Carboxylate Enhanced Rhodium(III)-Catalyzed Aryl C–H Alkylation with Conjugated Alkenes under Mild Conditions

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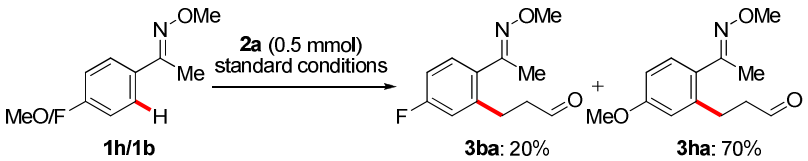
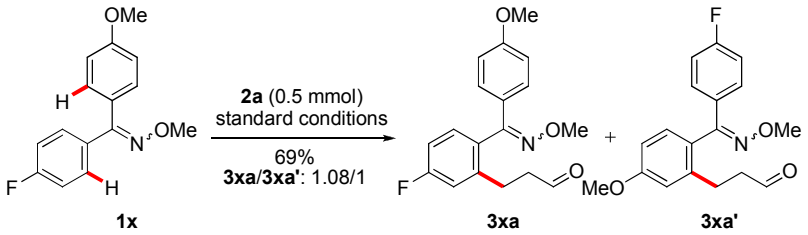
Intermolecular Competition Experiment between 1b and 1h

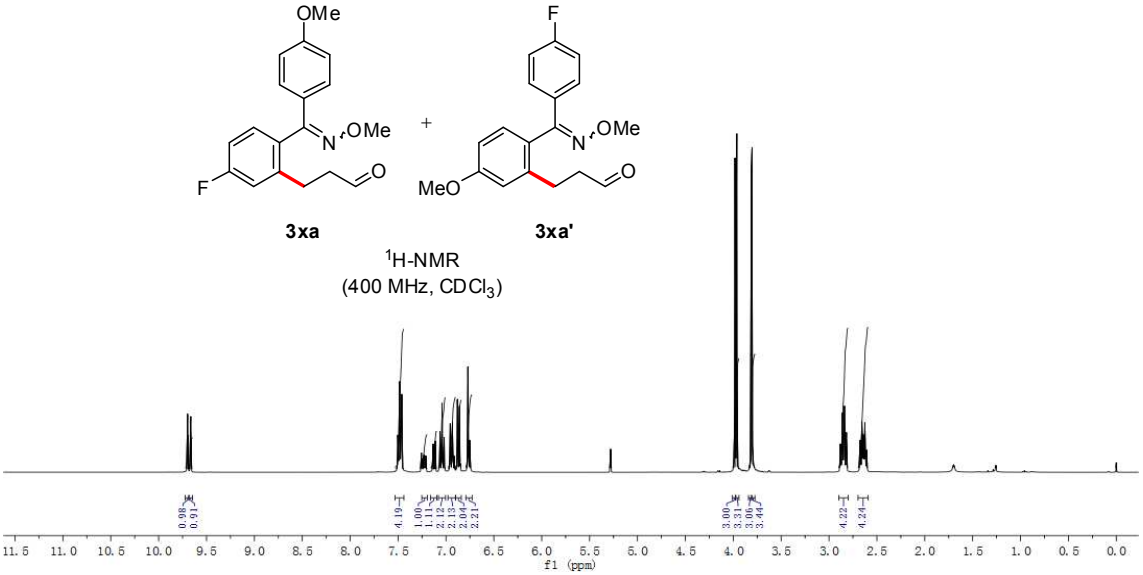


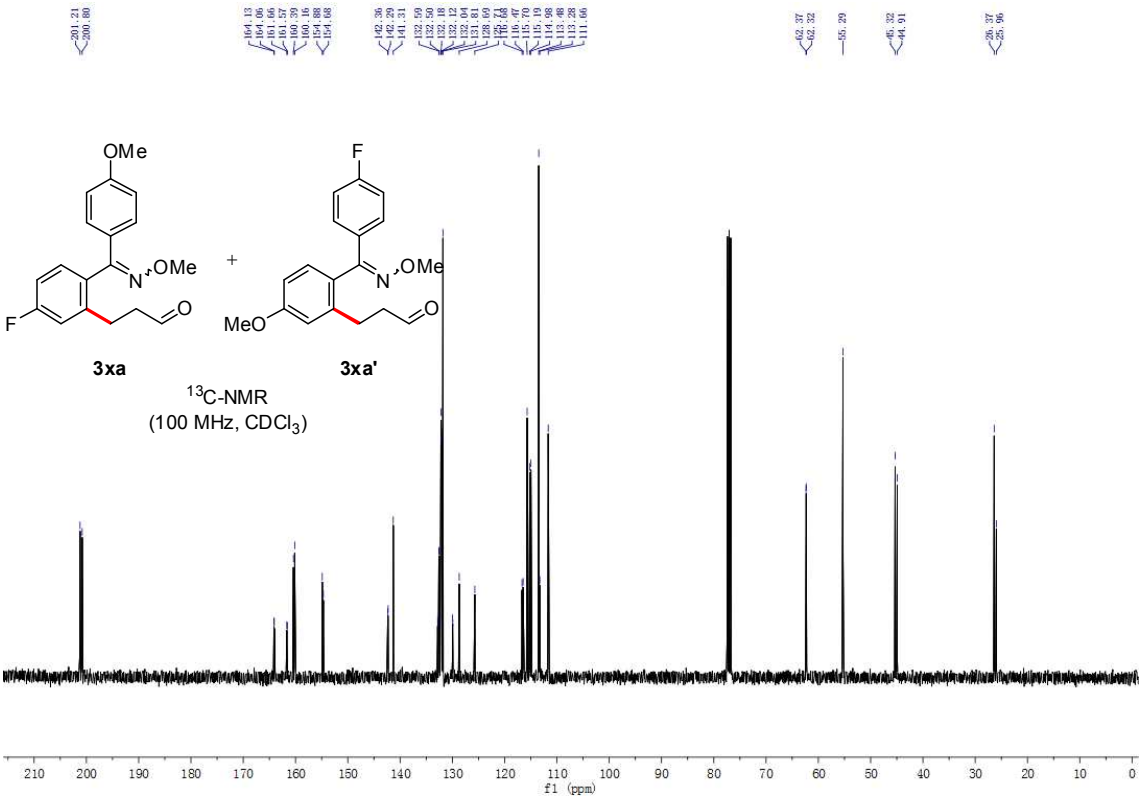
The general procedure was followed using 1-(4-fluorophenyl)ethanone *O*-methyl oxime **1b** (84.0 mg, 0.50 mmol), 1-(4-methoxyphenyl)ethanone *O*-methyl oxime **1h** (90.0 mg, 0.50 mmol) and **2a** (14.0 mg, 0.25 mmol) for 4 h. Purification by column chromatography (*n*-hexane/EtOAc 15:1→8:1) yielded products **3ba** (11 mg, 20%) and **3ha** (41 mg, 70%) as colorless oil, respectively.

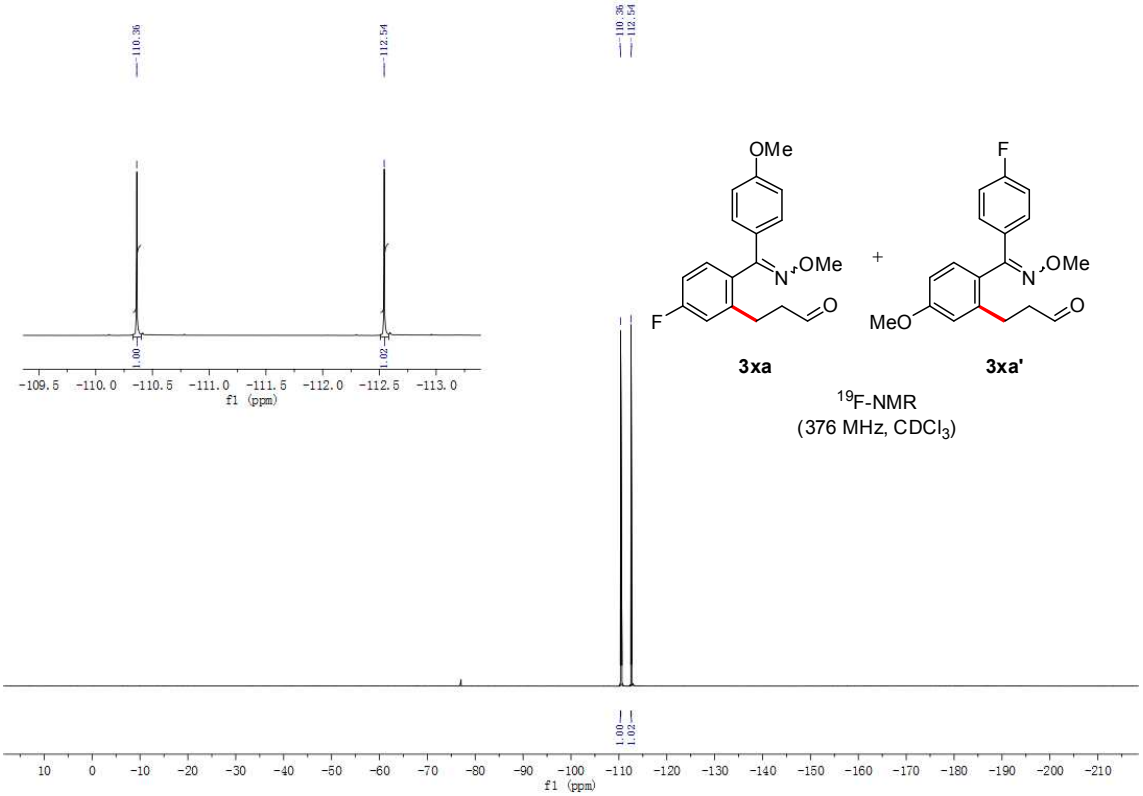
Intramolecular Competition Experiment of 1x



The general procedure was followed using (4-fluorophenyl)(4-methoxyphenyl)methanone *O*-methyl oxime **1x** (65.0 mg, 0.25 mmol) and **2a** (35.0 mg, 0.50 mmol) for 4 h. Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded the mixture of products **3xa** and **3xa'** (55 mg, 69%) as a colorless oil. The ratio of the products was estimated by ^{1}H-NMR and ^{19}F-NMR spectroscopy (**3xa**:**3xa'** 1:1).

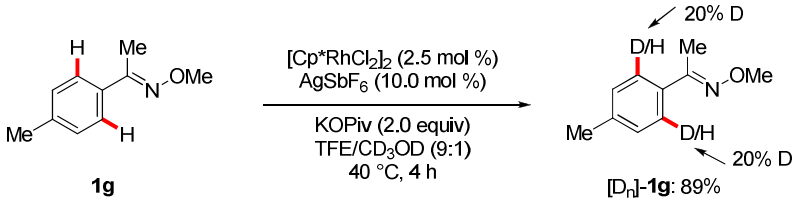

OMe
N
OMe
F
O
+
F
N
OMe
MeO
O
3xa
3xa'
1H-NMR
(400 MHz, CDCl3)
f1 (ppm)


OMe
N
OMe
F
O
+
F
N
OMe
MeO
O
3xa
3xa'
13C-NMR
(100 MHz, CDCl3)
f1 (ppm)

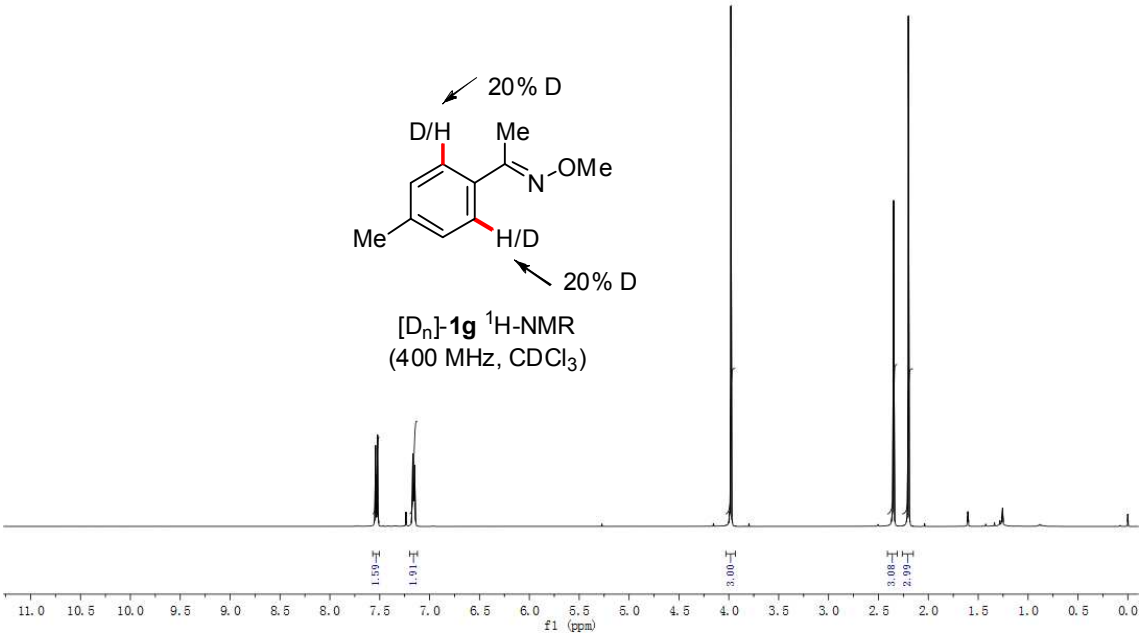

110.36
112.54
1.00
1.02
-109.5 -110.0 -110.5 -111.0 -111.5 -112.0 -112.5 -113.0
f1 (ppm)
OMe
N
OMe
F
O
+
F
N
OMe
MeO
O
3xa
3xa'
^{19}F-NMR
(376 MHz, $CDCl_3$)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

H/D Exchange Experiments:

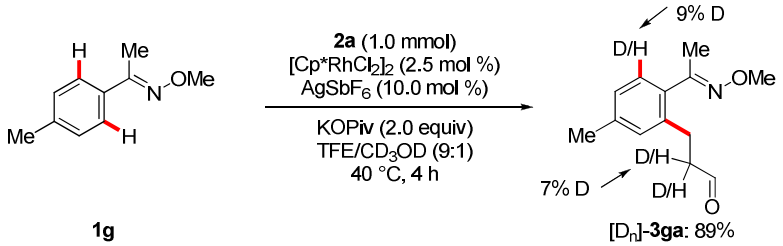
Rhodium(III)-Catalyzed H/D Exchange in Substrate 1g with CD_3OD as the Cosolvent without 2:



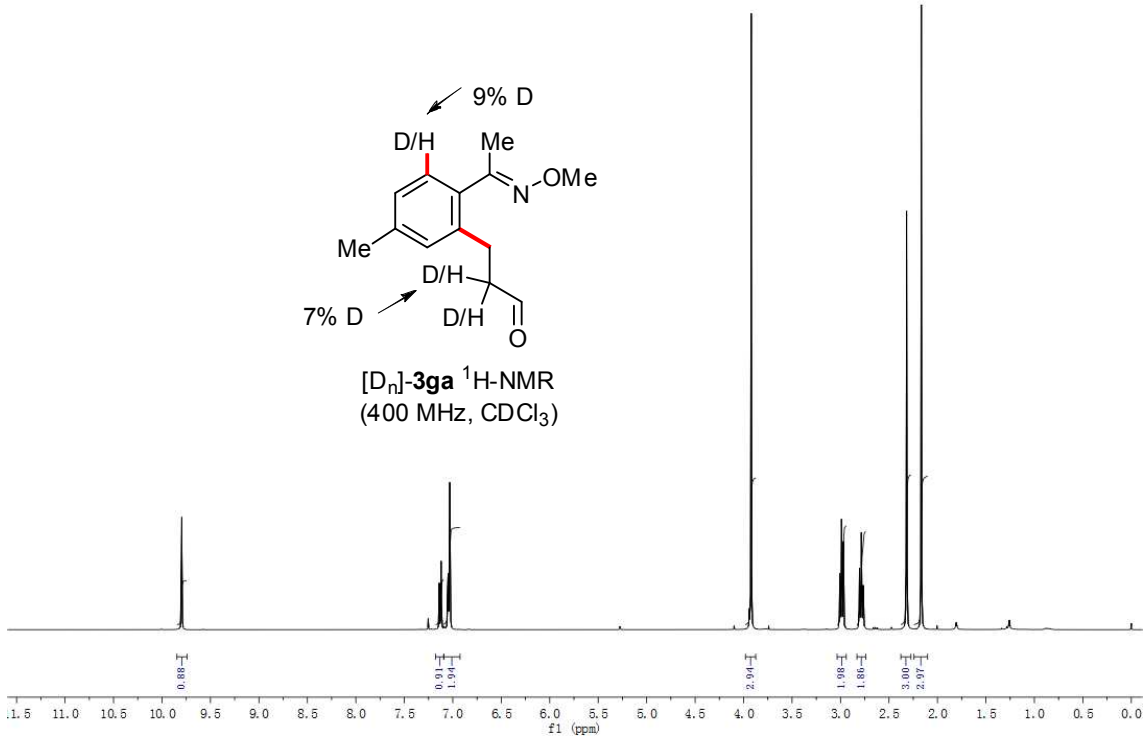
A suspemsion of 1-*p*-tolylethanone *O*-methyl oxime (**1g**) (82.0 mg, 0.50 mmol), $[Cp^*RhCl_2]_2$ (7.7 mg, 2.5 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %), KOPiv (140 mg, 2.0 equiv) in a solvent of mixture of TFE and, CD_3OD (1.8-0.2 mL) was stirred at 40 °C for 4 h under an atmosphere of Ar. At ambient temperature, the solvent was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 15:1) yielded the reisolated starting material $[D_n]$-**1g** (73 mg, 89%) as a colorless oil. The D-incorporation in $[D_n]$-**1g** was estimated by ^{1}H-NMR spectroscopy.



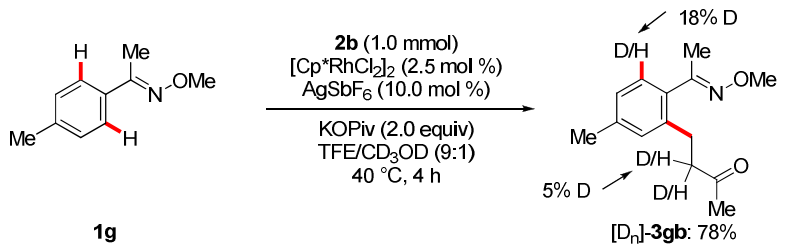
Rhodium(III)-Catalyzed H/D Exchange in Substrate 1g with CD_3OD as the Cosolvent with 2a:



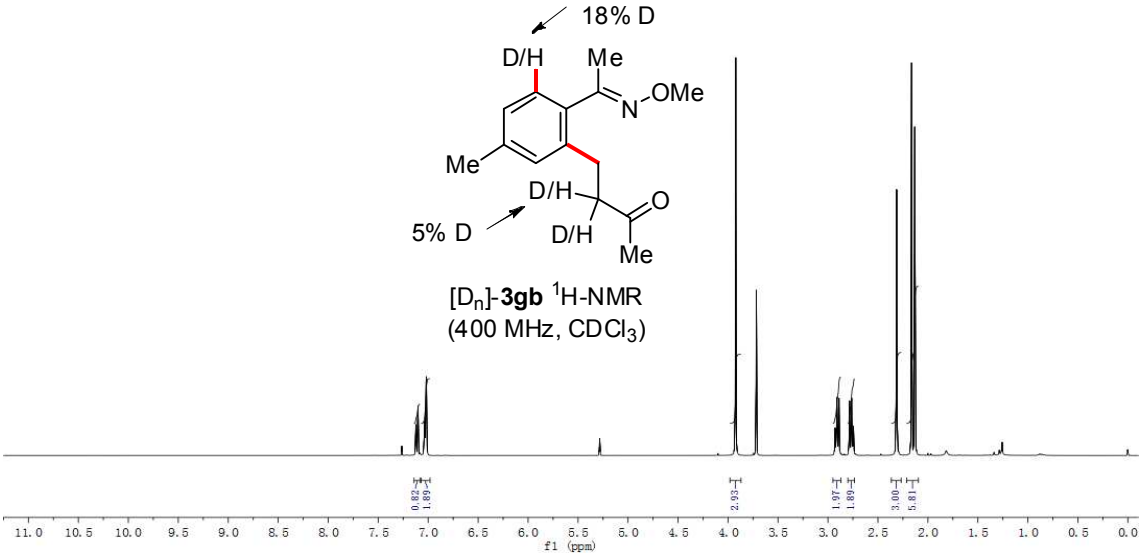
A suspemsion of 1-*p*-tolylethanone *O*-methyl oxime (**1g**) (41.0 mg, 0.25 mmol), $[Cp^*RhCl_2]_2$ (3.9 mg, 2.5 mol %), **2a** (28.0 mg, 0.5 mmol), $AgSbF_6$ (8.6 mg, 10.0 mol %), KOPiv (70.0 mg, 2.0 equiv) in a solvent of mixture of TFE and, CD_3OD (0.9-0.1 mL) was stirred at 40 °C for 4 h under an atmosphere of Ar. At ambient temperature, the solvent was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) yielded the product $[D_n]$-**3ga** (49 mg, 89%) as a colorless oil. The D-incorporation in $[D_n]$-**3ga** was estimated by ^{1}H-NMR spectroscopy.



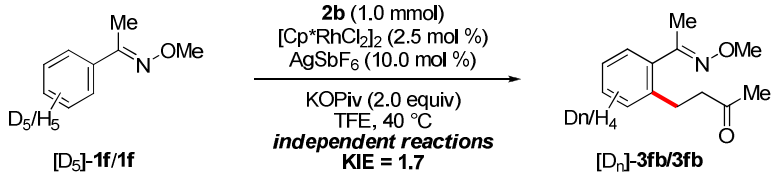
Rhodium(III)-Catalyzed H/D Exchange in Substrate 1g with CD_3OD as the Cosolvent with 2b:



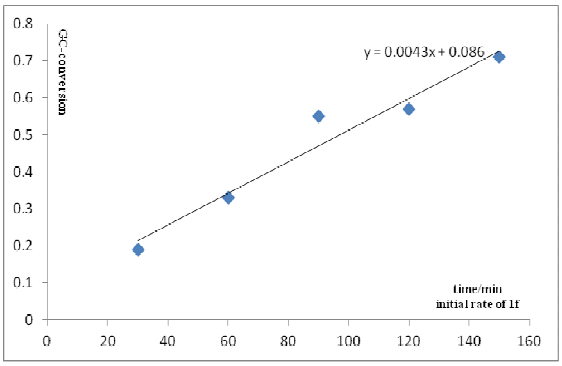
A suspemsion of 1-*p*-tolylethanone *O*-methyl oxime (**1g**) (41.0 mg, 0.25 mmol), $[Cp^*RhCl_2]_2$ (3.9 mg, 2.5 mol %), **2b** (35.0 mg, 0.5 mmol), $AgSbF_6$ (8.6 mg, 10.0 mol %), KOPiv (70.0 mg, 2.0 equiv) in a solvent of mixture of TFE and, CD_3OD (0.9-0.1 mL) was stirred at 40 °C for 4 h under an atmosphere of Ar. At ambient temperature, the solvent was evaporated *in vacuo* and the remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) yielded the product $[D_n]$-**3gb** (46 mg, 78%) as a colorless oil. The D-incorporation in $[D_n]$-**3gb** was estimated by ^{1}H-NMR spectroscopy.

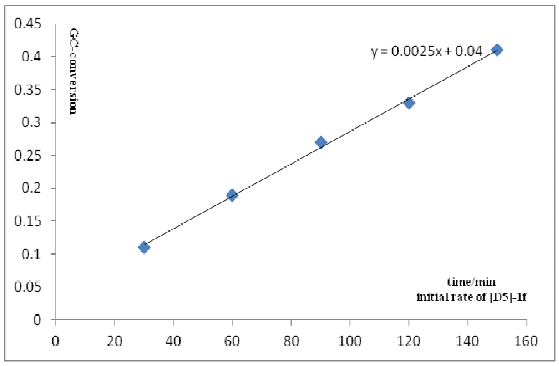


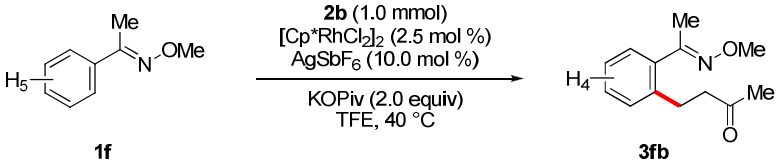
Kinetic Isotope Effect



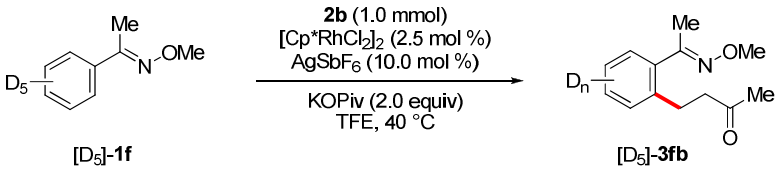
Two independent reactions with **1f** or deuterated substrate [D_5]-**1f** under the standard conditions were performed: Suspensions of MVK (**2b**) (70 mg, 1.0 mmol), substrates **1f** (75 mg, 0.5 mmol) or [D_5]-**1a** (77 mg, 0.5 mmol), [Cp*$RhCl_2$]$_2$ (7.7 mg, 2.5 mol %), $AgSbF_6$ (17.2 mg, 10.0 mol %) and KOPiv (140 mg, 2.0 equiv) in TFE (2.0 mL) were stirred at 40 °C for 0.5 h, 1.5 h, 2.0 h, 2.5 h, 3.5 h under an atmosphere of argon, respectively. The consumption of substrate **1f** or [D_5]-**1f** and the appearance of the products **3fb** or [D_n]-**3fb** were monitored by GC analysis. These experiments indicated that the C–H bond activation is not the turnover-limiting step of the rhodium(III)-catalyzed C–H alkylation reaction.





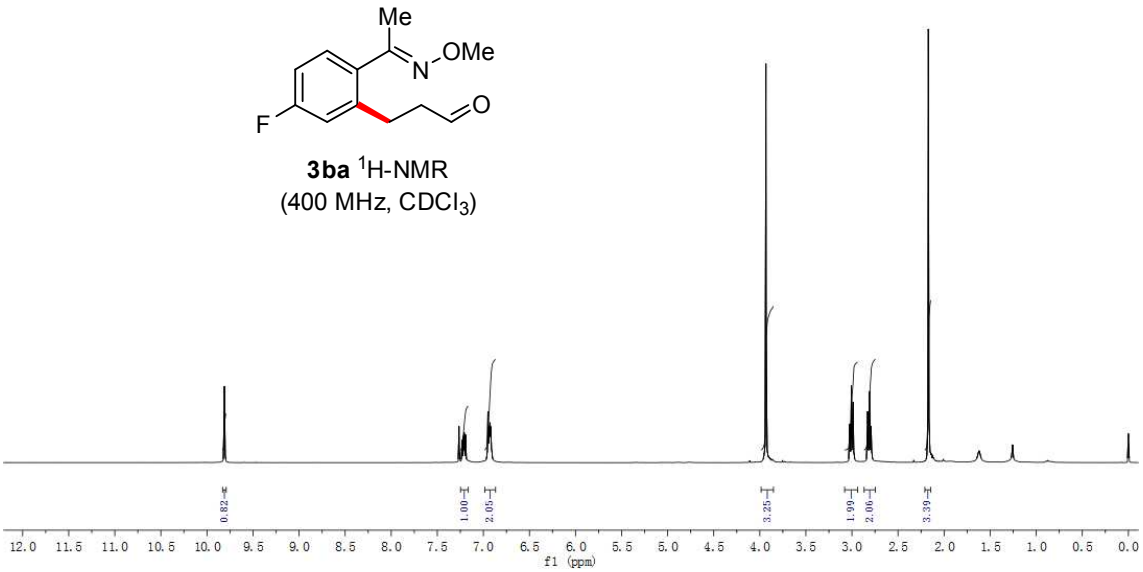


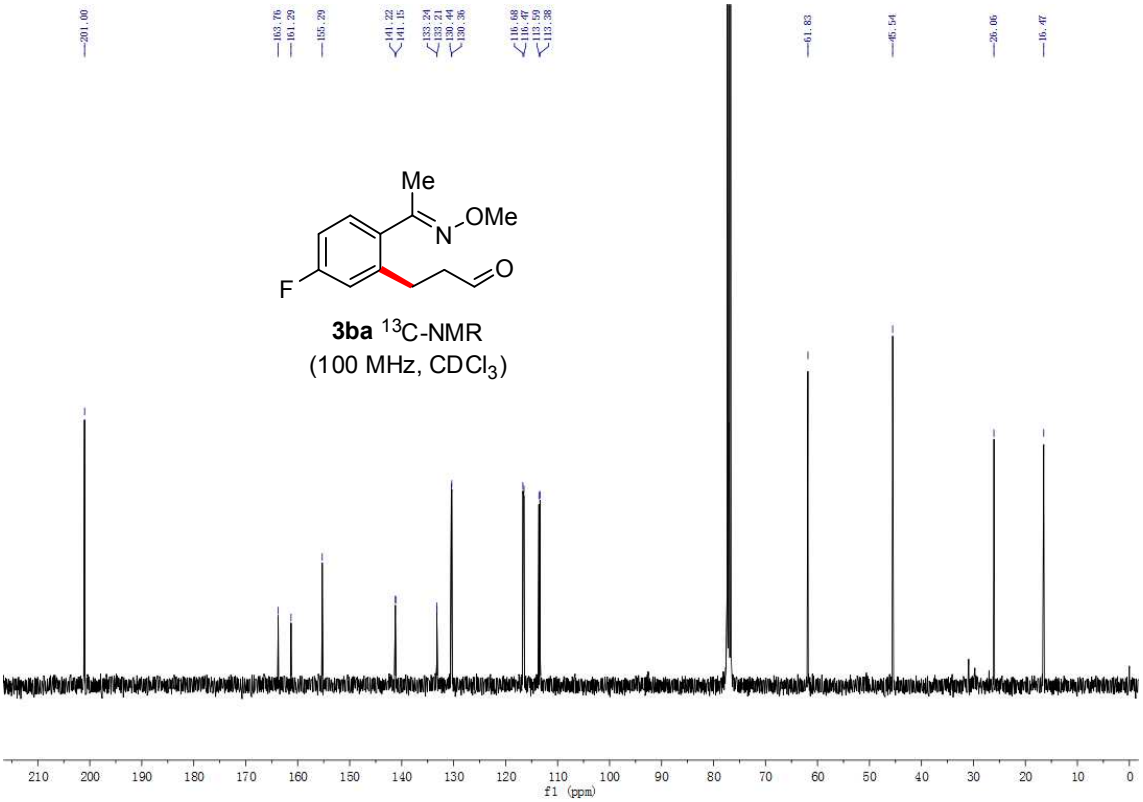
t/(h)	0.5	1.0	1.5	2.0	2.5
3fb	0.19	0.33	0.55	0.57	0.71
1f	0.81	0.67	0.45	0.43	0.29

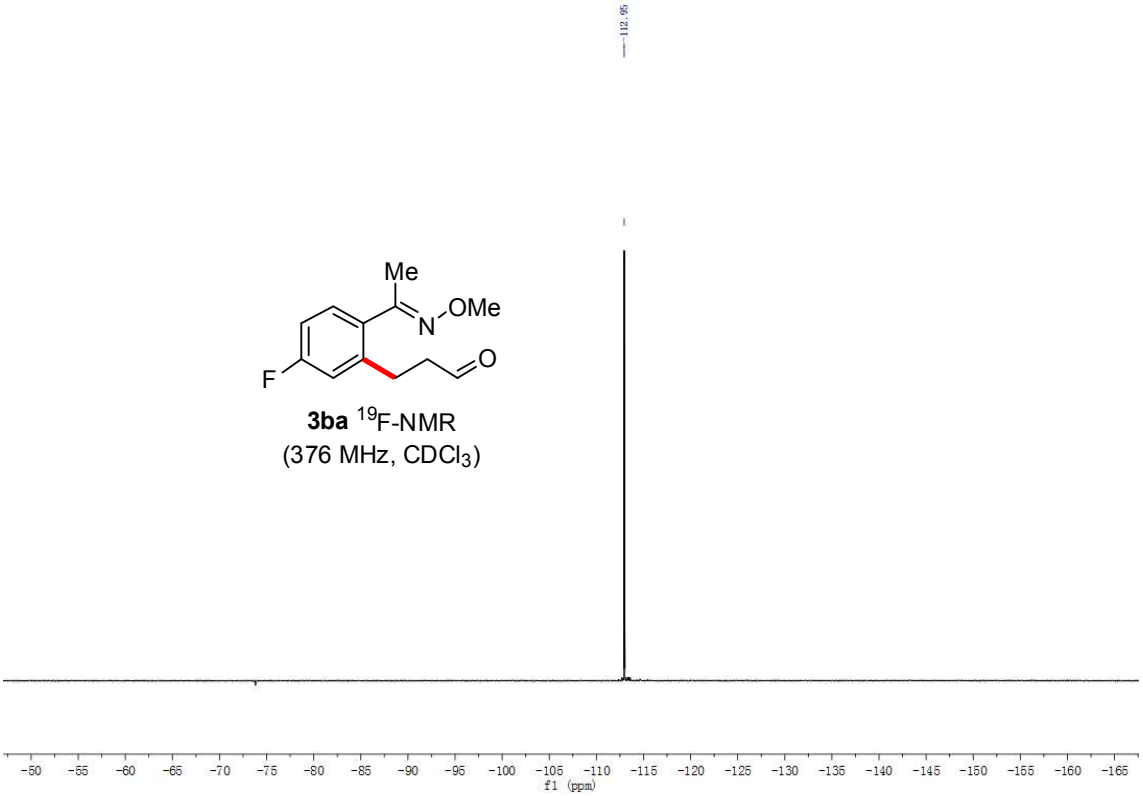


t/(h)	0.5	1.0	1.5	2.0	2.5
[D_n]-**3fb**	0.11	0.19	0.27	0.33	0.41
[D_5]-**1f**	0.89	0.81	0.73	0.77	0.59

