Z	4
ρ_{calcd} , gm/cm ³	1.110
μ , mm ⁻¹	0.074
θ range, deg	1.22 - 24.79
completeness to θ , %	98
reflections collected	4177
independent reflections	1649
R(int)	0.0519
restraints	283
parameters	183
Max., min. transmission	0.995, 0.985
R1 ^b (wR2) ^c [I>2sigma(I)]	0.0478 (0.0595)
R1 ^b (wR2) ^c	0.1322 (0.0760)
GOF(F ²) ^d	0.925
max, min peaks, e.Å ⁻³	0.103, -0.111

^aMo K α radiation ($\lambda = 0.71073$ Å). ^bR1 = $\Sigma||F_o| - |F_c|| / \Sigma|F_o|$. ^cwR2 = $\{\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]\}^{1/2}$.

^dGOF = $\{\Sigma[w(F_o^2 - F_c^2)^2] / (n-p)\}^{1/2}$, where n is the number of data and p is the number of refined parameters.

References.

1. *APEX II, 2009 Edition*; Bruker Analytical X-ray Systems, Inc.: Madison, WI, 2009.
2. G. M. Sheldrick, *Acta Crystallogr. Sect. A: Found. Crystallogr.* 2008, **64**, 112.
3. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.* 2009, **42**, 339.
4. L. J. Farrugia, *J. Appl. Crystallogr.* 1997, **30**, 565.
5. L. J. Farrugia, *J. Appl. Crystallogr.* 2012, **45**, 849.

Table 2: ¹H and ¹³C NMR comparison of Cananginone C (natural and synthetic).

δ_H of Natural (CDCl ₃ , 400 MHz)	δ_H of Synthetic (CDCl ₃ , 300 MHz)	δ_C of Natural (CDCl ₃ , 100 MHz)	δ_C of Synthetic (CDCl ₃ , 75MHz)
5.78 (ddt, 16.9, 10.2, 6.7, 1H)	5.84-5.72 (m, 1H)	179.5	179.7
4.99 (d, 17.1, 1H), 4.94 (d, 10.2, 1H)	5.04-4.92 (m, 2H)	138.4	138.6
4.58 (m, 1H)	4.62-4.56 (m, 1H)	114.6	114.8
3.54 (dd, $J=10.6, 3.5$ Hz, 1H),	3.56 (dd, $J=10.5, 3.6$ Hz, 1H),	77.5	Merged with CDCl ₃ signal
3.48 (dd, $J=10.6, 4.0$, 1H)	3.49 (dd, $J=10.8, 3.9$ Hz, 1H)	77.2	Merged with CDCl ₃ signal
3.37 (s, 3H)	3.38 (s, 3H)	76.7	Merged with CDCl ₃ signal
2.68 (m, 1H)	2.74-2.61 (m, 1H)	74.3	74.5
2.28 (m, 1H)	2.37-2.28 (m, 1H)	65.4	65.5
2.25 (t, $J=6.5$ Hz, 2H), 2.23 (t, $J=7.2$ Hz, 2H)	2.27-2.22 (m, 4H)	65.2	65.4
2.05 (q, $J=6.7$ Hz, 2H)	2.09-2.02 (m, 2H)	59.4	59.6
1.98 (ddd, $J=12.6, 8.5, 4.3$ Hz, 1H)	2.01-1.94 (m, 1H)	39.2	39.4
1.82 (m, 1H)	1.87-1.76 (m, 1H)	33.1	33.3
1.50 (m, 6H)	1.54-1.47 (m, 6H) marged with H ₂ O peak	31.1	31.3
1.38 (brs, 1H), 1.25-1.45 (m, 10H)	1.46-1.28 (m, 11H)	30.4	30.6
		29.2	29.4
		29.2	29.4
		28.9	29.1
		28.7	28.9
		28.3	28.4
		28.0	28.1
		27.7	27.9
		27.2	27.4
		19.1	19.3
		19.0	19.2

Table 3: ^1H and ^{13}C NMR comparison of Debilisone A (natural) and compound **13 (Reported Structure).**

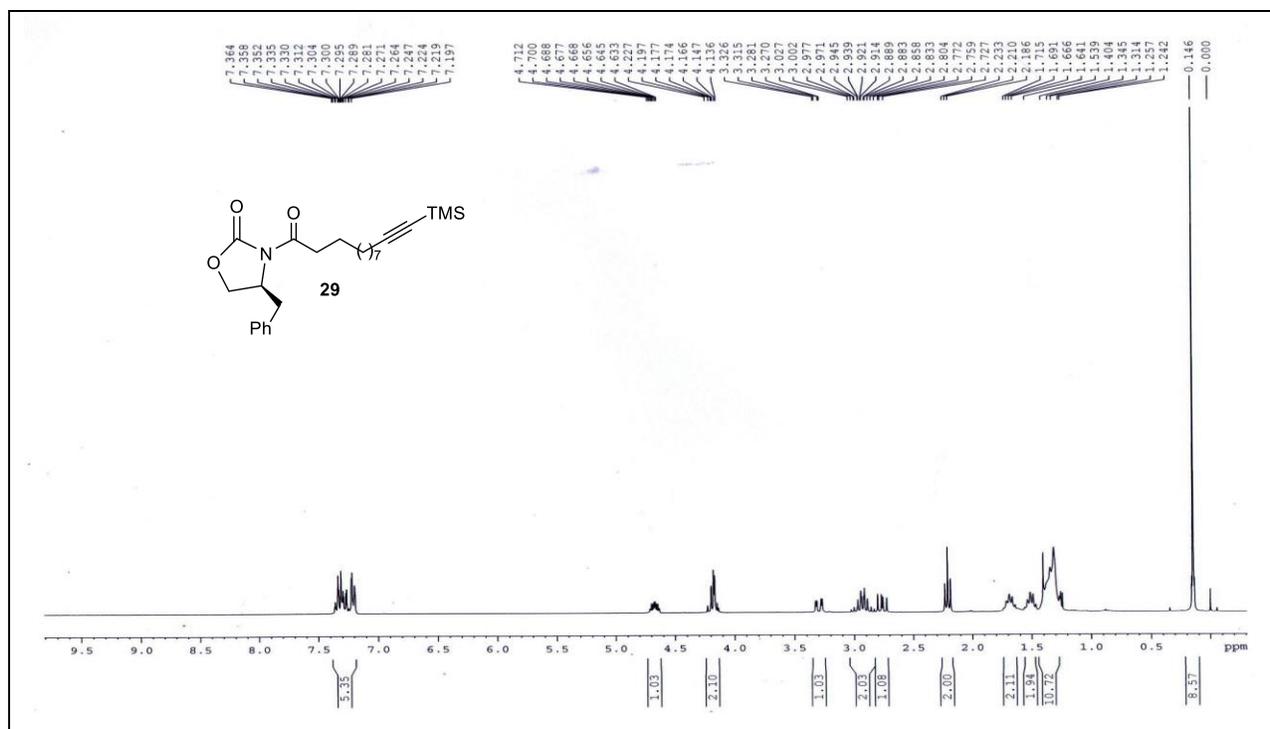
δ_{H} of Natural (CDCl ₃ , 400 MHz)	δ_{H} of compound 13 (CDCl ₃ , 300 MHz)	δ_{C} of Natural (CDCl ₃ , 100 MHz)	δ_{C} of compound 13 (CDCl ₃ , 125 MHz)
4.55 (m, 1H)	4.54-4.46 (m, 1H)	180.1	178.8
3.82 (dd, $J = 12.4, 3.6$ Hz, 1H),	3.92 (dd, $J = 12.3, 2.4$ Hz, 1H)	78.8	78.7
3.60 (dd, $J = 12.4, 4.6$ Hz, 1H)	3.63 (dd, $J = 12.6, 5.1$ Hz, 1H)	77.5	77.7
2.67 (m, 1H)	2.70-2.59 (m, 1H)	77.4	Merged with CDCl ₃ signal
2.28 (m, 1H)	2.39-2.22 (m, 1H)	65.2	65.4
2.20 (t, $J = 6.9$ Hz, 4H)	2.24 (t, $J = 6.9$ Hz, 4H)	65.2	65.4
1.95 (m, 1H)	1.95-1.85 (m, 1H)	64.3	64.1
1.77 (m, 1H)	1.82-1.74 (m, 1H)	39.6	40.8
1.47 (q, $J = 6.9$ Hz, 4H)	1.54-1.46 (m, 4H) marged with H ₂ O peak	31.2	31.4
1.23 (brs, 4H), 1.40-1.22 (m, 17 H)	1.43-1.25 (m, 21H)	31.2	30.5
0.85 (t, $J = 6.8$ Hz, 3H)	0.88 (t, $J = 6.9$ Hz, 3H)	29.6	29.8
		29.4	29.8
		29.4	29.6
		29.3	29.5
		29.3	29.5
		29.0	29.4
		28.8	29.2
		28.5	29.0
		28.3	28.7
		28.2	28.5
		27.2	27.5
		22.5	22.7
		19.1	19.4
		14.0	14.2

Table 4: ¹H and ¹³C NMR comparison of Debilisone A (natural) and Compound 33.

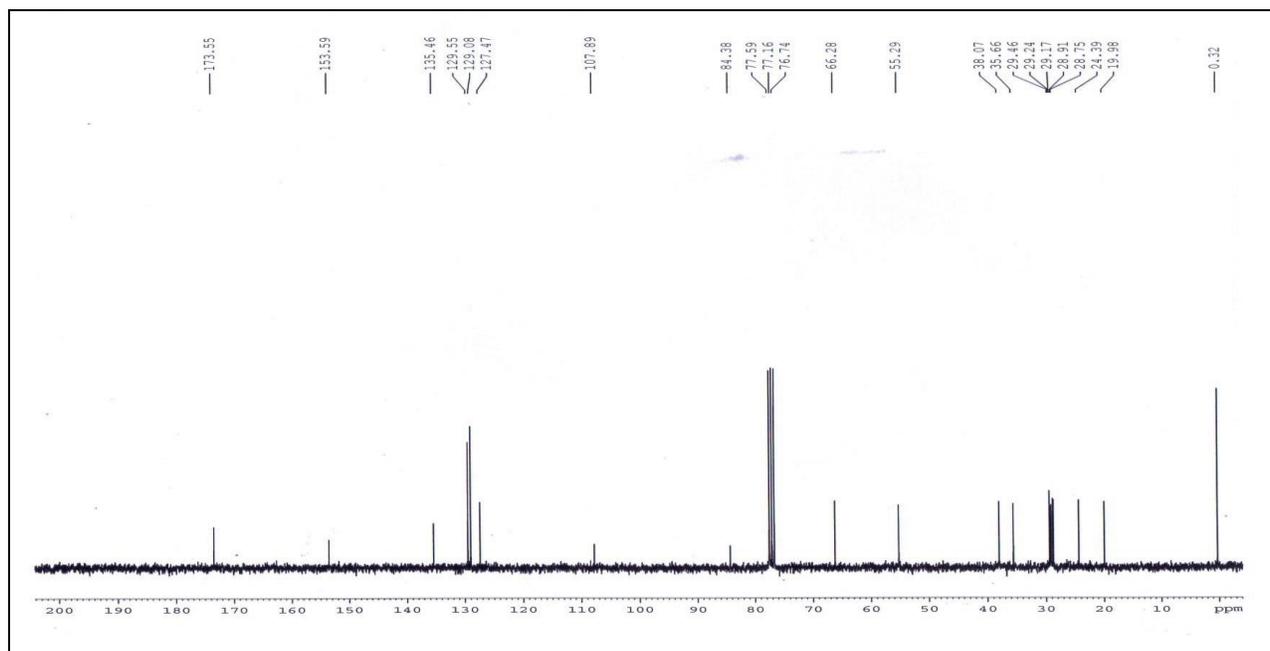
δ_{H} of Natural (CDCl ₃ , 400 MHz)	δ_{H} of compound 33 (CDCl ₃ , 300 MHz)	δ_{C} of Natural (CDCl ₃ , 100 MHz)	δ_{C} of compound 33 (CDCl ₃ , 75MHz)
4.55 (m, 1H)	4.63-4.56 (m, 1H)	180.1	179.7
3.82 (dd, $J = 12.4, 3.6$ Hz, 1H)	3.88-3.84 (m, 1H)	78.8	78.5
3.60 (dd, $J = 12.4, 4.6$ Hz, 1H)	3.67-3.63 (m, 1H)	77.5	Marged with CDCl ₃ signal
2.67 (m, 1H)	2.74-2.61 (m, 1H)	77.4	Marged with CDCl ₃ signal
2.28 (m, 1H)	2.34-2.28 (m, 1H)	65.2	65.4
2.20 (t, $J = 6.9$ Hz, 4H)	2.24 (t, $J = 6.6$ Hz, 4H)	65.2	65.4
1.95 (m, 1H)	2.05-1.96 (m, 1H)	64.3	64.9
1.77 (m, 1H)	1.85-1.81 (m, 1H)	39.6	39.7
1.47 (q, $J = 6.9$ Hz, 4H)	1.54-1.47 (m, 4H) marged with H ₂ O peak	31.2	31.4
1.23 (brs, 4H), 1.40-1.22 (m, 17 H)	1.41-1.25 (m, 21H)	31.2	31.4
0.85 (t, $J = 6.8$ Hz, 3H)	0.88 (t, $J = 6.9$ Hz, 3H)	29.6	29.8
		29.4	29.7
		29.4	29.6
		29.3	29.5
		29.3	29.5
		29.0	29.4
		28.8	29.2
		28.5	29.0
		28.3	28.7
		28.2	28.5
		27.2	27.4
		22.5	22.7
		19.1	19.4
		14.0	14.2

Spectra (^1H , ^{13}C , HRMS and 2D NMR) of compounds:

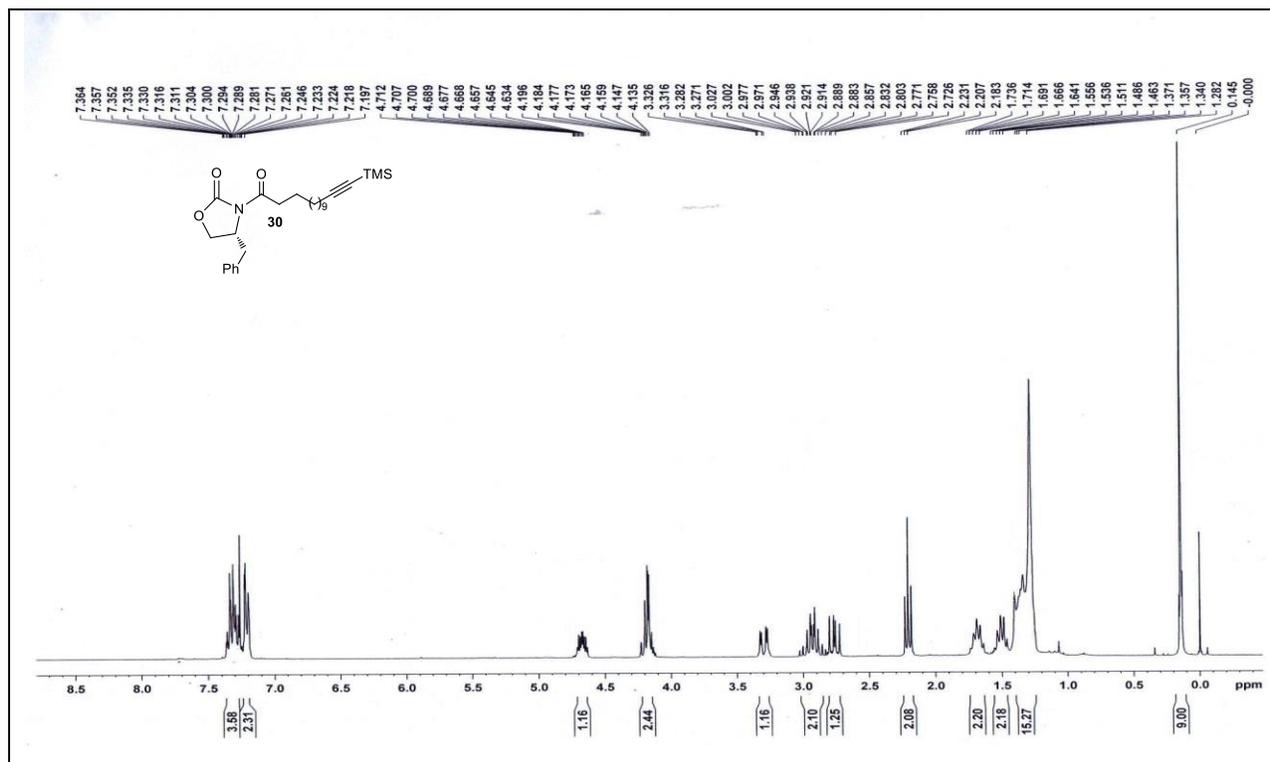
^1H NMR spectra of 29 (300 MHz, CDCl_3)



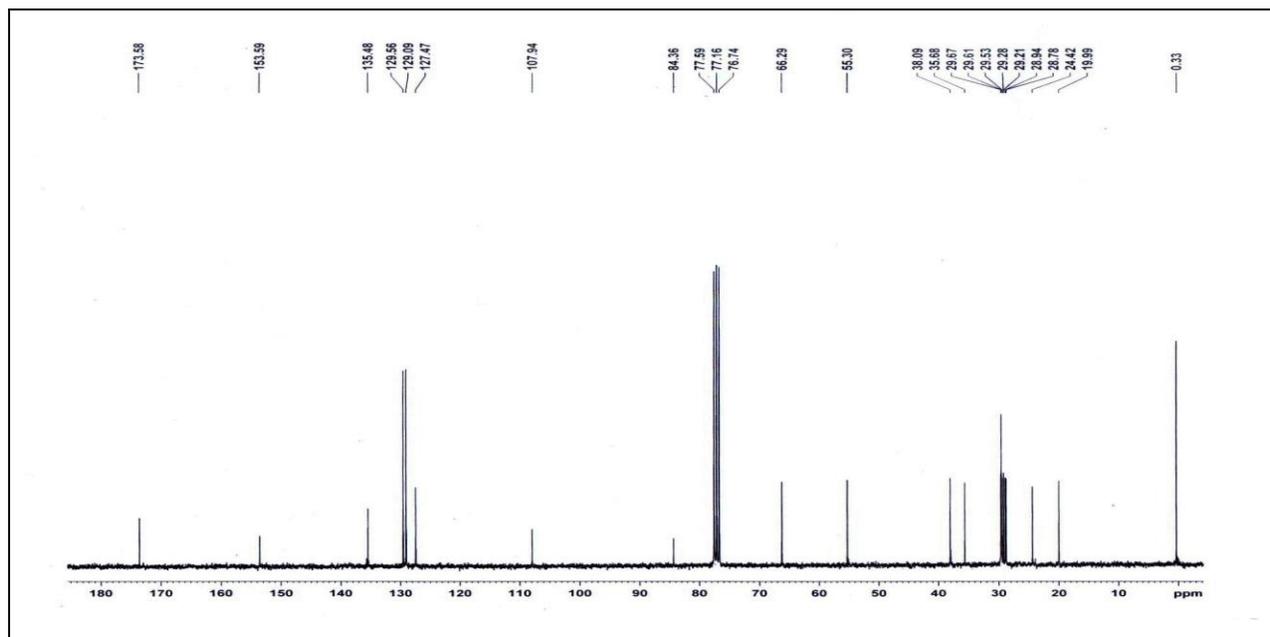
^{13}C NMR spectra of 29 (75 MHz, CDCl_3)



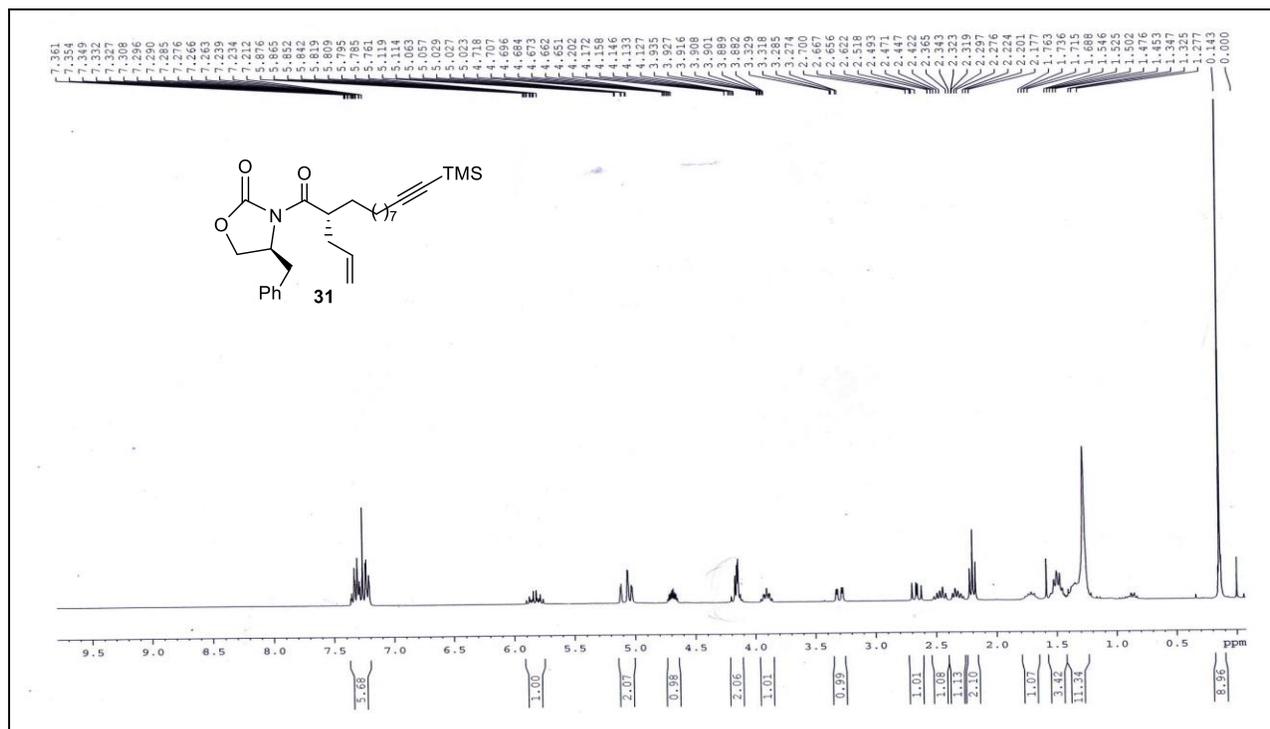
¹H NMR spectra of 30 (300 MHz, CDCl₃)



