

Kinetics and Mechanism of Isocyanide-Promoted Carbene Insertion into the Aryl Substituent of an *N*-Heterocyclic Carbene Ligand in Ruthenium-Based Metathesis Catalysts

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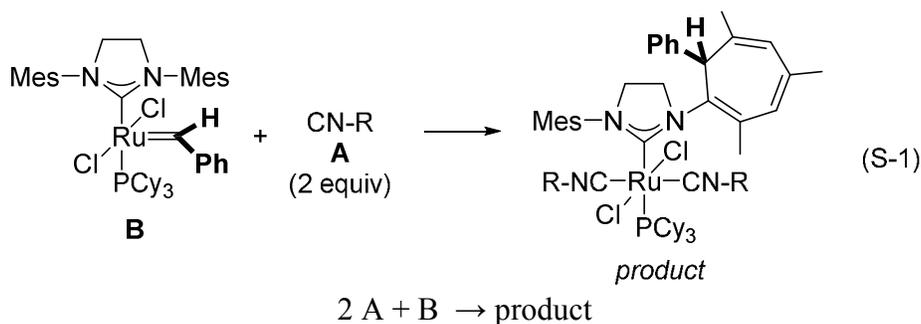
SUPPORTING INFORMATION

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Kinetic Treatment for Isocyanide-Promoted Buchner Reaction

The following kinetic treatment is derived for a second order reaction with the slow step being the initial binding of isocyanide. All steps to follow are assumed faster. This kinetic treatment applies to conditions in which the concentration of isocyanide is exactly twice that of the ruthenium carbene **3**. Plotting of $1/[A]_t$ vs. time give a straight line with the slope = k in $M^{-1} s^{-1}$.



$$\text{rate} = -\frac{1}{2} \frac{dA}{dt} = k[A][B]$$

Replace A with $a-x$, B with $b-(x/2)$ where $a=A_0$, $b=B_0$, and x = amount of A consumed

$$-\frac{1}{2} \frac{d(a-x)}{dt} = k(a-x) \left(b - \frac{x}{2}\right) = k(a-x) \frac{(2b-x)}{2} = \frac{1}{2} k(a-x)(2b-x)$$

or

$$-\frac{d(a-x)}{dt} = \frac{dx}{dt} = k(a-x)(2b-x)$$

If $a=2b$, then:

$$-\frac{d(a-x)}{dt} = \frac{dx}{dt} = k(a-x)^2$$

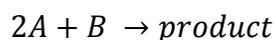
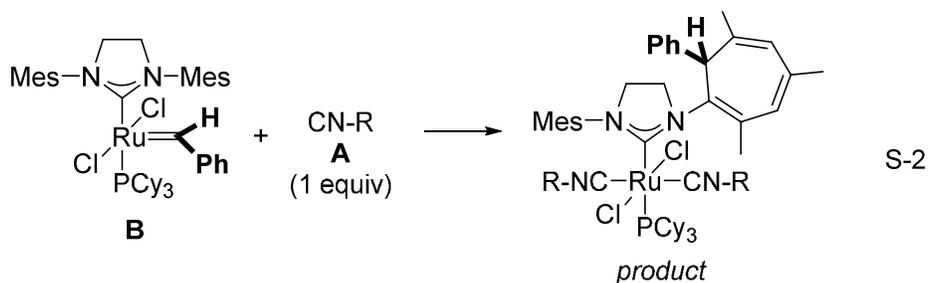
$$\int_0^x \frac{1}{(a-x)^2} dx = -\int_0^t k dt$$

$$= \frac{1}{-1(a-x)} \Big|_0^x = -kt$$

$$\text{Or } \frac{1}{a-x} - \frac{1}{a} = kt = \frac{1}{A} - \frac{1}{A_0} = kt$$

Kinetic Treatment for Determining Order of Reactants

In order to determine the order of each reactant, use of a modified kinetic treatment and alternative substrate concentrations was used. Assuming a first order dependence in both [isocyanide] and [3], using modified conditions (0.01 M 4-chlorophenyl isocyanide, 0.01 M 3, CH₂Cl₂, 0 °C) and plotting $\ln \left[\frac{2B_0 - x}{A_0 - x} \right]$ vs. time gives a line with slope = (2B₀-A₀)k. The slope of the line with units of s⁻¹ is then divided by (2B₀-A₀) to give *k* in M⁻¹ s⁻¹. If the reaction is indeed first order in [isocyanide]¹ and [3]¹ the *k* values would be identical to those obtained under the standard kinetic treatment (0.02 M 4-chlorophenyl isocyanide, 0.01 M 3). Indeed this is observed for the values listed in Table S1.



$$\text{rate} = -\frac{1}{2} \frac{dA}{dt} = k[A][B] = k(a-x) \left(b - \frac{x}{2} \right)$$

$$a = A(t = 0), b = B(t = 0)$$

$$-\frac{1}{2} \frac{d(a-x)}{dt} = k(a-x) \frac{(2b-x)}{2}$$

$$\text{Or } -\frac{dx}{dt} = k(a-x)(2b-x)$$

$$\text{Or } \int_0^x \frac{1}{(a-x)(2b-x)} dx = -\int_0^t k dt$$

$$\int \frac{dx}{u \cdot v} = \frac{1}{"k"} \log \frac{v}{u}$$

$$u = a + bx, v = c + dx, "k" = ad - bc$$

$$\frac{1}{2b-a} \ln \frac{2b-x}{(a-x)} \Big|_0^x = -kt$$

$$\frac{1}{2b-a} \left[\ln \frac{2b-x}{a-x} - \ln \frac{2b}{a} \right] = -kt$$

$$\text{or } \frac{1}{2b-a} \ln \left[\left(\frac{a}{2b} \right) \left(\frac{2b-x}{a-x} \right) \right] = -kt$$

$$x = A \text{ consumed}$$

$$\ln \left[\frac{2B_0 - x}{A_0 - x} \right] = (2B_0 - A_0)kt + \ln \frac{2B_0}{A_0}$$

$$\text{Plotting } \ln \left[\frac{2B_0 - x}{A_0 - x} \right] \text{ vs. time}$$

$$\text{Slope} = (2B_0 - A_0)k$$

Kinetic Data

4-Chlorophenyl Isocyanide

Performed according to the general procedure, 4-chlorophenyl isocyanide was reacted with **3**. The resulting data was plotted as $1/[\text{CNR}]_t$ to obtain k (shown in Table S1). A single product was observed.

Table S1. Kinetic Data for 4-Chlorophenyl Isocyanide with **3** in CH_2Cl_2 at 0°C .

Run	[Isocyanide], M	[3], M	k , ^a $\text{M}^{-1} \text{s}^{-1}$
1	0.02	0.01	2.94
2	0.02	0.01	3.15
3	0.02	0.01	3.14
4	0.02	0.01	2.70
5	0.02	0.01	3.04
6	0.02	0.01	3.18
7	0.02	0.01	2.50
8 ^b	0.01	0.01	2.89
9 ^b	0.01	0.01	2.57
10 ^b	0.01	0.01	2.47
11 ^b	0.01	0.01	2.50

Average			2.82(±0.29)
^a Error for the measurements is 5%. ^b Alternative kinetic treatment used to determine these values.			

4-Methoxyphenyl Isocyanide

Performed according to the general procedure, 4-methoxyphenyl isocyanide was reacted with **3**. The resulting data was plotted as $1/[\text{CNR}]_t$ to obtain k (shown in Table S2). A single product was observed, consistent with the reactivity observed for 4-chlorophenyl isocyanide.

Table S2. Kinetic Data for 4-Methoxyphenyl isocyanide Promoted Buchner Reaction

Run	[Isocyanide], M	[3], M	k , $\text{M}^{-1} \text{s}^{-1}$
1	0.02	0.01	1.35
2	0.02	0.01	1.59
3	0.02	0.01	1.30
Average			1.42(±0.12)
Conditions: 0.01 M 3 , CH_2Cl_2 , 0 °C, N_2 atm.			

NMR Studies

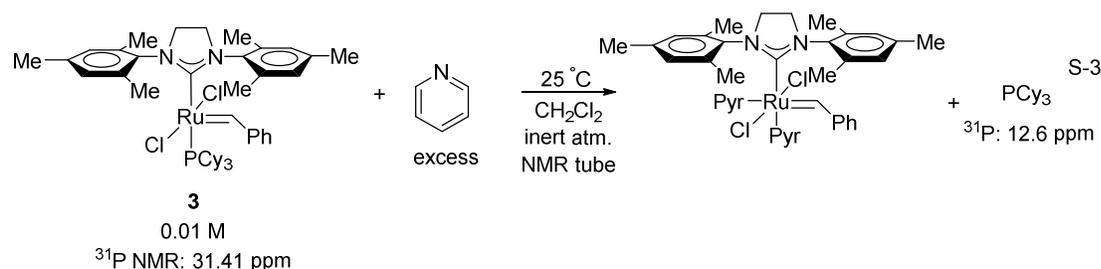
In an oven-dried screw cap NMR tube was added **3** (0.007 mmol) with 0.5 mL of CD_2Cl_2 under an inert atmosphere at 25 °C. Then mesitylene (0.007 mmol) was added. In one portion was added and isocyanide (0.021 mmol) in 200 μL of CD_2Cl_2 (total volume = 0.7 mL). The reaction was then analyzed by ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR tracking of cycloheptatriene and methylene resonances of the products and intermediates. This procedure was used for all NMR studies of the different isocyanides. The characteristic proton resonances used are indicated:

7d: δ 5.78 (s, 1 H, CH_{CHT}) and 5.57 (s, 1 H, CH_{CHT})

8d: δ 5.70 (s, 1 H, vinylic CH_{CHT}), 5.62 (s, 1 H, vinylic CH_{CHT}), and 4.88 (s, 1 H, benzylic methine)

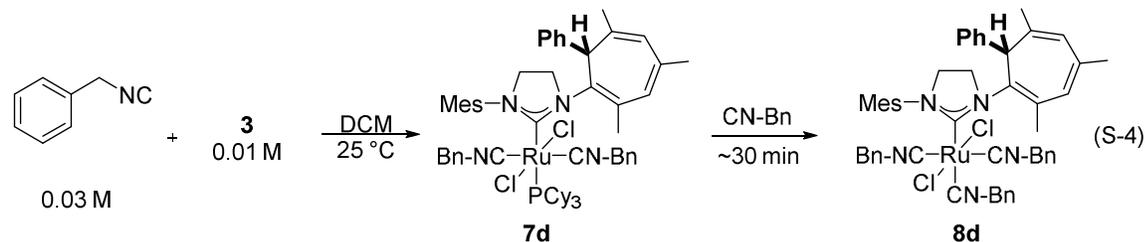
8f: δ 5.75 (s, 1 H, vinylic CH_{CHT}), 5.63 (s, 1 H, vinylic CH_{CHT}), 4.83 (s, 1 H, benzylic methine)

