Electronic Supplementary Material (ESI) for Chemical Communications.

-Electronic Supplementary Information-

Diastereoselective Access to [4,4]-Carbospirocycles: Governance of Thermodynamic Enolates with Organocatalyst in Vinylogous Cascade Annulation

Vinod Bhajammanavar,[a] Sumitava Mallik,[a] Venkata Surya Kumar Choutipalli,[b] Venkatesan Subramanian,[b] and Mahiuddin Baidya*[a]

[a]*Department of Chemistry, Indian Institute of Technology Madras, Chennai 600 036, Tamil Nadu, India.*
[b]*Inorganic and Physical Chemistry Laboratory, CSIR-Central Leather Research Institute, Chennai 600 020, Tamil Nadu, India.*
E-mail: mbaidya@iitm.ac.in

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General Experimental Information

All non-aqueous reactions were carried out in flame-dried glassware and were stirred using a magnetic stir plate. All reactions were carried out using anhydrous solvent unless otherwise noted. DMSO and DMF were purchased from Acros Organic company. Dry toluene, xylene, mesitylene, tetrahydrofuran and chlorobenzene were prepared by distilling over sodium ketyl. Dry DCE and CH_3CN were prepared by distilling over calcium hydride. Quinidine, quinine, cinchonine, and cinchonidine were purchased from Aldrich company.

All reactions were monitored by thin layer chromatography (TLC) on WhatmanPartisil® K6F TLC plates (silica gel 60 Å, 0.25 mm thickness) and visualized using a UV lamp (366 or 254 nm) or by use of one of the following visualization reagents: PMA: 10 g phosphomolybdic acid/ 100 mL ethanol, $KMnO_4$: 0.75 g potassium permanganate, 5 g K_2CO_3 / 100 mL water. Products were isolated by column chromatography (Merck silica gel 100-200μm). Yields refer to chromatographically and spectroscopically homogenous materials unless noted otherwise. ^{13}C and ^{1}H NMR spectra were recorded on a Bruker 400 or Bruker 500 MHz spectrometers. Chemical shift values (δ) are reported in ppm and calibrated to the residual solvent peak $CDCl_3$ δ = 7.260 ppm for ^{1}H, δ = 77.160 ppm for ^{13}C, DMSO-d_6 δ = 2.500 ppm for ^{1}H, δ = 39.500 ppm for ^{13}C or calibrated to tetramethylsilane (δ = 0.00). All NMR spectra were recorded at ambient temperature (290 K) unless otherwise noted. ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constant, integration). The following abbreviations are used to indicate multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet; dt, doublet of triplet; dq, doublet of quartet; td, triplet of doublet; ddd, doublet of doublet of doublet; br, broad; app, apparent.

Mass spectra were recorded by electron spray ionization (ESI) method on a Q-TOF Micro with lock spray source. The crystal data were collected and integrated using a BrukerAxs kappa apex2 CCD diffractometer, with graphite monochromated Mo-Kα radiation.

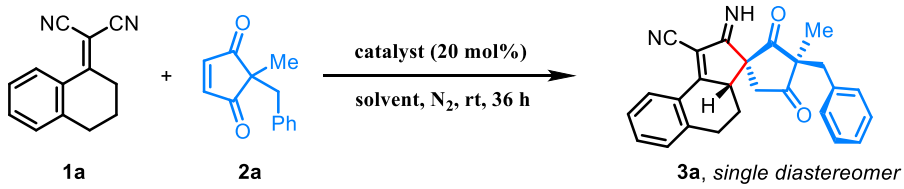
The vinyl malononitriles[1] **1** and cyclopentene-1,3-diones[2] **2** were synthesized following literature procedures published previously.

References:

(1) a) J. Lu, F. Liu and T.-P. Loh, *Adv. Synth. Catal*. 2008, **350**, 1781-1784; b) X. Li, X. Xu, W. Wei, A. Lin and H. Yao, *Org. Lett.* 2016, **18**, 428-431.

(2) a) M. S. Manna and S. Mukherjee, *Chem. Sci.* 2014, **5**, 1627-1633; b) Q. Gong, J. Wen and X. Zhang, *Chem. Sci.* 2019, **10**, 6350-6353.

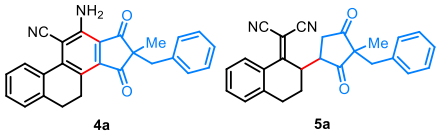
Table S1: Optimization of [4,4]-Carbospiroannulation Reaction Conditions[a]



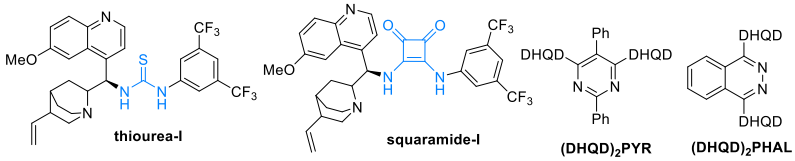
1a **2a** **3a**, *single diastereomer*

entry	solvent	catalyst	yield (%)[b]
1	DCE	quinidine	73
2	THF	quinidine	69
3	CH_3CN	quinidine	trace
4	**Toluene**	**quinidine**	**84**
5	Mesitylene	quinidine	66
6	PhCl	quinidine	51
7	Toluene	quinine	73
8	Toluene	cinchonine	47
9	Toluene	cinchonidine	40
10	Toluene	thiourea-I	20
11	Toluene	squaramide-I	27
12	Toluene	$(DHQD)_2PYR$	25
13	Toluene	$(DHQD)_2PHAL$	16
14	Toluene	DBU	33 (70)[d]
15	Toluene	DBN	27 (64)[d]
16	Toluene	DMAP	trace
17	Toluene	$^{i}Pr_2NEt$	NR
18	Toluene	DABCO	trace
19	Toluene	3-quinuclidinol	59[c]
20	Toluene	$LiO^{t}Bu/KO^{t}Bu$	27/36[e]
21	Toluene	K_2CO_3 or Cs_2CO_3	trace
22	Toluene+5µl H_2O	quinidine	35
23	Toluene+50µl H_2O	quinidine	NR
24	Toluene	–	NR

Undesired products:

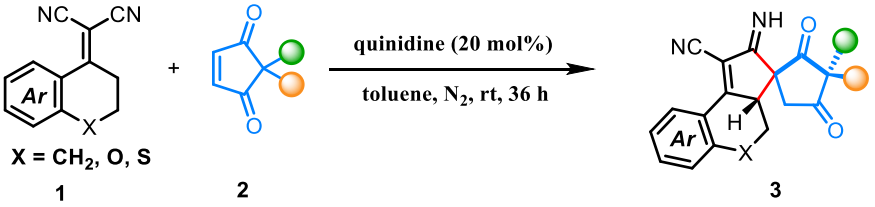


Chiral organocatalysts:



[a]Reaction conditions: **1a** (0.22 mmol), **2a** (0.26 mmol), N_2, solvent (4 mL), rt, 36 h. [b]Isolated yields were provided. The dr was determined by ^1H NMR analysis of crude reaction mixture. [c]Combined yield of **3a** and **5a**. [d]Reaction was stopped after 24 h. [e]Yield corresponds to (4+2) annulation product **4a**. NR: No reaction.

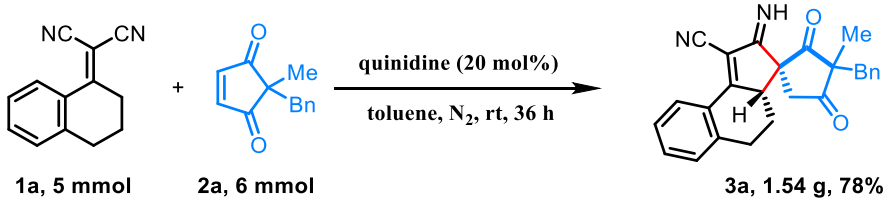
General Procedure for the Synthesis of [4,4]-Carbospirocycles 3:



The alkylidene malononitriles **1** (0.22 mmol, 1 equiv), cyclopentene-1,3-diones **2** (0.26 mmol, 1.2 equiv), and quinidine (20 mol%) were taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated, and backfilled with nitrogen gas. Then, dry toluene (4 mL) was added via a syringe under nitrogen. The reaction mixture was allowed to stir at room temperature for 36 h. After completion, the crude reaction mixture was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (5→15% EtOAc: hexane) to provide pure spirocyclic imine **3**.

*Note: DBU (20 mol%) base was used instead of quinidine and reaction was stopped after 24 h during the synthesis of compounds **3ao** to **3at**.*

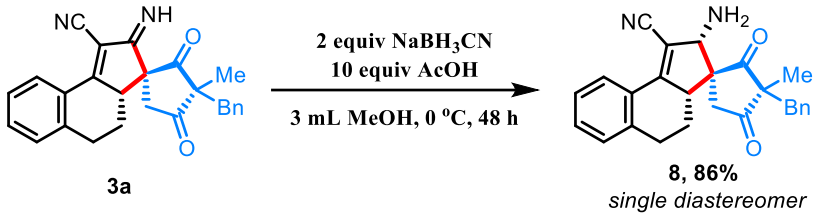
Procedure for the Gram Scale Synthesis of Compound 3a:



The α-tetralone derived malononitrile **1a** (0.97 g, 5.0 mmol, 1 equiv), cyclopentene-1, 3-dione **2a** (1.2 g, 6.0 mmol, 1.2 equiv), and quinidine (324 mg, 20 mol%) were taken in a 100 mL oven dried round bottom flask equipped with a magnetic stir. The round bottom flask was capped with a rubber septum, evacuated, and backfilled with nitrogen gas. Then, dry toluene (15 mL) was added via syringe under nitrogen. The mixture was allowed to stir at room temperature for 36 h. After completion, volatiles were carefully evaporated, and the crude product obtained was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (5→15% EtOAc: hexane) to provide pure spirocyclic imine **3a** (1.54 g, 78% yield).

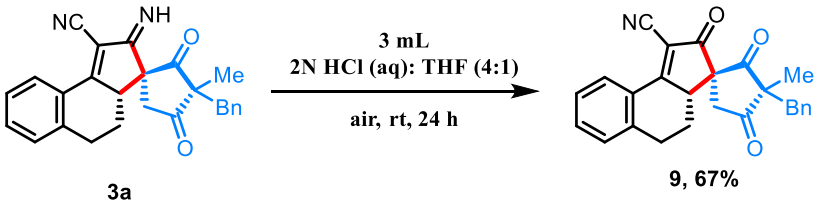
Post-Functionalizations

i. Chemoselective Reduction for the Synthesis of Compound 8:



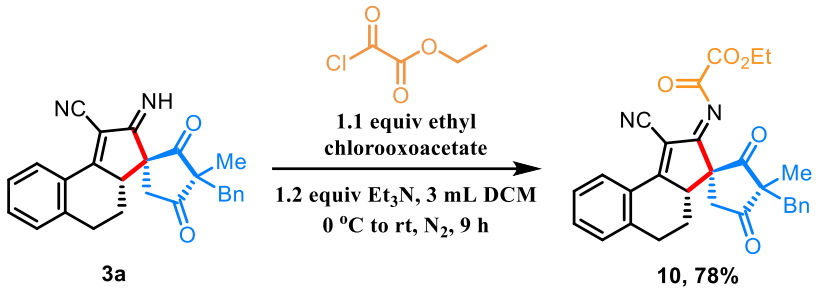
The product **3a** (0.22 mmol, 1 equiv) was taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated and backfilled with nitrogen gas. Then, dry MeOH (3 mL) and acetic acid (10 equiv) were added via syringe. The reaction mixture was cooled to 0 ^{o}C. Sodium cyanoborohydride (2 equiv) was added portion wise and reaction mixture was allowed to stir for 48 h at 0 ^{o}C. Then, the reaction mixture was quenched with aq. NH_4Cl solution, and extracted with DCM. The crude product obtained after evaporation of DCM was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (15→35% EtOAc: hexane) to provide pure spirocyclic amine **8** (75 mg, 86% yield) as a single diastereomer.

ii. Synthesis of Triketone Spirocyclic Compound 9:



The product **3a** (0.22 mmol, 1 equiv) was taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum. Then, 3 mL of 2N HCl (aq): THF (4:1) mixture were added via syringe. The reaction mixture was allowed to stir for 24 h. The reaction mixture was quenched with aq. NaCl solution and extracted with DCM. The crude product obtained after evaporation of DCM was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (5→15% EtOAc: hexane) to provide pure triketone spirocyclic compound **9** (58 mg, 67% yield) as a single diastereomer.

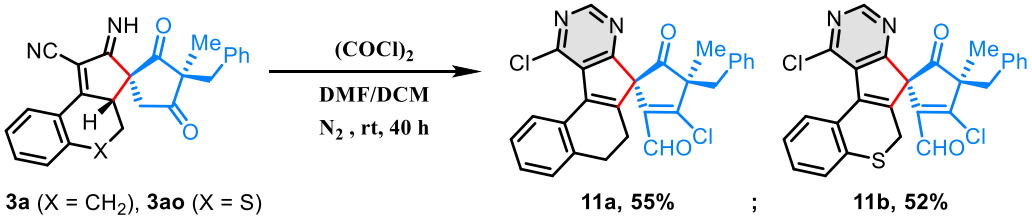
iii. Synthesis of *N*-Protected Carbospirocycle 10:



The product **3a** (0.22 mmol, 1 equiv) was taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated, and backfilled with nitrogen gas. Then, dry DCM (3 mL) and Et_3N (1.2 equiv) were added via syringe. The reaction mixture was cooled to 0 °C. Ethyl chlorooxoacetate (1.1 equiv) was added and reaction mixture was allowed to attain room temperature with stirring. After 9 h (TLC monitored), reaction mixture was quenched with aq. NH_4Cl solution, and extracted with DCM. After evaporation, the crude product was purified by crystallization technique using DCM and hexane solvents combination to get pure *N*-protected spirocycle **10** (85 mg, 78% yield) as a single diastereomer.

Skeletal Rearrangement Reactions

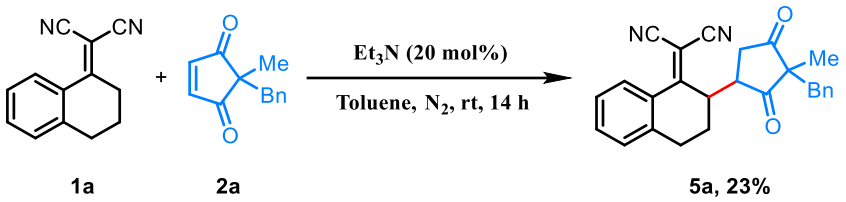
Synthesis of Pyrimidine Fused Spirocycles 11:



The corresponding spirocyclic product **3a** or **3ao** (0.2 mmol, 1 equiv) was taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated and backfilled with nitrogen gas. Then, dry DCM (2 mL) followed by dry DMF (50 μl) were added via syringe. The reaction mixture was cooled to 0 °C and oxalyl chloride (10 equiv) was added drop wise to the reaction mixture at 0 °C under the positive pressure of nitrogen gas (balloon). The reaction mixture was allowed to attain room temperature with stirring and stirred further for 40 h. After completion (TLC monitored), reaction mixture was workup with ice-cold brine solution, and extracted with DCM. Resulting organic layer was dried over anhydrous Na_2SO_4. The crude product obtained after evaporation of DCM was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (10→25% EtOAc: hexane) to provide pure indane-1,3-dione derivative **11a** (59 mg, 55%) or **11b** (58 mg, 52%) respectively.

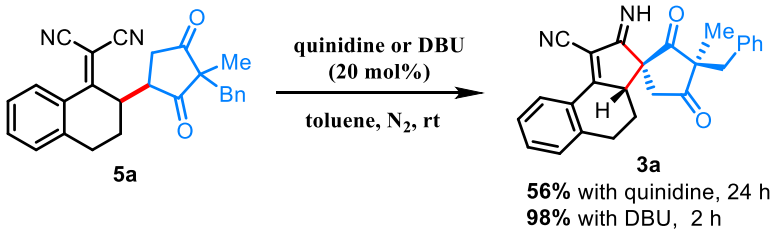
Mechanistic Investigations

Isolation of Reaction Intermediate 5a:



The α-tetralone derived malononitriles **1a** (0.22 mmol, 1 equiv), cyclopentene-1,3-diones **2a** (0.26 mmol, 1.2 equiv), and Et_3N (20 mol%) were taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated, and backfilled with nitrogen gas. Then, toluene (4 mL) was added via syringe. The mixture was allowed to stir at room temperature for 14 h. The crude reaction mixture was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (5→15% EtOAc: hexane) to provide Michael addition product **5a** (20 mg, 23% yield).

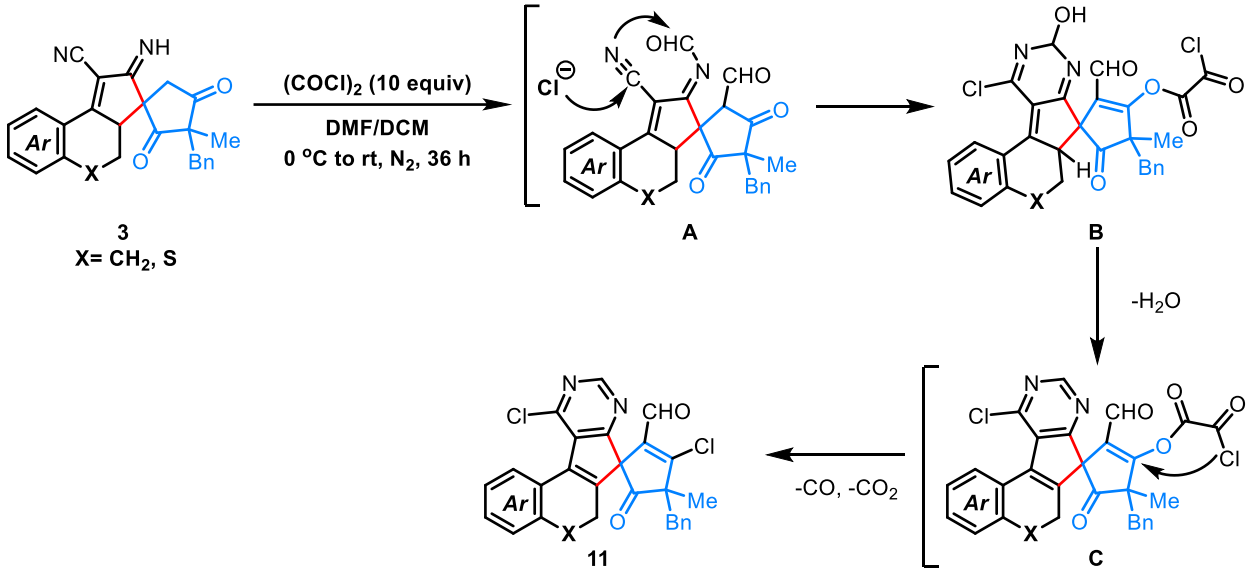
Spiroannulation Reaction with Intermediate 5a:



Isolated reaction intermediate **5a** (0.02 mmol, 1 equiv) and DBU (20 mol%) were taken in a 16×100 mm oven dried reaction tube equipped with a magnetic stir. The reaction tube was capped with a rubber septum, evacuated and backfilled with nitrogen gas. Then, dry toluene (2 mL) was added via syringe. The reaction mixture was allowed to stir at room temperature for 2 h. After completion (TLC monitored), the crude reaction mixture was loaded directly onto silica gel column and purified with a gradient eluent of hexane and ethyl acetate (5→15% EtOAc: hexane) to provide pure spirocyclic imine **3a** in 98% yield. Execution of the same reaction with quinidine catalyst resulted in 56% yield (44 mg) of spirocyclic imine **3a** after 24 h.

Skeletal Rearrangement Mechanism

Possible Mechanism for Pyrimidine Fused Carbospirocycles 11



List of detailed references 4, 7, and 8 from the manuscript

4. (a) T. H. Babu, A. A. Joseph, D. Muralidharan and P. T. Perumal, *Tetrahedron Lett.* 2010, **51**, 994-996; (b) X.-M. Shi, W.-P. Dong, L.-P. Zhu, X.-X. Jiang and R. Wang, *Adv. Synth. Catal.* 2013, **355**, 3119-3123; (c) S. E. Kiruthika, P. T. Perumal, C. Balachan dran and S. Ignacimuthu, *J. Chem. Sci.* 2014, **126**, 177-185; (d) T.-Z. Li, J. Xie, Y. Jiang, F. Sha and X.-Y. Wu, *Adv. Synth. Catal.* 2015, **357**, 3507-3511; (e) H. Mei, L. Lin, B. Shen, X. Liu and X. Feng, *Org. Chem. Front.* 2018, **5**, 2505-2509; (f) H.-L. Cui , X. Tang, M.-F. Li, X.-J. Xu and Y. Shi, *Synlett* 2019, **30**, 845-850; (g) Z. Zhou, Q. He, Y. Jiang, Q. Ouyang, W. Du and Y.-C. Chen, *Org. Lett.* 2019, **21**, 7184-7188; (h) P.-W. Xu, J.-S. Yu, C. Chen, Z.-Y. Cao, F. Zhou and J. Zhou, *ACS Catal.* 2019, **9**, 1820−1882.

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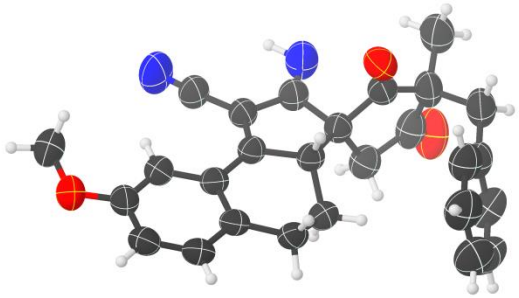
8 (a) S. Zhuo, T. Zhu, L. Zhou, C. Mou, H. Chai, Y. Lu, L. Pan, Z. Jin and Y. R. Chi, *Angew. Chem. Int. Ed.* 2019, **58,** 1784-1788; (b) E. Sánchez-Larios, J. M. Holmes, C. L. Daschner and M. Gravel, *Org. Lett.* 2010, **12**, 5772-5775; (c) S. Barik, S. Shee, S. Das, R. G. Gonnade, G. Jindal, S. Mukherjee and A. T. Biju, *Angew. Chem. Int. Ed.* 2021, **60,** 12264-12268; (d) B.-M. Yang, P.-J. Cai, Y.-Q. Tu, Z.-X. Yu, Z.-M. Chen, S.-H. Wang, S.-H. Wang and F.-M. Zhang, *J. Am. Chem. Soc.* 2015, **137**, 8344-8347; (e) S. Li, J.-W. Zhang, X.-L. Li, D.-J. Cheng and B. Tan, *J. Am. Chem. Soc.* 2016, **138**, 16561-16566; (f) J. Liu, Q. Li, Y. Wei and M. Shi, *Org. Lett.* 2020, **22**, 2494-2499.

Crystallographic Experimental Section:

Crystals of compounds **3b, 3aa, 3aq,** and **11a** were obtained through slow evaporation technique at room temperature from their respective solution in hexane: DCM solvent combinations.

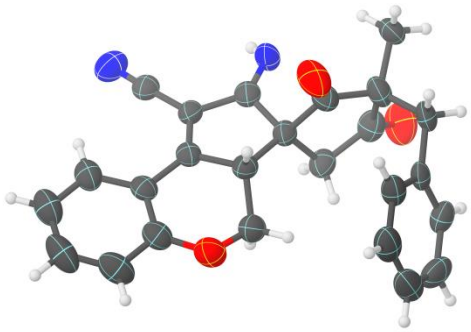
Crystal data and structure refinement for compound 3b (CCDC 2096229, Ellipsoid Probability 50%):



Identification code	Compound **3b**	
Empirical formula	C_{27} H_{24} N_2 O_3	
Formula weight	424.48	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.7603(4) Å	a= 90°.
	b = 7.2351(3) Å	b= 92.4650(10)°.
	c = 15.8107(6) Å	g = 90°.
Volume	1115.47(8) $Å^3$	
Z	2	
Density (calculated)	1.264 Mg/m^3	
Absorption coefficient	0.664 mm^{-1}	
F(000)	448	
Crystal size	0.300 x 0.250 x 0.200 mm^3	
Theta range for data collection	4.534 to 72.312°.	
Index ranges	-12<=h<=11, -8<=k<=8, -19<=l<=19	
Reflections collected	14745	
Independent reflections	4304 [R(int) = 0.0438]	
Completeness to theta = 67.679°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7536 and 0.6183	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4304 / 1 / 296	
Goodness-of-fit on F^2	1.080	
Final R indices [I>2sigma(I)]	R1 = 0.0484, wR2 = 0.1314	
R indices (all data)	R1 = 0.0536, wR2 = 0.1386	
Absolute structure parameter	0.20(13)	
Extinction coefficient	0.136(11)	

Largest diff. peak and hole	0.168 and -0.139 e.Å^{-3}

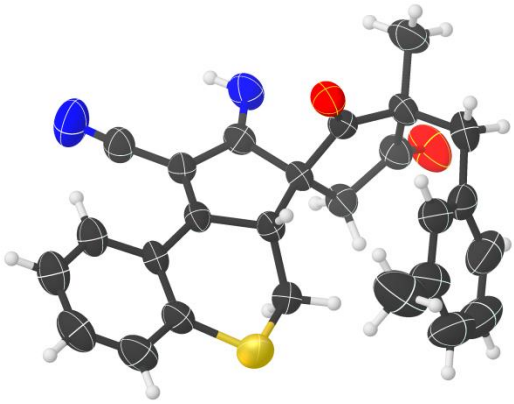
Crystal data and structure refinement for compound 3aa: (CCDC 2096228, Ellipsoid Probability 50%)



Identification code	Compound **3aa**
Chemical formula	$C_{25}H_{20}N_2O_3$
Formula weight	396.43 g/mol
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal size	0.190 x 0.220 x 0.250 mm
Crystal habit	clear light colourless Rectangular
Crystal system	monoclinic
Space group	P 1 21 1
Unit cell dimensions	a = 9.5635(6) Å α = 90°
	b = 6.7073(3) Å β = 90.829(3)°
	c = 15.8118(8) Å γ = 90°
Volume	1014.15(9) Å^3
Z	2
Density (calculated)	1.298 g/cm^3
Absorption coefficient	0.086 mm^{-1}
F(000)	416
Theta range for data collection	2.13 to 25.00°
Index ranges	-11<=h<=11, -7<=k<=7, -18<=l<=18
Reflections collected	7813
Independent reflections	3558 [R(int) = 0.0238]
Coverage of independent reflections	99.9%
Absorption correction	multi-scan
Max. and min. transmission	0.9840 and 0.9790
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick 2008)

Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	Σ w(Fo2 - Fc2)2
Data / restraints / parameters	3558 / 1 / 277
Goodness-of-fit on F2	1.039
Final R indices	2715 data; I>2σ(I) R1 = 0.0397, wR2 = 0.0798
	all data R1 = 0.0598, wR2 = 0.0909
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0388P)^2+0.0483P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	-0.3(7)
Extinction coefficient	0.0370(40)
Largest diff. peak and hole	0.105 and -0.120 eÅ^{-3}
R.M.S. deviation from mean	0.028 eÅ^{-3}

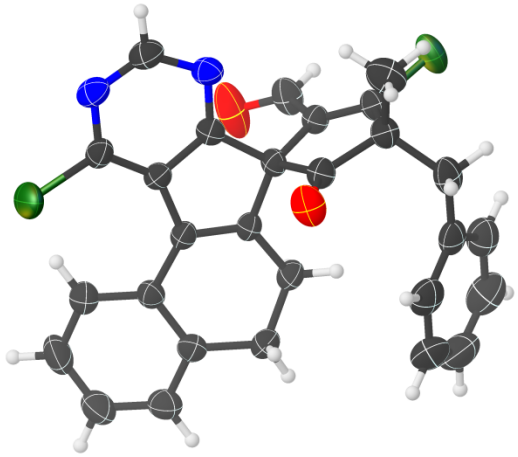
Crystal data and structure refinement for compound 3aq: (CCDC 2096230, Ellipsoid Probability 50%)



Identification code	Compound **3aq**	
Empirical formula	$C_{26}H_{22}N_2O_2S$	
Formula weight	426.51	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 11.4340(12) Å	α= 90°.
	b = 10.0679(10) Å	β= 102.571(6)°.
	c = 19.338(2) Å	γ = 90°.
Volume	2172.8(4) Å^3	
Z	4	
Density (calculated)	1.304 Mg/m^3	
Absorption coefficient	0.175 mm^{-1}	

F(000)	896
Crystal size	0.300 x 0.250 x 0.200 mm^3
Theta range for data collection	1.825 to 25.899°.
Index ranges	-14<=h<=14, -12<=k<=12, -23<=l<=23
Reflections collected	20693
Independent reflections	4204 [R(int) = 0.0751]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7453 and 0.6243
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4204 / 0 / 287
Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0525, wR2 = 0.1071
R indices (all data)	R1 = 0.1206, wR2 = 0.1400
Extinction coefficient	0.0107(10)
Largest diff. peak and hole	0.203 and -0.229 e.$Å^{-3}$

Crystal data and structure refinement for compound 11a: (CCDC 2096231, Ellipsoid Probability 50%)

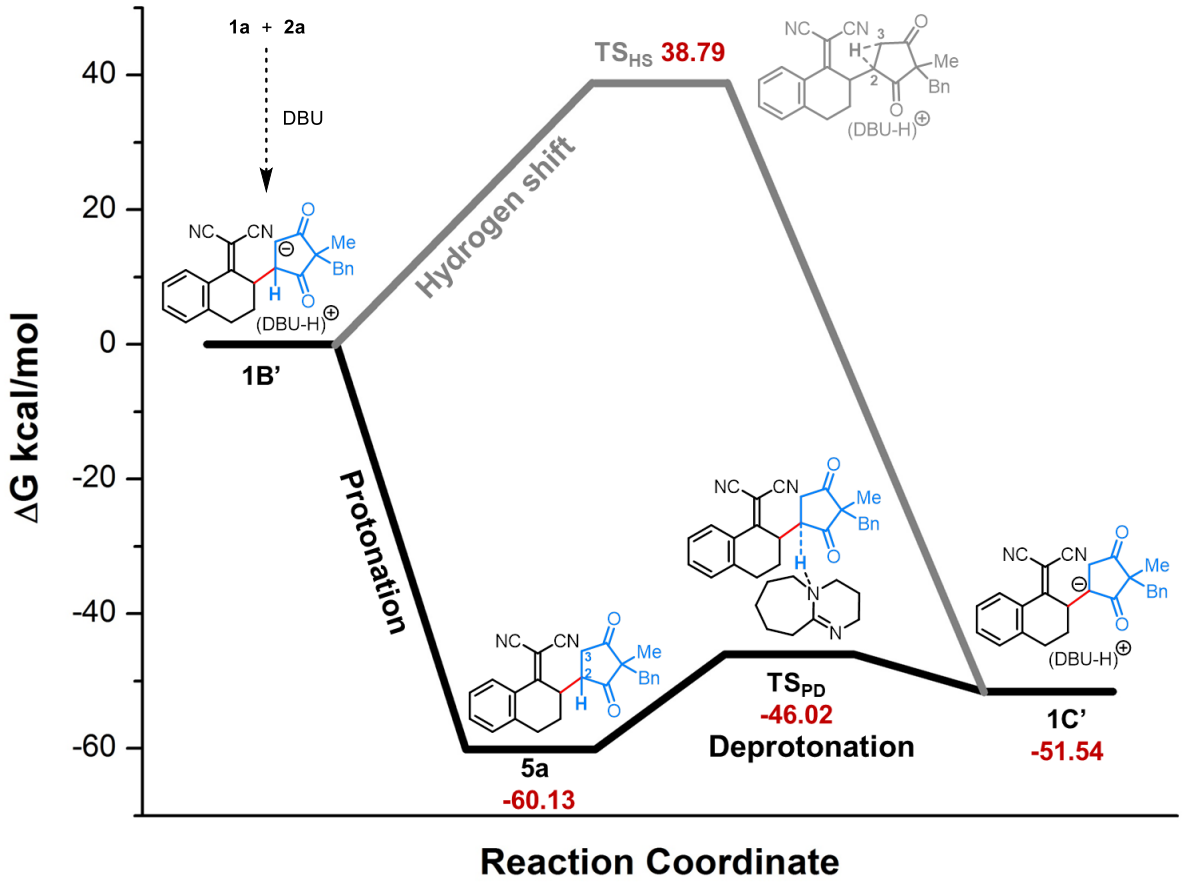


Identification code	Compound **11a**	
Chemical formula	$C_{28}H_{20}Cl_2N_2O_2$	
Formula weight	487.36 g/mol	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.220 x 0.250 mm	
Crystal habit	clear light colourless BLock	
Crystal system	orthorhombic	
Space group	P c a 21	
Unit cell dimensions	a = 12.4644(7) Å	α = 90°
	b = 11.8934(6) Å	β = 90°

	c = 15.4819(7) Å γ = 90°
Volume	2295.1(2) $Å^3$
Z	4
Density (calculated)	1.410 g/cm^3
Absorption coefficient	0.313 mm^{-1}
F(000)	1008
Theta range for data collection	1.71 to 25.00°
Index ranges	-14<=h<=14, -14<=k<=13, -18<=l<=18
Reflections collected	15384
Independent reflections	4038 [R(int) = 0.0509]
Coverage of independent reflections	100.0%
Absorption correction	multi-scan
Max. and min. transmission	0.9690 and 0.9260
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	Σ w(Fo2 - Fc2)2
Data / restraints / parameters	4038 / 1 / 308
Goodness-of-fit on F2	1.004
Final R indices	3284 data; I>2σ(I) R1 = 0.0378, wR2 = 0.0835
	all data R1 = 0.0524, wR2 = 0.0920
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0470P)^2]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.1(0)
Largest diff. peak and hole	0.152 and -0.181 $eÅ^{-3}$
R.M.S. deviation from mean	0.041 $eÅ^{-3}$

Computational Details

All the quantum chemical computations were carried out using the B3LYP[3] hybrid functional with the Grimme's dispersion parameter (D3) for dispersion corrections in conjunction with the 6-31G(d) basis set.[4] Standard convergence criteria and an ultrafine integration grid were used. All the thermodynamic data was computed at 298.15 K and 1 atm. All the optimized geometries were verified as minima or first order saddle points by the harmonic vibrational frequency analysis and thermal and zero point energy (ZPE) corrections were also included. As in the standard practice, the presence of one imaginary frequency criteria was used for the characterization of transition states (TS). Further, intrinsic reaction coordinate (IRC) calculations confirmed the nature of the transition states and provided the information that, they were connected to the respective minima (reactant and product). All the calculations were performed using G09RevC.01 suite of program.[5]



Scheme S1. Gibbs free energy reaction profile of direct hydrogen shift and protonation-deprotonation pathways calculated at B3LYP-D3/6-31G(d,p) level of theory.

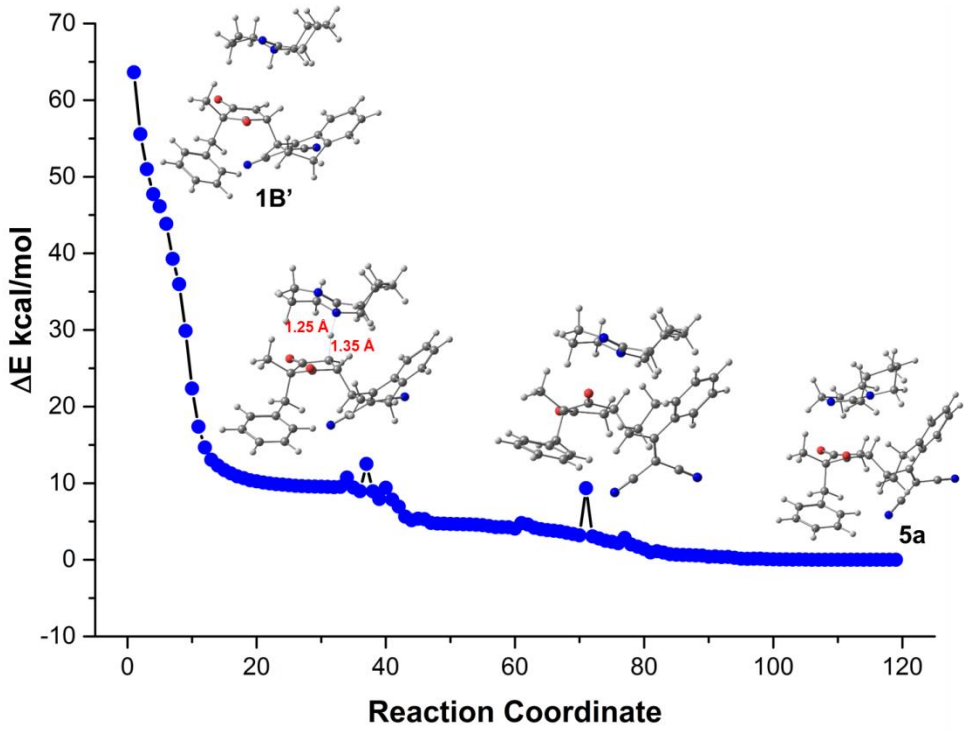


Figure S1. Energy profile (ΔE vs step size) for geometry relaxation of enolate with acid calculated at B3LYP-D3/6-31G(d,p) level of theory.