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3ba**

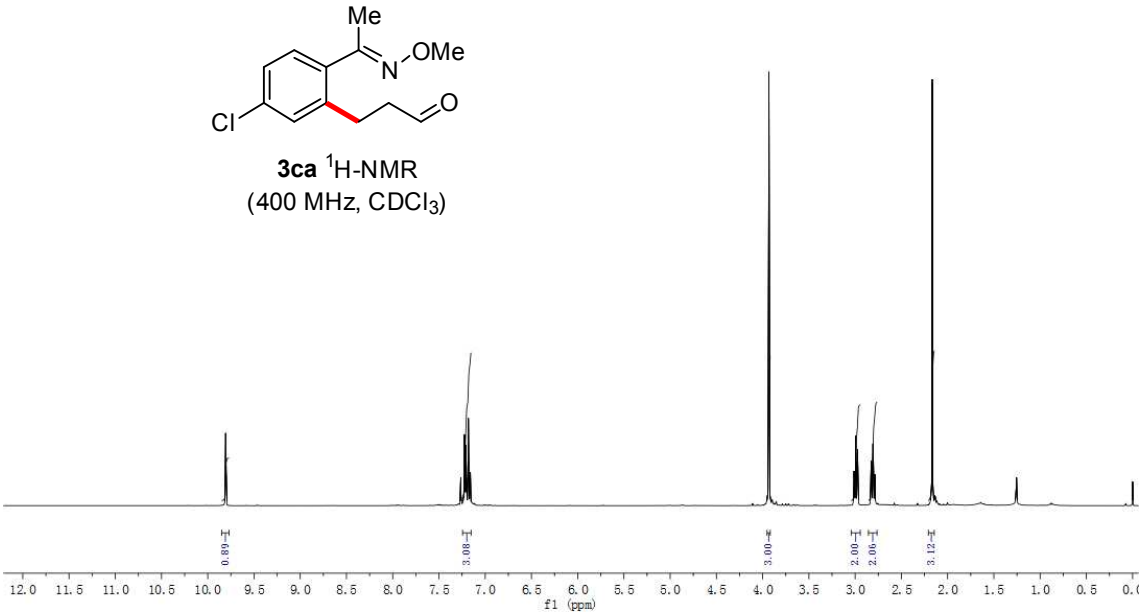


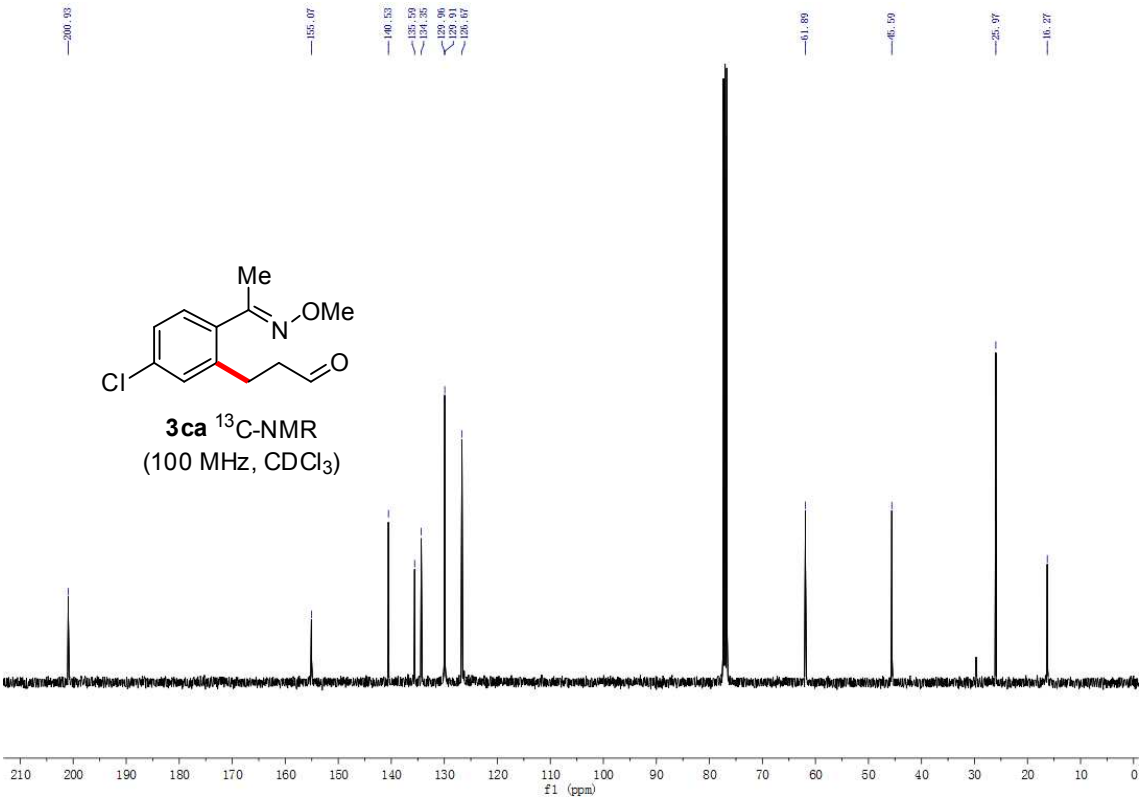




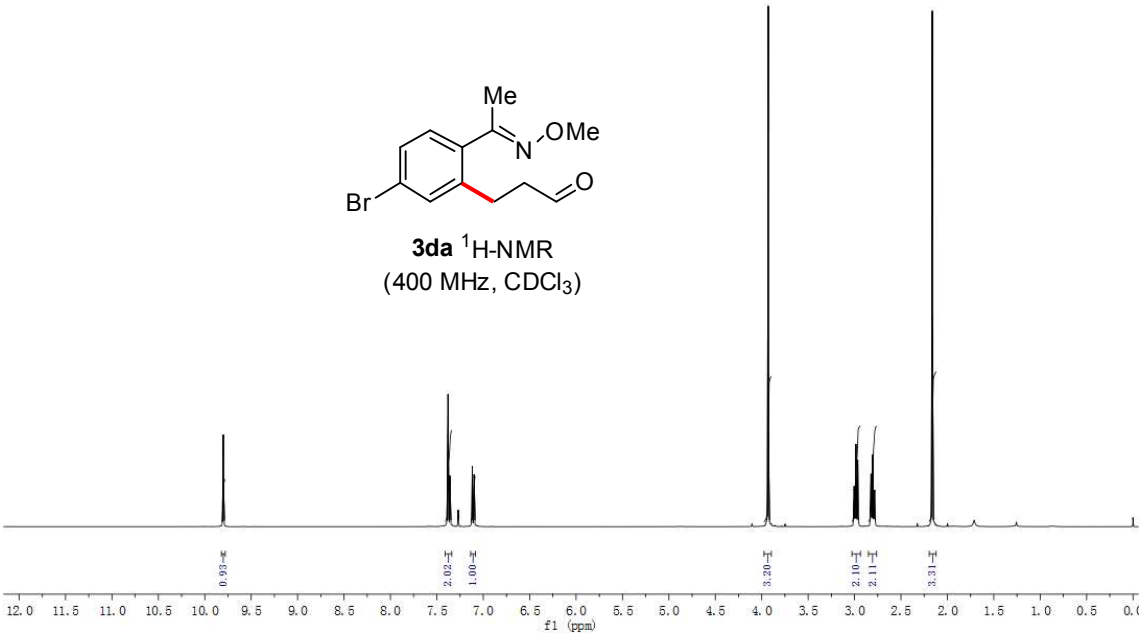
3ba ^{19}F-NMR
(376 MHz, $CDCl_3$)

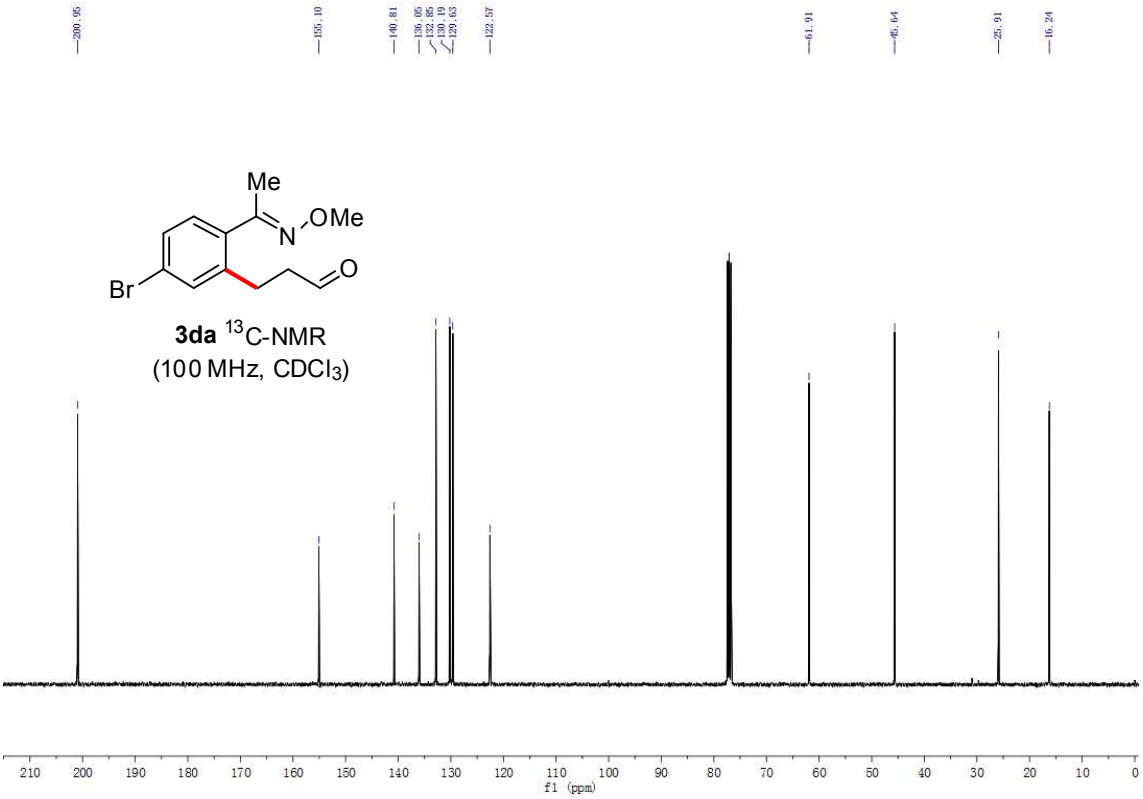
^{1}H NMR and ^{13}C NMR spectra of **3ca**



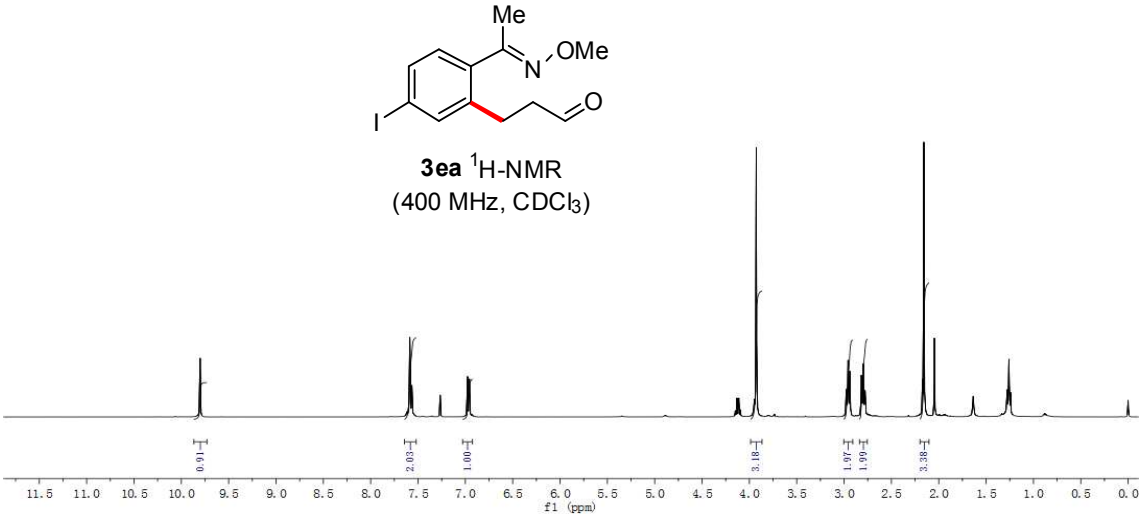


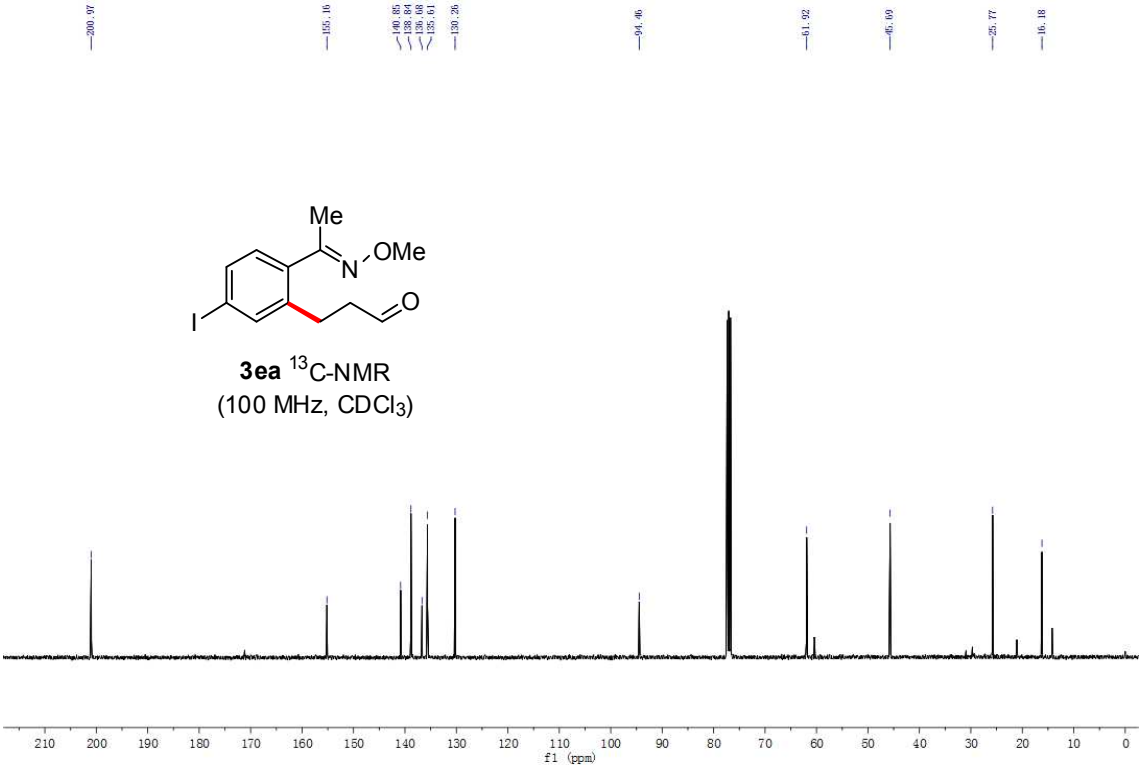
^{1}H NMR and ^{13}C NMR spectra of **3da**



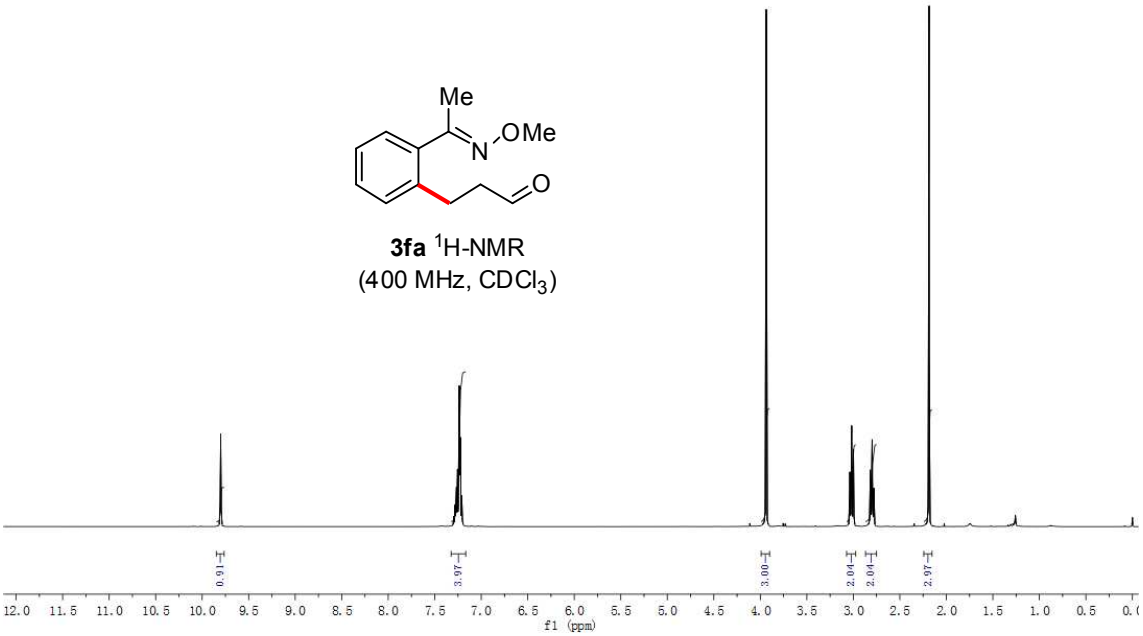


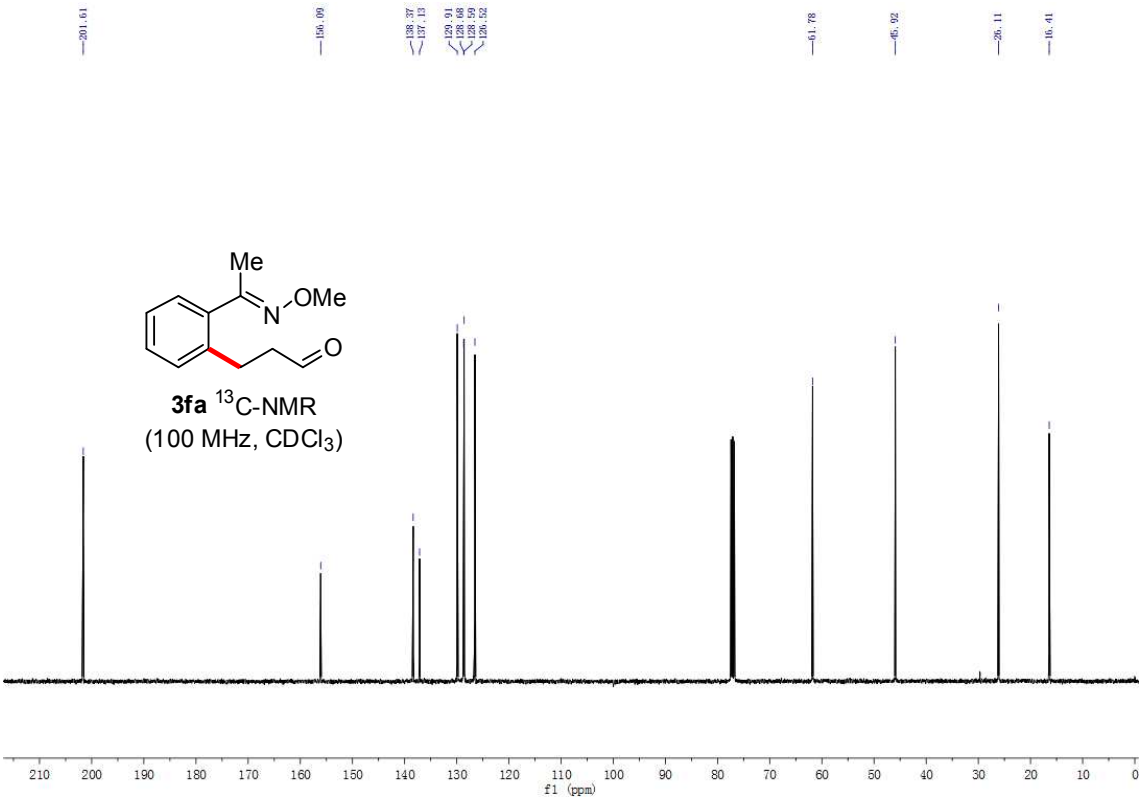
^{1}H NMR and ^{13}C NMR spectra of **3ea**



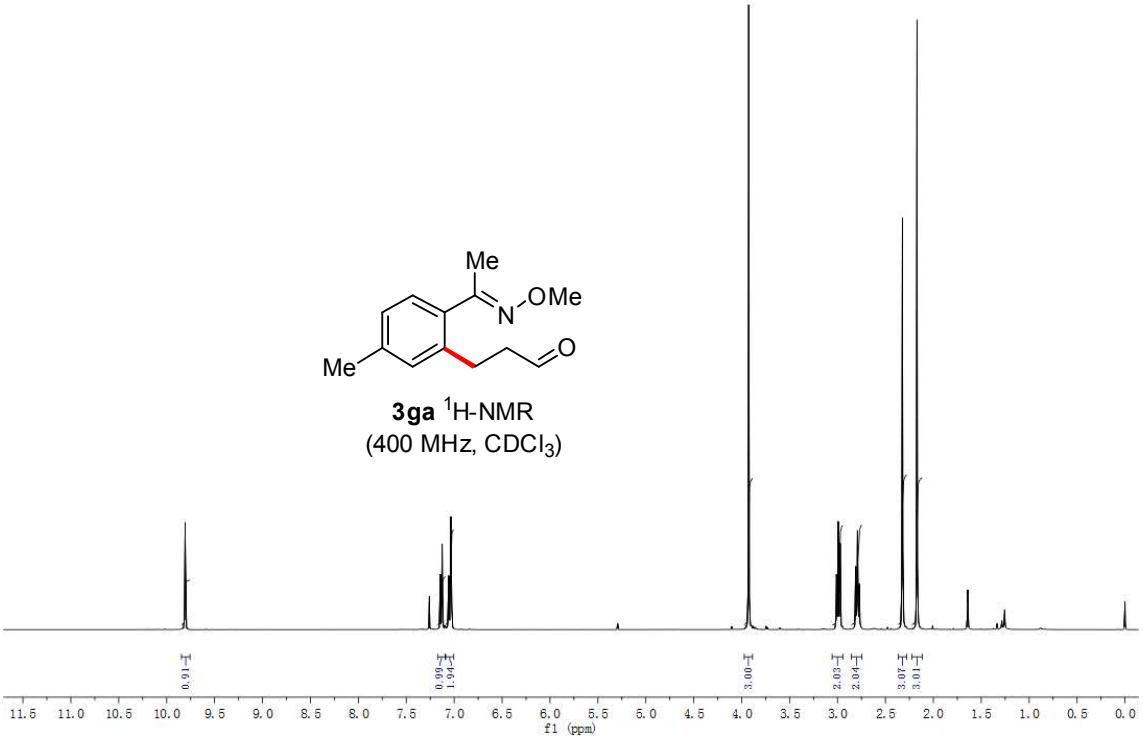


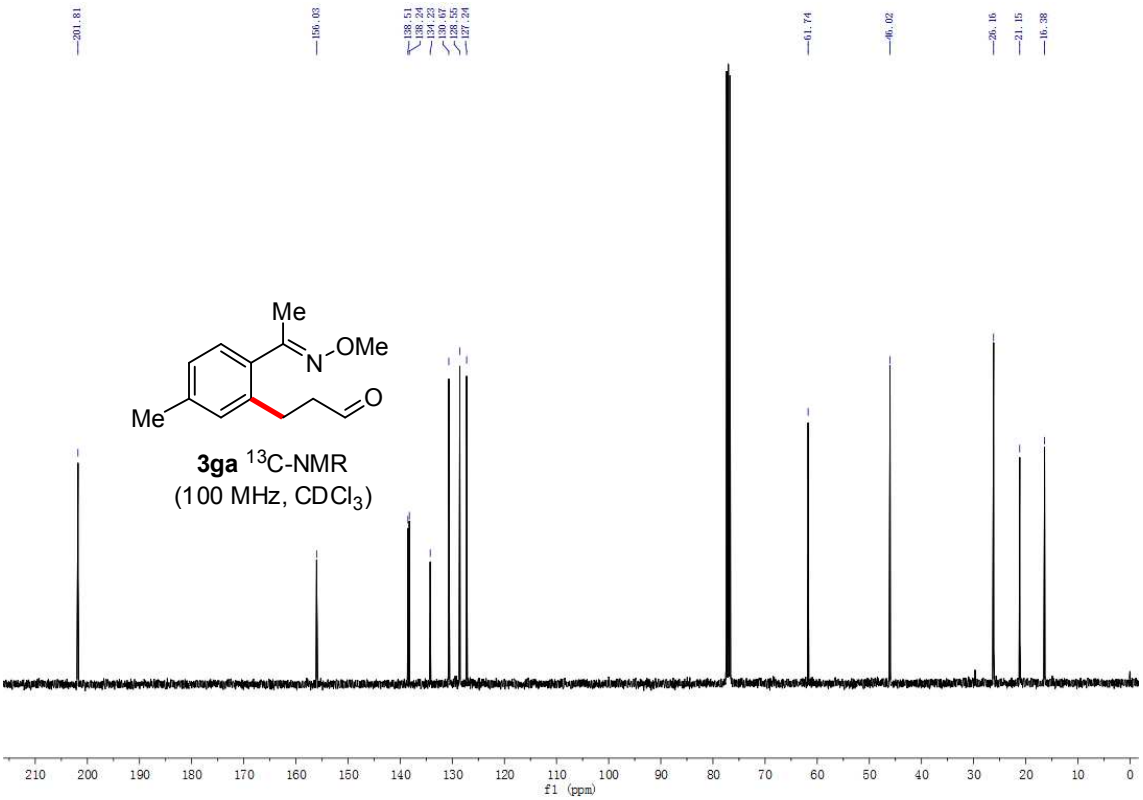
^{1}H NMR and ^{13}C NMR spectra of **3fa**



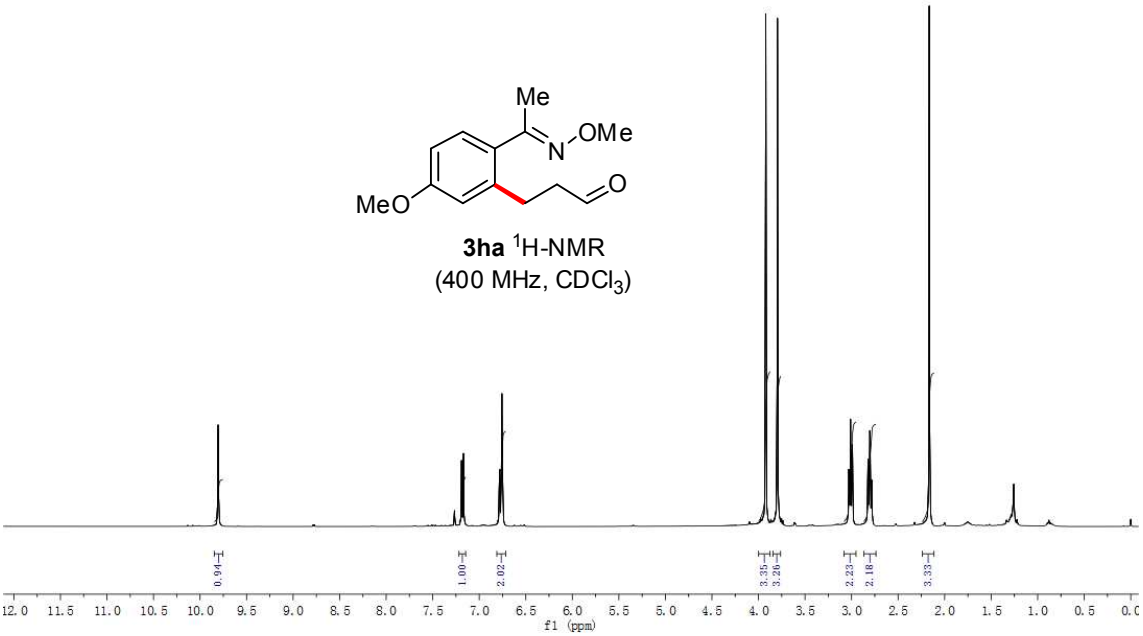


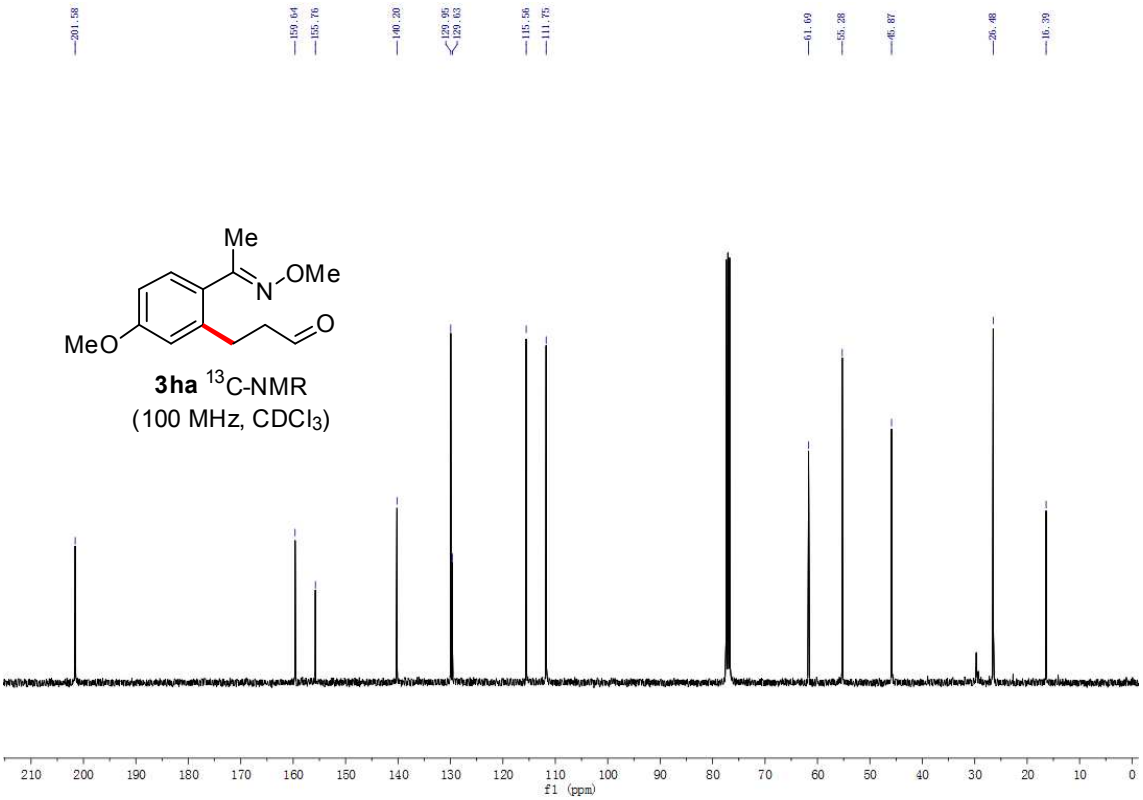
^{1}H NMR and ^{13}C NMR spectra of **3ga**



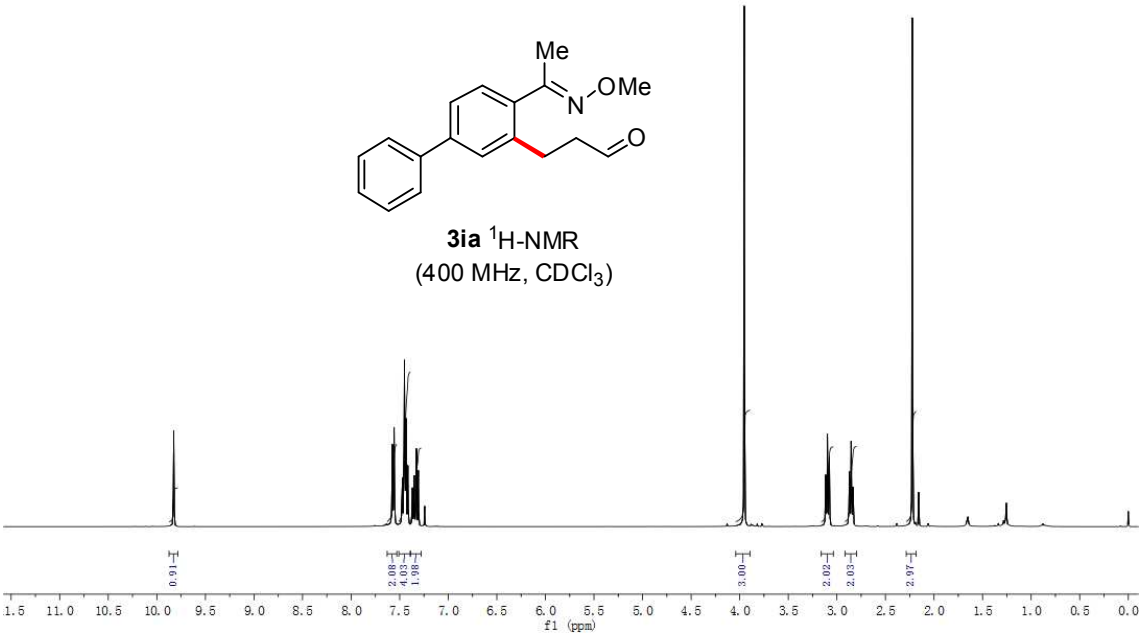


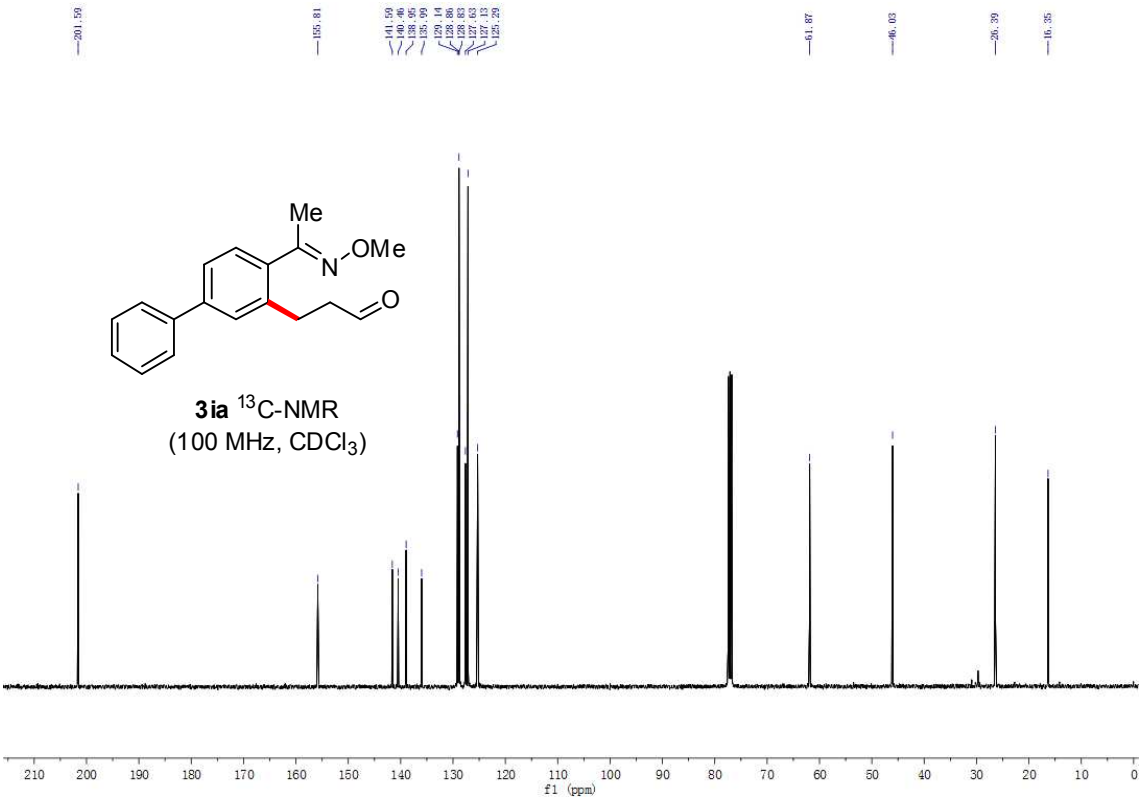
^{1}H NMR and ^{13}C NMR spectra of **3ha**



