

SUPPORTING INFORMATION

An Air-Stable Cationic Iridium Hydride as a Highly Active and General Catalyst for the Isomerization of Terminal Epoxides

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Supporting Information

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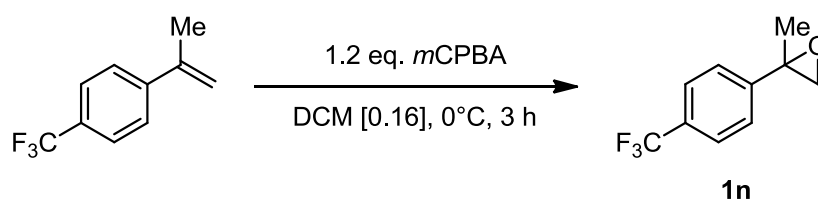
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General information

All reactions were carried out under an inert atmosphere of nitrogen using either two manifold vacuum/inert gas lines or a MBraun glove-box, unless otherwise noted. Solvents were dried over activated alumina columns and further degassed by three successive “freeze-pump-thaw” cycles if necessary. NMR spectra were recorded on ARX-300, ARX-400 and ARX-500 Bruker Avance spectrometers. ^1H and ^{13}C NMR chemical shifts are given in ppm relative to SiMe_4 , with the solvent resonance used as internal reference. ^{31}P NMR chemical shifts are reported in ppm relative to H_3PO_4 . The mass spectrometric data were obtained at the mass spectrometry facility of the University of Geneva (<http://www.unige.ch/sciences/sms/>). Chiral GC analyses were performed on a HP6890 gas chromatography. HPLC analyses were performed on an Agilent 1100 series or a Shimadzu CTO-20AA. Commercial reagents were purchased from Aldrich, Acros or Strem and used without purification, unless otherwise noted. Liquid reagents were transferred with stainless steel syringes or cannula. Flash chromatography was performed using silica gel 60 (230-400 ASTM) from Fluka or silica gel 60 (230-400 mesh) from Silicycle.

$[\text{Ir}(\text{COD})\text{Cl}]_2$,¹ Schwartz reagent² and NaBAR_f ³ were prepared according to literature procedures. $[(\text{Ph}_3\text{P})\text{CuH}]_6$, $[(\text{Ph}_3\text{P})_3\text{RhH}(\text{CO})]$ and $[(\text{Ph}_3\text{P})_3\text{RuH}(\text{Cl})]$. Tol were purchased from Aldrich and stored in a glove box. Epoxides **2a-m** and **2o-v** were synthesized according to literature procedures.⁴ Aldehydes **2a-m**,⁴ **2o-v**⁴ and **2n**⁵ have been characterized previously.

Synthesis of 1n



At room temperature, in a vacuum-dried Schlenk, *p*-trifluoromethyl- α -methylstyrene (300 mg, 1.61 mmol, 1.0 eq.) was dissolved in dry CH_2Cl_2 (10 mL) under a N_2 atmosphere. To this solution *m*-CPBA (< 77%, 433 mg, 1.93 mmol, 1.2 eq.) was added as a solid in a single portion at 0°C. The reaction mixture was stirred for 3 hours at 0°C and then quenched with a saturated solution of NaHCO_3 (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3×15 mL) and the combined organic layers were washed successively with a saturated solution of NaHCO_3 , H_2O and brine and dried over Na_2SO_4 . Evaporation of the solvents under reduced pressure followed by purification by flash column chromatography on silica gel using *n*-pentane/EtOAc/ Et_3N (95/4/1) as eluent afforded the analytically pure product (264 mg, 81%) as a clear oil. $R_f = 0.40$ (CyH/EtOAc = 95/5).

$^1\text{H NMR}$ (500 MHz, CDCl_3 , 298K): $\delta/\text{ppm} = 1.74$ (s, 3H, CH_3), 2.77 (d, $^2J_{\text{HH}} = 5.4$ Hz, 1H, CHH), 3.01 (d, $^2J_{\text{HH}} = 5.4$ Hz, 1H, CHH), 7.48 (d, $^3J_{\text{HH}} = 8.1$ Hz, 2H, H-Ar), 7.60 (d, $^3J_{\text{HH}} = 8.1$ Hz, 2H, H-Ar).

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3 , 298K): $\delta/\text{ppm} = 21.6$ (CH_3), 56.5 (C- CH_3), 57.2 (CH_2), 124.2 (q, $^1J_{\text{CF}} = 270$ Hz, CF_3), 125.5 (q, $^3J_{\text{CF}} = 3.6$ Hz, CH-Ar), 125.9 (CH-Ar), 129.9 (q, $^2J_{\text{CF}} = 32.5$ Hz, CCF_3), 145.5 (C^{IV} -Ar).

$^{19}\text{F}\{^1\text{H}\}$ NMR (282 MHz, CDCl_3 , 298K): $\delta/\text{ppm} = -62.5$.

IR (ATR): $\nu(\text{cm}^{-1}) = 2991, 1621, 1412, 1323, 1164, 1111, 1064, 1015$.

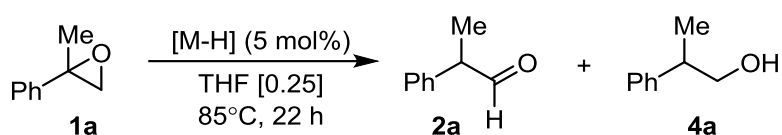
GLC (HP-1701): $t_R = 8.6$ min.

LR-MS (ESI) for $\text{C}_{10}\text{H}_9\text{F}_3\text{O}$: calcd. $(\text{M})^+ = 202.17$, found $(\text{M}-\text{CF}_3)^+ = 133.1$.

Catalyst optimization

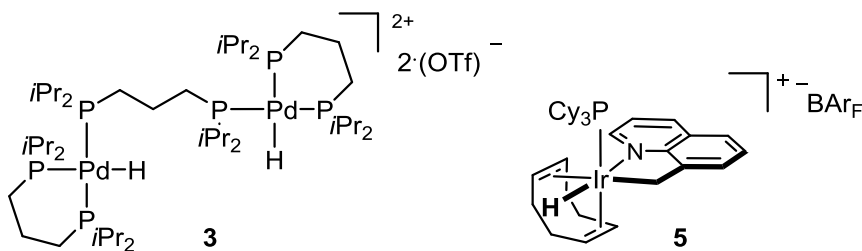
In a Young-valve Schlenk: to a solution of the selected metal hydride (5.0 mol%), and of the appropriate additive when necessary (7.5 mol%), in freshly distilled and degassed THF (0.6 mL) was added epoxide **1a** (20.0 mg, 0.15 mmol) at 23°C. The Schlenk was sealed and placed in a preheated oil bath (100°C) and stirred for 24 hours. The reaction was cooled to room temperature and the volatiles were removed under reduced pressure. Formation of a dark-brown residue was obtained upon addition of 20 mL of pentane. The precipitate was removed by filtration through a MS® PTFE organic stable syringe filter (0.22 µm pore size). The solvent was subsequently evaporated to afford the analytically pure aldehyde.

