Supporting Information

Acid-Catalyzed Oxidative Cross-Coupling of Acridans with Silyl Diazoenolates and Rh-Catalyzed Rearrangement: Two-step Synthesis of γ-(9-Acridanylidene)-β-keto Esters

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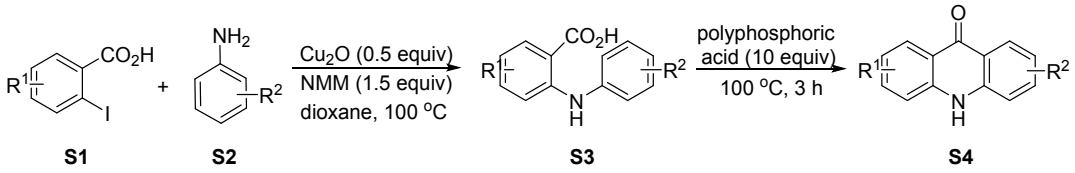
I. General information

Unless otherwise noted, all commercially available compounds and solvents were used as provided without further purification. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.5 mm). For column chromatography, 200-300 mesh silica gel (Qingdao, China) was used. High-resolution mass spectra (HRMS) were performed on ThermoFisher Q Exactive using orbitrap as the mass analyzer with APCI ionization techniques. ^{1}H NMR and ^{13}C NMR spectra were measured recorded on Brucker ARX 400 spectrometer at ambient temperature. Chemical shifts (δ) were given in ppm, referenced to the residual proton resonance of $CDCl_3$ (7.26), to the carbon resonance of $CDCl_3$ (77.16). Coupling constants (*J*) were given in Hertz (Hz). The term, d, t, m, dd referred to doublet, triplet, multiplet, doublet of doublet. UV-Vis spectra were recorded using a PerkinElmer LAMBDA950 spectrophotometer. Emission spectra were recorded on the HITACHI F-4500 fluorescence spectrophotometer and uncorrected.

II. Preparation of acridans

1. Synthesis of acridone

These compound was synthesized according to the known literature procedure.[1,2]

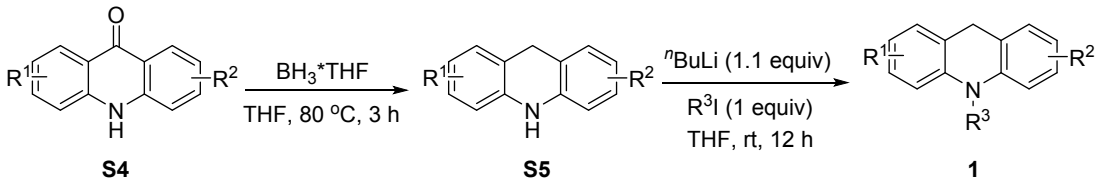


S1 **S2** **S3** **S4**

2-Iodobenzoic acid **S1** (30 mmol), aniline **S2** (36 mmol), N-methylmorpholine (45 mmol), and Cu_2O (15 mmol) were heated to reflux in dioxane (75 mL) under nitrogen atmosphere for 3 h. The reaction mixture was cooled to room temperature, and 200 mL of NaOH (1 N) was then added. The resulting mixture was extracted with DCM (100 mL), and the aqueous phase was acidified with HCl (3 N) to pH = 2. The precipitate was collected and dried in air overnight to give the 2-arylamino benzoic acid **S3**, which was used in the next step without further purification.

A mixture of **S3** (1 mmol) and polyphosphoric acid (10 mmol) was heated at 100 ^{o}C for 3 h. The reaction was completed when brown color of the reaction mixture was faded to yellow. Then, it was poured into hot water (200 ml), which was neutralized by aq. ammonia to PH = 7. The obtained yellow precipitate was filtered off, washed with hot water, and dried in air overnight to give acridone **S4** as a green powder.

2. Synthesis of N-alkyl acridans[3]

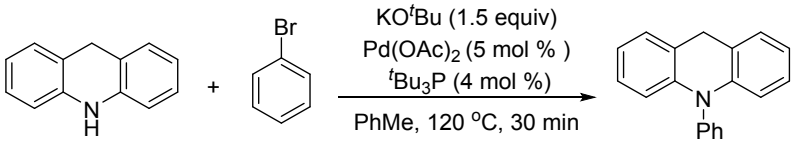


S4 **S5** **1**

To a slurry of acridone **S4** (10 mol) in THF (0.25 M), BH_3·THF solution (1.0 M in THF; 20 mmol) was added dropwise and the mixture was refluxed for 4 h under argon atmosphere. After the completion of the reaction, as monitored by TLC, the mixture was cooled to 0-5 °C and brine was cautiously added followed by the addition of aq. NaOH (2 M, 25 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (1 × 25mL). The collected organic layers were washed with saturated aq. $NaHCO_3$ (1 × 50 mL), dried over Na_2SO_4 and evaporated. The crude product was subjected to column chromatography on silica (eluent: petroleum ether/ethyl acetate = 25/1) to afford acridan **S5** as a light yellowish powder.

A Schlenk-tube equipped with a magnetic stirrer was evacuated and refilled with argon, then charged with a solution of acridan **S5** in THF (0.15 M). A solution of ^{n}BuLi (2.5 M in hexanes; 1.1 equiv) was added dropwise at 0-5 °C and the mixture stirred for 1 h. Then alkyl iodide (1.0 equiv) dissolved in THF (1 M) was added. After stirring at at 0-5 °C for 2 h, the mixture was warmed to room temperature and stirred overnight. The reaction was quenched by pouring into H_2O, and the product was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was subjected to column chromatography on silica (eluent: petroleum ether /ethyl acetate = 50/1) to afford N-alkyl acridine as a white solid.

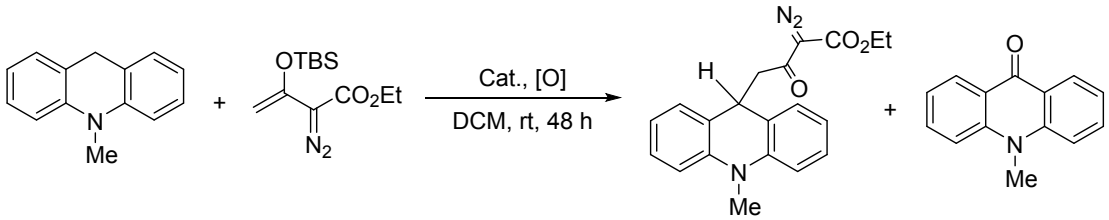
Synthesis of N-phenyl acridane 1d[3]



To a two-neck round bottle flask equipped with a magnetic stirrer and a reflux condenser was charged with 9,10-dihydroacridine (10.0 mmol), $Pd(OAc)_2$ (0.5 mmol), tris(^{t}butyl)phosphine (0.4 mmol), and KO^{t}Bu (15.0 mmol). The flask was evacuated and refilled with argon. Then bromobenzene (11.0 mmol) and toluene (12 mL) were injected via a syringe. The reaction mixture was stirred under reflux for 30 min and then was cooled to room temperature. After purification by column chromatography (eluent: petroleum ether/ethyl acetate =25/1), N-phenylacridane was obtained as a white solid.

III. Optimization of reaction conditions

Table S1. Oxidative coupling of **1a** and **2a** using various catalysts and oxidants [a]

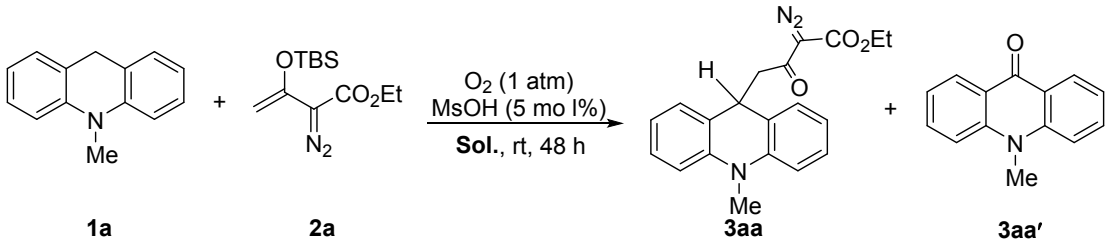


1a **2a** **3aa** **3aa′**

Entry	Cat. (mol%)	[O]	**3aa** [%][b]	**3aa'**[%][b]
1	$FeCl_2$ (10)	TBHP (2.0)	36	21
2	$FeCl_2$ (10)	DTBP (2.0)	trace	19
3	CuBr (10)	TBHP (2.0)	39	28
4	CuBr (10)	DTBP (2.0)	25	23
5	MsOH (5)	TBHP (2.0)	29	15
6	TfOH (5)	DTBP (2.0)	23	22
7	MsOH (5)	O_2 bar	91	trace
8	TfOH (5)	O_2 bar	67	5
9	MsOH (5)	Air	38	trace

[a] Reaction conditions: **1a** (0.5 mmol, 1.0 equiv), **2a** (1.0 mmol, 2.0 equiv), catalyst, oxidant and DCM (1.0 mL), room temperature, 48 h. [b] Yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S2. Oxidative coupling of **1a** and **2a** in various solvents [a]

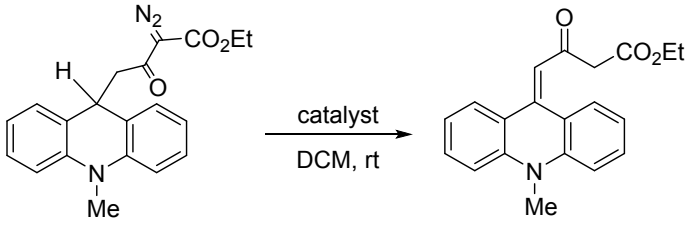


1a **2a** **3aa** **3aa′**

Entry	Solvent	**3aa** [%][b]	**3aa'**[%][b]
1	DCM	91	trace
2	acetone	60	trace
3	CH_3CN	77	trace
4	EtOAc	32	trace
5	MeOH	0	trace

[a] Reaction conditions: the 1 mL solution of **1a** (0.5 mmol, 1.0 equiv), **2a** (1.0 mmol, 2.0 equiv) and MsOH (5 mol%) was stirred at room temperature under 1 atm of O_2 for 48 h. [b] Yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S3. The effects of catalyst on the rearrangement of **3aa** [a]



3aa **7a**

Entry	catalyst	time	**7a** [%][b]
1	$Rh_2(OAc)_4$	15 min	93
2	$Cu(MeCN)_4PF_6$	8 h	76
3	$Cu(OTf)_2$	8 h	71

[a] The reaction was carried out using 0.2 mmol of **3aa**, 1 mol % of catalyst in 1 mL of CH_2Cl_2 at room temperature. [b] Isolated yield.

IV. The fluorescent properties of products

Addition of strong acids to **7a** in CD_3CN, such as trifluoro acetic acid (TFA), a significant color change from deep red to bright yellow was observed for a **7a** solution. When the solution was neutralized by a base, the color of the solution started to deepen gradually and return to the original deep red eventually. The UV-vis

absorbance spectra show that new bands rise at 260 nm and 370 nm, indicating the formation of an acridinium cation during the addition of TFA.

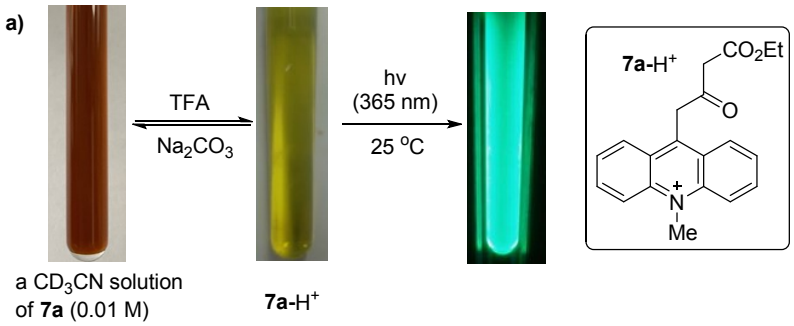


Figure S1. The CD_3CN solution of **7a** (left), protonated **7a** at daylight (middle) and upon irradiation at 365 nm (right).

UV/vis TFA titration of **7a**, 0.035 mM in MeCN. Arrows indicate the hyper –or hypochromic shift from low TFA – to high TFA concentration.

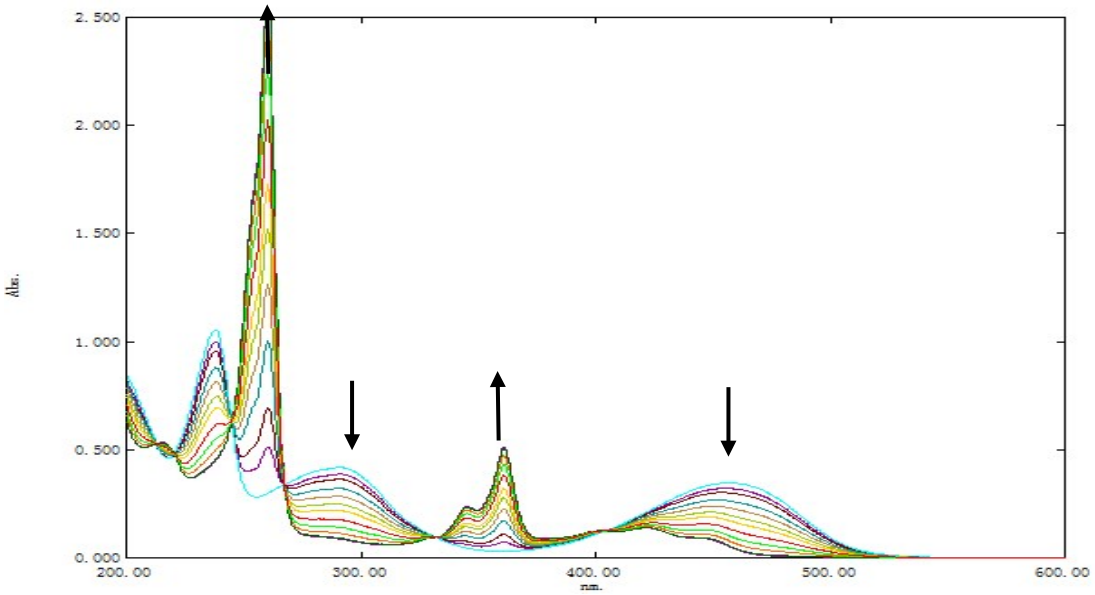


Figure S3. UV/Vis-monitored TFA titration of **7a** in MeCN

Emission spectra for protonated **7a**, **7b**, **7c** and **7e** excited at 370 nm, the acridinium cation **7a-H**$^+$ in MeCN displayed a maximum emission at 505 nm. The N-protected groups have little effects on the λ_{em}^{max} of acridinium cations (**7b-H**$^+$and **7c-H**$^+$), while the spectra of acridinium cation **7e-H**$^+$ bearing an methoxy group on the aromatic ring underwent a bathochromic-shift in emission (λ_{em}^{max} = 550 nm).

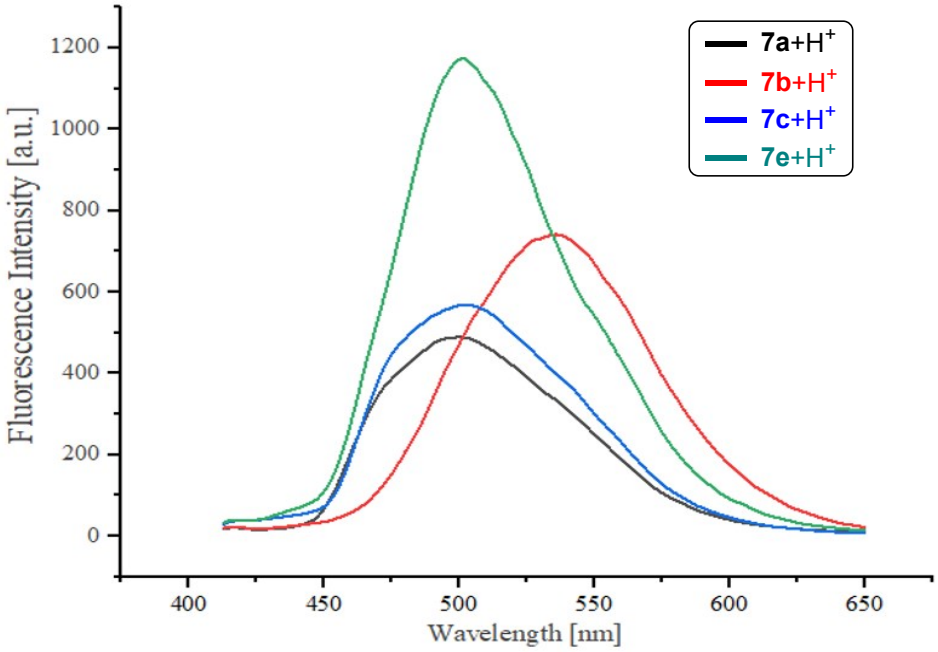


Figure S3. Emission spectra for protonated **7a**, **7b**, **7c** and **7e**.

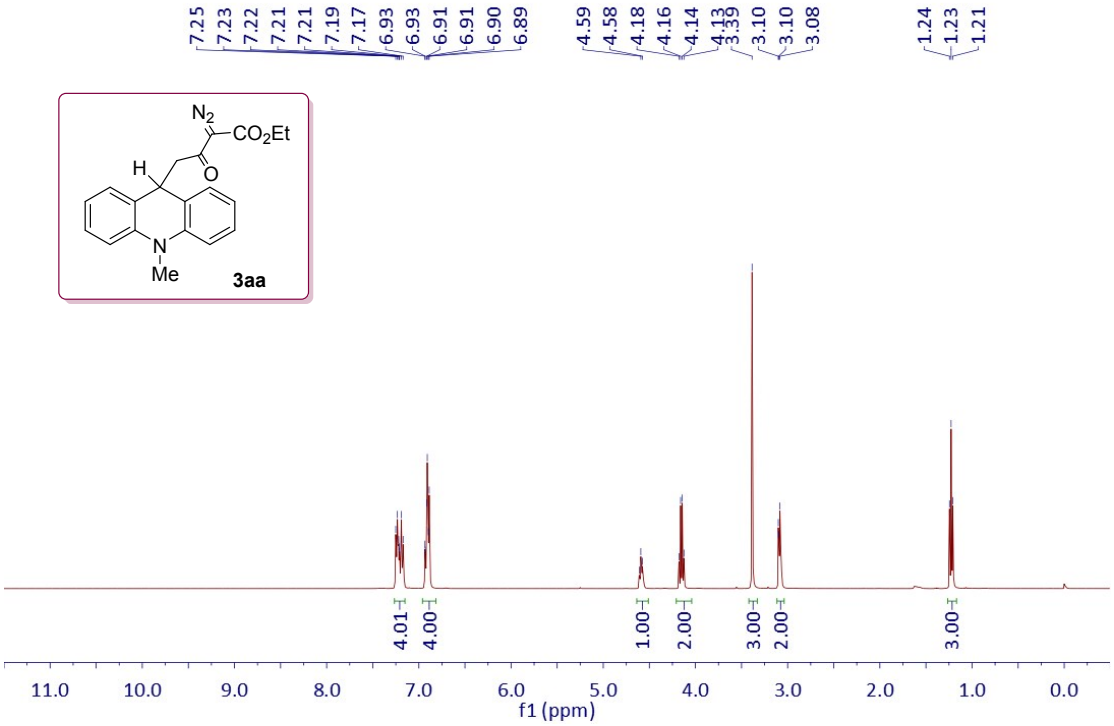
V. References

[1] Z. Zheng, L. Dian, Y Yuan, D. Zhang-Negrerie, Y. Du, K Zhao. *J. Org. Chem.* **2014**, *79*, 7451.

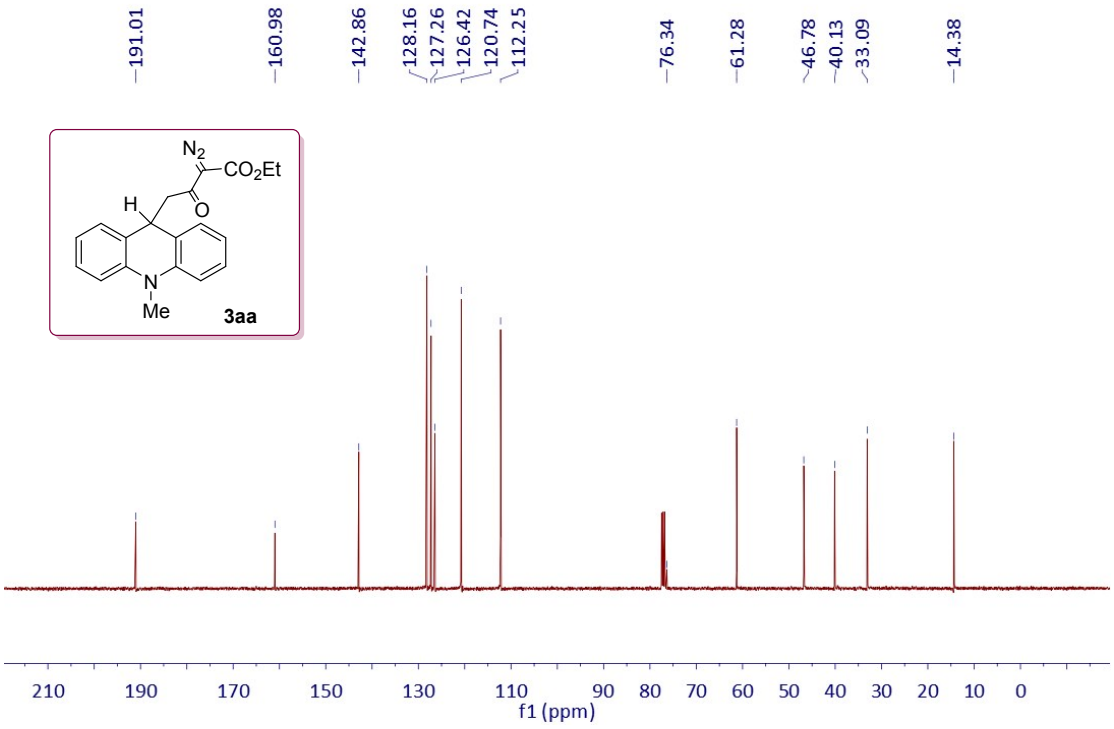
[2] M. Mohammadi-Khanaposhtani, M.Saeedi, N. S. Zafarghandi, M. Mahdavi, R. Sabourian, E. K. Razkenari, H. Alinezhad, M.Khanavi, A. Foroumadi, A.Shafiee, T. Akbarzadeh. *Eur. J. Med. Chem.* **2015**, *92*, 799.

[3] Á. Pintér, A. Sud, D. Sureshkumar, M. Klussmann. *Angew. Chem. Int. Ed.* **2010**, *49*, 5004.

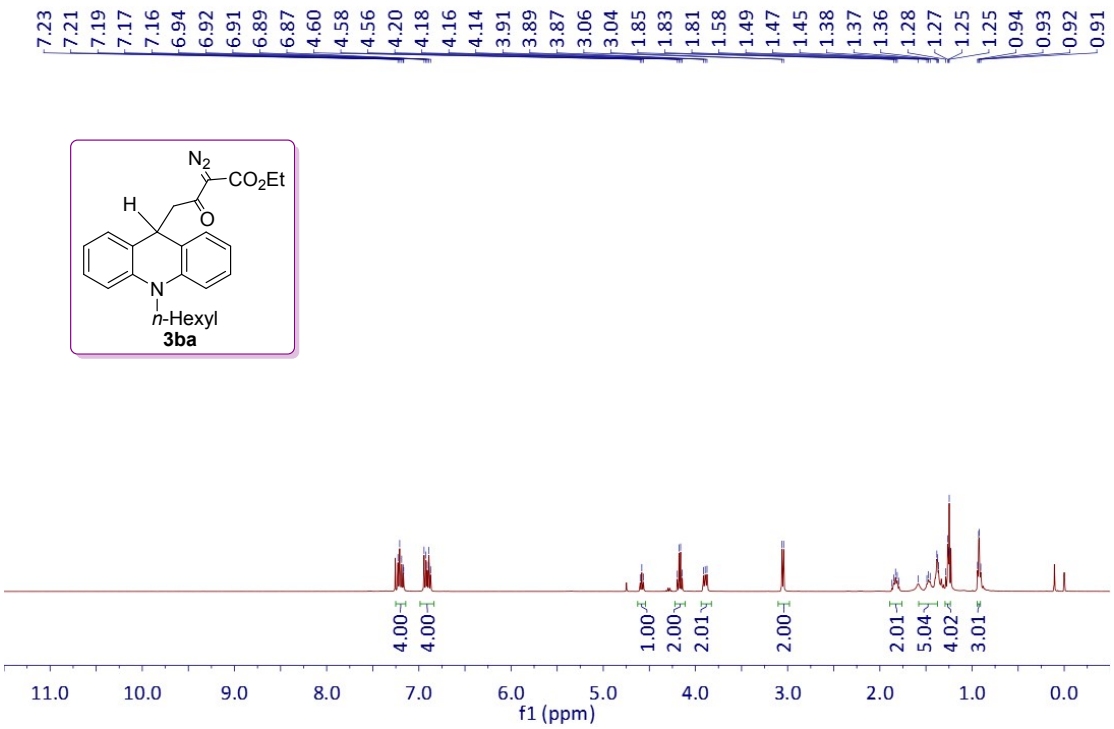
VI. Copies of ^{1}H and ^{13}C NMR spectra of products



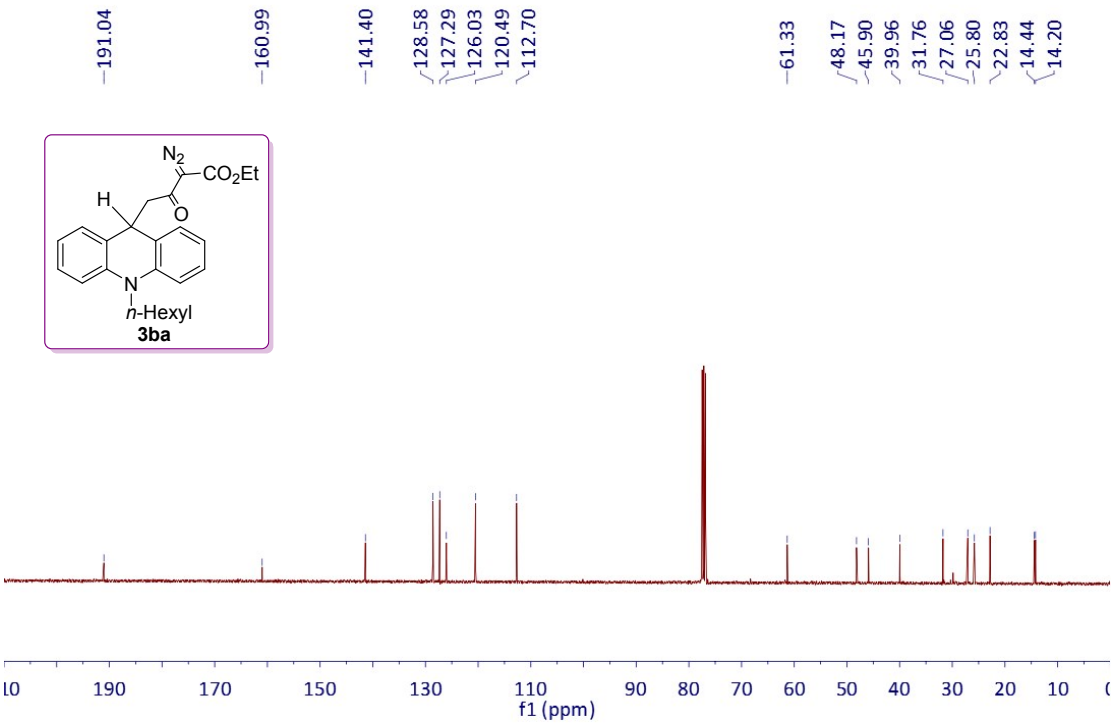
^{1}H-NMR of **3aa** ($CDCl_3$, 400Hz)