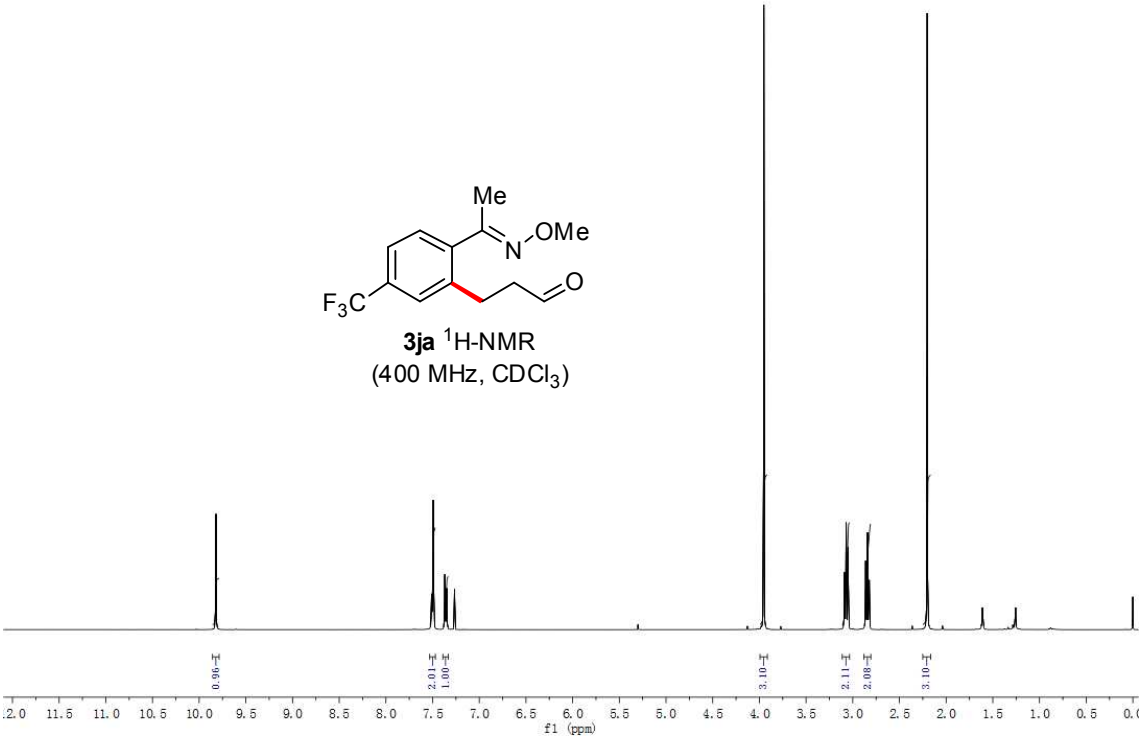


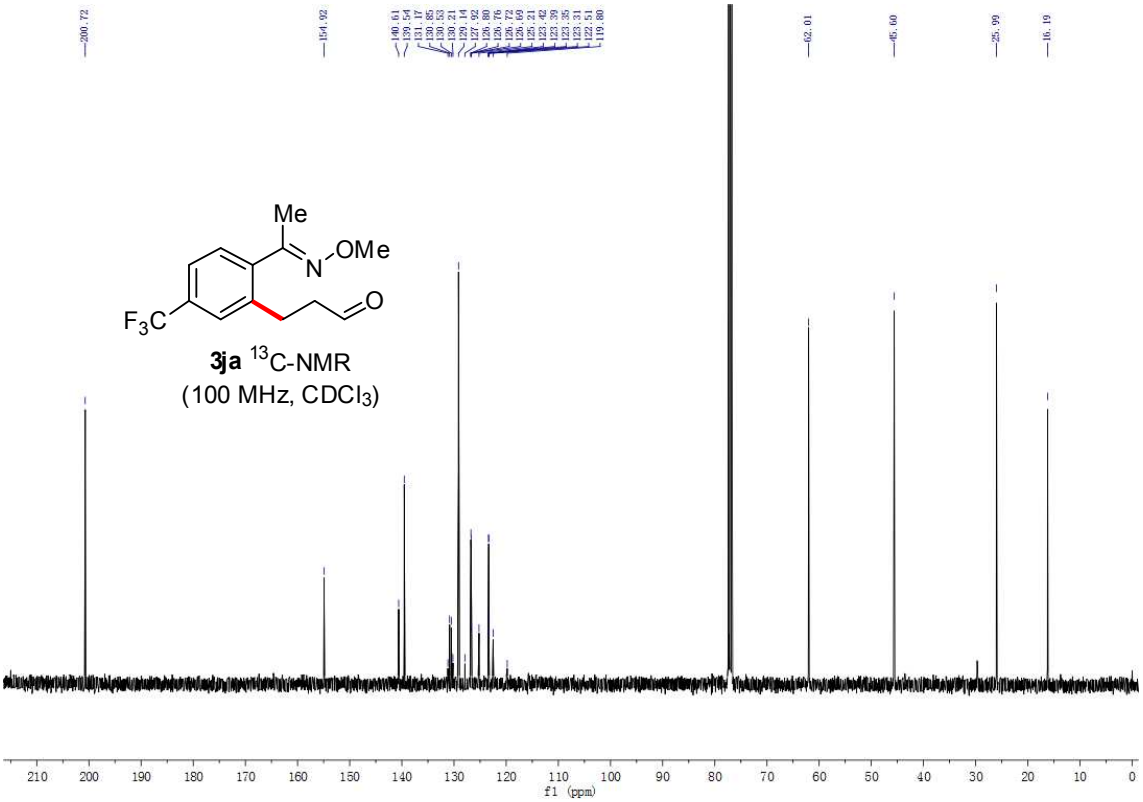
^{1}H NMR and ^{13}C NMR spectra of **3ia**



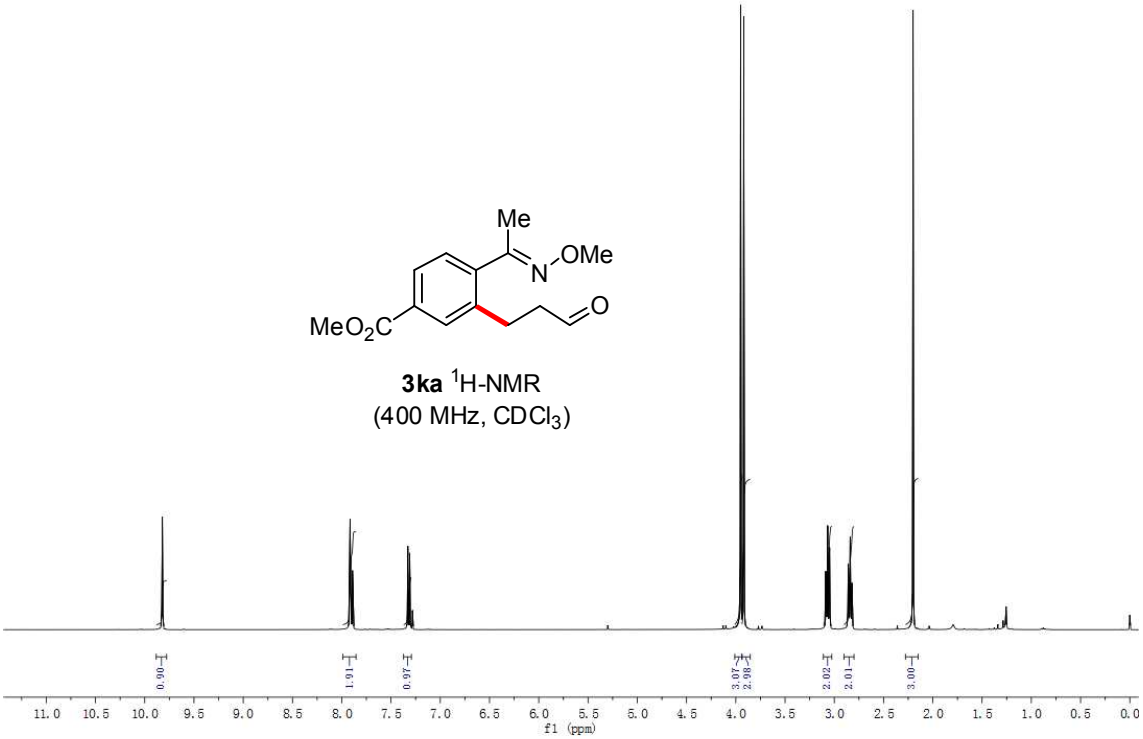


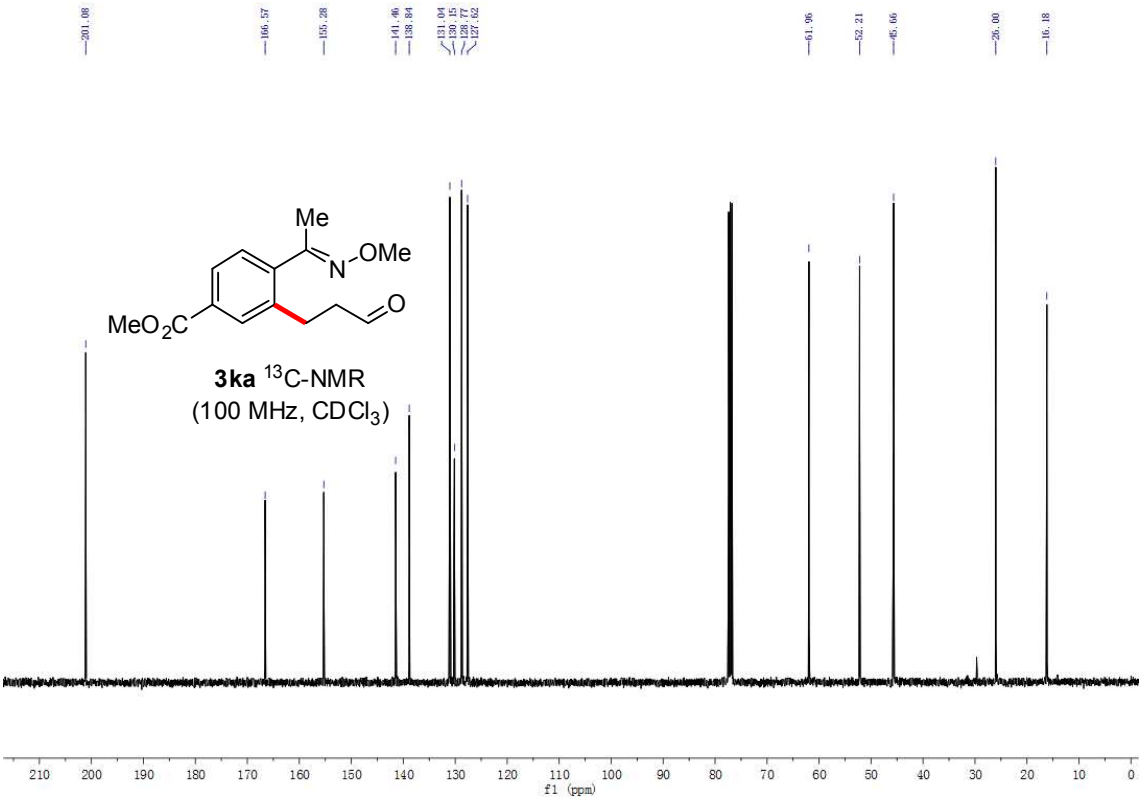
^{1}H NMR and ^{13}C NMR spectra of **3ja**



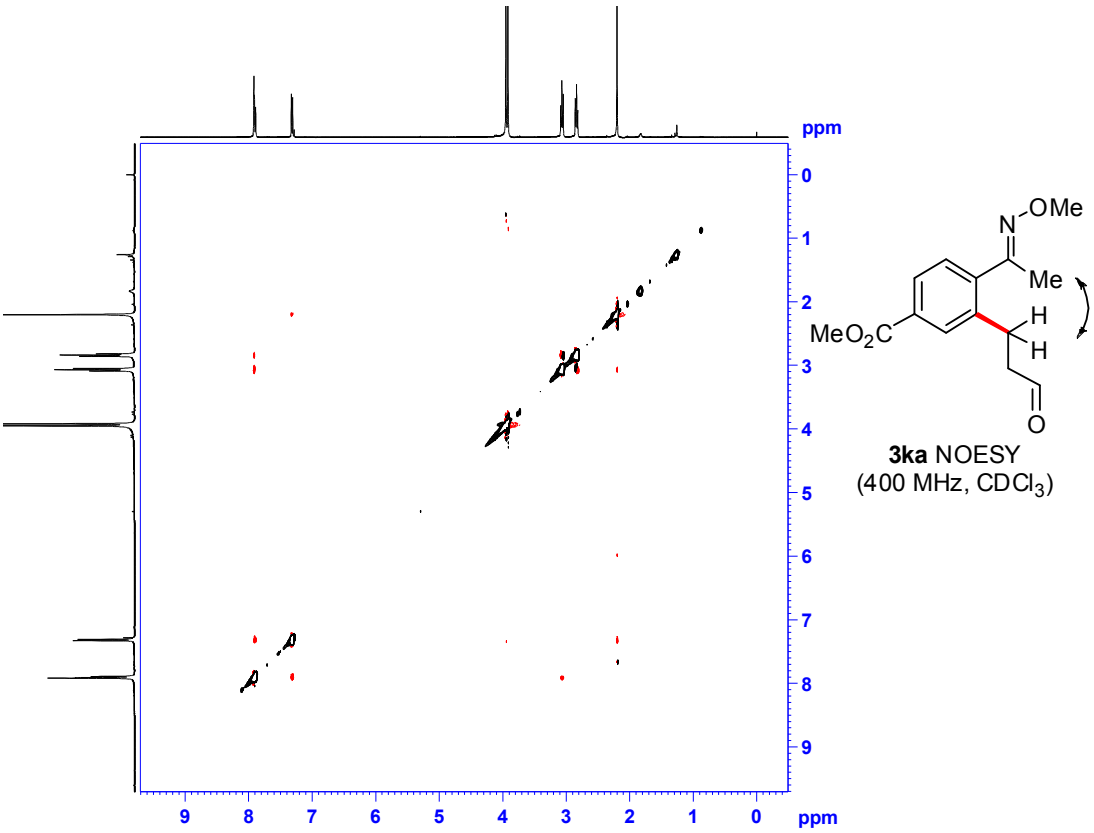


^{1}H NMR and ^{13}C NMR spectra of **3ka**

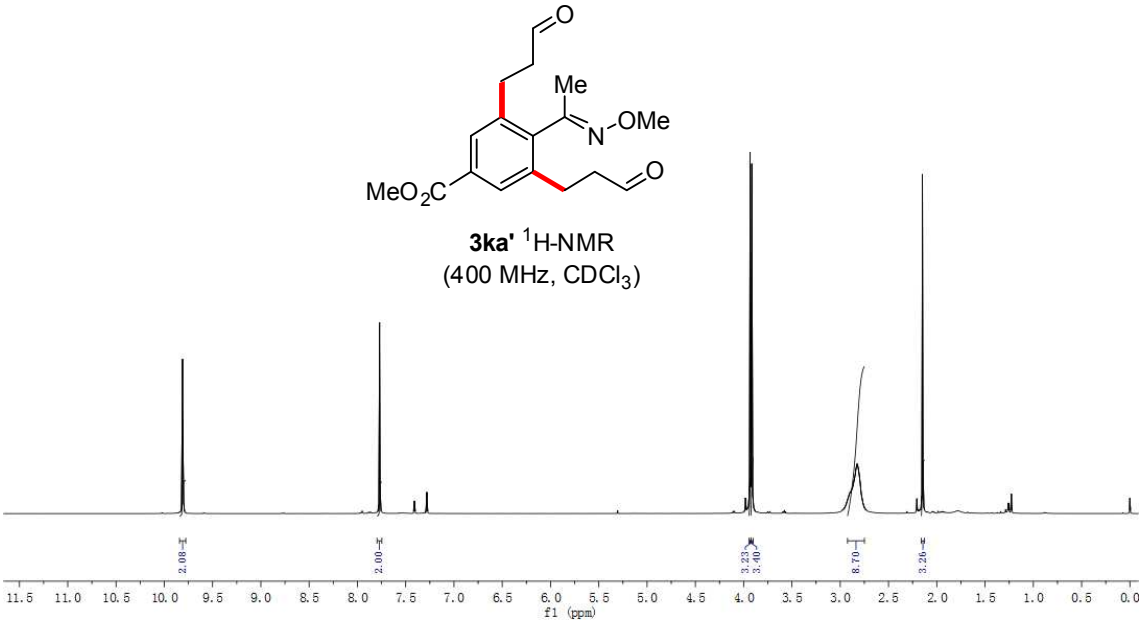


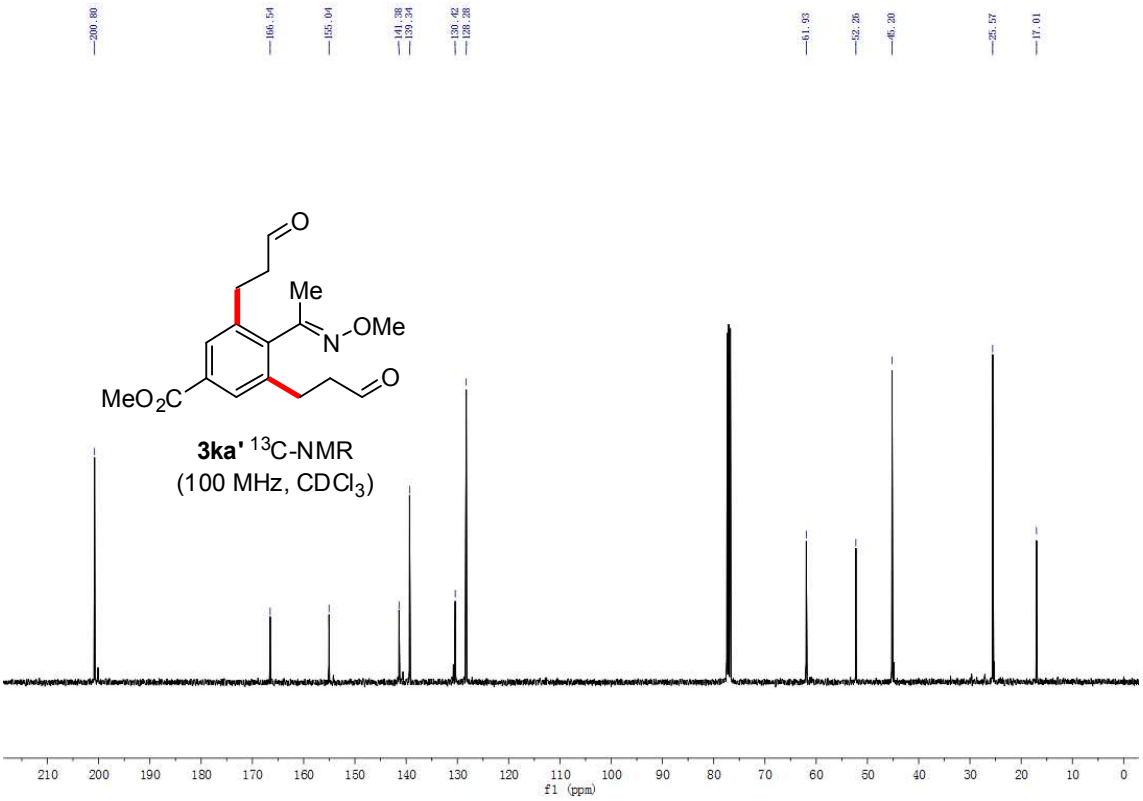


NOESY spectrum of **3ka**

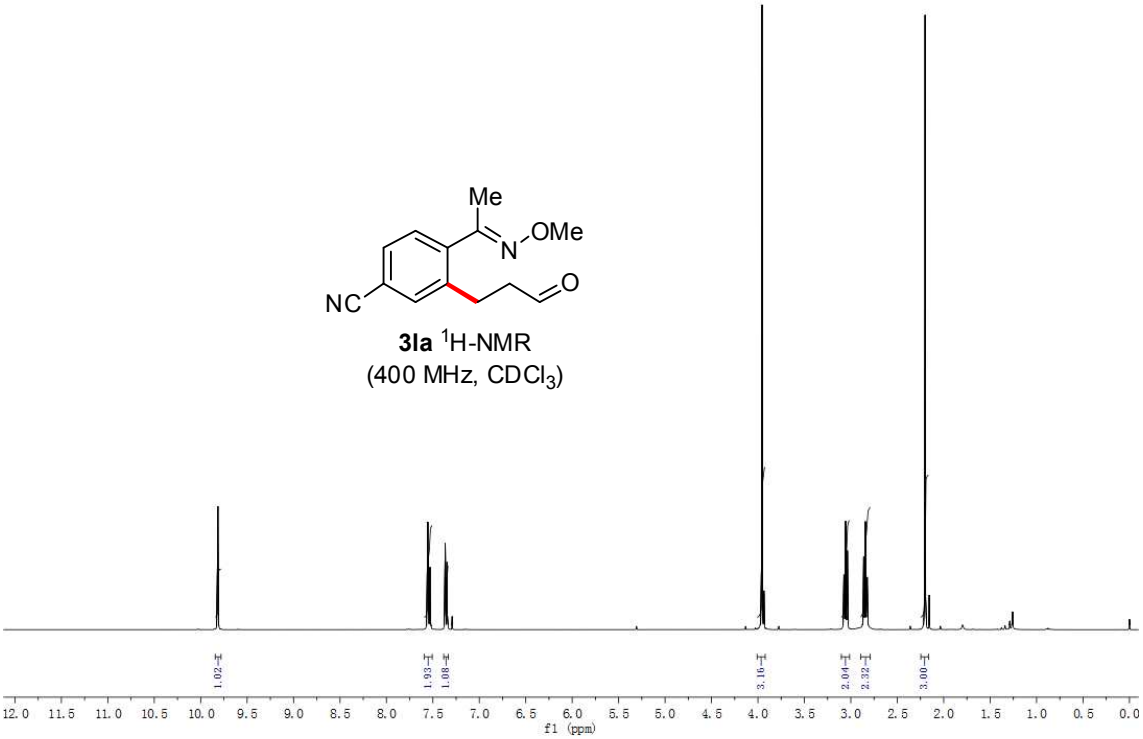


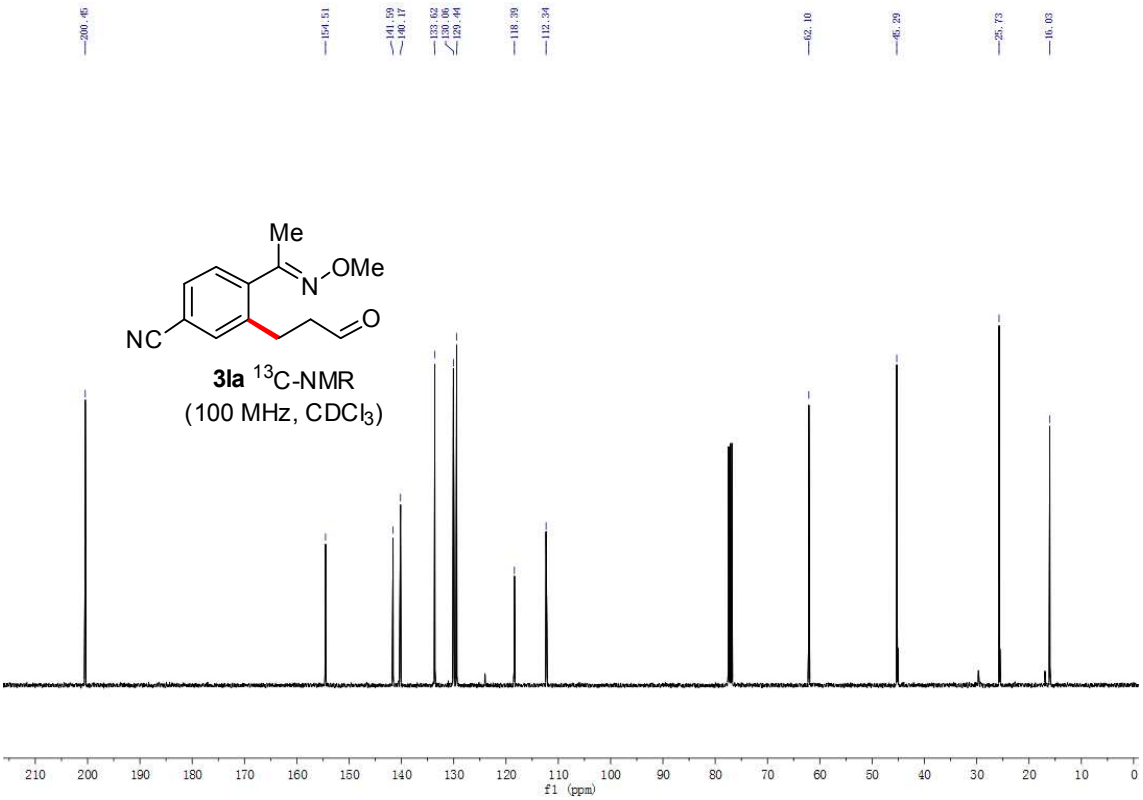
^{1}H NMR and ^{13}C NMR spectra of **3ka'**



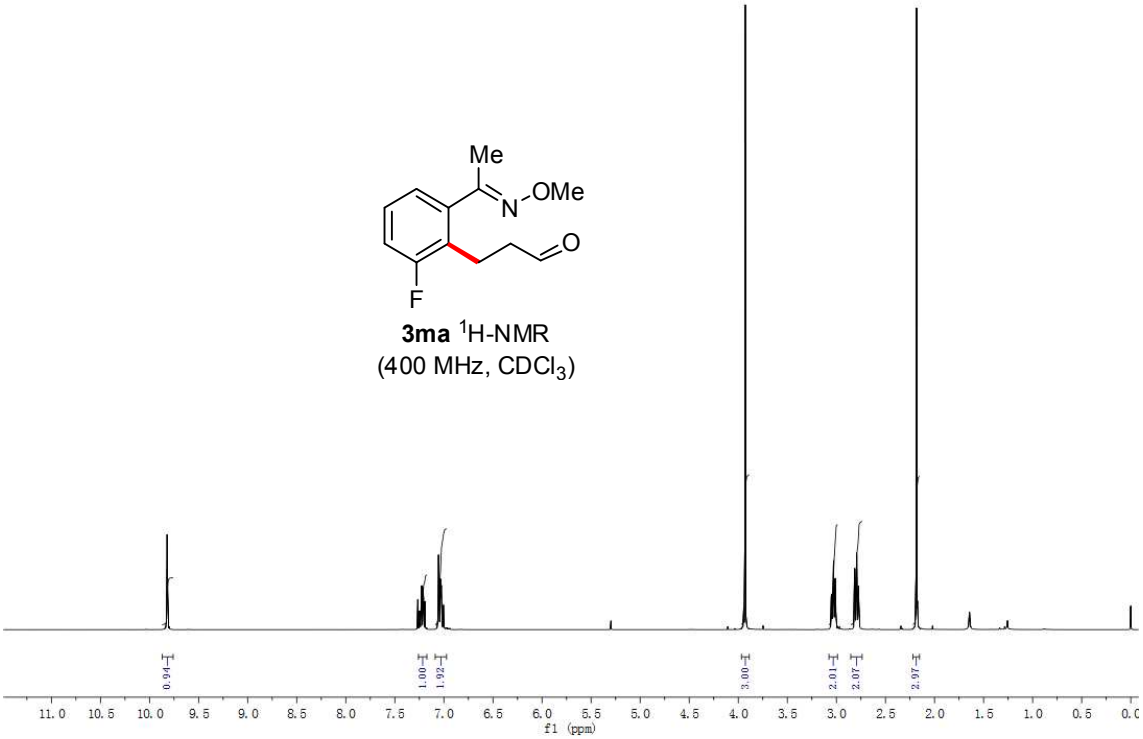


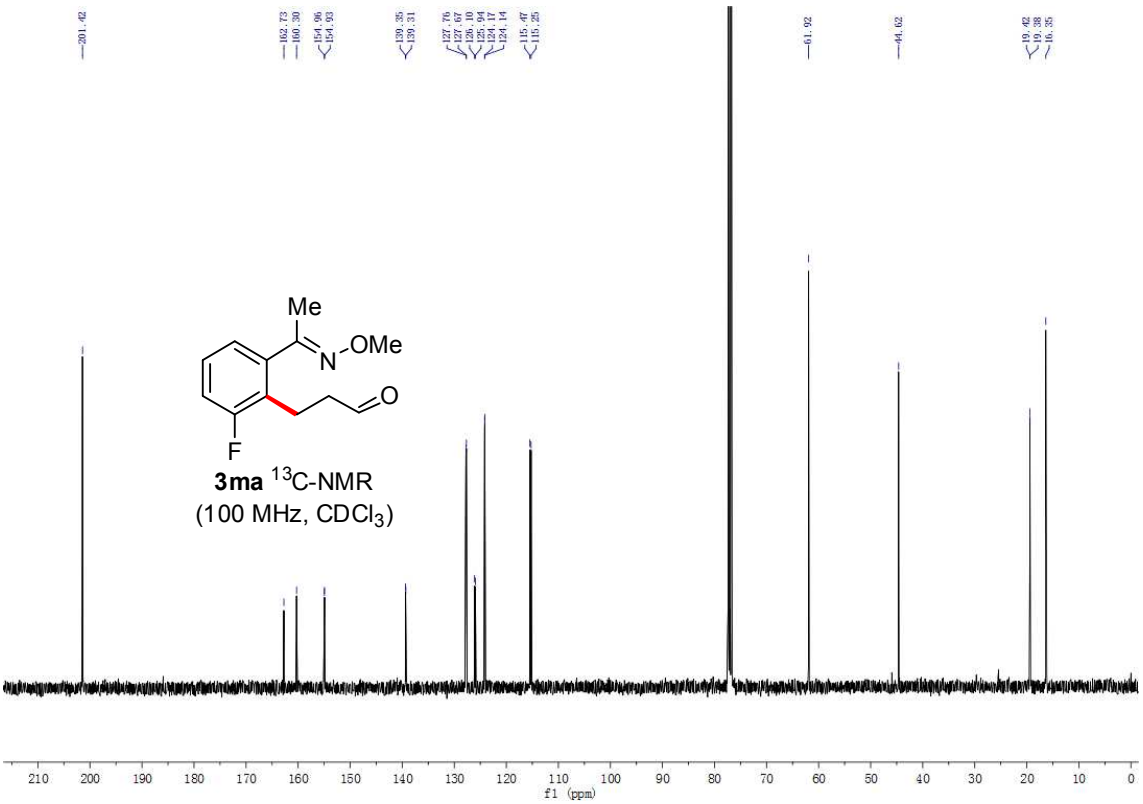
^{1}H NMR and ^{13}C NMR spectra of **3la**

