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SUPPORTING INFORMATION

Reactivity and properties of bis(chlorodifluoroacetyl) peroxide generated *in-situ* from chlorodifluoroacetic anhydride for chlorodifluoromethylation reactions

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1. General Experimental

General: All reactions involving air- and/or moisture-sensitive compounds were conducted in a dry vessel under a positive pressure of nitrogen gas by using a nitrogen-filled balloon. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel (Merck, Silica gel 60 F_{254}) containing a fluorescent indicator. Visualization was accomplished by means of ultraviolet irradiation at 254 nm and/or by spraying an ethanolic solution of 12-molybdo(VI)phosphoric acid as a developing agent. Flash column chromatography was performed using Silica gel N-60 (spherical, neutral, 40–50 μm, Kanto Chemical Co., Inc. (Kanto)) as described by Still *et al*.[1]

Instrumentation:

NMR analysis

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded at room temperature on a JEOL JNM-ECS-400 NMR spectrometer at 400, 100, and 376 MHz, respectively. The proton chemical shift values are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and referenced to the proton resonance of $CHCl_3$ (δ 7.26). The carbon chemical shift values are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and referenced to the carbon resonance of $CDCl_3$ (δ 77.16). The fluorine chemical shift values are reported in parts per million (ppm, δ scale) with $CFCl_3$ (δ 0.00) as an external standard. *J* values are reported in hertz (Hz). The data are presented in the following order: chemical shift, signal area integration in natural numbers, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet and/or multiple resonances, and br = broad). The *Z*-isomer of the allylic fluoroalkyl compounds was analogically identified by comparison of NMR spectra with literature data of trifluoromethyl analogues.[2]

IR analysis

Infrared spectra were measured on a Thermo Nicolet iS5. Only diagnostic absorptions are listed.

HRMS analysis

ESI-MS spectra were measured on a Brucker micrOTOF-QII-RSL. The samples were diluted with MeOH for the measurement. EI-MS and FI-MS were taken on a JMS-T100GCV.

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Solvents: Anhydrous dichloromethane was purchased from Kanto.

Materials: Chemical reagents were purchased from Wako Pure Chemical Industries, Ltd., Tokyo Chemical Industry Co., Ltd., Sigma-Aldrich Inc., and other commercial suppliers.

Preparation of known alkenes (1):

The known alkenes (**1a**,[3] **1c**,[4] **1e**,[5] **1g**,[6] **1h**,[7] **1i–l**,[8] **1m**,[9] **1n**,[10] **1o**,[11] **1p**,[12] **1q**,[5] **1r**,[5] **1s**,[13] **1t**,[14] **1u**,[11] **1v**[15]) were prepared according to the literatures.

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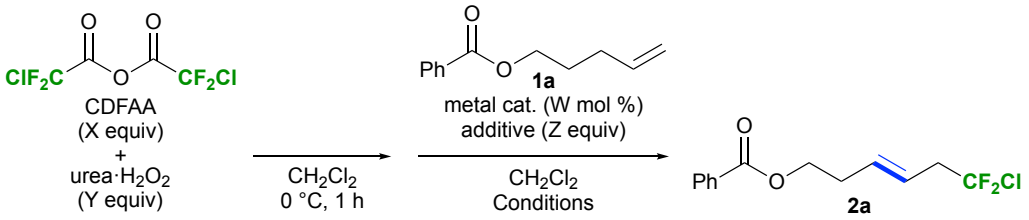
2. Additional Results

Table S1. Optimization of the conditions for the synthesis of 2a[a]

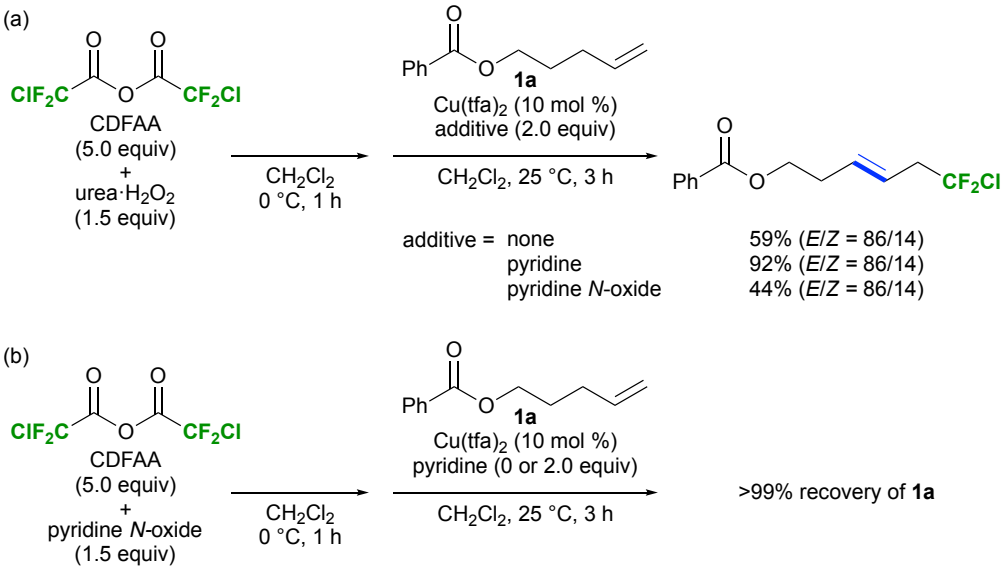


Entry	X	Y	metal cat. (W)	additive (Z)	Conditions	Yield of **2a** (%)[b] (*E*/*Z*)[b]	Recov. of **1a** (%)[c]
1	4.0	1.2	none	none	25 °C, 3 h	9 (82/18)	11
2	4.0	1.2	$[Cu(CH_3CN)_4]PF_6$ (10)	none	0 °C, 3 h	3 (90/10)	43
3	4.0	1.2	$[Cu(CH_3CN)_4]PF_6$ (10)	none	25 °C, 3 h	11 (81/19)	11
4[d]	4.0	1.2	$Cu(tfa)_2$ (10)	none	40 °C, 3 h	37 (83/17)	11
5	4.0	1.2	$Cu(tfa)_2$ (10)	none	40 °C, 3 h	40 (84/16)	19
6	4.0	1.2	$Cu(tfa)_2$ (10)	none	0 °C, 3 h	5 (85/15)	83
7	4.0	1.2	$Cu(tfa)_2$ (10)	none	25 °C, 3 h	53 (83/17)	13
8	4.0	1.2	$Cu(OTf)_2$ (10)	none	25 °C, 3 h	41 (84/16)	17
9	4.0	1.2	$Cu(OAc)_2$ (10)	none	25 °C, 3 h	44 (84/16)	19
10	4.0	1.2	$[Cu(tmeda)OH]_2Cl_2$ (10)	none	25 °C, 3 h	47 (89/11)	20
11	4.0	1.2	$CuCl_2$ (10)	none	25 °C, 3 h	33 (83/17)	20
12	4.0	1.2	$CuBr_2$ (10)	none	25 °C, 3 h	16 (82/18)	4
13	4.0	1.2	$Fe(acac)_3$ (10)	none	25 °C, 3 h	6 (82/18)	2
14	4.0	1.2	$Fe(OAc)_2$ (10)	none	25 °C, 3 h	6 (81/19)	6
15	4.0	1.2	$Fe(OTf)_2$ (10)	none	25 °C, 3 h	6 (81/19)	12
16	4.0	1.2	$Cu(tfa)_2$ (10)	K_2CO_3 (1.0)	25 °C, 3 h	58 (83/18)	13
17	4.0	1.2	$Cu(tfa)_2$ (10)	Cs_2CO_3 (1.0)	25 °C, 3 h	17 (82/18)	10
18	4.0	1.2	$Cu(tfa)_2$ (10)	$NaHCO_3$ (1,0)	25 °C, 3 h	48 (76/24)	31
19	4.0	1.2	$Cu(tfa)_2$ (10)	K_2HPO_4 (1.0)	25 °C, 3 h	23 (80/20)	8
20	4.0	1.2	$Cu(tfa)_2$ (10)	Et_3N (1.0)	25 °C, 3 h	54 (86/14)	31
21	4.0	1.2	$Cu(tfa)_2$ (10)	TMEDA (1.0)	25 °C, 3 h	44 (87/13)	31
22	4.0	1.2	$Cu(tfa)_2$ (10)	TMP (1.0)	25 °C, 3 h	61 (86/14)	43
23	4.0	1.2	$Cu(tfa)_2$ (10)	DBU (1.0)	25 °C, 3 h	66 (88/12)	20
24	4.0	1.2	$Cu(tfa)_2$ (10)	DMAP (1.0)	25 °C, 3 h	69 (88/12)	14
25	4.0	1.2	$Cu(tfa)_2$ (10)	pyridine (1.0)	25 °C, 3 h	74 (87/13)	14
26	4.0	1.2	$Cu(tfa)_2$ (10)	2,6-lutidine (1.0)	25 °C, 3 h	73 (87/13)	12
27	4.0	1.2	$Cu(tfa)_2$ (10)	2,2'-bipyridine (1.0)	25 °C, 3 h	5 (81/19)	2
28	4.0	1.2	$Cu(tfa)_2$ (10)	1,10-phenanthroline (1.0)	25 °C, 3 h	3 (80/20)	13
29	4.0	1.2	$Cu(tfa)_2$ (10)	pyridine (2.0)	25 °C, 3 h	84 (86/14)	10
30	4.0	1.2	$Cu(tfa)_2$ (10)	pyridine (2.0)	25 °C, 6 h	85 (86/14)	9
31	4.0	1.2	$Cu(tfa)_2$ (10)	pyridine (2.0)	0 °C, 3 h	24 (88/12)	72
32	4.0	1.2	$Cu(tfa)_2$ (10)	pyridine (4.0)	25 °C, 3 h	29 (86/16)	61
33	5.0	1.5	$Cu(tfa)_2$ (10)	pyridine (2.0)	25 °C, 3 h	92 (86/14)[e]	n.d.
34	5.0	1.5	$Cu(tfa)_2$ (10)	pyridine (2.0)	25 °C, 1 h	89 (86/14)	1
35	5.0	1.5	$Cu(tfa)_2$ (20)	pyridine (2.0)	25 °C, 3 h	91 (86/14)	n.d.
36	5.0	1.5	$Cu(tfa)_2$ (5)	pyridine (2.0)	25 °C, 3 h	81 (86/14)	n.d.
37	5.0	1.5	none	pyridine (2.0)	25 °C, 3 h	3 (90/10)	n.d.
38	5.0	1.5	$Cu(tfa)_2$ (10)	none	25 °C, 3 h	59 (86/14)	n.d.

[a]The reactions were conducted on a 0.20 mmol scale. n.d. = not detected. [b]The yields and *E*/*Z* ratio were estimated by means of ^{19}F NMR analysis by using α,α,α-trifluorotoluene as an internal standard. [c]The recovery of **1a** was estimated by means of ^{1}H NMR analysis by using dibromomethane as an internal standard. [d]The first step was carried out at –40 °C. [e]Isolated yield.

Pyridine was reported to be oxidized by bis-perfluoroacyl peroxide, affording acylated *N*-oxide.[16] Under our conditions containing excess chlorodifluoroacetic acid, pyridine should be converted to its chlorodifluoroacetate salt, not acylated *N*-oxide; however, it is still possible that a small amount of pyridine *N*-oxide was formed. Therefore, in order to clarify the effect of pyridine *N*-oxide, we performed a reaction using pyridine *N*-oxide as the additive instead of pyridine (Scheme S1(a)). In contrast to the case of pyridine, no significant improvement of the yield of the desired product was observed. In addition, since Stephenson reported that perfluoroacylated pyridine *N*-oxide prepared *in-situ* from perfluoroacid anhydride and pyridine *N*-oxide can be a perfluoroalkyl radical source under their photocatalytic conditions,[17] a reaction using pyridine *N*-oxide instead of urea·H_2O_2 was conducted (Scheme S1(b)). However, no reaction proceeded. These results indicated that neither pyridine *N*-oxide nor its acylated form would play a critical role in our experimental conditions.

Scheme S1. Reaction using pyridine *N*-oxide (a) as the additive instead of pyridine and (b) as the oxidant instead of urea·H_2O_2



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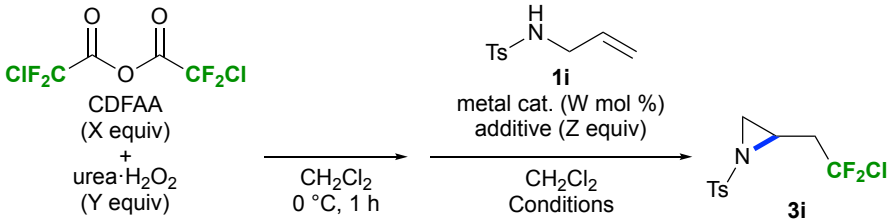
[17] (a) J. W. Beatty, J. J. Douglas, K. P. Cole and C. R. J. Stephenson, *Nat. Commun.*, 2015, **6**, 7919; (b) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole and C. R. J. Stephenson, *Chem*, 2016, **1**, 456; (c) R. C. McAtee, J. W. Beatty, C. C. McAtee and C. R. J. Stephenson, *Org. Lett.*, 2018, **20**, 3491.

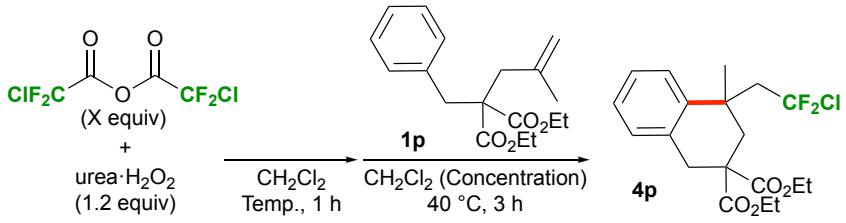
Table S2. Optimization of the conditions for the synthesis of 3i[a]



Entry	X	Y	metal cat. (W)	additive (Z)	Conditions	Yield of **3i** (%) [b]	Recov. of **1i** (%) [c]
1	4.0	1.2	$[Cu(CH_3CN)_4]PF_6$ (10)	none	0 °C, 1 h	n.d.	50
2	4.0	1.2	$[Cu(CH_3CN)_4]PF_6$ (10)	none	25 °C, 1 h	n.d.	45
3	4.0	1.2	$[Cu(CH_3CN)_4]PF_6$ (10)	none	40 °C, 1 h	n.d.	42
4	4.0	1.2	$Cu(tfa)_2$ (10)	none	0 °C, 1 h	n.d.	72
5	4.0	1.2	$Cu(tfa)_2$ (10)	none	25 °C, 1 h	22	25
6	4.0	1.2	$Cu(tfa)_2$ (10)	none	40 °C, 1 h	18	22
7	4.0	1.2	$Cu(tfa)_2$ (10)	none	25 °C, 3 h	25	4
8	5.0	1.5	$Cu(tfa)_2$ (10)	none	25 °C, 3 h	24	7
9	5.0	1.5	$Cu(tfa)_2$ (10)	$NaHCO_3$ (1.0)	25 °C, 3 h	34	n.d.
10	5.0	1.5	$Cu(tfa)_2$ (10)	Et_3N (1.0)	25 °C, 3 h	32	36
11	5.0	1.5	$Cu(tfa)_2$ (10)	DBU (1.0)	25 °C, 3 h	47	1
12	5.0	1.5	$Cu(tfa)_2$ (10)	DMAP (1.0)	25 °C, 3 h	36	7
13	5.0	1.5	$Cu(tfa)_2$ (10)	pyridine (1.0)	25 °C, 3 h	51	1

[a]The reactions were conducted on a 0.20 mmol scale. n.d. = not detected. [b]The yields were estimated by means of ^{19}F NMR analysis by using α,α,α-trifluorotoluene as an internal standard. [c]The recovery of **1i** was estimated by means of ^{1}H NMR analysis by using 1,1,2,2-tetrachloroethane as an internal standard.

Table S3. Optimization of the conditions for the synthesis of 4p[a]



Entry	X	Temp.	Concentration	Yield of **4p** (%)[c]	Recovery of **1p** (%)[d]
1	10	–40 °C	0.4 M	96	n.d.
2	4.0	–40 °C	0.4 M	91	n.d.
3	4.0	0 °C	0.4 M	96	n.d.
4	4.0	0 °C	0.2 M	99[d]	n.d.

[a]The reactions were conducted on a 0.20 mmol scale. n.d. = not detected. [b]The yields were estimated by means of ^{19}F NMR analysis by using α,α,α-trifluorotoluene as an internal standard. [c]The recovery of **1p** was estimated by means of ^{1}H NMR analysis by using dibromomethane as an internal standard. [d]Isolated yield.

3. Experimental Procedures

General procedure A (allylic and amino-chlorodifluoromethylation)

To a suspension of urea·H_2O_2 (28 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) chlorodifluoroacetic anhydride (175 μL, 1.0 mmol) was slowly added at 0 °C. After stirring for 1 h, alkene (0.20 mmol), pyridine (32 μL, 0.40 mmol), and $Cu(tfa)_2$ (5.8 mg, 0.020 mmol) were added at 0 °C. Then, the mixture was immediately warmed to 25 °C and stirred for 3 h. After addition of 5 mL of EtOAc, the reaction was quenched with aqueous $NaHCO_3$ solution at 0 °C and then stirred at rt for 20 min. The aqueous layer was extracted with 5 mL of EtOAc three times. The combined organic phase was checked with XploSens PS® to confirm the absence of peroxide, and the water phase was treated with saturated $Na_2S_2O_3$ to decompose H_2O_2. The combined organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel afforded the target compound.

General procedure B (chlorodifluoromethylation of aromatic alkenes)

To a suspension of urea·H_2O_2 (23 mg, 0.24 mmol) in CH_2Cl_2 (1.0 mL) chlorodifluoroacetic anhydride (140 μL, 0.80 mmol) was slowly added at 0 °C. After stirring for 1 h, alkene (0.20 mmol) was added at 0 °C. Then, the mixture was immediately warmed to 40 °C and stirred for 3 h. After addition of 5 mL of EtOAc, the reaction was quenched with aqueous $NaHCO_3$ solution at 0 °C and then stirred at rt for 20 min. The aqueous layer was extracted with 5 mL of EtOAc three times. The combined organic phase was checked with XploSens PS® to confirm the absence of peroxide, and the water phase was treated with saturated $Na_2S_2O_3$ to decompose H_2O_2. The combined organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel afforded the target compound.

General procedure C (chlorodifluoromethylation of *N*-heterocycles)

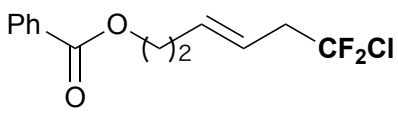
To a suspension of urea·H_2O_2 (45 mg, 0.48 mmol) in CH_2Cl_2 (0.25 mL) chlorodifluoroacetic anhydride (280 μL, 1.6 mmol) was slowly added at 0 °C. After stirring for 1 h, heterocycle (0.20 mmol) was added at 0 °C. Then, the mixture was immediately warmed to 40 °C and stirred for 3 h. After addition of 5 mL of EtOAc, the reaction was quenched with aqueous $NaHCO_3$ solution at 0 °C and then stirred at rt for 20 min. The aqueous layer was extracted with 5 mL of EtOAc three times. The combined organic phase was checked with XploSens PS® to confirm the absence of peroxide, and the water phase was treated with saturated $Na_2S_2O_3$ to decompose H_2O_2. The combined

organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel afforded the target compound.

Procedure for ^{19}F NMR experiment (Fig 1)

Fluoroacetic anhydride (2.0 mmol) was slowly added to a suspension of urea·H_2O_2 (23 mg, 0.25 mmol) in CD_2Cl_2 (0.5 mL) in a Schlenk tube at –40 °C, and the mixture was stirred for 1 h. The obtained colorless solution containing diacyl peroxide was carefully transferred to a valve NMR tube containing α,α,α-trifluorotoluene as an internal standard under a N_2 atmosphere. The ^{19}F NMR spectrum of the sample was measured at room temperature. ^{19}F NMR signals at –65.9, –65.7, and –61.5 ppm were assigned as CDFAA, CDFA, and BCDFAP.

Synthesis of 6-chloro-6,6-difluoro-3-hexenyl benzoate (2a):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (54 mg, 92% yield, *E*/*Z* = 86/14) after silica gel column chromatography (CH_2Cl_2/hexane = 40/60).

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

E-isomer, 2.53–2.60 (m, 2H), 2.95–3.05 (m, 2H), 4.38 (t, *J* = 6.6 Hz, 2H), 5.60 (dtt, *J* = 15.2, 6.8, 1.2 Hz, 1H), 5.78 (dt, *J* = 15.2, 6.8 Hz, 1H), 7.41–7.48 (m, 2H), 7.56 (tt, *J* = 7.2, 1.2 Hz, 1H), 8.01–8.06 (m, 2H);

Z-isomer, 2.53–2.60 (m, 2H), 3.05–3.15 (m, 2H), 4.37 (t, *J* = 6.7 Hz, 2H), 5.60 (overlap, 1H), 5.78 (overlap, 1H), 7.41–7.48 (m, 2H), 7.56 (m, 1H), 8.01–8.06 (m, 2H)

^{13}C NMR (*E*-isomer, 100 MHz, $CDCl_3$)

32.2, 45.2 (t, *J* = 25.1 Hz), 63.7, 122.0 (t, *J* = 3.9 Hz), 128.5 (2C), 129.7 (3C), 130.3 (t, *J* = 139 Hz), 133.1, 133.8, 166.6

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

E-isomer, –51.4 (t, *J* = 12.3 Hz); *Z*-isomer, –50.9 (t, *J* = 12.3 Hz)

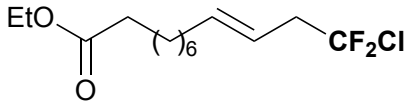
IR (neat, cm^{-1})

1720, 1452, 1315, 1274, 1202, 1178, 1110, 1071, 1027, 995, 968, 711, 687, 676

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{13}H_{13}ClF_2O_2$, 297.0464; found, 297.0476

Synthesis of ethyl 12-chloro-12,12-difluoro-9-dodecenoate (2b) on a gram-scale:



In a round-bottom flask (300–mL size) capped by a three-way cock, urea·H_2O_2 (1.4 g, 15 mmol) was allowed to settle under N_2 gas.[18] Then, CH_2Cl_2 (50 mL) was added, and the resulting suspension was cooled to 0 °C. To this mixture, chlorodifluoroacetic anhydride (8.8 mL, 50 mmol) was slowly added. After stirring for 1 h, ethyl 10-undecenoate (10 mmol, 2.2 g), pyridine (1.6 mL, 20 mmol), and $Cu(tfa)_2$ (290 mg, 1.0 mmol) were added. Then, the mixture was warmed to 25 °C and stirred for 3 h. After addition of 60 mL of EtOAc, the reaction was quenched with aqueous $NaHCO_3$ solution at 0 °C and stirred at rt for 20 min. The aqueous layer was extracted with 60 mL of EtOAc three times. The combined organic phase was checked with XploSens PS® to confirm the absence of peroxide, and the water phase was treated with saturated $Na_2S_2O_3$ to decompose H_2O_2. The combined organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel (CH_2Cl_2/hexane = 20/80) afforded the target compound as a colorless oil (2.4 g, 81%, *E*/*Z* = 88/12).

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

E-isomer, 1.23–1.42 (m, 8H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.61 (quint, *J* = 7.2 Hz, 2H), 2.05 (td, *J* = 7.2, 6.8 Hz, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.91–3.00 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 5.40 (dtt, *J* = 15.2, 6.8, 1.6 Hz, 1H), 5.69 (dt, *J* = 15.2, 6.8 Hz, 1H);

Z-isomer, 1.23–1.42 (m, 8H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.61 (quint, *J* = 7.2 Hz, 2H), 2.05 (td, *J* = 7.2, 6.8 Hz, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.99–3.08 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 5.40 (overlap, 1H), 5.69 (overlap, 1H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

14.4, 25.1, 28.9 (2C), 29.2 (2C), 32.6, 34.5, 45.3 (t, *J* = 24.9 Hz), 60.3, 118.9 (t, *J* = 3.8 Hz), 129.1 (t, *J* = 289 Hz), 138.8, 174.0

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

E-isomer, –51.4 (t, *J* = 11.7 Hz); *Z*-isomer, –50.8 (t, *J* = 11.7 Hz)

IR (neat, cm^{-1})

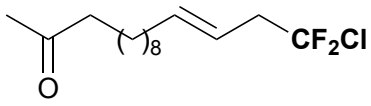
2985, 2931, 2854, 1736, 1466, 1445, 1425, 1372, 1347, 1302, 1242, 1184, 1095, 1034, 969, 948, 895, 800, 730, 667

[18] The reaction must be conducted under a slightly positive flow of N_2 gas in order to release CO_2 gas generated during the reaction.

HRMS-ESI (*m*/*z*)

[M+Na]$^+$ calcd. for $C_{14}H_{23}ClF_2O_2$, 319.1247; found, 319.1252

Synthesis of 15-chloro-15,15-difluoro-12-pentadecen-2-one (2c):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (39 mg, 67% yield, *E*/*Z* = 88/12) after silica gel column chromatography (CH_2Cl_2/hexane = 50/50).

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

E-isomer, 1.20–1.60 (m, 14H), 2.05 (td, *J* = 7.2, 6.4 Hz, 2H), 2.12 (s, 3H), 2.40 (t, *J* = 7.6 Hz, 2H), 2.90–3.00 (m, 2H), 5.40 (dtt, *J* = 15.2, 6.4, 1.6 Hz, 1H), 5.69 (dt, *J* = 15.2, 6.4 Hz, 1H);

Z-isomer, 1.20–1.60 (m, 14H), 2.05 (td, *J* = 7.2, 6.4 Hz, 2H), 2.12 (s, 3H), 2.40 (t, *J* = 7.6 Hz, 2H), 3.01–3.09 (m, 2H), 5.40 (overlap, 1H), 5.69 (overlap, 1H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

24.0, 29.0, 29.1, 29.2, 29.5 (3C), 30.0, 32.6, 43.9, 45.3 (t, *J* = 24.8 Hz), 118.9 (t, *J* = 14.7 Hz), 129.1 (t, *J* = 289 Hz), 138.9, 209.5

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

E-isomer, –51.4 (t, *J* = 11.3 Hz); *Z*-isomer, –50.8 (t, *J* = 11.3 Hz)

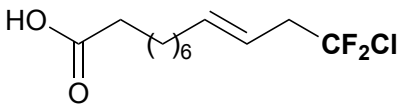
IR (neat, cm^{-1})

2927, 2854, 1719, 1462, 1440, 1425, 1358, 1236, 1186, 1094, 960, 949, 896, 721, 672, 666

HRMS-ESI (*m*/*z*)

[M+Na]$^+$ calcd. for $C_{15}H_{25}ClF_2O$, 317.1454; found, 317.1445

Synthesis of 13-chloro-13,13-difluoro-10-tridecenoic acid (2d):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (36 mg, 66% yield, *E*/*Z* = 88/12) after silica gel column chromatography (EtOAc/hexane = 16/84).

^{1}H NMR (400 MHz, $CDCl_3$)[19]

E-isomer, 1.25–1.44 (m, 8H), 1.63 (quint, 7.2 Hz, 2H), 2.05 (td, *J* = 7.2, 6.8 Hz, 2H), 2.35 (t, *J* = 7.6 Hz, 2H), 2.90–3.00 (m, 2H), 5.41 (dtt, *J* = 15.2, 6.4, 1.2

[19] The ^{1}H NMR signal of the OH group could not be identified.

Hz, 1H), 5.69 (dt, *J* = 15.2, 6.8 Hz, 1H);

Z-isomer, 1.25–1.44 (m, 8H), 1.63 (quint, 7.2 Hz, 2H), 2.05 (td, *J* = 7.2, 6.8 Hz, 2H), 2.35 (t, *J* = 7.6 Hz, 2H), 2.99–3.09 (m, 2H), 5.41 (overlap, 1H), 5.69 (overlap, 1H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

24.7, 28.9, 29.1 (2C), 29,8, 32.6, 34.2, 45.3 (t, *J* = 24.9 Hz), 118,9, 129.1 (t, *J* = 289 Hz), 138.8, 180.3

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

E-isomer, –51.4 (t, *J* = 11.7 Hz); *Z*-isomer, –50.8 (t, *J* = 11.7 Hz)

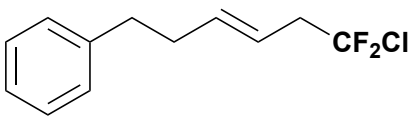
IR (neat, cm^{-1})

2929, 2857, 1709, 1457, 1419, 1287, 1239, 1186, 1095, 968, 947, 896, 668

HRMS-ESI (*m/z*)

$[M+Na]^+$ calcd. for $C_{12}H_{19}ClF_2O_2$, 291.0934; found, 291.0933

Synthesis of (6-chloro-6,6-difluoro-3-hexenyl)benzene (2e):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. Despite inseparable impurity contents after isolation by means of silica gel column chromatography (hexane), analytically pure sample was partly obtained as a colorless oil (6.0 mg, 13%, *E*/*Z* = 88/12). The yield of the reaction was estimated by means of ^{19}F NMR analysis by using α,α,α-trifluorotoluene as an internal standard.

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

E-isomer, 2.39 (t, *J* = 7.4 Hz, 2H), 2.72 (t, *J* = 7.4 Hz, 2H), 2.90–3.00 (m, 2H), 5.41 (m, 1H), 5.74 (dt, *J* = 15.2, 7.4 Hz, 1H), 7.14–7.22 (m, 3H), 7.24–7.31 (m, 2H);

Z-isomer, 2.39 (overlap, 2H), 2.70 (t, *J* = 7.2 Hz, 2H), 2.90–3.00 (m, 2H), 5.41 (overlap, 1H), 5.74 (overlap, 1H), 7.14–7.22 (m, 3H), 7.24–7.31 (m, 2H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

34.4, 35.5, 45.3 (t, *J* = 24.8 Hz), 118.6 (t, *J* = 3.8 Hz), 126.1, 128.5 (2C), 128.6 (2C), 129.0 (t, *J* = 289 Hz), 137.7, 141.6

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

E-isomer, –51.4 (t, *J* = 12.8 Hz); *Z*-isomer, –50.9 (t, *J* = 12.8 Hz)

IR (neat, cm^{-1})

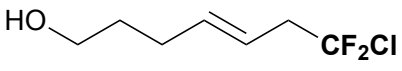
3025, 2922, 2857, 1604, 1496, 1454, 1425, 1237, 1186, 1102, 997, 969, 952,

894, 747, 698, 670

HRMS-EI (*m*/*z*)

[M] calcd. for $C_{12}H_{13}ClF_2$, 230.0674; found, 230.0670

Synthesis of 7-chloro-7,7-difluoro-4-heptenol (2f):



The reaction was carried out on a 0.40 mmol scale according to general procedure A. Diethyl ether was used instead of EtOAc for dilution and extraction of the reaction mixture. The organic phase after the extraction was slowly passed through a Et_3N-treated silica gel column prepared according to the literature.[20] The target compound was obtained as a colorless oil (35 mg, 47% yield, *E*/*Z* = 84/16) after silica gel column chromatography (CH_2Cl_2).

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

E-isomer, 1.25 (br, 1H), 1.68 (quint, *J* = 6.8 Hz, 2H), 2.17 (td, *J* = 7.2, 6.8 Hz, 2H), 2.91–3.01 (m, 2H), 3.02–3.12, 3.66 (br, 2H), 5.47 (dtt, *J* = 15.6, 6.8, 1.6 Hz, 1H), 5.73 (dt, *J* = 15.6, 6.8 Hz, 1H);

Z-isomer, 1.25 (br, 1H), 1.68 (overlap, 2H), 2.17 (td, *J* = 7.2, 6.8 Hz, 2H), 2.91–3.01(m, 2H), 3.02–3.12 (m, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 5.47 (overlap, 1H), 5.82 (dt, *J* = 14.8, 7.6 Hz, 1H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

29.0, 31.9, 45.3 (t, *J* = 23.9 Hz), 62.4, 119.6 (t, *J* = 3.8 Hz), 129.0 (t, *J* = 289 Hz), 137.9

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

E-isomer, –51.4 (t, *J* = 11.7 Hz); *Z*-isomer, –50.9 (t, *J* = 11.7 Hz)

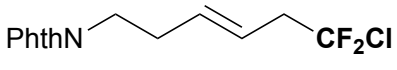
IR (neat, cm^{-1})

3383, 2923, 2856, 1725, 1461, 1240, 1189, 1093, 970, 668

HRMS-FI (*m*/*z*)

[M] calcd. for $C_7H_{11}ClF_2O$, 184.0467; found, 184.0468

Synthesis of *N*-(6-chloro-6,6-difluoro-3-hexenyl)phthalimide (2g):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (47 mg, 78% yield, *E*/*Z* = 84/16) after silica gel column

[20] L. Ou and D. Bai, *Organic Preparations and Procedures International: The New Journal for Organic Synthesis*, 1999, **31**, 333.

chromatography (CH_2Cl_2/hexane = 50/50).

