Supporting Information

Copper-Catalyzed Difluoromethylation of Propargylamide-Substituted Indoles: Synthesis of mono- and bis-Difluoromethylated Indoloazepinones Derivatives

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1. General Remarks

Column chromatography was carried out on silica gel and analytical TLC was performed with silica gel GF254 plates. NMR spectra were recorded on a Bruker advance Ⅲ 400 spectrometer in $CDCl_3$ at 400 MHz (1H NMR), 100 MHz (^{13}C NMR), 376 MHz (^{19}F NMR). Data collections for crystal structure were performed at room temperature (293 K) using MoKα radiation on a Bruker APEXII diffractometer. High-resolution massspectral analysis (HRMS) data were measured on a Bruker Apex II. All difluoromethylated products were further characterized by high resolution mass spectra (HRMS). Commercially available reagents and solvents were used without further purification.

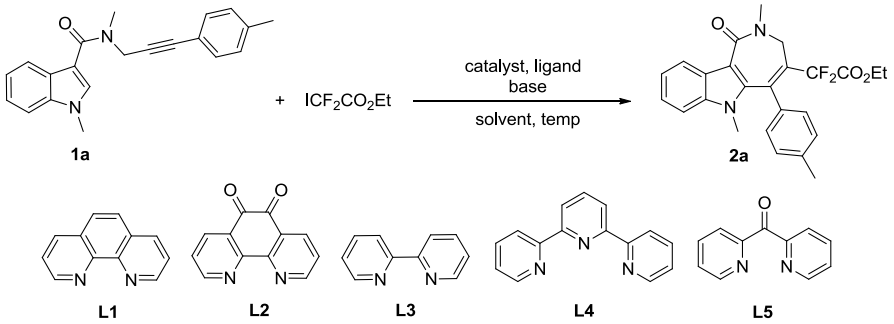
2. General Experimental Procedure for Synthesis of Product 2 or 6

In a dried tube, substrates **1(5)** (0.2 mmol), CuCl (10 mol %, 2.0 mg), 1,10-Phen (20 mol %, 7.2 mg), and Cs_2CO_3(0.5 mmol, 163.0 mg) was added, The tube was evacuated and back filled with argon (repeated three times). Anhydrous DCE (2 mL) and ethyl difluoroiodoacetate (0.5 mmol, 63.9 uL) was added, the mixture was stirred at 60 ℃ for 48 h. The resulting reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, appropriate mixture of petroleum ether/ethyl acetate) to afford **2(6)**.

3. General Experimental Procedure for Synthesis of Product 3 and 4

In a dried tube, corresponding substrates **2** (0.1 mmol), CuCl (10 mol %, 1.0 mg), 1,10-Phen (20 mol %, 3.6 mg), and Cs_2CO_3(0.25 mmol, 81.5 mg) was added, The tube was evacuated and back filled with argon (repeated three times). Anhydrous DCE (1 mL) and ethyl difluoroiodoacetate (0.8 mmol, 102.3 uL) was added, the mixture was stirred at 60 ℃ for 72 h. The resulting reaction mixture was concentrated in vacuo and the residue was purified by column chromatography (silica gel, appropriate mixture of petroleum ether/ethyl acetate) to afford **3** and **4**.

4. Optimization of the Reaction Conditions[a]

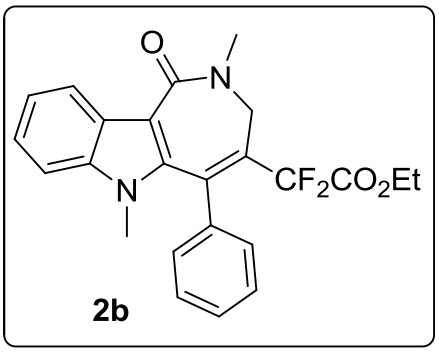


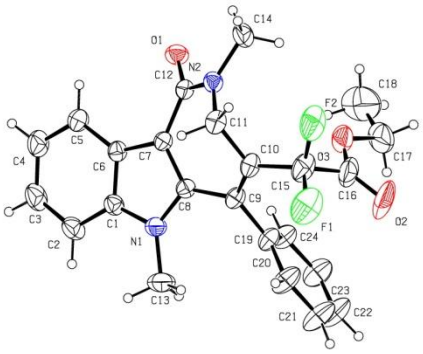
entry	cat. (mol %)	ligand	base (equiv)	solvent	yield[b] (%)
1	$CuCl_2$ (10)	**L1**	K_2CO_3 (2.0)	MeCN	27
2	$CuCl_2$ (10)	**L1**	Na_2CO_3 (2.0)	MeCN	trace
3	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	MeCN	42
4	$CuCl_2$ (10)	**L1**	C_SOAc (2.0)	MeCN	33
5	$CuCl_2$ (10)	**L1**	CsF (2.0)	MeCN	trace
6	$CuCl_2$ (10)	**L1**	$KHCO_3$ (2.0)	MeCN	trace

7	$CuCl_2$ (10)	**L1**	KOH (2.0)	MeCN	trace
8	$CuCl_2$ (10)	**L1**	*t*-BuONa (2.0)	MeCN	0
9	$CuCl_2$ (10)	**L1**	K_3PO_4 (2.0)	MeCN	trace
10	$CuCl_2$ (10)	**L2**	Cs_2CO_3 (2.0)	MeCN	37
11	$CuCl_2$ (10)	**L3**	Cs_2CO_3 (2.0)	MeCN	12
12	$CuCl_2$ (10)	**L4**	Cs_2CO_3 (2.0)	MeCN	30
13	$CuCl_2$ (10)	**L5**	Cs_2CO_3 (2.0)	MeCN	11
14	$CuCl_2$ (10)	DBU	Cs_2CO_3 (2.0)	MeCN	7
15	$CuCl_2$ (10)	NEt_3	Cs_2CO_3 (2.0)	MeCN	trace
16	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	THF	27
17	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	acetone	38
18	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	DMF	trace
19	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	toluene	trace
20	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	NMP	8
21	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	CH_3NO_2	trace
22	$CuCl_2$ (10)	**L1**	Cs_2CO_3 (2.0)	DCE	51
23	CuBr (10)	**L1**	Cs_2CO_3 (2.0)	DCE	56
24	CuI (10)	**L1**	Cs_2CO_3 (2.0)	DCE	50
25	$CuBr_2$ (10)	**L1**	Cs_2CO_3 (2.0)	DCE	47
26	$Cu(OTf)_2$ (10)	**L1**	Cs_2CO_3 (2.0)	DCE	33
27	$Cu(PPh_3)_3Br$ (10)	**L1**	Cs_2CO_3 (2.0)	DCE	27
28	CuCl (10)	**L1**	Cs_2CO_3 (2.0)	DCE	58
29	CuCl (5)	**L1**	Cs_2CO_3 (2.0)	DCE	46
30	CuCl (20)	**L1**	Cs_2CO_3 (2.0)	DCE	54
32	CuCl (10)	**L1**	Cs_2CO_3 (2.5)	DCE	62
33	CuCl (10)	**L1**	Cs_2CO_3 (3.0)	DCE	51
35[c]	**CuCl (10)**	**L1**	**Cs_2CO_3 (2.5)**	**DCE**	**68**
36[d]	CuCl (10)	**L1**	Cs_2CO_3 (2.5)	DCE	61
37[c,e]	—	**L1**	Cs_2CO_3 (2.5)	DCE	trace
38[c,f]	CuCl (10)	**L1**	—	DCE	0

[a]Reaction conditions: **1a** (0.2 mmol), ethyl difluoroiodoacetate (0.4 mmol), catalyst, ligand and base in anhydrous solvent (2 mL) with stirring at 60 ℃ under argon for 48 h. [b]Isolated yield. [c]ICF_2CO_2Et (0.5 mmol), [d]ICF_2CO_2Et (0.6 mmol), [e]Without copper catalyst. [f]Without base.

5. Crystallographic data of 2b, 3a and 4f





Bond precision: C-C = 0.0030 A Wavelength=1.54184

Cell: a=12.2175(2) b=15.8782(3) c=22.0697(4)
alpha=90 beta=90 gamma=90
Temperature: 291 K

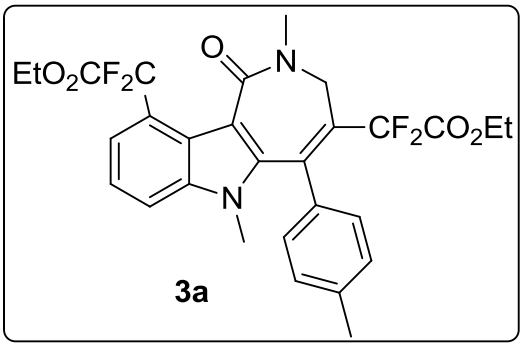
	Calculated	Reported
Volume	4281.34(13)	4281.35(12)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C24 H22 F2 N2 O3	C24 H22 F2 N2 O3
Sum formula	C24 H22 F2 N2 O3	C24 H22 F2 N2 O3
Mr	424.44	424.44
Dx,g cm-3	1.317	1.317
Z	8	8
Mu (mm-1)	0.827	0.827
F000	1776.0	1776.0
F000'	1782.05	
h,k,lmax	14,19,26	14,19,26
Nref	4041	3993
Tmin,Tmax	0.773,0.813	0.873,1.000
Tmin'	0.767	

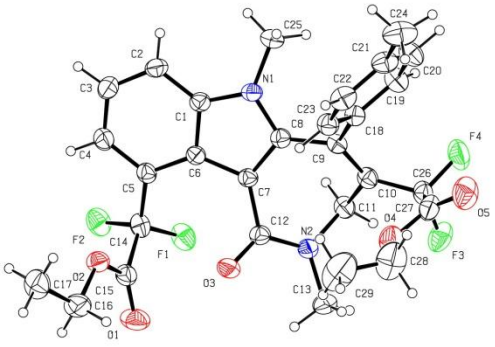
Correction method= # Reported T Limits: Tmin=0.873 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.988 Theta(max)= 69.710

R(reflections)= 0.0485(3110) wR2(reflections)= 0.1408(3993)

S = 1.026 Npar= 283





Bond precision: C-C = 0.0044 A Wavelength=0.71073

Cell: a=12.4966(6) b=9.7777(4) c=22.6334(12)
alpha=90 beta=100.263(4) gamma=90
Temperature: 291 K

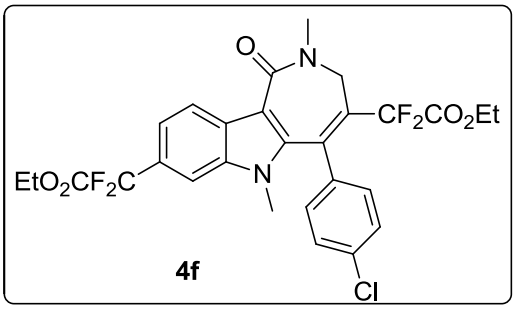
	Calculated	Reported
Volume	2721.3(2)	2721.3(2)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C29 H28 F4 N2 O5	C29 H28 F4 N2 O5
Sum formula	C29 H28 F4 N2 O5	C29 H28 F4 N2 O5
Mr	560.53	560.53
Dx,g cm-3	1.368	1.368
Z	4	4
Mu (mm-1)	0.112	0.112
F000	1168.0	1168.0
F000'	1168.75	
h,k,lmax	15,12,27	15,12,27
Nref	5358	5349
Tmin,Tmax	0.981,0.984	0.810,1.000
Tmin'	0.981	

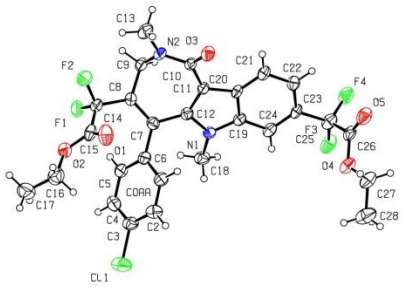
Correction method= # Reported T Limits: Tmin=0.810 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 26.020

R(reflections)= 0.0573(3083) wR2(reflections)= 0.1605(5349)

S = 1.027 Npar= 366





Bond precision: C-C = 0.0072 A Wavelength=0.71073

Cell:	a=12.8985(11)	b=14.8772(11)	c=27.961(3)
	alpha=90	beta=97.992(8)	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	5313.4(8)	5313.5(8)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C28 H25 Cl F4 N2 O5	C28 H25 Cl F4 N2 O5
Sum formula	C28 H25 Cl F4 N2 O5	C28 H25 Cl F4 N2 O5
Mr	580.95	580.95
Dx,g cm-3	1.452	1.452
Z	8	8
Mu (mm-1)	0.214	0.214
F000	2400.0	2400.0
F000'	2402.68	
h,k,lmax	15,18,34	15,18,34
Nref	10463	10440
Tmin,Tmax	0.957,0.970	0.470,1.000
Tmin'	0.950	

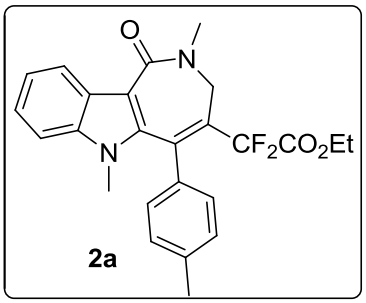
Correction method= # Reported T Limits: Tmin=0.470 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 26.020

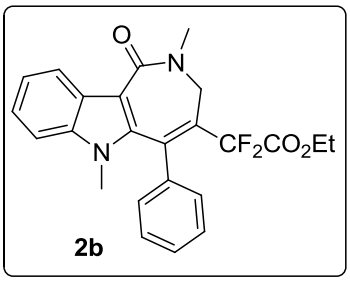
R(reflections)= 0.0888(5031) wR2(reflections)= 0.2627(10440)

S = 1.041 Npar= 729

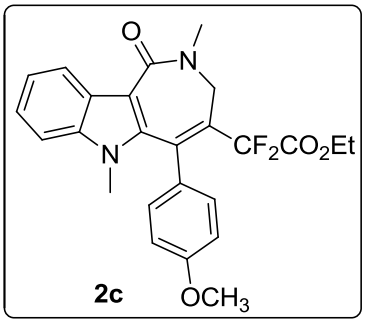
6. Characterization data of 2a-2t



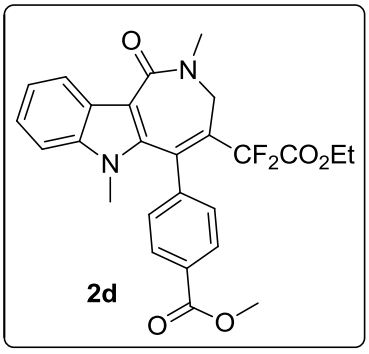
ethyl 2-(2,6-dimethyl-1-oxo-5-(p-tolyl)-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2a**): 59.3 mg, 68% yield, white solid. Mp = 180-182 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 2.38 (s, 3H), 3.03 (s, 3H), 3.30 (s, 3H), 3.61-3.69 (m, 1H), 3.82-3.90 (m, 1H), 4.00-4.05 (m, 1H), 4.14-4.18 (m, 1H), 7.17-7.23 (m, 4H), 7.27-7.51 (m, 3H), 8.34 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.4 (dd, J = 32.0 Hz, J = 37.0 Hz), 139.6, 139.1 (t, J = 8.0 Hz), 138.4, 138.3, 132.6, 130.2, 129.2, 128.4 (dd, J = 23.0 Hz, J = 29.0 Hz), 126.3, 124.6, 122.8, 121.7, 115.6, 112.3 (dd, J = 241.0 Hz, J = 249.0 Hz), 109.2, 62.9, 47.2 (d, J = 7.0 Hz), 34.2, 32.0, 21.3, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.01 (d, J = 285.8 Hz, 1F), -95.18 (d, J = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1834.



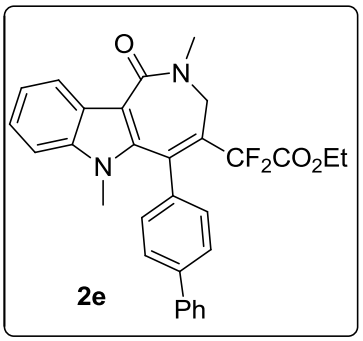
ethyl 2-(2,6-dimethyl-1-oxo-5-phenyl-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2b**): 54.2 mg, 64% yield, white solid. Mp = 172-174 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 6.8 Hz, 3H), 3.02 (s, 3H), 3.31 (s, 3H), 3.64-3.66 (m, 1H), 3.82-3.83 (m, 1H), 4.01-4.06 (m, 1H), 4.16-4.19 (m, 1H), 6.80 (s, 1H), 7.21-7.61 (m, 7H), 8.34 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 162.2 (dd, J = 31.0 Hz, J = 36.0 Hz), 138.9 (t, J = 8.0 Hz), 138.2, 138.1, 135.3, 129.4, 128.5 (dd, J = 23.0 Hz, J = 29.0 Hz), 128.4, 126.1, 124.6, 122.6, 121.7, 115.5, 112.1 (dd, J = 241.0 Hz, J = 249.0 Hz), 109.1, 62.9, 47.1 (d, J = 7.0 Hz), 34.1, 31.9, 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.26 (d, J = 286.1 Hz, 1F), -95.16 (d, J = 286.5 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{22}F_2N_2O_3$ $[M+H]^+$: 425.1671, found: 425.1674.



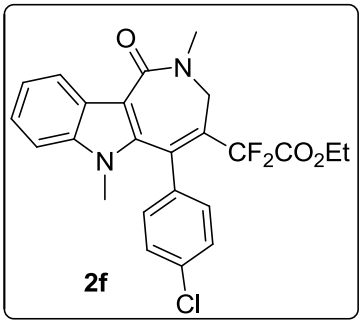
ethyl 2,2-difluoro-2-(5-(4-methoxyphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)acetate (**2c**): 59.0 mg, 65% yield, white solid. Mp = 158-160 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 3.05 (s, 3H), 3.30 (s, 3H), 3.64-3.72 (m, 1H), 3.84 (s, 3H), 3.86-3.92 (m, 1H), 3.99-4.04 (m, 1H), 4.14-4.18 (m, 1H), 6.88 (d, J = 5.6 Hz, 3H), 7.22-7.37 (m, 4H), 8.34 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.5 (dd, J = 31.0 Hz, J = 37.0 Hz), 160.5, 138.8 (t, J = 8.0 Hz), 138.5, 138.4, 131.8, 128.1 (dd, J = 24.0 Hz, J = 30.0 Hz), 127.7, 126.3, 124.6, 122.8, 121.8, 115.6, 113.9, 112.3 (d, J = 240.0 Hz, J = 249.0 Hz), 109.2, 62.9, 55.3, 47.1 (d, J = 7.0 Hz), 34.3, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.30 (d, J = 286.1 Hz, 1F), -95.07 (d, J = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_4$ $[M+H]^+$: 455.1777, found: 455.1780.



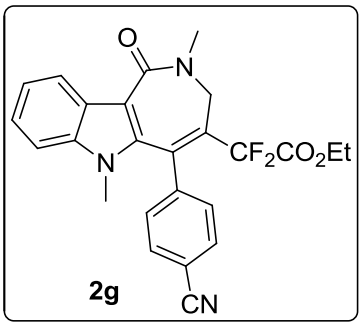
methyl 4-(4-(2-ethoxy-1,1-difluoro-2-oxoethyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-5-yl)benzoate (**2d**): 50.0 mg, 52% yield, white solid. Mp = 166-168 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, J = 7.2 Hz, 3H), 3.02 (s, 3H), 3.31 (s, 3H), 3.74-3.82 (m, 1H), 3.93-3.97 (m, 4H), 4.03-4.08 (m, 1H), 4.16-4.20 (m, 1H), 7.21-7.23 (m, 1H), 7.27-7.39 (m, 3H), 8.05 (s, 2H), 8.35 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.6, 162.4 (dd, J = 32.0 Hz, J = 36.0 Hz), 140.1, 138.4, 138.0 (t, J = 7.0 Hz), 137.6, 130.9, 129.6, 129.5 (dd, J = 24.0 Hz, J = 28.0 Hz), 126.2, 125.0, 122.9, 122.0, 116.0, 112.2 (dd, J = 245.0 Hz, J = 249.0 Hz), 109.3, 63.3, 52.4, 47.5 (d, J = 5.0 Hz), 34.4, 32.2, 26.9, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.11 (d, J = 282.0 Hz, 1F), -89.27, -96.54 (dd, J = 3.8 Hz, J = 282.4 Hz, 1F). HRMS (ESI) m/z calcd for $C_{26}H_{24}F_2N_2O_5$ $[M+H]^+$: 483.1726, found: 483.1725.



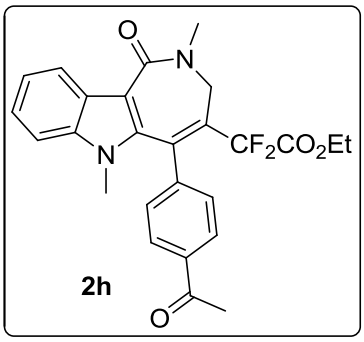
ethyl
2-(5-([1,1'-biphenyl]-4-yl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2e**): 46.8 mg, 47% yield, white solid. Mp = 180-182 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, J = 7.2 Hz, 3H), 3.09 (s, 3H), 3.32 (s, 3H), 3.66-3.74 (m, 1H), 3.82-3.90 (m, 1H), 4.04-4.09 (m, 1H), 4.17-4.21 (m, 1H), 7.23-7.26 (m, 2H), 7.29-7.48 (m, 6H), 7.62-7.64 (m, 4H), 8.36 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 162.5 (dd, J = 33.0 Hz, J = 37.0 Hz), 142.2, 139.6, 138.7 (t, J = 8.0 Hz), 138.4, 138.3, 134.4, 131.0, 129.0, 128.9 (dd, J = 23.0 Hz, J = 29.0 Hz), 128.0, 127.0, 127.0, 126.3, 124.8, 122.9, 121.9, 115.8, 112.4 (dd, J = 241.0 Hz, J = 249.0 Hz), 109.31, 63.1, 47.4 (d, J = 6.0 Hz), 34.4, 32.2(26.9), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.39 (d, J = 285.8 Hz, 1F), -96.54 (dd, J = 3.8 Hz, J = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{30}H_{26}F_2N_2O_3$ $[M+H]^+$: 501.1984, found: 501.1982.



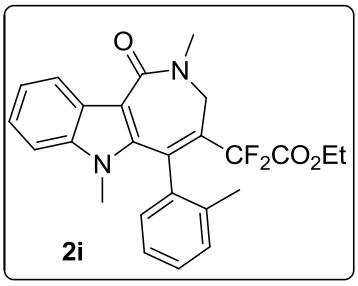
ethyl
2-(5-(4-chlorophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2f**): 49.5 mg, 54% yield, white solid. Mp = 162-164 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, J = 6.8 Hz, 3H), 3.06 (s, 3H), 3.30 (s, 3H), 3.76-3.84 (m, 1H), 3.91-4.05 (m, 2H), 4.14-4.18 (m, 1H), 6.87-7.18 (m, 1H), 7.22-7.37 (m, 6H), 8.34 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.5 (dd, J = 31.0 Hz, J = 36.0 Hz), 138.4, 137.8 (t, J = 7.0 Hz), 137.8 135.8, 134.0, 131.7, 129.2 (dd, J = 24.0 Hz, J = 28.0 Hz), 128.8, 126.2, 125.0, 122.9, 122.0, 116.0, 112.2 (dd, J = 244.0 Hz, J = 250.0 Hz), 109.2, 63.23, 47.40 (d, J = 6.0 Hz), 34.4, 32.2, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.20 (d, J = 283.1 Hz, 1F), -96.21 (dd, J = 3.8 Hz, J = 282.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{21}ClF_2N_2O_3$ $[M+H]^+$: 459.1282, found: 459.1286.



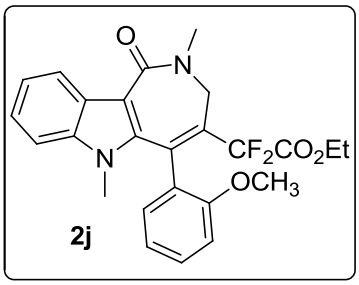
ethyl 2-(5-(4-cyanophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl) -2,2-difluoroacetate (**2g**): 42.8 mg, 48% yield, white solid. Mp = 134-136 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3H), 3.04 (s, 3H), 3.31 (s, 3H), 3.90-3.98 (m, 1H), 4.02-4.08 (m, 2H), 4.14-4.17 (m, 1H), 7.22-7.24 (m, 1H), 7.30-7.47 (m, 3H), 7.68 (s, 3H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 162.5 (dd, J = 32.0 Hz, J = 36.0 Hz), 140.4, 138.5, 137.1 (t, J = 7.0 Hz), 137.1, 132.2, 130.9, 130.2 (t, J = 25.0 Hz), 126.2, 125.3, 123.0, 122.2, 117.9, 116.3, 114.7 (t, J = 249.0 Hz), 113.2, 109.3, 63.5, 47.6 (dd, J = 3.0 Hz, J = 6.0 Hz), 34.5, 32.3, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.53 (d, J = 278.2 Hz, 1F), -97.59 (d, J = 278.6 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{21}F_2N_3O_3$ $[M+H]^+$: 450.1624, found: 450.1625.



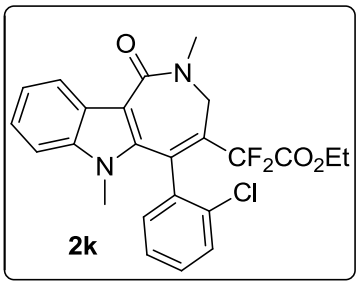
ethyl 2-(5-(4-acetylphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl) -2,2-difluoroacetate (**2h**): 57.7 mg, 62% yield, white solid. Mp = 286-288 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, J = 7.2 Hz, 3H), 2.64 (s, 3H), 3.03 (s, 3H), 3.31 (s, 3H), 3.78-3.86 (m, 1H), 3.93-4.01 (m, 1H), 4.03-4.08 (m, 1H), 4.16-4.19 (m, 1H), 7.01-7.23 (m, 2H), 7.29-7.65 (m, 3H), 7.96 (s, 2H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 164.5, 162.4 (dd, J = 32.0 Hz, J = 36.0 Hz), 140.3, 138.4, 137.9 (t, J = 7.0 Hz), 137.5, 137.3, 130.6, 129.5 (dd, J = 24.0 Hz, J = 26.0 Hz), 128.3, 126.2, 125.0, 122.9, 122.0, 116.0, 112.2 (dd, J = 246.0 Hz, J = 250.0 Hz), 109.2, 63.3, 47.5 (d, J = 5.0 Hz), 34.4, 32.2, 26.7, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -86.45 (d, J = 281.2 Hz, 1F), -96.21 (dd, J = 3.8 Hz, J = 281.2 Hz, 1F). HRMS (ESI) m/z calcd for $C_{26}H_{24}F_2N_2O_4$ $[M+H]^+$: 467.1777, found: 467.1782.



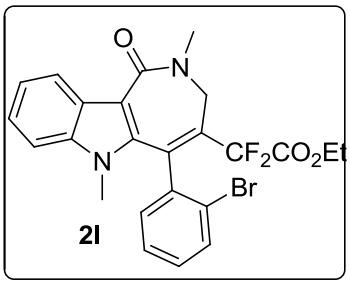
ethyl 2-(2,6-dimethyl-1-oxo-5-(o-tolyl)-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2i**): 54.0 mg, 62% yield, white solid. Mp = 162-164 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, J = 7.2 Hz, 3H), 1.55 (s, 3H), 3.03 (s, 3H), 3.34 (s, 3H), 3.60-3.68 (m, 1H), 3.74-3.82 (m, 1H), 4.04-4.21 (m, 2H), 7.10-7.12 (m, 1H), 7.21-7.23 (m, 1H), 7.27-7.36 (m, 4H), 7.46-7.48 (m, 1H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 162.3 (dd, J = 31.0 Hz, J = 36.0 Hz), 138.7 (t, J = 8.0 Hz), 138.2, 137.7 (d, J = 5.0 Hz), 134.1, 132.6 (d, J = 3.0 Hz), 130.6, 130.3, 130.1, 129.6 (dd, J = 24.0 Hz, J = 29.0 Hz), 126.3, 125.8, 124.7, 123.1, 121.9, 115.6, 112.2 (dd, J = 240.0 Hz, J = 250.0 Hz), 109.2, 62.9, 46.9 (d, J = 6.0 Hz), 34.2, 32.0, 19.5, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.54 (d, J = 286.1 Hz, 1F), -94.38--95.15 (m, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1831.



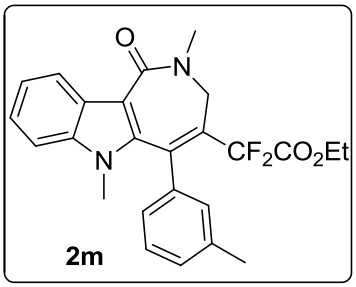
ethyl 2,2-difluoro-2-(5-(2-methoxyphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)acetate (**2j**): 54.7 mg, 60% yield, white solid. Mp = 184-186 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11-1.30 (m, 3H), 3.05-3.07 (m, 3H), 3.30-3.32 (m, 3H), 3.34-3.83 (m, 3H), 3.99-4.20 (m, 4H), 6.67-7.07 (m, 3H), 7.19-7.21 (m, 1H), 7.25-7.45 (m, 3H), 8.32-8.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 162.9 (t, J = 35.0 Hz), 156.5, 139.4, 138.1, 133.3 (d, J = 53.0 Hz), 130.8, 130.5, 130.1 (dd, J = 22.0 Hz, J = 25.0 Hz), 126.3, 124.7, 124.4, 122.7, 121.6, 120.7, 115.3, 112.6 (t, J = 242.0 Hz), 110.3,109.1, 62.8, 55.0, 48.5, 34.3, 31.2, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.22- -102.78 (m, 2F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_4$ $[M+H]^+$: 455.1777, found: 455.1775.



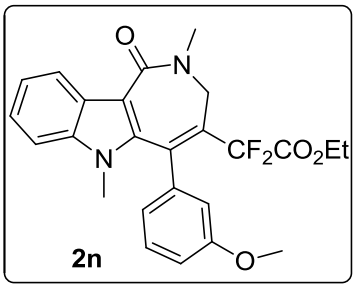
ethyl 2-(5-(2-chlorophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2k**): 53.3 mg, 58% yield, white solid. Mp = 170-172 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18-1.34 (m, 3H), 3.09-3.15 (m, 3H), 3.31-3.34 (m, 3H), 3.77-4.25 (m, 4H), 6.87-7.24 (m, 2H), 7.29-7.42 (m, 4H), 7.47-7.62 (m, 1H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.3, 138.3, 137.0, 135.0, 134.2, 133.6, 131.2, 130.2, 130.1, 129.5, 127.0, 126.5, 124.8, 123.1, 121.9, 116.3, 112.1 (dd, J = 243.0 Hz, J = 252.0 Hz), 109.2, 63.2, 47.0, 34.6, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.49- -103.31 (m, 2F). HRMS (ESI) m/z calcd for $C_{24}H_{21}ClF_2N_2O_3$ $[M+H]^+$: 459.1282, found: 459.1288.



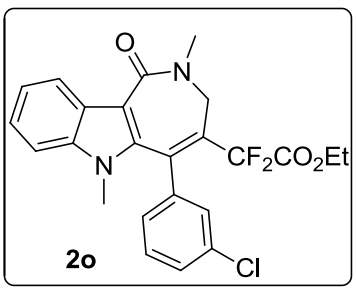
ethyl 2-(5-(2-bromophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2l**): 52.2 mg, 52% yield, white solid. Mp = 148-150 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20-1.34 (m, 3H), 3.08-3.19 (m, 3H), 3.30-3.34 (m, 3H), 3.82-4.23 (m, 4H), 6.87-7.25 (m, 2H), 7.28-7.55 (m, 4H), 7.60-7.67 (m, 1H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.2 (t, J = 34.0 Hz), 138.3, 137.8 (d, J = 7.0 Hz), 136.9, 135.5, 134.4, 133.5, 131.2, 130.3, 127.5, 126.5, 124.8, 123.9, 123.1, 121.9, 116.9, 112.0 (t, J = 250.0 Hz), 109.2, 63.3, 47.0 (d, J = 6.0 Hz), 34.3, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.69- -102.65 (m, 2F). HRMS (ESI) m/z calcd for $C_{24}H_{21}BrF_2N_2O_3$ $[M+H]^+$: 503.0776, found: 503.0780.



ethyl
2-(2,6-dimethyl-1-oxo-5-(m-tolyl)-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2l**): 35.2 mg, 40% yield, white solid. Mp = 154-156 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, J = 7.2 Hz, 3H), 2.32 (s, 3H), 3.05 (s, 3H), 3.31 (s, 3H), 3.57-3.65 (m, 1H), 3.81-3.89 (m, 1H), 4.00-4.05 (m, 1H), 4.15-4.19 (m, 1H), 7.20-7.38 (m, 6H), 8.35 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 162.4 (dd, J = 31.0 Hz, J = 36.0 Hz), 139.2 (t, J = 6.0 Hz), 138.4, 138.3, 138.2, 135.4, 130.2, 128.8, 128.5, 126.3, 124.7, 122.8, 121.8, 115.6, 112.3 (dd, J = 242.0 Hz, J = 250.0 Hz), 109.2, 62.9, 47.2 (d, J = 7.0 Hz), 34.3, 32.1(26.9), 21.2, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.20 (d, J = 286.5 Hz, 1F), -94.15- 95.54 (m, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1829.

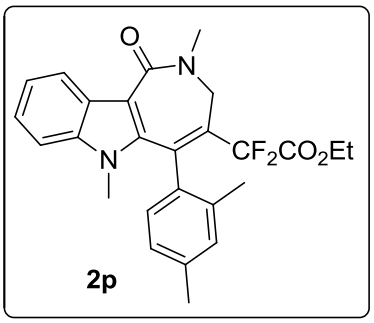


ethyl
2,2-difluoro-2-(5-(3-methoxyphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)acetate (**2l**): 28.1 mg, 31% yield, white solid. Mp = 162-164 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 7.2 Hz, 3H), 3.09 (s, 3H), 3.31 (s, 3H), 3.68-3.70 (m, 3H), 3.84-3.93 (m, 2H), 4.00-4.05 (m, 1H), 4.15-4.19 (m, 1H), 6.36 (s, 1H), 6.94-6.95 (m, 1H), 7.23-7.38 (m, 5H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 162.4 (dd, J = 31.0 Hz, J = 36.0 Hz), 162.2, 159.6, 156.4, 139.0 (d, J = 8.0 Hz), 138.4, 138.0, 136.7, 129.7, 128.9 (dd, J = 24.0 Hz, J = 27.0 Hz), 126.3, 124.8, 122.9, 121.9, 115.7, 112.3 (dd, J = 241.0 Hz, J = 249.0 Hz), 109.3, 63.0, 55.4, 47.4 (d, J = 7.0 Hz), 34.3, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.82--85.13 (m, 1F), -94.74 (dd, J = 3.8 Hz, J = 286.9 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_4$ $[M+H]^+$: 455.1777, found: 455.1779.



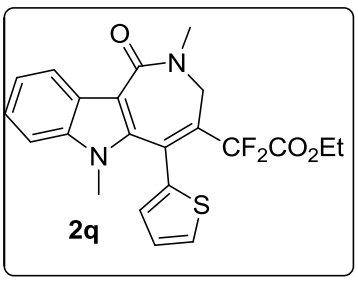
ethyl
2-(5-(3-chlorophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2o**): 32.0 mg, 35% yield, white solid. Mp = 110-112 ^{o}C. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.2 Hz, 3H), 3.09 (s, 3H), 3.31 (s, 3H), 3.83 (s, 1H), 3.93-4.05 (m, 2H), 4.15-4.18 (m, 1H), 6.85 (s, 1H), 7.23-7.52 (m, 6H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 162.4 (dd, J = 32.0 Hz, J = 37.0 Hz), 138.4, 134.6 (t, J = 7.0 Hz), 137.5, 137.3, 134.6, 129.9, 129.6, 129.4, 126.2, 125.0, 122.9, 122.0, 116.0, 112.2 (dd, J = 244.0 Hz, J = 248.0 Hz), 109.3, 63.3, 47.4 (d, J = 6.0 Hz), 34.4, 32.3(26.9), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.61- -86.67 (m, 1F), -95.89- -96.66 (m, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{21}ClF_2N_2O_3$ $[M+H]^+$: 459.1282, found: 459.1286.



2p

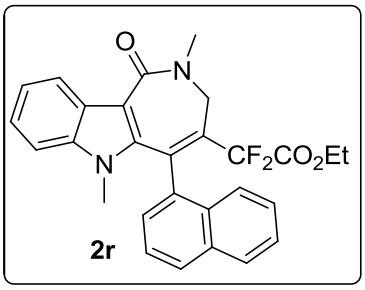
ethyl
2-(5-(2,4-dimethylphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2p**): 50.5 mg, 56% yield, white solid. Mp = 144-146 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, J = 7.2 Hz, 3H), 1.50 (s, 3H), 2.35 (s, 3H), 3.04 (s, 3H), 3.33 (s, 3H), 3.60-3.68 (m, 1H), 3.75-3.83 (m, 1H), 4.03-4.11 (m, 1H), 4.16-4.20 (m, 1H), 6.92 (s, 1H), 7.09-7.10 (m, 1H), 7.20-7.23 (m, 1H), 7.26-7.35 (m, 3H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.4 (dd, J = 31.0 Hz, J = 36.0 Hz), 140.1, 138.8 (dd, J = 7.0 Hz, J = 9.0 Hz), 138.2, 137.9, 137.5 (d, J = 2.0 Hz), 130.6 (d, J = 3.0 Hz), 131.3, 131.2, 129.4 (dd, J = 24.0 Hz, J = 30.0 Hz), 126.4, 126.3, 124.7, 123.0, 121.9, 115.4, 112.3 (dd, J = 240.0 Hz, J = 250.0 Hz), 109.2, 62.8, 47.9 (d, J = 7.0 Hz), 34.2, 32.0, 21.2, 19.4, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.27 (d, J = 285.8 Hz, 1F), -94.25- -95.01 (m, 1F). HRMS (ESI) m/z calcd for $C_{26}H_{26}F_2N_2O_3$ $[M+H]^+$: 453.1984, found: 453.1986.



2q

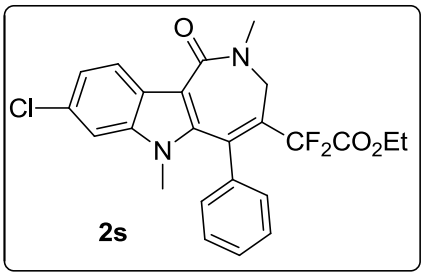
ethyl
2-(2,6-dimethyl-1-oxo-5-(thiophen-2-yl)-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2q**): 40.4 mg, 47% yield, white solid. Mp = 164-166 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, J = 7.2 Hz, 3H), 3.20 (s, 3H), 3.29 (s, 3H), 3.74-3.82 (m, 1H), 3.93-4.03 (m, 2H), 4.18-4.21 (m, 1H), 7.05-7.08 (m, 1H), 7.26-7.39 (m, 4H), 7.49-7.50 (m, 1H), 8.33 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6,

162.1 (dd, *J* = 31.0 Hz, *J* = 38.0 Hz), 138.5, 137.7, 136.6, 132.4 (d, *J* = 5.0 Hz), 131.6 (t, *J* = 8.0 Hz), 130.2 (dd, *J* = 22.0 Hz, *J* = 30.0 Hz), 130.2, 127.2, 126.1, 124.9, 122.8, 121.9, 115.5, 112.2 (dd, *J* = 240.0 Hz, *J* = 251.0 Hz), 109.4, 63.1, 46.8 (d, *J* = 7.0 Hz), 34.2, 31.3(26.8), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.01 (d, *J* = 287.3 Hz, 1F), -95.83 (dd, *J* = 4.1 Hz, *J* = 287.3 Hz, 1F). HRMS (ESI) m/z calcd for $C_{22}H_{20}F_2N_2O_3S$ $[M+H]^+$: 431.1235, found: 431.1234.



2r

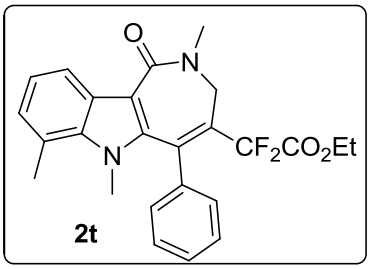
ethyl
2-(2,6-dimethyl-5-(naphthalen-1-yl)-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2r**): 39.9 mg, 42% yield, white solid. Mp = 206-208 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (t, *J* = 7.2 Hz, 3H), 2.46-2.54 (m, 1H), 2.82 (s, 3H), 3.27-3.31 (m, 1H), 3.38 (s, 3H), 4.15-4.20 (m, 1H), 4.26-4.30 (m, 1H), 7.05-7.08 (m, 2H), 7.16-7.20 (m, 1H), 7.26-7.30 (m, 2H), 7.36-7.40 (m, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 8.41 (dd, *J* = 2.8 Hz, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 161.9 (dd, *J* = 31.0 Hz, *J* = 36.0 Hz), 138.3, 137.9 (t, *J* = 8.0 Hz), 137.8, 133.3, 132.0 (t, *J* = 3.0 Hz), 131.9, 131.0, 130.8, 130.7, 130.5, 128.3, 127.6, 126.6, 125.1, 124.9, 124.7, 123.1, 121.9, 115.0, 112.3 (dd, *J* = 238.0 Hz, *J* = 248.0 Hz), 109.2, 62.4, 47.0 (d, *J* = 6.0 Hz), 34.3 (d, *J* = 2.0 Hz), 31.9(26.9), 13.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.29 (d, *J* = 289.1 Hz, 1F), -93.98 (dd, *J* = 2.6 Hz, *J* = 289.5 Hz, 1F). HRMS (ESI) m/z calcd for $C_{28}H_{24}F_2N_2O_3$ $[M+H]^+$: 475.1828, found: 475.1286.



2s

ethyl
2-(8-chloro-2,6-dimethyl-1-oxo-5-phenyl-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)-2,2-difluoroacetate (**2s**): 58.6 mg, 64% yield, white solid. Mp = 156-158 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.2 Hz, 3H), 2.98 (s, 3H), 3.00 (s, 3H), 3.62-3.70 (m, 1H), 3.81-3.89 (m, 1H), 4.00-4.06 (m, 1H), 4.16-4.20 (m, 1H), 7.21-7.58 (m, 7H), 8.35 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 162.3 (dd, *J* = 31.0 Hz, *J* = 36.0 Hz), 138.9 (d, *J* = 7.0 Hz), 138.8, 135.2, 130.8, 129.7,

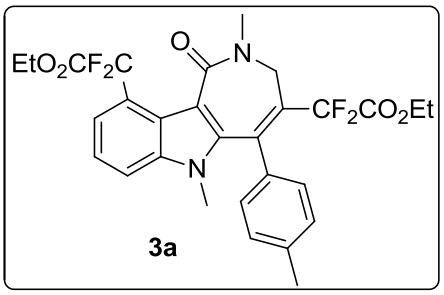
129.0 (dd, *J* = 24.0 Hz, *J* = 29.0 Hz), 128.6, 124.8, 123.9, 122.6, 115.8, 112.2 (dd, *J* = 242.0 Hz, *J* = 249.0 Hz), 109.3, 63.0, 47.3 (d, *J* = 6.0 Hz), 34.3, 32.2, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.61 (d, *J* = 286.1 Hz, 1F), -95.38 (dd, *J* = 4.1 Hz, *J* = 286.1 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{21}ClF_2N_2O_3$ $[M+H]^+$: 459.1282, found: 459.1283.



2t

ethyl
2,2-difluoro-2-(2,6,7-trimethyl-1-oxo-5-phenyl-1,2,3,6-tetrahydroazepino[4,3-b]indol-4-yl)acetate (**2t**): 44.0 mg, 50% yield, white solid. Mp = 150-152 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (t, *J* = 7.2 Hz, 3H), 2.63 (s, 3H), 3.30 (s, 3H), 3.31 (s, 3H), 3.58-3.66 (m, 1H), 3.80-3.88 (m, 1H), 4.03-4.08 (m, 1H), 4.15-4.19 (m, 1H), 7.04-7.42 (m, 7H), 8.22 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.3 (dd, *J* = 31.0 Hz, *J* = 36.0 Hz), 139.6, 139.1 (t, *J* = 8.0 Hz), 137.8, 135.8, 130.4, 129.4, 129.1, 128.9 (t, *J* = 5.0 Hz), 128.5, 127.8, 127.2, 121.8, 121.0, 116.0, 112.3 (dd, *J* = 241.0 Hz, *J* = 250.0 Hz), 63.0, 47.4 (d, *J* = 7.0 Hz), 35.4, 34.4, 20.4, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.60 (d, *J* = 286.5 Hz, 1F), -95.17 (dd, *J* = 4.1 Hz, *J* = 286.5 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1830.

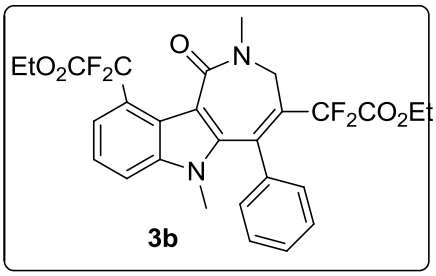
7. Characterization data of 3 and 4



3a

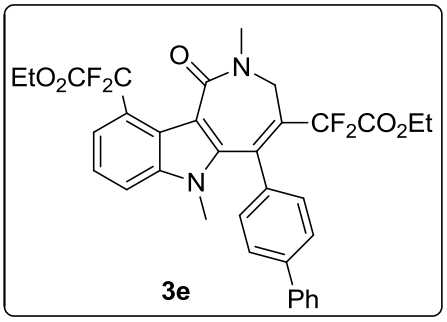
diethyl
2,2'-(2,6-dimethyl-1-oxo-5-(p-tolyl)-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,10-diyl) bis(2,2-difluoroacetate) (**3a**): white solid. Mp = 190-192 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.2 Hz, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 2.38 (s, 3H), 3.02 (s, 3H), 3.22 (s, 3H), 3.59-3.67 (m, 1H), 3.79-3.87 (m, 1H), 4.09-4.20 (m, 2H), 4.34-4.42 (m, 1H), 4.51-4.59 (m, 1H), 7.17-7.26 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (t, *J* = 34.0 Hz), 164.1, 162.4 (dd, *J* = 31.0 Hz, *J* = 36.0 Hz), 139.8, 139.3, 138.6 (t, *J* = 8.0 Hz),

138.4, 132.5, 131.7 (dd, *J* = 23.0 Hz, *J* = 30.0 Hz), 130.4, 129.3, 128.4 (t, *J* = 25.0 Hz), 123.9, 121.8 (d, *J* = 6.0 Hz), 121.2 (d, *J* = 7.0 Hz), 121.1 (d, *J* = 7.0 Hz), 116.1, 112.2, 117.0-109.7 (m, 4F), 62.9, 62.4, 47.0 (d, *J* = 7.0 Hz), 34.0, 32.4, 21.3, 14.1, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.23 (d, *J* = 287.3 Hz, 1F), -94.76 (d, *J* = 285.4 Hz, 1F), -95.09 (dd, *J* = 3.0 Hz, *J* = 287.3 Hz, 1F), -97.60 (d, *J* = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{29}H_{28}F_4N_2O_5$ $[M+H]^+$: 561.2007, found:561.2010.



3b

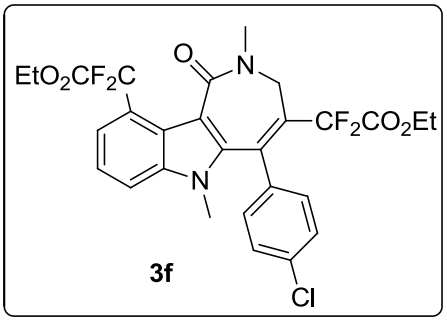
diethyl 2,2'-(2,6-dimethyl-1-oxo-5-phenyl-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,10-diyl)bis(2,2-difluoroacetate) (**3b**): white solid. Mp = 214-216 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.2 Hz, 3H), 1.44 (t, *J* = 7.2 Hz, 3H), 3.02 (s, 3H), 3.23 (d, *J* = 0.4 Hz, 3H), 3.59-3.67 (m, 1H), 3.79-3.87 (m, 1H), 4.11-4.22 (m, 2H), 4.35-4.43 (m, 1H), 4.51-4.59 (m, 1H), 7.23-7.30 (m, 2H), 7.34-7.44 (m, 5H), 7.64 (d, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (t, *J* = 34.0 Hz), 164.1, 162.3 (dd, *J* = 31.0 Hz, *J* = 37.0 Hz), 139.3, 138.5 (t, *J* = 7.0 Hz), 138.2, 135.4, 132.0 (dd, *J* = 24.0 Hz, *J* = 29.0 Hz), 130.6, 129.6, 128.6, 126.9 (t, *J* = 25.0 Hz), 123.9, 121.8 (d, *J* = 5.0 Hz), 121.3 (d, *J* = 7.0 Hz), 121.2 (d, *J* = 7.0 Hz), 116.2, 112.2, 116.9-109.8 (m, 4F), 63.0, 62.4, 47.0 (d, *J* = 7.0 Hz), 34.0, 32.4, 14.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.53 (d, *J* = 287.3 Hz, 1F), -94.76 (d, *J* = 285.8 Hz, 1F), -95.22 (d，*J* = 286.9 Hz, 1F), -97.60 (d, *J* = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{28}H_{26}F_4N_2O_5$ $[M+H]^+$: 547.1851, found: 547.1849.



3e

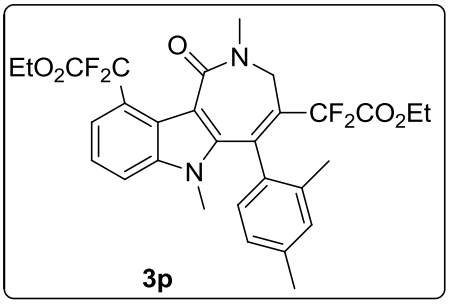
diethyl 2,2'-(5-([1,1'-biphenyl]-4-yl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,10-diyl)bis(2,2-difluoroacetate) (**3e**): white solid. Mp = 206-208 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7.2 Hz, 3H), 1.44 (t, *J* = 7.2 Hz, 3H), 3.09 (s, 3H), 3.24 (s, 3H), 3.63-3.72 (m, 1H), 3.79-3.87 (m, 1H), 4.13-4.23 (m, 2H), 4.35-4.43 (m, 1H), 4.52-4.60 (m, 1H), 7.26-7.49 (m, 7H), 7.62-7.65 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (t, *J* = 34.0 Hz), 164.1, 162.4 (dd, *J* = 31.0 Hz, *J* = 36.0 Hz), 142.2,

139.5, 139.3，138.2, 138.2 (t, *J* = 8.0 Hz), 134.3, 131.1 (dd, *J* = 23.0 Hz, *J* = 29.0 Hz), 131.0, 129.0, 128.1, 127.0, 127.0, 124.0, 121.8 (d, *J* = 6.0 Hz), 121.3 (d, *J* = 6.0 Hz), 121.2 (d, *J* = 6.0 Hz), 116.3, 112.2, 117.0-109.8 (m, 4F), 63.1, 62.4, 47.1 (d, *J* = 7.0 Hz), 34.1, 32.5(26.9), 14.1, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.55 (d, *J* = 286.9 Hz, 1F), -94.81 (d, *J* = 285.8 Hz, 1F), -95.05 (d，*J* = 287.3 Hz, 1F), -97.53 (d, *J* = 285.7 Hz, 1F). HRMS (ESI) m/z calcd for $C_{34}H_{30}F_4N_2O_5$ $[M+H]^+$: 623.2164, found: 623.2162.



3f

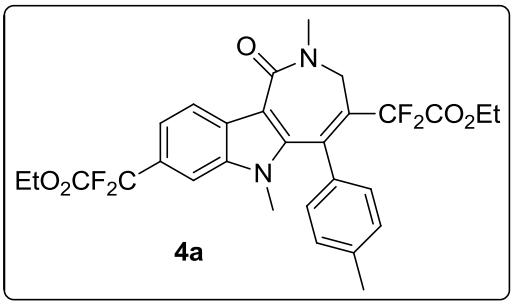
diethyl 2,2'-(5-(4-chlorophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,10-diyl)bis(2,2-difluoroacetate) (**3f**): white solid. Mp = 138-140 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.2 Hz, 3H), 1.43 (t, *J* = 7.2 Hz, 3H), 3.06 (s, 3H), 3.22 (s, 3H), 3.73-3.81 (m, 1H), 3.88-3.96 (m, 1H), 4.10-4.20 (m, 2H), 4.34-4.42 (m, 1H), 4.51-4.59 (m, 1H), 7.17-7.26 (m, 2H), 7.35-7.38 (m, 3H), 7.42-7.45 (m, 1H), 7.64 (d, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (t, *J* = 34.0 Hz), 163.9, 162.3 (dd, *J* = 31.0 Hz, *J* = 35.0 Hz), 139.3, 137.8，137.3 (t, *J* = 7.0 Hz), 135.9, 133.9, 132.4 (dd, *J* = 24.0 Hz, *J* = 29.0 Hz), 131.8, 128.9, 126.9 (t, *J* = 25.0 Hz), 124.2, 121.8 (d, *J* = 6.0 Hz), 121.4 (d, *J* = 6.0 Hz), 121.3 (d, *J* = 7.0 Hz), 116.4, 112.2, 116.9-109.7 (m, 4F), 63.3, 62.4, 47.1 (d, *J* = 7.0 Hz), 34.1, 32.6(26.9), 14.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.30 (d, *J* = 285.0 Hz, 1F), -94.85 (d, *J* = 285.8 Hz, 1F), -96.08 (d，*J* = 284.6 Hz, 1F), -97.61 (d, *J* = 286.1 Hz, 1F). HRMS (ESI) m/z calcd for $C_{28}H_{25}ClF_4N_2O_5$ $[M+H]^+$: 581.1461, found:581.1460.