Table 1 Reaction optimization.^a

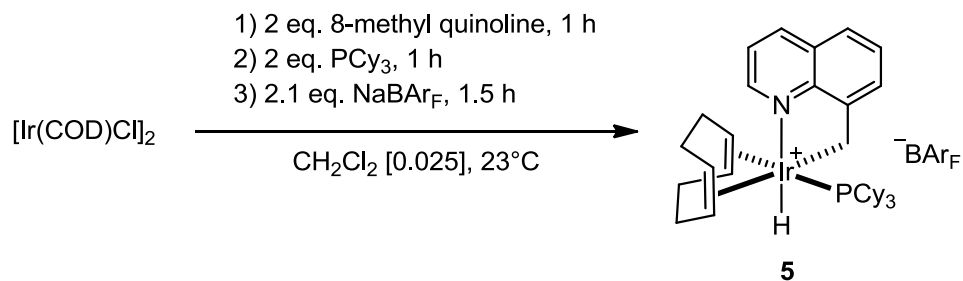


Entry	Catalyst	Additive ^b	Conv. (%) ^c	2a/4a
1	3	none	>99 (77) ^d	>99:1
2	[(Ph ₃ P)CuH] ₆	none	0	<i>nd</i> ^e
3	[(Ph ₃ P) ₃ RhH(CO)]	none	0	<i>nd</i>
4	[(Ph ₃ P) ₃ RuH(Cl)].Tol	none	49	66:34
5	[(Ph ₃ P) ₃ CuH] ₆	dipp	0	<i>nd</i>
6	[(Ph ₃ P) ₃ RhH(CO)]	dipp	0	<i>nd</i>
7	[(Ph ₃ P) ₃ RuH(Cl)].Tol	dipp	0	<i>nd</i>
8	[(Ph ₃ P) ₃ RuH(Cl)].Tol	NaBAR _F	>99 (70) ^d	77:23
9	[Cp ₂ Zr(H)Cl]	none	>99	73:27
10	5	none	>99	>99:1
11 ^f	5	none	>99(98) ^d	>99:1
12	5	dtbmp	>99	>99:1
13	5	TEMPO	0	<i>nd</i>

^a Average of two independent experiments (0.15 mmol scale). ^b Experiments performed according to the general procedure with 7.5 mol% of the appropriate additive. ^c Determined by GC or ¹H NMR. ^d Isolated yield of **2a**. ^e not determined. ^f 0.5 mol%, 100°C, 24 h.

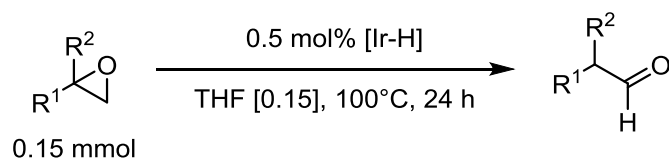


Synthesis of complex 5⁶



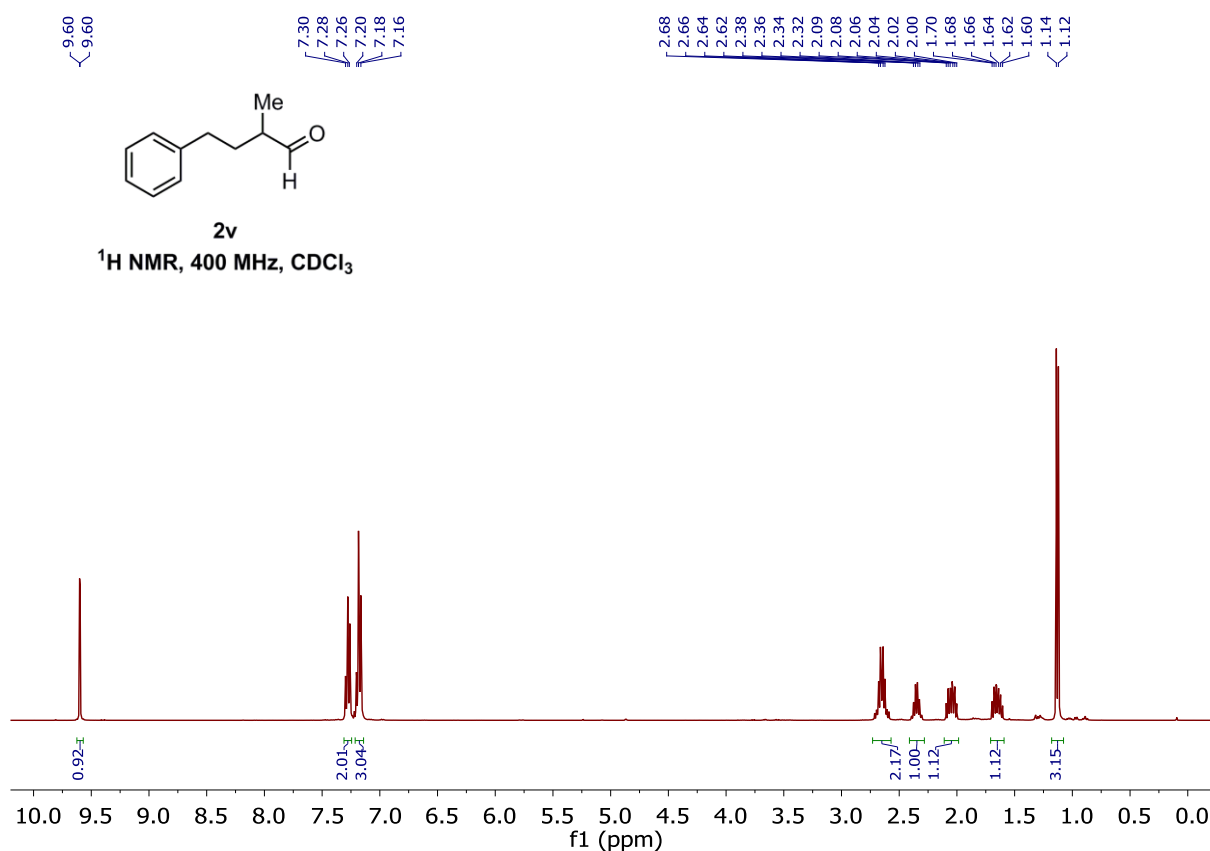
In a Schlenk equipped with a Young-valve, 8-methylquinoline (2.0 eq., 122 μL , 0.89 mmol) was added to a solution of [Ir(COD)Cl]₂ (1 eq., 300 mg, 0.45 mmol) in degassed CH₂Cl₂ (18 mL, 0.025 M) at 23°C. The reaction was stirred for 1 hour and then brought into a glove box. Tricyclohexylphosphine (2.0 eq., 250 mg, 0.89 mmol) was then added in one portion and the resulting solution stirred for 1 hour under inert atmosphere. Outside of the glove box, in open-air, NaBAR_F (2.1 eq., 831 mg, 0.94 mmol) was added to the mixture and the resulting suspension vigorously stirred for 1.5 hours. After evaporation of the solvent under reduced pressure, the crude mixture was purified by column chromatography (eluent: CH₂Cl₂; R_f = 0.9). A beige, air-stable solid was obtained (1.41 g, yield = 99%).

General procedure for the Ir-catalyzed isomerization of epoxides

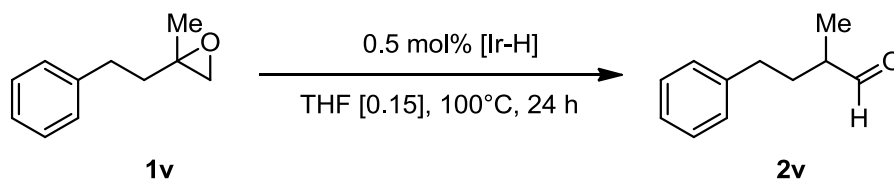


In a Young-valve Schlenk: to 1 mL of a stock solution (35.7 mg of **5** in 30 mL of freshly distilled and degassed THF) of complex **5** (0.5 mol%) was added the appropriate epoxide (0.15 mmol) at 23°C. The Schlenk was sealed and placed in a preheated oil bath (100°C) and stirred for 24 hours. The reaction was cooled to room temperature and the volatiles were removed under reduced pressure. Formation of a dark-brown residue was obtained upon addition of 2 mL of pentane. The precipitate was removed by filtration through a MS® PTFE organic stable syringe filter (0.22 μm pore size). The solvent was subsequently evaporated to afford the analytically pure aldehyde.

Below is shown a typical ¹H NMR obtained by this method for aldehyde **2v**.



