Photoredox/palladium co-catalyzed propargylic benzylation with internal propargylic carbonates

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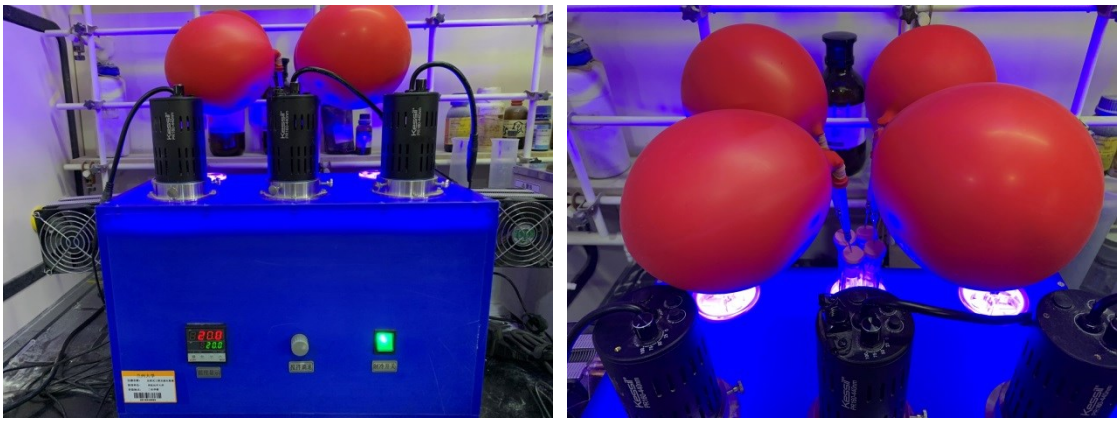
1. General Information and Materials:

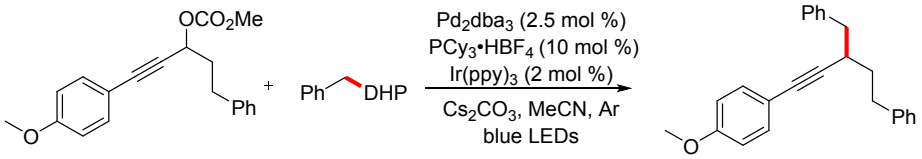
For product purification by flash column chromatography, silica gel (200~300 mesh) and *n*-pentane were used. ^{1}H NMR spectra were recorded on 400 MHz in $CDCl_3$, ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$, ^{19}F NMR spectra were recorded on 376 MHz in $CDCl_3$ using TMS as internal standard. Melting points were determined on a microscopic apparatus and were uncorrected. All products were further characterized by HRMS (high resolution mass spectra). Copies of their ^{1}H NMR and ^{13}C NMR spectra were provided. The starting materials were purchased from Sigma-Aldrich, Acros, TCI, Admas or J&K Chemicals and used without further purification.

Kessil brand 440 (± 15) nm LED was used in a reaction box equipped cooling fan to keep reaction temperature between 15 °C and 25 °C.



Photoredox devices with Kessil LED lights 440 (± 15) nm

2. General Procedure for the photoredox/palladium dual-catalyzed propargylic benzylation reaction:



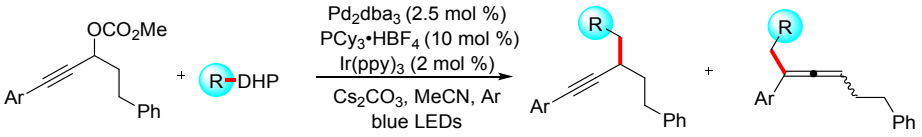
In a 5.0 mL snap vial with Teflon cover and magnetic stirring bar the internal propargylic carbonates **1a-1o**, **2a-2n** (0.2 mmol), benzyl 1,4-dihydropyridines derivatives **1b** (0.3 mmol, 1.5 equiv), Pd_2dba_3 (0.005 mmol, 2.5 mol %), PCy_3 (0.02 mmol, 10 mol %), $Ir(ppy)_3$ (0.004 mmol, 2 mol %) and Cs_2CO_3 (0.3 mmol, 1.5 equiv) were dissolved in 2.0 mL MeCN. After degassing with argon by syringe needle for 5 minutes, the reaction mixture was then irradiated in reactor with cooling device using a 440 (± 15) nm LED (50 W). The reaction progress was monitored by GC analysis. After full conversion, the reaction mixture was transferred into a separating funnel and 10 mL of distilled water and 2 mL of brine were added. The resulting mixture was extracted with Et_2O (10 mL *2) and combined organic layer were dried over $MgSO_4$, filtered and concentrated in vacuum. Purification of the crude product was achieved by flash column chromatography using *n*-pentane as eluents on silica gel.

3. Preparation of Starting Materials:

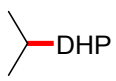
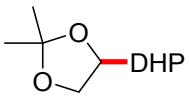
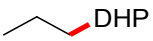
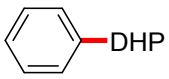
All of propargylic carbonates and benzyl 1,4-dihydropyridine derivatives (DHP) were synthesized according to the previous literatures, and the NMR spectroscopy and GC-MS data were in full accordance with the data in the reported literatures.[1,2]

4. Optimization of Reaction Conditions:

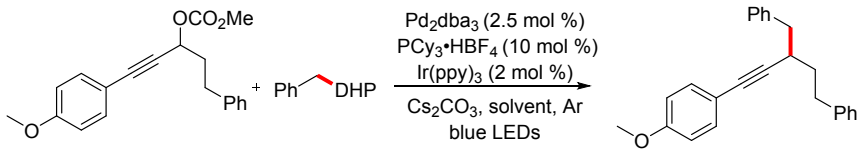
a) Screening of 1,4-dihydropyridines derivatives:



Ar = *p*-OMe-Ph

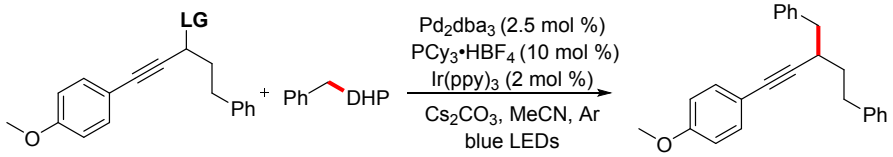
			
trace	14% yield (1:1)	trace	trace

b) Screening of solvents and loading of liagand:



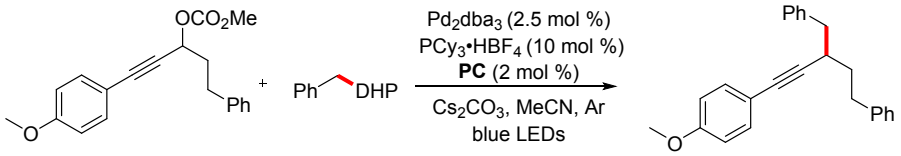
entries	Catalyst (2.5 mol %)	Ligand (7.5 mol %)	PC (2 mol %)	Base (1.5 equiv.)	**Solvent**	yield (%)
1	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**toluene**	11
2	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**acetone**	18
3	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**MeCN**	77
4	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**THF**	trace
5	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**dioxane**	trace
6	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**DMF**	trace
7	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**DMAc**	trace
8	Pd_2dba_3	**PCy_3 (10 mol %)**	$Ir(ppy)_3$	Cs_2CO_3	MeCN	82

c) Screening of leaving group on propargylic derivatives:



entries	Catalyst (2.5 mol %)	Ligand (10 mol %)	PC (2 mol %)	Base (1.5 equiv.)	**LG**	yield (%)
1	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**OH**	0
2	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**OAc**	44
3	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**OMs**	63
4	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**OCO_2Ph**	31
5	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**OCO_2Bn**	77
6	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**Br**	13
7	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	**Cl**	77

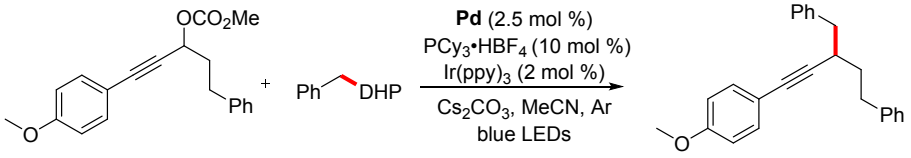
d) Screening of photocatalysis:



entries	Catalyst (2.5 mol %)	Ligand (10 mol %)	**PC (2 mol %)**	Base (1.5 equiv.)	yield (%)

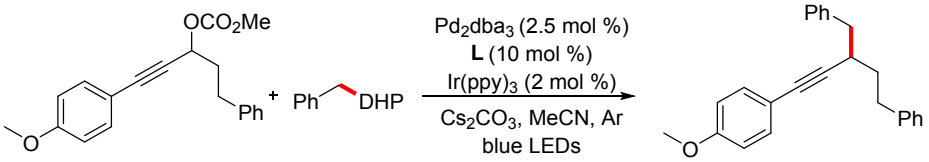
1	Pd_2dba_3	PCy_3	**$Ru(bpy)_3Cl_2·6H_2O$**	Cs_2CO_3	trace
2	Pd_2dba_3	PCy_3	**$Ir(ppy)_2(dtbbpy)PF_6$**	Cs_2CO_3	22
3	Pd_2dba_3	PCy_3	**4CzIPN**	Cs_2CO_3	11
4	Pd_2dba_3	PCy_3	**Eosin Y**	Cs_2CO_3	7

e) Screening of palladium catalysis:



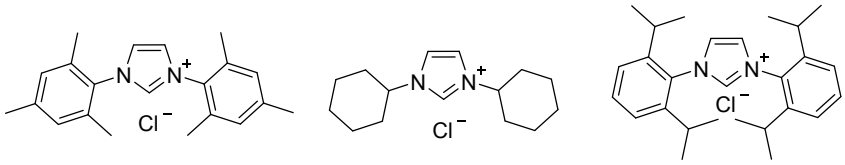
entries	**Catalyst (2.5 mol %)**	Ligand (10 mol %)	PC (2 mol %)	Base (1.5 equiv.)	Solvent	yield (%)
1	**$Pd(OAc)_2$**	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	68
2	**$Pd(dba)_2$**	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	61
3	**$Pd(PPh_3)_2Cl_2$**	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	67
4	**$Pd(MeCN)_2Cl_2$**	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	54
5	**$[Pd(allyl)Cl]_2$**	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	77

f) Screening of ligands:

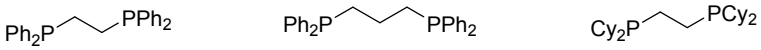


entries	Catalyst (2.5 mol %)	Ligand (10 mol %)	PC (2 mol %)	Base (1.5 equiv.)	Solvent	yield (%)
1	Pd_2dba_3	PCy_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	82
2	**Pd_2dba_3**	**$PCy_3·HBF_4$**	**$Ir(ppy)_3$**	**Cs_2CO_3**	**MeCN**	**87**
3	Pd_2dba_3	$P^tBu_3·HBF_4$	$Ir(ppy)_3$	Cs_2CO_3	MeCN	51
4	Pd_2dba_3	PPh_3	$Ir(ppy)_3$	Cs_2CO_3	MeCN	76
5	Pd_2dba_3	P(*o*-furan)$_3$	$Ir(ppy)_3$	Cs_2CO_3	MeCN	77
6	Pd_2dba_3	P(2-Me-Ph)$_3$	$Ir(ppy)_3$	Cs_2CO_3	MeCN	8
7	Pd_2dba_3	P(3-OMe-Ph)$_3$	$Ir(ppy)_3$	Cs_2CO_3	MeCN	61
8	Pd_2dba_3	DavePhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	76
9	Pd_2dba_3	CPhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	51
10	Pd_2dba_3	SPhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	78
11	Pd_2dba_3	RuPhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	72
12	Pd_2dba_3	CyJohnPhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	78
13	Pd_2dba_3	XPhos	$Ir(ppy)_3$	Cs_2CO_3	MeCN	61

14	Pd_2dba_3	dtbbpy	$Ir(ppy)_3$	Cs_2CO_3	MeCN	13
15	Pd_2dba_3	**L1-L6**	$Ir(ppy)_3$	Cs_2CO_3	MeCN	trace



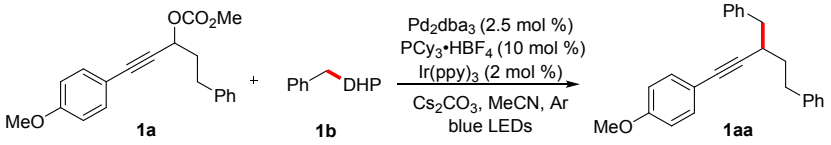
IMes•HCl (**L1**) ICy•HCl (**L2**) IPr•HCl (**L3**)



dppe (**L4**) dppp (**L5**) dcype (**L6**)

5. Mechanism characterization:

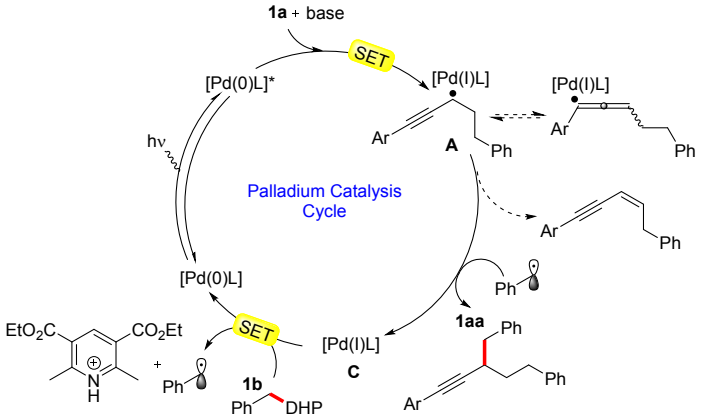
a) Control experiments:



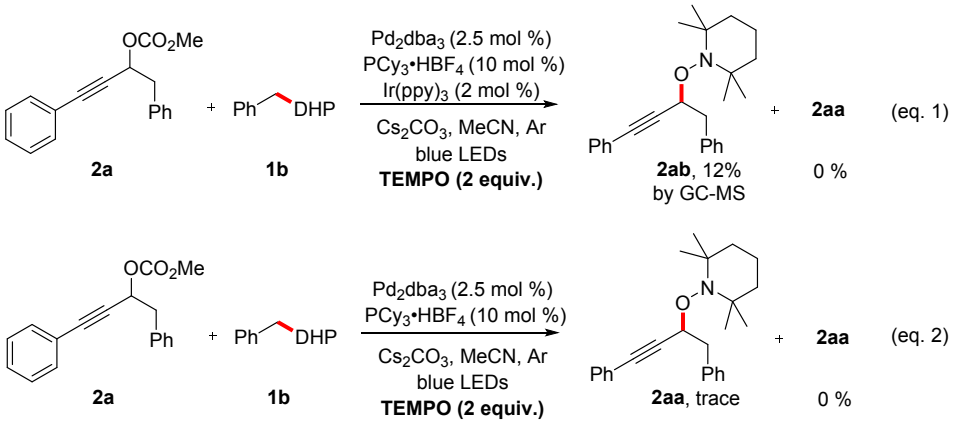
entries	Catalyst (2.5 mol %)	Ligand (10 mol %)	PC (2 mol %)	Base (1.5 equiv.)	yield (%)
	Pd_2dba_3	$PCy_3 \cdot HBF_4$	$Ir(ppy)_3$	Cs_2CO_3	
1	×	√	√	√	0
2	√	√	×	√	9
3	√	×	√	√	5
4	√	√	√	×	0
5*	√	√	√	√	0
6*	√	√	×	√	0

* In dark.

The control experiments revealed that photo catalyst $Ir(ppy)_3$ itself could not finish the catalytic cycle while Pd_2dba_3 with ligand gave 9% GC-MS yields under visible light. Meanwhile, ligand $PCy_3 \cdot HBF_4$ was proved to be the key factor for high yield and lack of base or visible light completely inhibited the reaction. It can be inferred from the entry 2 and 6, a visible-light-mediated palladium catalyzed propargylic benzylation would be proceed, even in only 9% yield by GC-MS. However, the dual catalytic system with $Ir(ppy)_3$ would accelerate this process.



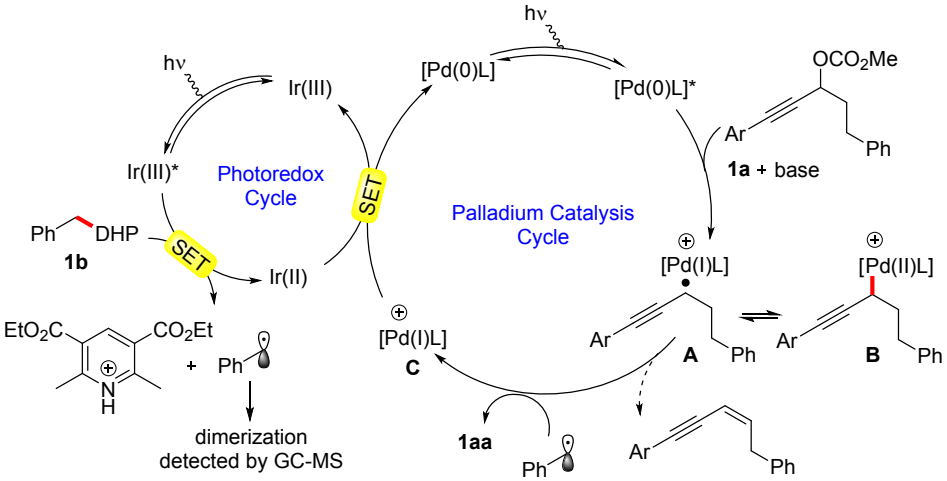
b) Radical capture experiments:



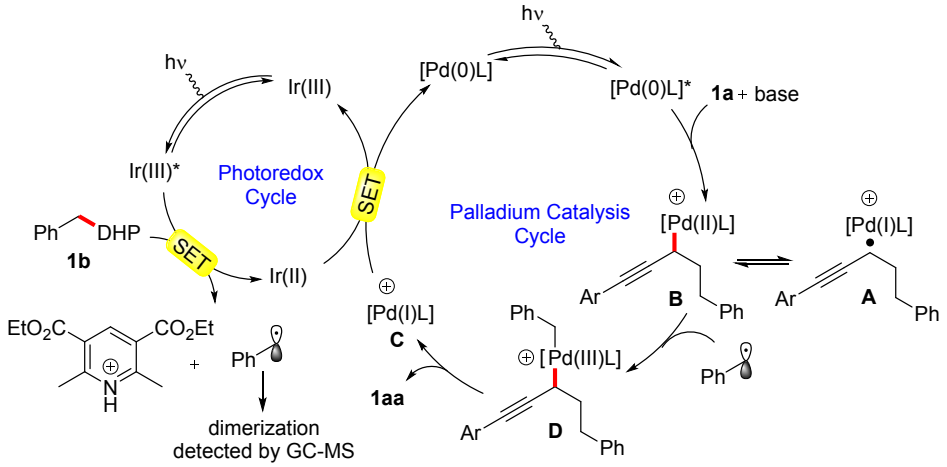
Radical capture product **2ab** was detected by GC-MS in 12% yield under standard conditions through radical inhibition experiments with TEMPO, while no product **2ab** was observed without $Ir(ppy)_3$. The results indicated that two possible pathway: 1) PC/Pd dual catalytic system accelerated the catalytic ability compared with visible-light-mediated palladium catalyzed propargylic benzylation, leading to high density of propargylic Pd(I) radical species;[3] 2) As proposed by Xiao[4] and Yu[5] group, low-valent Ir(II) reduced the propargylic Pd(II) species to generate Pd(0) and propargylic radical species. However, according to our control experiments, visible light is necessary for the generation of propargylic palladium species, namely propargylic Pd(I) radical species or propargylic Pd(II) species. Meanwhile, trace *β*-H elimination byproduct in our reaction (monitored by GC-MS) revealed that low-valent propargylic Pd(I) radical species would be more favorable (see plausible mechanism: Path A). Even though we thought that the radical coupling process with propargylic Pd(I) radical species might be more favorable, however, the addition of benzyl radical to propargylic Pd(II) species could not be fully ruled out (see plausible mechanism: Path B).[5,6]

c) Plausible mechanism:

Path A:



Path B:



6. References:

[1] (a) Z.-S. Chen, X.-H. Duan, L.-Y. Wu, S. Ali, K.-G. Ji, P.-X. Zhou, X.-Y. Liu and Y.-M. Liang, *Chem. Eur. J.,* 2011, **17**, 6918; (b) Y. Miyazaki, B. Zhou, H. Tsuji and M. Kawatsura, *Org. Lett.,* 2020, **22**, 2049; (c) P. Wu, M. Jia, W. Lin and S. Ma, *Org. Lett.,* 2018, **20**, 554; (d) C. R. Reddy, S. Z. Mohammed and P. Kumaraswamya, *Org. Biomol. Chem.,* 2015, **13**, 8310.

[2] (a) Á. Gutiérrez-Bonet, J. C. Tellis, J. K. Matsui, B. A. Vara and G. A. Molander, *ACS Catal.,* 2016, **6**, 8004; (b) Á Gutiérrez-Bonet, C. Remeur, J. K. Matsui and G. A. Molander, *J. Am. Chem. Soc.,* 2017, **139**, 12251.

[3] Z.-Z. Zhou, J.-H. Zhao, X.-Y. Gou, X.-M. Chen and Y.-M. Liang, *Org. Chem. Front.,* 2019, **6**, 1649.

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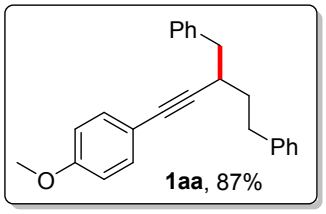
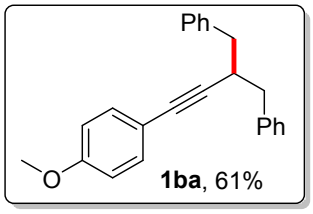
[5] H.-H. Zhang, J.-J. Zhao and S. Yu, *J. Am. Chem. Soc.,* 2018, **140**, 16914.

[6] (a) S. B. Lang, K. M. O'Nele and J. A. Tunge, *J. Am. Chem. Soc.,* 2014, **136**, 13606; (b) J. Xuan, T.-T. Zeng, Z.-J. Feng, Q.-H. Deng, J.-R. Chen, L.-Q. Lu, W.-J. Xiao and H. Alper, *Angew. Chem. Int. Ed.,* 2015, **54**, 1625; (c) W.-M. Cheng, R. Shang, H.-Z. Yu and Y. Fu, *Chem. Eur. J.,* 2015, **21**, 13191; (d) S. B. Lang, K. M. O'Nele, J. T. Douglas and J. A.Tunge, *Chem. Eur. J.,* 2015, **21**, 18589; (e) C. Zheng, W.-M. Cheng, H.-L. Li, R.-S. Na and R. Shang, *Org. Lett.,* 2018, **20**, 2559.

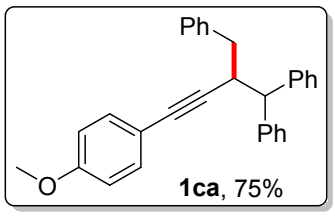
7. Characterization Data of Products 1aa-1ma:



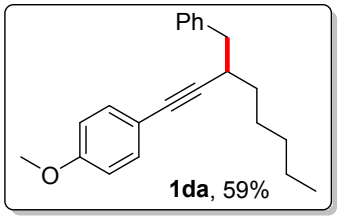
1aa: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.77-1.91（m, 2H), 2.73-2.99（m, 5H), 3.80 (s, 3H), 6.80-6.84（dt, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 4H), 7.16-7.23 (m, 4H), 7.25-7.33 (m, 8H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 33.7, 33.9, 36.3, 41.6, 55.3, 83.0, 90.9, 113.8, 116.1, 125.8, 126.2, 128.1, 128.3, 128.5, 129.4, 132.9, 139.5, 142.0, 159.1;
HRMS (ESI) calcd for $C_{25}H_{24}O$ $[M+H]^+$ m/z 341.1900, found 341.1903.



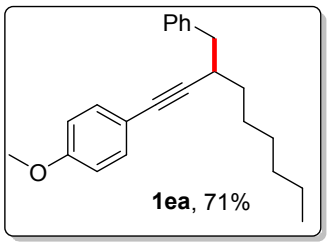
1ba: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.82-2.91 (m, 4H), 3.04-3.11 (m, 1H), 3.77 (s, 3H), 6.76-6.80 (dt, J_1 = 2.4 Hz, J_2 = 9.2 Hz, 4H), 7.21-7.24 (m, 4 H), 7.26-7.33 (m, 8H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.5, 41.0, 55.3, 83.3, 90.7, 113.8, 116.1, 126.3, 128.2, 129.4, 132.8, 139.6, 159.1;
HRMS (ESI) calcd for $C_{24}H_{22}O$ $[M+H]^+$ m/z 327.1743, found 327.1747.



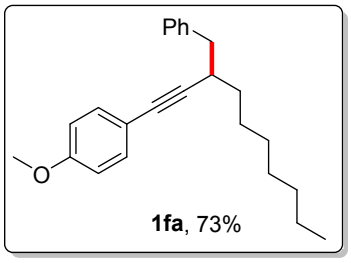
1ca: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 80/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.72-2.90 (m, 2H), 3.61-3.66 (m, 1H), 3.75 (s,3H), 4.05-4.07 (d, J = 8.4 Hz, 1H), 6.72-6.74 (d, J = 8.4 Hz, 2H), 7.05-7.07 (d, J = 8.4 Hz, 2H), 7.18-7.34 (m, 11H), 7.38-7.44 (m, 4H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 39.6, 39.9, 55.2, 55.4, 84.9, 89.9, 113.7, 116.0, 126.3, 126.4, 126.5, 128.0, 128.1, 128.2, 128.6, 129.0, 129.4, 132.6, 139.6, 142.7, 143.0, 159.0;
HRMS (ESI) calcd for $C_{30}H_{26}O$ $[M+H]^+$ m/z 403.2056, found 403.2062.



1da: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.88-0.91 (t, J = 6.4 Hz, 3H), 1.30-1.31 (m, 4H), 1.43-1.62 (m, 4H), 2.74-2.89 (m, 3H), 3.79 (s, 3H), 6.79-6.81 (d, J = 8.8 Hz, 2H), 7.20-7.32 (m, 7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.6, 27.1, 31.7, 34.4, 34.6, 41.7, 55.3, 82.3, 91.5, 113.8, 116.2, 126.1, 128.1, 129.4, 132.8, 139.9, 159.0;
HRMS (ESI) calcd for $C_{22}H_{26}O$ $[M+H]^+$ m/z 307.2056, found 307.2059.

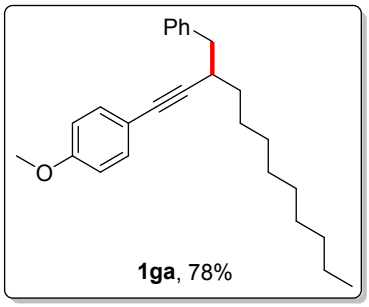


1ea: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.86-0.90 (t, J = 6.8 Hz, 3H), 1.26-1.36 (m, 6H), 1.45-1.62 (m, 4H), 2.76-2.89 (m, 3H), 3.79 (s, 3H), 6.78-6.81 (dt, J_1 = 3.6 Hz, J_2 = 9.6 Hz, 2H), 7.20-7.32 (m, 7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.7, 27.4, 29.3, 29.5, 29.6, 31.9, 34.4, 34.6, 41.7, 55.2, 82.3, 91.5, 113.7, 116.2, 126.1, 128.1, 129.4, 132.8, 139.9, 159.0;
HRMS (ESI) calcd for $C_{23}H_{28}O$ $[M+H]^+$ m/z 321.2213, found 321.2217.