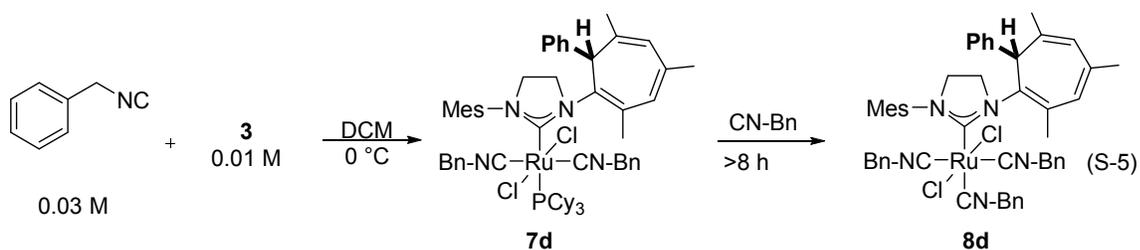
A simple ligand exchange reaction was used to confirm the presence of free tricyclohexylphosphine in solution (eq S-3). The phosphine species seen at 12.6 ppm is that of unbound PCy₃ which is ultimately extruded by ligand substitution.



Benzyl Isocyanide

Reactions with benzyl isocyanide ultimately produced a tris-isocyanide product **8d** (eq S-4). Analysis of different kinetic conditions using IR gave detailed information about the relative reactivity. Benzyl isocyanide promotes a rapid Buchner reaction and ligand exchange at 25 °C with complete reaction within 30 minutes. When cooled to 0 °C, the Buchner reaction still occurs; however, the secondary ligand exchange becomes drastically slower, taking longer than 8 h to go to completion (eq S-5).





Methyl Isocyanoacetate

Performed according to the general procedure, methyl isocyanoacetate was reacted with **3**. The resulting data were plotted as $1/[\text{CNR}]_t$ to obtain k (Table S3). The important observation from these data is that when performed at $0\text{ }^\circ\text{C}$ a product corresponding to $\text{Ru}(\text{NHC})\text{Cl}_2(\text{CNR})_2(\text{PCy}_3)$ is formed. Upon warming of the solution, decomposition and ligand exchange produces the tris-isocyanide product **8e**. The kinetic runs can still be used for determining the rate of the Buchner reaction and making meaningful comparisons to the data generated with aryl isocyanides.

Table S3. Kinetic Data for methyl isocyanoacetate Promoted Buchner Reaction

Run	$k, \text{M}^{-1}\text{s}^{-1}$
1	0.724
2	0.585
3	0.594
Average	0.63(\pm 0.08)
Conditions: 0.02 M methyl isocyanoacetate, 0.01 M 3 , CH_2Cl_2 , $0\text{ }^\circ\text{C}$	

As discussed earlier, the reaction of methyl isocyanoacetate and **3** at 25 °C produces product **8e** in about 4 h. Figure S1 provides a graphical representation of this reaction determined by in situ IR spectroscopy. Intermediate **7e** forms rapidly followed by a slow decay as the slower ligand substitution occurs. This plot has been converted to concentration vs. time, noting that the final maximum concentration of **8e** is 0.01 M as exact molar ratios are used for these reactions.

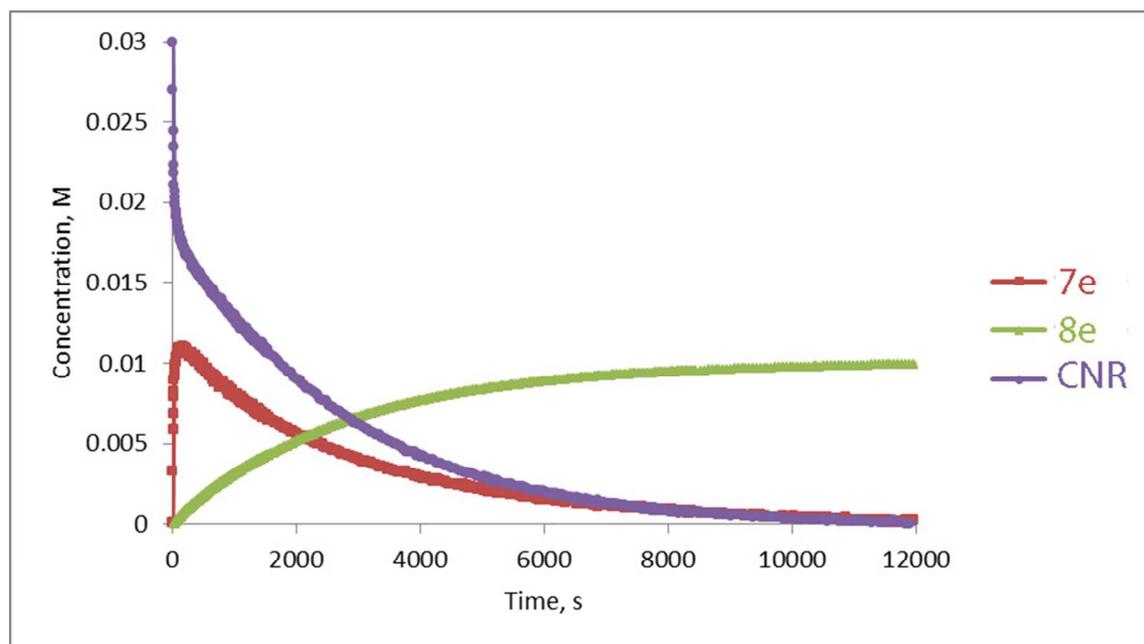
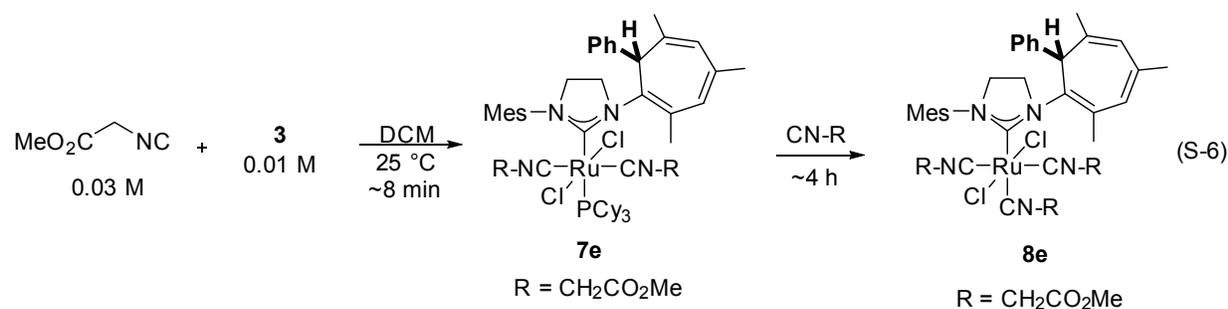


Figure S1. Plot of concentration vs. time for disappearance of methyl isocyanoacetate and formation of **7e** and **8e**.

Chromium Isocyanide Complexes

Complexes $\text{Cr}(\text{CO})_5(\text{CNR})$ have been prepared previously by reaction of the corresponding isocyanide with $\text{Cr}(\text{CO})_5(\text{THF})$, prepared by photolysis of $\text{Cr}(\text{CO})_6$ in THF solution.⁵ However, this method suffers from poor yields due to low photolytic conversion. We employed the reaction of trimethylamine oxide, which has been used previously to prepare $\text{Cr}(\text{CO})_5(\text{PR}_3)$.⁶

General Procedure

Reagents $\text{Cr}(\text{CO})_6$ (75 mg, 0.34 mmol), trimethylamine oxide dihydrate (38 mg, 0.34 mmol), and the isocyanide (0.34 mmol) were placed in a 50-mL Schlenk flask, equipped with magnetic stir bar, under an argon atmosphere. Then 10 mL of THF was added via syringe and the mixture was stirred. A bright yellow color change signified formation of $\text{Cr}(\text{CO})_5(\text{THF})$. The solution was stirred until the yellow color faded (ca. 3 h) or overnight. Then the solution was evaporated to dryness and the residue was purified by preparative TLC (silica, 10% CH_2Cl_2 in hexanes) the product was visualized by UV fluorescence and extracted with CH_2Cl_2 . Evaporation gave the product as colorless or very pale yellow solid.

$\text{Cr}(\text{CO})_5(\text{CNC}_6\text{H}_4\text{-4-Cl})$: Isolated as a colorless solid (72% yield). ^1H NMR (400 MHz, C_6D_6 , ppm): δ 6.60 (d, $^3J = 8.2$ Hz, 2 H, aromatic), 6.09 (d, $^3J = 8.2$ Hz, 2 H, aromatic). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, C_6D_6 , ppm): δ 216.48 (1 C, axial CO), 214.80 (4 C, equatorial CO), 134.64 (1 C, NC), 129.50 (2 C), 127.28 (2 C). IR (hexanes): 2133 (w, NC), 2051 (m, A_1''), 1966 (vs, A_1' , E) cm^{-1} . Previously reported, with spectral data measured for acetonitrile (IR) and THF (NMR) solutions.^{5b}

$\text{Cr(CO)}_5(\text{CNC}_6\text{H}_4\text{-4-OMe})$: Isolated as a colorless solid (76% yield). ^1H NMR (400 MHz, C_6D_6 , ppm): δ 6.53 (d, $^3J = 8.8$ Hz, 2 H, aromatic), 6.29 (d, $^3J = 8.8$ Hz, 2 H, aromatic), 3.10 (s, 3 H, methoxy). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, C_6D_6 , ppm): δ 217.16 (1 C, axial CO), 215.15 (4 C, equatorial CO), 159.94 (1 C, NC), 127.55 (2 C), 114.63 (2 C), 55.00 (1 C). IR (hexanes): 2138 (w, NC), 2057 (m, A_1''), 1962 (vs, A_1' , E) cm^{-1} .

