Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Palladium-catalyzed decarbonylative methylation of aryl carboxylic acids

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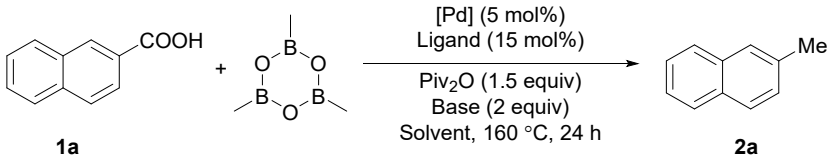
Contents

I. General remarks

NMR spectra were prepared on an Agilent 400-MR DD2 spectrometer (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz). The ^{1}H NMR (400 MHz) chemical shifts and the ^{13}C NMR (100 MHz) chemical shifts were measured relative to $CDCl_3$ or acetone-d_6 as the internal reference. High resolution mass spectra (HRMS) were prepared with a Shimadzu LCMS-IT-TOF (ESI) or an Agilent 1260/6530 (ESI). GC-MS spectra were recorded by an Agilent 8860-5977B. Purification by preparative HPLC was performed on a Shimadzu LC-20AR equipped with an SPD-20A UV-Vis detector and a Shimadzu (250 mm x20 mm; 5 μm C18 packing) column.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Toluene, 1,4-dioxane and $PhCF_3$ were distilled over sodium before use. $Pd(OAc)_2$ and $Pd(TFA)_2$ were purchased from Shanxi Kaida Chemical Engineering. $Pd(acac)_2$, XantPhos, dppb, dppe and XPhos was purchased from Energy Chemical. Aryl carboxylic acids (**1a-1v)** and trimethyboroxine (TMB, 3.5 *N* in THF) were also purchased from Energy Chemical. 2-Naphthoyl fluoride (**5**) was synthesized according to the literature procedure.[1] The yields of compound **2f-2h** and **3** were determined by GC-MS analysis using calibration curves based on the data from authentic samples of the corresponding compounds. For all GC-MS calibration curves, the ratio of molar concentration is taking as the horizontal axis and the ratio of GC area is taking as the vertical axis.Unless otherwise noted, all reactions were performed with dry solvents under argon in dried glassware with standard vacuum-line techniques.

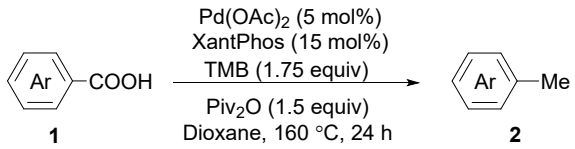
II. General procedure for the optimization study



1a **2a**

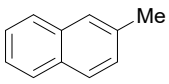
An oven-dried Schlenk tube equipped with a stirring bar was charged with 2-naphthoic acid **1a** (34.4 mg, 0.2 mmol, 1.0 equiv), TMB (100 μL, 3.5*N* in THF, 0.35 mmol, 1.75 equiv), Pd catalyst (5 mol%), ligand (15 mol%), Piv_2O (1.5 equiv), and base (2 equiv) under argon. Then solvent (1 mL) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 24 h. Next, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through celite, and concentrated. The resulting crude mixture was purified by column chromatography on silica gel (200-300 mesh, petroleum ether) to afford the corresponding methylated product **2a**.

III. General procedure for the decarbonylative methylation



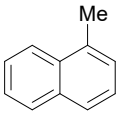
An oven-dried Schlenk tube equipped with a stirring bar was charged with aryl carboxylic acid **1** (0.2 mmol, 1.0 equiv), TMB (100 μL, 3.5*N* in THF, 0.35 mmol, 1.75 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol%), XantPhos (17.4 mg, 15 mol%) and Piv_2O (61 μL, 1.5 equiv) under argon. Then dioxane (1 mL) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 24 h. Next, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through celite, and concentrated. The resulting crude mixture was purified by column chromatography on silica gel (200-300 mesh) or neutral Al_2O_3 (200-300 mesh) to afford the corresponding methylated product **2**.

IV. Experimental data for the described substances



2-Methylnaphthalene (2a)

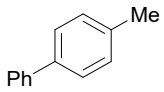
According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether) on silica gel afforded compound **2a** as colorless oil (25 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.53 (s, 3H), 7.33 (dd, *J* = 8.4 Hz, 1.6, 1H), 7.39 – 7.48 (m, 2H), 7.63 (s, 1H), 7.75 – 7.78 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 21.9, 125.1, 126.0, 127.0, 127.4, 127.7, 127.8, 128.2, 131.8, 133.8, 135.6 ppm. The NMR spectrum data are consistent with the literature.[2]



1-Methylnaphthalene (2b)

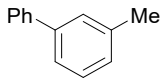
According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether) on silica gel afforded compound **2b** as colorless oil (25.6 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 2.72 (s, 3H), 7.34 (d, *J* = 6.8 Hz, 1H), 7.37 – 7.42 (m, 1H), 7.48 – 7.57 (m, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.89 (m, 1H), 8.02 (dd, *J* = 8.0 Hz, 1.0, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$):

δ = 19.5, 124.2, 125.67, 125.70, 125.8, 126.5, 126.7, 128.6, 132.7, 133.7, 134.4 ppm. The NMR spectrum data are consistent with the literature.[2]



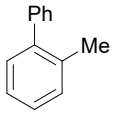
4-Methyl-1,1'-biphenyl (2c)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether) on silica gel afforded compound **2c** as a white solid (25.2 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3H), 7.25 (d, J = 8.0 Hz, 2H), 7.30 – 7.36 (m, 1H), 7.40 – 7.45 (m, 2H), 7.48 – 7.52 (m, 2H), 7.56 – 7.61 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 127.10, 127.11, 127.13, 128.8, 129.6, 137.2, 138.5, 141.3 ppm. The NMR spectrum data are consistent with the literature.[2]



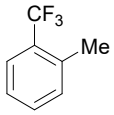
3-Methyl-1,1'-biphenyl (2d)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether) on silica gel afforded compound **2d** as yellowish oil (26.2 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3H), 7.17 – 7.22 (m, 1H), 7.34 – 7.39 (m, 2H), 7.41 – 7.49 (m, 4H), 7.59 – 7.64 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 124.4, 127.29, 127.31, 128.11, 128.12, 128.79, 128.82, 138.5, 141.4, 141.5 ppm. The NMR spectrum data are consistent with the literature.[2]



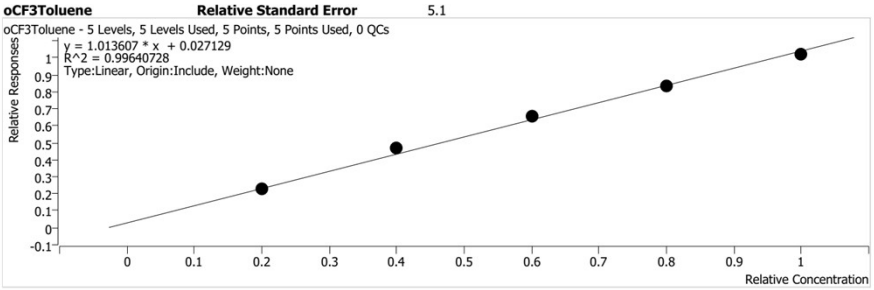
2-Methyl-1,1'-biphenyl (2e)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether) on silica gel afforded compound **2e** as yellowish oil (27.6 mg, 82% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 7.22 – 7.28 (m, 3H), 7.30 – 7.36 (m, 3H), 7.37 – 7.62 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 125.9, 126.9, 127.3, 127.4, 128.2, 128.9, 129.3, 129.9, 130.4, 135.5 ppm. The NMR spectrum data are consistent with the literature.[2]



2-Methylbenzotrifluoride (2f)

Following the general decarbonylative methylation procedure starting from **1f**, mesitylene (27.8 μL, 0.2 mmol) was subjected as internal standard after the completion of reaction. The yield of **2f** was determined by GC-MS analysis using calibration curves based on data from the authentic sample of **2f** and mesitylene (86% yield).



Calibration STD Path	Type	Level	Enable	Conc.	Response	RF	Level RSD
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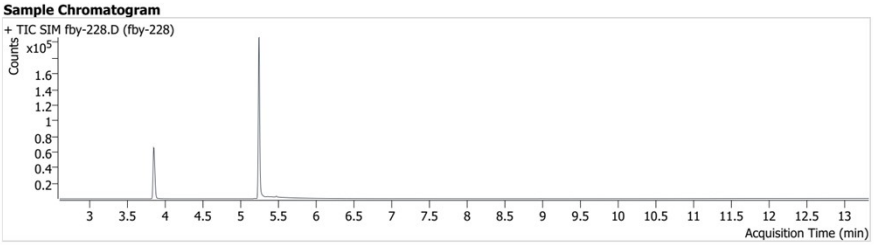
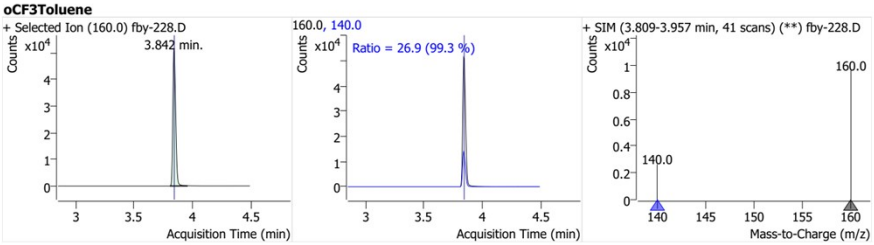
D:\MassHunter\GCMS\1\data\FBY\oCF3Toluene\oCF3Toluene0915-2.D	Calibration	2	x	0.4000	88667	1.1617	
D:\MassHunter\GCMS\1\data\FBY\oCF3Toluene\oCF3Toluene0915-3.D	Calibration	3	x	0.6000	138970	1.0886	
D:\MassHunter\GCMS\1\data\FBY\oCF3Toluene\oCF3Toluene0915-4.D	Calibration	4	x	0.8000	195626	1.0453	
D:\MassHunter\GCMS\1\data\FBY\oCF3Toluene\oCF3Toluene0915-5.D	Calibration	5	x	1.0000	233714	1.0183	

Sample Chromatogram

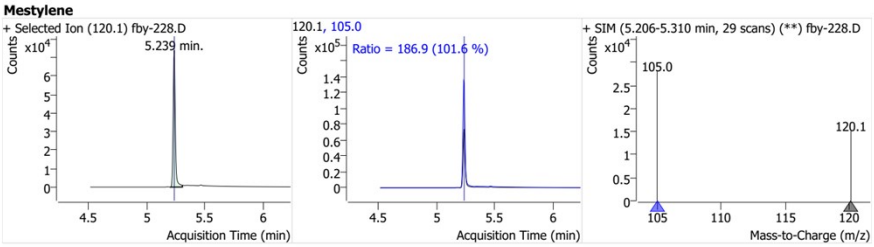


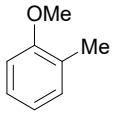
Name	ISTD	RT	Resp.	ISTD Resp.	RR	Final Conc.	Units	Ratio
oCF3Toluene	Mestylene	3.842	87402	96854	0.9024	0.8635		26.9

oCF3Toluene



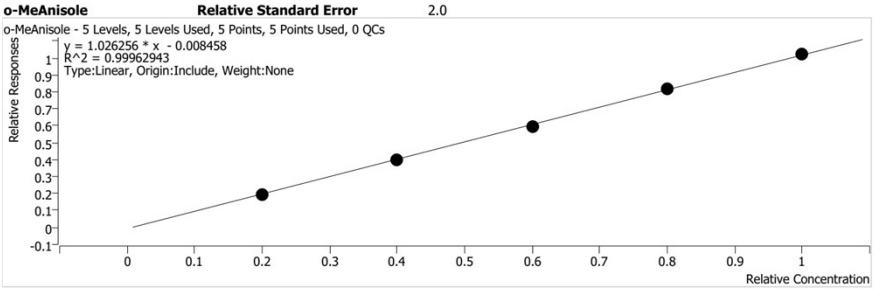
Mestylene





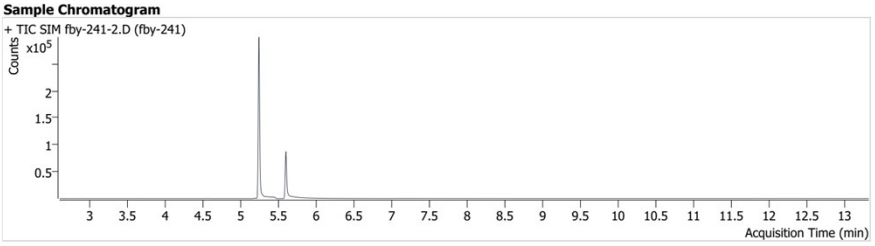
2-Methylanisole (2g)

Following the general decarbonylative methylation procedure starting from **1g**, mesitylene (27.8 μL, 0.2 mmol) was subjected as internal standard after the completion of reaction. The yield of **2g** was determined by GC-MS analysis using calibration curves based on data from the authentic sample of **2g** and mesitylene (57% yield).



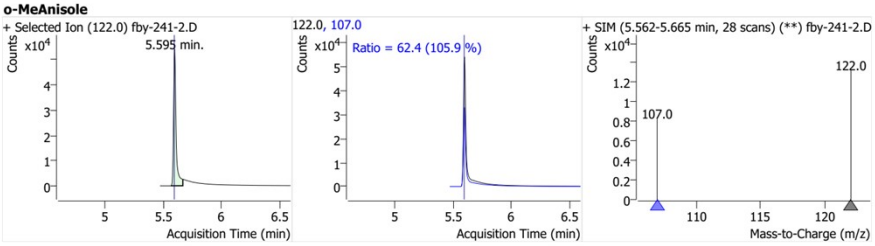
Calibration STD Path	Type	Level	Enable	Conc.	Response	RF	Level RSD
D:\MassHunter\GCMS\1\data\FBY\oMeAnisole\o-MeAnisole0915-1.D	Calibration	1	x	0.2000	35251	0.9541	
D:\MassHunter\GCMS\1\data\FBY\oMeAnisole\o-MeAnisole0915-2.D	Calibration	2	x	0.4000	64985	1.0002	
D:\MassHunter\GCMS\1\data\FBY\oMeAnisole\o-MeAnisole0915-3.D	Calibration	3	x	0.6000	105187	0.9954	
D:\MassHunter\GCMS\1\data\FBY\oMeAnisole\o-MeAnisole0915-4.D	Calibration	4	x	0.8000	159904	1.0252	
D:\MassHunter\GCMS\1\data\FBY\oMeAnisole\o-MeAnisole0915-5.D	Calibration	5	x	1.0000	199017	1.0197	

Sample Chromatogram

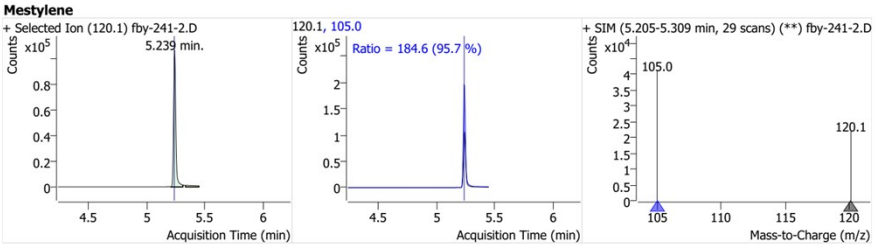


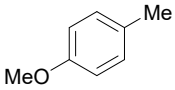
Name	ISTD	RT	Resp.	ISTD Resp.	RR	Final Conc.	Units	Ratio
o-MeAnisole	Mestylene	5.595	81783	141043	0.5798	0.5732		62.4

o-MeAnisole



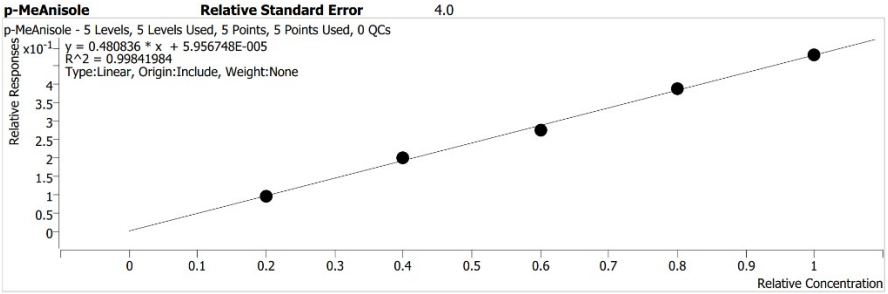
Mestylene





4-Methylanisole (2h)

Following the general decarbonylative methylation procedure starting from **1h**, mesitylene (27.8 μL, 0.2 mmol) was subjected as internal standard after the completion of reaction. The yield of **2h** was determined by GC-MS analysis using calibration curves based on data from the authentic sample of **2h** and mesitylene (45% yield).