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

E-isomer, 2.45–2.54 (m, 2H), 2.86–2.96 (m, 2H), 3.78 (t, *J* = 6.8 Hz, 2H), 5.45 (dtt, *J* = 15.2, 7.2, 1.2 Hz, 1H), 5.69 (dt, *J* = 15.2, 7.2 Hz, 1H), 7.69–7.73 (m, 2H), 7.82–7.86 (m, 2H);

Z-isomer, 2.45–2.54 (m, 2H), 2.96–3.06 (m, 2H), 3.78 (overlap, 2H), 5.54 (dtt, *J* = 15.2, 7.2, 1.2 Hz, 1H), 5.69 (overlap, 1H), 7.69–7.73 (m, 2H), 7.82–7.86 (m, 2H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

31.8, 37.2, 45.1 (t, *J* = 24.8 Hz), 122.3 (t, *J* = 3.8 Hz), 123.4 (2C), 128.6 (t, *J* = 289 Hz), 132.2, 134.1 (2C), 134.2 (2C), 168.4 (2C)

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

E-isomer, –51.4 (t, *J* = 11.3 Hz); *Z*-isomer, –51.0 (t, *J* = 11.3 Hz)

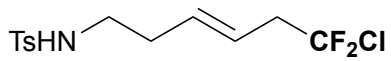
IR (neat, cm^{-1})

1773, 1710, 1468, 1437, 1395, 1360, 1237, 1188, 1080, 1059, 982, 957, 905, 791, 716, 667

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{14}H_{12}ClF_2NO_2$, 322.0417; found, 322.0416

Synthesis of *N*-(6-chloro-6,6-difluoro-3-hexenyl)-4-toluenesulfonamide (2h):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (43 mg, 66% yield, *E*/*Z* = 88/12) after silica gel column chromatography (CH_2Cl_2/hexane = 50/50).

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

E-isomer, 2.22 (m, 2H), 2.43 (s, 3H), 2.92 (td, *J* = 11.3, 6.8 Hz, 2H), 3.03 (m, 2H), 4.60 (s, 1H), 5.42 (dtt, *J* = 15.2, 6.8, 1.2 Hz, 1H), 5.54 (dt, *J* = 15.2, 6.8 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H);

Z-isomer, 2.22 (m, 2H), 2.43 (s, 3H), 2.92 (td, *J* = 11.3, 6.8 Hz, 2H), 3.03 (m, 2H), 4.60 (overlap, s, 1H), 5.42 (overlap, 1H), 5.54 (overlap, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (*E*-isomer; 100 MHz, $CDCl_3$)

21.6, 32.7, 42.3, 45.1 (t, *J* = 24.8 Hz), 122.7 (t, *J* = 3.8 Hz), 127.2 (2C), 128.7 (t, *J* = 289 Hz), 129.9 (2C), 134.0, 137.1, 143.7

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

E-isomer, –51.4 (t, *J* = 11.3 Hz); *Z*-isomer, –50.9 (t, *J* = 11.3 Hz)

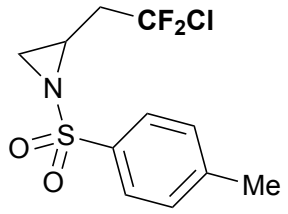
IR (neat, cm^{-1})

3281, 2915, 1599, 1425, 1325, 1239, 1159, 1093, 1009, 971, 897, 815, 664

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{13}H_{16}ClF_2NO_2S$, 346.0451; found, 346.0462

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-*N*-tosylaziridine on a gram-scale (3i):



In a round-bottom flask (300–mL size) capped by a three-way cock, urea·H_2O_2 (1.4 g, 15 mmol) was allowed to settle under N_2 gas.[18] Then, CH_2Cl_2 (50 mL) was added, and the resulting suspension was cooled to 0 °C. To this mixture, chlorodifluoroacetic anhydride (8.8 mL, 50 mmol) was slowly added. After stirring for 1 h, *N*-allyl-4-toluenesulfonamide **1i** (10 mmol, 2.1 g), pyridine (1.6 mL, 20 mmol), and $Cu(tfa)_2$ (290 mg, 1.0 mmol) were added. Then, the mixture was warmed to 25 °C and stirred for 3 h. After addition of 60 mL of EtOAc, the reaction was quenched with aqueous $NaHCO_3$ solution at 0 °C and then stirred at rt for 20 min. The aqueous layer was extracted with 60 mL of EtOAc three times. The combined organic phase was checked with XploSens PS® to confirm the absence of peroxide, and the water phase was treated with saturated $Na_2S_2O_3$ to decompose H_2O_2. The combined organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel (CH_2Cl_2/hexane = 60/40) afforded the target compound as a colorless oil (1.5 g, 52%).

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

2.18 (d, *J* = 4.4 Hz, 1H), 2.30–2.43 (m, 1H), 2.46 (s, 3H), 2.47–2.59 (m, 1H), 2.76 (d, *J* = 6.9 Hz, 1H), 2.98 (dtd, *J* = 6.9, 6.3, 4.4 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 8.3 Hz, 2H)

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

21.8, 32.0, 34.0 (t, *J* = 4.3 Hz), 43.8 (t, *J* = 25.1 Hz), 127.4 (t, *J* = 292 Hz), 128.3 (2C), 130.0 (2C), 134.5, 145.2

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

–51.1 (dt, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 11.6 Hz, 1F), –50.5 (dt, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 11.6 Hz, 1F)

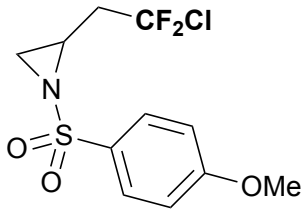
IR (neat, cm^{-1})

1597, 1410, 1327, 1306, 1261, 1232, 1194, 1162, 1134, 1088, 1005, 937, 903, 815, 773, 712, 694, 658

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{11}H_{12}ClF_2NO_2S$, 318.0138; found, 318.0148

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-*N*-((4-methoxyphenyl)sulfonyl)aziridine (3j):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (31 mg, 50% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 70/30).

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

2.17 (d, *J* = 4.6 Hz, 1H), 2.32–2.45 (m, 1H), 2.46–2.59 (m, 1H), 2.74 (d, *J* = 6.9 Hz, 1H), 2.95 (dtd, *J* = 6.9, 6.2, 4.6 Hz, 1H), 3.89 (s, 3H), 6.98–7.05 (m, 2H), 7.84–7.91 (m, 2H)

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

32.0, 34.0 (t, *J* = 5.8 Hz), 43.9 (t, *J* = 24.8 Hz), 55.9, 114.5 (2C), 127.5 (t, *J* = 290 Hz), 128.9, 130.5 (2C), 164.1

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

−51.1 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F), −50.5 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F)

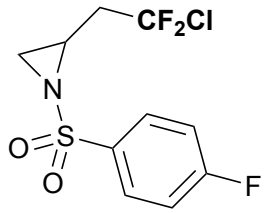
IR (neat, cm^{-1})

2845, 1596, 1579, 1499, 1461, 1442, 1415, 1328, 1301, 1262, 1232, 1194, 1156, 1114, 1089, 1009, 937, 899, 835, 806, 774, 722, 699, 660

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{11}H_{12}ClF_2NO_3S$, 334.0087; found, 334.0082

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-*N*-((4-fluorophenyl)sulfonyl)aziridine (3k):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (31 mg, 51% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 60/40).

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

2.23 (d, *J* = 4.4 Hz, 1H), 2.40–2.57 (m, 2H), 2.82 (dd, *J* = 7.2, 0.8 Hz, 1H), 3.00–3.07 (m, 1H), 7.22–7.30 (m, 2H), 7.96–8.03 (m, 2H)

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

32.0, 34.3 (t, *J* = 4.8 Hz), 43.8 (t, *J* = 24.8 Hz), 116.6 (d, *J* = 22.9 Hz, 2C), 127.3 (t, *J* = 290 Hz), 131.2 (d, *J* = 9.5 Hz, 2C), 133.7 (d, *J* = 3.9 Hz), 166.1 (d, *J* = 254 Hz)

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

–102.8 (m), –51.3 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F), –50.6 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F)

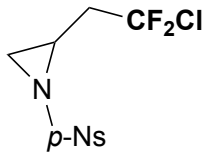
IR (neat, cm^{-1})

2919, 2846, 1592, 1494, 1408, 1333, 1293, 1237, 1194, 1170, 1155, 1135, 1088, 1005, 966, 937, 900, 840, 820, 719, 697, 660

HRMS-ESI (*m/z*)

$[M+Na]^+$ calcd. for $C_{10}H_9ClF_3NO_3S$, 321.9887; found, 321.9898

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-*N*-((4-nitrophenyl)sulfonyl)aziridine (3l):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a white solid (16 mg, 24% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 70/30).

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

2.28 (d, *J* = 4.4 Hz, 1H), 2.40–2.58 (m, 2H), 2.90 (d, *J* = 6.8 Hz, 1H), 3.08–3.16 (m, 1H), 8.13–8.20 (m, 2H), 8.37–8.44 (m, 2H)

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

32.3, 35.0 (t, *J* = 3.9 Hz), 43.8 (t, *J* = 24.8 Hz), 124.5 (2C), 127.2 (t, *J* = 290

Hz), 129.8 (2C), 143.4, 151.0

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

−51.4 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F), −50.6 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F)

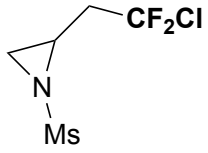
IR (neat, cm^{-1})

2917, 1608, 1535, 1403, 1352, 1313, 1263, 1234, 1194, 1169, 1134, 1089, 1006, 940, 898, 855, 799, 774, 753, 743, 692, 673, 627

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{10}H_9ClF_2N_2O_4S$, 348.9832; found, 348.9833

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-*N*-(methanesulfonyl)aziridine (3m):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a white solid (18 mg, 40% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 70/30).

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

2.21 (d, *J* = 4.0 Hz, 1H), 2.49–2.66 (m, 2H), 2.74 (d, *J* = 6.8 Hz, 1H), 2,96–3.02 (m, 1H), 3.10 (s, 3H)

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

30.7, 34.0, 39.8, 43.9 (t, *J* = 24.8 Hz), 127.7 (t, *J* = 290 Hz)

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

−51.1 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F), −50.3 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F)

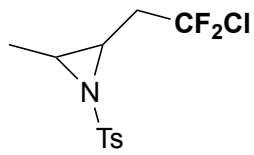
IR (neat, cm^{-1})

2923, 2820, 1415, 1326, 1263, 1235, 1196, 1159, 1102, 1011, 967, 943, 785

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_5H_8ClF_2NO_2S$, 241.9825; found, 241.9827

Synthesis of 2-(2-chloro-2,2-difluoroethyl)-3-methyl-1-tosylaziridine (3n):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The diastereomixture of the target compound was obtained as a colorless oil (26 mg, 41% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 60/40: *trans*/*cis* = 6/4, *trans*-product (R_f = 0.21) was very slightly less polar than *cis*-product (R_f = 0.18)).

^{1}H NMR (400 MHz, $CDCl_3$)[21]

trans-isomer, 1.56–1.60 (d, J = 6.0 Hz, 3H), 2.44 (s, 3H), 2.50–2.62 (m, 1H), 2.67–2.85 (m, 2H), 2.88–2.93 (m, 1H), 7.30–7.37 (m, 2H), 7.79–7.85 (m, 2H);

cis-isomer, 1.22–1.29 (m, 3H), 2.37–2.56 (m, 2H), 2.45 (s, 3H), 2.97–3.05 (m, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.79–7.83 (m, 2H)

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

trans-isomer, 14.6, 21.8, 42.4, 44.7 (t, J = 24.8 Hz), 127.7 (t, J = 292 Hz), 127.7 (2C), 129.8 (2C), 137.4, 144.5;

cis-isomer, 12.5, 21.8, 38.6, 38.7 (t, J = 4.3 Hz), 39.7 (t, J = 25.3 Hz), 127.6 (t, J = 289 Hz), 128.2 (2C), 129.9 (2C), 134.9, 144.9

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

trans-isomer: –51.0 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F), –50.2 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 8.6 Hz, 1F);

cis-isomer: –50.9 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F),–50.4 (dt, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.3 Hz, 1F)

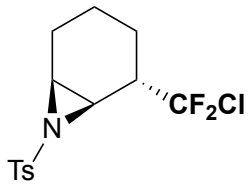
IR (neat, cm^{-1})

1597, 1456, 1326, 1260, 1194, 1161, 1111, 1088, 1053, 1010, 995, 976, 944, 902, 815, 710, 685

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{12}H_{14}ClF_2NO_2S$, 332.0294; found, 332.0295

Synthesis of (1*R*,2*S*,6*S*)-2-(chlorodifluoromethyl)-7-tosyl-7-azabicyclo[4.1.0]-heptane (3o):



The reaction was carried out on a 0.20 mmol scale according to general procedure A. The target compound was obtained as a colorless oil (23 mg, 34% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 60/40).

^{1}H NMR (400 MHz, $CDCl_3$)[21]

1.15–1.26 (m, 1H), 1.29–1.40 (m, 1H), 1.50–1.60 (m, 1H), 1.63–1.73 (m, 1H), 1.75–1.84 (m, 1H), 2.02–2.09 (m, 1H), 2.40–2.51 (m, 1H), 2,45 (s, 3H), 3.01 (d, J = 6.8 Hz, 1H), 3.14–3.18 (m, 1H), 7.32–7.37 (m, 2H), 7.79–7.85 (m, 2H)

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

16.4, 21.8, 22.0, 22.7, 38.4 (t, J = 4.8 Hz), 39.3, 45.6 (t, J = 22.9 Hz), 128.0

[21] The stereochemistry was confirmed by means of a NOESY experiment.

(2C), 129.9 (2C), 130.5 (t, J = 292 Hz), 135.1, 144.8

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

–57.0 (dd, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 11.7 Hz, 1F), –56.5 (dd, $J_{F–F}$ = 164 Hz, $J_{F–H}$ = 8.6 Hz, 1F)

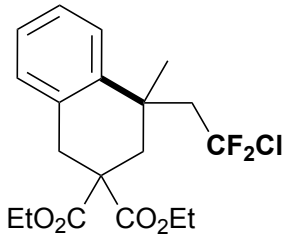
IR (neat, cm^{-1})

2949, 1597, 1495, 1452, 1412, 1327, 1305, 1242, 1160, 1091, 1049, 1024, 984, 955, 944, 907, 893, 869, 830, 813, 776, 729, 698, 670

HRMS-ESI (m/z)

$[M+Na]^+$ calcd. for $C_{14}H_{16}ClF_2NO_2S$, 358.0451; found, 358.0451

Synthesis of diethyl 4-(2-chloro-2,2-difluoroethyl)-4-methyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate (4p):



The reaction was carried out on a 0.21 mmol scale according to general procedure B. The target compound was obtained as a colorless oil (80 mg, 99% yield) after silica gel column chromatography (EtOAc/hexane = 10/90).

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

1.19 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.45 (d, J = 1.8 Hz, 3H), 2.43 (d, J = 14.6 Hz, 1H), 2.71 (d, J = 14.6 Hz, 1H), 2.64–2.89 (m, 2H), 3.15 (d, J = 15.9 Hz, 1H), 3.32 (d, J = 15.9 Hz, 1H), 4.05–4.28 (m, 4H), 7.14–7.27 (m, 4H)

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

14.0 (2C), 29.8, 35.2, 37.0, 39.9, 52.6, 53.9 (t, J = 21.7 Hz), 61.5, 61.9, 126.2, 126.9, 127.0, 129.2, 129.3 (t, J = 296 Hz), 133.3, 140.9, 171.3, 171.8

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

–47.0 (ddd, $J_{F–F}$ = 156 Hz, $J_{F–H}$ = 23.1 Hz, $J_{F–H'}$ = 7.2 Hz, 1F), –45.4 (ddd, $J_{F–F}$ = 156 Hz, $J_{F–H}$ = 23.8 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

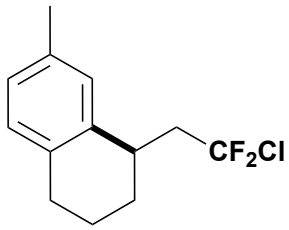
IR (neat, cm^{-1})

1732, 1299, 1258, 1211, 1193, 1145, 1128, 1081, 1046, 973, 926, 902, 860, 759, 730

HRMS-ESI (m/z)

$[M+Na]^+$ calcd. for $C_{19}H_{23}ClF_2O_4$, 411.1145; found, 411.1146

Synthesis of 1-(2-chloro-2,2-difluoroethyl)-7-methyl-1,2,3,4-tetrahydronaphthalene (4q):



The reaction was carried out on a 0.20 mmol scale according to general procedure B. The target compound was obtained as a white amorphous material (32 mg, 65% yield) after silica gel column chromatography (hexane).

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

1.75–1.85 (m, 2H), 1.86–1.99 (m, 2H), 2.31 (s, 3H), 2.54–2.80 (m, 4H), 3.22–3.28 (m, 1H), 6.94–6.99 (m, 3H)

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

19.3, 21.2, 27.9, 29.0, 33.6, 49.0 (t, J = 22.2 Hz), 127.3, 129.3, 129.4, 130.0 (t, J = 293 Hz), 134.2, 135.7, 138.7

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

–50.0 (dt, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 15.9 Hz, 1F), –47.0 (ddd, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 14.5 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

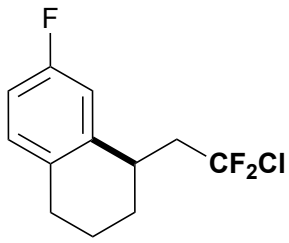
IR (neat, cm^{-1})

2935, 1506, 1457, 1437, 1363, 1245, 1206, 1105, 1069, 1048, 989, 949, 924, 806, 679, 668

HRMS-ESI (*m/z*)

$[M]^+$ calcd. for $C_{13}H_{15}ClF_2$, 244.0825; found, 244.0807

Synthesis of 1-(2-chloro-2,2-difluoroethyl)-7-fluoro-1,2,3,4-tetrahydro-naphthalene (4r):



The reaction was carried out on a 0.20 mmol scale according to general procedure B. The target compound was obtained as a colorless oil (35 mg, 70% yield) after silica gel column chromatography (hexane).

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

1.76–1.83 (m, 2H), 1.85–2.00 (m, 2H), 2.56–2.80 (m, 4H), 3.24–3.29 (m, 1H), 6.82–6.89 (m, 2H), 7.02–7.05 (m, 1H)

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

19.3, 27.8, 28.7, 33.8, 48.9 (t, J = 22.2 Hz), 113.7 (d, J = 21.2 Hz), 114.9 (d, J

= 21.2 Hz), 129.8 (t, J = 293 Hz), 130.9 (d, J = 7.7 Hz), 132.7 (d, J = 2.9 Hz), 140.7 (d, J = 6.7 Hz), 161.3 (d, J = 244 Hz)

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

–50.2 (dt, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 15.9 Hz, 1F), –116.8 (m), –47.4 (dt, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 11.6 Hz, 1F)

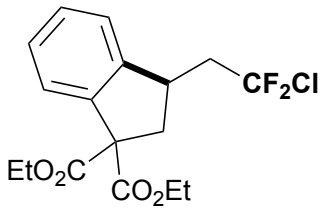
IR (neat, cm^{-1})

2939, 1617, 1591, 1501, 1366, 1244, 1224, 1206, 1143, 1100, 990, 922, 873, 808, 679

HRMS-ESI (*m/z*)

$[M]^+$ calcd. for $C_{12}H_{12}ClF_3$, 248.0574; found, 248.0567

Synthesis of diethyl 3-(2-chloro-2,2-difluoroethyl)-2,3-dihydro-1H-indene-1,1-dicarboxylate (4s):



The reaction was carried out on a 0.20 mmol scale according to general procedure B. The target compound was obtained as a white amorphous material (64 mg, 88% yield) after silica gel column chromatography (EtOAc/hexane = 4/96).

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

1.24 (t, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 2.44–2.58 (m, 2H), 2.86–2.98 (m, 1H), 3.08–3.14 (dd, J = 13.8, 7.8 Hz, 1H), 3.66–3.73 (m, 1H), 4.19 (q, J = 7.1 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 7.19–7.22 (m, 1H), 7.29–7.38 (m, 2H), 7.59–7.61 (m, 1H)

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

14.1, 14.2, 38.4, 40.9, 47.4 (t, J = 23.6 Hz), 61.96, 62.02, 64.9, 123.5, 127.1, 127.9, 129.2, 129.5 (t, J = 293 Hz), 139.1, 144.9, 170.2, 170.6

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

–50.4 (dt, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 15.2 Hz, 1F), –48.2 (ddd, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 15.9 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

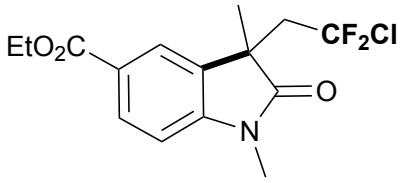
IR (neat, cm^{-1})

1734, 1457, 1368, 1242, 1188, 1106, 1022, 948, 860, 753, 679, 668

HRMS-ESI (*m/z*)

$[M+Na]^+$ calcd. for $C_{17}H_{19}ClF_2O_4$, 383.0832; found, 383.0838

Synthesis of ethyl 3-(2-chloro-2,2-difluoroethyl)-1,3-dimethyl-2-oxoindoline-5-carboxylate (4t):



The reaction was carried out on a 0.20 mmol scale according to general procedure B. The target compound was obtained as a white solid (57 mg, 86% yield) after silica gel column chromatography (EtOAc/hexane = 20/80).

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

1.39 (t, *J* = 7.1 Hz, 3H), 1.40 (s, 3H), 2.95 (m, 1H), 3.16 (m, 1H), 3.26 (s, 3H), 4.36 (q, *J* = 7.1 Hz, 2H), 6.90 (d, *J* = 8.3 Hz, 1H), 7.92 (s, 1H), 8.05 (dd, *J* = 8.3 Hz, 1H)

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

14.5, 25.6, 26.8, 45.3, 48.4 (t, *J* = 23.6 Hz), 61.1, 108.1, 125.07, 125.13, 127.3 (t, *J* = 294 Hz), 130.9, 131.2, 147.0, 166.4, 178.8

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

–49.3 (ddd, $J_{F–H}$ = 162 Hz, $J_{F–H}$ = 17.3 Hz, $J_{F–H'}$ = 8.7 Hz, 1F), –46.6 (ddd, $J_{F–H}$ = 162 Hz, $J_{F–H}$ = 17.3 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

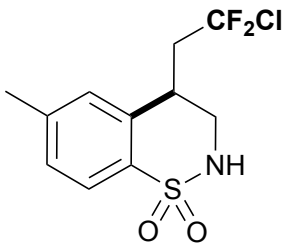
IR (neat, cm^{-1})

1710, 1616, 1500, 1459, 1373, 1350, 1283, 1234, 1133, 1103, 1051, 1027, 1001, 978, 930, 772

HRMS-ESI (*m/z*)

$[M+Na]^+$ calcd. for $C_{15}H_{16}ClF_2NO_3$, 354.0679; found, 354.0689

Synthesis of 4-(2-chloro-2,2-difluoroethyl)-6-methyl-3,4-dihydro-2H-benzo[1,2]thiazine-1,1-dioxide (4i):



The reaction was carried out on a 0.20 mmol scale according to general procedure B, stirring the reaction mixture at 25 °C for 3 h instead of 40 °C. The target compound was obtained as a white solid (43 mg, 72% yield) after silica gel column chromatography (EtOAc/hexane = 25/75).

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

2.39 (s, 3H), 2.54–2.70 (m, 1H), 2.83–3.00 (m, 1H), 3.26 (m, 1H), 3.71 (ddd, *J* = 15.4, 5.3, 3.7 Hz, 1H), 4.00 (ddd, *J* = 15.4, 9.4, 4.0 Hz, 1H), 5.32 (br, 1H), 7.07 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H)

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

21.7, 33.2, 44.8, 46.0 (t, J = 23.6 Hz), 124.6, 128.7 (t, J = 292 Hz), 129.52, 129.53, 134.8, 137.4, 143.6

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

–50.5 (dt, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 15.9 Hz, 1F), –48.2 (ddd, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 15.9 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

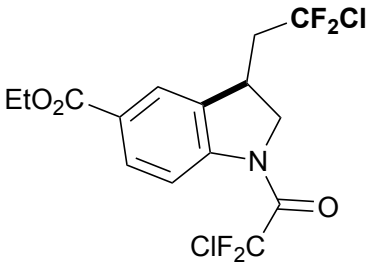
IR (neat, cm^{-1})

3266, 1606, 1438, 1320, 1174, 1148, 1114, 1078, 1006, 953, 817, 708, 672

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{11}H_{12}ClF_2NO_2S$, 318.0138; found, 318.0148

Synthesis of ethyl 1-(2-chloro-2,2-difluoroacetyl)-3-(2-chloro-2,2-difluoroethyl)indoline-5-carboxylate (4u):



The reaction was carried out on a 0.21 mmol scale according to general procedure B. The target compound was obtained as a white solid (48 mg, 59% yield) after silica gel column chromatography (EtOAc/hexane = 10/90).

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

1.41 (t, J = 7.1 Hz, 3H), 2.56–2.68 (m, 1H), 2.96 (dtd, J = 15.1, 15.1, 2.8 Hz, 1H), 3.91 (m, 1H), 4.22 (dd, J = 11.6, 6.7 Hz, 1H), 4.33–4.44 (m, 2H), 4.60 (q, J = 11.6, 11.6 Hz, 1H), 7.93 (s, 1H), 8.05 (m, 1H), 8.26 (d, J = 8.6 Hz, 1H)

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

14.5, 36.2, 46.5 (t, J = 24.1 Hz), 54.9, 61.5, 117.9, 118.4 (t, J = 302 Hz), 125.2, 128.4, 128.5, 131.4, 132.8, 145.3, 156.6 (t, J = 31.3 Hz), 165.7

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

–61.2 (d, J = 165 Hz, 1F), –60.6 (d, J = 165 Hz, 1F), –51.2 (dt, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 15.1 Hz, 1F), –49.4 (ddd, $J_{F–F}$ = 165 Hz, $J_{F–H}$ = 14.5 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

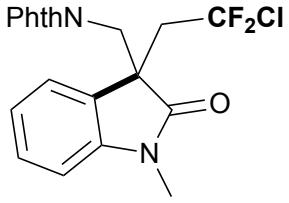
IR (neat, cm^{-1})

1701, 1609, 1488, 1445, 1405, 1368, 1291, 1265, 1178, 1112, 1087, 1020, 952, 908, 849, 828, 769, 742, 709, 679, 668, 614

HRMS-ESI (*m*/*z*)

[M+Na]$^+$ calcd. for $C_{15}H_{13}Cl_2F_4NO_3$, 424.0101; found, 424.0102

Synthesis of *N*-((3-(2-chloro-2,2-difluoroethyl)-*N*-methyl-3-oxindolinyl)methyl) phthalimide (4v):



The reaction was carried out on a 0.20 mmol scale according to general procedure B. The target compound was obtained as a white solid (66 mg, 81% yield) after silica gel column chromatography (EtOAc/hexane = 30/70).

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

3.24 (s, 3H), 3.21–3.42 (m, 2H), 3.86 (d, *J* = 14.1 Hz, 1H), 3.98 (d, *J* = 14.1 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 7.03 (td, *J* = 7.6, 1.0 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.31 (td, *J* = 7.6, 1.0 Hz, 1H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H)

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

26.8, 44.4, 45.7 (t, *J* = 23.6 Hz), 49.5, 108.8, 122.5, 123.8 (2C), 124.9, 126.6, 127.3 (t, *J* = 294 Hz), 129.4, 131.7 (2C), 134.4 (2C), 143.6, 168.1 (2C), 175.7

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

–48.8 (ddd, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 17.3 Hz, $J_{F–H'}$ = 11.6 Hz, 1F), –45.3 (ddd, $J_{F–F}$ = 162 Hz, $J_{F–H}$ = 17.3 Hz, $J_{F–H'}$ = 8.7 Hz, 1F)

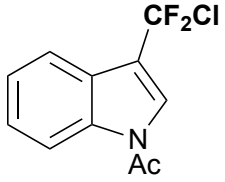
IR (neat, cm^{-1})

1778, 1717, 1613, 1495, 1472, 1424, 1395, 1339, 1193, 1110, 1087, 1021, 920, 755, 721, 604

HRMS-ESI (*m*/*z*)

[M+Na]$^+$ calcd. for $C_{20}H_{15}ClF_2N_2O_3$, 427.0632; found, 427.0627

Synthesis of *N*-acetyl-3-(chlorodifluoromethyl)indole (5w):



The reaction was carried out on a 0.20 mmol scale according to general procedure C. The target compound was obtained as a white solid (14 mg, 28% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 30/70).

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

2.86 (s, 3H), 7.20 (s, 1H), 7.33 (td, *J* = 7.2, 0.8 Hz, 1H), 7.47 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.86 (dd, *J* = 8.4, 0.8 Hz, 1H)

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

27.34, 113.8 (t, *J* = 6.2 Hz), 115.0, 123.0, 124.0, 122.1 (t, *J* = 286 Hz), 127.1, 127.3, 132.8, 137.1, 168.7

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

–43.6 (s)

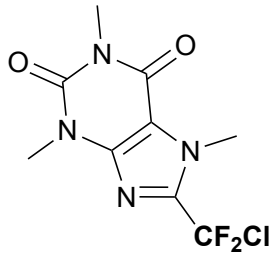
IR (neat, cm^{-1})

2923, 2852, 1723, 1558, 1476, 1460, 1434, 1378, 1358, 1341, 1329, 1296, 1267, 1220, 1178, 1163, 1125, 1099, 1084, 1028, 929, 891, 863, 832, 796, 750, 741, 689, 670

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{11}H_8ClF_2NO$, 266.0155; found, 266.0155

Synthesis of 8-(chlorodifluoromethyl)caffeine (5x):



The reaction was carried out on a 0.20 mmol scale according to general procedure C. The desired compound was obtained as a white solid (36 mg, 65% yield) after silica gel column chromatography (EtOAc/hexane = 20/80).

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

3.41 (s, 3H), 3.59 (s, 3H), 4.17 (t, *J* = 1.4 Hz, 3H)

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

28.3, 30.0, 33.6, 109.7, 119.8 (t, *J* = 289 Hz), 142.6 (t, *J* = 32.8 Hz), 146.4, 151.4, 155.6

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

–50.9 (s)

IR (neat, cm^{-1})

1711, 1666, 1546, 1458, 1234, 1134, 1090, 1040, 986, 961, 908, 763, 746, 648

HRMS-ESI (*m*/*z*)

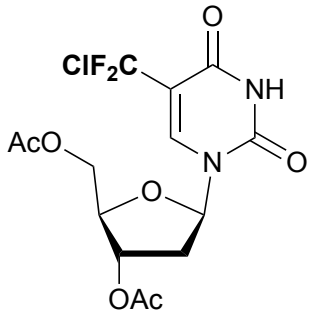
$[M+H]^+$ calcd. for $C_9H_{10}ClF_2N_4O_2$, 279.0455; found, 279.0463

<Gram-scale synthesis of **5x**>

In a round-bottom flask (300–mL size) equipped with a reflux condenser, urea·H_2O_2 (1.2 g, 12 mmol) was allowed to settle under N_2 gas.[18] Then, CH_2Cl_2 (13 mL) was added, and the resulting suspension was cooled to 0 °C. To this mixture, chlorodifluoroacetic

anhydride (7.2 mL, 41 mmol) was added dropwise. After stirring for 1 h, caffeine (10 mmol, 2.0 g) was added. Then, the mixture was warmed to 40 °C and stirred for 3 h. After cooling to 0 °C, the reaction was quenched with aqueous $NaHCO_3$ solution and diluted with 60 mL of EtOAc, and then stirred at rt for 20 min. The aqueous layer was extracted with 60 mL of EtOAc three times. The combined organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash column chromatography of the crude product on silica gel (100% CH_3Cl) afforded the target compound as a white solid (1.7 g, 62%).

Synthesis of 5-(chlorodifluoromethyl)-3',5'-di-*O*-acetyl-2'-deoxyuridine (5y):



The reaction was carried out on a 0.20 mmol scale according to general procedure C. The target compound was obtained as a white solid (43 mg, 54% yield) after silica gel column chromatography (EtOAc/hexane = 50/50).