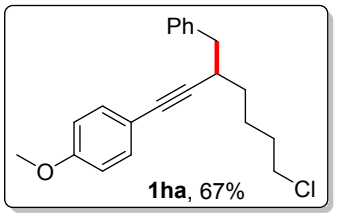


1fa: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.86-0.89 (t, J = 6.8 Hz, 3H), 1.27-1.28 (m, 8H), 1.41-1.62 (m,

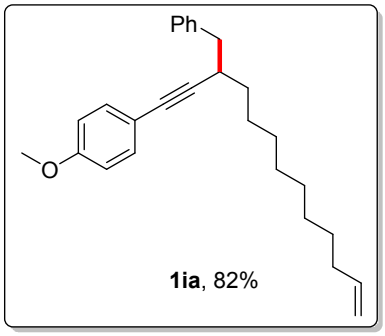
4H), 2.74-2.89 (m, 3H), 3.79 (s, 3H), 6.78-6.81 (dt, J_1 = 2.8 Hz, J_2 = 8.8 Hz, 2H), 7.19-7.32 (m, 7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.7, 27.4, 29.3, 29.4, 31.9, 34.4, 34.6, 41.7, 55.2, 82.3, 91.5, 113.7, 116.2, 126.1, 128.1, 129.4, 132.8, 139.9, 159.0;
HRMS (ESI) calcd for $C_{24}H_{30}O$ $[M+H]^+$ m/z 335.2369, found 335.2374.



1ga: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.86-0.89 (t, J = 6.8 Hz, 3H), 1.26-1.27 (m, 12H), 1.42-1.63 (m, 4H), 2.74-2.89 (m, 3H), 3.79 (s, 3H), 6.79-6.82 (d, J = 14.4 Hz, 2H), 7.20-7.33 (m, 7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.1, 22.7, 27.4, 29.3, 29.5, 29.6, 31.9, 34.4, 34.6, 41.7, 55.2, 82.3, 91.5, 113.7, 116.2, 126.1, 128.1, 129.4, 132.8, 139.9, 159.0;
HRMS (ESI) calcd for $C_{26}H_{34}O$ $[M+H]^+$ m/z 363.2682, found 363.2688.

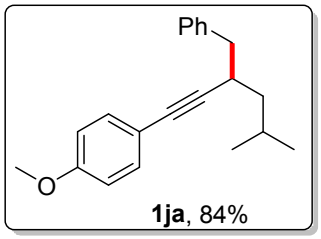


1ha: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.47-1.84 (m, 6H), 2.78-2.89 (m, 3H), 3.52-3.55 (t, J = 6.4 Hz, 2H), 3.79 (s, 3H), 6.78-6.88 (dt, J_1 = 2.8 Hz, J_2 = 9.6 Hz, 2H), 7.20-7.33 (m, 7H),
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 24.8, 32.4, 33.7, 34.3, 41.6, 44.9, 55.2, 82.6, 90.8, 113.8, 116.0, 126.3, 127.2, 128.1, 128.8, 129.3, 132.8, 139.6, 159.0;
HRMS (ESI) calcd for $C_{21}H_{23}ClO$ $[M+H]^+$ m/z 327.1510, found 327.1515.



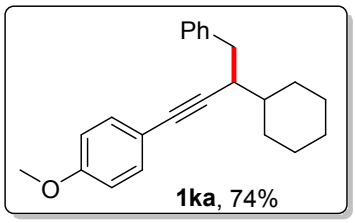
1ia: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;

^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.26-1.38 (m, 10H), 1.46-1.62 (m, 4H), 2.00-2.06 (dd, J_1 = 6.8 Hz, J_2 = 14.0 Hz, 2H), 2.74-2.89 (m, 3H), 3.79 (s,3H), 4.91-5.01 (m, 2H), 5.76-5.86 (m,1H), 6.78-6.81 (d, J = 8.8 Hz, 2H), 7.20-7.33 (m, 7H),
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 27.4, 28.9, 29.1, 29.4, 29.5, 33.8, 34.4, 34.6, 41.7, 55.2, 82.3, 91.5, 113.7, 114.1, 116.2, 126.1, 127.2, 128.1, 128.8, 132.8, 139.2, 139.9, 159.0;
HRMS (ESI) calcd for $C_{27}H_{34}O$ $[M+H]^+$ m/z 375.2682, found 375.2689.



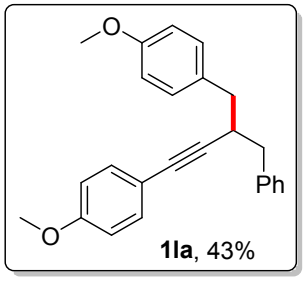
1ja, 84%

1ja: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.89-0.96 (m, 6H), 1.26-1.32 (m, 2H), 1.48-1.54(m, 1H), 1.90-2.00 (m, 1H), 2.79-2.89 (m, 2H), 3.79 (s, 3H), 6.78-6.81 (dt, J_1 = 2.8 Hz, J_2 = 9.6 Hz, 2H), 7.20-7.33 (m,7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 21.6, 23.5, 26.1, 32.5, 42.1, 44.0, 55.2, 82.3, 91.3, 113.7, 116.2, 126.2, 128.1, 129.4, 132.8, 139.9, 159.0;
HRMS (ESI) calcd for $C_{21}H_{24}O$ $[M+H]^+$ m/z 293.1900, found 293.1904.



1ka, 74%

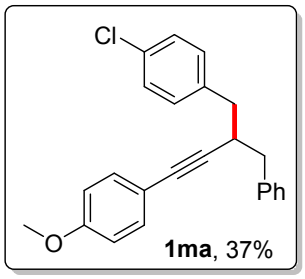
1ka: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.16-1.45 (m, 6H), 1.66-1.80 (m, 4H), 1.94-1.96 (d, J = 11.2 Hz, 1H), 2.65-2.69 (m, 1H), 2.79-2.90 (m, 2H), 3.78 (s, 3H), 6.77-6.81 (dt, J_1 = 3.6 Hz, J_2 = 11.6 Hz, 2H), 7.18-7.32 (m, 7H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 26.3, 26.4, 26.5, 28.9, 31.9, 38.9, 40.8, 41.0, 55.2, 83.3, 90.2, 113.7, 116.4, 126.0, 128.1, 129.2, 132.8, 140.4, 159.0;
HRMS (ESI) calcd for $C_{23}H_{26}O$ $[M+H]^+$ m/z 319.2056, found 319.2060.



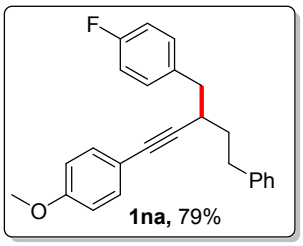
1la, 43%

1la: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 80/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.76-2.89 (m, 4H), 2.99-3.07 (m, 1H), 3.78 (s, 3H), 3.79 (s,

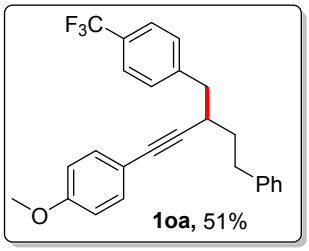
3H), 6.77-6.79 (d, J = 8.8 Hz, 2H), 6.84-6.86 (d, J = 8.8 Hz, 2H), 7.19-7.32 (m, 9H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.6, 40.1, 40.9, 55.2, 83.2, 90.9, 113.6, 113.7, 116.1, 126.2, 128.1, 129.4, 130.3, 131.6, 132.7, 139.6, 158.1, 159.0;
HRMS (ESI) calcd for $C_{25}H_{24}O_2$ $[M+H]^+$ m/z 357.1849, found 357.1854.



1ma: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.74-2.91 (m, 4H), 3.00-3.07 (m, 1H), 3.78 (s, 3H), 6.77-6.81 (dt, J_1 = 2.8 Hz, J_2 = 11.6 Hz, 2H), 7.19-7.33 (m, 11H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.3, 40.2, 41.1, 55.2, 83.6, 90.2, 113.8, 115.8, 126.4, 128.2, 129.3, 130.7, 132.1, 132.7, 138.0, 139.3, 159.2;
HRMS (ESI) calcd for $C_{24}H_{21}ClO$ $[M+H]^+$ m/z 361.1354, found 361.1359.

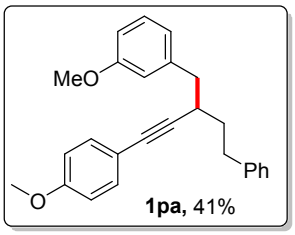


1na: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.76-1.88 (m, 2H), 2.74-2.83 (m, 4H), 2.91-2.98 (m, 1H), 3.80 (s, 3H), 6.81-6.83 (d, J = 8.8 Hz, 2H), 6.95-6.99 (t, J = 8.8 Hz, 2H), 7.16-7.32 (m, 9H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 33.7, 34.0, 36.3, 40.7, 55.3, 83.2, 90.5, 113.8, 114.7-114.9 (d, J = 20.9 Hz), 115.9, 125.8, 127.1, 128.4-128.5 (d, J = 15.4 Hz), 130.6-130.7 (d, J = 7.7 Hz), 132.8, 135.1, 141.9, 159.2;
^{19}F NMR (376 MHz, $CDCl_3$, δ ppm): -117.2 (s, 1F);
HRMS (ESI) calcd for $C_{25}H_{23}FO$ $[M+H]^+$ m/z 359.1806, found 359.1879.

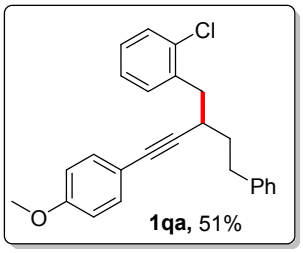


1oa: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.83-1.88 (m, 2H), 2.75-2.99 (m, 5H), 3.81 (s, 3H), 6.82-6.84 (d, J = 8.8 Hz, 2H), 7.18-7.31 (m, 7H), 7.36-7.38 (d, J = 8.0 Hz, 2H), 7.53-7.55 (d, J = 8.0 Hz, 2H);

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 33.6, 33.7, 36.5, 41.3, 55.3, 83.5, 90.0, 113.9, 115.7, 125.0-125.1 (q, J = 3.7 Hz, CF3), 125.9, 128.4, 128.5, 129.6, 132.8, 141.7, 143.6, 159.2;
^{19}F NMR (376 MHz, $CDCl_3$, δ ppm): -62.3 (s, 3F);
HRMS (ESI) calcd for $C_{26}H_{23}F_3O$ $[M+H]^+$ m/z 409.1774, found 409.1771.

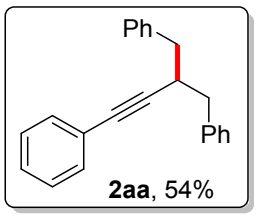


1pa: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.80-1.87 (m, 2H), 2.73-2.99 (m, 5H), 3.77 (s, 3H), 3.81 (s, 3H), 6.75-6.85 (m, 5H), 7.16-7.34 (m, 8H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 33.7, 33.8, 36.3, 41.6, 55.1, 55.3, 83.0, 90.9, 111.8, 113.8, 114.9, 116.1, 121.8, 125.8, 128.3, 128.5, 129.0, 132.9, 141.1, 142.0, 159.1, 159.4;
HRMS (ESI) calcd for $C_{26}H_{26}O_2$ $[M+H]^+$ m/z 371.2006, found 371.2004.



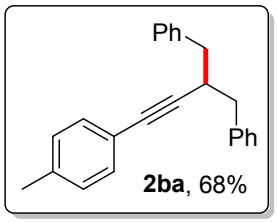
1qa: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.87-1.94 (m, 2H), 2.76-3.07 (m, 5H), 3.80 (s, 3H), 6.79-6.83 (m, 2H), 7.16-7.35 (m, 11H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 32.3, 33.7, 36.6, 39.1, 55.3, 83.0, 90.4, 113.8, 116.0, 125.8, 126.4, 127.8, 128.3, 128.5, 129.4, 131.7, 132.8, 134.2, 137.3, 141.9, 159.1;
HRMS (ESI) calcd for $C_{25}H_{23}ClO$ $[M+H]^+$ m/z 375.1510, found 375.1509.

8. Characterization Data of Products 2aa-2la:

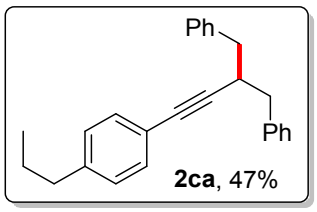


2aa: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.83-2.92 (m, 4H), 3.10-3.13 (m, 1H), 7.21-7.33 (m, 15H),
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.4, 41.0, 83.6, 92.3, 123.8, 126.3, 127.6, 128.1, 128.2, 129.4, 131.4, 139.4;

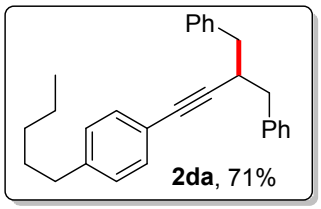
HRMS (ESI) calcd for $C_{23}H_{20}$ $[M+H]^+$ m/z 297.1638, found 297.1642.



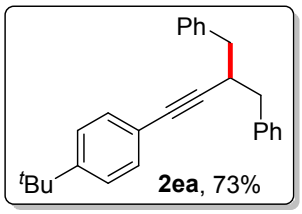
2ba: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.30-2.31 (d, *J* = 2.4 Hz, 3H), 2.82-2.88 (m, 4H), 3.04-3.13 (m, **1**H), 7.04-7.06 (d, *J* = 8.0 Hz, 2H), 7.17-7.33 (m, 12H),
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 21.4, 36.4, 41.0, 83.6, 91.5, 120.7, 126.3, 128.1, 128.9, 129.4, 131.3, 137.5, 139.5;
HRMS (ESI) calcd for $C_{24}H_{22}$ $[M+H]^+$ m/z 311.1794, found 311.1800.



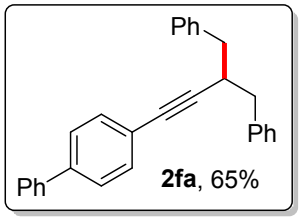
2ca: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.90-0.93 (t, *J* = 7.2 Hz, 3H), 1.56-1.65 (m, 2H), 2.53-2.56 (t, *J* = 8.0 Hz, 2H), 2.82-2.91 (m, 4H), 3.04-3.11 (m, 1H), 7.05-7.07 (d, *J* = 8.0 Hz, 2H), 7.19-7.33 (m, 12H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 13.7, 24.4, 36.4, 37.9, 41.0, 83.6, 91.5, 121.0, 126.3, 128.1, 128.3, 129.4, 131.3, 139.5, 142.3;
HRMS (ESI) calcd for $C_{26}H_{26}$ $[M+H]^+$ m/z 339.2107, found 339.2113.



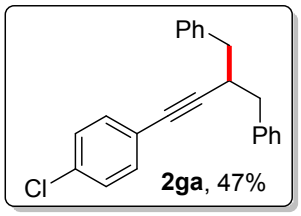
2da: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 0.86-0.89 (t, *J* = 6.8 Hz, 3H), 1.26-1.34 (m, 4H), 1.54-1.61 (m, 2H), 2.54-2.57 (t, *J* = 8.0 Hz, 2H), 2.82-2.91 (m, 4H), 3.04-3.11 (m, 1H), 7.05-7.07 (d, *J* = 6.8 Hz, 2H),
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 14.0, 22.5, 31.0, 31.4, 35.8, 36.4, 41.0, 83.6, 91.5, 121.0, 126.3, 128.1, 128.2, 129.4, 131.3, 139.5, 142.6;
HRMS (ESI) calcd for $C_{28}H_{30}$ $[M+H]^+$ m/z 367.2420, found 367.2426.



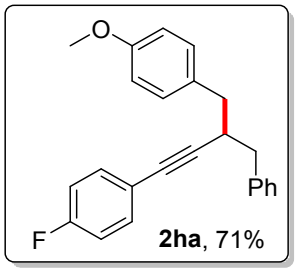
2ea: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.29 (s, 9H), 2.82-2.91 (m, 4H), 3.04-3.11 (m, 1H), 7.20-7.32 (m, 14H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 31.2, 34.7, 36.4, 41.0, 83.5, 91.6, 120.8, 125.1, 126.3, 128.1, 129.4, 131.1, 139.5, 150.7;
HRMS (ESI) calcd for $C_{27}H_{28}$ $[M+H]^+$ m/z 353.2264, found 353.2269.



2fa: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.85-2.94 (m, 4H), 3.08-3.15 (m, 1H), 7.22-7.57 (m, 19H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.5, 40.9, 83.4, 93.1, 122.8, 126.4, 126.8, 127.0, 127.5, 128.2, 128.8, 129.4, 131.8, 139.4, 140.3, 140.5;
HRMS (ESI) calcd for $C_{29}H_{24}$ $[M+H]^+$ m/z 373.1951, found 373.1957.

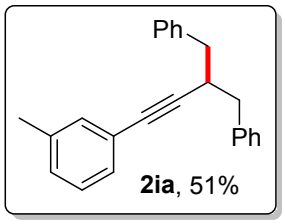


2ga: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.81-2.92 (m, 4H), 3.04-3.12 (m, 1H), 7.16-7.33 (m, 14H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.5, 40.8, 82.6, 93.4, 122.3, 126.4, 128.2, 128.4, 129.3;
HRMS (ESI) calcd for $C_{23}H_{19}Cl$ $[M+H]^+$ m/z 331.1248, found 331.1254.

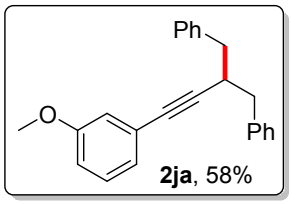


2ha: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.76-2.90 (m, 4H), 2.99-3.06 (m, 1H), 3.80 (s, 3H), 6.84-6.86

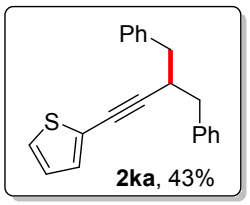
(d, J = 8.8 Hz, 2H), 6.92-6.97 (m, 2H), 7.12-7.33 (m, 9H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.6, 40.0, 40.8, 55.2, 82.5, 92.1, 113.6, 115.2, 115.4, 119.9, 126.3, 128.2, 129.3, 130.3, 131.5, 133.1, 133.2, 139.5, 158.2, 160.9-163.3 (d, J = 246.7 Hz);
^{19}F NMR (376 MHz, $CDCl_3$, δ ppm): -112.2 (s, 1F).
HRMS (ESI) calcd for $C_{24}H_{21}FO$ $[M+H]^+$ m/z 345.1649, found 345.1653.



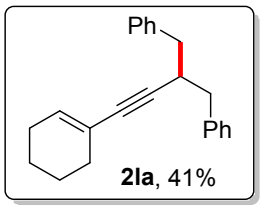
2ia: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.29 (s, 3H), 2.82-2.91 (m, 4H), 3.04-3.11 (m, 1H), 7.05-7.33 (m, 14H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 21.2, 36.4, 40.9, 83.7, 91.9, 123.6, 126.3, 128.0, 128.2, 128.5, 128.5, 129.4, 132.0, 137.7, 139.5;
HRMS (ESI) calcd for $C_{24}H_{22}$ $[M+H]^+$ m/z 311.1794, found 311.1799.



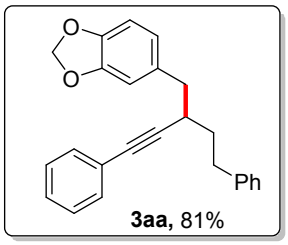
2ja: according to **GP**; colorless oil; Eluent: *n*-hexane/EtOAc = 100/1;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.83-2.92 (m, 4H), 3.05-3.12 (m, 1H), 3.77 (s, 3H), 6.80-6.90 (m, 3H), 7.14-7.33 (m, 11H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.4, 40.9, 55.2, 83.5, 92.2, 114.1, 116.4, 123.9, 124.8, 126.3, 128.2, 129.2, 129.4, 139.4, 159.2;
HRMS (ESI) calcd for $C_{24}H_{22}O$ $[M+H]^+$ m/z 327.1743, found 327.1747.



2ka: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 2.83-2.91 (m, 4H), 3.07-3.14 (m, 1H), 6.90-6.98 (dd, J_1 = 3.6 Hz, J_2 = 5.2 Hz, 1H), 7.03-7.04 (d, J = 2.8 Hz, 1H), 7.14-7.16 (d, J = 6.0 Hz, 1H), 7.21-7.33 (m, 10H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 36.7, 40.7, 96.3, 123.9, 126.0, 126.4, 126.7, 128.2, 129.3, 130.9, 139.2;
HRMS (ESI) calcd for $C_{21}H_{18}S$ $[M+H]^+$ m/z 303.1202, found 303.1205.

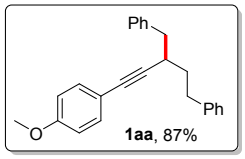


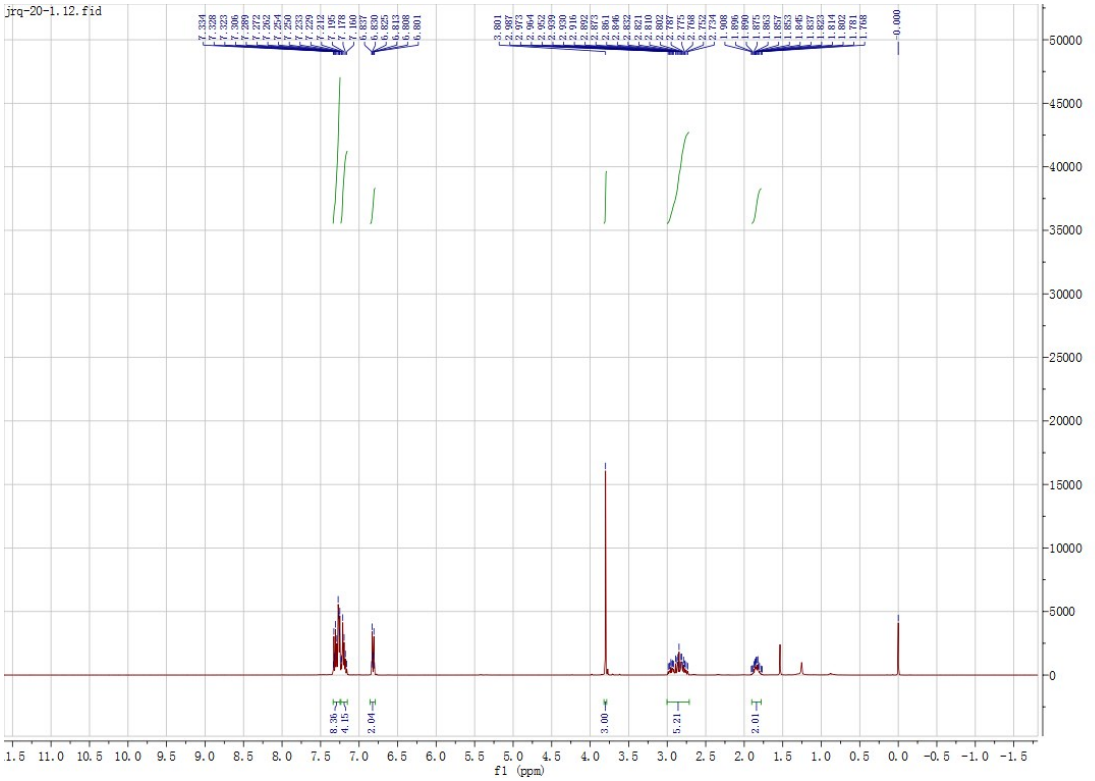
2la: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.52-1.61 (m, 4H), 1.99-2.15 (m, 4H), 2.73-3.02 (m, 5H), 5.87-5.93 (m, 1H), 7.12-7.33 (m, 10H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 21.6, 22.3, 25.5, 29.3, 36.2, 41.0, 85.3, 89.4, 120.9, 126.2, 128.1, 129.3, 133.2, 139.6;
HRMS (ESI) calcd for $C_{23}H_{24}$ $[M+H]^+$ m/z 301.1951, found 301.1955.

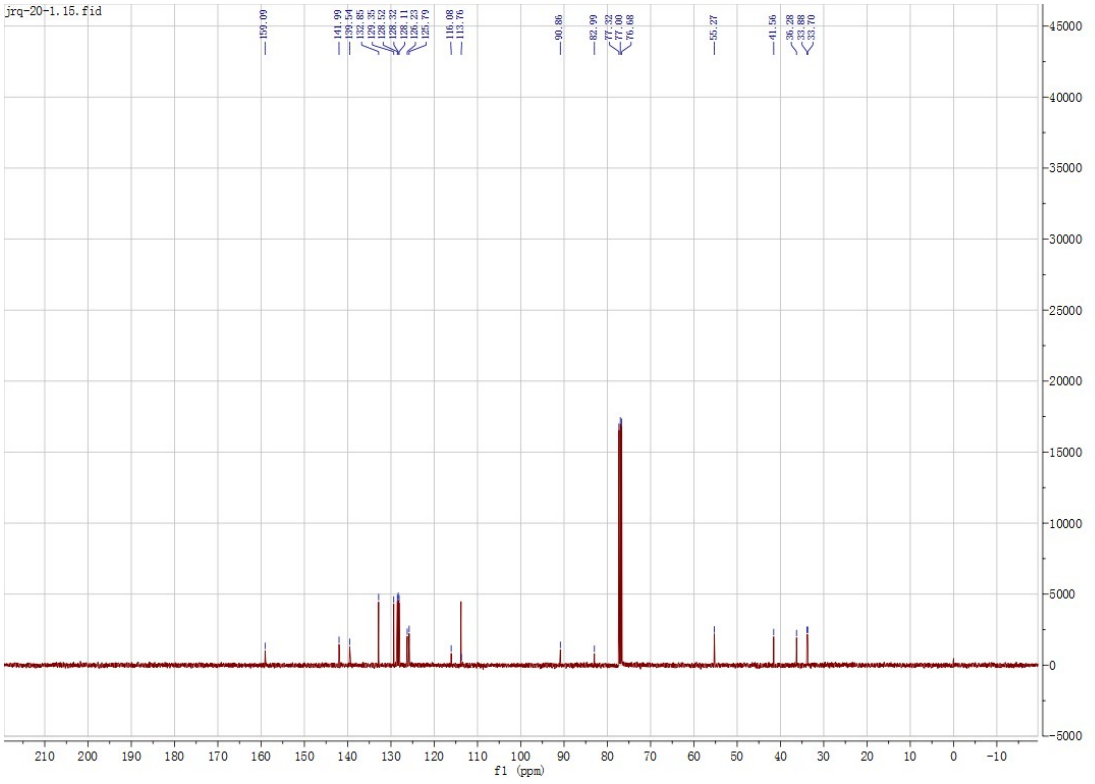


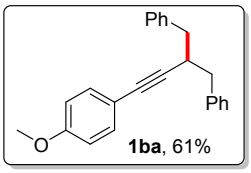
3aa: according to **GP**; colorless oil; Eluent: *n*-hexane;
^{1}H NMR (400 MH_Z $CDCl_3$, δ ppm): 1.80-1.88 (m, 2H), 2.74-2.98 (m, 5H), 5.91 (s, 2H), 6.58-6.77 (m, 3H), 7.16-7.40 (m, 10H);
^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 33.7, 34.1, 36.1, 41.1, 83.4, 92.4, 100.8, 107.9, 109.7, 122.3, 125.8, 127.6, 128.2, 128.3, 128.5, 131.5, 133.2, 141.9, 146.0, 147.4;
HRMS (ESI) calcd for $C_{25}H_{22}O_2$ $[M+H]^+$ m/z 355.1693, found 355.1697.