Gram scale experiment for the isomerization of epoxide **1v**



In a Young-valve Schlenk: to a solution of **5** (0.5 mol%, 48.9 mg, 0.031 mmol) in freshly distilled and degassed THF (41 mL) was added epoxide **1v** (1.0 g, 6.16 mmol) at 23°C. The Schlenk was sealed and placed in a preheated oil bath (100°C) and stirred for 24 hours. The reaction was cooled to room temperature and the volatiles were removed under reduced pressure. Formation of a dark-brown residue was obtained upon addition of 20 mL of pentane. The precipitate was removed by filtration through a MS[®] PTFE organic stable syringe filter (0.22 μm pore size). The solvent was subsequently evaporated to afford the analytically pure aldehyde **2v** (1.01 g, > 99%).

Deuterium labelling experiments

Preparation of the stock solution. In a Young-valve Schlenk under N₂ were added successively 115 mg of epoxide **1a-d**₁₀ (0.1 mmol), 96 mg of mesitylene (0.1 mmol) as internal standard and 4 mL of THF-*d*₈. The stock solution was kept in a glove box.

Data acquisition. All NMR labelling experiments were conducted in separate Young-valve NMR tubes using the following protocol: the Young-valve NMR tube was charged with the appropriate amount of the iridium hydride precatalyst **5** (5–35 mol%). The tube was conditioned by three successive vacuum-nitrogen cycles and brought into the glove box. Next, 0.5 mL of the above-prepared stock solution was added at room temperature. The tube was taken out of the glove box and a first ¹H NMR experiment was recorded (*t* = 0, Table 2). This measurement provided the exact initial catalyst loading. The tube was then placed into a pre-heated oil bath (100°C) to initiate the catalytic reaction. After 24 h the mixture was cooled to room temperature before recording a second ¹H NMR experiment (*t* = 24 h). The extent of incorporation of hydrogen in the aldehydic position (H_a; δ = 9.64 ppm) and the amount of degradation complexes [Ir]_{deg.} in the hydride region ([Ir]_{deg.}-**1** δ = -11.4 (t); [Ir]_{deg.}-**2** δ = -11.7 (d) ppm) was quantified with this experiment. Potential incorporation in the benzylic position (H_b; δ = 3.62 ppm) could not be assessed because of overlap with the most deshielded signal of residual THF and degradation complexes [Ir]_{deg.}. The volatiles were removed under vacuum, the resulting brown oil suspended in pentane and filtered through a MS® PTFE organic stable syringe filter (0.22 μm pore size). Pentane was removed under vacuum and final ¹H NMR experiment recorded in CDCl₃ (*t* = 24 h; CDCl₃). The extent of H incorporation in the benzylic position (H_b; δ = 3.64 ppm) was thus accessible retrospectively.

A representative set of experiments is given below for a load of 35 mol% (Figure 1). Table 2 contains the results of this specific experiment. Table 3 summarizes the results of 5 experiments with 5 different catalyst loadings. Table 4 corresponds to three independent experiments with a catalyst loading of ca. 10 mol% performed at *t* = 2h, *t* = 4 h and *t* = 24 h. Conversions were measured by ²H NMR spectroscopy.