Calibration STD Path	Type	Level	Enable	Conc.	Response	RF	Level RSD
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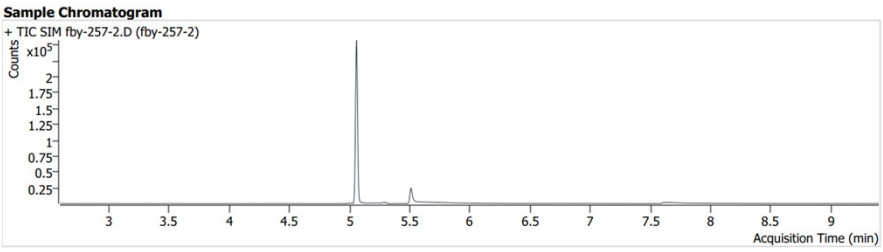
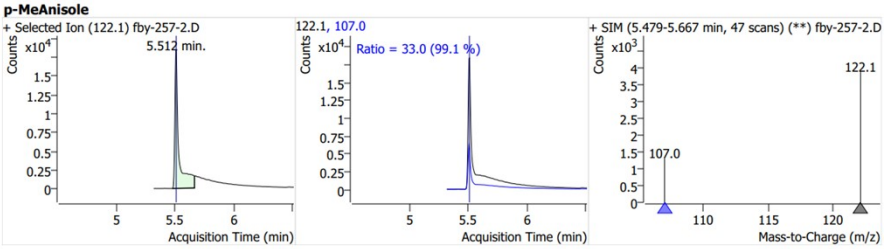
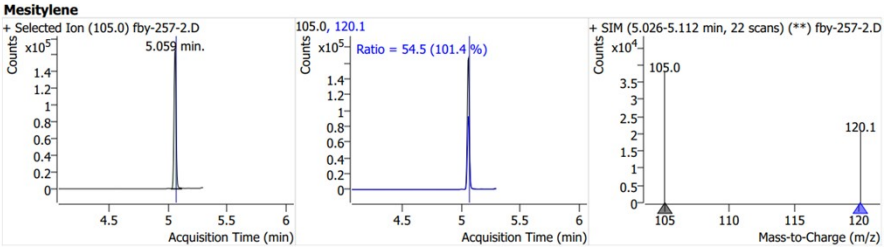
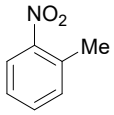
D:\MassHunter\GCMS\1\data\FBY\pMANISOLE\p-Meanisole-2.D	Calibration	2	x	0.4000	73016	0.5037	
D:\MassHunter\GCMS\1\data\FBY\pMANISOLE\p-Meanisole-3.D	Calibration	3	x	0.6000	102645	0.4621	
D:\MassHunter\GCMS\1\data\FBY\pMANISOLE\p-Meanisole-4.D	Calibration	4	x	0.8000	141135	0.4886	
D:\MassHunter\GCMS\1\data\FBY\pMANISOLE\p-Meanisole-5.D	Calibration	5	x	1.0000	166956	0.4797	



Name	ISTD	RT	Resp.	ISTD Resp.	RR	Final Conc. Units	Ratio
p-MeAnisole	Mesitylene	5.512	43760	204288	0.2142	0.4454	33.0

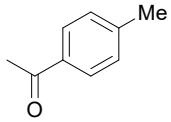






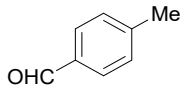
1-Methyl-2-nitrobenzene (2i)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/CH_2Cl_2 = 8/1) on silica gel afforded compound **2i** as yellow oil (23 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.61 (s, 3H), 7.30 – 7.39 (m, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 124.8, 127.0, 132.9, 133.1, 133.7, 149.5 ppm. The NMR spectrum data are consistent with the literature.[3]



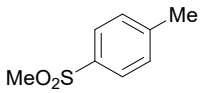
4-Methylacetophenone (2j)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/ethyl acetate = 50/1) on silica gel afforded compound **2j** as colorless oil (21.7 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3H), 2.58 (s, 3H), 7.26 (d, J = 8.8 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 26.7, 128.6, 129.4, 134.8, 144.0, 198.0 ppm. The NMR spectrum data are consistent with the literature.[4]



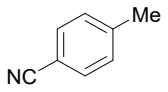
4-Methylbenzaldehyde (2k)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/ethyl acetate = 50/1) on silica gel afforded compound **2k** as colorless oil (20.6 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3H), 7.33 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 9.96 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 129.8, 130.0, 134.3, 145.7, 192.2 ppm. The NMR spectrum data are consistent with the literature.[3]



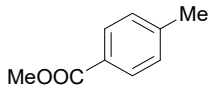
1-Methyl-4-(methylsulfonyl)benzene (2l)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/ethyl acetate = 2/1) on silica gel afforded compound **2l** as a white solid (26.2 mg, 77% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3H), 3.03 (s, 3H), 7.36 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 44.7, 127.5, 130.1, 137.8, 144.8 ppm. The NMR spectrum data are consistent with the literature.[5]



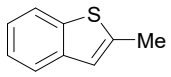
4-Methylbenzonitrile (2m)

According to the general procedure for decarbonylative methylation, purification by prepared TLC (petroleum ether/ CH_2Cl_2 = 6/1) afforded compound **2m** as colorless oil (15.4 mg, 66% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 2.42 (s, 3H), 7.27 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 22.0, 109.4, 119.3, 130.0, 132.2, 143.8 ppm. The NMR spectrum data are consistent with the literature.[6]



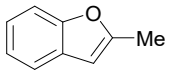
Methyl 4-methylbenzoate (2n)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/ethyl acetate = 30/1) on silica gel afforded compound **2n** as a white solid (16 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.40 (s, 3H), 3.90 (s, 3H), 7.23 (d, J = 8.0 Hz, 2H), 7.93 (d, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.8, 52.1, 127.5, 129.2, 129.7, 143.7, 167.3 ppm. The NMR spectrum data are consistent with the literature.[7]



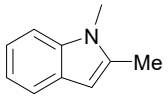
2-Methylbenzo[*b*]thiophene (2o)

According to the general procedure for decarbonylative methylation, purification by prepared TLC (petroleum ether) afforded compound **2o** as colorless oil (15.4 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, J = 1.2 Hz, 3H), 6.97 – 7.00 (m, 1H), 7.23 – 7.28 (m, 1H), 7.29 – 7.34 (m, 1H), 7.65 – 7.68 (m, 1H), 7.74 – 7.78 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3, 121.7, 122.1, 122.6, 123.5, 124.2, 139.8, 140.6, 141.0 ppm. The NMR spectrum data are consistent with the literature.[3]



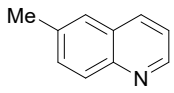
2-Methylbenzofuran (2p)

According to the general procedure for decarbonylative methylation, purification by prepared TLC (petroleum ether) afforded compound **2p** as colorless oil (11.9 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3H), 6.37 (p, J = 1.0 Hz, 1H), 7.15 – 7.23 (m, 2H), 7.38 – 7.42 (m, 1H), 7.45 – 7.49 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 102.7, 110.7, 120.2, 122.5, 123.2, 129.3, 154.8, 155.5 ppm. The NMR spectrum data are consistent with the literature.[3]



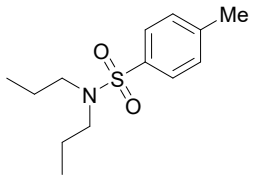
1,2-Dimethyl-1*H*-indole (2q)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/CH_2Cl_2 = 10/1) on silica gel afforded compound **2q** as brown liquid (17.7 mg, 61% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 2.44 (s, 3H), 3.67 (s, 3H), 6.21 (s, 1H), 7.05 – 7.11 (m, 1H), 7.14 – 7.19 (m, 1H), 7.27 (d, J = 7.2 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.9, 29.5, 99.7, 108.8, 119.3, 119.7, 120.5, 128.0, 136.9, 137.4 ppm. The NMR spectrum data are consistent with the literature.[8]



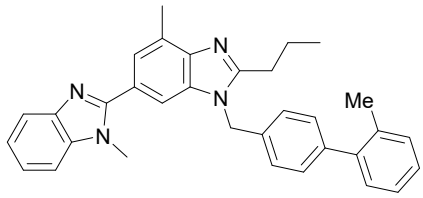
6-Methylquinoline (2r)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/ethyl acetate = 20/1) on Al_2O_3 afforded compound **2r** as yellow liquid (20.6 mg, 72% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 2.52 (s, 3H), 7.31 – 7.37 (m, 1H), 7.51 – 7.58 (m, 2H), 7.99 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.83 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.7, 121.2, 126.7, 128.4, 129.2, 131.9, 135.5, 136.5, 147.0, 149.6 ppm. The NMR spectrum data are consistent with the literature.[3]



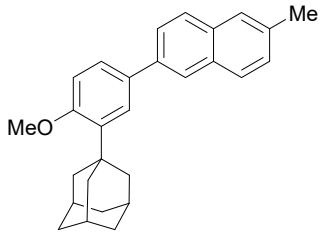
4-Methyl-*N*,*N*-dipropylbenzenesulfonamide (2s)

According to the general procedure for decarbonylative methylation, the reaction mixture was first purified by column chromatography (petroleum ether/ethyl acetate = 16/1) on silica gel. Further purification by preparative HPLC (90% MeCN in aq. as eluent) afforded compound **2s** as colorless liquid (32.7 mg, 64% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ =0.86 (td, J = 7.2, 1.6 Hz, 6H), 1.49 – 1.58 (m, 4H), 2.41 (s, 3H), 3.05 (td, J = 7.6, 1.6 Hz, 4H), 7.23 – 7.32 (m, 2H), 7.62 – 7.71 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.3, 21.6, 22.2, 50.2, 127.2, 129.7, 137.3, 143.0 ppm. The NMR spectrum data are consistent with the literature.[8]



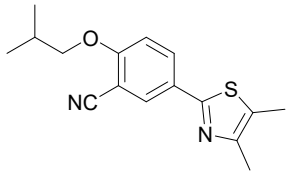
1,7'-Dimethyl-3'-((2'-methyl-[1,1'-biphenyl]-4-yl)methyl)-2'-propyl-1*H*,3'*H*-2,5'-bibenzo[*d*]imidazole (2t)

According to the general procedure for decarbonylative methylation, purification by column chromatography (CH_2Cl_2/ethyl acetate = 3/2) on Al_2O_3 afforded compound **2t** as a white solid (77.5 mg, 80% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 1.01 – 1.08 (m, 3H), 1.83 – 1.90 (m, 2H), 2.21 (s, 3H), 2.77 (s, 3H), 2.90 – 2.98 (m, 2H), 3.80 (s, 3H), 5.45 (s, 2H), 7.10 (d, J = 7.6 Hz, 2H), 7.16 (d, J = 7.6 Hz, 1H), 7.19 – 7.25 (m, 4H), 7.27 (s, 1H), 7.28 – 7.32 (m, 2H), 7.34 – 7.39 (m, 1H), 7.43 (s, 1H), 7.52 (s, 1H), 7.77 – 7.83 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ =14.2, 17.1, 20.6, 22.0, 30.0, 31.9, 47.2, 109.1, 109.6, 119.7, 122.5, 122.7, 123.98, 124.02, 126.0, 126.1, 127.6, 129.6, 129.8, 130.0, 130.5, 134.5, 135.2, 135.4, 136.8, 141.2, 141.8, 143.0, 143.3, 154.9, 156.7 ppm. HRMS (ESI$^+$) calcd for $C_{33}H_{32}N_4$ $[M+H]^+$ 485.2700, found 485.2696.



2-Methyl-6-(3-(1-adamantyl)-4-methoxylphenyl)-naphthalene (2u)

According to the general procedure for decarbonylative methylation, purification by column chromatography (petroleum ether/CH_2Cl_2 = 8/1) on silica gel afforded compound **2u** as a white solid (42.1 mg, 55% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 1.83 (s, 6H), 2.13 (s, 3H), 2.18 – 2.25 (m, 6H), 2.54 (s, 3H), 7.00 (d, J = 8.4 Hz, 1H), 7.34 (dd, J = 8.4, 1.6 Hz, 1H), 7.54 (dd, J = 8.4, 2.4 Hz, 1H), 7.60 – 7.65 (m, 2H), 7.71 (dd, J = 8.4, 1.6 Hz, 1H), 7.79 – 7.83 (m, 2H), 7.96 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.9, 29.3, 37.3, 37.3, 40.7, 55.3, 112.2, 124.9, 125.6, 125.8, 126.0, 126.7, 127.7, 128.0, 128.6, 132.1, 132.6, 133.4, 135.3, 138.2, 138.9, 158.5 ppm. The NMR spectrum data are consistent with the literature.[9]

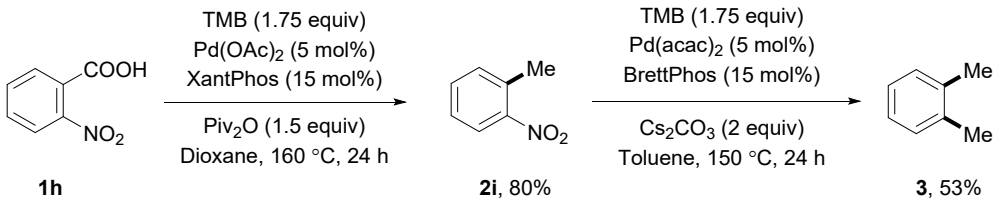


5-(4,5-Dimethylthiazol-2-yl)-2-isobutoxybenzonitrile (2v)

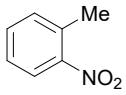
According to the general procedure for decarbonylative methylation, the product was firstly purified by column chromatography (petroleum ether/ethyl acetate = 5/1) on silica gel. Further purification on preparative HPLC (90% MeCN in aq. as eluent) afforded compound **2v** as a white solid (20.0 mg, 35% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 1.08 (d, J = 6.8 Hz, 6H), 2.13 – 2.24 (m, 1H), 2.36 (s, 3H), 2.39 (s, 3H), 3.86 (d, J = 6.4 Hz, 2H), 6.96 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 8.8 Hz, 1H), 8.04 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.6, 14.9, 19.2, 28.3, 75.7, 102.7, 112.6, 116.0, 126.9, 127.3, 131.4, 131.9, 149.6, 160.9, 161.5 ppm. HRMS (ESI$^+$) calcd for $C_{16}H_{18}N_2OS$ $[M+H]^+$ 287.1213, found 287.1209.

V. Sequential cross-couplings

(a) Combination with C–NO_2 activation

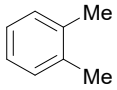


1h **2i**, 80% **3**, 53%



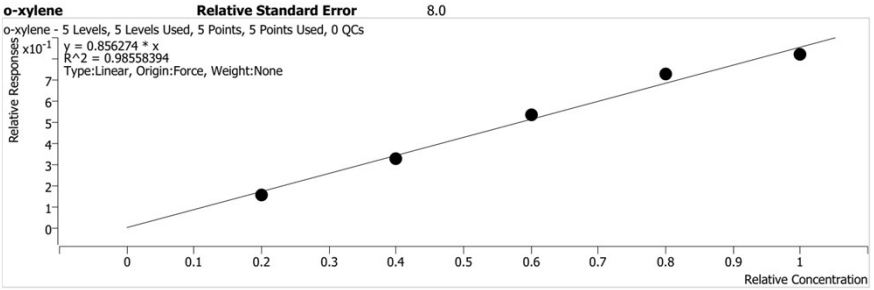
1-Methyl-2-nitrobenzene (2i)

An oven-dried Schlenk tube equipped with a stirring bar was charged with 2-nitrobenzoic acid **1i** (1 mmol, 1.0 equiv), TMB (0.5 mL, 3.5*N* in THF, 1.75 mmol, 1.75 equiv), $Pd(OAc)_2$ (11 mg, 5 mol%), XantPhos (87 mg, 15 mol%) and Piv_2O (305 μL, 1.5 equiv) under argon. Then dioxane (5 mL) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 24 h. Next, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (50 mL), filtered through celite, and concentrated. The resulting crude mixture was purified by column chromatography (petroleum ether/CH_2Cl_2 = 8/1) on silica gel afforded compound **2i** as yellow oil (109.5 mg, 80% yield).

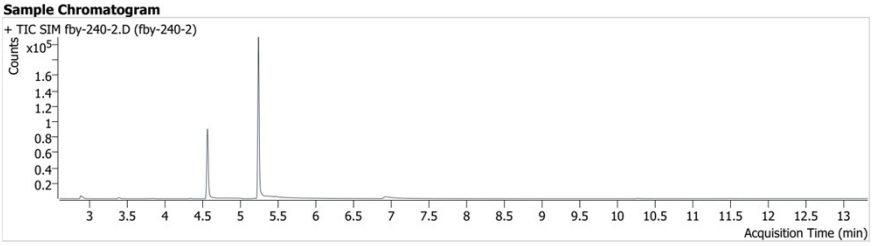


***o*-xylene (3)**

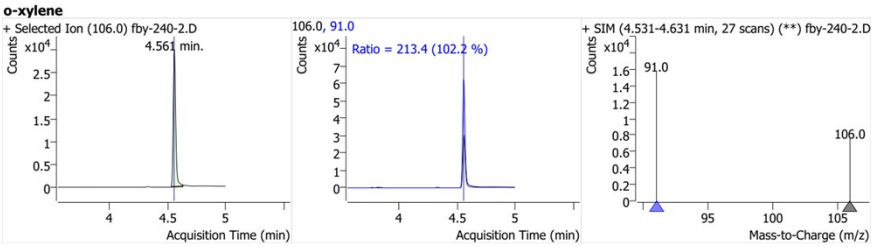
A modified procedure of You's work was used for the synthesis of **3**.[9] An oven-dried Schlenk tube equipped with a stirring bar was charged with 1-methyl-2-nitrobenzene **2i** (0.2 mmol, 1.0 equiv), TMB (100 μL, 3.5*N* in THF, 0.35 mmol, 1.75 equiv), $Pd(acac)_2$ (3.1 mg, 5 mol%), BrettPhos (16.1 mg, 15 mol%) and Cs_2CO_3 (130 mg, 2 equiv) under argon. Then toluene (0.6 ml) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 150 °C, and stirred for 24 h. Mesitylene (27.8 μL, 0.2 mmol) was subjected as internal standard after the completion of reaction. The yield of **3** was determined by GC-MS analysis using calibration curves based on data from the authentic sample of **3** and mesitylene (53% yield).

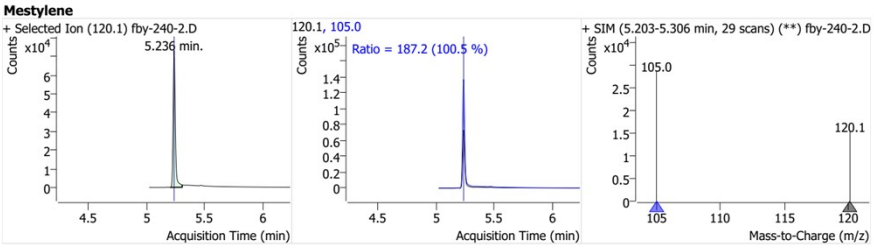


Calibration STD Path	Type	Level	Enable	Conc.	Response	RF	Level RSD
D:\MassHunter\GCMS\1\data\FBY\o-xylene\o-xylene-1.D	Calibration	1	x	0.2000	18403	0.7769	
D:\MassHunter\GCMS\1\data\FBY\o-xylene\o-xylene-2.D	Calibration	2	x	0.4000	53277	0.8089	
D:\MassHunter\GCMS\1\data\FBY\o-xylene\o-xylene-3.D	Calibration	3	x	0.6000	63875	0.8905	
D:\MassHunter\GCMS\1\data\FBY\o-xylene\o-xylene-4.D	Calibration	4	x	0.8000	103211	0.9119	
D:\MassHunter\GCMS\1\data\FBY\o-xylene\o-xylene-5.D	Calibration	5	x	1.0000	107616	0.8191	

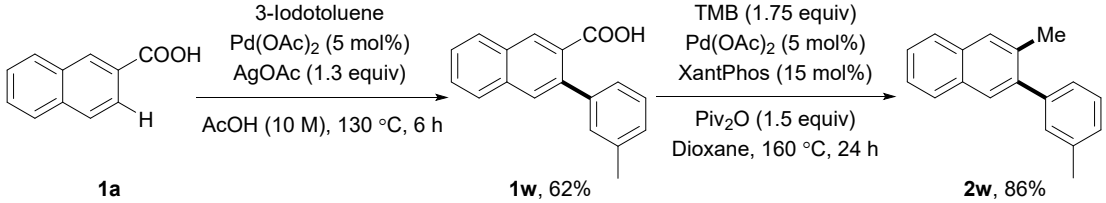


Name	ISTD	RT	Resp.	ISTD Resp.	RR	Final Conc. Units	Ratio
o-xylene	Mestylene	4.561	44448	97837	0.4543	0.5306	213.4

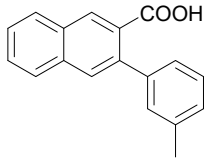




(b) Combination with C–H activation

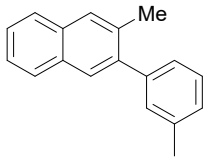


1a **1w**, 62% **2w**, 86%



3-(*m*-Tolyl)-2-naphthoic acid (1w)

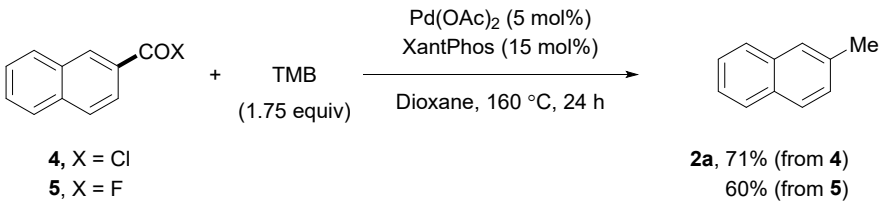
A modified procedure of Daugulis' work was used for the synthesis of **1w**.[10] An oven-dried vial equipped with a stirring bar was charged with 2-naphthoic acid (172.2 mg, 1.0 mmol), Pd(OAc) (11.4 mg, 0.05 mmol), AgOAc (215.6 mg, 1.3 mmol), 3-iodotoluene (385 μL, 3 mmol) and AcOH (200 μL) under argon. The vial was then sealed and placed in a preheated oil bath at 130 °C, and stirred for 6 h. The reaction mixture was then cooled down to room temperature, diluted with CH_2Cl_2 (20 mL), filtered through celite, and concentrated. The resulting crude mixture was first purified by flash chromatography on silica gel (200-300 mesh, dichloromethane/ethyl acetate = 10/1), and then purified by prepared HPLC afford the corresponding pure product as a yellow solid (162.6 mg, 62%). The preparative HPLC runs were performed using 80% to 100% MeOH (0.2% acetic acid was added) in aq. as gradient eluent. ^{1}H NMR (400MHz, Acetone-d_6) δ = 2.38 (s, 3H), 7.15 – 7.33 (m, 4H), 7.57 – 7.68 (m, 2H), 7.89 (s, 1H), 8.00 (d, J = 7.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.44 (s, 1H) ppm. ^{13}C NMR (100 MHz, Acetone-d_6) δ = 21.5, 126.7, 127.6, 128.5, 128.70, 128.74, 129.0, 129.3, 130.2, 130.4, 131.1, 131.2, 132.5, 135.2, 138.2, 139.7, 142.4 ppm. The NMR spectrum data are consistent with the literature.[10]



2-Methyl-3-(*m*-tolyl)naphthalene (2w)

According to the general procedure for decarbonylative methylation starting from **2w**, purification by column chromatography (petroleum ether) on silica gel afforded compound **2w** as colorless oil (40.0 mg, 86% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ = 2.42 (s, 3H), 2.44 (s, 3H), 7.18 – 7.25 (m, 3H), 7.34 (t, J = 7.6 Hz, 1H), 7.40 – 7.49 (m, 2H), 7.71 (d, J = 10.4 Hz, 2H), 7.77 – 7.83 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.2, 21.7, 125.5, 126.0, 126.5, 127.0, 127.7, 127.8, 128.1, 128.3, 128.4, 130.2, 132.1, 133.0, 134.1, 137.8, 141.2, 141.9 ppm. HRMS (ESI$^+$) calcd for $C_{18}H_{16}$ $[M+H]^+$ 233.1325, found 233.1330.