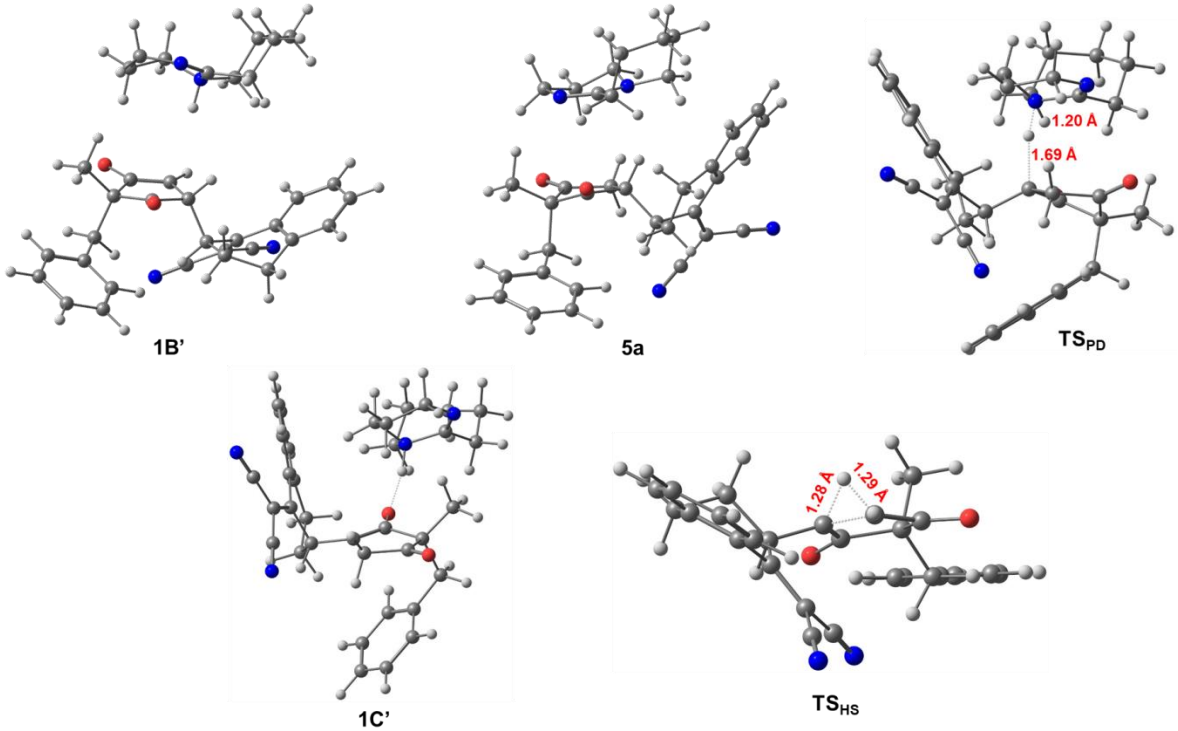


Figure S2. Optimized geometries of intermediates involved calculated at B3LYP-D3/6-31G(d,p) level of theory

Table S2. Cartesian coordinates of intermediate geometries calculated at B3LYP-D3/6-31G(d,p) level of theory.

	1B'				**5a**		
C	3.22076700	3.81635300	-1.93499100	C	4.15403100	1.83776000	-1.95026400
C	1.91390200	3.82578200	-2.42862600	C	2.88691300	1.66212600	-2.50160000
C	0.84518600	3.45686800	-1.61309700	C	1.72625500	1.88579600	-1.75344200
C	1.09844600	3.07969300	-0.27479000	C	1.85082900	2.31700500	-0.40609100
C	2.41338800	3.07262300	0.21688200	C	3.14121900	2.46507100	0.14569900
C	3.47074200	3.43750100	-0.61323700	C	4.27973200	2.23346400	-0.61562400
H	4.04443500	4.10219200	-2.58257800	H	5.03819500	1.65633700	-2.55397000
H	1.71897500	4.12272900	-3.45548000	H	2.78475300	1.34239800	-3.53517800
H	2.60541900	2.76966300	1.23983900	H	3.25483800	2.73862200	1.18620000
H	4.48646700	3.42356000	-0.23081100	H	5.26035500	2.35185800	-0.16616700
C	-0.06510900	2.66779800	0.51988900	C	0.63208300	2.53046100	0.39419300
C	-0.58851800	3.46022100	-2.07750700	C	0.38301600	1.62627900	-2.40019600
H	-1.11736200	4.30272900	-1.61047300	H	0.36242400	2.08654400	-3.39449300
H	-0.64249500	3.60587100	-3.16085500	H	0.26732200	0.54587600	-2.55398900
C	-1.05328900	1.76790000	-0.18451700	C	-0.58861300	1.76480500	-0.07188200
H	-2.00632000	1.80110000	0.34967200	H	-1.46748200	2.08886000	0.49014200
C	-1.27254000	2.13997600	-1.68058400	C	-0.79987600	2.10531200	-1.56072500
H	-2.34624000	2.19645600	-1.87916800	H	-0.91605600	3.19286200	-1.64420900
H	-0.88867200	1.33270300	-2.30925000	H	-1.71864300	1.63688900	-1.91704800
C	-0.24753300	3.00491900	1.83551000	C	0.53750100	3.36234100	1.48247100
C	0.66437700	3.82610100	2.57556700	C	1.56893500	4.24093700	1.94769300
C	-1.40615700	2.57109700	2.56194500	C	-0.67693300	3.42720800	2.24448300
N	1.39713500	4.48111700	3.19856000	N	2.38189400	4.97135300	2.34748700
N	-2.36061200	2.23290500	3.13569200	N	-1.66567900	3.44659500	2.85879300
C	-0.49628200	0.30066700	-0.05757700	C	-0.36071700	0.25614100	0.21395000
C	-1.57513400	-0.69368000	-0.53025700	C	-1.45478000	-0.64145500	-0.38437400
C	-0.22256900	-0.18545900	1.33660500	C	-0.30649600	-0.09879100	1.71045900
C	-2.15629000	-1.43185500	0.68263900	C	-2.26242600	-1.29659000	0.72053800
C	-1.09293000	-1.13811000	1.71246000	C	-1.32002600	-1.22624800	1.91876800
O	-1.88798000	-0.88011200	-1.68461100	O	-1.62253000	-0.80461400	-1.57579800
O	-1.11692100	-1.83125900	2.86719000	O	-1.40411600	-1.91309500	2.91423200
C	-2.32283000	-2.92623900	0.38492200	C	-2.74198700	-2.70052500	0.37706100
H	-2.73042700	-3.43169800	1.26634500	H	-3.27848200	-3.12183600	1.23302300
H	-3.00667700	-3.05468000	-0.45744600	H	-3.40239400	-2.66303700	-0.49223100
H	-1.35676100	-3.37838500	0.13772500	H	-1.87630400	-3.32837700	0.14651800
C	-3.50805300	-0.78074500	1.13956400	C	-3.44897100	-0.32623100	1.10876700
H	-3.84396600	-1.35739900	2.00878700	H	-3.96580900	-0.81889800	1.93958200
H	-3.30388200	0.23547400	1.49345600	H	-3.03875900	0.61451000	1.49618000
H	0.58401800	0.18703500	1.95690100	H	-0.59631400	0.73912600	2.35582000
H	0.37396400	0.23818600	-0.72512900	H	0.57405800	-0.03368700	-0.26386700
C	-4.57506700	-0.75407100	0.07566900	C	-4.39942700	-0.02927200	-0.02171800
C	-5.43300500	-1.84351500	-0.11933400	C	-5.42546500	-0.92176100	-0.35682600
C	-4.71267100	0.36379200	-0.75659300	C	-4.26125500	1.14739600	-0.76790400
C	-6.39777600	-1.82124900	-1.12783600	C	-6.28202500	-0.65155300	-1.42499600
H	-5.34078300	-2.71172300	0.52741600	H	-5.55097600	-1.82867900	0.22711500
C	-5.67672200	0.39400000	-1.76383400	C	-5.11599800	1.42352100	-1.83529300
H	-4.05801300	1.21880500	-0.60616600	H	-3.48449100	1.85757100	-0.49849800
C	-6.52127100	-0.70220400	-1.95441300	C	-6.12711000	0.52003900	-2.16985200
H	-7.05613300	-2.67454300	-1.26482200	H	-7.07366700	-1.35296800	-1.67226900
H	-5.77042400	1.27110100	-2.39803600	H	-4.99698600	2.34377000	-2.40005500
H	-7.27355700	-0.68226600	-2.73764200	H	-6.79518000	0.73129500	-2.99963100
C	5.24429000	-1.64886000	0.72845600	C	4.39058500	-1.86943800	-0.91407400
C	5.75657000	-1.26454900	-0.66613100	C	3.79547700	-2.10639800	-2.30837200
C	4.99675900	-1.90810900	-1.83186000	C	2.46722600	-2.87490800	-2.32923000
C	3.79225800	-1.20704900	0.98449900	C	3.45113100	-1.08506300	0.01817000
C	3.48171000	-1.61038500	-1.83323700	C	1.33392700	-2.18058800	-1.54021600

C	2.72841900	-2.49469700	-0.86064600
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H	5.68730300	-0.17108300	-0.76414800
H	5.14131400	-2.99614300	-1.82560000
H	3.31099000	-0.55033100	-1.62397100
H	3.61721200	-0.23155100	0.51705400
H	5.88776800	-1.17933300	1.48229100
H	6.82035800	-1.51988100	-0.74345600
H	5.42366900	-1.53829700	-2.77157800
H	3.62031800	-1.07907200	2.05787800
H	3.06390100	-1.82809700	-2.81799600
C	2.54076300	-3.28805300	1.42856100
C	1.46703900	-4.48679200	-0.48049600
C	1.30390600	-4.06629400	0.98726000
H	3.42566700	-3.94345500	1.42925400
H	2.41744900	-2.88976300	2.44098700
H	0.48440400	-4.69779000	-0.91926400
H	2.03966800	-5.42282300	-0.54595300
H	0.42379800	-3.42803900	1.09334000
H	1.16879700	-4.94422600	1.62856800
N	2.75782800	-2.14553900	0.51719800
N	2.13534400	-3.51981000	-1.34409300
H	1.91809100	-1.61304900	0.62348600

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H	4.64859500	-2.82477400	-0.43753300
H	3.63190500	-1.12441200	-2.77475400
H	2.60496200	-3.89091700	-1.93746500
H	1.38978100	-1.10460600	-1.73651000
H	2.97395200	-0.27597100	-0.54029600
H	5.32486800	-1.30415200	-1.02308700
H	4.52871700	-2.63506900	-2.93000700
H	2.14602800	-2.98063600	-3.37216500
H	4.02778100	-0.60945500	0.81709600
H	0.35943800	-2.53010700	-1.88041000
C	2.83377600	-2.54757800	1.92302800
C	0.73169300	-3.90301600	1.74490500
C	1.61254200	-3.06396300	2.68002800
H	3.52535200	-3.37847400	1.70714700
H	3.38222400	-1.81369200	2.52413600
H	-0.26535500	-4.00794300	2.18414500
H	1.14520000	-4.91803400	1.65052400
H	1.03036800	-2.22636700	3.07035700
H	1.93740000	-3.66220800	3.53858500
N	2.42456600	-1.89553900	0.67472600
N	0.57860800	-3.37685600	0.38940100
H	0.68831700	-0.43144200	2.01526400

TS_{PD}

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C	0.91627000	2.04159900	-1.96249400
C	0.86340200	2.61619900	-0.66267500
C	1.93362400	3.44091300	-0.24910100
C	3.01469500	3.70392100	-1.08136800
H	3.89410400	3.34915800	-3.02414400
H	2.03491800	1.89242600	-3.78238400
H	1.94214900	3.85782700	0.74717900
H	3.82171300	4.33816800	-0.72839600
C	-0.29475000	2.32194000	0.20186200
C	-0.16075600	1.12462000	-2.48974600
H	-0.34599900	1.35994100	-3.54471900
H	0.18792400	0.08616500	-2.45409200
C	-1.14072600	1.12123800	-0.17087000
H	-2.10776200	1.22968900	0.32758500
C	-1.44435900	1.18675600	-1.67505600
H	-1.97693700	2.12586200	-1.87022100
H	-2.10678600	0.36420400	-1.94512900
C	-0.68330800	3.07891000	1.28639500
C	-0.05979800	4.27558100	1.76617200
C	-1.86002800	2.73787200	2.03650900
N	0.41275300	5.25033200	2.19362900
N	-2.81186800	2.47586000	2.65409900
C	-0.51499300	-0.18950200	0.35014200
C	-0.98369200	-1.42835100	-0.25573000
C	-0.61933000	-0.36933400	1.87791700
C	-1.60544800	-2.34767400	0.82816300
C	-0.82988500	-1.87404900	2.04722100
O	-0.90024600	-1.78848500	-1.44048700
O	-0.40297600	-2.57178400	2.94403100
C	-1.53705900	-3.84243700	0.54339900
H	-2.09802400	-4.39699800	1.30170700
H	-1.96195100	-4.04589400	-0.44435500
H	-0.51083200	-4.21120900	0.55921200
C	-3.11427700	-1.89432900	1.06921700

1C'

C	2.42466600	3.68641400	-1.52367600
C	1.66760100	2.77956900	-2.26049800
C	0.43016800	2.30127600	-1.80338100
C	-0.09002700	2.80038000	-0.57767700
C	0.71587000	3.68100700	0.17924200
C	1.95339400	4.11810300	-0.28021900
H	3.37591600	4.04421300	-1.90742900
H	2.03347800	2.42107400	-3.22008600
H	0.37623000	4.02548300	1.14544500
H	2.53950900	4.80136300	0.32651000
C	-1.45774800	2.41991400	-0.16593400
C	-0.24724400	1.21297400	-2.59369500
H	-0.11457600	1.39960100	-3.66645700
H	0.26573500	0.27917600	-2.33061400
C	-2.02443300	1.14162300	-0.74911000
H	-3.11578500	1.18768700	-0.67907200
C	-1.72127500	1.03022600	-2.25105000
H	-2.31397900	1.80496500	-2.75463800
H	-2.07702200	0.05849500	-2.60190500
C	-2.25268700	3.16807400	0.68244900
C	-1.88665800	4.38620800	1.33760400
C	-3.61537300	2.79825300	0.93685000
N	-1.63185000	5.38174800	1.88680500
N	-4.72681800	2.51955600	1.14545700
C	-1.60928400	0.01758400	0.18399300
C	-0.60605700	-0.91769200	0.09736500
C	-2.53468900	-0.25565700	1.34979800
C	-0.85349100	-2.05468700	1.10089500
C	-1.97357600	-1.51553900	1.98509800
O	0.39130800	-1.03522400	-0.73236600
O	-2.34304800	-2.02857300	3.02284000
C	0.36049400	-2.47775000	1.92658600
H	0.07040200	-3.26591200	2.62786900
H	1.14480200	-2.85901100	1.26543200
H	0.76521800	-1.64605900	2.51020300
C	-1.36763000	-3.30898400	0.32287200

H	-3.67233300	-2.81101200	1.29098200	H	-0.54116900	-3.63487600	-0.31909000
H	-3.17521500	-1.27738600	1.97171400	H	-1.56645300	-4.09381300	1.06184300
H	-1.48849600	0.15148100	2.30809500	H	-3.57417600	-0.43951200	1.03620300
C	-3.79730600	-1.13946400	-0.04961500	C	-2.59835000	-3.05155600	-0.50978400
C	-3.92089900	-1.68925400	-1.33328100	C	-2.47806600	-2.55288300	-1.81348500
C	-4.33239500	0.13235600	0.19138800	C	-3.87761000	-3.23864100	0.02721600
C	-4.55545700	-0.97926400	-2.35209000	C	-3.61312500	-2.25667100	-2.56877000
H	-3.49018700	-2.66301100	-1.53900400	H	-1.48300200	-2.37469300	-2.21212900
C	-4.96647800	0.84755900	-0.82769700	C	-5.01637400	-2.93815900	-0.72413500
H	-4.23779100	0.57387300	1.18069700	H	-3.97478700	-3.60516000	1.04570800
C	-5.07959000	0.29294000	-2.10340500	C	-4.88690700	-2.44762400	-2.02516200
H	-4.63651500	-1.41704900	-3.34304900	H	-3.50550300	-1.87157600	-3.57942100
H	-5.36886500	1.83514100	-0.62091800	H	-6.00247800	-3.08460600	-0.29269700
H	-5.57142500	0.84588500	-2.89872100	H	-5.77136300	-2.21436500	-2.61105300
H	0.25274700	-0.05220000	2.46104800	H	-2.58798300	0.55216700	2.09517900
C	3.58619300	-2.01836200	-1.82138100	C	4.81277100	-0.46834100	-1.44945400
C	3.37037800	-3.52907500	-1.65439700	C	5.46878900	-1.85705200	-1.44852300
C	3.10685700	-3.97567000	-0.21324700	C	5.33362600	-2.62670500	-0.13100600
C	2.33702600	-1.17809500	-1.52652100	C	3.28462800	-0.52034600	-1.37855500
C	1.93493800	-3.22726400	0.45733700	C	3.88441500	-2.75216000	0.38870200
C	2.31709500	-1.84973500	0.92007000	C	3.37402800	-1.46781300	0.98655300
H	4.42591200	-1.68066500	-1.19954200	H	5.20508300	0.14525300	-0.62732300
H	2.51530800	-3.82126300	-2.27884600	H	5.01661100	-2.44649400	-2.25793000
H	4.00655300	-3.84057300	0.40022900	H	5.93294300	-2.14498500	0.65145200
H	1.09136400	-3.16465100	-0.23658800	H	3.21252500	-3.08693200	-0.41087800
H	1.41840000	-1.69952600	-1.79984300	H	2.88658100	-1.41232800	-1.86639900
H	3.87352800	-1.81620400	-2.85938000	H	5.08068100	0.05060400	-2.37601800
H	4.24590900	-4.06144000	-2.04411700	H	6.53223900	-1.75252000	-1.69160600
H	2.87709900	-5.04686800	-0.21067500	H	5.73882500	-3.63542800	-0.26656700
H	2.36189800	-0.23934600	-2.08146500	H	2.82193000	0.34635800	-1.85383800
H	1.60380900	-3.75913000	1.35068700	H	3.85025500	-3.49142500	1.19122100
C	3.11906700	0.36717900	0.24433800	C	2.65091200	0.87741900	0.56642000
C	3.01489700	-0.32164700	2.62759900	C	2.93853700	-0.03397500	2.85689900
C	2.80693800	0.84630600	1.65106600	C	2.05265200	0.83286400	1.95863100
H	4.14096400	-0.02076500	0.17698800	H	3.66489500	1.28719800	0.56393100
H	2.98336000	1.14116000	-0.50531400	H	2.02941200	1.43414000	-0.12391200
H	2.41151100	-0.18601000	3.53243400	H	2.39331700	-0.36548000	3.74714300
H	4.06067400	-0.36686200	2.95816500	H	3.80289000	0.53811600	3.21946000
H	1.77318000	1.20145600	1.67834100	H	1.03635300	0.42974300	1.88472400
H	3.45346800	1.69051000	1.90880300	H	1.97447300	1.85140000	2.34911700
N	2.18490100	-0.75405800	-0.08878000	N	2.72401000	-0.51925600	0.02279400
N	2.68755600	-1.64082100	2.10772900	N	3.47026000	-1.23552200	2.22066400
H	1.12685300	-0.41462000	0.02411100	H	1.79099300	-0.80508900	-0.12457400

TS_{HS}

C	6.45673000	-0.85348100	0.68759800
C	5.57521400	-1.83133500	0.22211000
C	4.27362300	-1.50747200	-0.15782600
C	3.82522200	-0.15999500	-0.07899900
C	4.72157500	0.81082300	0.41899100
C	6.01815000	0.46927800	0.79135200
H	7.46817200	-1.12304900	0.97990900
H	5.89449000	-2.86904000	0.15444200
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H	6.68300300	1.23838000	1.17467800
C	2.45687300	0.14181500	-0.51404200
C	3.29954500	-2.56310600	-0.60831300
H	3.14632600	-2.50732600	-1.69683700
H	3.68893200	-3.56233900	-0.38140600
C	1.40052200	-0.93369800	-0.37215000
H	0.95669300	-1.09112100	-1.36751100

C	1.95835700	-2.29012900	0.08681900
H	1.20918100	-3.05529500	-0.13810300
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C	2.05377800	1.38862900	-0.99134000
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C	0.21699700	-0.48185600	0.45170300
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C	0.21258800	0.70456800	1.45450500
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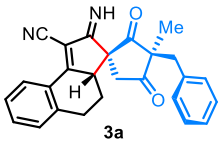
C	-1.13851700	1.13315200	1.65343500
O	-1.48011100	-1.47661600	-0.89503500
O	-1.56585500	2.07959100	2.32773700
C	-2.74165400	-0.74712300	1.97783600
H	-3.33852000	-0.11248500	2.64310900
H	-3.38870800	-1.49801200	1.51477100
H	-1.97954000	-1.25837200	2.57893400
C	-3.12640700	0.94122200	0.08538600
H	-3.31516000	1.85316400	0.66339300
H	-2.65480100	1.24001900	-0.85762700
H	0.26471200	-0.55880100	1.73282800
H	1.10616400	1.24350700	1.73903600
C	-4.45192400	0.26340900	-0.18953000
C	-5.63701100	0.82292200	0.30641400
C	-4.53700500	-0.92161600	-0.93898300
C	-6.87837900	0.22994400	0.05912800
H	-5.57876400	1.73619400	0.89417600
C	-5.77504600	-1.51689000	-1.18481400
H	-3.61185100	-1.36881600	-1.29170200
C	-6.95221500	-0.94491400	-0.69062800
H	-7.78418300	0.68467600	0.45414900
H	-5.82216300	-2.43581200	-1.76519100
H	-7.91475200	-1.41245200	-0.88529700

References:

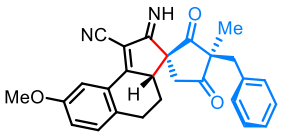
3. C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B* 1988, **37**, 785-789.
4. a) W. J. Hehre, L. Radom, P. R. Schleyer and J. A. Pople, *Ab Initio Molecular Orbital theory; Wiley: New York,* 1986; b) P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta* 1973, **28**, 213-222.
5. M. J. Frisch, *et. al,* Gaussian 09, Revision C.01, Gaussian, Inc., Wallingford, CT, USA, 2010.

Spectroscopic Data of Synthesized Compounds



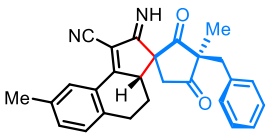
3a

Compound **3a** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (73 mg, 84%), melting point = 119 - 121 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.30 (bs, 1H), 8.26 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.07 – 7.05 (m, 2H), 3.24 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.07 – 2.97 (m, 2H), 2.87 – 2.76 (m, 2H), 2.70 (d, *J* = 18.3 Hz, 1H), 1.93 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.18 – 1.07 (m, 1H), 0.69 – 0.63 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.6, 214.7, 182.1, 171.5, 140.7, 136.4, 133.5, 130.2, 129.8, 128.8, 128.1, 127.9, 127.5, 127.3, 113.9, 103.2, 62.8, 59.2, 47.7, 45.2, 44.3, 29.8, 25.7, 21.6. **IR**: 3240, 2921, 2855, 2212, 1755, 1725, 1634, 1590, 1457, 1335, 757 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_2+H]^+$ [M + H$^+$] m/z 395.1754, found 395.1750.



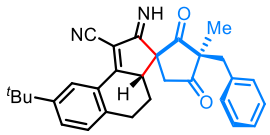
3b

Compound **3b** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1b** (0.22 mmol, 49 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (73 mg, 78%), melting point = 165-167 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.75 (d, *J* = 2.6 Hz, 1H), 7.27 – 7.25 (m, 3H), 7.11 (d, *J* = 8.6 Hz, 1H), 7.06 – 7.01 (m, 3H), 3.84 (s, 3H), 3.23 – 3.18 (m, 1H), 3.06 – 2.96 (m, 2H), 2.78 – 2.63 (m, 3H), 1.93 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.14 – 1.04 (m, 1H), 0.67 – 0.62 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.6, 214.6, 182.1, 171.7, 158.3, 136.4, 133.2, 130.7, 130.2, 128.8, 128.6, 127.5, 121.8, 114.0, 110.4, 103.2, 62.9, 59.2, 55.6, 47.7, 45.1, 44.2, 29.1, 26.0, 21.6. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{24}N_2O_3+H]^+$ [M + H$^+$] m/z 425.1860, found 425.1865.



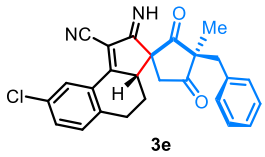
3c

Compound **3c** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1c** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (68 mg, 76%), melting point = 157-159 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.28 (bs, 1H), 8.06 (s, 1H), 7.27 – 7.25 (m, 4H), 7.10 (d, *J* = 7.9 Hz, 1H), 7.06 – 7.04 (m, 2H), 3.21 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.12 – 2.93 (m, 2H), 2.81 – 2.66 (m, 3H), 2.38 (s, 3H), 1.93 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.15 – 1.04 (m, 1H), 0.68 – 0.63 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.6, 214.7, 182.2, 171.6, 137.9, 137.1, 136.4, 134.6, 130.2, 129.6, 128.8, 128.2, 127.9, 127.5, 113.9, 102.9, 62.9, 59.2, 47.8, 45.2, 44.3, 29.5, 25.9, 21.6, 21.2. **IR**: 3450, 3368, 2925, 2212, 1620, 1585, 1487, 1456, 1270, 1068, 1011, 703 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{24}N_2O_2+H]^+$ [M + H$^+$] m/z 409.1911, found 409.1918.



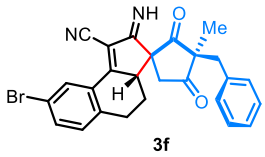
3d

Compound **3d** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1d** (0.22 mmol, 55 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (71 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.28 (bs, 1H), 8.32 (s, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.27 – 7.25 (m, 3H), 7.17 (s, 1H), 7.06 – 7.05 (m, 2H), 3.24 – 3.19 (m, 1H), 3.02 (q, *J* = 12.7 Hz, 2H), 2.82 – 2.67 (m, 3H), 1.94 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.34 (s, 9H), 1.18 – 1.05 (m, 1H), 0.69 – 0.64 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.6, 214.7, 182.2, 172.3, 150.5, 137.8, 136.4, 131.1, 130.2, 129.4, 128.8, 127.6, 127.5, 124.9, 114.0, 102.9, 62.9, 59.2, 47.8, 45.1, 44.2, 35.0, 31.2, 29.3, 25.9, 21.6. **IR**: 3271, 2963, 2881, 2222, 1781, 1727, 1632, 1589, 1437, 1365, 1330, 1224, 1011, 875 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{30}H_{30}N_2O_2+H]^+$ [M + H^+] m/z 451.2380, found 451.2381.



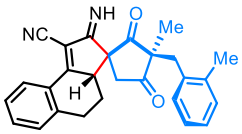
3e

Compound **3e** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1e** (0.22 mmol, 50 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (81 mg, 86%), melting point = 196-198 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (bs, 1H), 8.26 (d, *J* = 7.9 Hz, 1H), 7.46-7.43 (m, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.28-7.25 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.06-7.04 (m, 2H), 3.23 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.05 (d, *J* = 12.8 Hz, 1H), 2.98 (d, *J* = 12.8 Hz, 1H), 2.88 – 2.75 (m, 2H), 2.70 (d, *J* = 18.3 Hz, 1H), 1.94 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.16-1.08 (m, 1H), 0.69 – 0.65 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.5, 214.6, 182.1, 171.4, 140.7, 136.4, 133.5, 130.2, 129.7, 128.8, 128.1, 128.0, 127.5, 127.3, 113.8, 103.2, 62.8, 59.2, 47.7, 45.1, 44.2, 29.8, 25.7, 21.6. **IR**: 2951, 2905, 2212, 1771, 1724, 1624, 1586, 1452, 1332, 1189, 1021, 861 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_2Cl+K]^+$ [M + K^+] m/z 467.0923, found 467.0875.



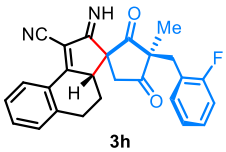
3f

Compound **3f** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1f** (0.22 mmol, 60 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (84 mg, 81%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.31 (bs, 1H), 8.26 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.27 – 7.26 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.07 – 7.04 (m, 2H), 3.23 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.02 (q, *J* = 12.7 Hz, 2H), 2.85 – 2.75 (m, 2H), 2.70 (d, *J* = 18.3 Hz, 1H), 1.94 (d, *J* = 18.3 Hz, 1H), 1.50 (s, 3H), 1.18 – 1.07 (m, 1H), 0.70 – 0.64 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.5, 214.6, 182.1, 171.4, 140.7, 136.4, 133.5, 130.2, 129.8, 128.8, 128.1, 128.0, 127.5, 127.3, 113.8, 103.2, 62.9, 59.2, 47.7, 45.2, 44.3, 29.9, 25.7, 21.6. **IR**: 3125, 3065, 2212, 1755, 1715, 1630, 1580, 1452, 1335, 1173, 859 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_2Br+H]^+$ [M + H^+] m/z 475.0839, found 475.0881.



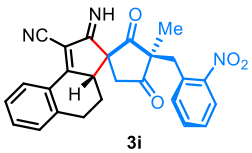
3g

Compound **3g** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (75 mg, 83%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.17 – 7.14 (m, 2H), 7.10 – 7.07 (m, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 3.29 – 3.26 (m, 1H), 3.13 – 3.06 (m, 2H), 2.88 – 2.81 (m, 2H), 2.66 (d, *J* = 17.8 Hz, 1H), 2.27 (s, 3H), 2.01 (d, *J* = 17.8 Hz, 1H), 1.50 (s, 3H), 1.20 – 1.12 (m, 1H), 0.86 – 0.82 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.7, 214.6, 182.2, 171.7, 140.7, 137.5, 134.9, 133.5, 131.4, 130.8, 129.8, 128.1, 128.0, 127.7, 127.3, 126.0, 113.8, 103.2, 63.0, 58.6, 47.5, 45.1, 41.1, 29.9, 25.8, 21.7, 19.8. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{24}N_2O_2+H]^+$ [M + H$^+$] m/z 409.1911, found 409.1915.



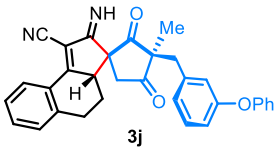
3h

Compound **3h** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (68 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.31 (bs, 1H), 8.28 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.12 – 7.01 (m, 3H), 3.40 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.05 (s, 2H), 2.91 – 2.86 (m, 2H), 2.74 (d, *J* = 17.9 Hz, 1H), 2.26 (d, *J* = 17.9 Hz, 1H), 1.50 (s, 3H), 1.37 – 1.26 (m, 1H), 1.09 – 1.03 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.4, 212.9, 182.1, 171.3, 160.9 (d, *J* = 247.9 Hz), 140.7, 133.6, 132.8 (d, *J* = 4.0 Hz), 129.8, 129.6 (d, *J* = 8.1 Hz), 128.2, 128.0, 127.4, 124.4 (d, *J* = 3.7 Hz), 123.2 (d, *J* = 15.8 Hz), 115.8 (d, *J* = 22.3 Hz), 113.8, 103.1, 63.1, 57.5, 47.5, 44.6, 36.8, 29.9, 25.9, 21.0. **^{19}F NMR** (461 MHz, $CDCl_3$) δ -113.9 ppm. **IR**: 3343, 3073, 2929, 2218, 1759, 1729, 1588, 1509, 1447, 1369, 1223, 1051, 827 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_2F+H]^+$ [M + H$^+$] m/z 413.1660, found 413.1663.



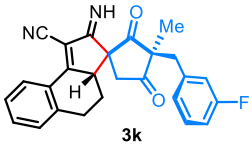
3i

Compound **3i** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (69 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (bs, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.46 – 7.42 (m, 2H), 7.38 (d, *J* = 7.7 Hz, 1H), 3.68 – 3.62 (m, 2H), 3.29 – 3.11 (m, 4H), 2.93 (d, *J* = 17.6 Hz, 1H), 2.28 – 2.25 (m, 1H), 1.78 – 1.67 (m, 1H), 1.53 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 213.7, 212.5, 182.0, 172.1, 149.1, 141.1, 134.3, 133.6, 133.5, 131.1, 129.9, 128.9, 128.2, 128.1, 127.3, 125.7, 113.9, 102.9, 63.4, 55.4, 47.8, 43.3, 39.6, 30.1, 26.4, 20.4. **IR**: 3250, 2931, 2885, 2217, 1771, 1727, 1639, 1589, 1526, 1437, 1343, 1275, 1023, 864 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_3O_4+Na]^+$ [M + Na$^+$] m/z 462.1424, found 462.1424.



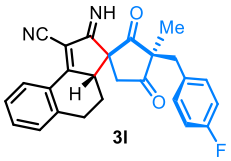
3j

Compound **3j** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (78 mg, 73%), melting point = 157-159 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.32 (bs, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.37 – 7.31 (m, 3H), 7.28 – 7.25 (m, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.94 – 6.87 (m, 3H), 6.79 – 6.78 (m, 1H), 6.73 (t, *J* = 2.1 Hz, 1H), 3.37 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.04 (d, *J* = 12.7 Hz, 1H), 2.95 – 2.91 (m, 3H), 2.74 (d, *J* = 18.2 Hz, 1H), 2.00 (d, *J* = 18.2 Hz, 1H), 1.49 (s, 3H), 1.35 – 1.21 (m, 1H), 1.02 – 0.97 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.3, 214.1, 182.0, 171.3, 157.8, 156.7, 140.8, 138.5, 133.5, 130.1, 130.0, 129.8, 128.2, 128.0, 127.3, 124.9, 123.9, 120.4, 119.0, 117.5, 113.8, 103.2, 63.0, 58.9, 47.7, 45.2, 43.9, 29.9, 25.9, 21.7. **IR**: 3255, 3062, 2936, 2222, 1776, 1727, 1634, 1587, 1485, 1427, 1254, 1138, 798 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{32}H_{26}N_2O_3+H]^+$ [M + H$^+$] m/z 487.2016, found 487.2005.



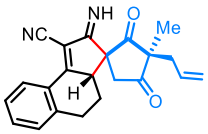
3k

Compound **3k** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (73 mg, 80%), melting point = 139-141 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.34 (bs, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.27 – 7.23 (m, 2H), 7.00 – 6.96 (m, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.79 – 6.76 (m, 1H), 3.32 (dd, *J* = 14.2, 4.3 Hz, 1H), 3.06 (d, *J* = 12.7 Hz, 1H), 2.97 (d, *J* = 12.7 Hz, 1H), 2.92 – 2.80 (m, 2H), 2.75 (d, *J* = 18.3 Hz, 1H), 1.94 (d, *J* = 18.4 Hz, 1H), 1.51 (s, 3H), 1.27 – 1.18 (m, 1H), 0.84 – 0.80 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 216.3, 214.1, 181.9, 171.3, 162.9 (d, *J* = 247.6 Hz), 140.7, 139.0 (d, *J* = 7.1 Hz), 133.6, 130.5 (d, *J* = 8.2 Hz), 129.8, 128.2, 127.9, 127.4, 126.0 (d, *J* = 3.2 Hz), 117.0 (d, *J* = 21.0 Hz), 114.5 (d, *J* = 21.0 Hz), 113.8, 103.2, 62.9, 59.0, 47.8, 45.1, 43.5, 29.8, 25.9, 21.7. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -111.9. **IR**: 3255, 2955, 2926, 2217, 1758, 1727, 1623, 1589, 1451, 1363, 1259, 1153, 869 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_2F+H]^+$ [M + H$^+$] m/z 413.1660, found 413.1648.



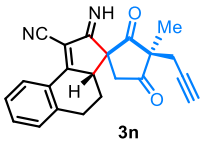
3l

Compound **3l** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (71 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.34 (bs, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.06 – 6.95 (m, 4H), 3.24 (d, *J* = 14.0 Hz, 1H), 3.05 – 2.89 (m, 3H), 2.83 – 2.75 (m, 2H), 2.00 (d, *J* = 18.4 Hz, 1H), 1.49 (s, 3H), 1.27 – 1.21 (m, 1H), 0.78 – 0.75 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.5, 214.5, 181.9, 171.1, 162.2 (d, *J* = 247.3 Hz), 140.6, 133.6, 132.2 (d, *J* = 3.0 Hz), 131.8 (d, *J* = 7.7 Hz), 129.8, 128.1, 127.8, 127.3, 115.6 (d, *J* = 21.2 Hz), 113.8, 103.2, 62.8, 59.2, 47.7, 45.1, 42.9, 29.7, 25.8, 21.6. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -115.5. **IR**: 2922, 2835, 2222, 1777, 1725, 1620, 1593, 1450, 1346, 1225, 1051, 857 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_2F+H]^+$ [M + H$^+$] m/z 413.1660, found 413.1669.



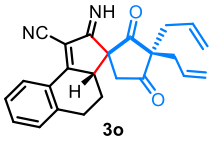
3m

Compound **3m** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc : hexane) to provide pure compound as white solid (58 mg, 79%), melting point = 180-182 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.39 (bs, 1H), 8.35 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.33 – 7.24 (m, 1H), 5.66 – 5.55 (m, 1H), 5.12 – 5.08 (m, 2H), 3.72 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.13 – 3.09 (m, 2H), 2.93 (d, *J* = 17.9 Hz, 1H), 2.79 (d, *J* = 17.9 Hz, 1H), 2.46 – 2.35 (m, 2H), 2.08 – 2.02 (m, 1H), 1.76 – 1.65 (m, 1H), 1.40 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.5, 213.3, 181.8, 170.9, 140.8, 133.6, 132.0, 129.9, 128.2, 128.0, 127.5, 120.4, 113.9, 103.2, 63.3, 57.1, 47.5, 44.8, 41.9, 29.9, 26.6, 20.3. **HRMS** (TOF MS ES+) calcd. for $[C_{22}H_{20}N_2O_2+Na]^+$ [M + Na^+] m/z 367.1417, found 367.1441.



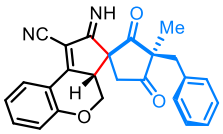
3n

Compound **3n** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (65 mg, 87%), melting point = 110-112 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.31 – 7.27 (m, 1H), 3.87 – 3.82 (m, 1H), 3.13 – 3.04 (m, 4H), 2.62 – 2.46 (m, 2H), 2.21 – 2.16 (m, 1H), 2.03 2.01 (m, 1H), 1.79 – 1.68 (m, 1H), 1.40 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 214.5, 212.2, 181.7, 171.1, 140.8, 133.7, 129.9, 128.2, 128.0, 127.4, 113.9, 103.1, 79.9, 71.0, 63.4, 55.5, 47.6, 45.6, 29.9, 26.9, 26.2, 20.6. **IR**: 3296, 2971, 2850, 2212, 1776, 1727, 1636, 1588, 1452, 1366, 1282, 1087, 732 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{22}H_{18}N_2O_2+H]^+$ [M + H^+] m/z 343.1441, found 343.1432.



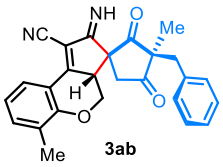
3o

Compound **3o** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (67 mg, 82%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.46 (bs, 1H), 8.35 (d, *J* = 6.9 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.40 – 7.36 (m, 1H), 7.29 – 7.27 (m, 1H), 5.87 (dq, *J* = 16.0, 7.3 Hz, 1H), 5.57 (dq, *J* = 17.1, 8.5 Hz, 1H), 5.18 – 5.06 (m, 4H), 3.62 – 3.59 (m, 1H), 3.09 – 3.01 (m, 3H), 2.79 (d, *J* = 19.4 Hz, 1H), 2.70 – 2.58 (m, 2H), 2.50 – 2.40 (m, 2H), 2.02 – 1.97 (m, 1H), 1.74 – 1.63 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 214.4, 212.8, 181.5, 170.6, 140.6, 133.6, 132.2, 131.7, 129.9, 128.2, 128.0, 127.5, 120.5, 119.7 (2×C), 113.9, 63.0, 60.6, 48.6, 45.1, 38.9, 38.5, 29.9, 26.7. **HRMS** (TOF MS ES+) calcd. for $[C_{24}H_{22}N_2O_2+Na]^+$ [M + Na^+] m/z 393.1573, found 393.1571.