9. ^{1}H NMR and ^{13}C NMR Spectra of the Products 1aa-1ma:

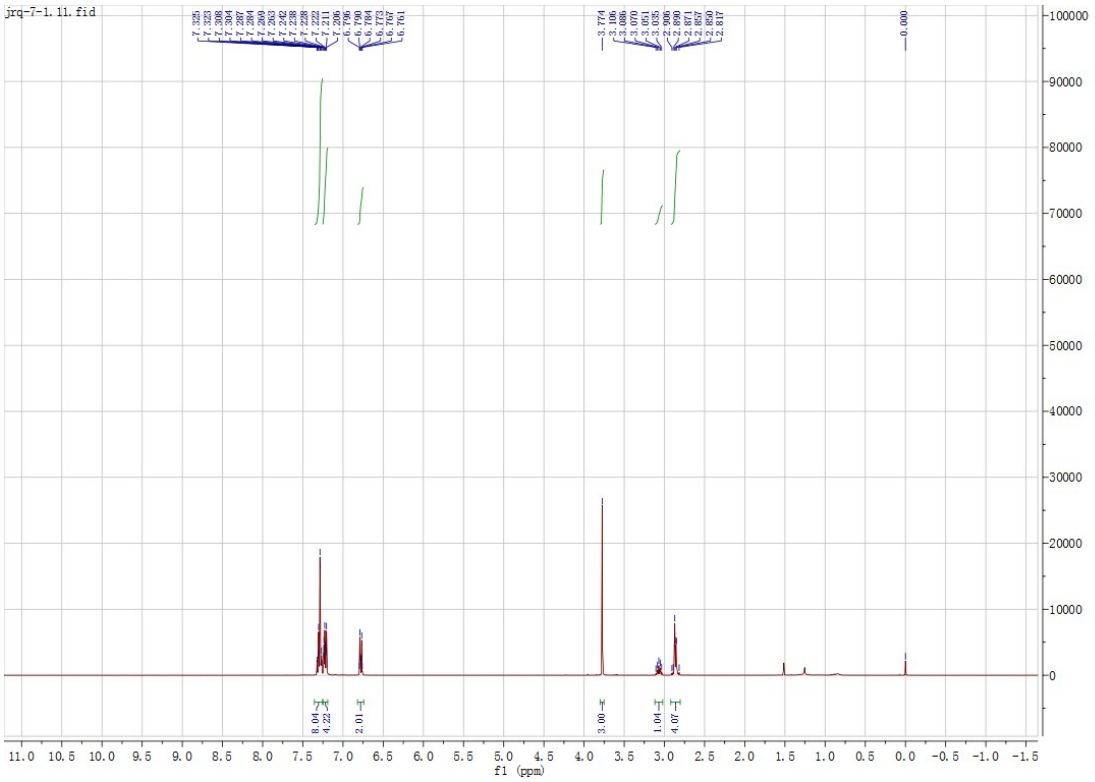


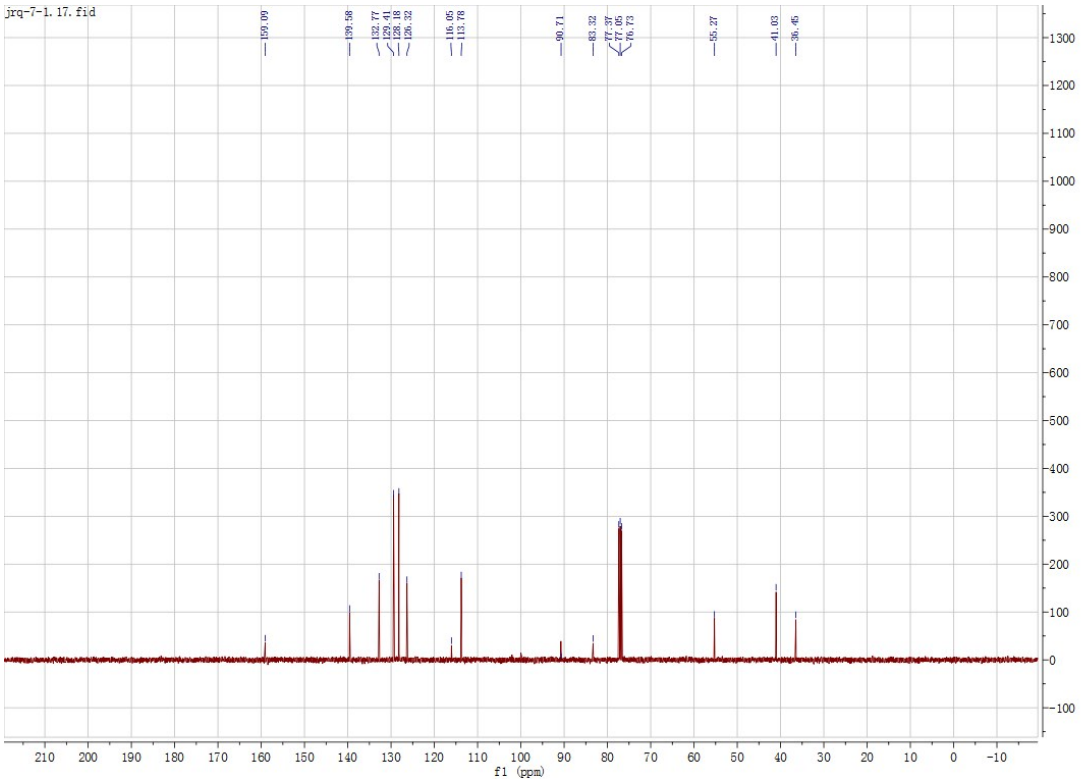


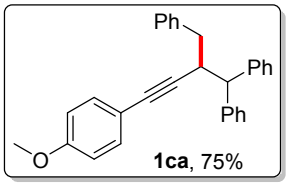




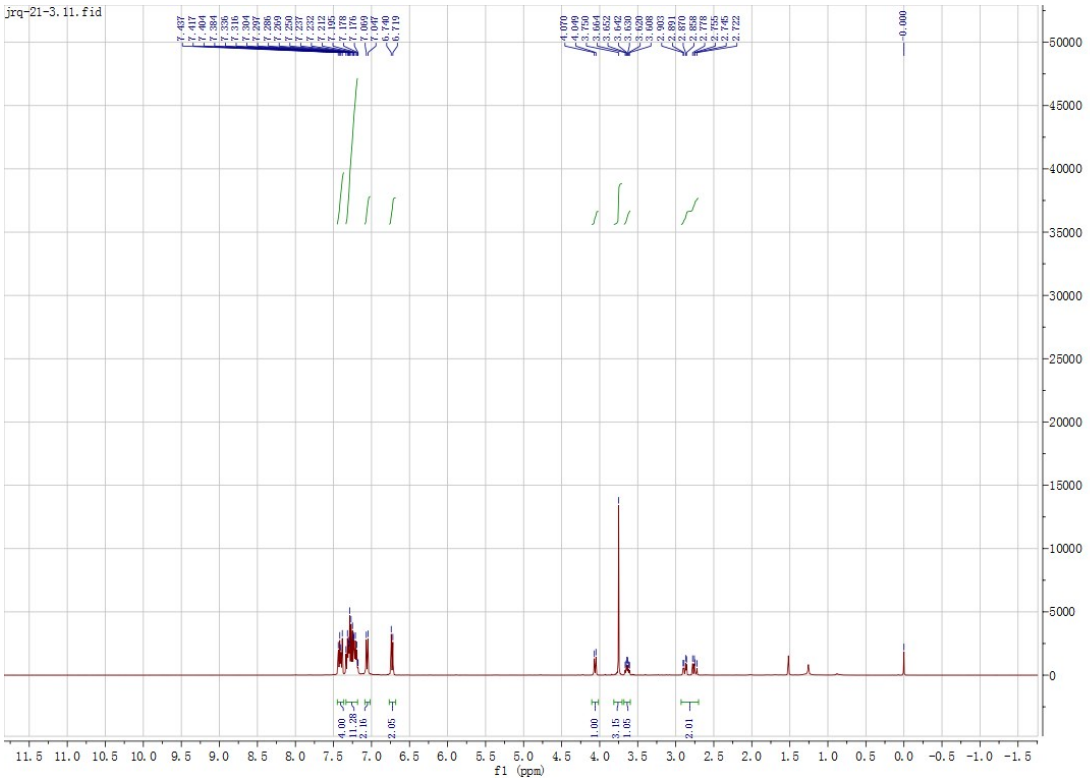
1ba, 61%

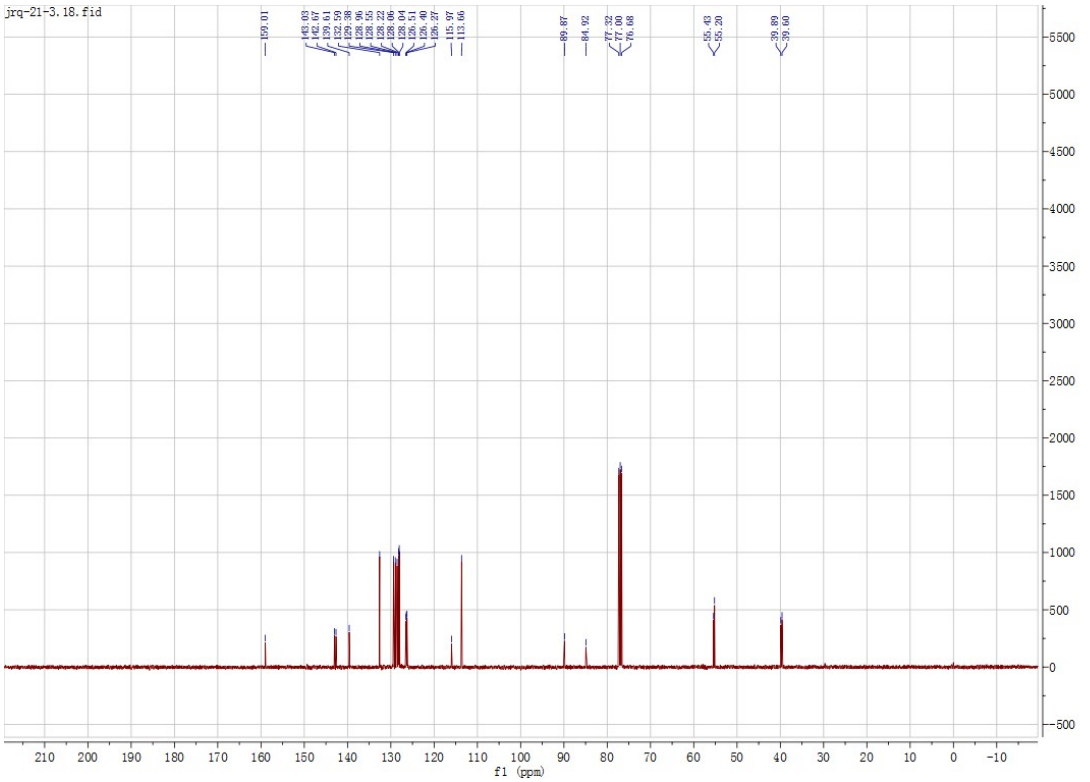


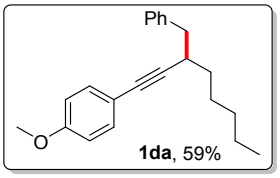


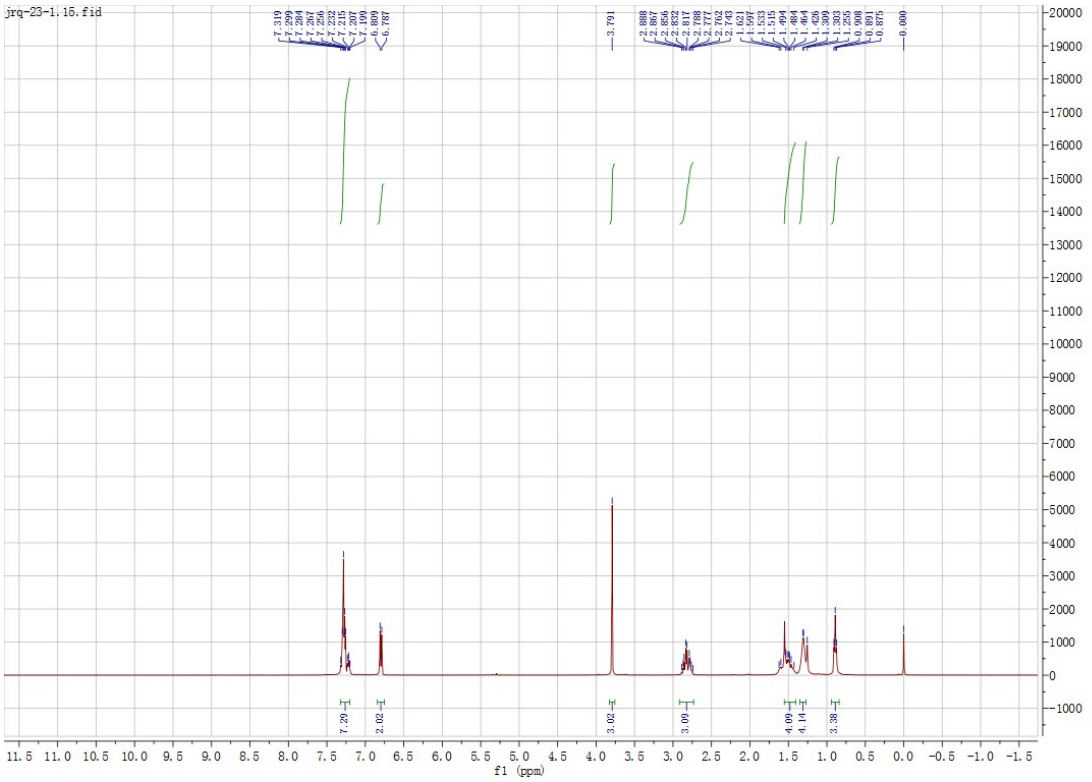


1ca, 75%






Ph
O
1da, 59%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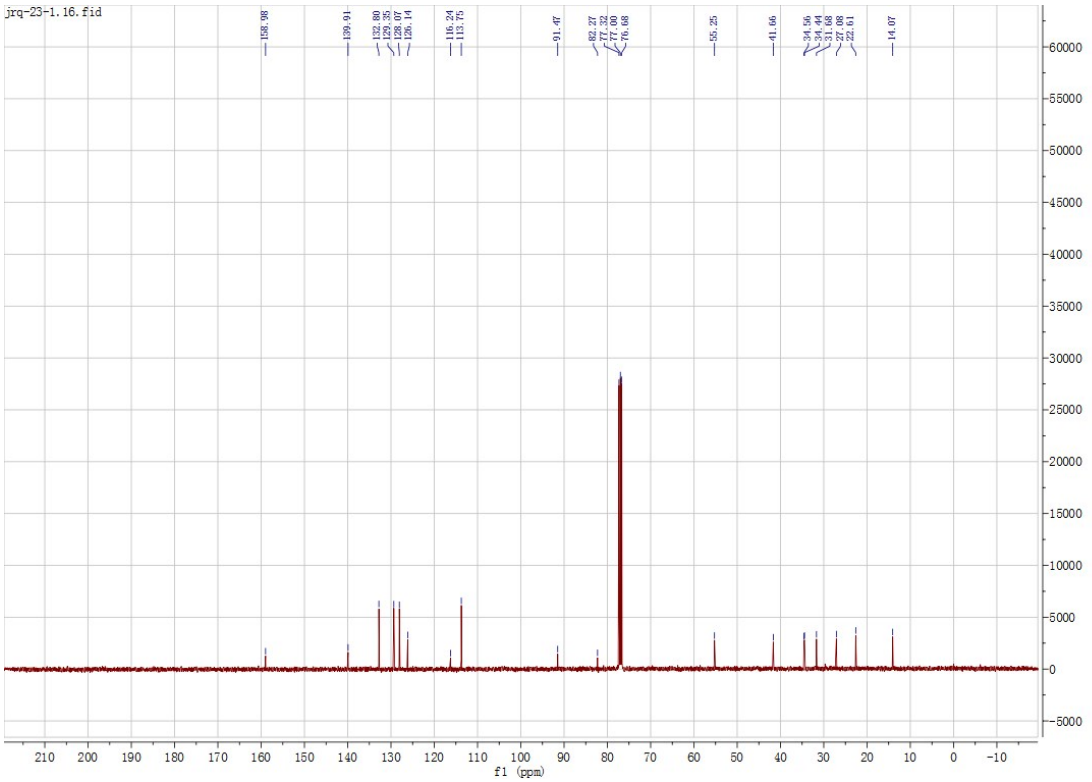
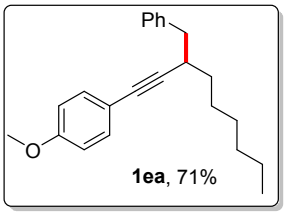
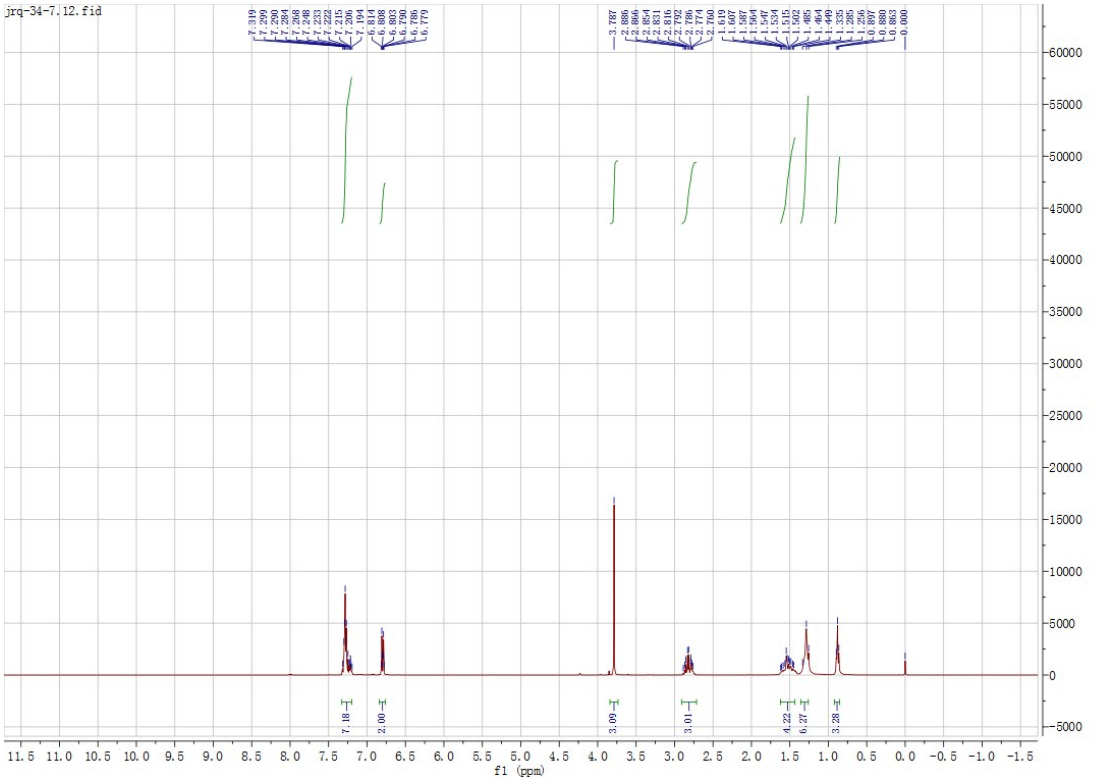
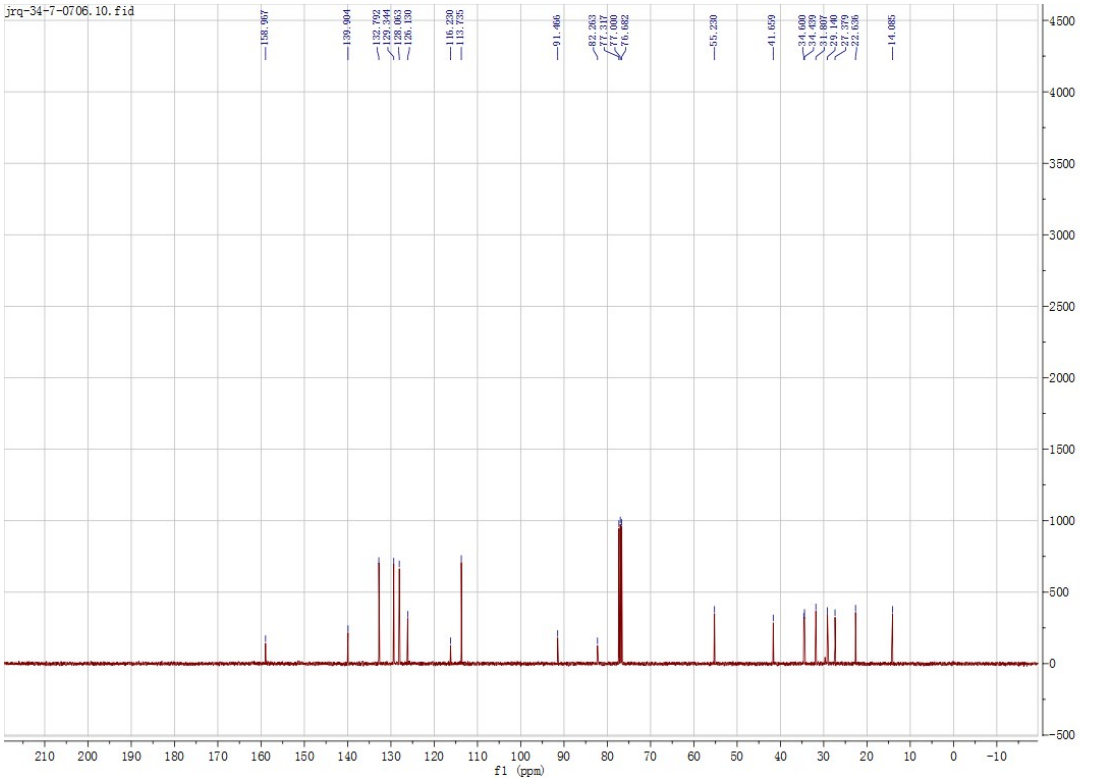
f1 (ppm)

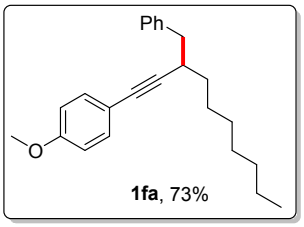

jrq-23-1.16.fid
f1 (ppm)