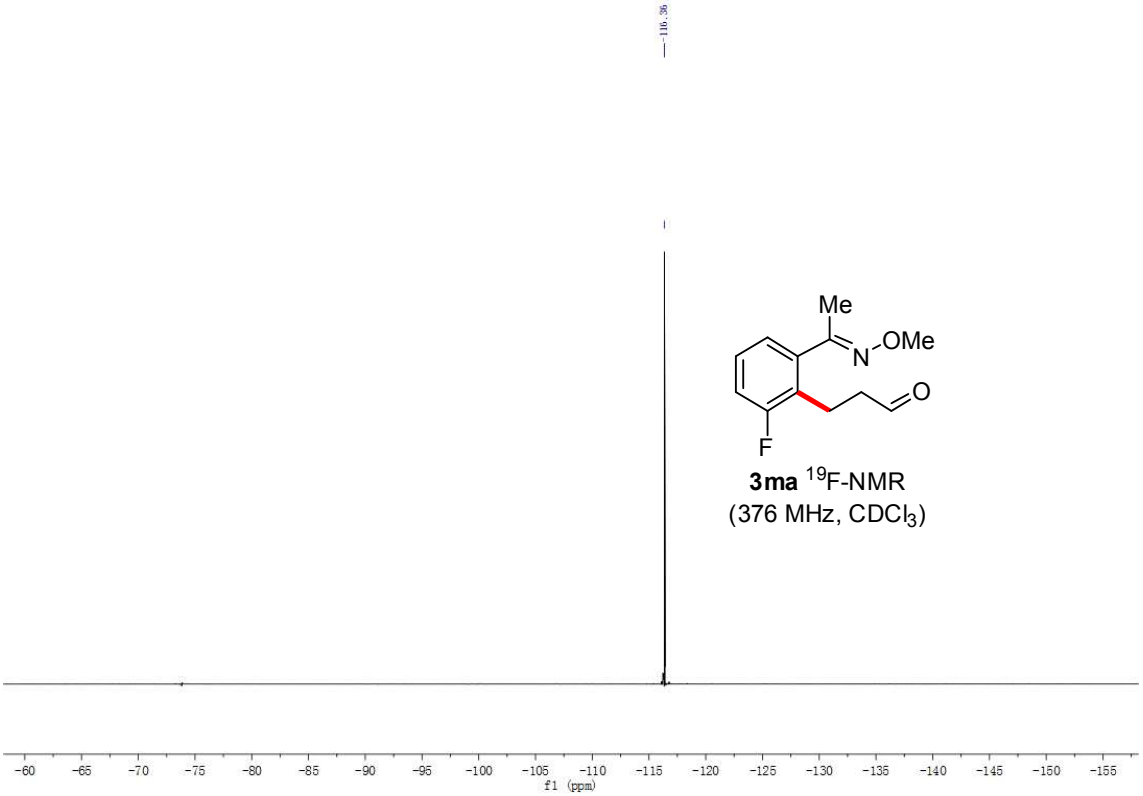




^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3ma**

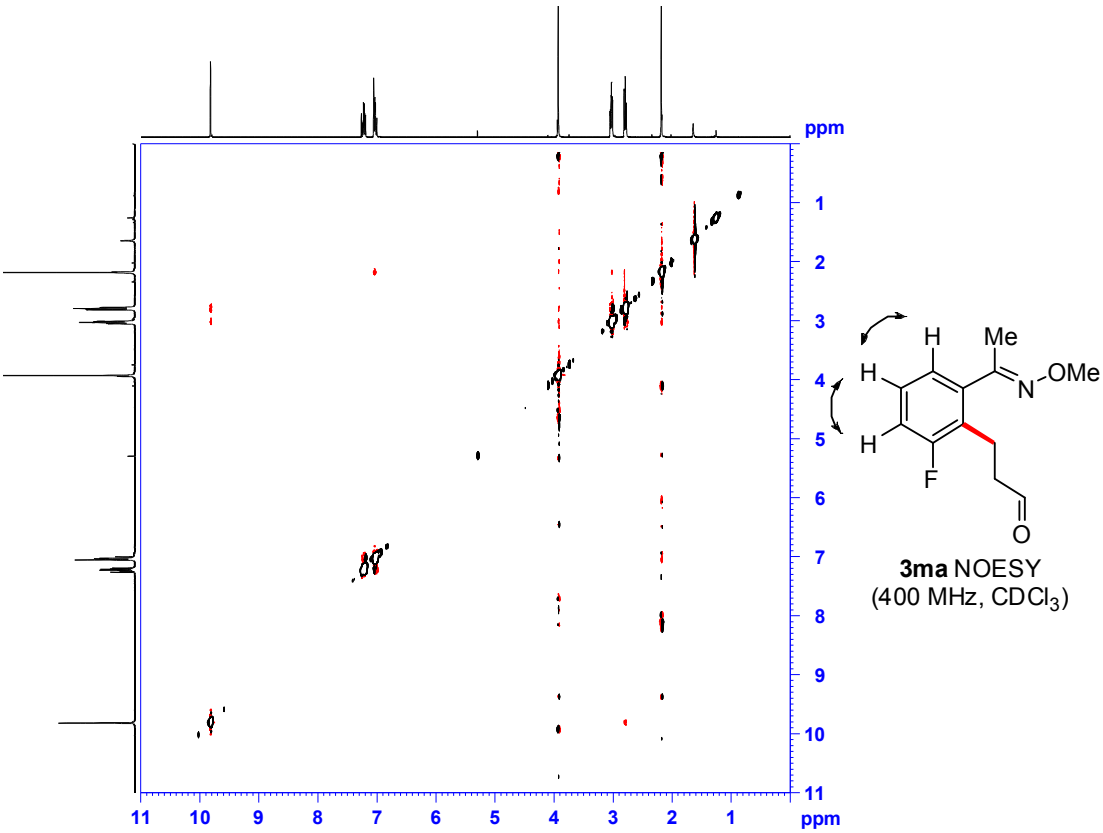




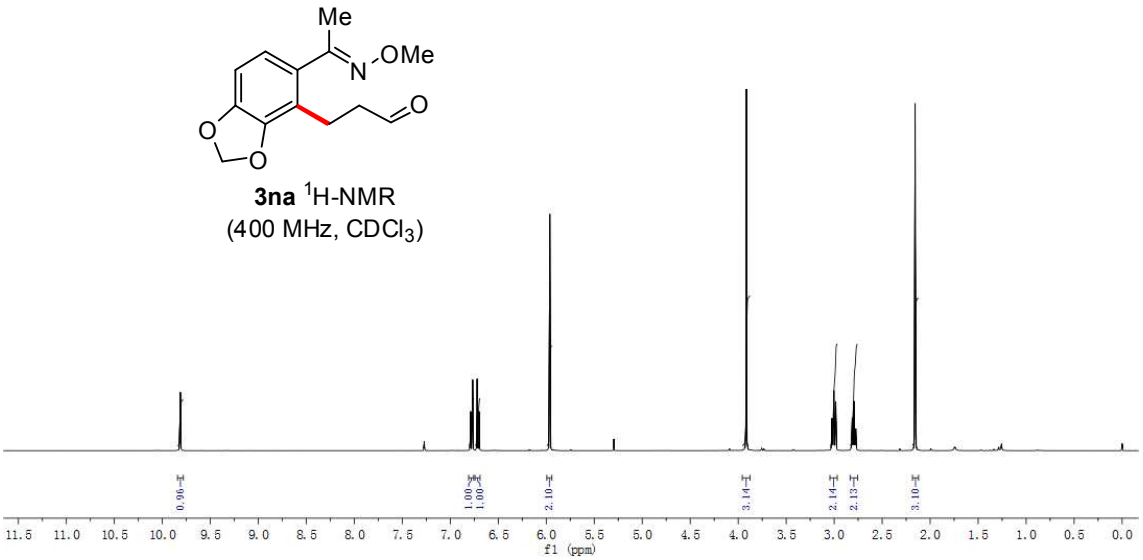


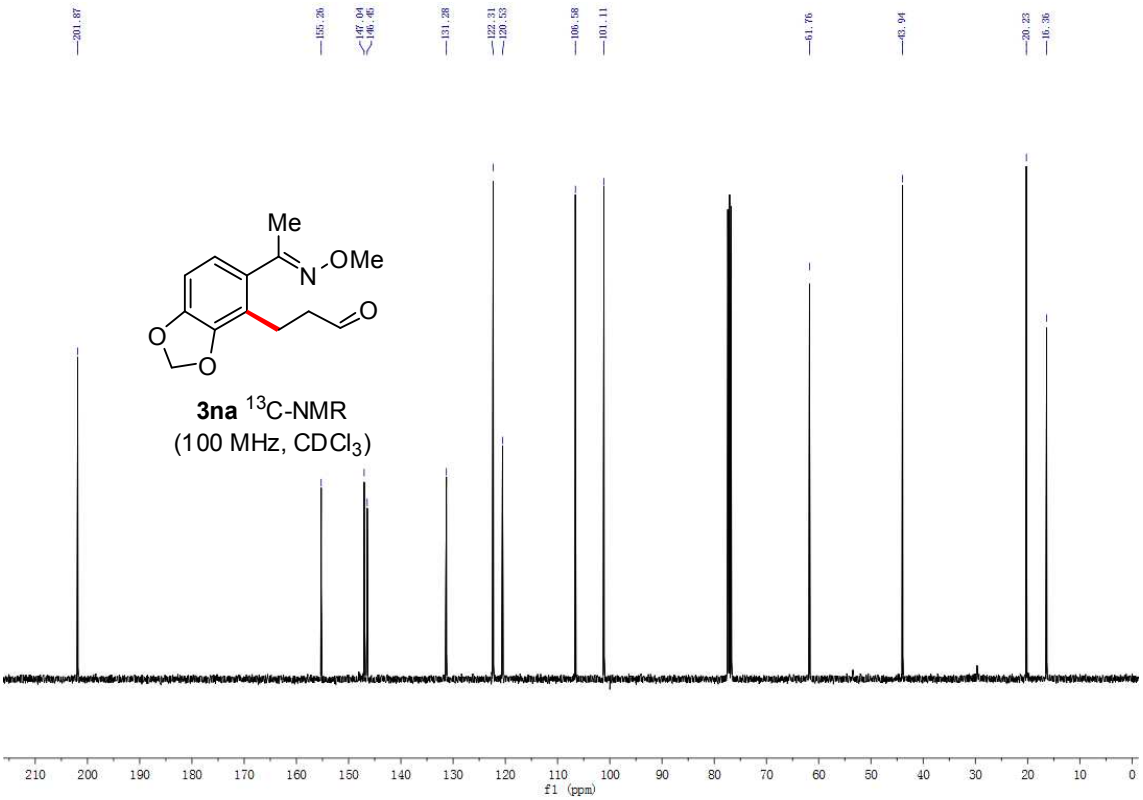
3ma ^{19}F-NMR
(376 MHz, $CDCl_3$)

NOESY spectrum of **3ma**

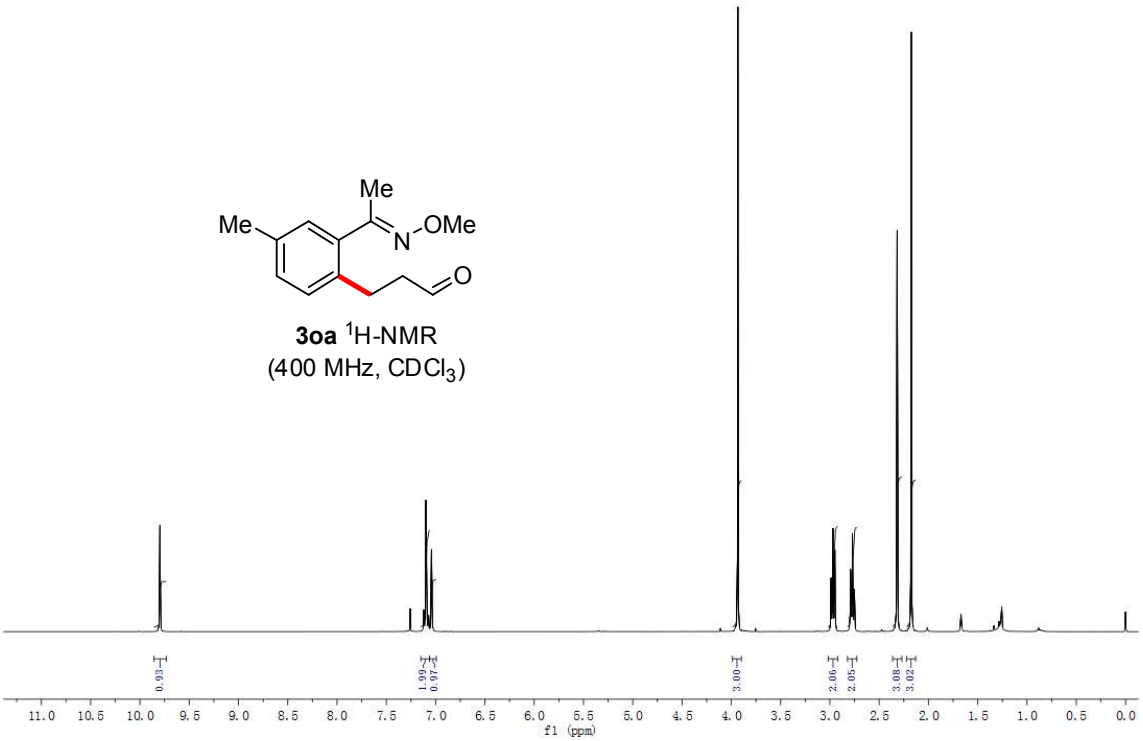


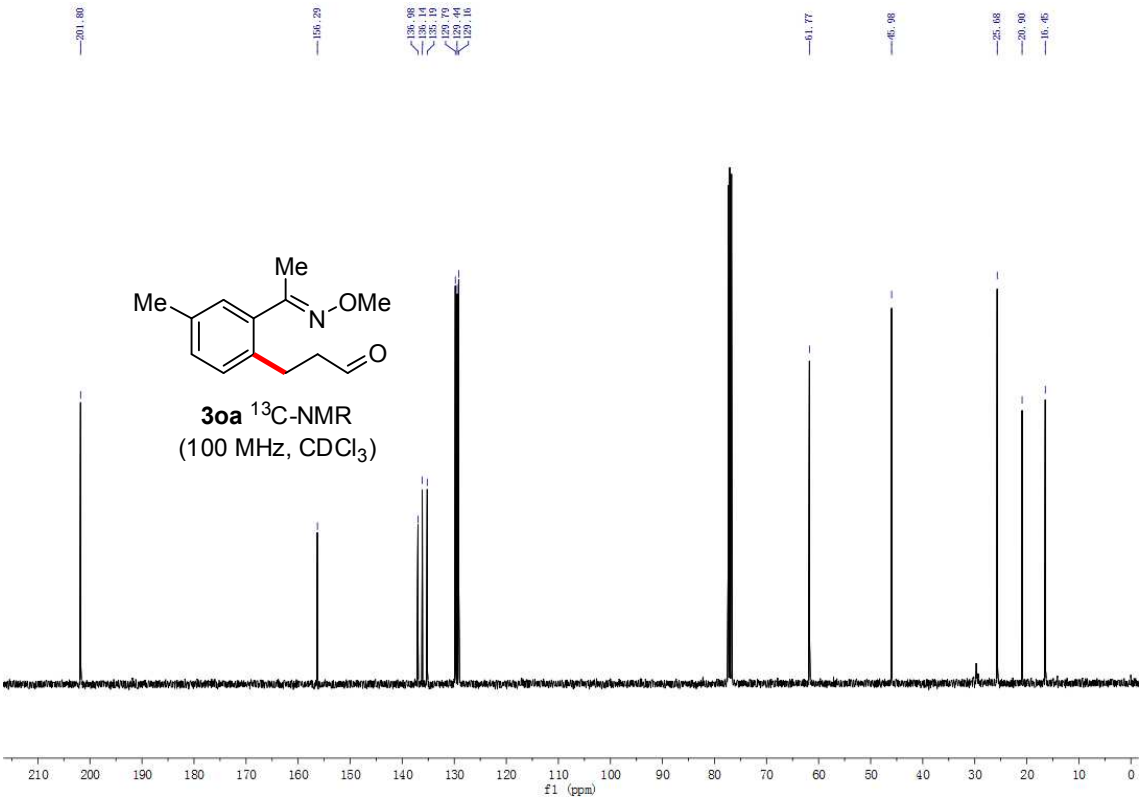
^{1}H NMR and ^{13}C NMR spectra of **3na**



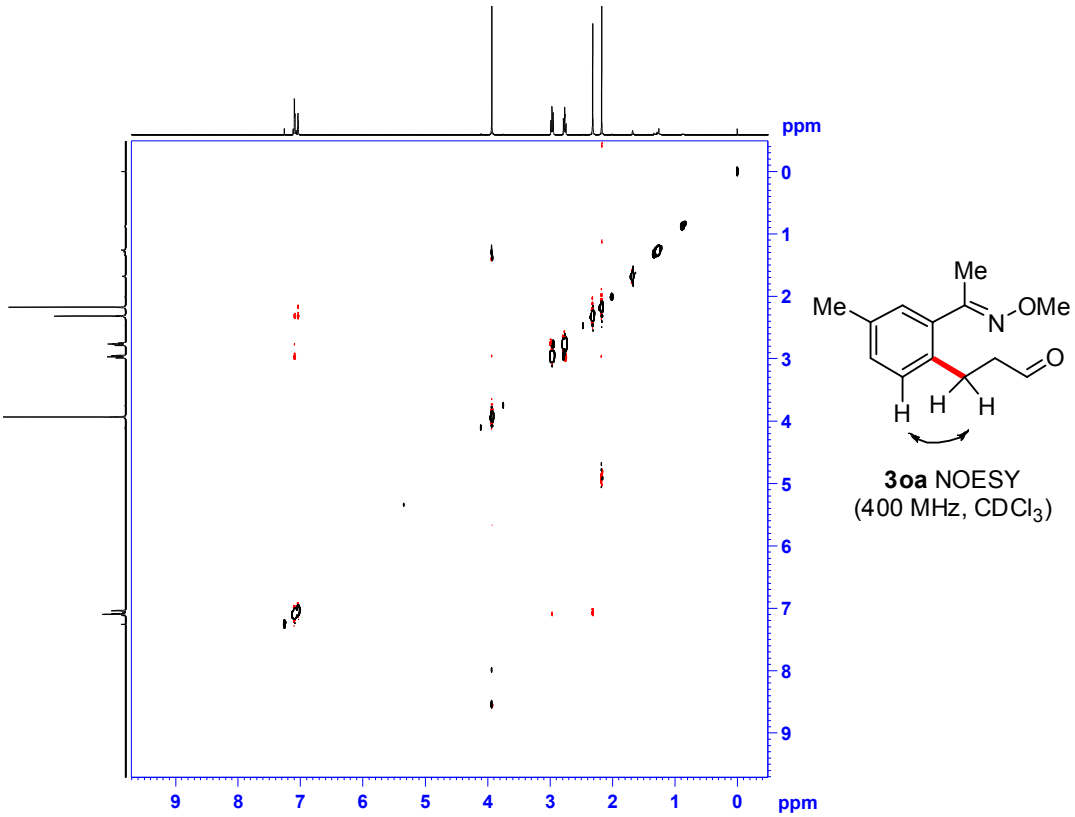


^{1}H NMR and ^{13}C NMR spectra of **3oa**

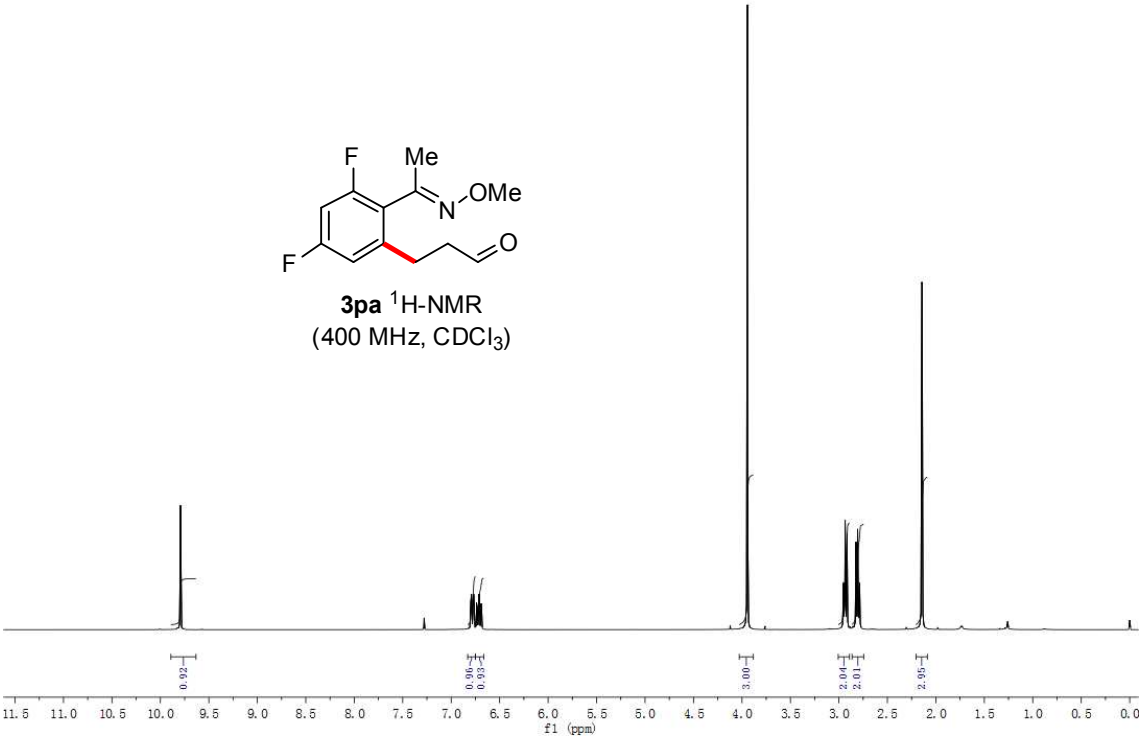


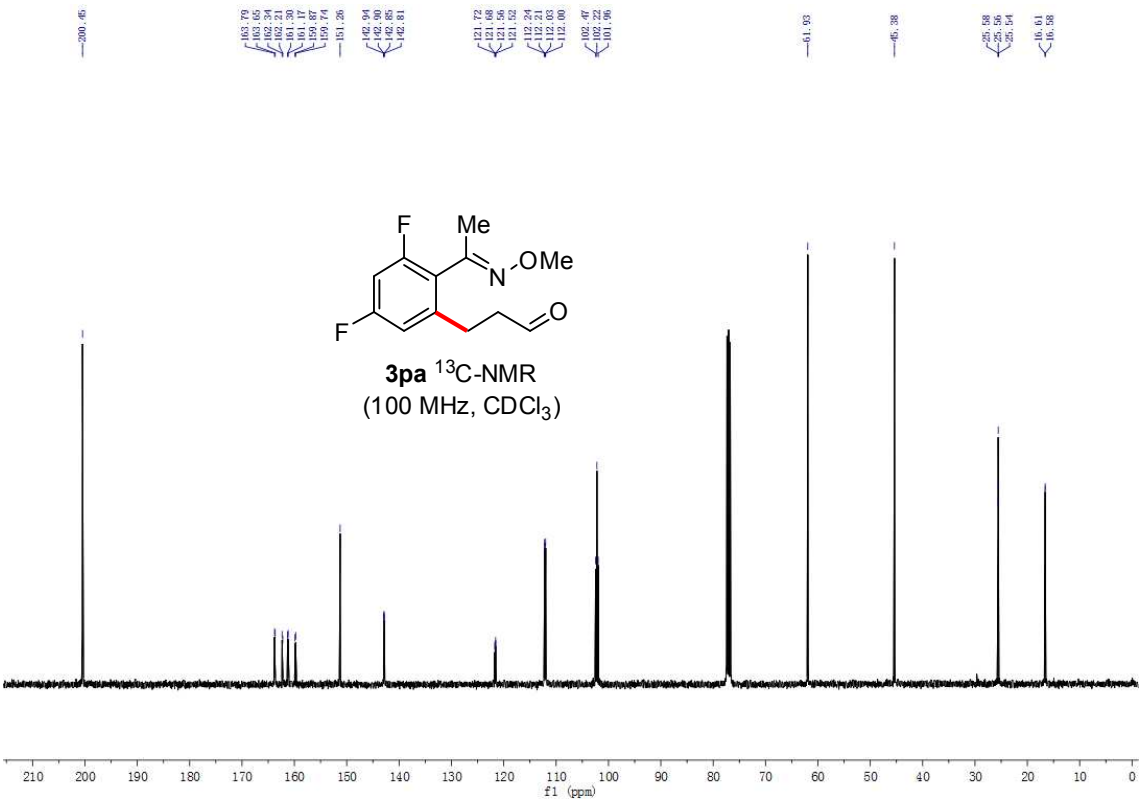


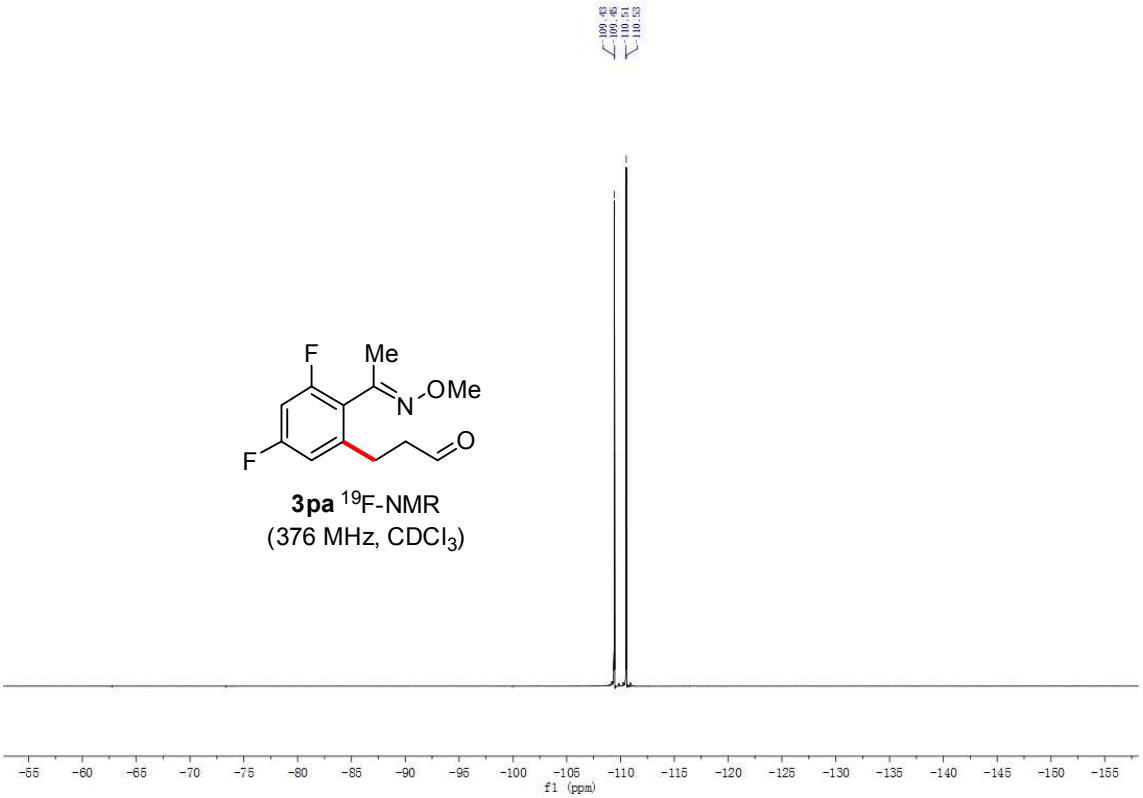
NOESY spectrum of **3oa**



^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3pa**

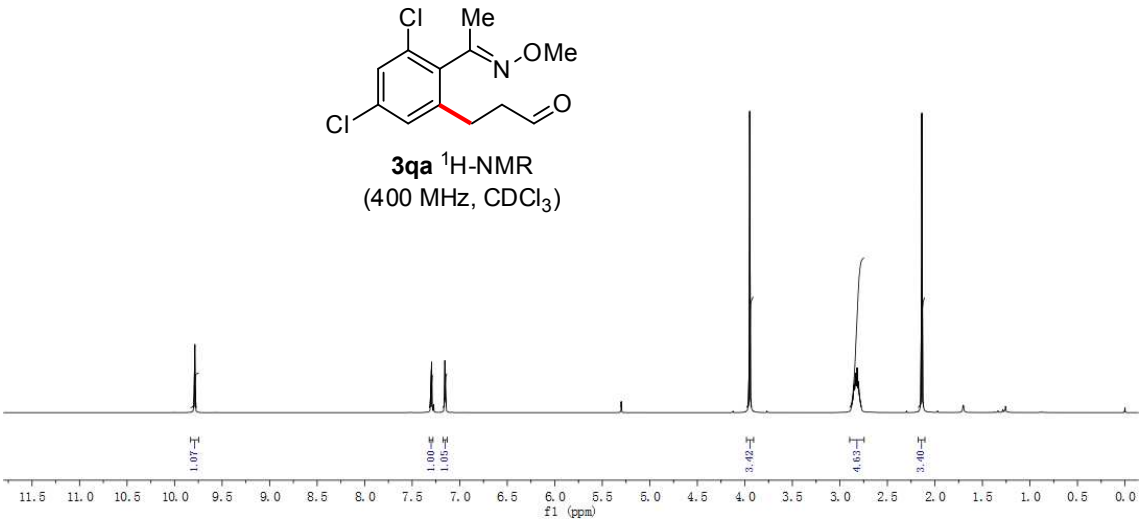


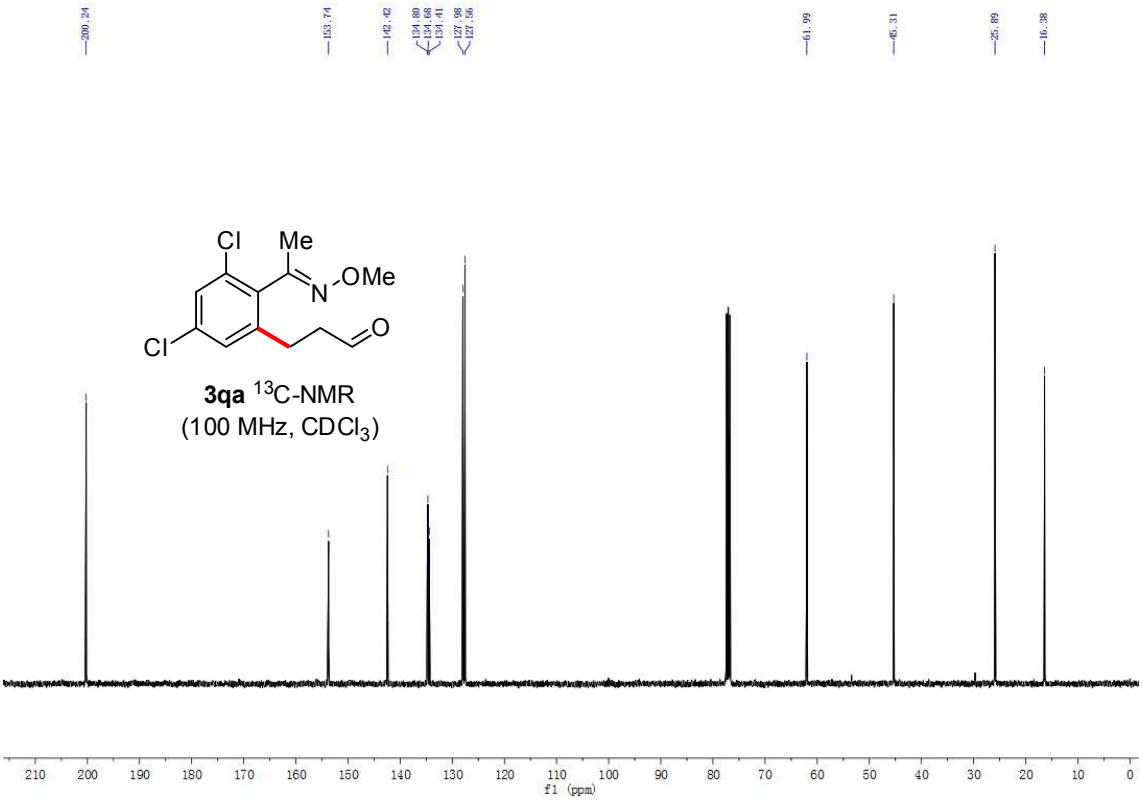




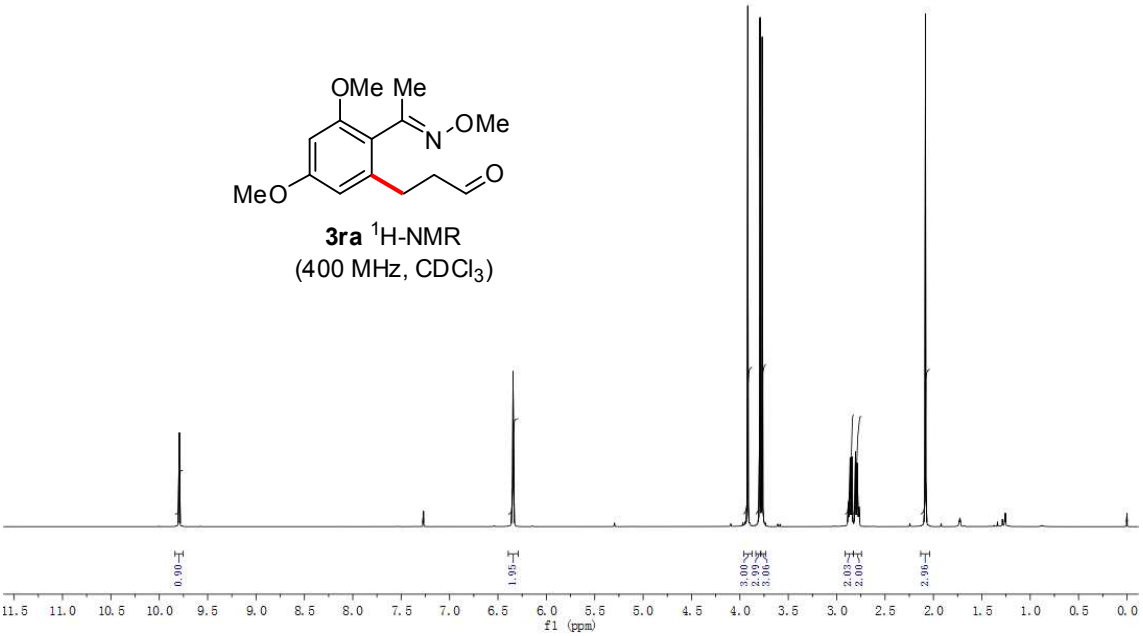
3pa ^{19}F-NMR
(376 MHz, $CDCl_3$)

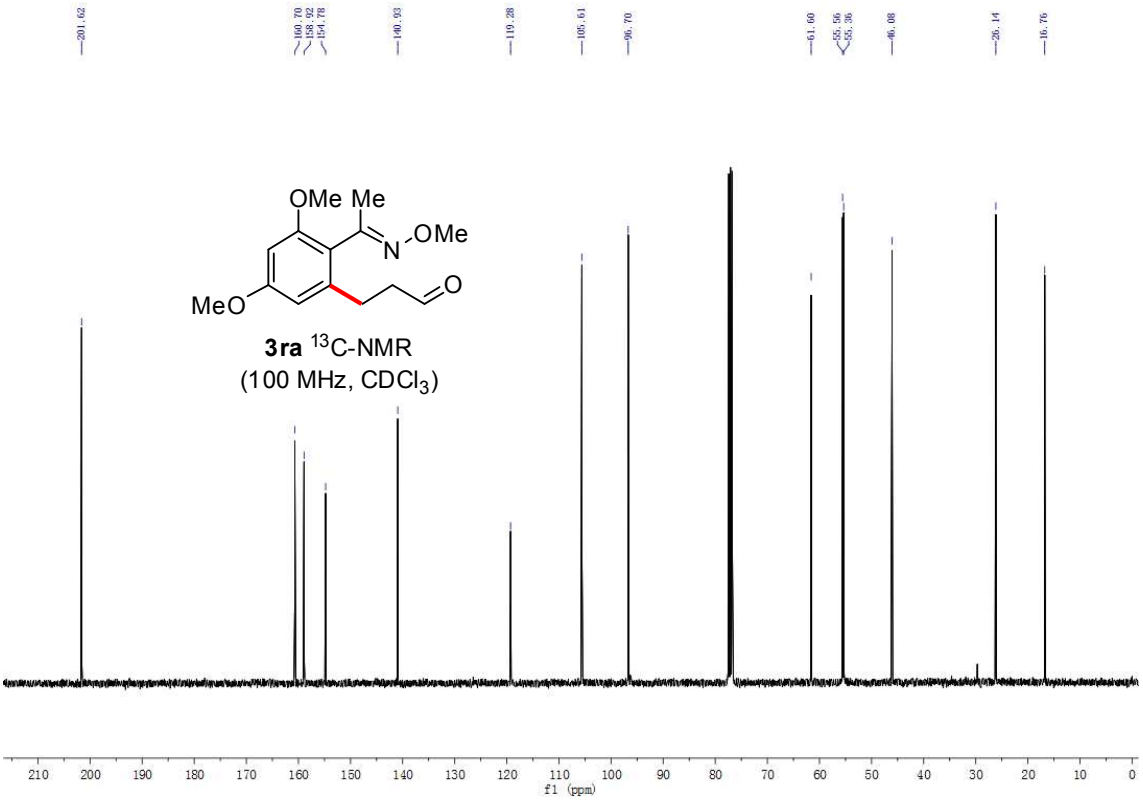
^{1}H NMR and ^{13}C NMR spectra of **3qa**