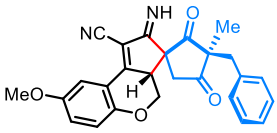
3aa

Compound **3aa** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1aa** (0.22 mmol, 43 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (66 mg, 76%), melting point = 190-191 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.09 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.47 – 7.44 (m, 1H), 7.35 – 7.33 (m, 3H), 7.08 – 7.05 (m, 3H), 6.94 (d, *J* = 8.4 Hz, 1H), 3.65 (dd, *J* = 13.8, 5.6 Hz, 1H), 3.40 – 3.34 (m, 1H), 3.10 (d, *J* = 12.7 Hz, 1H), 3.04 (dd, *J* = 10.2, 5.6 Hz, 1H), 2.97 (d, *J* = 12.7 Hz, 1H), 2.58 (d, *J* = 17.8 Hz, 1H), 1.54 – 1.49 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.4, 213.5, 181.4, 164.3, 157.2, 136.2, 136.1, 130.1, 129.2, 127.9, 127.8, 122.2, 118.3, 115.8, 113.2, 101.2, 66.4, 60.5, 58.9, 44.9, 44.3, 42.3, 21.4. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{20}N_2O_3+H]^+$ [M + H^+] m/z 397.1547, found 397.1524.



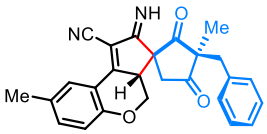
3ab

Compound **3ab** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ab** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (67 mg, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.30 (m, 4H), 7.08 – 7.06 (m, 2H), 6.96 (t, *J* = 7.7 Hz, 1H), 3.68 – 3.63 (m, 1H), 3.41 – 3.35 (m, 1H), 3.17 – 3.09 (m, 2H), 2.99 (d, *J* = 12.6 Hz, 1H), 2.58 (d, *J* = 17.7 Hz, 1H), 2.19 (s, 3H), 1.53 – 1.48 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.4, 213.6, 181.5, 164.9, 155.5, 137.1, 136.2, 130.0, 129.2, 127.9, 127.7, 125.4, 121.6, 115.3, 113.4, 100.9, 66.5, 60.6, 58.9, 44.9, 44.3, 42.3, 21.5, 16.1. **IR**: 3261, 2931, 2217, 1766, 1724, 1624, 1588, 1421, 1329, 1218, 1133, 862 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_3+Na]^+$ [M + Na^+] m/z 433.1523, found 433.1525.



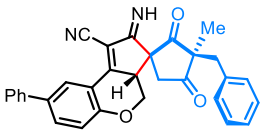
3ac

Compound **3ac** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ac** (0.22 mmol, 49 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (72 mg, 77%), melting point = 205-209 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.53 – 7.52 (m, 1H), 7.35 – 7.33 (m, 3H), 7.08 – 7.05 (m, 3H), 6.87 (d, *J* = 9.1 Hz, 1H), 3.80 (s, 3H), 3.65 – 3.62 (m, 1H), 3.35 – 3.29 (m, 1H), 3.10 (d, *J* = 12.6 Hz, 1H), 3.00 – 2.95 (m, 2H), 2.57 (d, *J* = 17.8 Hz, 1H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.5, 213.5, 181.4, 164.5, 154.3, 151.9, 136.2, 130.0, 129.2, 127.9, 125.3, 119.4, 115.5, 113.4, 108.3, 100.9, 66.5, 60.6, 58.9, 55.9, 44.9, 44.3, 42.4, 21.3. **IR**: 3204, 2943, 2207, 1761, 1725, 1623, 1588, 1491, 1447, 1325, 1031, 854 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_4+H]^+$ [M + H^+] m/z 427.1652, found 427.1659.



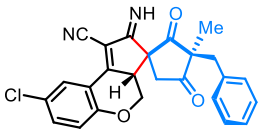
3ad

Compound **3ad** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ad** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (71 mg, 79%), melting point = 143-145 ºC. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.34 – 7.33 (m, 3H), 7.06 – 7.04 (m, 2H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 3.62 (dd, *J* = 13.9, 5.5 Hz, 1H), 3.35 – 3.30 (m, 1H), 3.09 (d, *J* = 12.6 Hz, 1H), 3.02 – 2.95 (m, 2H), 2.57 (d, *J* = 17.8 Hz, 1H), 2.36 (s, 3H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.5, 213.5, 181.6, 164.3, 157.3, 148.0, 136.2, 130.0, 129.1, 127.9, 127.5, 123.6, 118.3, 113.4, 113.3, 100.0, 66.3, 60.5, 58.9, 44.9, 44.3, 42.3, 22.2, 21.3. **IR**: 2906, 2813, 2217, 1766, 1730, 1634, 1579, 1437, 1330, 1224, 1143, 854 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_3+H]^+$ [M + H^+] m/z 411.1703, found 411.1715.



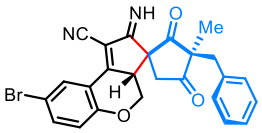
3ae

Compound **3ae** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ae** (0.22 mmol, 60 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (73 mg, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.36 (bs, 1H), 8.30 (s, 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.35 (m, 4H), 7.08 – 7.00 (m, 3H), 3.68 (dd, *J* = 13.9, 5.6 Hz, 1H), 3.40 (dd, *J* = 13.9, 10.1 Hz, 1H), 3.12 – 3.04 (m, 2H), 2.98 (d, *J* = 12.7 Hz, 1H), 2.60 (d, *J* = 17.8 Hz, 1H), 1.54 – 1.50 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.4, 213.4, 181.3, 164.3, 156.5, 139.0, 136.2, 135.3, 134.8, 130.0, 129.2 (2×C), 127.9, 127.8, 126.7, 125.5, 118.7, 115.9, 113.2, 101.4, 66.5, 60.6, 58.9, 44.9, 44.3, 42.4, 21.4. **IR**: 3250, 3032, 2217, 1761, 1728, 1631, 1603, 1480, 1452, 1204, 1037, 762 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{31}H_{24}N_2O_3+H]^+$ [M + H^+] m/z 473.1860, found 473.1883



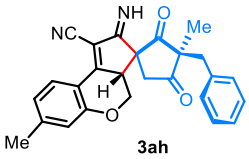
3af

Compound **3af** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1af** (0.22 mmol, 50 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (68 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.02 (s, 1H), 7.40 – 7.33 (m, 4H), 7.06 – 7.04 (m, 2H), 6.90 (d, *J* = 8.9 Hz, 1H), 3.60 (dd, *J* = 13.9, 5.5 Hz, 1H), 3.35 (t, *J* = 12.0 Hz, 1H), 3.11 – 2.96 (m, 3H), 2.58 (d, *J* = 17.8 Hz, 1H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.2, 213.2, 181.0, 162.5, 155.6, 136.2, 135.8, 130.0, 129.2, 127.9, 127.4, 126.6, 119.8, 116.6, 112.6, 102.2, 66.4, 60.4, 58.9, 44.9, 44.2, 42.1, 21.3. **IR**: 3260, 3058, 2936, 2850, 2217, 1761, 1728, 1640, 1598, 1453, 1376, 1341, 1207, 1092, 875 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_3Cl+H]^+$ [M + H^+] m/z 431.1157, found 431.1166.



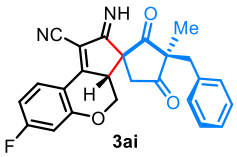
3ag

Compound **3ag** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ag** (0.22 mmol, 60 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (79 mg, 76%), melting point = 188-190 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.15 (s, 1H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.33 – 7.32 (m, 3H), 7.05 – 7.03 (m, 2H), 6.83 (d, *J* = 9.0 Hz, 1H), 3.61 – 3.56 (m, 1H), 3.37 – 3.31 (m, 1H), 3.10 – 2.95 (m, 3H), 2.57 (d, *J* = 17.8 Hz, 1H), 1.51 – 1.46 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.1, 213.2, 180.9, 162.4, 156.1, 138.6, 136.1, 130.0, 129.7, 129.2, 127.9, 120.1, 117.2, 114.5, 112.6, 102.2, 66.4, 60.4, 58.9, 44.9, 44.2, 42.1, 21.3. **IR**: 3265, 3062, 2222, 1766, 1728, 1643, 1603, 1476, 1452, 1332, 1219, 861 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_3Br+H]^+$ [M + H^+] m/z 475.0652, found 475.0671.



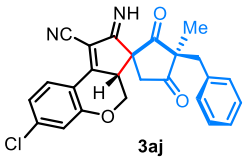
3ah

Compound **3ah** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ah** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (66 mg, 73%), melting point = 184-186 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.86 (s, 1H), 7.34 – 7.33 (m, 3H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.06 – 7.04 (m, 2H), 6.84 (d, *J* = 8.6 Hz, 1H), 3.63 (dd, *J* = 14.0, 5.5 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.09 (d, *J* = 12.7 Hz, 1H), 3.02 – 2.95 (m, 2H), 2.57 (d, *J* = 17.8 Hz, 1H), 2.32 (s, 3H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.4, 213.5, 181.5, 164.4, 155.3, 137.3, 136.2, 131.7, 130.0, 129.1, 127.9, 127.2, 118.0, 115.4, 113.3, 100.8, 66.3, 60.5, 58.9, 44.9, 44.3, 42.4, 21.3, 20.6. **IR**: 2922, 2835, 2222, 1776, 1725, 1620, 1593, 1450, 1346, 1225, 1051, 857 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_3+H]^+$ [M + H^+] m/z 411.1703, found 411.1715.



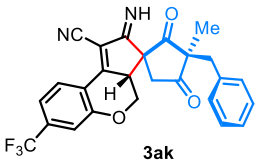
3ai

Compound **3ai** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ai** (0.22 mmol, 47 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (62 mg, 68%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.11 (dd, *J* = 8.9, 6.2 Hz, 1H), 7.35 – 7.34 (m, 3H), 7.07 – 7.05 (m, 2H), 6.83 – 6.79 (m, 1H), 6.65 (dd, *J* = 9.6, 2.6 Hz, 1H), 3.62 (dd, *J* = 13.8, 5.6 Hz, 1H), 3.39 – 3.35 (m, 1H), 3.10 (d, *J* = 12.7 Hz, 1H), 3.02 (dd, *J* = 10.2, 5.6 Hz, 1H), 2.98 (d, *J* = 12.7 Hz, 1H), 2.58 (d, *J* = 17.8 Hz, 1H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.4, 213.4, 181.2, 167.1 (d, *J* = 258.4 Hz), 163.0, 159.0 (d, *J* = 13.5 Hz), 136.2, 130.1, 129.9 (d, *J* = 11.1 Hz), 129.2, 127.9, 113.2, 112.5 (d, *J* = 2.8 Hz), 110.8 (d, *J* = 23.1 Hz), 105.4 (d, *J* = 24.7 Hz), 100.8, 66.6, 60.4, 58.9, 44.9, 44.3, 42.1, 21.3; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -98.8. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_3F+Na]^+$ [M + Na^+] m/z 437.1272, found 437.1265.



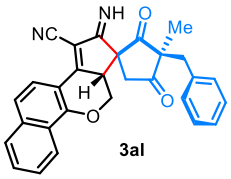
3aj

Compound **3aj** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1aj** (0.22 mmol, 50 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (62 mg, 65%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 8.02 (d, J = 8.6 Hz, 1H), 7.36 – 7.33 (m, 3H), 7.07 – 7.04 (m, 3H), 6.97 (d, *J* = 2.0 Hz, 1H), 3.61 (dd, *J* = 13.9, 5.6 Hz, 1H), 3.36 (dd, *J* = 13.9, 10.2 Hz, 1H), 3.10 (d, *J* = 12.7 Hz, 1H), 3.02 (dd, *J* = 10.2, 5.6 Hz, 1H), 2.98 (d, *J* = 12.7 Hz, 1H), 2.58 (d, *J* = 17.8 Hz, 1H), 1.52 – 1.48 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.3, 213.3, 181.1, 162.9, 157.5, 141.9, 136.2, 130.1, 129.2, 128.6, 127.9, 123.0, 118.5, 114.3, 113.0, 101.5, 66.5, 60.4, 58.9, 44.9, 44.3, 42.1, 21.3. **IR**: 3054, 2986, 2308, 1768, 1731, 1623, 1595, 1422, 1352, 1266, 896, 740 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_3Cl+H]^+$ [M + H^+] m/z 431.1157, found 431.1155.



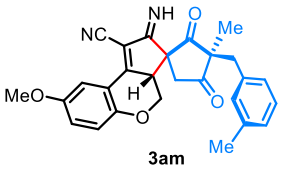
3ak

Compound **3ak** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ak** (0.22 mmol, 58 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (73 mg, 72%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.37 – 7.33 (m, 3H), 7.30 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.22 (d, *J* = 1.8 Hz, 1H), 7.07 – 7.05 (m, 2H), 3.62 (dd, *J* = 13.8, 5.6 Hz, 1H), 3.41 (dd, *J* = 13.8, 10.3 Hz, 1H), 3.11 – 3.06 (m, 2H), 2.99 (d, *J* = 12.7 Hz, 1H), 2.61 (d, *J* = 17.8 Hz, 1H), 1.54 – 1.51 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.2, 213.1, 180.8, 162.4, 156.9, 136.9 (q, *J* = 33.3 Hz), 136.2, 130.1, 129.2, 128.5, 128.0, 123.0 (q, *J* = 273.1 Hz), 118.5 (q, *J* = 3.6 Hz), 118.3, 115.7 (q, *J* = 4.0 Hz), 112.6, 103.4, 66.6, 60.4, 58.9, 44.9, 44.2, 42.2, 21.3; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -63.8. **IR**: 3266, 3077, 2950, 2869, 2218, 1759, 1729, 1629, 1606, 1499, 1376, 1207, 1066, 858 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{19}N_2O_3F_3+H]^+$ [M + H^+] m/z 465.1421, found 465.1444



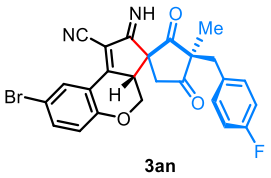
3al

Compound **3al** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1al** (0.22 mmol, 54 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (63 mg, 64%), melting point = 172-174 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 6.9 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.42 – 7.34 (m, 3H), 7.17 – 7.03 (m, 2H), 3.78 (dd, *J* = 14.1, 5.6 Hz, 1H), 3.53 (dd, *J* = 14.2, 10.1 Hz, 1H), 3.30 (dd, *J* = 10.1, 5.7 Hz, 1H), 3.12 (d, *J*= 12.7 Hz, 1H), 3.00 (d, *J* = 12.7 Hz, 1H), 2.62 (d, *J* = 17.8 Hz, 1H), 1.59 – 1.55 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.5, 213.6, 181.7, 163.7, 155.4, 137.1, 136.3, 130.2, 130.1, 129.2, 128.2, 127.9, 127.0, 124.6, 123.8, 122.2, 122.0, 113.7, 110.3, 100.2, 67.1, 60.6, 59.0, 44.9, 44.3, 41.9, 21.4. **IR**: 2923, 2850, 2212, 1736, 1680, 1614, 1536, 1508, 1368, 1269, 1108, 806 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{29}H_{22}N_2O_3+H]^+$ [M + H^+] m/z 447.1703, found 447.1715.



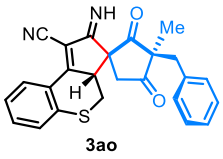
3am

Compound **3am** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ac** (0.22 mmol, 49 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (75 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.53 (d, *J* = 2.9 Hz, 1H), 7.27 – 7.19 (m, 1H), 7.16 – 7.14 (m, 1H), 7.07 (dd, *J* = 9.1, 3.0 Hz, 1H), 6.89 – 6.84 (m, 3H), 3.80 (s, 3H), 3.65 (dd, *J* = 13.9, 5.5 Hz, 1H), 3.36 – 3.30 (m, 1H), 3.07 – 2.99 (m, 2H), 2.91 (d, *J* = 12.6 Hz, 1H), 2.55 (d, *J* = 17.7 Hz, 1H), 2.33 (s, 3H), 1.50 – 1.45 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.6, 213.5, 181.5, 164.6, 154.2, 152.0, 139.1, 136.1, 130.5, 129.1, 128.5, 127.0, 125.2, 119.4, 115.5, 113.3, 108.3, 101.0, 66.6, 60.6, 58.8, 55.9, 44.9, 44.2, 42.5, 21.4, 21.2. **IR**: 3260, 2952, 2869, 2218, 1770, 1729, 1634, 1600, 1490, 1330, 1209, 1044, 733 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{24}N_2O_4+H]^+$ [M + H$^+$] m/z 441.1809, found 441.1790.



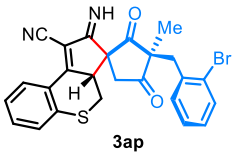
3an

Compound **3an** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ag** (0.22 mmol, 60 mg) and purified by silica gel column chromatography (5→15% EtOAc : hexane) to provide pure compound as yellow solid (77 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.44 (bs, 1H), 8.15 (s, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.03 – 7.01 (m, 4H), 6.85 (d, *J* = 9.0 Hz, 1H), 3.64 - 3.59 (m, 1H), 3.48 – 3.41 (m, 1H), 3.19 – 3.15 (m, 1H), 3.06 (d, *J* = 13.0 Hz, 1H), 2.94 (d, *J* = 12.9 Hz, 1H), 2.64 (d, *J* = 17.9 Hz, 1H), 1.56 – 1.39 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.0, 212.9, 180.7, 162.3 (d, *J* = 248.1 Hz), 162.1, 156.0, 138.7, 131.9 (d, *J* = 3.5 Hz), 131.6 (d, *J* = 7.7 Hz), 129.6, 120.2, 117.1, 116.0 (d, *J* = 21.2 Hz), 114.5, 112.6, 102.2, 66.5, 60.4, 58.8, 44.2, 43.6, 42.1, 21.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -113.4. **IR**: 3250, 2960, 2900, 2217, 1787, 1729, 1644, 1603, 1509, 1391, 1325, 1221, 850 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{18}N_2O_3FBr+H]^+$ [M + H$^+$] m/z 493.0558, found 493.0555.



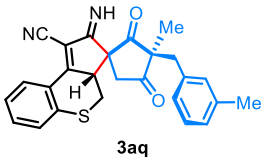
3ao

Compound **3ao** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1am** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (64 mg, 71%), melting point = 167-199 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.37 (bs, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.29 (m, 4H), 7.22 – 7.18 (m, 2H), 7.06 – 7.05 (m, 2H), 3.62 – 3.57 (m, 1H), 3.07 (d, *J* = 12.6 Hz, 1H), 2.95 (d, *J* = 12.6 Hz, 1H), 2.69 – 2.64 (m, 1H), 2.52 – 2.45 (m, 1H), 1.71 (d, *J* = 18.2 Hz, 1H), 1.47 (s, 3H), 1.45 – 1.41 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.2, 213.7, 180.7, 167.1, 138.2, 136.2, 133.4, 130.0, 129.8, 129.2, 127.8, 127.4, 125.4, 125.3, 113.6, 104.6, 62.8, 58.9, 45.5, 44.9, 44.6, 27.3, 21.5. **IR**: 3055, 2986, 2308, 1765, 1731, 1266, 896, 740, 706 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{20}N_2O_2S+H]^+$ [M + H$^+$] m/z 413.1318, found 413.1325.



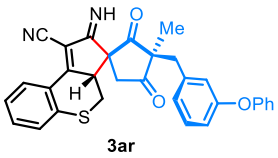
3ap

Compound **3ap** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above by using **1am** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc : hexane) to provide pure compound as yellow solid (69 mg, 64%), melting point = 185-187 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.37 (bs, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.13 (m, 4H), 3.75 (dd, *J* = 14.1, 4.2 Hz, 1H), 3.31 (d, *J* = 13.3 Hz, 1H), 3.15 (d, *J* = 13.3 Hz, 1H), 2.74 – 2.63 (m, 2H), 2.15 (d, *J* = 17.3 Hz, 1H), 1.83 – 1.79 (m, 1H), 1.49 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 213.9, 211.4, 180.6, 167.1, 138.0, 135.7 (2×C), 133.9, 133.4, 132.7, 129.8, 129.5, 127.9, 127.4, 125.4 (2×C), 113.5, 104.7, 63.1, 57.3, 45.4, 44.3, 43.3, 27.7, 21.2. **IR**: 3250, 2921, 2843, 2217, 1762, 1730, 1633, 1586, 1438, 1349, 1041, 1021, 879 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_2BrS+H]^+$ [M + H^+] m/z 491.0423, found 491.0430.



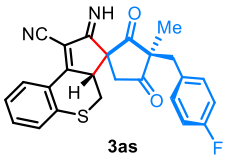
3aq

Compound **3aq** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1am** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (62 mg, 66%), melting point = 211-213 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.36 (bs, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.23 – 7.17 (m, 3H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.86 – 6.64 (m, 2H), 3.62 (dd, *J* = 14.1, 4.2 Hz, 1H), 3.04 (d, *J* = 12.6 Hz, 1H), 2.90 (d, *J* = 12.6 Hz, 1H), 2.63 (d, *J* = 17.9 Hz, 1H), 2.51 (dd, *J* = 14.0, 12.1 Hz, 1H), 2.34 (s, 3H), 1.68 (d, *J* = 17.9 Hz, 1H), 1.52 – 1.47 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.2, 213.6, 180.7, 167.1, 139.2, 138.2, 136.1, 133.4, 130.6, 129.8, 129.1, 128.4, 127.3, 127.0, 125.4, 125.3, 113.6, 104.7, 62.8, 58.8, 45.4, 45.0, 44.7, 27.4, 21.6, 21.5. **IR**: 3270, 2916, 2860, 2217, 1766, 1728, 1634, 1583, 1437, 1348, 1306, 859 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_2S+H]^+$ [M + H^+] m/z 427.1475, found 427.1483.



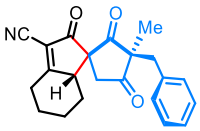
3ar

Compound **3ar** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1am** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (69 mg, 62%), melting point = 207-209 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.40 (bs, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.27 – 7.21 (m, 3H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.91 – 6.89 (m, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.70 (s, 1H), 3.71 (dd, *J* = 14.1, 4.2 Hz, 1H), 3.05 (d, *J* = 12.6 Hz, 1H), 2.91 (d, *J* = 12.6 Hz, 1H), 2.73 (d, *J* = 17.8 Hz, 1H), 2.64 (t, *J* = 13.1 Hz, 1H), 1.83 – 1.78 (m, 2H), 1.47 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 214.8, 213.2, 180.5, 167.0, 158.3, 156.3, 138.2 (2×C), 133.4, 130.4, 130.1, 129.8, 127.4, 125.4, 125.3, 124.3, 124.2, 119.8, 119.5, 117.3, 113.6, 104.7, 62.9, 58.6, 45.4, 44.7, 44.5, 27.5, 21.8. **IR**: 3286, 3058, 2212, 1771, 1728, 1630, 1583, 1486, 1437, 1345, 1258, 1143, 870 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{31}H_{24}N_2O_3S+H]^+$ [M + H^+] m/z 505.1580, found 505.1592.



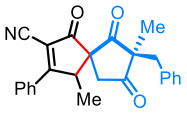
3as

Compound **3as** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1am** (0.22 mmol, 46 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (66 mg, 70%), melting point = 160-162 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.41 (bs, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.24 – 7.18 (m, 2H), 7.05 – 6.98 (m, 4H), 3.60 – 3.55 (m, 1H), 3.04 (d, *J* = 12.9 Hz, 1H), 2.94 (d, *J* = 12.9 Hz, 1H), 2.76 (d, *J* = 18.1 Hz, 1H), 2.59 (t, *J* = 13.1 Hz, 1H), 1.78 (d, *J* = 18.1 Hz, 1H), 1.59 – 1.56 (m, 1H), 1.46 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 215.1, 213.5, 180.4, 166.9, 162.3 (d, *J* = 248.3 Hz), 138.1, 133.4, 132.0 (d, *J* = 3.3 Hz), 131.7 (d, *J* = 7.7 Hz), 129.8, 127.4, 125.4 (2×C), 116.0 (d, *J* = 21.2 Hz), 113.6, 104.7, 62.8, 58.8, 45.7, 44.5, 43.5, 27.6, 21.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -113.6. **IR**: 3255, 3062, 2976, 2864, 2223, 1766, 1729, 1633, 1586, 1439, 1371, 1241, 1040, 866 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{19}N_2O_2FS+Na]^+$ [M + Na^+] m/z 453.1043, found 453.1054.



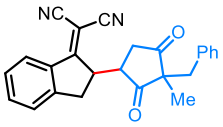
3at

Compound **3at** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1an** (0.22 mmol, 32 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white sticky solid (47 mg, 62%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 3H), 7.02 – 6.98 (m, 2H), 3.17 – 3.13 (m, 1H), 3.02 – 2.95 (m, 2H), 2.68 (d, *J* = 18.6 Hz, 1H), 2.59 – 2.55 (m, 1H), 2.52 – 2.44 (m, 1H), 2.15 – 2.10 (m, 1H), 1.73 (d, *J* = 18.5 Hz, 2H), 1.36 – 1.29 (m, 5H), 0.97 – 0.94 (m, 1H), 0.70 – 0.60 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 213.4, 212.8, 198.0, 197.5, 136.1, 130.0, 128.9, 127.7, 111.0, 110.6, 67.6, 59.3, 48.2, 43.9, 41.9, 31.5, 31.4, 27.3, 24.6, 21.1. **IR**: 2941, 2860, 2227, 1767, 1730, 1712, 1624, 1585, 1451, 1224, 1021, 847 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{22}H_{21}N_2O_3+Na]^+$ [M + Na^+] m/z 370.1414, found 370.1417.



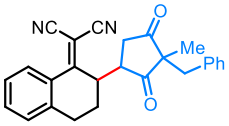
3au, 1:5 dr

Compound **3au** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ao** (0.22 mmol, 40 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow solid (32 mg, 38%). **^{1}H NMR** (500 MHz, $CDCl_3$) (major diastereomer) δ 9.35 (s, 1H), 7.76 – 7.73 (m, 2H), 7.59 – 7.51 (m, 3H), 7.33 – 7.24 (m, 3H), 7.09 – 7.05 (m, 2H), 3.33 – 3.27 (m, 1H), 3.06 (d, *J* = 12.8 Hz, 1H), 2.96 (d, *J* = 12.7 Hz, 1H), 2.84 (d, *J* = 17.8 Hz, 1H), 1.74 (d, *J* = 17.8 Hz, 1H), 1.43 (s, 3H), 0.55 (d, *J* = 7.4 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 214.1 CC*, 214.0 CC*, 179.5 CC*, 177.0 CC*, 136.3 CC*, 135.1 C*, 134.0 C, 132.7 C, 131.0 C*, 130.0 CC*, 129.7 C*, 129.5 C, 129.0 C*, 128.9 C, 128.4 C*, 128.2 C, 127.7 CC*, 113.6 CC*, 107.6 C, 101.9 C*, 69.7 C*, 65.2 C, 59.1 CC*, 44.6 C*, 44.4 C, 43.8 C*, 43.6 C, 42.6 C*, 42.4 C, 22.6 C, 21.6 C*, 17.1 C*, 16.4 C. [C= major diastereomer, C*= minor diastereomer, & CC*= both diastereomers peaks were merging]. **IR**: 3260, 3067, 2956, 2855, 2218, 1767, 1728, 1637, 1600, 1493, 1372, 1224, 1092, 879 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{22}N_2O_2+H]^+$ [M + H^+] m/z 383.1754, found 383.1757.



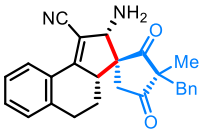
3av, 1:9 dr

Compound **3av** was prepared by general procedure for synthesis of [4,4]-carbospirocycles described above using **1ap** (0.22 mmol, 40 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (57 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$) of major diastereomer: δ 8.27 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.33 – 7.27 (m, 3H), 7.11 – 7.07 (m, 2H), 6.97 (d, *J* = 7.8 Hz, 1H), 4.14 – 4.11 (m, 1H), 3.52 – 3.46 (m, 1H), 3.09 – 3.02 (m, 2H), 2.76 (dd, *J* = 18.6, 7.1 Hz, 1H), 2.37 (dd, *J* = 18.6, 10.1 Hz, 1H), 1.29 (s, 3H), 1.24 – 1.18 (m, 1H), 0.85 (d, *J* = 18.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) of major diastereomer : δ 214.7, 213.8, 179.9, 152.3, 136.8, 135.8, 135.6, 130.7, 128.8, 128.6, 127.3, 126.1, 125.5, 113.0, 112.7, 75.1, 59.1, 48.0, 43.9, 40.9, 37.6, 32.6, 22.8. **IR**: 3457, 3062, 2925, 2855, 2225, 1763, 1728, 1608, 1570, 1493, 1373, 1244, 1046, 738 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{25}H_{20}N_2O_2+H]^+$ [M + H^+] m/z 381.1598, found 381.1598.



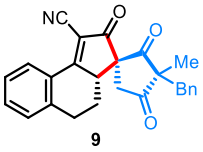
5a

Compound **5a** was prepared by general procedure for isolation of reaction of intermediate **5a** described above using **1a** (0.22 mmol, 42 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as yellow sticky solid (20 mg, 23%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.30 – 7.27 (m, 1H), 7.17 – 7.15 (m, 1H), 7.09 – 7.05 (m, 2H), 7.02 – 7.01 (m, 1H), 6.91 – 6.89 (m, 2H), 3.45 – 3.41 (m, 1H), 3.03 (d, *J* = 12.9 Hz, 1H), 2.85 – 2.80 (m, 1H), 2.78 (d, *J* = 12.9 Hz, 1H), 2.75 – 2.66 (m, 2H), 2.28 – 2.23 (m, 1H), 2.05 – 1.99 (m, 2H), 1.58 – 1.56 (m, 1H), 1.23 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 215.4, 213.6, 174.7, 140.0, 135.9, 133.7, 129.8, 129.3, 128.7, 128.5, 128.4, 127.5, 127.1, 113.3, 113.0, 80.3, 59.4, 47.0, 43.8, 42.7, 40.6, 24.9, 24.8, 20.2. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{22}N_2O_2+H]^+$ [M + H^+] m/z 395.1754, found 395.1752.



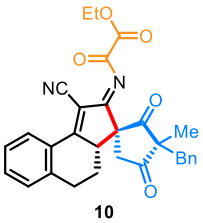
8

Compound **8** was prepared by general procedure for chemoselective reduction for synthesis of compound described above using **3a** (0.22 mmol, 87 mg) and purified by silica gel column chromatography (15→35% EtOAc: hexane) to provide pure compound as yellow solid (75 mg, 86%), melting point = 142-144 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.18 (m, 4H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.05 – 6.99 (m, 3H), 4.43 (d, *J* = 6.4 Hz, 1H), 4.30 (bs, 2H), 3.06 – 2.97 (m, 2H), 2.61 – 2.53 (m, 2H), 2.40 – 2.32 (m, 1H), 2.01 (d, *J* = 19.2 Hz, 1H), 1.81 – 1.76 (m, 1H), 1.33 (s, 3H), 1.11 – 1.00 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 216.1, 215.3, 159.3, 136.2, 136.0, 134.4, 129.9, 129.7, 128.9, 128.5, 127.8, 126.8, 126.5, 117.7, 84.8, 66.2, 59.3, 43.8, 43.6, 43.2, 41.8, 28.7, 22.5, 21.7. **IR**: 3356, 2956, 2934, 2197, 1723, 1644, 1579, 1457, 1376, 1224, 1088, 748 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{24}N_2O_2+Na]^+$ [M + Na^+] m/z 419.1730, found 419.1730.



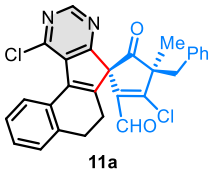
9

Compound **9** was prepared by general procedure for synthesis of triketone spirocyclic compound described above using **3a** (0.22 mmol, 87 mg) and purified by silica gel column chromatography (5→15% EtOAc: hexane) to provide pure compound as white solid (58 mg, 67%), melting point = 189-191 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.28 – 7.27 (m, 4H), 7.05 – 7.03 (m, 2H), 3.23 (dd, *J* = 14.3, 4.3 Hz, 1H), 3.07 – 2.99 (m, 2H), 2.91 – 2.80 (m, 2H), 2.72 (d, *J* = 18.7 Hz, 1H), 1.91 (d, *J* = 18.7 Hz, 1H), 1.43 (s, 3H), 1.26 – 1.19 (m, 1H), 0.77 – 0.71 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 214.1, 213.4, 199.4, 182.7, 141.4, 136.3, 134.9, 130.2, 130.0, 129.2, 128.9, 127.9, 127.6 (2×C), 113.1, 105.2, 66.3, 59.3, 46.4, 43.7, 42.5, 29.8, 25.9, 20.8. **IR**: 3055, 2982, 2926, 2855, 2303, 1763, 1730, 1688, 1578, 1432, 1266, 890, 706 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{26}H_{21}N_2O_3+H]^+$ [M + H^+] m/z 396.1594, found 396.1589.



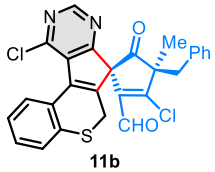
10

Compound **10** was prepared by general procedure for synthesis of *N*-protected carbospirocycle described above using **3a** (0.22 mmol, 87 mg) and purified by crystallization technique to provide pure compound as white solid (85 mg, 78%), melting point = 101-103 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.29 – 7.20 (m, 4H), 7.08 – 7.03 (m, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.21 (dd, *J* = 14.2, 4.3 Hz, 1H), 3.03 (q, *J* = 12.8 Hz, 2H), 2.91 – 2.76 (m, 3H), 2.00 (d, *J* = 18.6 Hz, 1H), 1.45 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.22 – 1.14 (m, 1H), 0.71 – 0.66 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 214.1, 213.5, 179.3, 173.5, 165.3, 158.6, 141.5, 136.1, 134.9, 130.2, 129.9, 128.9, 128.5, 127.7 (2×C), 127.5, 113.6, 100.3, 63.7, 63.6, 59.0, 47.6, 44.5, 44.3, 29.8, 25.9, 21.5, 14.0. **IR**: 3266, 2978, 2917, 2223, 1765, 1727, 1708, 1584, 1453, 1269, 1232, 1082, 821 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{30}H_{26}N_2O_5+Na]^+$ [M + Na^+] m/z 517.1734, found 517.1727.



11a

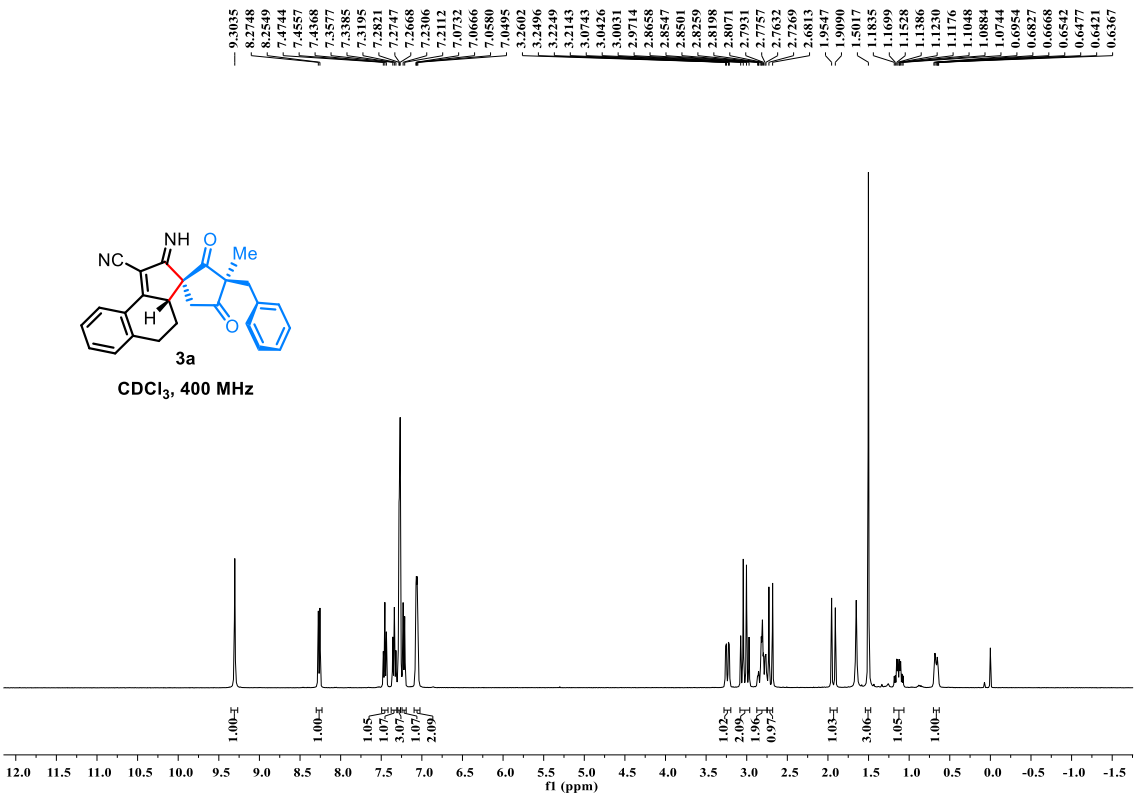
Compound **11a** was prepared by general procedure for synthesis of pyrimidine fused spirocycles described above using **3a** (0.22 mmol, 87 mg) and purified by silica gel column chromatography (10→25% EtOAc: hexane) to provide pure compound as white solid (59 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.63 (s, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.30 – 7.26 (m, 4H), 7.23 – 7.19 (m, 3H), 7.13 (d, *J* = 7.5 Hz, 1H), 3.26 (d, *J* = 13.9 Hz, 1H), 3.13 (d, *J* = 13.9 Hz, 1H), 2.43 – 2.37 (m, 2H), 1.76 (s, 3H), 1.07 – 0.99 (m, 1H), 0.68 – 0.59 (m, 1H); IR: 3067, 2958, 2843, 1755, 1728, 1629, 1589, 1453, 1328, 1264, 1088, 745 cm^{-1}. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.7, 184.5, 174.7, 158.8, 154.0, 150.1, 148.1, 137.0, 136.8, 135.7, 135.3, 133.3, 130.7, 129.6, 129.0, 127.9, 127.6 (2×C), 127.4, 126.1, 73.6, 63.9, 40.8, 29.0, 24.2, 20.5. **IR**: 2906, 2813, 2217, 1766, 1730, 1634, 1579, 1437, 1330, 1224, 1143, 854 cm^{-1}. **HRMS** (TOF MS ES+) calcd. for $[C_{28}H_{20}N_2O_2Cl_2+Na]^+$ [M + Na^+] m/z 509.0794, found 509.0792.