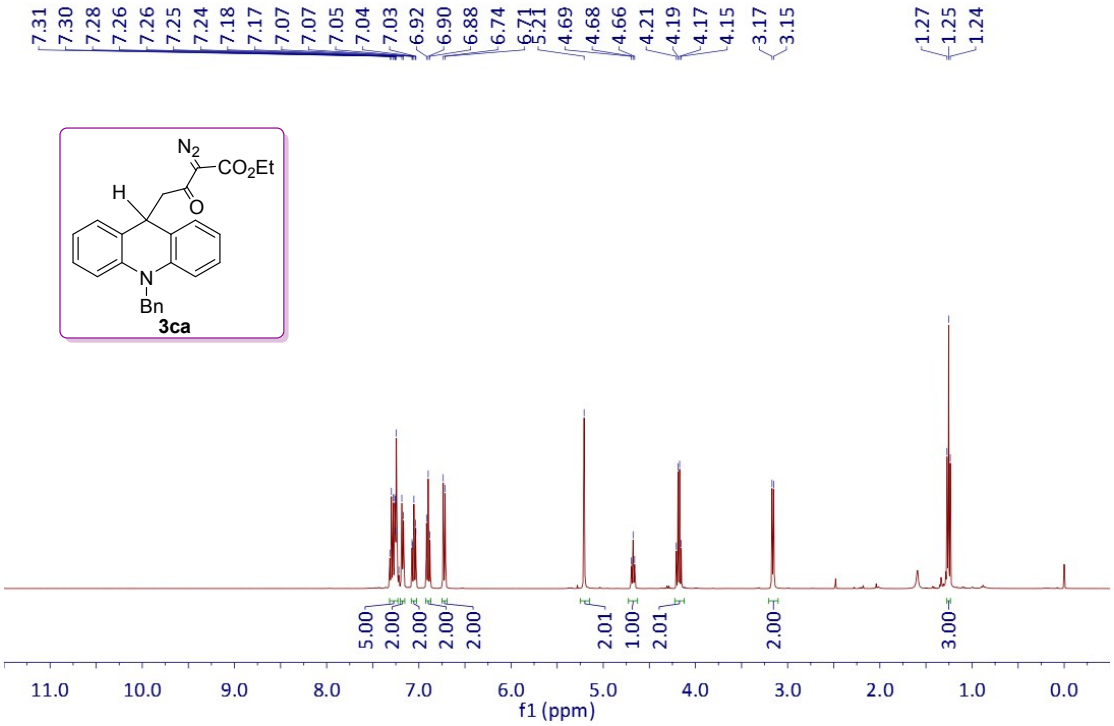
^{13}C-NMR of **3aa** ($CDCl_3$, 100Hz)



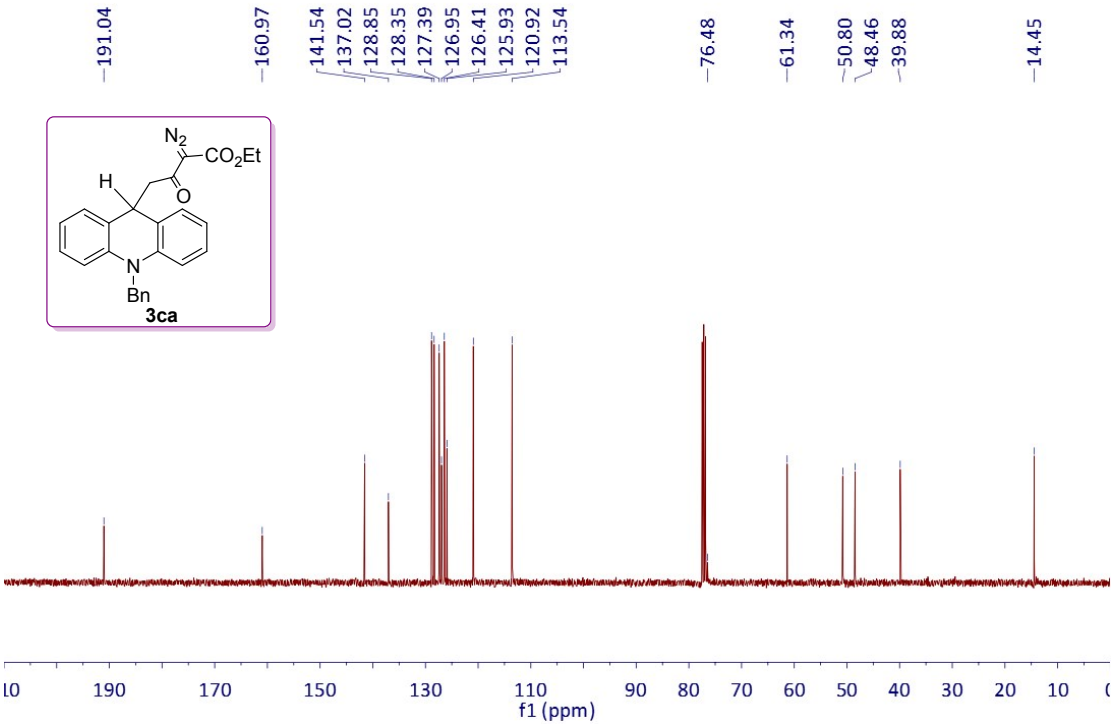
^{1}H-NMR of **3ba** ($CDCl_3$, 400Hz)



^{13}C-NMR of **3ba** ($CDCl_3$, 100Hz)



^{1}H-NMR of **3ca** ($CDCl_3$, 400Hz)



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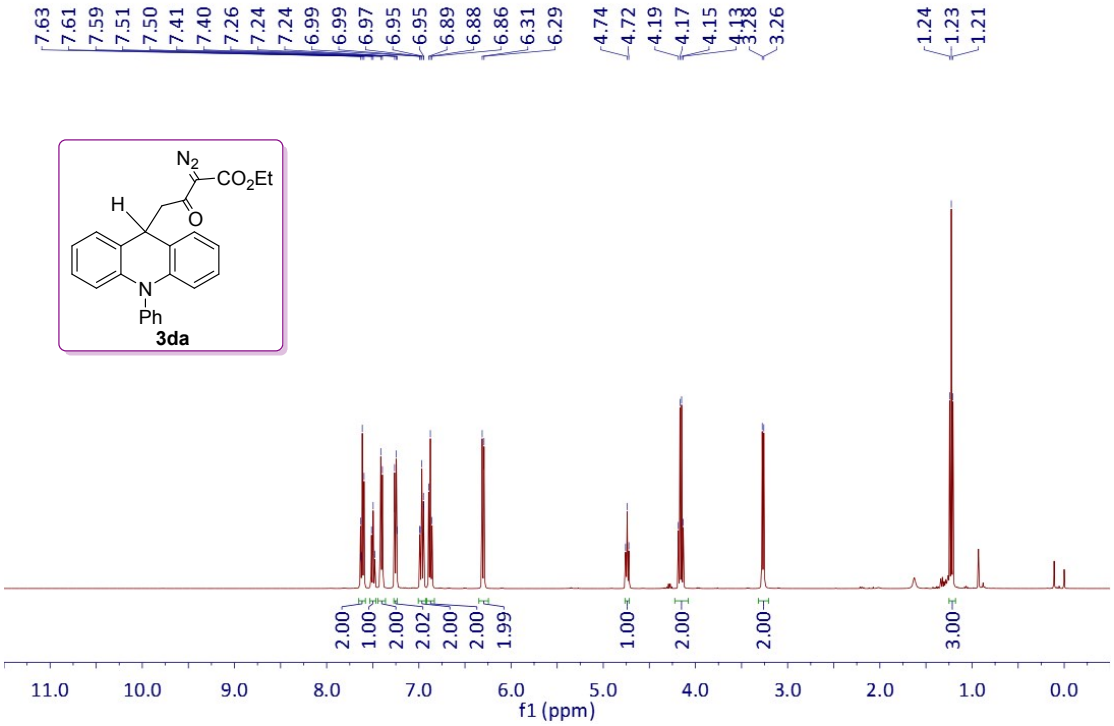

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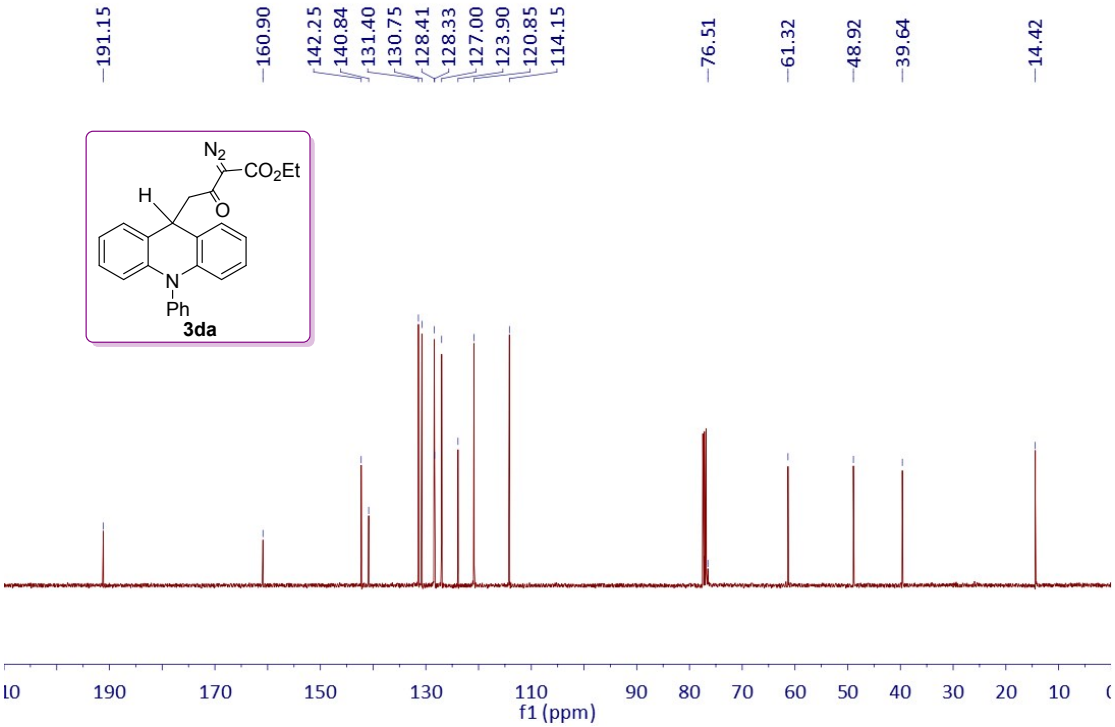

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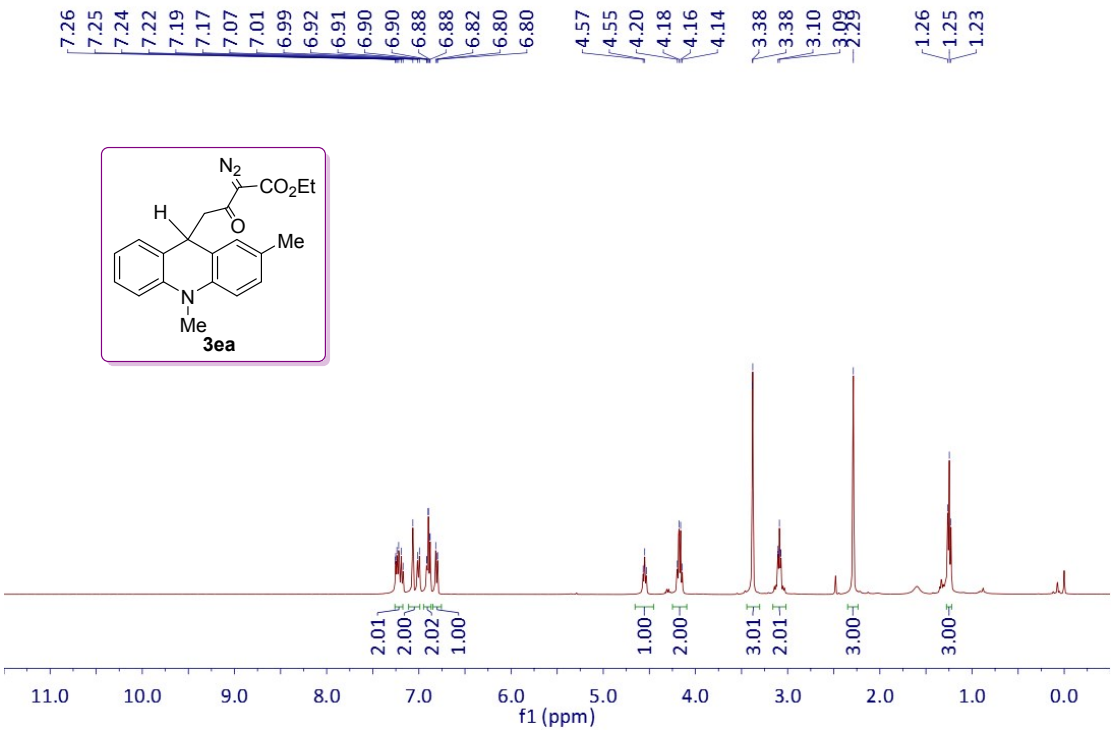

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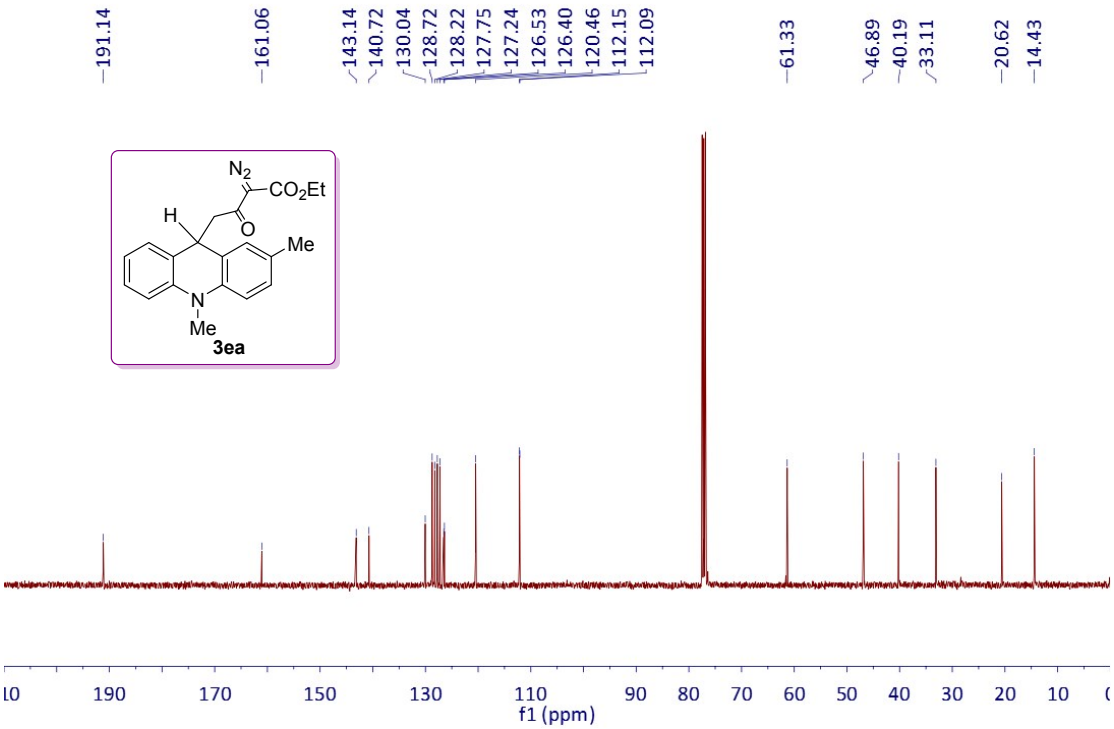

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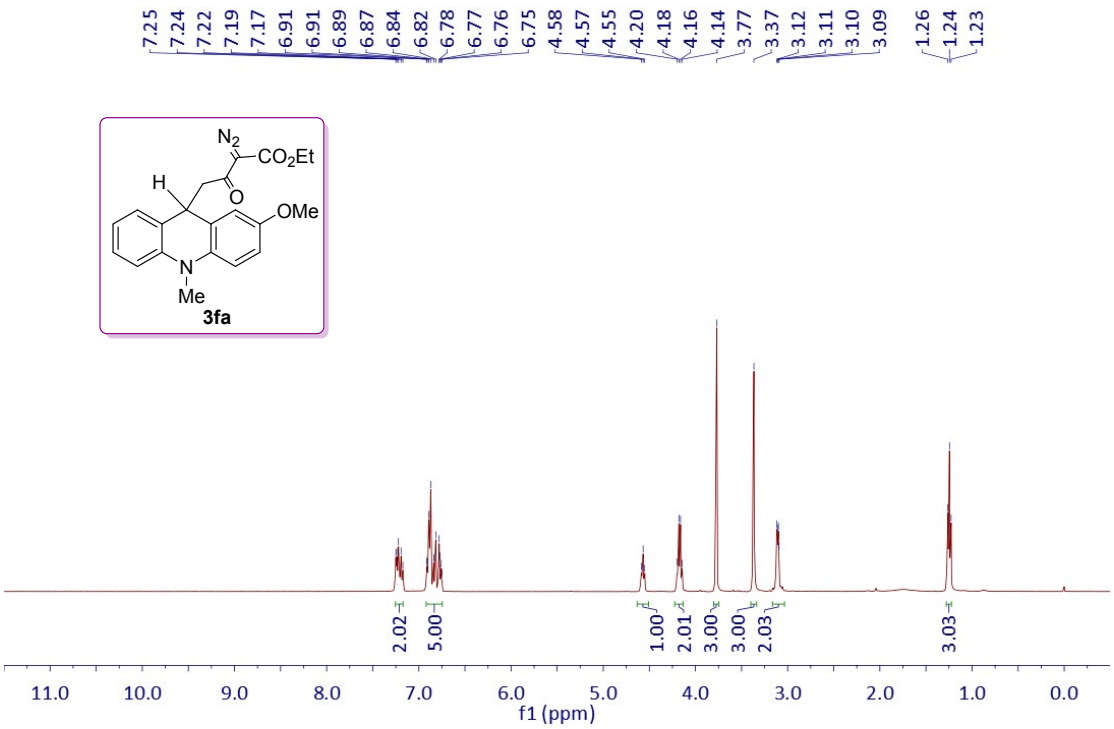

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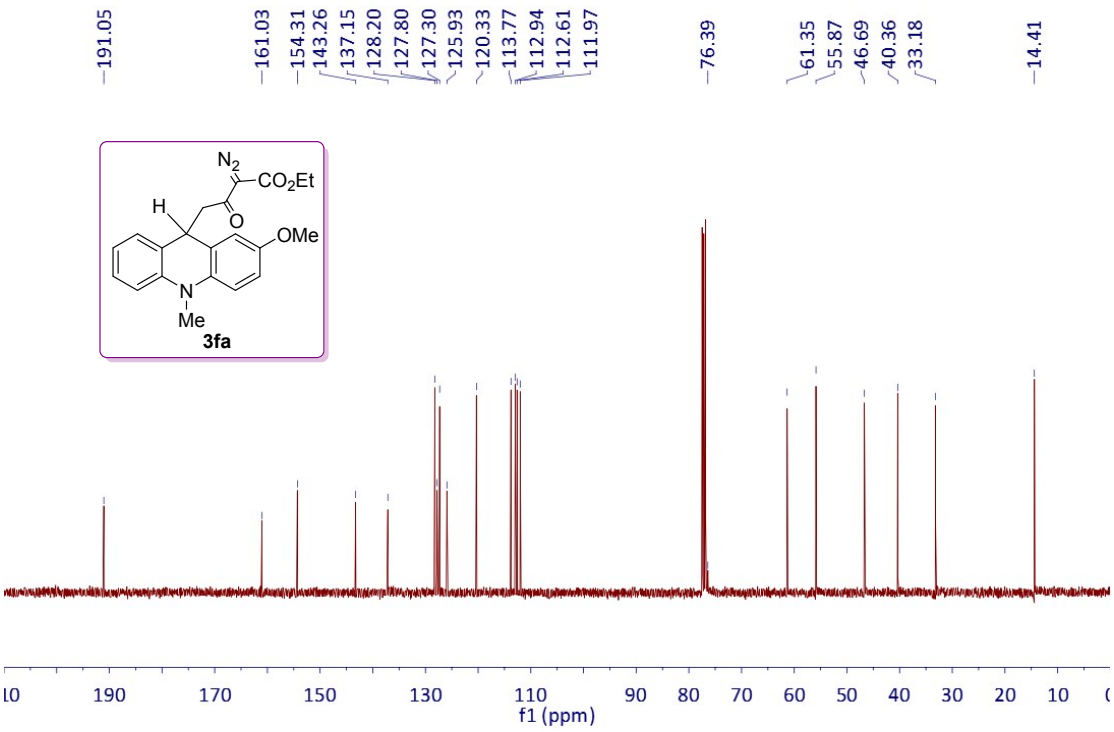

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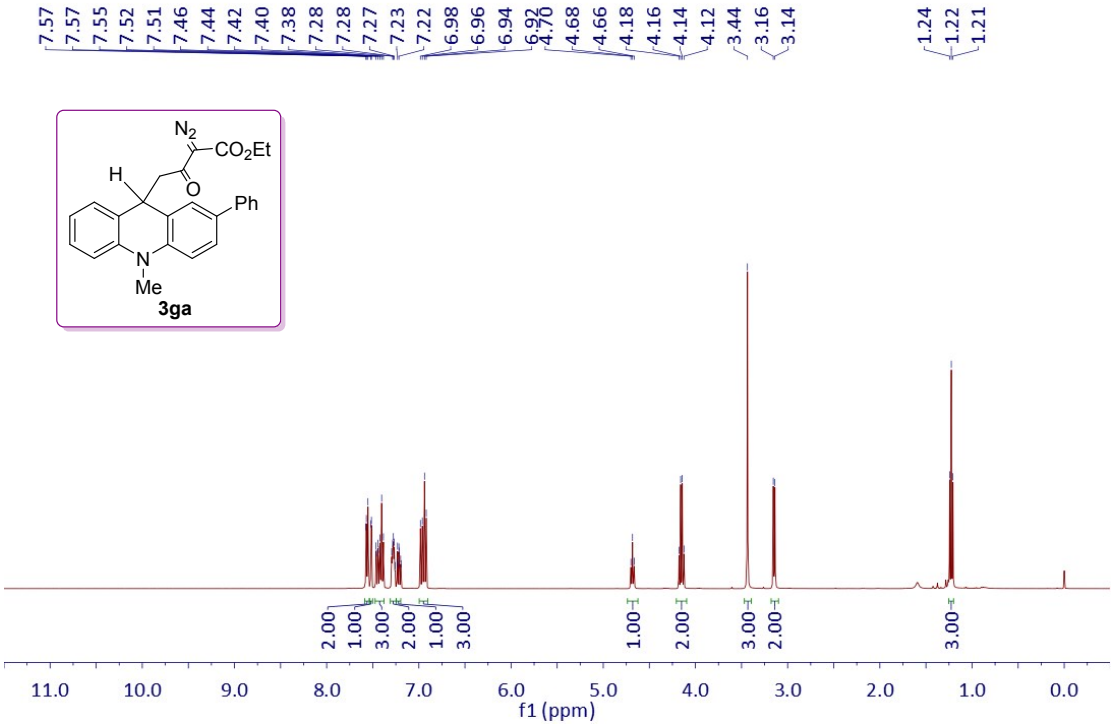

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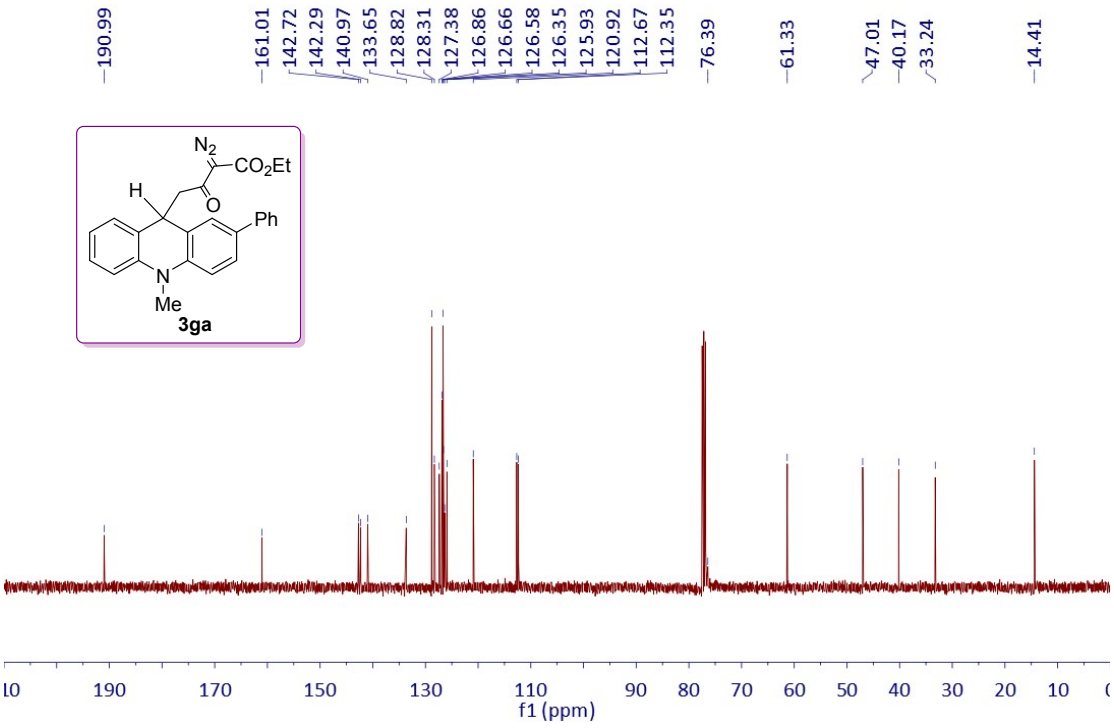

