
Supporting Information

**Cu(I)-Catalyzed Addition-Cycloisomerization Difunctionalization Reaction of
1,3-Enyne-Alkylidenecyclopropanes (ACPs)**

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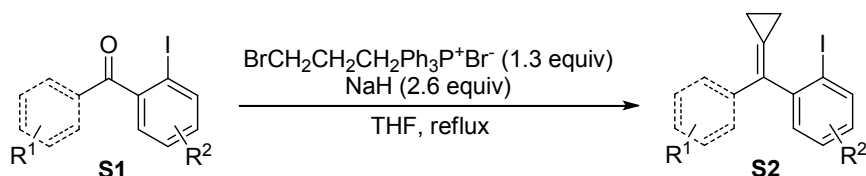
Fax: (+86)-21-6416-6128; e-mail: mshi@mail.sioc.ac.cn

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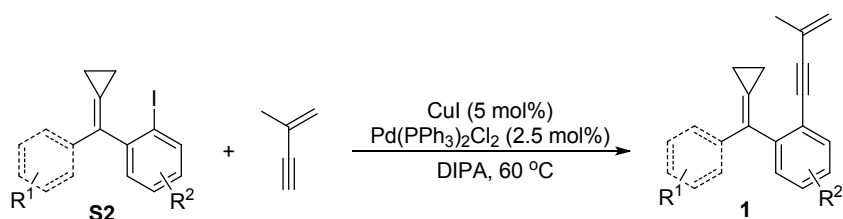
1 General procedure for the preparation of starting materials

1.1 Preparation of substrates 1a-1k



Preparation of substrates **S2**

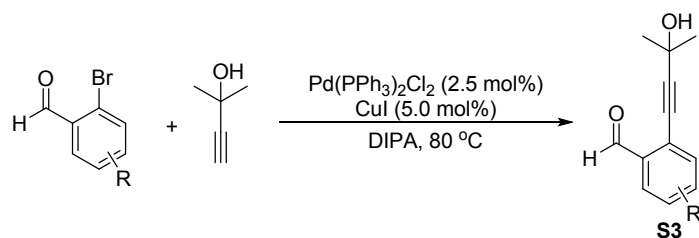
A solution of (4-bromobutyl)triphenylphosphonium bromide (1.3 equiv) and NaH (2.6 equiv) in THF (25 mL) was stirred at 70 °C under N_2 for 2-6 h. Upon the reaction system becomes orange, the compound **S1**¹ (1.0 equiv) in THF (10 mL) was added after 0.5 h. The reaction mixture was stirred for another 4-10 h until the completion of compound **S1**. The reaction mixture was cooled to room temperature and filtered through a celite. The filtrate was concentrated under reduced pressure and the residue was purified by a silica gel flash chromatography (eluent: petroleum ether) to afford the products **S2** in moderate yields.



Preparation of substrates 1a-1k

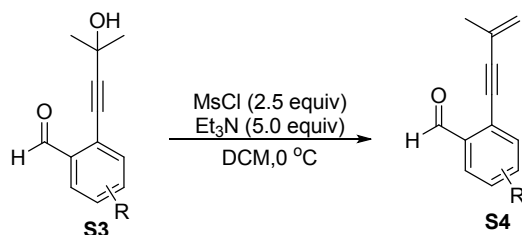
To a stirred solution of **S2** (1.0 equiv) and 2-methyl-1-buten-3-yne (1.2 equiv) in degassed diisopropylamine (DIPA) (30 mL) was added $\text{PdCl}_2(\text{PPh}_3)_2$ (2.5 mol%) and CuI (5 mol%). The resulted mixture was stirred at 60 °C for 4 h. After the separation of ammonium salt by filtration and the removal of solvent under reduced pressure, the residue was purified by a column chromatography on silica gel (eluent: petroleum ether) to afford the corresponding products **1a-1k** in moderate yields.

1.2 Preparation of substrates 11-1v



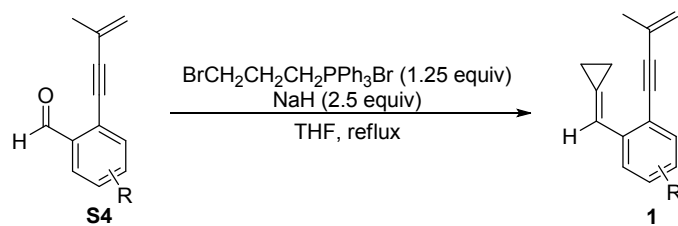
Preparation of substrates **S3**

To a stirred solution of substituted 2-bromobenzaldehyde (1.0 equiv) and 3-methyl butynol (1.2 equiv) in degassed diisopropylamine (DIPA) (30 mL) was added PdCl₂(PPh₃)₂ (2.5 mol%) and CuI (5 mol%). The resulted mixture was stirred at 80 °C overnight. After the separation of ammonium salt by filtration and the removal of solvent under reduced pressure, the residue was purified by a column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10/1) to afford the corresponding products **S3** in excellent yields.



Preparation of substrates **S4**²

To a stirred solution of **S3** (1.0 equiv) in dry dichloromethane (DCM) (15 mL) was added Et₃N (5.0 equiv) and methanesulfonyl chloride (MsCl) (2.5 equiv) at 0 °C sequentially and slowly. The resulted mixture was stirred at 0 °C for 30-60 min. Upon completion, the reaction was quenched by addition of water, and washed with a saturated NaCl solution, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by a column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 25/1) to afford the corresponding products **S4** in good yields.

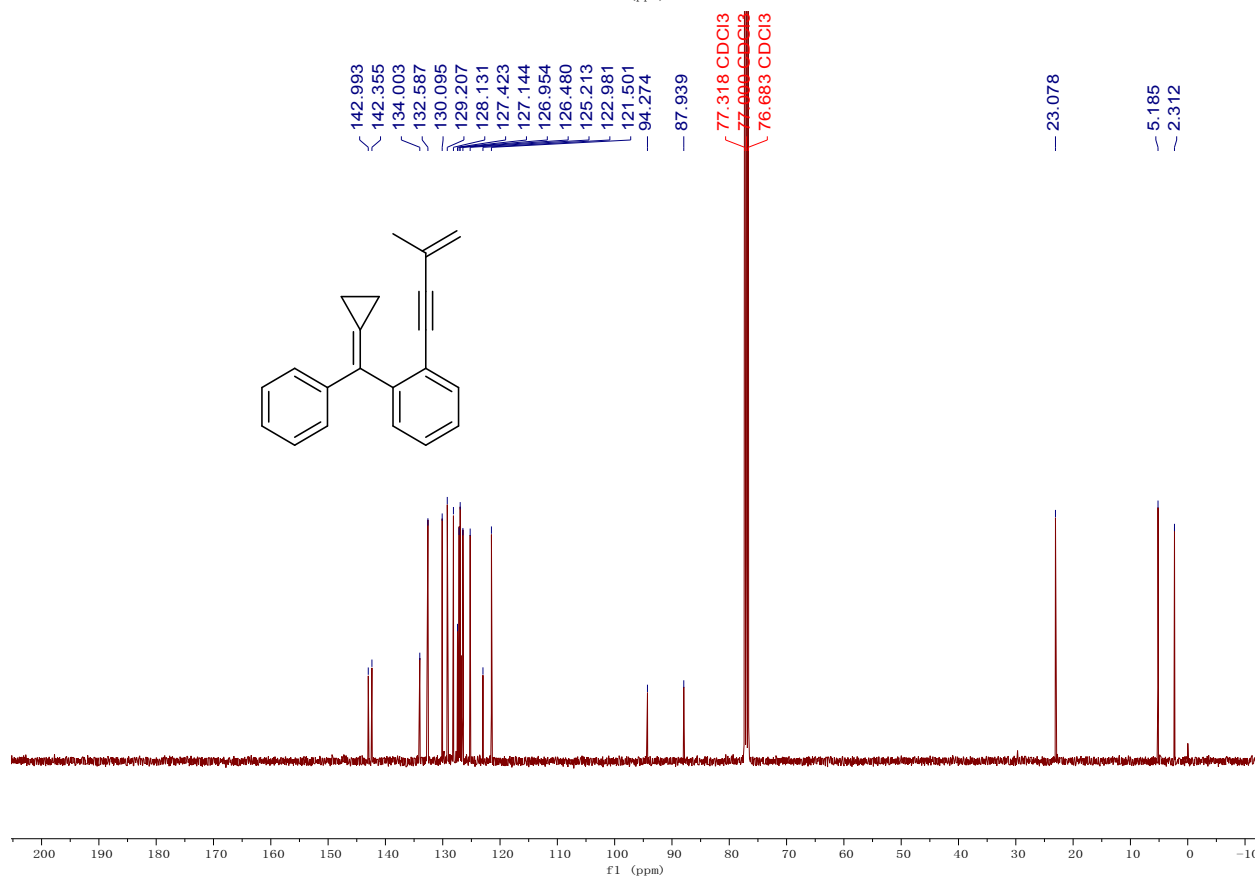
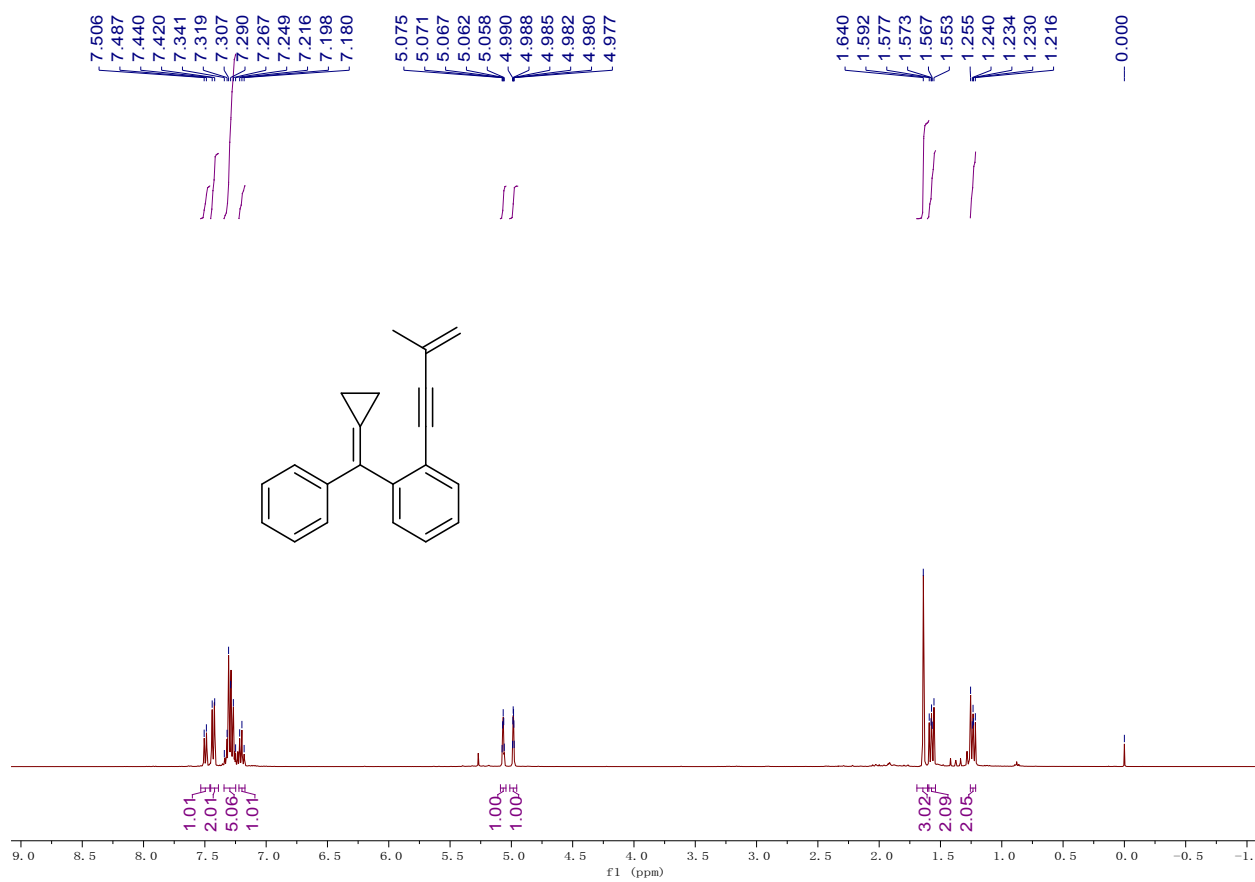


Preparation of substrates **11-1v**

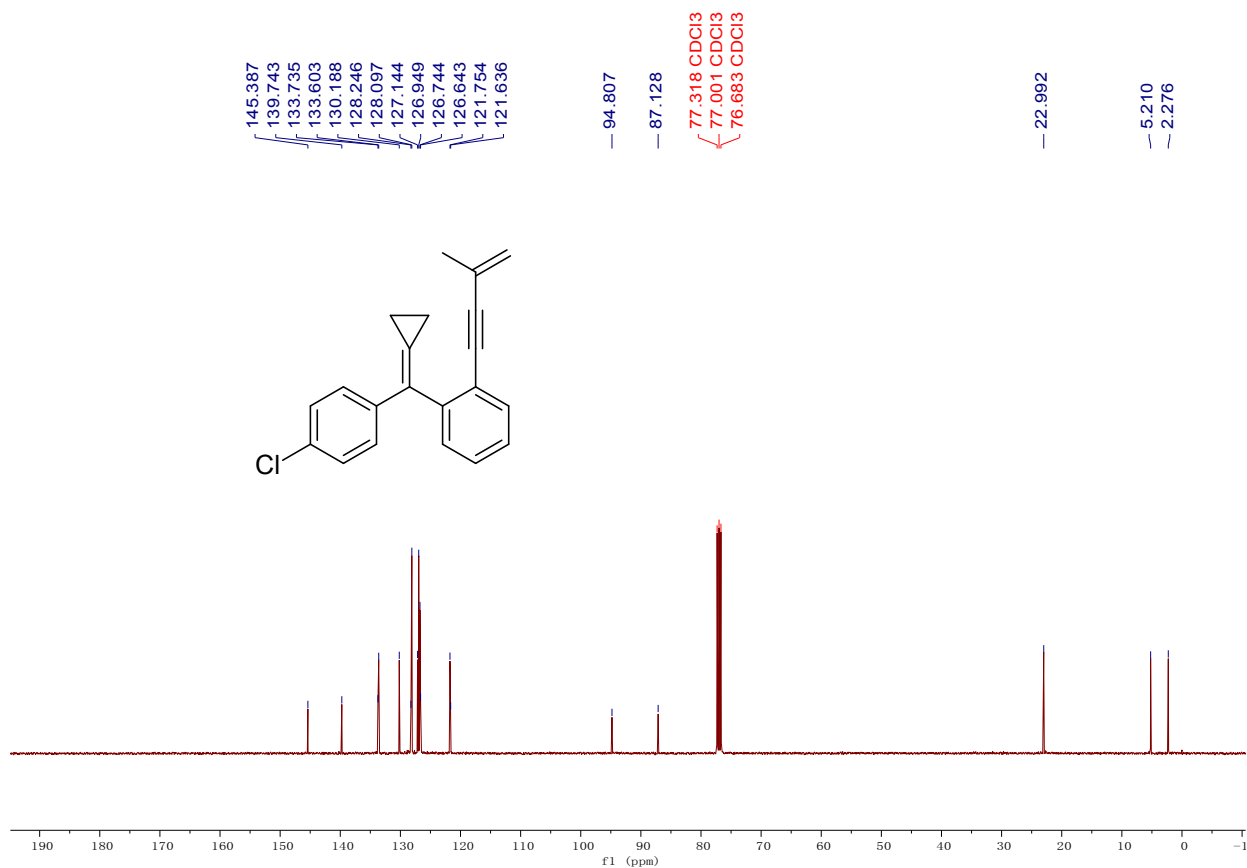
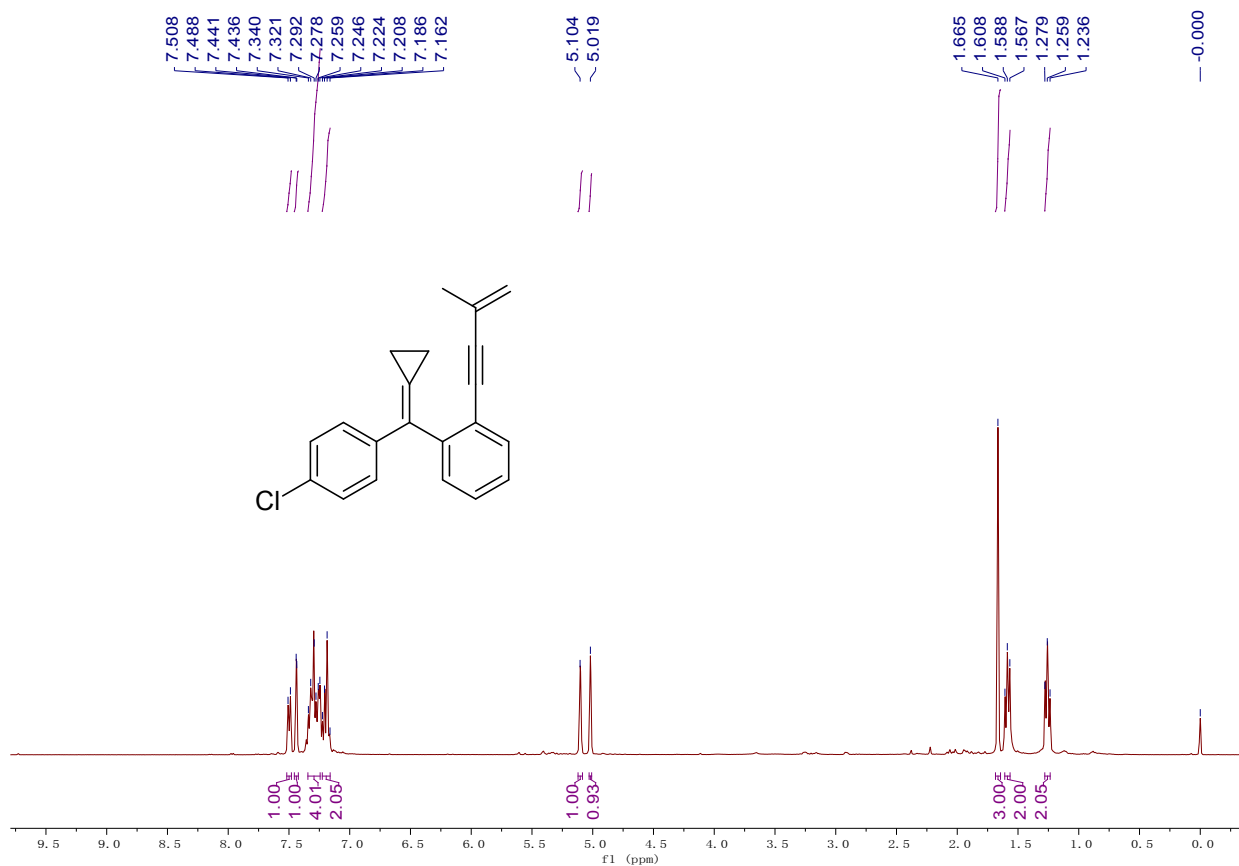
A solution of compound **S4** (1.0 equiv), (4-bromobutyl)triphenylphosphonium bromide (1.3 equiv) and NaH (2.6 equiv) in THF (25 mL) was stirred at 70 °C under N_2 for 12 h. Upon completion, the reaction mixture was cooled to room temperature and the mixture was filtered through a celite. The filtrate was concentrated under reduced pressure and the residue was purified by a silica gel flash chromatography (eluent: petroleum ether) to afford the products **11-1v** in moderate yields.

2 Copies of NMR spectra of all compounds

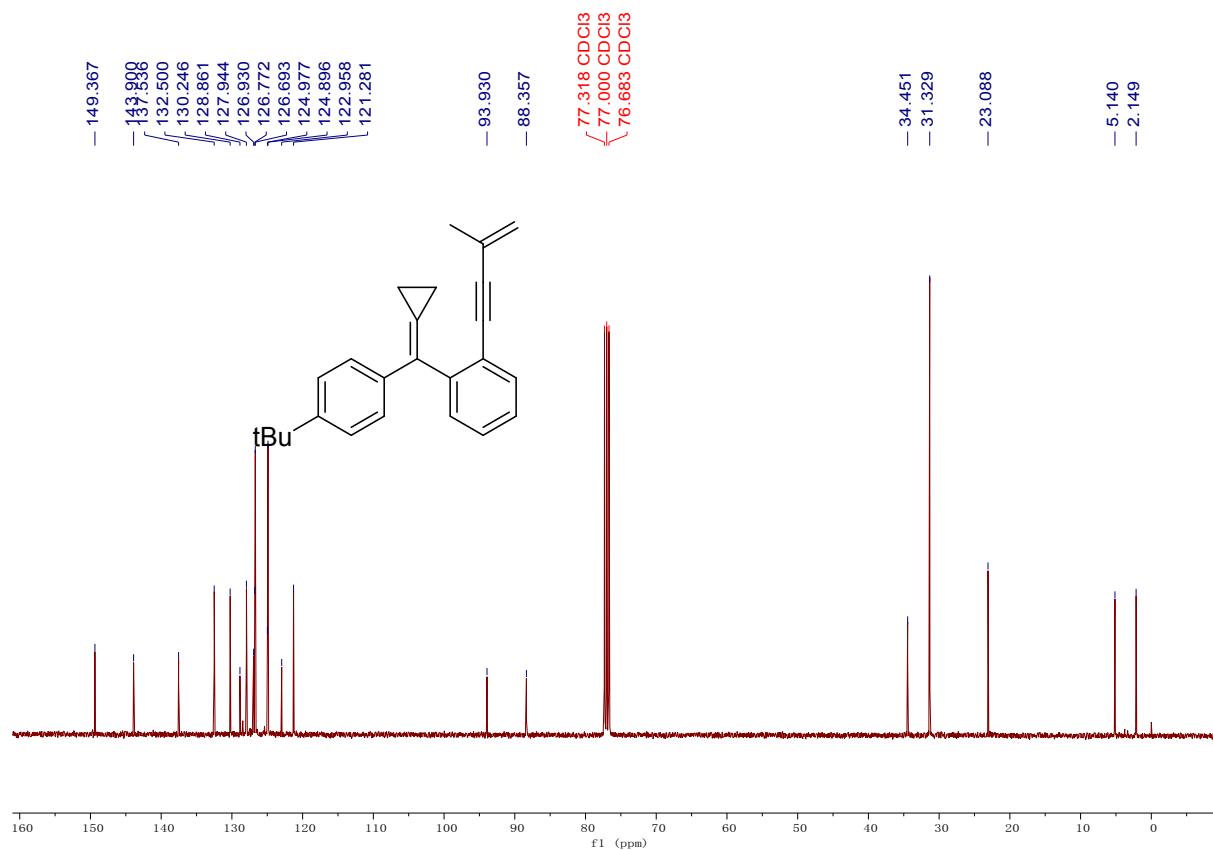
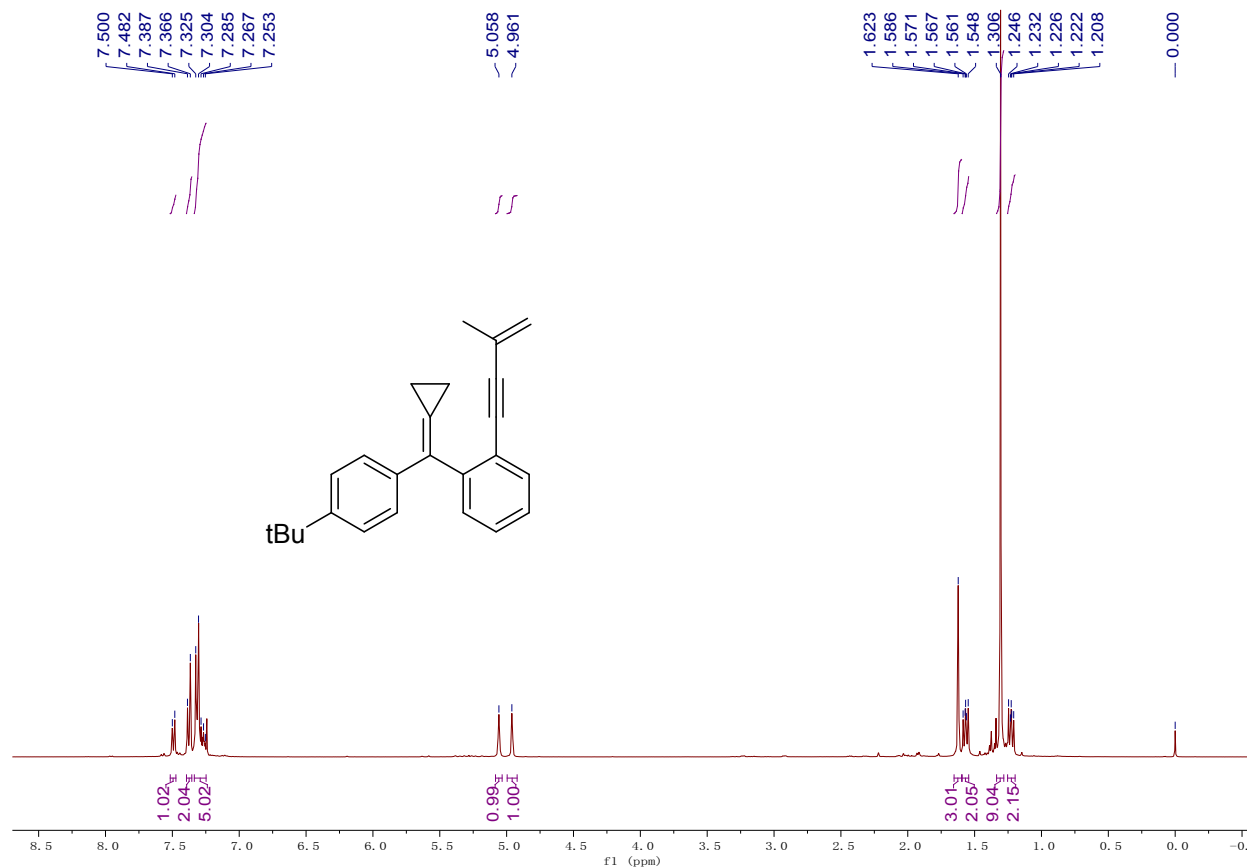
1-(cyclopropylidene(phenyl)methyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1a)



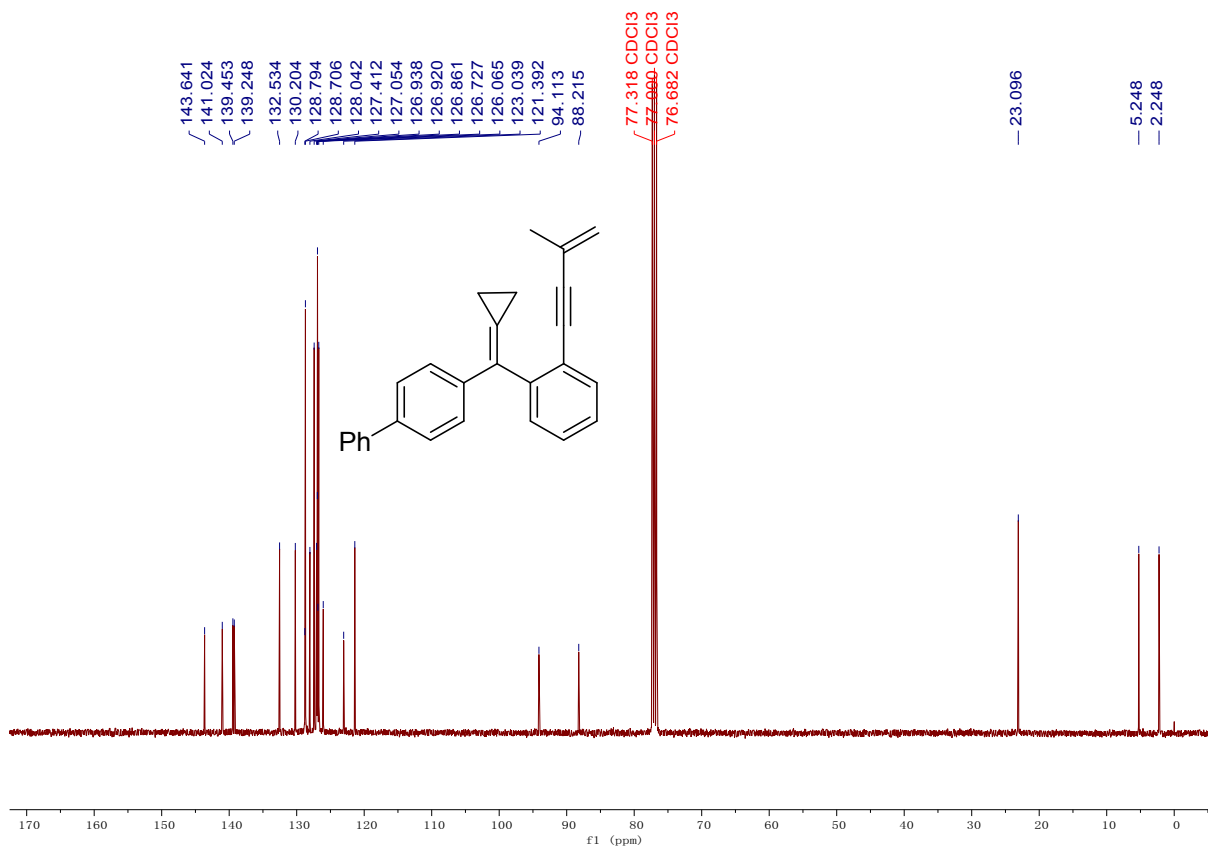
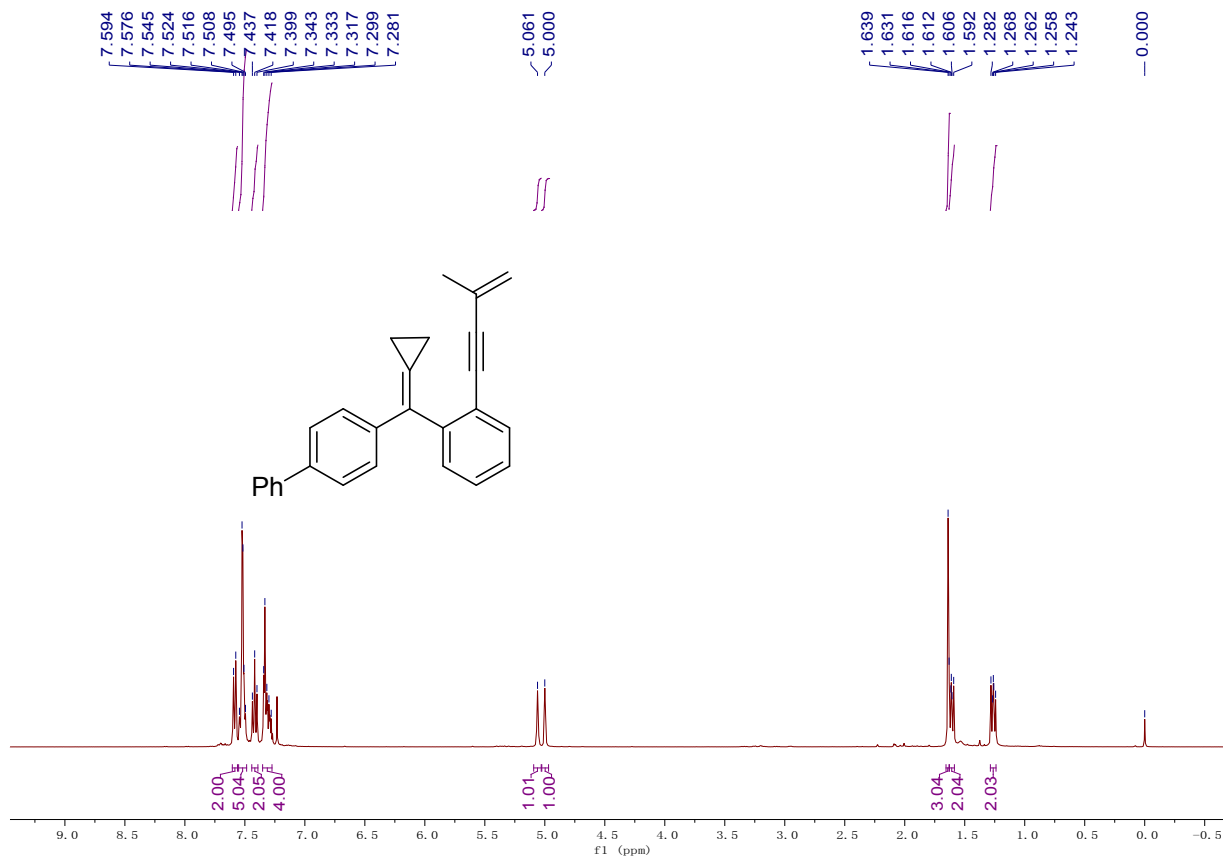
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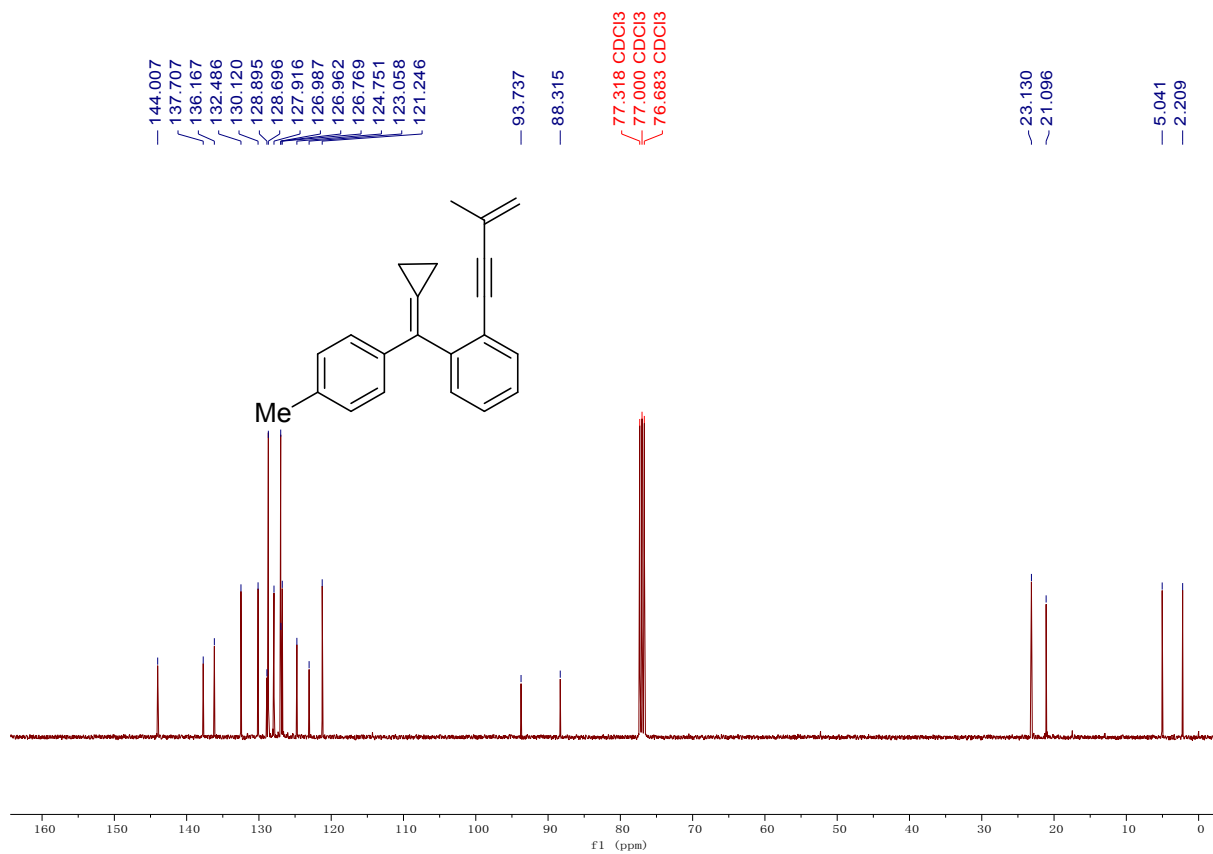
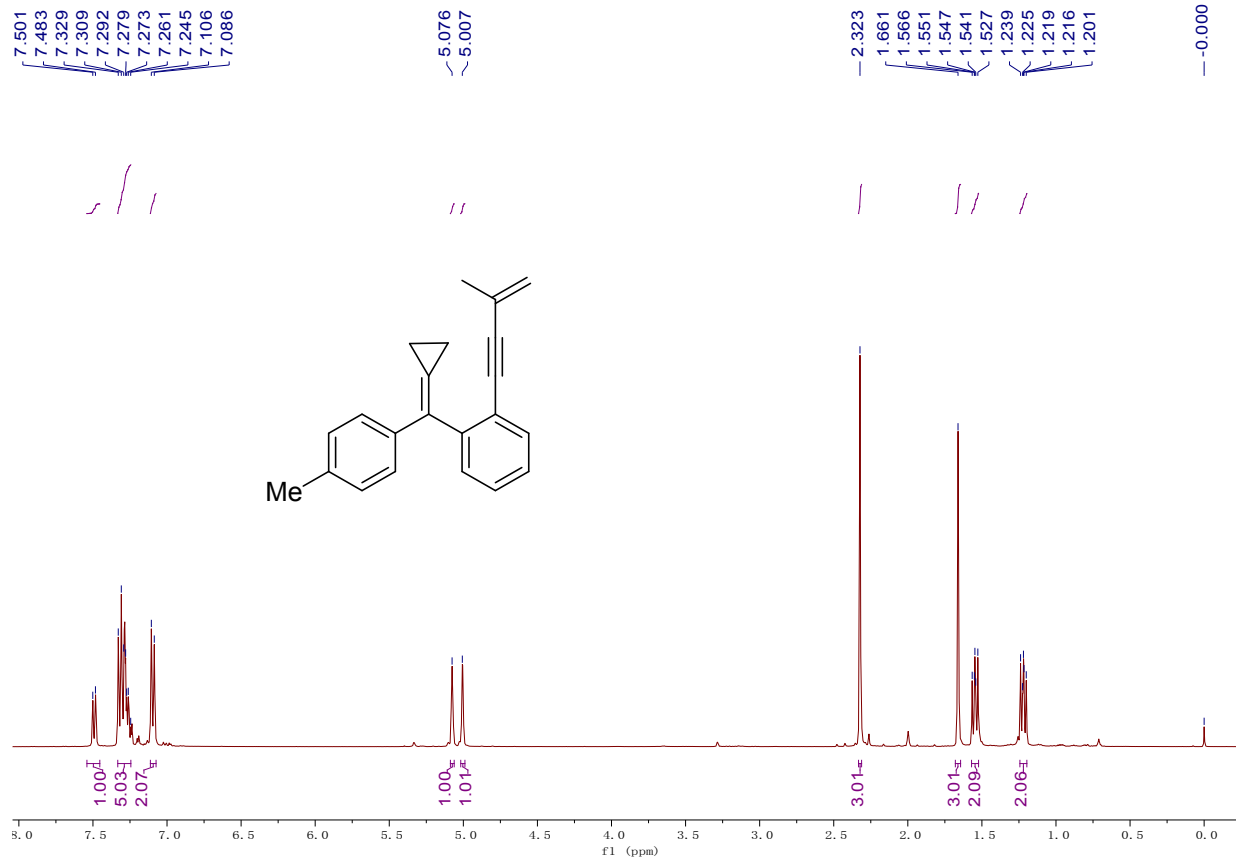
1-((4-(*tert*-butyl)phenyl)(cyclopropylidene)methyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1c)



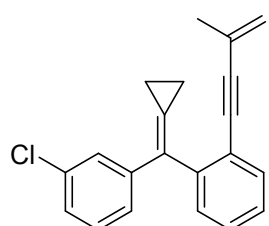
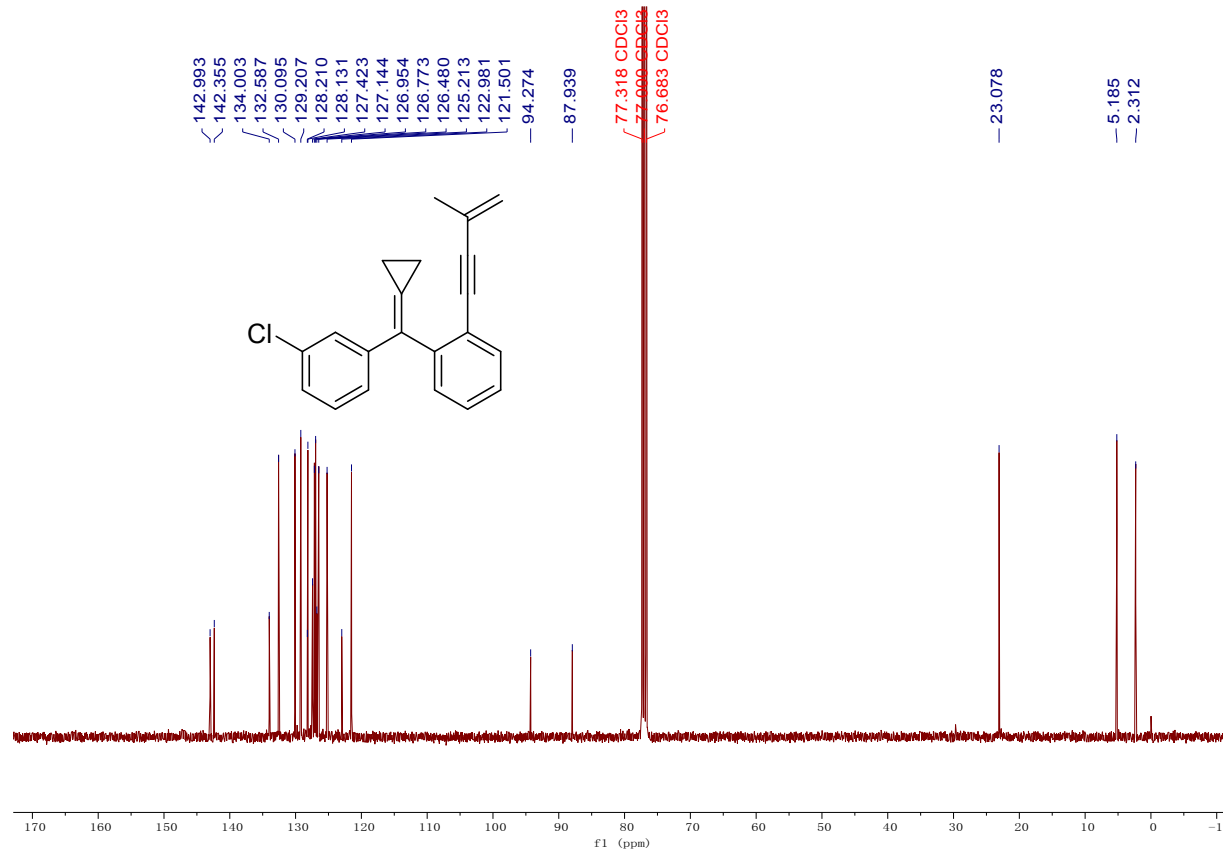
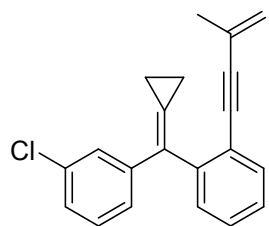
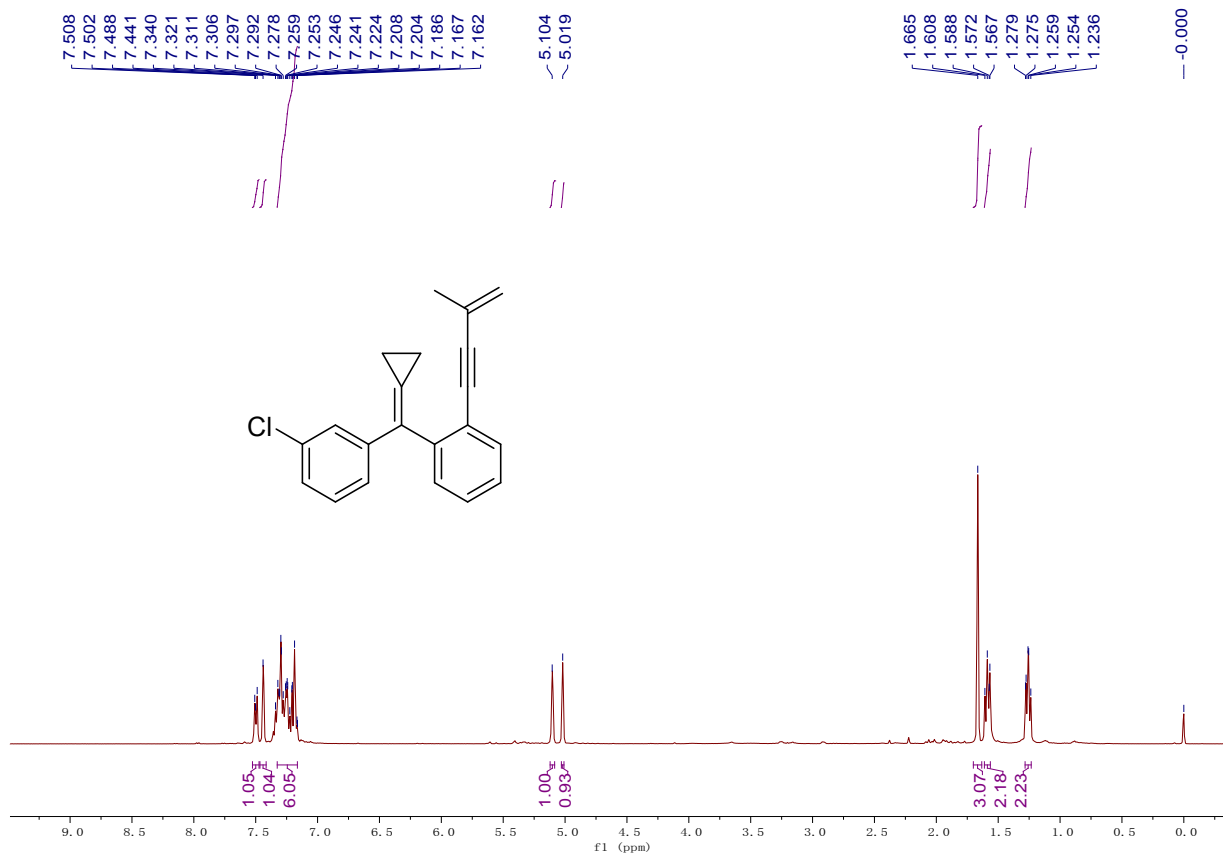
4-(cyclopropylidene(2-(3-methylbut-3-en-1-yn-1-yl)phenyl)methyl)-1,1'-biphenyl (1d)



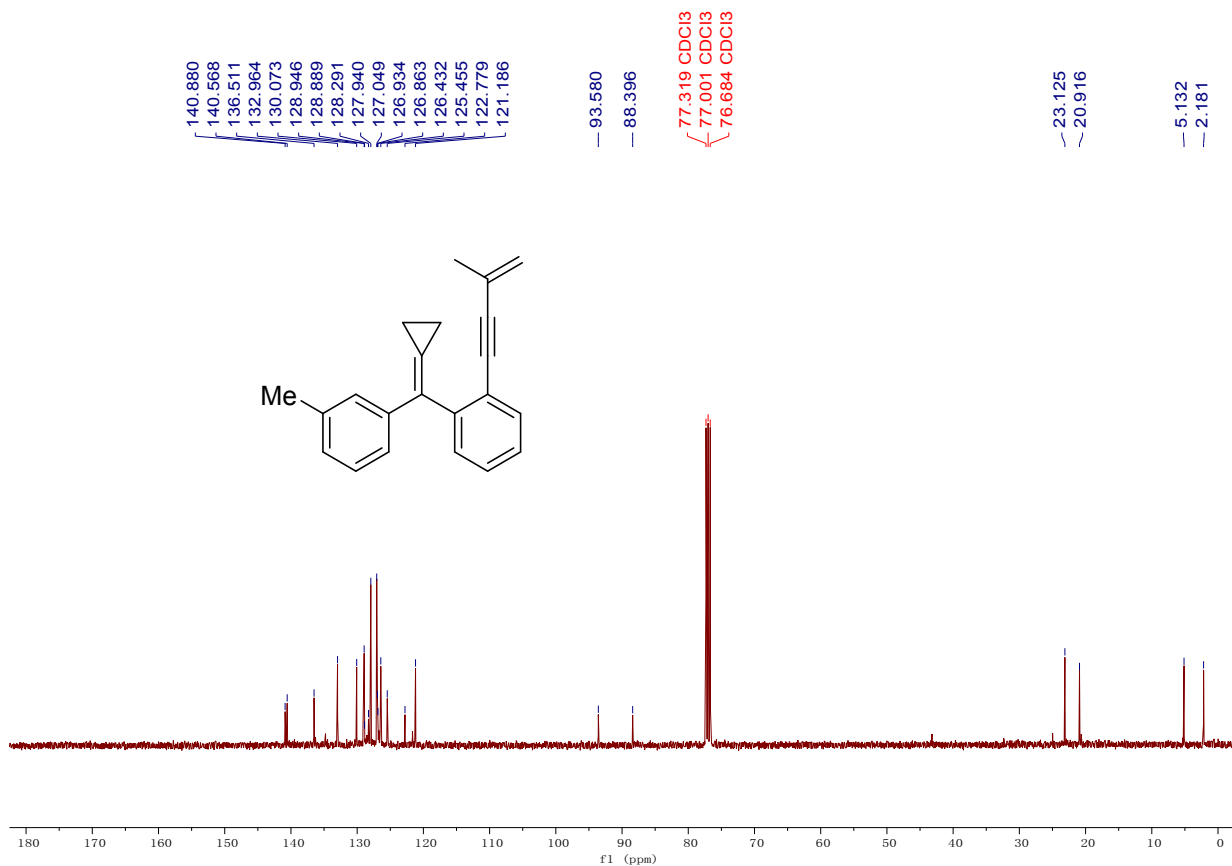
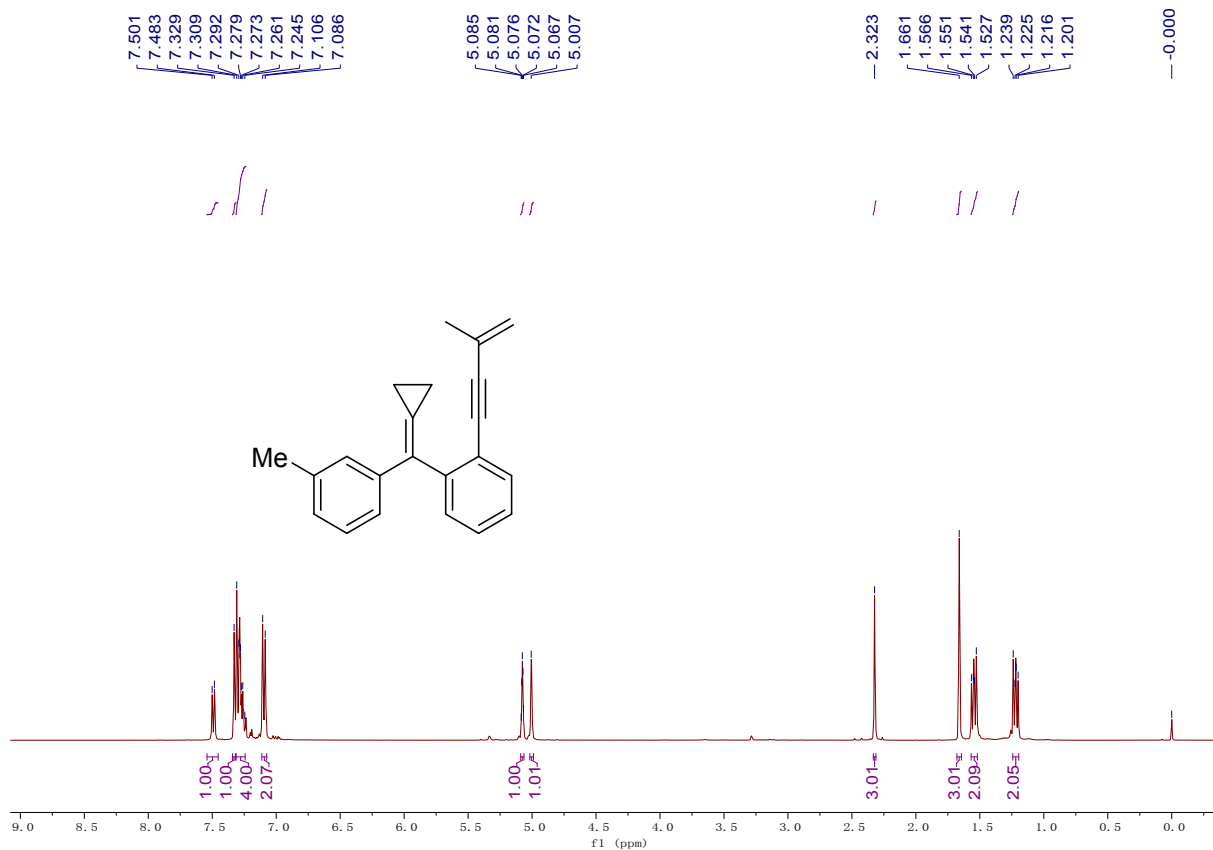
1-(cyclopropylidene(*p*-tolyl)methyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1e)