VI. Decarbonylative methylation of aroyl derivatives

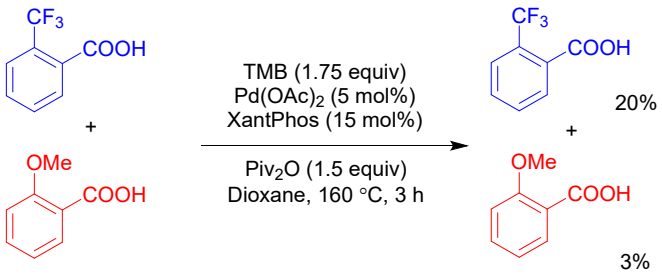


4, X = Cl
5, X = F

2a, 71% (from **4**)
60% (from **5**)

An oven-dried Schlenk tube equipped with a stirring bar was charged with aroyl chloride **4** or aroyl fluoride **5** (0.2 mmol, 1.0 equiv), TMB (100 μL, 3.5*N* in THF, 0.35 mmol, 1.75 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol%), XantPhos (17.4 mg, 15 mol%) under argon. Then dioxane (1 mL) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 24 h. Next, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered through celite, and concentrated. The resulting crude mixture was purified by column chromatography on silica gel (200-300 mesh) to afford the corresponding methylated product **2a**.

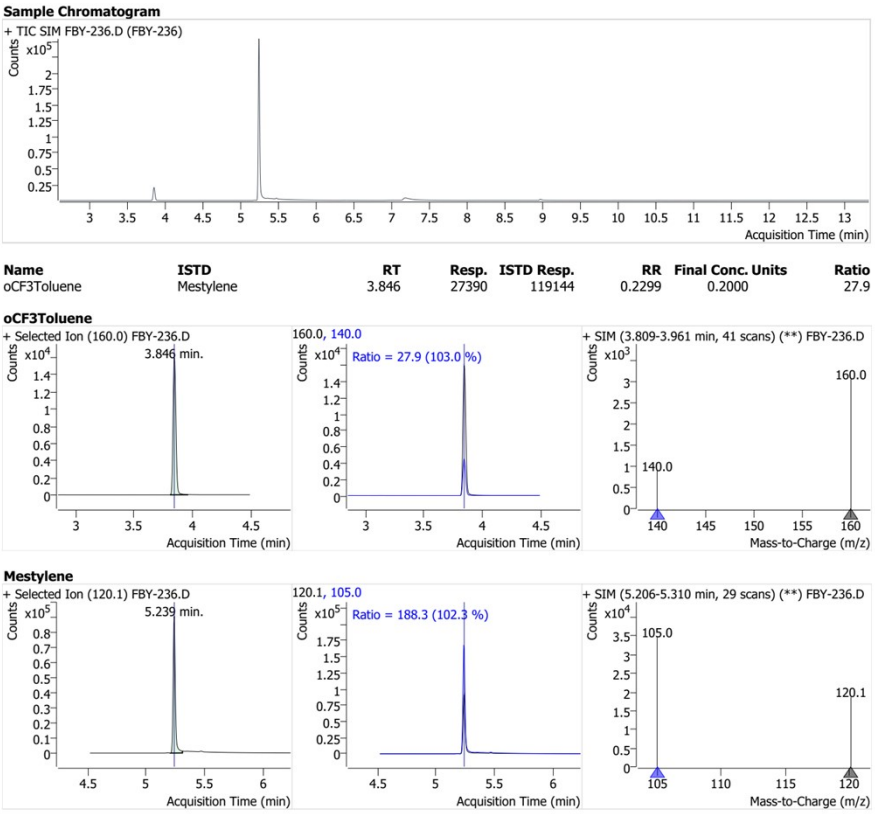
VII. Competition Experiment



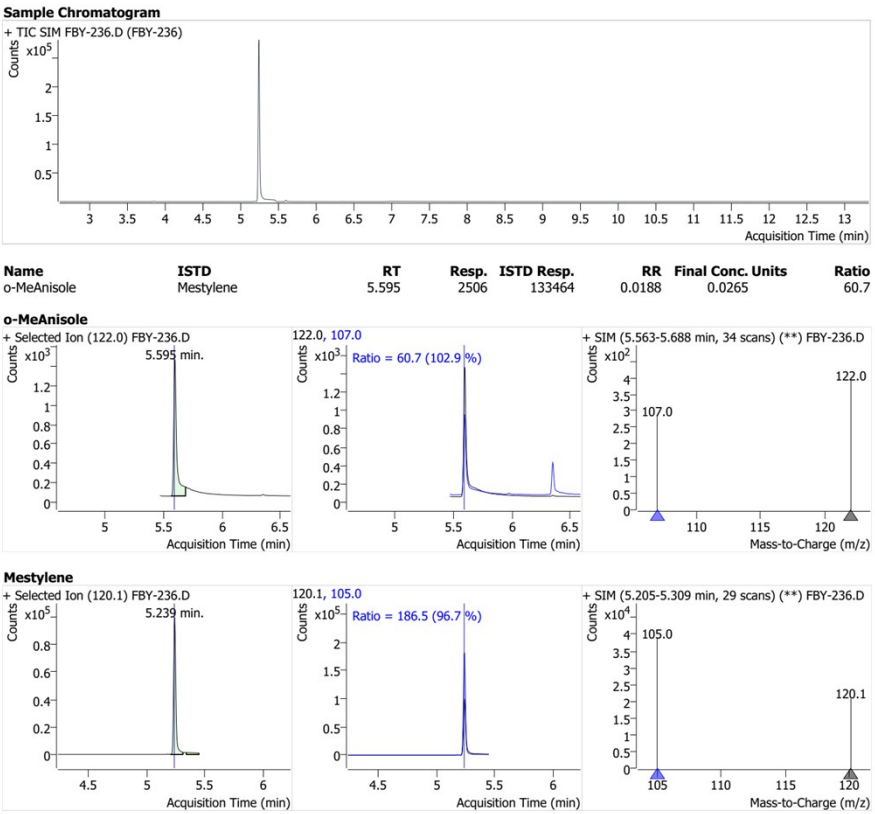
Scheme S1 Competition experiment of **1f** and **1g**

An oven-dried Schlenk tube equipped with a stirring bar was charged with **1f** and **1g** (0.2 mmol for each, 1.0 equiv), TMB (100 μL, 3.5N in THF, 0.35 mmol, 1.75 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol%), XantPhos (17.4 mg, 15 mol%), Piv_2O (61μL, 1.5 equiv) under argon. Then dioxane (1 mL) was added at room temperature. The reaction mixture was placed in a preheated oil bath at 160 °C, and stirred for 4h. The reaction mixture was then cooled down to room temperature. Mesitylene (27.8 μL, 0.2 mmol) was subjected as internal standard after the completion of reaction. The yields of **2f** and **2g** were separately determined by GC-MS analysis using mesitylene as the internal standard (yield of **2f**: 20%, yield of **2g**: 3%).

GC-MS analysis of **2f**:



GC-MS analysis of **2g**:



VIII. References

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(2) T. Morioka, A. Nishizawa, K. Nakamura, M. Tobisu and N. Chatani, *Chem. Lett.*, 2015, **44**, 1729.

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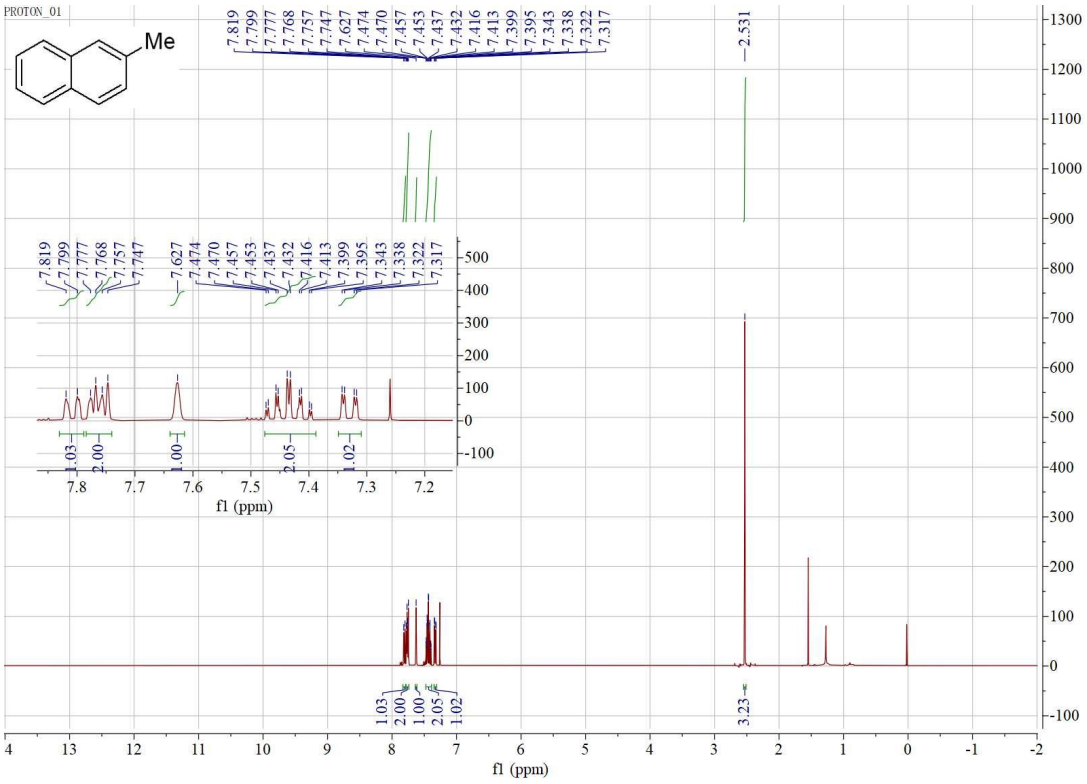
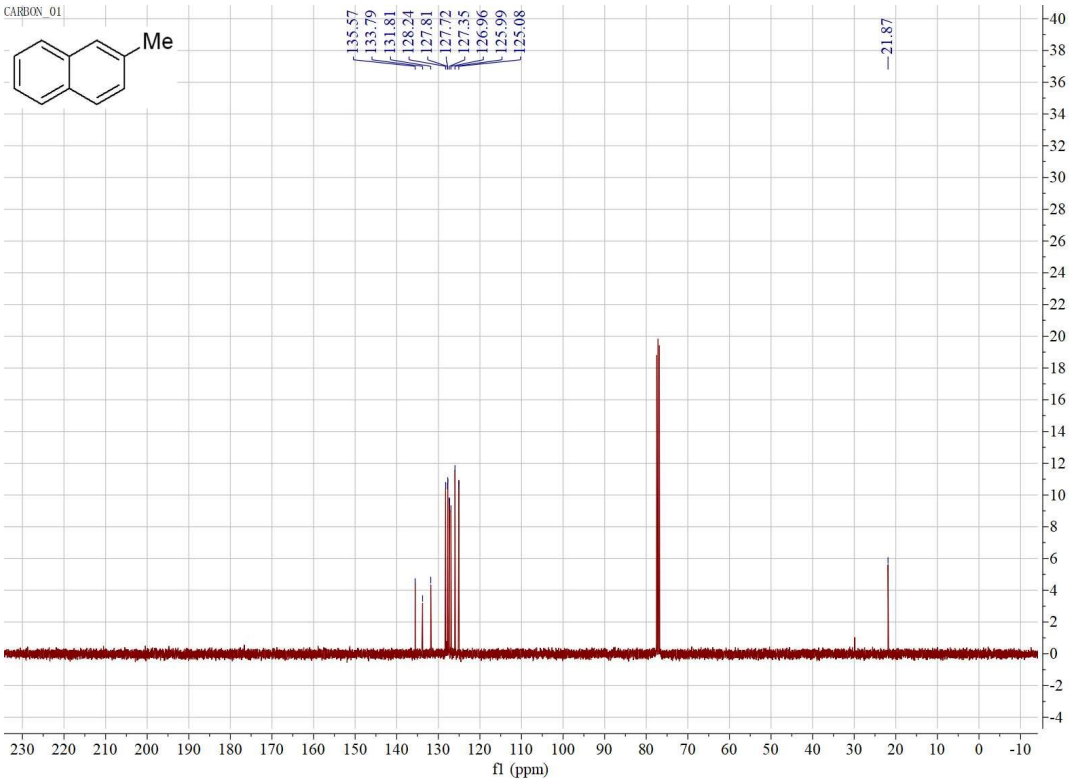
IX. Copies of NMR spectra

^{1}H NMR spectra of compound **2a**:



^{13}C NMR spectra of compound **2a**:



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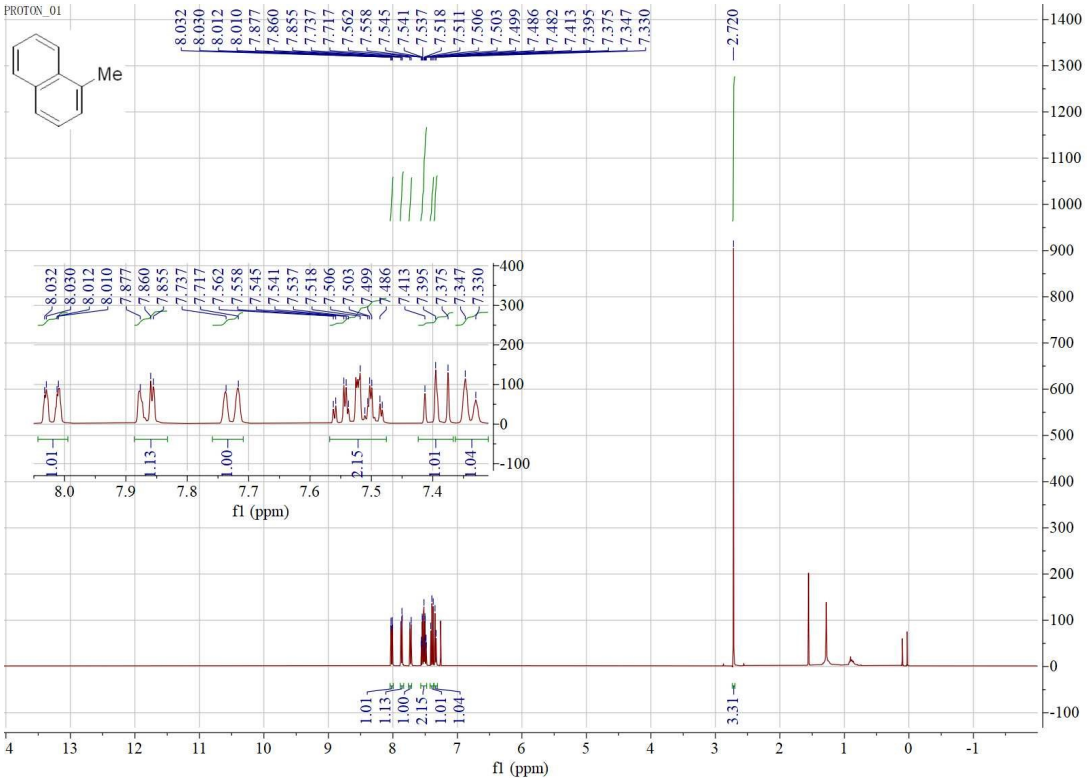

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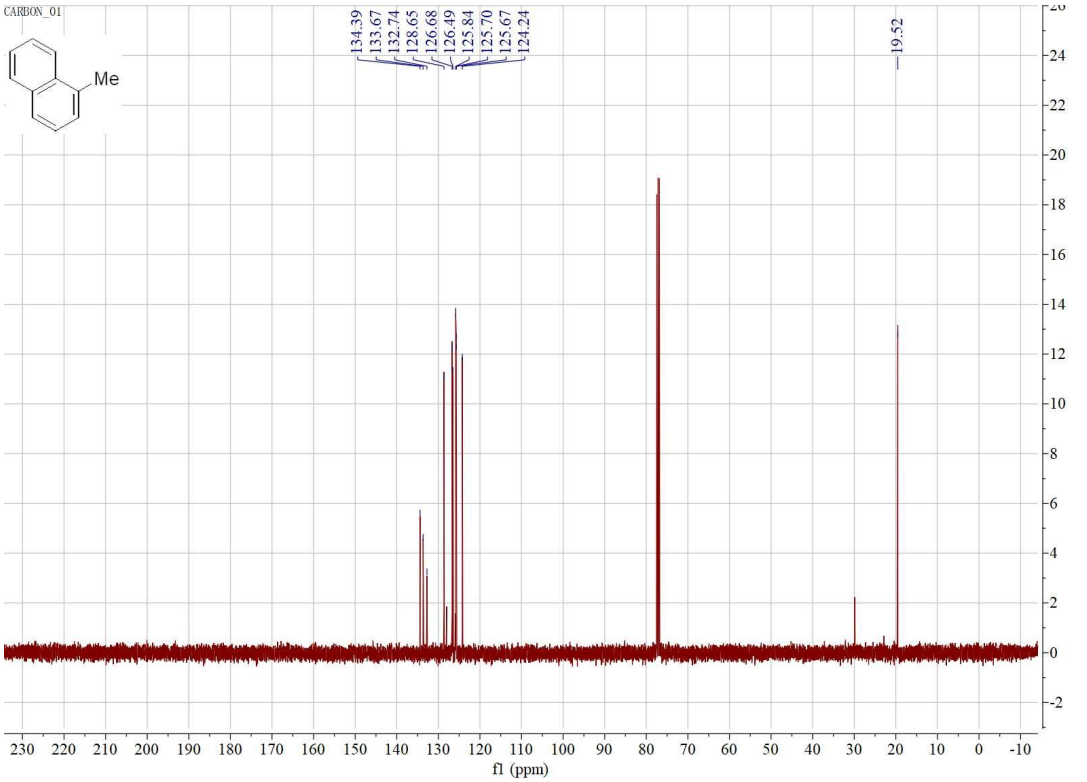
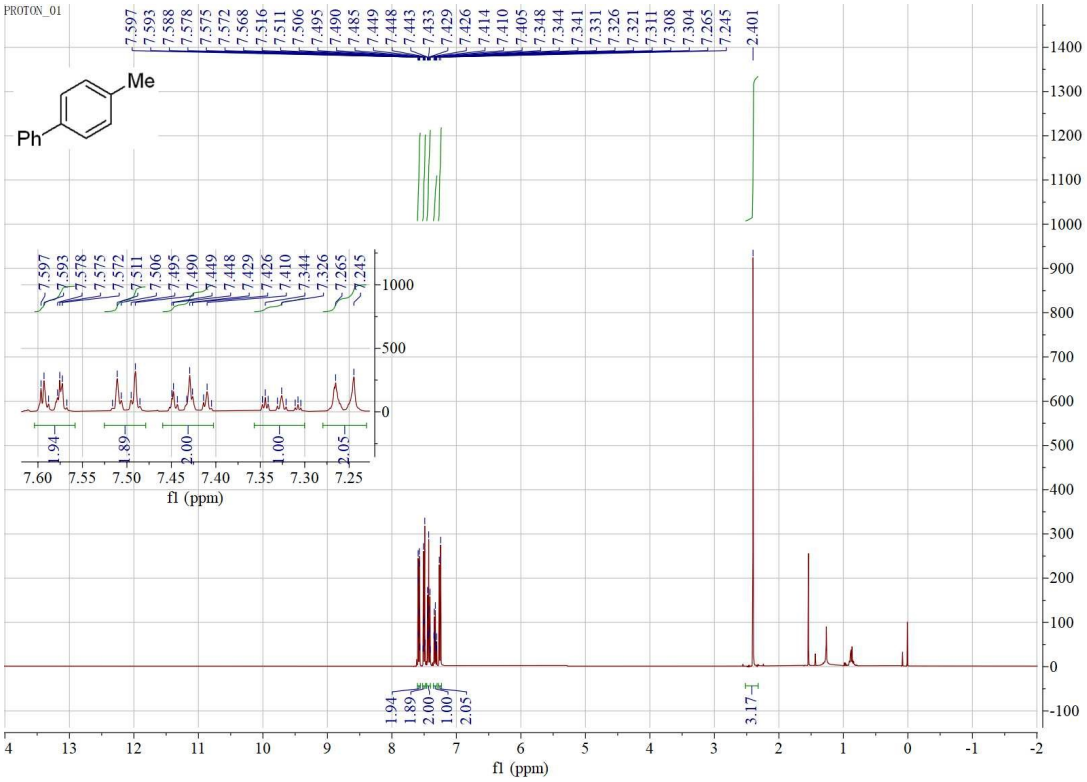