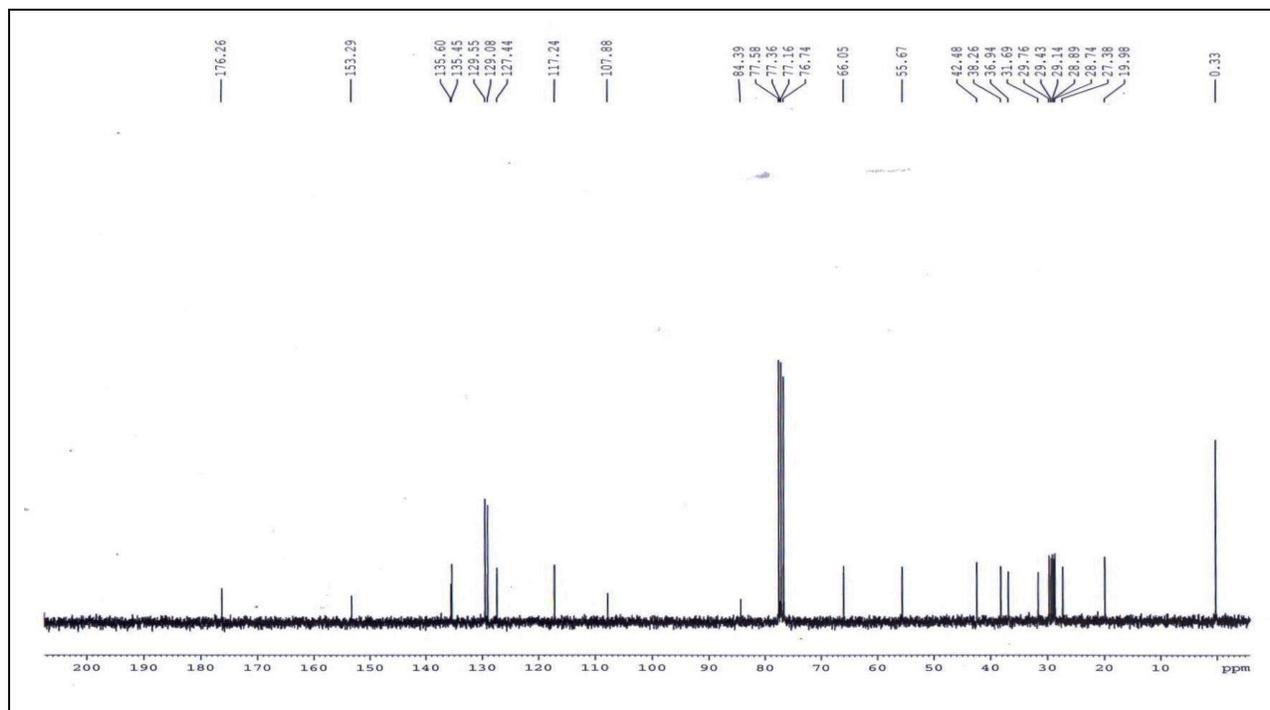
¹³C NMR spectra of 30 (75 MHz, CDCl₃)



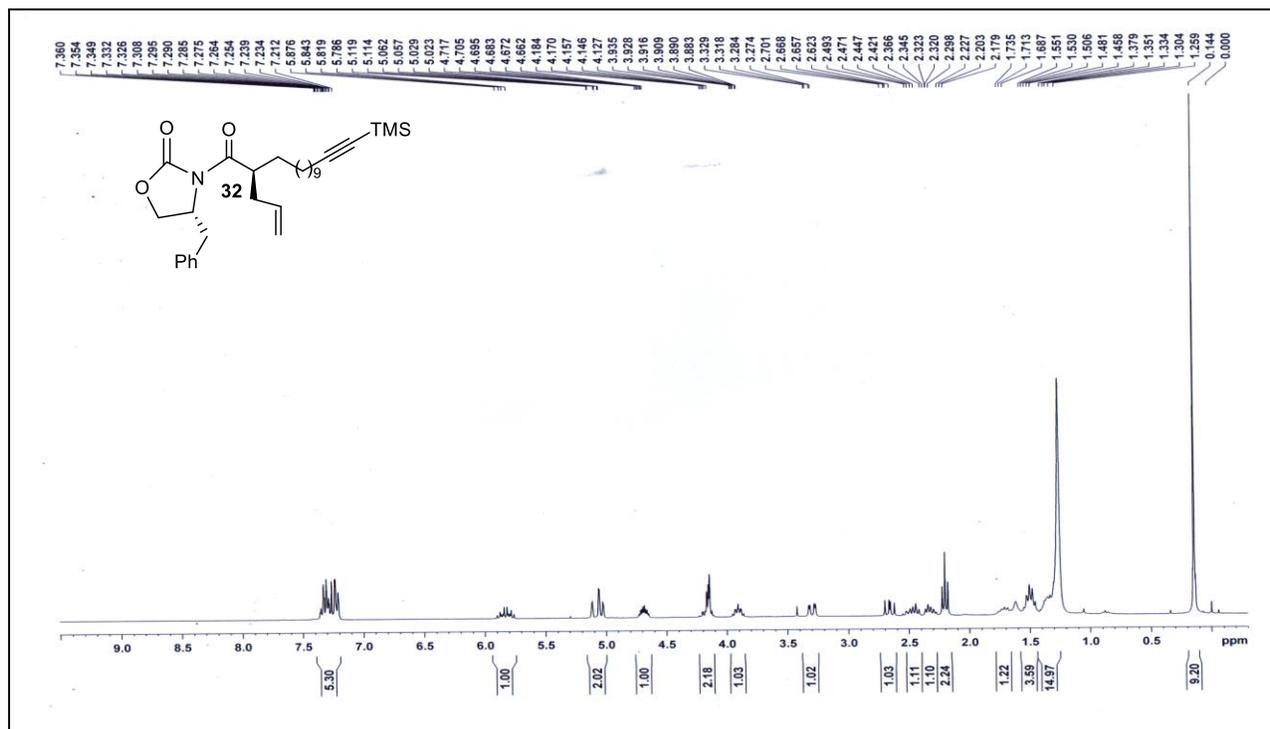
¹H NMR spectra of 31 (300 MHz, CDCl₃)



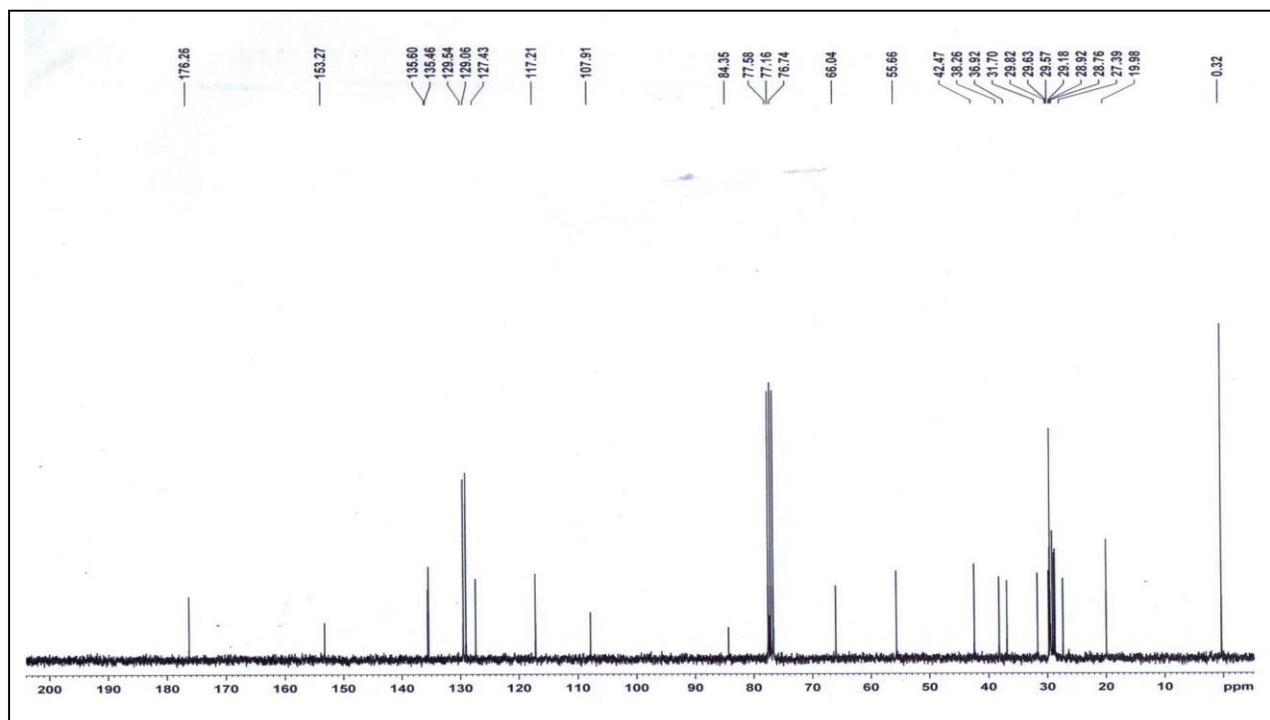
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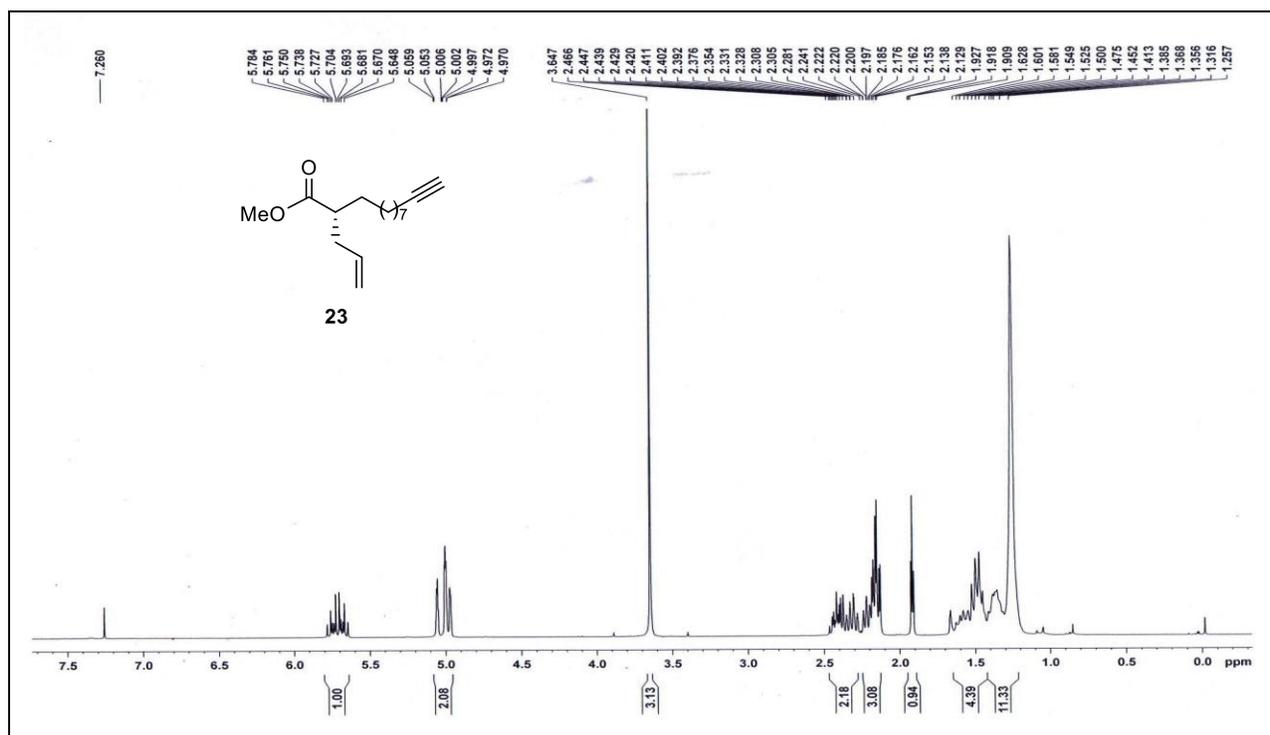
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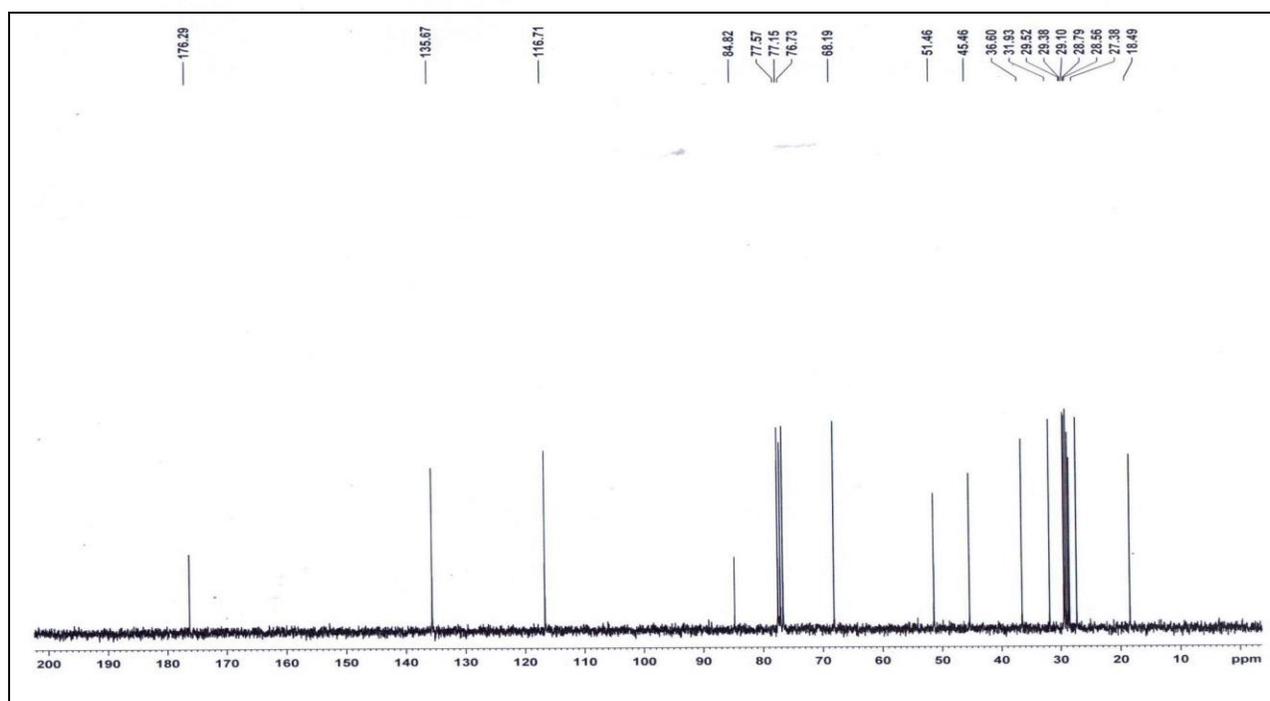
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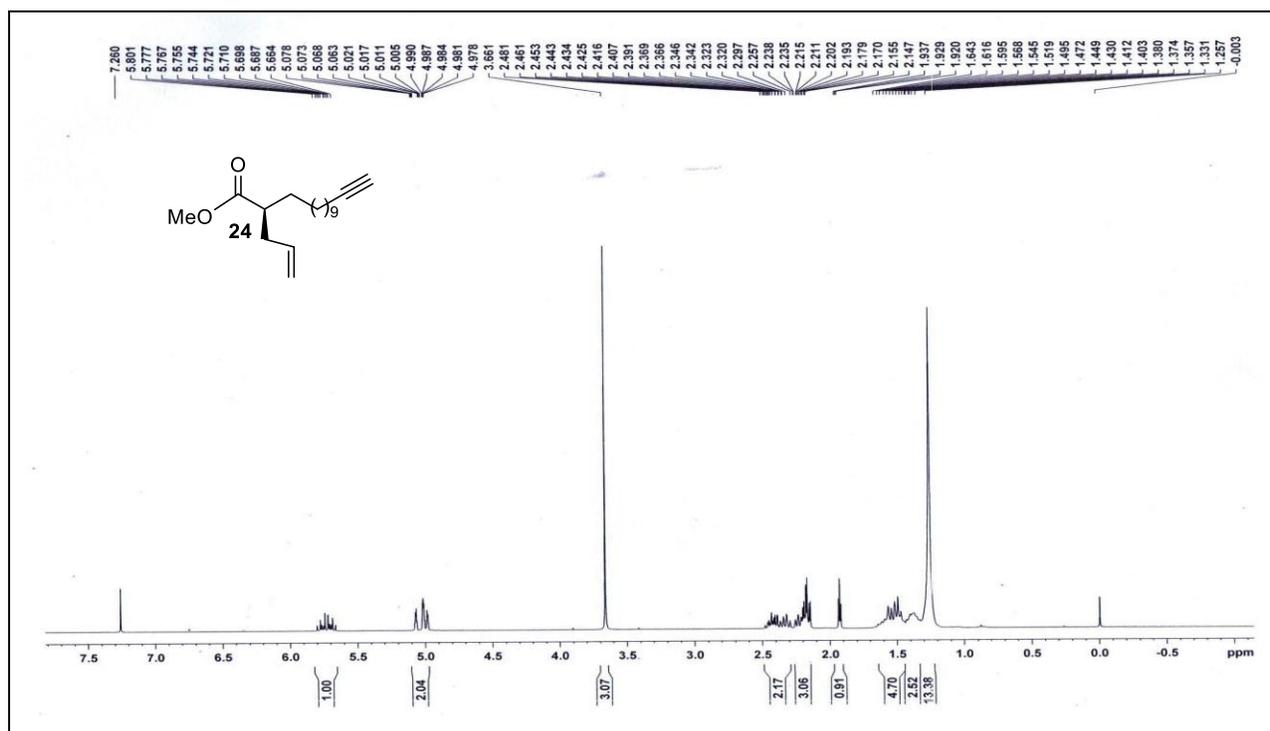
¹H NMR spectra of 23 (300 MHz, CDCl₃)



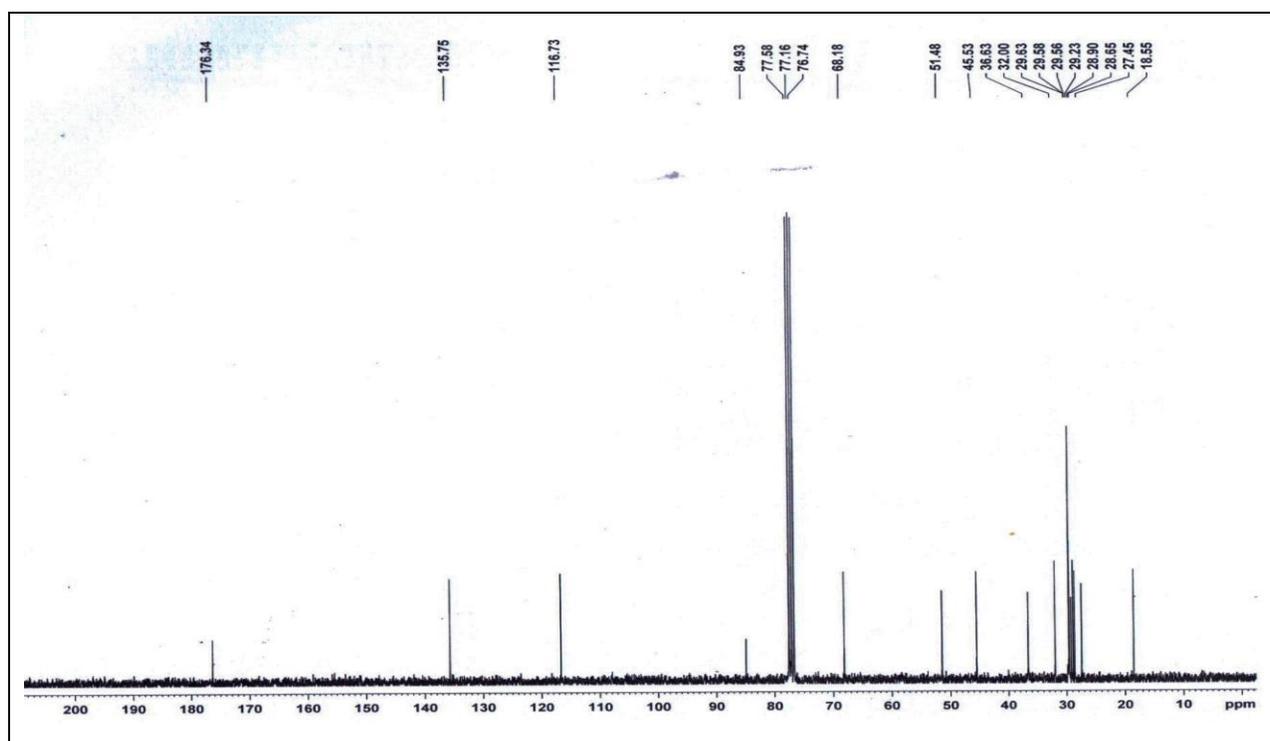
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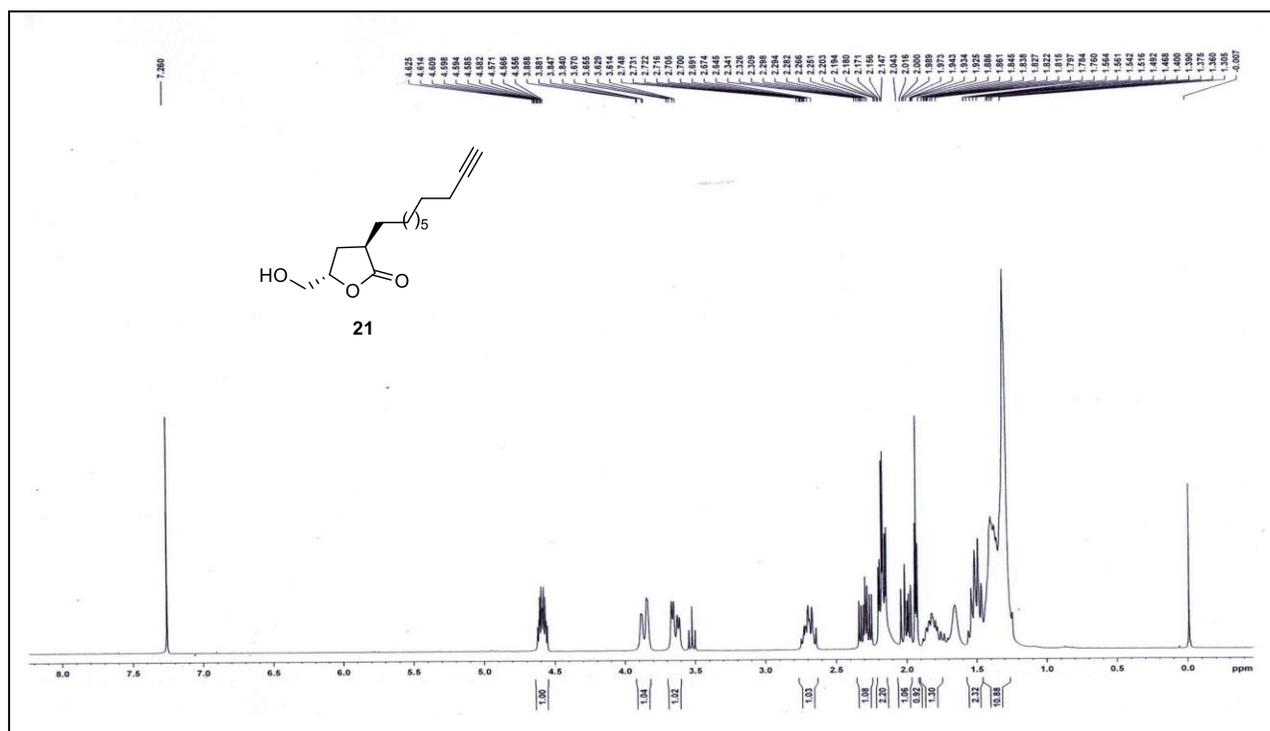
¹H NMR spectra of 24 (300 MHz, CDCl₃)