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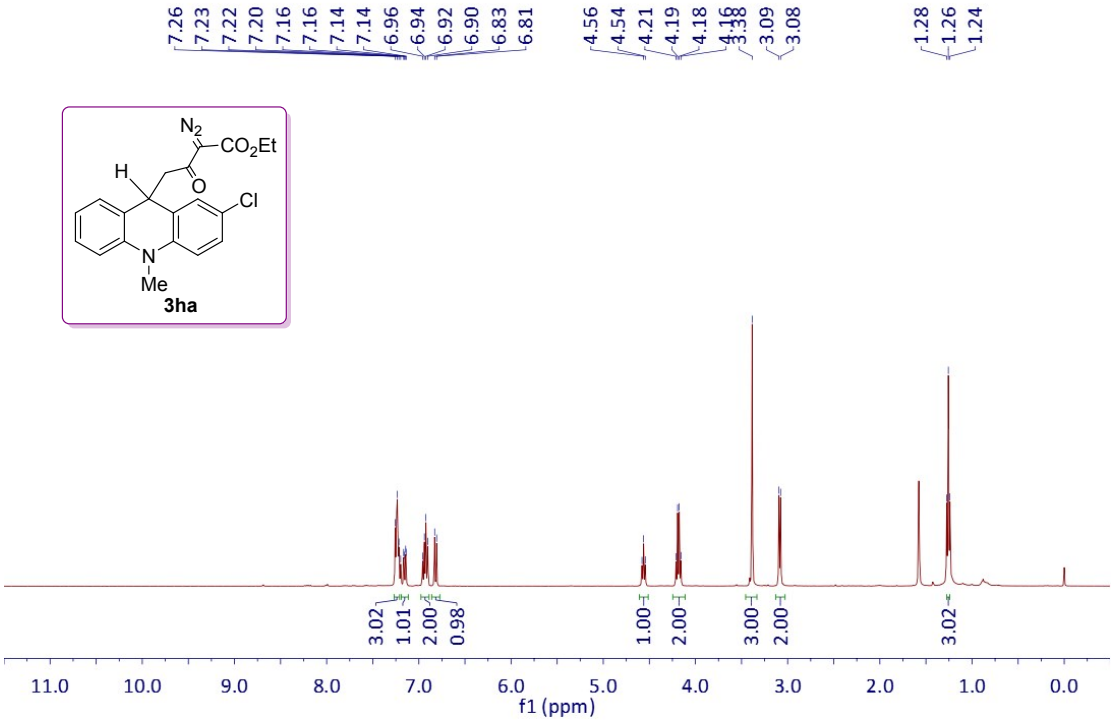

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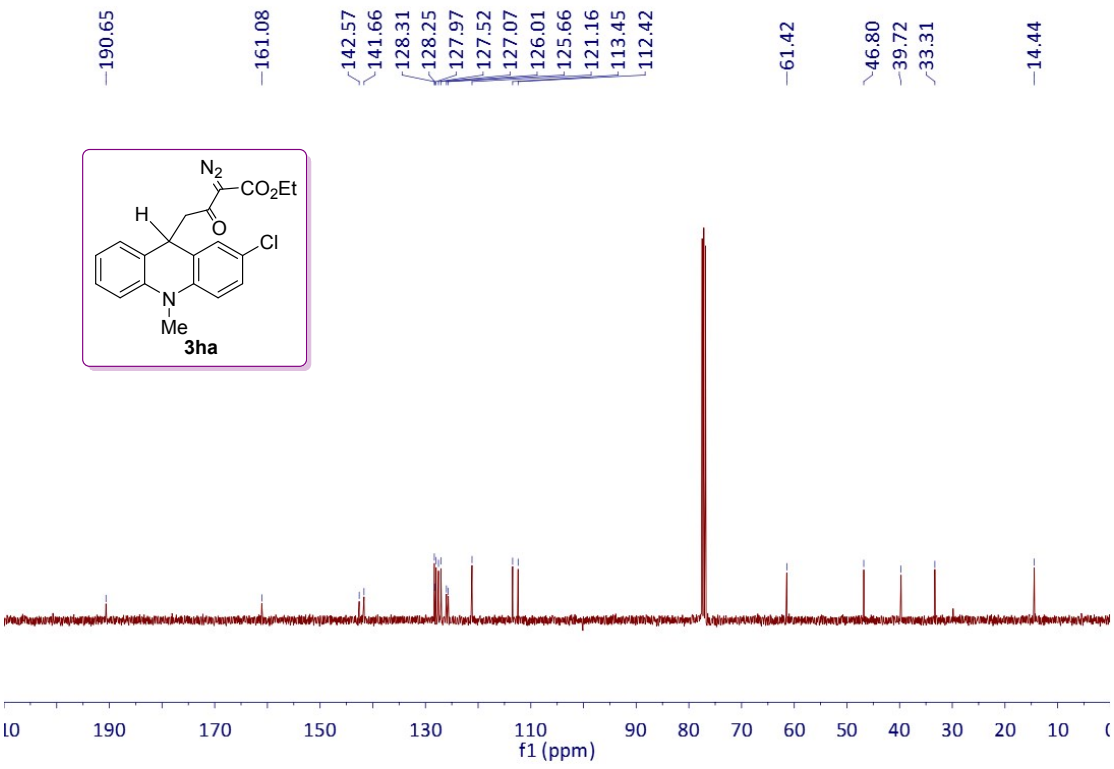

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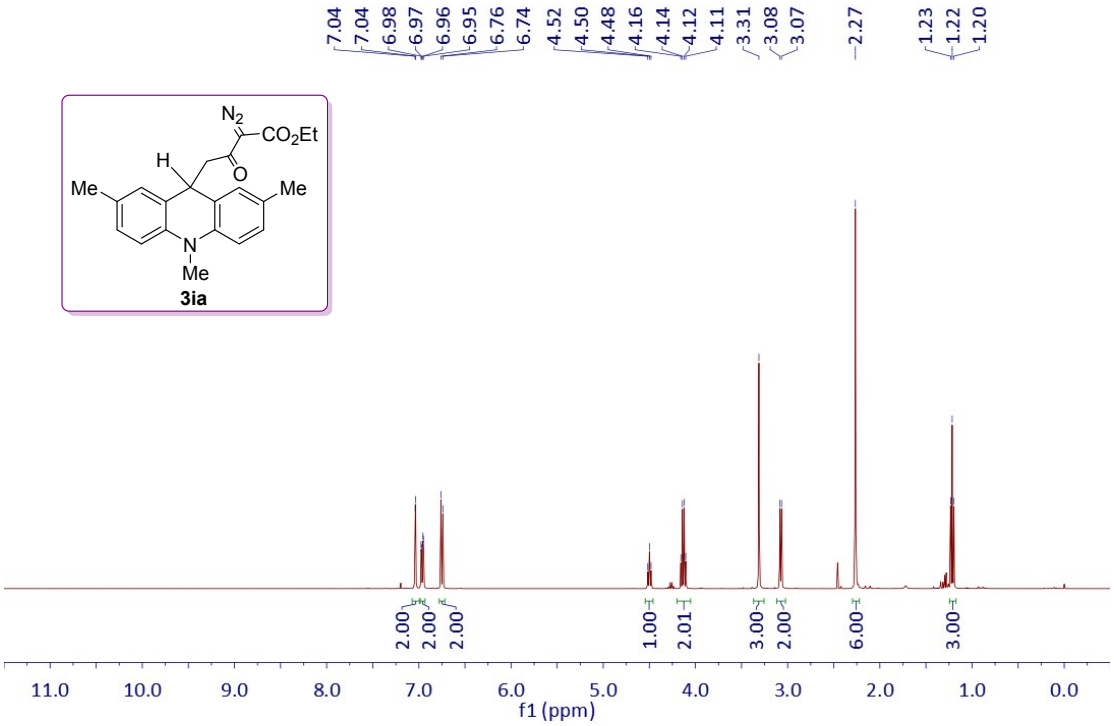

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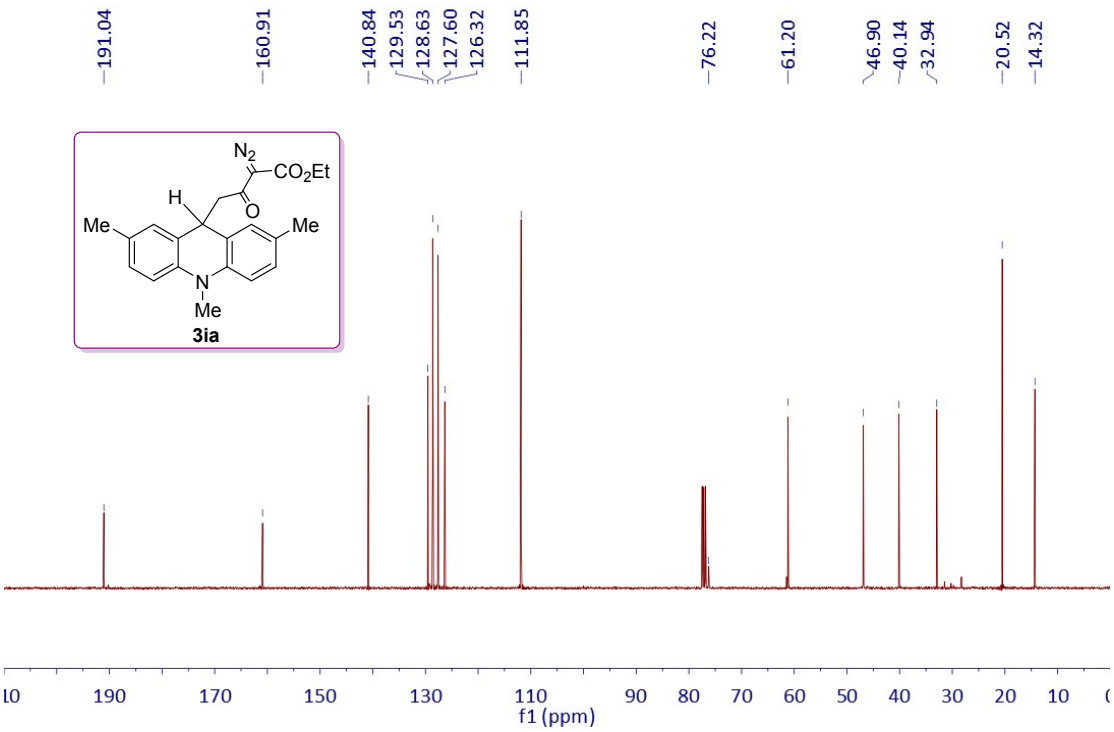

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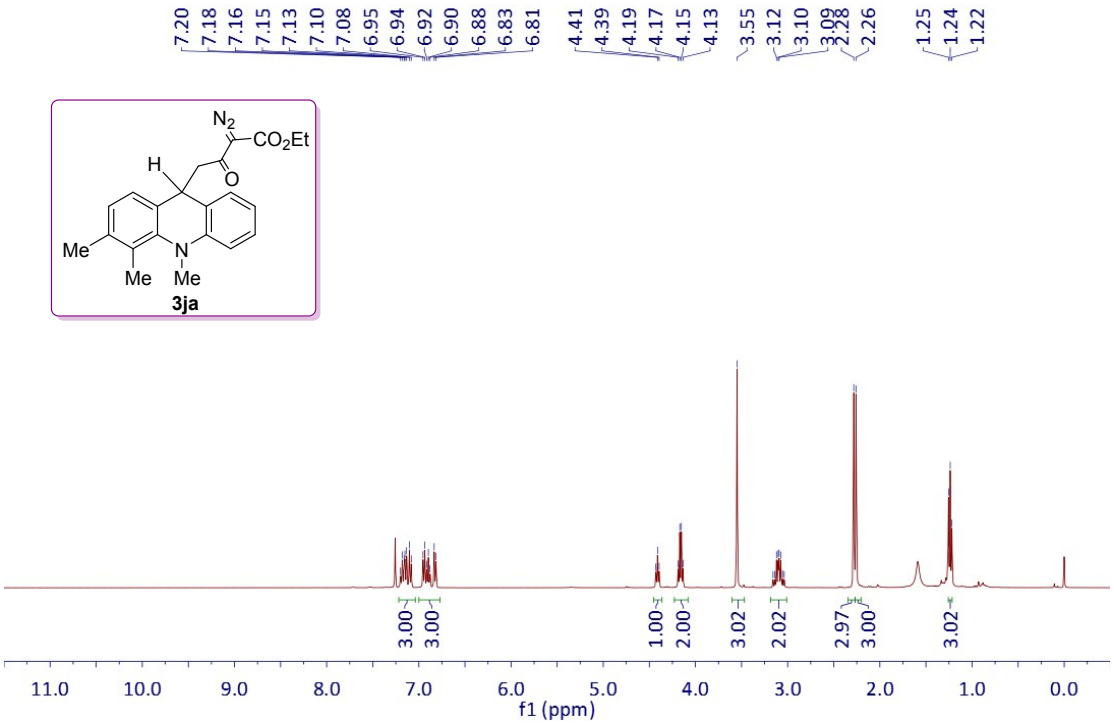

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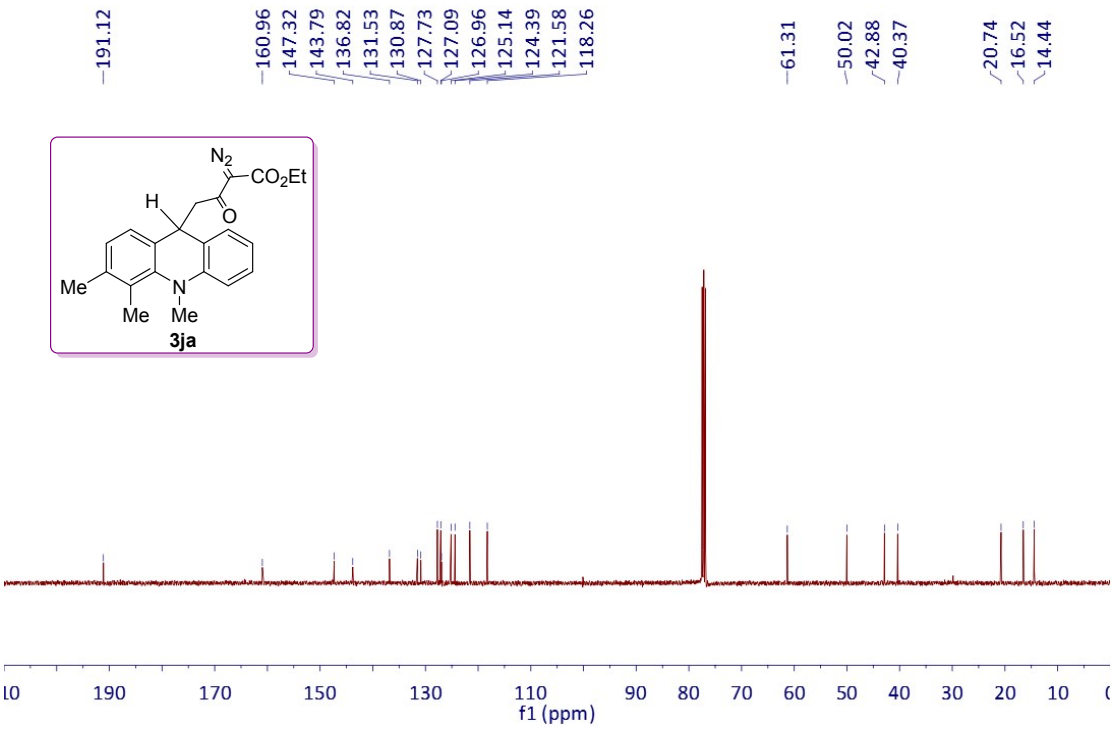

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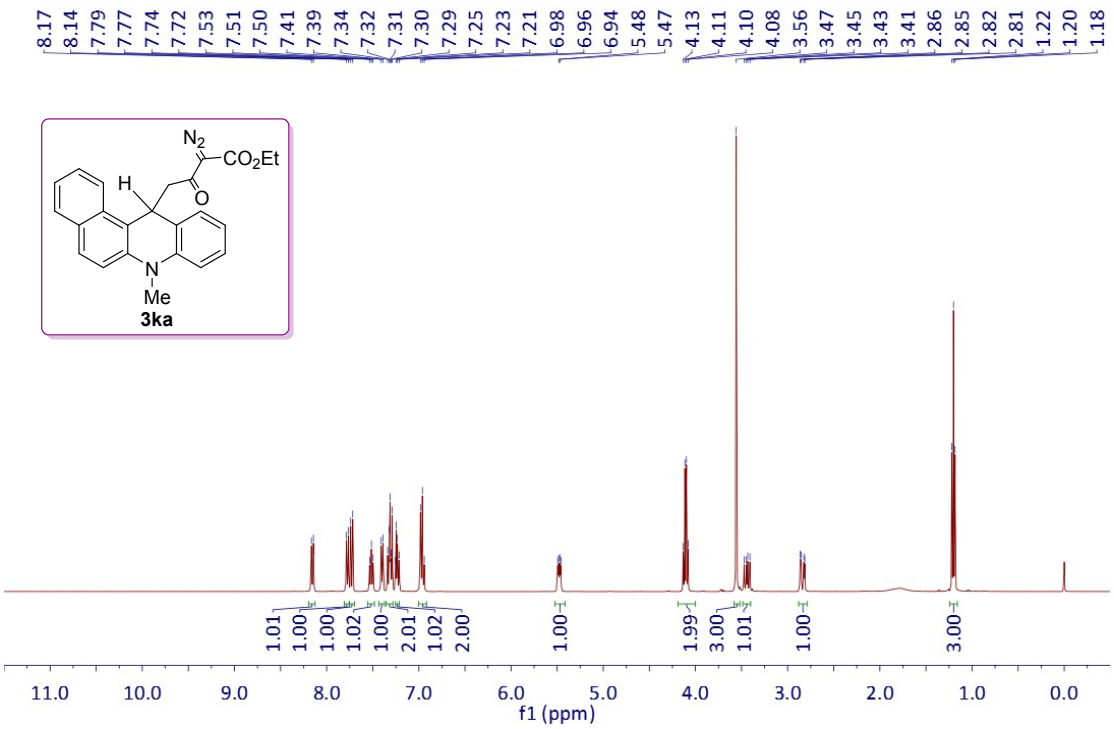

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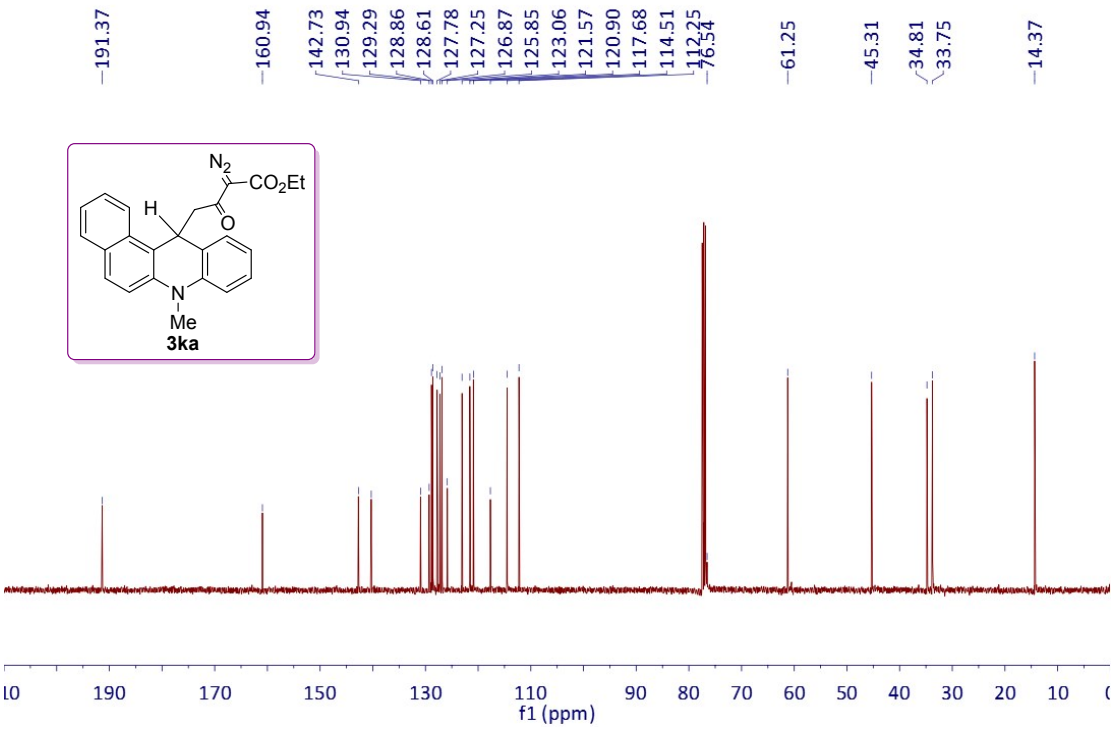

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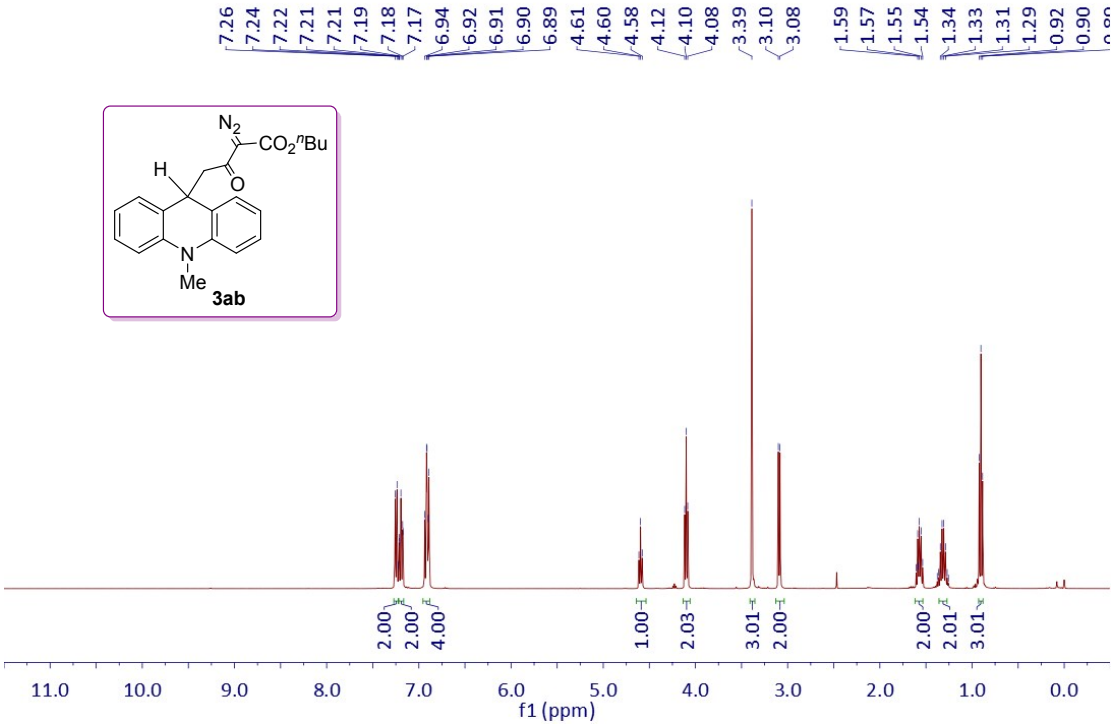