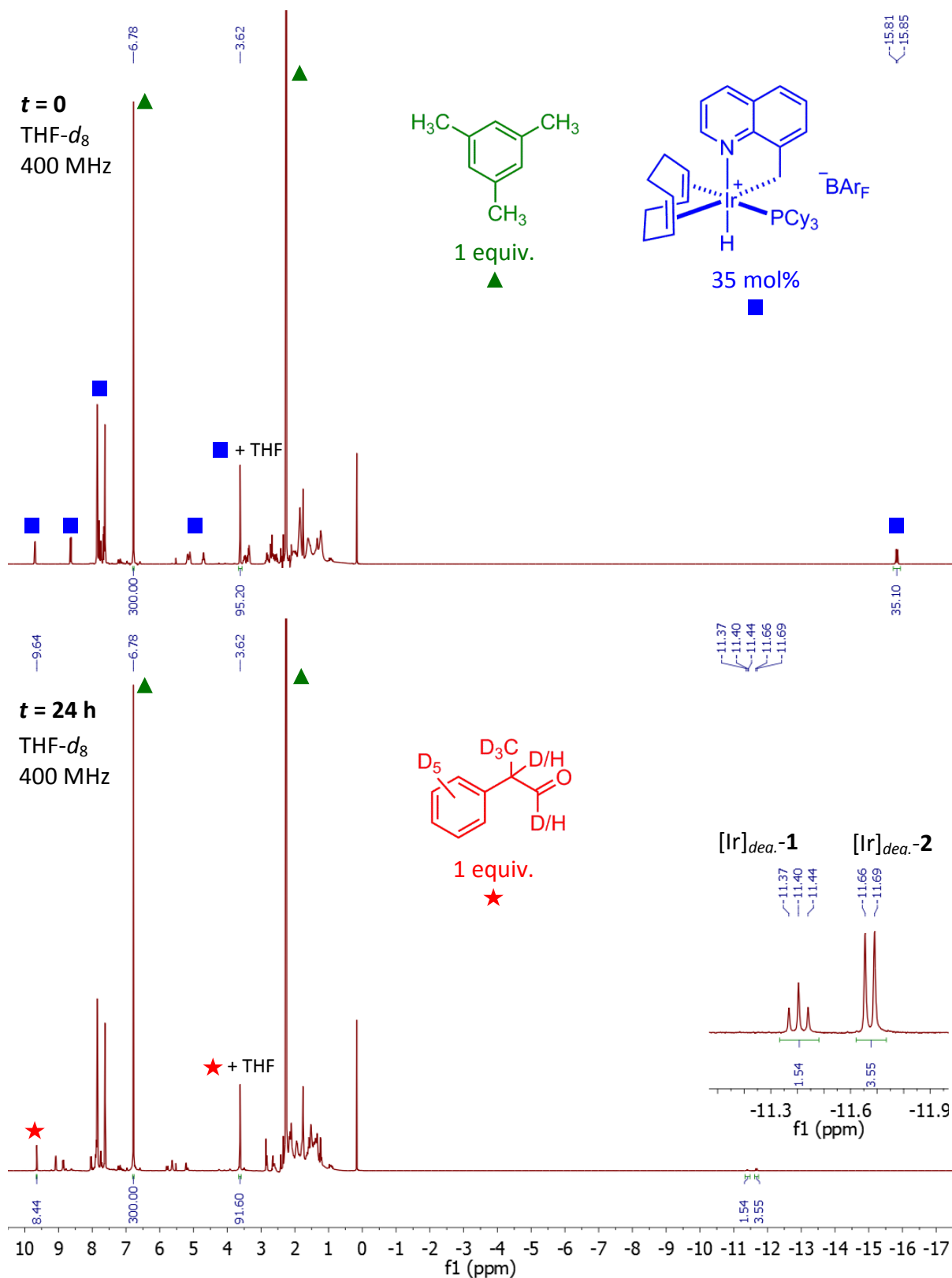


Figure 1 (Part 1) NMR experiments for a labelling reaction at 35 mol%

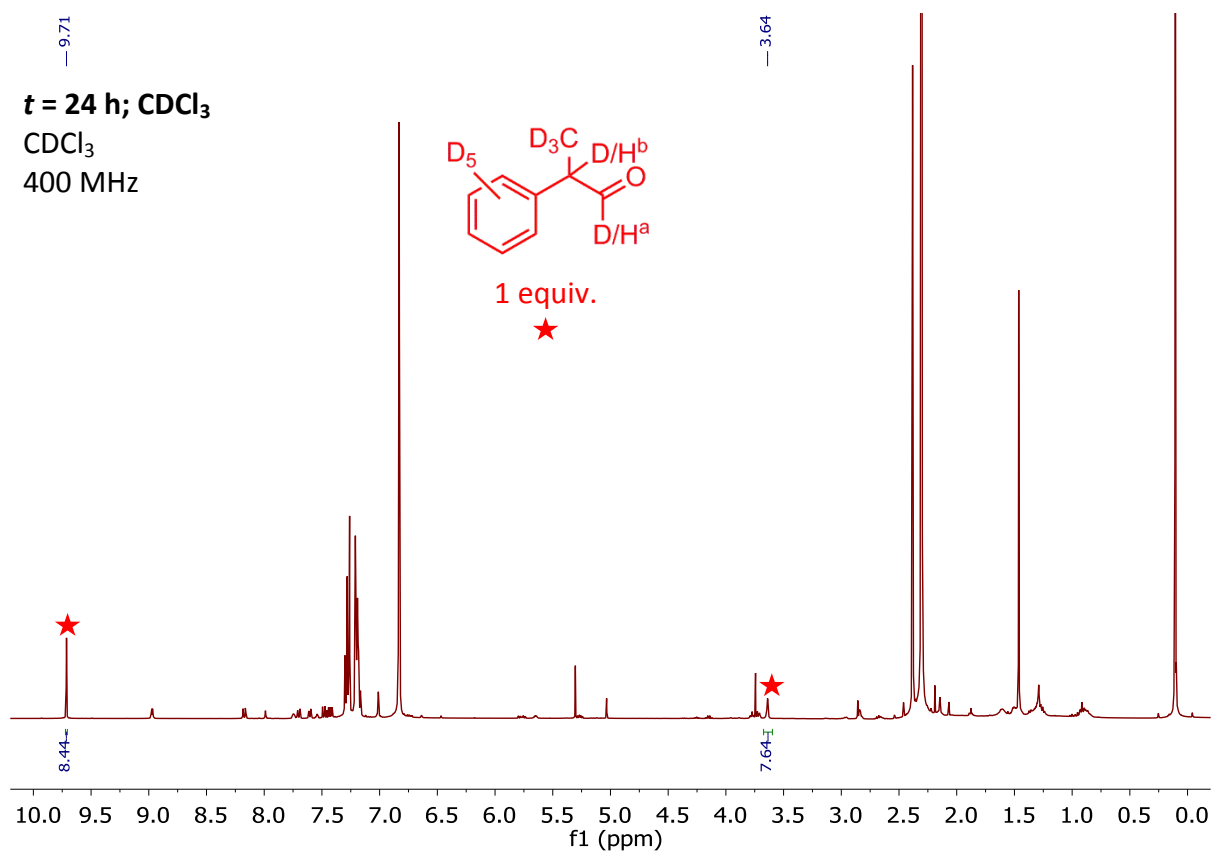


Figure 1 (Part 2) NMR experiments for a labelling reaction at 35 mol%

Table 2 Labelling experiment for a 35 mol% catalyst loading

$t = 0$	$t = 24 \text{ h}$		$t = 24 \text{ h; CDCl}_3$	Total
[Ir-H] 5	H_a	$[\text{Ir}]_{deg.-1}$	$[\text{Ir}]_{deg.-2}$	
			H_b	
35.1	8.4	1.5	3.6	7.6
				21.1

Results are expressed in mol%. Numbers in parenthesis represent the percentage of incorporated with respect to the initial catalyst loading.

Table 3 Labelling experiments with different catalyst loading

t = 0	t = 24 h			t = 24 h; CDCl₃	Total
[Ir-H] 5	H _a	[Ir]_{deg.}-1	[Ir]_{deg.}-2	H _b	
5.2	1.7	0.2	0.1	3.7	5.7
10.4	4.8	0.5	0.5	5.3	11.1
20.0	7.7	1.0	1.4	6.8	16.9
28.0	9.6	1.3	2.1	9.8	22.8
35.1	8.4	1.5	3.6	7.6	21.1

Table 4 Labelling experiments with different reaction time

Reaction time	t = 0	t = X h			t = X h; CDCl₃	Total
	[Ir-H] 5	H _a	[Ir]_{deg.}-1	[Ir]_{deg.}-2	H _b	
2 h ^a	9.6	1.5	0.1	0.5	5.8	7.9
4 h ^b	9.4	2.2	0.1	0.6	6.2	9.1
24 h ^b	10.4	4.8	0.5	0.5	5.3	11.1

^a 97% conversion based on ²H NMR. ^b >99% conversion based on ²H NMR.

Attempt to isolate and characterize [Ir]_{deg.}

At the end of the gram scale experiment with substrate **1v**, the remaining dark-brown residue (30 mg) was analyzed by ¹H and ³¹P{¹H} NMR spectroscopy (CDCl₃). Intriguingly, only signals corresponding to [Ir]_{deg.}-1 were observed in the hydride region. Signals attributable to the 8-methylquinoline were visible whereas no olefinic signals of the cyclooctadiene ligand were detectable. A singlet that resonates at $\delta = 28.1$ ppm was observed by ³¹P{¹H} spectroscopy. Repeated attempts to purify [Ir]_{deg.}-1 by either crystallization or column chromatography were unsuccessful.

X-Ray Diffraction experiment

A yellow single crystal of complex **5** was mounted on a mitegen cryoloop using fomblin oil. Data were collected using Mo radiation on a SuperNova dual-source Agilent diffractometer equipped with an Atlas diffractometer. The crystal was kept at 180 K during data collection. Using Olex2⁷, the structure was solved with the Superflip⁸ structure solution program and refined with the ShelXL⁹ refinement package using Least Squares minimisation.

Crystallographic information is summarized in the table below.

The BAr_f ions (residue 1 and 2) have disordered CF_3 group. Four CF_3 groups for residue 1 and three for residue 2 were refined using 2 components. Restraints were applied on distances and anisotropic displacement parameters.

Residue 4 and 5 are two components of a disordered complex with respective occupancies 0.72 and 0.28. Restraints were also applied to regularize the geometry.

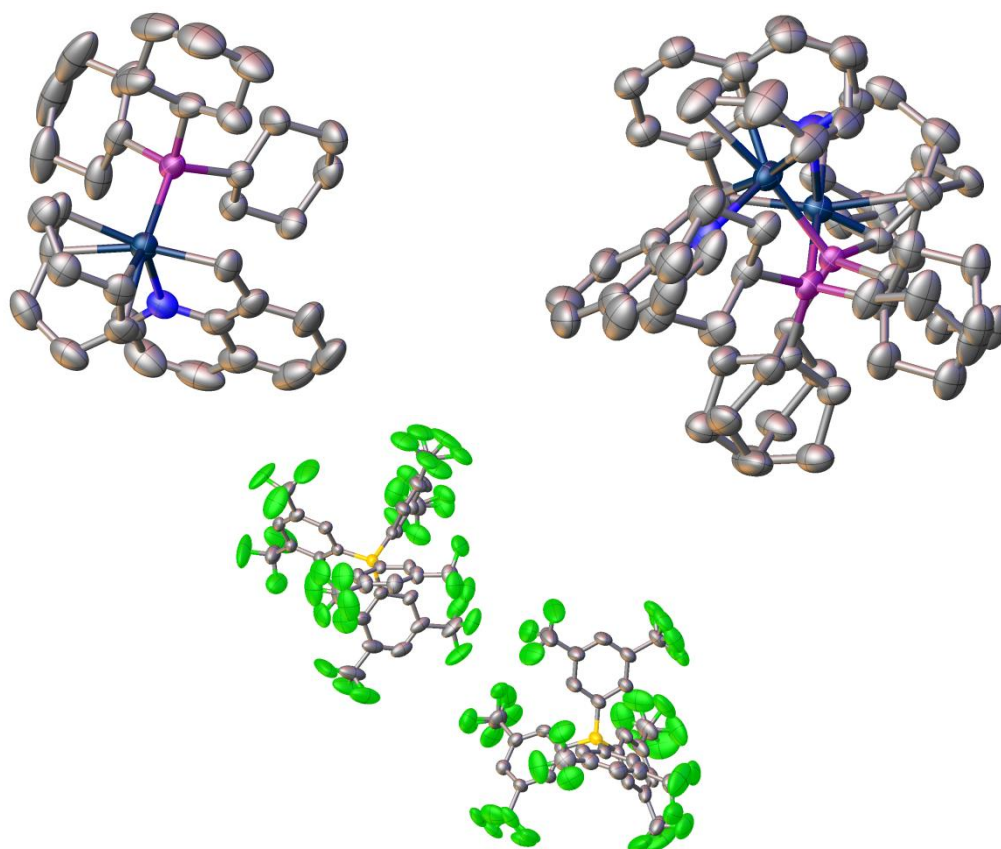


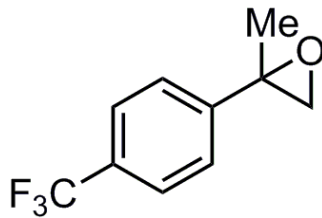
Figure 2 Ellipsoid representation (50 percent probability) of complex **5**, disordered complex **5** and the BAr_f ions.