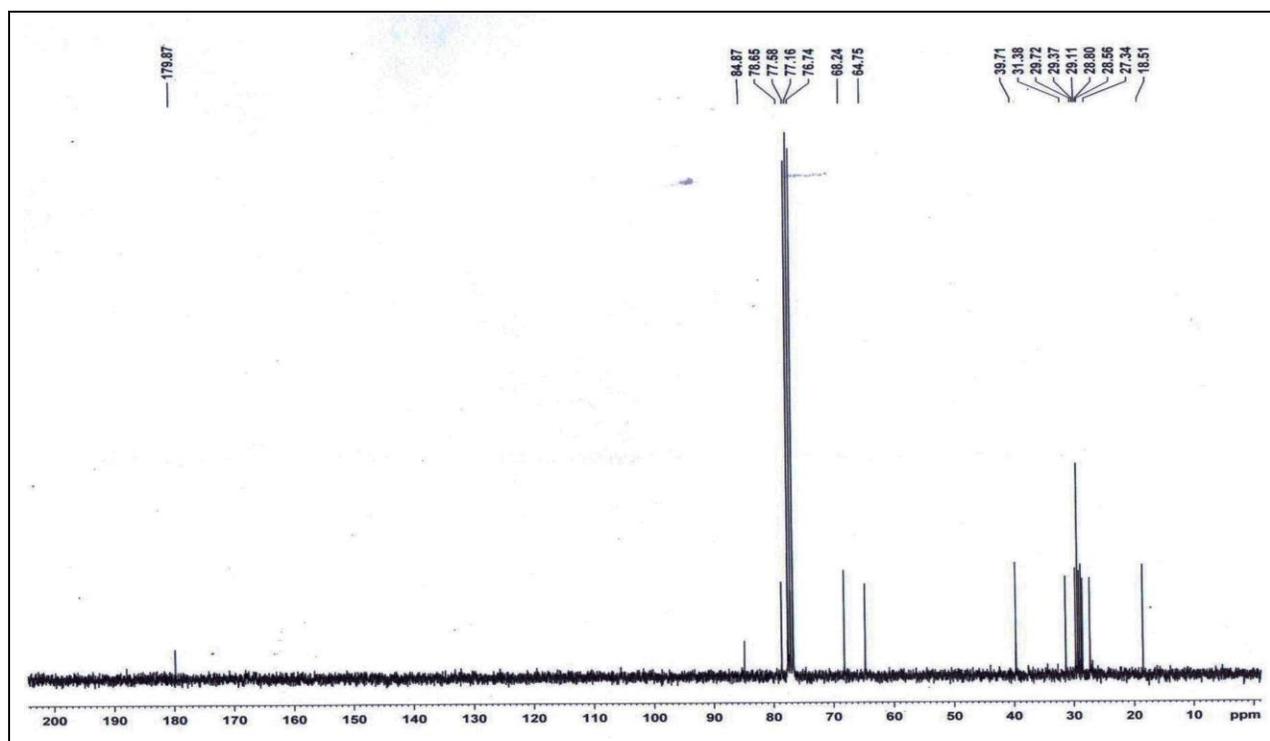
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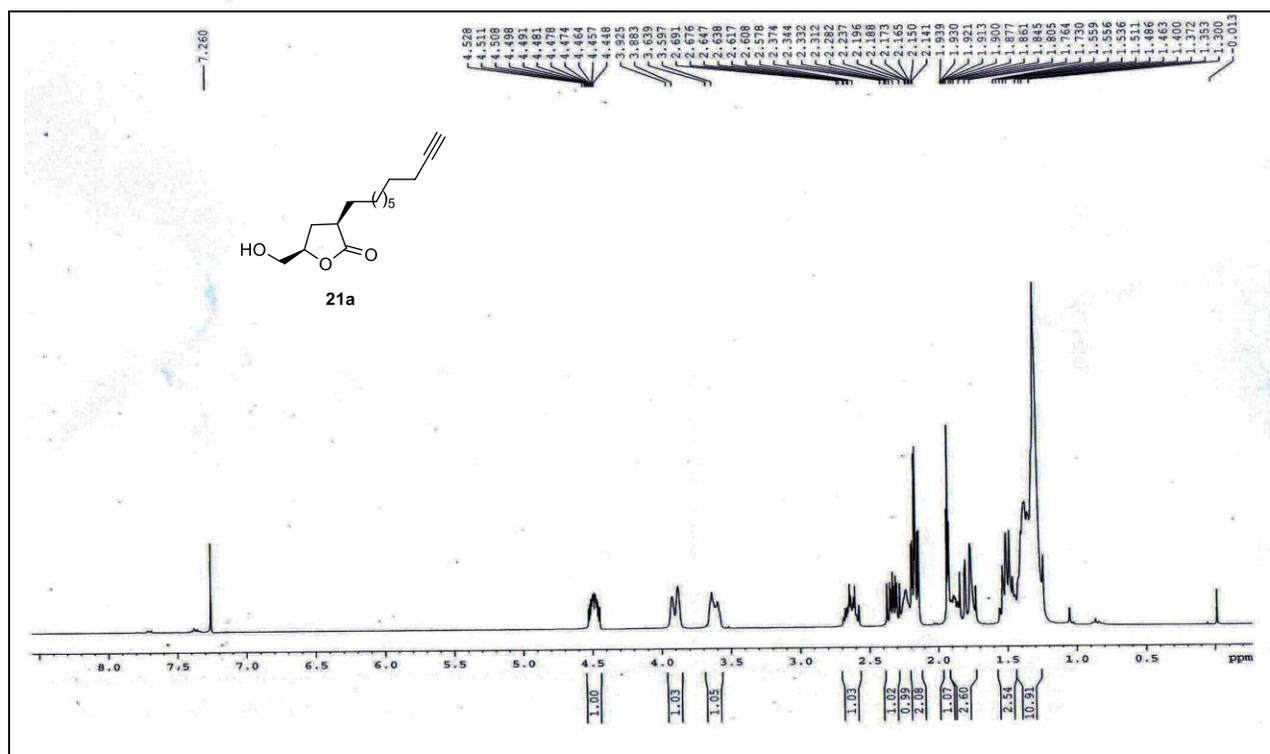
¹H NMR spectra of 21 (300 MHz, CDCl₃)



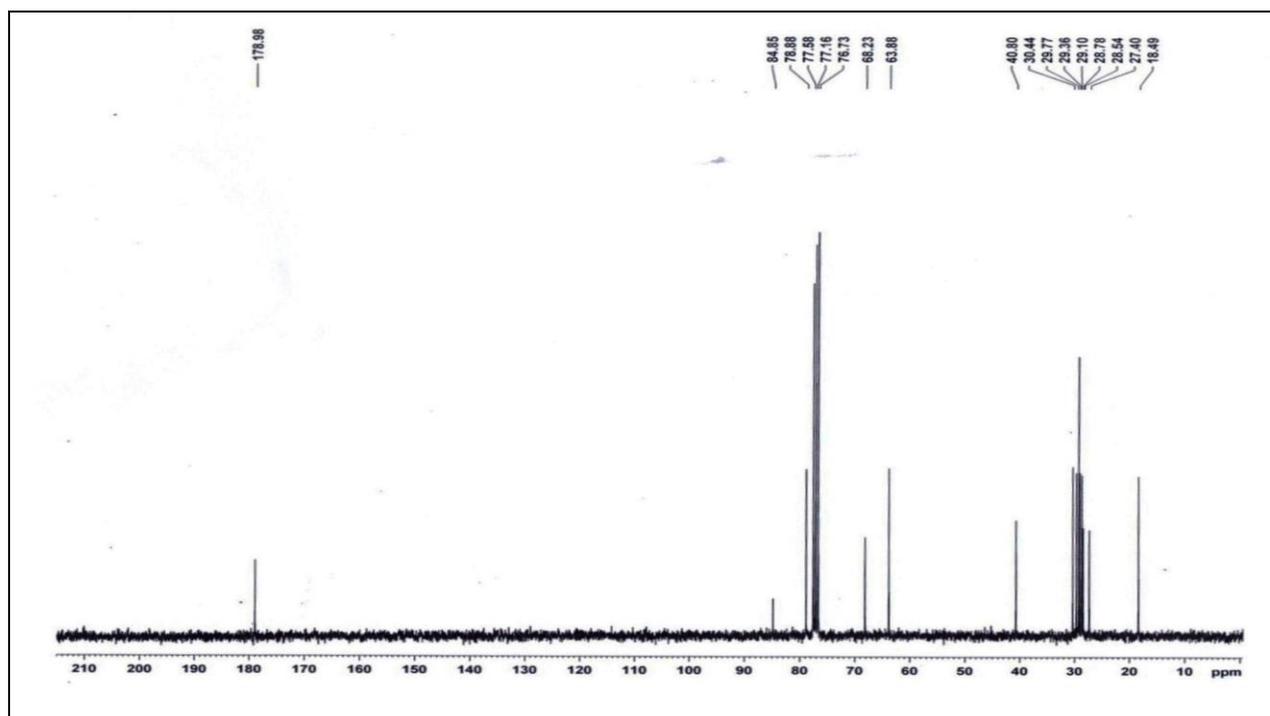
¹H NMR spectra of 21 (75 MHz, CDCl₃)



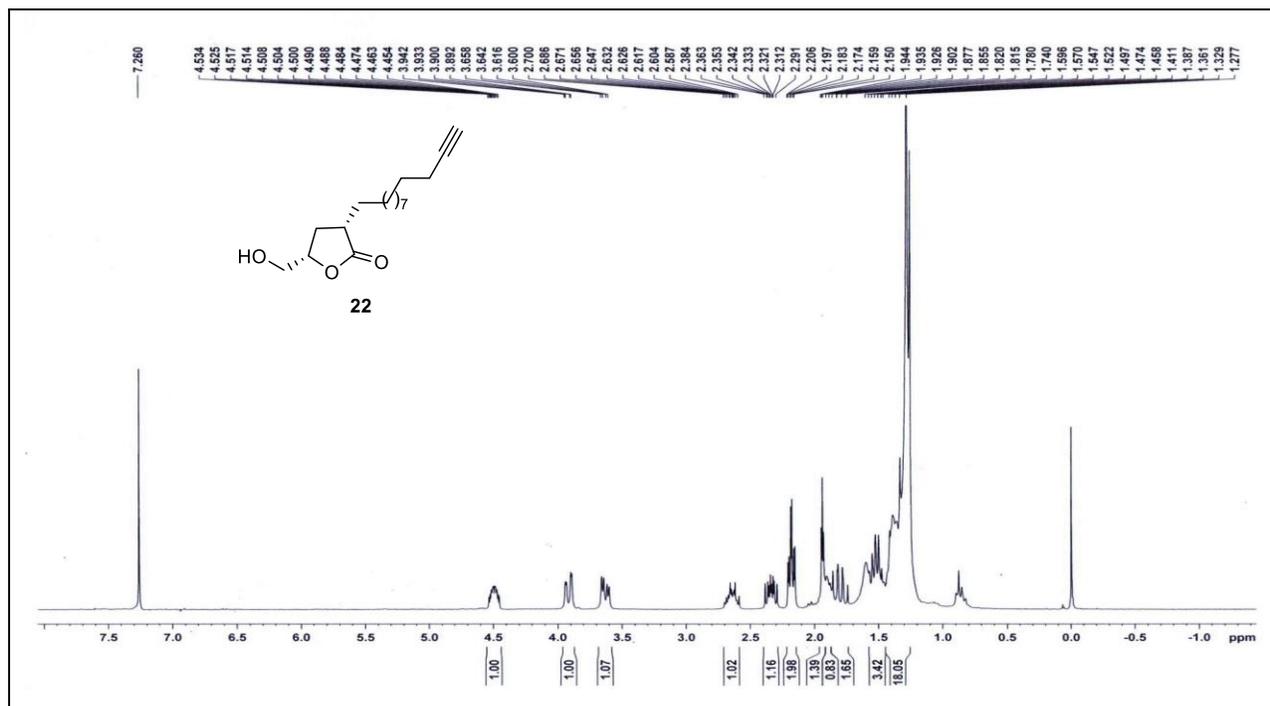
¹H NMR spectra of 21a (300 MHz, CDCl₃)



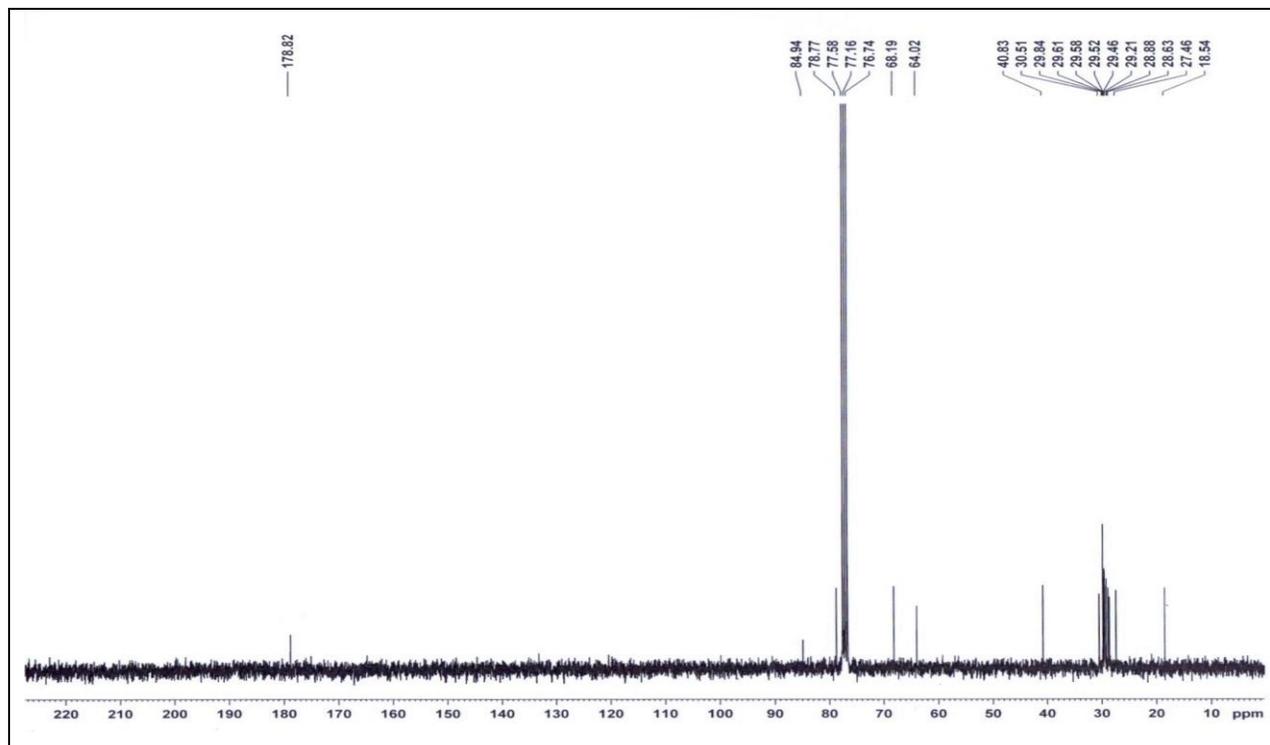
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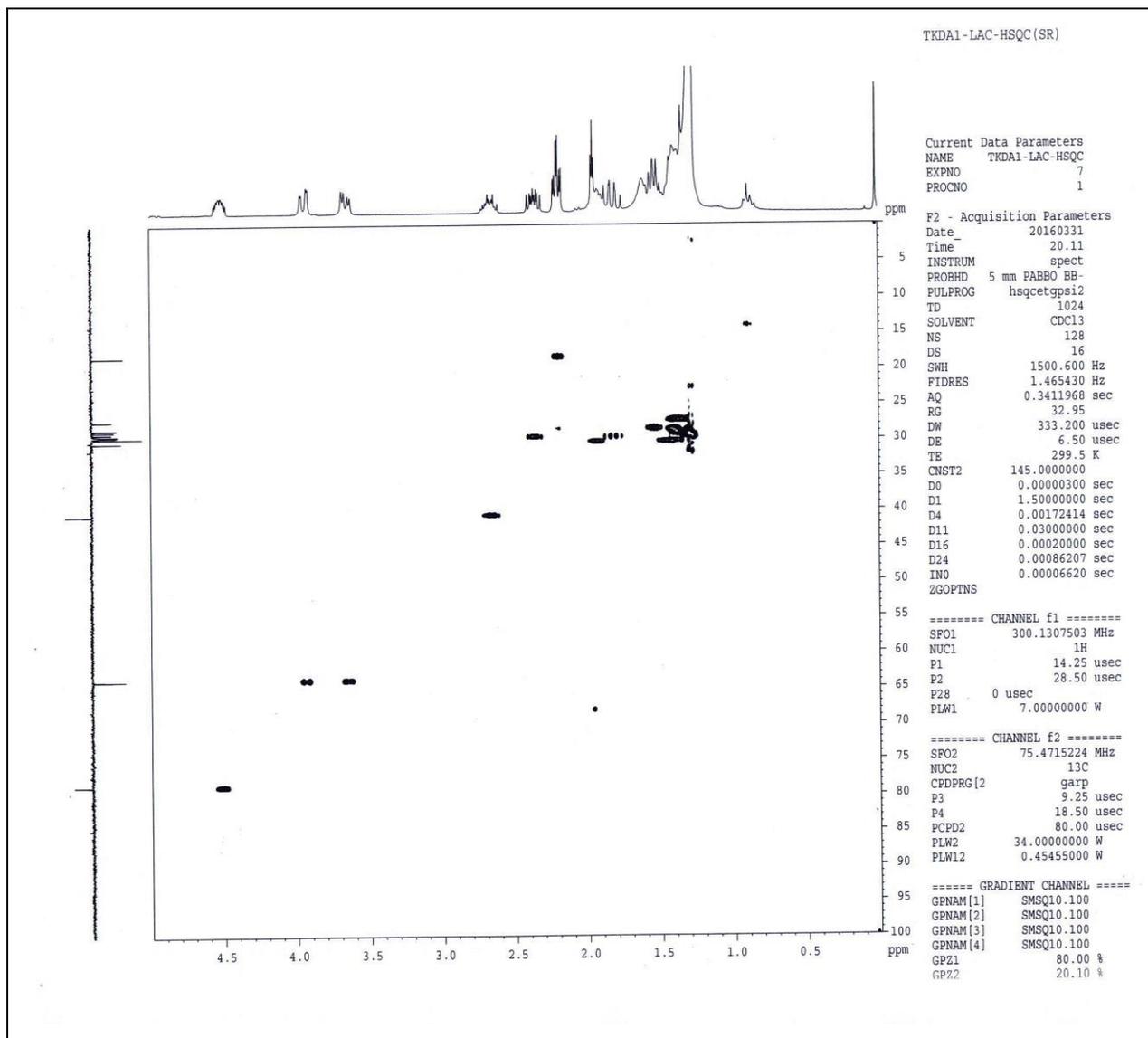
¹H NMR spectra of 22 (300 MHz, CDCl₃)