3p

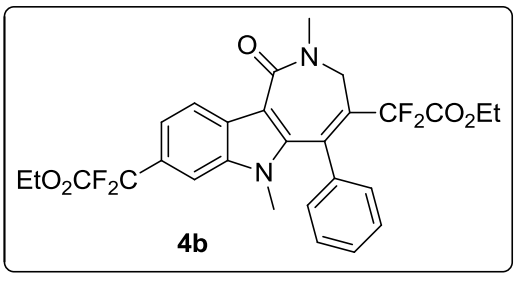
diethyl 2,2'-(5-(3,4-dimethylphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,10-diyl)bis(2,2-difluoroacetate) (**3p**): white solid. Mp = 184-186 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, *J* = 7.2 Hz, 3H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.53 (s, 3H), 2.35 (s, 3H), 3.05 (s, 3H), 3.24 (s, 3H), 3.57-3.65 (m, 1H), 3.73-3.81 (m, 1H),

4.13-4.22 (m, 2H), 4.35-4.53 (m, 2H), 6.94 (s, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.32-7.42 (m, 3H), 7.61 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 163.9 (t, *J* = 34.0 Hz), 162.3 (dd, *J* = 31.0 Hz, *J* = 35.0 Hz), 140.2, 139.0, 138.1 (t, *J* = 9.0 Hz), 137.7, 137.4, 132.7 (dd, *J* = 23.0 Hz, *J* = 26.0 Hz), 132.6 (d, *J* = 3.0 Hz), 131.3, 131.1, 127.0 (t, *J* = 24.0 Hz), 126.5, 123.8, 121.9 (d, *J* = 5.0 Hz), 121.3 (d, *J* = 6.0 Hz), 121.1 (d, *J* = 7.0 Hz), 116.1, 112.1, 116.9-109.8 (m, 4F), 62.9, 62.4, 47.0 (d, *J* = 7.0 Hz), 34.0, 32.4, 21.3, 14.1, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.29 (d, *J* = 286.2 Hz, 1F), -93.71- -95.28 (m, 2F), -98.06 (d，*J* = 285.0 Hz, 1F). HRMS (ESI) m/z calcd for $C_{30}H_{30}F_4N_2O_5$ $[M+H]^+$: 575.2164, found: 575.2163.



4a

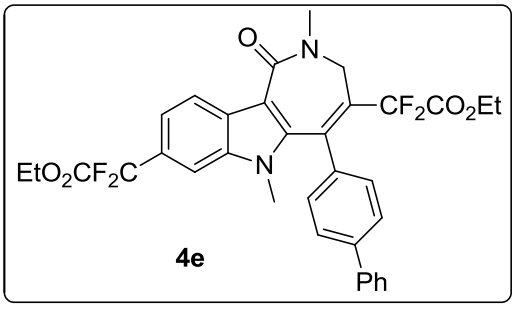
diethyl 2,2'-(2,6-dimethyl-1-oxo-5-(p-tolyl)-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,8-diyl)bis(2,2-difluoroacetate) (**4a**): white solid. Mp = 156-158 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.12 (m, 3H), 1.28-1.32 (m, 3H), 2.38 (d, *J* = 6.0 Hz, 3H), 3.07-3.20 (s, 3H), 3.30 (s, 3H), 3.60-3.72 (m, 1H), 3.80-3.91 (m, 1H), 3.99-4.09 (m, 1H), 4.16-4.21 (m, 1H), 4.26-4.36 (m, 2H), 7.05-7.27 (m, 4H), 7.28-7.51 (m, 2H), 8.39-8.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4(164.1), 164.2 (t, *J* = 35.0 Hz), 162.6-161.9 (m) 141.6, 140.3, 140.0 (t, *J* = 20.0 Hz), 139.2-138.8 (m), 137.6, 135.3, 132.7 (d, *J* = 33.0 Hz), 130.2, 129.4, 129.2, 128.9 (d, *J* = 70 Hz), 128.0, 126.7, 123.3 120.7, 124.8-106.9 (m, 4F), 63.4-63.0 (m), 47.2 (dd, *J* = 8.0 Hz, *J* = 11.0 Hz), 36.7-34.3 (m), 32.3 (26,9), 21.3 (*J* = 2.0 Hz), 13.9 (*J* = 3.0 Hz), 13.5 (*J* = 3.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.29- -84.88 (m, 1F), -88.42- -89.97 (m, 1F), -94.88- -95.93(m, 1F), -101.88- -103.42 (m, 1F). HRMS (ESI) m/z calcd for $C_{29}H_{28}F_4N_2O_5$ $[M+H]^+$: 561.2007, found:561.2010.



4b

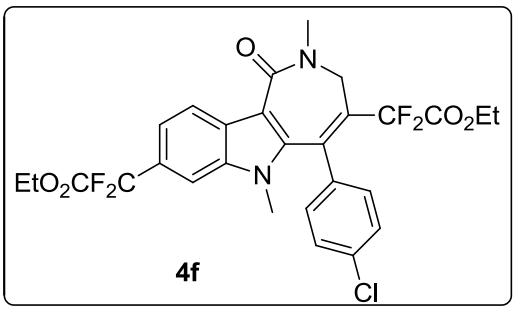
diethyl 2,2'-(2,6-dimethyl-1-oxo-5-phenyl-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,8-diyl)bis(2,2-difluoroacetate) (**4b**): white solid. Mp = 160-162 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.12 (m, 3H), 1.28-1.32 (m, 3H), 3.06-3.19 (s, 3H), 3.31 (s, 3H),

3.59-3.71 (m, 1H), 3.80-3.90 (m, 1H), 4.01-4.11 (m, 1H), 4.17-4.23 (m, 1H), 4.27-4.35 (m, 2H), 7.09-7.23 (m, 1H), 7.29-7.51 (m, 6H), 8.40-8.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4(164.1), 164.2 (d, J = 34.0 Hz), 162.2 (t, J = 40.0 Hz), 141.5, 140.0, 137.7, 135.4, 151.1, 130.1 (d, J = 24.0 Hz), 129.8, 129.6, 128.8, 128.7, 128.6, 128.0, 126.7, 123.3, 120.7, 125.0-106.9 (m, 4F), 63.5-63.1 (m), 47.3 (d, J = 8.0 Hz), 36.7-34.4 (m), 32.3, 13.9 (d, J = 2.0 Hz), 13.6 (J = 2.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.54- -85.15 (m, 1F), -88.37- -90.07 (m, 1F), -94.95- -95.95 (m, 1F), -101.91- -103.50 (m, 1F). HRMS (ESI) m/z calcd for $C_{28}H_{26}F_4N_2O_5$ $[M+H]^+$: 547.1851, found: 547.1850.



4e

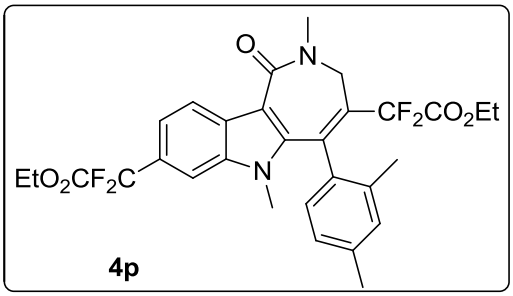
diethyl 2,2'-(5-([1,1'-biphenyl]-4-yl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,8-diyl)bis(2,2-difluoroacetate) (**4e**): white solid. Mp = 168-170 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.12 (m, 3H), 1.30 (t, J = 7.2 Hz, 3H), 3.13-3.26 (s, 3H), 3.32 (s, 3H), 3.54-3.76 (m, 1H), 3.81-3.91 (m, 1H), 4.03-4.13 (m, 1H), 4.18-4.24 (m, 1H), 4.27-4.35 (m, 2H), 7.30-7.41 (m, 3H), 7.44-7.52 (m, 4H), 7.60-7.62 (m, 4H), 8.41-8.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4(164.1), 164.2 (d, J = 34.0 Hz), 162.4-161.6 (m), 142.4, 142.2, 141.5, 139.6, 139.5, 138.7, 137.7, 135.3, 134.4, 134.0, 130.8, 129.0 (d, J = 9.0 Hz), 129.0, 128.1, 128.0, 127.0 (d, J = 2.0 Hz), 126.9 (d, J = 43.0 Hz), 123.3, 120.8, 124.9-106.9 (m, 4F), 63.5-63.1 (m), 47.3 (d, J = 8.0 Hz), 36.7-34.4 (m), 32.3(26.9), 13.9 (d, J = 2.0 Hz), 13.6 (J = 2.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.65- -85.25 (m, 1F), -88.40- -89.95 (m, 1F), -94.78- -95.84 (m, 1F), -101.85- -103.38 (m, 1F). HRMS (ESI) m/z calcd for $C_{34}H_{30}F_4N_2O_5$ $[M+H]^+$: 623.2164, found: 623.2163.



4f

diethyl 2,2'-(5-(4-chlorophenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,8-diyl)bis(2,2-difluoroacetate) (**4f**): white solid. Mp = 158-160 ^{o}C. ^{1}H NMR (400

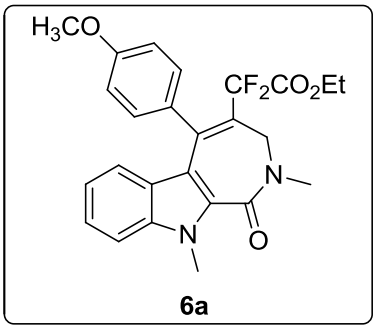
MHz, $CDCl_3$) δ 1.12-1.18 (m, 3H), 1.28-1.33 (m, 3H), 3.11-3.23 (s, 3H), 3.30 (s, 3H), 3.74-3.86 (m, 1H), 3.92-4.01 (m, 1H), 4.03-4.10 (m, 1H), 4.15-4.21 (m, 1H), 4.27-4.37 (m, 2H), 7.09-7.52 (m, 6H), 8.39-8.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2(163.9), 164.2 (d, J = 34.0 Hz), 162.3 (t, J = 40.0 Hz), 145.4, 141.1, 139.6, 137.8 (d, J = 14.0 Hz), 136.0 (d, J = 18.0 Hz), 135.4, 133.9, 133.6, 131.6, 130.3 (d, J = 24.0 Hz), 129.0, 128.8, 126.8, 123.4, 120.9, 125.2-106.9 (m, 4F), 63.5-63.2 (m), 47.4 (d, J = 8.0 Hz), 36.9-34.5 (m), 32.5 (26.9), 13.9 (d, J = 2.0 Hz), 13.6 (J = 2.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.44- -86.05 (m, 1F), -89.25 (s, 1F), -95.84- -96.88 (m, 1F), -101.97- -103.45 (m, 1F). HRMS (ESI) m/z calcd for $C_{28}H_{25}ClF_4N_2O_5$ $[M+H]^+$: 581.1461, found:581.1460.



4p

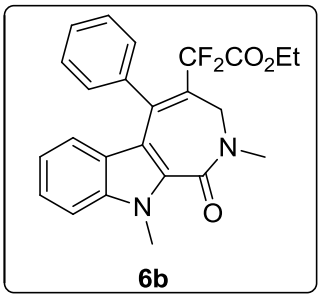
diethyl 2,2'-(5-(3,4-dimethylphenyl)-2,6-dimethyl-1-oxo-1,2,3,6-tetrahydroazepino[4,3-b]indole-4,8-diyl)bis(2,2-difluoroacetate) (**4p**): white solid. Mp = 184-186 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09-1.14 (m, 3H), 1.29 (t, J = 7.2 Hz, 3H), 1.46-1.49 (m, 3H), 2.34-2.56 (d, J = 6.0 Hz, 3H), 3.08-3.21 (m, 3H), 3.33 (s, 3H), 3.58-3.70 (m, 1H), 3.73-4.81 (m, 1H), 4.02-4.14 (m, 1H), 4.17-4.23 (m, 1H), 4.26-4.35 (m, 2H), 6.91-6.94 (m, 1H), 7.07-7.12 (m, 1H), 7.28-7.50 (m, 3H), 8.39-8.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4 (d, J = 34.0 Hz), 164.2(163.9), 162.3 (dd, J = 24.0 Hz, J = 36.0 Hz), 141.4, 140.4 (d, J = 24.0 Hz), 139.7, 138.8-138.5(m), 137.5, 137.3 (d, J = 5.0 Hz), 135.2, 132.7 (dd, J = 4.0 Hz, J = 38.0 Hz), 131.4 (d, J = 6.0 Hz), 131.0 (d, J = 25.0 Hz), 130.4 (d, J = 23.0 Hz), 128.9 (d, J = 6.0 Hz), 128.1, 126.9, 126.6 d, J = 20.0 Hz), 123.5, 120.7, 125.0-106.8 (m, 4F), 63.4-62.9 (m), 47.0-46.8 (m), 36.9-34.3 (m), 32.2 (26.9), 21.2 (d, J = 3.0 Hz), 19.4 (d, J = 12.0 Hz), 13.9 (d, J = 7.0 Hz), 13.5 (J = 3.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.48- -86.12 (m, 1F), -88.16- -90.30 (m, 1F), -94.25- -95.38 (m, 1F), -101.80- -103.51 (m, 1F). HRMS (ESI) m/z calcd for $C_{30}H_{30}F_4N_2O_5$ $[M+H]^+$: 575.2164, found: 575.2162.

8. Characterization data of 6a-6i and 7b



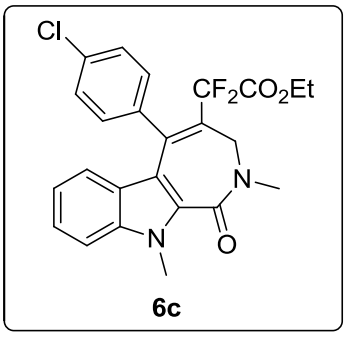
6a

ethyl
2,2-difluoro-2-(5-(4-methoxyphenyl)-2,10-dimethyl-1-oxo-1,2,3,10-tetrahydroazepin o[3,4-b]indol-4-yl)acetate (**6a**): 56.4 mg, 62% yield, white solid. Mp = 290-292 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 3.05 (s, 3H), 3.30 (s, 3H), 3.64-3.72 (m, 1H), 3.84 (s, 3H), 3.86-3.92 (m, 1H), 3.99-4.04 (m, 1H), 4.00-4.05 (m, 1H), 4.14-4.18 (m, 1H), 6.87-7.03 (m, 3H), 7.07-7.37 (m, 4H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.4 (dd, J = 31.0 Hz, J = 37.0 Hz), 160.5, 138.9 (t, J = 7.0 Hz), 138.5, 138.4, 131.8, 128.2 (dd, J = 23.0 Hz, J = 29.0 Hz), 127.7, 126.3, 124.6, 122.8, 121.8, 115.6, 113.9, 112.4 (dd, J = 240.0 Hz, J = 249.0 Hz), 109.2, 62.9, 55.3, 47.2 (d, J = 7.0 Hz), 34.3, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.33 (d, J = 285.8 Hz, 1F), -95.10 (dd, J = 4.5 Hz, J = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_4$ $[M+H]^+$: 455.1777, found: 455.1773.



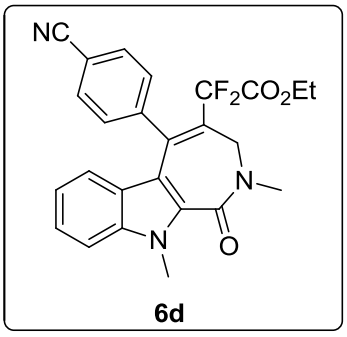
6b

ethyl
2-(2,10-dimethyl-1-oxo-5-phenyl-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-dif luoroacetate (**6b**): 50.5 mg, 60% yield, white solid. Mp = 190-192 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 3.02 (s, 3H), 3.31 (s, 3H), 3.61-3.69 (m, 1H), 3.81-3.90 (m, 1H), 4.02-4.07 (m, 1H), 4.16-4.20 (m, 1H), 7.21-7.26 (m, 2H), 7.28-7.41 (m, 6H), 8.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.4 (dd, J = 31.0 Hz, J = 35.0 Hz), 139.1 (t, J = 7.0 Hz), 138.4, 138.2, 135.5, 139.5, 128.6, 127.7, 127.2, 126.3, 124.8, 122.9, 121.9, 115.7, 112.3 (dd, J = 243.0 Hz, J = 250.0 Hz), 109.2, 63.0, 47.3 (d, J = 8.0 Hz), 34.3, 32.0, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.32 (d, J = 285.8 Hz, 1F), -95.28 (dd, J = 4.5 Hz, J = 285.8 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{22}F_2N_2O_3$ $[M+H]^+$: 425.1671, found: 425.1676.



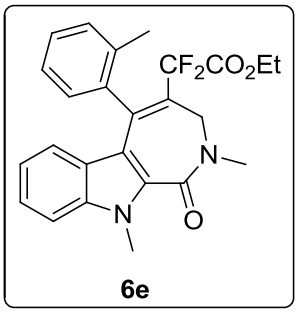
6c

ethyl 2-(5-(4-chlorophenyl)-2,10-dimethyl-1-oxo-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-difluoroacetate (**6c**): 37.6 mg, 41% yield, white solid. Mp = 184-186 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (t, J = 7.2 Hz, 3H), 3.06 (s, 3H), 3.30 (s, 3H), 3.77-3.85 (m, 1H), 3.90-3.98 (m, 1H), 4.00-4.05 (m, 1H), 4.14-4.18 (m, 1H), 7.10-7.24 (m, 2H), 7.26-7.38 (m, 5H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.3 (dd, J = 31.0 Hz, J = 36.0 Hz), 138.4, 139.1 (t, J = 7.0 Hz), 137.8, 135.7, 134.0, 131.6, 129.2 (dd, J = 23.0 Hz, J = 28.0 Hz), 128.8, 126.2, 125.0, 122.9, 122.0, 116.0, 112.2 (dd, J = 243.0 Hz, J = 249.0 Hz), 109.2, 63.2, 47.4 (d, J = 6.0 Hz), 34.4, 32.0(26.9), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.23 (d, J = 282.8 Hz, 1F), -96.23 (dd, J = 3.8 Hz, J = 283.1 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{21}ClF_2N_2O_3$ $[M+H]^+$: 459.1282, found: 459.1284.



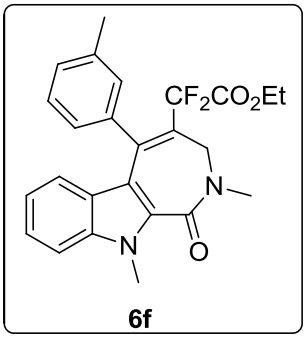
6d

ethyl 2-(5-(4-cyanophenyl)-2,10-dimethyl-1-oxo-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-difluoroacetate (**6d**) 33.3 mg, 37% yield, white solid. Mp = 198-200 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3H), 3.04 (s, 3H), 3.31 (s, 3H), 3.91-3.98 (m, 1H), 4.02-4.08 (m, 2H), 4.14-4.17 (m, 1H), 7.22-7.40 (m, 4H), 7.47-7.68 (m, 3H), 8.34 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 162.4 (dd, J = 33.0 Hz, J = 37.0 Hz), 140.4, 138.5, 137.2 (t, J = 6.0 Hz), 137.1, 132.1, 130.9, 130.1 (dd, J = 24.0 Hz, J = 26.0 Hz), 126.2, 125.3, 123.0, 122.2, 117.9, 116.3, 113.2, 112.2 (dd, J = 248.0 Hz, J = 250.0 Hz), 109.3, 63.5, 47.6 (d, J = 4.0 Hz), 34.5, 32.3(26.9), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -87.54 (d, J = 278.2 Hz, 1F), -97.59 (dd, J = 3.8 Hz, J = 278.2 Hz, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{21}F_2N_2O_3$ $[M+H]^+$: 450.1624, found: 450.1625.



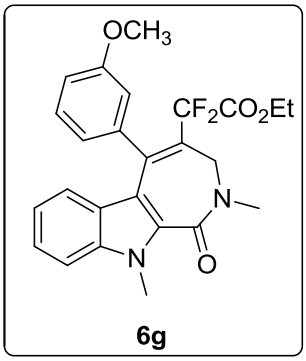
6e

ethyl 2-(2,10-dimethyl-1-oxo-5-(o-tolyl)-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-difluoroacetate (**6e**): 50.8 mg, 58% yield, white solid. Mp = 134-136 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07-1.20 (m, 3H), 2.07-2.31 (m, 3H), 2.64-3.31 (m, 3H), 2.97-3.04 (m, 3H), 3.59-4.22 (m, 4H), 6.42-6.97 (m, 2H), 7.20-7.42 (m, 5H), 5.96 and 8.34 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 162.4 (dd, *J* = 31.0 Hz, *J* = 37.0 Hz), 150.7, 140.9 (t, *J* = 65.0 Hz), 139.2 (t, *J* = 7.0 Hz), 138.4 (d, *J* = 15.0 Hz), 138.3, 135.4, 130.2, 128.9 140.9 (d, *J* = 34.0 Hz), 128.4, 127.6 (t, *J* = 18.0 Hz), 126.3, 124.6, 122.8, 127.8, 115.6, 112.3 (dd, *J* = 241.0 Hz, *J* = 249.0 Hz), 109.2, 62.9, 47.3 (d, *J* = 6.0 Hz), 34.3(29.3), 32.0(26.9), 21.2, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -84.27(d, *J* = 286.1 Hz, 1F), -94.28- -101.70 (m, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1834.



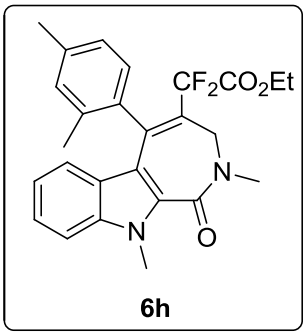
6f

ethyl 2-(2,10-dimethyl-1-oxo-5-(m-tolyl)-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-difluoroacetate (**6f**): 36.0 mg, 41% yield, white solid. Mp = 170-172 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.2 Hz, 3H), 1.55 (s, 3H), 3.03 (s, 3H), 3.34 (s, 3H), 3.62-3.67 (m, 1H), 3.77-3.81 (m, 1H), 4.05-4.10 (m, 1H), 4.18-4.22 (m, 1H), 7.10-7.12 (m, 1H), 7.20-7.22 (m, 1H), 7.26-7.36 (m, 4H), 7.46-7.48 (m, 1H), 8.35 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 162.4 (dd, *J* = 31.0 Hz, *J* = 35.0 Hz), 138.7 (t, *J* = 8.0 Hz), 138.2, 137.7, 137.7, 134.2, 132.6 (d, *J* = 3.0 Hz) , 130.6, 130.1, 129.6 (dd, *J* = 24.0 Hz, *J* = 29.0 Hz), 126.3, 125.8, 124.8, 123.1, 121.9, 115.6, 112.3 (dd, *J* = 240.0 Hz, *J* = 250.0 Hz), 109.2, 62.9, 47.2 (d, *J* = 7.0 Hz), 34.2, 32.0, 21.3, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.58(d, *J* = 285.8 Hz, 1F), -94.42- -95.19 (m, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_3$ $[M+H]^+$: 439.1828, found: 439.1827.



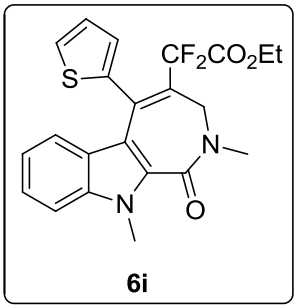
6g

ethyl
2,2-difluoro-2-(5-(3-methoxyphenyl)-2,10-dimethyl-1-oxo-1,2,3,10-tetrahydroazepin o[3,4-b]indol-4-yl)acetate (**6g**): 40.8 mg, 45% yield, white solid. Mp = 188-190 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (s, 3H), 3.09 (s, 3H), 3.31 (s, 3H), 3.63-3.71 (m, 3H), 3.81-3.90 (m, 2H), 4.00-4.05 (m, 1H), 4.15-4.18 (m, 1H), 6.45-7.04 (m, 3H), 7.22-7.37 (m, 4H), 8.34 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 162.4 (dd, J = 31.0 Hz, J = 35.0 Hz), 159.6, 150.7, 140.6, 138.9 (t, J = 7.0 Hz), 138.4, 138.0, 136.7, 129.7, 129.1 (t, J = 25.0 Hz), 128.7 (dd, J = 7.0 Hz, J = 16.0 Hz), 126.3, 124.7, 122.8, 121.9, 115.7, 112.3 (dd, J = 242.0 Hz, J = 250.0 Hz), 109.2, 63.0, 55.4, 47.3 (d, J = 7.0 Hz), 34.3, 32.0, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -83.89- -85.14 (m, 1F), -94.42- -95.19 (m, 1F). HRMS (ESI) m/z calcd for $C_{25}H_{24}F_2N_2O_4$ $[M+H]^+$: 455.1777, found: 455.1776.



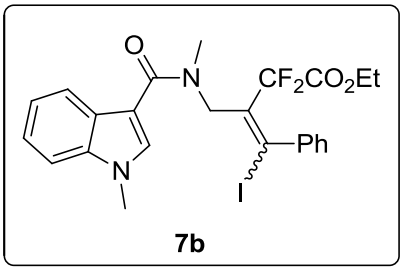
6h

ethyl
2-(5-(2,4-dimethylphenyl)-2,10-dimethyl-1-oxo-1,2,3,10-tetrahydroazepino[3,4-b]ind ol-4-yl)-2,2-difluoroacetate (**6h**): 45.3 mg, 50% yield, white solid. Mp = 160-162 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, J = 7.2 Hz, 3H), 1.52 (s, 3H), 2.37 (s, 3H), 3.07 (s, 3H), 3.35 (s, 3H), 3.62-3.70 (m, 1H), 3.77-3.84 (m, 1H), 4.05-4.10 (m, 1H), 4.18-4.22 (m, 1H), 6.95 (s, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.23-7.37 (m, 4H), 8.37 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.4 (dd, J = 32.0 Hz, J = 36.0 Hz), 140.1, 138.8 (t, J = 8.0 Hz), 138.2, 137.9, 137.5, 132.6 (d, J = 4.0 Hz) , 131.3, 131.2, 129.4 (dd, J = 24.0 Hz, J = 30.0 Hz), 126.4, 126.4, 124.7, 123.1, 121.9, 115.4, 112.3 (dd, J = 240.0 Hz, J = 250.0 Hz), 109.2, 62.8, 46.9 (d, J = 6.0 Hz), 34.2 (d, J = 1.0 Hz), 32.0(26.9), 21.2, 19.5, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -85.28 (d, J = 285.8 Hz, 1F), -94.26- -95.02 (m, 1F). HRMS (ESI) m/z calcd for $C_{26}H_{26}F_2N_2O_3$ $[M+H]^+$: 453.1984, found: 453.1981.



6i

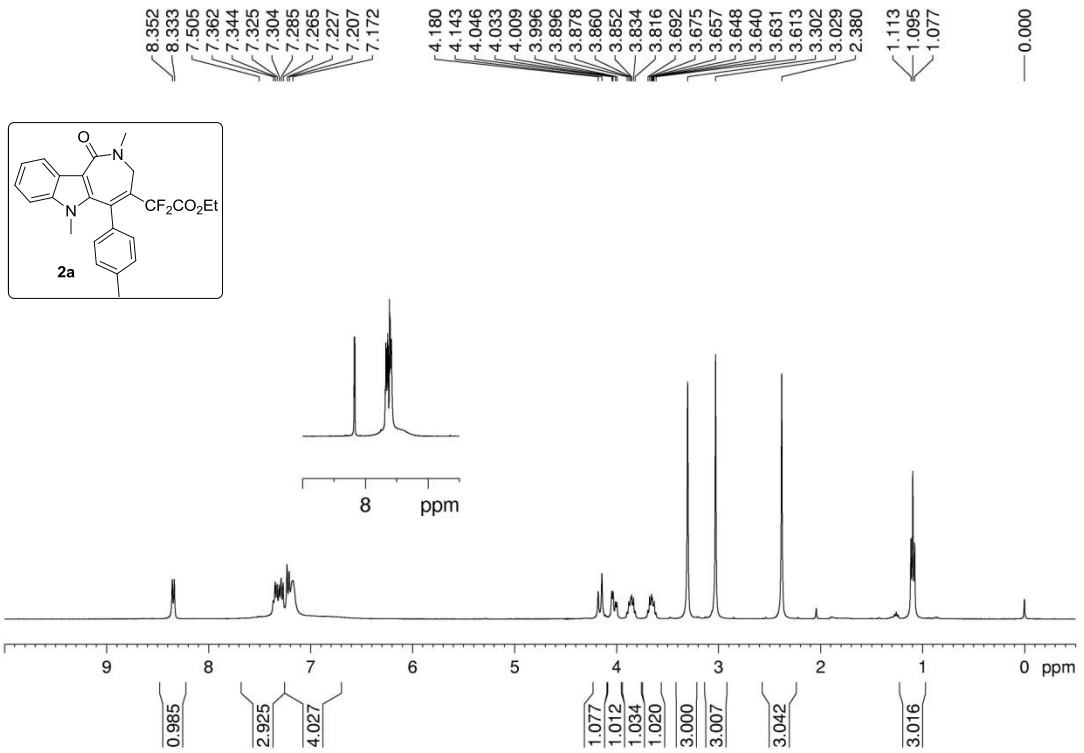
ethyl 2-(2,10-dimethyl-1-oxo-5-(thiophen-2-yl)-1,2,3,10-tetrahydroazepino[3,4-b]indol-4-yl)-2,2-difluoroacetate (**6i**): 26.8 mg, 31% yield, white solid. Mp = 128-130 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, J = 7.2 Hz, 3H), 3.20 (s, 3H), 3.30 (s, 3H), 3.74-3.82 (m, 1H), 3.94-4.04 (m, 2H), 4.18-4.21 (m, 1H), 7.06-7.08 (m, 1H), 7.26-7.32 (m, 3H), 7.35-7.39 (m, 1H), 7.49 (dd, J = 0.8 Hz, J = 5.2 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 162.1 (dd, J = 31.0 Hz, J = 37.0 Hz), 138.5, 137.7, 136.6, 132.4 (d, J = 6.0 Hz), 131.7 (dd, J = 6.0 Hz, J = 8.0 Hz), 130.3 (dd, J = 22.0 Hz, J = 32.0 Hz), 130.2, 127.2, 126.2, 124.9, 122.8, 122.0, 115.6, 112.2 (dd, J = 240.0 Hz, J = 250.0 Hz), 109.4, 63.1, 46.9 (d, J = 8.0 Hz), 34.3, 31.3, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.01 (d, J = 287.3 Hz, 1F), -95.44- -96.21 (m, 1F). HRMS (ESI) m/z calcd for $C_{22}H_{20}F_2N_2O_3S$ $[M+H]^+$: 431.1235, found: 431.1236.

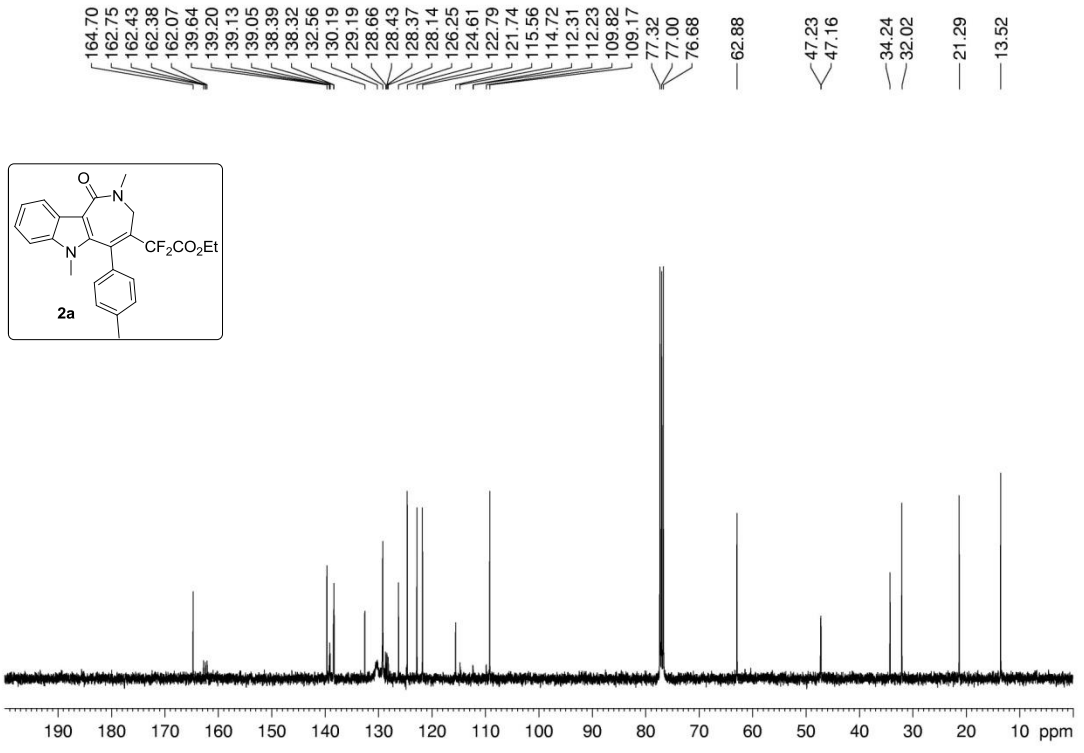


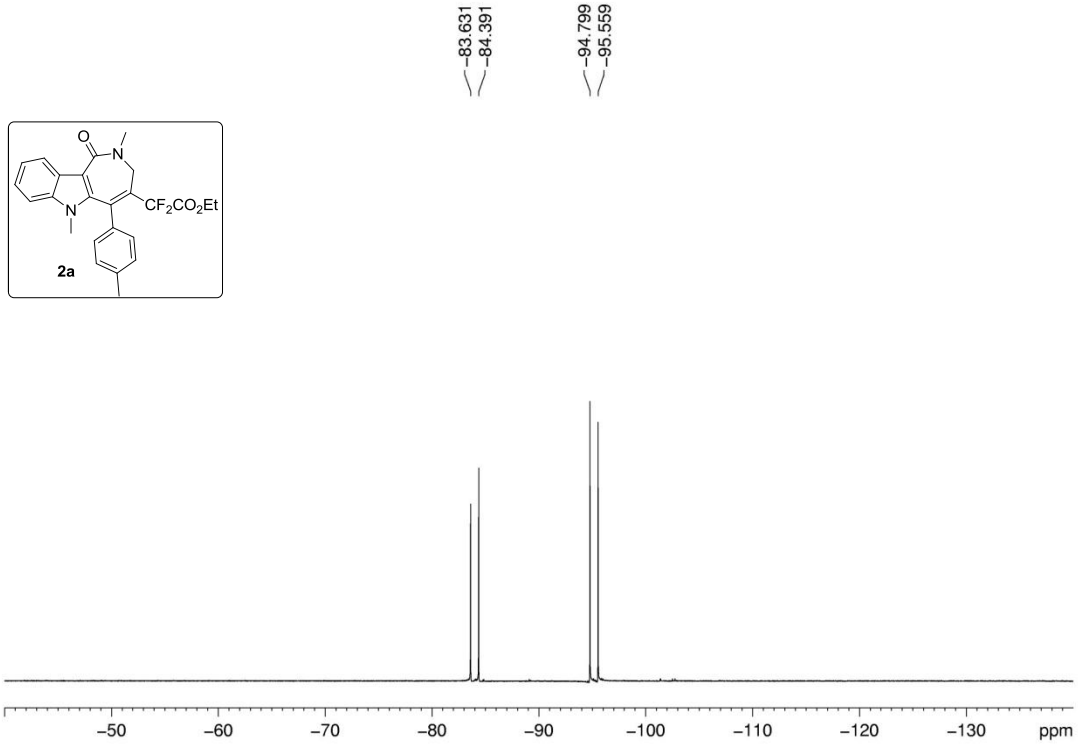
7b

(E/Z)-ethyl 3-((N,1-dimethyl-1H-indole-3-carboxamido)methyl)-2,2-difluoro-4-iodo-4-phenylbut-3-enoate (**7b**): 11.0 mg, 10% yield, yellow solid. Mp = 130-132 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, J = 7.2 Hz, 3H), 2.20 (s, 3H), 3.01 (s, 3H), 3.99 (dd, J = 6.8 Hz, J = 16.8 Hz, 1H), 4.14 (s, 2H), 4.21-4.26 (m, 2H), 6.16 (d, J = 8.0 Hz, 1H), 6.64-6.71 (m, 3H), 6.83 (d, J = 7.6 Hz, 1H), 7.05-7.26 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 162.1 (t, J = 33.0 Hz), 138.5, 151.6, 143.8 (d, J = 5.0 Hz), 141.2, 131.9, 129.8 (d, J = 5.0 Hz), 128.6 (d, J = 17.0 Hz), 127.3 (d, J = 25.0 Hz), 118.8, 114.3 (d, J = 251.0 Hz), 110.5, 108.5 (d, J = 7.0 Hz), 107.4, 107.0 (d, J = 7.0 Hz), 99.3, 76.1-74.4 (m), 63.0-59.8 (m), 34.9 (34.3), 29.9 (29.7), 14.2 (13.2); ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.21 (d, J = 286.5 Hz, 1F), -102.97 (d, J = 286.5 Hz, 1F). HRMS (ESI) m/z calcd for $C_{24}H_{23}F_2N_2O_3I$ $[M+H]^+$: 553.0794, found: 553.0791.

9. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 2a-2t



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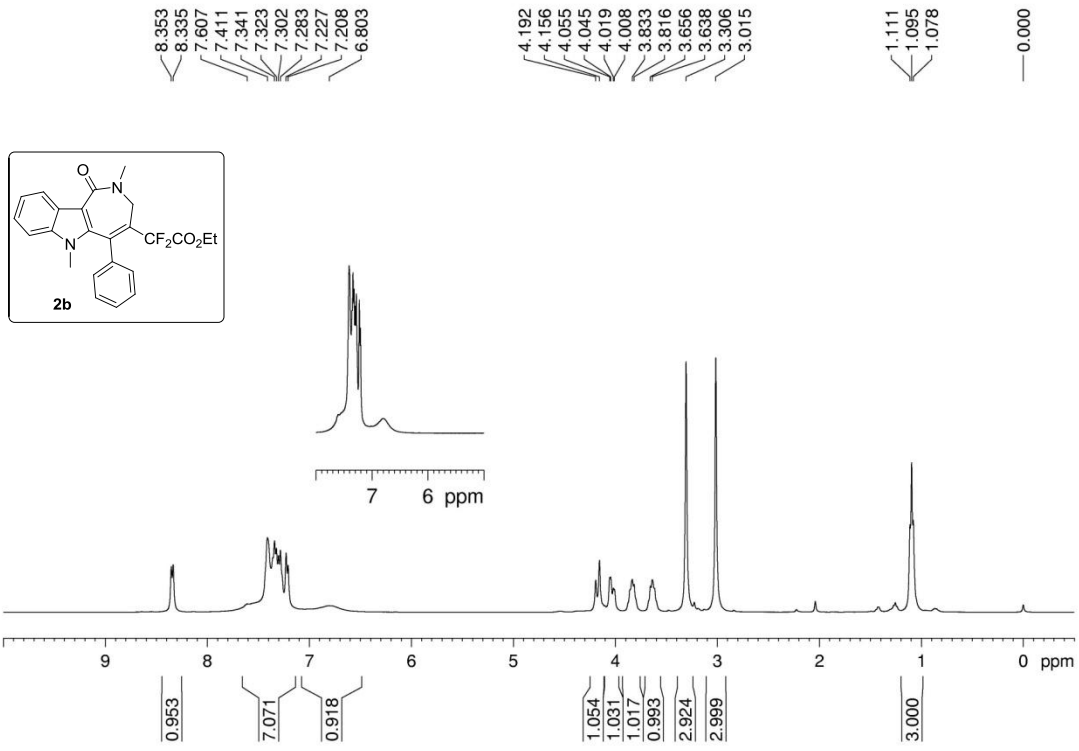
−95.559
O
N
N
CF2CO2Et
2a
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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8.335
7.607
7.411
7.341
7.323
7.302
7.283
7.227
7.208
6.803
4.192
4.156
4.055
4.045
4.019
4.008
3.833
3.816
3.656
3.638
3.306
3.015
1.111
1.095
1.078
0.000
O
N
N
CF2CO2Et
2b
7
6 ppm
9
8
7
6
5
4
3
2
1
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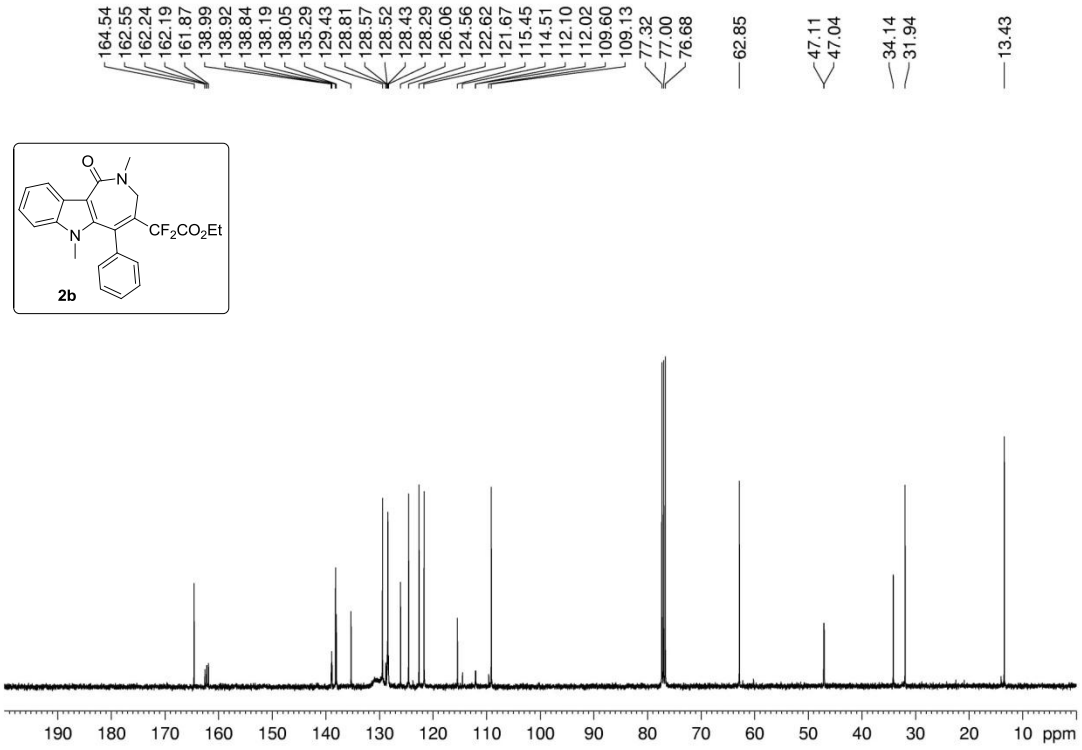
7.071
0.918
1.054
1.031
1.017
0.993
2.924
2.999
3.000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162.24
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138.99
138.92
138.84
138.19
138.05
135.29
129.43
128.81
128.57
128.52
128.43
128.29
126.06
124.56
122.62
121.67
115.45
114.51
112.10
112.02
109.60
109.13
77.32
77.00
76.68
62.85
47.11
47.04
34.14
31.94
13.43
O
N
N
CF2CO2Et
2b
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180
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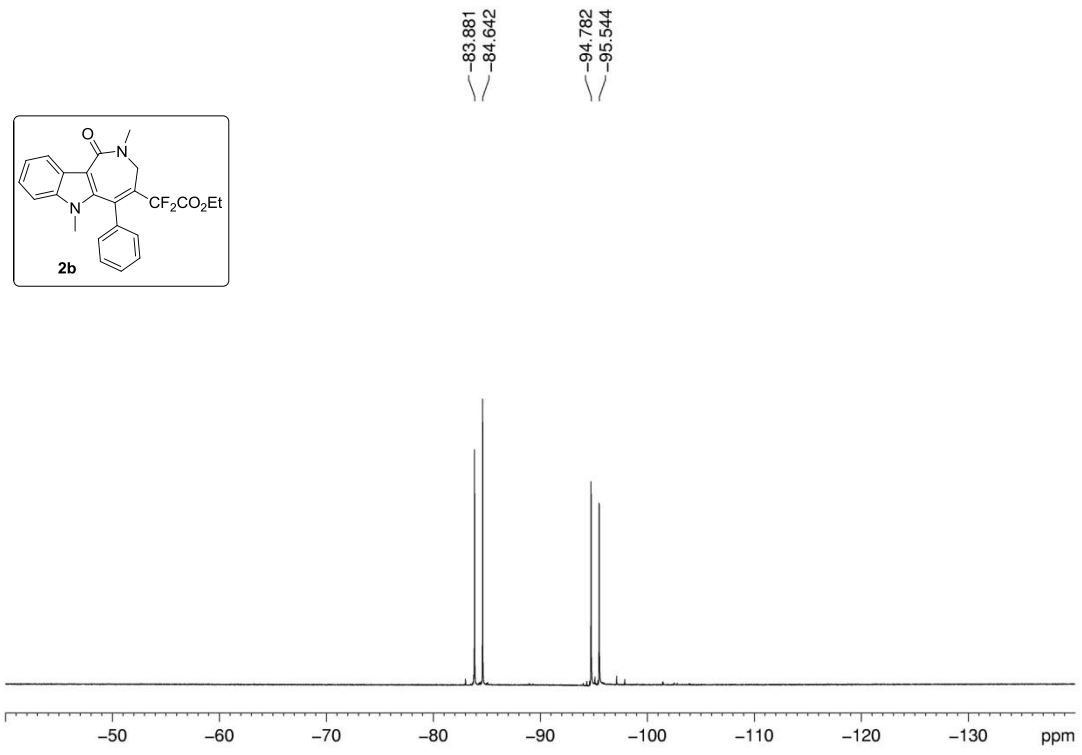
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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−94.782
−95.544
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N
CF2CO2Et
2b
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−60
−70
−80
−90
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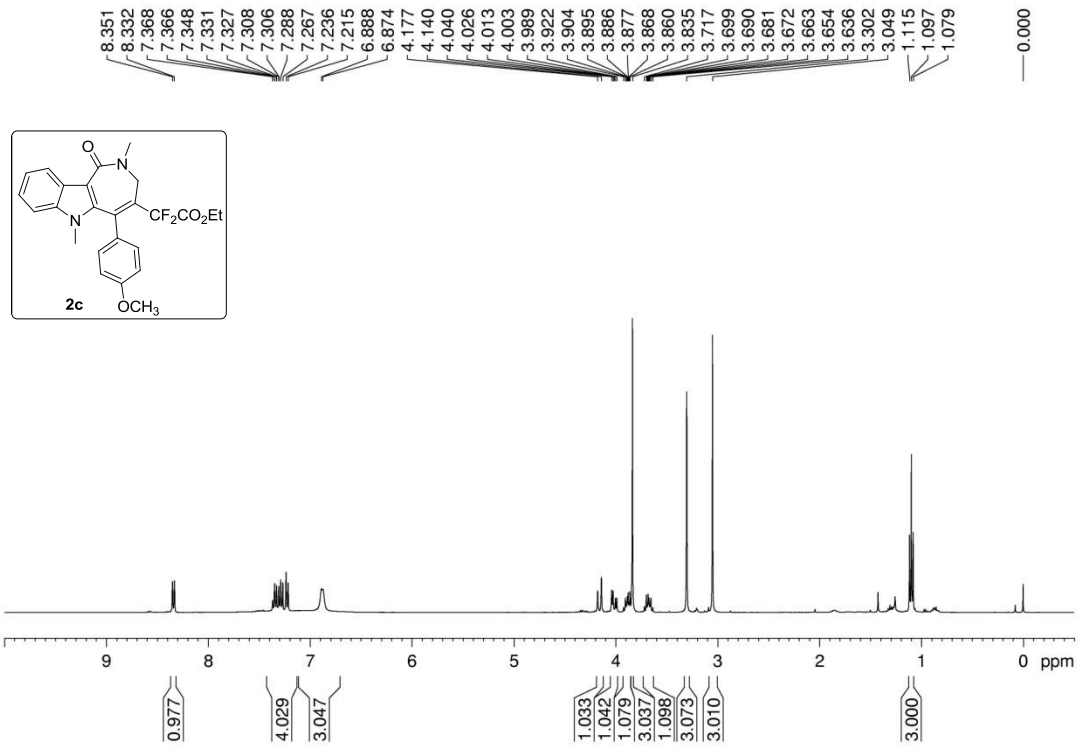
−110
−120
−130
ppm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7.327
7.308
7.306
7.288
7.267
7.236
7.215
6.888
6.874
4.177
4.140
4.040
4.026
4.013
4.003
3.989
3.922
3.904
3.895
3.886
3.877
3.868
3.860
3.835
3.717
3.699
3.690
3.681
3.672
3.663
3.654
3.636
3.302
3.049
1.115
1.097
1.079
0.000
CF2CO2Et
2c
OCH3
9
8
7
6
5
4
3
2
1
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3.047
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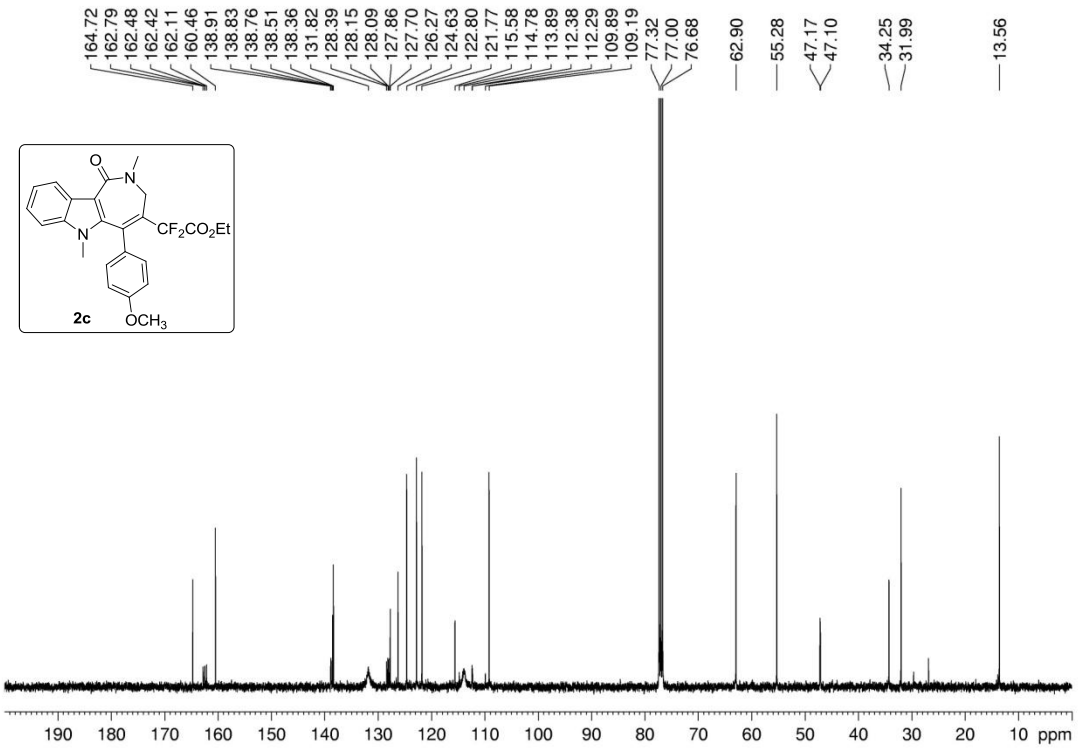
3.037
1.098
3.073
3.010
3.000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160.46
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138.83
138.76
138.51
138.36
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128.39
128.15
128.09
127.86
127.70
126.27
124.63
122.80
121.77
115.58
114.78
113.89
112.38
112.29
109.89
109.19
77.32
77.00
76.68
62.90
55.28
47.17
47.10
34.25
31.99
13.56
CF2CO2Et
2c
OCH3
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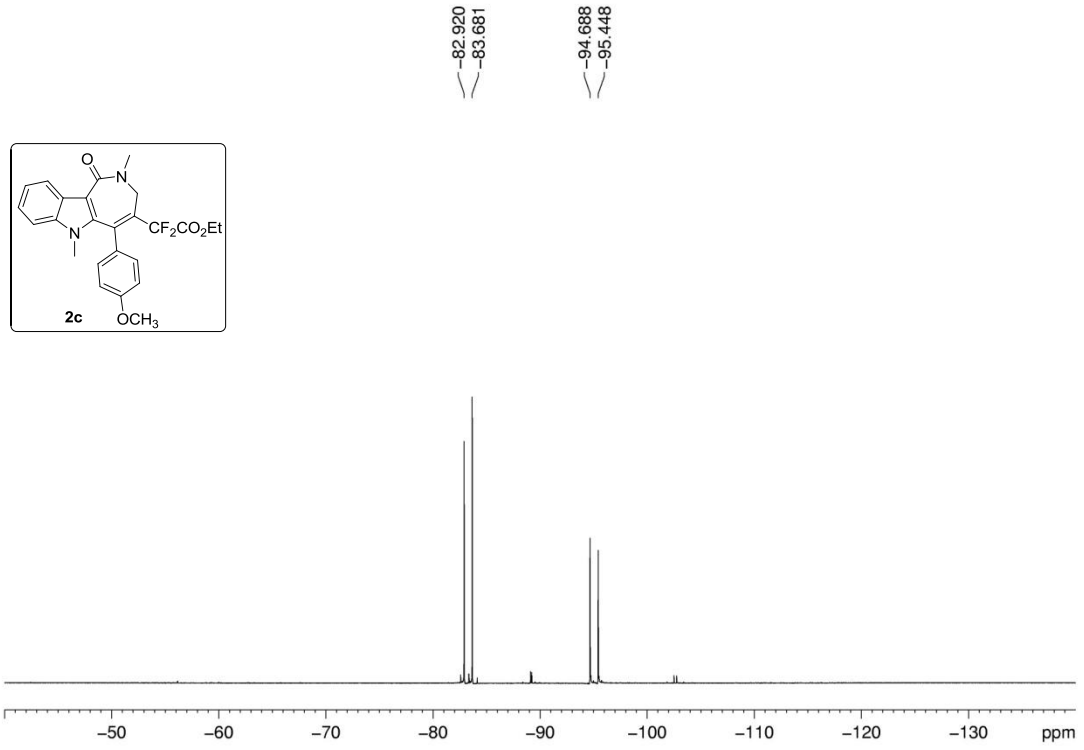
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm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-94.688
-95.448
2c
CF_2CO_2Et
OCH_3
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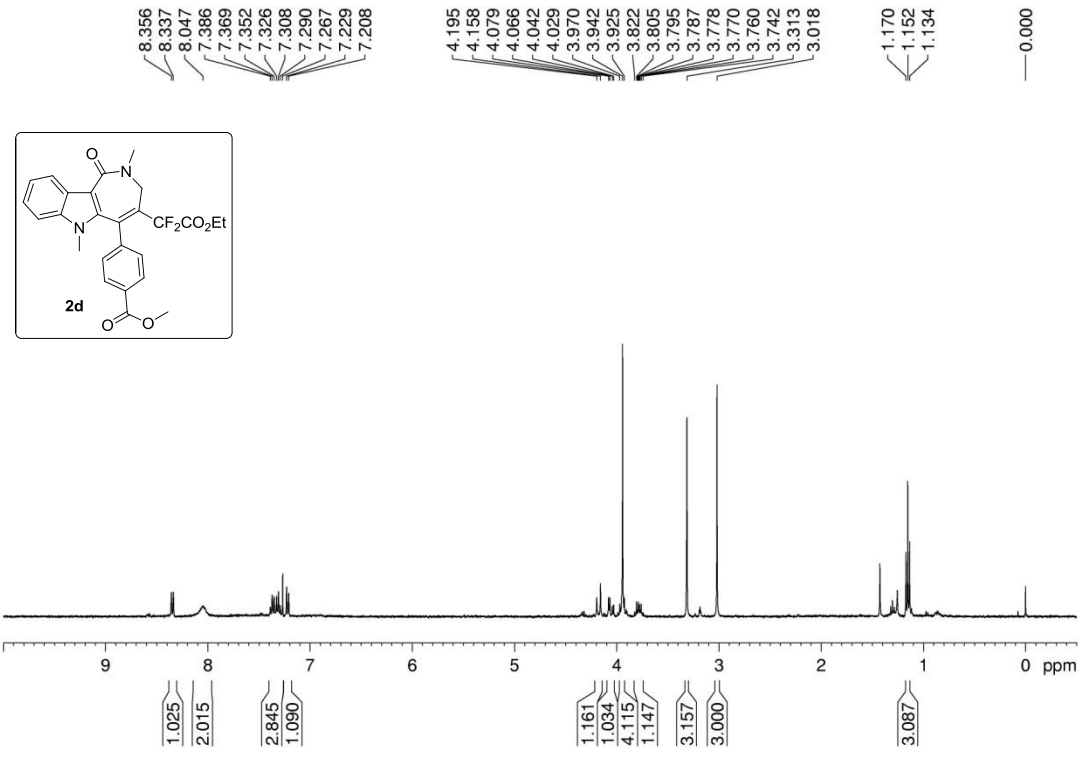
−60
−70
−80
−90
−100
−110
−120
−130
ppm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7.369
7.352
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7.308
7.290
7.267
7.229
7.208
4.195
4.158
4.079
4.066
4.042
4.029
3.970
3.942
3.925
3.822
3.805
3.795
3.787
3.778
3.770
3.760
3.742
3.313
3.018
1.170
1.152
1.134
0.000
2d
CF_2CO_2Et
9
8
7
6
5
4
3
2
1
0 ppm
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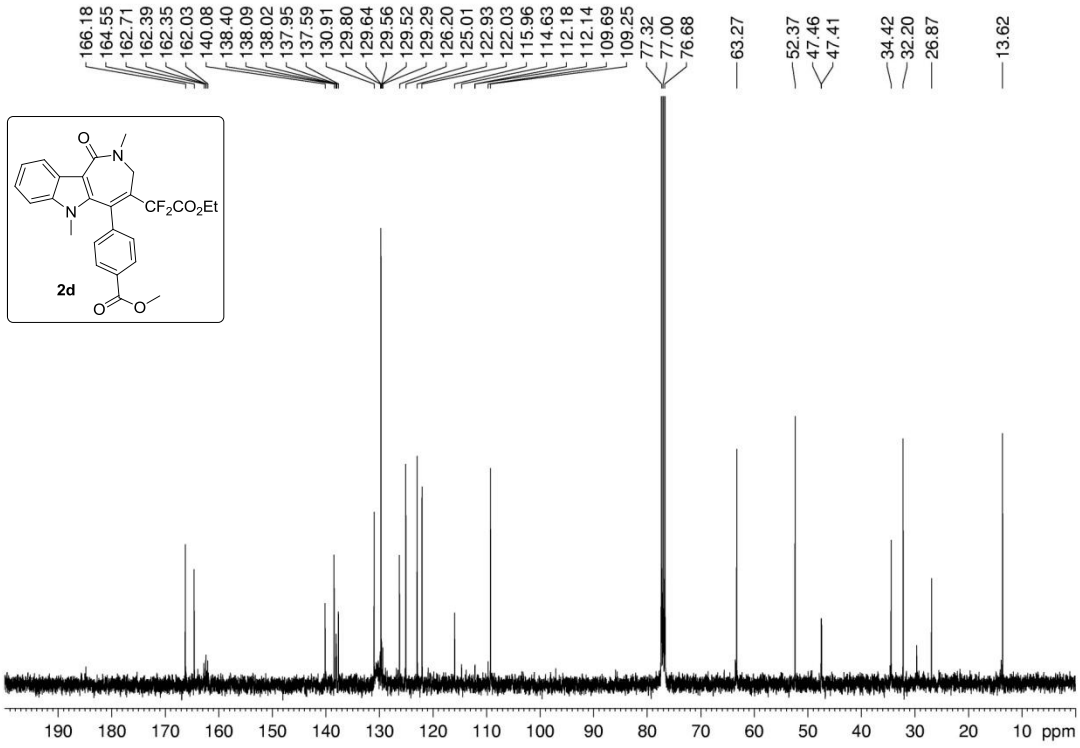
2.015
2.845
1.090
1.161
1.034
4.115
1.147
3.157
3.000
3.087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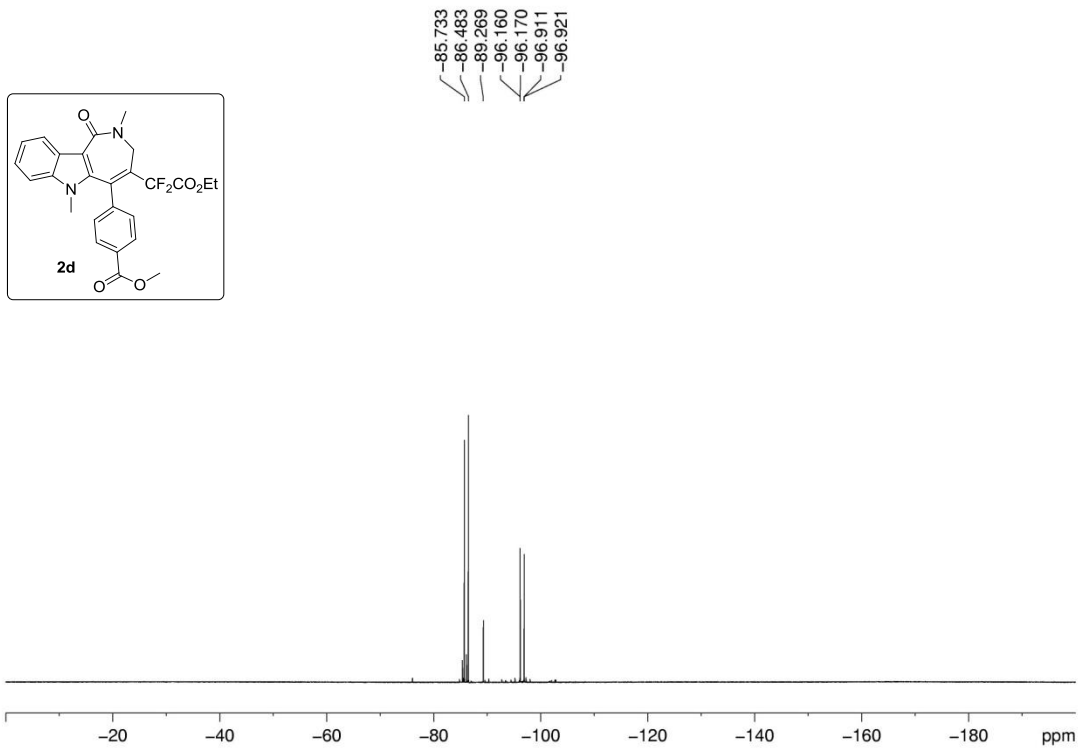
162.35
162.03
140.08
138.40
138.09
138.02
137.95
137.59
130.91
129.80
129.64
129.56
129.52
129.29
126.20
125.01
122.93
122.03
115.96
114.63
112.18
112.14
109.69
109.25
77.32
77.00
76.68
63.27
52.37
47.46
47.41
34.42
32.20
26.87
13.62
2d
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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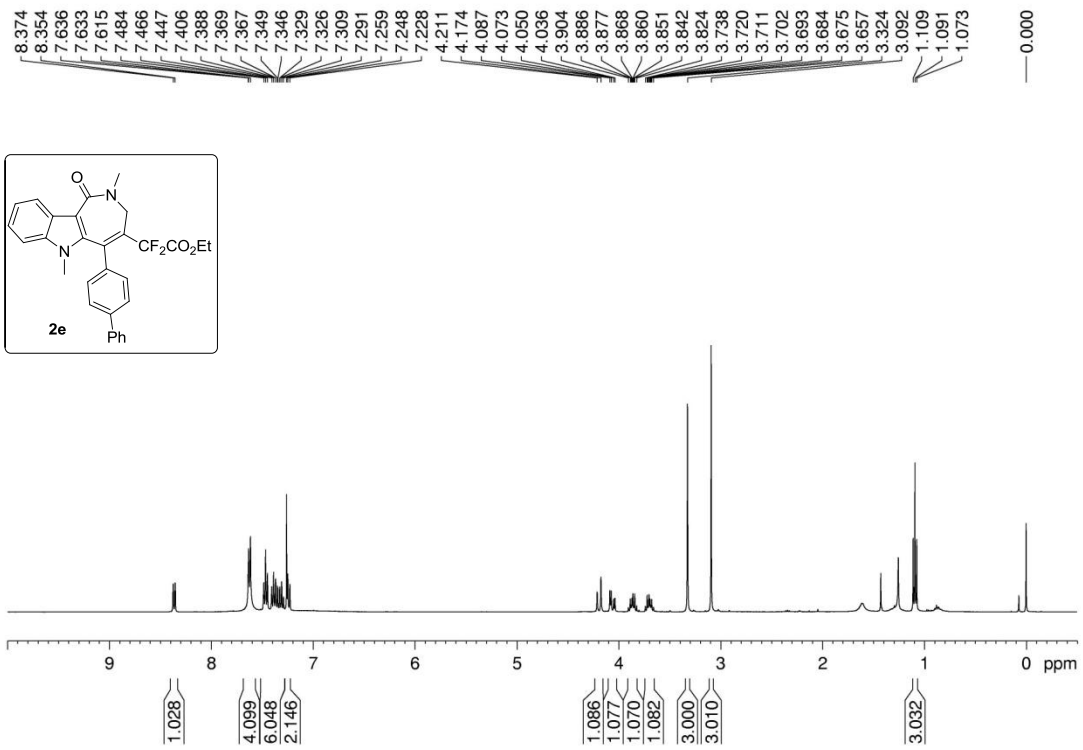
-86.483
-89.269
-96.160
-96.170
-96.911
-96.921
2d
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm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7.484
7.466
7.447
7.406
7.388
7.369
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7.349
7.346
7.329
7.326
7.309
7.291
7.259
7.248
7.228
4.211
4.174
4.087
4.073
4.050
4.036
3.904
3.886
3.877
3.868
3.860
3.851
3.842
3.824
3.738
3.720
3.711
3.702
3.693
3.684
3.675
3.657
3.324
3.092
1.109
1.091
1.073
0.000
CF2CO2Et
2e
Ph
9
8
7
6
5
4
3
2
1
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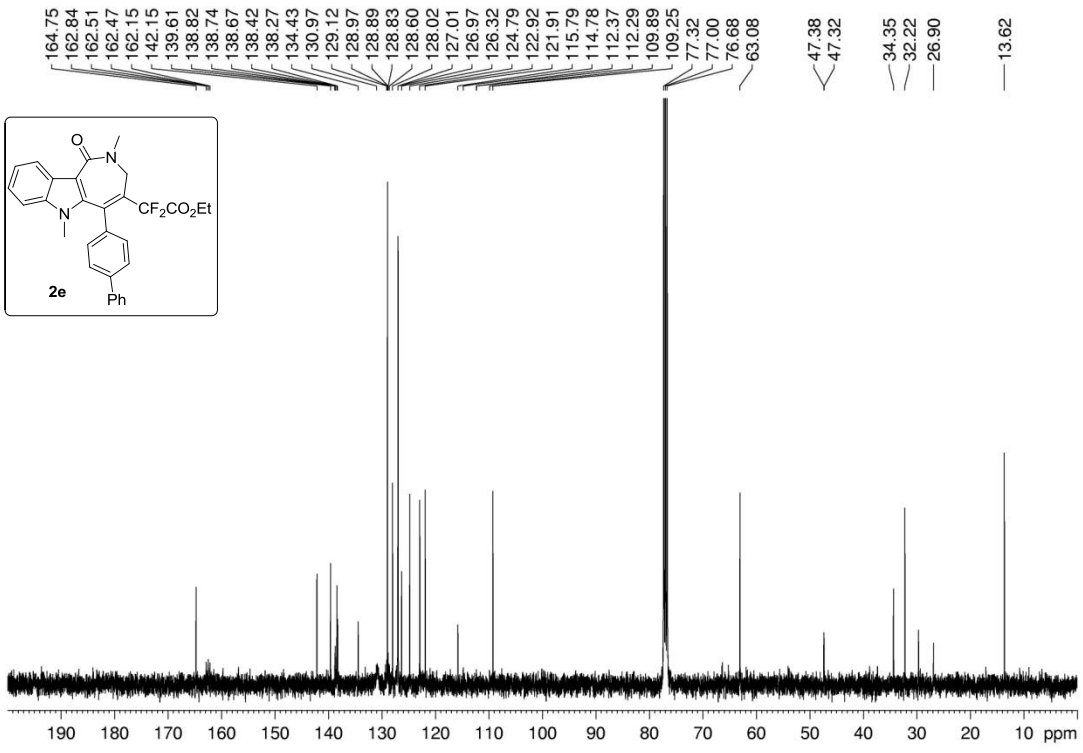
3.032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138.82
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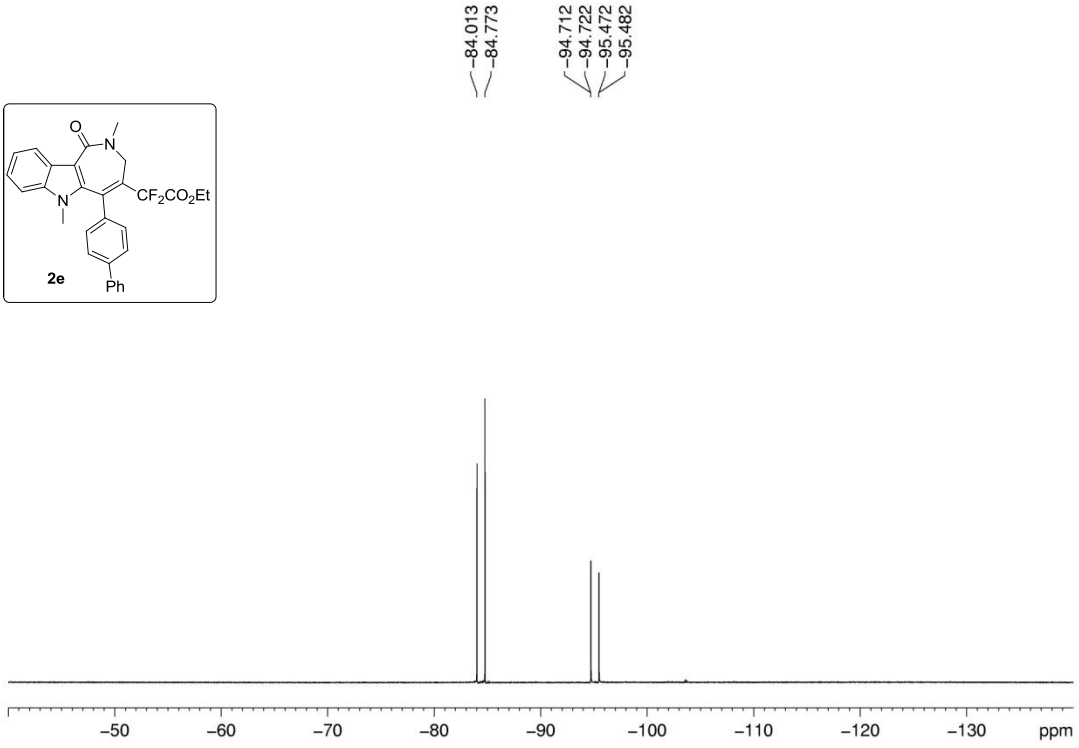
138.27
134.43
130.97
129.12
128.97
128.89
128.83
128.60
128.02
127.01
126.97
126.32
124.79
122.92
121.91
115.79
114.78
112.37
112.29
109.89
109.25
77.32
77.00
76.68
63.08
47.38
47.32
34.35
32.22
26.90
13.62
CF2CO2Et
2e
Ph
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm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O
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N
CF2CO2Et
2e
Ph
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-80
-90
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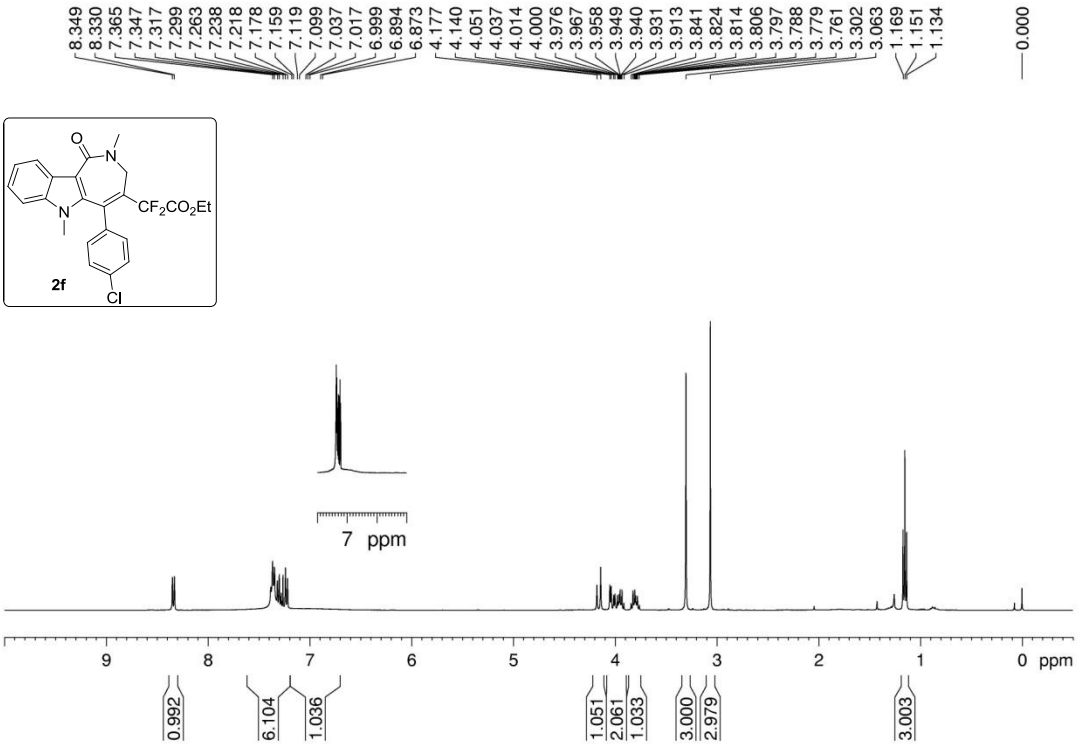
-130
ppm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7.299
7.263
7.238
7.218
7.178
7.159
7.119
7.099
7.037
7.017
6.999
6.894
6.873
4.177
4.140
4.051
4.037
4.014
4.000
3.976
3.967
3.958
3.949
3.940
3.931
3.913
3.841
3.824
3.814
3.806
3.797
3.788
3.779
3.761
3.302
3.063
1.169
1.151
1.134
0.000
O
N
N
CF2CO2Et
2f
Cl
7 ppm
9
8
7
6
5
4
3
2
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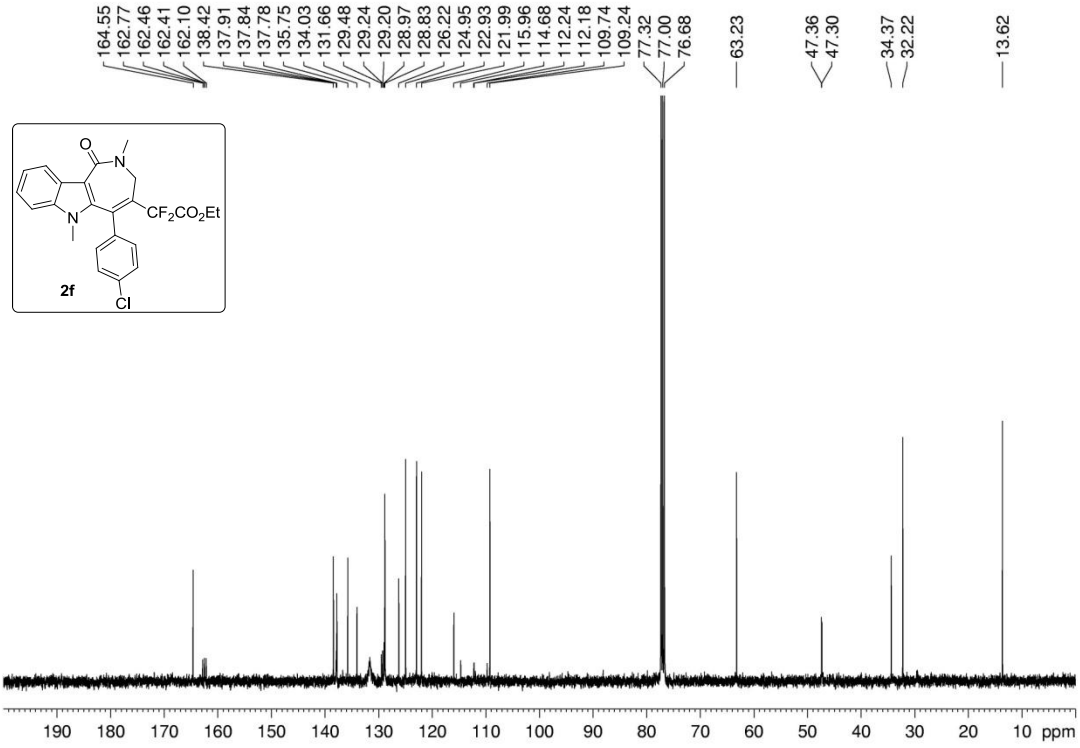
3.003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137.84
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134.03
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129.48
129.24
129.20
128.97
128.83
126.22
124.95
122.93
121.99
115.96
114.68
112.24
112.18
109.74
109.24
77.32
77.00
76.68
63.23
47.36
47.30
34.37
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O
N
N
CF2CO2Et
Cl
2f
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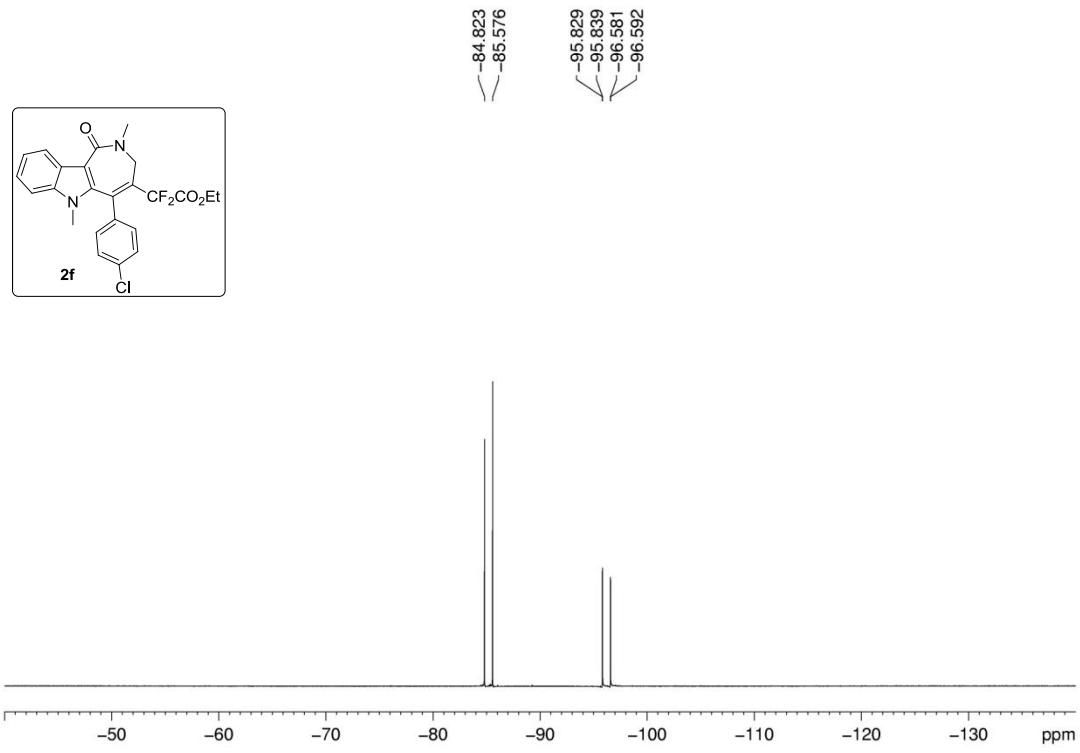
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-95.839
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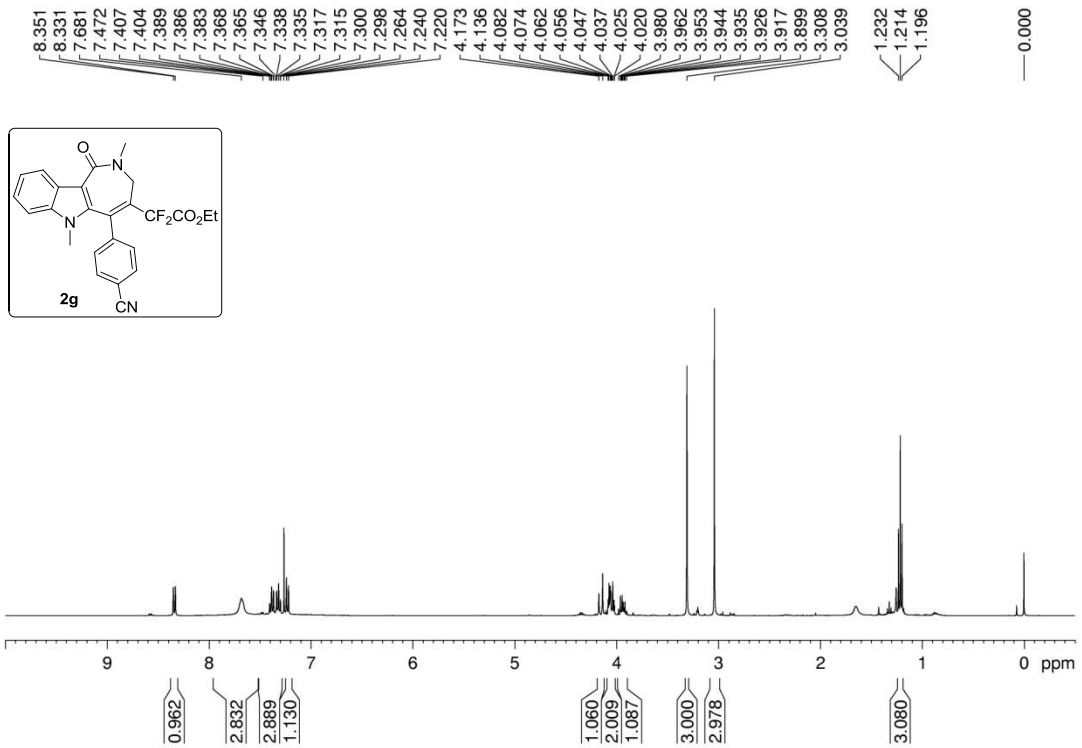
-96.592
O
N
N
CF2CO2Et
Cl
2f
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm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7.383
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7.365
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7.220
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4.136
4.082
4.074
4.062
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4.037
4.025
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3.953
3.944
3.935
3.926
3.917
3.899
3.308
3.039
1.232
1.214
1.196
0.000
O
N
CF2CO2Et
N
2g
CN
9
8
7
6
5
4
3
2
1
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2.009
1.087
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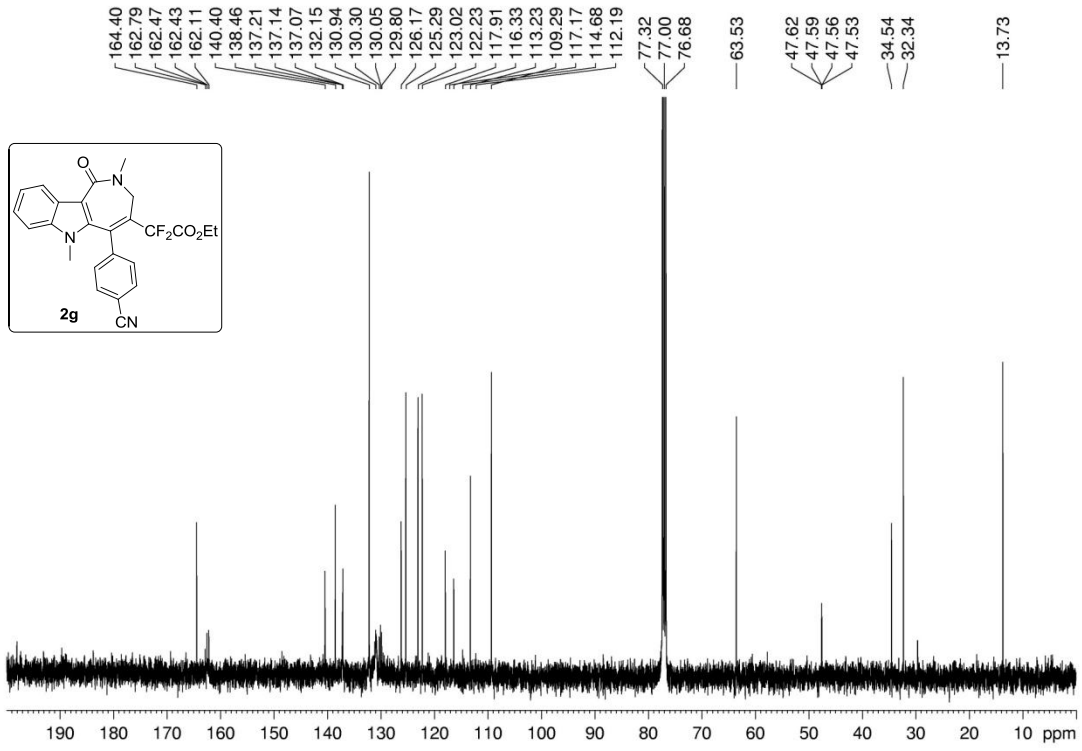
2.978
3.080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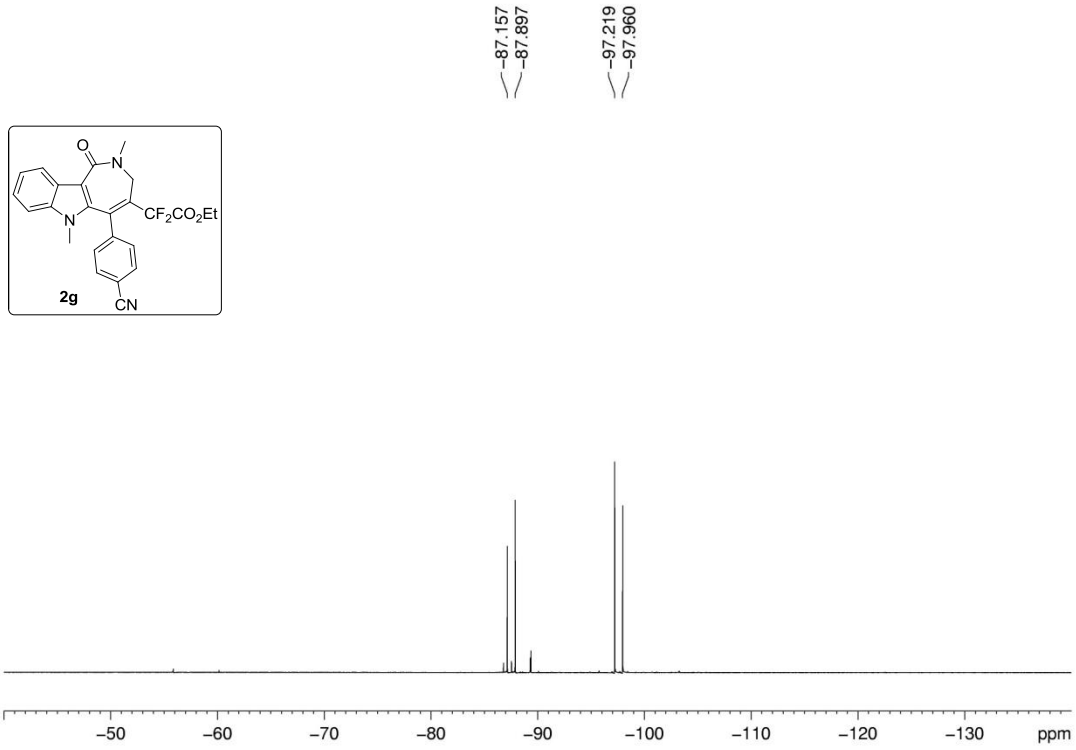
137.21
137.14
137.07
132.15
130.94
130.30
130.05
129.80
126.17
125.29
123.02
122.23
117.91
116.33
113.23
109.29
117.17
114.68
112.19
77.32
77.00
76.68
63.53
47.62
47.59
47.56
47.53
34.54
32.34
13.73
O
N
CF2CO2Et
N
2g
CN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm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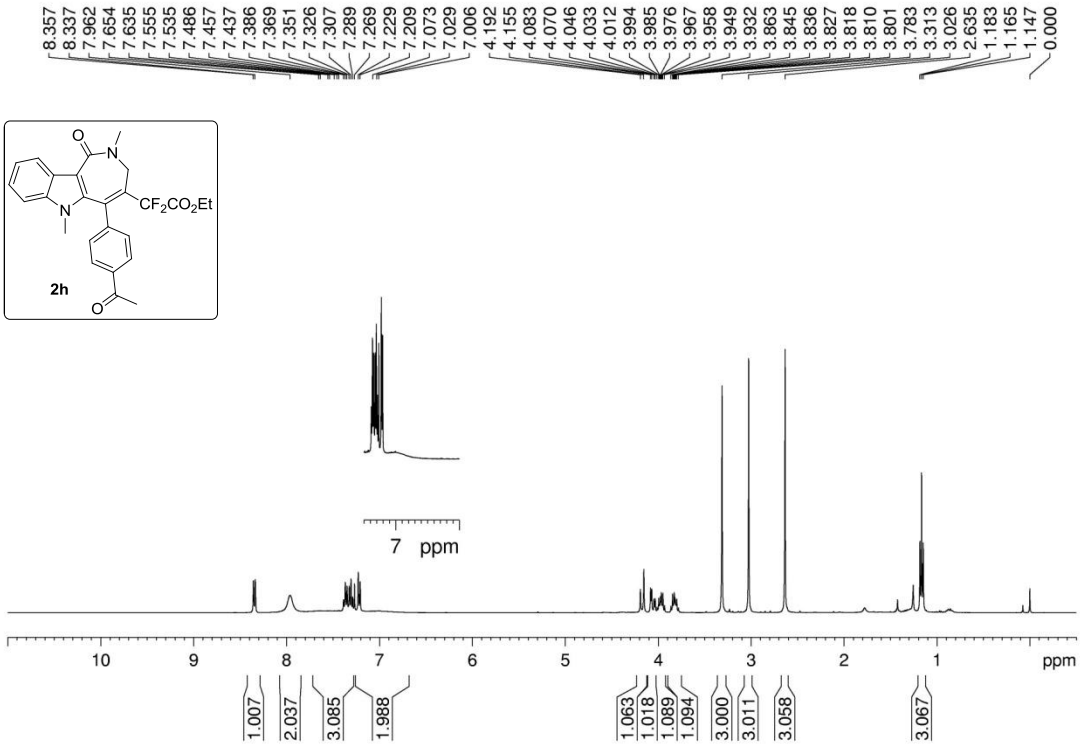
−97.960
O
N
N
CF2CO2Et
2g
CN
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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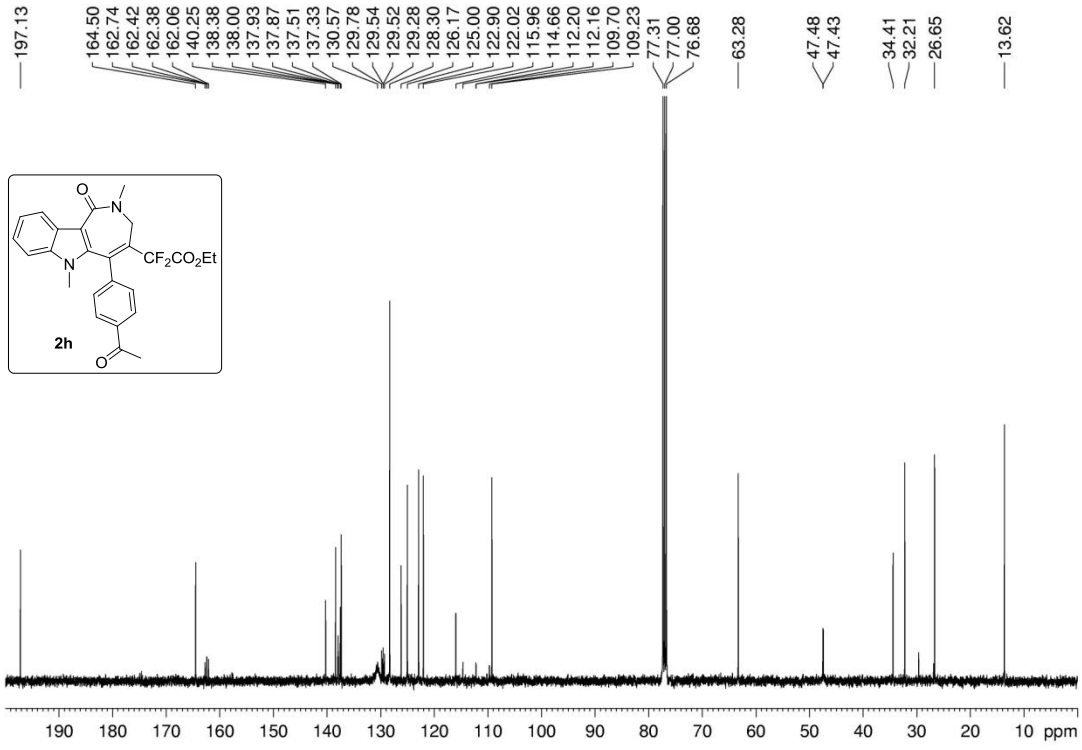
8.337
7.962
7.654
7.635
7.555
7.535
7.486
7.457
7.437
7.386
7.369
7.351
7.326
7.307
7.289
7.269
7.229
7.209
7.073
7.029
7.006
4.192
4.155
4.083
4.070
4.046
4.033
4.012
3.994
3.985
3.976
3.967
3.958
3.949
3.932
3.863
3.845
3.836
3.827
3.818
3.810
3.801
3.783
3.313
3.026
2.635
1.183
1.165
1.147
0.000
O
N
N
CF2CO2Et
2h
O
7 ppm
10
9
8
7
6
5
4
3
2
1
ppm
1.007
2.037
3.085
1.988
1.063
1.018
1.089
1.094
3.000
3.011
3.058
3.067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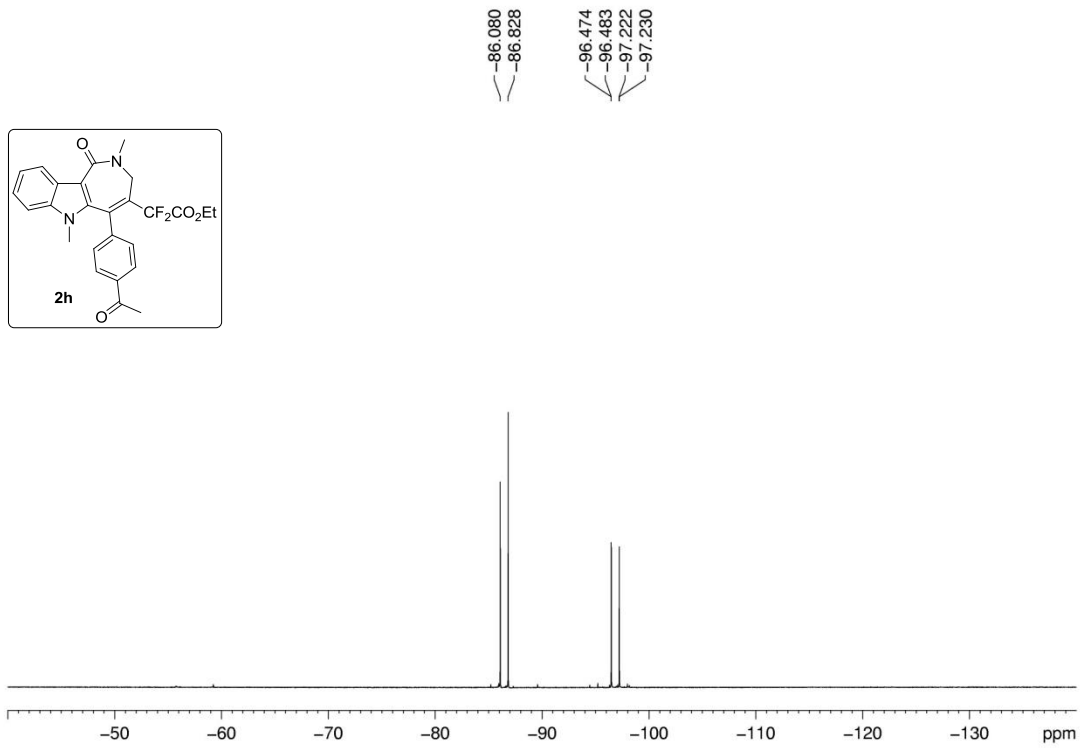
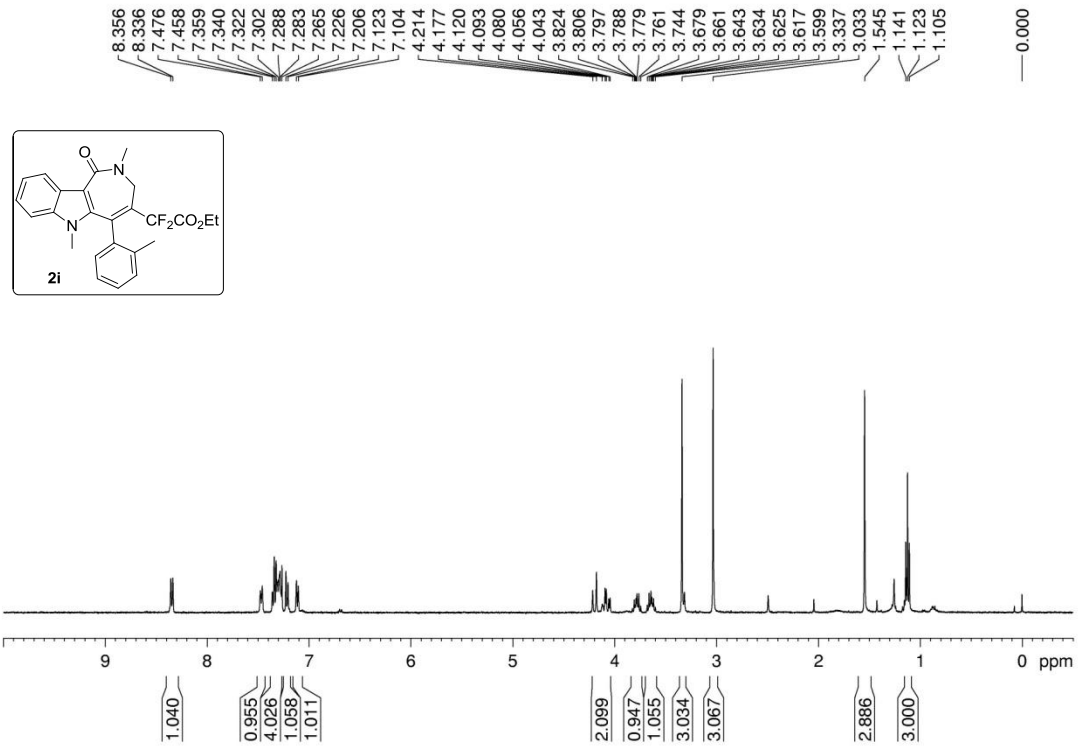
162.74
162.42
162.38
162.06
140.25
138.38
138.00
137.93
137.87
137.51
137.33
130.57
129.78
129.54
129.52
129.28
128.30
126.17
125.00
122.90
122.02
115.96
114.66
112.20
112.16
109.70
109.23
77.31
77.00
76.68
63.28
47.48
47.43
34.41
32.21
26.65
13.62
CF2CO2Et
2h
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


