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Supporting Information

Non-Directed C–H Arylation of Anisole Derivatives via Pd/S,O-Ligand Catalysis

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Supporting Information
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Ke-Zuan Deng, Verena Sukowski and M. Ángeles Fernández-Ibáñez*

Abstract: Non-directed C–H Arylation is one of the most efficient methods to synthesize biaryl compounds without the need of the prefuctionalization of starting materials, or the installment and removal of directing groups on the substrate. A direct C–H arylation of simple arenes as limiting reactants remains a challenge. Here we disclose a non-directed C–H arylation of anisole derivatives as limiting reagents with aryl iodides under mild reaction conditions. The arylated products are obtained in synthetically useful yields and the arylation of bioactive molecules is also demonstrated. Key to the success of this methodology is the use of a one-step synthesized S,O-ligand.

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SUPPORTING INFORMATION

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SUPPORTING INFORMATION

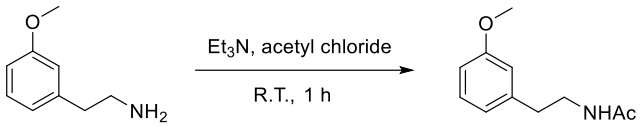
1. General Information

Chromatography: Flash column chromatography was performed using Macherey-Nagel Silica 60 (particle size 0.04–0.063 mm) under compressed air flow or a Buchi C-850 automatic column machine with FlashPure silica cartridges, TLC: Merck TLC plates (0.25 mm) precoated with silica gel 60 F_{254}, preparative TLC: Analtech silica gel G 1500 um 20x20 cm. Visualization of the chromatogram was performed by UV and $KMnO_4$ solution. Mass spectra were recorded on AccuTOF GC v 4g, JMS-T100GCV mass spectrometers. ^1H and ^{13}C were recorded on Bruker 500 AMX, 400 and Bruker DRX 300 using $CDCl_3$ as the solvent otherwise it will be noted. Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. IR spectra were recorded on a Bruker Alpha FTIR machine and wavelengths are reported in cm^{-1}. Mass spectrometry spectra were recorded on a JEOL JMS-T100LP AccuTOF 2012 (ESI), JEOL JMS-T100GCv AccuTOF 2012, (EI, FD). The FD/FI probe was equipped with an FD Emitter, Carbotec, FD = 10 µm. Current rate = 51.2 mA/min over 1.2 min using field desorption (FD) as an ionization method. The melting point was measured in Melting Point apparatus Büchi M-565. All reagents and solvents were used as received unless it was specified. $Pd(OAc)_2$ was purchased from Strem.

2. Synthesis of anisole derivatives and aryl iodide 2j

Substrates **1a-b, 1d-h, 1j-m, 1r-s, 1u-1w, 1y-1ab** and aryl iodides **2b-i** were purchased from commercial suppliers and were used without further purification.

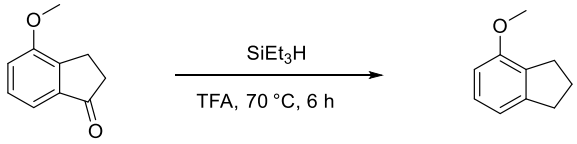
Synthesis of *N*-(3-methoxyphenethyl)acetamide (1n).[1]



To a solution of 2-(3-methoxyphenyl)ethan-1-amine (1.5 mL, 10.0 mmol, 1.0 equiv.) in DCM (10 mL) was added Et_3N (2.1 mL, 15 mmol, 1.5 equiv.) and the resulting mixture was cooled to 0-5 °C. To the mixture was added acetyl chloride (0.78 mL, 11 mmol, 1.1 equiv.) dropwise. After stirring at room temperature for 1 h, the mixture was quenched with cold water and extracted three times with DCM. The organic layer was washed with 0.6 M aqueous HCl and saturated $NaHCO_3$, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (1:1-0:1 v/v) as an eluent provided the titled compound as a yellow oil (1.39 g, 72%).

^1H NMR (300 MHz, $CDCl_3$) δ 7.22 (t, *J* = 8.1 Hz, 1H), 6.79 (d, *J* = 2.1 Hz, 1H), 6.77 – 6.73 (m, 2H), 5.54 (s, 1H), 3.90 (s, 3H), 3.51 (q, *J* = 6.6 Hz, 2H), 2.79 (t, *J* = 6.9 Hz, 2H), 1.93 (s, 3H). ^1H NMR spectra data of the product matched with the spectra data reported in the literature.[2]

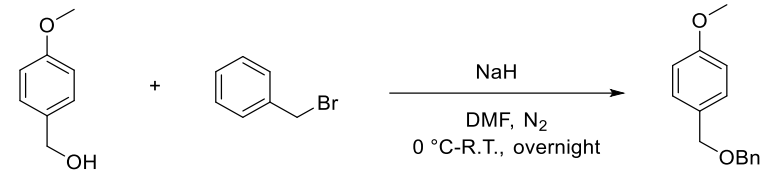
Synthesis of 4-methoxy-2,3-dihydro-1*H*-indene (1q).[3]



A mixture of 4-methoxy-2,3-dihydro-1*H*-inden-1-one (324 mg, 2.0 mmol, 1.0 equiv.), triethylsilane (1.5 g, 13.0 mmol, 6.5 equiv.) and TFA (6.5 mL) was refluxed at 70 °C. After 6 h, the mixture was poured into ice water and extracted with EtOAc. The combined organic layers were neutralized with aqueous $NaHCO_3$ solution and washed with water. Then the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/DCM (30:1-20:1 v/v) as an eluent provided the titled compound as a colorless liquid (590 mg, 79%).

^1H NMR (300 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.84 (s, 3H), 2.96 – 2.86 (m, 4H), 2.13 – 2.03 (m, 2H). ^1H NMR spectra data of the product matched with the spectra data reported in the literature.[4]

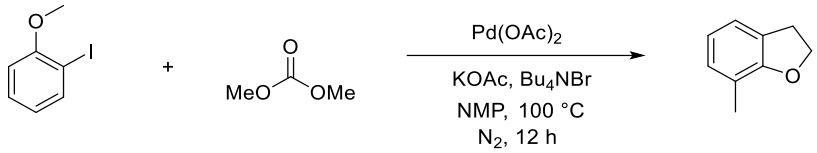
Synthesis of 1-((benzyloxy)methyl)-4-methoxybenzene (1t).[5]



4-Methoxybenzyl alcohol (0.621 mL, 5.0 mmol, 1.0 equiv.) was dissolved in dry DMF (5.0 mL) under N_2 atmosphere. The mixture was cooled down in an ice bath and was slowly added pre-washed NaH (400 mg, 10.0 mmol, 2.0 equiv., 60% dispersion in mineral oil). After stirring for 30 min, benzyl bromide (0.718 mL, 6 mmol, 1.2 equiv.) was added slowly by syringe and the mixture was allowed to room temperature. After stirring overnight, the mixture was quenched with cold water and extracted three times with Et_2O. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (30:1-10:1 v/v) as an eluent provided the titled compound as a pale yellow oil (0.917 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 4H), 7.34 – 7.28 (m, 3H), 6.92 – 6.87 (m, 2H), 4.54 (s, 2H), 4.50 (s, 2H), 3.82 (s, 3H). ^{1}H NMR spectra data of the product matched with the spectra data reported in the literature.[6]

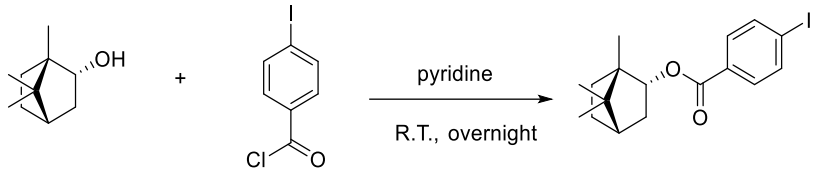
Synthesis of methyl 4-(7-methyl-2,3-dihydrobenzofuran-5-yl)benzoate (1x).[7]



A Schlenk flask equipped with a stirring bar was charged with $Pd(OAc)_2$ (90 mg, 0.4 mmol, 10 mol%), KOAc (0.98 g, 10 mmol, 2.5 equiv.), Bu_4NBr (5.16 g, 16 mmol, 4.0 equiv.), 1-iodo-2-methoxybenzene (0.94 g, 4 mmol, 1.0 equiv.) and NMP (30 mL). The flask was then evacuated and backfilled with nitrogen for 5 times. The dimethyl carbonate (2.7 mL, 32 mmol, 8.0 equiv.) was added by syringe. After stirring at 100 °C for 12 h, the mixture was cooled down to room temperature. The mixture was diluted with EtOAc, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/DCM (15:1-10:1 v/v) as an eluent provided the titled compound as a colorless liquid (324 mg, 60%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 – 7.02 (m, 1H), 6.96 – 6.92 (m, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 4.56 (t, *J* = 8.7 Hz, 2H), 3.22 (t, *J* = 9.0 Hz, 2H), 2.22 (s, 3H). ^{1}H NMR spectra data of the product matched with the spectra data reported in the literature.[7]

Synthesis of (1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 4-iodobenzoate (2j).[8]



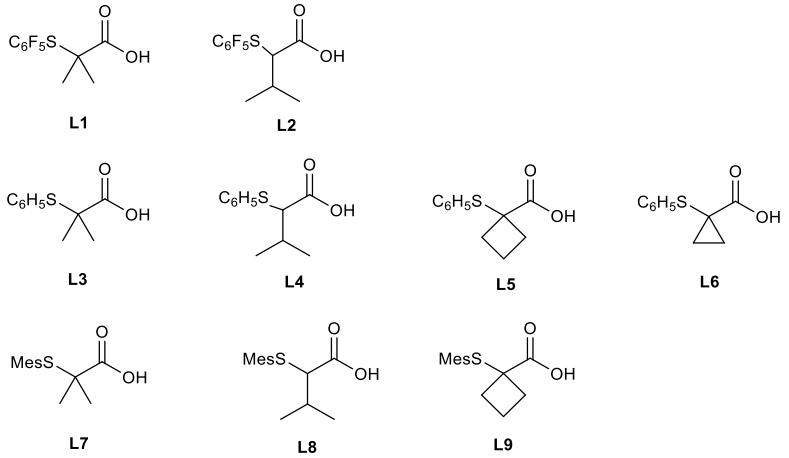
To a solution of L(-)-borneol (0.78 g, 5 mmol, 1.0 equiv.) in pyridine (15 mL) was added 4-iodobenzoyl chloride (2.65 g, 10 mmol, 2.0 equiv.). After stirring at room temperature overnight, the mixture was quenched with 0.6 M aqueous HCl and extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (100:1-1:2 v/v) as an eluent provided the titled compound as a white solid (1.80 g, 94%).[8]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.80 (m, 4H), 5.12 – 5.08 (m, 1H), 2.51 – 2.43 (m, 1H), 2.12 – 2.05 (m, 1H), 1.85 – 1.76 (m, 1H), 1.75 – 1.73 (m, 1H), 1.45 – 1.37 (m, 1H), 1.33 – 1.27 (m, 1H), 1.10 (dd, *J* = 14.0, 3.6 Hz, 1H), 0.962 (s, 3H), 0.914 (s, 3H), 0.901 (s, 3H). ^{1}H NMR spectra data of the product matched with the spectra data reported in the literature.[8]

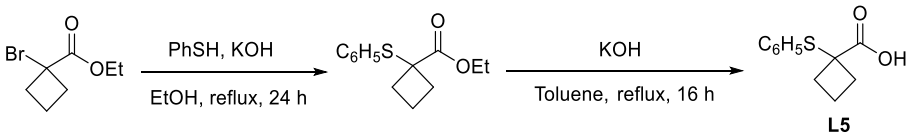
3. Synthesis of S,O-ligands

Ligand **L1** was synthesized according to the reported procedure.[9] Ligands **L2-L4, L6-L8** were synthesized according to the reported procedure.[10]

Table S1. Overview of screened S,O-ligands.



Synthesis of L5.



Step1:

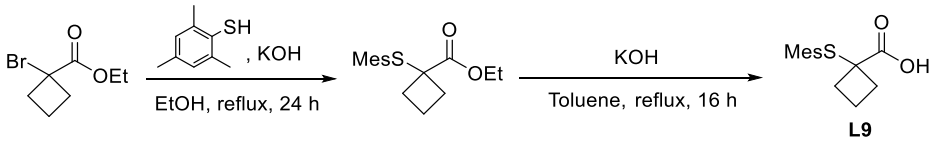
To a solution of thiophenol (0.51 mL, 5.0 mmol, 1.0 equiv.) in EtOH (6 mL) was slowly added KOH (0.28 g, 5 mmol, 1.0 equiv.) and the resulting suspension was heated at 60 °C until all the KOH was dissolved. The resulting solution was cooled to 0 °C and ethyl 1-bromocyclobutane-1-carboxylate (0.81 mL, 5.0 mmol, 1.0 equiv.) was added dropwise. The mixture was then heated to reflux for 24 h before it was cooled to room temperature. KBr (white solid) was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was diluted with DCM, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The resulting liquid was used for the next step without further purification.

Step2:

KOH (1.26 g, 22.5 mol, 4.5 equiv.) was dissolved in hot toluene (20 mL) and ethyl 1-(phenylthio)cyclobutane-1-carboxylate was added. The mixture was refluxed for 16 h. After the mixture was cooled to room temperature, water was added and the mixture was extracted with Et_2O. The aqueous phase was acidified with 1.0 M aqueous HCl to pH 1. The acidified aqueous layer was extracted with Et_2O and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/Et_2O (100:1-1:2 v/v) as an eluent provided the titled compound as a pale yellow solid (594 mg, 57% in two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 2H), 7.33 – 7.28 (m, 3H), 2.78 – 2.63 (m, 2H), 2.33 – 2.17 (m, 3H), 2.03 – 1.89 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.00, 133.32 (2C), 132.77, 129.08 (2C), 128.39, 52.87, 31.84 (2C), 15.99. **IR**: v 2986, 2943, 2852, 2657, 2558, 1690, 1572, 1472, 1454, 1436, 1404, 1287, 1250, 1209, 1175, 1156, 1125, 1089, 1069, 1042, 1021, 1001, 975, 922, 896, 803, 752, 691, 627, 615, 546, 489, 435, 408 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{11}H_{12}O_2S$ $[M]^+$ = 208.0565; found: 208.0558. **M.P.** = 61– 63 °C.

Synthesis of L9.



Step1:

To a solution of 2,4,6-trimethylbenzenethiol (0.76 mL, 5.0 mmol, 1.0 equiv.) in EtOH (6 mL) was added KOH (0.28 g, 5 mmol, 1.0 equiv.) slowly and the resulting suspension was heated at 60 °C until all the KOH was dissolved. The resulting solution was cooled to 0 °C and ethyl 1-bromocyclobutane-1-carboxylate (0.81 mL, 5.0 mmol, 1.0 equiv.) was added dropwise. The mixture was then heated to reflux for 24 h before it was cooled to room temperature. KBr (white solid) was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was diluted with DCM, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/Et_2O (100:1-20:1 v/v) as an eluent provided the titled compound (1.04 g, 75%).

Step2:

KOH (0.94 g, 16.8 mol, 4.5 equiv.) was dissolved in hot toluene (16 mL) and the ethyl 1-(mesitylthio)cyclobutane-1-carboxylate (1.04 g, 3.73 mmol, 1.0 equiv.) was added. The mixture was refluxed for 16 h. After the mixture was cooled to room temperature, water was added and the mixture was extracted with Et_2O. The aqueous phase was acidified with 1.0 M aqueous HCl to pH 1. The acidified aqueous layer was extracted with Et_2O and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/Et_2O (100:1-5:1 v/v) as an eluent provided the titled compound as a pale yellow solid (731 mg, 78%).

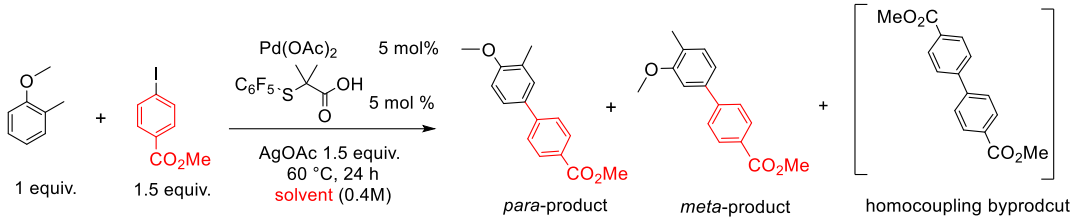
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (s, 2H), 2.63 – 2.56 (m, 2H), 2.49 (s, 6H), 2.27 (s, 3H), 2.26 – 2.18 (m, 2H), 2.12 – 2.02 (m, 1H), 1.91 – 1.80 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.30, 144.93 (2C), 139.39, 129.24 (2C), 127.29, 54.39, 32.67 (2C), 22.50 (2C), 21.22, 16.45. **IR**: v 3078, 2992, 2976, 2928, 2867, 1693, 1599, 1559, 1465, 1454, 1429, 1398, 1375, 1275, 1225, 1216, 1183, 1136, 1046, 1032, 1014, 1000, 922, 878, 864, 840, 779, 737, 720, 701, 638, 553, 511, 441, 426 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{14}H_{18}O_2S$ $[M]^+$ = 250.1027; found: 250.1036. **M.P.** = 80 – 82 °C.

4. Reaction optimization for C–H arylation of anisole derivatives

4.1 Optimization of the C–H Arylation of 2-methylanisole (1a)

In a pressure tube containing a suitable stirring bar was added $Pd(OAc)_2$, S,O-ligand, methyl 4-iodobenzoate (**2a**), AgOAc, solvent and 2-methyl anisole (12.6 µL, 0.1 mmol, 1.0 equiv.). The tube was put in a pre-heated oil bath at an appropriate temperature and was stirred for a certain time. After cooling to room temperature, the resulting mixture was diluted with DCM, filtered through a plug of Celite® and concentrated under reduced pressure. The ^{1}H NMR yield was determined by adding CH_2Br_2 (10 µL, 0.144 mmol) as internal standard and $CDCl_3$ as deuterated solvent.

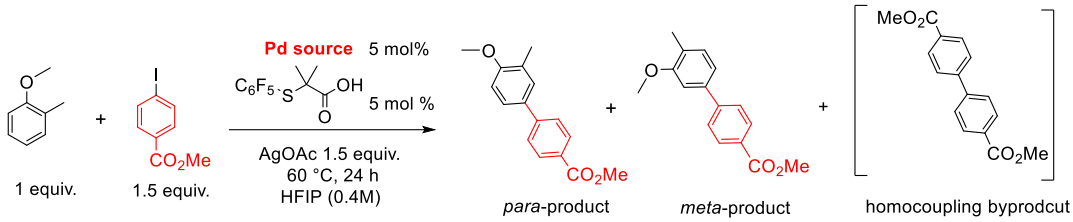
Table S2. Initial solvent screening.



Entry	solvent	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	**HFIP**	**37**	**11**	**48**	**3.4:1**	**14**
2	DCE	traces	traces	traces	-	traces
3	^{t}BuOH	3	traces	3	-	3
4	AcOH	traces	traces	traces	-	traces
5	DCM	traces	traces	traces	-	traces
6	TFE	34	4	38	8.5:1	5

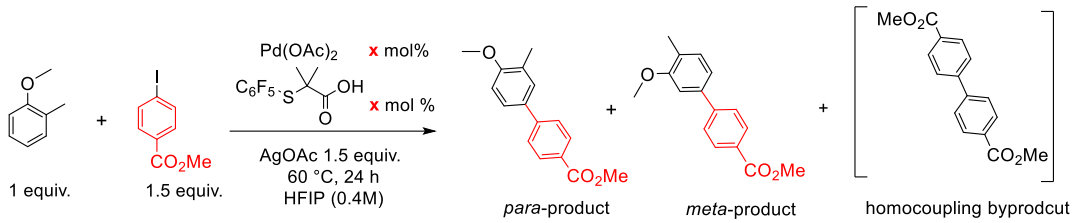
7	$(CF_3)_3COH$	37	6	43	6.2:1	10

Table S3. Pd source screening.



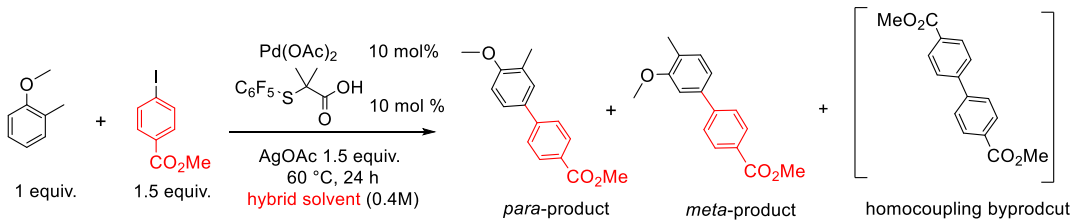
Entry	Pd source	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	**$Pd(OAc)_2$**	**37**	**11**	**48**	**3.4:1**	**14**
2	$Pd(OPiv)_2$	33	9	42	3.7:1	14
3	$Pd(TFA)_2$	23	6	29	4:1	12
4	$Pd(acac)_2$	traces	traces	traces	-	traces
5	$PdCl_2(PPh_3)_2$	13	4	17	3.2:1	29

Table S4. Screening amount of catalyst.



Entry	$Pd(OAc)_2$/mol%	S,O-L/mol%	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	2.5	2.5	25	8	33	3.1:1	10
2	5	5	37	11	48	3.4:1	14
3	7.5	7.5	44	11	55	4.0:1	18
4	**10**	**10**	**49**	**11**	**60**	**4.4:1**	**16**

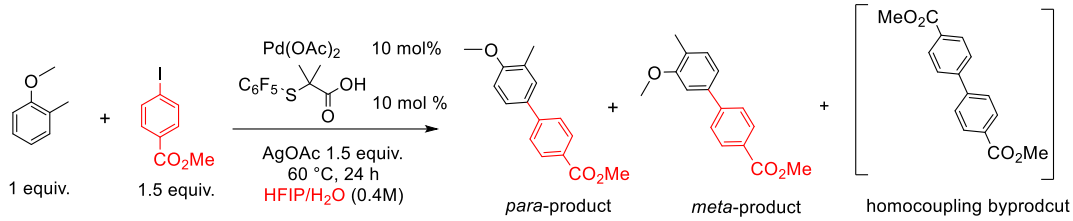
Table S5. Hybrid solvent screening.



Entry	HFIP+solvent 1.5:1	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	**-**	49	11	60	4.4:1	16

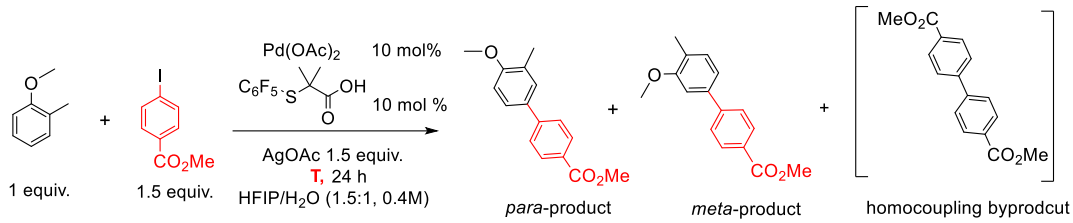
2	DCE	62	12	74	5.2:1	8
3	$CHCl_3$	67	12	79	5.6:1	10
4	pentane	52	9	61	5.8:1	15
5	tBuOH	50	7	57	7.1:1	3
6	AcOH	30	10	40	3:1	7
7	**H_2O**	**79**	**6**	**85**	**13.2:1**	**8**

Table S6. Screening of HFIP/H_2O ratio.



Entry	ratio of HFIP/H_2O	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	1:0	50	11	61	4.5:1	14
2	10:1	76	7	83	10.9:1	11
3	**1.5:1**	**79**	**6**	**85**	**13.2:1**	**8**
4	1:1	77	5	82	15.4:1	7
5	1:1.5	67	4	71	16.8:1	4
6	1:4	37	2	39	18.5:1	2

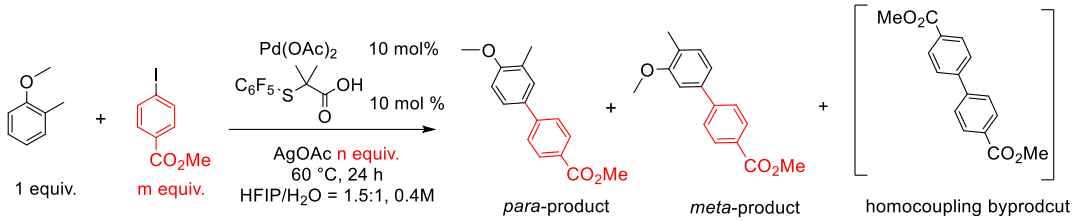
Table S7. Temperature screening.



Entry	Temperature/℃	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	40	58	3	61	19.3:1	2
2	**60**	**79**	**6**	**85**	**13.2:1**	**8**
3	80	73	7	80	10.4:1	10
4	100	58	6	64	9.7:1	10

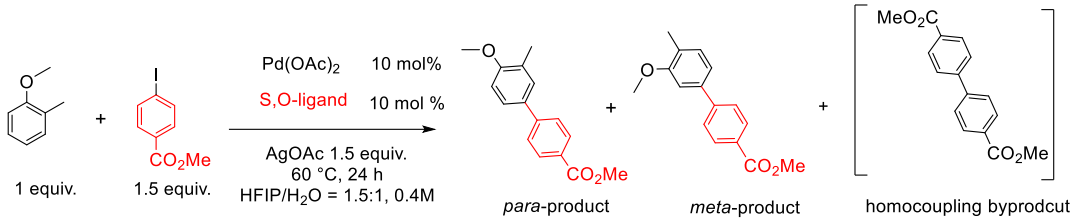
SUPPORTING INFORMATION

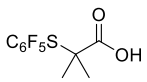
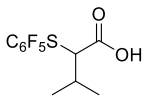
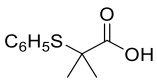
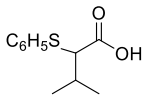
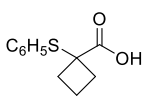
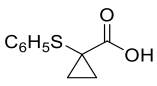
Table S8. Screening of the amount of ArI and AgOAc.



Entry	ArI/eq.	AgOAc/eq.	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	1.0	1.0	71	5	76	14.2:1	8
2	1.5	1.0	70	4	74	17.5:1	10
3	**1.5**	**1.5**	**78**	**5**	**83**	**15.6:1**	**8**
4	1.5	2.0	78	5	83	15.6:1	7
5	2.0	2.0	73	5	78	14.6:1	6
6	3.0	3.0	74	6	80	12.3:1	4

Table S9. S,O-ligand screening.



Entry	S,O-ligand	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1		**80**	**6**	**86**	**13.3:1**	**8**
2		77	5	82	15.4:1	9
3		58	9	67	6.4:1	13
4		45	5	50	9:1	12
5		56	8	64	7:1	16
6		53	7	60	7.6:1	17

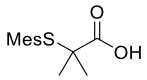
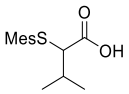
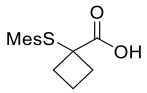
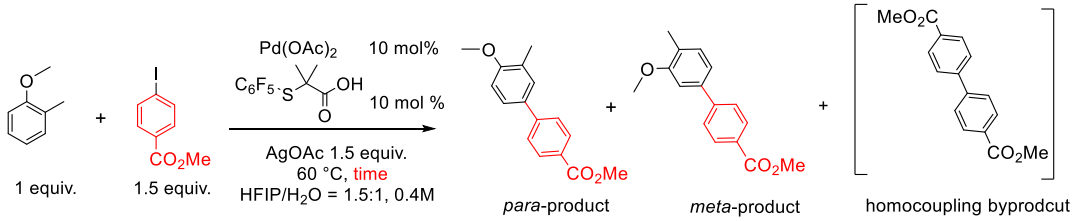
7		53	15	68	3.5:1	14
8		58	11	69	5.3:1	18
9		56	13	69	4.3:1	19

Table S10. Reaction time studies.

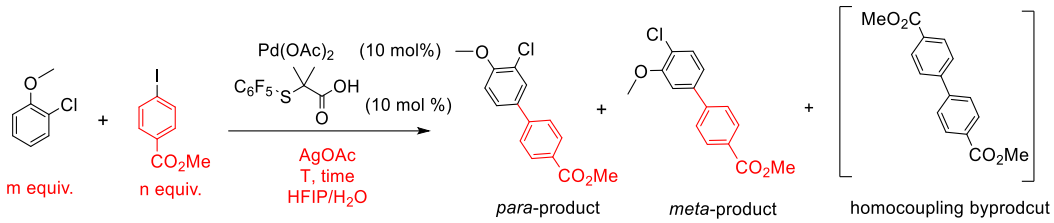


Entry	time	yield of *para*/%	yield of *meta*/%	total yield/%	*para*:*meta*	byproduct/%
1	5 min	13	2	15	6.5:1	1
2	10 min	24	2	26	12:1	2
3	15 min	31	2	33	15.5:1	2
4	30 min	55	3	58	18.3:1	5
5	1 h	74	4	78	18.5:1	7
6	2 h	84	5	89	16.8:1	8
7	4 h	84	6	90	14:1	8
8	8 h	82	5	87	16.4:1	7
9	24 h	80	6	86	13.3:1	8
10	72 h	81	6	87	13.5:1	11

4.2 Optimization of the C–H Arylation of 2-chloroanisole (1f)

In a pressure tube containing a suitable stirring bar was added $Pd(OAc)_2$, S,O-ligand, methyl 4-iodobenzoate (**2a**), AgOAc, solvent and 2-chloroanisole. The tube was put in a pre-heated oil bath at an appropriate temperature and was stirred for a certain time. After cooling to room temperature, the resulting mixture was diluted with DCM, filtered through a plug of Celite® and concentrated under reduced pressure. The ^1H NMR yield was determined by adding CH_2Br_2 (10 µL, 0.144 mmol) as internal standard and $CDCl_3$ as deuterated solvent.

Table S11. Optimization of the C–H Arylation of 2-chloroanisole (**1f**)



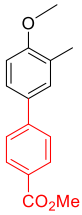
Entry	m:n	T/°C	time/h	conc. of solvent/M	yield of *para*/%	byproduct/ %
1[a]	1:1.5	60	4	0.4	14	3
2[a]	1:1.5	60	6	0.4	17	4
3[a]	1:1.5	60	20	0.4	25	6
4[a]	1:1.5	60	48	0.4	28	7
5[a]	1:1.5	80	20	0.4	25	14
6[a]	1:1.5	100	20	0.4	24	22
7[b]	1.5:1	60	20	0.4	38	11
8[b]	2:1	60	20	0.4	41	14
9[b]	3:1	60	20	0.4	45	14
10[b]	3:1	60	20	0.6	52	14
11[b]	3:1	60	20	0.8	49	12
12[a]	**3:1**	**60**	**20**	**0.6**	**58**	**17**
13[c]	3:1	60	20	0.6	58	19
14[d]	3:1	60	20	0.6	52	16

All reactions were performed on a 0.1 mmol scale. [a] 1.5 equiv. AgOAc. [b] 1.0 equiv. AgOAc. [c] 2 equiv. AgOAc. [d] 3 equiv. AgOAc.

5. C–H arylation of anisole derivatives

General Procedure: In a pressure tube containing a suitable stirring bar was added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 10 mol%), aryl iodide (0.375 mmol-0.25 mmol, 1.5-1.0 equiv.), AgOAc (62.5 mg, 0.375 mmol, 1.5 equiv.), (F_5)-S,O-ligand **L1** (2-methyl-2-[(perfluorophenyl)thio]propanoic acid) (250 µL, 0.1 M stock solution in HFIP, 0.025 mmol, 10 mol%), HFIP, H_2O and the corresponding anisole (0.25 mmol-0.75 mmol, 1.0-3.0 equiv.). The tube was put in a pre-heated oil bath at 25-80 °C and was stirred for 4 or 20 h. After cooling to room temperature, the resulting mixture was diluted with DCM, filtered through a plug of Celite® and concentrated under reduced pressure. The ^{1}H NMR yield was determined by adding CH_2Br_2 (10 µL, 0.144 mmol) as an internal standard. The crude mixture was purified by column chromatography on silica gel to obtain the desired product.

Methyl 4'-methoxy-3'-methyl-[1,1'-biphenyl]-4-carboxylate (3a)



3a

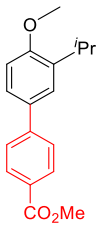
General procedure was followed using 2-methylanisole (**1a**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3a** in 87% (*p*/*m*, 94:6) ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (51.4 mg, 80%, *p*/*m* 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.34 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.24, 158.20, 145.58, 132.05, 130.17(2C), 129.64, 128.20, 127.30, 126.58(2C), 125.78, 110.34, 55.56, 52.17, 16.51. **IR**: ν 2950, 2922, 2844, 1704, 1600, 1519, 1494, 1464, 1446, 1433, 1394, 1284, 1269, 1249, 1178, 1139, 1106, 1049, 1022, 1014, 961, 901, 888, 857, 815, 772, 754, 727, 717, 701, 622, 595, 558, 524, 491, 440 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{16}H_{16}O_3$ $[M]^+$ = 256.1099; found: 256.1113.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Gram-scale reaction of 2-methylanisole (**1a**)

In a 50 mL flask containing a suitable stirring bar was added $Pd(OAc)_2$ (56 mg, 0.25 mmol, 5 mol%), (F_5)-S,O-ligand **L1** (2-methyl-2-[(perfluorophenyl)thio]propanoic acid) (72 mg, 0.25 mmol, 5 mol%), methyl 4-iodobenzoate (**2a**) (1.97 g, 7.5 mmol, 1.5 equiv.), AgOAc (1.25 g, 7.5 mmol, 1.5 equiv.), 7.5 mL HFIP, 5 mL H_2O and 2-methylanisole (**1a**) (630 µL, 5.0 mmol, 1.0 equiv.). The flask was put in a pre-heated oil bath at 60 °C and was stirred for 4 h. After cooling to room temperature, the resulting mixture was filtered through Celite®, extracted with DCM, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (930 mg, 73%, *p*/*m* 95:5).

Methyl 3'-isopropyl-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3b)

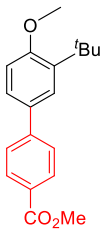


3b

General procedure was followed using 2-iso-propylanisole (**1b**) (40.9 µL, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3b** in 94% (*p*/*m*, 95:5) ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (64.1 mg, 90%, *p*/*m*, 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 – 7.98 (m, 2H), 7.56 – 7.53 (m, 2H), 7.39 (d, *J* = 2.4 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.32 – 3.26 (m, 1H), 1.20 (s, 3H), 1.18 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.25, 157.27, 145.95, 137.66, 132.32, 130.17(2C), 128.20, 126.67(2C), 125.57, 125.20, 110.80, 55.62, 52.17, 27.05, 22.79(2C). **IR**: ν 2946, 2867, 2835, 1713, 1603, 1488, 1459, 1437, 1397, 1315, 1280, 1264, 1244, 1196.1691, 1185, 1174, 1161, 1107, 1081, 1040, 1027, 1012, 960, 896, 857, 845, 821, 814, 768, 742, 702, 628, 617, 515, 483, 436 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{18}H_{20}O_3$ $[M]^+$ = 284.1412; found: 284.1409.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 3'-(tert-butyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3c)



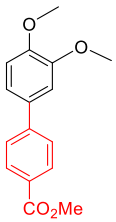
3c

General procedure was followed using 2-tert-butylanisole (**1c**) (41.1 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3c** in 93% (*p*/*m*, 96:4) ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (64.7 mg, 87%, p/m 96:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 – 8.09 (m, 2H), 7.66 – 7.64 (m, 2H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.21, 158.95, 146.06, 138.81, 131.92, 130.16(2C), 128.15, 126.67(2C), 125.93, 125.82, 111.98, 55.24, 52.13, 35.11, 29.80(3C). **IR**: ν 2997, 2952, 2834, 1713, 1602, 1487, 1452, 1437, 1421, 1390, 1359, 1315, 1277, 1248, 1235, 1193, 1180, 1156, 1105, 1094, 1051, 1031, 1012, 960, 900, 856, 824, 815, 769, 728, 703, 629, 621, 588, 514, 500, 485, 421 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{19}H_{22}O_3$ $[M]^+$ = 298.1569; found: 298.1576.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

SUPPORTING INFORMATION

Methyl 3',4'-dimethoxy-[1,1'-biphenyl]-4-carboxylate (3d)

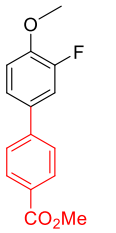


3d

General procedure was followed using 1,2-dimethoxybenzene (**1d**) (51.4 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 25 °C for 40 h, providing **3d** in 62% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/DCM (2:1-1:2 v/v) as an eluent provided the titled compound as a white solid (42.3 mg, 62% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.18 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.10, 149.44, 149.39, 145.50, 132.93, 130.18 (2C), 128.49, 126.70 (2C), 119.87, 111.59, 110.46, 56.09 (2C), 52.18. **IR**: v 2950, 2839, 1714, 1600, 1590, 1530, 1503, 1469, 1446, 1433, 1401, 1322, 1290, 1278, 1256, 1219, 1187, 1172, 1149, 1111, 1026, 875, 855, 844, 816, 767, 699 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{16}H_{16}O_4$ $[M]^+$ = 272.1049; found: 272.1056. **M.P.** =117-119 °C.

A parallel reaction without ligand was also performed, and traces of product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 3'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3e)

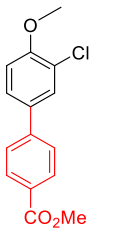


3e

General procedure was followed using 2-fluoroanisole (**1e**) (84 µL, 0.75 mmol, 3.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 417 µL, 0.6 M) at 60 °C for 20 h, providing **3e** in 49% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (10:1-1:8 v/v) as an eluent provided the titled compound as a white solid (28.0 mg, 43% yield, p/m 80:20). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 3.939 (s, 3H), 3.935 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.04, 152.74 (d, $J_{C\text{-}F}$ = 246.44 Hz), 147.92 (d, $J_{C\text{-}F}$ = 11.11 Hz), 144.16 (d, $J_{C\text{-}F}$ = 1.92 Hz), 133.16 (d, $J_{C\text{-}F}$ = 6.06 Hz), 130.32 (2C), 128.93, 126.64 (2C), 123.09 (d, $J_{C\text{-}F}$ = 3.43 Hz), 115.04 (d, $J_{C\text{-}F}$ = 19.29 Hz), 113.80 (d, $J_{C\text{-}F}$ = 2.22 Hz), 56.48, 52.27. **IR**: v 2955, 2845, 1708, 1604, 1585, 1530, 1502, 1470, 1444, 1430, 1400, 1323, 1279, 1214, 1190, 1177, 1136, 1112, 1035, 1013, 960, 893, 876, 852, 825, 810, 766, 716, 696, 637, 618, 596, 518, 500, 486, 451, 427 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{15}H_{13}O_3$ $[M]^+$ = 260.0849; found: 260.0851.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 3'-chloro-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3f)

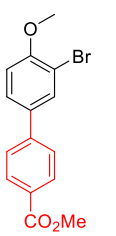


3f

General procedure was followed using 2-chloroanisole (**1f**) (97.2 µL, 0.75 mmol, 3.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 417 µL, 0.6 M) at 60 °C for 20 h, providing **3f** in 60% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (10:1-1:8 v/v) as an eluent provided the titled compound as a white solid (35.8 mg, 52% yield, *p*/other isomers 93:7). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 2H), 7.65 (d, *J* = 2.8 Hz, 1H), 7.61-7.58 (m, 2H), 7.49 (dd, *J* =11.2, 3.2 Hz, 1H), 7.01 (d, *J* = 11.6 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.02, 155.20, 143.99, 133.42, 130.32 (2C), 129.10, 128.92, 126.63 (2C), 123.16, 112.43, 56.40, 52.27. **IR**: v 2974, 2953, 2845, 1712, 1603, 1519, 1488, 1468, 1443, 1431, 1390, 1371, 1310, 1280, 1262, 1192, 1179, 1155, 1104, 1063, 1040, 1015, 973, 957, 936, 891, 857, 847, 841, 811, 765, 734, 719, 703, 638, 619, 601, 560, 501, 447, 428 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{15}H_{13}ClO_3$ $[M]^+$ = 276.0553; found: 276.0542.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 3'-bromo-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3g)

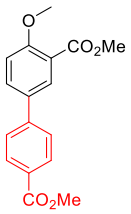


3g

General procedure was followed using 2-bromoanisole (**1g**) (96.0 µL, 0.75 mmol, 3.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 417 µL, 0.6 M) at 60 °C for 20 h, providing **3g** in 53% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (10:1-1:8 v/v) as an eluent provided the titled compound as a colorless oil (37.6 mg, 47% yield, *p*/other isomers 74:26). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 2H), 7.83 (d, *J* = 2.4 Hz, 1H), 7.63-7.57 (m, 2H), 7.54 (dd, *J* =8.8, 2.4 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.05, 156.11, 143.92, 133.94, 132.19, 130.35, 130.33 (2C), 128.94, 127.41, 127.39, 126.68 (2C), 112.40, 112.26, 56.51, 52.29. **IR**: v 3003, 2950, 2839, 1711, 1599, 1575, 1523, 1489, 1463, 1433, 1387, 1280, 1187, 1160, 1114, 1056, 1030, 1016, 965, 859, 839, 815, 770, 760, 728, 700, 677 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{15}H_{13}BrO_3$ $[M]^+$ = 320.0048; found: 320.0045.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Dimethyl 4-methoxy-[1,1'-biphenyl]-3,4'-dicarboxylate (3h)

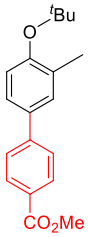


3h

General procedure was followed using methyl 2-methoxybenzoate (**1h**) (107.8 µL, 0.75 mmol, 3.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 417 µL, 0.6 M) at 60 °C for 20 h. Purification by column chromatography on silica gel using cyclohexane/EtOAc (20:1-1:1 v/v) as an eluent provided the titled compound as a brown solid (39.2 mg, 52% yield, *p*/*m* 96:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 3H), 7.72 (dd, *J* =11.6, 3.2 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.06 (d, *J* = 11.6 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.92 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.04, 166.54, 159.27, 144.16, 132.14, 132.01, 130.54, 130.28 (2C), 128.81, 126.60 (2C), 120.54, 112.66, 56.30, 52.30, 52.23. **IR**: v 2952, 2923, 2847, 1702, 1606, 1518, 1490, 1434, 1422, 1393, 1321, 1308, 1272, 1243, 1182, 1158, 1112, 1097, 1049, 1015, 974, 960, 916, 868, 855, 833, 820, 796, 784, 768, 731, 716, 700, 673, 622, 572, 511, 492, 457, 422 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{17}H_{16}O_5$ $[M]^+$ = 300.0998; found: 300.0995.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4'-(tert-butoxy)-3'-methyl-[1,1'-biphenyl]-4-carboxylate (3i)

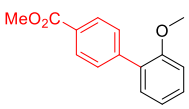


3i

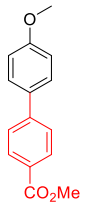
General procedure was followed using 2-tert-butoxytoluene (**1i**) (41.1 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 80 °C for 20 h, providing **3i** in 56% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (5:1-1:10 v/v) as an eluent provided the titled compound as a white solid (40.4 mg, 54%, *p*/*m* 92:8). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 8.06 (m, 2H), 7.64 – 7.62 (m, 2H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.36 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 3.93 (s, 3H), 2.31 (s, 3H), 1.44 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.24, 155.01, 145.54, 133.99, 132.52, 130.15 (2C), 129.84, 128.37, 126.71 (2C), 125.08, 122.15, 76.84, 52.18, 29.36 (3C), 17.53. **IR**: v 2977, 2953, 1714, 1605, 1521, 1493, 1439, 1390, 1366, 1322, 1280, 1265, 1174, 1131, 1110, 1015, 928, 910, 868, 854, 834, 775, 757, 702 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{19}H_{22}O_3$ $[M]^+$ = 298.1569; found: 298.1574.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

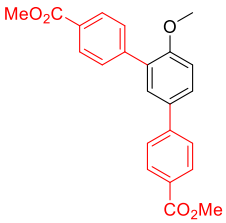
Methyl 2'-methoxy-[1,1'-biphenyl]-4-carboxylate (3j-*ortho*), methyl 4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3j-*para*) and dimethyl 4'-methoxy-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (3j-di)



3j-*ortho*



3j-*para*



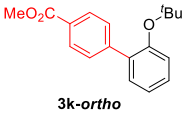
3j-di

General procedure was followed using anisole (**1j**) (54.3 µL, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h. Purification by column chromatography on silica gel using pentane/DCM (10:1-0:1 v/v) as an eluent provided **3j-*ortho*** (20.4 mg, 34%), **3j-*para*** (15.4 mg, 25%) and **3j-di** (5.6 mg, 6%) as white solids. **^{1}H NMR of 3j-*ortho*** (300 MHz, $CDCl_3$) δ 8.09 – 8.05 (m, 2H), 7.63 – 7.59 (m, 2H), 7.39 – 7.32 (m, 2H), 7.07 – 7.00 (m, 2H), 3.93 (s, 3H), 3.82 (s, 3H). **^{1}H NMR of 3j- *para*** (300 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 2H), 7.64 – 7.55 (m, 4H), 7.02 – 6.97 (m, 2H), 3.94 (s, 3H), 3.86 (s, 3H). **^{1}H NMR** spectra data of the **3j-*ortho*** and **3j-*para*** matched with the spectra data reported in the literature.[11]

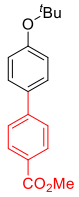
^{1}H NMR of 3j-di (400 MHz, $CDCl_3$) δ 8.12 – 8.08 (dd, *J* = 8.4, 2.4 Hz, 4H), 7.67 – 7.59 (m, 6H), 7.10 – 7.08 (d, *J* = 8.4 Hz, 1H), 7.07 – 7.00 (m, 2H), 3.945 (s, 3H), 3.938 (s, 3H), 3.88 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.19, 167.15, 156.83, 144.98, 143.09, 132.84, 130.31 (2C), 130.28, 129.79, 129.71 (2C), 129.51 (2C), 128.93, 128.64, 128.23, 126.69 (2C), 111.90, 55.94, 52.26 (2C). **IR**: v 2951, 2852, 1720, 1607, 1519, 1490, 1462, 1435, 1407, 1387, 1278, 1181, 1151, 1112, 1058, 1019, 858, 816, 773, 739, 705 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{23}H_{20}O_5$ $[M]^+$ = 376.1311; found: 376.1314.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 2'-(*tert*-butoxy)-[1,1'-biphenyl]-4-carboxylate (3k-*ortho*) and methyl 4'-(*tert*-butoxy)-[1,1'-biphenyl]-4-carboxylate (3k-*para*)



3k-*ortho*



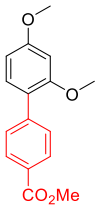
3k-*para*

General procedure was followed using *tert*-butoxybenzene (**1k**) (78.0 µL, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h. Purification by column chromatography on silica gel using pentane/EtOAc (100:1-0:1 v/v) as an eluent provided **3k-*ortho*** as a colorless oil (11.6 mg, 16% yield) and a mixture of **3k-*para*** and **3k-*meta*** (24.7 mg, 35% yield; *p*/*m* 85:15) as a yellow solid. **^{1}H NMR of 3k-*ortho*** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.18 – 7.13 (m, 2H), 3.94 (s, 3H), 1.10 (s, 9H). **^{13}C NMR of 3k-*ortho*** (101 MHz, $CDCl_3$) δ 167.39, 153.14, 145.04, 136.19, 130.73, 130.08 (2C), 129.27 (2C), 128.71, 128.40, 124.59, 123.79, 80.43, 52.21, 28.94 (3C). **IR of 3k-*ortho***: ν 2978, 2951, 2362, 2340, 2323, 1724, 1609, 1563, 1512, 1479, 1461, 1435, 1402, 1391, 1366, 1278, 1180, 1162.01, 1111, 1102, 1024, 1008, 924, 896, 856, 817, 780, 748, 706 cm^{-1}. **HRMS of 3k-*ortho*** (FD): m/z calculated for $C_{18}H_{20}O_3$ $[M]^+$ = 284.1412; found: 284.1426.

^{1}H NMR of 3k-*para* (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 3.93 (s, 3H), 1.39 (s, 9H). **^{13}C NMR of 3k-*para*** (101 MHz, $CDCl_3$) δ 167.21, 155.95, 145.35, 134.92, 130.21 (2C), 128.56, 127.88 (2C), 126.80 (2C), 124.46 (2C), 79.04, 52.22, 29.02 (3C).

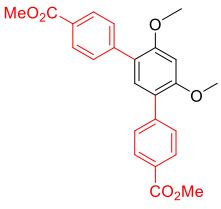
A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 2',4'-dimethoxy-[1,1'-biphenyl]-4-carboxylate (3l-mono) and dimethyl 4',6'-dimethoxy-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (3l-di)



3l-mono

General procedure was followed using 1,3-dimethoxybenzene (**1l**) (65.5 µL, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 25 °C for 20 h. Purification by column chromatography on silica gel using pentane/EtOAc (20:1-1:1 v/v) as an eluent provided **3l-mono** as a colorless crystal (43.4 mg, 64% yield) and **3l-di** as a yellow solid (4.1 mg, 4% yield). **^{1}H NMR of 3l-mono** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.50 – 6.44 (m, 2H), 3.83 (s, 3H), 3.76 (s, 3H), 3.71 (s, 3H). **^{13}C NMR of 3l-mono** (101 MHz, $CDCl_3$) δ 167.27, 161.02, 157.65, 143.35, 131.40, 129.44 (2C), 129.37 (2C), 128.07, 122.48, 104.94, 99.14, 55.65, 55.53, 52.11. **IR of 3l-mono**: ν 3000, 2950, 2837, 1719, 1607, 1581, 1561, 1522, 1494, 1463, 1436, 1401, 1278, 1251, 1209, 1182, 1161, 1138, 1104, 1051, 1032, 1004, 967, 936, 861, 827, 803, 774, 727, 706, 556 cm^{-1}. **HRMS of 3l-mono** (FI): m/z calculated for $C_{16}H_{16}O_4$ $[M]^+$ = 272.1049; found: 272.1035. **M.P. of 3l-mono** =116-118 °C.