Table 5 Crystal Data for complex 5

Compound	5
Formula	C ₃₂ H ₁₂ BF ₂₄ , C ₃₆ H ₅₄ Ir N P
Empirical formula	C ₆₈ H ₆₆ BF ₂₄ IrNP
Formula weight	1587.19
Temperature/K	180.15
Crystal system	triclinic
Space group	P-1
a/Å	13.42933(10)
b/Å	18.87158(14)
c/Å	27.7213(2)
α/°	77.2224(6)
β/°	88.4024(6)
γ/°	77.9371(6)
Volume/Å ³	6698.97(9)
Z	4
ρ _{calc} /mg/mm ³	1.574
m/mm ⁻¹	2.125
F(000)	3176.0
Crystal size/mm ³	0.4478 × 0.2515 × 0.1980
Radiation	Mo Kα (λ = 0.7107)
2θ range for data collection	2.982 to 52.626°
Index ranges	-16 ≤ h ≤ 16, -23 ≤ k ≤ 23, -34 ≤ l ≤ 34
Reflections collected	122524
Independent reflections	26772[R(int) = 0.0525]
Data/restraints/parameters	26772/815/2277
Goodness-of-fit on F ²	1.047
Final R indexes [I ≥ 2σ(I)]	R ₁ = 0.0591, wR ₂ = 0.1641
Final R indexes [all data]	R ₁ = 0.0624, wR ₂ = 0.1674
Largest diff. peak/hole / e Å ⁻³	3.38/-1.61

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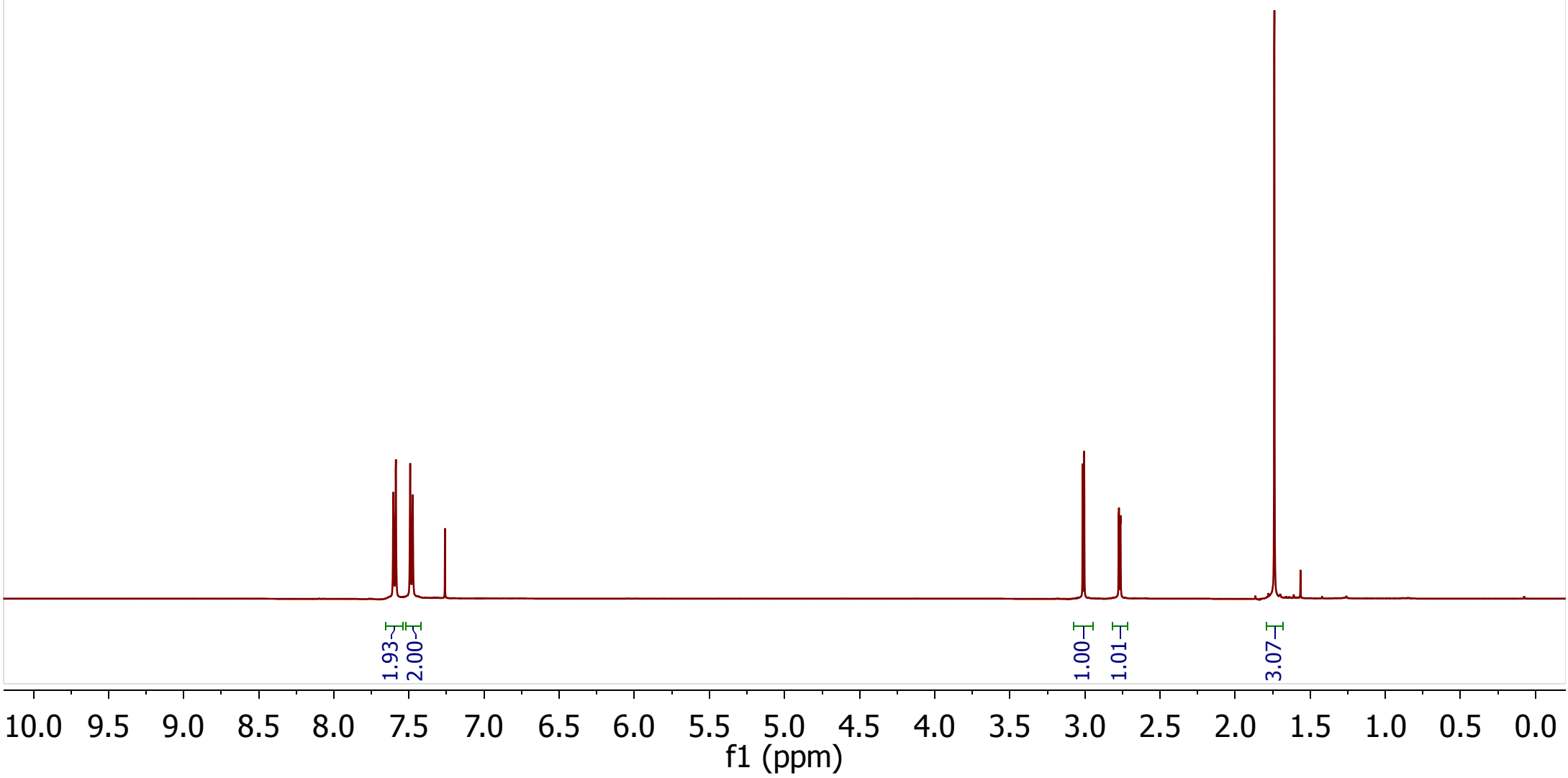
1n