86.080
86.828
96.474
96.483
97.222
97.230
CF2CO2Et
2h
−50 −60 −70 −80 −90 −100 −110 −120 −130 ppm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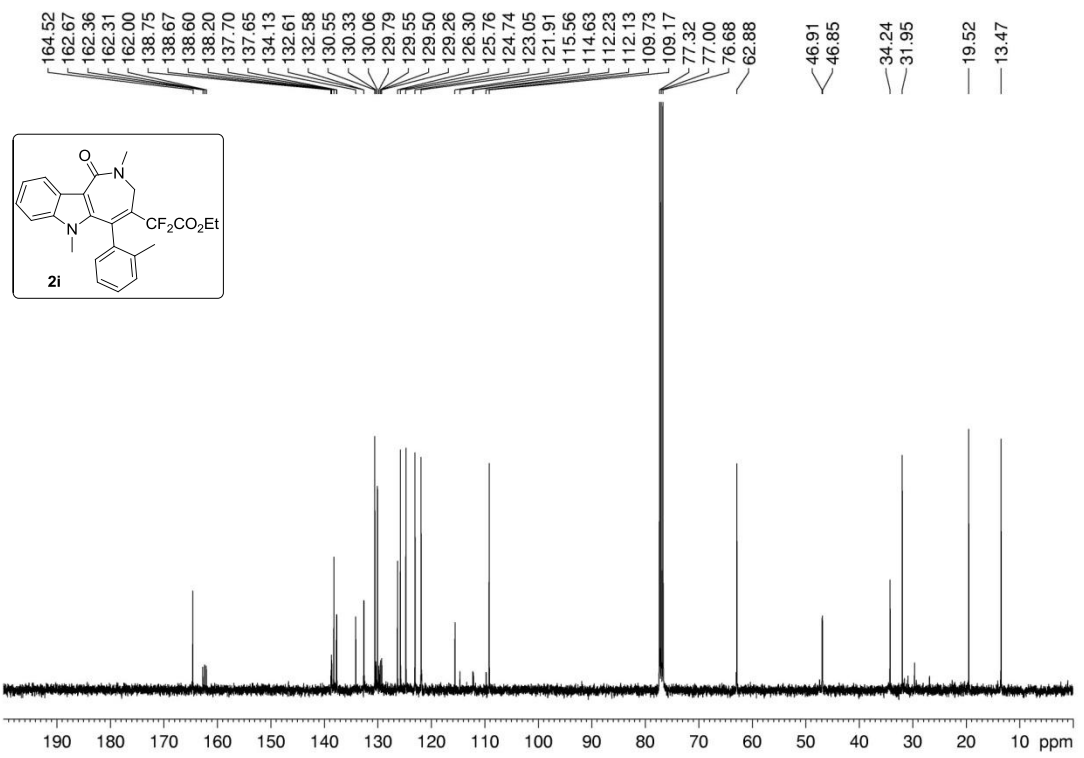
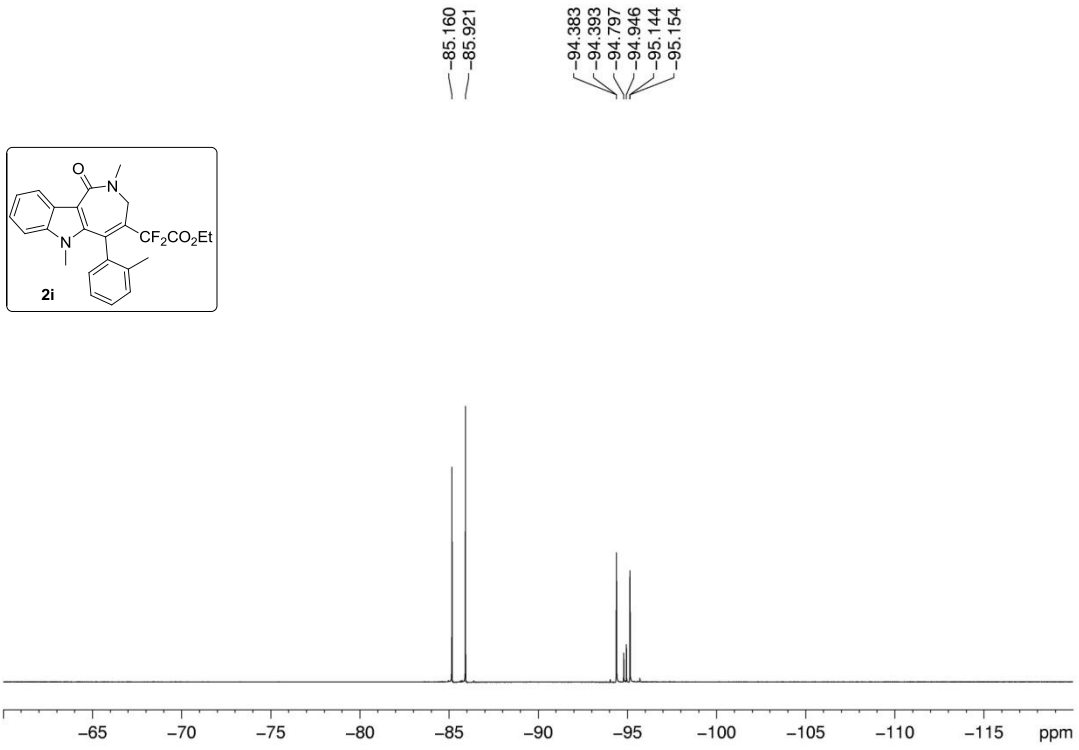
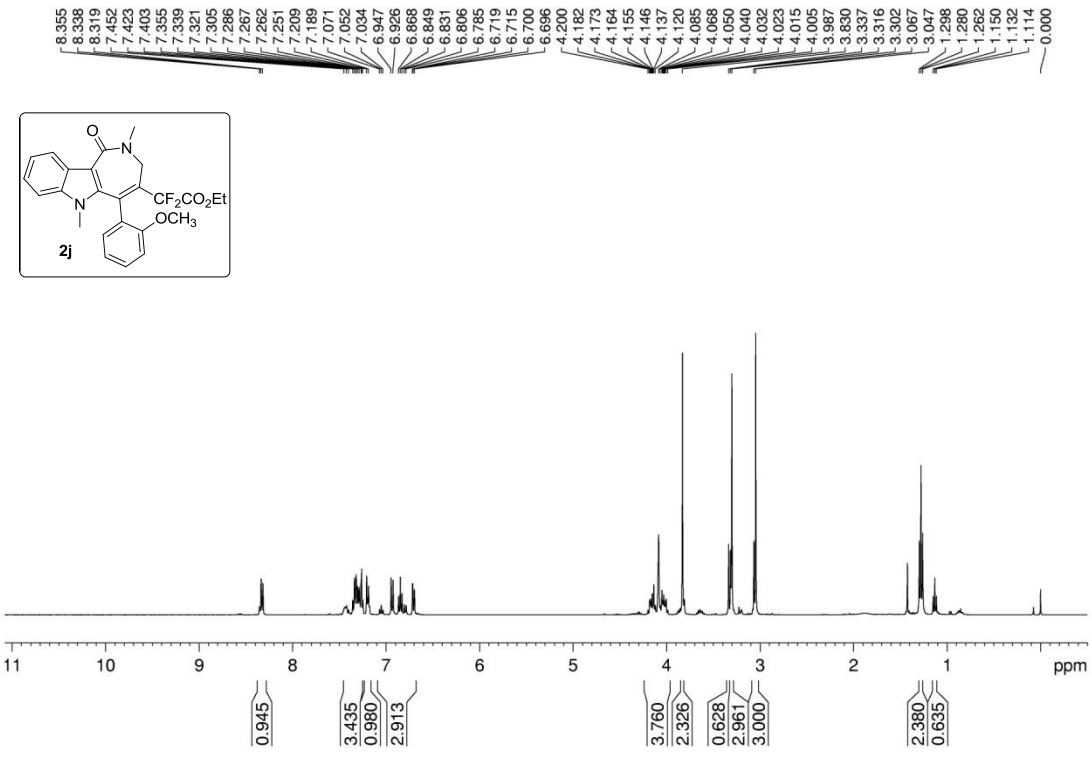
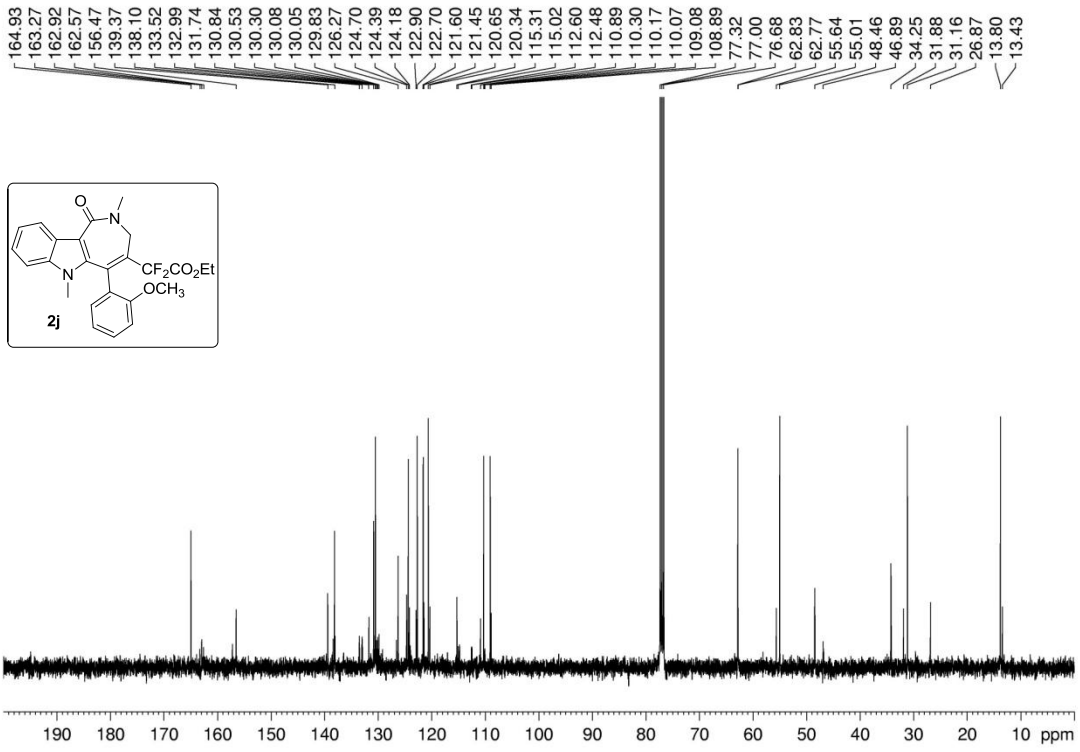
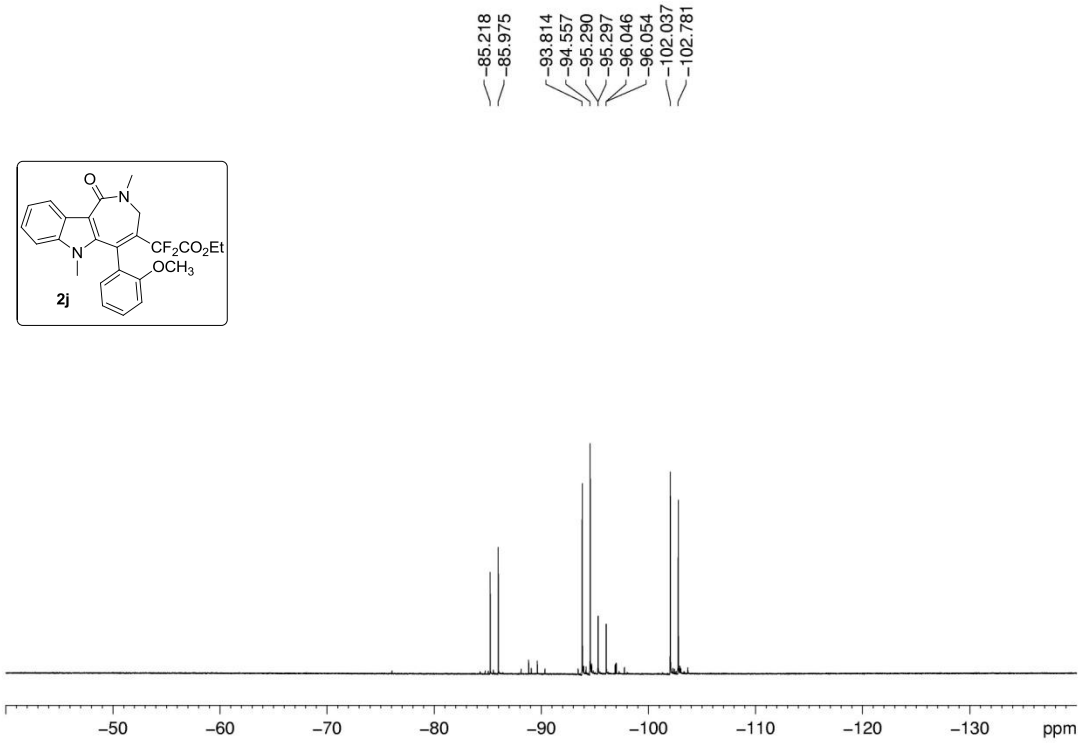
8.336
7.476
7.458
7.359
7.340
7.322
7.302
7.288
7.283
7.265
7.226
7.206
7.123
7.104
4.214
4.177
4.120
4.093
4.080
4.056
4.043
3.824
3.806
3.797
3.788
3.779
3.761
3.744
3.679
3.661
3.643
3.634
3.625
3.617
3.599
3.337
3.033
1.545
1.141
1.123
1.105
0.000
CF2CO2Et
2i
9
8
7
6
5
4
3
2
1
0 ppm
1.040
0.955
4.026
1.058
1.011
2.099
0.947
1.055
3.034
3.067
2.886
3.000

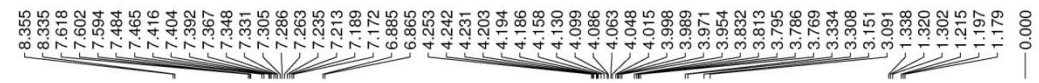

164.52
162.67
162.36
162.31
162.00
138.75
138.67
138.60
138.20
137.70
137.65
134.13
132.61
132.58
130.55
130.33
130.06
129.79
129.55
129.50
129.26
126.30
125.76
124.74
123.05
121.91
115.56
114.63
112.23
112.13
109.73
109.17
77.32
77.00
76.68
62.88
46.91
46.85
34.24
31.95
19.52
13.47
CF2CO2Et
2i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


-85.160
-85.921
-94.383
-94.393
-94.797
-94.946
-95.144
-95.154
O
N
N
CF2CO2Et
2i
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
ppm


8.355
8.338
8.319
7.452
7.423
7.403
7.355
7.339
7.321
7.305
7.286
7.267
7.262
7.251
7.209
7.189
7.071
7.052
7.034
6.947
6.926
6.868
6.849
6.831
6.806
6.785
6.719
6.715
6.700
6.696
4.200
4.182
4.173
4.164
4.155
4.146
4.137
4.120
4.085
4.068
4.050
4.040
4.032
4.023
4.015
4.005
3.987
3.830
3.337
3.316
3.302
3.067
3.047
1.298
1.280
1.262
1.150
1.132
1.114
0.000
O
N
N
CF2CO2Et
OCH3
2j
11
10
9
8
7
6
5
4
3
2
1
ppm
0.945
3.435
0.980
2.913
3.760
2.326
0.628
2.961
3.000
2.380
0.635


164.93
163.27
162.92
162.57
156.47
139.37
138.10
133.52
132.99
131.74
130.84
130.53
130.30
130.08
130.05
129.83
126.27
124.70
124.39
124.18
122.90
122.70
121.60
121.45
120.65
120.34
115.31
115.02
112.60
112.48
110.89
110.30
110.17
110.07
109.08
108.89
77.32
77.00
76.68
62.83
62.77
55.64
55.01
48.46
46.89
34.25
31.88
31.16
26.87
13.80
13.43
O
N
N
CF2CO2Et
OCH3
2j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


−85.218
−85.975
−93.814
−94.557
−95.290
−95.297
−96.046
−96.054
−102.037
−102.781
O
N
N
CF2CO2Et
OCH3
2j
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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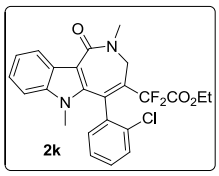
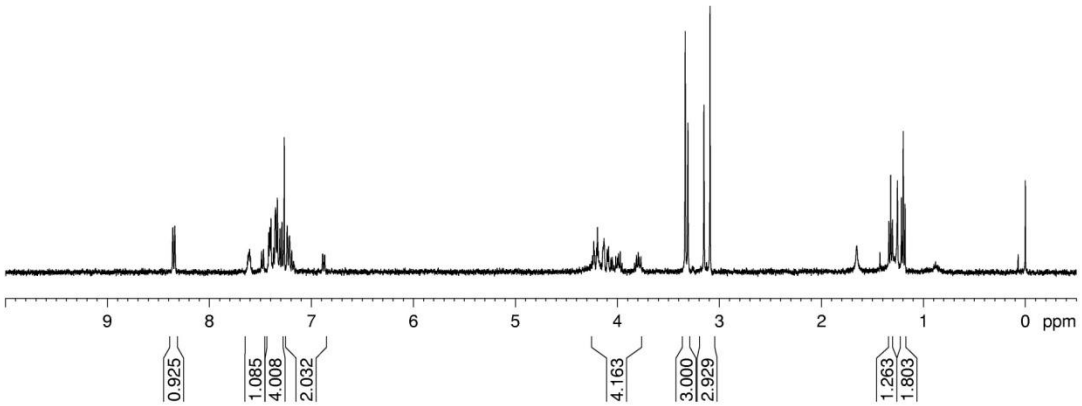
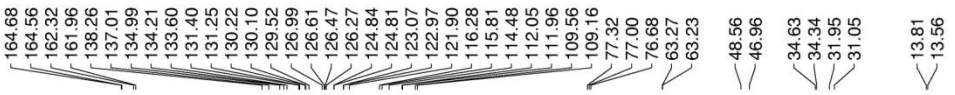
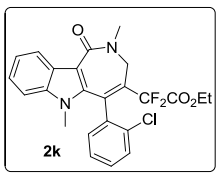
8.335
7.618
7.602
7.594
7.484
7.465
7.416
7.404
7.392
7.367
7.348
7.331
7.305
7.286
7.263
7.235
7.213
7.189
7.172
6.885
6.865
4.253
4.242
4.231
4.203
4.194
4.186
4.158
4.130
4.099
4.086
4.063
4.048
4.015
3.998
3.989
3.971
3.954
3.832
3.813
3.795
3.786
3.769
3.334
3.308
3.151
3.091
1.338
1.320
1.302
1.215
1.197
1.179
0.000

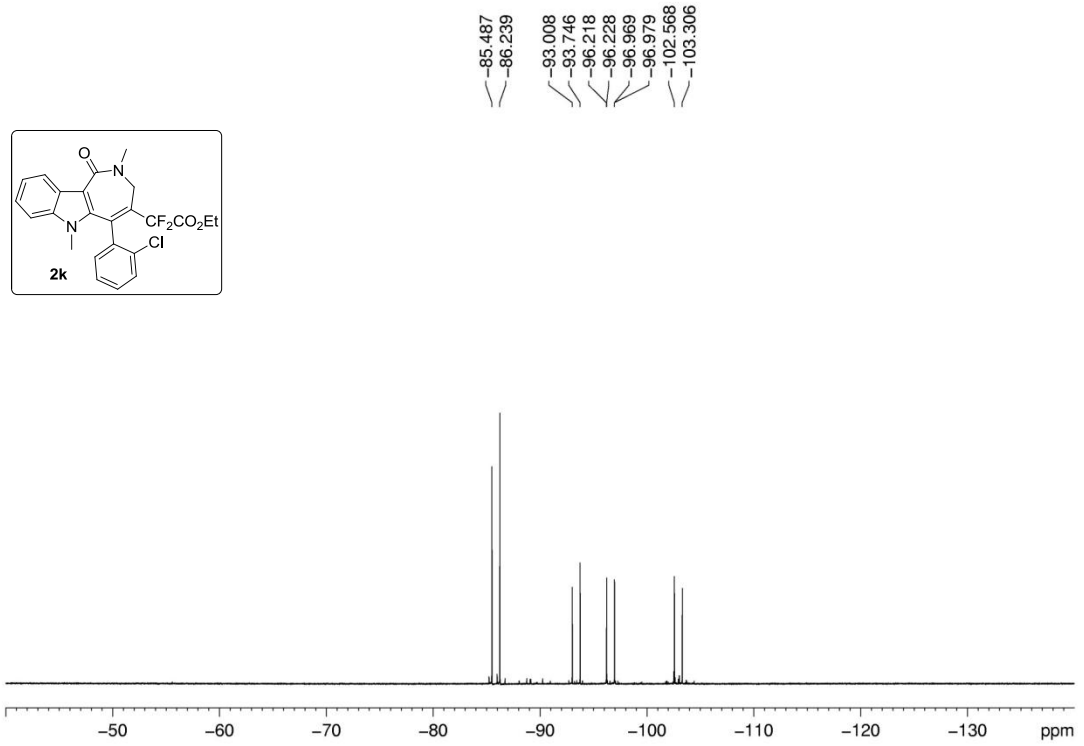

O
N
CF2CO2Et
N
Cl
2k

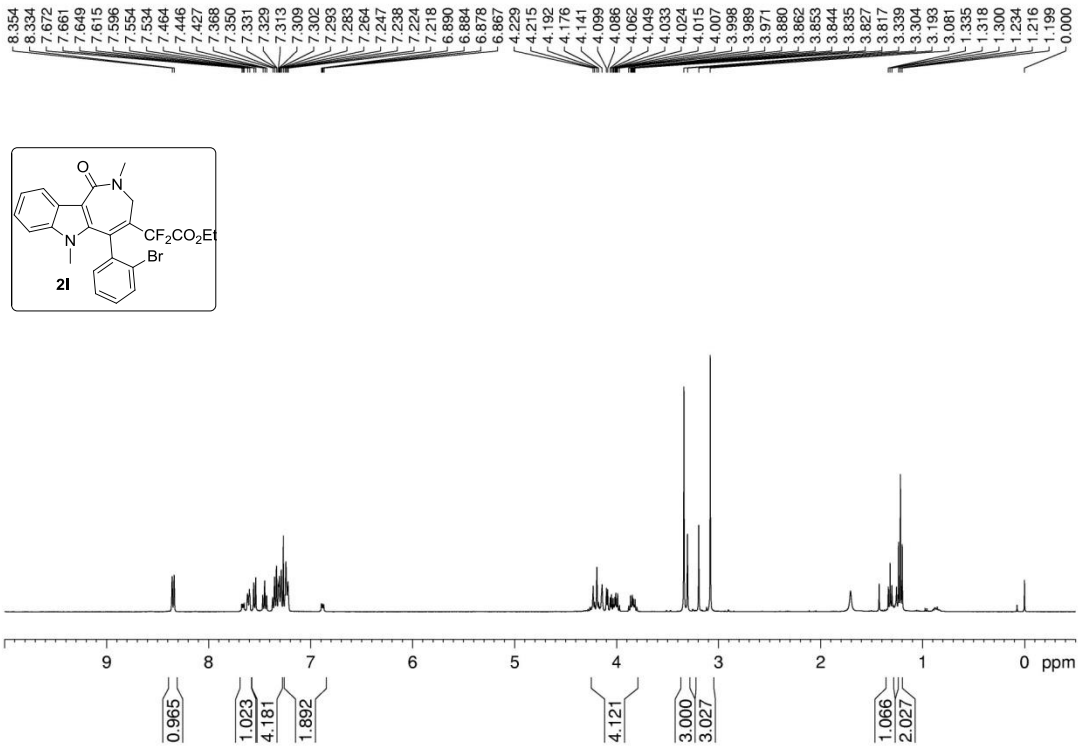

9
8
7
6
5
4
3
2
1
0 ppm
0.925
1.085
4.008
2.032
4.163
3.000
2.929
1.263
1.803


164.68
164.56
162.32
161.96
138.26
137.01
134.99
134.21
133.60
131.40
131.25
130.22
130.10
129.52
126.99
126.61
126.47
126.27
124.84
124.81
123.07
122.97
121.90
116.28
115.81
114.48
112.05
111.96
109.56
109.16
77.32
77.00
76.68
63.27
63.23
48.56
46.96
34.63
34.34
31.95
31.05
13.81
13.56


O
N
CF2CO2Et
N
Cl
2k

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


-85.487
-86.239
-93.008
-93.746
-96.218
-96.228
-96.969
-96.979
-102.568
-103.306
O
N
N
CF2CO2Et
Cl
2k
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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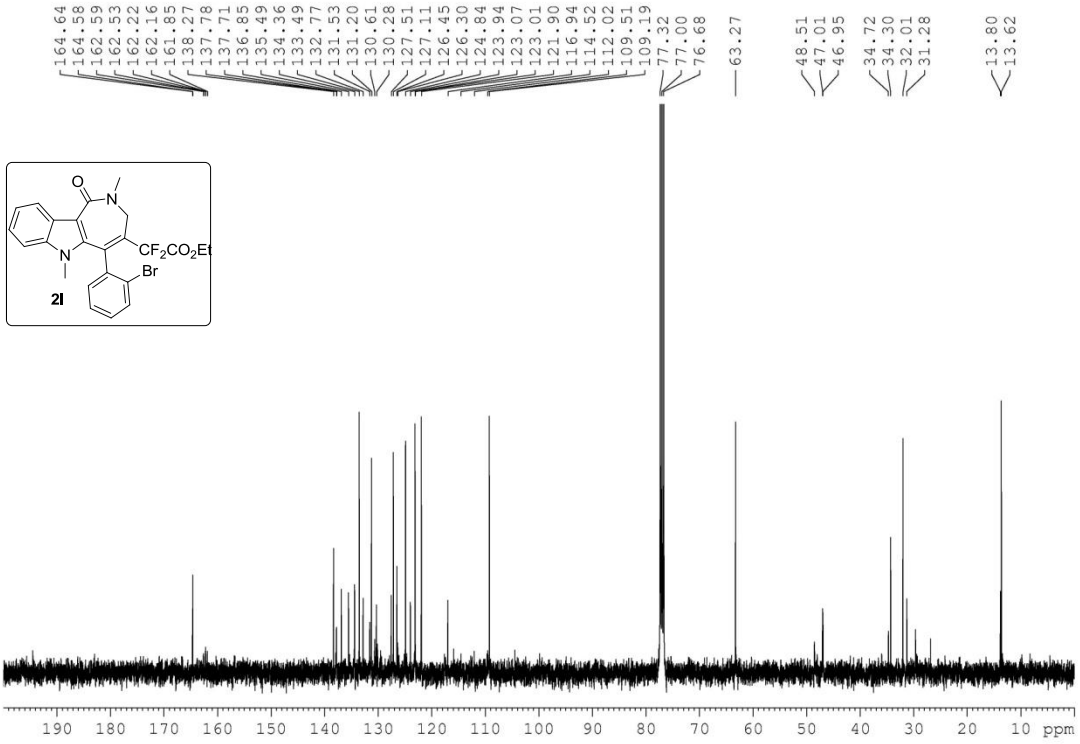
7.661
7.649
7.615
7.596
7.554
7.534
7.464
7.446
7.427
7.368
7.350
7.331
7.329
7.313
7.309
7.302
7.293
7.283
7.264
7.247
7.238
7.224
7.218
6.890
6.884
6.878
6.867
4.229
4.215
4.192
4.176
4.141
4.099
4.086
4.062
4.049
4.033
4.024
4.015
4.007
3.998
3.989
3.971
3.880
3.862
3.853
3.844
3.835
3.827
3.817
3.339
3.304
3.193
3.081
1.335
1.318
1.300
1.234
1.216
1.199
0.000
O
N
N
CF2CO2Et
Br
2l
9
8
7
6
5
4
3
2
1
0 ppm
0.965
1.023
4.181
1.892
4.121
3.000
3.027
1.066
2.027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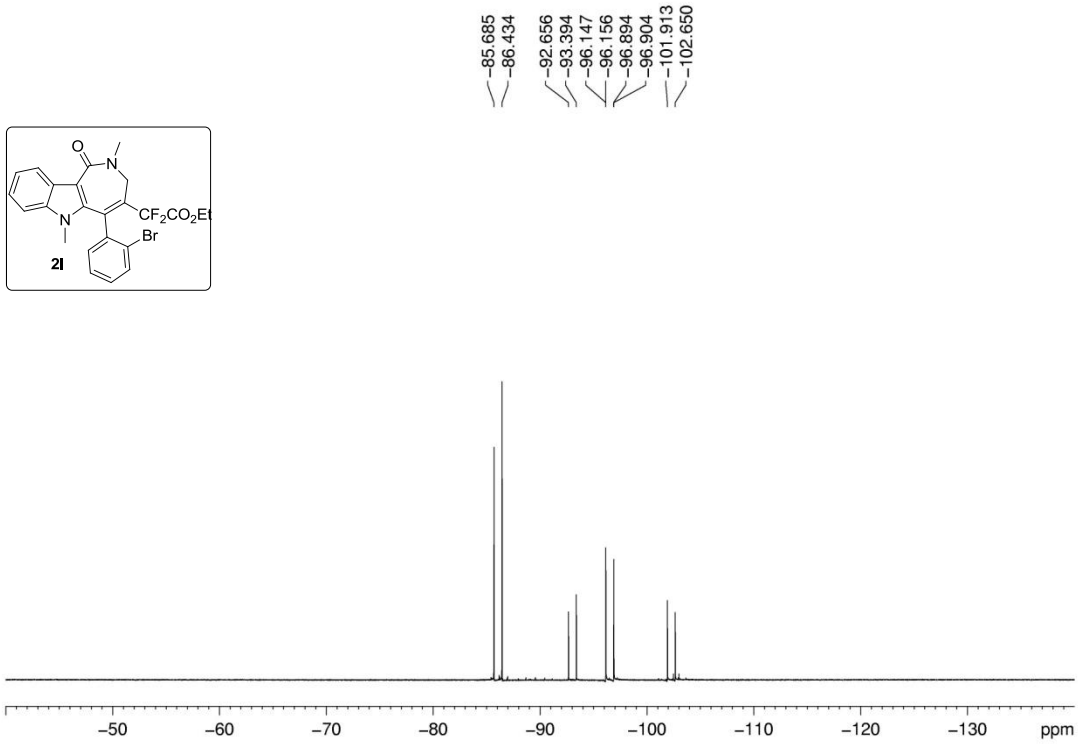
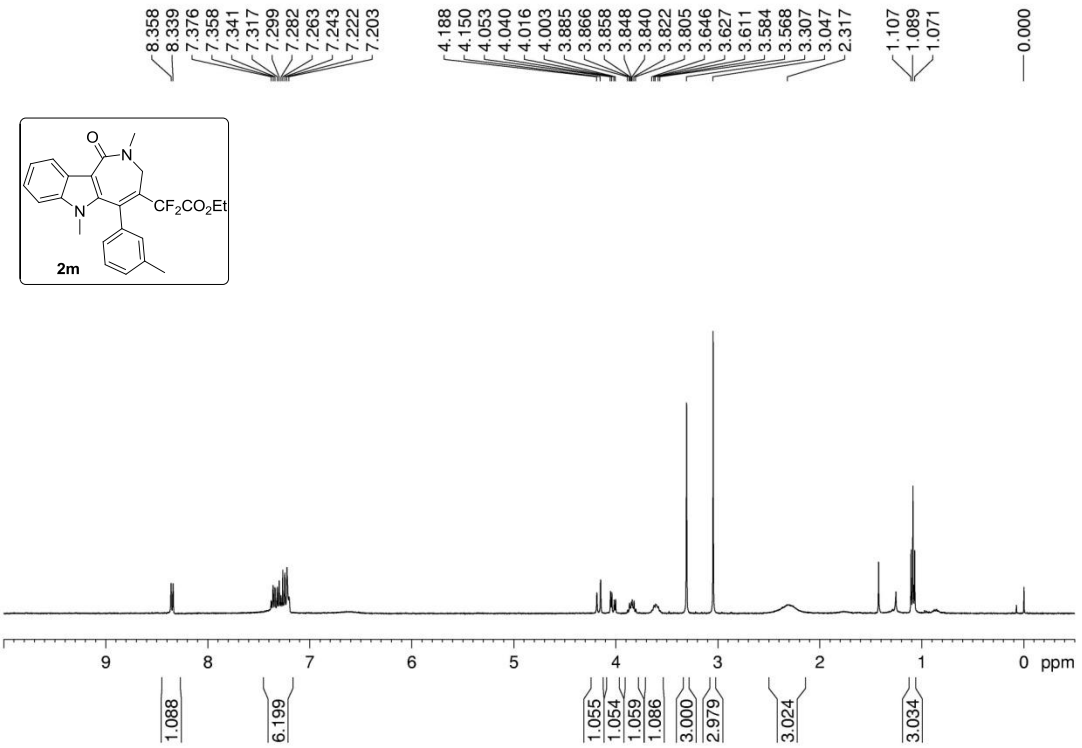
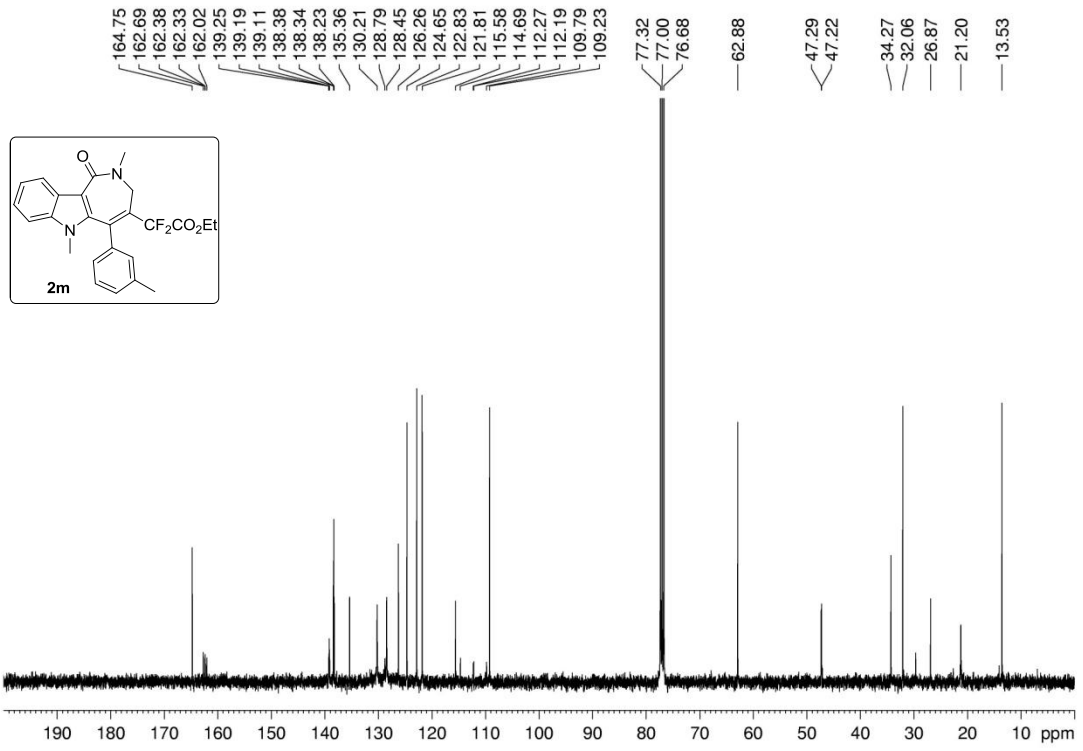
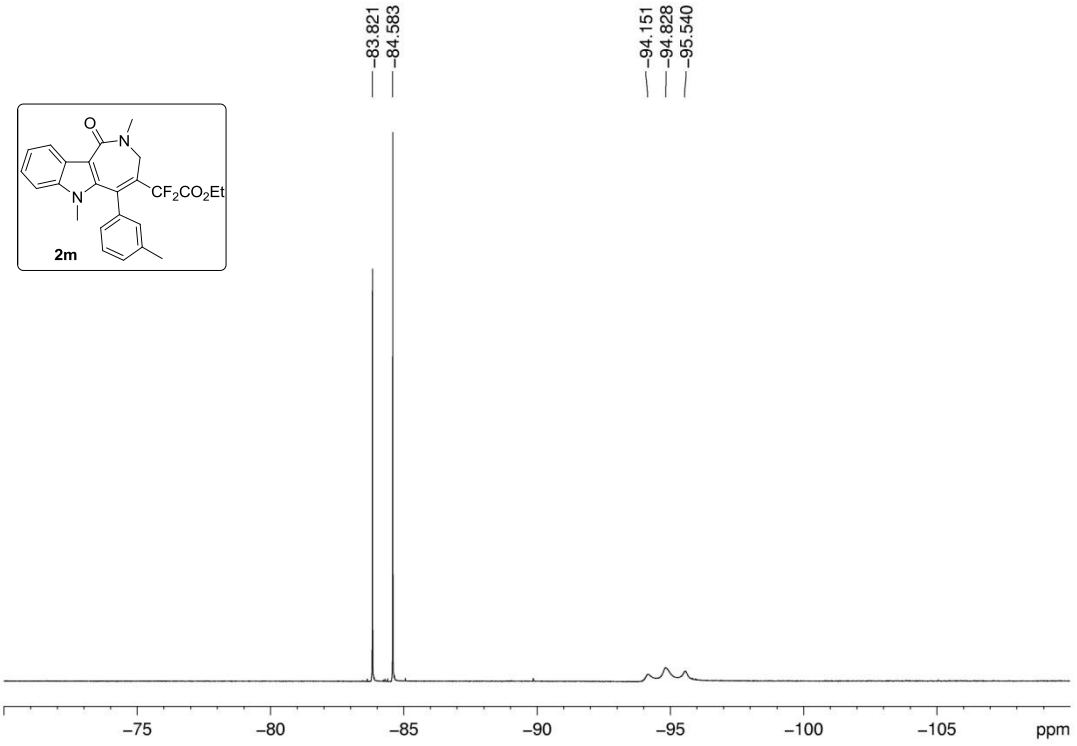
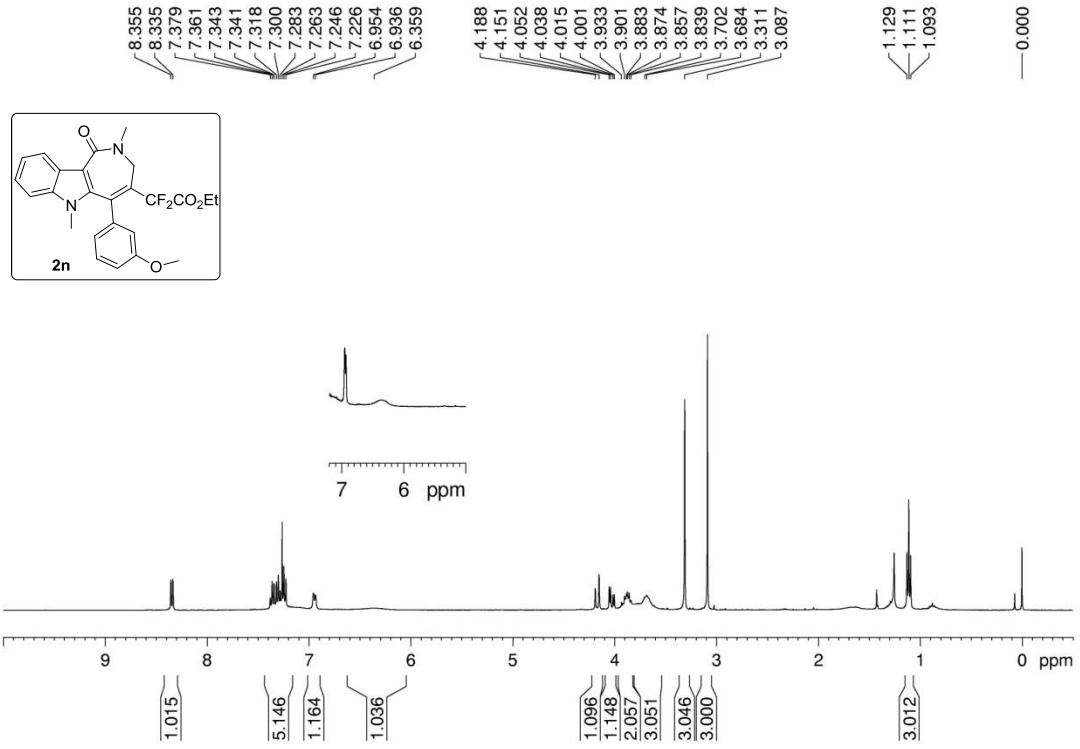
164.58
162.59
162.53
162.22
162.16
161.85
138.27
137.78
137.71
136.85
135.49
134.36
133.49
132.77
131.53
131.20
130.61
130.28
127.51
127.11
126.45
126.30
124.84
123.94
123.07
123.01
121.90
116.94
114.52
112.02
109.51
109.19
77.32
77.00
76.68
63.27
48.51
47.01
46.95
34.72
34.30
32.01
31.28
13.80
13.62
O
N
N
CF2CO2Et
Br
2l
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

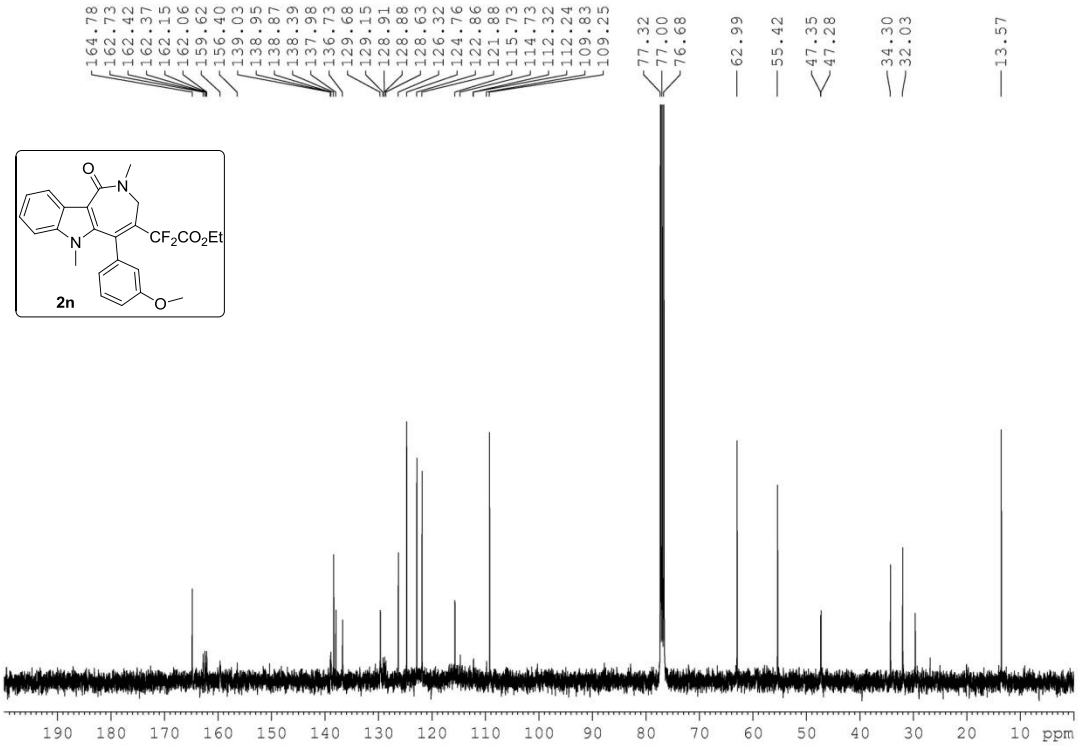

-85.685
-86.434
-92.656
-93.394
-96.147
-96.156
-96.894
-96.904
-101.913
-102.650
O
N
N
CF2CO2Et
Br
2l
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm

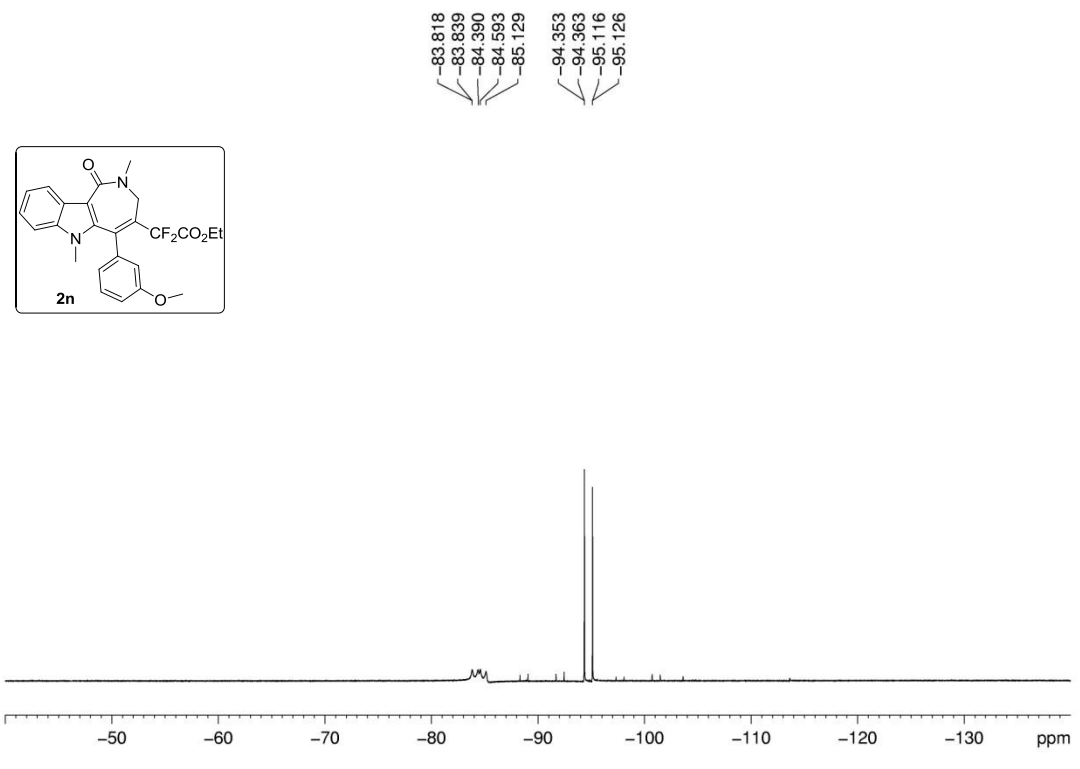

8.358
8.339
7.376
7.358
7.341
7.317
7.299
7.282
7.263
7.243
7.222
7.203
4.188
4.150
4.053
4.040
4.016
4.003
3.885
3.866
3.858
3.848
3.840
3.822
3.805
3.646
3.627
3.611
3.584
3.568
3.307
3.047
2.317
1.107
1.089
1.071
0.000
2m
9
8
7
6
5
4
3
2
1
0 ppm
1.088
6.199
1.055
1.054
1.059
1.086
3.000
2.979
3.024
3.034

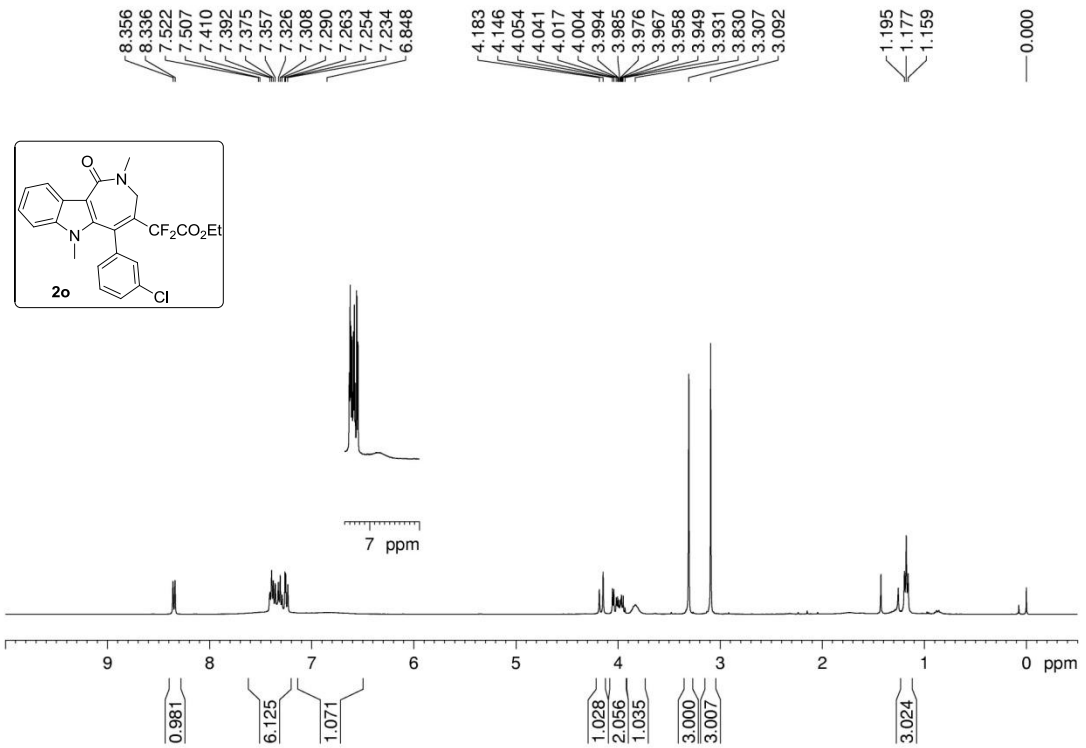

164.75
162.69
162.38
162.33
162.02
139.25
139.19
139.11
138.38
138.34
138.23
135.36
130.21
128.79
128.45
126.26
124.65
122.83
121.81
115.58
114.69
112.27
112.19
109.79
109.23
77.32
77.00
76.68
62.88
47.29
47.22
34.27
32.06
26.87
21.20
13.53
2m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


-83.821
-84.583
-94.151
-94.828
-95.540
O
N
N
CF2CO2Et
2m
−75
−80
−85
−90
−95
−100
−105
ppm


8.355
8.335
7.379
7.361
7.343
7.341
7.318
7.300
7.283
7.263
7.246
7.226
6.954
6.936
6.359
4.188
4.151
4.052
4.038
4.015
4.001
3.933
3.901
3.883
3.874
3.857
3.839
3.702
3.684
3.311
3.087
1.129
1.111
1.093
0.000
O
N
N
CF2CO2Et
2n
O
7
6
ppm
9
8
7
6
5
4
3
2
1
0
ppm
1.015
5.146
1.164
1.036
1.096
1.148
2.057
3.051
3.046
3.000
3.012


164.78
162.73
162.42
162.37
162.15
162.06
159.62
156.40
139.03
138.95
138.87
138.39
137.98
136.73
129.68
129.15
128.91
128.88
128.63
126.32
124.76
122.86
121.88
115.73
114.73
112.32
112.24
109.83
109.25
77.32
77.00
76.68
62.99
55.42
47.35
47.28
34.30
32.03
13.57
CF2CO2Et
2n
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-83.818
-83.839
-84.390
-84.593
-85.129
-94.353
-94.363
-95.116
-95.126
CF2CO2Et
2n
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm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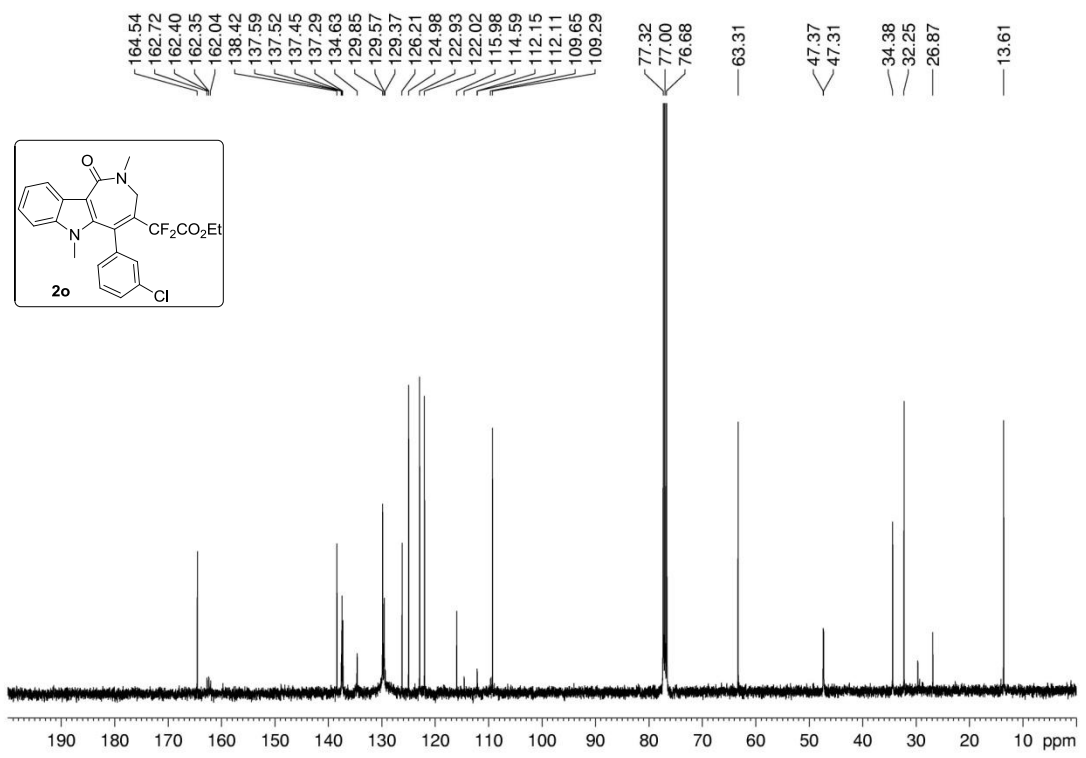
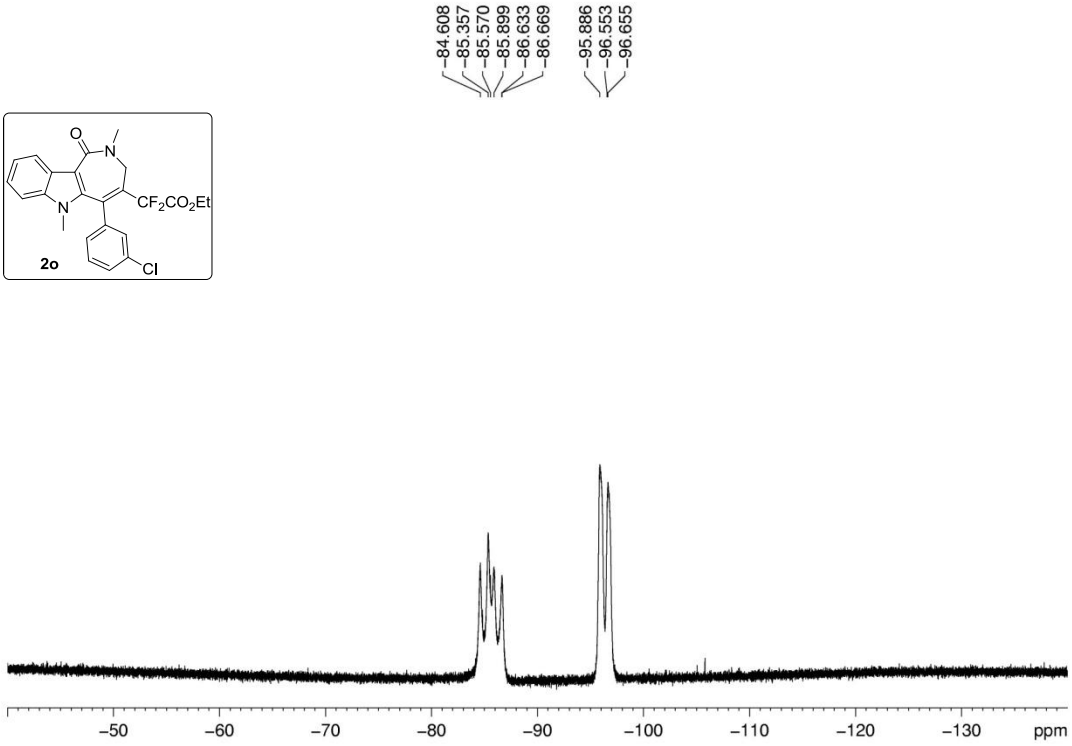
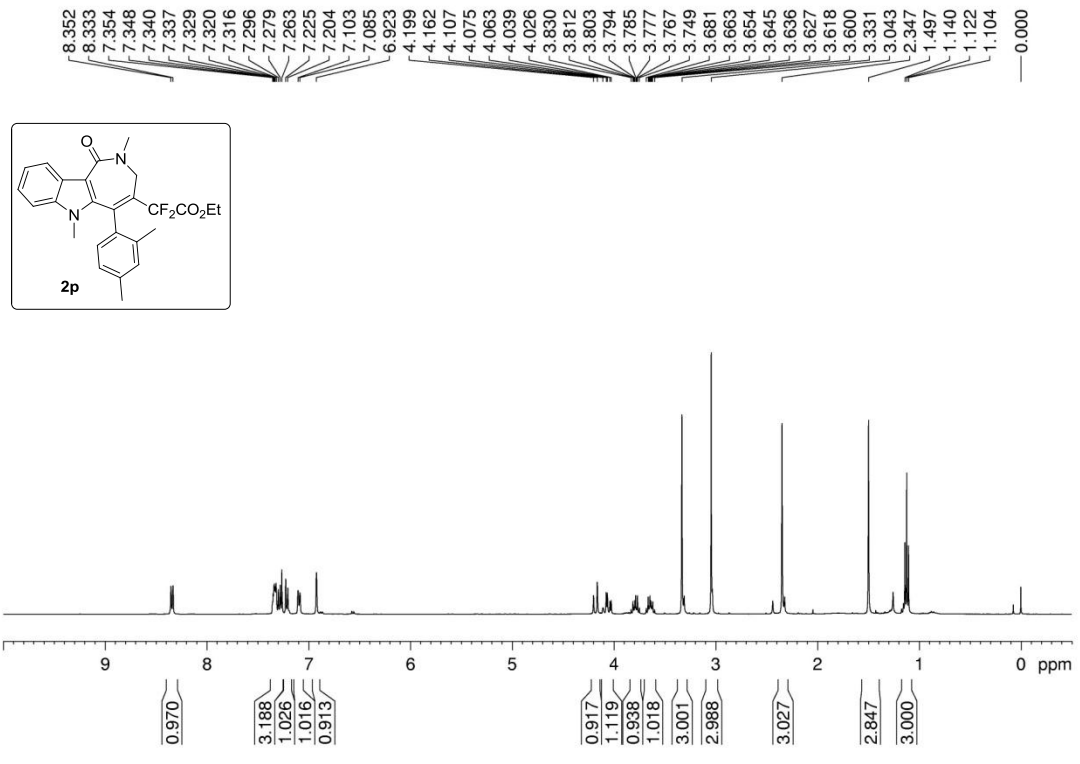
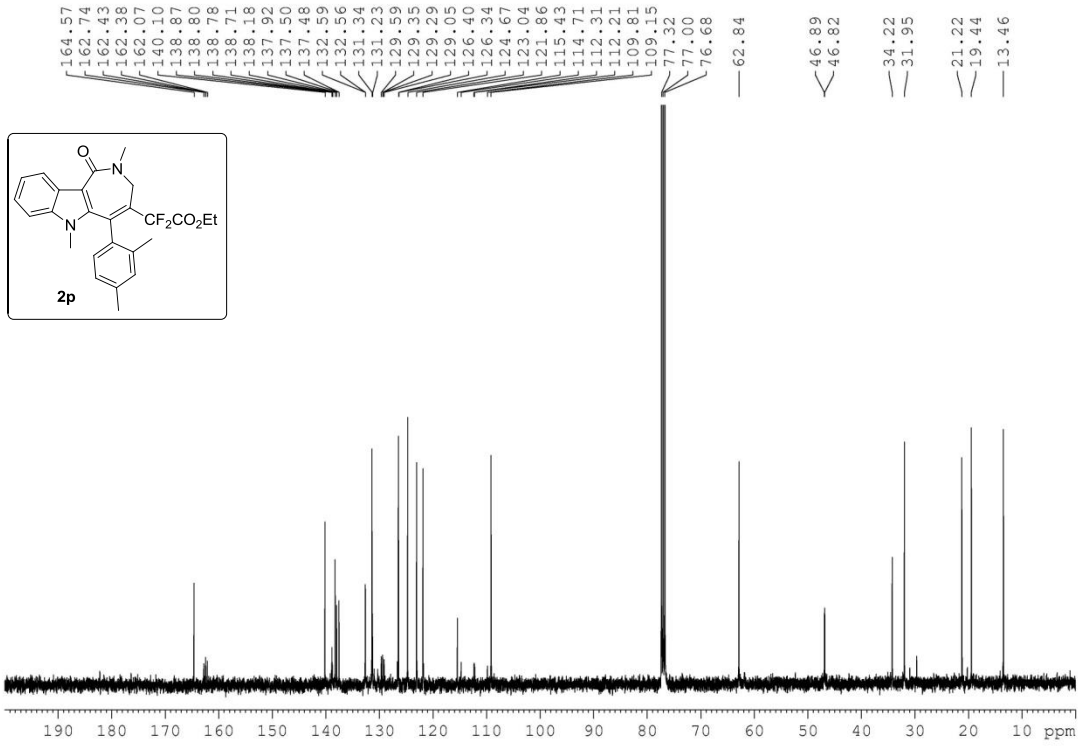
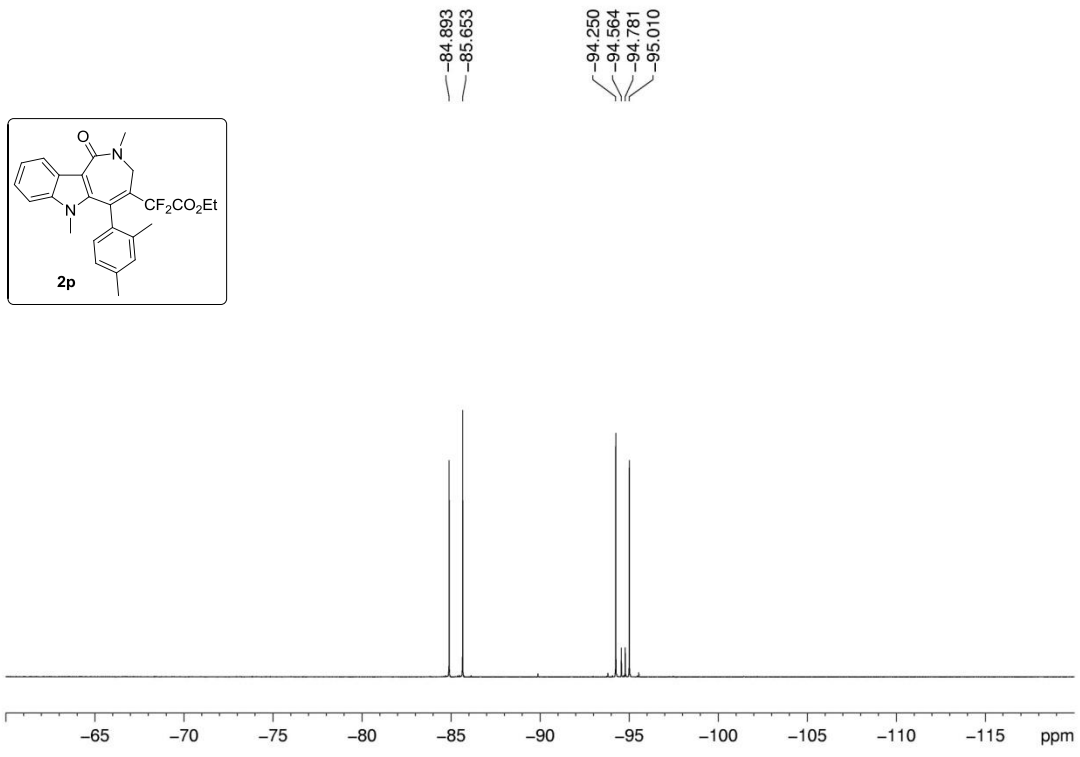
8.336
7.522
7.507
7.410
7.392
7.375
7.357
7.326
7.308
7.290
7.263
7.254
7.234
6.848
4.183
4.146
4.054
4.041
4.017
4.004
3.994
3.985
3.976
3.967
3.958
3.949
3.931
3.830
3.307
3.092
1.195
1.177
1.159
0.000
2o
7 ppm
9
8
7
6
5
4
3
2
1
0 ppm
0.981
6.125
1.071
1.028
2.056
1.035
3.000
3.007
3.024