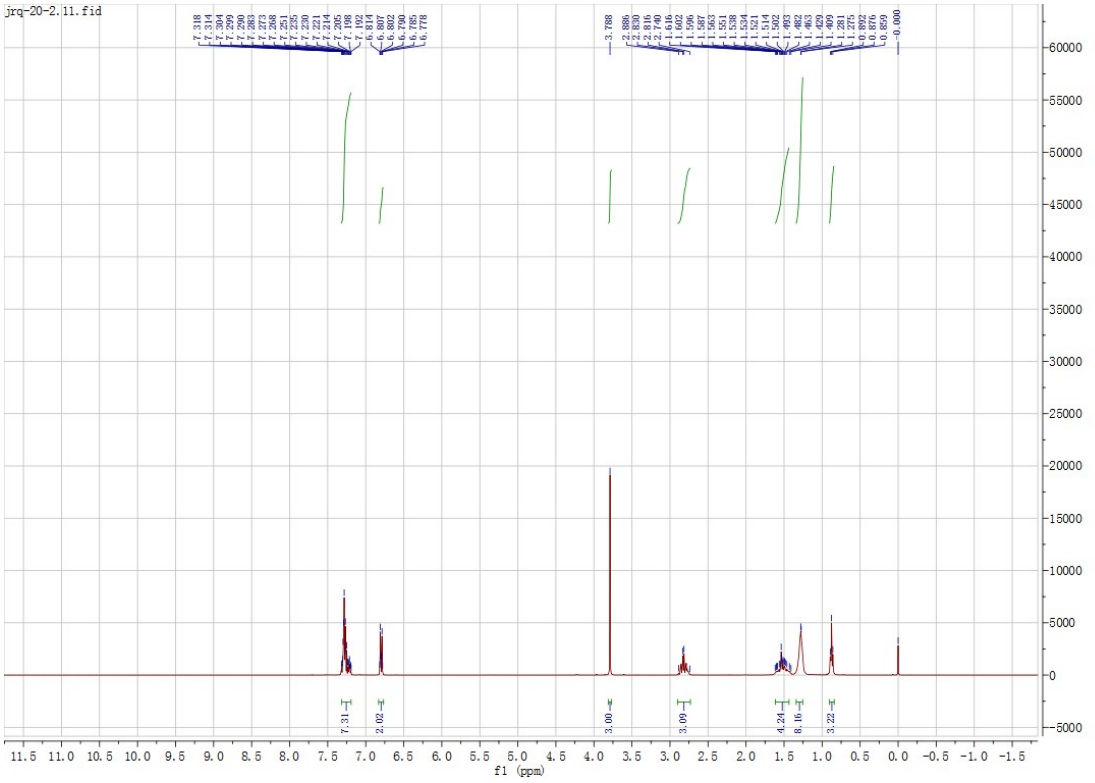
1ea, 71%

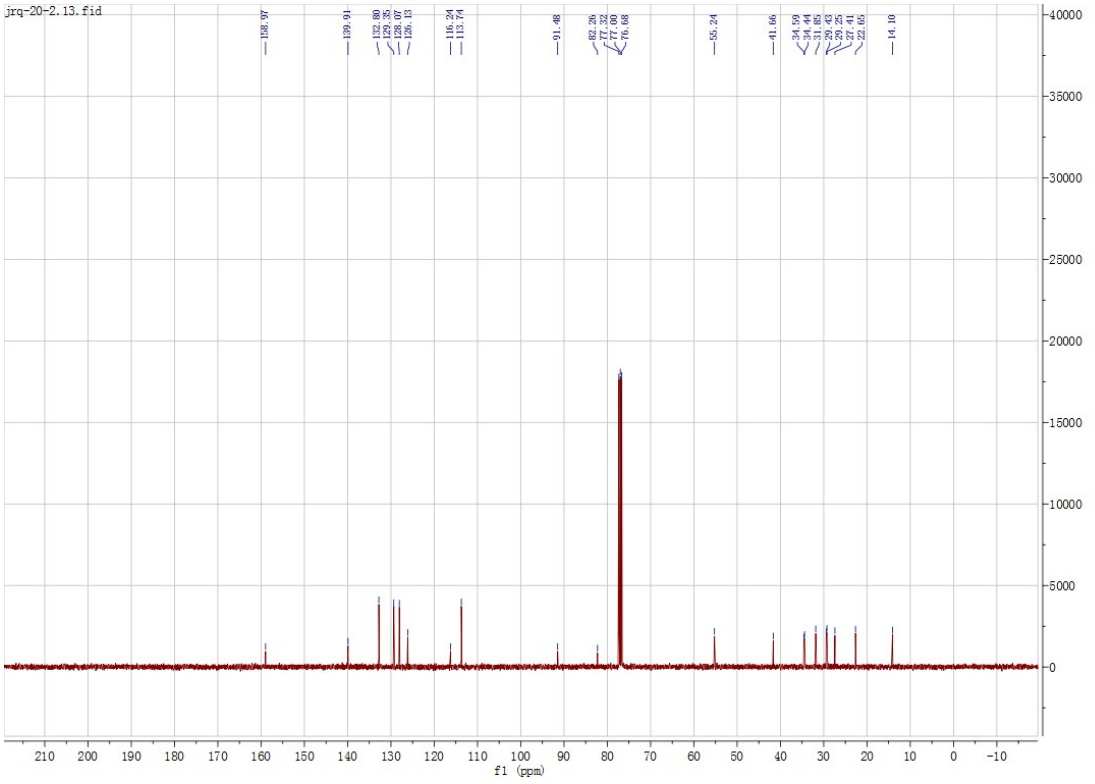


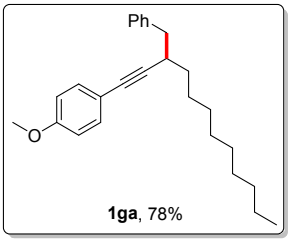




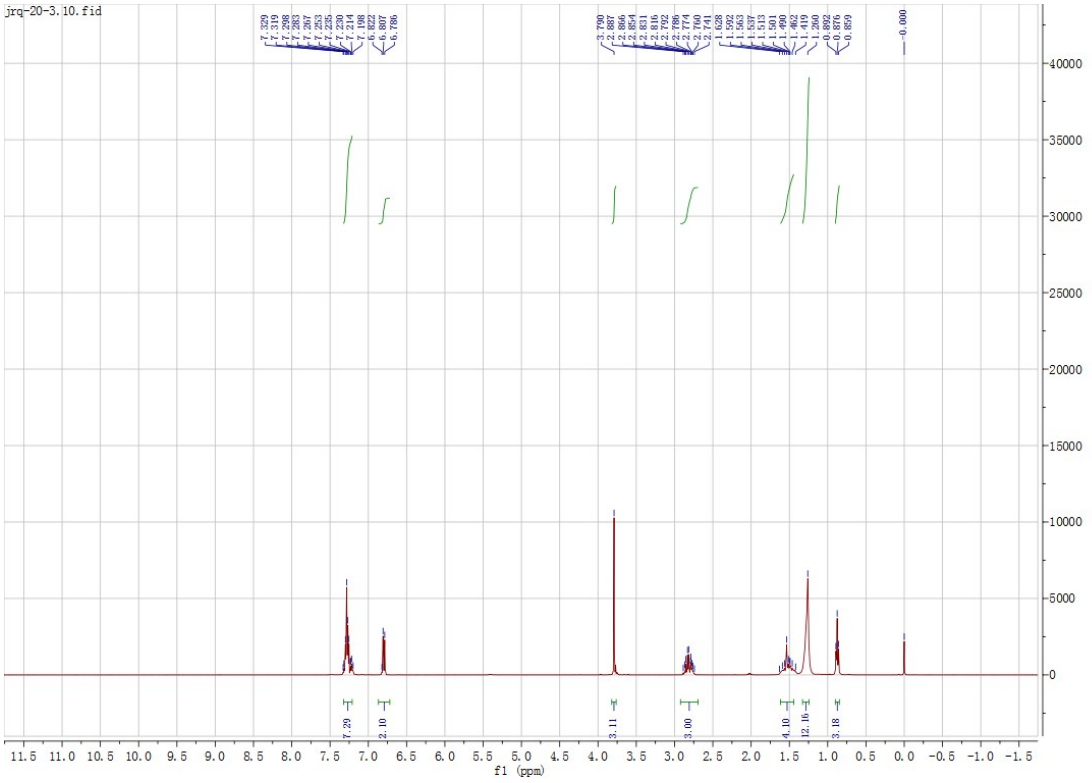
1fa, 73%

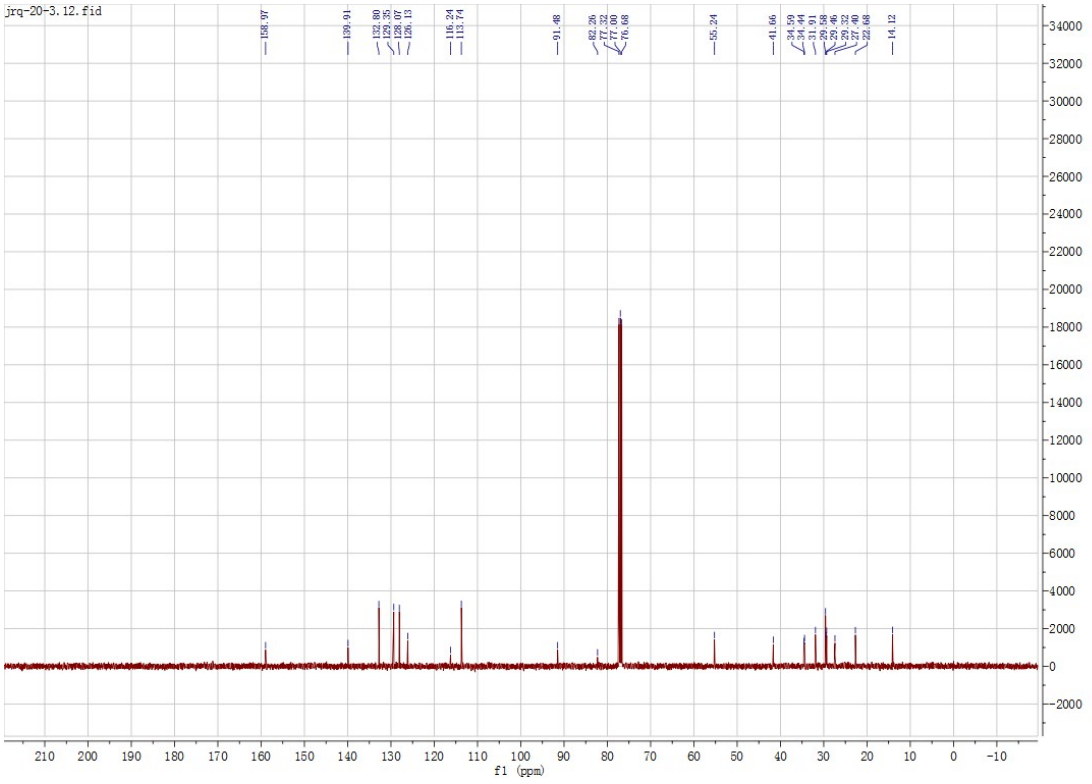


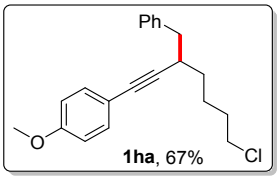




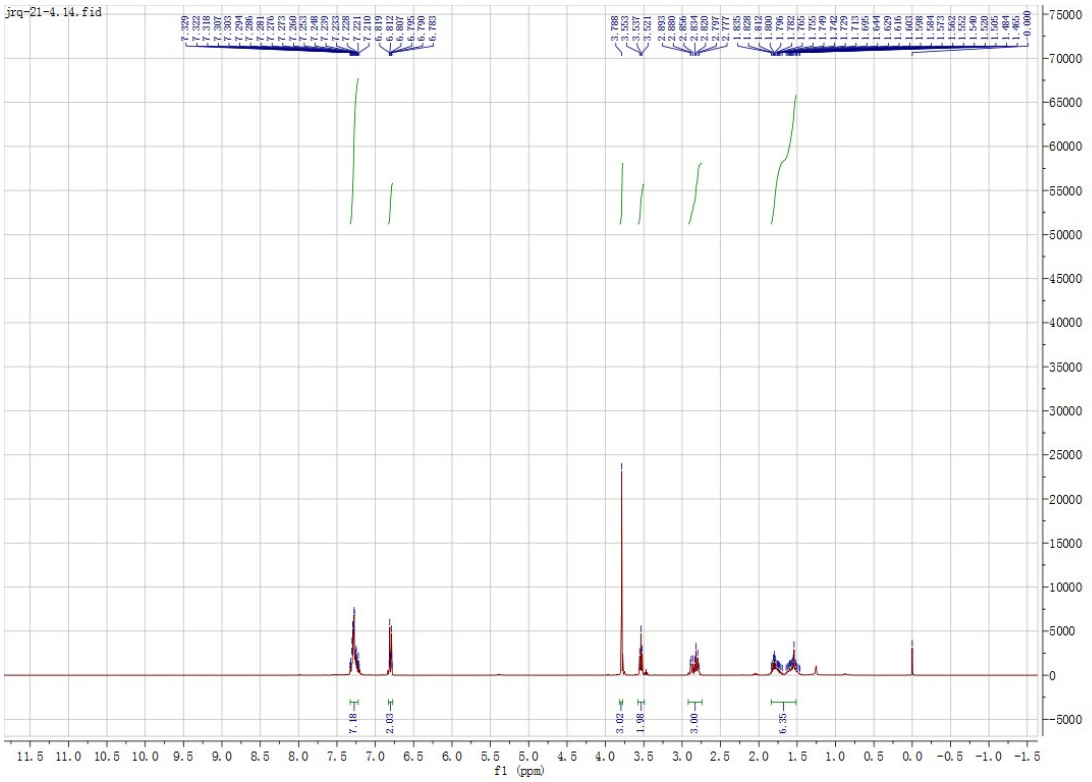
1ga, 78%

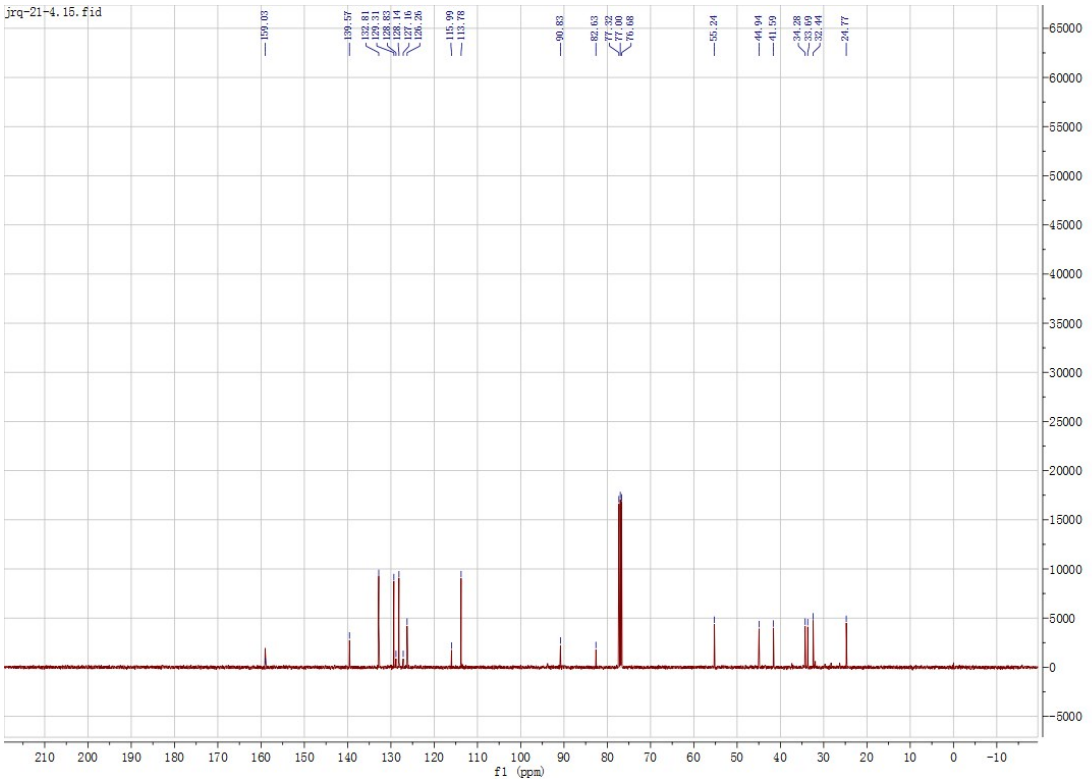


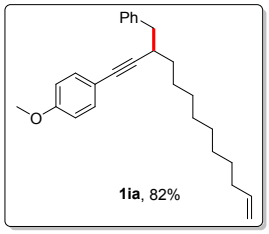




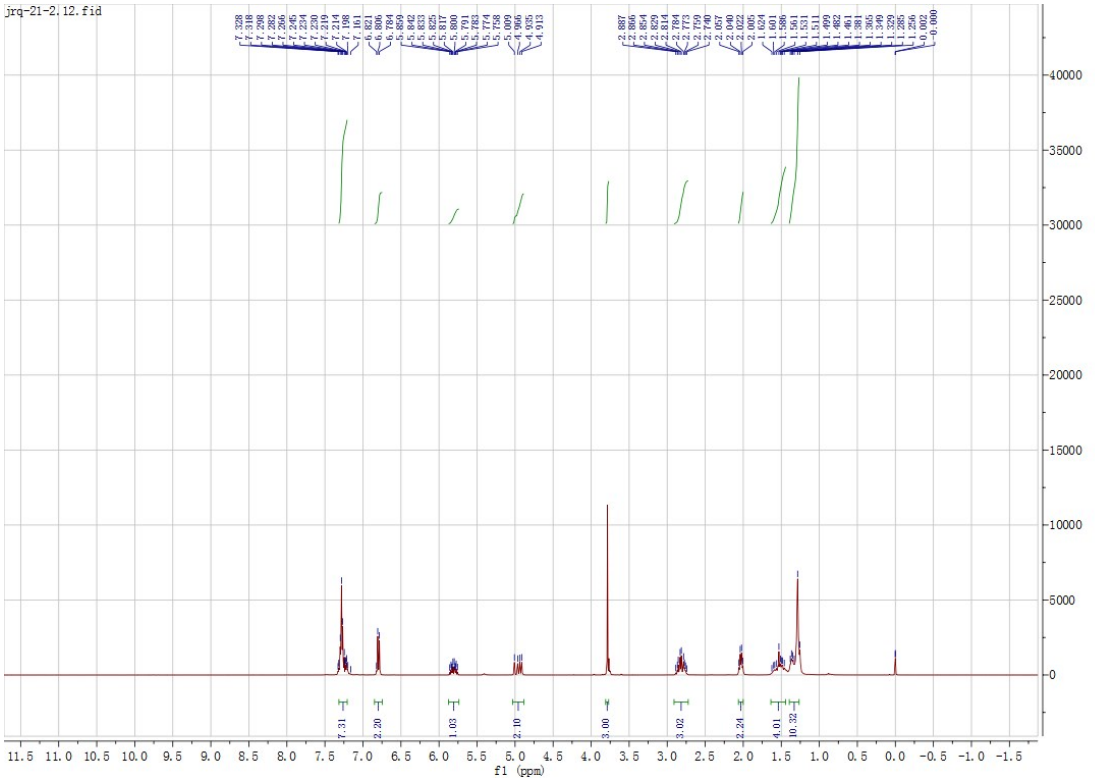
1ha, 67%

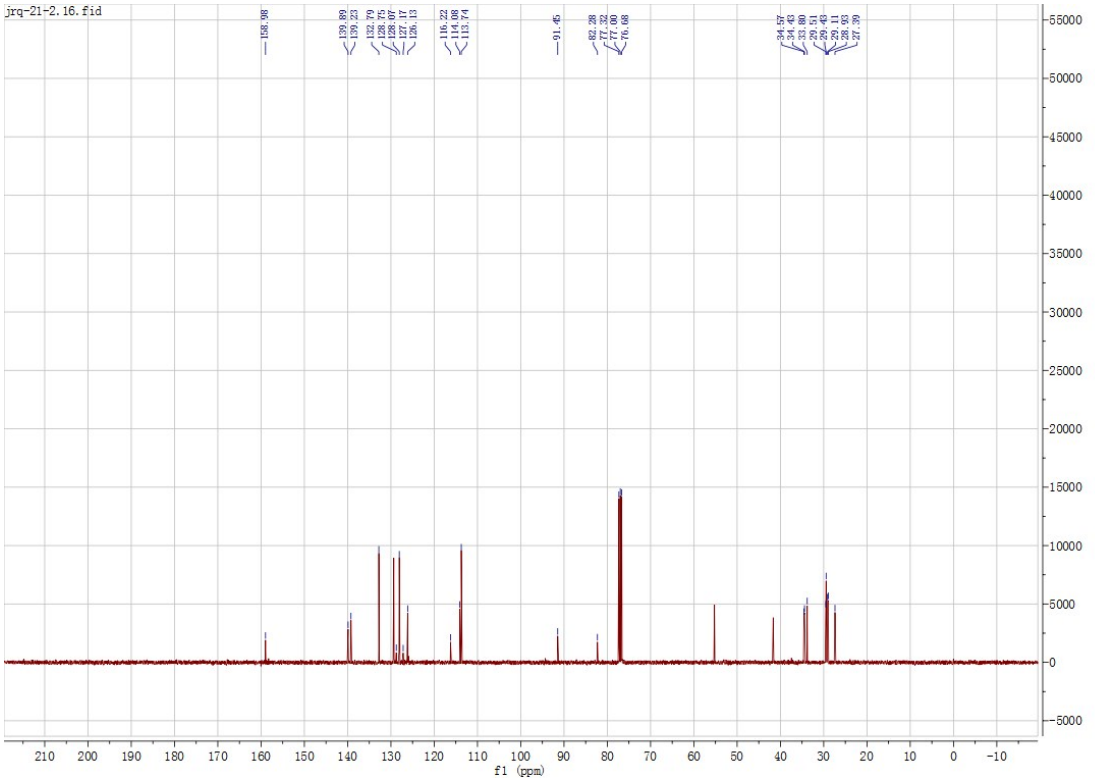


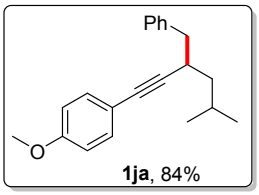




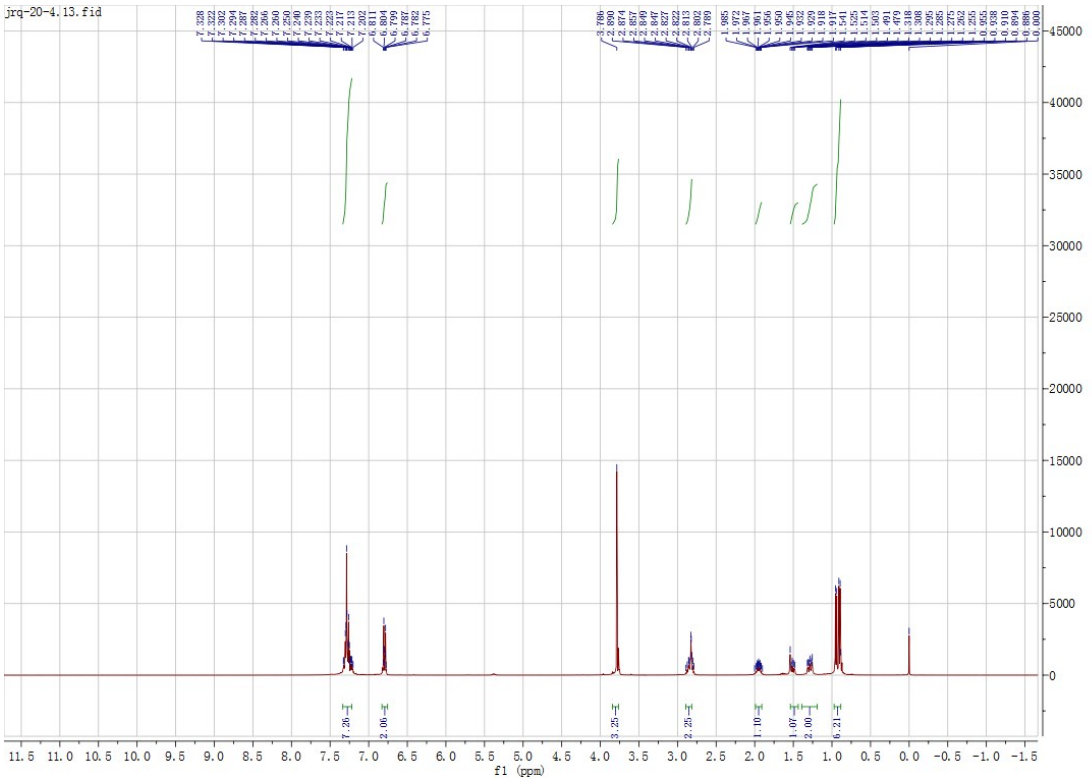
1ia, 82%

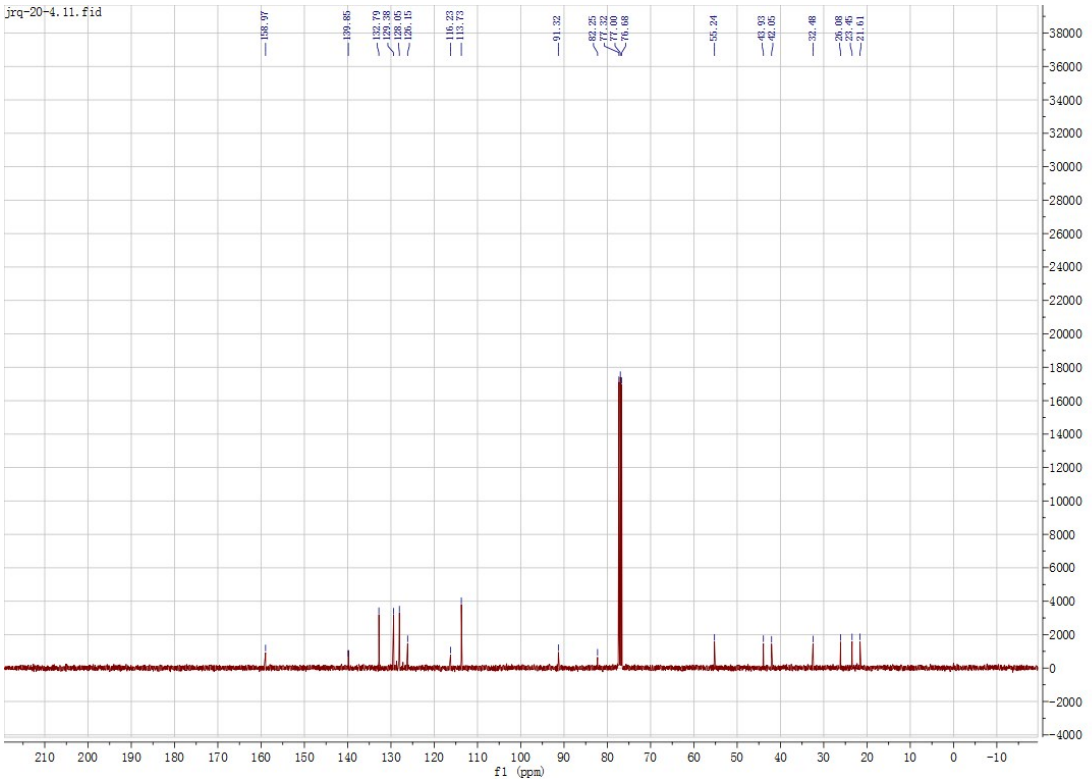


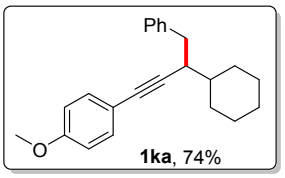




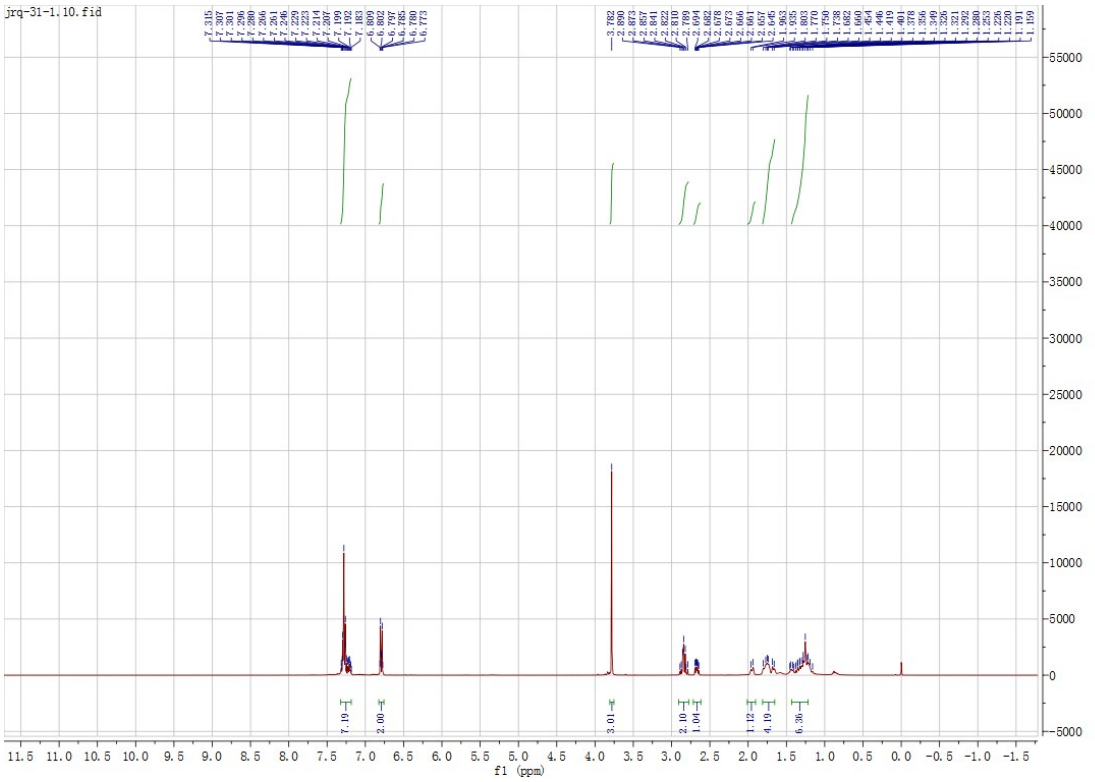
1ja, 84%