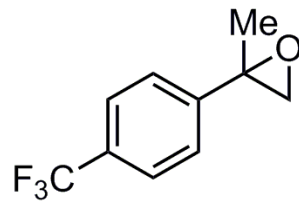
¹H NMR, 500 MHz, CDCl₃

7.61
7.60
7.59
7.59
7.59
7.49
7.49
7.49
7.48
7.47

3.02
3.00
2.78
2.77
2.76
2.76

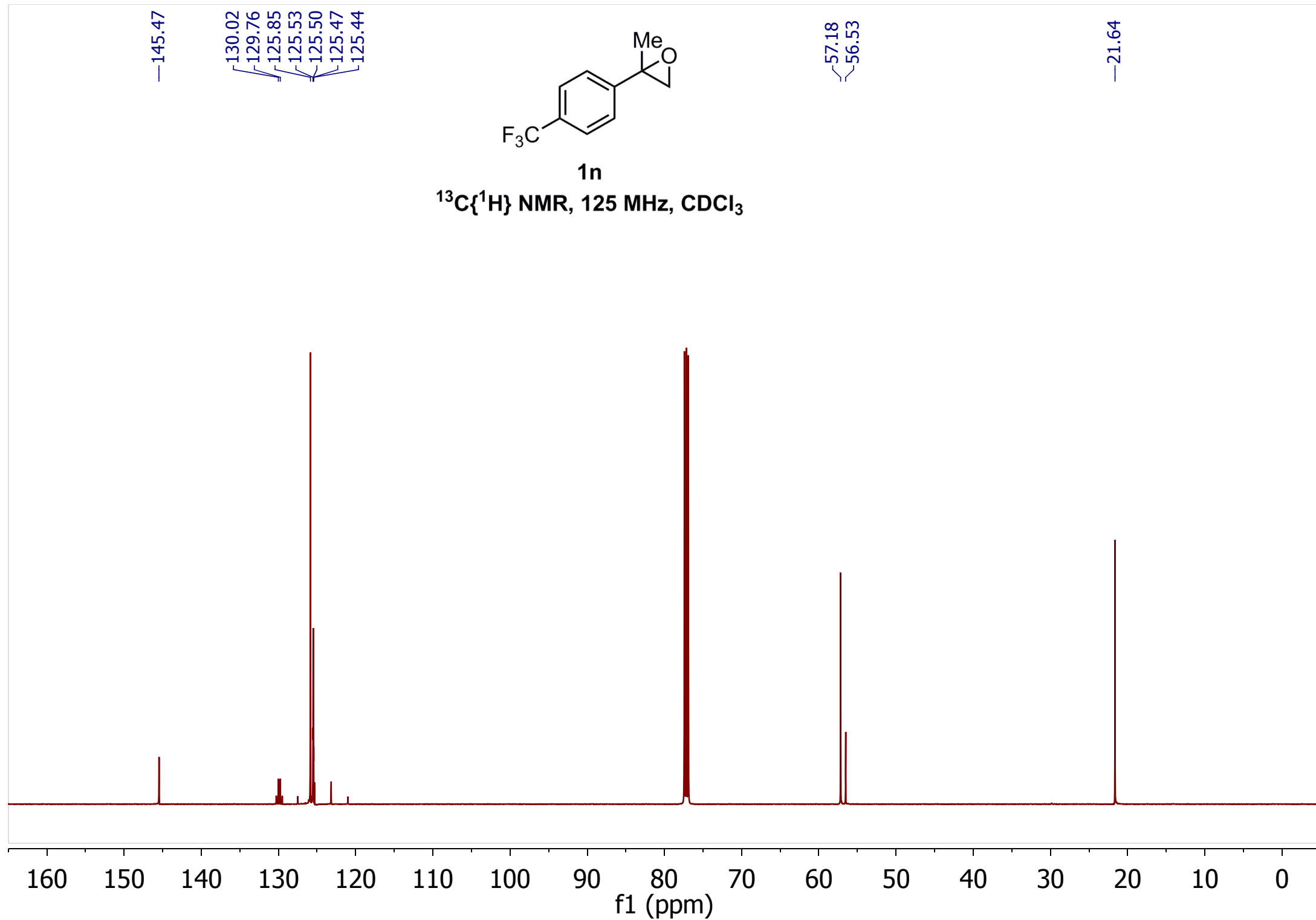
1.74
1.74

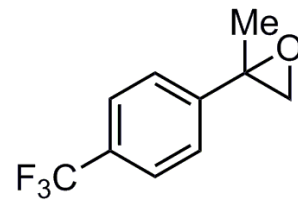




1n

$^{13}\text{C}\{^1\text{H}\}$ NMR, 125 MHz, CDCl_3