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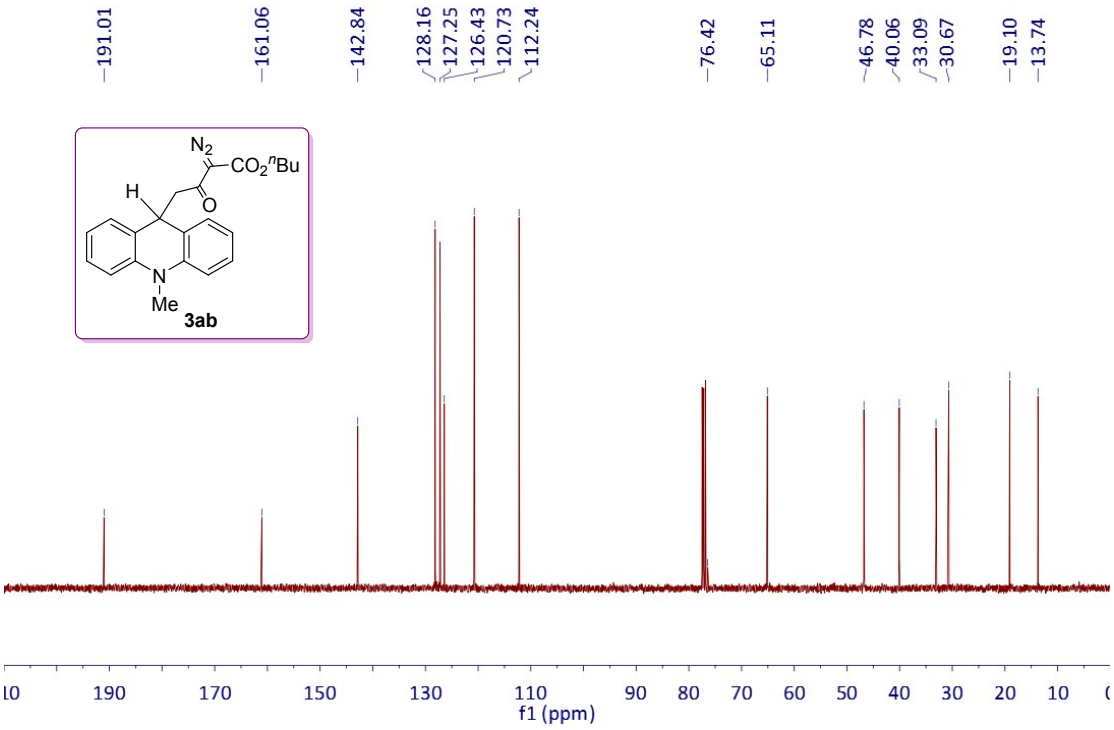
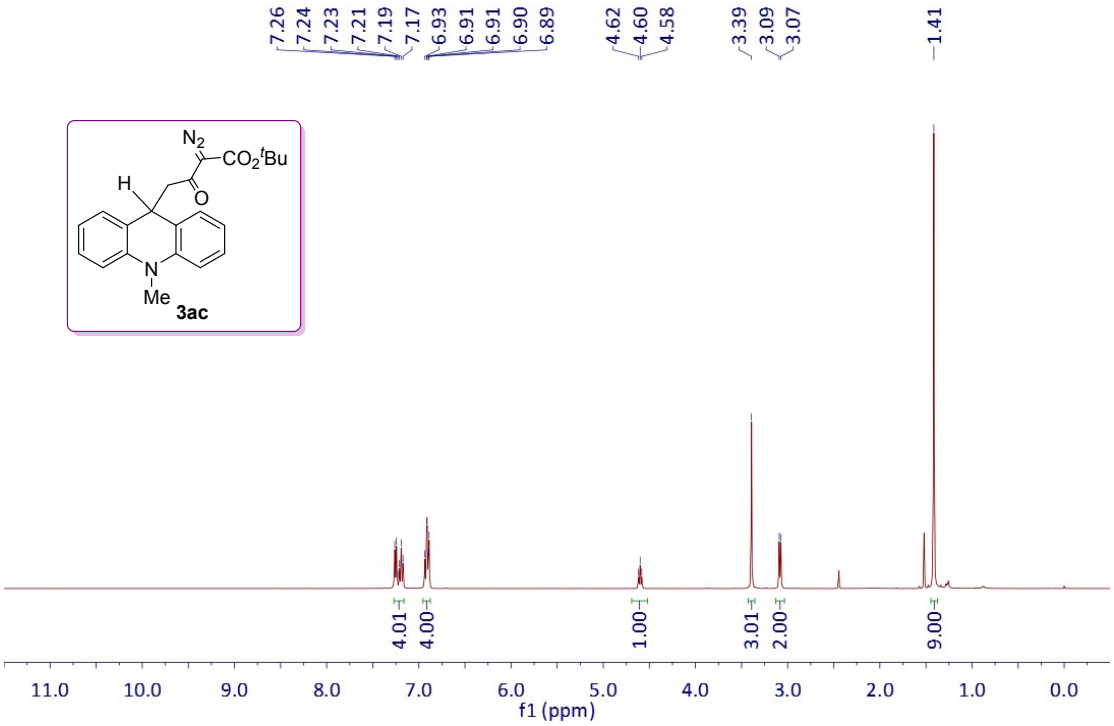
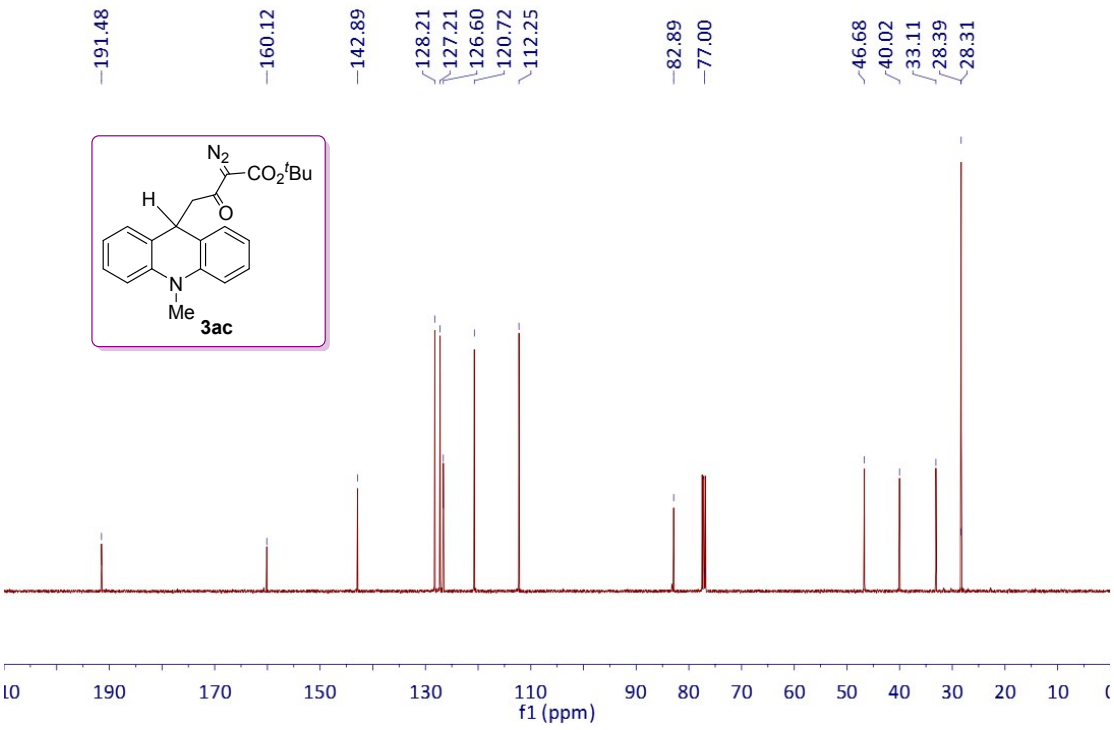


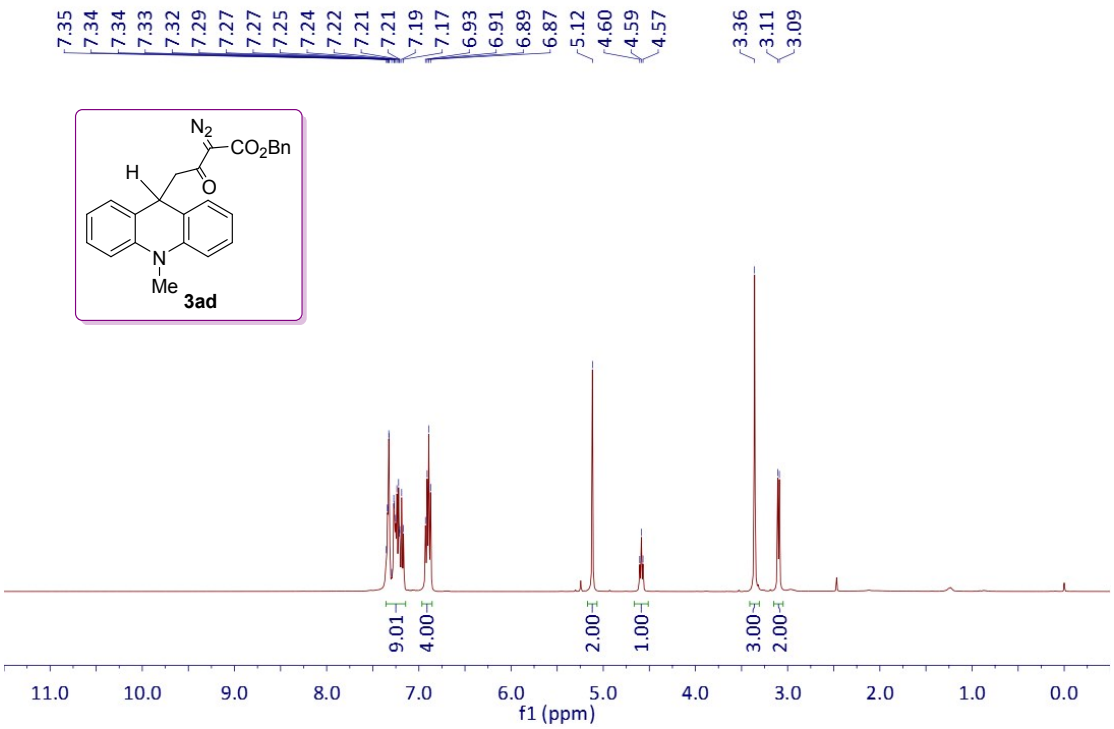
^{13}C-NMR of **3ab** ($CDCl_3$, 100Hz)



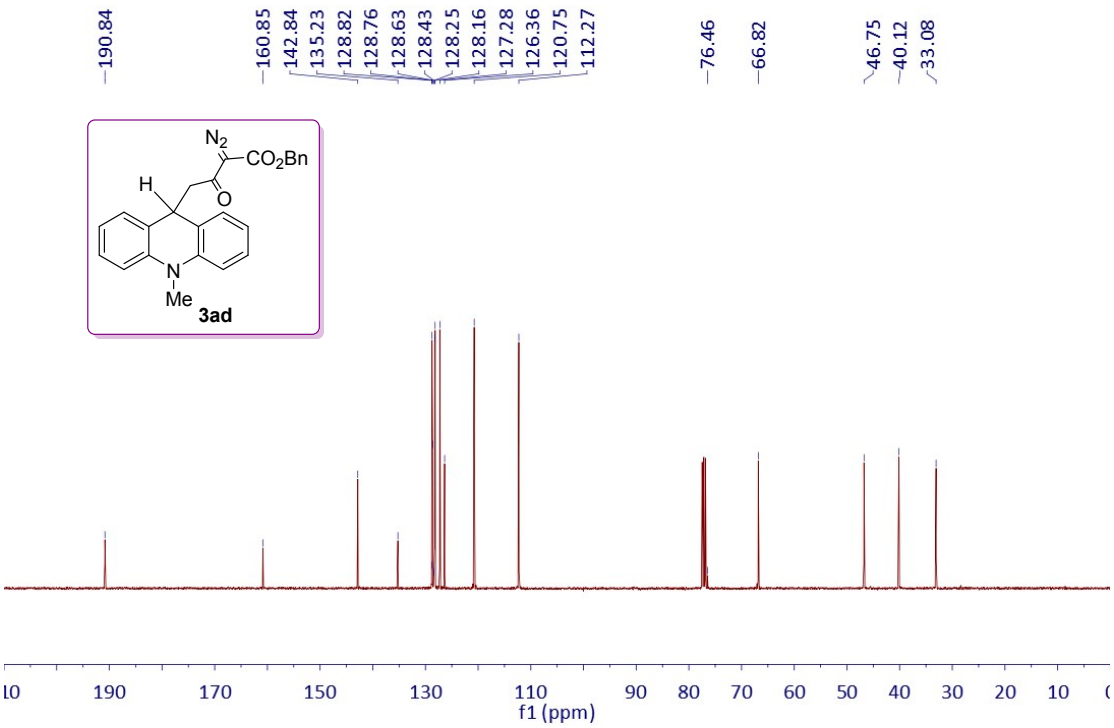
^{1}H-NMR of **3ac** ($CDCl_3$, 400Hz)



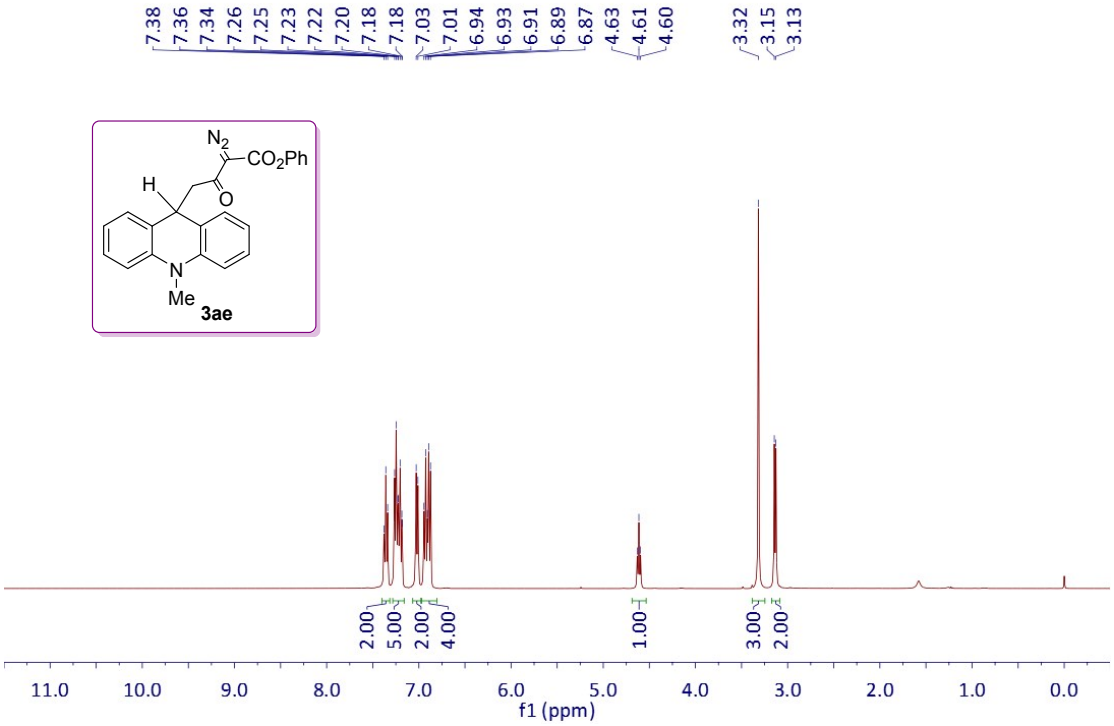
^{13}C-NMR of **3ac** ($CDCl_3$, 100Hz)



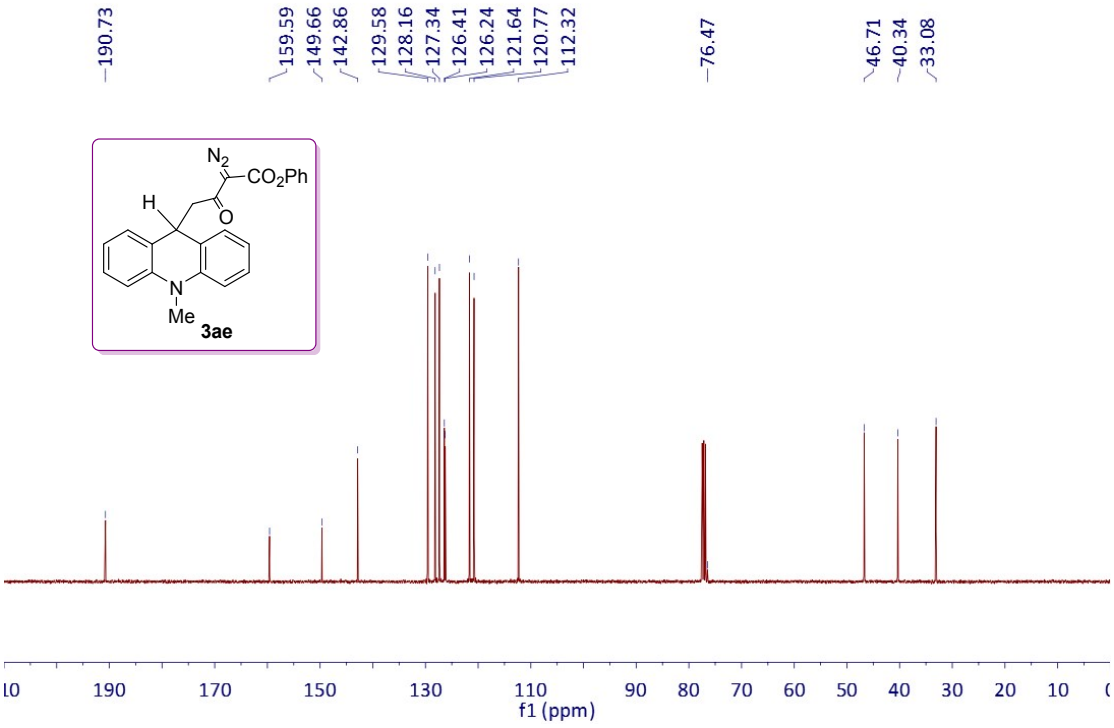
^{1}H-NMR of **3ad** ($CDCl_3$, 400Hz)



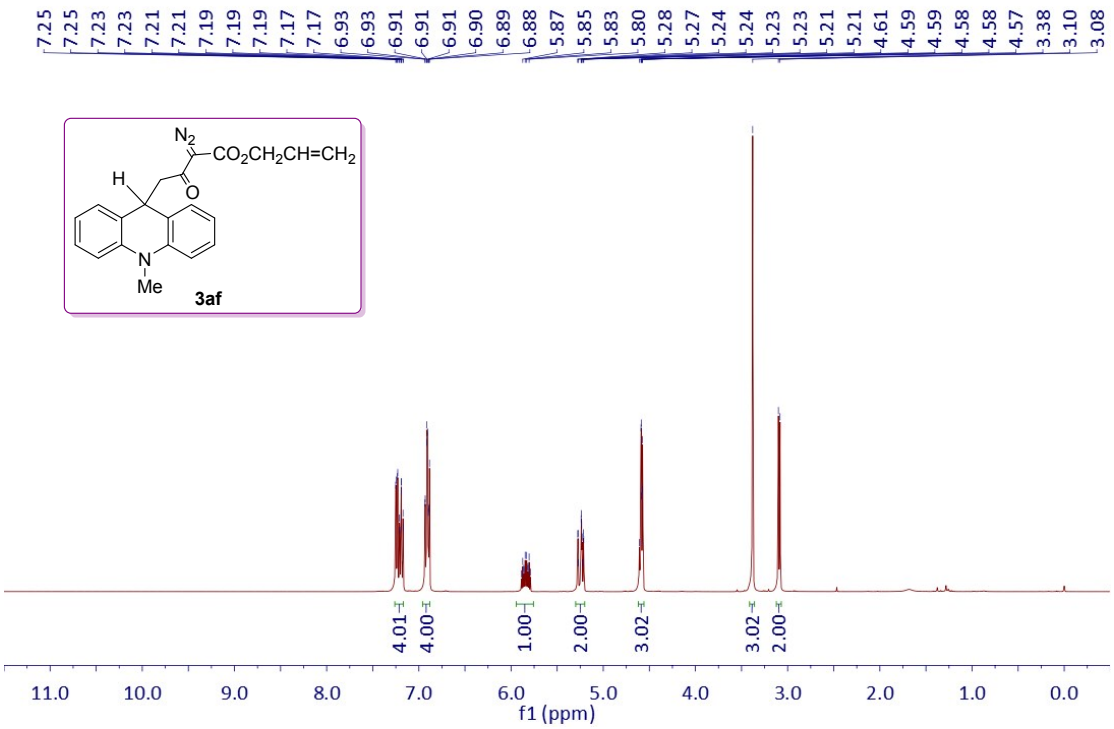
^{13}C-NMR of **3ad** ($CDCl_3$, 100Hz)



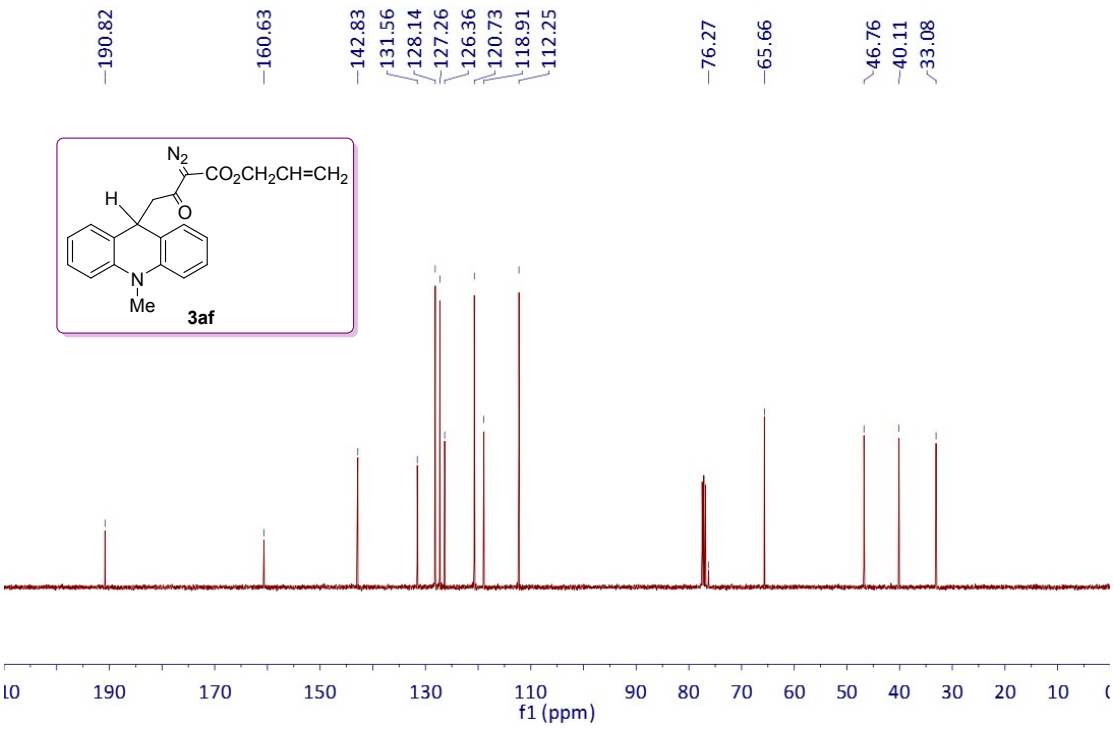
^{1}H-NMR of **3ae** ($CDCl_3$, 400Hz)



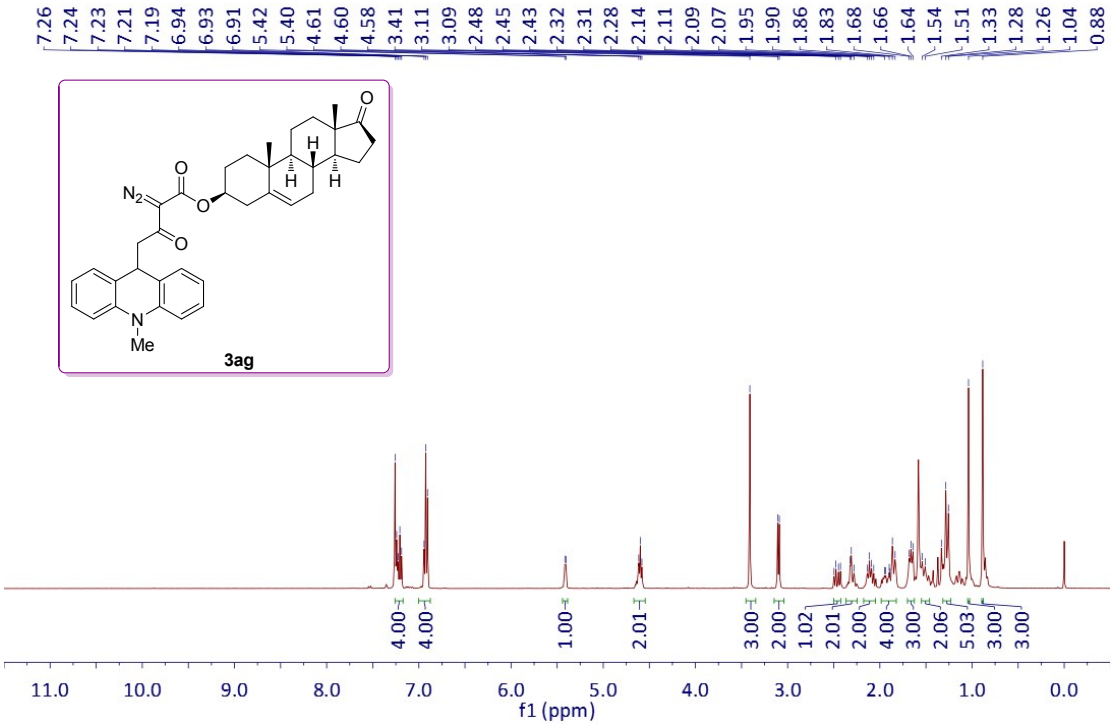
^{13}C-NMR of **3ae** ($CDCl_3$, 100Hz)



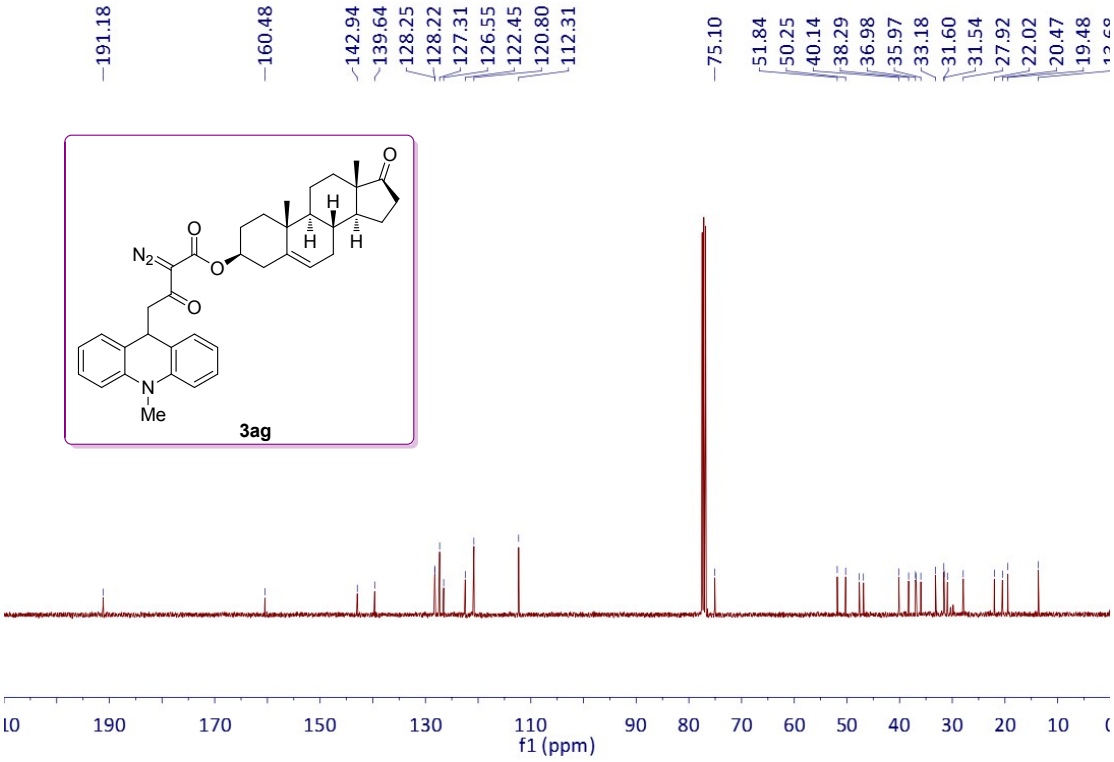
^{1}H-NMR of **3af** ($CDCl_3$, 400Hz)



