Supporting Information

Mechanochemical Cu(II) complexes and propargylamine synthetic adventures

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Contents

Experimental section

Materials

All reagents were purchased from Sigma Aldrich, Fluorochem, Tokyo Chemical Industry, Apollo Scientific, Fischer Scientific or Alfa Aesar and used without further purification. Experiments were performed under aerobic conditions or argon.

Instrumentation

NMR spectra were recorded with a Varian VNMRS 600 at 25 °C, at either 600 MHz or 151 MHz in CDCl3 or DMSO-d_6. Chemical shifts are quoted in parts per million (ppm). Coupling constants (J) are recorded in units of Hz. FT-IR spectra were recorded over the range of 4000–650 cm^{-1} on a PerkinElmer Spectrum One FT-IR spectrometer fitted with a UATR polarisation accessory. HRMS data were obtained with a Bruker Daltonics Fourier Transform (FTMS) Apex II spectrometer with electrospray ionisation (ESI) and methanol as solvent. HR-MS data were obtained on a VG Autospec Fissions instrument (EI at 70 eV). Molecular ions are reported as mass/charge (m/z) ratios. Thermogravimetric analysis was carried out with a Thermogravimetric analyser Q-50 V20.13 using a platinum pan, in a nitrogen atmosphere from 25 – 800 °C, at a scan rate of 5 °C/min. UV-Vis was recoded over the range of 320-1100 nm at 25 °C using an Avantor v-3000pc spectrophotometer. Purification of compounds with normal-phase silica flash column chromatography was conducted on a Teledyne Isco Combiflash with UV detection at all wavelengths. Elemental analysis was carried out at the London Metropolitan University.

PXRD and SXRD

Single crystal diffraction data for ligands *SS*-H_2L2_BM80min and *SS*-H_2L2_BM10min, *SS*-Cu**L2**, *RR*-Cu**L2** and *RR*-FeCl**L2** were collected at the National Crystallography Service, University of Southampton.[1] Suitable crystals were mounted on a MITIGEN holder in oil on a Rigaku 007HF diffractometer with HF Varimax confocal mirrors, a UG2 goniometer and HyPix 6000HE detector and data were collected at *T* = 100(2)K. The data were processed with CrysAlisPro and solved by intrinsic phasing methods with SHELXT.[2] All crystal structures were then refined on Fo^2 by full-matrix least-squares refinements using SHELXL[2] or olex2.refine 1.5-alpha (*SS*-Cu**L2** and *RR*-Cu**L2**)[3]. Single crystal diffraction data for ligands RR-H_2L2_solvent_made, RR_H_2L2_BM10min and SS-H_2L2_BM80min_MeOH and recovered materials *SS*-Cu**L2** and *RR*-Cu**L2** were collected at University of Sussex in a Rigaku rotating anode diffractometer at *T* = 100(2)K. Geometric/crystallographic calculations were performed using PLATON,[3]Olex2,[4] and WINGX[5] packages; graphics were prepared with Crystal Maker.[6] Structures have been given CCDC deposition numbers 2284741–2284750.

PXRD data were collected at the National Crystallography Service, University of Southampton on a Rigaku MiniFlex in theta-2theta geometry using Cu (Ka1/Ka2) radiation and a Ni Kb filter (detector side). Additional beam optics and settings: primary & secondary axial Soller slit (2.5°), fixed 1.25mm divergence & receiving slits, 1mm anti-scatter-screen, Detector: NaI scintillation counter, Generator: 600W (40kV, 15mA). Data collection range 5˚<=θ<=50˚, step size 0.01˚, collection time 0.2˚/min.

Synthesis

Ligand synthesis H_2L1

All three N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamine ligands were synthesised using high-vibration ball milling (HVBM). N,N'-1,2-diaminocyclohexane (0.111g, 0.12ml, 1.00 mmol) (racemic or RR or SS) and 3,5-di-tert-butyl-2-hydroxybenzaldehyde (0.468 g, 2.00mmol) were combined in 25 ml ball mill Teflon jar with two Ceramic medium size balls and mixed for 10 minutes at 25 Hz frequency. The yellow solid was collected in excellent yields (>99%, based on N,N'-1,2-diaminocyclohexane). ^{1}H NMR (600 MHz, CDCl3) δ 13.72 (s, 2H), 8.30 (s, 2H), 7.30 (d, *J* = 2.4 Hz, 2H), 6.98 (d, *J* = 2.4 Hz, 2H), 3.34 – 3.29 (m, 2H), 1.94 (d, *J* = 13.4 Hz, 2H), 1.73 (d, *J* = 12.2 Hz, 3H), 1.55 (s, 2H), 1.46 (t, *J* = 10.8 Hz, 2H), 1.41 (s, 19H), 1.23 (s, 18H). ^{13}C NMR (151 MHz, CDCl3) δ 165.78, 157.98, 139.85, 136.30, 126.72, 126.02, 117.82, 72.41, 34.93, 34.01, 33.27, 31.40, 29.40, 24.34.

Ligand synthesis H_2L2

(S,S) H_2**L2** and (R,R) H_2**L2** ligands were synthesised using high-vibration ball milling (HVBM). (S,S) 1,2-diphenylethylenediamine (0.212g, 1.00 mmol) and 3,5-di-tert-butyl-2-hydroxybenzaldehyde (0.468 g, 2.00 mmol) ball mill Teflon jar with two Ceramic medium size balls and mixed for 10 minutes at 25 Hz frequency.

The yellow solid was collected in excellent yields (>99%, based on S,S-1,2-diphenylethylenediamine). ^{1}H NMR (600 MHz, CDCl3) δ 8.41 (s, 2H), 7.31 (d, *J* = 2.4 Hz, 2H), 7.23 – 7.18 (m, 4H), 7.18 – 7.13 (m, 6H), 6.98 (d, *J* = 2.4 Hz, 2H), 4.73 (s, 2H), 1.42 (s, 18H), 1.22 (s, 18H). ^{13}C NMR (151 MHz, CDCl3) δ 167.23, 128.25, 128.02, 31.39, 29.41.

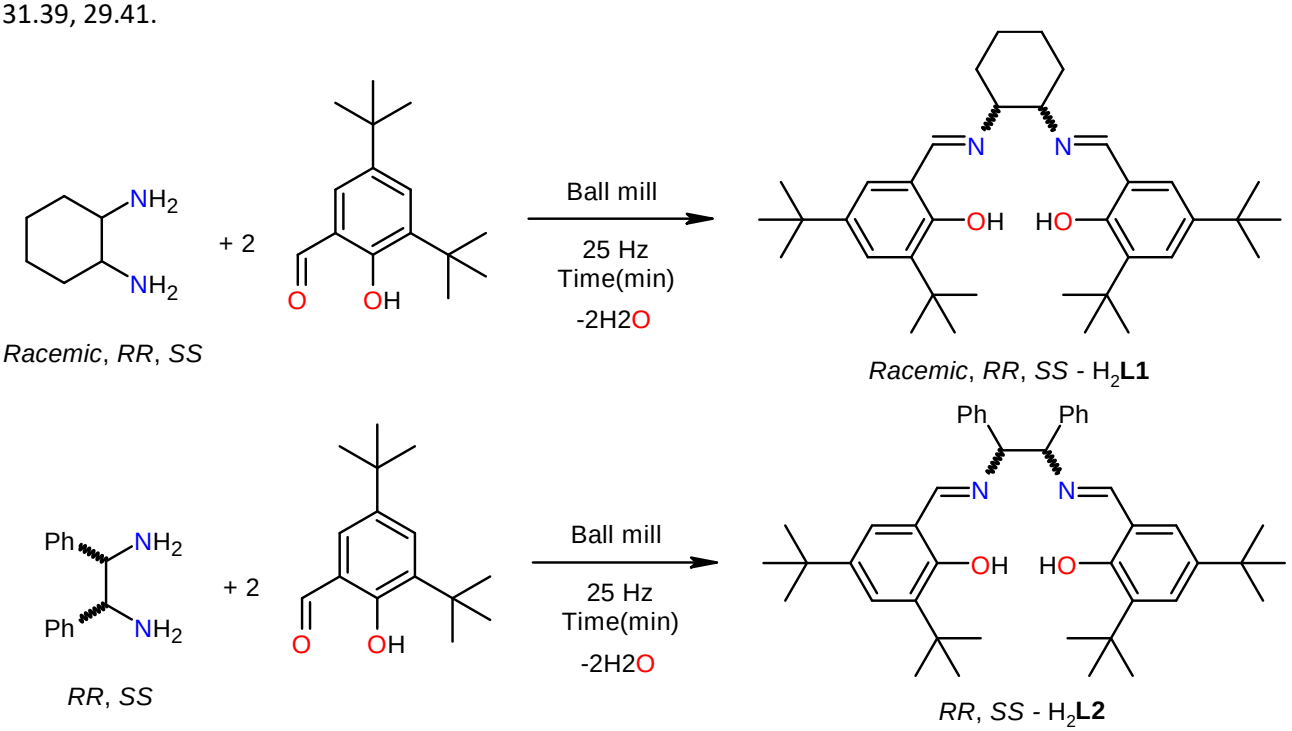


Table S1. Optimisation table for the ball mill synthesis of the ligand *racemic*-H_2**L1.** Amine-aldehyde ratio 1:2 Optimum conditions have been highlighted in bold.

Entry	Number of balls (diameter/ millimeter)	Ball Material	Jar Material	Time (min)	Frequency (Hz)	Yield (%)
1	2(6mm)	Stainless steel	Stainless steel	5	3	-
2	4(3mm)	Stainless steel	Stainless steel	5	3	-
3	2(8mm)	Ceramic	Stainless steel	5	3	-
4	2(8mm)	Ceramic	Teflon	5	3	-
5	2(6mm)	Stainless steel	Stainless steel	5	5	-
6	4(3mm)	Stainless steel	Stainless steel	5	5	-
7	3(8mm&3mm)	1 Ceramic, 2 Stainless steel	Stainless steel	5	5	-
8	2(8mm)	Ceramic	Teflon	5	5	-
9	2(6mm)	Stainless steel	Stainless steel	5	10	-
10	4(3mm)	Stainless steel	Stainless steel	5	10	-
11	2(8mm)	Ceramic	Stainless steel	5	10	-
12	2(8mm)	Ceramic	Teflon	5	10	-
13	4(3mm)	Stainless steel	Stainless steel	5	10	-
14	3(8mm&3mm)	1 Ceramic, 2 Stainless steel	Stainless steel	5	10	-
15	2(6mm)	Stainless steel	Stainless steel	5	15	50
16	4(3mm)	Stainless steel	Stainless steel	5	15	50
17	2(8mm)	Ceramic	Stainless steel	5	15	50
18	2(8mm)	Ceramic	Teflon	5	15	60
19	2(6mm)	Stainless steel	Stainless steel	5	20	70
20	4(3mm)	Stainless steel	Stainless steel	5	20	70
21	2(8mm)	Ceramic	Stainless steel	5	20	70
22	2(8mm)	Ceramic	Teflon	5	20	75

23	2(6mm)	Stainless steel	Stainless steel	5	25	80
24	2(6mm)	Stainless steel	Stainless steel	10	25	96
25	4(3mm)	Stainless steel	Stainless steel	10	25	96
26	2(8mm)	Ceramic	Stainless stile	10	25	97
27	**2(8mm)**	**Ceramic**	**Teflon**	**10**	**25**	**>99**

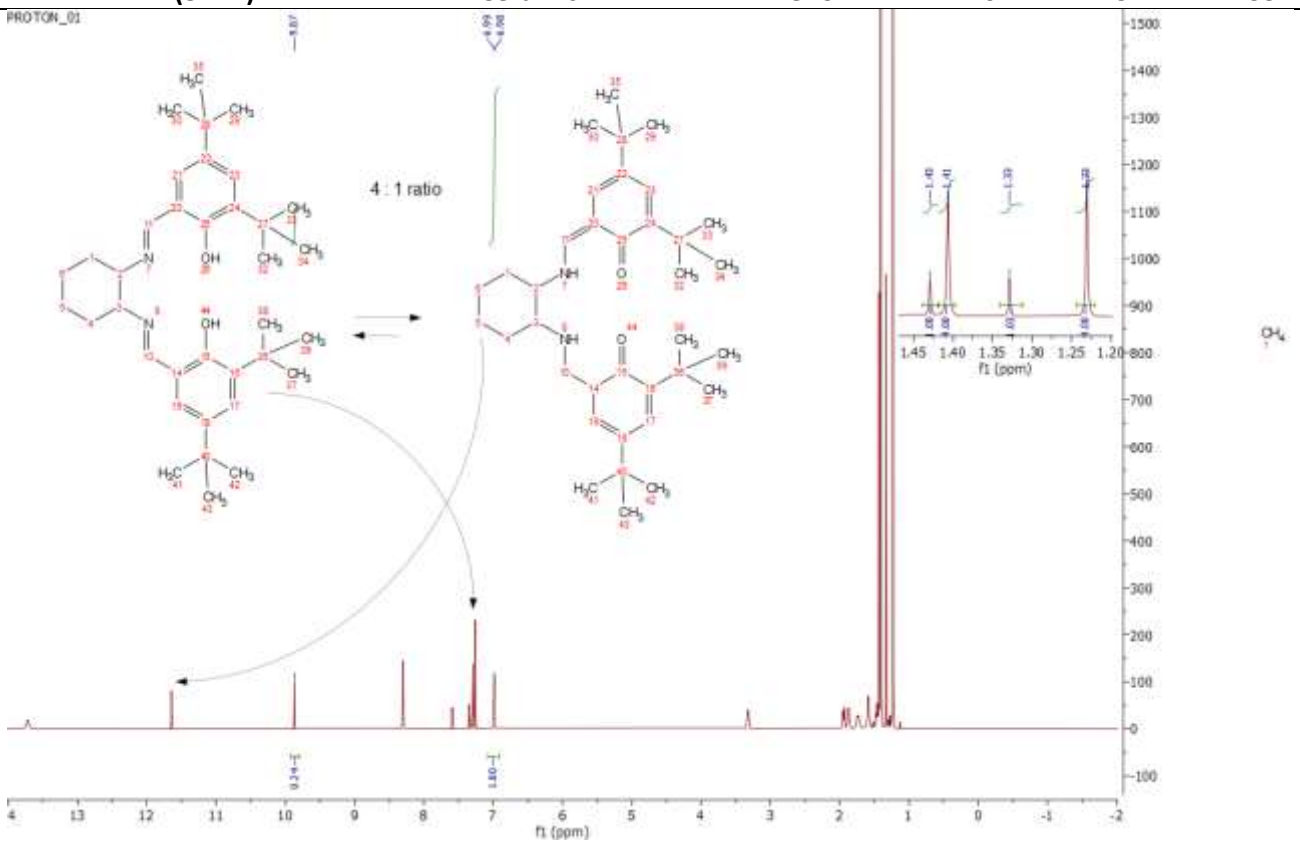


Figure S1. ^{1}H NMR of the ligand racemic-H_2**L1** after 80 minutes

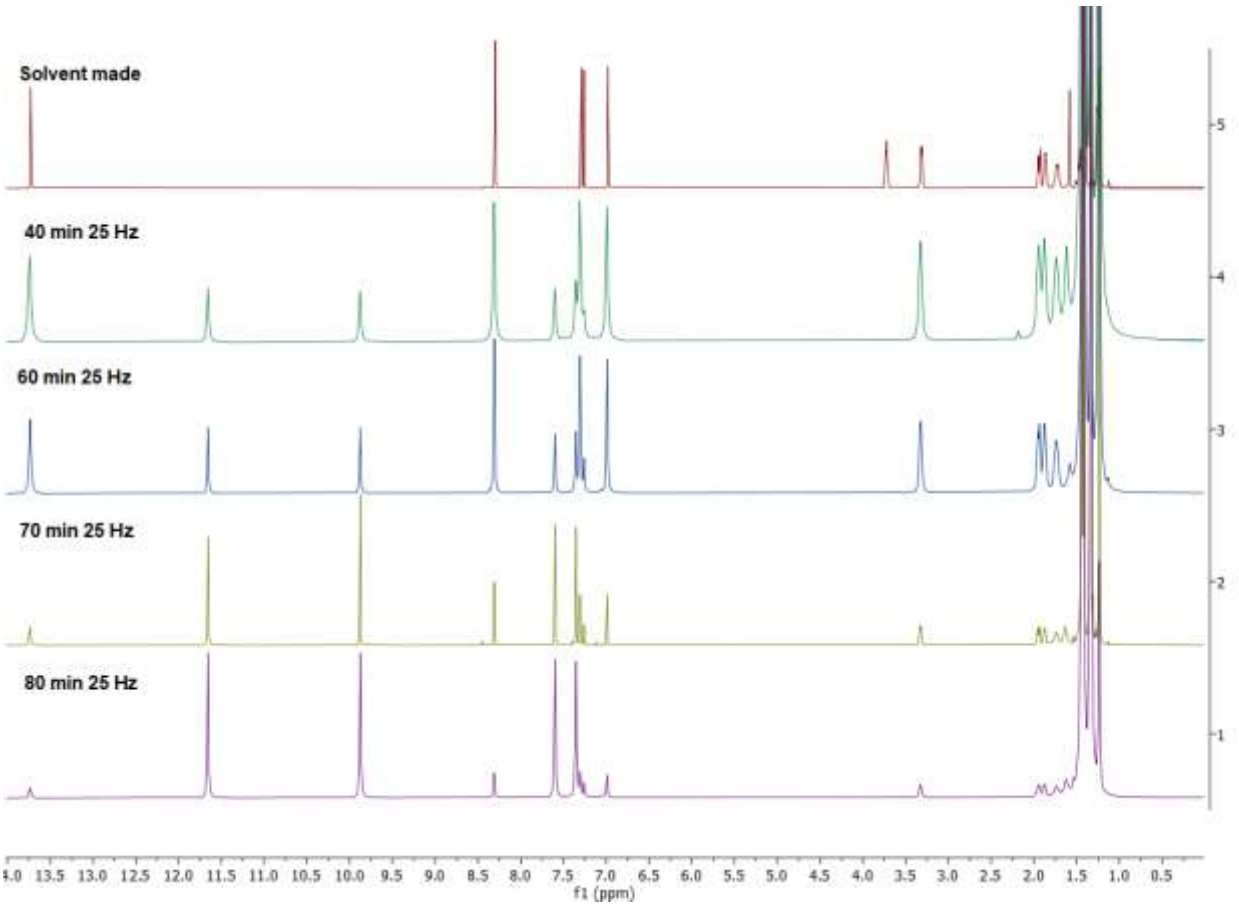


Figure S2. ^{1}H NMR of racemic-H_2**L1** after different milling timings, using steel balls and jars (Entries 1 & 27).

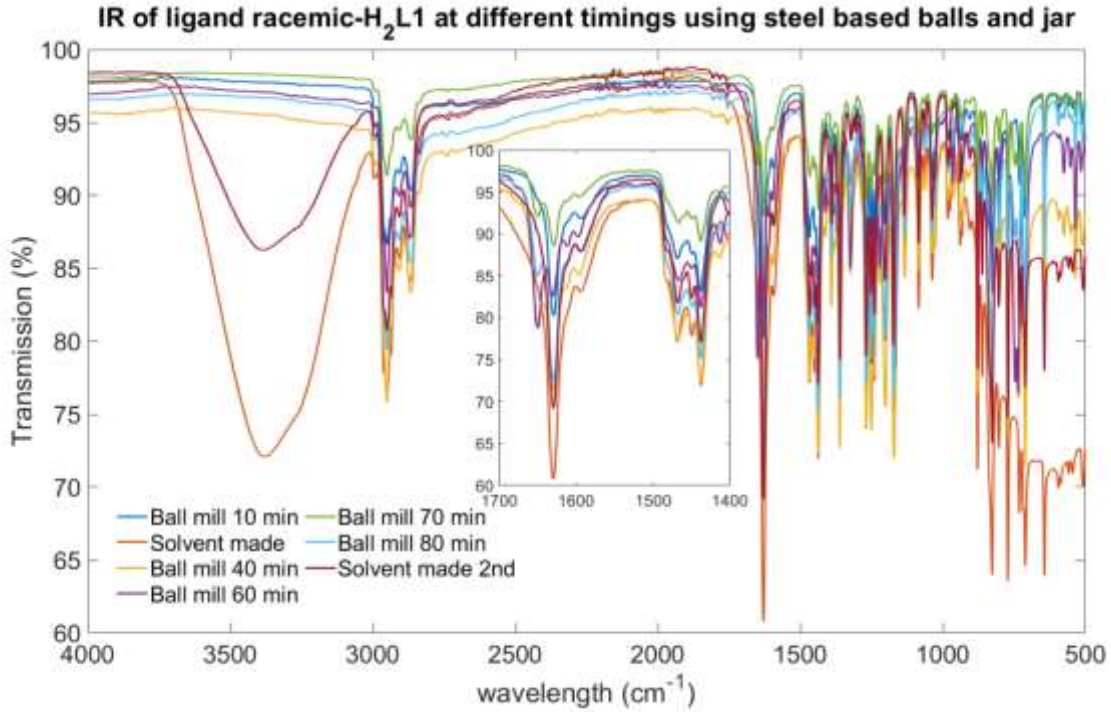
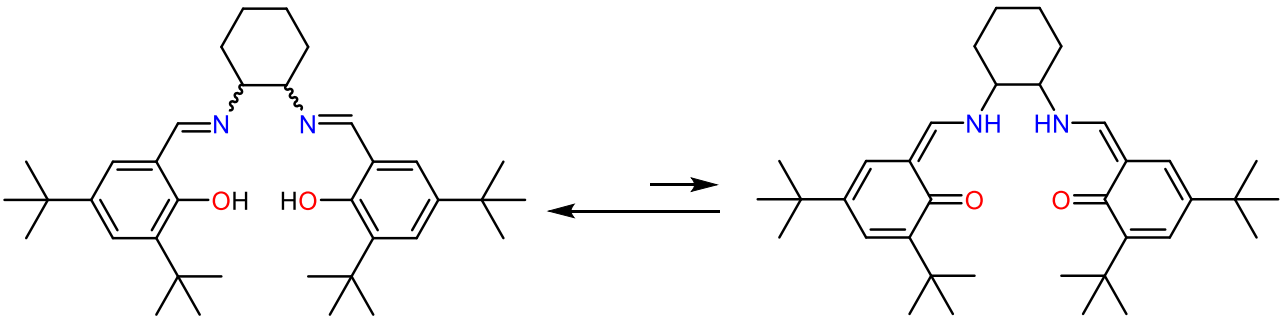


Figure S3. IR spectra of racemic-H_2**L1**synthesized at different timings.



Racemic H_2**L1** - diol form

Racemic H_2**L1** - ketone form

Scheme S1. Resonance structures of the diol (desired) and ketone forms (unwanted) of racemic-H_2**L1**.

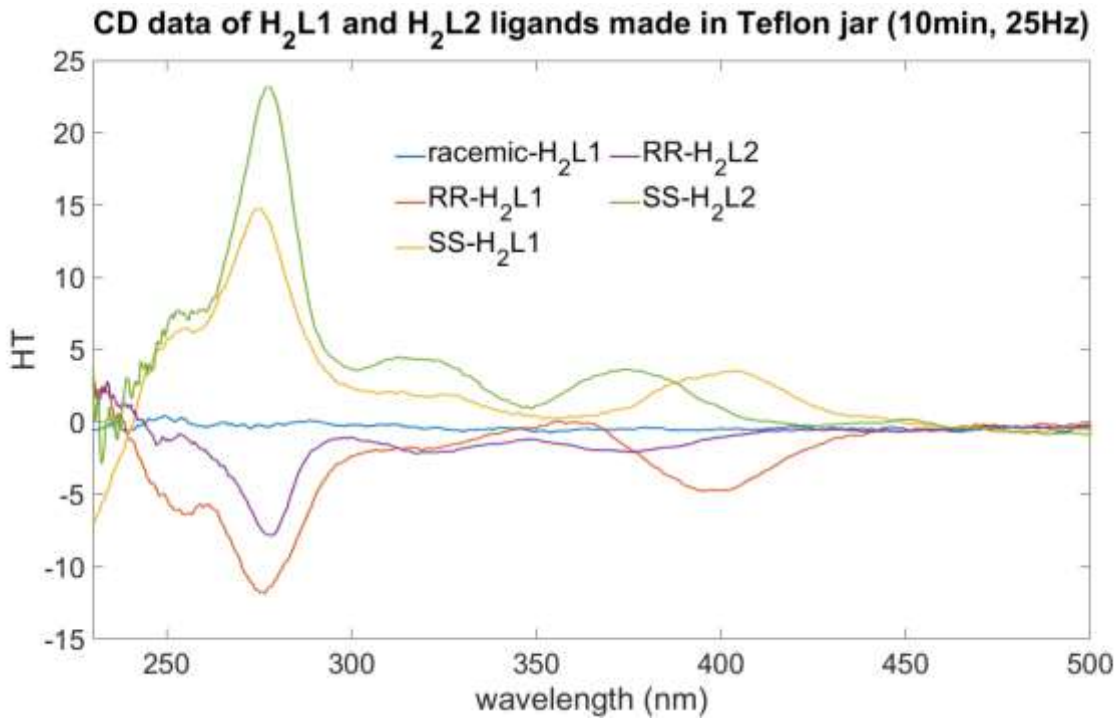


Figure S4. Circular Dichroism data for all ligands

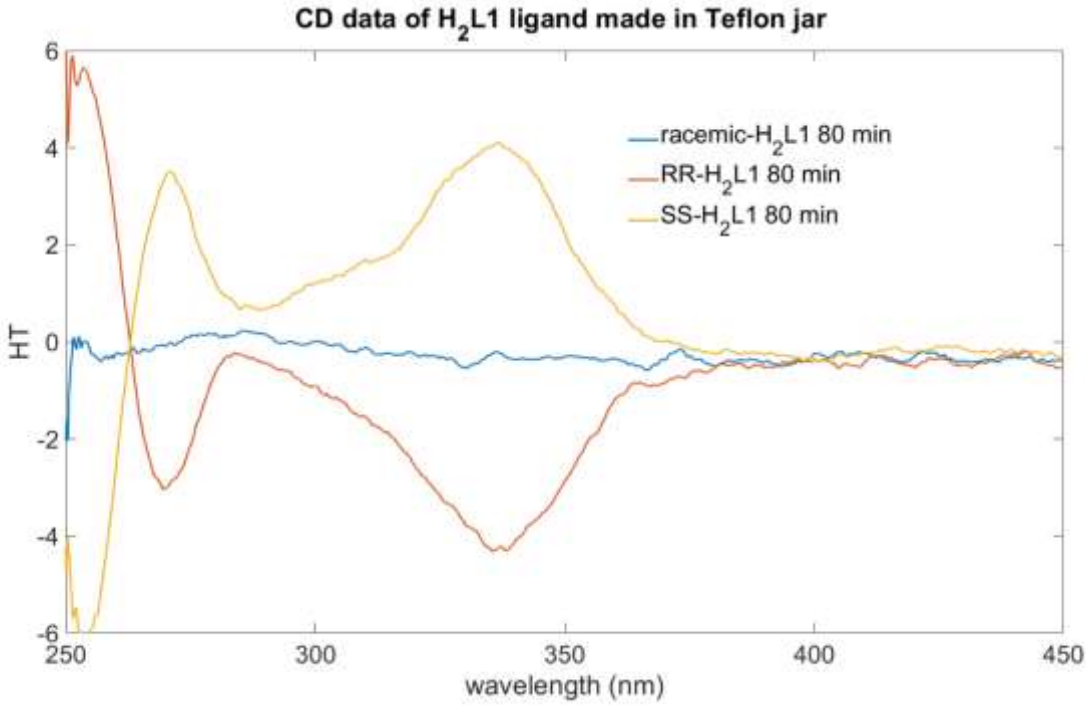


Figure S5. Circular Dichroism data for ligands H_2**L1**, after 80 minutes with Teflon jar and ceramic balls.

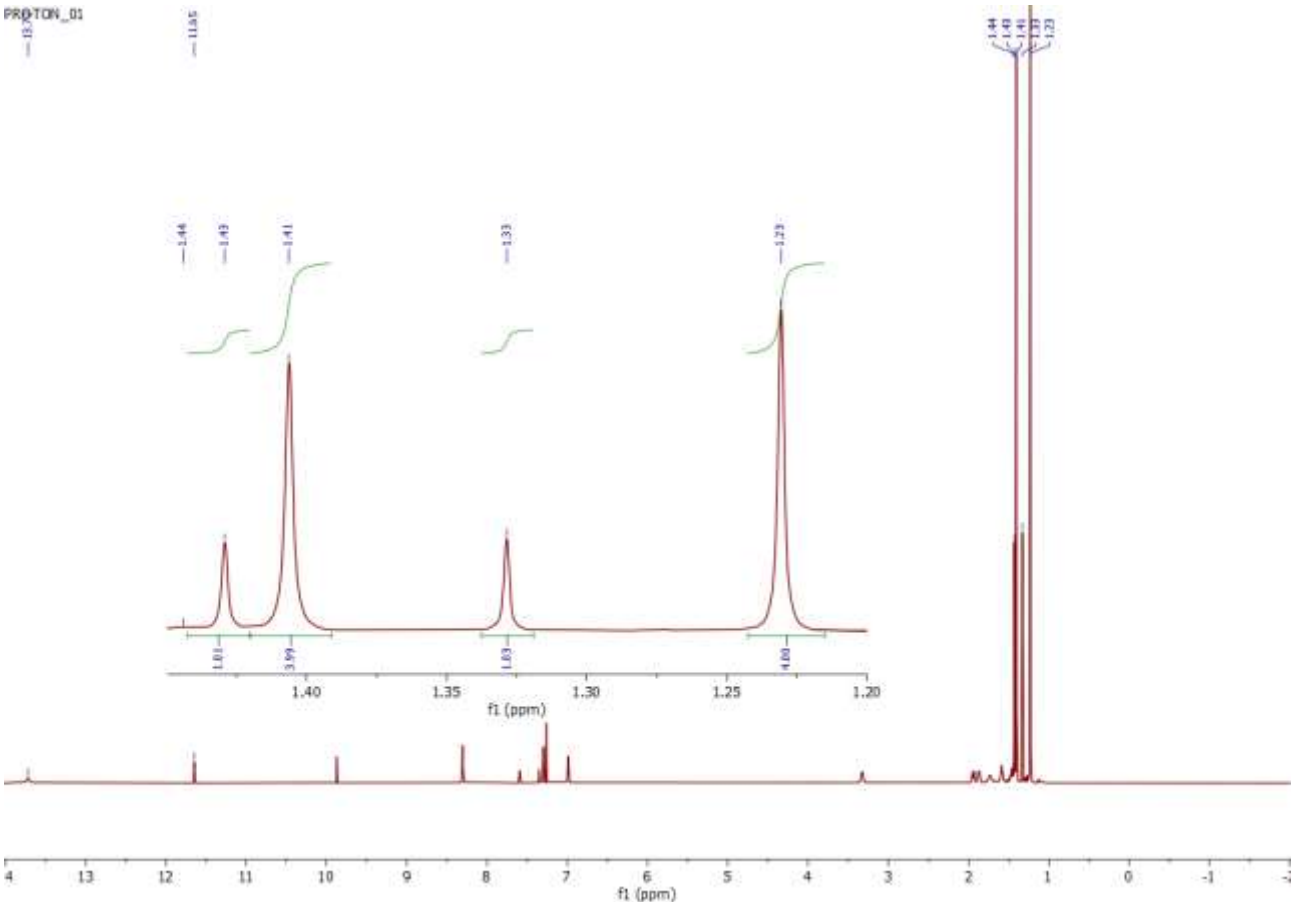


Figure S6. ^{1}H NMR of *RR*-H_2**L2** after 80 minutes

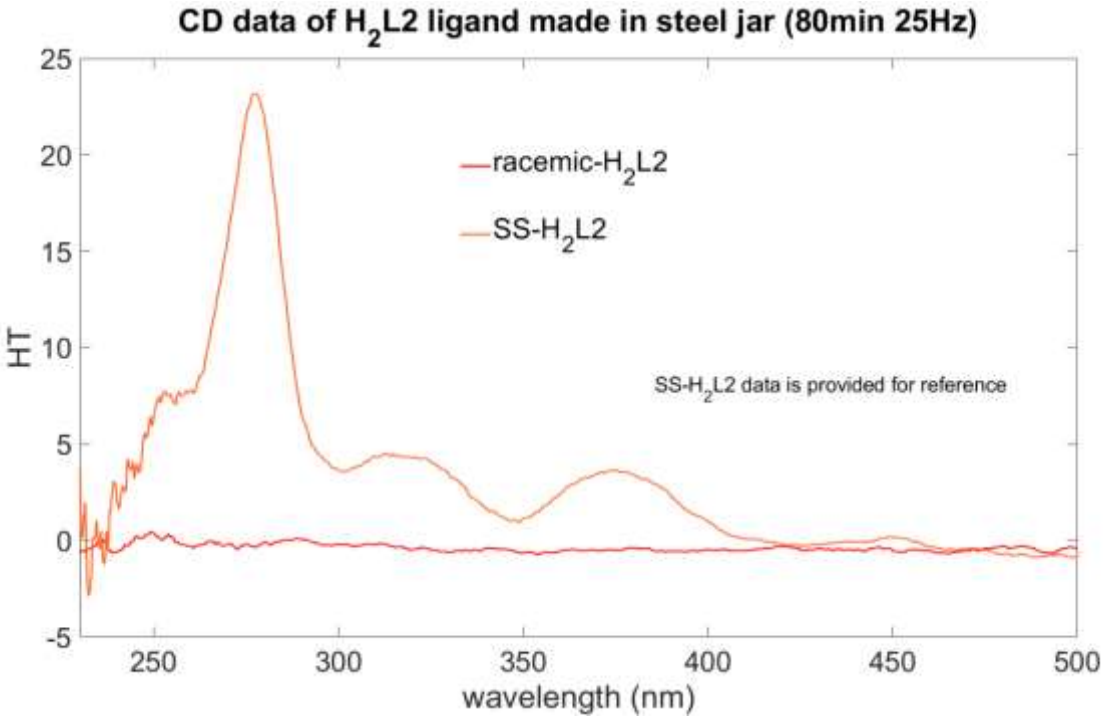


Figure S7. Circular Dichroism data for H_2**L2** that loses chirality (see Table S2 first entry)

Table S2 Crystal data and structure refinement for ligands

Identification code	**SS-H_2L2-BM80min**	**SS-H_2L2-BM10min**	**SS-H_2L2-BM80min_MeOH**	**RR-H_2L2-BM10min**	**RR-H_2L2_Solvent_made**
Empirical formula	$C_{44}H_{56}N_2O_2$	$C_{44}H_{56}N_2O_2$	$C_{44}H_{56}N_2O_2$	$C_{44}H_{56}N_2O_2$	$C_{44}H_{56}N_2O_2$
Formula weight	644.90	644.90	644.90	644.90	644.90
Temperature/K	100(2)	100.00(10)	100.01(10)	100.00(10)	100.00(11)
Crystal system	triclinic	monoclinic	orthorhombic	orthorhombic	orthorhombic
Space group	P-1	I2	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	9.4526(2)	10.8545(2)	10.04086(13)	10.03506(7)	10.03785(4)
b/Å	13.5974(4)	10.17090(10)	19.8914(2)	19.89824(17)	19.90232(11)
c/Å	16.3518(7)	35.9232(5)	20.0896(3)	20.08814(14)	20.09076(10)
α/°	66.069(3)	90	90	90	90
β/°	75.352(3)	95.1270(10)	90	90	90
γ/°	81.926(2)	90	90	90	90
Volume/Å^3	1856.89(11)	3950.05(10)	4012.41(8)	4011.20(5)	4013.66(3)
Z	2	4	4	4	4
ρ_{calc}g/cm^3	1.153	1.084	1.068	1.068	1.067
μ/mm^{-1}	0.533	0.501	0.493	0.493	0.493
F(000)	700.0	1400.0	1400.0	1400.0	1400.0
Crystal size/mm^3	0.04 × 0.02 × 0.01	0.209 × 0.125 × 0.09	0.1 × 0.08 × 0.05	0.08 × 0.04 × 0.02	0.1 × 0.05 × 0.03
Radiation	Cu Kα (λ = 1.54178)	Cu Kα (λ = 1.54178)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.118 to 154.054	4.94 to 136.432	9.868 to 132.658	8.888 to 134.19	8.802 to 132.676
Index ranges	-10 ≤ h ≤ 11, -17 ≤ k ≤ 16, -20 ≤ l ≤ 20	-12 ≤ h ≤ 13, -12 ≤ k ≤ 12, -43 ≤ l ≤ 43	-11 ≤ h ≤ 11, -23 ≤ k ≤ 23, -18 ≤ l ≤ 23	-11 ≤ h ≤ 10, -23 ≤ k ≤ 23, -21 ≤ l ≤ 23	-11 ≤ h ≤ 11, -23 ≤ k ≤ 23, -23 ≤ l ≤ 23
Reflections collected	35872	66029	23123	39138	28720
Independent reflections	7452 [R_{int} = 0.0500, R_{sigma} = 0.0350]	7205 [R_{int} = 0.0416, R_{sigma} = 0.0166]	6686 [R_{int} = 0.0323, R_{sigma} = 0.0239]	7102 [R_{int} = 0.0385, R_{sigma} = 0.0231]	6928 [R_{int} = 0.0358, R_{sigma} = 0.0258]
Data/restraints/parameters	7452/0/447	7205/1/447	6686/0/477	7102/30/459	6928/0/477
Goodness-of-fit on F^2	1.033	1.040	1.039	1.051	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.0459, wR_2 = 0.1137	R_1 = 0.0347, wR_2 = 0.0930	R_1 = 0.0293, wR_2 = 0.0767	R_1 = 0.0316, wR_2 = 0.0816	R_1 = 0.0291, wR_2 = 0.0754
Final R indexes [all data]	R_1 = 0.0565, wR_2 = 0.1209	R_1 = 0.0351, wR_2 = 0.0933	R_1 = 0.0297, wR_2 = 0.0775	R_1 = 0.0326, wR_2 = 0.0826	R_1 = 0.0303, wR_2 = 0.0759
Largest diff. peak/hole / e Å^{-3}	0.23/-0.26	0.16/-0.20	0.16/-0.12	0.25/-0.25	0.13/-0.13
Flack parameter		0.04(8)	0.03(7)	0.04(7)	0.01(7)

Complex synthesis

The complexation reaction of *racemic*-H_2**L1** and $CuCl_2$, in a molar ratio (1:1) was performed using high-vibration ball milling (HVBM). The *racemic*-H_2**L1** (0.544 g, 1.00 mmol) and $CuCl_2$ (0.134 g, 1.00 mmol) were combined in 25 ml ball mill Teflon jar with two Ceramic medium size balls and mixed for 3 hr at 25 Hz frequency. The resulting compound was washed with five drops (~0.25 ml) of H_2O and recrystallised from Acetone (5 ml) and obtained as brown crystals (599 mg, 98% yield)

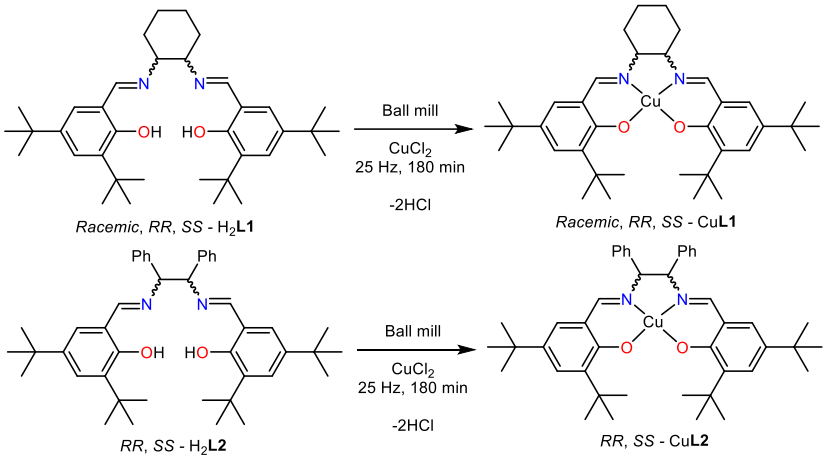


Table S3. Optimisation table for the ball mill synthesis of *racemic*-Cu**L1.** Optimum conditions have been highlighted in bold.