^{1}H NMR spectra of compound **2c**:



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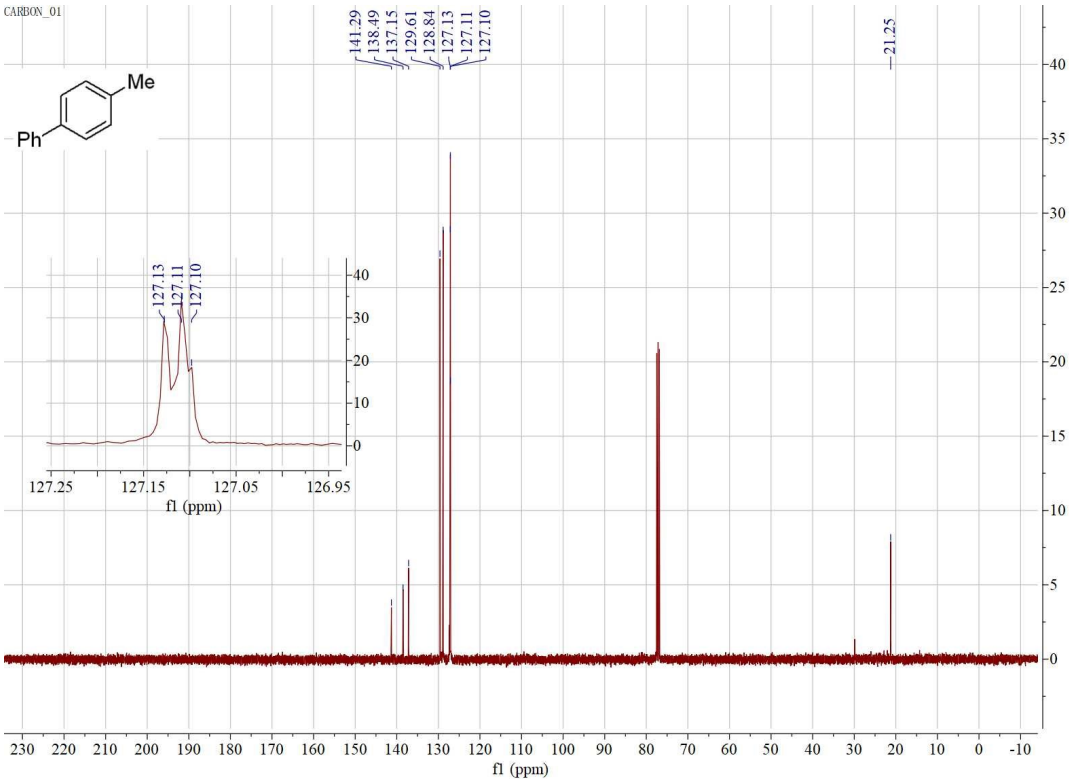

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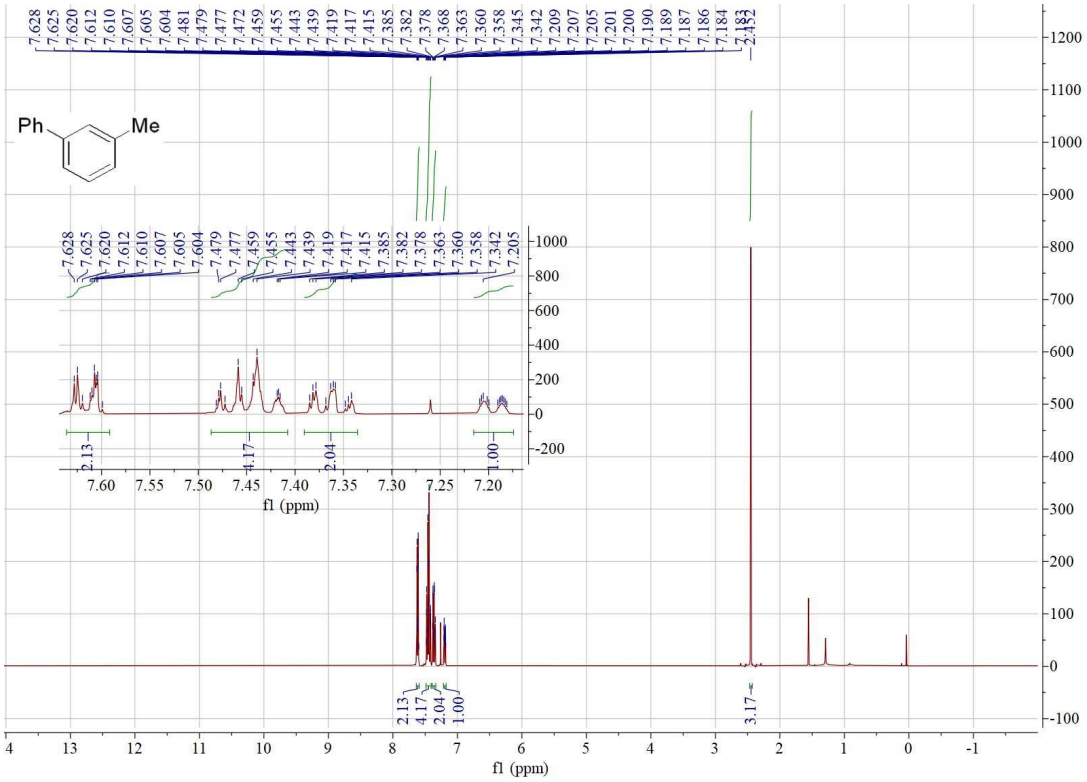

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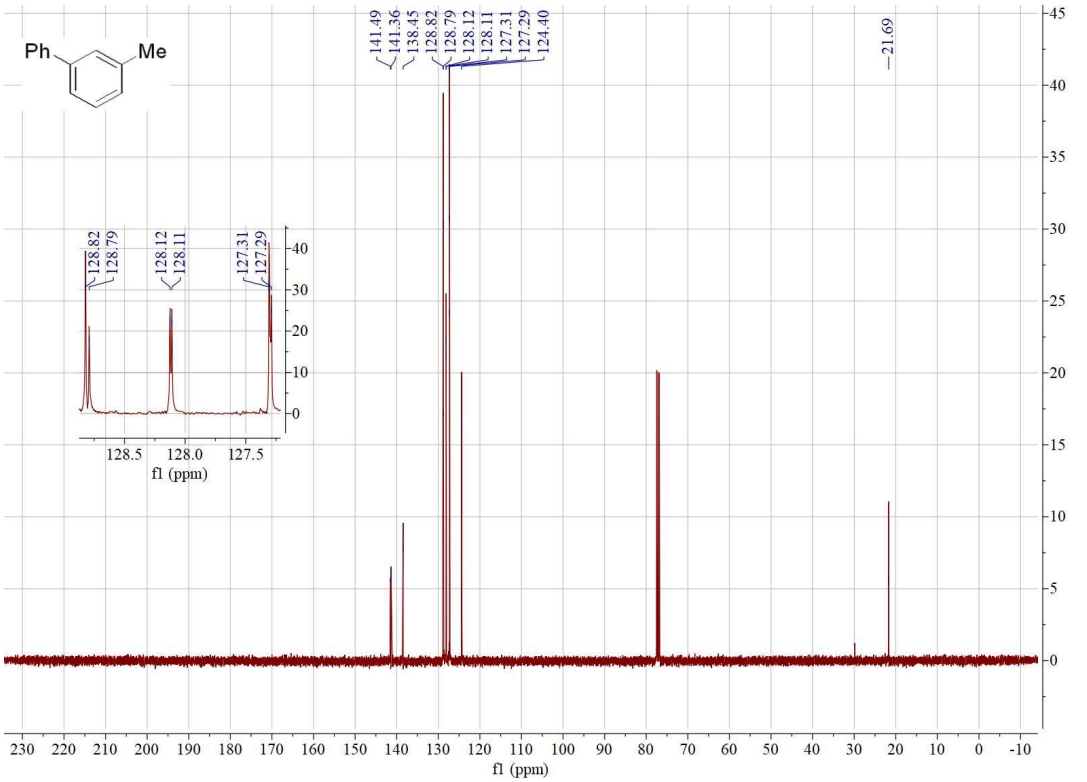

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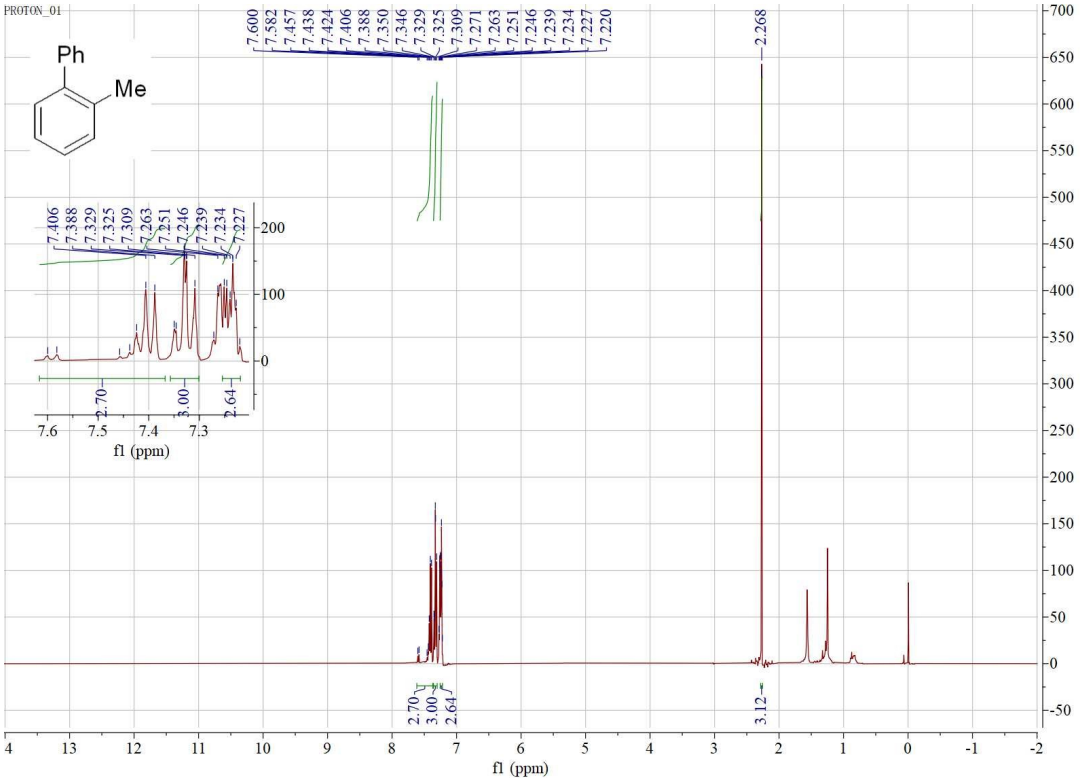

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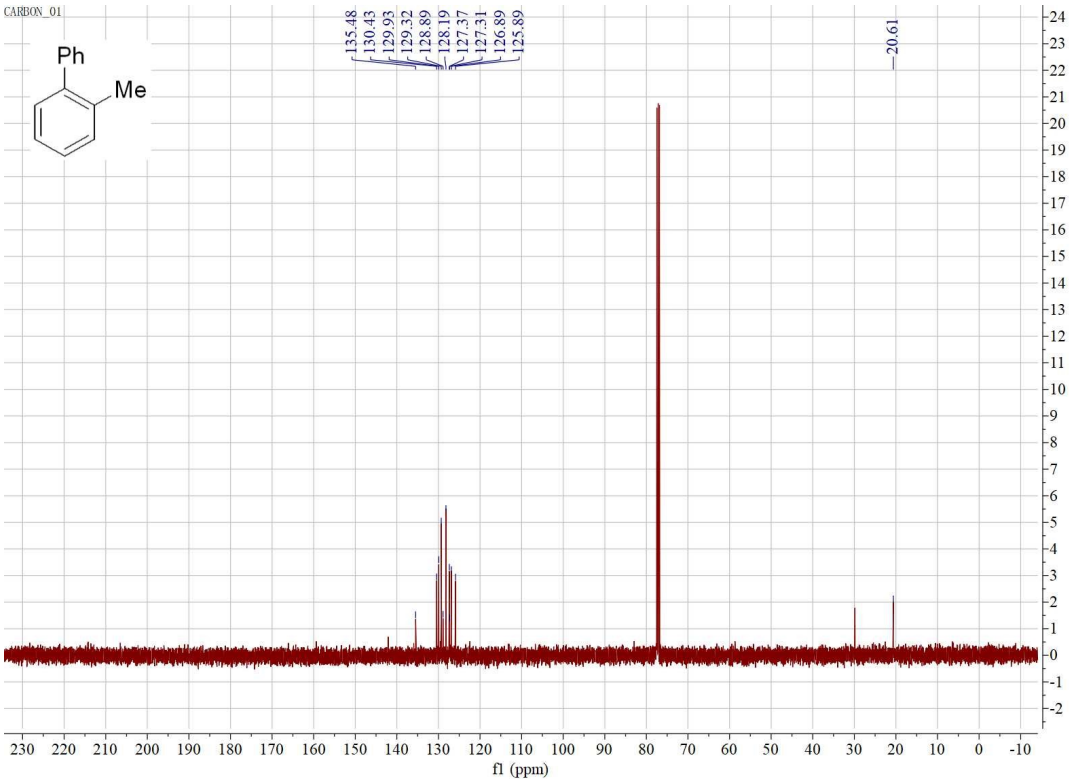

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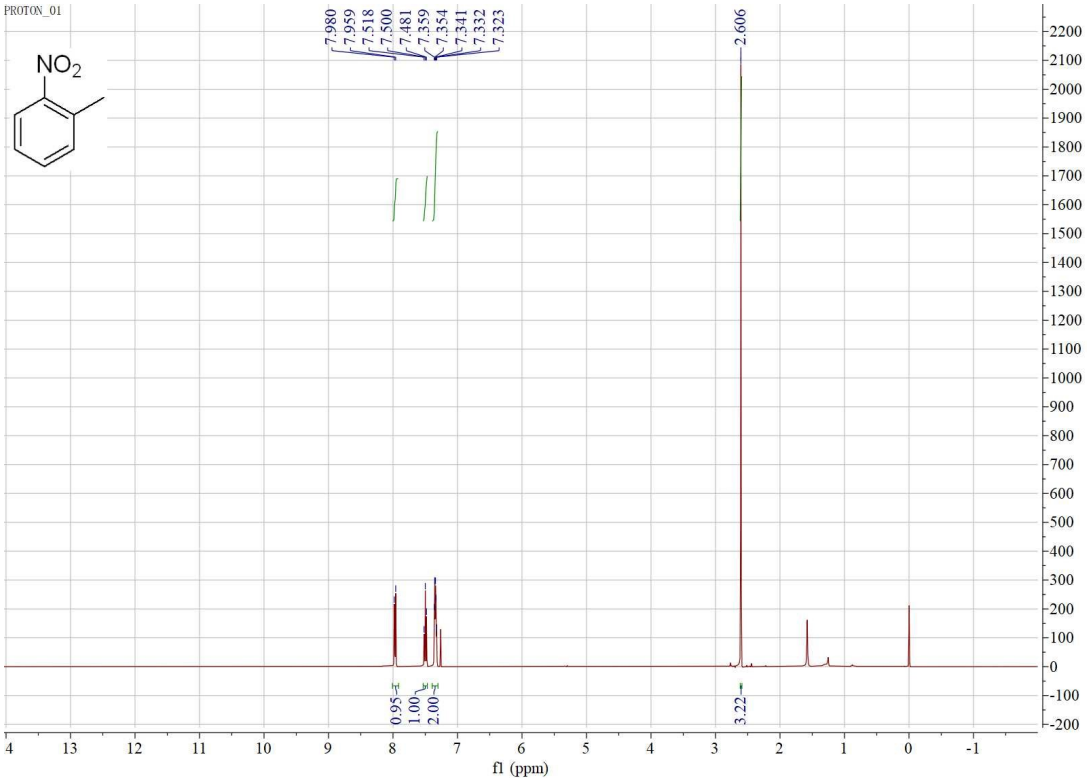