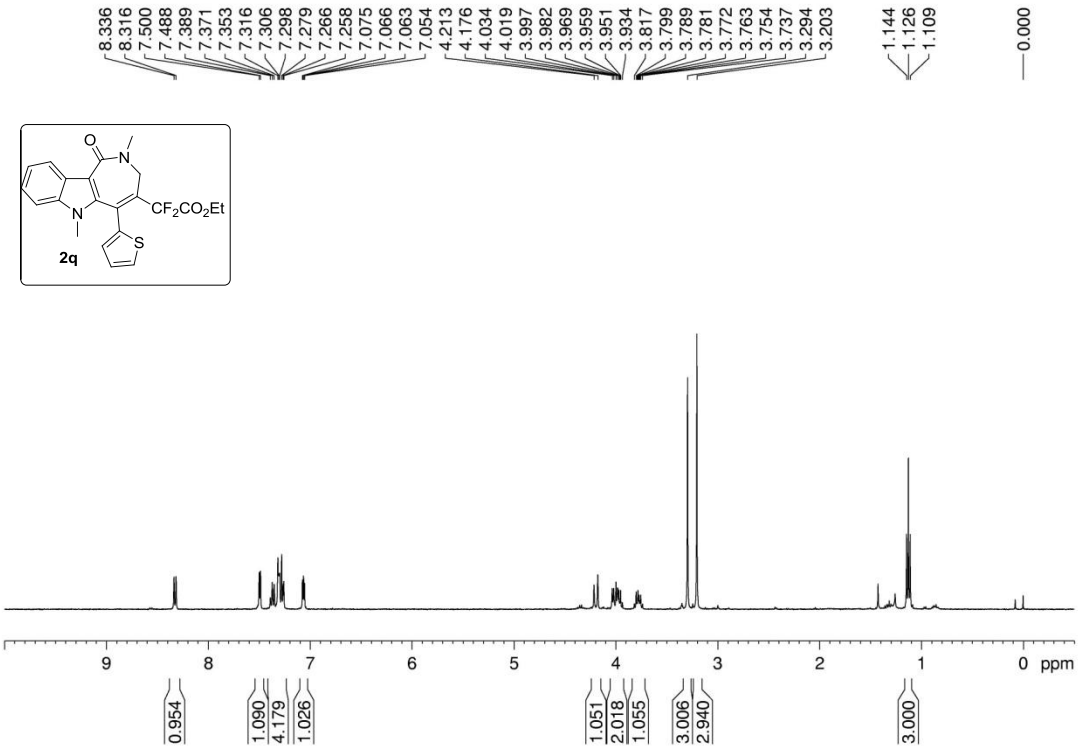

164.54
162.72
162.40
162.35
162.04
138.42
137.59
137.52
137.45
137.29
134.63
129.85
129.57
129.37
126.21
124.98
122.93
122.02
115.98
114.59
112.15
112.11
109.65
109.29
77.32
77.00
76.68
63.31
47.37
47.31
34.38
32.25
26.87
13.61
2o
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

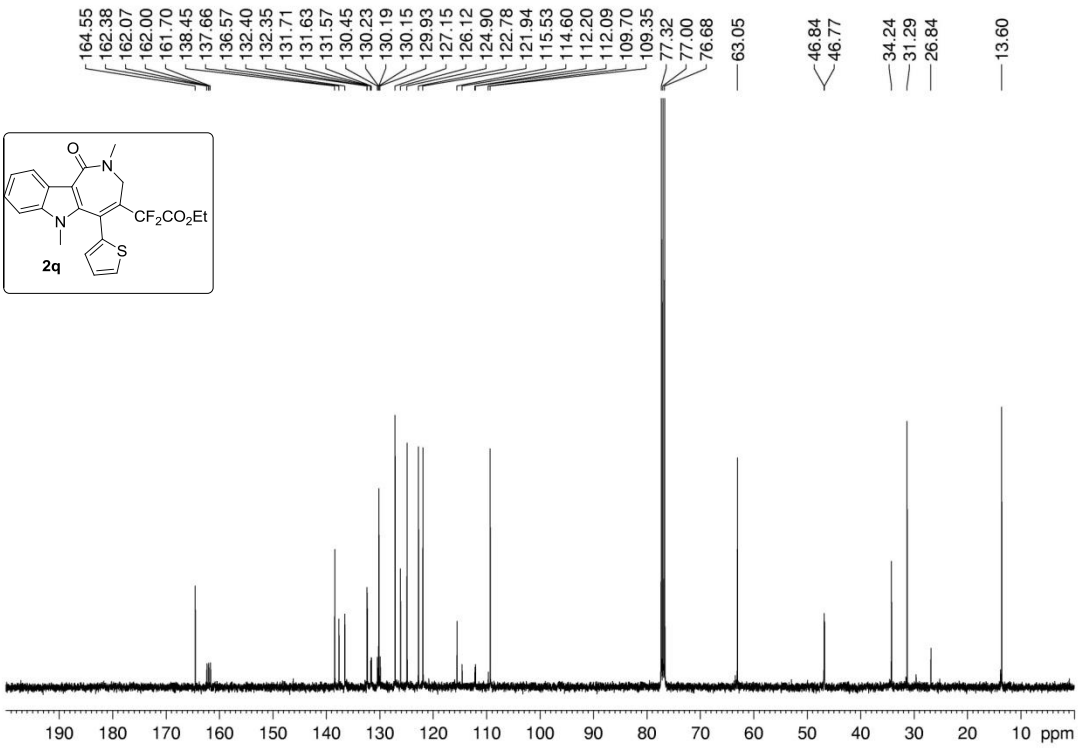

-84.608
-85.357
-85.570
-85.899
-86.633
-86.669
-95.886
-96.553
-96.655
O
N
CF2CO2Et
N
Cl
2o
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm

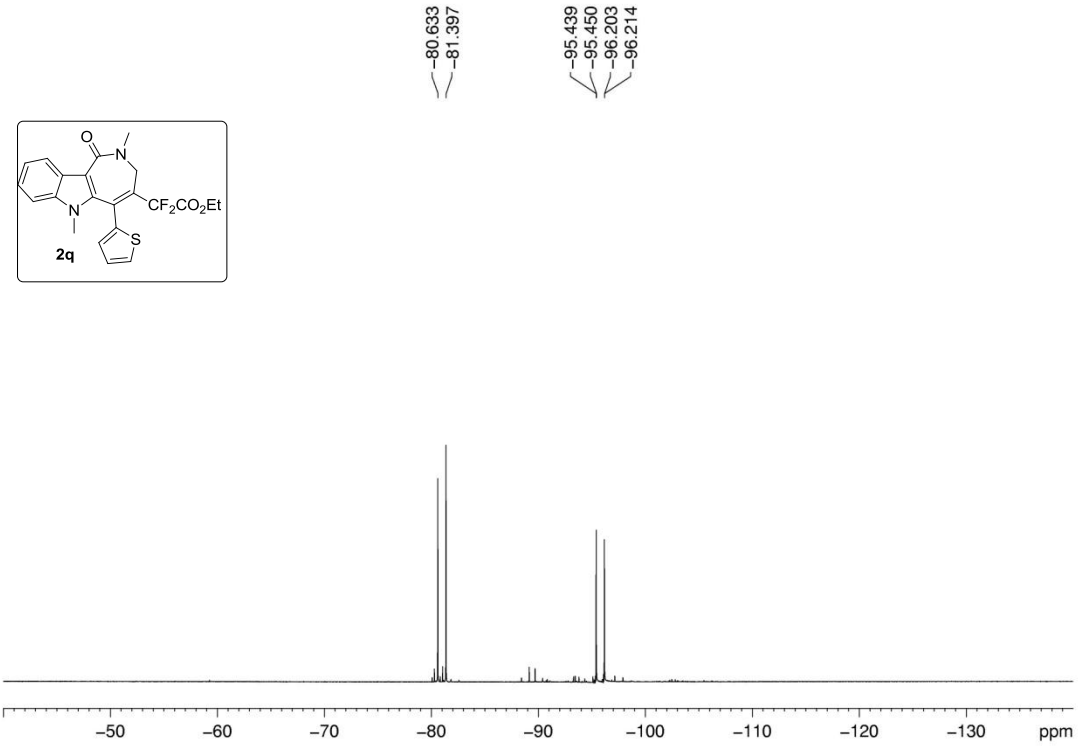

8.352
8.333
7.354
7.348
7.340
7.337
7.329
7.320
7.316
7.296
7.279
7.263
7.225
7.204
7.103
7.085
6.923
4.199
4.162
4.107
4.075
4.063
4.039
4.026
3.830
3.812
3.803
3.794
3.785
3.777
3.767
3.749
3.681
3.663
3.654
3.645
3.636
3.627
3.618
3.600
3.331
3.043
2.347
1.497
1.140
1.122
1.104
0.000
O
N
CF2CO2Et
N
2p
9
8
7
6
5
4
3
2
1
0 ppm
0.970
3.188
1.026
1.016
0.913
0.917
1.119
0.938
1.018
3.001
2.988
3.027
2.847
3.000

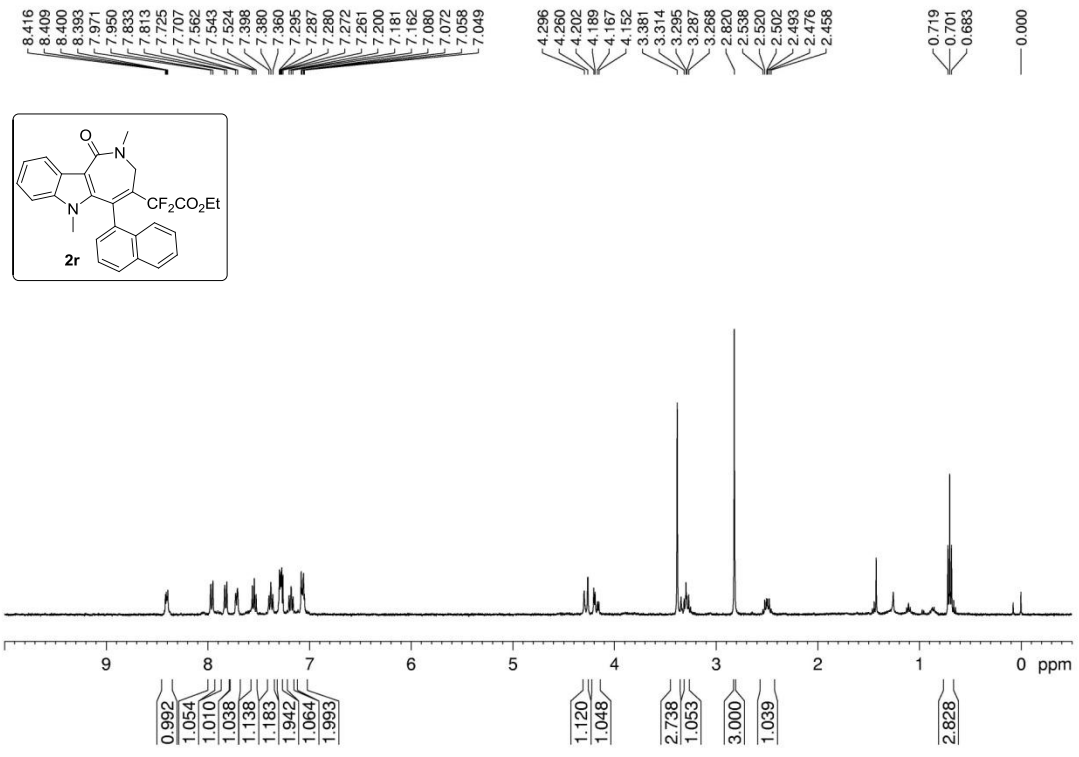

164.57
162.74
162.43
162.38
162.07
140.10
138.87
138.80
138.78
138.71
138.18
137.92
137.50
137.48
132.59
132.56
131.34
131.23
129.59
129.35
129.29
129.05
126.40
126.34
124.67
123.04
121.86
115.43
114.71
112.31
112.21
109.81
109.15
77.32
77.00
76.68
62.84
46.89
46.82
34.22
31.95
21.22
19.44
13.46
O
N
N
CF2CO2Et
2p
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

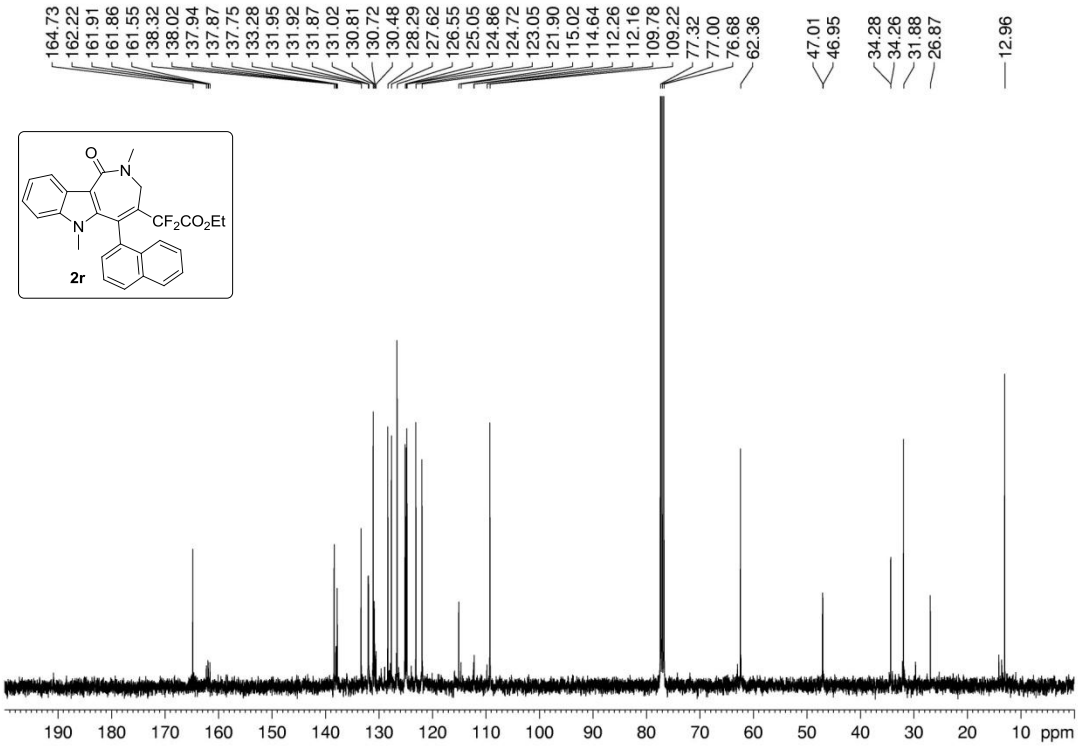

-84.893
-85.653
-94.250
-94.564
-94.781
-95.010
O
N
N
CF2CO2Et
2p
-65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 ppm

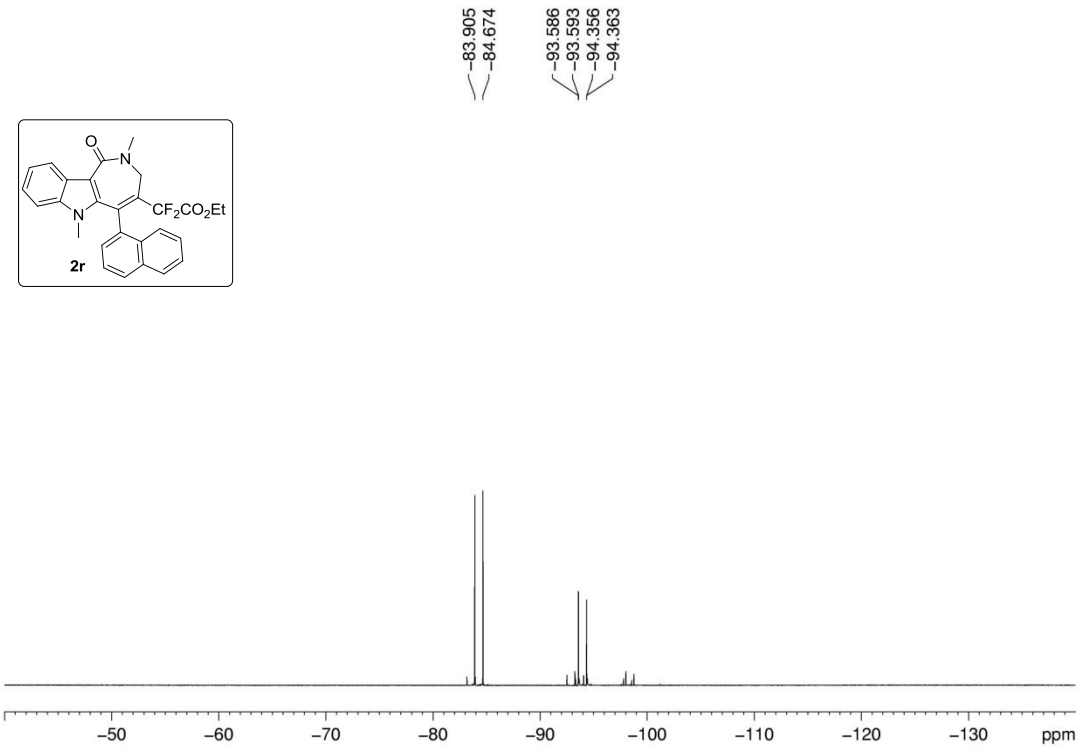

8.336
8.316
7.500
7.488
7.389
7.371
7.353
7.316
7.306
7.298
7.279
7.266
7.258
7.075
7.066
7.063
7.054
4.213
4.176
4.034
4.019
3.997
3.982
3.969
3.959
3.951
3.934
3.817
3.799
3.789
3.781
3.772
3.763
3.754
3.737
3.294
3.203
1.144
1.126
1.109
0.000
CF2CO2Et
2q
9
8
7
6
5
4
3
2
1
0 ppm
0.954
1.090
4.179
1.026
1.051
2.018
1.055
3.006
2.940
3.000

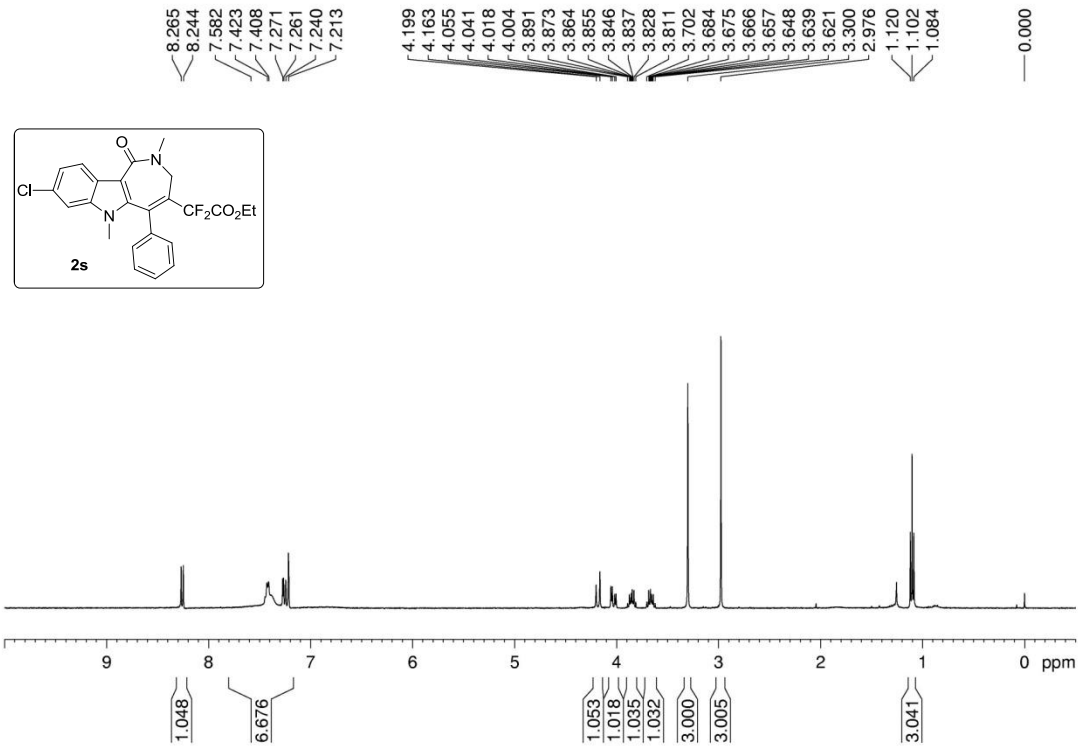

164.55
162.38
162.07
162.00
161.70
138.45
137.66
136.57
132.40
132.35
131.71
131.63
131.57
130.45
130.23
130.19
130.15
129.93
127.15
126.12
124.90
122.78
121.94
115.53
114.60
112.20
112.09
109.70
109.35
77.32
77.00
76.68
63.05
46.84
46.77
34.24
31.29
26.84
13.60
CF2CO2Et
2q
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

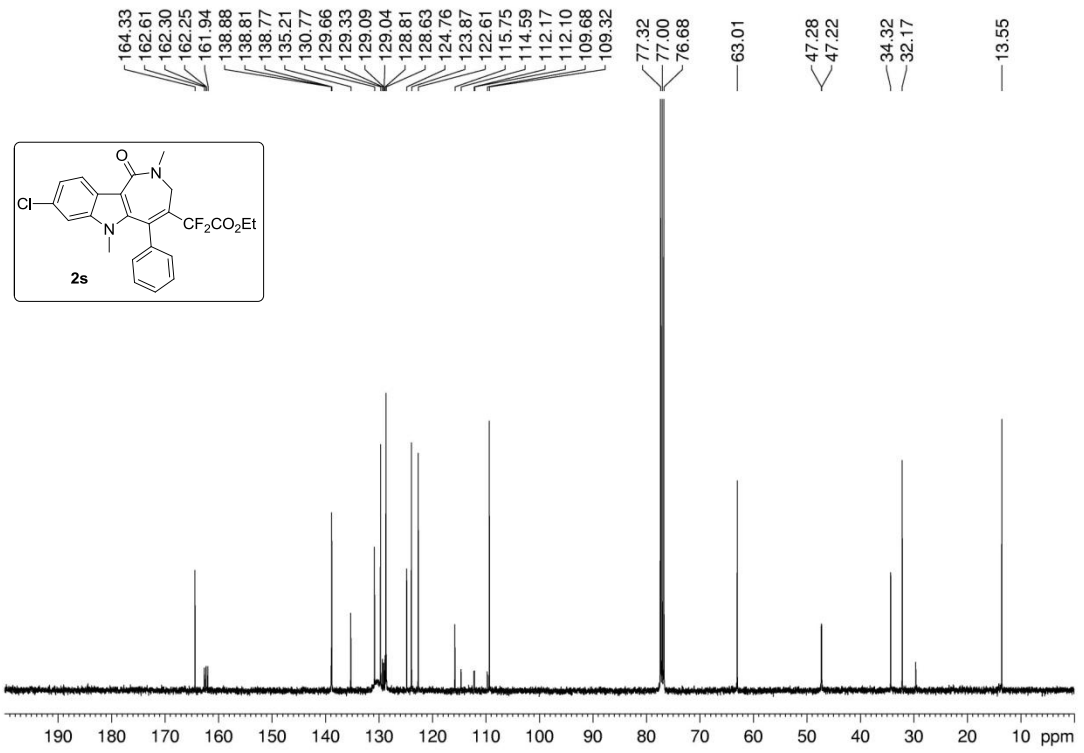

−80.633
−81.397
−95.439
−95.450
−96.203
−96.214
2q
CF2CO2Et
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm

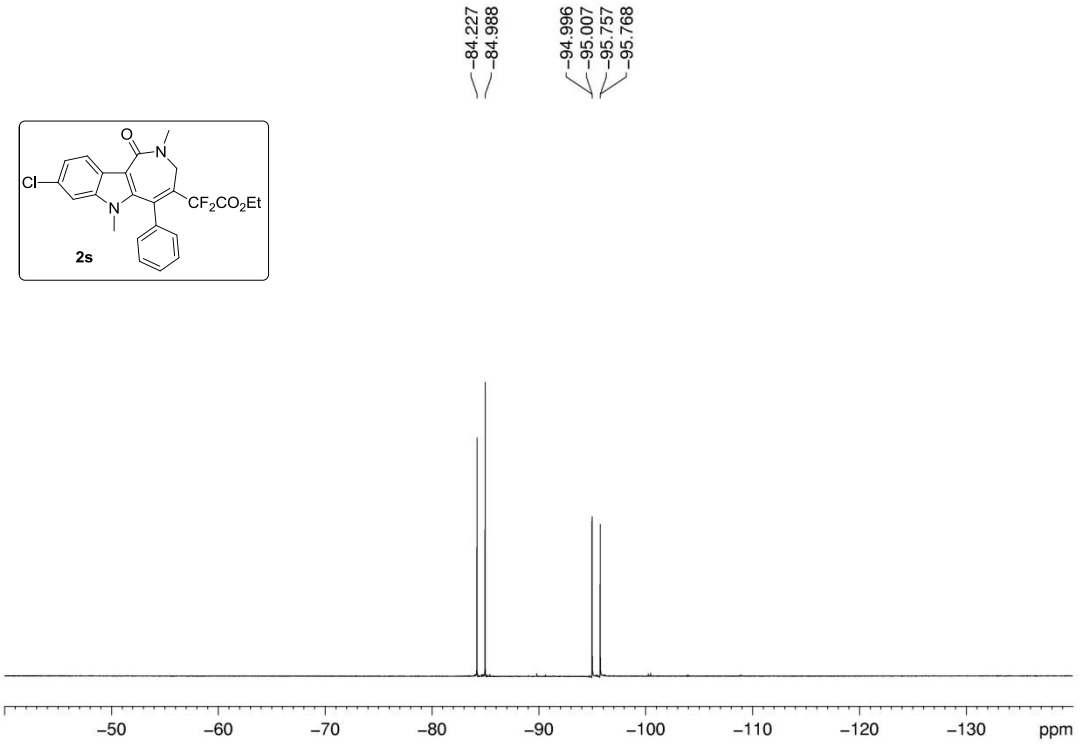

8.416
8.409
8.400
8.393
7.971
7.950
7.833
7.813
7.725
7.707
7.562
7.543
7.524
7.398
7.380
7.360
7.295
7.287
7.280
7.272
7.261
7.200
7.181
7.162
7.080
7.072
7.058
7.049
4.296
4.260
4.202
4.189
4.167
4.152
3.381
3.314
3.295
3.287
3.268
2.820
2.538
2.520
2.502
2.493
2.476
2.458
0.719
0.701
0.683
0.000
2r
CF2CO2Et
9
8
7
6
5
4
3
2
1
0 ppm
0.992
1.054
1.010
1.038
1.138
1.183
1.942
1.064
1.993
1.120
1.048
2.738
1.053
3.000
1.039
2.828

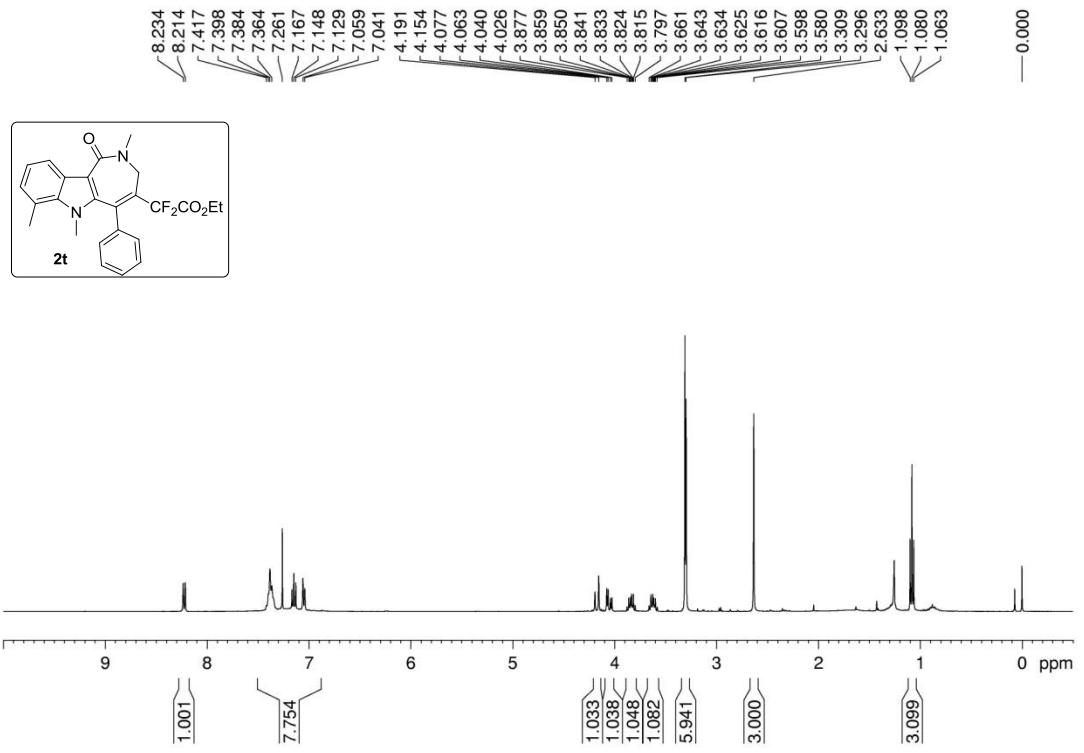

164.73
162.22
161.91
161.86
161.55
138.32
138.02
137.94
137.87
137.75
133.28
131.95
131.92
131.87
131.02
130.81
130.72
130.48
128.29
127.62
126.55
125.05
124.86
124.72
123.05
121.90
115.02
114.64
112.26
112.16
109.78
109.22
77.32
77.00
76.68
62.36
47.01
46.95
34.28
34.26
31.88
26.87
12.96
O
N
N
CF2CO2Et
2r
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

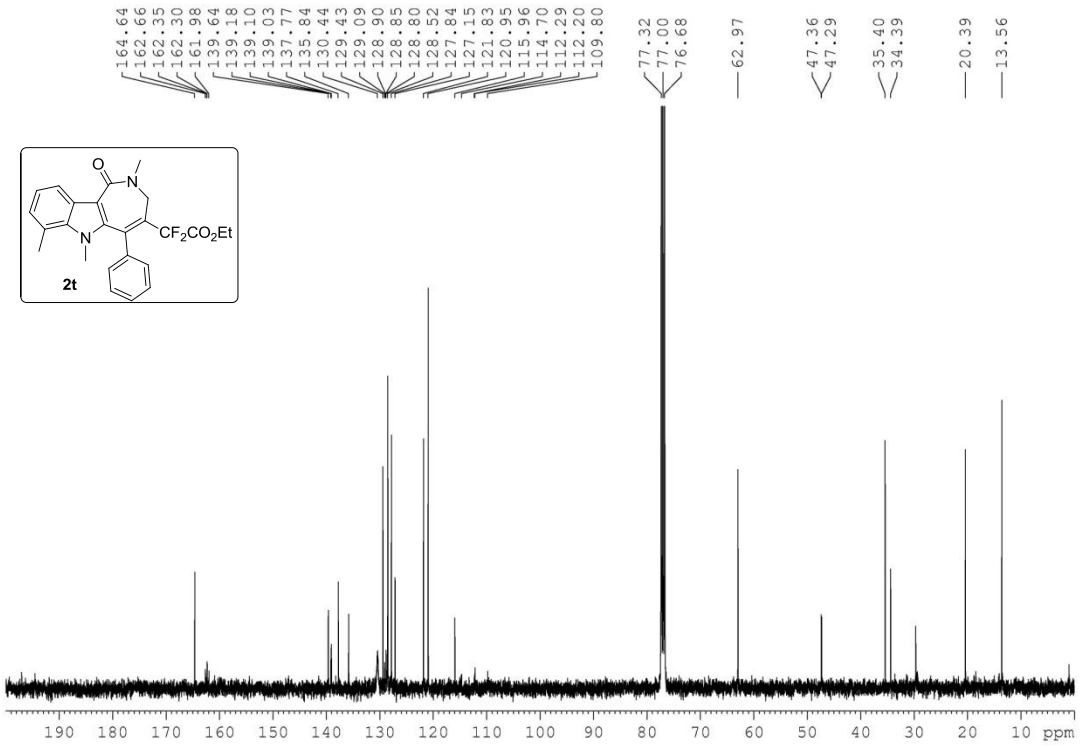

-83.905
-84.674
-93.586
-93.593
-94.356
-94.363
O
N
N
CF2CO2Et
2r
−50 −60 −70 −80 −90 −100 −110 −120 −130 ppm

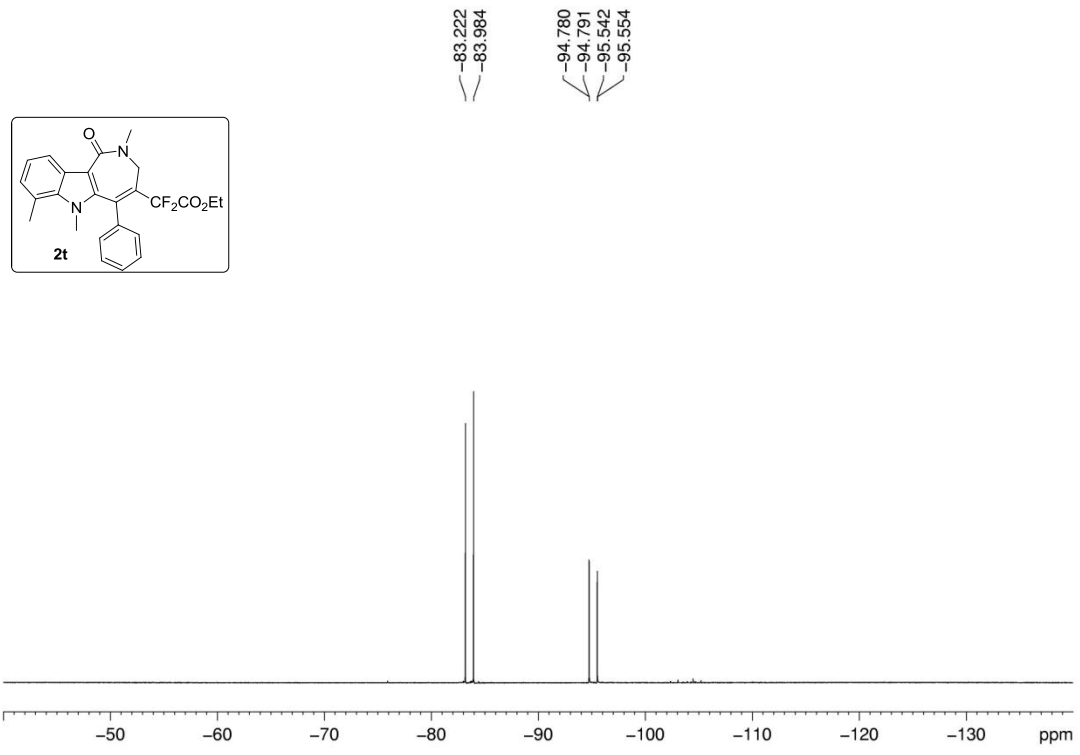

8.265
8.244
7.582
7.423
7.408
7.271
7.261
7.240
7.213
4.199
4.163
4.055
4.041
4.018
4.004
3.891
3.873
3.864
3.855
3.846
3.837
3.828
3.811
3.702
3.684
3.675
3.666
3.657
3.648
3.639
3.621
3.300
2.976
1.120
1.102
1.084
0.000
Cl
N
O
CF2CO2Et
2s
9
8
7
6
5
4
3
2
1
0 ppm
1.048
6.676
1.053
1.018
1.035
1.032
3.000
3.005
3.041


164.33
162.61
162.30
162.25
161.94
138.88
138.81
138.77
135.21
130.77
129.66
129.33
129.09
129.04
128.81
128.63
124.76
123.87
122.61
115.75
114.59
112.17
112.10
109.68
109.32
77.32
77.00
76.68
63.01
47.28
47.22
34.32
32.17
13.55
Cl
N
O
CF2CO2Et
2s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

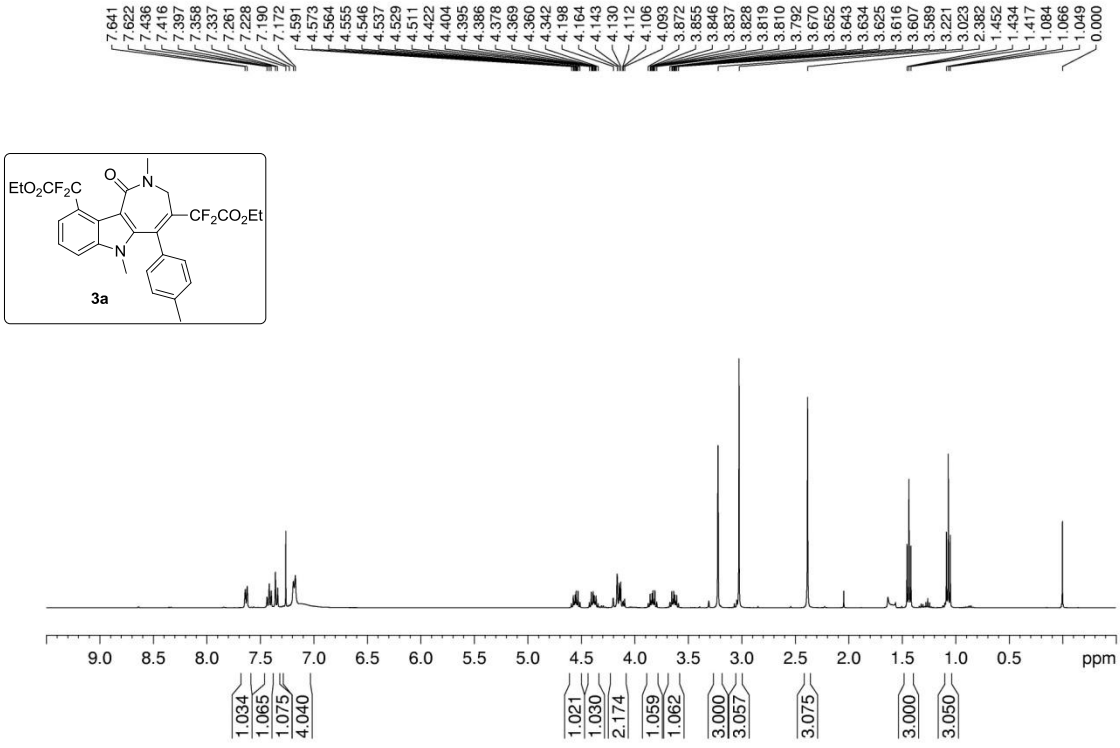

-84.227
-84.988
-94.996
-95.007
-95.757
-95.768
Cl
CF2CO2Et
2s
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm

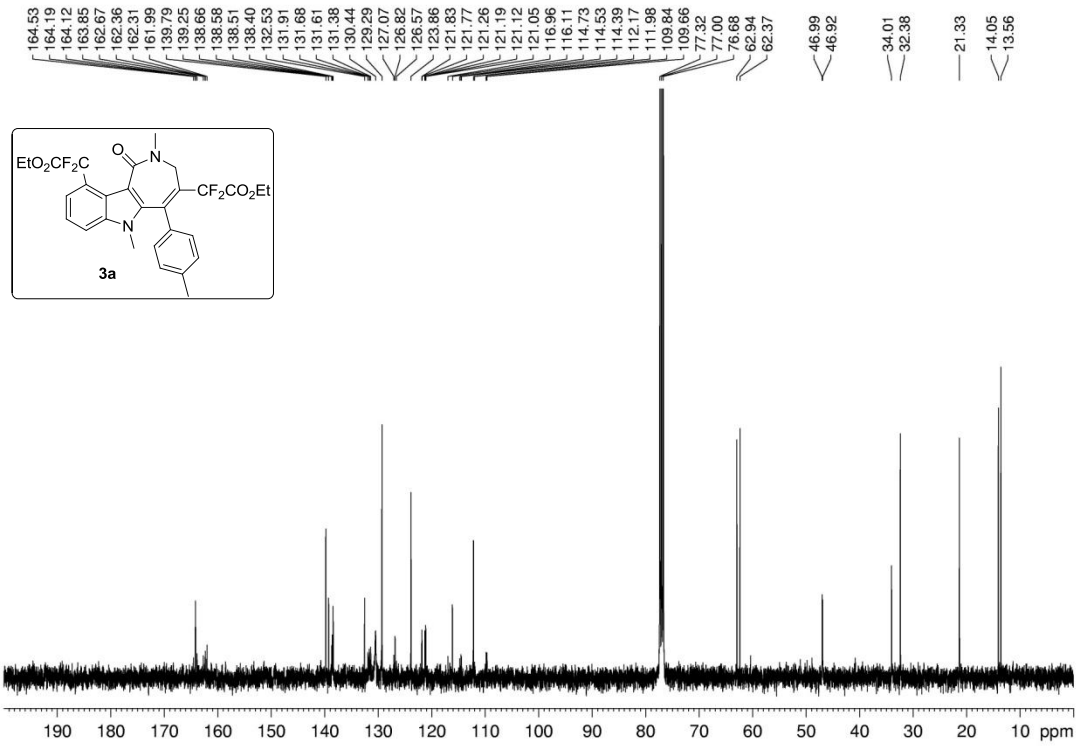

8.234
8.214
7.417
7.398
7.384
7.364
7.261
7.167
7.148
7.129
7.059
7.041
4.191
4.154
4.077
4.063
4.040
4.026
3.877
3.859
3.850
3.841
3.833
3.824
3.815
3.797
3.661
3.643
3.634
3.625
3.616
3.607
3.598
3.580
3.309
3.296
2.633
1.098
1.080
1.063
0.000
CF2CO2Et
2t
9
8
7
6
5
4
3
2
1
0 ppm
1.001
7.754
1.033
1.038
1.048
1.082
5.941
3.000
3.099

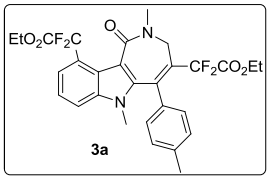

164.64
162.66
162.35
162.30
161.98
139.64
139.18
139.10
139.03
137.77
135.84
130.44
129.43
129.09
128.90
128.85
128.80
128.52
127.84
127.15
121.83
120.95
115.96
114.70
112.29
112.20
109.80
77.32
77.00
76.68
62.97
47.36
47.29
35.40
34.39
20.39
13.56
O
N
N
CF2CO2Et
2t
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

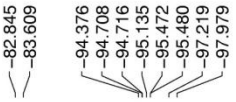

-83.222
-83.984
-94.780
-94.791
-95.542
-95.554
O
N
N
CF2CO2Et
2t
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm

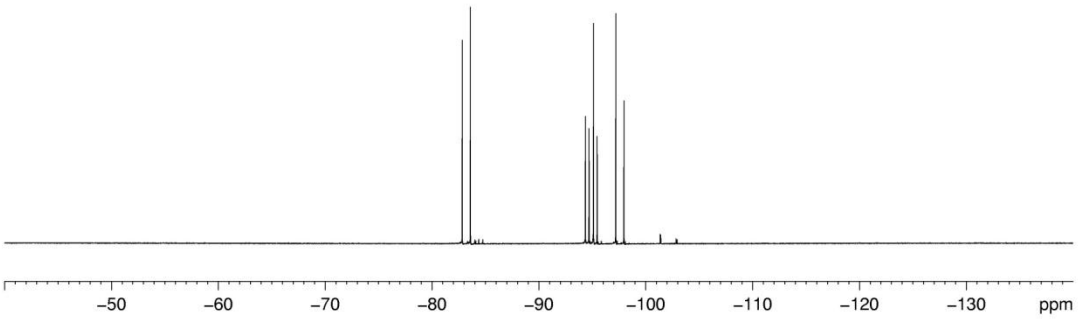
10. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3 and 4

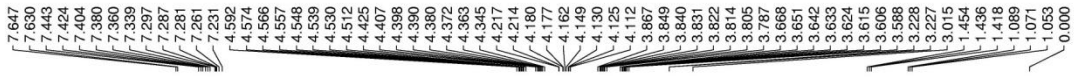


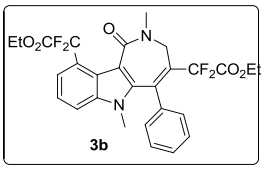


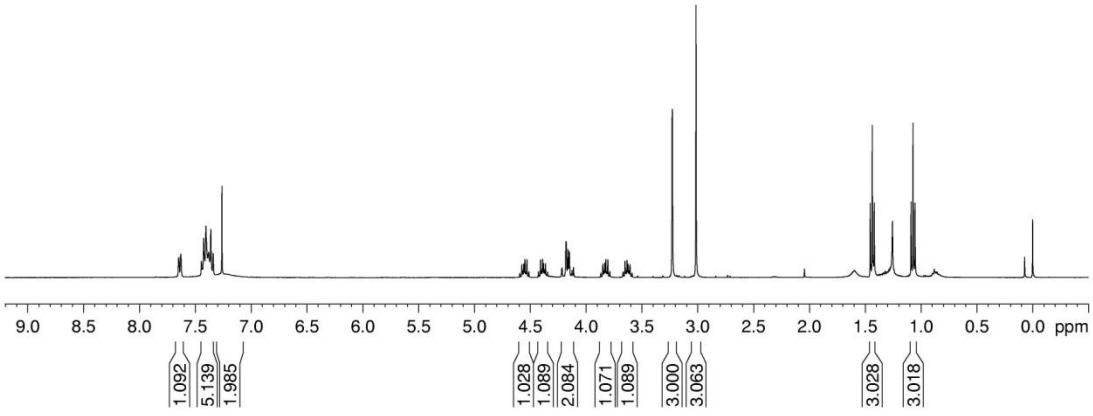

EtO2CF2C
CF2CO2Et
O
N
N
3a

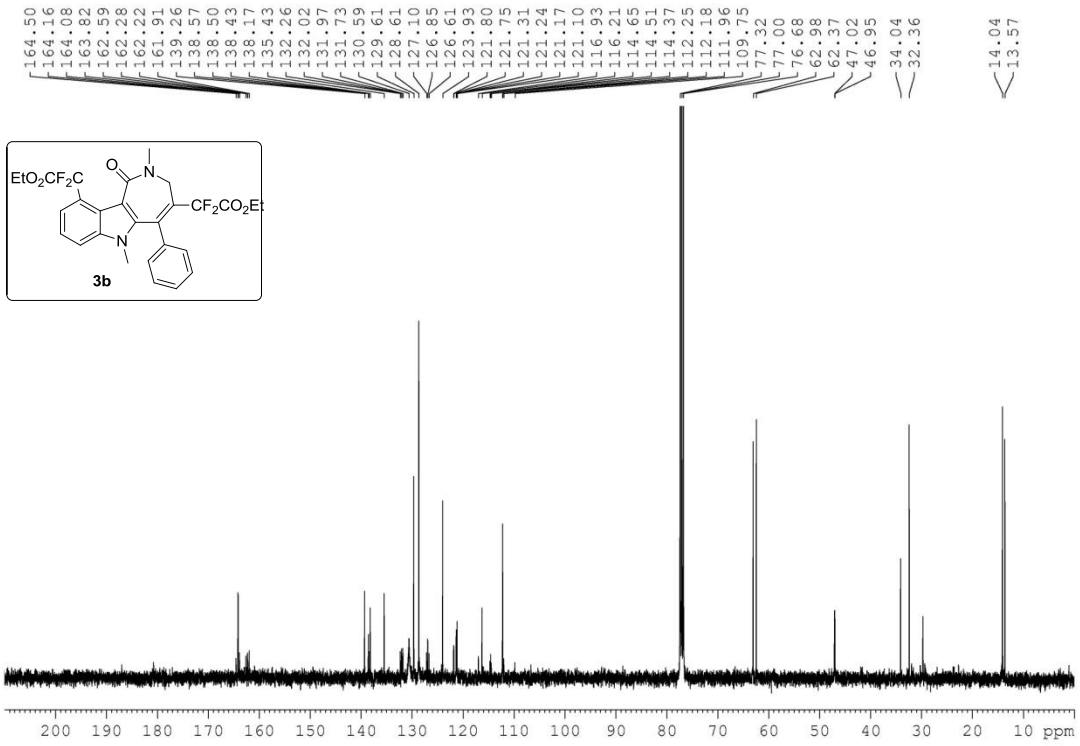

-82.845
-83.609
-94.376
-94.708
-94.716
-95.135
-95.472
-95.480
-97.219
-97.979

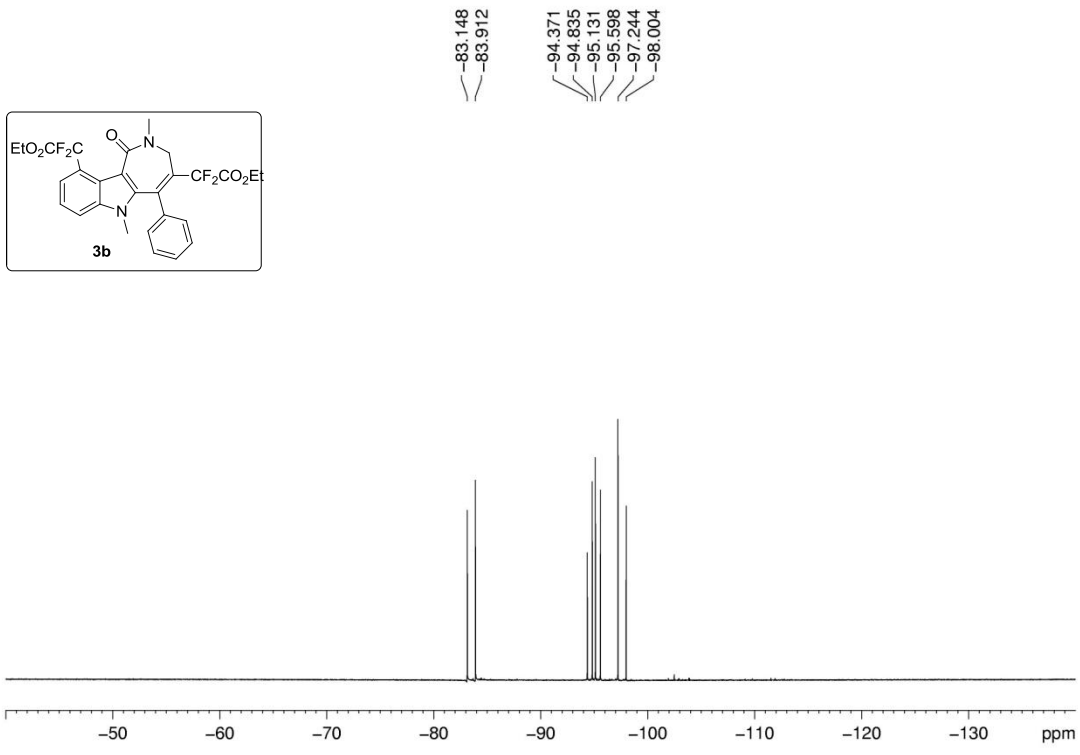

-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm


7.647
7.630
7.443
7.424
7.404
7.380
7.360
7.339
7.297
7.287
7.281
7.261
7.231
4.592
4.574
4.566
4.557
4.548
4.539
4.530
4.512
4.425
4.407
4.398
4.390
4.380
4.372
4.363
4.345
4.217
4.214
4.180
4.177
4.162
4.149
4.130
4.125
4.112
3.867
3.849
3.840
3.831
3.822
3.814
3.805
3.787
3.668
3.651
3.642
3.633
3.624
3.615
3.606
3.588
3.228
3.227
3.015
1.454
1.436
1.418
1.089
1.071
1.053
0.000