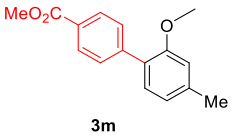


3l-di

^{1}H NMR of 3l-di (400 MHz, $CDCl_3$) δ 8.08 – 8.05 (m, 4H), 7.63 – 7.60 (m, 4H), 7.34 (s, 1H), 6.66 (s, 1H), 3.93 (s, 6H), 3.90 (s, 6H). **^{13}C NMR of 3l-di** (101 MHz, $CDCl_3$) δ 167.28 (2C), 157.67 (2C), 142.90 (2C), 132.83, 129.50 (8C), 128.34 (2C), 122.39 (2C), 96.24, 56.03 (2C), 52.21 (2C). **IR of 3l-di**: ν 2999, 2951, 2844, 1718, 1606, 1578, 1561, 1514, 1491, 1463, 1436, 1407, 1383, 1313, 1277, 1240, 1204, 1183, 1168, 1106, 1031, 1008, 980, 858, 821, 774, 709 cm^{-1}. **HRMS of 3l-di** (FI): m/z calculated for $C_{24}H_{22}O_6$ $[M]^+$ = 406.1416; found: 406.1398. **M.P. of 3l-di** =132-135 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4'-methoxy-2'-methyl-[1,1'-biphenyl]-4-carboxylate (3m)

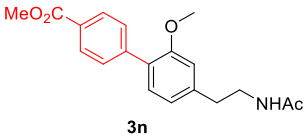


3m

General procedure was followed using 3-methylanisole (**1m**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 25 °C for 20 h, providing **3m** in 68% (*o*/other isomers, 92:8) ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/DCM (3:1-1:3 v/v) as an eluent provided the titled compound as a colorless oil (38.4 mg, 60%, *o*/other isomers 92:8). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.83 (s, 1H), 3.94 (s, 3H), 3.82 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.28, 156.44, 143.56, 139.78, 130.65, 129.58 (2C), 129.37 (2C), 128.34, 126.81, 121.73, 112.37, 55.63, 52.14, 21.73. **IR**: ν 2950, 1720, 1608, 1578, 1519, 1494, 1464, 1435, 1397, 1313, 1277, 1181, 1168, 1138, 1112, 1103, 1039, 1006, 966, 925, 862, 814, 776, 737, 705, 593, 566, 546, 454 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{16}H_{16}O_3$ $[M]^+$ = 256.1099; found: 256.1088.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 2'-(2-acetamidoethyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3n)

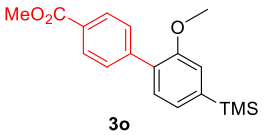


3n

General procedure was followed using *N*-(3-methoxyphenethyl)acetamide (**1n**) (48.2 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3n** in 67% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (1:1-0:1 v/v) as an eluent provided the titled compound as a brown solid (49.8 mg, 61%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.84 (s, 1H), 5.81 (s, 1H), 3.94 (s, 3H), 3.82 (s, 3H), 3.57 (q, *J* = 6.8 Hz, 2H), 2.88 (t, *J* = 7.2 Hz, 2H), 1.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.26, 167.20, 156.68, 143.18, 140.70, 130.91, 129.51 (2C), 129.34 (2C), 128.45, 127.82, 121.24, 111.90, 55.68, 52.14, 40.68, 35.83, 23.40. **IR**: v 3292, 2925, 2853, 1715, 1637, 1607, 1574, 1547, 1519, 1492, 1462, 1434, 1397, 1374, 1274, 1180, 1165, 1142, 1101, 1034, 1005, 957, 866, 847, 821, 776, 729, 704, 595, 557, 515, 487, 473, 451, 424 cm^{-1}. **HRMS** (ESI): m/z calculated for $C_{19}H_{21}NO_4$ $[M+H]^+$ = 328.1549; found: 328.1547. **M.P.** 134-136 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4'-methoxy-2'-(trimethylsilyl)-[1,1'-biphenyl]-4-carboxylate (3o)

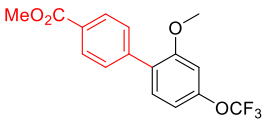


3o

General procedure was followed using 3-trimethylsilylanisole (**1o**) (45.1 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h. Purification by column chromatography on silica gel using pentane/EtOAc (100:1-1:2 v/v) as an eluent provided the titled compound as a yellow solid (33.4 mg, 42%, *o*/other isomers 94:6). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 – 8.09 (m, 2H), 7.66 – 7.63 (m, 2H), 7.36 (d, *J* = 9.6 Hz, 1H), 7.23 (d, *J* = 9.6, 1.2 Hz, 1H), 7.16 (s, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 0.35 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.21, 155.98, 143.45, 142.46, 130.29, 130.21, 129.61 (2C), 129.37 (2C), 128.60, 126.15, 115.87, 55.67, 52.14, -0.98 (3C). **IR**: v 2998, 2953, 2900, 2842, 1721, 1609, 1570, 1540, 1515, 1491, 1462, 1435, 1407, 1383, 1312, 1278, 1247, 1181, 1145, 1111, 1037, 1005, 968, 888, 834, 777, 756, 735, 705, 677, 625 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{18}H_{22}O_3Si$ $[M]^+$ = 314.1338; found: 314.1349.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4'-methoxy-2'-(trifluoromethoxy)-[1,1'-biphenyl]-4-carboxylate (3p)

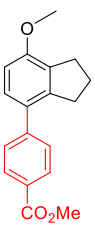


3p

General procedure was followed using 3-trifluoromethoxyanisole (**1p**) (96.1 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h, providing **3p** in 32% ^{1}H NMR yield (*o*/other isomers, 83:17). Purification by column chromatography on silica gel using pentane/DCM (20:1-2:1 v/v) as an eluent provided the titled compound as a colorless oil (23.9 mg, 29%, *o*/other isomers 84:16). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 2H), 7.57 – 7.55 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 6.84 (s, 1H), 3.94 (s, 3H), 3.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.12, 157.48, 142.19, 131.48, 129.69, 129.60 (2C), 129.51 (2C), 129.32, 129.02, 128.38, 112.87, 104.85, 55.97, 52.26. **IR**: v 2953, 2845, 1722, 1611, 1565, 1520, 1493, 1465, 1437, 1398, 1254, 1218, 1165, 1113, 1037, 1007, 975, 879, 862, 847, 820, 776, 730, 705, 647, 607, 564 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{16}H_{13}F_3O_4$ $[M]^+$ = 326.0766; found: 326.0779.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(7-methoxy-2,3-dihydro-1H-inden-4-yl)benzoate (3q)

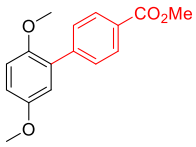


3q

General procedure was followed using 4-methoxy-2,3-dihydro-1*H*-indene (**1q**) (74.0 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 40 °C for 4 h, providing **3q** in 67% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (1:1-0:1 v/v) as an eluent provided the titled compound as a white solid (44.8 mg, 63%, *p*/*m* 97.5:2.5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 2H), 7.50 – 7.48 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 3.95 (s, 3H), 3.89 (s, 3H), 2.99 (t, *J* = 7.2 Hz, 2H), 2.94 (t, *J* = 7.2 Hz, 2H), 2.08 (m, *J* = 7.2 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.22, 156.04, 146.18, 143.99, 132.60, 130.03, 129.66 (2C), 128.48 (2C), 128.18, 128.10, 108.66, 55.39, 52.16, 33.53, 29.70, 25.53. **IR**: v 2950, 2839, 1719, 1603, 1586, 1563, 1516, 1486, 1462, 1435, 1397, 1310, 1268, 1180, 1113, 1105, 1085, 1068, 1018, 967, 942, 860, 808, 774, 721, 708 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{18}H_{18}O_3$ $[M]^+$ = 282.1256; found: 282.1261.

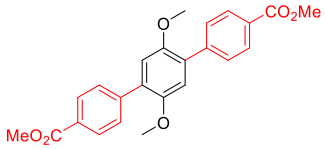
A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 2',5'-dimethoxy-[1,1'-biphenyl]-4-carboxylate (3r-mono) and dimethyl 2',5'-dimethoxy-[1,1':4',1''-terphenyl]-4,4''-dicarboxylate (3r-di)



3r-mono

General procedure was followed using 1,4-dimethoxybenzene (**1r**) (34.5 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 25 °C for 20 h. Purification by column chromatography on silica gel using pentane/DCM (5:1-1:10 v/v) as an eluent provided **3r-mono** (39.6 mg, 30%) as a white solid and **3r-di** (19.1 mg, 19%) as a white solid. **^{1}H NMR of 3r-mono** (400 MHz, $CDCl_3$) δ 8.09 – 8.06 (m, 2H), 7.62 – 7.60 (m, 2H), 6.95 – 6.87 (m, 3H), 3.94 (s, 3H), 3.81 (s, 3H), 3.76 (s, 3H). **^{13}C NMR of 3r-mono** (101 MHz, $CDCl_3$) δ 167.21, 153.94, 150.88, 143.31, 130.63, 129.60 (2C), 129.44 (2C), 128.76, 116.73, 114.00, 112.92, 56.44, 55.96, 52.21. **IR of 3r-mono**: ν 2947, 2838, 1705, 1604, 1579, 1562, 1492, 1456, 1435, 1393, 1378, 1318, 1289, 1277, 1256, 1229, 1209, 1180, 1145, 1104, 1050, 1014, 986, 957, 862, 845, 824, 799, 778, 742, 719, 704, 659, 636, 604, 546, 511, 487, 454, 433 cm^{-1}. **M.P. of 3r-mono** = 77-79 °C. **HRMS** (EI): m/z calculated for $C_{16}H_{16}O_4$ $[M]^+$ = 272.1049; found: 272.1040.

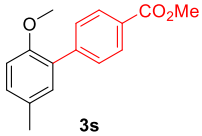


3r-di

^{1}H NMR of 3r-di (400 MHz, $CDCl_3$) δ 8.12-8.10 (d, *J* = 8.4 Hz, 4H), 7.68-7.66 (d, *J* = 8.4 Hz, 4H), 6.99 (s, 2H), 3.95 (s, 6H), 3.81 (s, 6H). **^{13}C NMR of 3r-di** (101 MHz, $CDCl_3$) δ 167.17 (2C), 150.89 (2C), 142.99 (2C), 130.18 (2C), 129.60 (4C), 129.56 (4C), 128.95 (2C), 114.75 (2C), 56.62 (2C), 52.28 (2C). **IR of 3r-di**: ν 2952, 2920, 2851, 1716, 1605, 1567, 1523, 1494, 1464, 1434, 1418, 1389, 1315, 1275, 1213, 1188, 1103, 1057, 1031, 1017, 973, 880, 853, 824, 790, 764, 705, 631, 534, 509, 498, 464 cm^{-1}. **HRMS** (FD): m/z calculated for $C_{24}H_{22}O_6$ $[M]^+$ = 406.1416; found: 406.1420. **M.P. of 3r-di** = 217-219 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 2'-methoxy-5'-methyl-[1,1'-biphenyl]-4-carboxylate (3s)

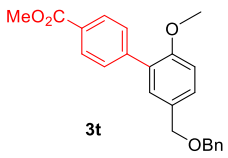


3s

General procedure was followed using 4-methylanisole (**1s**) (94.8 µL, 0.75 mmol, 3.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3s** in 58% ^{1}H NMR yield. Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a colorless oil (37.4 mg, 58%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.06 (m, 2H), 7.62 – 7.60 (m, 2H), 7.17 – 7.15 (m, 2H), 6.92 – 6.90 (m, 1H), 3.94 (s, 3H), 3.79 (s, 3H), 2.35 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.27, 154.52, 143.62, 131.52, 130.27, 129.78, 129.62 (2C), 129.43, 129.36 (2C), 128.50, 111.54, 55.84, 52.16, 20.57. **^{1} IR**: ν 2998, 2950, 2838, 1721, 1609, 1514, 1496, 1463, 1435, 1395, 1311, 1276, 1240, 1180, 1147, 1111, 1103, 1046, 1028, 967, 858, 808, 779, 747, 834, 718, 704, 580 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{16}H_{16}O_3$ $[M]^+$ = 256.1099; found: 256.1094.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 5'-((benzyloxy)methyl)-2'-methoxy-[1,1'-biphenyl]-4-carboxylate (3t)

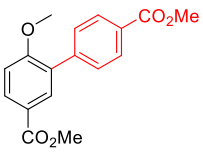


3t

General procedure was followed using 1-((benzyloxy)methyl)-3-methoxybenzene (**1t**) (57.1 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3t** in 58% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/DCM (2:1-1:2 v/v) as an eluent provided the titled compound as a colorless oil (49.0 mg, 54%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.40 – 7.28 (m, 7H), 6.99 (d, *J* = 8.4 Hz, 1H), 4.59 (s, 2H), 4.55 (s, 2H), 3.94 (s, 3H), 3.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.24, 156.22, 143.33, 138.38, 130.82, 130.78, 129.66 (2C), 129.64, 129.39 (2C), 129.26, 128.65, 128.54 (2C), 127.95 (2C), 127.78, 111.44, 72.23, 71.81, 55.84, 52.19. **IR**: ν 2949, 2855, 1721, 1609, 1514, 1496, 1454, 1435, 1401, 1359, 1277, 1244, 1180, 1145, 1103, 1072, 1045, 1027, 859, 816, 779, 738, 702, 464 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{23}H_{22}O_4$ $[M]^+$ = 362.1518; found: 362.1522.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Dimethyl 6-methoxy-[1,1'-biphenyl]-3,4'-dicarboxylate (3u)

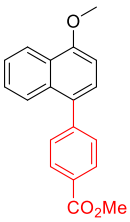


3u

General procedure was followed using methyl 4-methoxybenzoate (**1u**) (83.0 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h, providing **3u** in 56% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (10:1-2:1 v/v) as an eluent provided the titled compound as a white solid (36.1 mg, 48%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 4H), 7.61 – 7.59 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.10, 166.78, 160.22, 142.36, 132.40, 131.54, 129.63 (2C), 129.57, 129.45 (2C), 129.01, 122.91, 110.84, 55.91, 52.22, 52.10. **^{1} IR**: v 2951, 2843, 1718, 1606, 1514, 1495, 1435, 1396, 1312, 1277, 1239, 1183, 1140, 1111, 1040, 1021, 970, 861, 827, 770, 733, 706, 631 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{17}H_{16}O_5$ $[M]^+$ = 300.0998; found: 300.1005. **M.P.** = 115-117 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(4-methoxynaphthalen-1-yl)benzoate (3v)

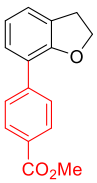


3v

General procedure was followed using 1-methoxynaphthalene (**1v**) (79.0 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3v** in 52% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/DCM (10:1-0:1 v/v) as an eluent provided the titled compound as a white solid (36.8 mg, 50%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 – 8.36 (m, 1H), 8.16 (d, *J* = 8.0 Hz, 2H), 7.84 – 7.82 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.54 – 7.45 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 4.06 (s, 3H), 3.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.25, 155.58, 145.92, 132.20, 131.64, 130.38 (2C), 129.69 (2C), 128.74, 127.20, 126.95, 125.83, 125.44 (2C), 122.47, 103.48, 55.73, 52.26. **^{1} IR**: v 3077, 3047, 3018, 2999, 2949, 2837, 1724, 1606, 1581, 1512, 1461, 1431, 1388, 1371, 1326, 1307, 1272, 1252, 1232, 1204, 1189, 1178, 1152, 1109, 1097, 1082, 1028, 1015, 992, 972, 949, 924, 913, 874, 860, 847, 820, 806, 782, 767, 753, 724, 705, 650, 631, 619, 590, 558, 493, 469, 431, 417 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{19}H_{16}O_3$ $[M]^+$ = 292.1099; found: 292.1110. **M.P.** = 204-206 °C.

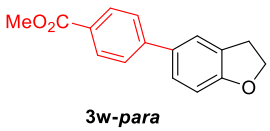
A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(2,3-dihydrobenzofuran-7-yl)benzoate (3w-*ortho*), methyl 4-(2,3-dihydrobenzofuran-5-yl)benzoate (3w-*para*) and dimethyl 4,4'-(2,3-dihydrobenzofuran-5,7-diyl)dibenzoate (3w-di)



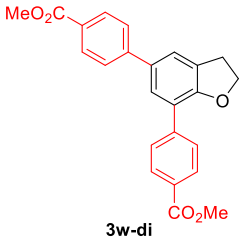
3w-*ortho*

General procedure was followed using 2,3-dihydrobenzofuran (**1w**) (56.5 µL, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h. Purification by column chromatography on silica gel using pentane/DCM (10:1-1:10 v/v) as an eluent provided **3w-*ortho*** (19.8 mg, 30%) as a white solid, **3w-*para*** (18.3 mg, 29%) as a white solid and **3w-di** (14.5 mg, 15%) as a yellow solid. **^{1}H NMR of 3w-*ortho*** (400 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 2H), 7.80 – 7.77 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 4.64 (t, *J* = 8.8 Hz, 2H), 3.93 (s, 3H), 3.28 (t, *J* = 8.4 Hz, 2H). **^{13}C NMR of 3w-*ortho*** (101 MHz, $CDCl_3$) δ 167.22, 157.55, 142.17, 129.79 (2C), 128.61, 128.33 (2C), 128.22, 127.87, 125.00, 122.44, 121.16, 71.34, 52.21, 29.89. **IR of 3w-*ortho***: v 2950, 2924, 2898, 2854, 1718, 1609, 1566, 1476, 1450, 1436, 1400, 1312, 1278, 1200, 1160, 1111, 1062, 1019, 987, 946, 898, 860, 832, 819, 785, 762, 738, 703, 559, 479 cm^{-1}. **HRMS of 3w-*ortho*** (FI): m/z calculated for $C_{16}H_{14}O_3$ $[M]^+$ = 254.0943; found: 254.0938. **M.P. of 3w-*ortho*** = 112-114 °C.



3w-*para*

^{1}H NMR of 3w-*para* (400 MHz, $CDCl_3$) δ 8.08 – 8.06 (m, 2H), 7.61 – 7.59 (m, 2H), 7.47 (s, 1H), 7.39 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 4.64 (t, *J* = 8.8 Hz, 2H), 3.93 (s, 3H), 3.28 (t, *J* = 8.8 Hz, 2H). **^{13}C NMR of 3w-*para*** (101 MHz, $CDCl_3$) δ 167.24, 160.63, 145.88, 132.76, 130.22 (2C), 128.23, 128.08, 127.52, 126.65 (2C), 124.05, 109.81, 71.75, 52.21, 29.80. **IR of 3w-*para***: v 2951, 2924, 2854, 1715, 1604, 1489, 1436, 1404, 1325, 1287, 1242, 1191, 1154, 1116, 980, 942, 856, 846, 820, 771, 700 cm^{-1}. **HRMS of 3w-*para*** (FI): m/z calculated for $C_{16}H_{14}O_3$ $[M]^+$ = 254.0943; found: 254.0938. **M.P. of 3w-*para*** = 124-126 °C.



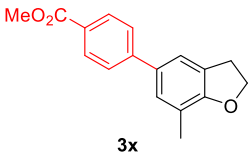
3w-di

^{1}H NMR of 3w-di (300 MHz, $CDCl_3$) δ 8.12 – 8.08 (m, 4H), 7.84-7.81 (m, 2H), 7.66 – 7.63 (m, 2H), 7.57 (d, *J* = 2.1 Hz, 1H), 7.49 (s, 1H), 4.71 (t, *J* = 8.7 Hz, 2H), 3.94 (s, 6H), 3.36 (t, *J* = 8.7 Hz, 2H). **^{13}C NMR of 3w-di** (75 MHz, $CDCl_3$) δ 167.14 (2C), 157.94, 145.56, 141.75, 133.54, 130.30 (2C), 129.89 (2C), 129.30, 128.95, 128.53, 128.40 (2C), 127.27, 126.77 (2C), 123.91, 122.74, 71.91, 52.26 (2C), 29.86. **IR of 3w-di**: v 2951, 2924, 2853, 1720, 1607, 1463, 1435,

1391, 1280, 1185, 1110, 1018, 987, 947, 853, 773, 704 cm^{-1}. **HRMS of 3w-di** (EI): m/z calculated for $C_{24}H_{20}O_5$ $[M]^+$ = 388.1311; found: 388.1303. **M.P. of 3w-di** = 156-158 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^1H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(7-methyl-2,3-dihydrobenzofuran-5-yl)benzoate (3x)

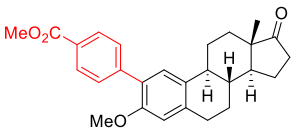


3x

General procedure was followed using 7-methyl-2,3-dihydrobenzofuran (**1x**) (67.0 mg, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2a**) (65.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3x** in 96% ^{1}H NMR yield (*p*/other isomers, 91:9). Purification by column chromatography on silica gel using pentane/DCM (15:1-10:1 v/v) as an eluent provided the titled compound as a white solid (58.5 mg, 87%, *p*/*m*/*m'* 92:3:3). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.30 (s, 1H), 7.23 (s, 1H), 4.62 (t, *J* = 8.8 Hz, 2H), 3.93 (s, 3H), 3.27 (t, *J* = 8.8 Hz, 2H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.22, 159.03, 146.02, 132.61, 130.13 (2C), 128.69, 128.04, 127.21, 126.58 (2C), 121.40, 119.98, 71.39, 52.14, 30.09, 15.48. **IR**: v 2949, 2915, 1716, 1602, 1566, 1479, 1434, 1401, 1379, 1333, 1315, 1276, 1238, 1182, 1167, 1105, 1066, 1029, 1017, 983, 940, 885, 851, 823, 773, 704, 531, 486 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{17}H_{16}O_3$ $[M]^+$ = 268.1099; found: 268.1108.

A parallel reaction without ligand was also performed, and no product was observed by ^1H NMR analysis with CH_2Br_2 as internal standard.

2-(4-Methoxycarbonylphenyl)-estrone methyl ether (3y)

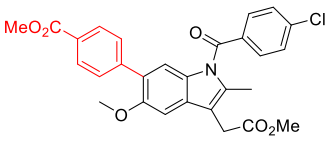


3y

General procedure was followed using estrone methyl ether (**1y**) (71.1 mg, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3y** in 80% ^{1}H NMR yield. Purification by column chromatography on silica gel using pentane/EtOAc (2:1-1:1 v/v) as an eluent provided the titled compound as a white solid (78.3 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.26 (s, 1H), 6.75 (s, 1H), 3.94 (s, 3H), 3.80 (s, 3H), 3.00 – 2.97 (m, 2H), 2.56 – 2.49 (m, 1H), 2.48 – 2.42 (m, 1H), 2.35 – 2.28 (m, 1H), 2.21 – 2.05 (m, 3H), 1.99 – 1.95 (m, 1H), 1.71 – 1.44 (m, 6H), 0.94 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.18, 154.52, 143.64, 137.96, 132.26, 129.51 (2C), 129.32 (2C), 128.32, 127.95 (2C), 127.22, 111.80, 55.70, 52.10, 50.43, 48.05, 43.99, 38.46, 35.92, 31.63, 29.77, 26.60, 26.05, 21.65, 13.92. **^{1} IR**: v 2936, 2881, 2851, 1733, 1718, 1609, 1516, 1492, 1459, 1434, 1394, 1377, 1318, 1307, 1288, 1274, 1251, 1227, 1187, 1159, 1138, 1114, 1103, 1084, 1053, 1040, 1020, 1008, 964, 918, 898, 865, 848, 825, 777, 744, 733, 720, 703, 654, 577, 564, 489, 458, 423 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{27}H_{30}O_4$ $[M]^+$ = 418.2144; found: 418.2150. **M.P.** = 204-206 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^1H NMR analysis with CH_2Br_2 as internal standard.

2-(4-Methoxycarbonylphenyl)-indomethacin methyl ether (3z)

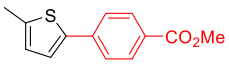


3z

General procedure was followed using indomethacin methyl ether (**1z**) (37.2 mg, 0.1 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (39.3 mg, 0.15 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h. Purification by column chromatography on silica gel using pentane/DCM (2:1-0:1 v/v) as an eluent provided the titled compound as a yellow solid (30.8 mg, 61%, *o*/other isomers 80:20). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.69 – 7.66 (m, 2H), 7.49 – 7.46 (m, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.05 (s, 1H), 7.01 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.73 (s, 3H), 3.71 (s, 2H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.40, 168.36, 167.22, 153.44, 143.82, 139.57, 136.30, 133.92, 131.31 (2C), 130.95, 130.36, 129.68 (2C), 129.33 (2C), 129.27 (2C), 128.38, 126.23, 116.57, 112.54, 100.25, 56.14, 52.35, 52.17, 30.35, 13.62. **^{1} IR**: v 2926, 2850, 1766, 1730, 1719, 1674, 1589, 1467, 1434, 1400, 1347, 1315, 1261, 1217, 1194, 1168, 1147, 1112, 1085, 1040, 1013, 971, 939, 910, 834, 803, 777, 755, 733, 713, 689, 671, 648, 620, 593, 570, 529, 481, 431 cm^{-1}. **HRMS** (FD): m/z calculated for $C_{28}H_{24}ClNO_6$ $[M]^+$ = 505.1292; found: 505.1302.

A parallel reaction without ligand was also performed, and no product was observed by ^1H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(5-methylthiophen-2-yl)benzoate (3aa)

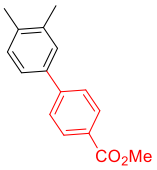


3aa

General procedure was followed using 2-methylthiophene (**1aa**) (24.8 µL, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **3aa** in 47% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (2:1-1:2 v/v) as an eluent provided the titled compound as a brown solid (26.6 mg, 46%, C2/C3 85:15). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 3.6 Hz, 1H), 6.76 (dd, *J* = 3.6, 1.2 Hz, 1H), 3.92 (s, 3H), 2.52 (s, 3H). **IR**: v2955, 2918, 2849, 1708, 1602, 1464, 1440, 1410, 1289, 1273, 1259, 1214, 1193, 1180, 1108, 1055, 1012, 964, 950, 877, 851, 803, 768, 743, 712, 695, 632, 495, 467, 438 cm^{-1}. **^{1}H NMR** spectra data of **3z** matched with the spectra data reported in the literature.[12]

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4-(3,4-dimethylphenyl)benzoate (3ab)

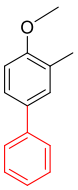


3ab

General procedure was followed using *o*-xylene (**1ab**) (30.5 µL, 0.25 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (**2a**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 40 °C for 20 h, providing **3ab** in 55% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (5:1-1:1 v/v) as an eluent provided the titled compound as a white solid (31.7 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.41 (s, 1H), 7.37 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 3.94 (s, 3H), 2.35 (s, 3H), 2.32 (s, 3H). **^{1}H NMR** spectra data of **3aa** matched with the spectra data reported in the literature.[13]

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4-Methoxy-3-methyl-1,1'-biphenyl (4b)

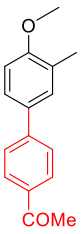


4b

General procedure was followed using 2-methylanisole (**1a**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and iodobenzene (**2b**) (41.8 µL, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **4b** in 48% ^{1}H NMR yield (regioselectivity not determined). Purification by column chromatography on silica gel using pentane/DCM (5:1-1:10 v/v) as an eluent provided the titled compound as a white solid (22.4 mg, 45%, *p*/*m* 97:3). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 – 7.61 (m, 2H), 7.48 – 7.44 (m, 4H), 7.37 – 7.33 (m, 1H), 6.95 – 6.93 (m, 1H), 3.91 (s, 3H), 2.36 (s, 3H). **^{1}H NMR** spectra data of **4b** matched with the spectra data reported in the literature.[14]

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

1-[4-(4-Methoxy-3-methylphenyl)phenyl]ethanone (4c)

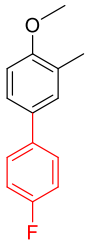


4c

General procedure was followed using 2-methylanisole (**1a**) (63.0 µL, 0.5 mmol, 2.0 equiv.) and methyl 4-iodobenzoate (**2c**) (62.8 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h. Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a pink solid (54.2 mg, 90%, p/m 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.98 (m, 2H), 7.66 – 7.62 (m, 2H), 7.47 – 7.43 (m, 2H), 6.92 – 6.89 (m, 1H), 3.88 (s, 3H), 2.62 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.81, 158.25, 145.69, 135.24, 131.83, 129.58, 128.98 (2C), 127.30, 126.67 (2C), 125.77, 110.33, 55.51, 26.68, 16.49. **IR**: v 2946, 2922, 2843, 1672, 1598, 1556, 1521, 1494, 1468, 1449, 1422, 1395, 1360, 1307, 1296, 1268, 1253, 1191, 1177, 1141, 1119, 1049, 1024, 960, 848, 833, 811, 757, 649, 586 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{16}H_{16}O_2$ $[M]^+$ = 240.1150; found: 240.1160.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4'-Fluoro-4-methoxy-3-methyl-1,1'-biphenyl (4d)

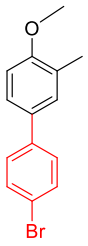


4d

General procedure was followed using 2-methylanisole (**1a**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and 1-fluoro-4-iodobenzene (**2d**) (43.2 µL, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h. Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (40.1 mg, 74%, p/m 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.47 (m, 2H), 7.37 – 7.22 (m, 2H), 7.14 – 7.07 (m, 2H), 6.91 – 6.88 (m, 1H), 3.88 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.17 (d, $J_{C\text{-}F}$ = 246.2 Hz), 157.48, 137.32 (d, $J_{C\text{-}F}$ = 3.23 Hz), 132.53, 129.50, 128.34 (d, $J_{C\text{-}F}$ = 7.88 Hz, 2C), 127.13, 125.38, 115.58 (d, $J_{C\text{-}F}$ = 21.4 Hz, 2C), 110.32, 55.56, 16.51. **NMR** spectra data of **4d** matched with the spectra data reported in the literature.[15] **IR**: v 3001, 2952, 2836, 1606, 1495, 1465, 1442, 1423, 1391, 1307, 1291, 1275, 1244, 1226, 1173, 1159, 1138, 1097, 1054, 1031, 887, 837, 808, 754, 581, 538, 507, 442 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{14}H_{13}FO$ $[M]^+$ = 216.0950; found: 216.0942.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4'-Bromo-4-methoxy-3-methyl-1,1'-biphenyl (4e)

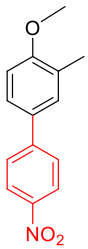


4e

General procedure was followed using 2-methylanisole (**1a**) (63.0 µL, 0.5 mmol, 2.0 equiv.) and 1-bromo-4-iodobenzene (**2e**) (70.8 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h. Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (33.8 mg, 49%, *p*/*m* 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.51 (m, 2H), 7.42 – 7.40 (m, 2H), 7.37 – 7.34 (m, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.78, 140.10, 132.18, 131.86 (2C), 129.38, 128.45 (2C), 127.26, 125.36, 120.76, 110.36, 55.58, 16.52. **NMR** spectra data of **4e** matched with the spectra data reported in the literature.[15] **IR**: v 3016, 2964, 2941, 2923, 2837, 1605, 1515, 1486, 1469, 1440, 1384, 1305, 1289, 1274, 1261, 1140, 1050, 1026, 1005, 884, 829, 805, 502 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{14}H_{13}BrO$ $[M]^+$ = 276.0150; found: 276.0145.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4-Methoxy-3-methyl-4'-nitro-1,1'-biphenyl (4f)

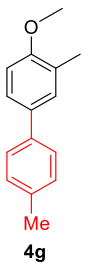


4f

General procedure was followed using 2-methylanisole (**1a**) (63.0 µL, 0.5 mmol, 2.0 equiv.) and 1-iodo-4-nitrobenzene (**2f**) (62.3 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **4f** in 44% ^{1}H NMR yield (*p*/*m*, 93:7). Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as am orange solid (24.8 mg, 41%, pure *para*-). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 – 8.25 (m, 2H), 7.71 – 7.68 (m, 2H), 7.47 – 7.43 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.83, 147.61, 146.57, 130.73, 129.73, 127.69, 127.17 (2C), 126.09, 124.23 (2C), 110.48, 55.62, 16.54. **IR**: v 2926, 2839, 1594, 1559, 1512, 1487, 1465, 1442, 1393, 1341, 1310, 1276, 1253, 1190, 1174, 1140, 1110, 1053, 1028, 887, 851, 812, 755, 722, 696 cm^{-1}. **HRMS** (FI): m/z calculated for $C_{14}H_{13}NO_3$ $[M]^+$ = 243.0895; found: 243.0889. **M.P.** = 83-85 °C.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4-Methoxy-3,4'-dimethyl-1,1'-biphenyl (4g)

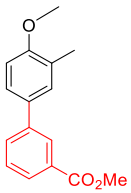


4g

General procedure was followed using 2-methylanisole (**1a**) (94.5 µL, 0.75 mmol, 3.0 equiv.) and 4-iodotoluene (**2g**) (54.5 mg, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 20 h. Purification by column chromatography on silica gel using cyclohexane/EtOAc (1:0-10:1 v/v) as an eluent provided the titled compound as a white solid (18.0 mg, 34%, *p*/*m* 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.40 – 7.37 (m, 2H), 7.23 – 7.21 (m, 2H), 6.90 – 6.88 (m, 1H), 3.87 (s, 3H), 2.39 (s, 3H), 2.29 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.31, 138.33, 136.33, 133.46, 129.52 (2C), 129.47, 126.97, 126.74 (2C), 125.29, 110.30, 55.57, 21.19, 16.53. **NMR** spectra data of **4g** matched with the spectra data reported in the literature.[16] **IR**: v 3026, 2945, 2918, 2856, 2837, 1607, 1497, 1466, 1440, 1291, 1274, 1249, 1214, 1195, 1173, 1138, 1051, 1024, 885, 824, 806, 754, 506 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{15}H_{16}O$ $[M]^+$ = 212.1201; found: 212.1211.

A parallel reaction without ligand was also performed, and 5% product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

Methyl 4'-methoxy-3'-methyl-[1,1'-biphenyl]-3-carboxylate (4h)

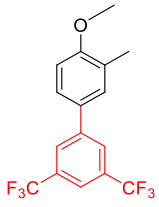


4h

General procedure was followed using 2-methylanisole (**1a**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and methyl 3-iodobenzoate (**2h**) (98.2 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 60 °C for 4 h, providing **4h** in 81% ^{1}H NMR yield (*p*/*m*, 95:5). Purification by column chromatography on silica gel using pentane/DCM (1:2-1:1 v/v) as an eluent provided the titled compound as a colorless oil (48.1 mg, 75%, *p*/*m* 96:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.52 – 7.45 (m, 3H), 6.94 – 6.92 (m, 1H), 3.98 (s, 3H), 3.90 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.31, 157.83, 141.37, 132.22, 131.19, 130.67, 129.52, 128.84, 127.88, 127.69, 127.20, 125.54, 110.31, 55.52, 52.25, 16.47. **IR**: ν 2998, 2951, 2837, 1722, 1610, 1510, 1482, 1438, 1391, 1318, 1284, 1244, 1192, 1173, 1140, 1112, 1085, 1063, 1032, 979, 886, 810, 758, 730, 693, 606 cm^{-1}. **HRMS** (EI): m/z calculated for $C_{16}H_{16}O_3$ $[M]^+$ = 256.1099; found: 256.1111.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

4-Methoxy-3-methyl-3',5'-bis(trifluoromethyl)-1,1'-biphenyl (4i)

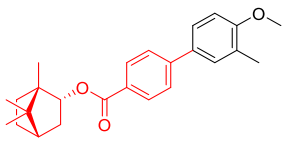


4i

General procedure was followed using 2-methylanisole (**1a**) (63.0 µL, 0.5 mmol, 2.0 equiv.) and 1-iodo-3,5-bis(trifluoromethyl)benzene (**2i**) (44.3 µL, 0.25 mmol, 1.0 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 80 °C for 4 h, providing **4i** in 52% ^{1}H NMR yield (*p*/*m*, 85:15). Purification by column chromatography on silica gel using pentane/DCM (1:0-4:1 v/v) as an eluent provided the titled compound as a colorless oil (40.2 mg, 48%, *p*/*m* 96:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (s, 2H), 7.79 (s, 1H), 7.44 – 7.39 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 3H), 2.31 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.69, 143.26, 132.09 (q, $J_{C\text{-}F}$ = 33.33 Hz, 2C), 130.29, 129.53, 127.86, 126.77 (d, $J_{C\text{-}F}$ = 4.14 Hz, 2C), 125.85, 124.99, 122.27, 120.17 (d, $J_{C\text{-}F}$ = 3.84 Hz), 110.55, 55.64, 16.51. **IR**: ν 2958, 2842, 1611, 1514, 1465, 1442, 1404, 1375, 1278, 1251, 1180, 1130, 1108, 1073, 1034, 923, 884, 846, 811, 705, 683, 609 cm^{-1}. **HRMS** (FD): m/z calculated for $C_{16}H_{12}F_6O$ $[M]^+$ = 334.0792; found: 334.0793.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

(1*S*,2*R*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 4'-methoxy-3'-methyl-[1,1'-biphenyl]-4-carboxylate (4j)



4j

General procedure was followed using 2-methylanisole (**1a**) (31.5 µL, 0.25 mmol, 1.0 equiv.) and (1*S*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 4-iodobenzoate (**2j**) (114 mg, 0.375 mmol, 1.5 equiv.) in HFIP/H_2O (1.5:1, 625 µL, 0.4 M) at 80 °C for 4 h, providing **4j** in 59% ^{1}H NMR yield (*p*/*m*, 90:10). Purification by column chromatography on silica gel using pentane/DCM (5:1-1:1 v/v) as an eluent provided the titled compound as a white solid (53.4 mg, 56%, *p*/*m* 92:8). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 2H), 7.55 – 7.53 (m, 2H), 7.37 – 7.34 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 1H), 5.08 – 5.04 (m, 1H), 3.79 (s, 3H), 2.45 – 2.37 (m, 1H), 2.21 (s, 3H), 2.12 – 2.04 (m, 1H), 1.78 – 1.69 (m, 1H), 1.66 (t, *J* = 8.4 Hz, 1H), 1.38 – 1.30 (m, 1H), 1.28 – 1.21 (m, 1H), 1.06 (dd, *J* = 14.0, 3.6 Hz, 1H), 0.897 (s, 3H), 0.849 (s, 3H), 0.842 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.94, 158.17, 145.47, 132.18, 130.10 (2C), 129.65, 128.97, 127.31, 126.59 (2C), 125.78, 110.35, 80.53, 55.56, 49.25, 48.02, 45.15, 37.08, 28.25, 27.56, 19.87, 19.07, 16.54, 13.77. **IR**: ν 2986, 2954, 2875, 2837, 1703, 1606, 1522, 1492, 1467, 1453, 1441, 1392, 1380, 1368, 1325, 1314, 1281, 1270, 1249, 1180, 1140, 1103, 1054, 1030, 1015, 978, 952, 909, 886, 860, 847, 813, 771, 754, 730, 718, 702, 654, 636, 624, 596, 565, 528, 512, 498, 486, 445 cm^{-1}. **HRMS** (FD): m/z calculated for $C_{25}H_{30}O_3$ $[M]^+$ = 378.2195; found: 378.2194.

A parallel reaction without ligand was also performed, and no product was observed by ^{1}H NMR analysis with CH_2Br_2 as internal standard.

SUPPORTING INFORMATION

Overview of unsuccessful substrates

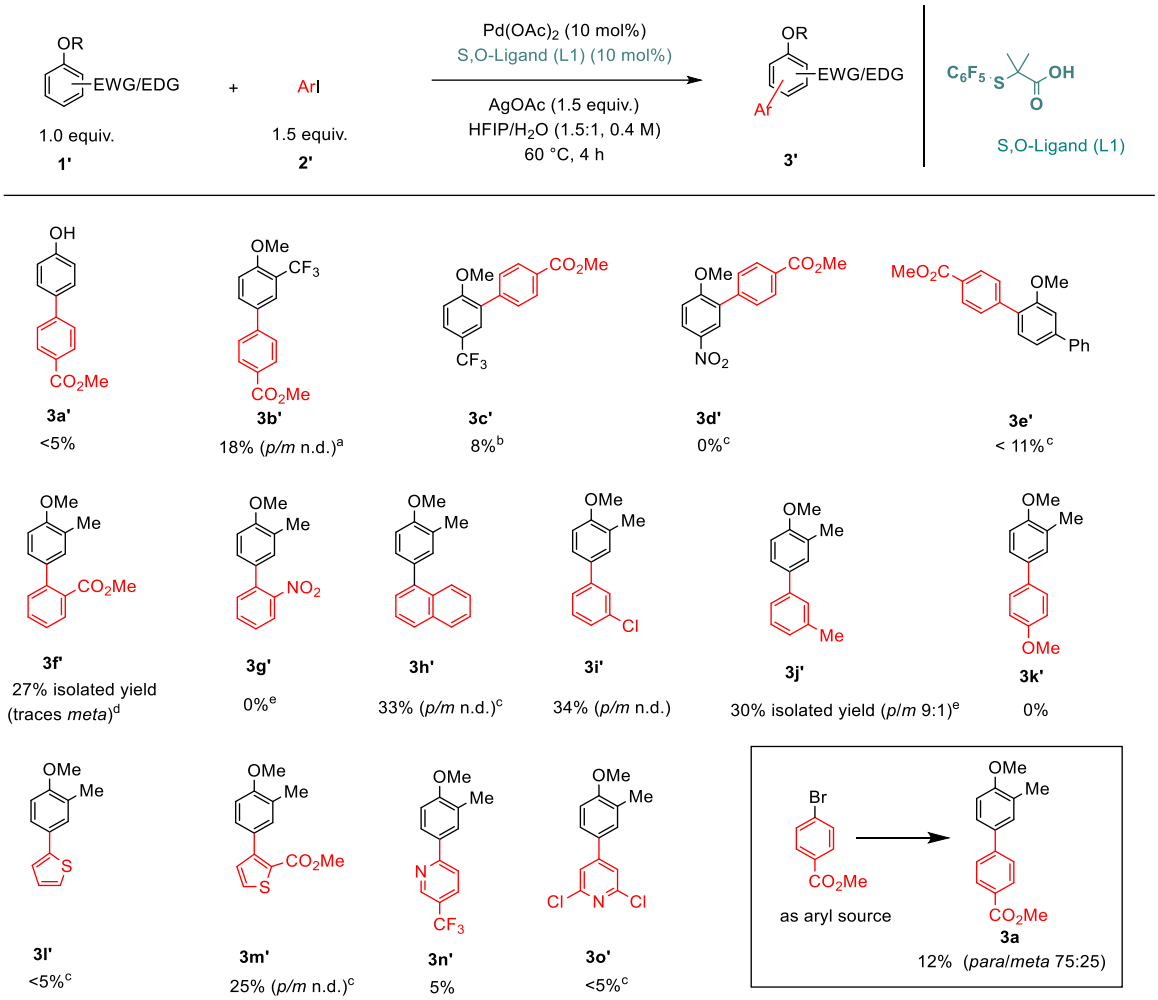


Figure S1. Overview of unsuccessful substrates. **1** (0.1 mmol, 1.0 equiv.), **2** (1.5 equiv.), $Pd(OAc)_2$ (10 mol%), **L1** (10 mol%) and AgOAc (1.5 equiv.) in HFIP/H_2O (1.5:1, 0.4 M) at 60 °C for 4 h; ^1H NMR yields. [a] **1** (2 equiv.), 20 h. [b] **1** (3 equiv.), 20 h. [c] 20 h. [d] 48 h. [e] **1** (2 equiv.).

6. Structural determination of arylated products

Structural determination of arylated products was confirmed by ^1H NMR and 2D NOESY (or 1D NOESY).

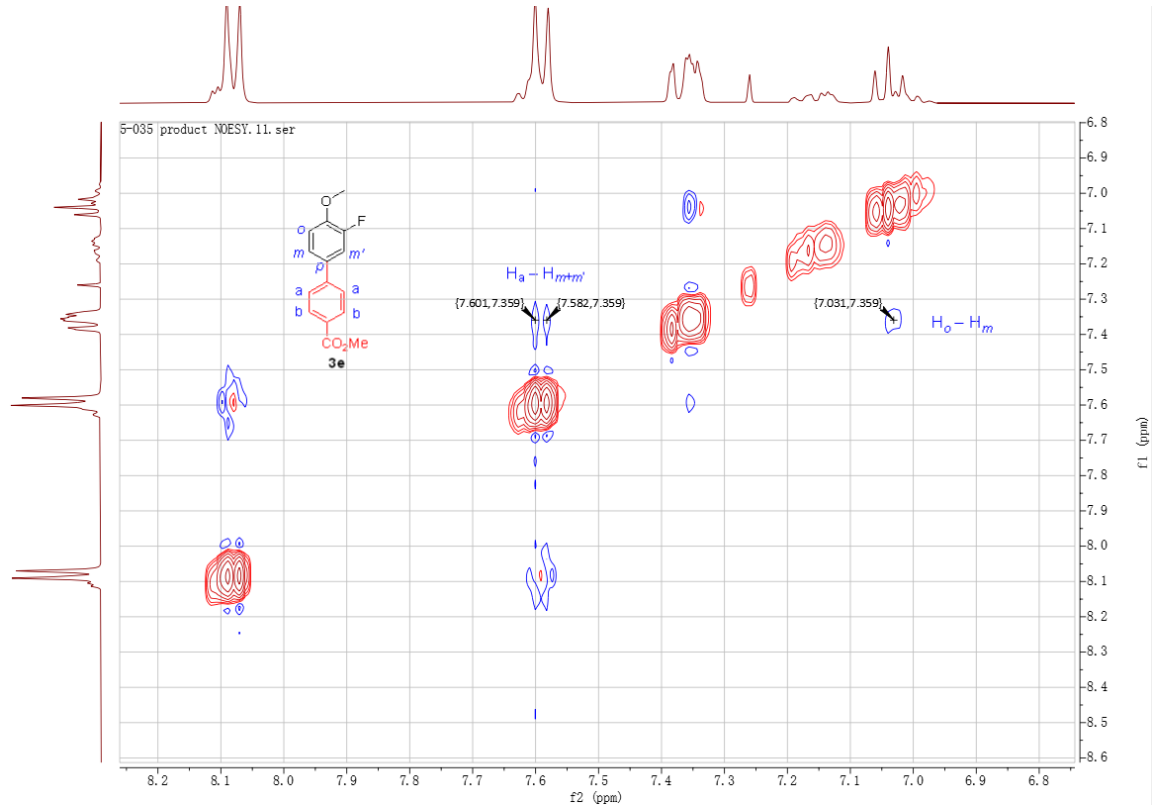


Figure S2. The structure assignment of **3e** by 2D NOESY.

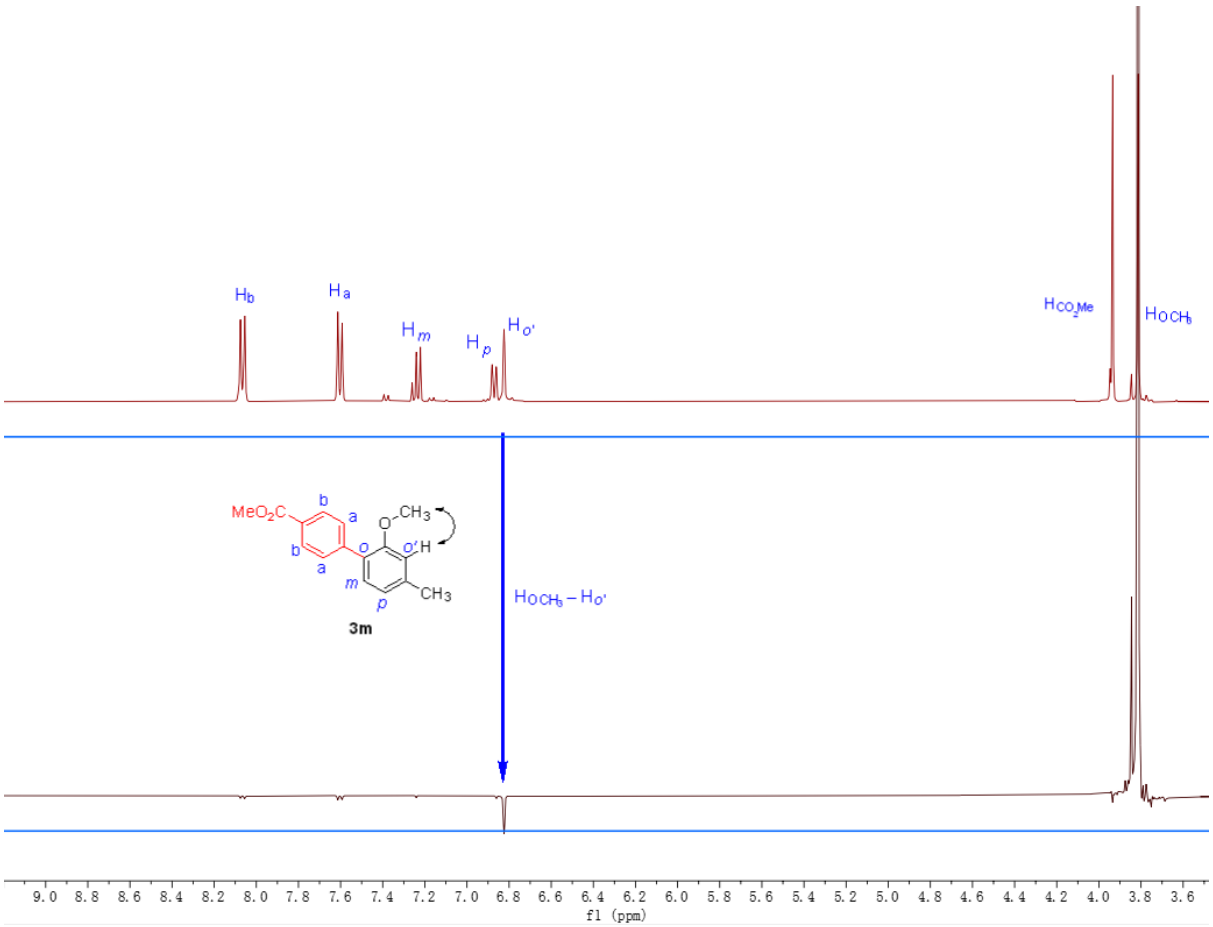


Figure S3. The structure assignment of **3m** by 1D NOESY.

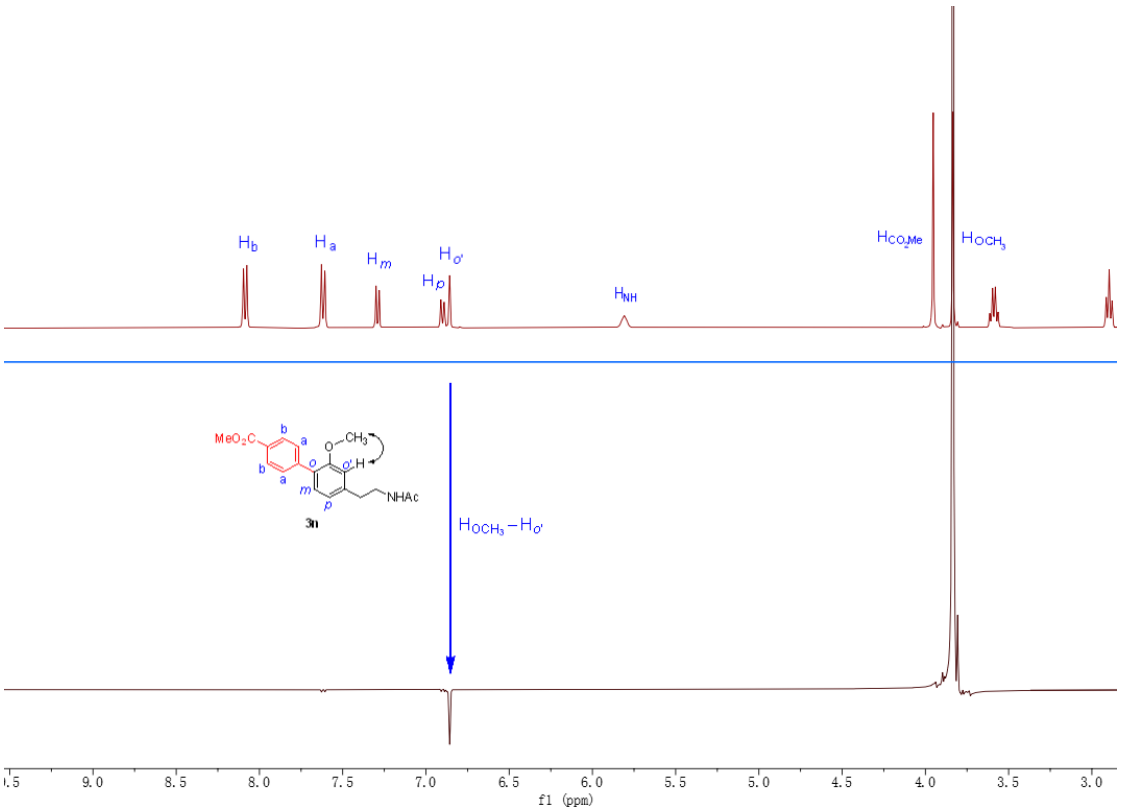


Figure S4. The structure assignment of **3n** by 1D NOESY.