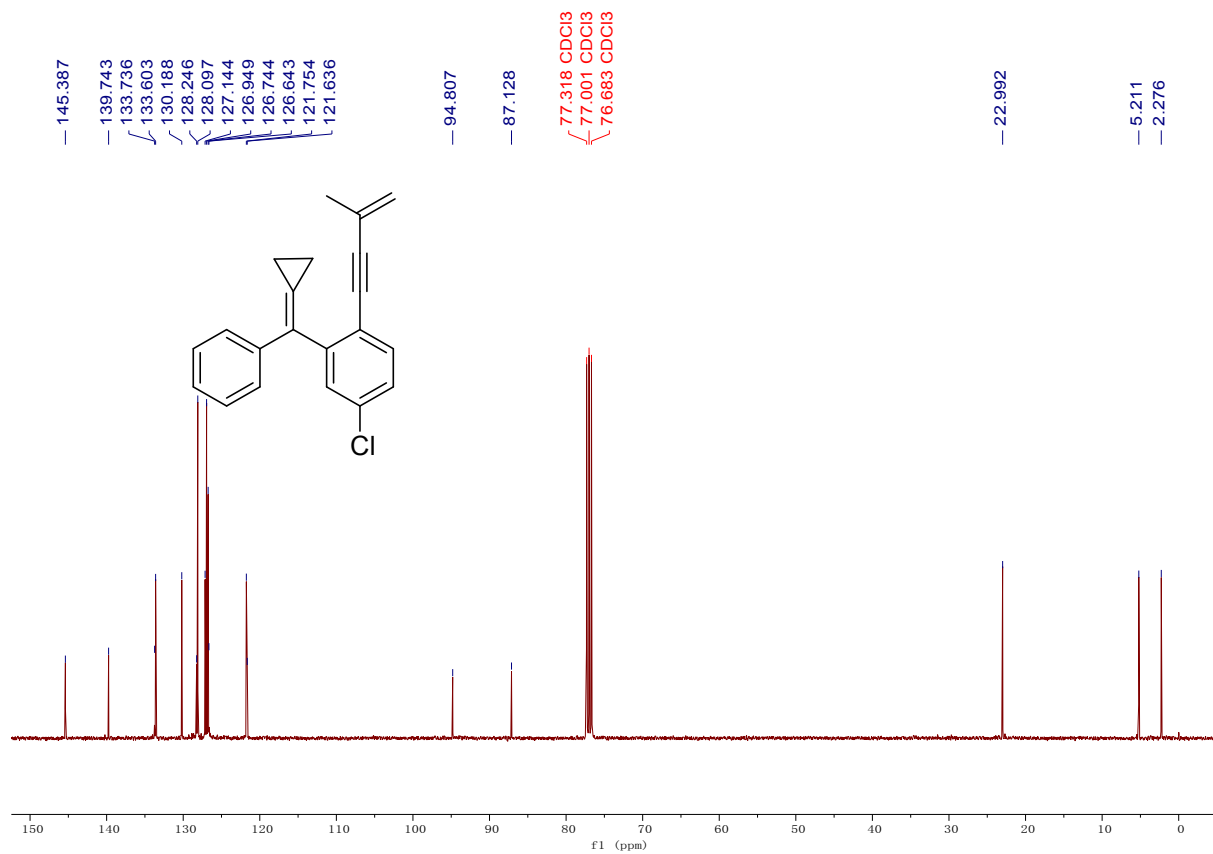
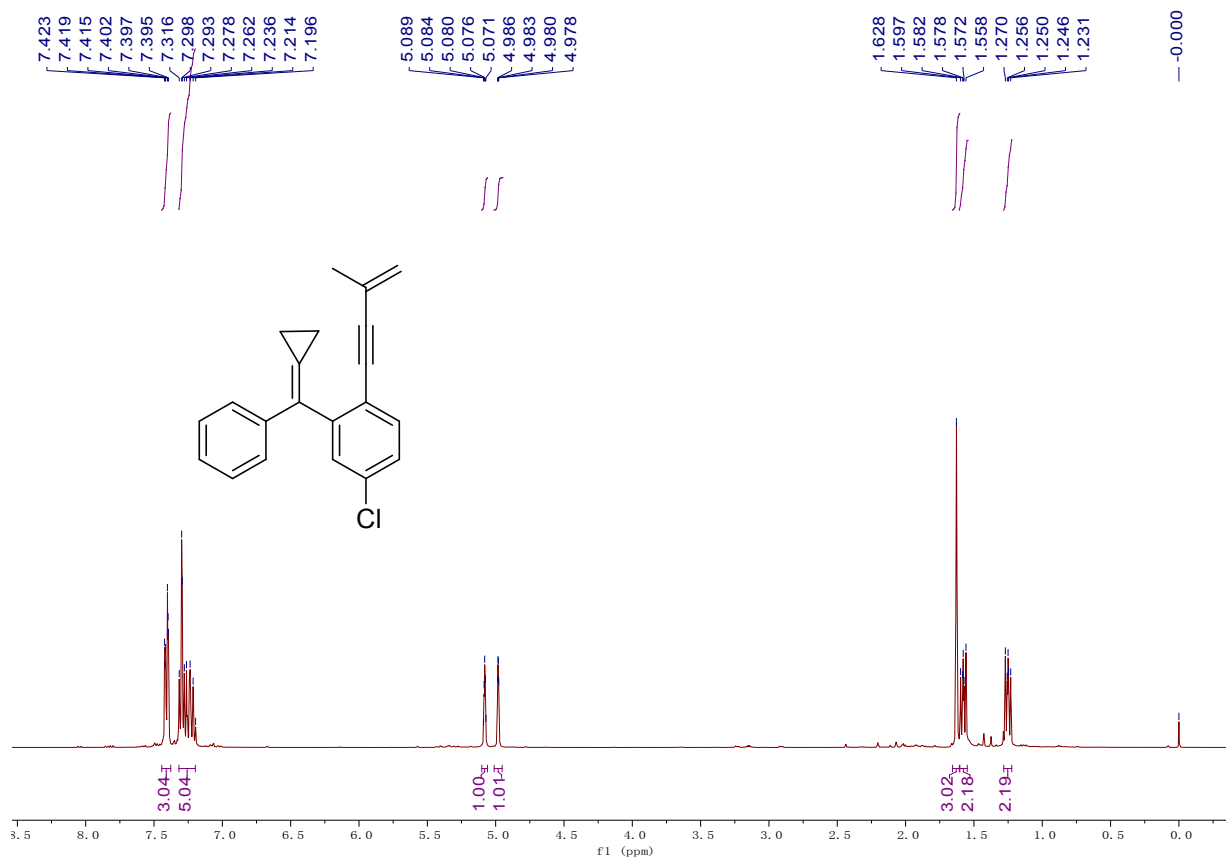
1-((3-chlorophenyl)(cyclopropylidene)methyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1f)



1-(cyclopropylidene(*m*-tolyl)methyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1g)

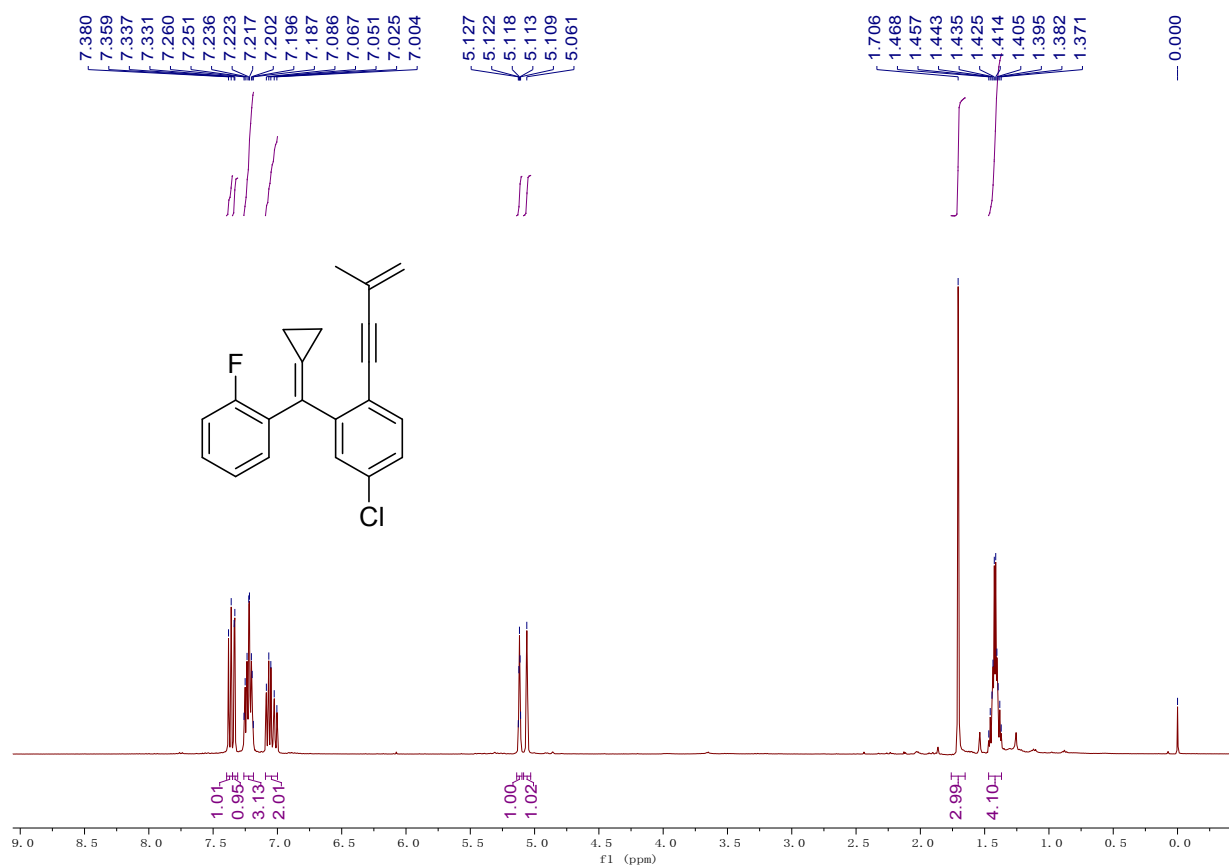


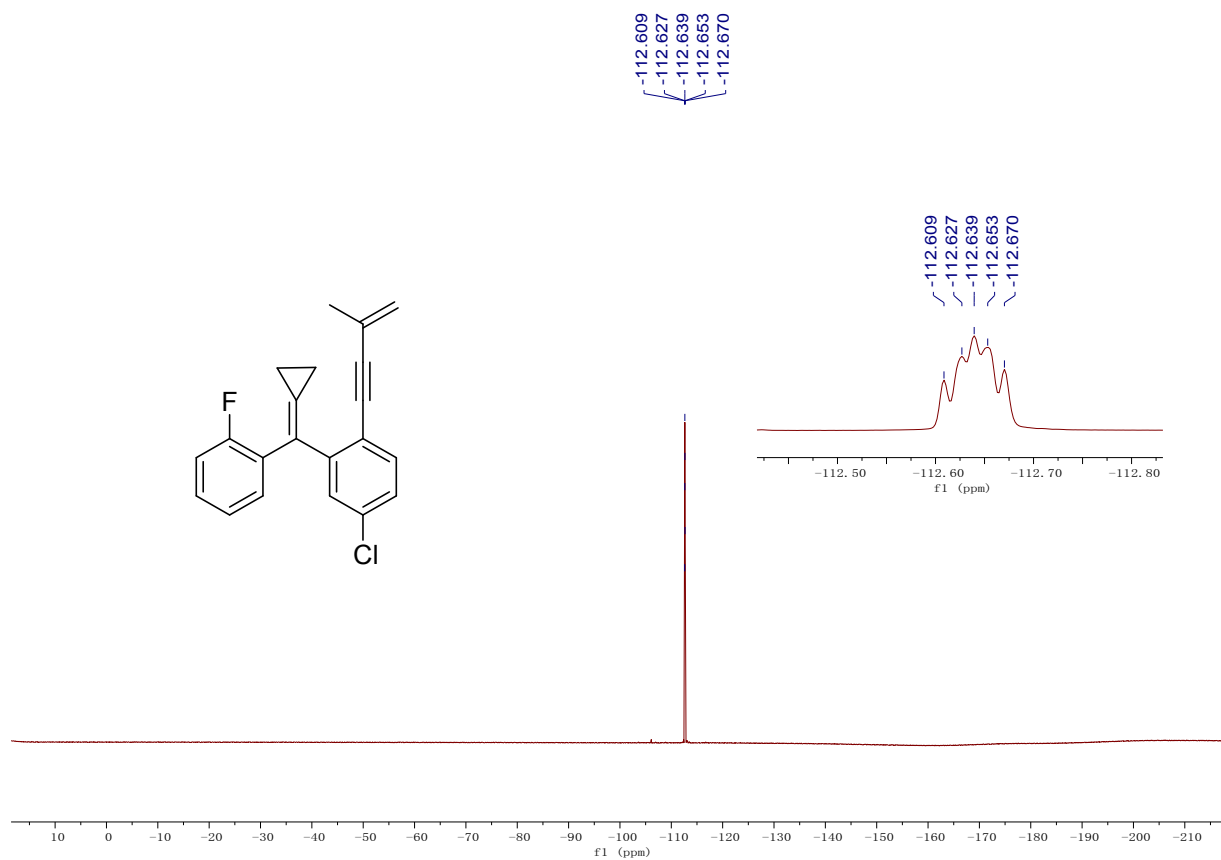
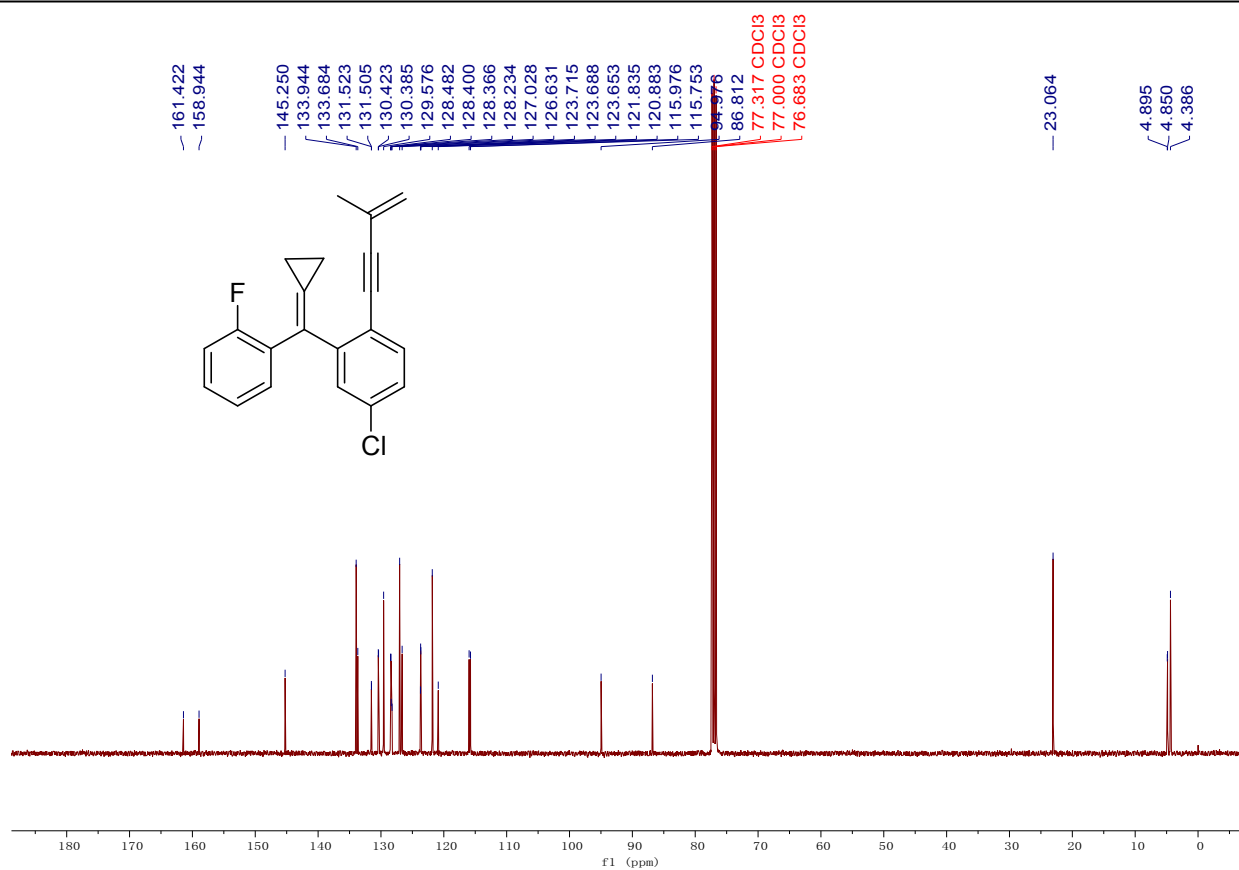
4-chloro-2-(cyclopropylidene(phenyl)methyl)-1-(3-methylbut-3-en-1-yn-1-yl)benzene (1h)



4-chloro-2-(cyclopropylidene(2-fluorophenyl)methyl)-1-(3-methylbut-3-en-1-yn-1-yl)benzene

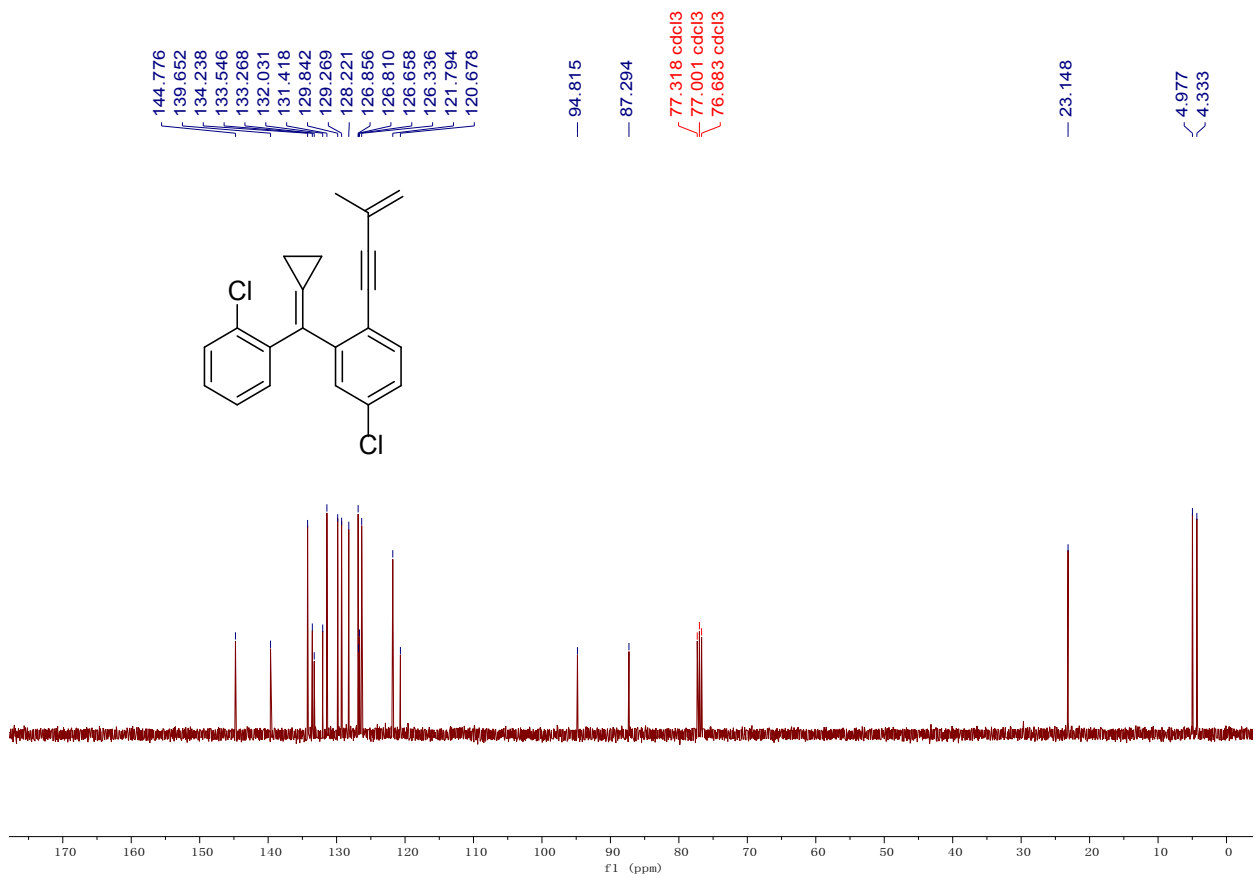
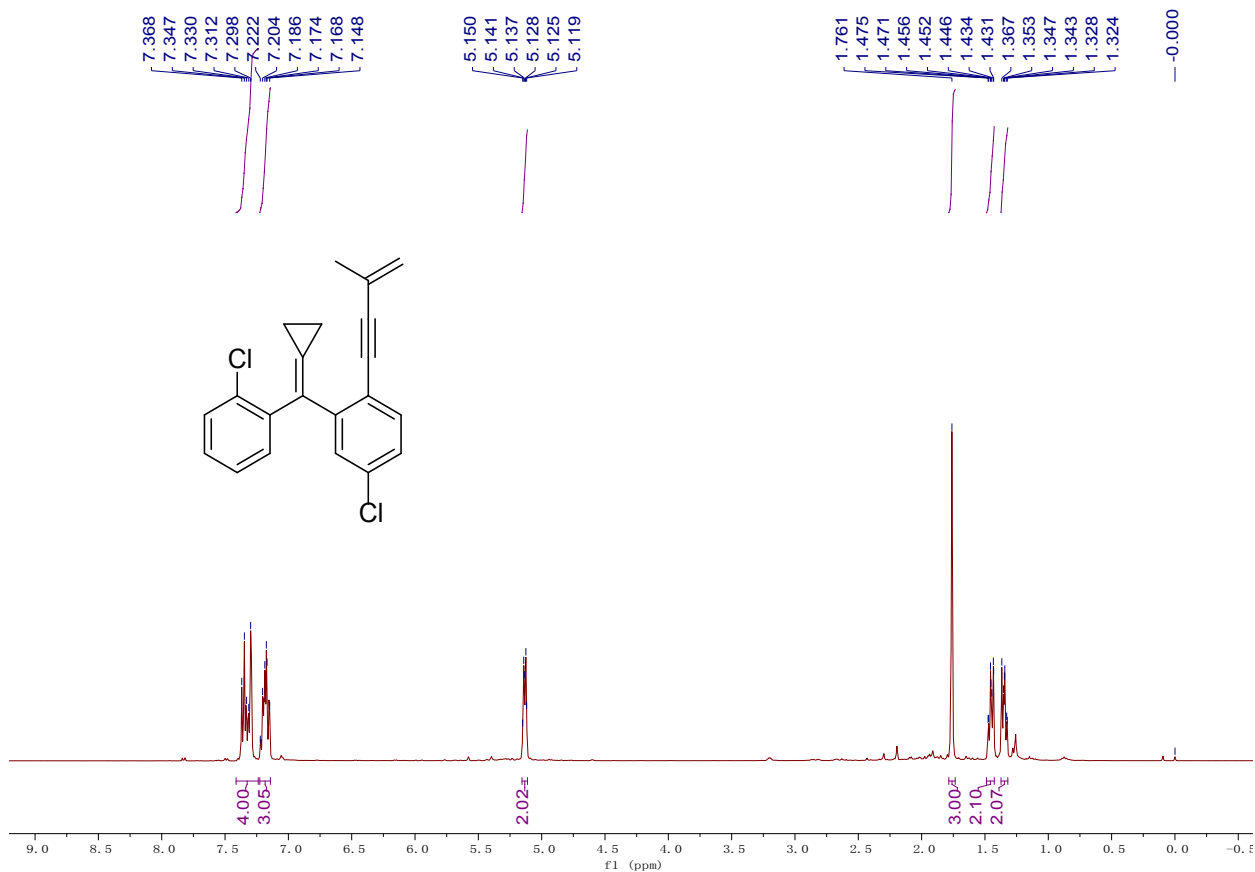
(1i)



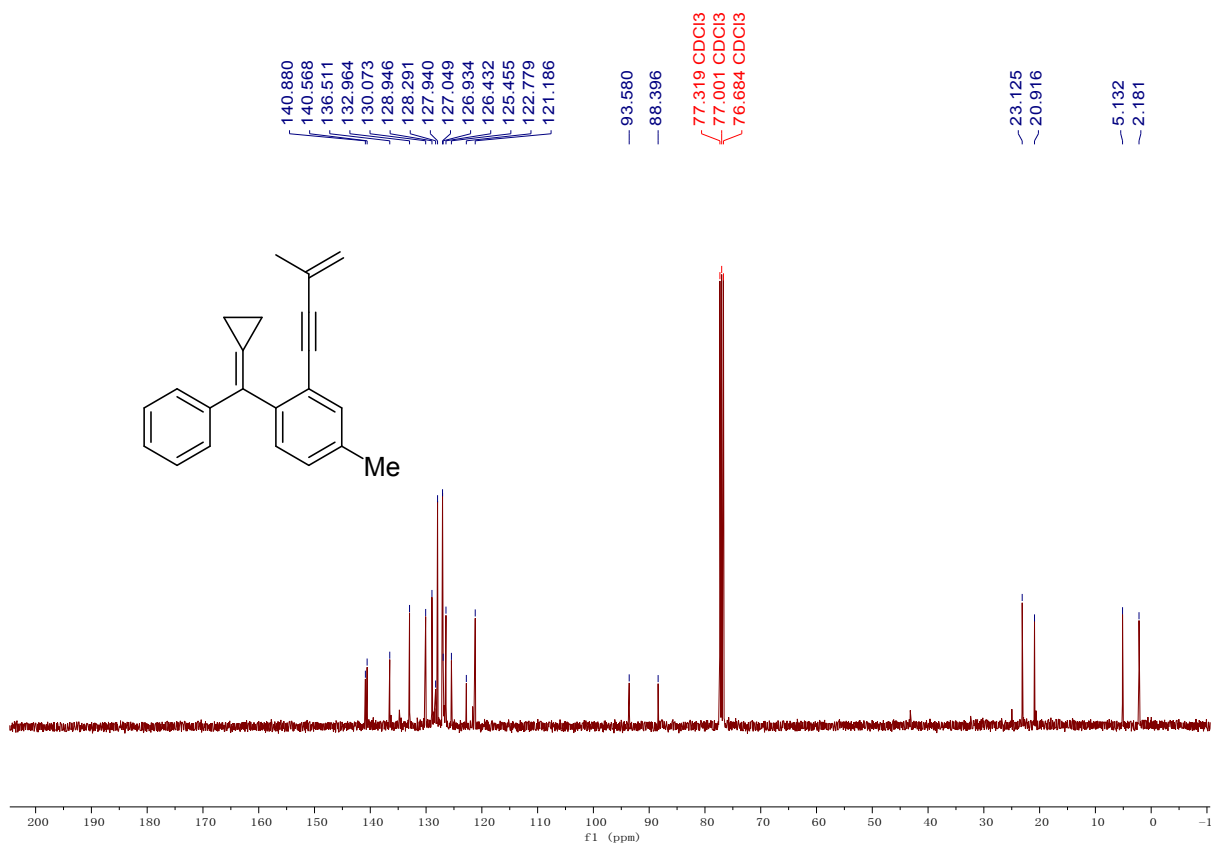
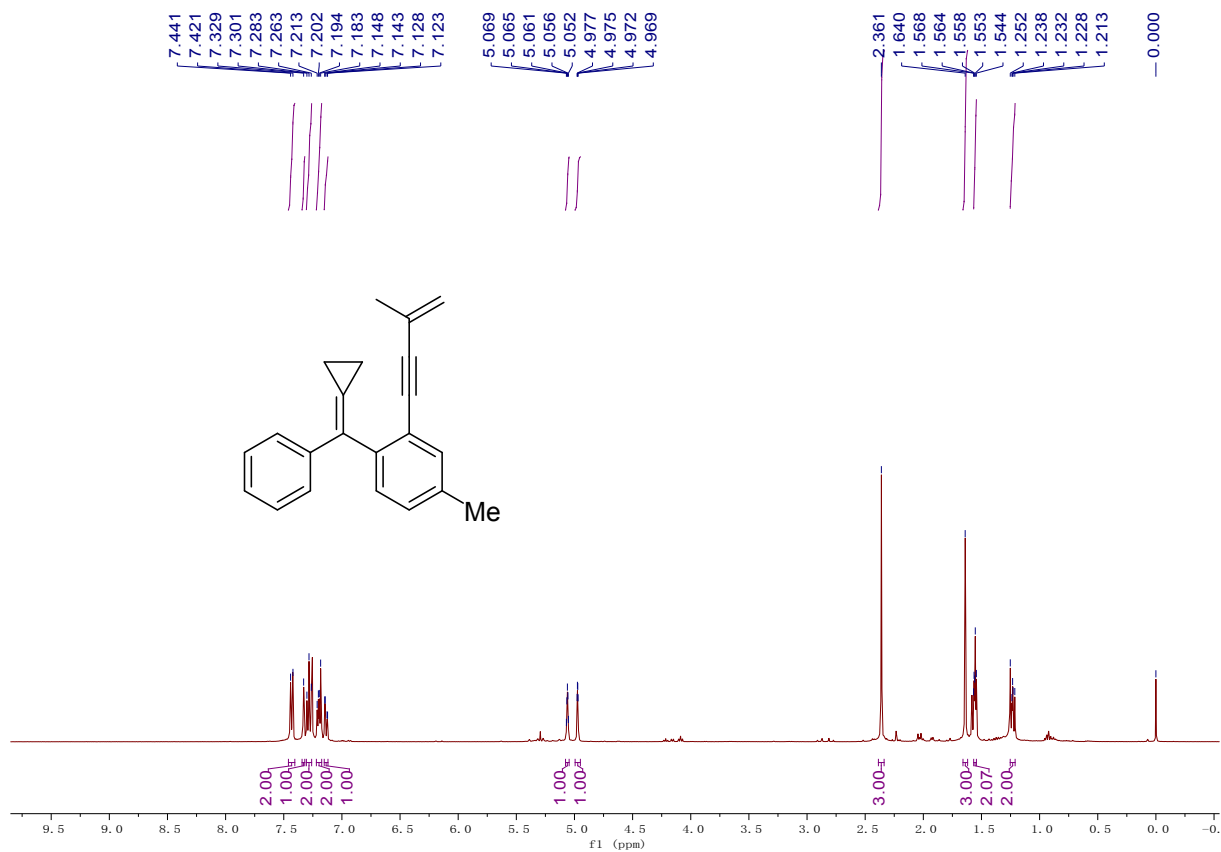


4-chloro-2-((2-chlorophenyl)(cyclopropylidene)methyl)-1-(3-methylbut-3-en-1-yn-1-

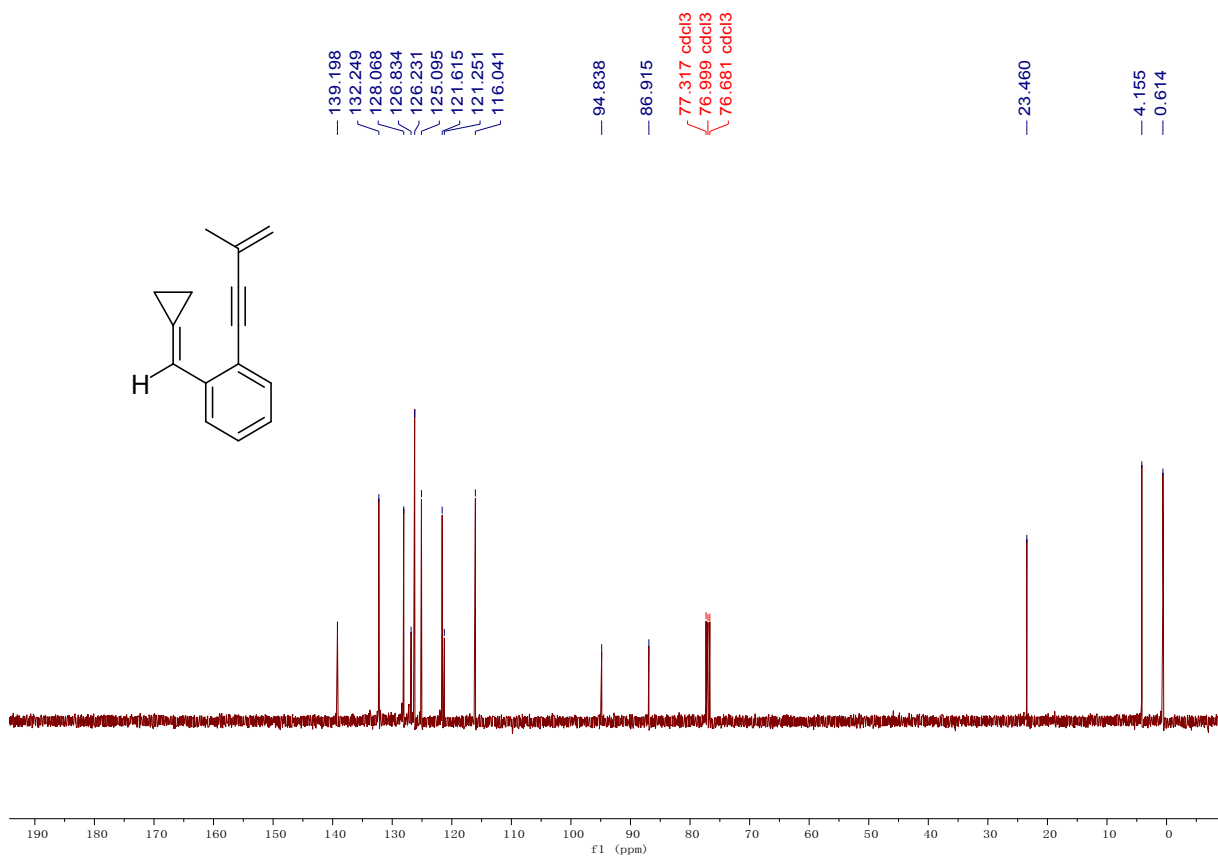
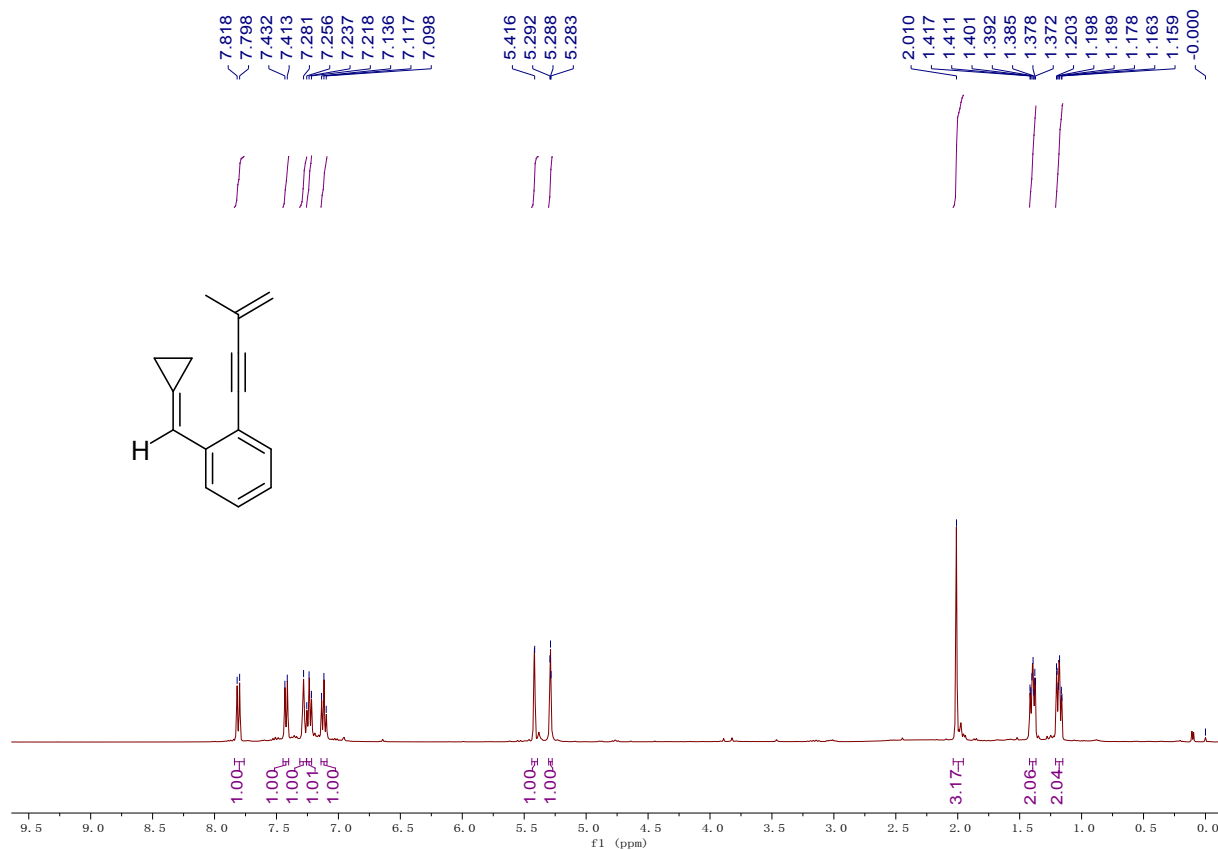
yl)benzene(1j)



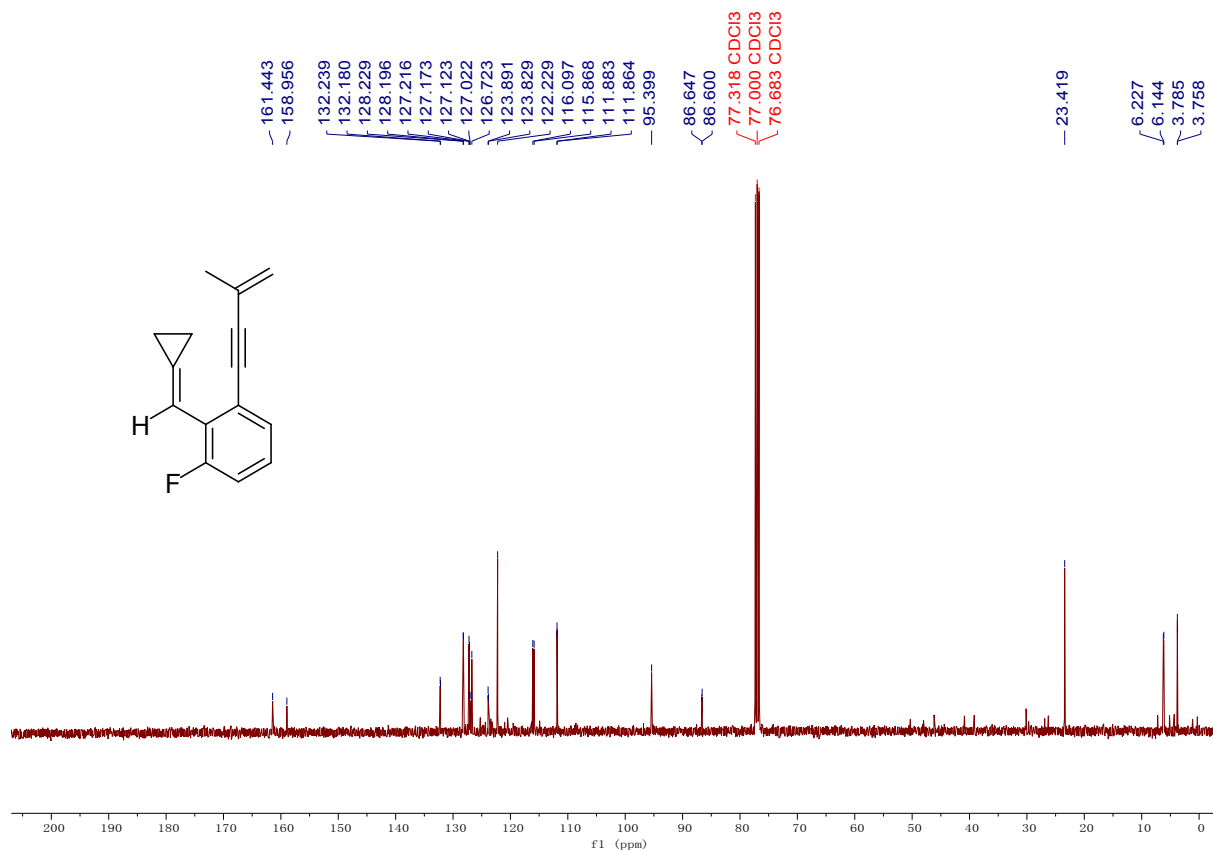
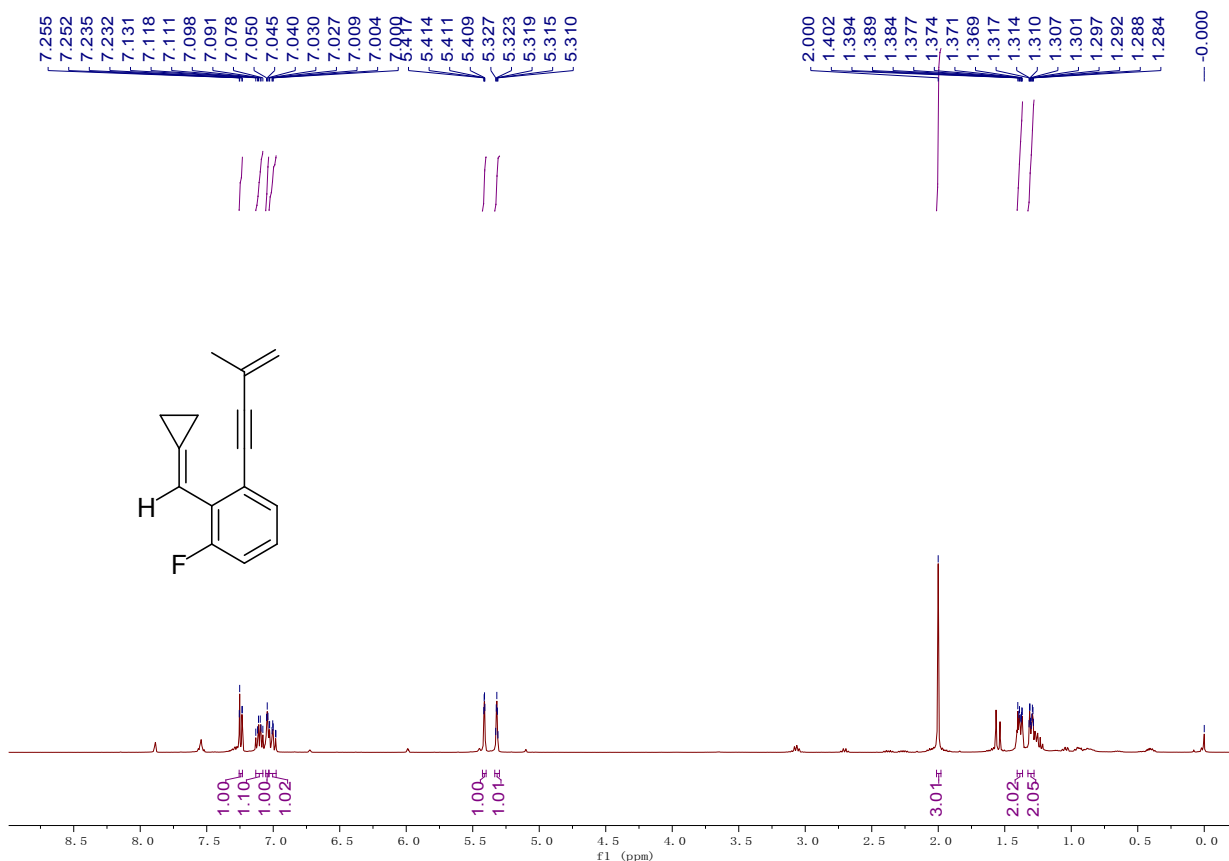
1-(cyclopropylidene(phenyl)methyl)-4-methyl-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1k)

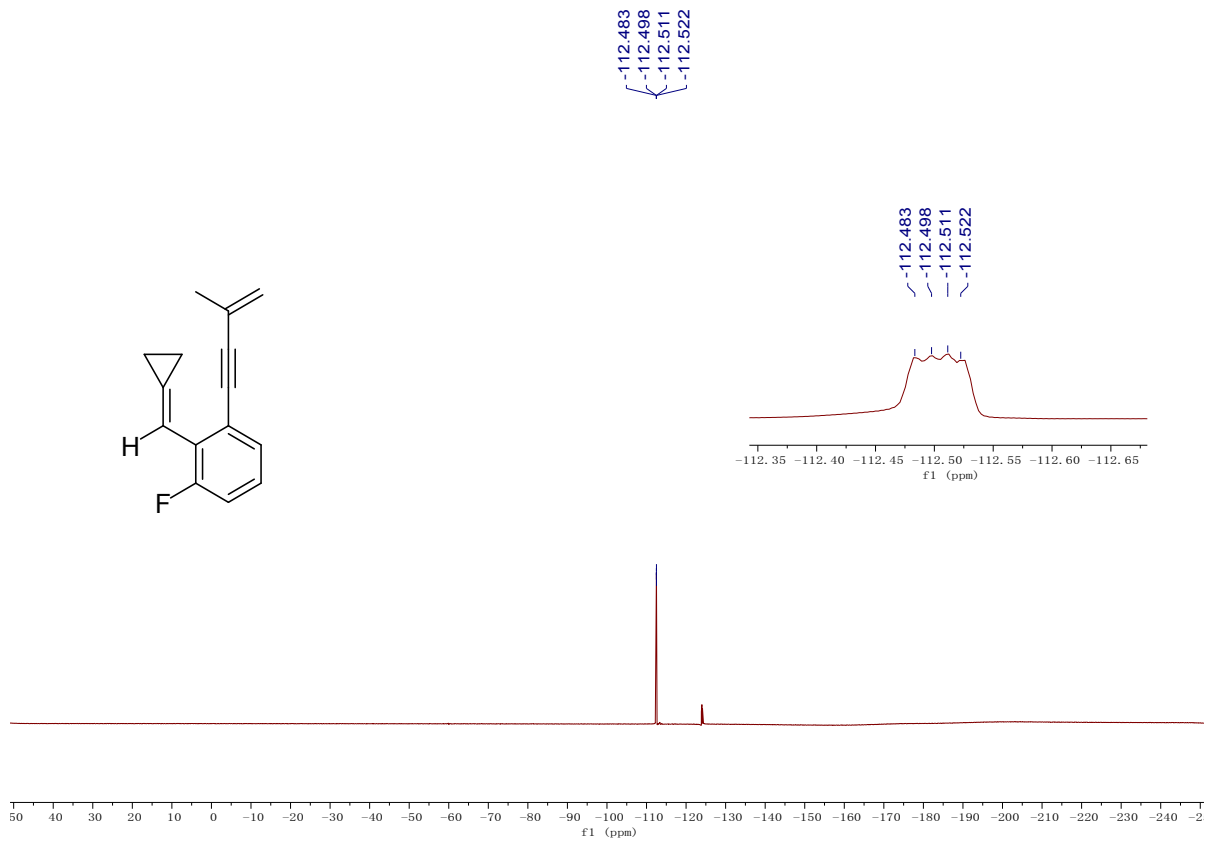


1-(cyclopropylidenemethyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (11)