EtO2CF2C
CF2CO2Et
O
N
N
3b


9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.092
5.139
1.985
1.028
1.089
2.084
1.071
1.089
3.000
3.063
3.028
3.018


164.50
164.16
164.08
163.82
162.59
162.28
162.22
161.91
139.26
138.57
138.50
138.43
138.17
135.43
132.26
132.02
131.97
131.73
130.59
129.61
128.61
127.10
126.85
126.61
123.93
121.80
121.75
121.31
121.24
121.17
121.10
116.93
116.21
114.65
114.51
114.37
112.25
112.18
111.96
109.75
77.32
77.00
76.68
62.98
62.37
47.02
46.95
34.04
32.36
14.04
13.57
EtO2CF2C
CF2CO2Et
3b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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-83.912
-94.371
-94.835
-95.131
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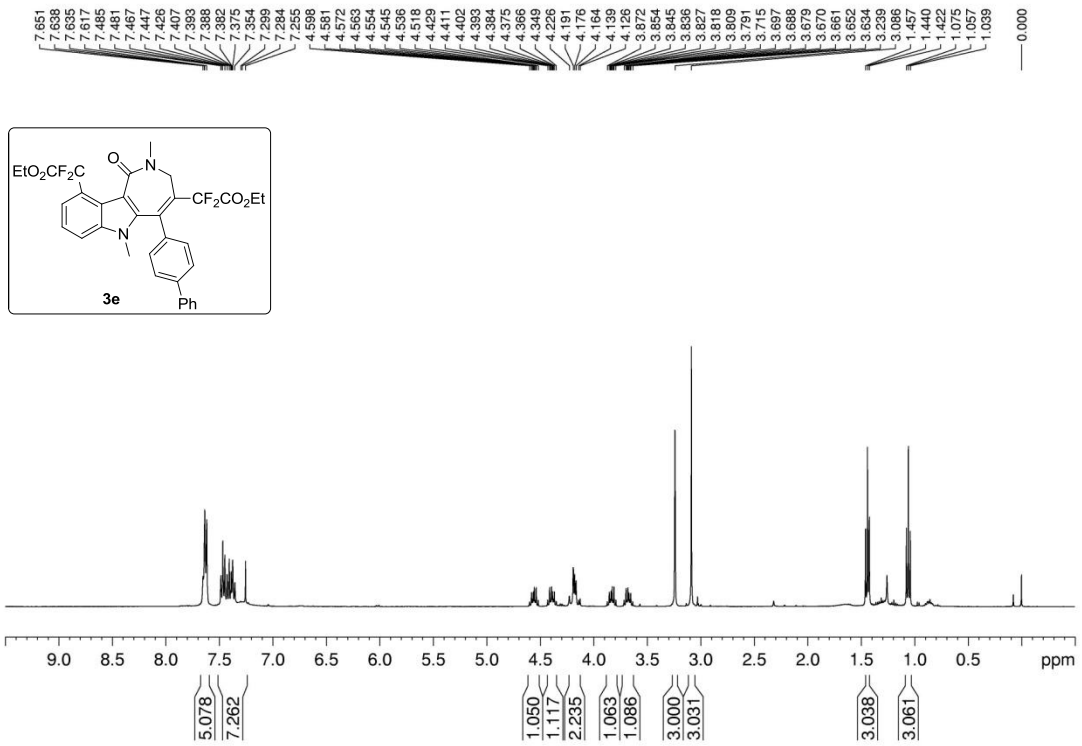
-97.244
-98.004
EtO2CF2C
CF2CO2Et
3b
−50 −60 −70 −80 −90 −100 −110 −120 −130 ppm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7.635
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7.447
7.426
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7.393
7.388
7.382
7.375
7.354
7.299
7.284
7.255
4.598
4.581
4.572
4.563
4.554
4.545
4.536
4.518
4.429
4.411
4.402
4.393
4.384
4.375
4.366
4.349
4.226
4.191
4.176
4.164
4.139
4.126
3.872
3.854
3.845
3.836
3.827
3.818
3.809
3.791
3.715
3.697
3.688
3.679
3.670
3.661
3.652
3.634
3.239
3.086
1.457
1.440
1.422
1.075
1.057
1.039
0.000
EtO2CF2C
CF2CO2Et
Ph
3e
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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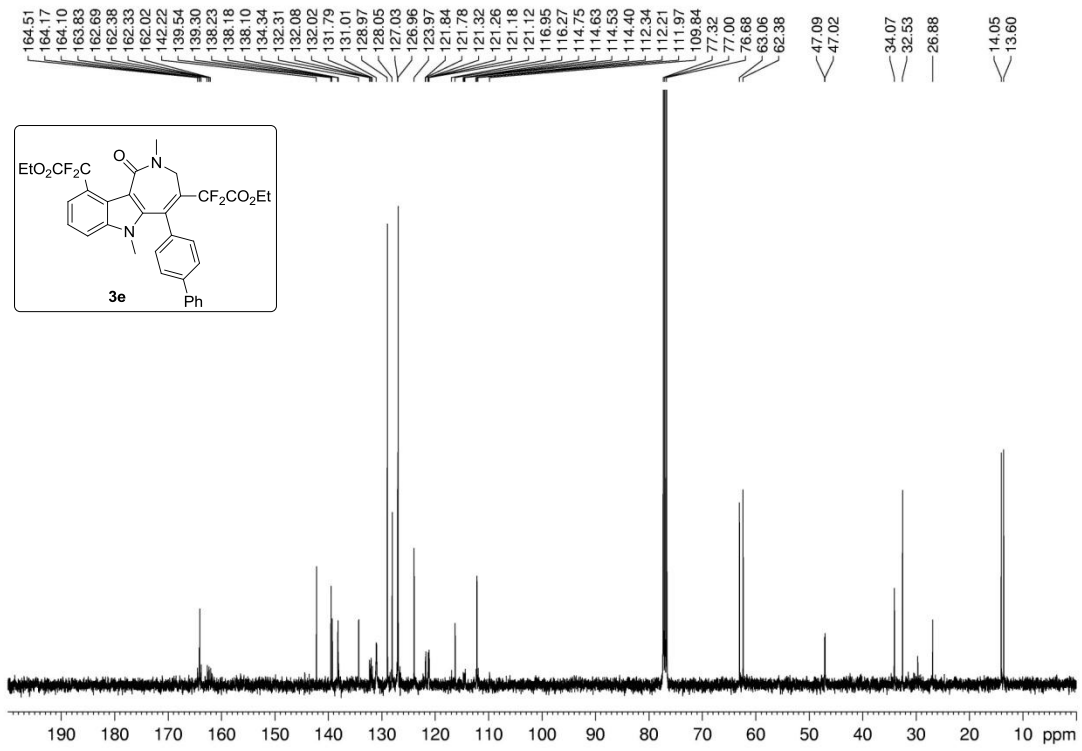
7.262
1.050
1.117
2.235
1.063
1.086
3.000
3.031
3.038
3.061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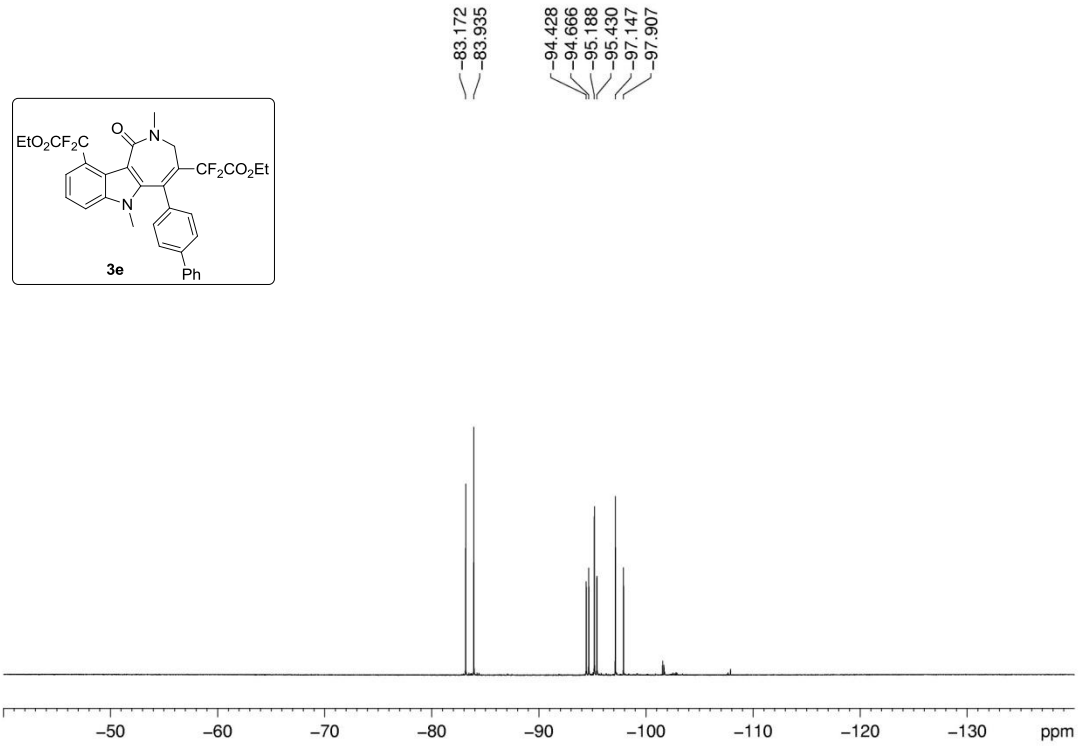
162.33
162.02
142.22
139.54
139.30
138.23
138.18
138.10
134.34
132.31
132.08
132.02
131.79
131.01
128.97
128.05
127.03
126.96
123.97
121.84
121.78
121.32
121.26
121.18
121.12
116.95
116.27
114.75
114.63
114.53
114.40
112.34
112.21
111.97
109.84
77.32
77.00
76.68
63.06
62.38
47.09
47.02
34.07
32.53
26.88
14.05
13.60
EtO2CF2C
CF2CO2Et
Ph
3e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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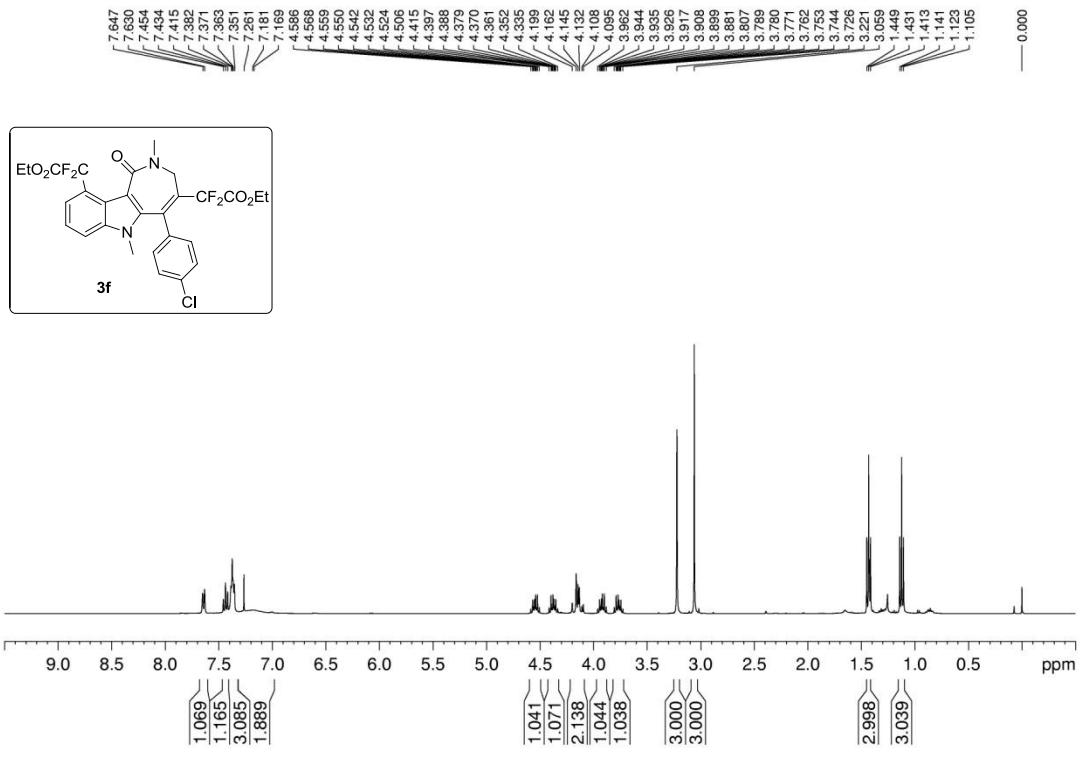
-95.430
-97.147
-97.907
EtO2CF2C
CF2CO2Et
3e
Ph
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm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7.630
7.454
7.434
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7.371
7.363
7.351
7.261
7.181
7.169
4.586
4.568
4.559
4.550
4.542
4.532
4.524
4.506
4.415
4.397
4.388
4.379
4.370
4.361
4.352
4.335
4.199
4.162
4.145
4.132
4.108
4.095
3.962
3.944
3.935
3.926
3.917
3.908
3.899
3.881
3.807
3.789
3.780
3.771
3.762
3.753
3.744
3.726
3.221
3.059
1.449
1.431
1.413
1.141
1.123
1.105
0.000
EtO2CF2C
CF2CO2Et
3f
Cl
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.069
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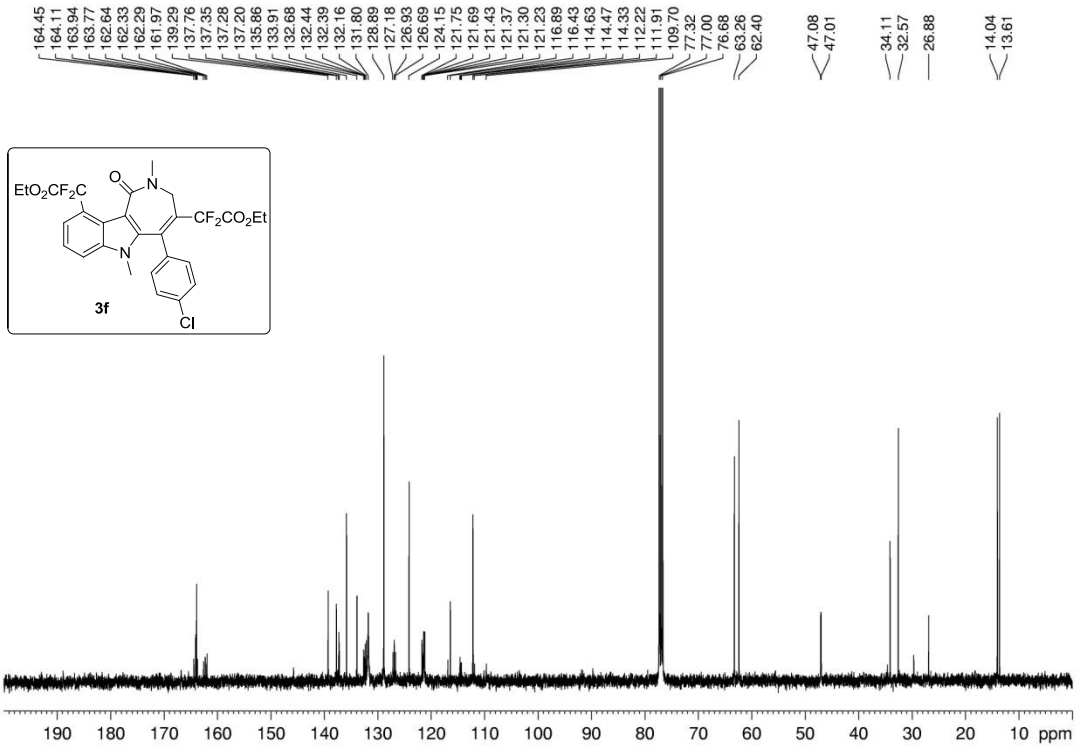
1.889
1.041
1.071
2.138
1.044
1.038
3.000
3.000
2.998
3.039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162.29
161.97
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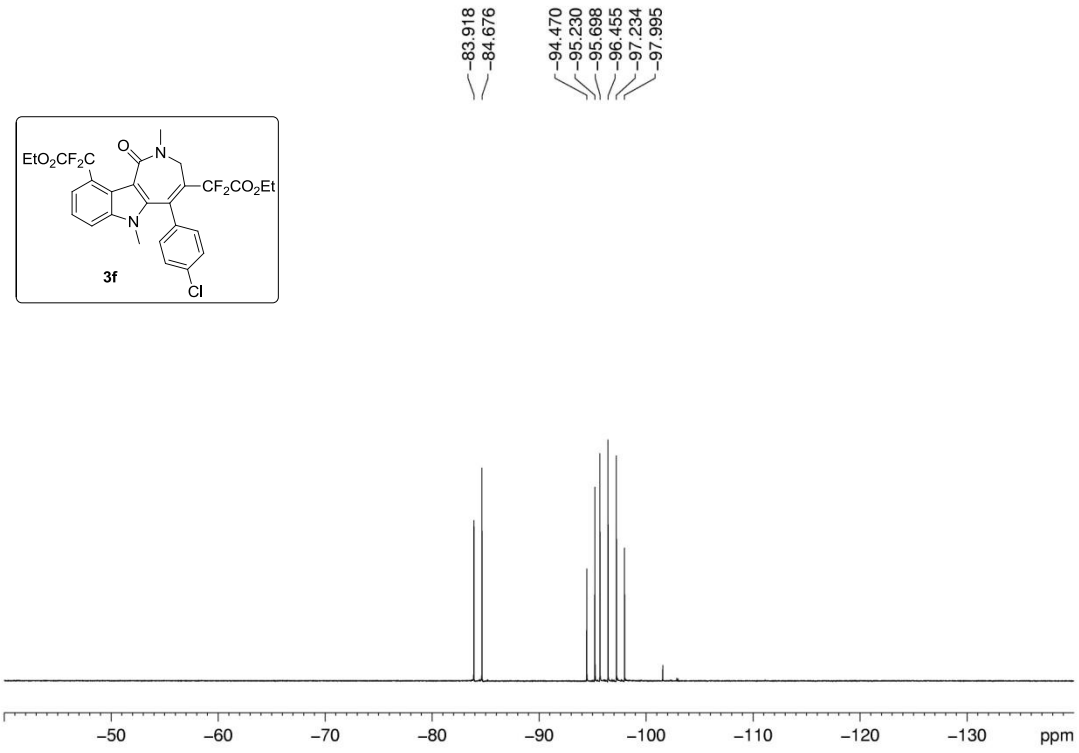
137.76
137.35
137.28
137.20
135.86
133.91
132.68
132.44
132.39
132.16
131.80
128.89
127.18
126.93
126.69
124.15
121.75
121.69
121.43
121.37
121.30
121.23
116.89
116.43
114.63
114.47
114.33
112.22
111.91
109.70
77.32
77.00
76.68
63.26
62.40
47.08
47.01
34.11
32.57
26.88
14.04
13.61
EtO2CF2C
CF2CO2Et
O
N
N
3f
Cl
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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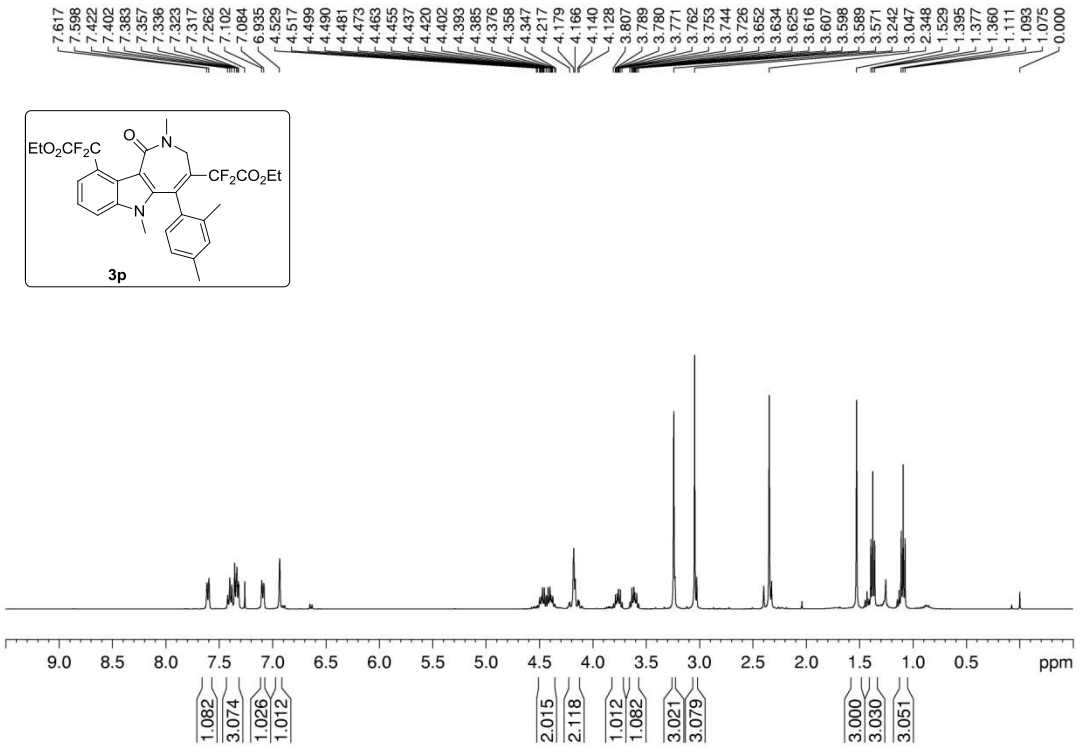
-95.230
-95.698
-96.455
-97.234
-97.995
EtO2CF2C
CF2CO2Et
O
N
N
3f
Cl
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm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7.422
7.402
7.383
7.357
7.336
7.323
7.317
7.262
7.102
7.084
6.935
4.529
4.517
4.499
4.490
4.481
4.473
4.463
4.455
4.437
4.420
4.402
4.393
4.385
4.376
4.358
4.347
4.217
4.179
4.166
4.140
4.128
3.807
3.789
3.780
3.771
3.762
3.753
3.744
3.726
3.652
3.634
3.625
3.616
3.607
3.598
3.589
3.571
3.242
3.047
2.348
1.529
1.395
1.377
1.360
1.111
1.093
1.075
0.000
EtO2CF2C
CF2CO2Et
3p
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.082
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1.012
2.015
2.118
1.012
1.082
3.021
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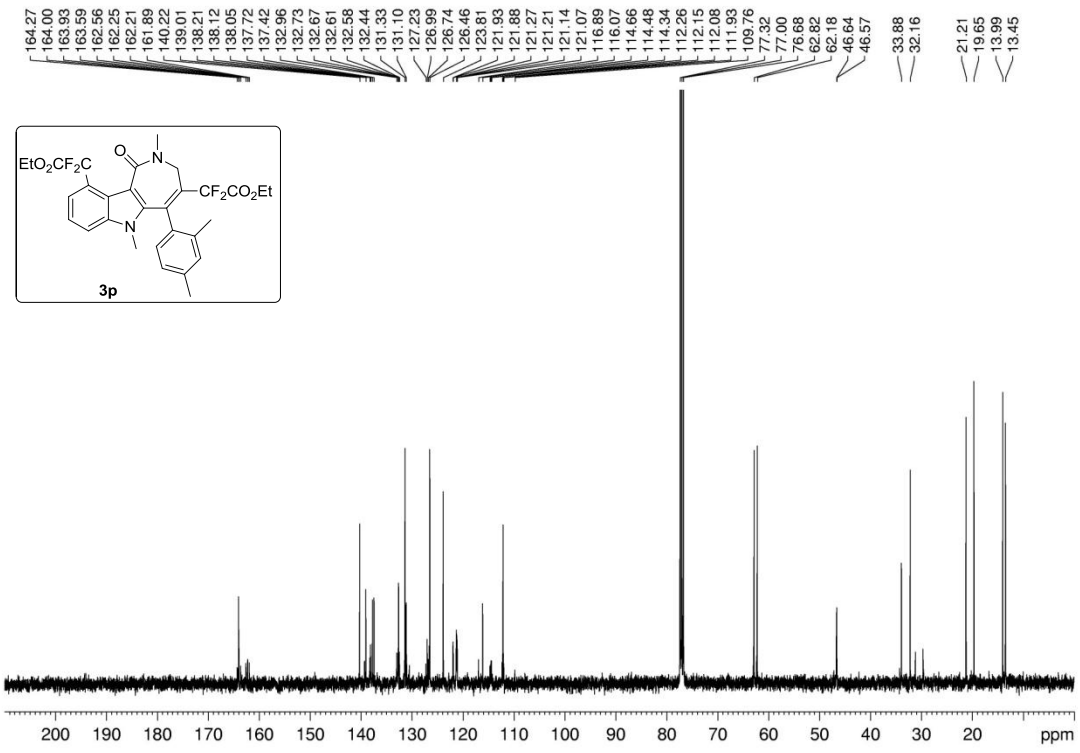
3.000
3.030
3.051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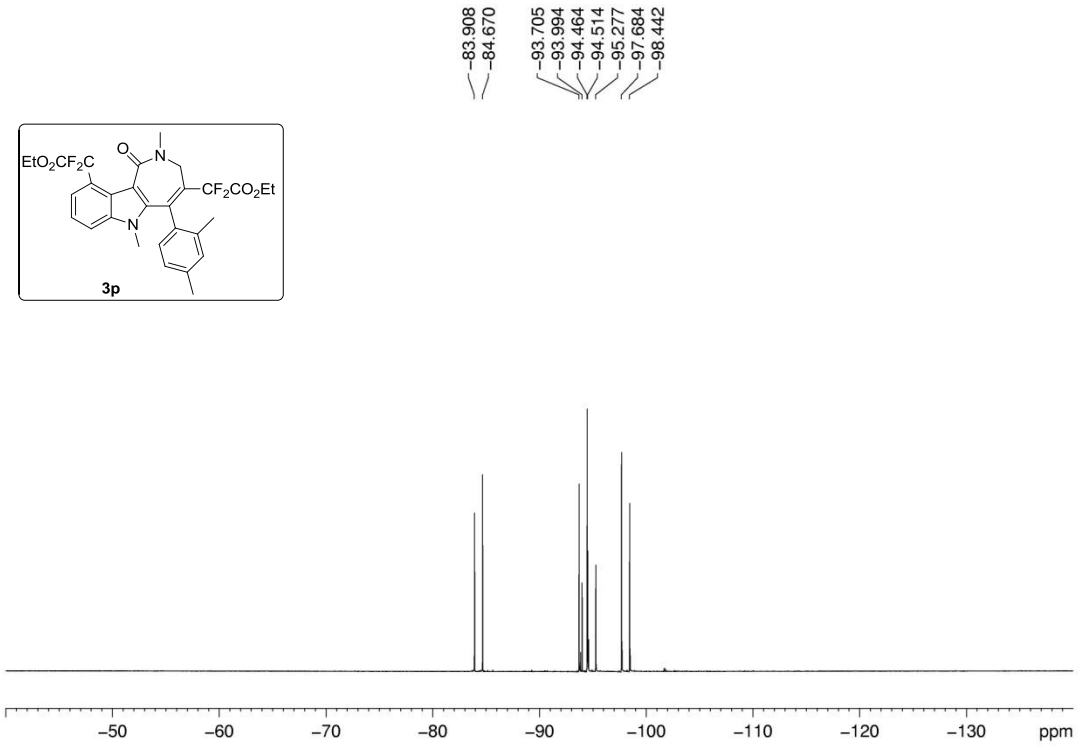
138.12
138.05
137.72
137.42
132.96
132.73
132.67
132.61
132.58
132.44
131.33
131.10
127.23
126.99
126.74
126.46
123.81
121.93
121.88
121.27
121.21
121.14
121.07
116.89
116.07
114.66
114.48
114.34
112.26
112.15
112.08
111.93
109.76
77.32
77.00
76.68
62.82
62.18
46.64
46.57
33.88
32.16
21.21
19.65
13.99
13.45
EtO2CF2C
CF2CO2Et
3p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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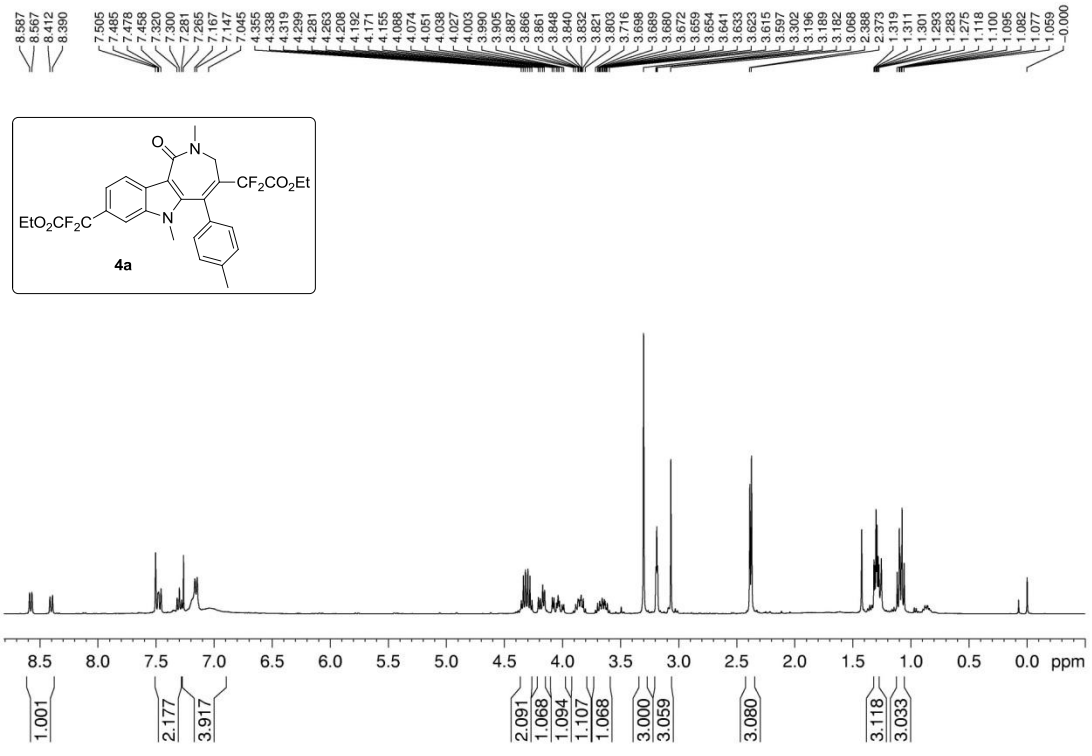
−84.670
−93.705
−93.994
−94.464
−94.514
−95.277
−97.684
−98.442
EtO2CF2C
CF2CO2Et
3p
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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7.485
7.478
7.458
7.320
7.300
7.281
7.265
7.167
7.147
7.045
4.355
4.338
4.319
4.299
4.281
4.263
4.208
4.192
4.171
4.155
4.088
4.074
4.051
4.038
4.027
4.003
3.990
3.905
3.887
3.866
3.861
3.848
3.840
3.832
3.821
3.803
3.716
3.698
3.689
3.680
3.672
3.659
3.654
3.641
3.633
3.623
3.615
3.597
3.302
3.196
3.189
3.182
3.068
2.388
2.373
1.319
1.311
1.301
1.293
1.283
1.275
1.118
1.100
1.095
1.082
1.077
1.059
−0.000
EtO2CF2C
CF2CO2Et
4a
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.001
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1.068
3.000
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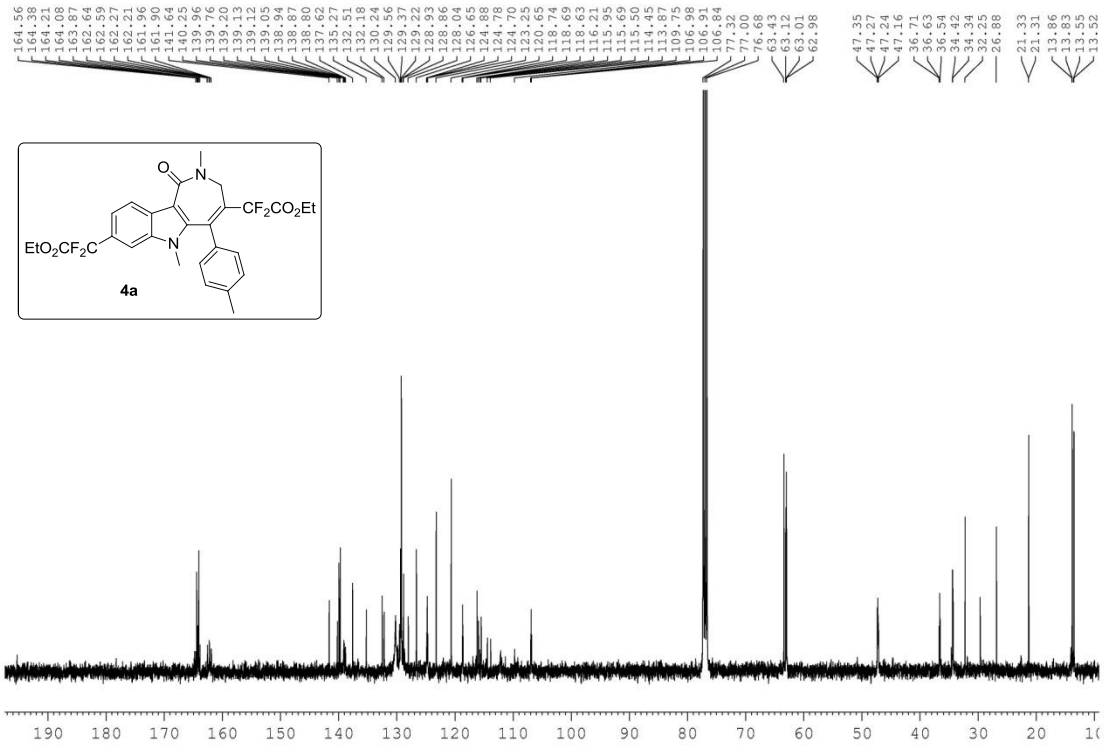
3.118
3.033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141.64
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139.96
139.76
139.20
139.13
139.12
139.05
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138.87
138.80
137.62
135.27
132.51
132.18
130.24
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129.37
129.22
128.93
128.86
128.04
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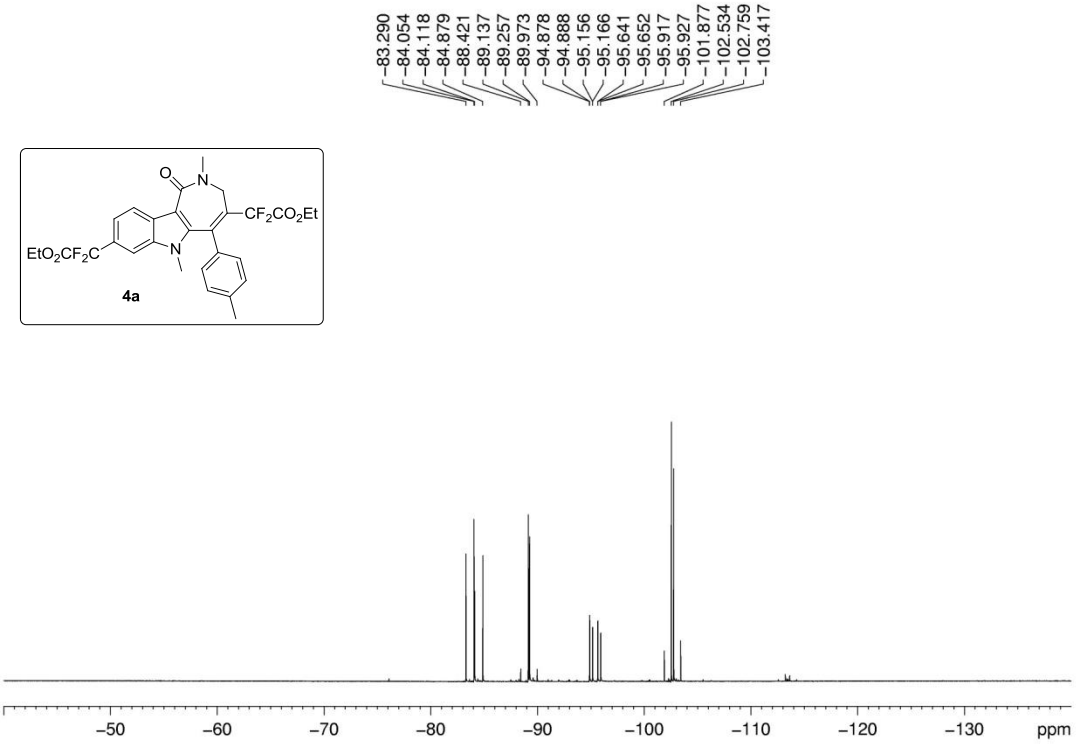
124.88
124.78
124.70
123.25
120.65
118.74
118.69
118.63
116.21
115.95
115.69
115.50
114.45
113.87
109.75
106.98
106.91
106.84
77.32
77.00
76.68
63.43
63.12
63.01
62.98
47.35
47.27
47.24
47.16
36.71
36.63
36.54
34.42
34.34
32.25
26.88
21.33
21.31
13.86
13.83
13.55
13.52
O
N
CF2CO2Et
EtO2CF2C
N
4a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20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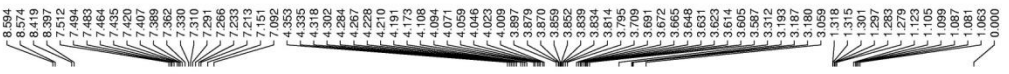
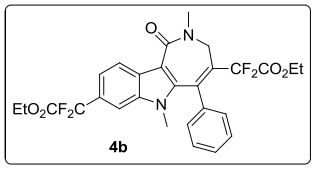
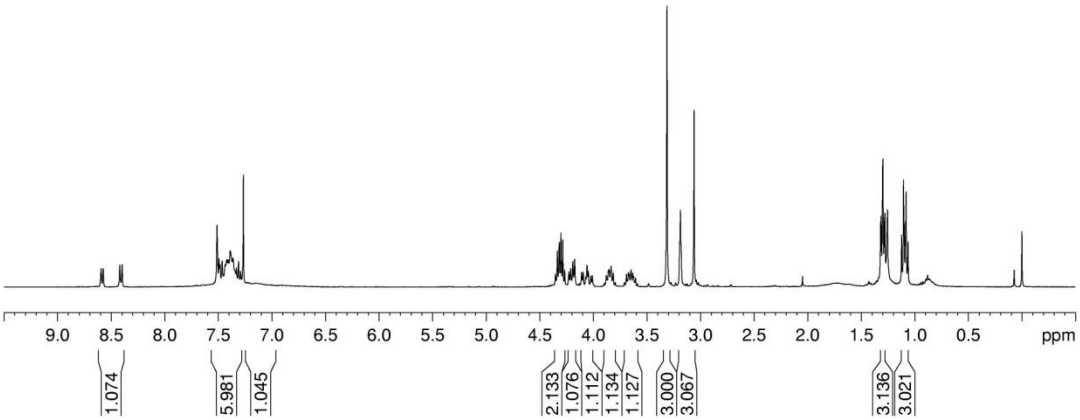
-89.257
-89.973
-94.878
-94.888
-95.156
-95.166
-95.641
-95.652
-95.917
-95.927
-101.877
-102.534
-102.759
-103.417
O
N
CF2CO2Et
EtO2CF2C
N
4a
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm




O
N
CF2CO2Et
EtO2CF2C
N
4b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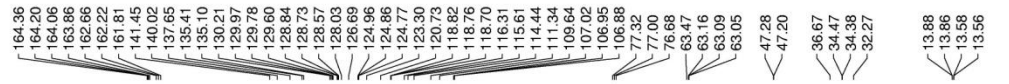
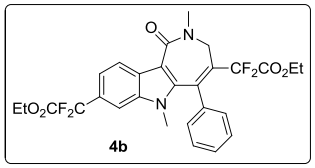
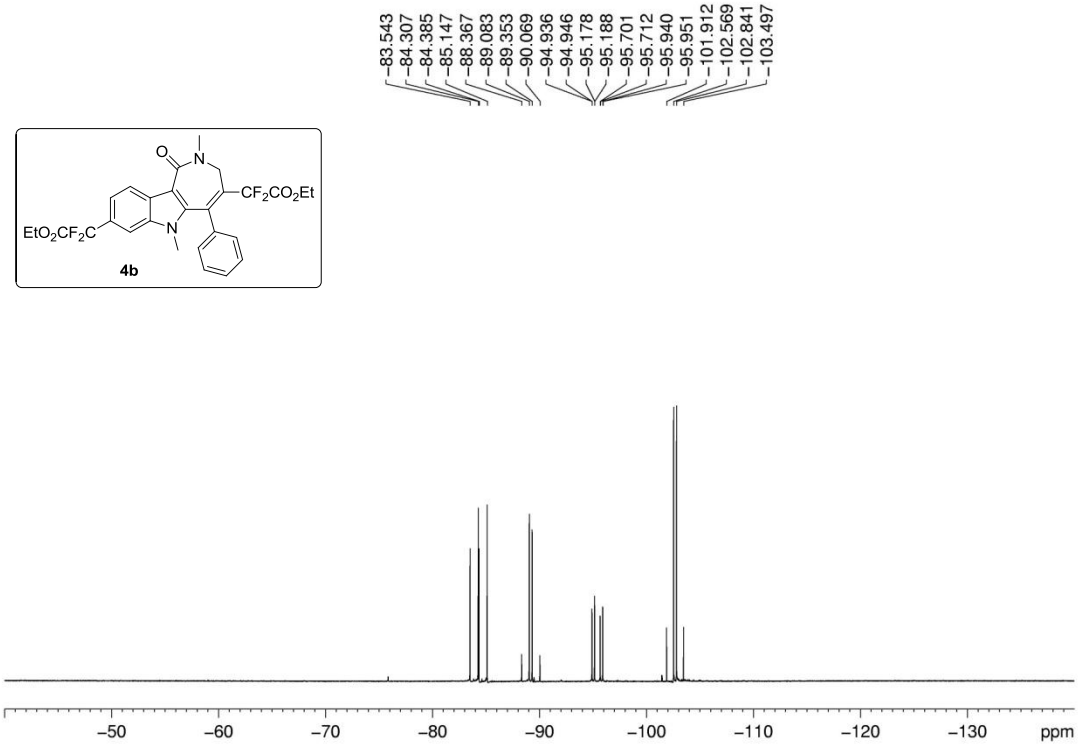
1.045
2.133
1.076
1.112
1.134
1.127
3.000
3.067
3.136
3.021




O
N
CF2CO2Et
EtO2CF2C
N
4b

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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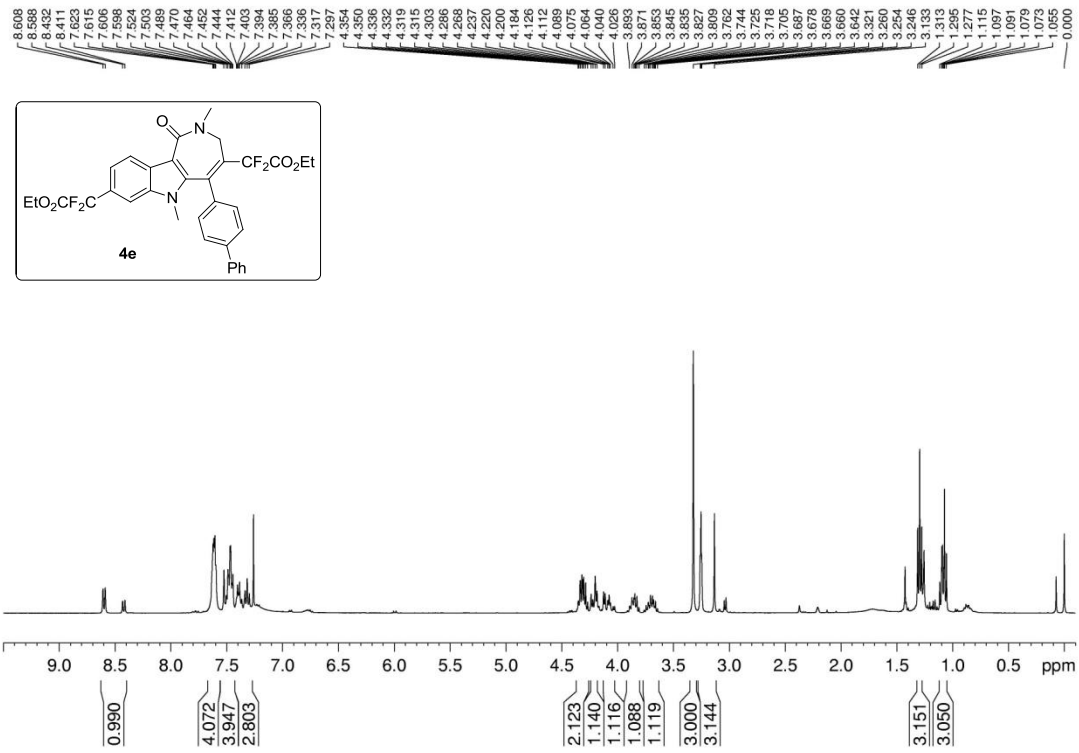
-89.353
-90.069
-94.936
-94.946
-95.178
-95.188
-95.701
-95.712
-95.940
-95.951
-101.912
-102.569
-102.841
-103.497
O
N
CF2CO2Et
EtO2CF2C
N
4b
−50
−60
−70
−80
−90
−100
−110
−120
−130
ppm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7.464
7.452
7.444
7.412
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7.394
7.385
7.366
7.336
7.317
7.297
4.354
4.350
4.336
4.332
4.319
4.315
4.303
4.286
4.268
4.237
4.220
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4.075
4.064
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3.744
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3.718
3.705
3.697
3.678
3.669
3.660
3.642
3.321
3.260
3.254
3.246
3.133
1.313
1.295
1.277
1.115
1.097
1.091
1.079
1.073
1.055
0.000
O
N
CF2CO2Et
EtO2CF2C
N
4e
Ph
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.990
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2.123
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1.119
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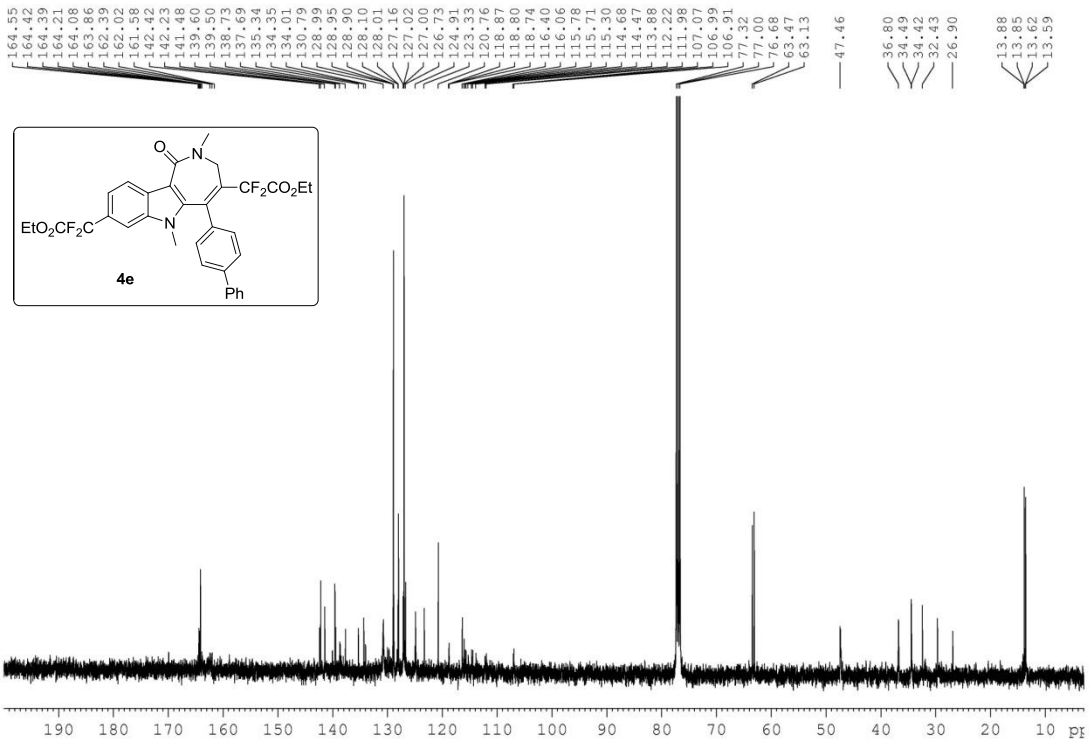
3.151
3.050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162.02
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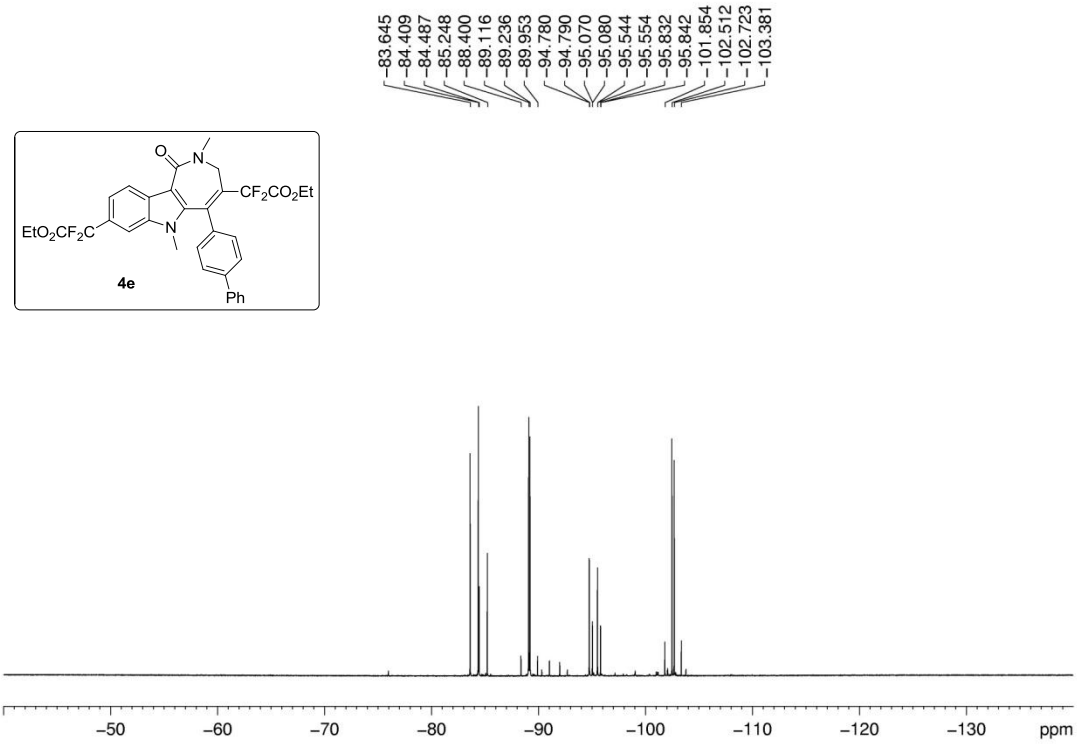
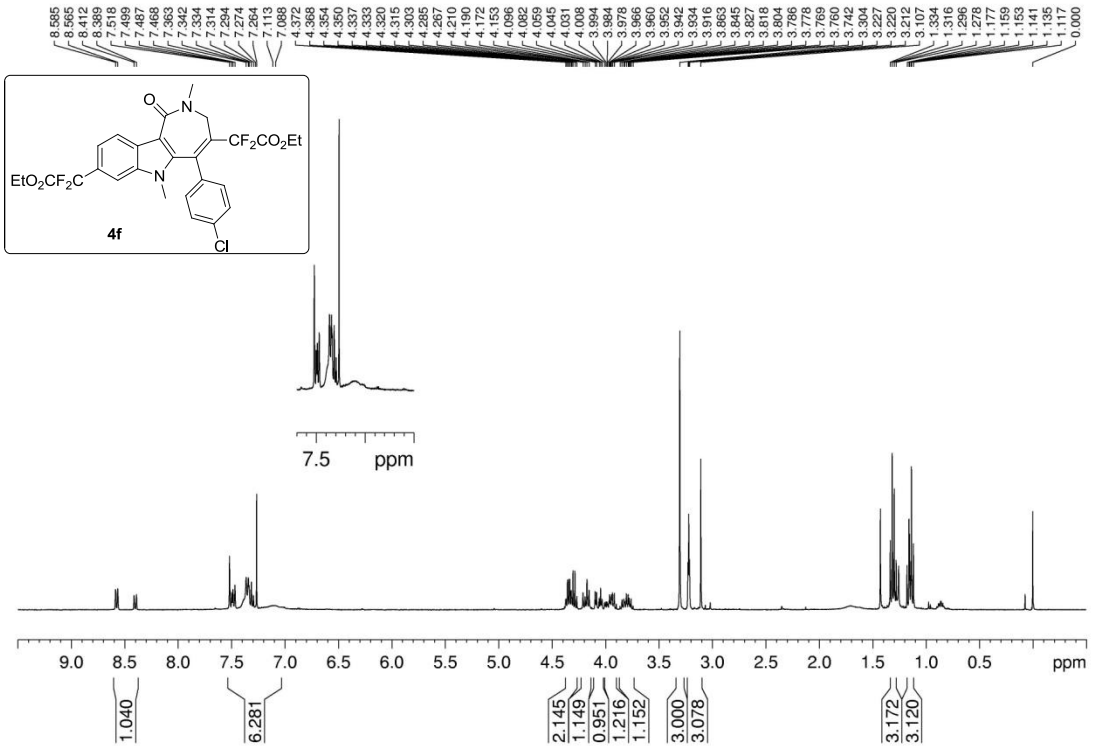
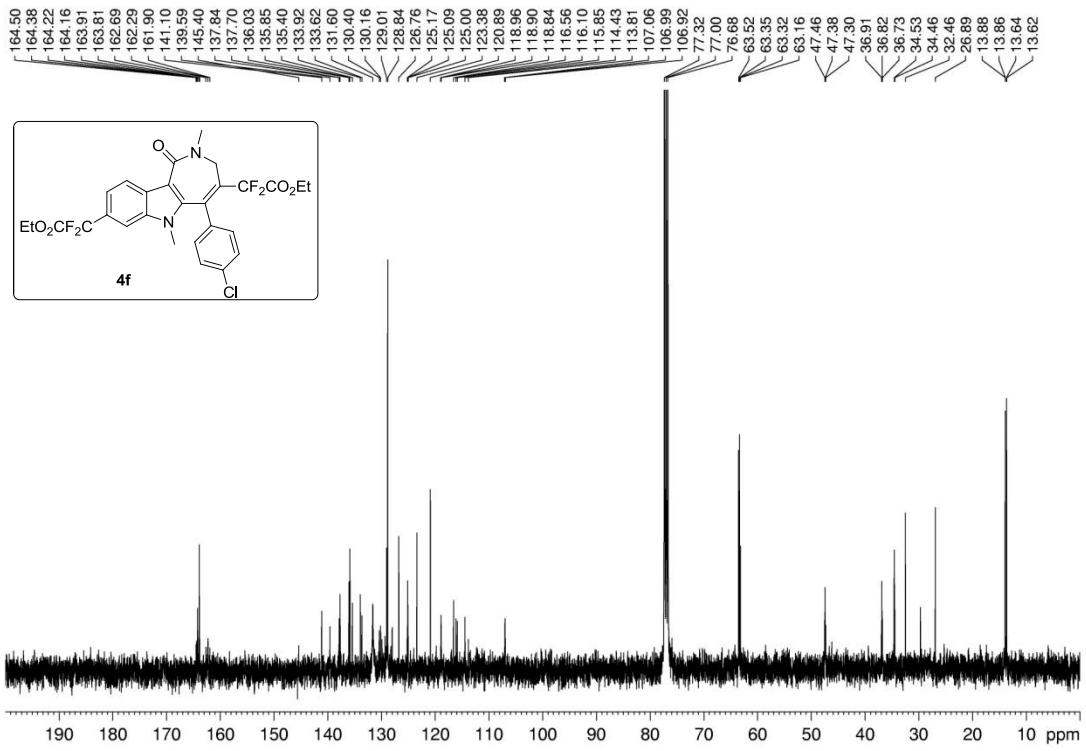
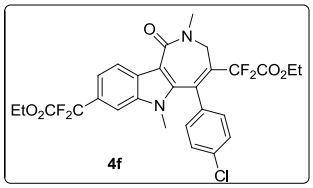
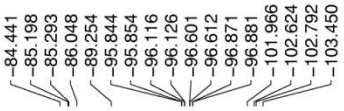
142.23
141.48
139.60
139.50
138.73
137.69
135.34
134.35
134.01
130.79
128.99
128.95
128.90
128.10
128.01
127.16
127.02
127.00
126.73
124.91
123.33
120.76
118.87
118.80
118.74
116.40
116.06
115.78
115.71
115.30
114.68
114.47
113.88
112.22
111.98
107.07
106.99
106.91
77.32
77.00
76.68
63.47
63.13
47.46
36.80
34.49
34.42
32.43
26.90
13.88
13.85
13.62
13.59
O
N
CF2CO2Et
EtO2CF2C
N
4e
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 pp