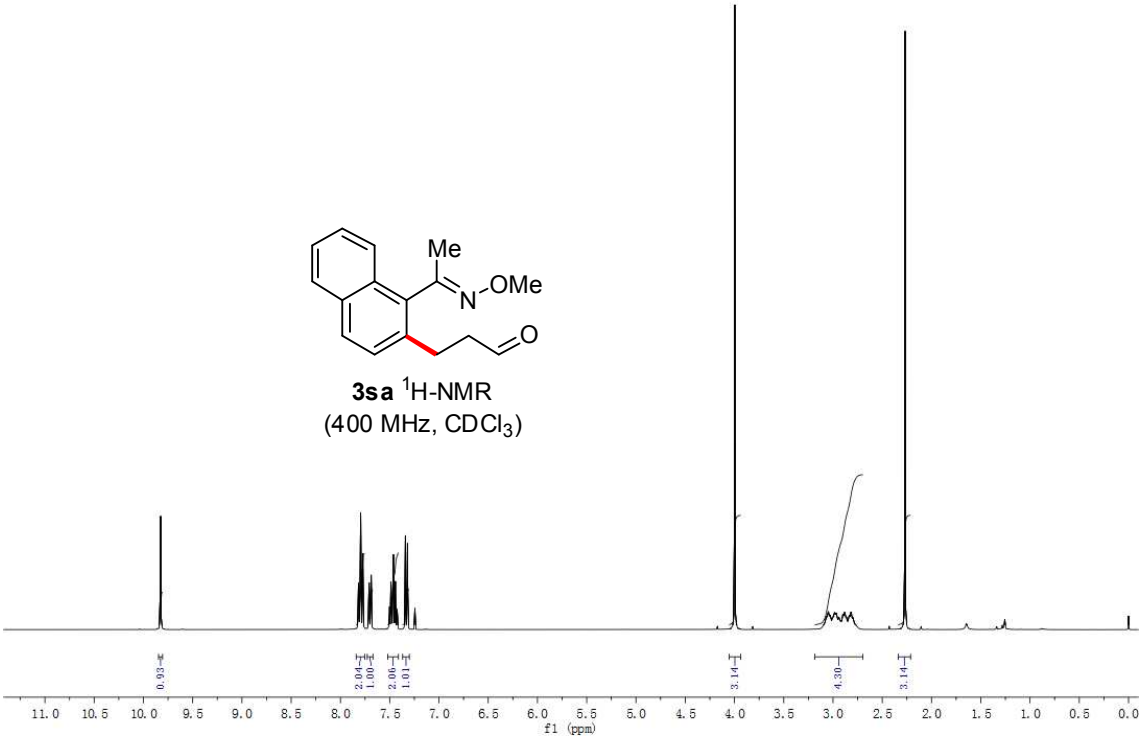


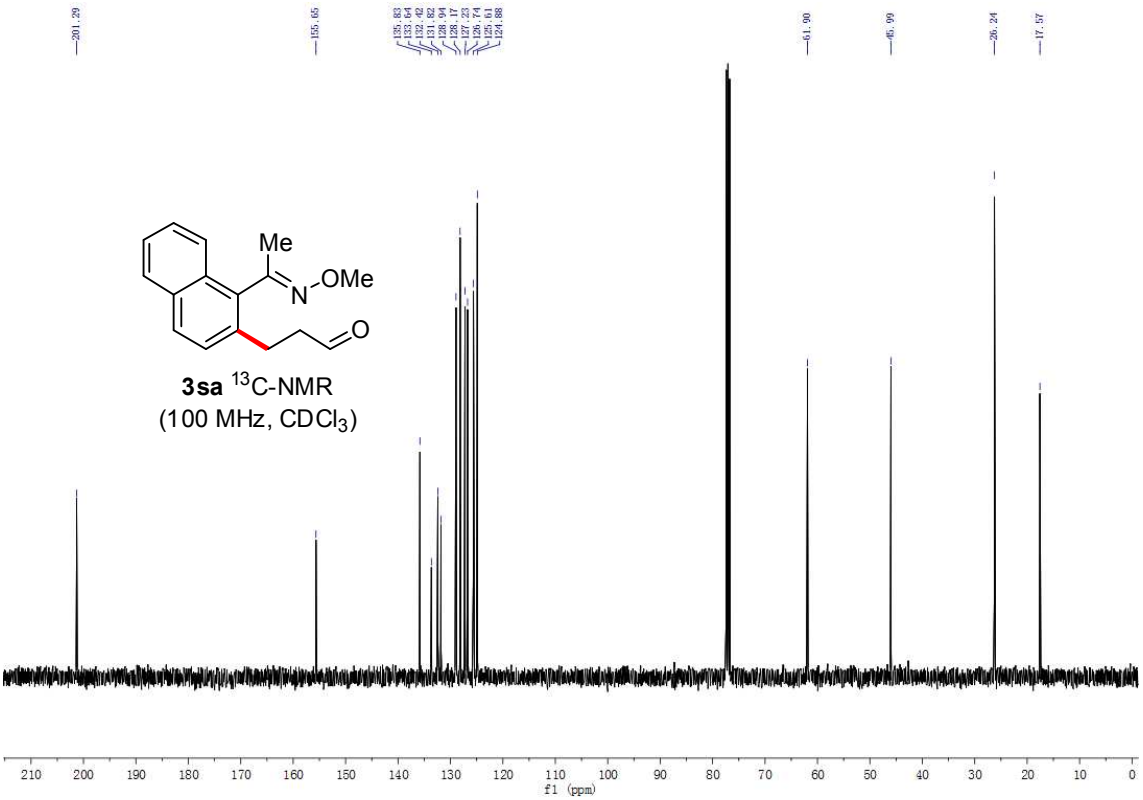
^{1}H NMR and ^{13}C NMR spectra of **3ra**



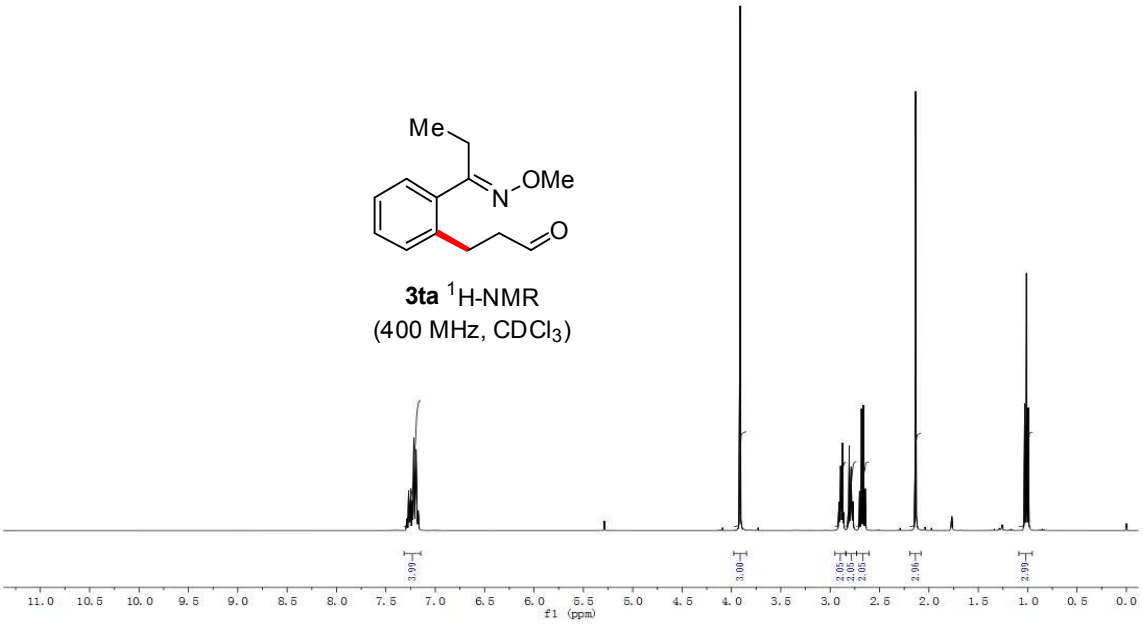


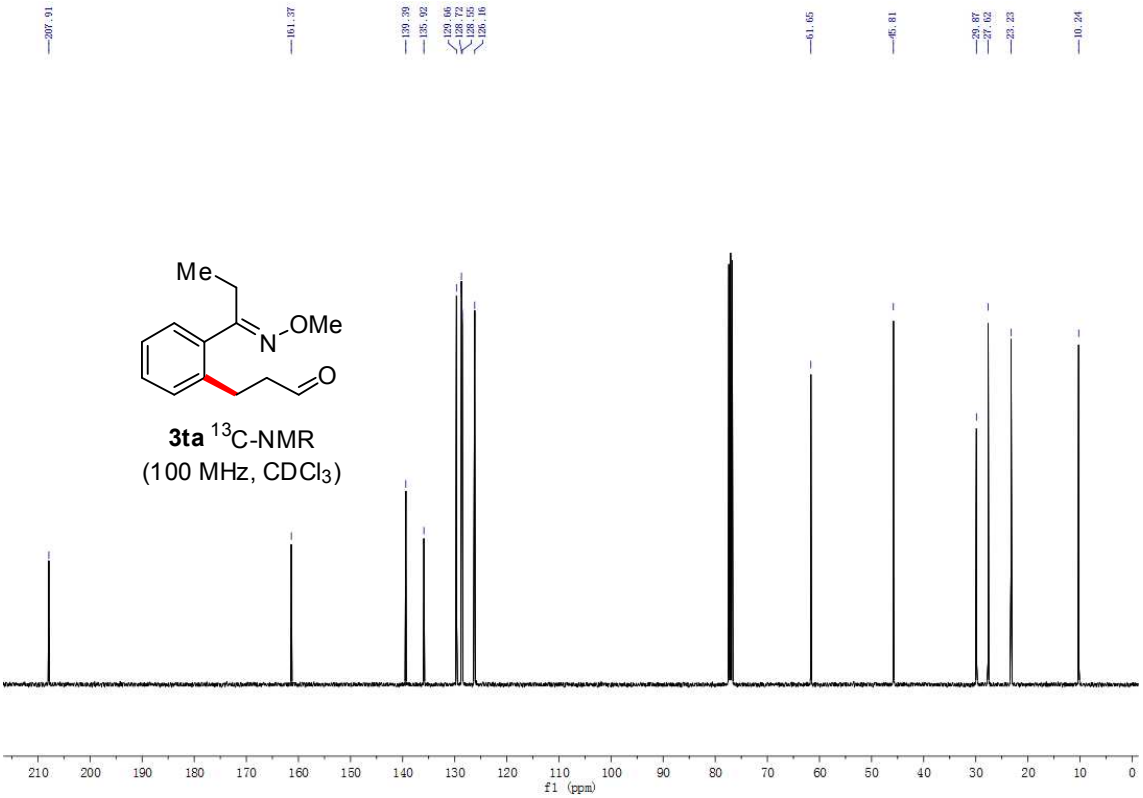
^{1}H NMR and ^{13}C NMR spectra of **3sa**



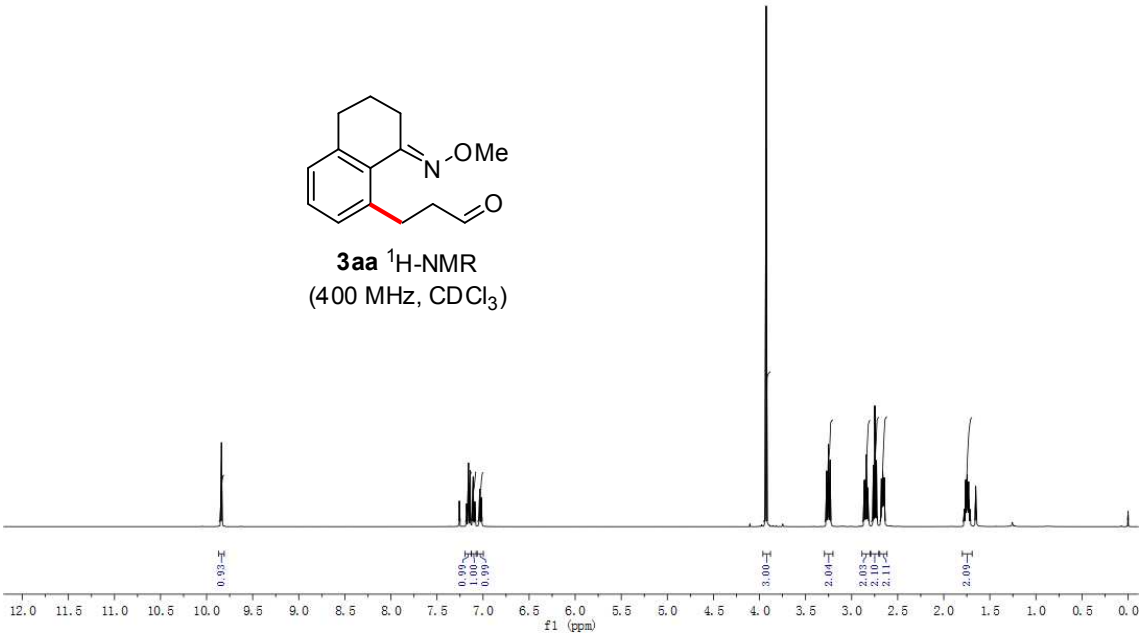


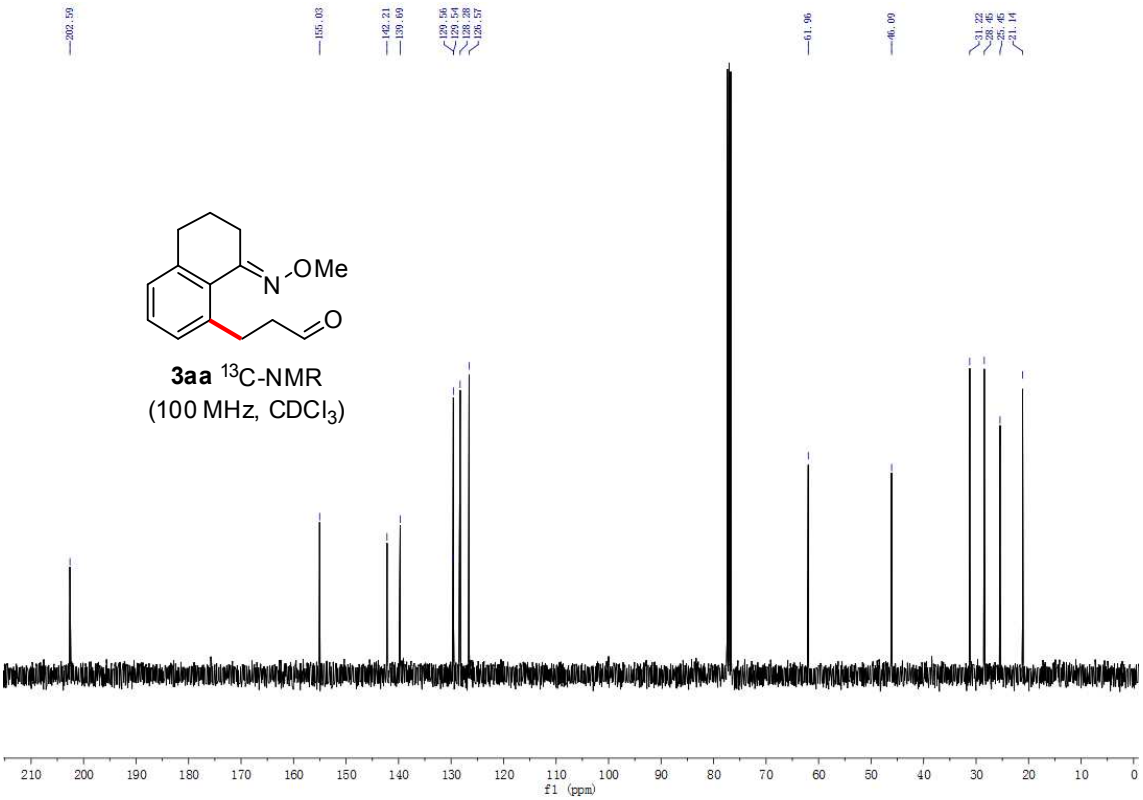
^{1}H NMR and ^{13}C NMR spectra of **3ta**



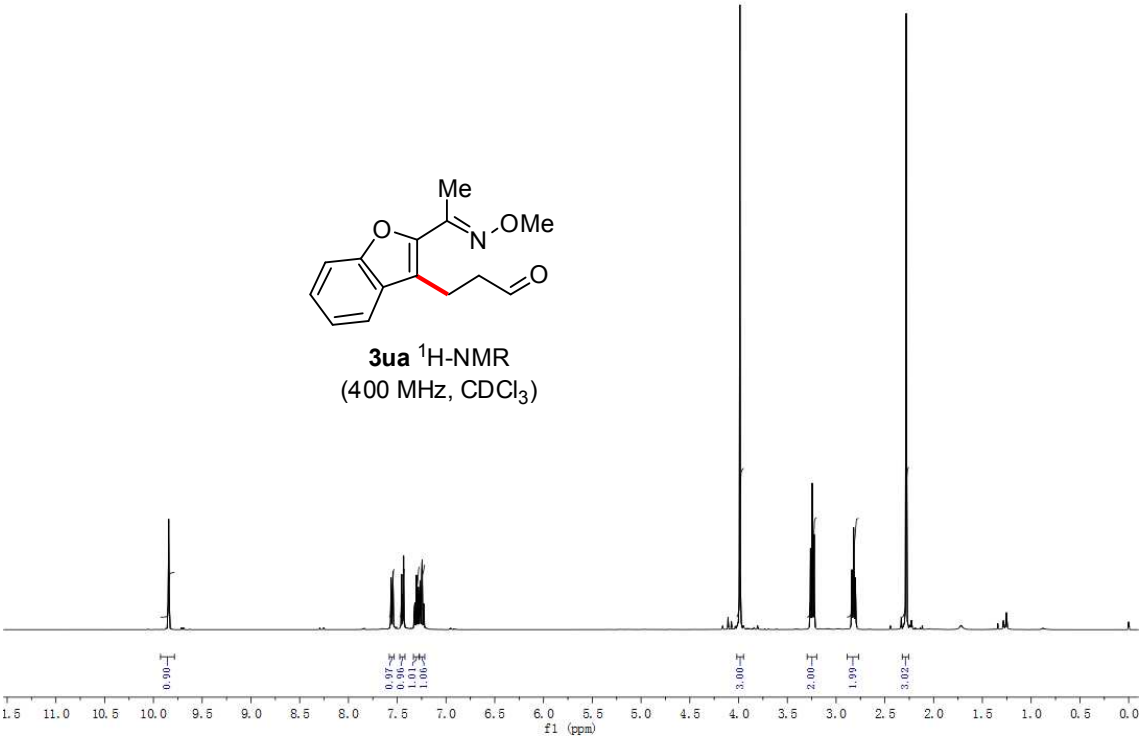


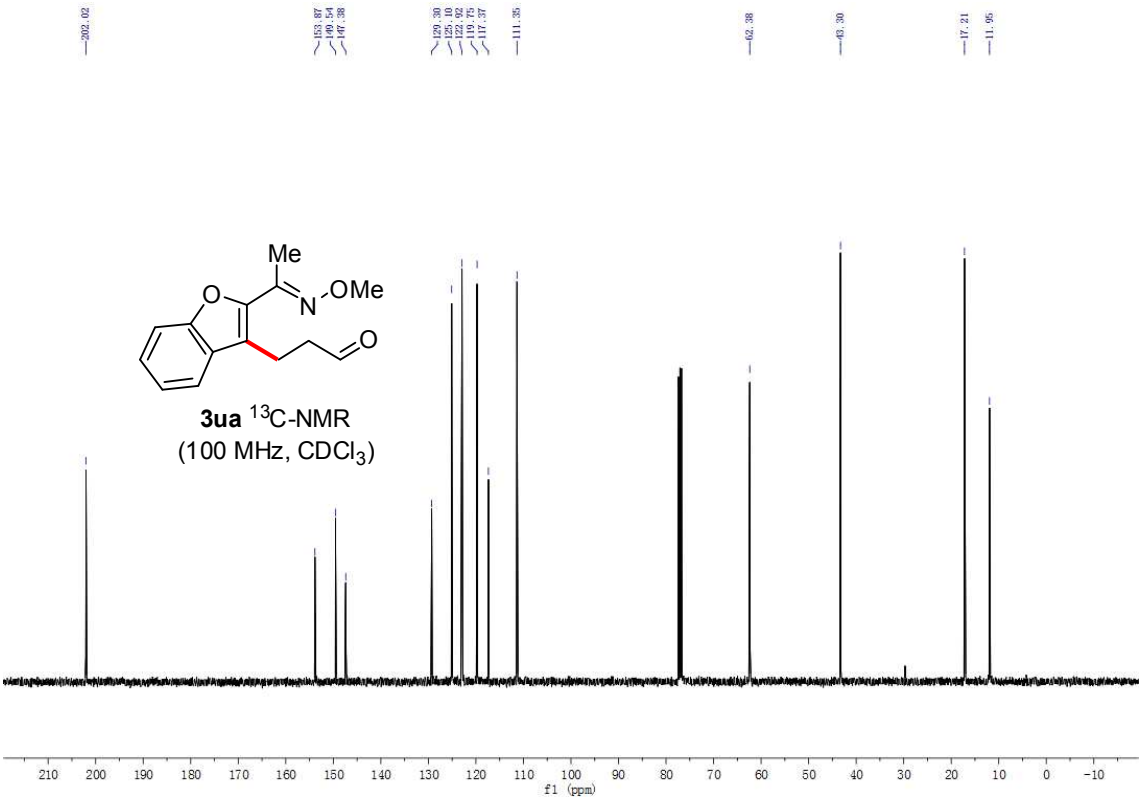
^{1}H NMR and ^{13}C NMR spectra of **3aa**



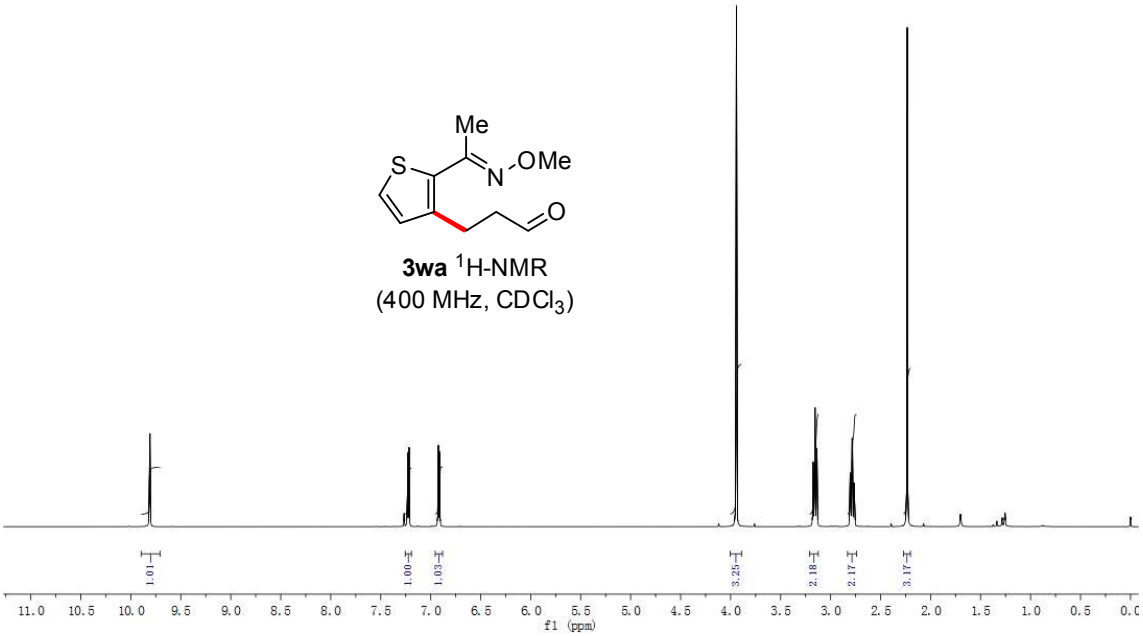


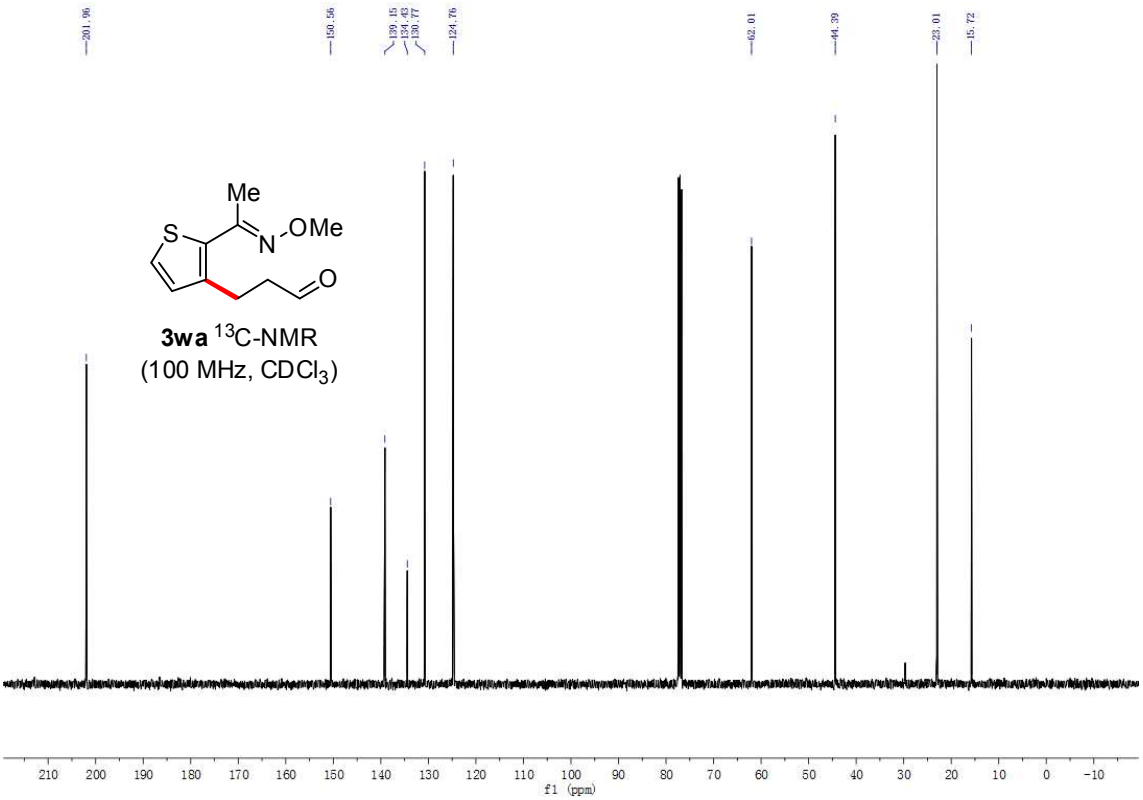
^{1}H NMR and ^{13}C NMR spectra of **3ua**



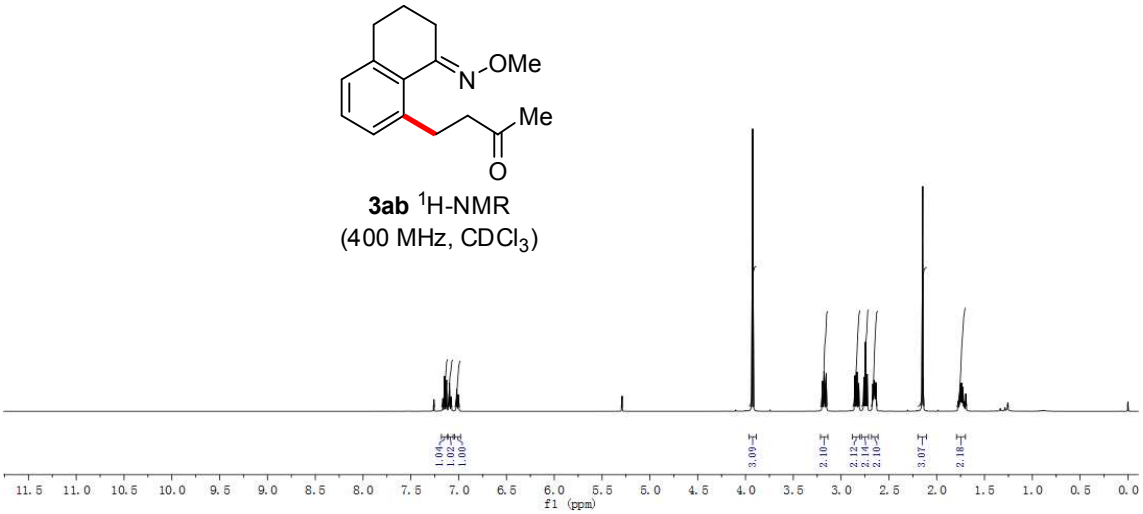


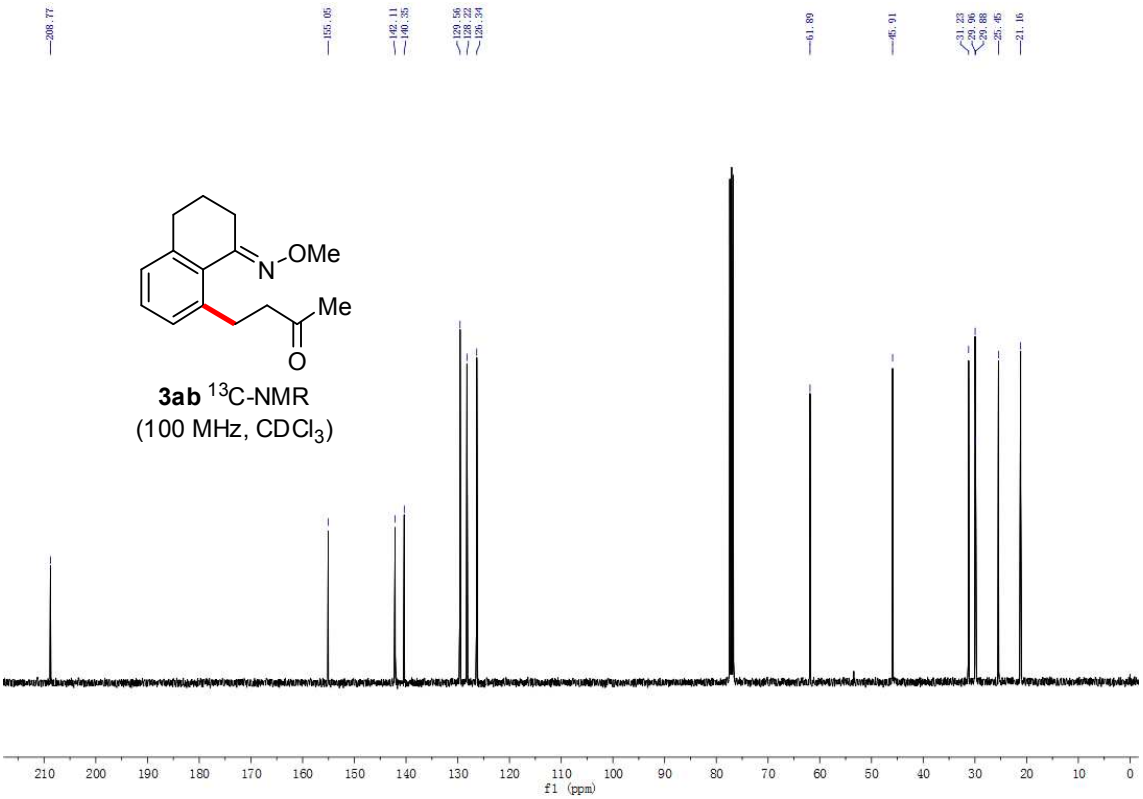
^{1}H NMR and ^{13}C NMR spectra of **3wa**



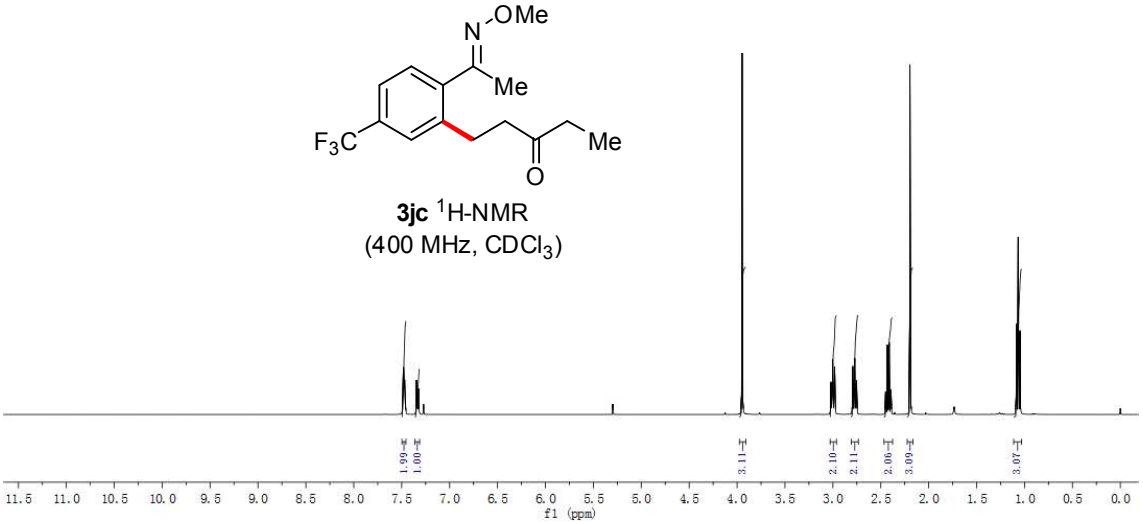


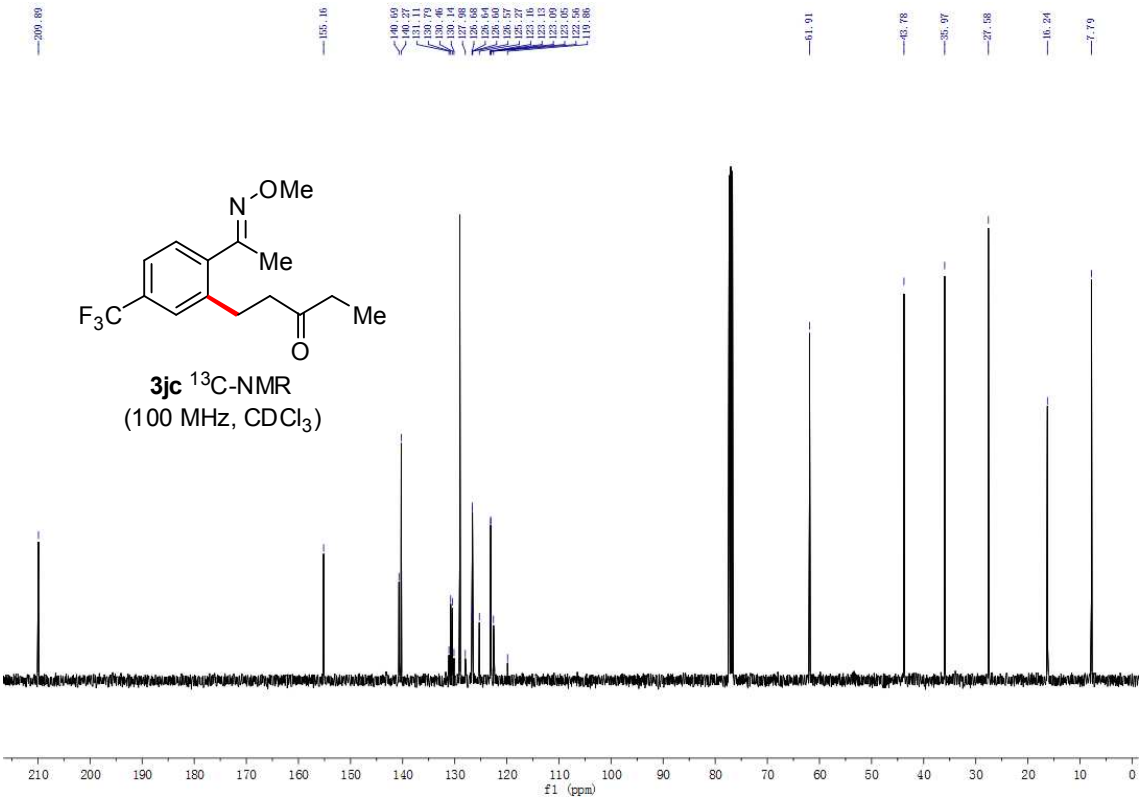
^{1}H NMR and ^{13}C NMR spectra of **3ab**