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

2.09 (s, 3H), 2.11 (s, 3H), 2.18 (ddd, *J* = 14.5, 8.0, 6.6 Hz, 1H), 2.62 (ddd, *J* = 14.5, 5.6, 2.0 Hz, 1H), 4.44–4.29 (m, 3H), 5.22 (dt, *J* = 6.4, 1.8 Hz, 1H), 6.26 (dd, *J* = 8.0, 5.6 Hz, 1H), 8.04 (s, 1H), 9.59 (br, 1H)

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

20.7, 21.0, 38.7, 63.9, 74.2, 83.2, 86.2, 110.9 (t, *J* = 27.0 Hz), 122.9 (t, *J* = 287 Hz), 138.4 (t, *J* = 7.7 Hz), 149.4, 158.1, 170.3, 170.5

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

–51.2 (d, $J_{F\text{-}F}$ = 173 Hz, 1F), –50.6 (d, $J_{F\text{-}F}$ = 173 Hz, 1F)

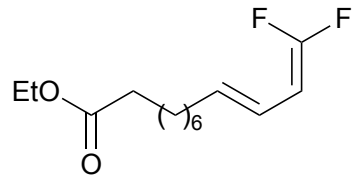
IR (neat, cm^{-1})

1701, 1465, 1240, 1193, 1101, 1073, 1035, 977, 915, 859, 757, 686, 668

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{14}H_{15}ClF_2N_2O_7$, 419.0428; found, 419.0424

Synthesis of ethyl (*E*)-12,12-difluorododeca-9,11-dienoate (6):



Compound **6** was synthesized according to the literature on 0.20 mmol scale.[22] The desired compound was obtained as a colorless oil (37 mg, 72% yield) after silica gel column chromatography (CH_2Cl_2).

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

1.22–1.42 (m, 11H), 1.55–1.65 (m, 2H), 2.01–2.10 (m, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 4.89 (ddd, *J* = 23.8, 10.8 Hz, 1H), 5.59 (dt, *J* = 15.2, 7.2 Hz, 1H), 5.84–5.94 (dd, *J* = 15.2, 10.8 Hz, 1H)

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

14.4, 25.1, 29.1, 29.2 (3C), 32.9, 34.5, 60.3, 82.1 (dd, *J* = 26.7, 17.2 Hz) 118.7, 133.7 (dd, *J* = 11.4, 2.8 Hz), 155.9 (dd, *J* = 292, 286 Hz), 174.1

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

–90.5 (d, $J_{F\text{-}F}$ = 34.2 Hz, 1F), –87.8 (dd, $J_{F\text{-}F}$ = 34.2, $J_{F\text{–}H}$ = 23.8 Hz, 1F)

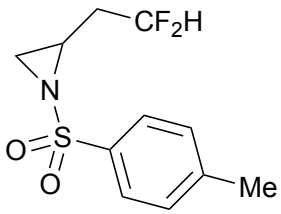
IR (neat, cm^{-1})

2932, 2855, 1734, 1724, 1646, 1465, 1369, 1286, 1184, 1097, 1034, 965, 917, 834, 724

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{14}H_{22}F_2O_2$, 283.1480; found, 283.1473

Synthesis of 2-(2,2-difluoroethyl)-1-tosylaziridine (7):



Compound **7** was synthesized according to the literature on 0.20 mmol scale.[23] The target compound was obtained as a colorless oil (52 mg, 100% yield) after silica gel column chromatography (CH_2Cl_2/hexane = 60/40).

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

1.75–1.93 (m, 1H), 2.04–2.20 (m, 1H), 2.15 (d, *J* = 4.4 Hz, 1H), 2.45 (s, 3H), 2.72 (d, *J* = 7.2 Hz, 1H), 2.80–2.87 (m, 1H), 5.62 (tdd, *J* = 55, 6.4, 3.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.79–7.84 (m, 2H)

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

21.8, 32.9, 33.9 (dd, *J* = 9.6, 5.8 Hz), 36.2 (t, *J* = 22 Hz), 115.3 (t, *J* = 239 Hz),

[22] P. Salomon and S. Z. Zard, *Org. Lett.*, 2014, **16**, 2926.
[23] A. Wegert, M. Hein, H. Reinke, N. Hoffmann and R. Miethchen, *Carbohydr. Res.*, 2006, **341**, 2641.

128.2 (2C), 129.9 (2C), 134.5, 145.1

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

–117.4 (dddd, $J_{F\text{-}F}$ = 288 Hz, $J_{F\text{-}H}$ = 55 Hz, $J_{F\text{-}H'}$ =23 Hz, $J_{F\text{-}H''}$ =17 Hz, 1F), –115.3 (ddt, $J_{F\text{-}F}$ = 288 Hz, $J_{F\text{-}H}$ = 55 Hz, $J_{F\text{-}H}$ =12 Hz, 1F)

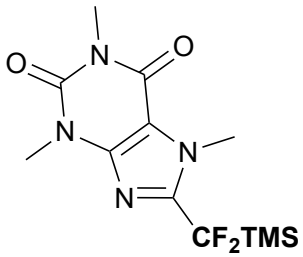
IR (neat, cm^{-1})

2919, 1597, 1495, 1456, 1416, 1393, 1325, 1291, 1230, 1186, 1162, 1121, 1092, 1073, 1054, 1019, 937, 886, 855, 816, 714, 694, 665

HRMS-ESI (*m*/*z*)

$[M+Na]^+$ calcd. for $C_{11}H_{13}F_2NO_2S$, 284.0527; found, 284.0532

Synthesis of 8-(difluoro(trimethylsilyl)methyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (8):



Compound **8** was synthesized according to the literature on 0.10 mmol scale.[24] The target compound was obtained as a white solid (17 mg, 54% yield) after silica gel column chromatography (EtOAc/CH_2Cl_2 = 5/95) .

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

0.34 (s, 9H), 3.41 (s, 3H), 3.54 (s, 3H), 4.15 (s, 3H)

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

–3.82 (3C), 28.2, 29.8, 33.3 (t, *J* = 3.9 Hz), 109.1, 124.3 (t, *J* = 255 Hz), 146.4, 146.7, 151.7, 155.9

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

–111.2 (s)

IR (neat, cm^{-1})

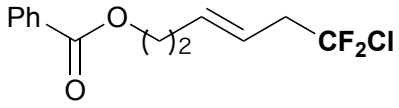
2957, 1710, 1668, 1608, 1546, 1444, 1423, 1342, 1291, 1251, 1227, 1091, 1045, 968, 875, 848, 762, 748

HRMS-ESI (*m*/*z*)

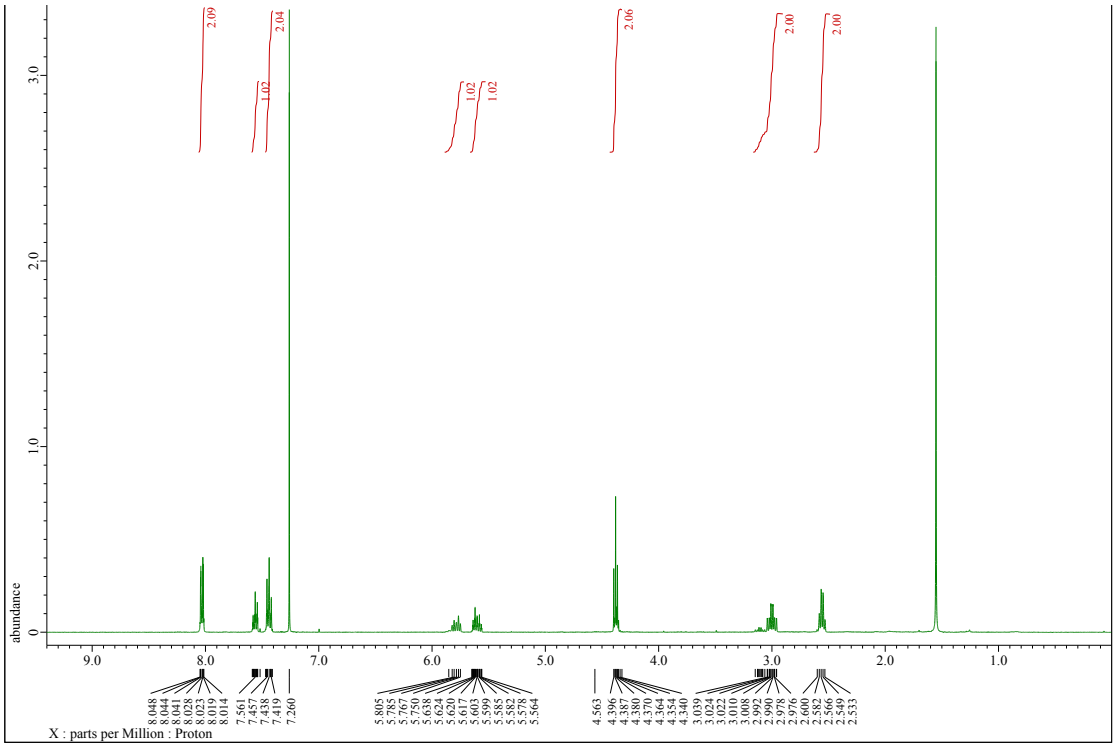
$[M+Na]^+$ calcd. for $C_{12}H_{18}F_2N_4O_2Si$, 339.1059; found, 339.1045

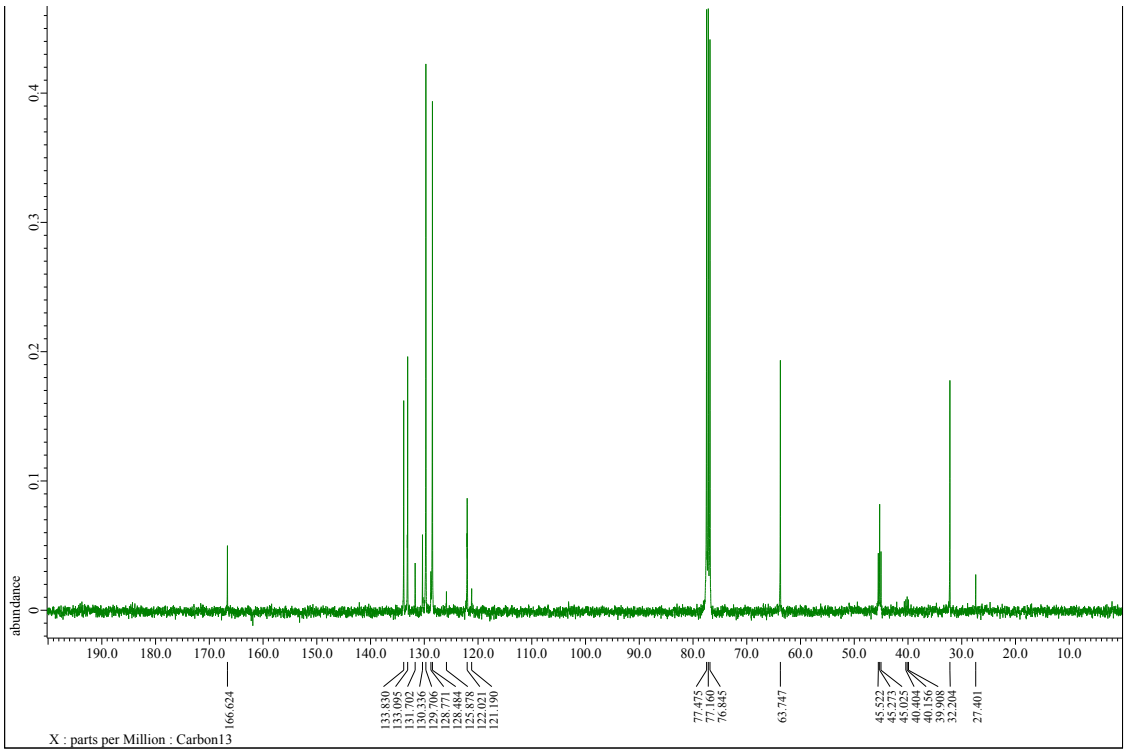
[24] J. Guidotti, F. Metz, M. Tordeux and C. Wakselman, *Synlett,* 2004, **10**, 1759.

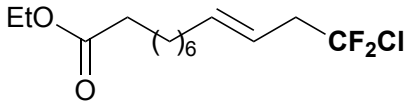
4. ^{1}H and ^{13}C NMR spectra



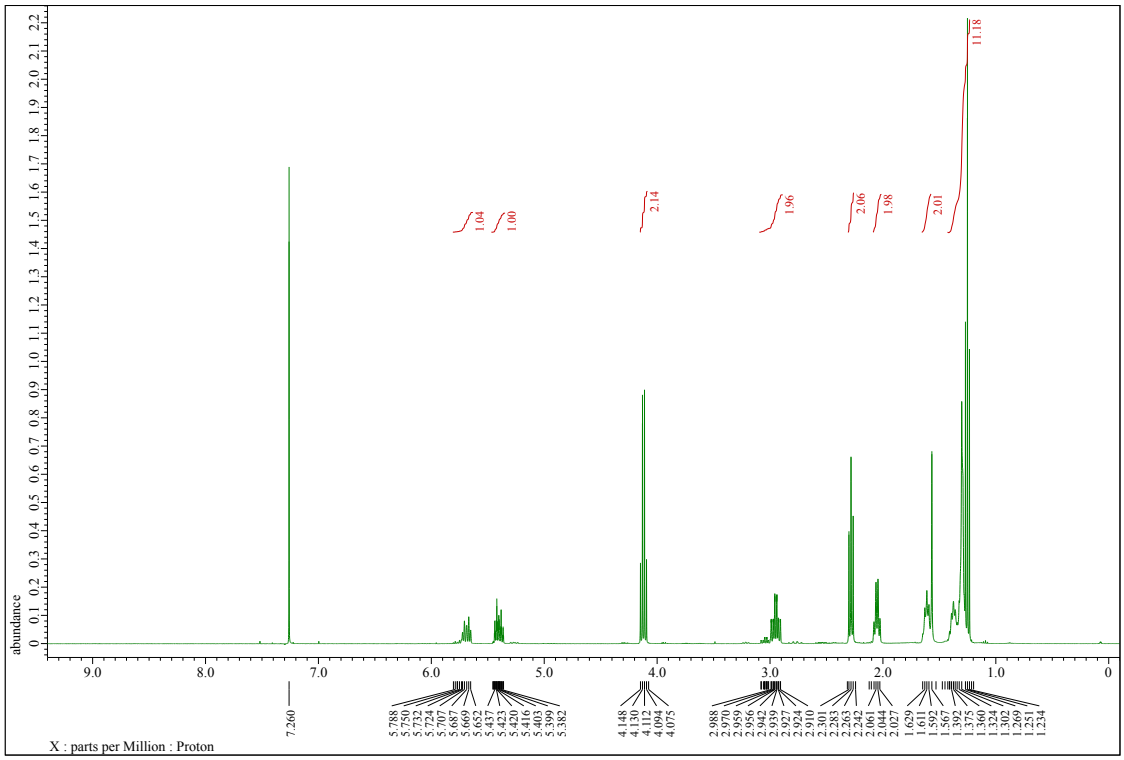
(**2a**)

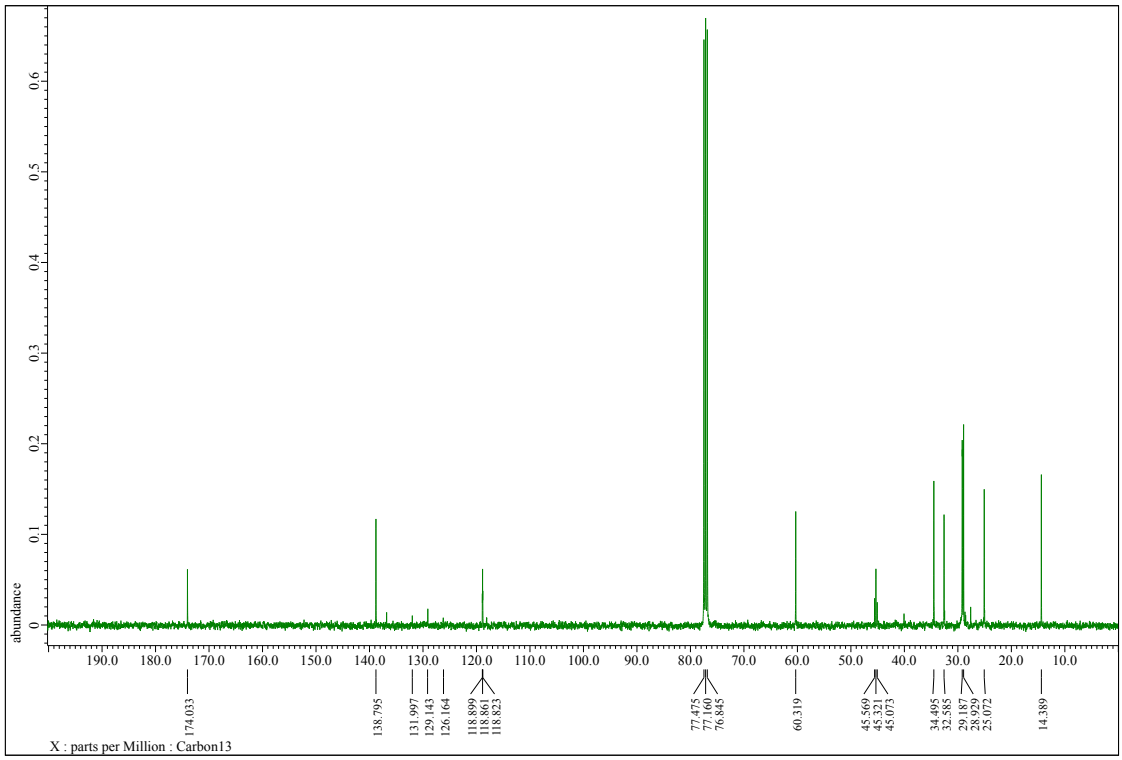


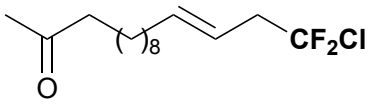



EtO
6
O
CF2Cl

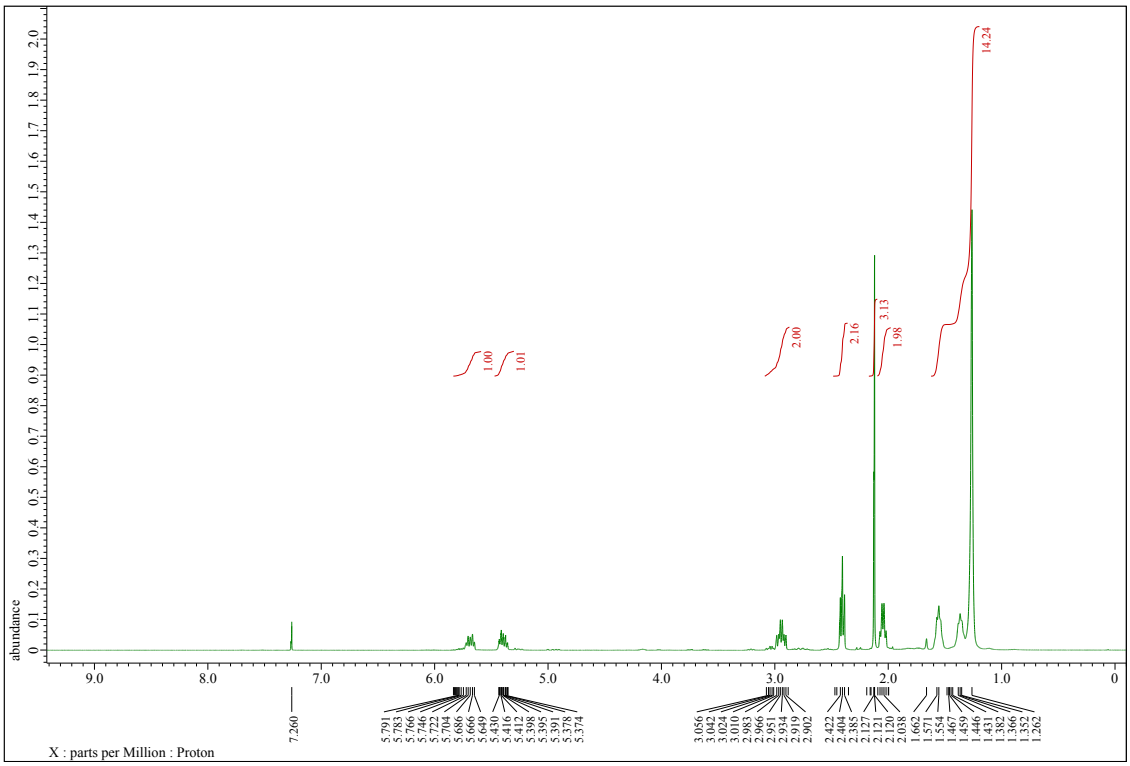
(**2b**)


abundance
X : parts per Million : Proton
11.18
2.14
1.96
2.06
1.98
2.01
1.04
1.00


abundance
X : parts per Million : Carbon13
174.033
138.795
131.997
129.143
126.164
118.899
118.861
118.823
77.475
77.160
76.845
60.319
45.569
45.321
45.073
34.495
32.585
29.187
28.929
25.072
14.389


O
8
CF2Cl

(**2c**)


abundance
X : parts per Million : Proton
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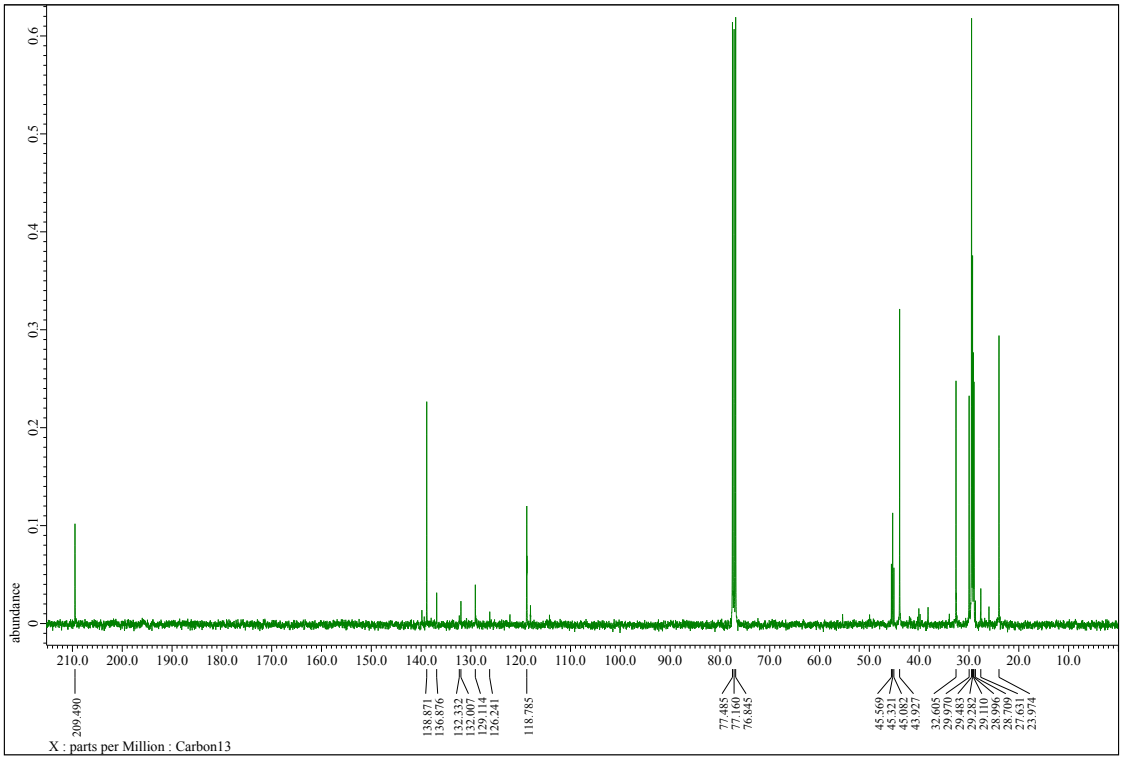
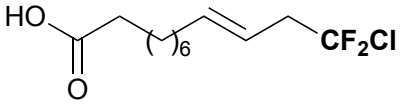
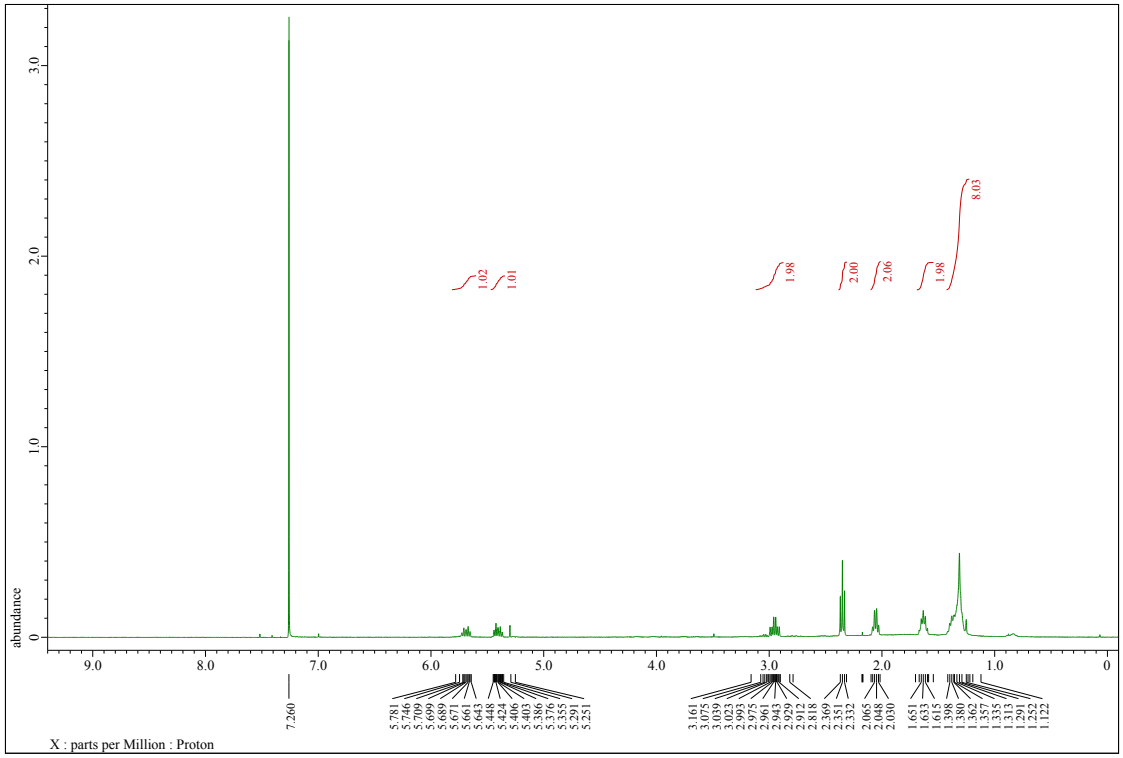
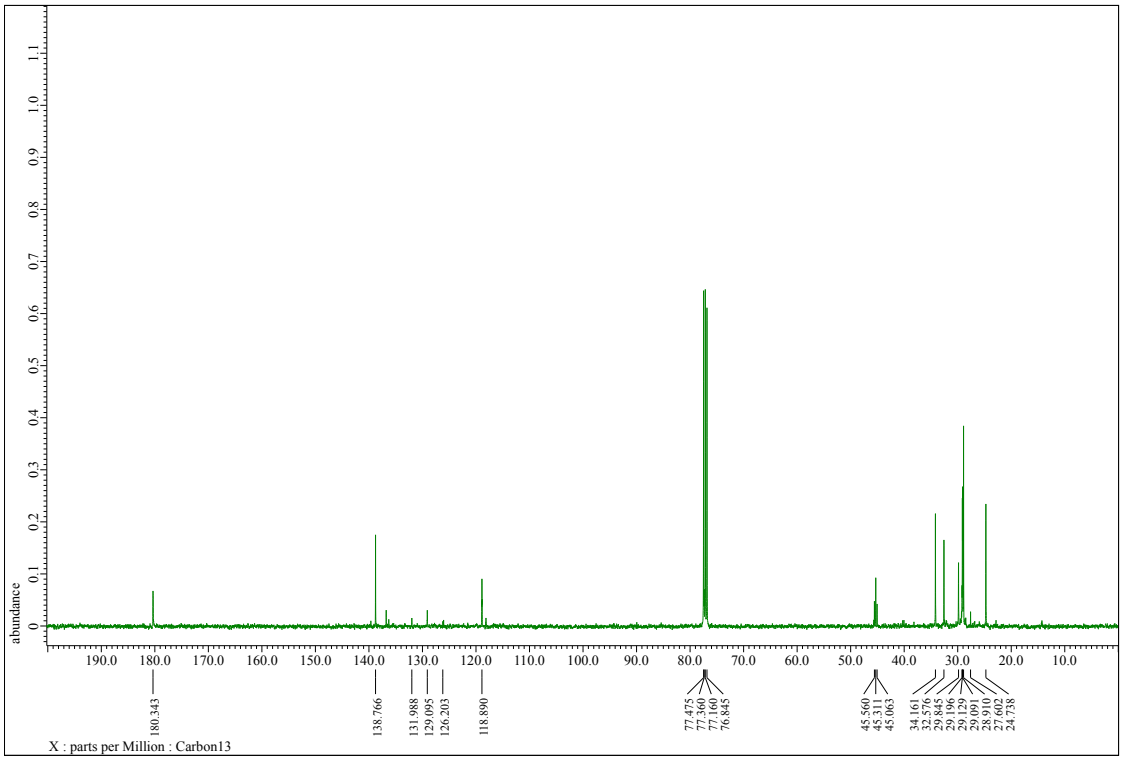
3.13
2.16
2.00
1.98
1.00
1.01


abundance
X : parts per Million : Carbon13


HO
O
6
CF2Cl

(**2d**)


abundance
X : parts per Million : Proton
7.260
1.02
1.01
1.98
2.00
2.06
1.98
8.03


abundance
X : parts per Million : Carbon13
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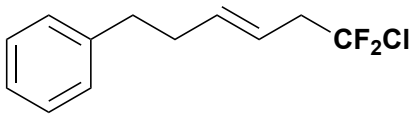
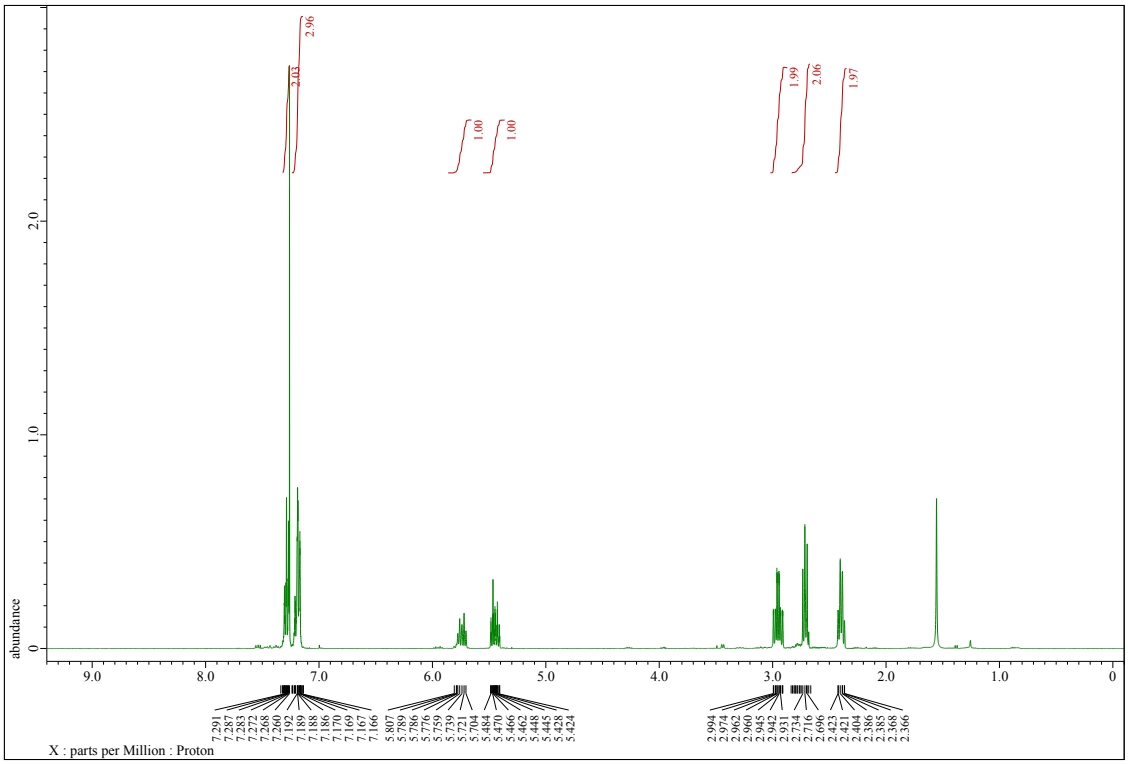
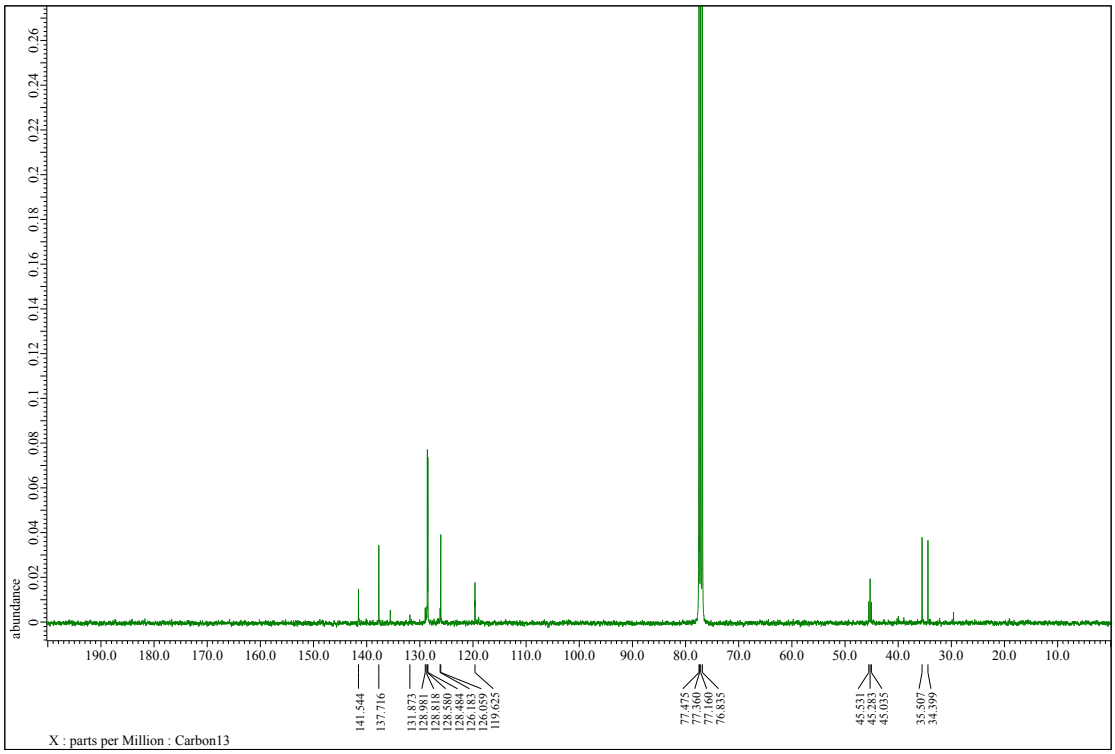
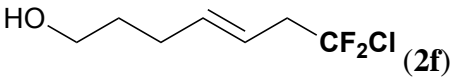
138.766
131.988
129.095
126.203
118.890
77.475
77.160
76.845
45.560
45.311
45.063
34.161
32.576
29.845
29.196
29.129
29.091
28.910
27.602
24.738