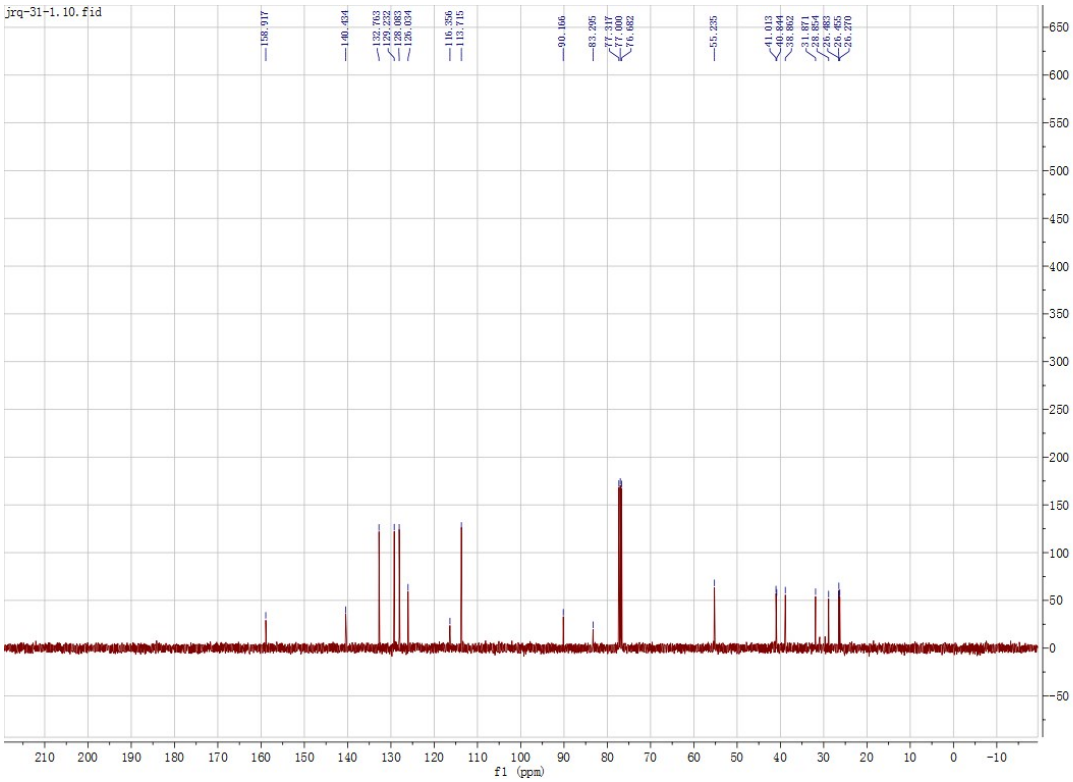


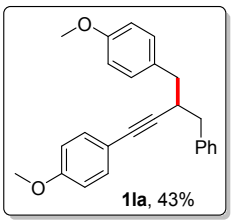




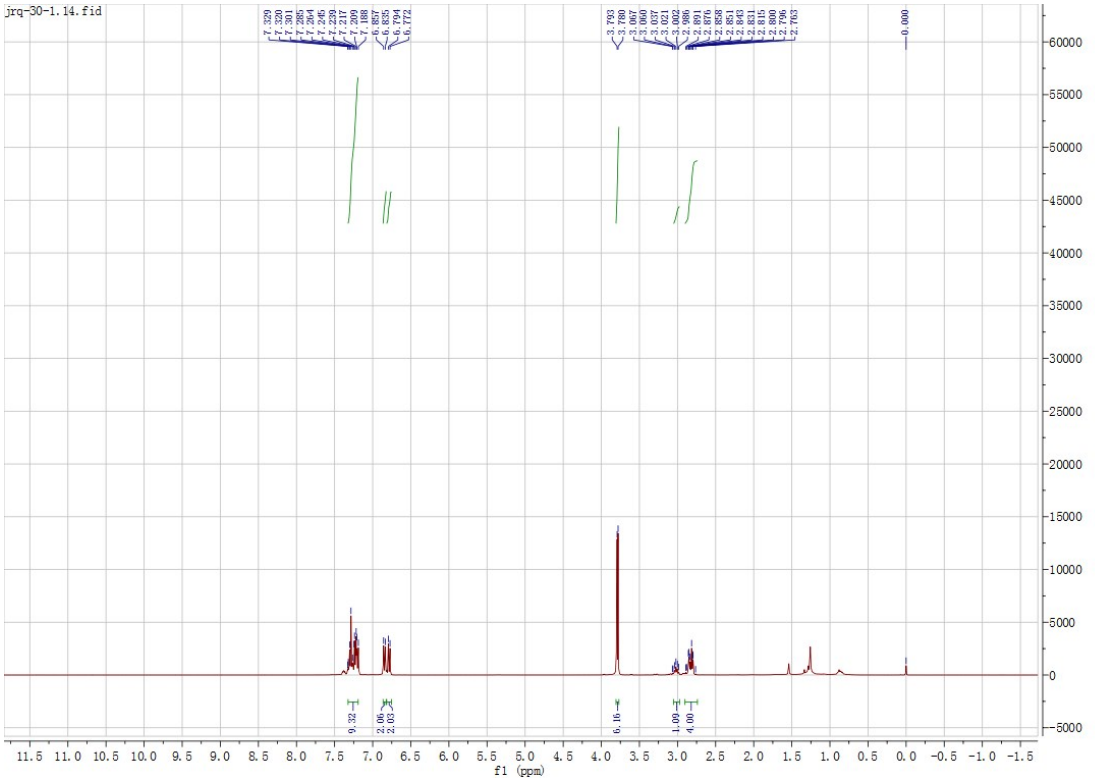
1ka, 74%

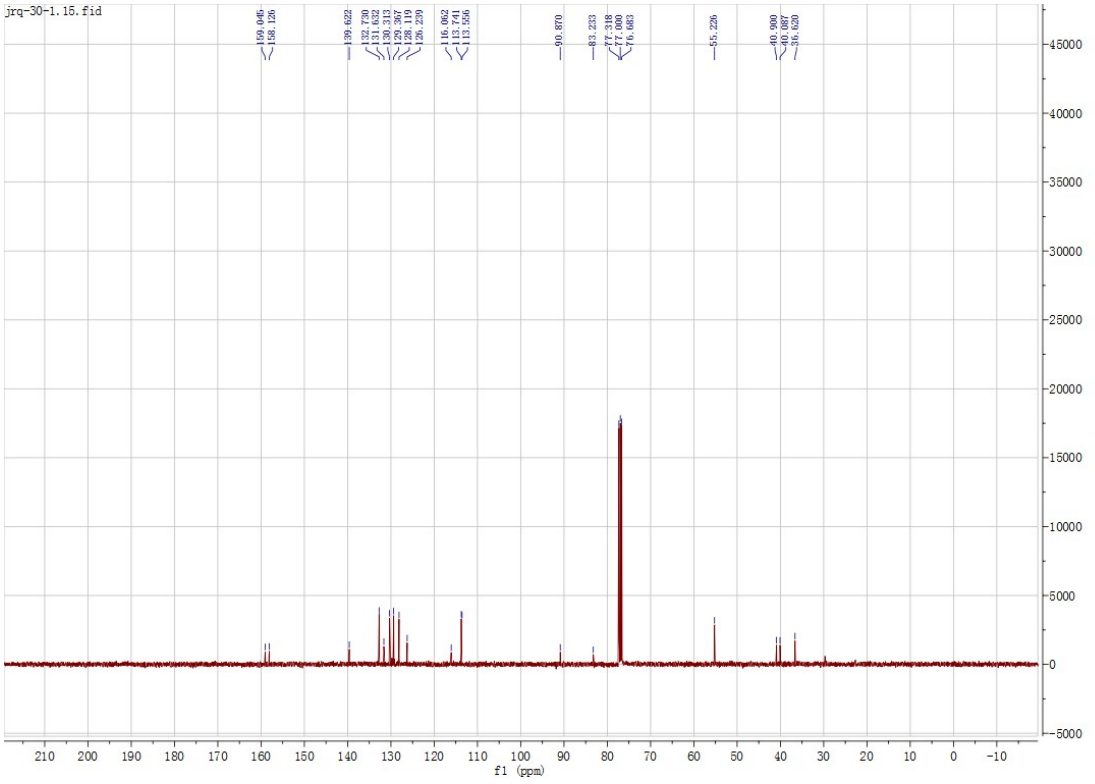


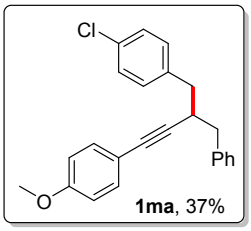




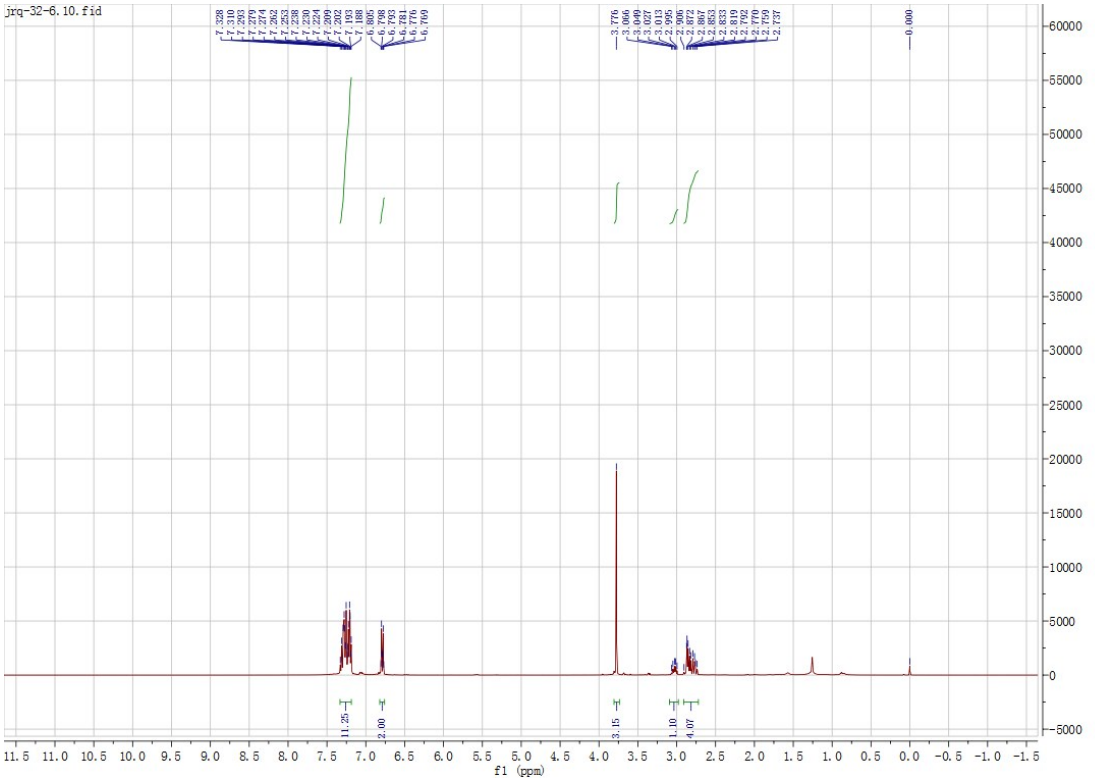
1la, 43%

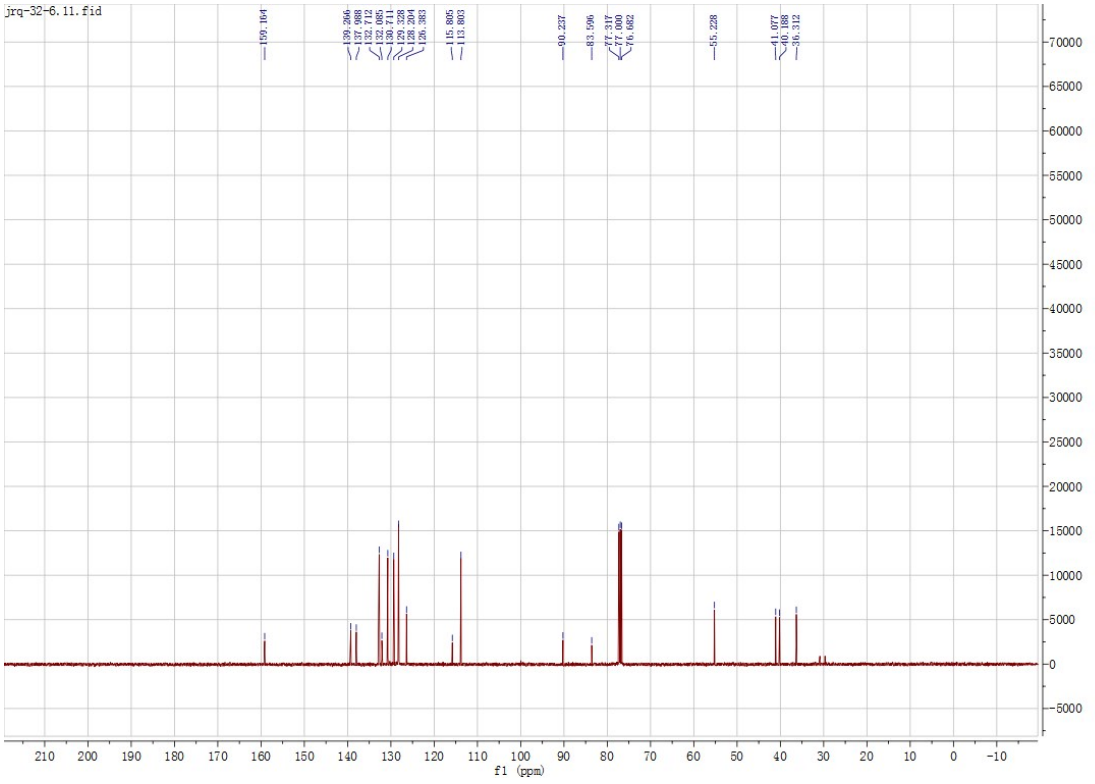


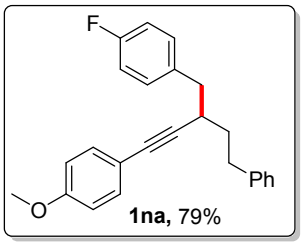




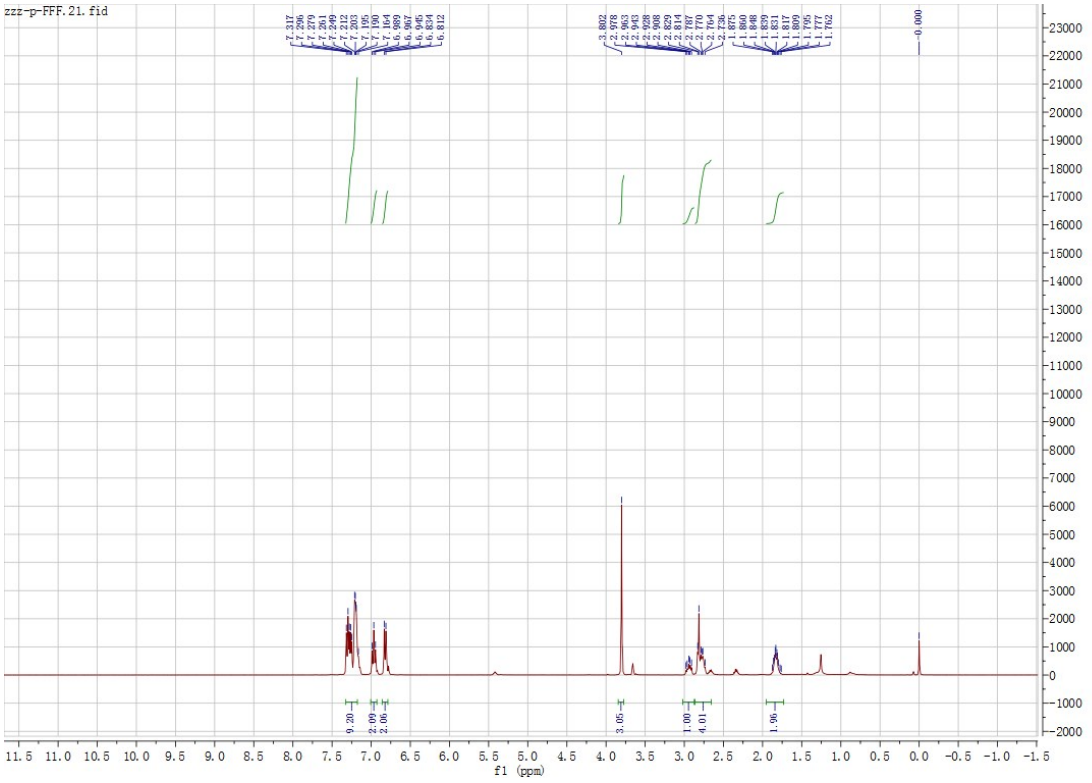
1ma, 37%

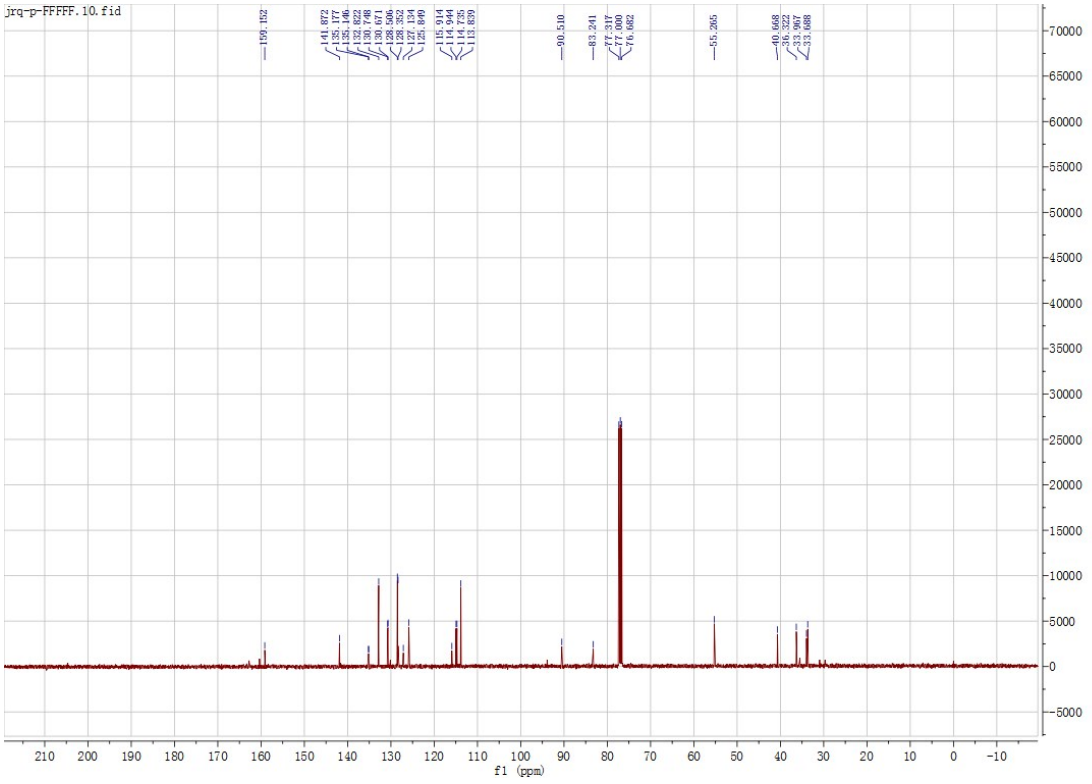


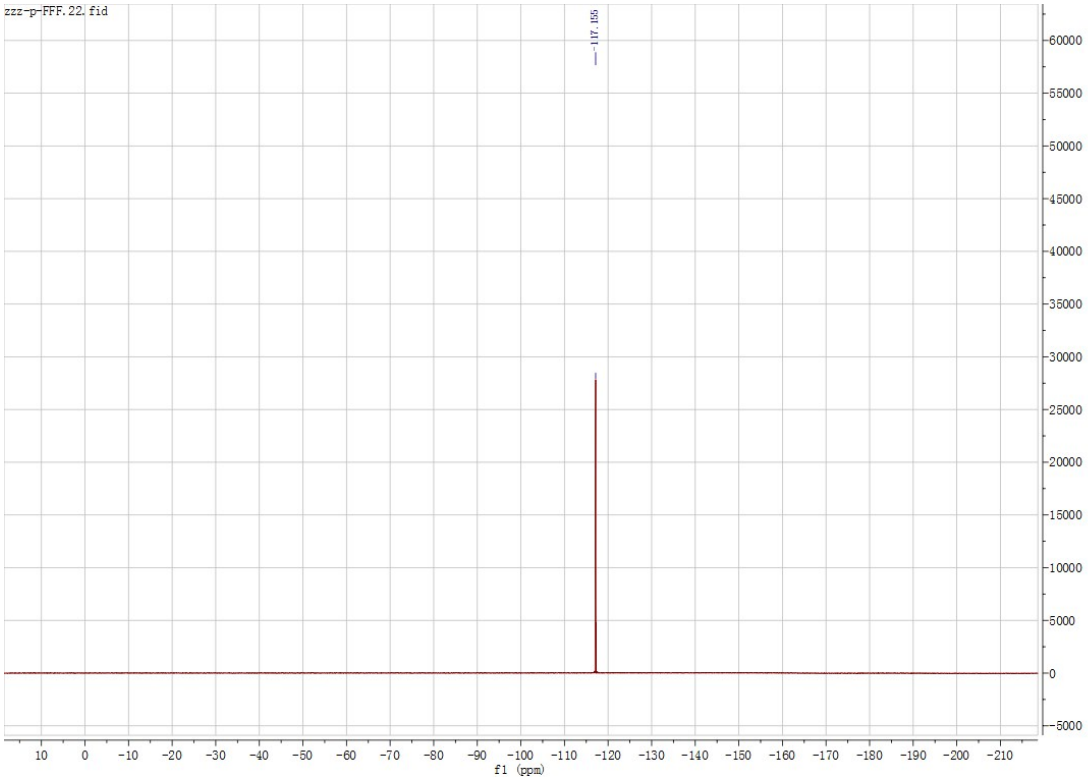


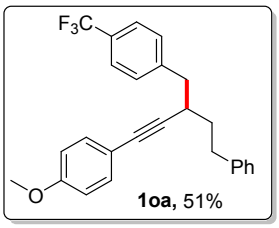


1na, 79%

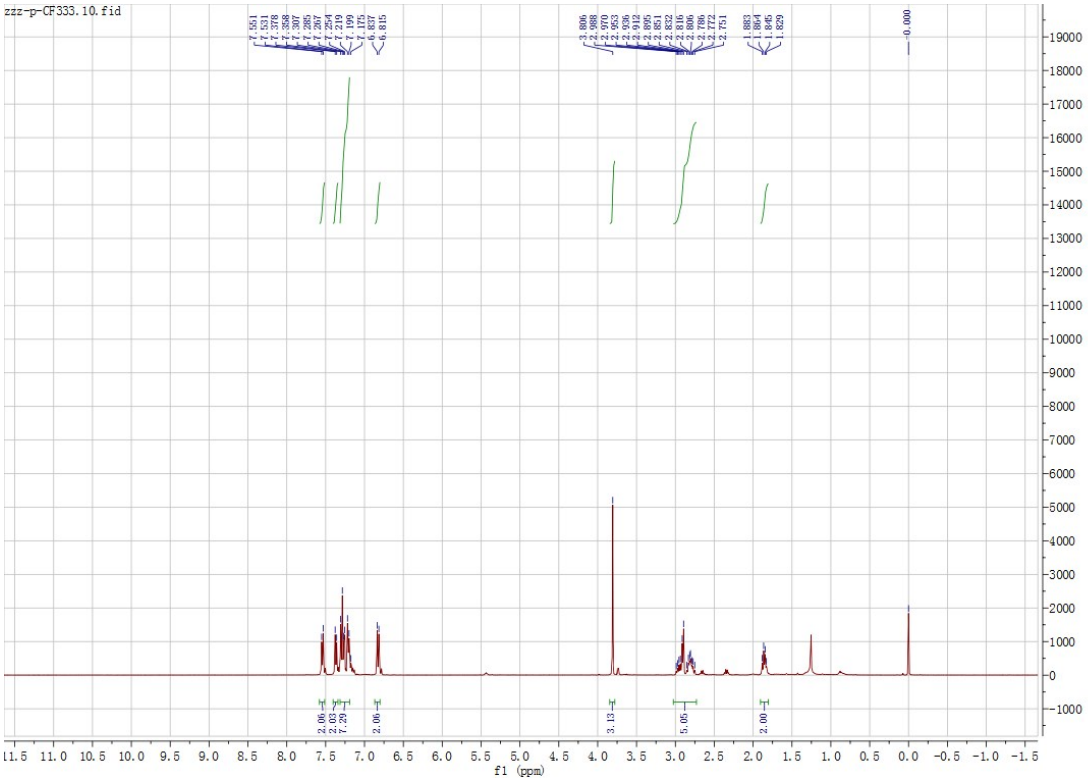


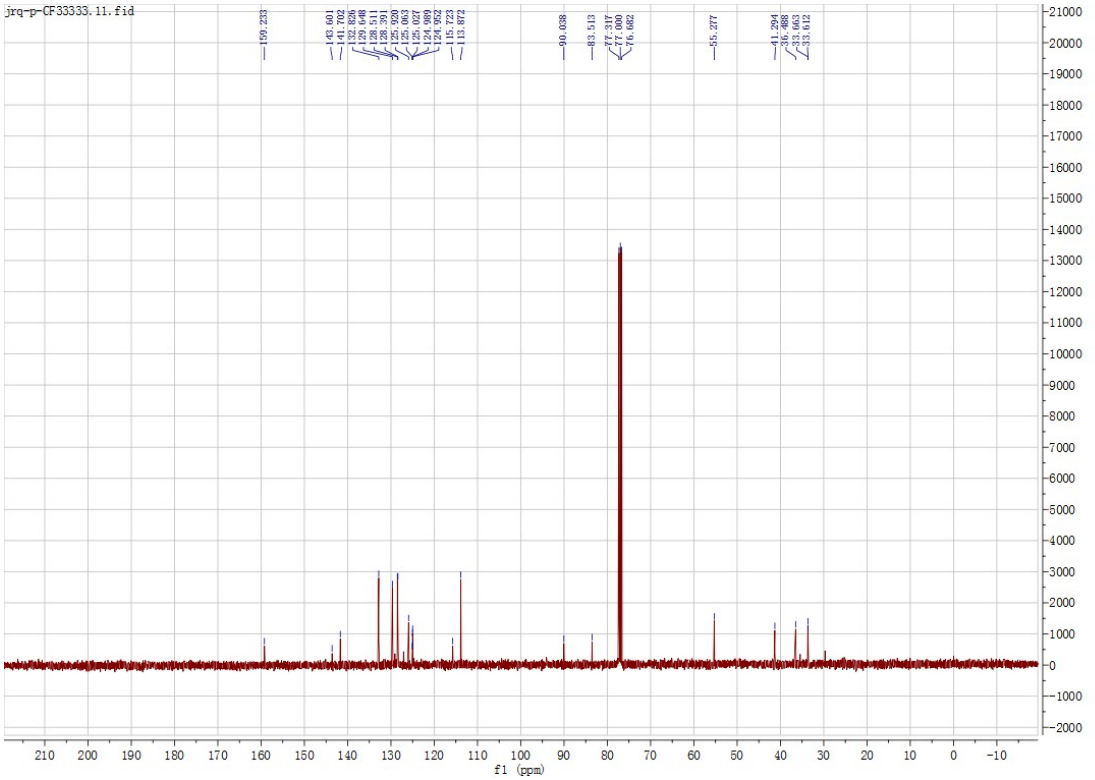


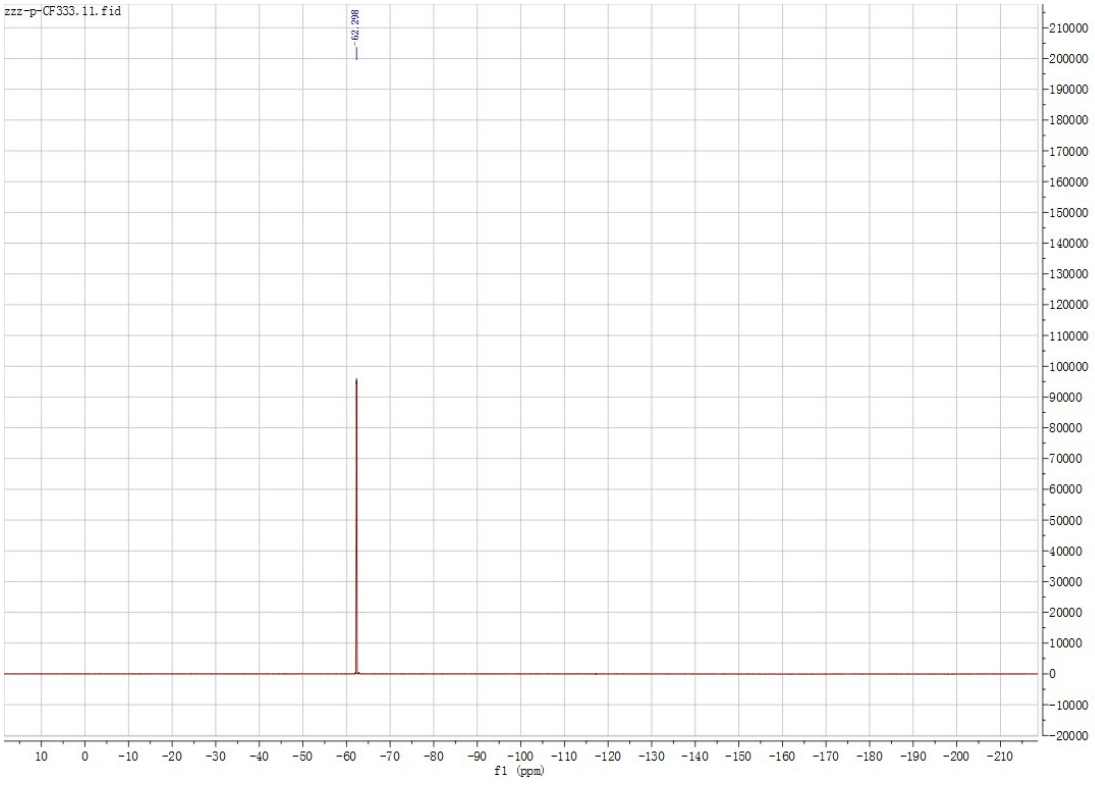


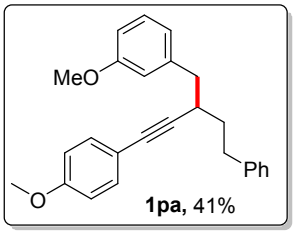


1oa, 51%

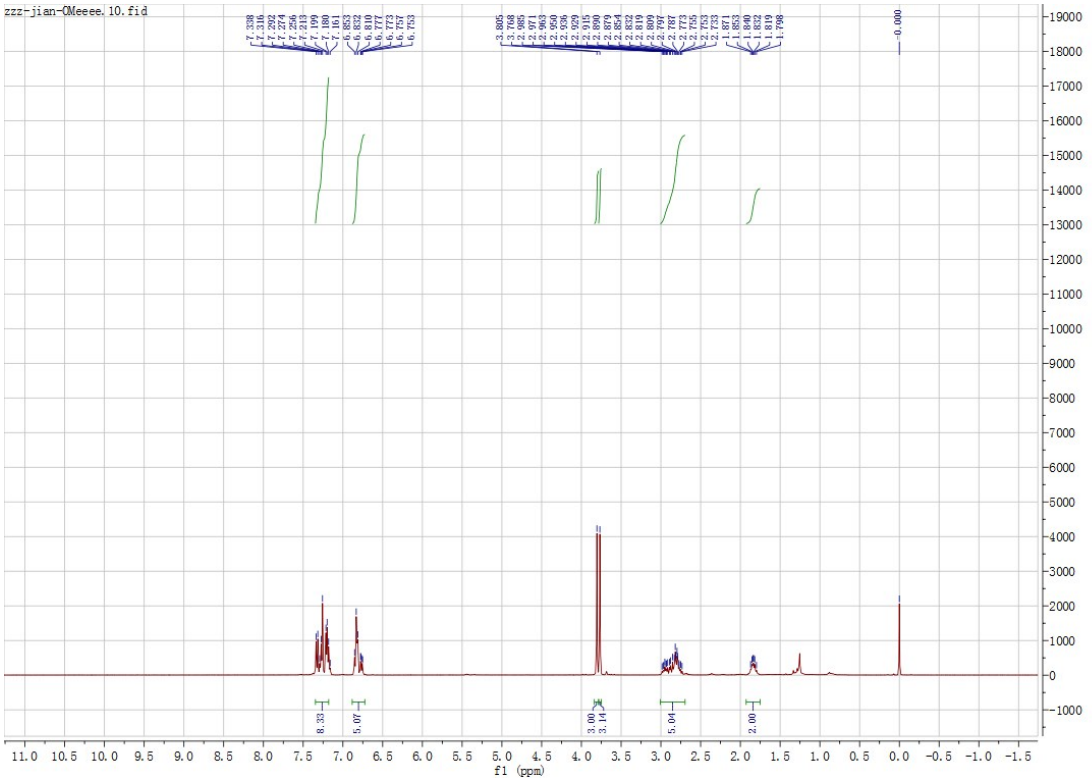