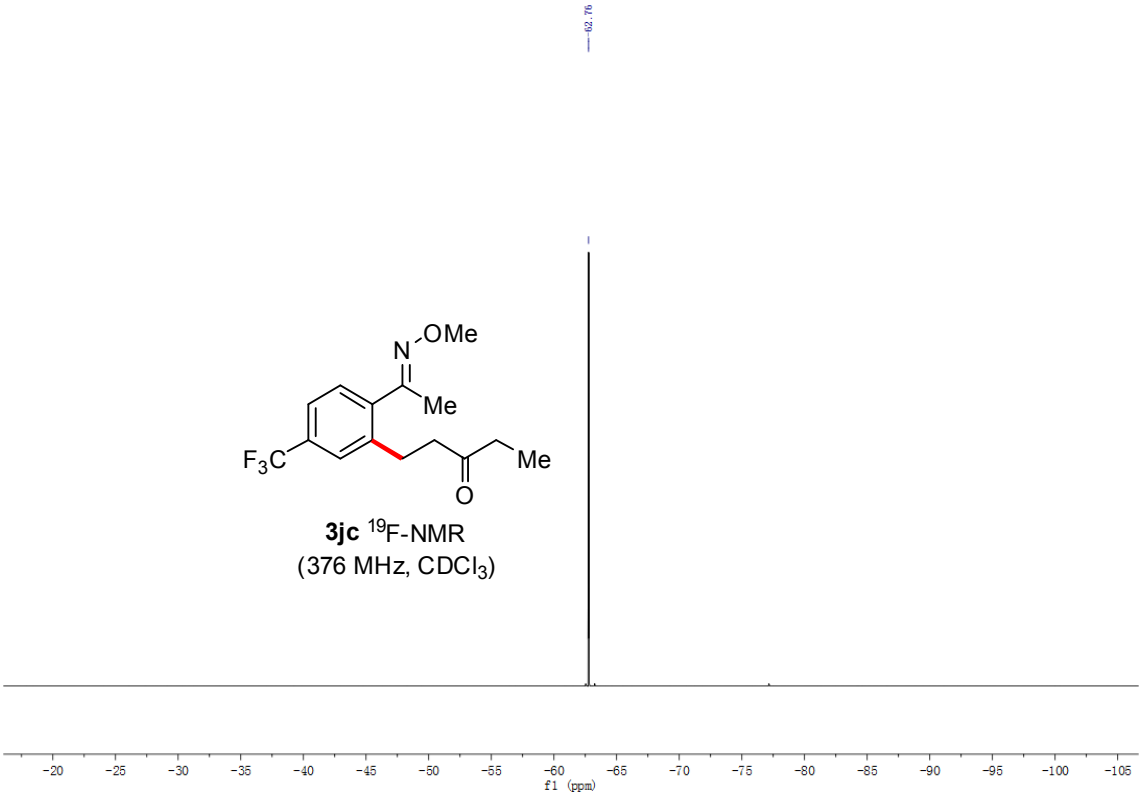




^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3jc**



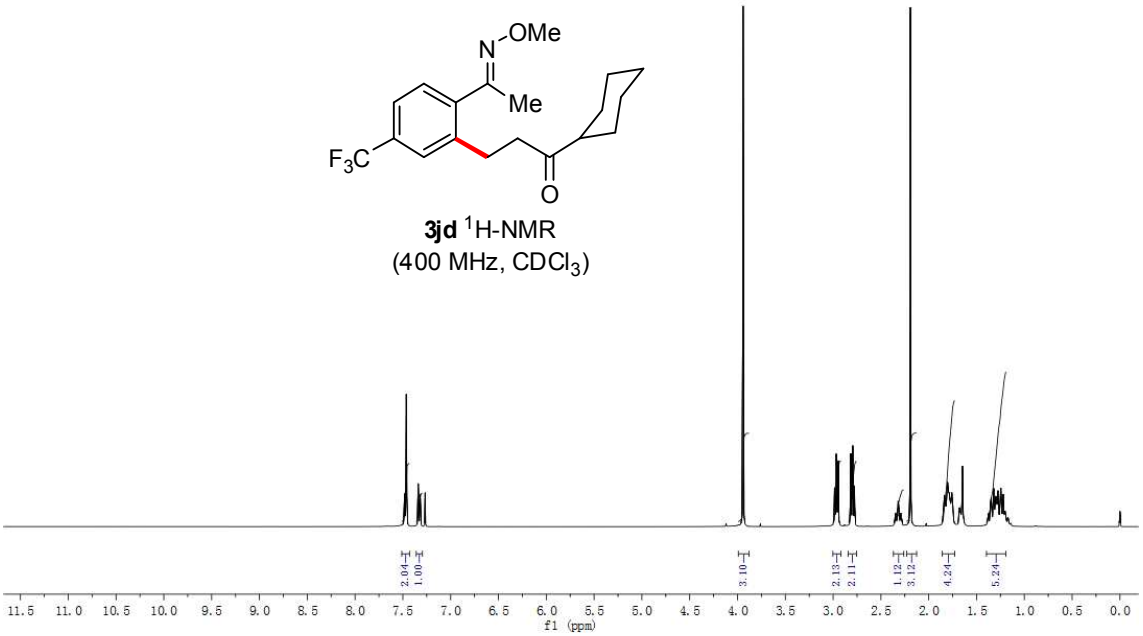




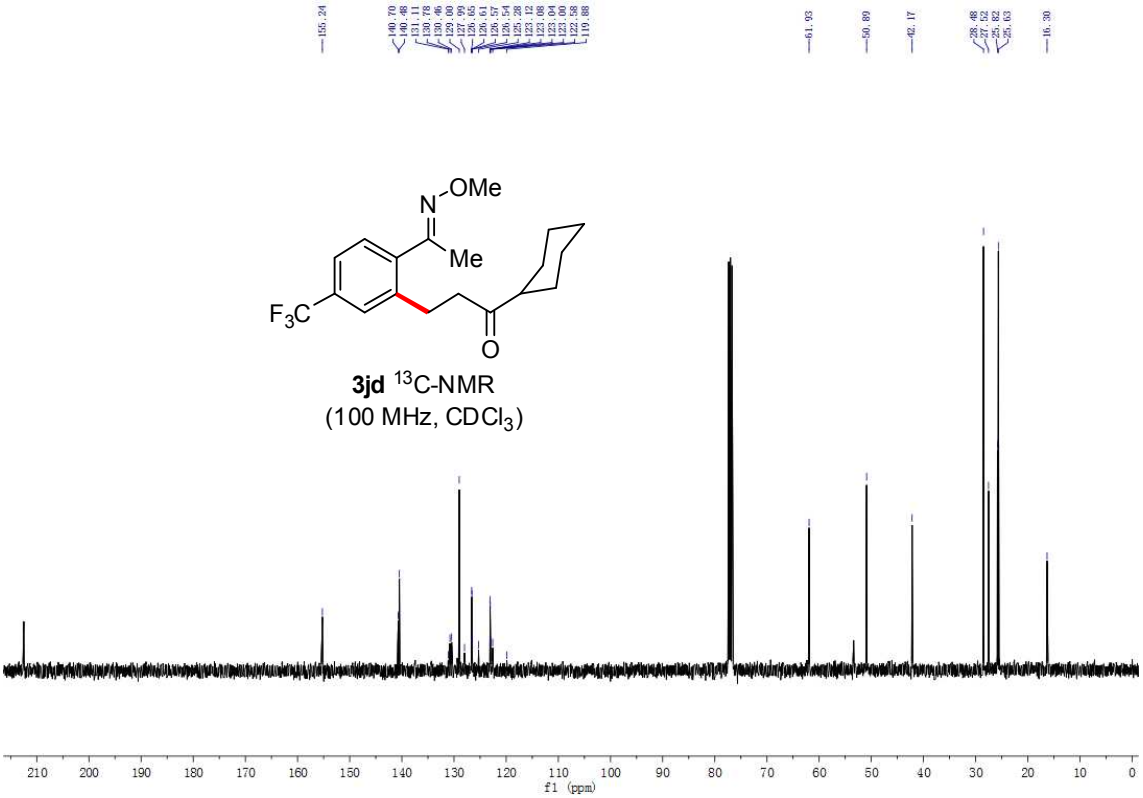
3jc ^{19}F-NMR
(376 MHz, $CDCl_3$)

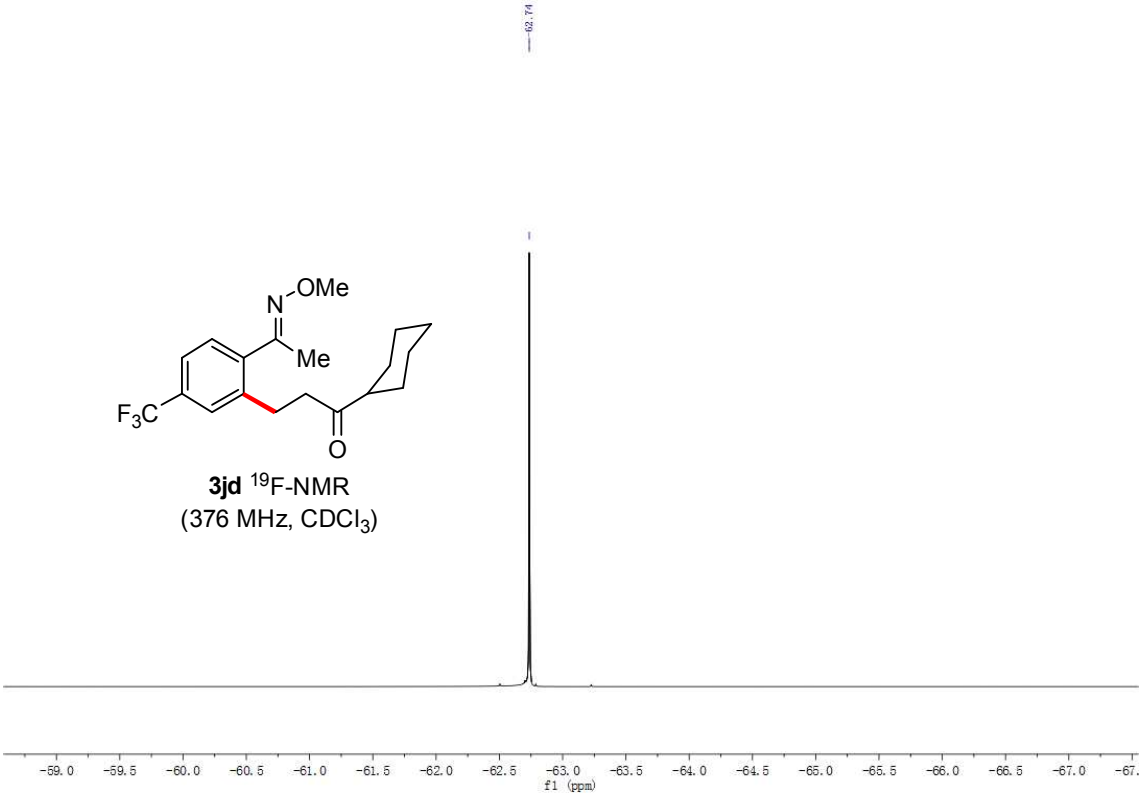
^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3jd**

3jd ^{1}H-NMR
(400 MHz, $CDCl_3$)



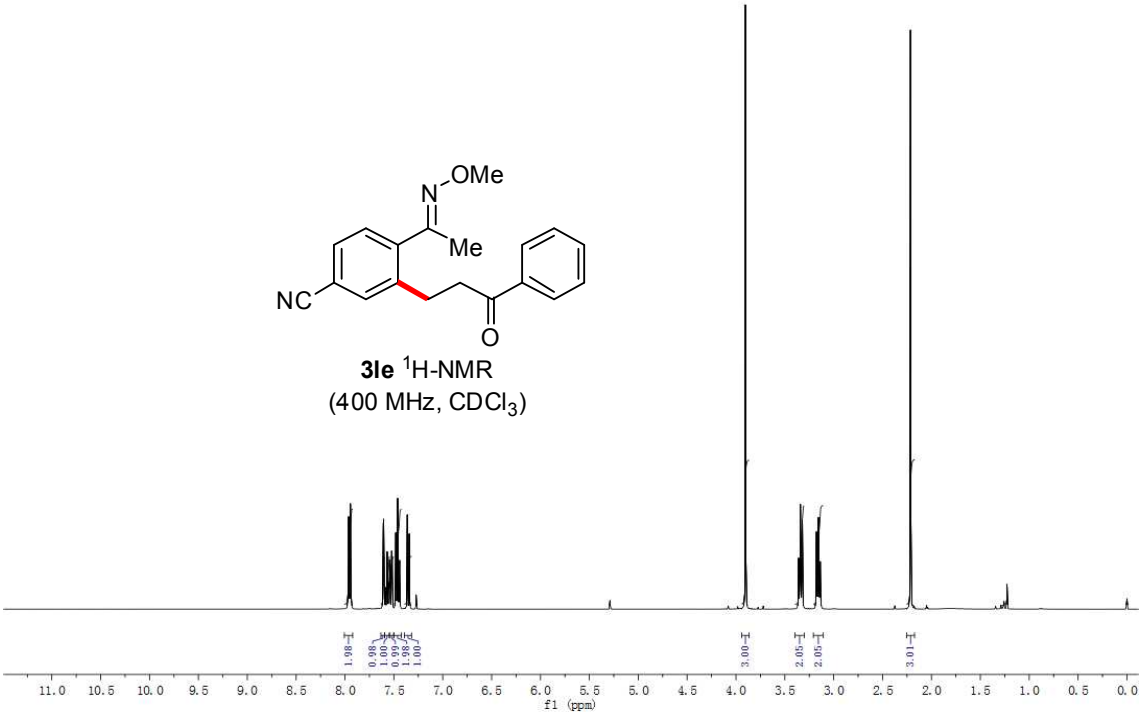
3jd ^{13}C-NMR
(100 MHz, $CDCl_3$)

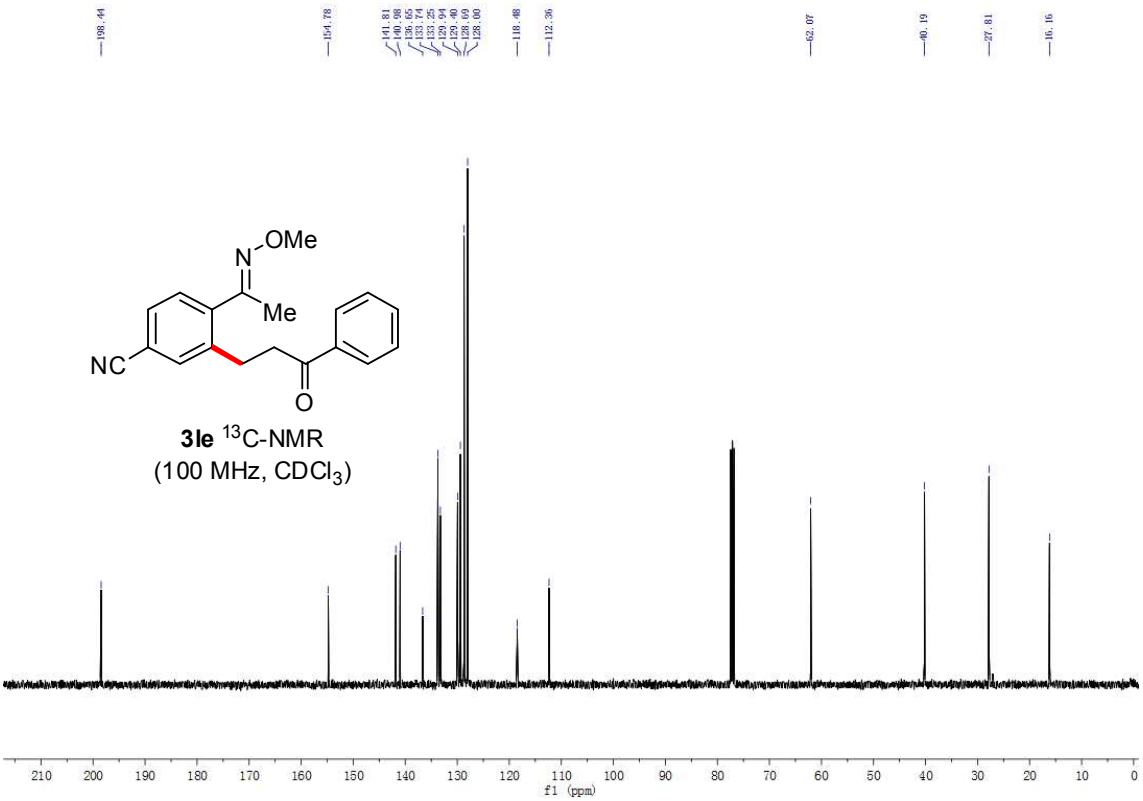




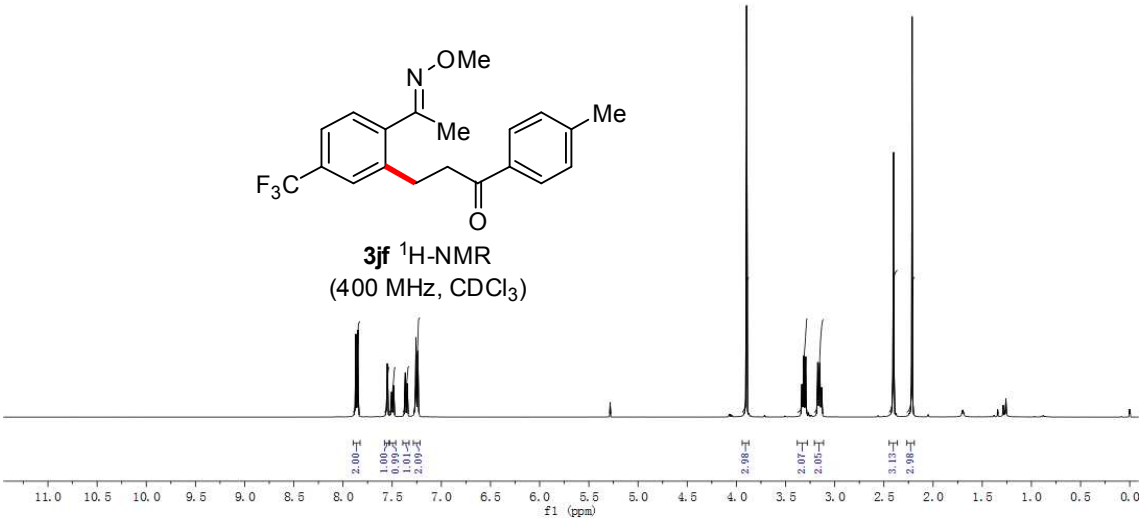
3jd ^{19}F-NMR
(376 MHz, $CDCl_3$)

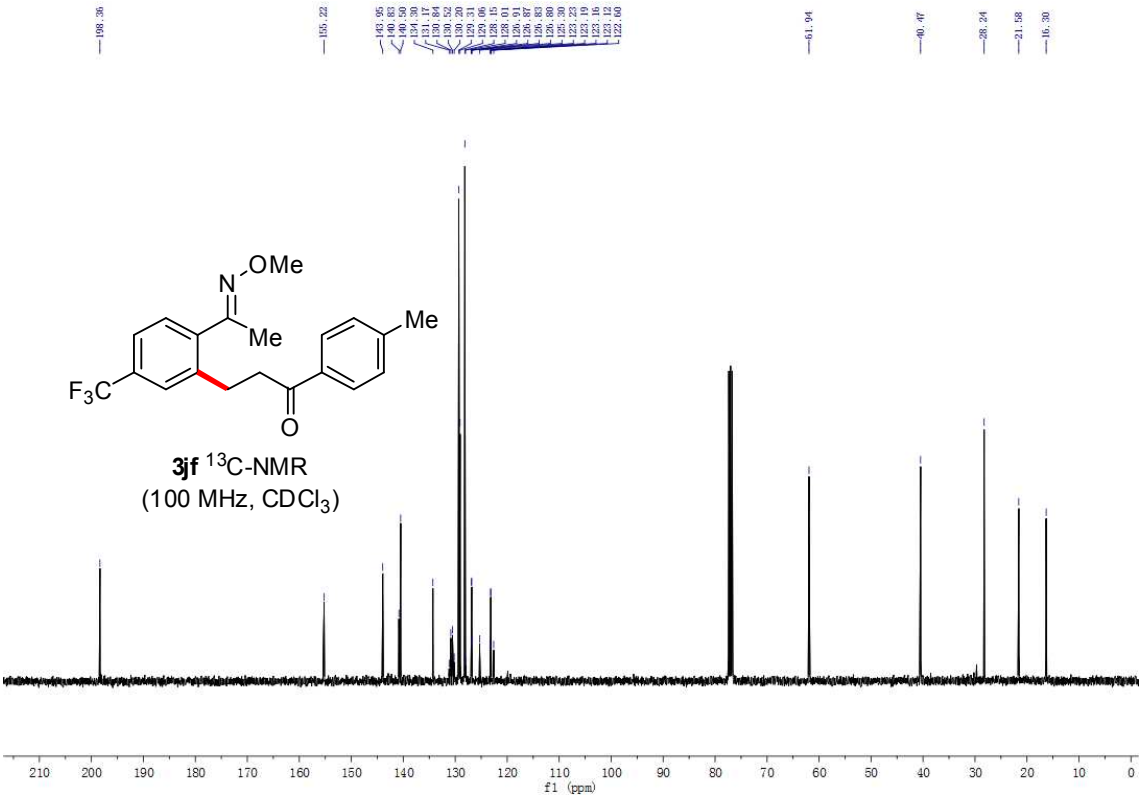
^{1}H NMR and ^{13}C NMR spectra of **3le**



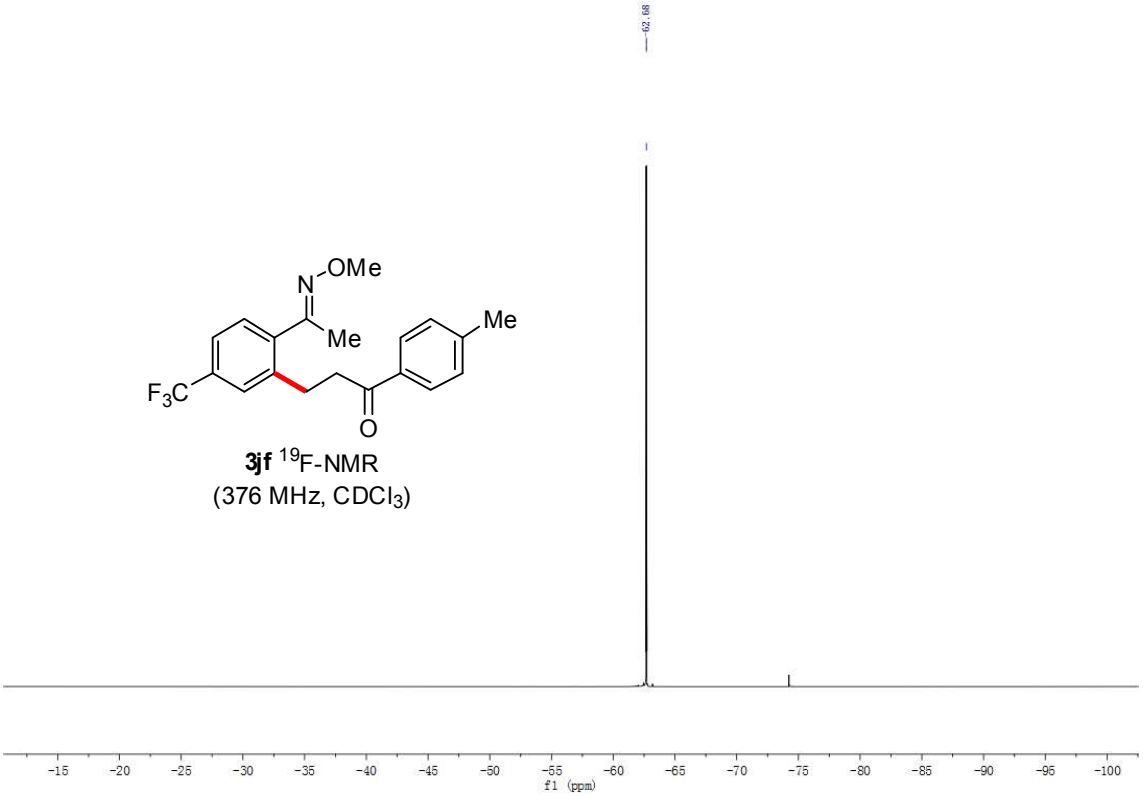


^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3jf**

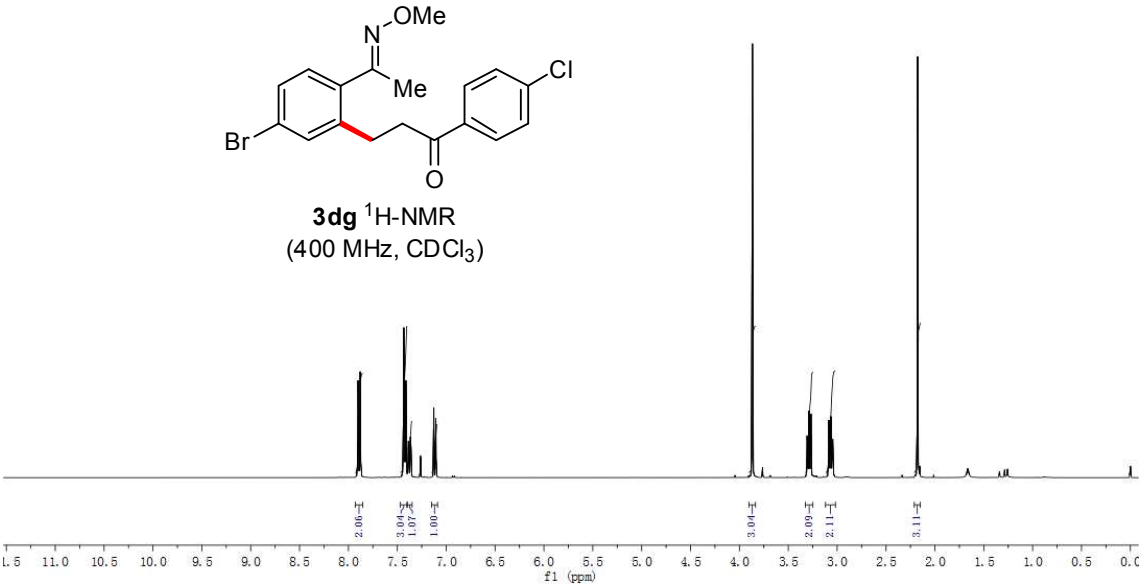




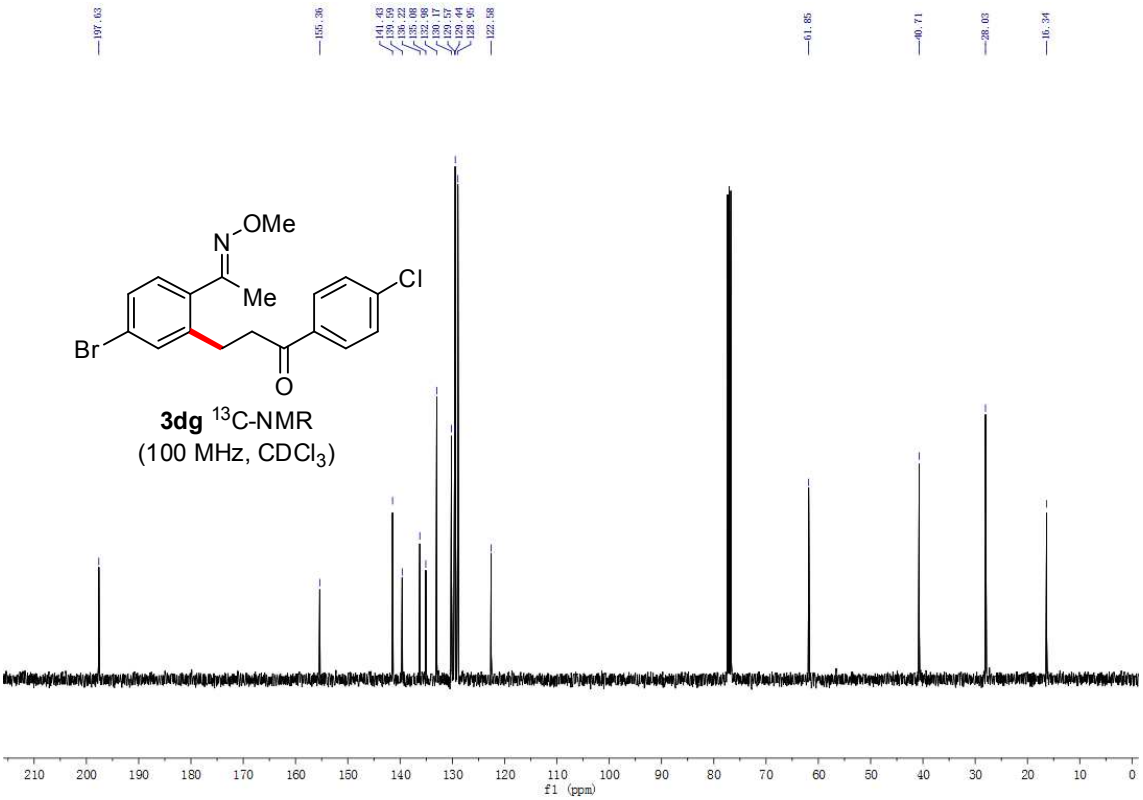
3jf ^{19}F-NMR
(376 MHz, $CDCl_3$)



^{1}H NMR and ^{13}C NMR spectra of **3dg**

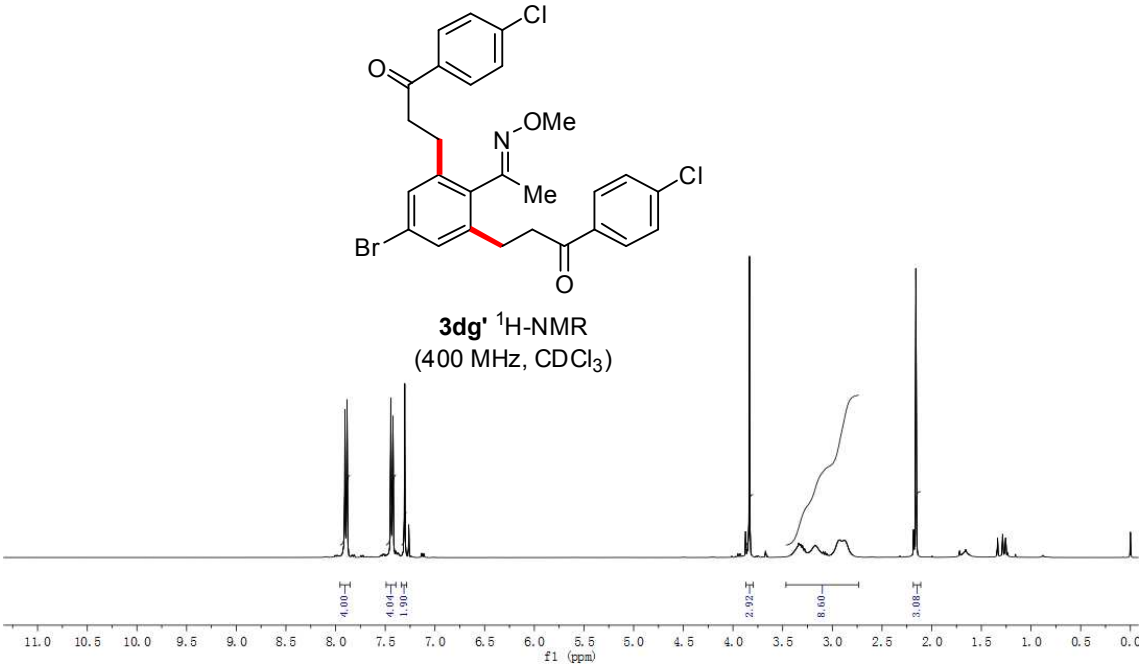


3dg ^{1}H-NMR
(400 MHz, $CDCl_3$)

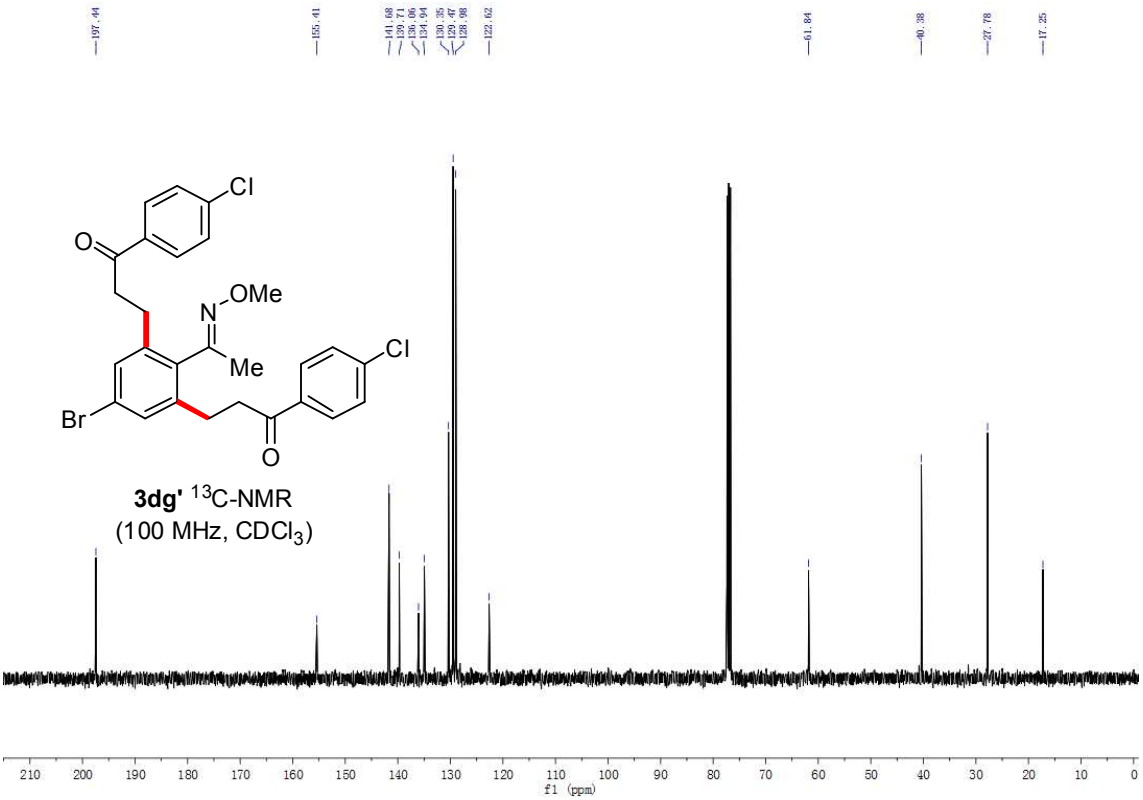


3dg ^{13}C-NMR
(100 MHz, $CDCl_3$)