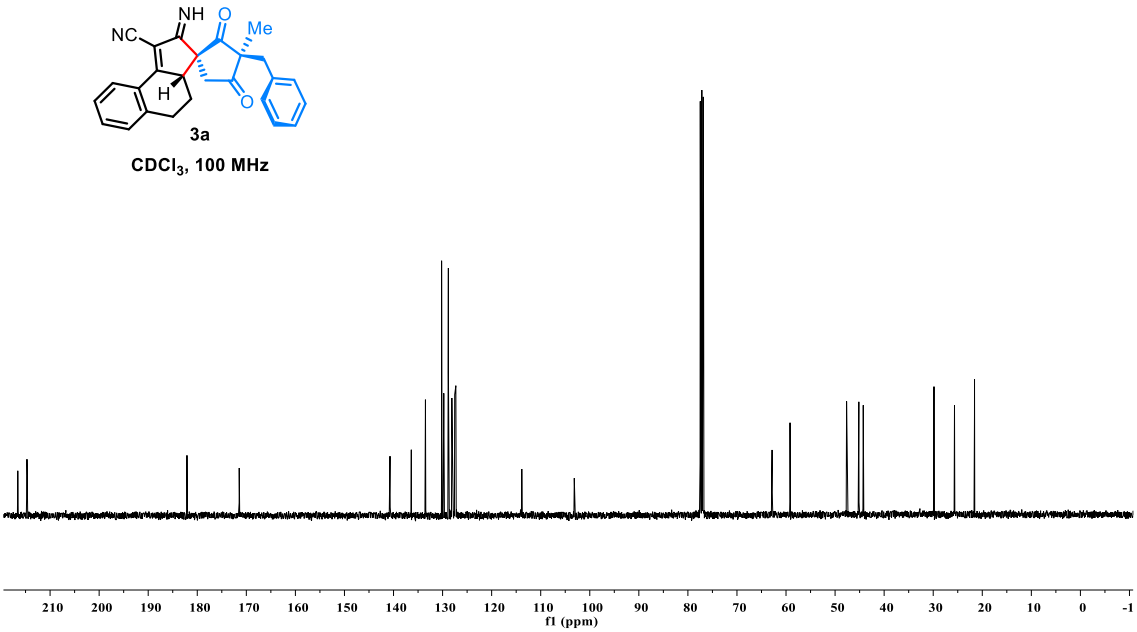


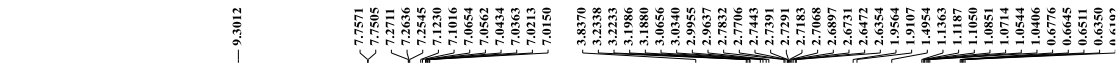
11b

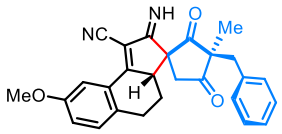
Compound **11b** was prepared by general procedure for synthesis of pyrimidine fused spirocycles described above using **3ao** (0.22 mmol, 90 mg) and purified by silica gel column chromatography (10→25% EtOAc: hexane) to provide pure compound as white solid (58 mg, 52%), melting point = 135-137 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.65 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.36 – 7.31 (m, 4H), 7.25 – 7.19 (m, 4H), 3.29 (d, *J* = 13.9 Hz, 1H), 3.16 (d, *J* = 13.9 Hz, 1H), 2.15 (d, *J* = 15.9 Hz, 1H), 1.76 (s, 3H), 1.19 (d, *J* = 15.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.1, 184.4, 174.0, 159.2, 154.5, 150.9, 142.4, 137.7, 135.7, 134.5, 134.1, 132.6, 130.7, 129.2, 129.0, 128.9, 128.5, 128.4, 127.9, 125.4, 73.6, 64.4, 40.9, 24.2, 22.5. **HRMS** (TOF MS ES+) calcd. for $[C_{27}H_{18}N_2O_2Cl_2S+H]^+$ [M + H^+] m/z 505.0539, found 505.0521.

NMR SPECTRA


NC
NH
O
Me
H
O
3a
CDCl3, 400 MHz
fl (ppm)

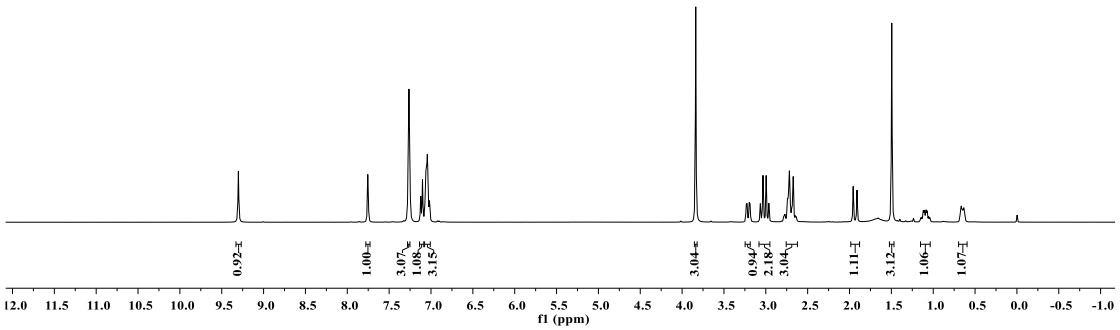

NC
NH
O
Me
H
O
3a
CDCl3, 100 MHz
fl (ppm)

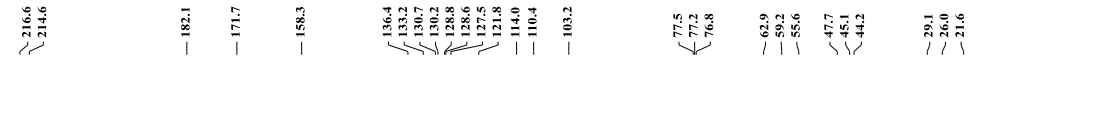


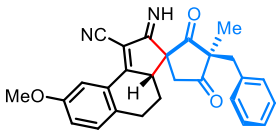


3b

$CDCl_3$, 400 MHz

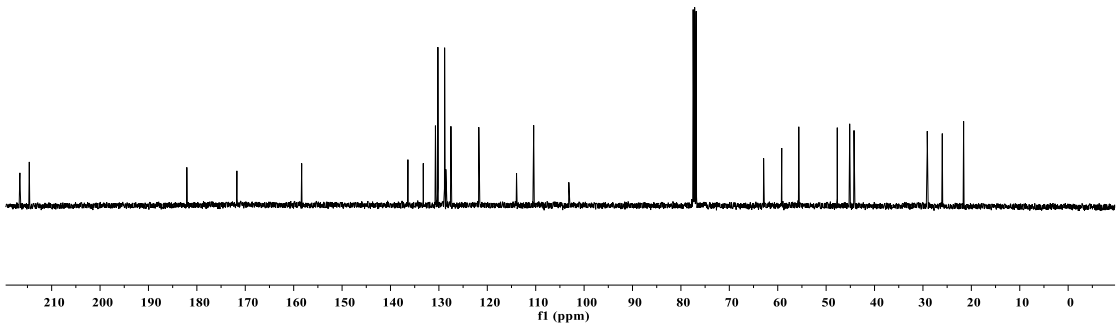


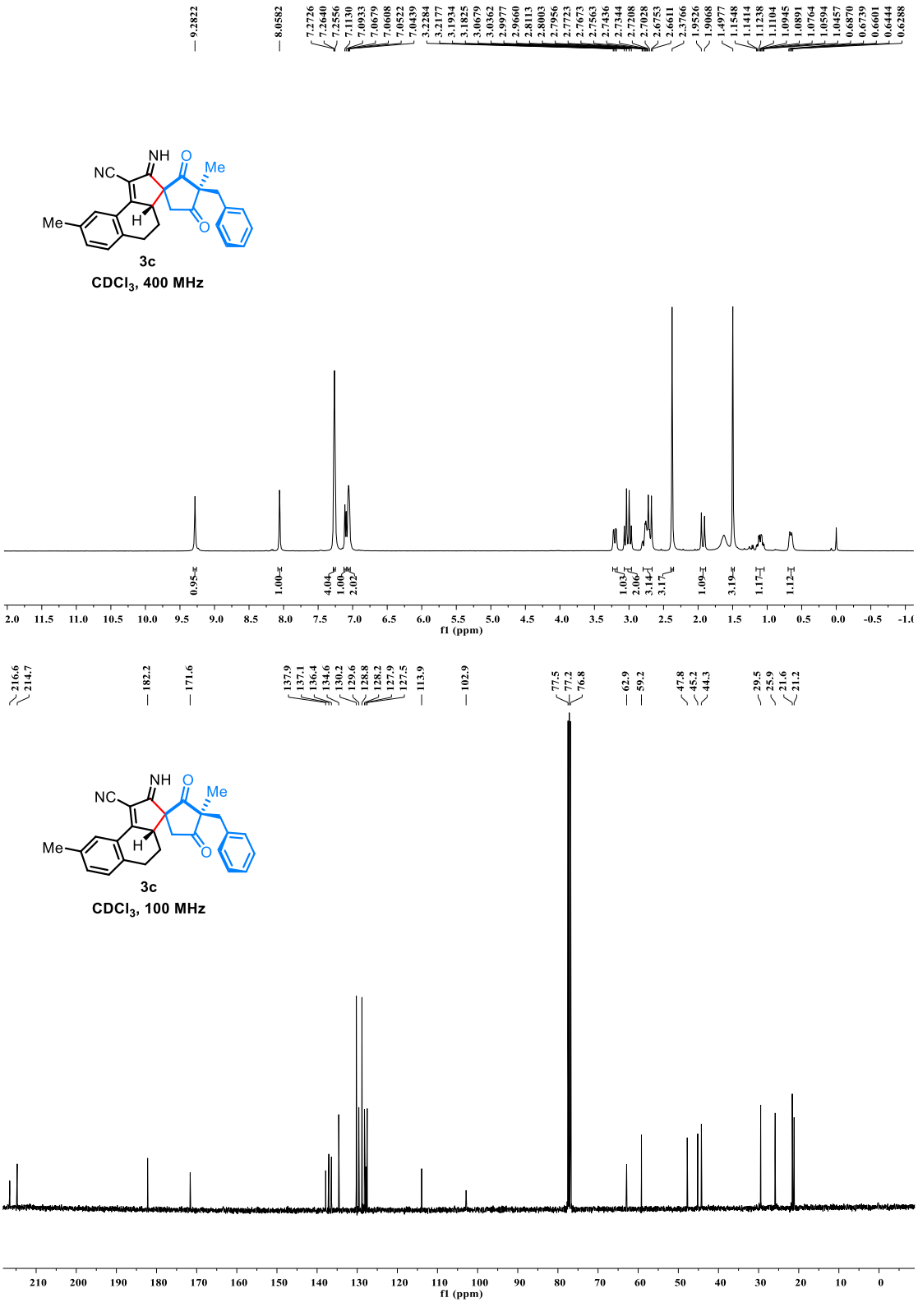


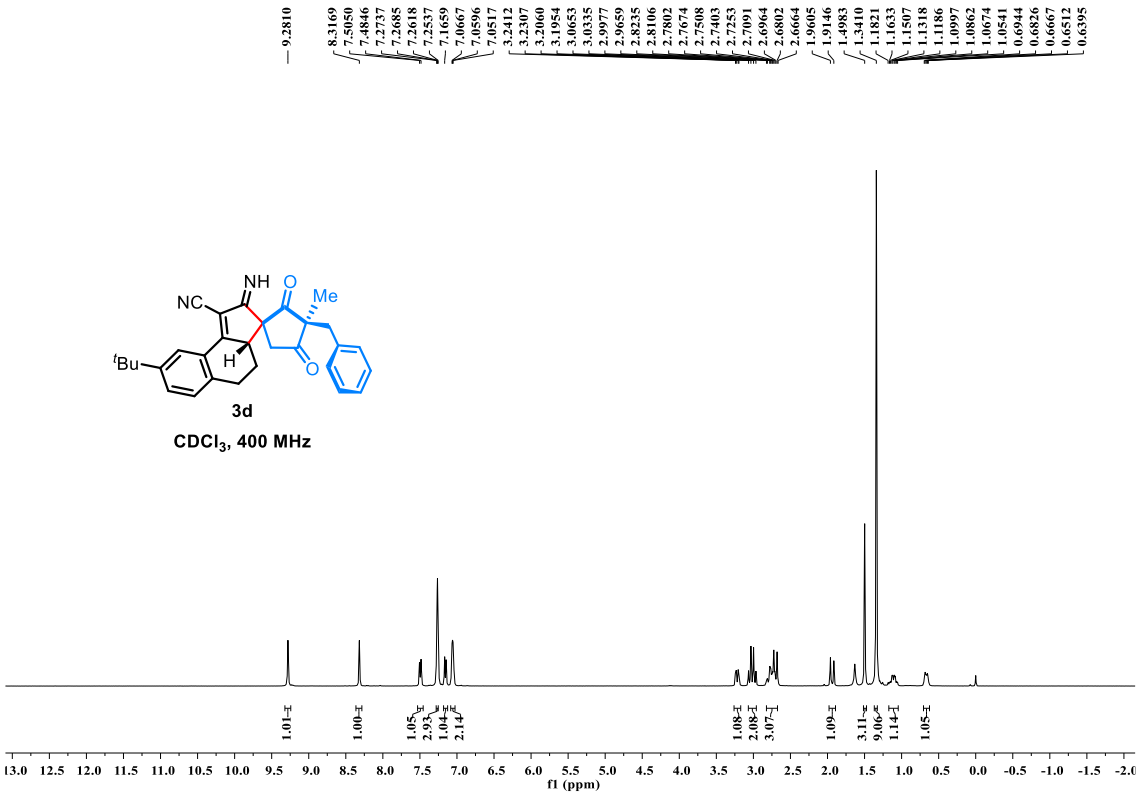


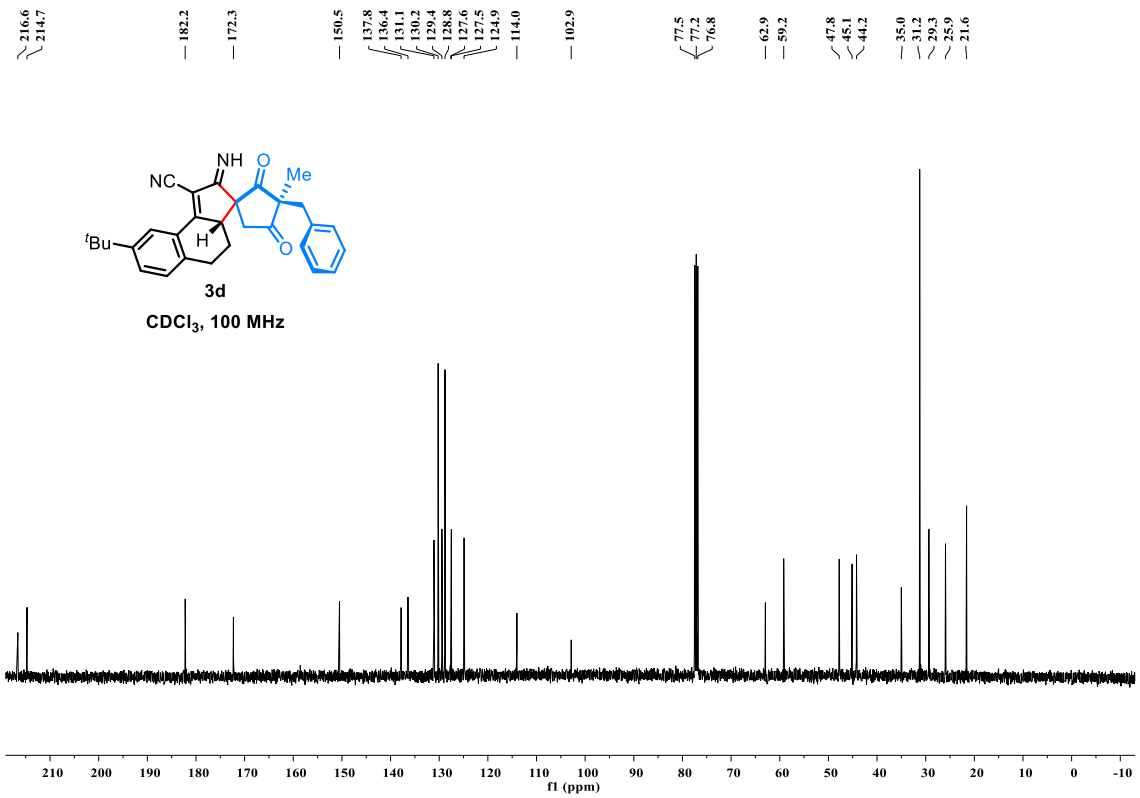
3b

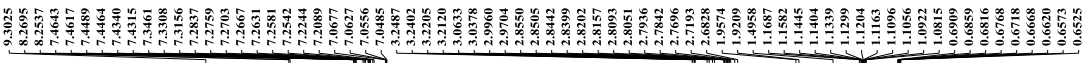
$CDCl_3$, 100 MHz

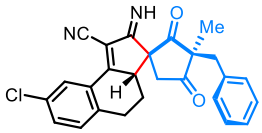



NC
NH
O
Me
Me
H
O
3c
CDCl3, 400 MHz
fl (ppm)
3c
CDCl3, 100 MHz
fl (ppm)


NC
NH
O
Me
H
O
tBu
3d
CDCl3, 400 MHz
f1 (ppm)

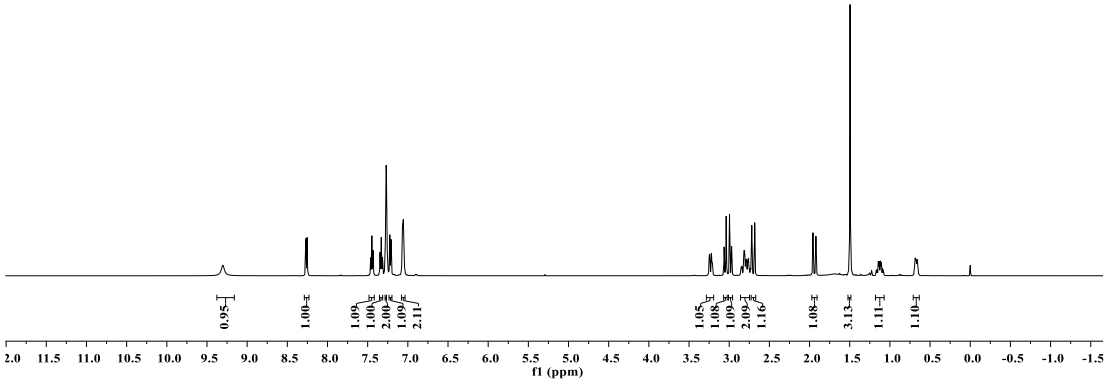

NC
NH
O
Me
H
O
tBu
3d
CDCl3, 100 MHz
f1 (ppm)

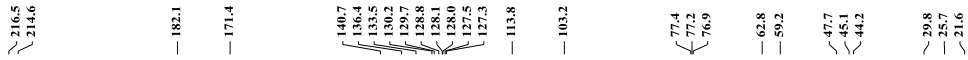


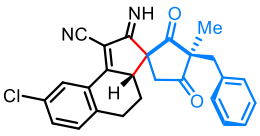


3e

$CDCl_3$, 500 MHz

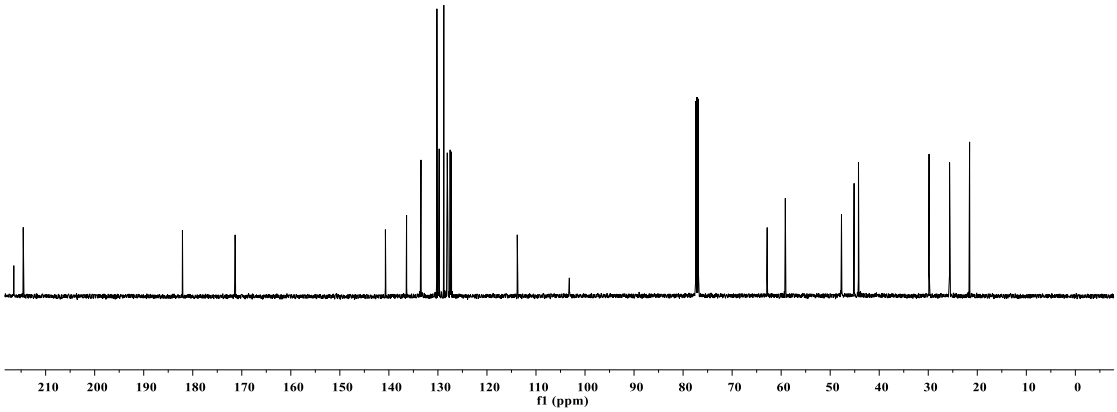


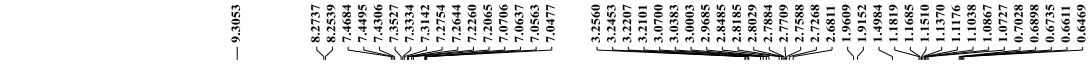


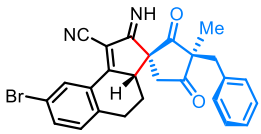


3e

$CDCl_3$, 125 MHz

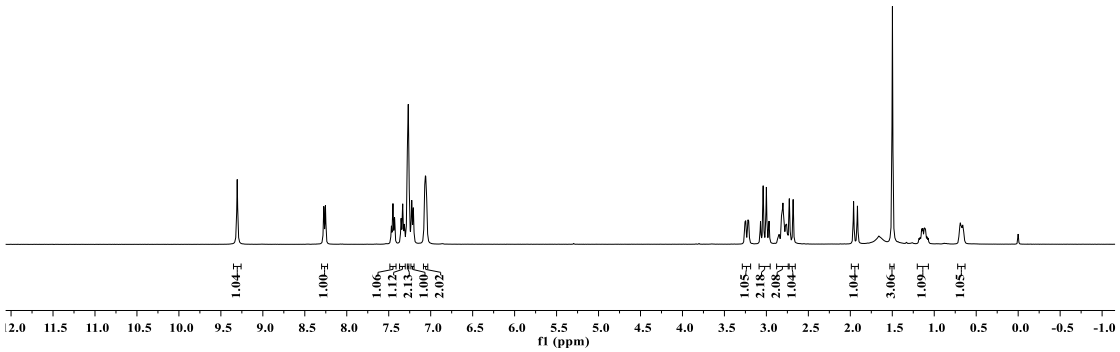


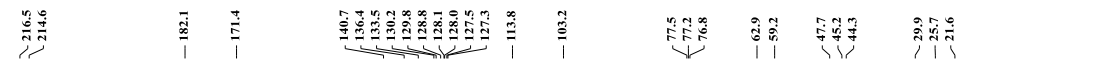


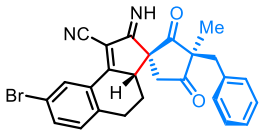


3f

$CDCl_3$, 400 MHz

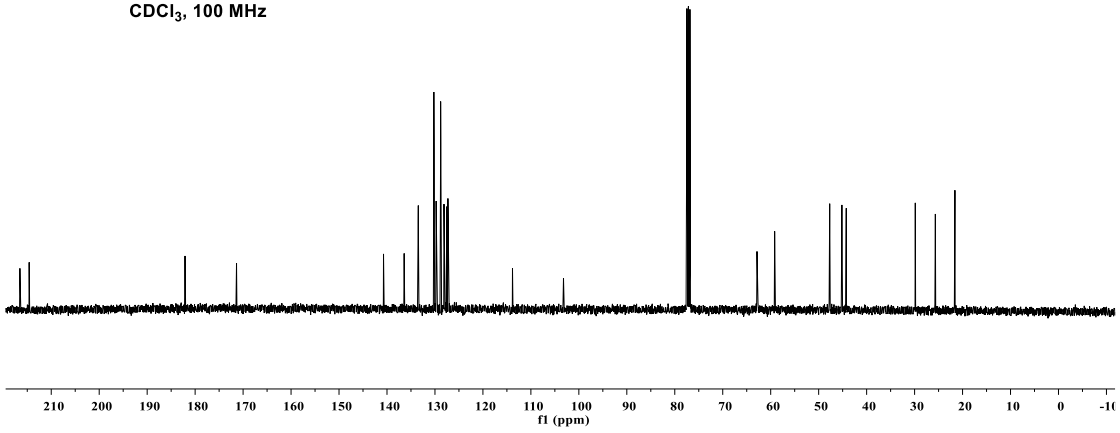


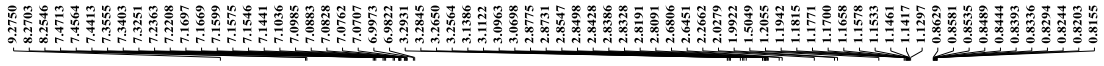


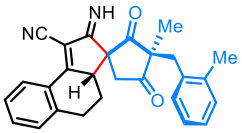


3f

$CDCl_3$, 100 MHz

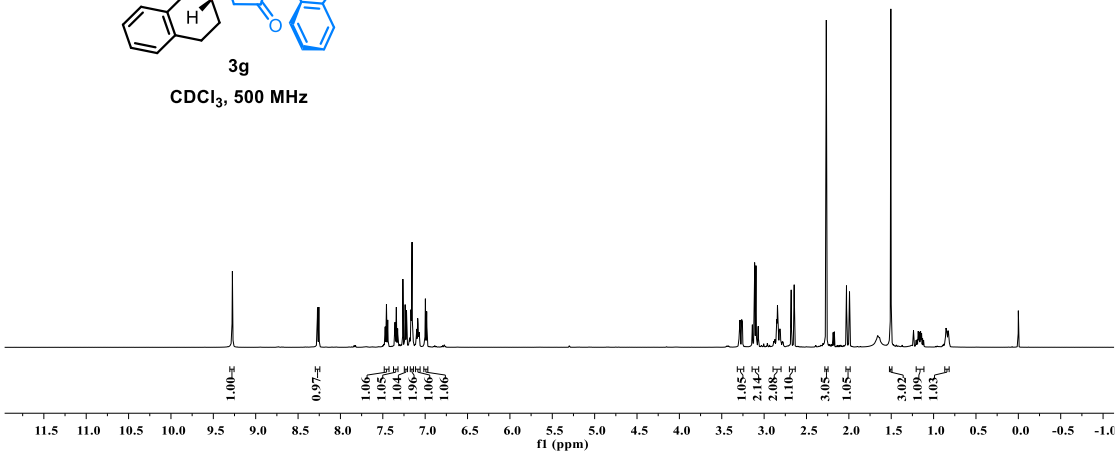


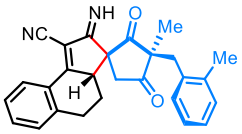




3g

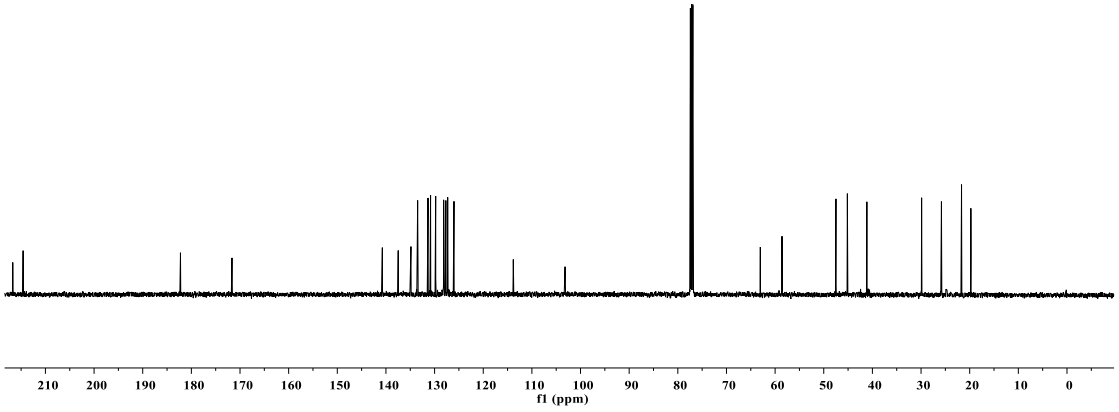
$CDCl_3$, 500 MHz

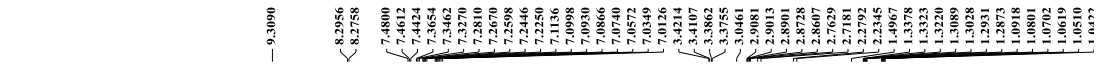


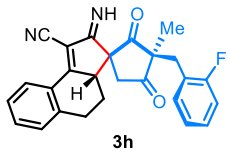


3g

$CDCl_3$, 125 MHz

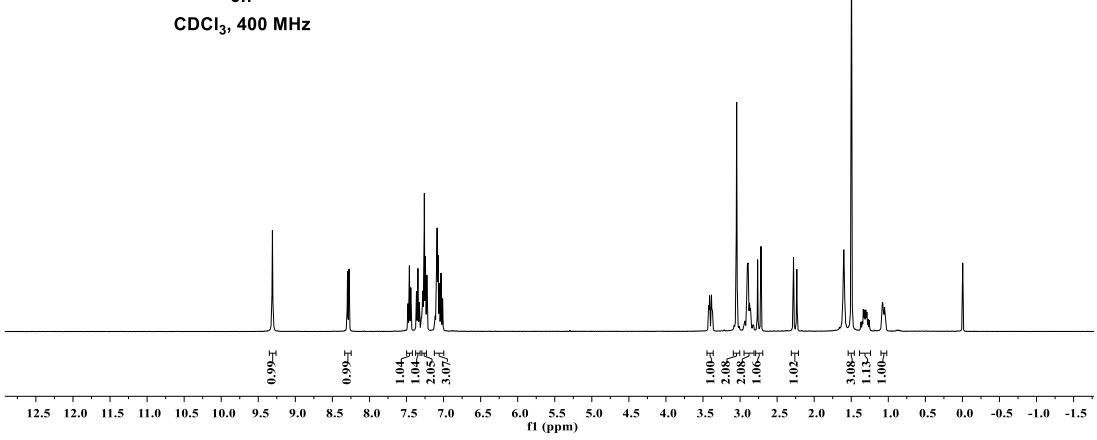


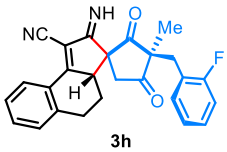




3h

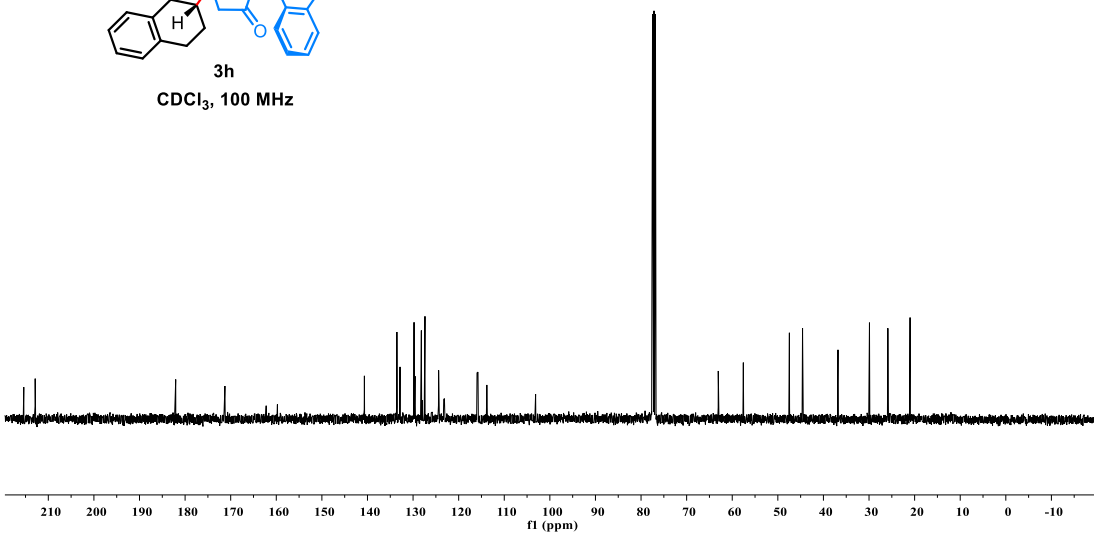
$CDCl_3$, 400 MHz

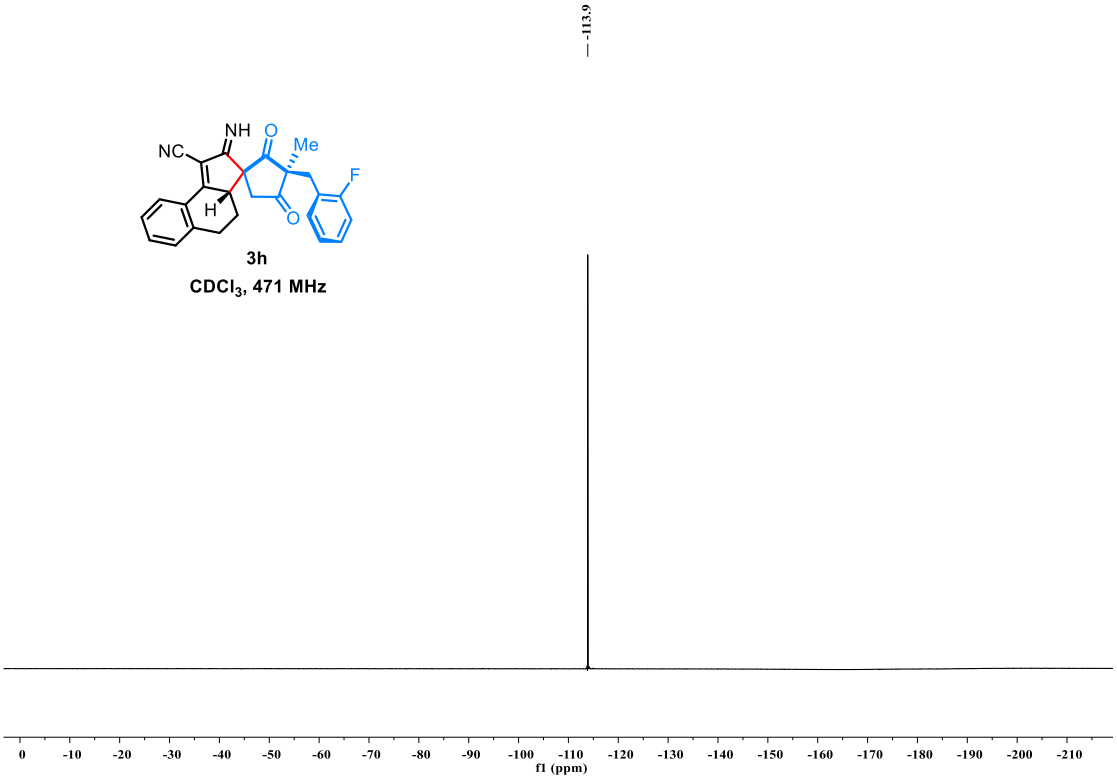


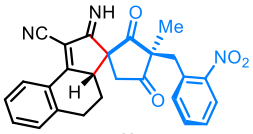


3h

$CDCl_3$, 100 MHz

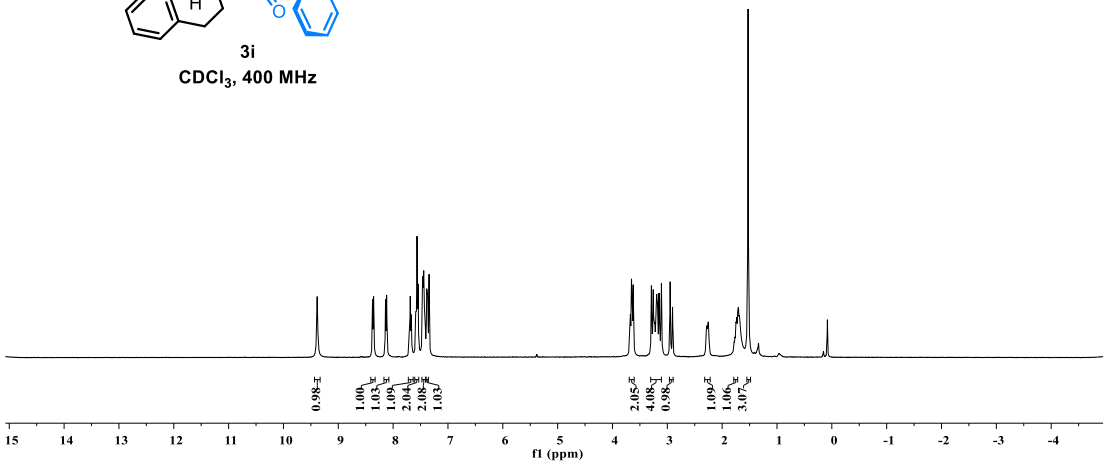


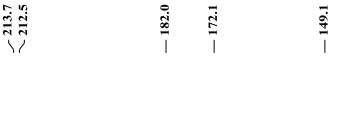

-113.9
NC
NH
O
Me
F
H
O
3h
CDCl3, 471 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