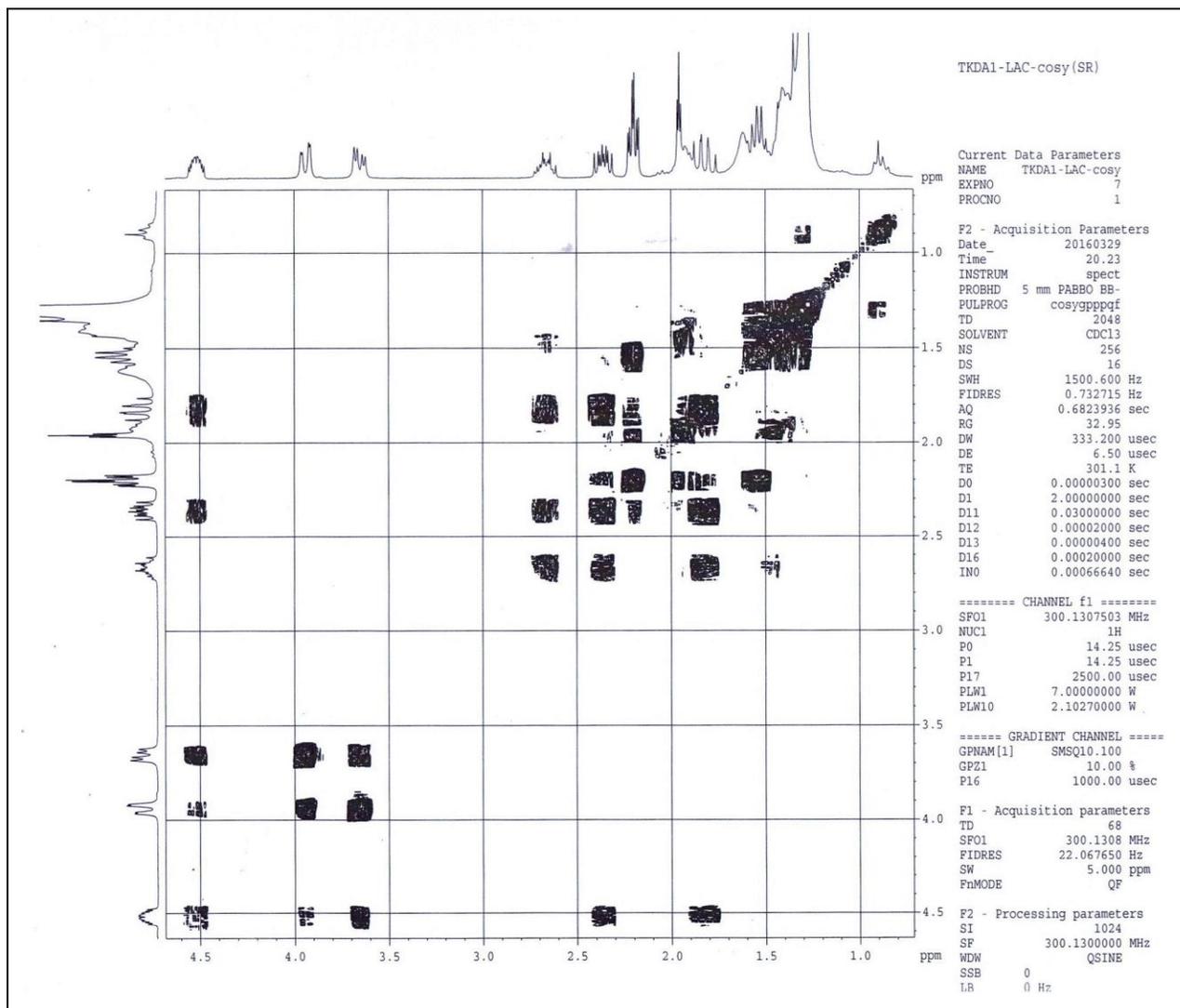
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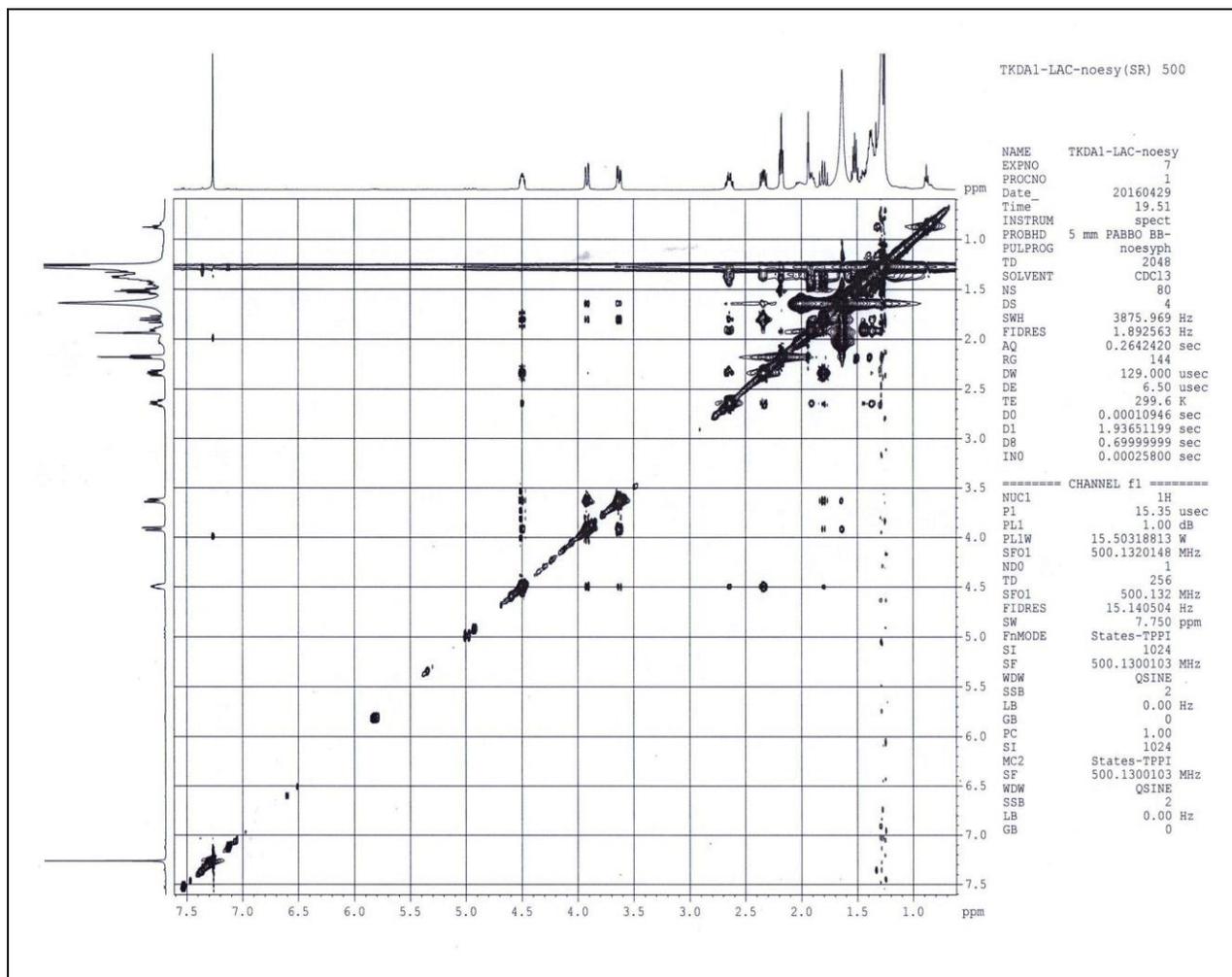
HSQC spectra of 22 (75 MHz, CDCl₃)



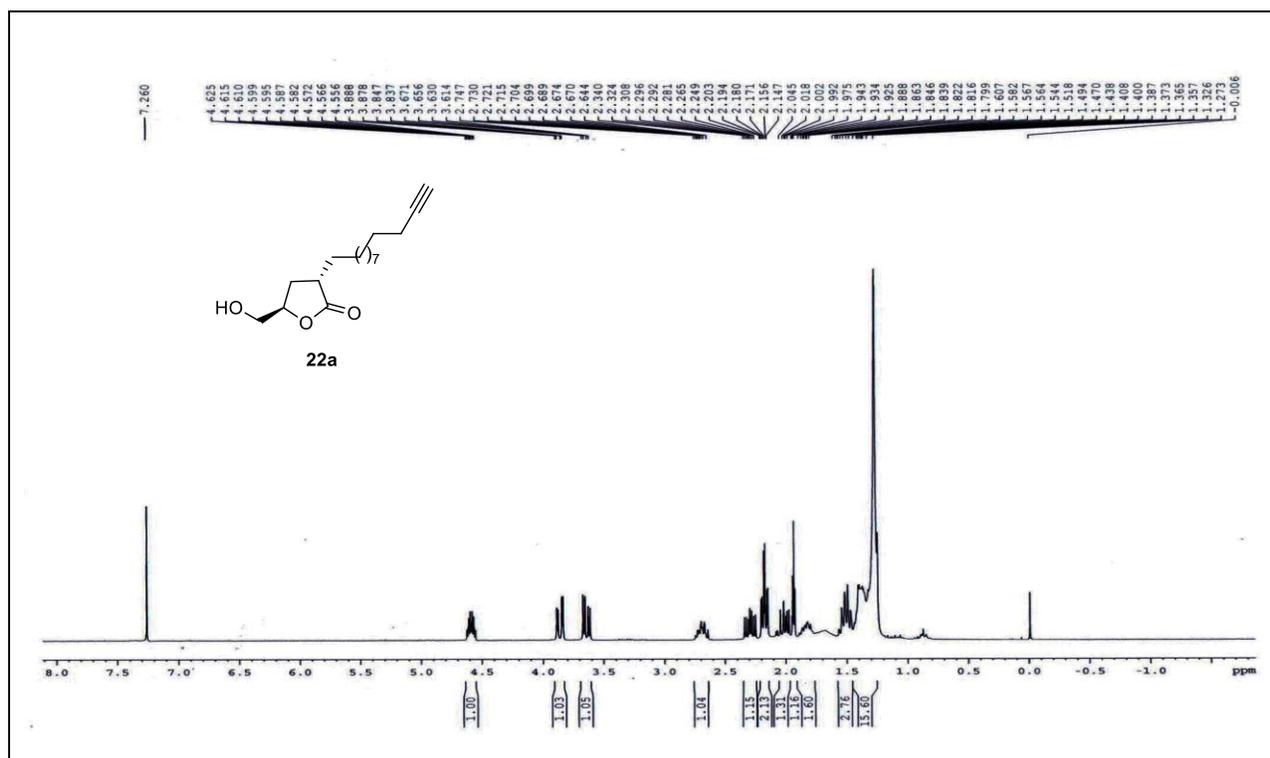
COSY spectra of 22 (300 MHz, CDCl₃)



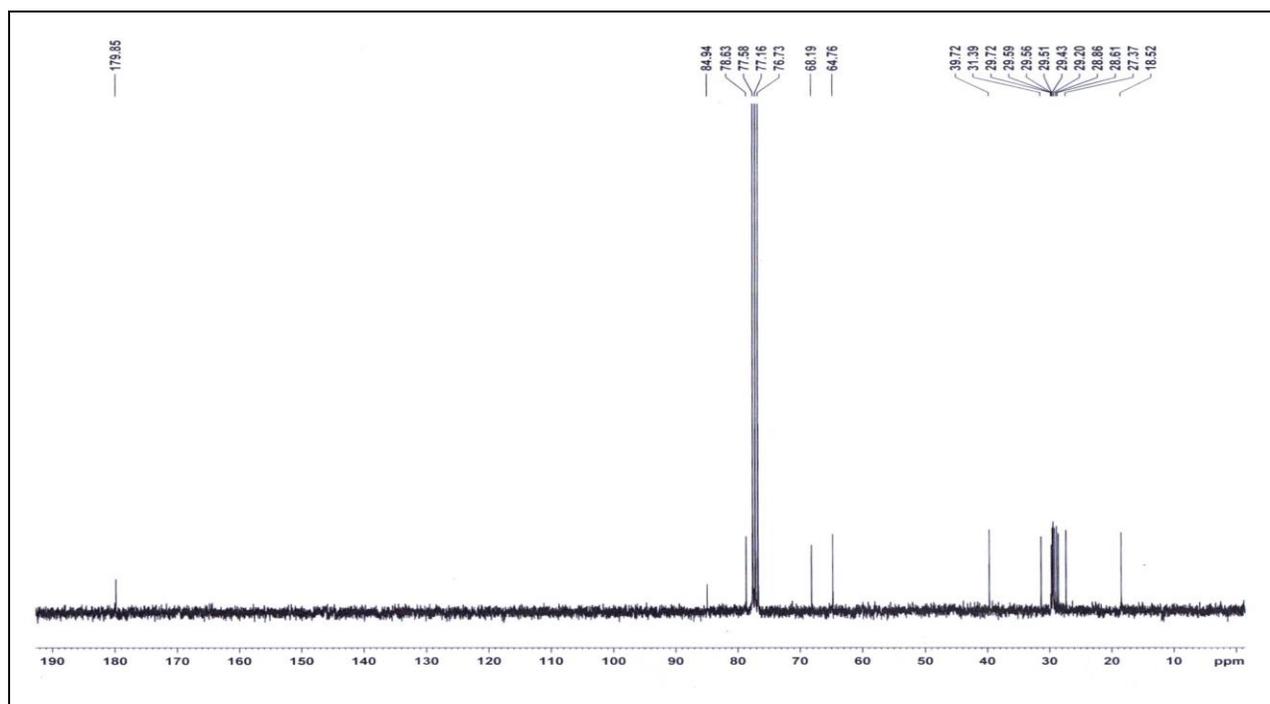
NOESY spectra of 22 (500 MHz, CDCl₃)



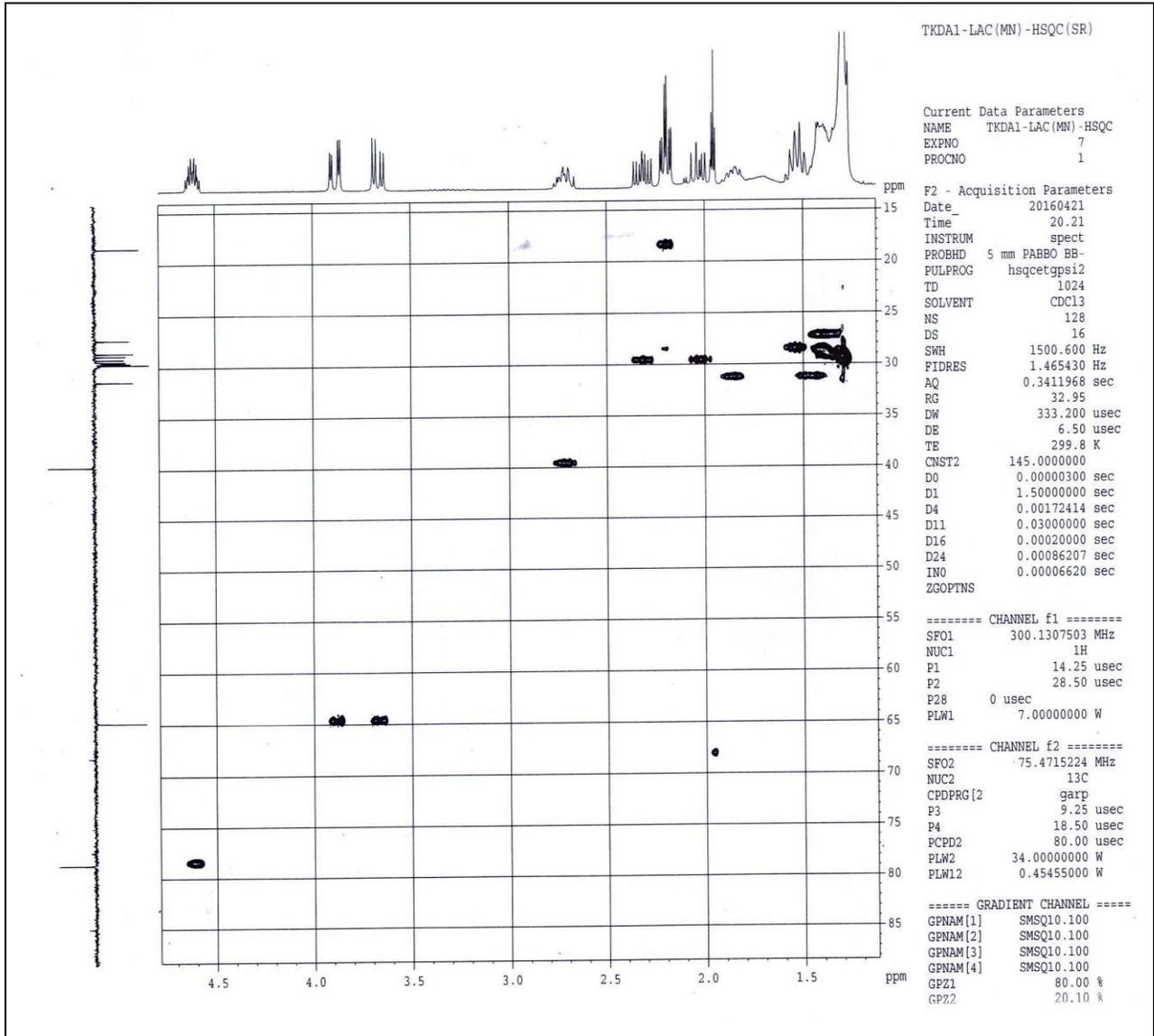
¹H NMR spectra of 22a (300 MHz, CDCl₃)



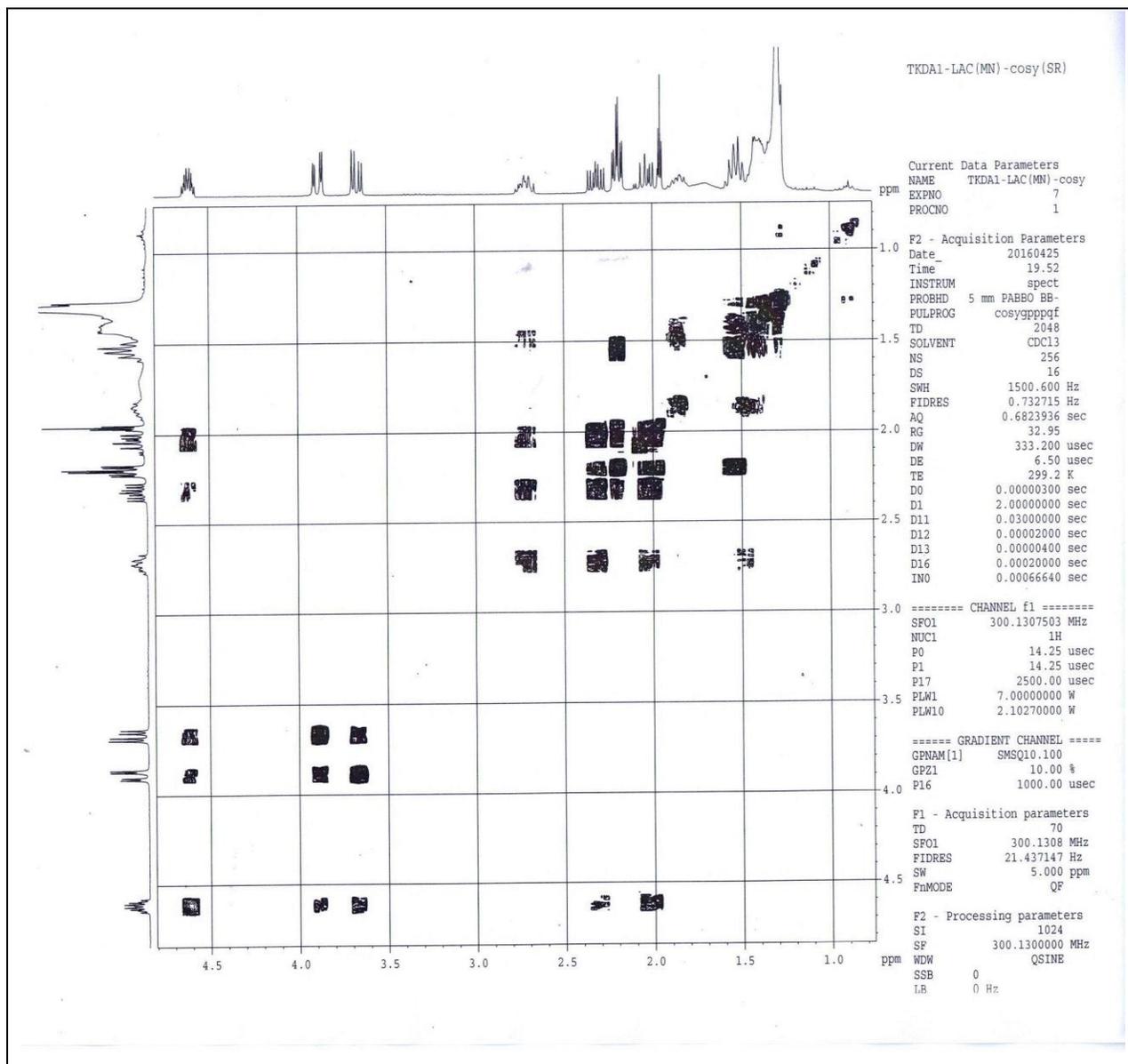
¹³C NMR spectra of 22a (75 MHz, CDCl₃)