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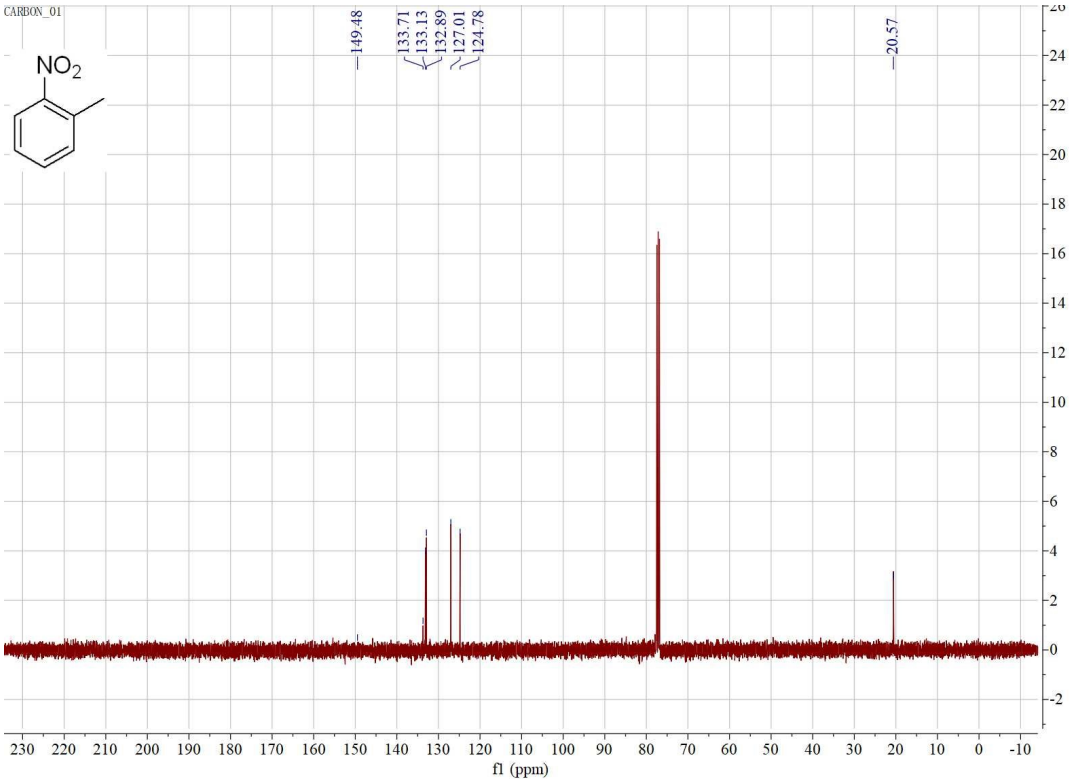

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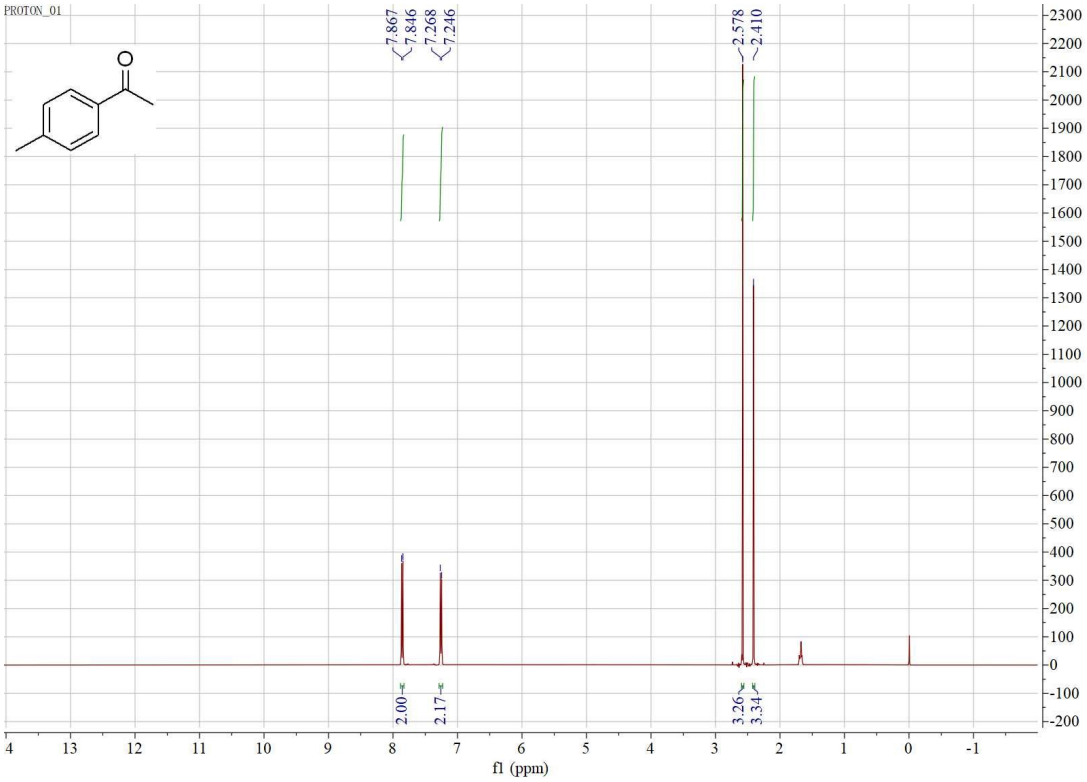

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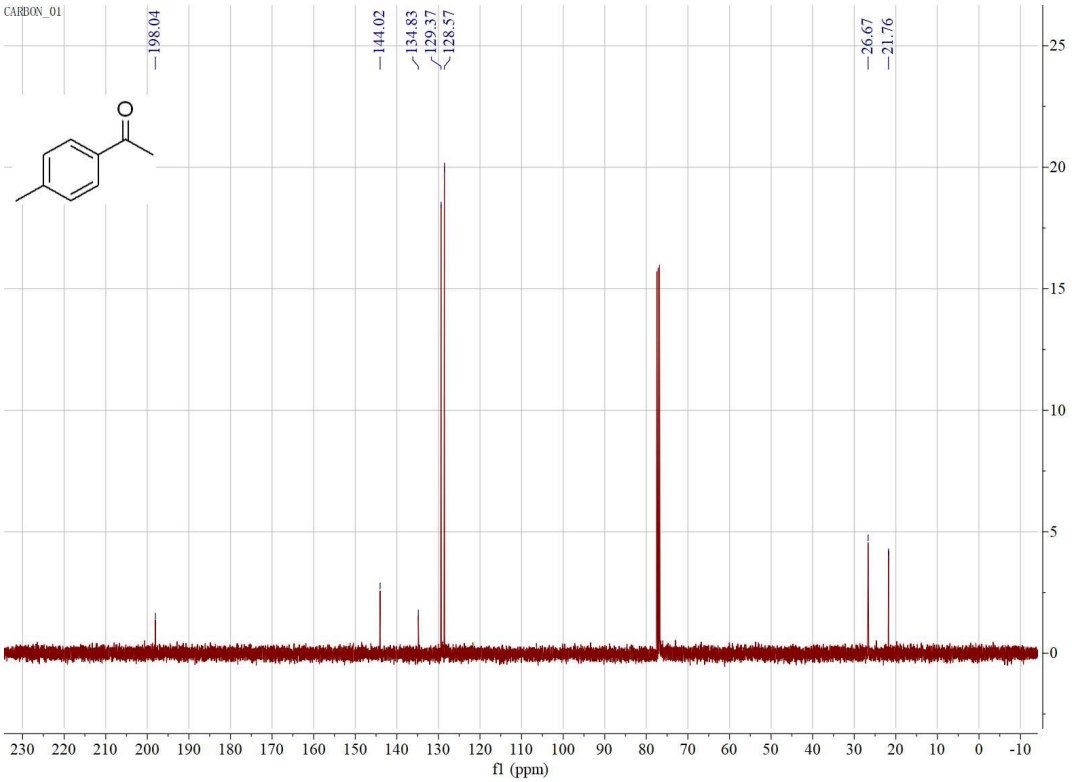

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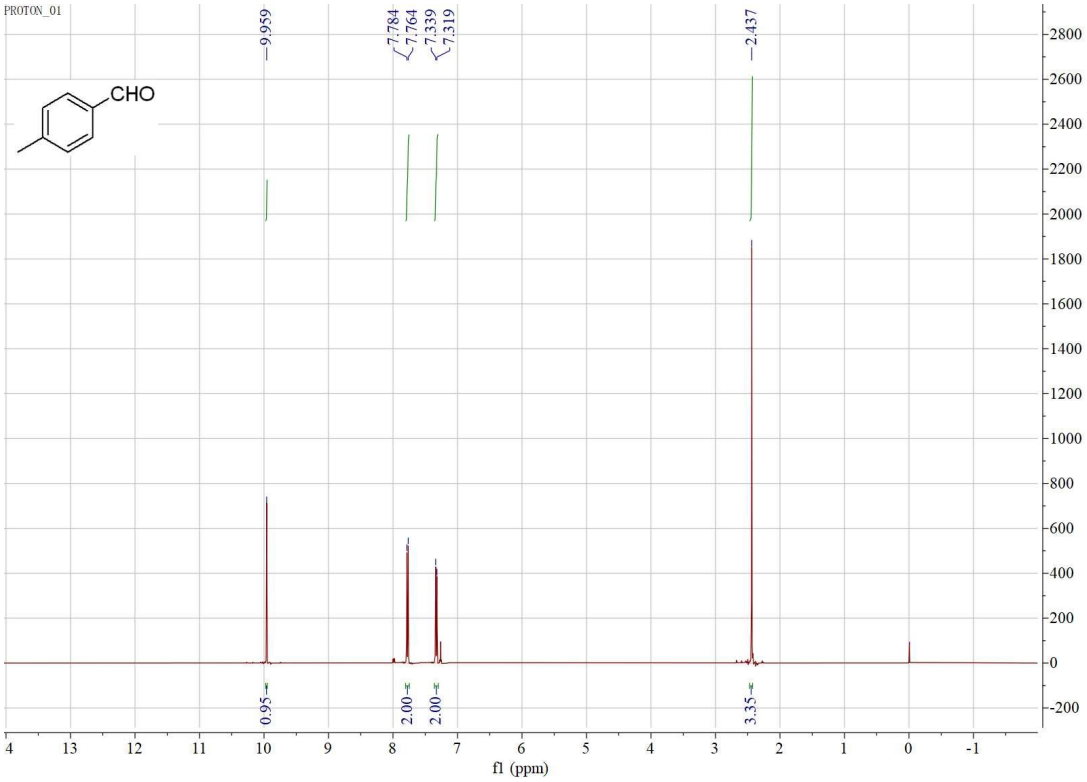

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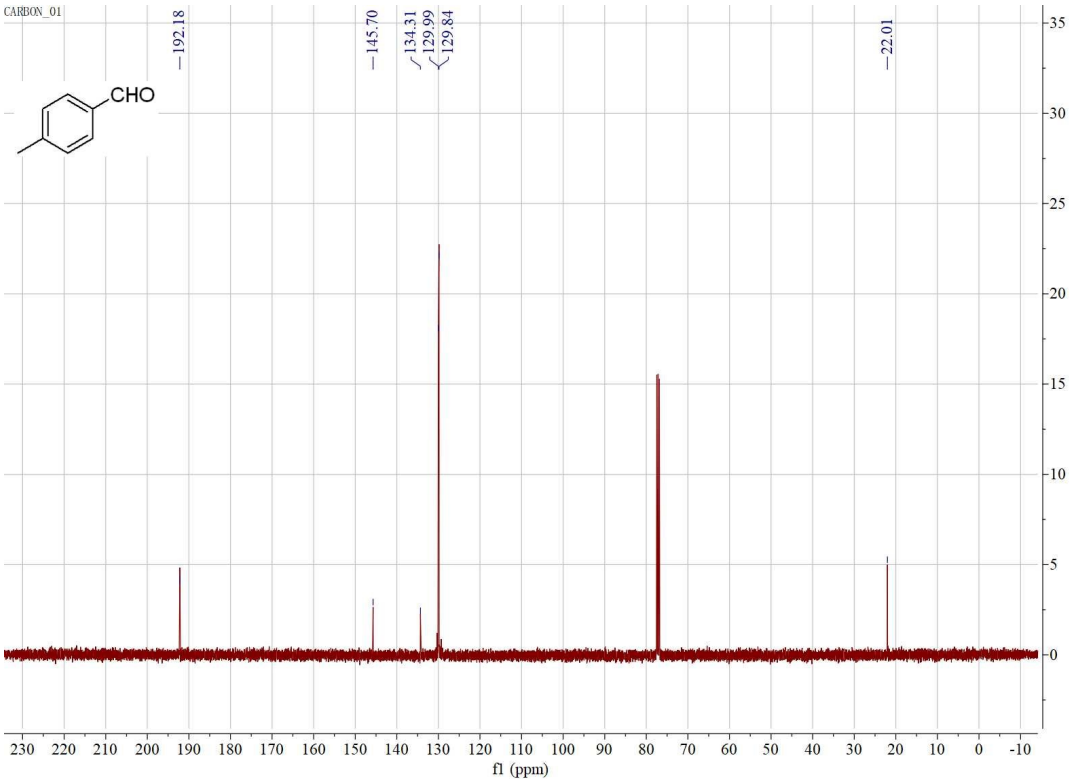

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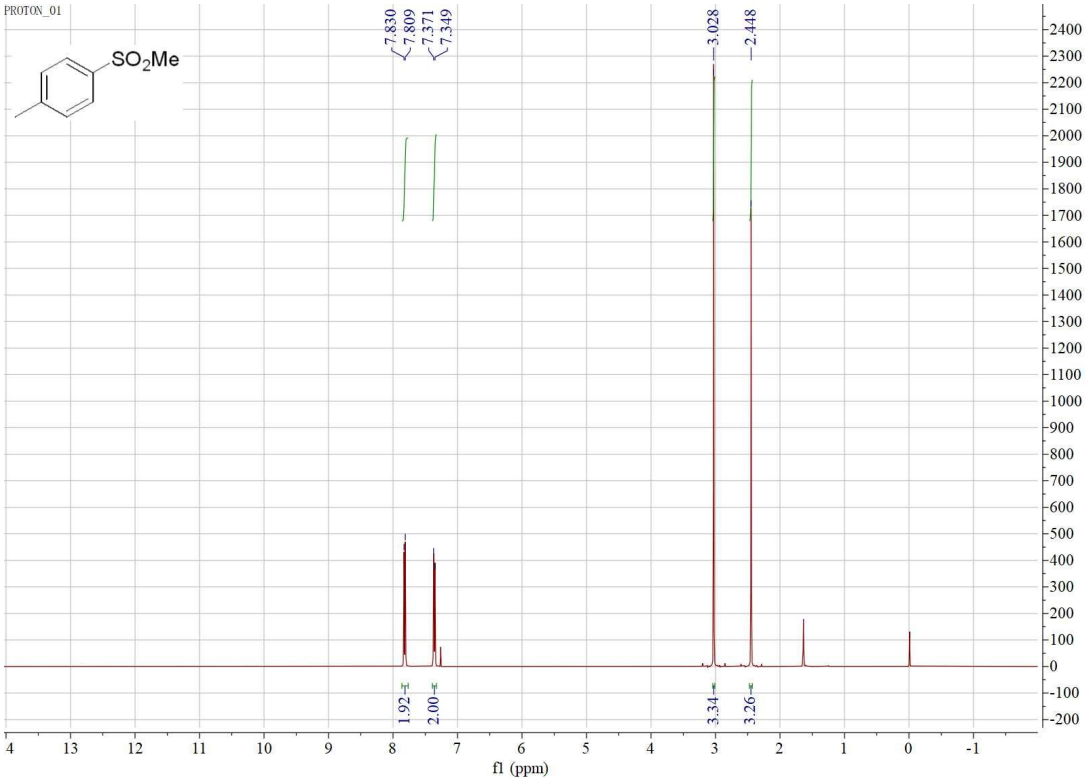

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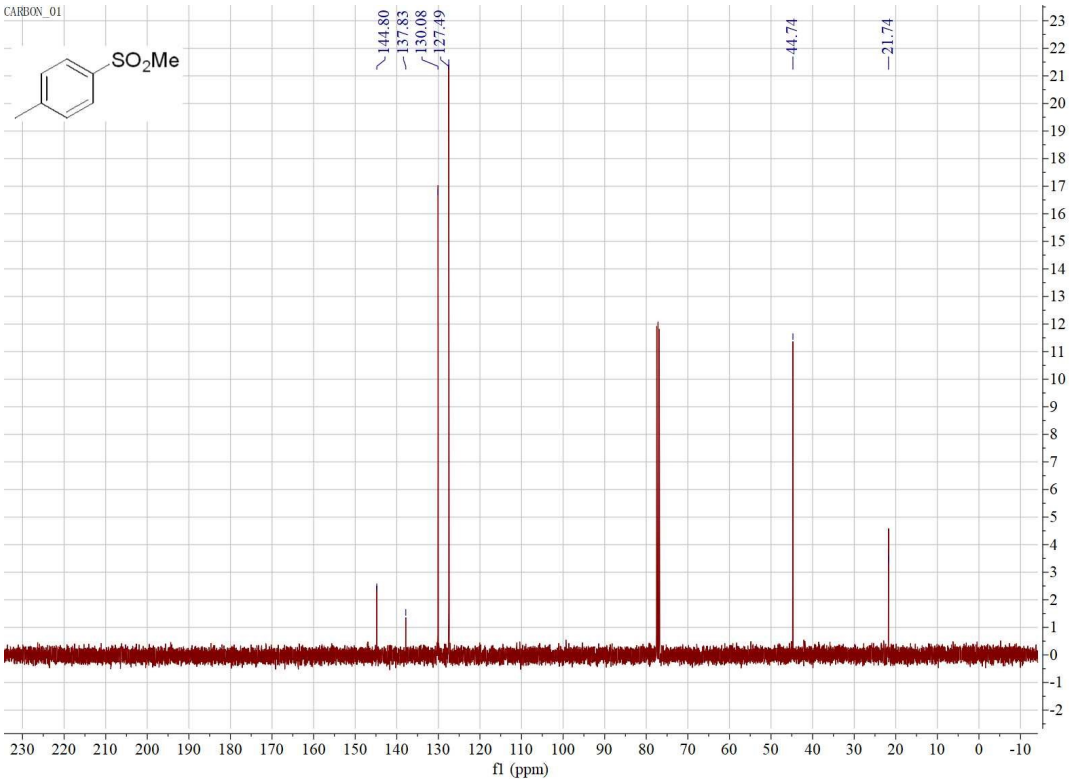

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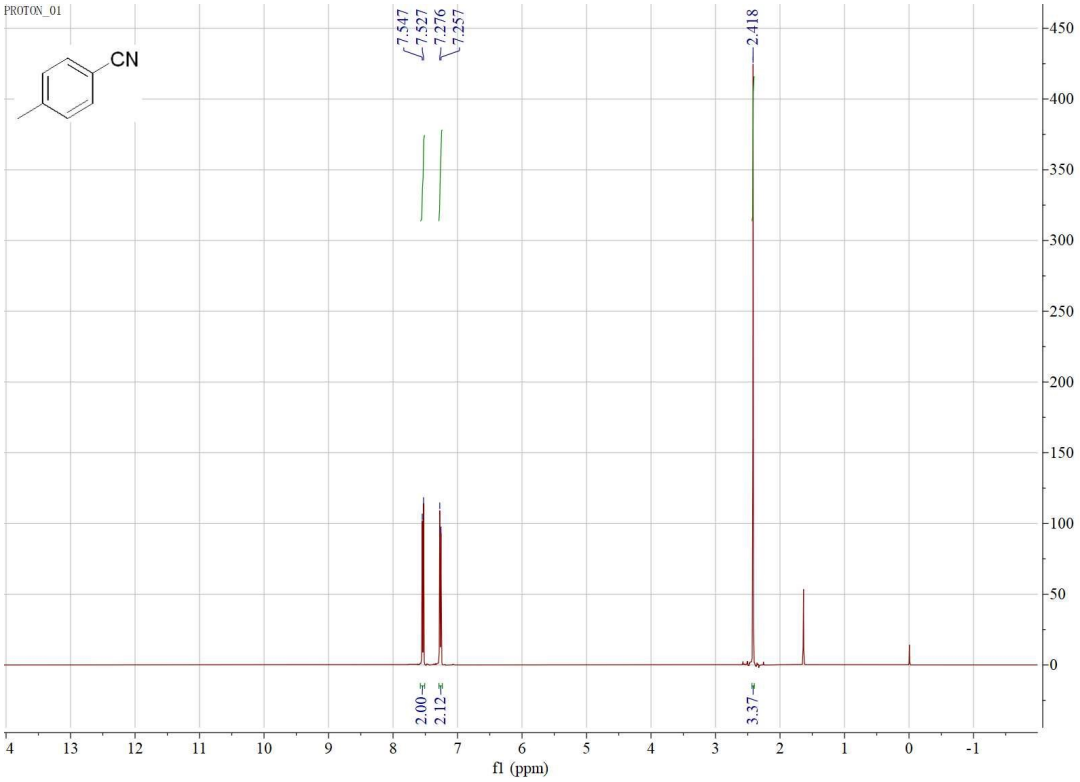