3i

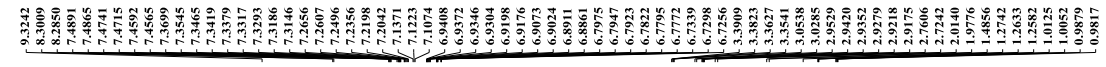
$CDCl_3$, 400 MHz

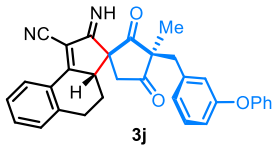




3i

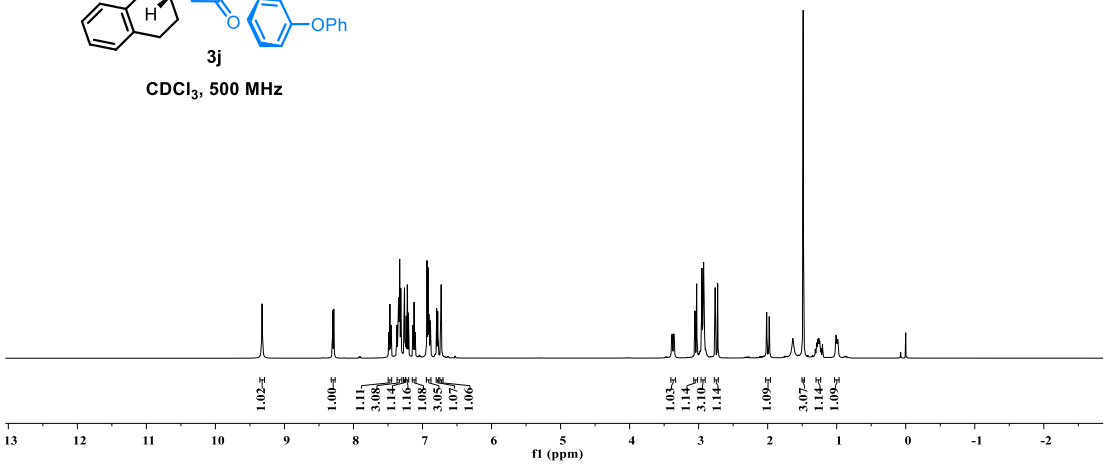
$CDCl_3$, 100 MHz

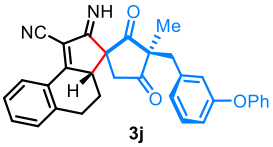




3j

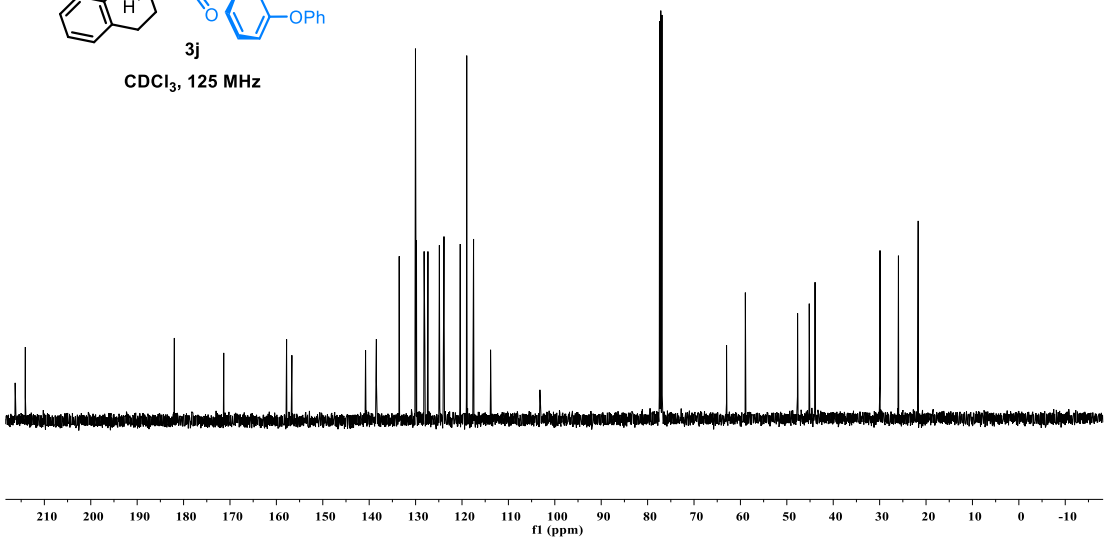
$CDCl_3$, 500 MHz

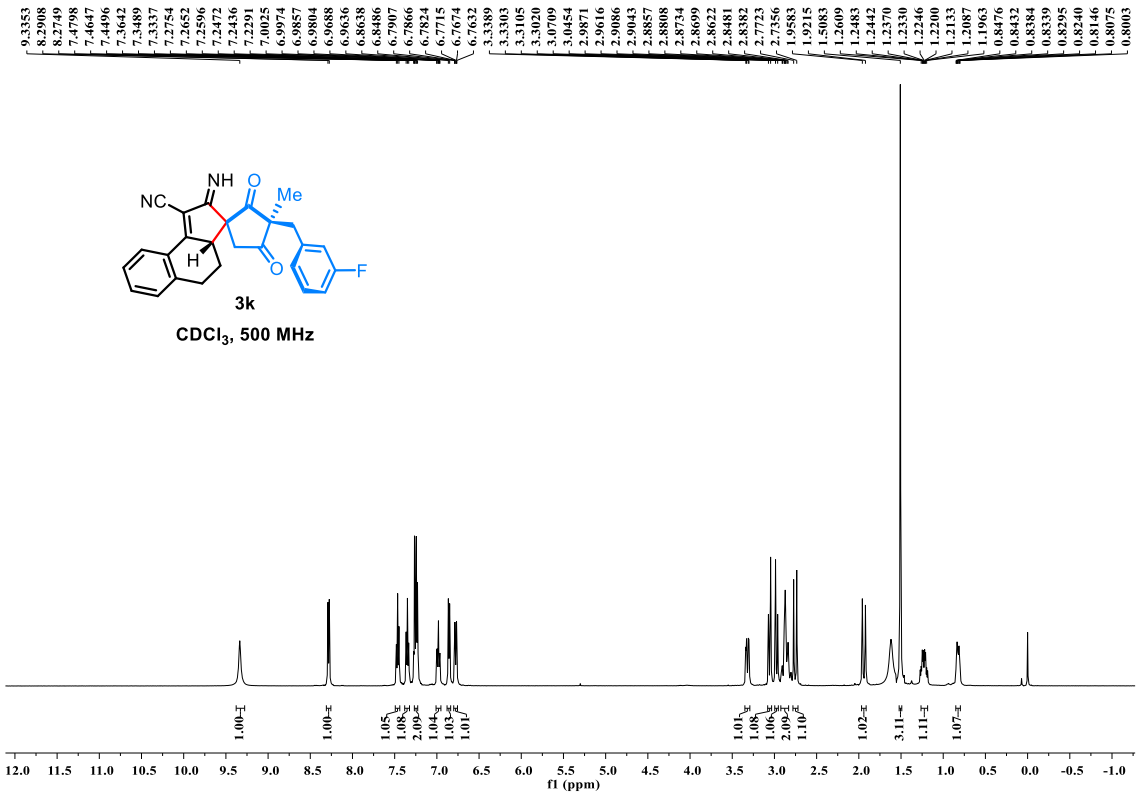


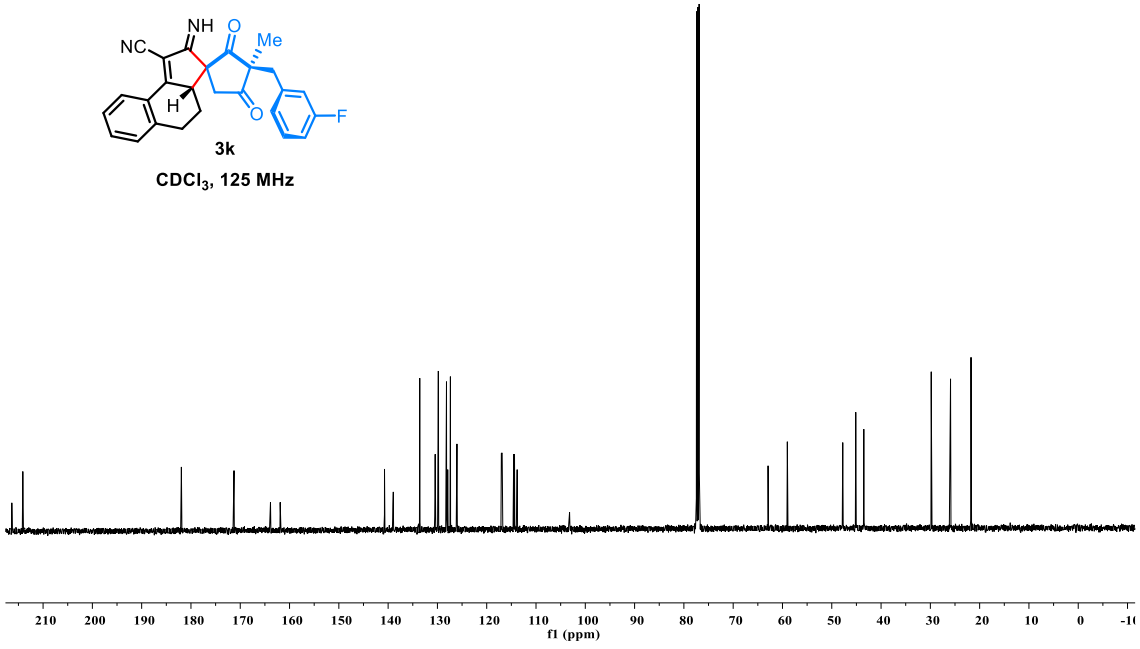


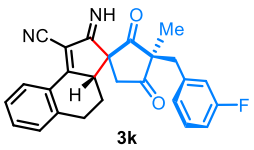
3j

$CDCl_3$, 125 MHz



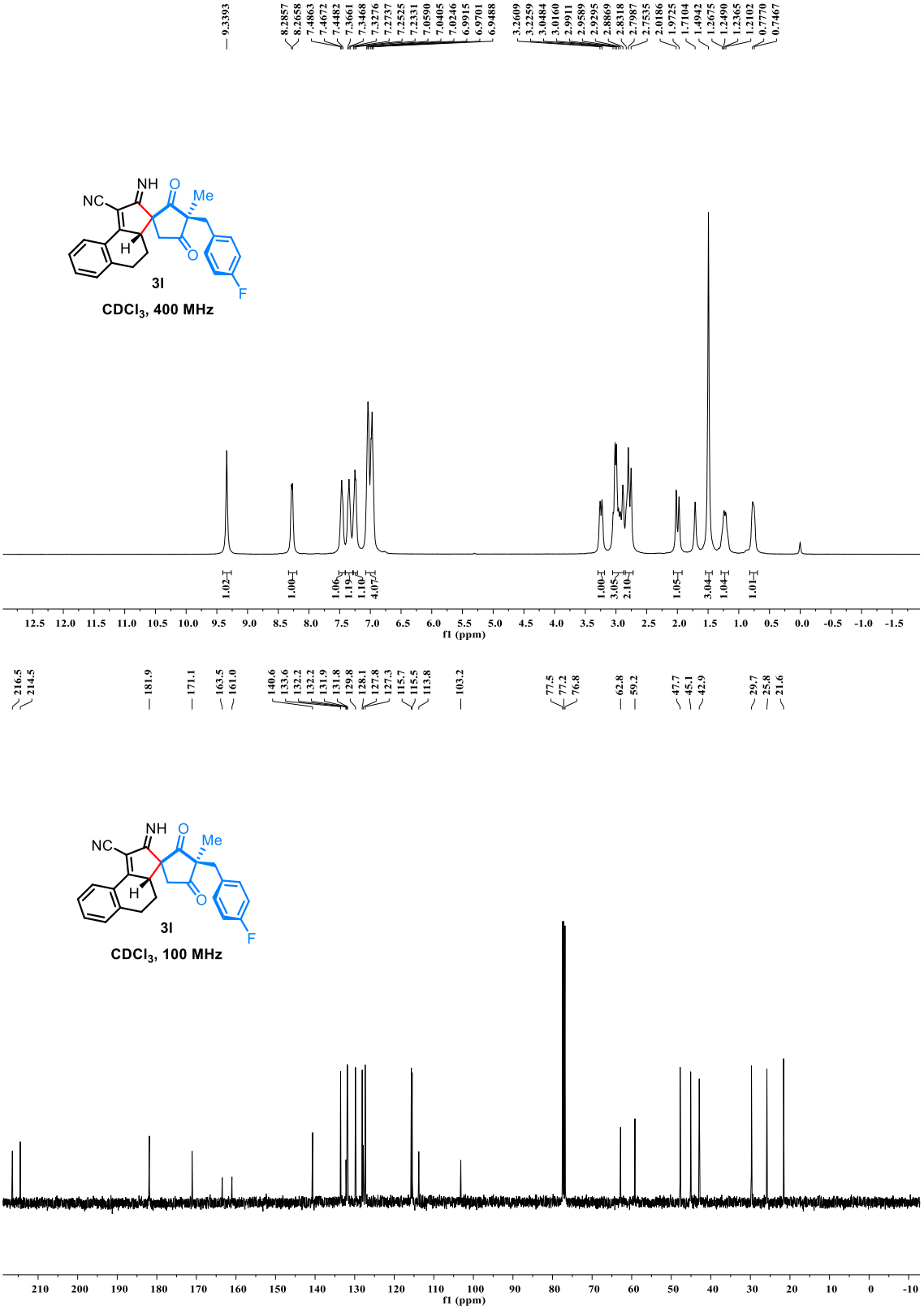

NC
NH
O
Me
H
O
F
3k
CDCl3, 500 MHz
f1 (ppm)

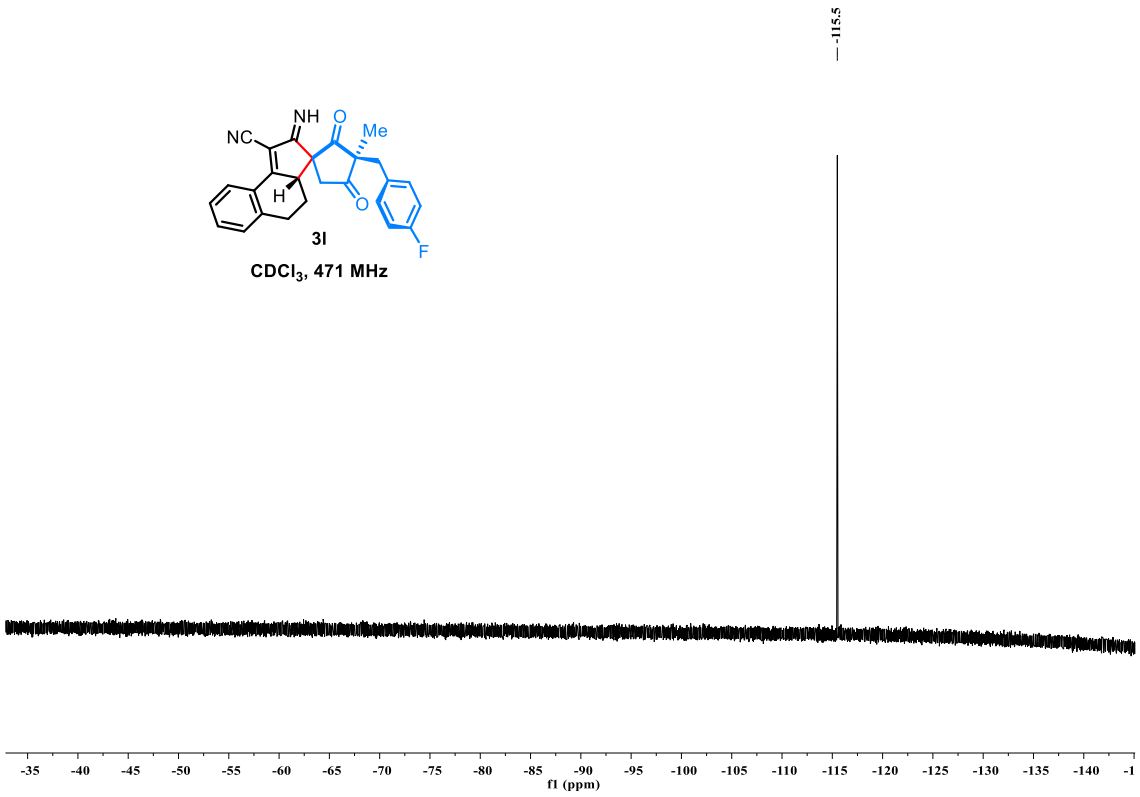

NC
NH
O
Me
H
O
F
3k
CDCl3, 125 MHz
f1 (ppm)

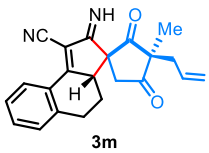


3k

$CDCl_3$, 471 MHz

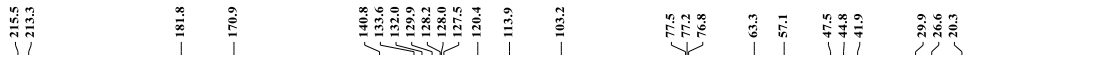

9.3393
8.2857
8.2658
7.4863
7.4672
7.4482
7.3661
7.3468
7.3276
7.2737
7.2525
7.2331
7.0590
7.0405
7.0246
6.9915
6.9701
6.9488
3.2609
3.2259
3.0484
3.0160
2.9911
2.9589
2.9295
2.8869
2.8318
2.7987
2.7535
2.0186
1.9725
1.7104
1.4942
1.2675
1.2490
1.2365
1.2102
0.7770
0.7467
NC
NH
O
Me
H
O
F
3l
CDCl3, 400 MHz
1.02
1.00
1.06
1.19
1.10
4.07
1.00
3.05
2.10
1.05
3.04
1.04
1.01
f1 (ppm)
216.5
214.5
181.9
171.1
163.5
161.0
140.6
133.6
132.2
132.2
131.9
131.8
129.8
128.1
127.8
127.3
115.7
115.5
113.8
103.2
77.5
77.2
76.8
62.8
59.2
47.7
45.1
42.9
29.7
25.8
21.6
NC
NH
O
Me
H
O
F
3l
CDCl3, 100 MHz
f1 (ppm)

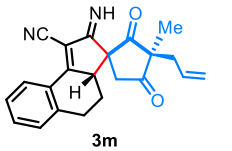

NC
NH
O
Me
H
O
F
3l
CDCl3, 471 MHz
-115.5
-35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140
f1 (ppm)



3m

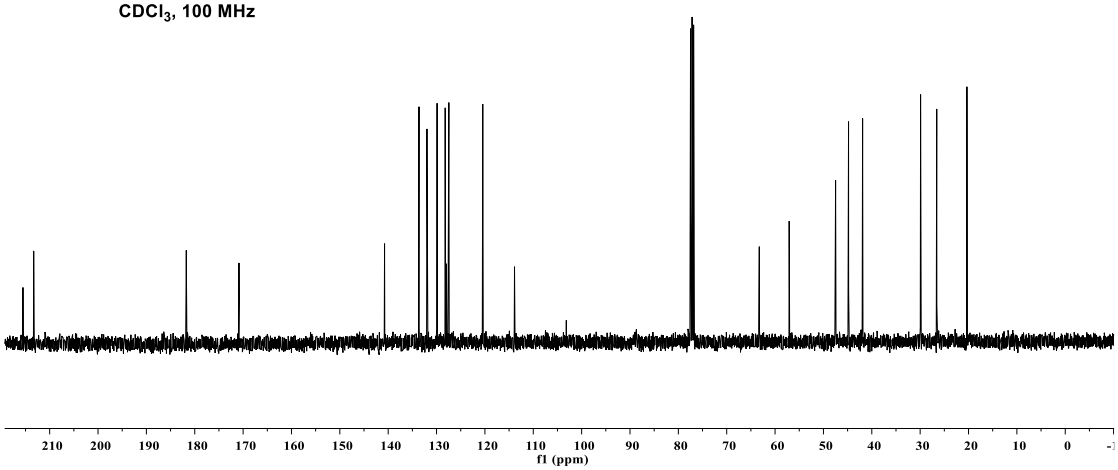
$CDCl_3$, 400 MHz

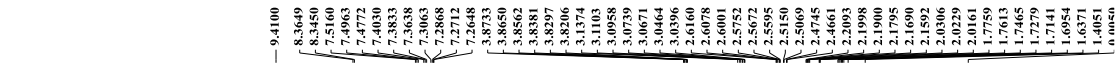


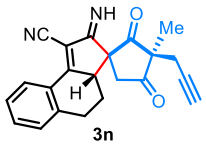


3m

$CDCl_3$, 100 MHz

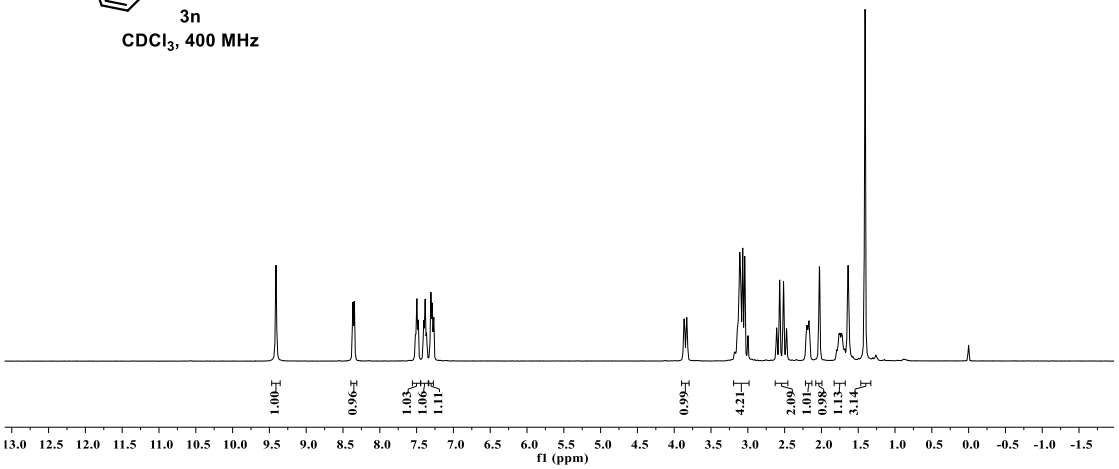


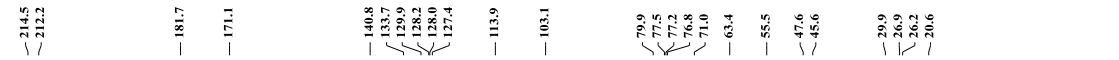


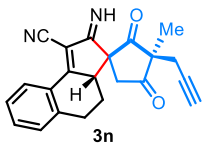


3n

$CDCl_3$, 400 MHz

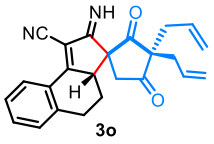






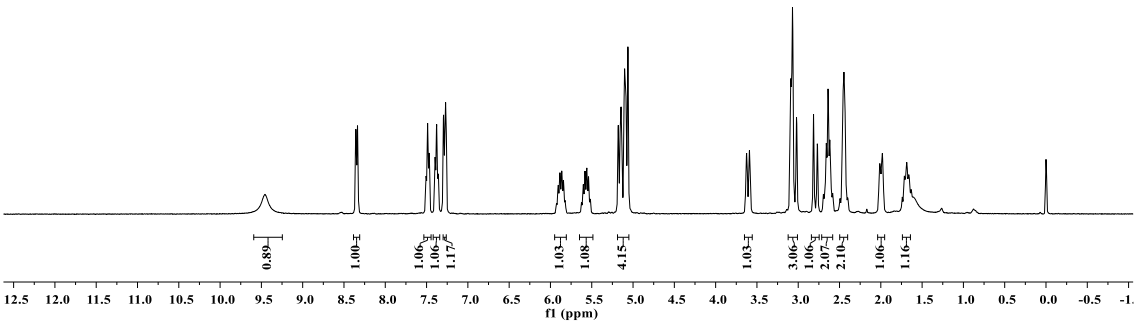
3n

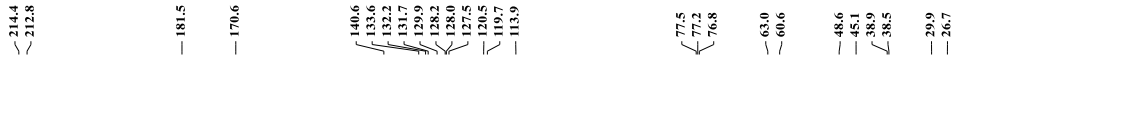
$CDCl_3$, 100 MHz

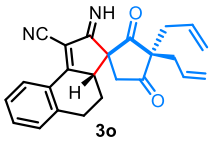


3o

$CDCl_3$, 400 MHz

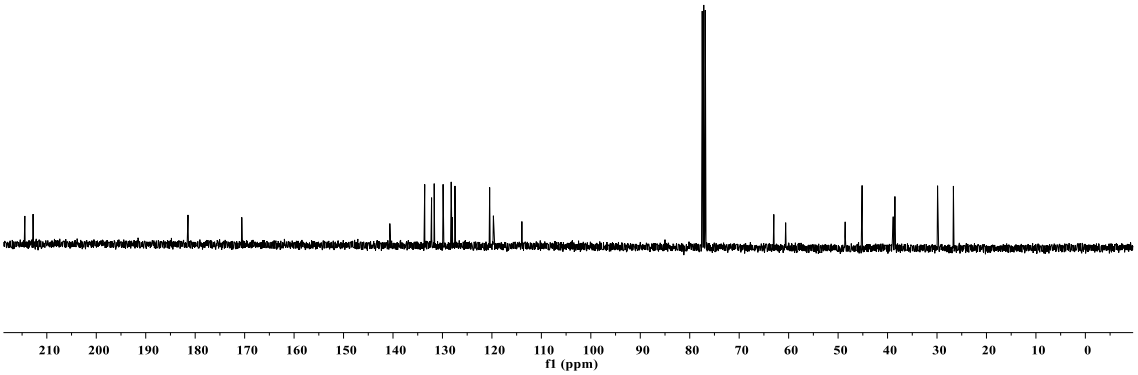


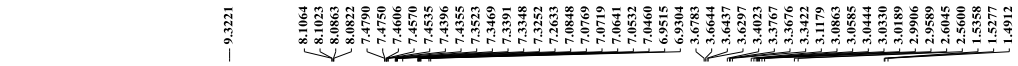


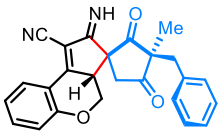


3o

$CDCl_3$, 100 MHz

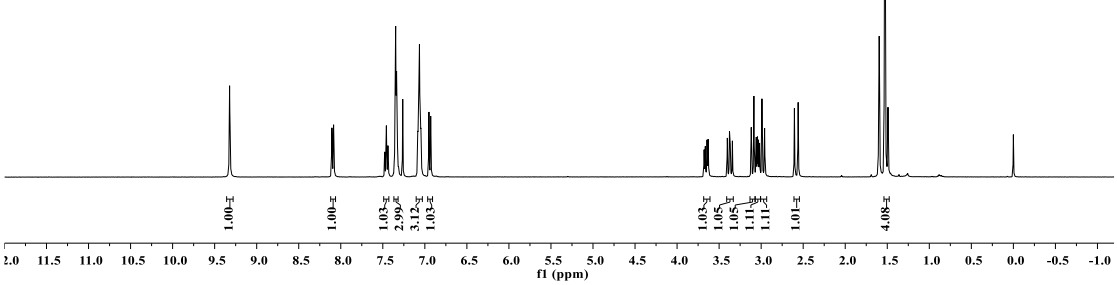


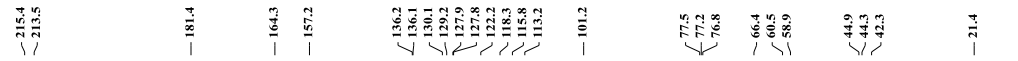


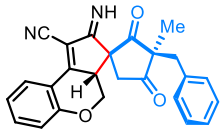


3aa

$CDCl_3$, 400 MHz

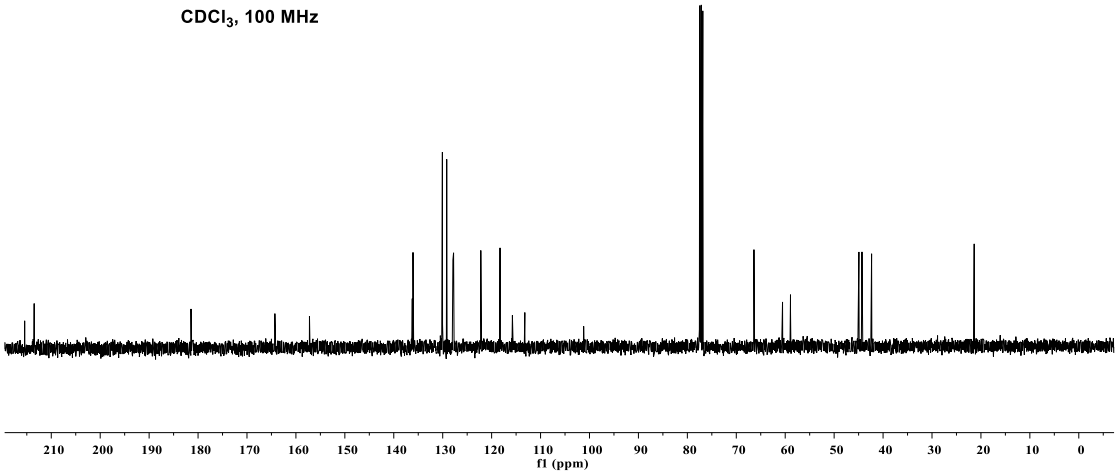


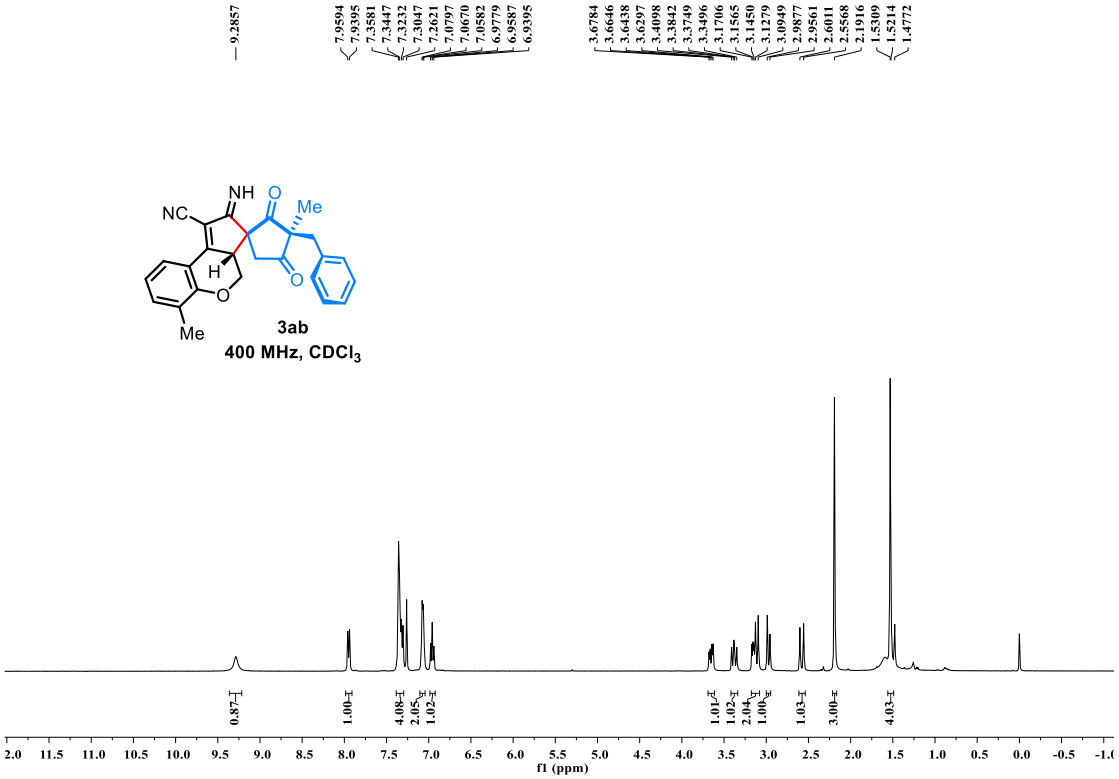


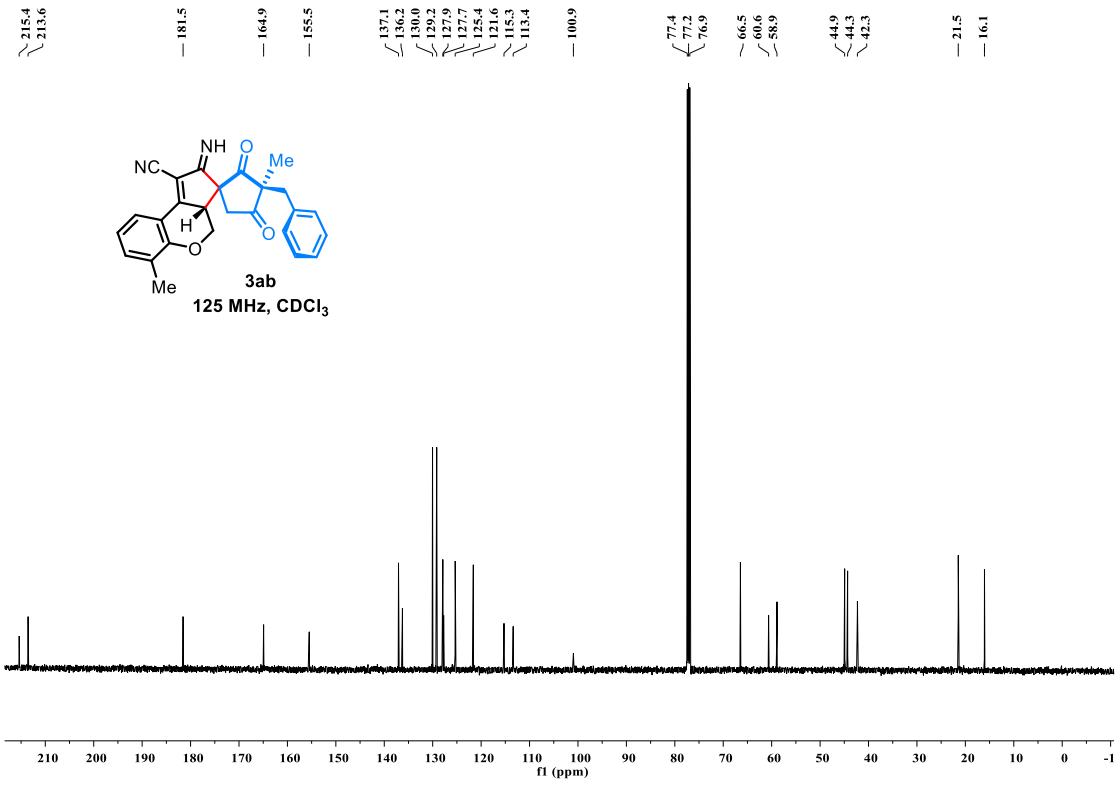


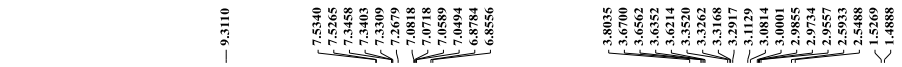
3aa

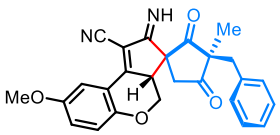
$CDCl_3$, 100 MHz




9.2857
7.9594
7.9395
7.3581
7.3447
7.3232
7.3047
7.2621
7.0797
7.0670
7.0582
6.9779
6.9587
6.9395
3.6784
3.6646
3.6438
3.6297
3.4098
3.3842
3.3749
3.3496
3.1706
3.1565
3.1450
3.1279
3.0949
2.9877
2.9561
2.6011
2.5568
2.1916
1.5309
1.5214
1.4772
NC
NH
O
Me
H
O
O
Me
3ab
400 MHz, CDCl3
0.87
1.00
4.08
2.05
1.02
1.01
1.02
2.04
1.00
1.03
3.00
4.03
f1 (ppm)

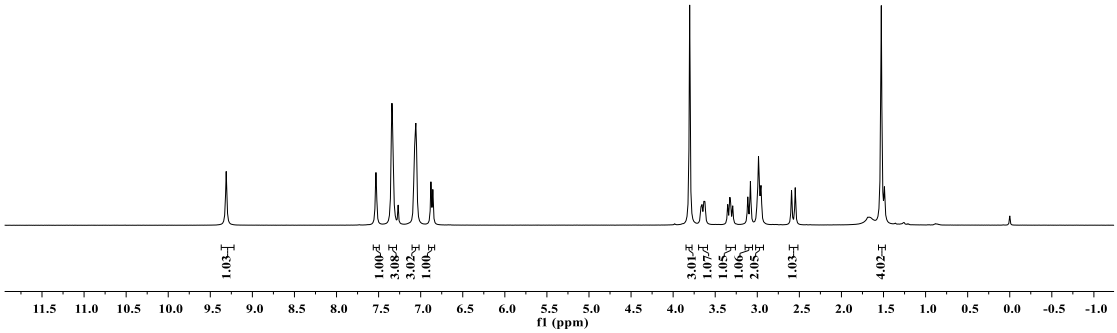

215.4
213.6
181.5
164.9
155.5
137.1
136.2
130.0
129.2
127.9
127.7
125.4
121.6
115.3
113.4
100.9
77.4
77.2
76.9
66.5
60.6
58.9
44.9
44.3
42.3
21.5
16.1
NC
NH
O
Me
H
O
O
Me
3ab
125 MHz, CDCl3
f1 (ppm)