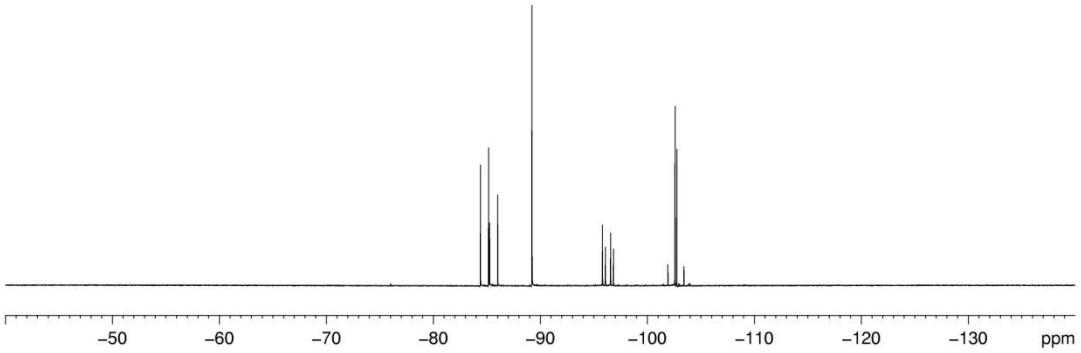

-83.645
-84.409
-84.487
-85.248
-88.400
-89.116
-89.236
-89.953
-94.780
-94.790
-95.070
-95.080
-95.544
-95.554
-95.832
-95.842
-101.854
-102.512
-102.723
-103.381
O
N
CF2CO2Et
EtO2CF2C
N
4e
Ph
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm

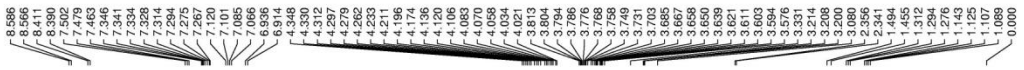

4f
7.5 ppm
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.040
6.281
2.145
1.149
0.951
1.216
1.152
3.000
3.078
3.172
3.120

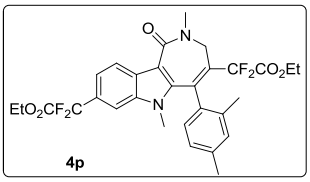

4f
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

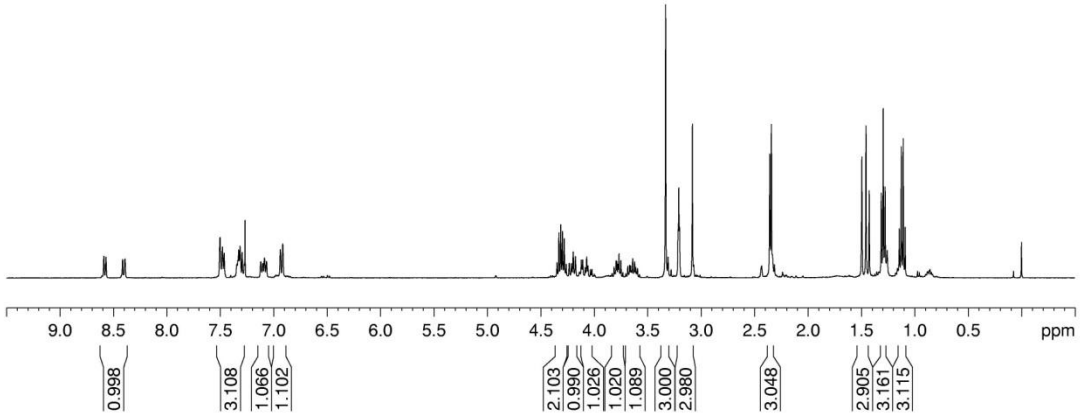

O
N
CF2CO2Et
EtO2CF2C
N
4f
Cl

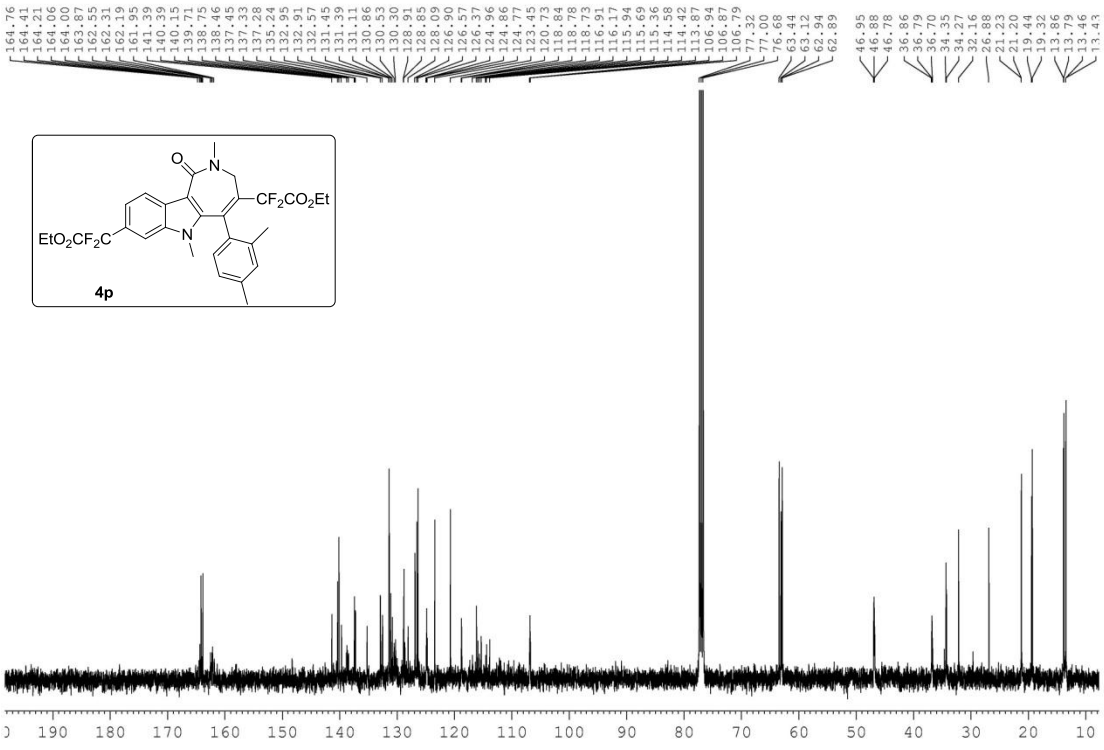

-84.441
-85.198
-85.293
-86.048
-89.254
-95.844
-95.854
-96.116
-96.126
-96.601
-96.612
-96.871
-96.881
-101.966
-102.624
-102.792
-103.450

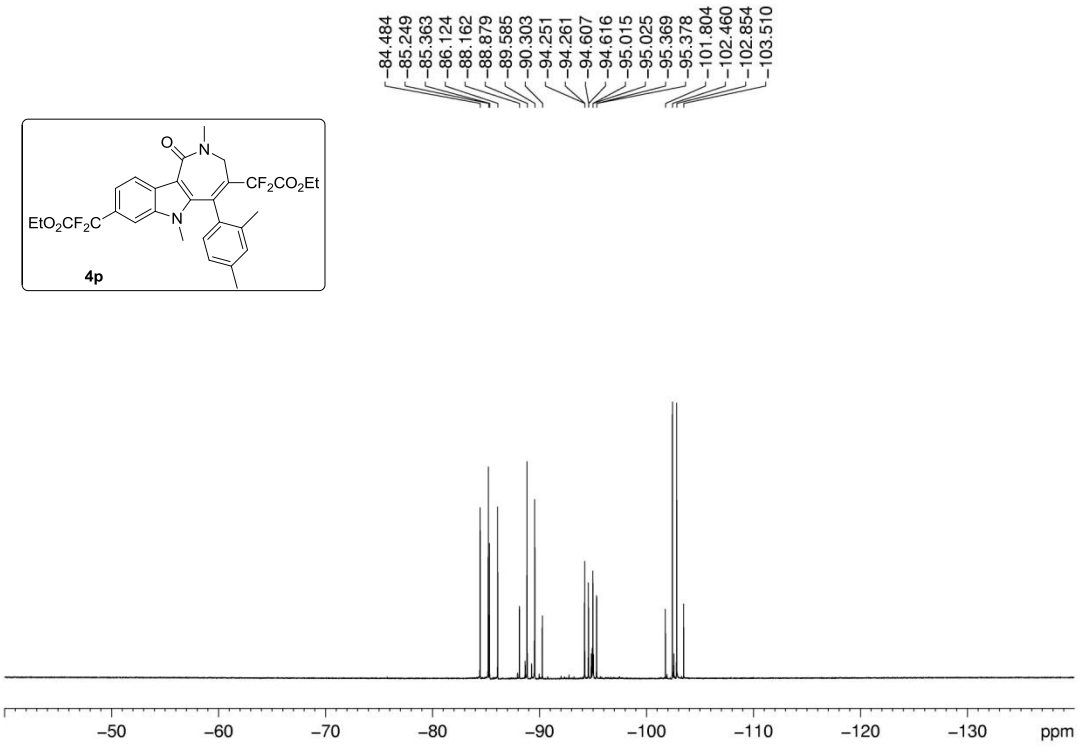

-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm



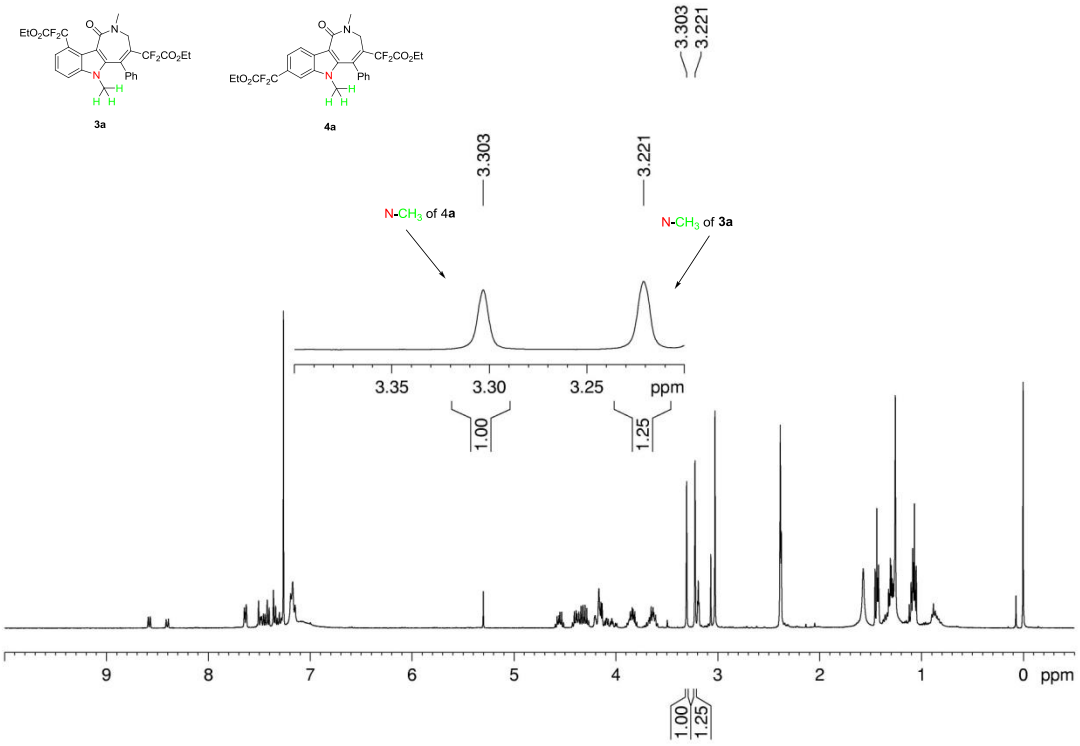

O
N
CF2CO2Et
EtO2CF2C
N
4p

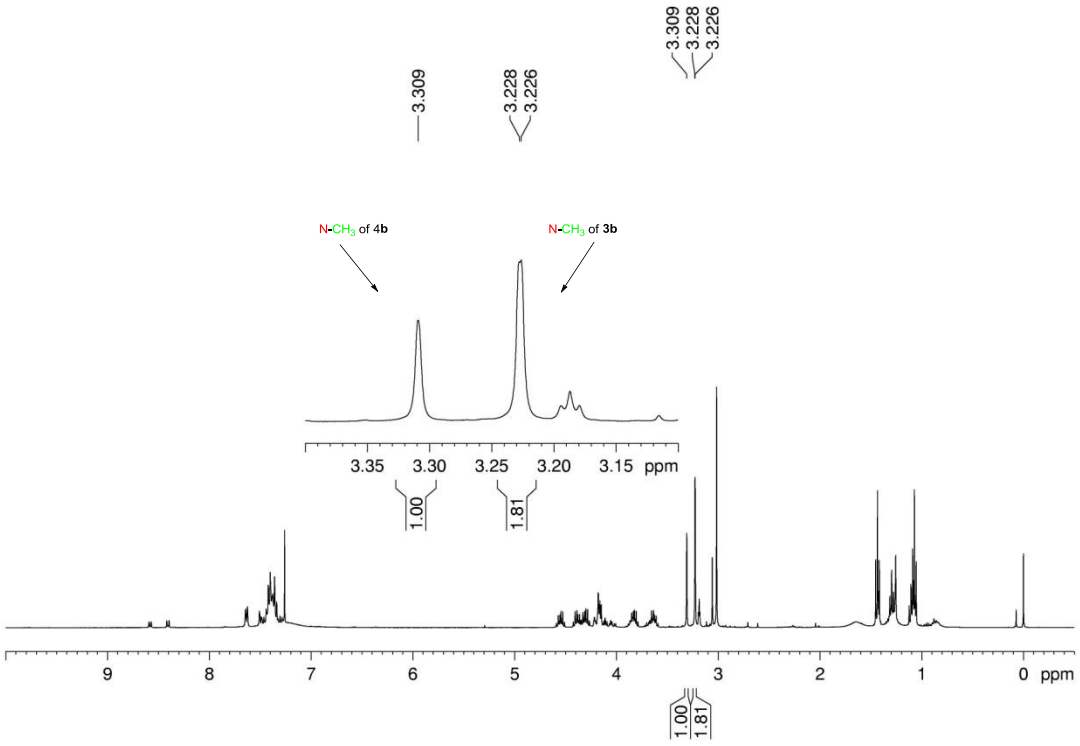

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.998
3.108
1.066
1.102
2.103
0.990
1.026
1.020
1.089
3.000
2.980
3.048
2.905
3.161
3.115

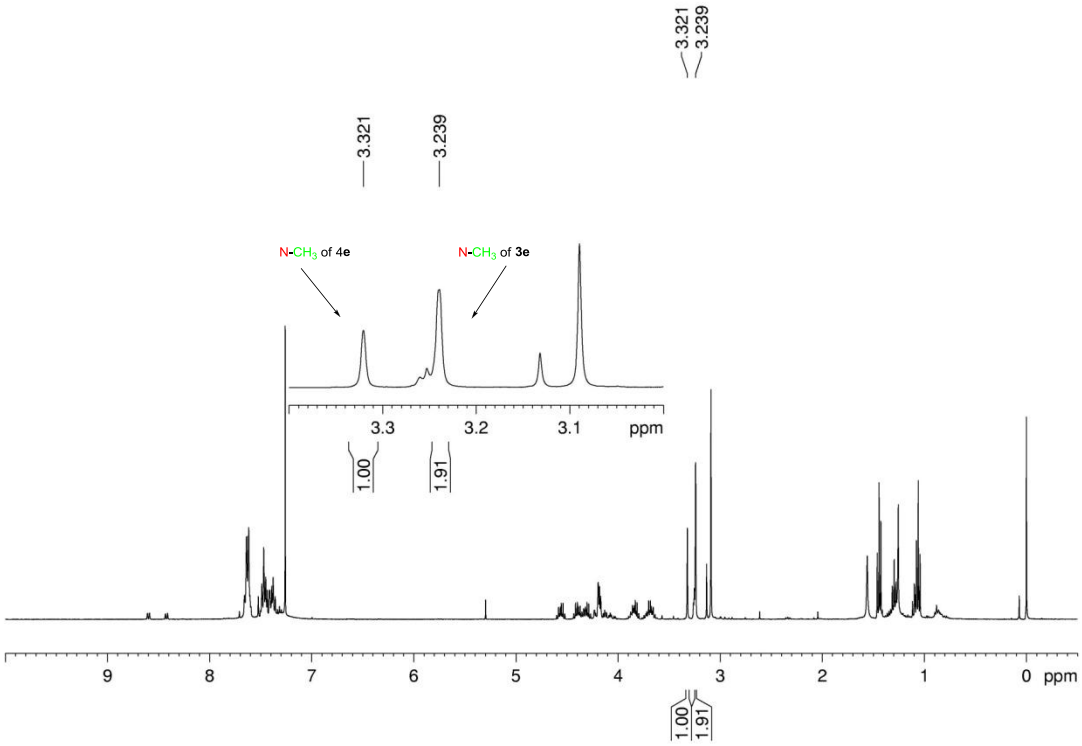

4p

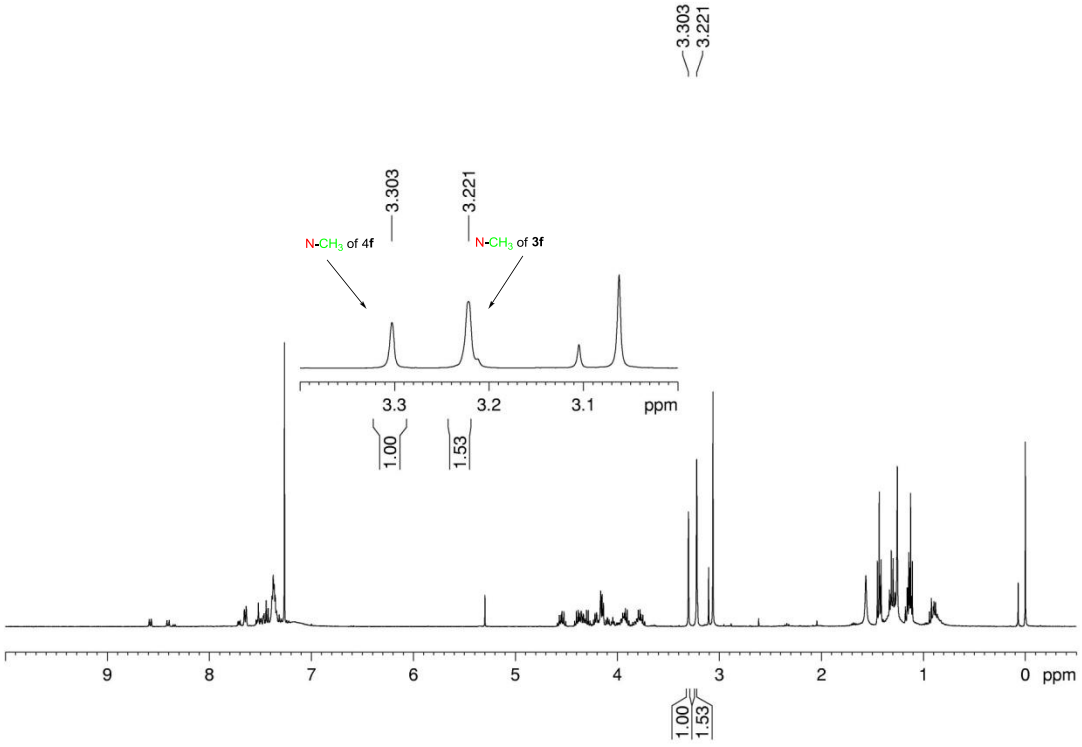

4p
ppm

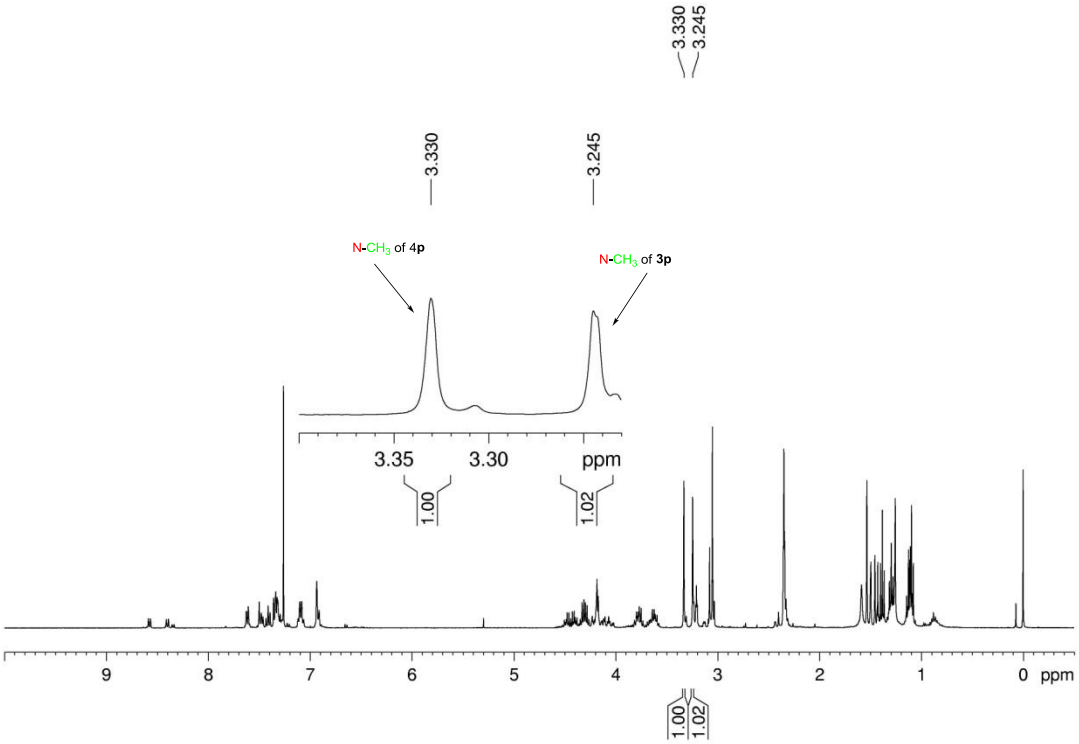
11. The ratio of 3 and 4 was determined by crude ^{1}H NMR spectra



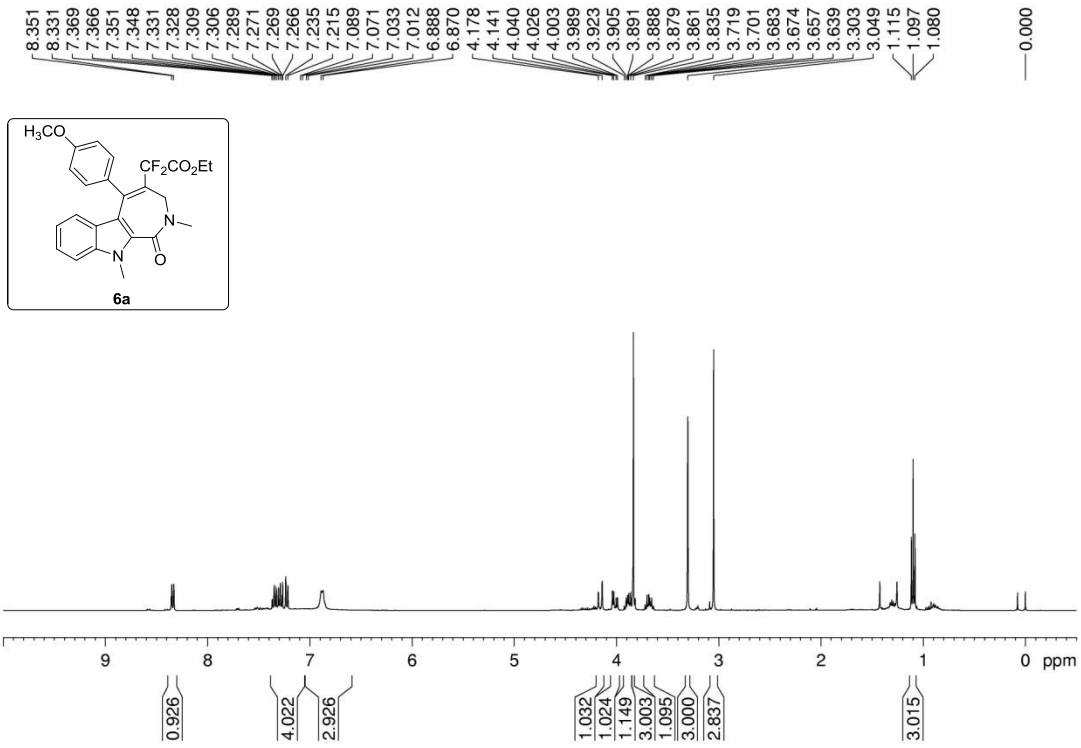


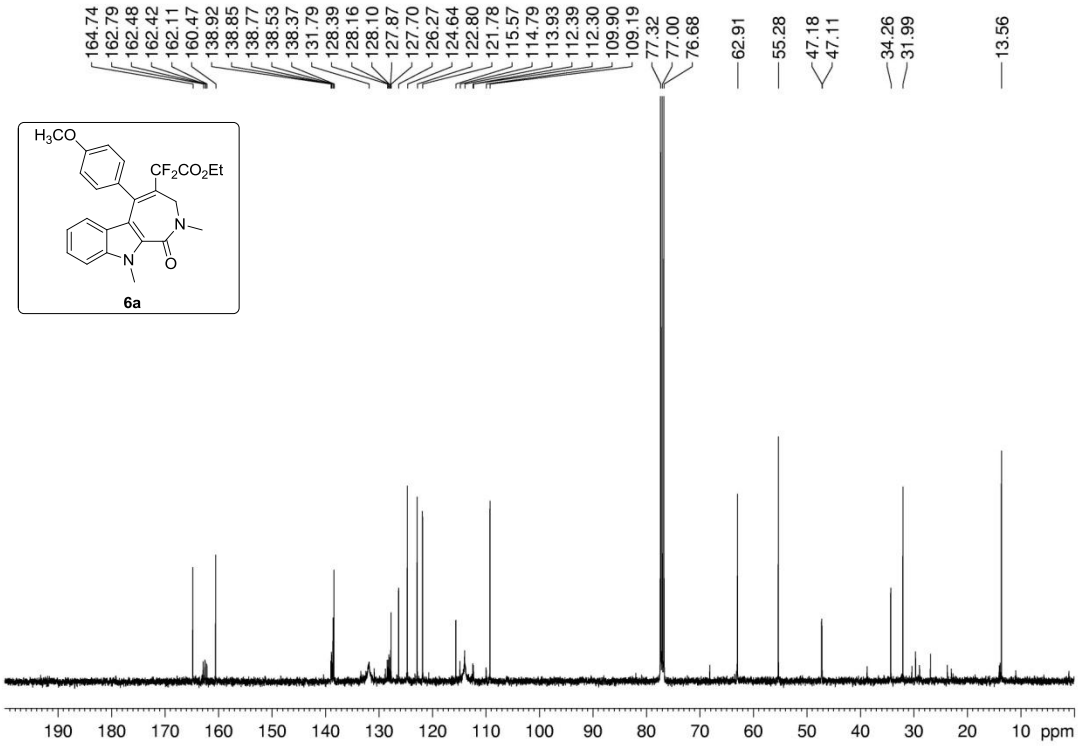

3.321
3.239
3.321
3.239
N-CH3 of 4e
N-CH3 of 3e
3.3
3.2
3.1
ppm
1.00
1.91
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.91

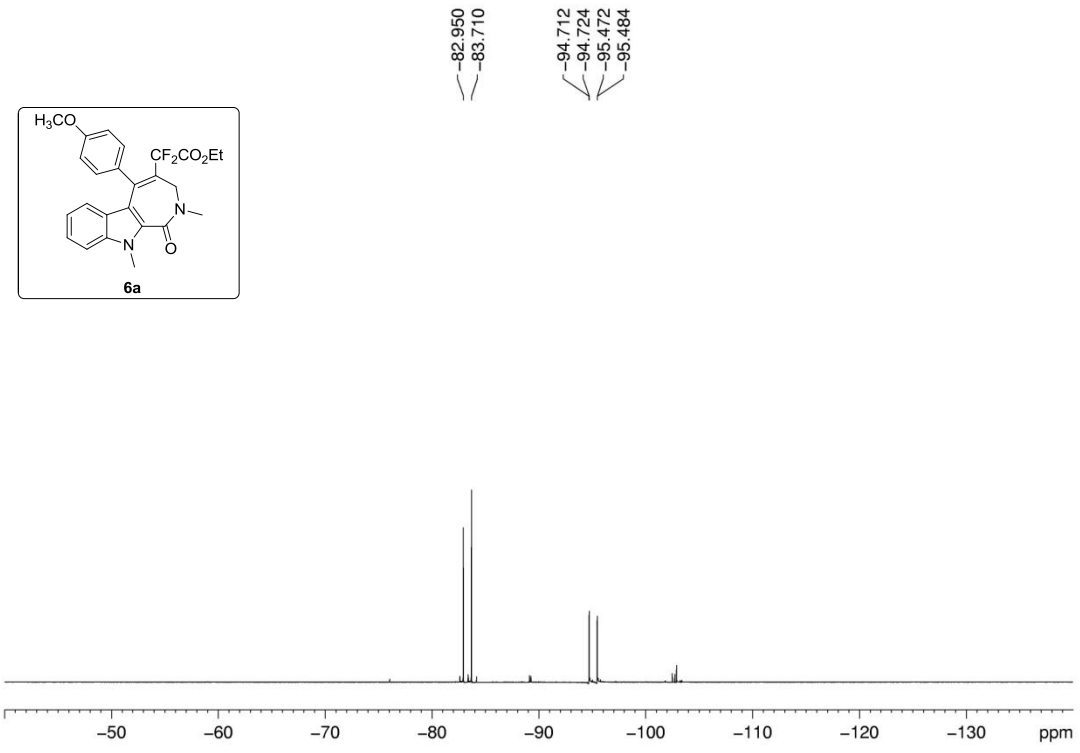

3.303
3.221
3.303
3.221
N-CH3 of 4f
N-CH3 of 3f
3.3
3.2
3.1
ppm
1.00
1.53
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.53

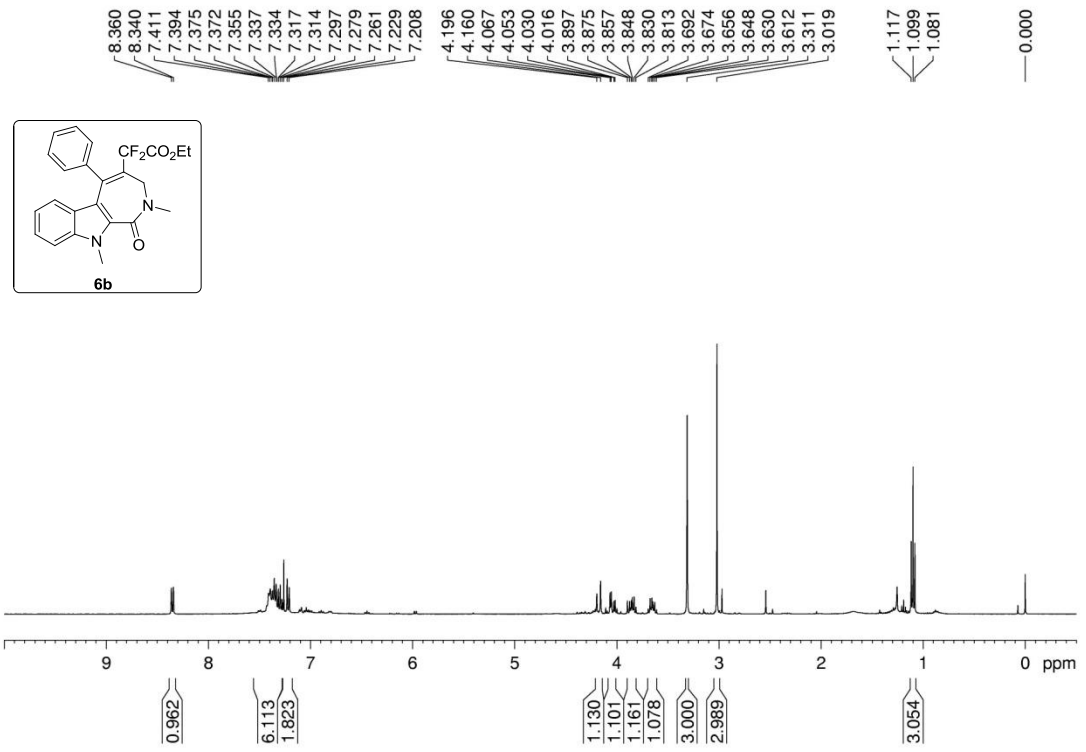


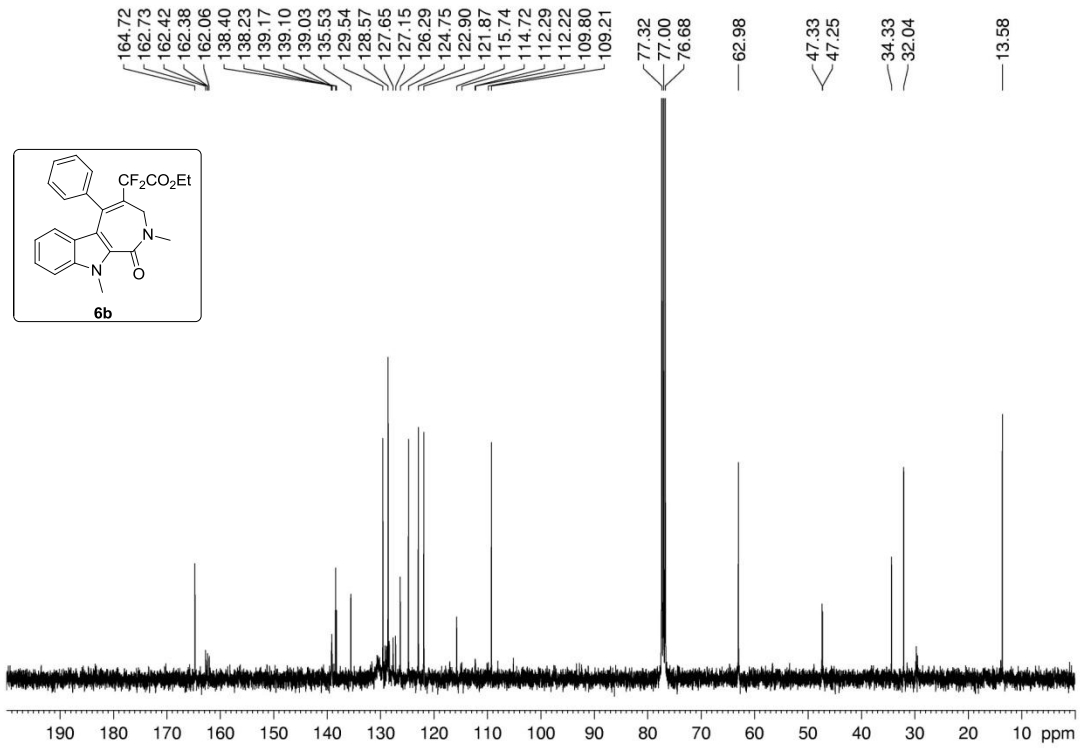
12. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 6a-6i and 7b

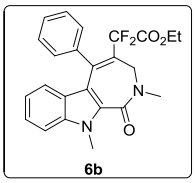



164.74
162.79
162.48
162.42
162.11
160.47
138.92
138.85
138.77
138.53
138.37
131.79
128.39
128.16
128.10
127.87
127.70
126.27
124.64
122.80
121.78
115.57
114.79
113.93
112.39
112.30
109.90
109.19
77.32
77.00
76.68
62.91
55.28
47.18
47.11
34.26
31.99
13.56
H3CO
CF2CO2Et
N
N
O
6a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-82.950
-83.710
-94.712
-94.724
-95.472
-95.484
H3CO
CF2CO2Et
N
N
O
6a
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm

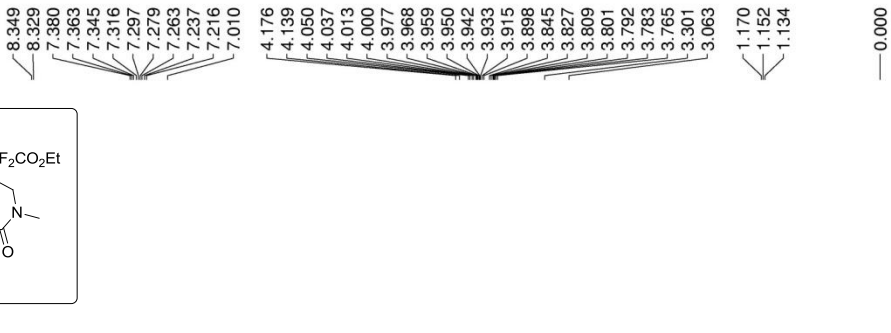

8.360
8.340
7.411
7.394
7.375
7.372
7.355
7.337
7.334
7.317
7.314
7.297
7.279
7.261
7.229
7.208
4.196
4.160
4.067
4.053
4.030
4.016
3.897
3.875
3.857
3.848
3.830
3.813
3.692
3.674
3.656
3.648
3.630
3.612
3.311
3.019
1.117
1.099
1.081
0.000
CF2CO2Et
N
N
O
6b
9
8
7
6
5
4
3
2
1
0 ppm
0.962
6.113
1.823
1.130
1.101
1.161
1.078
3.000
2.989
3.054

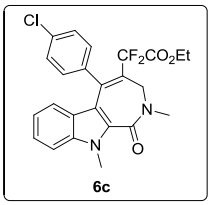

164.72
162.73
162.42
162.38
162.06
138.40
138.23
139.17
139.10
139.03
135.53
129.54
128.57
127.65
127.15
126.29
124.75
122.90
121.87
115.74
114.72
112.29
112.22
109.80
109.21
77.32
77.00
76.68
62.98
47.33
47.25
34.33
32.04
13.58
CF2CO2Et
N
N
O
6b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


CF2CO2Et
N
O
N

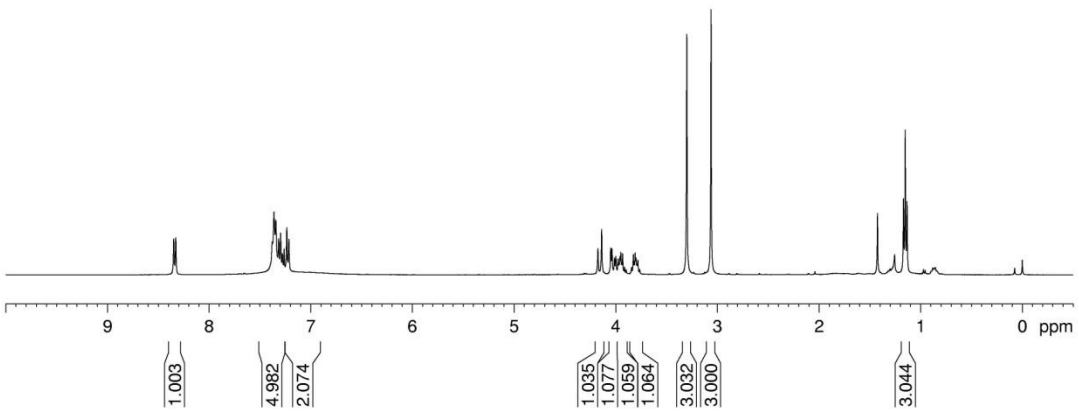
6b

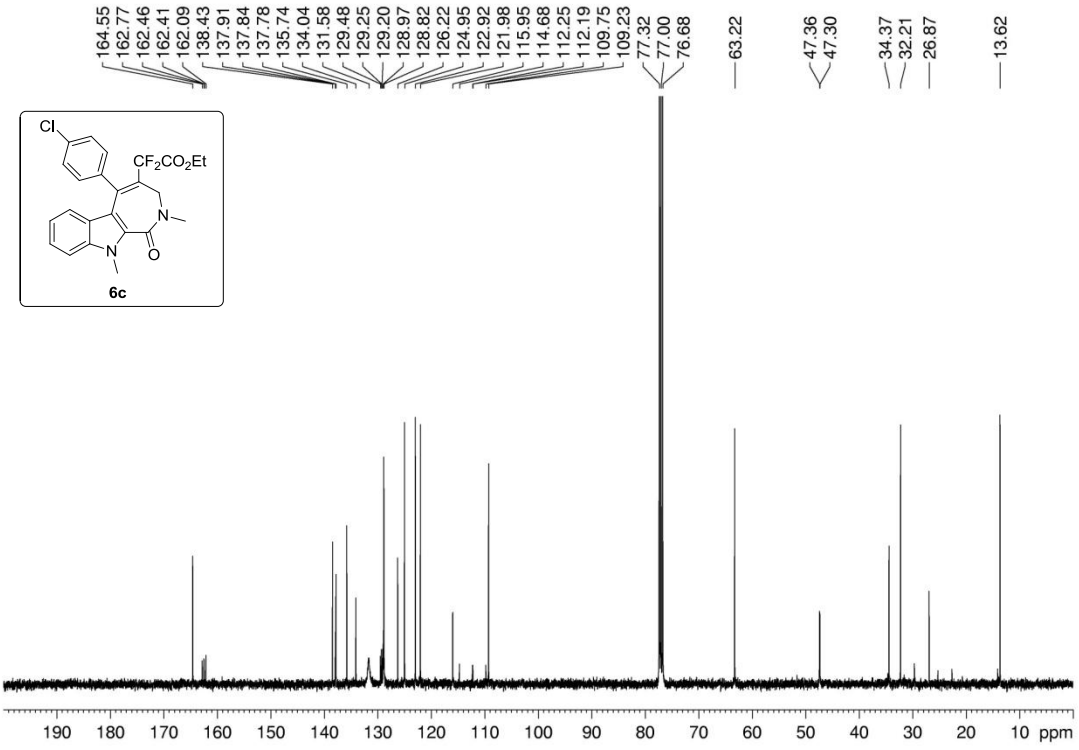
-83.943
-84.703
-94.896
-94.907
-95.656
-95.668
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm

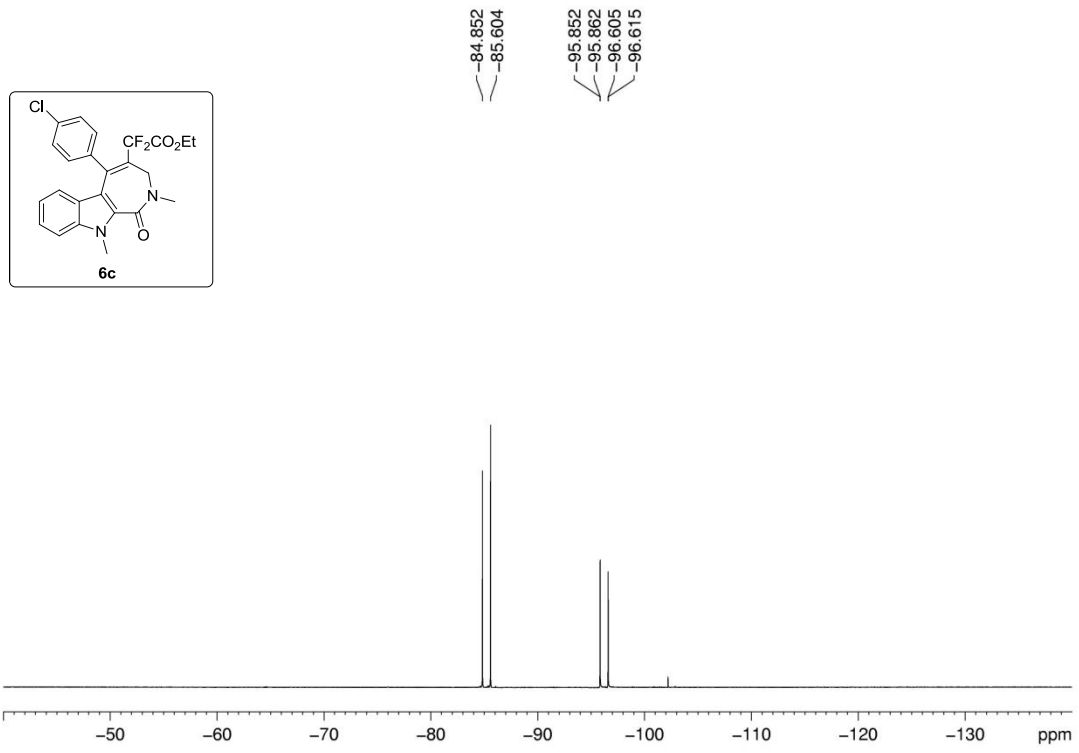

8.349
8.329
7.380
7.363
7.345
7.316
7.297
7.279
7.263
7.237
7.216
7.010
4.176
4.139
4.050
4.037
4.013
4.000
3.977
3.968
3.959
3.950
3.942
3.933
3.915
3.898
3.845
3.827
3.809
3.801
3.792
3.783
3.765
3.301
3.063
1.170
1.152
1.134
0.000

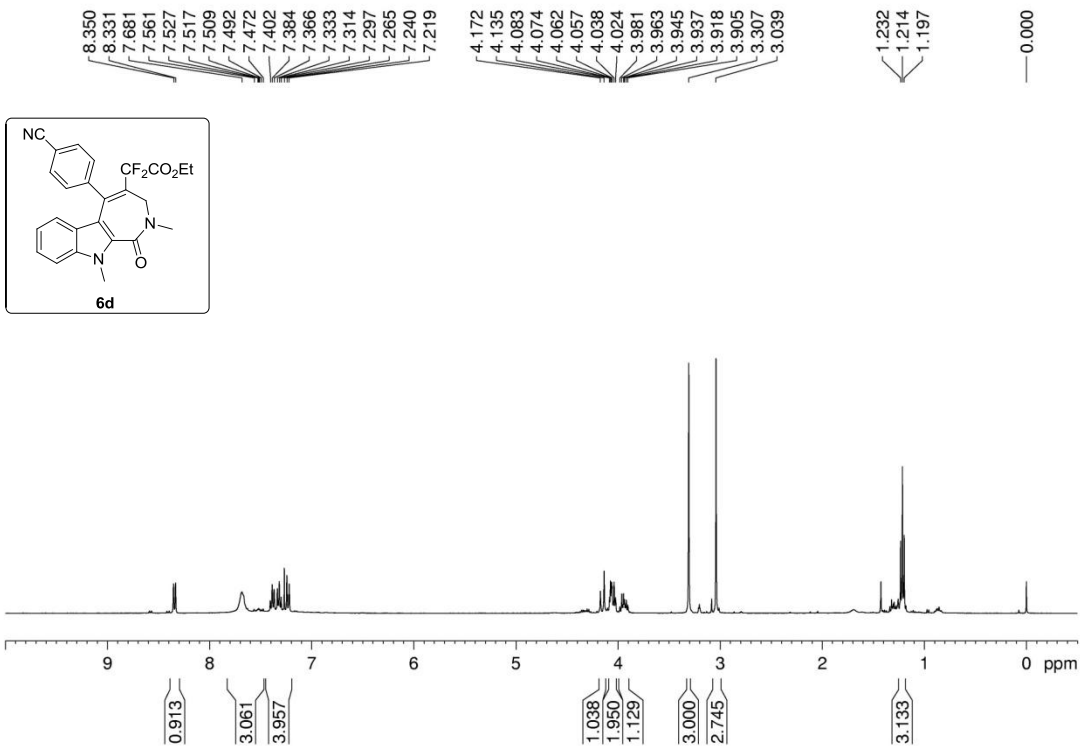

Cl
CF2CO2Et
N
O
N

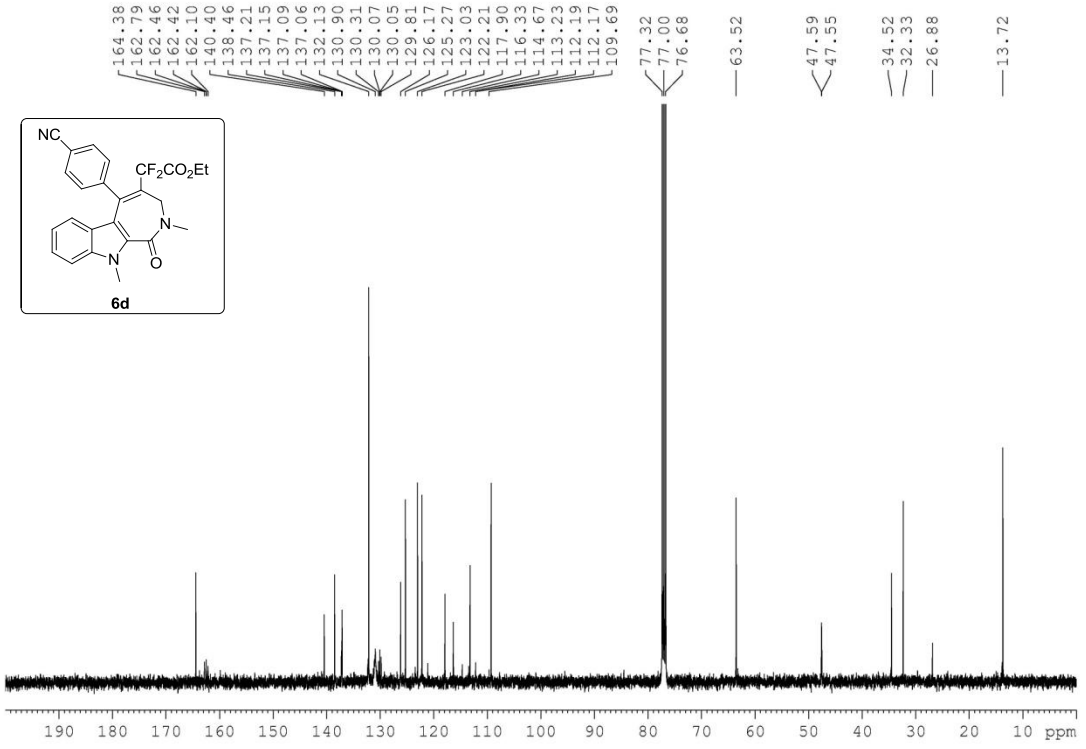
6c

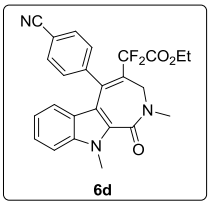

9
8
7
6
5
4
3
2
1
0 ppm
1.003
4.982
2.074
1.035
1.077
1.059
1.064
3.032
3.000
3.044