Entry	Method	Metal salt	Metal salt: Ligand ratio	Time (min)	Frequency (Hz)	Jar - balls	Yield (%)
1	BMML+Metal salt	$Cu(OTf)_2$	1:1	10	25	Stainless steel	-
2	BMML+Metal salt	$Cu(OTf)_2$	1:1	20	25	Stainless steel	-
3	BMML+Metal salt	$Cu(OTf)_2$	1:1	30	25	Stainless steel	-
4	BMML+Metal salt	$Cu(OTf)_2$	1:1	40	25	Stainless steel	20
5	BMML+Metal salt	$Cu(OTf)_2$	1:1	50	25	Stainless steel	38
6	BMML+Metal salt	$Cu(OTf)_2$	1:1	60	25	Stainless steel	50
7	BMML+Metal salt	$Cu(OTf)_2$	1:1	70	25	Stainless steel	55
8	BMML+Metal salt	$Cu(OTf)_2$	1:1	80	25	Stainless steel	64
9	BMML+Metal salt	$Cu(OTf)_2$	1:1	90	25	Stainless steel	70
10	BMML+Metal salt	$Cu(OTf)_2$	1:1	120	25	Stainless steel	85
11	BMML+Metal salt	$Cu(NO_3)_2$	1:1	120	25	Stainless steel	75
12	BMML+Metal salt	$CuBr_2$	1:1	120	25	Stainless steel	88
13	BMML+Metal salt	$Cu(BF_4)_2$	1:1	120	25	Stainless steel	90
14	BMML+Metal salt	$CuCl_2$	1:1	120	25	Stainless steel	97
15	**BMML+Metal salt**	**$CuCl_2$**	**1:1**	**120**	**25**	**Teflon, ceramic**	**>99**
16	SML+Metal salt	$Cu(OTf)_2$	1:1	10	25	Stainless steel	-
17	SML+Metal salt	$Cu(OTf)_2$	1:1	20	25	Stainless steel	-
18	SML+Metal salt	$Cu(OTf)_2$	1:1	30	25	Stainless steel	-
19	SML+Metal salt	$Cu(OTf)_2$	1:1	40	25	Stainless steel	-
20	SML+Metal salt	$Cu(OTf)_2$	1:1	50	25	Stainless steel	-
21	SML+Metal salt	$Cu(OTf)_2$	1:1	60	25	Stainless steel	30
22	SML+Metal salt	$Cu(OTf)_2$	1:1	70	25	Stainless steel	48
23	SML+Metal salt	$Cu(OTf)_2$	1:1	80	25	Stainless steel	55
24	SML+Metal salt	$Cu(OTf)_2$	1:1	90	25	Stainless steel	58
25	SML+Metal salt	$Cu(OTf)_2$	1:1	120	25	Stainless steel	62
26	SML+Metal salt	$Cu(OTf)_2$	1:1	120	25	Teflon, ceramic	72
27	SML+Metal salt	$CuCl_2$	1:1	120	25	Teflon, ceramic	75
28	All in one step	$CuCl_2$	1:2:1	120	25	Teflon, ceramic	30

Ball mill made ligand (BMML); Solvent made ligand (SML)

PXRD

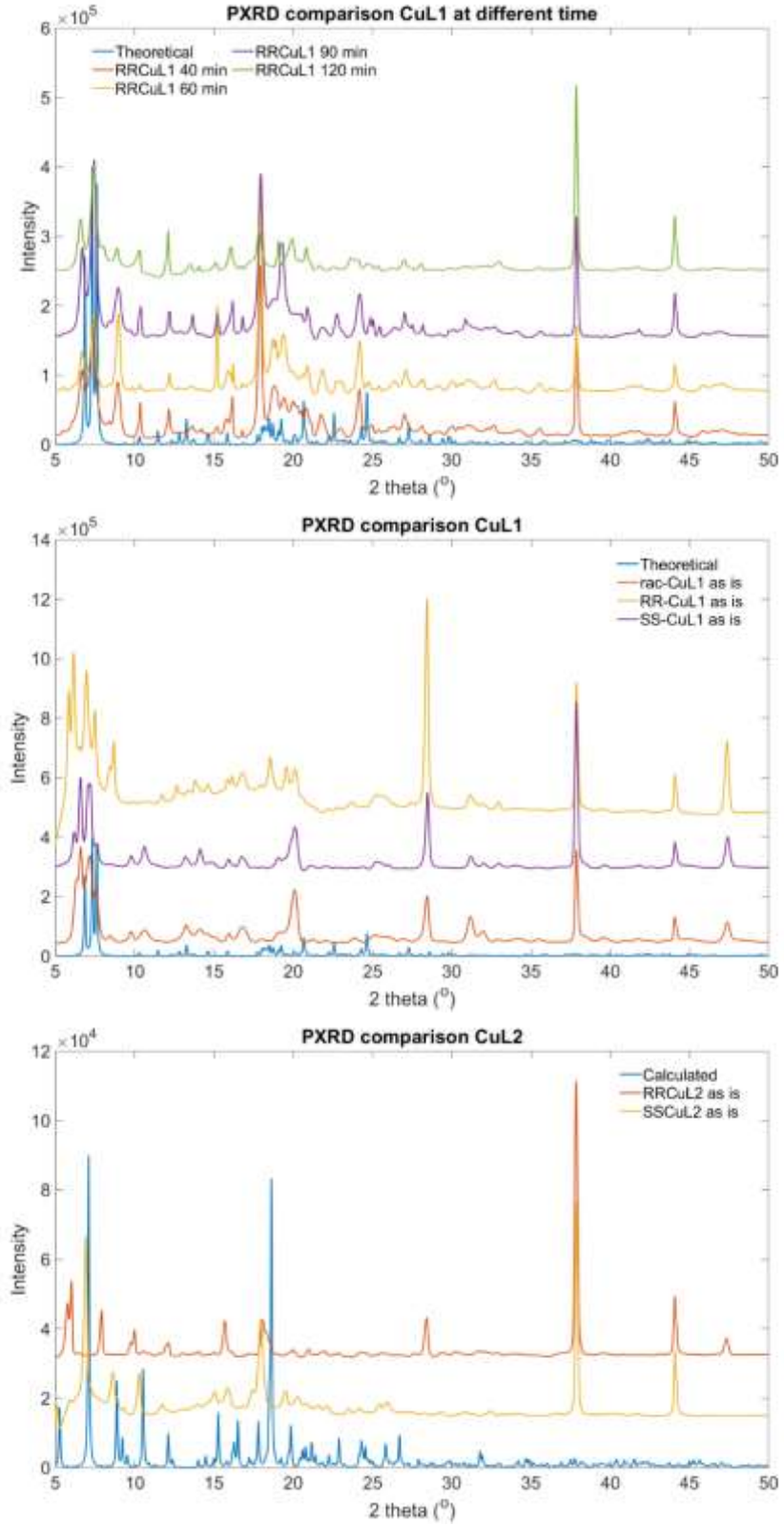
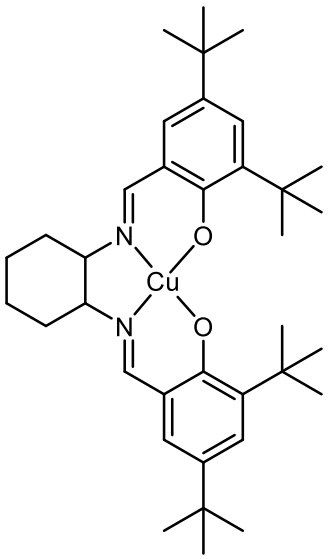


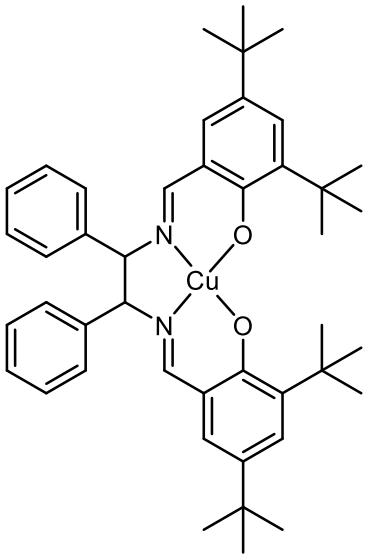
Figure S8. The Powder XRD data for Cu**L1**/ Cu**L2** at different timings (upper) and after 3 hours (middle, lower). These data suggest either the presence of impurities (these are complexes with coordinated water molecules) or crystallisation of the expected compound in a different space group.

Elemental analyses

Elemental analysis results for all complexes were recorded at London Metropolitan University. The samples, upon synthesis, were stored in Eppendorf vials. There is a deviation in the data; we assume this deviation is caused by losing their crystallinity and absorbing moisture from the atmosphere; therefore, we provide estimated formulae that match the experimental values. The TG, PXRD and EPR studies further validate our estimation, confirming all complexes' phase purity.



Chemical Formula: $C_{36}H_{52}CuN_2O_2$
Exact Mass: 607.33
Molecular Weight: 608.37
Elemental Analysis:
C, 71.07; H, 8.62; Cu, 10.45; N, 4.60; O, 5.26



Chemical Formula: $C_{44}H_{54}CuN_2O_2$
Exact Mass: 705.35
Molecular Weight: 706.47
Elemental Analysis:
C, 74.81; H, 7.70; Cu, 8.99; N, 3.97; O, 4.53

Rac-CuL1, Calculated for [**CuL**] C: 71.07; H: 8.62 ; N: 4.60; Found C: 67.09; H: 7.79 ; N:4.36; corresponding to [**CuL1**] 2(**H_2O**) C: 67.15; H: 8.01; N:4.35

RR-CuL1 Calculated for [**CuL**] C: 71.07; H: 8.62 ; N: 4.60; Found C: 68.99; H: 7.82 ; N:4.23, corresponding to [**RR-CuL1**] (**H_2O**) C: 68.73; H: 7.83; N:4.31.

SS-CuL1, Calculated for [**CuL**] C: 71.07; H: 8.62 ; N: 4.60; Found C: 65.81; H: 7.70 ; N:4.62, corresponding to [**SS-CuL1**] 3(**H_2O**) C: 65.91; H: 7.85; N:4.76.

RR-CuL2, Calculated for [**CuL**] C: 74.81; H: 7.70; N: 3.97; Found C: 63.39; H: 8.58; N: 3.51; corresponding to [**RR-CuL2**] 7(**H_2O**) C: 63.48; H: 8.23; N: 3.36;

SS-CuL2, Calculated for [**CuL**] C: 74.81; H: 7.70; N: 3.97; Found C: 62.86; H: 8.26; N: 3.30; corresponding to [**SS-CuL2**] **7.5**(**H_2O**) C: 62.80; H: 8.26; N: 3.33;

Circular Dichroism

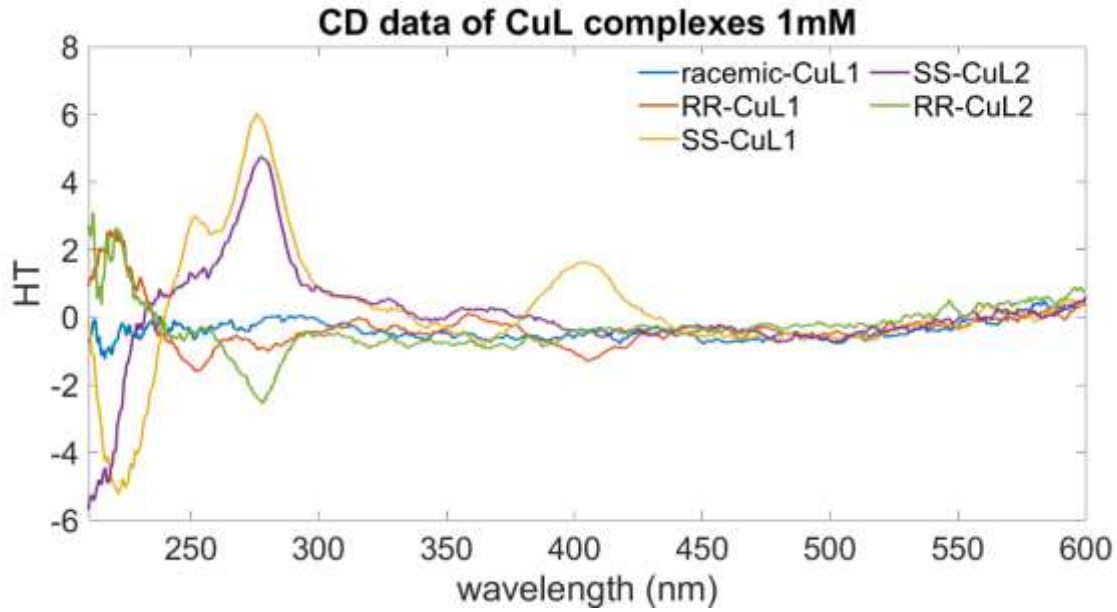


Figure S9. CD data for all complexes at 1 mM in MeOH

UV-Vis

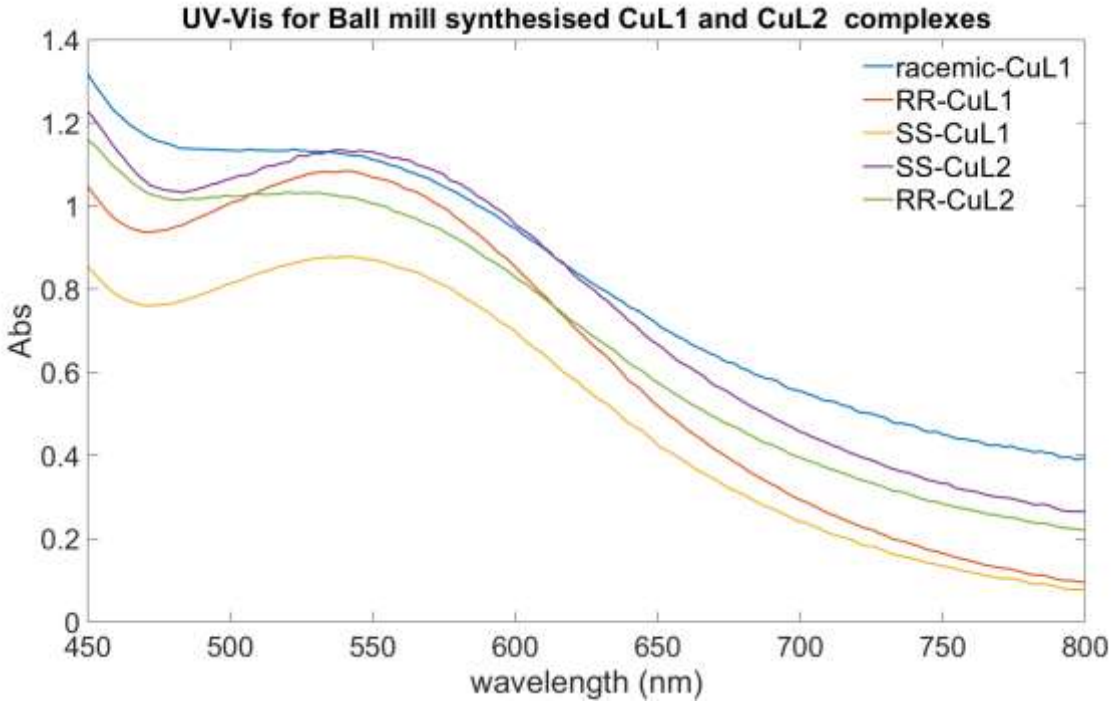
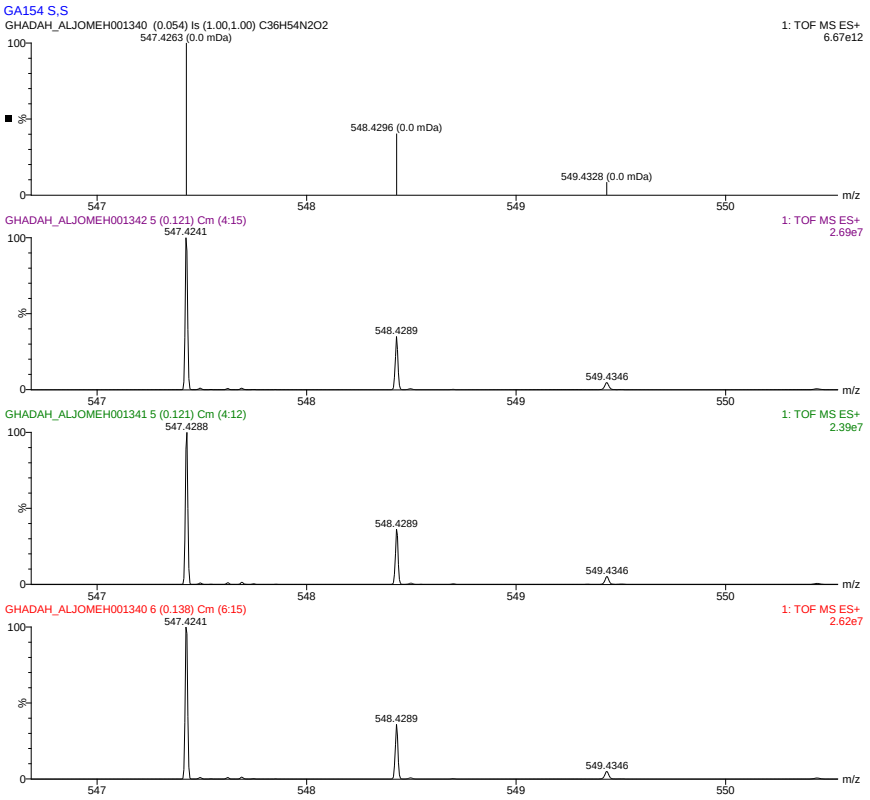


Figure S10. UV-Vis of all complexes at 1 mM in DCM

ESI-MS

H_2L1



H_2L2

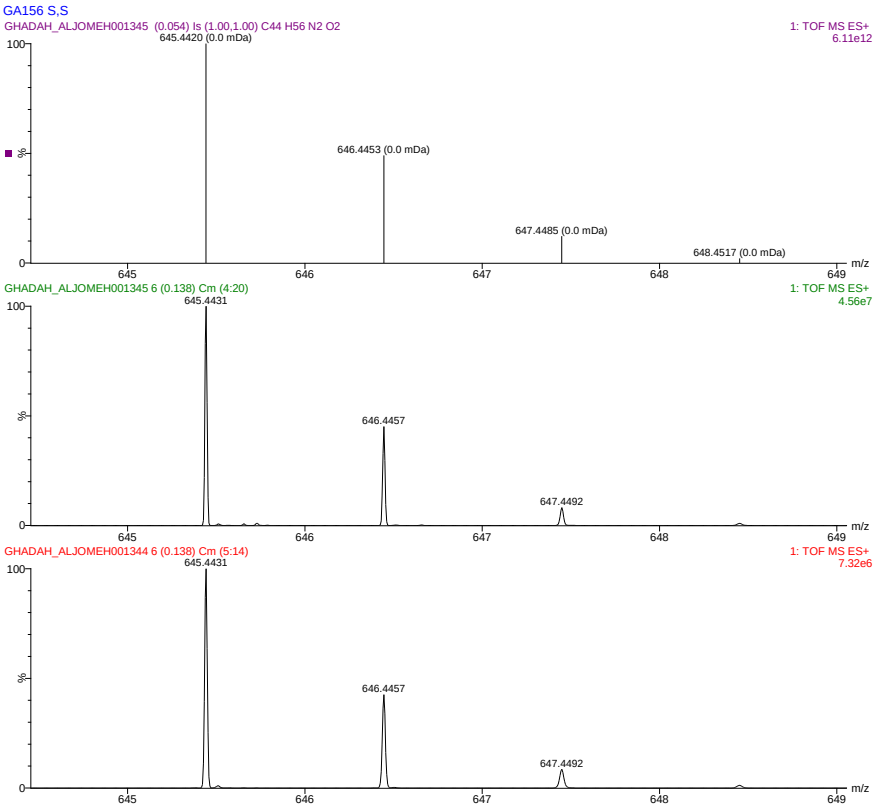
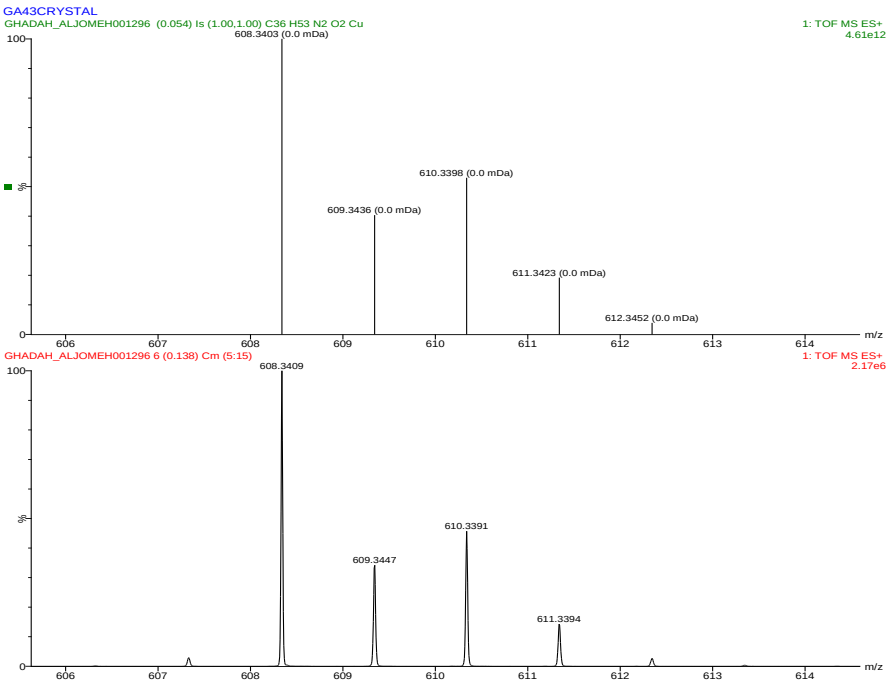


Figure S11. ESI – MS of ligands.

CuL1



CuL2

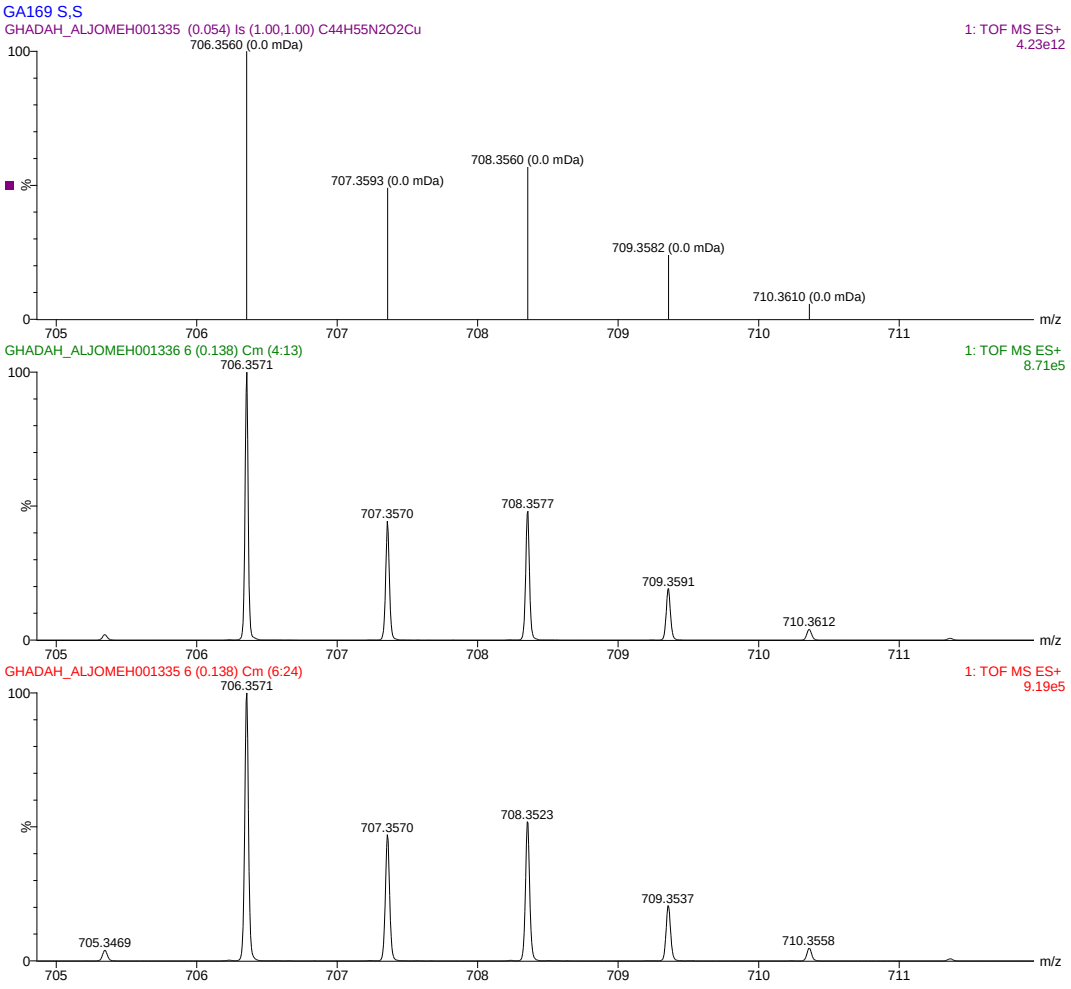


Figure S12. ESI – MS of complexes

Table S4 Crystal data and structure refinement for complexes

Identification code	**SS-CuL2**	**RR-CuL2**	**SS-CuL2_recovered**	**RR-CuL2_recovered**
Empirical formula	$C_{44}H_{54}CuN_2O_2$	$C_{44}H_{54}CuN_2O_2$	$C_{176}H_{216}Cu_4N_8O_8$	$C_{44}H_{54}CuN_2O_2$
Formula weight	706.477	706.477	2825.72	706.43
Temperature/K	100(2)	100(2)	100.00(10)	100.02(11)
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1$	$P2_1$	$P2_1$	$P2_1$
a/Å	12.2627(2)	12.2761(2)	12.2563(2)	12.2439(2)
b/Å	18.5521(2)	18.5554(2)	18.5591(2)	18.5343(2)
c/Å	17.4656(2)	17.4532(2)	17.4919(3)	17.4600(2)
α/°	90	90	90	90
β/°	105.761(1)	105.807(2)	105.757(2)	105.7640(10)
γ/°	90	90	90	90
Volume/Å^3	3824.02(9)	3825.29(10)	3829.29(11)	3813.21(9)
Z	4	4	1	4
ρ_{calc}g/cm^3	1.227	1.227	1.225	1.231
μ/mm^{-1}	1.089	1.089	1.088	1.093
F(000)	1504.2	1504.2	1508.0	1508.0
Crystal size/mm^3	0.23 × 0.2 × 0.04	0.2 × 0.1 × 0.04	0.1 × 0.02 × 0.01	0.05 × 0.04 × 0.03
Radiation	Cu Kα (λ = 1.54178)	Cu Kα (λ = 1.54178)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.26 to 153.7	5.26 to 153.34	5.25 to 134.294	5.26 to 134.37
Index ranges	-14 ≤ h ≤ 15, -19 ≤ k ≤ 23, -21 ≤ l ≤ 22	-14 ≤ h ≤ 14, -23 ≤ k ≤ 18, -21 ≤ l ≤ 22	-14 ≤ h ≤ 14, -22 ≤ k ≤ 22, -20 ≤ l ≤ 20	-14 ≤ h ≤ 14, -20 ≤ k ≤ 21, -20 ≤ l ≤ 20
Reflections collected	35313	36390	68220	143353
Independent reflections	12825 [R_{int} = 0.0512, R_{sigma} = 0.0513]	12418 [R_{int} = 0.0449, R_{sigma} = 0.0417]	13484 [R_{int} = 0.0835, R_{sigma} = 0.0508]	13388 [R_{int} = 0.0795, R_{sigma} = 0.0332]
Data/restraints/parameters	12825/1/907	12418/1/907	13484/1/907	13388/1/907
Goodness-of-fit on F^2	1.039	1.041	1.036	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0658, wR_2 = 0.1733	R_1 = 0.0400, wR_2 = 0.1005	R_1 = 0.0662, wR_2 = 0.1788	R_1 = 0.0419, wR_2 = 0.0985
Final R indexes [all data]	R_1 = 0.0698, wR_2 = 0.1794	R_1 = 0.0461, wR_2 = 0.1050	R_1 = 0.0703, wR_2 = 0.1833	R_1 = 0.0453, wR_2 = 0.0999
Largest diff. peak/hole / e Å^{-3}	0.74/-1.07	0.34/-0.40	1.44/-0.64	0.35/-0.43
Flack parameter	-0.016(16)	-0.003(16)	0.03(3)	0.008(15)

EPR

CW X-band EPR spectra (T = 120 and 290 K) were recorded on a Bruker EMX spectrometer equipped with an ER4119HS resonator, employing 100 kHz field modulation, 0.3 mT modulation depth and 10.0 mw microwave power. Computer simulations were performed using the Matlab toolbox in Easyspin,[4] implementing the chili function for slow motion and pepper function for solid state spectra.

The room temperature spectra of all samples indicate anisotropic rotation in the solution phase, and are characterized by an axial diffusion tensor, described using a rotational correlation time (in seconds), t_{corr}. Notably, no evidence of organic radicals were detected in the room temperature measurements.

Table S5 Spin Hamiltonian parameters for *SS*-Cu**L2** in the presence of A^3 substrates

Complex	$g^{a,b}$				A/ MHz		
	g_1	g_2	g_3		$^cA_1$	$^dA_2$	$^eA_3$
SS-Cu**L2**	2.15	2.01	2.01	^{63,65}Cu	590	90	90
				^{14}N	50	37	38
				^{1}H	20	16	24
	$t_{corr} = [0.15, 0.02] \times 10^{-9}$ s						
SS-Cu**L2**: phenylacetylene	2.27	2.09	2.09	^{63,65}Cu	500	100	100
				^{14}N	50	37	38
				^{1}H	20	16	24
	$t_{corr} = [0.2, 0.1] \times 10^{-9}$ s						
SS-Cu**L2**: Pyrrolidine:aldehyde	2.27	2.078	2.078	^{63,65}Cu	500	90	90
				^{14}N	40	37	38
				^{1}H	20	16	24
SS-Cu**L2**: A^3	2.27	2.06	2.06	^{63,65}Cu	500	60	60
				^{14}N	40	38	50
				^{1}H	20	24	20

[a] *g*- and *A*-frames are all taken as coincident with the molecular frame; [b] ± 0.005; [c] ± 20; [d] ± 10

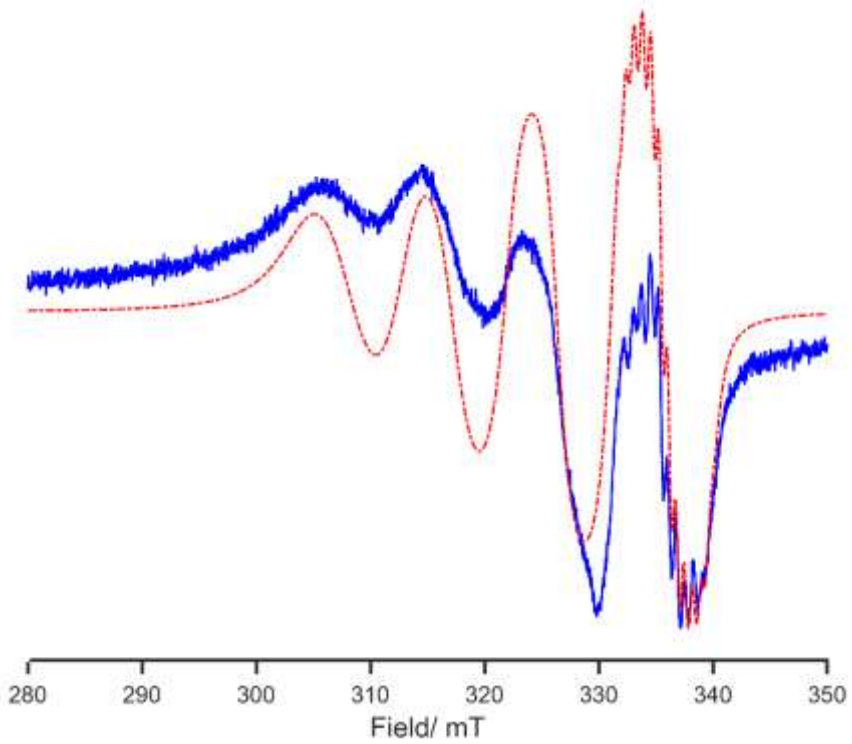


Figure S13 CW X-band EPR spectrum (T = 290 K) of *SS*-Cu**L2** in toluene:DCM solvent; (blue, solid) experimental, (red, dotted) simulation

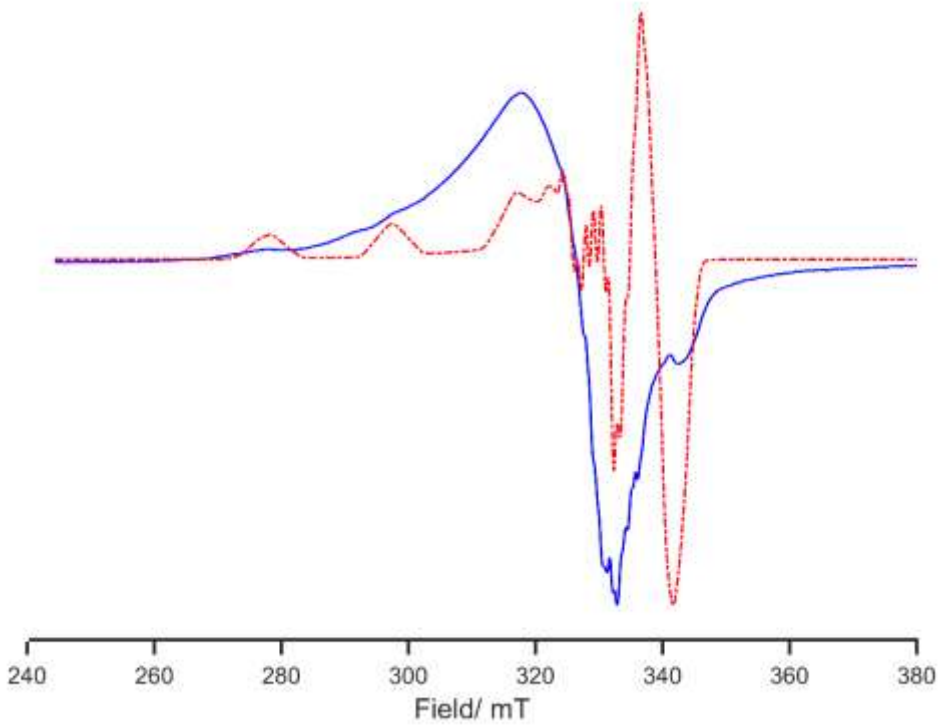


Figure S14 CW X-band EPR spectrum (T = 120 K) of *SS*-Cu**L2** in toluene:DCM solvent; (blue, solid) experimental, (red, dotted) simulation

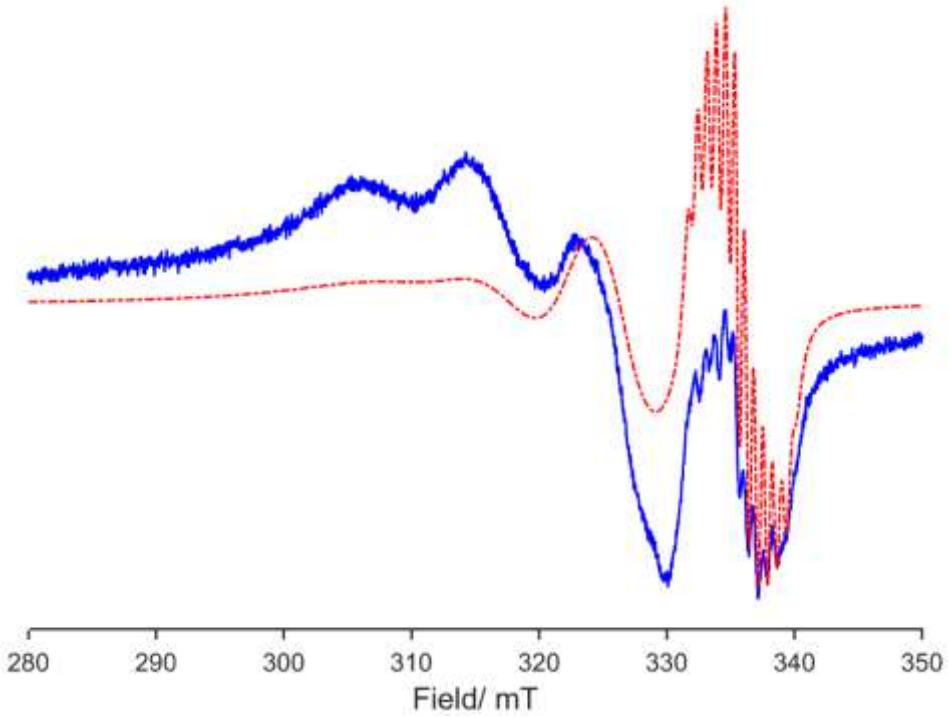


Figure S15 CW X-band EPR spectrum (T = 290 K) of *SS*-Cu**L2** with phenyacetylene; (blue, solid) experimental, (red, dotted) simulation

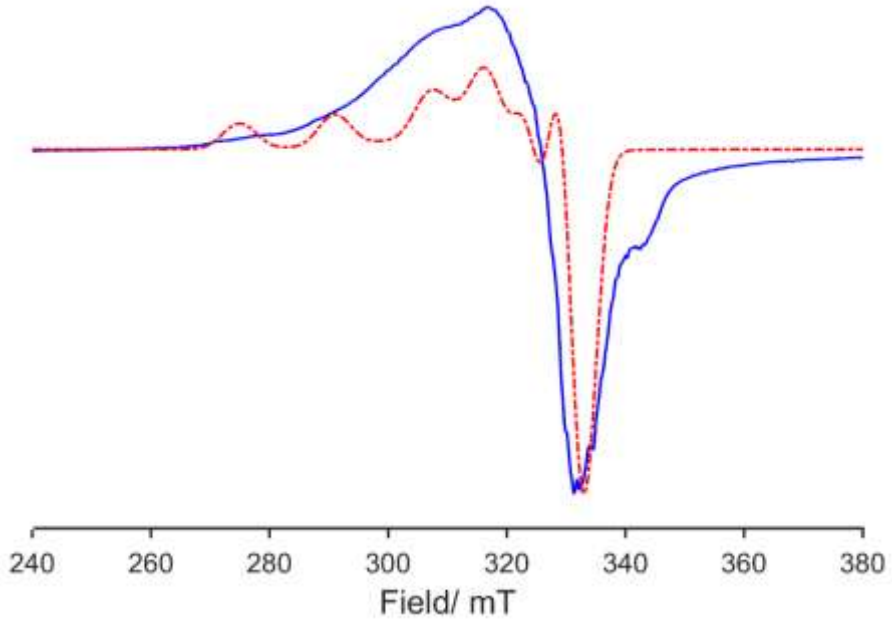


Figure S16 CW X-band EPR spectrum (T = 120 K) of *SS*-Cu**L2** with phenyacetylene; (blue, solid) experimental, (red, dotted) simulation

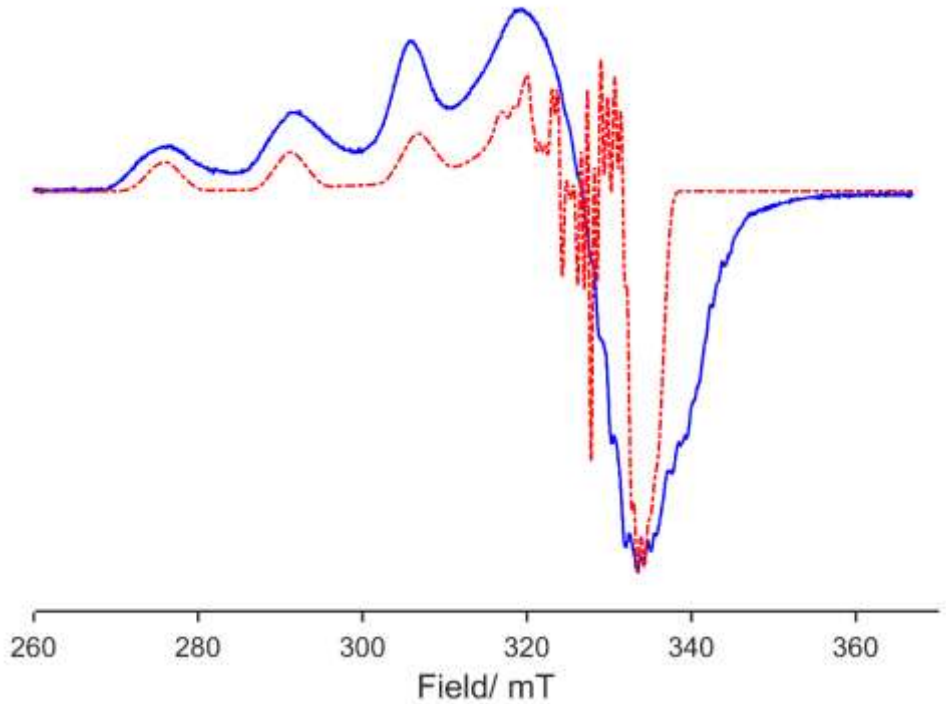


Figure S17 CW X-band EPR spectrum (T = 120 K) of *SS*-Cu**L2** with pyrrolidine + cyclohexanecarboxaldehyde; (blue, solid) experimental, (red, dotted) simulation

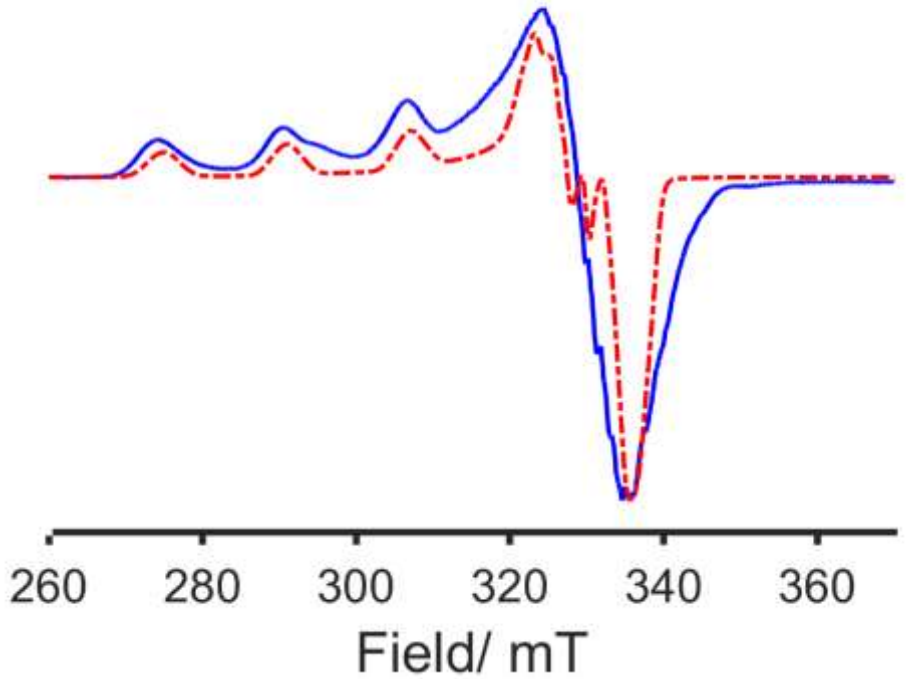


Figure S18 CW X-band EPR spectrum (T = 120 K) of *SS*-Cu**L2** with complete A^3 coupling substrates; (blue, solid) experimental, (red, dotted) simulation

Catalysis

Standard procedure for synthesis of propargylamines

Aldehyde (1.5 mmol, 1.5 eq.), amine (1.5 mmol, 1.5 eq.), alkyne (1.0 mmol, 1.0 eq.) and Cu catalyst (2 mol%, based on aldehyde) were placed in a 25 ml ball mill Teflon jar with two Ceramic medium size balls and mixed for 180 minutes. Then, the mixture was extracted with CH_2Cl_2 (2 mL) and filtered through a metal scavenger. The resultant solution was concentrated under reduced pressure, and the resulting oily residue was then loaded into flash column chromatography. The product was isolated through silica gel using a diethyl ether/petroleum ether (fraction 40-60) mixture as the gradient eluent (99:01-30:70 v/v) to afford pure propargylamines (**1** - **23**). Propargylamine **24** can be synthesised under microwave irradiation in a gram scale (Method A) and mechanochemically up to 500 mg scale (Method B).