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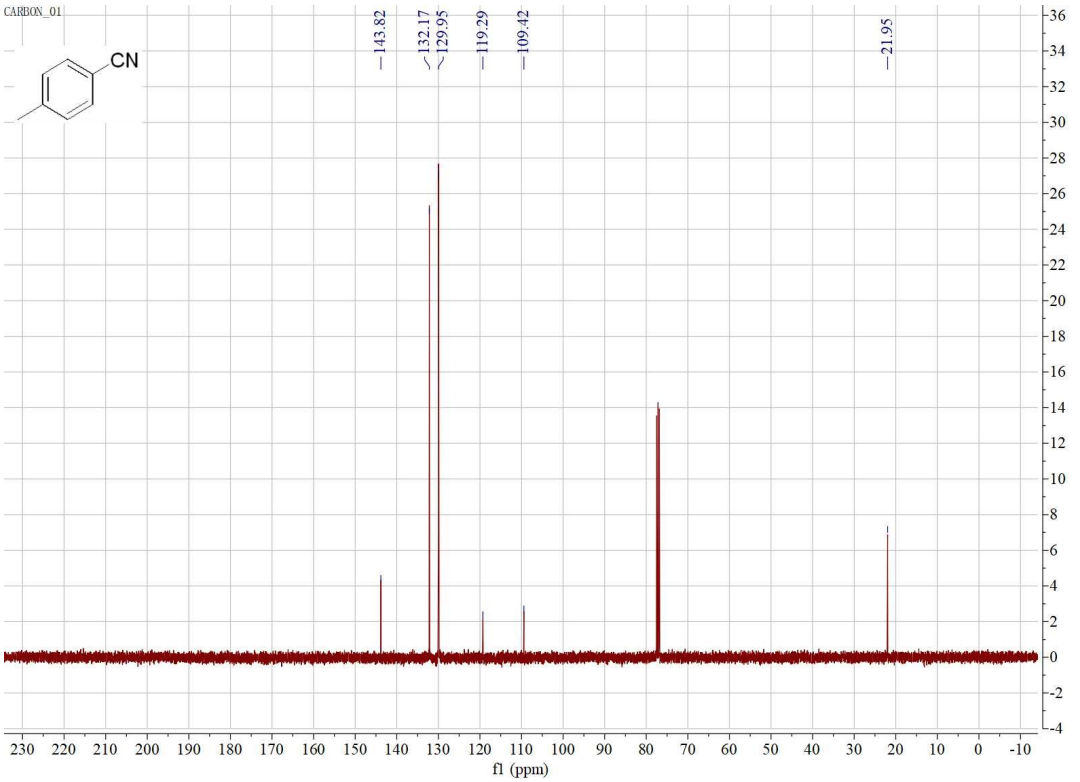

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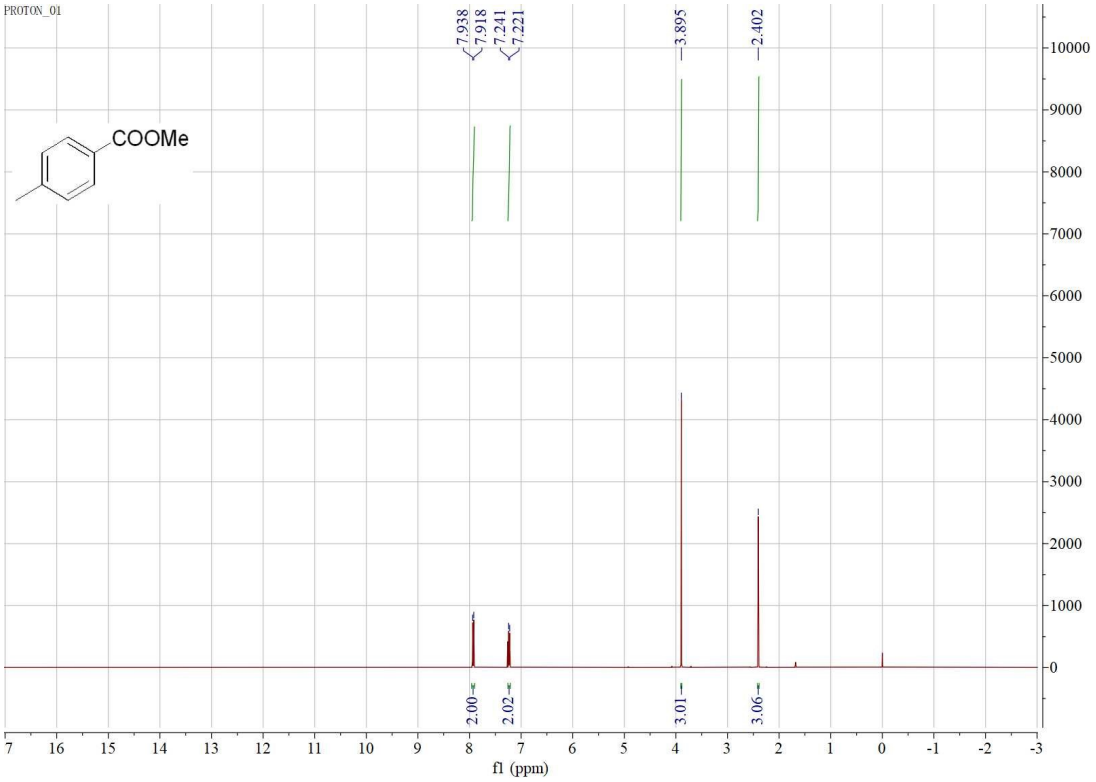

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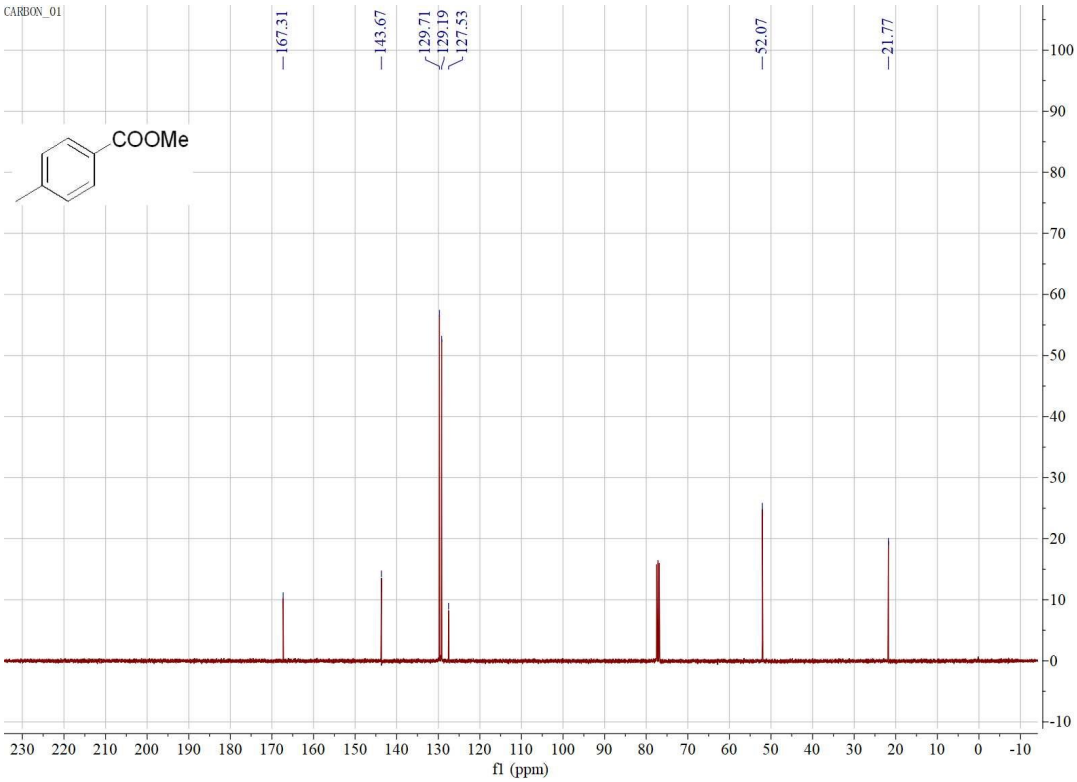

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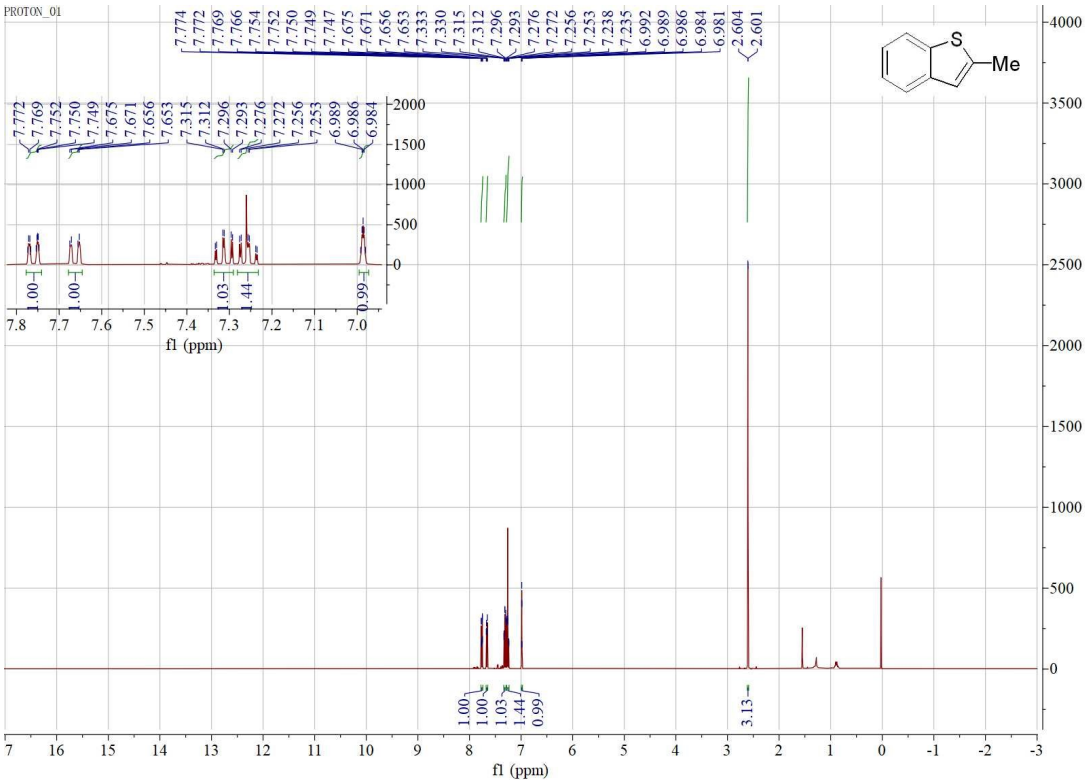

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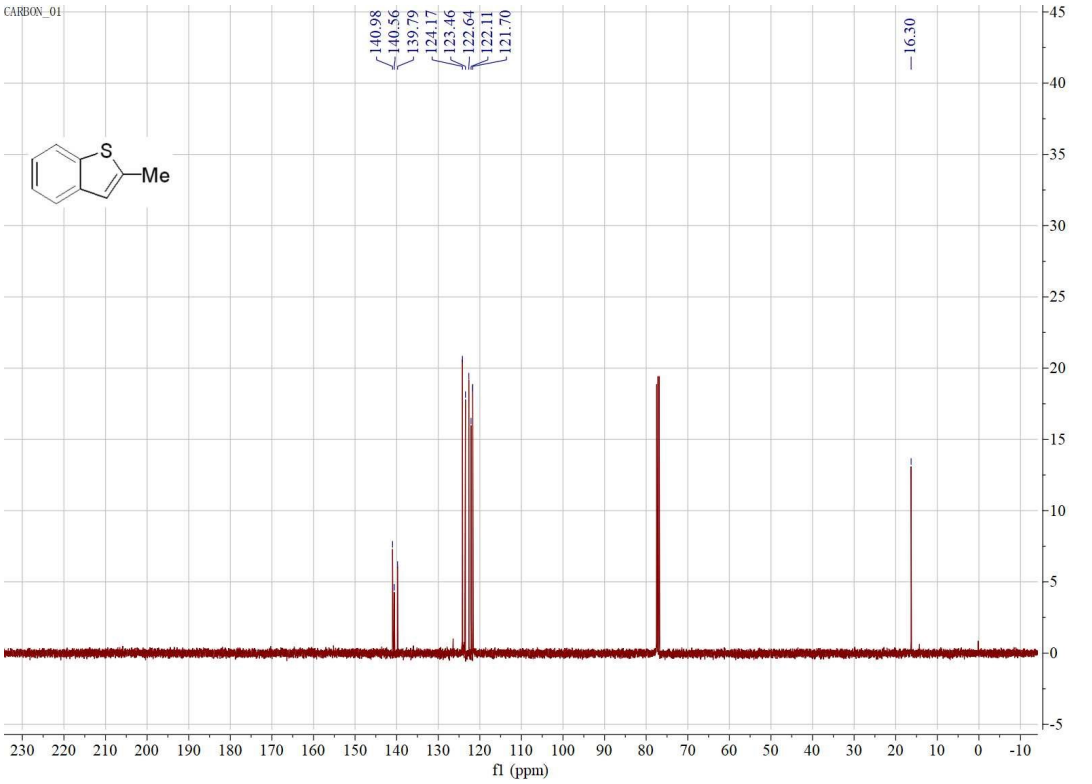

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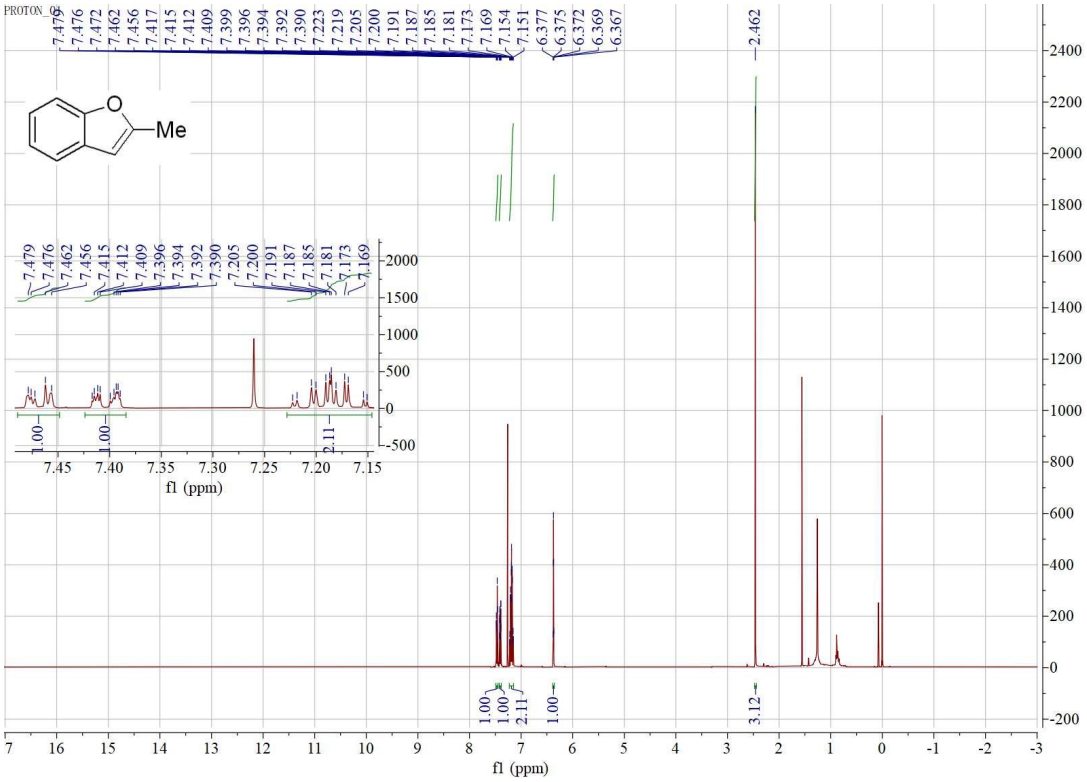

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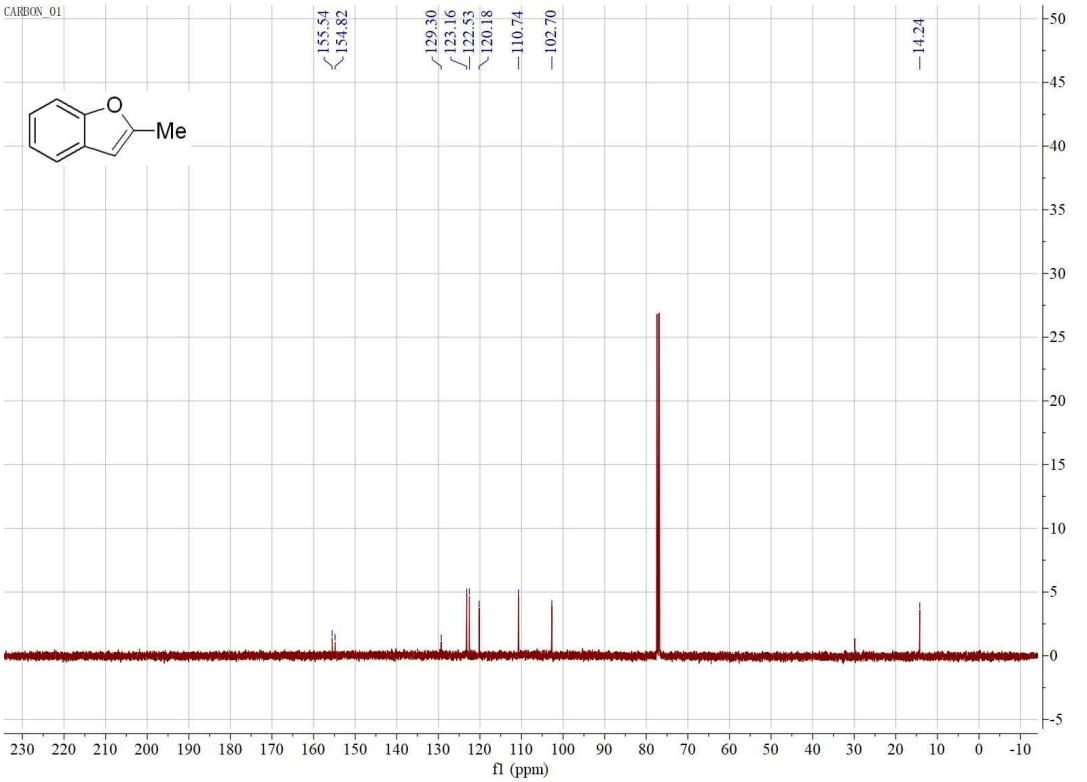