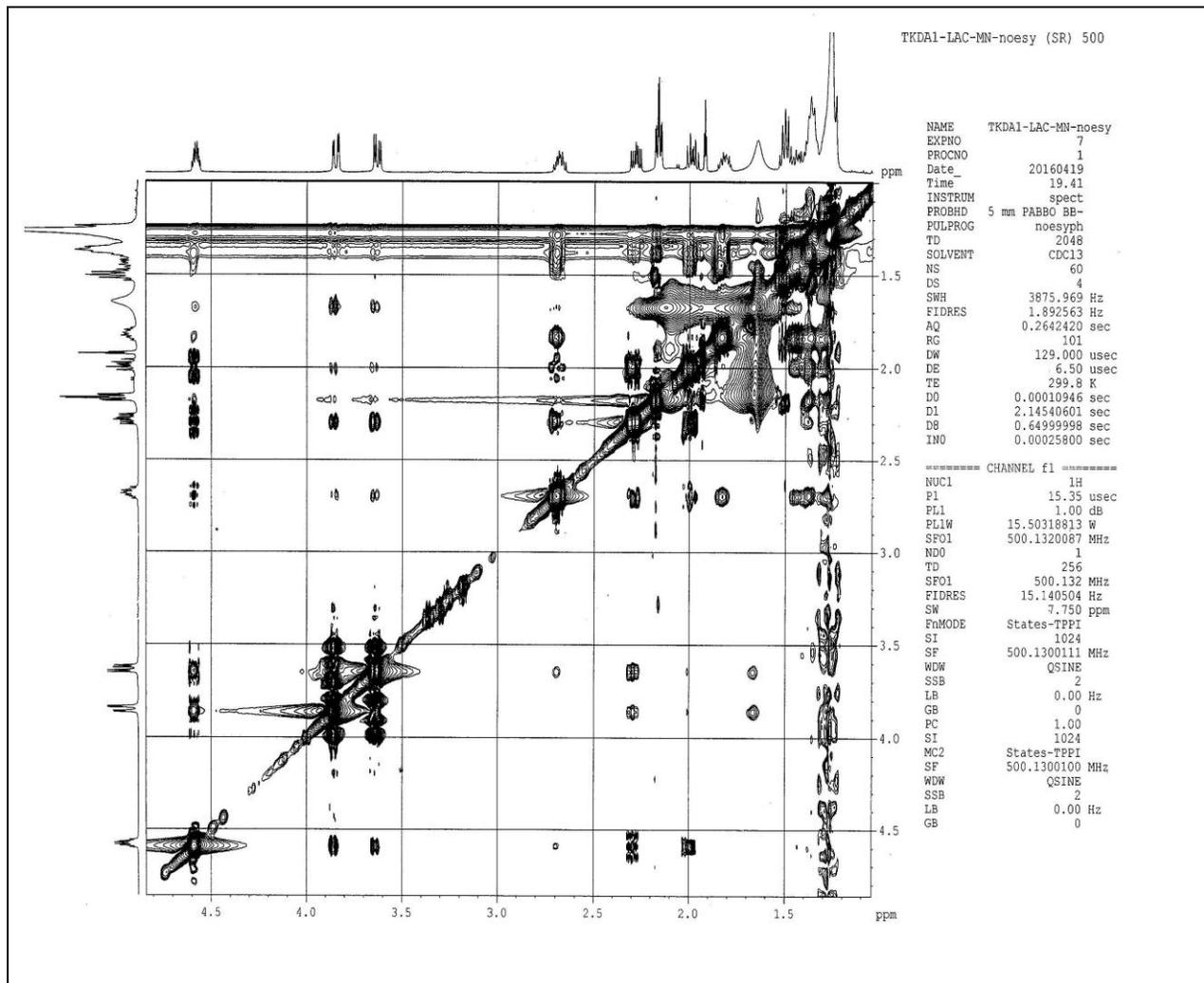
HSQC spectra of 22a (75 MHz, CDCl₃)



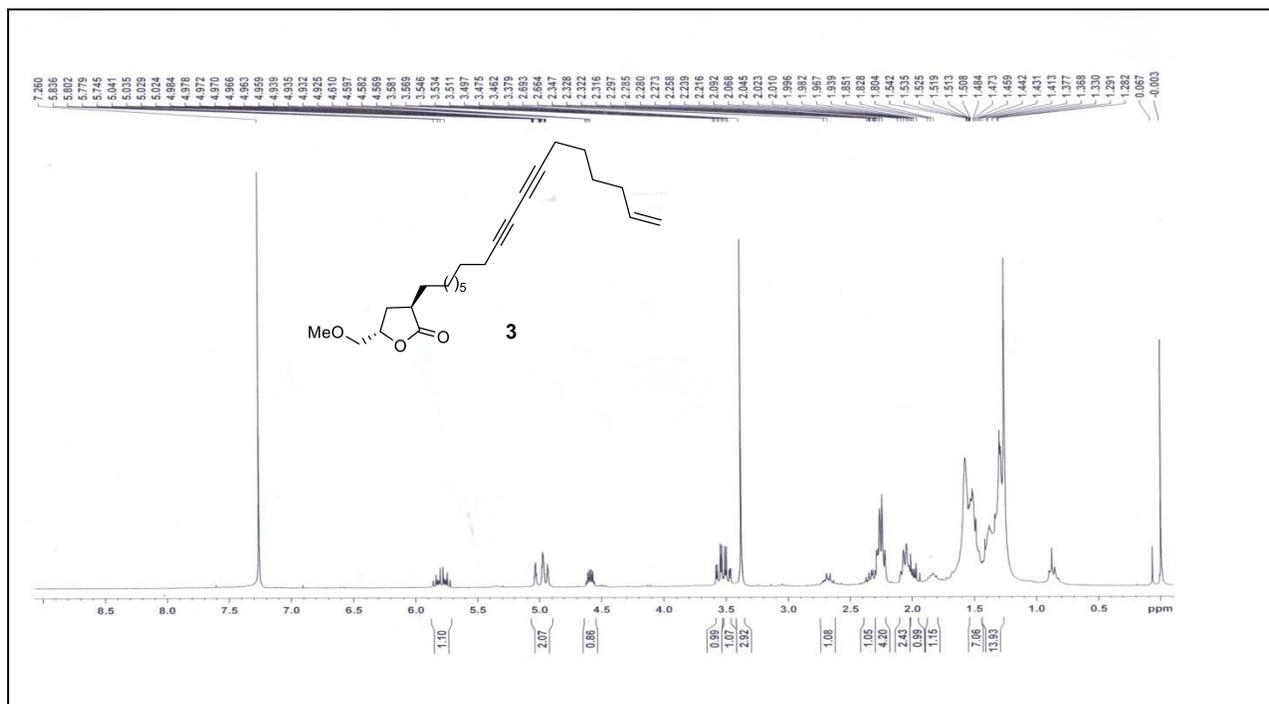
COSY spectra of 22a (300 MHz, CDCl₃)



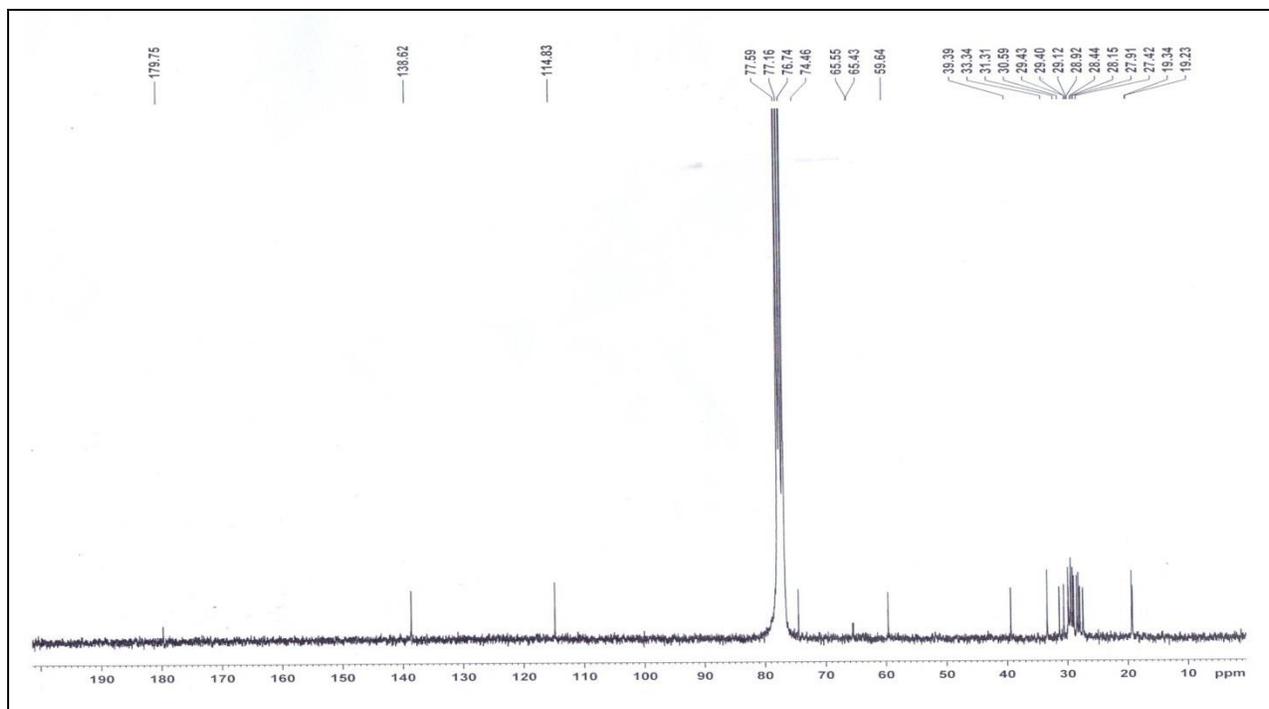
NOESY spectra of 22a (500 MHz, CDCl₃)



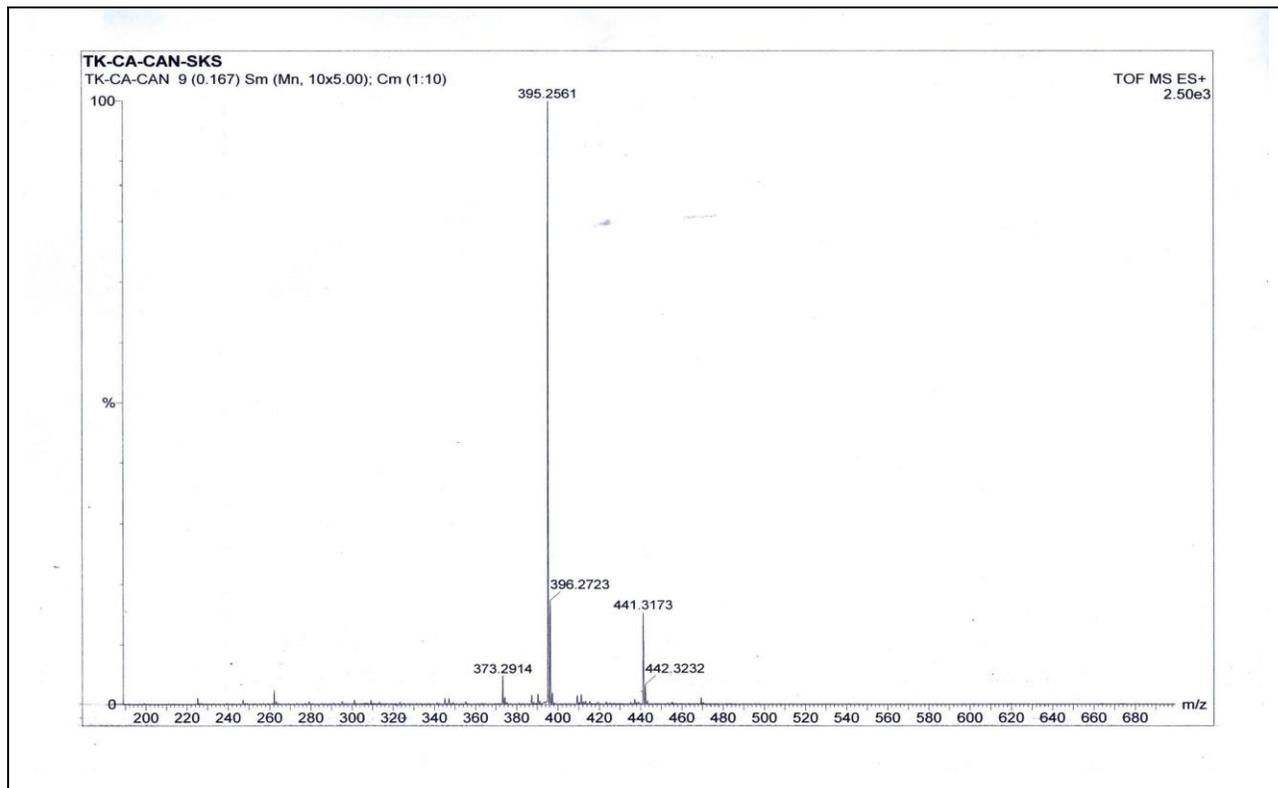
¹H NMR spectra of 3 (300 MHz, CDCl₃)



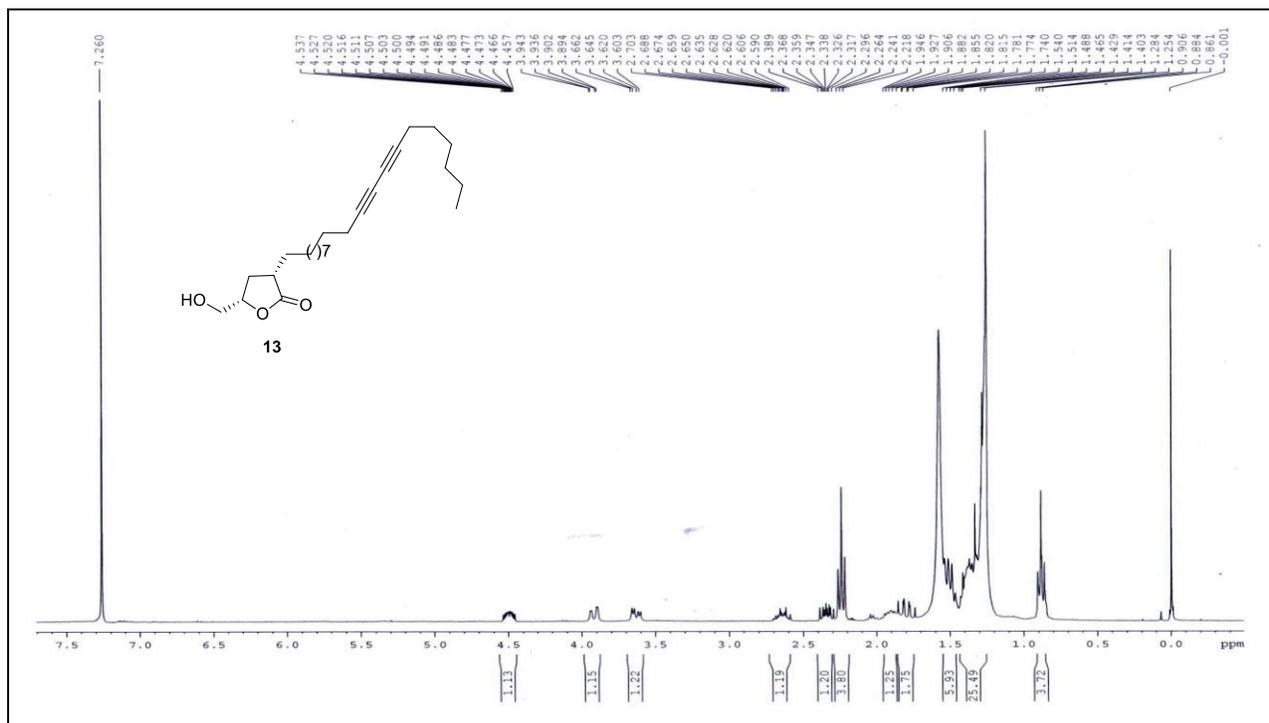
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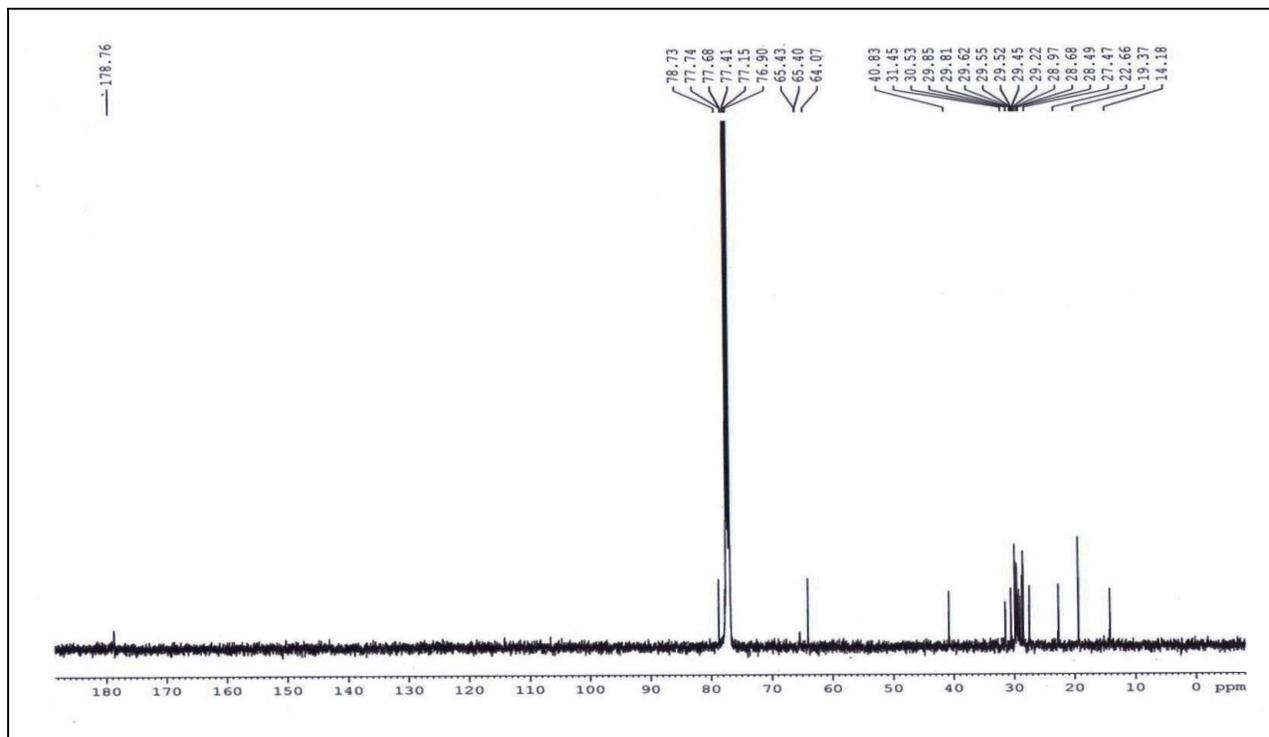
HRMS spectrum of 3:



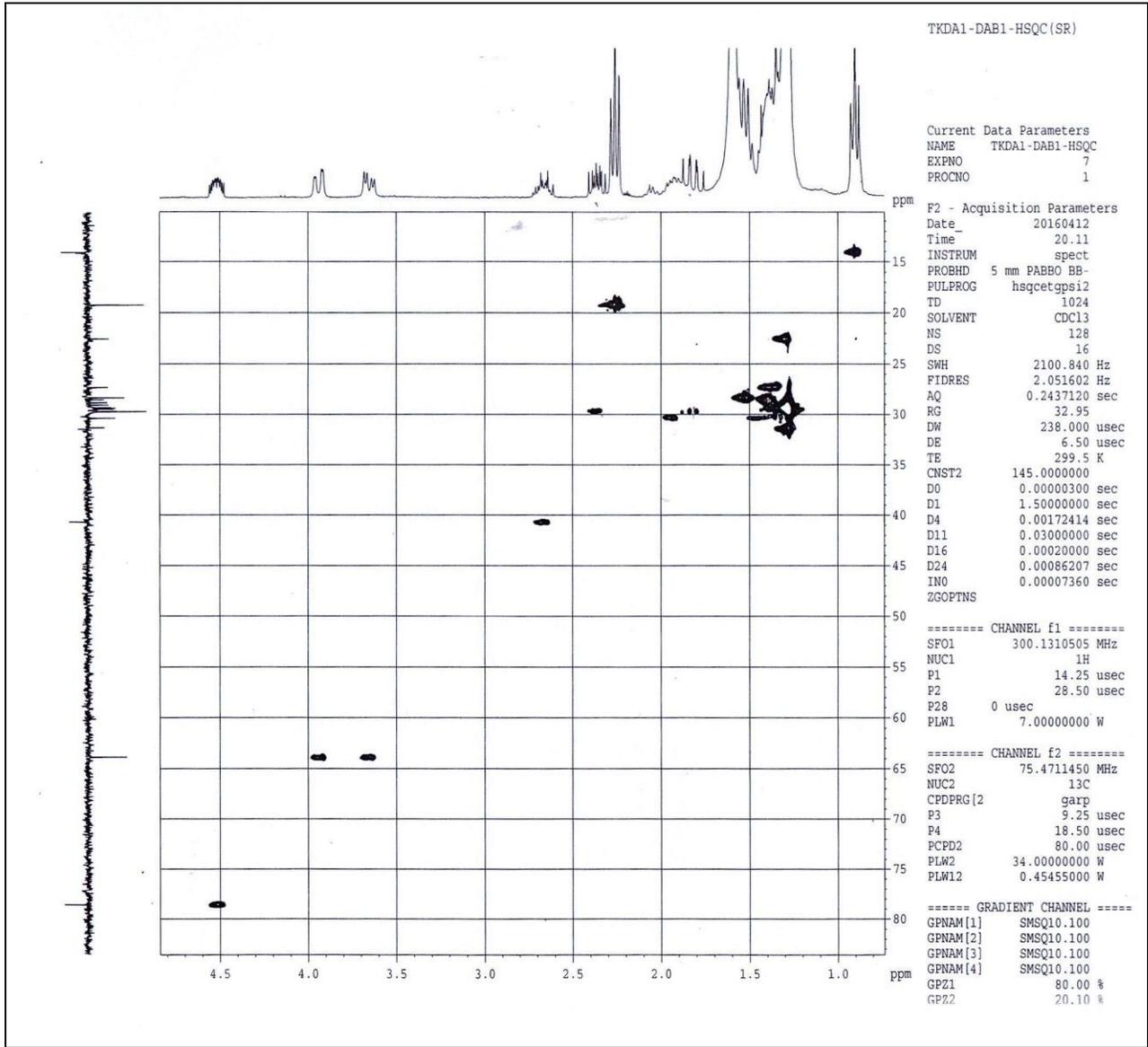
¹H NMR spectra of 13 (300 MHz, CDCl₃)