164.55
162.77
162.46
162.41
162.09
138.43
137.91
137.84
137.78
135.74
134.04
131.58
129.48
129.25
129.20
128.97
128.82
126.22
124.95
122.92
121.98
115.95
114.68
112.25
112.19
109.75
109.23
77.32
77.00
76.68
63.22
47.36
47.30
34.37
32.21
26.87
13.62
Cl
CF2CO2Et
N
N
O
6c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


84.852
85.604
95.852
95.862
96.605
96.615
Cl
CF2CO2Et
N
N
O
6c
−50 −60 −70 −80 −90 −100 −110 −120 −130 ppm

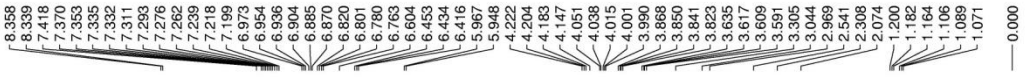

8.350
8.331
7.681
7.561
7.527
7.517
7.509
7.492
7.472
7.402
7.384
7.366
7.333
7.314
7.297
7.265
7.240
7.219
4.172
4.135
4.083
4.074
4.062
4.057
4.038
4.024
3.981
3.963
3.945
3.937
3.918
3.905
3.307
3.039
1.232
1.214
1.197
0.000
NC
CF2CO2Et
N
O
N
6d
9
8
7
6
5
4
3
2
1
0 ppm
0.913
3.061
3.957
1.038
1.950
1.129
3.000
2.745
3.133

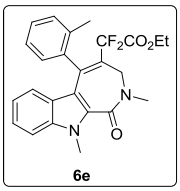

164.38
162.79
162.46
162.42
162.10
140.40
138.46
137.21
137.15
137.09
137.06
132.13
130.90
130.31
130.07
130.05
129.81
126.17
125.27
123.03
122.21
117.90
116.33
114.67
113.23
112.19
112.17
109.69
77.32
77.00
76.68
63.52
47.59
47.55
34.52
32.33
26.88
13.72
NC
CF2CO2Et
N
O
N
6d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


NC
CF2CO2Et
N
O
N

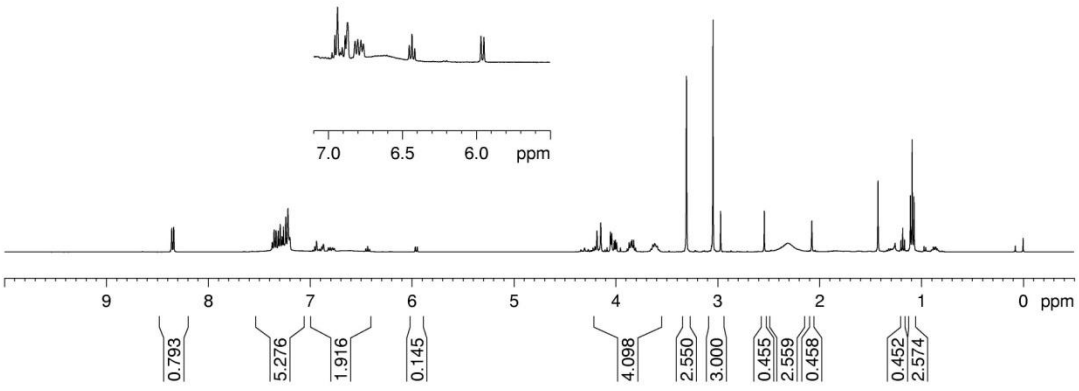
6d

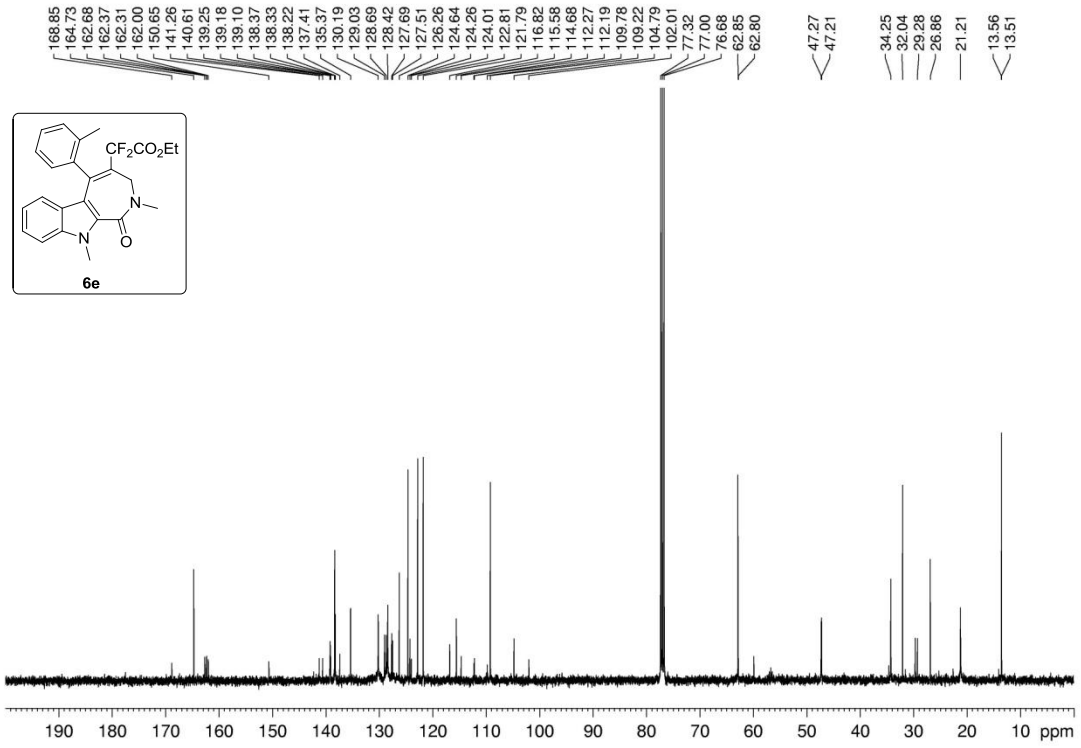
-87.166
-87.906
-97.216
-97.225
-97.956
-97.966
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm


8.358
8.339
7.418
7.370
7.353
7.335
7.332
7.311
7.293
7.276
7.262
7.239
7.218
7.199
6.973
6.954
6.936
6.904
6.885
6.870
6.820
6.801
6.780
6.763
6.604
6.453
6.434
6.416
5.967
5.948
4.222
4.204
4.183
4.147
4.051
4.038
4.015
4.001
3.990
3.868
3.850
3.841
3.823
3.635
3.617
3.609
3.591
3.305
3.044
2.969
2.541
2.308
2.074
1.200
1.182
1.164
1.106
1.089
1.071
0.000


CF2CO2Et
N
O
N

6e


7.0
6.5
6.0
ppm
9
8
7
6
5
4
3
2
1
0
ppm
0.793
5.276
1.916
0.145
4.098
2.550
3.000
0.455
2.559
0.458
0.452
2.574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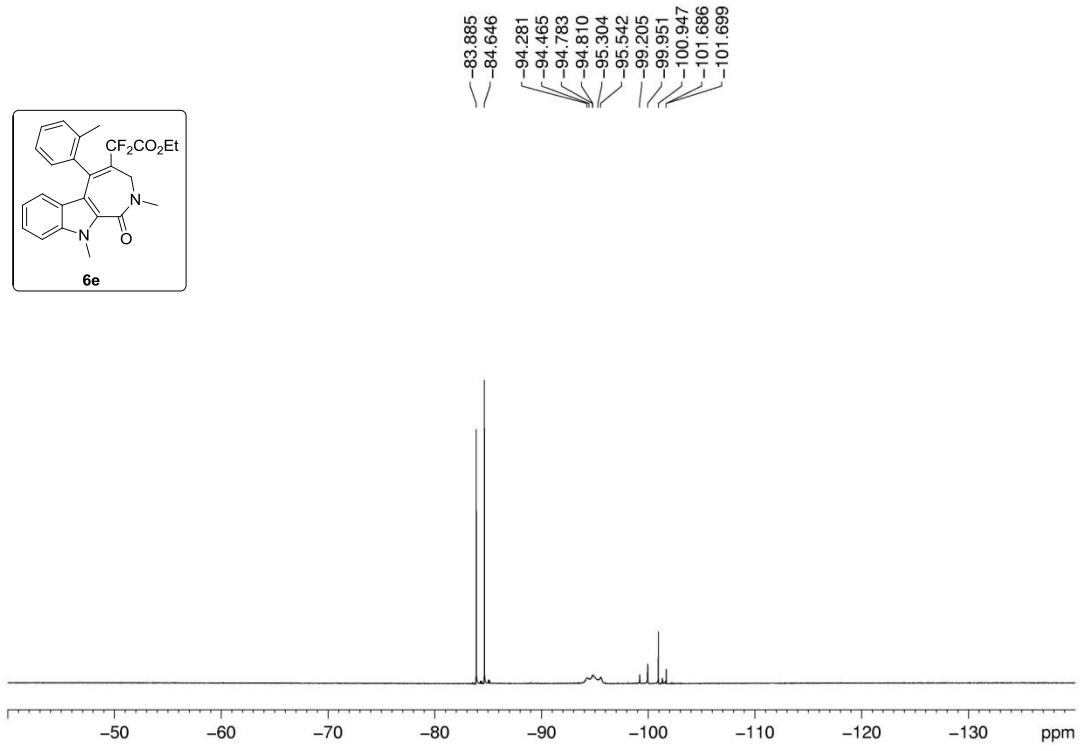
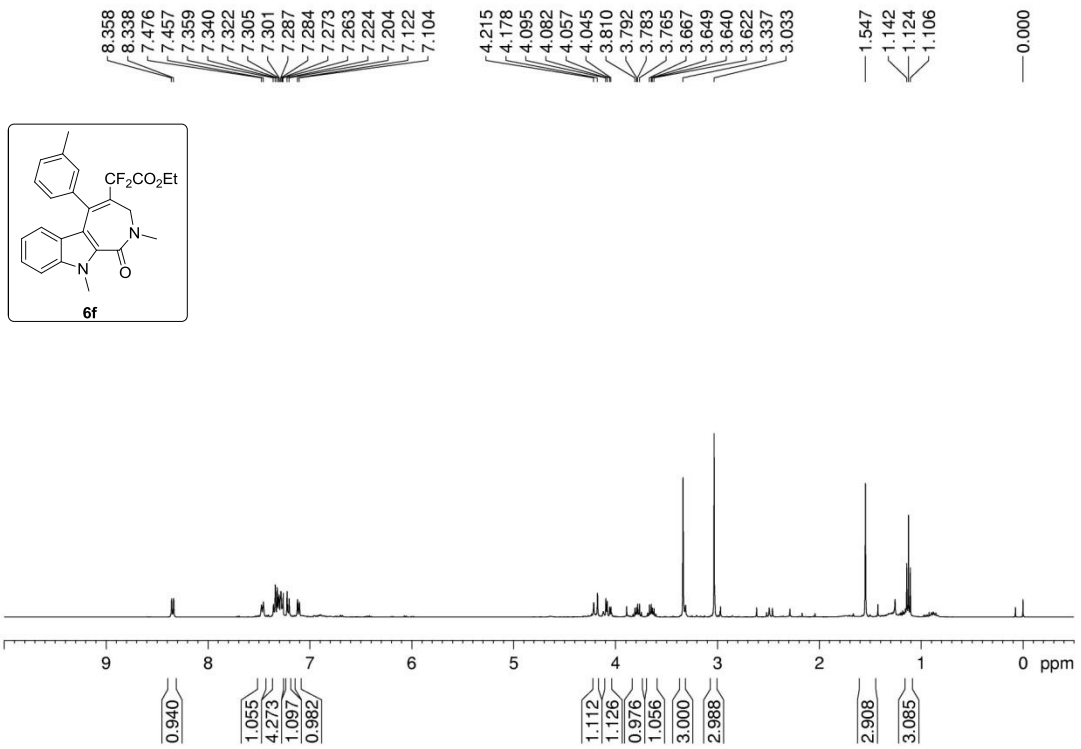
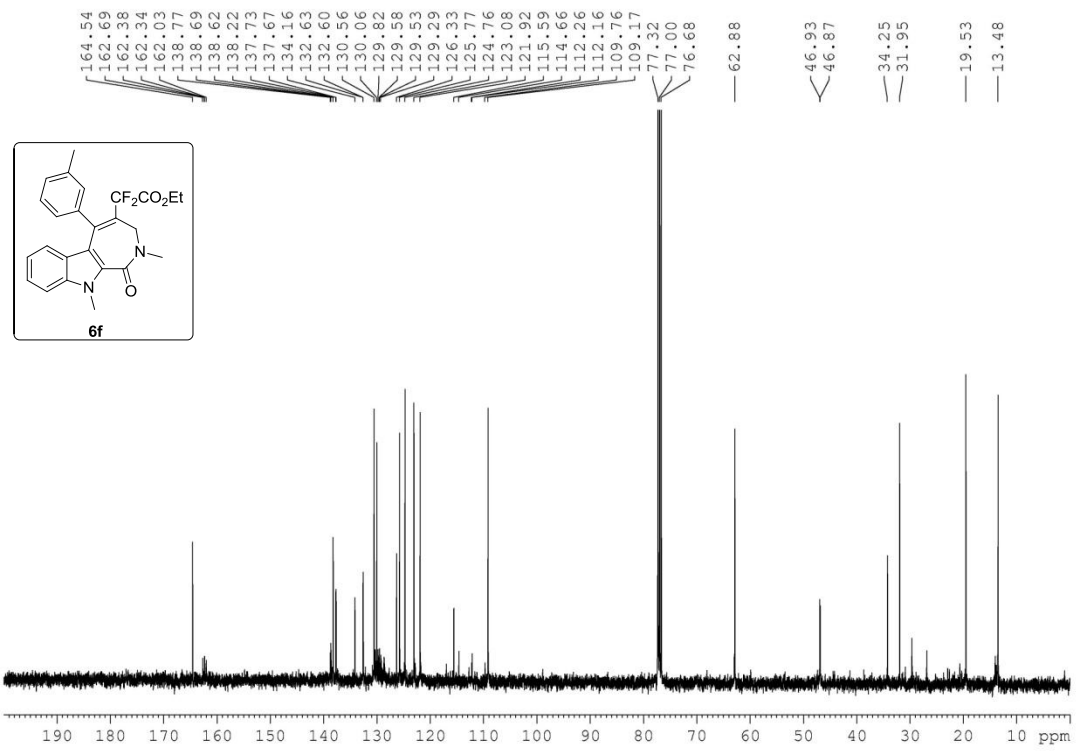
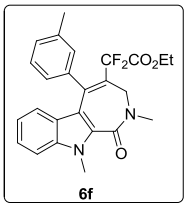
164.73
162.68
162.37
162.31
162.00
150.65
141.26
140.61
139.25
139.18
139.10
138.37
138.33
138.22
137.41
135.37
130.19
129.03
128.69
128.42
127.69
127.51
126.26
124.64
124.26
124.01
122.81
121.79
116.82
115.58
114.68
112.27
112.19
109.78
109.22
104.79
102.01
77.32
77.00
76.68
62.85
62.80
47.27
47.21
34.25
32.04
29.28
26.86
21.21
13.56
13.51
CF2CO2Et
N
N
O
6e
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

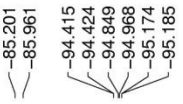

-83.885
-84.646
-94.281
-94.465
-94.783
-94.810
-95.304
-95.542
-99.205
-99.951
-100.947
-101.686
-101.699
CF2CO2Et
N
N
O
6e
−50 −60 −70 −80 −90 −100 −110 −120 −130 ppm

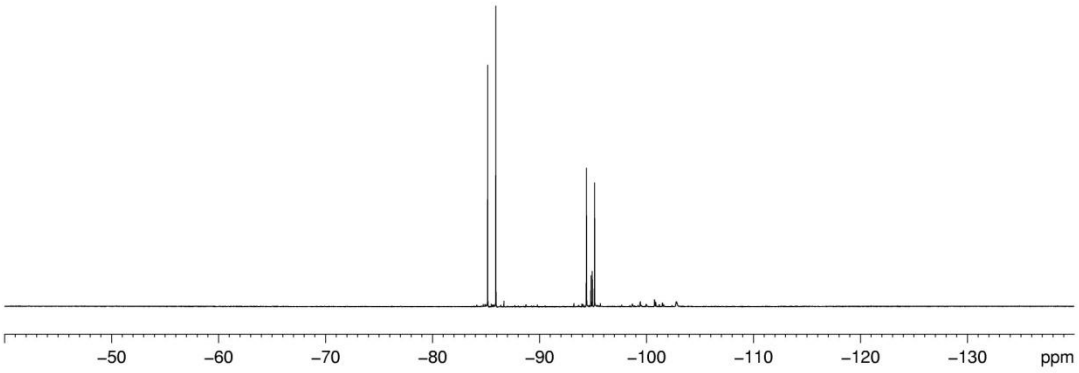

8.358
8.338
7.476
7.457
7.359
7.340
7.322
7.305
7.301
7.287
7.284
7.273
7.263
7.224
7.204
7.122
7.104
4.215
4.178
4.095
4.082
4.057
4.045
3.810
3.792
3.783
3.765
3.667
3.649
3.640
3.622
3.337
3.033
1.547
1.142
1.124
1.106
0.000
CF2CO2Et
N
N
O
6f
9
8
7
6
5
4
3
2
1
0 ppm
0.940
1.055
4.273
1.097
0.982
1.112
1.126
0.976
1.056
3.000
2.988
2.908
3.085

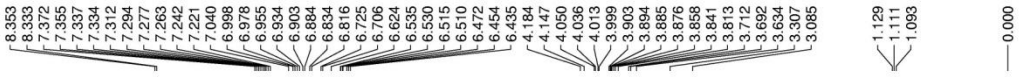

164.54
162.69
162.38
162.34
162.03
138.77
138.69
138.62
138.22
137.73
137.67
134.16
132.63
132.60
130.56
130.06
129.82
129.58
129.53
129.29
126.33
125.77
124.76
123.08
121.92
115.59
114.66
112.26
112.16
109.76
109.17
77.32
77.00
76.68
62.88
46.93
46.87
34.25
31.95
19.53
13.48
CF2CO2Et
N
N
O
6f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

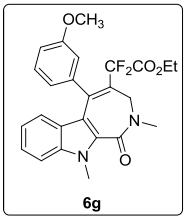

CF2CO2Et
N
O
N

6f

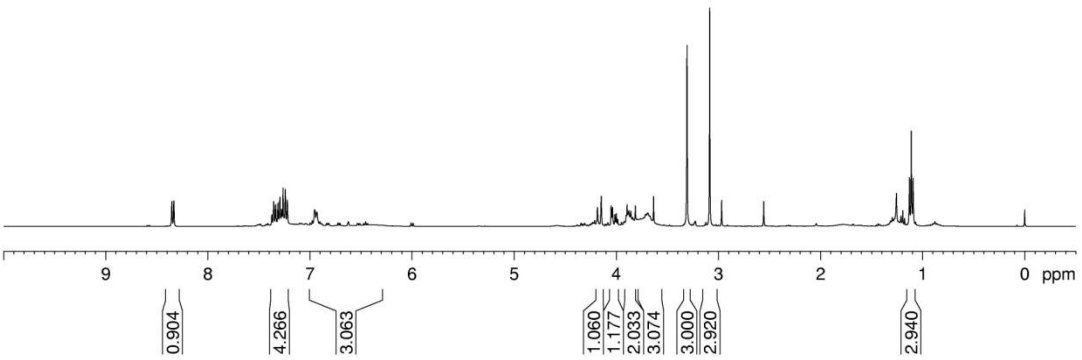

-85.201
-85.961
-94.415
-94.424
-94.849
-94.968
-95.174
-95.185

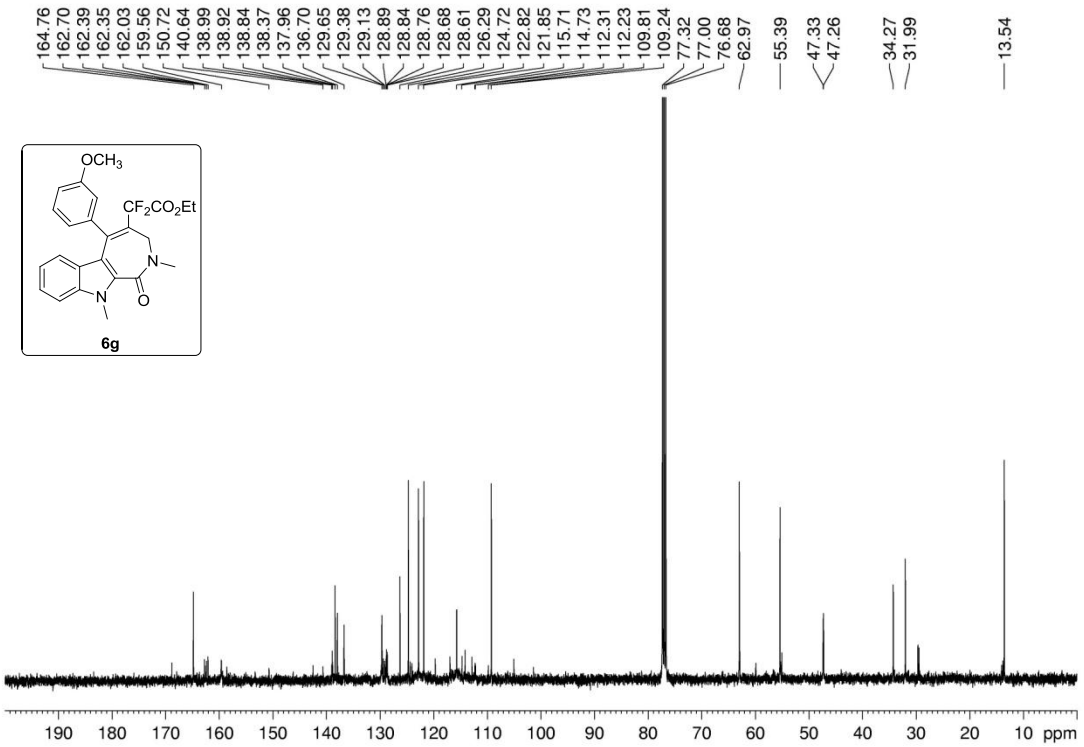

-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm

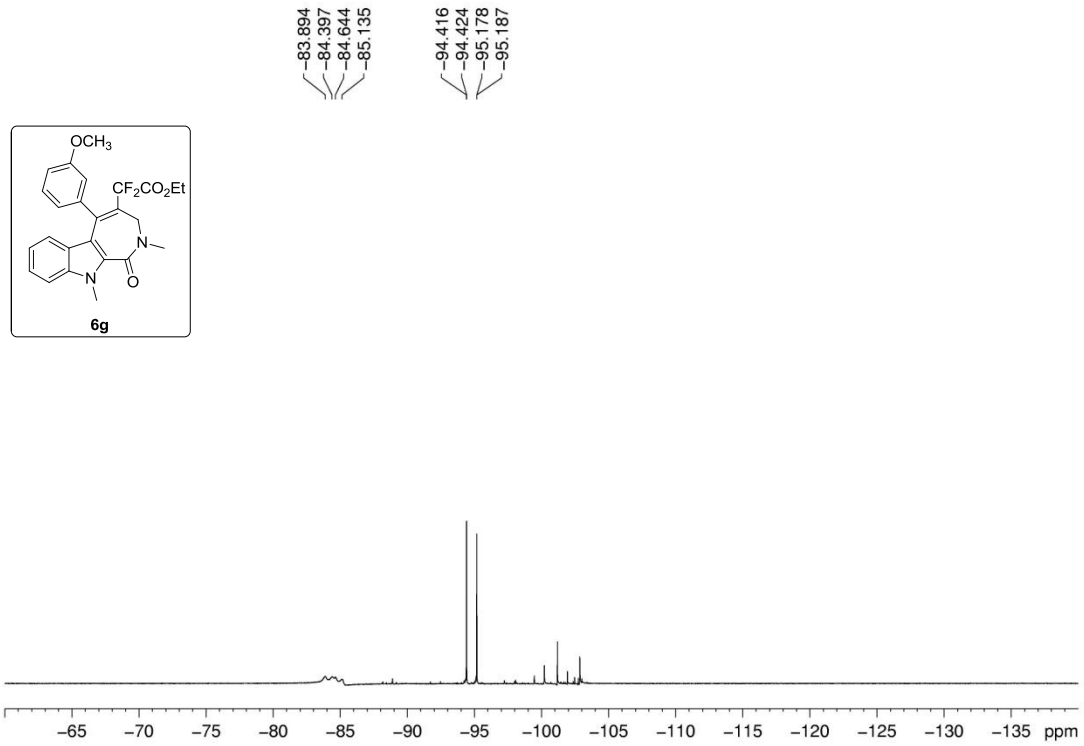

8.353
8.333
7.372
7.355
7.337
7.334
7.312
7.294
7.277
7.263
7.242
7.221
7.040
6.998
6.978
6.955
6.934
6.903
6.884
6.834
6.816
6.725
6.706
6.624
6.535
6.530
6.515
6.510
6.472
6.454
6.435
4.184
4.147
4.050
4.036
4.013
3.999
3.903
3.894
3.885
3.876
3.858
3.841
3.813
3.712
3.692
3.634
3.307
3.085
1.129
1.111
1.093
0.000

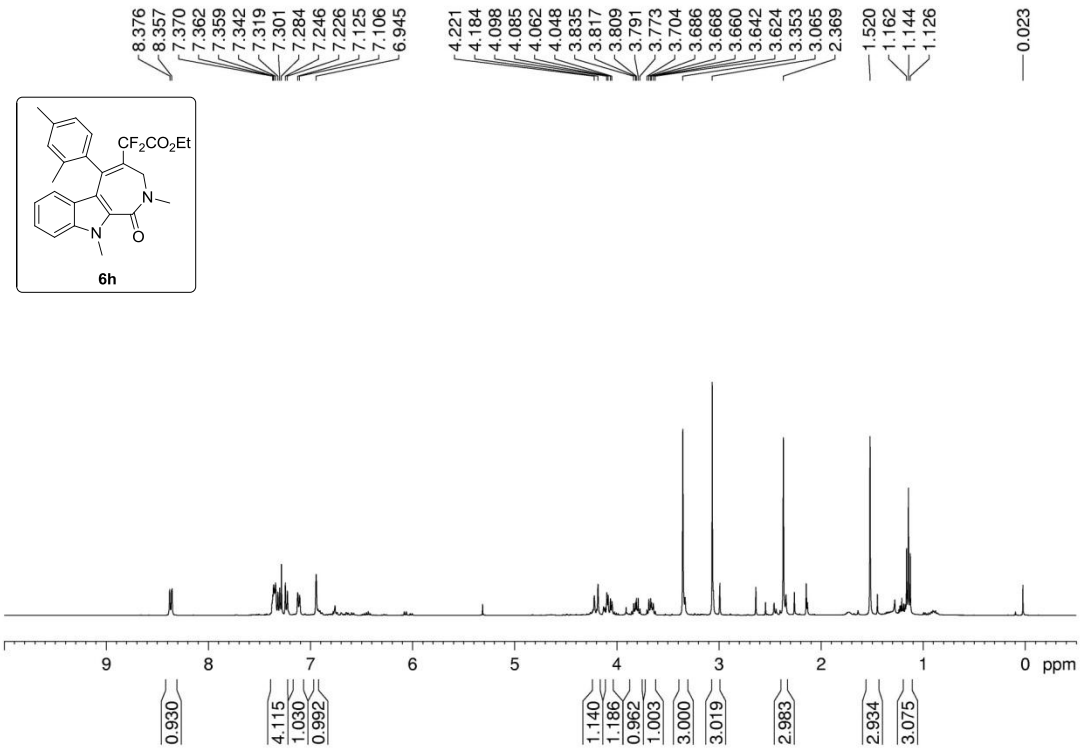

OCH3
CF2CO2Et
N
O
N

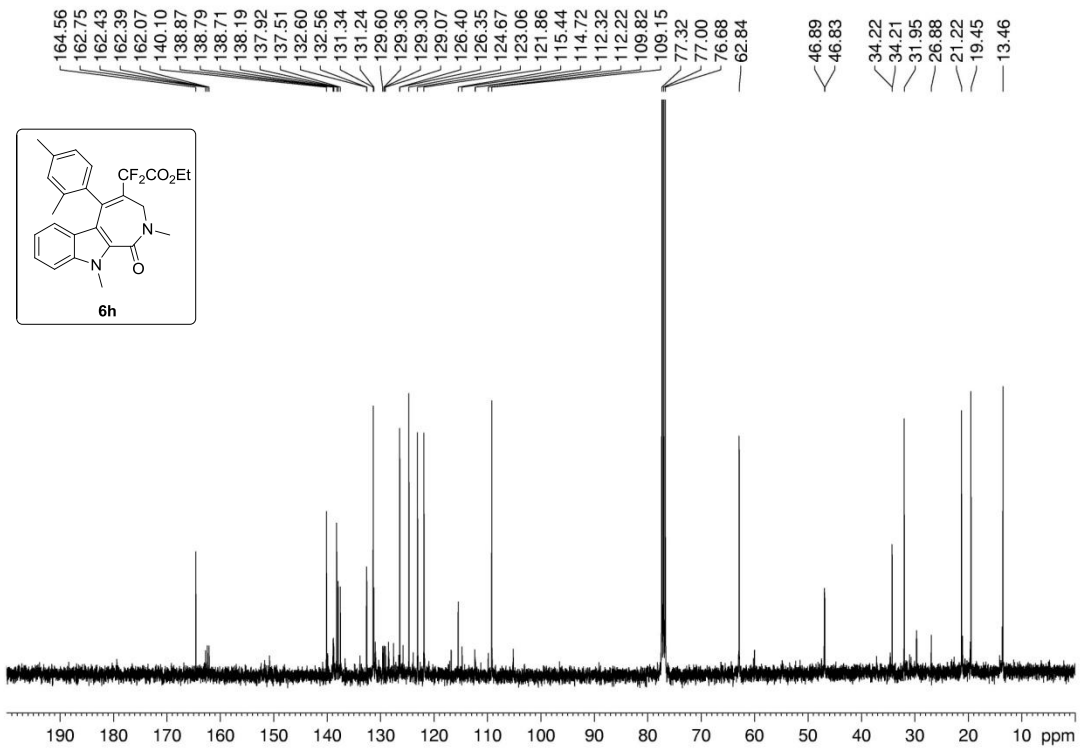
6g

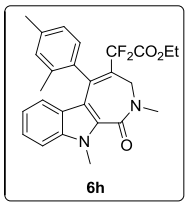

9
8
7
6
5
4
3
2
1
0 ppm
0.904
4.266
3.063
1.060
1.177
2.033
3.074
3.000
2.920
2.940


164.76
162.70
162.39
162.35
162.03
159.56
150.72
140.64
138.99
138.92
138.84
138.37
137.96
136.70
129.65
129.38
129.13
128.89
128.84
128.76
128.68
128.61
126.29
124.72
122.82
121.85
115.71
114.73
112.31
112.23
109.81
109.24
77.32
77.00
76.68
62.97
55.39
47.33
47.26
34.27
31.99
13.54
OCH3
CF2CO2Et
N
N
O
6g
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

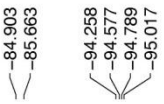

−83.894
−84.397
−84.644
−85.135
−94.416
−94.424
−95.178
−95.187
OCH3
CF2CO2Et
N
N
O
6g
−65 −70 −75 −80 −85 −90 −95 −100 −105 −110 −115 −120 −125 −130 −135 ppm

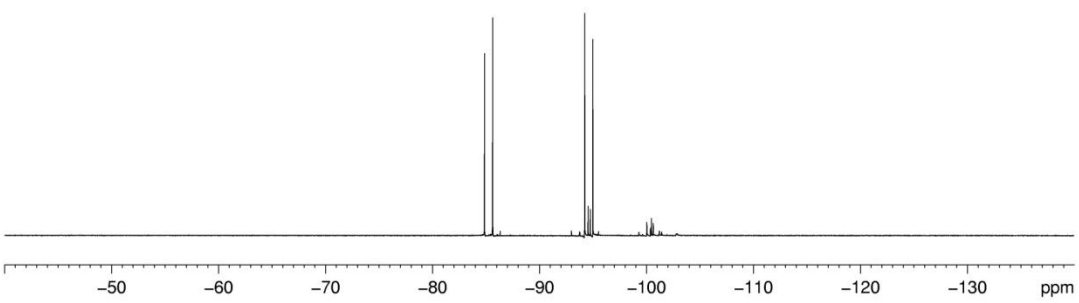

8.376
8.357
7.370
7.362
7.359
7.342
7.319
7.301
7.284
7.246
7.226
7.125
7.106
6.945
4.221
4.184
4.098
4.085
4.062
4.048
3.835
3.817
3.809
3.791
3.773
3.704
3.686
3.668
3.660
3.642
3.624
3.353
3.065
2.369
1.520
1.162
1.144
1.126
0.023
CF2CO2Et
N
N
O
6h
9
8
7
6
5
4
3
2
1
0 ppm
0.930
4.115
1.030
0.992
1.140
1.186
0.962
1.003
3.000
3.019
2.983
2.934
3.075

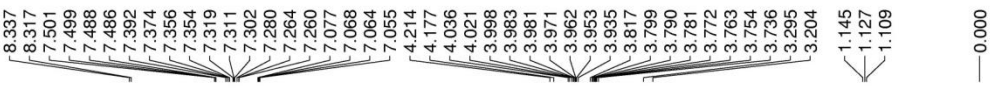

164.56
162.75
162.43
162.39
162.07
140.10
138.87
138.79
138.71
138.19
137.92
137.51
132.60
132.56
131.34
131.24
129.60
129.36
129.30
129.07
126.40
126.35
124.67
123.06
121.86
115.44
114.72
112.32
112.22
109.82
109.15
77.32
77.00
76.68
62.84
46.89
46.83
34.22
34.21
31.95
26.88
21.22
19.45
13.46
CF2CO2Et
N
N
O
6h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

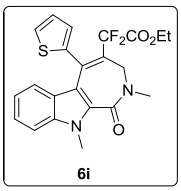

CF2CO2Et
N
O
N

6h

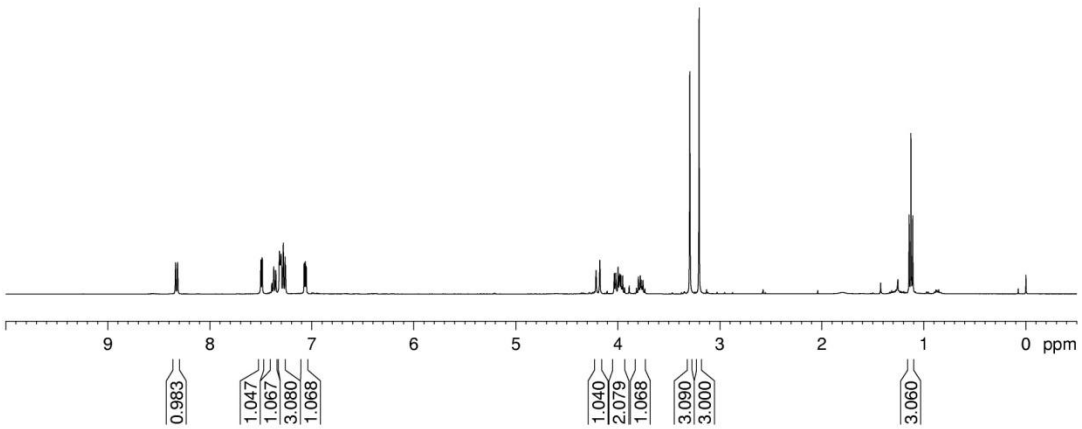

-84.903
-85.663
-94.258
-94.577
-94.789
-95.017

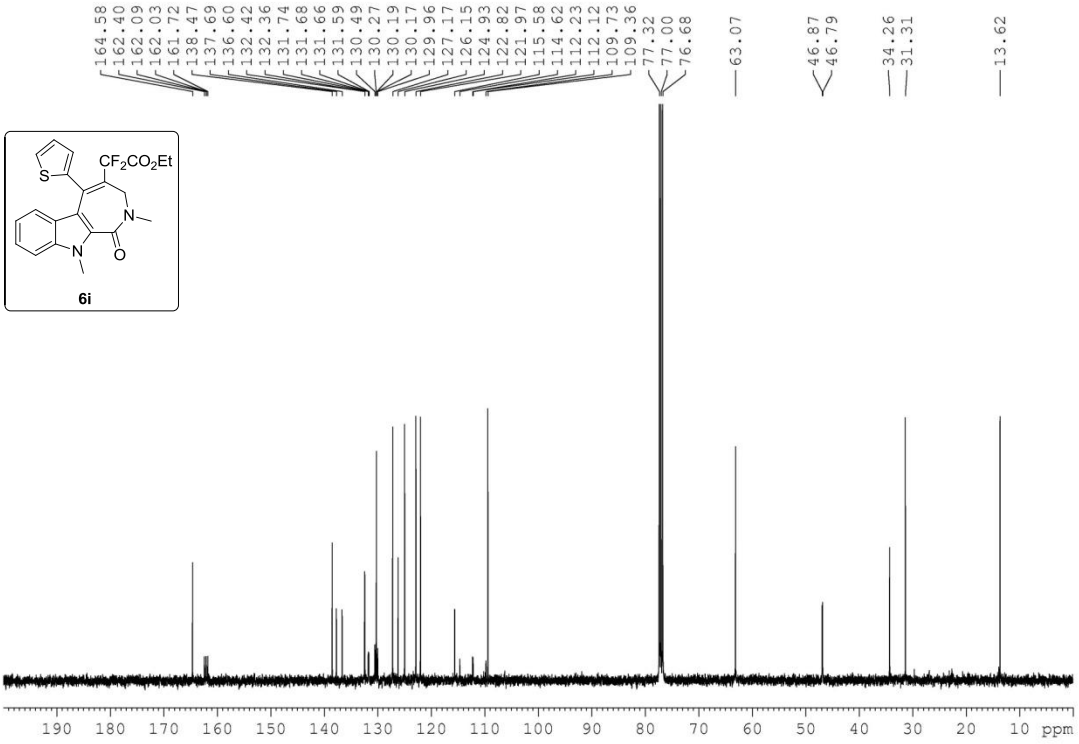

-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm

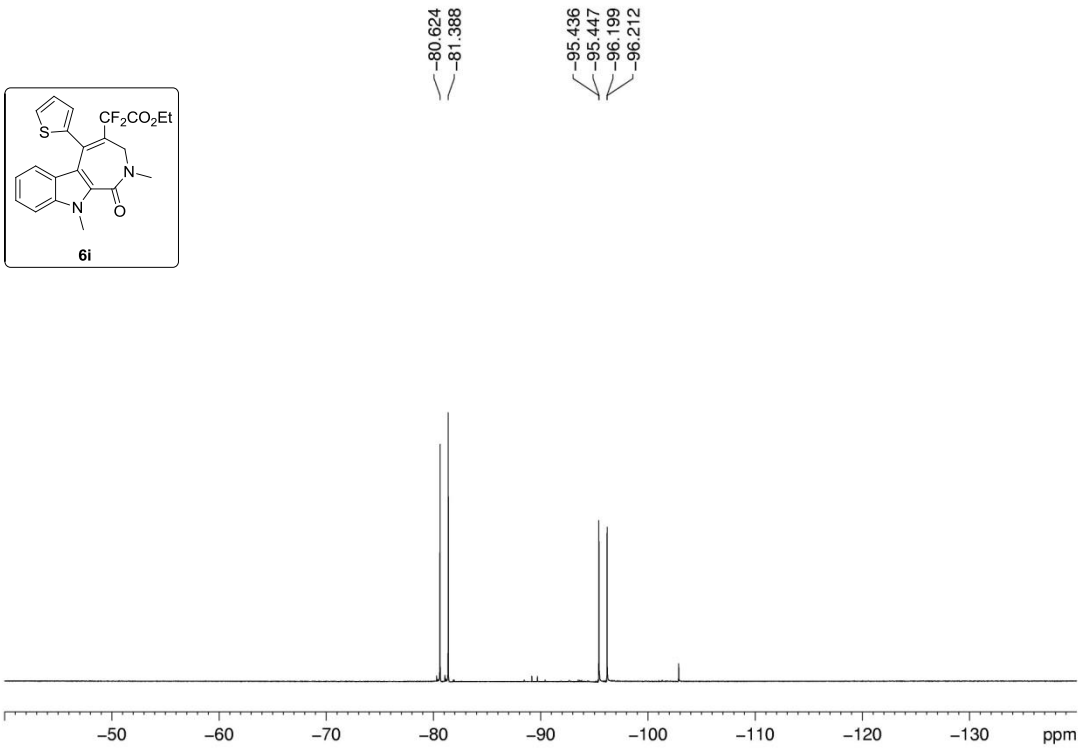

8.337
8.317
7.501
7.499
7.488
7.486
7.392
7.374
7.356
7.354
7.319
7.311
7.302
7.280
7.264
7.260
7.077
7.068
7.064
7.055
4.214
4.177
4.036
4.021
3.998
3.983
3.981
3.971
3.962
3.953
3.935
3.817
3.799
3.790
3.781
3.772
3.763
3.754
3.736
3.295
3.204
1.145
1.127
1.109
0.000

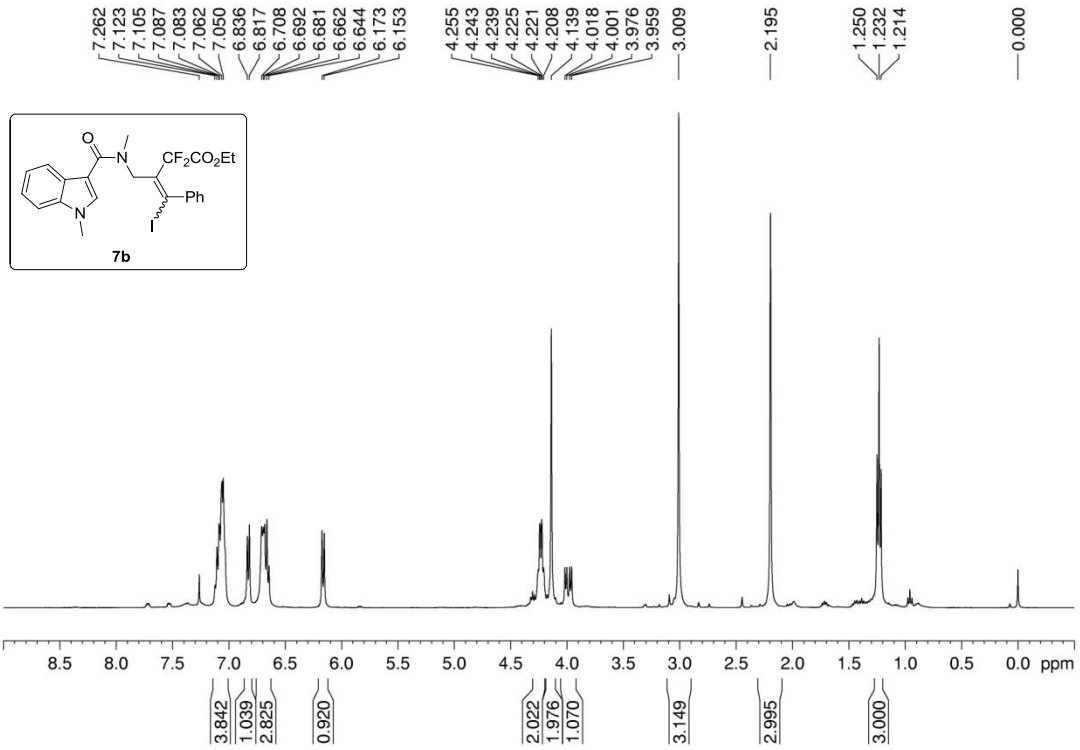

S
CF2CO2Et
N
O
N

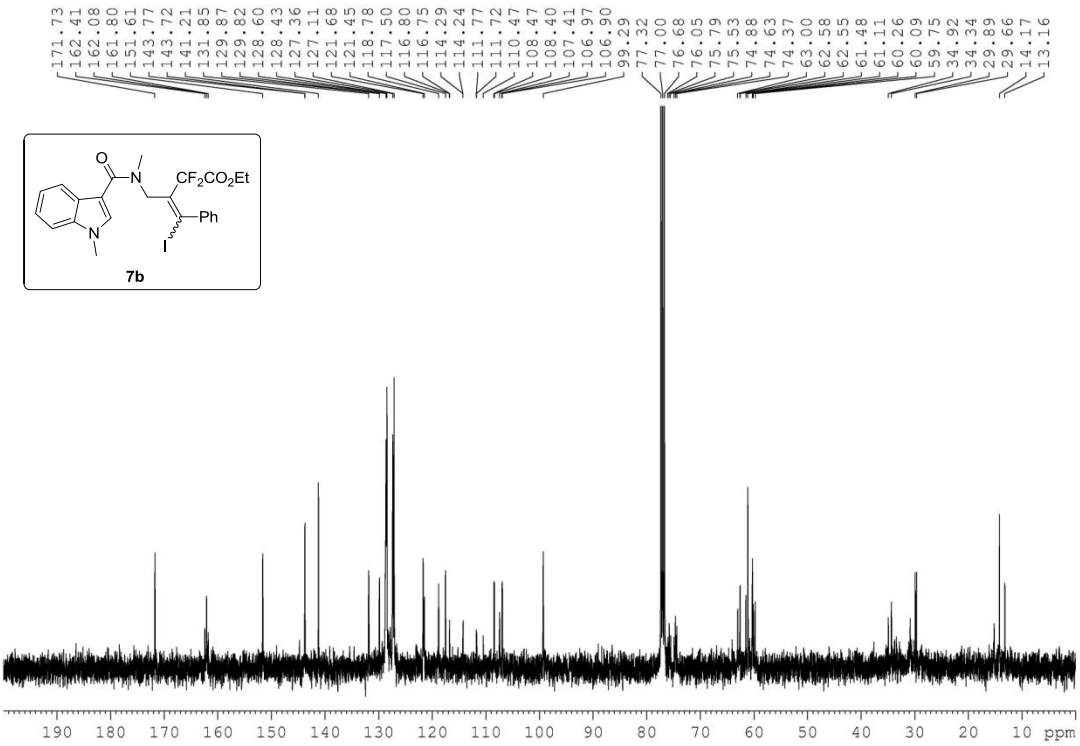
6i

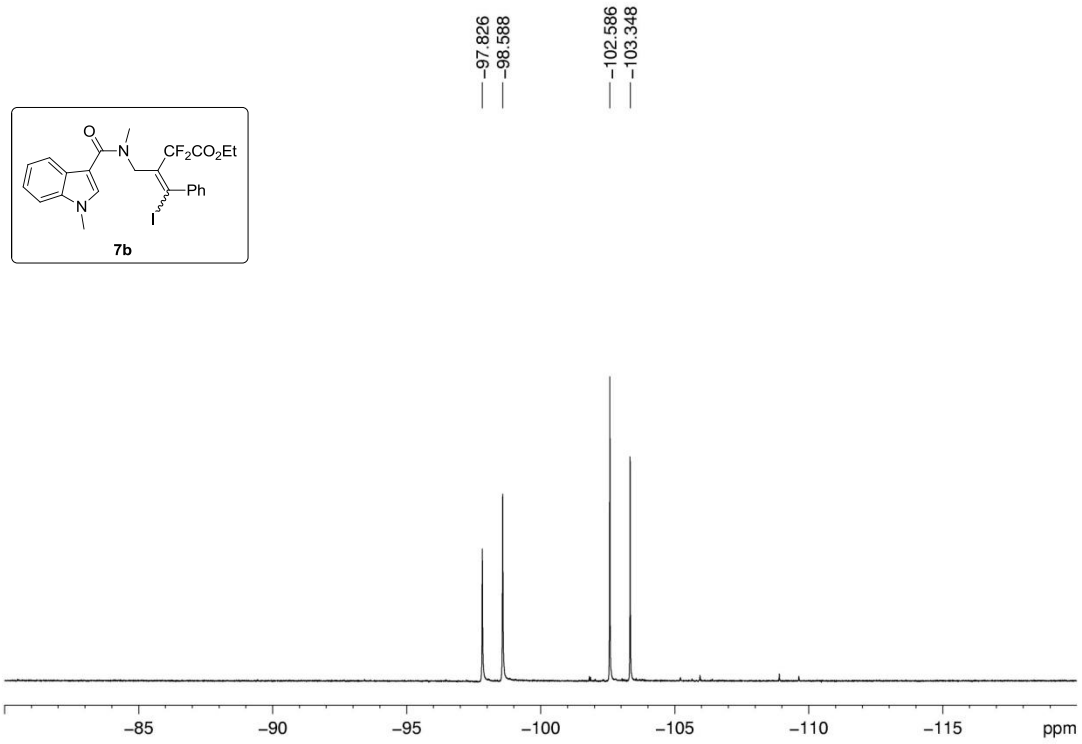

9
8
7
6
5
4
3
2
1
0 ppm
0.983
1.047
1.067
3.080
1.068
1.040
2.079
1.068
3.090
3.000
3.060


164.58
162.40
162.09
162.03
161.72
138.47
137.69
136.60
132.42
132.36
131.74
131.68
131.66
131.59
130.49
130.27
130.19
130.17
129.96
127.17
126.15
124.93
122.82
121.97
115.58
114.62
112.23
112.12
109.73
109.36
77.32
77.00
76.68
63.07
46.87
46.79
34.26
31.31
13.62
CF2CO2Et
S
N
N
O
6i
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-80.624
-81.388
-95.436
-95.447
-96.199
-96.212
CF2CO2Et
S
N
N
O
6i
-50 -60 -70 -80 -90 -100 -110 -120 -130 ppm


7.262
7.123
7.105
7.087
7.083
7.062
7.050
6.836
6.817
6.708
6.692
6.681
6.662
6.644
6.173
6.153
4.255
4.243
4.239
4.225
4.221
4.208
4.139
4.018
4.001
3.976
3.959
3.009
2.195
1.250
1.232
1.214
0.000
7b
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
3.842
1.039
2.825
0.920
2.022
1.976
1.070
3.149
2.995
3.000


171.73
162.41
162.08
161.80
151.61
143.77
143.72
141.21
131.85
129.87
129.82
128.60
128.43
127.36
127.11
121.68
121.45
118.78
117.50
116.80
116.75
114.29
114.24
111.77
111.72
110.47
108.47
108.40
107.41
106.97
106.90
99.29
77.32
77.00
76.68
76.05
75.79
75.53
74.88
74.63
74.37
63.00
62.58
62.55
61.48
61.11
60.26
60.09
59.75
34.92
34.34
29.89
29.66
14.17
13.16
7b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


−97.826
−98.588
−102.586
−103.348
O
N
CF2CO2Et
Ph
I
N
7b
−85
−90
−95
−100
−105
−110
−115
ppm