^{1}H NMR and ^{13}C NMR spectra of **3dg'**

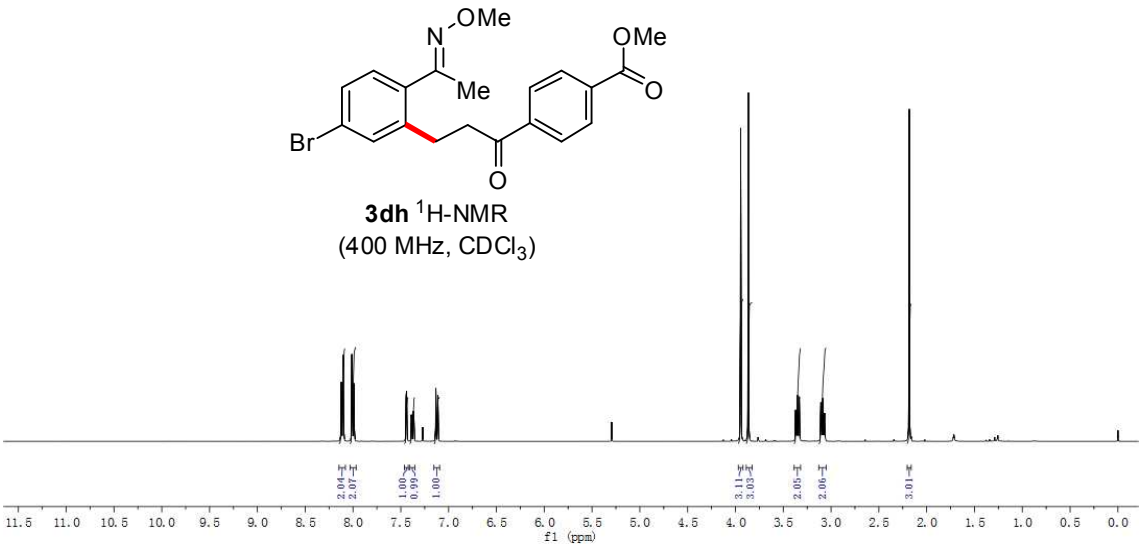


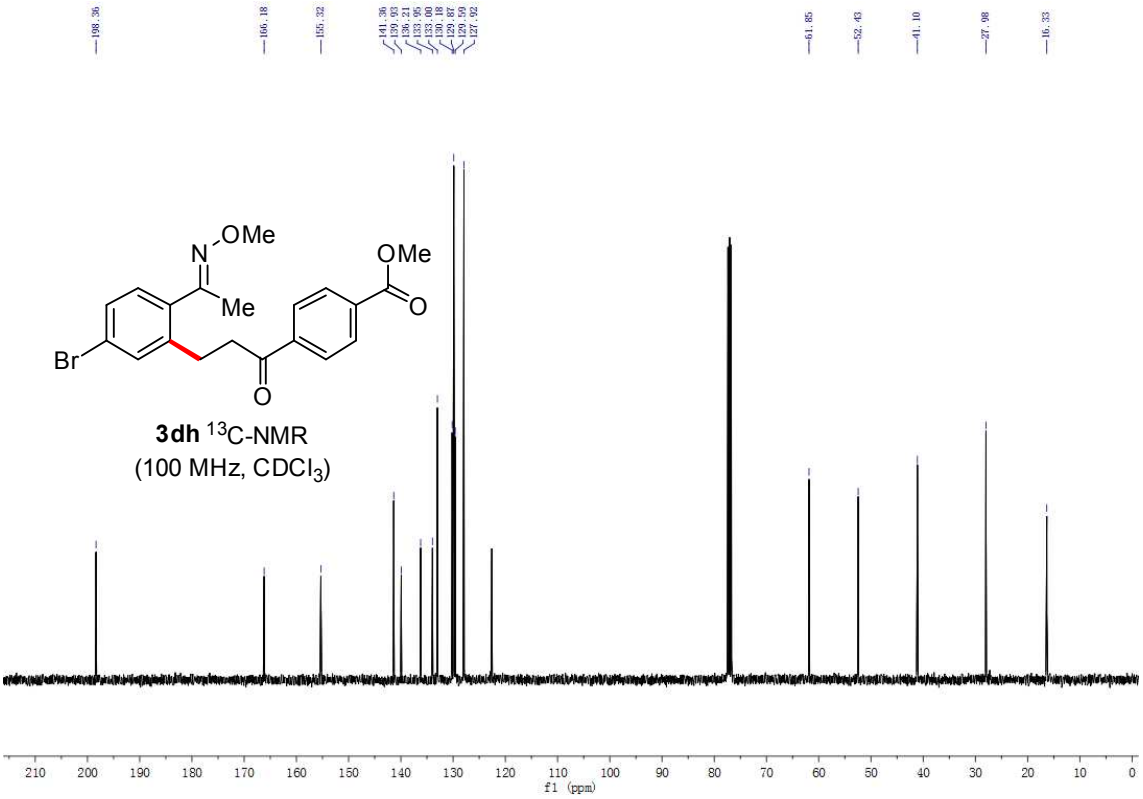
3dg' ^{1}H-NMR
(400 MHz, $CDCl_3$)



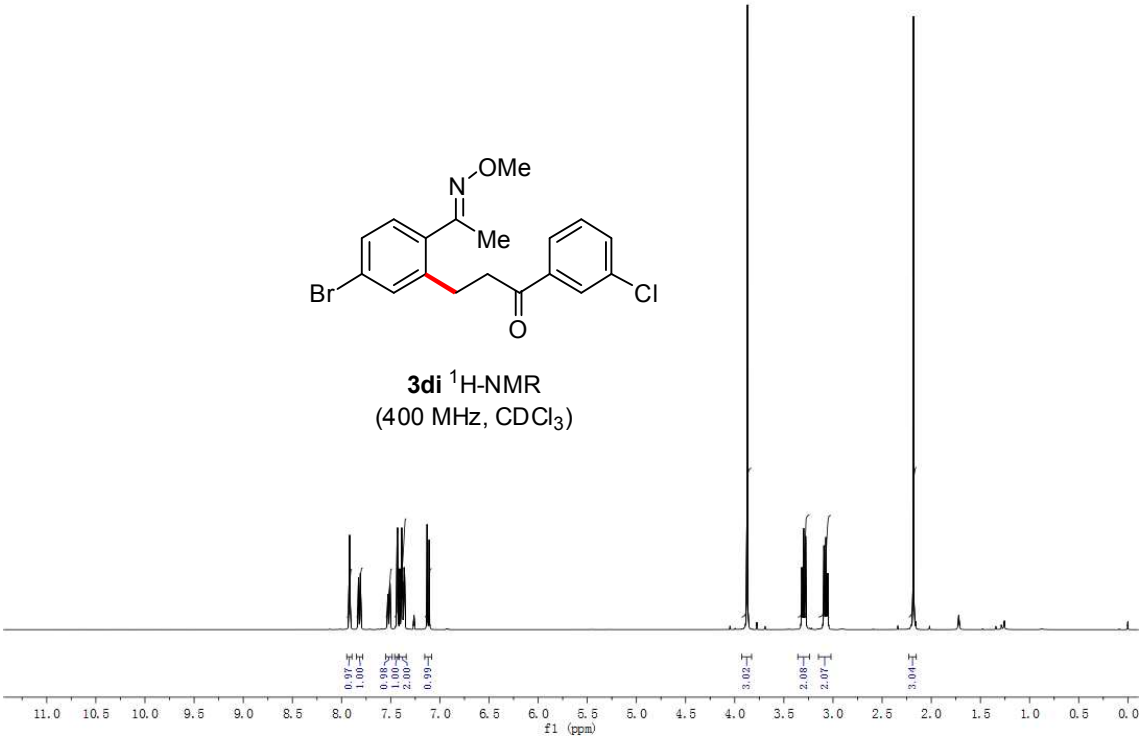
3dg' ^{13}C-NMR
(100 MHz, $CDCl_3$)

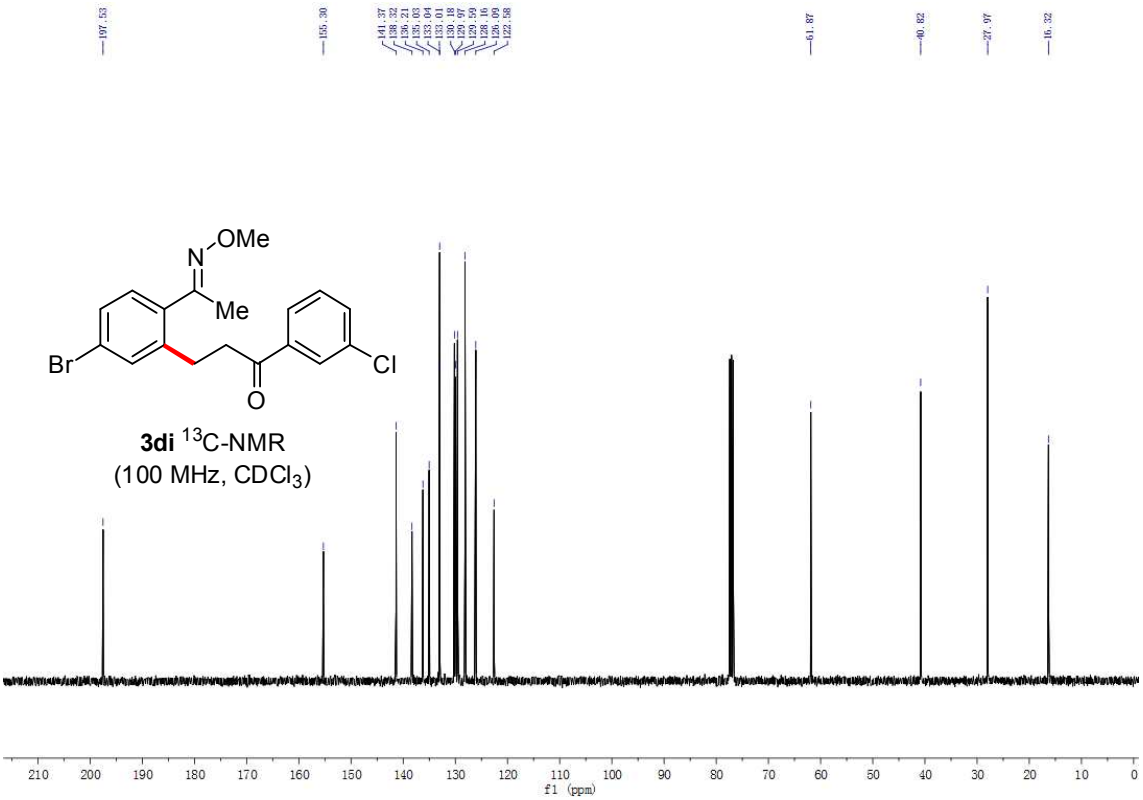
^{1}H NMR and ^{13}C NMR spectra of **3dh**



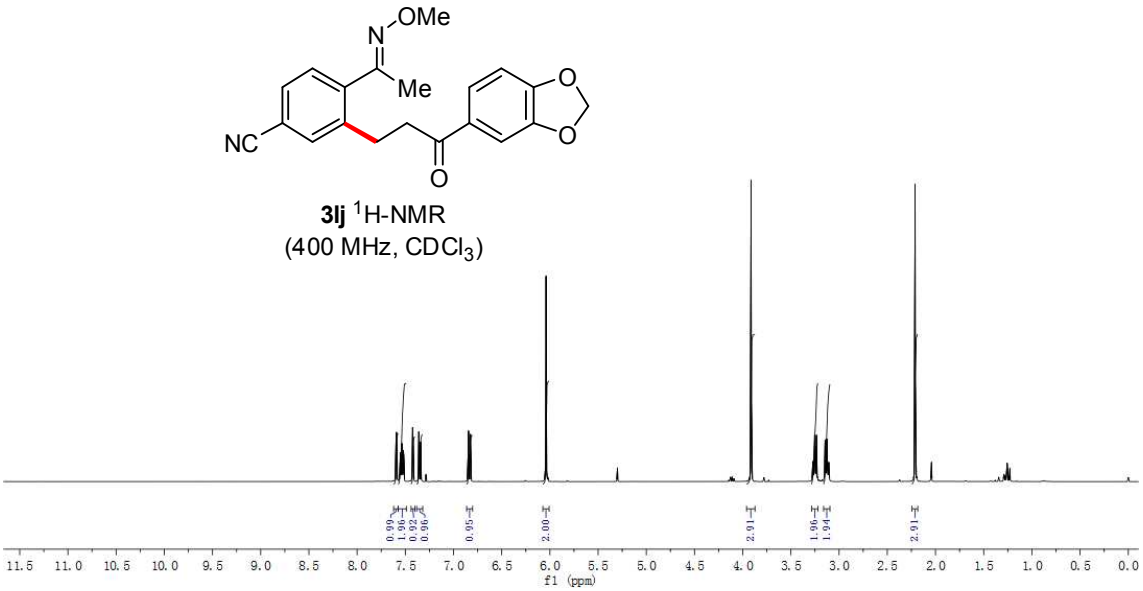


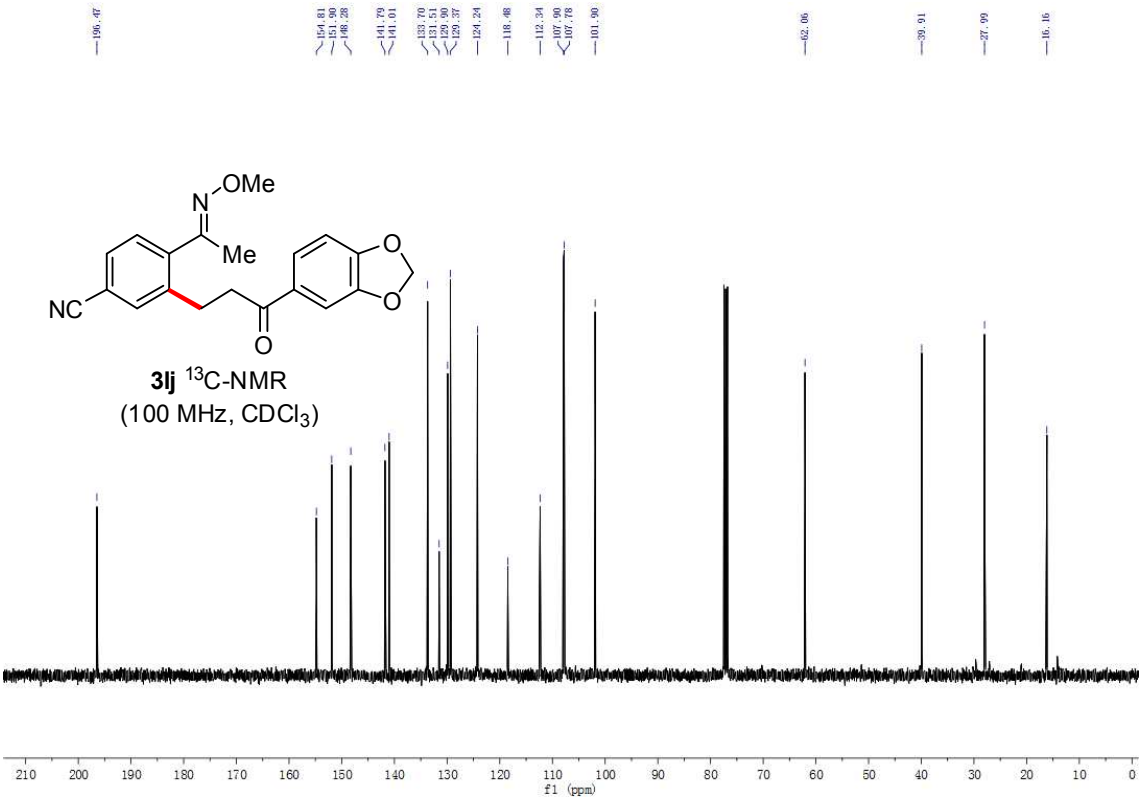
^{1}H NMR and ^{13}C NMR spectra of **3di**



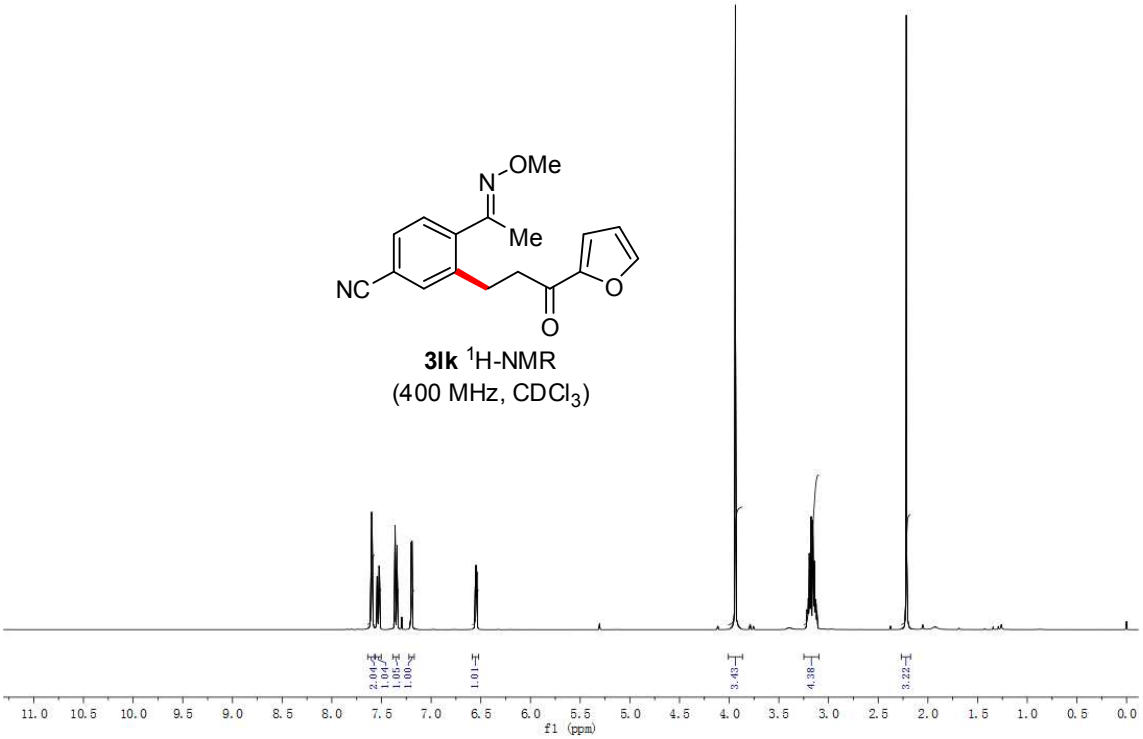


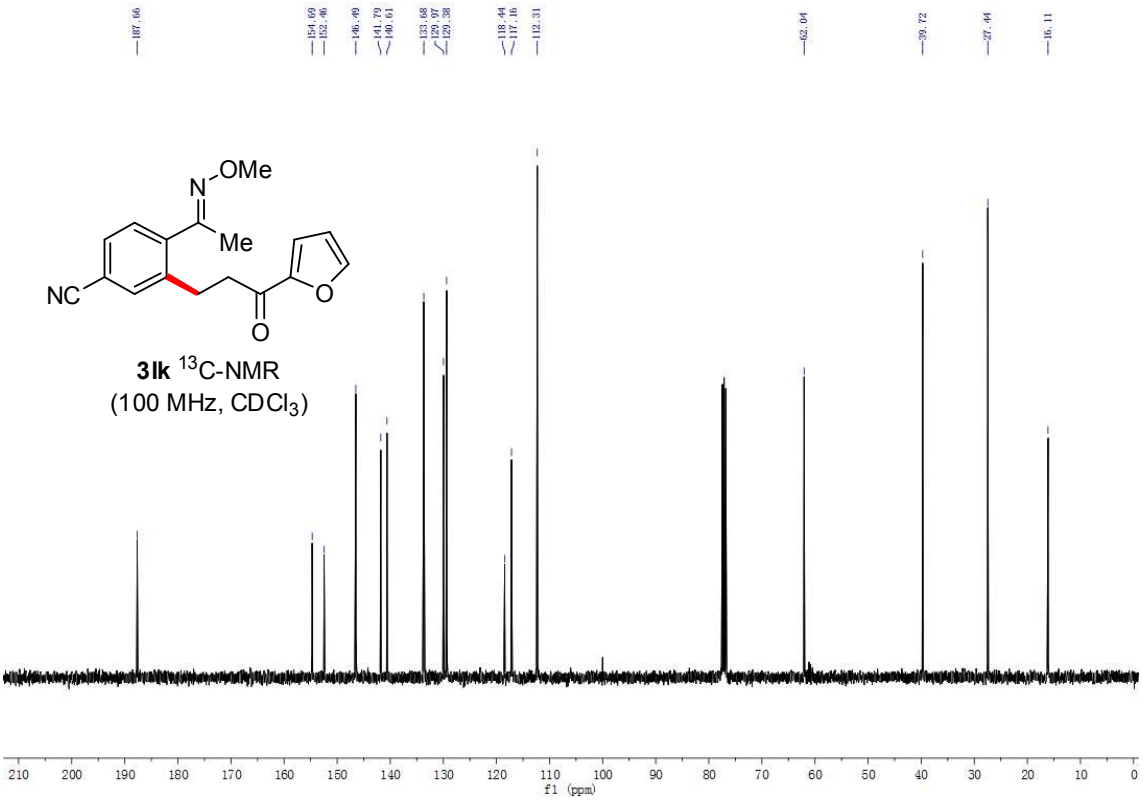
^{1}H NMR and ^{13}C NMR spectra of **3lj**



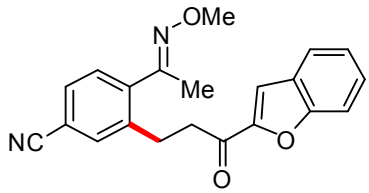


^{1}H NMR and ^{13}C NMR spectra of **3lk**

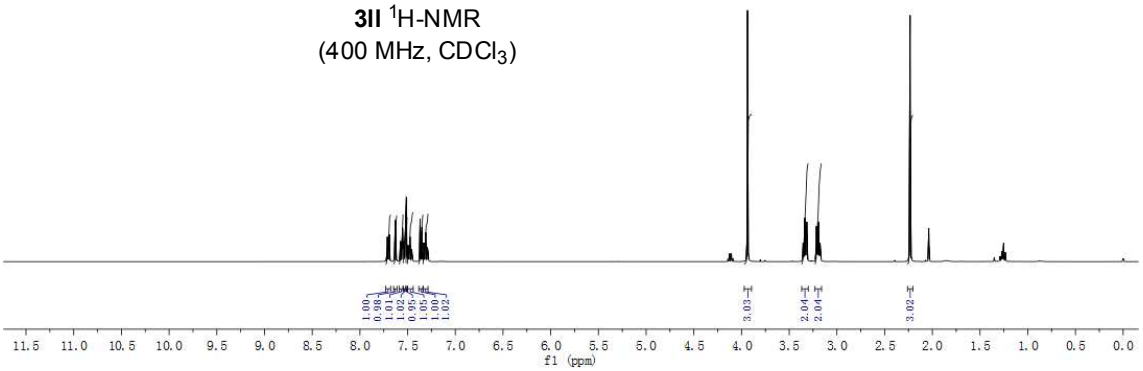


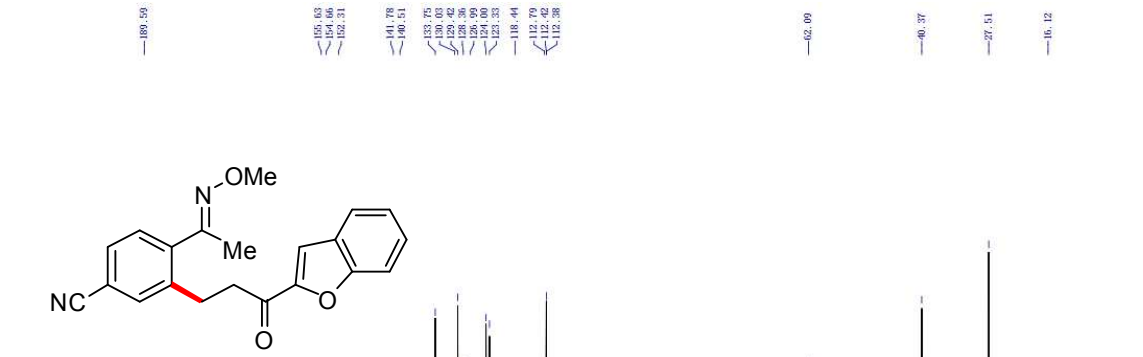


^{1}H NMR and ^{13}C NMR spectra of **3ll**

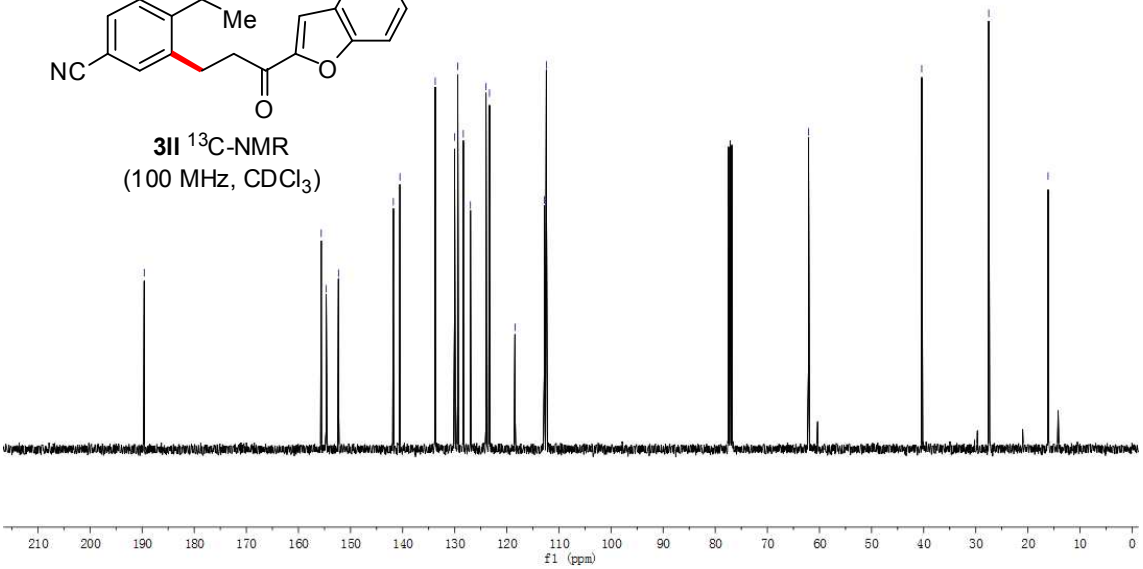


3ll ^{1}H-NMR
(400 MHz, $CDCl_3$)

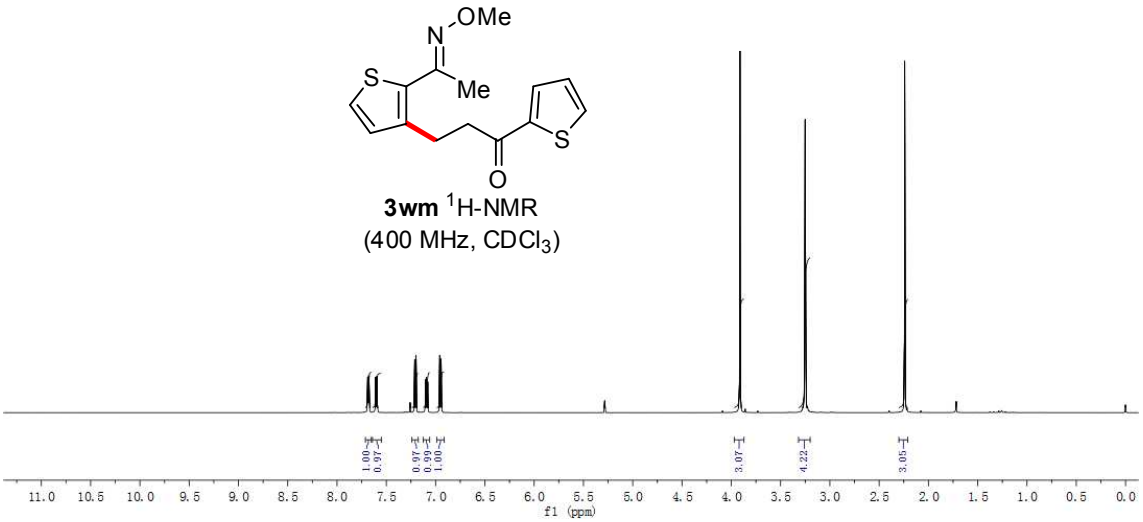


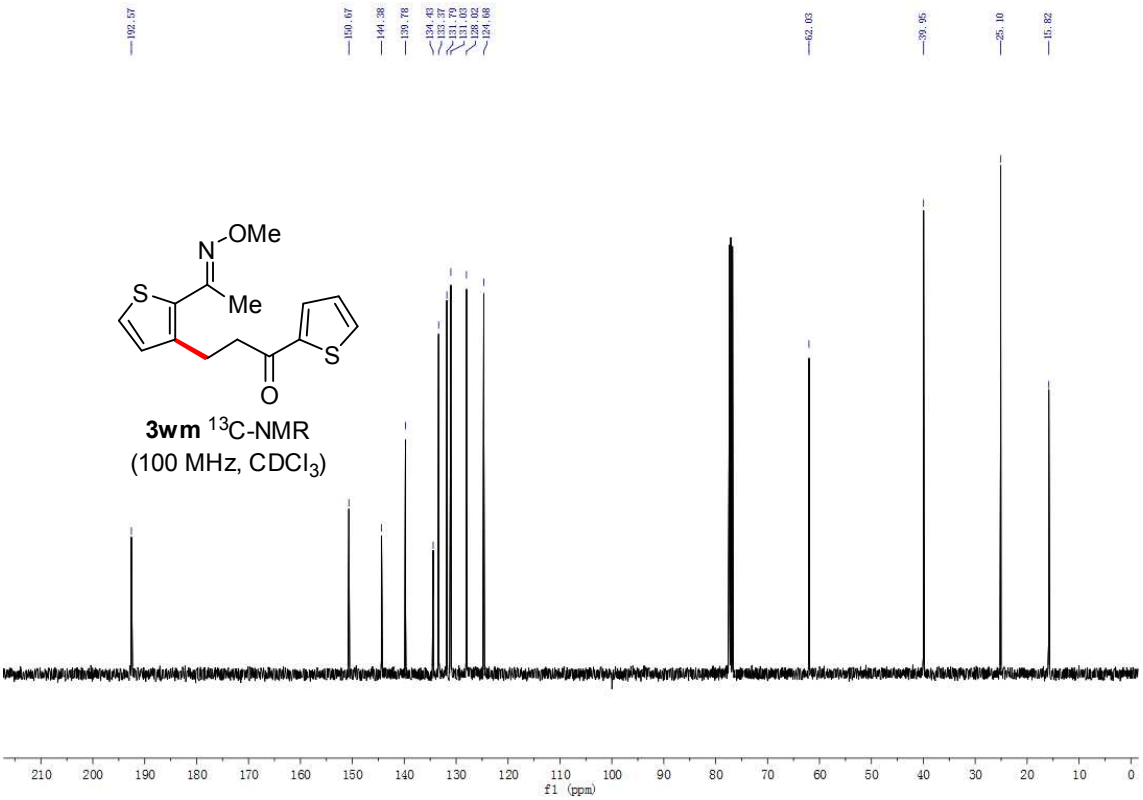


3ll ^{13}C-NMR
(100 MHz, $CDCl_3$)

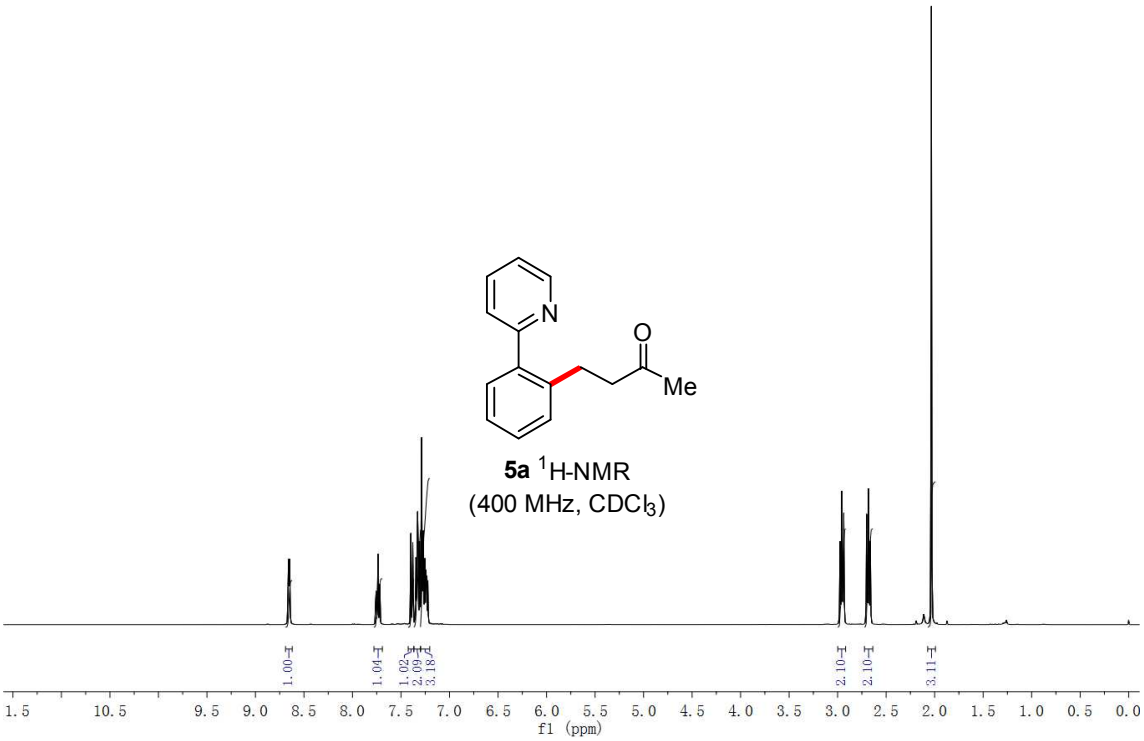


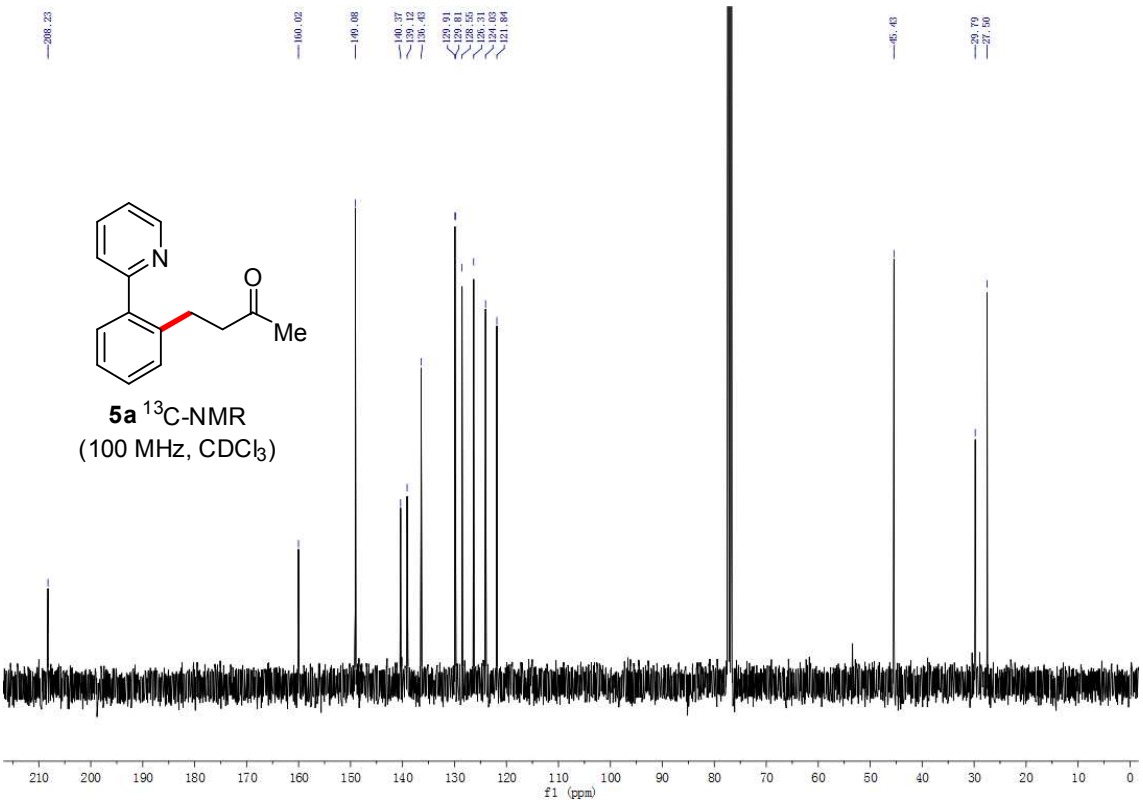
^{1}H NMR and ^{13}C NMR spectra of **3wm**