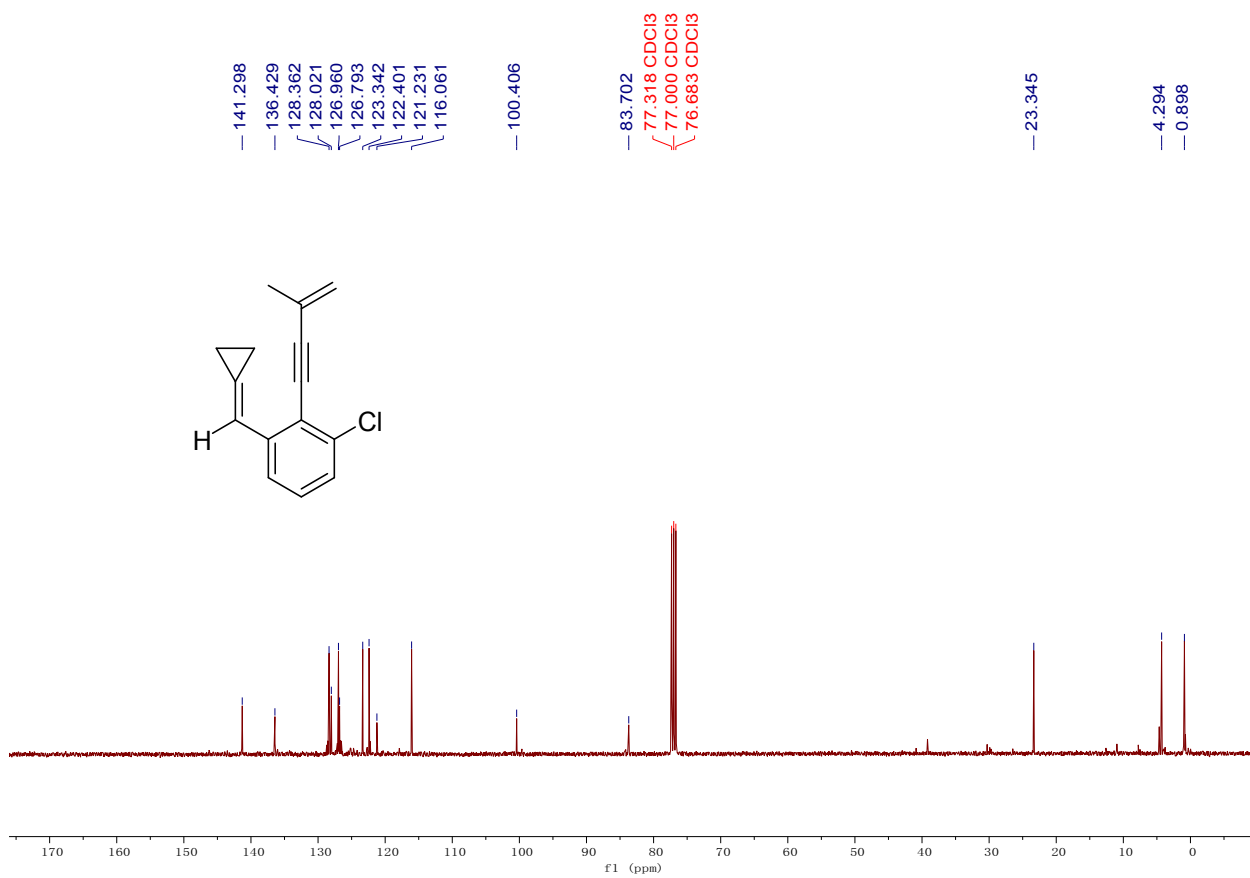
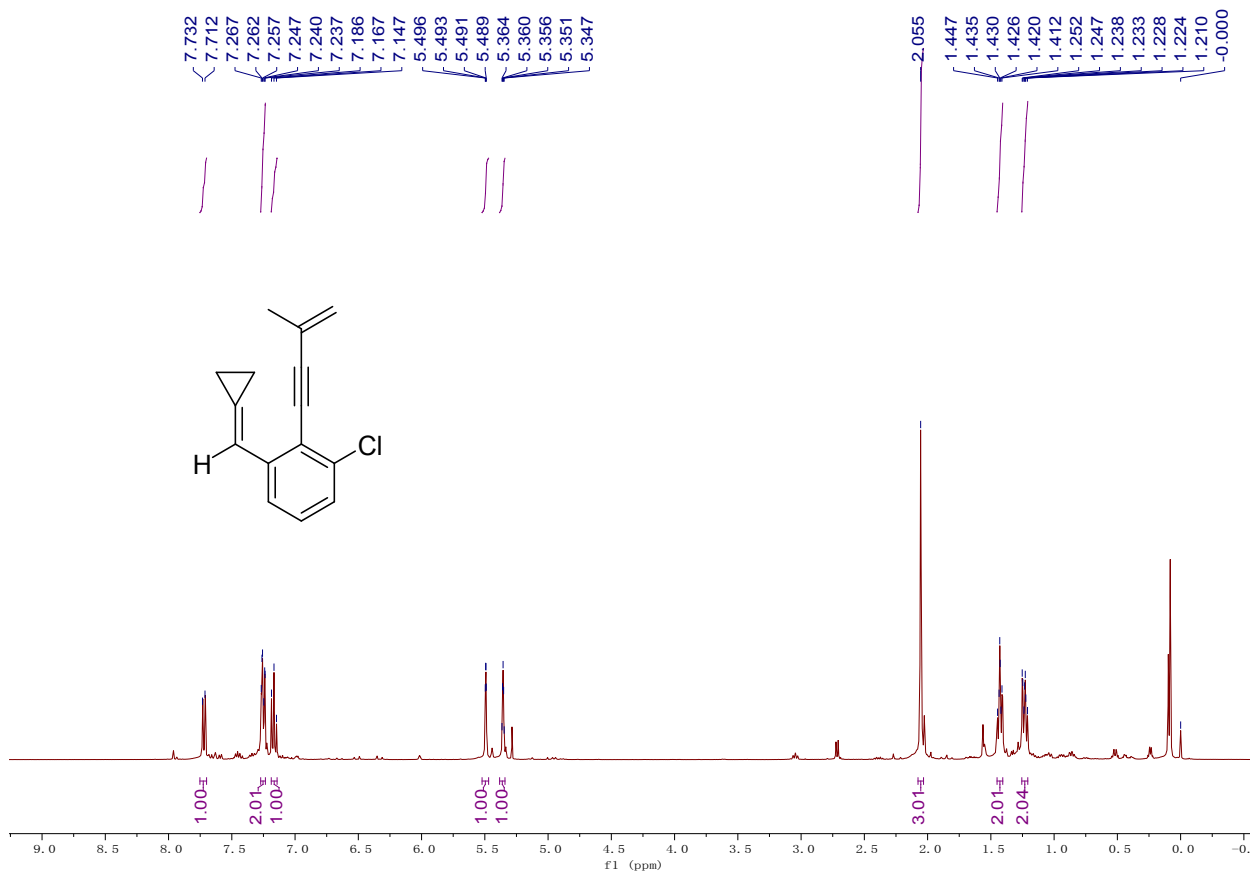


2-(cyclopropylidenemethyl)-1-fluoro-3-(3-methylbut-3-en-1-yn-1-yl)benzene (1m)

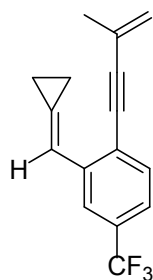
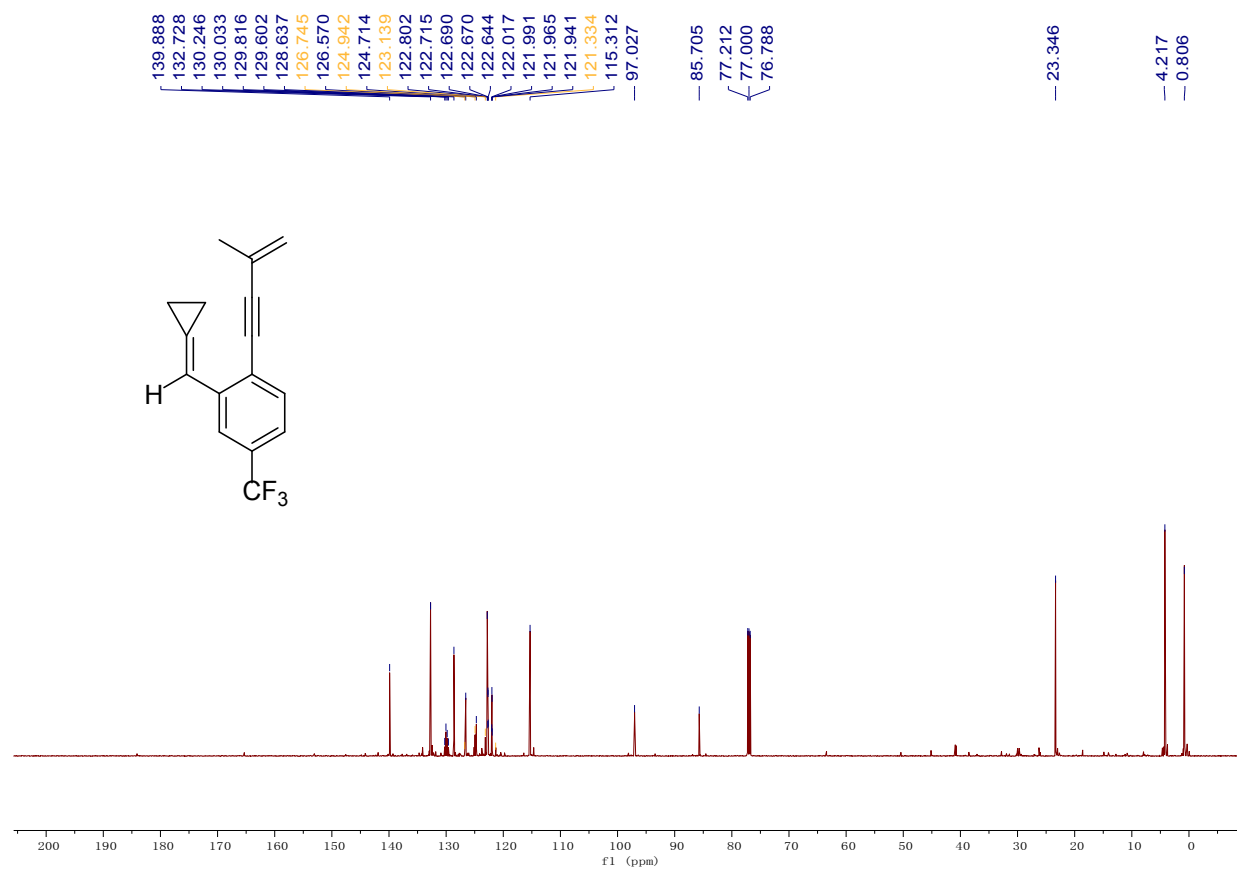
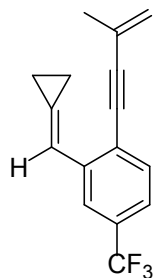
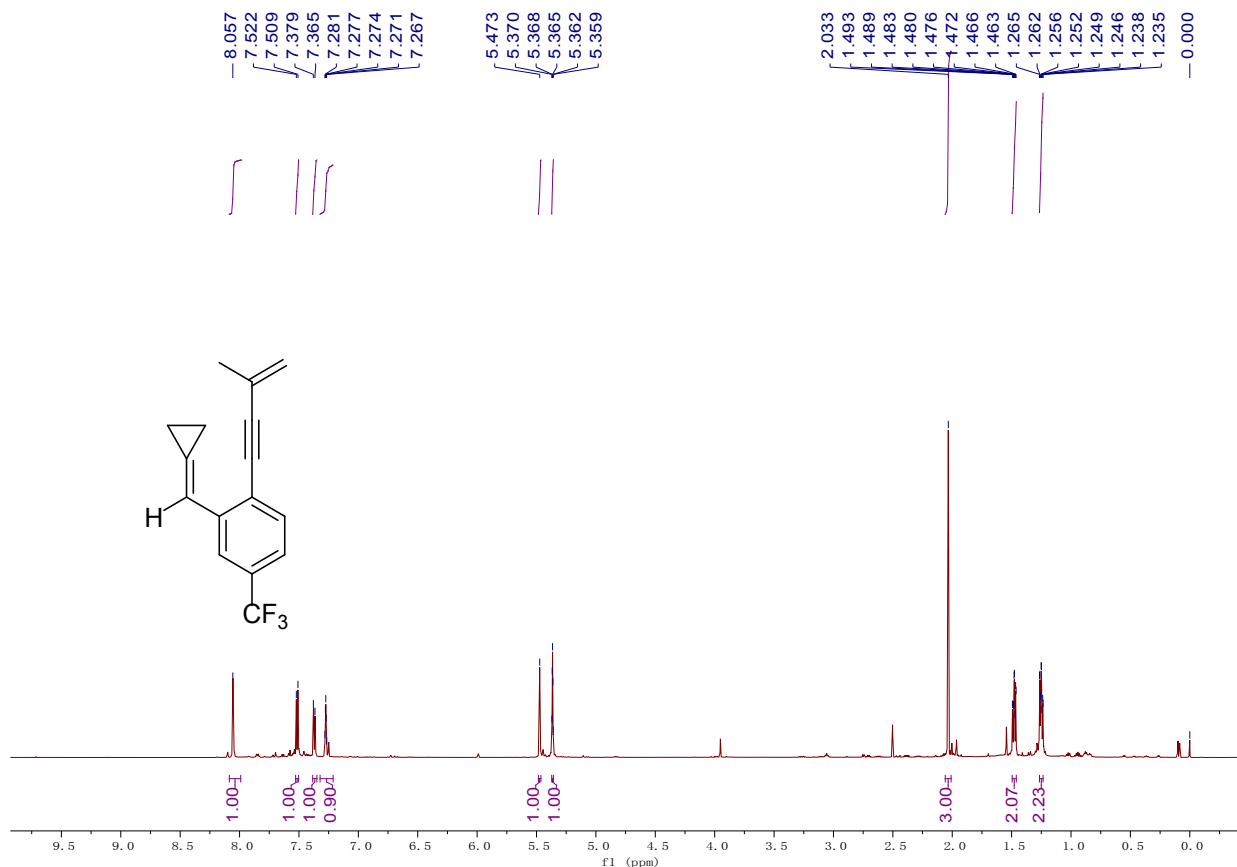


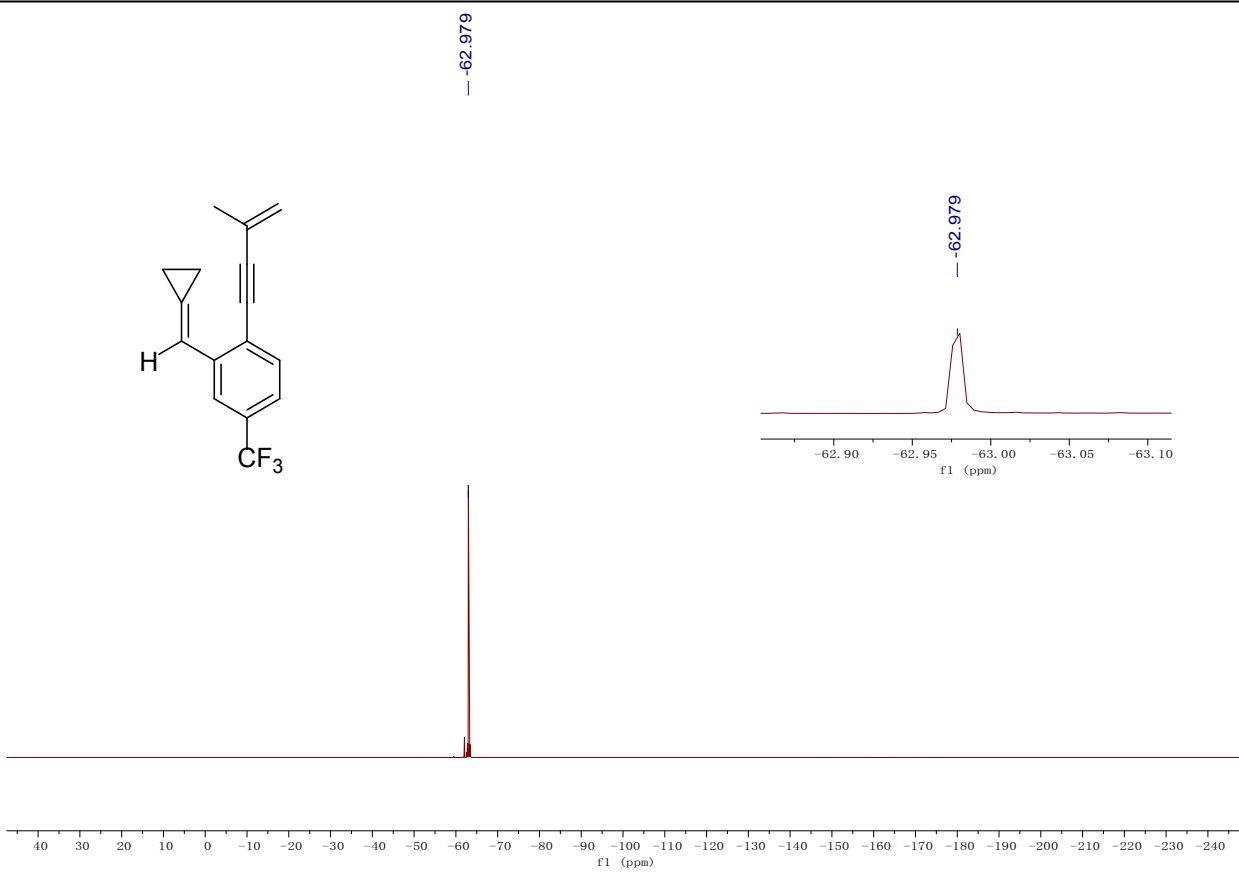


1-chloro-3-(cyclopropylidenemethyl)-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1n)

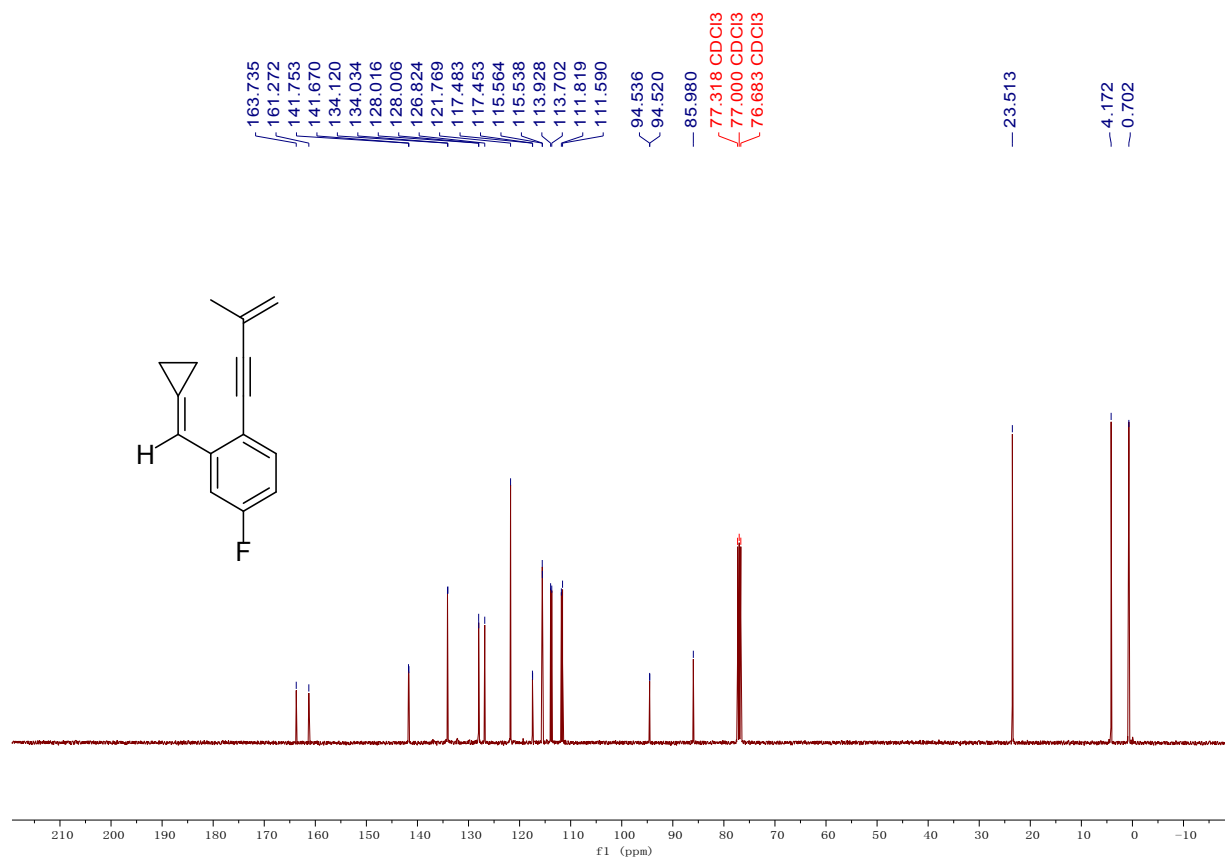
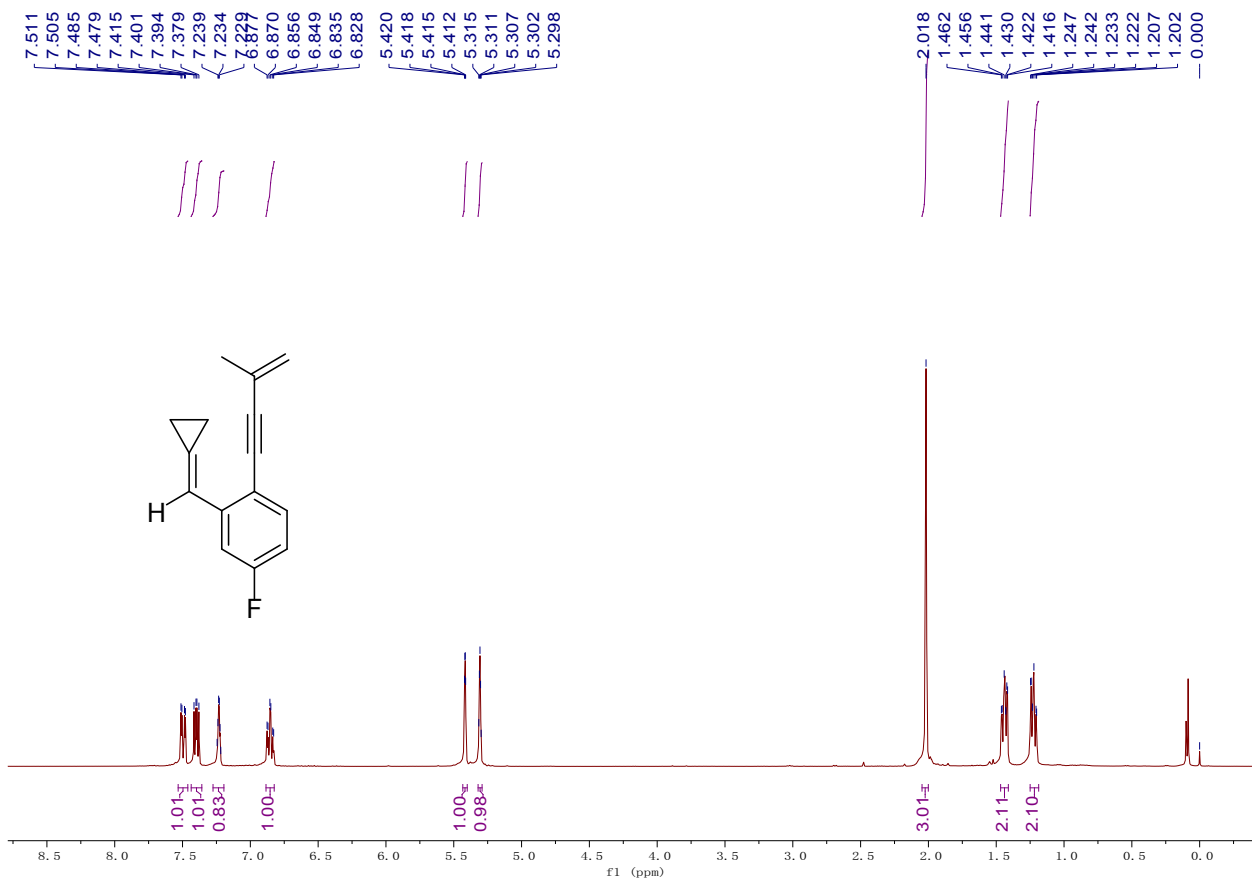


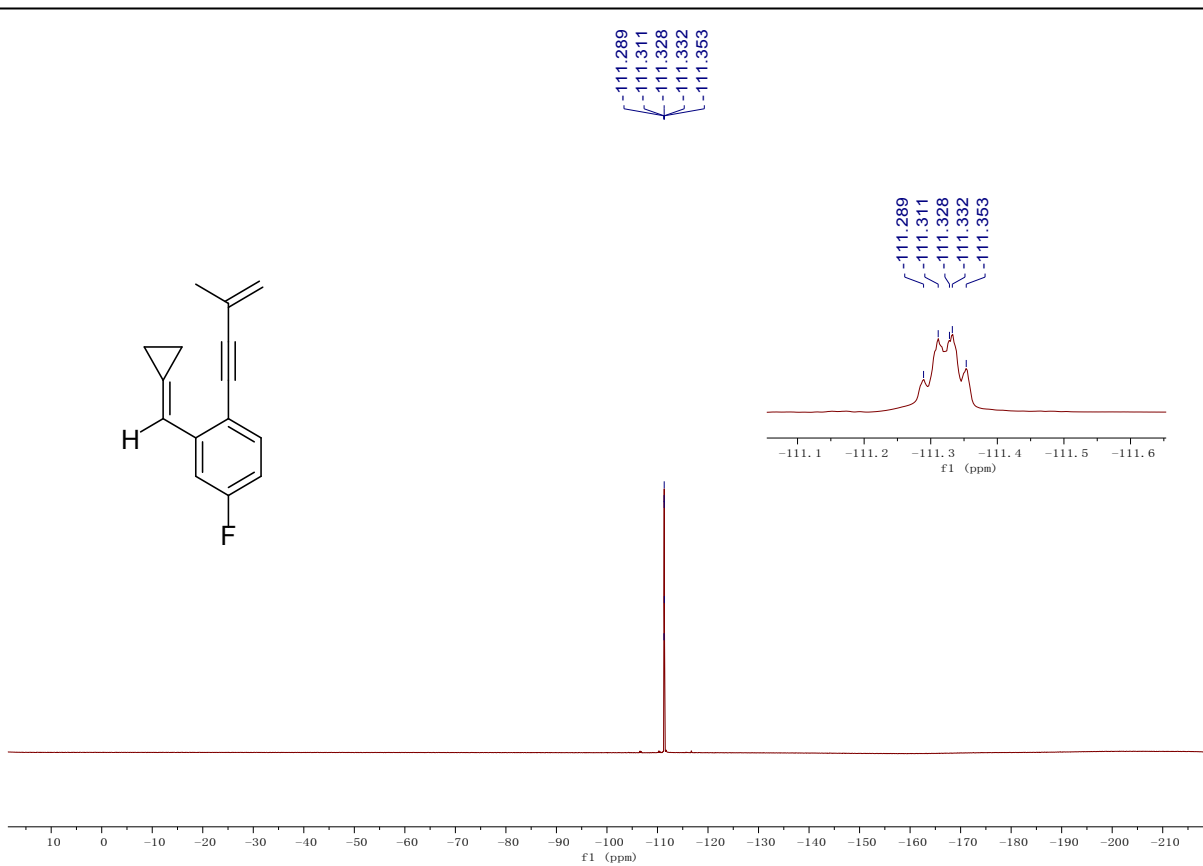
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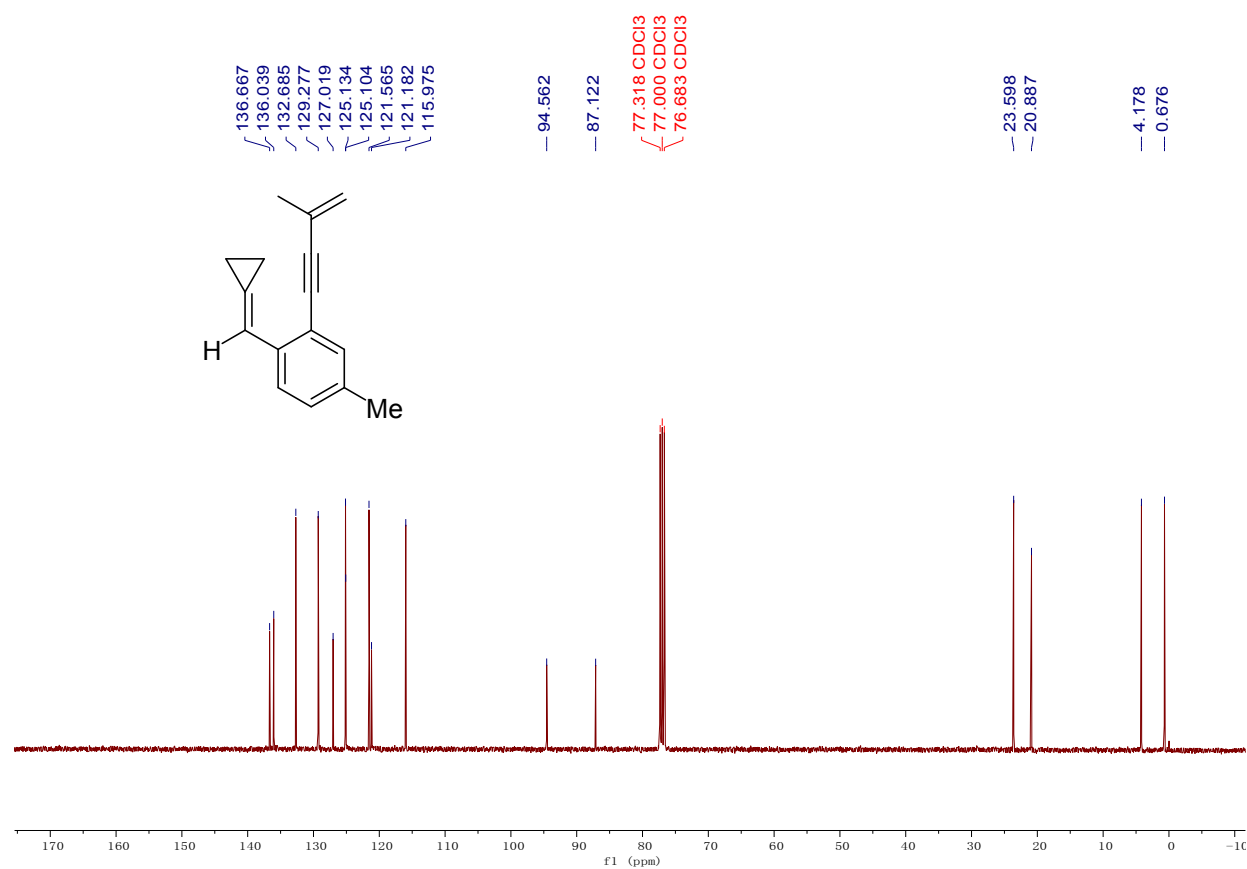
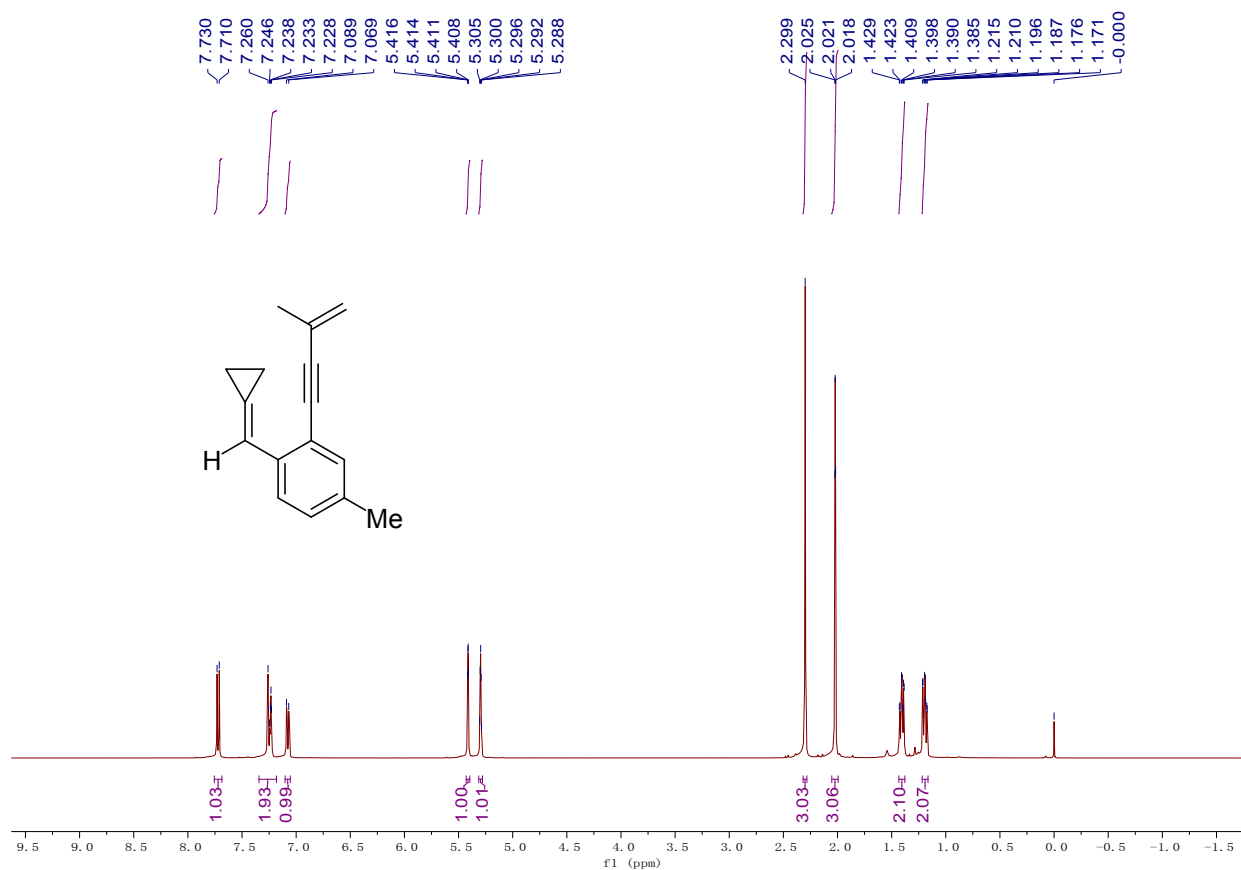


2-(cyclopropylidenemethyl)-4-fluoro-1-(3-methylbut-3-en-1-yn-1-yl)benzene (1p)

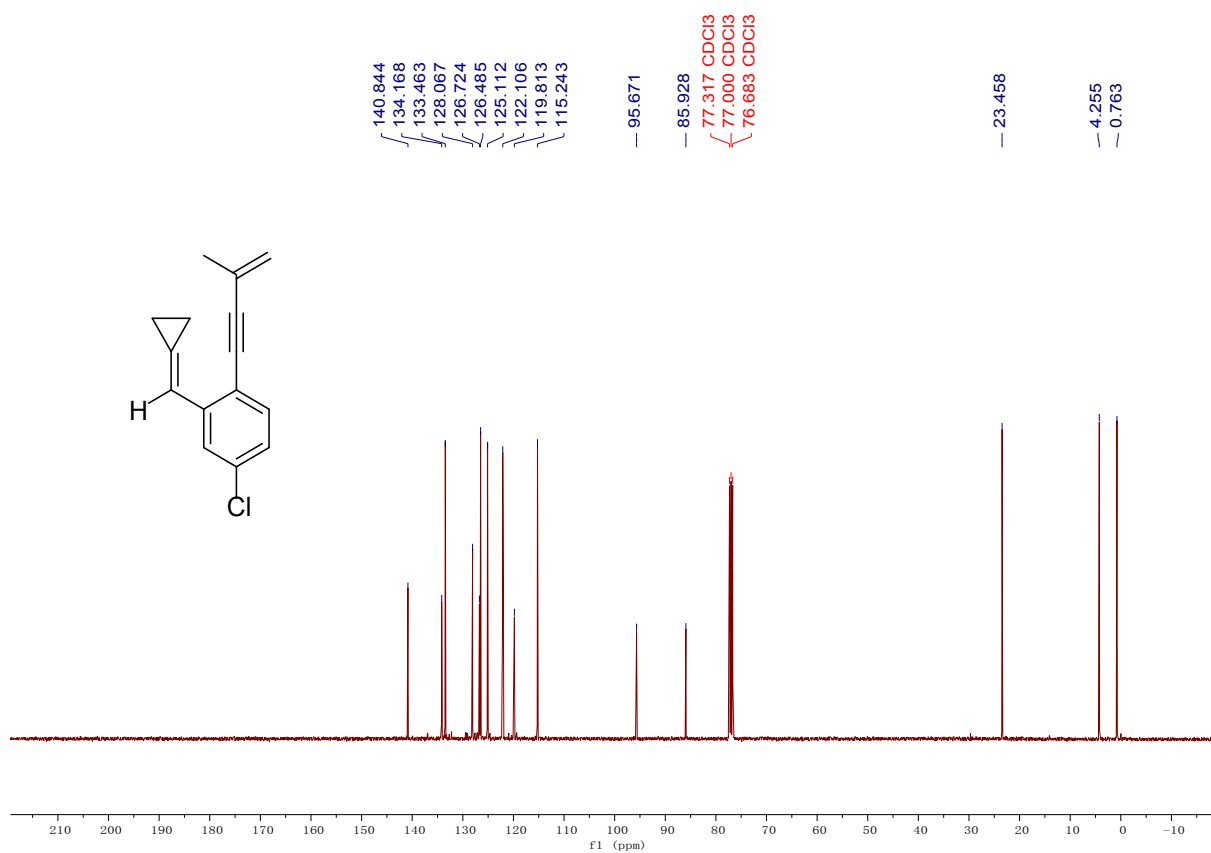
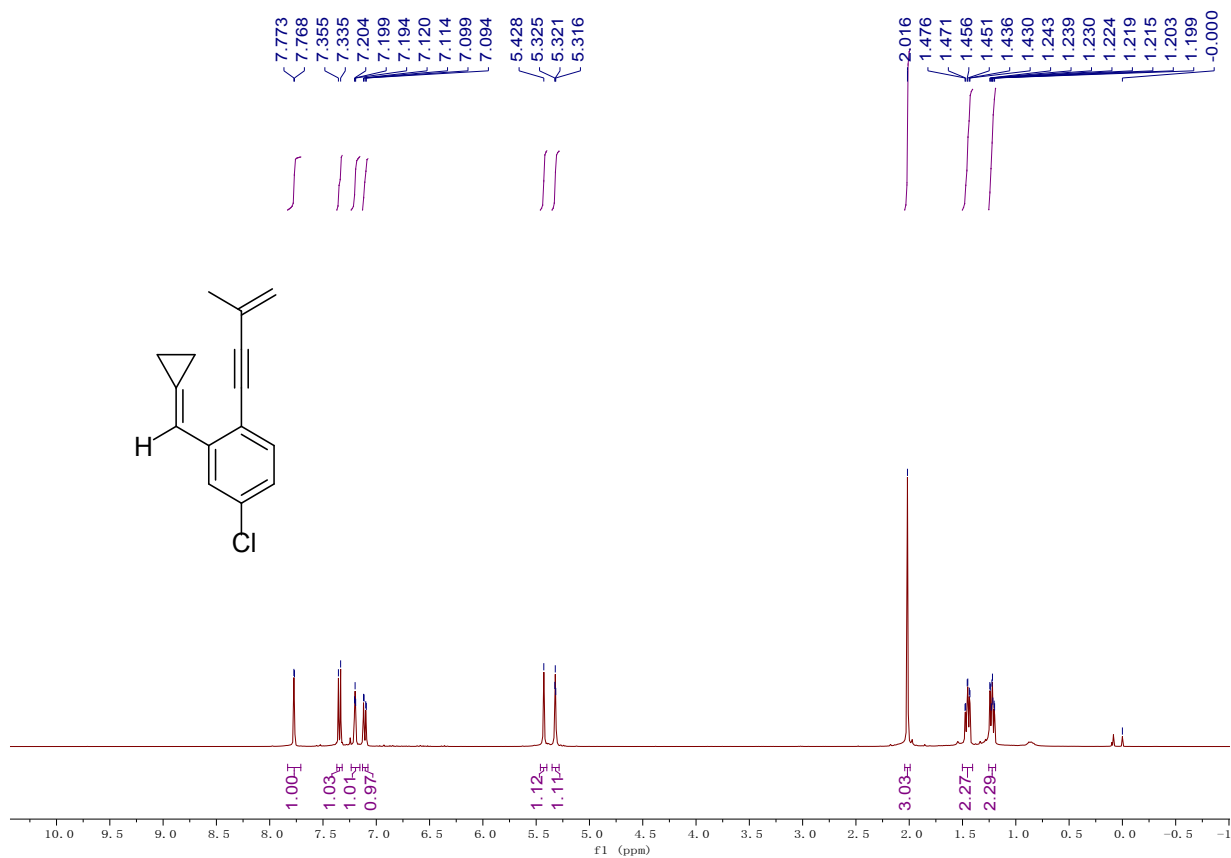




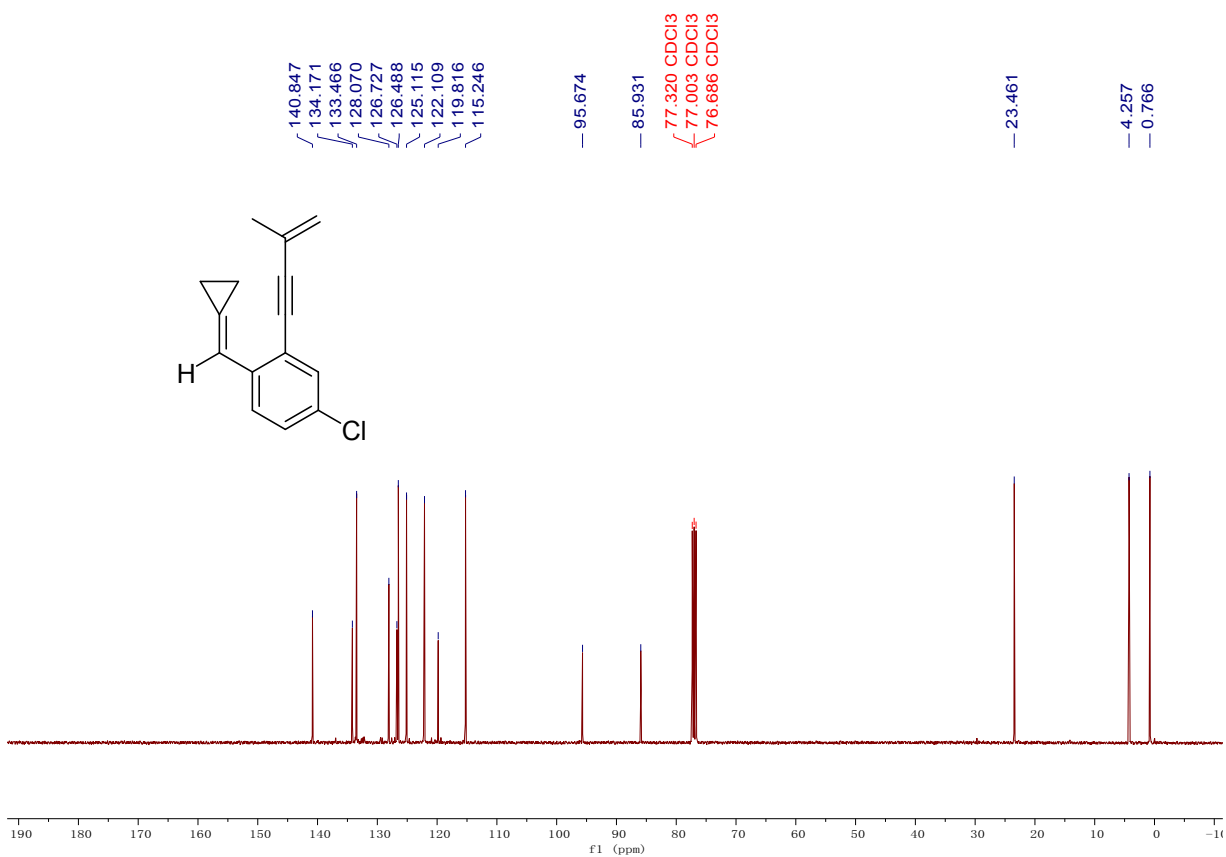
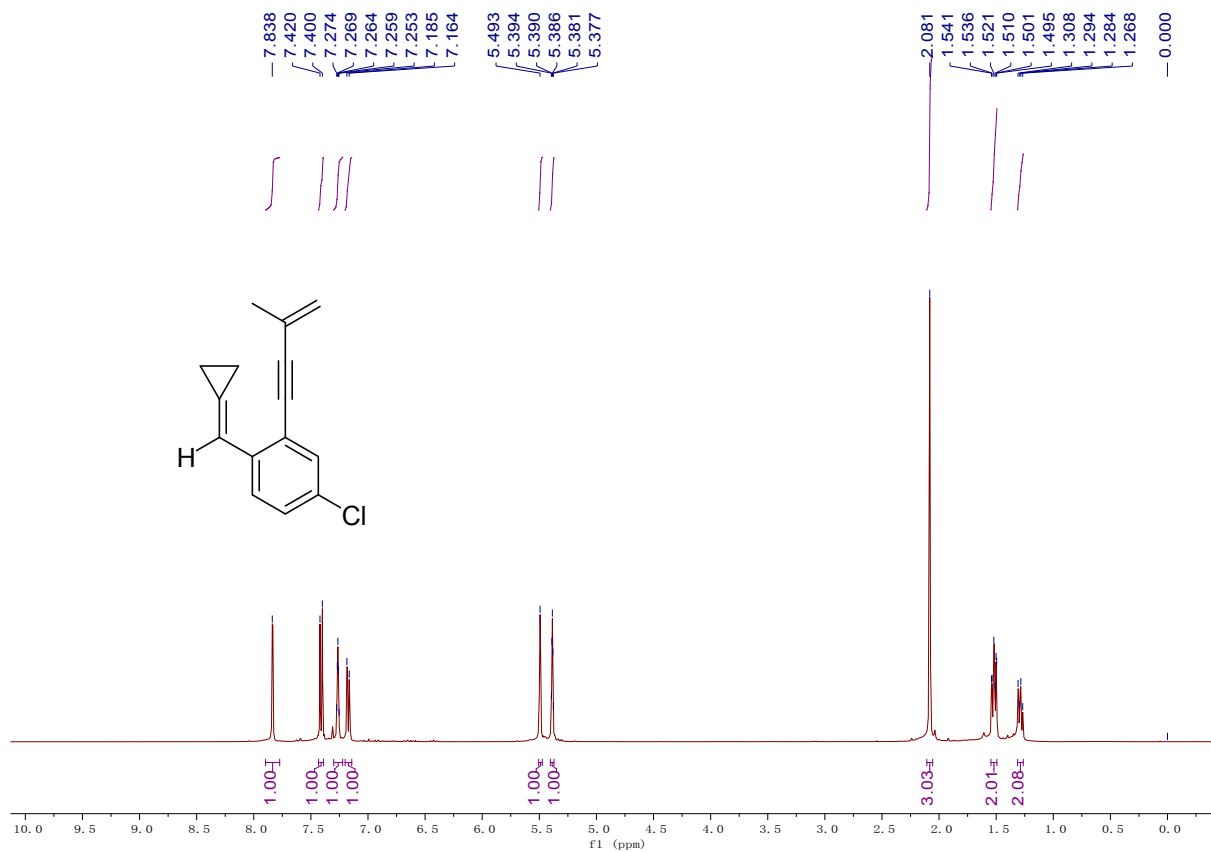
1-(cyclopropylidenemethyl)-4-methyl-2-(3-methylbut-3-en-1-yn-1-yl)benzene (1q)



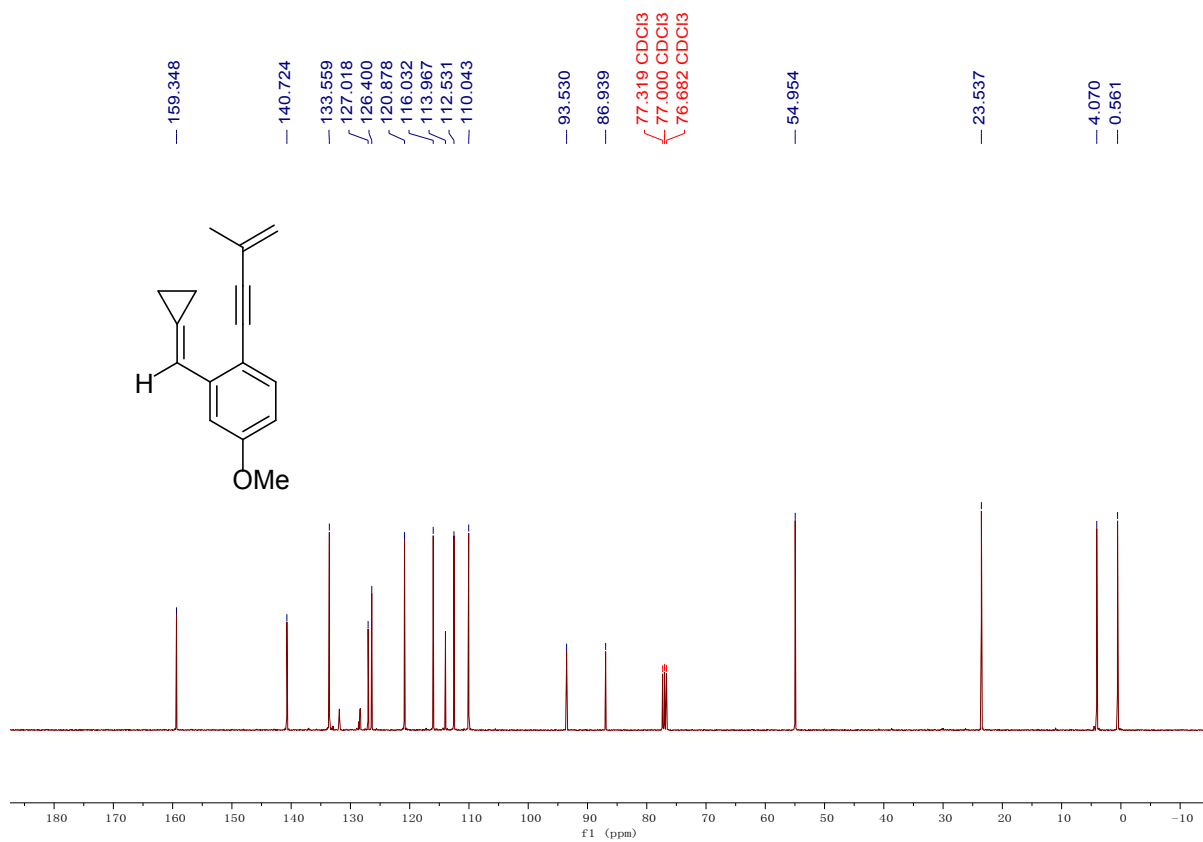
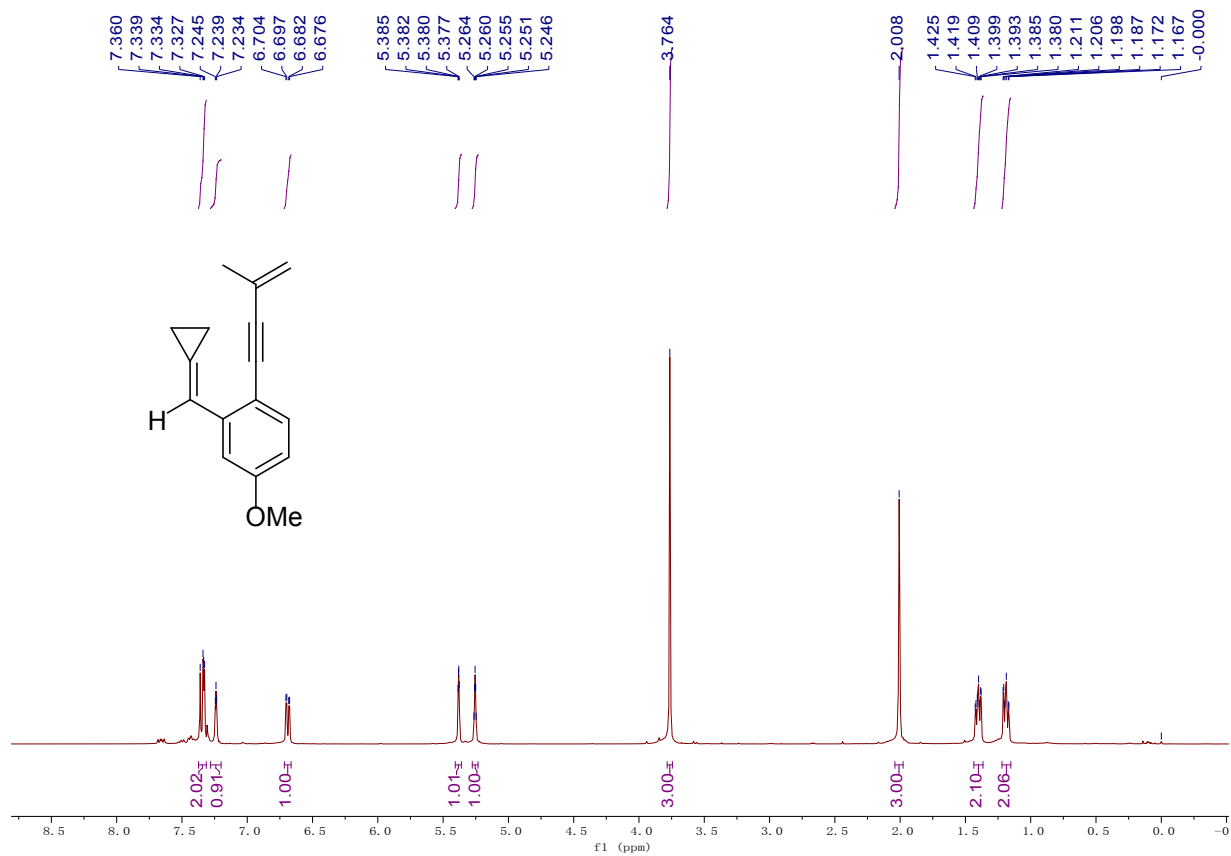
4-chloro-2-(cyclopropylidenemethyl)-1-(3-methylbut-3-en-1-yn-1-yl)benzene (1r)