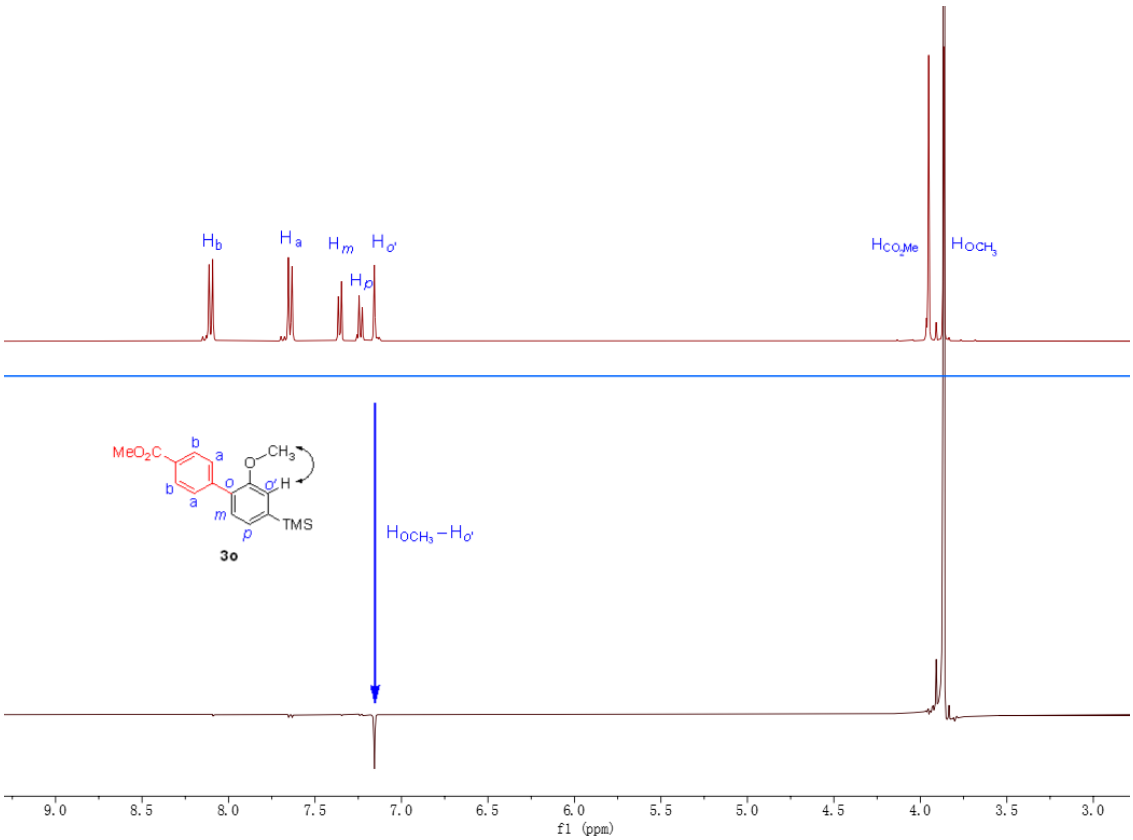


Figure S5. The structure assignment of **3o** by 1D NOESY.

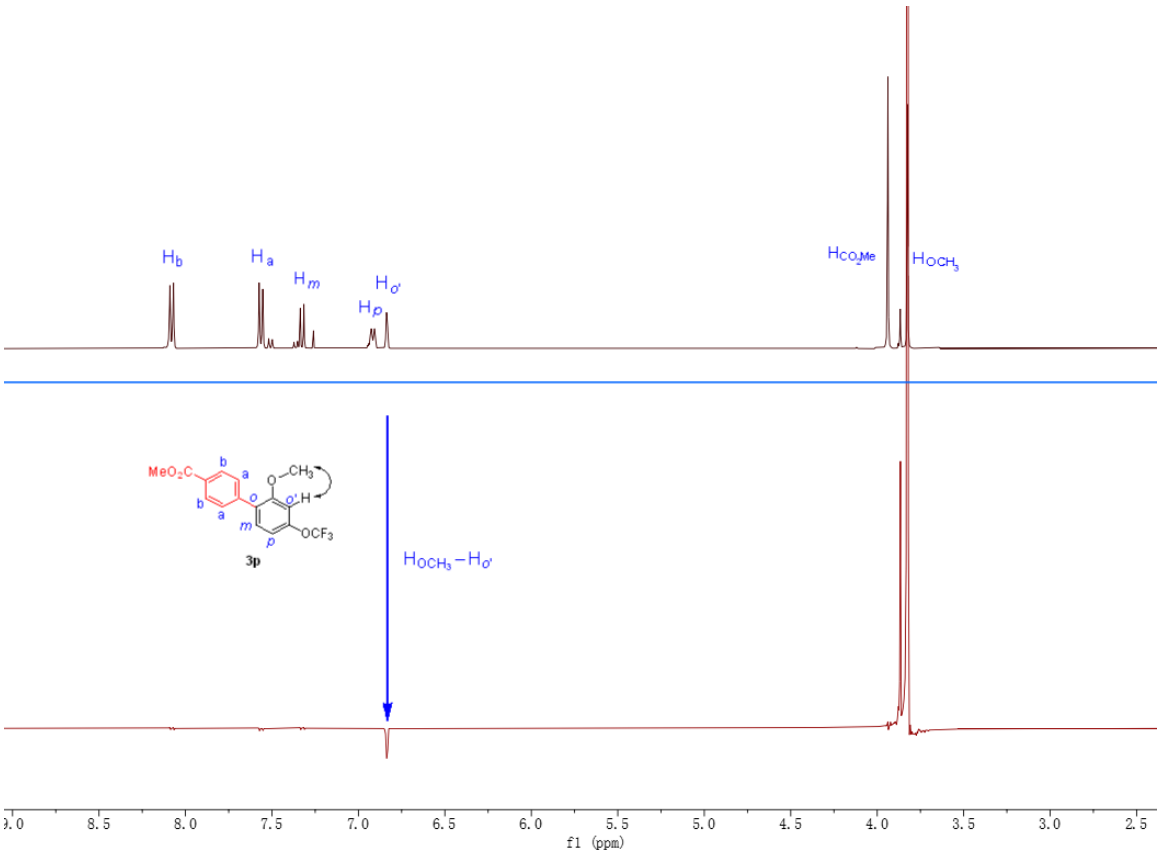


Figure S6. The structure assignment of **3p** by 1D NOESY.

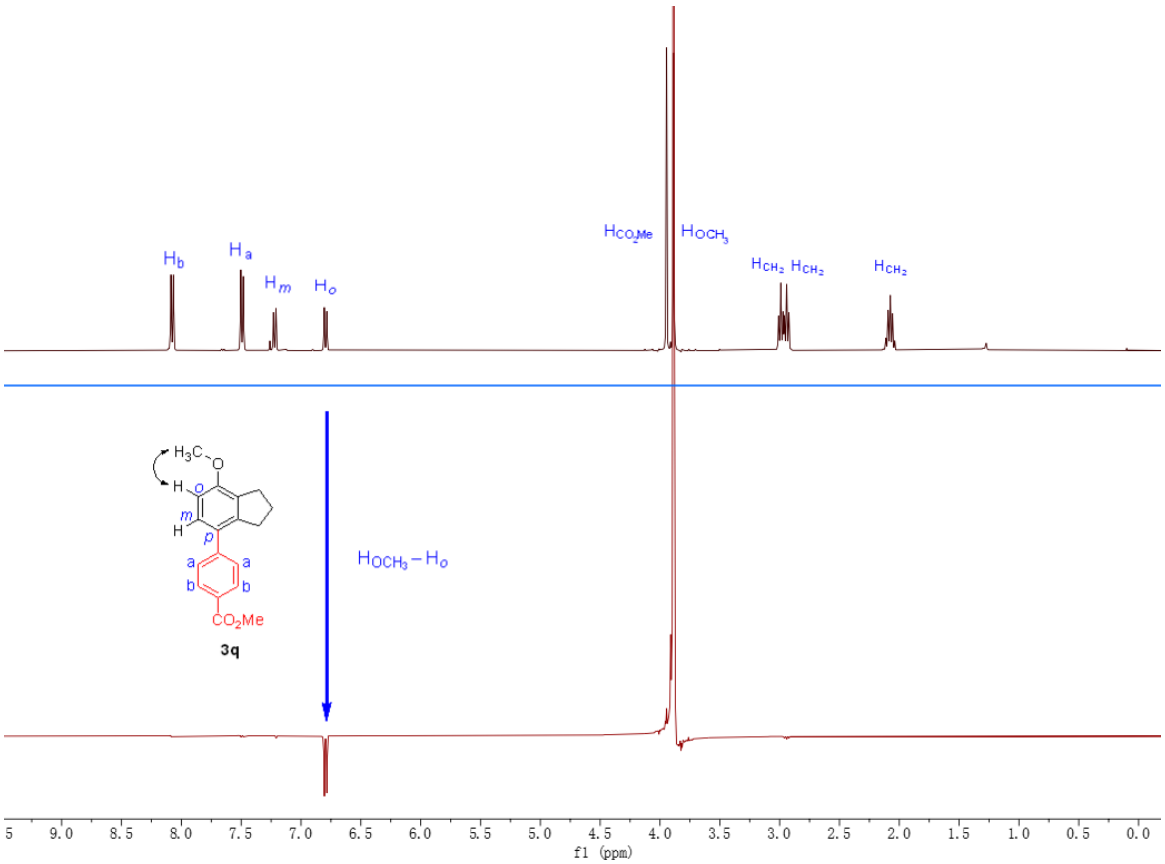


Figure S7. The structure assignment of **3q** by 1D NOESY.

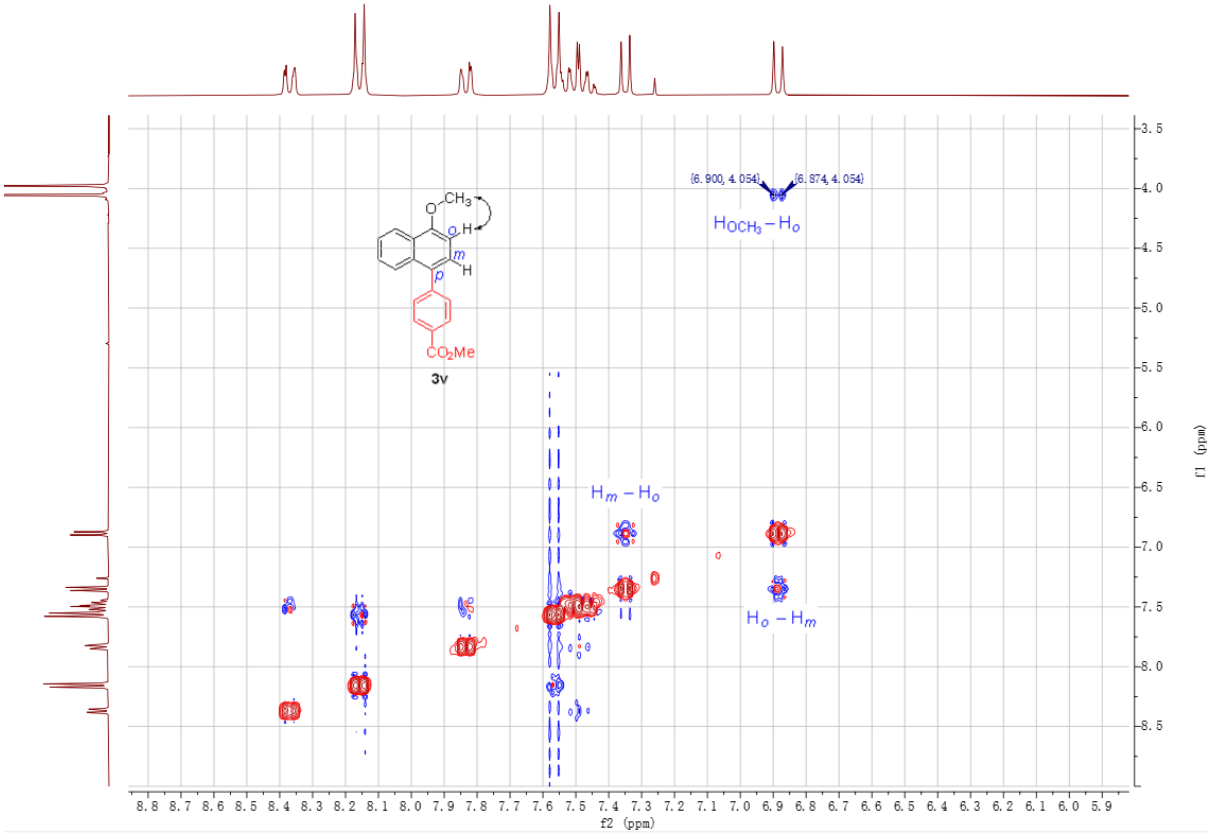


Figure S8. The structure assignment of **3v** by 2D NOESY.

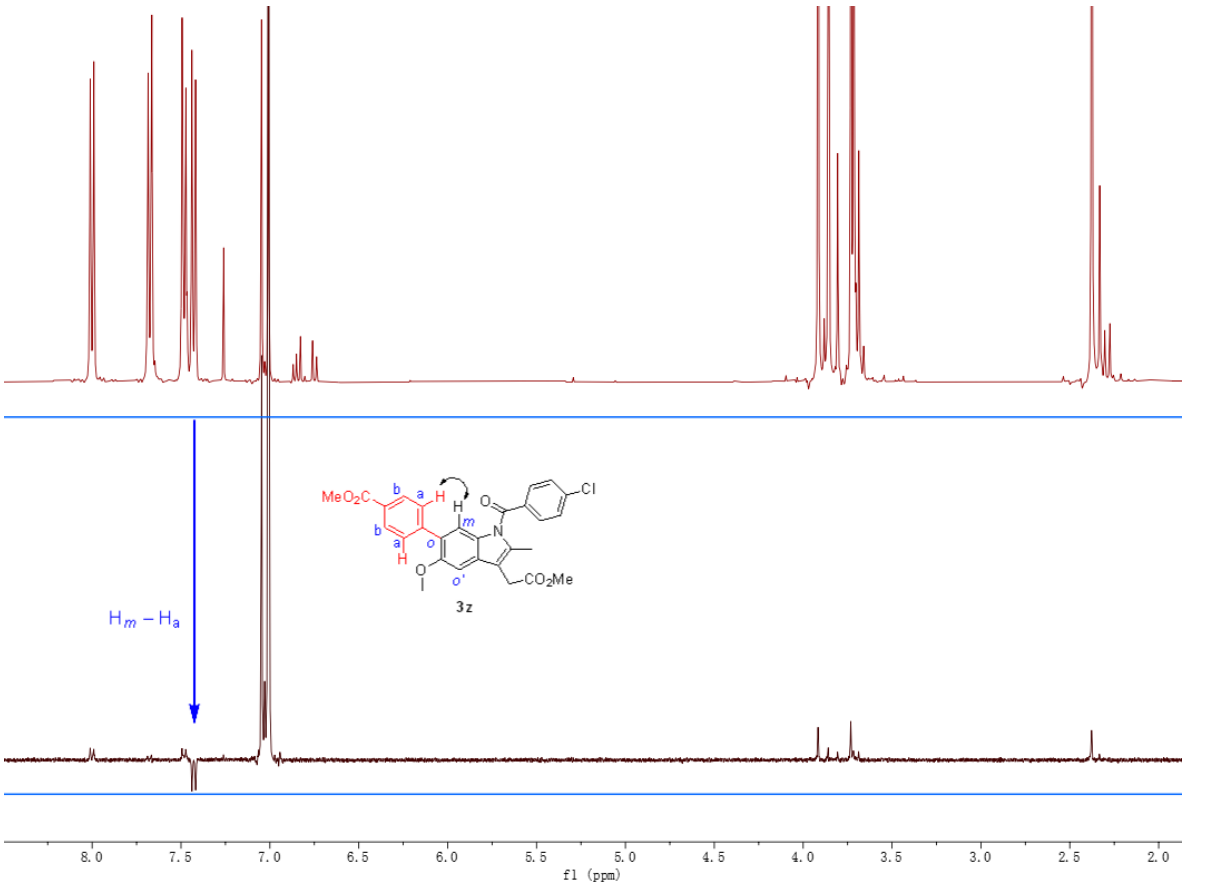
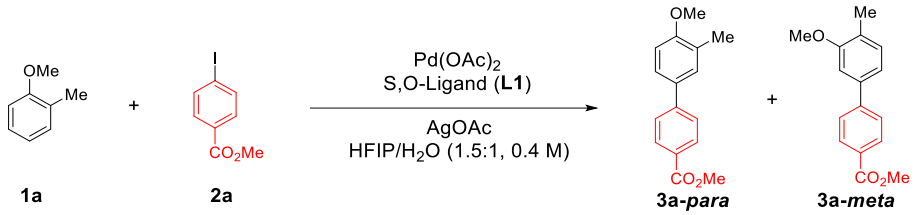


Figure S9. The structure assignment of **3z** by 1D NOESY.

7. Kinetic experiments

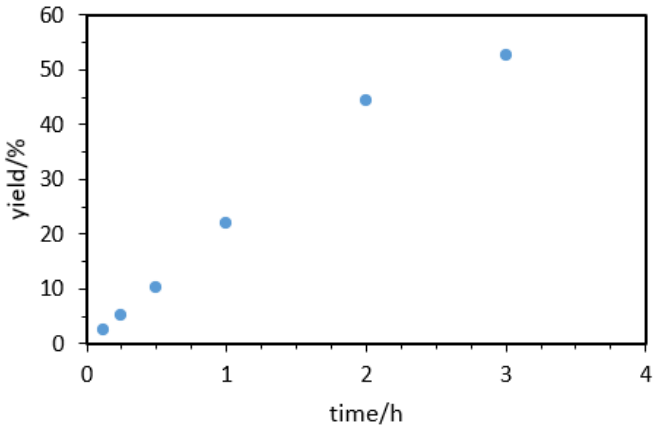
7.1 Kinetic order measurement



1a **2a** **3a-*para*** **3a-*meta***

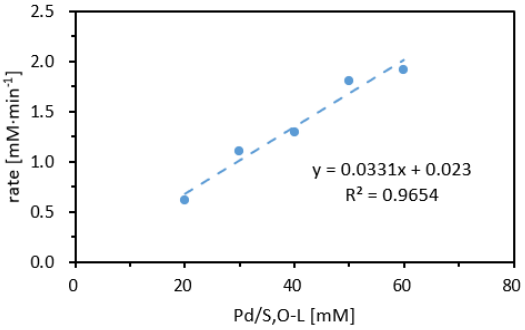
Procedure: The kinetic order of each reagent in the arylation reaction was determined using the method of initial rates.[17] A stock solution of $Pd(OAc)_2$ and S,O-ligand **L1** in HFIP was prepared. Pressure tubes containing a suitable stirring bar were equipped with methyl 4-iodobenzoate, AgOAc, the stock solution of $Pd(OAc)_2$ and S,O-ligand **L1**, HFIP, H_2O and 2-methylanisole **1a** (reaction scale: 0.1 mmol). The tubes were put into a pre-heated oil bath at 25 °C and were stirred for 30 min (according to the reaction profile**, Table S12**). Afterwards, the tubes were promptly cooled using a mixture of dry ice and acetone, each reaction was filtered through Celite® and rinsed with DCM. To each crude mixture, CH_2Br_2 (10 µL, 0.144 mmol) was added as internal standard, the mixture was dissolved in $CDCl_3$ and ^1H NMR was measured.

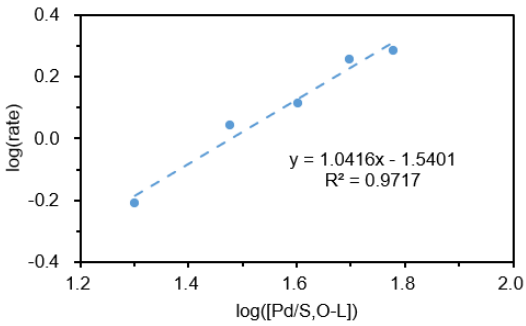
Table S12. Reaction profile at 25 °C



Entry	time/h	yield of *para*/%	yield of *meta*/%	total yield/%
1	7.5 min	2.5	0	2.5
2	15 min	5.2	0	5.2
3	30 min	9.8	0.5	10.3
4	1	20.2	1.9	22.1
5	2	40.8	3.7	44.5
6	3	47.9	4.7	52.6

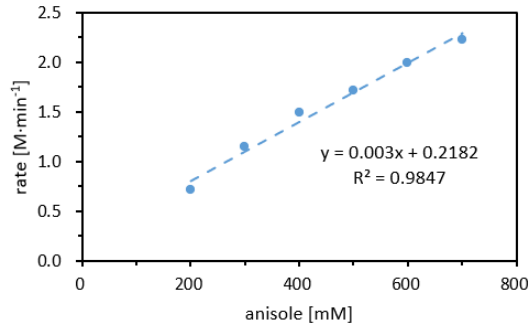
Table S13. Kinetic order of Pd/S,O-ligand.

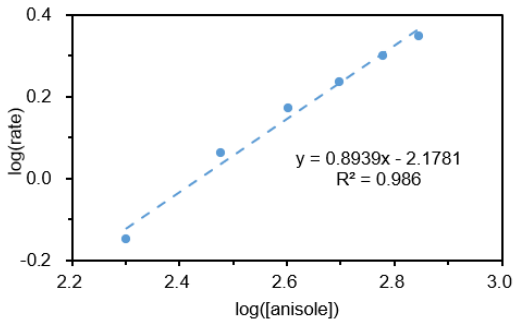




[Pd/S,O-L]/mol%	[Pd/S,O-L]/mM	log[mM]	yield/%	rate/mM*min^{-1}	log[rate]
5	20	1.30	4.6	0.61	-0.21
7.5	30	1.48	8.3	1.10	0.04
10	40	1.60	9.7	1.30	0.11
12.5	50	1.70	13.5	1.80	0.26
15	60	1.78	14.4	1.92	0.28

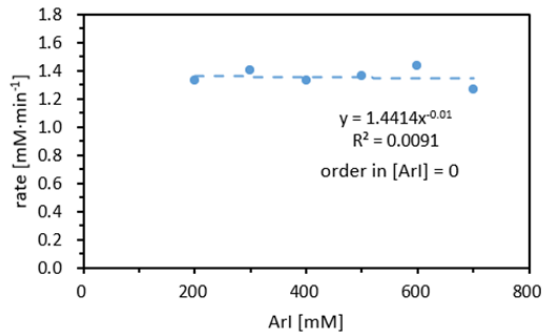
Table S14. Kinetic order of anisole.





[anisole]/equiv.	[anisole]/mM	log[mM]	yield/%	rate/mM*min^{-1}	log[rate]
0.5	200	2.30	5.3	0.71	-0.15
0.75	300	2.48	8.6	1.15	0.06
1	400	2.60	11.2	1.49	0.17
1.25	500	2.70	12.9	1.72	0.24
1.5	600	2.78	15.0	2.00	0.30
1.75	700	2.85	16.7	2.23	0.35

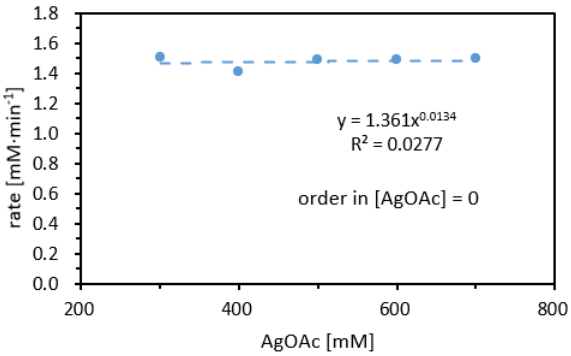
Table S15. Kinetic order of aryl iodide.



[ArI]/equiv.	[ArI]/mM	yield/%	rate/mM*min^{-1}
0.5	200	10.0	1.33
0.75	300	10.6	1.40
1	400	9.9	1.33
1.25	500	10.2	1.37
1.5	600	10.7	1.43
1.75	700	9.5	1.27

The plots of the reaction rates against [ArI] provide a straight line with slope close to zero, revealing that the reaction is of zero order in aryl iodide.

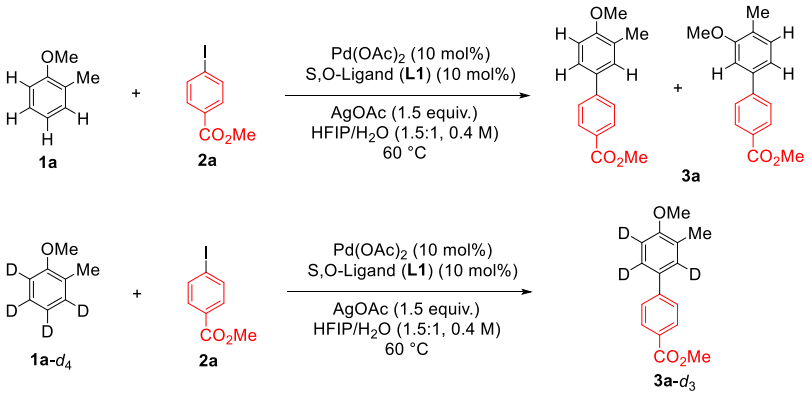
Table S16. Kinetic order of AgOAc.



[ArI]/equiv	[ArI]/mM	yield/%	rate/mM*min^{-1}
0.75	300	11.3	1.51
1	400	10.6	1.41
1.25	500	11.2	1.49
1.5	600	11.2	1.49
1.75	700	11.2	1.50

The plots of the reaction rates against [AgOAc] provide a straight line with slope close to zero, revealing that the reaction is of zero order in AgOAc.

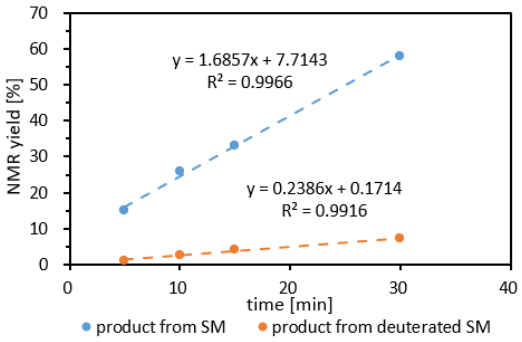
7.2 Parallel KIE experiment



Deuterated 2-methylanisole (**1a-*d*$_4$**) was synthesized according to the reported procedure.[18] A stock solution of $Pd(OAc)_2$ (9.0 mg, 0.04 mmol) and S,O-ligand **L1** (11.4 mg, 0.04 mmol) in 400 µL HFIP was prepared. Pressure tubes containing a suitable stirring bar were equipped with deuterated 2-methylanisole (**1a-*d*$_4$**) (12.6 mg, 0.1 mmol, 1.0 equiv.), methyl 4-iodobenzoate (**2a**) (39.3 mg, 0.15 mmol, 1.5 equiv.), AgOAc (25.0 mg, 0.15 mmol, 1.5 equiv.), 100 µL of the Pd/S,O-ligand stock solution, 50 µL HFIP and 100 µL H_2O. The tubes were put into a pre-heated oil bath at 60 °C and were stirred for 5, 10, 15, 30 min. Afterwards, the tubes were promptly cooled using a mixture of dry ice and acetone, each reaction was filtered through Celite® and rinsed with DCM. To each crude

mixture, CH_2Br_2 (10 μL, 0.144 mmol) was added as internal standard, the mixture was dissolved in $CDCl_3$ and ^1H NMR was measured. A parallel experiment using 2-methylanisole **1a** was performed as well.

Table S17. Parallel KIE experiment.

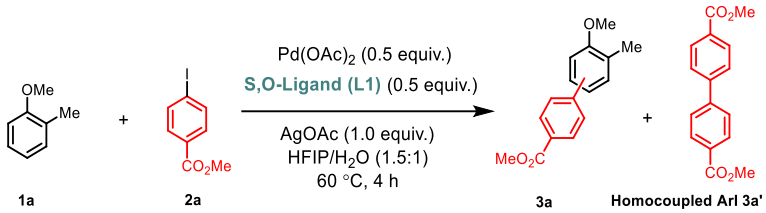


Deuterium KIE = 1.68/0.24 = 7

Product from deuterated 2-methylanisole **1a-*d*$_4$**				
Entry	Time/min	yield of *para*/%	yield of *meta*/%	total yield/%
1	5	1.2	0	1.2
2	10	2.5	0	2.5
3	15	4.1	0	4.1
4	30	7.2	0	7.2

Product from 2-methylanisole **1a**				
Entry	Time/min	yield of *para*/%	yield of *meta*/%	total yield/%
1	5	13	2	15
2	10	24	2	26
3	15	31	2	33
4	30	55	3	58

8. Control experiments

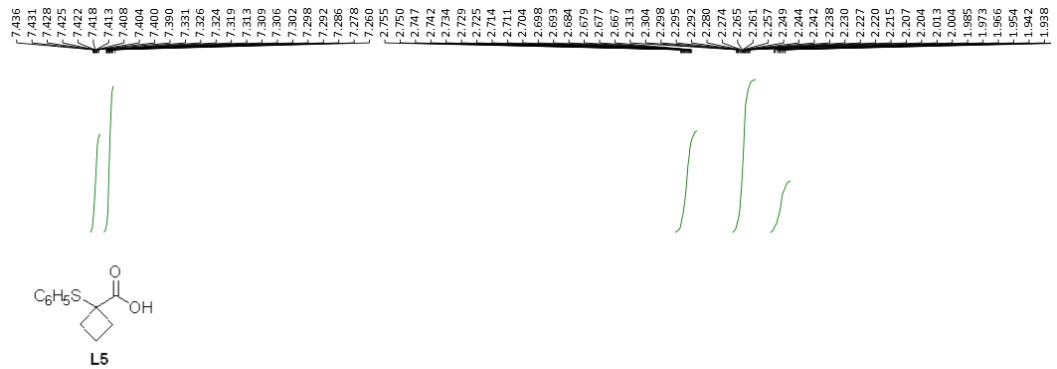


Procedure: Pressure tubes containing a suitable stirring bar were equipped with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol, 0.5 equiv.) and S,O-ligand **L1** (14.3 mg, 0.05 mmol, 0.5 equiv.), methyl 4-iodobenzoate **2a** (26.2 mg, 0.1 mmol, 1.0 equiv.), AgOAc (16.7 mg, 0.1 mmol, 1.0 equiv.), 150 µL HFIP, 100 µL H_2O and the corresponding amount of 2-methylanisole **1a** (0-6.3 µL, 0-0.05 mmol, 0-0.5 equiv.). The tubes were put into a pre-heated oil bath at 60 °C and were stirred for 4 h. After cooling to room temperature, the resulting mixture was diluted with DCM, filtered through a plug of Celite® and concentrated under reduced pressure. To each crude mixture, CH_2Br_2 (10 µL, 0.144 mmol) was added as internal standard, the mixture was dissolved in $CDCl_3$ and ^1H NMR was measured.

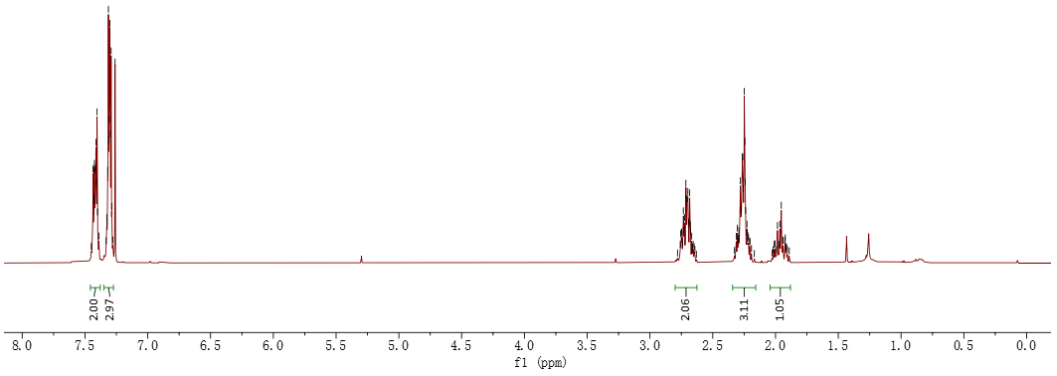
Table S18. Control experiments.

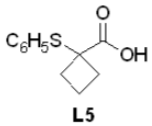
Entry	**1a** (equiv.)	**2a** (equiv.)	Yield of **3a**/%[a]	Yield of **3a'**/%[a]
1	0	1	0	0
2	0.1	1	5	5
3	0.2	1	11	9
4	0.5	1	21	14