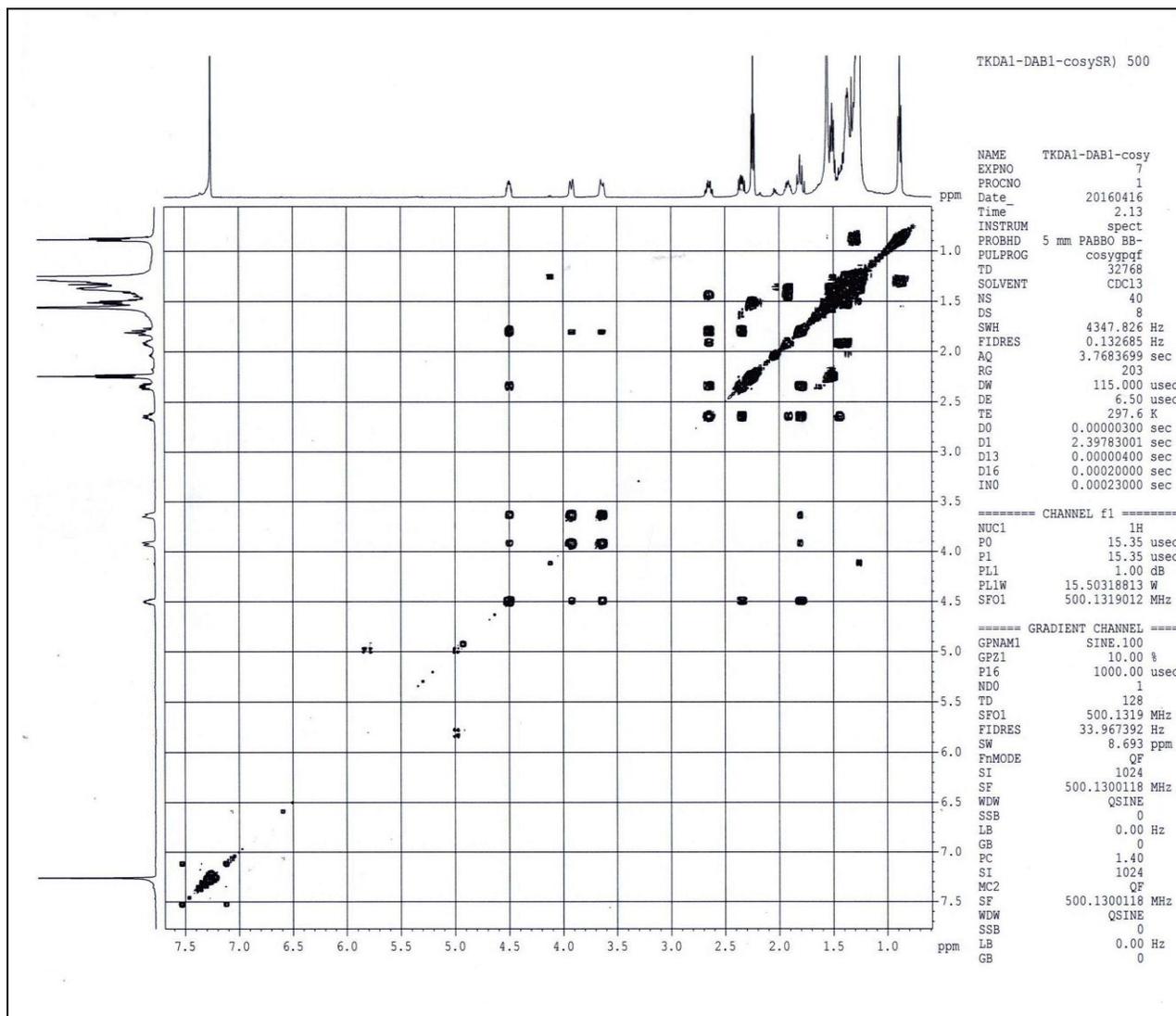
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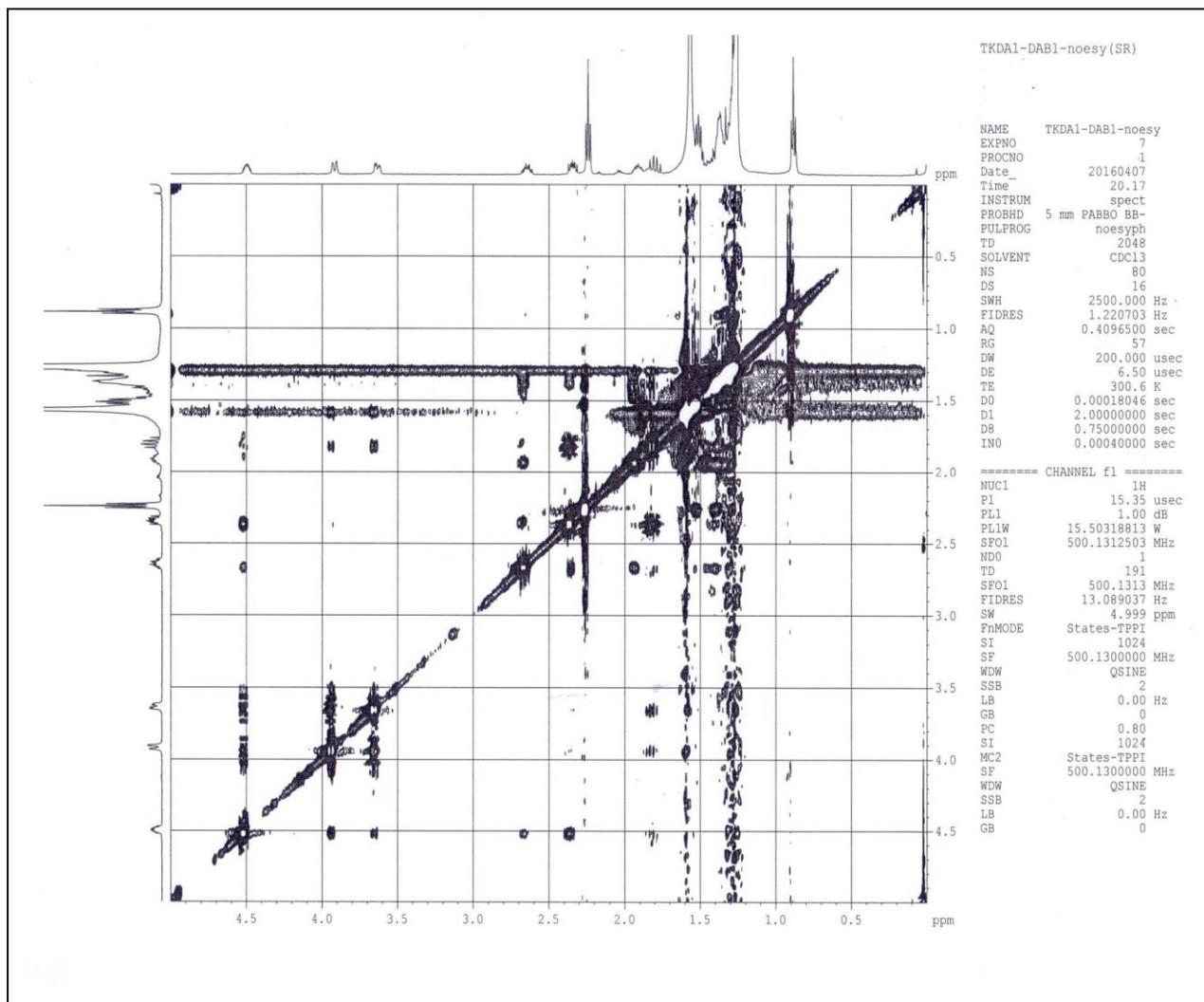
HSQC spectra of 13 (75 MHz, CDCl₃)



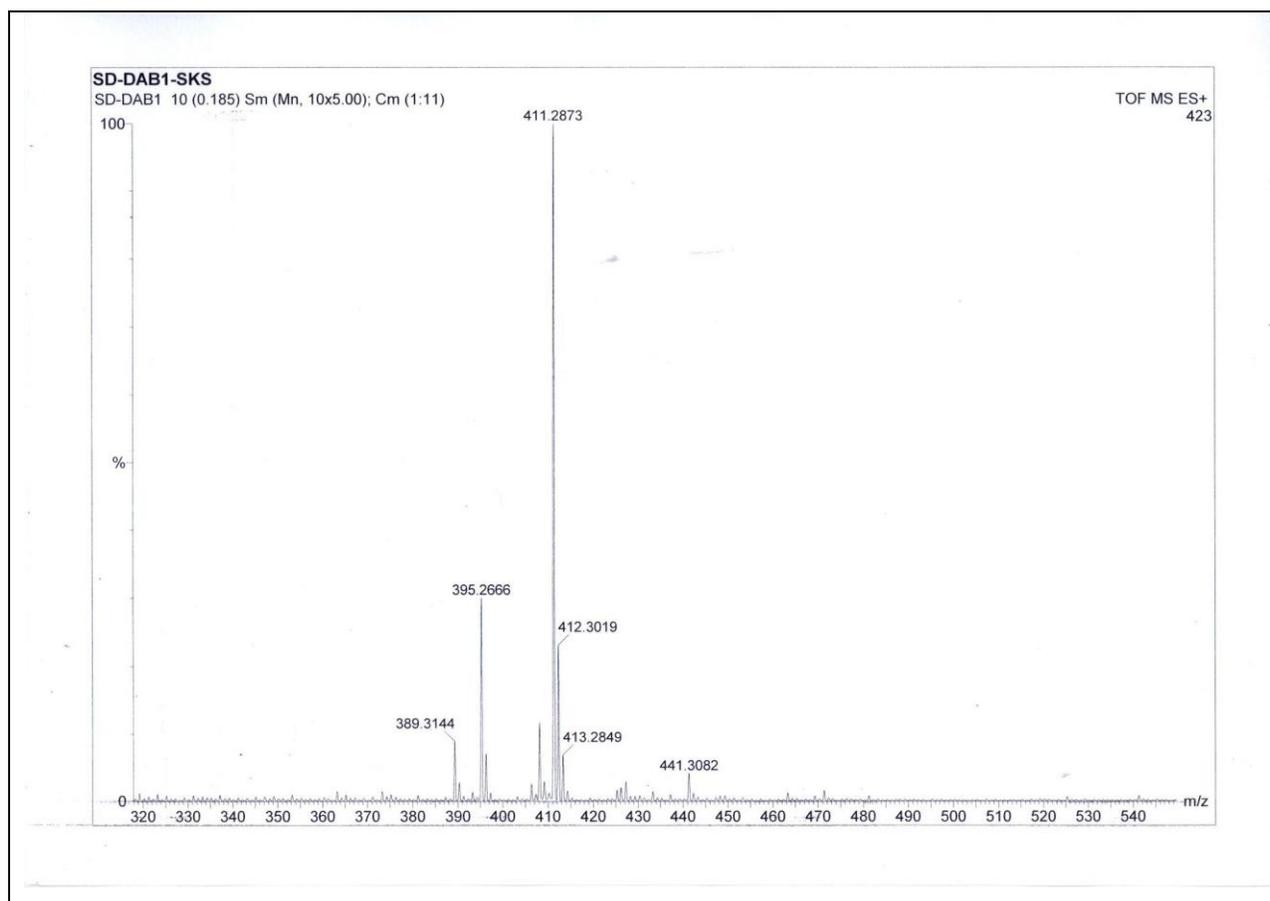
COSY spectra of 13 (500 MHz, CDCl₃)



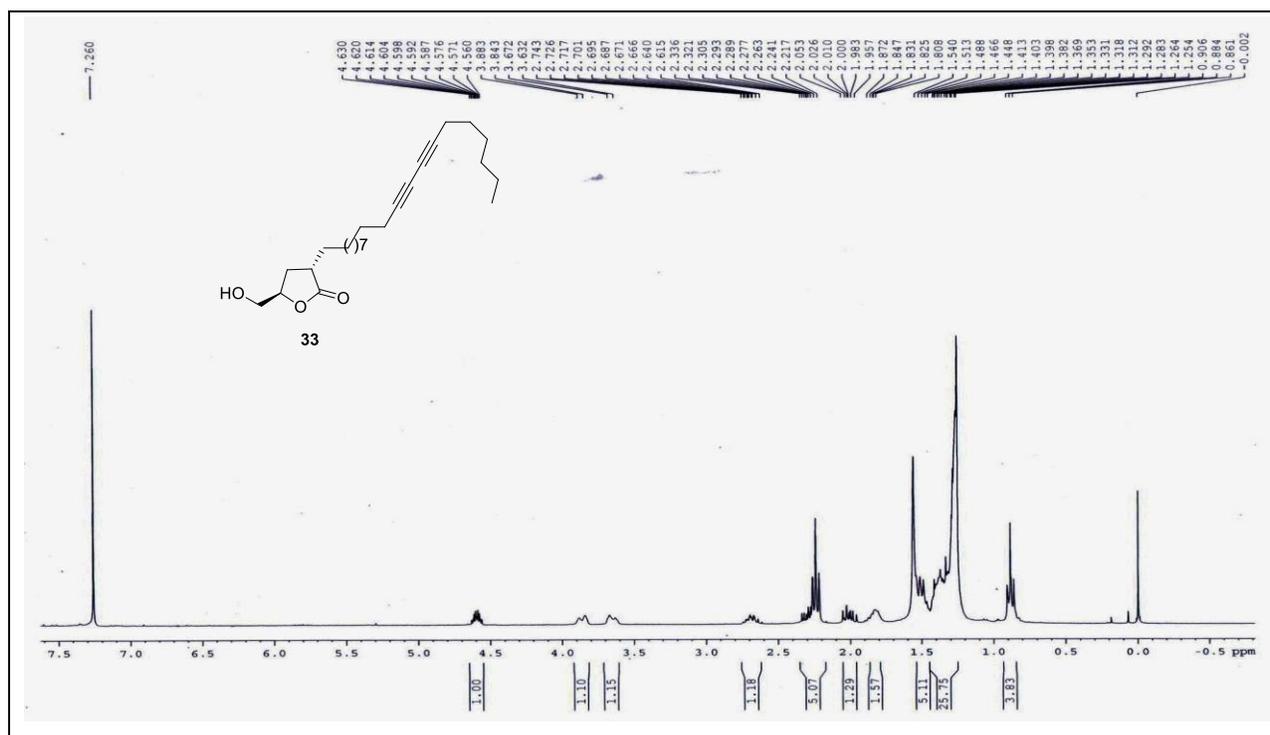
NOESY spectra of 13 (500 MHz, CDCl₃)



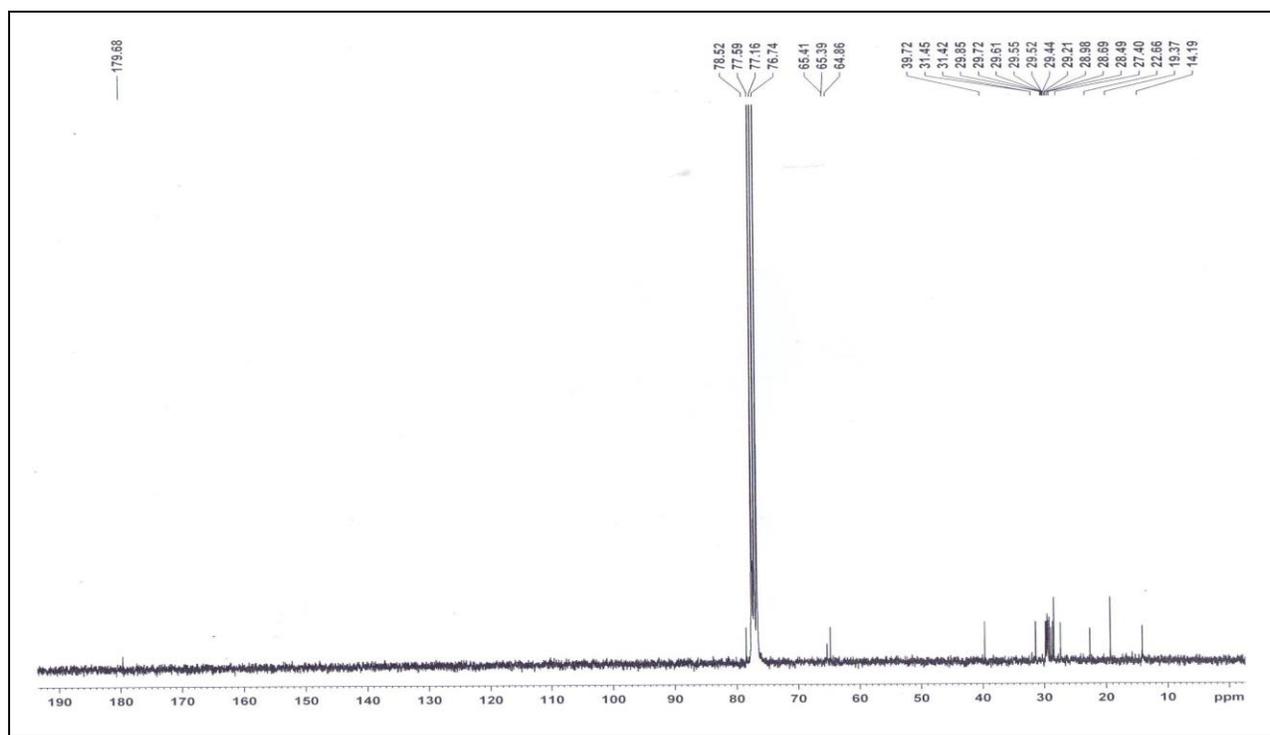
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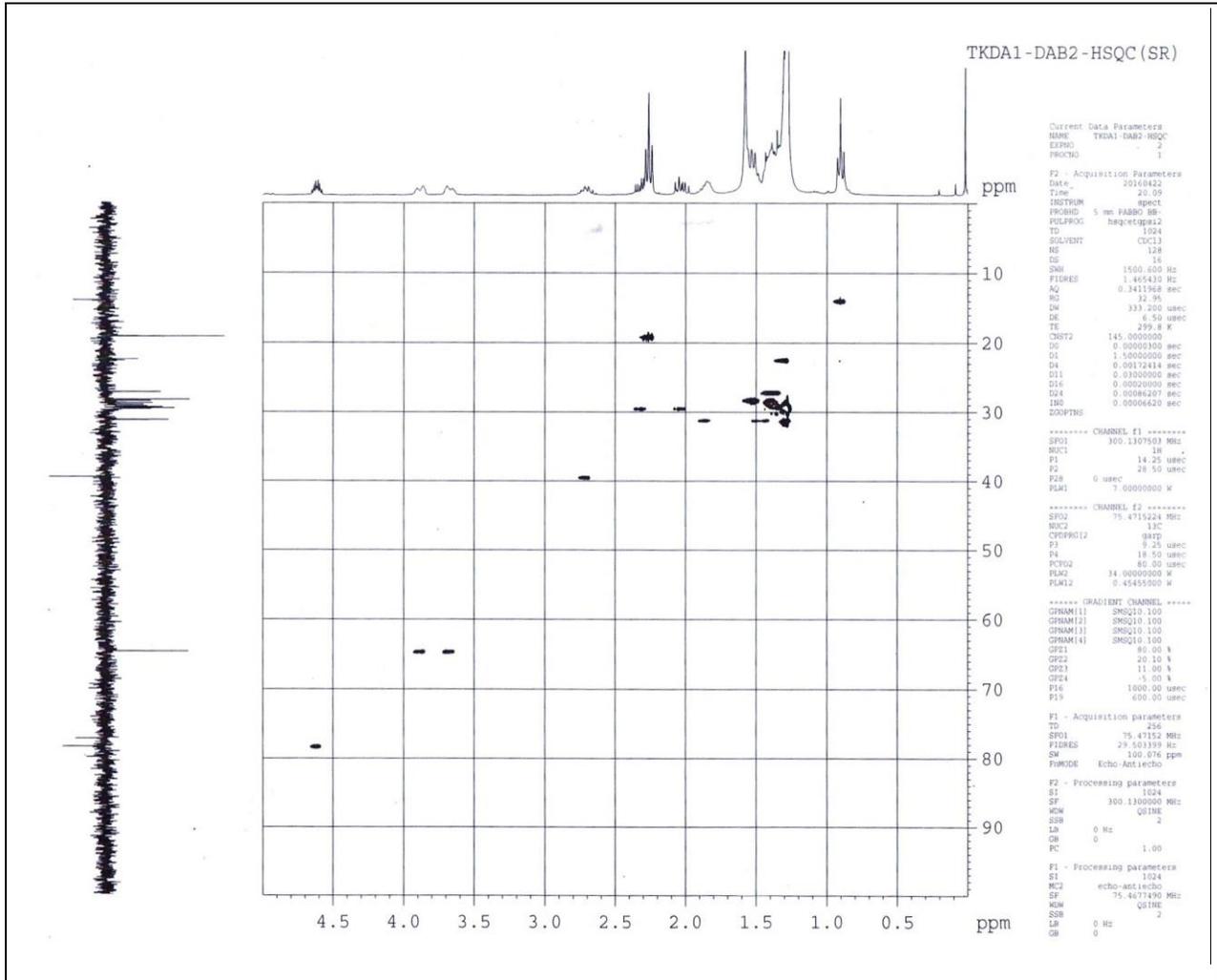
¹H NMR spectra of 33 (300 MHz, CDCl₃)