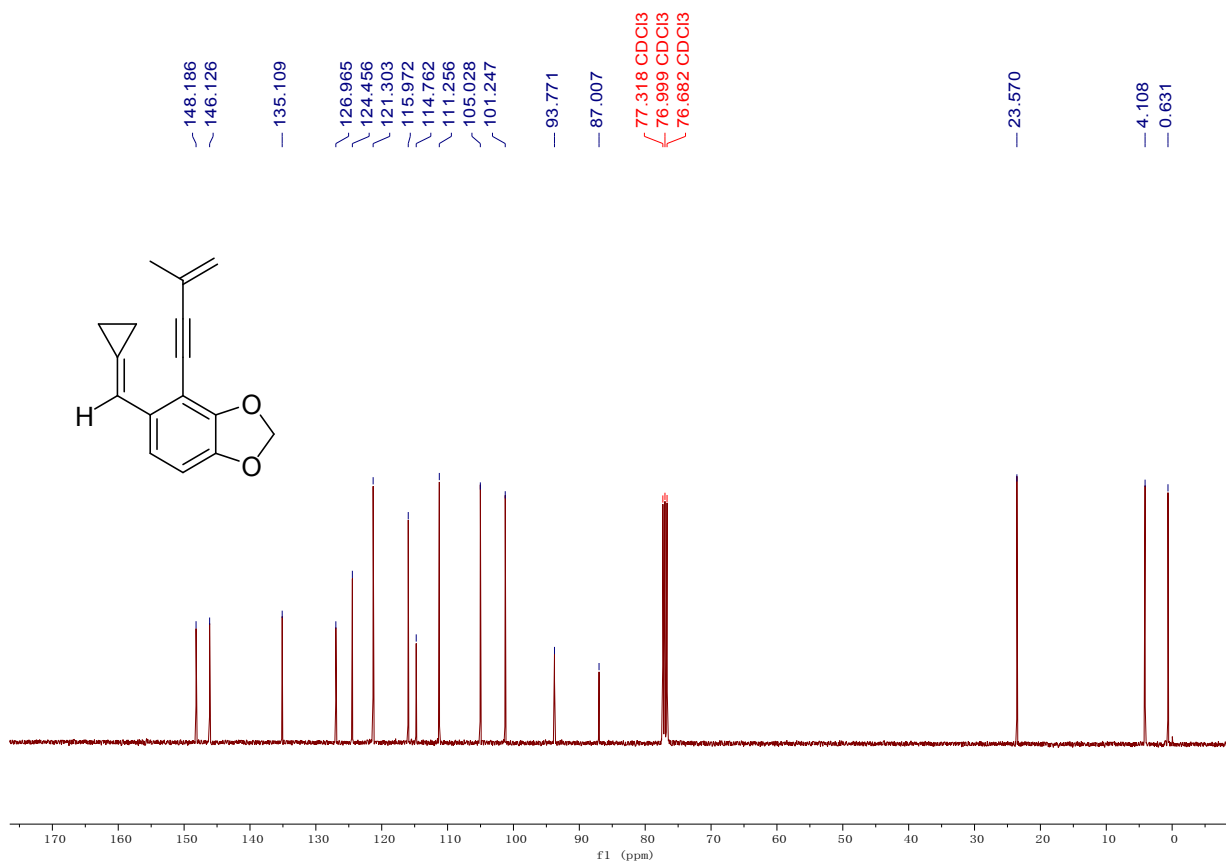
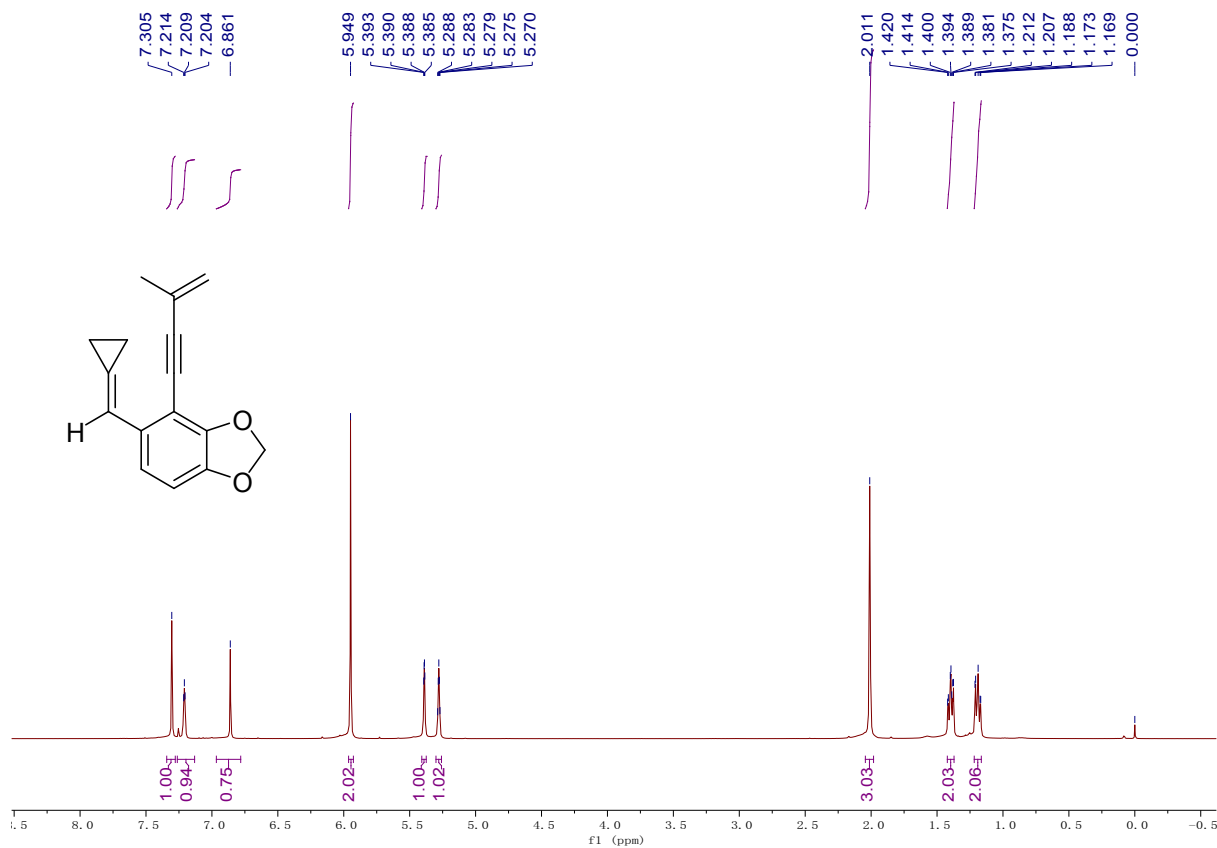
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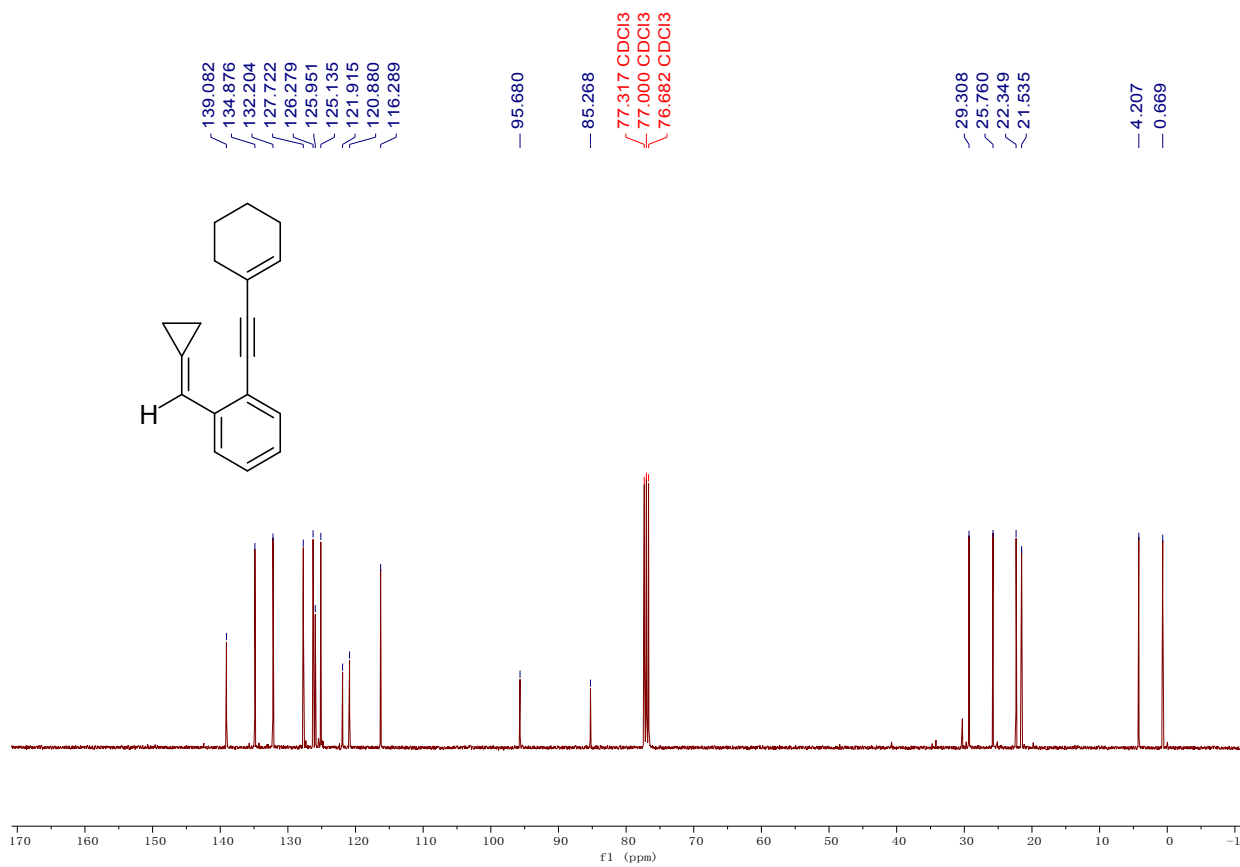
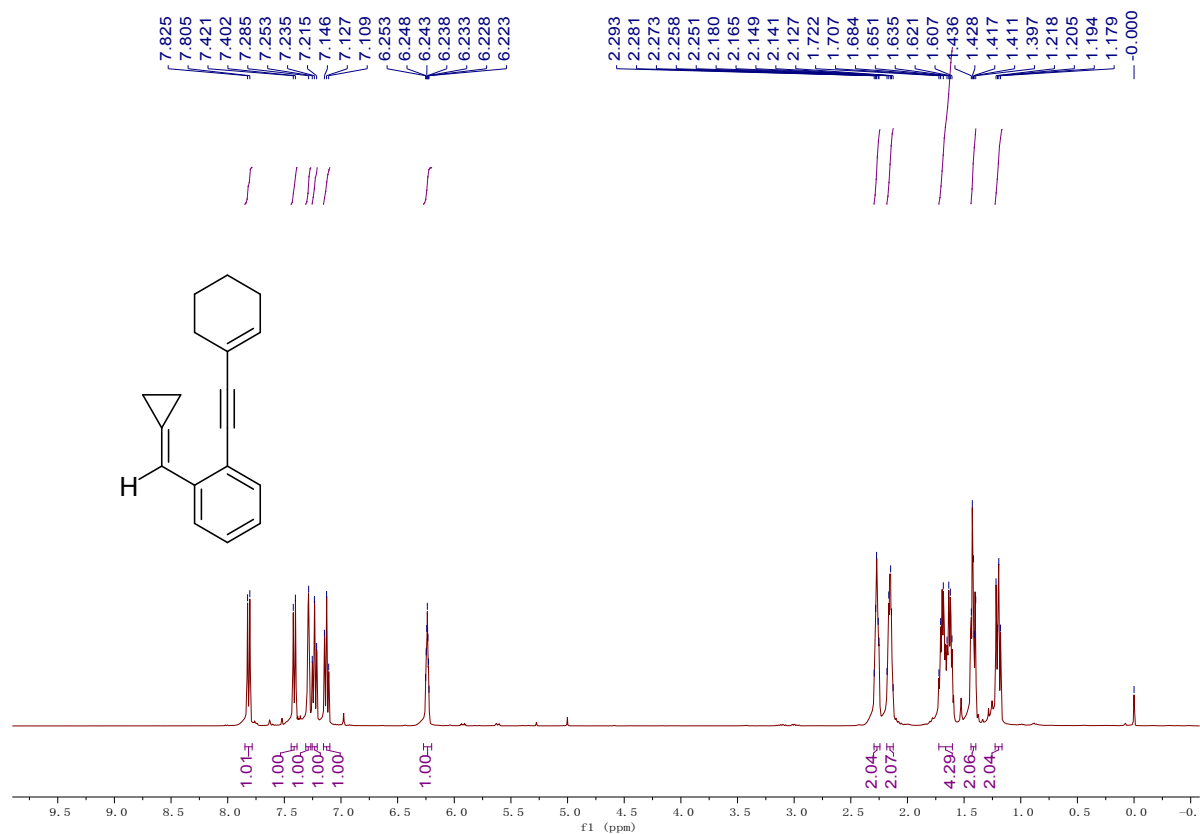
2-(cyclopropylidenemethyl)-4-methoxy-1-(3-methylbut-3-en-1-yn-1-yl)benzene (1t)



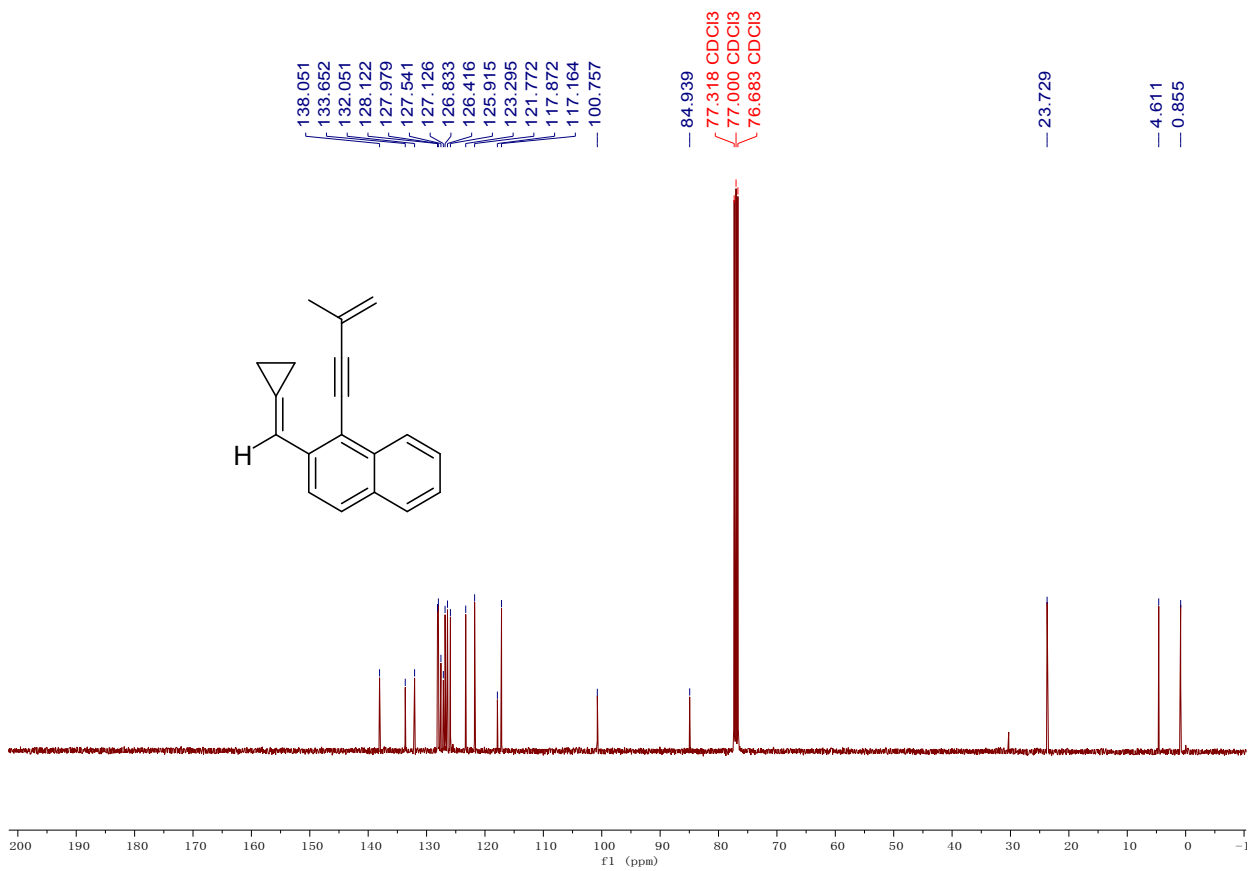
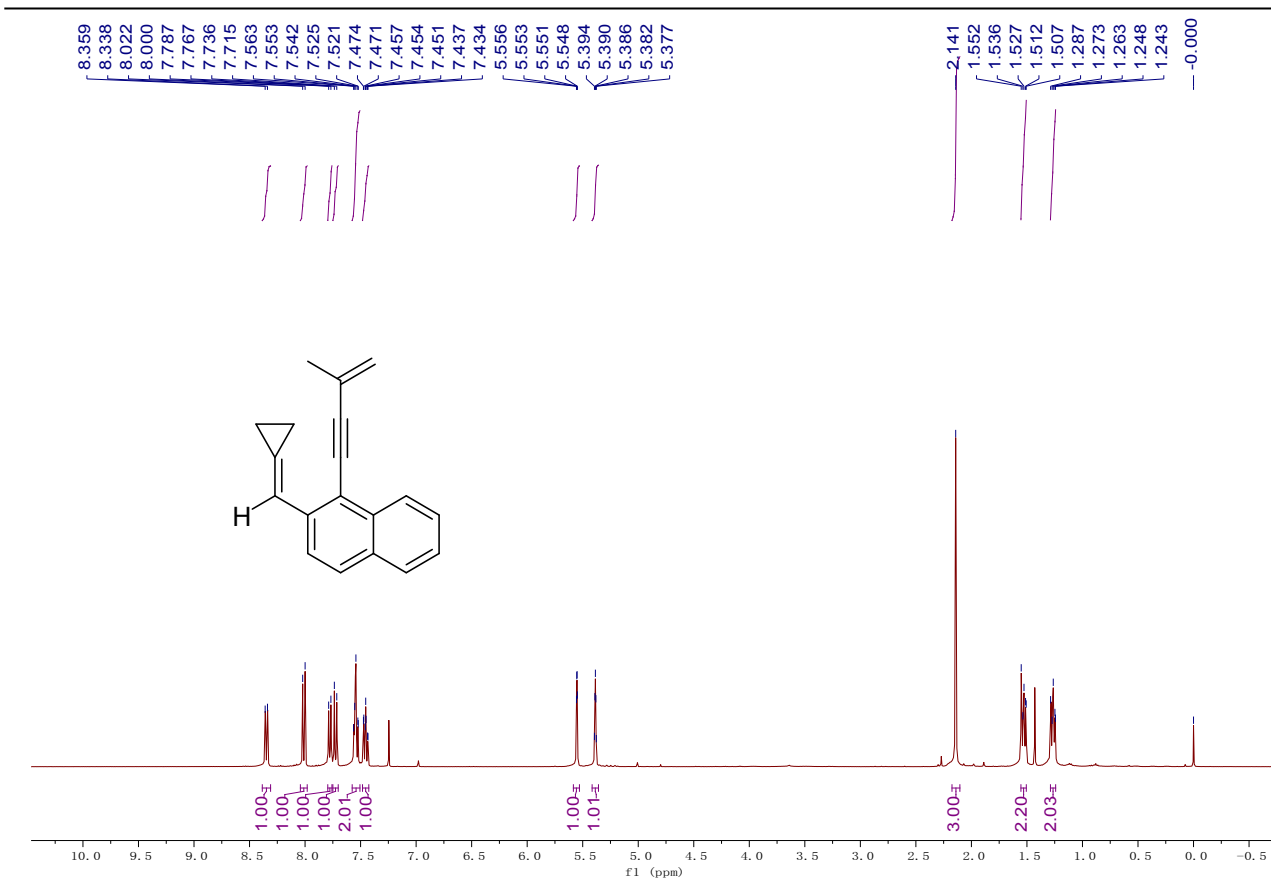
5-(cyclopropylidenemethyl)-4-(3-methylbut-3-en-1-yn-1-yl)benzo[d][1,3]dioxole (1u)



1-(cyclohex-1-en-1-ylethynyl)-2-(cyclopropylidenemethyl)benzene (1v)



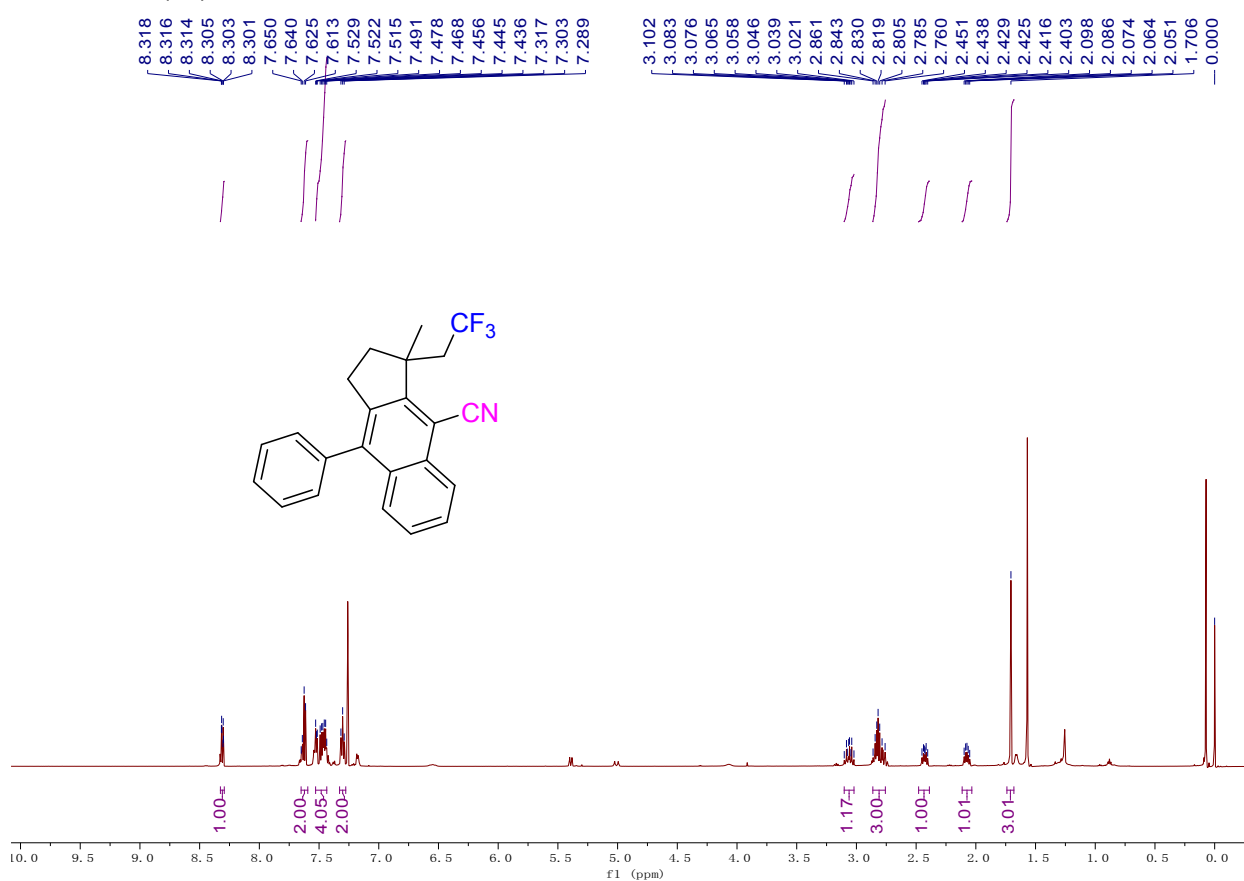
2-(cyclopropylidenemethyl)-1-(3-methylbut-3-en-1-yn-1-yl)naphthalene (1w)

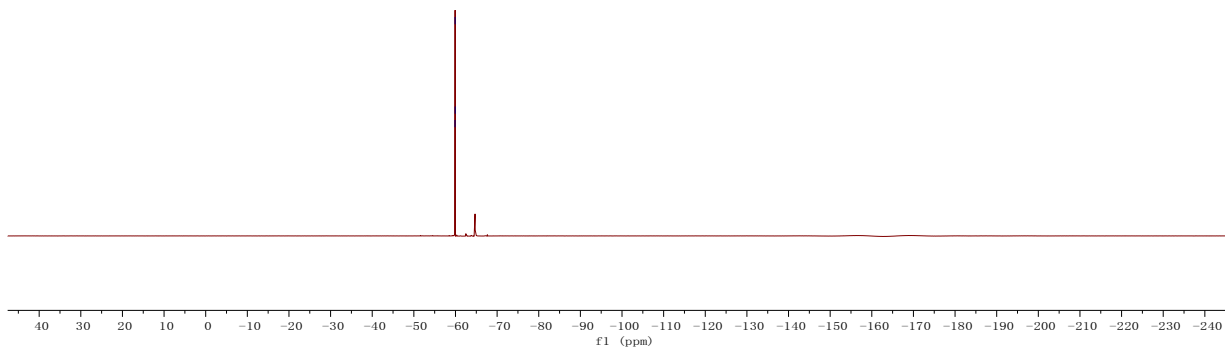
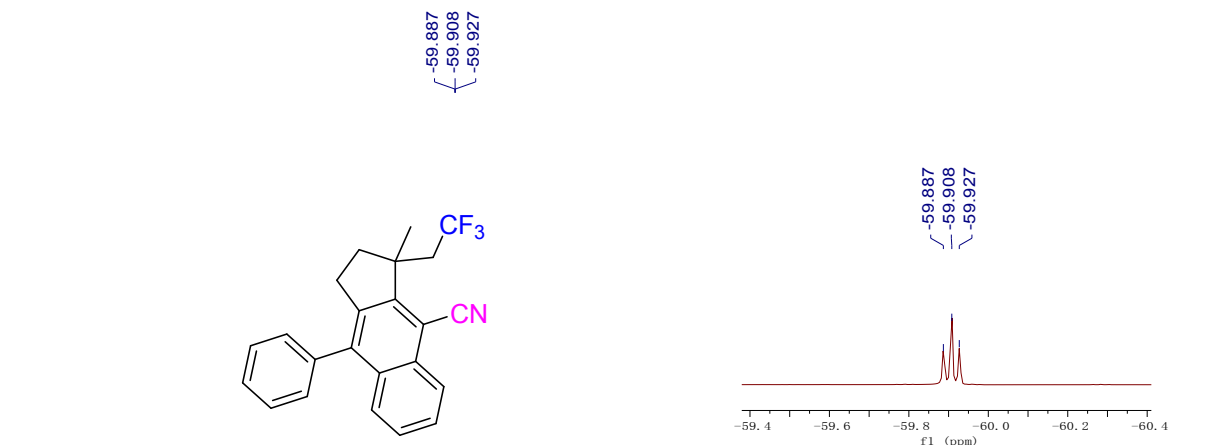
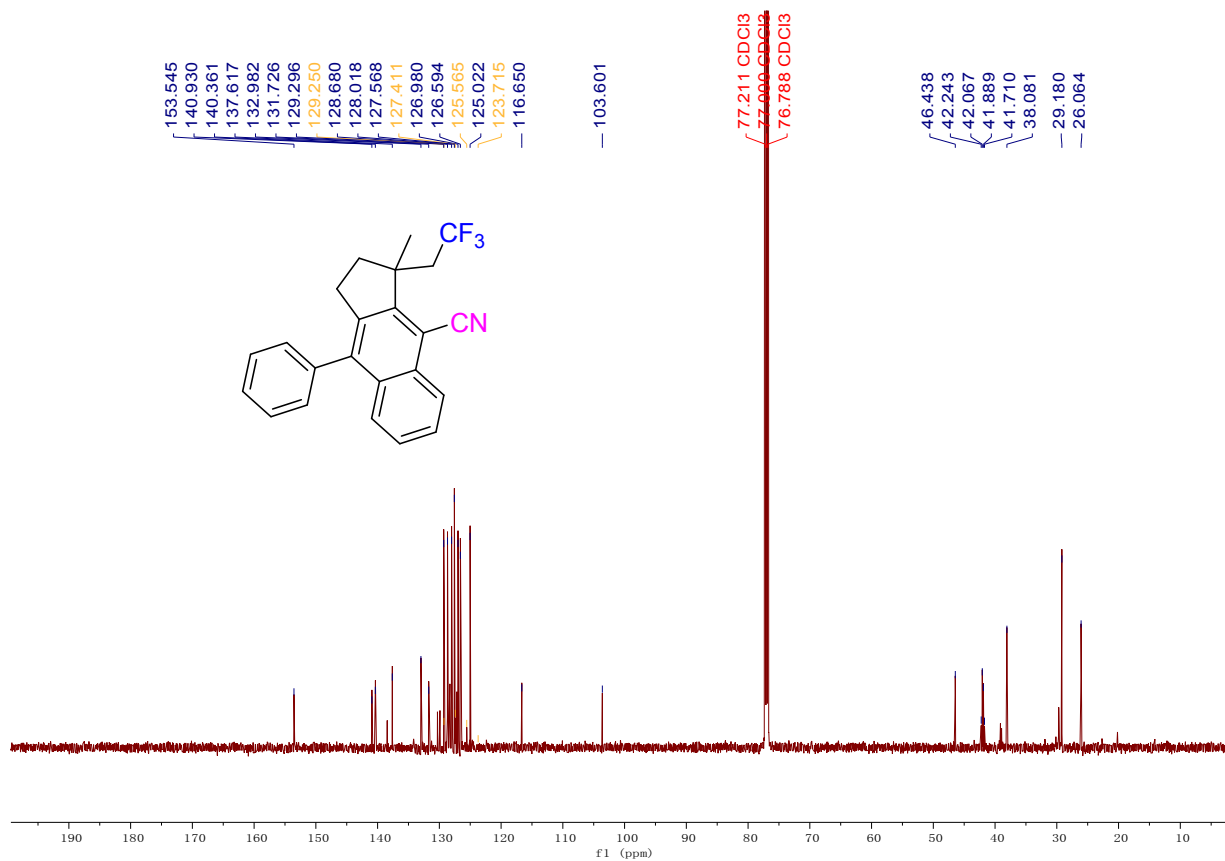


Note: Due to the low polarity, products **2** and **3** could not be separated completely via a column

chromatography on silica gel in some cases. Therefore, the isolated total yield of inseparable mixture is marked. The ratio of 2/3 was determined from the crude ^{19}F -NMR spectra detected with $\text{CF}_3\text{-DMAc}$ as an internal standard and the data of major product are listed below in most cases.

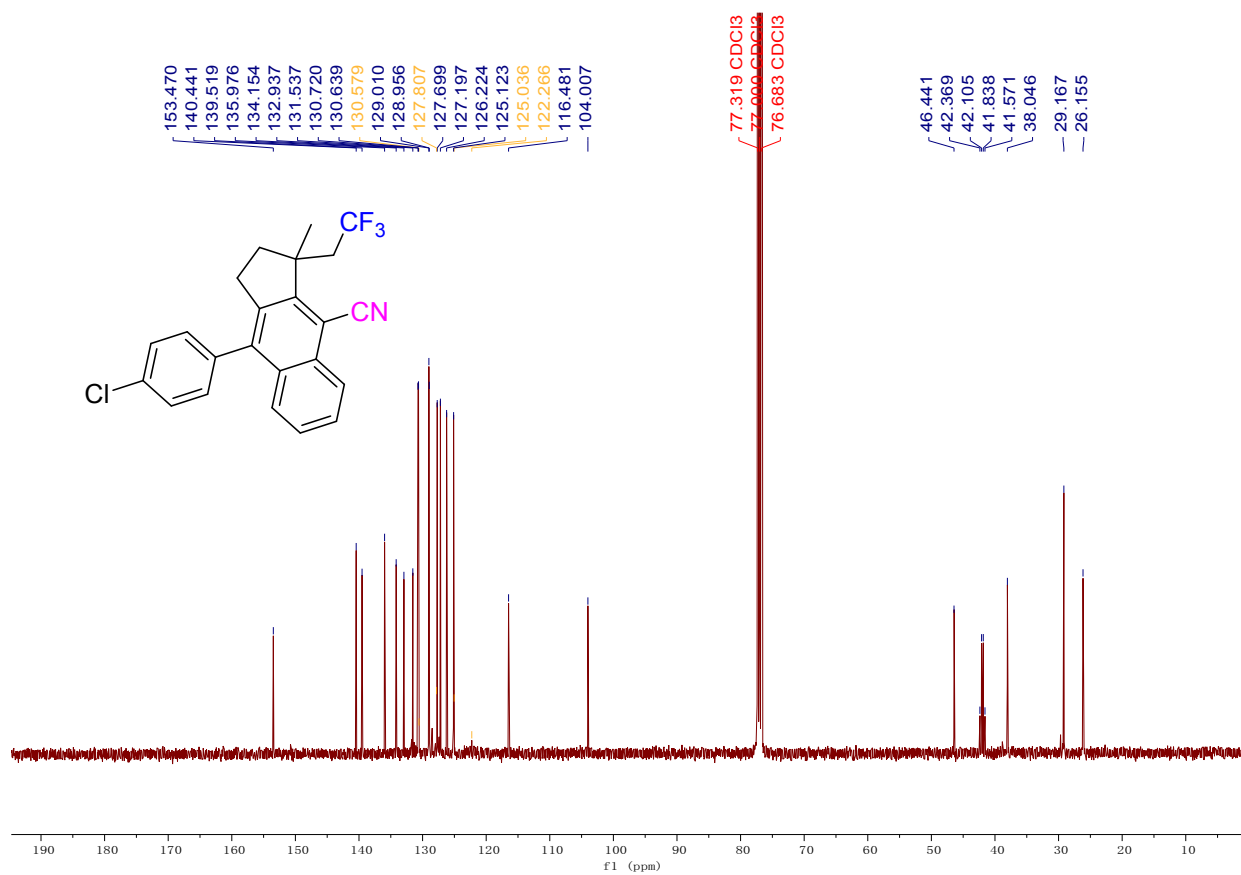
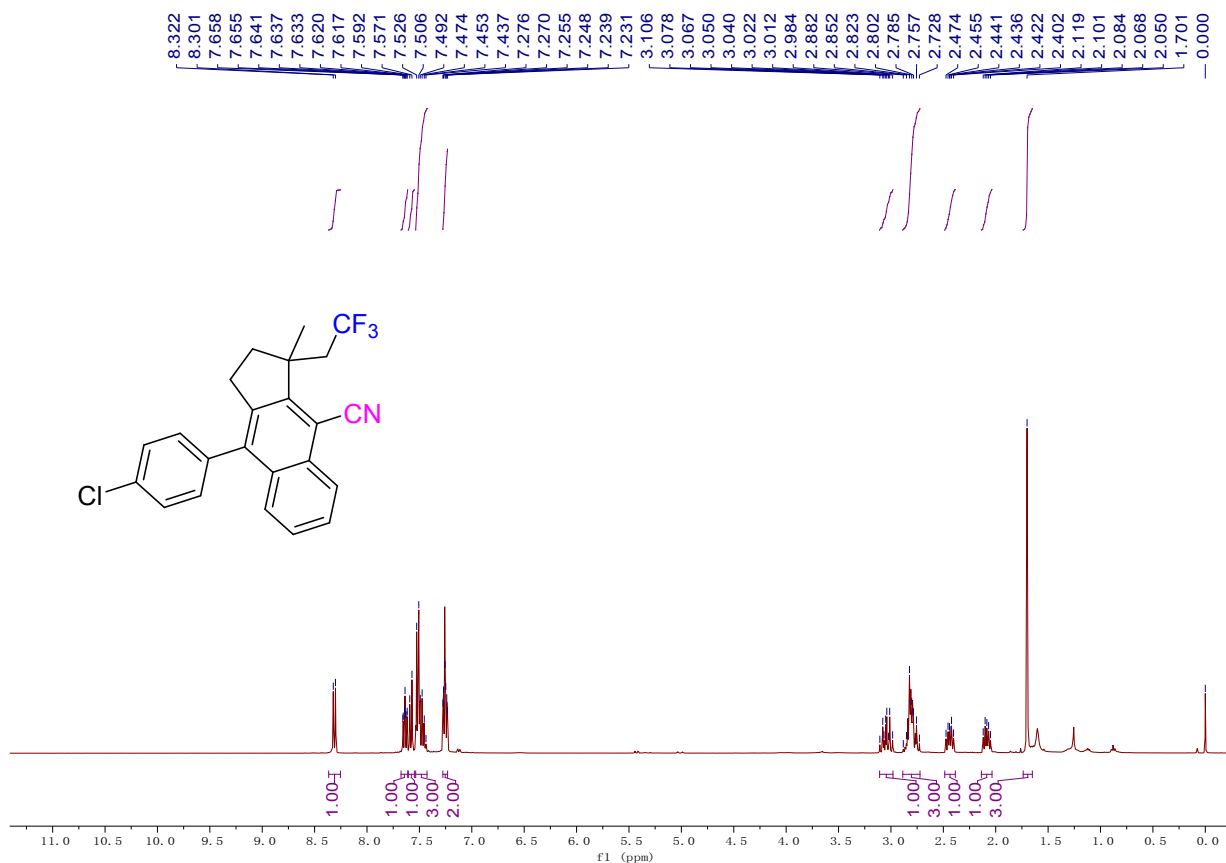
3-methyl-9-phenyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2a)

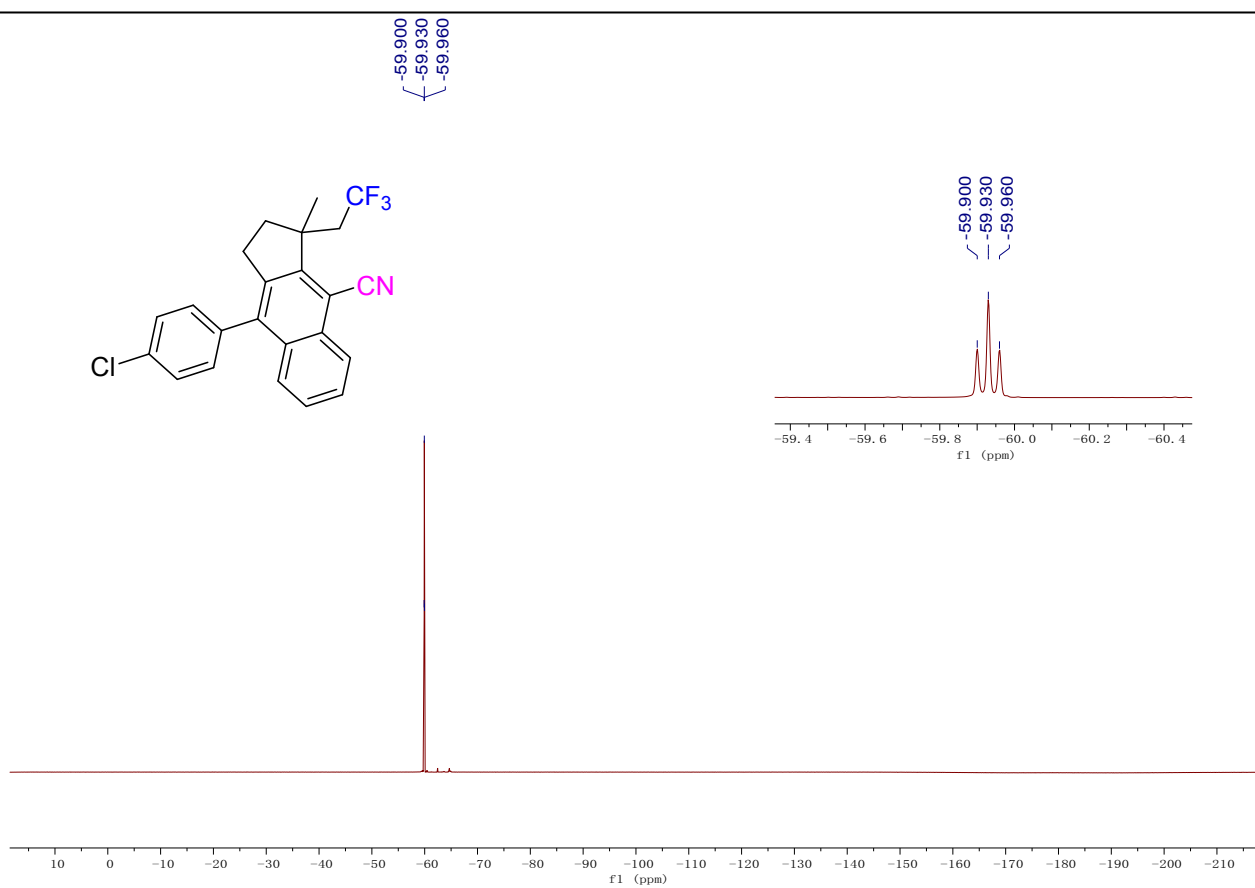




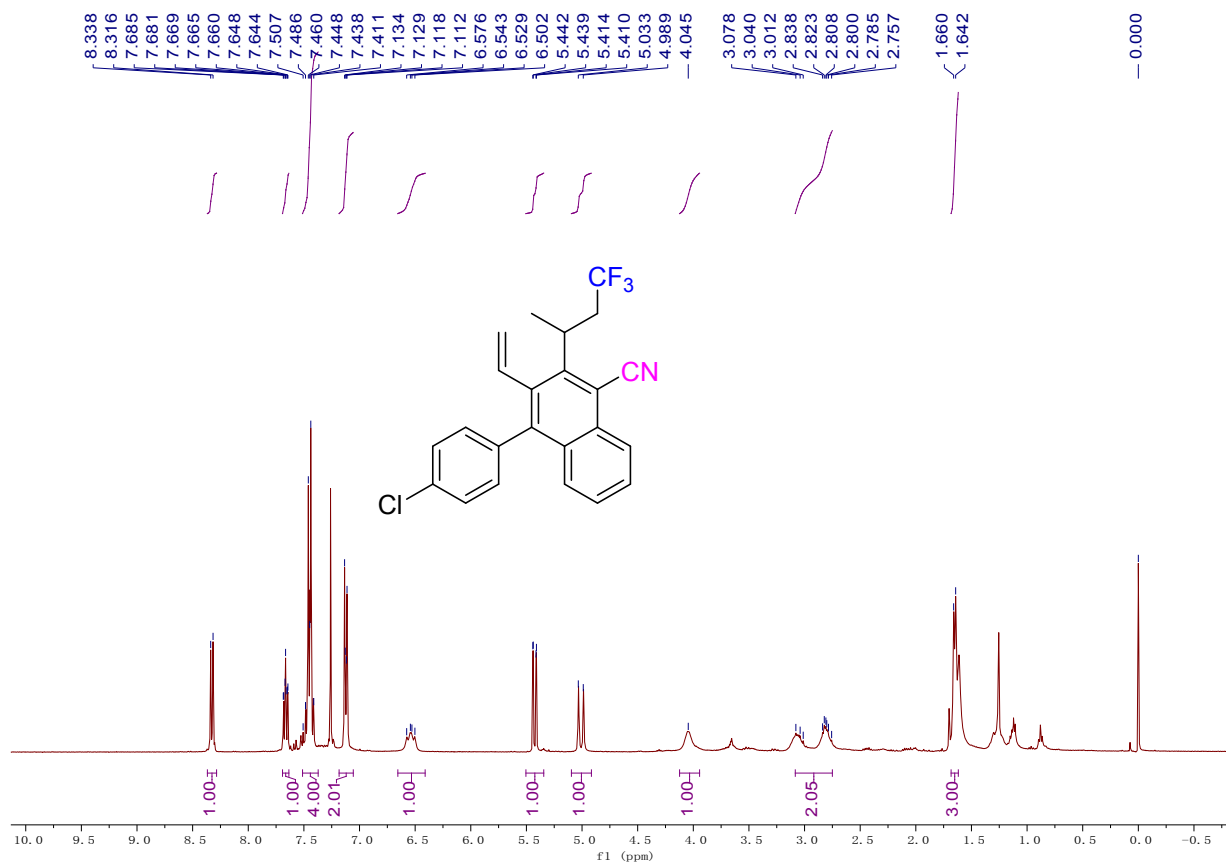
9-(4-chlorophenyl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-

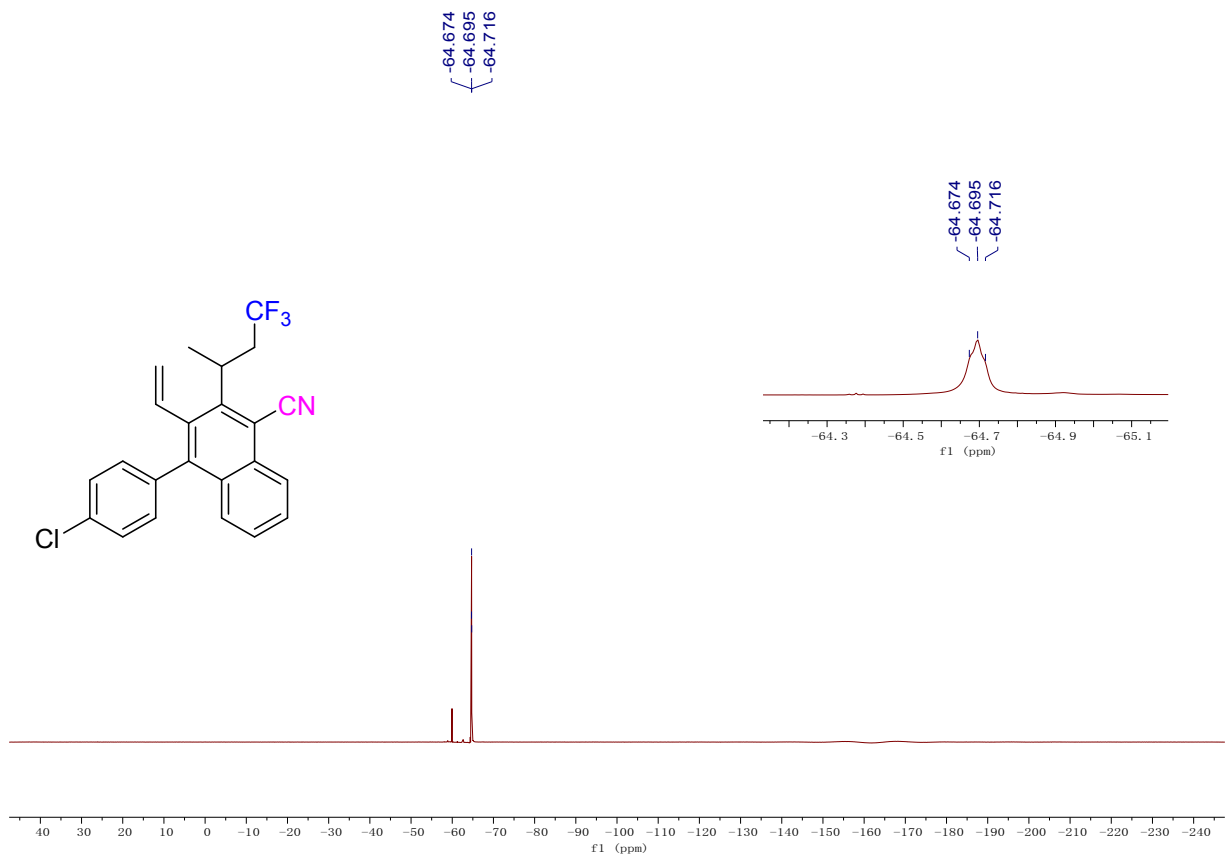
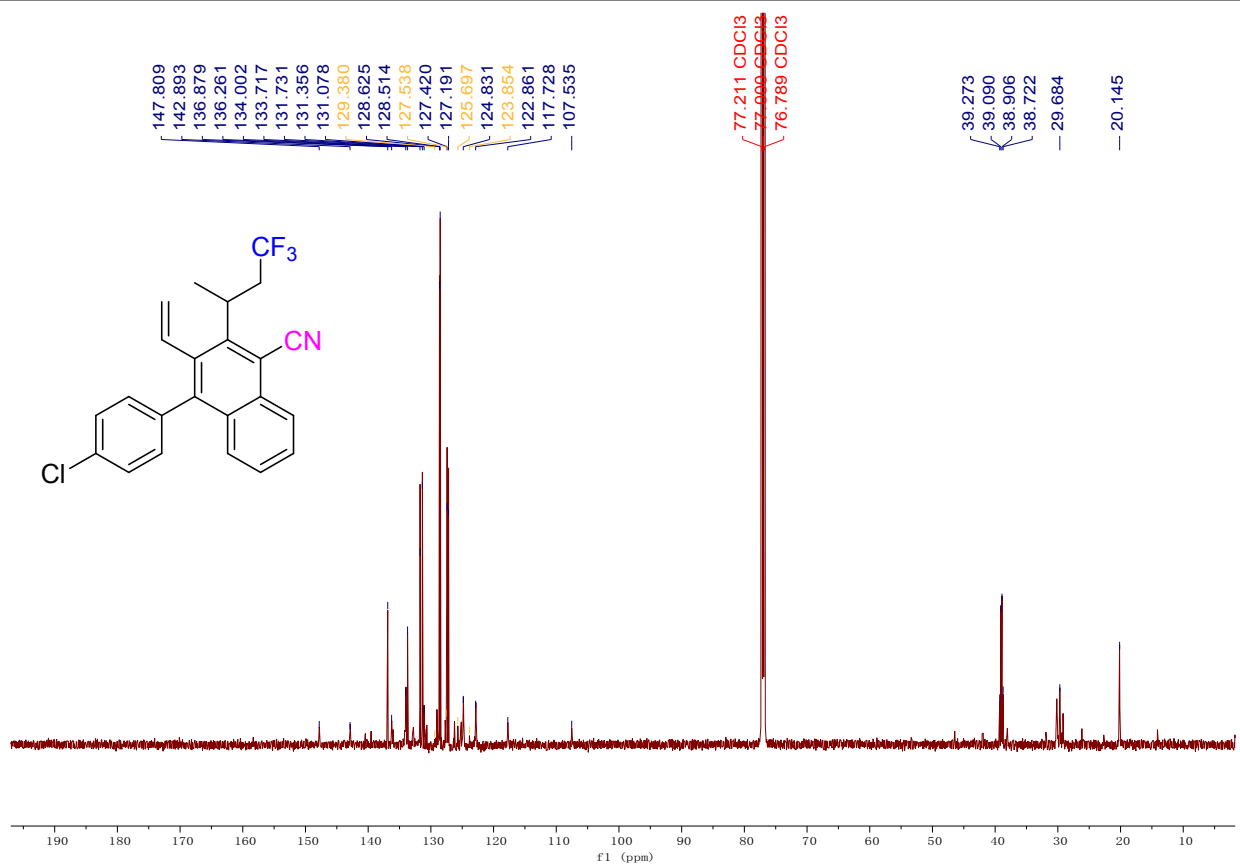
cyclopenta[*b*]naphthalene-4-carbonitrile (2b)