9. ^{1}H NMR and ^{13}C NMR spectra

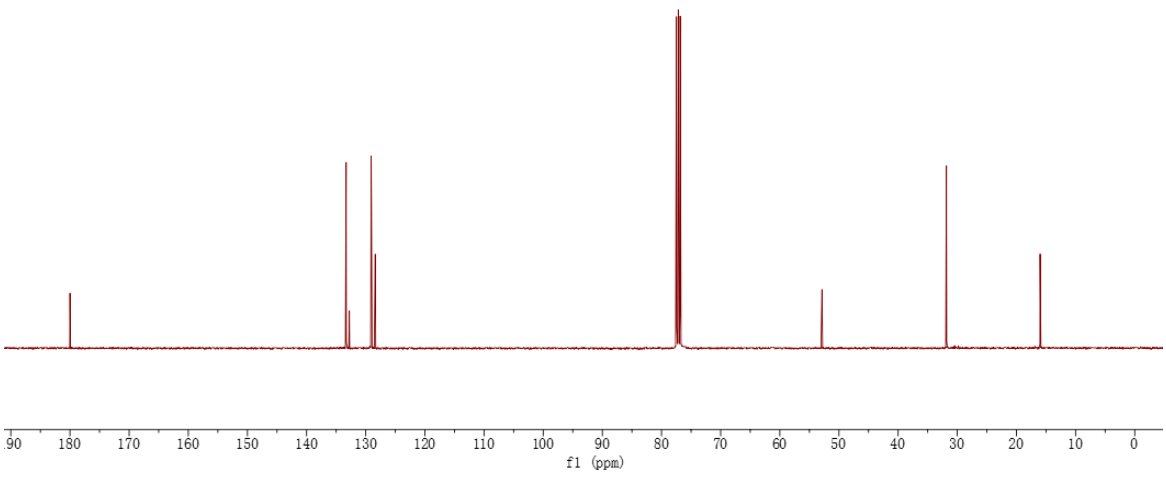


L5

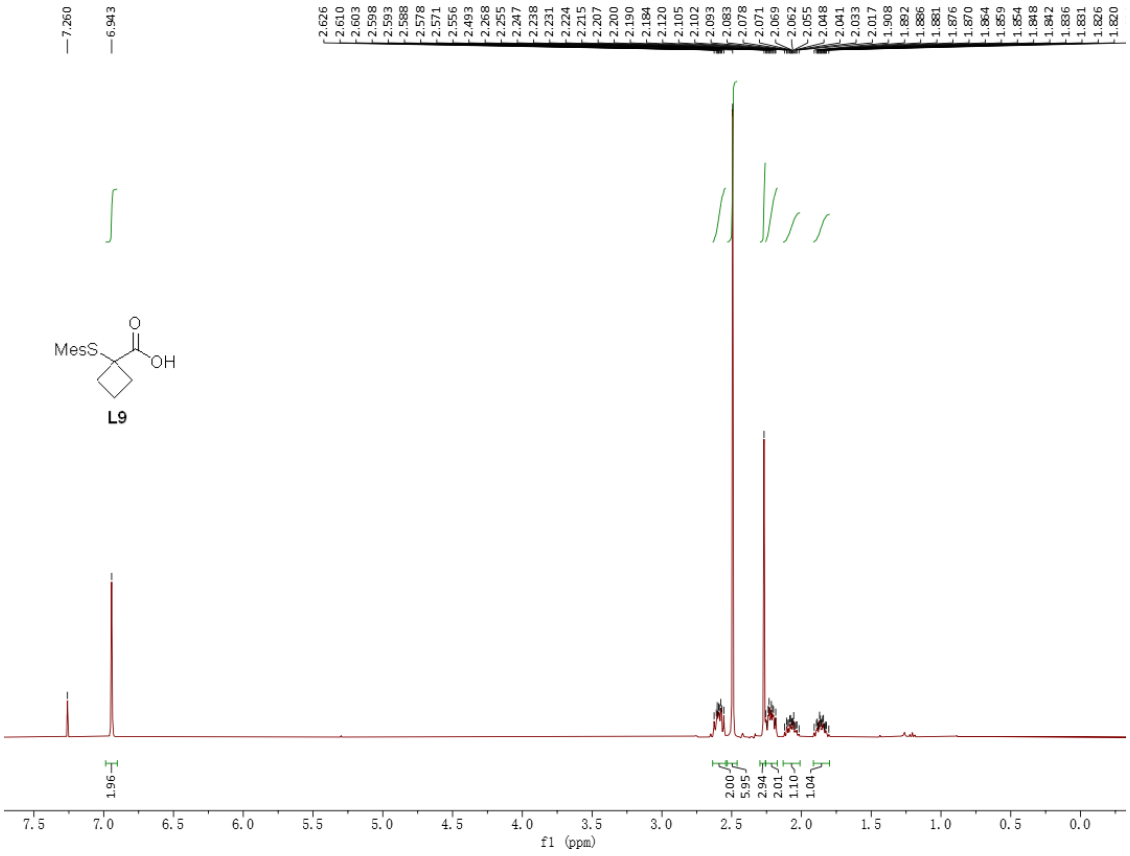


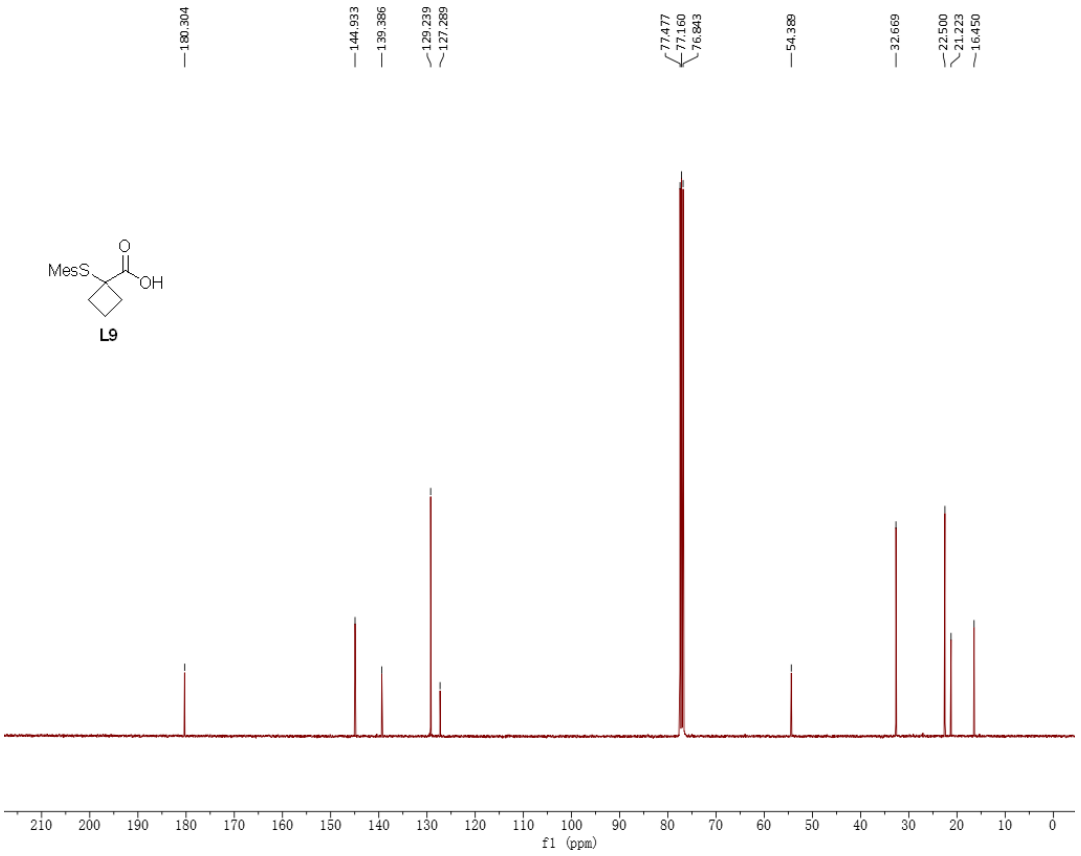


L5

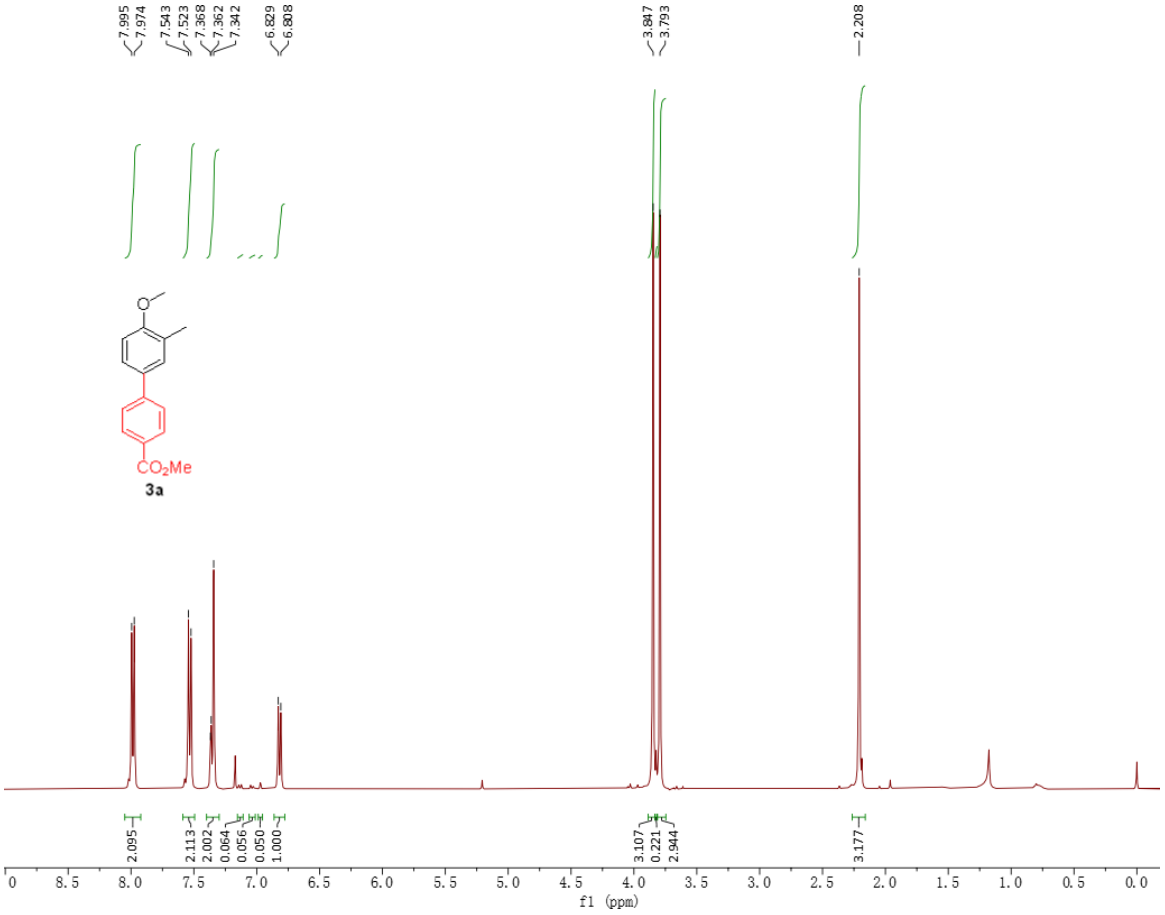


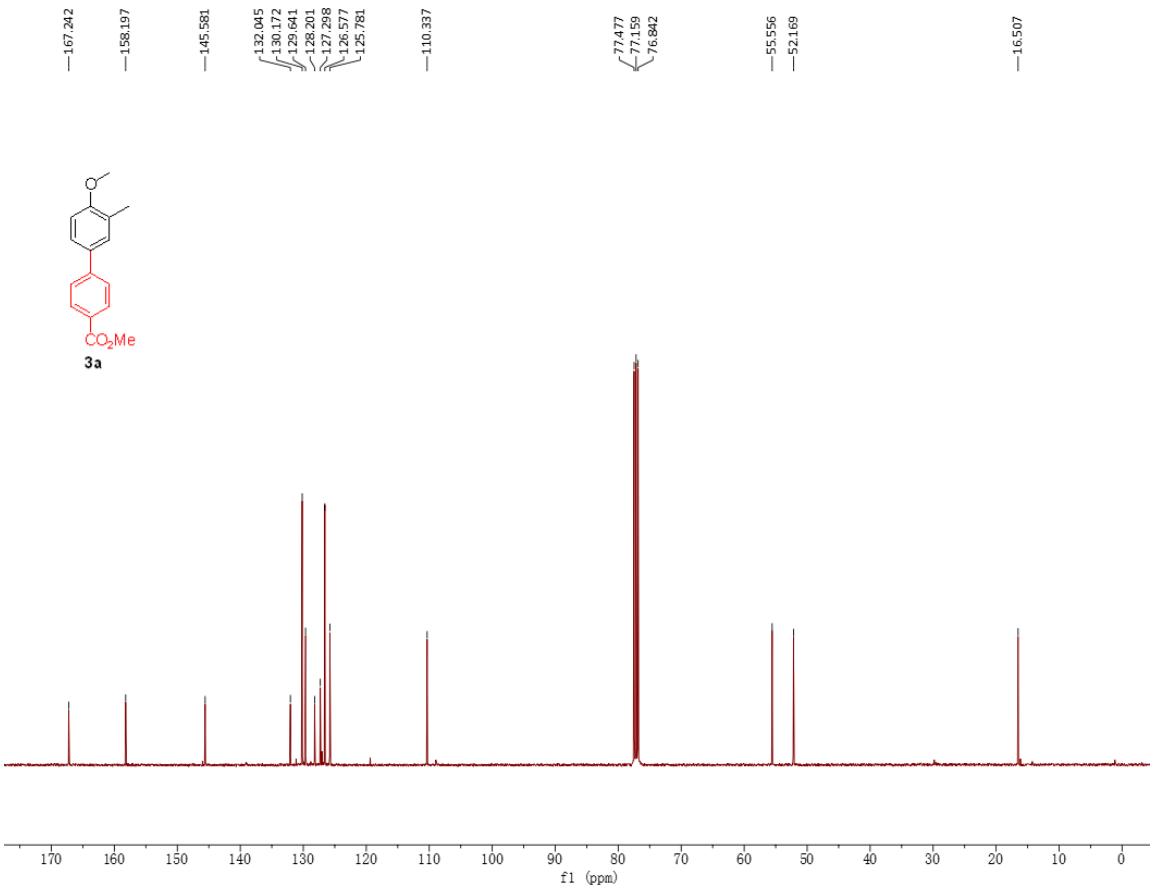
SUPPORTING INFORMATION

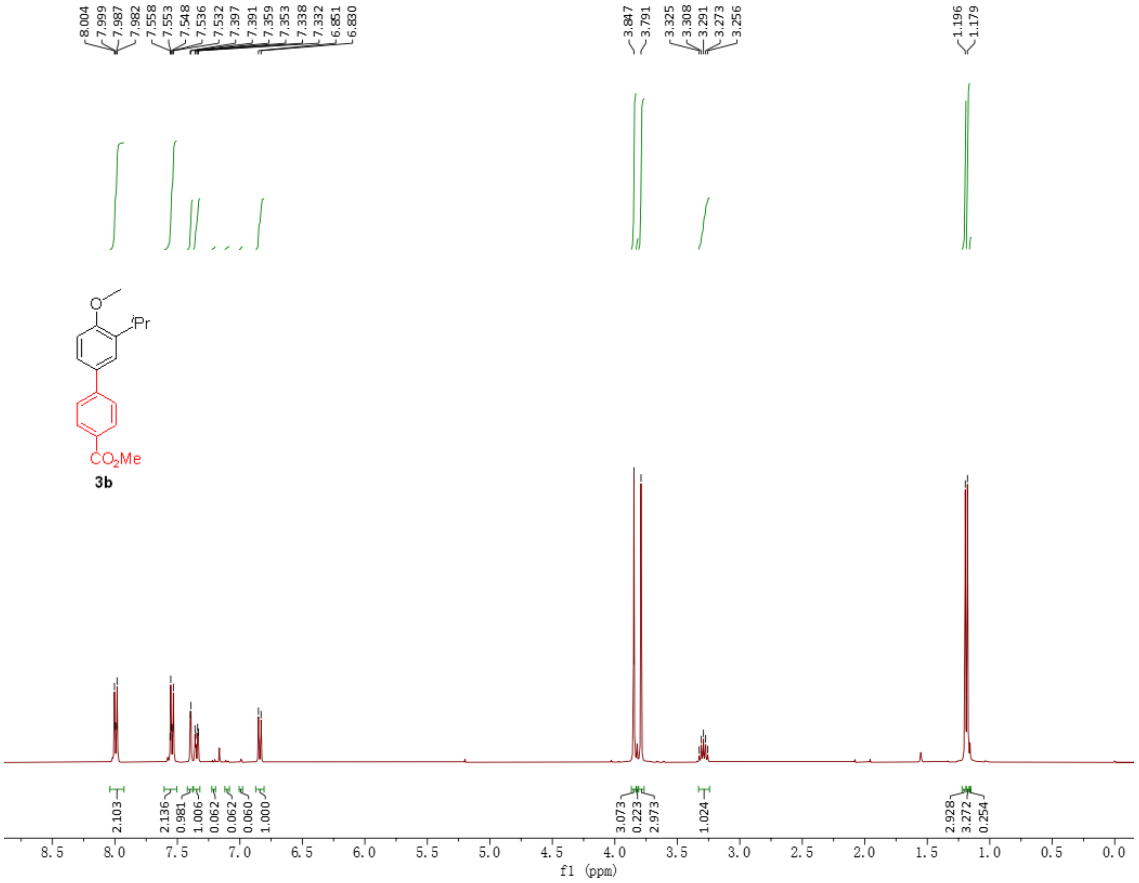




SUPPORTING INFORMATION



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7.353
7.338
7.332
6.851
6.830
3.847
3.791
3.325
3.308
3.291
3.273
3.256
1.196
1.179
iPr
O
CO2Me
3b
2.103
2.136
0.981
1.006
0.062
0.062
0.060
1.000
3.073
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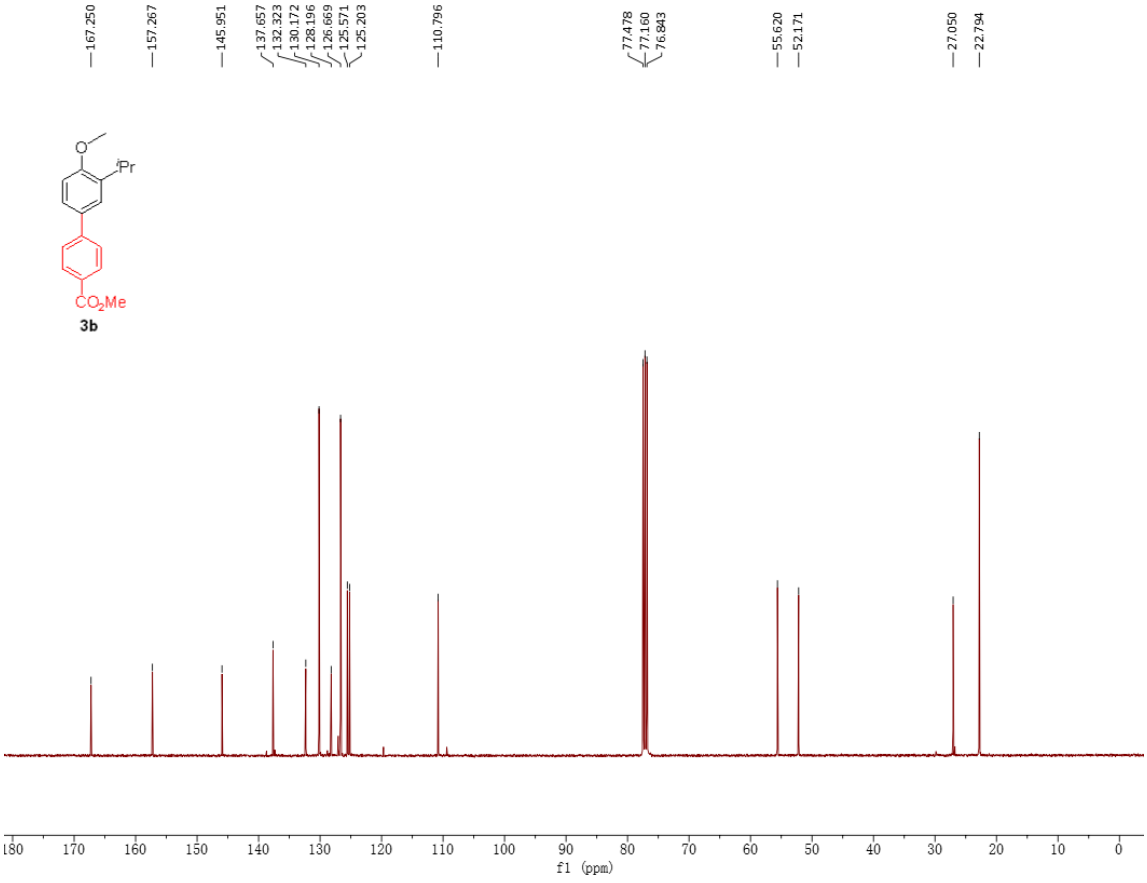
2.928
3.272
0.254
f1 (ppm)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126.669
125.571
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76.843
55.620
52.171
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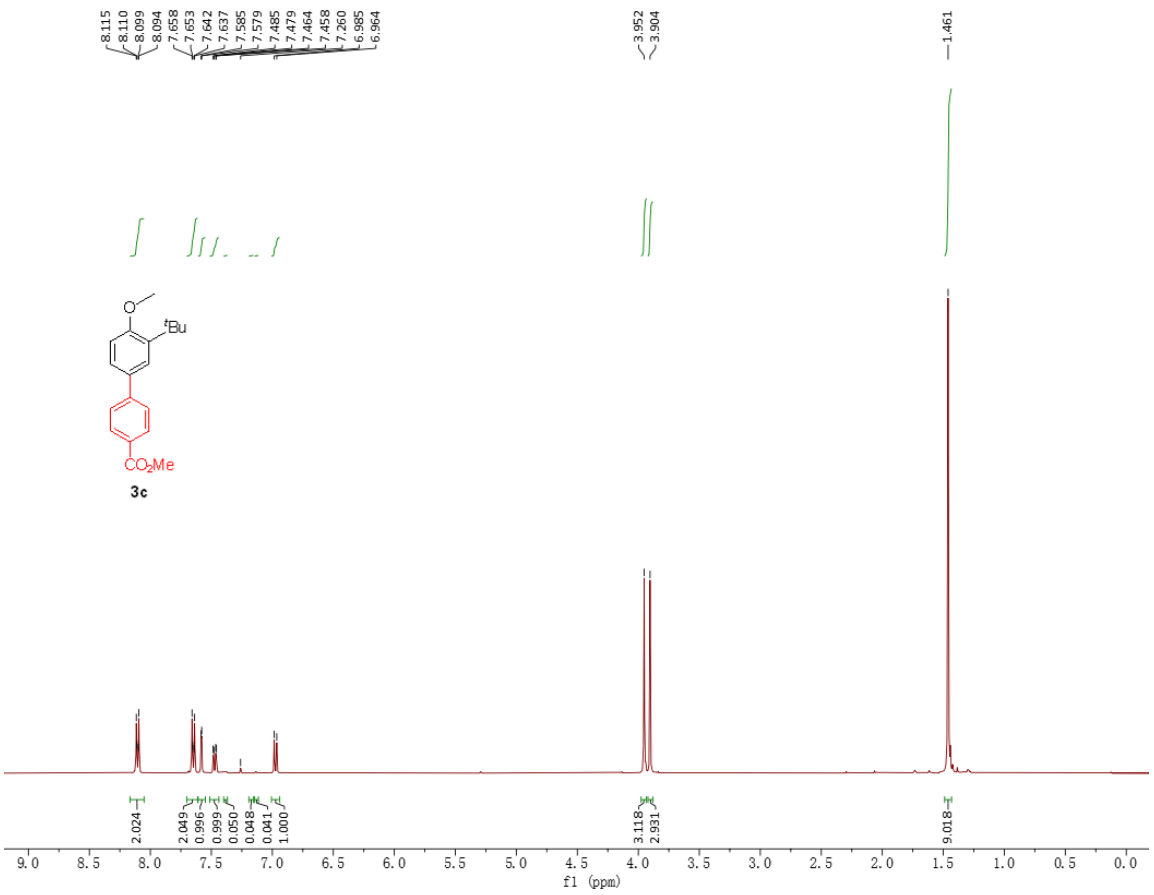
22.794
iPr
O
CO2Me
3b
f1 (ppm)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7.485
7.479
7.464
7.458
7.260
6.985
6.964
3.952
3.904
1.461
tBu
CO2Me
3c
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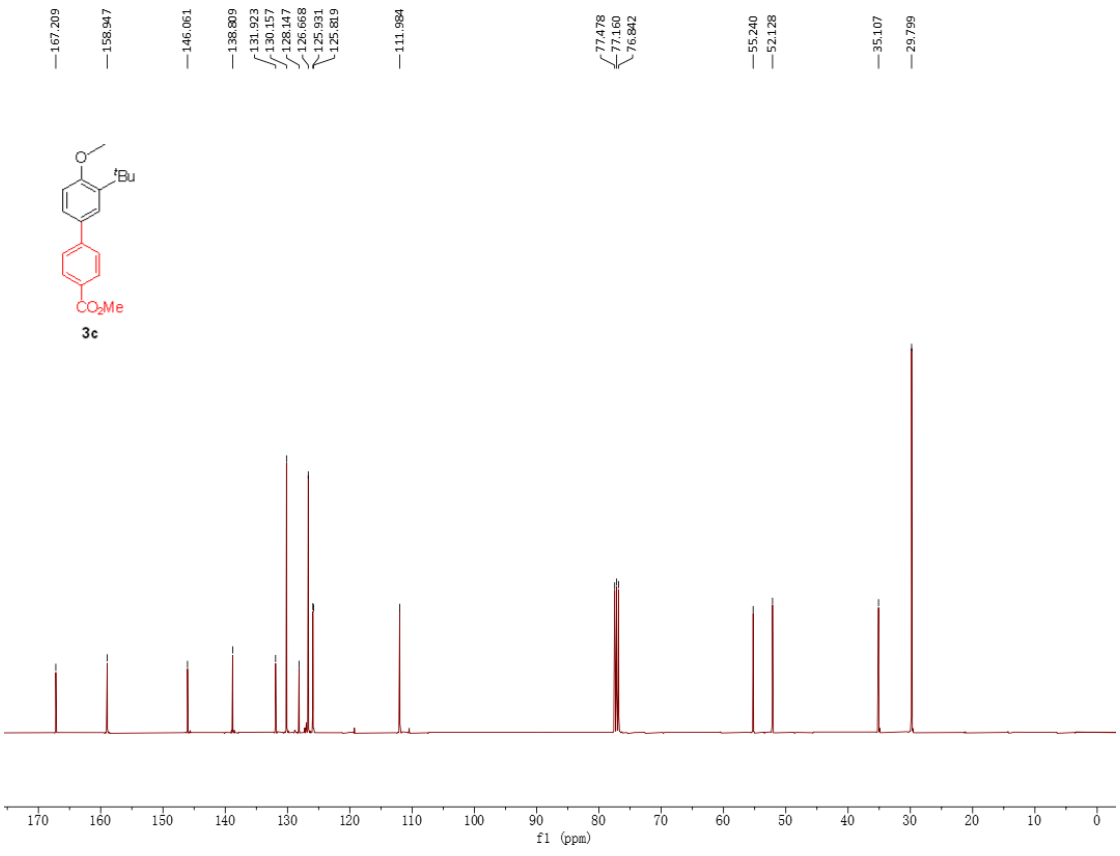
f1 (ppm)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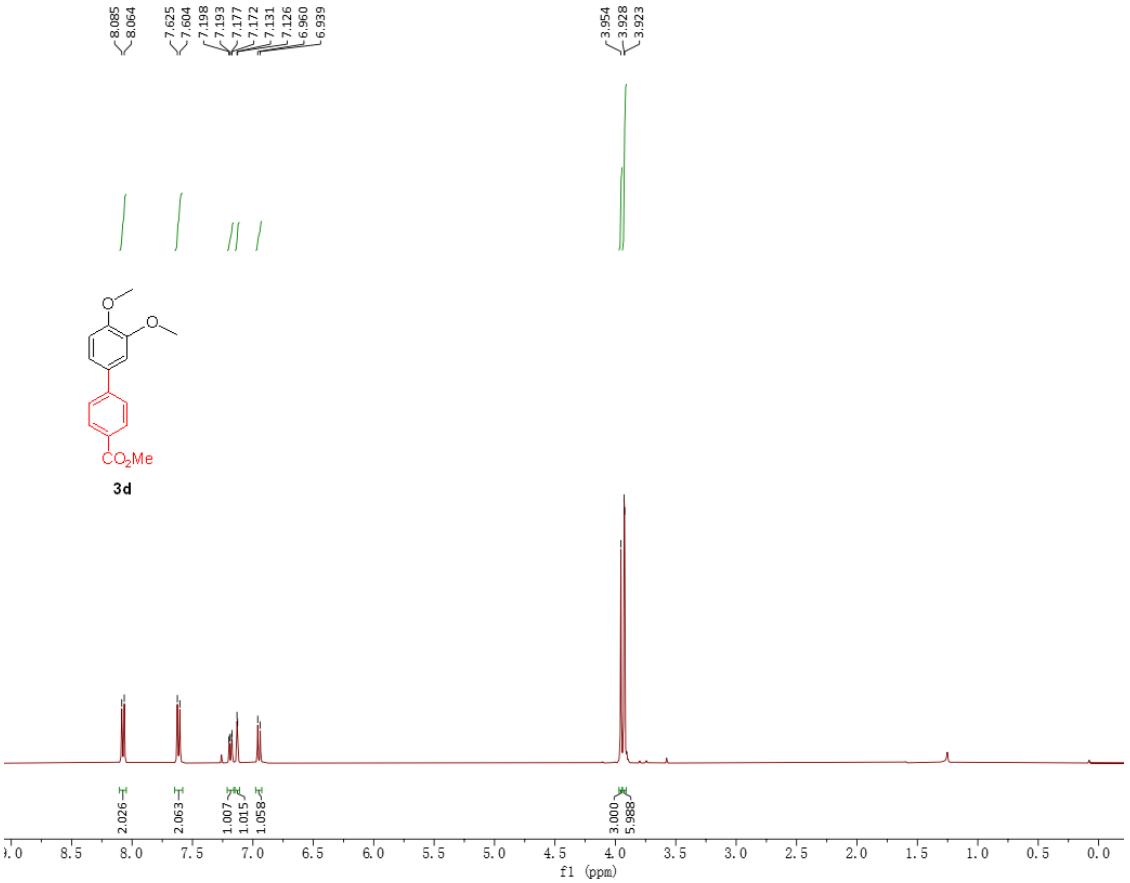
tBu
CO2Me
3c
f1 (ppm)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7.172
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7.126
6.960
6.939
3.954
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3d
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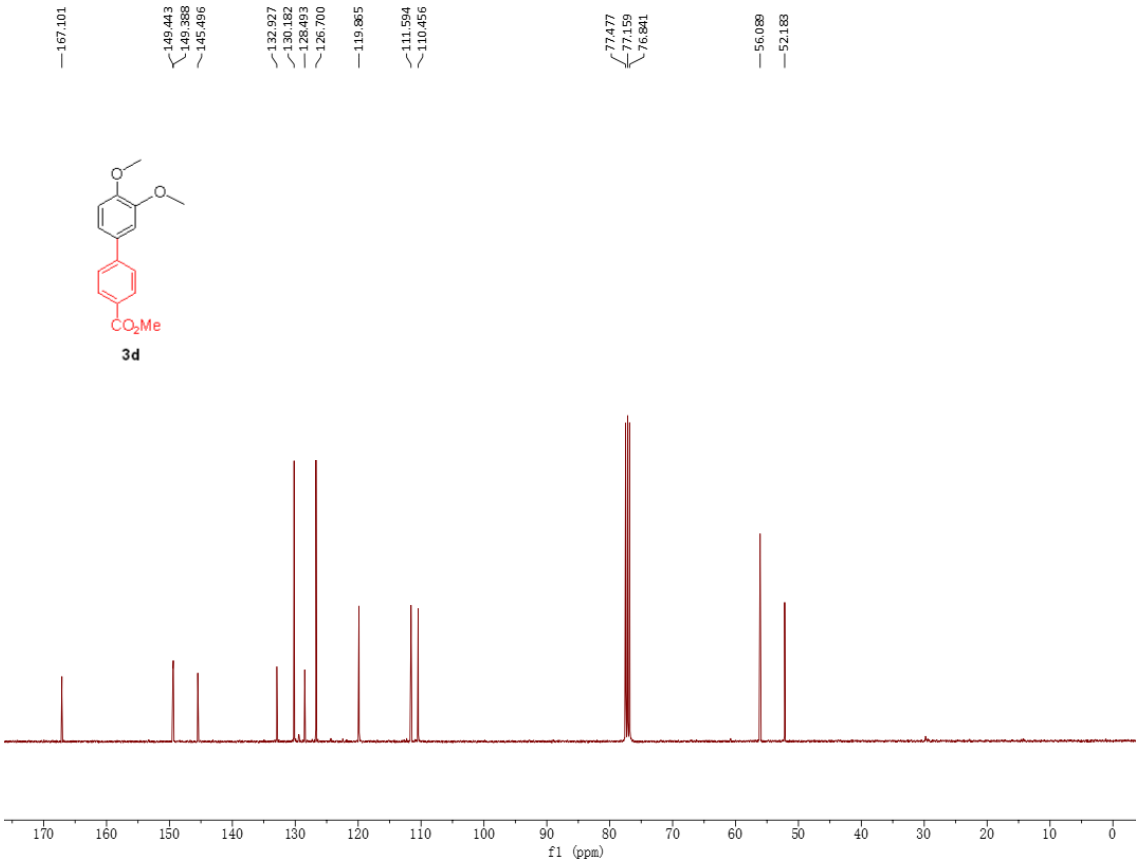
5.988
f1 (ppm)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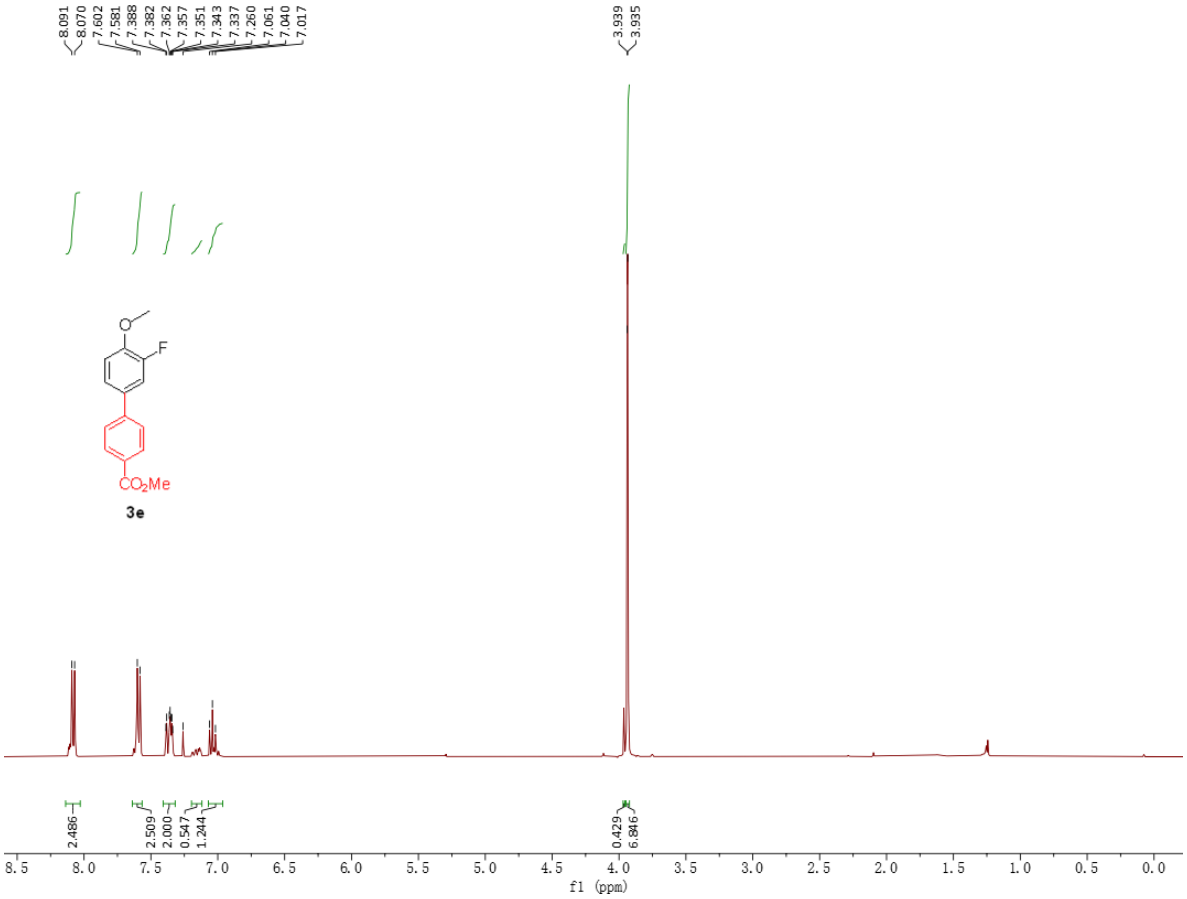
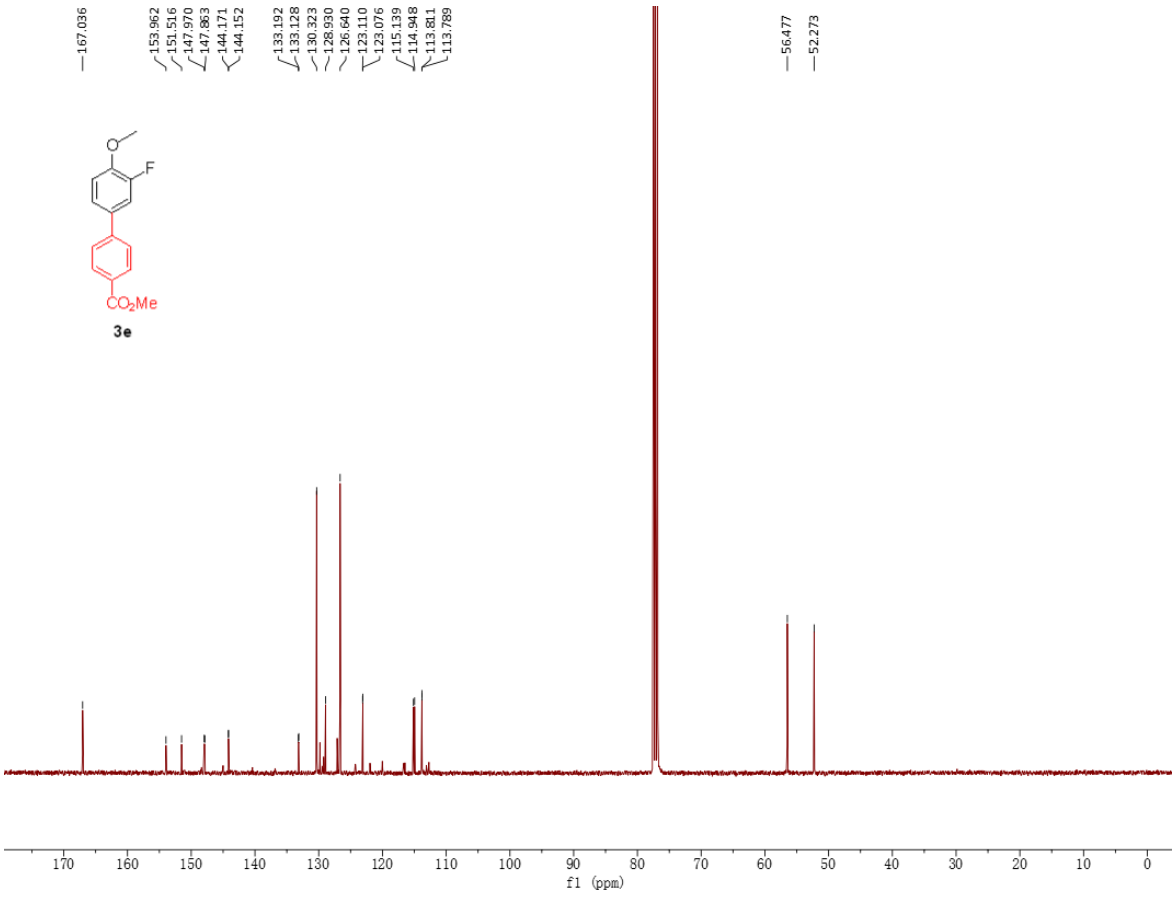
CO2Me
3d
f1 (ppm)

SUPPORTING INFORMATION





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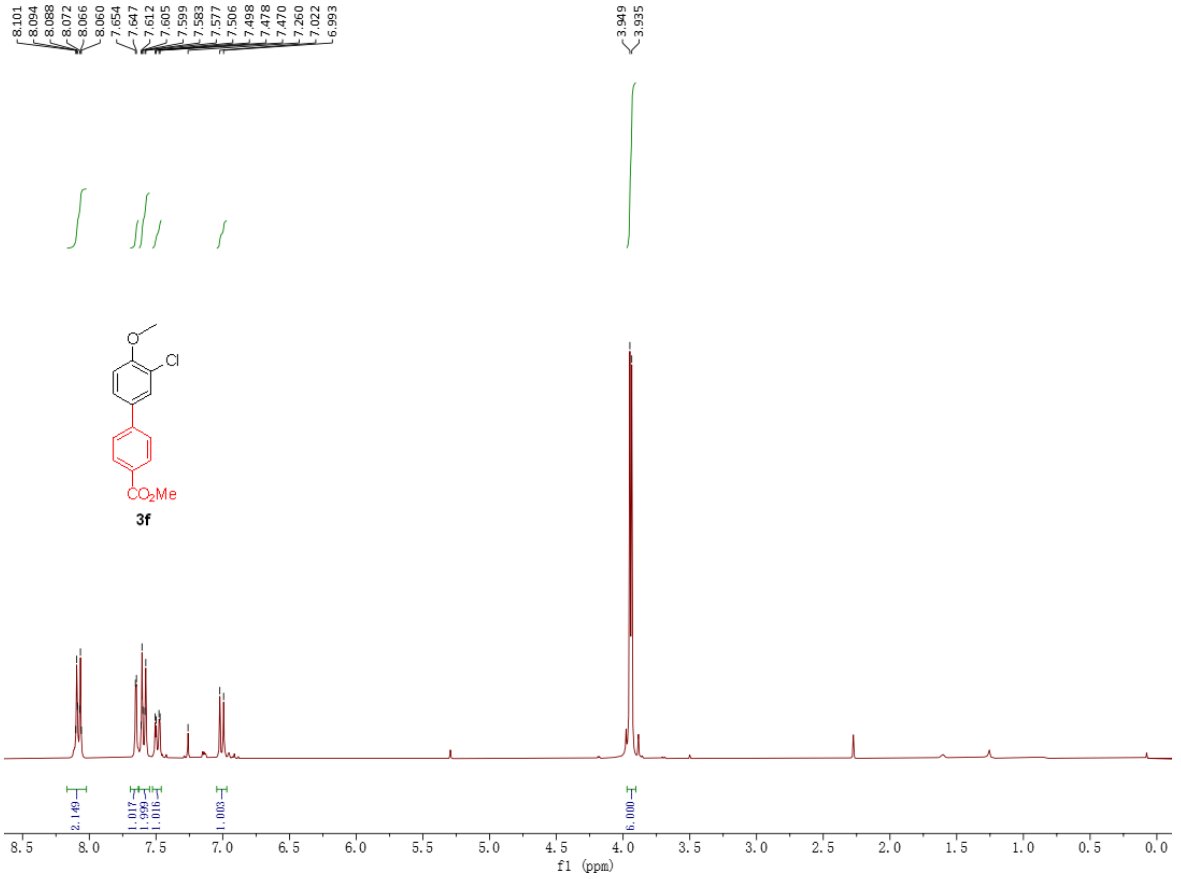
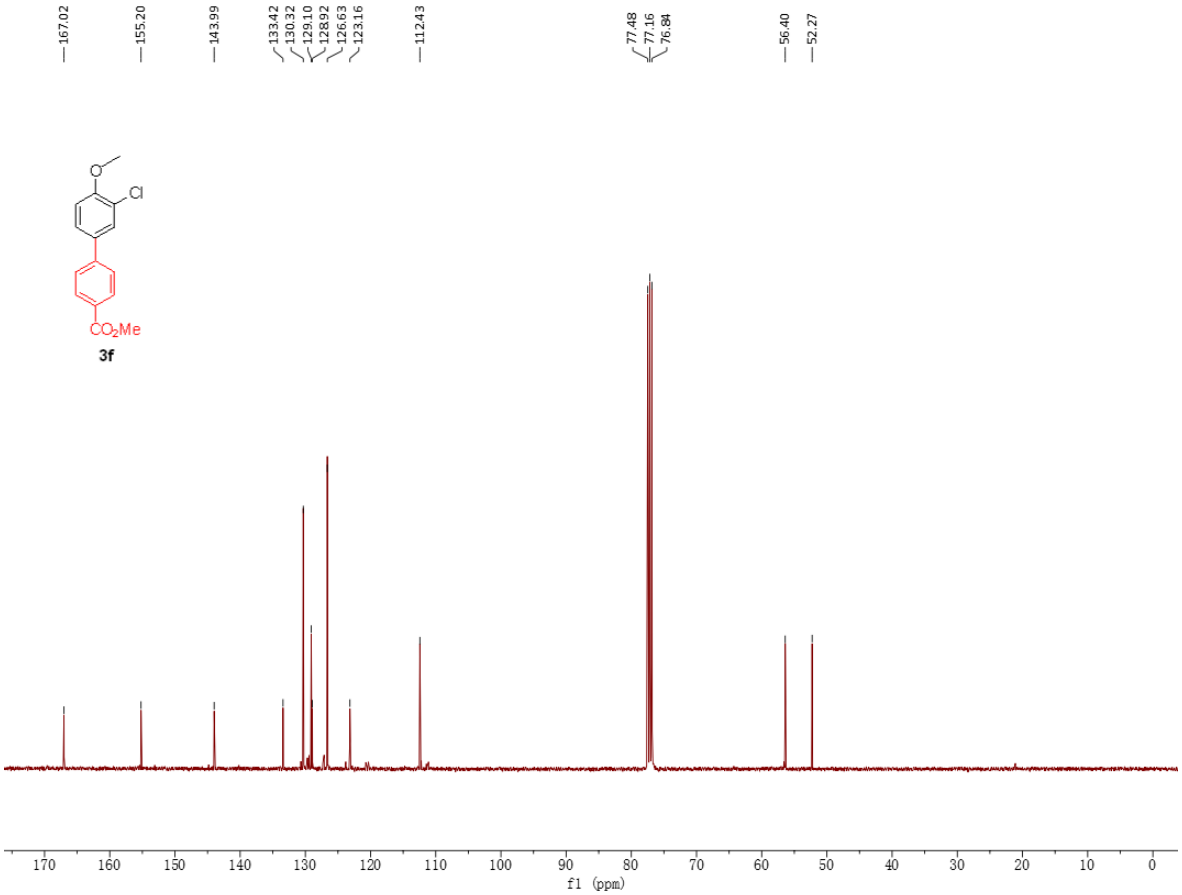
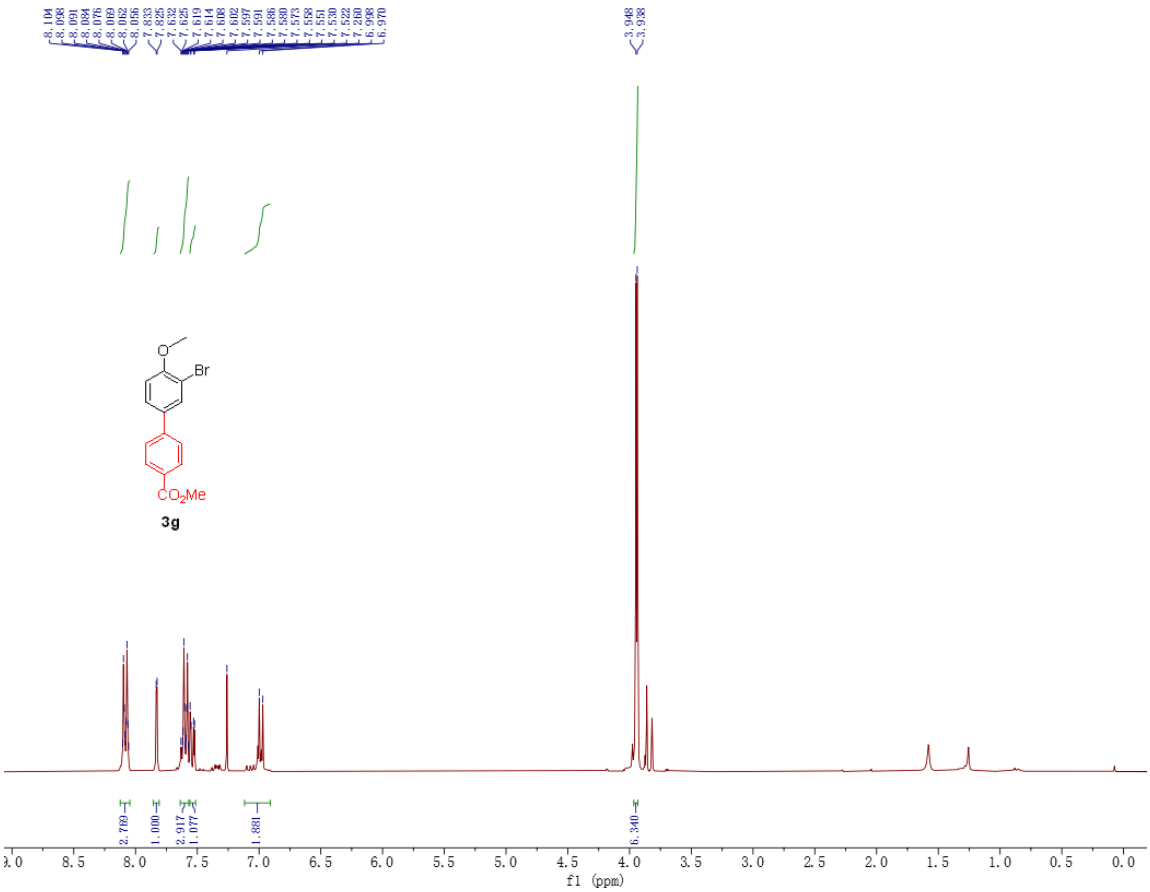
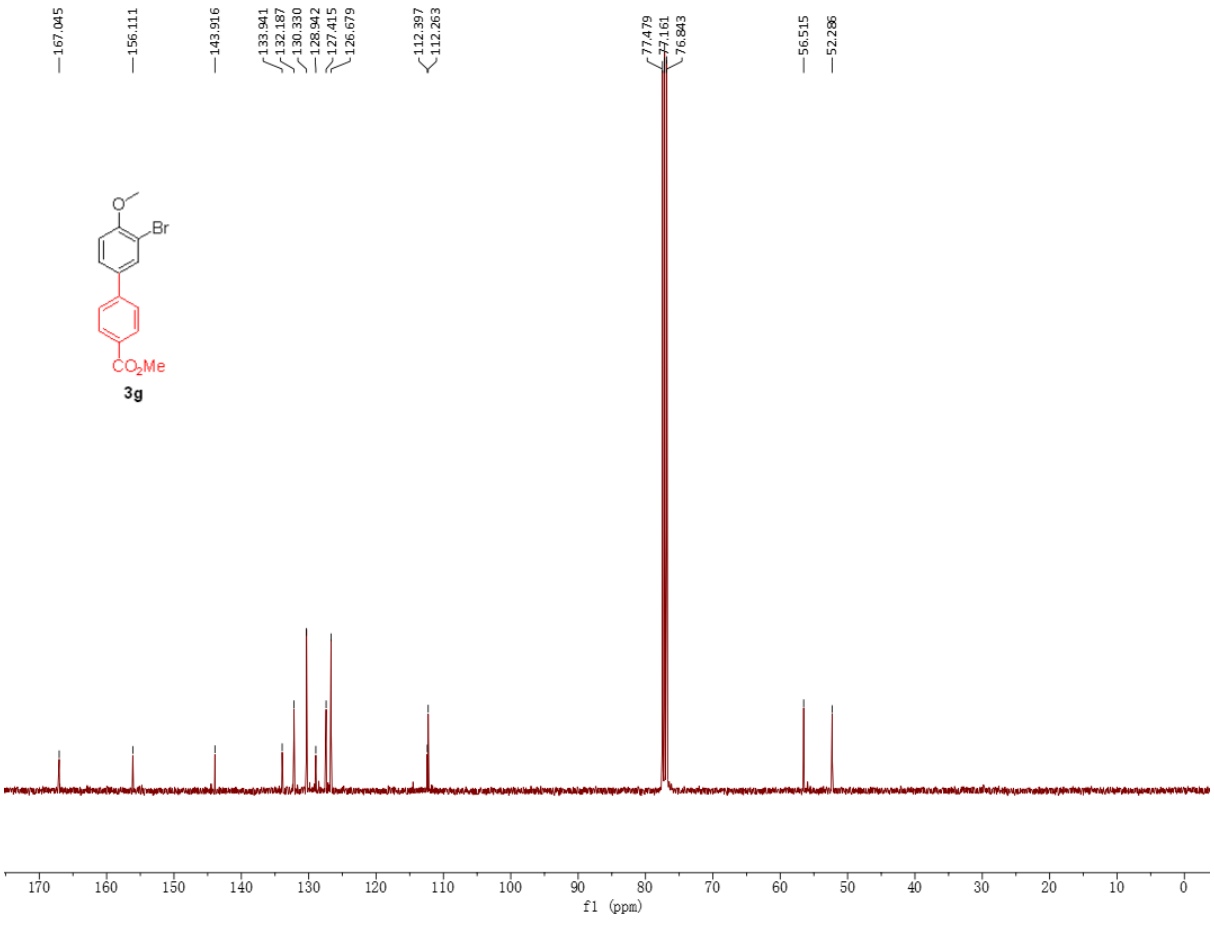
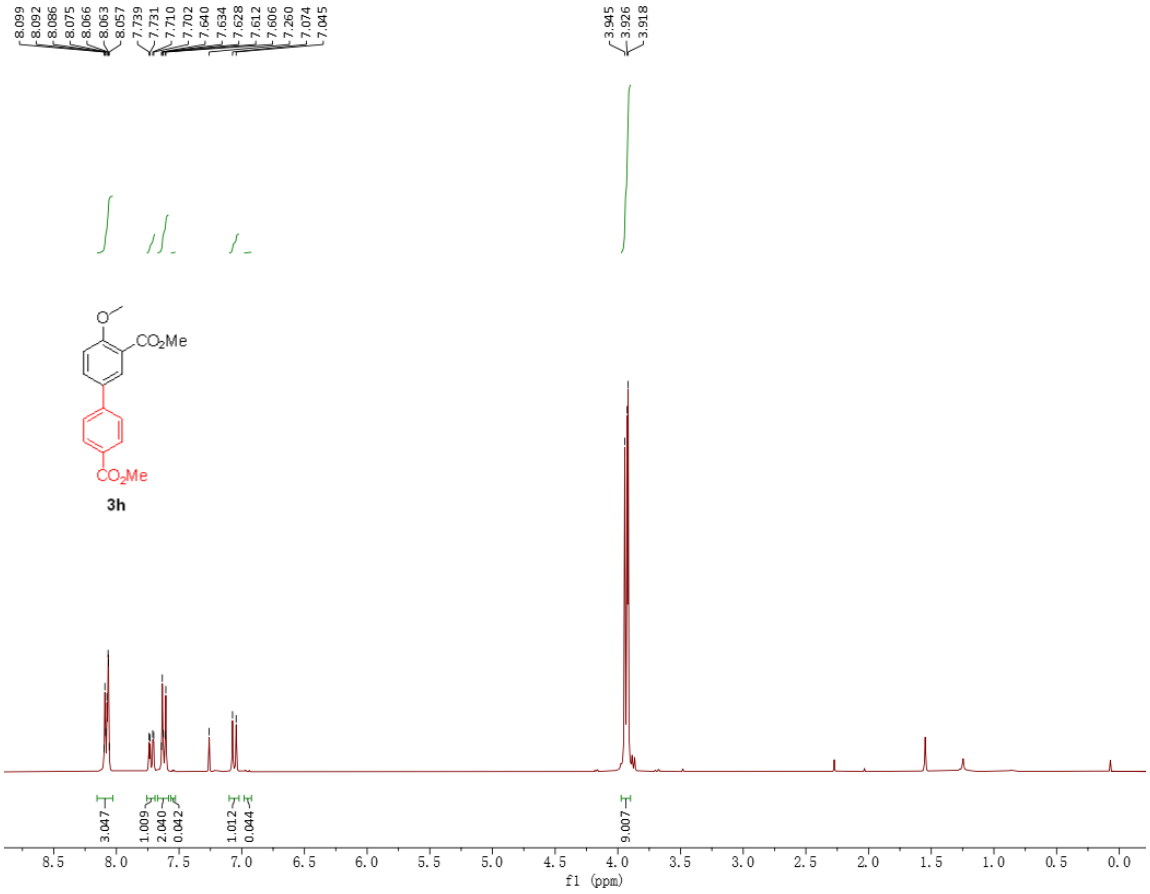




SUPPORTING INFORMATION



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8.075
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8.063
8.057
7.739
7.731
7.710
7.702
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7.628
7.612
7.606
7.260
7.074
7.045
3.945
3.926
3.918
CO2Me
CO2Me
3h
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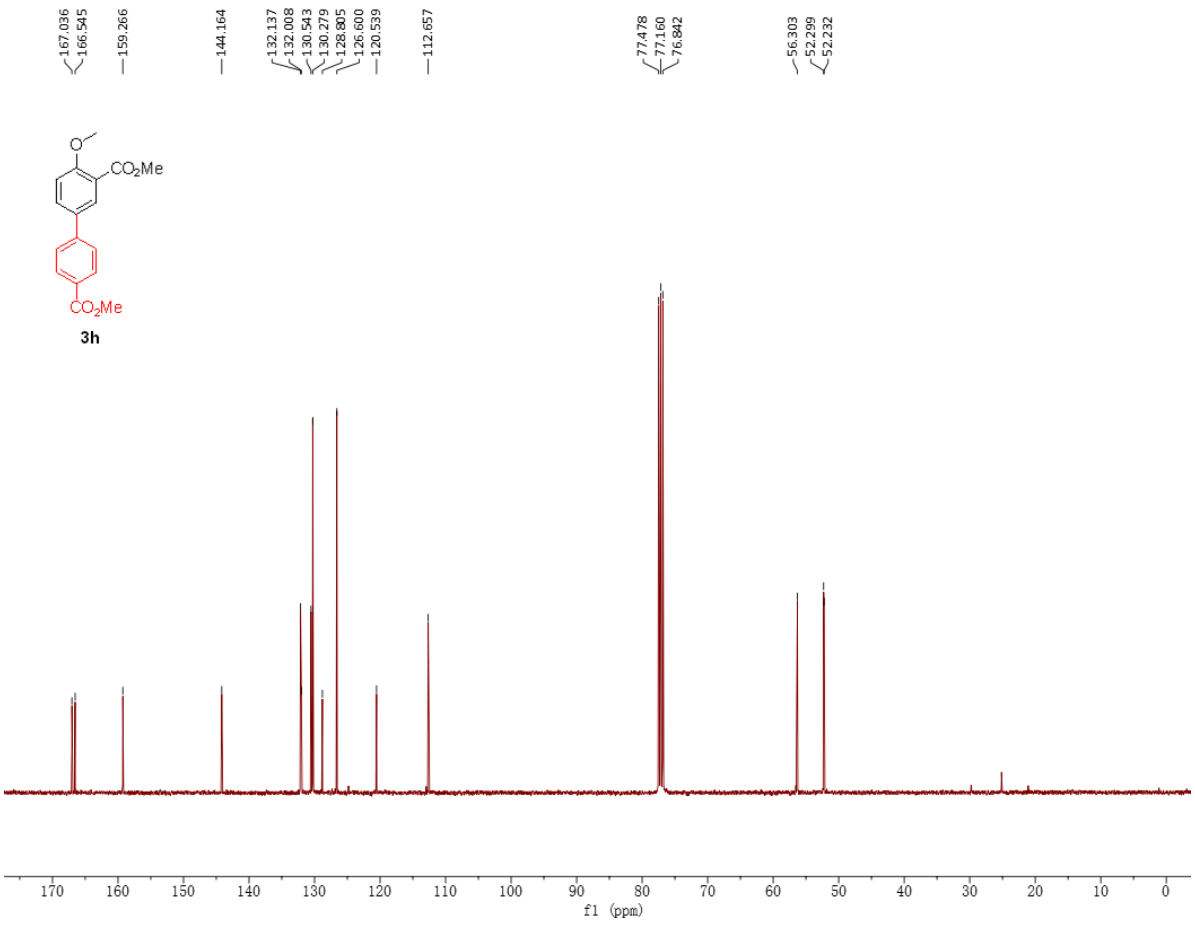
1.009
2.040
0.042
1.012
0.044
9.007
f1 (ppm)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120.539
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76.842
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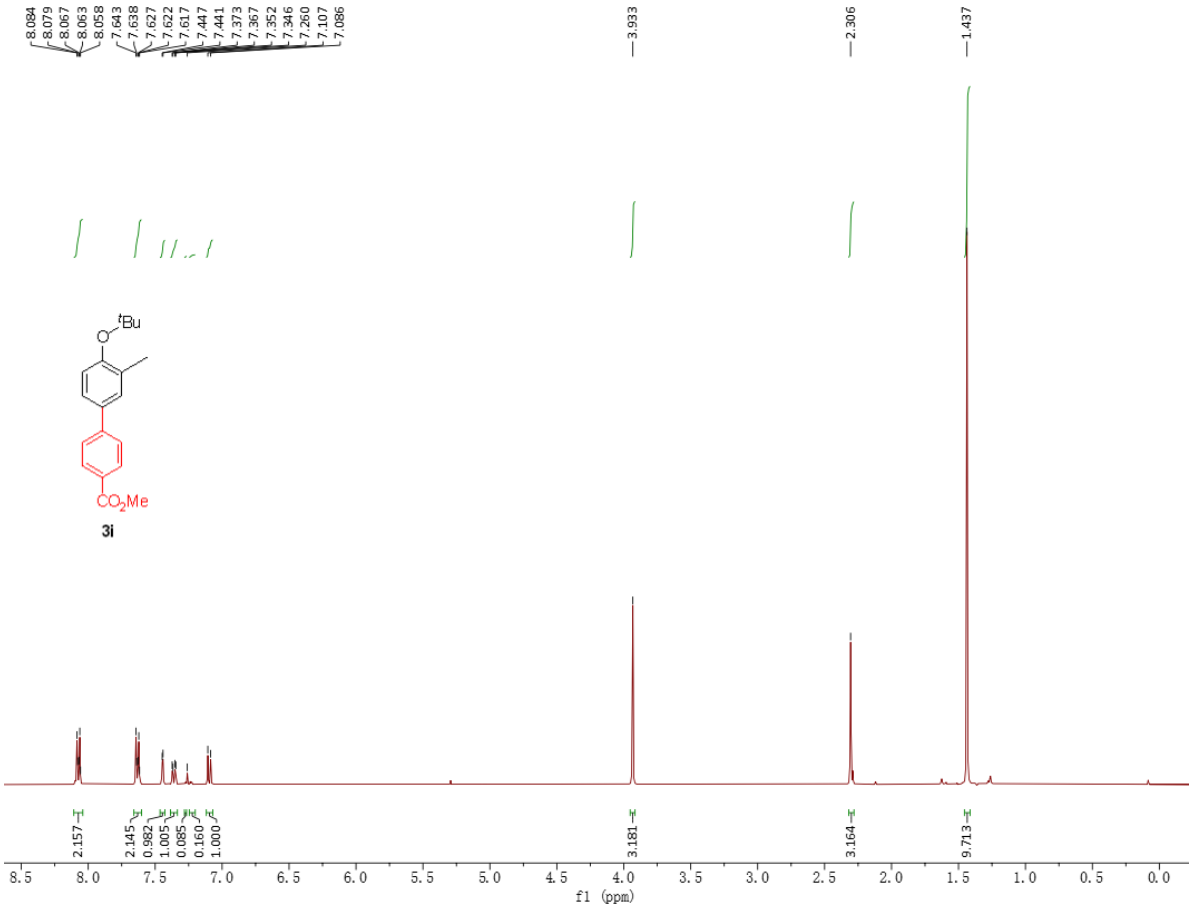
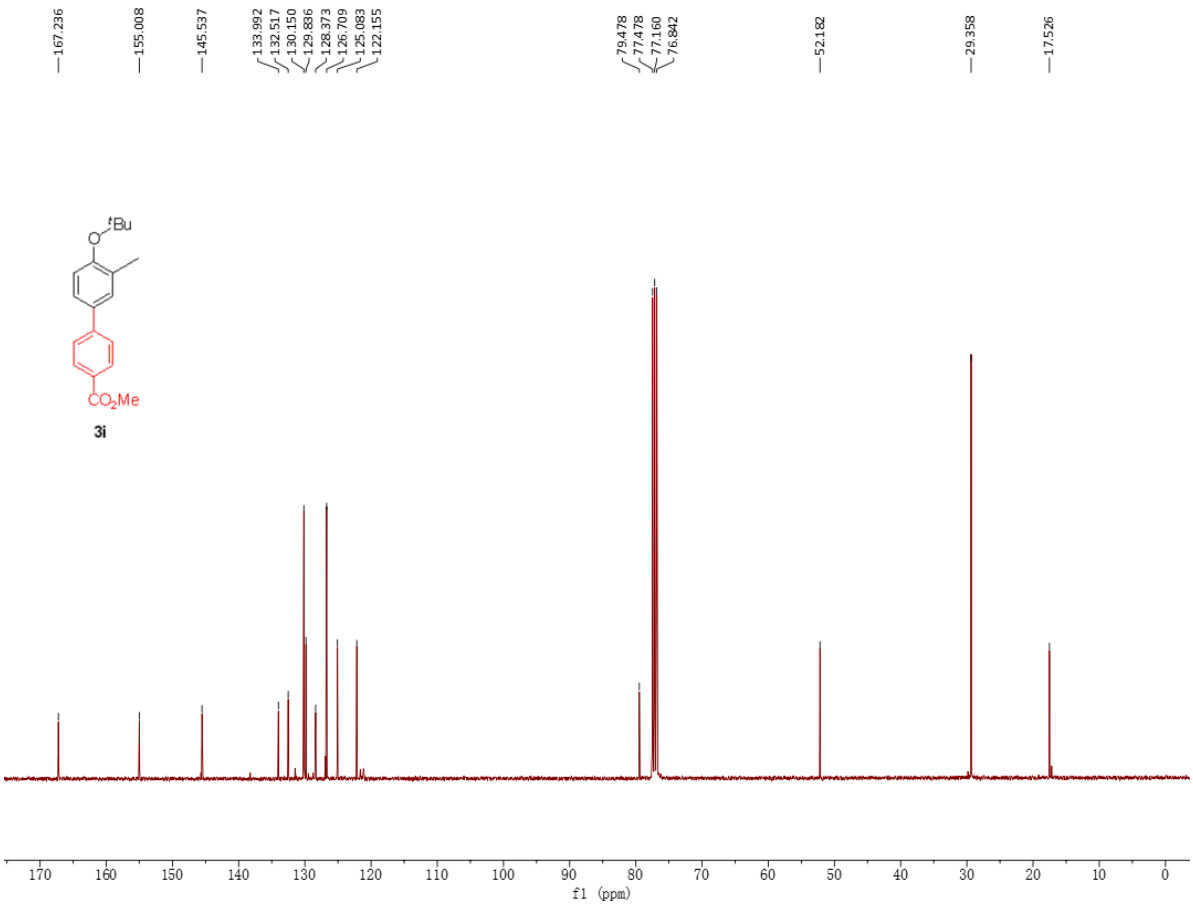
CO2Me
CO2Me
3h
f1 (ppm)

SUPPORTING INFORMATION





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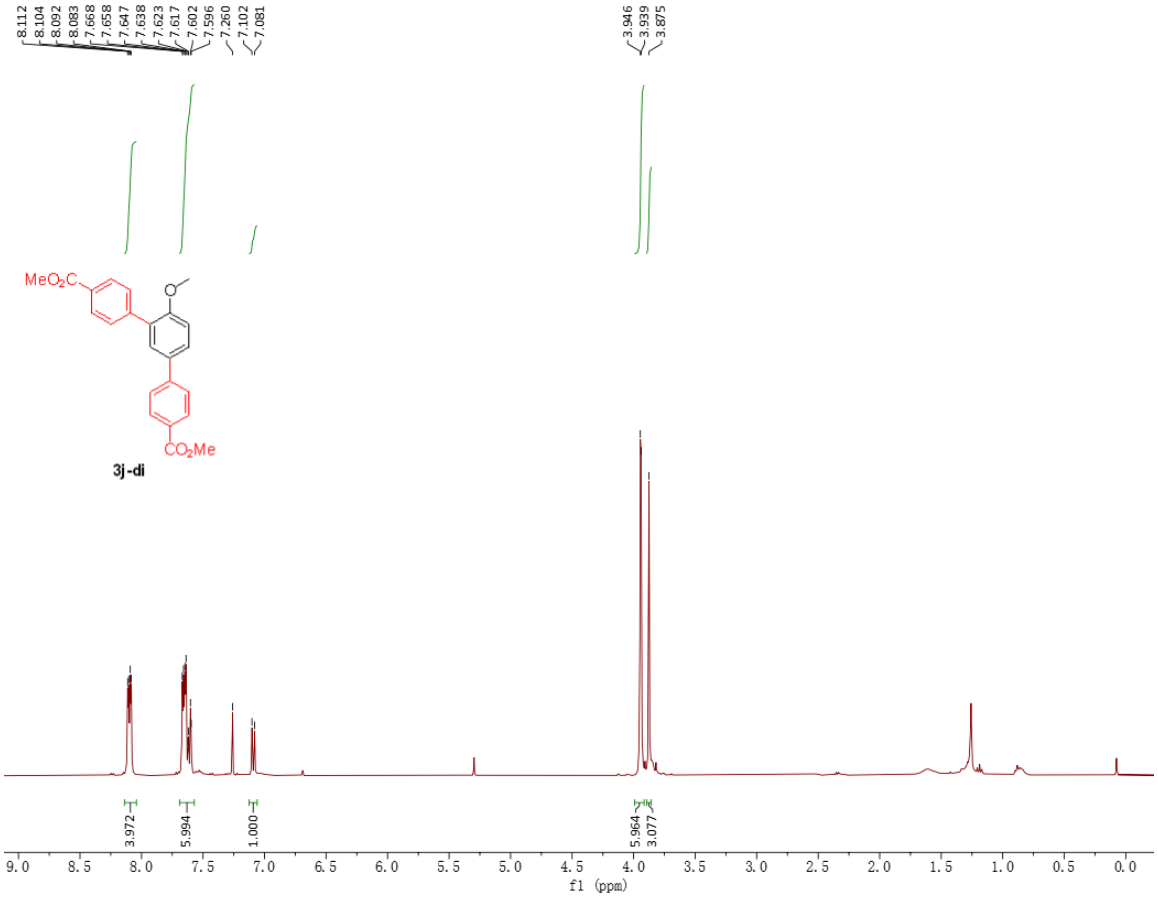