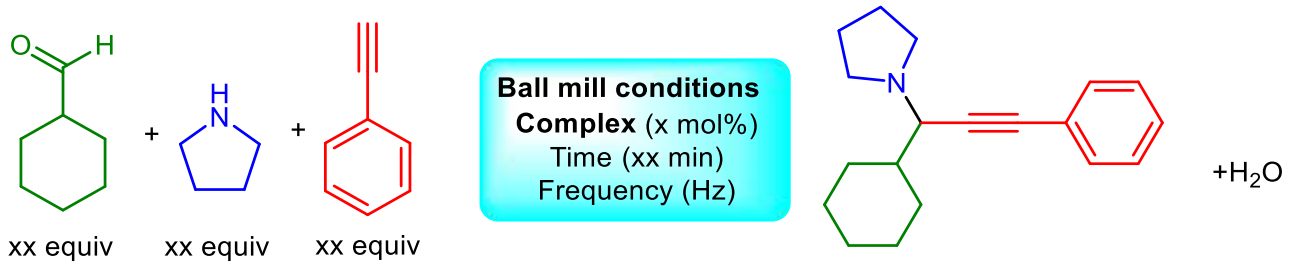
Method A

Inside a 25 ml microwave vial 4-(N-BOC-amino)piperidine (5314.9 mg, 1.0 eq), cyclohexanecarboxaldehyde (3213.7 µL, 1.0 eq) and $CuBr_2$ (591.6 mg, 0.1 eq) were suspended in MeCN (15 ml). The mixture was sonicated for 15 minutes leading to the formation of a pale blue suspension which was then treated with 3-butyn-1-ol (2000 µL, 1.0 eq) and irradiated in a Biotage Initiator microwave reactor at 60°C for 3 hours. Upon completion a brown solution had formed which was diluted with aq. $NaHCO_3$ (20 ml). This mixture was extracted into DCM (3 x 20 ml) and the combined organics were washed with aq. $NaHCO_3$ (3 x 30 ml) until the aqueous layer was clear and colourless. The organics were dried over $MgSO_4$ and concentrated to residue which was dissolved in minimal MeOH and passed through a Isolute Si-Thiol column. The filtrate was concentrated yielding a pale yellow, viscous oil. The oil was further purified by column chromatography (80g SiO_2, hexanes: ethyl acetate. 100% hexanes to 100% ethyl acetate over 22 minutes).

Method B

Aldehyde (1.0 mmol, 1.0 eq.), amine (1.0 mmol, 1.0 eq.), alkyne (1.0 mmol, 1.0 eq.)Cu catalyst (2 mol%, based on aldehyde) and 0.1mL of CH_3CN were placed in a 25 ml ball mill Teflon jar with two Ceramic medium size balls and mixed for 180 minutes. Then, the mixture was extracted with CH_2Cl_2 (2 mL) and filtered through a metal scavenger.

Table S6. Optimisation table for propargylamine synthesis



Entry	Aldehyde (mmol)	Amine (mmol)	Alkyne (mmol)	Complex (% mol)	Time	Frequency (Hz)	Yield (%)
1	1.0	1.1	1.2	2	30 min	25	34
2	1.0	1.1	1.2	5	60 min	25	52
3	1.0	1.1	1.2	7	99 min	25	59
4	1	1	1	5	2 hr	25	72
5	1.2	1.1	1.0	5	2 hr	25	81
6	1.5	1.5	1.0	2	2 hr	25	89
7	1.5	1.5	1.0	2	3 hr	25	95
8	0.75	0.75	1	2	3 hr	25	28

NMR figures with impurities / control experiments

Figure S19. Crude ^{1}H NMR of reaction entry 1, Table 2

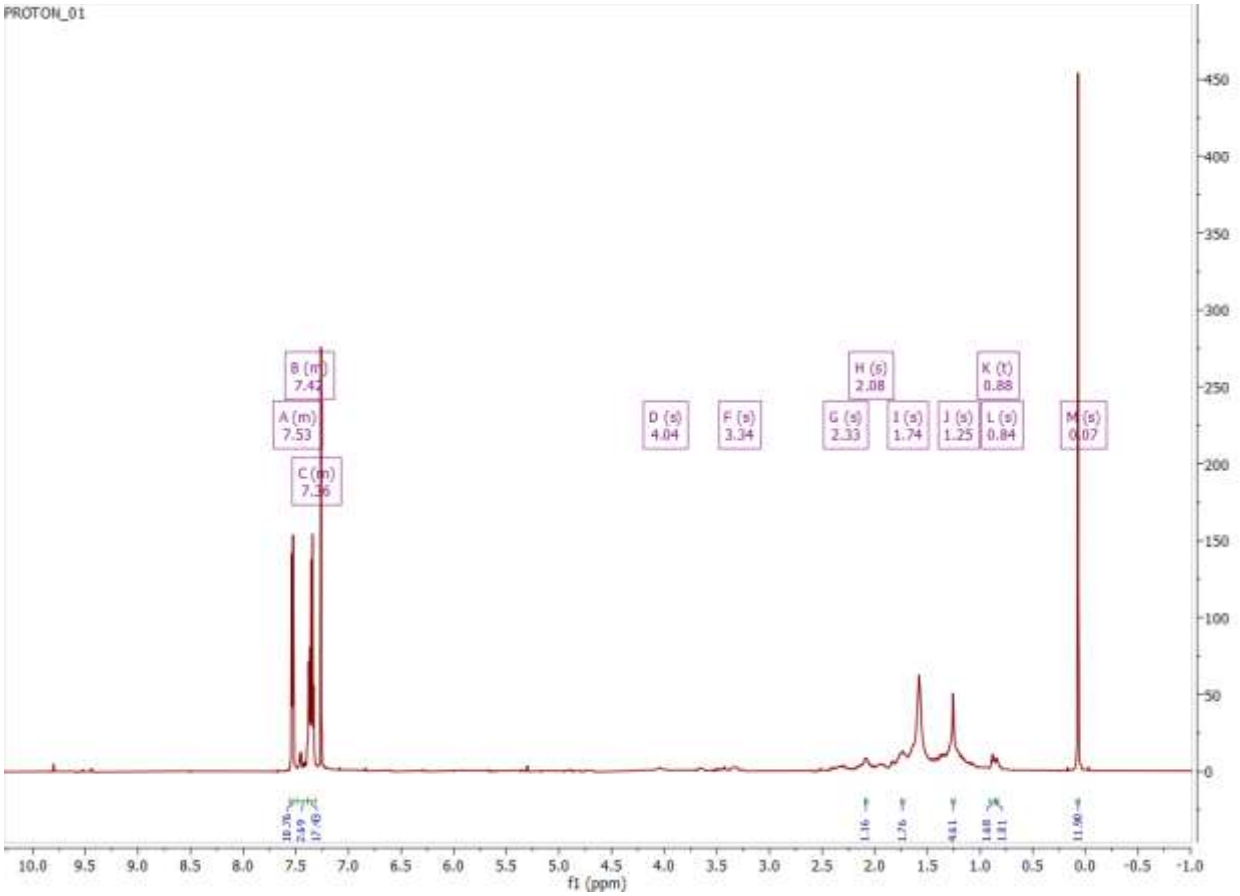


Figure S20. Crude ^{1}H NMR of the reaction with $CuCl_2$ (2% loading) entry 12, Table 2

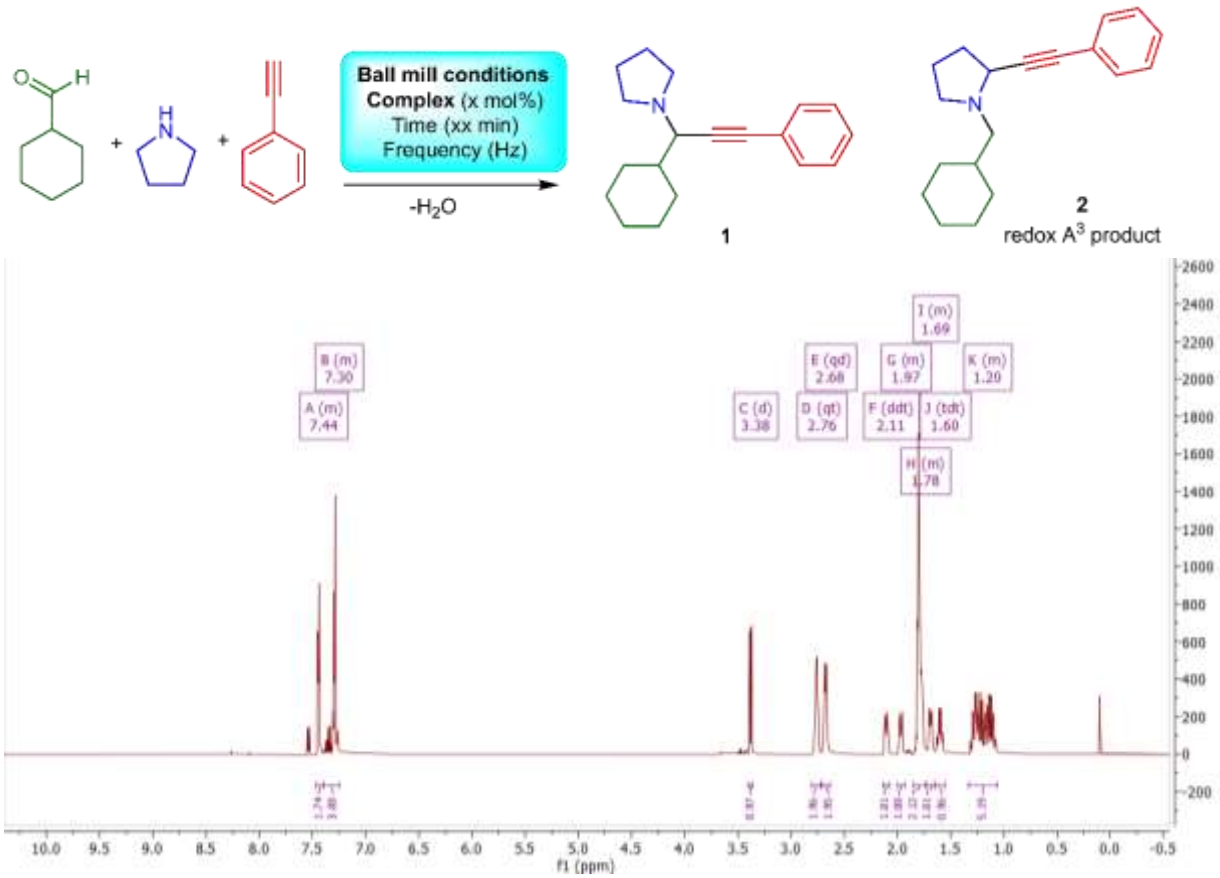
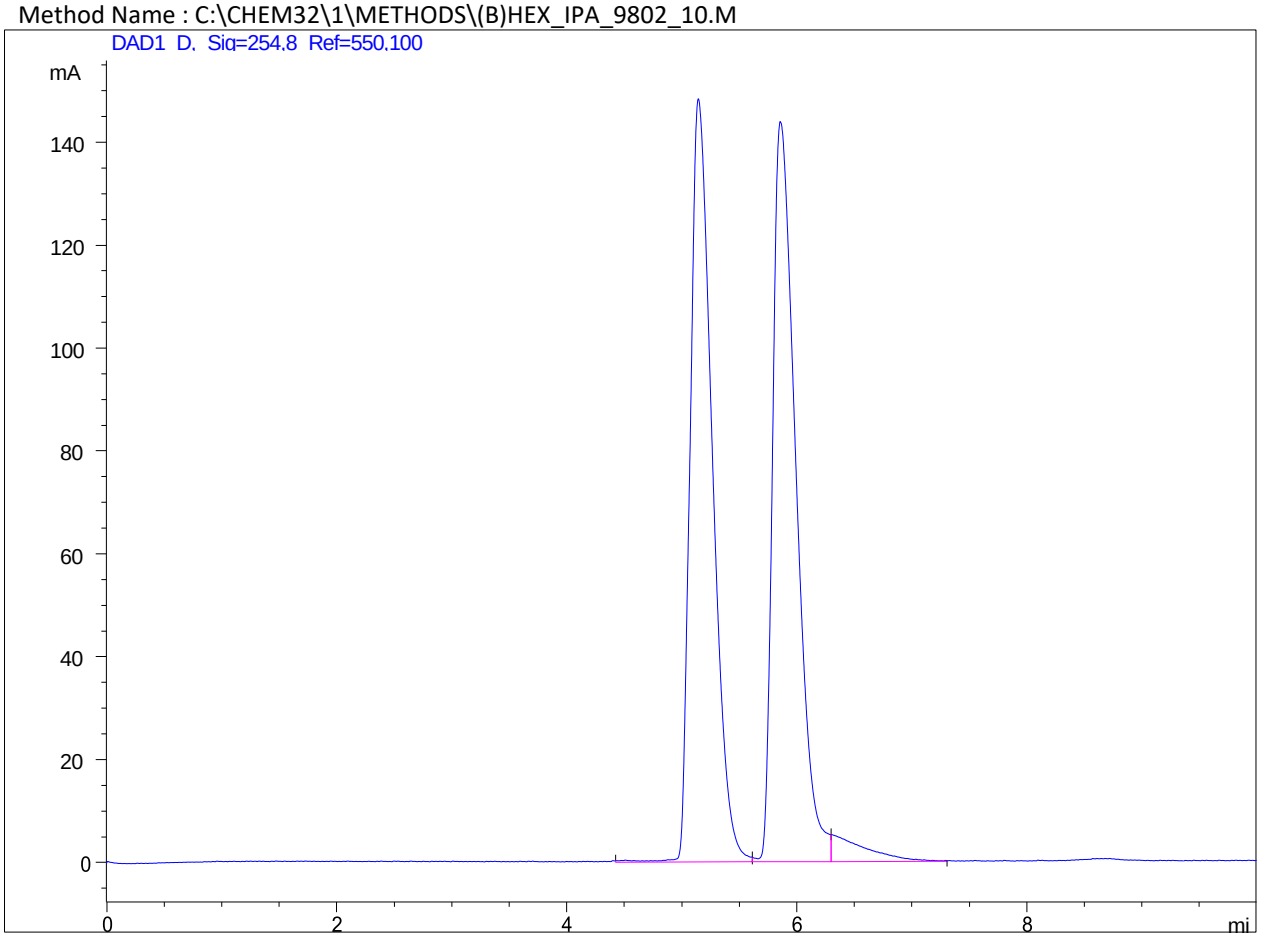


Figure S21. The crude ^{1}H NMR of the reaction with $CuCl_2$ (20% loading) entry 14, Table 2

Enantiomeric determination

Sample ID : US18
Method Name : C:\CHEM32\1\METHODS\(B)HEX_IPA_9802_10.M

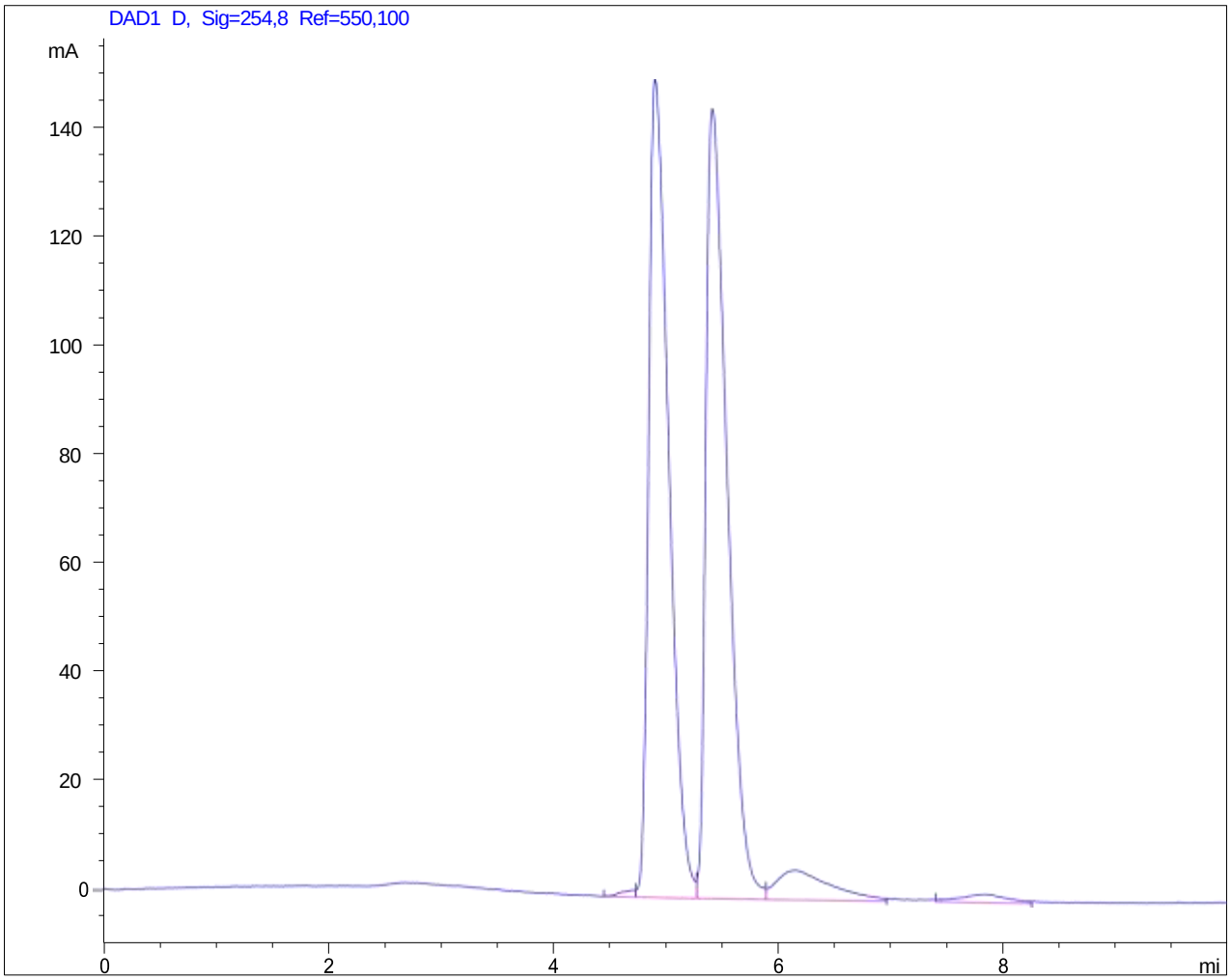


#	Meas. R	Height	Width	Area	Area %	Symmetry
1	5.157	1.488e3	0.220	1.990e4	48.161	0.715
2	5.853	1.440e3	0.235	2.032e4	49.186	0.461
3	6.300	53.220	0.343	1.096e3	2.654	0.000

Figure S22. HPLC profile for entry 11, Table 2

Sample ID : US20

Method Name : C:\CHEM32\1\METHODS\(B)HEX_IPA_9802_10.M

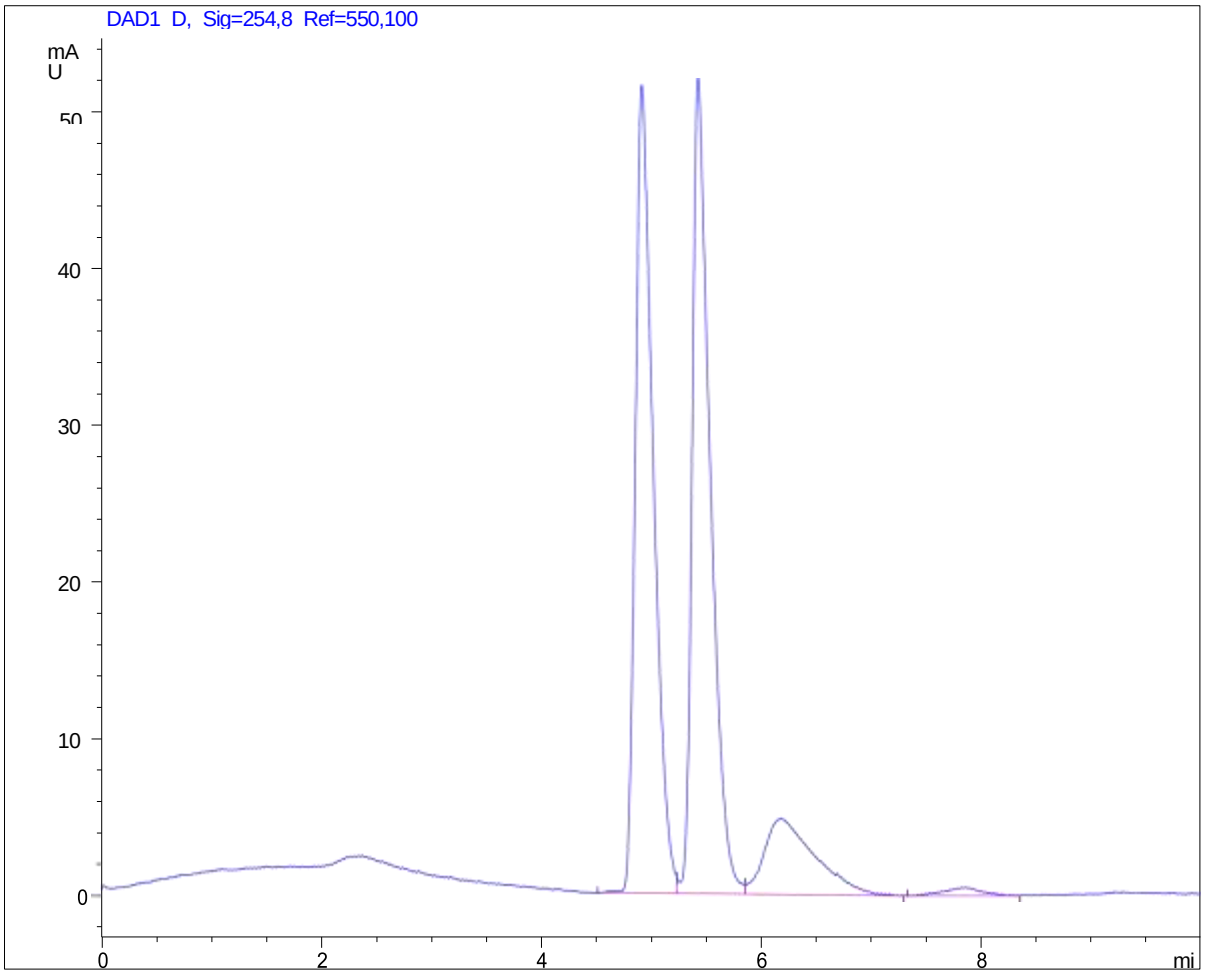


#	Meas. R	Height	Width	Area	Area %	Symmetry
1	4.736	14.179	0.155	132.211	0.327	0.000
2	4.904	1.503e3	0.208	1.874e4	46.402	0.439
3	5.416	1.450e3	0.221	1.921e4	47.559	0.424
4	6.154	54.531	0.557	1.822e3	4.510	0.505
5	7.840	16.118	0.502	485.355	1.202	1.043

Figure S23. HPLC profile for entry 21, Table 2

Sample ID : US23

Method Name : C:\CHEM32\1\METHODS\(B)HEX_IPA_9802_10.M

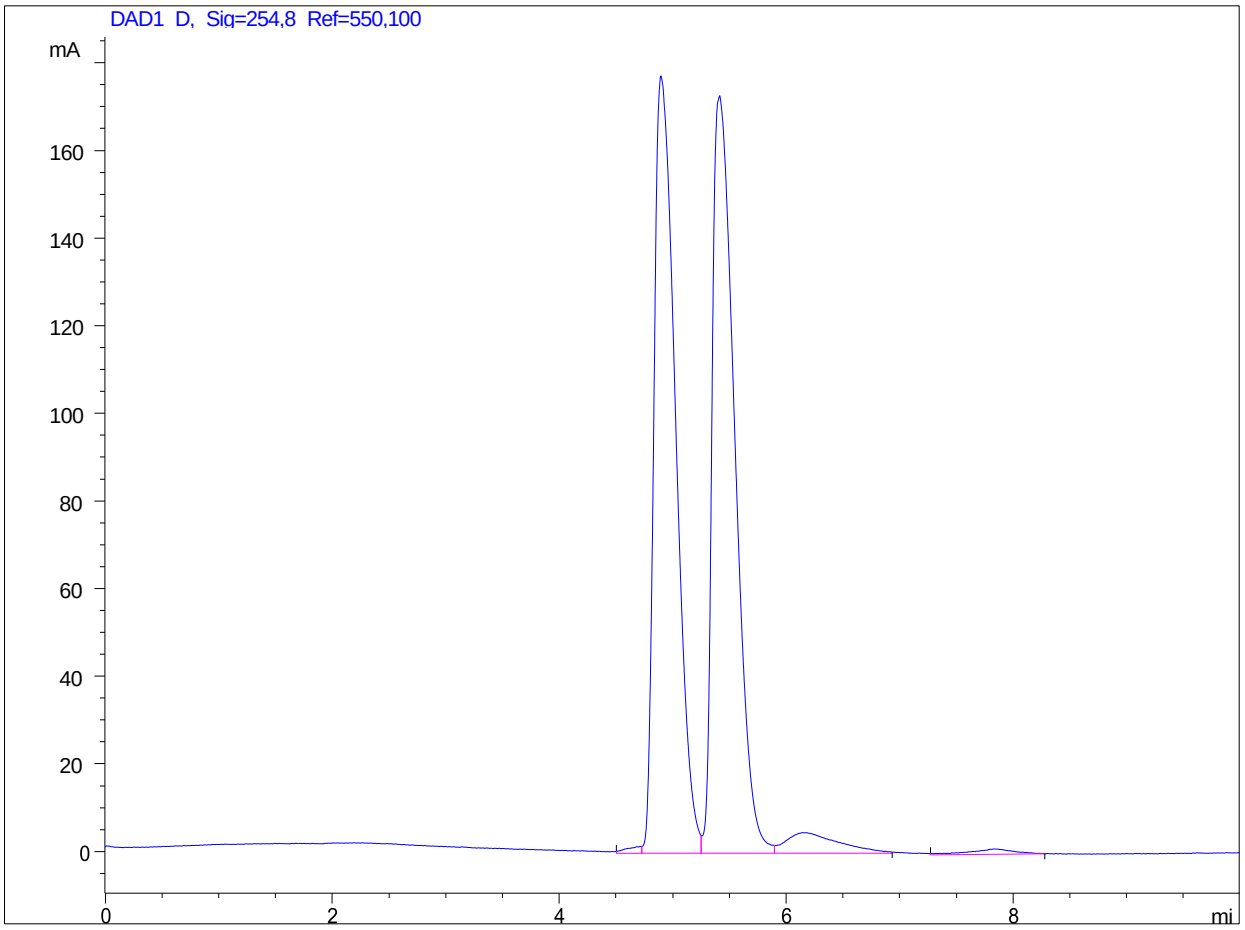


#	Meas. R	Height	Width	Area	Area %	Symmetr
1	4.927	490.633	0.188	5.883e3	43.407	0.724
2	5.442	503.405	0.186	5.974e3	44.080	0.642
3	6.184	48.343	0.465	1.561e3	11.516	0.485
4	7.844	5.128	0.380	135.170	0.997	1.159

Figure S24. HPLC profile for entry 22, Table 2

Sample ID : US21

Method Name : C:\CHEM32\1\METHODS\(B)HEX_IPA_9802_10.M

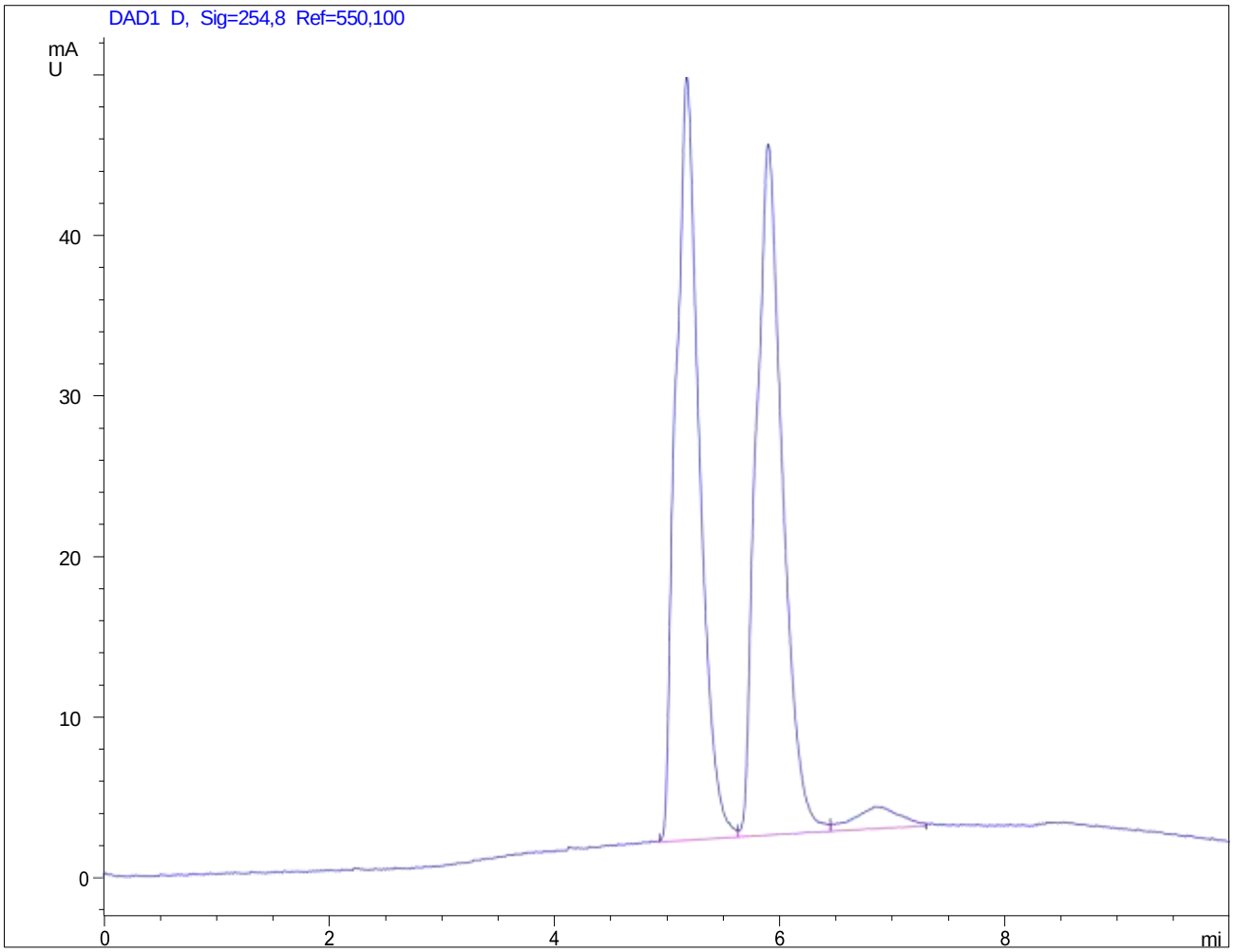


#	Meas. R	Height	Width	Area	Area %	Symmetr
1	4.724	15.446	0.156	144.641	0.292	0.000
2	4.894	1.774e3	0.221	2.353e4	47.428	0.467
3	5.411	1.729e3	0.232	2.406e4	48.497	0.483
4	6.147	47.023	0.539	1.520e3	3.064	0.472
5	7.832	12.431	0.478	356.712	0.719	1.283

Figure S25. HPLC profile for entry 23, Table 2

Sample ID : US24

Method Name : C:\CHEM32\1\METHODS\(B)HEX_IPA_9802_10.M

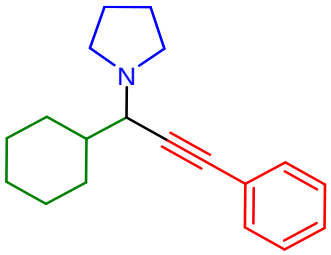


#	Meas. R	Height	Width	Area	Area %	Symmetr
1	5.172	474.798	0.242	6.898e3	48.321	0.822
2	5.896	430.134	0.270	6.980e3	48.896	0.795
3	6.839	13.974	0.474	397.295	2.783	0.871

Figure S26. HPLC profile for entry 24, Table 2

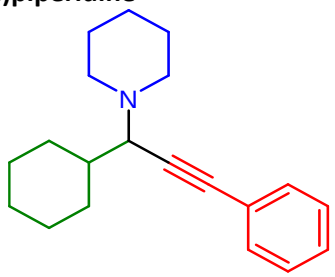
Characterisation for the A^3 Coupling products.

1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) pyrrolidine



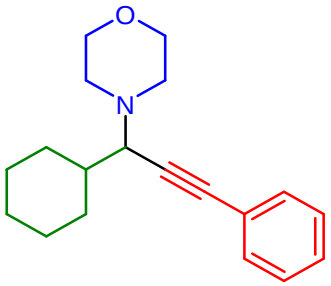
1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) pyrrolidine, (**1**), was synthesised using the standard procedure. Yellow oil (264 mg average of 262-265 mg, 0. 99 mmol 99%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.1, 2.5 Hz, 2H), 7.29 (h, *J* = 3.7 Hz, 3H), 3.35 (d, *J* = 8.4 Hz, 1H), 2.73 (dd, *J* = 8.6, 5.2 Hz, 2H), 2.64 (dd, *J* = 10.0, 4.9 Hz, 2H), 2.09 (dt, *J* = 13.0, 3.3 Hz, 1H), 1.98 – 1.92 (m, 1H), 1.84 – 1.73 (m, 6H), 1.70 – 1.65 (m, 1H), 1.59 (ditty, *J* = 11.5, 8.2, 3.8 Hz, 1H), 1.32 – 1.04 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.7, 128.2, 127.7, 123.6, 87.9, 85.7, 61.3, 41.3, 30.7, 30.3, 26.7, 26.2 (d, J = 3.2 Hz), 23.5; (HRMS + pTOF-ES) cald $C_{19}H_{26}N$ = [M + H]+: 268.2065, observed: 268.2065.