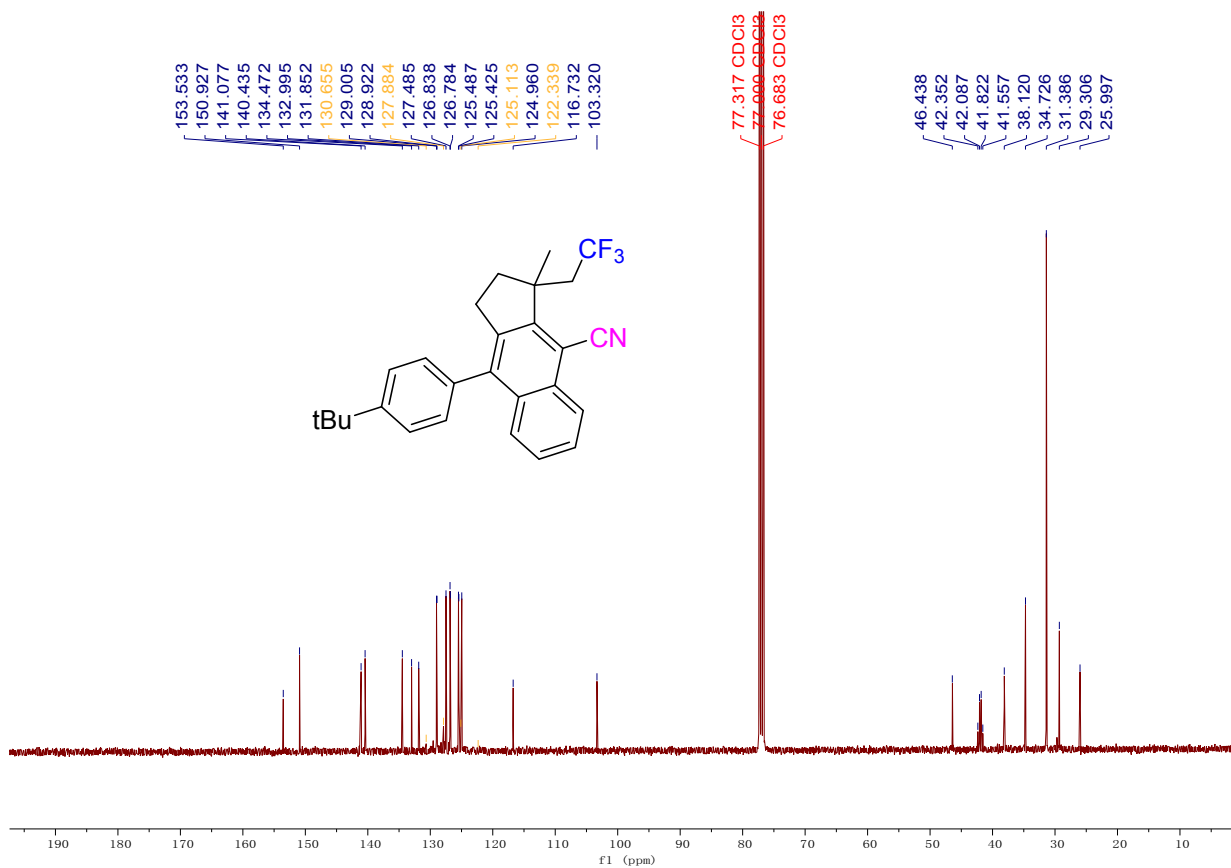
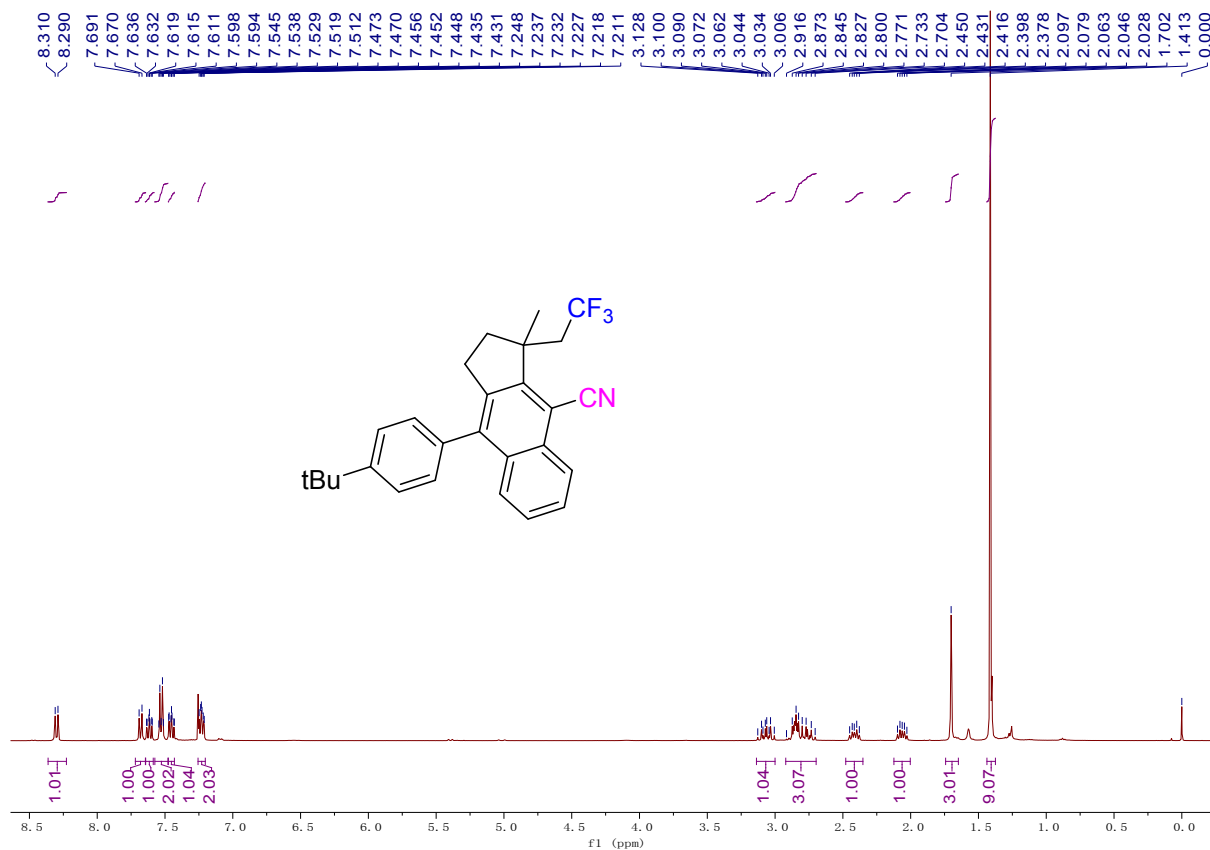


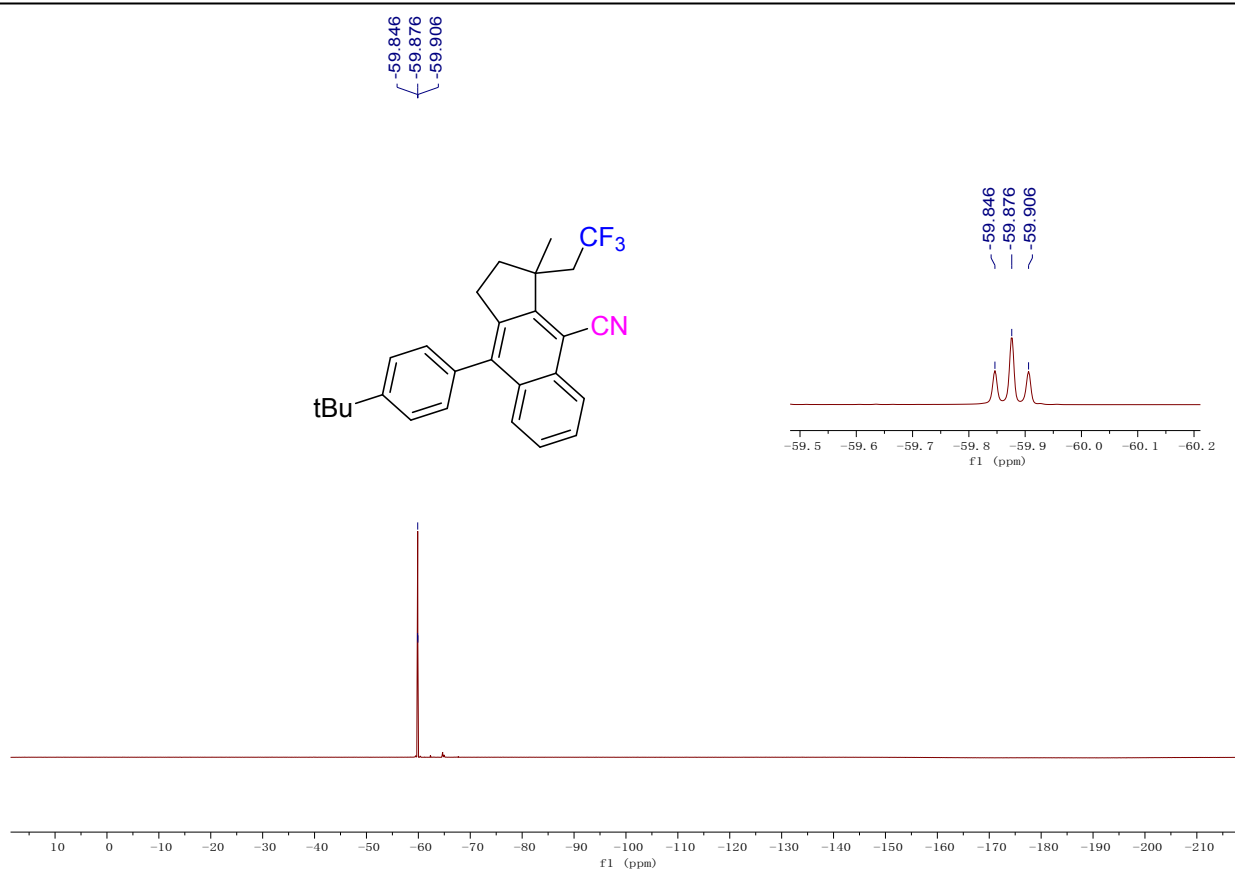
4-(4-chlorophenyl)-2-(4,4,4-trifluorobutan-2-yl)-3-vinyl-1-naphthonitrile (3b)



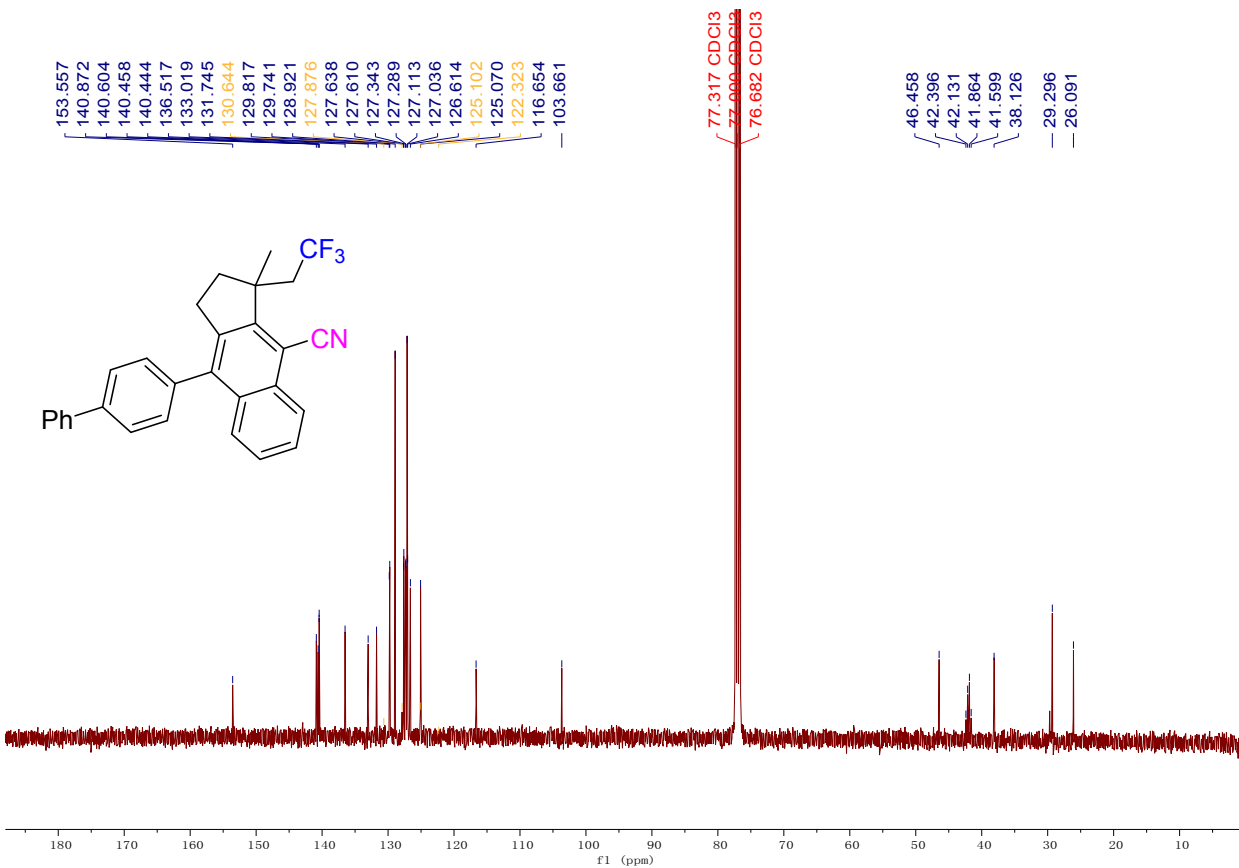
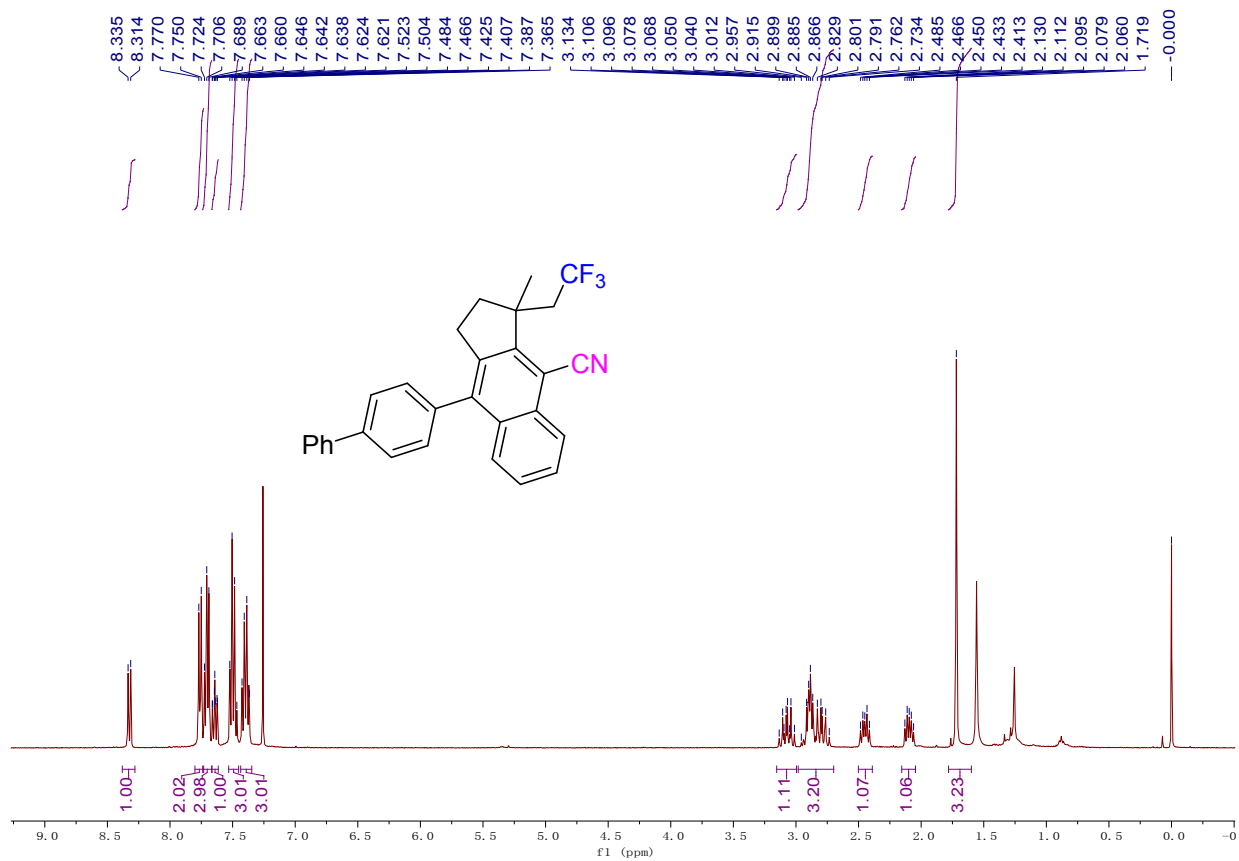


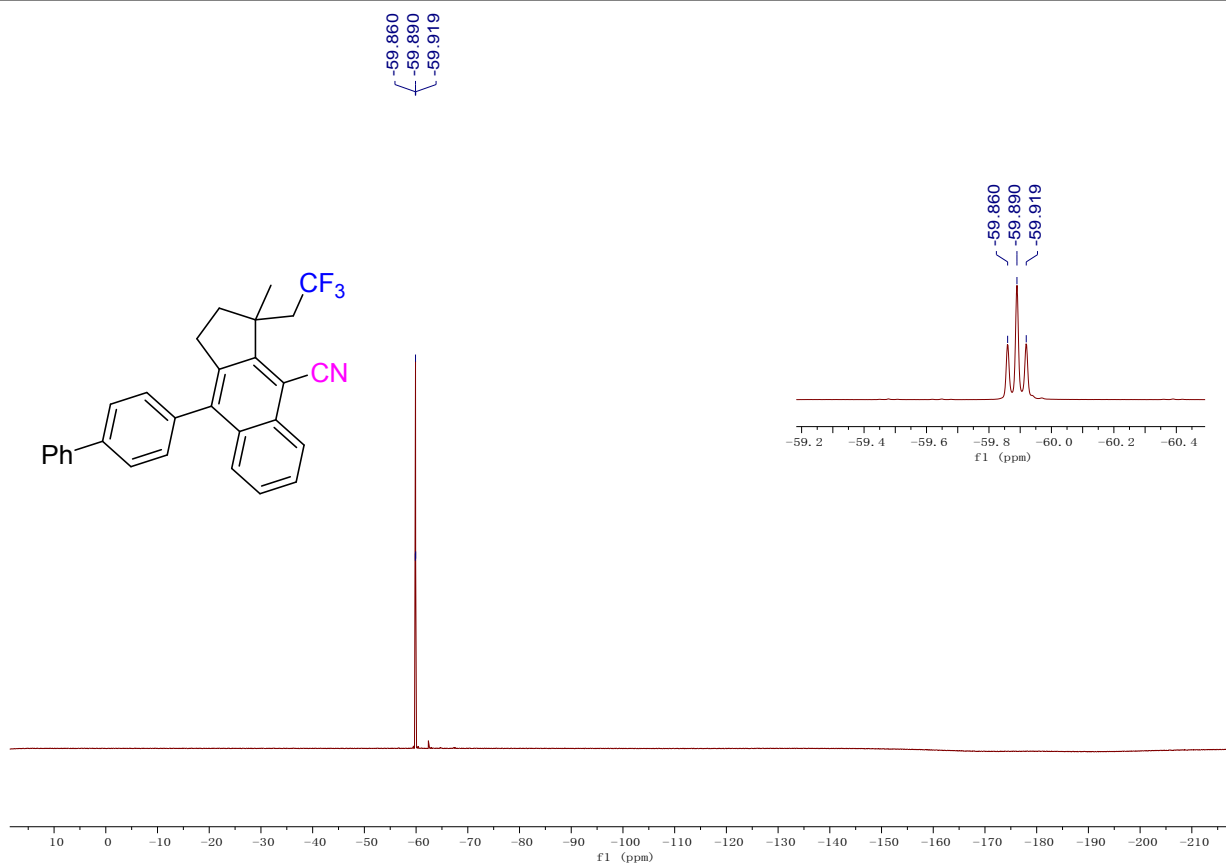
9-(4-(*tert*-butyl)phenyl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[*b*]naphthalene-4-carbonitrile (2c)



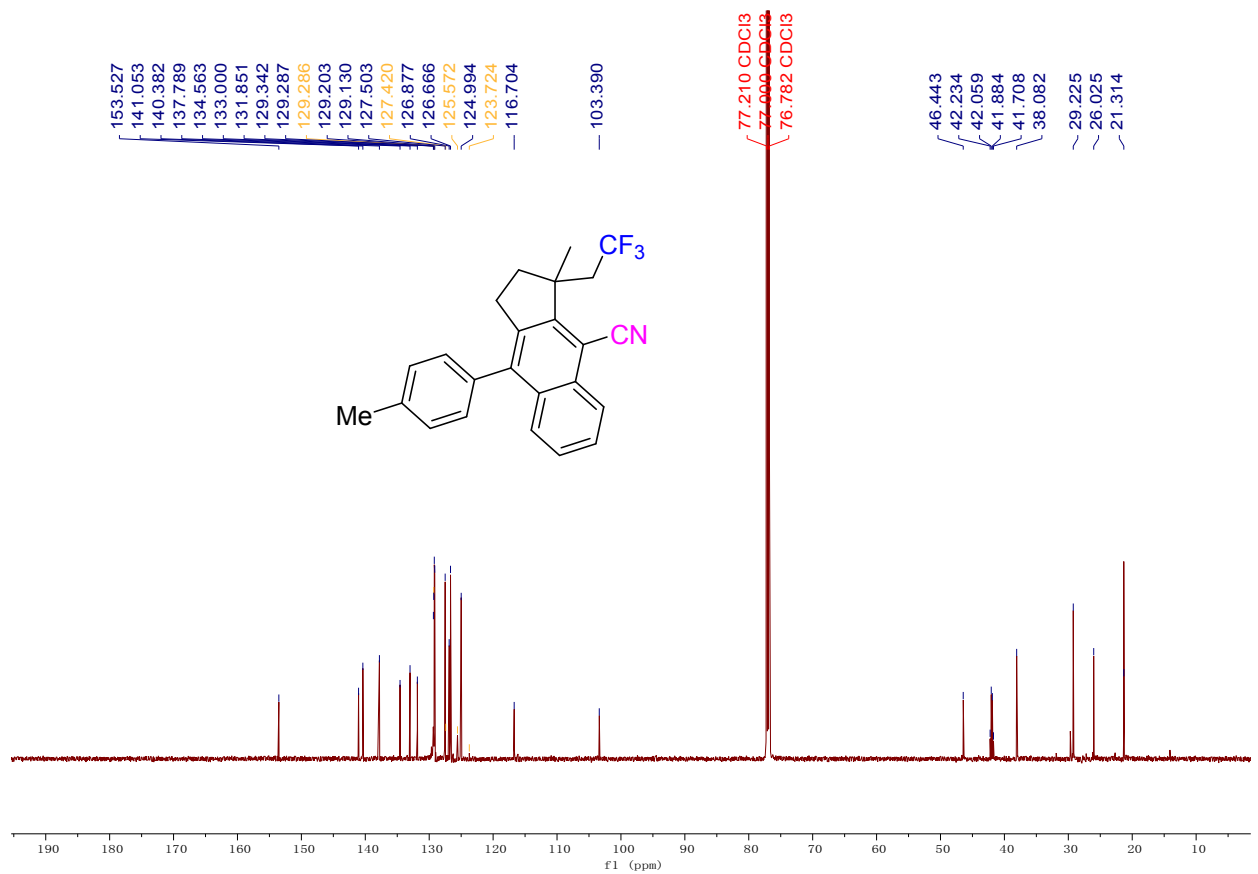
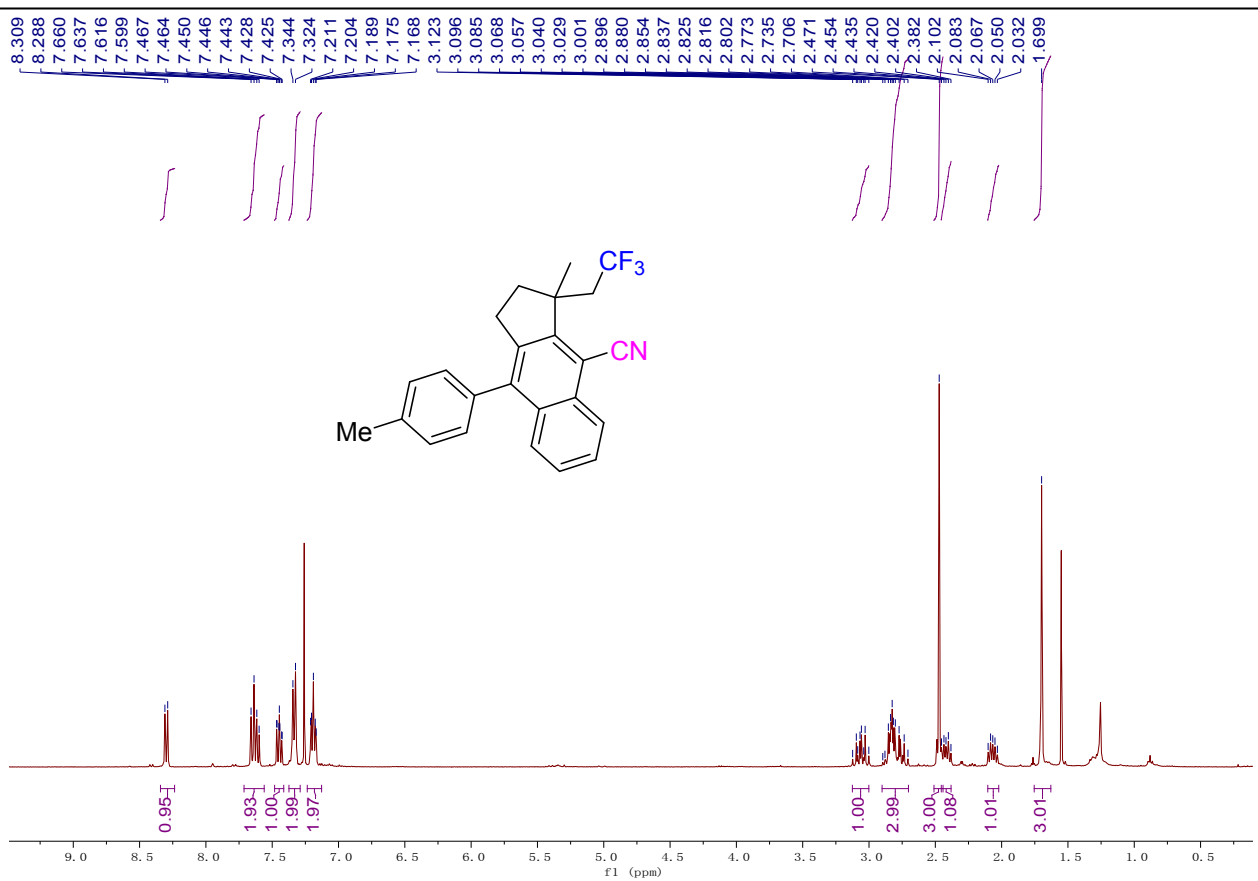


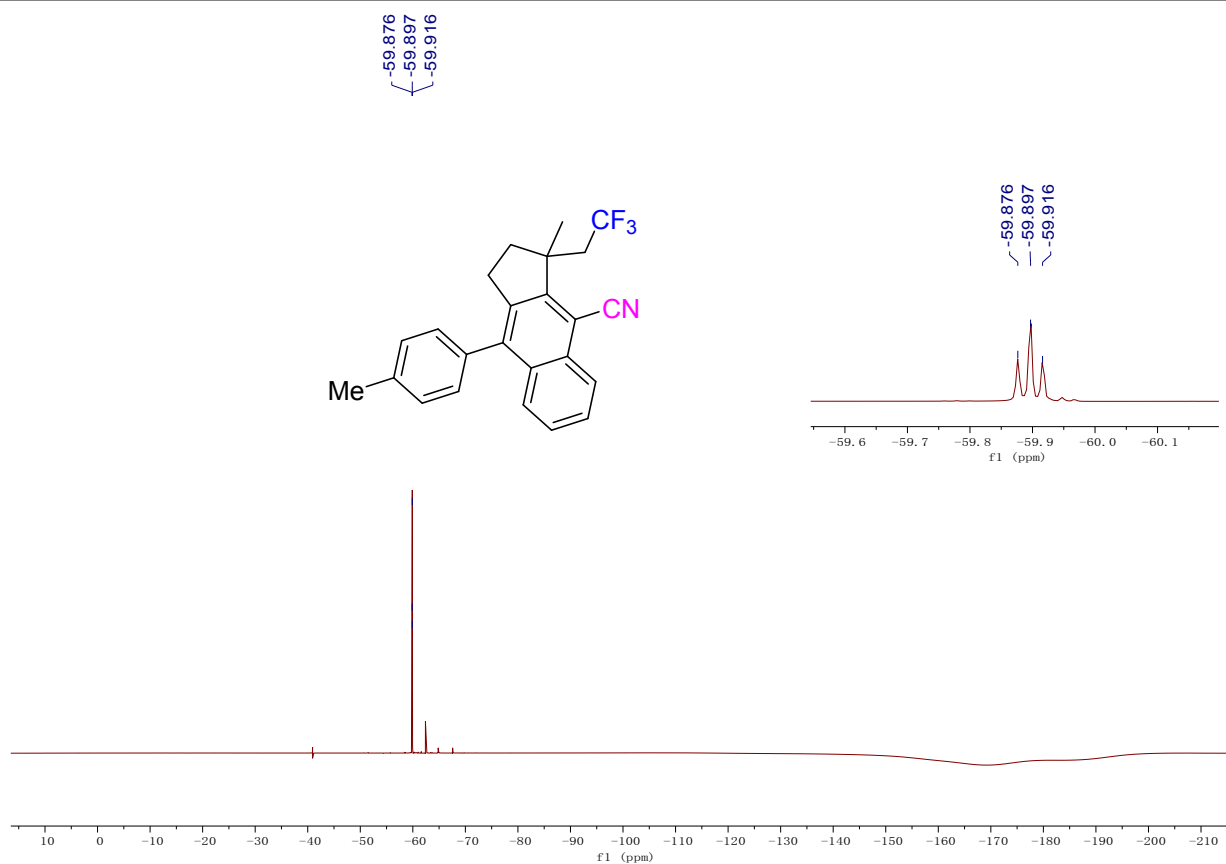
9-([1,1'-biphenyl]-4-yl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2d)



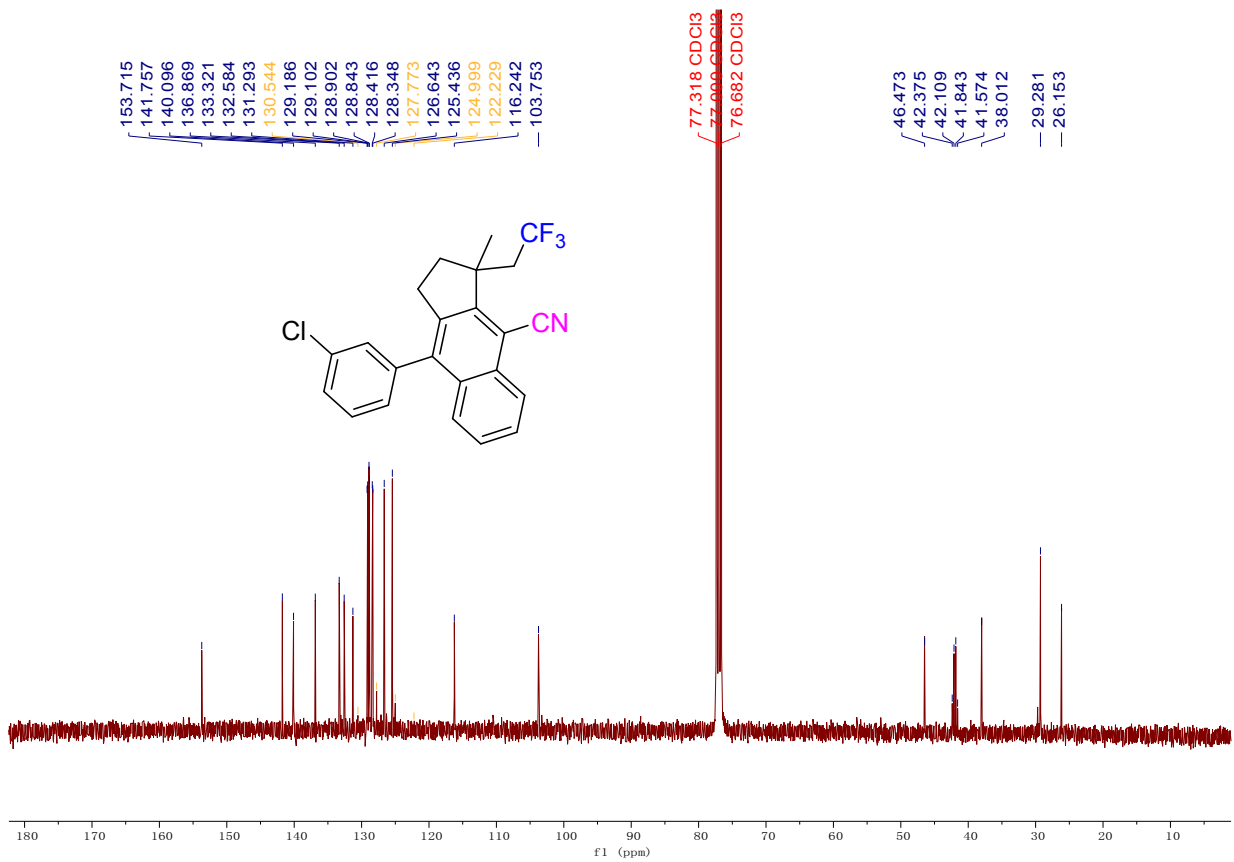
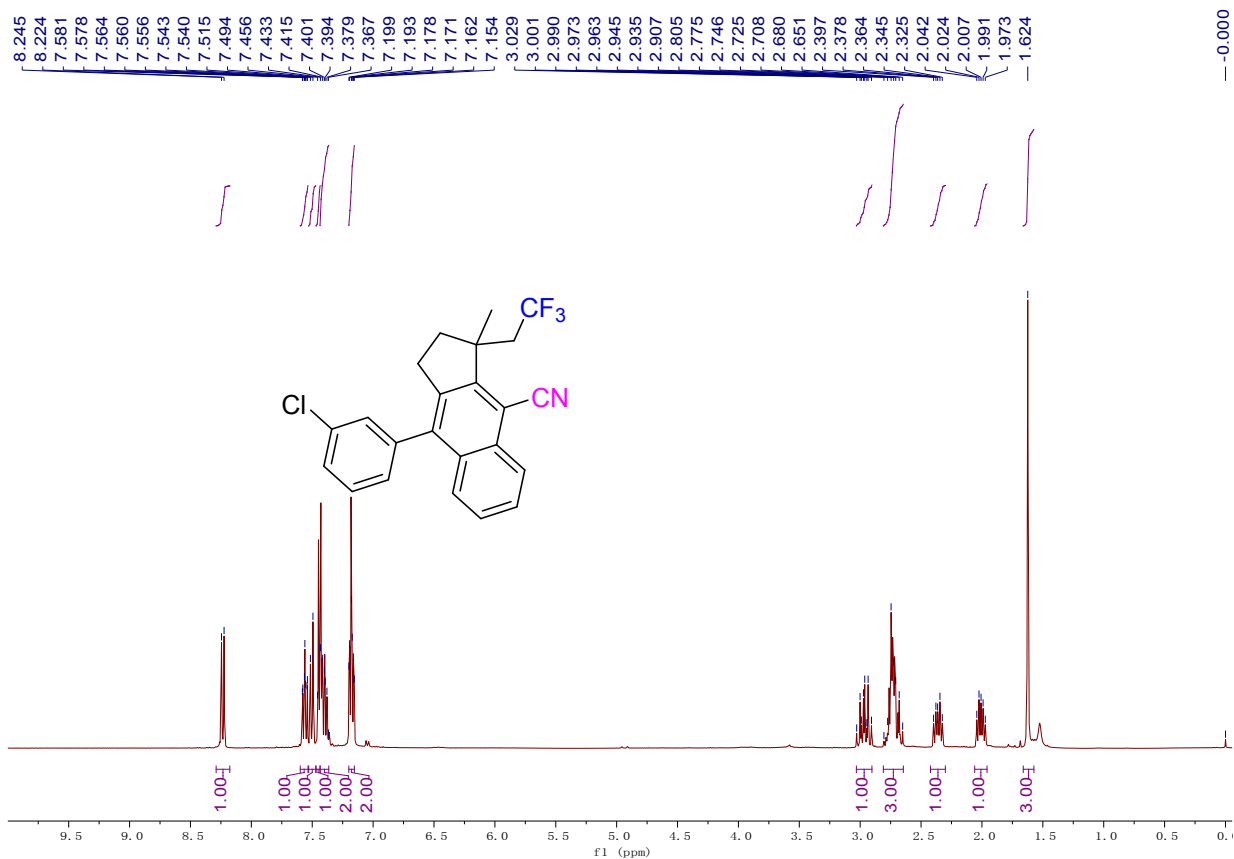


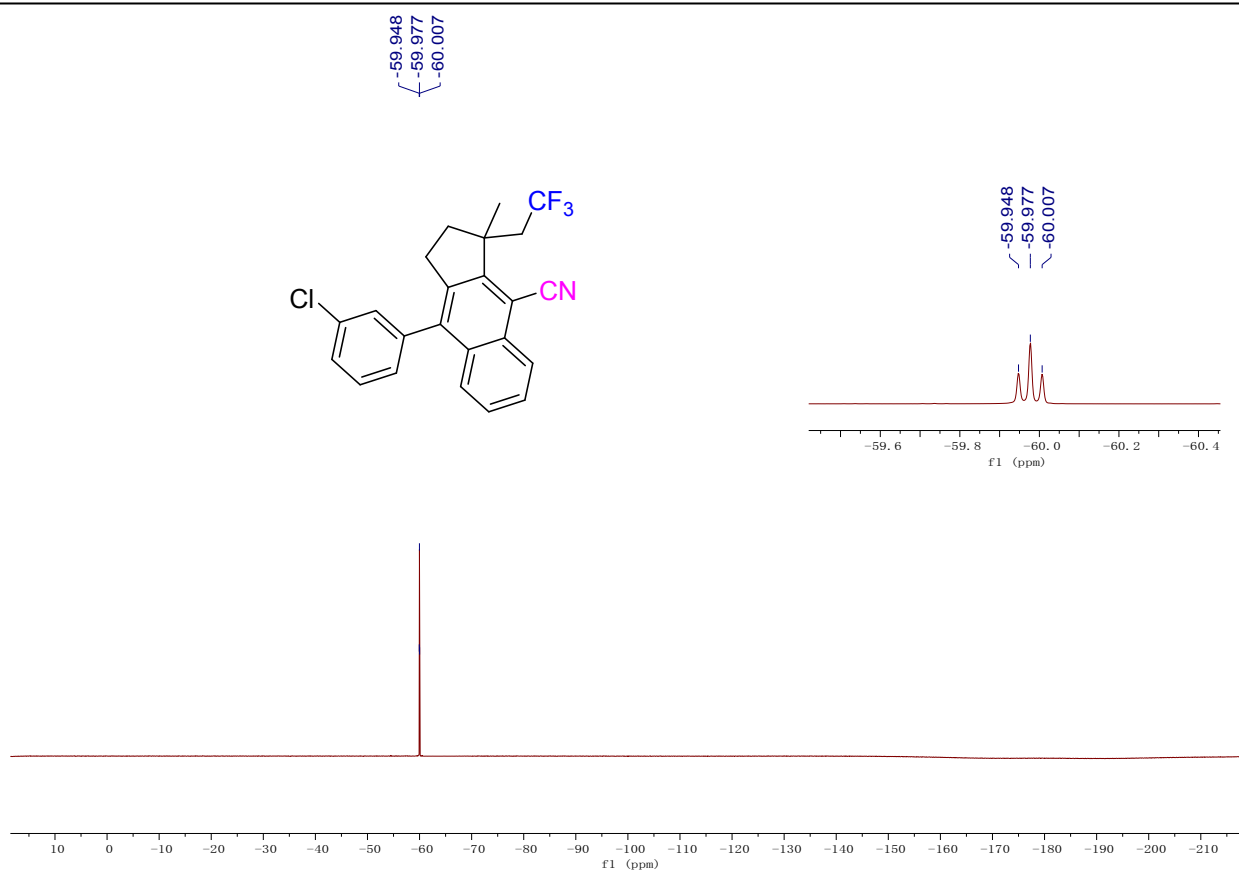
3-methyl-9-(*p*-tolyl)-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1*H*-cyclopenta[*b*]naphthalene-4-carbonitrile (2e)



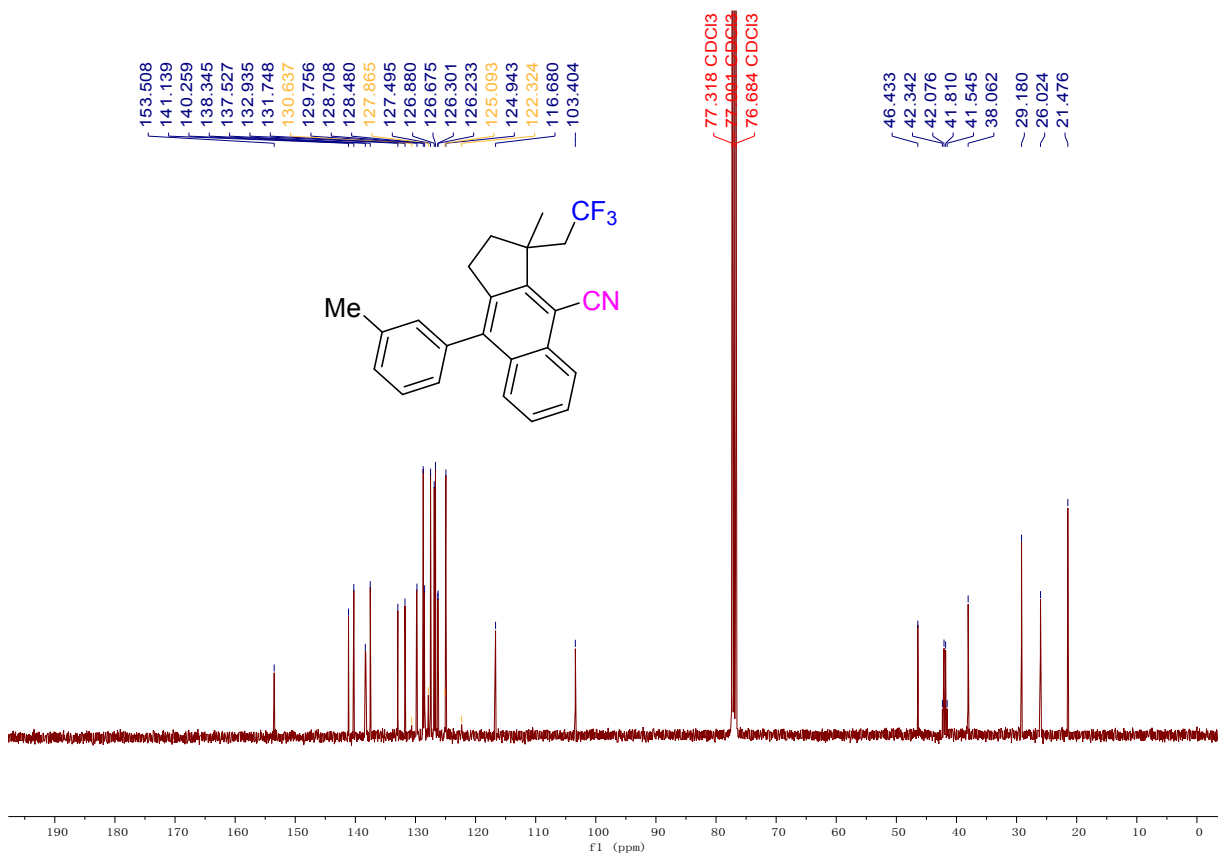
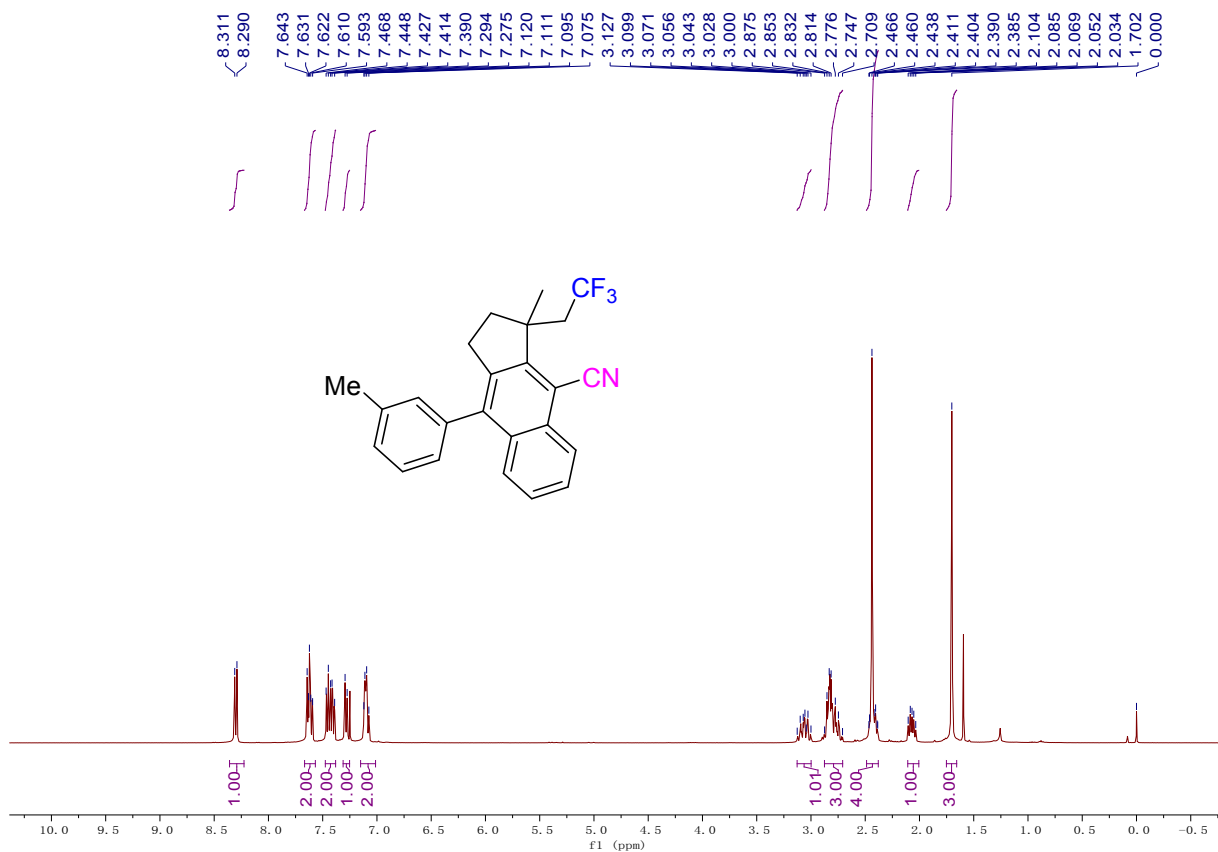


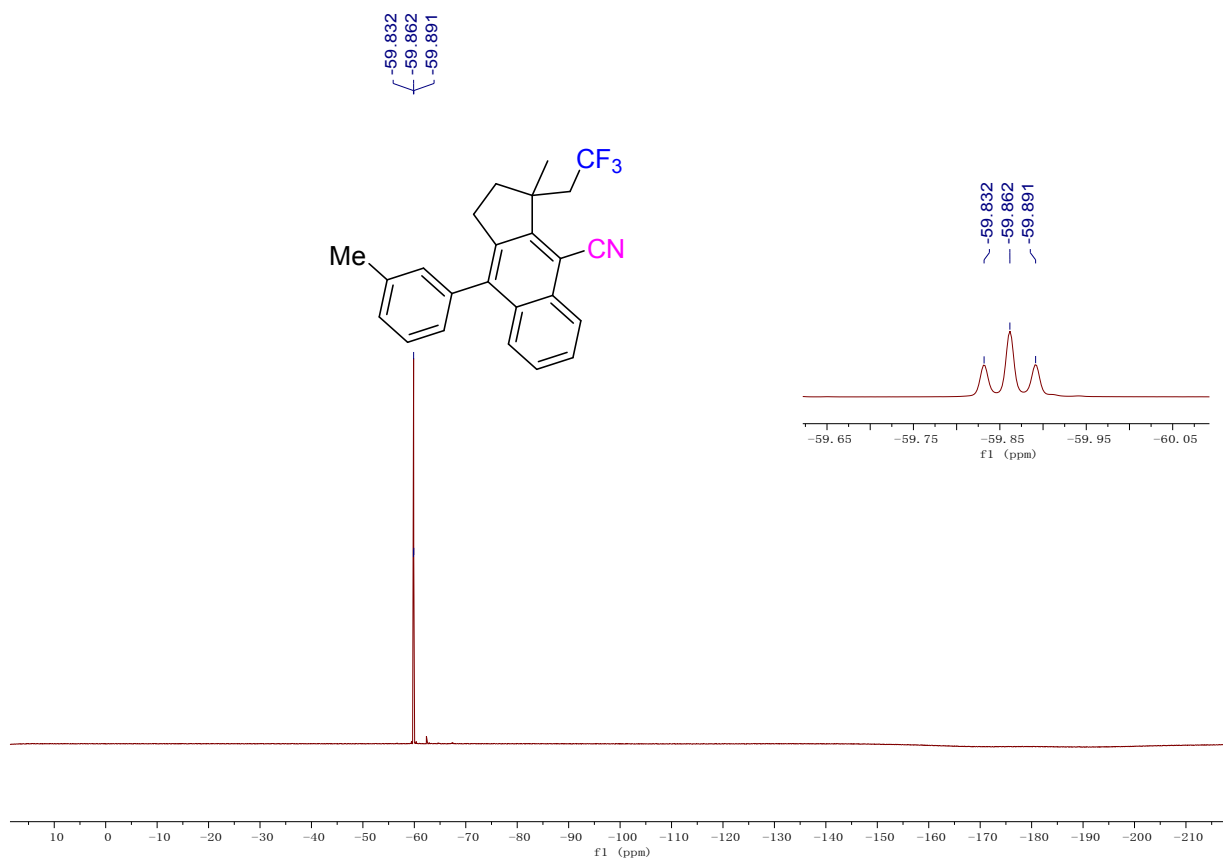
9-(3-chlorophenyl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2f)