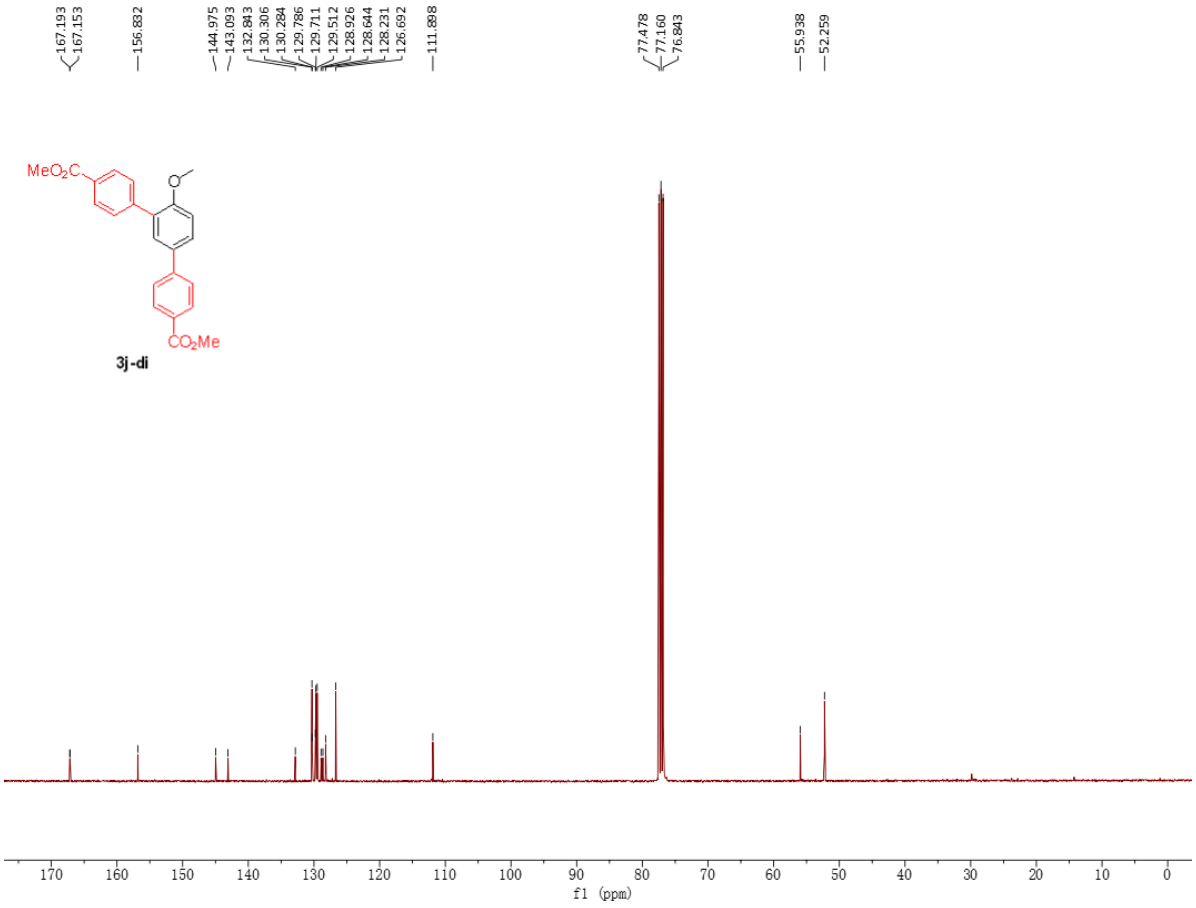

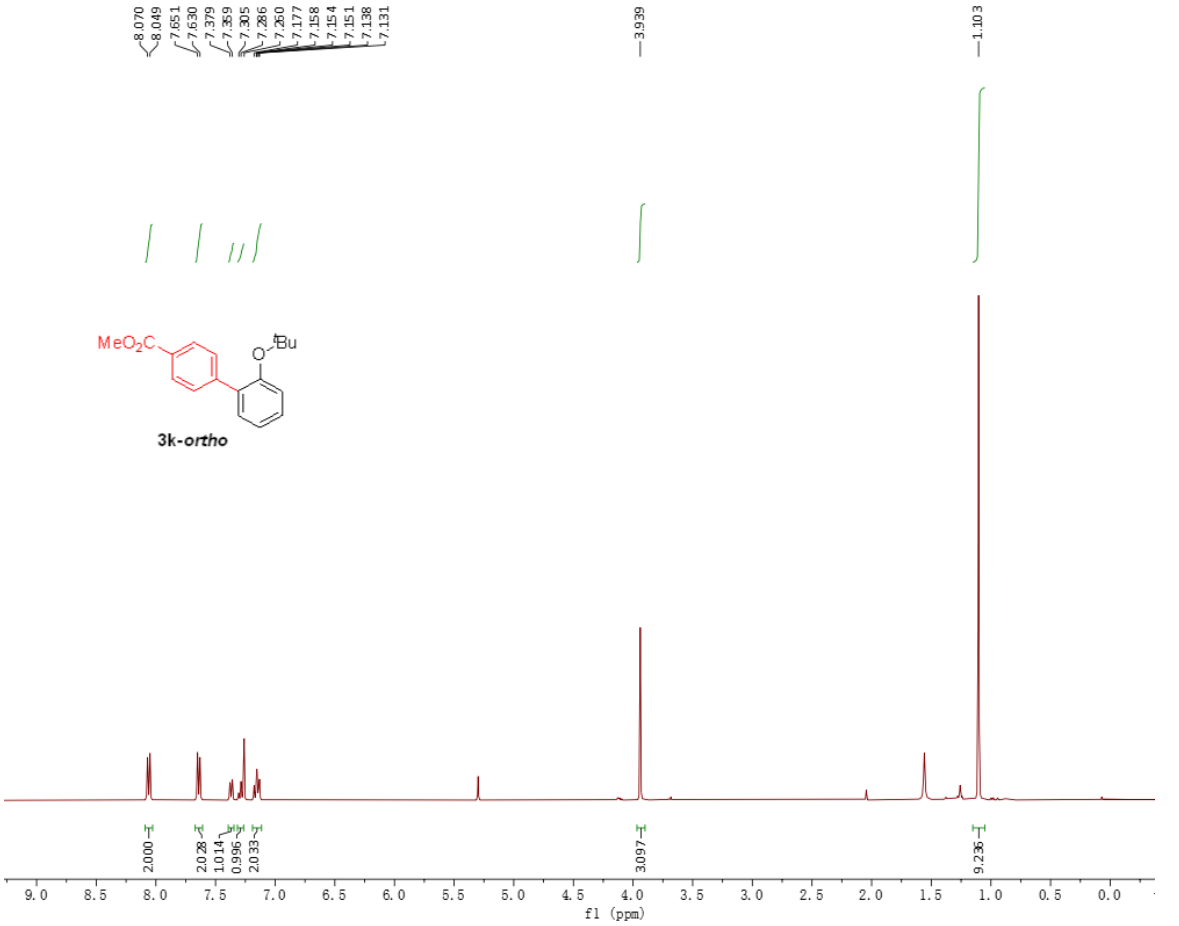
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7.260
7.177
7.158
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7.151
7.138
7.131
3.939
1.103
MeO2C
tBu
O
3k-ortho
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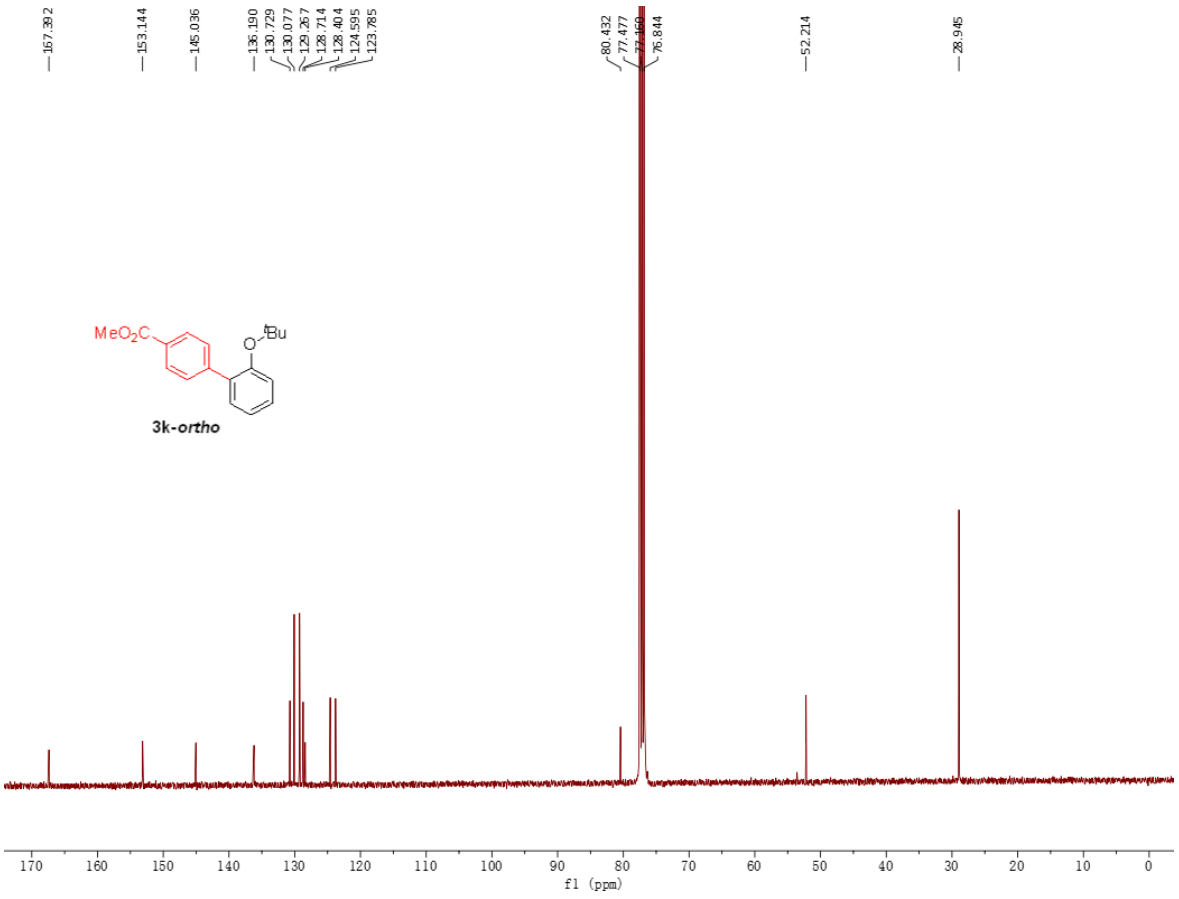
0.996
2.033
3.097
9.236
f1 (ppm)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128.404
124.595
123.785
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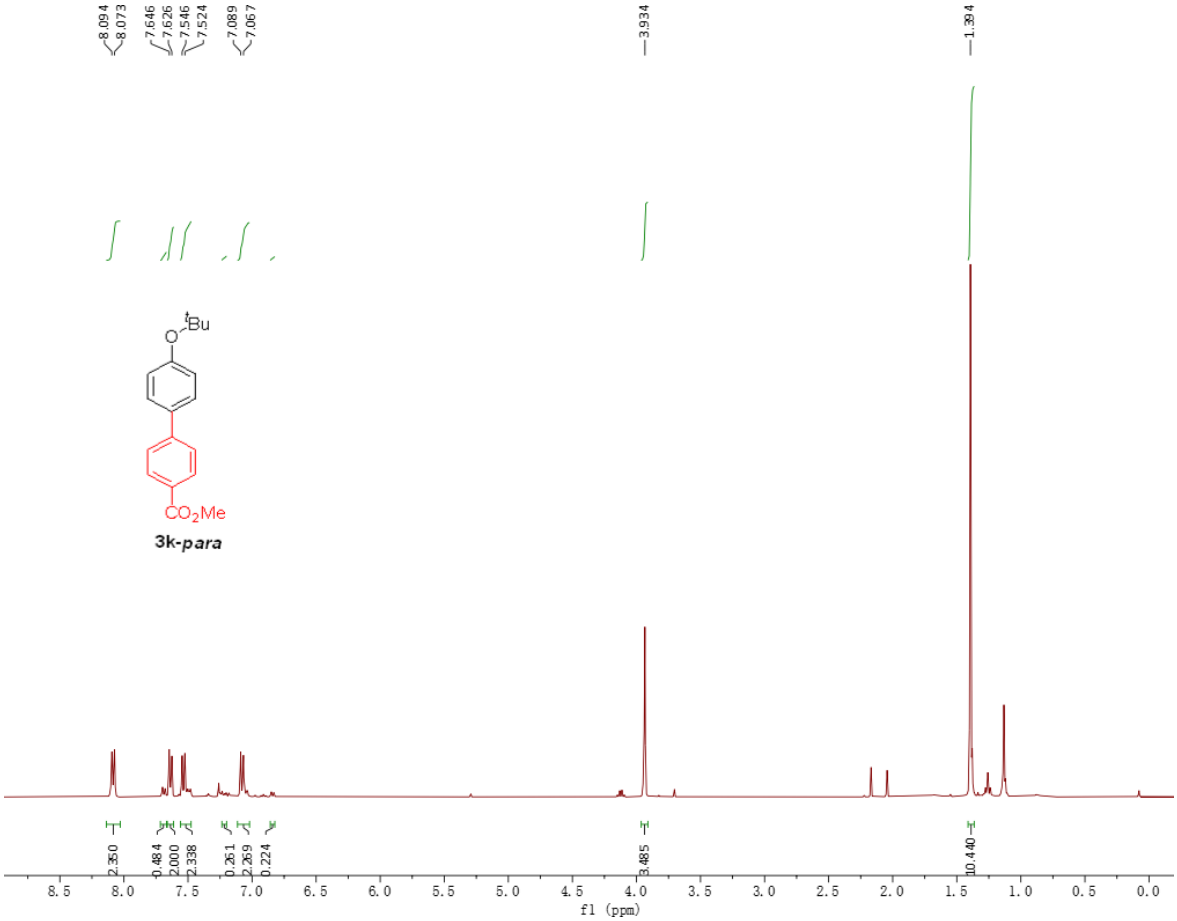
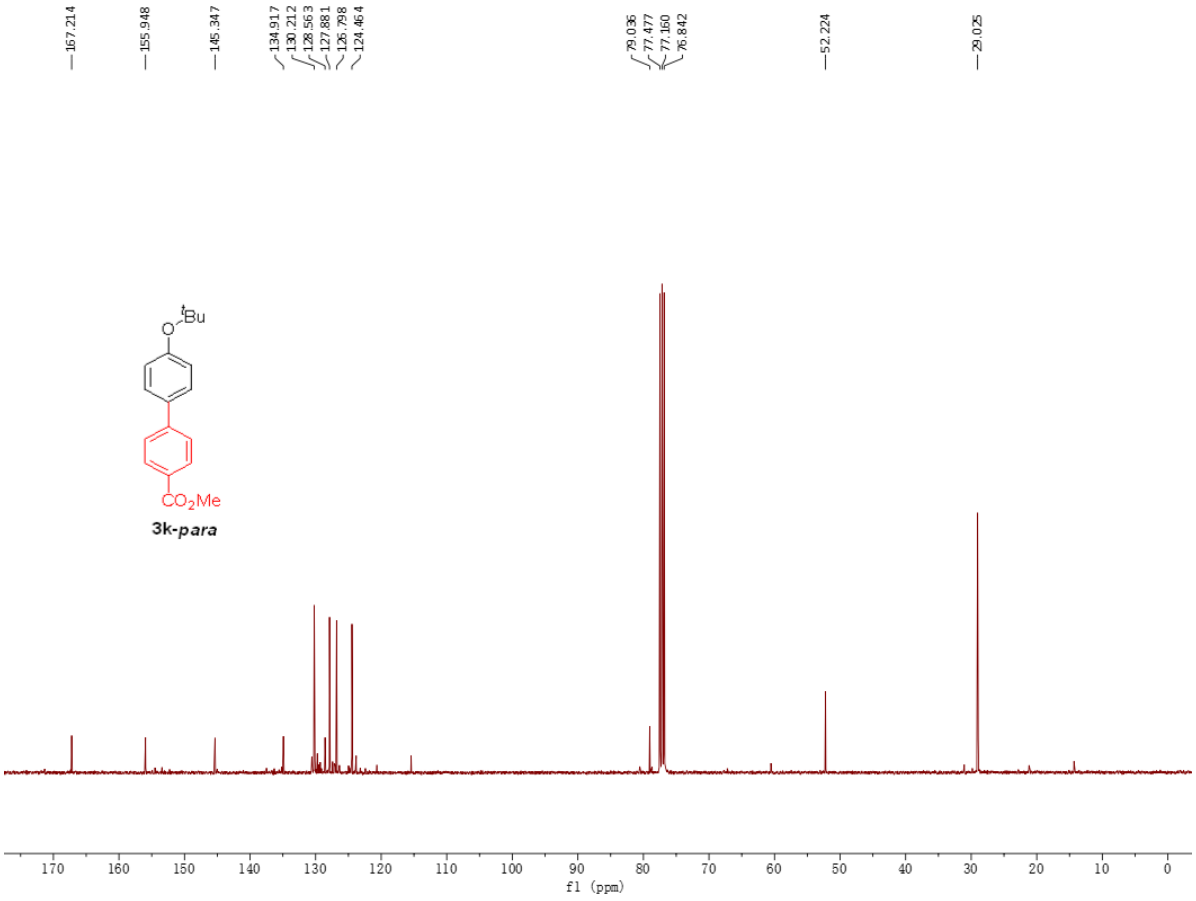
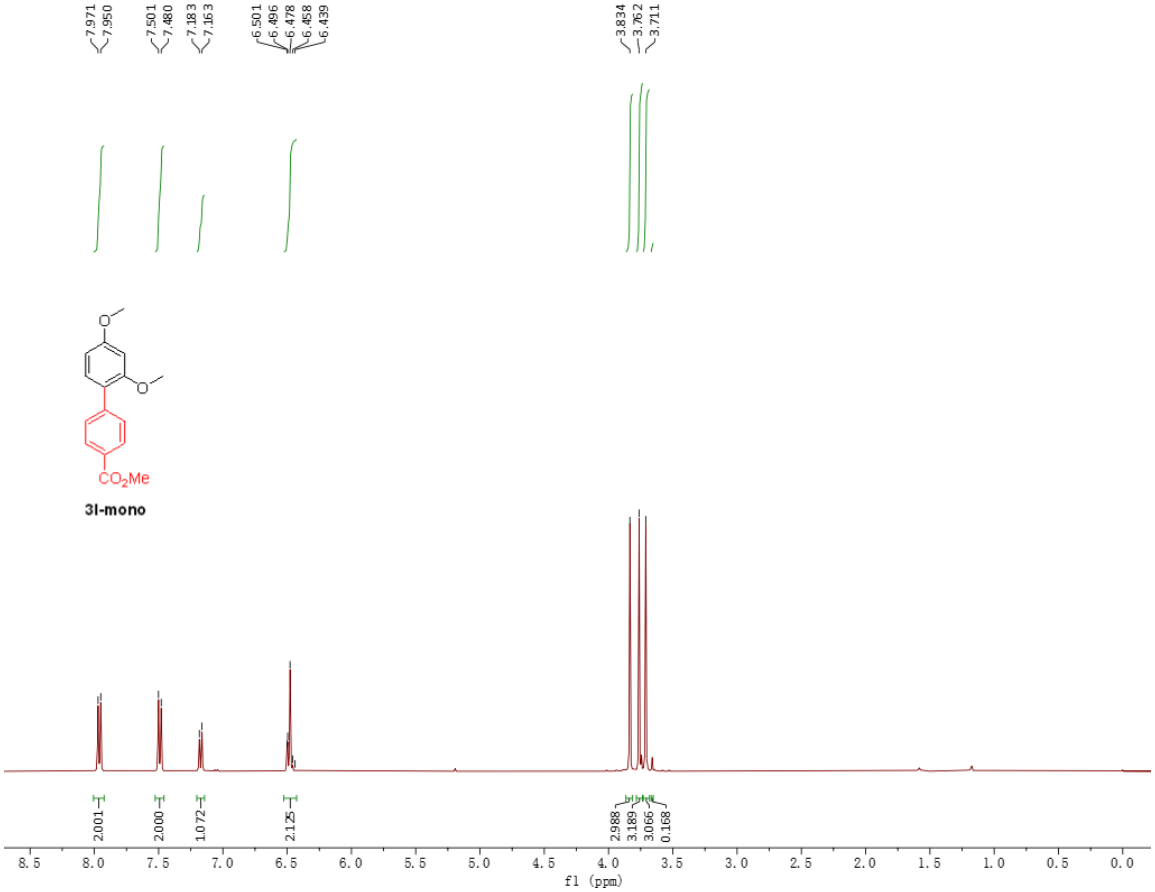
52.214
28.945
MeO2C
tBu
O
3k-ortho
f1 (ppm)

SUPPORTING INFORMATION



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6.458
6.439
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3.762
3.711
CO2Me
3l-mono
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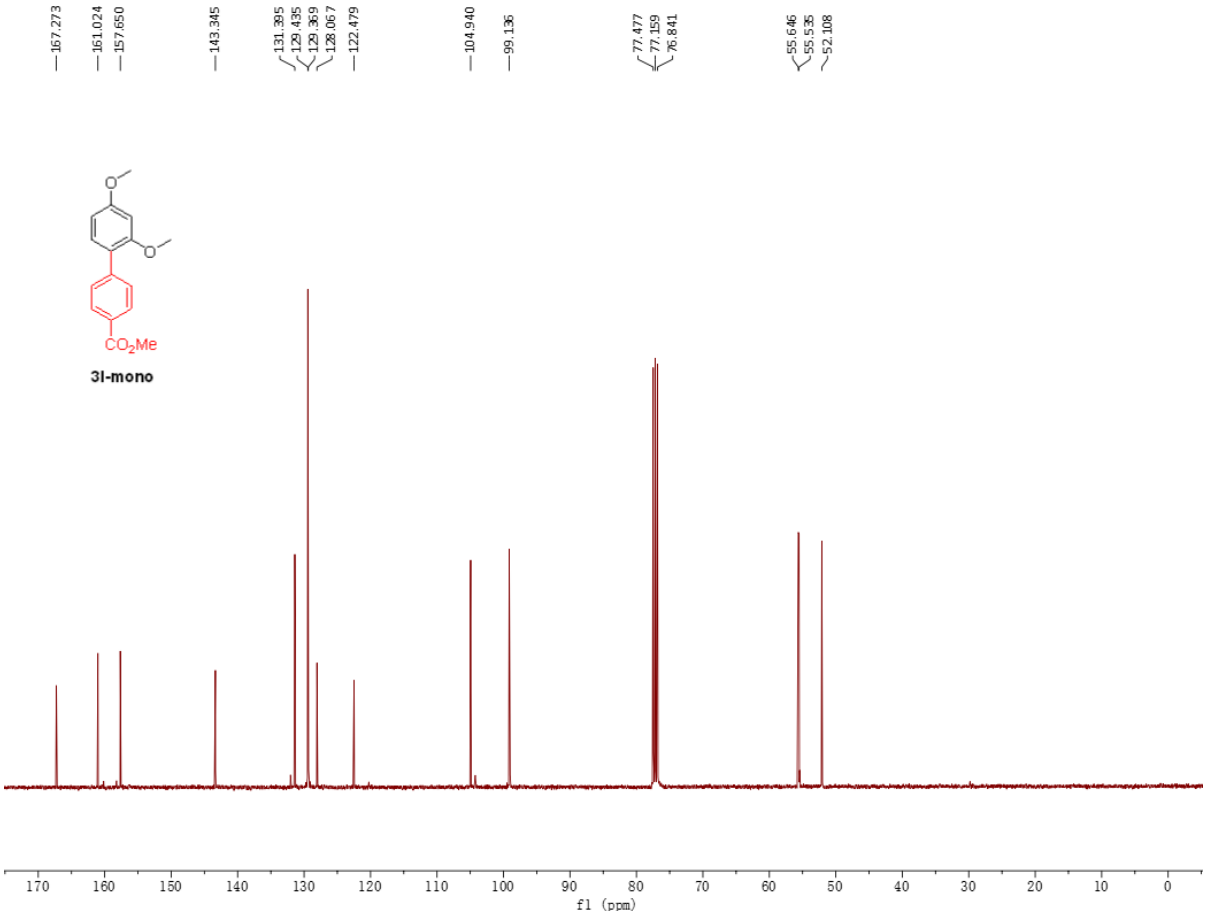
2.000
1.072
2.125
2.988
3.189
3.066
0.168
f1 (ppm)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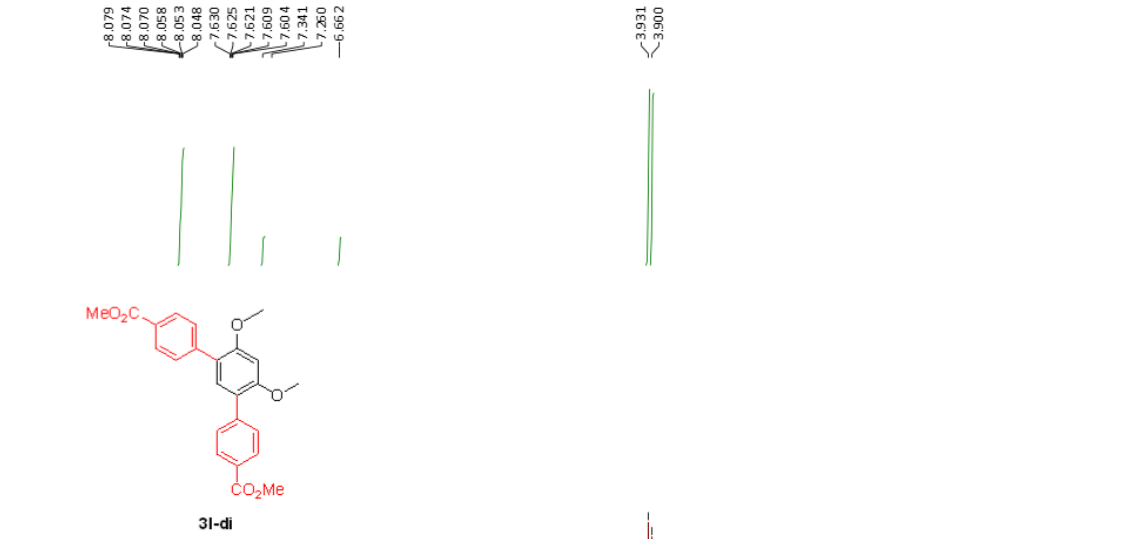
CO2Me
3l-mono
f1 (ppm)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7.260
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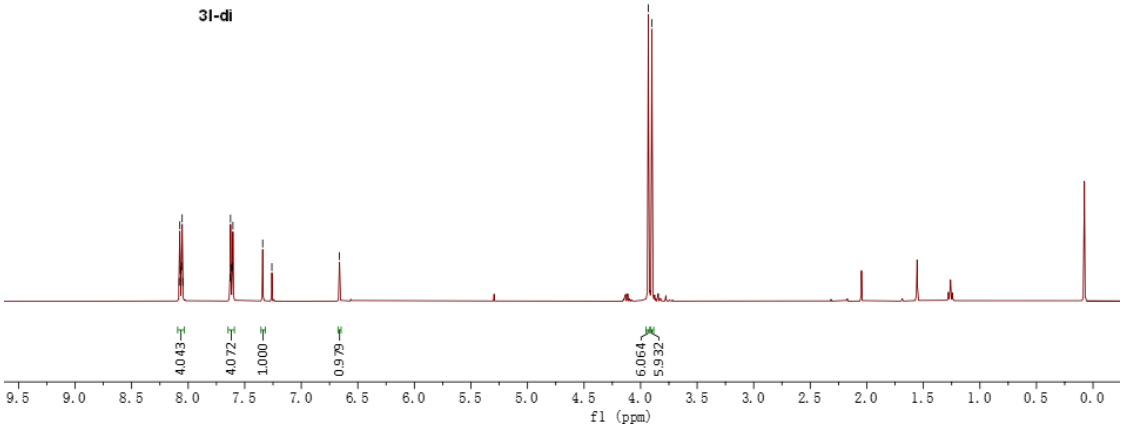
MeO2C
O
O
CO2Me

3l-di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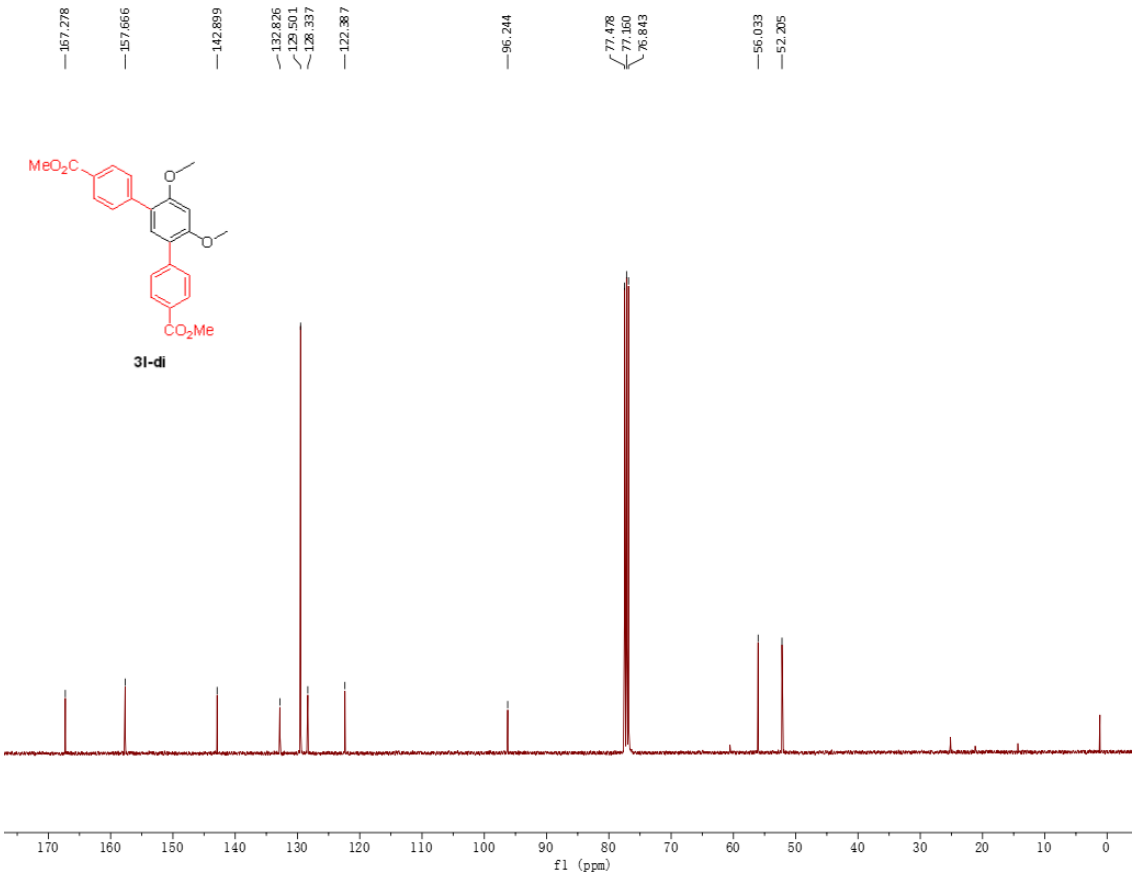
f1 (ppm)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128.337
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77.478
77.160
76.843
56.033
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MeO2C
O
O
CO2Me
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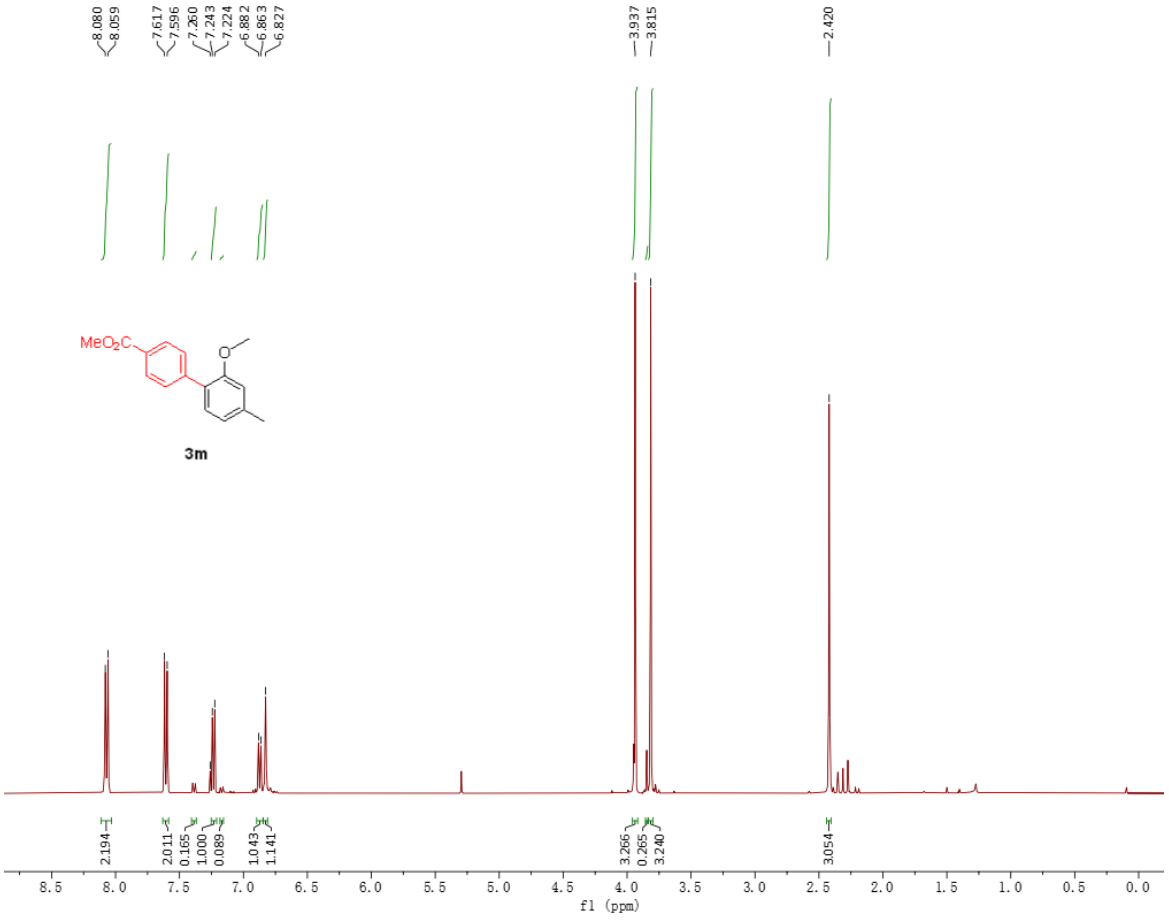
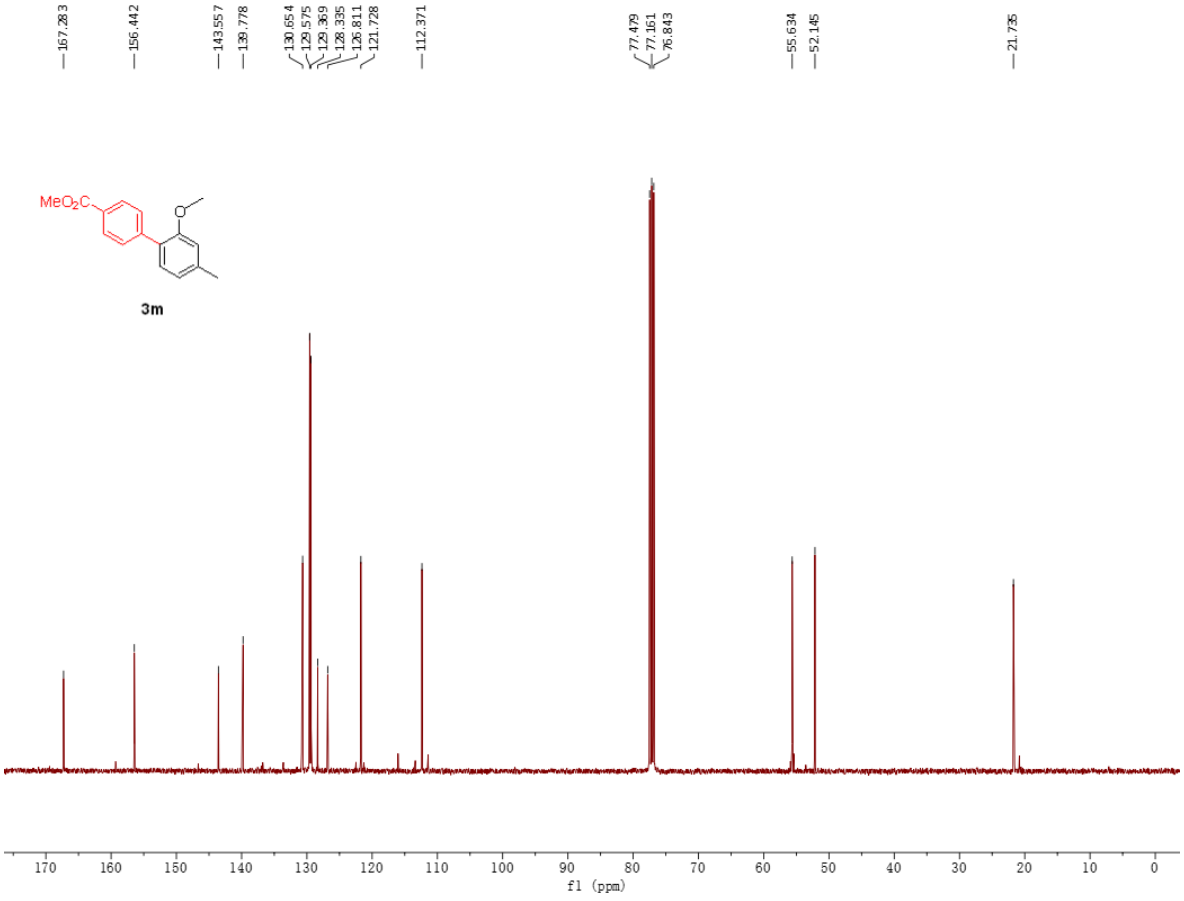
f1 (ppm)

3l-di

SUPPORTING INFORMATION





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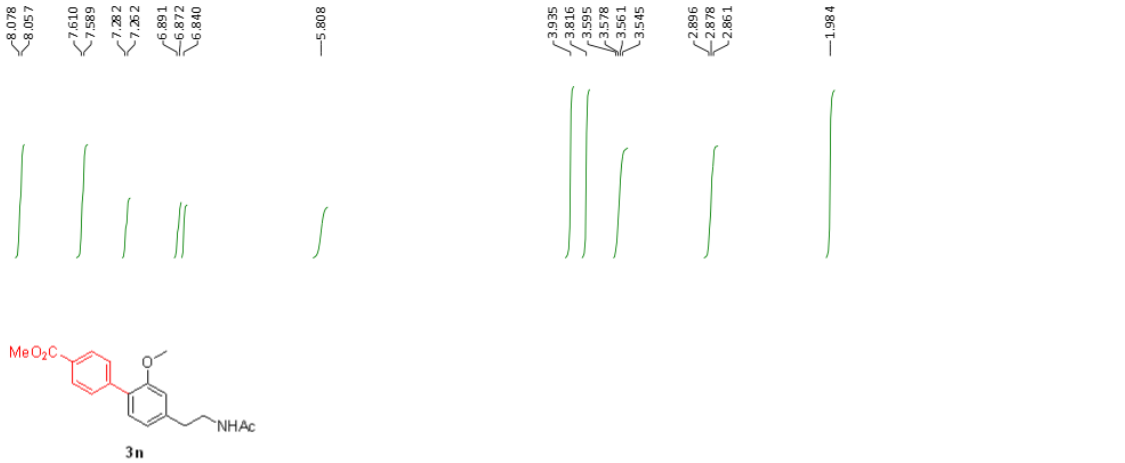

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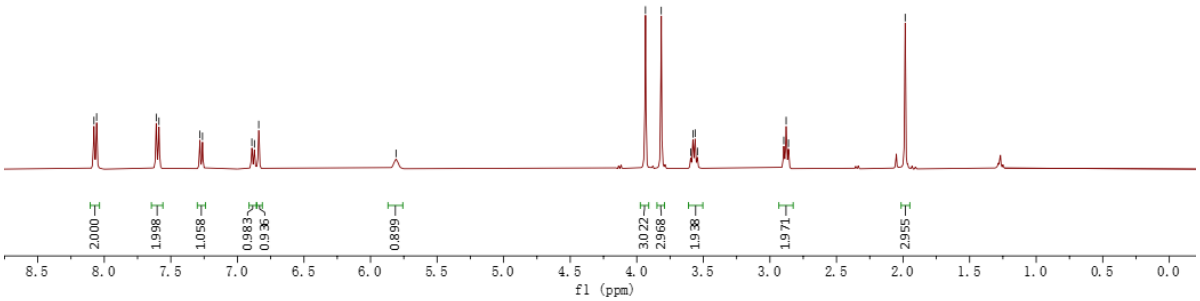

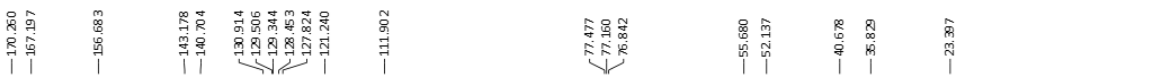

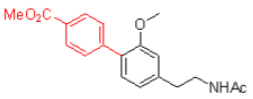

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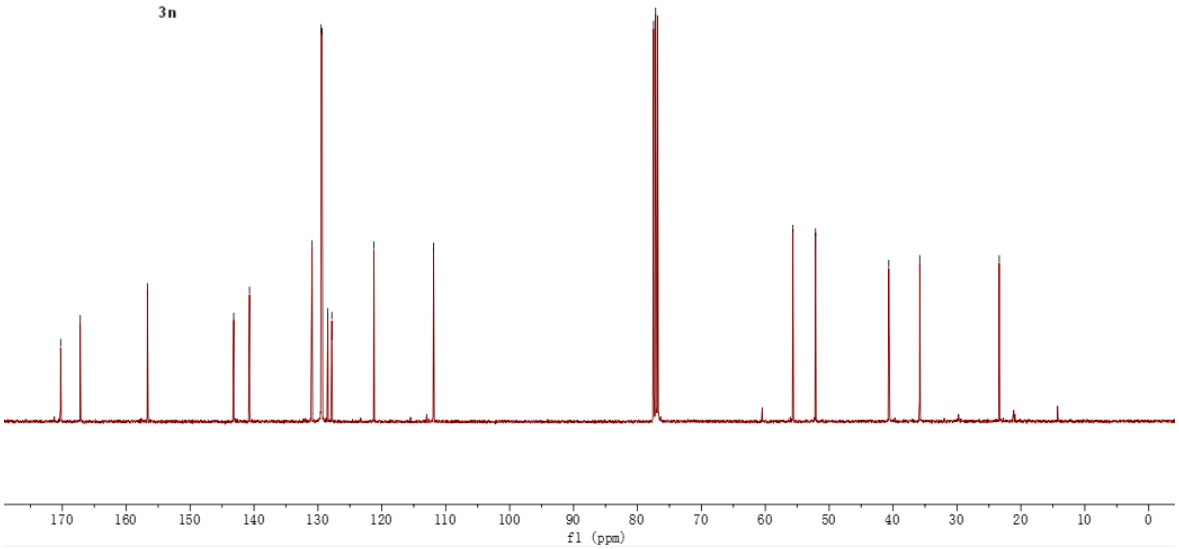

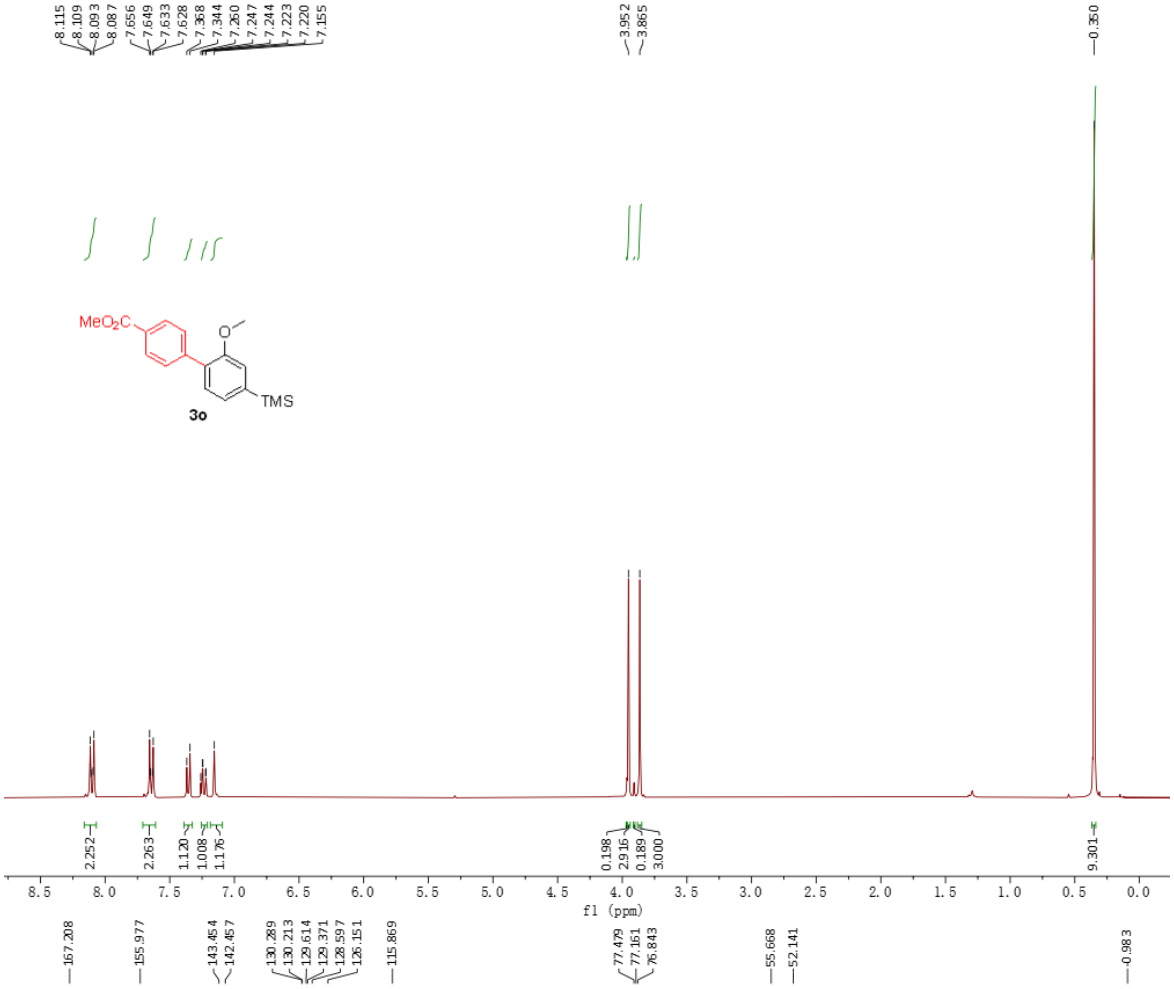
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7.649
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7.368
7.344
7.260
7.247
7.244
7.223
7.220
7.155
3.952
3.865
0.350
MeO2C
O
TMS
3o
2.252
2.263
1.120
1.008
1.176
0.198
2.916
0.189
3.000
9.301
f1 (ppm)
167.208
155.977
143.454
142.457
130.289
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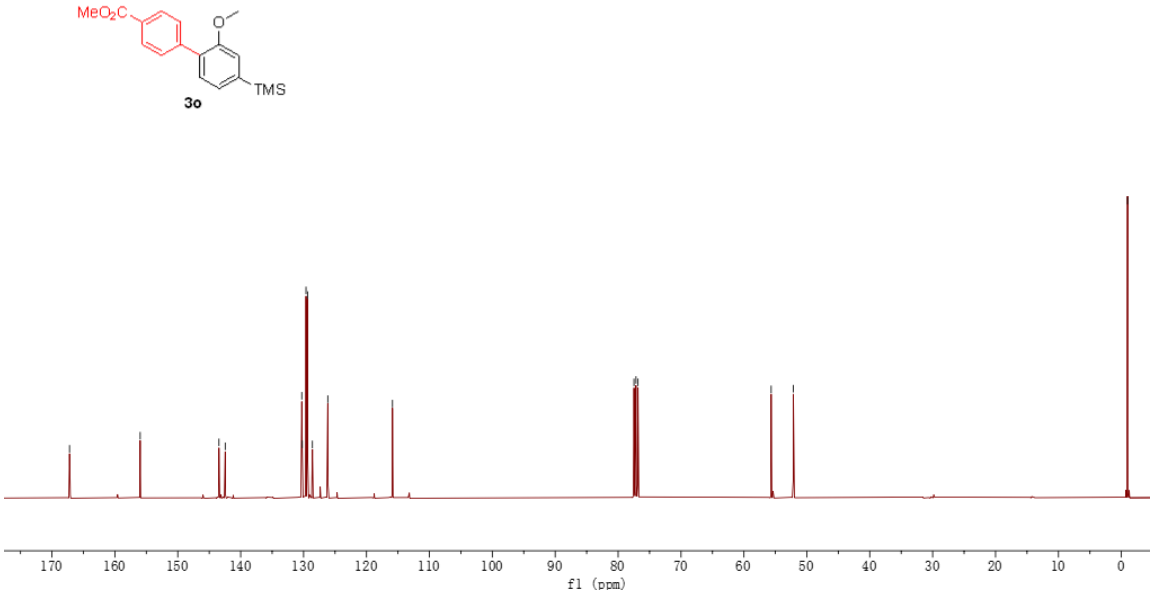
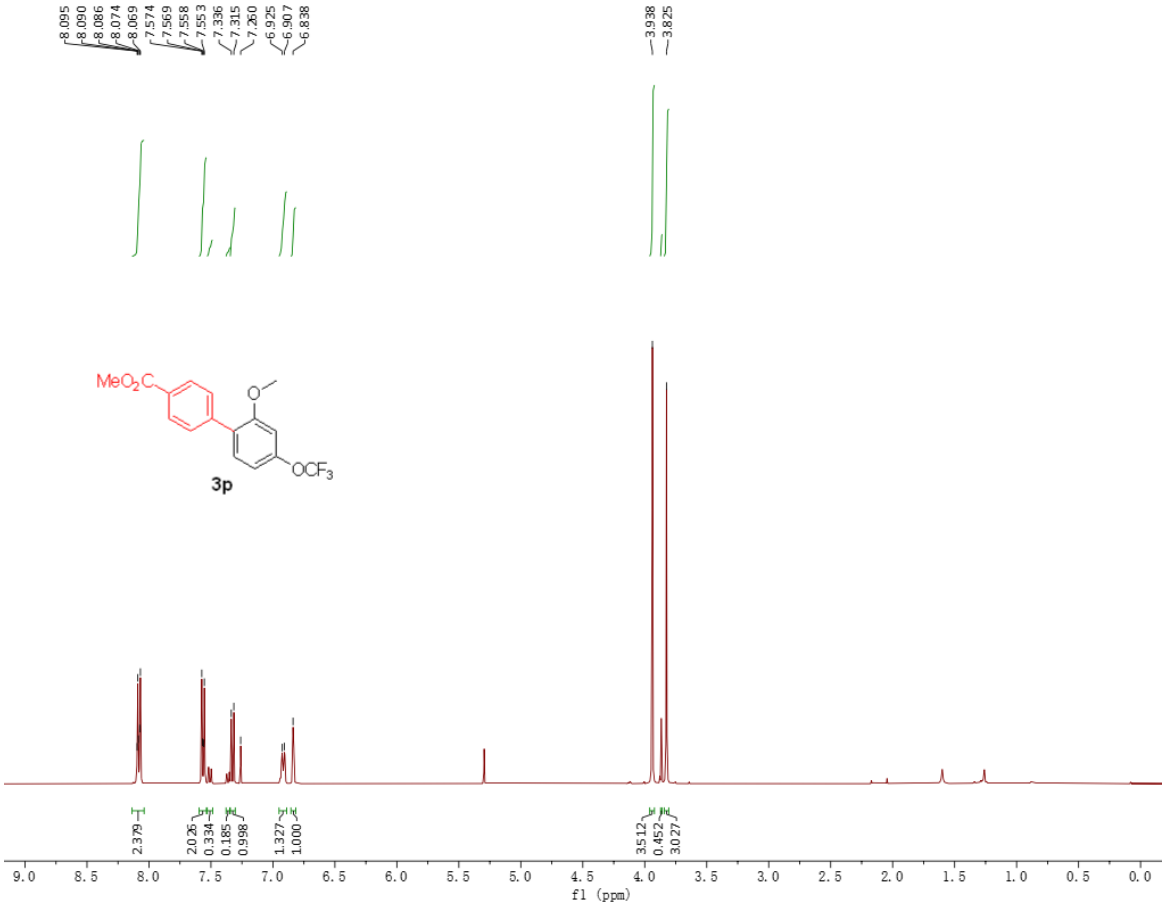
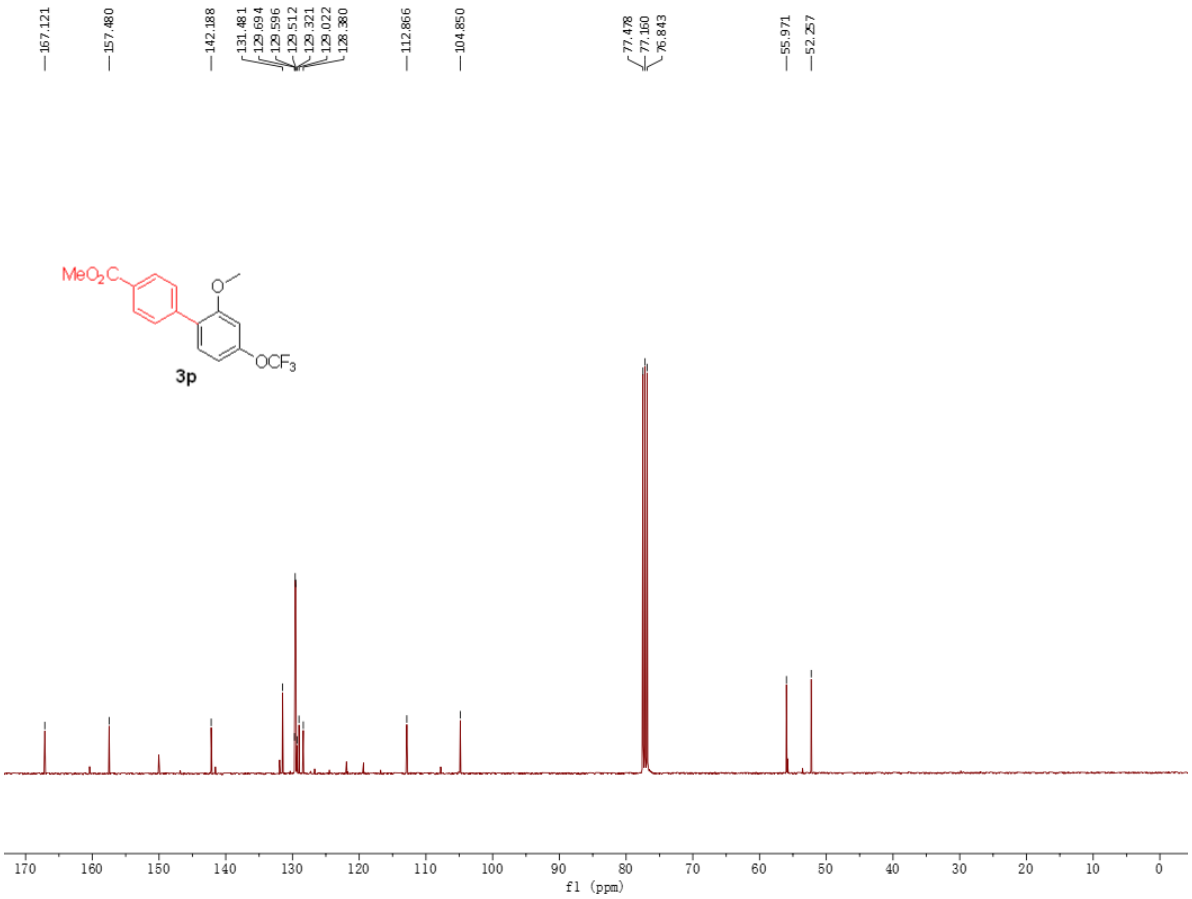
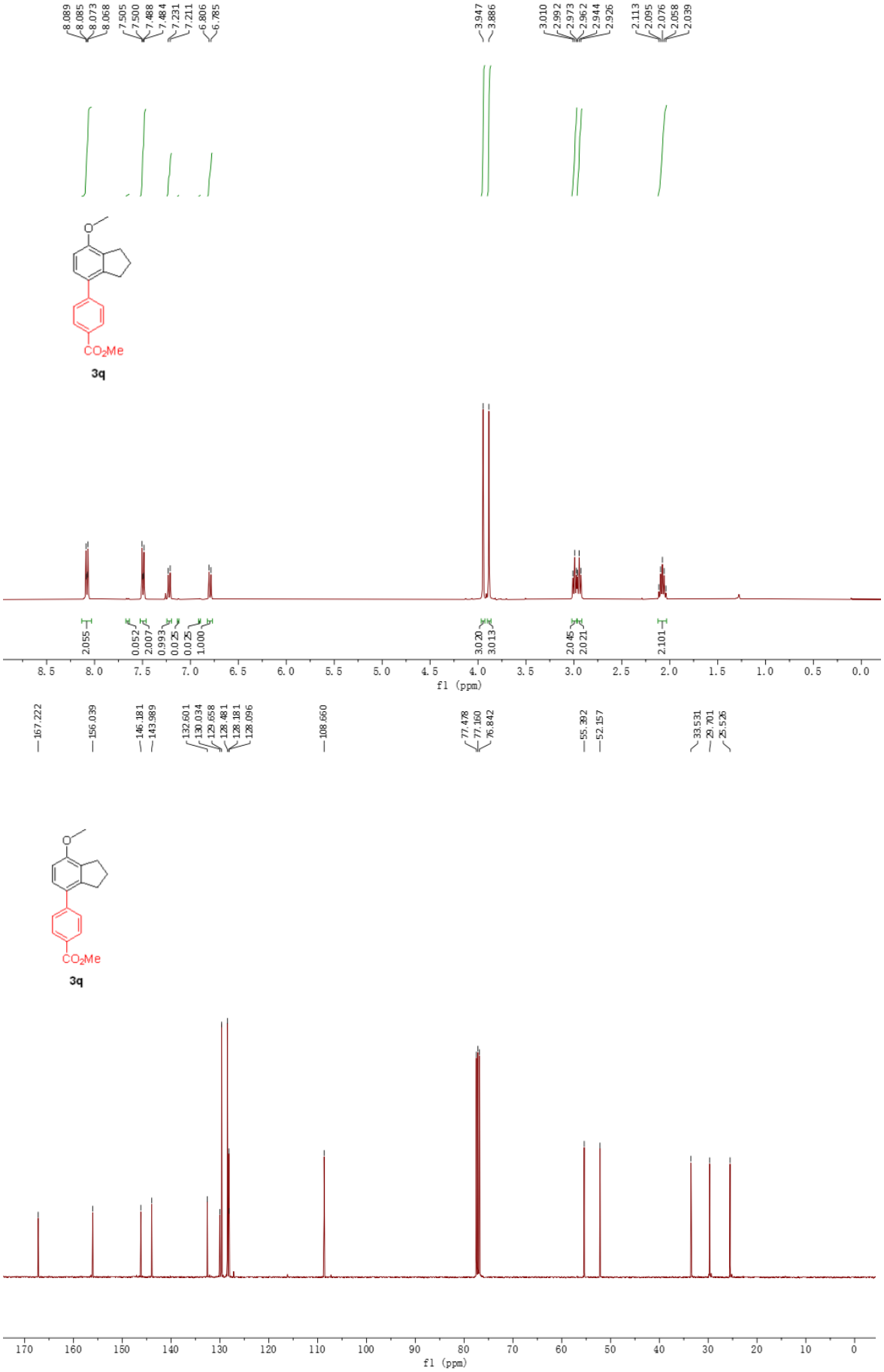