$\text{Cr(CO)}_5(\text{CNCH}_2\text{CO}_2\text{Me})$: Isolated as a colorless solid (73% yield). ^1H NMR (300 MHz, C_6D_6 , ppm): δ 3.20 (s, 3 H, methoxy), 3.00 (s, 2 H, methylene). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, C_6D_6 , ppm): δ 217.02 (1 C, axial CO), 215.19 (4 C, equatorial CO), 168.41 (1 C, CN), 163.98 (1 C), 52.67 (1 C), 44.73 (1 C). IR (hexanes): 2163 (w, NC), 2064 (m, A_1''), 1961 (vs, A_1' , E), 1764 (w, C=O) cm^{-1} .

$\text{Cr(CO)}_5(\text{CNCH}_2\text{SO}_2\text{C}_6\text{H}_4\text{-4-Me})$: Isolated as a colorless solid (68% yield). ^1H NMR (300 MHz, C_6D_6 , ppm): δ 7.63 (d, $^3J = 8.1$ Hz, 2 H, aromatic), 6.80 (d, $^3J = 8.1$ Hz, 2 H, aromatic), 3.36 (s, 2 H, methylene), 1.84 (s, 3 H, methyl). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, C_6D_6 , ppm): δ 215.74 (1 C, axial CO), 214.44 (4 C, equatorial CO), 174.10 (1 C, NC), 146.55 (1 C), 133.05 (1 C), 130.35 (2 C), 129.24 (2 C), 62.20 (1 C), 21.23 (1 C). IR (dichloromethane): 2153 (w, NC), 2063 (m, A_1''), 1953 (vs, A_1' , E) cm^{-1} .

$\text{Cr(CO)}_5(\text{CNC}_8\text{H}_{17})$: Isolated as a colorless oil (72% yield). ^1H NMR (300 MHz, C_6D_6 , ppm): δ 2.46–2.28 (m, 2 H, aliphatic), 1.38–1.04 (m, 6 H, aliphatic), 0.99–0.87 (m, 9 H, aliphatic). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, C_6D_6 , ppm): δ 217.44 (1 C, axial CO), 215.60 (4 C,

equatorial CO), 160.63 (1 C, NC), 43.89 (1 C), 31.96 (1 C), 29.28 (1 C), 28.97 (1 C), 28.68 (1 C), 26.25 (1 C), 22.99 (1 C), 14.29 (1 C). IR (hexanes): 2166 (w, NC), 2065 (m, A₁''), 1957 (vs, A₁', E) cm⁻¹.

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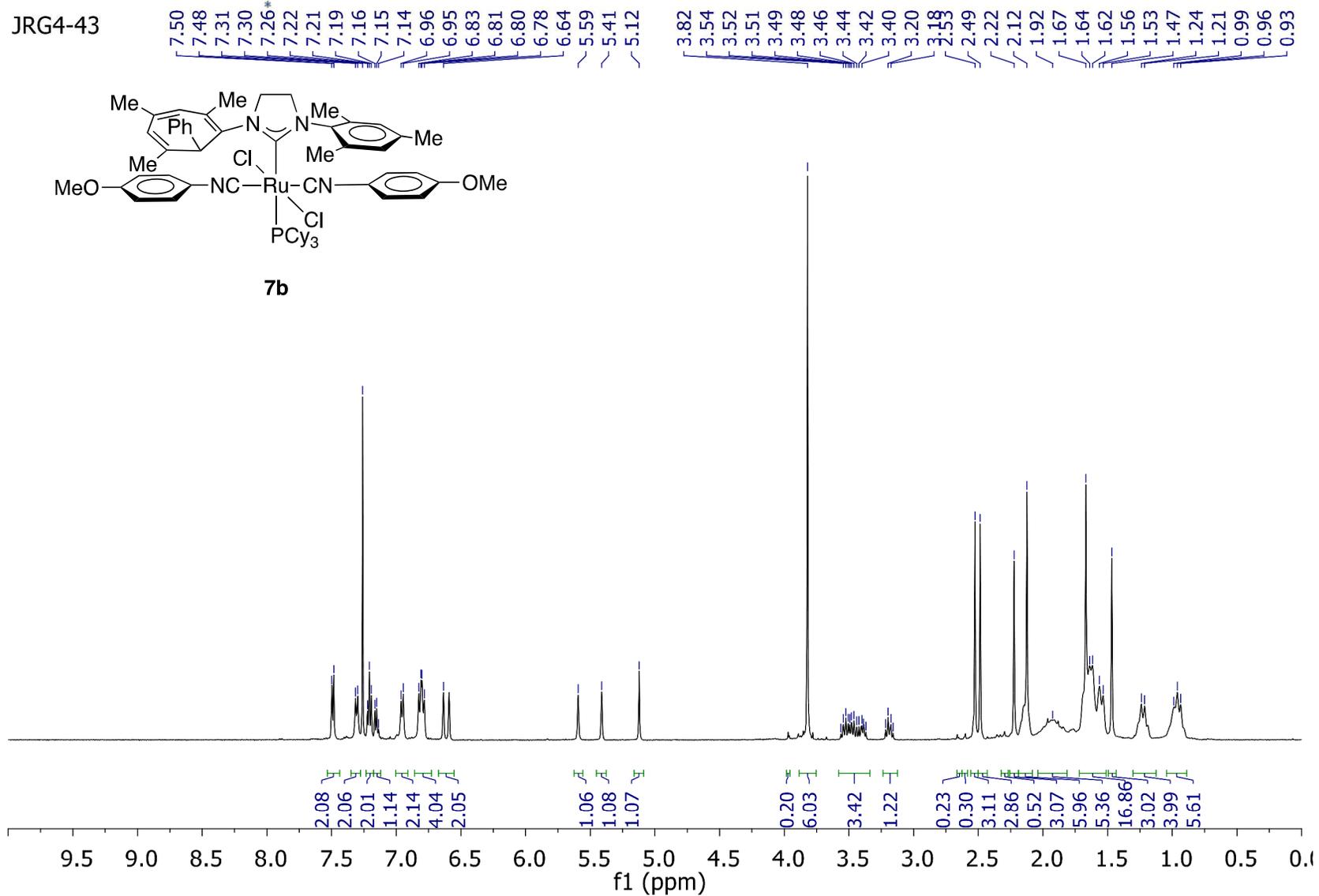


Figure S2. ¹H NMR spectrum of complex **7b** in CDCl₃. An asterisk marks solvent peak.

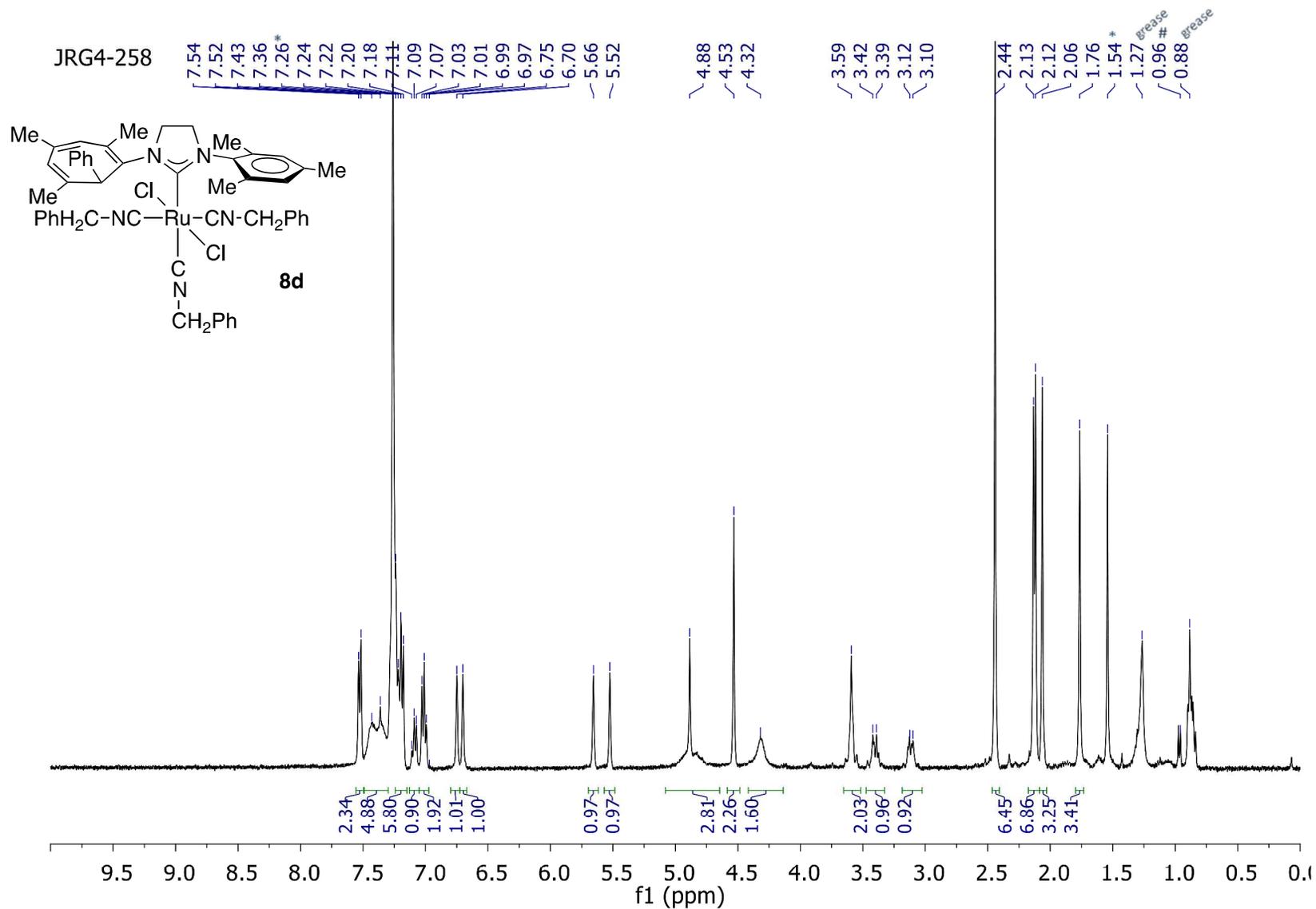


Figure S3. ¹H NMR spectrum of complex **8d** in CDCl₃. An asterisk marks solvent peak and H₂O; # is unidentified impurities.