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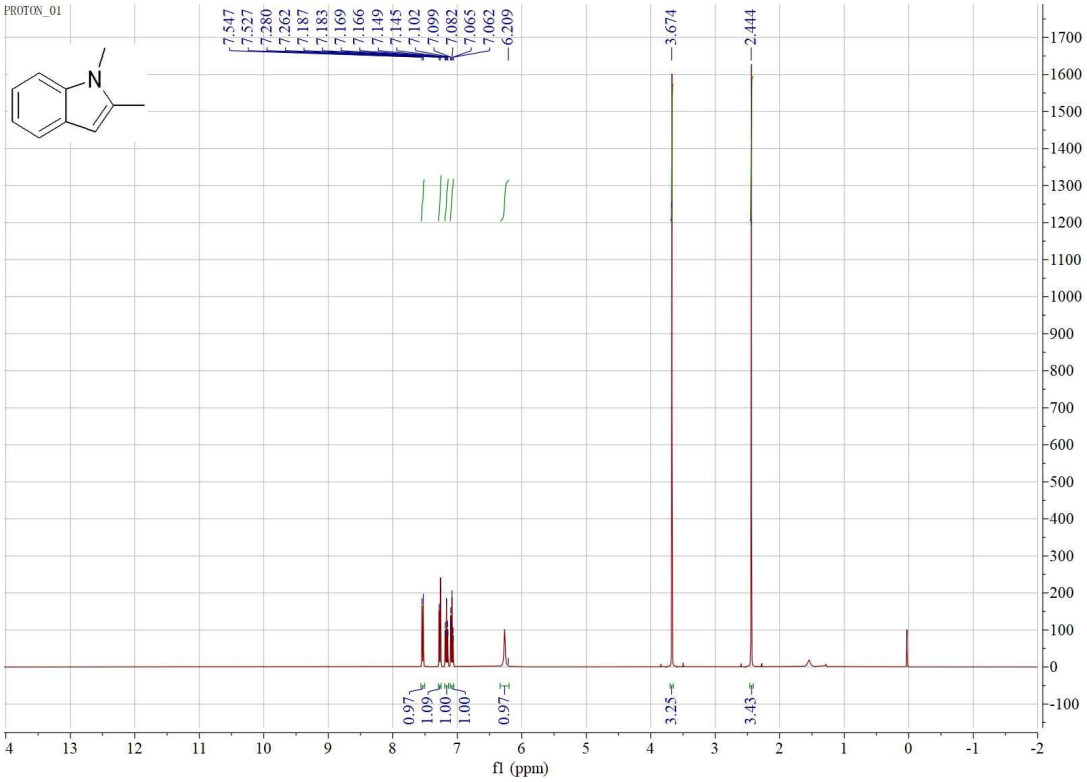

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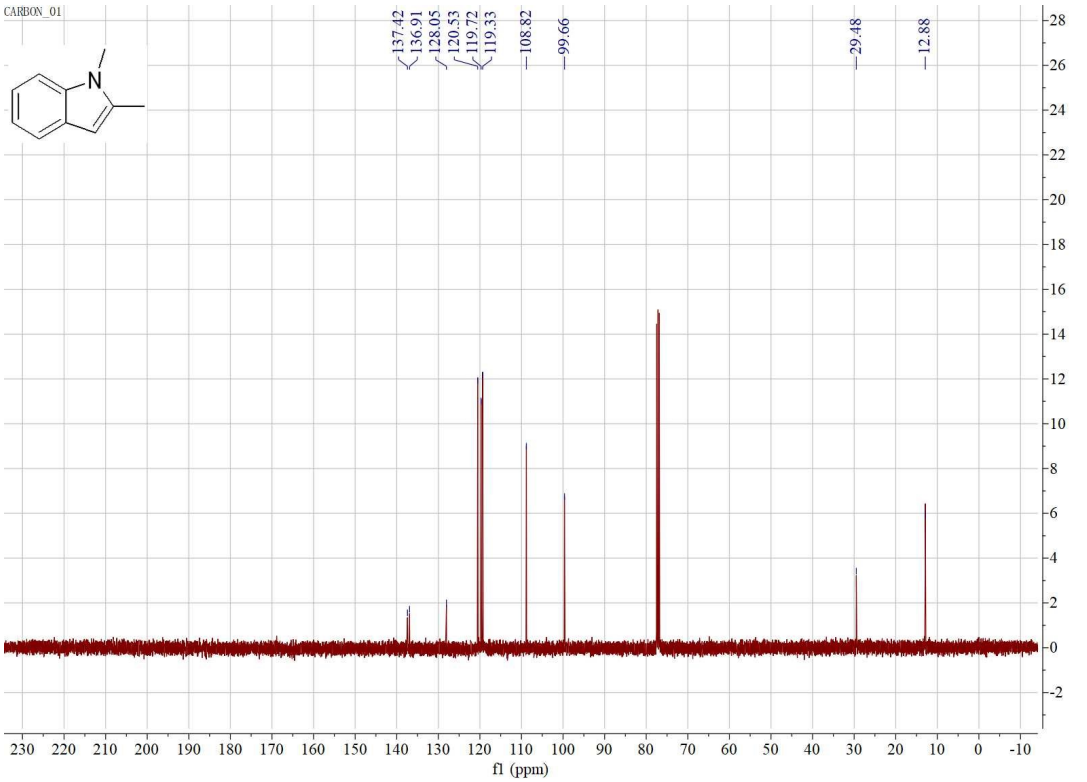

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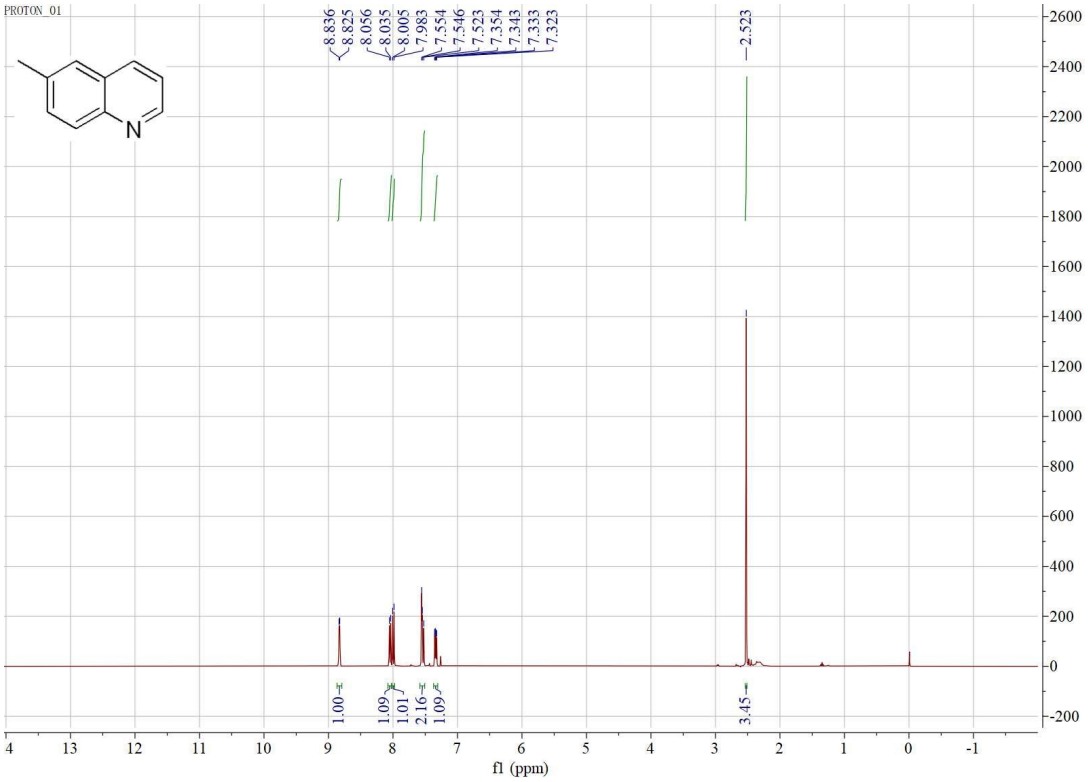

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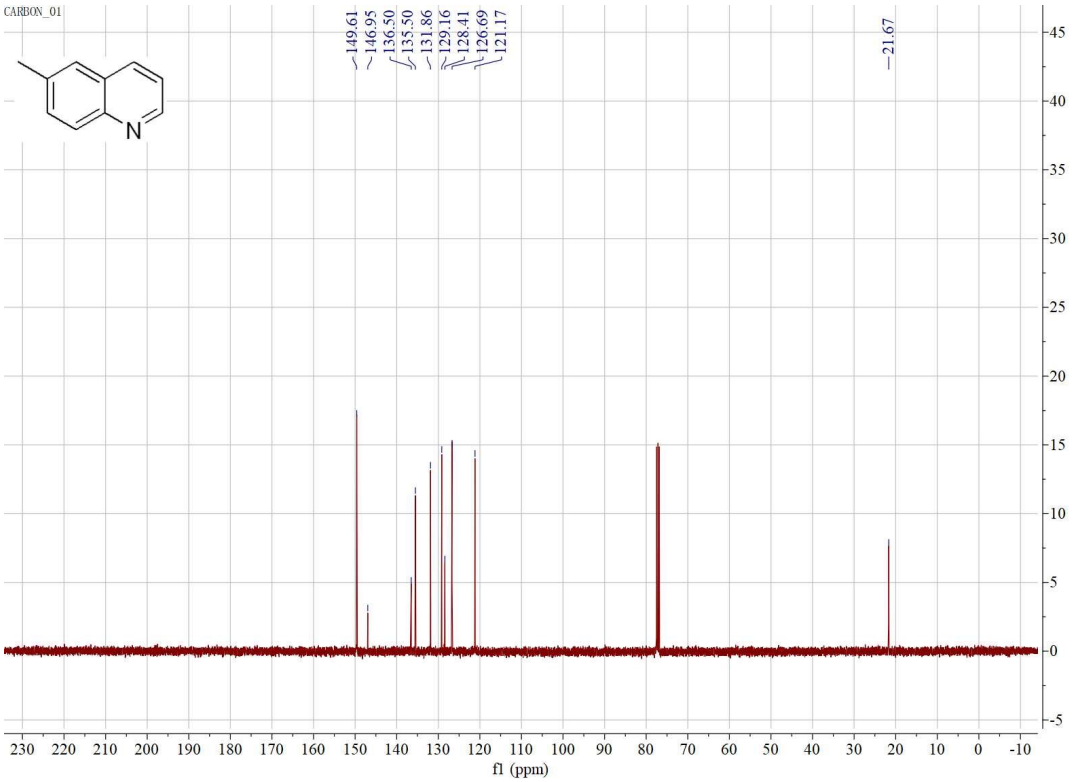

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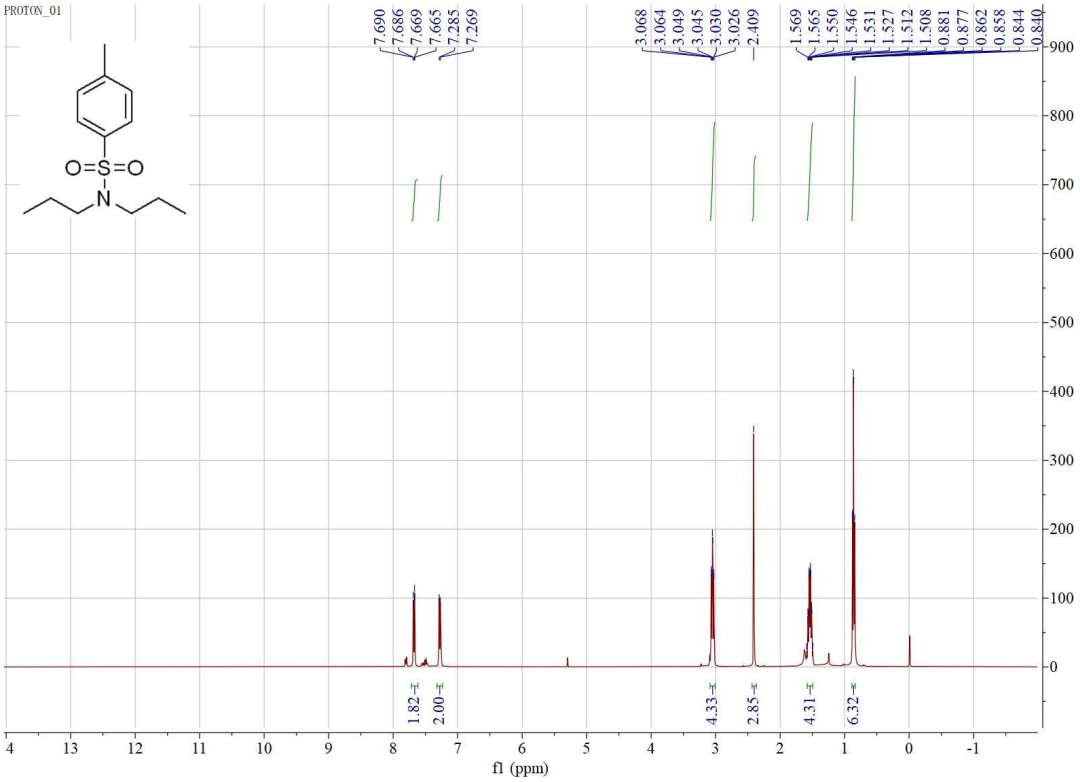

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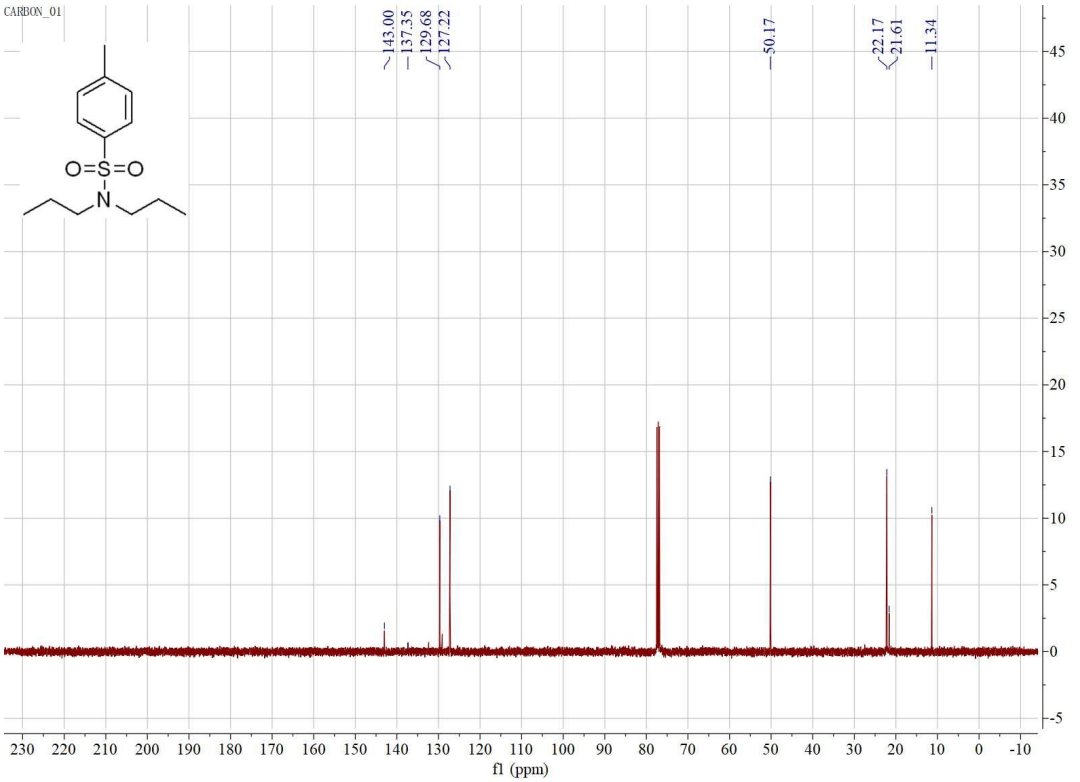

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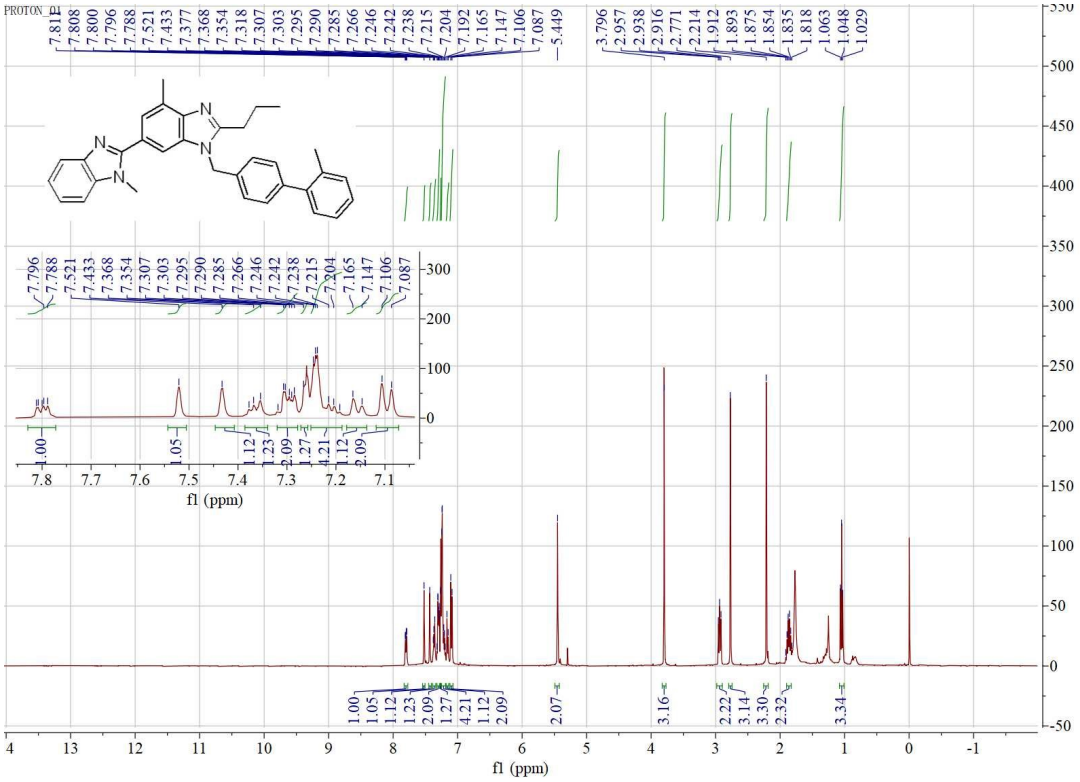

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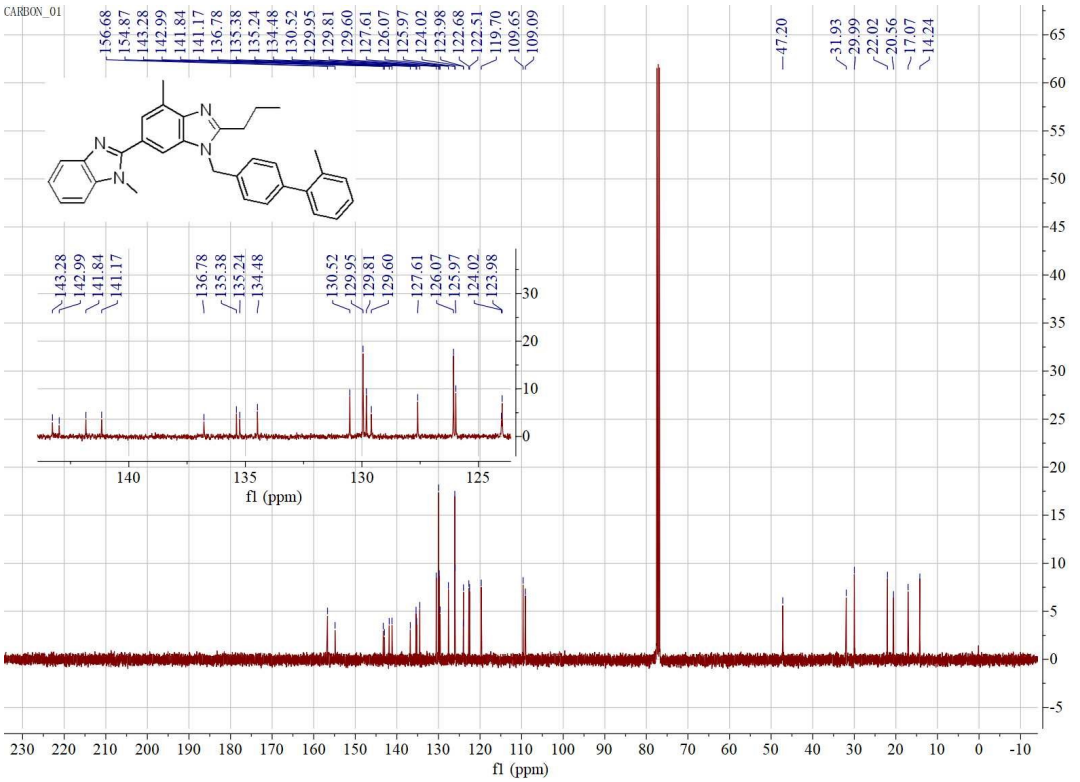