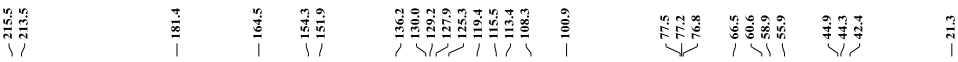


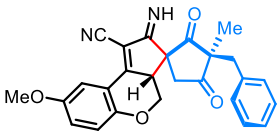


3ac

$CDCl_3$, 400 MHz

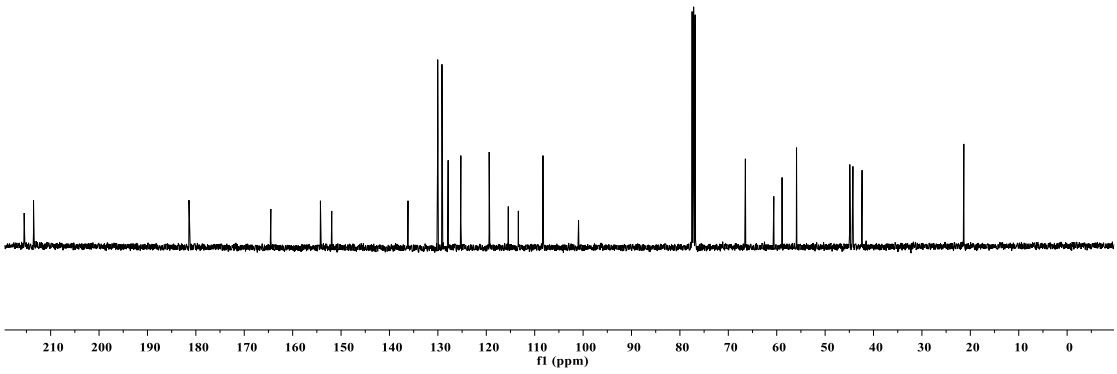


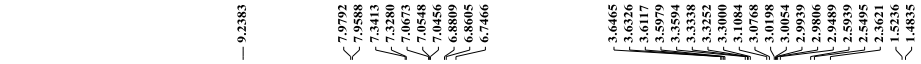


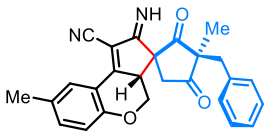


3ac

$CDCl_3$, 100 MHz

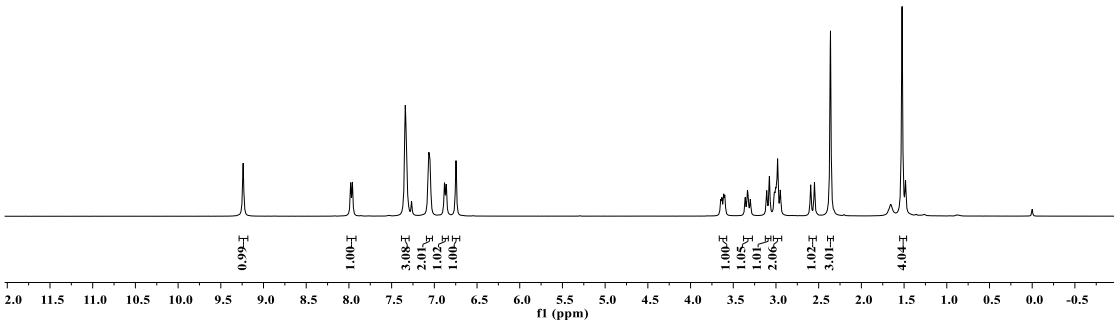


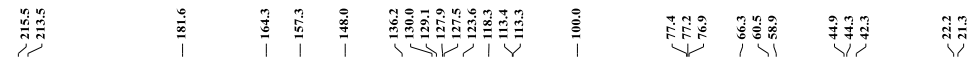


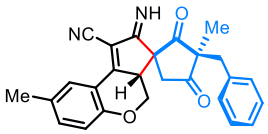


3ad

$CDCl_3$, 400 MHz

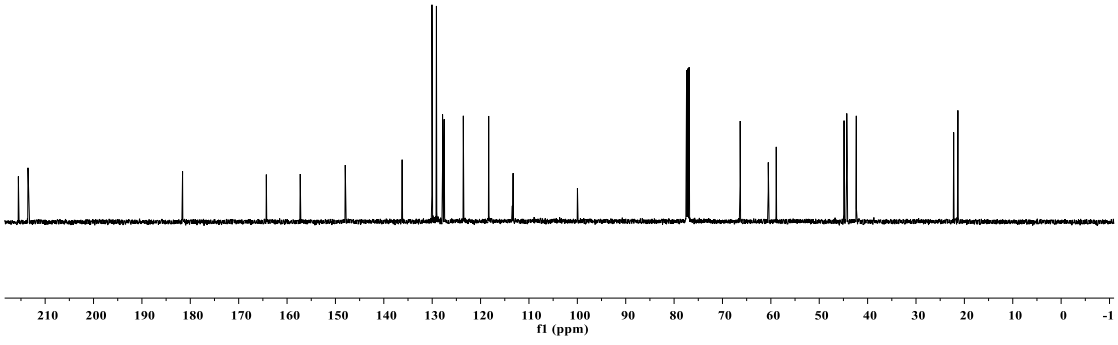


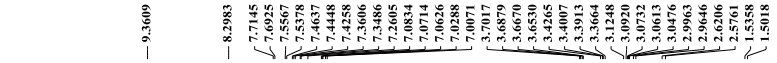


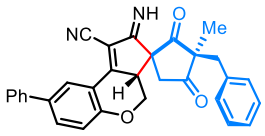


3ad

$CDCl_3$, 125 MHz

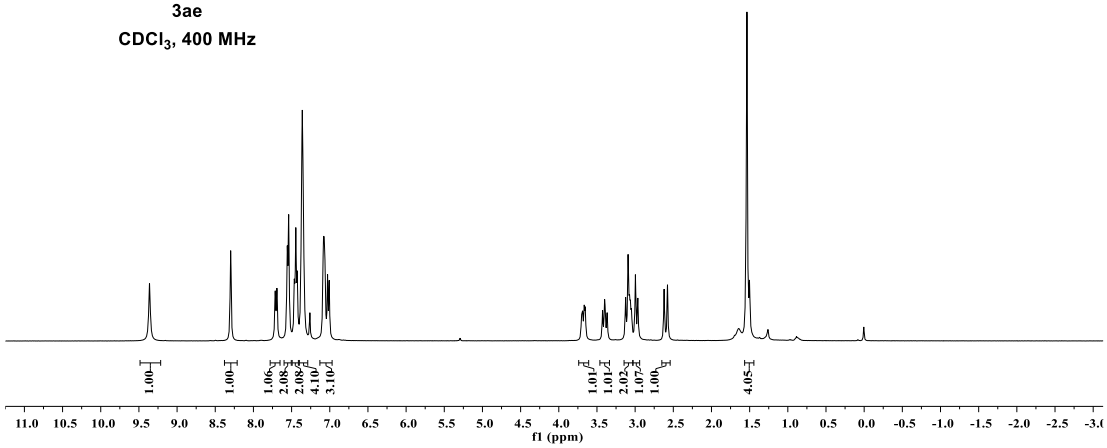


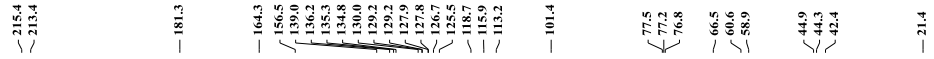


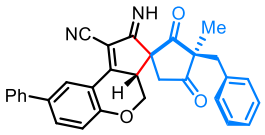


3ae

$CDCl_3$, 400 MHz

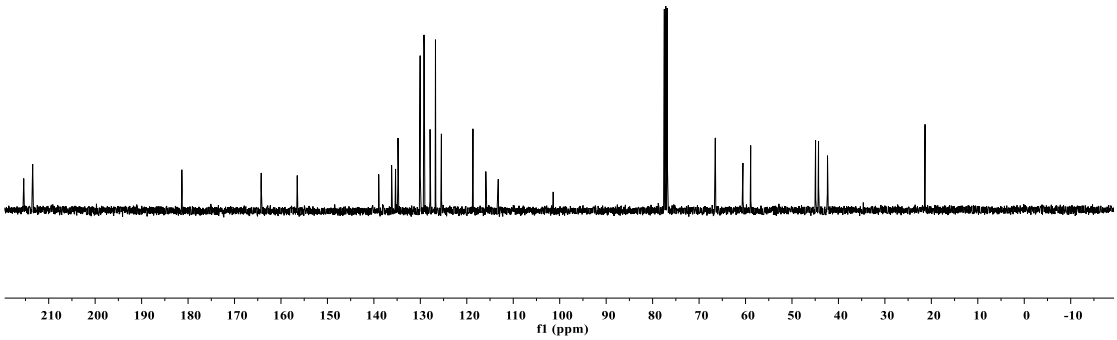


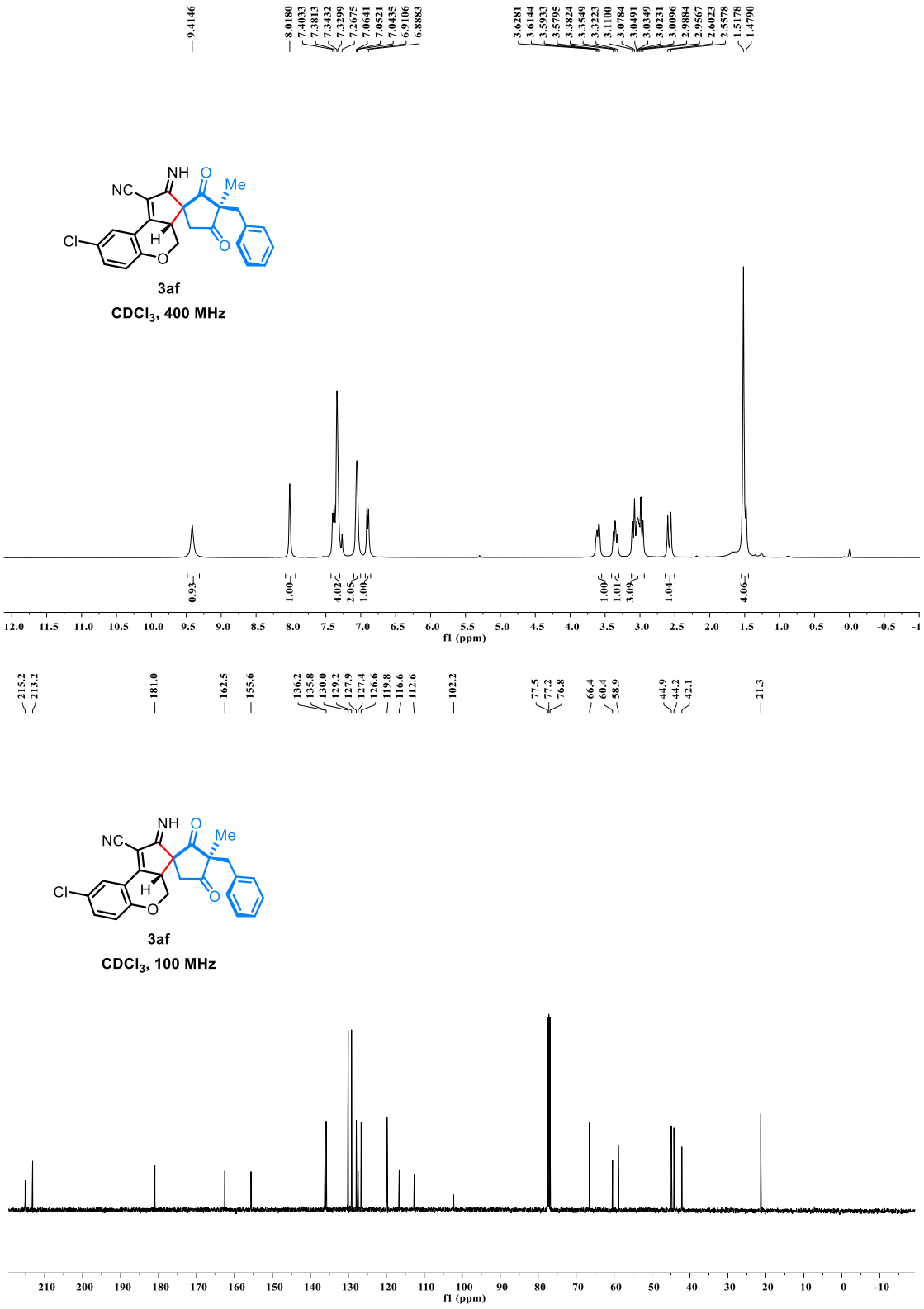


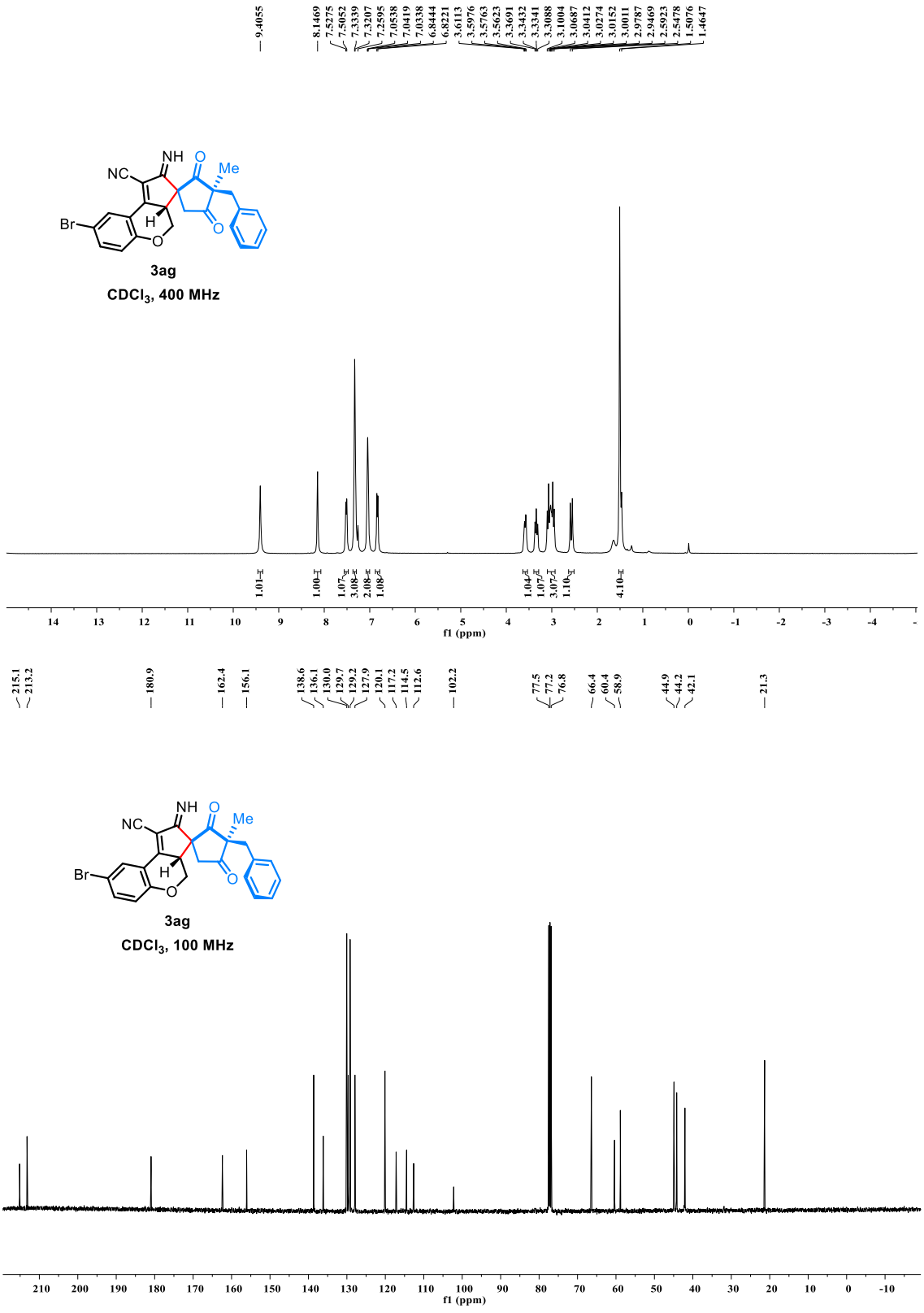


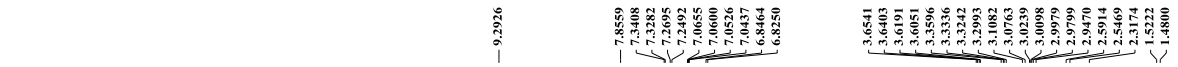
3ae

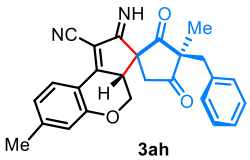
$CDCl_3$, 100 MHz




9.4146
8.0180
7.4033
7.3813
7.3432
7.3299
7.2675
7.0641
7.0521
7.0435
6.9106
6.8883
3.6281
3.6144
3.5933
3.5795
3.3824
3.3549
3.3323
3.1100
3.0784
3.0491
3.0349
3.0231
3.0096
2.9884
2.9567
2.6023
2.5578
1.5178
1.4790
NC
NH
O
Me
Cl
H
O
O
3af
CDCl3, 400 MHz
0.93
1.00
4.02
2.05
1.00
1.00
1.01
3.09
1.04
4.06
f1 (ppm)
215.2
213.2
181.0
162.5
155.6
136.2
135.8
130.0
129.2
127.9
127.4
126.6
119.8
116.6
112.6
102.2
77.5
77.2
76.8
66.4
60.4
58.9
44.9
44.2
42.1
21.3
NC
NH
O
Me
Cl
H
O
O
3af
CDCl3, 100 MHz
f1 (ppm)

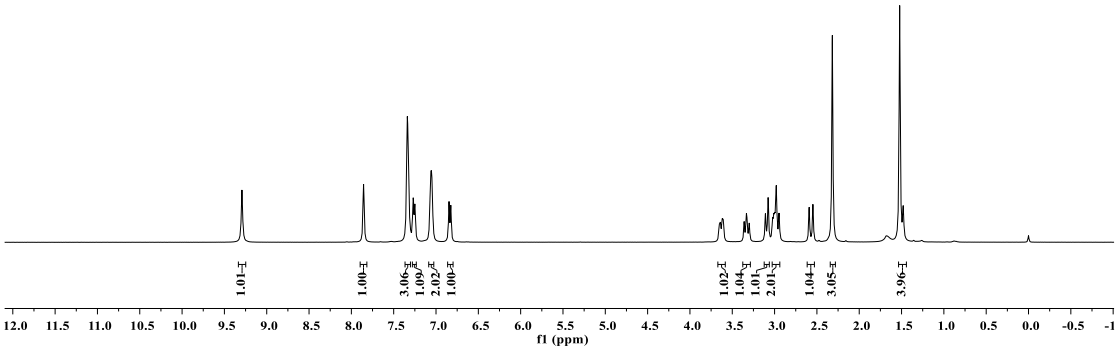

9.4055
8.1469
7.5275
7.5052
7.3339
7.3207
7.2595
7.0538
7.0419
7.0338
6.8444
6.8221
3.6113
3.5976
3.5763
3.5623
3.3691
3.3432
3.3341
3.3088
3.1004
3.0687
3.0412
3.0274
3.0152
3.0011
2.9787
2.9469
2.5923
2.5478
1.5076
1.4647
NC
NH
O
Me
Br
H
O
O
3ag
CDCl3, 400 MHz
1.01
1.00
1.07
3.08
2.08
1.08
1.04
1.07
3.07
1.10
4.10
f1 (ppm)
215.1
213.2
180.9
162.4
156.1
138.6
136.1
130.0
129.7
129.2
127.9
120.1
117.2
114.5
112.6
102.2
77.5
77.2
76.8
66.4
60.4
58.9
44.9
44.2
42.1
21.3
NC
NH
O
Me
Br
H
O
O
3ag
CDCl3, 100 MHz
f1 (ppm)

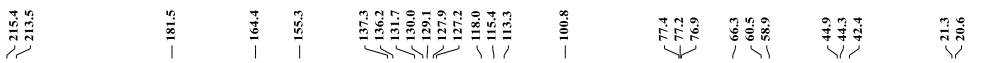


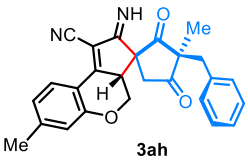


3ah

$CDCl_3$, 500 MHz

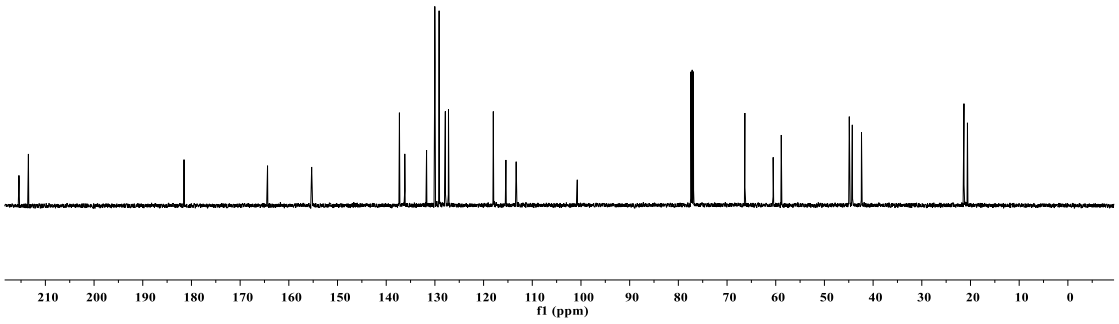


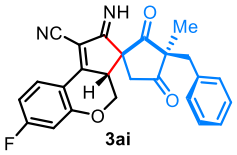




3ah

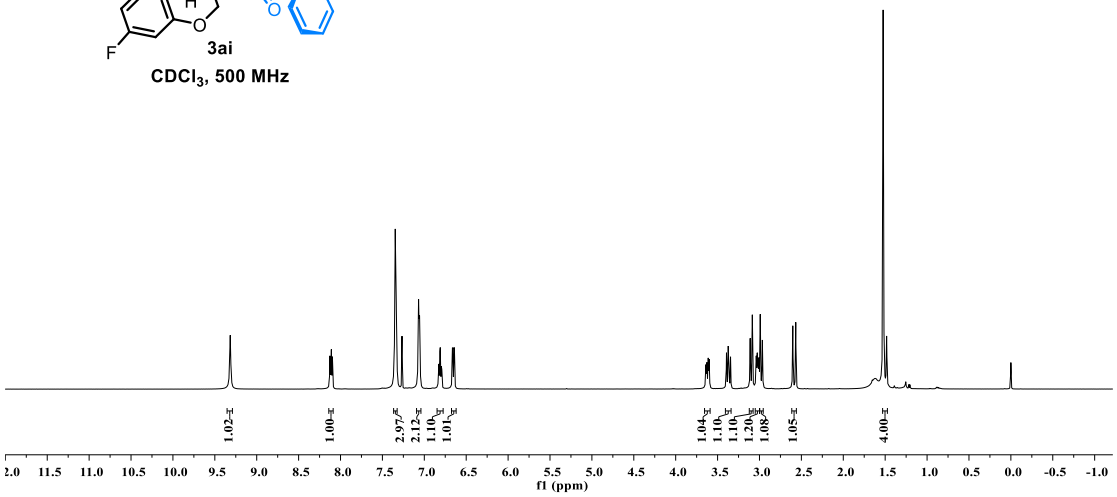
$CDCl_3$, 125 MHz

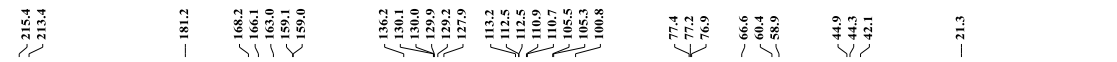


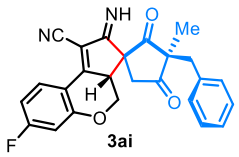


3ai

$CDCl_3$, 500 MHz

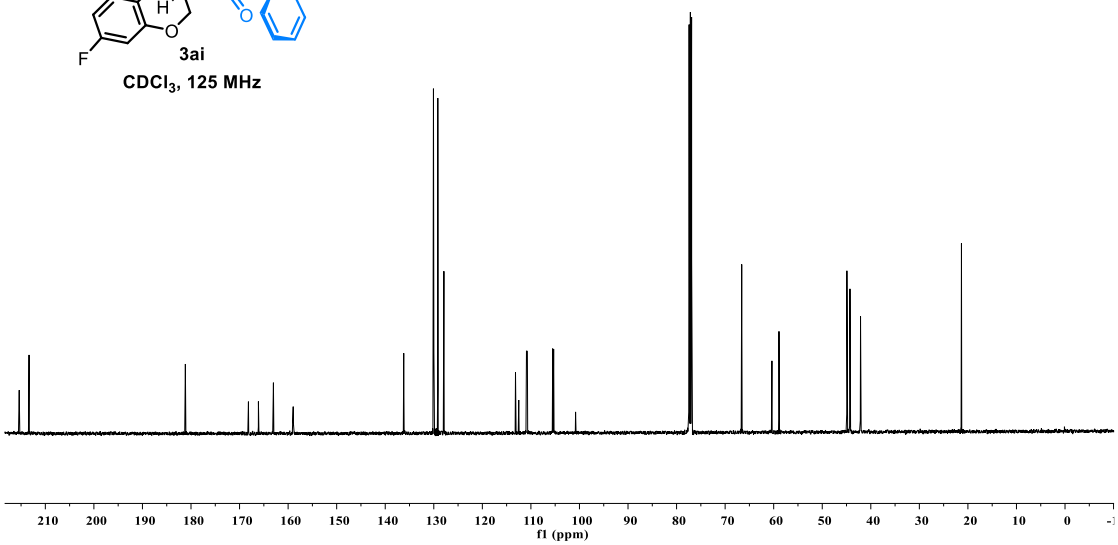


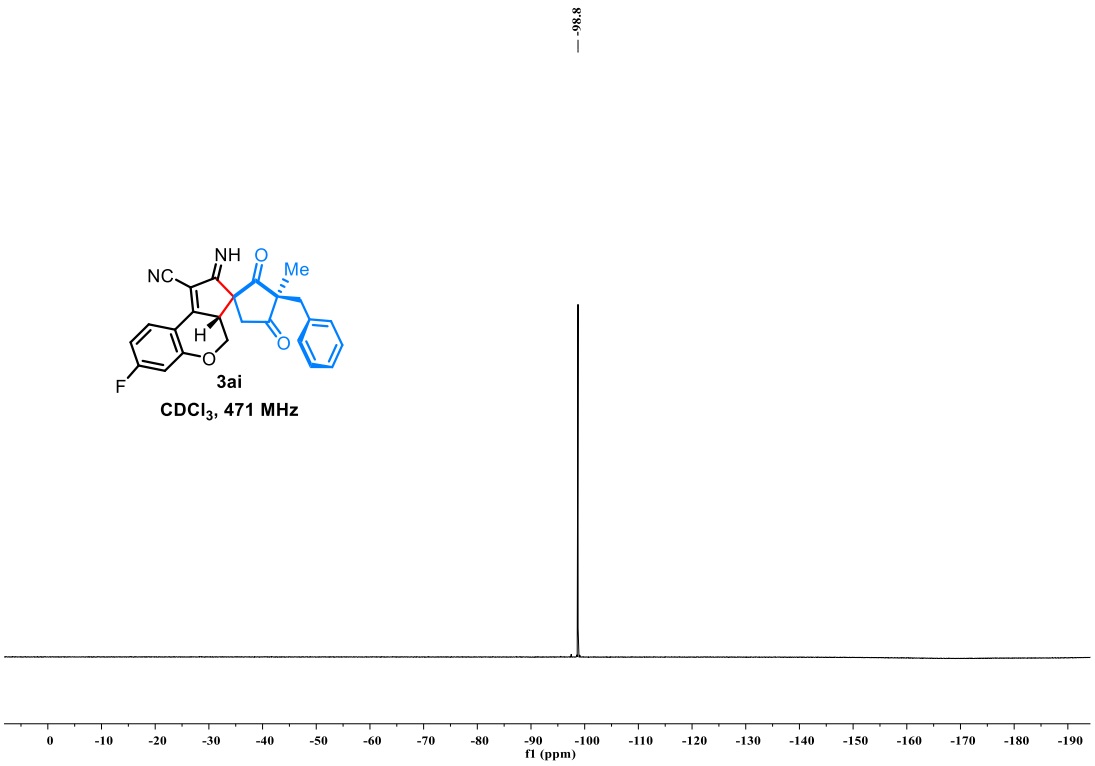


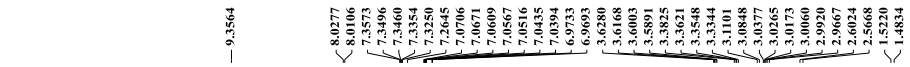


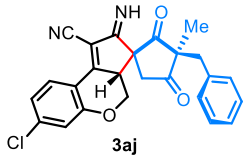
3ai

$CDCl_3$, 125 MHz



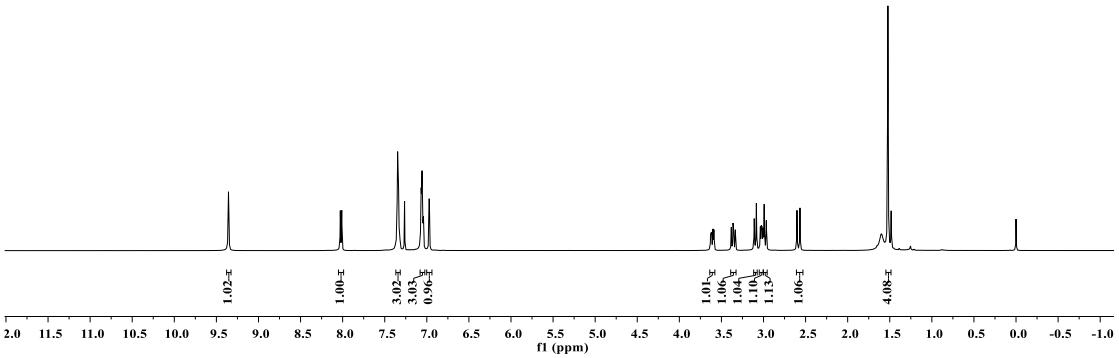

-98.8
NC
NH
O
Me
H
O
O
F
3ai
CDCl3, 471 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

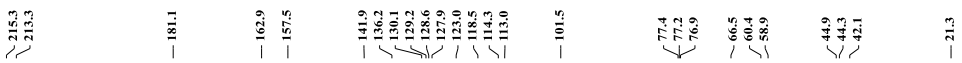


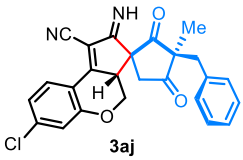


3aj

$CDCl_3$, 500 MHz

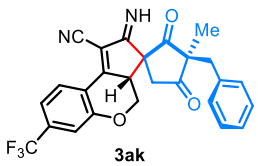






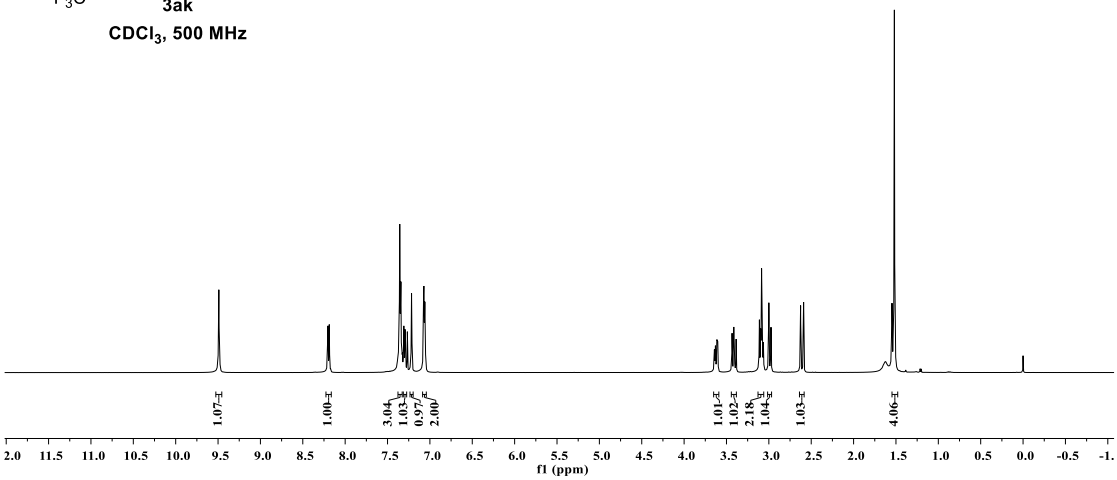
3aj

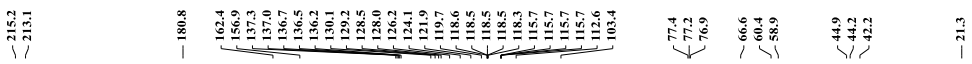
$CDCl_3$, 125 MHz

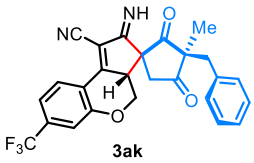


3ak

$CDCl_3$, 500 MHz

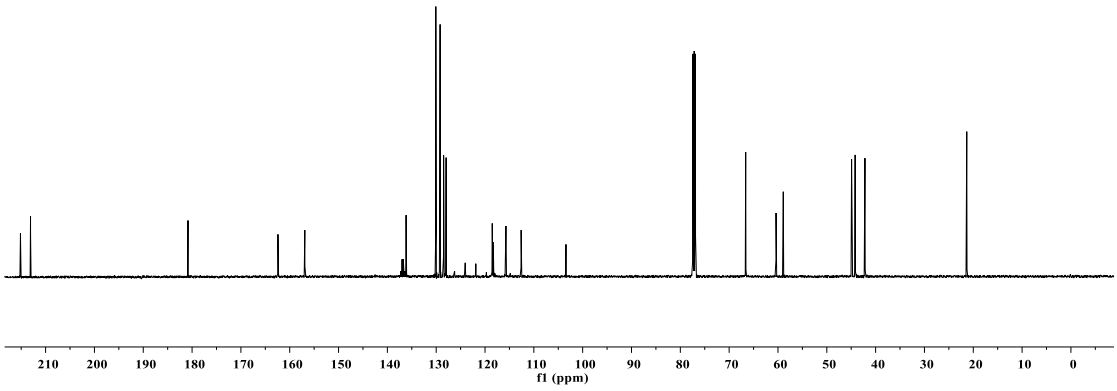


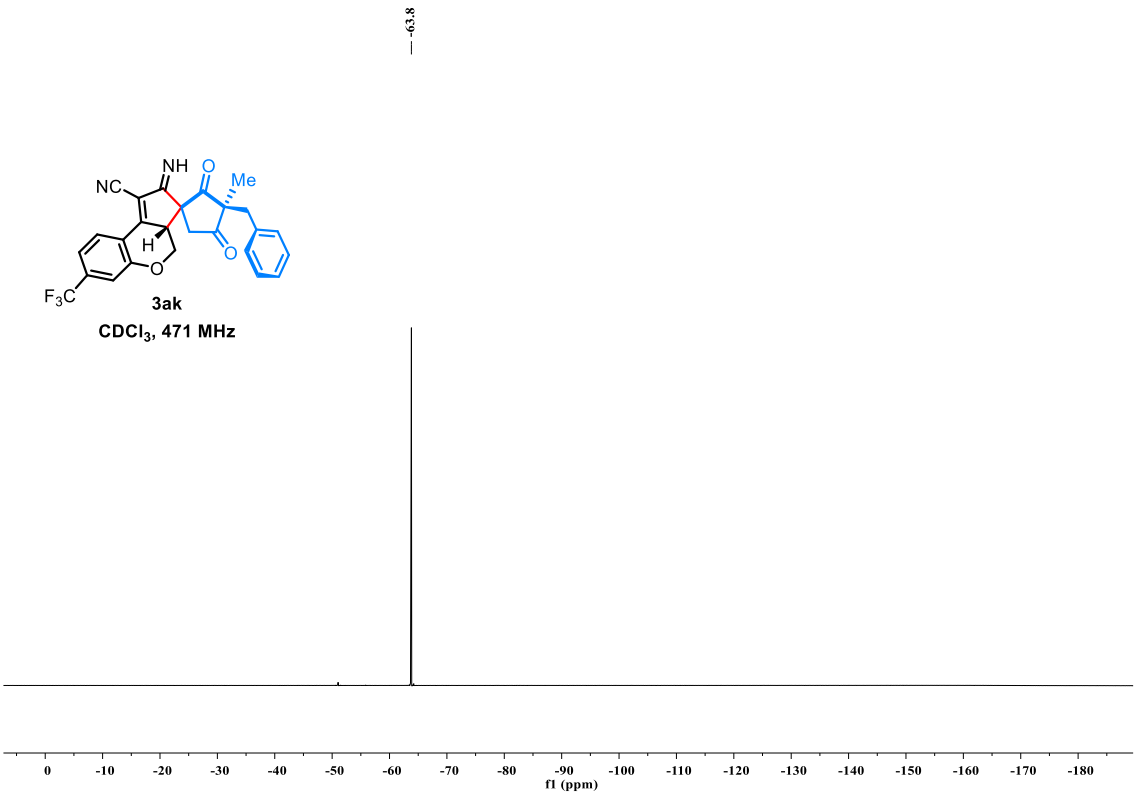


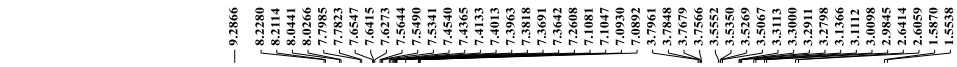


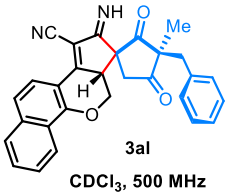
3ak

$CDCl_3$, 125 MHz



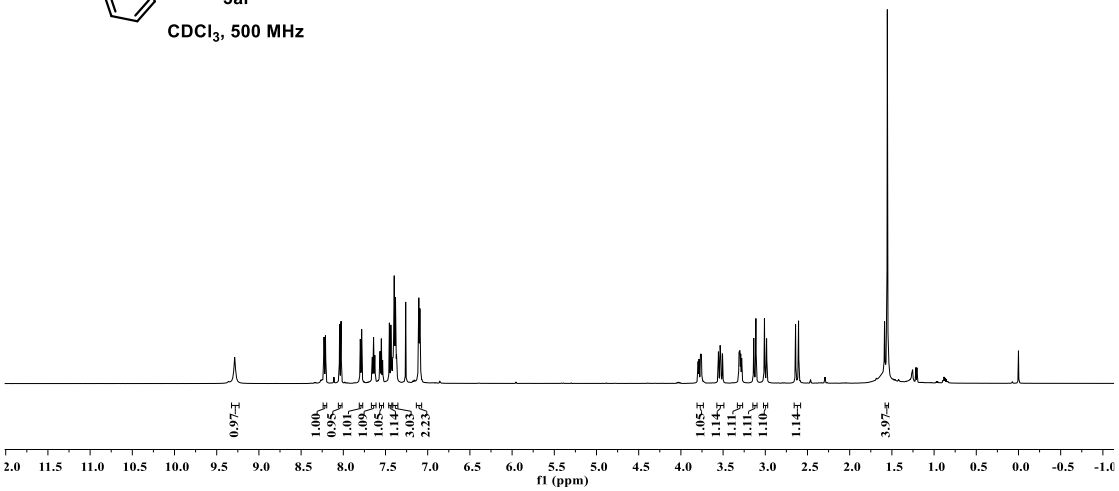

-63.8
NH
O
NC
Me
H
O
O
F3C
3ak
CDCl3, 471 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)