MeO2C
O
TMS
3o
f1 (ppm)

SUPPORTING INFORMATION



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3.886
3.010
2.992
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2.944
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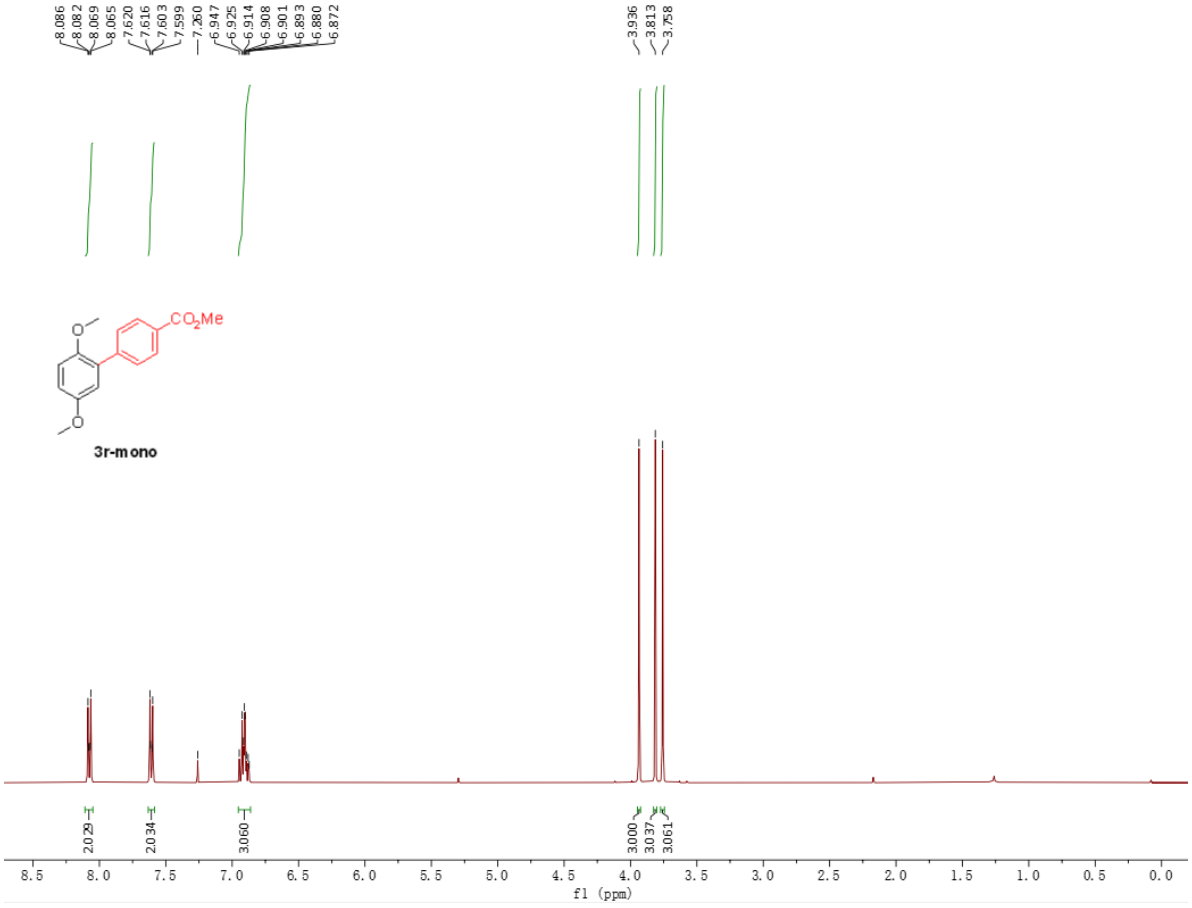
2.113
2.095
2.076
2.058
2.039
CO2Me
3q
2.055
0.052
2.007
0.993
0.025
0.025
1.000
3.020
3.013
2.045
2.021
2.101
f1 (ppm)
167.222
156.039
146.181
143.989
132.601
130.034
129.658
128.481
128.181
128.096
108.660
77.478
77.160
76.842
55.392
52.157
33.531
29.701
25.526
CO2Me
3q
f1 (ppm)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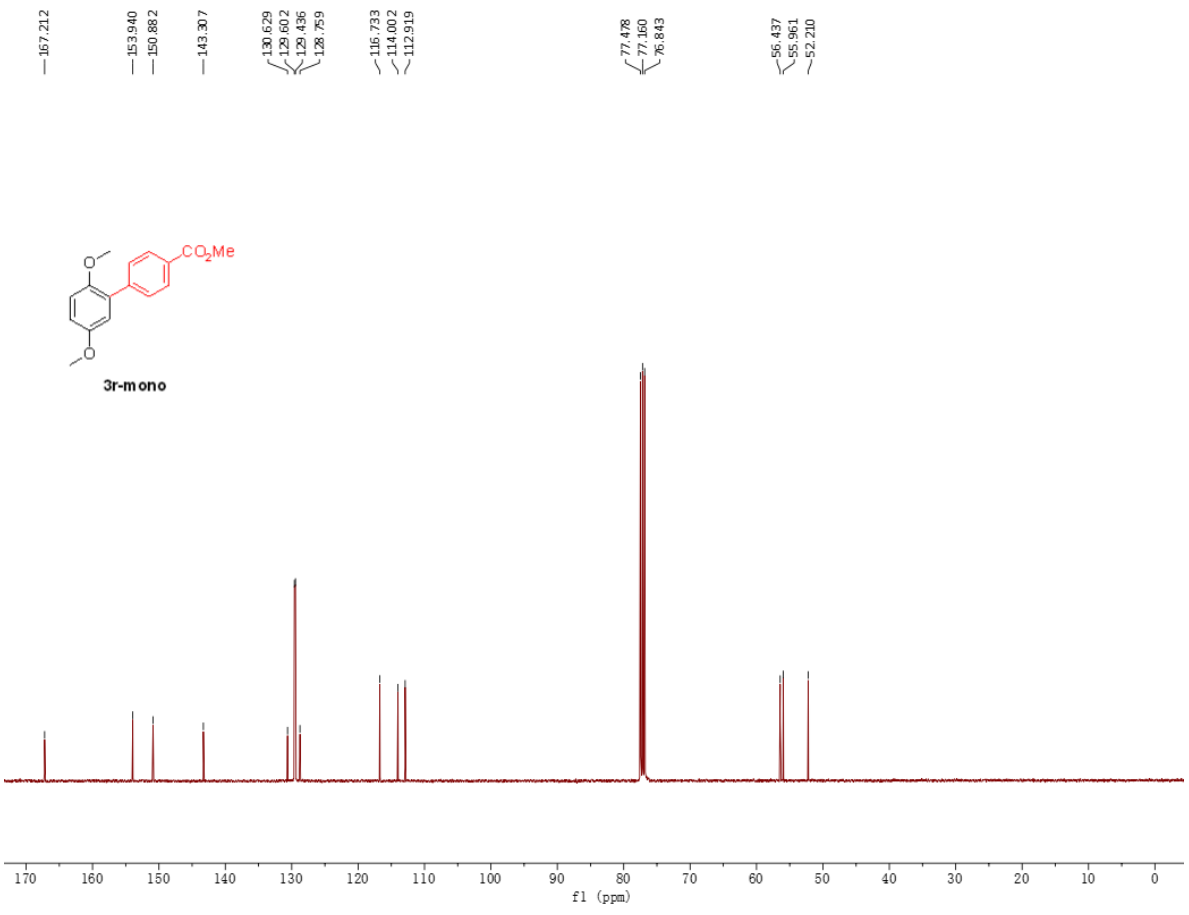
8.082
8.069
8.065
7.620
7.616
7.603
7.599
7.260
6.947
6.925
6.914
6.908
6.901
6.893
6.880
6.872
3.936
3.813
3.758
CO2Me
3r-mono
2.029
2.034
3.060
3.000
3.037
3.061
f1 (ppm)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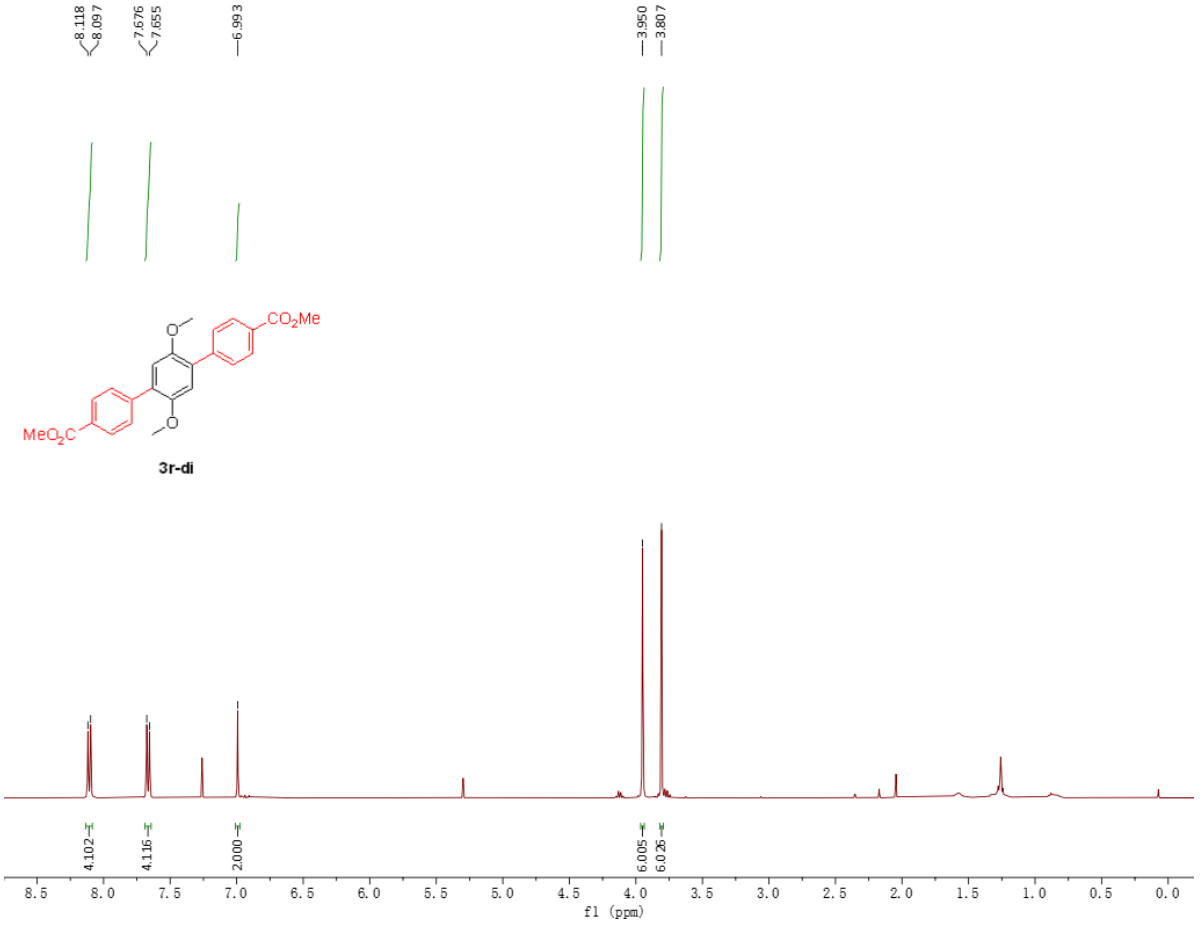
153.940
150.882
143.307
130.629
129.602
129.436
128.759
116.733
114.002
112.919
77.478
77.160
76.843
56.437
55.961
52.210
CO2Me
3r-mono
f1 (ppm)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8.097
7.676
7.655
6.993
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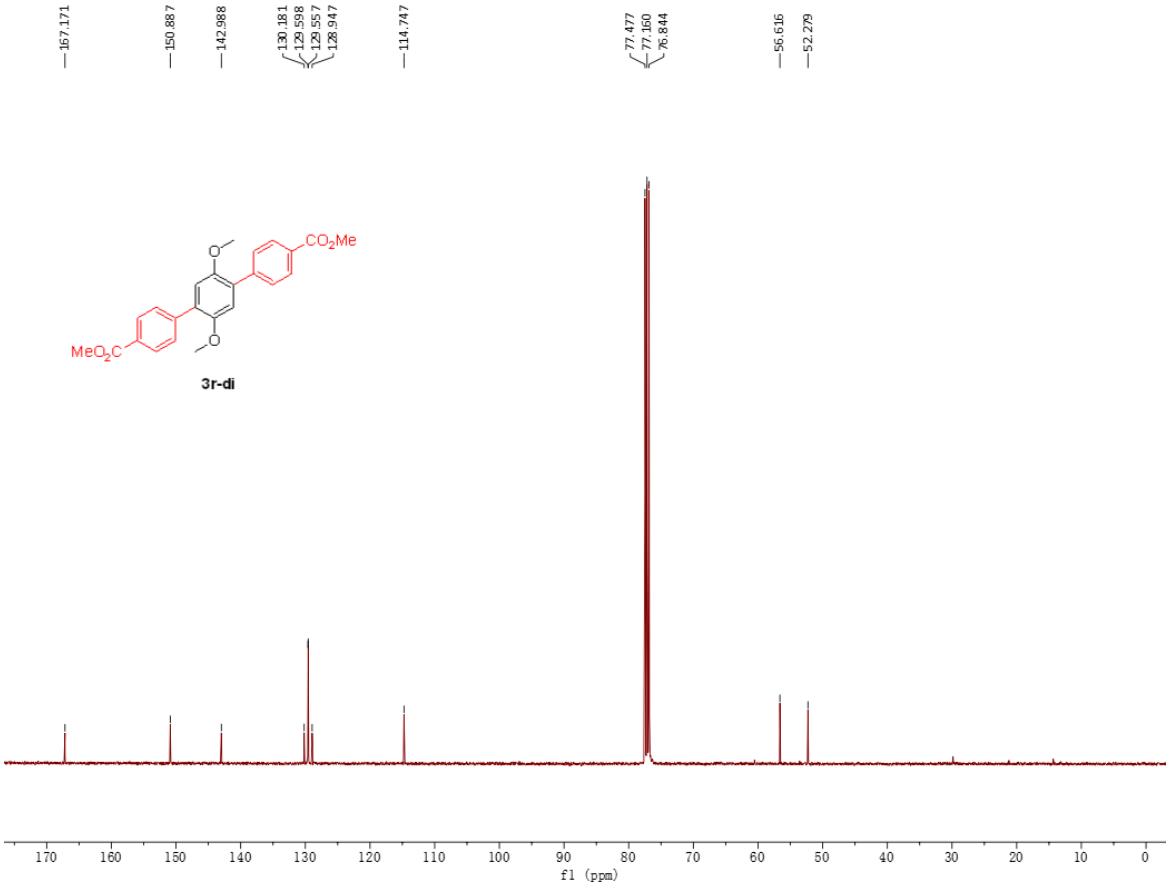
3.807
CO2Me
MeO2C
3r-di
4.102
4.116
2.000
6.005
6.026
f1 (ppm)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142.988
130.181
129.598
129.557
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114.747
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77.160
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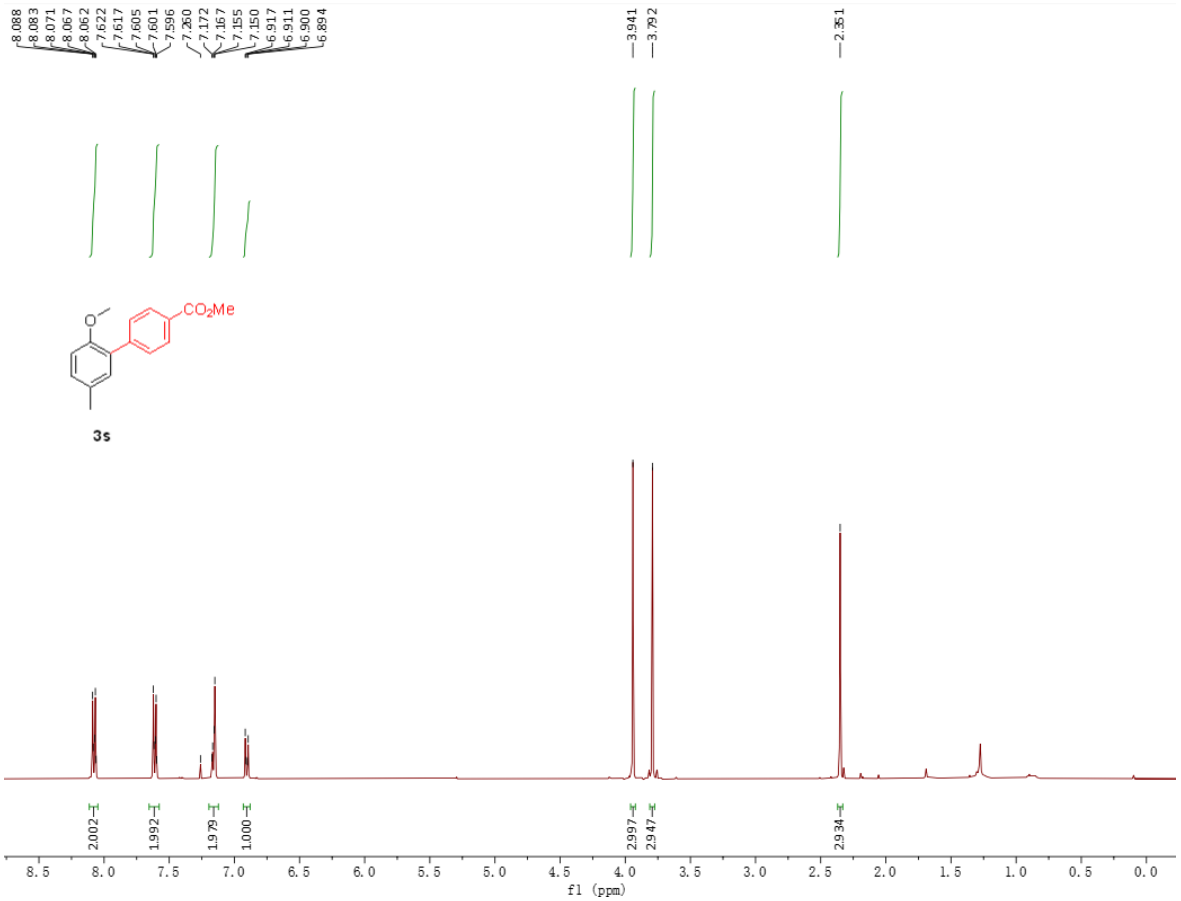
56.616
52.279
CO2Me
MeO2C
3r-di
f1 (ppm)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8.083
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8.067
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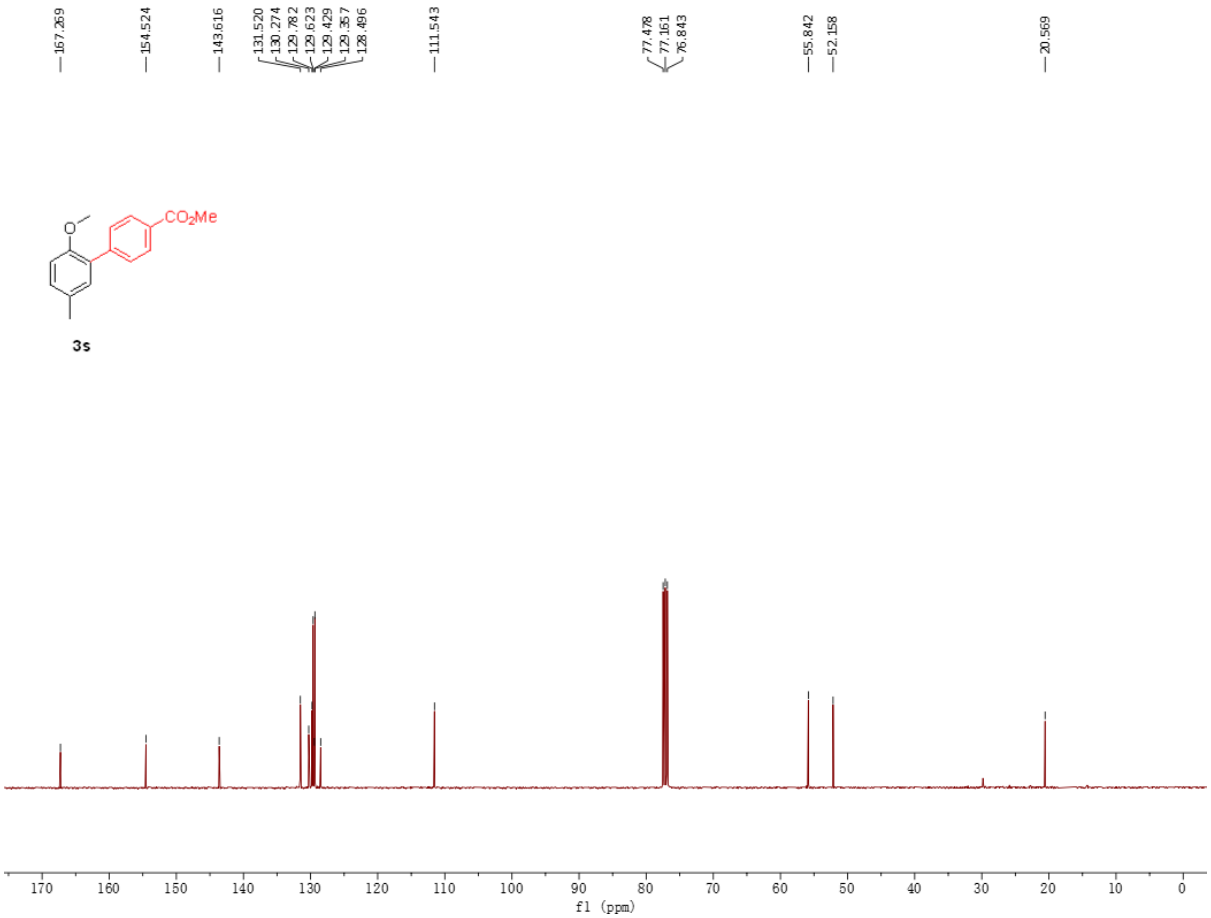
7.617
7.605
7.601
7.596
7.260
7.172
7.167
7.155
7.150
6.917
6.911
6.900
6.894
3.941
3.792
2.351
CO2Me
3s
2.002
1.992
1.979
1.000
2.997
2.947
2.934
f1 (ppm)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131.520
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129.782
129.623
129.429
129.357
128.496
111.543
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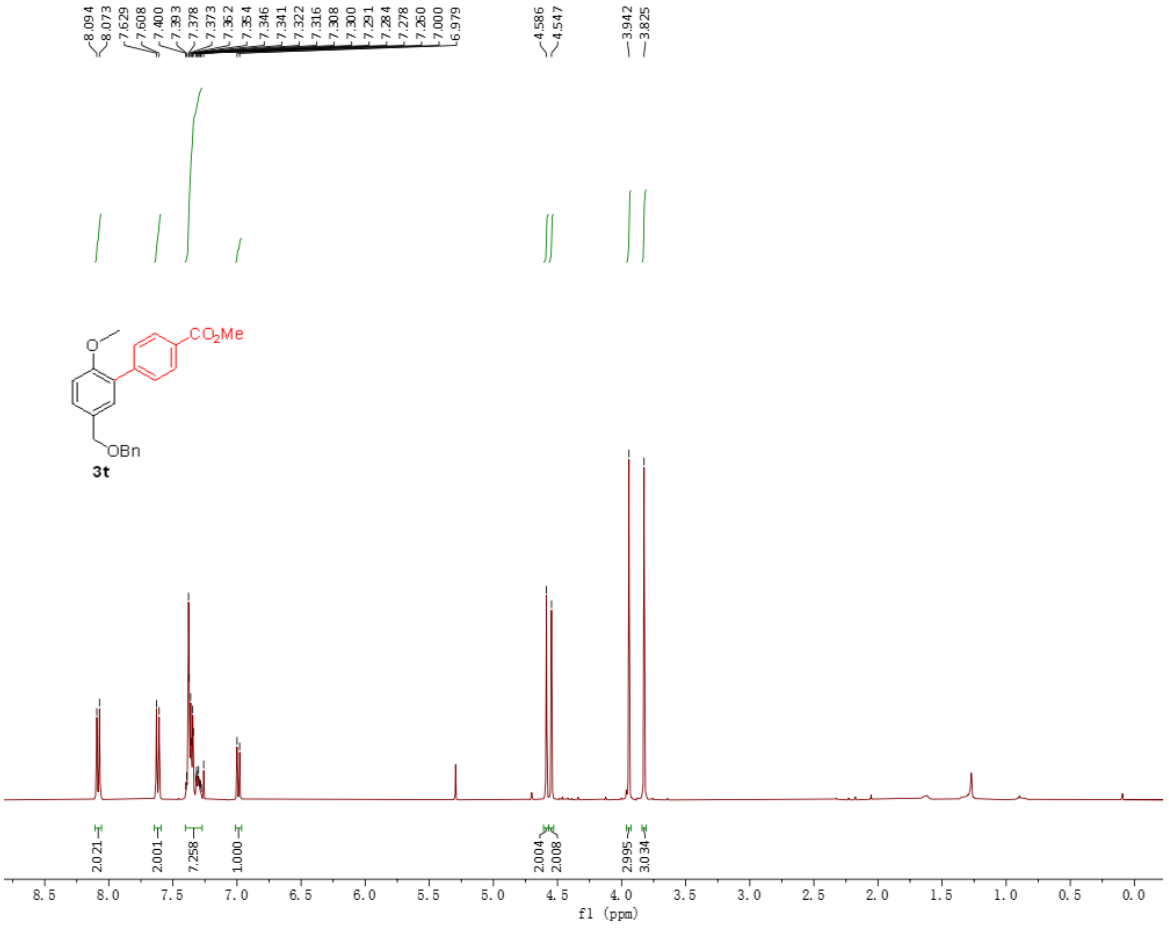
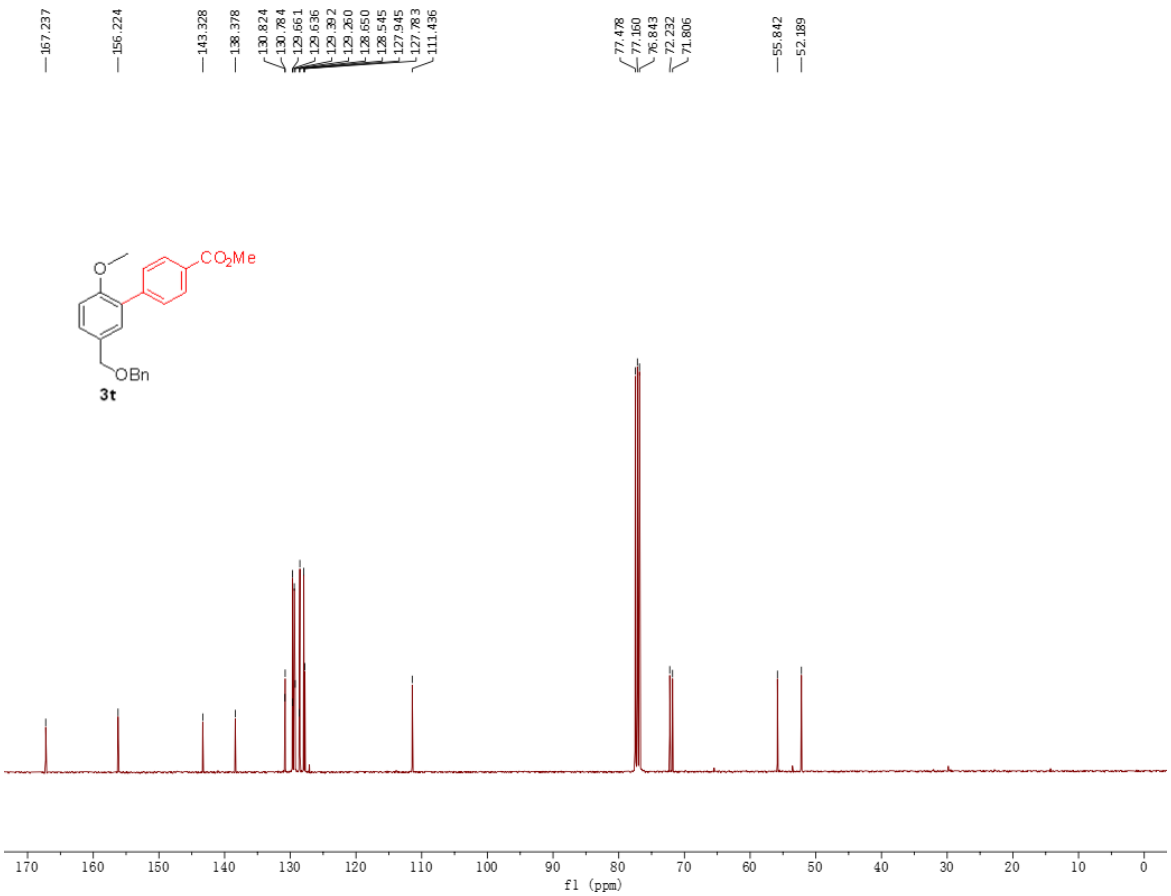
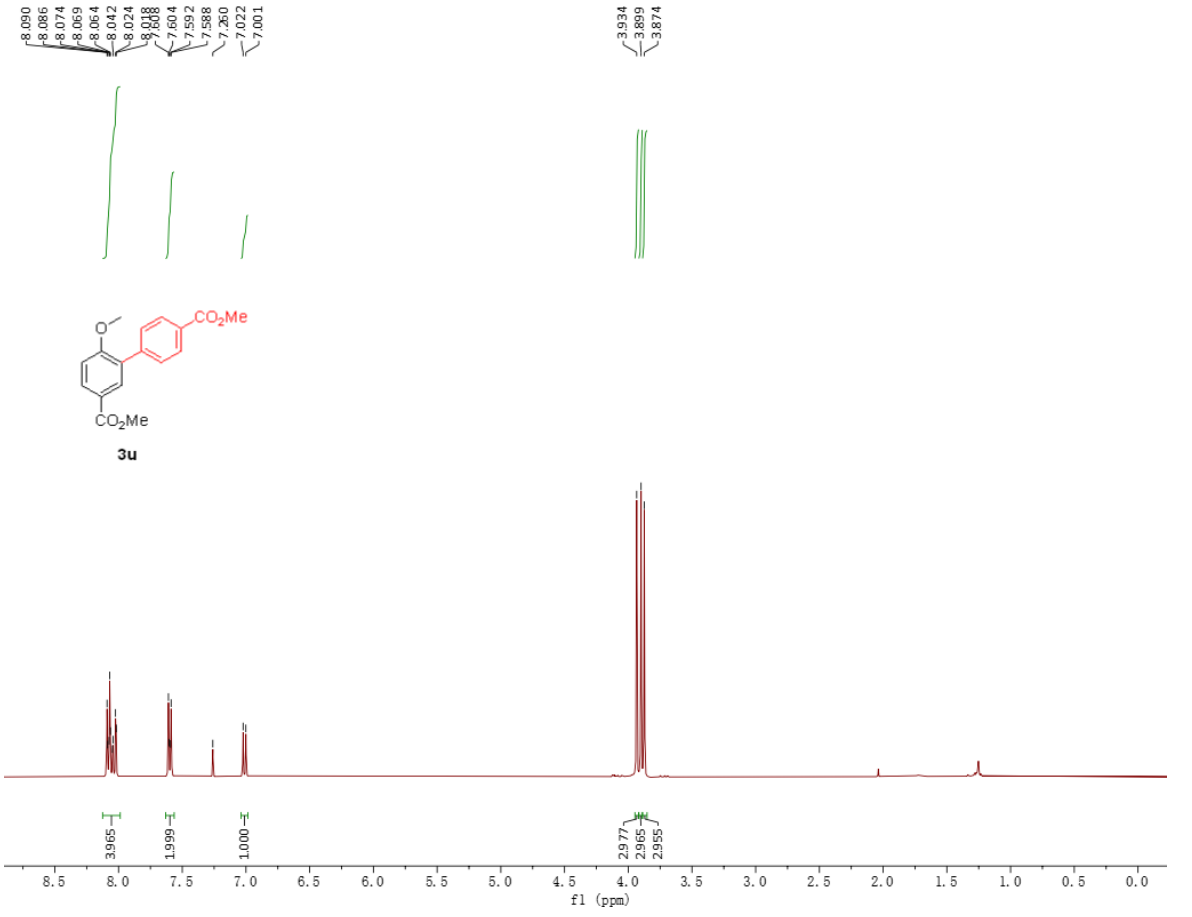
77.161
76.843
55.842
52.158
20.569
CO2Me
3s
f1 (ppm)

SUPPORTING INFORMATION



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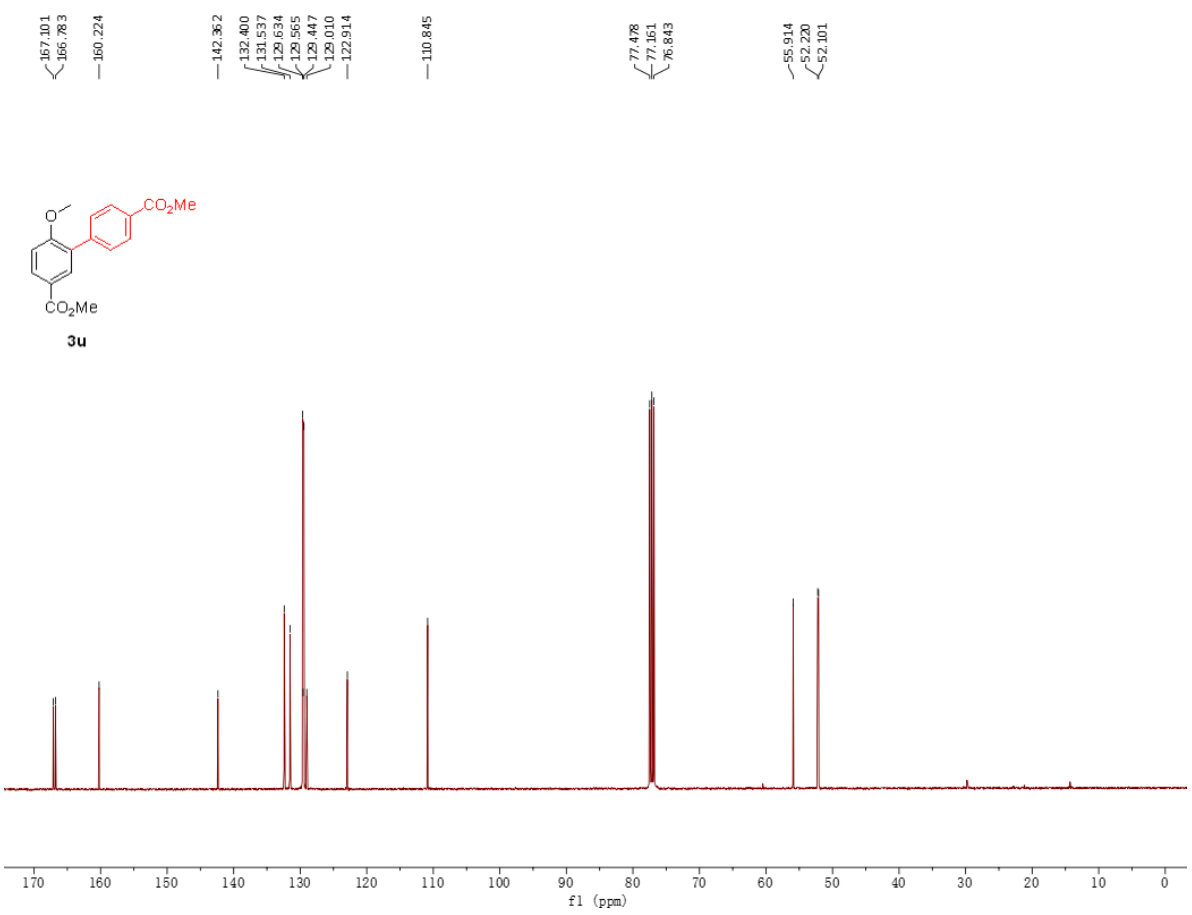
8.069
8.064
8.042
8.024
8.018
8.008
7.604
7.592
7.588
7.260
7.022
7.001
3.934
3.899
3.874
CO2Me
CO2Me
3u
3.965
1.999
1.000
2.977
2.965
2.955
f1 (ppm)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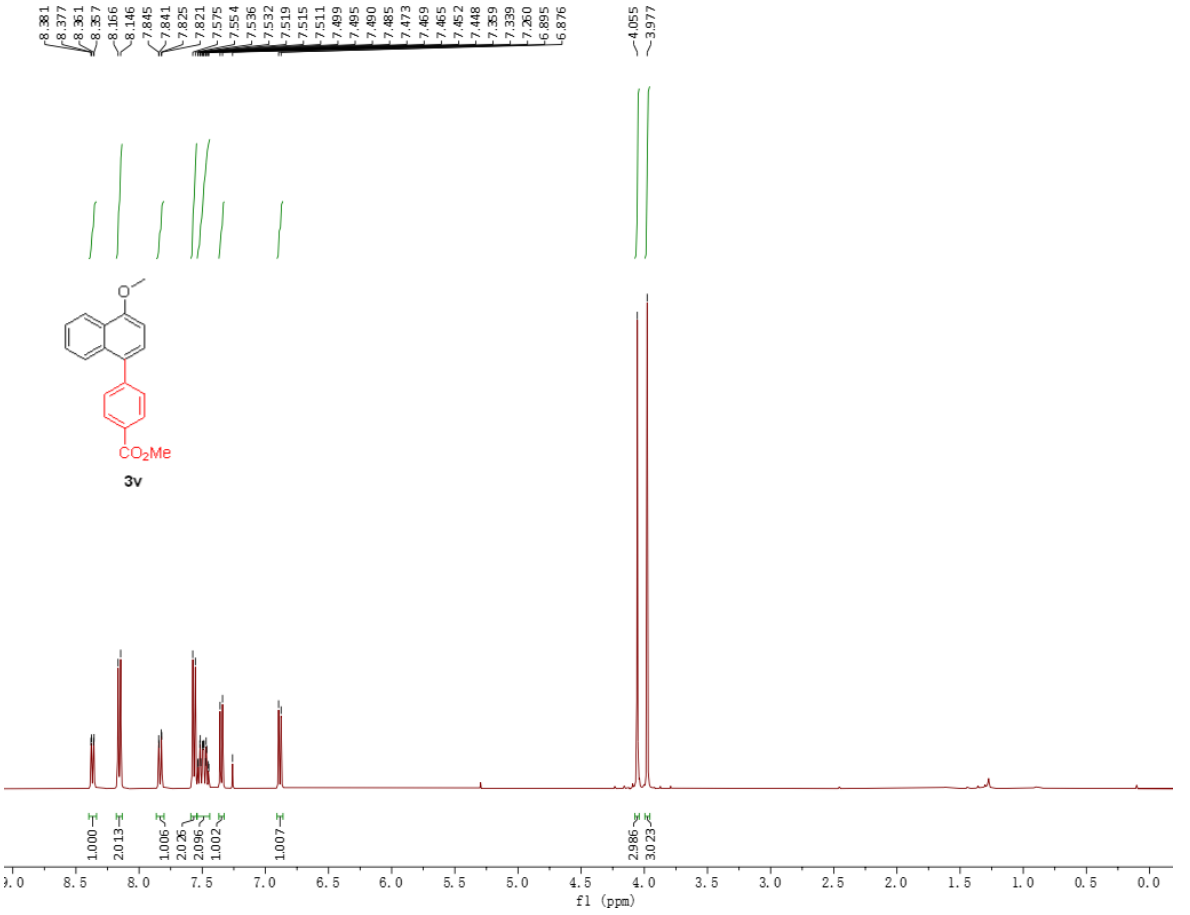
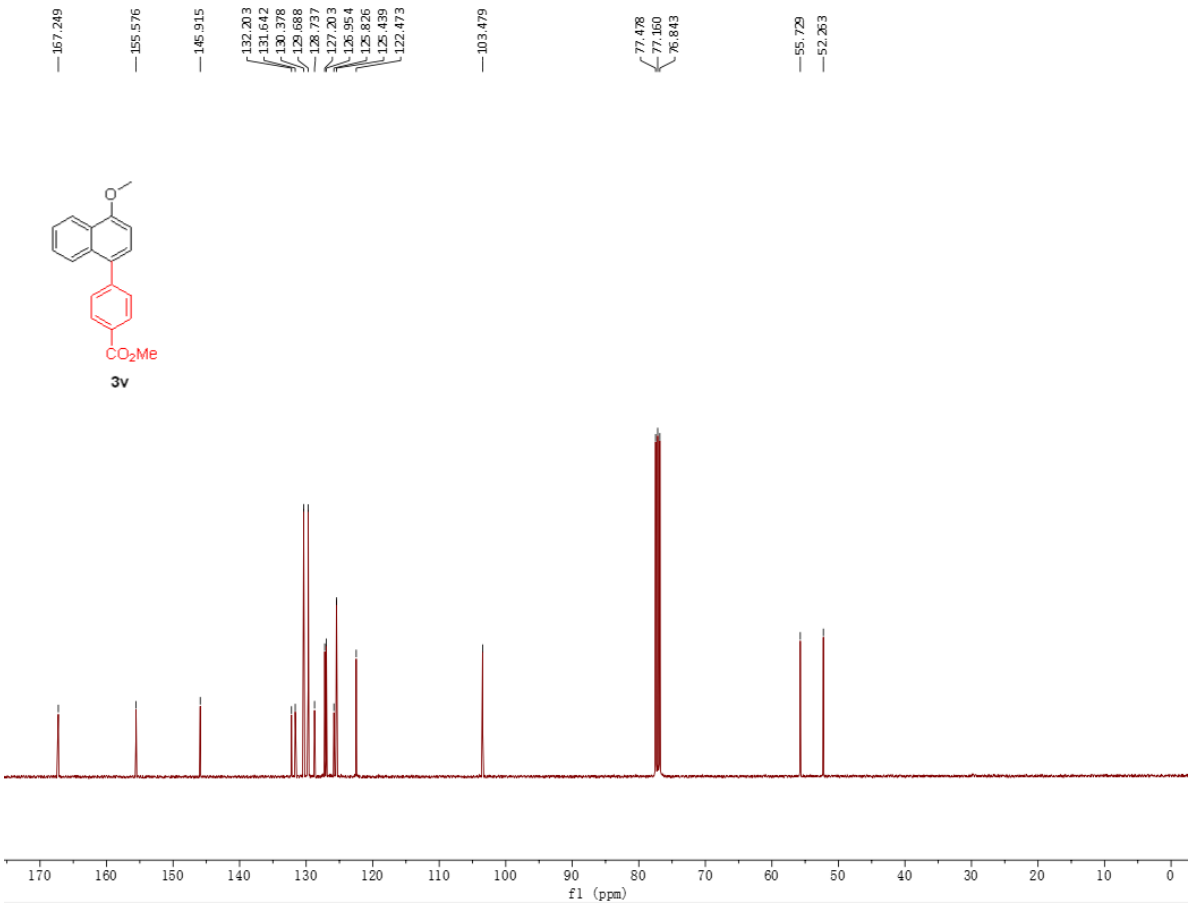
166.783
160.224
142.362
132.400
131.537
129.634
129.565
129.447
129.010
122.914
110.845
77.478
77.161
76.843
55.914
52.220
52.101
CO2Me
CO2Me
3u
f1 (ppm)