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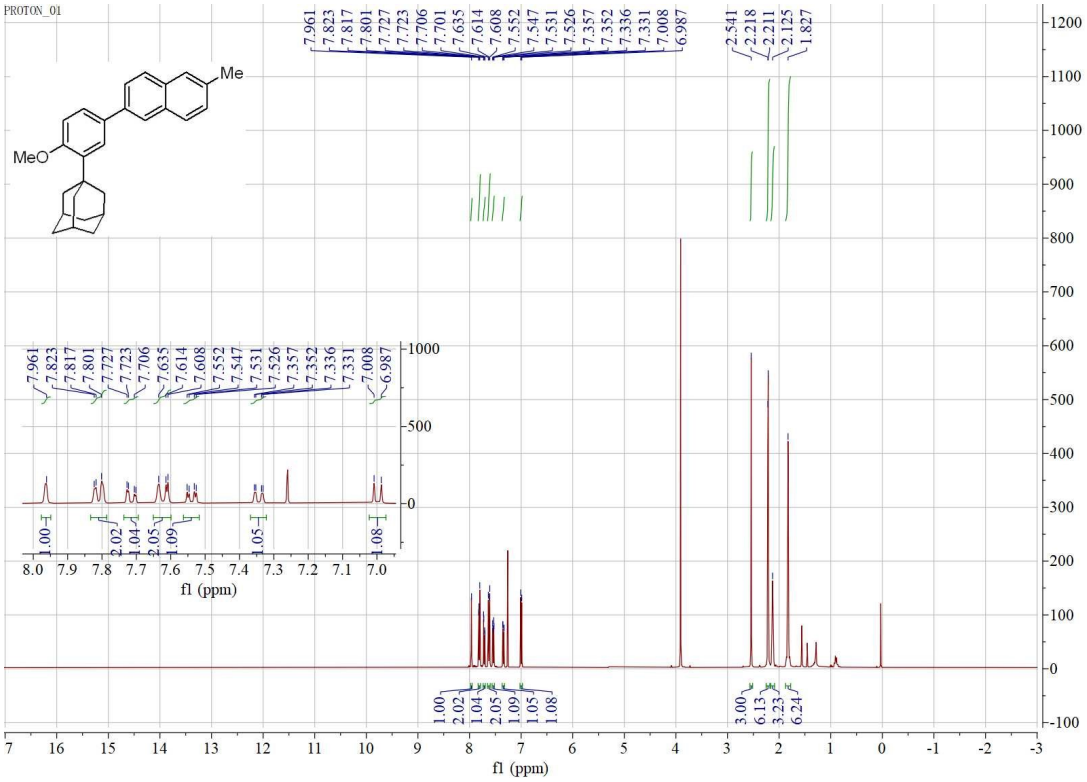

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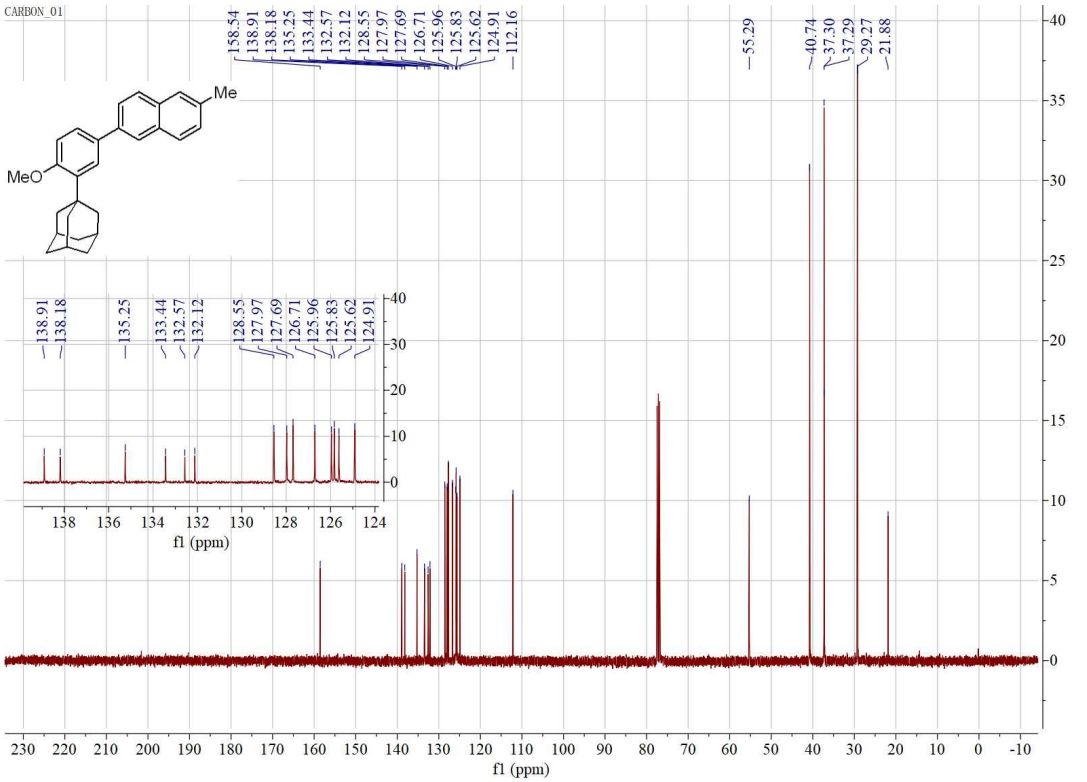

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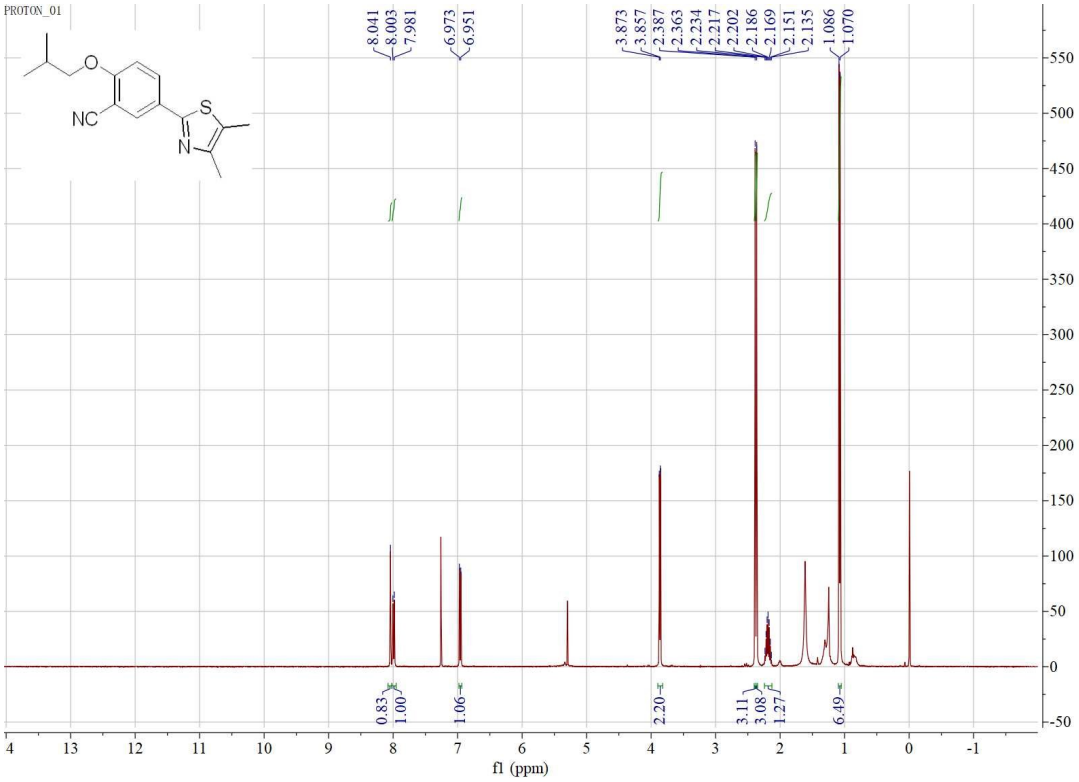

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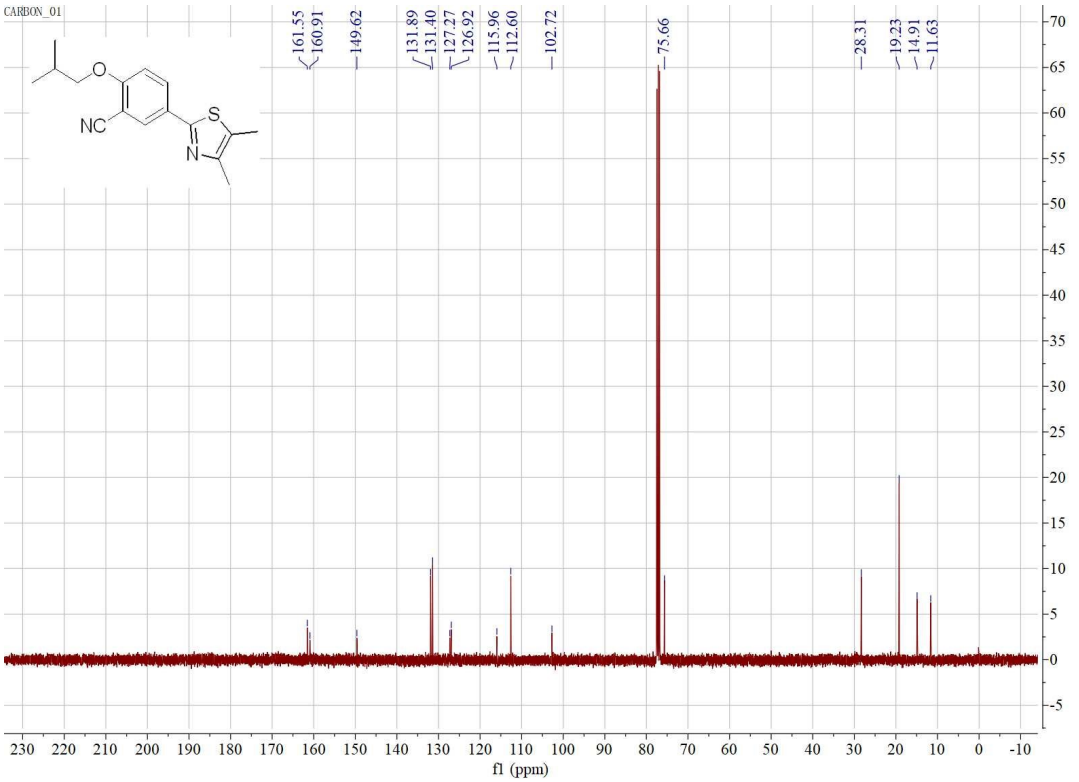

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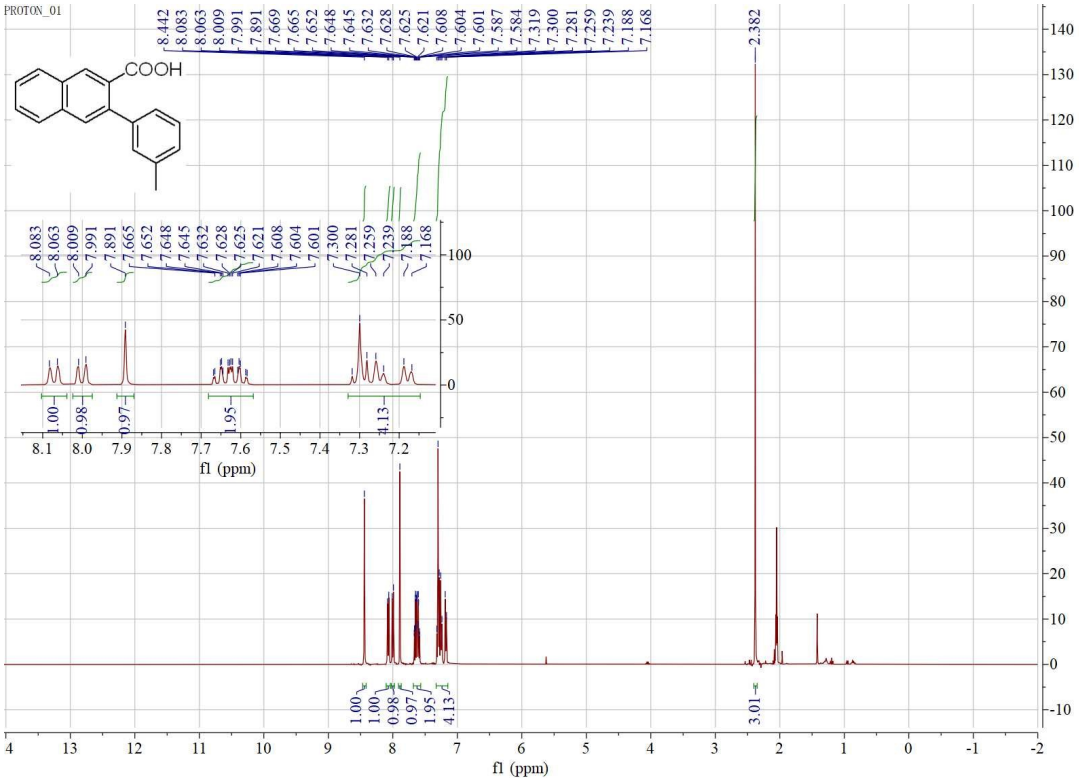

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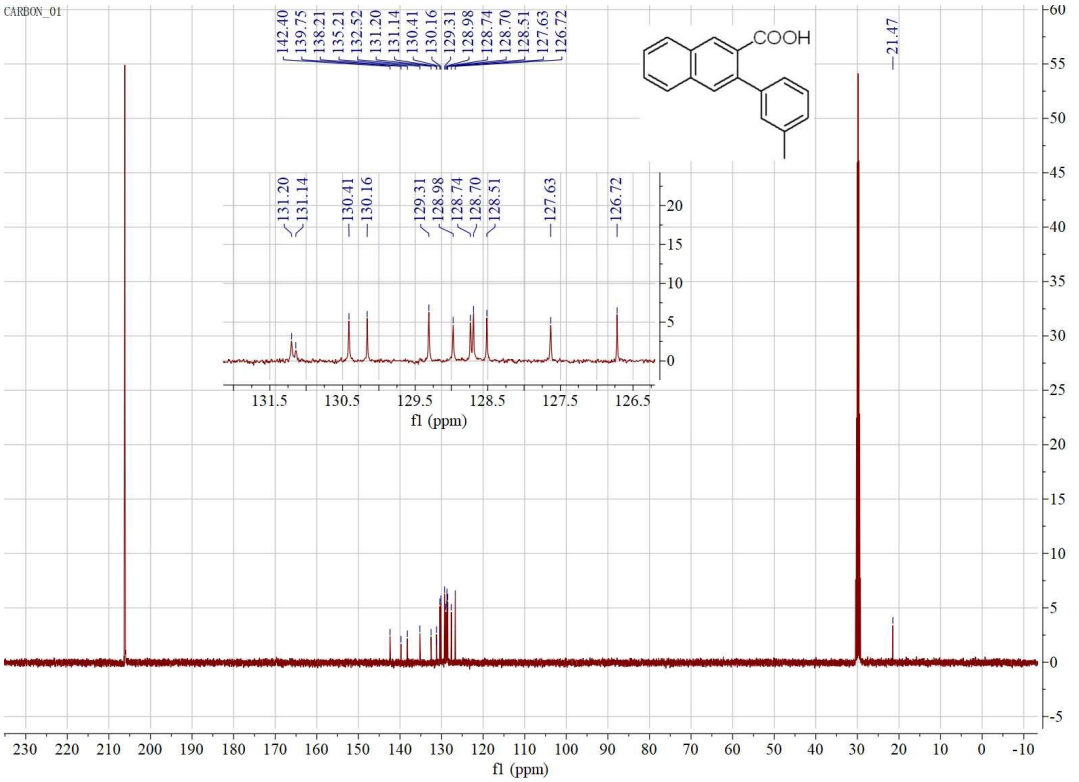

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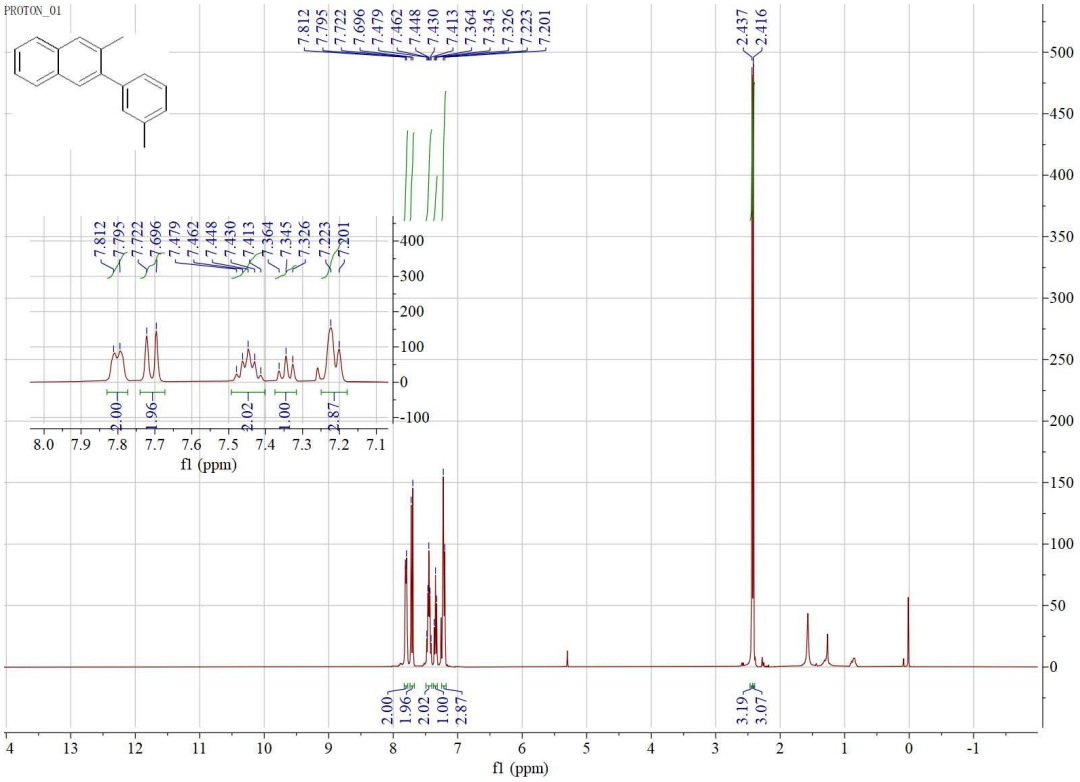

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