1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)piperidine



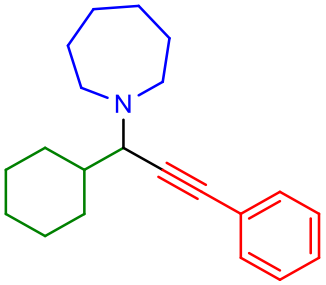
1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)piperidine, (**2**) was synthesised using the standard procedure. Dark Yellow oil (273 mg, average of 270-276 mg, 0. 97 mmol 97%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.32 – 7.24 (m, 3H), 3.12 (d, *J* = 9.8 Hz, 1H), 2.64 (td, *J* = 9.0, 7.0, 3.7 Hz, 2H), 2.42 (d, *J* = 9.8 Hz, 2H), 2.11 (ddt, *J* = 12.5, 3.7, 1.8 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.80 – 1.70 (m, 2H), 1.72 – 1.63 (m, 1H), 1.63 – 1.59 (m, 2H), 1.59 – 1.53 (m, 1H), 1.44 (dq, *J* = 9.4, 4.9, 4.0 Hz, 2H), 1.37 – 1.10 (m, 3H), 1.03 (qd, *J* = 12.6, 3.6 Hz, 1H), 0.99 – 0.89 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.7,128.2, 127.6, 123.8, 87.8, 86.1, 64.4, 39.5, 31.3, 30.4, 26.8, 26.3 (d, J = 2.7 Hz), 26.1, 24.7; (HRMS +pTOF-ES) cald $C_{20}H_{28}N$= [M + H]+: 282.2222, observed: 282.2235.

4-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)morpholine



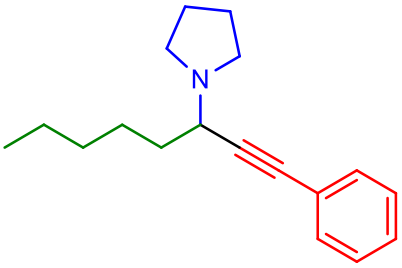
4-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)morpholine, (**3**), was synthesised using the standard procedure. Yellow oil (194 mg, average of 175-212 mg, 0.68 mmol 68%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.33 – 7.26 (m, 3H), 3.80 – 3.69 (m, 4H), 3.13 (d, *J* = 9.9 Hz, 1H), 2.70 (ddd, *J* = 10.4, 6.1, 3.0 Hz, 2H), 2.51 (ddd, *J* = 11.4, 6.1, 3.2 Hz, 2H), 2.14 – 2.07 (m, 1H), 2.07 – 2.01 (m, 1H), 1.77 (ddd, *J* = 17.4, 8.3, 3.5 Hz, 2H), 1.71 – 1.65 (m, 1H), 1.60 (dtd, *J* = 14.6, 11.1, 3.5 Hz, 1H), 1.34 – 1.22 (m, 1H), 1.25 – 1.18 (m, 1H), 1.18 (dt, *J* = 9.6, 3.3 Hz, 1H), 1.05 (qd, *J* = 12.5, 3.5 Hz, 1H), 0.97 (qd, *J* = 12.4, 3.7 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.7, 128.2, 127.8, 123.4, 86.7, 86.6, 67.2,63.9, 39.0, 31.0, 30.3, 26.7, 26.2; (HRMS + pTOF-ES) cald $C_{19}H_{26}NO$ = [M + H]+: 284.2014, observed: 284.1014

1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)azepane



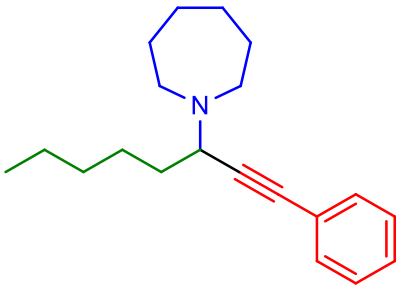
1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)azepane (**4**) was synthesised using the standard procedure. Yellow oil (244 mg, average of 238-250 mg, 0.83 mmol 83%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 3H), 7.31 – 7.24 (m, 5H), 3.65 (dd, *J* = 8.8, 6.0 Hz, 2H), 3.46 (s, 1H), 3.54 – 3.40 (m, 1H), 2.79 – 2.67 (m, 4H), 2.70 – 2.60 (m, 4H), 2.47 – 2.34 (m, 1H), 2.25 (dd, *J* = 9.4, 6.9 Hz, 1H), 1.92 (dtd, *J* = 11.9, 9.4, 9.0, 6.4 Hz, 1H), 1.86 – 1.64 (m, 11H), 1.63 – 1.56 (m, 1H), 1.55 (dq, *J* = 8.6, 6.0, 4.2 Hz, 1H), 1.52 – 1.46 (m, 1H), 1.48 – 1.38 (m, 1H), 1.33 (tdd, *J* = 8.4, 6.7, 3.9 Hz, 8H), 1.31 – 1.20 (m, 1H), 0.95 – 0.80 (m, 11H), 0.82 (s, 1H).^{13}C NMR (151 MHz, $CDCl_3$) δ 131.8, 128.3, 127.6, 124.1, 89.1, 85.0, 77.4, 76.9, 65.4, 52.8, 41.0, 31.3, 30.8, 29.4, 27.3, 27.0, 26.4, 26.2. (HRMS + pTOF-ES) cald $C_{21}H_{30}N$ = [M + H]+: 296.2065, observed: 296.2057.

1-(1-phenyloct-1-yn-3-yl) pyrrolidine



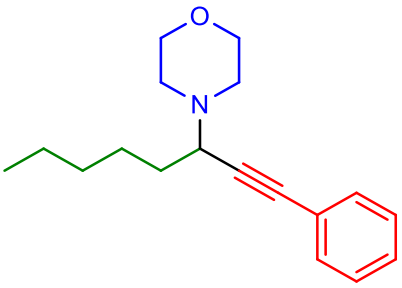
1-(1-phenyloct-1-yn-3-yl) pyrrolidine (**5**) was synthesised using the standard procedure. Yellow oil (238 mg, average of 231-244 mg, 0.93 mmol 93%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 3H), 7.31 – 7.24 (m, 5H), 3.65 (dd, *J* = 8.8, 6.0 Hz, 2H), 3.46 (s, 1H), 3.54 – 3.40 (m, 1H), 2.79 – 2.67 (m, 4H), 2.70 – 2.60 (m, 4H), 2.47 – 2.34 (m, 1H), 2.25 (dd, *J* = 9.4, 6.9 Hz, 1H), 1.92 (dtd, *J* = 11.9, 9.4, 9.0, 6.4 Hz, 1H), 1.86 – 1.64 (m, 11H), 1.63 – 1.56 (m, 1H), 1.55 (dq, *J* = 8.6, 6.0, 4.2 Hz, 1H), 1.52 – 1.46 (m, 1H), 1.48 – 1.38 (m, 1H), 1.33 (tdd, *J* = 8.4, 6.7, 3.9 Hz, 8H), 1.31 – 1.20 (m, 1H), 0.95 – 0.80 (m, 11H), 0.82 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.9, 128.3, 127.9, 123.7, 88.5, 85.4, 55.3, 54.7, 49.9, 46.7, 45.7, 35.2, 31.8, 26.6, 23.7, 22.7, 14.2. (HRMS + pTOF-ES) cald $C_{18}H_{26}N$ = [M + H]+: 256.2065, observed: 256.2057.

1-(1-phenyloct-1-yn-3-yl)azepane



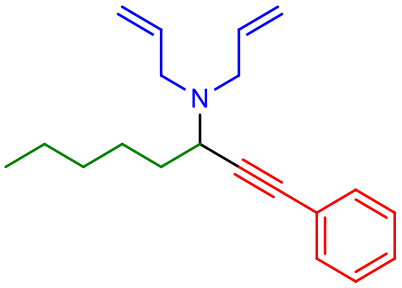
1-(1-phenyloct-1-yn-3-yl)azepane (**6**) was synthesised using the standard procedure. Yellow oil (274 mg, average of 268-280 mg, 0.97 mmol 97%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.31 – 7.23 (m, 3H), 3.51 (dd, *J* = 8.5, 6.5 Hz, 1H), 3.47 (s, 1H), 2.81 (ddd, *J* = 12.7, 7.1, 3.6 Hz, 2H), 2.62 (ddd, *J* = 12.5, 7.8, 3.9 Hz, 2H), 1.68 (ddd, *J* = 13.5, 6.6, 3.2 Hz, 2H), 1.67 – 1.58 (m, 2H), 1.58 (dd, *J* = 6.1, 3.1 Hz, 3H), 1.56 – 1.38 (m, 2H), 1.32 (tt, *J* = 6.1, 2.7 Hz, 4H), 0.89 (t, *J* = 6.9 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 131.9, 128.3, 127.9, 123.7, 88.5, 85.4, 55.3, 54.7, 49.9, 46.7, 45.7, 35.2, 31.8, 26.6, 23.7, 22.7, 14.2. (HRMS + pTOF-ES) cald $C_{20}H_{30}N$ = [M + H]+: 284.2378, observed: 284.2378.

4-(1-phenyloct-1-yn-3-yl)morpholine



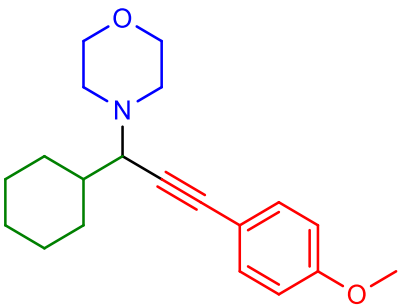
4-(1-phenyloct-1-yn-3-yl) morpholine (**7**) was synthesised using the standard procedure. Yellow oil (185 mg, average of 176-195 mg, 0.68mmol 68%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.32 – 7.24 (m, 3H), 3.81 – 3.61 (m, 5H), 3.50 – 3.45 (m, 1H), 2.92 – 2.87 (m, 1H), 2.73 (ddd, *J* = 11.4, 6.3, 3.2 Hz, 2H), 2.56 (ddd, *J* = 11.4, 6.3, 3.2 Hz, 2H), 1.76 – 1.65 (m, 2H), 1.60 – 1.38 (m, 2H), 1.33 (tq, *J* = 8.5, 4.3 Hz, 4H), 0.94 – 0.85 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.9, 130.1, 128.4, 85.6, 85.2, 83.0, 41.0, 34.0, 31.6, 28.6, 26.4, 24.0, 22.7, 20.9, 17.6, 17.4, 14.8, 14.2, 8.1(HRMS + pTOF-ES) cald $C_{18}H_{26}NO$ = [M + H]+: 272.2014, observed: 272.2016.

N,N-diallyl-1-phenyloct-1-yn-3-amine



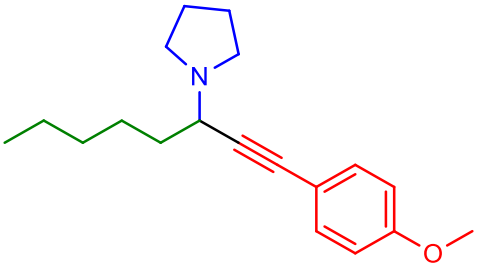
N,N-diallyl-1-phenyloct-1-yn-3-amine (**8**) was synthesised using the standard procedure. Yellow oil (245 mg, average of 248-260 mg, 0.90 mmol 90%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 2H), 7.35 – 7.27 (m, 3H), 5.89 (dddd, *J* = 17.7, 10.1, 7.9, 4.7 Hz, 2H), 5.29 (q, *J* = 1.7 Hz, 1H), 5.26 (q, *J* = 1.7 Hz, 1H), 5.15 (dd, *J* = 10.2, 2.1 Hz, 2H), 3.75 (t, *J* = 7.6 Hz, 1H), 3.37 (ddt, *J* = 14.2, 4.3, 1.9 Hz, 2H), 3.03 (dd, *J* = 14.2, 7.9 Hz, 2H), 1.77 – 1.69 (m, 2H), 1.58 – 1.44 (m, 2H), 1.35 (dddd, *J* = 12.6, 9.3, 6.7, 3.7 Hz, 4H), 0.93 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.8, 131.8, 128.3, 127.9, 123.7, 117.1, 88.5, 85.1, 76.9, 54.1, 53.2, 34.0, 31.7, 26.4, 22.7, 14.2. (HRMS + pTOF-ES) cald $C_{20}H_{28}N$ = [M + H]+: 282.2014, observed: 282.2223.

4-(1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl)morpholine



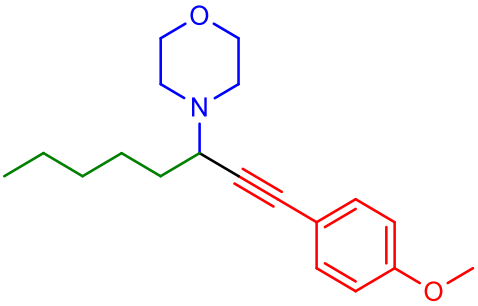
4-(1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl)morpholine (**9**) was synthesised using the standard procedure. Yellow oil (228 mg, average of 215-240 mg, 0.73mmol 73%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 6.84 – 6.79 (m, 2H), 3.79 (s, 3H), 3.78 – 3.68 (m, 4H), 3.10 (d, *J* = 9.8 Hz, 1H), 2.68 (t, *J* = 9.4 Hz, 2H), 2.49 (ddd, *J* = 11.2, 6.2, 3.0 Hz, 2H), 2.09 (ddt, *J* = 13.0, 3.6, 1.7 Hz, 1H), 2.06 – 1.99 (m, 1H), 1.79 – 1.71 (m, 1H), 1.70 – 1.63 (m, 1H), 1.63 – 1.55 (m, 1H), 1.26 (qt, *J* = 12.8, 3.5 Hz, 1H), 1.23 – 1.14 (m, 2H), 1.03 (qd, *J* = 12.2, 3.4 Hz, 1H), 0.95 (q, *J* = 11.0, 9.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.4, 133.2, 115.7, 114.0, 110.2, 86.7, 85.1, 67.4, 64.2, 55.4, 50.1, 39.3, 31.1, 30.6, 26.9, 26.3, 26.2. (HRMS + pTOF-ES) cald $C_{20}H_{28}NO$ = [M + H]+: 314.2119, observed: 314.2119.

1-(1-(4-methoxyphenyl)oct-1-yn-3-yl)pyrrolidine



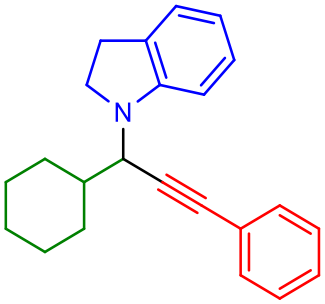
1-(1-(4-methoxyphenyl)oct-1-yn-3-yl)pyrrolidine (**10**) was synthesised using the standard procedure. Yellow oil (262 mg, average of 252-272 mg, 0.92mmol 92%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 6.86 – 6.79 (m, 2H), 3.81 (s, 3H), 3.01 (s, 4H), 1.92 (s, 5H), 1.76 – 1.66 (m, 1H), 1.47 (s, 1H), 1.36 – 1.29 (m, 4H), 0.94 – 0.85 (m, 4H).^{13}C NMR (151 MHz, $CDCl_3$) δ 159.9, 133.4, 114.1, 56.0, 55.5, 50.3, 49.9, 39.6, 34.2, 31.5, 26.4, 23.9, 22.6, 14.1. (HRMS + pTOF-ES) cald $C_{19}H_{28}NO$ = [M + H]+: 286.2170, observed: 286.2171.

4-(1-(4-methoxyphenyl)oct-1-yn-3-yl)morpholine



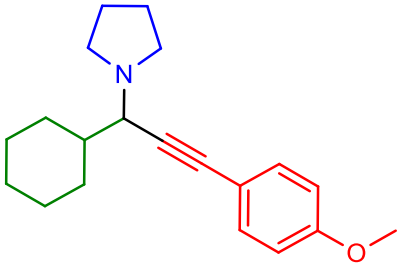
4-(1-(4-methoxyphenyl)oct-1-yn-3-yl)morpholine (**11**) was synthesised using the standard procedure. Yellow oil (220 mg, average of 203-237 mg, 0.73mmol 73%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 6.85 – 6.79 (m, 2H), 3.80 (s, 2H), 3.48 (s, 1H), 3.45 (s, 1H), 2.74 (s, 2H), 2.57 (s, 2H), 1.70 (s, 2H), 1.58 – 1.56 (m, 2H), 1.53 (t, *J* = 7.4 Hz, 1H), 1.45 (dt, *J* = 13.6, 7.2 Hz, 1H), 1.33 (dp, *J* = 8.0, 4.3, 3.6 Hz, 4H), 0.92 – 0.87 (m, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 133.3, 114.0, 67.2, 58.5, 55.5, 49.9, 33.0, 31.7, 26.4, 22.7, 14.2. (HRMS + pTOF-ES) cald $C_{19}H_{28}NO_2$ = [M + H]+: 302.2119, observed: 302.2119.

1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)indoline



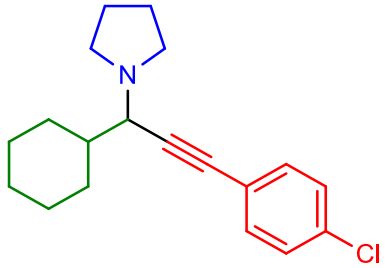
1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)indoline(**12**) was synthesized using the standard procedure. Yellow oil (259 mg, average of 242-275 mg, 0.82mmol 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 6.8, 2.9 Hz, 2H), 7.24 (tt, *J* = 5.9, 3.1 Hz, 3H), 7.08 (t, *J* = 7.2 Hz, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.56 (d, *J* = 8.1 Hz, 1H), 4.14 (d, *J* = 10.0 Hz, 1H), 3.54 – 3.41 (m, 2H), 3.05 – 3.00 (m, 1H), 3.00 – 2.93 (m, 1H), 2.24 – 2.17 (m, 1H), 2.10 (ddt, *J* = 13.5, 3.9, 2.0 Hz, 1H), 1.86 – 1.81 (m, 1H), 1.81 – 1.67 (m, 3H), 1.39 – 1.11 (m, 5H), 1.07 – 0.97 (m, 1H).^{13}C NMR (151 MHz, $CDCl_3$) δ 151.8, 131.9, 130.2, 128.2, 128.0, 127.3, 124.5, 123.4, 118.0, 107.8, 87.1, 85.3, 55.4, 48.4, 41.2, 31.6, 31.1, 30.3, 29.6, 28.5, 26.7, 26.2, 26.1. (HRMS + pTOF-ES) cald $C_{23}H_{26}N$ = [M + H]+: 316.2065, observed: 316.1057.

1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl]pyrrolidine



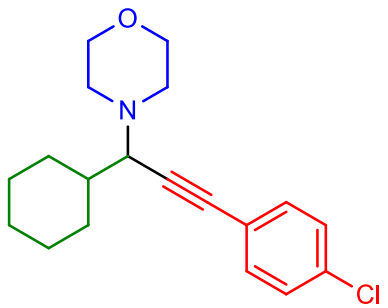
1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl]pyrrolidine (**13**) was synthesised using the standard procedure. Yellow oil (274 mg, average of 266-282 mg, 0.92mmol 92%). 1H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 6.86 – 6.79 (m, 2H), 3.80 (s, 2H), 3.33 (d, J = 8.3 Hz, 1H), 2.72 (t, J = 7.0 Hz, 2H), 2.64 (p, J = 5.8 Hz, 2H), 2.11 – 2.04 (m, 1H), 1.98 – 1.91 (m, 1H), 1.78 (q, J = 4.1, 2.6 Hz, 4H), 1.71 – 1.64 (m, 1H), 1.57 (tdt, J = 11.6, 8.2, 3.4 Hz, 1H), 1.32 – 1.04 (m, 4H). 13C NMR (151 MHz, $CDCl_3$) δ 159.3, 133.2, 116.0, 114.0, 86.4, 85.7, 61.5, 55.4, 50.2, 41.5, 30.9, 30.4, 26.9, 26.4, 26.4, 23. (HRMS + pTOF-ES) cald $C_{20}H_{28}NO$ = [M + H]+: 298.205, observed: 298.1057.

1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]pyrrolidine



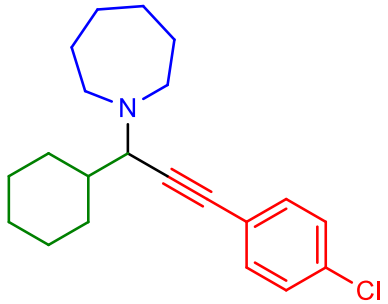
1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]pyrrolidine (**14**) was synthesised using the standard procedure. Yellow oil (269 mg, average of 258-280 mg, 0.89mmol 89%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.28 – 7.23 (m, 2H), 3.34 (d, *J* = 8.4 Hz, 1H), 2.75 – 2.69 (m, 2H), 2.66 – 2.60 (m, 2H), 2.09 – 2.03 (m, 1H), 1.97 – 1.91 (m, 1H), 1.82 – 1.73 (m, 5H), 1.71 – 1.65 (m, 1H), 1.62 – 1.53 (m, 1H), 1.31 – 1.03 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.64, 132.93, 128.48, 122.08, 84.71, 61.25, 50.08, 41.23, 30.94, 30.66, 30.23, 26.65, 26.17 (d, *J* = 3.4 Hz), 23.50. (HRMS + pTOF-ES) cald $C_{19}H_{25}N$ Cl = [M + H]+: 302.1691, observed: 302.1676.

4-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]morpholine



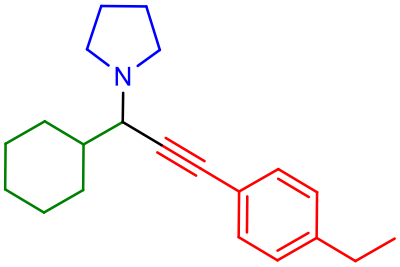
4-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]morpholine (**15**) was synthesised using the standard procedure. Yellow oil (214 mg, average of 199-229 mg, 0.67 mmol 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.28 (s, 1H), 3.79 – 3.69 (m, 3H), 3.12 (d, *J* = 9.9 Hz, 1H), 2.68 (ddd, *J* = 10.2, 5.8, 3.1 Hz, 2H), 2.49 (ddd, *J* = 11.3, 6.1, 3.2 Hz, 2H), 2.10 – 2.01 (m, 2H), 1.80 – 1.71 (m, 2H), 1.71 – 1.66 (m, 1H), 1.64 – 1.55 (m, 1H), 1.27 (tdd, *J* = 13.1, 6.8, 3.6 Hz, 1H), 1.20 (tq, *J* = 8.4, 5.7, 4.5 Hz, 2H), 0.99 (dqd, *J* = 48.4, 12.2, 3.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.78, 132.93, 128.52, 121.86, 87.74, 85.69, 67.19, 63.93, 38.99, 30.99, 30.32, 26.68, 26.13, 25.97. (HRMS + pTOF-ES) cald $C_{19}H_{25}N$ O Cl= [M + H]+: 318.1628, observed: 318.1625.

1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl] azepane



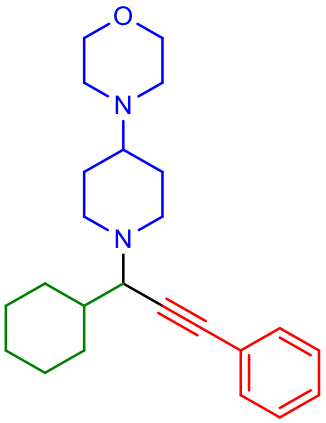
1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl] azepane (**16**) was synthesised using the standard procedure. Yellow oil (267 mg, average of 257-277 mg, 0.81 mmol 81%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 1H), 7.28 – 7.23 (m, 2H), 3.14 (d, *J* = 10.2 Hz, 0H), 2.77 (ddd, *J* = 12.4, 7.0, 3.6 Hz, 1H), 2.54 (ddd, *J* = 12.6, 7.5, 4.4 Hz, 1H), 2.15 (d, *J* = 13.6 Hz, 0H), 2.08 – 2.02 (m, 1H), 1.75 (td, *J* = 10.3, 9.8, 3.2 Hz, 1H), 1.69 – 1.67 (m, 1H), 1.67 – 1.61 (m, 2H), 1.61 (s, 0H), 1.58 (s, 3H), 1.54 – 1.41 (m, 1H), 1.33 – 1.27 (m, 1H), 1.25 (s, 2H), 1.21 (dt, *J* = 12.0, 3.0 Hz, 1H), 1.18 – 1.12 (m, 1H), 1.02 – 0.86 (m, 2H), 0.84 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.64, 132.93, 128.48, 122.08, 84.71, 61.25, 50.08, 41.23, 30.94, 30.66, 30.23, 26.65, 26.17 (d, *J* = 3.4 Hz), 23.50. (HRMS + pTOF-ES) cald $C_{21}H_{29}NCl$= [M + H]+: 330.1975, observed: 330.1989.

1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl]pyrrolidine



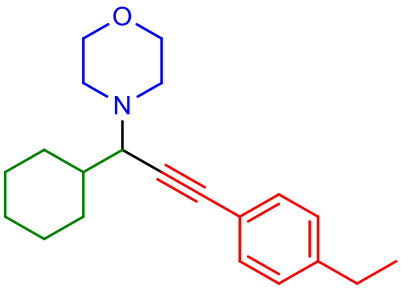
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl]pyrrolidine (**17**) was synthesised using the standard procedure. Yellow oil (252 mg, average of 232-272 mg, 0.85 mmol 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 3.34 (d, *J* = 8.4 Hz, 1H), 2.74 (s, 2H), 2.64 (q, *J* = 7.6 Hz, 4H), 2.09 (d, *J* = 12.9 Hz, 1H), 1.95 (dd, *J* = 13.5, 3.5 Hz, 1H), 1.80 (s, 2H), 1.79 – 1.74 (m, 5H), 1.68 (d, *J* = 11.7 Hz, 2H), 1.28 (q, *J* = 4.4, 3.3 Hz, 1H), 1.27 – 1.20 (m, 6H), 1.20 – 1.15 (m, 1H), 1.10 (dtd, *J* = 19.1, 12.5, 11.9, 3.4 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.15, 133.02, 115.83, 113.78, 86.17, 85.48, 61.29, 55.26, 50.05, 41.37, 30.70, 30.23, 26.68, 26.22, 26.19, 23.52. (HRMS + pTOF-ES) cald $C_{21}H_{30}N$ = [M + H]+: 296.2395, observed: 296.2378.

4-{1-[1-cyclohexyl-3-(4-phenylprop-2-yn-1-yl]piperidin-4-yl}morpholine



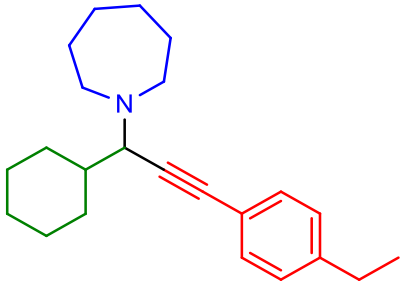
1-[1-cyclohexyl-3-(4-phenylprop-2-yn-1-yl](piperidin-4-yl)morpholine (**18**) was synthesised using the standard procedure. Red oil (287 mg, average of 278 -296 mg, 0.78 mmol 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H), 7.32 – 7.24 (m, 3H), 3.72 (t, *J* = 4.7 Hz, 4H), 3.14 (d, *J* = 10.0 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.73 (dp, *J* = 11.3, 2.9 Hz, 1H), 2.58 – 2.51 (m, 5H), 2.24 – 2.14 (m, 2H), 2.13 – 2.07 (m, 1H), 2.04 – 1.97 (m, 1H), 1.84 (dq, *J* = 13.2, 3.4 Hz, 2H), 1.79 – 1.70 (m, 2H), 1.70 – 1.64 (m, 1H), 1.57 (qdd, *J* = 11.8, 7.0, 3.8 Hz, 2H), 1.47 (qd, *J* = 12.0, 4.0 Hz, 1H), 1.32 – 1.21 (m, 1H), 1.24 – 1.11 (m, 2H), 1.01 (qd, *J* = 12.6, 3.5 Hz, 1H), 0.90 (qd, *J* = 12.2, 3.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.69, 128.20, 127.71, 123.60, 87.26, 86.27, 67.34, 63.54, 62.36, 52.82, 49.83, 45.51, 39.79, 31.28, 30.33, 28.67, 28.23, 26.76, 26.21, 26.05. (HRMS + pTOF-ES) cald $C_{24}H_{35}N_2O$= [M + H]+: 367.2753, observed: 367.2749.

1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] morpholine



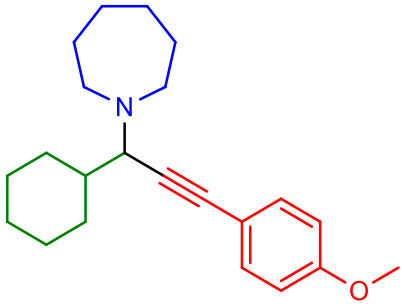
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] morpholine (**19**) was synthesised using the standard procedure. Dark red oil (211 mg, average of 192 -230 mg, 0.68 mmol 68%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 3.75 (tdd, *J* = 18.0, 8.9, 5.6 Hz, 4H), 3.12 (d, *J* = 9.8 Hz, 1H), 2.70 (ddd, *J* = 11.7, 6.1, 2.9 Hz, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.51 (ddd, *J* = 11.4, 6.1, 3.1 Hz, 2H), 2.14 – 2.08 (m, 1H), 2.07 – 2.01 (m, 1H), 1.77 (tdd, *J* = 11.5, 5.6, 3.1 Hz, 2H), 1.71 – 1.66 (m, 1H), 1.60 (dtd, *J* = 14.3, 11.0, 3.4 Hz, 1H), 1.33 – 1.15 (m, 5H), 1.01 (dqd, *J* = 48.5, 12.3, 3.5 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.19, 131.67, 127.77, 120.57, 86.83, 85.81, 67.22, 63.96, 39.11, 31.52, 30.97, 30.37, 28.78, 26.73, 26.18, 26.03, 25.95, 25.01, 15.46. (HRMS + pTOF-ES) cald $C_{21}H_{30}NO$= [M + H]+: 312.2328, observed: 312.2327 .

1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] azepane



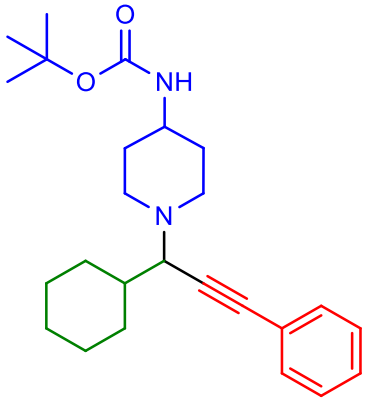
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] azepane. morpholine (**20**) was synthesised using the standard procedure. Dark red oil (234 mg, average of 223 -245 mg, 0.72 mmol 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 3.15 (d, *J* = 10.1 Hz, 1H), 2.78 (td, *J* = 8.3, 7.3, 4.4 Hz, 2H), 2.66 – 2.52 (m, 5H), 2.15 (d, *J* = 13.4 Hz, 1H), 1.75 (ddd, *J* = 12.5, 8.3, 4.1 Hz, 3H), 1.69 – 1.57 (m, 7H), 1.54 – 1.44 (m, 2H), 1.32 – 1.11 (m, 8H), 1.02 – 0.83 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.89, 131.64, 127.72, 121.04, 88.01, 84.94, 65.20, 52.62, 50.87, 45.45, 40.80, 31.13, 30.94, 30.66, 29.19, 28.77, 27.13, 26.82, 26.26, 26.08, 15.50. (HRMS + pTOF-ES) cald $C_{23}H_{34}N$ = [M + H]+: 324.2699, observed: 324.2691.

1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl] azepane



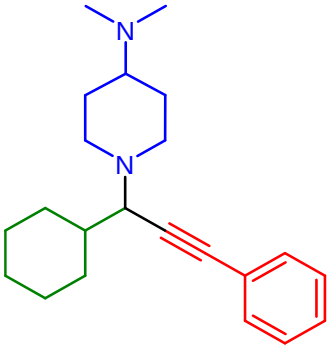
1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl] azepane (**21**) was synthesised using the standard procedure. Yellow oil (271 mg, average of 255 -288 mg, 0.83 mmol 83%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 3H), 3.80 (s, 4H), 3.13 (d, *J* = 10.2 Hz, 2H), 2.77 (s, 2H), 2.57 – 2.52 (m, 3H), 2.18 (s, 1H), 1.74 (s, 2H), 1.66 (s, 2H), 1.58 (s, 6H), 1.25 (s, 2H), 1.18 (d, *J* = 10.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.01, 133.00, 116.11, 113.76, 87.24, 84.53, 65.22, 55.27, 53.42, 52.63, 40.83, 31.59, 31.17, 30.66, 29.29, 27.13, 26.84, 26.28, 26.09, 22.66, 14.12. (HRMS + pTOF-ES) cald $C_{22}H_{32}NO$ = [M + H]+: 326.2489, observed: 326.2484.

tert-butyl N-[1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) piperidin-4-yl]carbamate



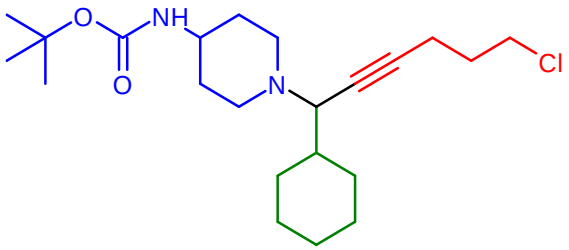
tert-butyl N-[1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) piperidin-4-yl]carbamate (**22**) was synthesised using the standard procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 2H), 7.33 – 7.26 (m, 3H), 4.44 (s, 1H), 3.48 (s, 1H), 3.13 (d, *J* = 10.0 Hz, 1H), 2.76 (dd, *J* = 9.8, 5.8 Hz, 1H), 2.63 (d, *J* = 6.6 Hz, 2H), 2.31 (t, *J* = 11.4 Hz, 1H), 2.10 (d, *J* = 13.2 Hz, 1H), 1.99 (d, *J* = 13.5 Hz, 1H), 1.94 (s, 1H), 1.75 (t, *J* = 14.0 Hz, 2H), 1.68 (s, 1H), 1.56 (d, *J* = 4.4 Hz, 3H), 1.45 (s, 8H), 1.40 – 1.33 (m, 1H), 1.31 – 1.14 (m, 5H), 1.06 – 0.97 (m, 1H), 0.91 (q, *J* = 12.3, 11.9 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.67, 128.21, 127.75, 123.47, 87.00, 86.43, 79.16, 63.69, 51.42, 48.05, 45.58, 39.69, 33.02, 32.70, 31.23, 30.37, 29.70, 28.42, 26.72, 26.18, 26.03. (HRMS + pTOF-ES) cald $C_{25}H_{37}N_2O_2$ = [M + H]+: 397.2868, observed: 397.2855

1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)-N,N-dimethylpiperidin-4-amine



1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)-N,N-dimethylpiperidin-4-amine (**23**) was synthesised using the standard procedure ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 1H), 7.32 – 7.24 (m, 2H), 3.14 (d, *J* = 9.9 Hz, 1H), 2.86 – 2.79 (m, 1H), 2.75 – 2.69 (m, 1H), 2.54 (td, *J* = 11.7, 2.4 Hz, 1H), 2.27 (s, 4H), 2.20 (td, *J* = 11.8, 2.3 Hz, 1H), 2.12 (tq, *J* = 12.3, 4.1 Hz, 2H), 2.05 – 1.98 (m, 1H), 1.85 – 1.78 (m, 2H), 1.81 – 1.73 (m, 1H), 1.76 – 1.70 (m, 1H), 1.70 – 1.64 (m, 1H), 1.63 – 1.55 (m, 1H), 1.57 – 1.50 (m, 1H), 1.45 (qd, *J* = 12.2, 4.0 Hz, 1H), 1.27 (tdd, *J* = 16.4, 9.8, 3.5 Hz, 1H), 1.24 – 1.12 (m, 1H), 1.06 – 0.96 (m, 1H), 0.96 – 0.87 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.69, 128.18, 127.68, 123.64, 87.34, 86.25, 63.59, 62.52, 52.97, 45.57, 41.69, 39.80, 31.28, 30.38, 28.75, 28.41, 26.77, 26.23, 26.07. (HRMS + pTOF-ES) cald $C_{22}H_{33}N_2$ = [M + H]+: 325.2644, observed: 325.2644

tert-butyl N-[1-(6-chloro-1-cyclohexylhex-2-yn-1-yl) piperidin-4-yl]carbamate



tert-butyl N-[1-(6-chloro-1-cyclohexylhex-2-yn-1-yl) piperidin-4-yl]carbamate (**24**) was synthesised synthesised under microwave irradiation in a gram scale (Method A); Scheme 3 however, using our protocol, **24** can be synthesized up to 500 mg scale (Method B).

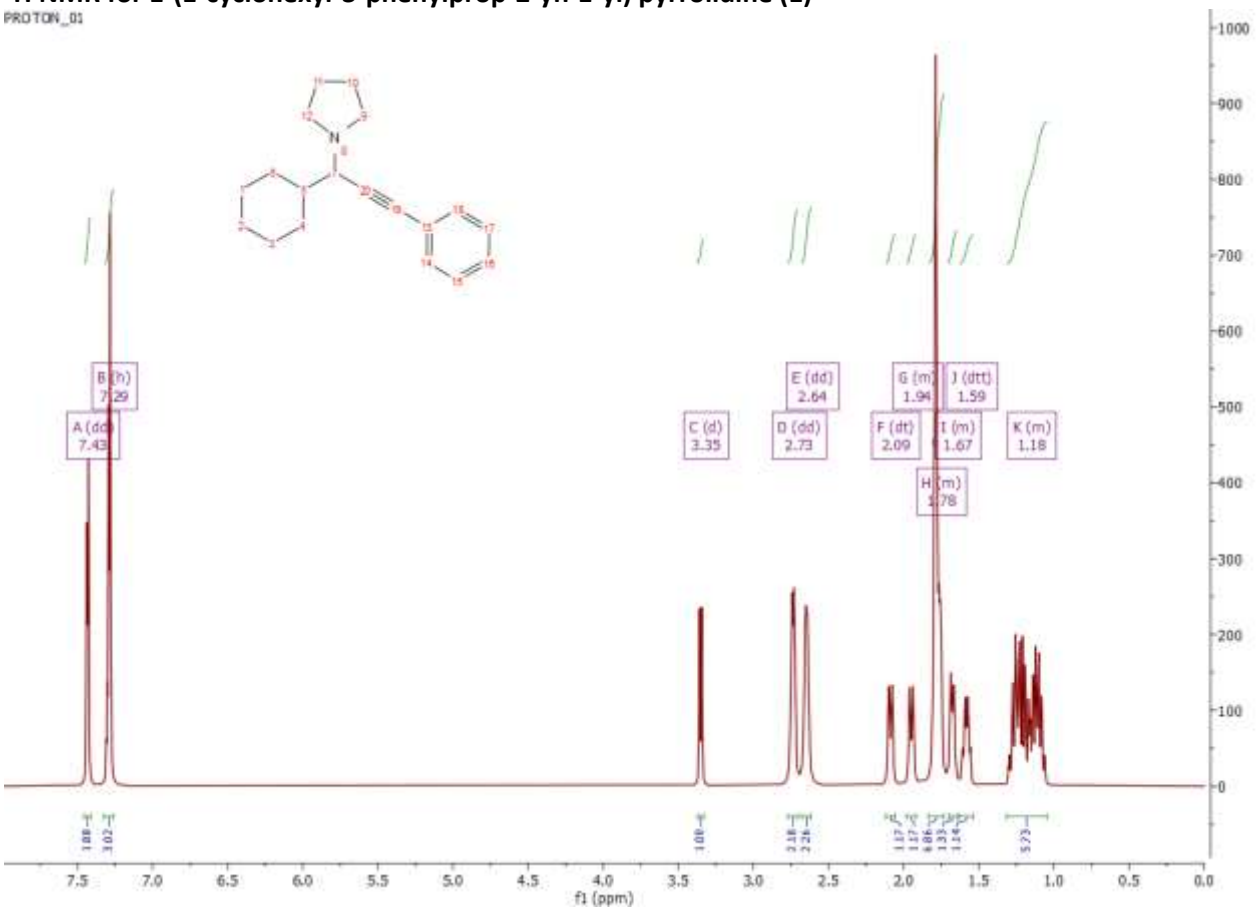
^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.43 (d, *J* = 8.0 Hz, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.44 (s, 1H), 2.87 (dt, *J* = 10.0, 2.2 Hz, 1H), 2.69 – 2.63 (m, 1H), 2.53 (dd, *J* = 12.1, 4.2 Hz, 1H), 2.47 (dt, *J* = 12.7, 6.4 Hz, 1H), 2.41 (td, *J* = 6.8, 2.1 Hz, 2H), 2.15 (t, *J* = 11.4 Hz, 1H), 2.00 – 1.88 (m, 6H), 1.76 – 1.67 (m, 2H), 1.67 – 1.62 (m, 1H), 1.44 (s, 9H), 1.43 – 1.29 (m, 2H), 1.23 (qt, *J* = 12.1, 3.4 Hz, 1H), 1.19 – 1.08 (m, 2H), 0.88 (dqd, *J* = 45.9, 12.3, 3.5 Hz, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 155.2, 84.0, 79.2, 78.0, 63.2, 45.5, 43.8, 39.7, 33.0, 32.7, 31.8, 31.1, 30.3, 28.4, 26.7, 26.2, 26.0, 16.1. (HRMS + pTOF-ES) cald $C_{22}H_{37}ClN_2O_2$ [M+H] = 397.2622. Calculated mass [M+H] = 397.2627 (ppm = 5.8).