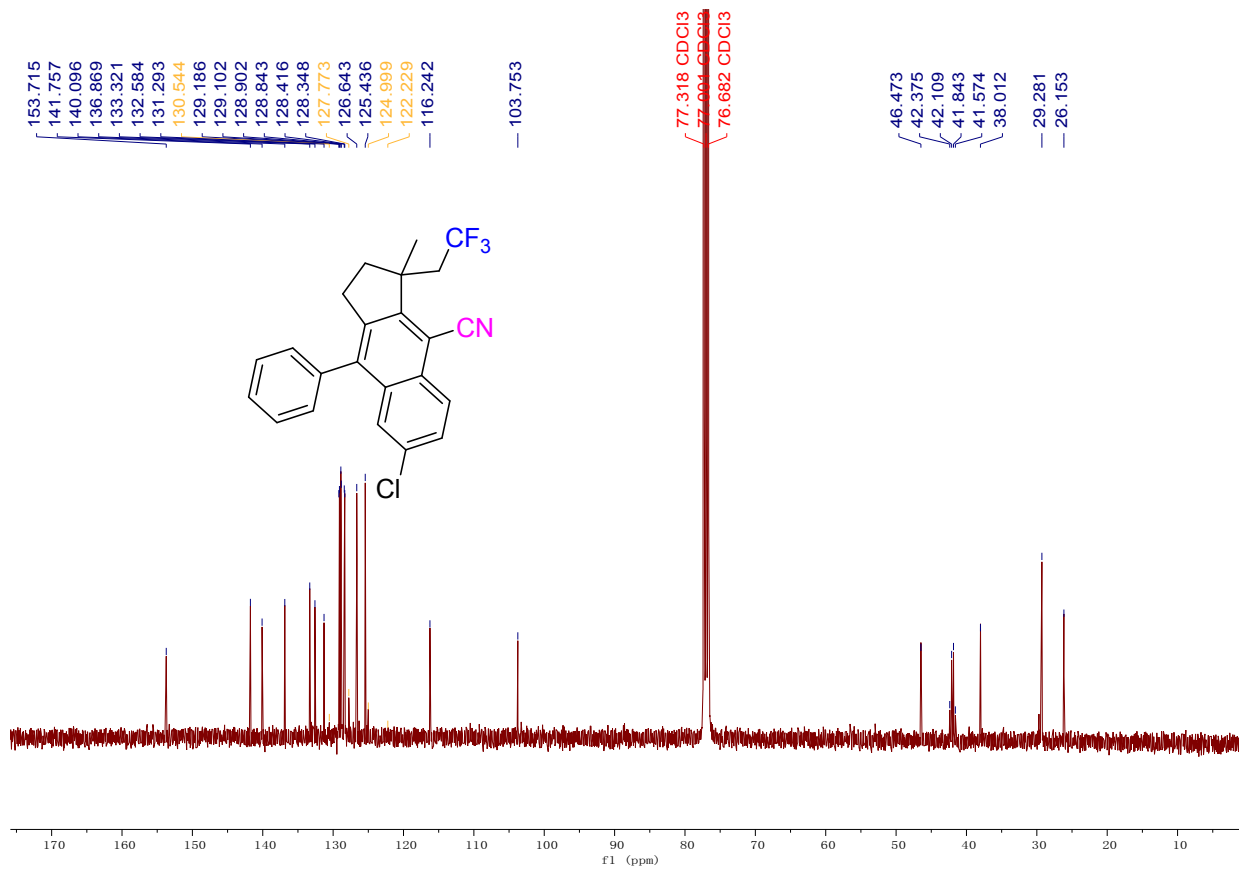
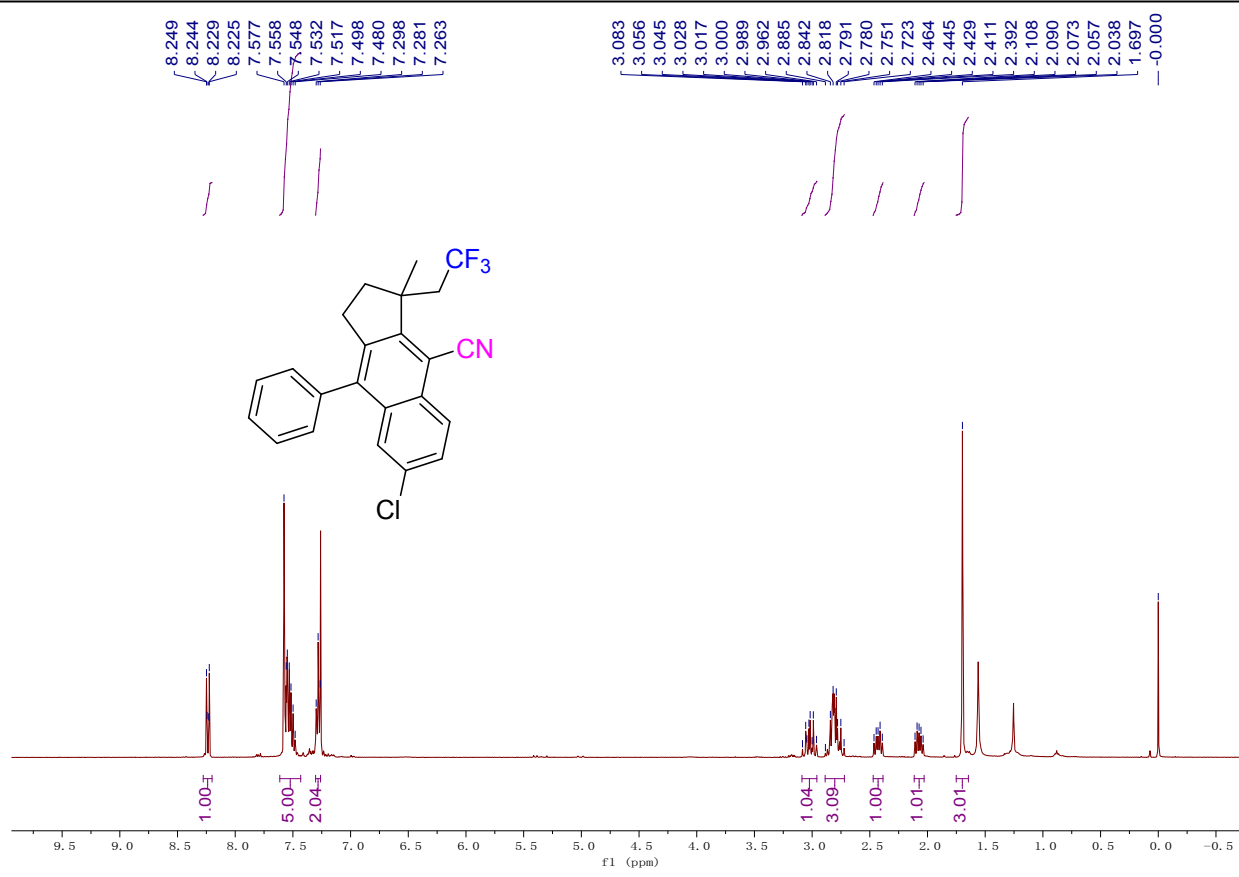


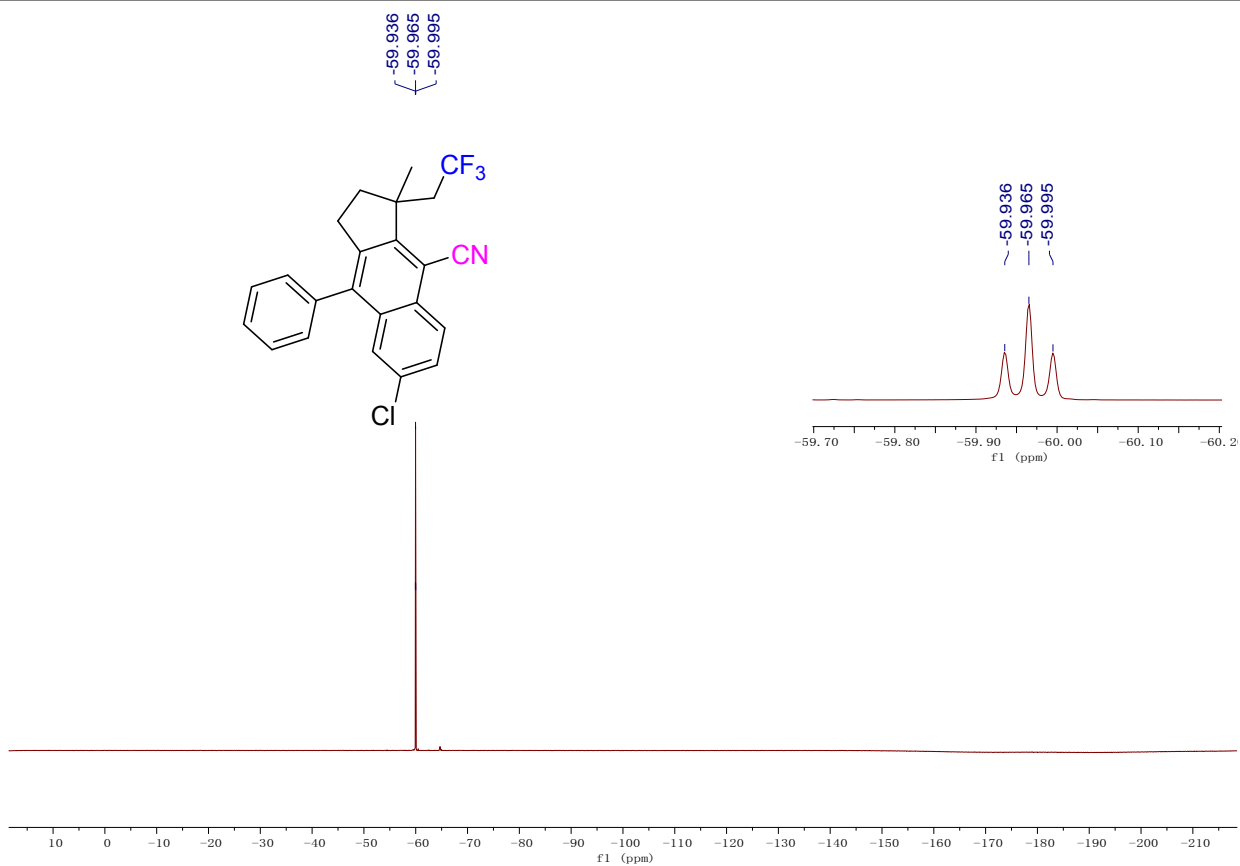
3-methyl-9-(*m*-tolyl)-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1*H*-cyclopenta[*b*]naphthalene-4-carbonitrile (2g)



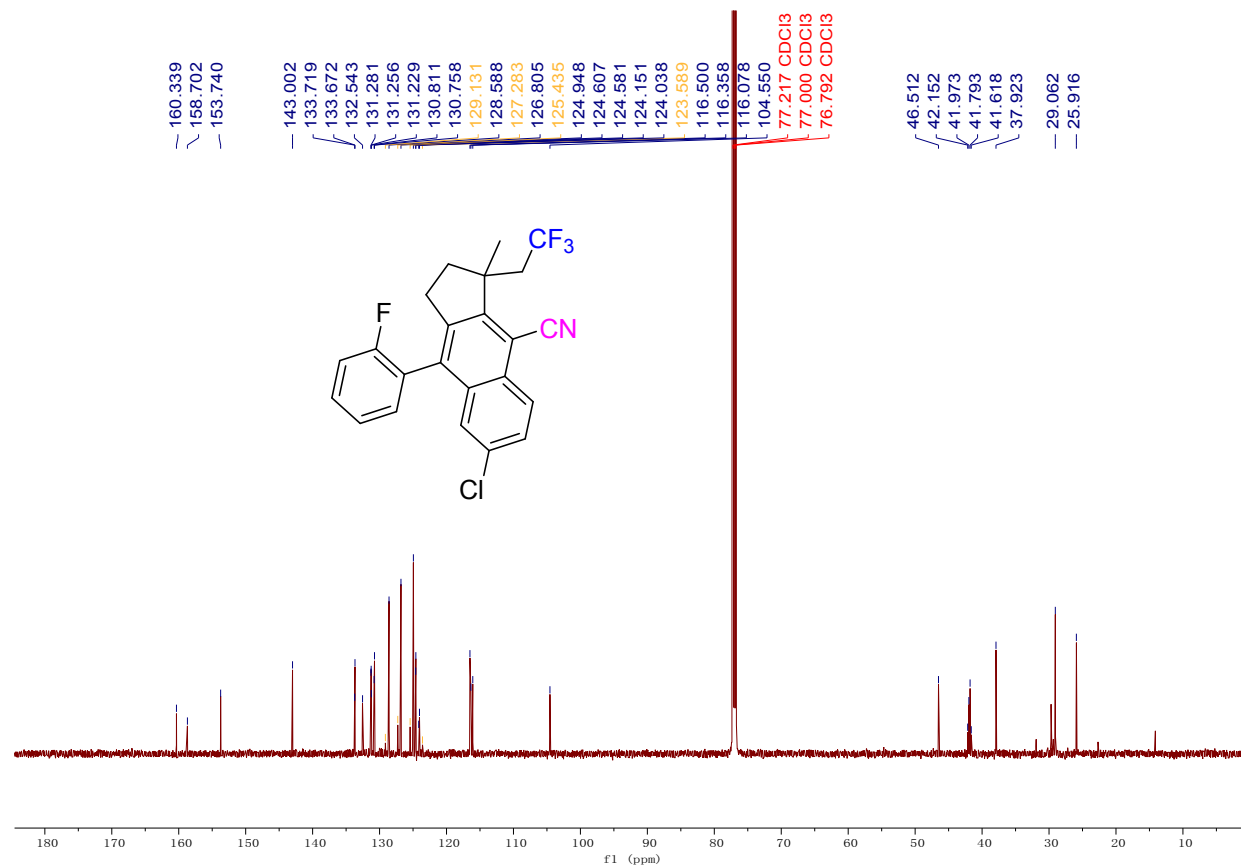
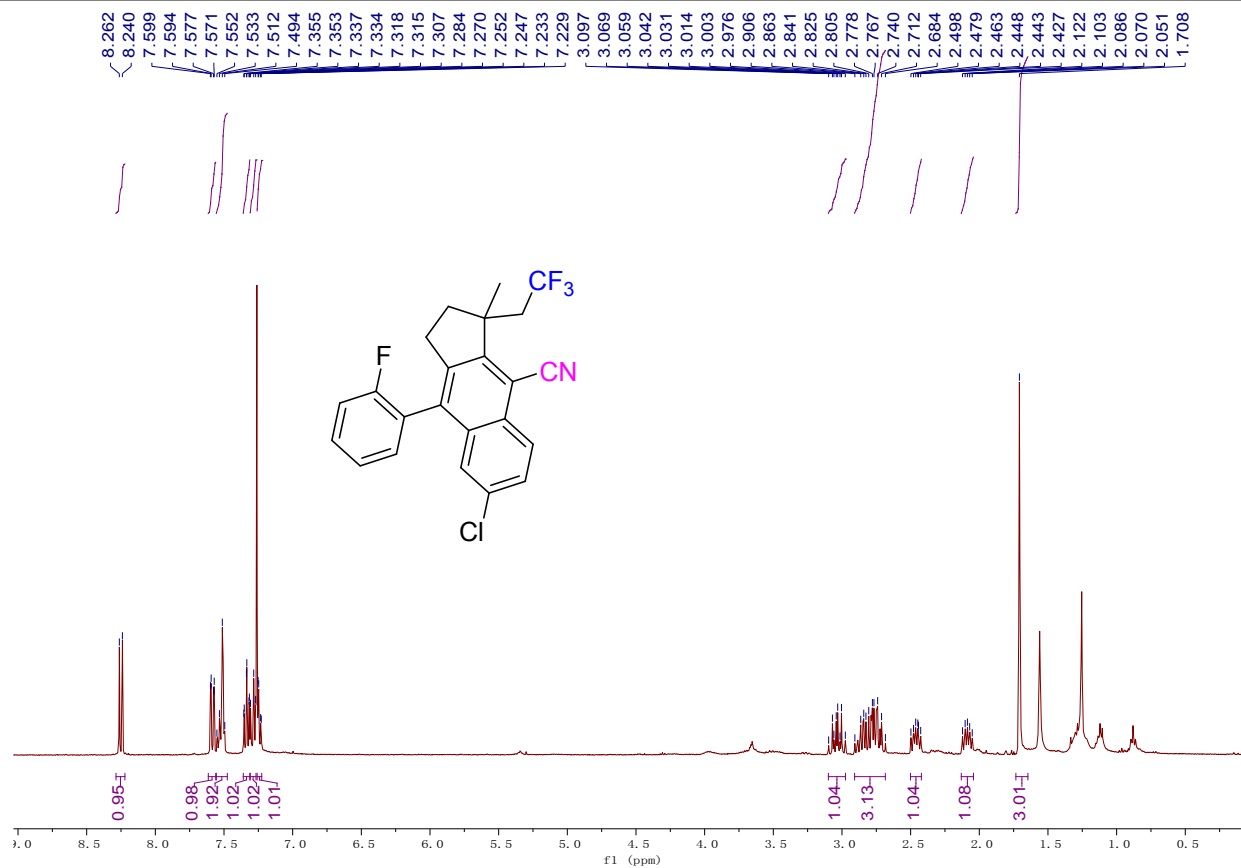


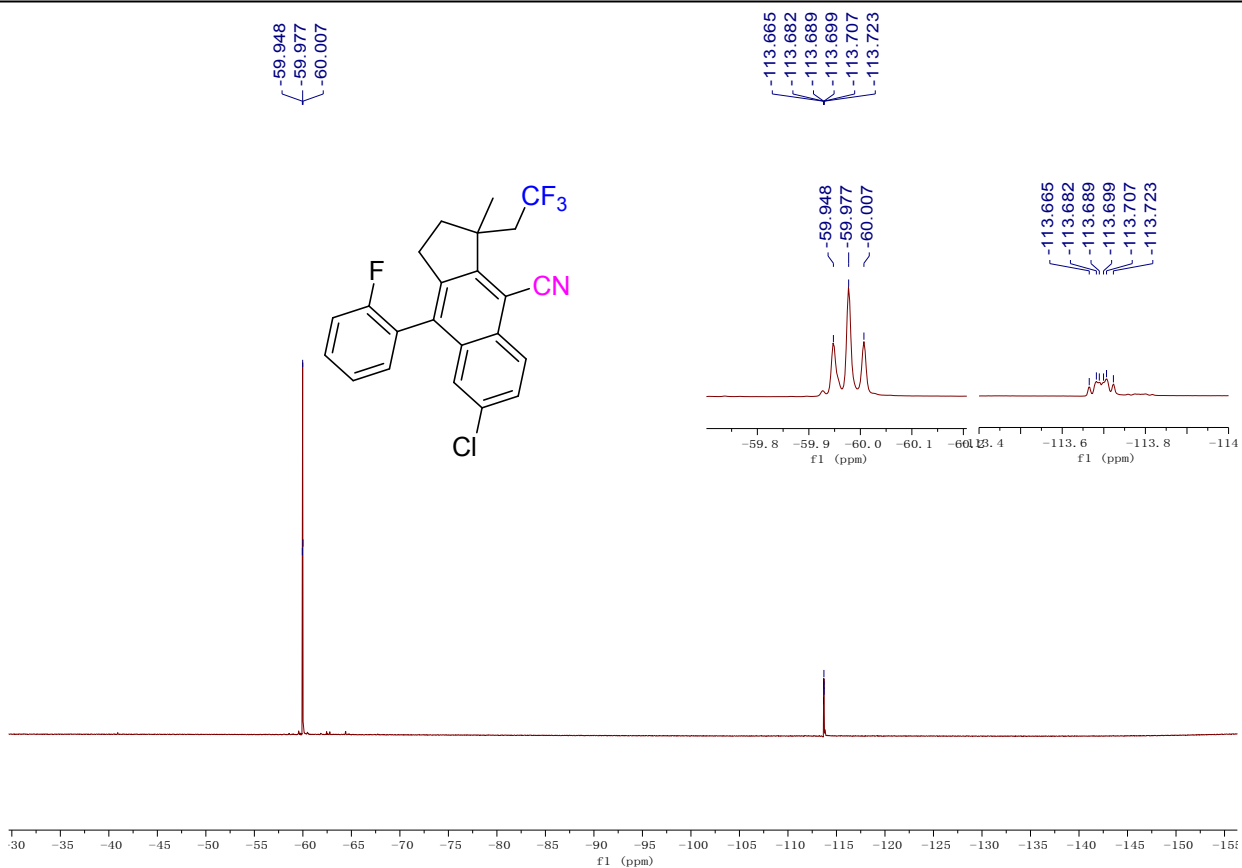
7-chloro-3-methyl-9-phenyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2h)



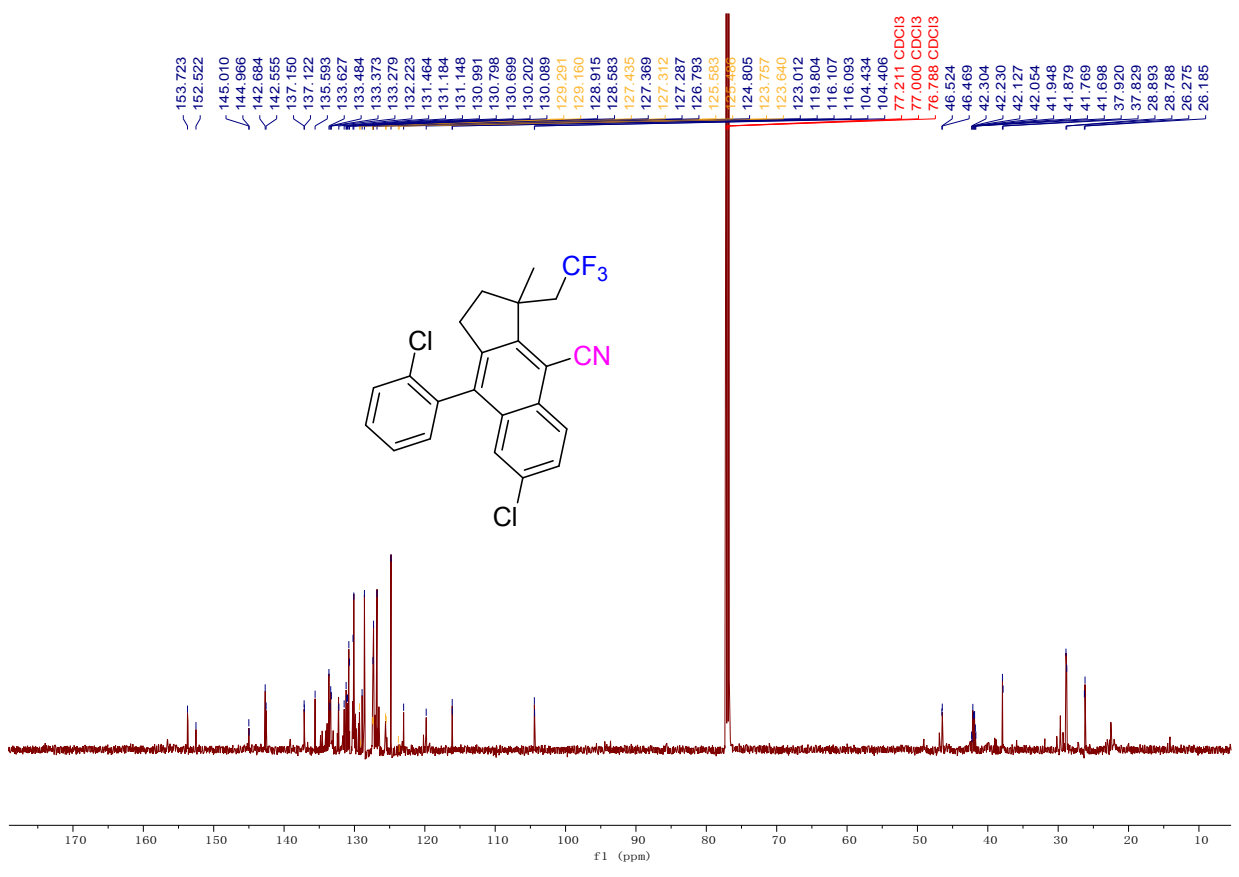
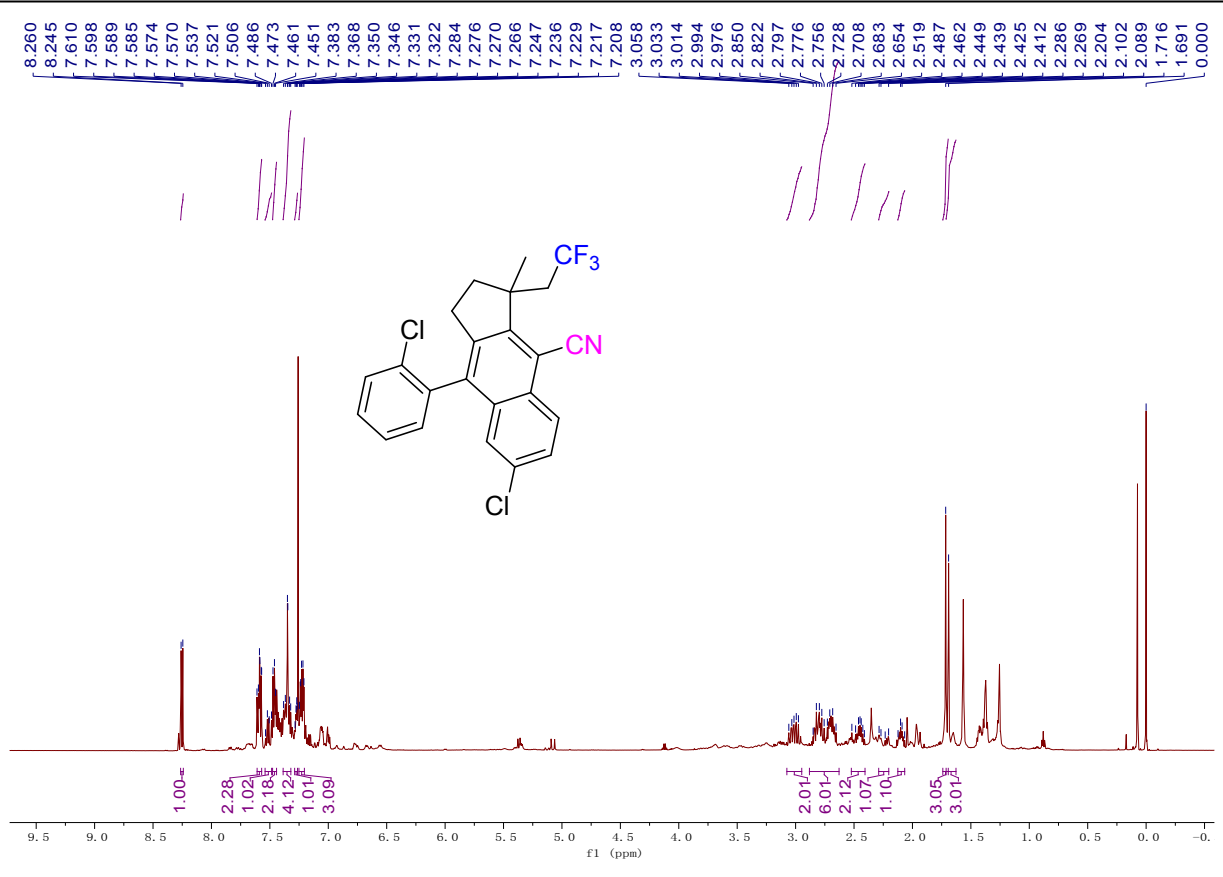


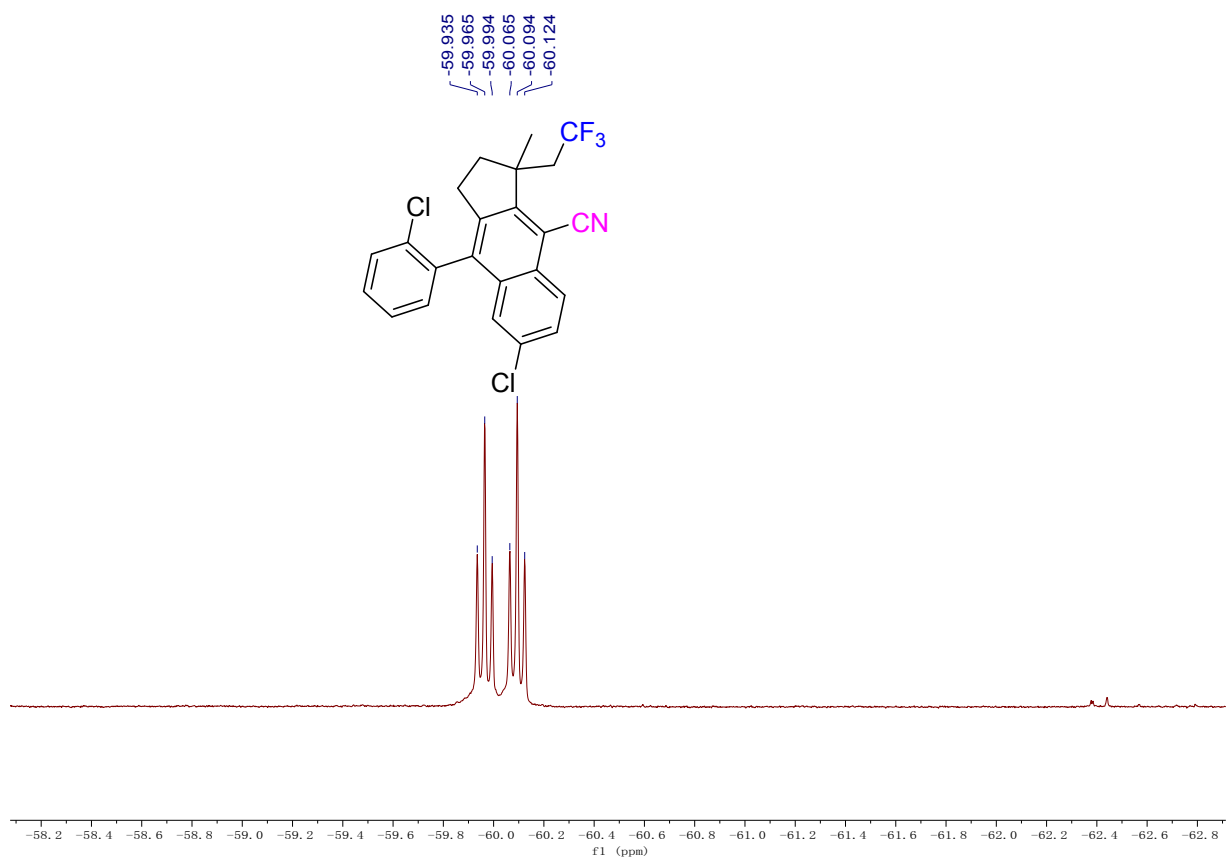
7-chloro-9-(2-fluorophenyl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2i)



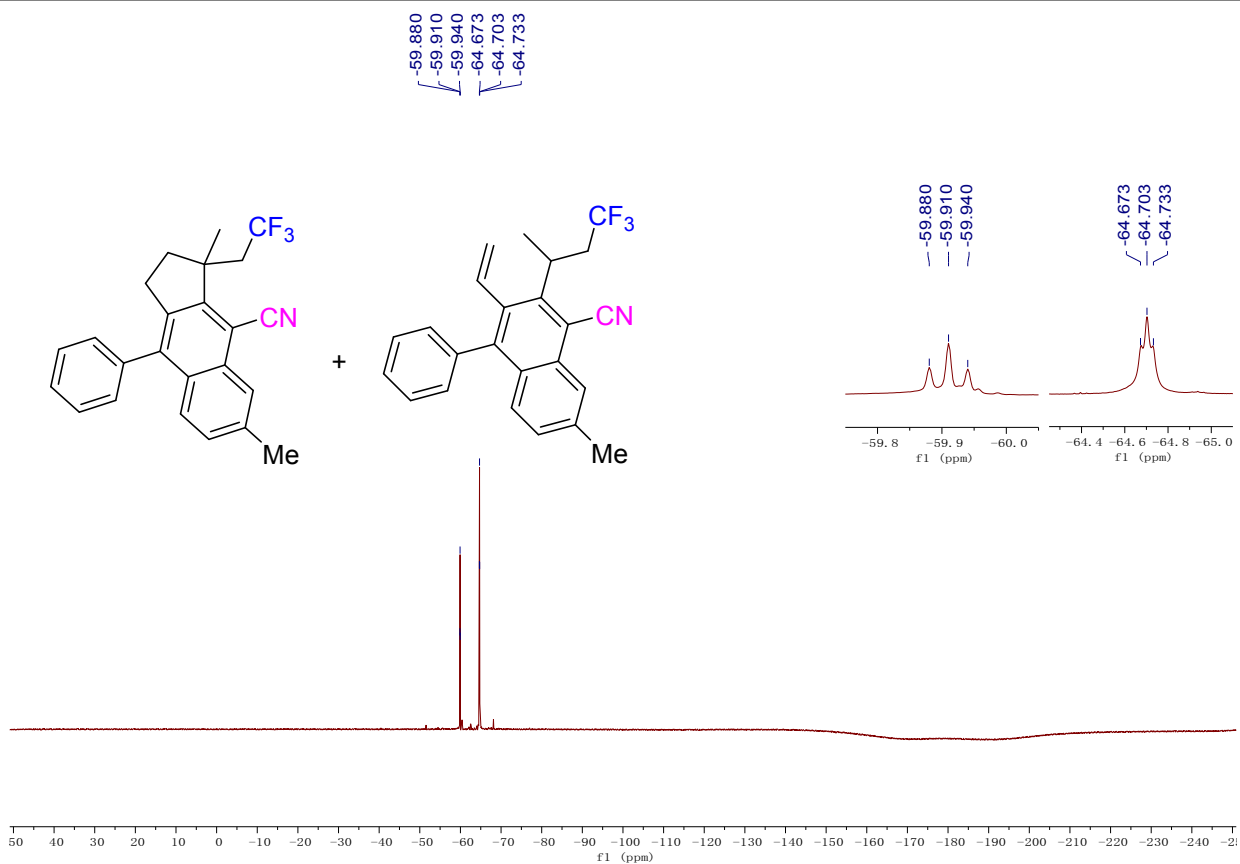


7-chloro-9-(2-chlorophenyl)-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2j)

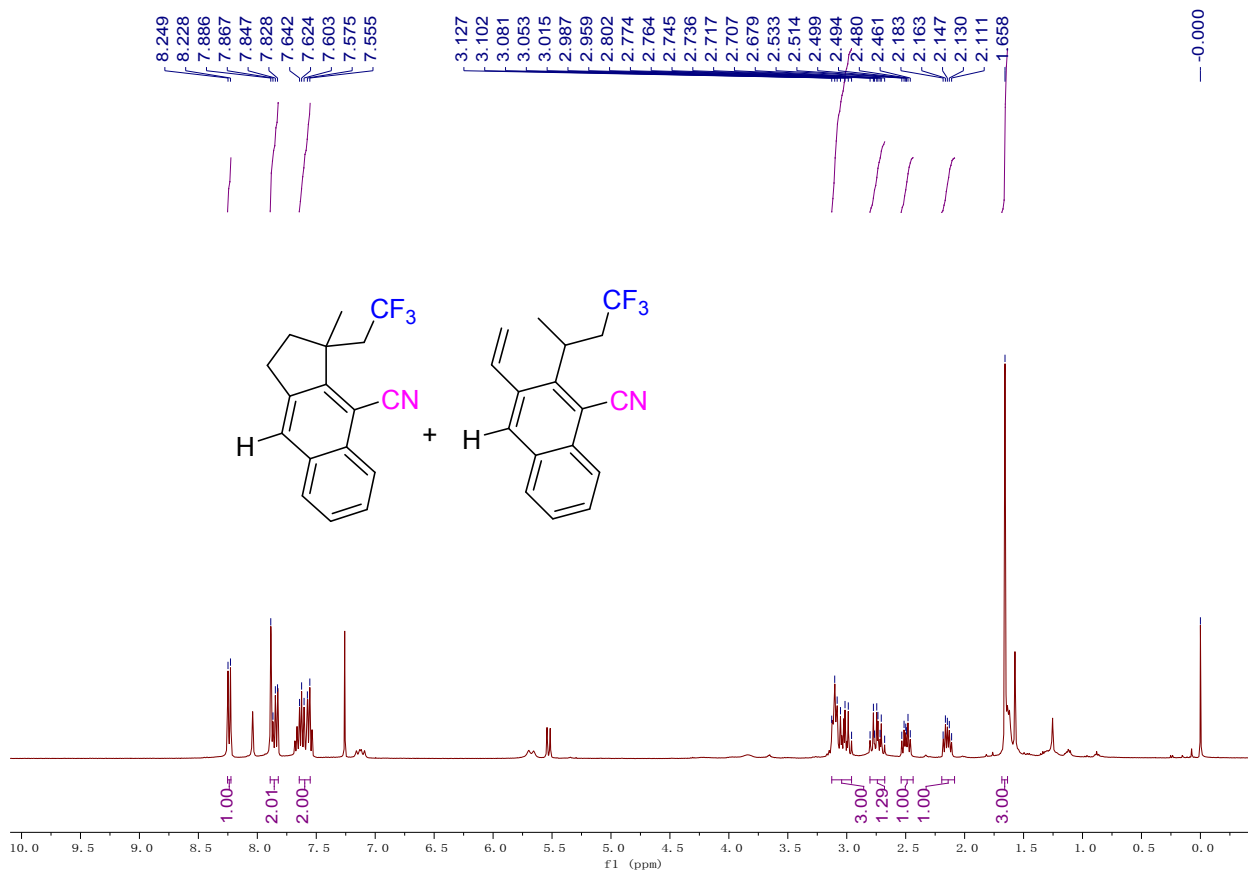


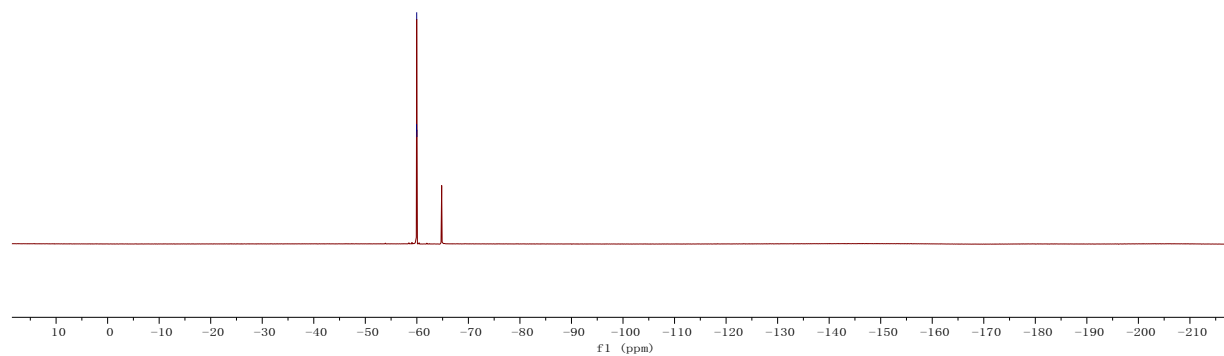
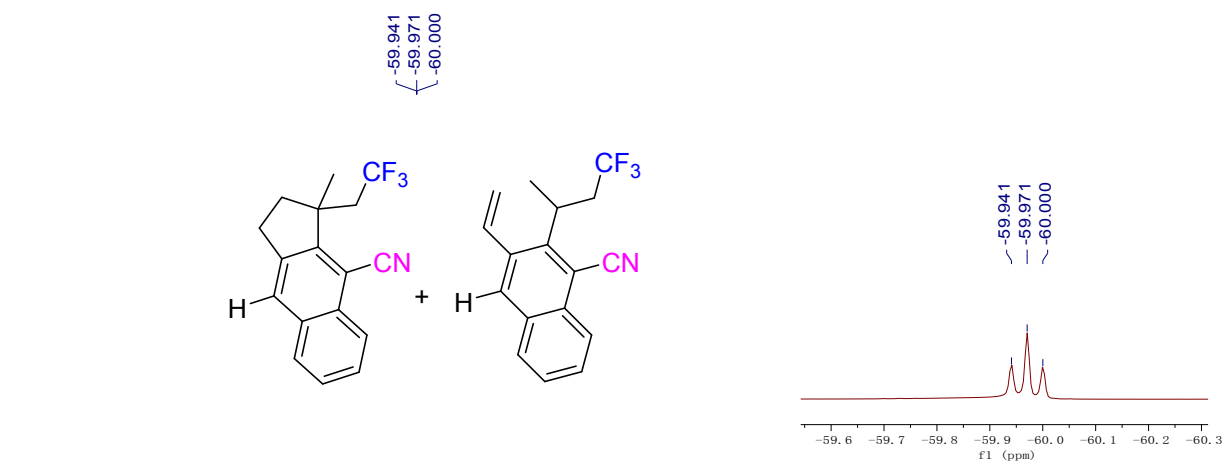
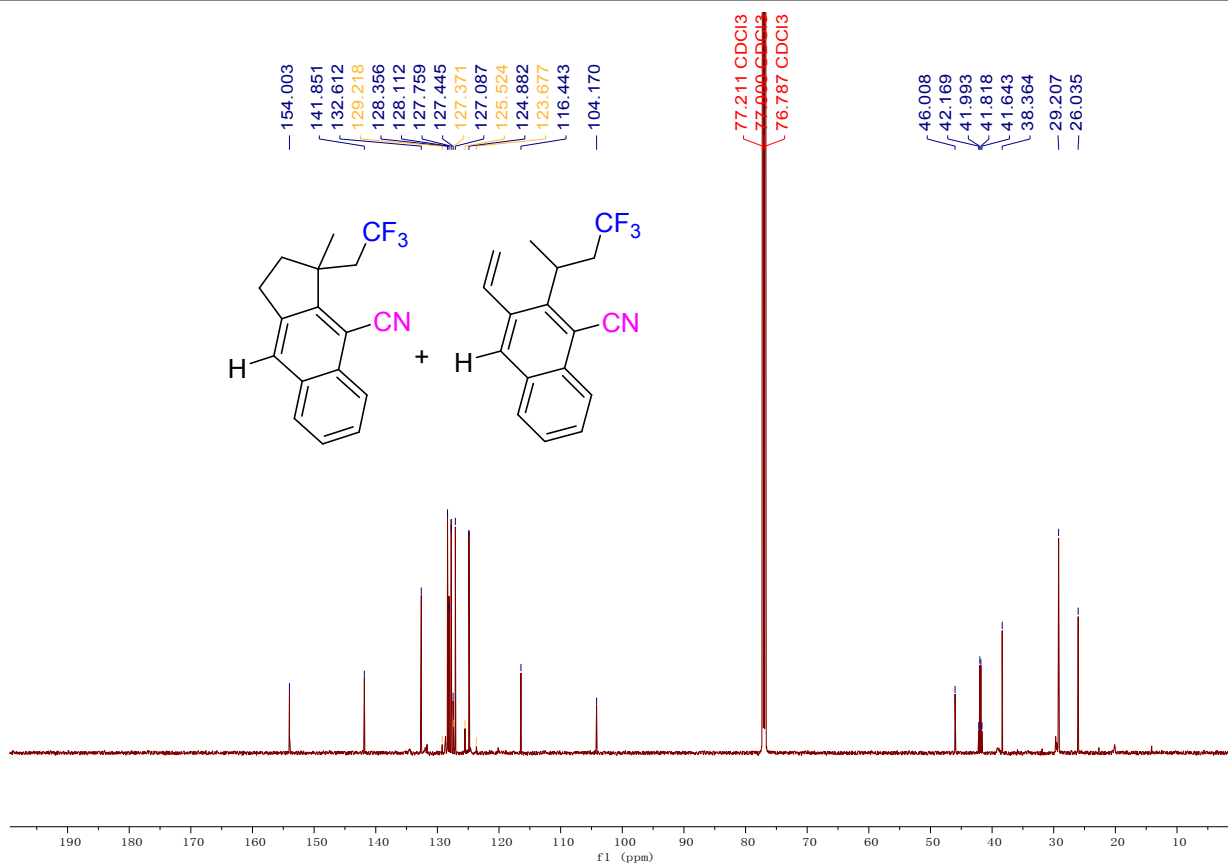


3,6-dimethyl-9-phenyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2k) + 7-methyl-4-phenyl-2-(4,4,4-trifluorobutan-2-yl)-3-vinyl-1-naphthonitrile (3k)

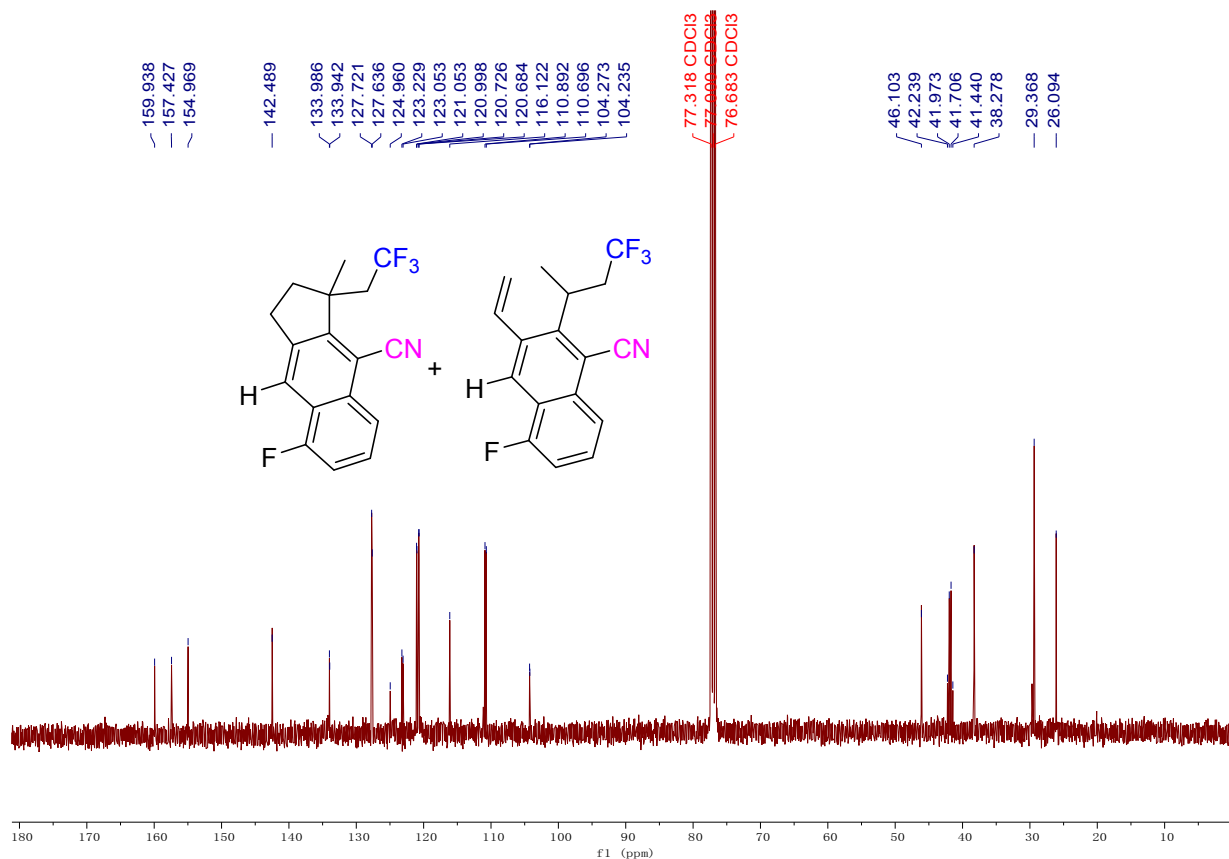
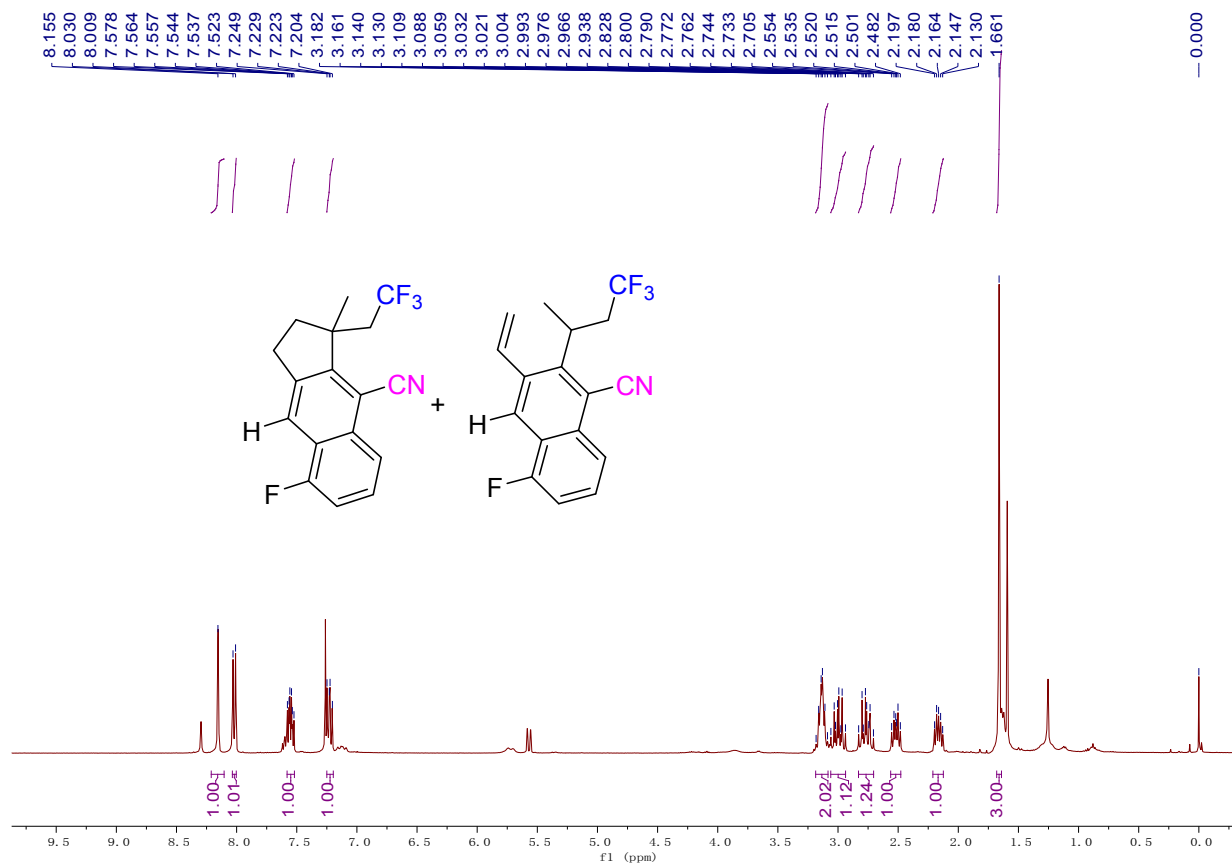


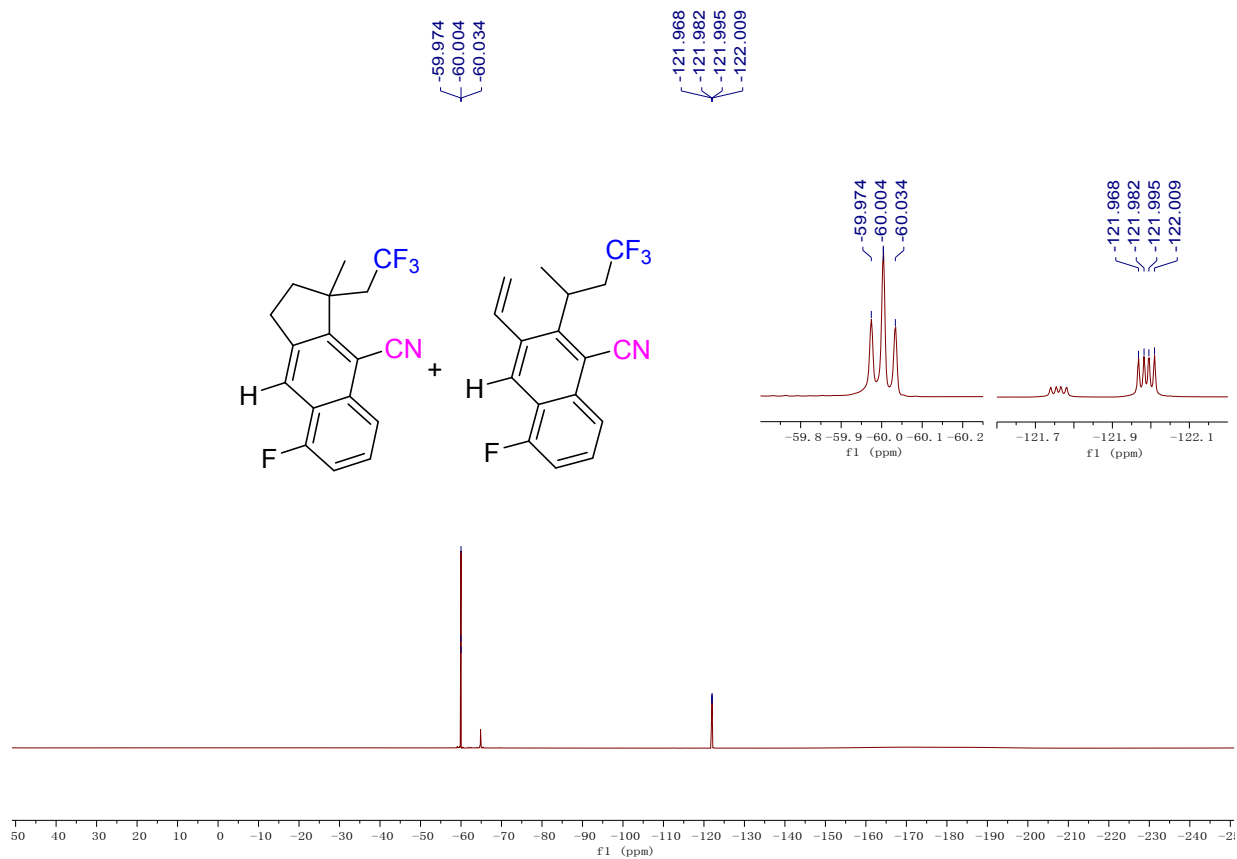
3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2l)