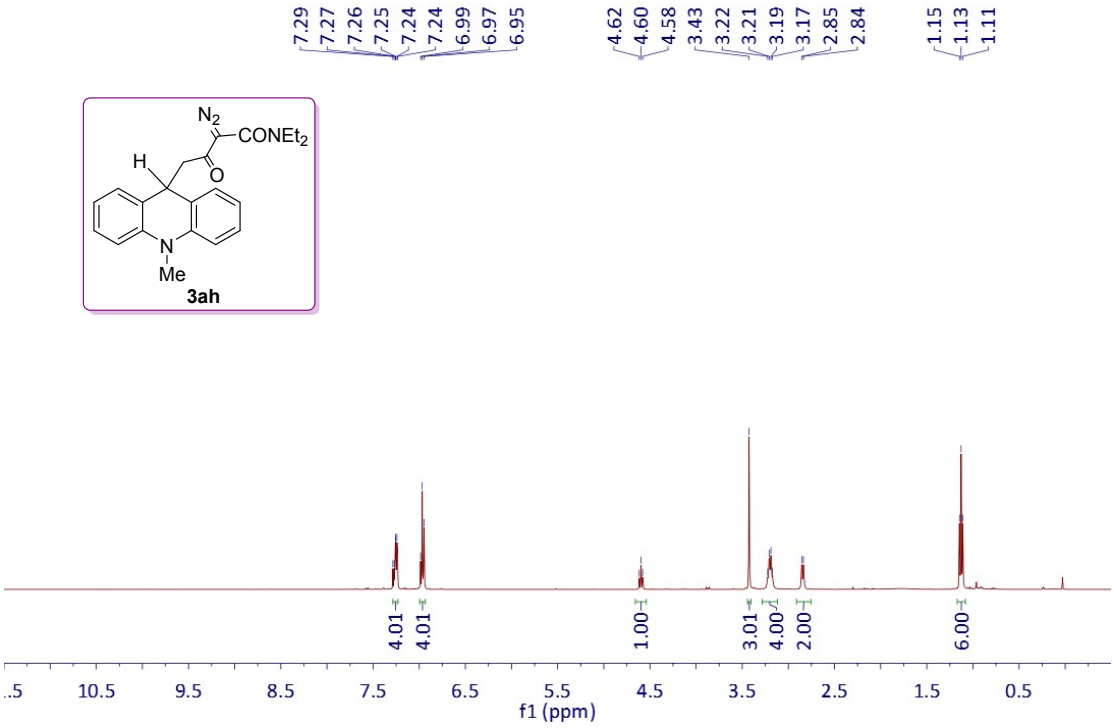
^{13}C-NMR of **3af** ($CDCl_3$, 100Hz)



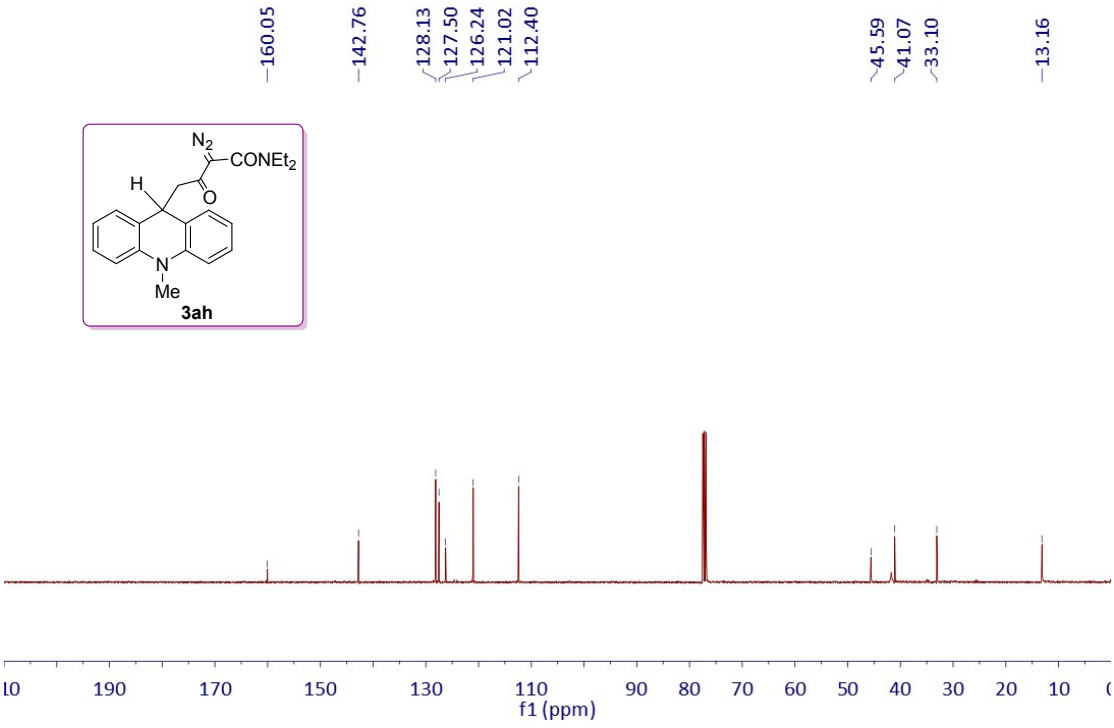
^{1}H-NMR of **3ag** ($CDCl_3$, 400Hz)



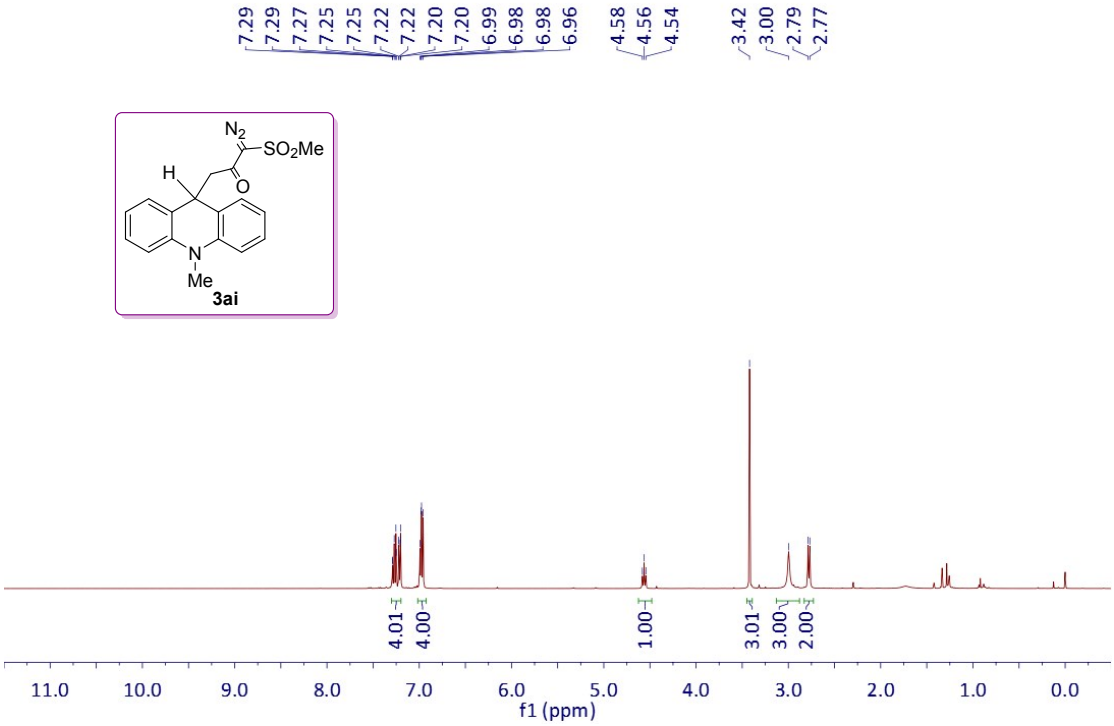
^{13}C-NMR of **3ag** ($CDCl_3$, 100Hz)



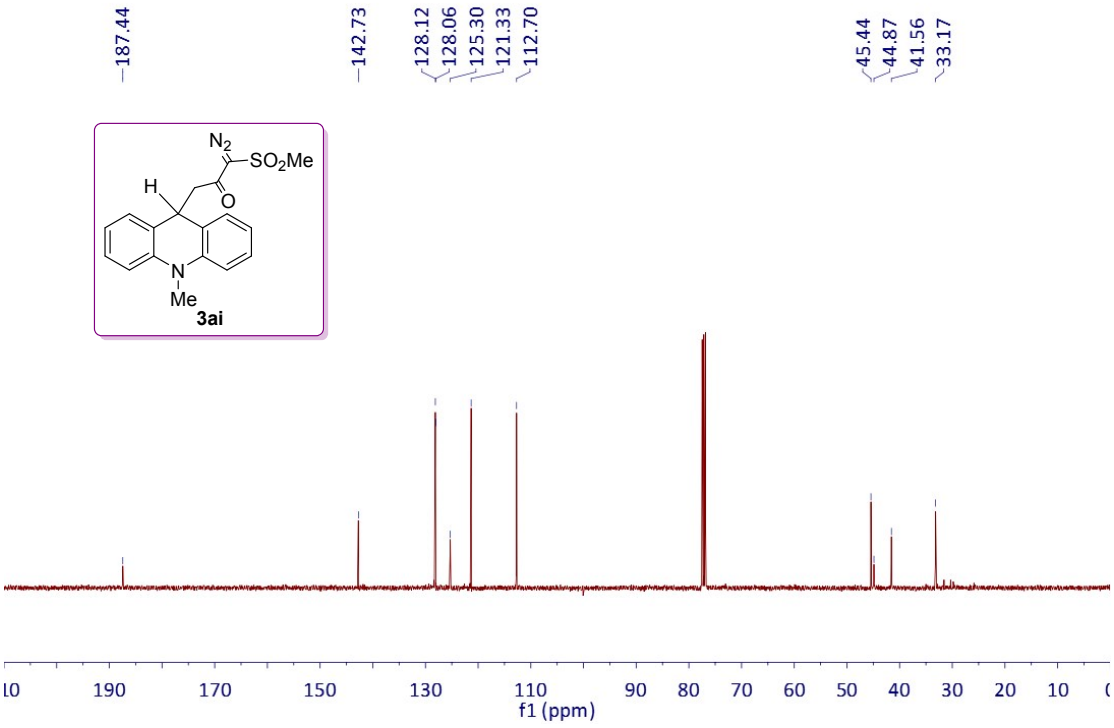
^{1}H-NMR of **3ah** ($CDCl_3$, 400Hz)



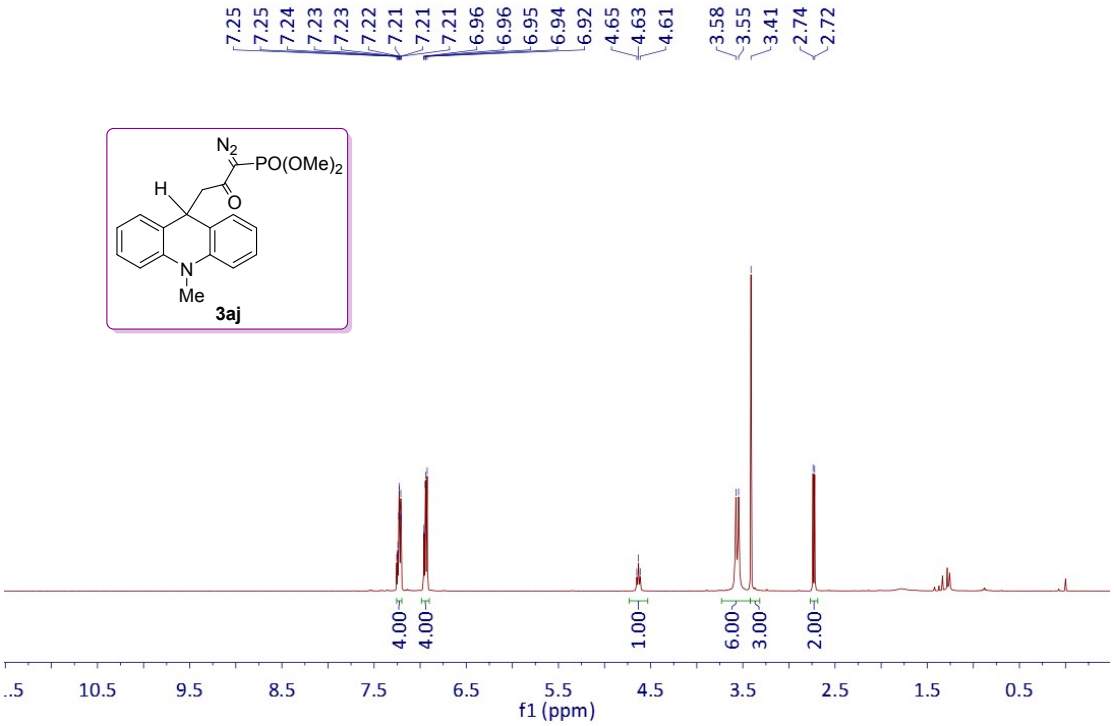
^{13}C-NMR of **3ah** ($CDCl_3$, 100Hz)



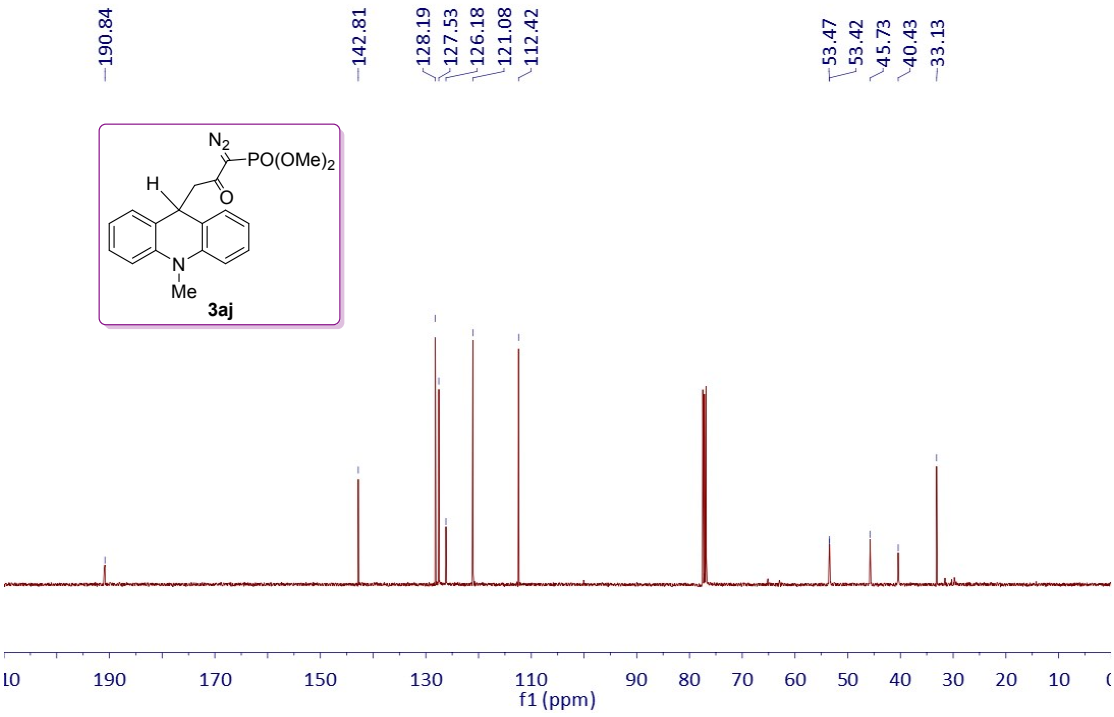
^{1}H-NMR of **3ai** ($CDCl_3$, 400Hz)



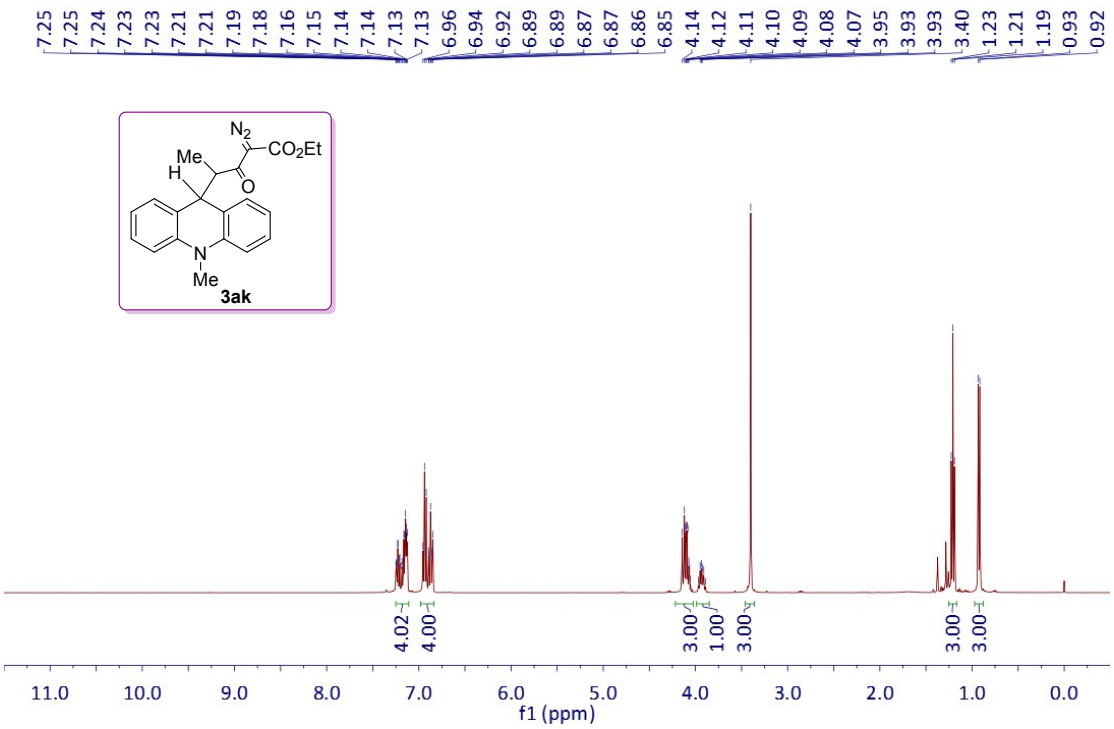
^{13}C-NMR of **3ai** ($CDCl_3$, 100Hz)



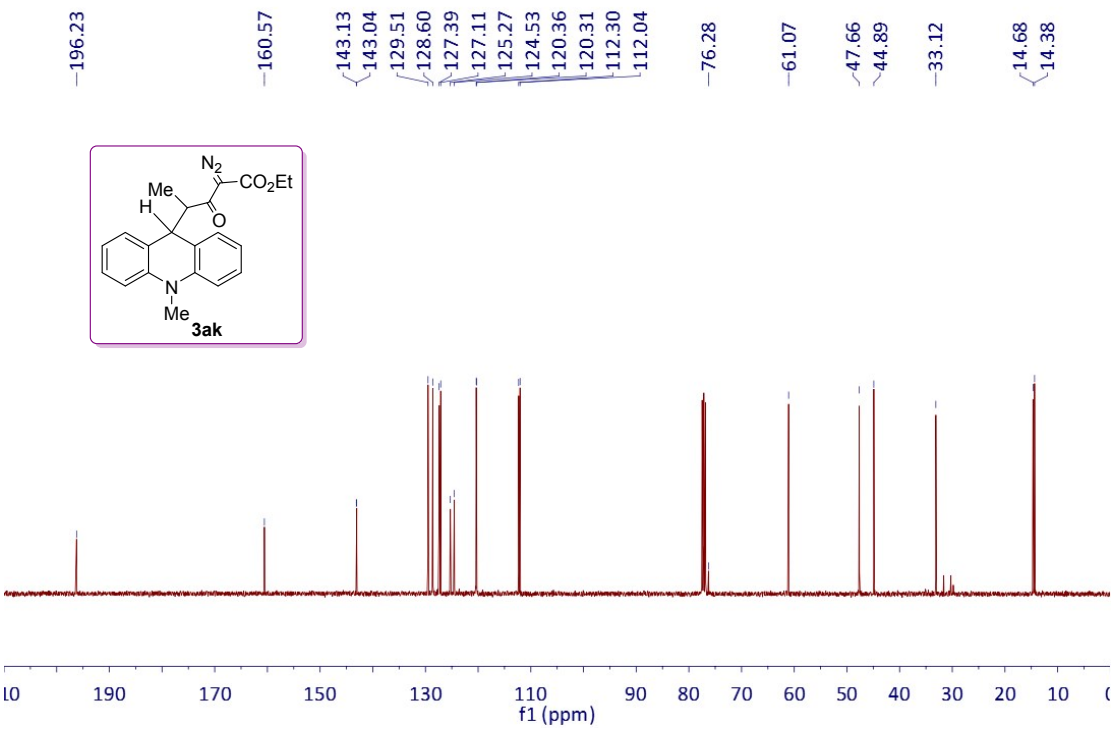
^{1}H-NMR of **3aj** ($CDCl_3$, 400Hz)



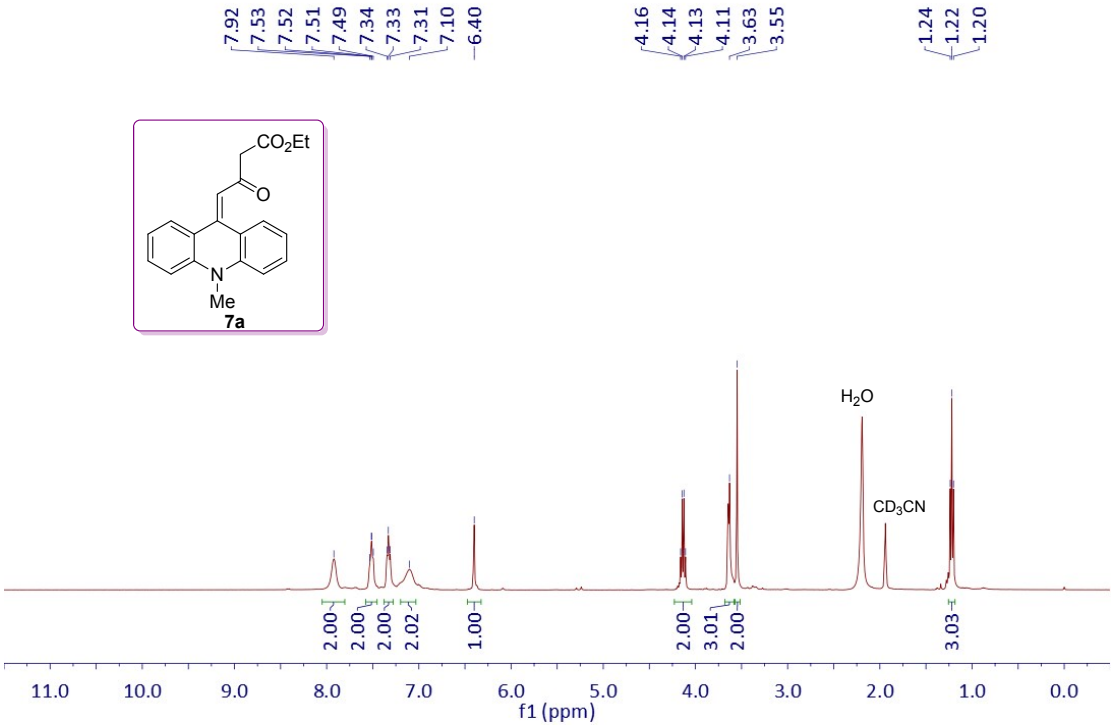
^{13}C-NMR of **3aj** ($CDCl_3$, 100Hz)



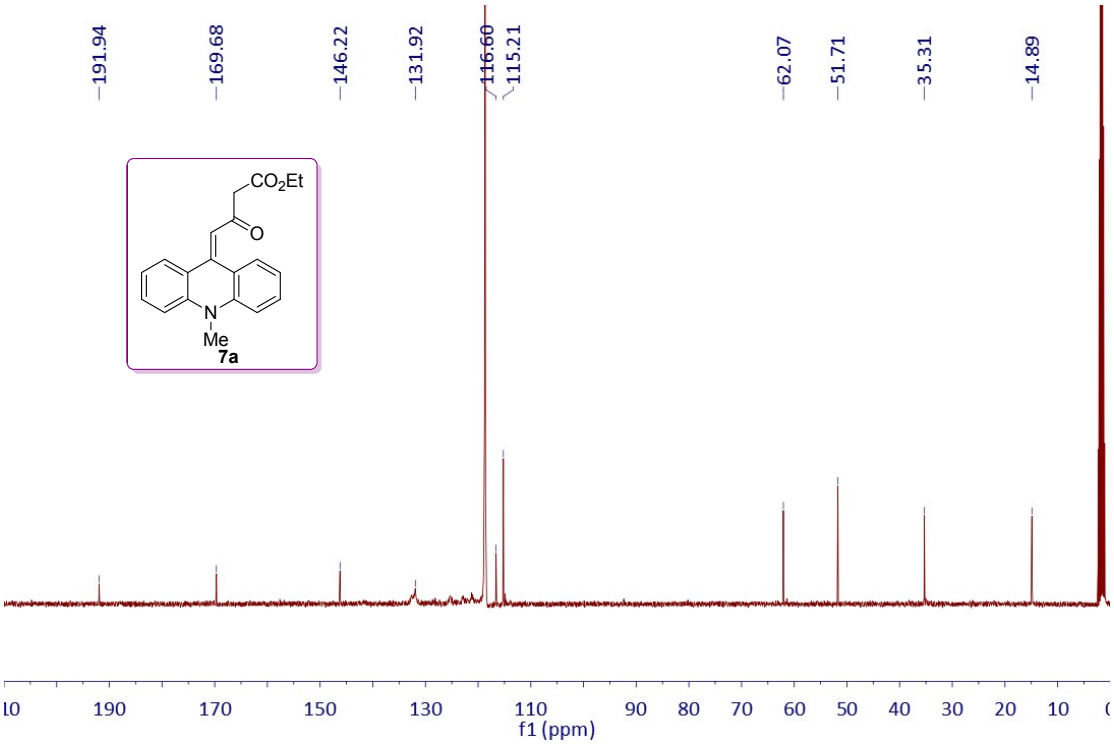
^{1}H-NMR of **3ak** ($CDCl_3$, 400Hz)