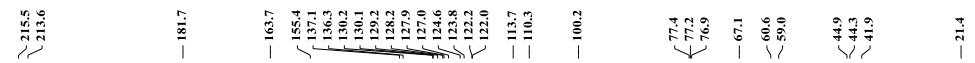


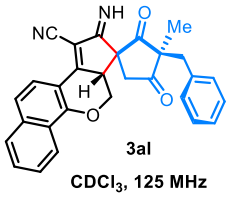


3al

$CDCl_3$, 500 MHz

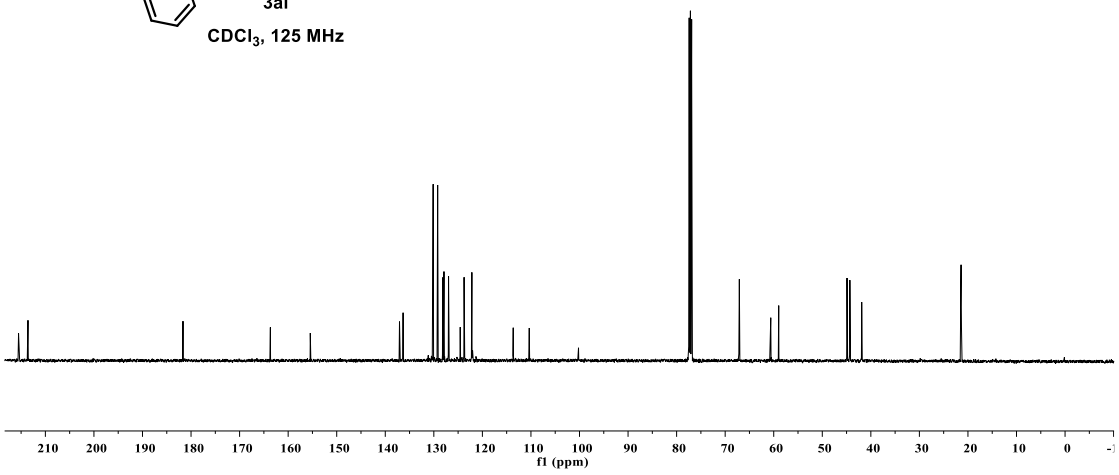


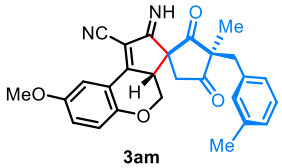




3al

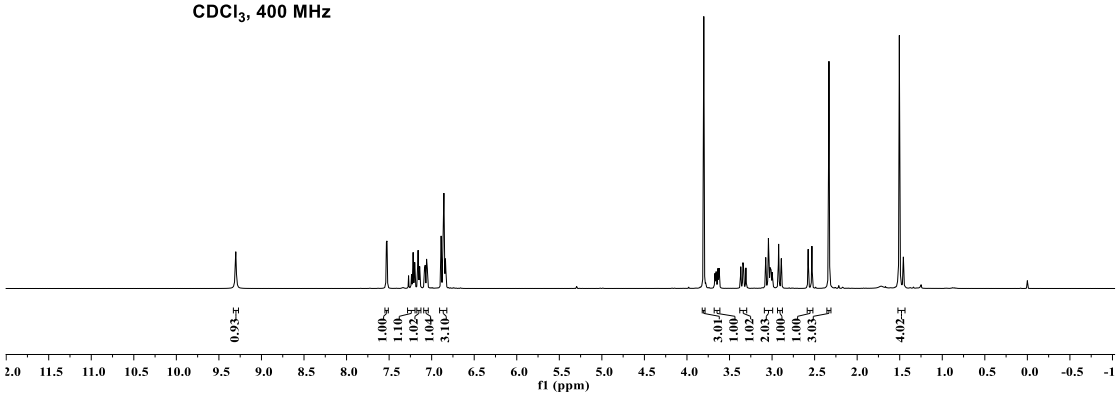
$CDCl_3$, 125 MHz

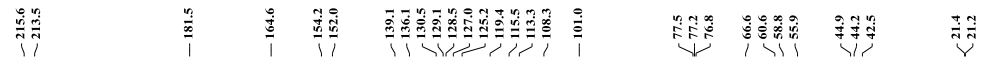


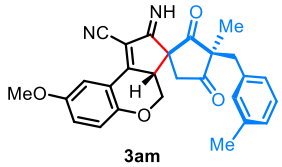


3am

$CDCl_3$, 400 MHz

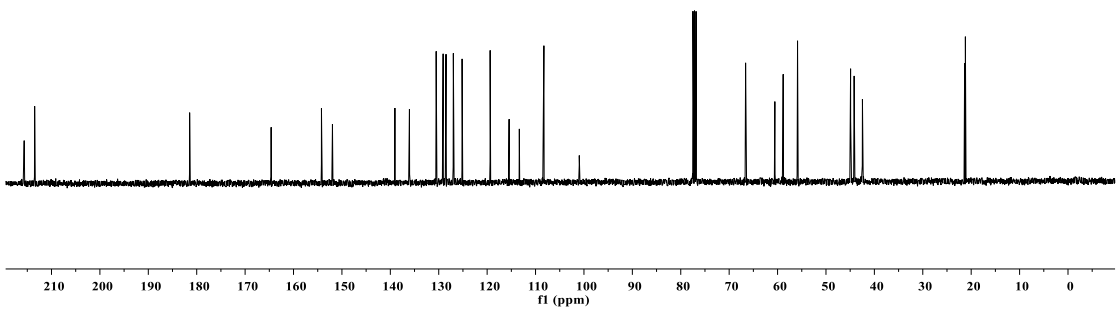


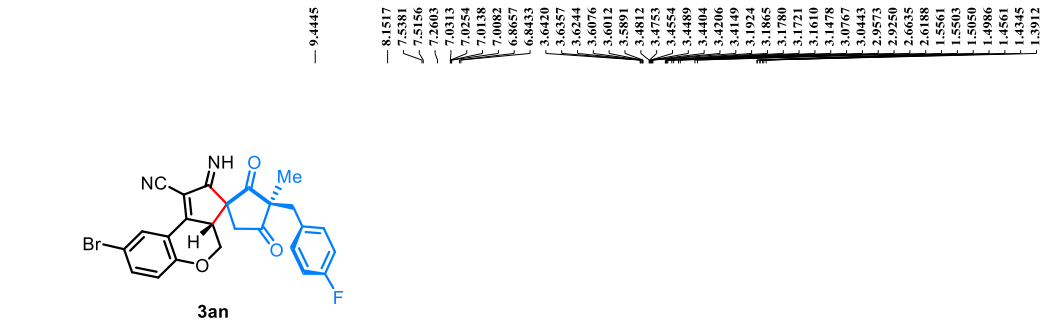




3am

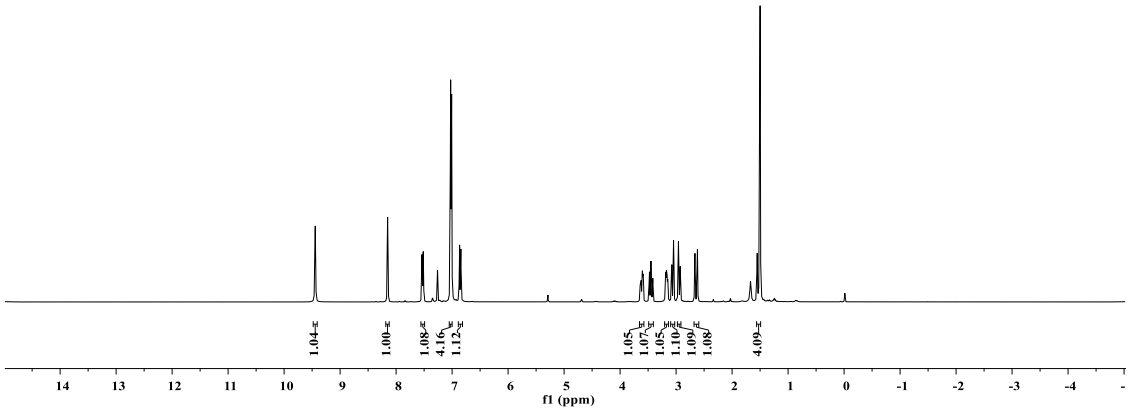
$CDCl_3$, 100 MHz

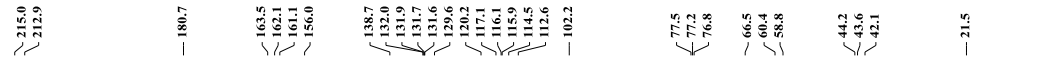


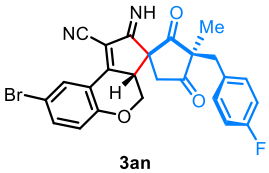


3an

$CDCl_3$, 400 MHz

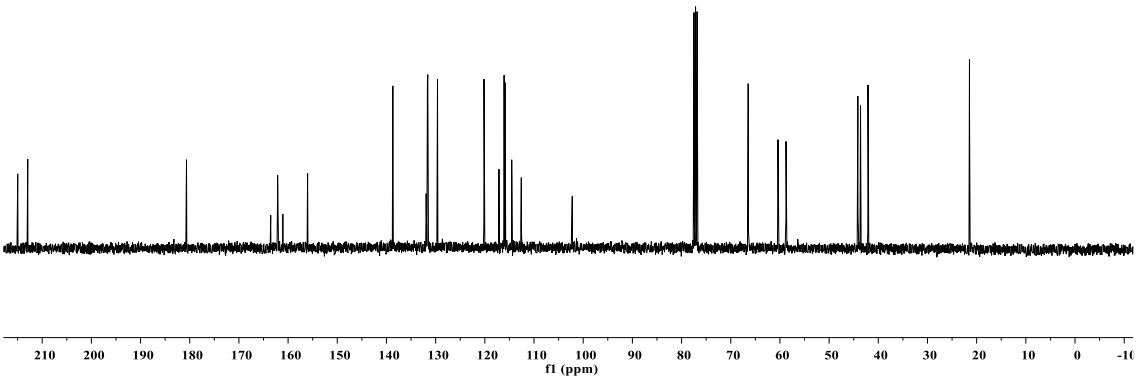


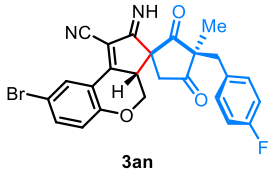




3an

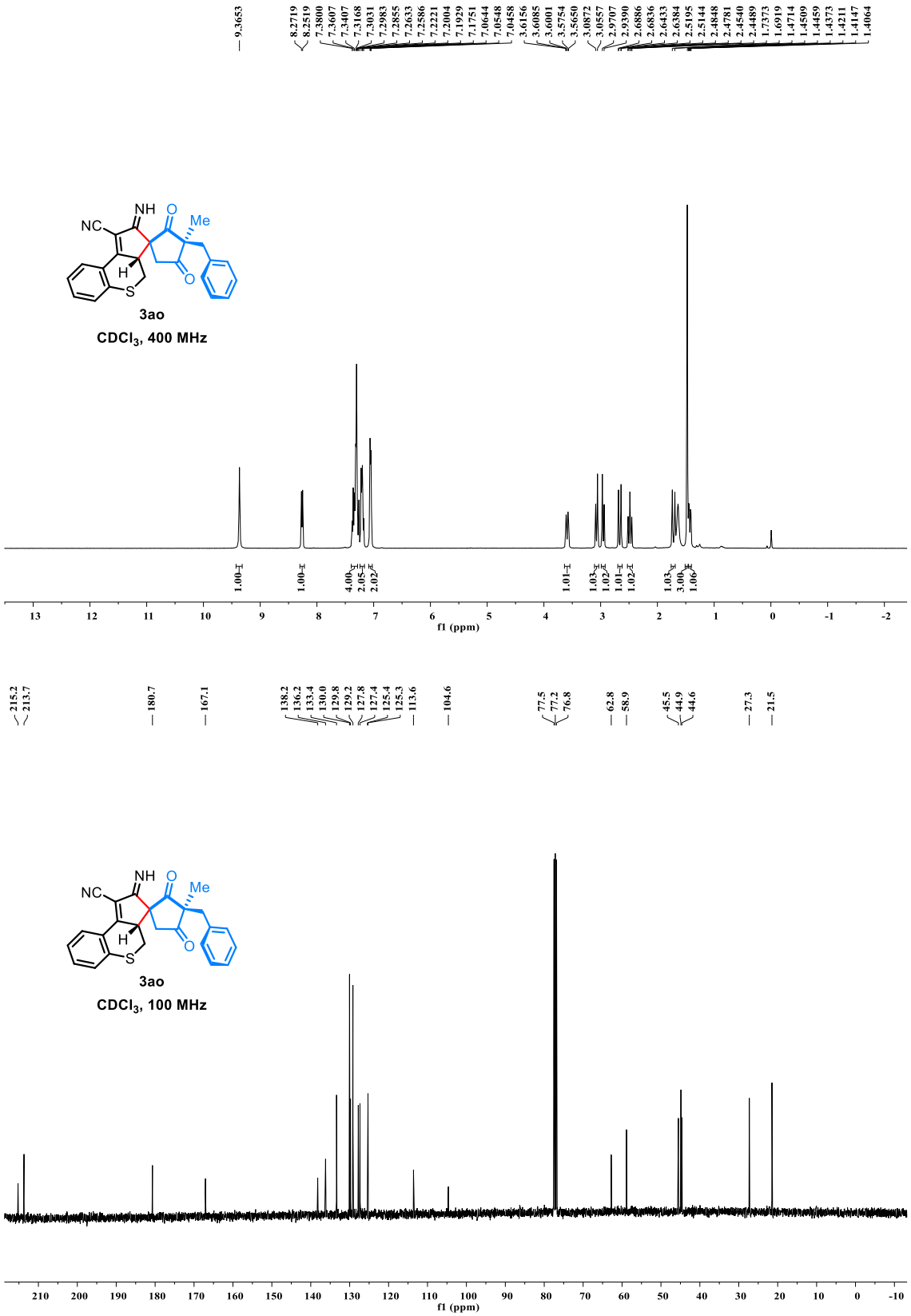
$CDCl_3$, 100 MHz

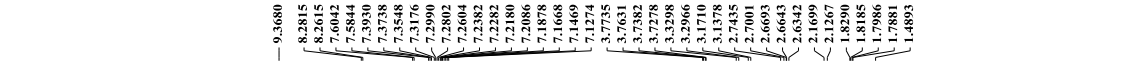


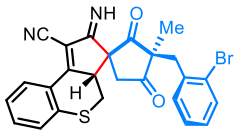


3an

$CDCl_3$, 471 MHz

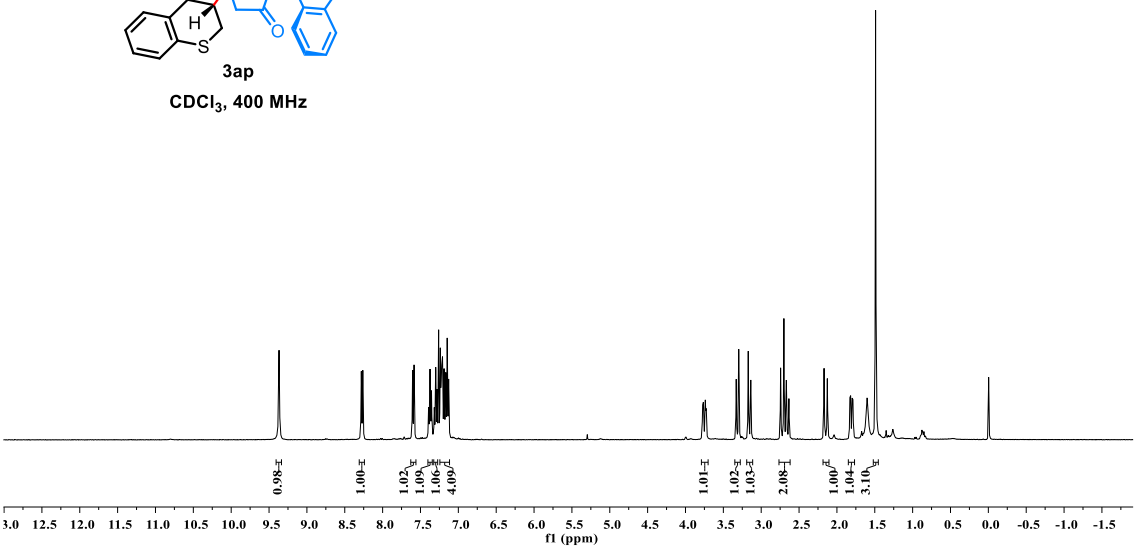

3ao
CDCl3, 400 MHz
f1 (ppm)
3ao
CDCl3, 100 MHz
f1 (ppm)

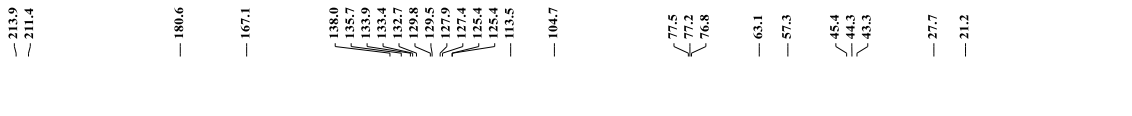


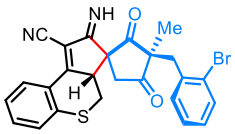


3ap

$CDCl_3$, 400 MHz

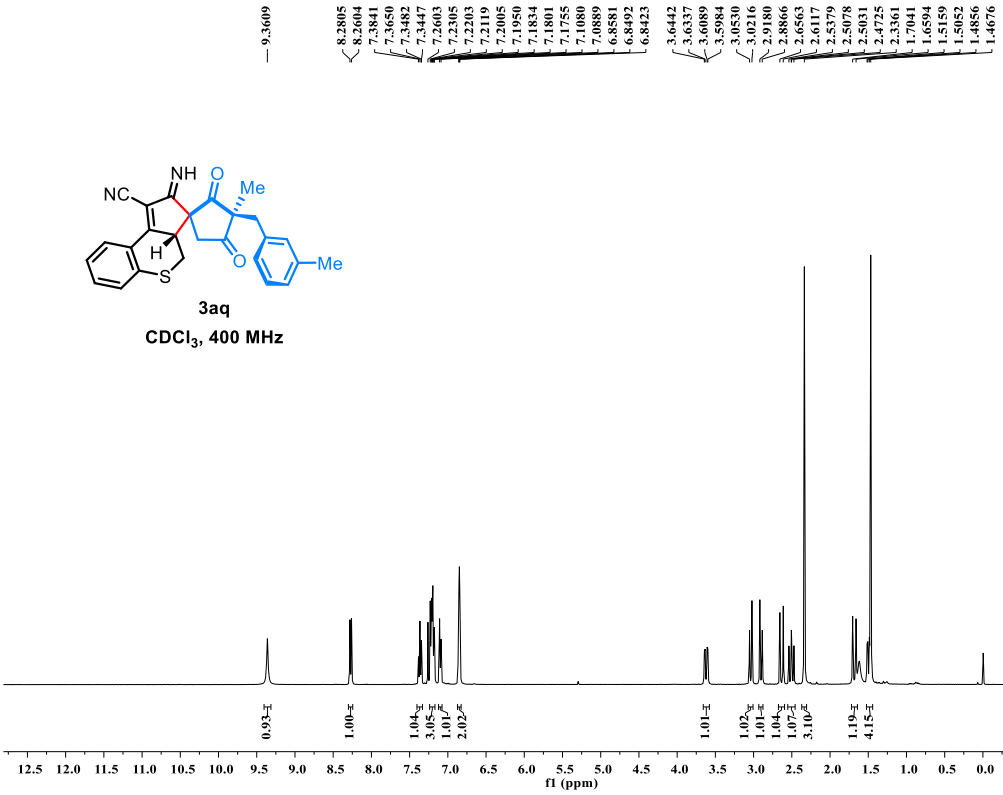


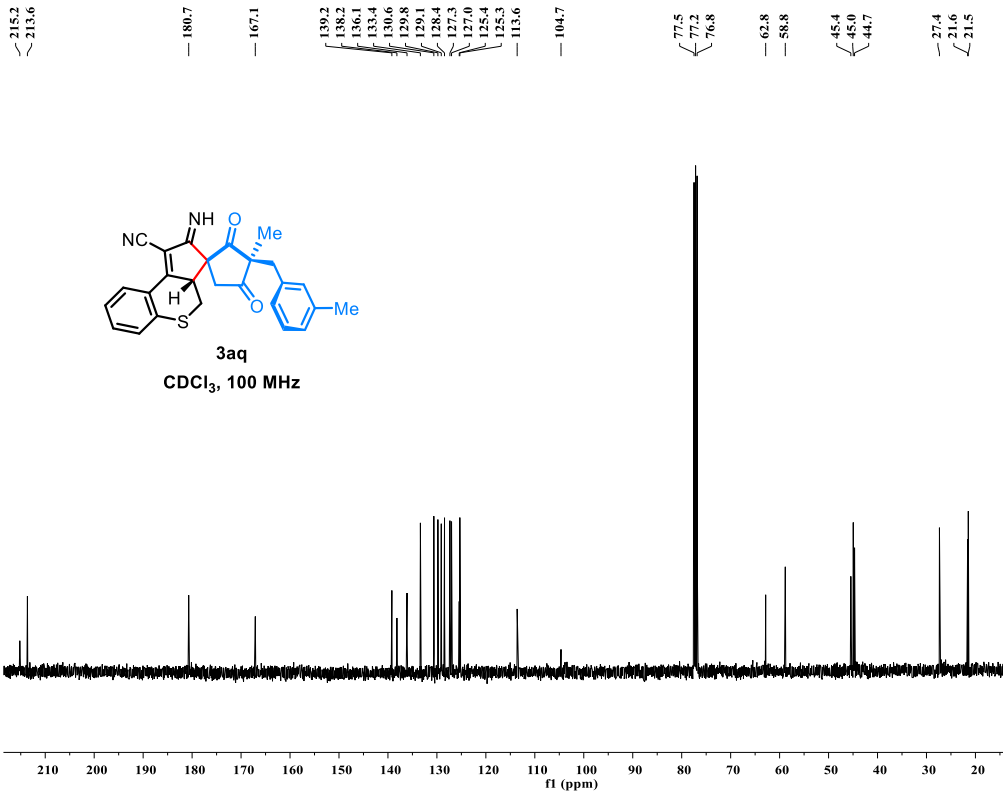


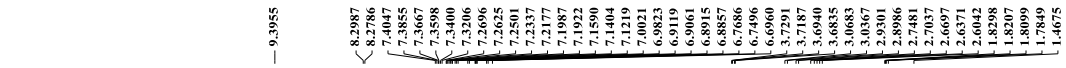


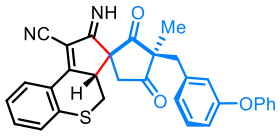
3ap

$CDCl_3$, 100 MHz


9.3609
8.2805
8.2604
7.3841
7.3650
7.3482
7.3447
7.2603
7.2305
7.2203
7.2119
7.2005
7.1950
7.1834
7.1801
7.1755
7.1080
7.0889
6.8581
6.8492
6.8423
3.6442
3.6337
3.6089
3.5984
3.0530
3.0216
2.9180
2.8866
2.6563
2.6117
2.5379
2.5078
2.5031
2.4725
2.3361
1.7041
1.6594
1.5159
1.5052
1.4856
1.4676
NH
O
Me
NC
H
S
O
Me
3aq
CDCl3, 400 MHz
0.93
1.00
1.04
3.05
1.01
2.02
1.01
1.02
1.01
1.04
1.07
3.10
1.19
4.15
f1 (ppm)

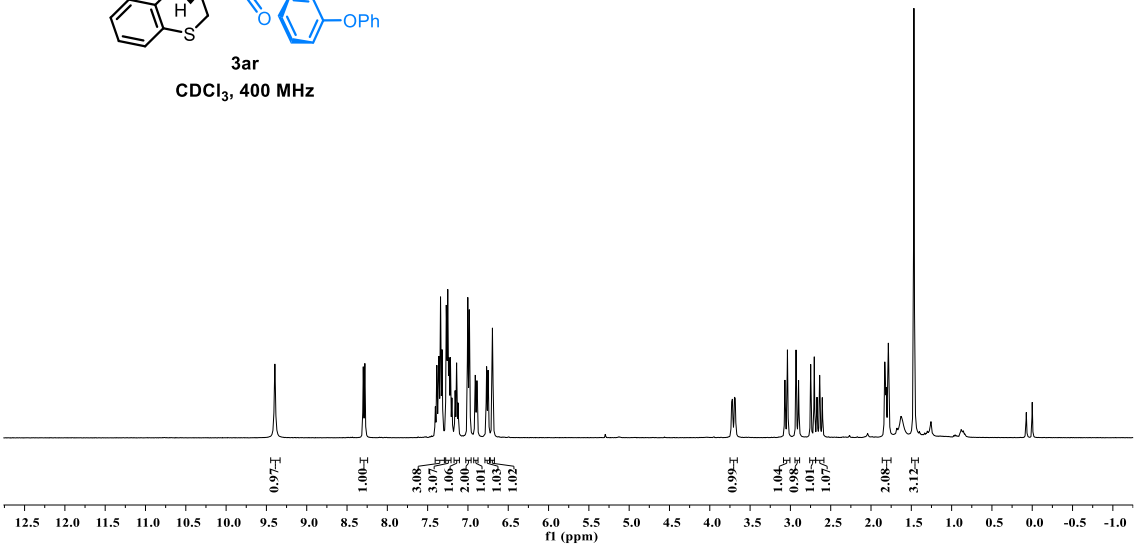

215.2
213.6
180.7
167.1
139.2
138.2
136.1
133.4
130.6
129.8
129.1
128.4
127.3
127.0
125.4
125.3
113.6
104.7
77.5
77.2
76.8
62.8
58.8
45.4
45.0
44.7
27.4
21.6
21.5
NH
O
Me
NC
H
S
O
Me
3aq
CDCl3, 100 MHz
f1 (ppm)

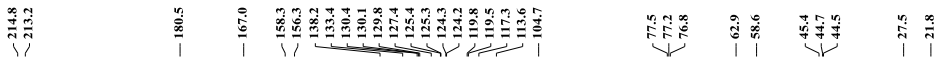


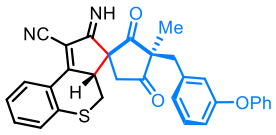


3ar

$CDCl_3$, 400 MHz

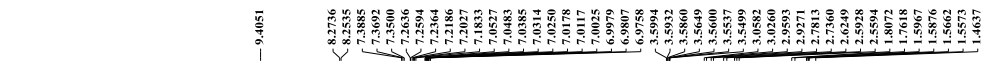


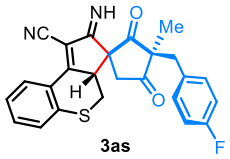




3ar

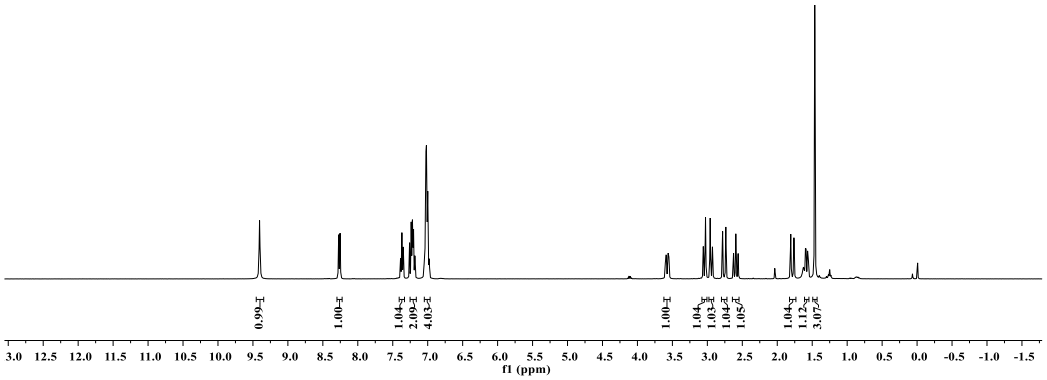
$CDCl_3$, 100 MHz

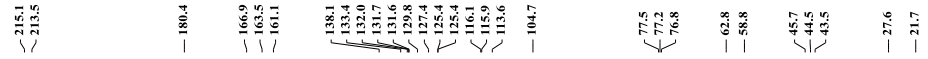


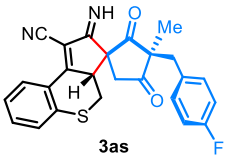


3as

$CDCl_3$, 400 MHz

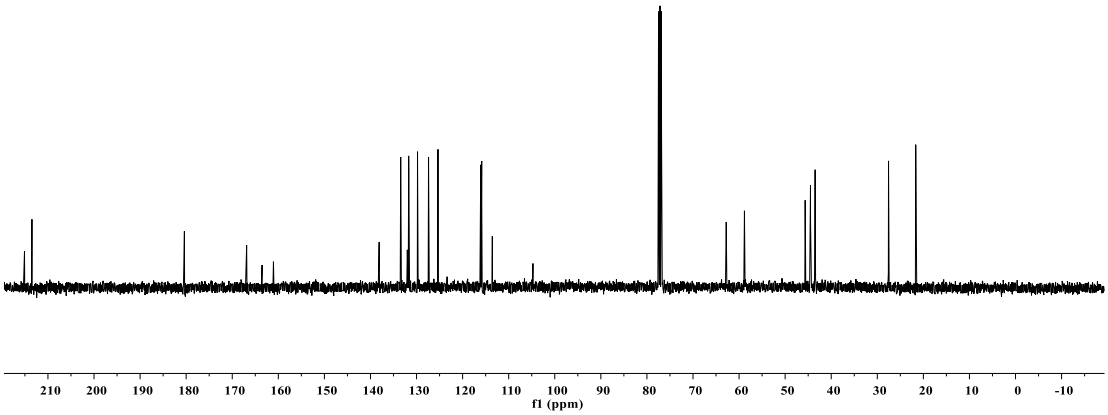


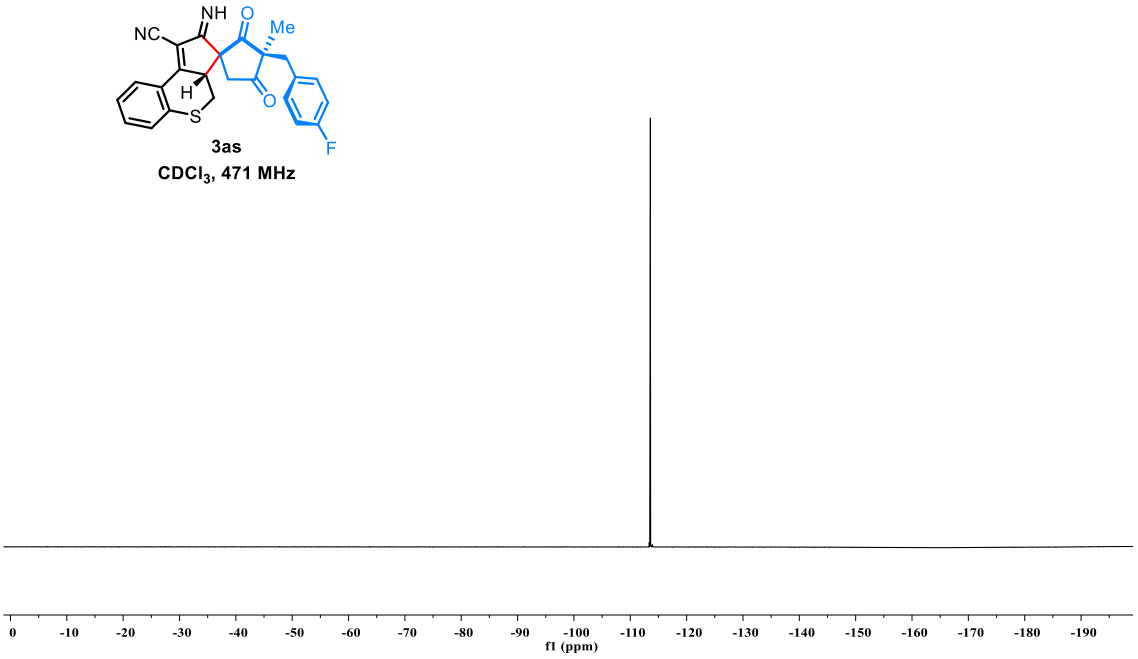


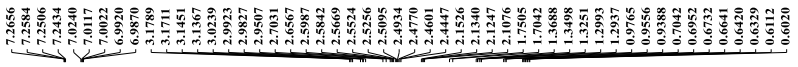


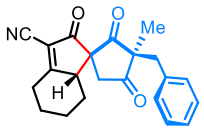
3as

$CDCl_3$, 100 MHz



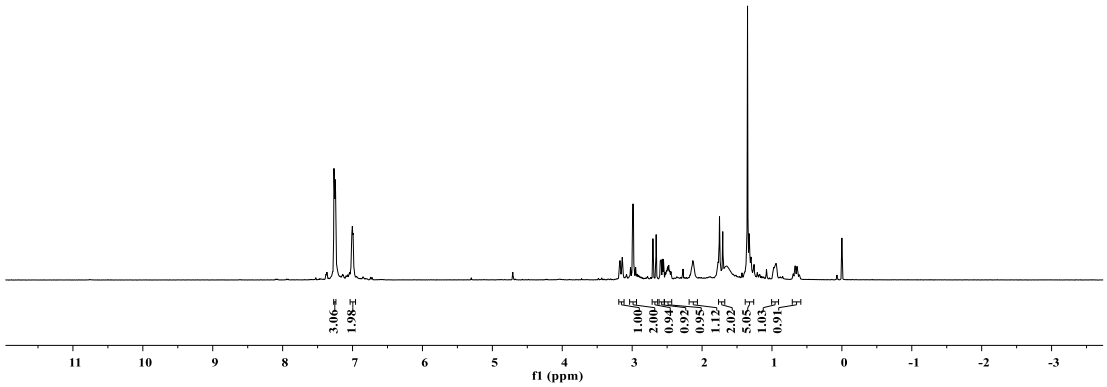

-113.6
NC
NH
O
Me
H
S
O
F
3as
CDCl3, 471 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