CF2Cl

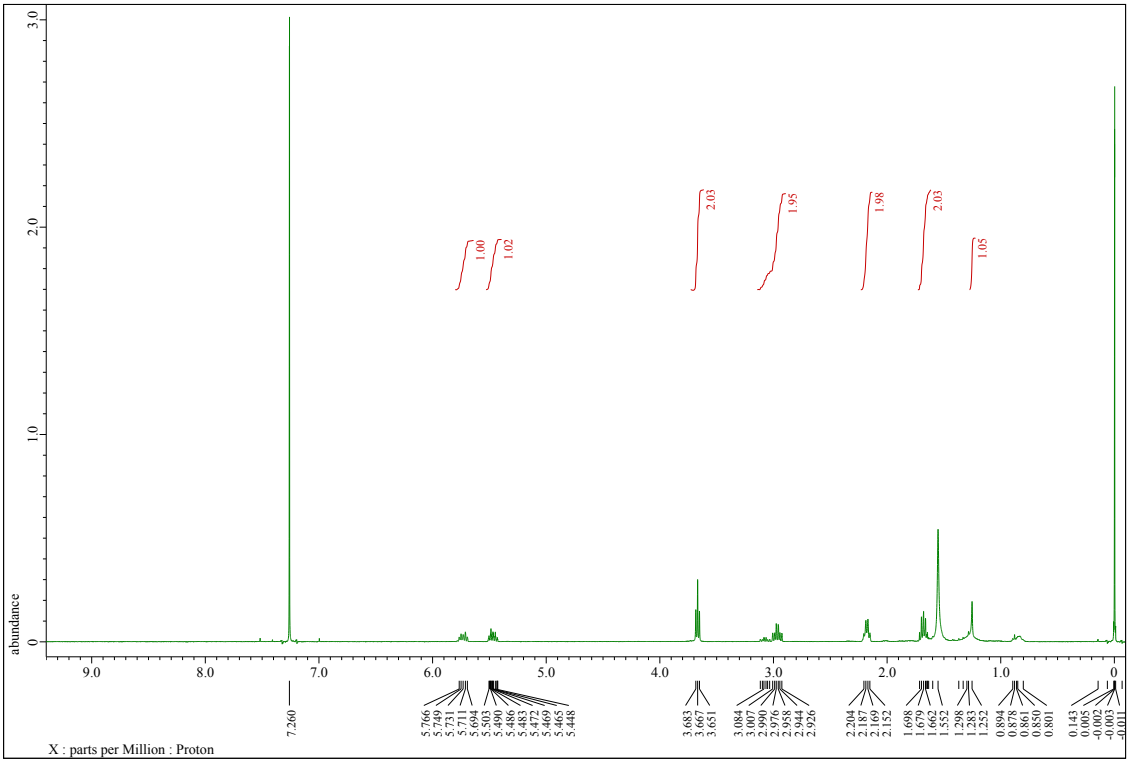
(**2e**)

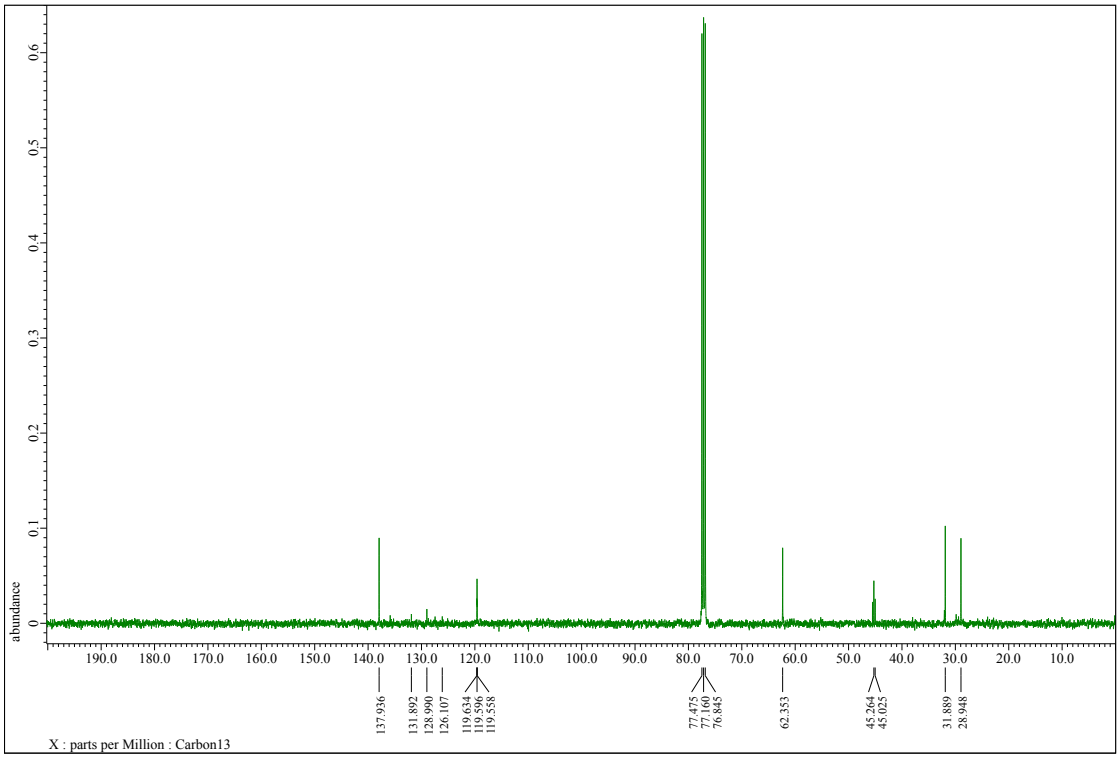

2.96
2.03
1.00
1.00
1.99
2.06
1.97
abundance
X : parts per Million : Proton

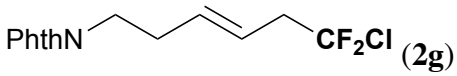

abundance
141.544
137.716
131.873
128.981
128.810
128.580
128.484
126.183
126.059
119.625
77.475
77.360
77.160
76.835
45.531
45.283
45.035
35.507
34.399
X : parts per Million : Carbon13


HO
CF2Cl

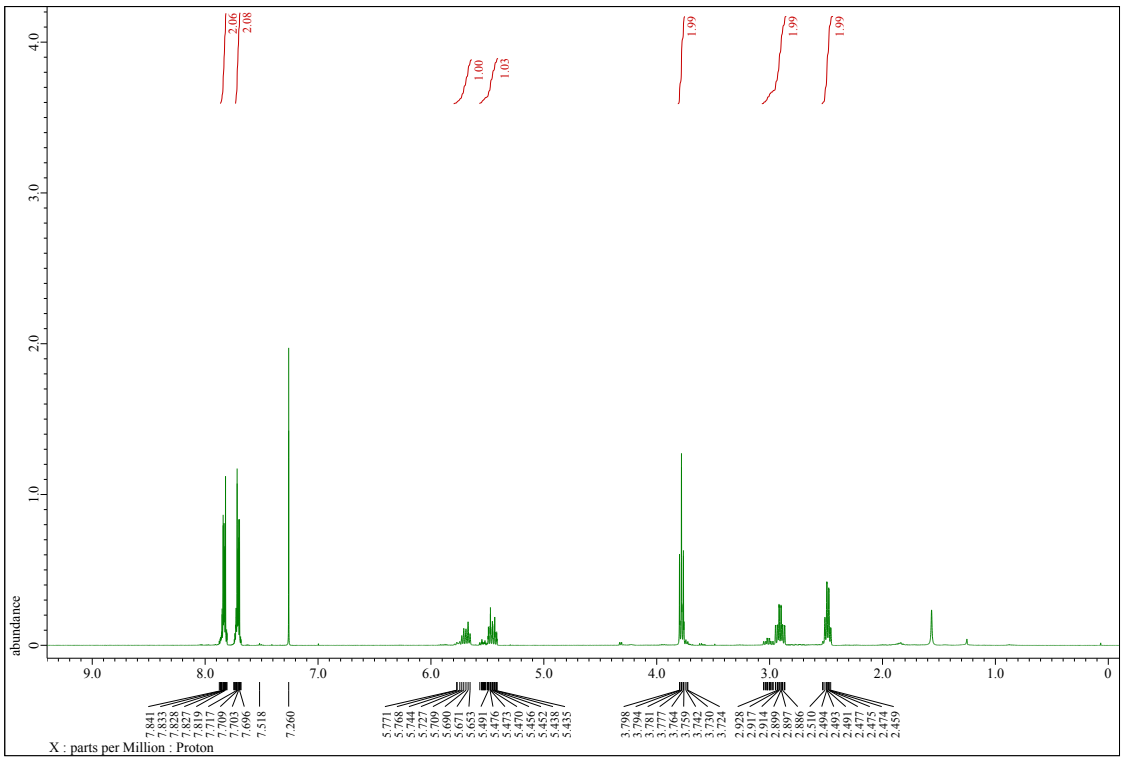
(**2f**)

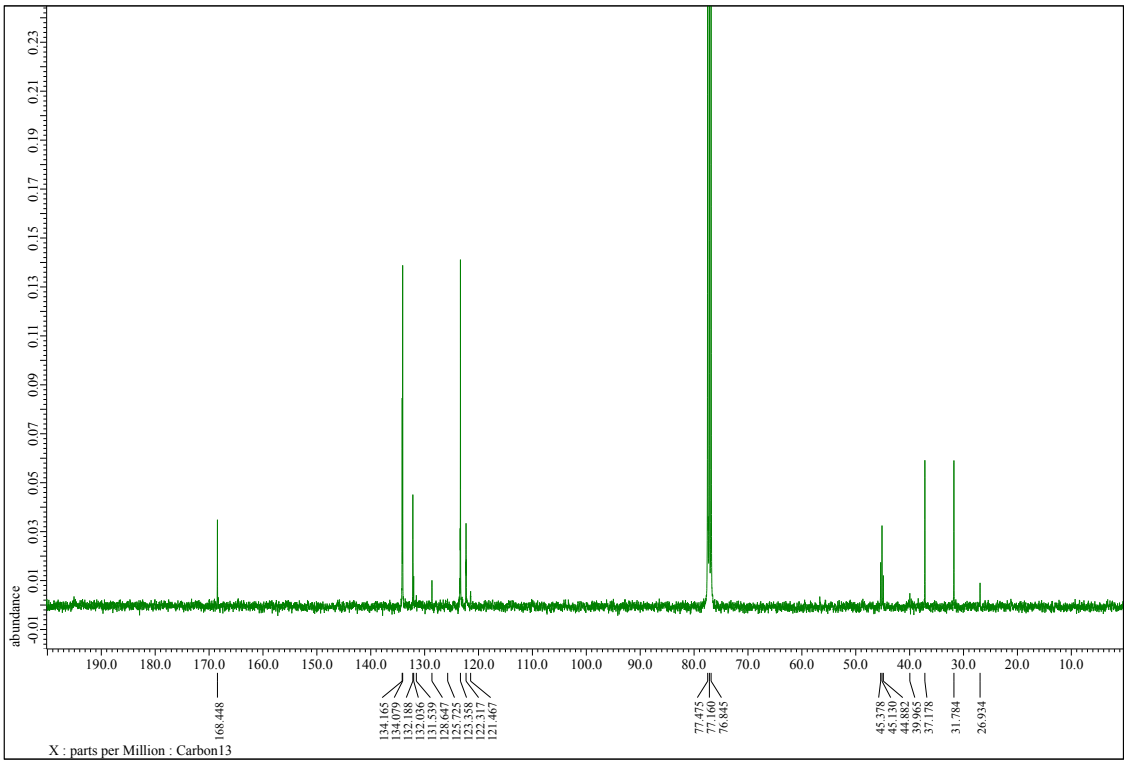

abundance
X : parts per Million : Proton
1.00
1.02
2.03
1.95
1.98
2.03
1.05

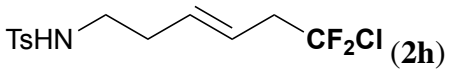

abundance
X : parts per Million : Carbon13


PhthN
CF2Cl

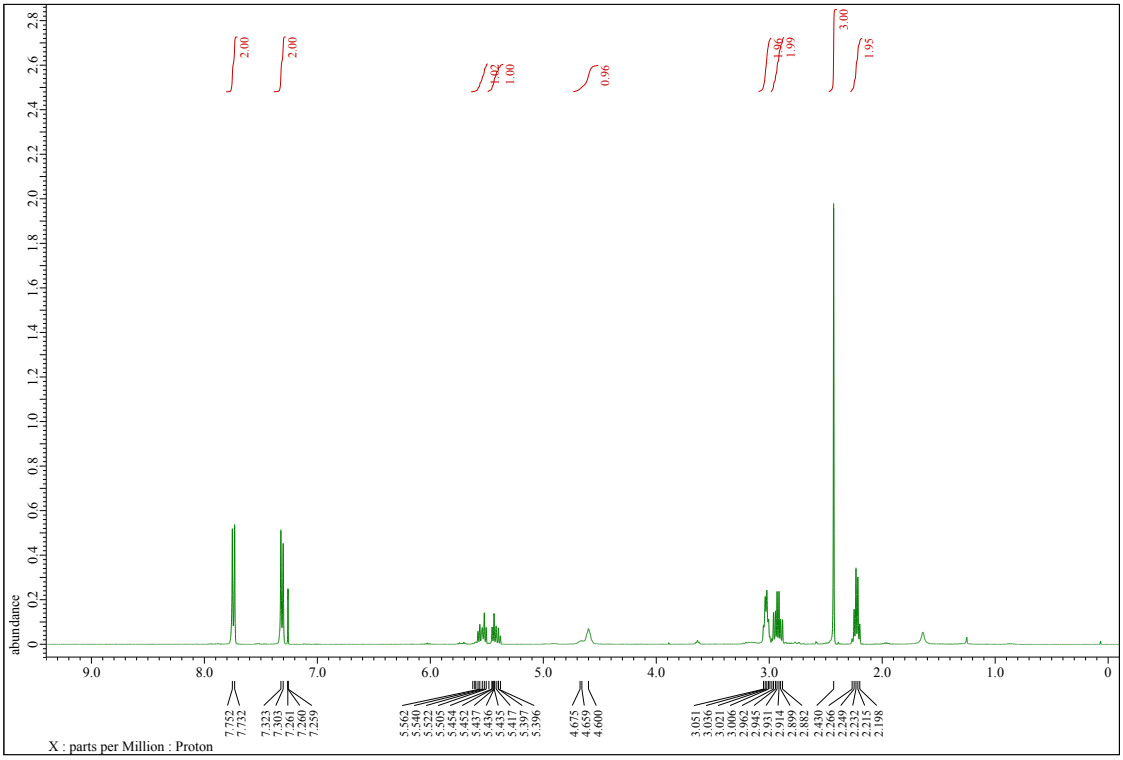
(2g)

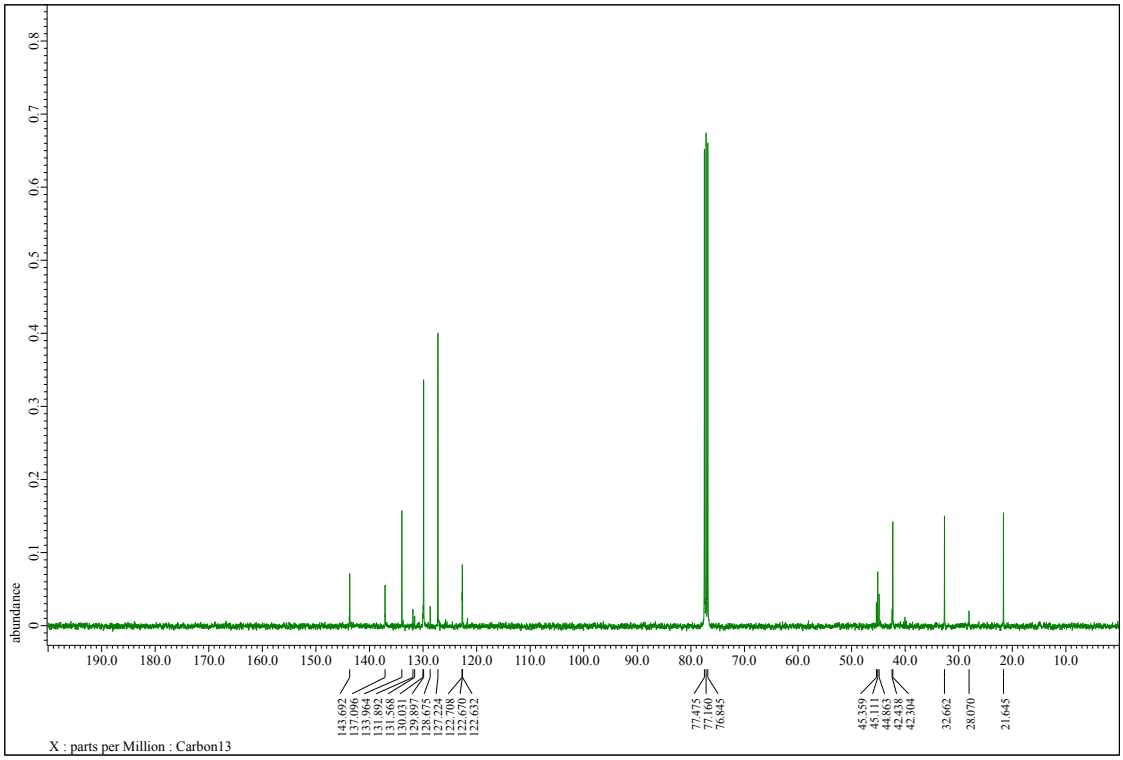

abundance
X : parts per Million : Proton

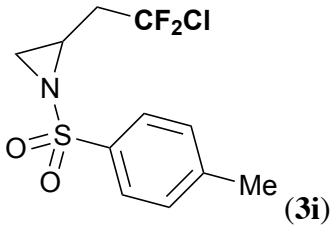

abundance
X : parts per Million : Carbon13


TsHN
CF2Cl

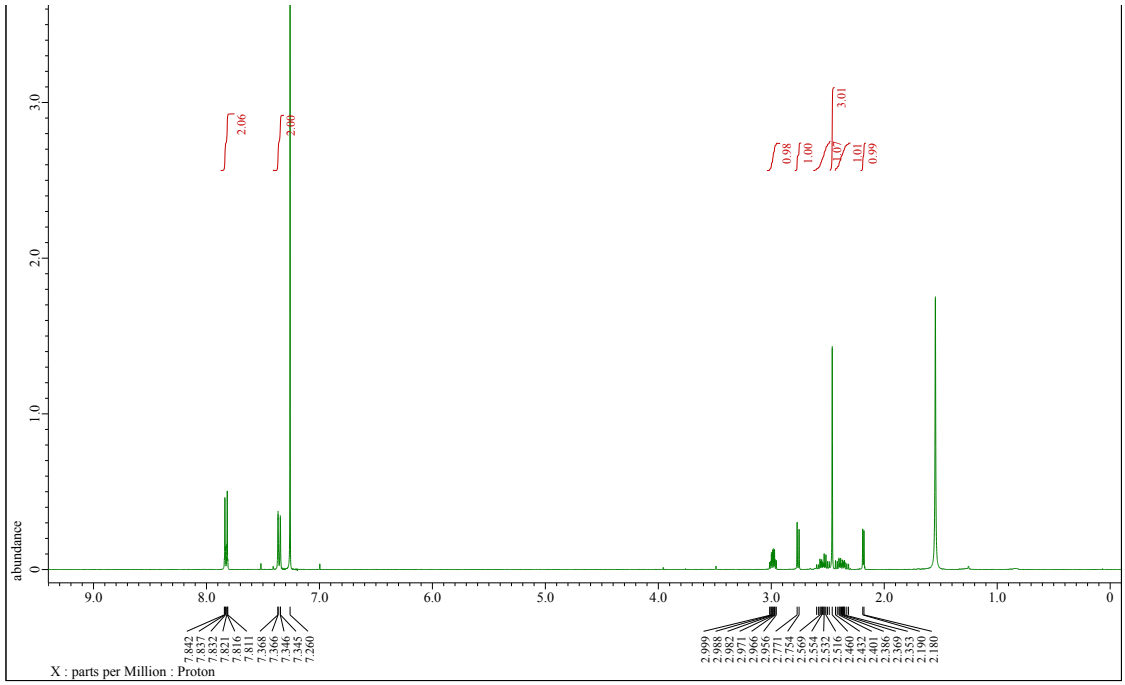
(2h)

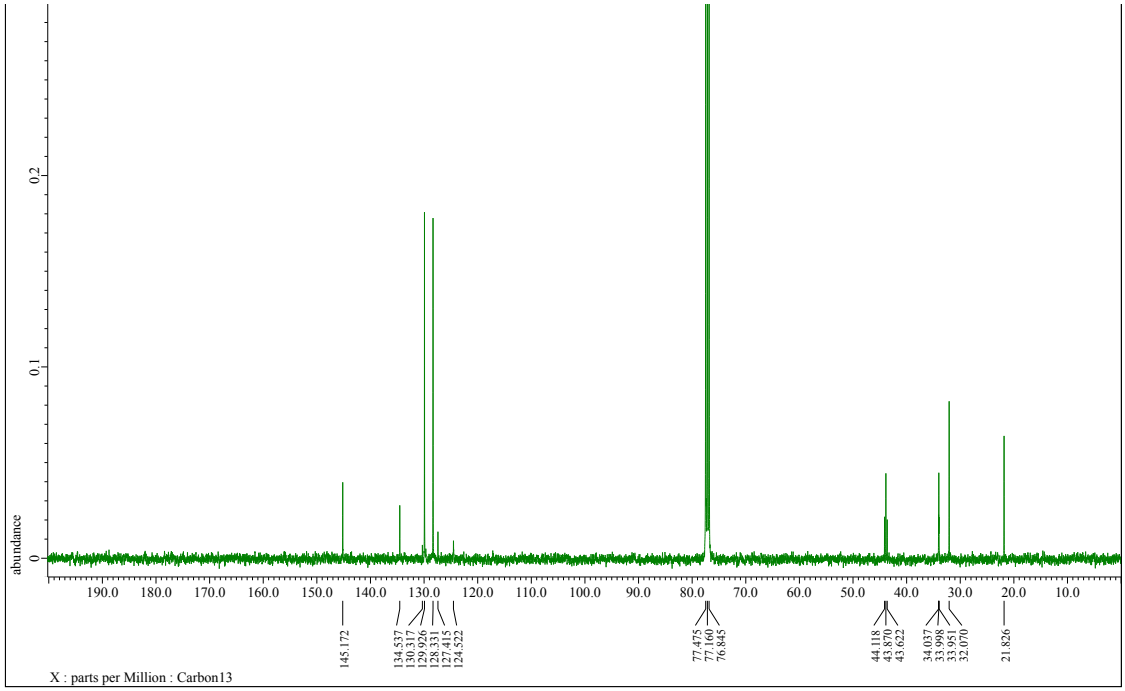

abundance
X : parts per Million : Proton

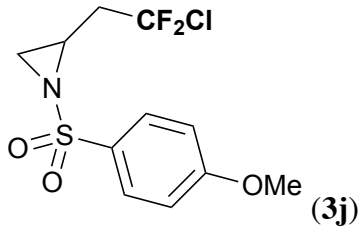

abundance
X : parts per Million : Carbon13


CF2Cl
N
O
S
O
Me

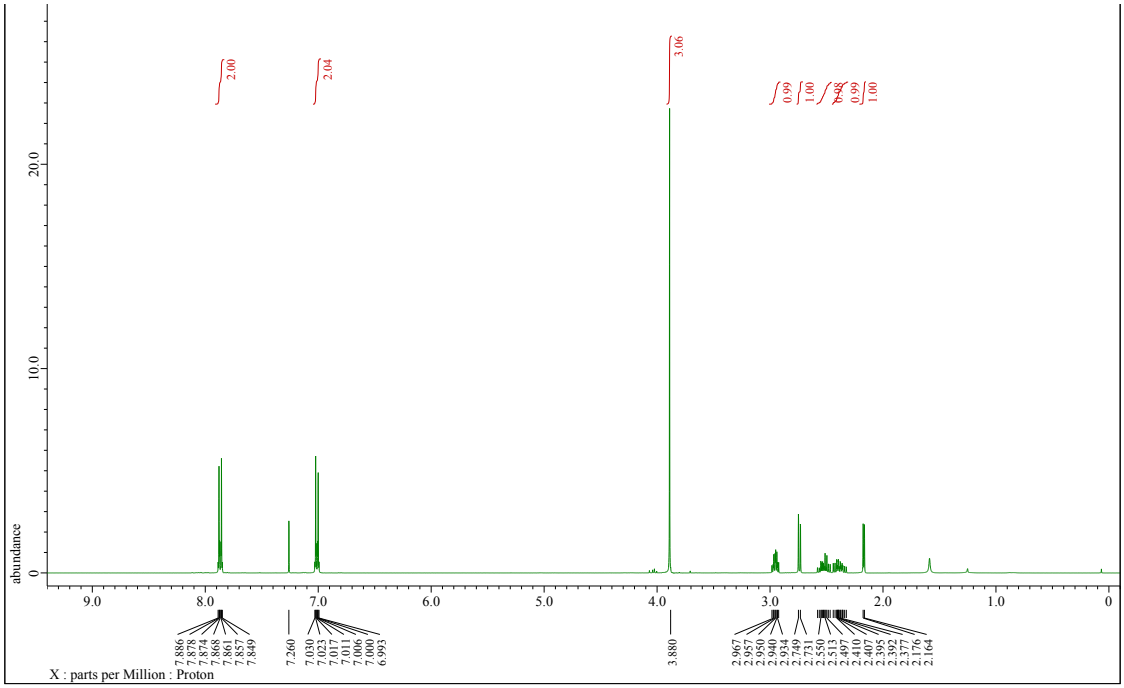
(**3i**)

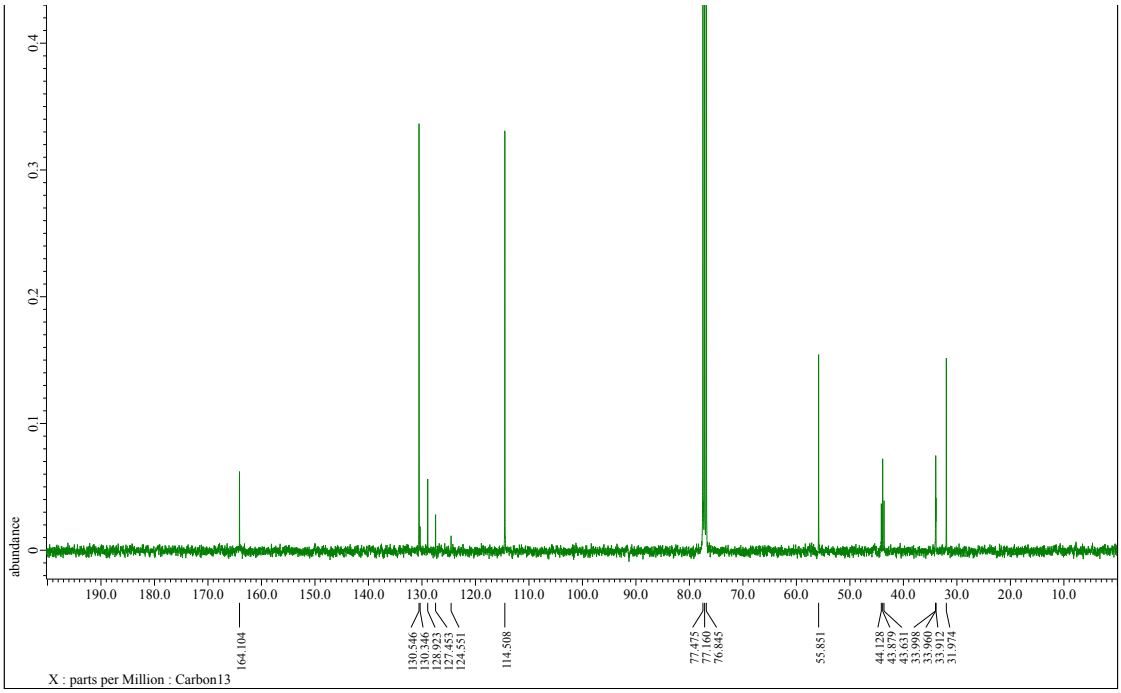

abundance
X : parts per Million : Proton

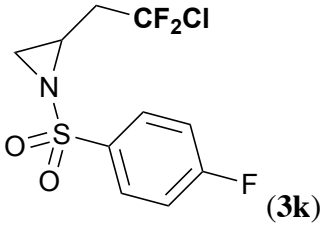

abundance
X : parts per Million : Carbon13


CF2Cl
N
O
S
O
OMe

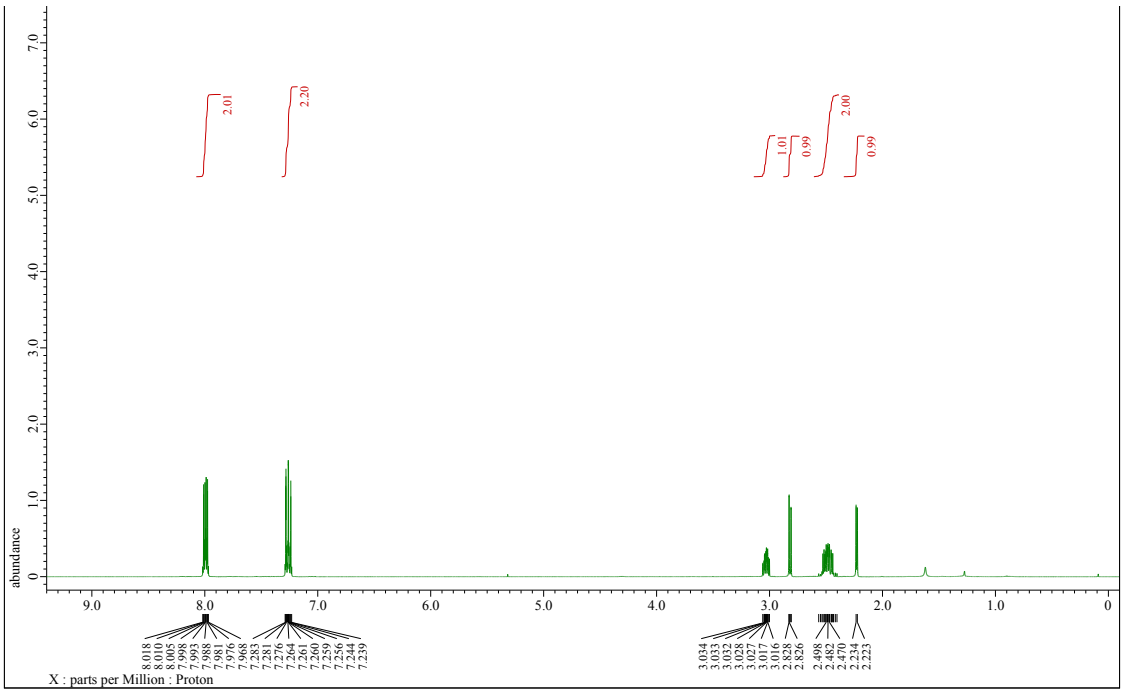
(**3j**)