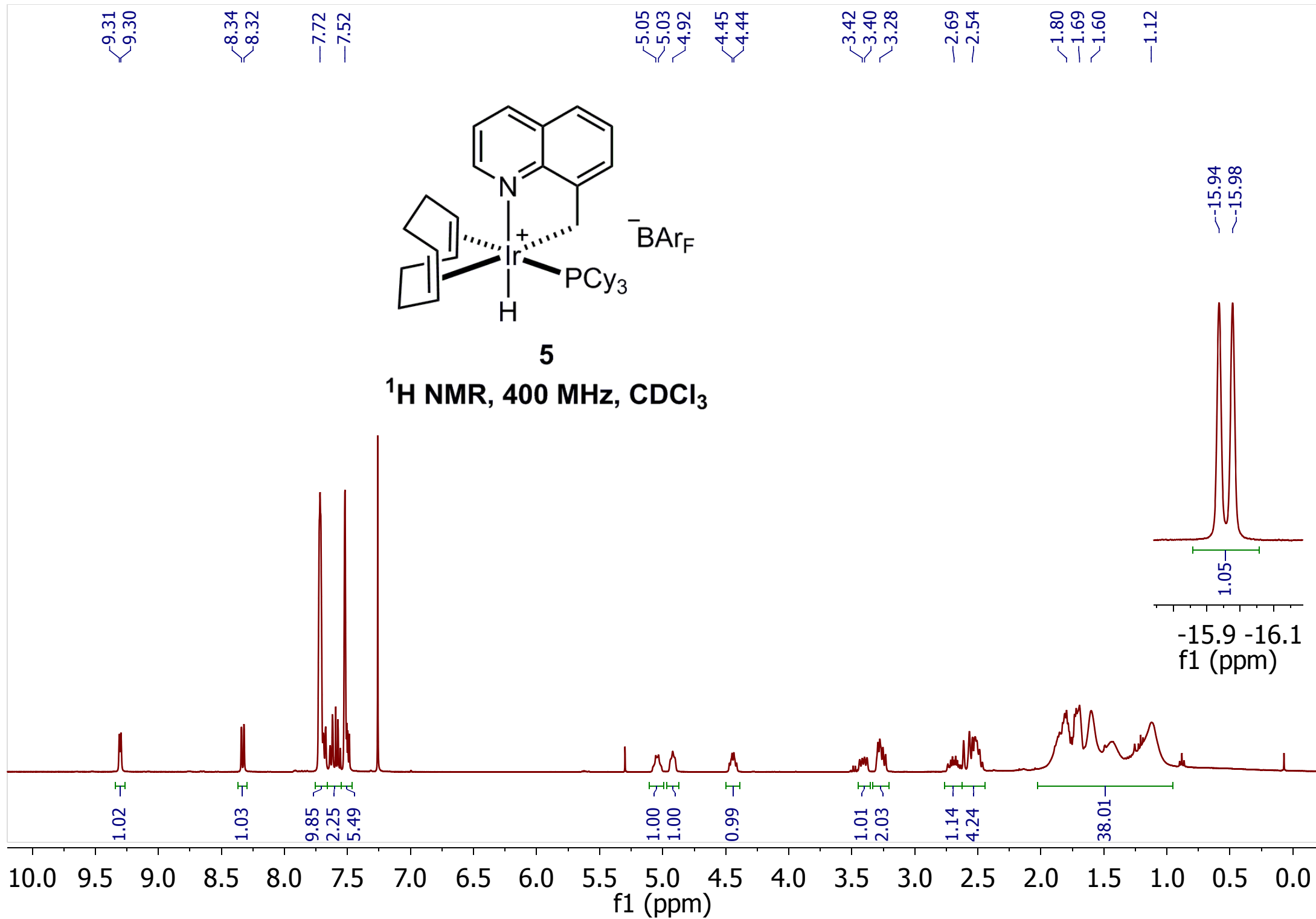
1n

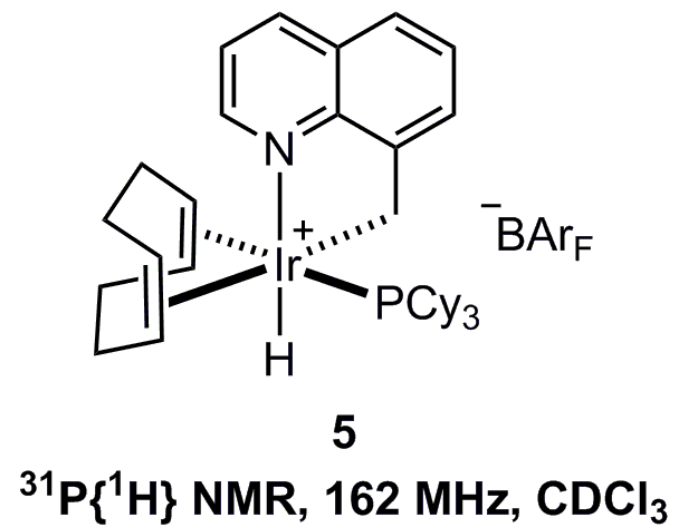
¹⁹F{¹H} NMR, 282 MHz, CDCl₃

---62.52

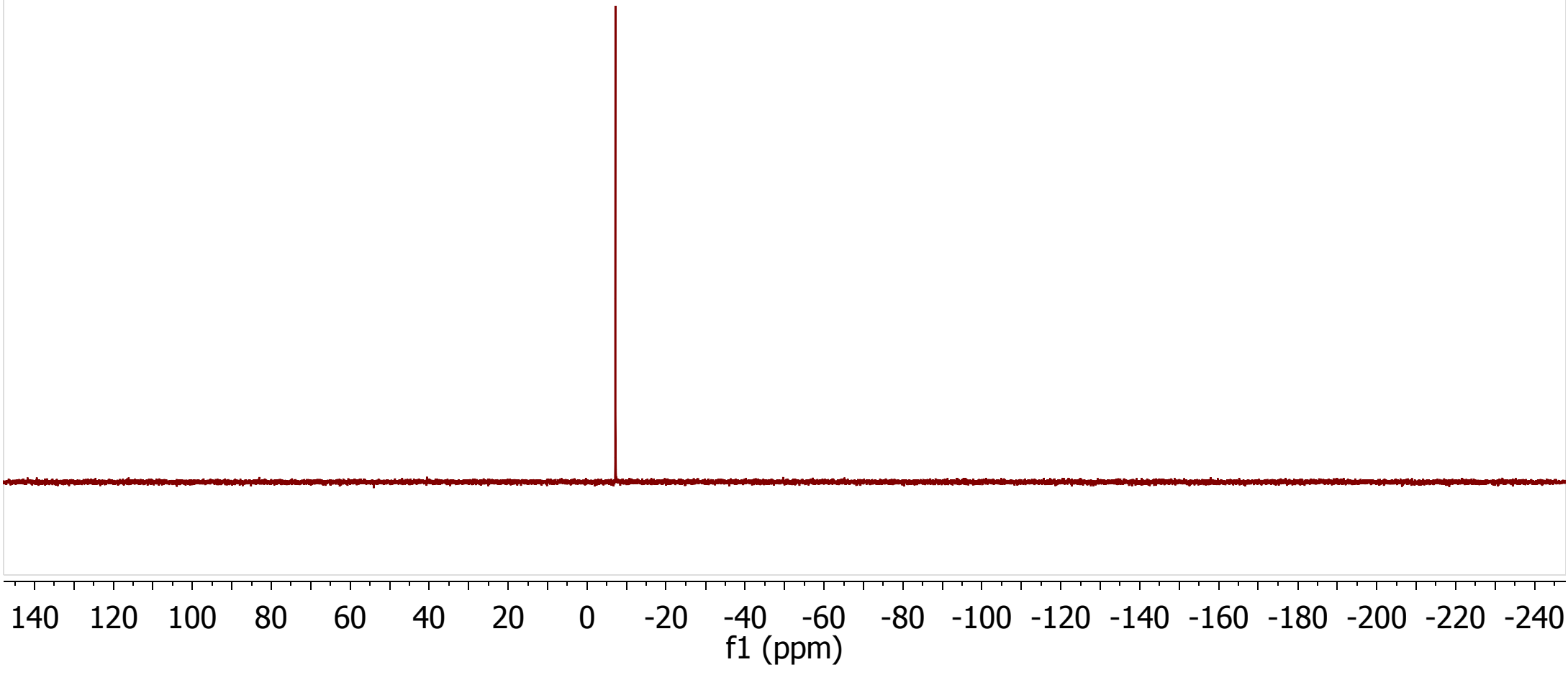


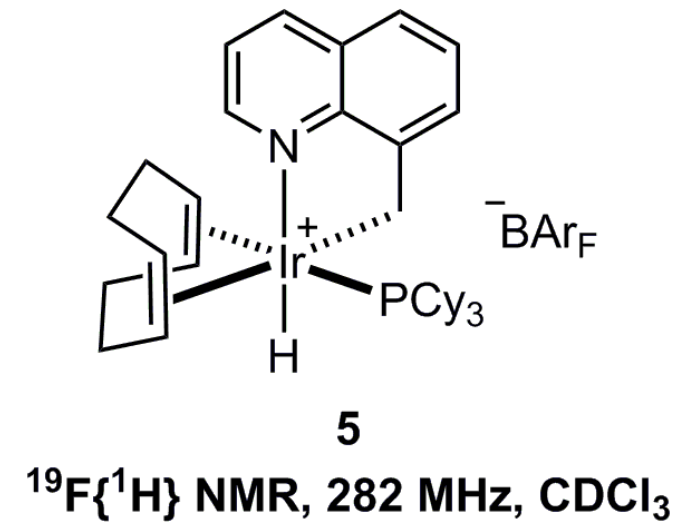
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)