References

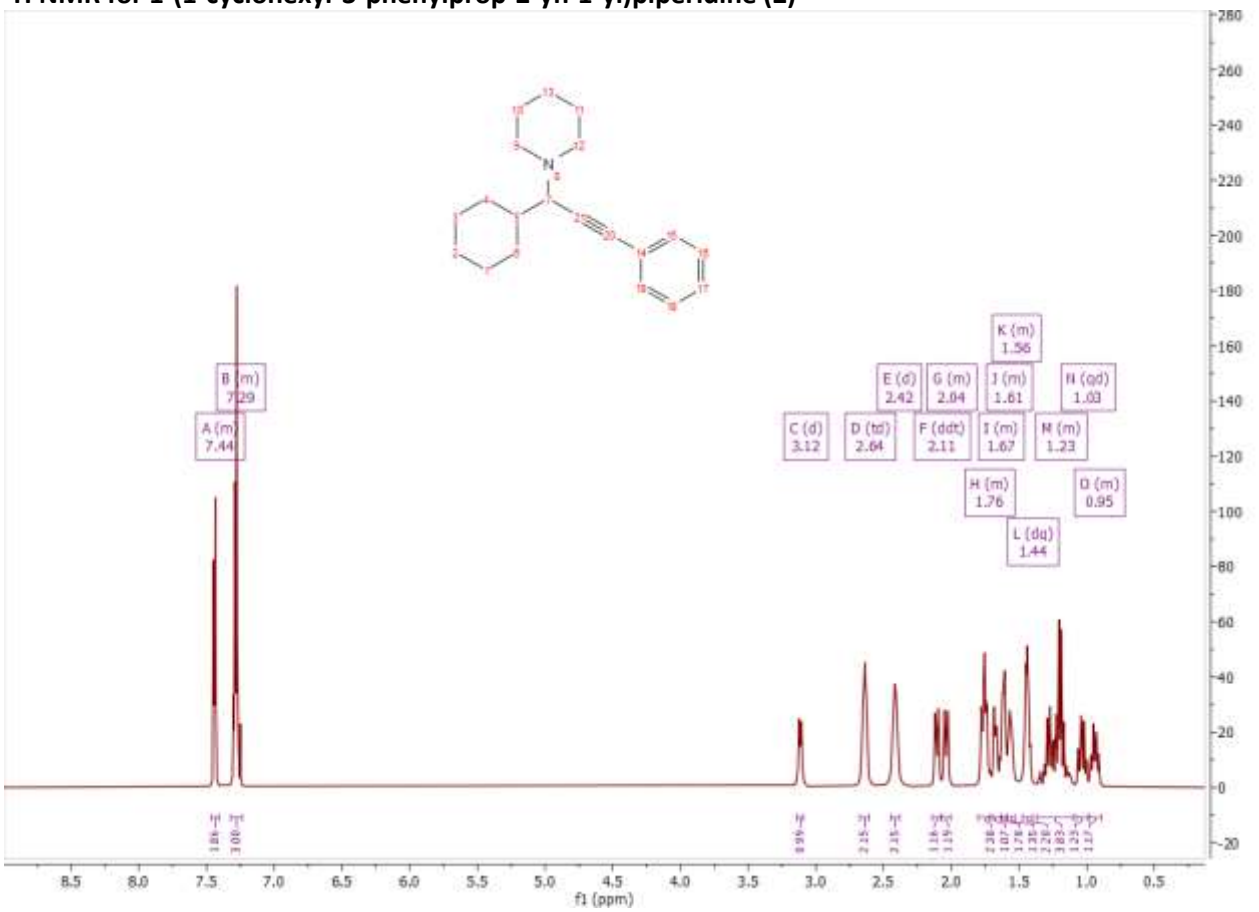
1 S. J. Coles and P. A. Gale, *Chem. Sci.*, 2012, **3**, 683–689.
2 G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.*, 2015, **71**, 3–8.
3 L. J. Bourhis, O. V. Dolomanov, R. J. Gildea, J. A. K. Howard and H. Puschmann, *Acta Crystallogr. Sect. A Found. Crystallogr.*, 2015, **71**, 59–75.
4 S. Stoll and A. Schweiger, *J. Magn. Reson.*, 2006, **178**, 42–55.

NMR Data

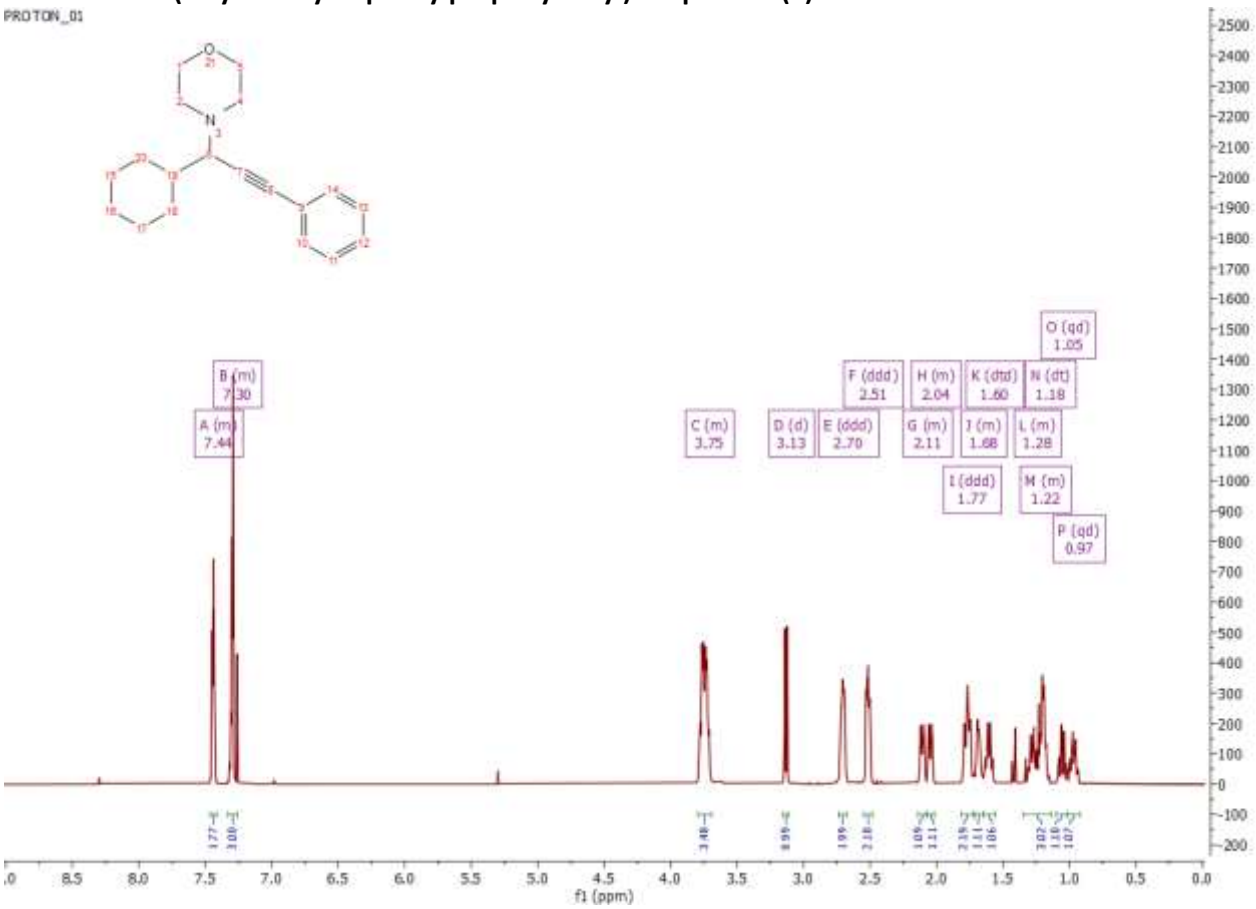
^{1}H NMR for 1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) pyrrolidine (1)



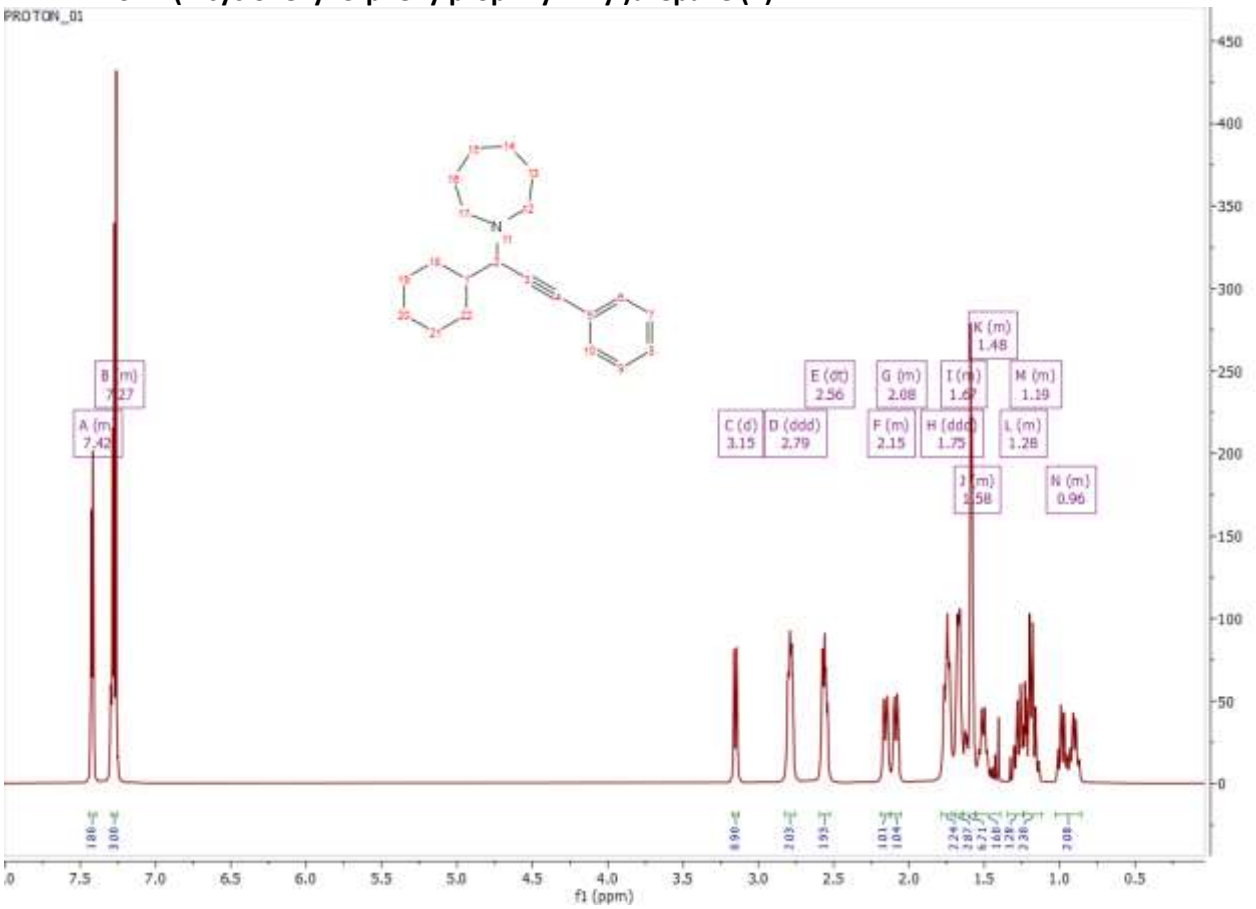
^{1}H NMR for 1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)piperidine (2)



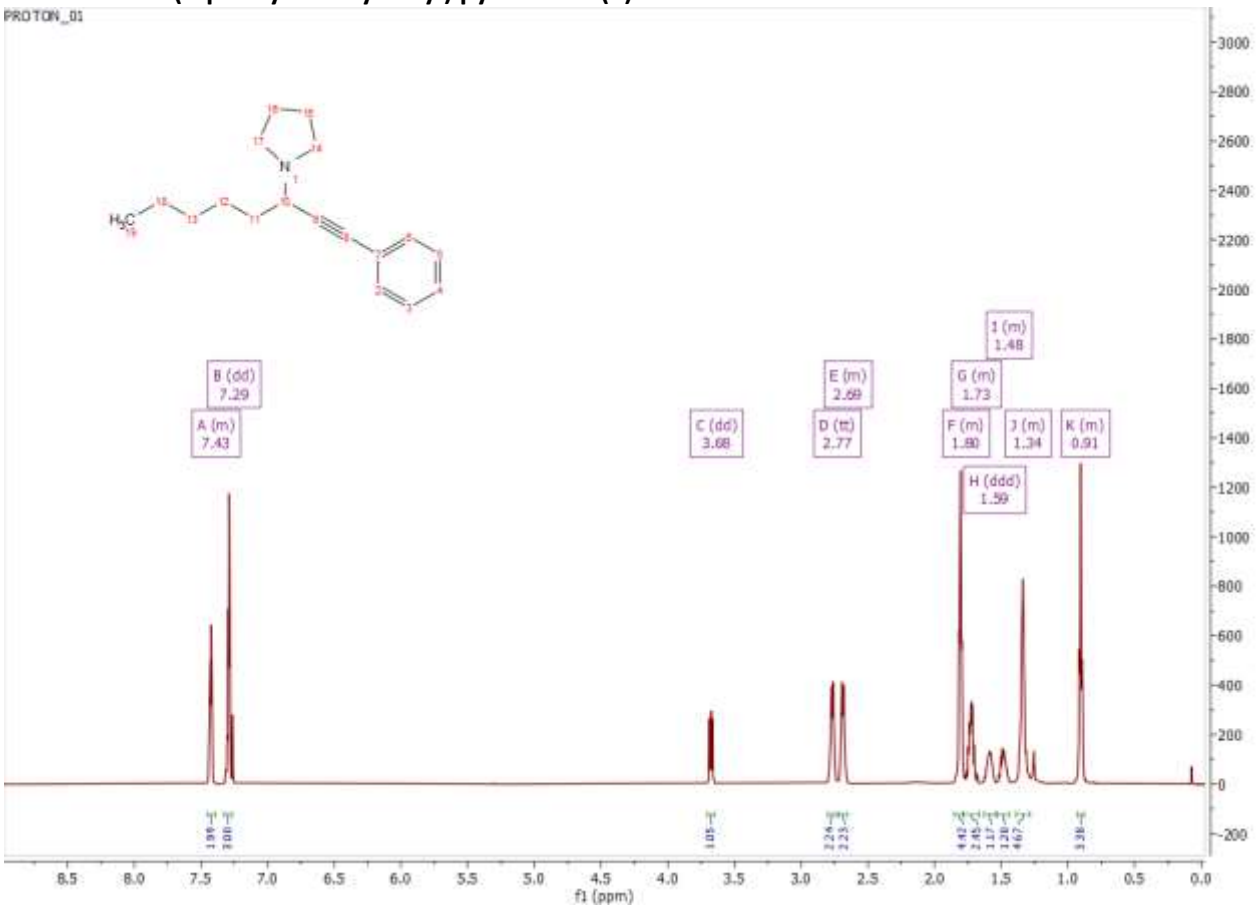
^{1}H NMR for 4-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)morpholine (3)



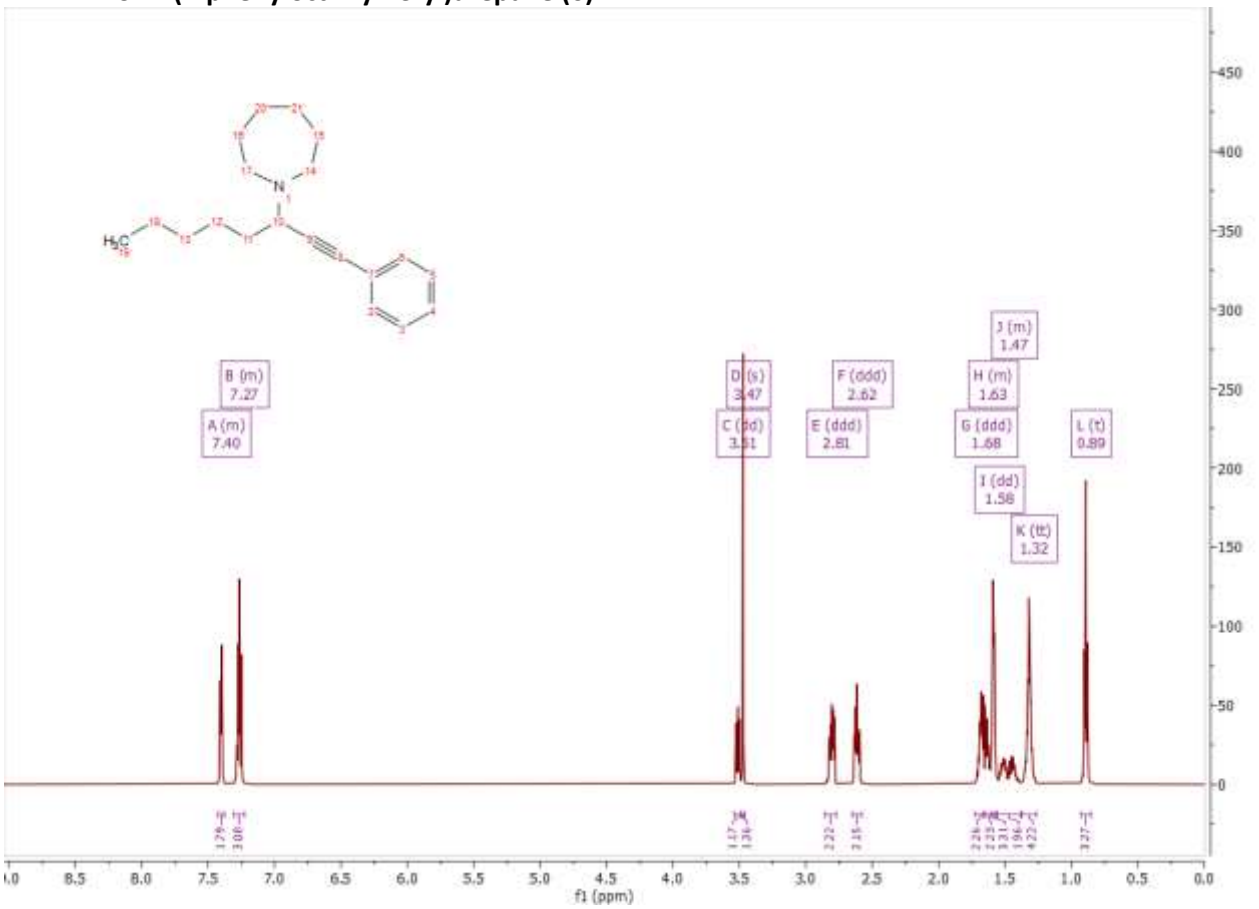
^{1}H NMR for 1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)azepane (4)



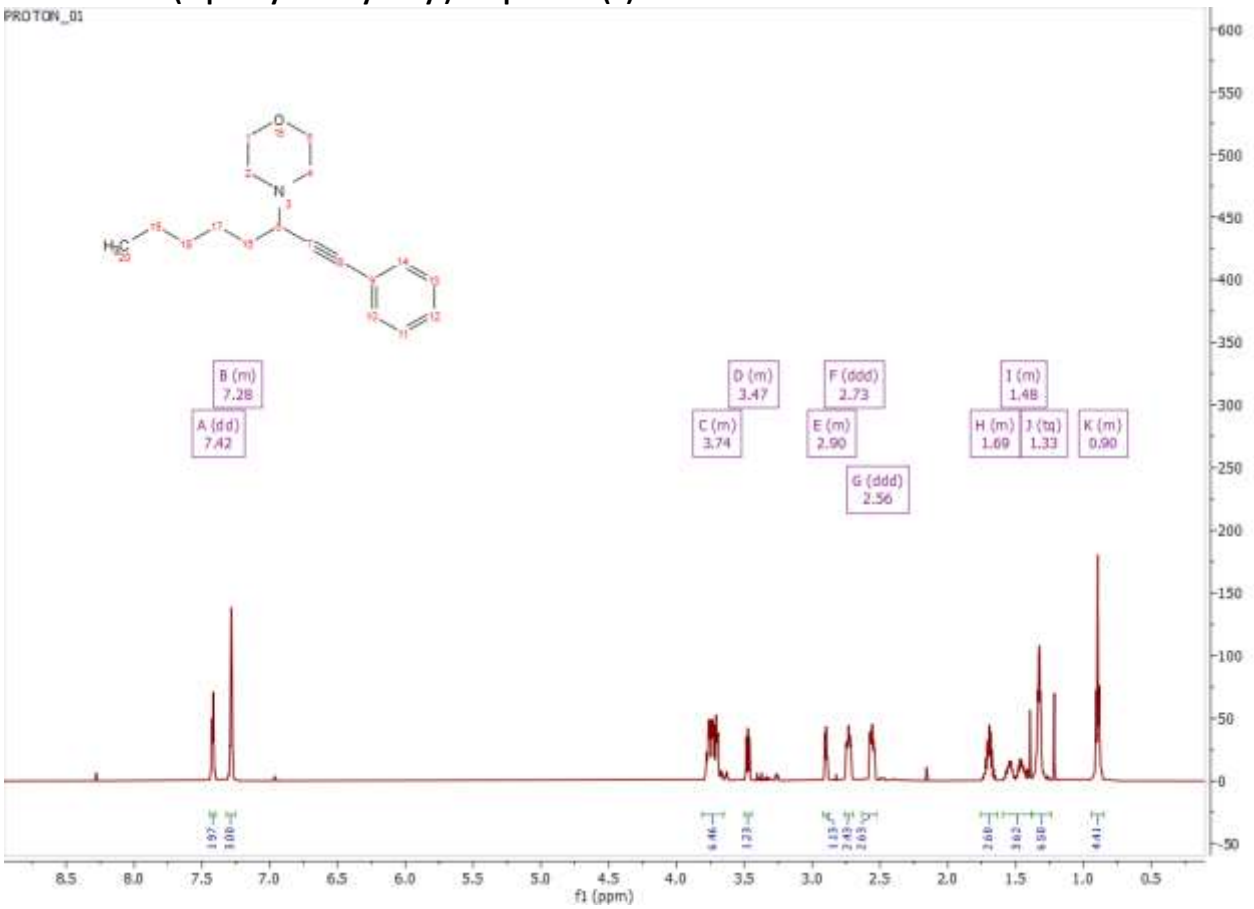
^{1}H NMR for 1-(1-phenyloct-1-yn-3-yl) pyrrolidine (5)



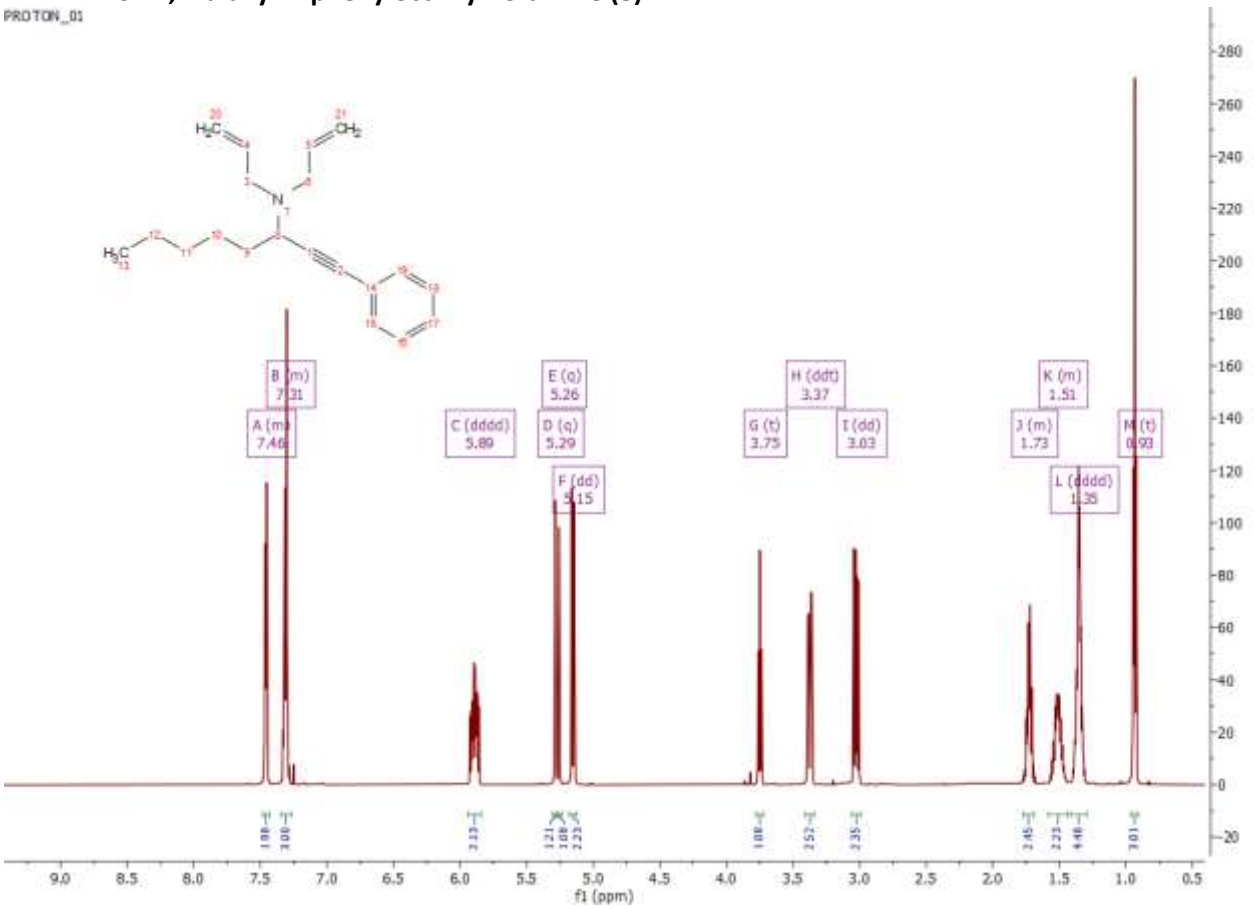
^{1}H NMR for 1-(1-phenyloct-1-yn-3-yl)azepane (6)



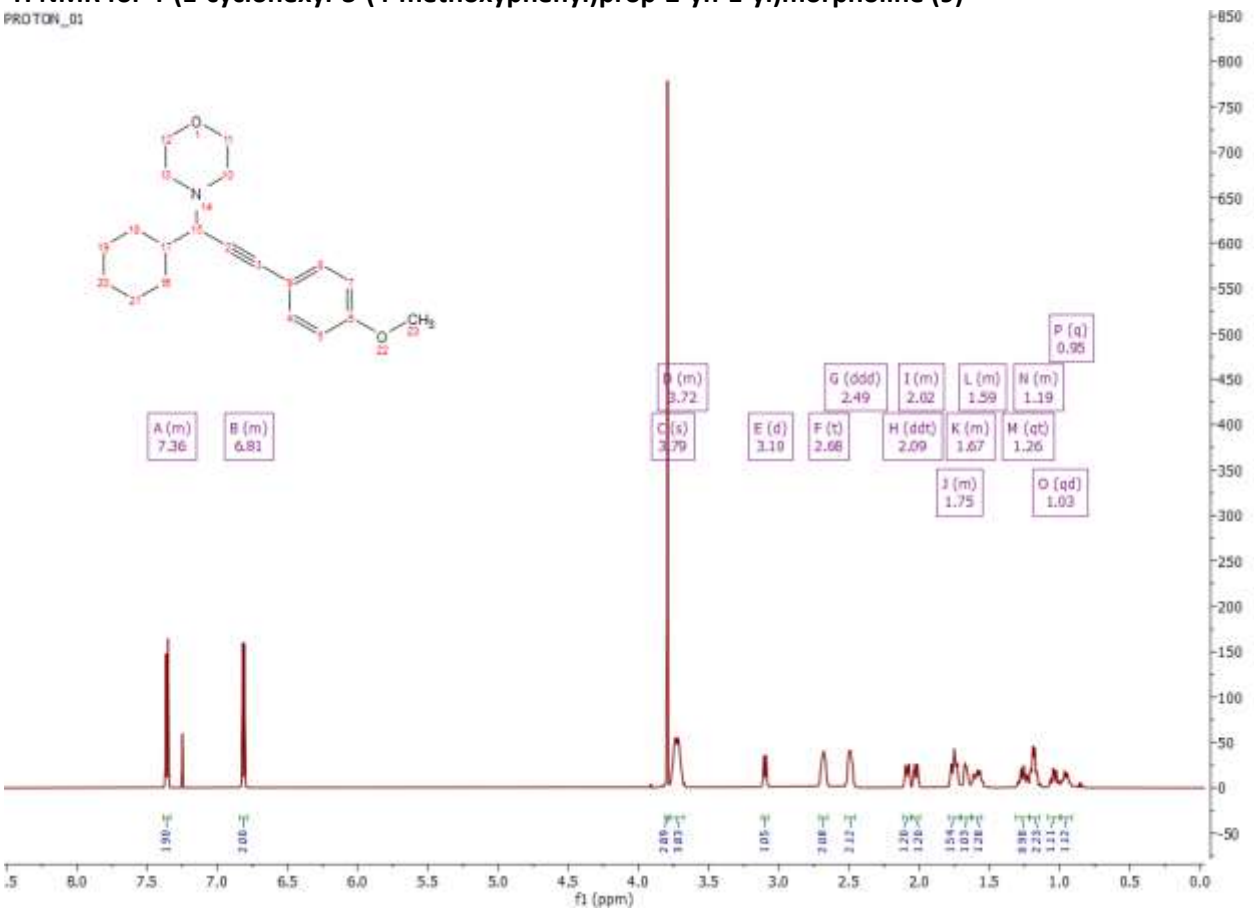
^{1}H NMR for 4-(1-phenyloct-1-yn-3-yl)morpholine (7)



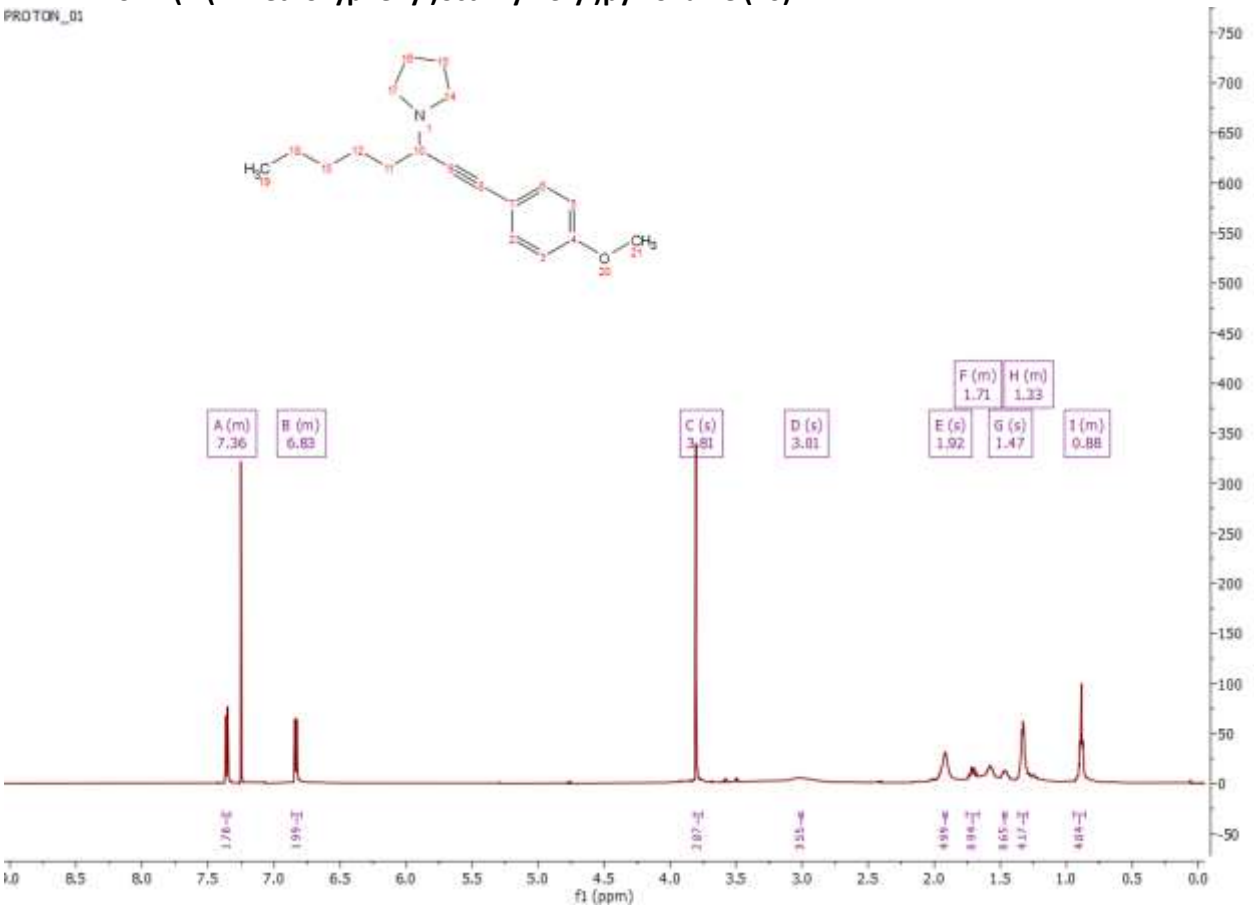
^{1}H NMR for N,N-diallyl-1-phenyloct-1-yn-3-amine (8)



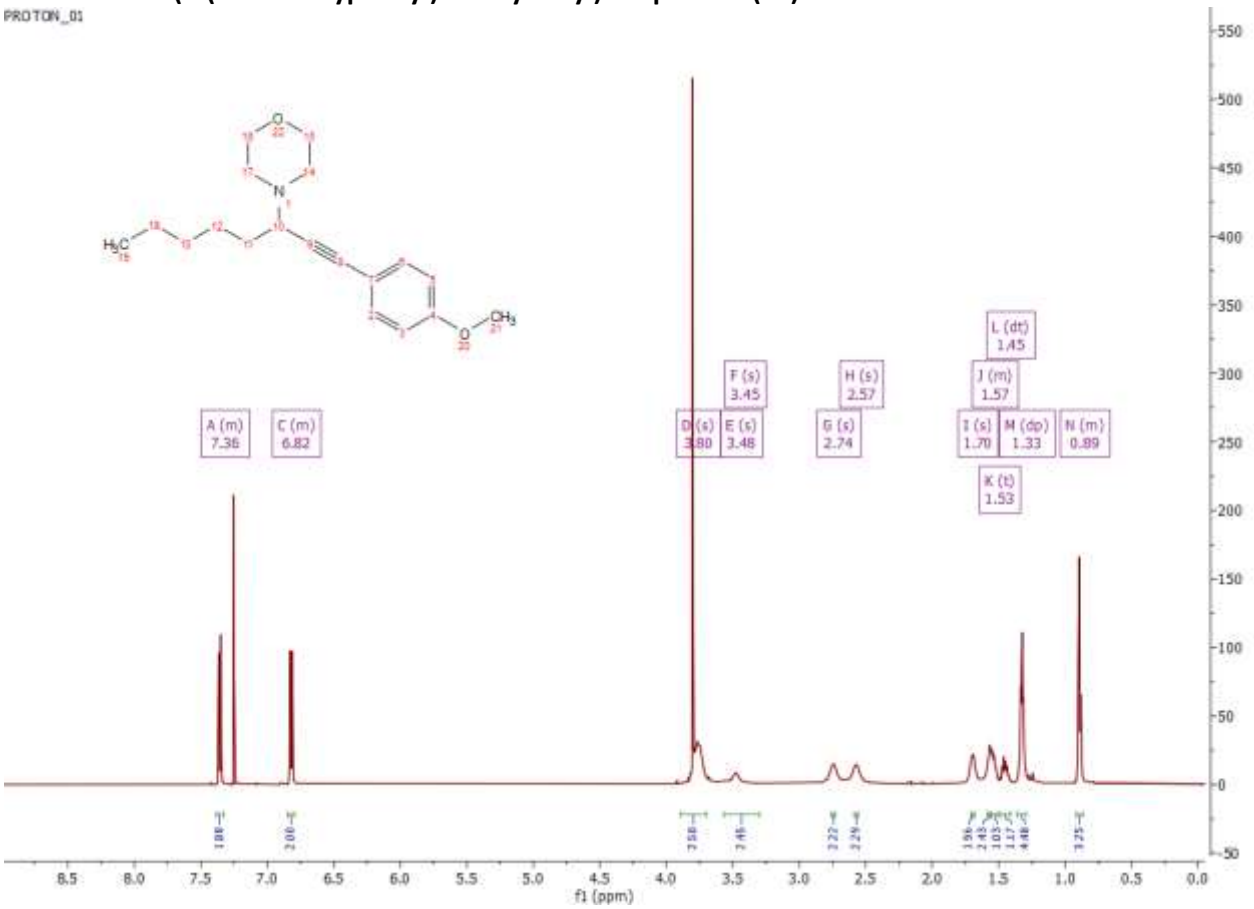
^{1}H NMR for 4-(1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl)morpholine (9)