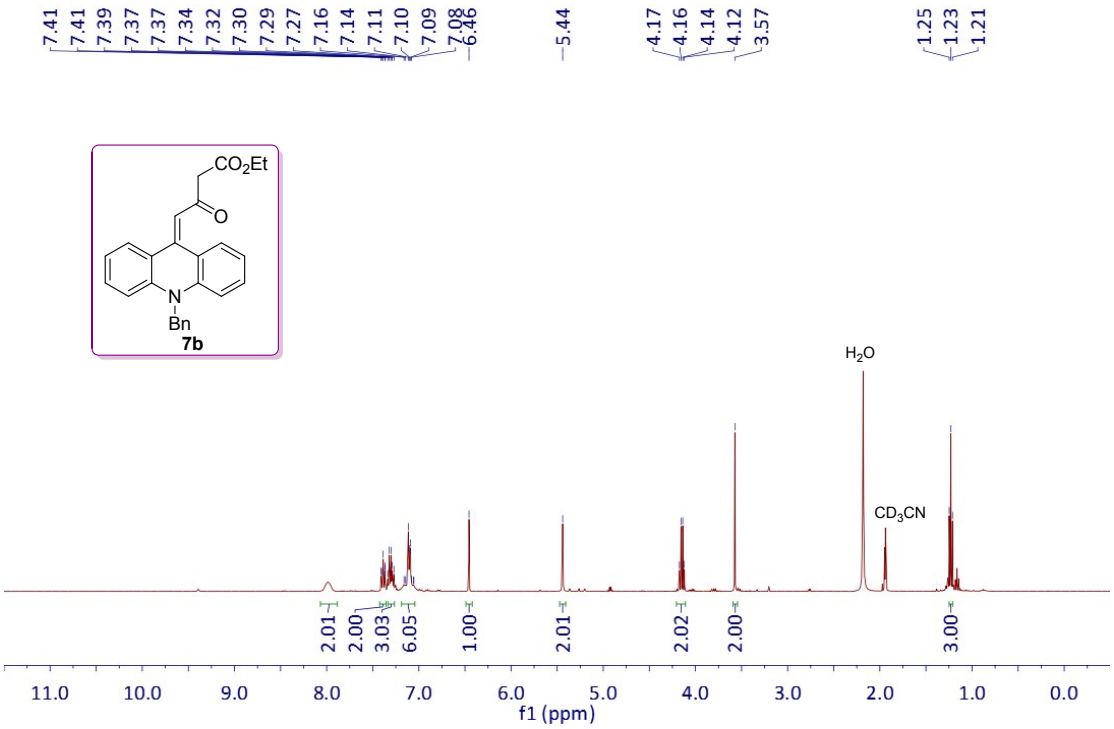
^{13}C-NMR of **3ak** ($CDCl_3$, 100Hz)



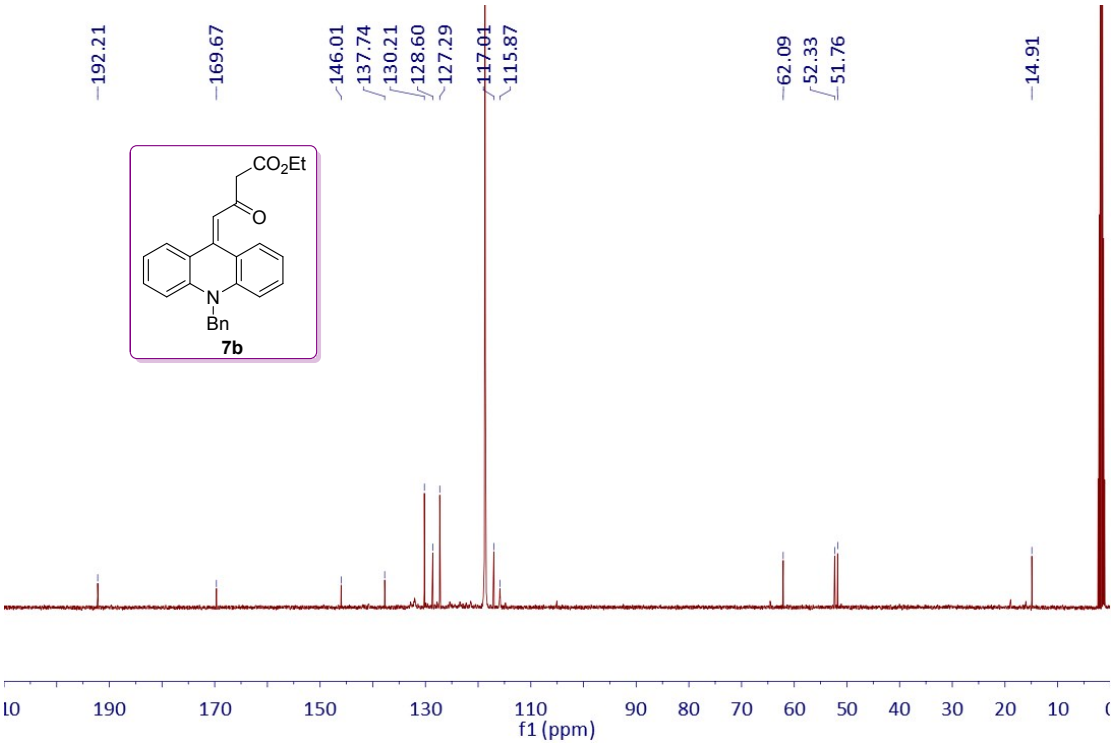
^{1}H-NMR of **7a** (CD_3CN, 400Hz)



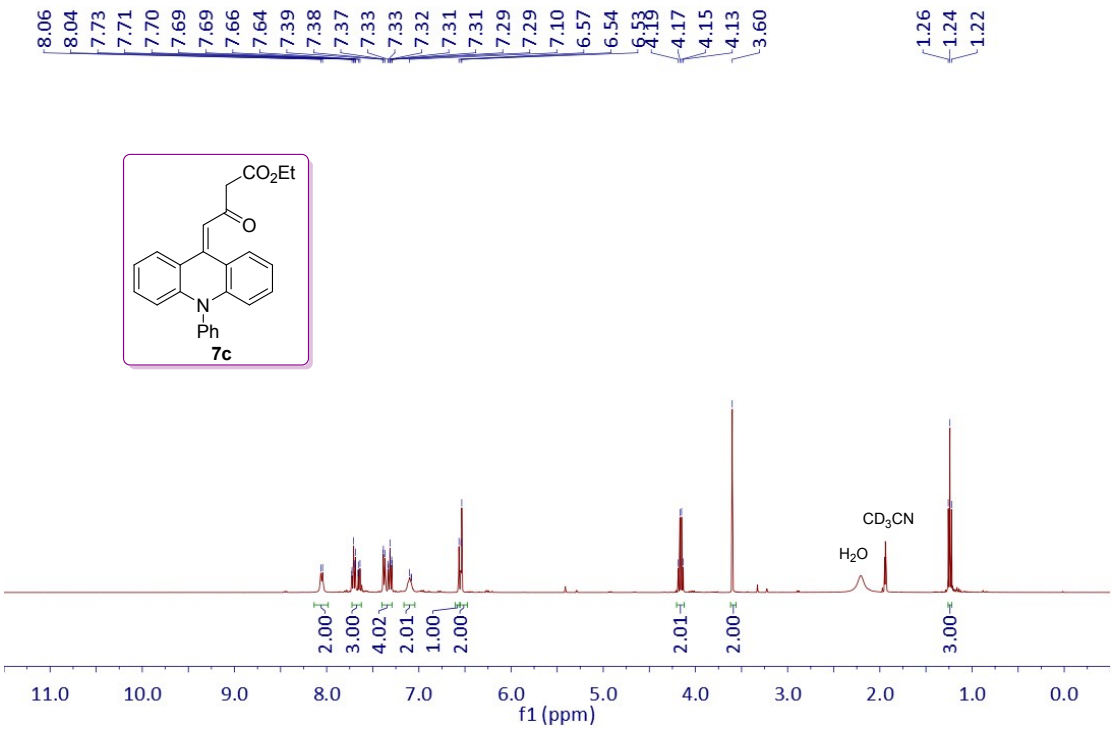
^{13}C-NMR of **7a** (CD_3CN, 100Hz)



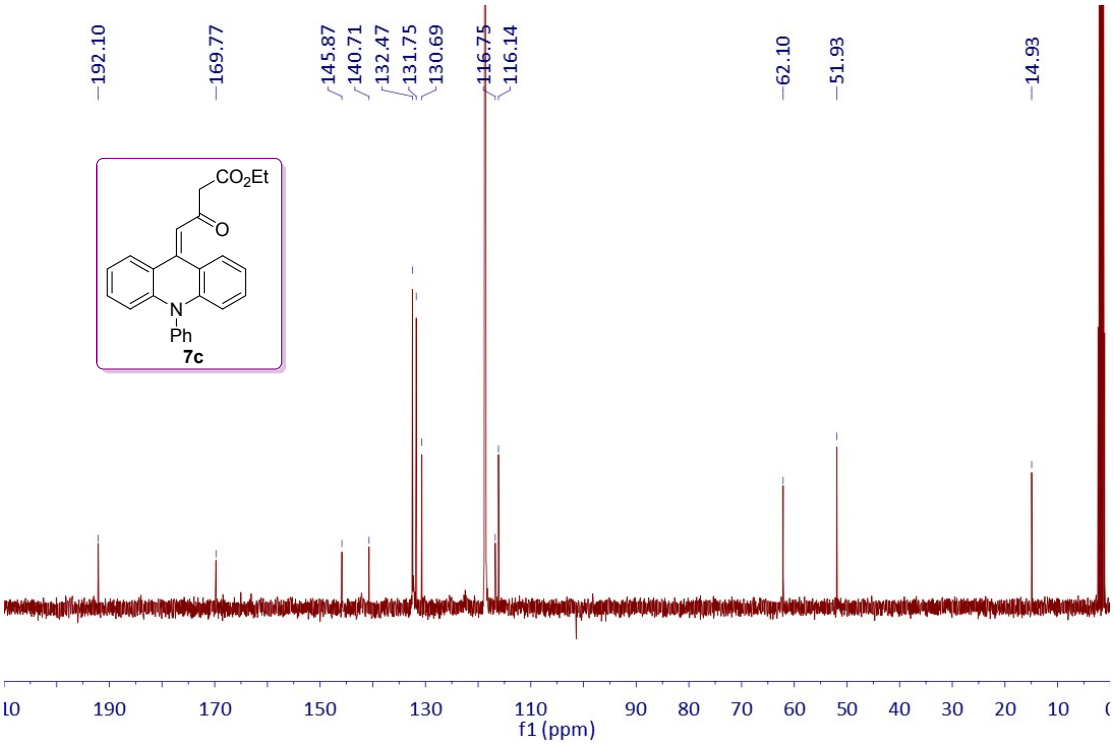
^{1}H-NMR of **7b** (CD_3CN, 400Hz)



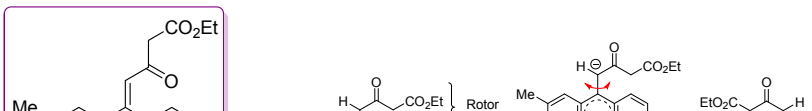
^{13}C-NMR of **7b** (CD_3CN, 100Hz)

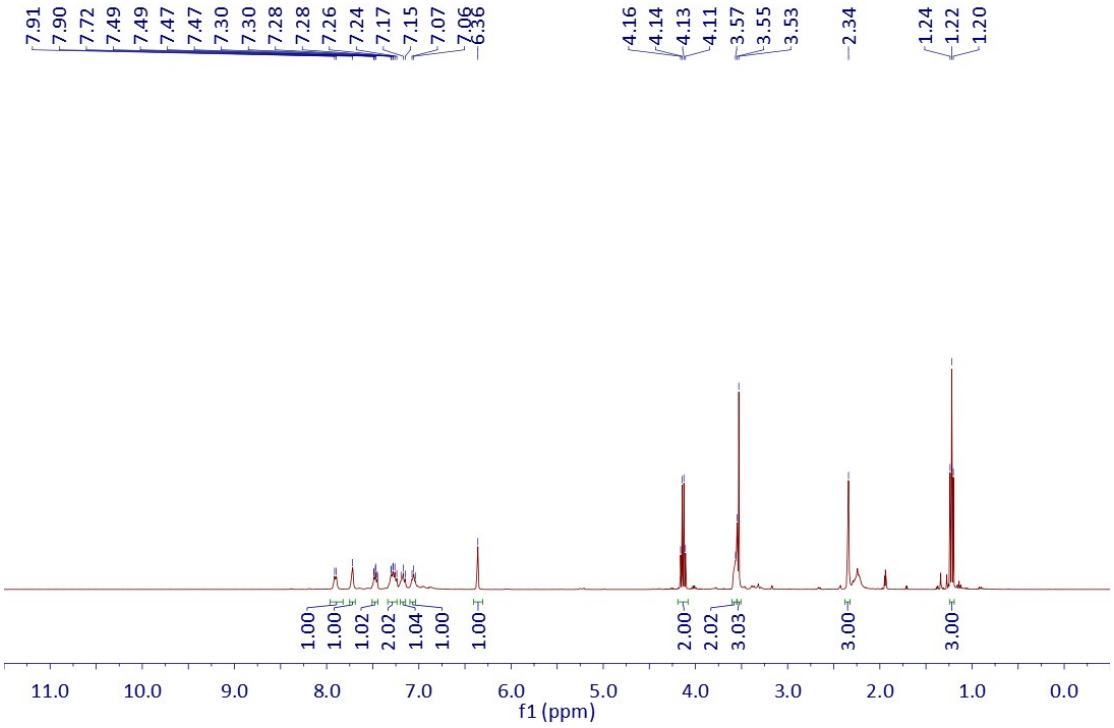


^{1}H-NMR of **7c** (CD_3CN, 400Hz)

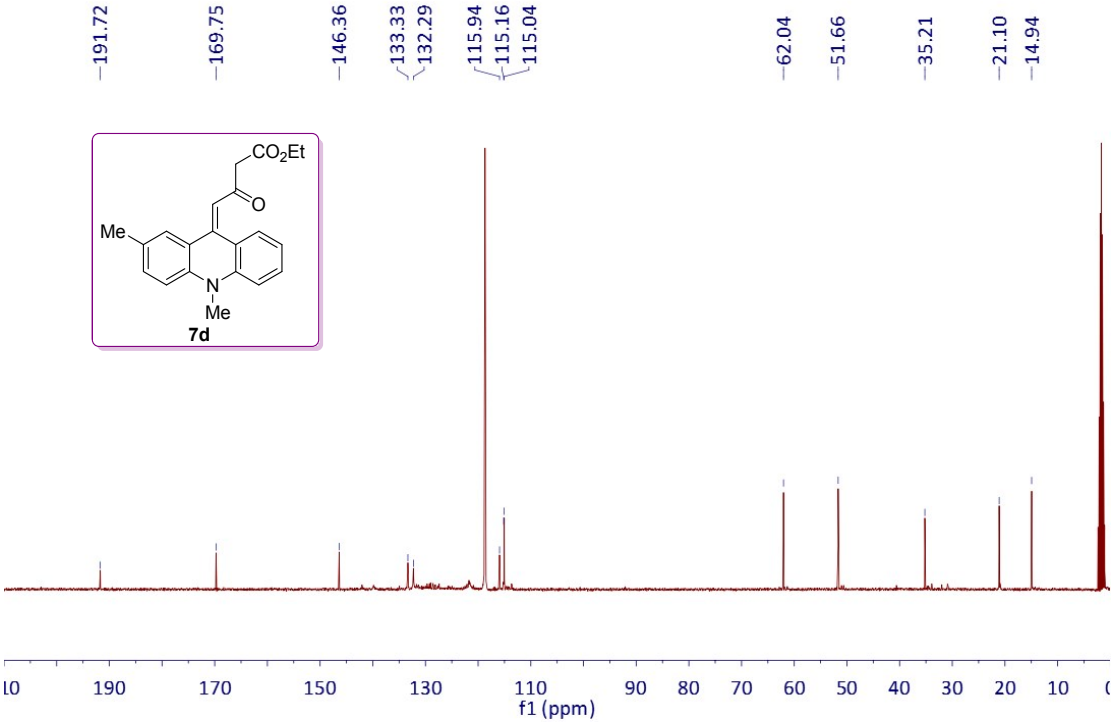


^{13}C-NMR of **7c** (CD_3CN, 100Hz)

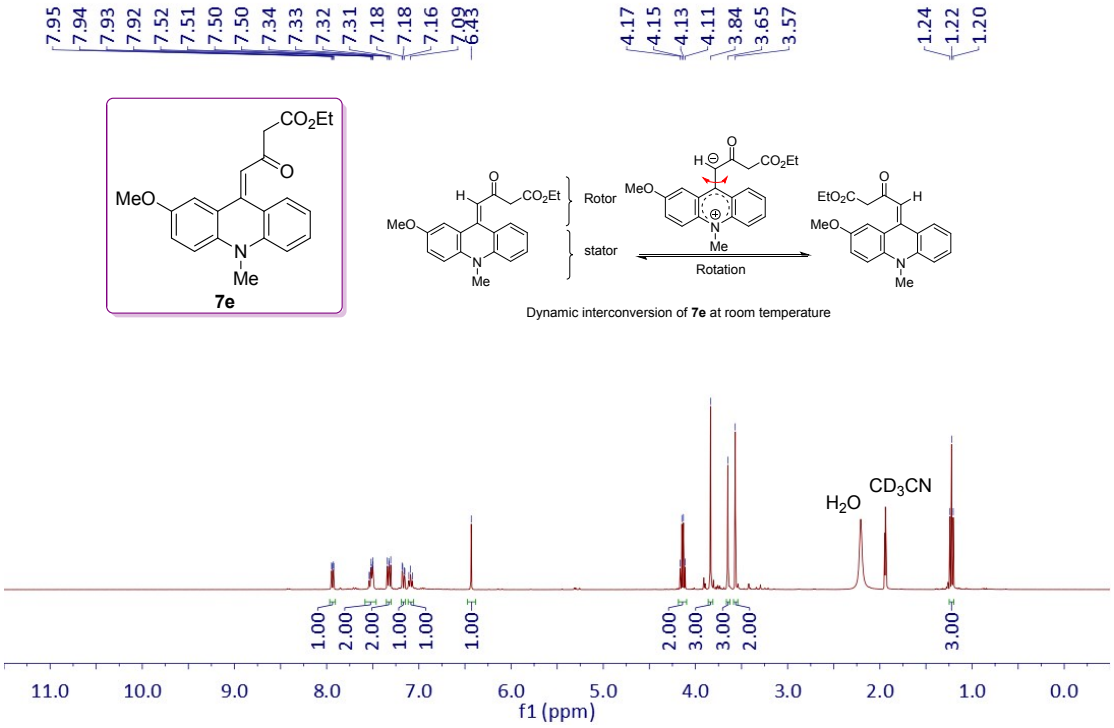




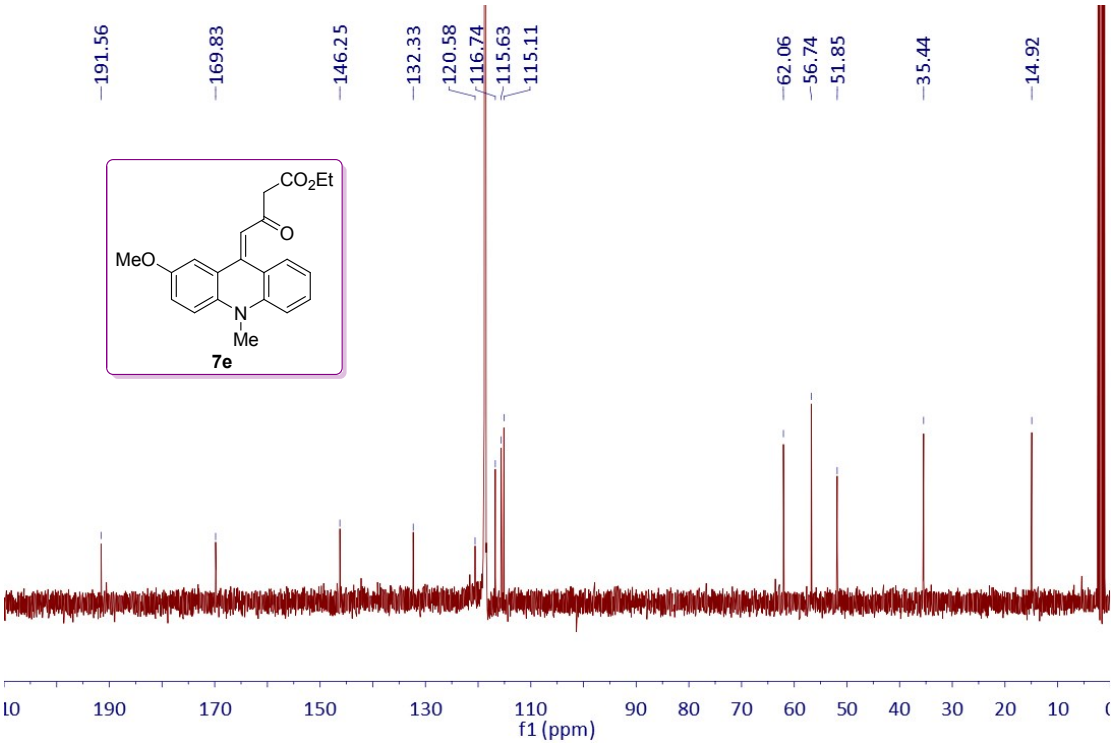
^{1}H-NMR of **7d** (CD_3CN, 400Hz)



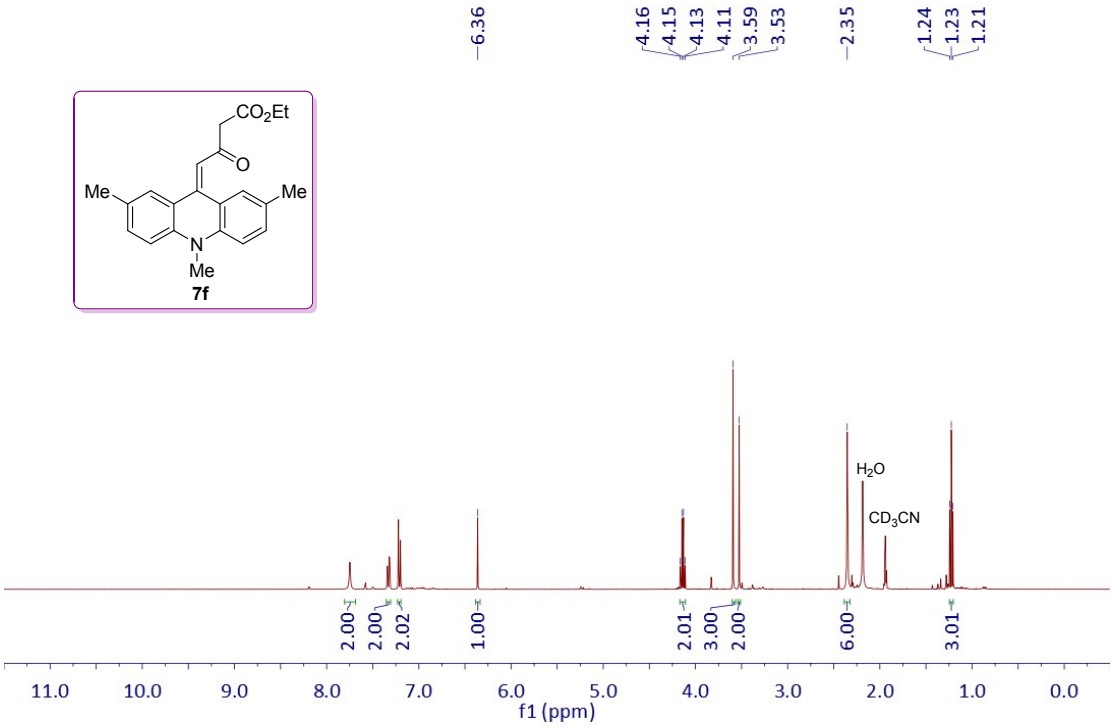
^{13}C-NMR of **7d** (CD_3CN, 100Hz)



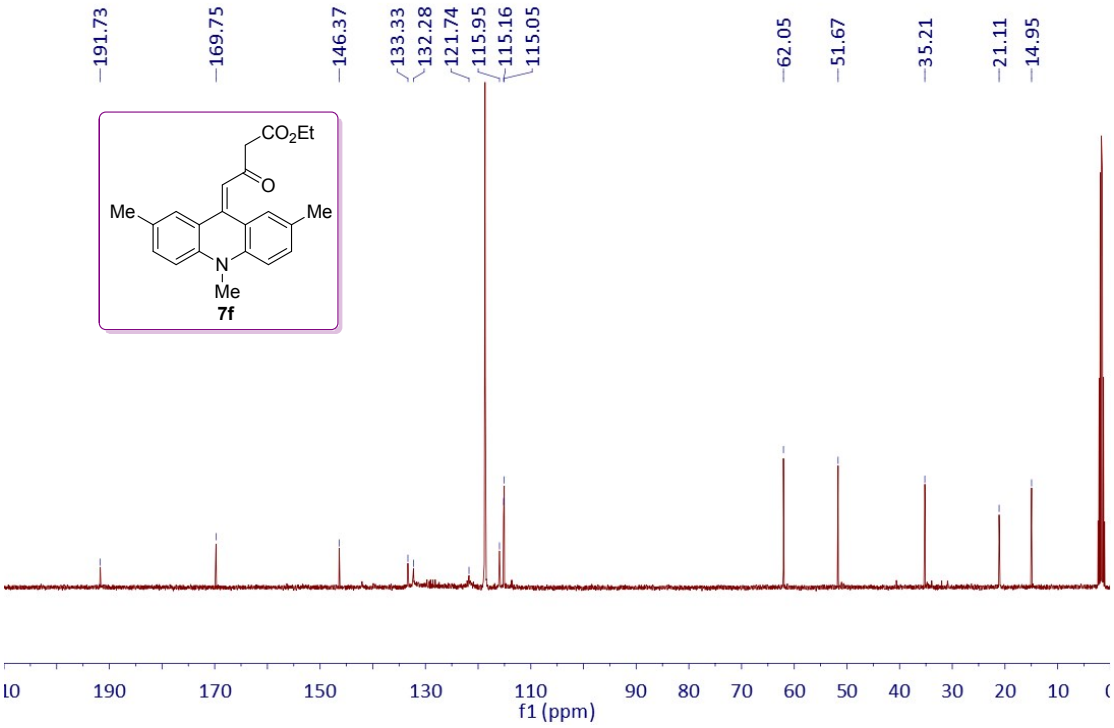
^{1}H-NMR of **7e** (CD_3CN, 400Hz)