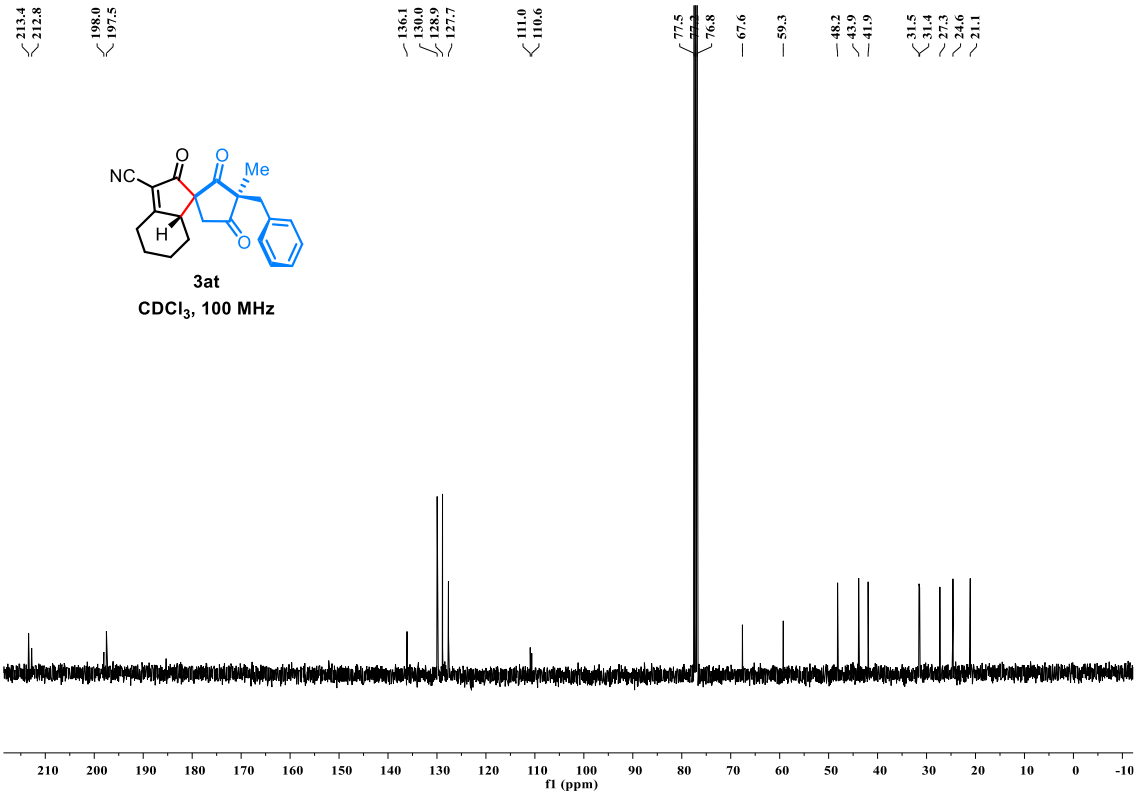




3at

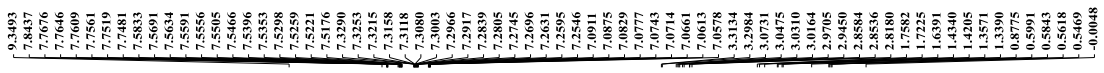
$CDCl_3$, 400 MHz

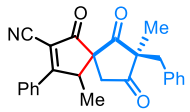




3at

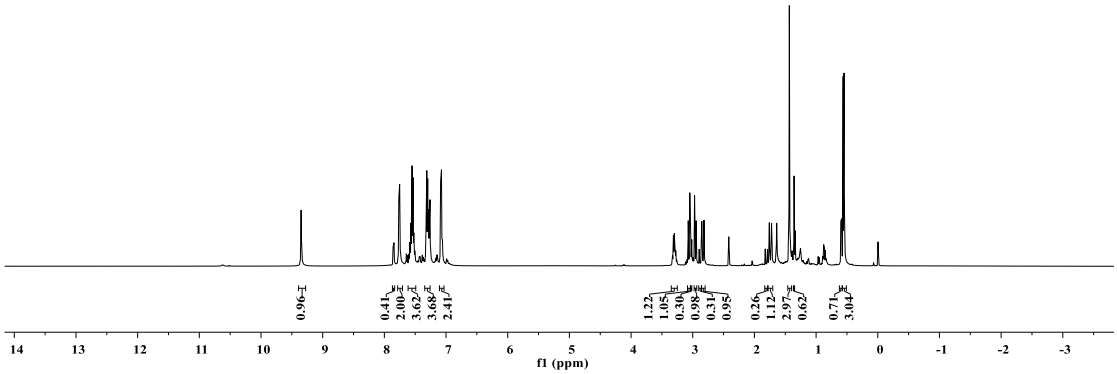
$CDCl_3$, 100 MHz

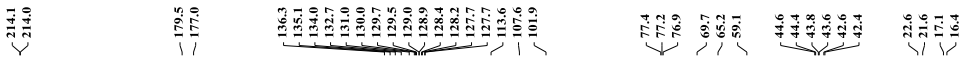


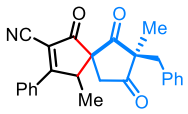


3au, 1:5 dr

$CDCl_3$, 500 MHz

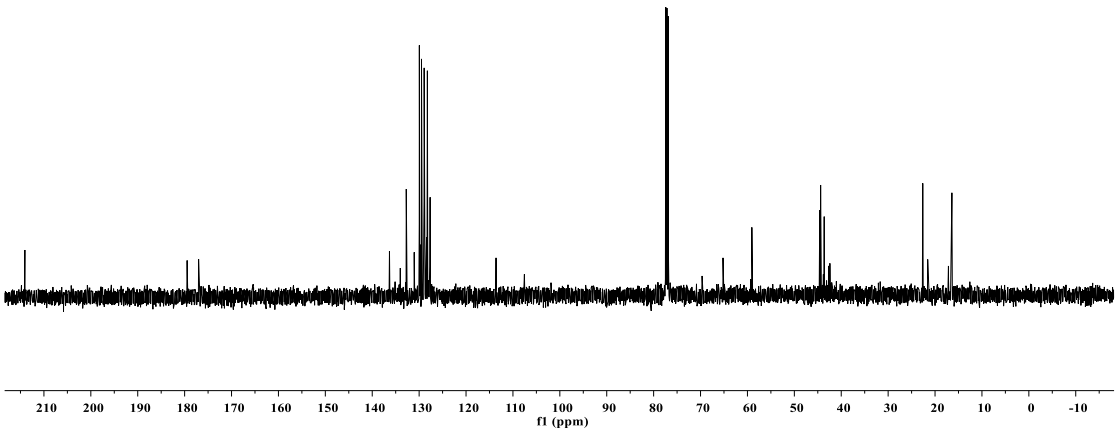


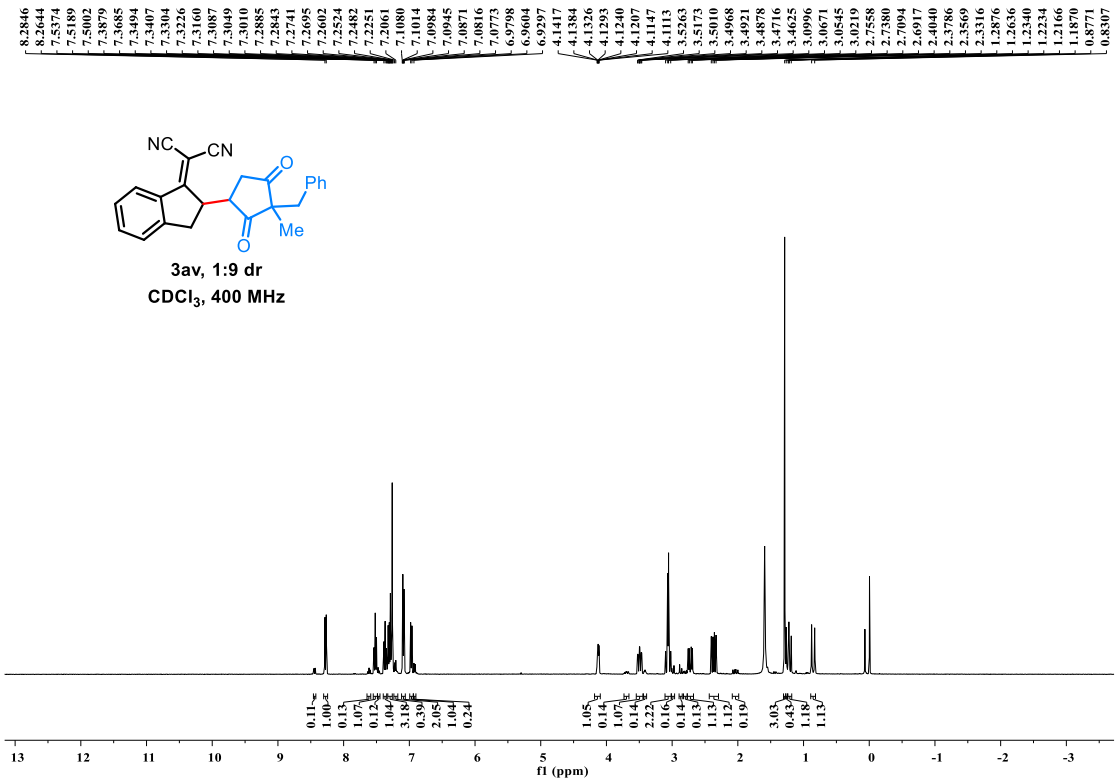


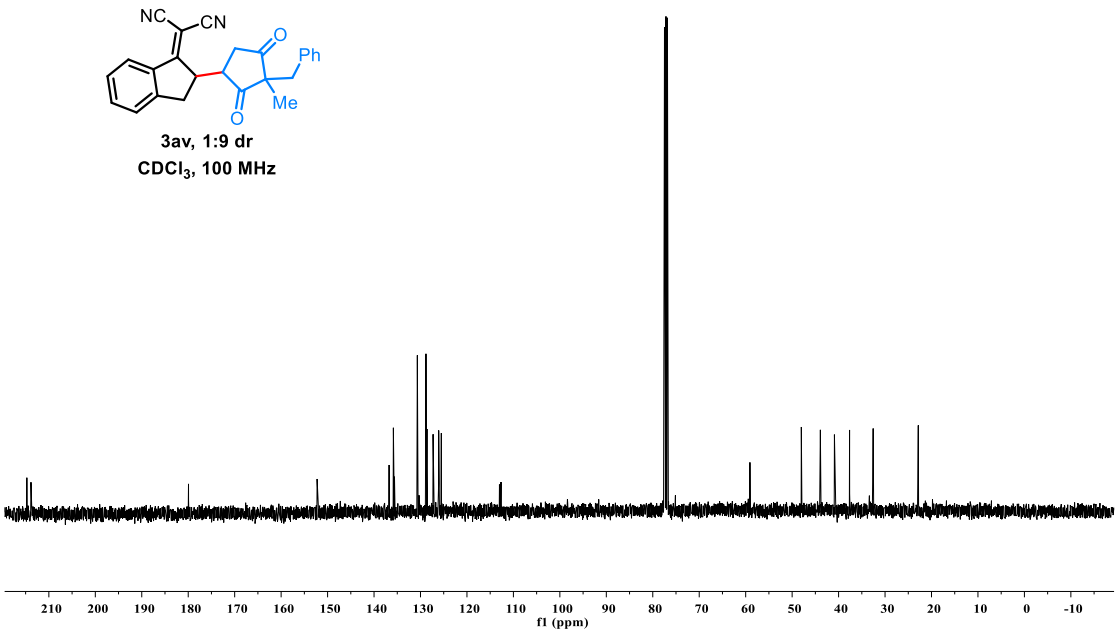


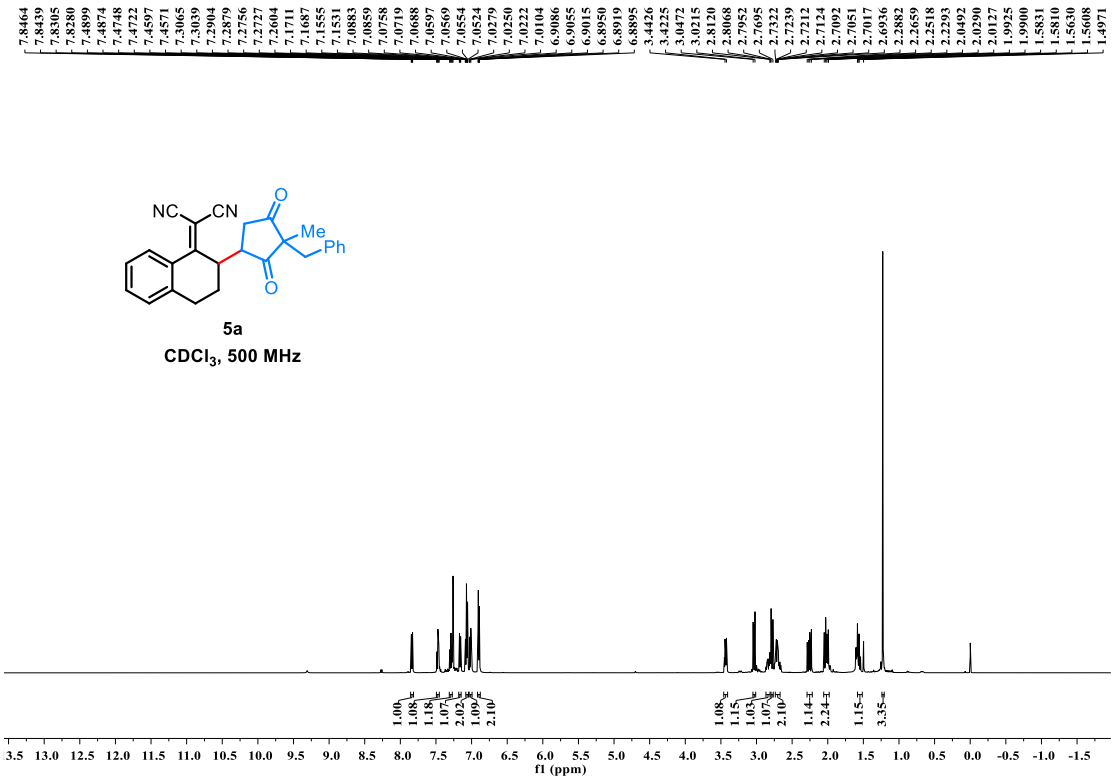
3au, 1:5 dr

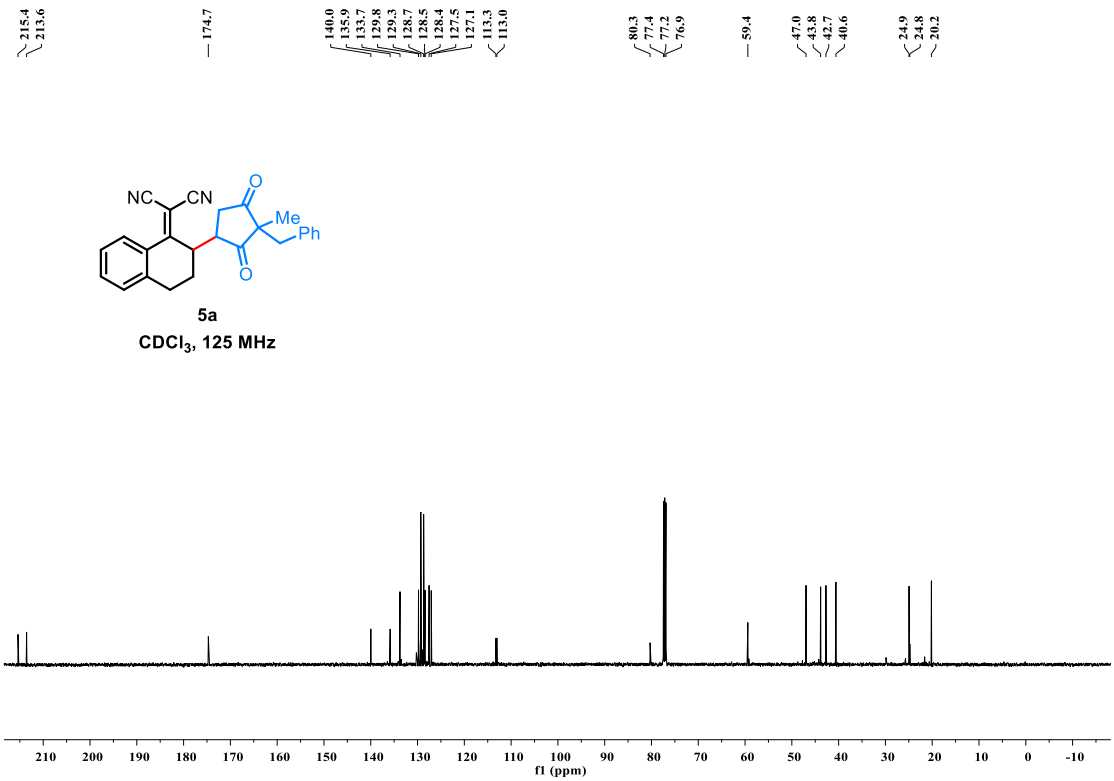
$CDCl_3$, 125 MHz

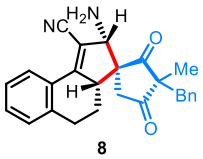



NC
CN
O
Ph
Me
O
3av, 1:9 dr
CDCl3, 400 MHz
f1 (ppm)


NC
CN
O
Ph
Me
O
3av, 1:9 dr
CDCl3, 100 MHz
f1 (ppm)

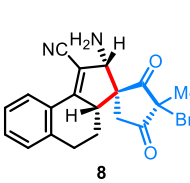

NC
CN
O
Me
Ph
O
5a
CDCl3, 500 MHz
f1 (ppm)


NC
CN
O
Me
Ph
O
5a
CDCl3, 125 MHz
f1 (ppm)



8

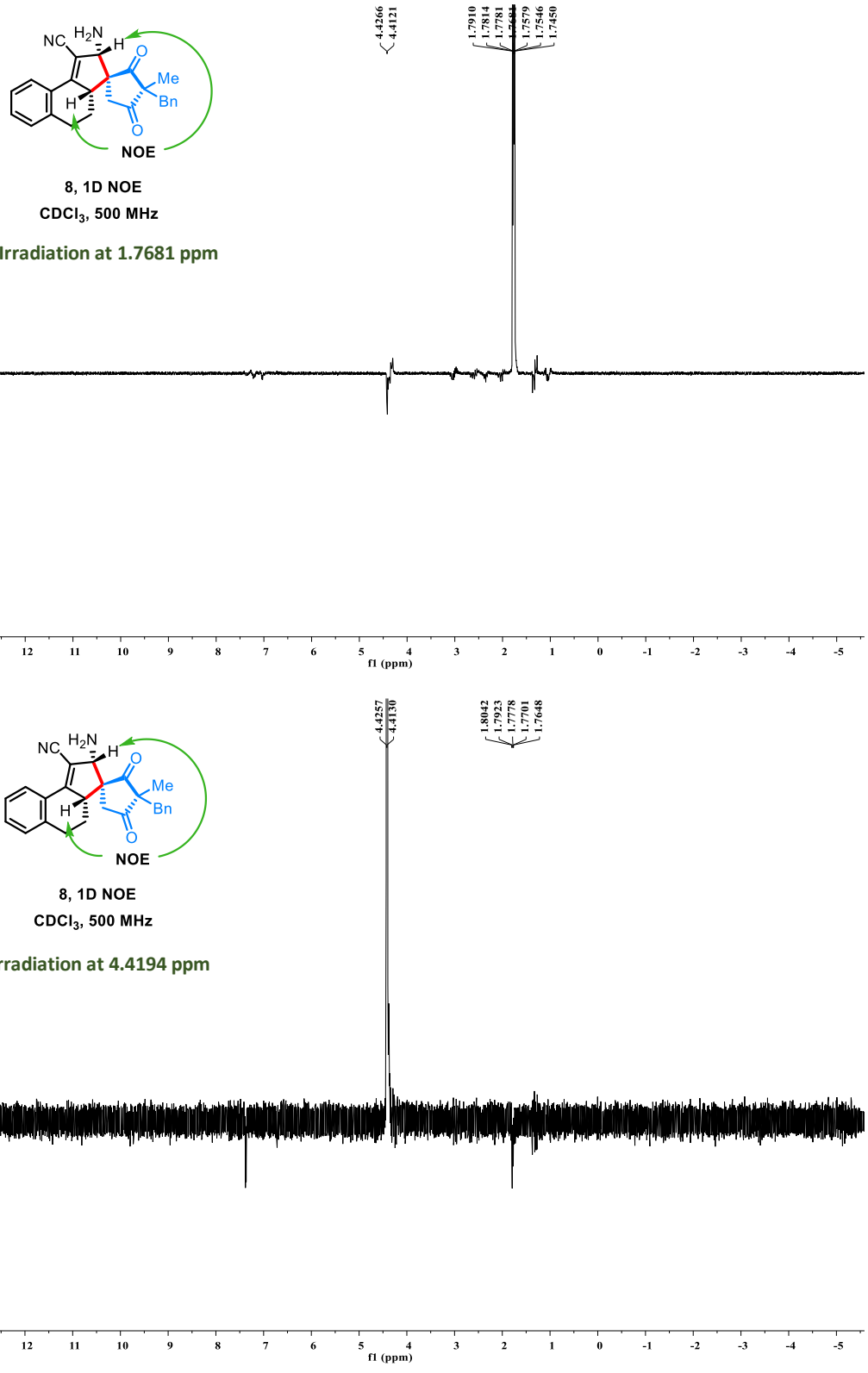
$CDCl_3$, 400 MHz



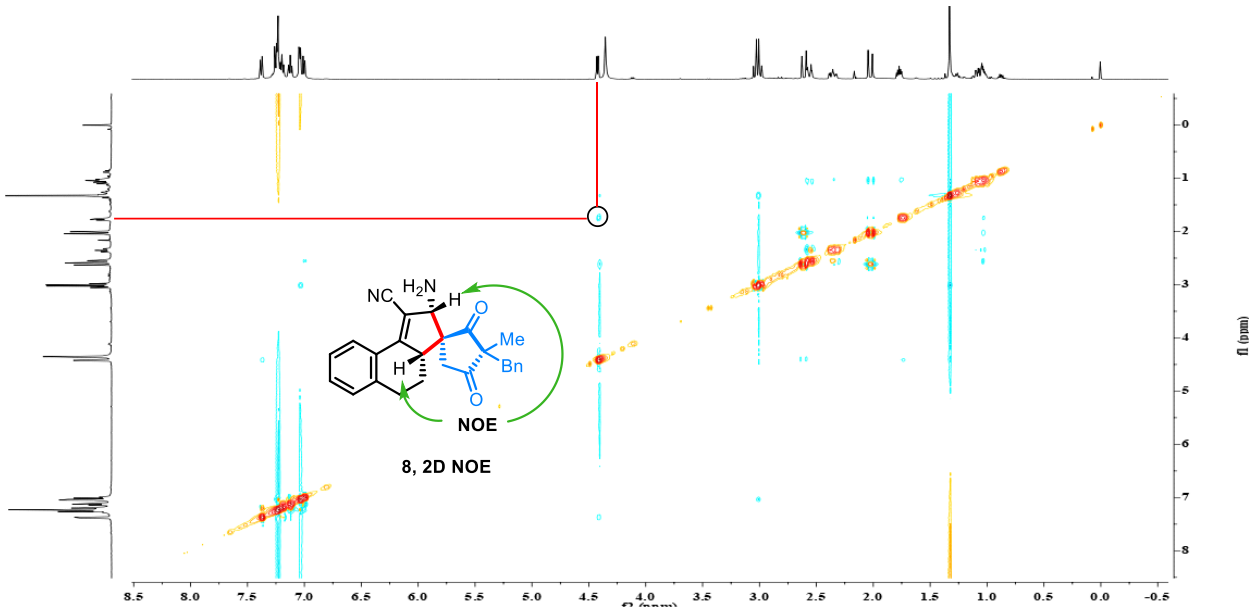
8

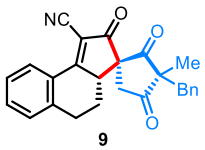
$CDCl_3$, 100 MHz

1D NOE spectra of compound **8**



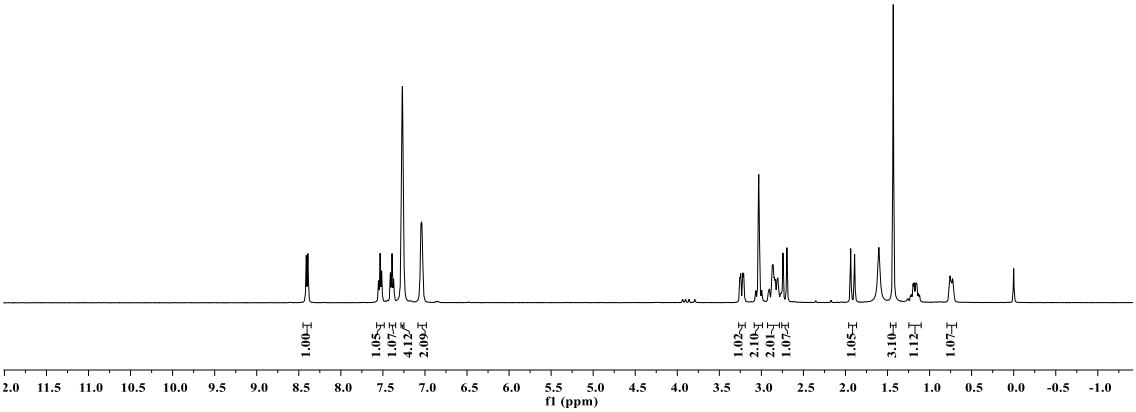
2D NOE spectrum of compound **8**

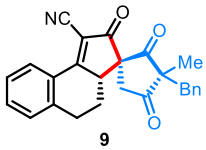




9

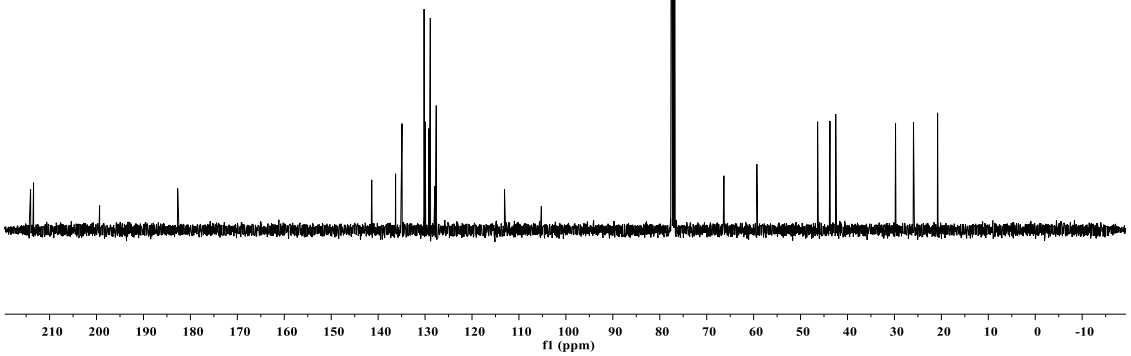
$CDCl_3$, 400 MHz

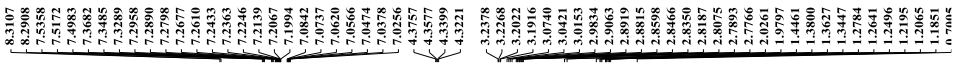


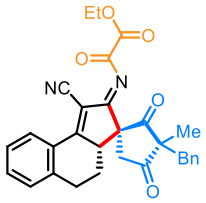


9

$CDCl_3$, 100 MHz

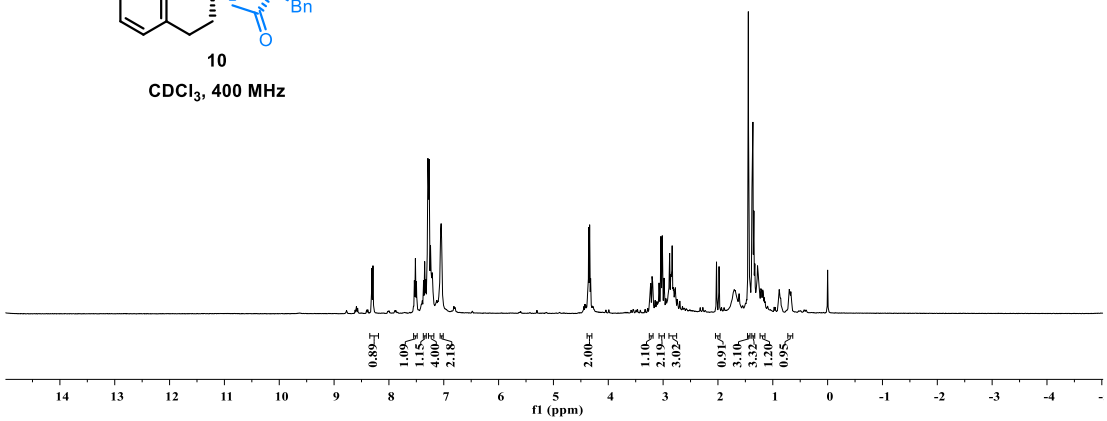


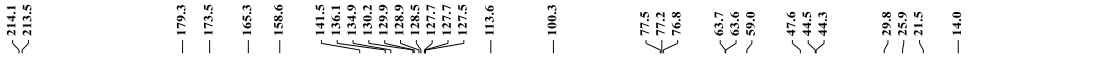


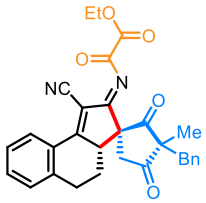


10

$CDCl_3$, 400 MHz

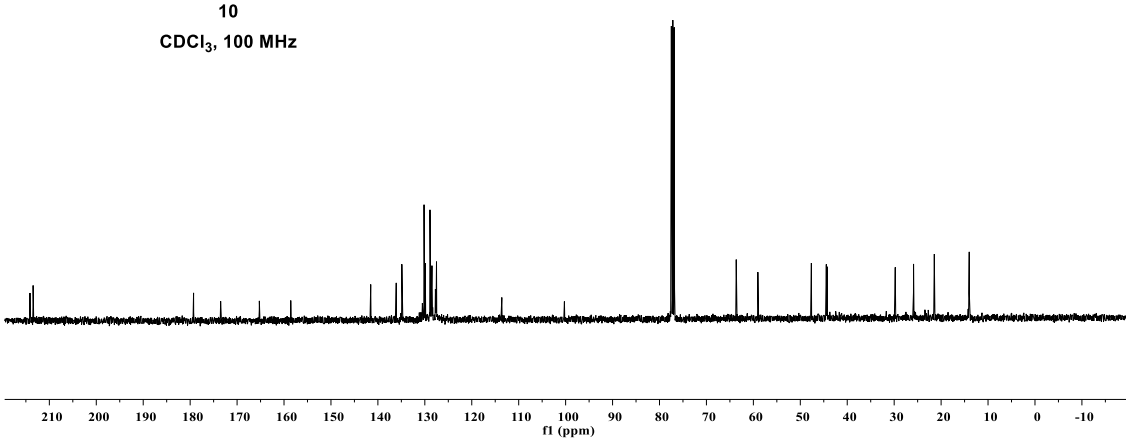


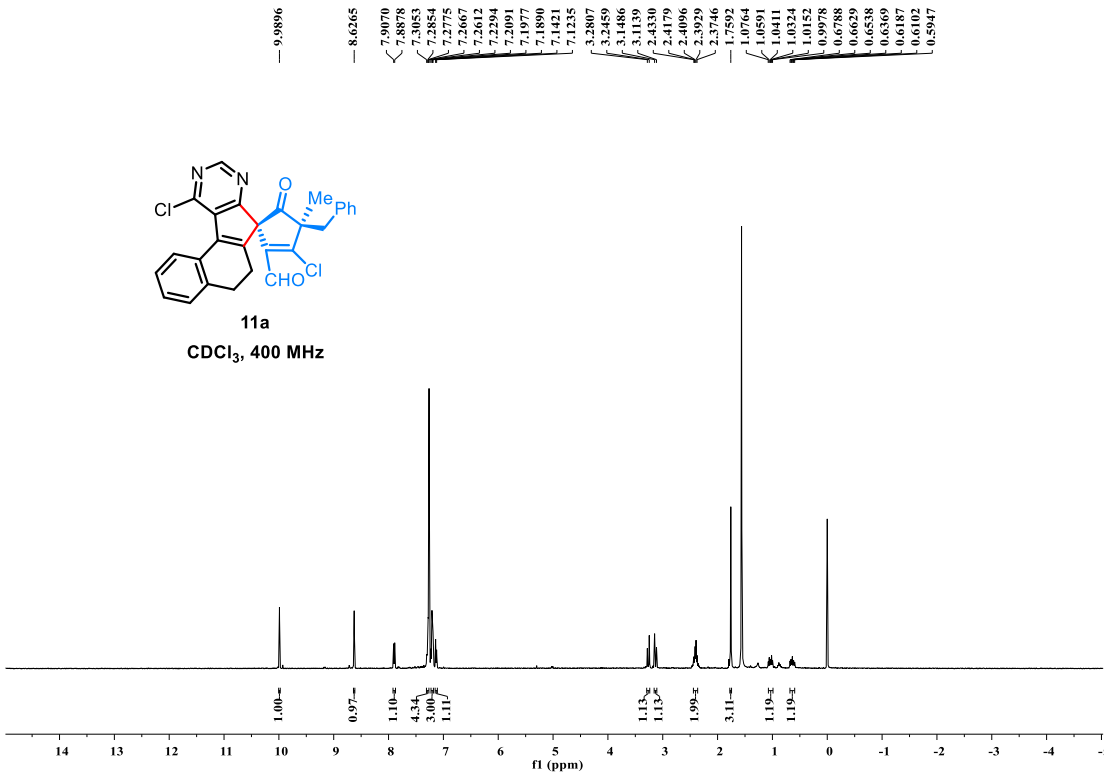


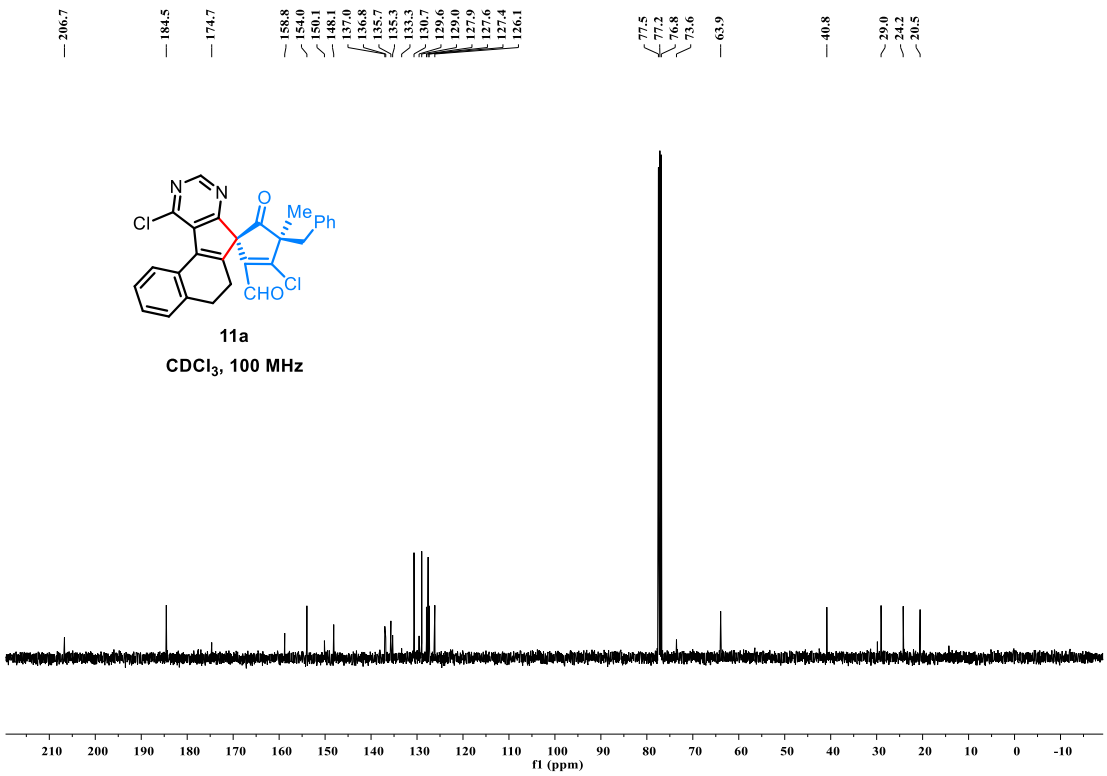


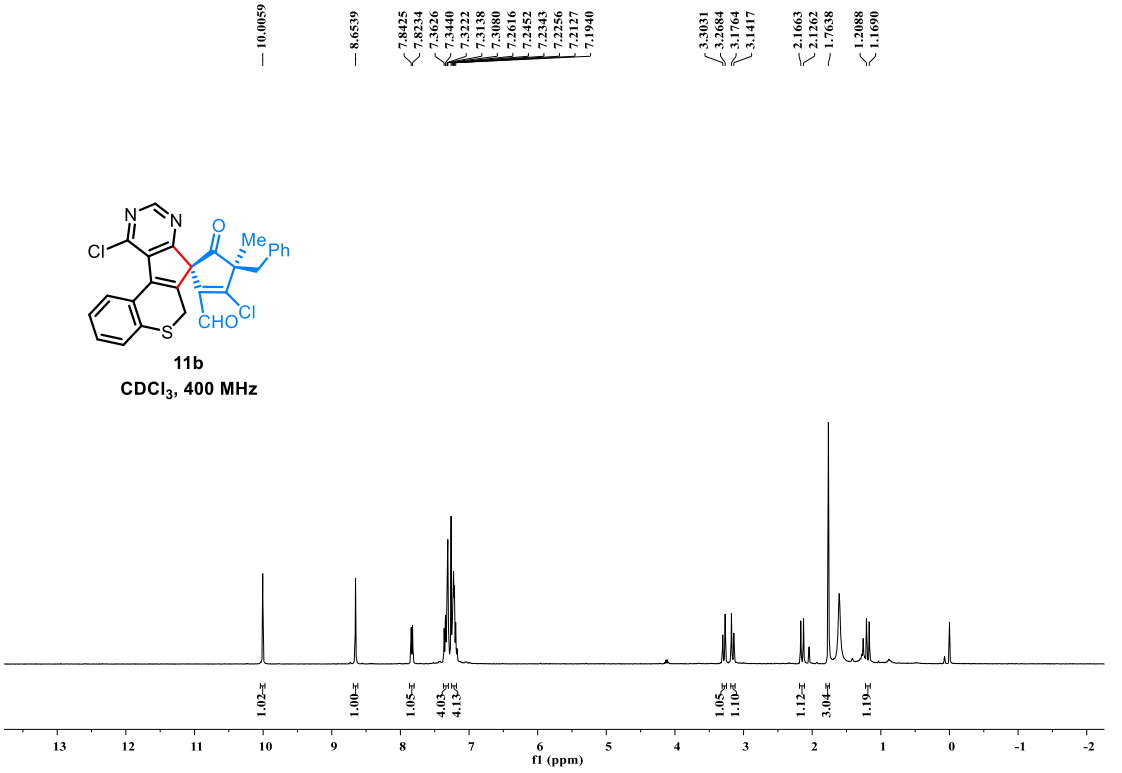
10

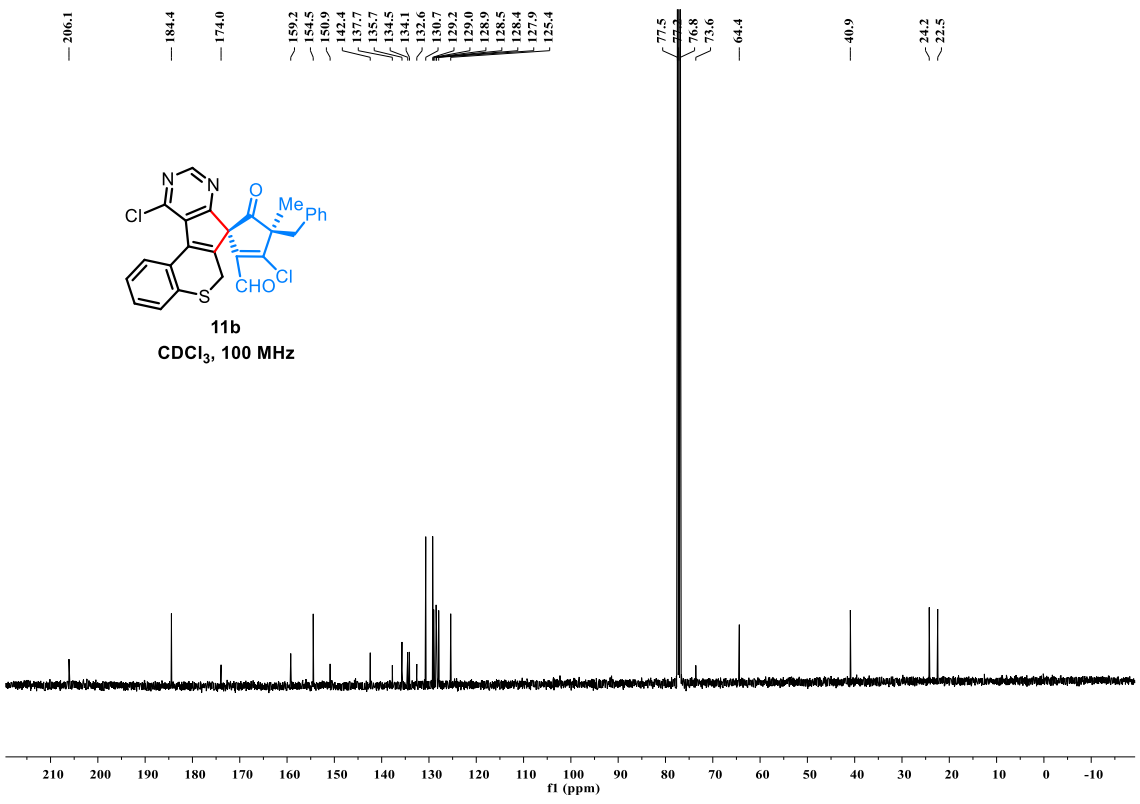
$CDCl_3$, 100 MHz




9.9896
8.6265
7.9070
7.8878
7.3053
7.2854
7.2775
7.2667
7.2612
7.2294
7.2091
7.1977
7.1890
7.1421
7.1235
3.2807
3.2459
3.1486
3.1139
2.4330
2.4179
2.4096
2.3929
2.3746
1.7592
1.0764
1.0591
1.0411
1.0324
1.0152
0.9978
0.6788
0.6629
0.6538
0.6369
0.6187
0.6102
0.5947
Cl
N
N
O
Me
Ph
CHO
Cl
11a
CDCl3, 400 MHz
1.00
0.97
1.10
4.34
3.00
1.11
1.13
1.13
1.99
3.11
1.19
1.19
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


206.7
184.5
174.7
158.8
154.0
150.1
148.1
137.0
136.8
135.7
135.3
133.3
130.7
129.6
129.0
127.9
127.6
127.4
126.1
77.5
77.2
76.8
73.6
63.9
40.8
29.0
24.2
20.5
Cl
N
N
O
Me
Ph
CHO
Cl
11a
CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


10.0059
8.6539
7.8425
7.8234
7.3626
7.3440
7.3322
7.3138
7.3080
7.2616
7.2452
7.2343
7.2256
7.2127
7.1940
3.3031
3.2684
3.1764
3.1417
2.1663
2.1262
1.7638
1.2088
1.1690
Cl
N
N
O
Me
Ph
CHO
Cl
S
11b
CDCl3, 400 MHz
1.02
1.00
1.05
4.03
4.13
1.05
1.10
1.12
3.04
1.19
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)


206.1
184.4
174.0
159.2
154.5
150.9
142.4
137.7
135.7
134.5
134.1
132.6
130.7
129.2
129.0
128.9
128.5
128.4
127.9
125.4
77.5
76.8
73.6
64.4
40.9
24.2
22.5
Cl
N
N
O
Me
Ph
CHO
Cl
S
11b
CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)