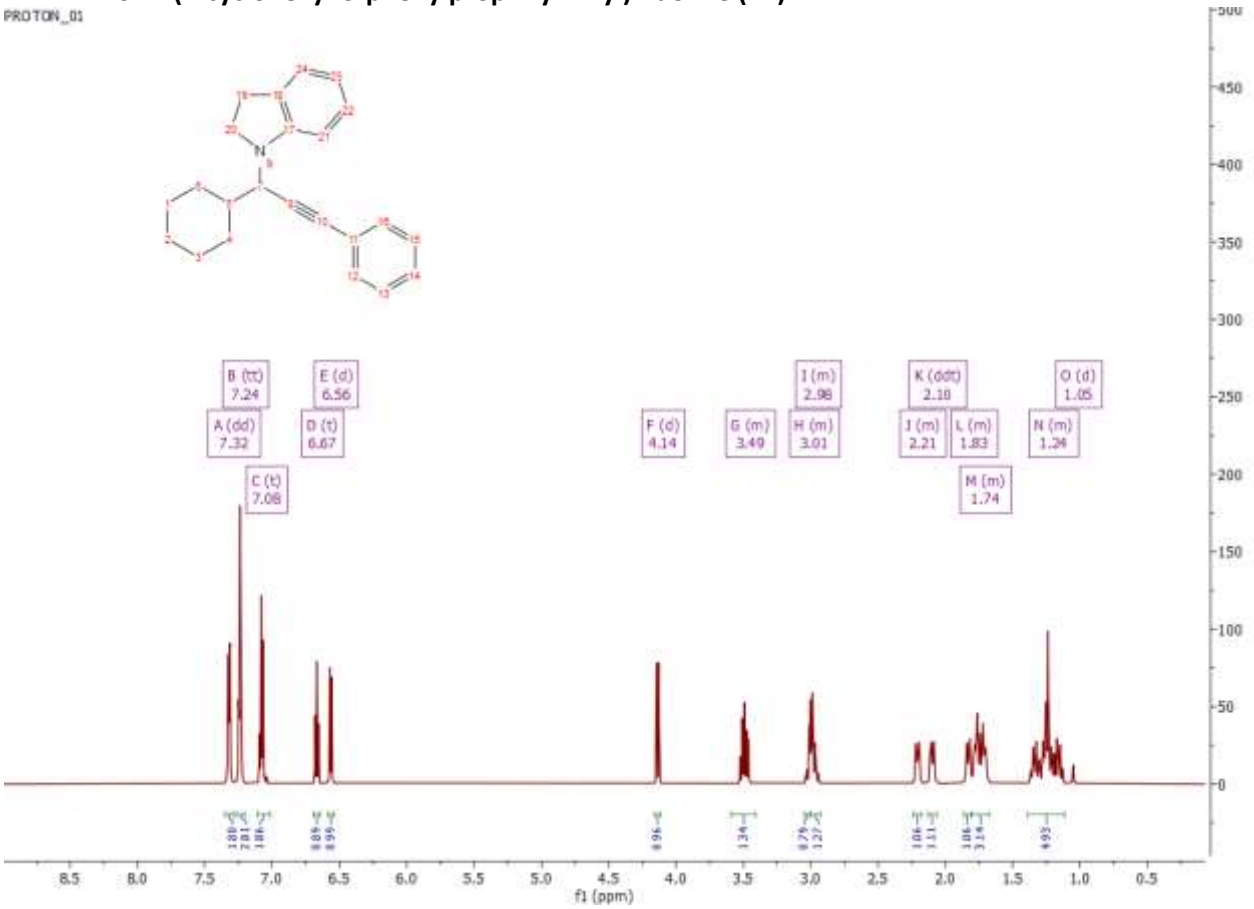
^{1}H NMR for 1-(1-(4-methoxyphenyl)oct-1-yn-3-yl)pyrrolidine (10)



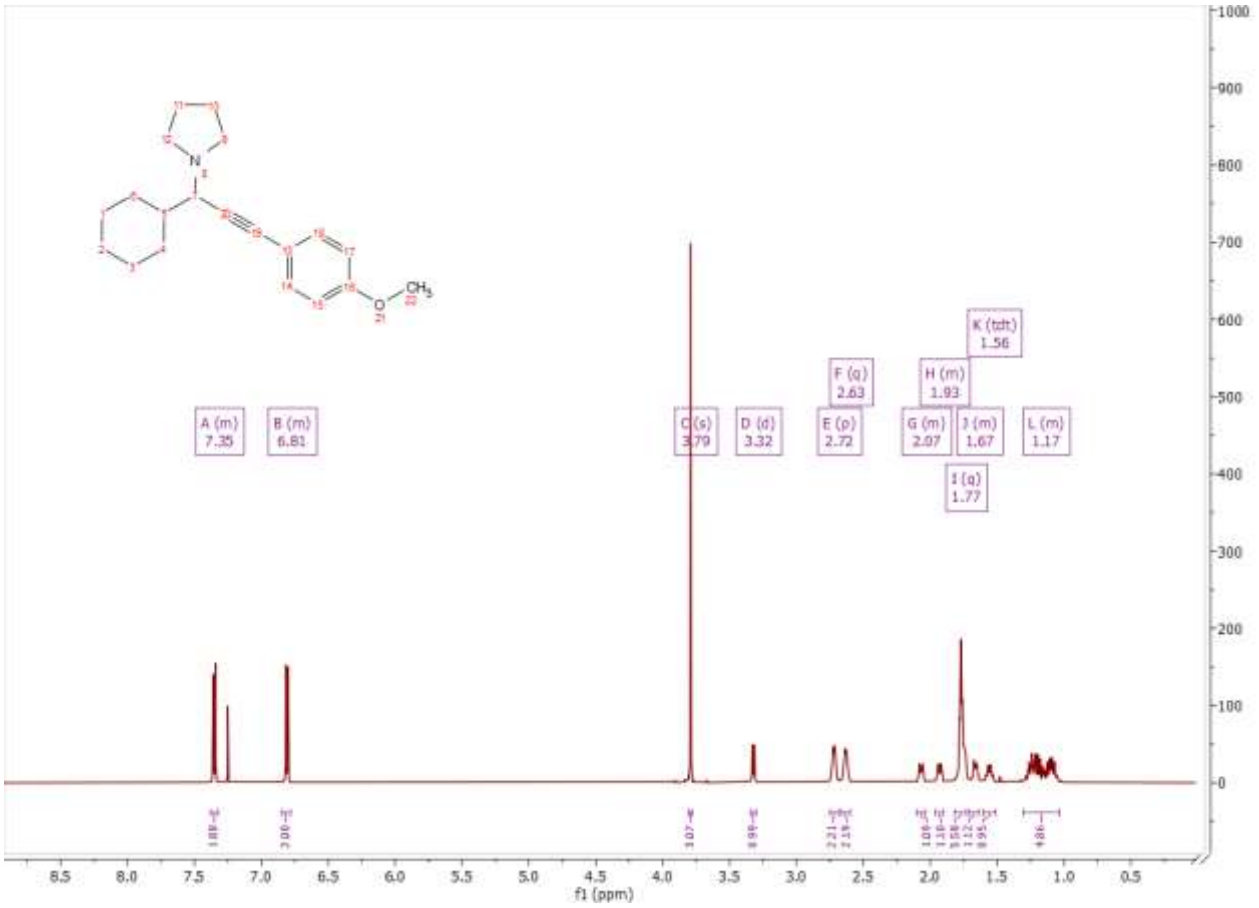
^{1}H NMR for 4-(1-(4-methoxyphenyl)oct-1-yn-3-yl)morpholine (11)



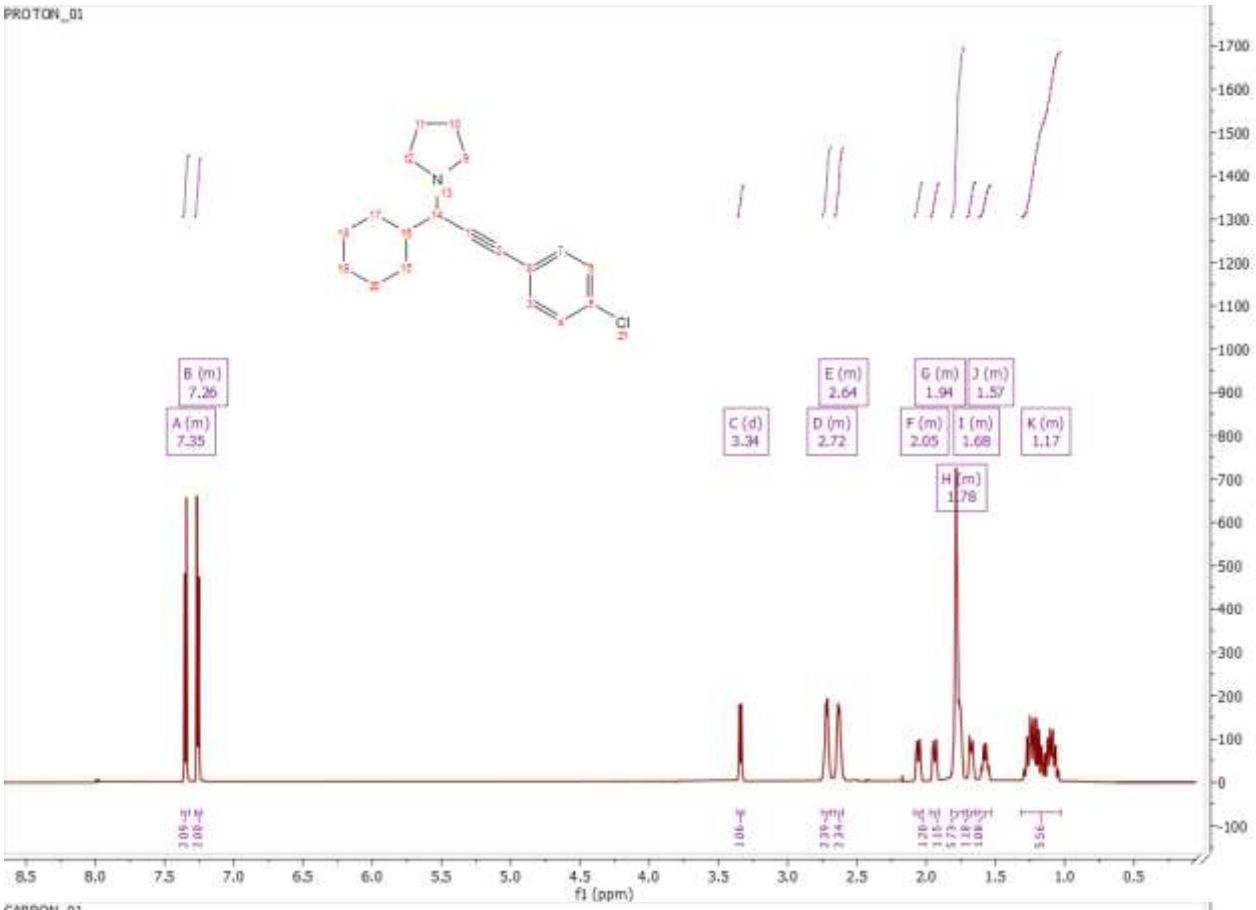
^{1}H NMR for 1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)indoline (12)

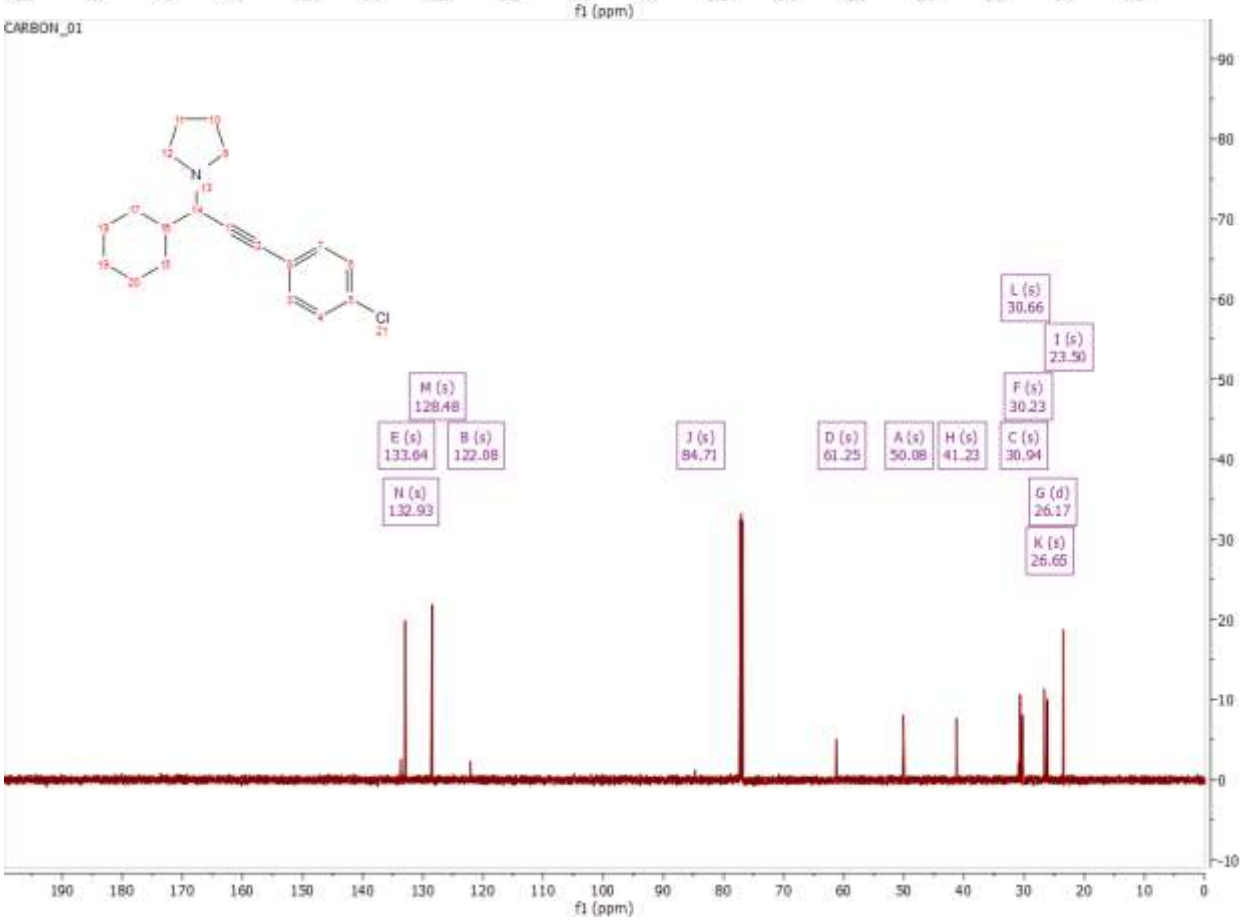


^{1}H NMR for 1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl]pyrrolidine (13)

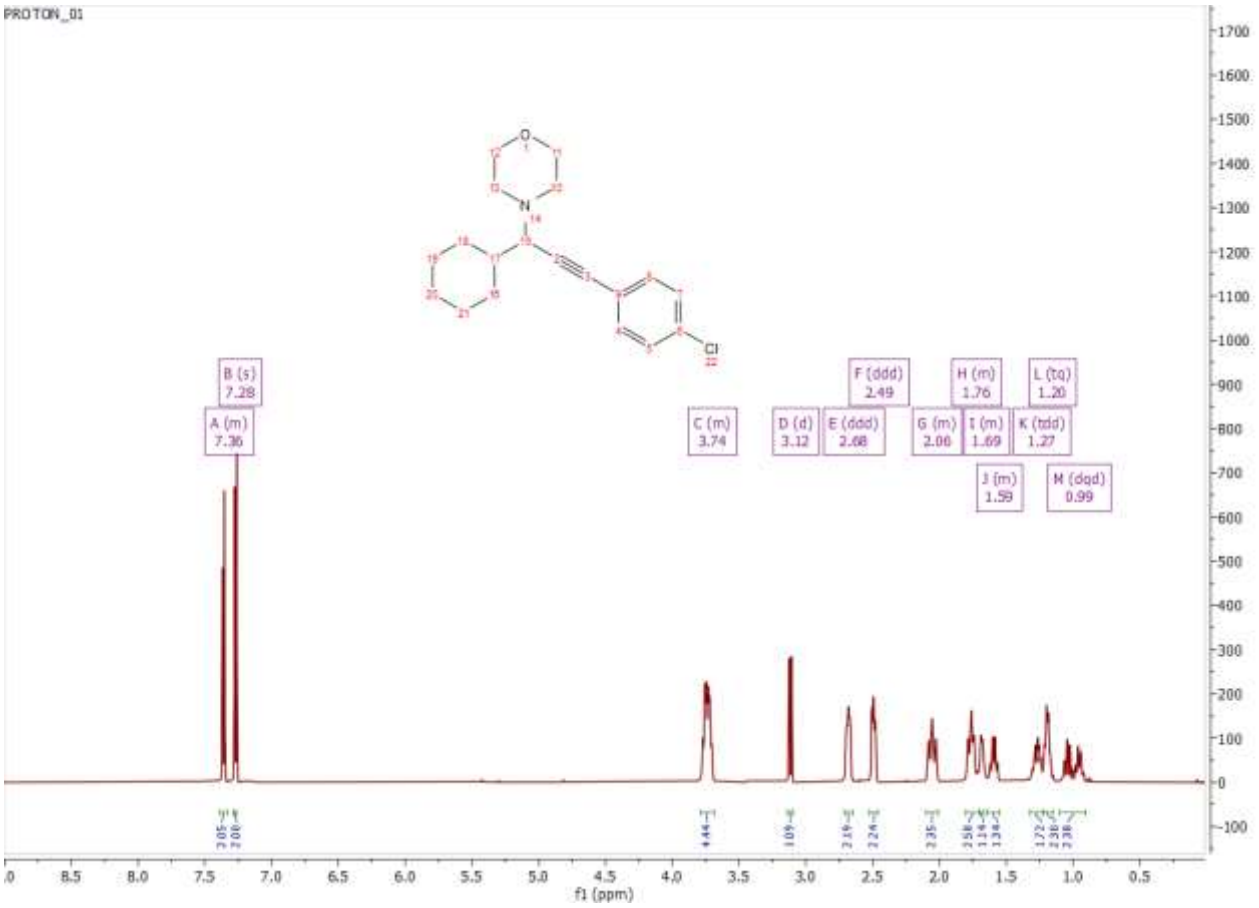


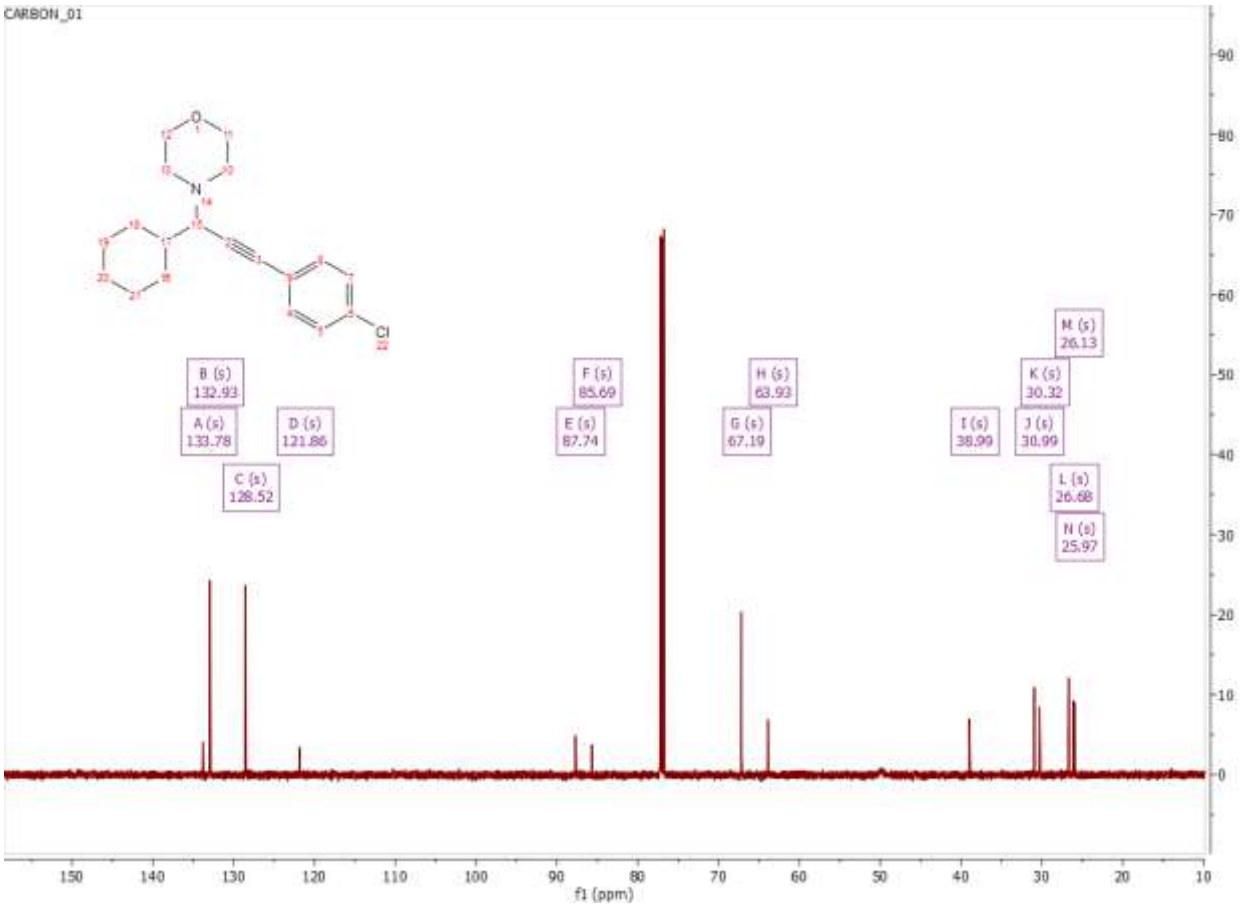
^{1}H NMR and ^{13}C NMR for 1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]pyrrolidine(14)



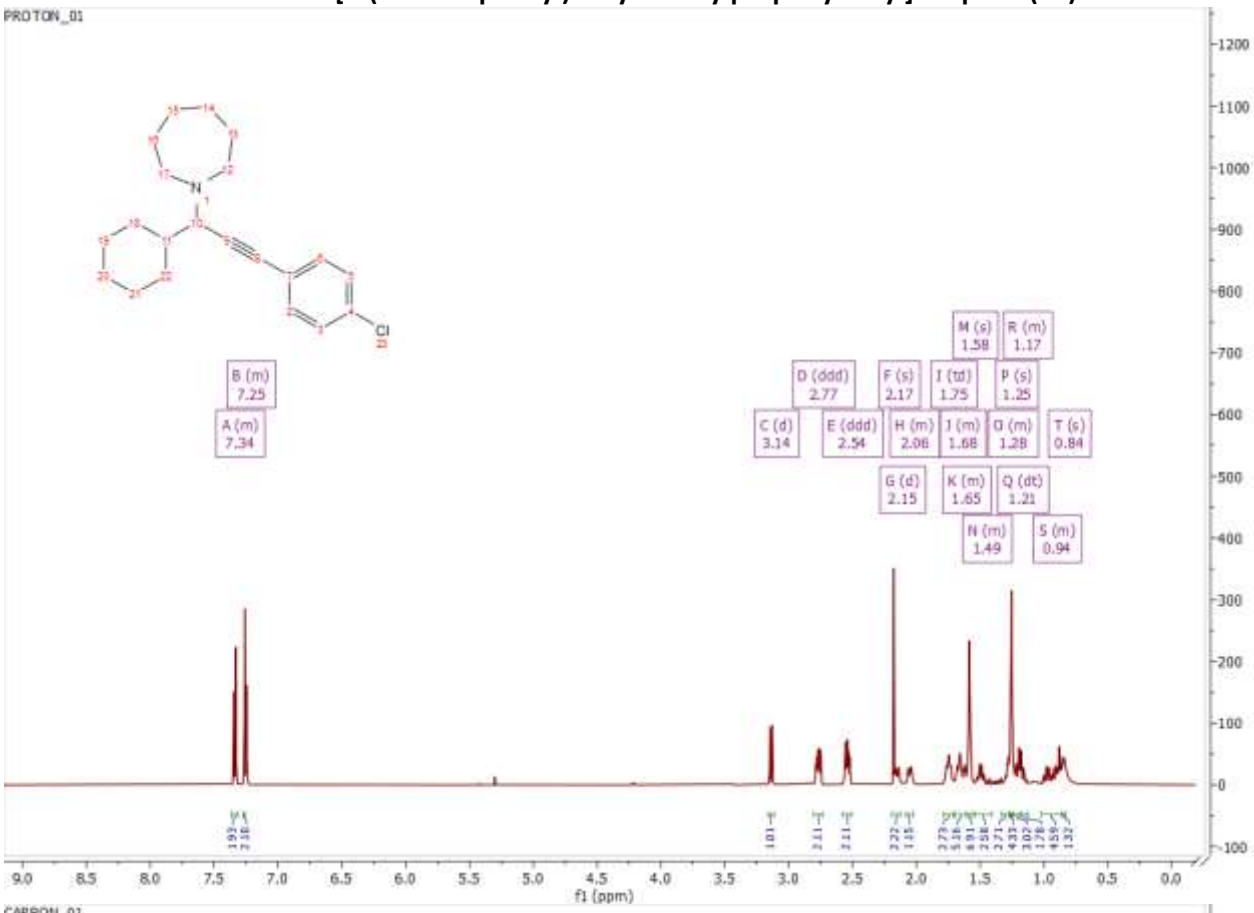


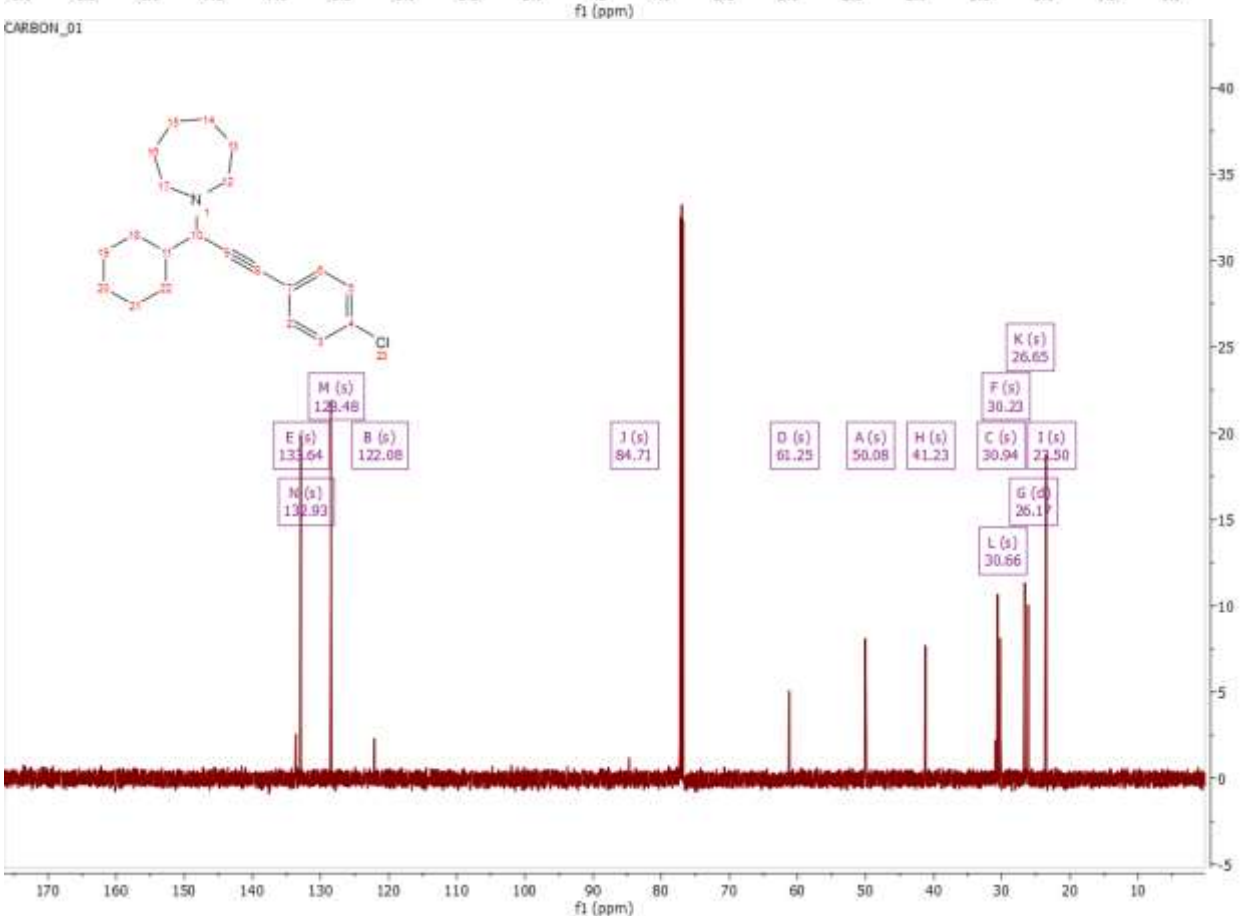
^{1}H NMR and ^{13}C NMR for 4-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]morpholine (15)



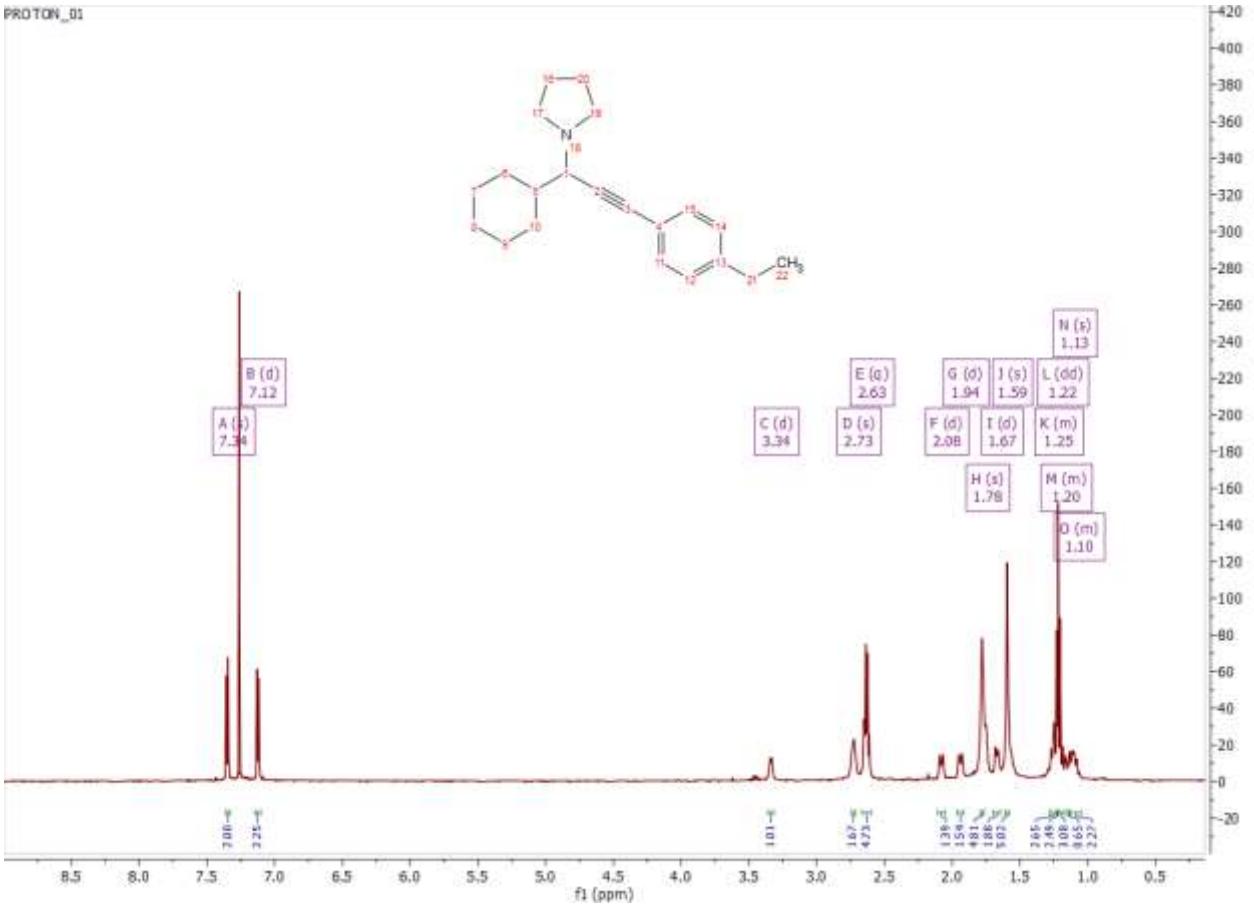


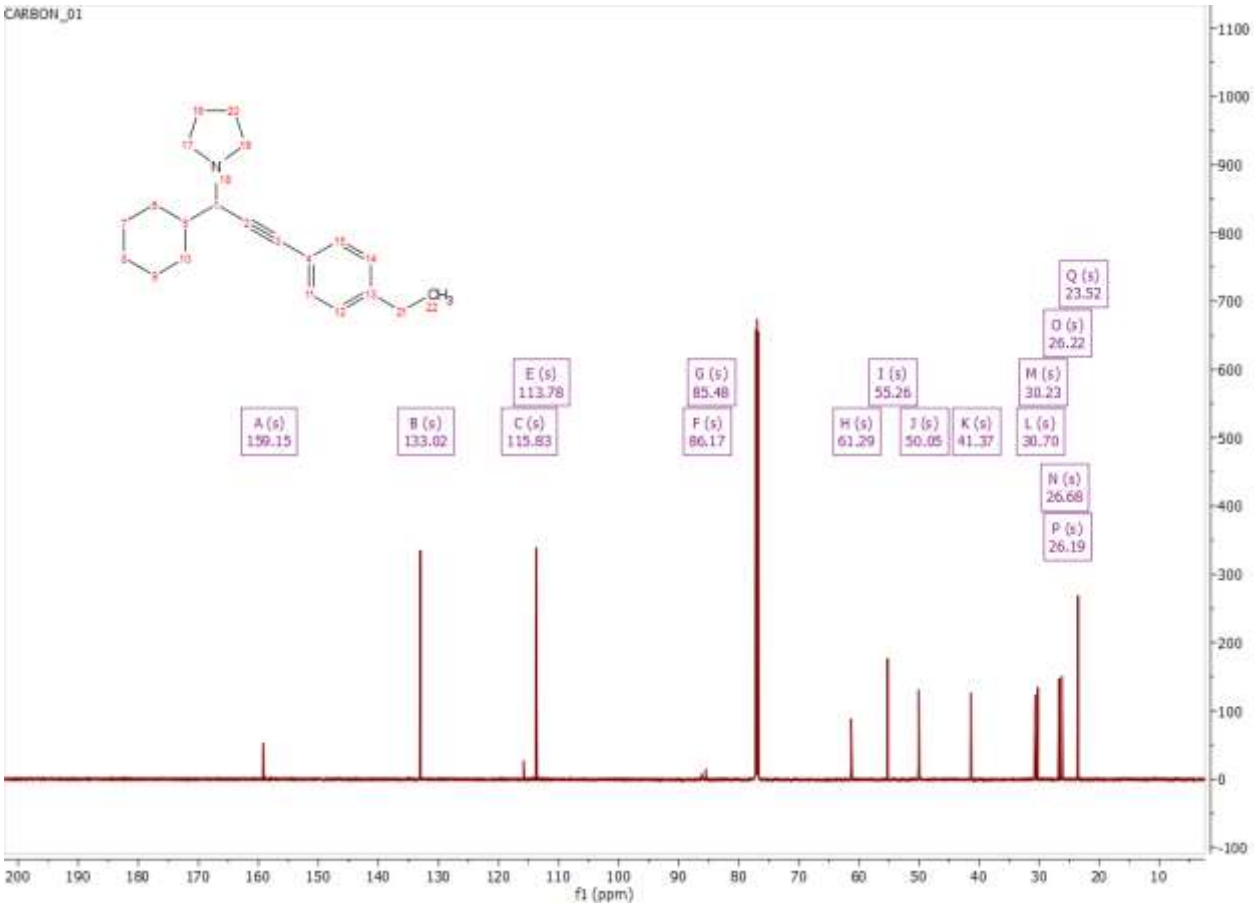
^{1}H NMR and ^{13}C NMR for 1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl] azepane (16)