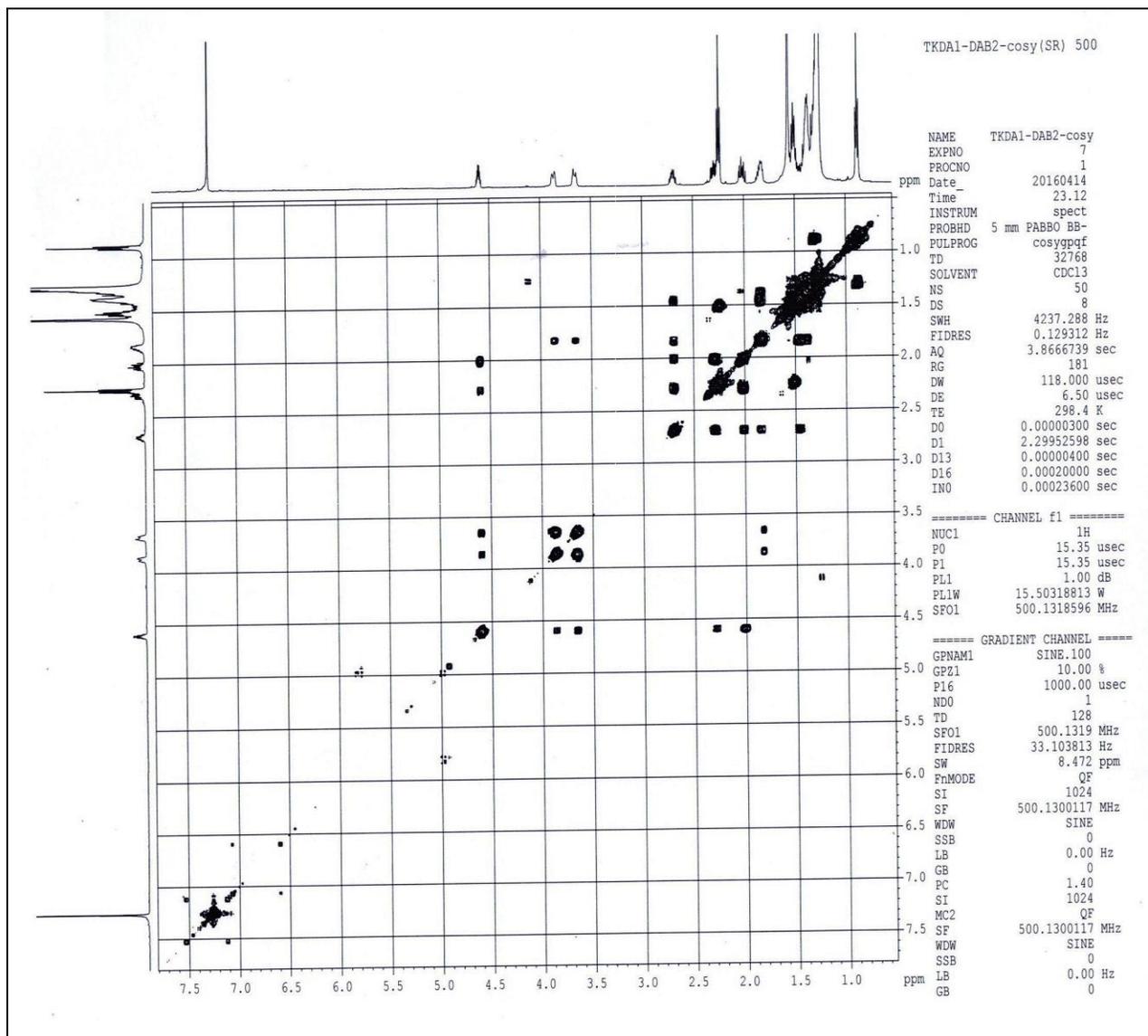
¹³C NMR spectra of 33 (75 MHz, CDCl₃)



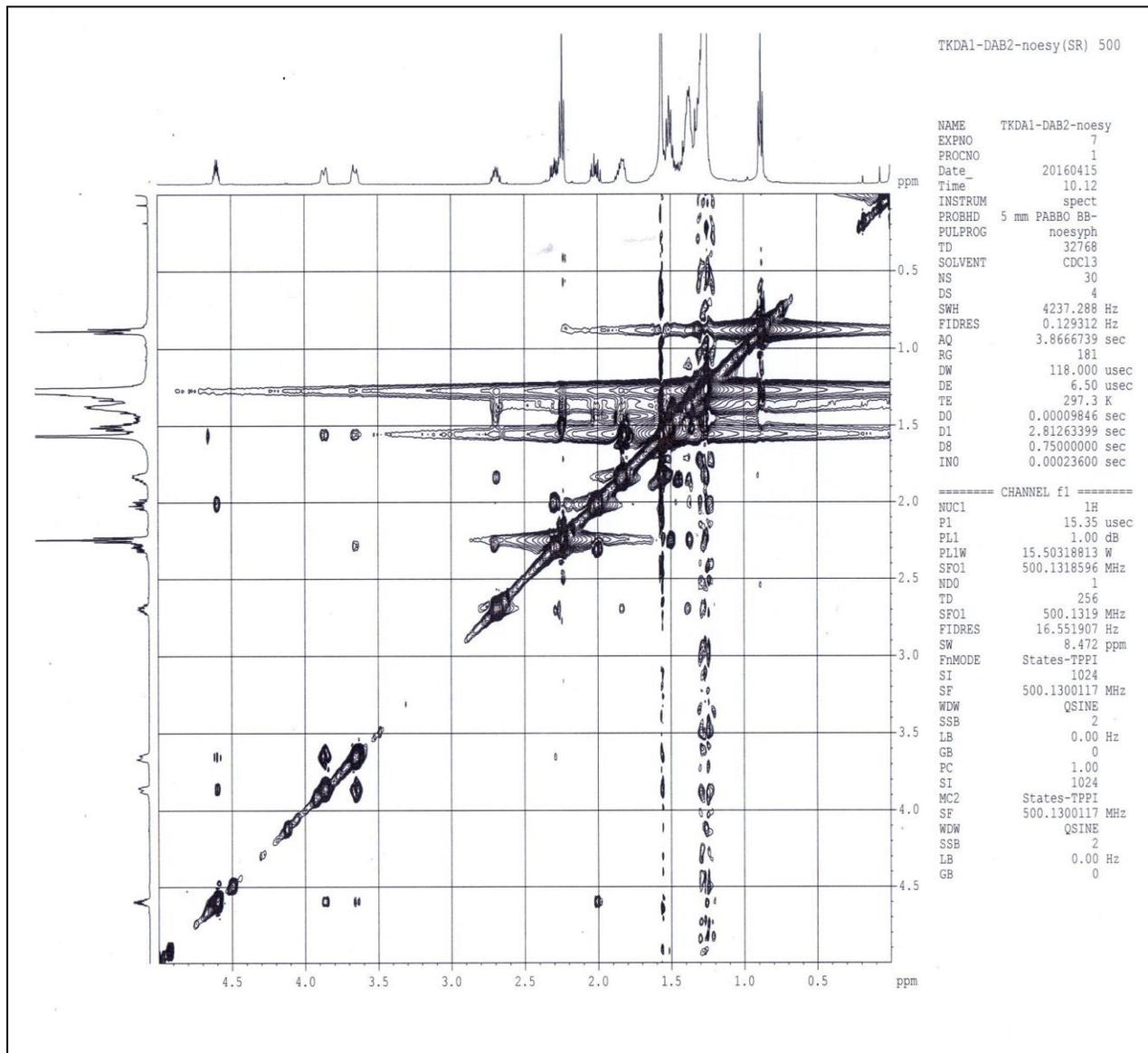
HSQC spectra of 33 (75 MHz, CDCl₃)



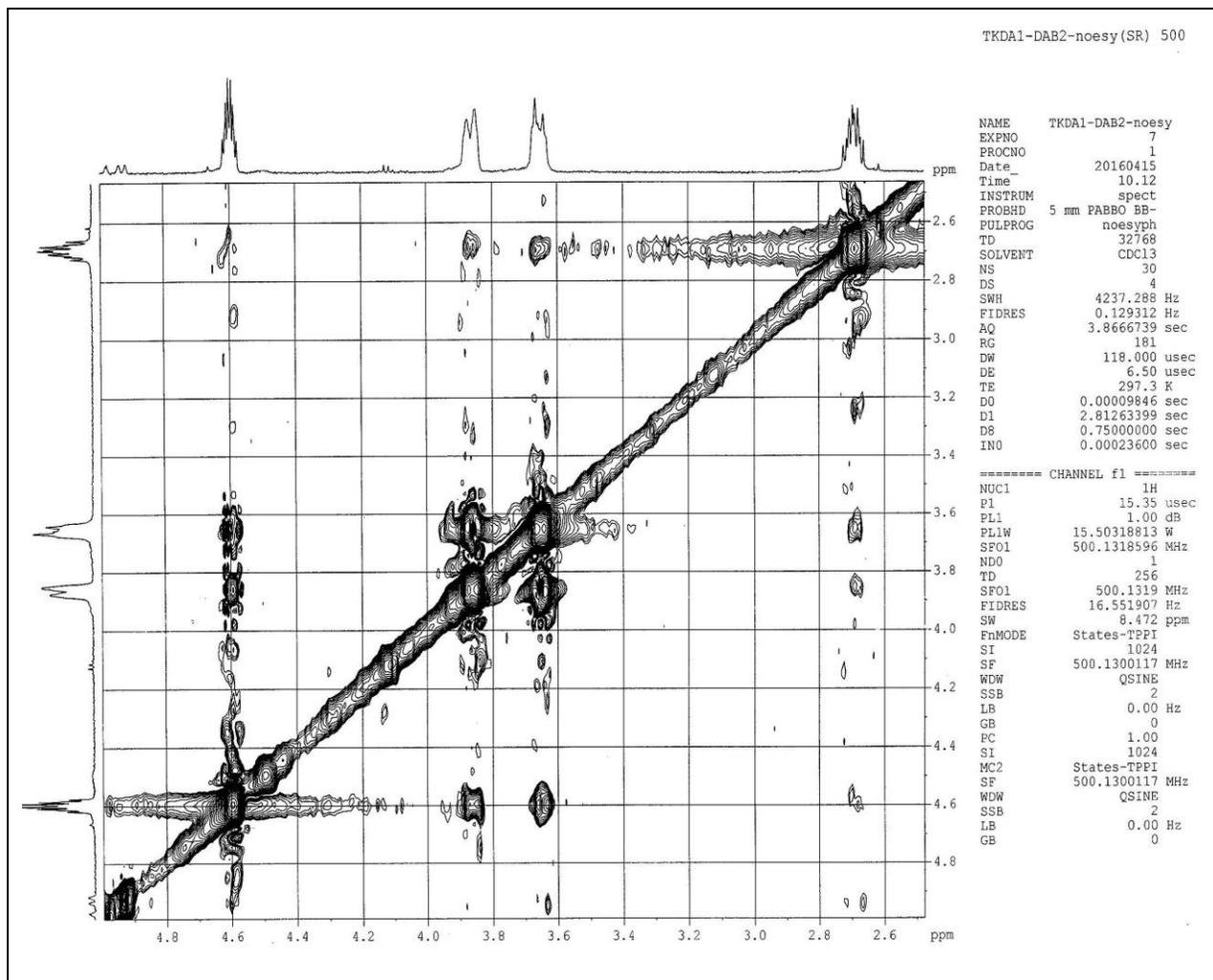
COSY spectra of 33 (500 MHz, CDCl₃)



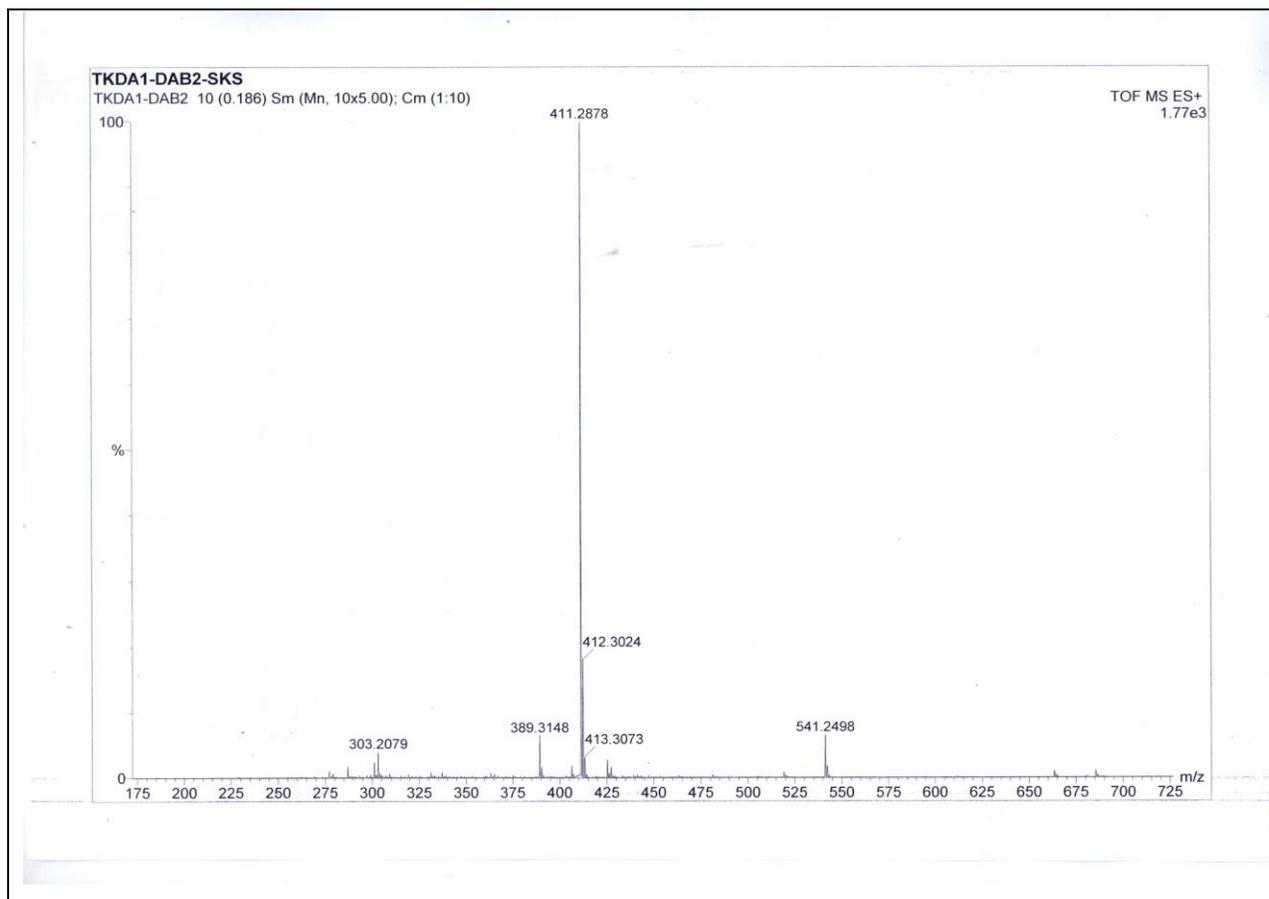
NOESY spectra of 33 (500 MHz, CDCl₃)



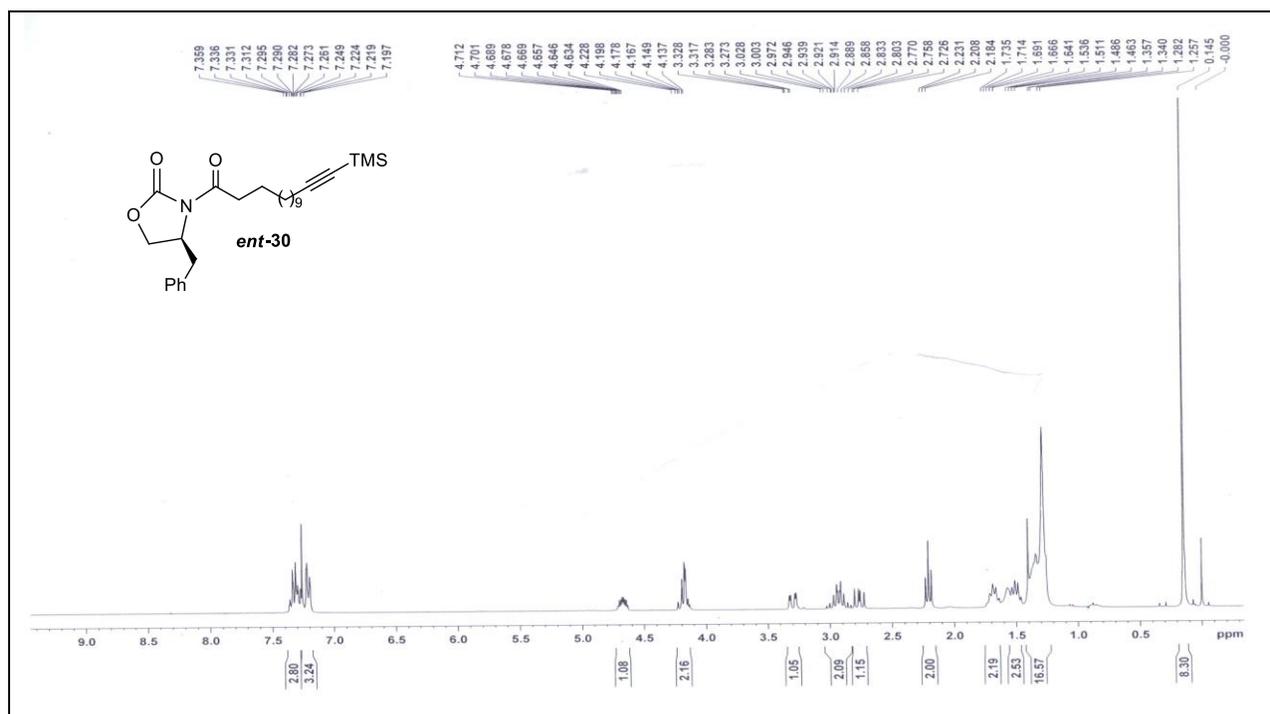
Zoomed NOESY spectra of 33 (500 MHz, CDCl₃)



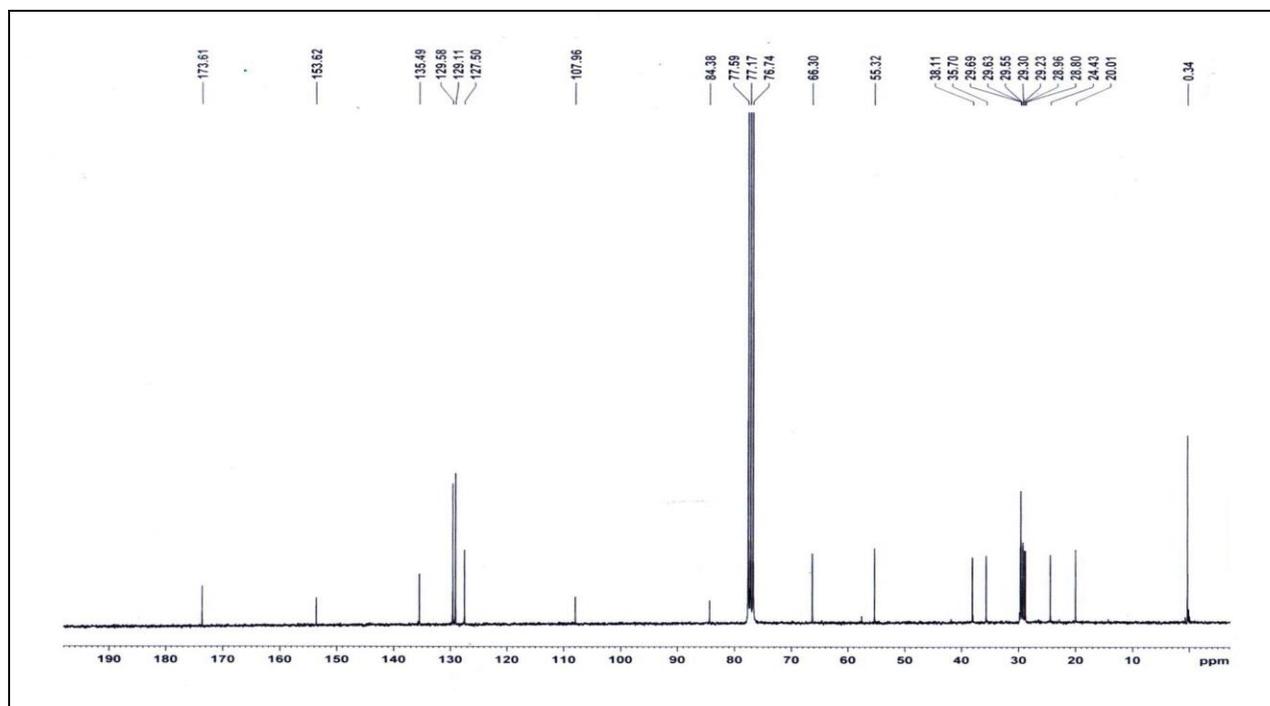
HRMS spectrum of 33:



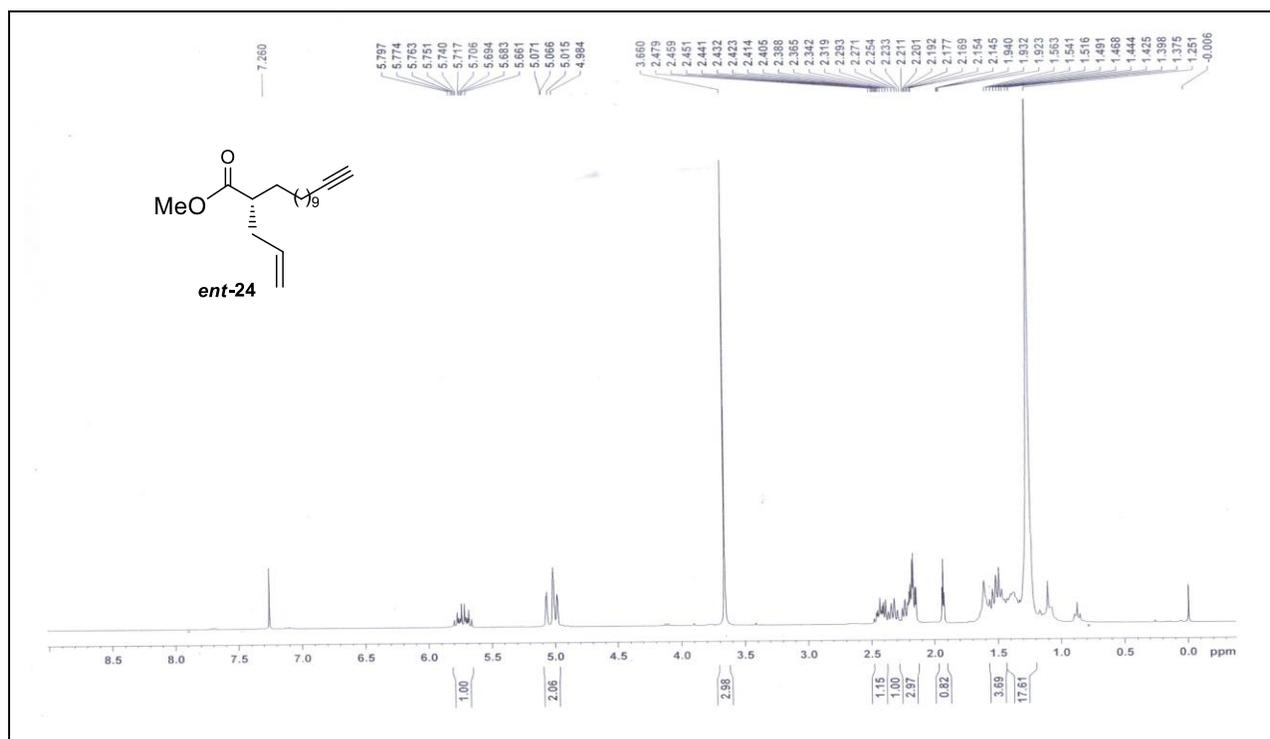
¹H NMR spectra of *ent*-30 (300 MHz, CDCl₃)