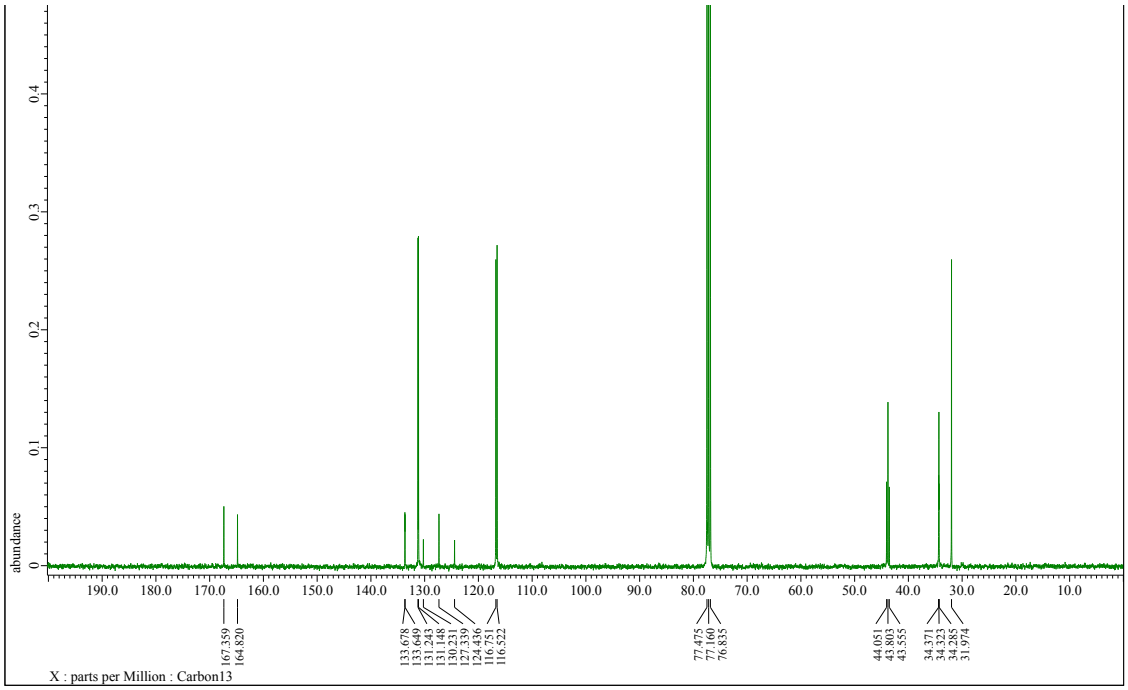

2.00
2.04
3.06
0.99
1.00
0.99
1.00
abundance
X : parts per Million : Proton

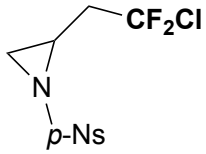

abundance
164.104
130.546
130.346
128.923
127.453
124.551
114.508
77.475
77.160
76.845
55.851
44.128
43.879
43.631
33.960
33.912
31.974
X : parts per Million : Carbon13


CF2Cl
N
O
S
O
F

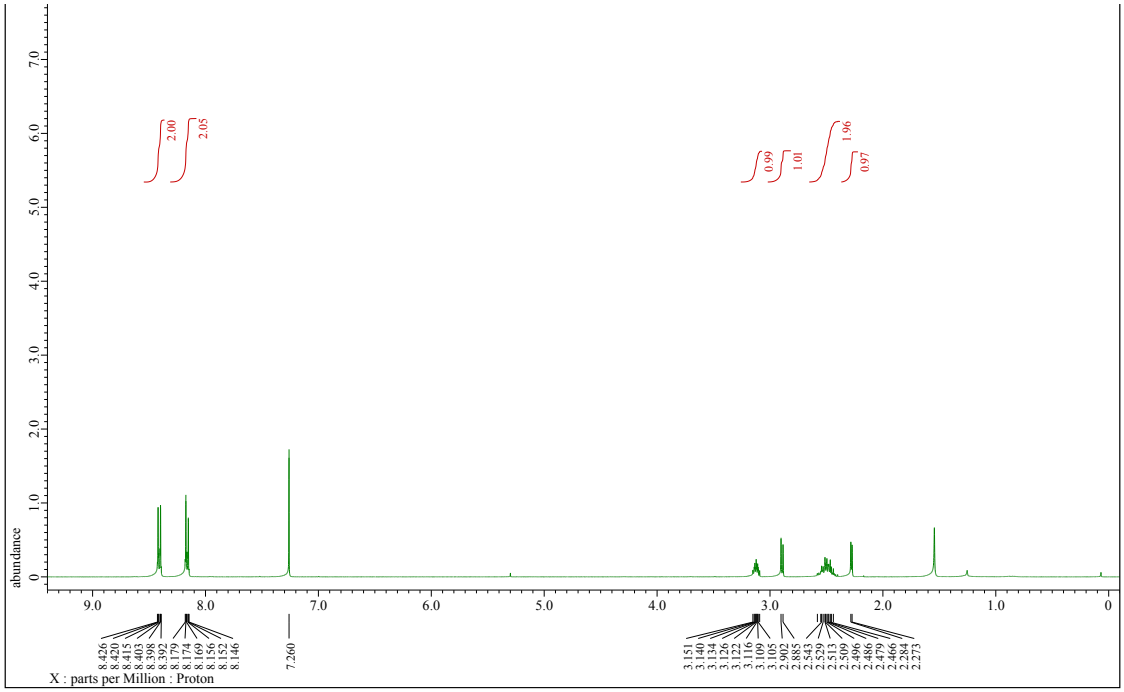
(**3k**)

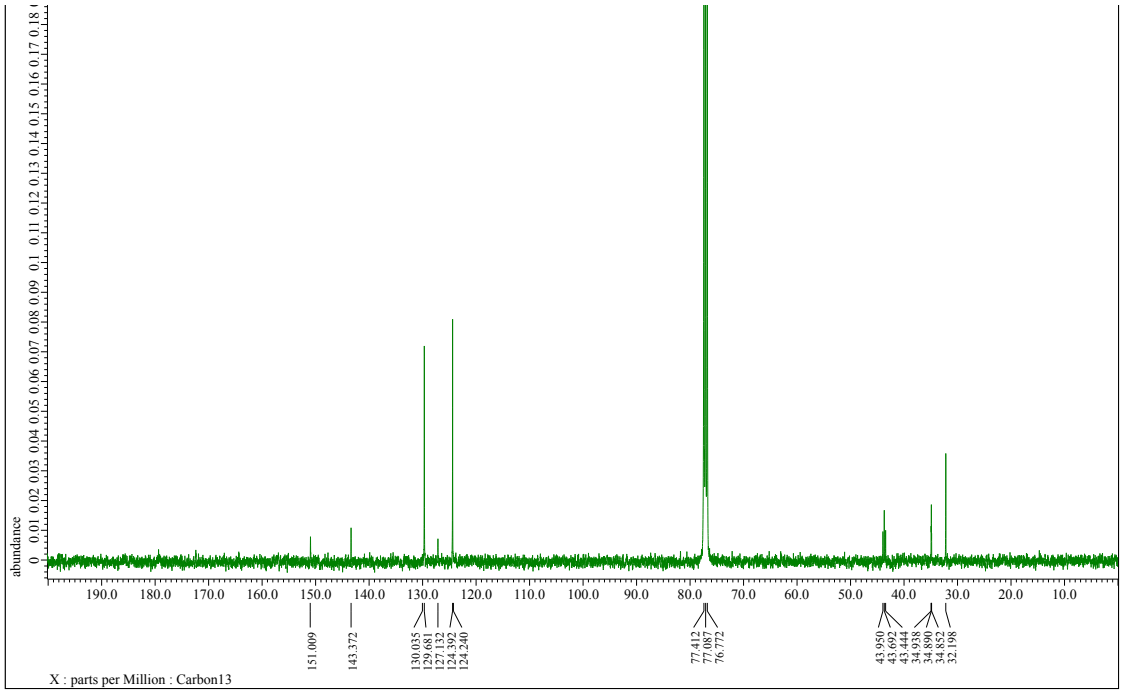

abundance
X : parts per Million : Proton
2.01
2.20
1.01
0.99
2.00
0.99

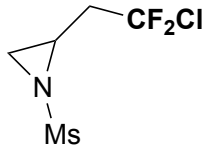

abundance
X : parts per Million : Carbon13


CF2Cl
N
p-Ns

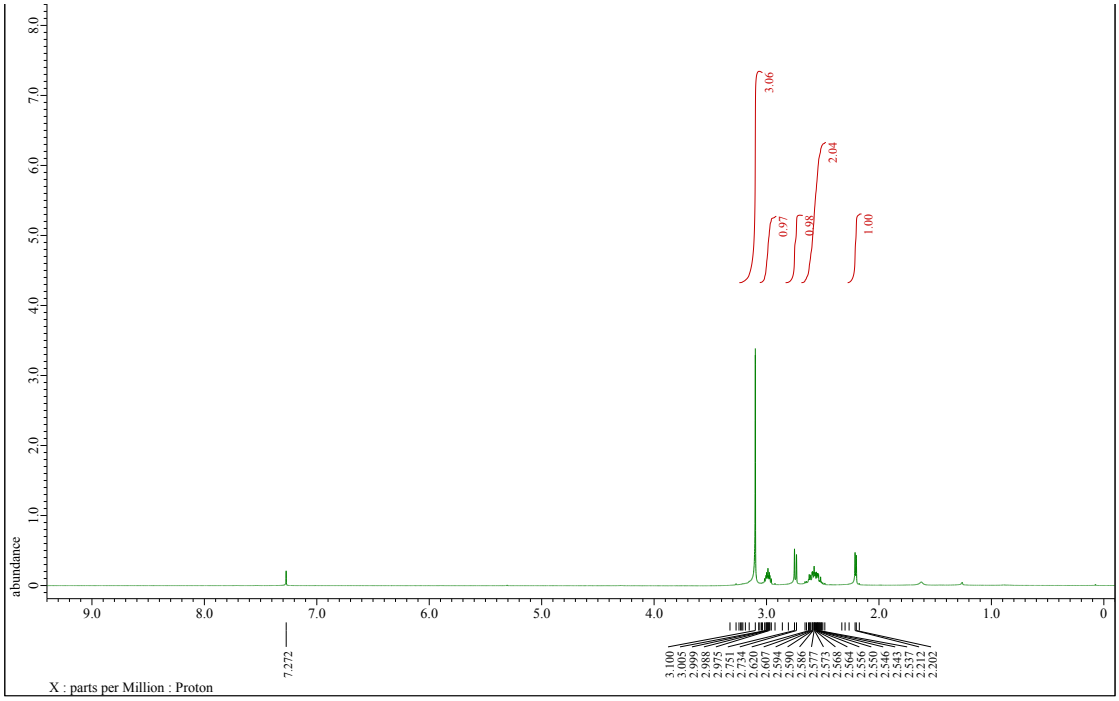
(**3l**)

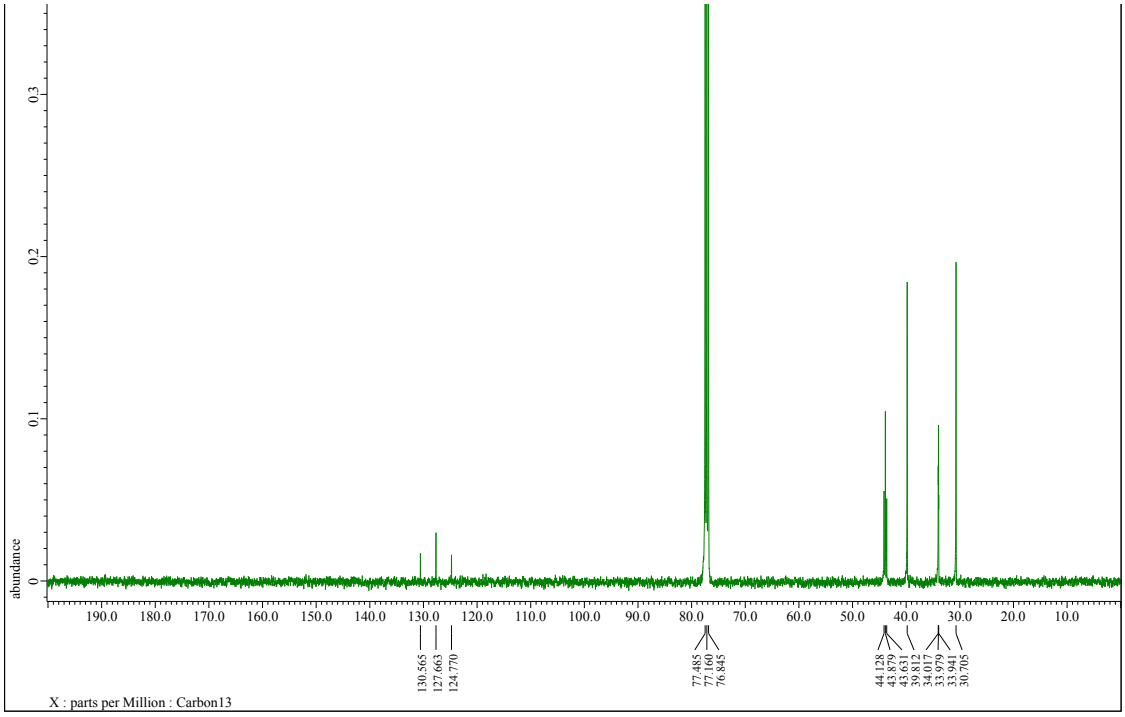

abundance
2.00
2.05
0.99
1.01
1.96
0.97
8.436
8.420
8.415
8.403
8.398
8.392
8.179
8.174
8.160
8.156
8.152
8.146
7.260
3.151
3.140
3.134
3.126
3.122
3.116
3.109
3.105
2.902
2.885
2.543
2.529
2.513
2.499
2.486
2.479
2.466
2.284
2.273
X : parts per Million : Proton

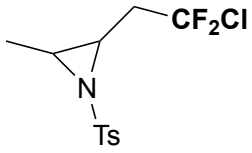

abundance
151.009
143.372
130.035
129.681
127.132
124.392
124.240
77.412
77.095
76.772
43.950
43.692
43.444
43.198
34.890
34.852
32.198
X : parts per Million : Carbon13


CF2Cl
N
Ms

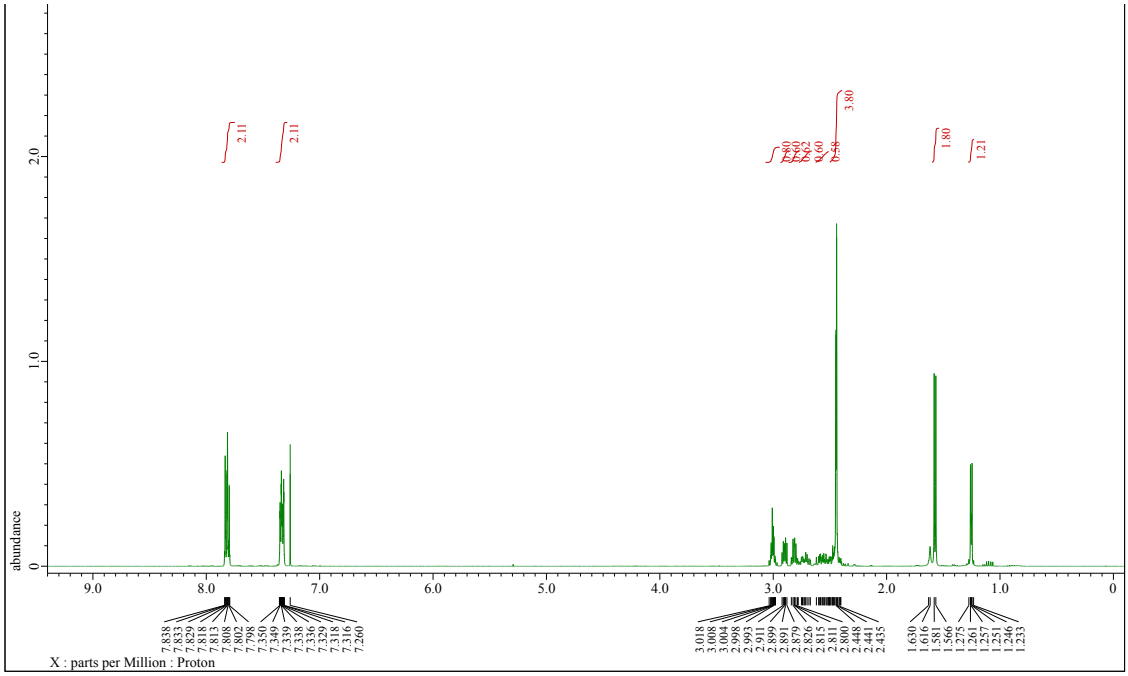
(**3m**)

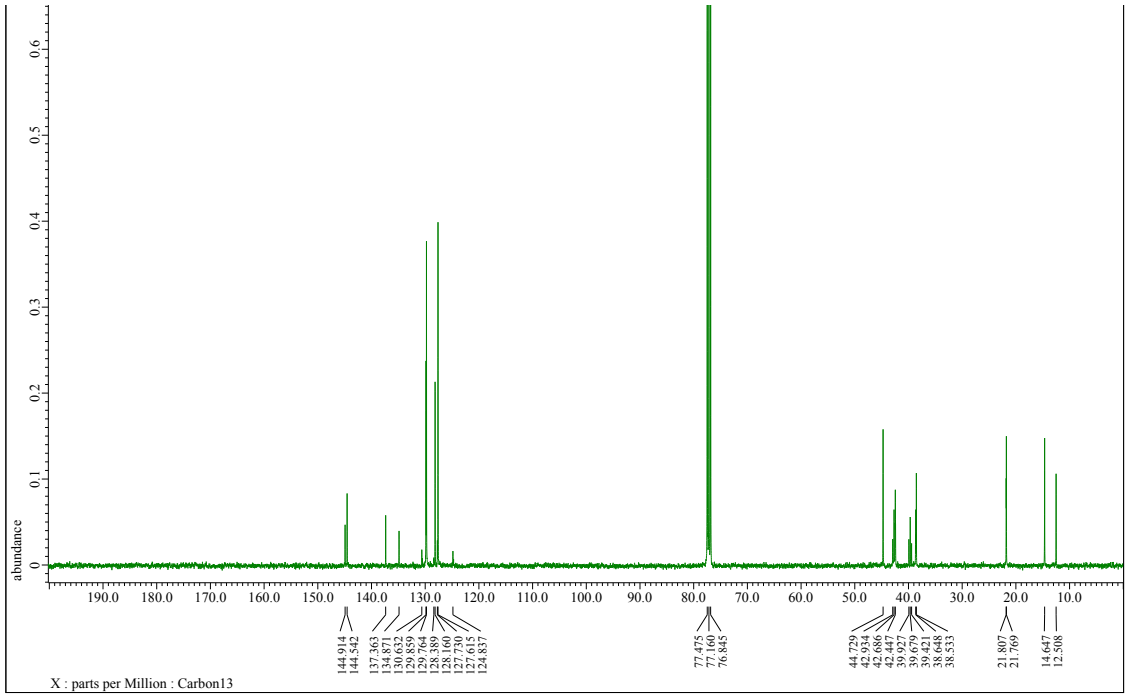

abundance
3.06
2.04
0.97
0.98
1.00
7.272
X : parts per Million : Proton

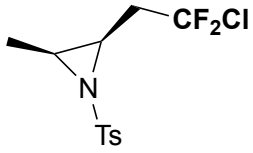

abundance
130.565
127.663
124.770
77.485
77.160
76.845
44.128
43.879
43.631
39.812
34.410
33.970
33.941
30.705
X : parts per Million : Carbon13



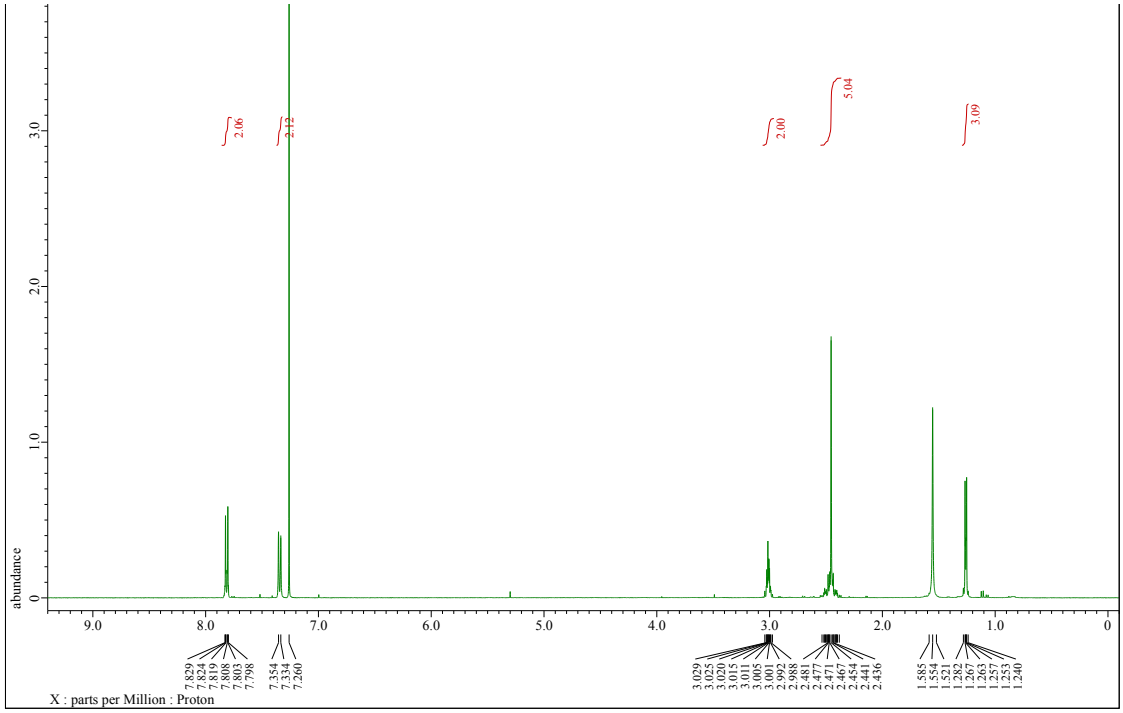
(**3n**; diastereomixture)

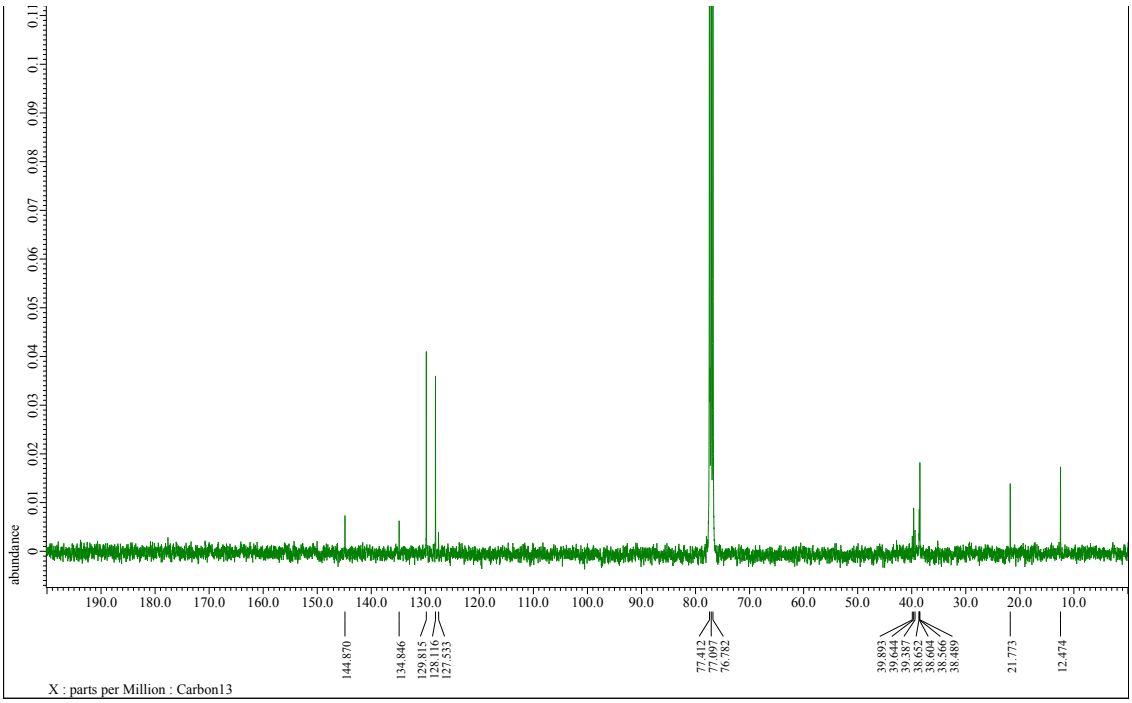


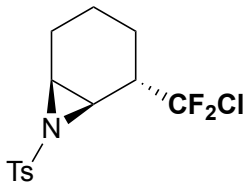



CF2Cl
N
Ts

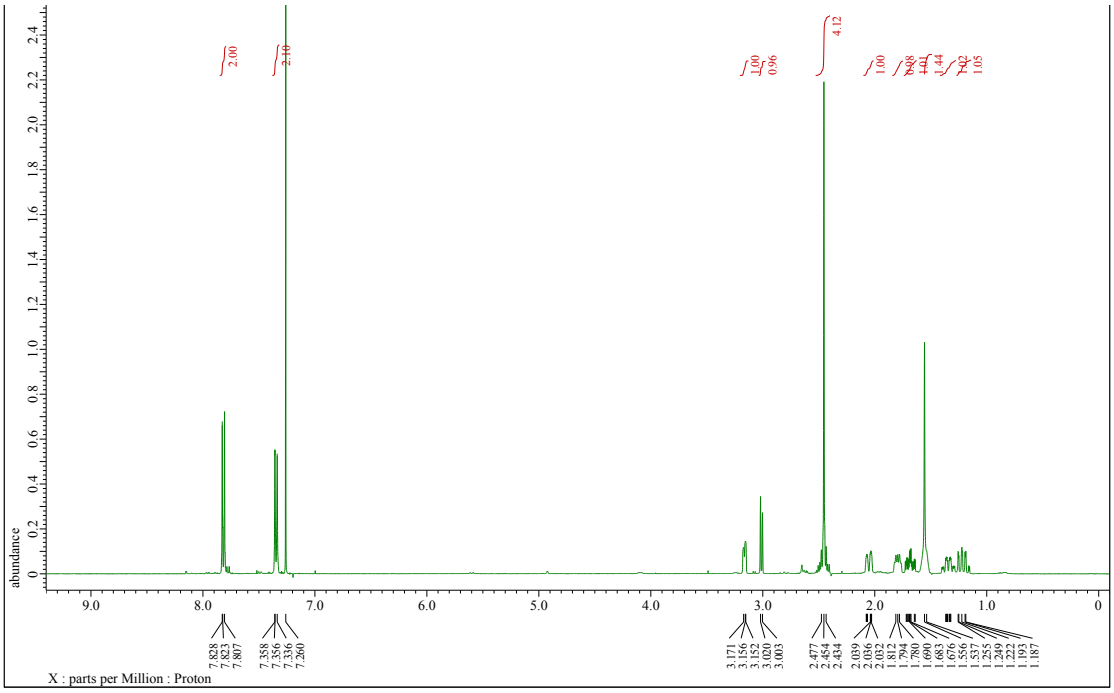
(*cis*-**3n**)

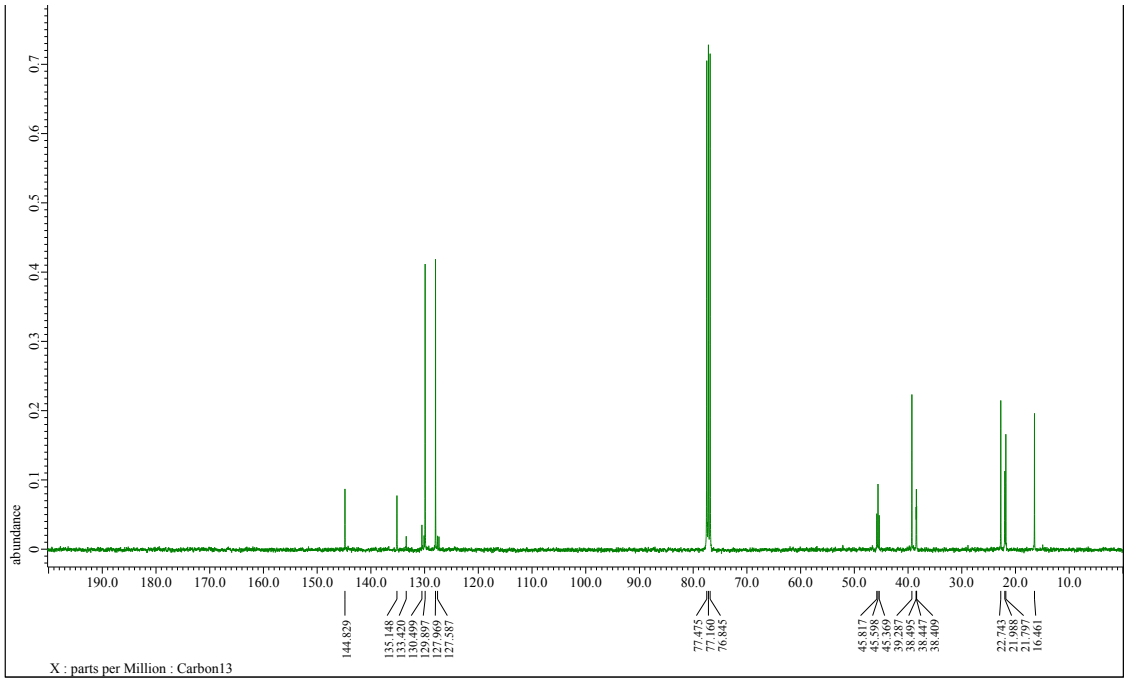

abundance
2.06
2.12
2.00
5.04
3.09
7.829
7.824
7.819
7.808
7.803
7.798
7.354
7.334
7.260
3.029
3.025
3.020
3.015
3.011
3.005
3.001
2.992
2.988
2.481
2.477
2.471
2.467
2.454
2.441
2.436
1.585
1.554
1.521
1.282
1.267
1.263
1.257
1.253
1.240
X : parts per Million : Proton

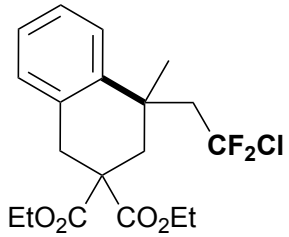

abundance
144.870
134.846
129.815
128.116
127.533
77.412
77.097
76.782
39.893
39.644
39.387
38.652
38.604
38.566
38.489
21.773
12.474
X : parts per Million : Carbon13