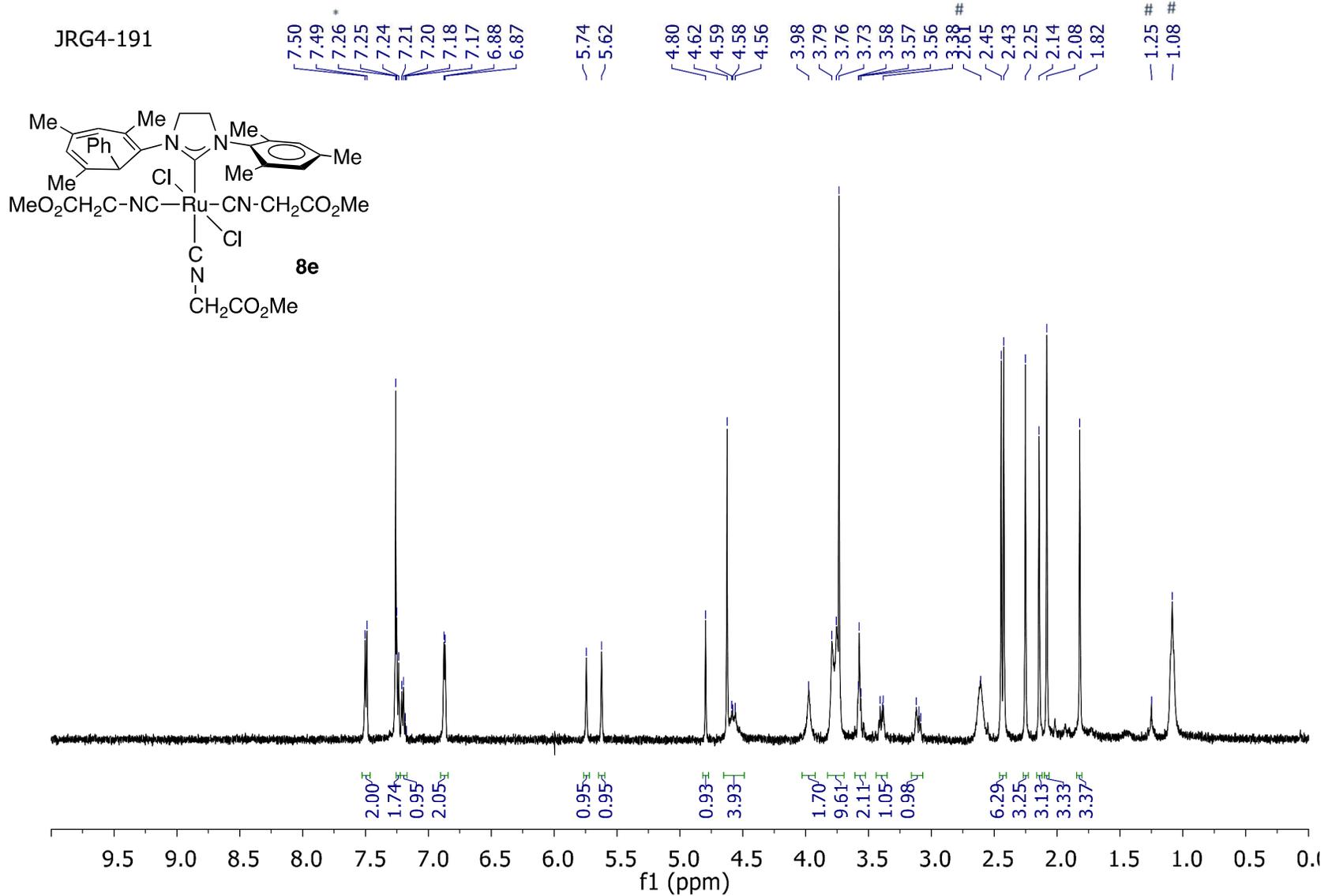
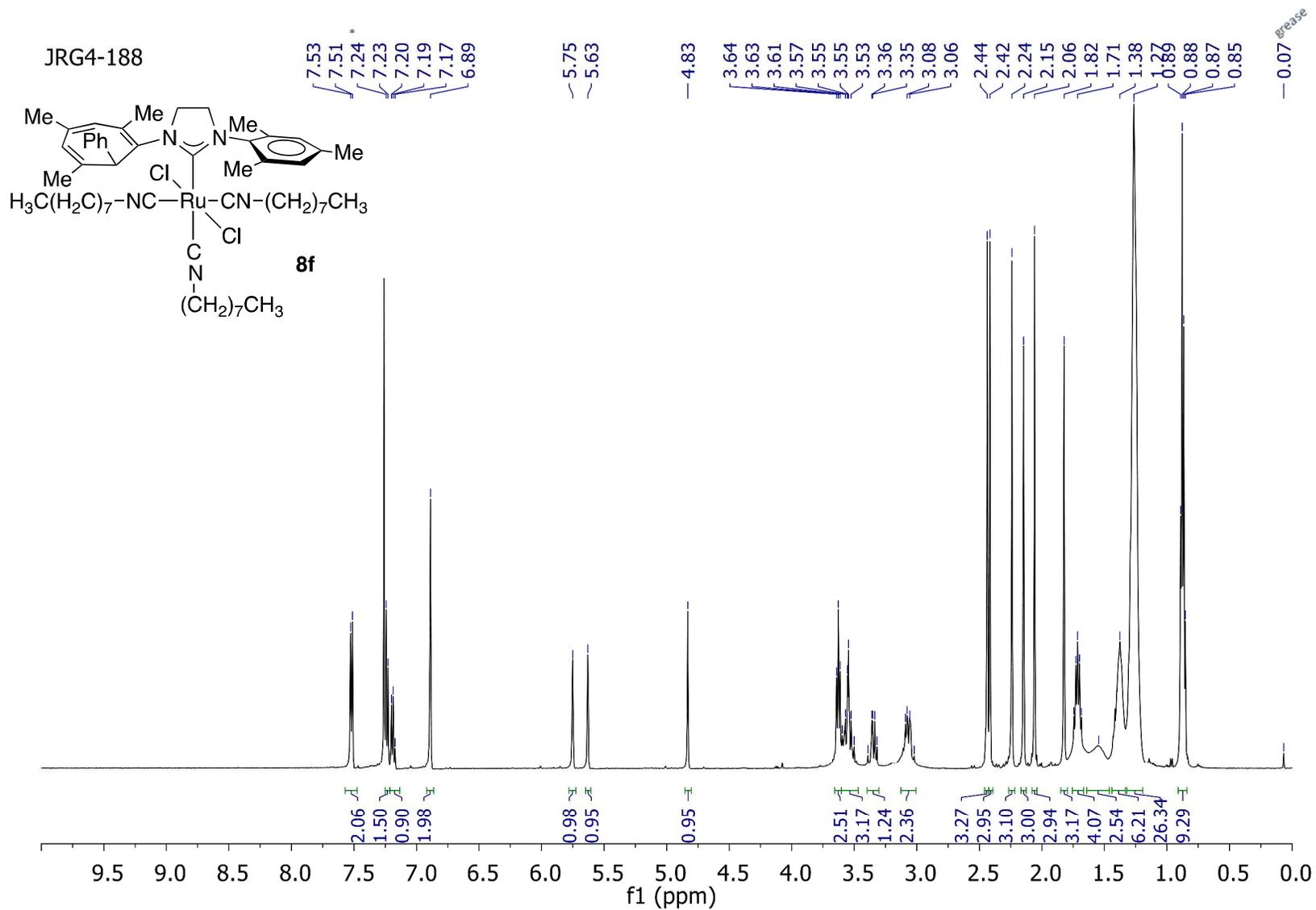


Figure S4. ¹H NMR spectrum of complex **8e** in CDCl₃. An asterisk marks solvent peak.



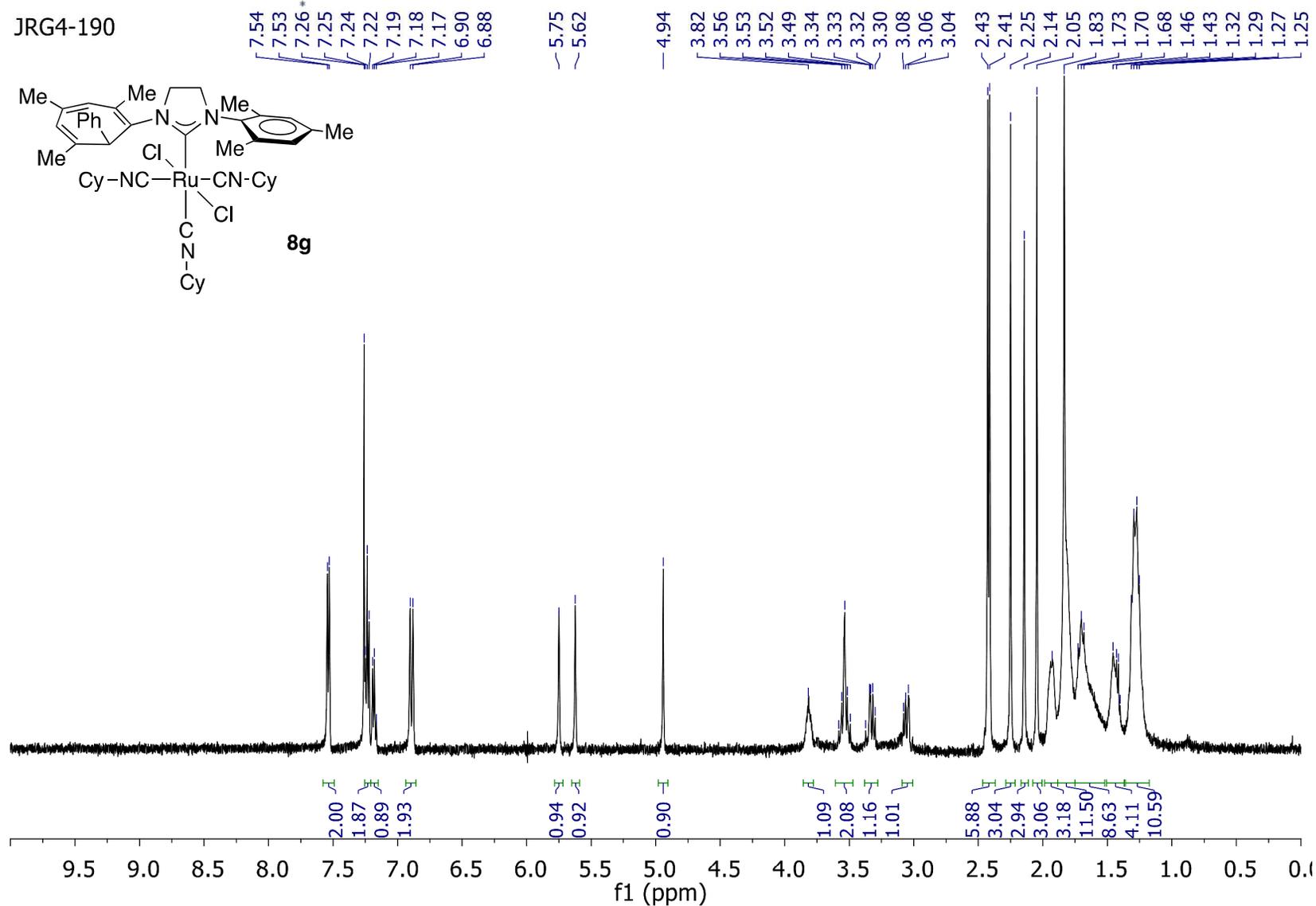


Figure S6. ^1H NMR spectrum of complex **8g** in CDCl_3 . An asterisk marks solvent peak.