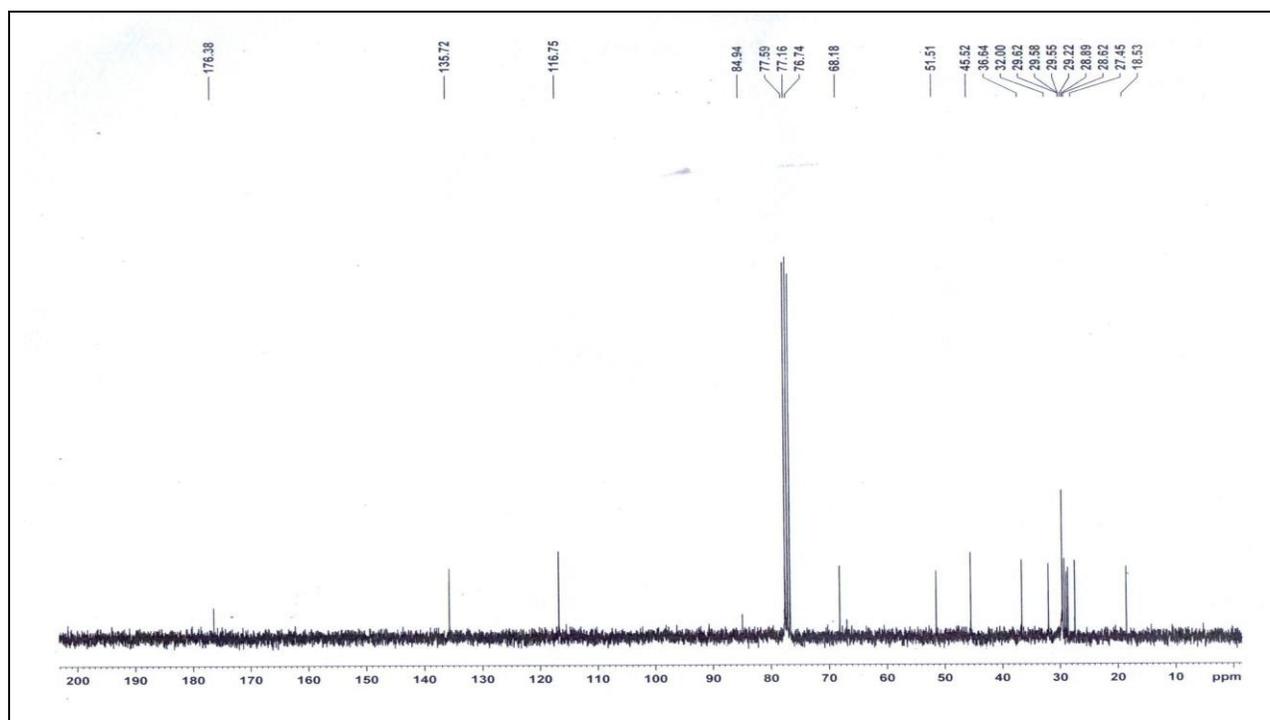
¹³C NMR spectra of *ent*-30 (75 MHz, CDCl₃)



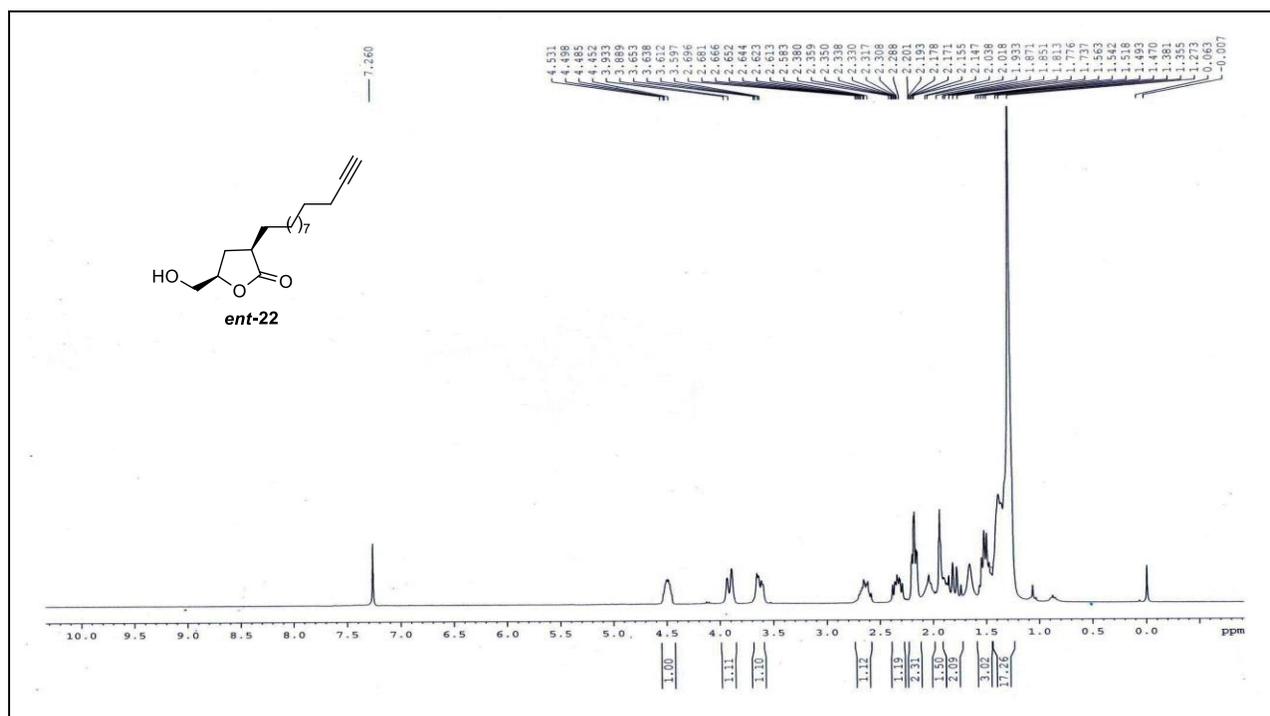
¹H NMR spectra of *ent*-24 (300 MHz, CDCl₃)



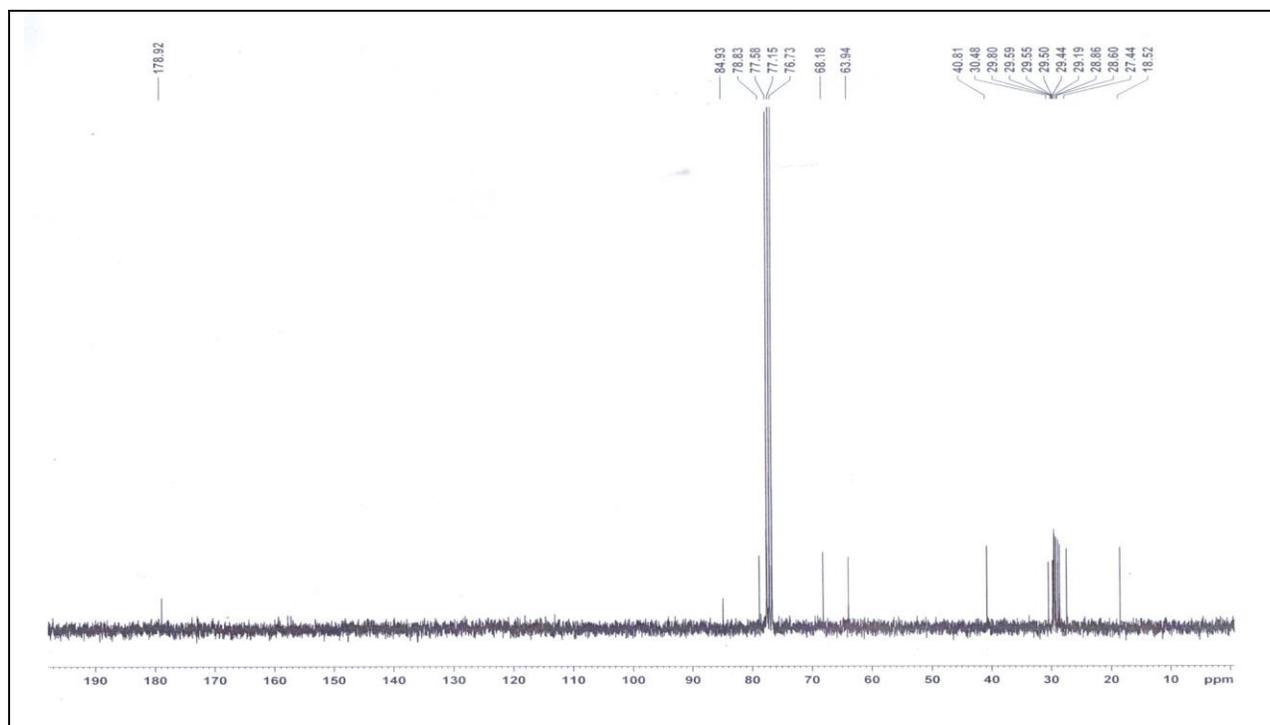
¹³C NMR spectra of *ent*-24 (75 MHz, CDCl₃)



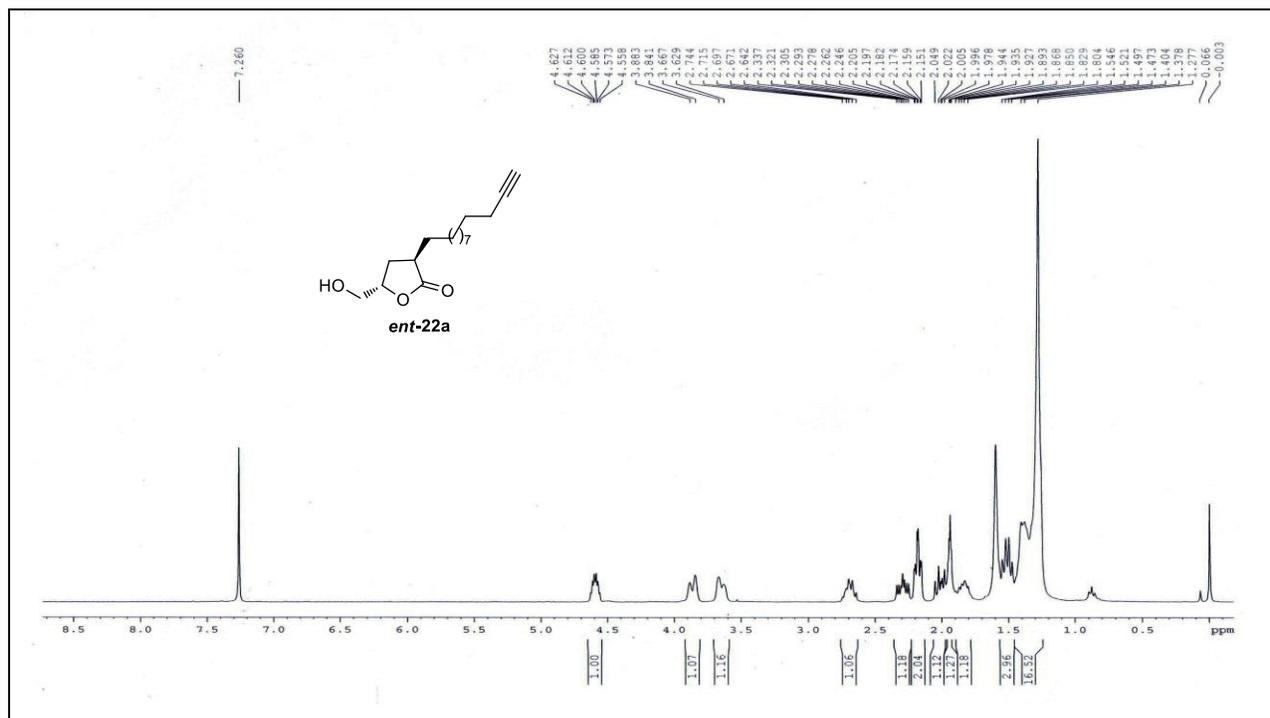
¹H NMR spectra of *ent*-22 (300 MHz, CDCl₃)



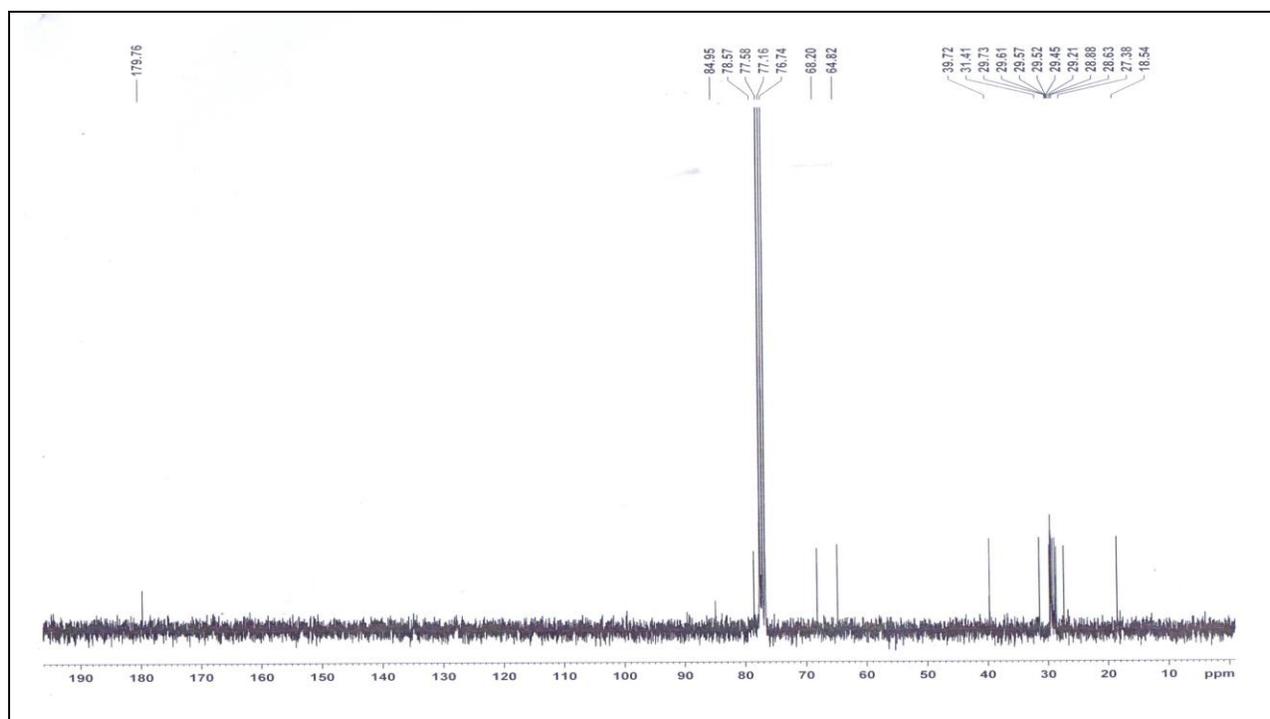
¹³C NMR spectra of *ent*-22 (75 MHz, CDCl₃)



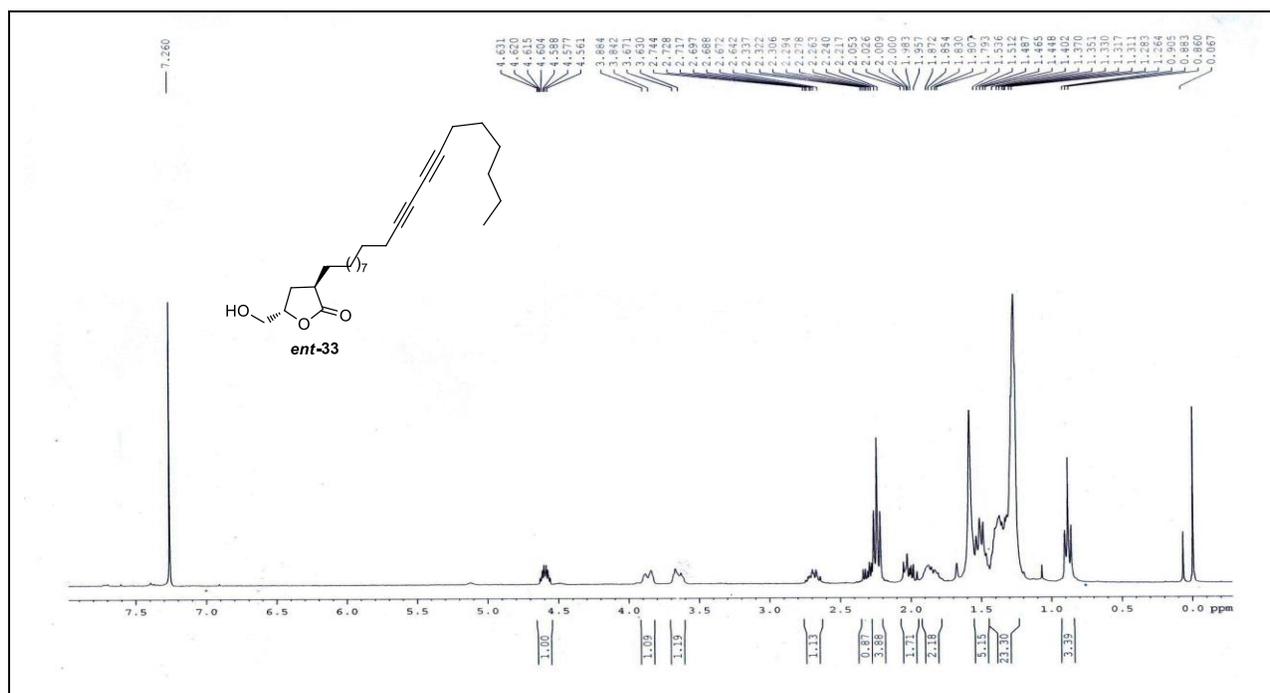
¹H NMR spectra of *ent*-22a (300 MHz, CDCl₃)



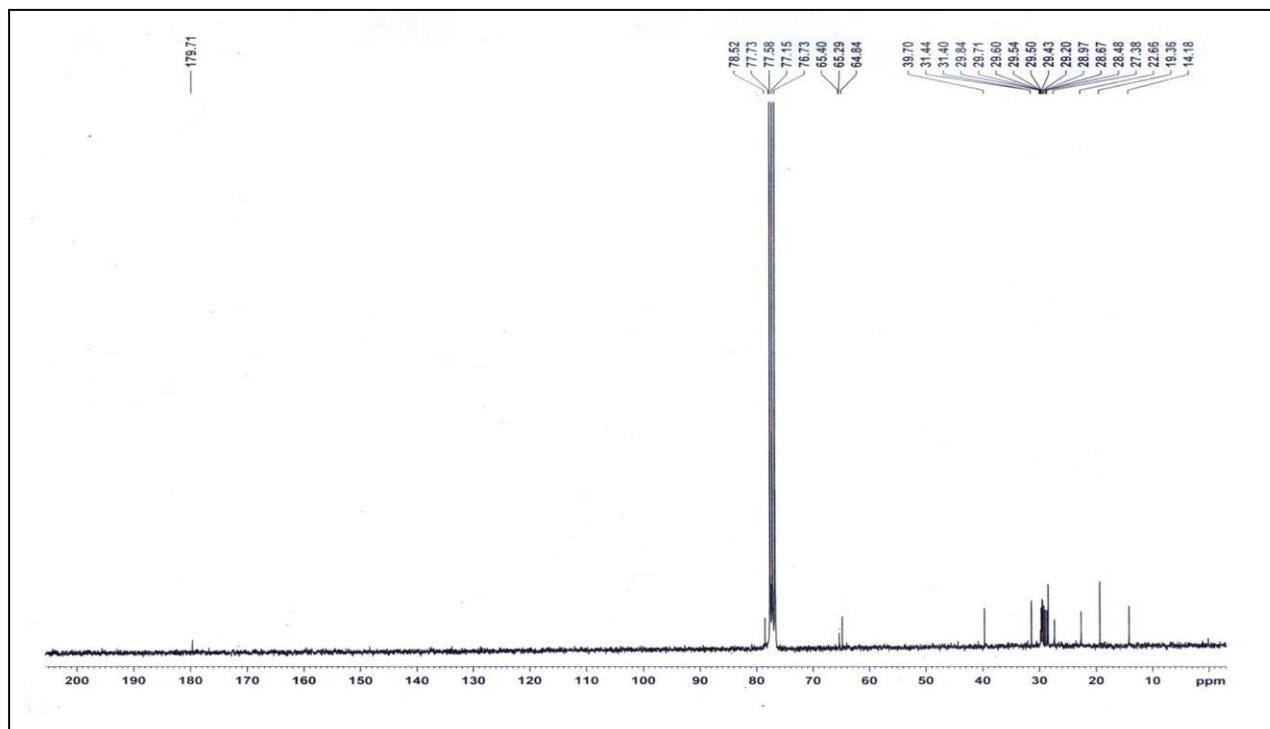
¹³C NMR spectra of *ent*-22a (75 MHz, CDCl₃)



^1H NMR spectra of *ent*-33 (300 MHz, CDCl_3)



^{13}C NMR spectra of *ent*-33 (75 MHz, CDCl_3)



HRMS spectrum of *ent*-33:

