Supporting information

A practical route to Acridines framework from 2-nitrobenzaldehyde and cyclohexenone derivatives via aldol reaction and reductive cyclization

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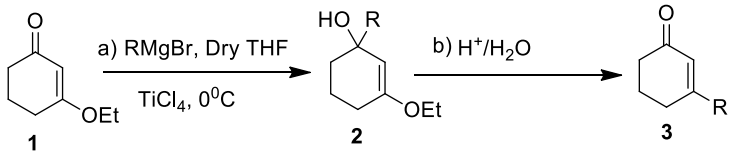
A. General methods:

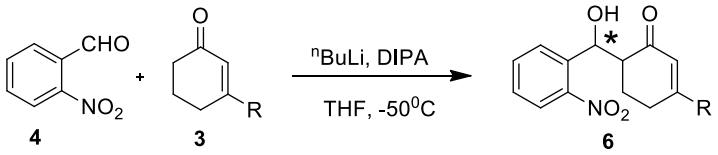
All reactions were performed under an atmosphere of nitrogen in oven-dried flasks. TLC was performed using 100-200 mesh silica gel plates. Column chromatography was performed using silica gel 100−200 mesh. TLC plates were visualized under UV light at 254 nm and iodine vapour. ^{1}H NMR spectra were recorded on Bruker 400 MHz spectrometer and ^{13}C NMR spectra were recorded on a Bruker 100 MHz spectrometer using $CDCl_3$ as a solvent with TMS as the internal standard. The chemical shifts value at 7.26 and 77.0 ppm are referenced for $CDCl_3$ solvent. The data of HRMS was carried out on a high-resolution mass spectrometer instrument. Melting points were measured with a Lab X India digital melting point apparatus and are uncorrected. X-ray structural analysis was conducted Bruker D8-Venture X-ray analysis instrument. All the commercial reagents were used from a different commercial source. DIPA, triethylamine, and ethanol were purified by using the traditional drying procedure.

B. Typical procedure for the synthesis of product 3:



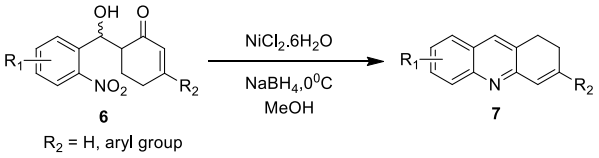
An oven-dry 50ml Round bottom flask was charged with dry Mg turnings (9.0mmol) and solvent (0.25N) in an inert atmosphere. A pinch of molecular iodine was then added to the solution which turned brown immediately. After that, bromobenzene (3.0mmol) in solvent was added slowly to the reaction mixture and continued stirring for 30min to prepare the Grignard reagent. Another dry 50mL round bottom flask was charged with compound 1 (1.0mmol) insolvent and $TiCl_4$ (10.0mmol%) was added at $0^{\circ}C$.Then the prepared Grignard reagent was added to the solution and the resulting mixture was stirred for an hour. The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis which was performed on silica gel 60 F_{254}. After completion of the reaction, the reaction mixture was extracted with 10% HCl solution and EtOAc (3 × 50 mL). The combined organic layer was washed with brine solution and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: pet ether/EtOAc = 3:1) to yield the desired product **3a** as a yellow solid.

General procedure for Aldol reaction between cyclohexenone and 2-nitro benzaldehyde derivatives 6:



An oven-dry 50ml Round bottom flask was charged with solvent (0.5N) and DIPA (2.0 mmol) and stirred for 10-15min at -50°C.Then base ^{n}BuLi (2.25mmol) was added to the solution and continued stirring for 30min. After that, compound **3** in THF solvent was added to the resulting mixture and the mixture was stirred for another 30min. Again the compound **4** (1.0mmol) in dry THF solvent was added and the resulting reaction mixture was continued stirring for an hour at -50 to 0°C. After completion of the reaction, the reaction mixture was extracted with sodium bicarbonate solution and Ethar (3 × 50 ml) The combined organic layer was washed with brine solution and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: pet ether/EtOAc = 3:1) to yield the desired product **6a** as a yellow solid.

Typical procedure for the synthesis of product 7:

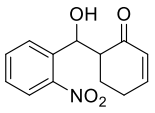


In a dry 25 ml, round bottom flask $NiCl_2.6H_2O$ (970mg, 10.0mmole) in methanol was charged at 0°C temperature and after 5-10 min $NaBH_4$ (169mg, 11.0mmole)was added to the solution. Then the reaction mixture was stirred at 0°C for half an hour. After that, the compound **8a** (100mg, 1.0mmole) which was dissolved in methanol, was added to the reaction mixture and the resulting mixture was stirred at 0°C to room temperature The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis which was performed on silica gel 60 F_{254}. After completion of the reaction, the reaction mixture was extracted with EtOAc (3 × 50 mL) and a short filtration column was performed. The combined organic layer was washed with brine solution and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: pet ether/EtOAc = 3:1) to yield the desired product **7a** as a yellow solid.

C. X-ray crystallographic data :

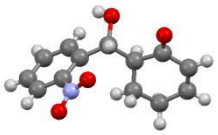
Single crystal X-ray Diffraction data were collected on Bruker APEX II diffractometer using monochromated Mo K_α radiation (λ = 0.71073 Å) at 100 K using an Oxford cryostream low-temperature device. Unit cell measurements, data integration, scaling, and absorption corrections for the crystals were done with Bruker APEXII software.[1] Data reduction was carried out with the Bruker SAINT suite.[2] Absorption correction was performed by multi-scan method, implemented in SADABS[3]. The structure was solved by direct methods using SIR 2014.[4] The crystal structure refinement was done in the program package OLEX2[5] and all non-hydrogen atoms were refined anisotropically by full-matrix least-squares calculations based on F^2 with SHELXL-2016[6], hydrogen atoms were included in calculated positions as riding atoms. The refinement of data has been performed with complete molecules in disorder (71:29). Additionally, restraints such as SIMU and RIGU have been implemented during structure refinement, to have a better-fitted model. The absolute structure could not be determined as the Flack parameter for the data is unreliable due to the presence of light scattering atoms in the molecule. The PARST[7] was used for crystal structure analysis and Mercury 4.0[8] was used for drawing molecular and crystal structure.

Table 1 : Checkcif data for 6a



6a

≡



CCDC NO: 2119316

Bond precision: C-C = 0.0071 A Wavelength=0.71073

Cell: a=8.283(4) b=8.309(4) c=9.834(5)
alpha=81.847(12) beta=84.967(12) gamma=61.229(12)

Temperature: 292 K

	Calculated	Reported
Volume	587.1(5)	587.1(5)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C13 H13 N O4	?
Sum formula	C13 H13 N O4	C13 H13 N O4
Mr	247.24	247.24

Dx,g cm-3	1.399	1.399
Z	2	2
Mu (mm-1)	0.105	0.105
F000	260.0	260.0
F000'	260.15	
h,k,lmax	11,11,13	10,11,13
Nref	2933	2803
Tmin,Tmax	0.989,0.996	
Tmin'	0.989	

Correction method= Not given

Data completeness= 0.956 Theta(max)= 28.357

R(reflections)= 0.1125(1662) wR2(reflections)= 0.3291(2803)

S = 1.043 Npar= 164

Table 2 : Checkcif data for 7b

CCDC NO 2048682

Bond precision: = 0.0000 A Wavelength=0.71073

Cell: a=7.5986(13) b=6.1021(10) c=14.110(2)
alpha=90 beta=96.293(6) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	650.30(18)	650.30(18)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C19 H15 N	C19 H15 N
Sum formula	C19 H15 N	C19 H15 N
Mr	257.32	257.32
Dx,g cm-3	1.314	1.314
Z	2	2
Mu (mm-1)	0.076	0.076
F000	272.0	272.0
F000'	272.09	
h,k,lmax	10,8,18	10,8,18
Nref	3213[1755]	3192
Tmin,Tmax	0.980,0.988	0.617,0.746
Tmin'	0.964	

Correction method= # Reported T Limits: Tmin=0.617 Tmax=0.746 AbsCorr = MULTI-SCAN

Data completeness= 1.82/0.99 Theta(max)= 28.273

R(reflections)= 0.0636(2007) wR2(reflections)= 0.1074(3192)

S = 1.032 Npar= 363

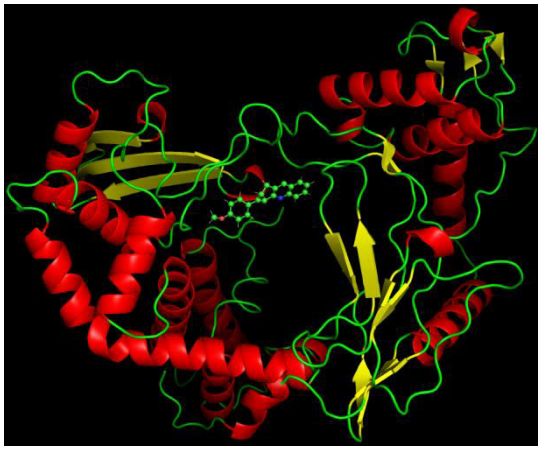
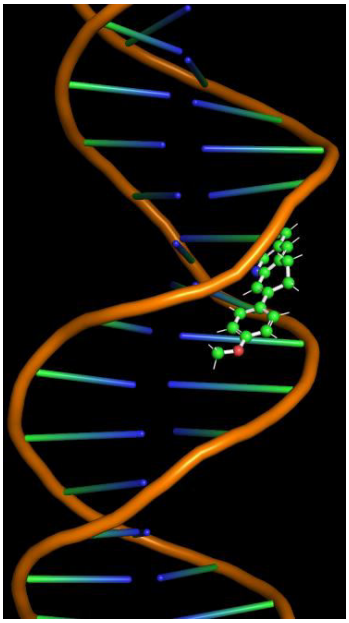
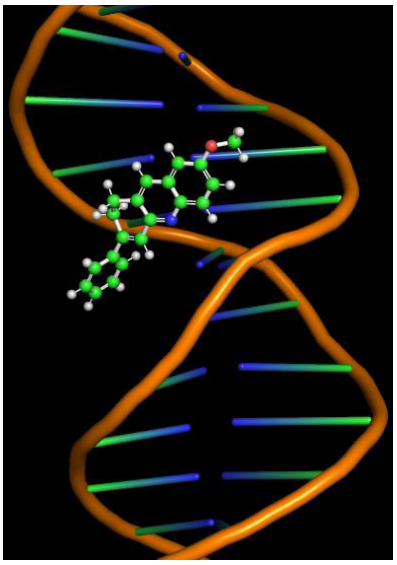
References:

1. Bruker (**2014**) APEX2, version 2014.11-0, Bruker AXS Inc., Madison, Wisconsin, USA.
2. Bruker (**2013**) SAINT, version V8.34A, Bruker AXS Inc., Madison, Wisconsin, USA.
3. Bruker (**2014**) SADABS, version 2014/5, Bruker AXS Inc., Madison, Wisconsin, USA.
4. Gruene, T.; Hahn, H. W.; Luebben, A. V.; Meilleur, F.; Sheldrick, G. M. Refinement of macromolecular structures against neutron data with *SHELXL2013*. *J. Appl. Crystallogr.*2014, *47* (1), 462–466.
5. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J. A. K.; Puschmann, H. OLEX2: a complete structure solution, refinement and analysis program. J. Appl. Crystallogr.2009, 42, 339-341.
6. Sheldrick, G. M. Crystal structure refinement with *SHELXL*. *Acta Cryst.*2015, C*71*, 3−8.
7. Nardelli, M. *PARST*95 - an update to *PARST*: a system of Fortran routines for calculating molecular structure parameters from the results of crystal structure analyses. *J. Appl. Crystallogr.*1995, *28*, 659.
8. Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T. A.; McCabe, P.; Pidcock, E.; Platings, M.; Shields, G. P.; Stevens, J. S.; Towler, M.; Wood, P. A. *Mercury 4.0*: from visualization to analysis, design and prediction. *J. Appl. Crystallogr.*2020, 5*3* (1), 226–235.

D. The details of docking study:

Method:

To check how the reported derivatives interact with DNA and also to check topoisomerase inhibitory activity we have used molecular docking method and calculate the binding affinity. X-ray crystal structure of the human topoisomerase I-DNA complex (PDB code: 1A35, resolution: 2.50Å) [M.R. Redinbo, L. Stewart, P. Kuhn, J. J. Champoux, W. G. Hol, crystal structures of human topoisomerase I in covalent and noncovalent complexes with DNA. SCIENCE, 279, 1504, 1998] has been downloaded from protein data bank (www.rcsb.org) to use as a model system for docking. The enzyme-DNA complex is used for both enzyme-derivatives and DNA-derivatives docking. To build the optimized 3D structure of the three derivatives (molecules **7d**, **7j** and **7m**) Avogadro software package [Marcus D Hanwell, Donald E Curtis, David C Lonie, Tim Vandermeersch, Eva Zurek and Geoffrey R Hutchison "Avogadro: An advanced semantic chemical editor, visualization, and analysis platform" Journal of Cheminformatics 2012, 4:17] has been used. AutoDock Vina [Trott, O.; Olson, A. J. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J. Comput. Chem. 2010, 31, 455], was used for docking and calculating the binding affinity of the best binding pose of the ligand. Three independent docking runs are performed for each complex.

	Topoisomerase I	DNA
7d	a) 	e) 
7j	b) 	f) 

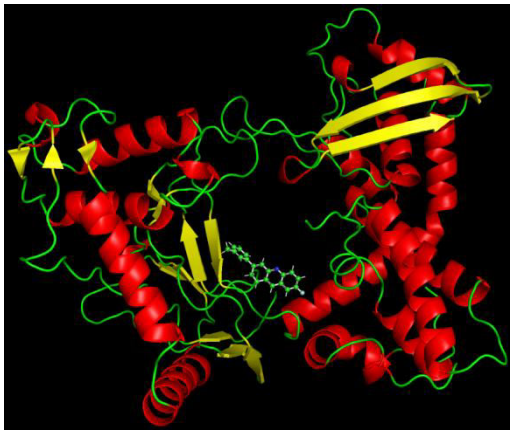
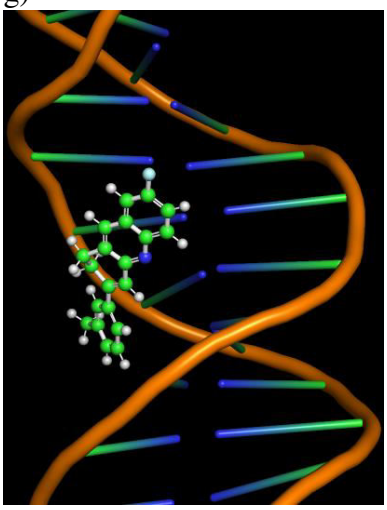
7m	c) 	g) 

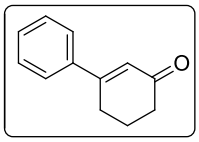
Figure: (**a-c)** Binding of derivatives **7d**, **7j** and **7m** at the topoisomerase I binding site. The derivatives molecules are show in ball and stick, enzyme is shown in cartoon.(**f-g)** Binding \ofderivatives **7d**, **7j** and **7m** at the DNA major and minor grooves.

Table 3:

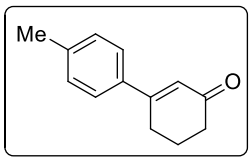
Binding affinity calculated from AutoDock Vina. Three independent dockings are performed and standard errors are calculated.

Arcidine derivatives	Average binding affinity (kcal/mol)	
	Topoisomerase I	DNA
7d	-6.05 ± 0.43	-6.07 ± 0.22
7j	-5.7 ± 0.2	-6.07 ± 0.27
7m	-6.0 ± 0.15	-6.5 ± 0.4

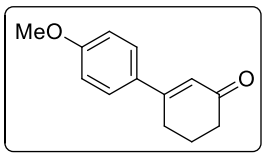
E. Analytical data:



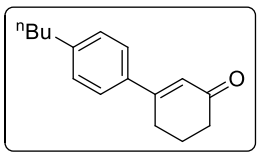
5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3a): Yellow solid(550mg, yield 87%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.47-7.45(m, 2H), 7.34(t, J=3.2Hz, 2H), 6.35(s, 1H), 2.70(t, J=5.6Hz, 2H), 2.41(t, J=6.0Hz, 2H), 2.11-2.05(m, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 199.9, 159.8, 138.8,130.0, 128.7, 126.1, 125.4, 37.2, 28.1, 22.8. HRMS ESI (m/z): Calculated for $C_{12}H_{12}O$ $[M+ H]^+$: 173.0922, found 173.09928.



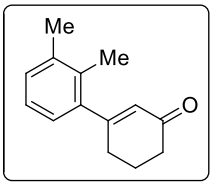
4'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3b): Yellow solid(540 mg, yield 85%) **^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.35(t, J=8.2Hz, 2H), 7.12 (d, J=7.9Hz, 1H), 6.32(s, 1H), 2.68-2.65(m, 2H), 2.38(t, J=6.2Hz, 2H), 2.29(s, 3H), 2.08-2.02(m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.0, 159.7, 140.4, 135.8, 129.5, 126.0, 124.6, 37.2, 28.0, 22.8, 21.3. HRMS ESI (m/z): Calculated for $C_{13}H_{14}O$ $[M+ H]^+$: 187.1078, found: 187.1086.



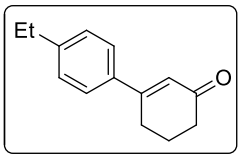
4'-methoxy-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3c): Yellow solid(500mg, yield 72%). **^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.53-7.50(m, 2H), 6.94-6.91(m, 2H), 6.39(s, 1H), 3.84(s, 3H), 2.77-2.72(m, 2H), 2.46(t, J=8.4Hz, 2H), 2.18-2.11(m, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 199.9, 159.8, 159.7, 140.3, 129.7, 125.6, 118.5, 115.4, 111.7, 55.3, 37.2, 28.2, 22.8. HRMS ESI (m/z): Calculated for $C_{13}H_{14}O_2$ $[M+ H]^+$: 203.1027, found: 203.1030.



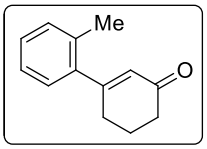
4'-butyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3d): Yellow liquid(510ml, yield 86%). **^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.46(d, J=8.1Hz, 2H), 7.23(t, J=8.0Hz, 2H), 6.42(s, 1H), 2.76(t, J=5.8Hz, 2H), 2.63(t, J=7.6Hz, 2H), 2.47(t, J=6.5Hz, 2H), 2.17-2.11(m, 2H), 1.64-1.57(m, 2H), 1.38-1.25(m, 2H), 0.93(t, J=7.2Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.1, 159.8, 145.4, 135.9, 128.8, 126.0, 124.6, 37.2, 35.4, 33.4, 28.0, 22.8, 22.3, 13.9. HRMS ESI (m/z): Calculated for $C_{16}H_{20}O$ $[M+ H]^+$: 229.1548, found: 229.1560.



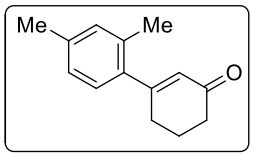
2', 3'-dimethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3e): Yellow solid(480mg, yield 83%).**^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.15-7.09(m, 2H), 6.93(d, J=6.7Hz, 1H), 5.96(s, 1H), 2.56(t, J=5.4Hz, 2H), 2.50(t, J=6.7Hz, 2H), 2.30(s, 3H), 2.16(t, J=7.5, 2H), 1.57(s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 199.6, 164.6, 141.1, 137.5, 132.3, 129.8, 128.6, 125.6, 124.5, 37.3, 31.7, 23.1, 20.3, 16.7. Calculated for $C_{14}H_{16}O$ $[M+ H]^+$: 201.1235, found: 201.1239.



4'-ethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3f): Yellow liquid(570ml, yield 78%)**. ^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.47(t, J=8.1Hz, 2H), 7.25(t, J=8.1Hz, 2H), 6.42(s, 1H), 2.76(t, J=6.0Hz,2H),2.70-2.64(m, 2H), 2.47(t, J=6.5Hz, 2H),2.17-2.11(m, 2H), 1.25(t, J=7.6Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.0, 159.8, 146.7, 136.0, 128.3, 126.1, 124.7, 37.2, 28.6, 28.0, 22.8, 15.3. . Calculated for $C_{14}H_{16}O$ $[M+ H]^+$: 201.1235, found: 201.1241.

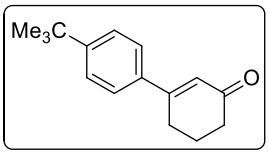


2'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3g): Yellow solid(500mg, yield 80%). **^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.26-7.18(m,3H), 7.10(d, J=7.2Hz, 1H),5.98(s, 1H), 2.59(t, J=5.7Hz, 2H), 2.50(t, J=6.7Hz, 2H), 2.30(s, 3H),2.19-2.12(m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 199.6, 163.6, 140.7, 133.9, 130.6, 128.6, 128.3, 126.9, 125.9, 37.3, 31.2, 23.1, 20.0. Calculated for $C_{13}H_{14}O$ $[M+ H]^+$: 187.1078, found: 187.1080.

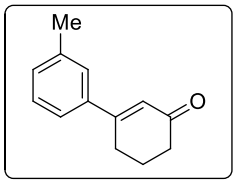


2',4'-dimethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3h): Yellow solid(530mg, yield 86%).**^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.14(s, 2H), 7.05(s, 1H), 6.39(s, 1H), 2.75(t,

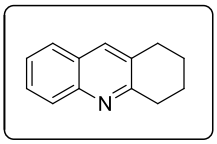
J=5.6Hz, 2H), 2.47(t, J=7.2Hz, 2H), 2.34(s, 6H), 2.16-2.12(m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.3, 160.7, 156.1, 138.3, 131.7, 125.1, 124.0, 122.0, 113.1, 37.2, 28.2, 22.8, 21.3, 21.2. Calculated for $C_{14}H_{16}O$ [M+ H]$^+$: 201.1235, found: 201.1237.



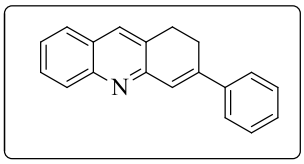
4'-(tert-butyl)-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3i): Yellow liquid(560ml, yield 87%).**^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.49(t, J=6.1Hz, 2H), 7.42(t, J=6.4Hz, 2H), 6.44(s, 1H), 2.77(t, J=5.4Hz, 2H), 2.48(t, J=6.6Hz, 2H), 2.17-2.12(m, 2H), 1.33(s, 9H).). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.1, 159.7, 153.6, 135.7, 126.3, 125.9, 125.7, 124.7, 114.8, 37.2, 34.8, 31.5, 31.1, 27.9, 22.8. Calculated for $C_{16}H_{20}O$ [M+ H]$^+$: 229.1548, found: 229.1550.



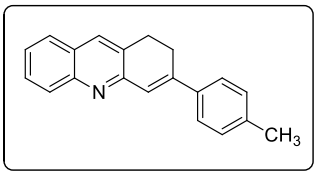
3'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3j): Yellow solid(550mg, yield 79%).**^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 7.27-7.24(m, 3H), 7.15(d, J=7.2Hz, 1H), 6.33(s, 1H), 2.69(t, J=6.1Hz, 2H), 2.41(t, J=7.0Hz, 2H), 2.31(s, 3H), 2.11-2.04(m, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 200.0, 160.0, 138.8, 138.4, 130.7, 128.6, 126.8, 125.3, 123.2, 37.3, 28.2, 22.8, 21.5. Calculated for $C_{13}H_{14}O$ [M+ H]$^+$: 187.1078, found: 187.1084.



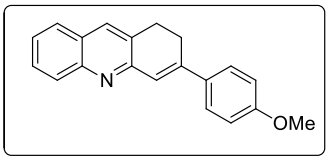
1,2,3,4-tetrahydroacridine(7a): Yellow solid, (120 mg, yield 67%), mp. 85-95˚C.
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.89(d, J=8.4Hz, 1H), 7.72(s, 1H), 7.62(d, J=8.0Hz, 1H), 7.54-7.50(m, 1H), 7.35(t, j=7.2Hz, 1H), 3.05(t, J=6.4Hz, 2H), 2.90(t, J=6.4Hz, 2H), 1.95-1.89(m, 2H), 1.85-1.79(m, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 159.3, 154.1, 147.1, 137.1,135.1,133.0, 129.9, 126.9,125.9, 33.4, 29.2, 27.4, 23.3. **HRMS ESI** (m/z): Calculated for $C_{13}H_{14}N$ [M+ H]$^+$: 184.1082, found:.184.1163.



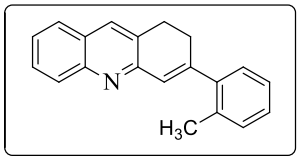
3-phenyl-1,2-dihydroacridine (7b) : Yellow solid, (117 mg, yield 84%), mp 80-90˚C. **^{1}H NMR** (400MHz, $CDCl_3$) δ (ppm) : 7.94 (d, *J*=8.4Hz, 1H), 7.76 (s, 1H), 7.64 (d, J=8.08Hz, 1H), 7.59-7.52 (m, 3H), 7.39-7.33 (m, 3H), 7.27 (t, *J*=7.2Hz, 1H), 3.11 (t, *J*=7.6Hz, 2H), 2.83 (t, J=7.8Hz, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm):154.8, 147.6, 146.7, 140.0, 132.6, 129.0, 132.6, 128.8, 128.7, 128.5, 127.8, 127.0, 126.1, 125.9, 125.6, 28.0, 26.2. **HRMS ESI** (m/z): Calculated for $C_{19}H_{16}N$ [M+ H]$^+$: 258.1238, found: 258.1297.



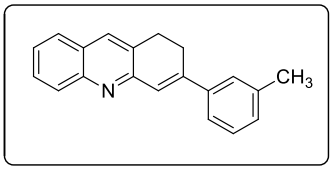
3-(p-tolyl)-1,2-dihydroacridine (7c): Yellow solid, (125 mg, yield 62%), mp 115-120˚C. **^{1}H NMR** (400 MHz,$CDCl_3$) δ (ppm): 7.99 (d, J=8.4Hz, 1H), 7.82 (s, 1H), 7.70 (d, J=8.0Hz, 1H), 7.63-7.54 (m, 2H), 7.43 (t, J=7.2Hz, 1H), 7.26-7.22 (m, 4H), 3.17 (t, J=7.6Hz, 2H), 2.88 (t, J=7.6Hz, 2H), 2.39 (s, 3H).**^{13}C NMR** (100 MHz,$CDCl_3$) δ (ppm): 158.7, 154.7, 147.4, 146.6, 145.4, 139.9, 135.0, 132.6, 129.0, 128.7, 128.6, 126.9, 125.5, 41.0, 40.4, 30.3, 27.9, 26.1. **HRMS ESI** (m/z): Calculated for $C_{20}H_{17}N$ [M+ H]$^+$: 272.1395, found : 272.1459.



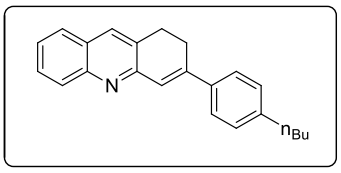
3-(4-methoxyphenyl)-1,2-dihydroacridine (7d): White solid (144 mg, yield 65%), mp 125-130˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.99 (d, J=8.4Hz, 1H), 7.78 (s, 1H), 7.68 (s, J=8.0Hz, 1H), 7.61-7.58 (m, 3H), 7.41 (t, J=7.6Hz, 1H), 7.19 (s, 1H), 6.93 (d, J=8.4Hz, 2H), 3.83 (s, 3H), 3.14 (t, J=7.6Hz, 2H), 2.85 (t, J=7.6Hz, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 160.1, 155.0, 147.3, 146.5, 132.6, 132.3, 129.0, 128.7, 128.4, 127.7, 126.9, 125.8, 124.1, 114.1, 55.4, 27.9, 26.1. **HRMS ESI** (m/z): Calculated for $C_{20}H_{18}NO$ [M+ H]$^+$: 288.1344, found: 288.1419.



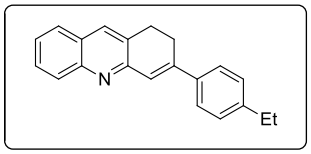
3-(o-tolyl)-1,2-dihydroacridine (7e): Yellow solid, (150 mg, yield 62%), m.p 90-95˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, *J*=7.6Hz, 1H), 7.87 (d, J=22.4Hz, 1H), 7.72 (t, J=7.6Hz, 1H), 7.65-7.59 (m, 1H), 7.48-7.43 (m, 1H), 7.25-7.15 (m, 4H), 6.81 (s, 1H), 3.43 (d, J=14Hz, 1H), 3.17 (t, J=7.2Hz, 2H) 2.72 (t, J=7.6Hz, 1H), 2.41 (d, J=5.6, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 150.7, 147.2, 142.4, 137.4, 133.4, 132.9, 129.3, 128.9, 128.8, 128.6, 128.2, 127.8, 127.0, 125.9, 125.7, 125.6, 29.5, 28.2, 20.6, 17.1. **HRMS ESI** (m/z): Calculated for $C_{20}H_{18}N$ [M+ H]$^+$: 272.1395 , found: 272.1569.



3-(m-tolyl)-1, 2-dihydroacridine (7f): Yellow solid, (157 mg, yield 43%), m.p 80-90˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, J=8.4Hz, 1H), 7.83 (s, 1H), 7.71 (d, J=8.0Hz, 1H), 7.63-7.60 (m, 1H), 7.48-7.42 (m, 3H), 7.31 (t, J=7.6Hz, 1H), 7.25 (s, 1H), 7.17 (d, J=7.2Hz, 1H), 3.17 (t, J=7.2Hz, 2H), 2.89 (t, J=7.6Hz, 2H), 2.40 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 194.0,154.8, 147.5, 146.8, 139.9, 138.1,135.7,135.1, 132.5, 129.2, 129.0, 128.7, 128.6, 128.5, 127.7, 126.9, 126.3, 125.8, 125.8, 122.7,116.3,116.0, 27.9, 26.1, 21.5. **HRMS ESI** (m/z): Calculated for $C_{20}H_{18}N$ [M+ H]+ : 272.1395, found : 272.1336.

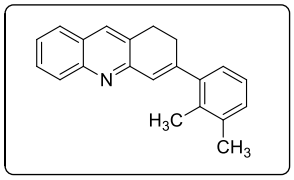


3-(4-butylphenyl)-1,2-dihydroacridine (7g): Yellow solid, (200 mg, yield 55%), mp 95-105˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, J=8.4Hz, 1H), 7.78 (s, 1H), 7.68 (d, J=8.0Hz, 1H), 7.61-7.55 (m, 3H), 7.42 (t, J=7.2Hz, 1H), 7.23 (t, J=8.0Hz, 3H), 3.14 (t, J=7.6Hz, 2H), 2.86 (t, J=7.2Hz, 2H), 2.63 (t, J=7.6Hz, 2H), 1.66-1.58 (m,2H), 1.42-1.34 (m,2H), 0.94 (t, J=7.2Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 154.9, 147.5, 146.6, 143.5, 137.1, 132.4, 129.0, 128.6, 126.9, 125.4, 125.2, 125.1, 35.4, 33.5, 27.9, 26.0, 22.4, 14.0. **HRMS ESI** (m/z): Calculated for $C_{23}H_{24}N$ [M+ H]$^+$: 314.1864, found : 314.1920.

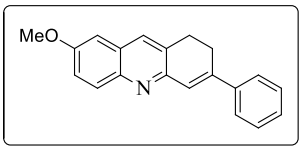


3-(4-ethylphenyl)-1,2-dihydroacridine (7h) : Yellow solid, (250mg, yield 49%), mp 85-90˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) : 8.02 (d, J=8.0Hz, 1H), 7.78 (s, 1H), 7.68 (d, J=12Hz, 1H), 7.62-7.56 (m, 3H), 7.43 (t, J=8.0Hz, 1H), 7.24 (t, J=8.0Hz, 3H), 3.14 (t, J=8.0Hz, 2H), 2.87 (t, J=8.0Hz, 2H), 2.71-2.64 (m, 2H), 1.27 (t, J=8.0Hz, 3H).**^{13}C NMR** (100

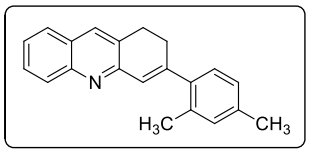
MHz, $CDCl_3$) δ (ppm): 154.9, 147.4, 146.7, 144.8, 137.2, 132.5, 129.0, 128.6, 128.5, 128.1, 126.9, 126.7, 125.7, 125.5, 125.0, 28.6, 27.9, 26.0, 15.4. **HRMS ESI** (m/z): Calculated for $C_{21}H_{20}N$ [M+ H]+ : 286.1551, found : 286.1595.



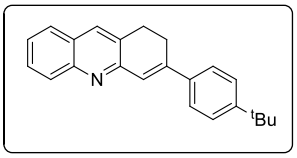
3-(2, 3-dimethylphenyl)-1,2-dihydroacridine (7i): Yellow solid, (200 mg, yield 67%), mp 95-105˚C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.01 (d, J=8.0Hz, 1H), 7.85 (s, 1H), 7.72 (d, J=8.0Hz, 1H), 7.62 (t, J=7.2Hz, 1H), 7.45 (t, J=7.2Hz, 1H), 7.28 (s, 1H), 7.13 (t, J=6.8Hz, 3H), 6.79 (s, 1H), 3.19 (t, J=7.2Hz, 2H), 2.69 (t, J=7.2Hz, 2H), 2.40-2.31 (m, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 150.7, 147.2, 142.4, 137.4, 133.4, 132.9, 129.3, 128.9, 128.8, 128.6, 128.2, 127.8, 127.0, 125.9, 125.7, 125.6, 29.5, 28.2, 20.6, 17.1. **HRMS ESI** (m/z): Calculated for $C_{21}H_{20}N$ [M+ H]+ : 286.1519, found : 286.1610.



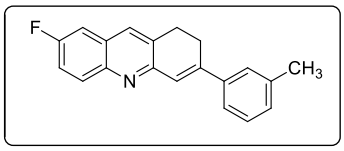
7-methoxy-3-phenyl-1,2-dihydroacridine (7j): Yellow solid, (200 mg, yield 65%), mp. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.90 (d, J=9.2Hz, 1H), 7.73 (s, 1H), 7.64 (d, J=7.6Hz, 2H), 7.41 (t, J=7.2Hz, 2H), 7.34 (d, J=7.2Hz, 1H),7.28 (t, J=2.0Hz, 1H), 7.22 (s, 1H), 7.01 (s, 1H), 3.92 (s, 3H), 3.16 (t, J=7.2Hz, 2H), 2.88 (t, J=7.6 Hz, 2H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm):157.5, 152.6, 145.3, 140.1, 131.6, 130.0, 129.4, 128.6, 128.6, 128.2, 125.4, 120.9, 105.2, 55.5, 28.0, 26.1. **HRMS ESI** (m/z): Calculated for $C_{20}H_{18}NO$ [M+ H]+ : 288.1388, found : 288.1414.



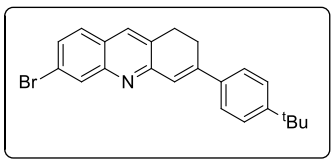
3-(2,4-dimethylphenyl)-1,2-dihydroacridine (7k) : Yellow liquid, (300 mg, yield 69%), mp. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.02 (d, J=8.4Hz, 1H), 7.82 (s, 1H), 7.70 (d, J=8.4Hz, 1H), 7.61 (t, J=7.2Hz, 1H), 7.44 (t, J=7.2Hz, 1H), 7.26 (d, J=8.0Hz, 3H), 7.00 (s, 1H), 3.15 (d, J=7.2Hz, 2H), 2.87 (d, J=7.6Hz, 2H), 2.36 (s, 5H), 2.32 (s,1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 154.8, 147.6, 147.1, 139.9, 138.1, 135.4, 132.9, 130.3, 129.2, 128.9, 128.2, 128.1, 127.8, 127.7, 127.0, 125.9, 125.5, 125.2, 124.7, 123.6, 27.9, 26.2, 21.4. **HRMS ESI** (m/z): Calculated for $C_{21}H_{19}N$ [M+ H]$^+$: 286.1596, found : 286.1617.



3-(4-(tert-butyl) phenyl)-1,2-dihydroacridine (7l): White solid, (250 mg, yield 79%), mp. **^{1}H NMR** (400 MHz, CDCl3) δ (ppm):.8.0 (d, J=8.4Hz, 1H), 7.82 (s, 1H), 7.70 (d, J=8.0Hz, 1H), 7.63-7.57 (m, 3H), 7.45-7.41(m, 1H), 7.23(d, J=8.4Hz, 3H), 3.17(t, J=7.6Hz, 2H), 2.91-2.87 (m, 2H), 2.64 (t, J=8.0Hz, 2H), 1.67-1.59 (m, 5H), 1.41-1.33 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm):155.0, 151.8, 147.6, 146.5, 137.0, 132.5, 129.1, 128.7, 128.7, 127.7, 127.0, 125.8, 125.6, 125.4, 125.3, 34.7, 31.3, 28.0, 36.1. **HRMS ESI** (m/z): Calculated for $C_{23}H_{24}N$ [M+ H]+ : 314.1909, found: 314.1917.



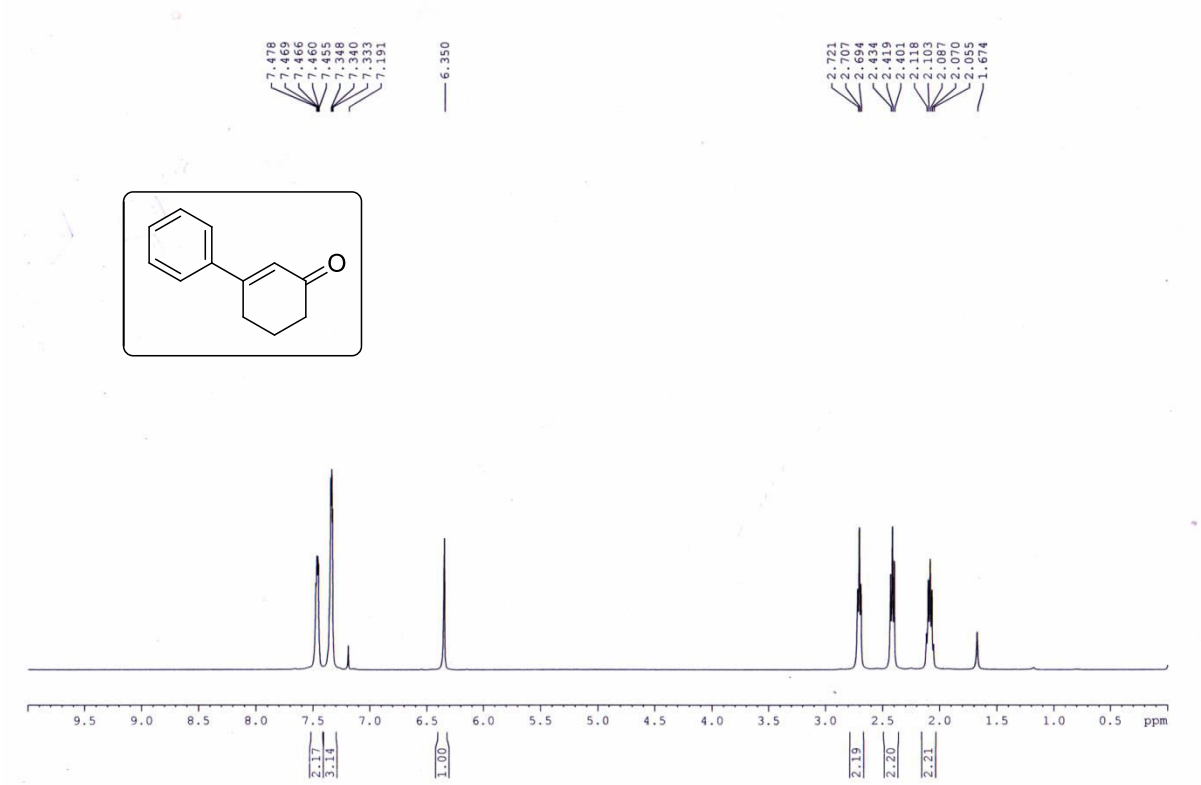
7-fluoro-3-(m-tolyl)-1,2-dihydroacridine (7m): White solid, (170 mg, yield 43%), mp. **^{1}H NMR** (400 MHz, CDCl3) δ (ppm): 8.00-7.96 (m, 1H), 7.77 (s, 1H), 7.45 (t, J=5.6Hz, 2H), 7.40-7.29 (m, 3H), 7.21 (s, 1H), 7.18 (d, J=7.2Hz, 1H), 3.17 (t, J=7.2Hz, 2H), 2.89 (t, J=8.0Hz, 2H), 2.40 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 161.5, 159.0, 154.4, 146.9, 144.5, 139.9, 138.3, 130.1, 129.4, 128.6, 126.4, 125.6, 122.7, 118.7, 118.5, 110.4, 110.2, 28.0, 26.1, 21.6.**HRMS ESI** (m/z): Calculated for $C_{20}H_{17}FN$ [M+ H]+ : 290.1345, found : 290.1344.

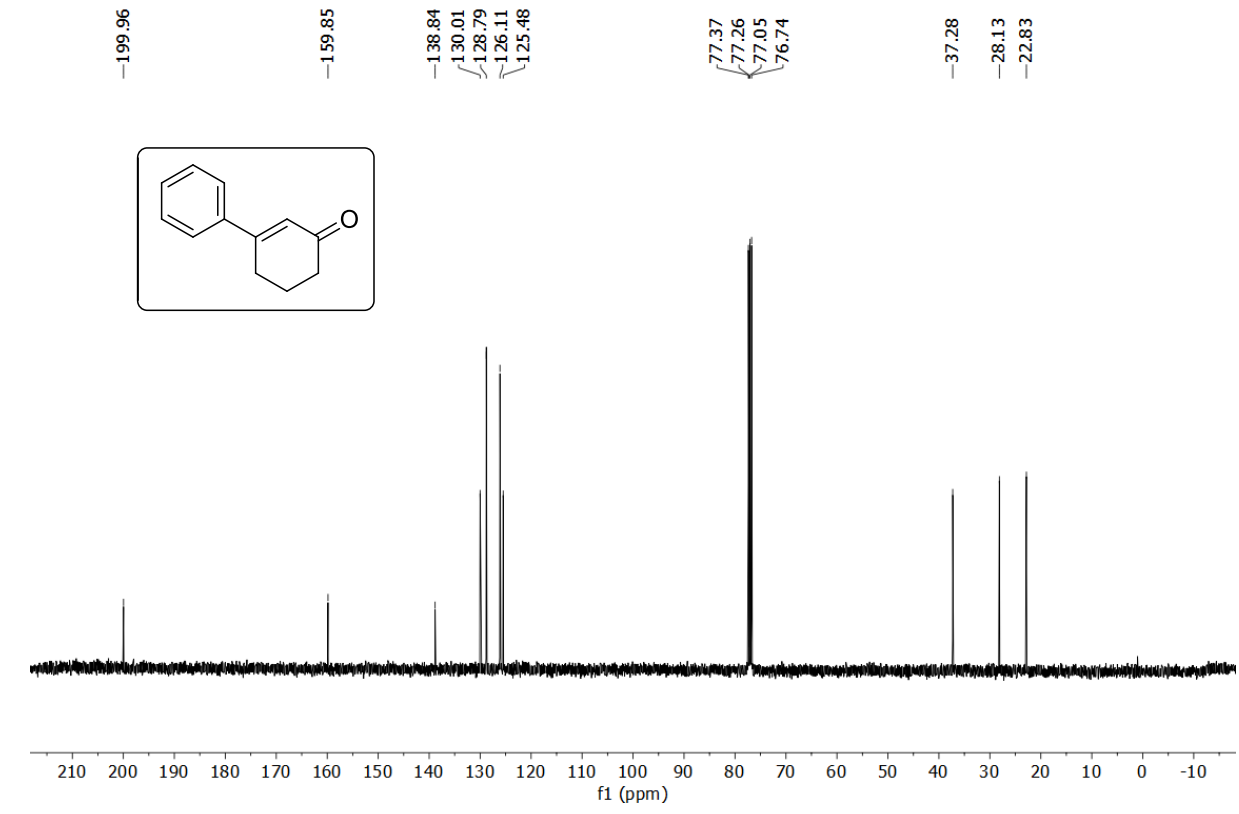


6-bromo-3-(4-(tert-butyl)phenyl)-1,2-dihydroacridine (7n): Yellow solid, (200 mg, yield 43%), mp70-75˚C.**^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, J=4.0Hz, 1H), 7.98 (d, J=4.0Hz, 1H), 7.87-7.69 (m, 1H), 7.64-7.56 (m, 2H), 7.45 (t, J=8.0Hz, 3H), 7.25-7.14 (m, 1H), 3.48 (d, J=16Hz, 3H), 3.29-3.09 (m, 1H), 2.66-2.58 (m, 2H), 1.66-1.56 (m, 2H), 1.40-1.34 (m, 2H),0.95-0.91 (m, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm): 158.8, 154.9, 147.4, 143.5, 142.6, 140.9, 137.1, 134.9, 132.4, 128.5, 128.3, 126.9, 126.6, 125.4, 125.1, 41.0, 40.0, 30.4, 28.8, 26.0, 22.4, 13.9. **HRMS ESI** (m/z): Calculated for $C_{23}H_{23}BrN$ [M+ H]+ : 392.1013, found: 392.0991

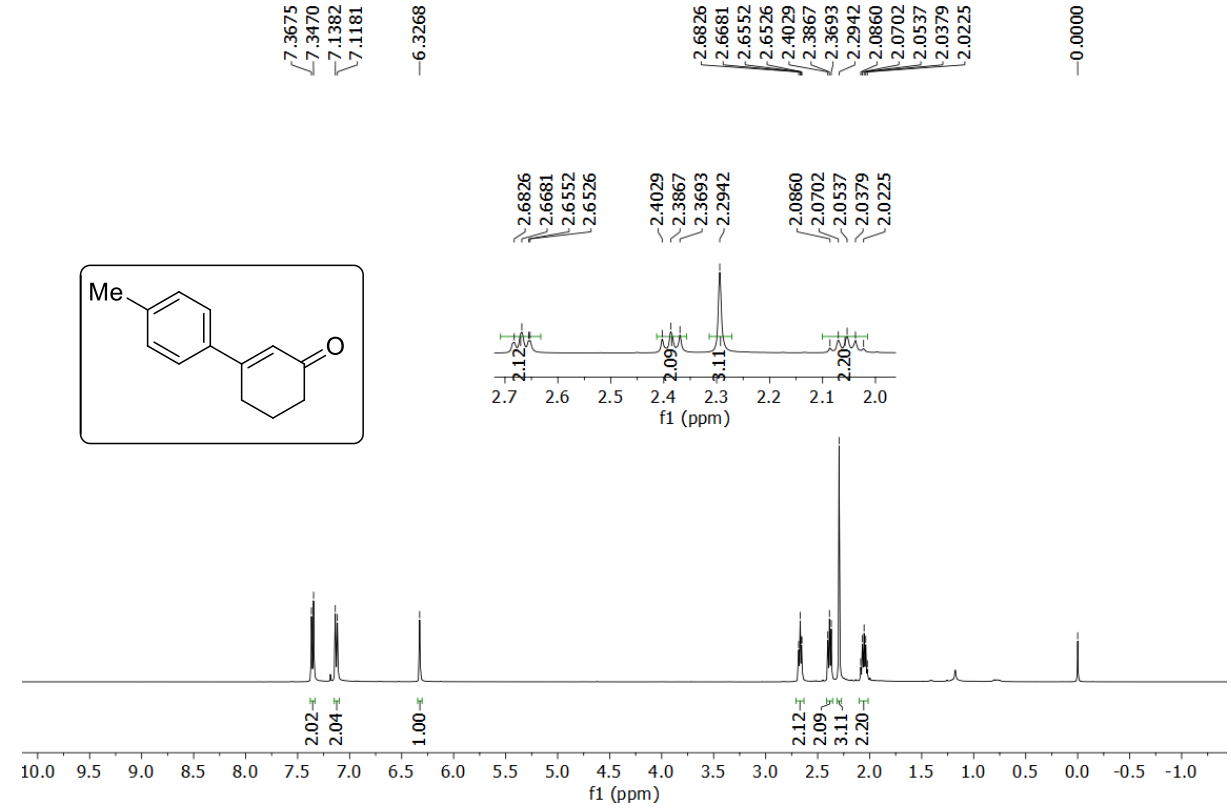
F. Copies of NMR Spectra :

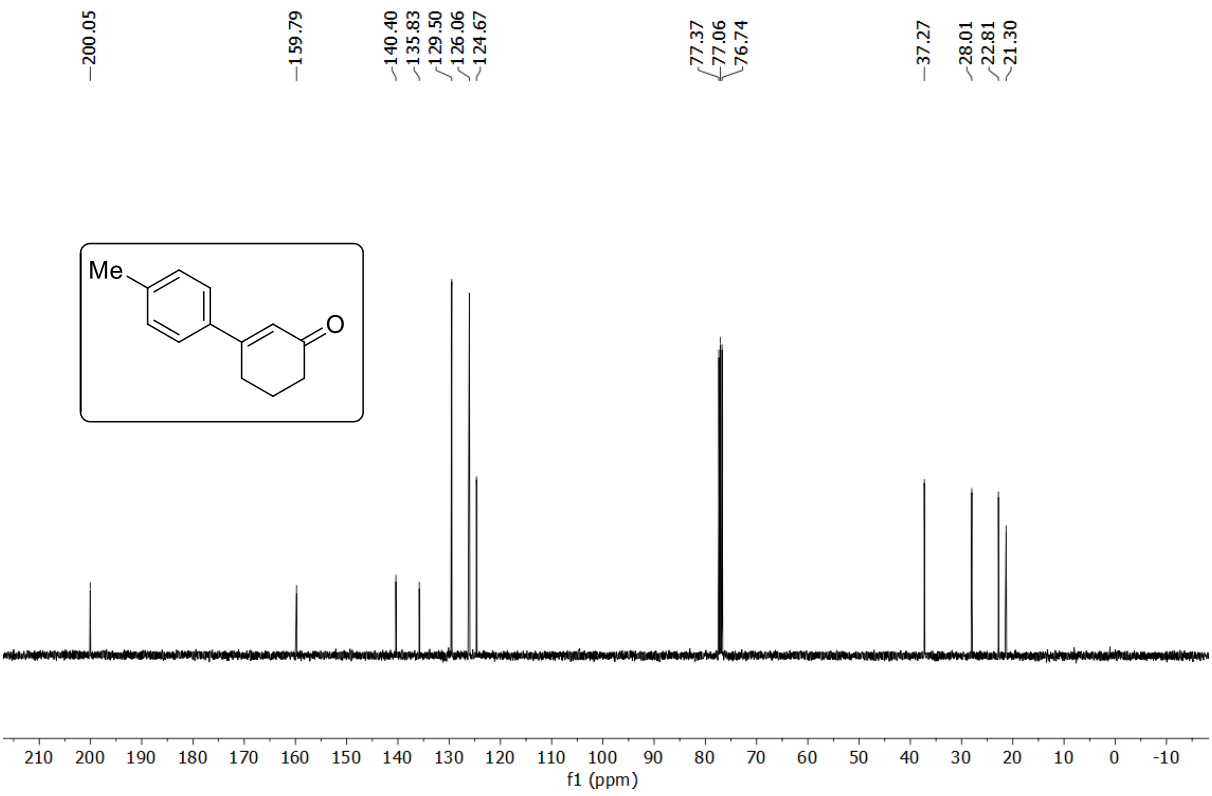
5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3a):



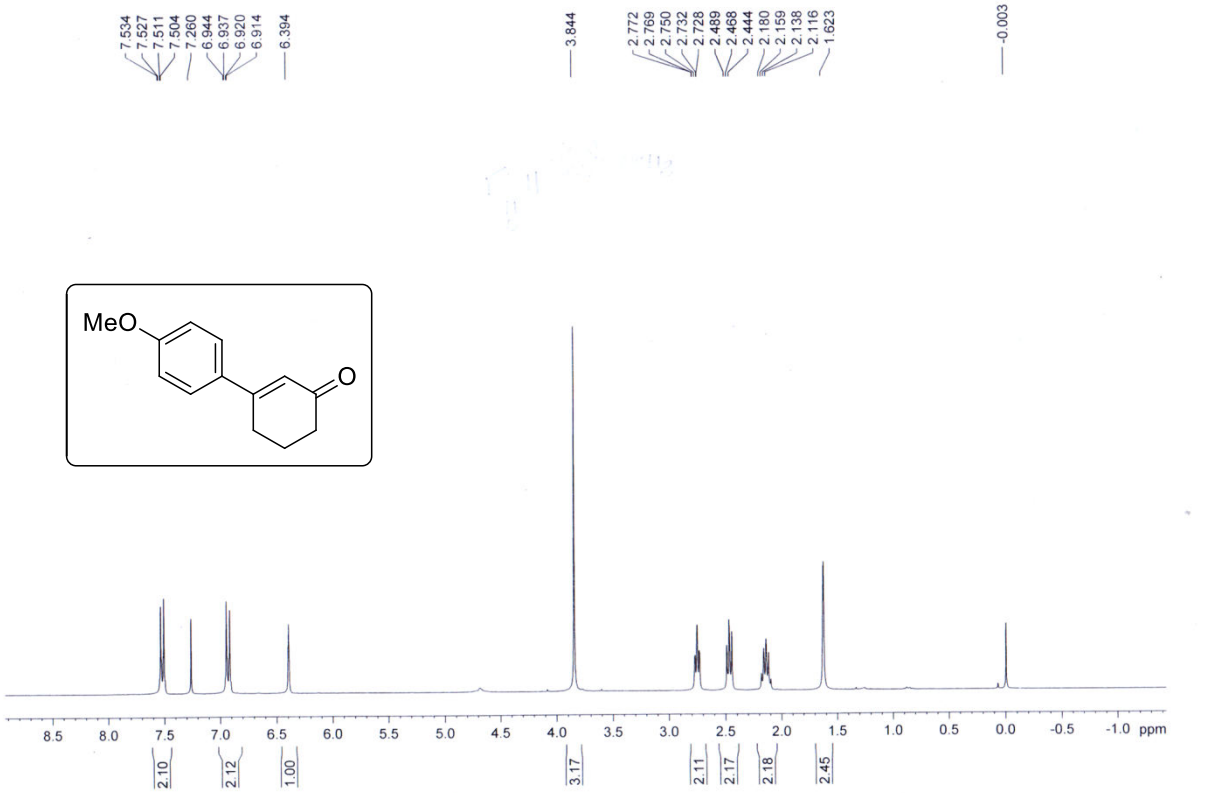


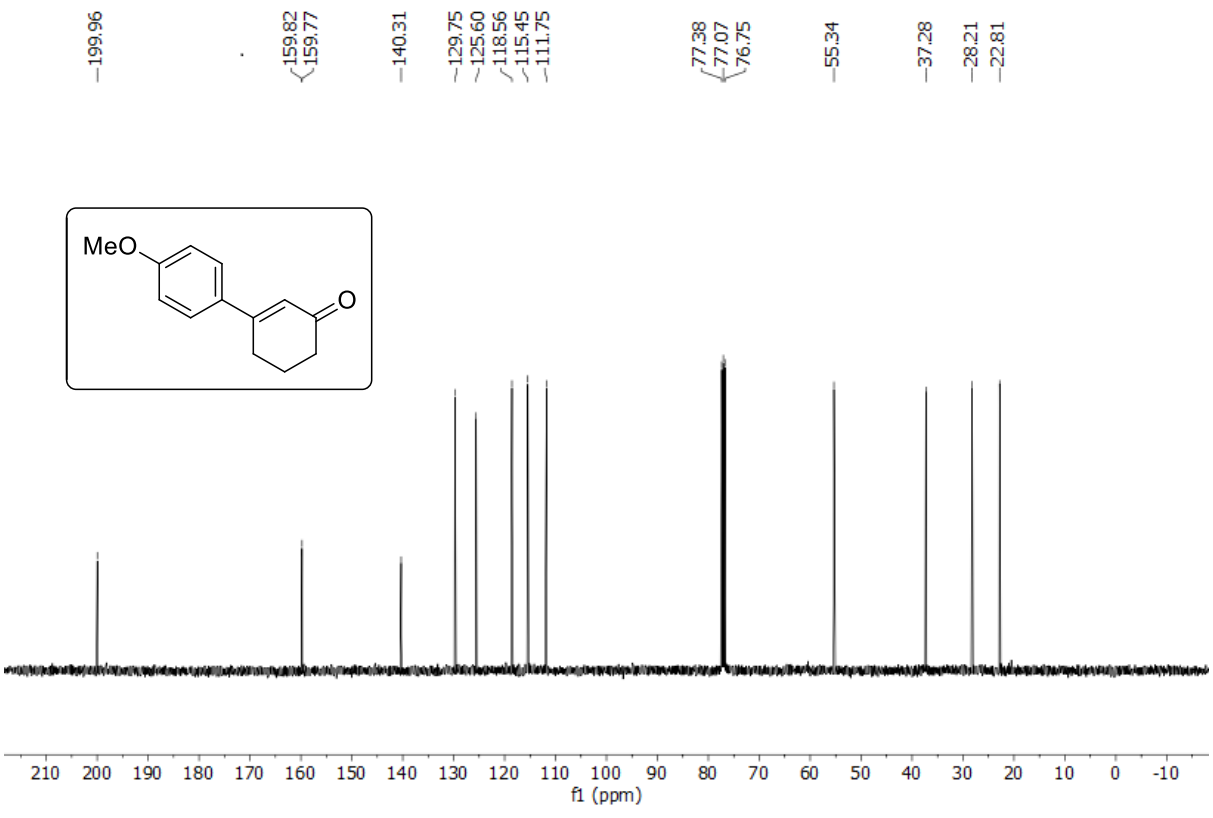
4'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3b):



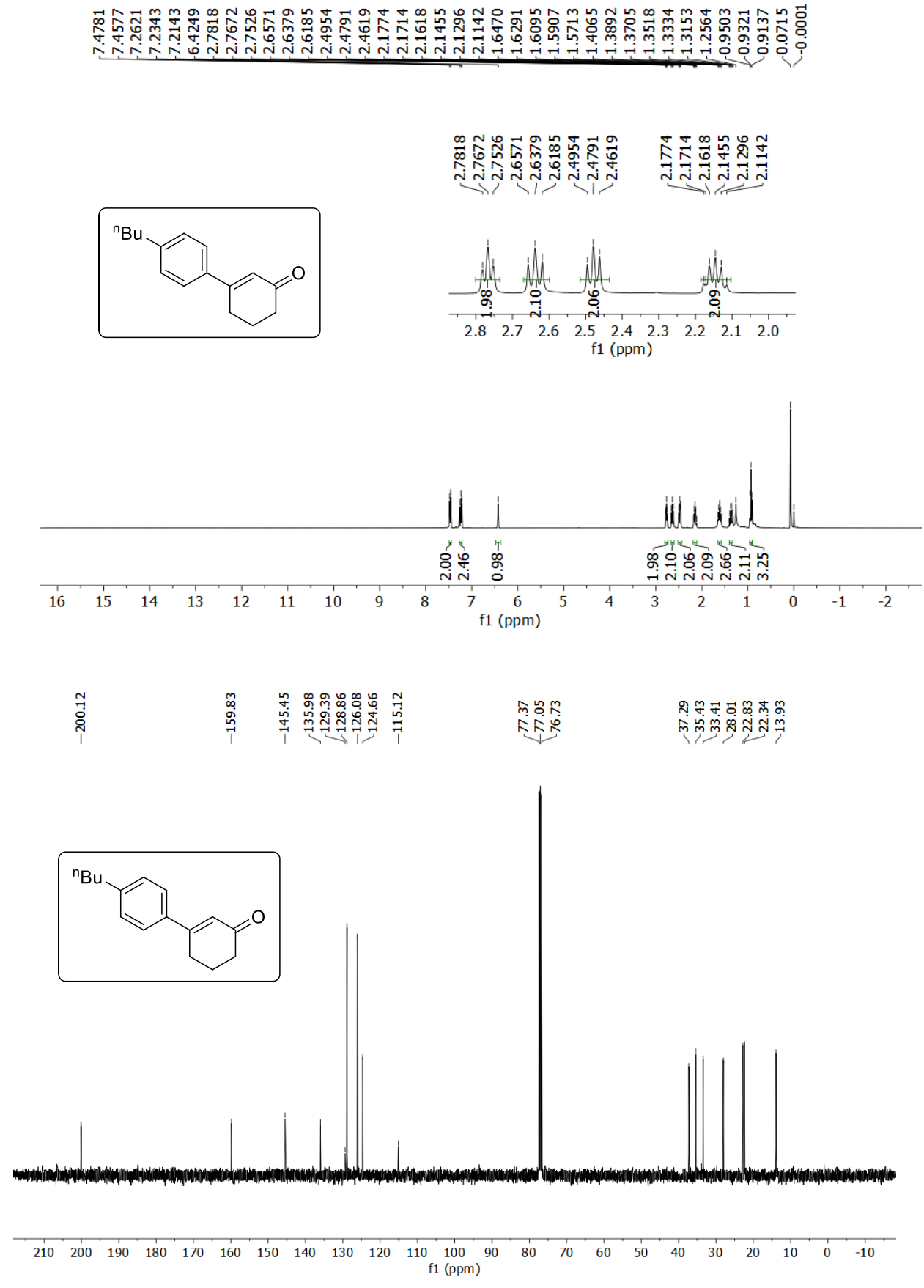


4'-methoxy-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3c):

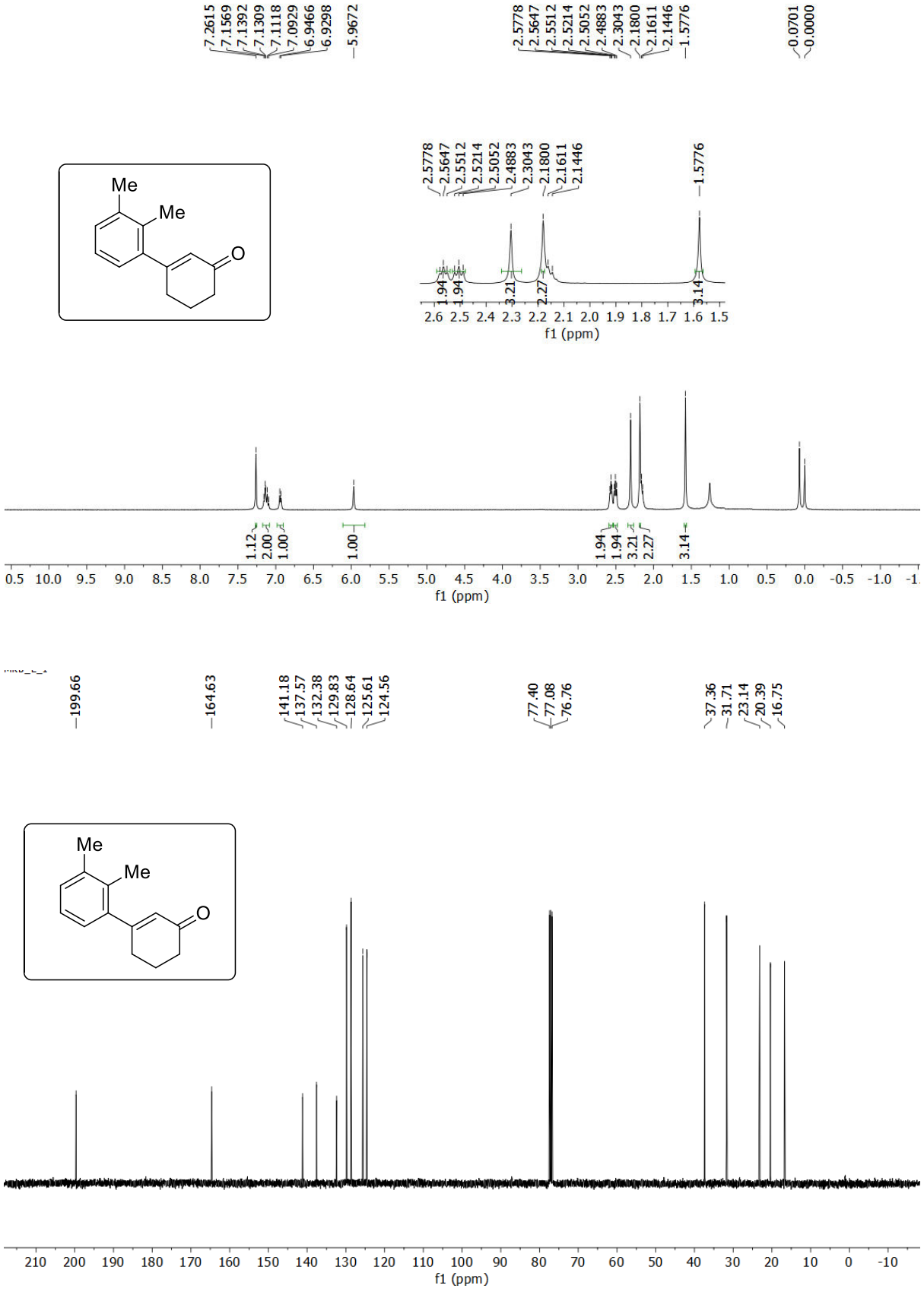




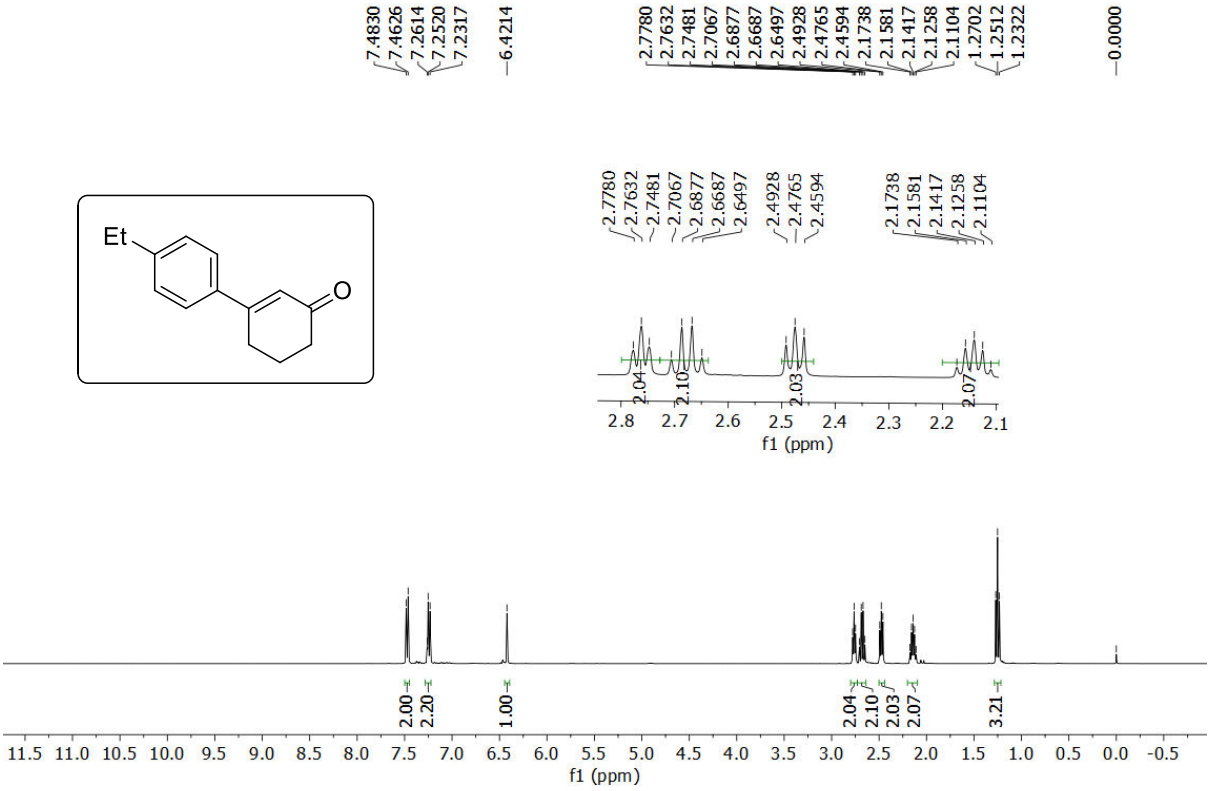
4'-butyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one(3d):

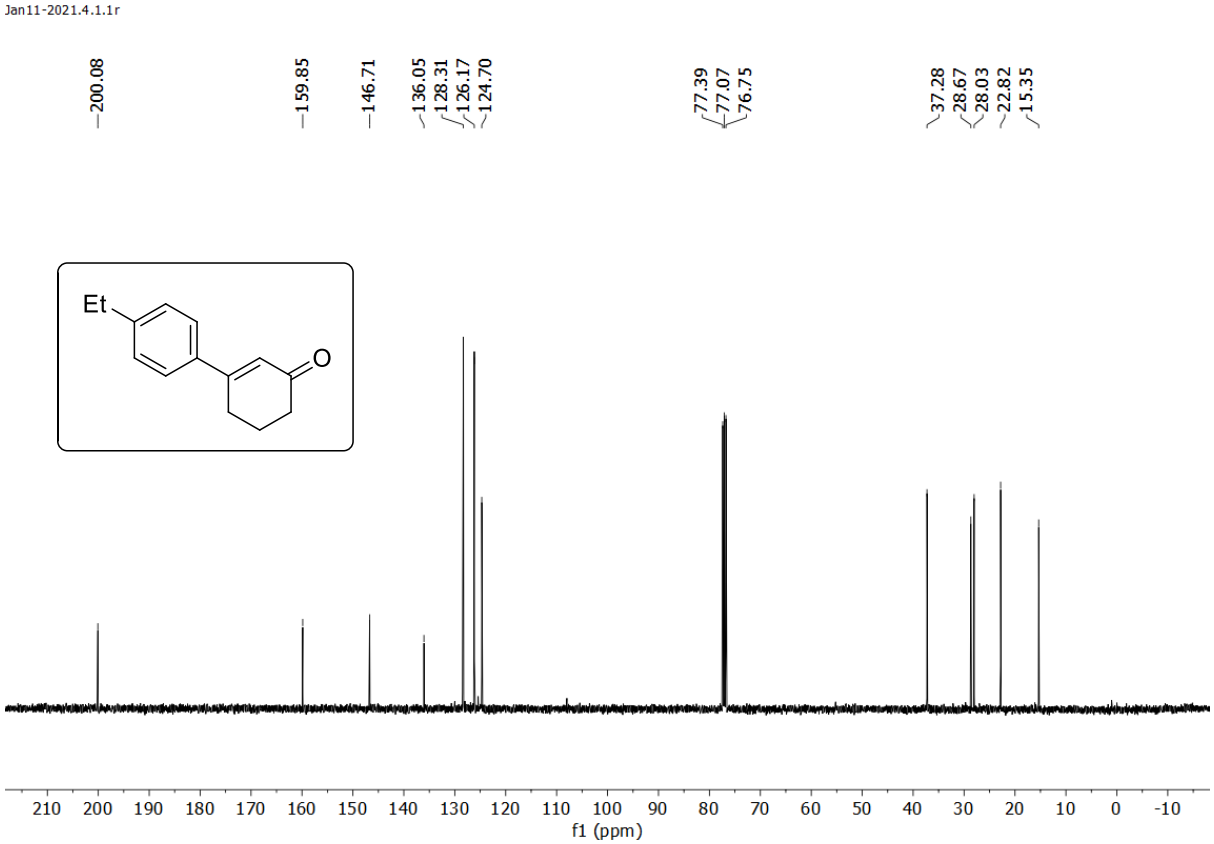


2',3'-dimethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3e):

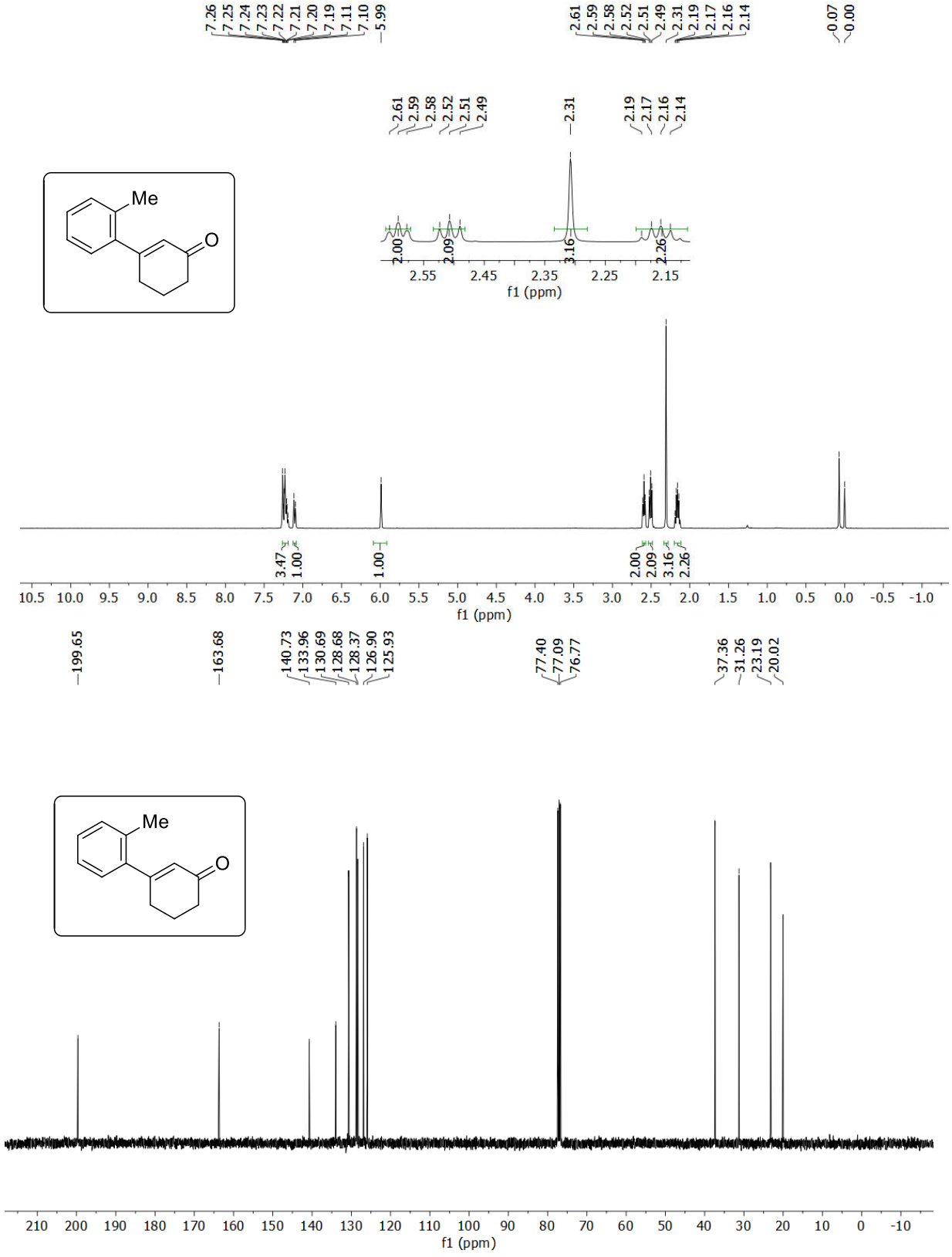


4'-ethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3f):

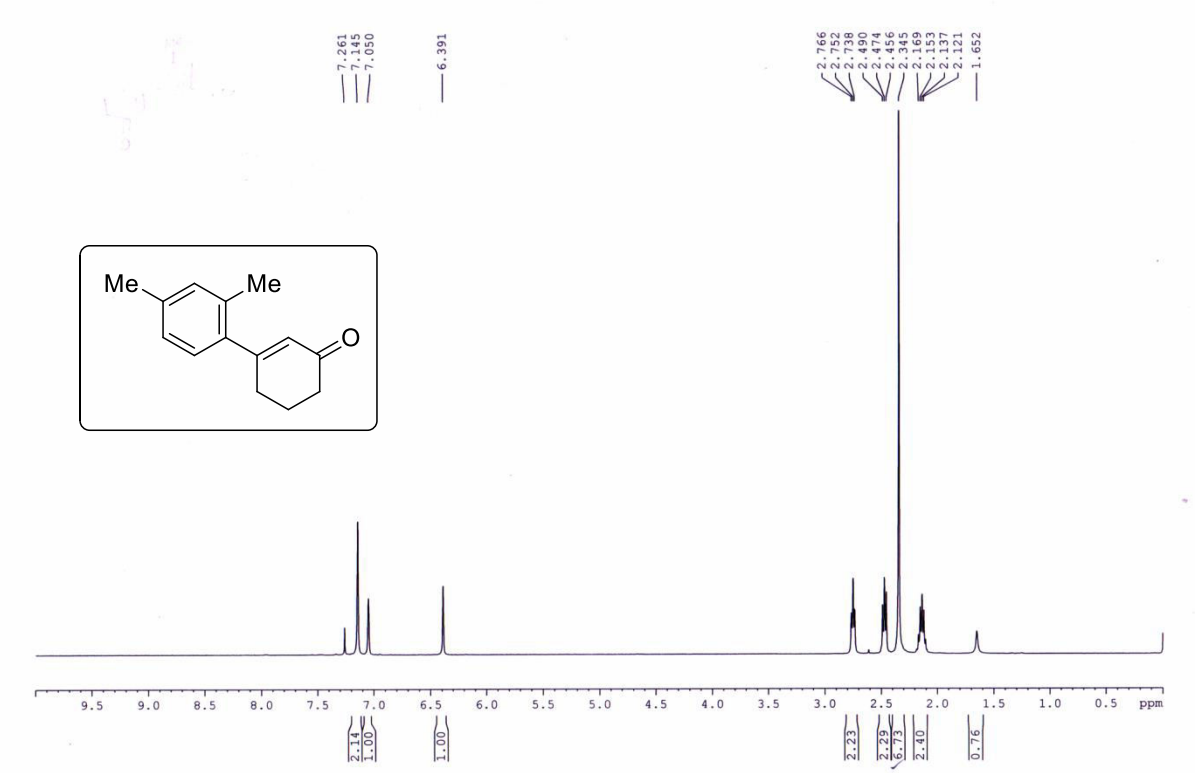


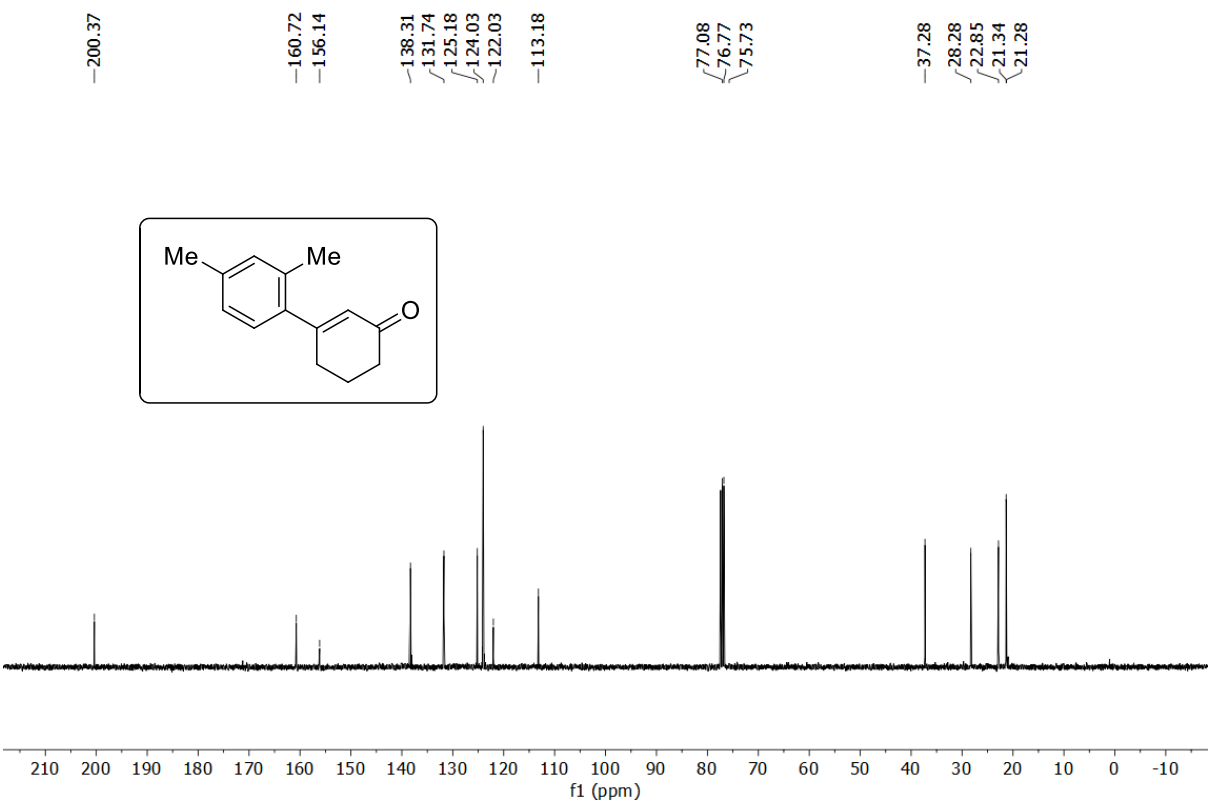


2'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3g):

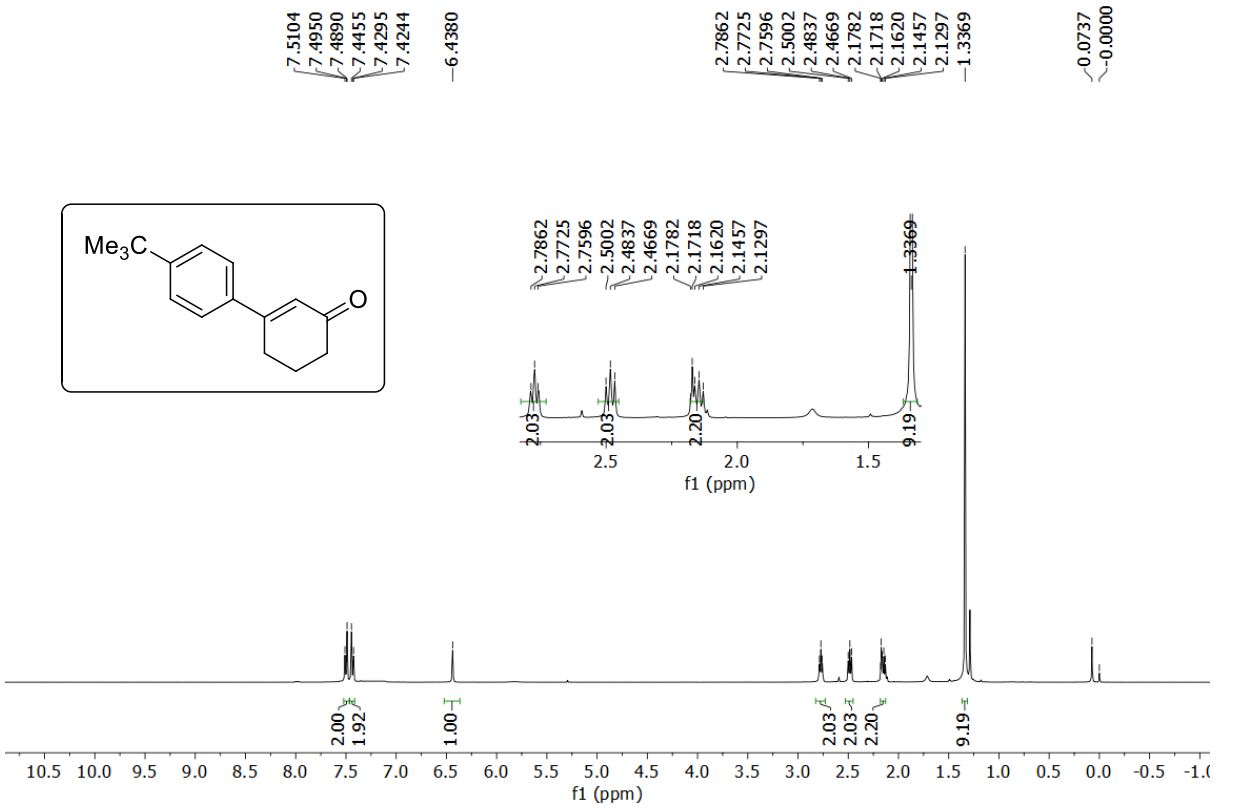


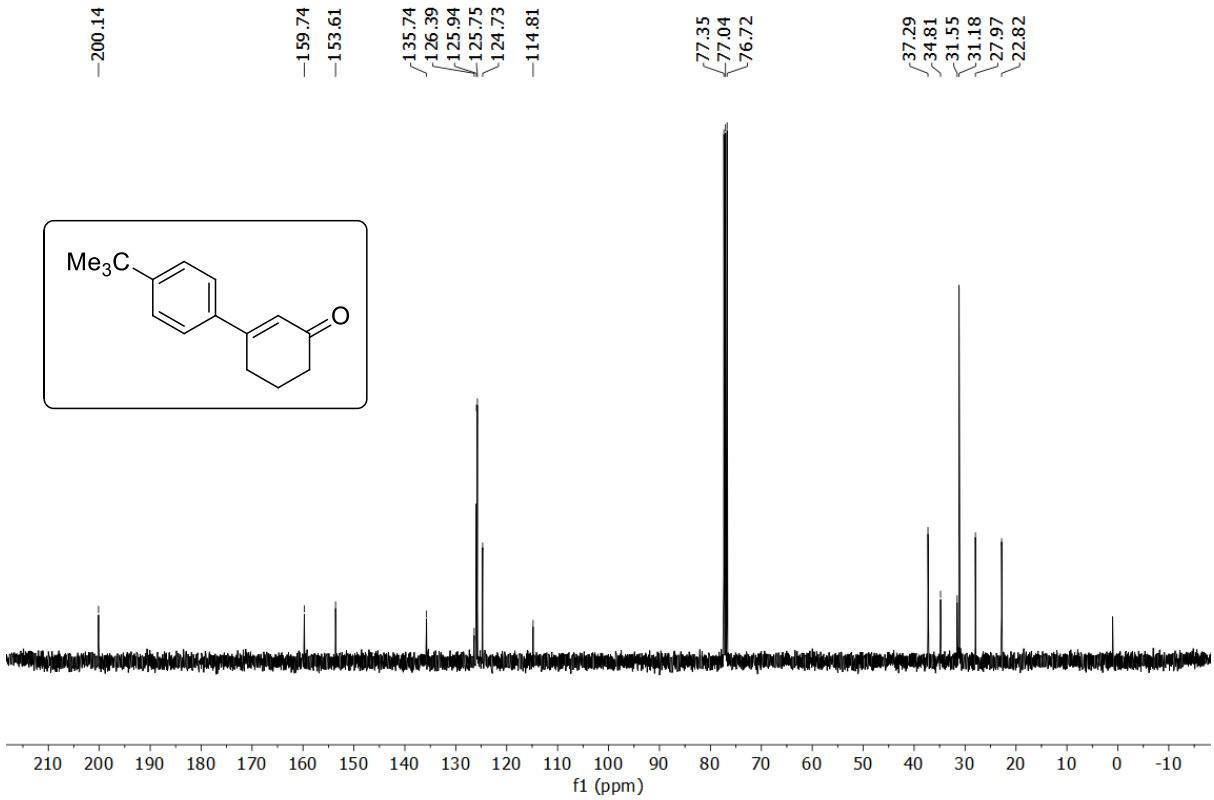
2',4'-dimethyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3h):



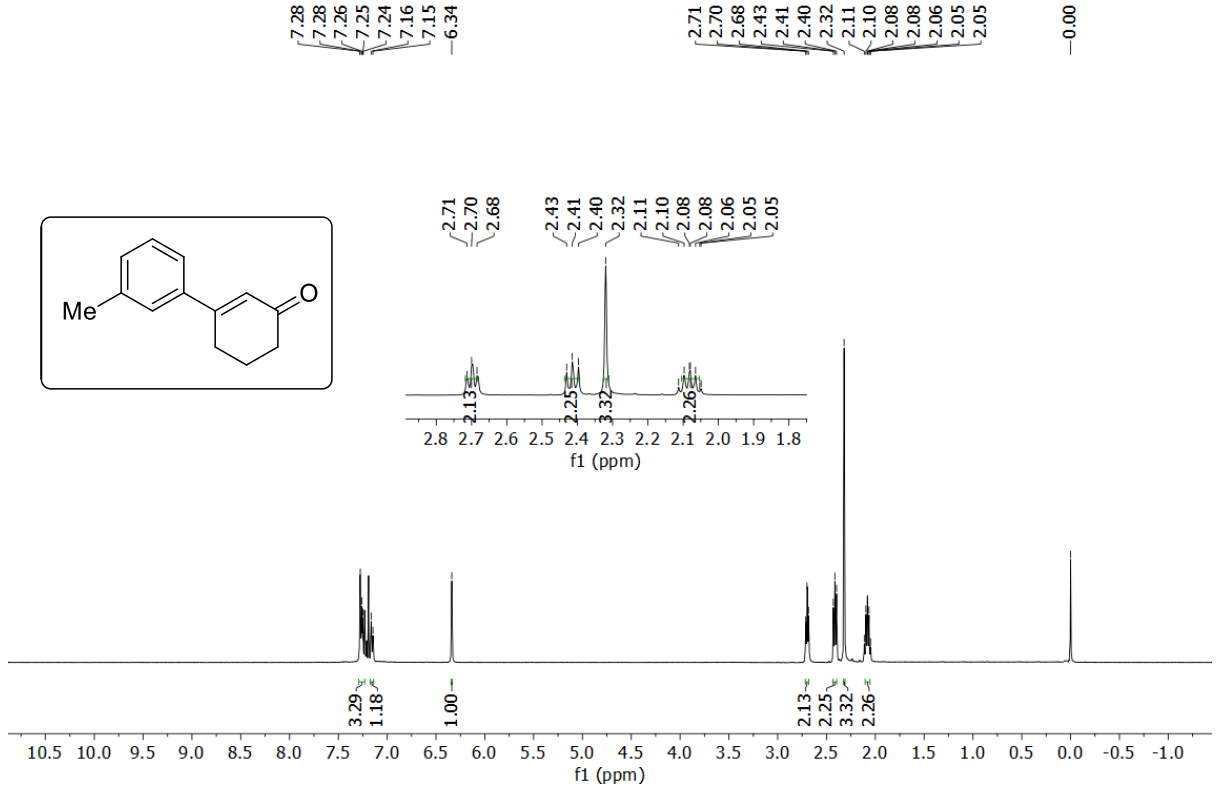


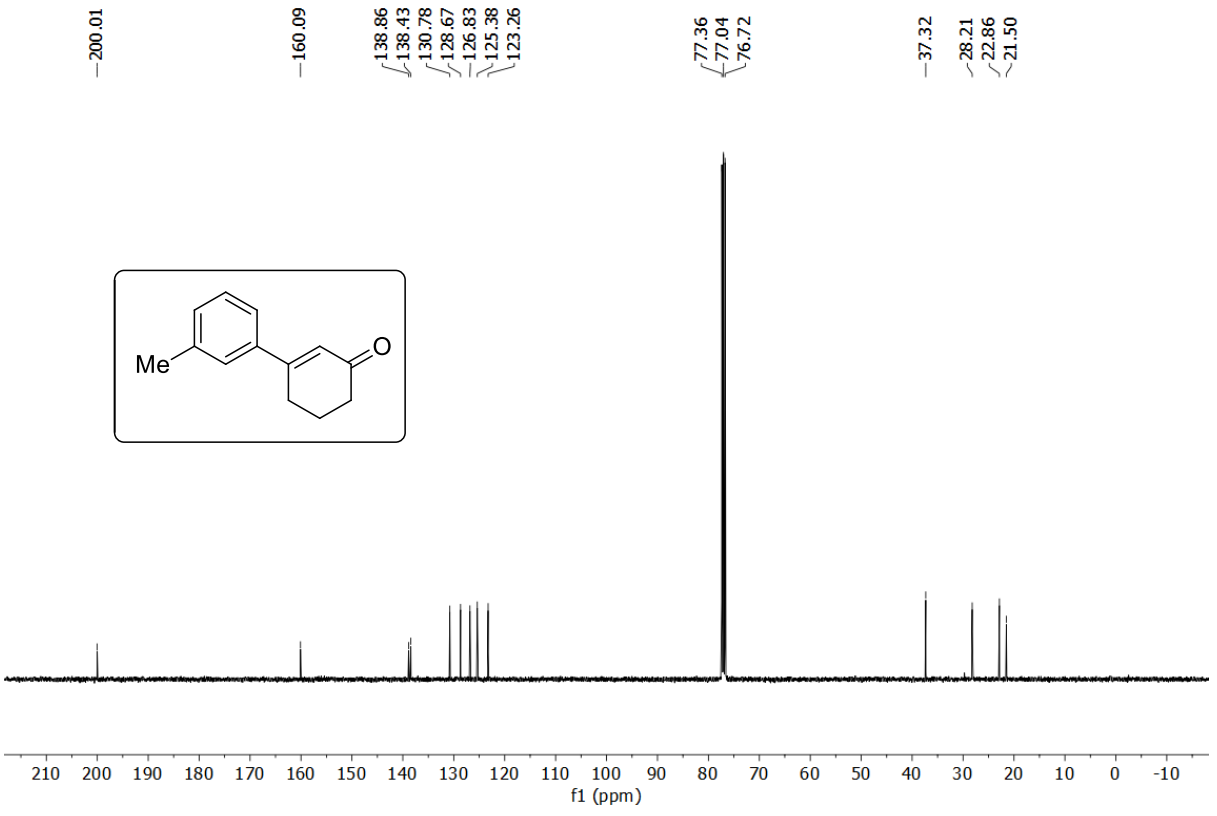
4'-(tert-butyl)-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3i):



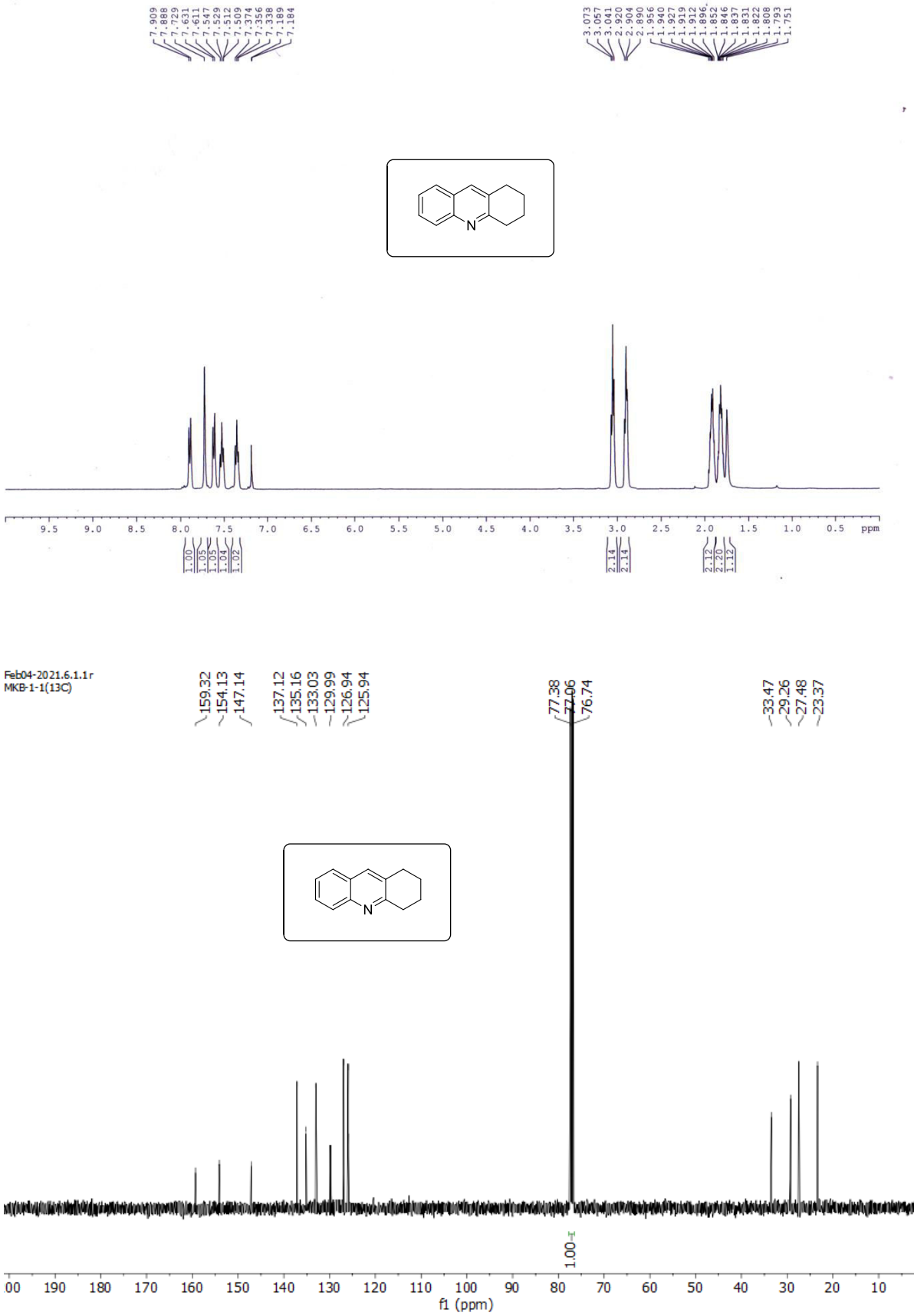


3'-methyl-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (3j):

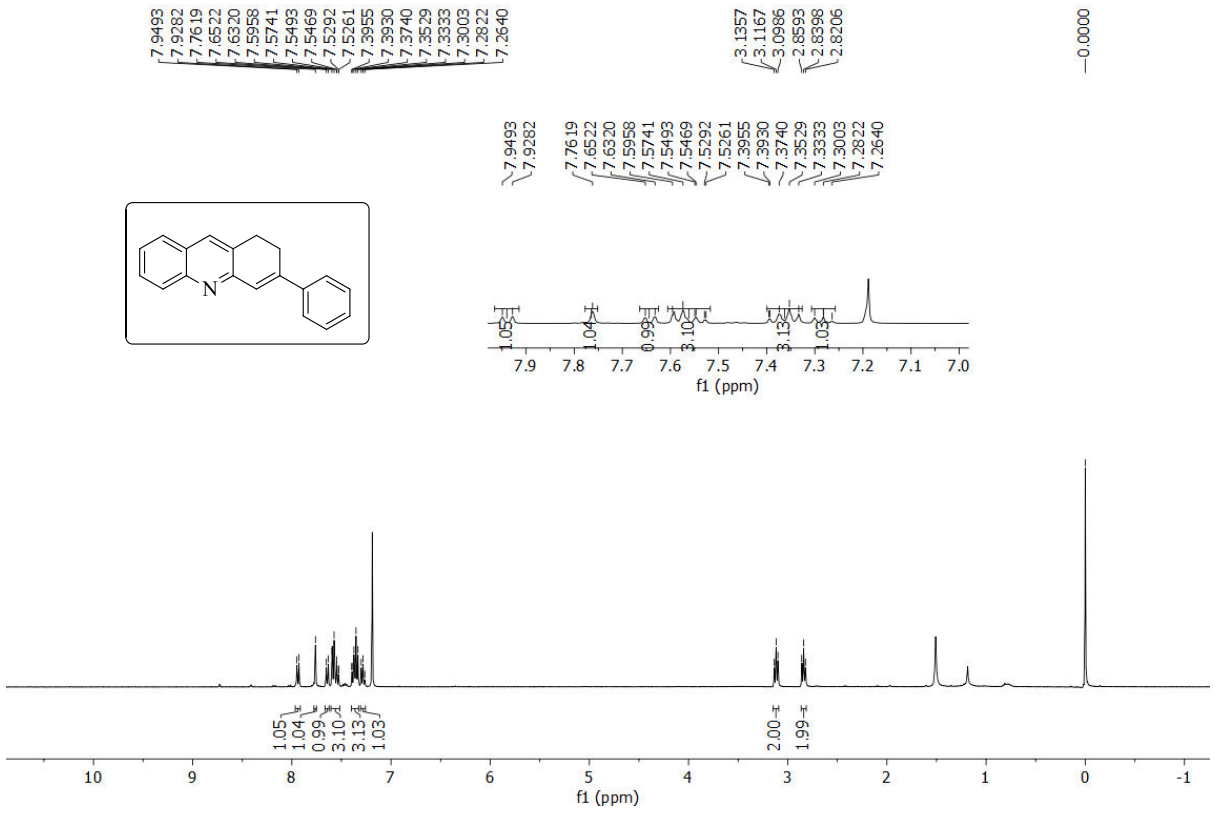


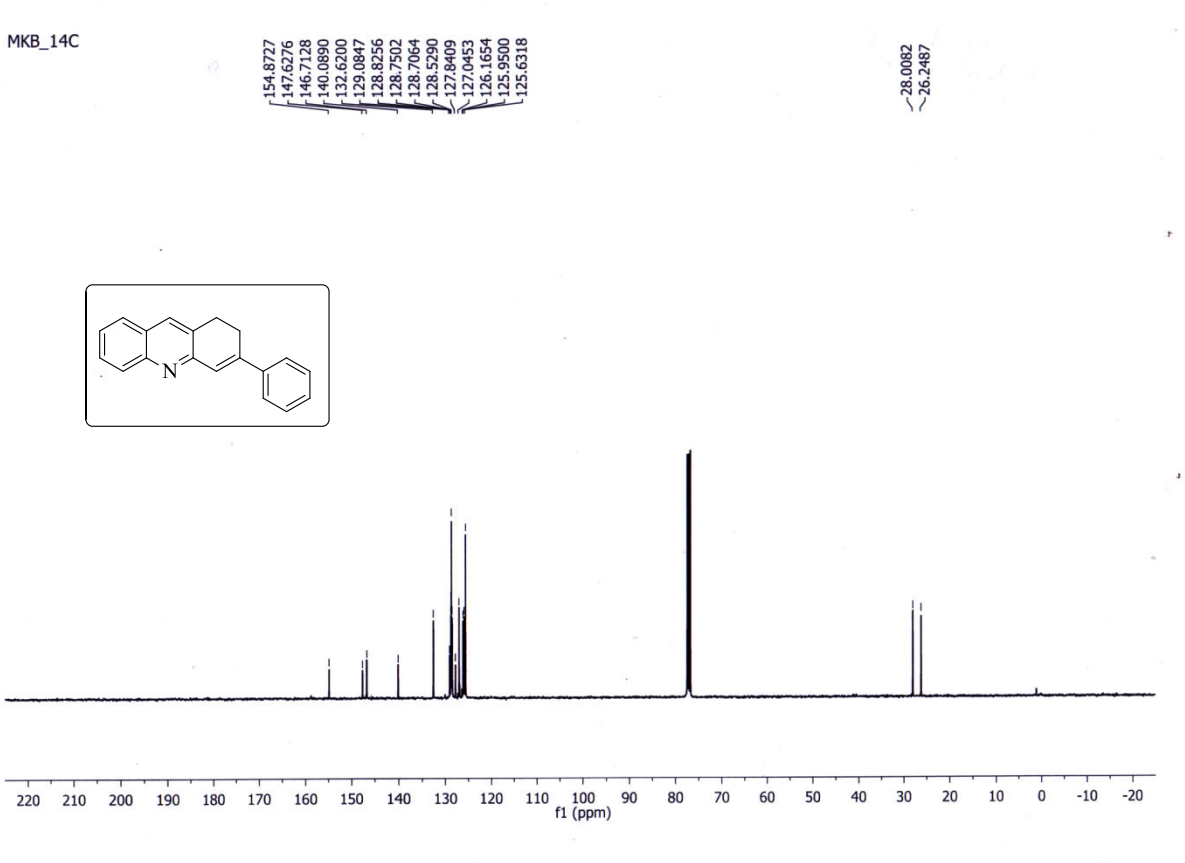


1,2,3,4-tetrahydroacridine (7a):

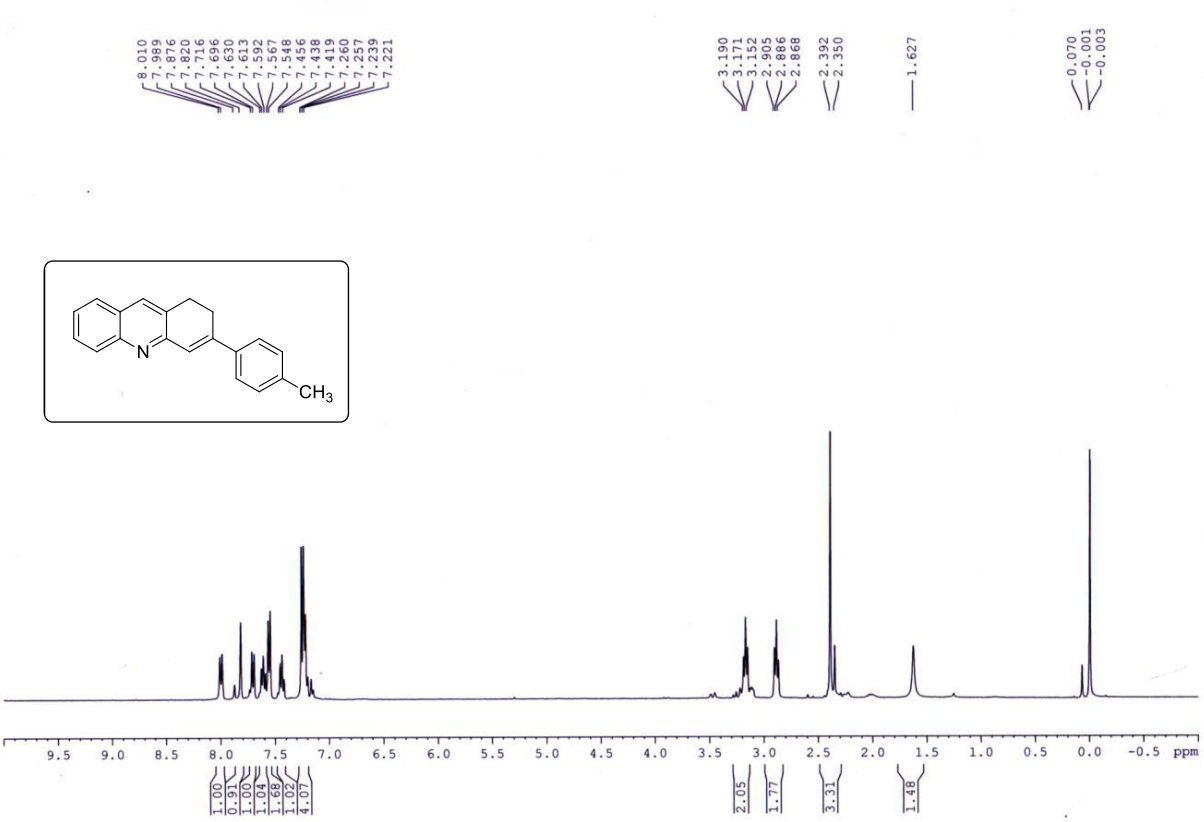


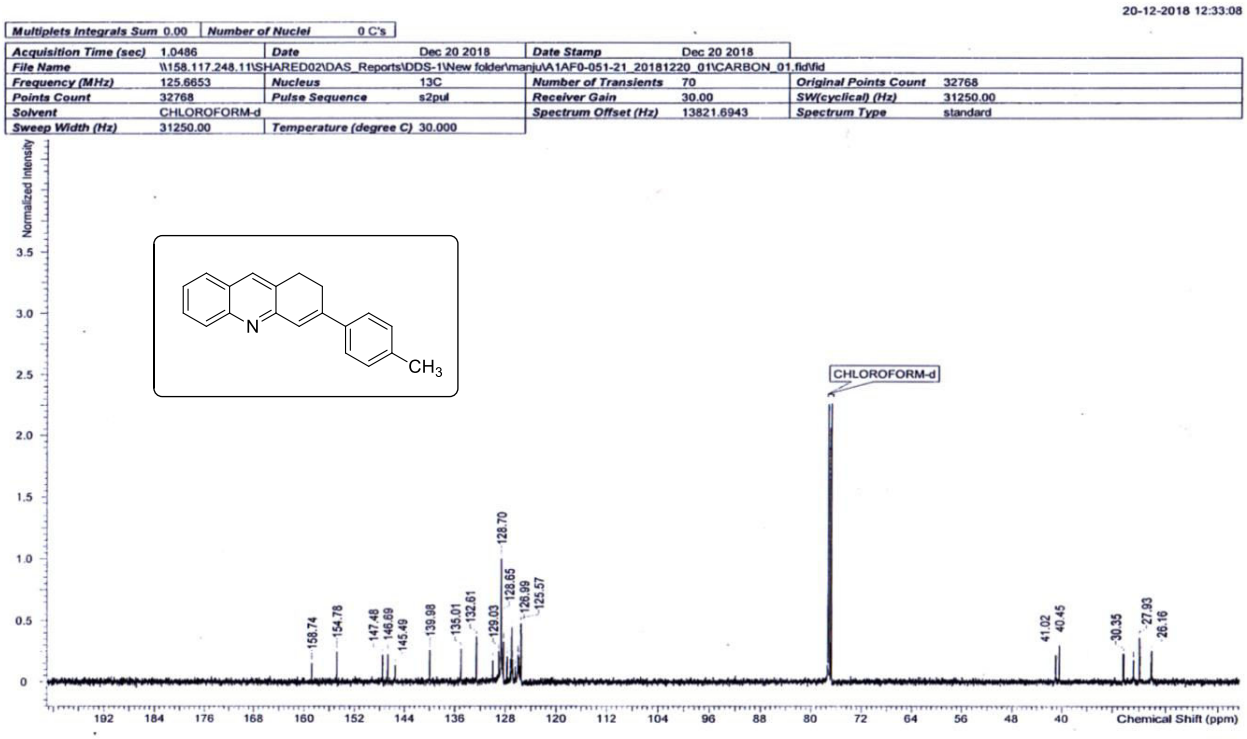
3-phenyl-1,2-dihydroacridine (7b):



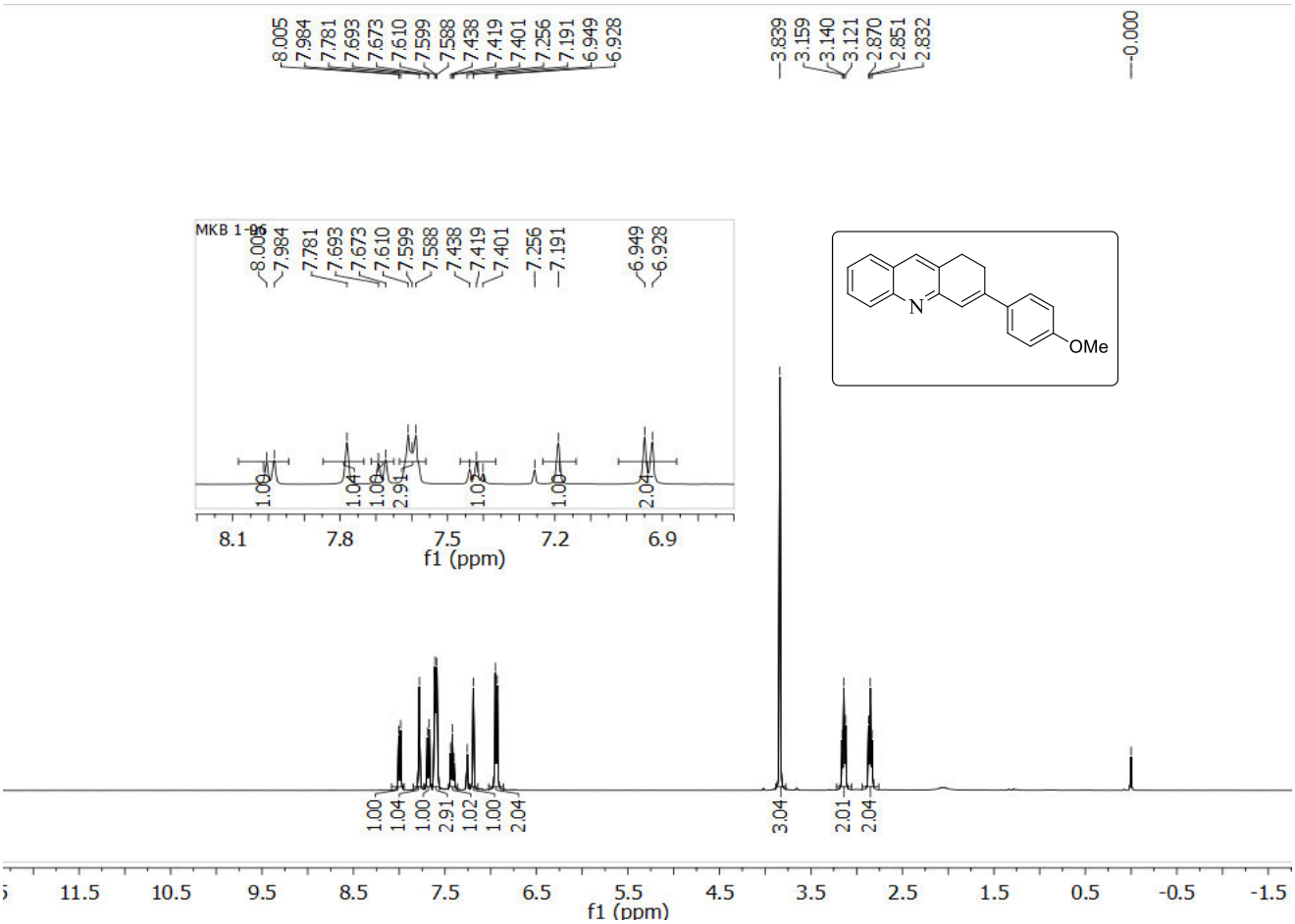


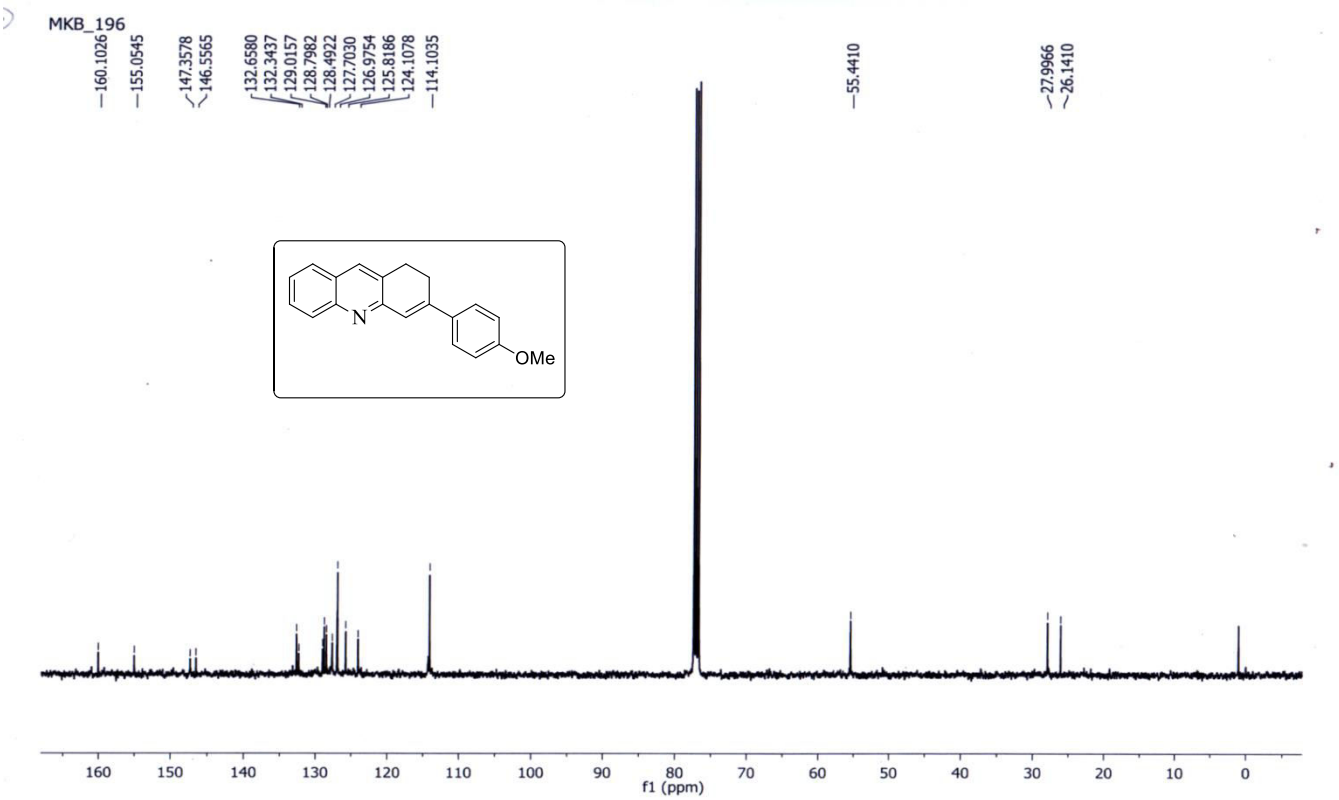
3-(p-tolyl)-1,2-dihydroacridine (7c):



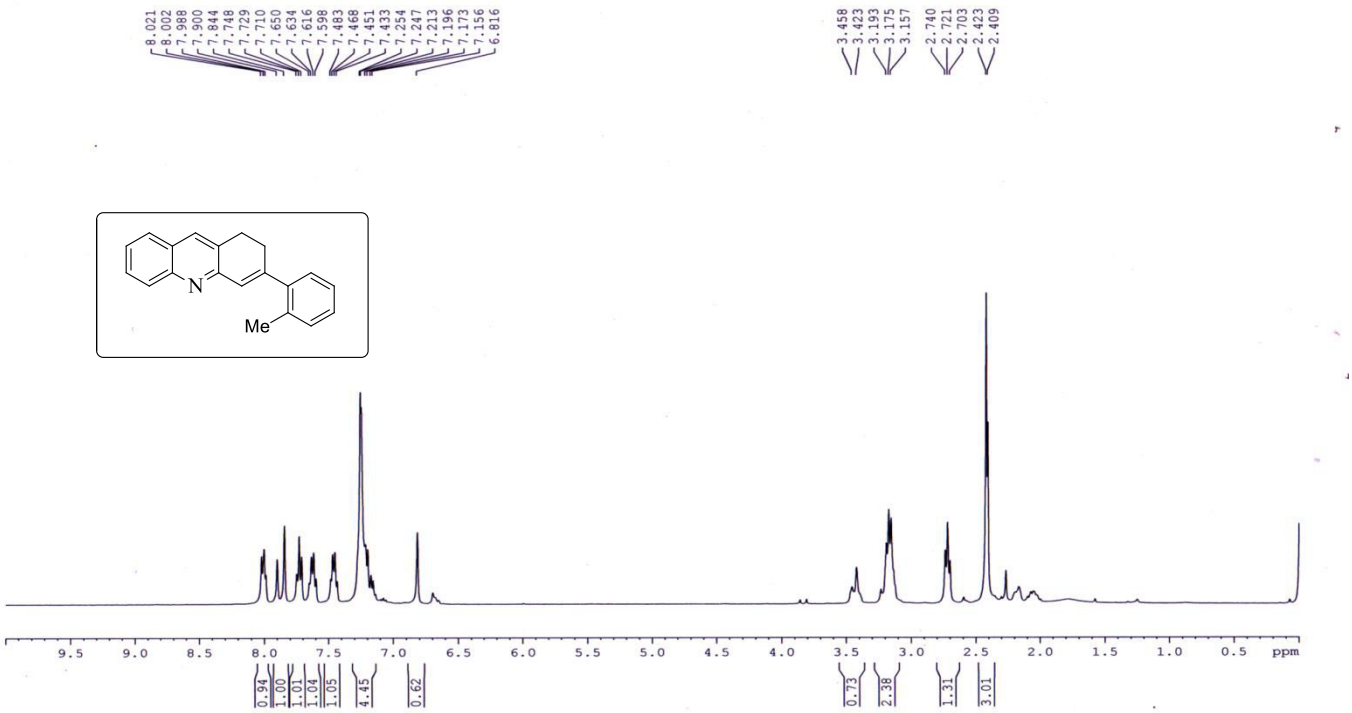


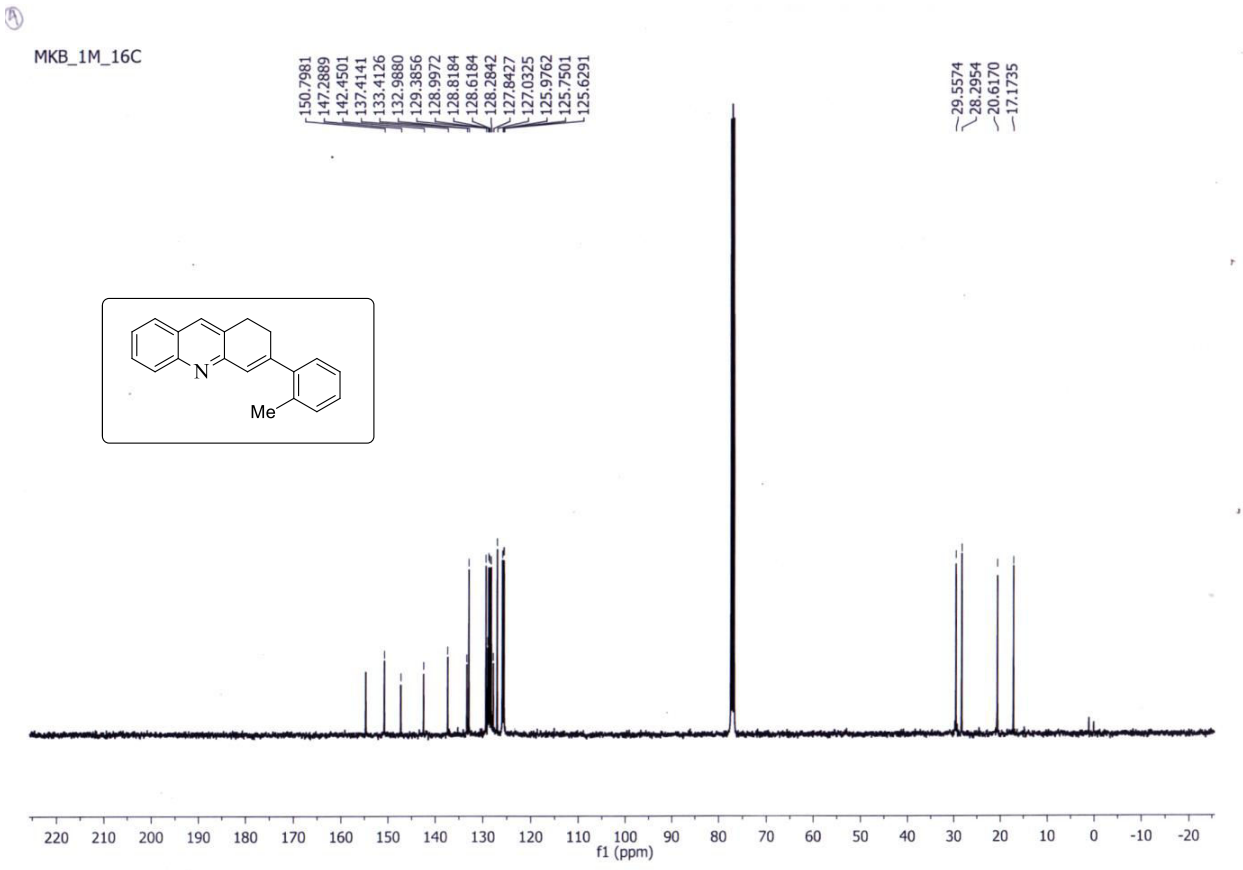
3-(4-methoxyphenyl)-1,2-dihydroacridine (7d):



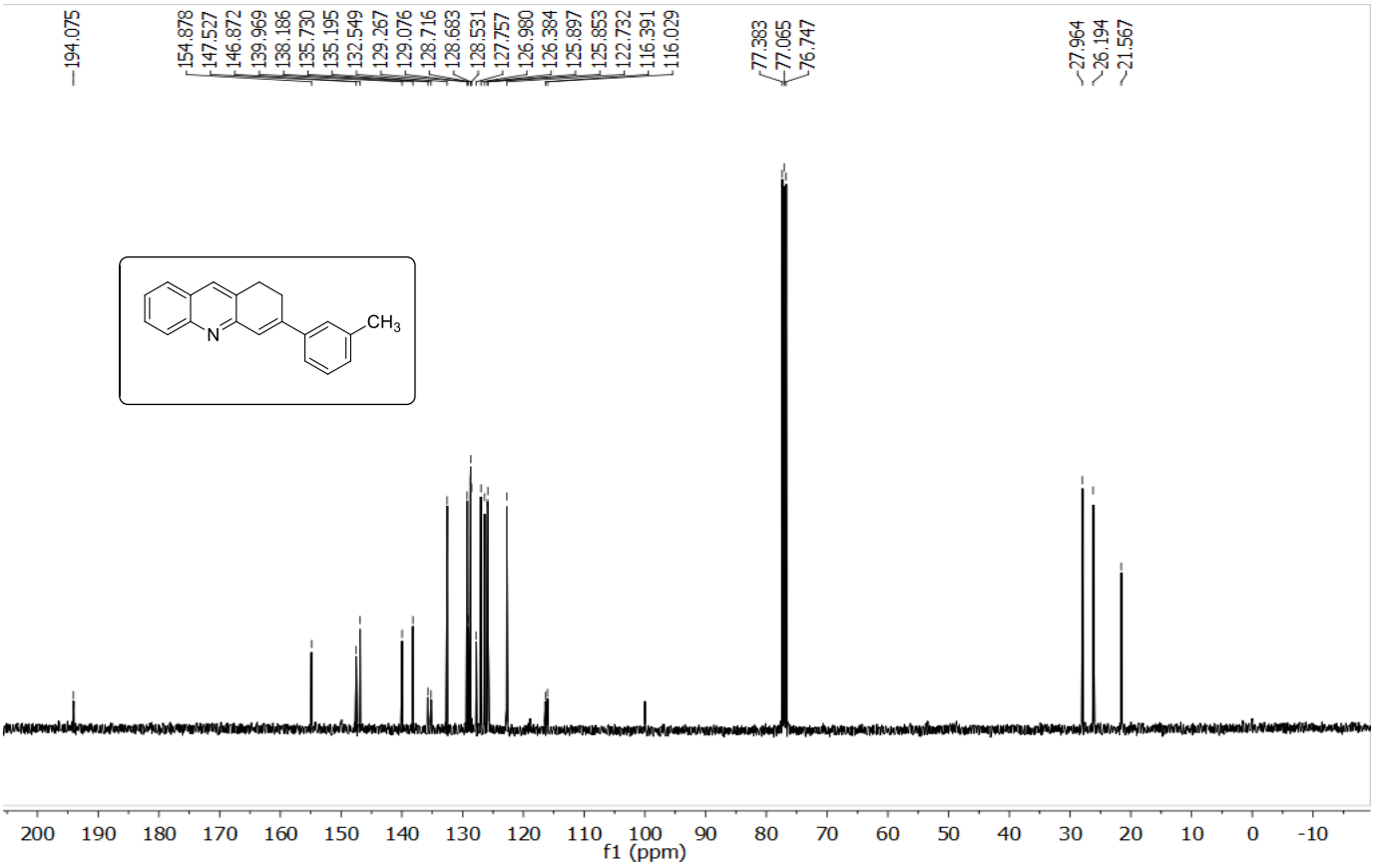


3-(o-tolyl)-1,2-dihydroacridine (7e):

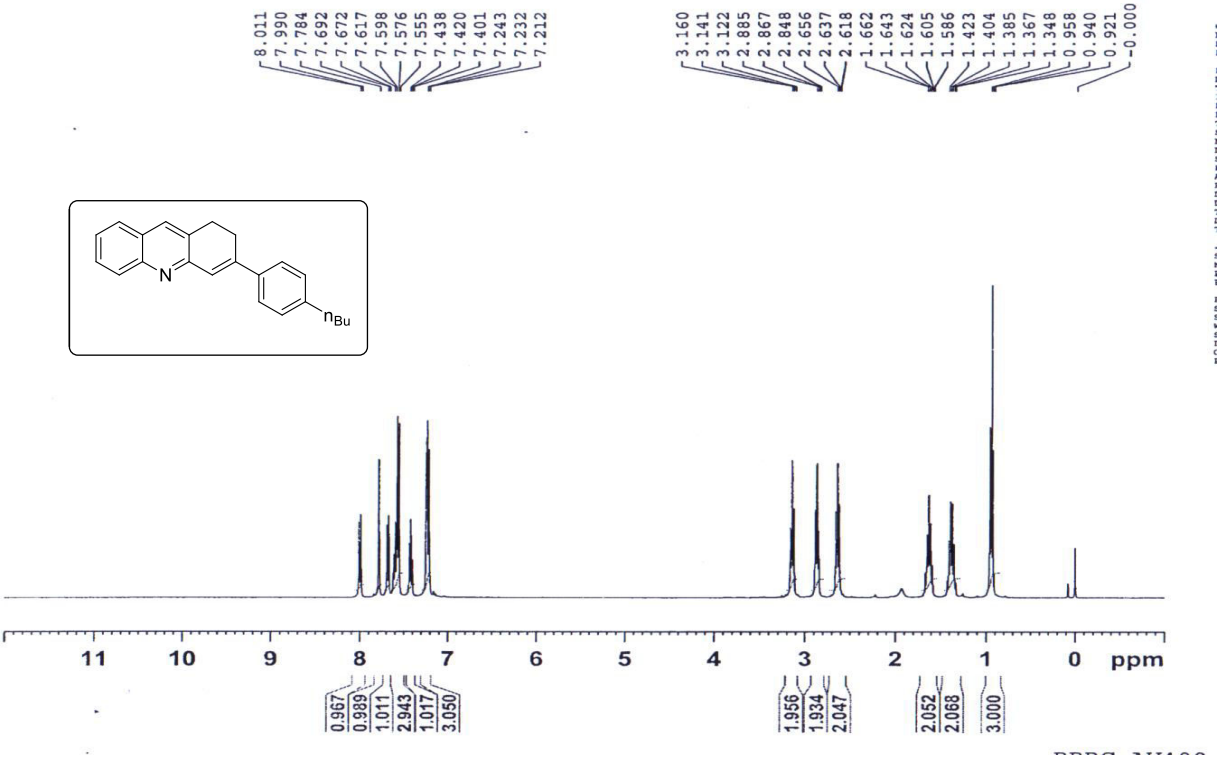


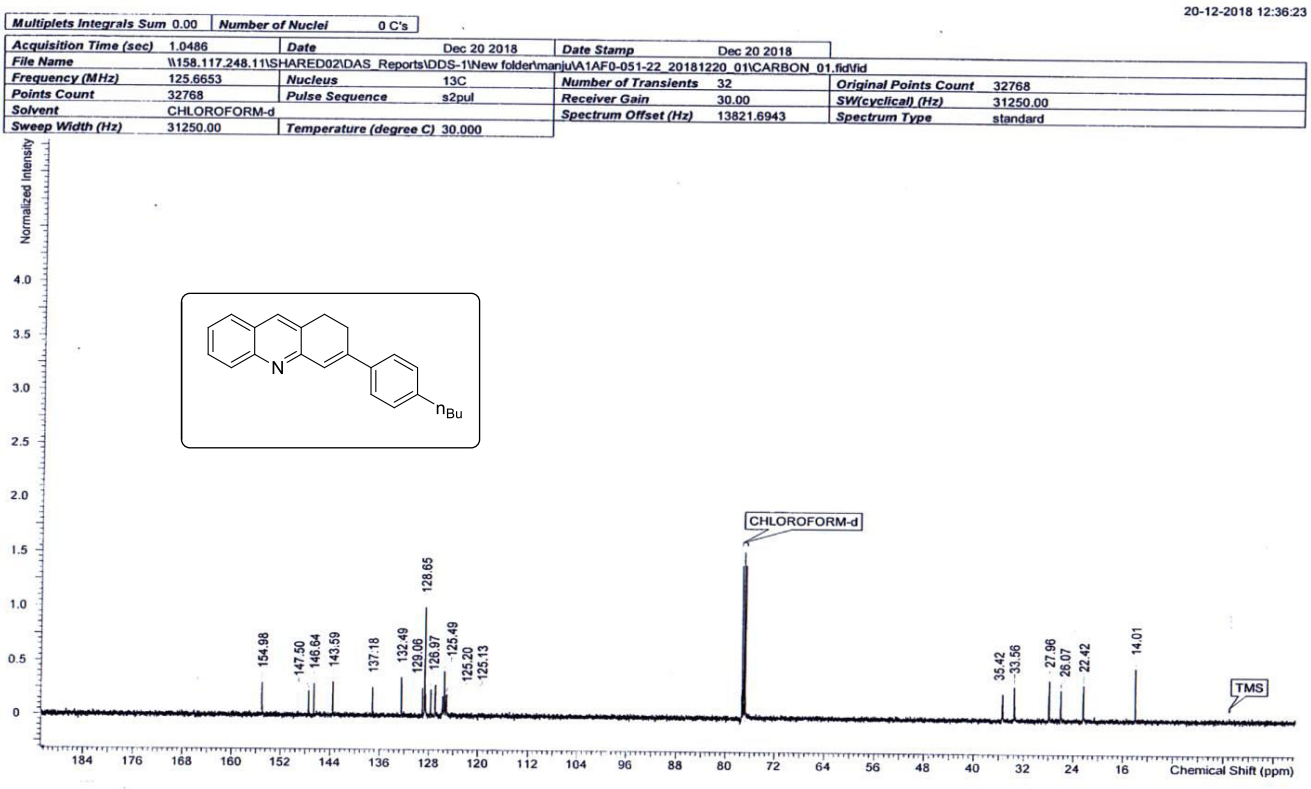


3-(m-tolyl)-1,2-dihydroacridine (7f):

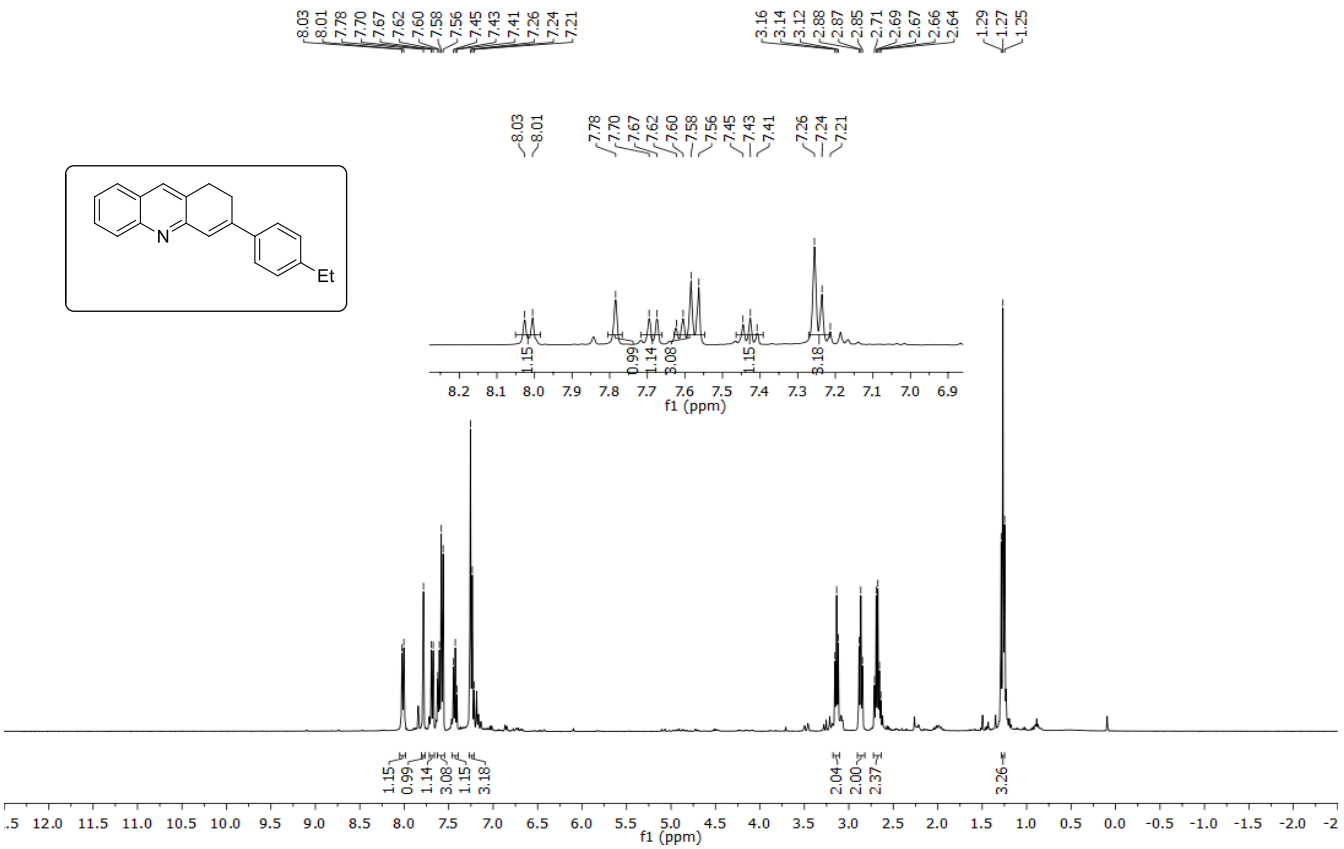


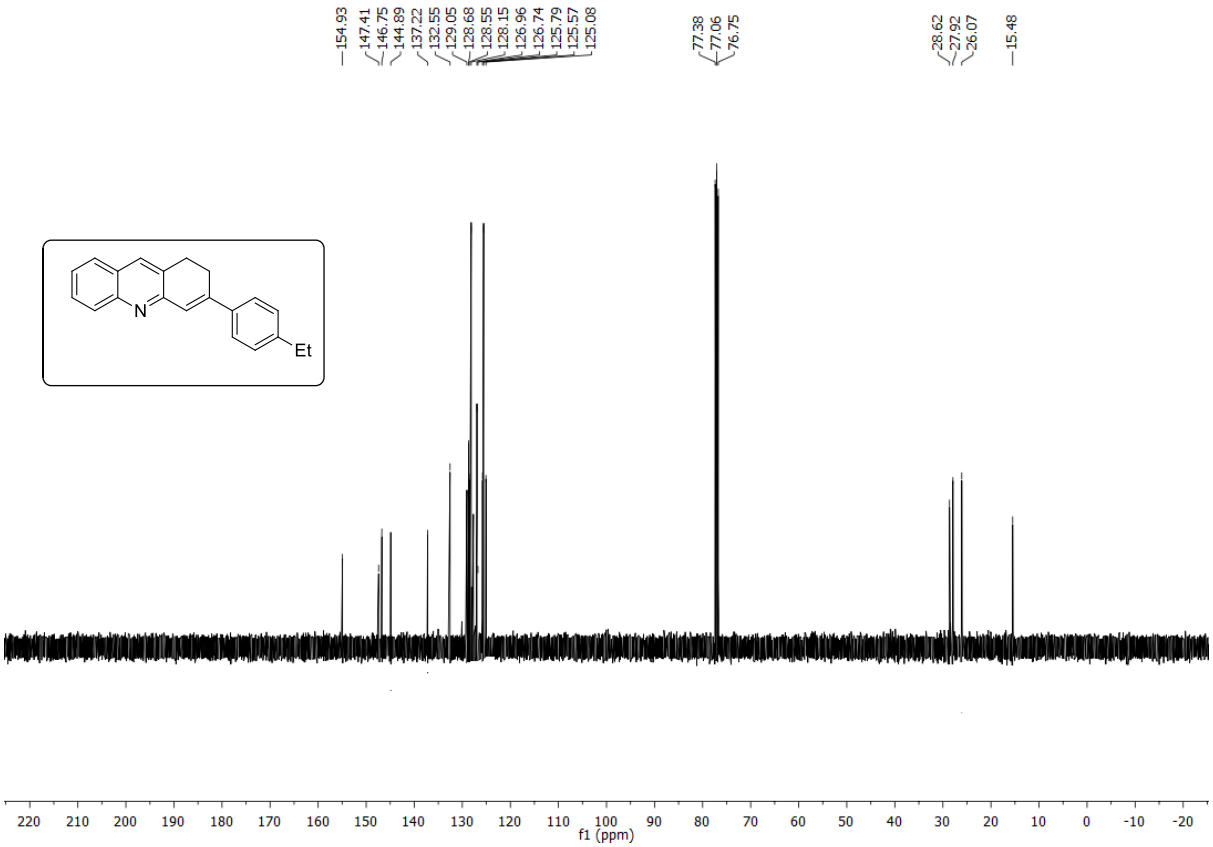
3-(4-butylphenyl)-1,2-dihydroacridine (7g):



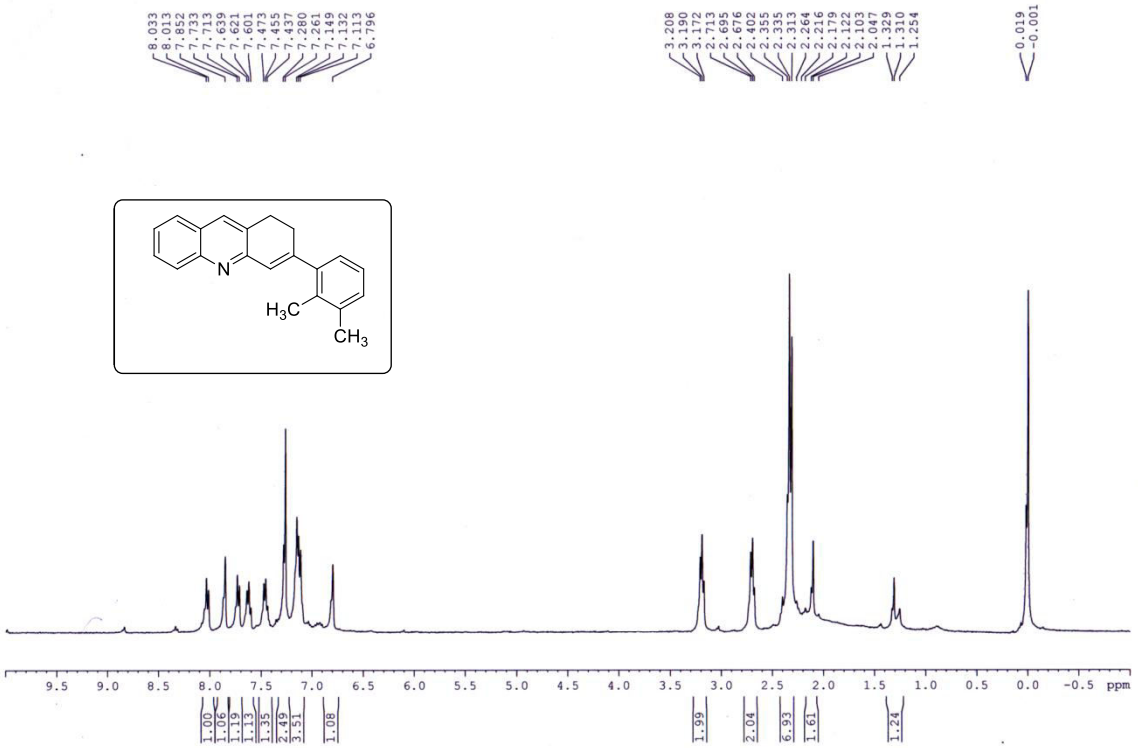


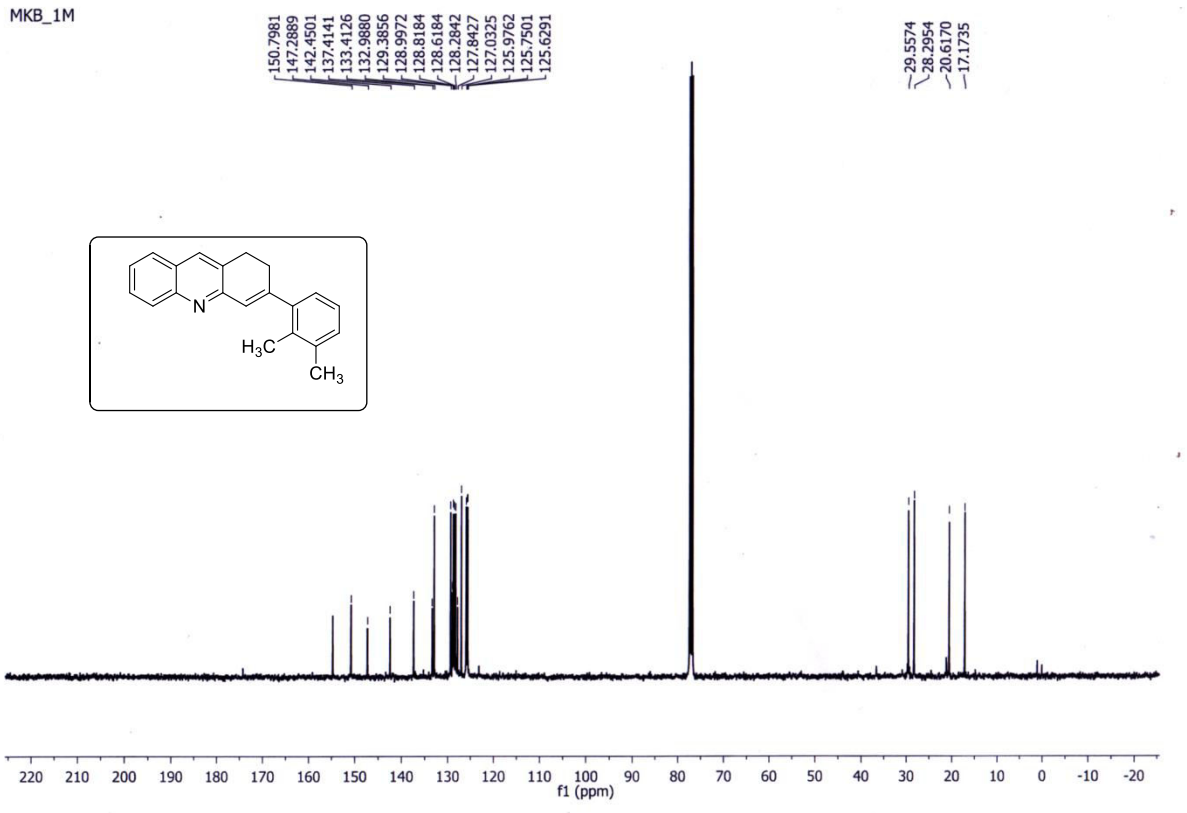
3-(4-ethylphenyl)-1,2-dihydroacridine (7h):



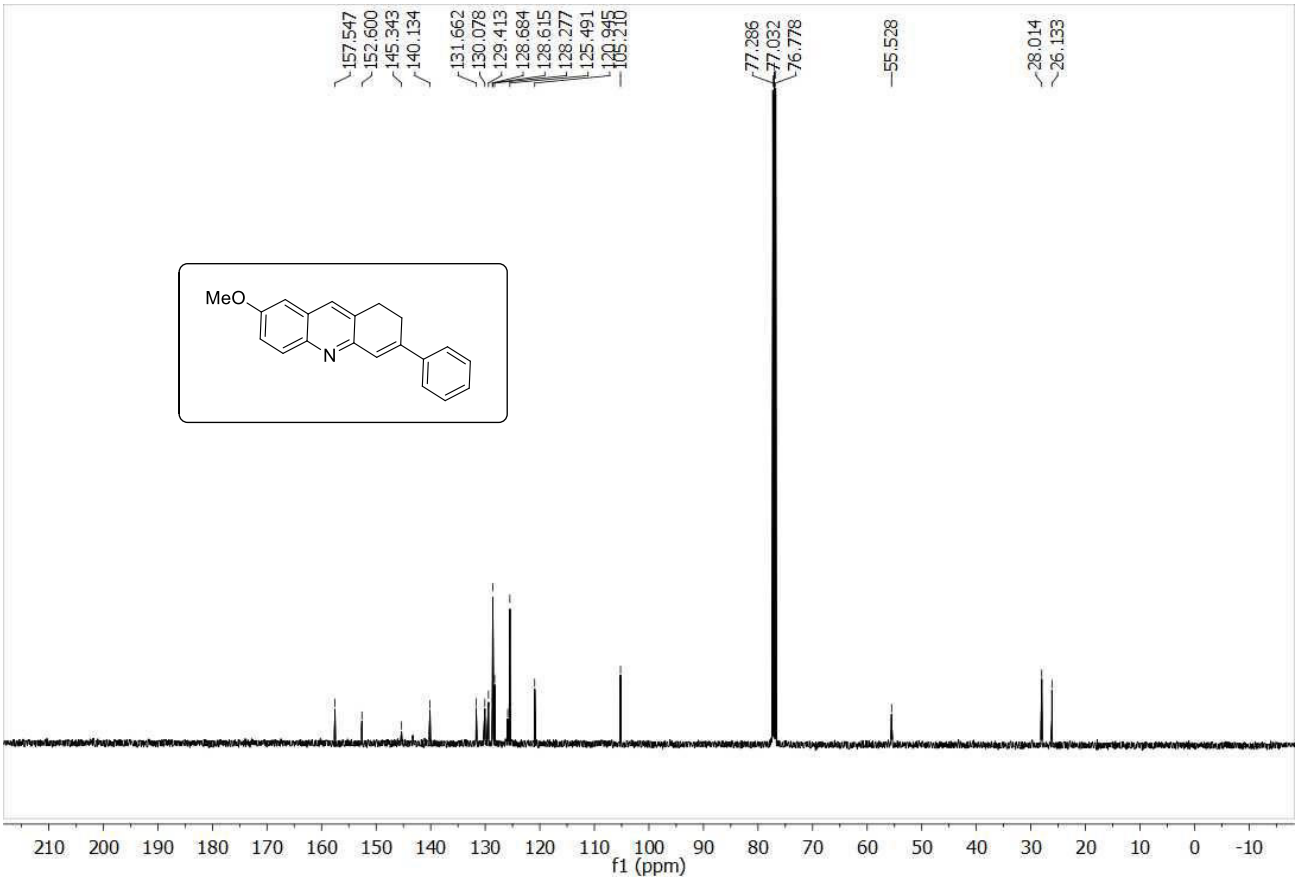


3-(2,3-dimethylphenyl)-1,2-dihydroacridine (7i):

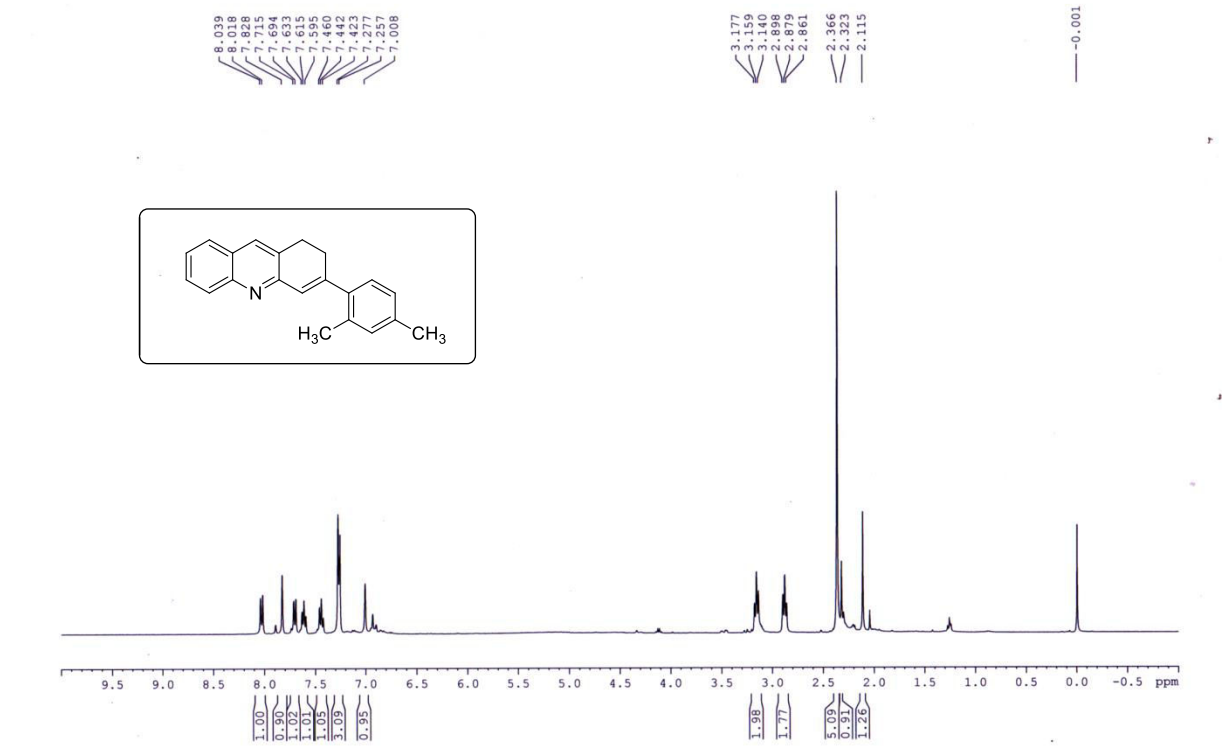


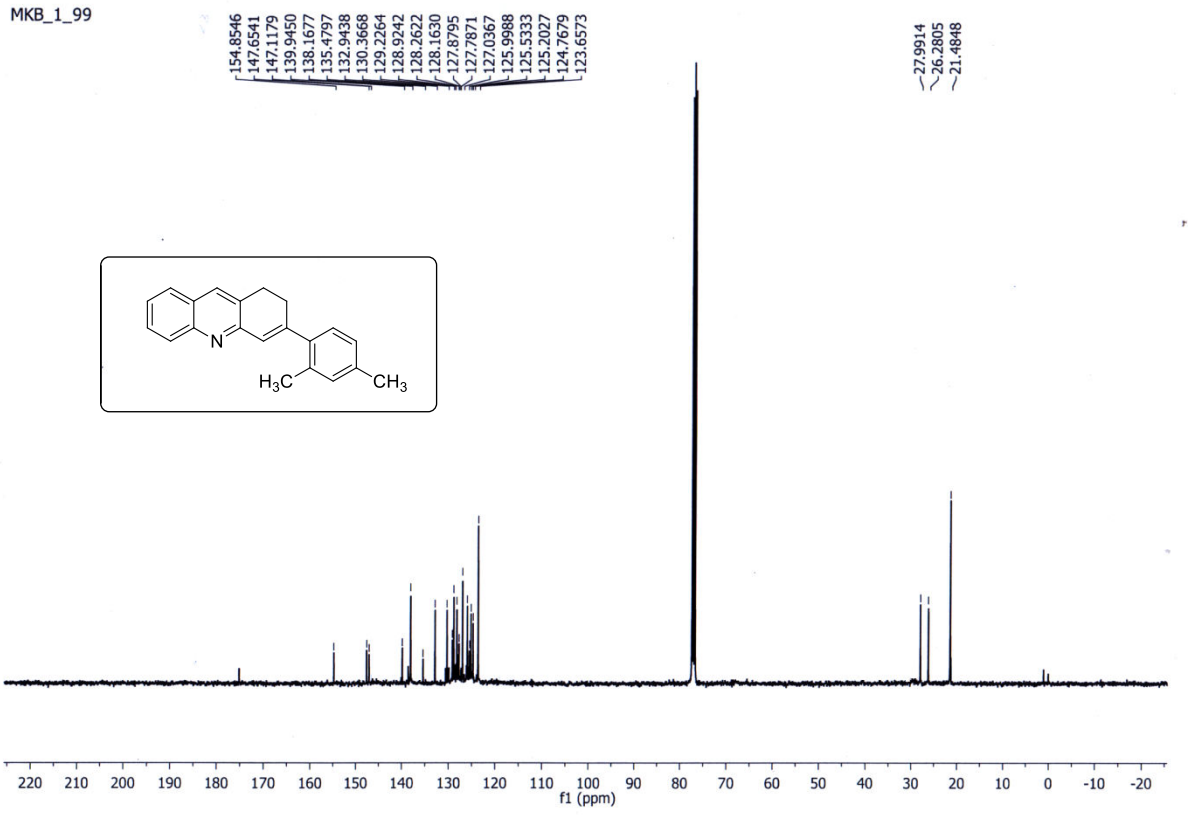


7-methoxy-3-phenyl-1,2-dihydroacridine (7j):

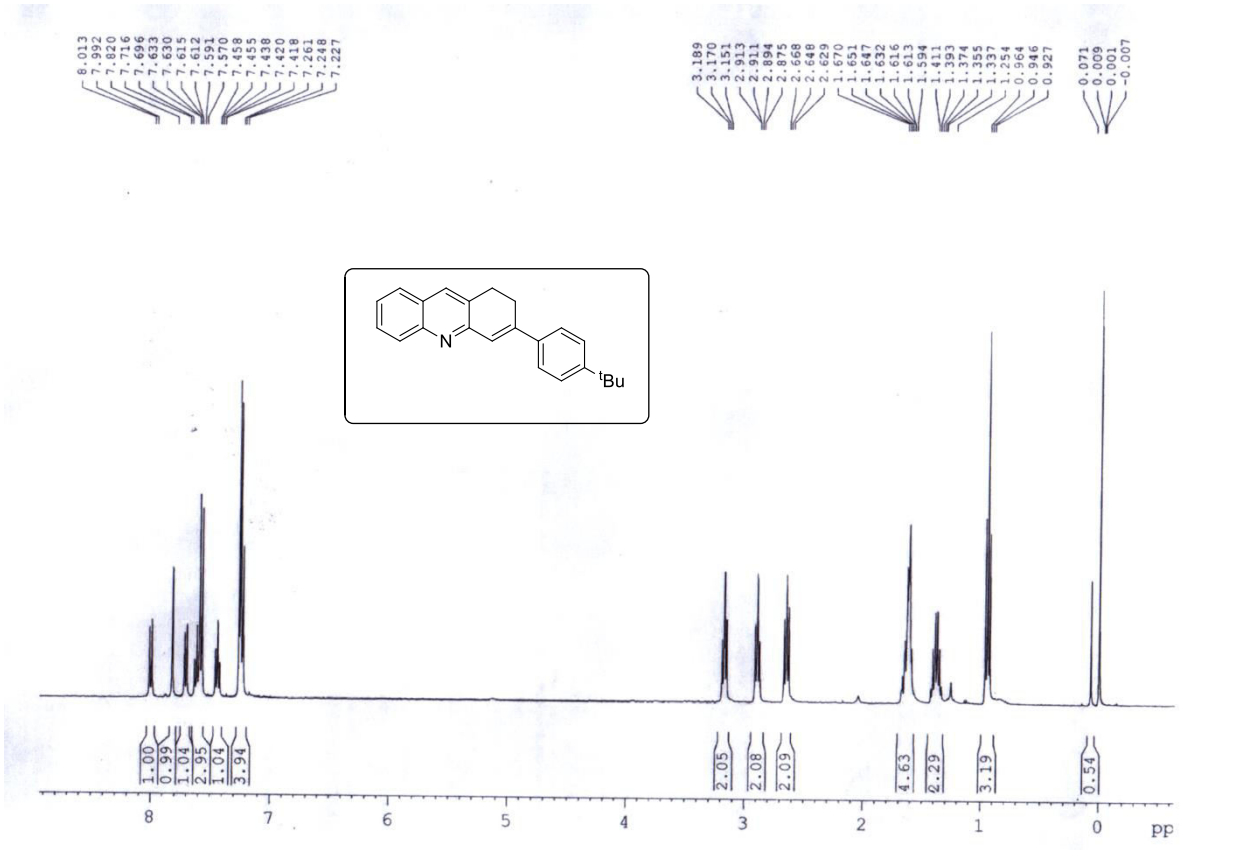


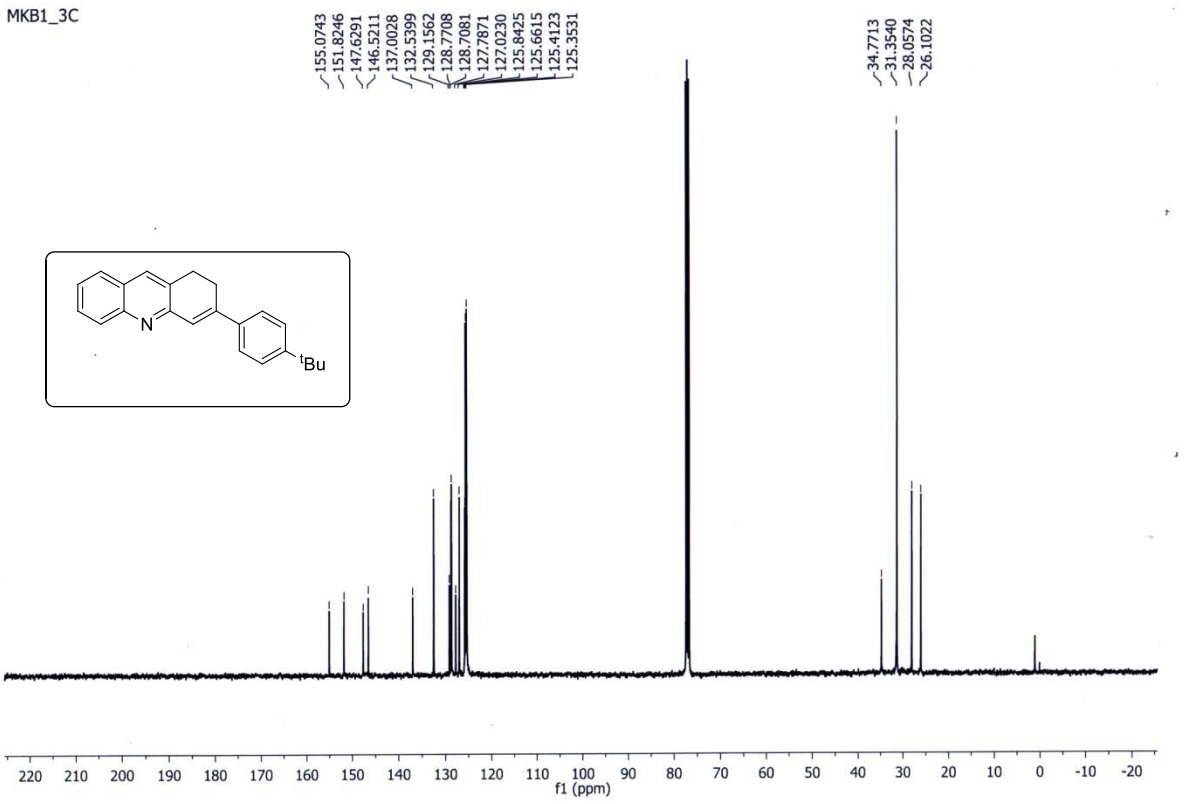
3-(2,4-dimethylphenyl)-1,2-dihydroacridine (7k) :



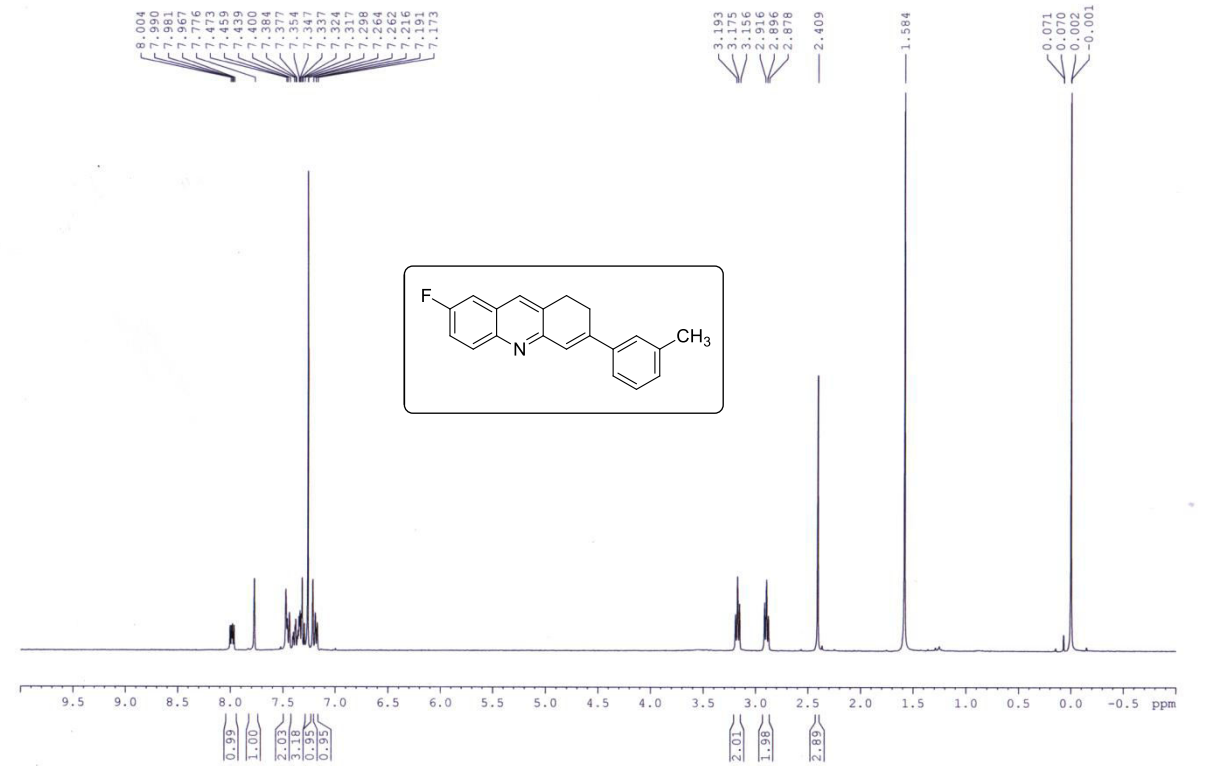


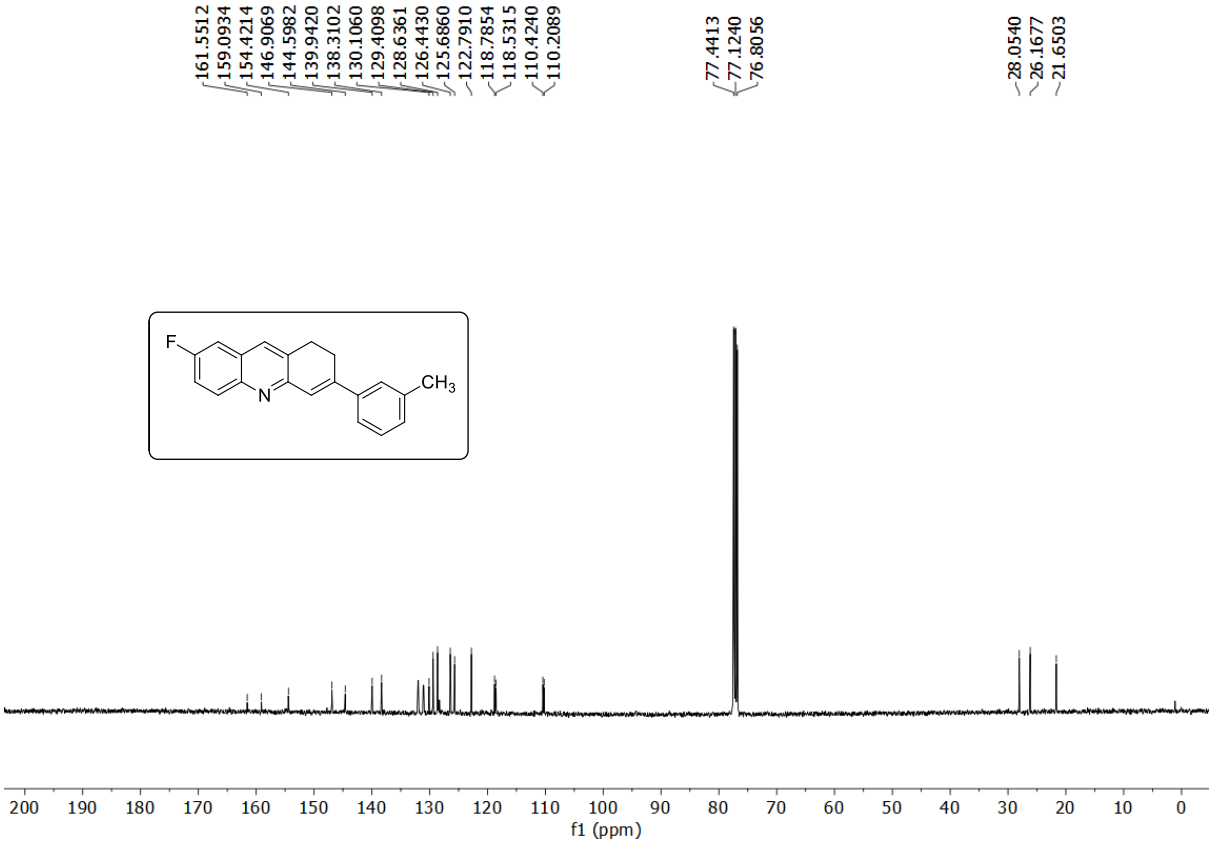
3-(4-(tert-butyl)phenyl)-1,2-dihydroacridine (7l):





7-fluoro-3-(m-tolyl)-1,2-dihydroacridine (7m):





6-bromo-3-(4-butylphenyl)-1,2-dihydroacridine (7n):