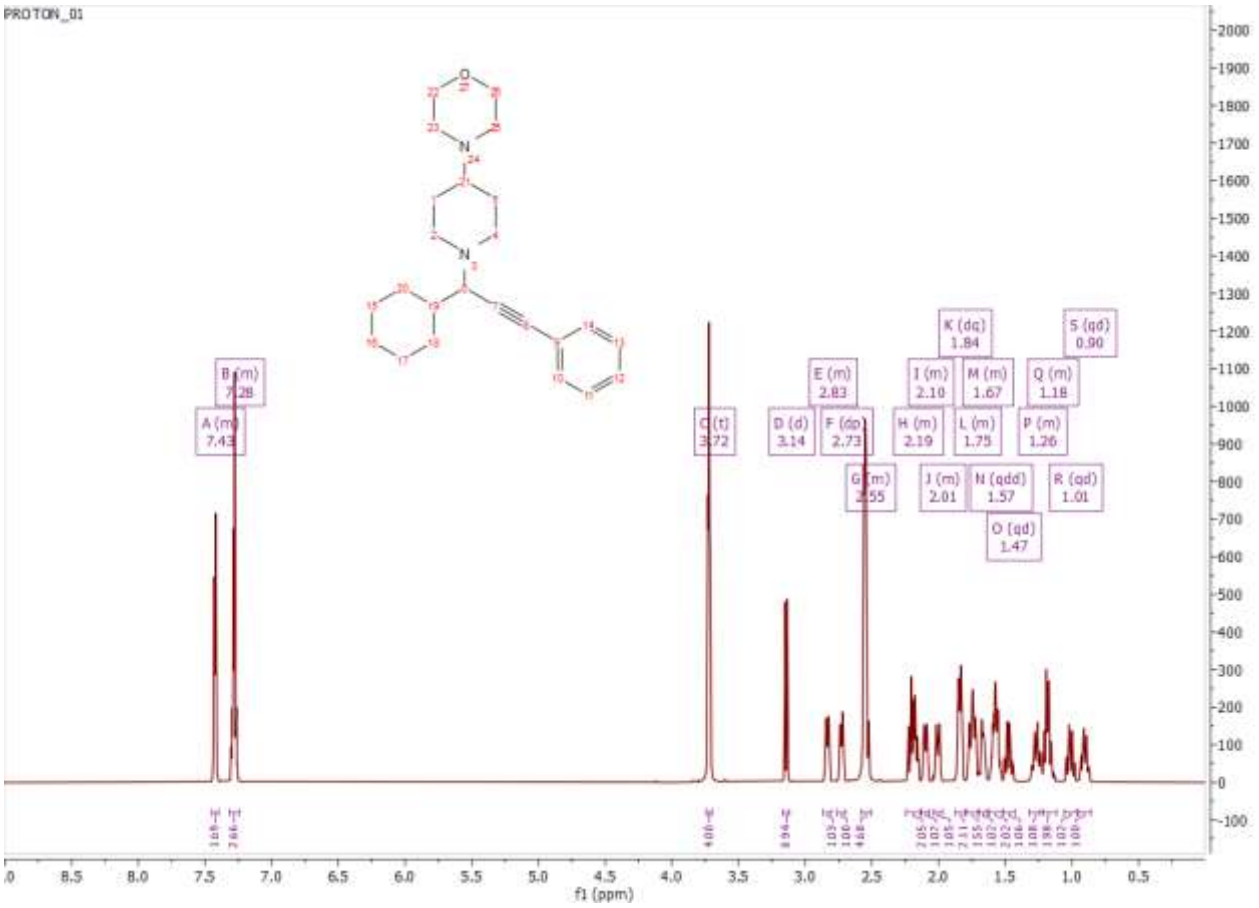


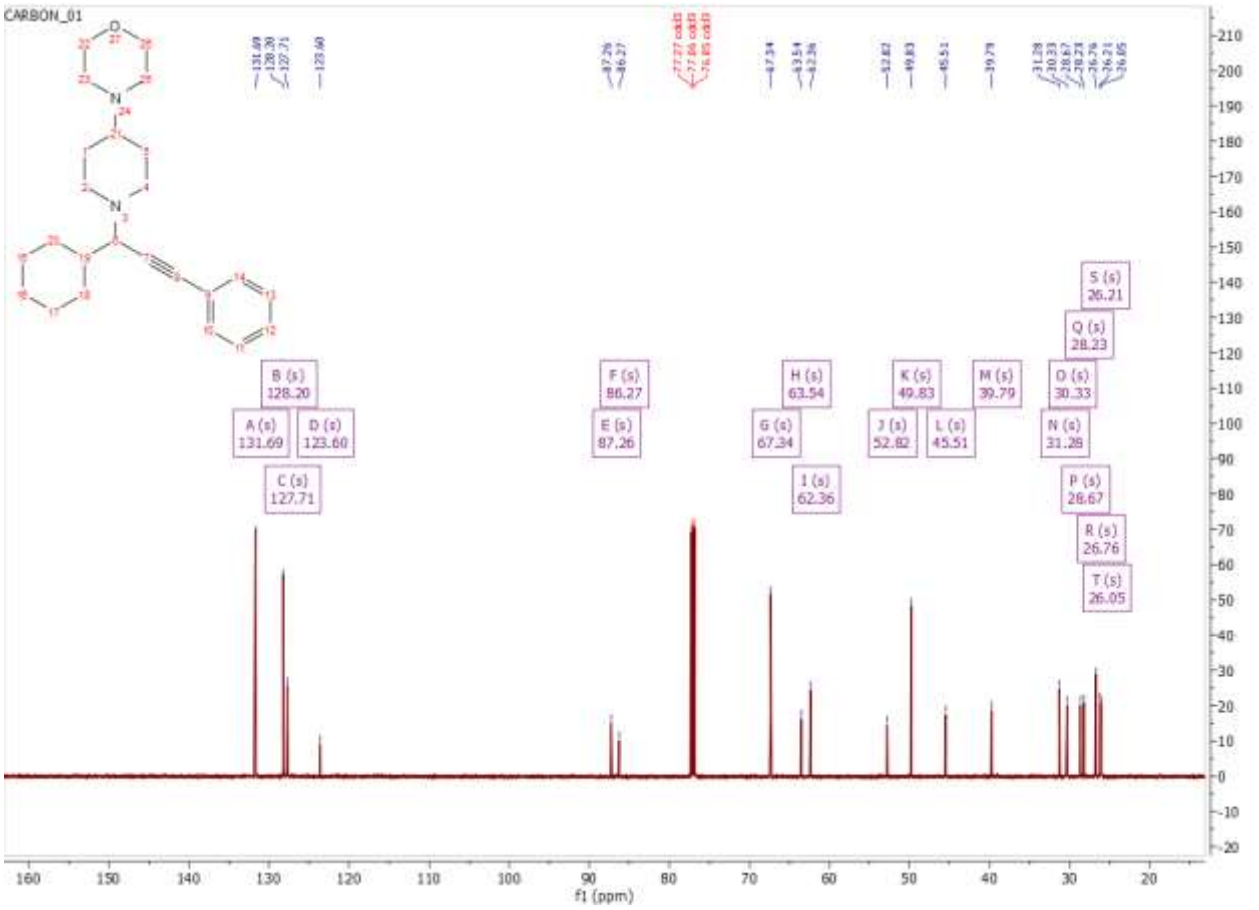
^{1}H NMR and ^{13}C NMR for 1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl]pyrrolidine (17)



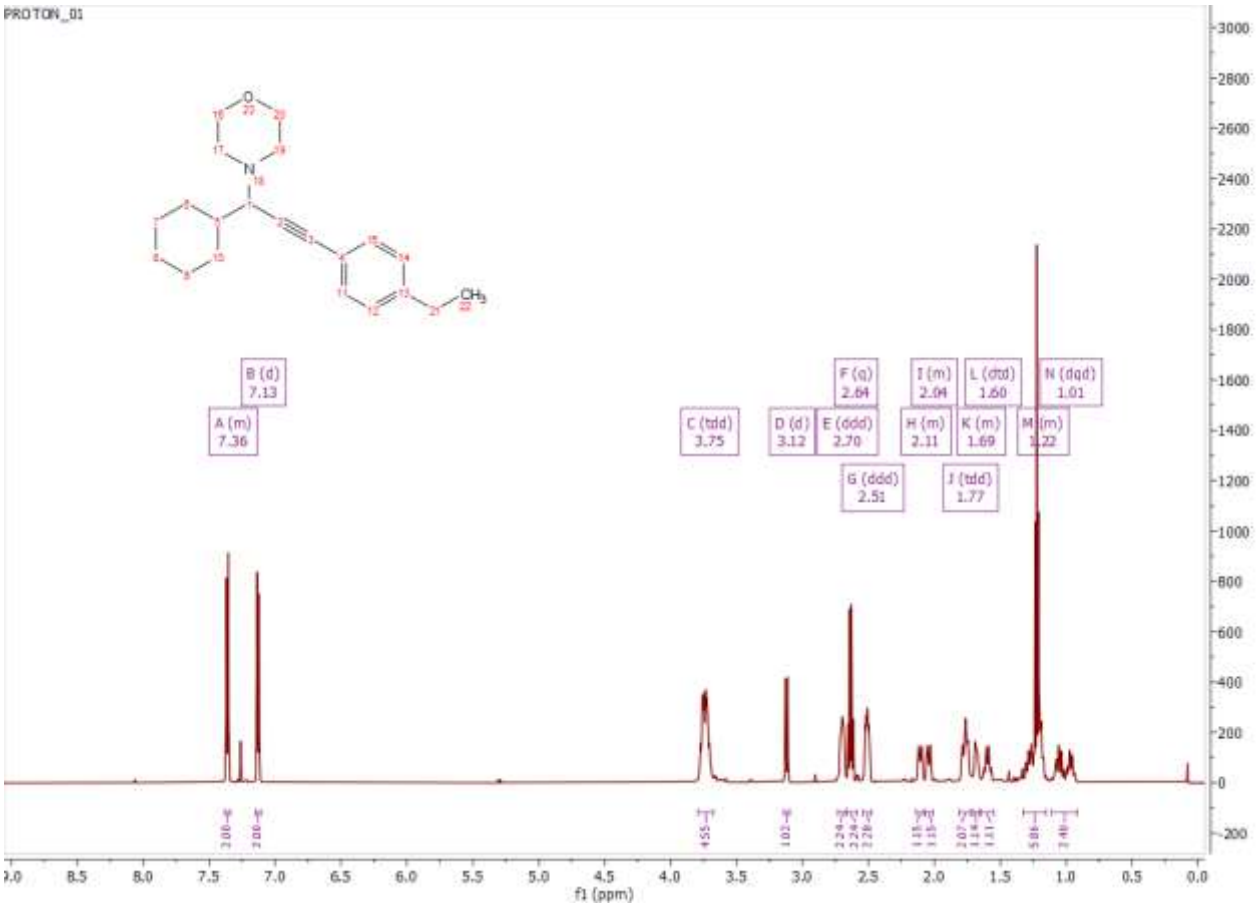


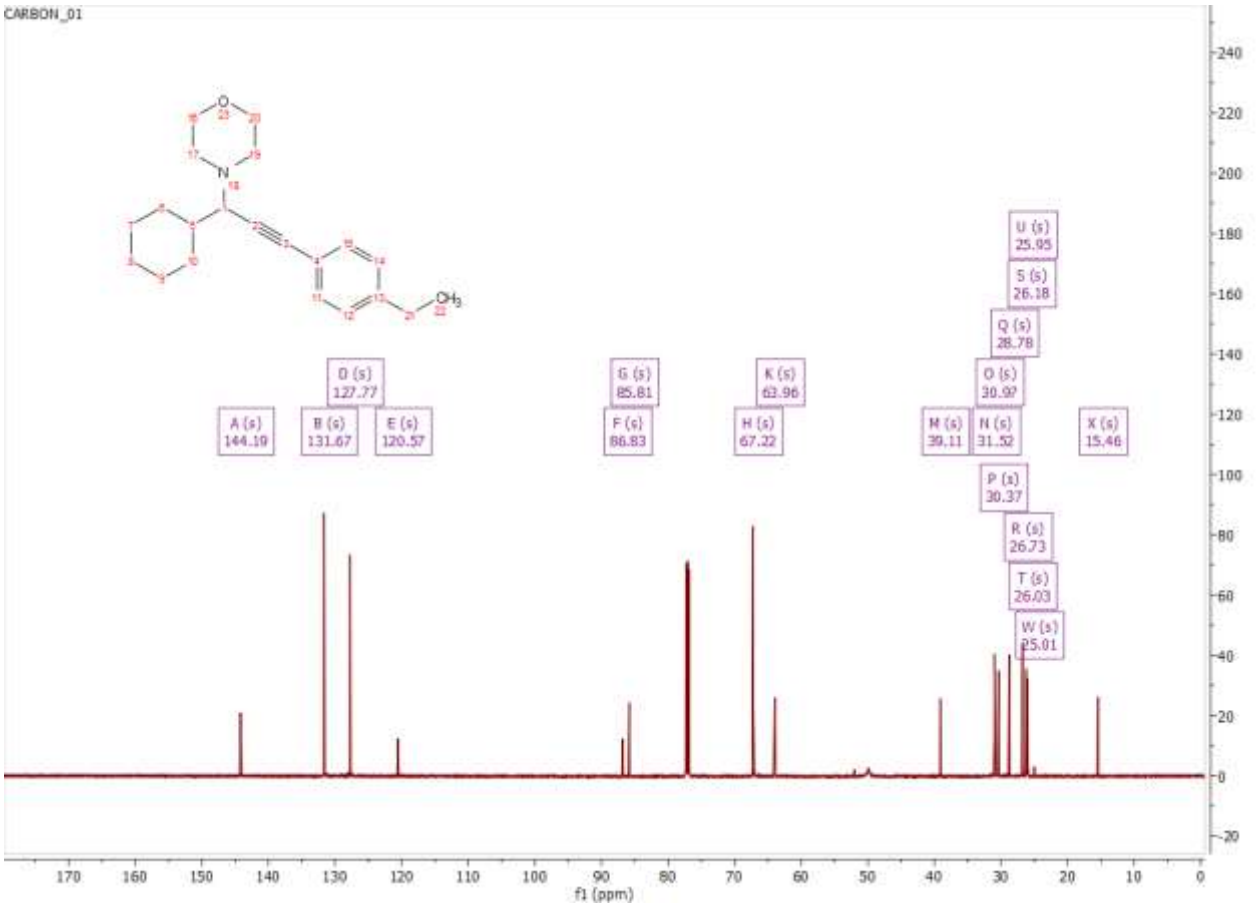
^{1}H NMR and ^{13}C NMR for 4-{1-[1-cyclohexyl-3-(4-phenylprop-2-yn-1-yl]piperidin-4-yl}morpholine (18)



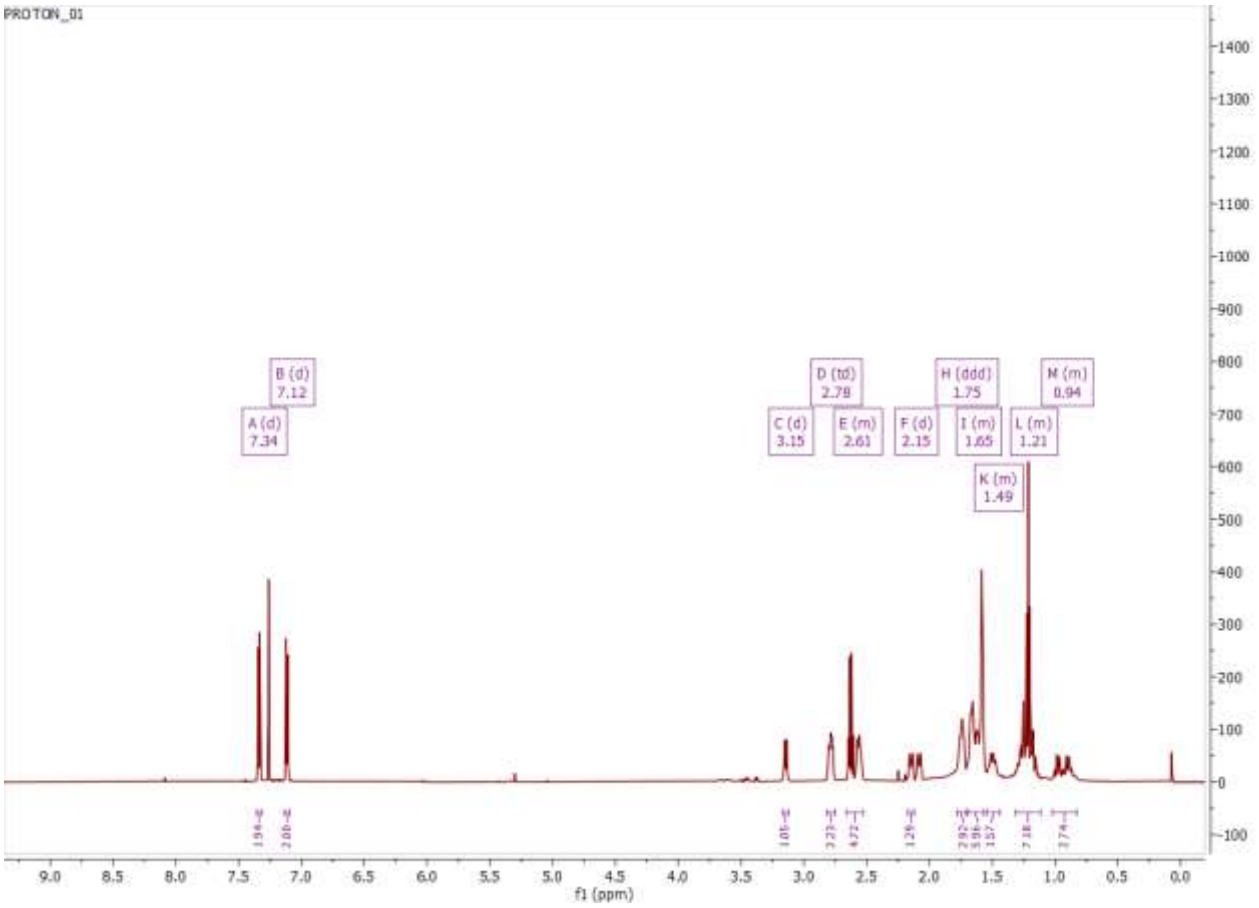


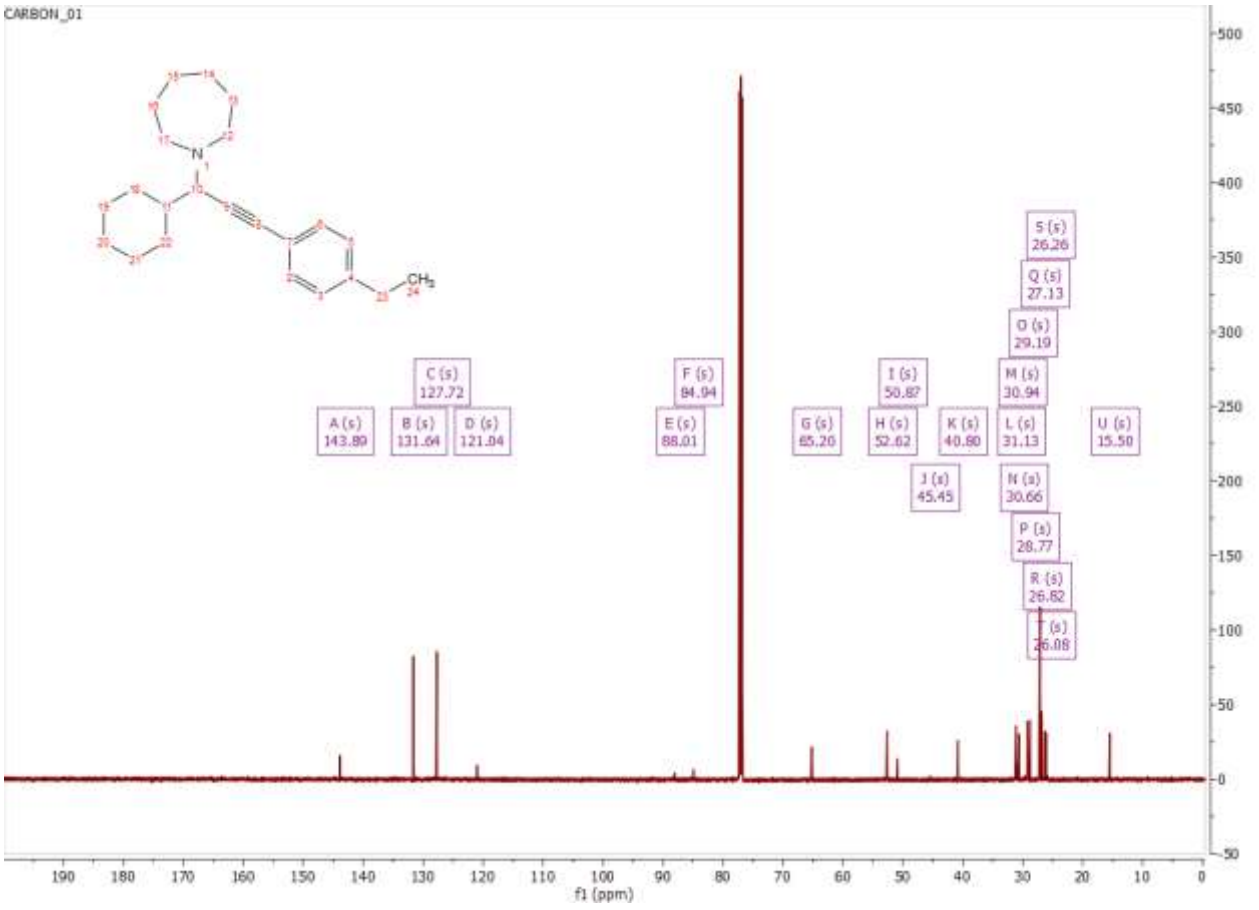
^{1}H NMR and ^{13}C NMR for 1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] morpholine (19)



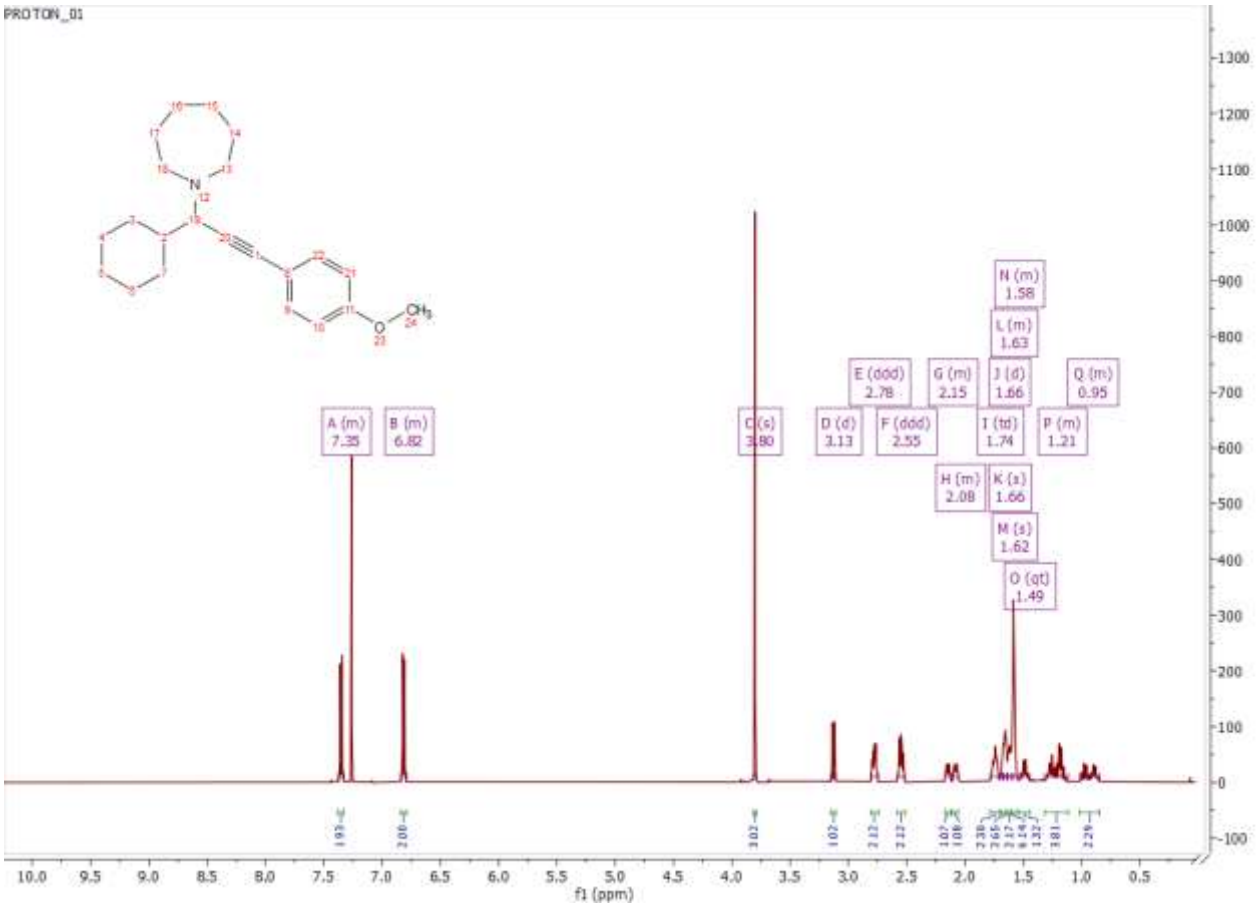


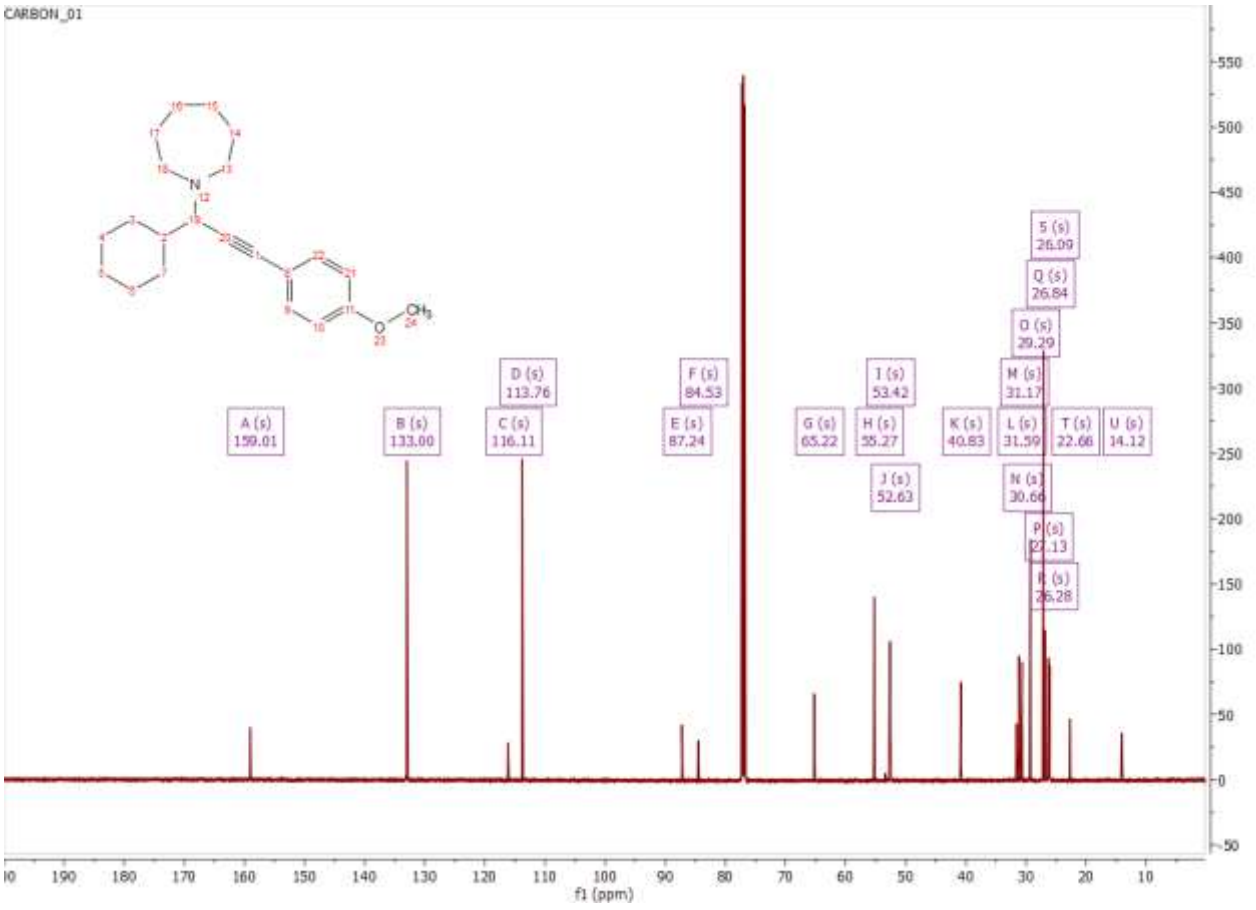
^{1}H NMR and ^{13}C NMR for 1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] azepane(20)



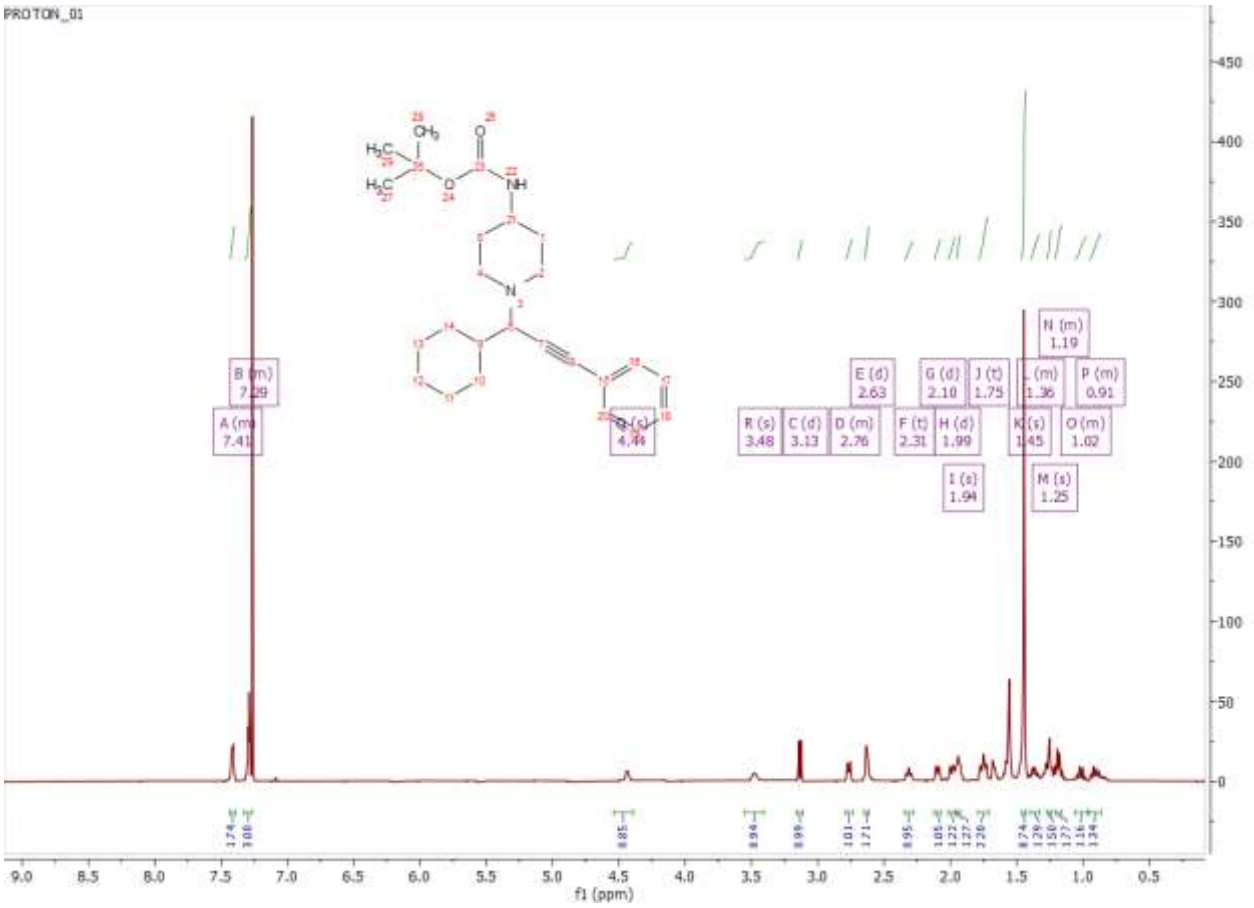


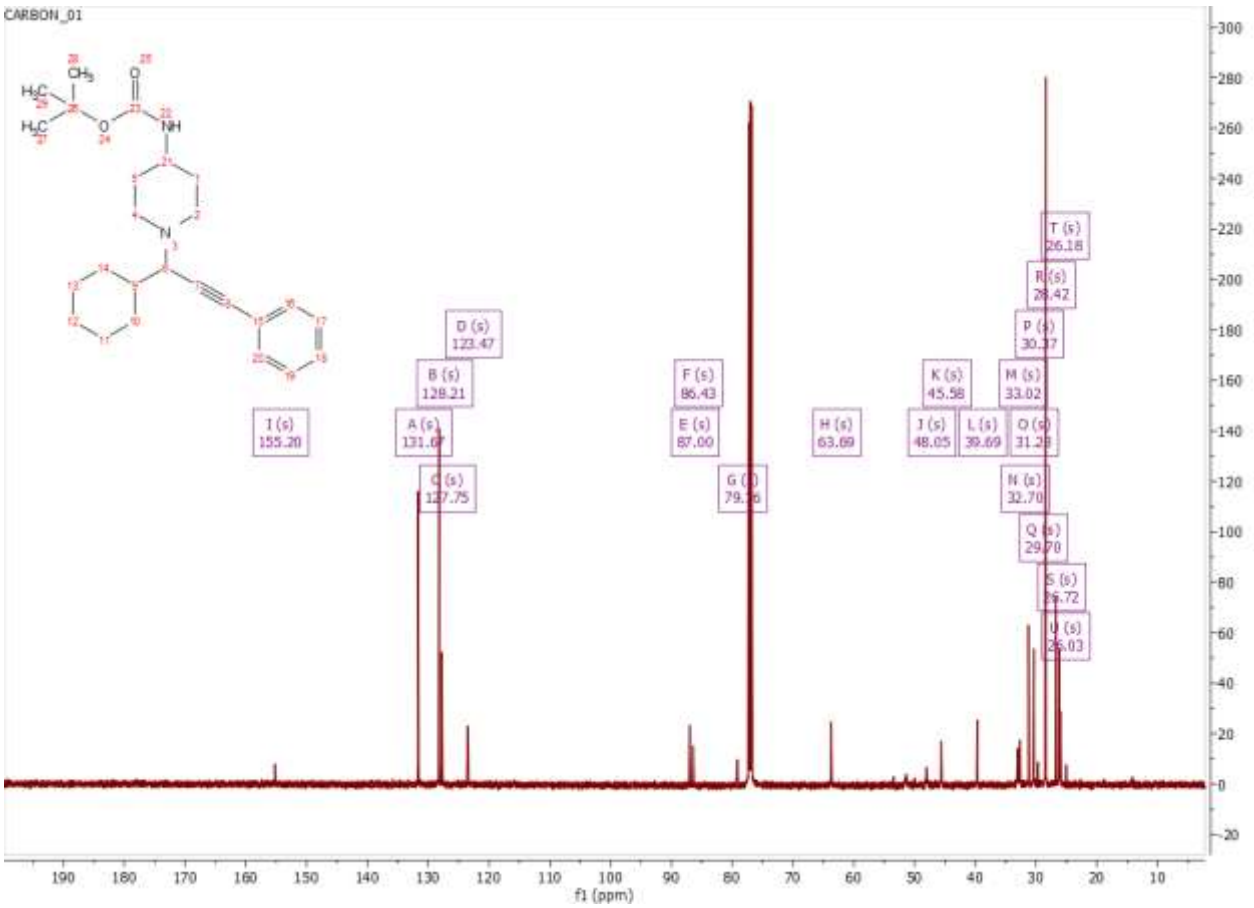
^{1}H NMR and ^{13}C NMR for 1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl] azepane (21)



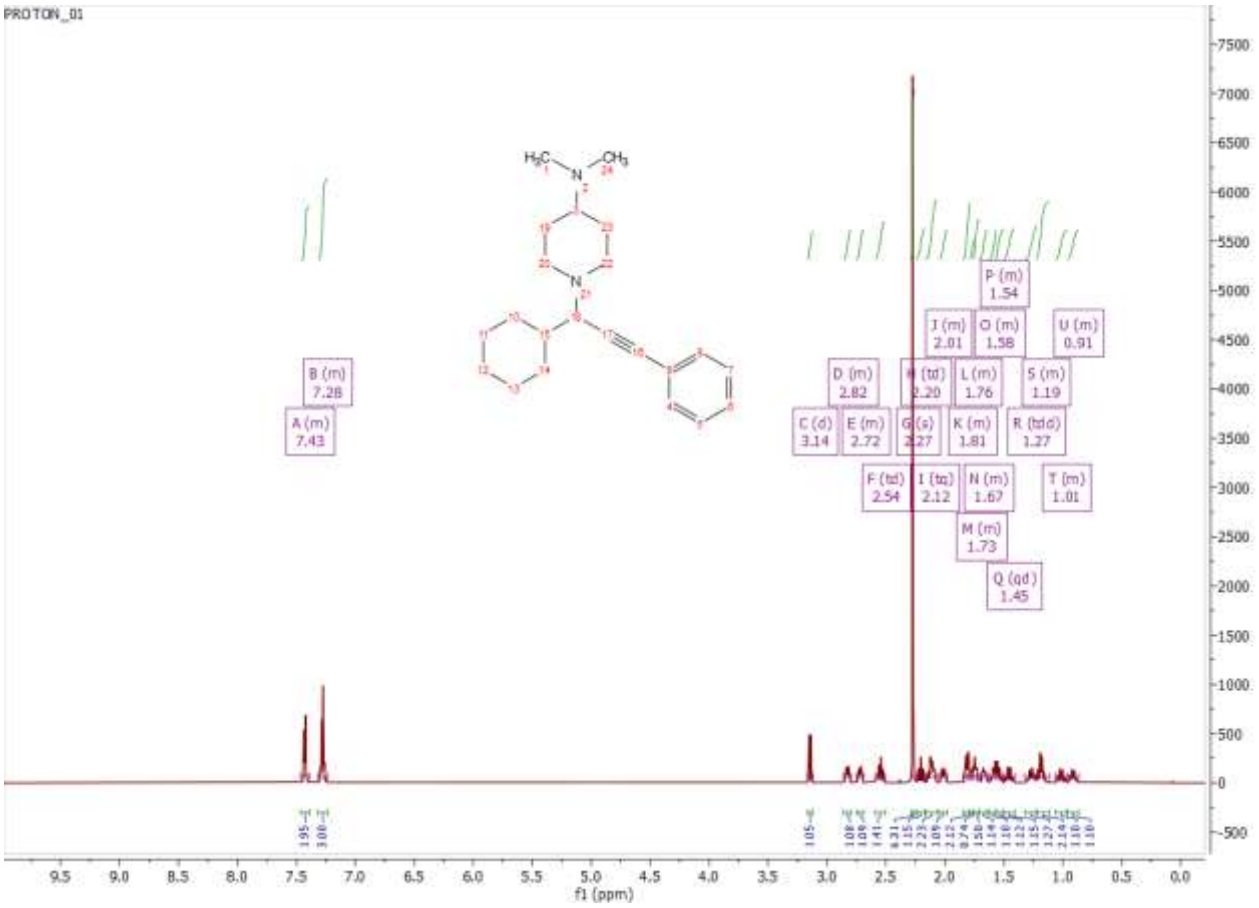


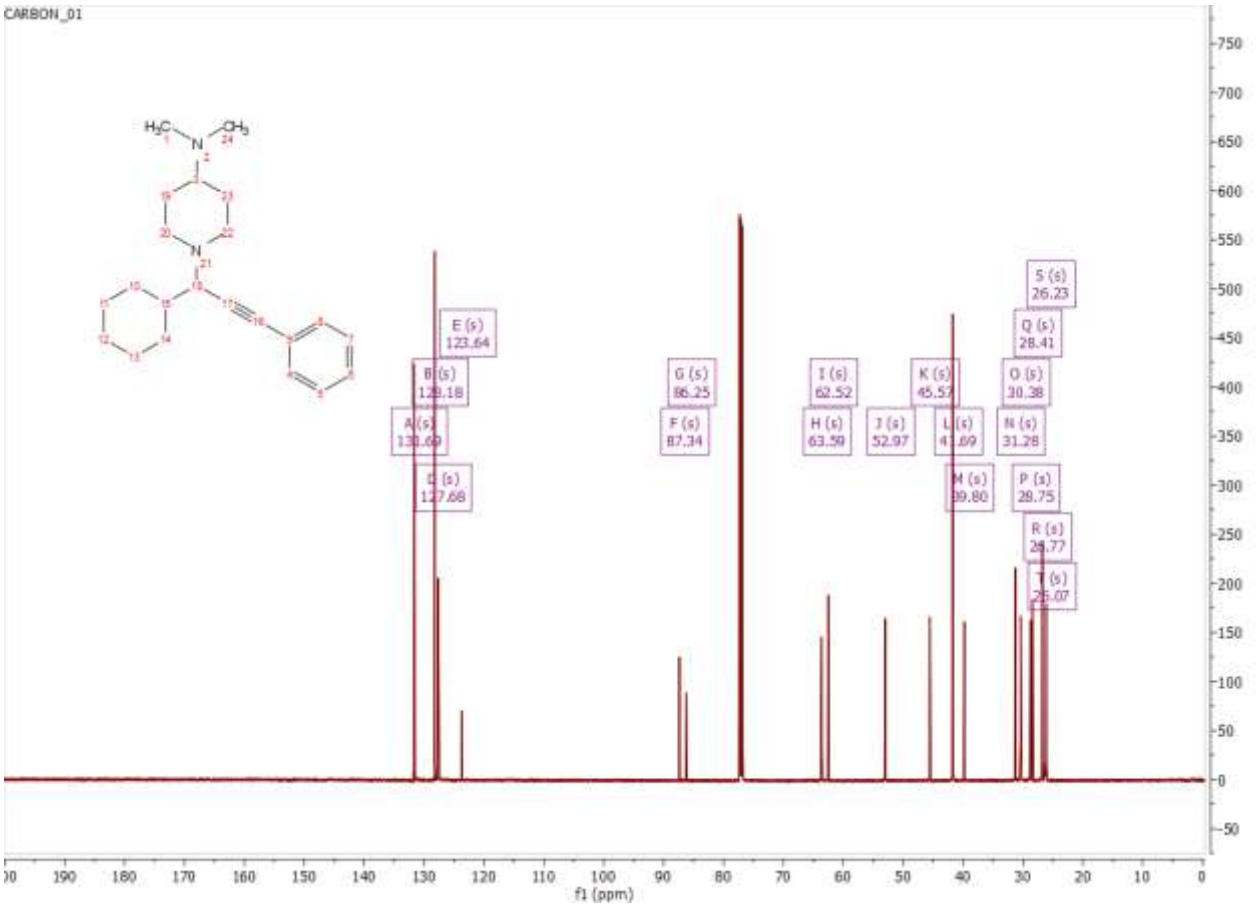
^{1}H NMR and ^{13}C NMR for tert-butyl N-[1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) piperidin-4-yl]carbamate (22)