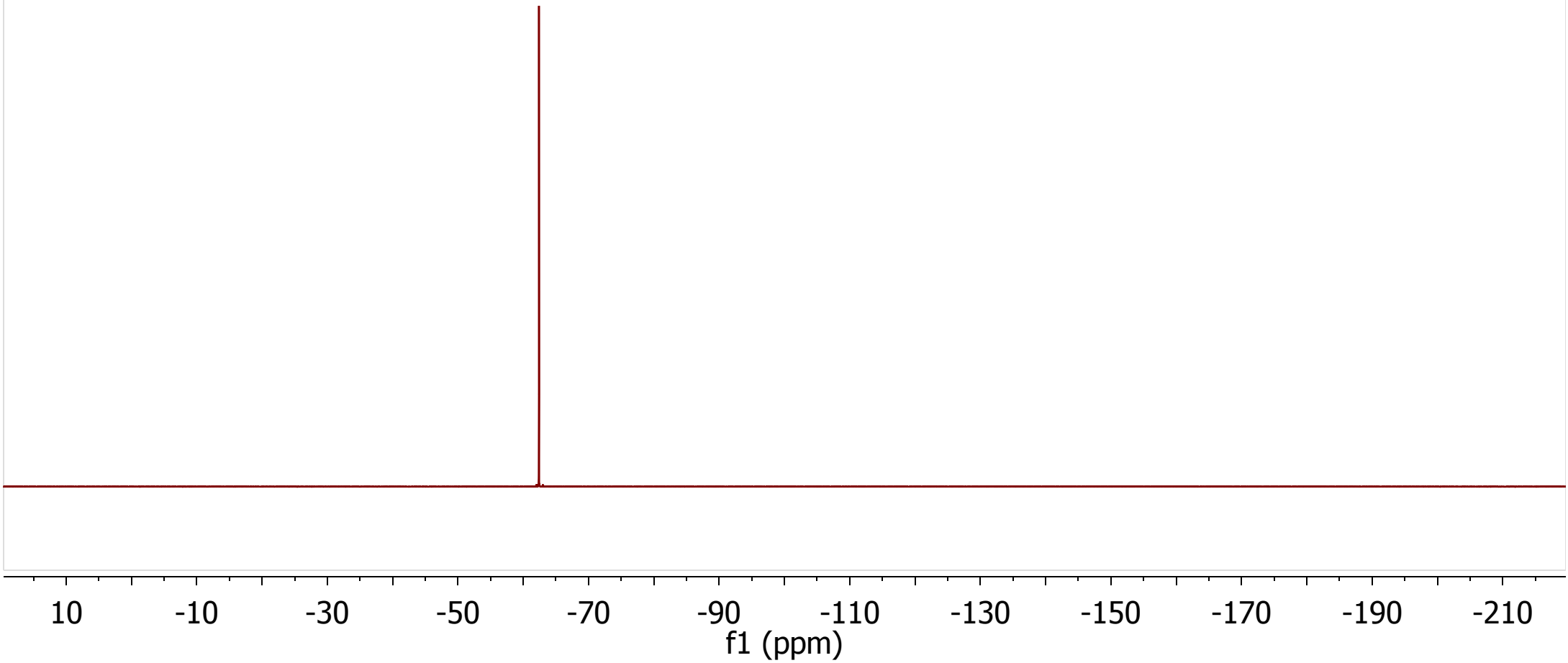


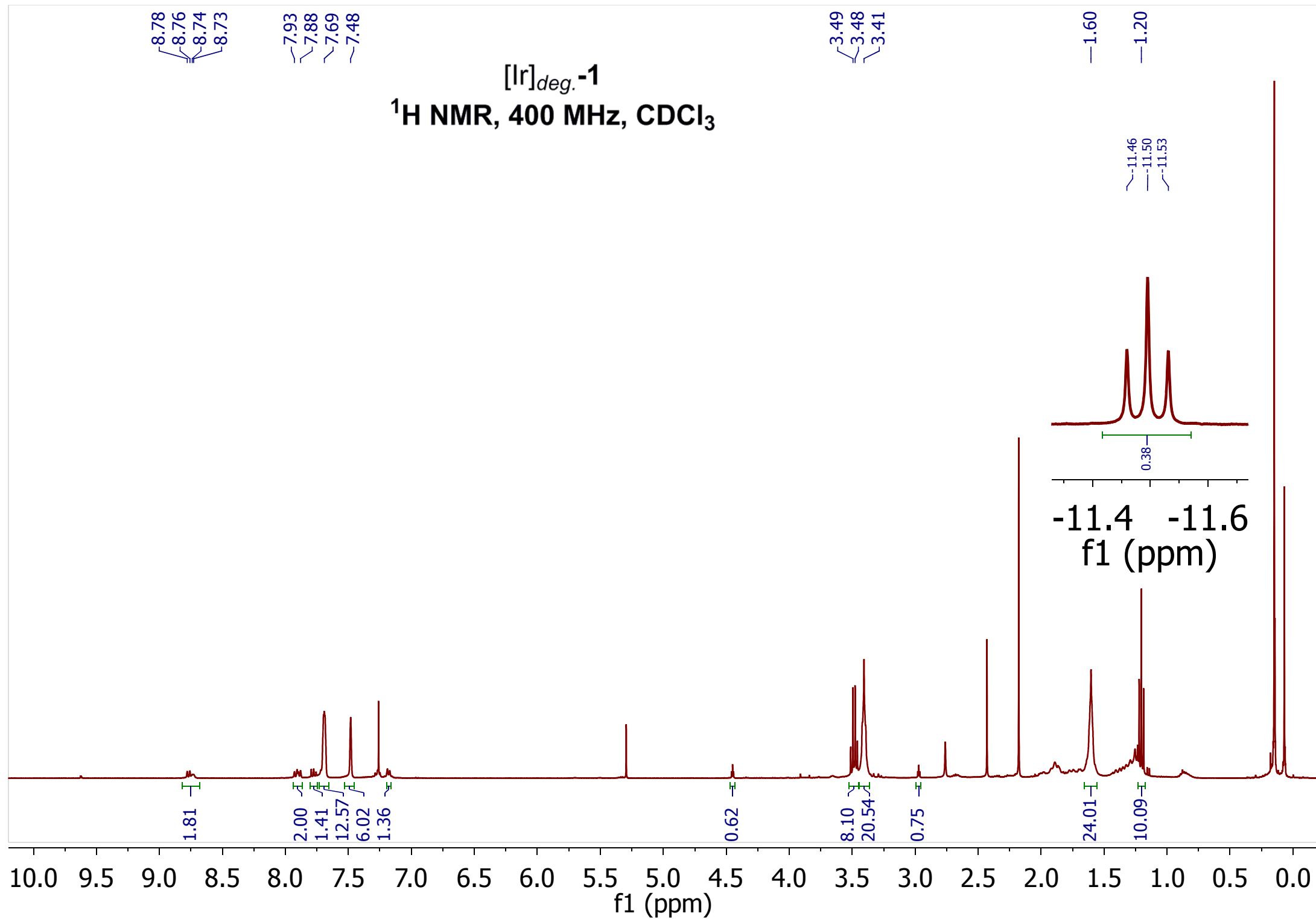
—7.16

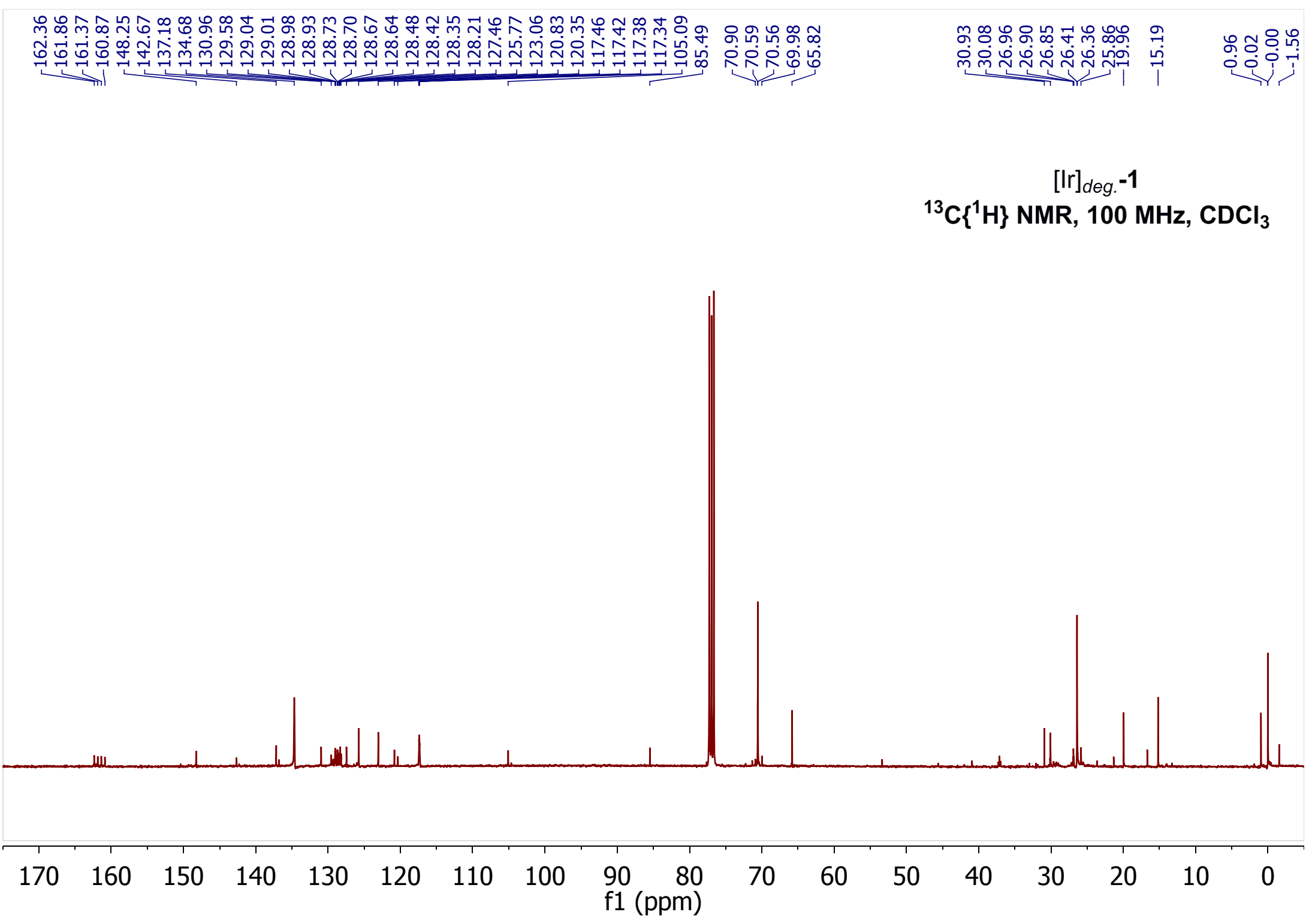




---62.40







$[lr]_{deg.}^{-1}$
 $^{31}\text{P}\{^1\text{H}\}$ NMR, 162 MHz, CDCl_3

—28.14