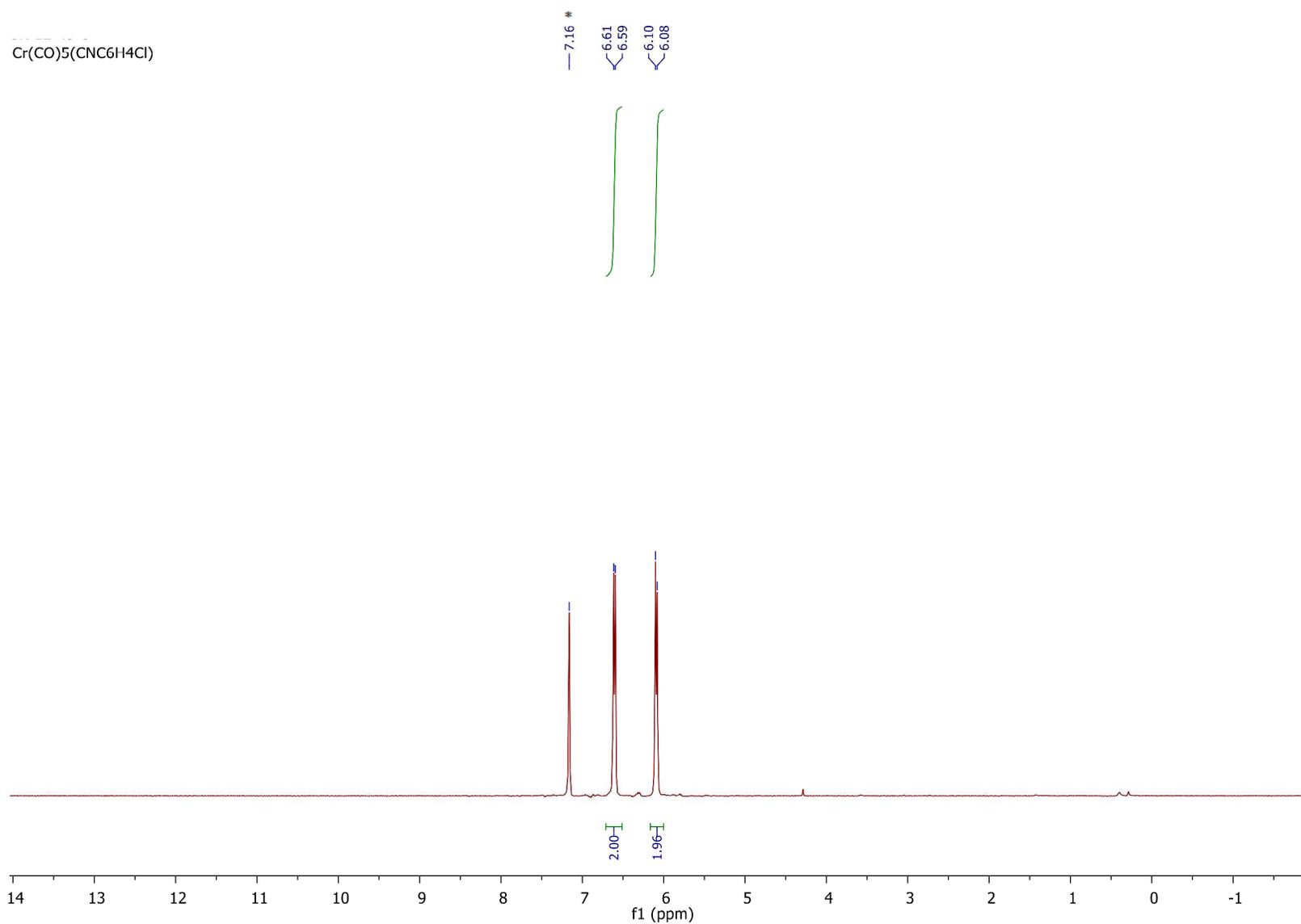


Figure S7. ^1H NMR spectrum of $\text{Cr}(\text{CO})_5(\text{CNC}_6\text{H}_4\text{Cl})$ in C_6D_6 . An asterisk marks solvent peak.

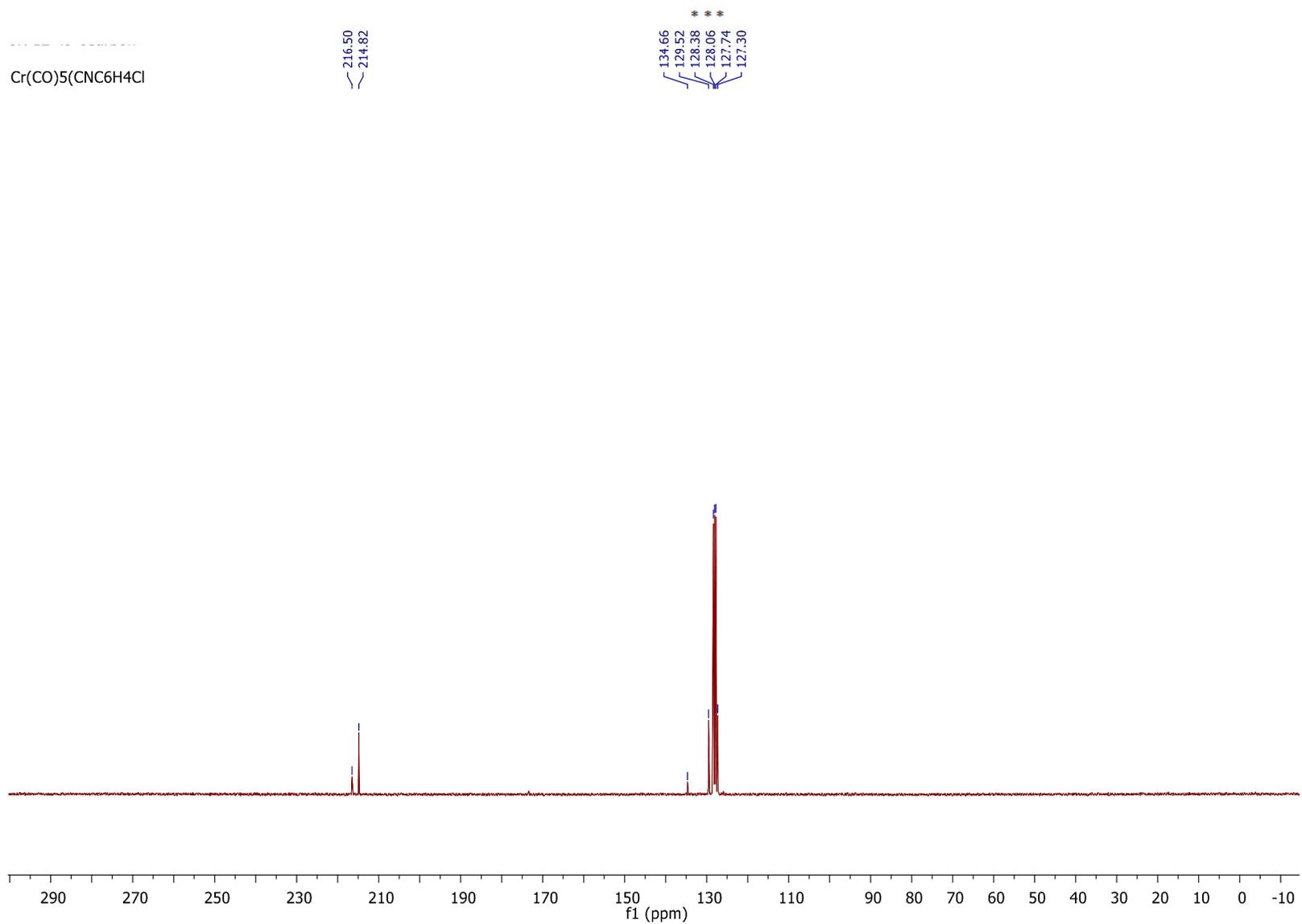


Figure S8. ¹³C NMR spectrum of Cr(CO)₅(CNC₆H₄Cl) in C₆D₆. An asterisk marks solvent peaks.

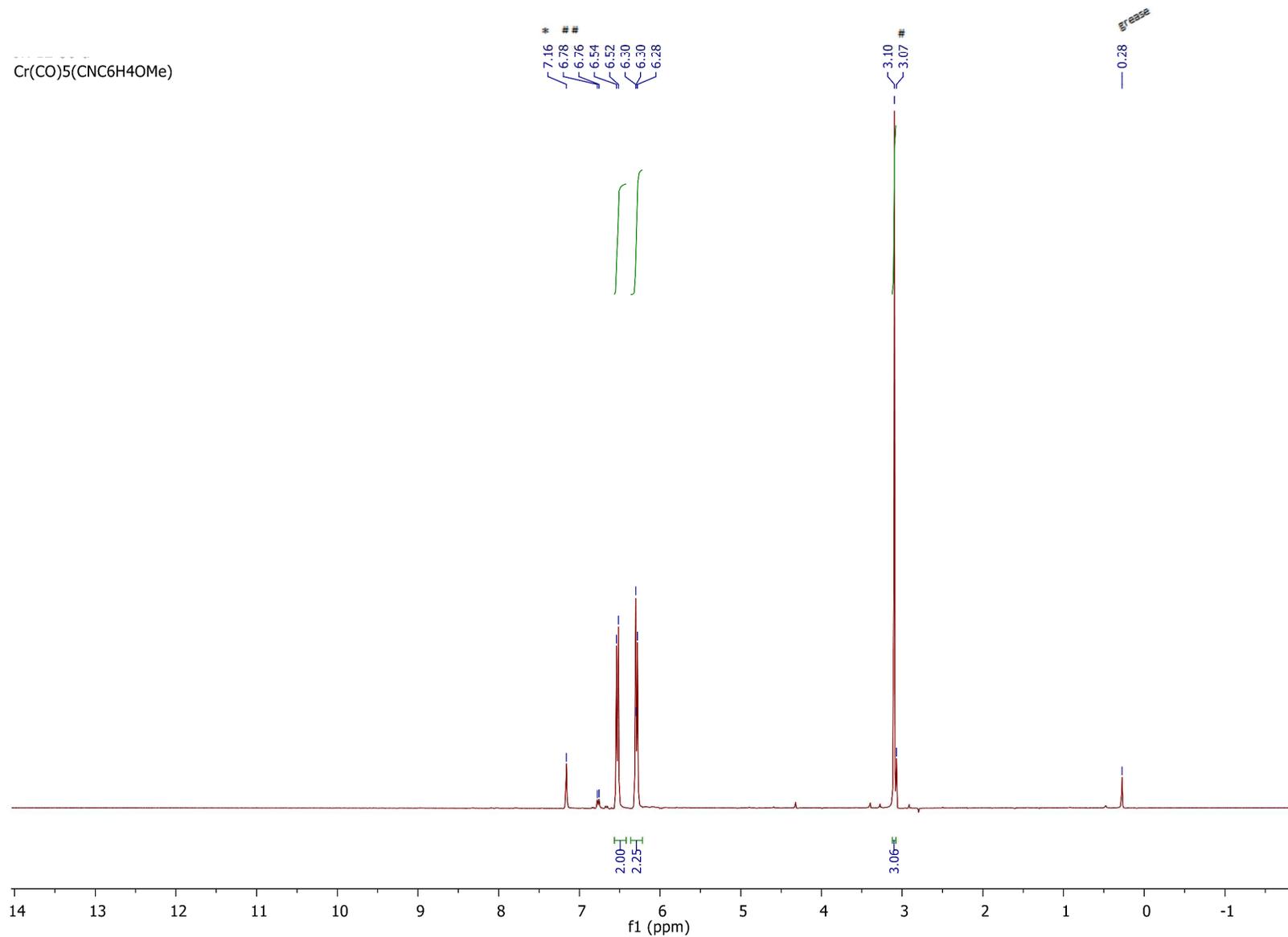


Figure S9. ¹H NMR spectrum of Cr(CO)₅(CNC₆H₄-4-OMe) in C₆D₆. An asterisk marks solvent peak and # marks impurities.

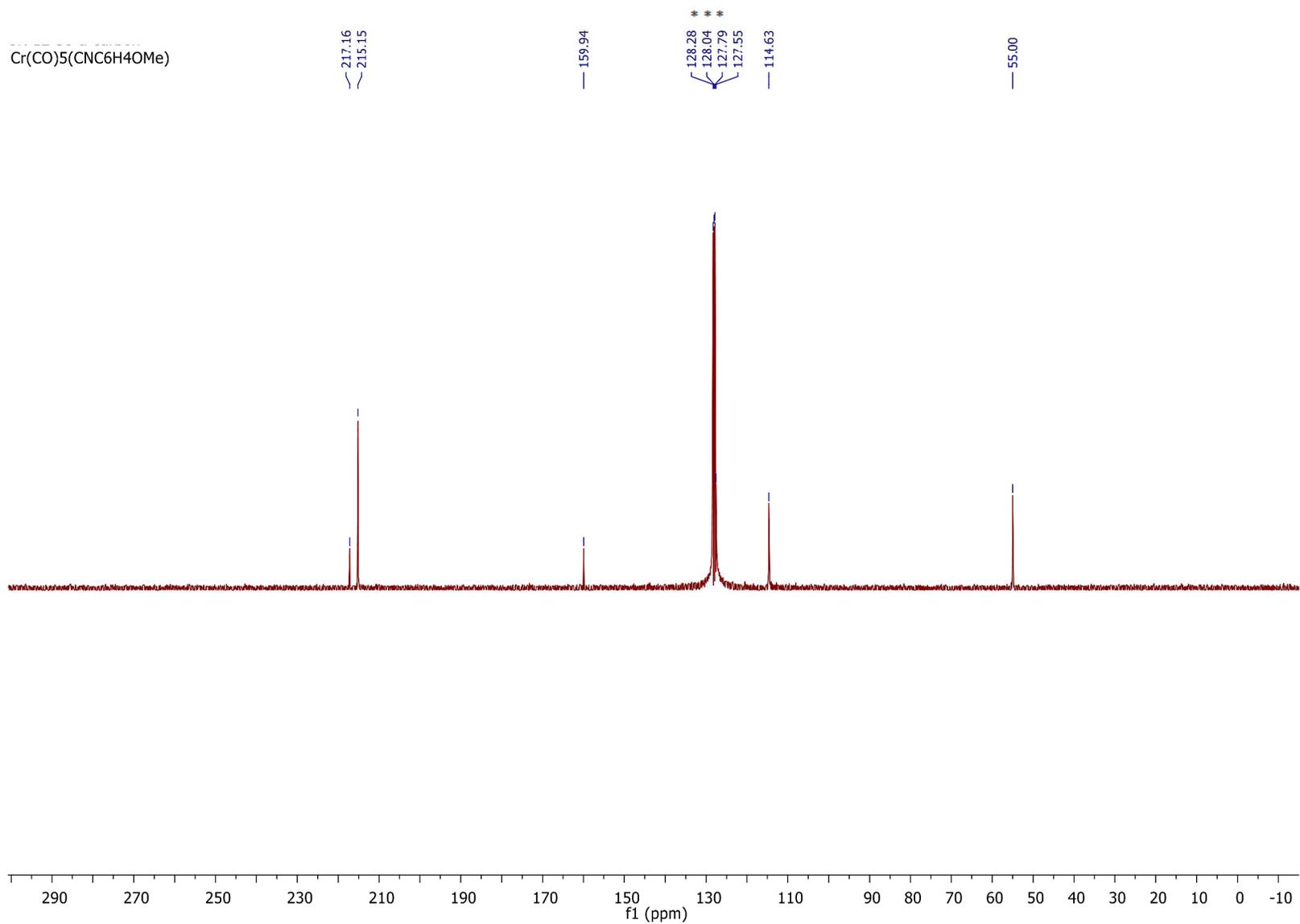


Figure S10. ¹³C NMR spectrum of Cr(CO)₅(CNC₆H₄-4-OMe) in C₆D₆. Asterisks mark solvent peaks.

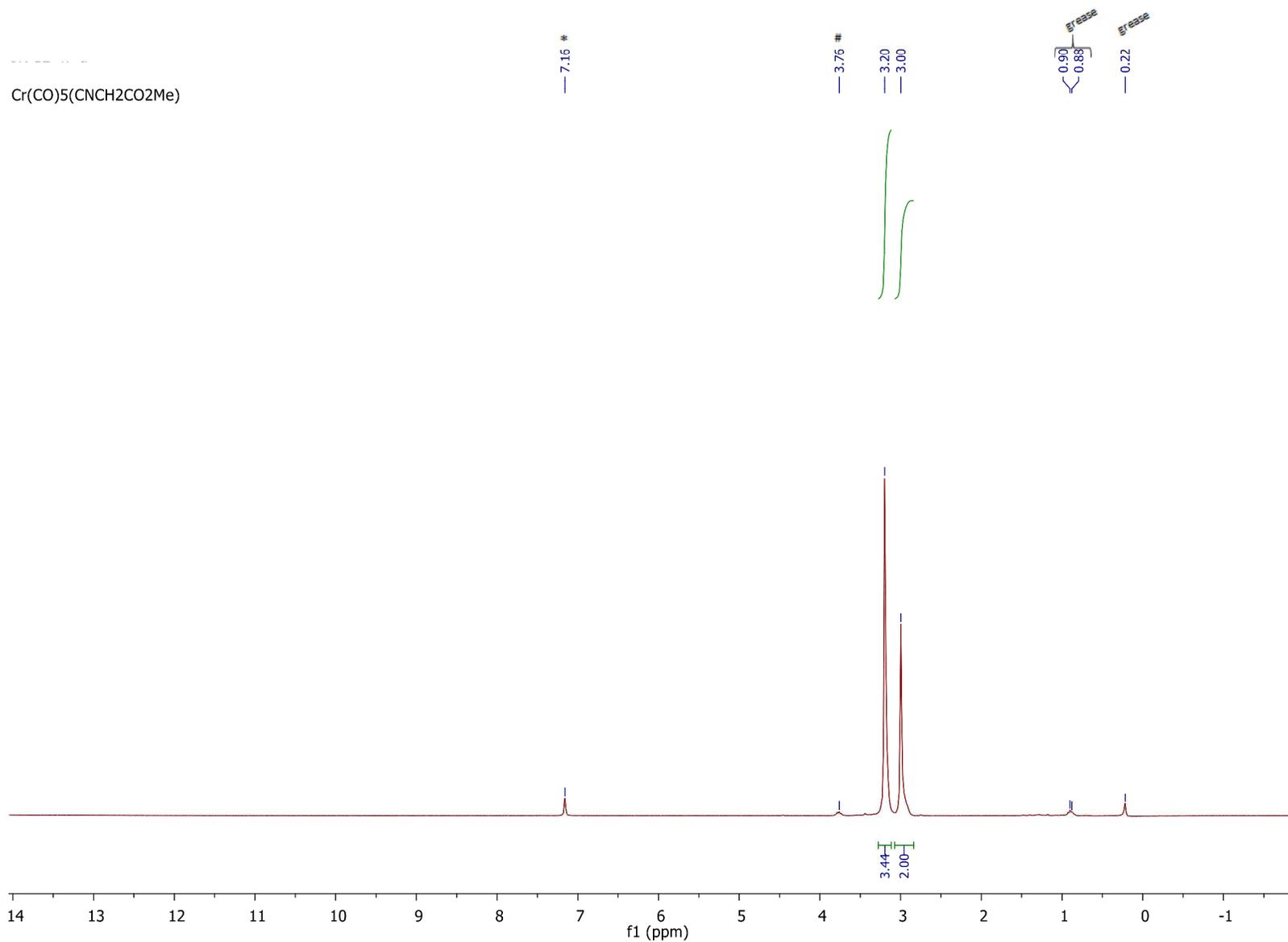


Figure S11. ¹H NMR spectrum of Cr(CO)₅(CNCH₂CO₂Me) in C₆D₆. An asterisk marks solvent peak and # marks impurities.