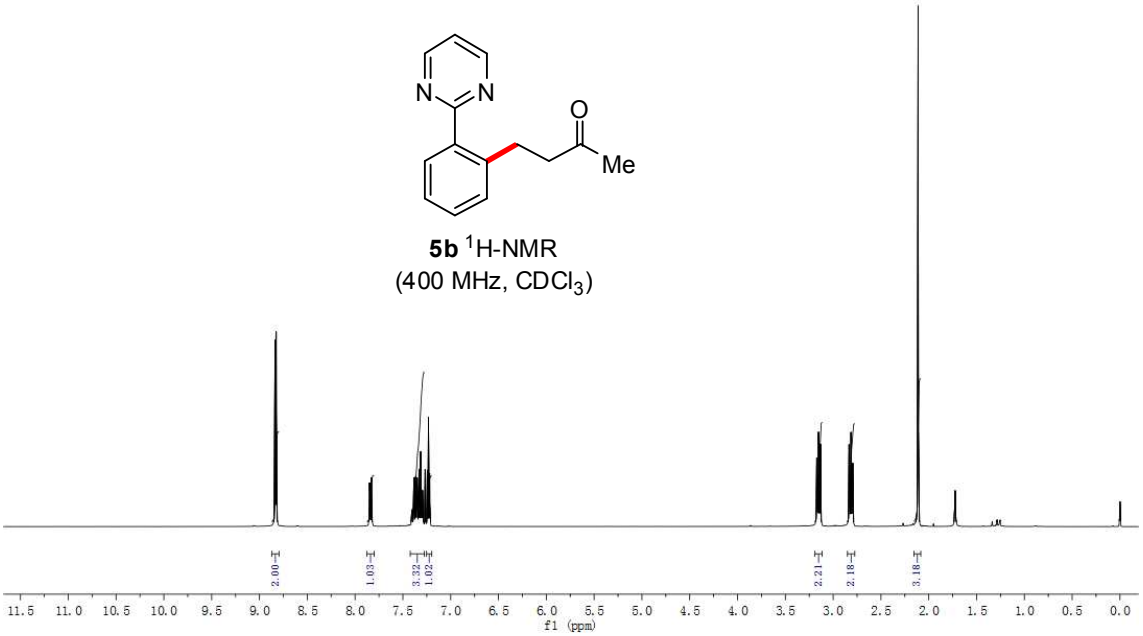


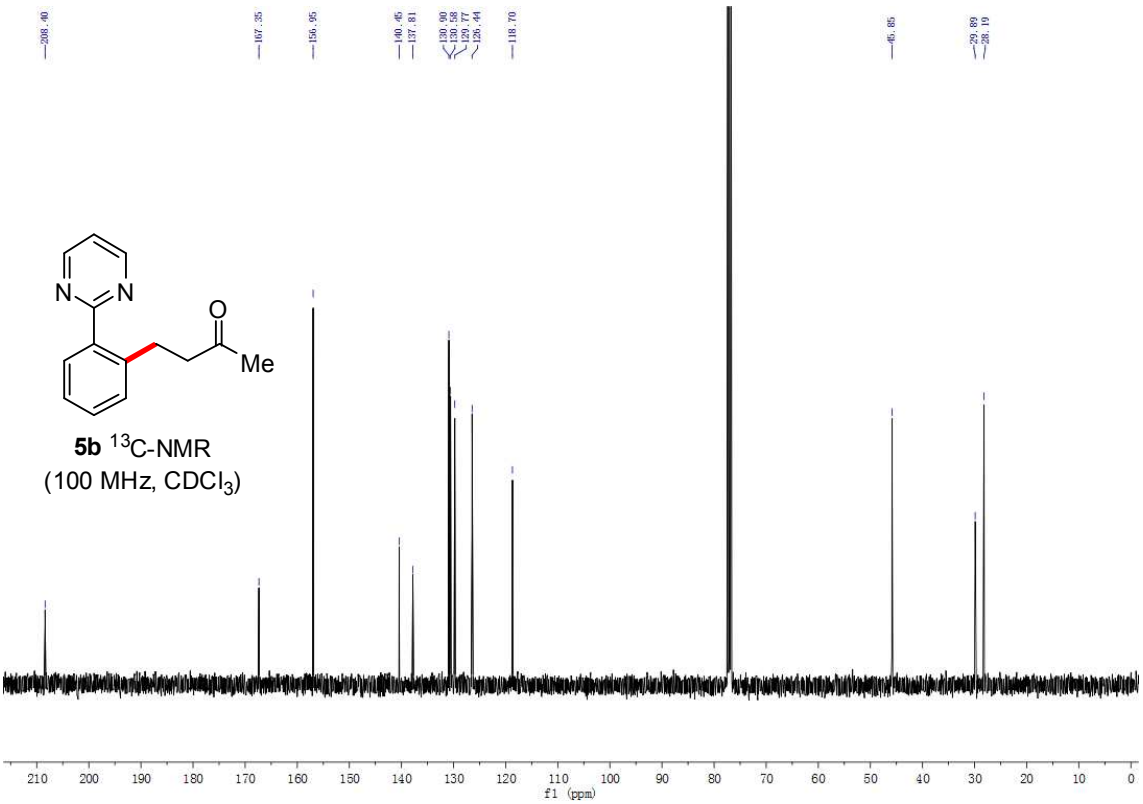
^{1}H NMR and ^{13}C NMR spectra of **5a**



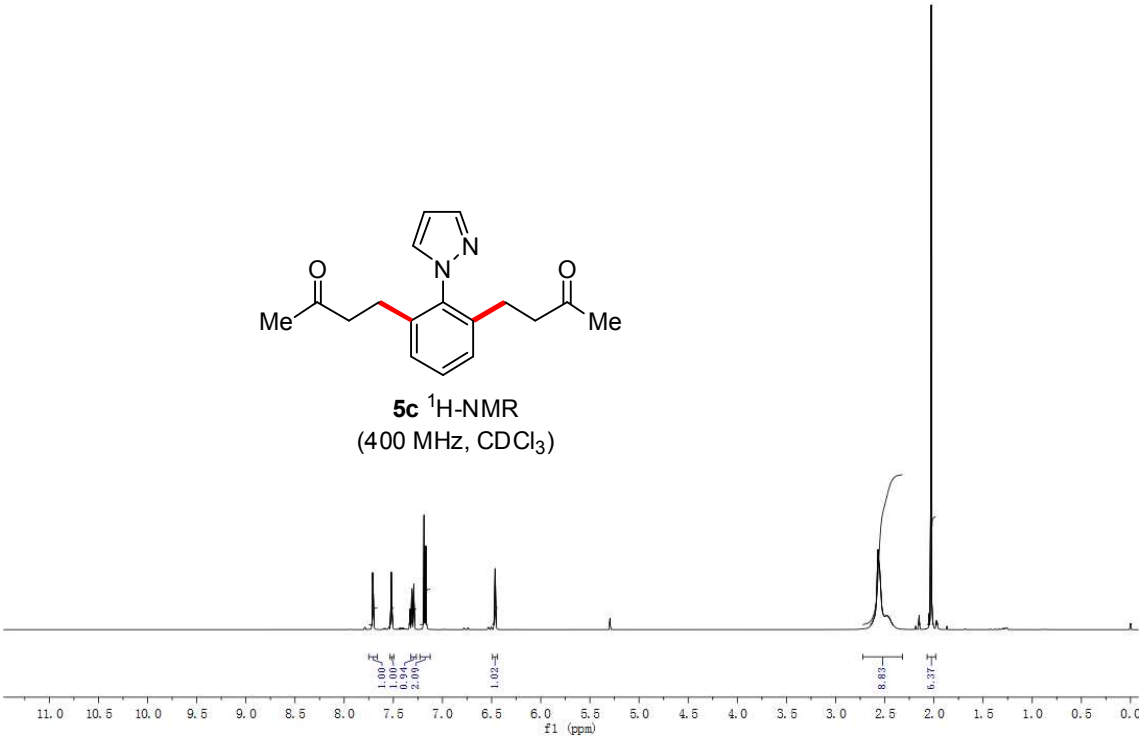


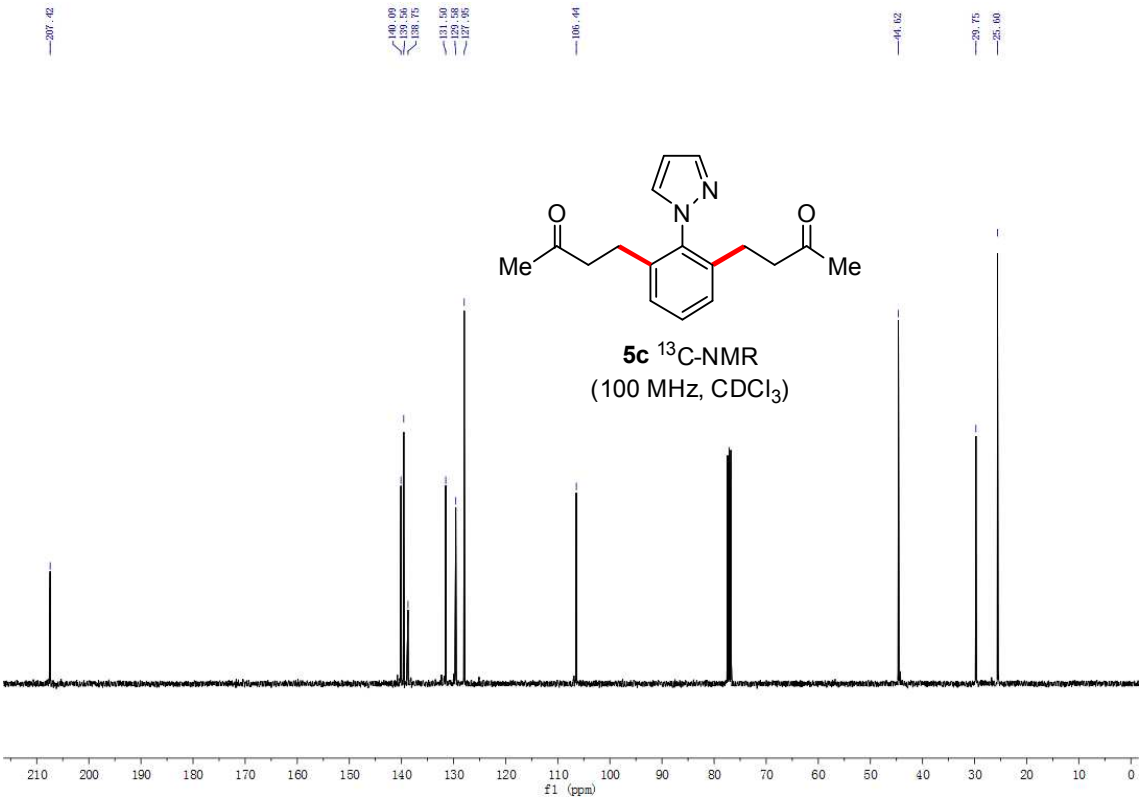
^{1}H NMR and ^{13}C NMR spectra of **5b**



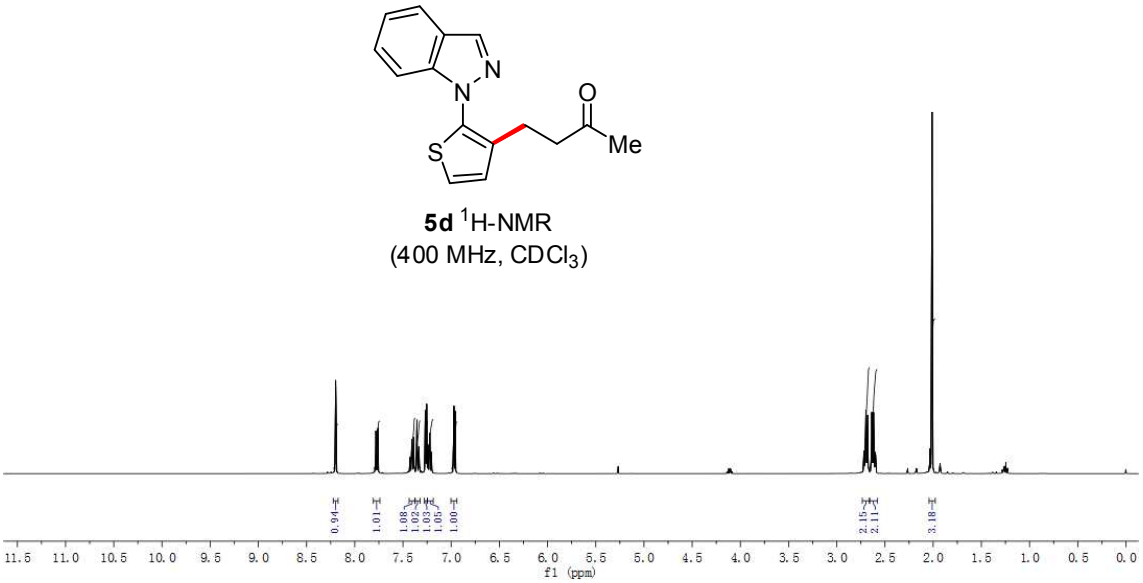


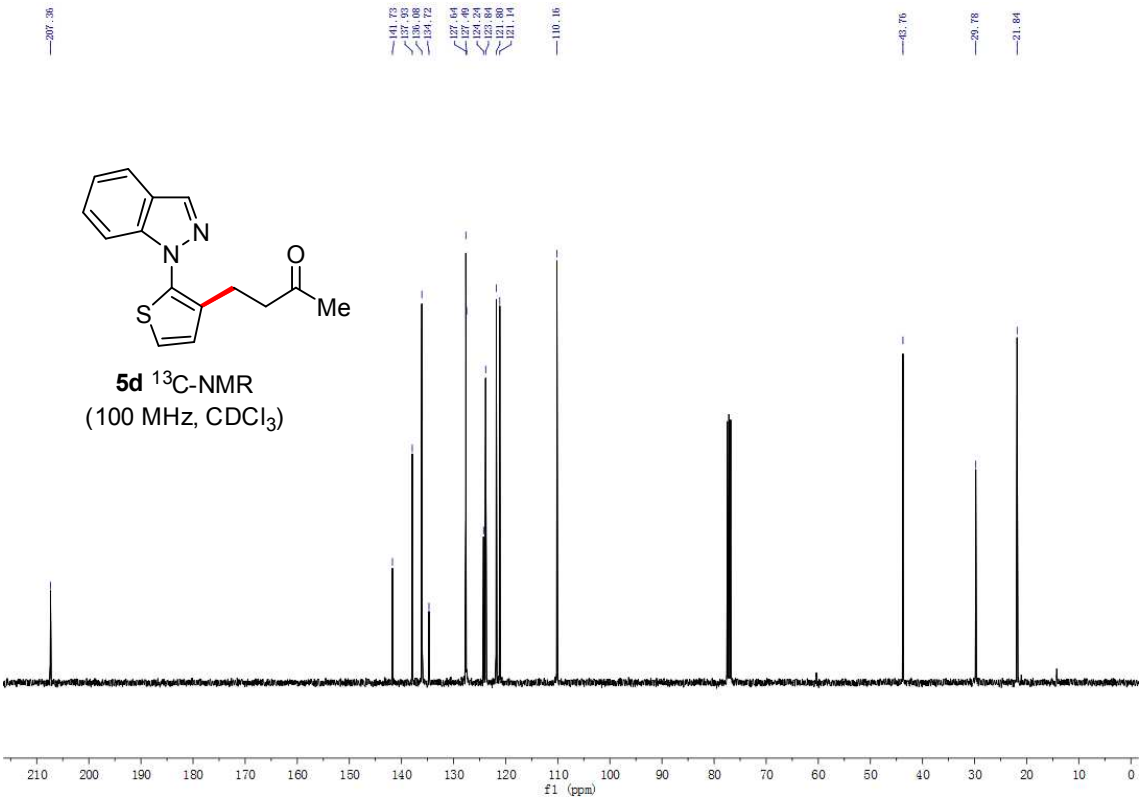
^{1}H NMR and ^{13}C NMR spectra of **5c**



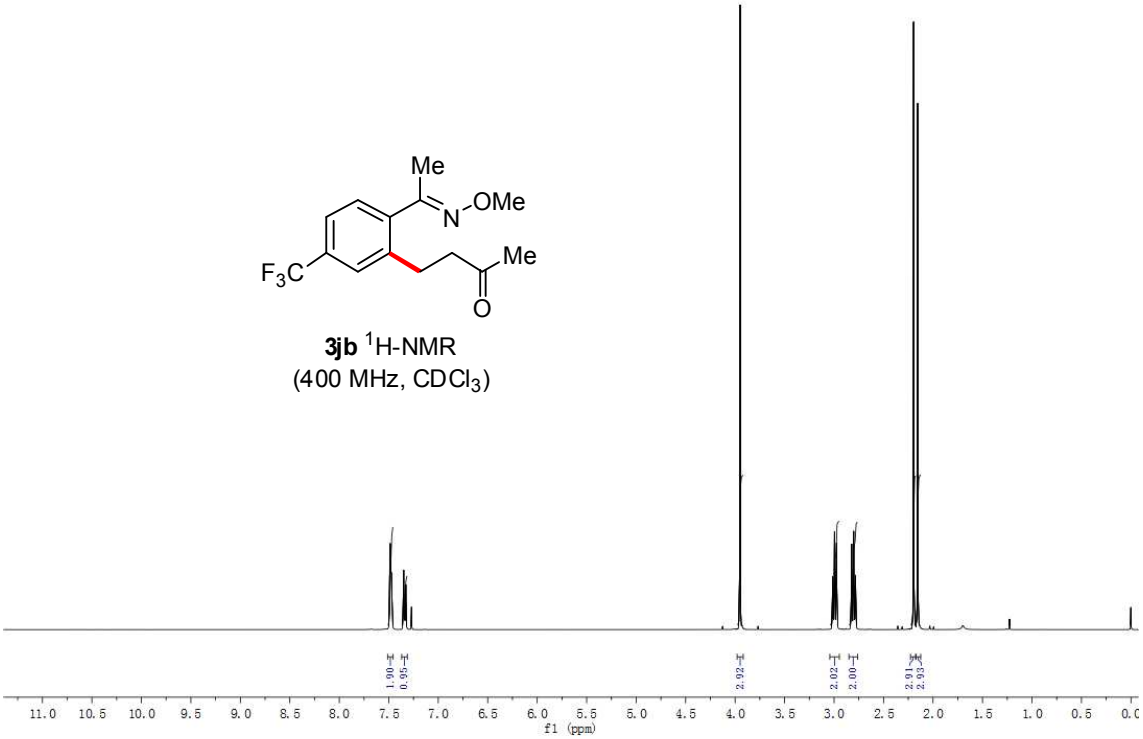


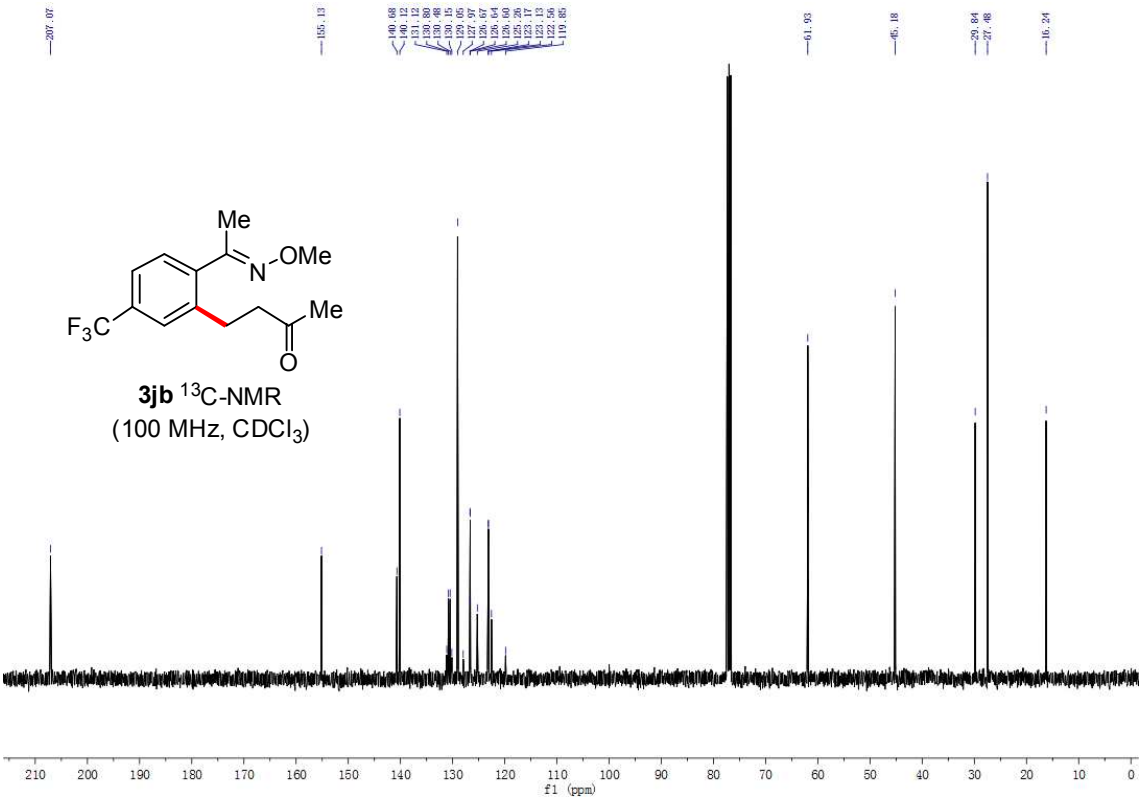
^{1}H NMR and ^{13}C NMR spectra of **5d**

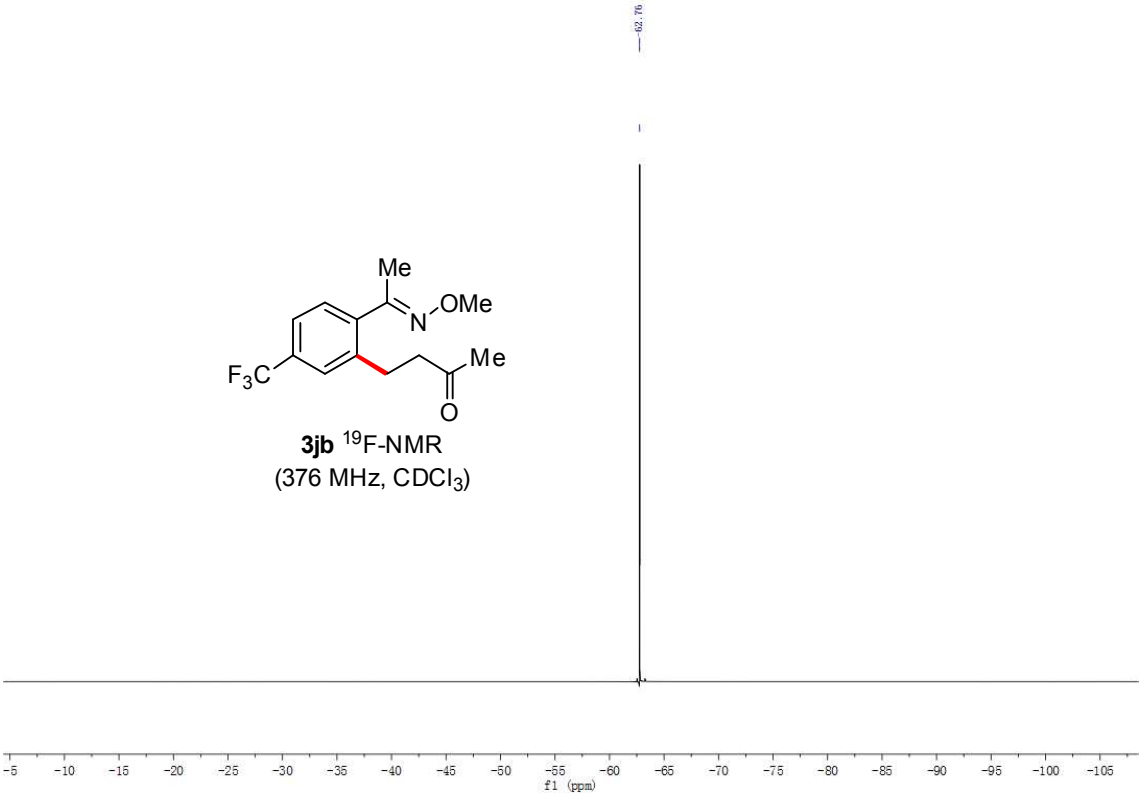




^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **3jb**

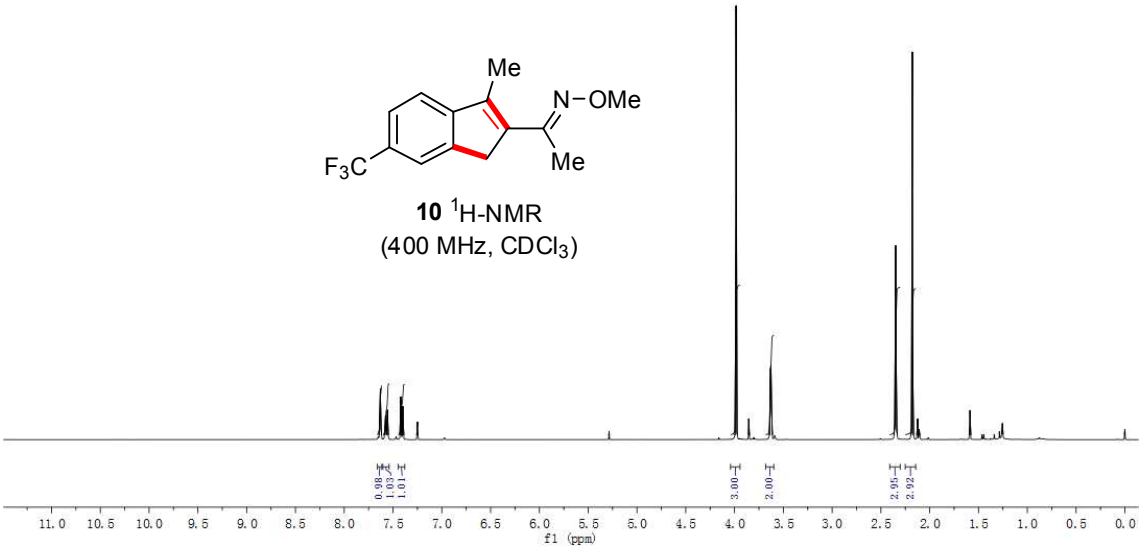


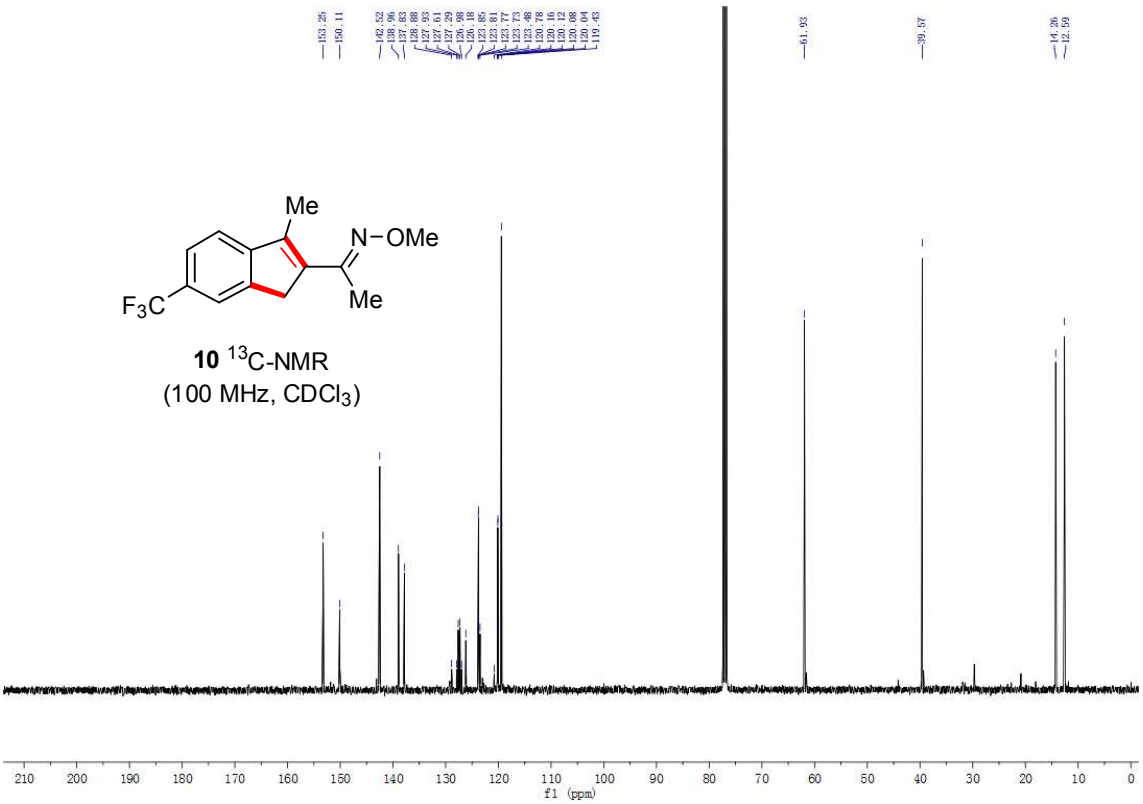


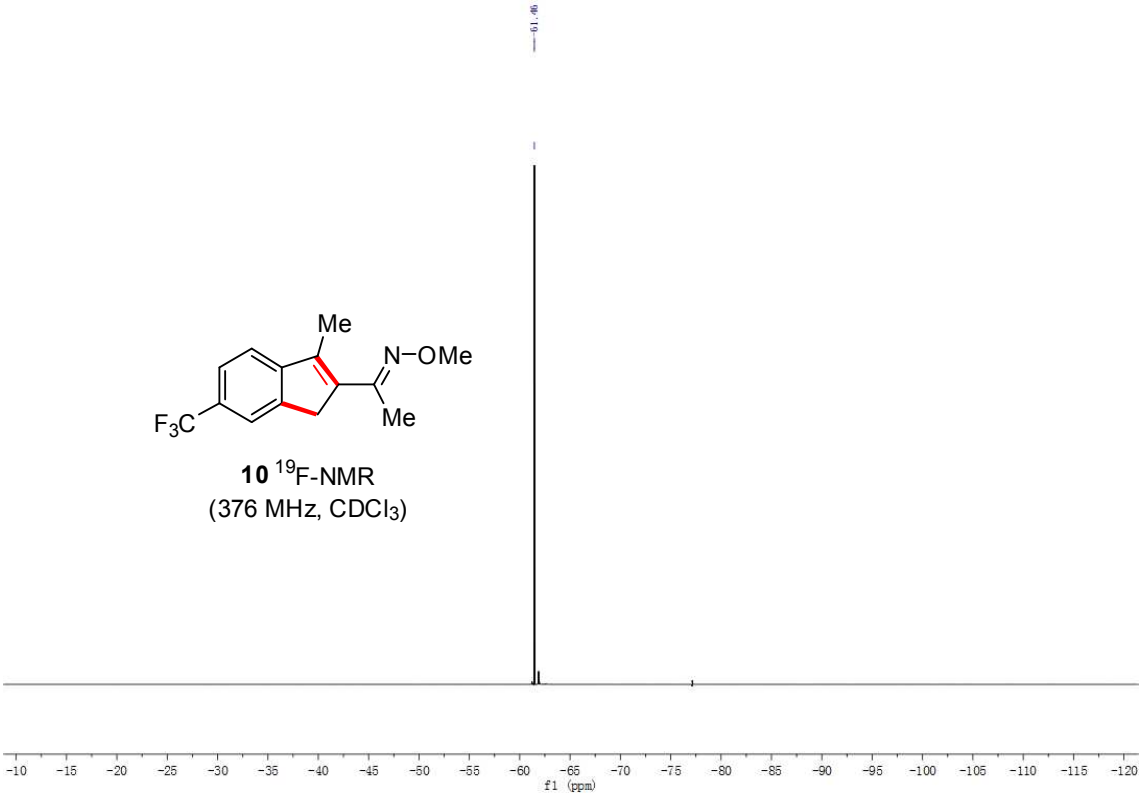


3jb ^{19}F-NMR
(376 MHz, $CDCl_3$)

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of **10**

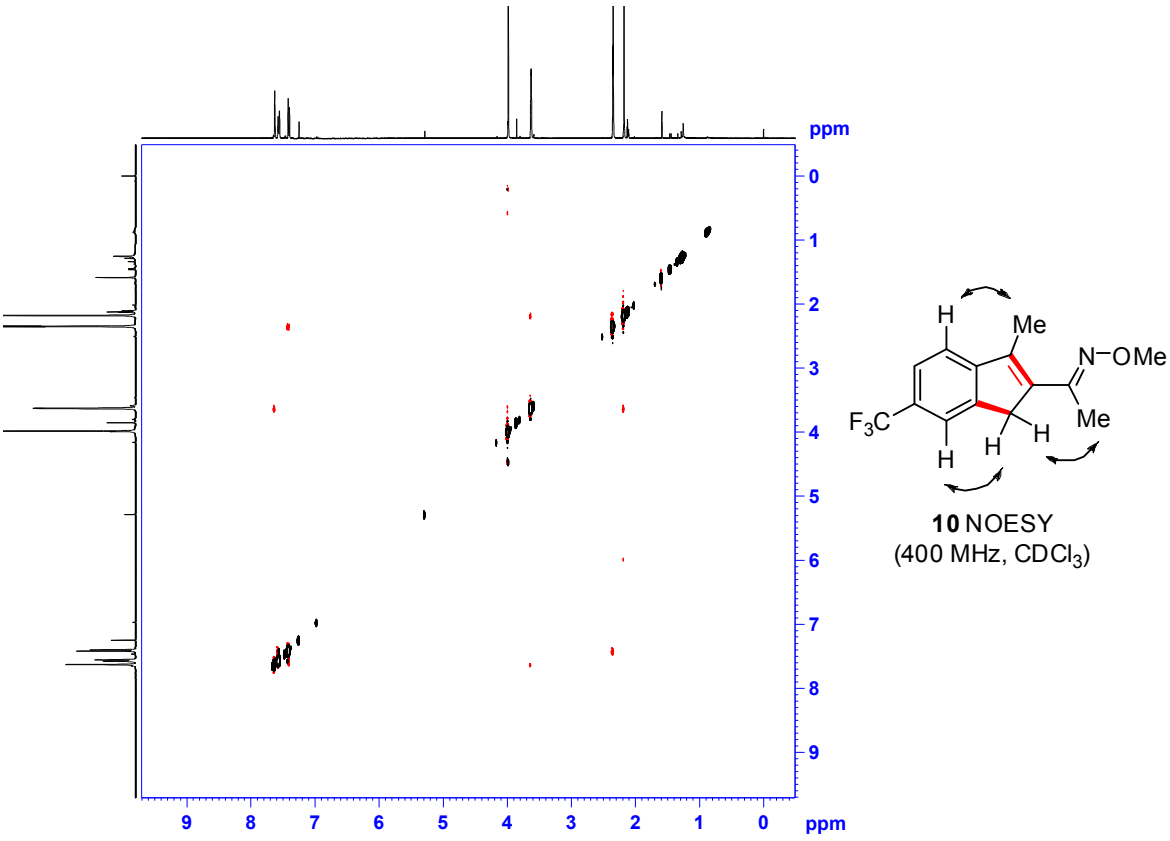






10 ^{19}F-NMR
(376 MHz, $CDCl_3$)

NOESY spectrum of **10**



10 NOESY
(400 MHz, $CDCl_3$)