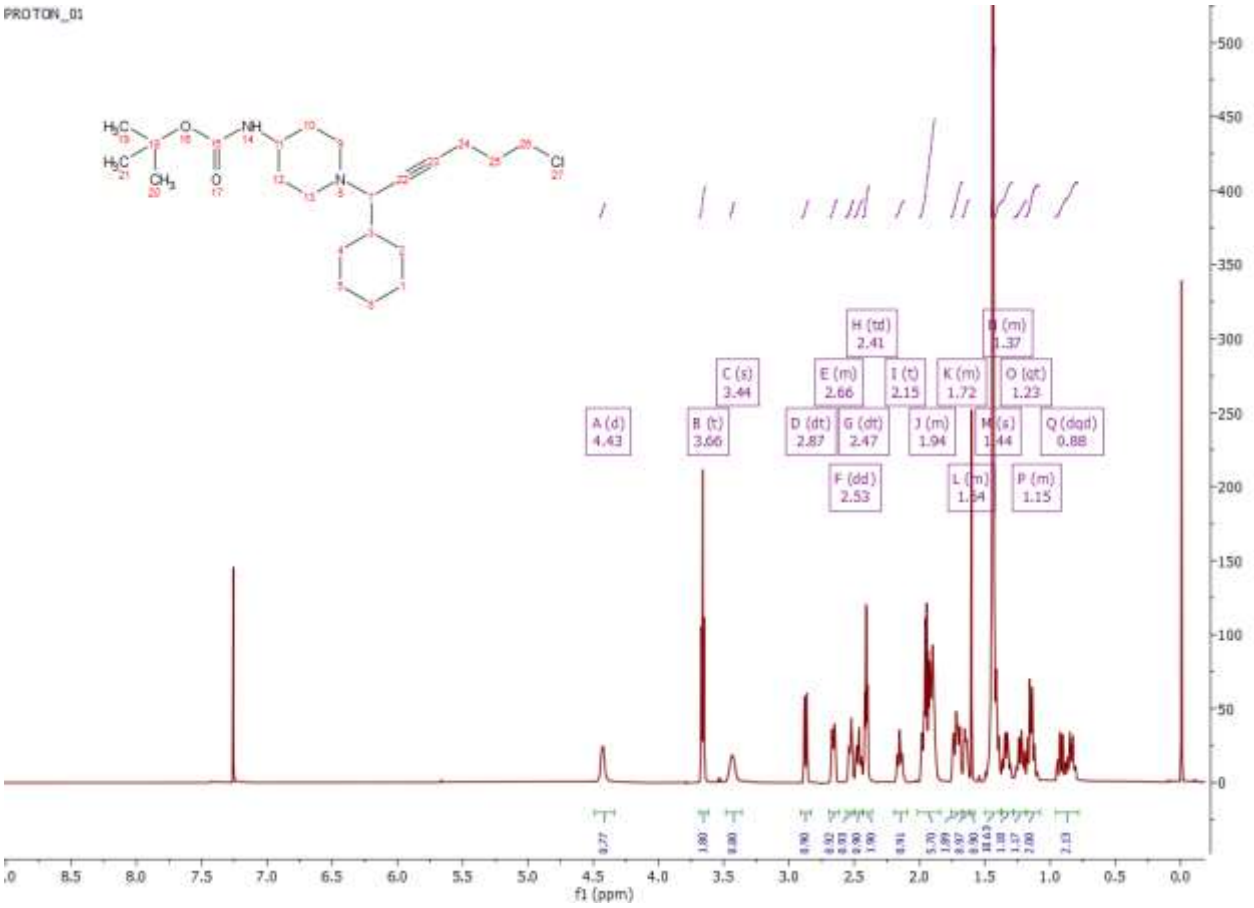


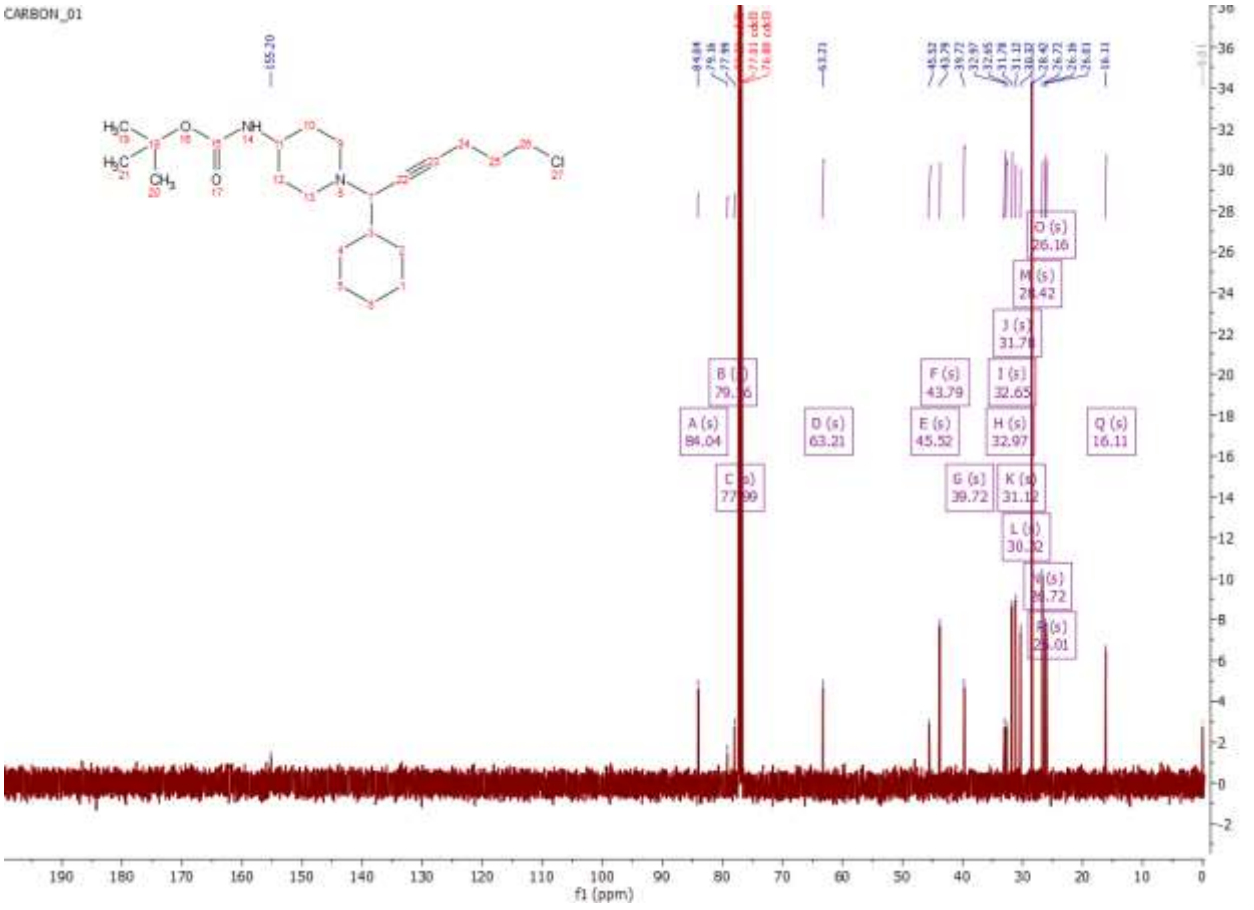
^{1}H NMR and ^{13}C NMR for 1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)-N,N-dimethylpiperidin-4-amine (23)





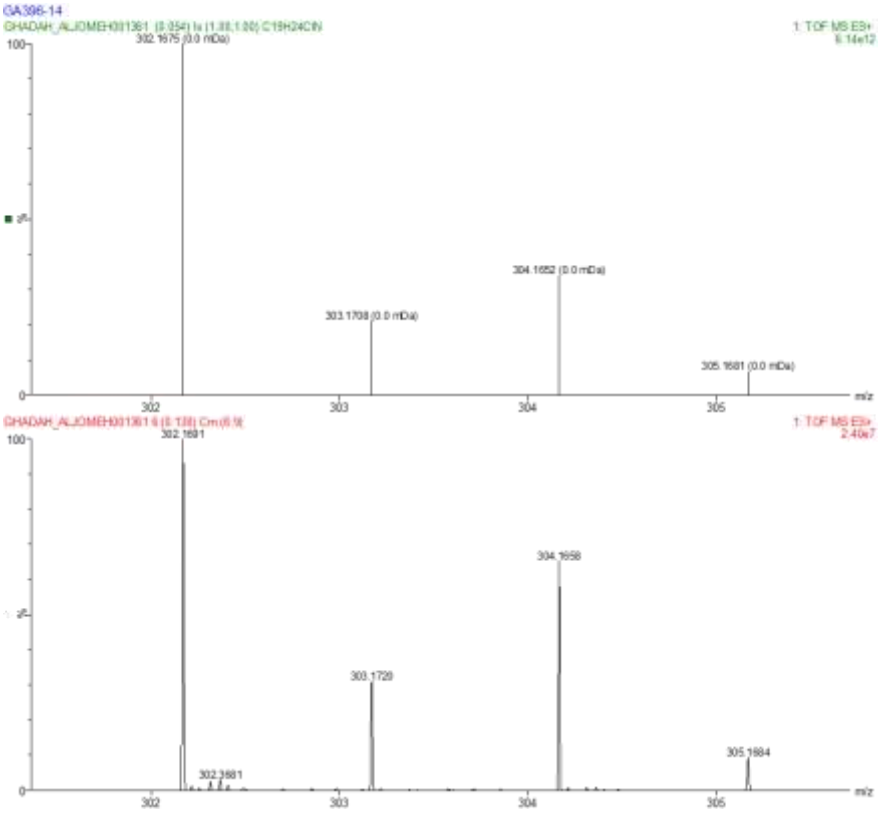
^{1}H NMR and ^{13}C NMR for tert-butyl N-[1-(6-chloro-1-cyclohexylhex-2-yn-1-yl) piperidin-4-yl]carbamate (24)



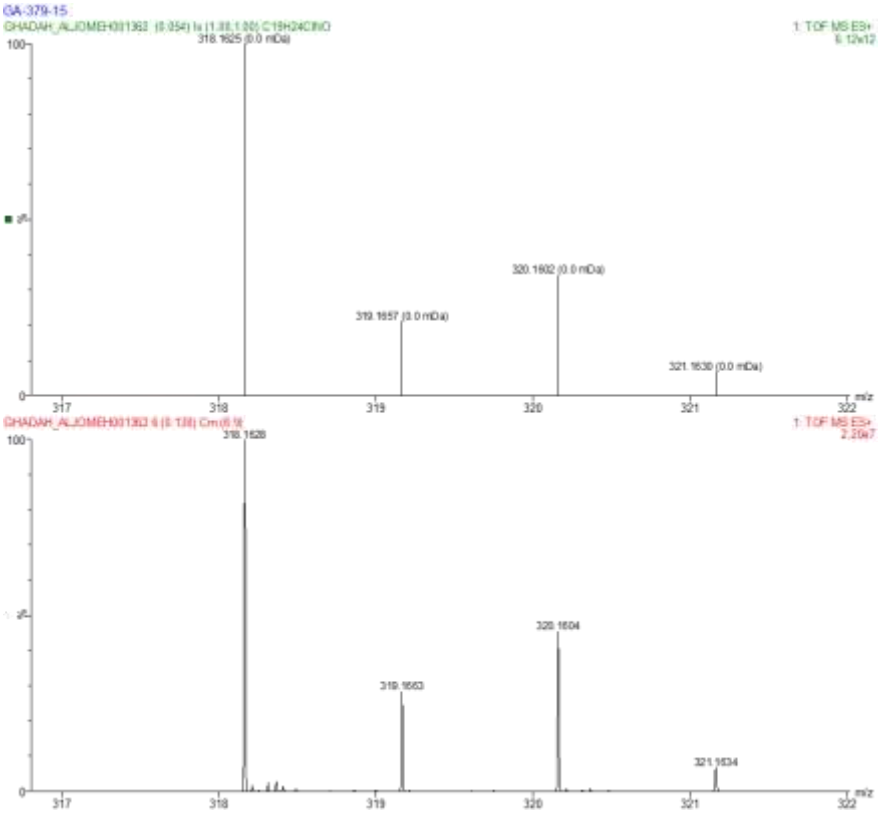


ESI-MS Data

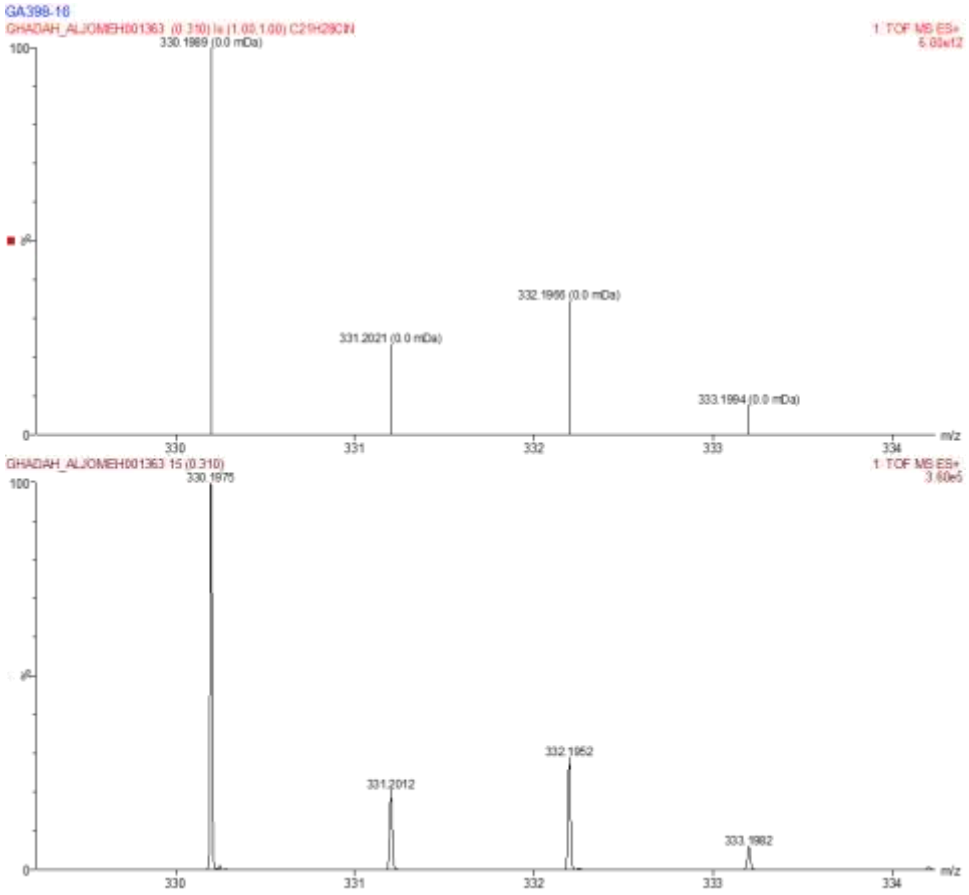
1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]pyrrolidine(14)



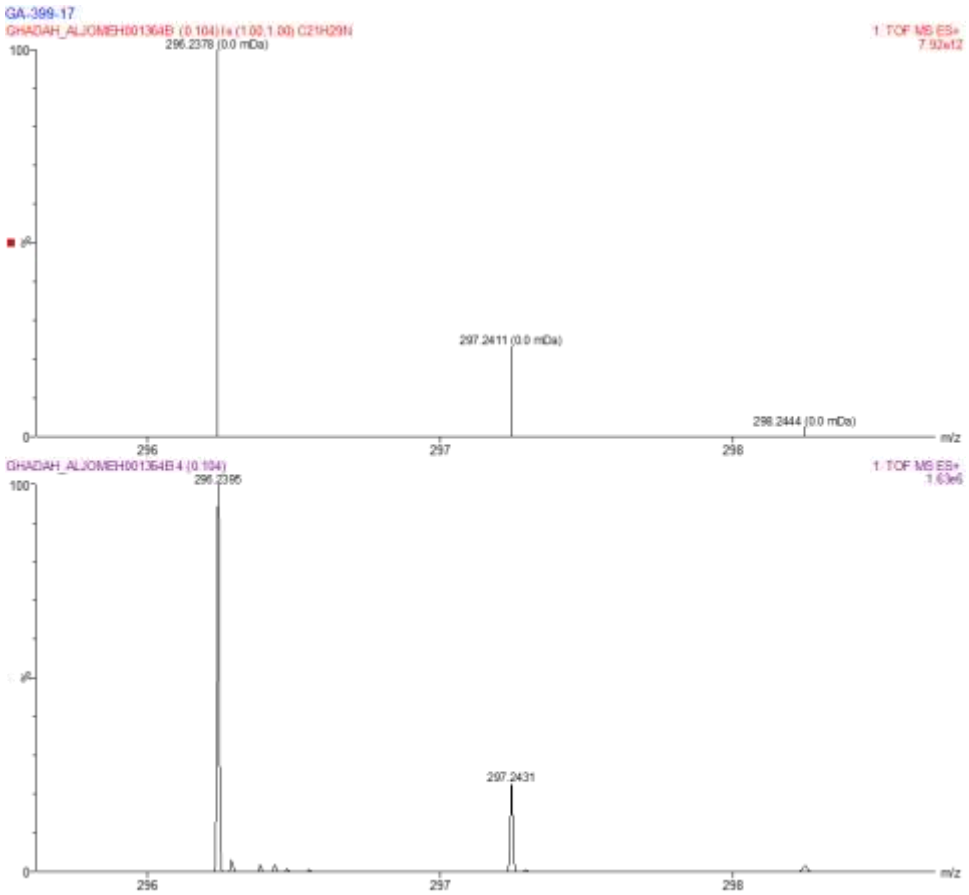
4-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl]morpholine (15)



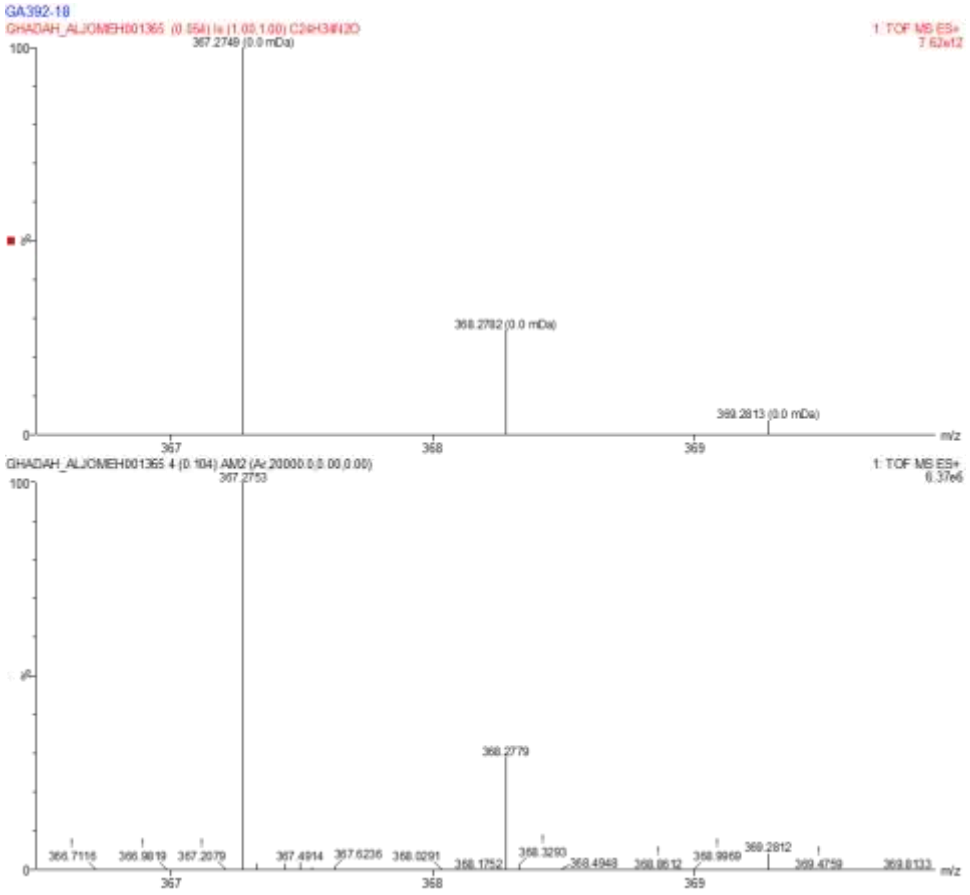
1-[3-(4-chlorophenyl)-1-cyclohexylprop-2-yn-1-yl] azepane (16)



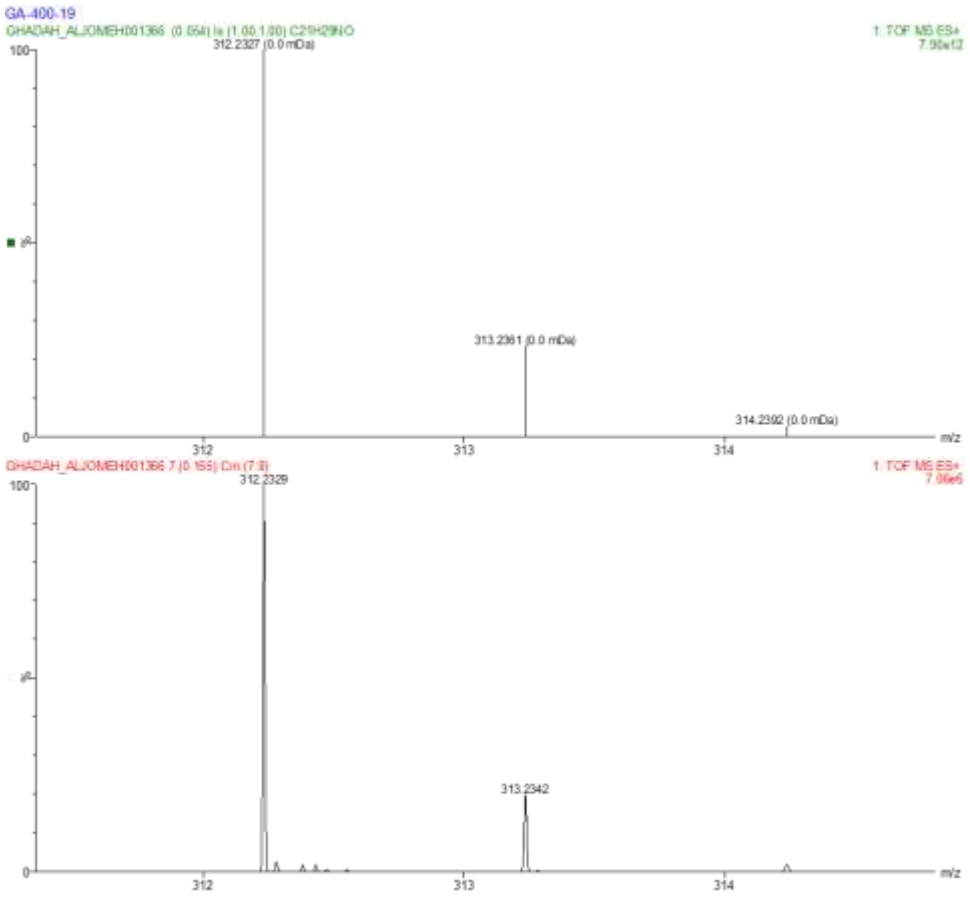
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl]pyrrolidine (17)



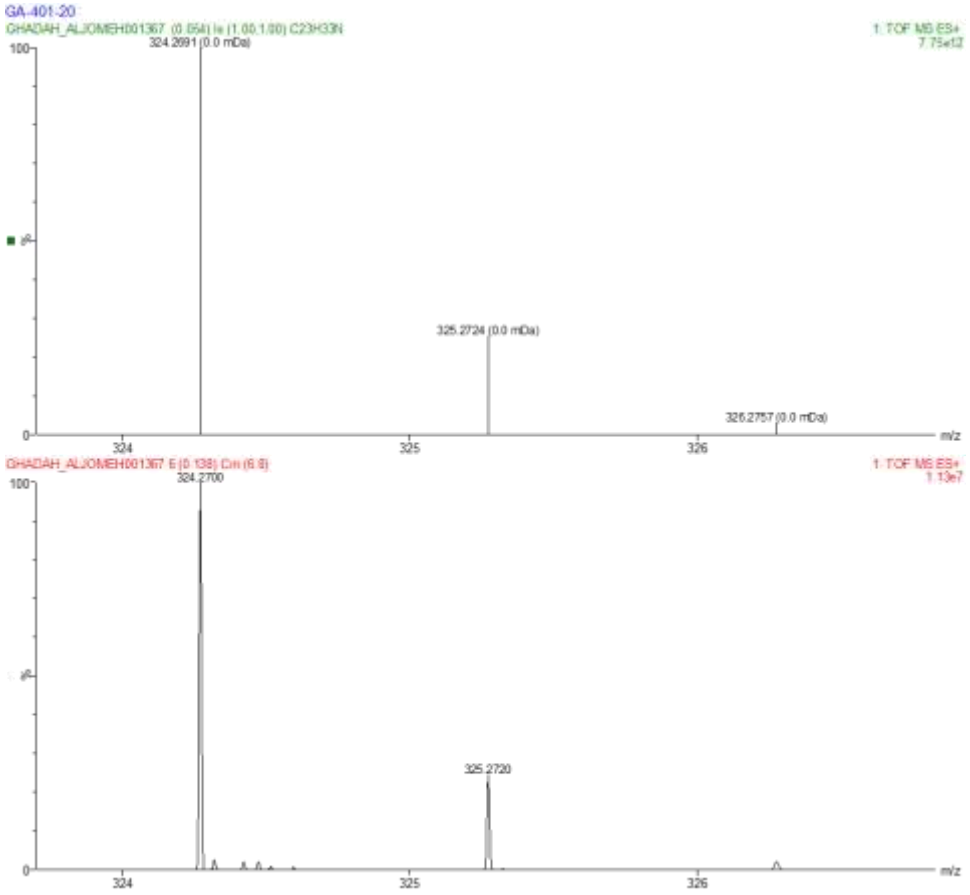
4-{1-[1-cyclohexyl-3-(4-phenylprop-2-yn-1-yl]piperidin-4-yl}morpholine (18)



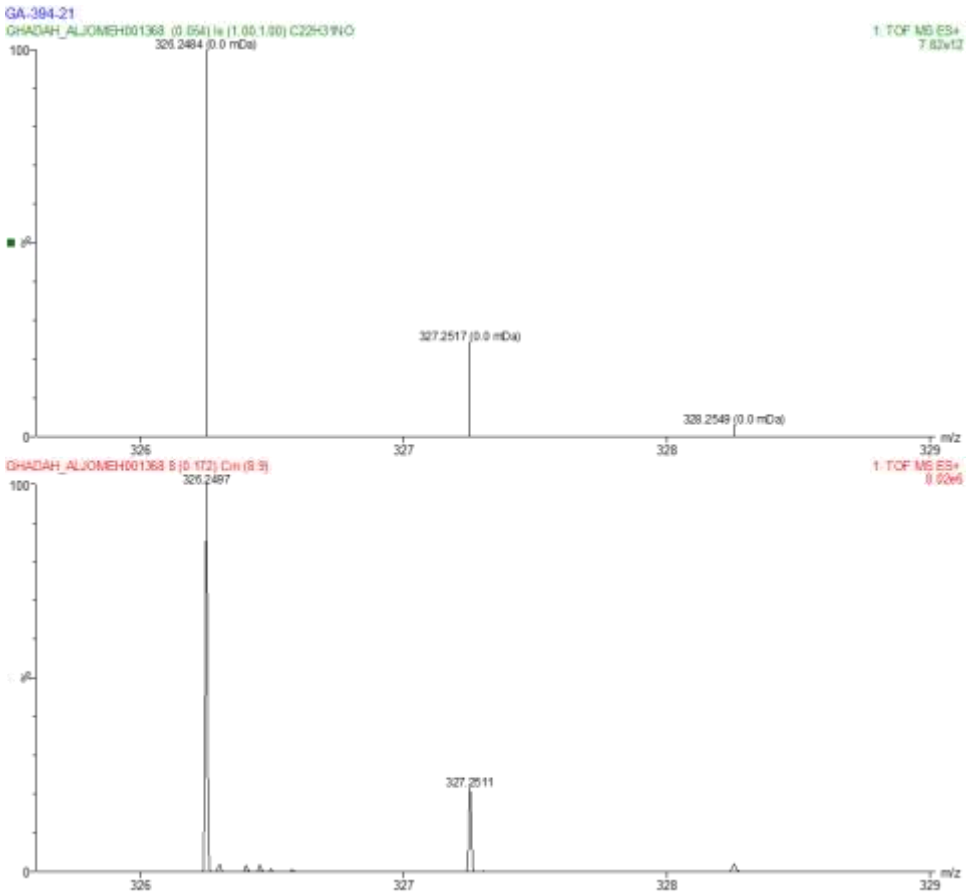
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] morpholine (19)



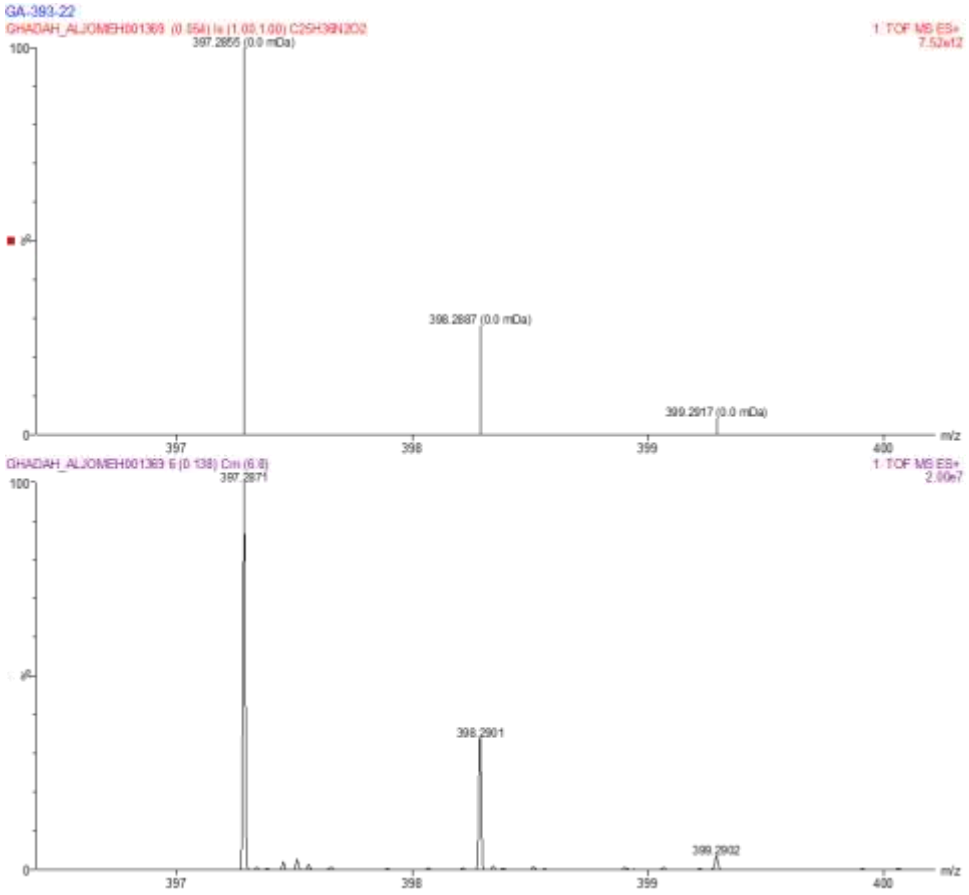
1-[1-cyclohexyl-3-(4-ethylphenyl)prop-2-yn-1-yl] azepane (20)



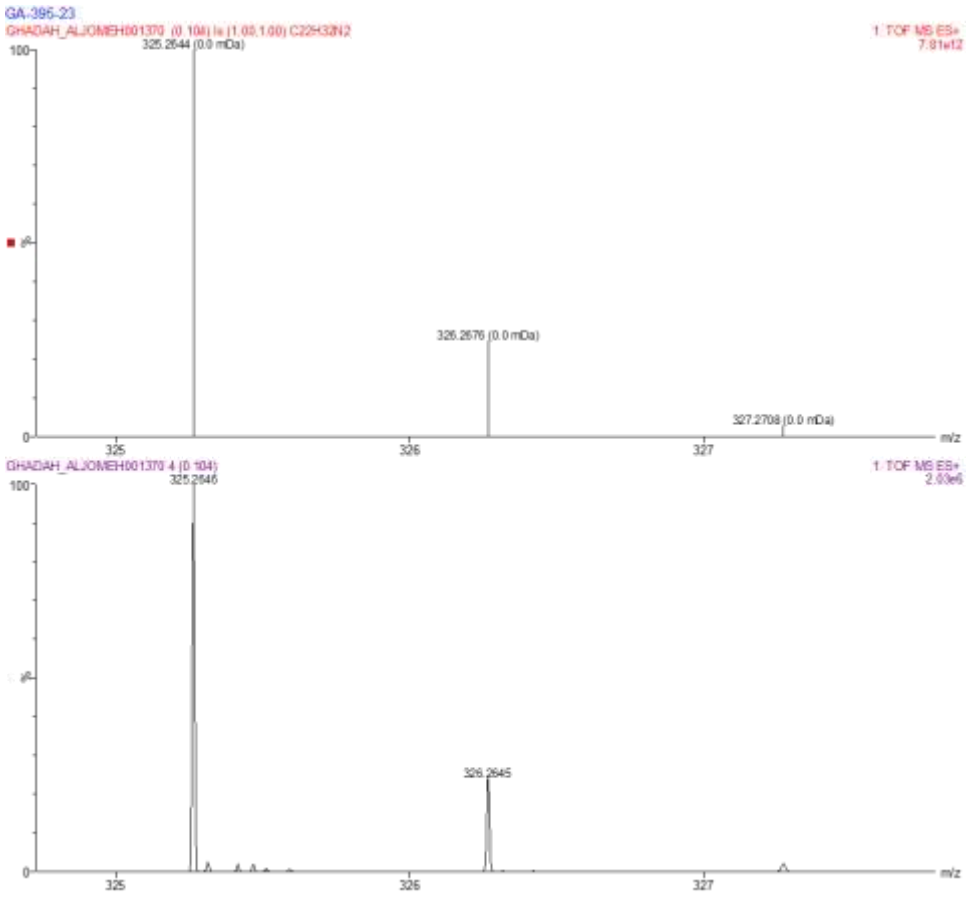
1-[1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-yl] azepane (21)



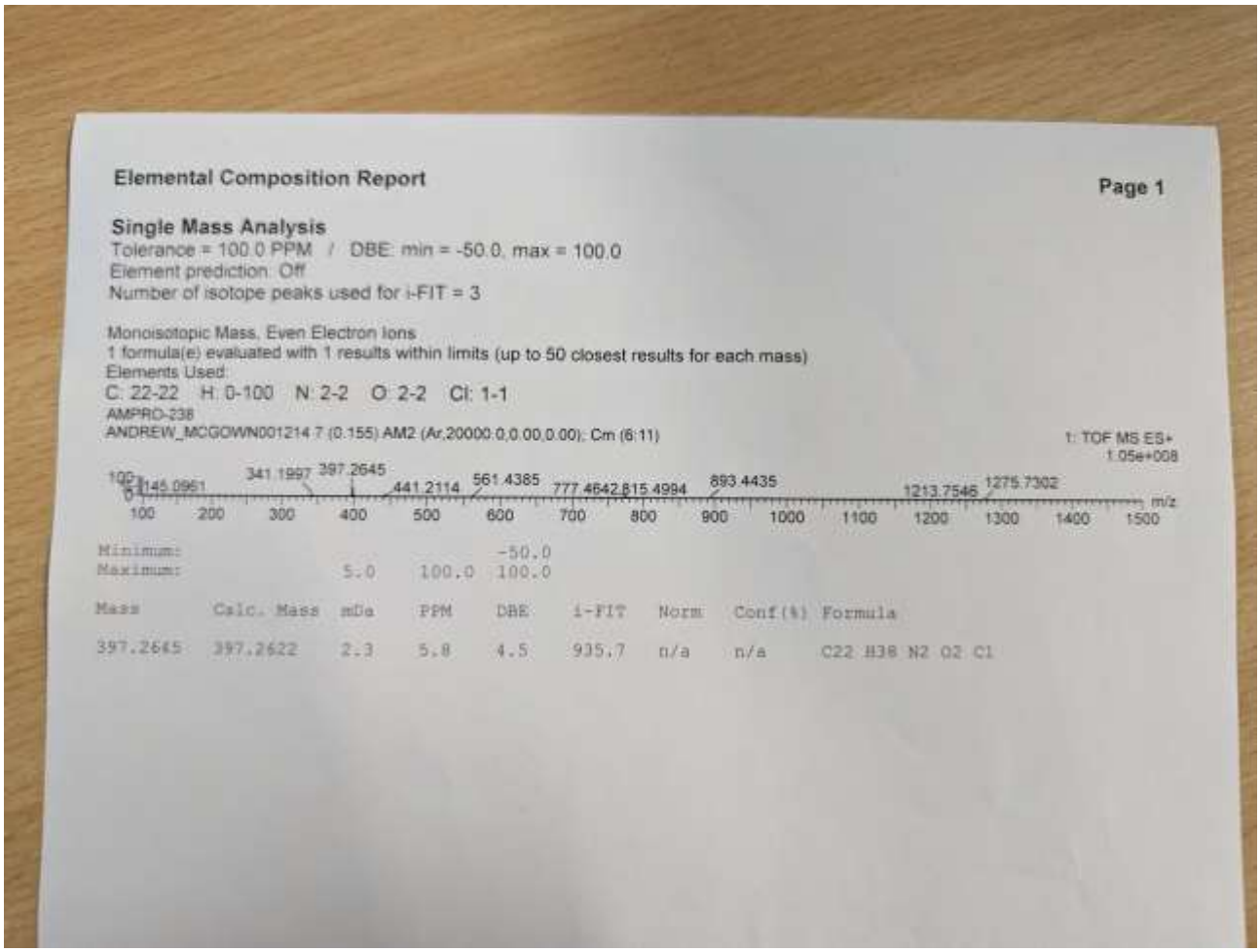
tret-butyl N-[1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) piperidin-4-yl]carbamate (22)



1-(1-cyclohexyl-3-phenylprop-2-yn-1-yl)-N,N-dimethylpiperidin-4-amine (23)



tert-butyl N-[1-(6-chloro-1-cyclohexylhex-2-yn-1-yl) piperidin-4-yl]carbamate (**24**)



Elemental Composition Report

Page 1

Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -50.0, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 22-22 H: 0-100 N: 2-2 O: 2-2 Cl: 1-1
AMPRO-238
ANDREW_MCGOWN001214 7 (0.155) AM2 (Ar,20000.0,0.00,0.00); Cm (6:11)

1: TOF MS ES+
1.05e+008

Minimum:				-50.0				
Maximum:		5.0	100.0	100.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
397.2645	397.2622	2.3	5.8	4.5	935.7	n/a	n/a	C22 H38 N2 O2 Cl