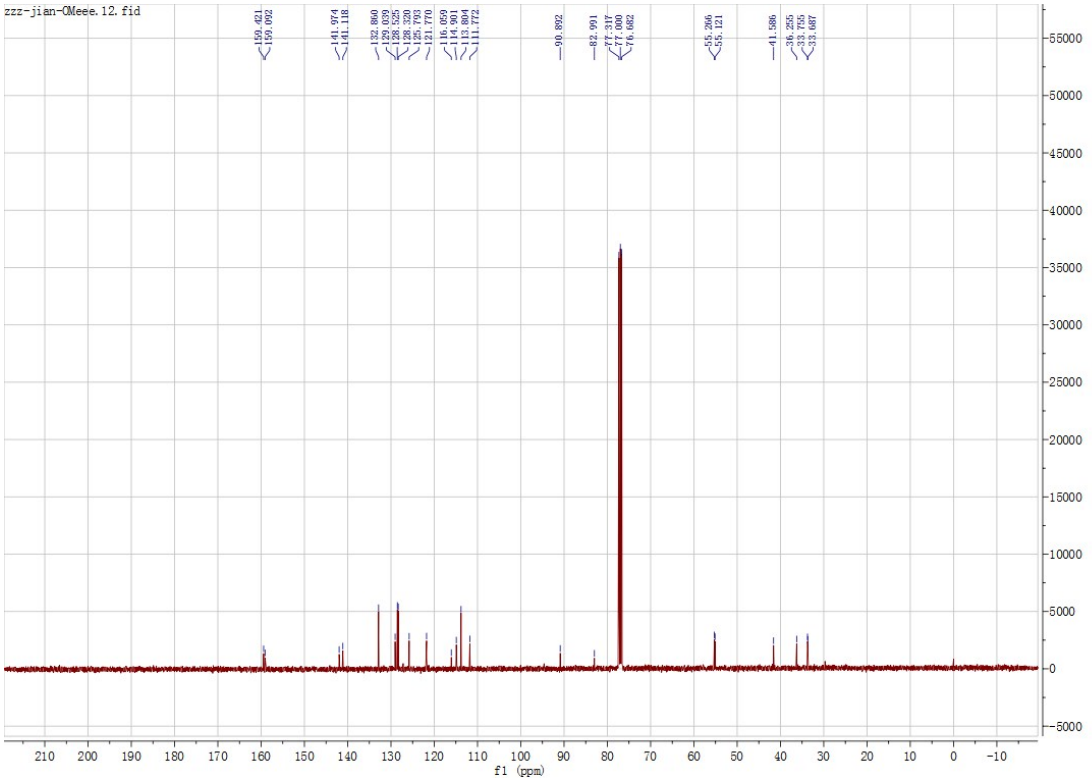

jrq-p-CF33333.11.fid
159.233
143.601
141.702
133.895
129.648
128.511
128.391
125.903
125.669
125.027
124.989
124.952
115.772
113.872
90.638
83.513
77.317
77.000
76.682
55.277
41.294
34.888
33.663
33.612
f1 (ppm)

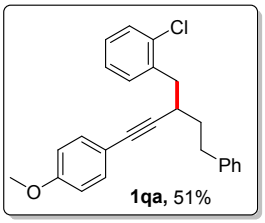

zzz-p-CF333.11.fid
-62.298
f1 (ppm)


MeO
Ph
O

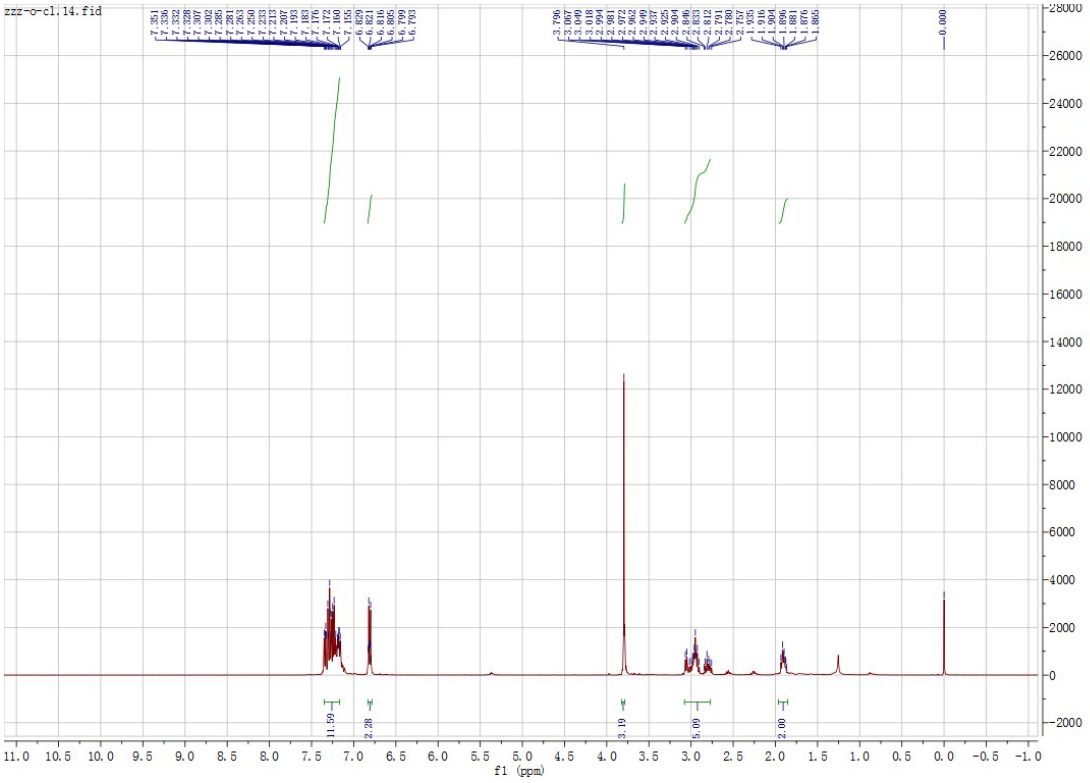
1pa, 41%

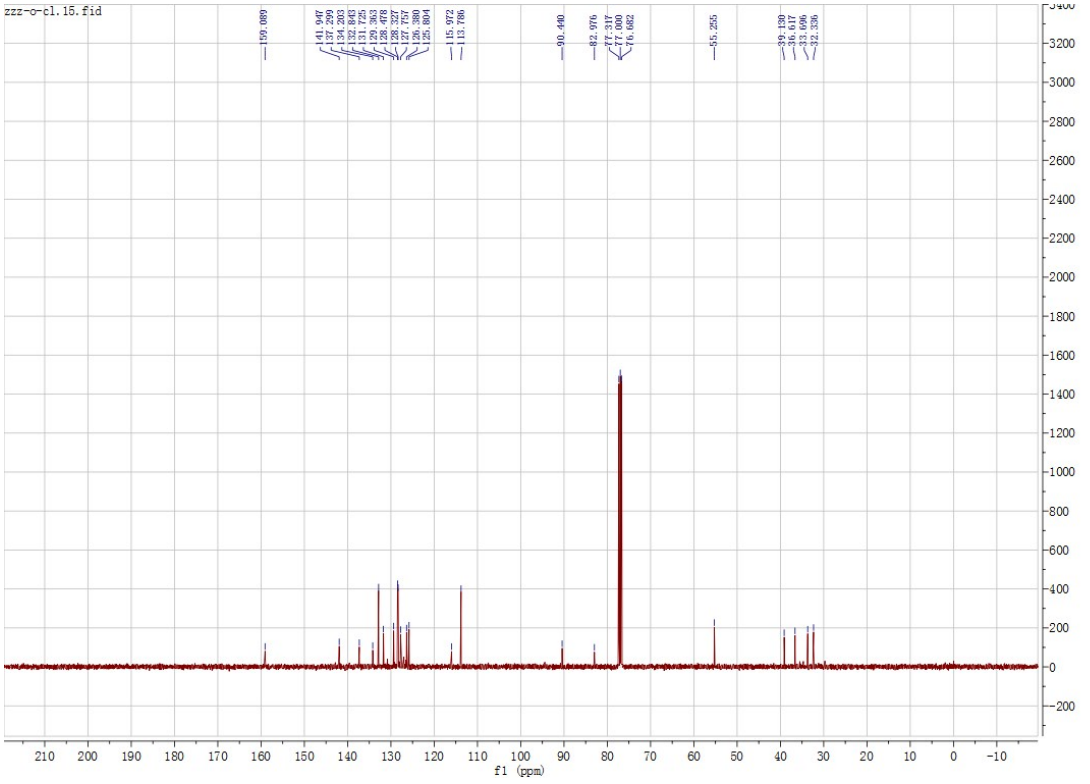

zzz-jian-OMeeee.10.fid
f1 (ppm)


zzz-jian-OMeee.12.fid
f1 (ppm)

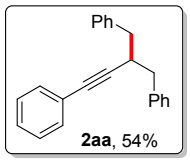


1qa, 51%

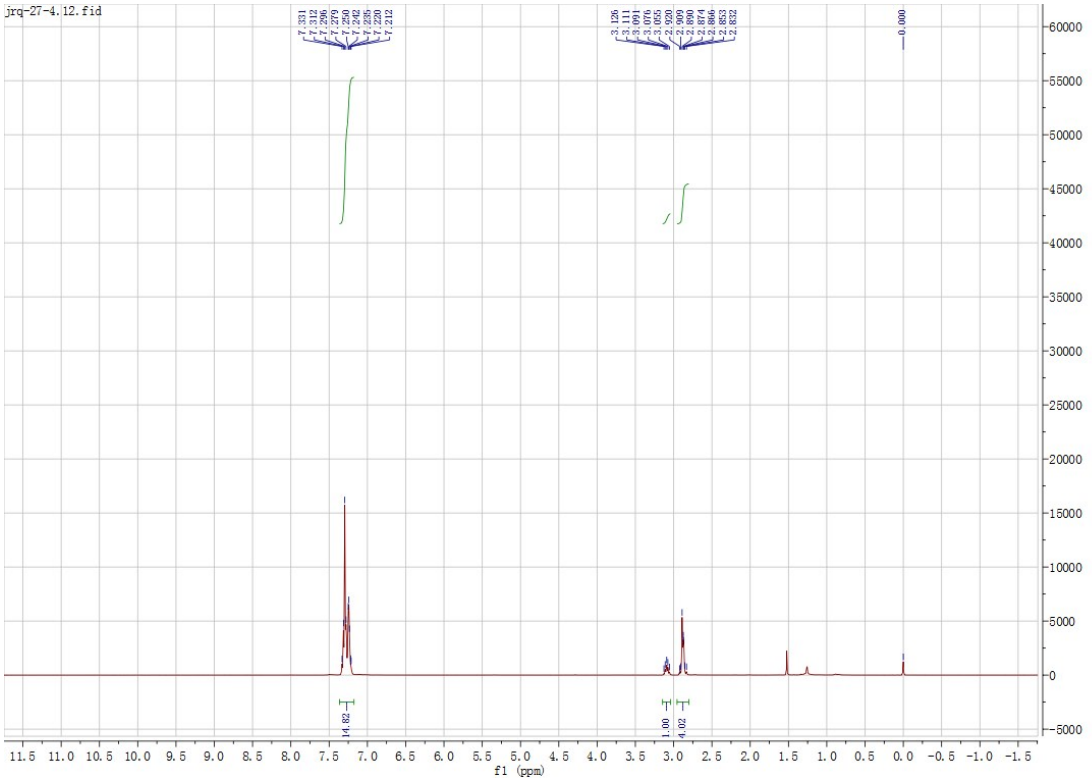


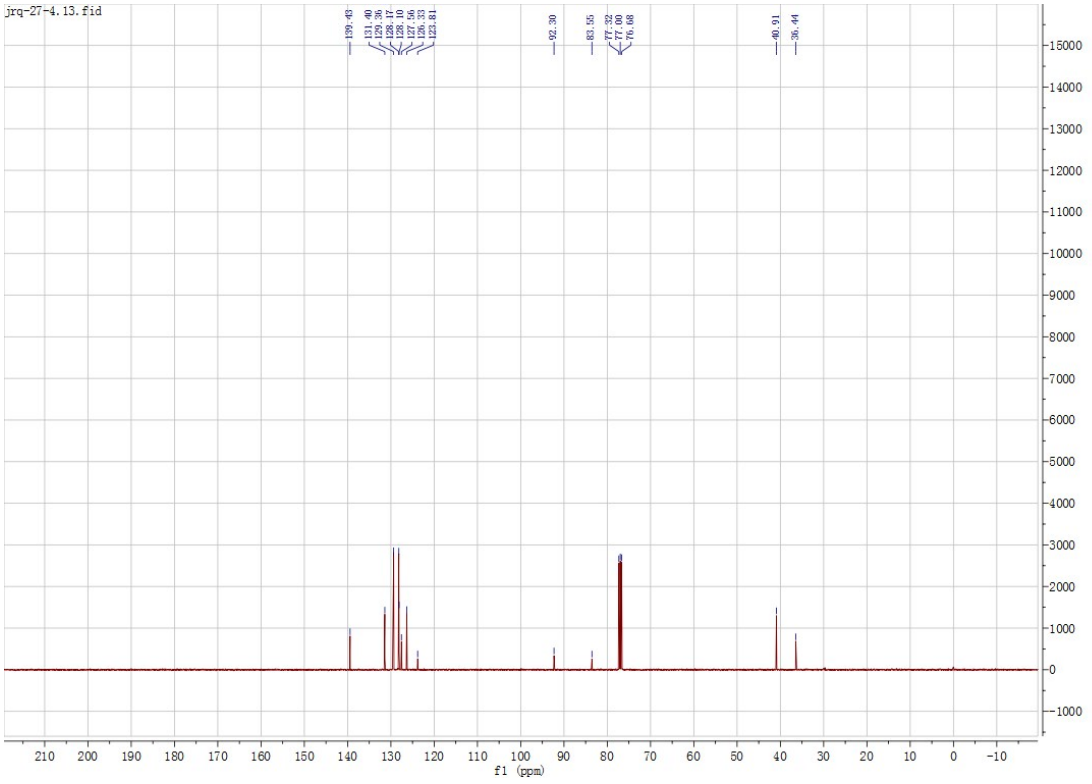


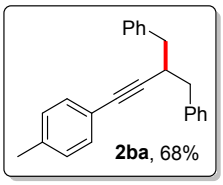
10. ^{1}H NMR and ^{13}C NMR Spectra of the Products 2aa-2la, 3aa:



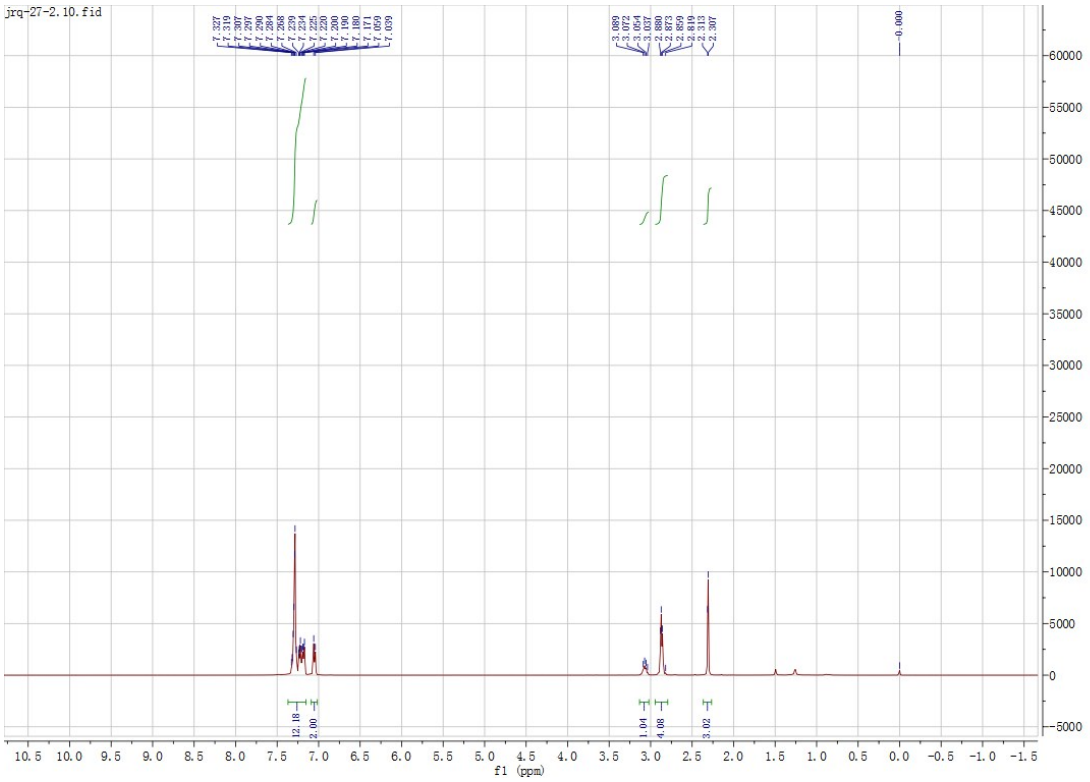
2aa, 54%

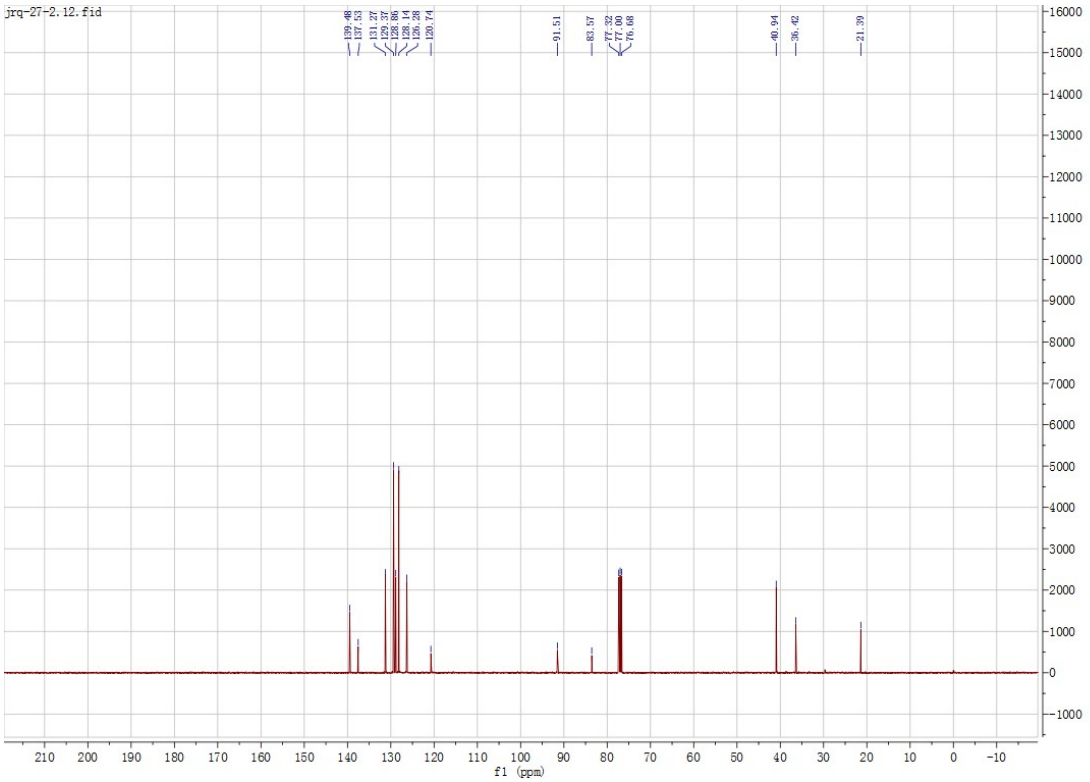


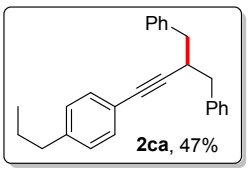




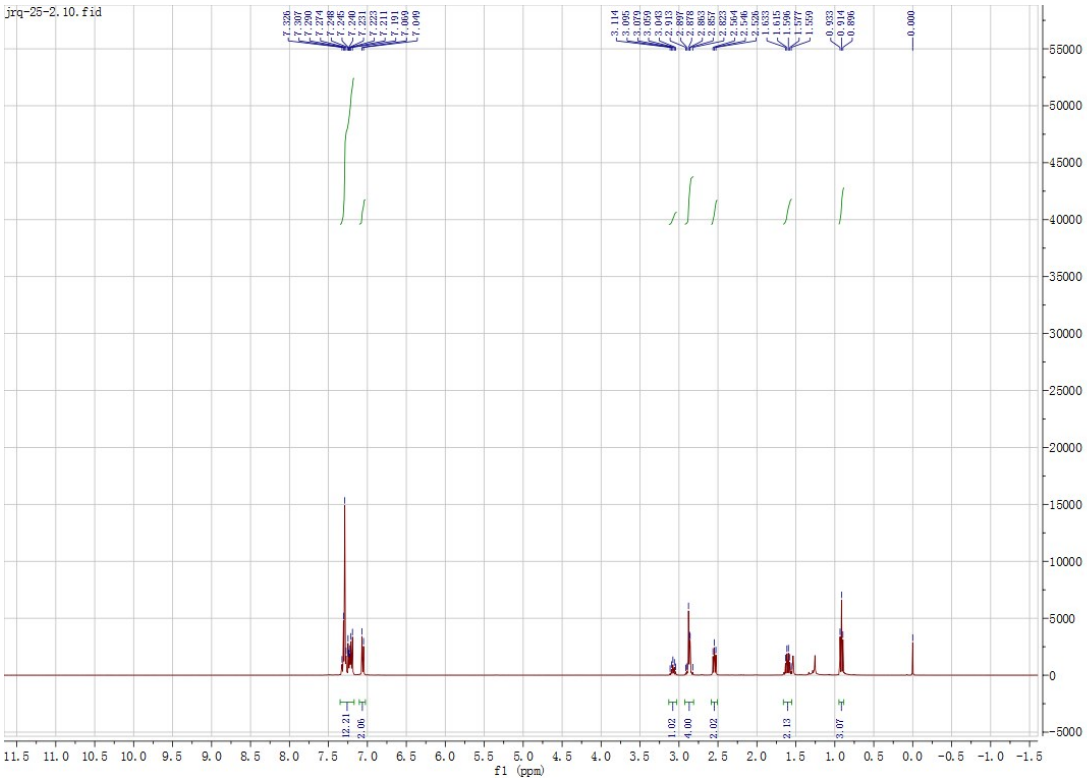
2ba, 68%

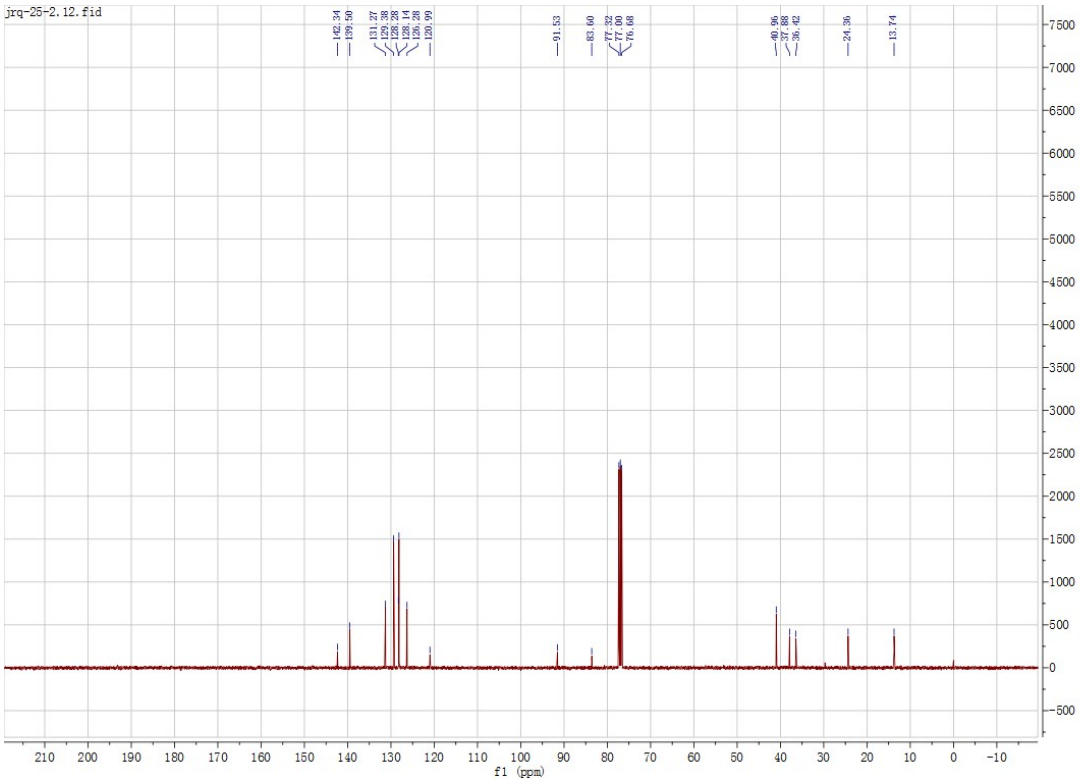


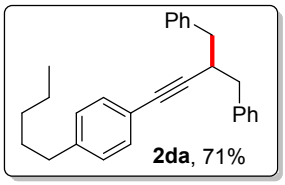




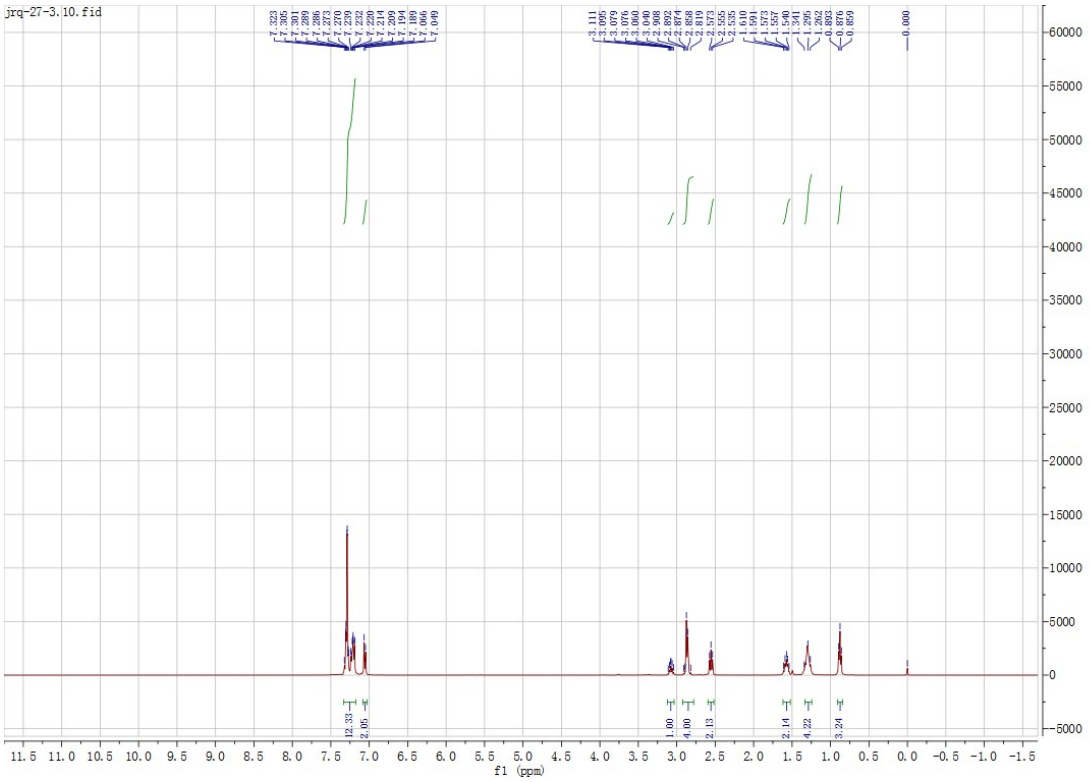
2ca, 47%

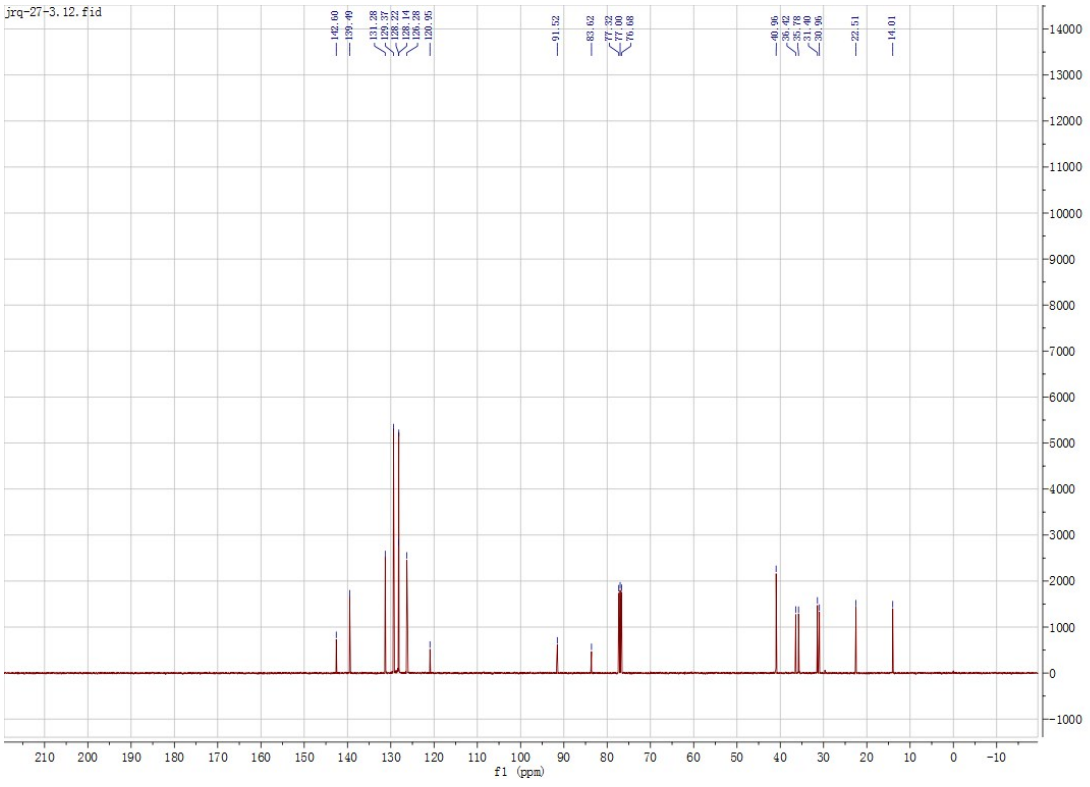


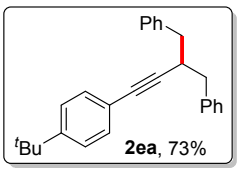




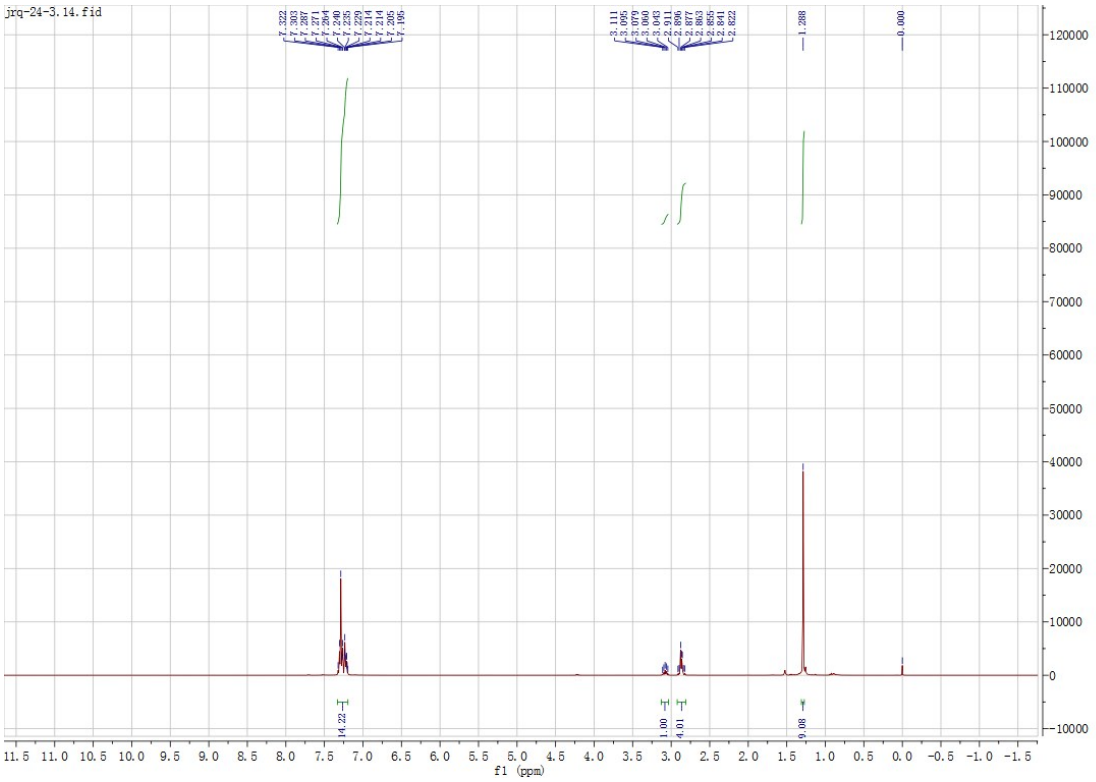
2da, 71%

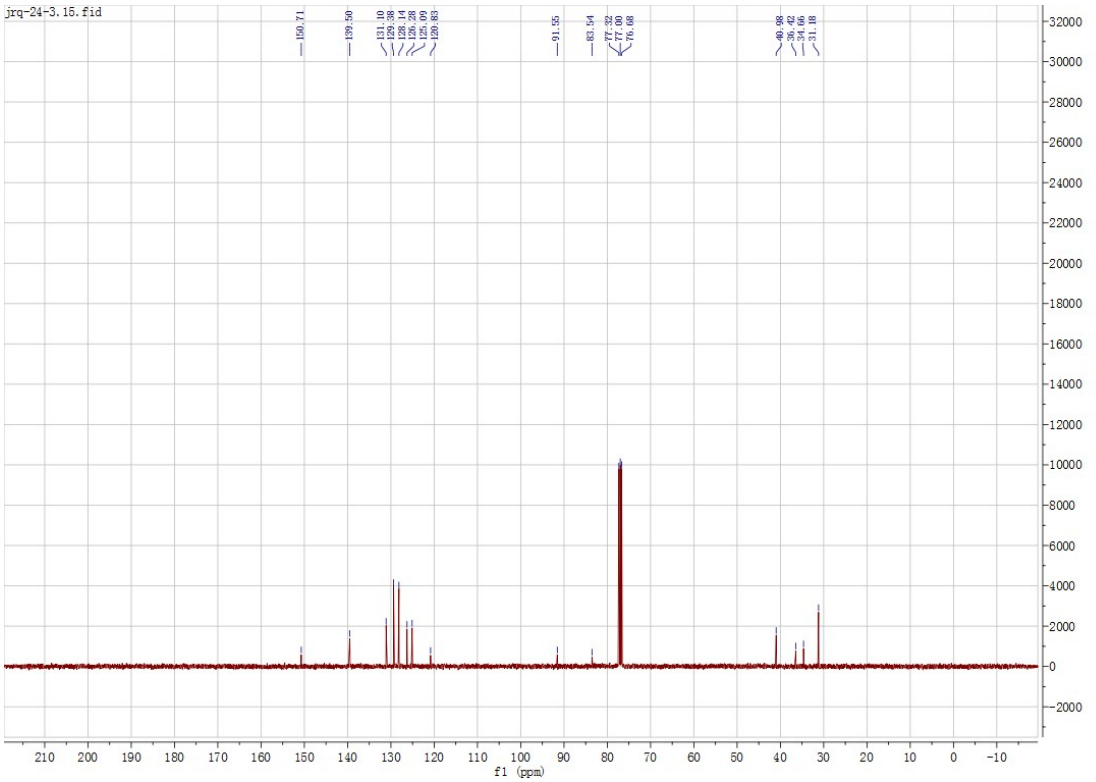


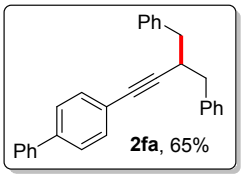




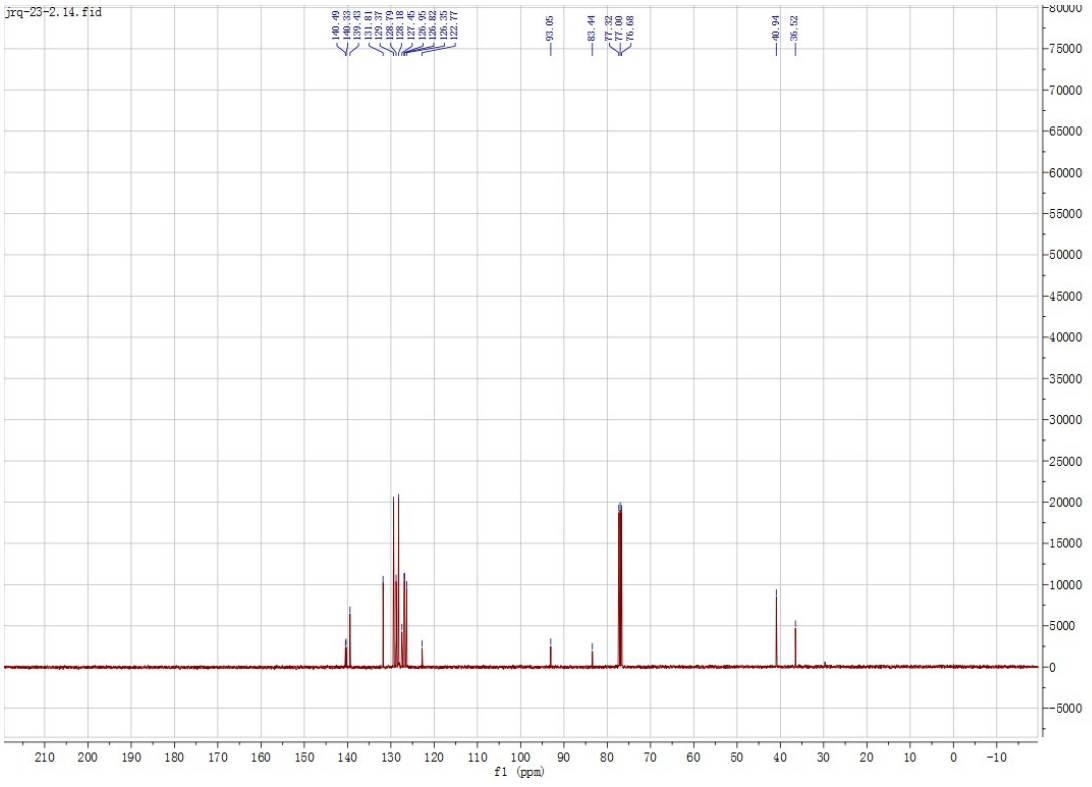
2ea, 73%

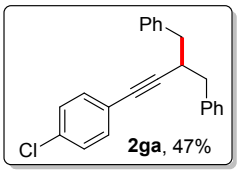


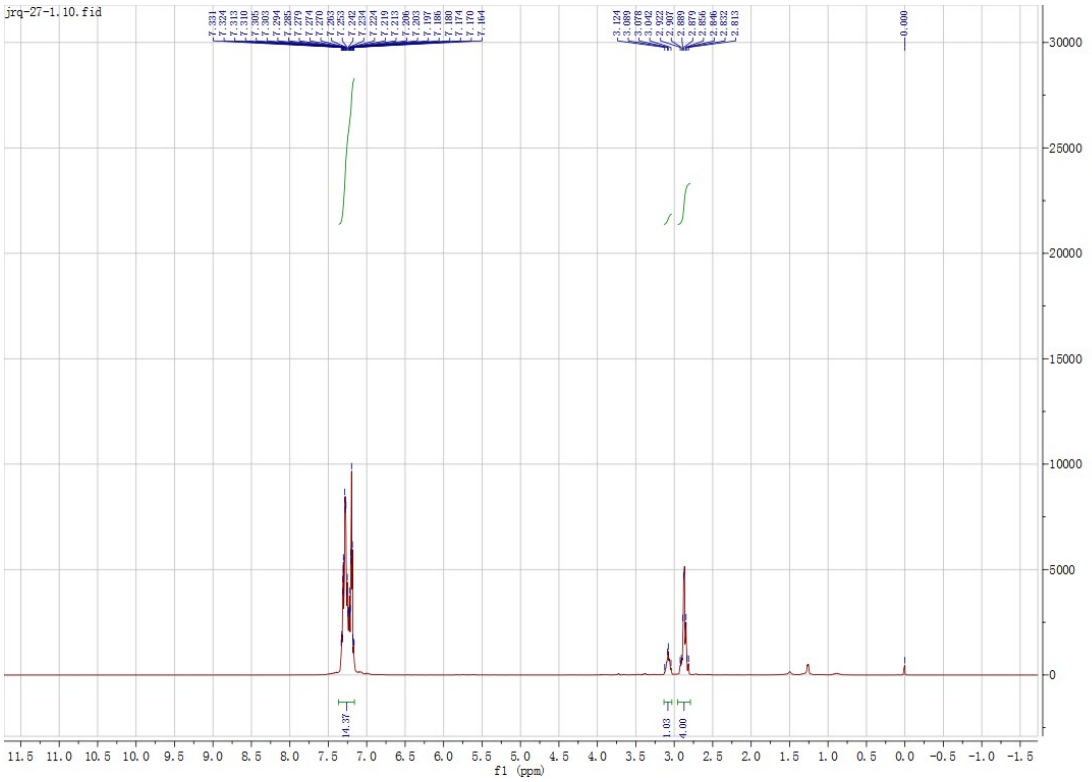


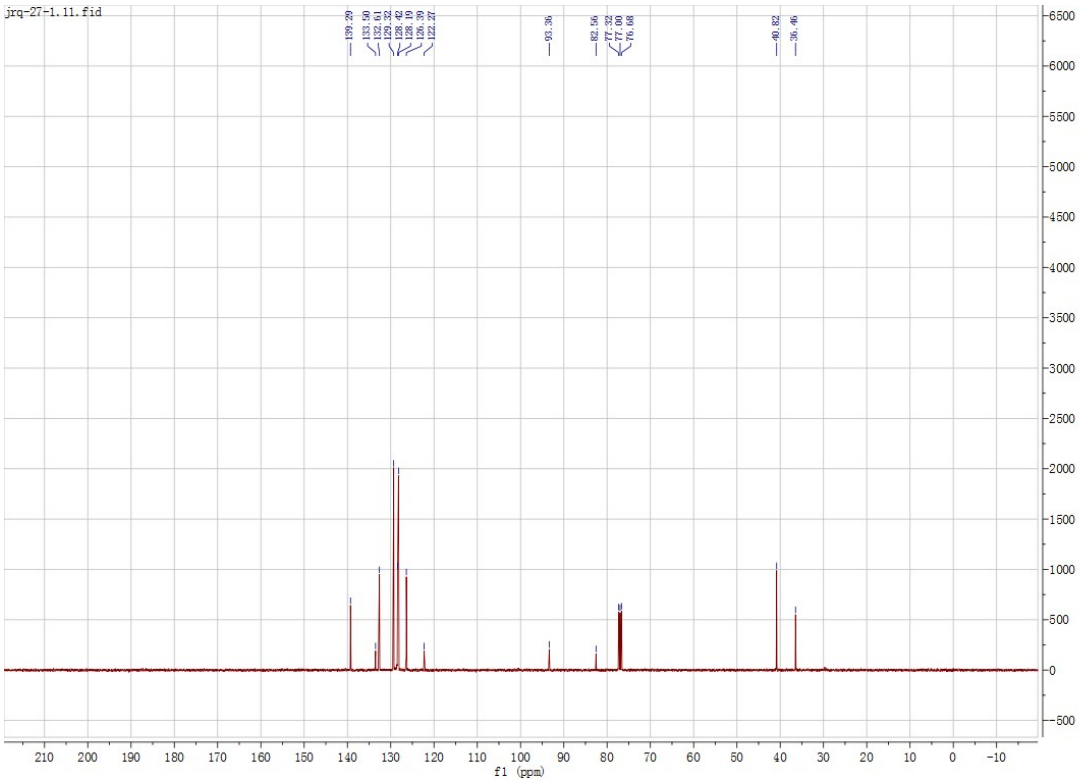

Ph
Ph
Ph
2fa, 65%

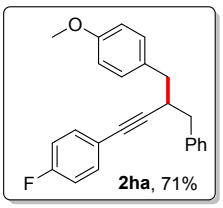

jrq-23-2.13.fid
f1 (ppm)


jrq-23-2.14.fid
f1 (ppm)

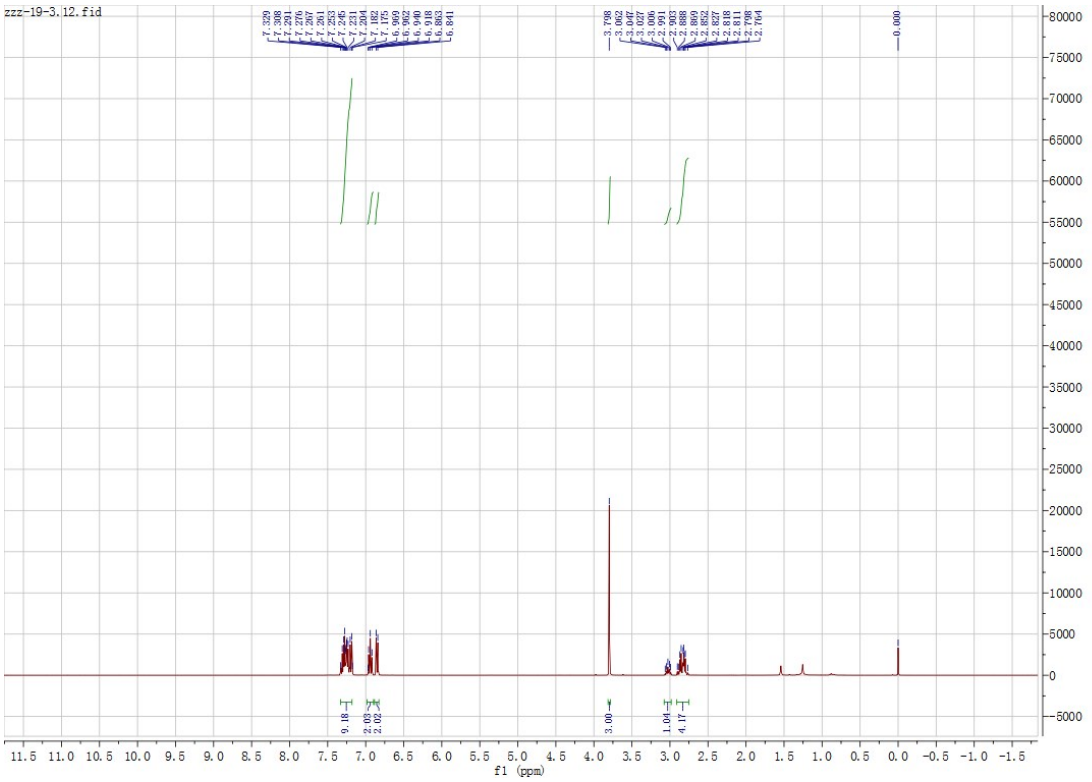

Ph
Ph
Cl
2ga, 47%

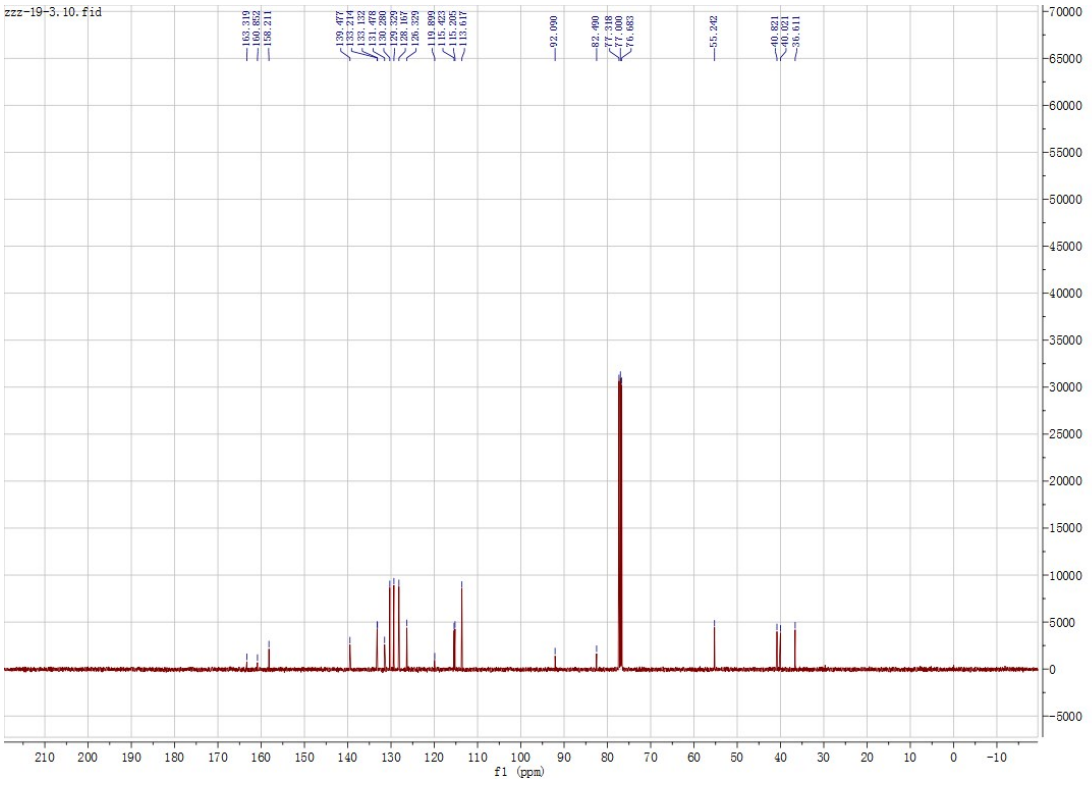

jrq-27-1.10.fid
f1 (ppm)