CF2Cl
N
Ts

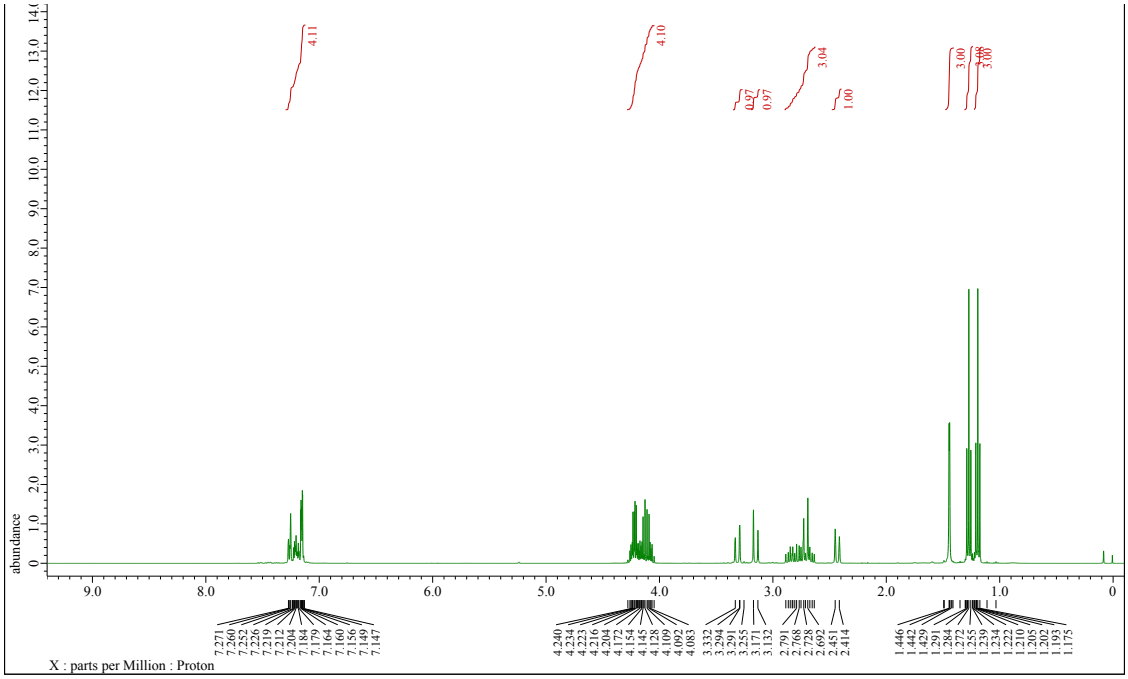
(**3o**)

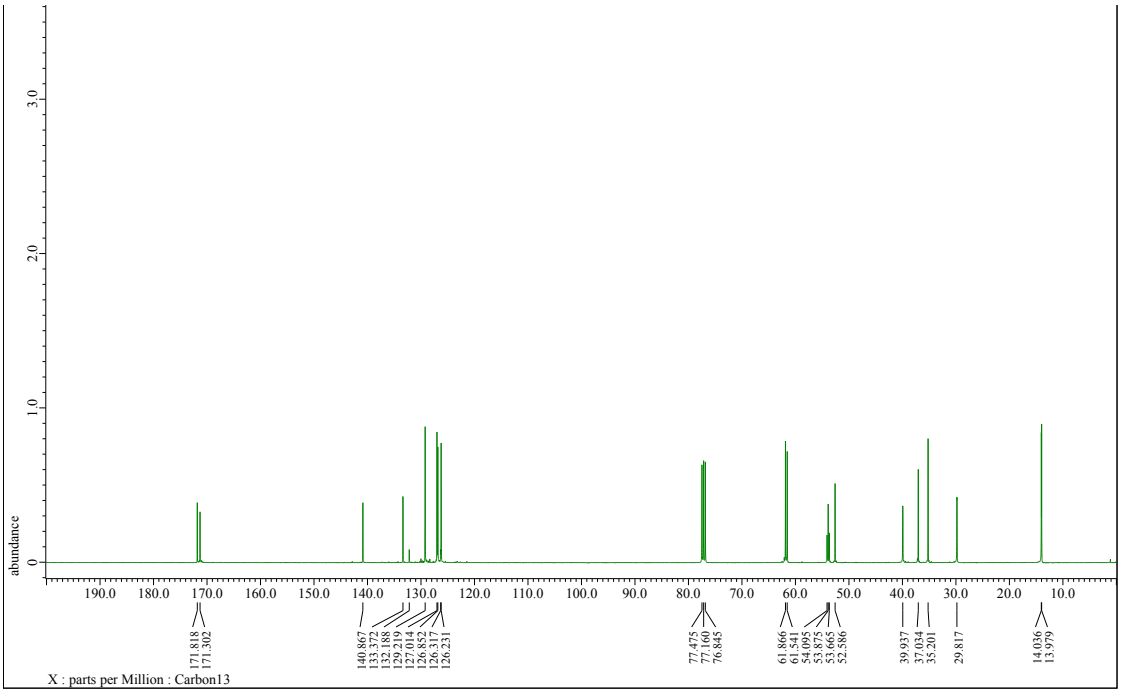

abundance
X : parts per Million : Proton

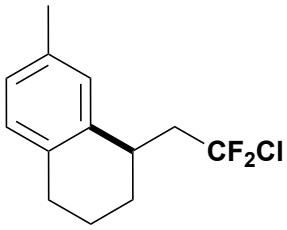

abundance
X : parts per Million : Carbon13


CF2Cl
EtO2C
CO2Et

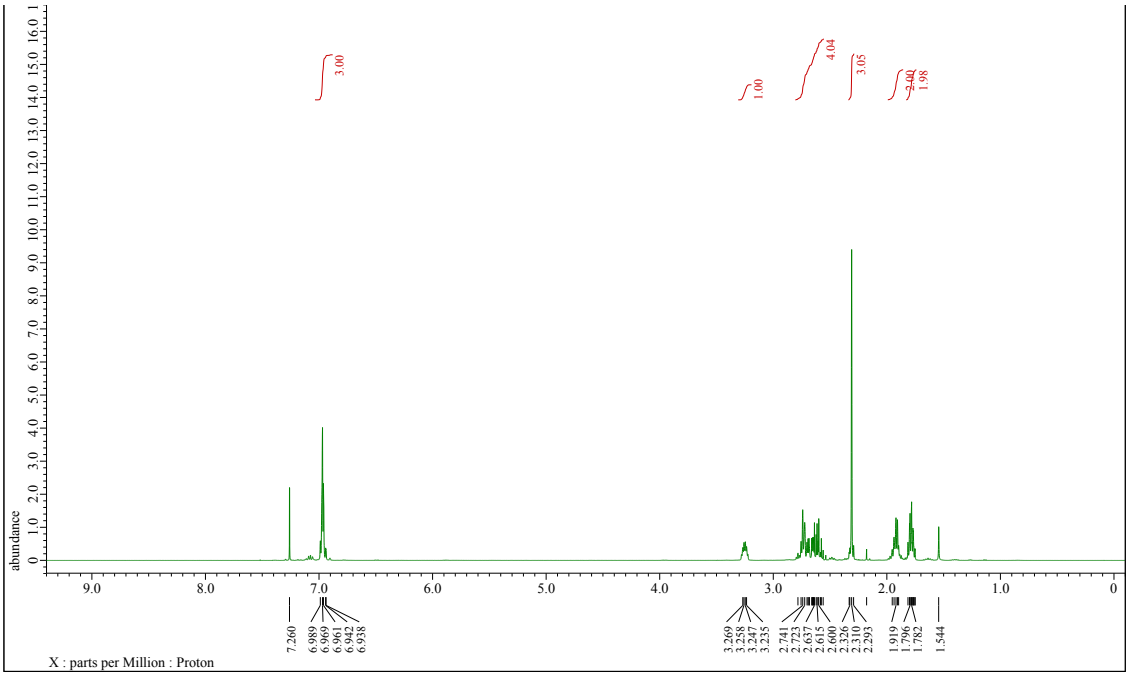
(**4p**)

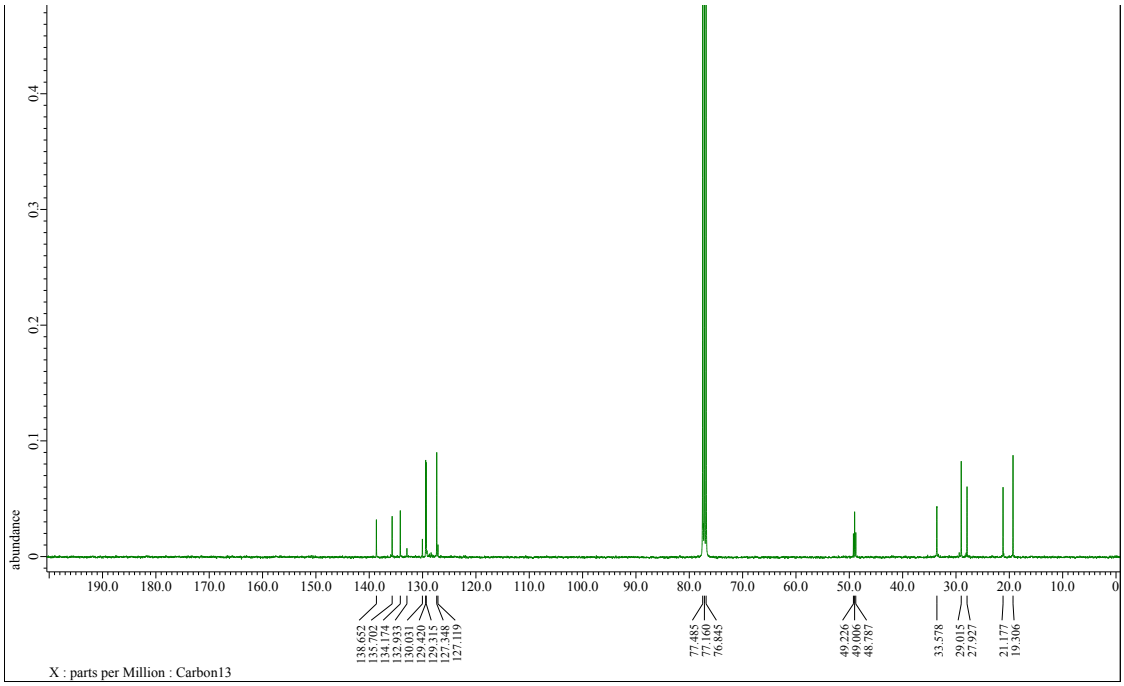

4.11
4.10
0.97
0.97
3.04
1.00
3.00
3.00
3.00
abundance
X : parts per Million : Proton

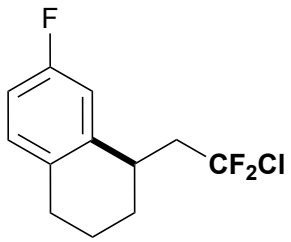

abundance
X : parts per Million : Carbon13


CF2Cl

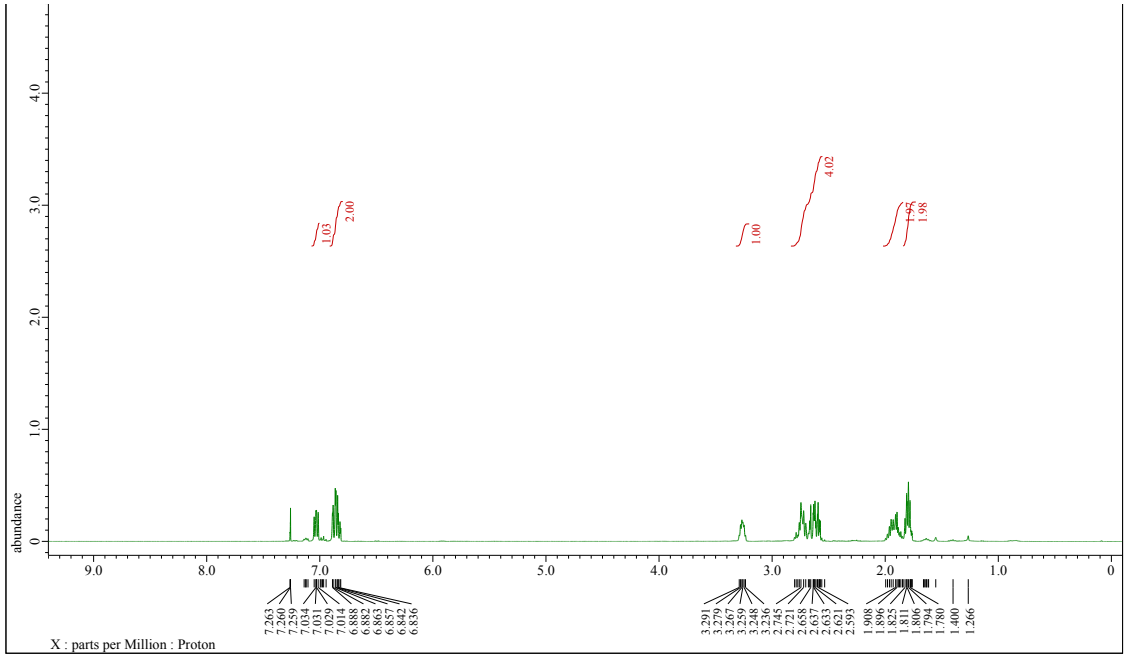
(**4q**)

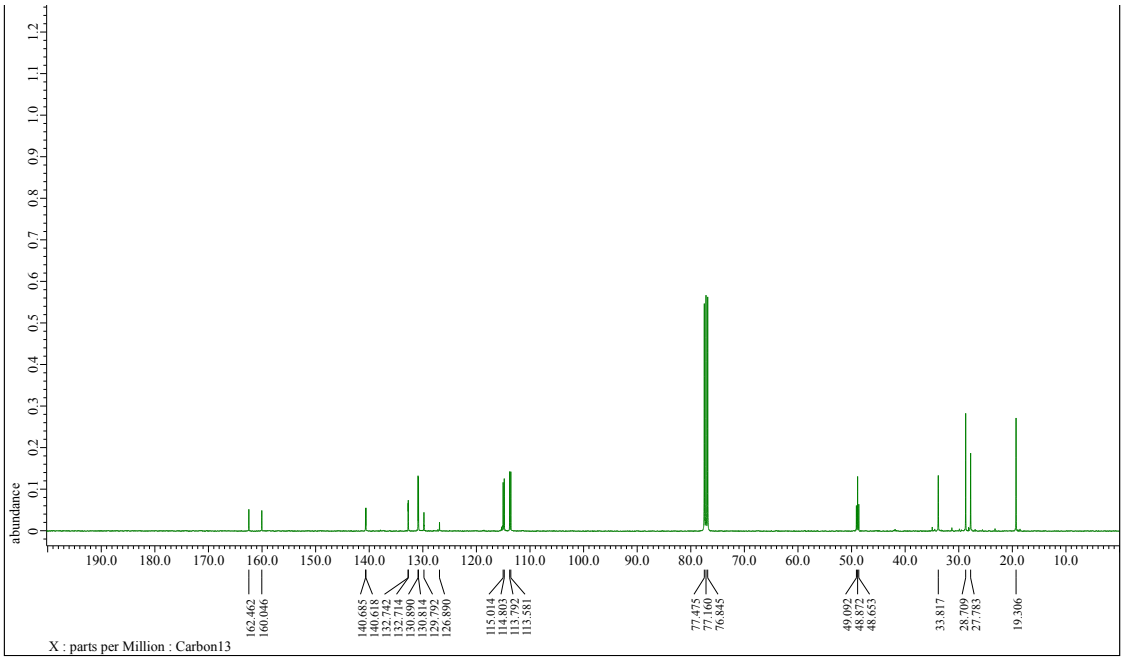

abundance
X : parts per Million : Proton

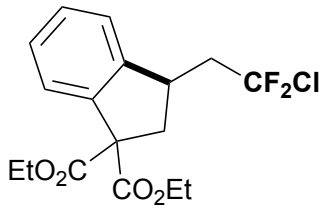

abundance
X : parts per Million : Carbon13


F
CF2Cl

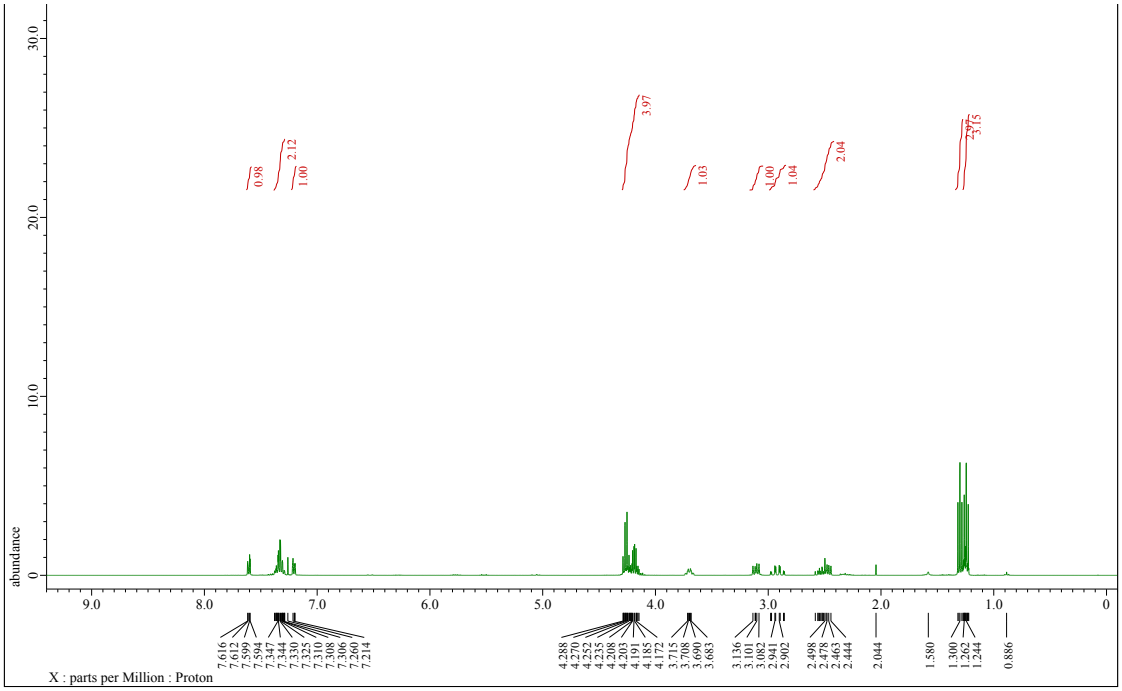
(**4r**)

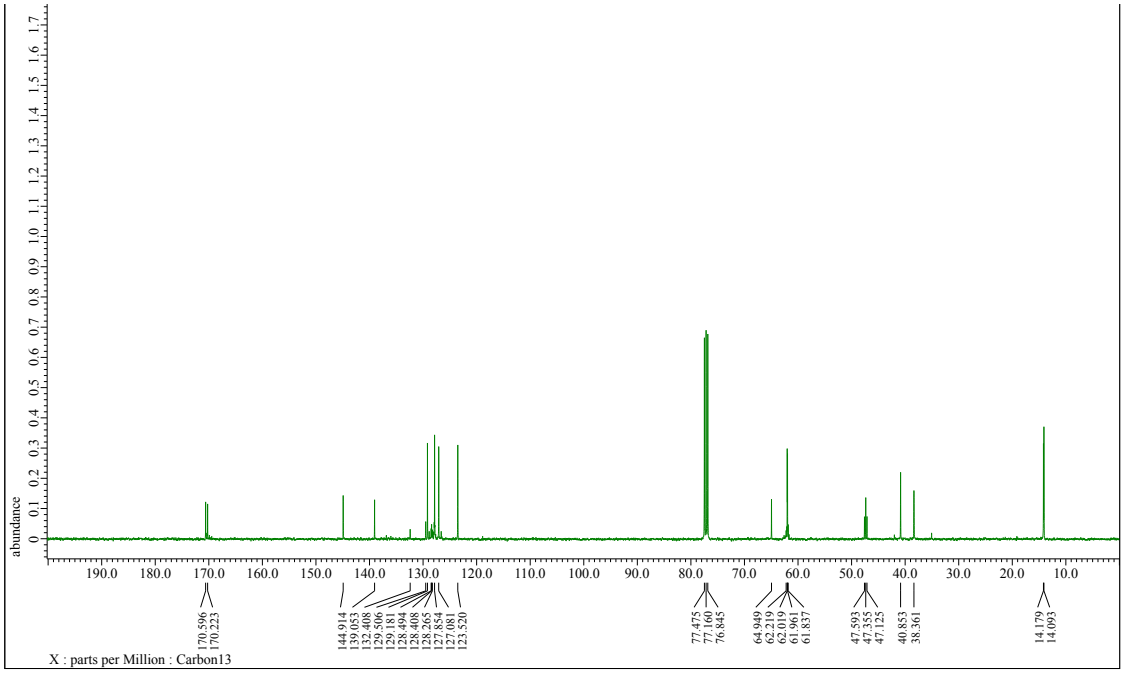

abundance
X : parts per Million : Proton
1.03
2.00
1.00
4.02
1.95
1.98

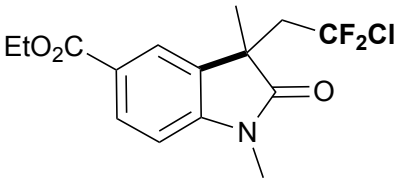

abundance
X : parts per Million : Carbon13


CF2Cl
EtO2C
CO2Et

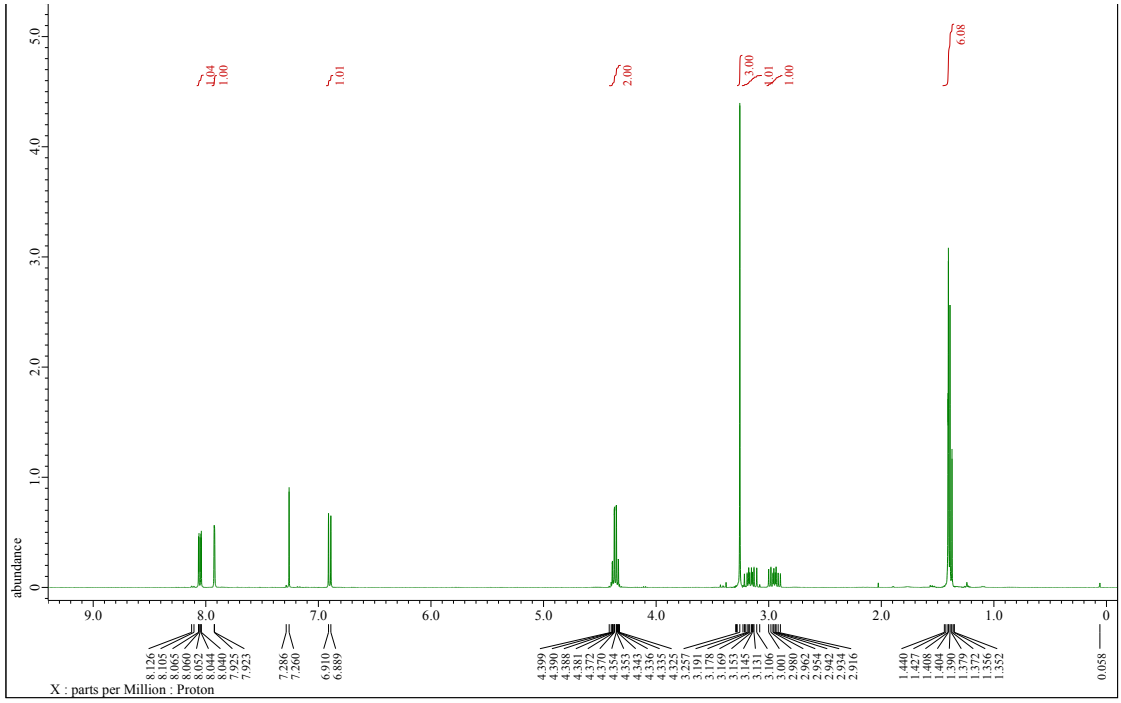
(**4s**)

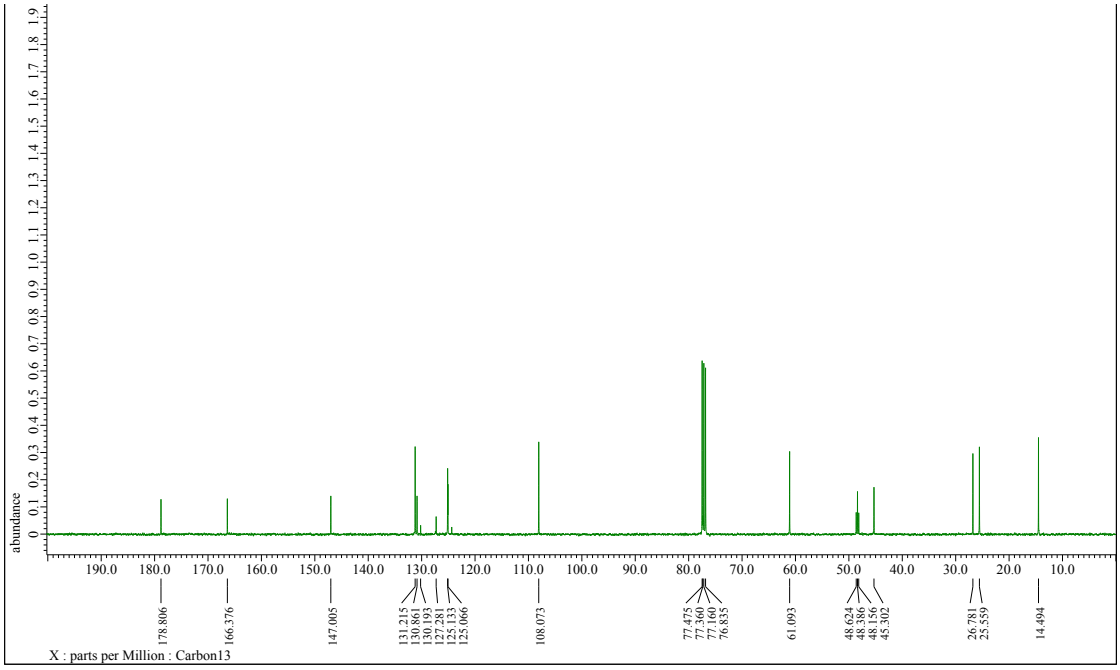

abundance
X : parts per Million : Proton

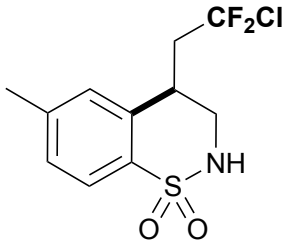

abundance
X : parts per Million : Carbon13


EtO2C
CF2Cl
O
N

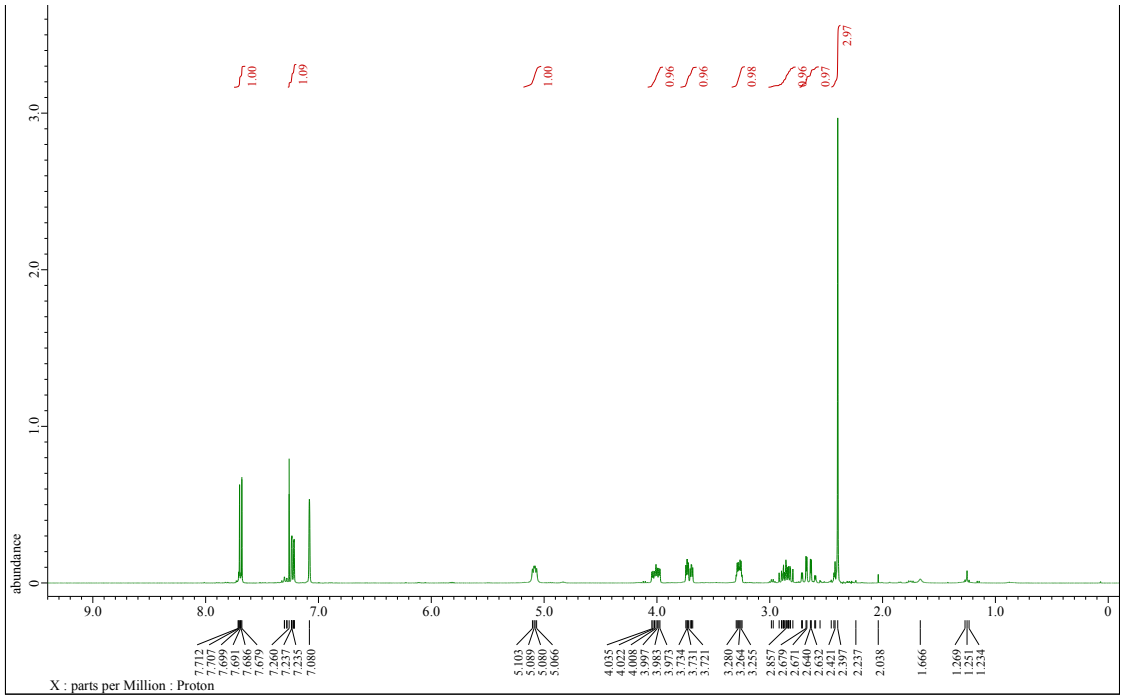
(**4t**)

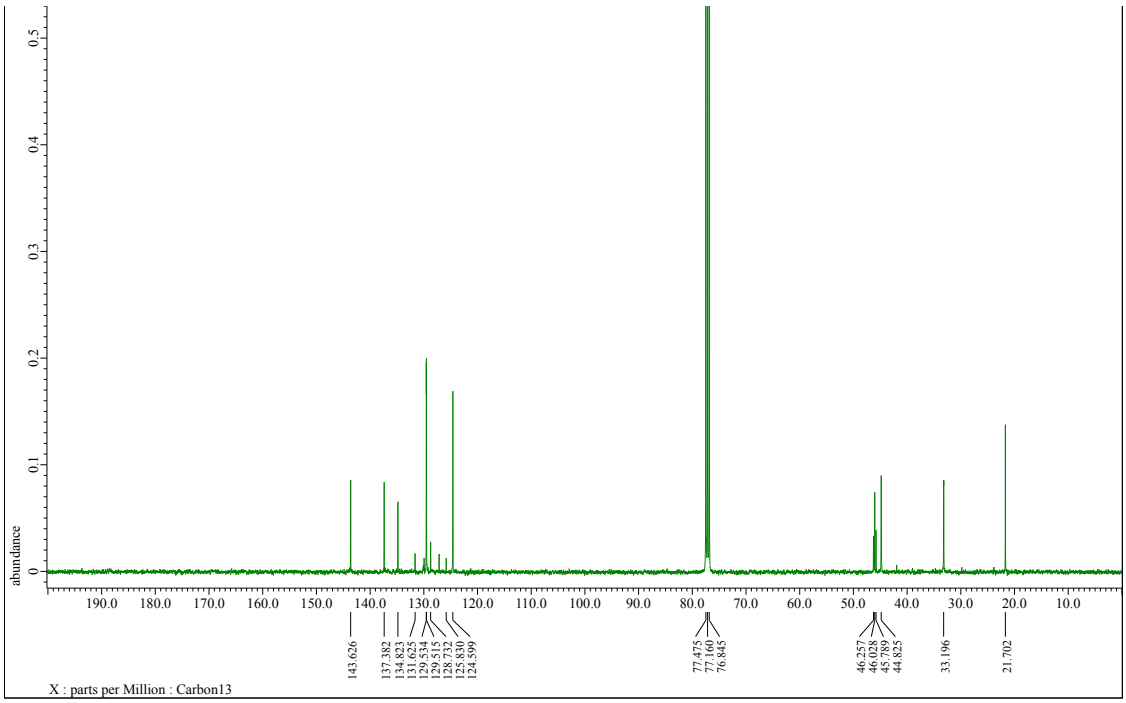

abundance
X : parts per Million : Proton

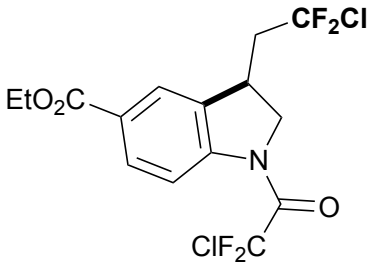

abundance
X : parts per Million : Carbon13


CF2Cl
NH
S
O
O

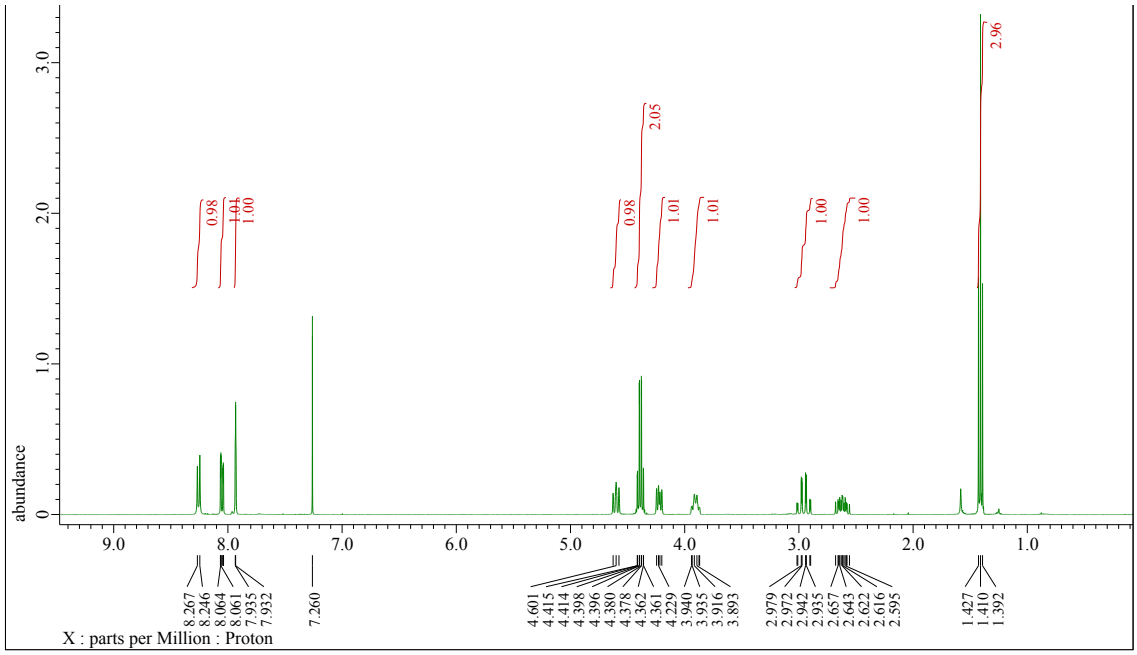
(**4i**)