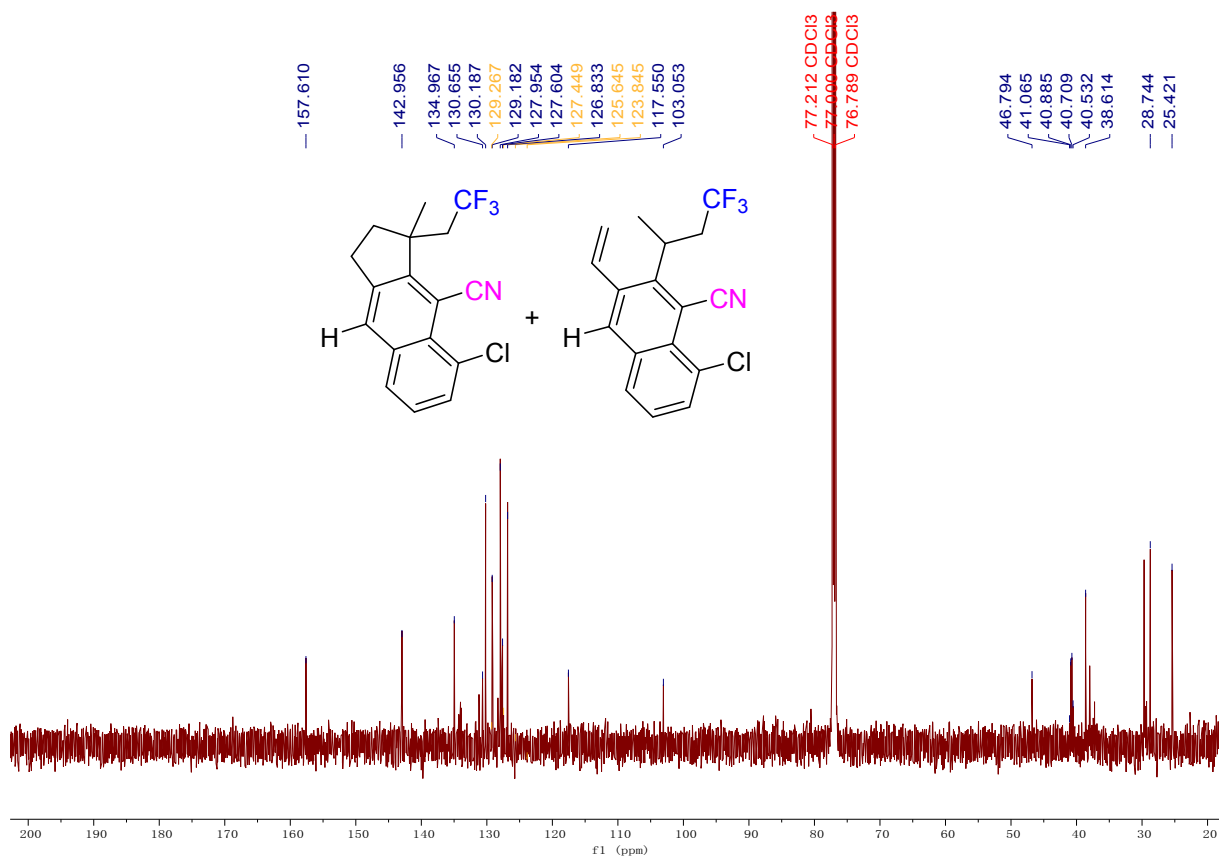
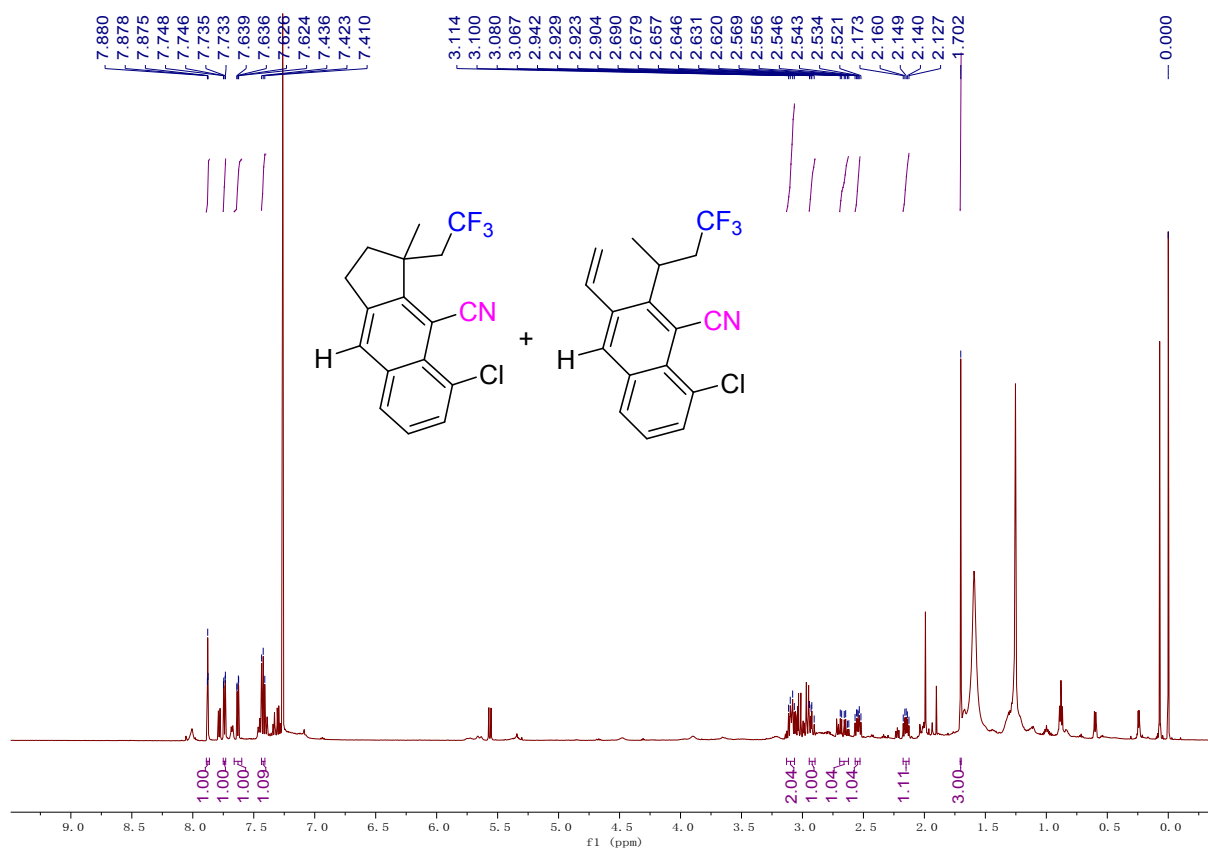


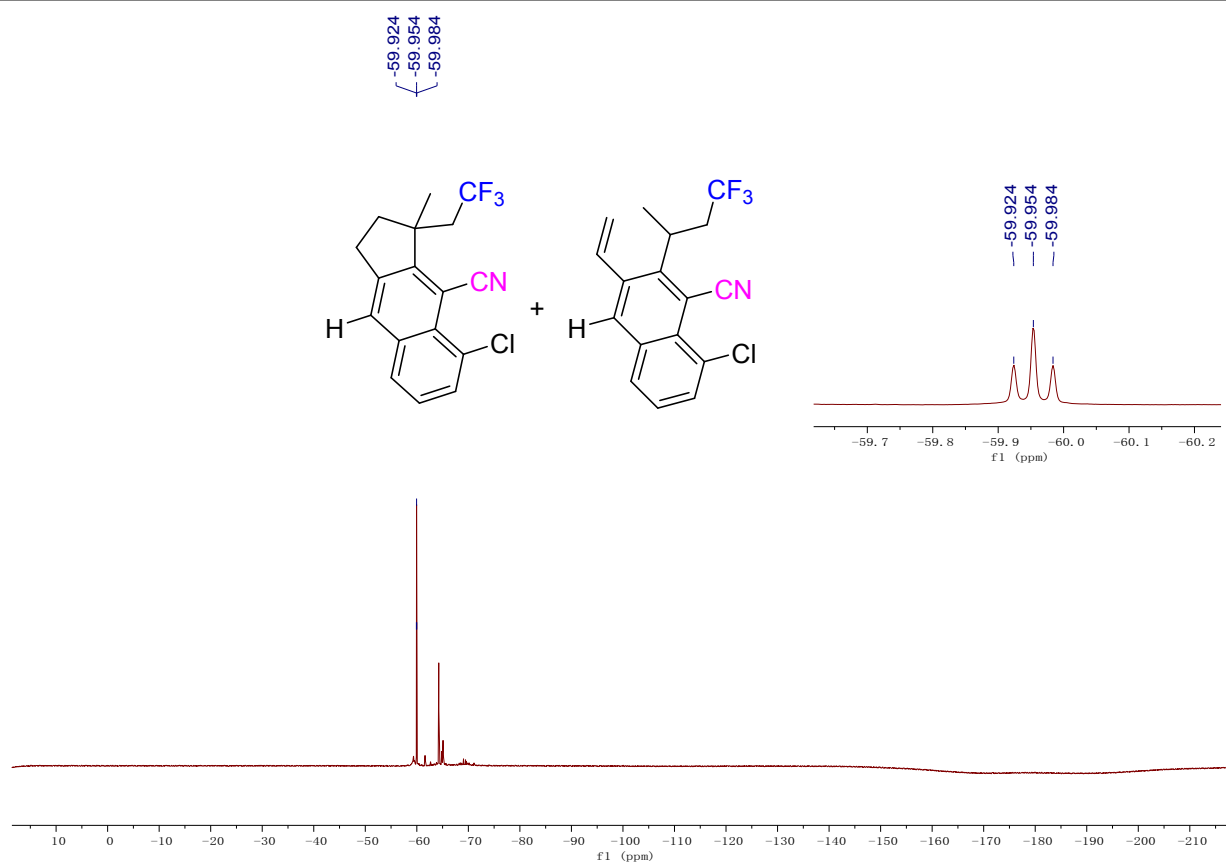
8-fluoro-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2m)



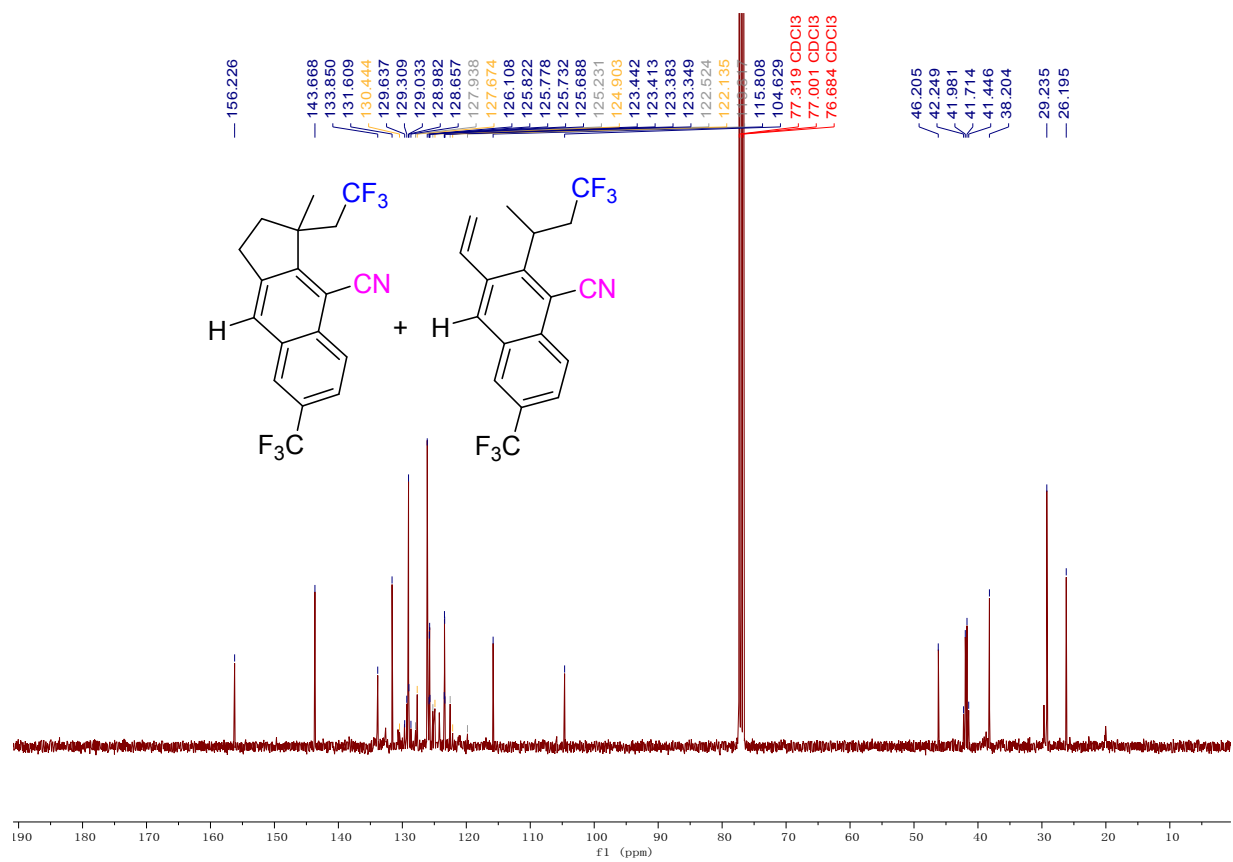
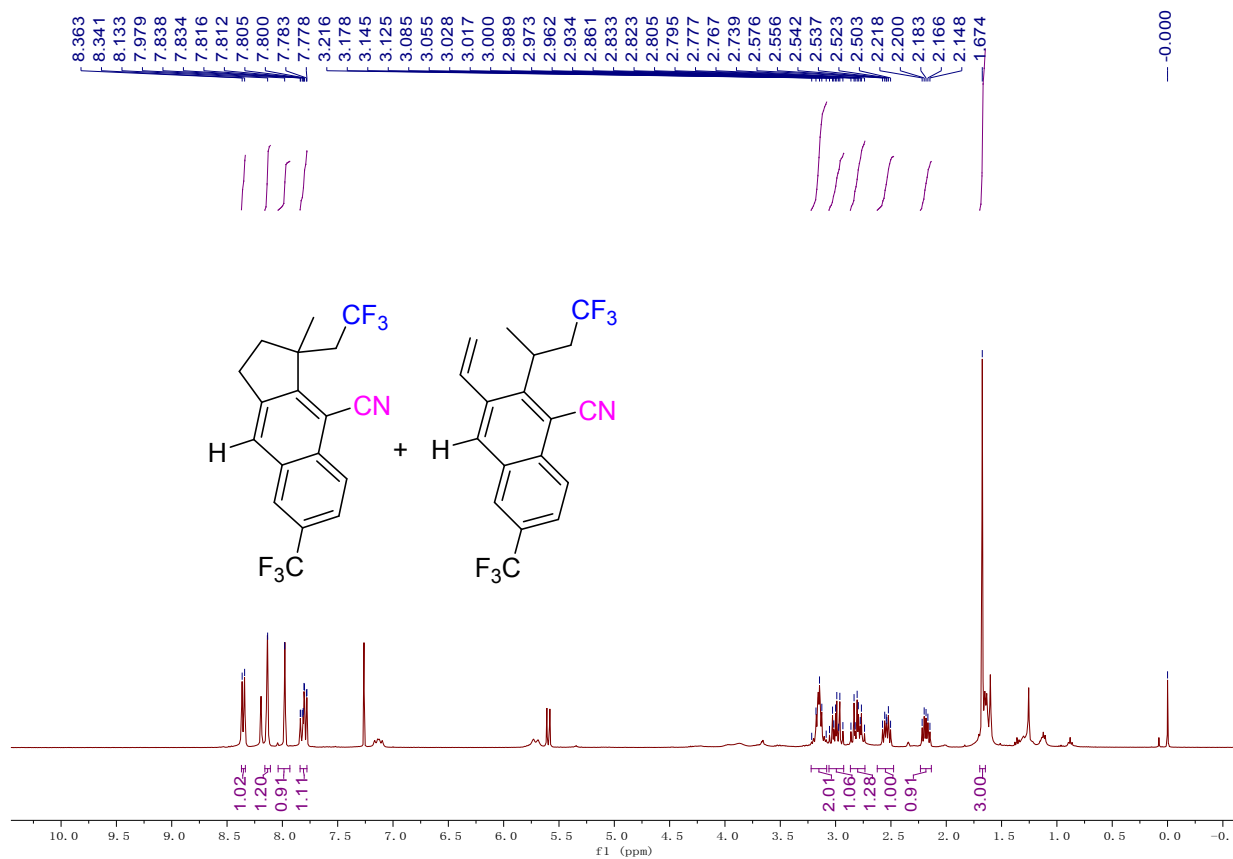


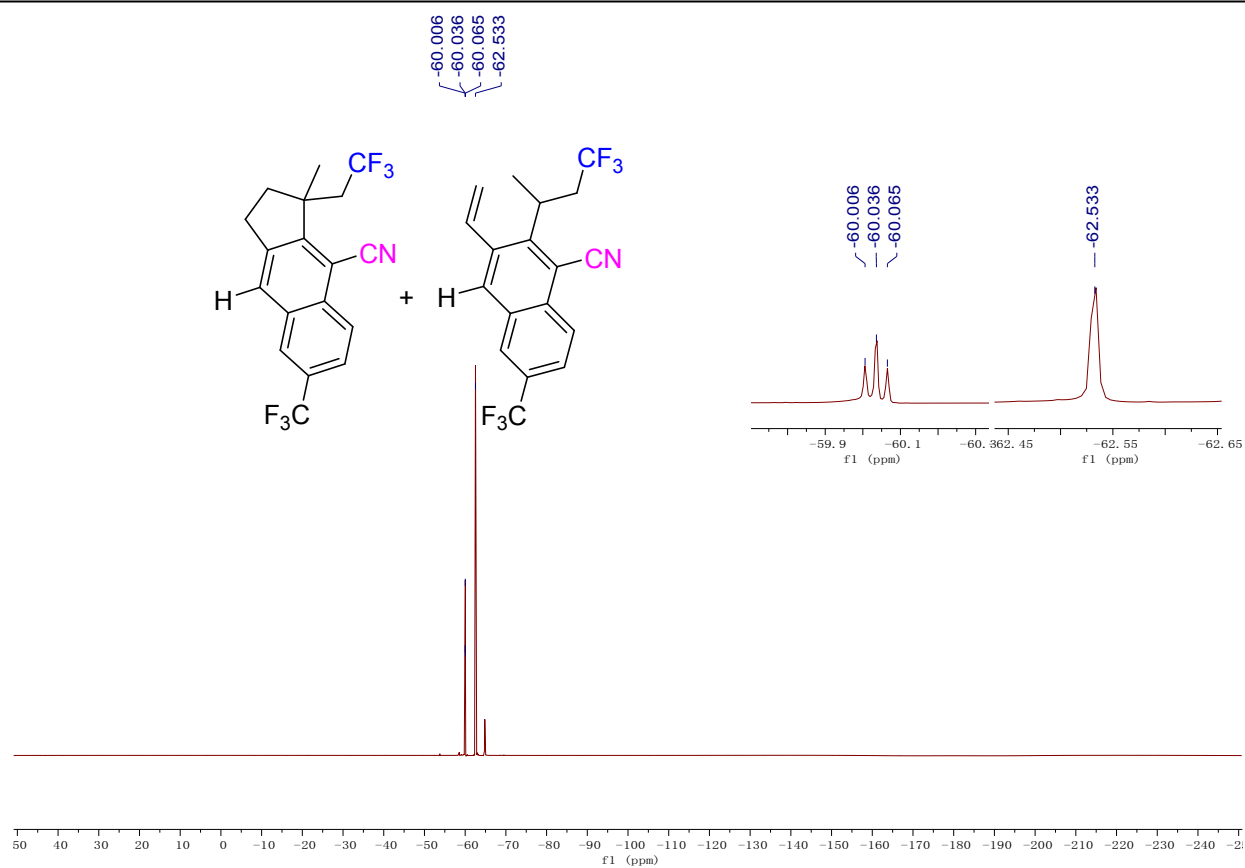
5-chloro-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[*b*]naphthalene-4-carbonitrile (2n)



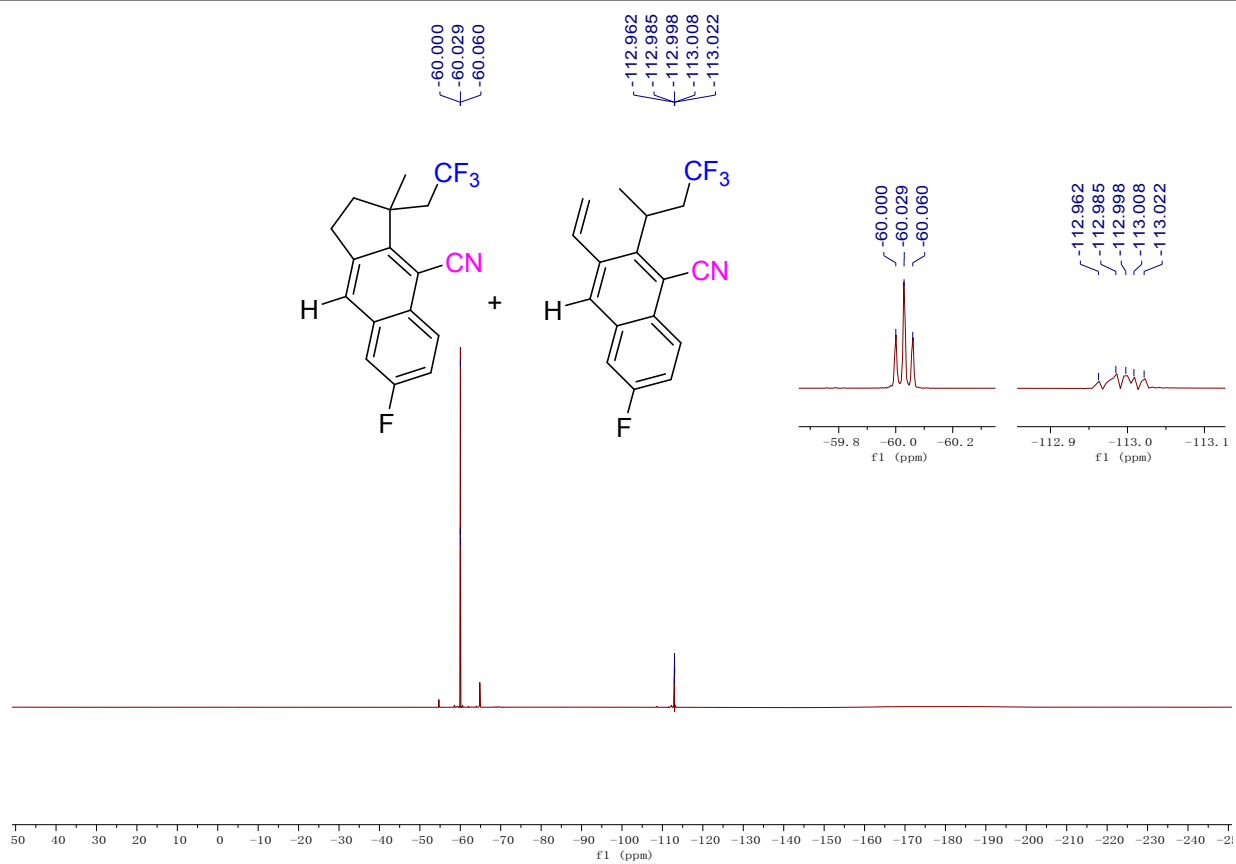


3-methyl-3-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-2,3-dihydro-1H-cyclopenta[*b*]naphthalene-4-carbonitrile (2o)

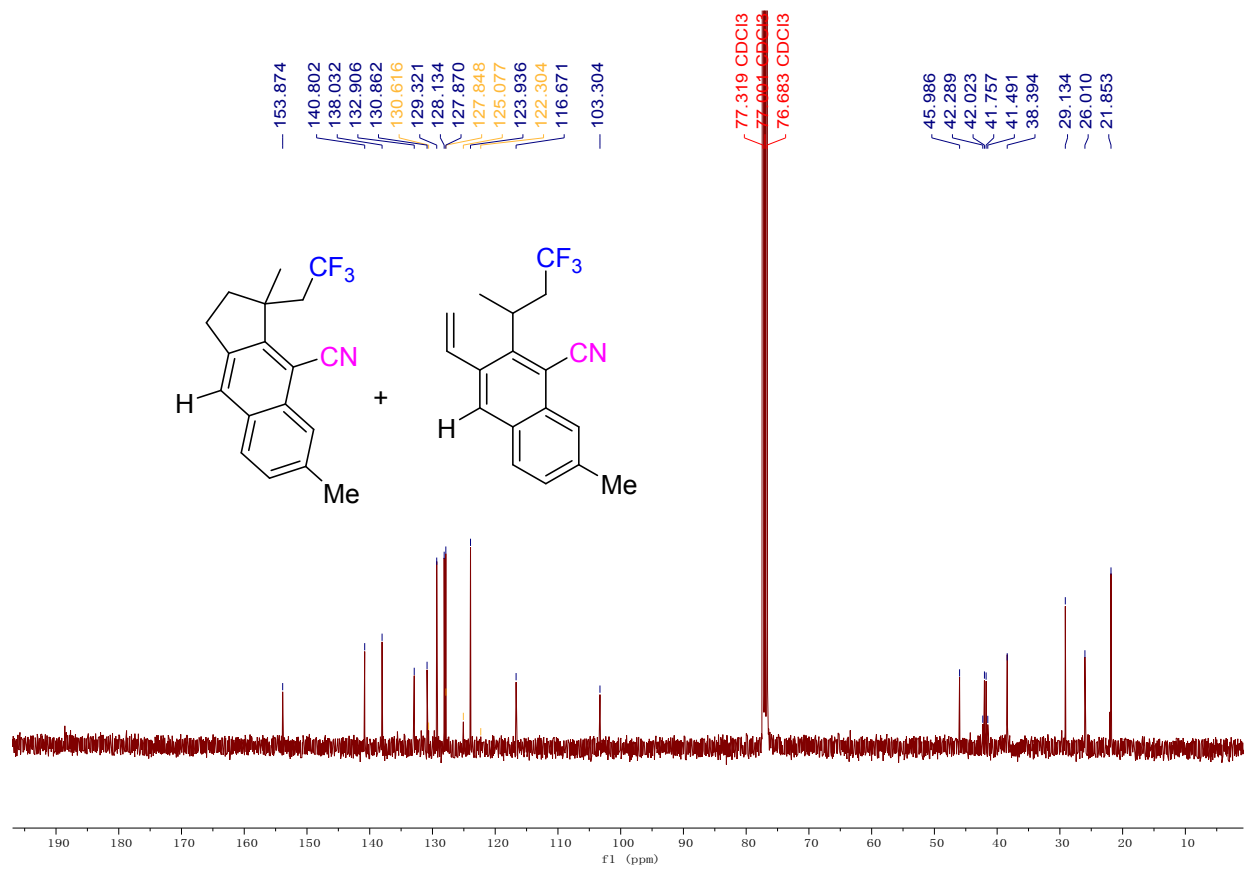
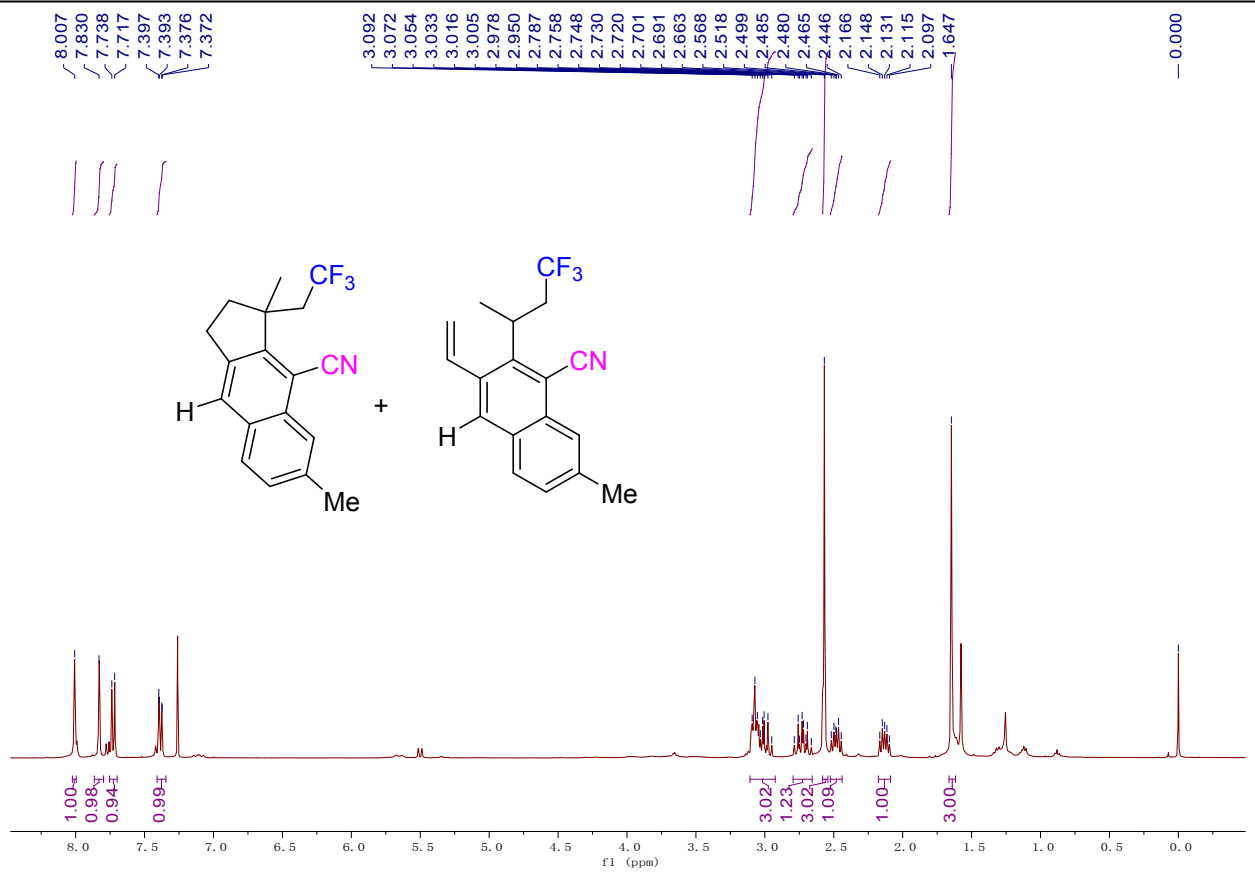


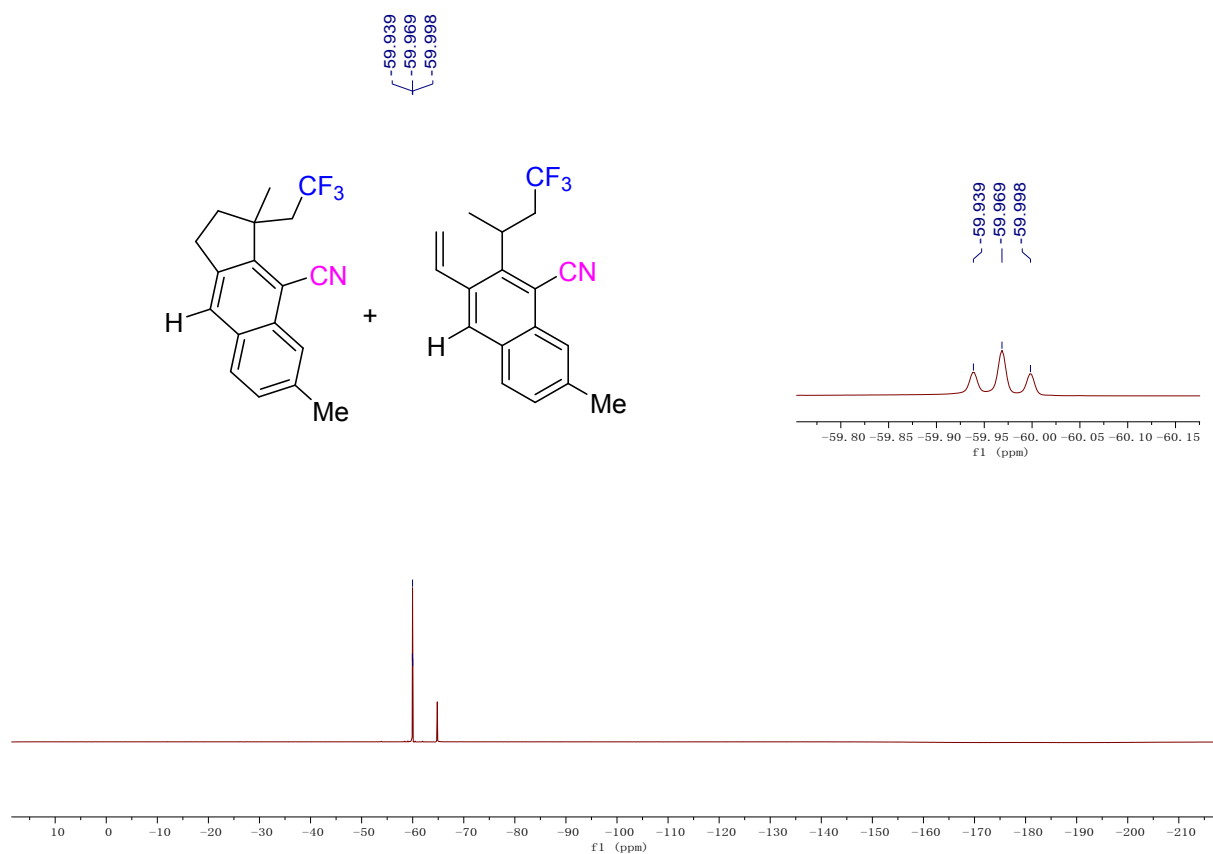


7-fluoro-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2p)

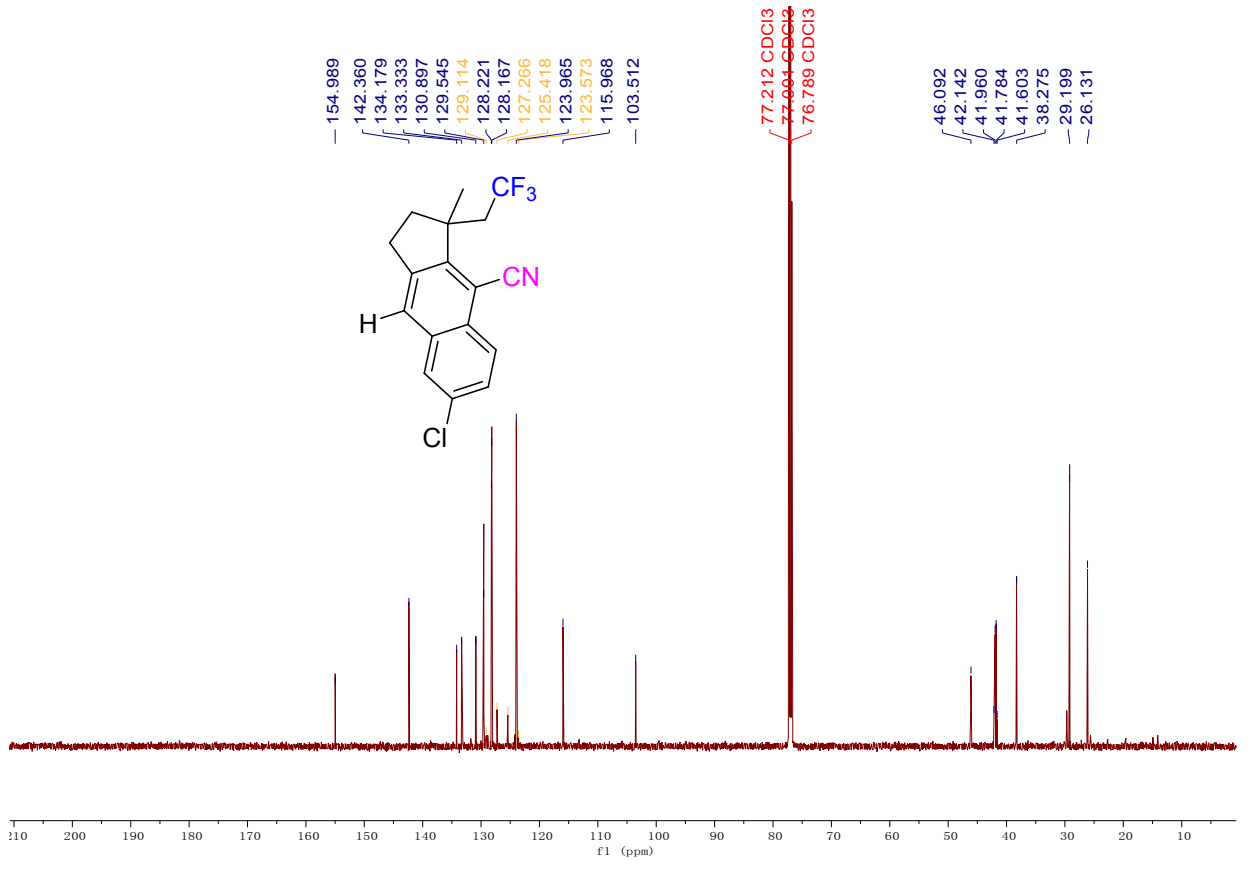
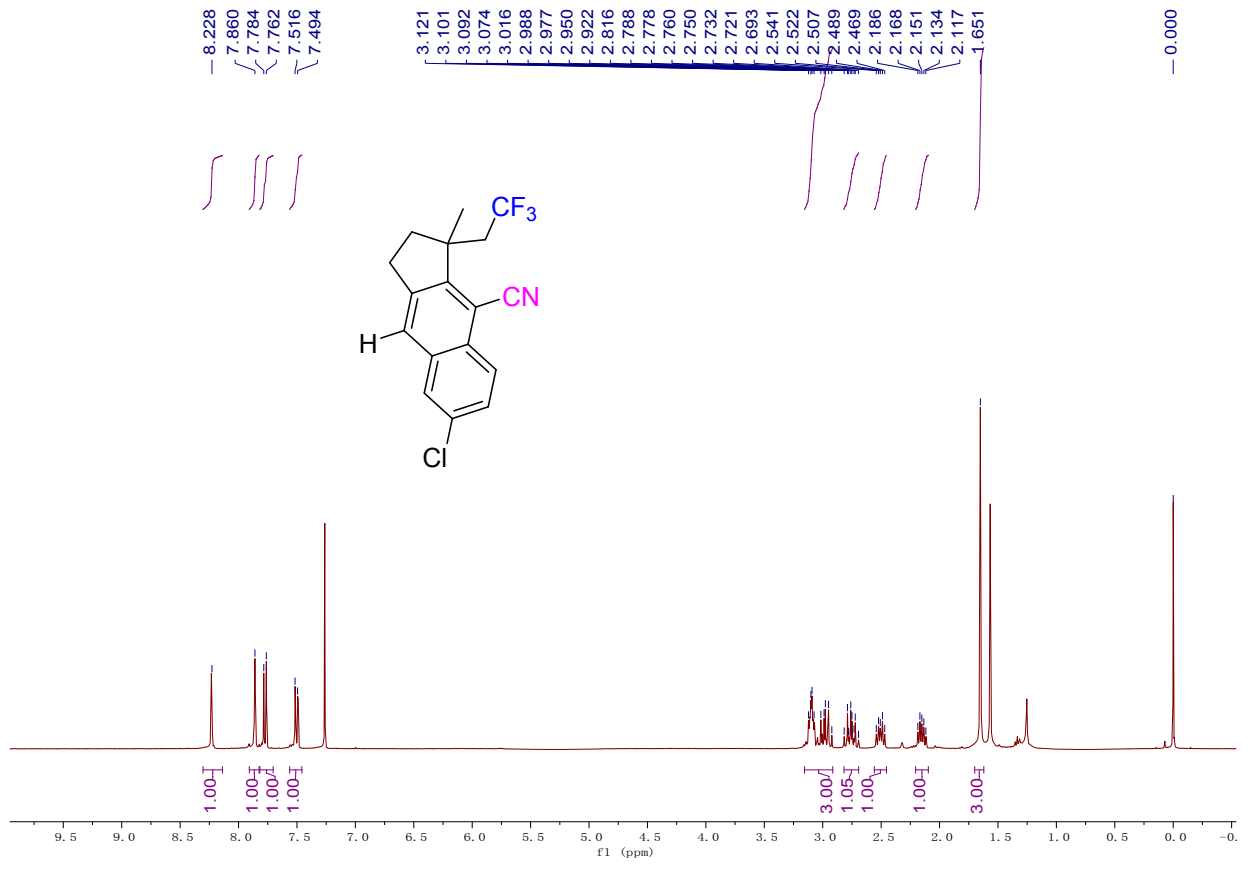


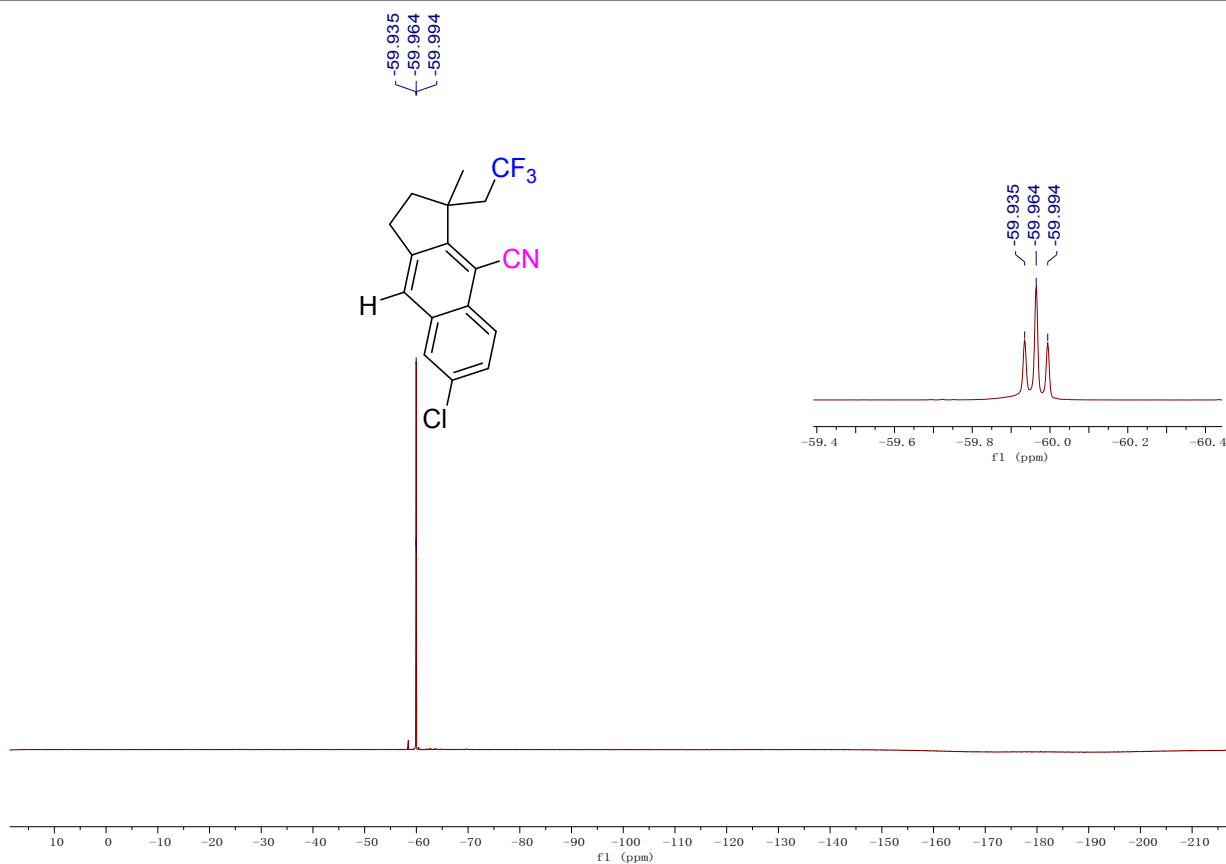
3,6-dimethyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[*b*]naphthalene-4-carbonitrile (2q)



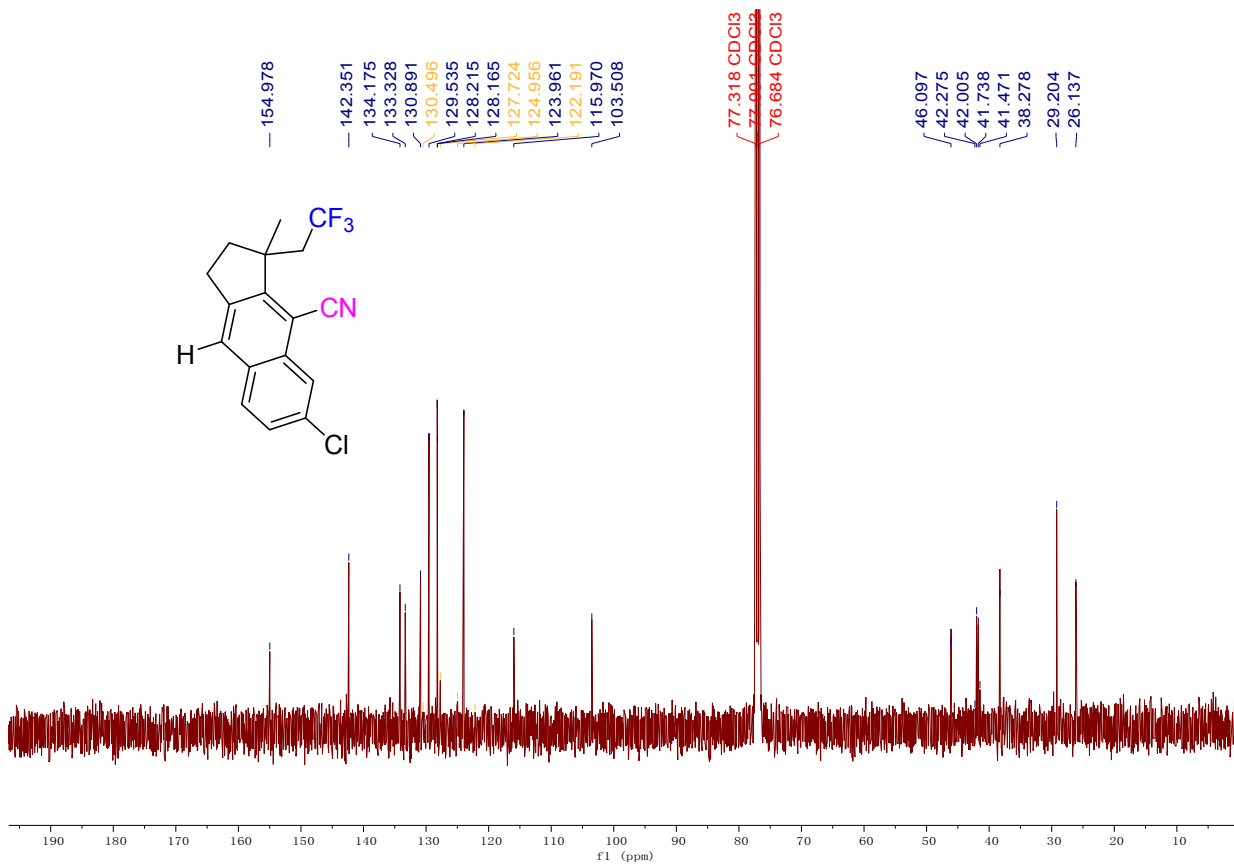
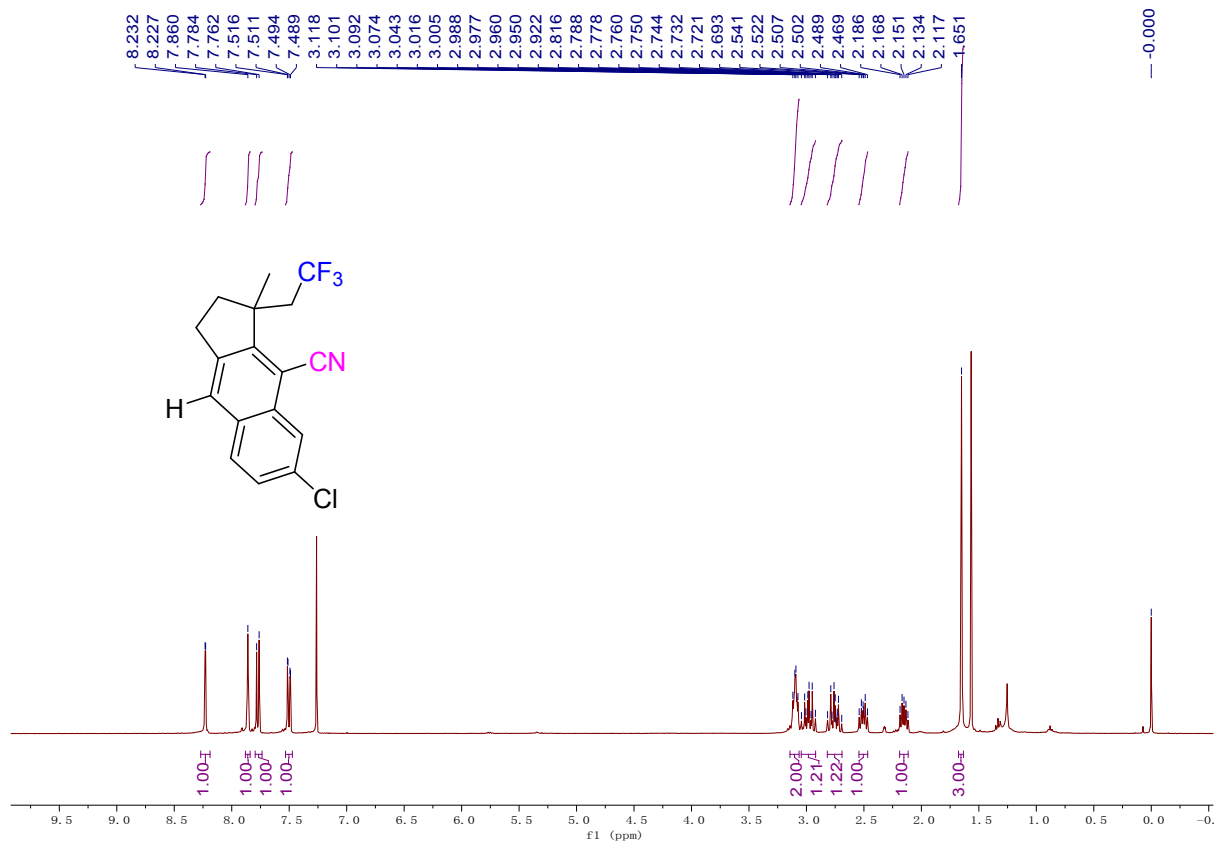