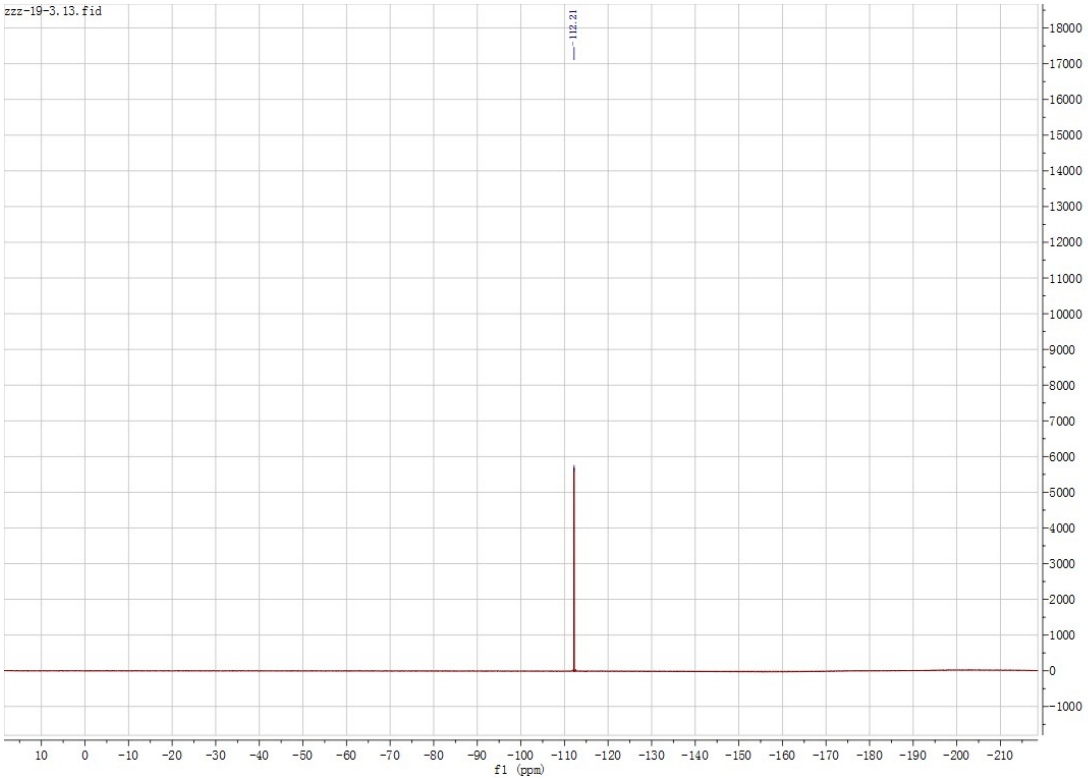

jrq-27-1.11.fid
f1 (ppm)



2ha, 71%






zzz-19-3.13.fid
-112.21
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
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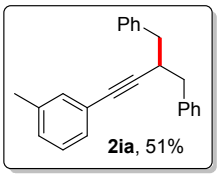
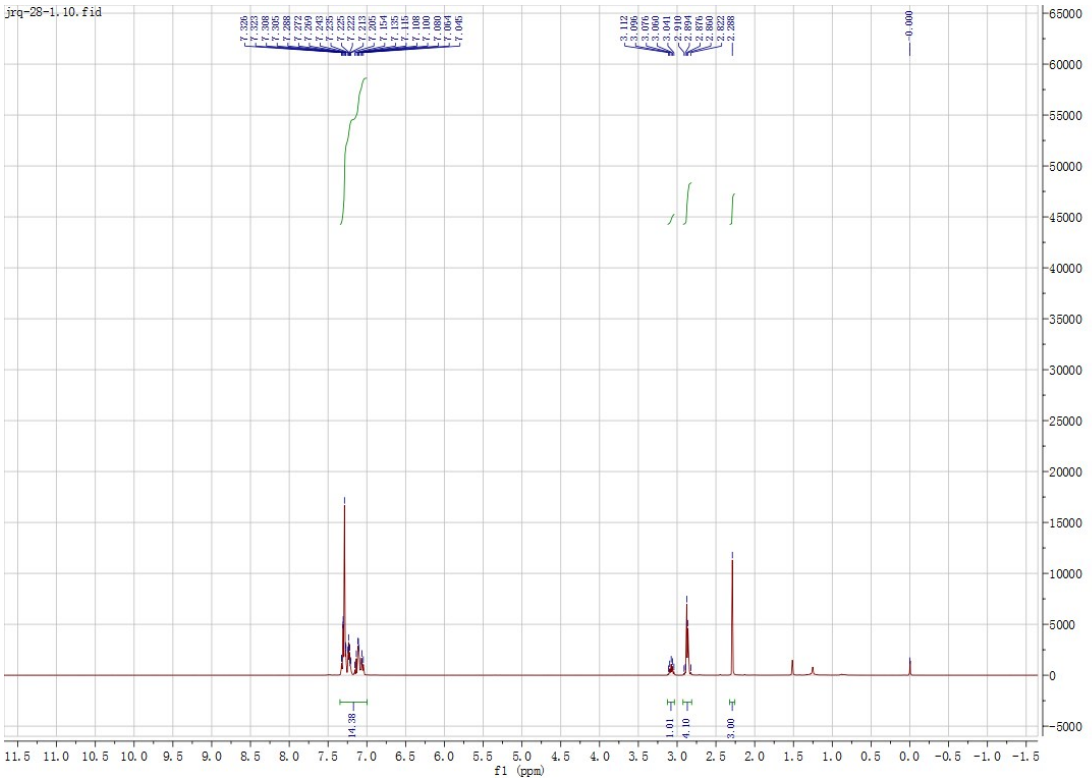
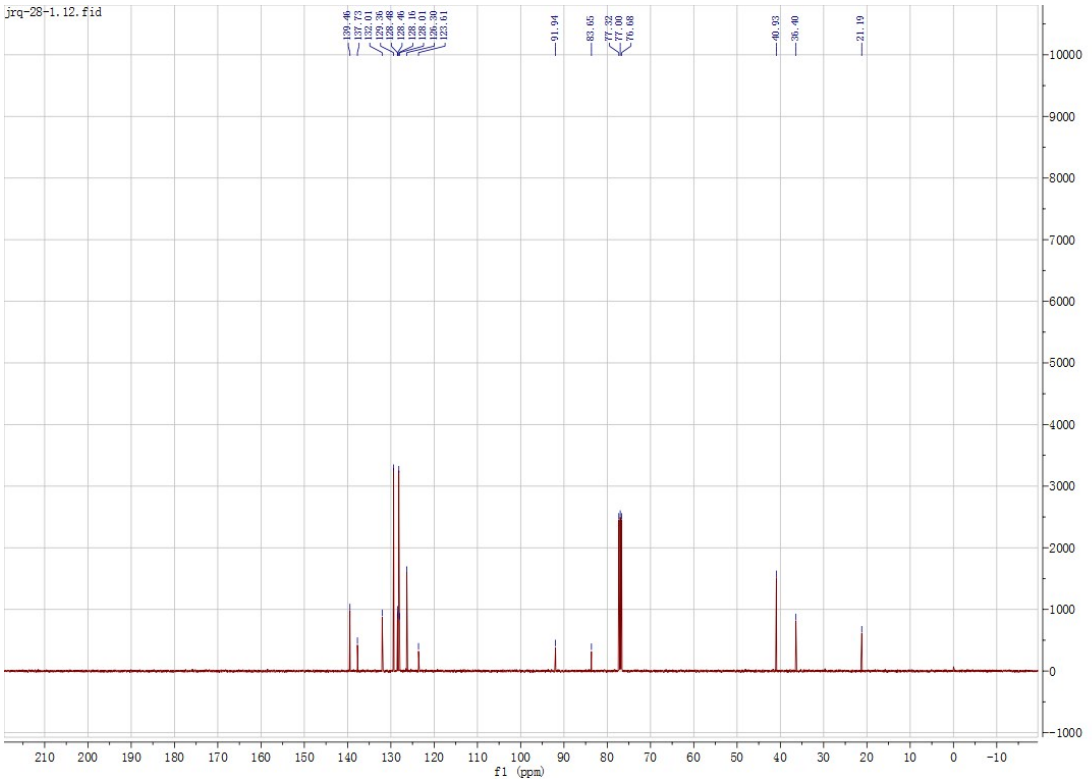
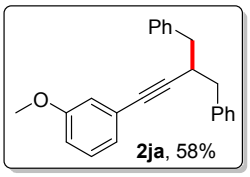
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



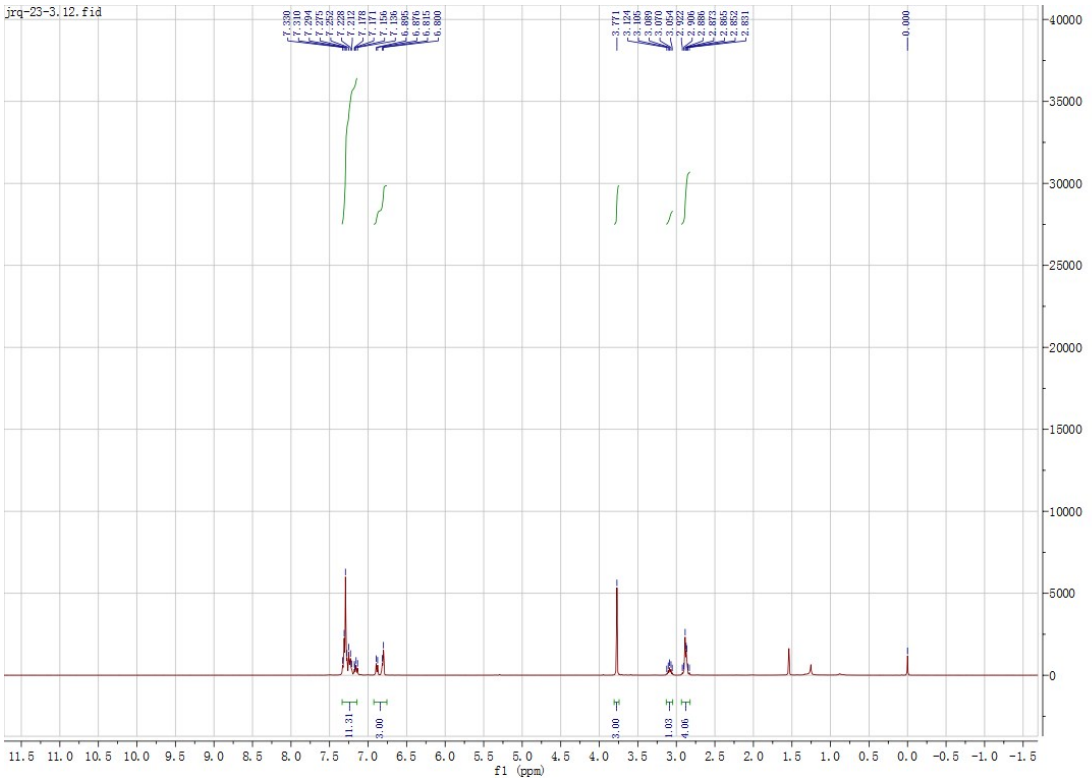
2ia, 51%

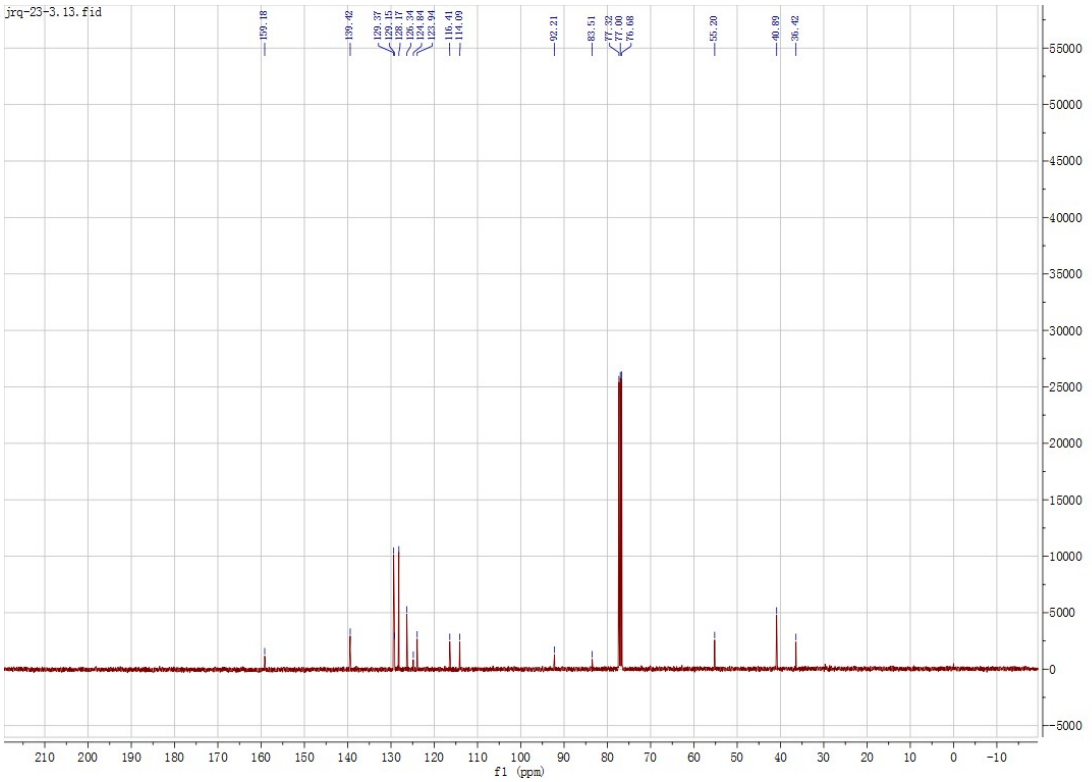


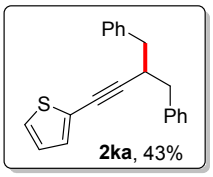




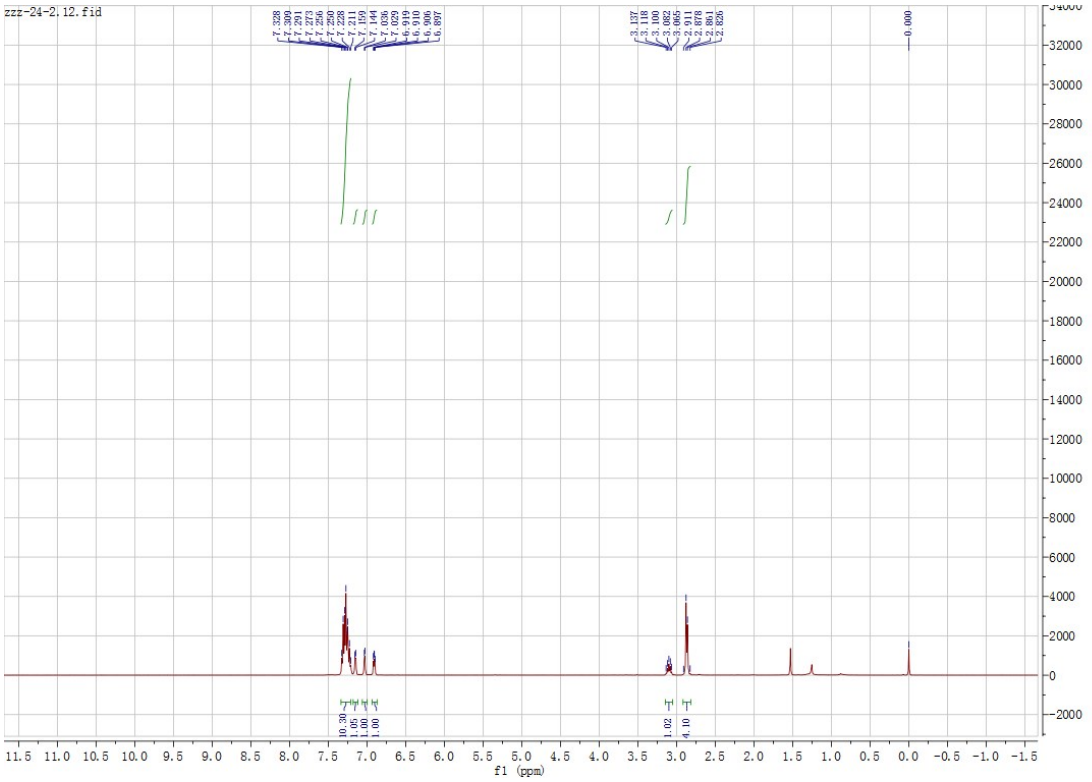
2ja, 58%

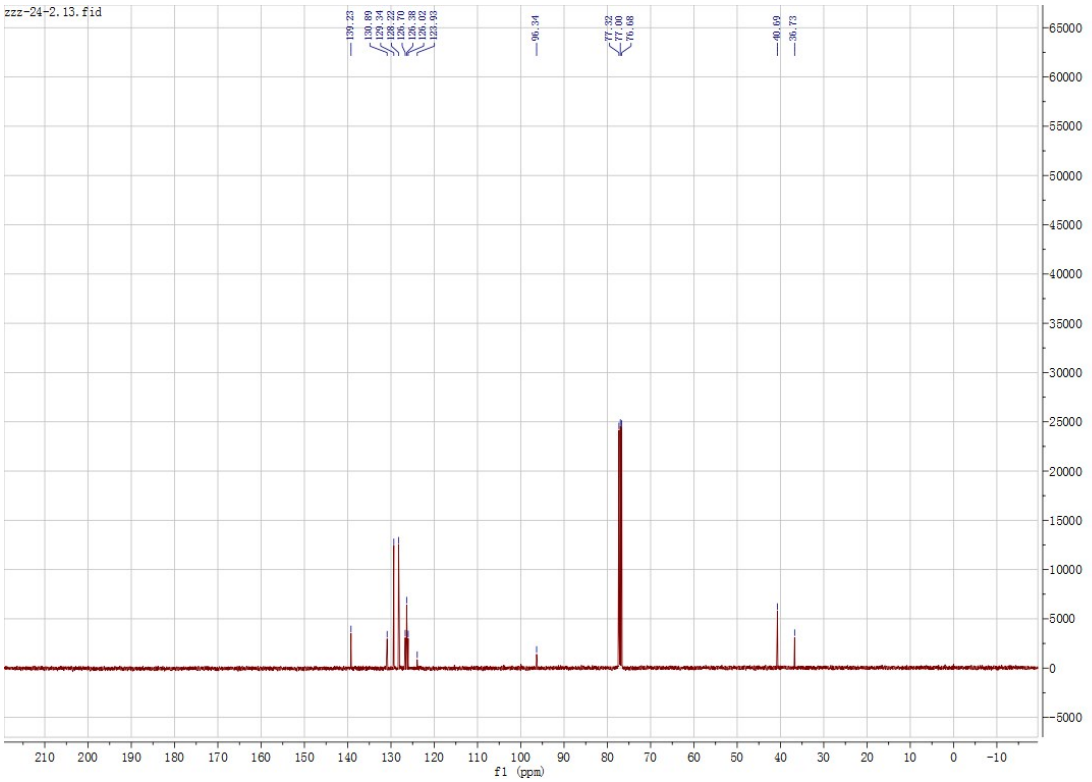


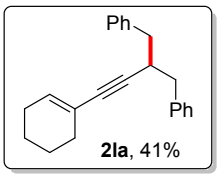




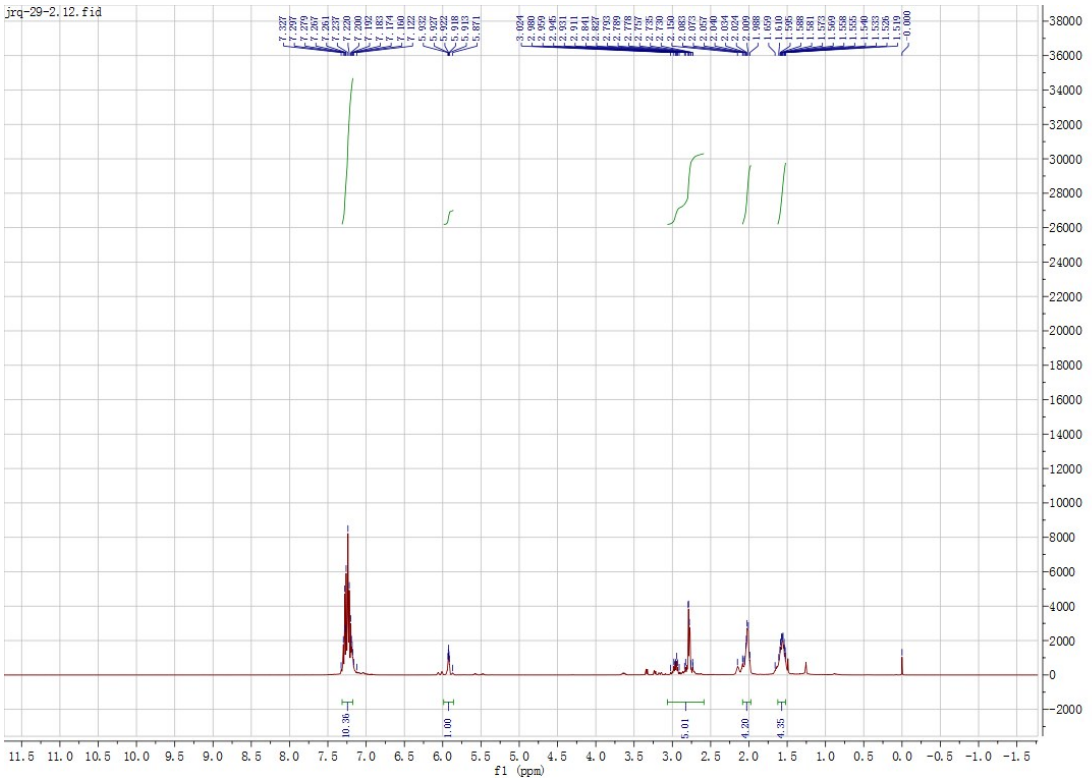
2ka, 43%

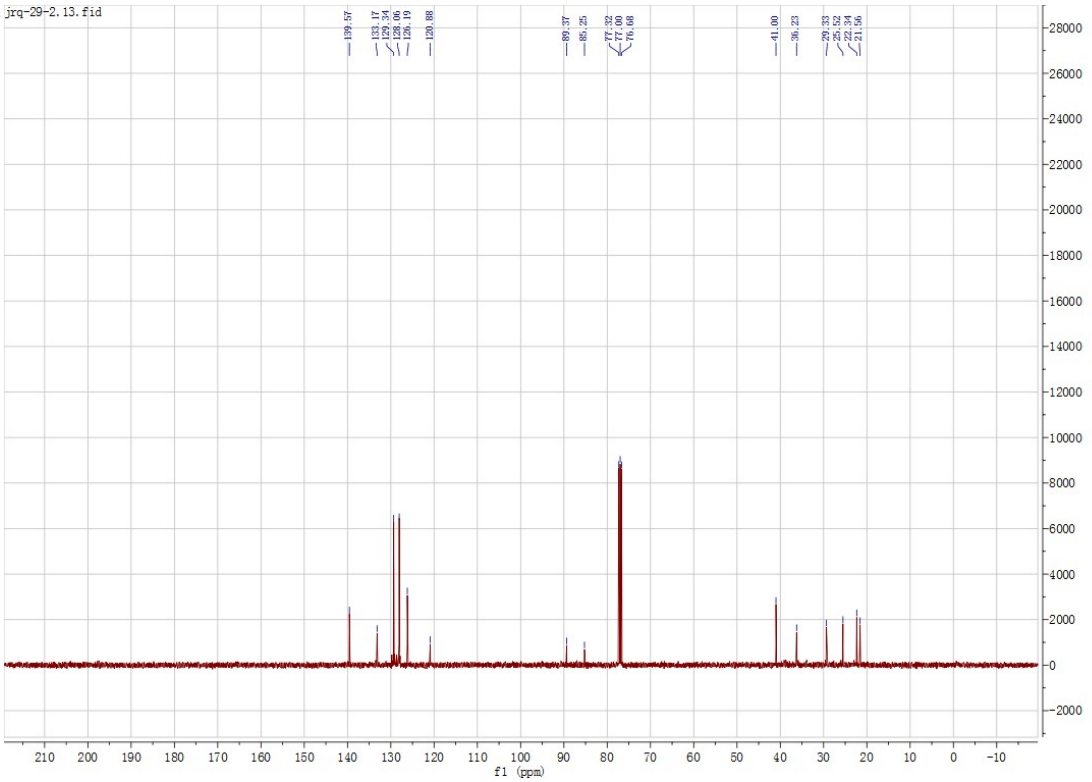


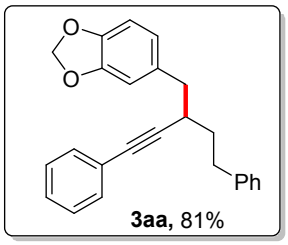




2la, 41%







3aa, 81%