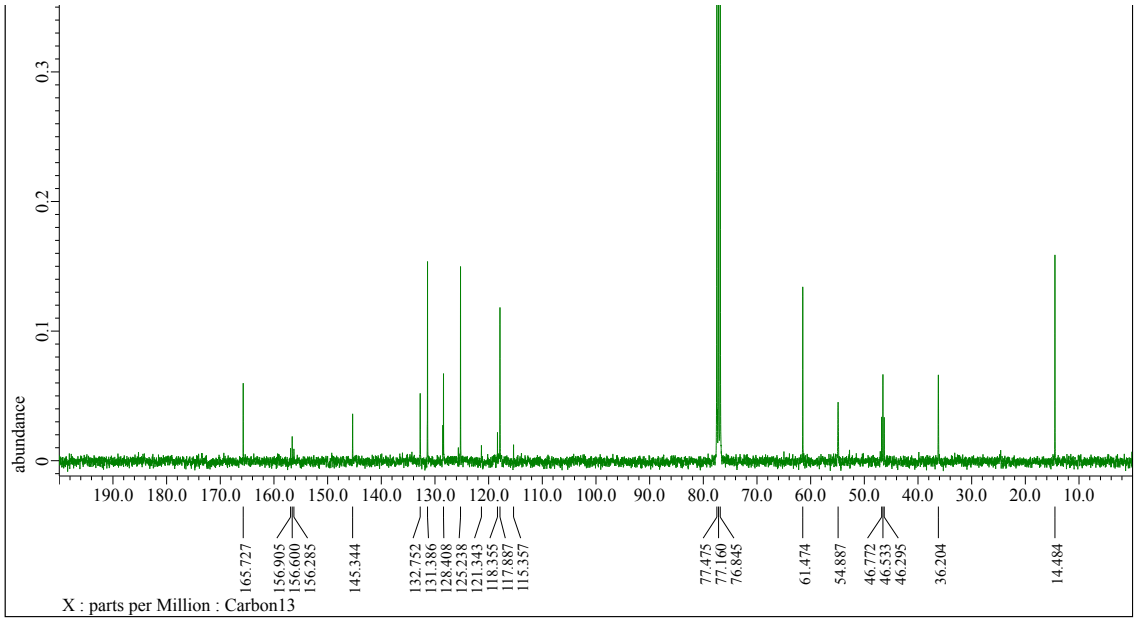

abundance
X : parts per Million : Proton

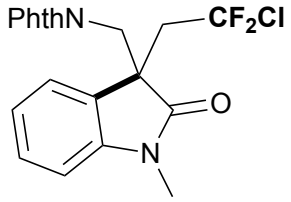

abundance
X : parts per Million : Carbon13


CF2Cl
EtO2C
N
O
ClF2C

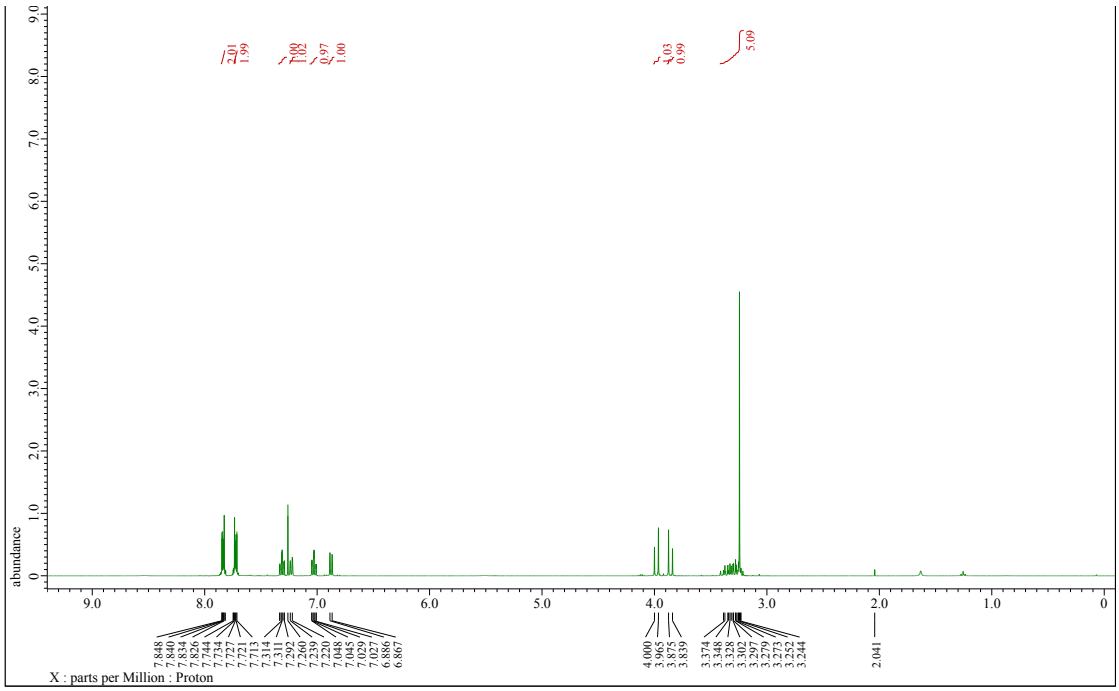
(**4u**)

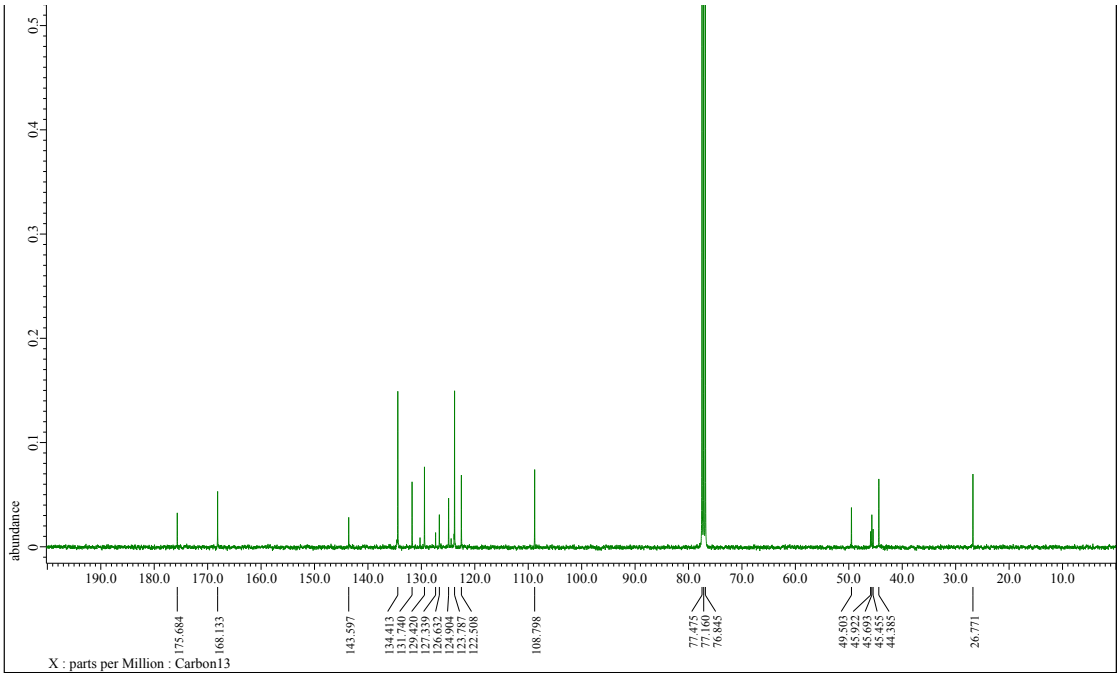

abundance
X : parts per Million : Proton
8.267
8.246
8.064
8.061
7.935
7.932
7.260
4.601
4.415
4.414
4.398
4.396
4.380
4.378
4.362
4.361
4.229
3.940
3.935
3.916
3.893
2.979
2.972
2.942
2.935
2.657
2.643
2.622
2.616
2.595
1.427
1.410
1.392

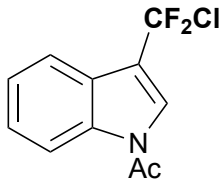

abundance
X : parts per Million : Carbon13
165.727
156.905
156.600
156.285
145.344
132.752
131.386
128.408
125.238
121.343
118.355
117.887
115.357
77.475
77.160
76.845
61.474
54.887
46.772
46.533
46.295
36.204
14.484


PhthN
CF2Cl
O
N

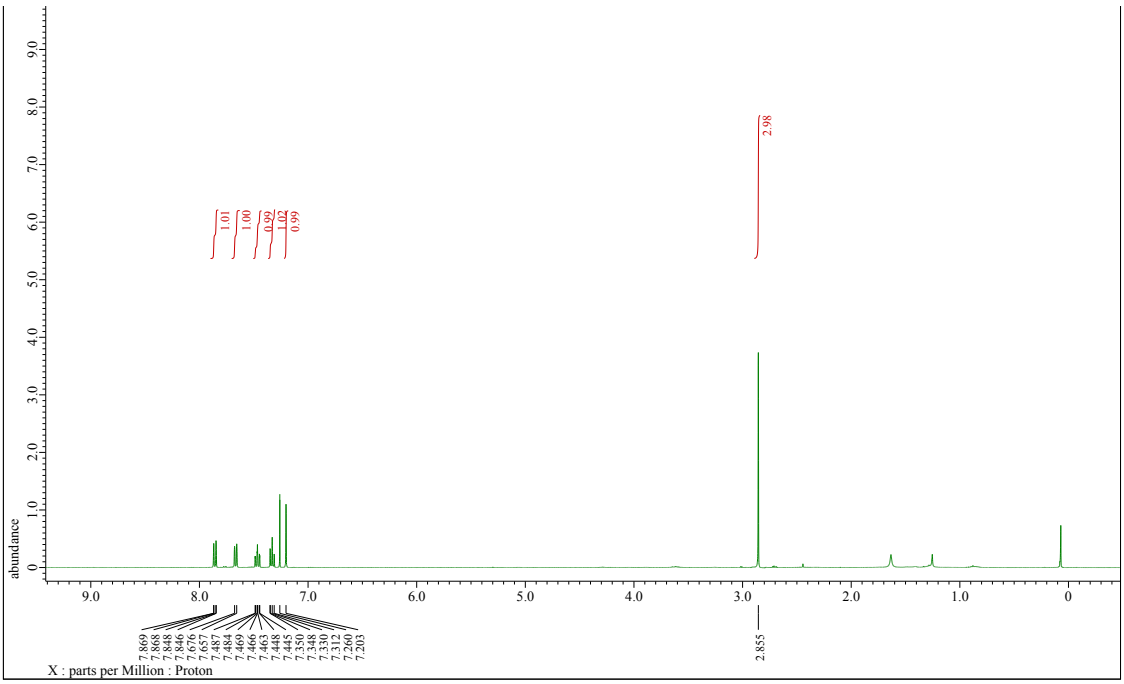
(**4v**)

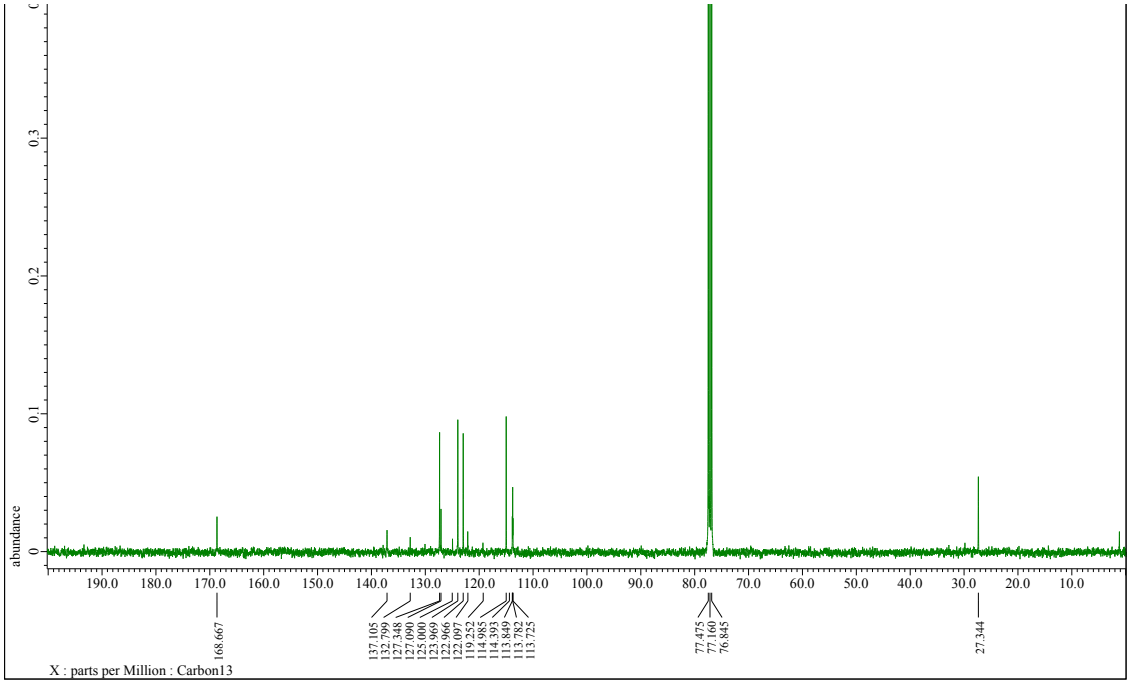

abundance
X : parts per Million : Proton

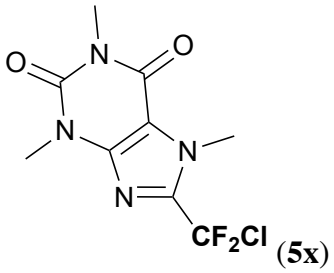

abundance
X : parts per Million : Carbon13


CF2Cl
N
Ac

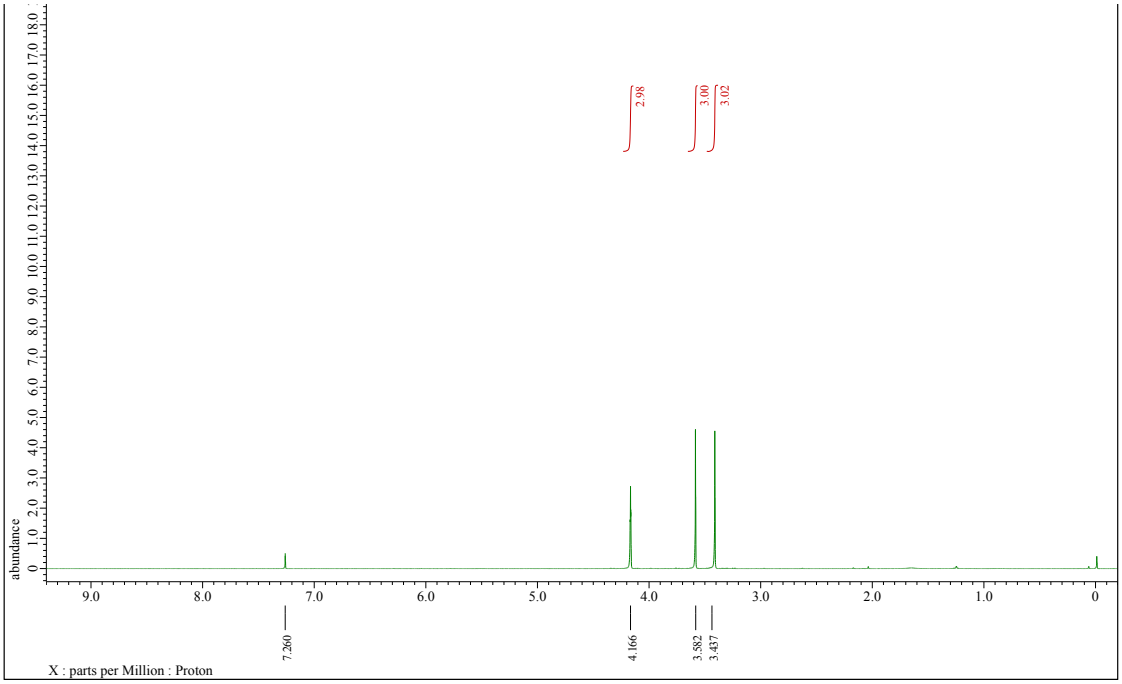
(5w)

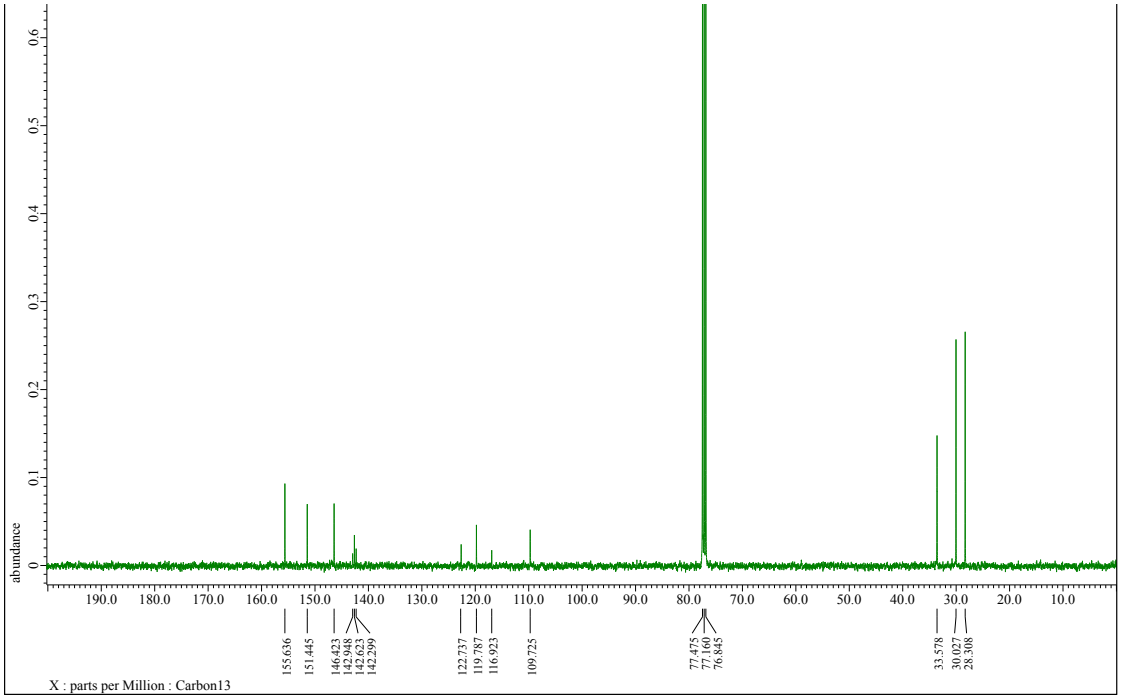

abundance
1.01
1.00
0.92
1.02
0.99
2.98
7.869
7.868
7.848
7.846
7.676
7.657
7.487
7.484
7.469
7.466
7.463
7.448
7.446
7.350
7.348
7.330
7.312
7.260
7.203
2.855
X : parts per Million : Proton

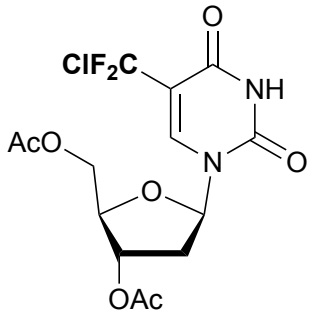

abundance
168.667
137.105
132.799
127.348
127.090
125.000
123.969
122.966
122.097
119.252
114.985
114.393
113.849
113.782
113.725
77.475
77.160
76.845
27.344
X : parts per Million : Carbon13


O
N
O
N
N
N
CF2Cl

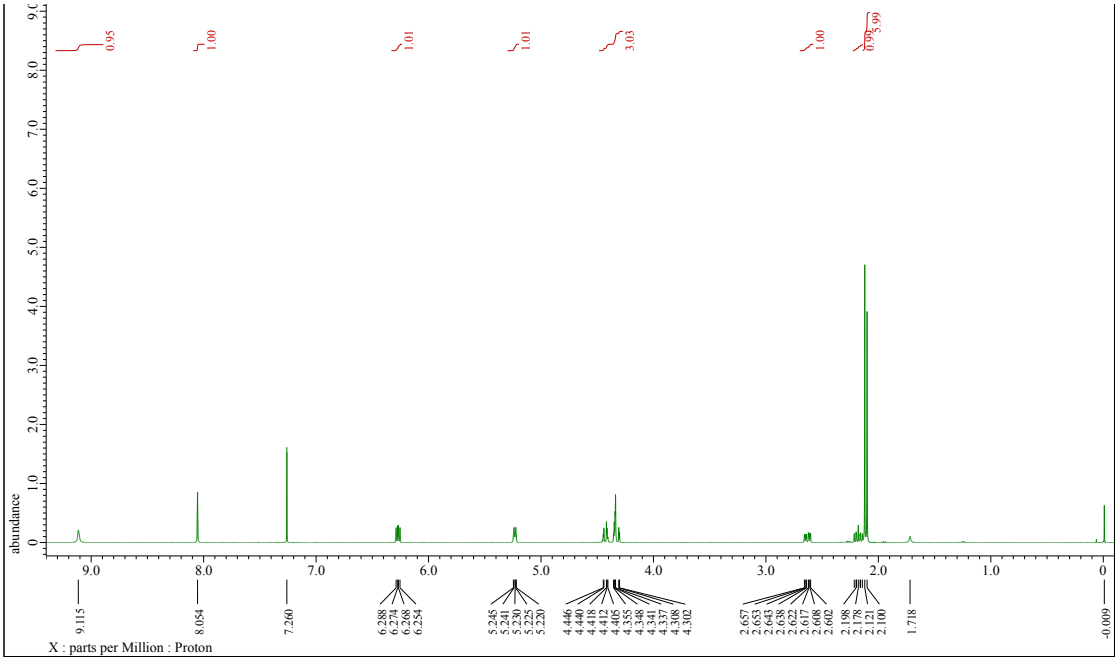
(5x)

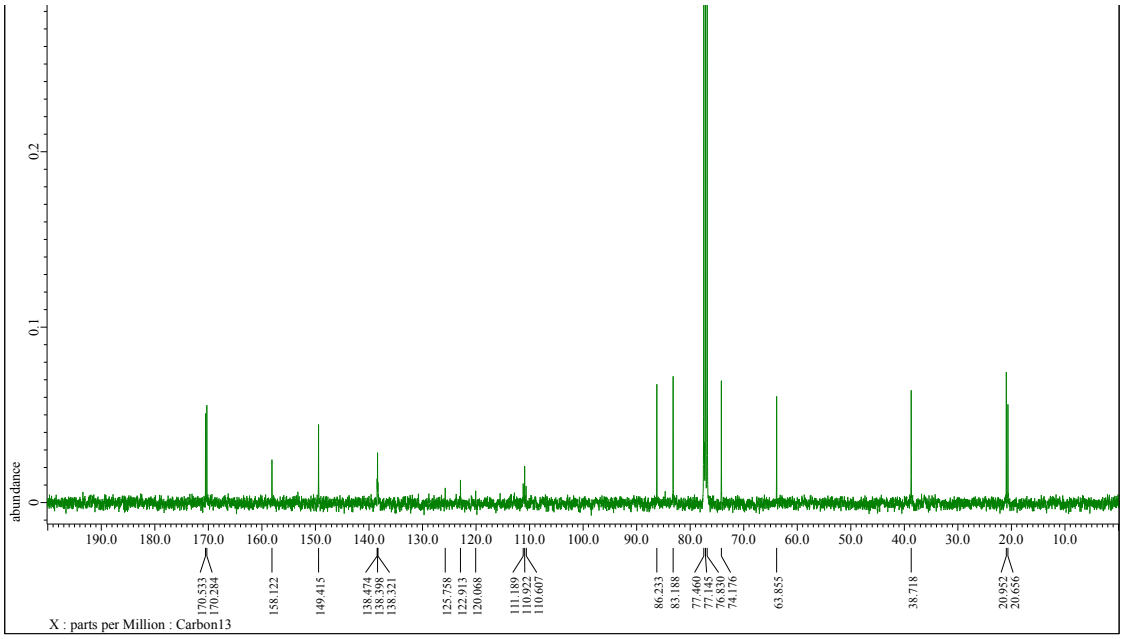

abundance
2.98
3.00
3.02
7.260
4.166
3.582
3.437
X : parts per Million : Proton

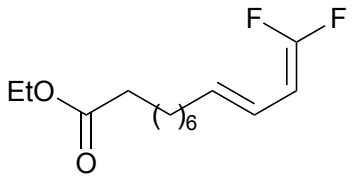

abundance
155.636
151.445
146.423
142.948
142.623
142.299
122.737
119.787
116.923
109.725
77.475
77.160
76.845
33.578
30.027
28.308
X : parts per Million : Carbon13


O
ClF2C
NH
AcO
N
O
O
OAc

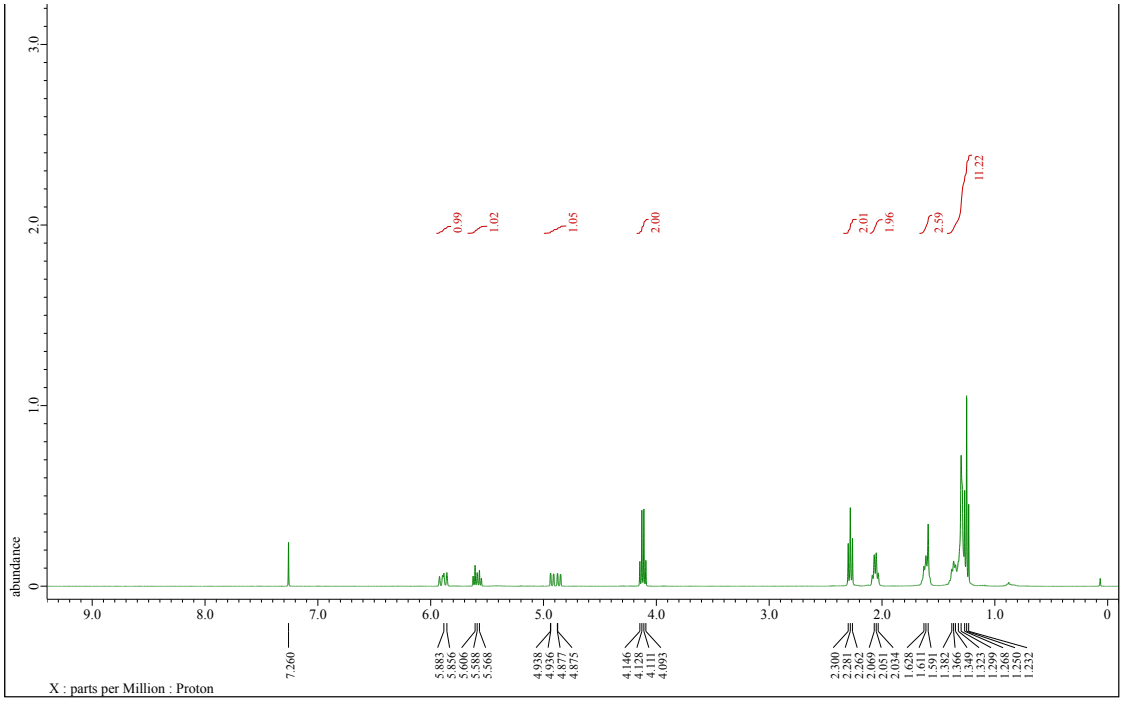
(**5y**)

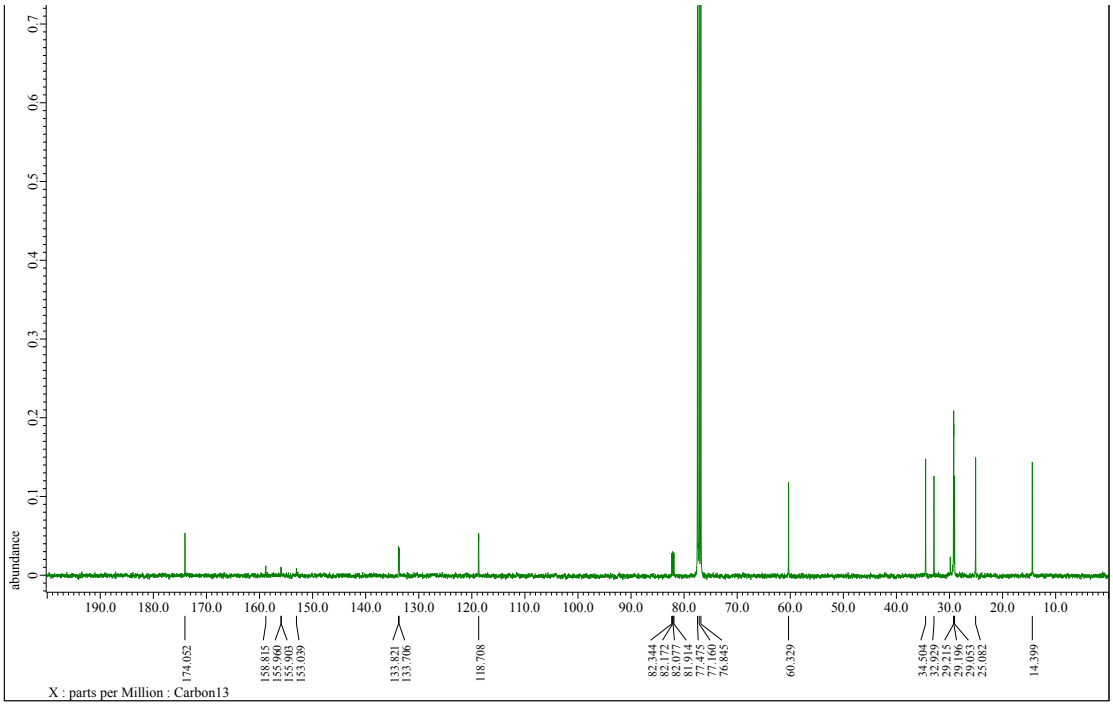

abundance
X : parts per Million : Proton

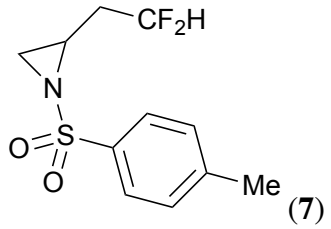

abundance
X : parts per Million : Carbon13


F
F
EtO
6
O

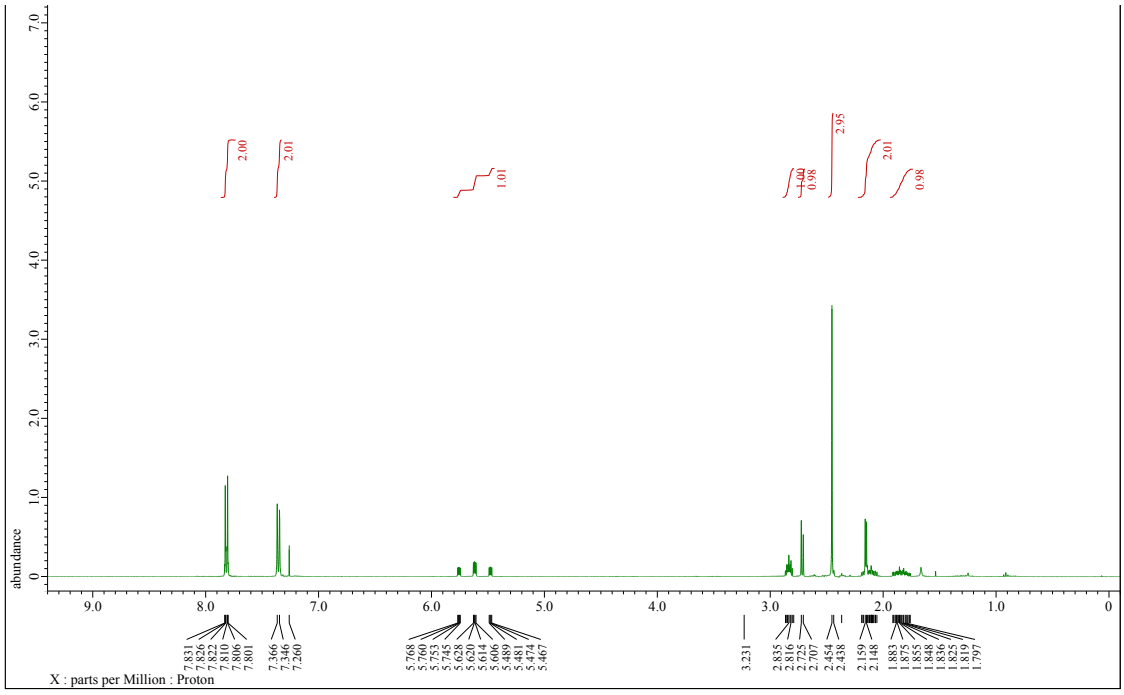
(**6**)