SUPPORTING INFORMATION





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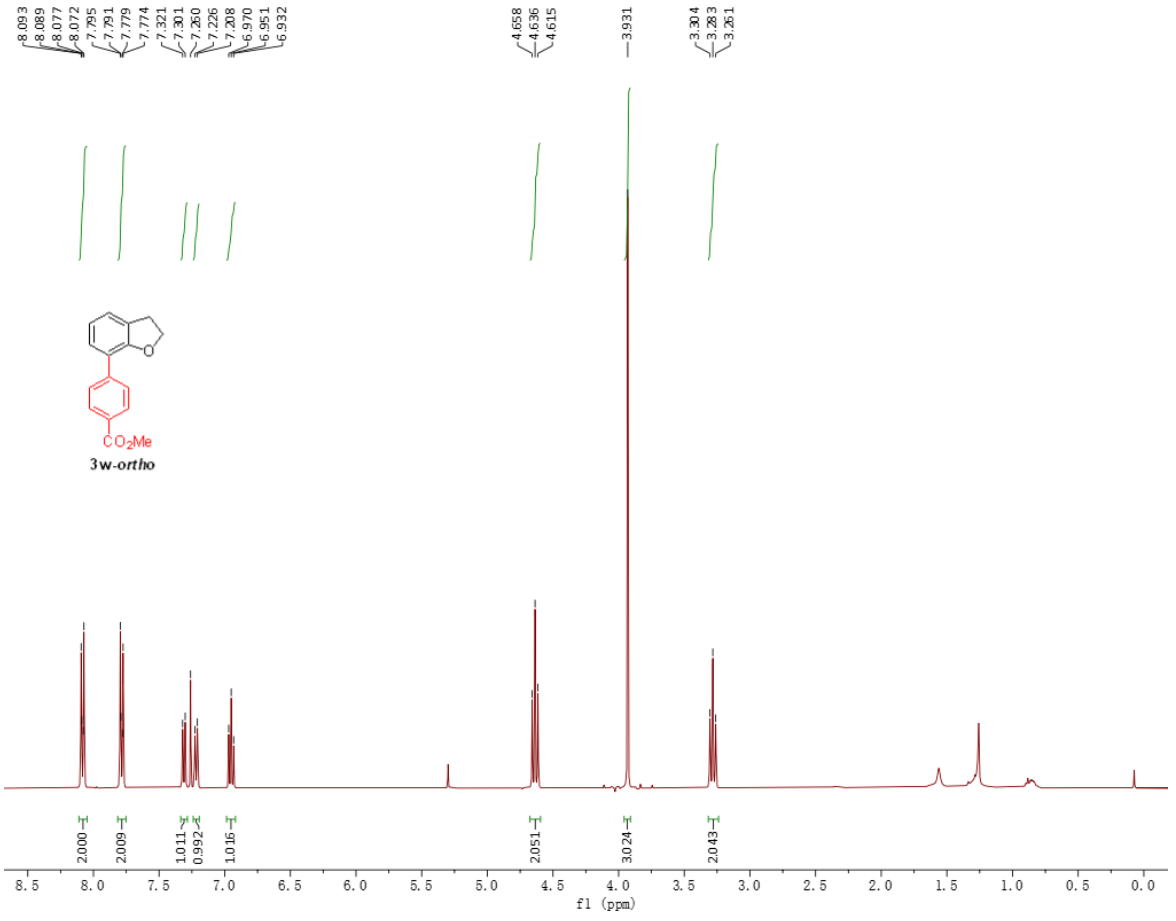

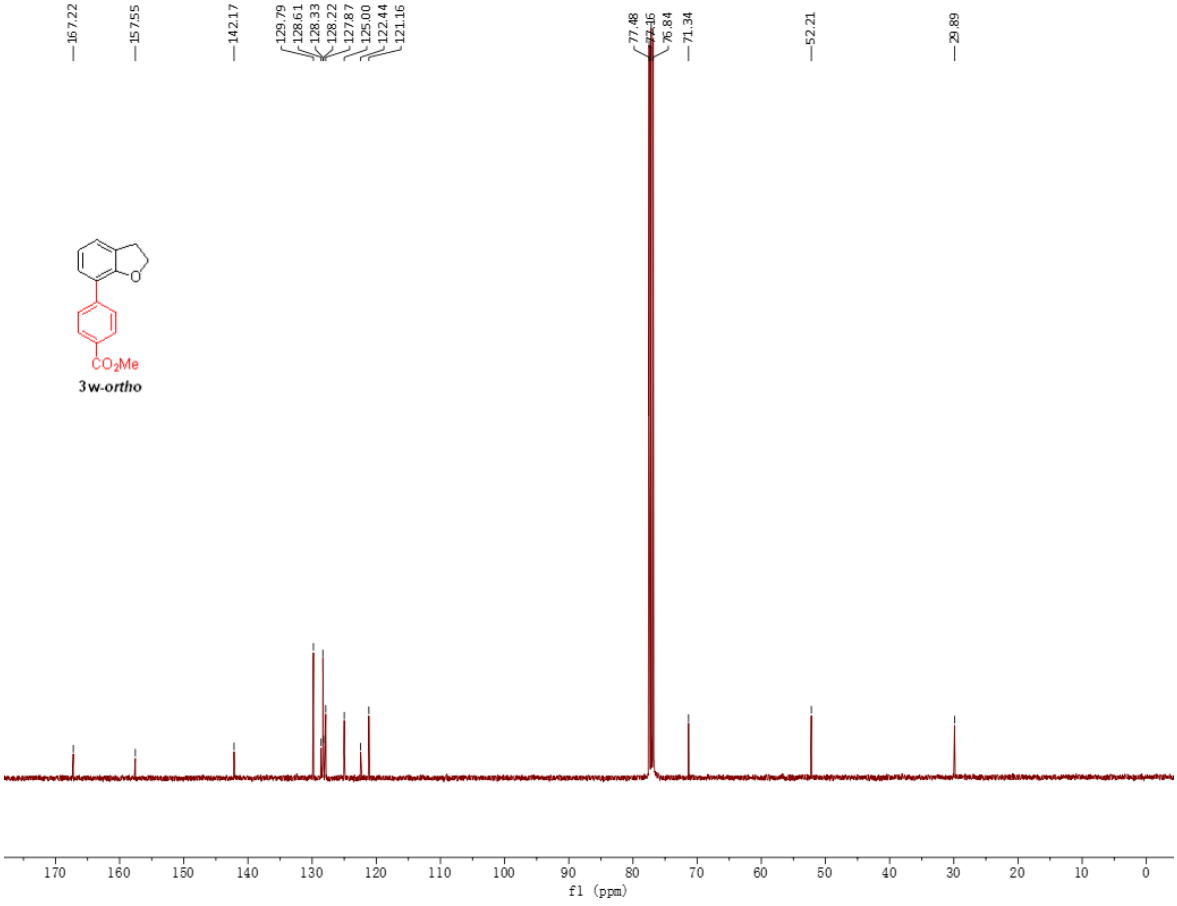

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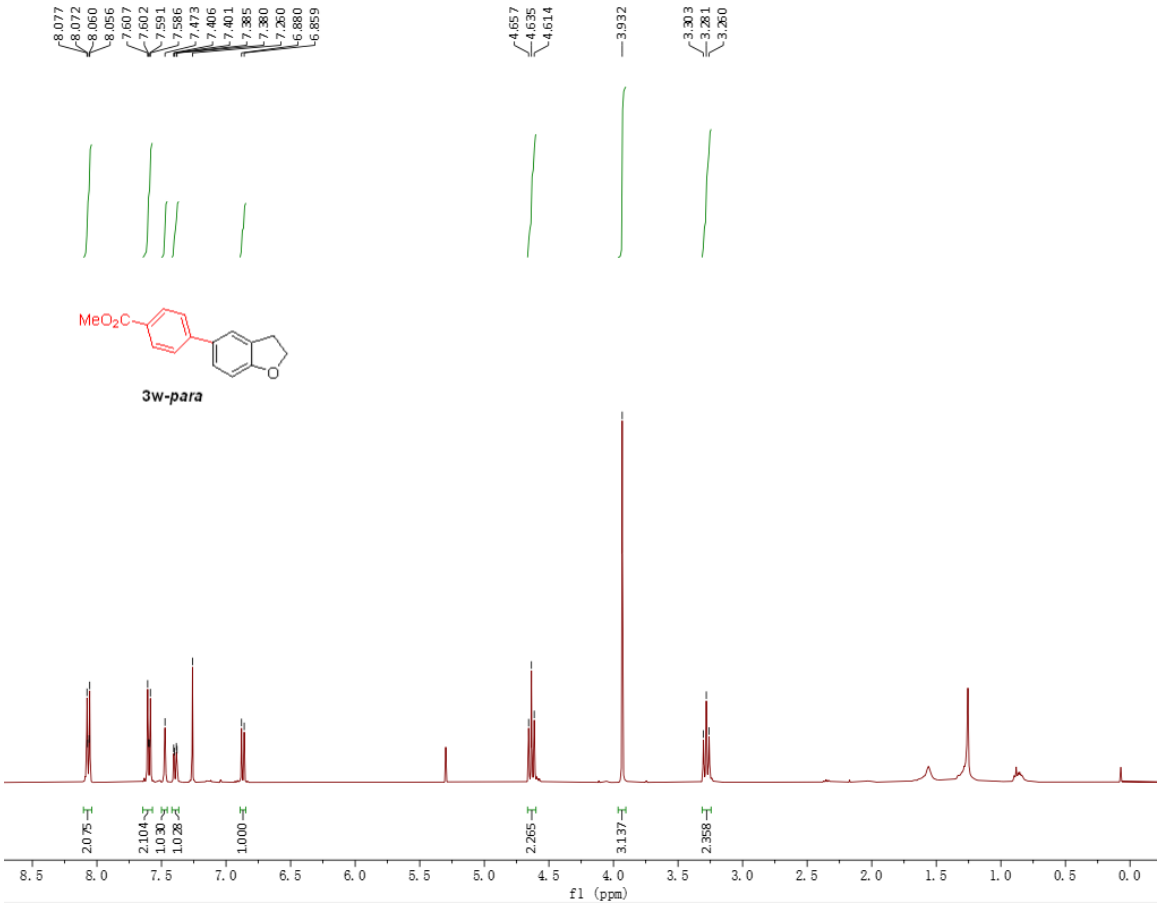

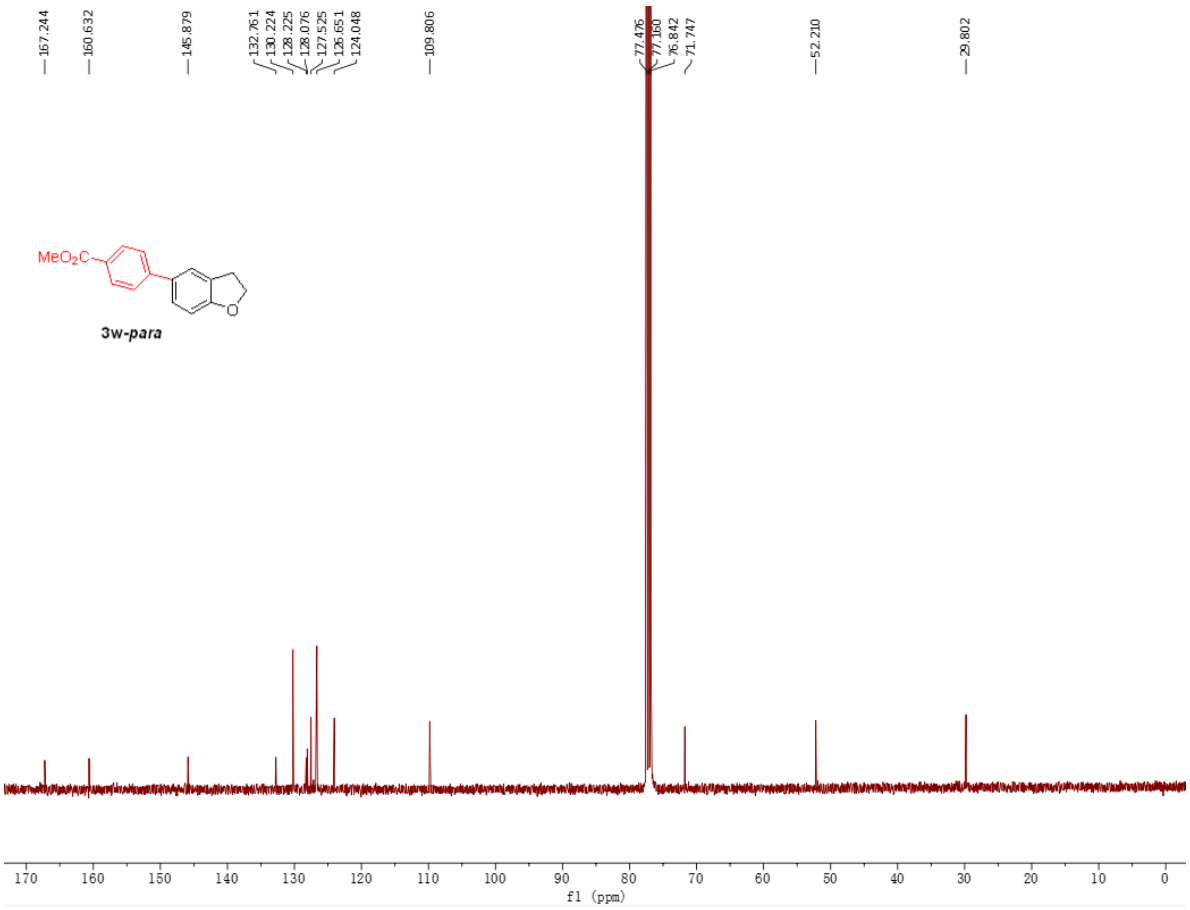

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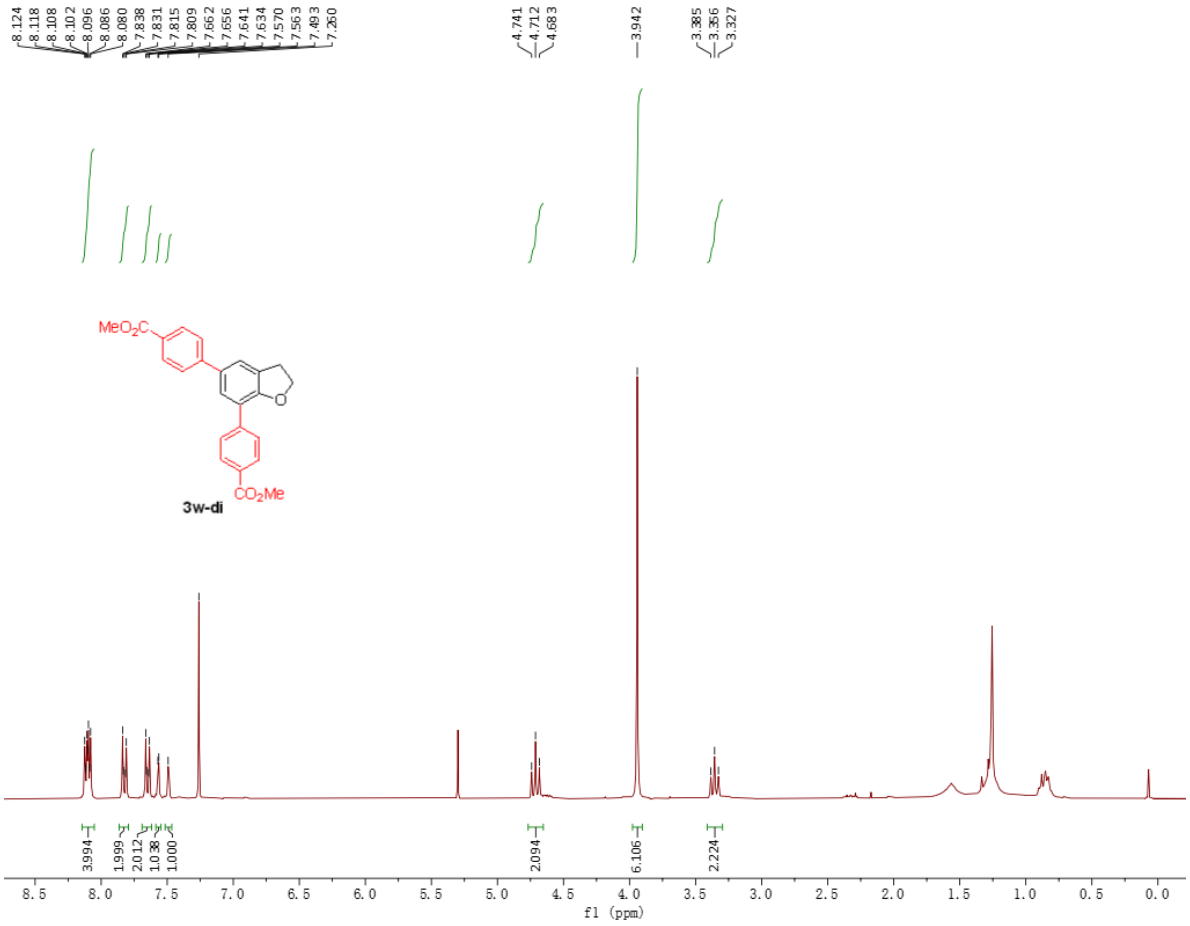

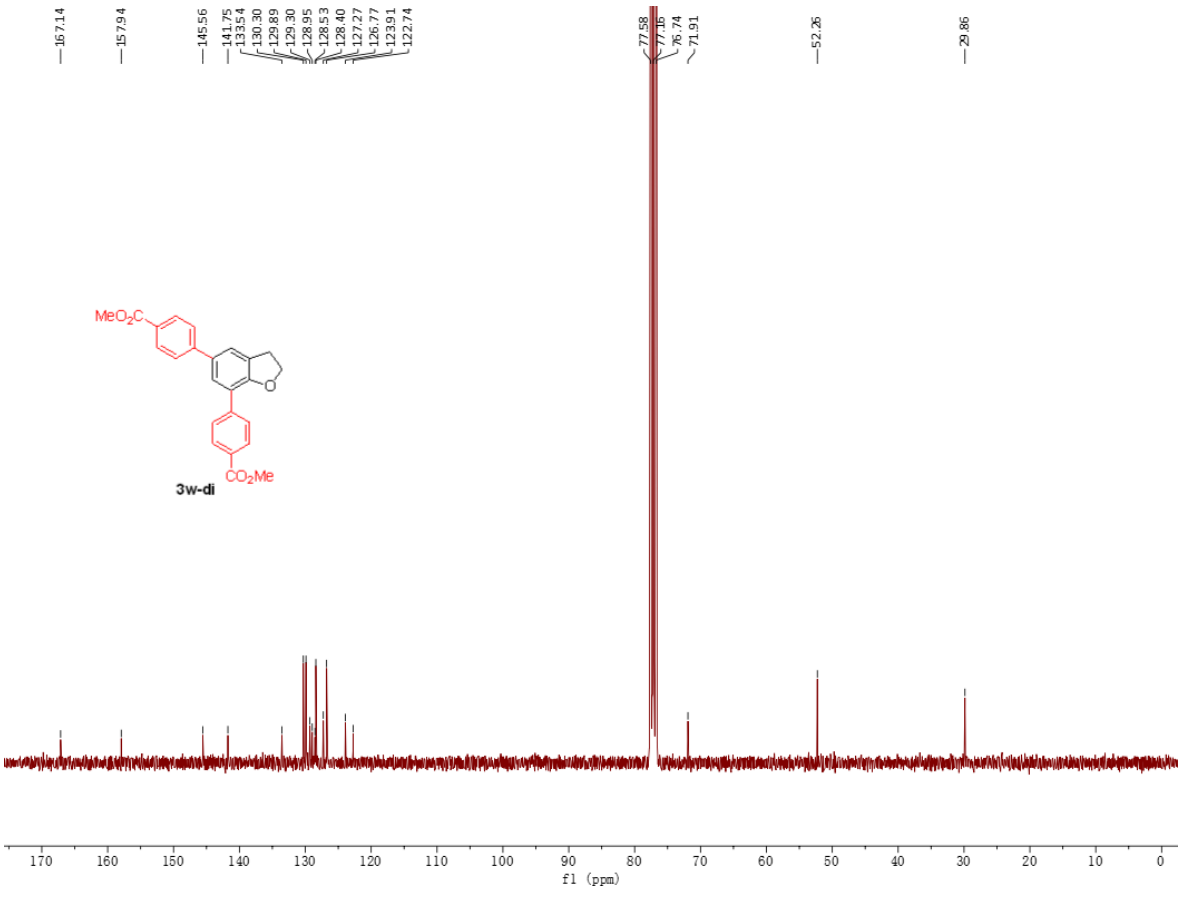

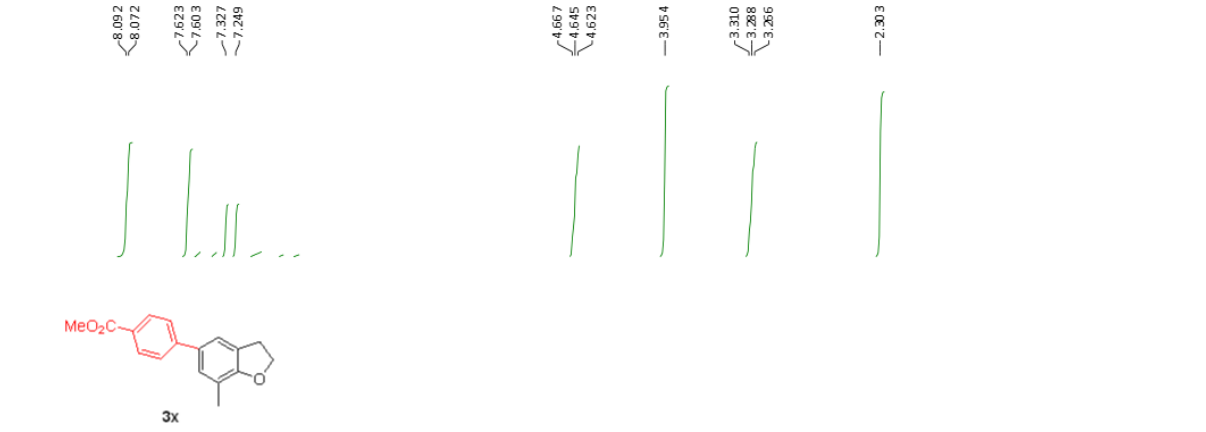
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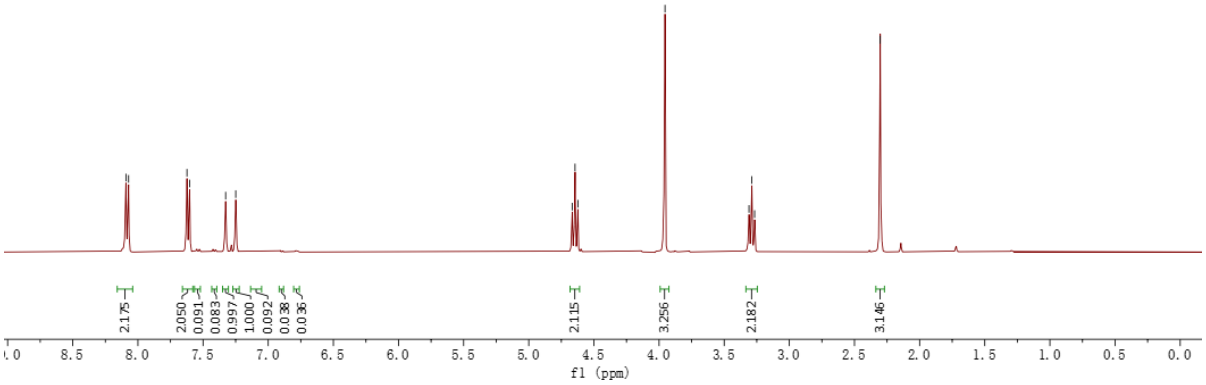
8.072
7.623
7.603
7.327
7.249
4.667
4.645
4.623
3.954
3.310
3.288
3.266
2.303
MeO2C
O

3x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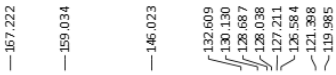
2.050
0.091
0.083
0.997
1.000
0.092
0.038
0.036
2.115
3.256
2.182
3.146
f1 (ppm)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159.034
146.023
132.609
130.130
128.687
128.038
127.211
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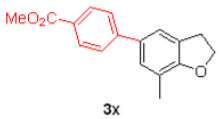
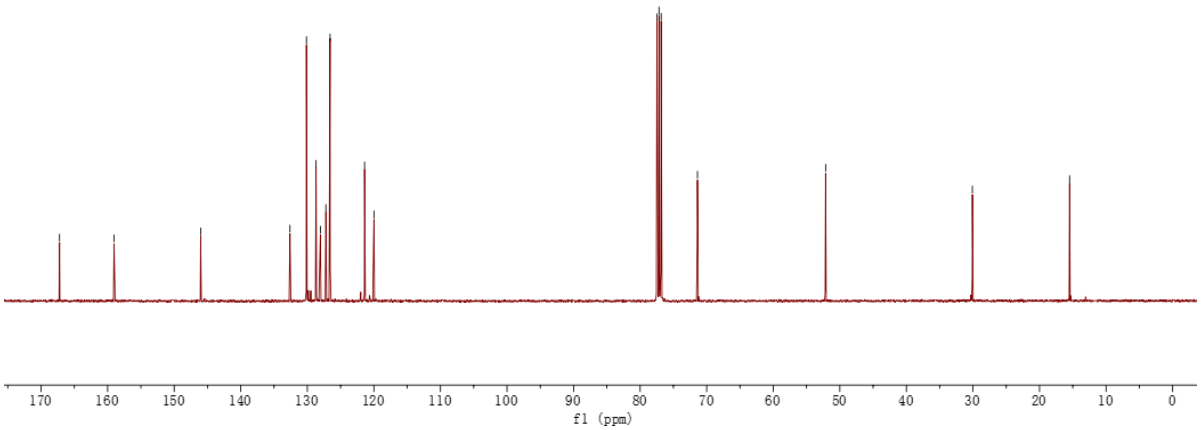
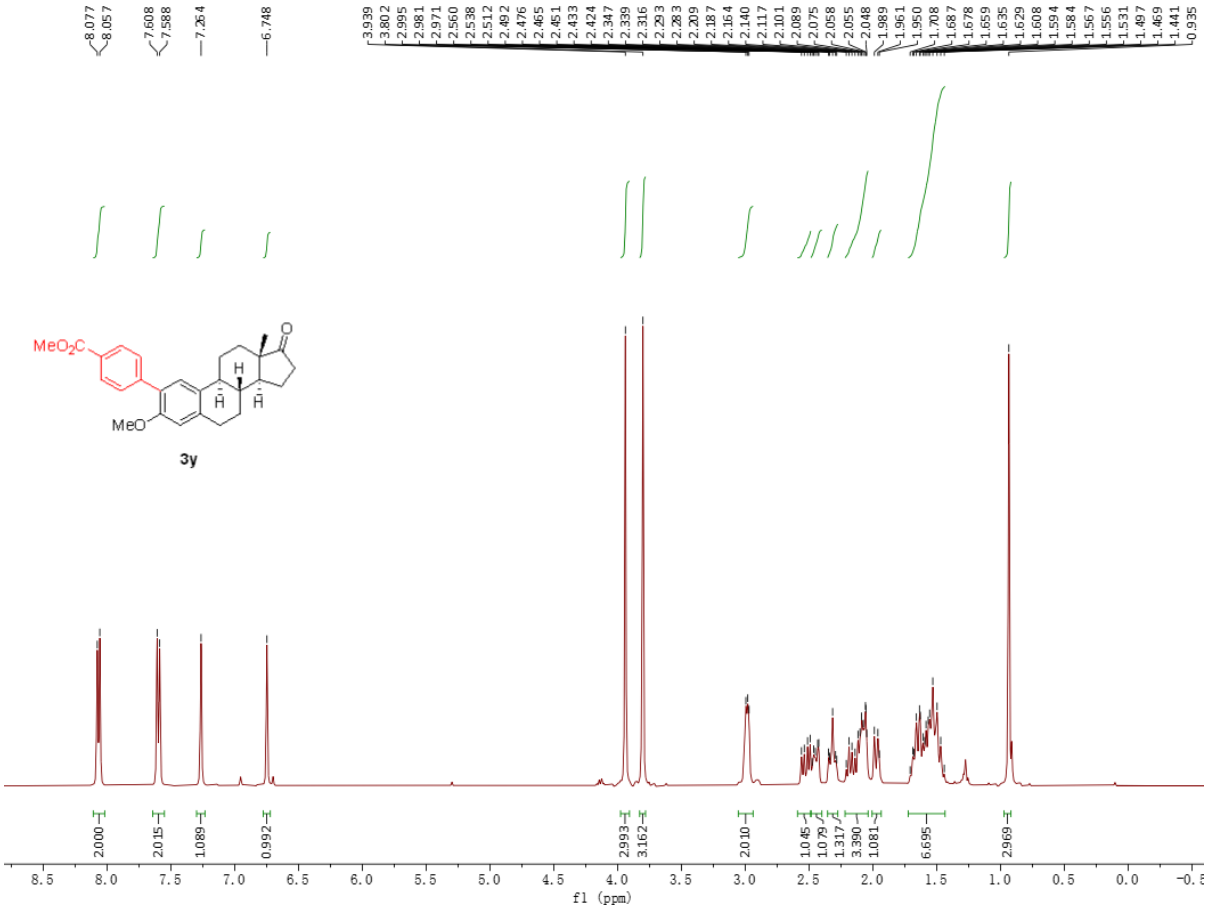
121.398
119.985
77.478
77.160
76.842
71.390
52.135
30.086
15.482


MeO2C
O

3x


f1 (ppm)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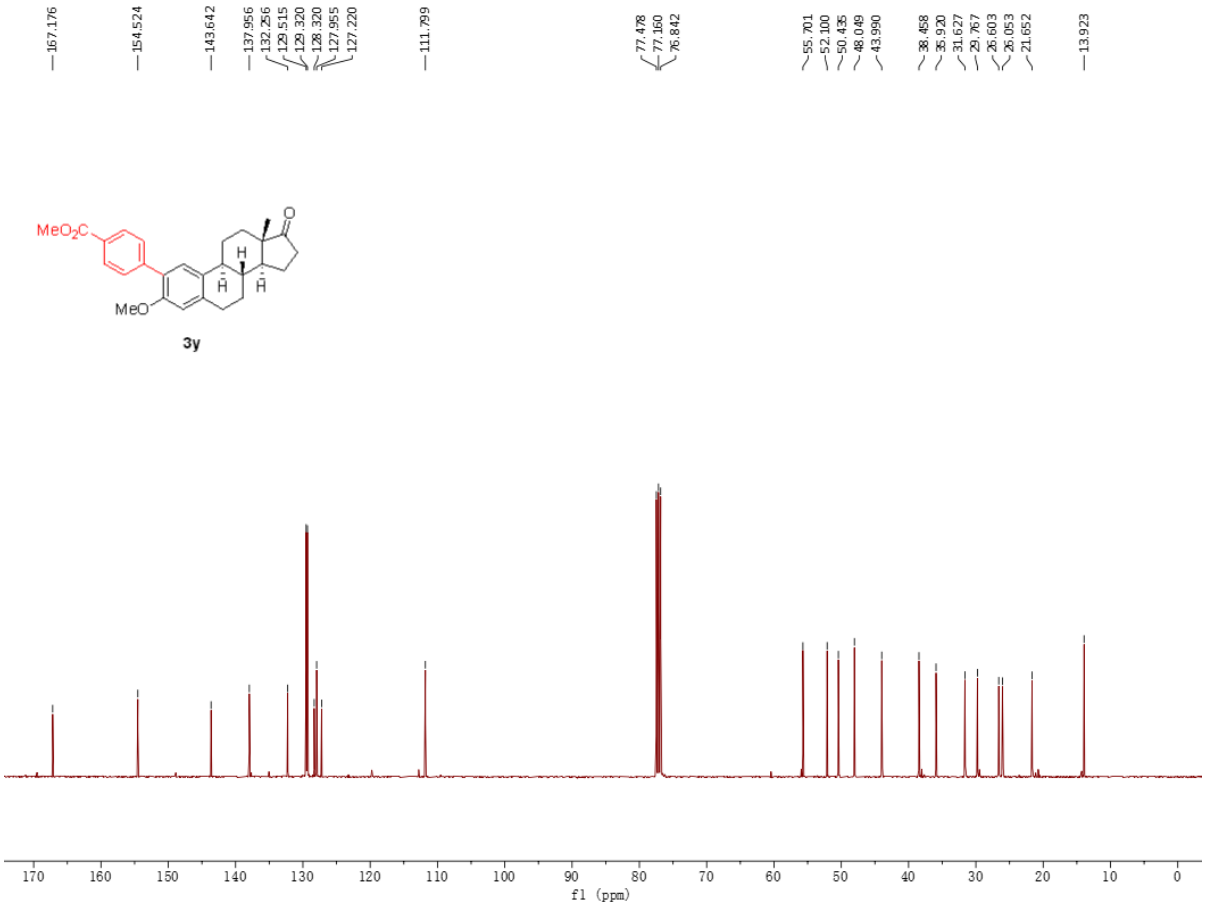
8.057
7.608
7.588
7.264
6.748
MeO2C
MeO
3y
2.000
2.015
1.089
0.992
2.993
3.162
2.010
1.045
1.079
1.317
3.390
1.081
6.695
2.969
f1 (ppm)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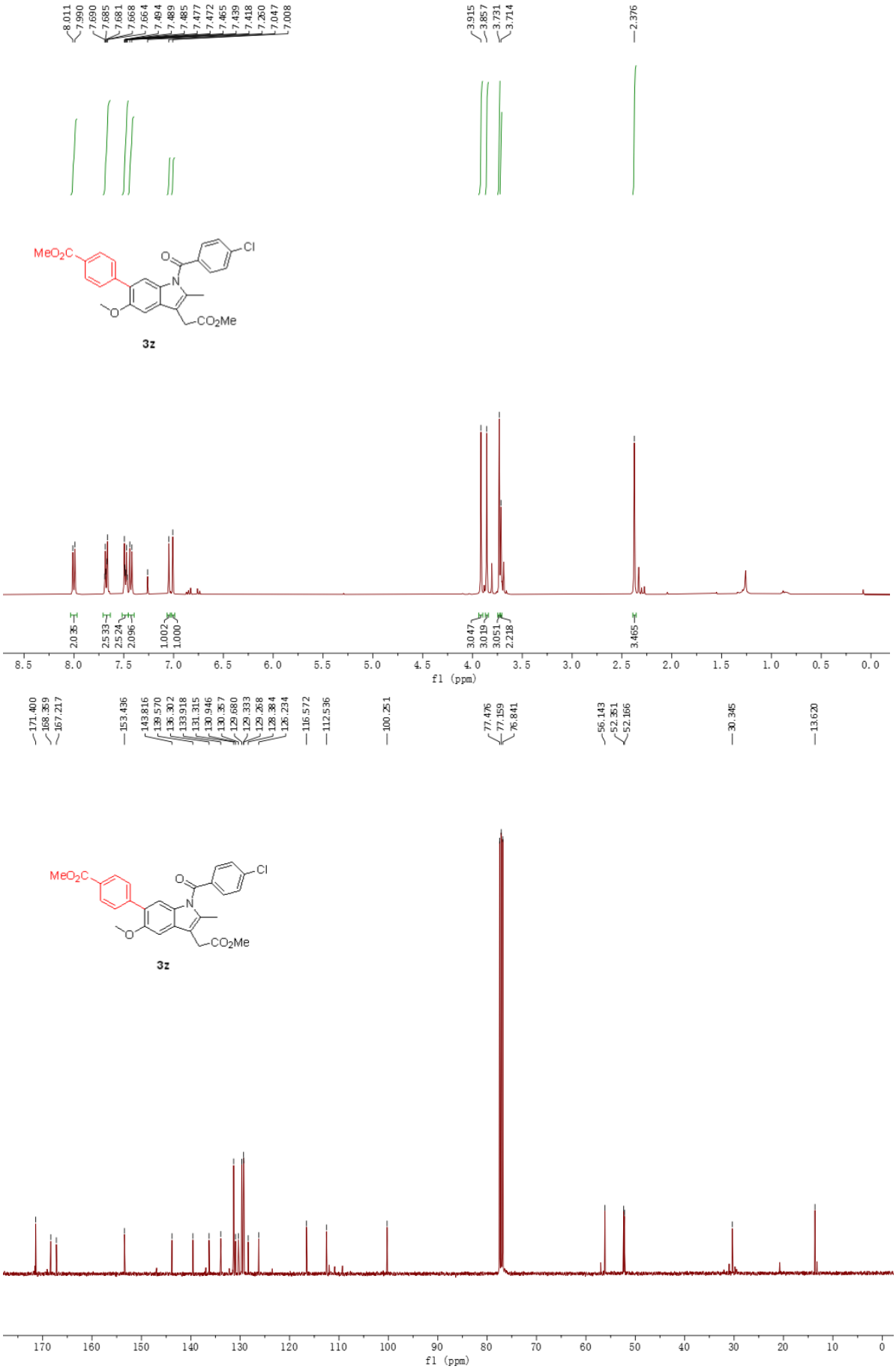
128.320
127.955
127.220
111.799
77.478
77.160
76.842
55.701
52.100
50.435
48.049
43.990
38.458
35.920
31.627
29.767
26.603
26.053
21.652
13.923
MeO2C
MeO
3y
f1 (ppm)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7.494
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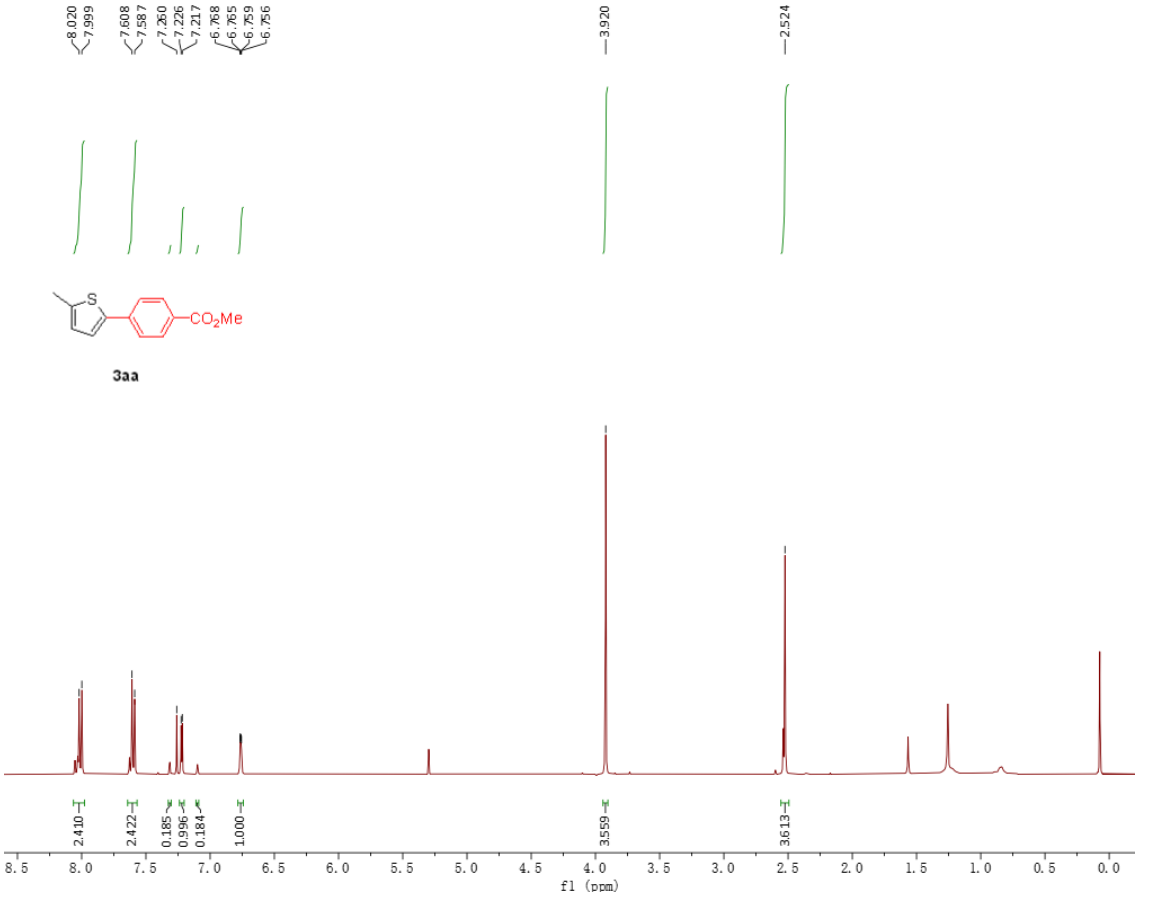
7.485
7.477
7.472
7.465
7.439
7.418
7.260
7.047
7.008
3.915
3.857
3.731
3.714
2.376
MeO2C
O
N
Cl
O
CO2Me
3z
20.35
25.33
25.24
20.96
1.002
1.000
30.47
30.19
30.51
2.218
3.465
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
171.400
168.359
167.217
153.436
143.816
139.570
136.302
133.918
131.315
130.946
130.357
129.680
129.333
129.268
128.384
126.234
116.572
112.536
100.251
77.476
77.159
76.841
56.143
52.351
52.166
30.345
13.620
MeO2C
O
N
Cl
O
CO2Me
3z
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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6.759
6.756
3.920
2.524
S
CO2Me
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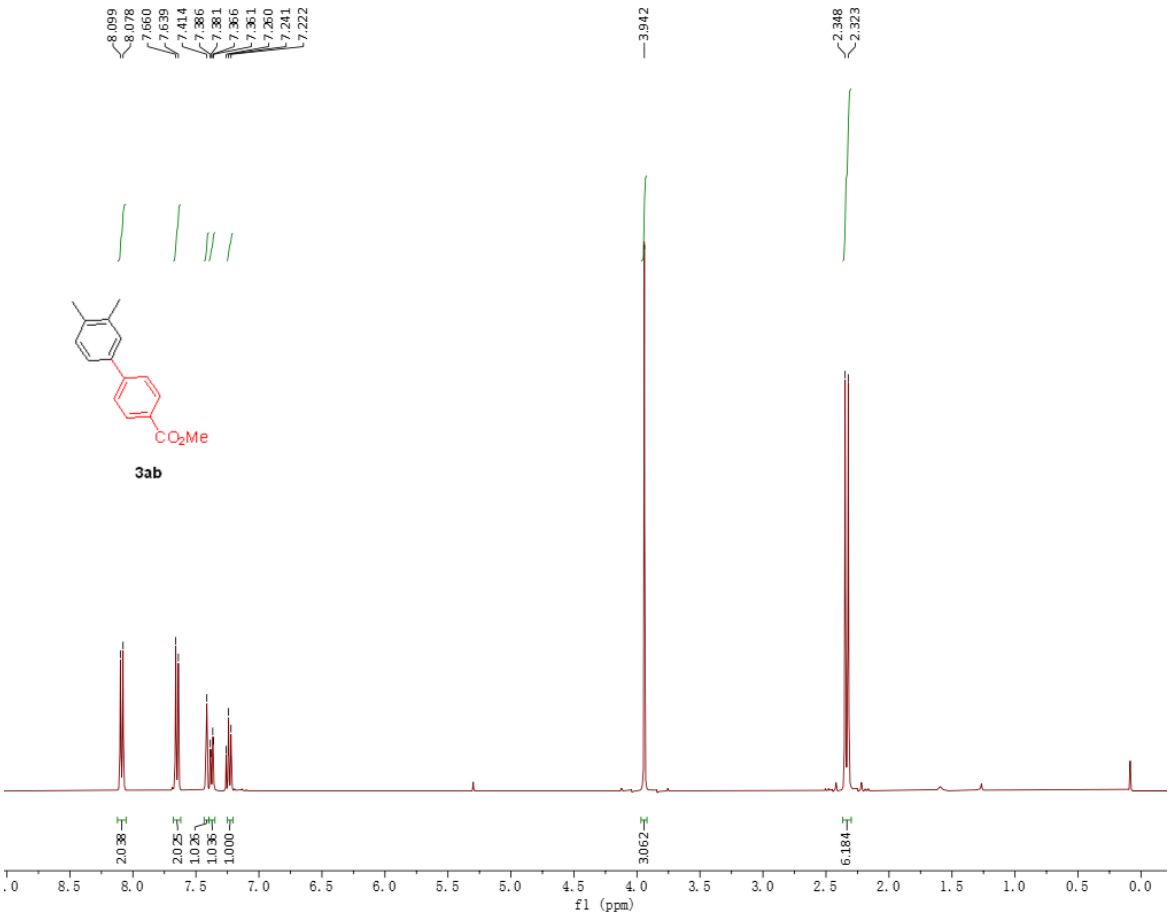
3.559
3.613
f1 (ppm)

3aa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7.222
3.942
2.348
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CO2Me
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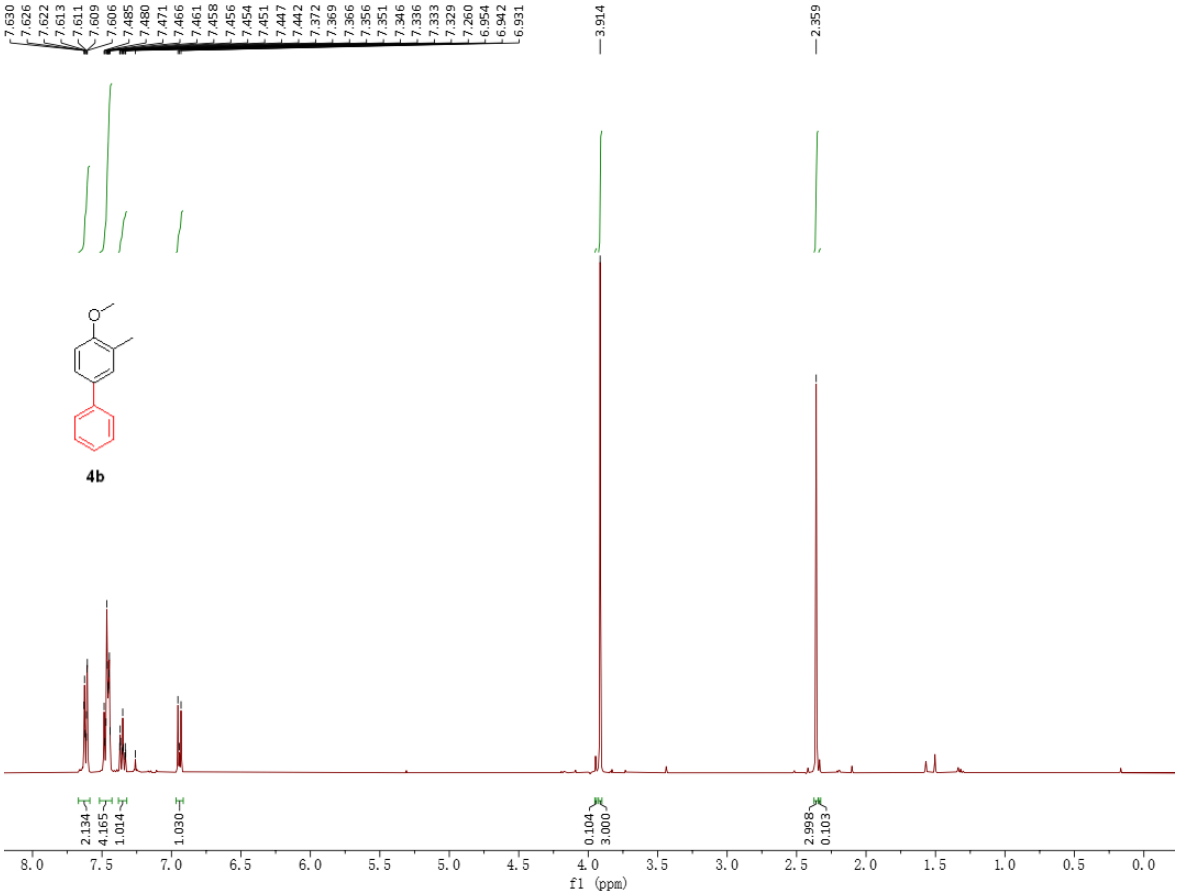
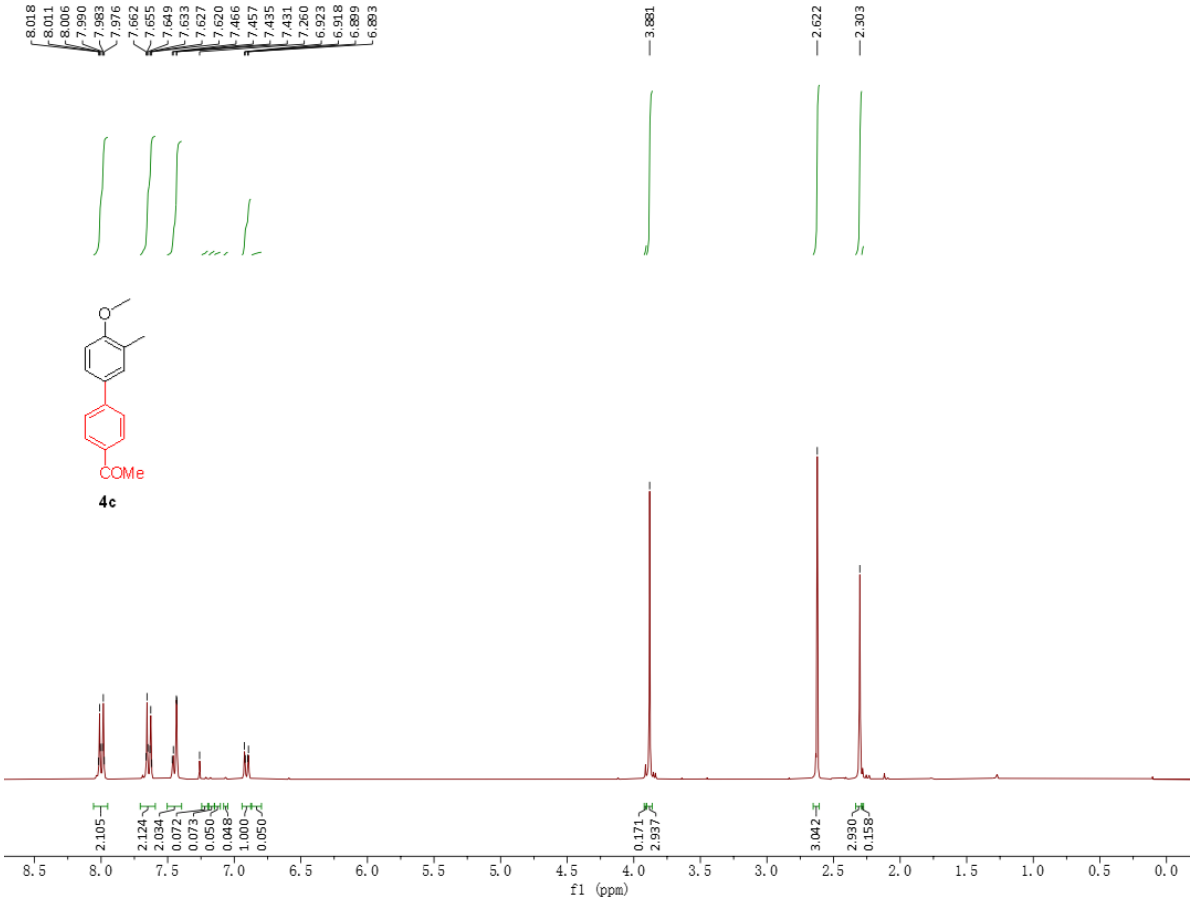
6.184
f1 (ppm)