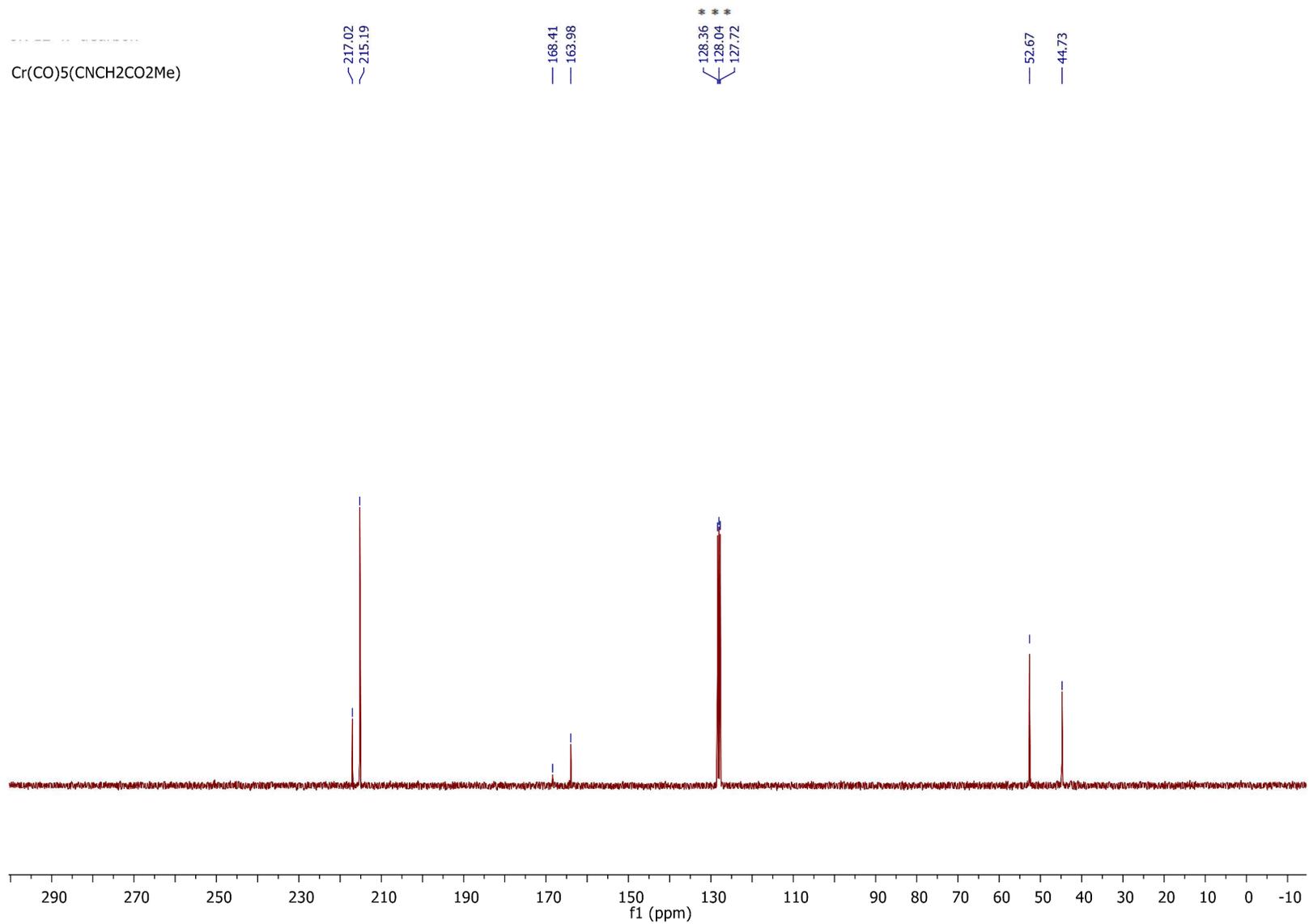


Figure S12. ¹³C NMR spectrum of Cr(CO)₅(CNCH₂CO₂Me) in C₆D₆. Asterisks mark solvent peaks.

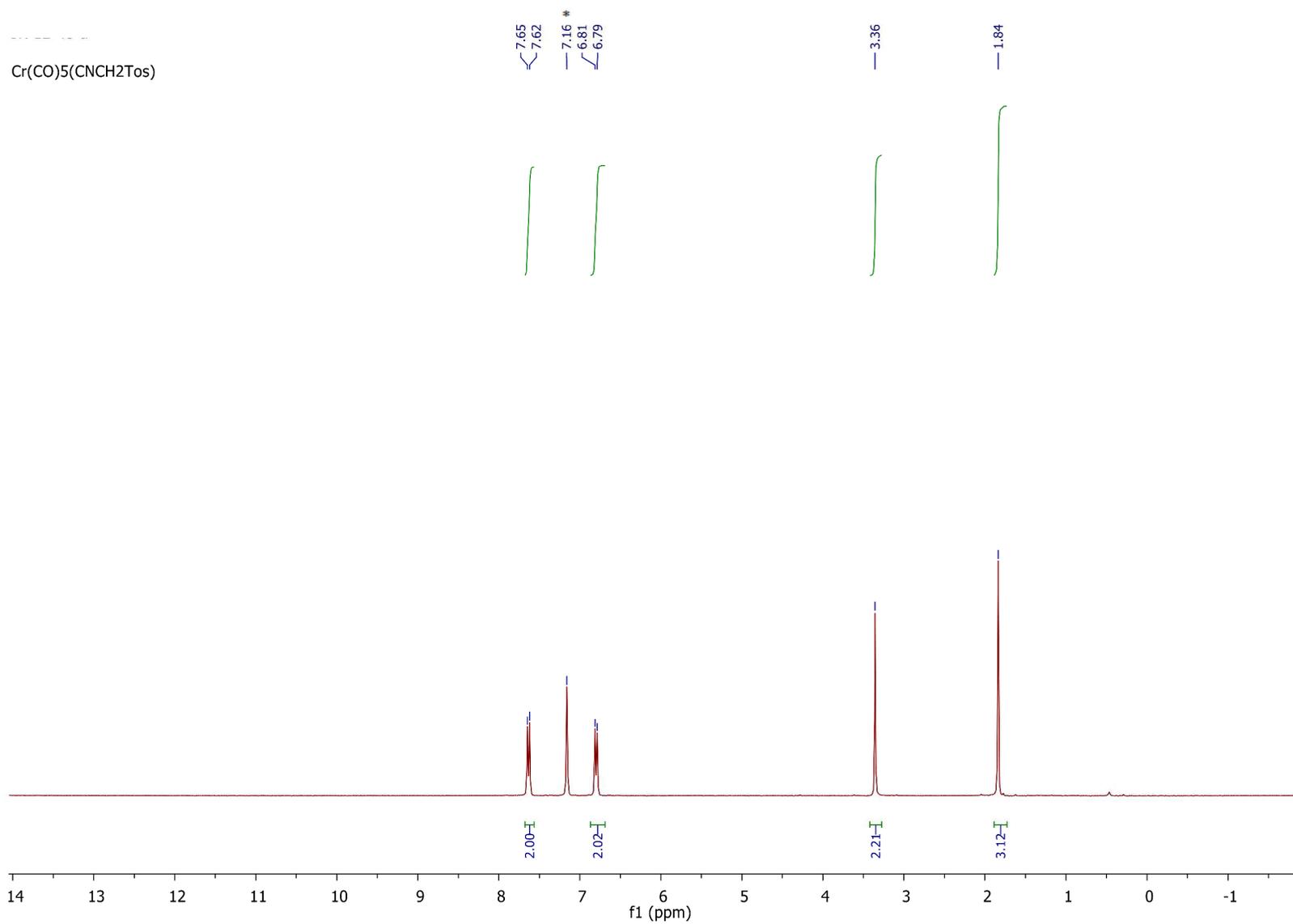


Figure S13. ¹H NMR spectrum of Cr(CO)₅(CNCH₂SO₂C₆H₄-4-Me) in C₆D₆. An asterisk marks solvent peak.