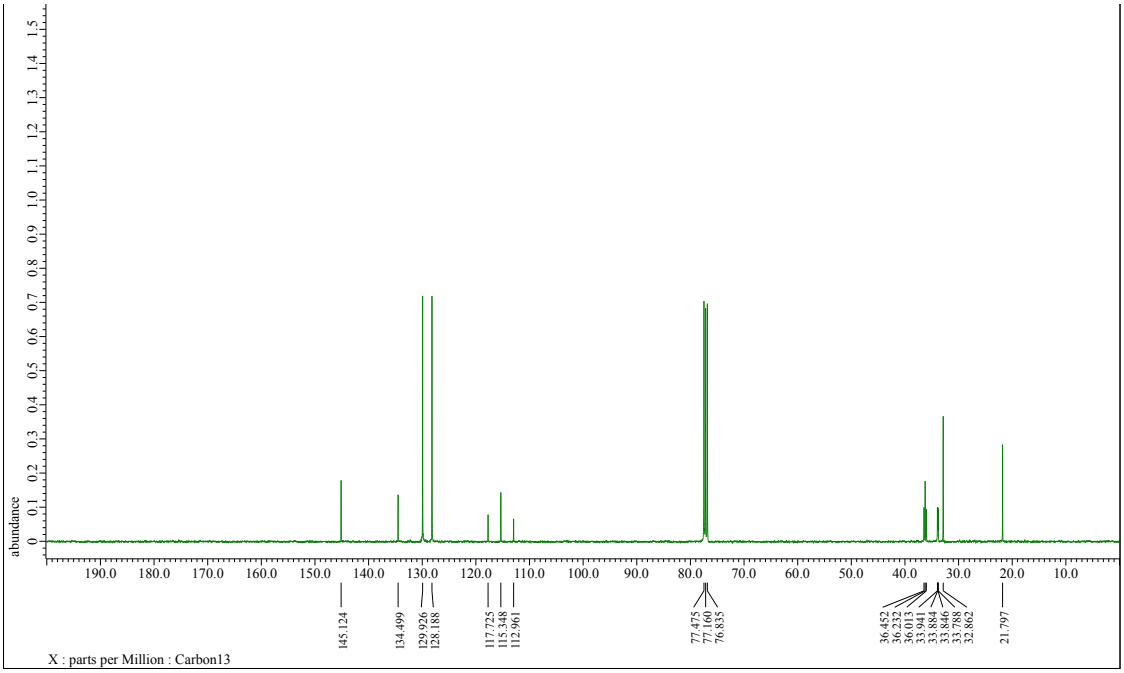

abundance
0.99
1.02
1.05
2.00
2.01
1.96
2.59
11.22
7.260
5.883
5.856
5.606
5.588
5.568
4.938
4.936
4.877
4.875
4.146
4.128
4.111
4.093
2.300
2.281
2.262
2.069
2.051
2.034
1.628
1.611
1.591
1.382
1.366
1.349
1.323
1.299
1.268
1.250
1.232
X : parts per Million : Proton

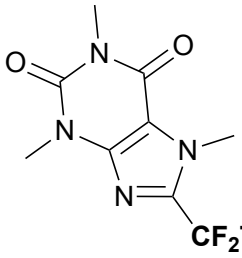

abundance
174.052
158.815
155.960
155.903
153.039
133.821
133.706
118.708
82.344
82.172
82.077
81.914
77.475
77.160
76.845
60.329
34.504
32.929
29.215
29.196
29.053
25.082
14.399
X : parts per Million : Carbon13


CF2H
N
O
S
O
Me

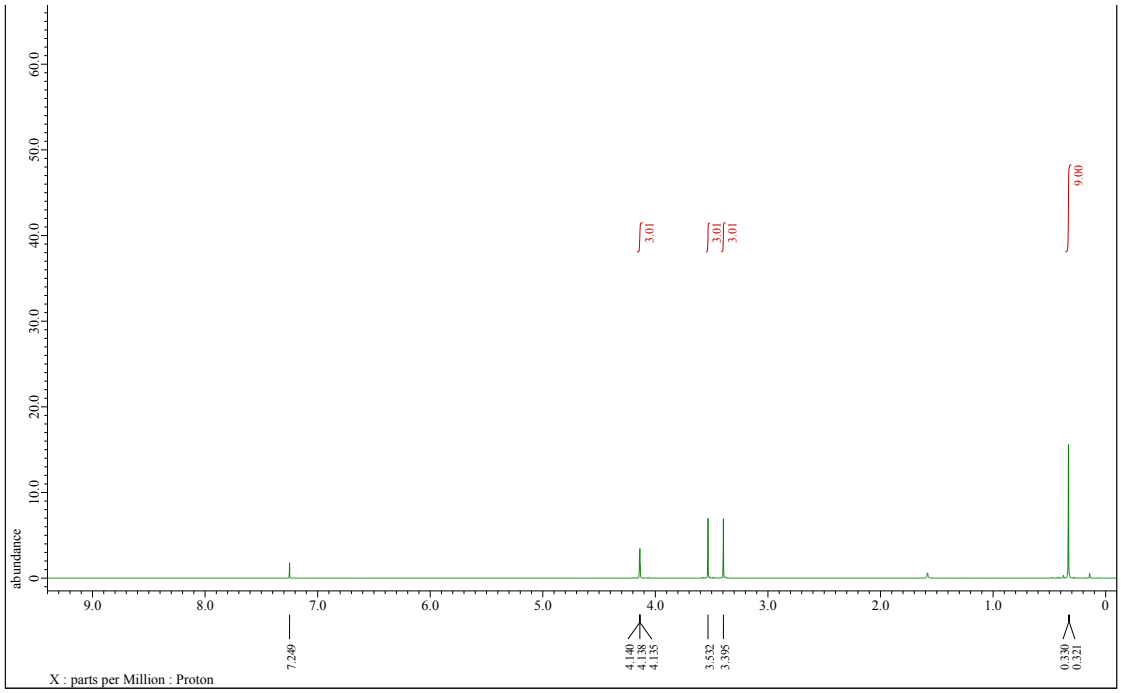
(**7**)

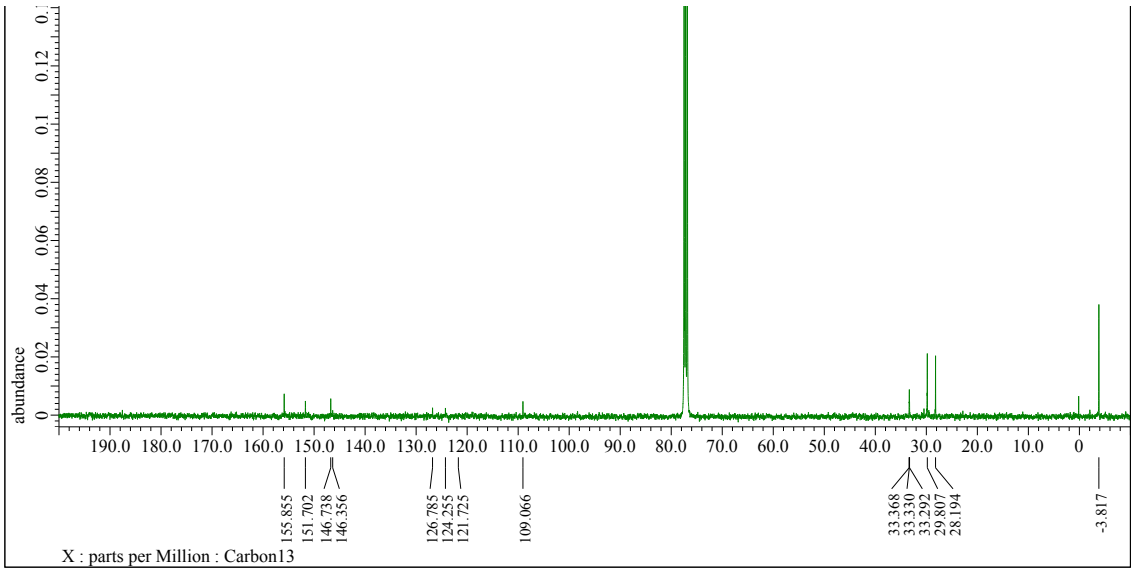

abundance
2.00
2.01
1.01
1.00
0.98
2.95
2.01
0.98
7.831
7.826
7.822
7.810
7.806
7.801
7.366
7.346
7.260
5.768
5.760
5.753
5.745
5.628
5.620
5.604
5.606
5.489
5.481
5.474
5.467
3.231
2.835
2.816
2.725
2.707
2.454
2.438
2.159
2.148
1.883
1.875
1.855
1.848
1.836
1.825
1.819
1.797
X : parts per Million : Proton


abundance
145.124
134.499
129.926
128.188
117.725
115.348
112.961
77.475
77.160
76.835
36.452
36.232
36.013
33.941
33.844
33.846
33.788
32.862
21.797
X : parts per Million : Carbon13


O
N
O
N
N
N
CF2TMS

(**8**)


abundance
60.0
50.0
40.0
30.0
20.0
10.0
0
3.01
3.01
3.01
9.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.249
4.140
4.138
4.135
3.532
3.395
0.330
0.321
X : parts per Million : Proton


abundance
0.12
0.1
0.08
0.06
0.04
0.02
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
155.855
151.702
146.738
146.356
126.785
124.255
121.725
109.066
33.368
33.330
33.292
29.807
28.194
-3.817
X : parts per Million : Carbon13

Computational details:[25]

DFT calculations were conducted with the Gaussian 16 series of programs. The structures in Fig 2 were optimized at the UM06-2X level of theory, and 6-311G(d,p) basis set was used. The enthalpies given in Fig 3 were estimated with thermal correction by using vibrational analysis at the same level of theory. The CPCM solvation model (dichloromethane) was used to reflect the solvent effect. The structures in Scheme 2 were optimized at the UB3LYP level of theory, and 6-31+G(d,p) basis set was used. The single-point energy calculation was performed using UMPWB1K/6-311+G(2df,2p), except that LanL2DZ was used for Cu. The CPCM solvation model (dichloromethane) was used to reflect the solvent effect. The free energies described in this work were estimated from the ZPEs from UMPWB1K with thermal corrections by using vibrational analysis at the UB3LYP level of theory. No imaginary frequencies for intermediates and one imaginary frequency for the transition state were observed. The reaction pathway from the transition state was confirmed by IRC calculation and the vibration mode of the imaginary frequency. DFT calculations were conducted according to the literature procedure reported by Houk and Buchwald.[26] The activation energy ($\Delta G^{\ddagger}$) of SET was estimated according to the Marcus equation with parameters as shown in Scheme S1 (n = 1.424, ε = 8.93 for CH_2Cl_2).

$$\Delta^{\ddagger}G = \left({}^{\lambda}/_{4}\right)\left(1 + {}^{\Delta G}/_{\lambda}\right)^2$$

$$\lambda \approx 332 \times \left(\frac{1}{2r_A} + \frac{1}{2r_B} - \frac{1}{R}\right)\left(\frac{1}{n^2} - \frac{1}{\varepsilon}\right)$$; reorganization energy (kcal/mol)

ΔG; reaction energy (kcal/mol), r; radius of molecules (Å)

$R = r_A + r_B$ (Å), n; index of refraction, ε; dielectric constant

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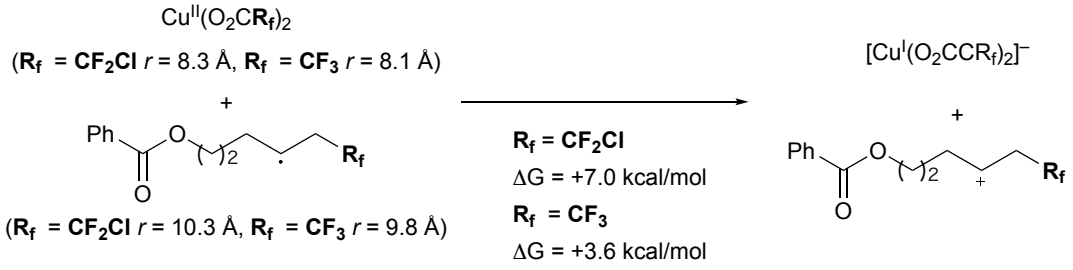
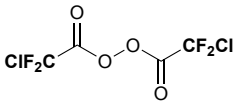
[25] Gaussian 16, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

[26] G. O. Jones, P. Liu, K. N. Houk and S. L. Buchwald, *J. Am. Chem. Soc.*, 2010, **132**, 6205.



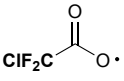
Scheme S1. Parameters for estimation of the activation energies of SET

Cartesian coordinates and energies



E (UM06-2X) = -1112526.865
Sum of electronic and thermal Enthalpies= = -1112483.867
Charge = 0 Multiplicity = 1

C	-2.85190500	0.19787600	0.25738500
F	-3.50893700	1.32581600	0.02611800
F	-2.82642400	-0.02479900	1.57020500
C	-1.41975800	0.35266000	-0.29264100
O	-1.07900400	1.15797400	-1.08263800
O	-0.64204900	-0.60411500	0.28255800
O	0.64205000	-0.60410800	-0.28258400
C	1.41975800	0.35265600	0.29263800
O	1.07899800	1.15795600	1.08264700
C	2.85190800	0.19787900	-0.25738000
F	2.82643600	-0.02478200	-1.57020400
F	3.50894000	1.32581600	-0.02610000
Cl	-3.66057100	-1.14371900	-0.55897200
Cl	3.66056500	-1.14372500	0.55896900



E (UM06-2X) = -556241.4169
Sum of electronic and thermal Enthalpies= = -556221.7213
Charge = 0 Multiplicity = 1

O	1.67694000	-0.22249800	-1.15937400
C	1.16252200	0.20350300	-0.02847000
O	1.70871900	0.94148000	0.73038400
C	-0.26837600	-0.35261900	0.19599700
F	-0.41539700	-1.52750000	-0.41754400
F	-0.45022600	-0.52058400	1.49881100
Cl	-1.45056100	0.79856500	-0.42968500

• CF_2Cl

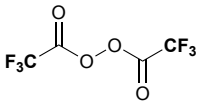
E (UM06-2X) = -437936.6505
Sum of electronic and thermal Enthalpies= = -437927.1456
Charge = 0 Multiplicity = 2

C	-0.51715000	-0.17036100	0.00000000
F	-0.51715000	-0.92067100	1.08011000
F	-0.51715000	-0.92067100	-1.08011000
Cl	0.73009400	1.03495500	0.00000000

CO_2

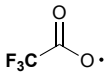
E (UM06-2X) = -118331.1375
Sum of electronic and thermal Enthalpies= = -118321.4312
Charge = 0 Multiplicity = 1

C	0.00000000	0.00000000	0.00000000
O	0.00000000	0.00000000	1.15436700
O	0.00000000	0.00000000	-1.15436700



E (UM06-2X) = -660289.24710
Sum of electronic and thermal Enthalpies= = -660244.288
Charge = 0 Multiplicity = 1

C	-2.85082600	0.01128700	-0.04972000
F	-3.57968200	-0.91417600	0.54487600
F	-2.93413600	-0.14354400	-1.36610700
C	-1.38392200	-0.12642600	0.41258100
O	-0.97243800	-0.92923200	1.17074400
O	-0.66678700	0.84253800	-0.21774800
O	0.66678900	0.84253900	0.21774800
C	1.38392400	-0.12642600	-0.41258100
O	0.97243600	-0.92923300	-1.17074200
C	2.85082600	0.01128700	0.04972000
F	2.93413700	-0.14356500	1.36610500
F	3.57968400	-0.91416400	-0.54489300
F	-3.32238600	1.21154200	0.26751300
F	3.32238000	1.21154900	-0.26749500



E (UM06-2X) = -330122.3288
Sum of electronic and thermal Enthalpies= = -330101.6379
Charge = 0 Multiplicity = 2

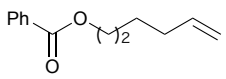
O	-1.51517000	-1.14413000	-0.00168800
C	-0.98467200	0.05844300	-0.01235600
O	-1.60715600	1.07421600	-0.00388400
C	0.56661900	0.00956400	-0.00504400
F	1.01835600	-1.15985400	-0.44342500
F	1.03312900	0.97761300	-0.77496600
F	1.00261800	0.19904800	1.23494400

• CF_3

E (UM06-2X) = -211814.5409
Sum of electronic and thermal Enthalpies= = -211804.0565
Charge = 0 Multiplicity = 2

C	-0.27740100	0.17885200	0.00000000
F	-0.27740100	-0.56535900	1.08351700
F	-0.27740100	-0.56535900	-1.08351700

F	0.73973500	1.01148300	0.00000000



E (UMPWB1K) = -386564.1403
Sum electronic and thermal free energies = -386445.155
Charge = 0 Multiplicity = 1

C	4.0026	0.37032	-0.18044
H	4.17652	0.9581	0.72931
H	4.07069	1.06685	-1.02897
C	5.07396	-0.67769	-0.32034
H	5.0143	-1.30082	-1.21436
C	6.06326	-0.89182	0.55383
H	6.16246	-0.29643	1.45937
H	6.80748	-1.6667	0.39198
C	2.58576	-0.23587	-0.15305
H	2.48777	-0.90539	0.70951
H	2.42363	-0.84082	-1.05359
C	1.51816	0.84394	-0.07816
H	1.55539	1.51351	-0.94303
H	1.61261	1.44846	0.82915
O	0.22539	0.18293	-0.06052
C	-0.86367	0.97046	0.00372
O	-0.80163	2.19155	0.04638
C	-2.13882	0.19678	0.01658
C	-2.16048	-1.20647	-0.03535
C	-3.34665	0.90898	0.08262
C	-3.37979	-1.88578	-0.0212
H	-1.22895	-1.75804	-0.08634
C	-4.56288	0.22648	0.09651
H	-3.31869	1.99254	0.12241
C	-4.58118	-1.17191	0.04462
H	-3.39262	-2.97068	-0.06144
H	-5.49405	0.78242	0.14765
H	-5.52829	-1.70326	0.05543

· CF_2Cl

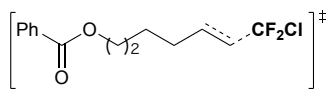
E (UMPWB1K) = -438002.1954
Sum electronic and thermal free energies = -438013.4097
Charge = 0 Multiplicity = 2

C	-0.51353	-0.17287	0.
F	-0.51353	-0.93705	1.09221
F	-0.51353	-0.93705	-1.09221
Cl	0.72498	1.05319	0.

· CF_3

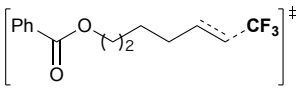
E (UMPWB1K) = -211832.6605
Sum electronic and thermal free energies = -211841.477
Charge = 0 Multiplicity = 2

C	0.	0.	0.33189
F	0.	1.26667	-0.07375
F	-1.09696	-0.63333	-0.07375
F	1.09696	-0.63333	-0.07375



E (UMPWB1K) = -824563.9721
Sum electronic and thermal free energies = -824445.5792
Charge = 0 Multiplicity = 2

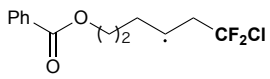
C	1.60149	-0.04996	0.07661
H	1.79385	-0.63222	-0.83242
H	1.72217	-0.73708	0.92815
C	2.61051	1.05379	0.19904
H	2.51464	1.70003	1.07207
C	3.64075	1.26321	-0.65736
H	3.72058	0.70158	-1.5848
H	4.28373	2.13188	-0.55503
C	5.44508	-0.07622	0.22904
F	4.99607	-1.34015	0.29038
F	5.66769	0.35534	1.4806
C	0.15166	0.47621	0.07304
H	0.00017	1.13639	-0.7887
H	-0.02862	1.0723	0.9757
Cl	6.90978	0.04102	-0.76378
C	-0.85171	-0.66492	0.01762
H	-0.76195	-1.3275	0.884
H	-0.73526	-1.26638	-0.88907
O	-2.1796	-0.07941	0.01772
C	-3.22218	-0.92917	-0.03483
O	-3.08891	-2.14421	-0.08171
C	-4.54009	-0.23121	-0.02943
C	-4.6429	1.16811	0.03106
C	-5.70498	-1.01244	-0.08669
C	-5.89977	1.77521	0.03416
H	-3.74466	1.77287	0.07562
C	-6.95896	-0.40189	-0.08362
H	-5.61442	-2.09235	-0.13321
C	-7.05814	0.99278	-0.02319
H	-5.97532	2.85727	0.08122
H	-7.85666	-1.01087	-0.12818
H	-8.03467	1.468	-0.02069



E (UMPWB1K) = -598395.3246
Sum electronic and thermal free energies = -598275.8625
Charge = 0 Multiplicity = 2

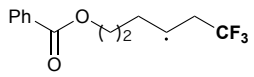
C	2.00903	-0.03389	-0.01025
H	2.18637	-0.61588	-0.92252
H	2.14829	-0.71964	0.8393
C	3.01683	1.07335	0.09274
H	2.93906	1.7153	0.97081
C	4.01702	1.29691	-0.79069
H	4.0851	0.73193	-1.71719
H	4.66802	2.16033	-0.69351
C	5.92167	-0.07006	0.04507
F	5.55705	-1.35752	0.14251
F	6.30251	0.3757	1.25172
C	0.55779	0.48767	0.01272
H	0.38847	1.14729	-0.84614
H	0.39197	1.08324	0.9185
C	-0.44267	-0.65677	-0.02422
H	-0.33409	-1.31947	0.83989
H	-0.34152	-1.25739	-0.93333
O	-1.77231	-0.07584	0.00153
C	-2.81267	-0.9294	-0.02946
O	-2.67591	-2.14401	-0.07738
C	-4.13277	-0.23625	0.00048
C	-4.23955	1.16272	0.06185
C	-5.29564	-1.02181	-0.03436
C	-5.49837	1.76523	0.08791
H	-3.34287	1.77081	0.08921
C	-6.55157	-0.41584	-0.00841
H	-5.20196	-2.10143	-0.08166
C	-6.65472	0.97851	0.05271
H	-5.577	2.84705	0.13554
H	-7.44771	-1.02812	-0.03577

H	-7.63277	1.45016	0.07298
F	6.95045	0.03652	-0.81266



E (UMPWB1K) = -824599.3507
Sum electronic and thermal free energies = -824478.1259
Charge = 0 Multiplicity = 2

C	-1.68098	0.25191	-0.33047
H	-1.78213	0.93737	-1.18473
H	-1.8475	0.87959	0.56434
C	-2.73281	-0.80589	-0.40825
H	-2.53762	-1.77753	0.03911
C	-4.1226	-0.52142	-0.88408
H	-4.14197	0.32037	-1.58407
H	-4.55395	-1.39131	-1.39147
C	-5.08372	-0.171	0.25184
F	-4.66727	0.92818	0.9423
F	-5.17107	-1.18064	1.16301
C	-0.25465	-0.32091	-0.27743
H	-0.05907	-0.91058	-1.18059
H	-0.16186	-0.9986	0.57976
Cl	-6.76102	0.16732	-0.33626
C	0.78752	0.77948	-0.15961
H	0.65453	1.37047	0.75192
H	0.76209	1.45934	-1.01675
O	2.09125	0.14336	-0.11221
C	3.16311	0.95195	-0.01973
O	3.07575	2.17137	0.02332
C	4.45221	0.20321	0.02376
C	4.50234	-1.1994	-0.0264
C	5.64404	0.9388	0.11844
C	5.73387	-1.85491	0.01798
H	3.58324	-1.76906	-0.09928
C	6.87255	0.28001	0.16231
H	5.59418	2.02165	0.15675
C	6.91922	-1.11779	0.11222
H	5.7687	-2.93937	-0.02078
H	7.79124	0.85395	0.23548
H	7.87591	-1.63066	0.14658



E (UMPWB1K) = -598435.7524
Sum electronic and thermal free energies = -598312.7712
Charge = 0 Multiplicity = 2

C	-2.09661	0.28265	-0.40396
H	-2.17962	0.9614	-1.26594
H	-2.27084	0.92097	0.48185
C	-3.15617	-0.76724	-0.4889
H	-2.96489	-1.74892	-0.06257
C	-4.54737	-0.46312	-0.95093
H	-4.56393	0.3922	-1.63557
H	-4.98744	-1.32002	-1.47425
C	-5.51481	-0.12604	0.17405
F	-5.13247	0.97074	0.88273
F	-5.64425	-1.13965	1.07177
C	-0.67579	-0.29996	-0.32597
H	-0.47215	-0.89897	-1.22123
H	-0.59985	-0.97086	0.53821
C	0.37281	0.7937	-0.20308
H	0.23164	1.3934	0.70149
H	0.36412	1.46644	-1.06618
O	1.67132	0.14899	-0.13236
C	2.74703	0.95092	-0.02793
O	2.66727	2.17112	0.00737
C	4.03036	0.194	0.03896
C	4.07177	-1.20924	-0.0002
C	5.22565	0.92237	0.14498
C	5.2981	-1.87254	0.06647
H	3.14996	-1.77333	-0.08183
C	6.44897	0.25581	0.21111
H	5.18255	2.00579	0.17448
C	6.48694	-1.14261	0.17205
H	5.32617	-2.95748	0.03626
H	7.37037	0.82418	0.29299
H	7.43957	-1.66153	0.22378
F	-6.76544	0.13487	-0.29689

$Cu^{II}(O_2C\mathbf{CF_2Cl})_2$

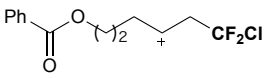
E (UMPWB1K) = -1235823.850
Sum electronic and thermal free energies = -1235822.398
Charge = 0 Multiplicity = 2

Cu	0.	-0.00013	0.0027
O	1.70296	0.26016	1.09035
O	1.70347	0.10874	-1.09671
O	-1.70228	-0.26414	-1.08517
O	-1.70344	-0.10533	1.1018
C	-2.33008	-0.24718	0.01209
C	2.33008	0.24759	-0.00702
C	-3.86619	-0.37034	0.02072
C	3.86608	0.37109	-0.01727
F	-4.27626	-1.11497	-1.02621
F	-4.27362	-0.98119	1.15251
F	4.27005	1.0025	-1.13895
F	4.27913	1.09612	1.04192
Cl	4.61323	-1.24745	0.04949
Cl	-4.61316	1.24623	-0.07743

$Cu^{II}(O_2C\mathbf{CF_3})_2$

E (UMPWB1K) = -783493.6334
Sum electronic and thermal free energies = -783488.0931
Charge = 0 Multiplicity = 2

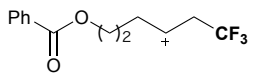
Cu	0.00012	0.00136	-0.01709
O	-1.70978	-1.11041	-0.01095
O	-1.72118	1.08256	-0.01158
O	1.71222	1.11079	-0.02418
O	1.71929	-1.08218	-0.02494
C	2.34439	0.01738	-0.0227
C	-2.34405	-0.01832	-0.00713
C	3.88759	0.00413	0.00812
C	-3.88764	-0.00629	0.00975
F	4.39372	1.22586	-0.20988
F	4.36847	-0.83305	-0.92884
F	4.31263	-0.42439	1.21458
F	-4.35695	0.68569	-1.04609
F	-4.38951	-1.24795	-0.03733
F	-4.32943	0.59084	1.13428



E (UMPWB1K) = -824470.2489
Sum electronic and thermal free energies = -824347.9222
Charge = 1 Multiplicity = 1

C	1.56862	-0.5925	-0.33488
H	1.67817	-1.29661	-1.16483
H	1.76037	-1.22545	0.59781

C	2.74372	0.15732	-0.04508
H	2.66093	0.98224	0.66699
C	4.05738	-0.14354	-0.61302
H	4.14954	-1.18324	-0.93963
H	4.05867	0.46062	-1.5442
C	5.24753	0.28562	0.24757
F	5.24747	-0.41909	1.40927
F	5.1349	1.59642	0.58424
C	0.19479	0.0741	-0.2017
H	0.02549	0.66592	-1.10707
H	0.1832	0.75663	0.6531
Cl	6.79526	0.02706	-0.58559
C	-0.90915	-0.9672	-0.05717
H	-0.81845	-1.52747	0.87859
H	-0.90723	-1.67895	-0.88817
O	-2.15167	-0.23843	-0.05827
C	-3.28255	-0.97713	0.03784
O	-3.26159	-2.19465	0.12902
C	-4.51783	-0.14882	0.01896
C	-4.47795	1.25001	-0.10317
C	-5.75477	-0.80484	0.12522
C	-5.66655	1.98097	-0.11904
H	-3.52442	1.75847	-0.18543
C	-6.93959	-0.06996	0.10922
H	-5.77398	-1.88525	0.21889
C	-6.89697	1.32355	-0.0131
H	-5.63323	3.06187	-0.21416
H	-7.89373	-0.58107	0.1917
H	-7.81999	1.89548	-0.02593



E (UMPWB1K) = -598306.7574

Sum electronic and thermal free energies = -598182.4823

Charge = 1 Multiplicity = 1

C	-1.98535	-0.59204	0.4274
H	-2.088	-1.31438	1.24244
H	-2.19608	-1.20453	-0.51683
C	-3.16136	0.16281	0.161
H	-3.08252	1.00455	-0.53165
C	-4.47316	-0.15092	0.72337
H	-4.5662	-1.1942	1.03908
H	-4.48202	0.44644	1.65955
C	-5.67158	0.27879	-0.11885
F	-5.74165	-0.43866	-1.2619
F	-5.59684	1.58355	-0.46162
C	-0.61151	0.07137	0.28745
H	-0.42998	0.65034	1.1988
H	-0.60805	0.76571	-0.55793
C	0.48856	-0.96991	0.11491
H	0.37963	-1.52432	-0.82244
H	0.5024	-1.68679	0.94136
O	1.73076	-0.24103	0.09581
C	2.85924	-0.97802	-0.03542
O	2.83671	-2.19475	-0.1361
C	4.09386	-0.14856	-0.04252
C	4.05565	1.24956	0.08815
C	5.32832	-0.80245	-0.18464
C	5.24342	1.98194	0.0766
H	3.10404	1.75641	0.19791
C	6.51231	-0.06615	-0.19595
H	5.34628	-1.88231	-0.28469
C	6.47136	1.32665	-0.06528
H	5.21137	3.0623	0.17814
H	7.46452	-0.57559	-0.3063
H	7.39373	1.8997	-0.07399
F	-6.81567	0.08893	0.5615

$[Cu^{I}(O_2C\mathbf{CF_2Cl})_2]^-$

E (UMPWB1K) = -1235943.889

Sum electronic and thermal free energies = -1235945.625

Charge = -1 Multiplicity = 1

Cu	0.	0.00002	0.17021
O	-2.59123	1.65612	-0.37192
O	-1.85206	-0.42135	0.18638
O	2.5912	-1.65612	-0.37189
O	1.85207	0.42138	0.18634
C	2.72967	-0.46723	-0.08534
C	-2.72968	0.46723	-0.08535
C	4.17414	0.12207	-0.02977
C	-4.17413	-0.12209	-0.02977
F	5.12424	-0.80095	-0.28436
F	4.44811	0.64978	1.19084
F	4.33221	1.11841	-0.93903
F	-4.44813	-0.6497	1.19087
F	-5.12424	0.80089	-0.28446
F	-4.33216	-1.11851	-0.93896

$[Cu^{I}(O_2C\mathbf{CF_3})_2]^-$

E (UMPWB1K) = -783617.1494

Sum electronic and thermal free energies = -783614.8051

Charge = -1 Multiplicity = 1

Cu	0.	0.00002	0.17021
O	-2.59123	1.65612	-0.37192
O	-1.85206	-0.42135	0.18638
O	2.5912	-1.65612	-0.37189
O	1.85207	0.42138	0.18634
C	2.72967	-0.46723	-0.08534
C	-2.72968	0.46723	-0.08535
C	4.17414	0.12207	-0.02977
C	-4.17413	-0.12209	-0.02977
F	5.12424	-0.80095	-0.28436
F	4.44811	0.64978	1.19084
F	4.33221	1.11841	-0.93903
F	-4.44813	-0.6497	1.19087
F	-5.12424	0.80089	-0.28446
F	-4.33216	-1.11851	-0.93896