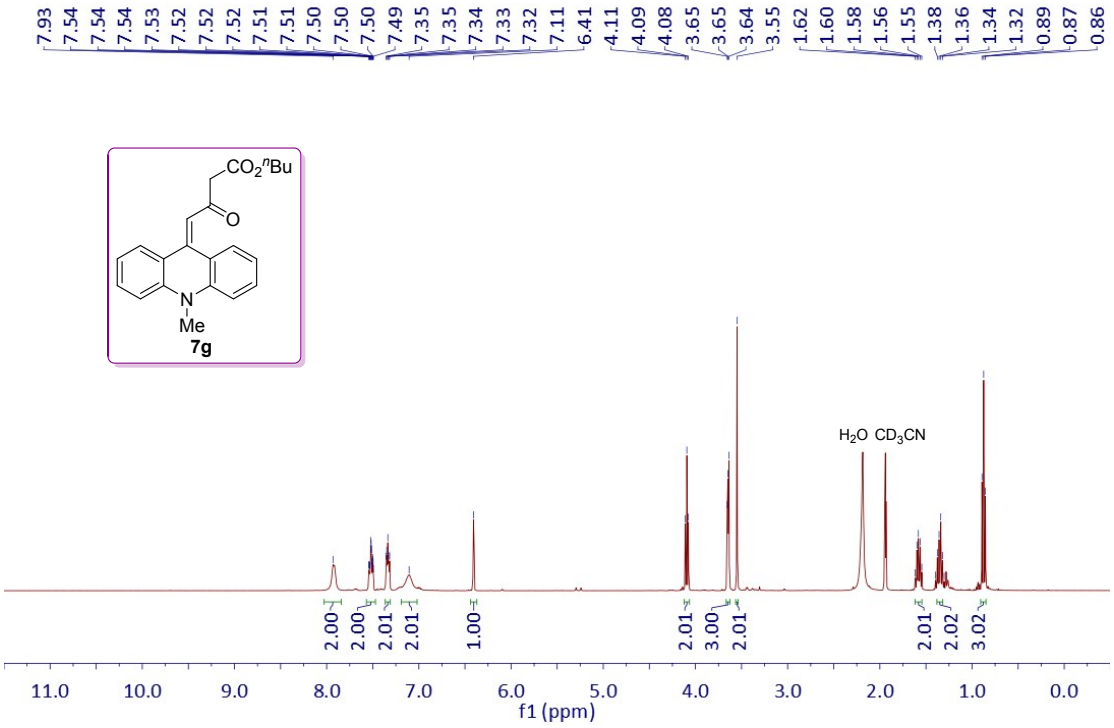
^{13}C-NMR of **7e** (CD_3CN, 100Hz)



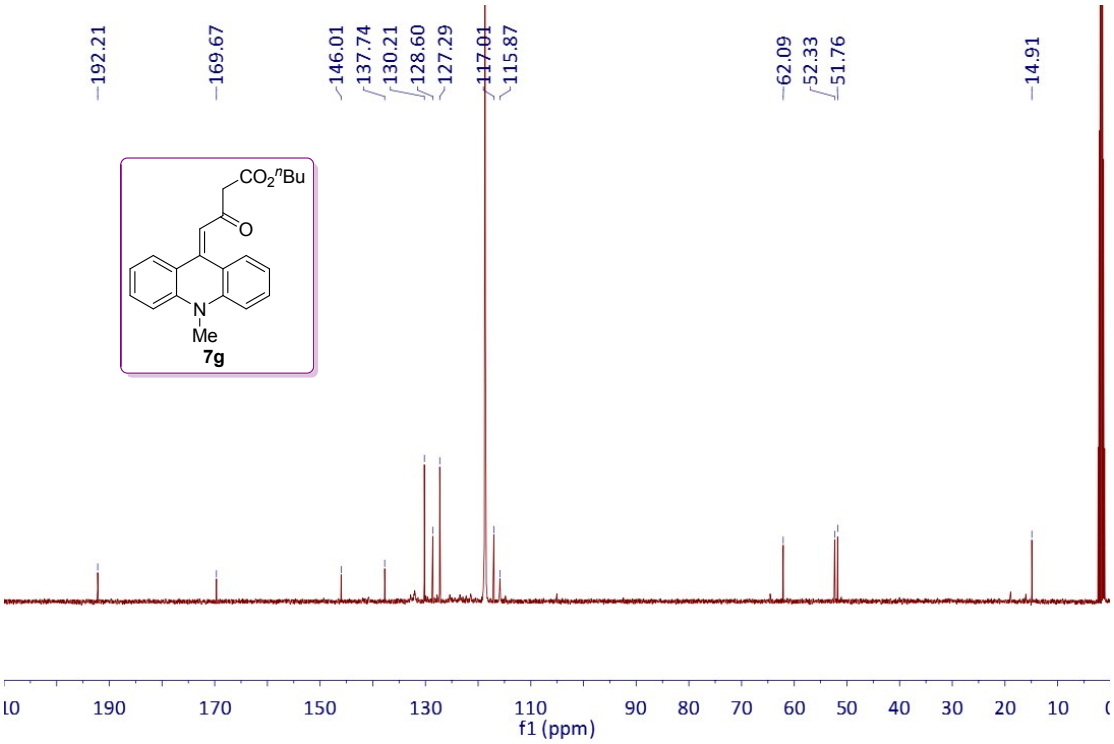
^{1}H-NMR of **7f** (CD_3CN, 400Hz)



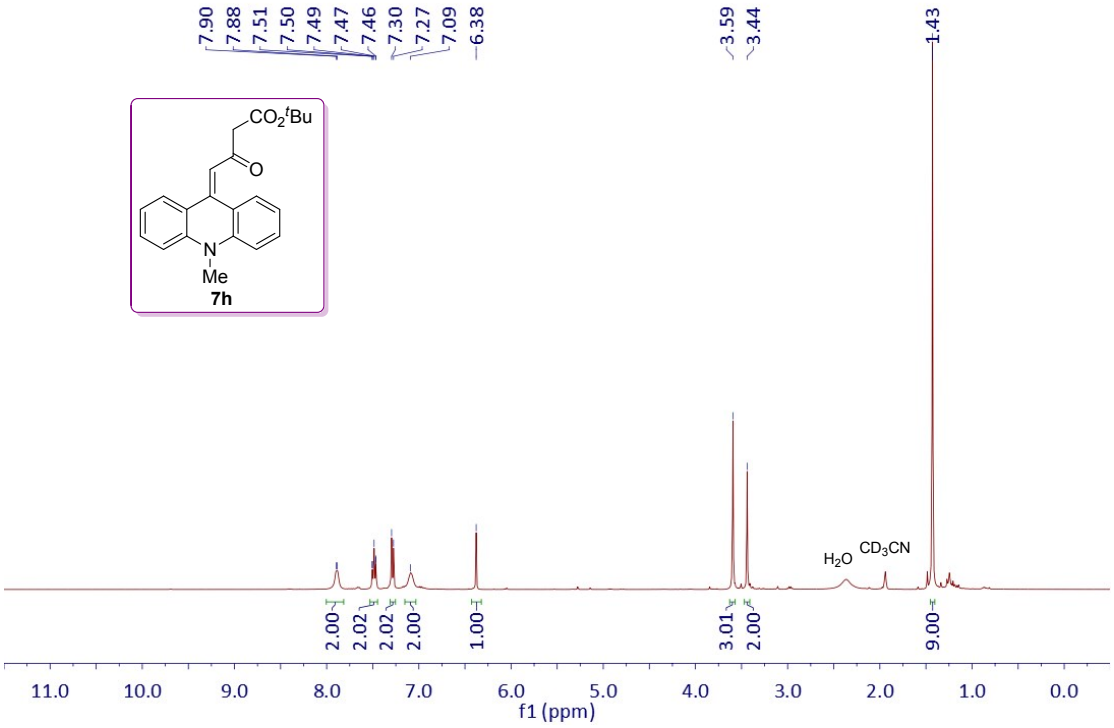
^{13}C-NMR of **7f** (CD_3CN, 100Hz)



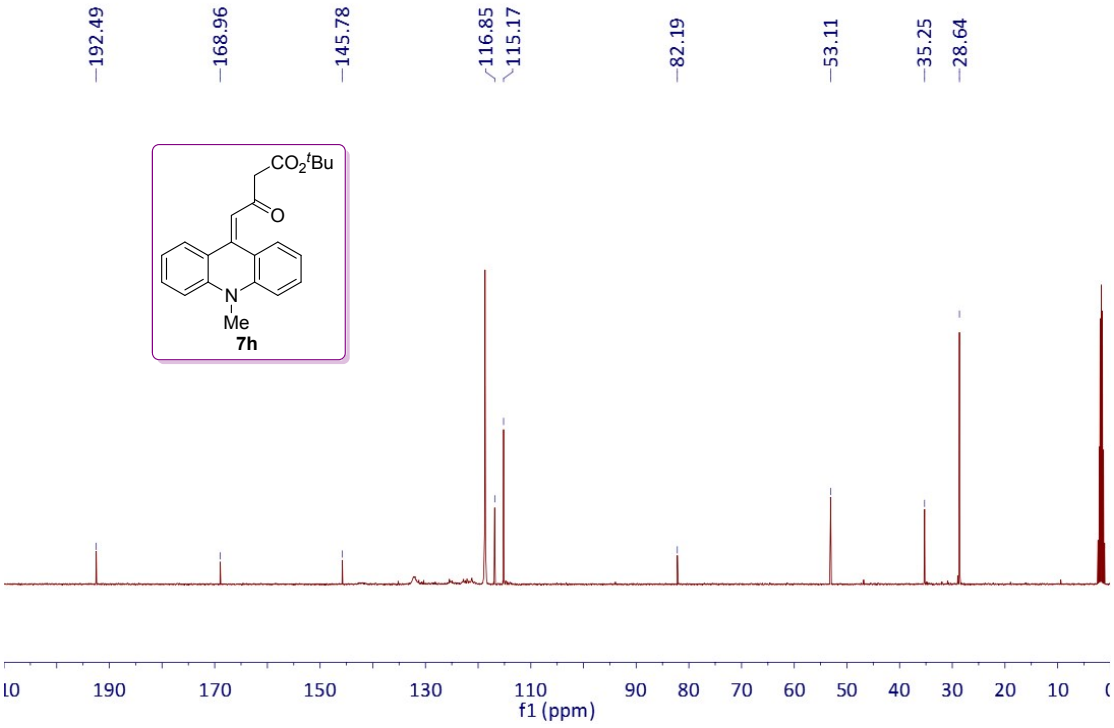
^{1}H-NMR of **7g** (CD_3CN, 400Hz)



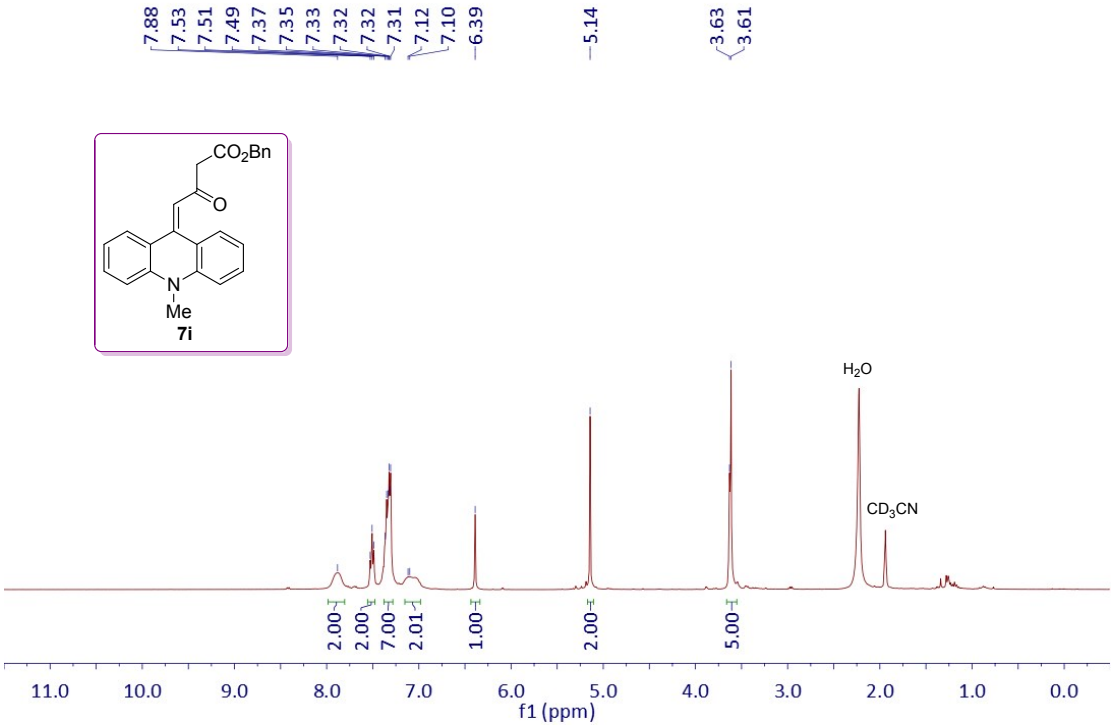
^{13}C-NMR of **7g** (CD_3CN, 100Hz)



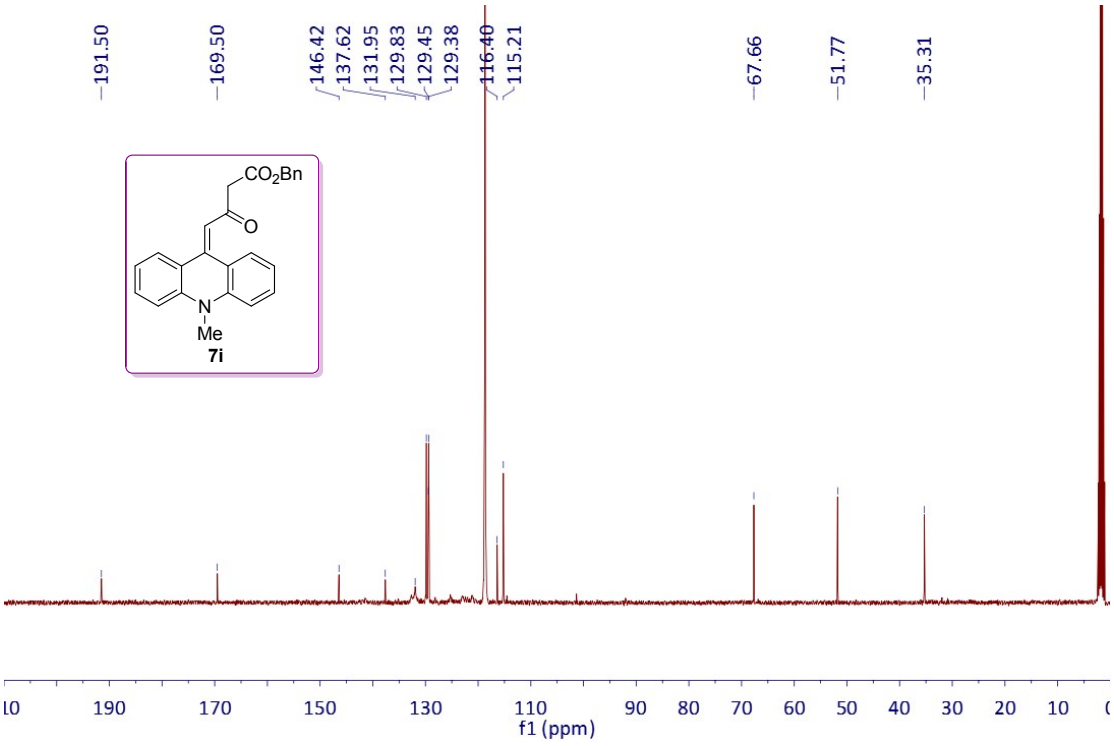
^{1}H-NMR of **7h** (CD_3CN, 400Hz)



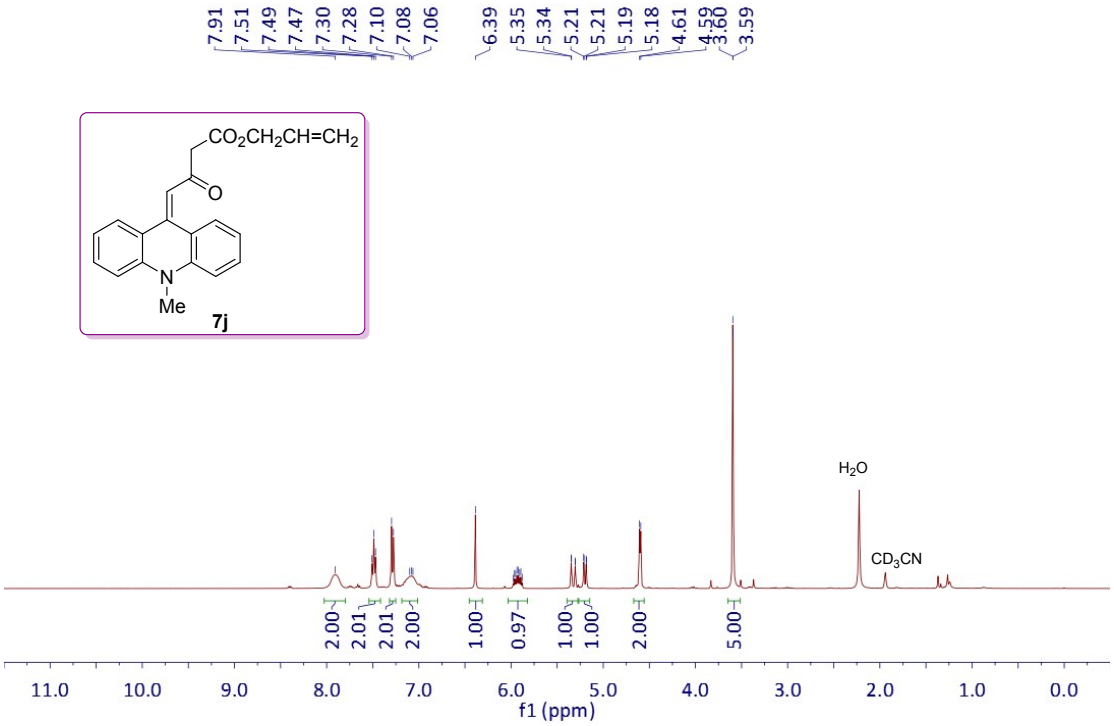
^{13}C-NMR of **7h** (CD_3CN, 100Hz)



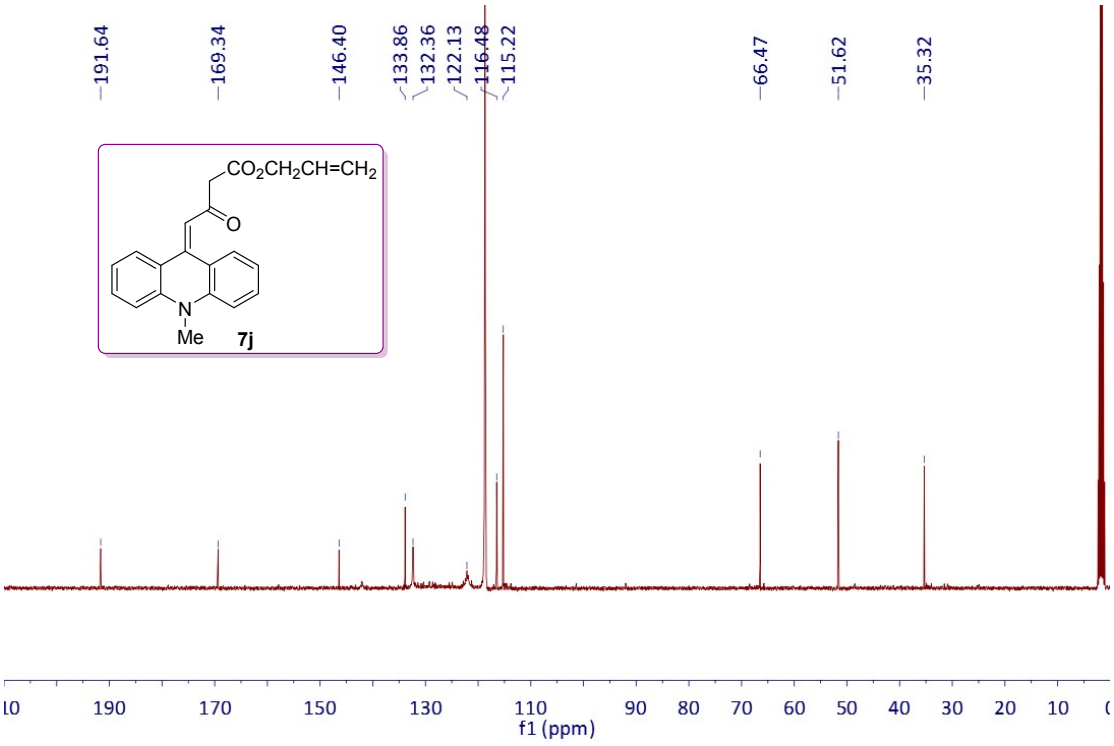
^{1}H-NMR of **7i** (CD_3CN, 400Hz)



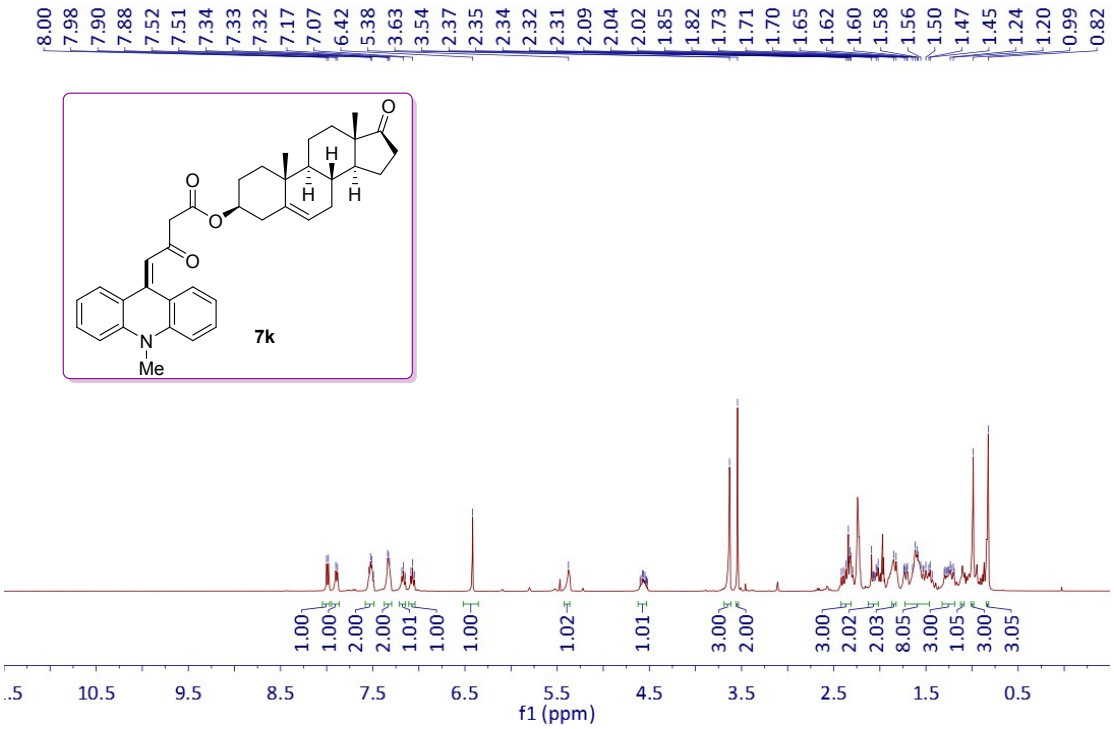
^{13}C-NMR of **7i** (CD_3CN, 100Hz)



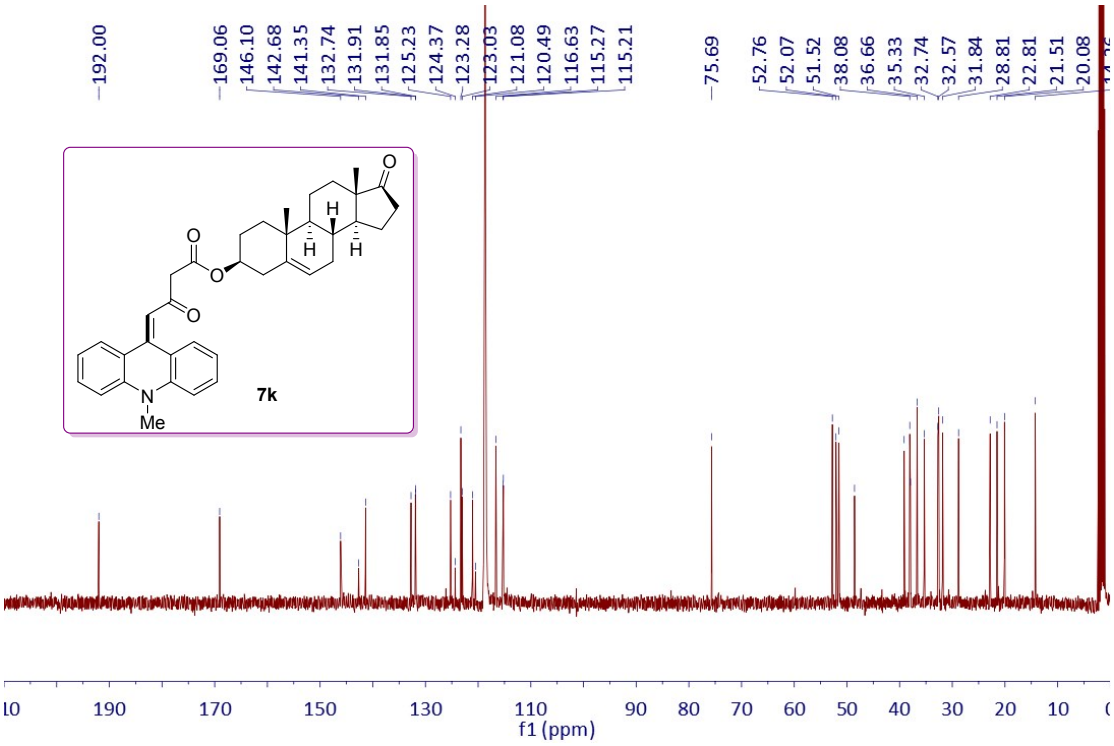
^{1}H-NMR of **7j** (CD_3CN, 400Hz)