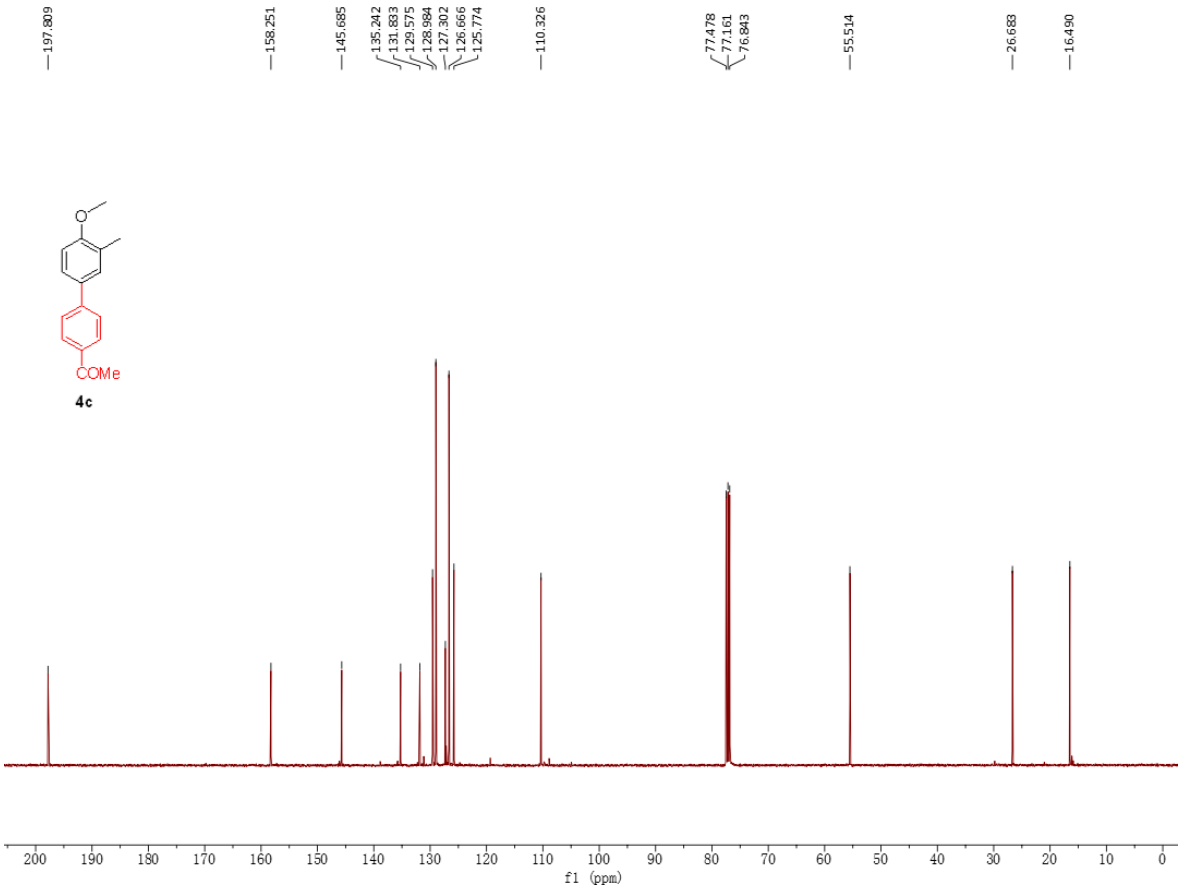
3ab

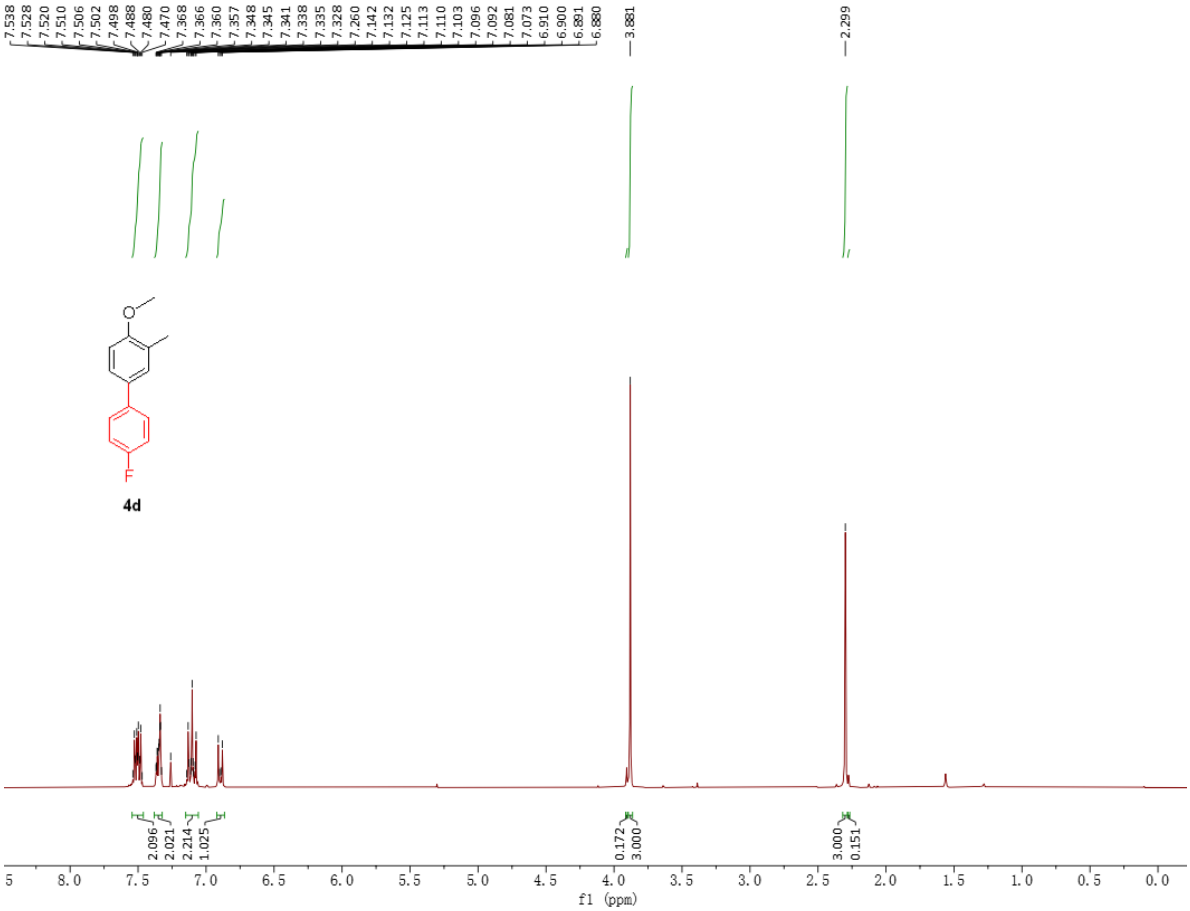
SUPPORTING INFORMATION

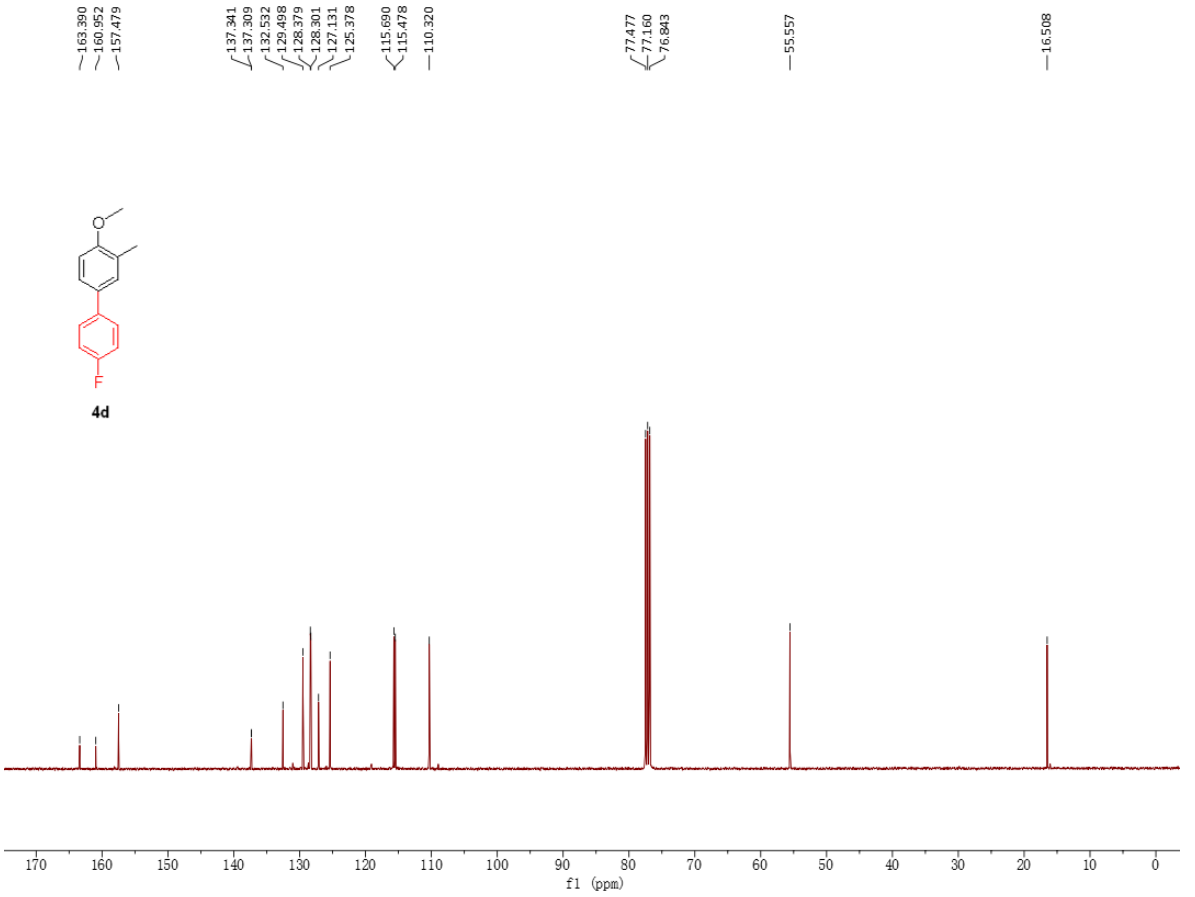




SUPPORTING INFORMATION



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132.532
129.498
128.379
128.301
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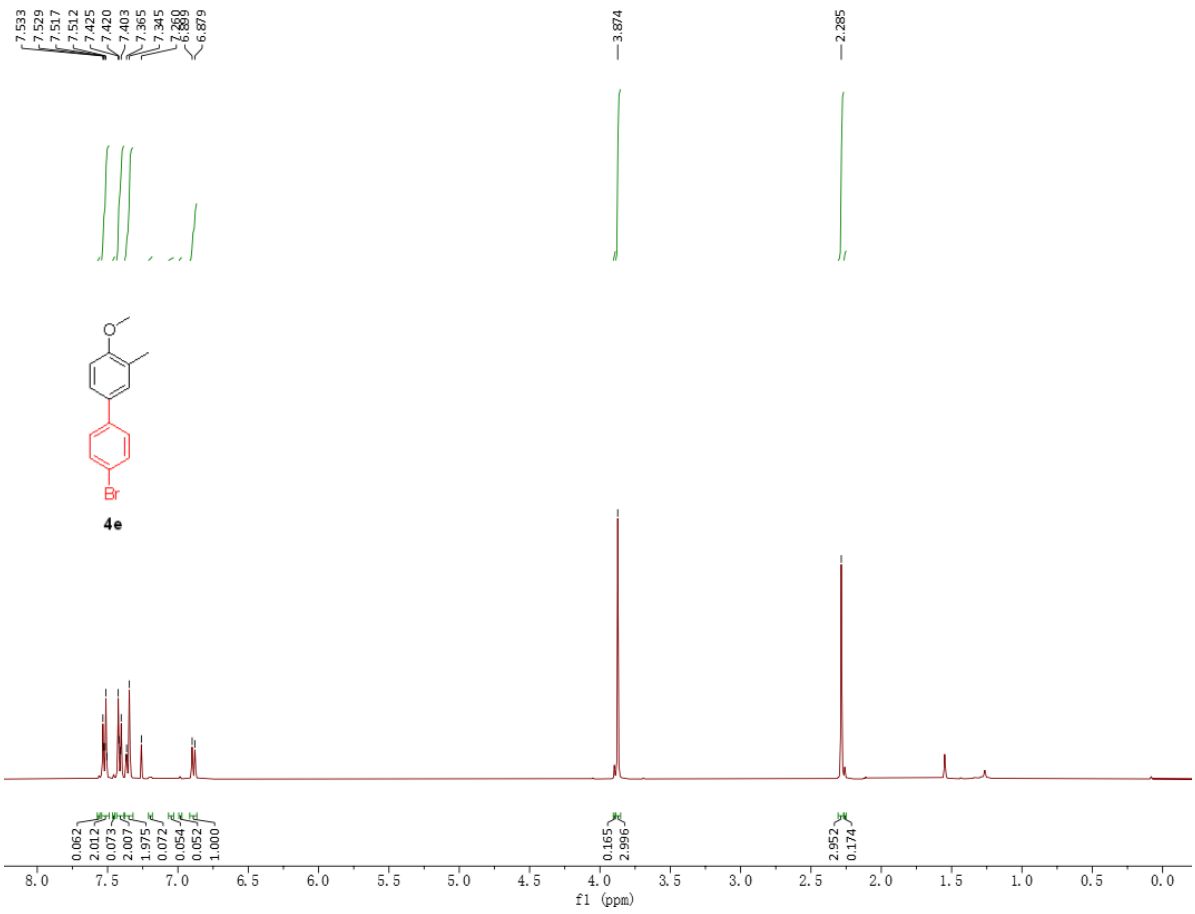
115.478
110.320
77.477
77.160
76.843
55.557
16.508
4d
f1 (ppm)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7.529
7.517
7.512
7.425
7.420
7.403
7.365
7.345
6.879
3.874
2.285
4e
0.062
2.012
0.073
2.007
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0.054
0.052
1.000
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2.996
2.952
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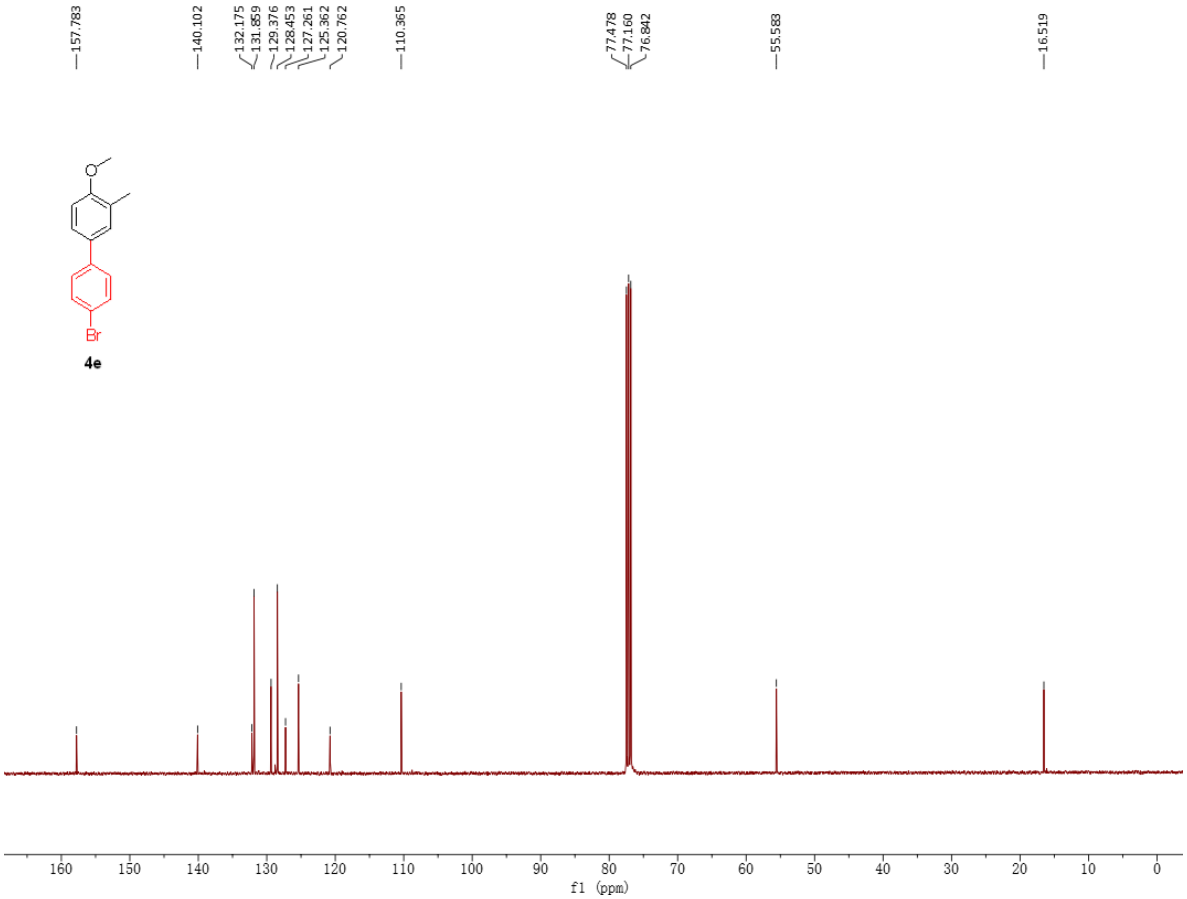
f1 (ppm)


157.783
140.102
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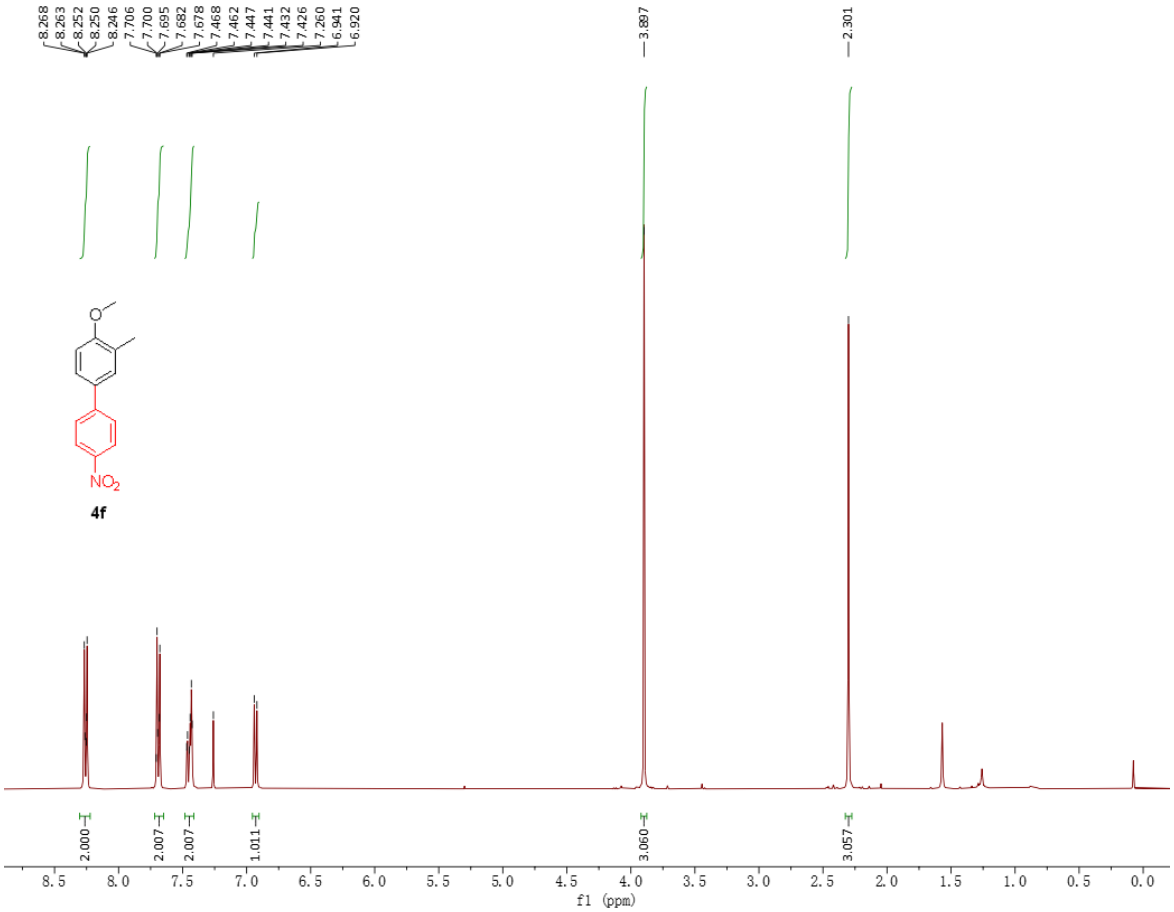
76.842
55.583
16.519
Br
4e
f1 (ppm)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7.695
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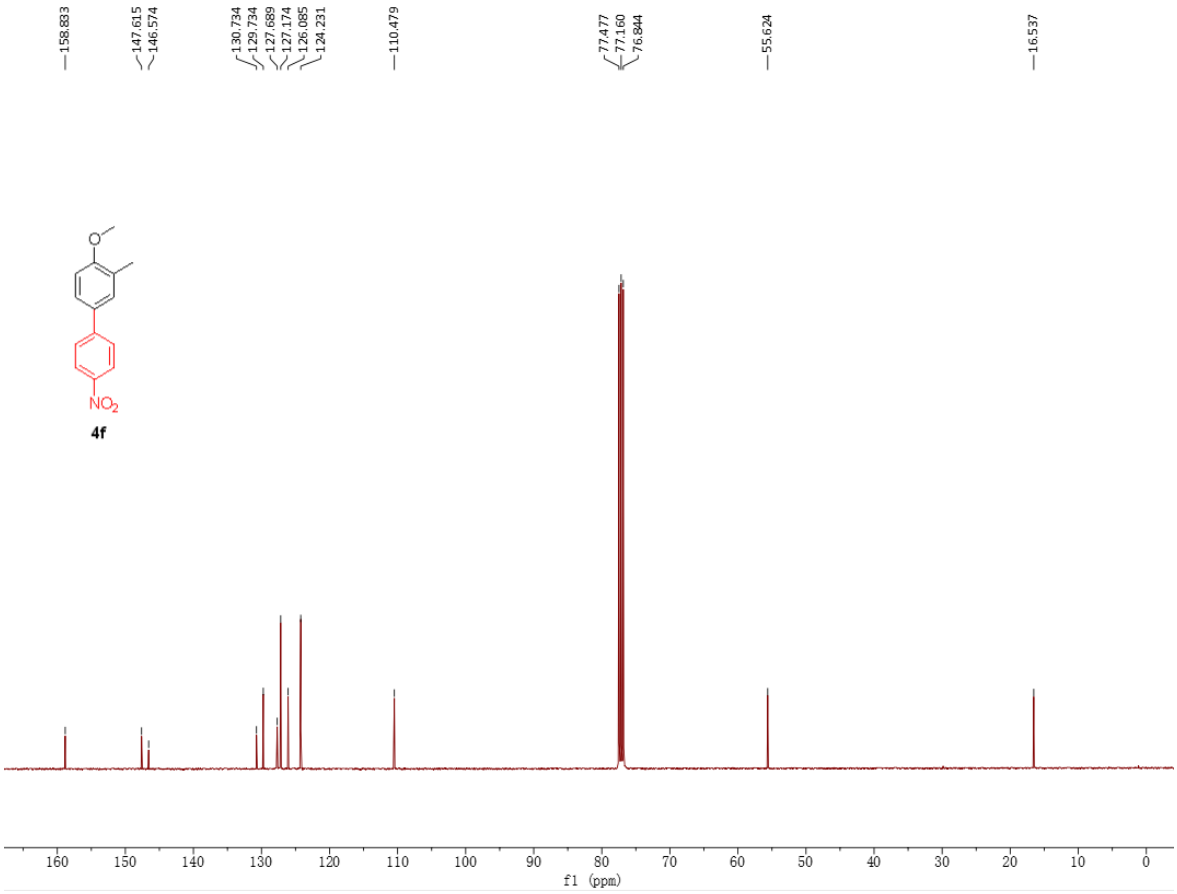
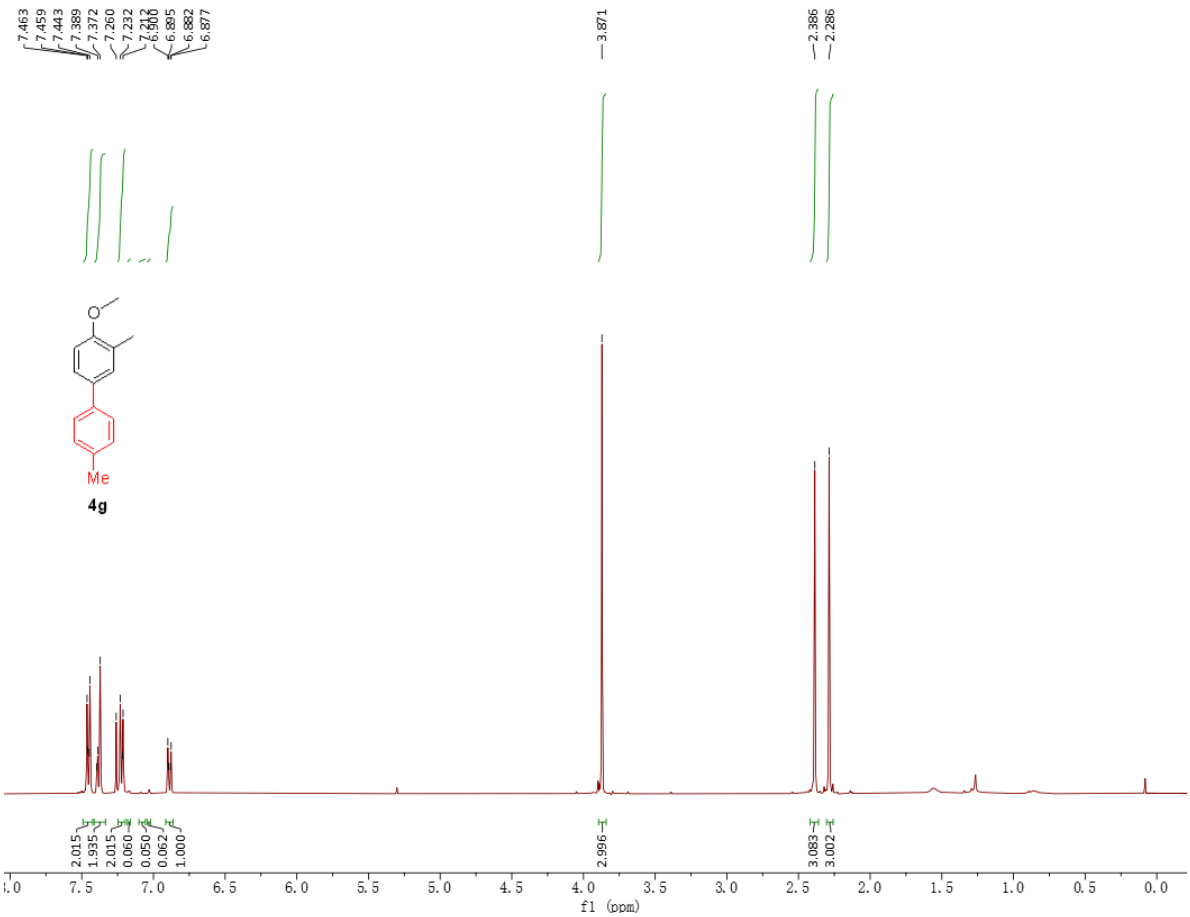
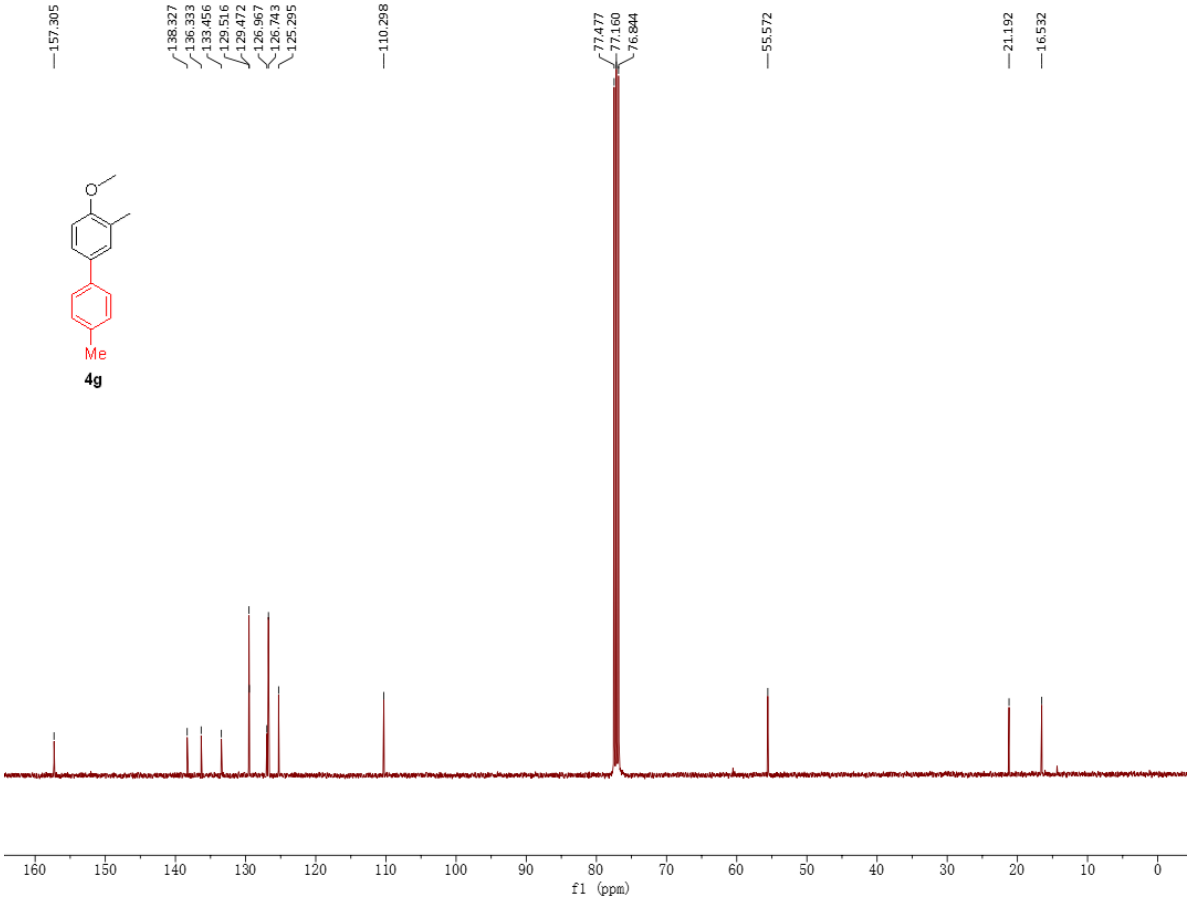
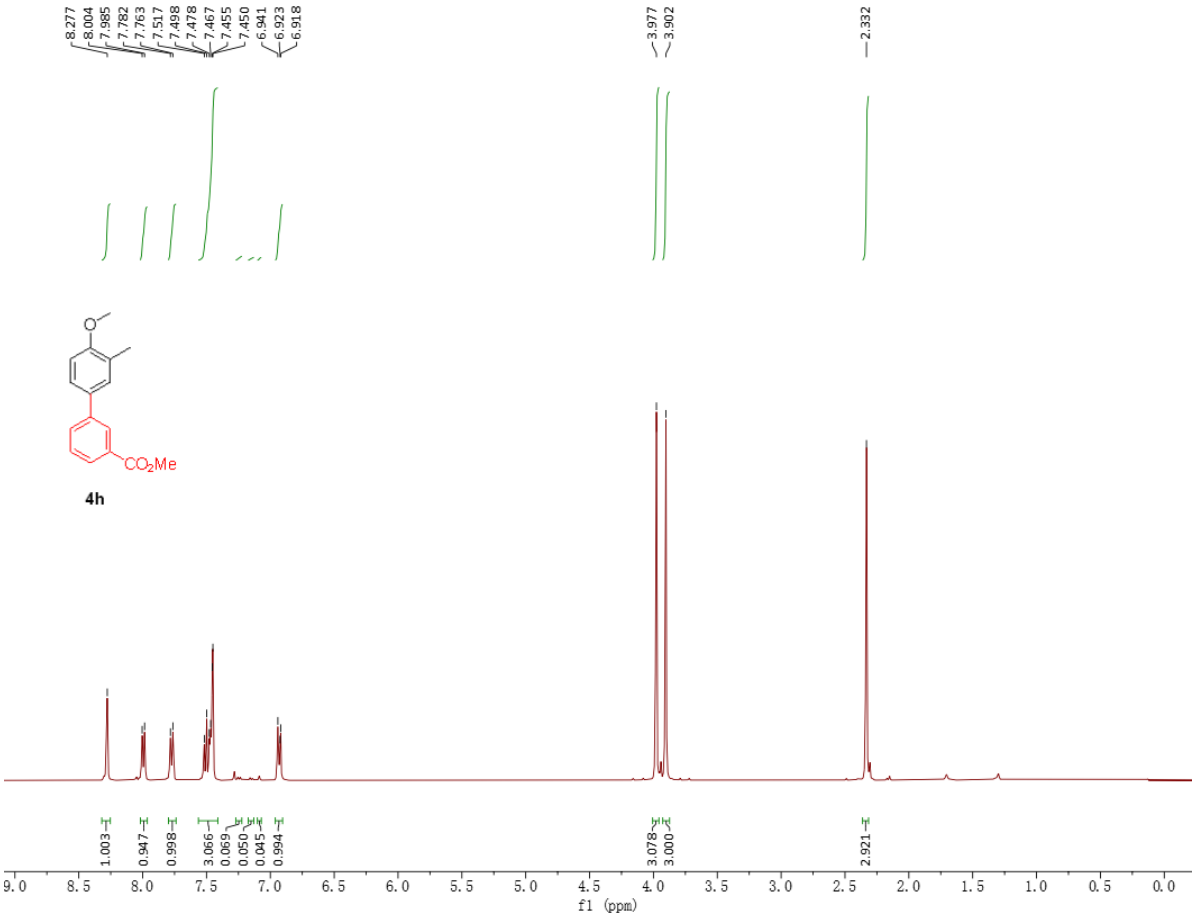
7.462
7.447
7.441
7.432
7.426
7.260
6.941
6.920
3.897
2.301
NO2
4f
2.000
2.007
2.007
1.011
3.060
3.057
f1 (ppm)

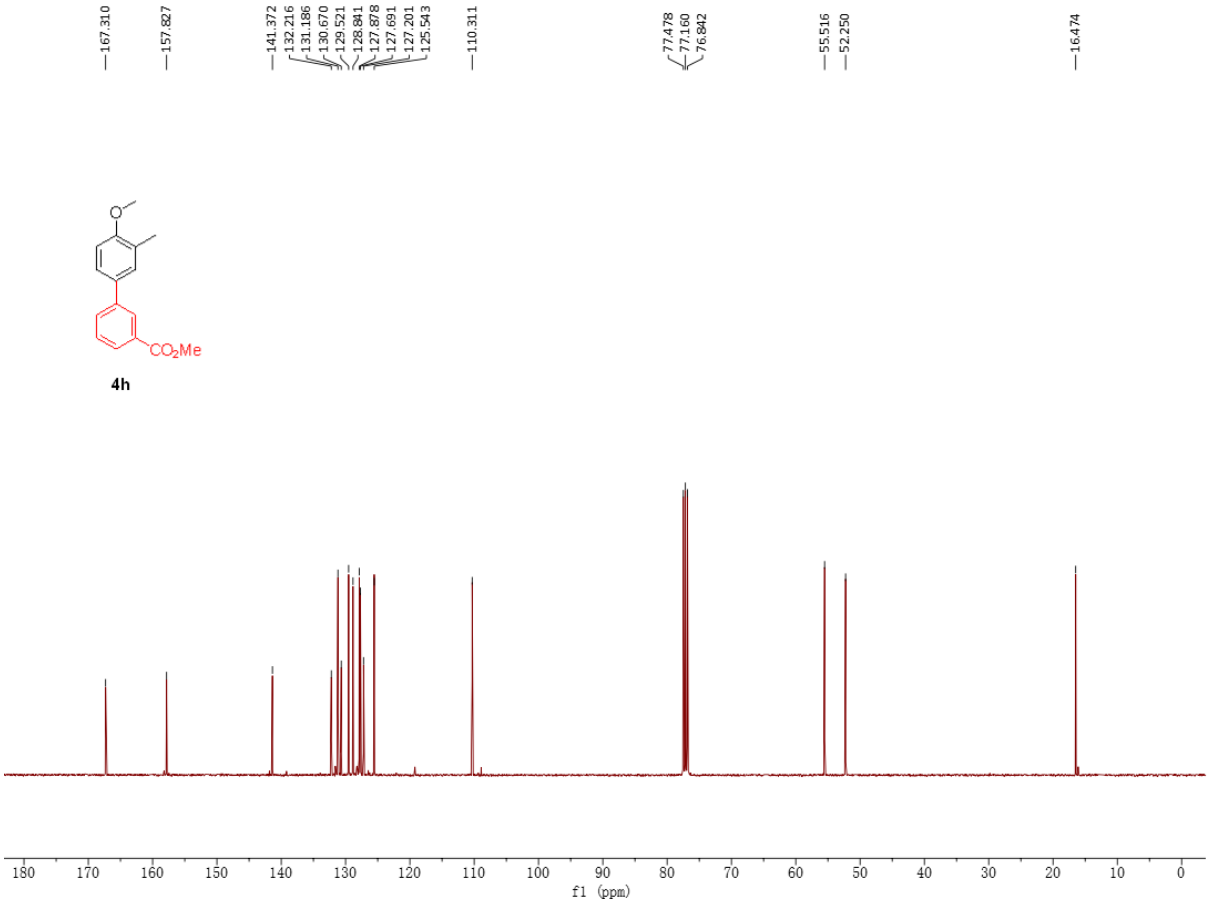

158.883
147.615
146.574
130.734
129.734
127.689
127.174
126.085
124.231
110.479
77.477
77.160
76.844
55.624
16.537
NO2
4f
f1 (ppm)

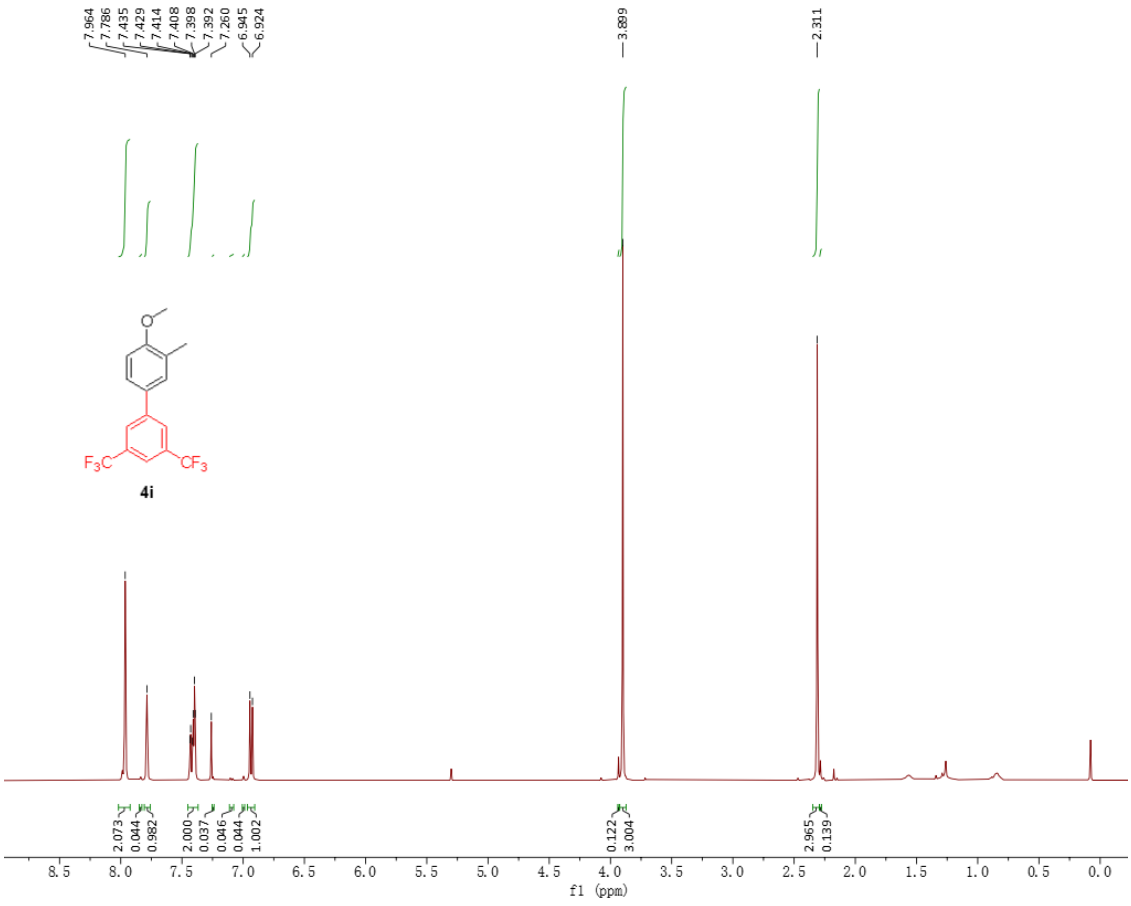

7.463
7.459
7.443
7.389
7.372
7.260
7.232
7.212
6.900
6.895
6.882
6.877
3.871
2.386
2.286
Me
4g
2.015
1.935
2.015
0.060
0.050
0.062
1.000
2.996
3.083
3.002
f1 (ppm)

SUPPORTING INFORMATION

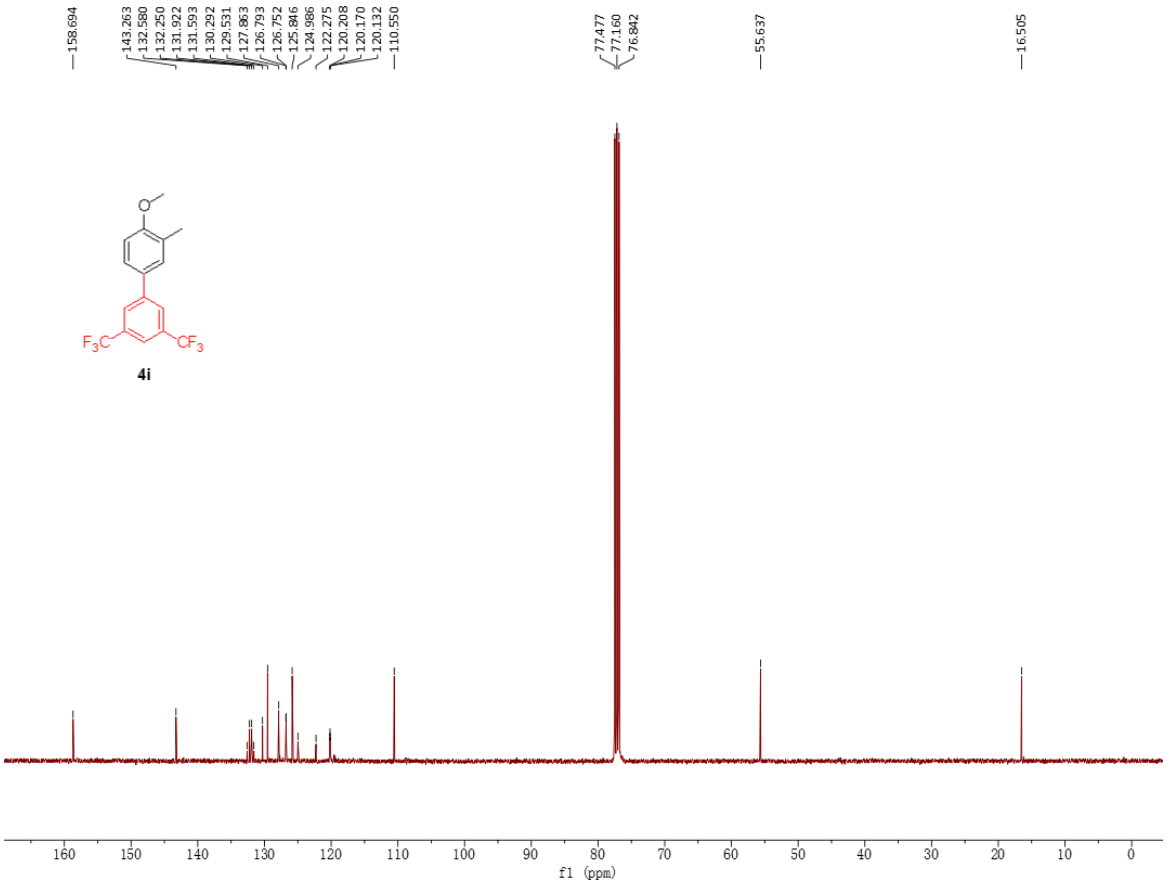


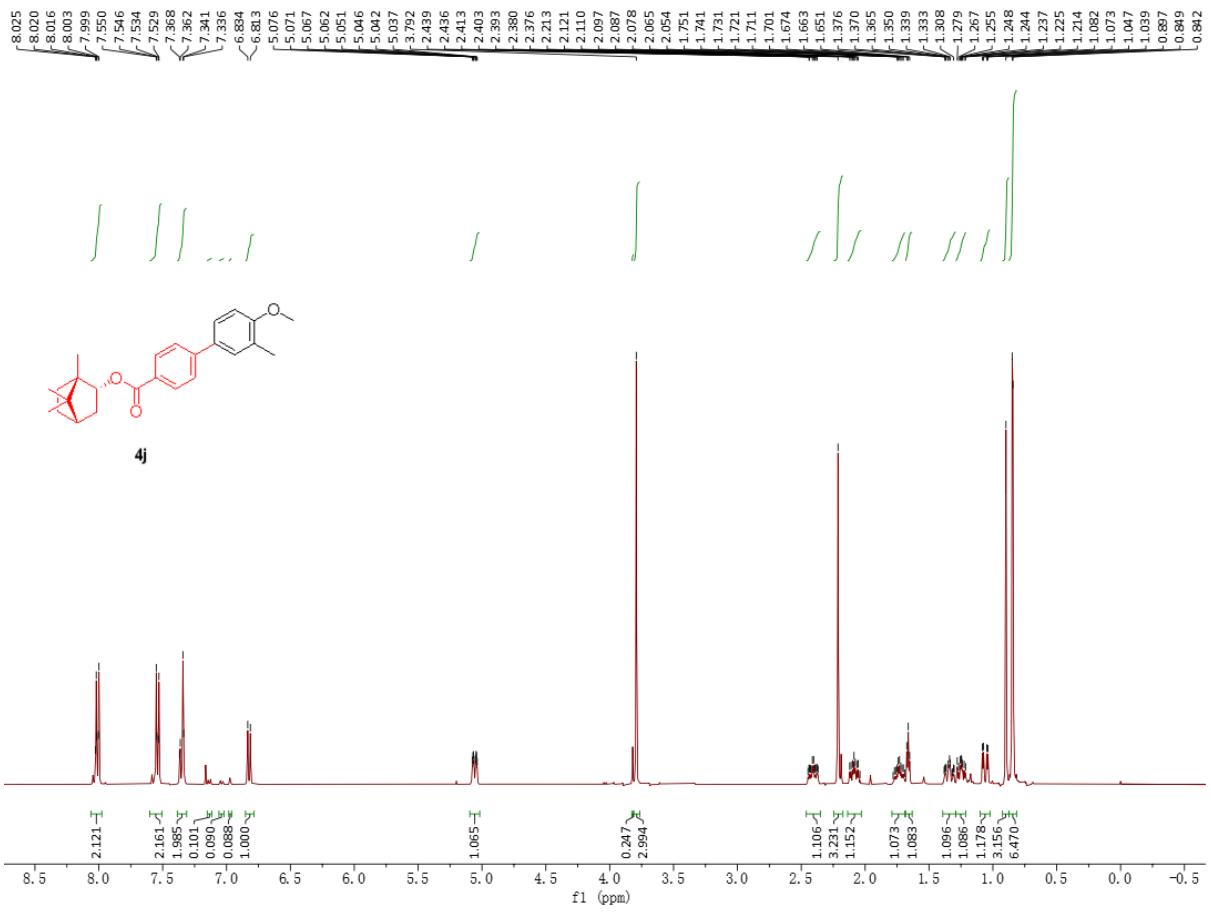


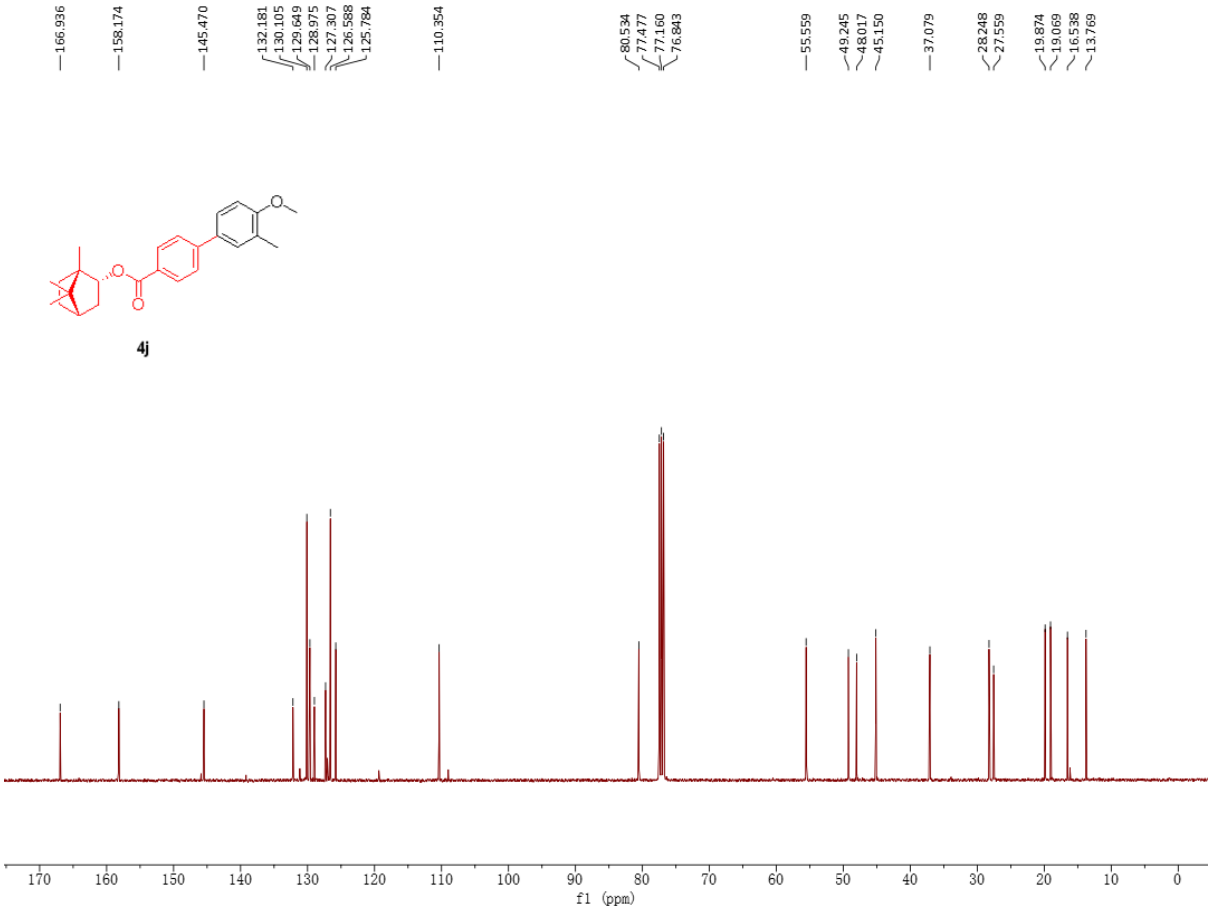

167.310
157.827
141.372
132.216
131.186
130.670
129.521
128.841
127.878
127.691
127.201
125.543
110.311
77.478
77.160
76.842
55.516
52.250
16.474
CO2Me
4h
f1 (ppm)


7.964
7.786
7.435
7.429
7.414
7.408
7.398
7.392
7.260
6.945
6.924
3.889
2.311
F3C
CF3
4i
2.073
0.044
0.982
2.000
0.037
0.046
0.044
1.002
0.122
3.004
2.965
0.139
f1 (ppm)

SUPPORTING INFORMATION






166.936
158.174
145.470
132.181
130.105
129.649
128.975
127.307
126.588
125.784
110.354
80.534
77.477
77.160
76.843
55.559
49.245
48.017
45.150
37.079
28.248
27.559
19.874
19.069
16.538
13.769
4j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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