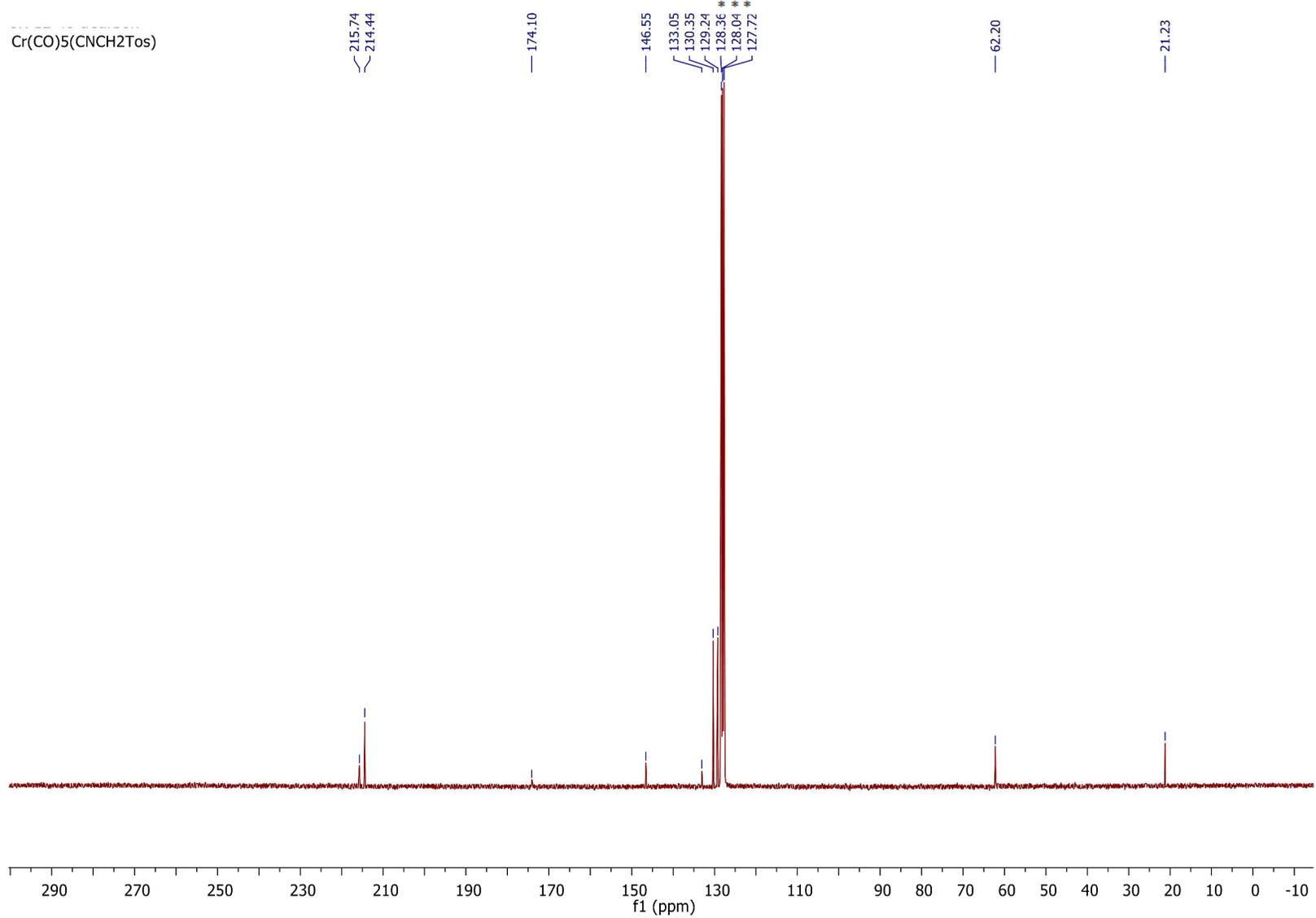


Figure S14. ^{13}C NMR spectrum of $\text{Cr}(\text{CO})_5(\text{CNCH}_2\text{SO}_2\text{C}_6\text{H}_4\text{-4-Me})$ in C_6D_6 . Asterisks mark solvent peaks.

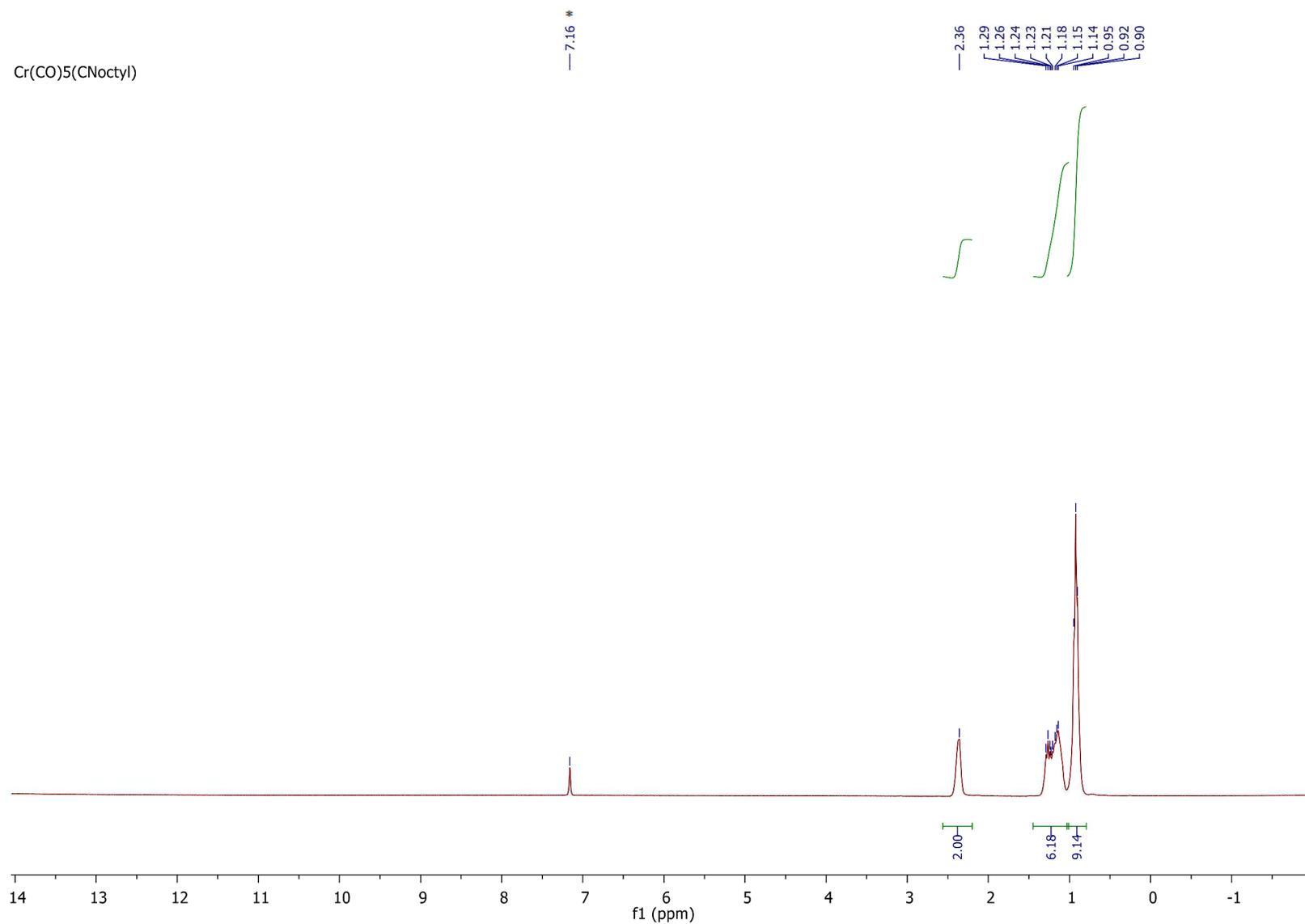


Figure S15. ¹H NMR spectrum of Cr(CO)₅(CNC₈H₁₇) in C₆D₆. An asterisk marks solvent peak.

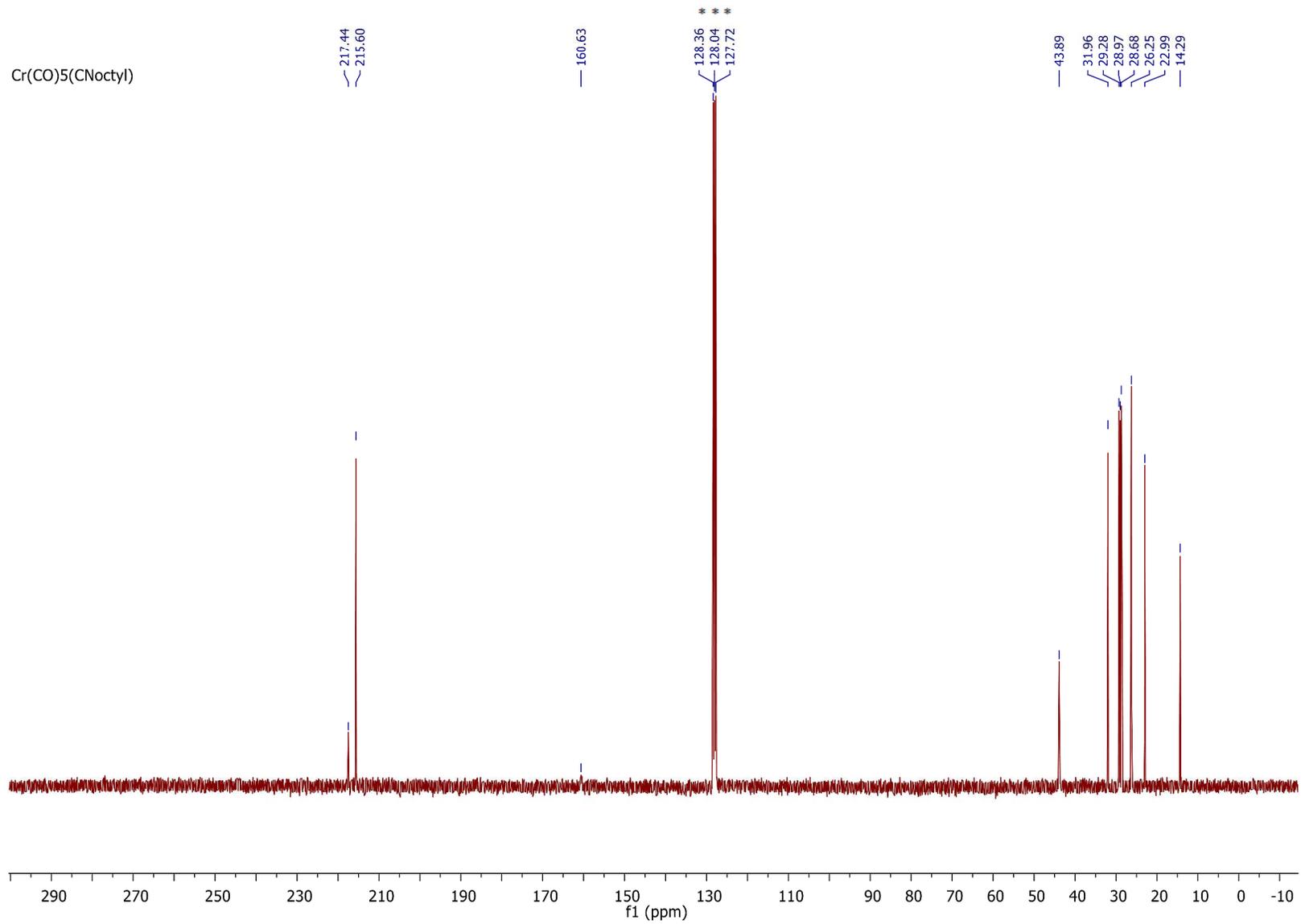


Figure S16. ¹H NMR spectrum of Cr(CO)₅(C₈H₁₇) in C₆D₆. Asterisks mark solvent peaks.