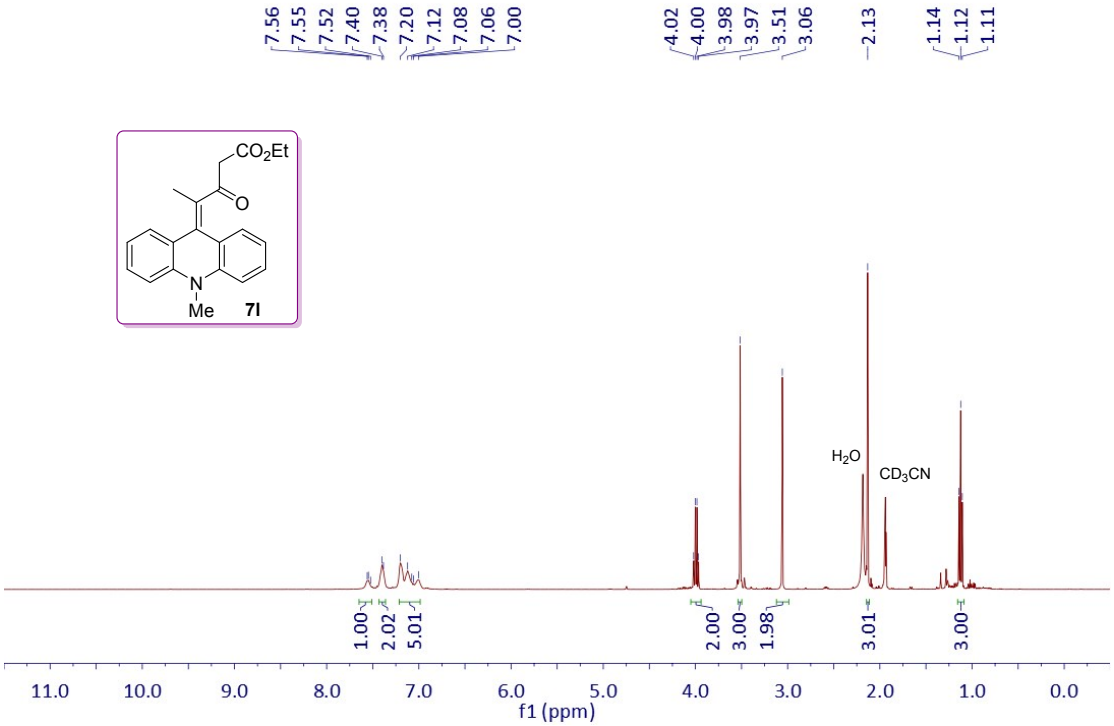
^{13}C-NMR of **7j** (CD_3CN, 100Hz)



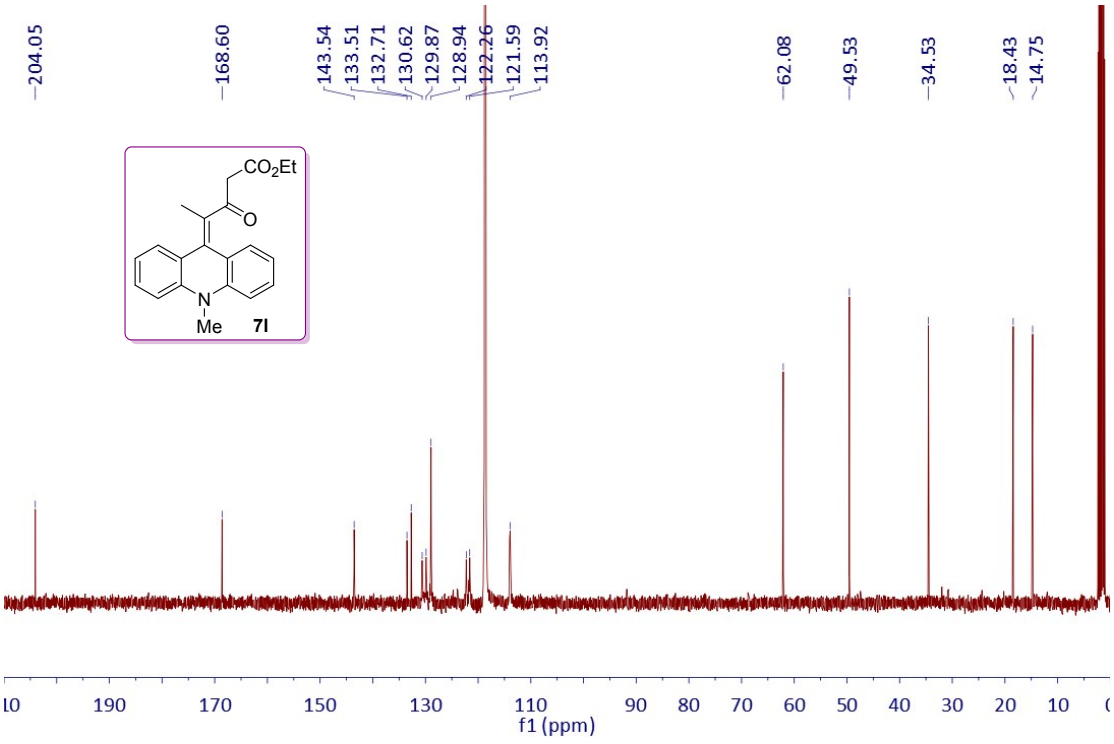
^{1}H-NMR of **7k** (CD_3CN, 400Hz)



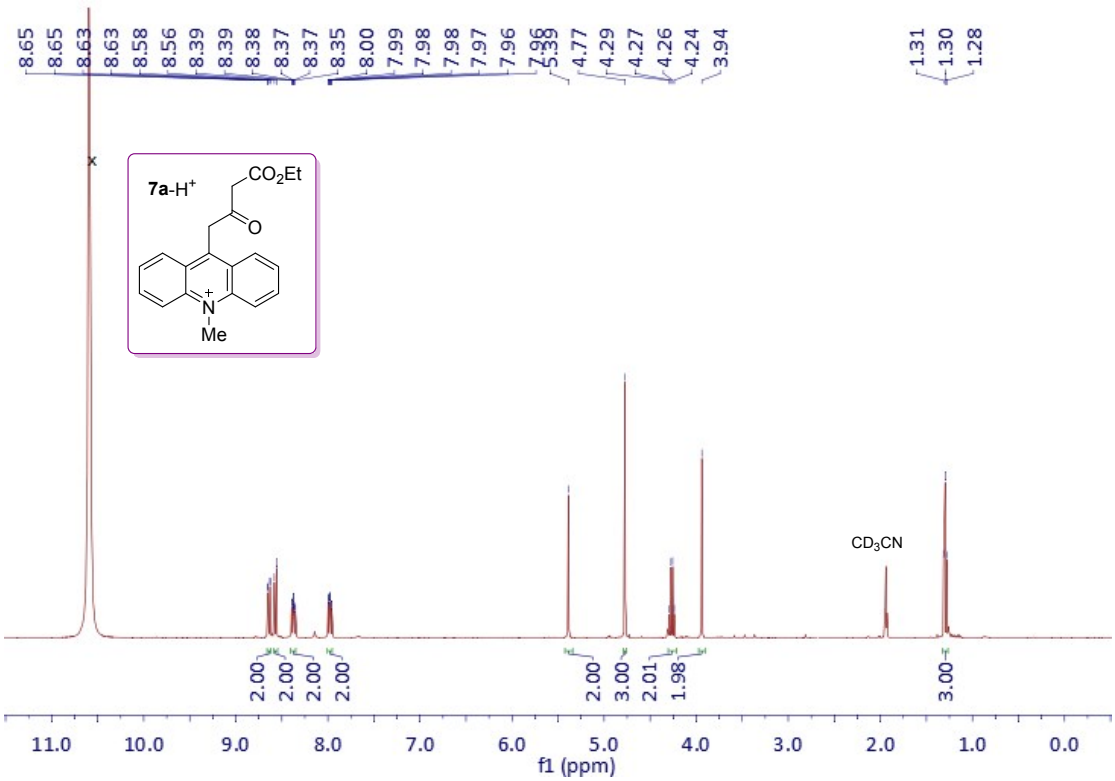
^{13}C-NMR of **7k** (CD_3CN, 100Hz)



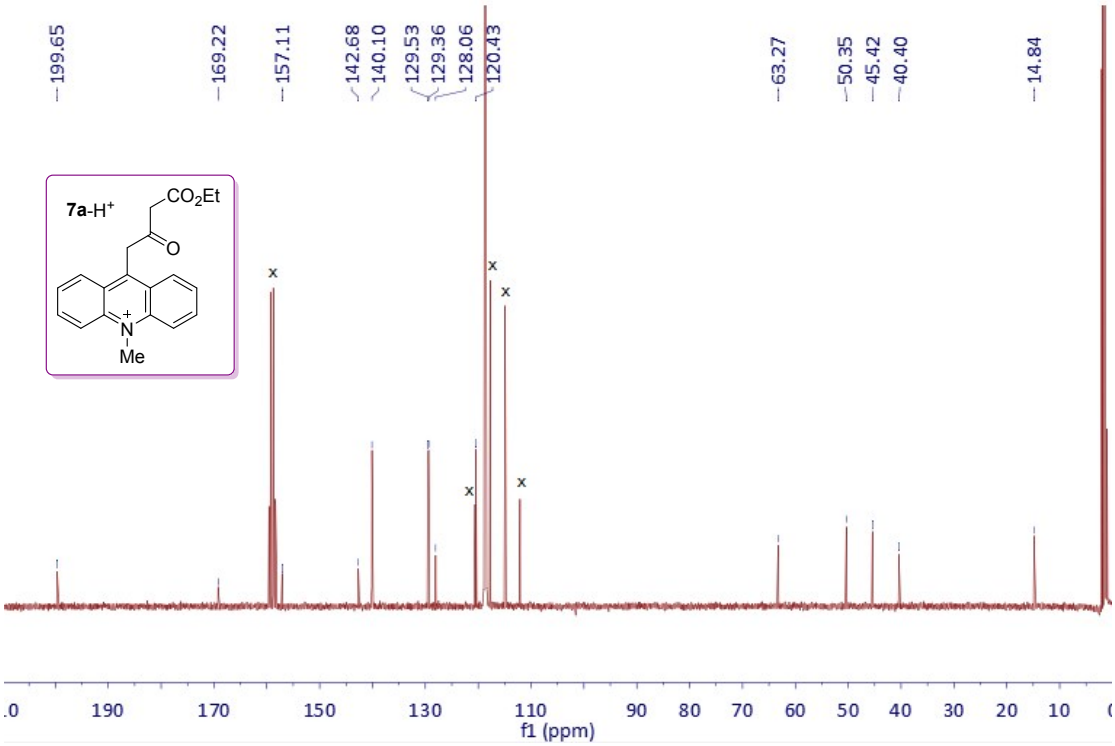
^{1}H-NMR of **7l** (CD_3CN, 400Hz)



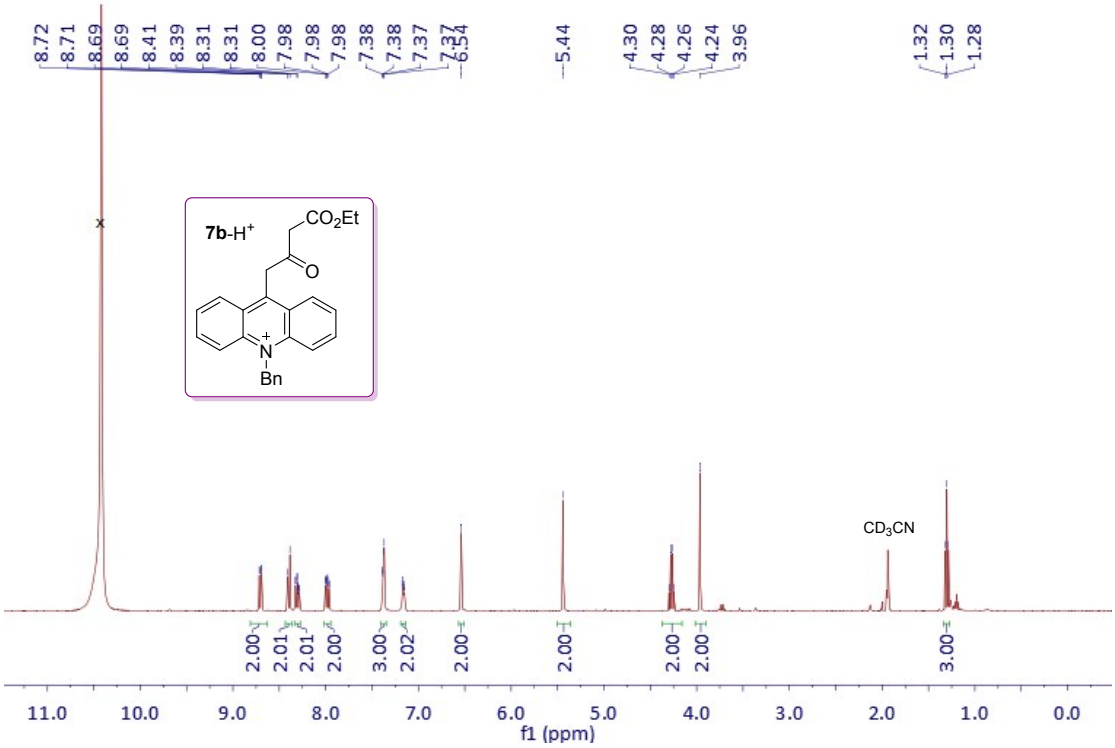
^{13}C-NMR of **7l** (CD_3CN, 100Hz)



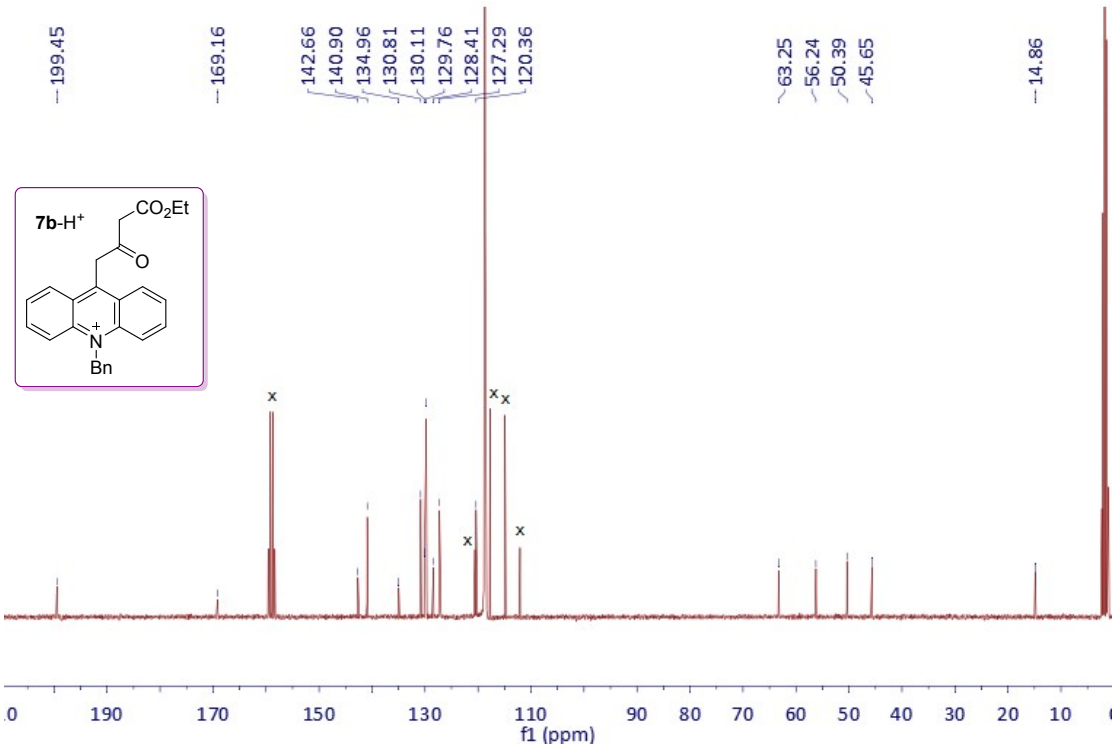
^{1}H-NMR of **7a-H**$^{+}$ (CD_3CN, 400Hz), "X" indicates the peaks of CF_3CO_2H



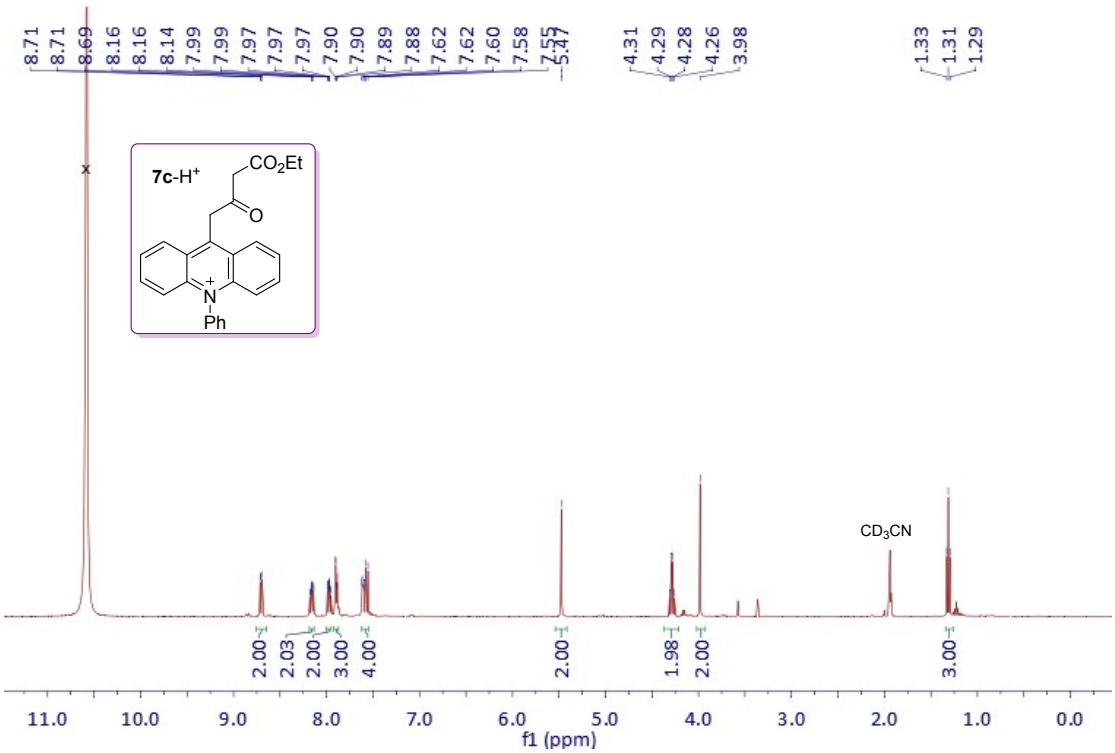
^{13}C-NMR of **7a-H**$^{+}$ (CD_3CN, 100Hz), "X" indicates the peaks of CF_3CO_2H



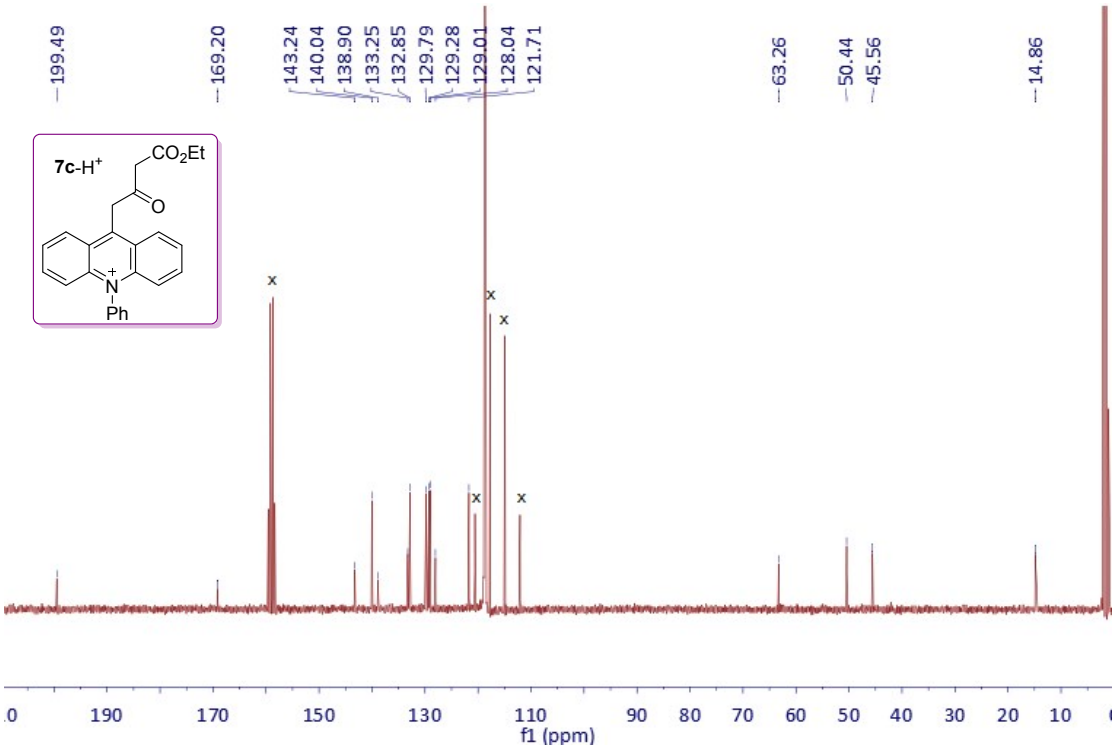
^{1}H-NMR of **7b-H**$^{+}$ (CD_3CN, 400Hz), "X" indicates the peaks of CF_3CO_2H



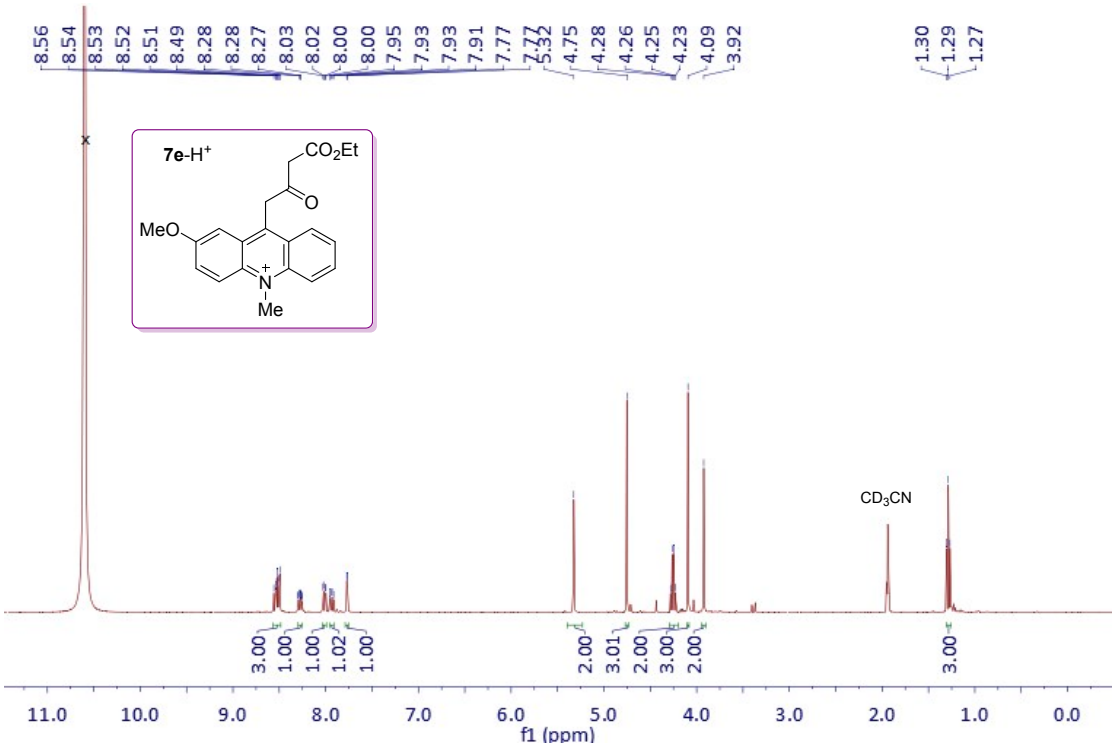
^{13}C-NMR of **7b-H**$^{+}$ (CD_3CN, 100Hz), "X" indicates the peaks of CF_3CO_2H



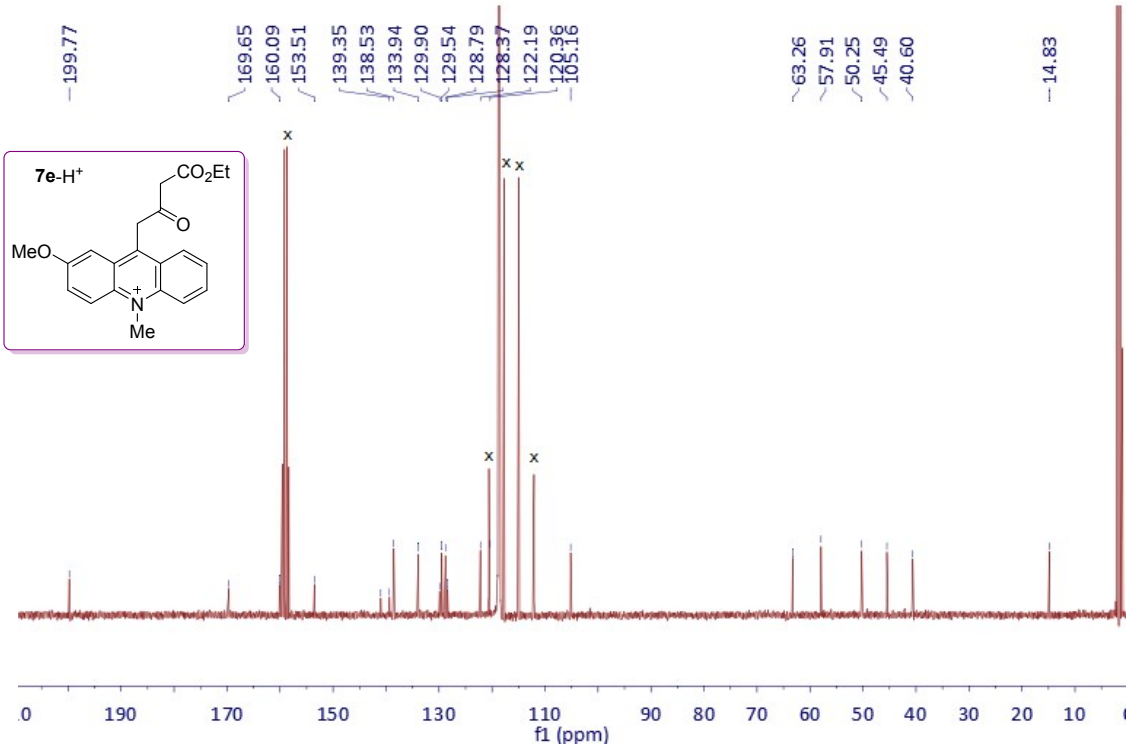
^{1}H-NMR of **7c-H**$^{+}$ (CD_3CN, 400Hz), "X" indicates the peaks of CF_3CO_2H



^{13}C-NMR of **7c-H**$^{+}$ (CD_3CN, 100Hz), "X" indicates the peaks of CF_3CO_2H



^{1}H-NMR of **7e-H**$^{+}$ (CD_3CN, 400Hz), "X" indicates the peaks of CF_3CO_2H



^{13}C-NMR of **7e-H**$^{+}$ (CD_3CN, 100Hz), "X" indicates the peaks of CF_3CO_2H