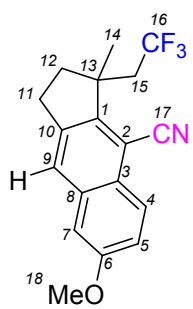
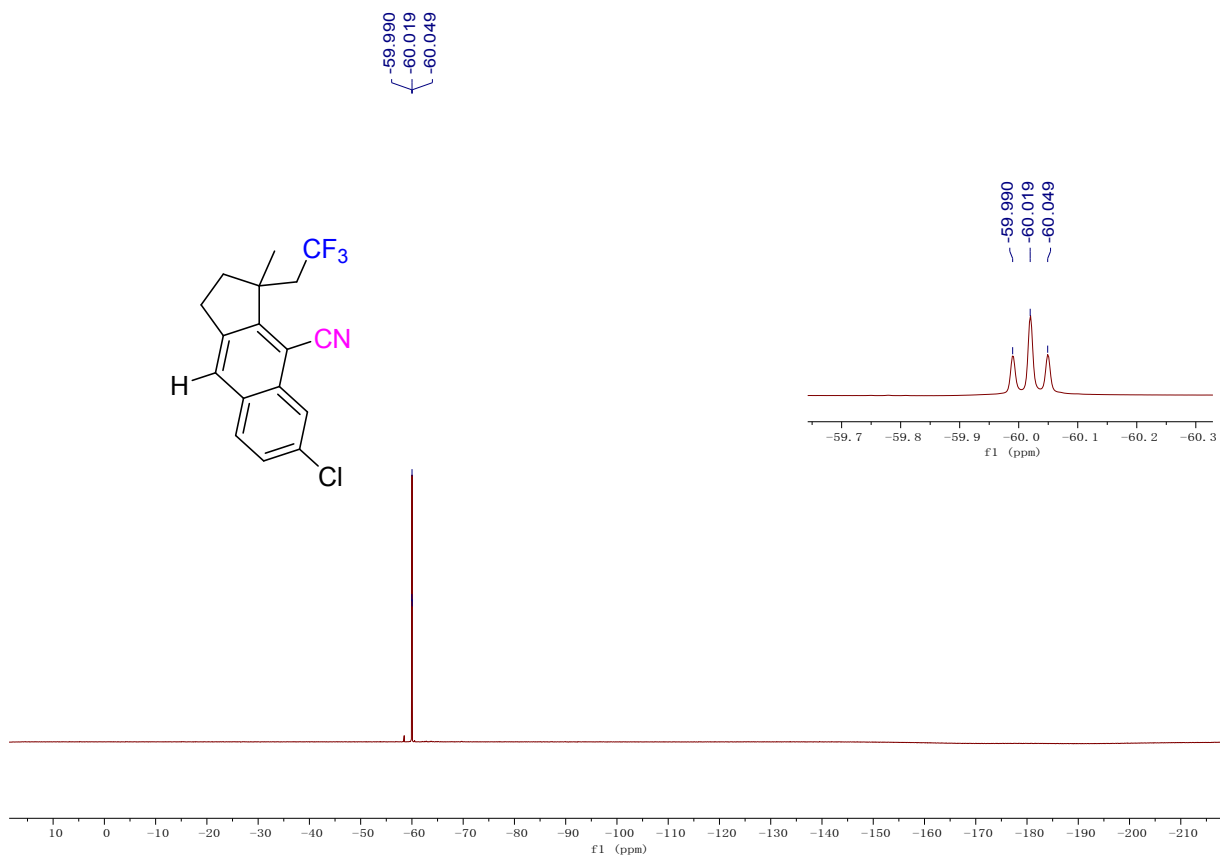
7-chloro-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2r)



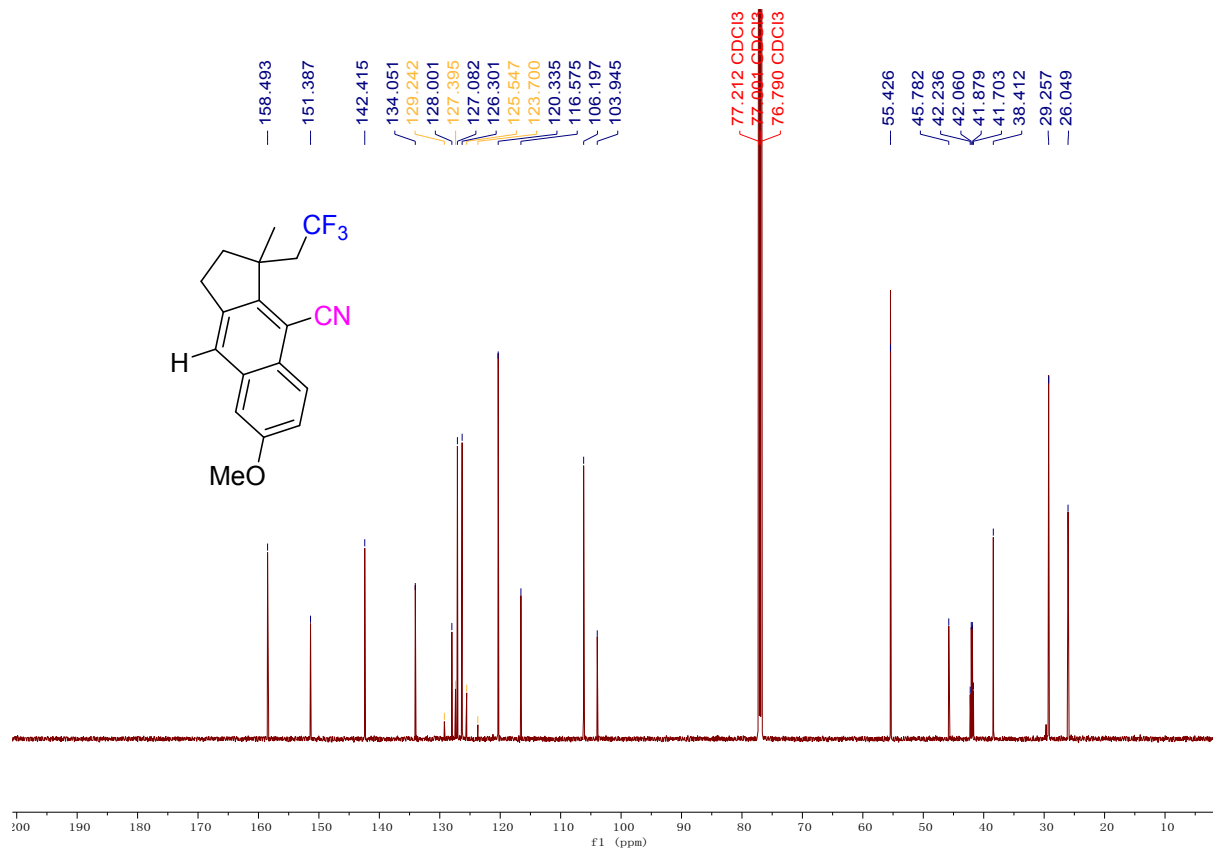
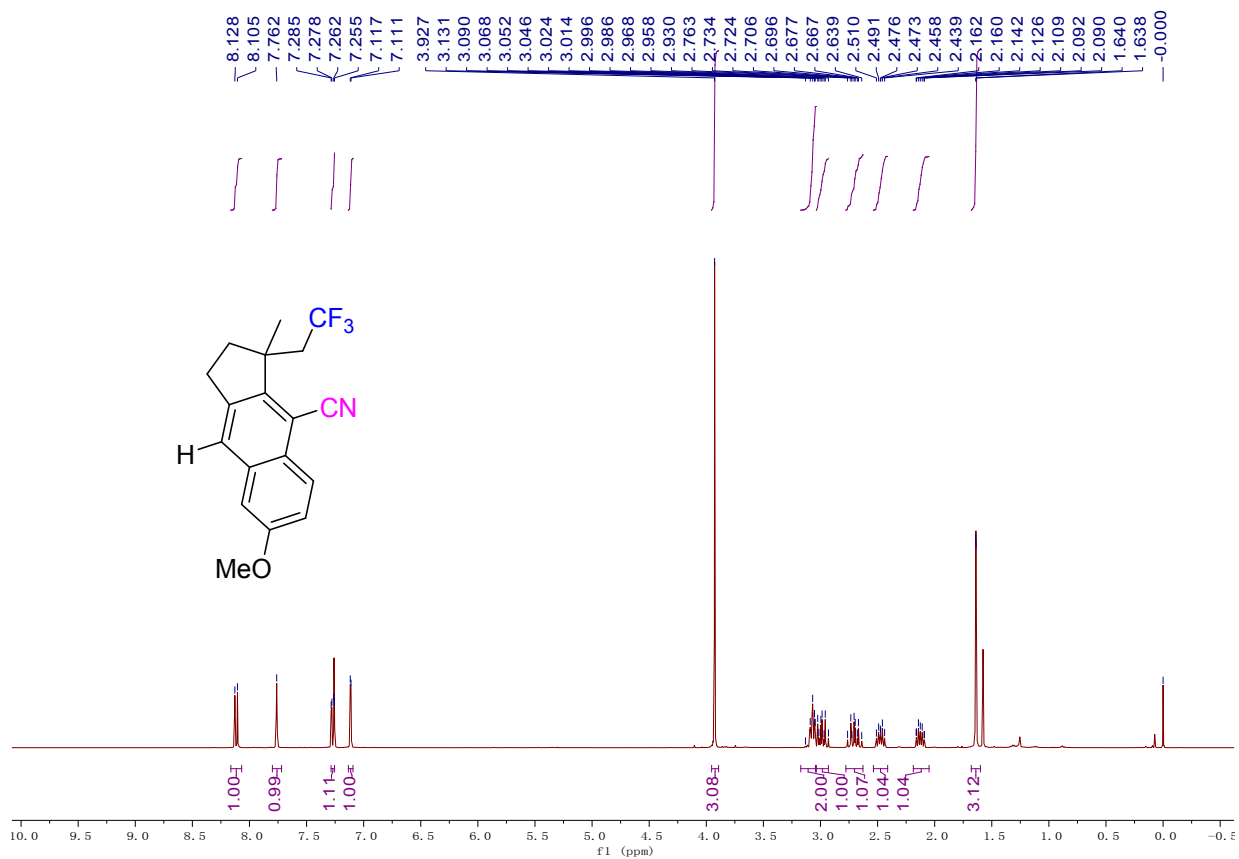


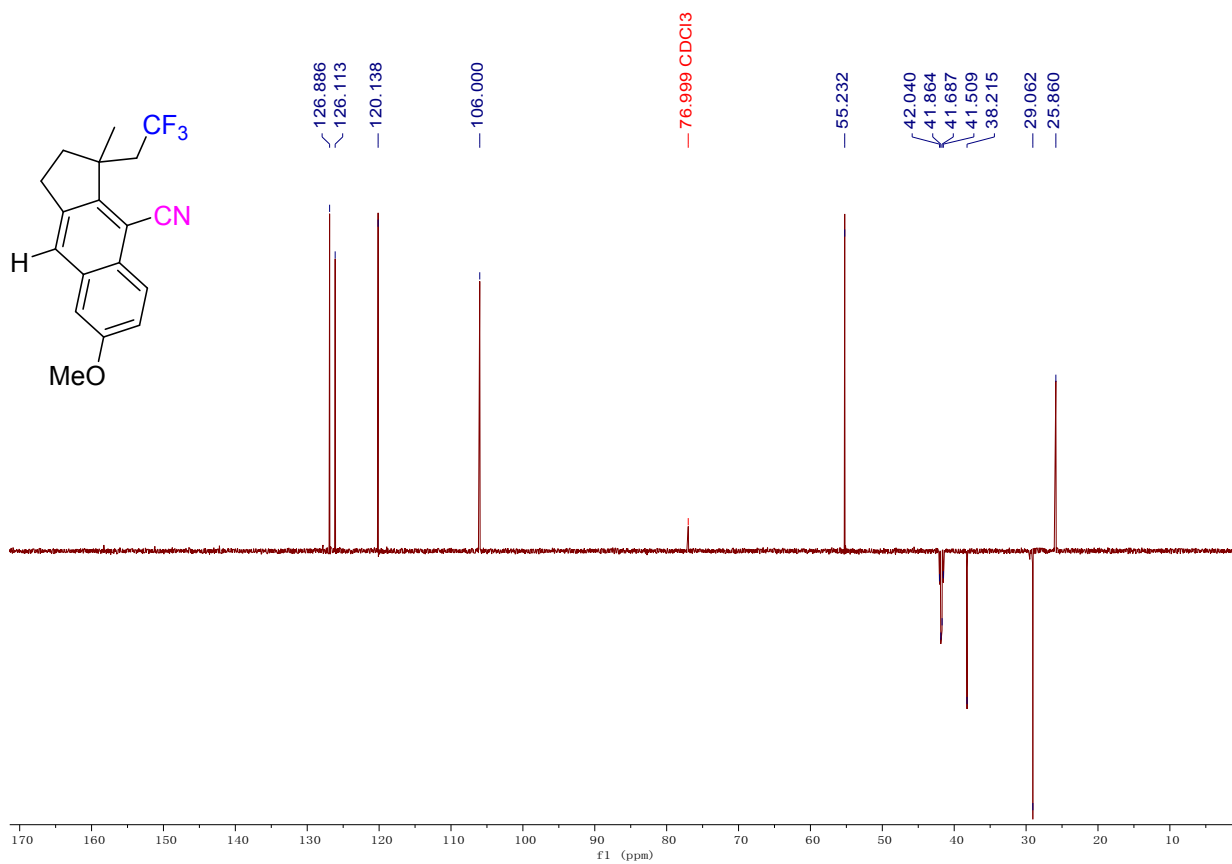
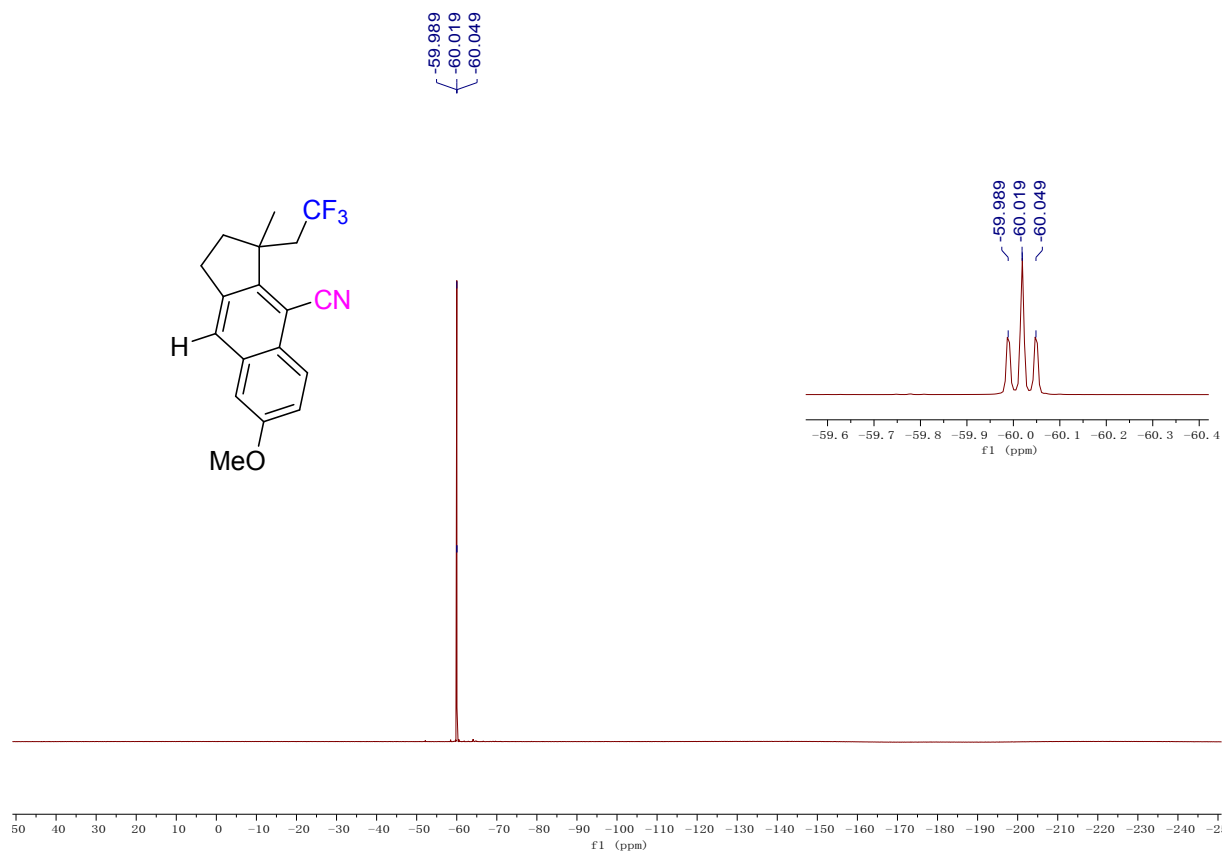
6-chloro-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2s)



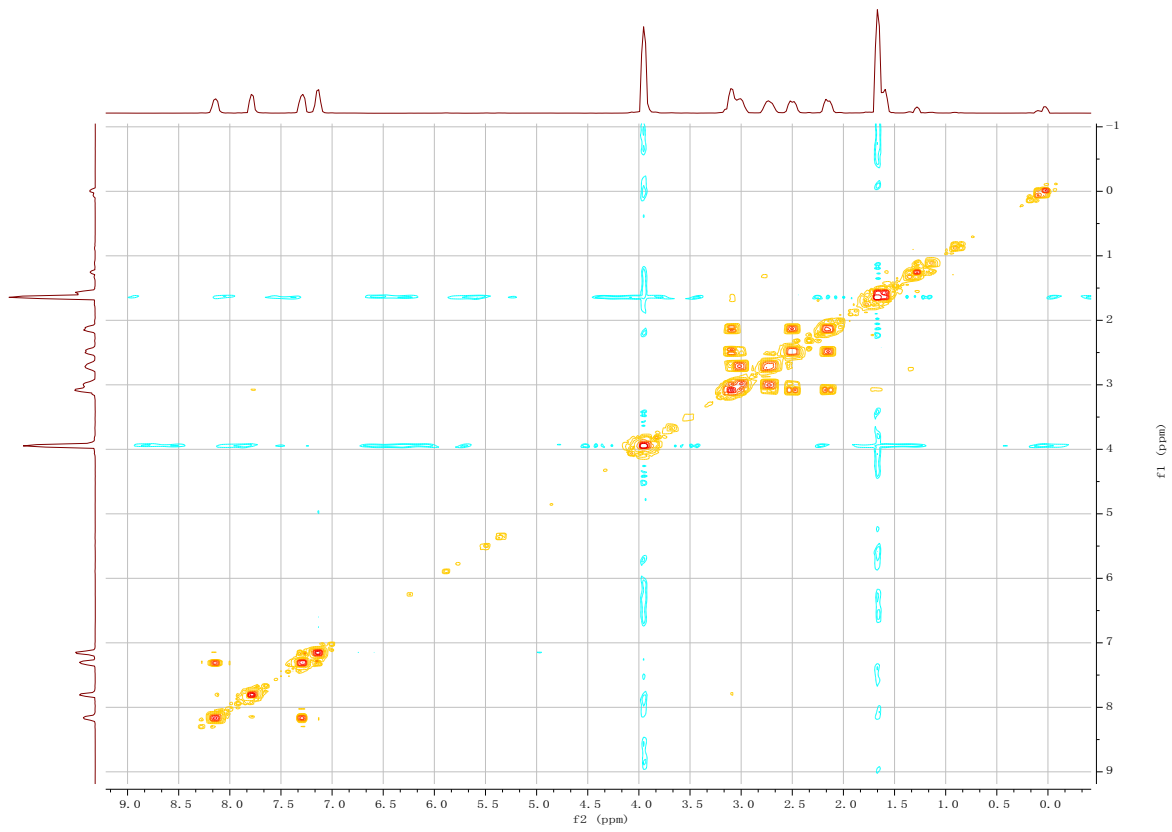


7-methoxy-3-methyl-3-(2,2,2-trifluoroethyl)-2,3-dihydro-1H-cyclopenta[b]naphthalene-4-carbonitrile (2t)

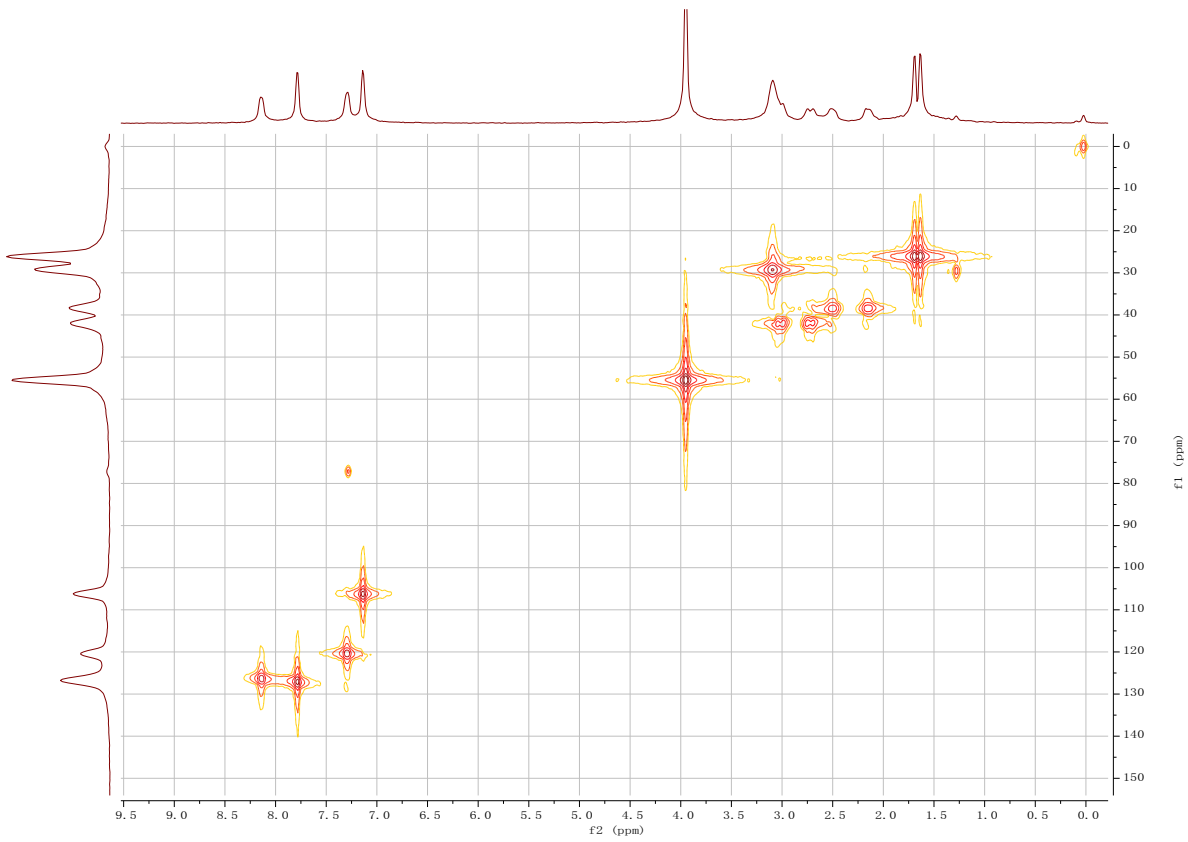




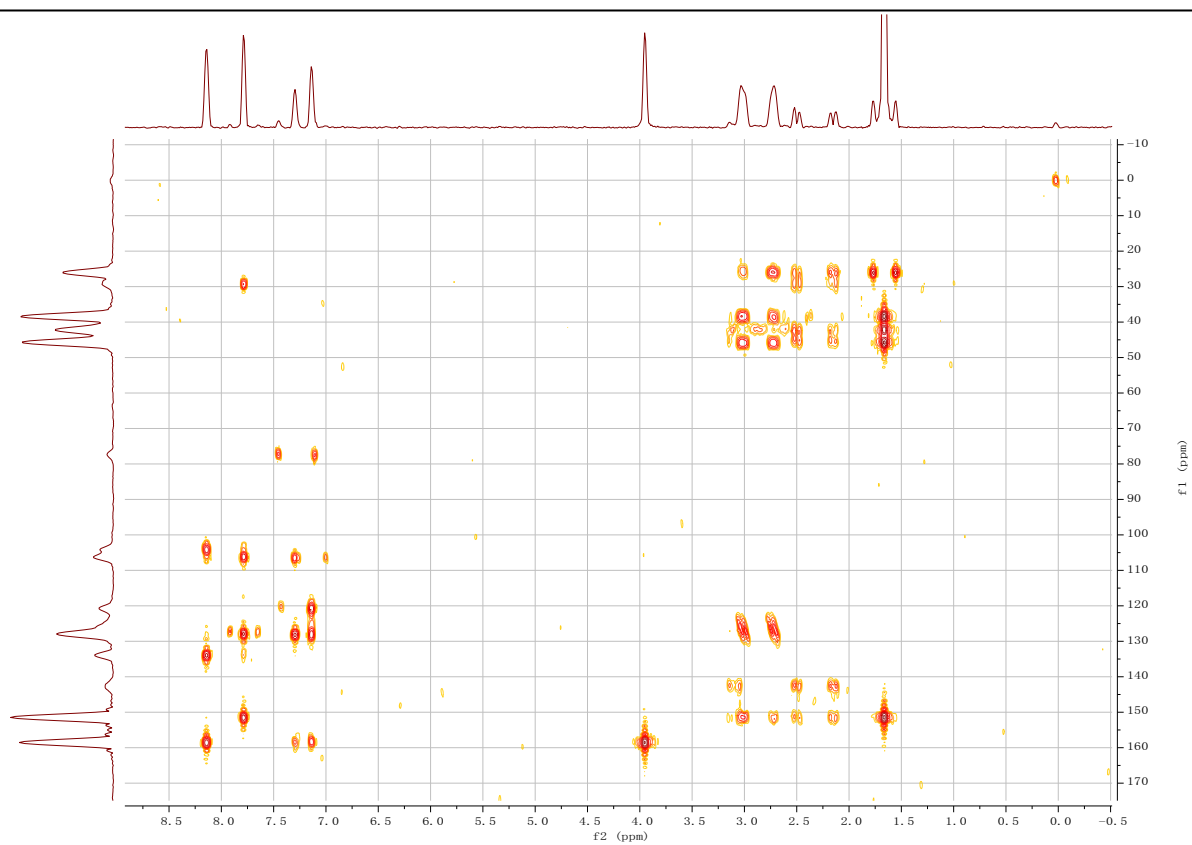
Distortionless Enhancement by Polarization Transfer 135 (DEPT 135)



H-H Correlation Spectroscopy (COSY)

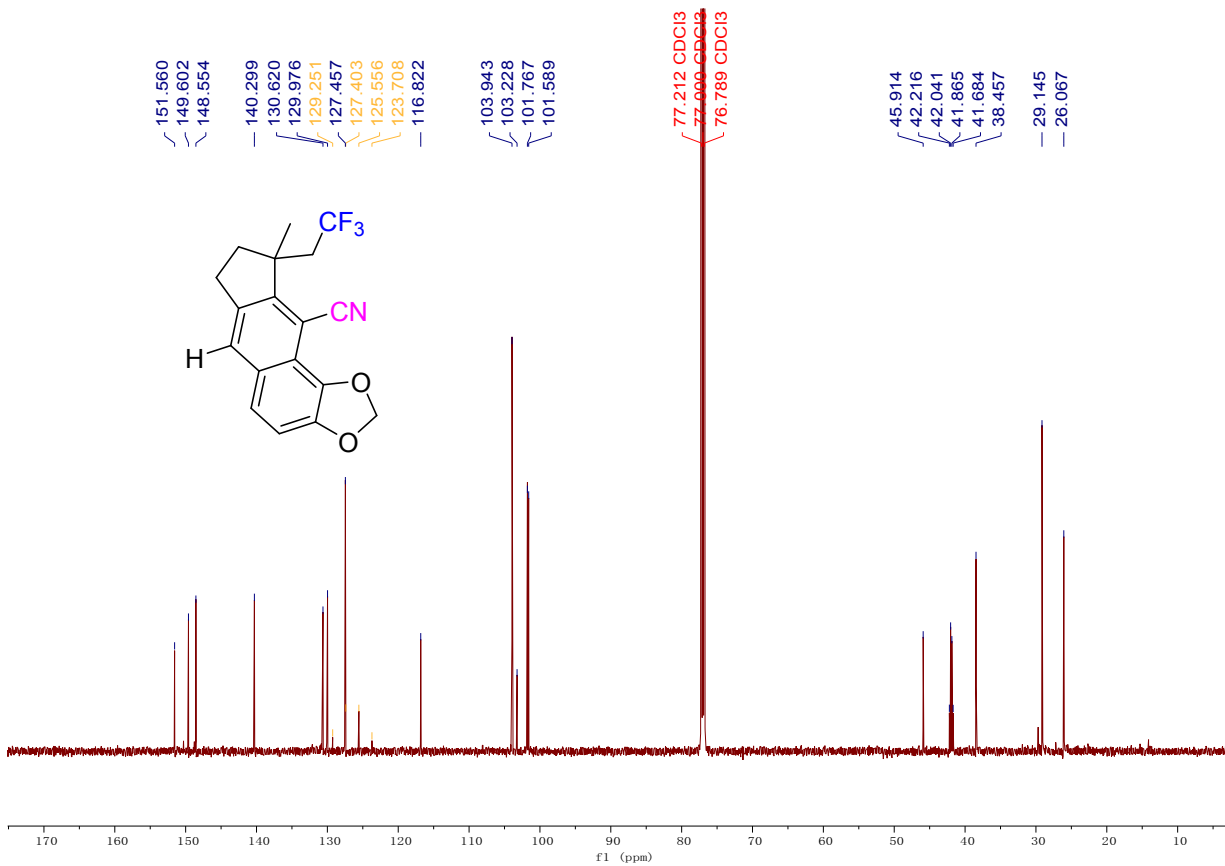
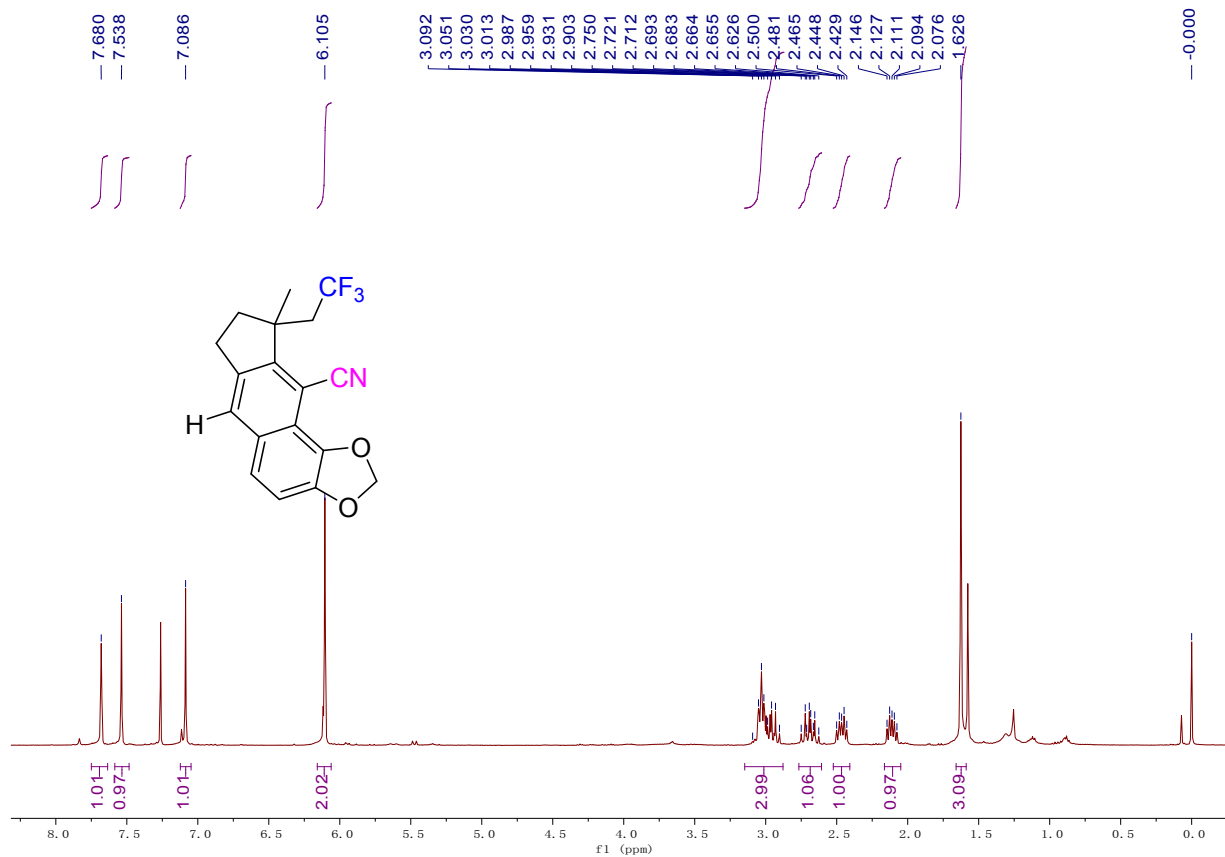


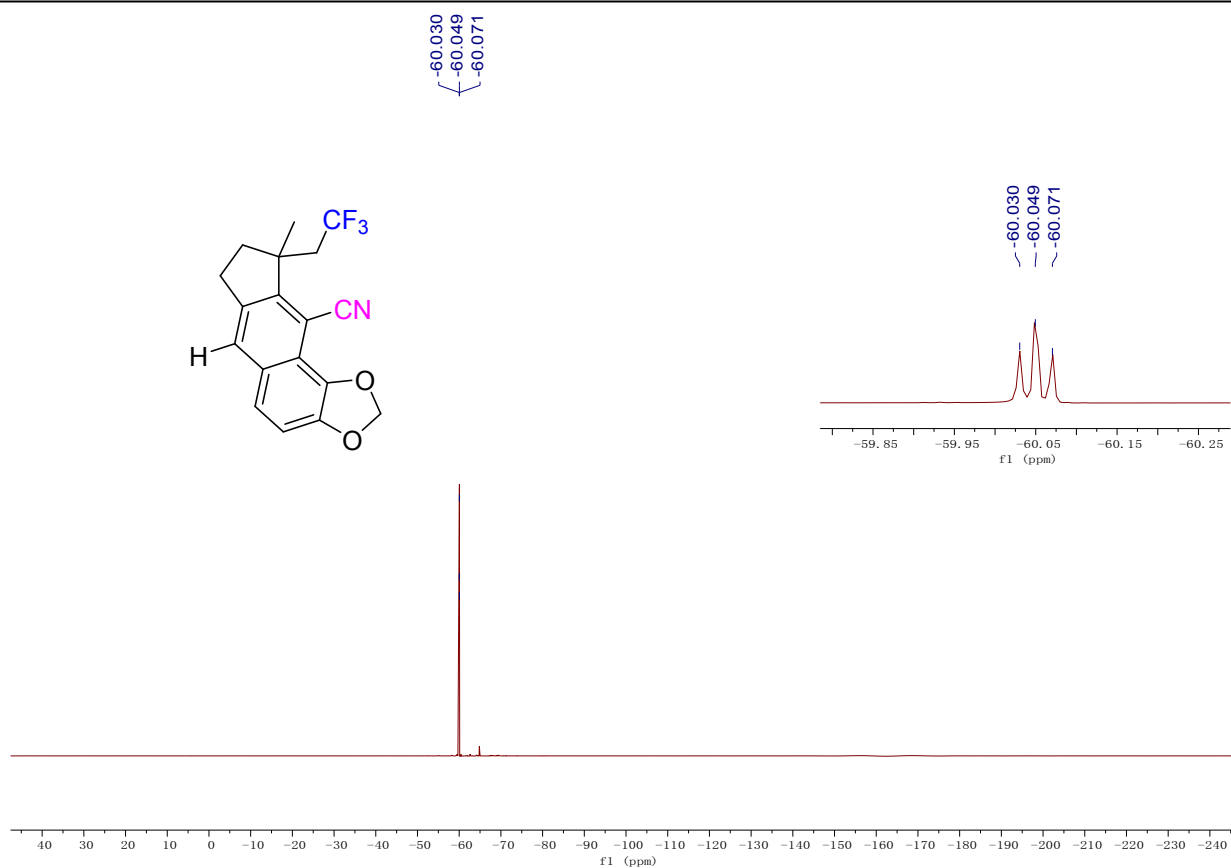
Heteronuclear Multiple-Quantum Correlation (HMQC)



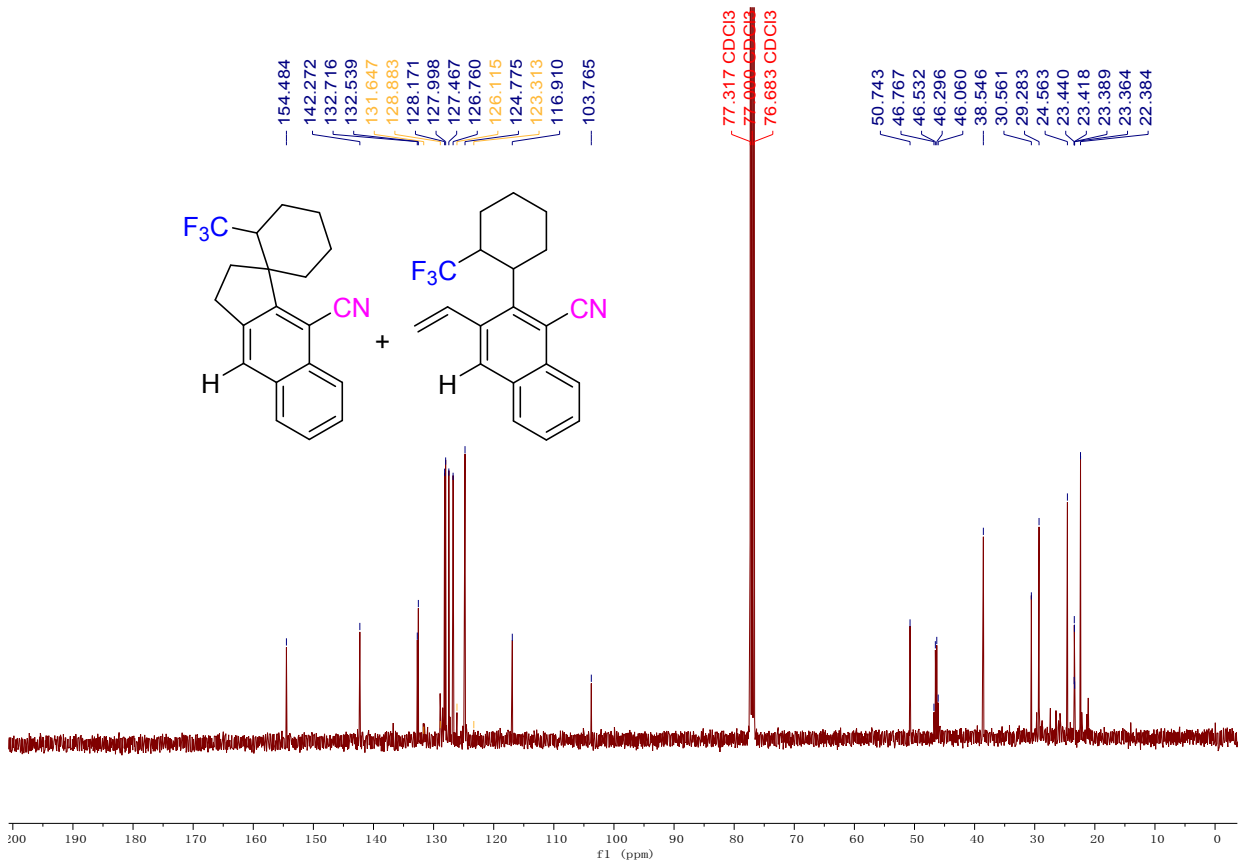
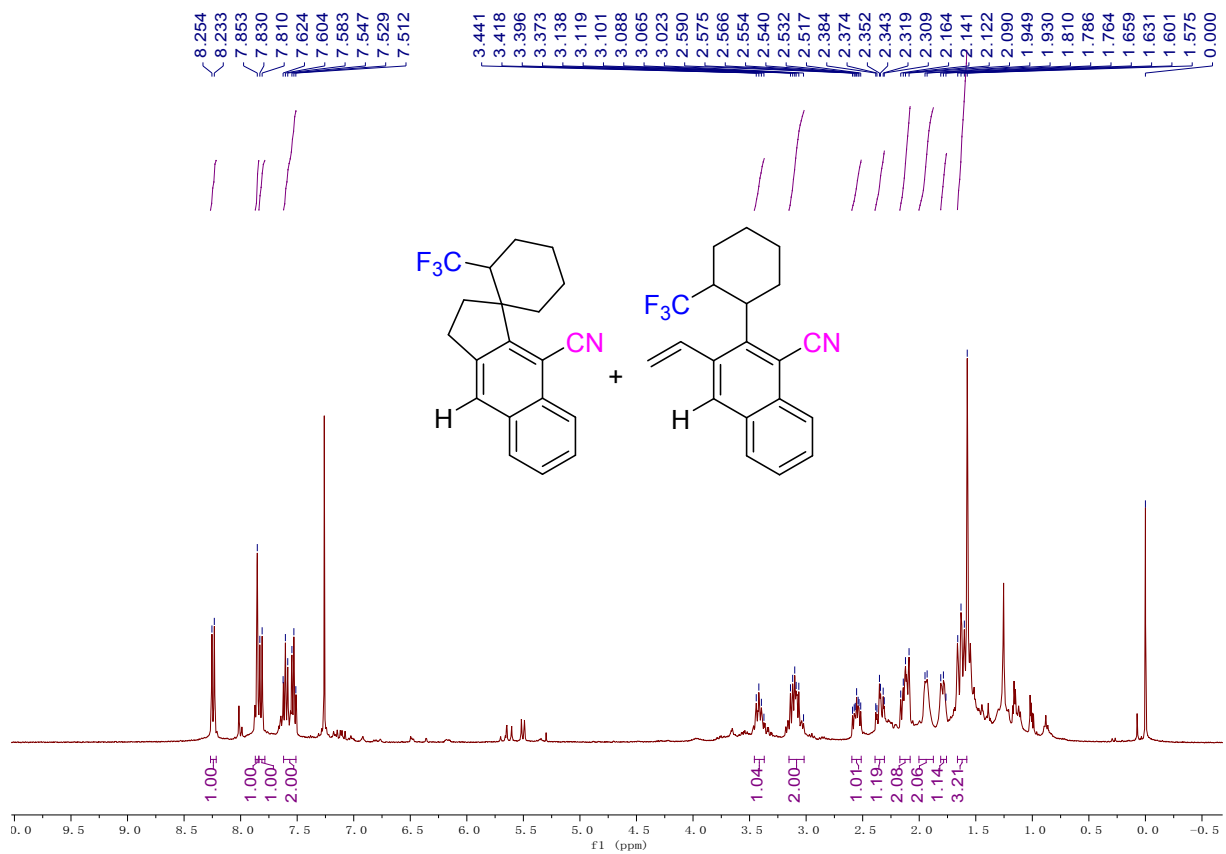
Heteronuclear Multiple Bond Correlation (HMBC)

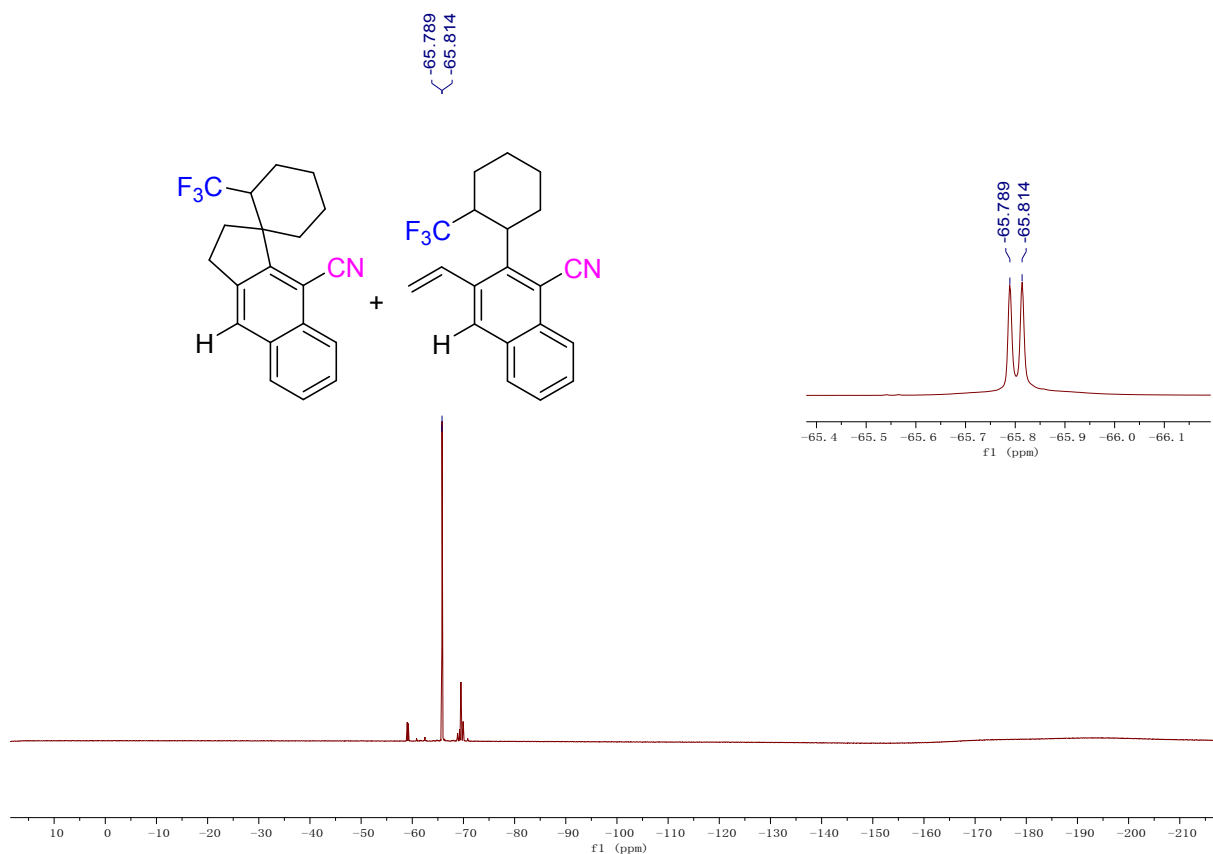
9-methyl-9-(2,2,2-trifluoroethyl)-8,9-dihydro-7*H*-cyclopenta[6,7]naphtho[1,2-*d*][1,3]dioxole-10-carbonitrile (2u)



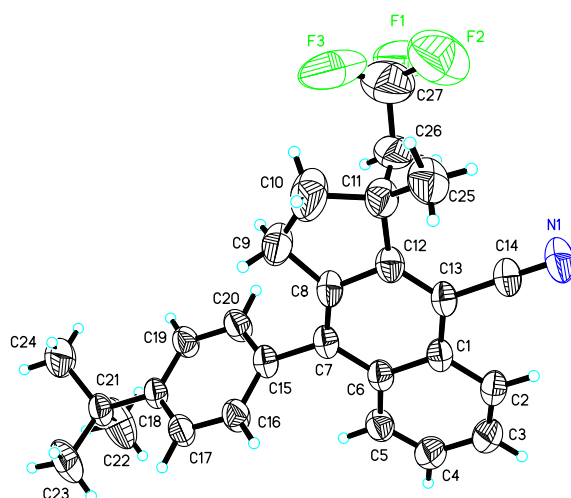


2-(trifluoromethyl)-2',3'-dihydrospiro[cyclohexane-1,1'-cyclopenta[*b*]naphthalene]-9'-carbonitrile (2v)

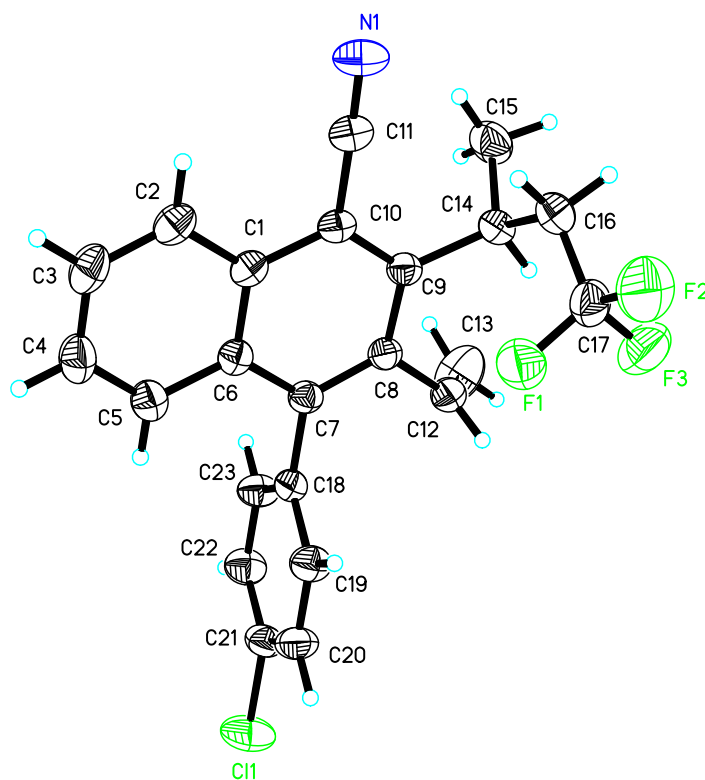




3 X-ray crystal data of compounds 2c and 3b



The crystal data of **2c** have been deposited in CCDC with number 2017000. Empirical Formula: $C_{27}H_{26}F_3N$; Formula Weight: 421.49; Crystal Color, Habit: colorless, Crystal Dimensions: 0.190 x 0.140 x 0.080 mm³; Crystal System: Triclinic; Lattice Parameters: $a = 8.7540(3)\text{\AA}$, $b = 13.9202(5)\text{\AA}$, $c = 20.4884(7)\text{\AA}$, $\alpha = 70.8050(10)^\circ$, $\beta = 84.4830(10)^\circ$, $\gamma = 81.5860(10)^\circ$, $V = 2329.40(14)\text{\AA}^3$; Space group: $P -1$; $Z = 4$; $D_{calc} = 1.202\text{ g/cm}^3$; $F_{000} = 888$; Final R indices [$I > 2\sigma(I)$] $R1 = 0.1232$, $wR2 = 0.3304$.



The crystal data of **3b** have been deposited in CCDC with number 1967399. Empirical Formula: $C_{23}H_{17}ClF_3N$; Formula Weight: 399.83; Crystal Color, Habit: colorless, Crystal Dimensions: 0.200 x 0.160 x 0.130 mm³; Crystal System: Triclinic; Lattice Parameters: $a = 8.6636(9)\text{\AA}$, $b = 8.9777(11)\text{\AA}$, $c = 13.8142(16)\text{\AA}$, $\alpha = 83.784(4)^\circ$, $\beta = 78.625(3)^\circ$, $\gamma = 68.828(3)^\circ$, $V = 981.4(2)\text{\AA}^3$; Space group: P -1; $Z = 2$; $D_{calc} = 1.353\text{ g/cm}^3$; $F_{000} = 412$; Final R indices [$I > 2\sigma(I)$] $R1 = 0.0484$, $wR2 = 0.1324$.

4 References

1. a) K. Utimoto, M. Tamura and K. Sisido, *Tetrahedron*, 1973, **29**, 1169; b) J. A. Stafford and J. E. McMurry, *Tetrahedron Lett.*, 1988, **29**, 2531; c) S. V. Frye, M. C. Johnson and N. L. Valvano, *J. Org. Chem.*, 1991, **56**, 3750; d) K. Chen, Z. Zhang, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 7696; e) T. M. Acker, A. Khatri, K. M. Vance, C. Slabber, J. Bacsa, J. P. Snyder, S. F. Traynelis and D. C. Liotta, *J. Med. Chem.*, 2013, **56**, 6434; f) K. Chen, Z. Z. Zhu, Y. S. Zhang, X. Y. Tang and M. Shi, *Angew. Chem., Int. Ed.*, 2014, **53**, 6645; g) L. Z. Yu, Y. Wei and M. Shi, *Chem. Commun.*, 2016, **52**, 13163; h) P. H. Li, L. Z. Yu, X. Y. Zhang and M. Shi, *Org. Lett.*, 2018, **20**, 4516.
2. X. Zhu, W. Deng, M. F. Chiou, C. Ye, W. Jian, Y. Zeng, Y. Jiao, L. Ge, Y. Li, X. Zhang and H. Bao, *J. Am. Chem. Soc.*, 2019, **141**, 548.