

Oxidative C-N coupling of azoles with cycloheptatriene using an Oxoammonium Salt Bearing the Nitrate Anion

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SUPPORTING INFORMATION

General Considerations.....	2
Chemicals	2
General procedure for the preparation of 1-(cyclohepta-2,5,6-trien-1-yl)azoles	2
Product Characterization	3
References	4
¹ H-, ¹³ C-NMR Spectra of Synthesized Compounds.....	5
¹ H-NMR (400 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7a)	5
¹³ C-NMR (101 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7a)	6
¹ H-NMR (400 MHz CDCl ₃) 3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b)	7
¹³ C-NMR (101 MHz CDCl ₃) 3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b)	8
¹⁹ F-NMR (376 MHz CDCl ₃) 3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b)	9
¹ H-NMR (400 MHz CDCl ₃) 3-Phenyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7c)	10
¹³ C-NMR (101 MHz CDCl ₃) 3-Phenyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7c)	11
¹ H-NMR (400 MHz CDCl ₃) 4-Methyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7d)	12
¹³ C-NMR (101 MHz CDCl ₃) 4-Methyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7d)	13
¹ H-NMR (400 MHz CDCl ₃) 4-Chloro-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7e)	14
¹³ C-NMR (101 MHz CDCl ₃) 4-Chloro-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7e)	15
¹ H-NMR (400 MHz CDCl ₃) 4-Bromo-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7f)	16
¹³ C-NMR (101 MHz CDCl ₃) 4-Bromo-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7f)	17
¹ H-NMR (400 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)	18
¹³ C-NMR (101 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)	19
¹⁹ F-NMR (376 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)	20
¹ H-NMR (400 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-1,2,3-triazole (7h)	21

¹³ C-NMR (101 MHz CDCl ₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-1,2,3-triazole (7h)	22
¹ H-NMR (400 MHz CDCl ₃) Crude NMR of 1-(Cyclohepta-2,4,6-trienyl-1-yl)-1H-1,2,4-triazole (7i)	23
¹ H-NMR (400 MHz CDCl ₃) Crude NMR of 1-(Cyclohepta-2,4,6-trienyl-1-yl)-1H-imidazole (7j)	24
¹ H-NMR (400 MHz CDCl ₃) 1-Cyclohepta-2,4,6-trienyl-1H-indazole (7k)	25
¹³ C-NMR (101 MHz CDCl ₃) 1-Cyclohepta-2,4,6-trienyl-1H-indazole (7k)	26
¹ H-NMR (400 MHz CDCl ₃) Crude NMR of 7-phenylthiocycloheptatriene(7l)	27

General Considerations

NMR spectra (¹H-, ¹³C-, and ¹⁹F-) were performed at 300 K using either a Brüker Avance 300 MHz with BBO probe, or Brüker Avance NEO 400 400 MHz with TBO probe spectrometers. ¹H-NMR spectra were referenced to residual CHCl₃ (7.26 ppm) in CDCl₃. ¹³C-NMR spectra were referenced to CDCl₃ (77.16 ppm). ¹⁹F-NMR spectra were referenced to hexafluorobenzene (C₆F₆; -161.64 ppm).¹ Reactions were monitored by TLC on silica gel plates (60 Å porosity, 250 μm thickness). TLC analysis was performed using UV light. Melting points were obtained using a Barnstead electrothermal Mel-Temp model 1001D.

Chemicals

Deuterated chloroform (CDCl₃) was purchased from Cambridge Isotope Laboratories. 4-acetamido-2,2,6,6-tetramethyl-oxo-piperidinium nitrate (Nitrate salt) was prepared and recrystallized using a previously reported protocol.² All chemicals were purchased from Oakwood Chemicals, Sigma Aldrich, Fisher Scientific, or TCI America.

General procedure for the preparation of 1-(cyclohepta-2,5,6-trien-1-yl)azoles

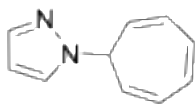
For convention heating:

To a 4-dram reaction vial equipped with a stir bar were added 4-acetamido-2,2,6,6-tetramethyl-oxo-piperidinium nitrate (BSNO₃, 165mg, 0.6 equiv.), and 2ml of acetonitrile. Then nucleophile (1 mmol, 1 equiv.), cycloheptatriene (1.1 mmol, 1.1 equiv.) were added and the vial was closed tightly. The contents were then heated in an oil bath at 50 °C for 20 minutes. Upon completion, the product mixture was filtered through a pad of silica, the silica was washed with an 85:15 mixture of hexanes and ethyl acetate to elute the product. The solvent was then removed from the filtrate under vacuum, affording the pure product.

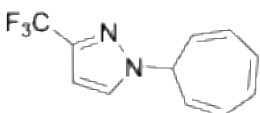
For Microwave heating:

In a 10-mL glass microwave vial equipped with a stir bar were added 4-acetamido-2,2,6,6-tetramethyl-oxo-piperidinium nitrate (BSNO₃, 165mg, 0.6 equiv.), and 2ml of acetonitrile. Then nucleophile (1 mmol, 1 equiv.), cycloheptatriene (1.1 mmol, 1.1 equiv.) were added and the vial was closed tightly. The contents were then heated in an oil bath at 45 °C for 30 minutes. Upon completion, the product mixture was filtered through a pad of silica, the silica was washed with an 85:15 mixture of hexanes and ethyl acetate to elute the product. The solvent was then removed from the filtrate under vacuum, affording the pure product.

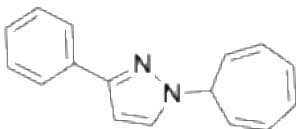
Product Characterization



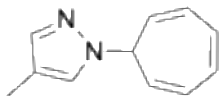
1-(Cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7a). With a reaction time of 20 min, the product was obtained as a yellow oil (0.151g, 95.5%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.61 (d, $J = 1.8$ Hz, 1H), 7.49 (dd, $J = 2.3, 0.7$ Hz, 1H), 6.75 (dd, $J = 3.7, 2.7$ Hz, 2H), 6.33 – 6.21 (m, 3H), 5.70 (ddt, $J = 9.5, 5.2, 0.9$ Hz, 2H), 4.29 (tt, $J = 5.1, 1.5$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 139.87, 131.40, 128.62, 124.10, 123.81, 105.74, 60.68.³



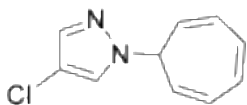
3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b). With a reaction time of 20 min, the product was obtained as a yellow oil (0.205g, 91%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.52 (dd, $J = 2.4, 1.1$ Hz, 1H), 6.76 (dd, $J = 3.7, 2.7$ Hz, 2H), 6.56 (d, $J = 2.4$ Hz, 1H), 6.30 (dddd, $J = 9.3, 4.0, 2.6, 1.5$ Hz, 2H), 5.73 – 5.64 (m, 2H), 4.37 (tt, $J = 5.3, 1.6$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 142.73 (q, $J = 38.1$ Hz), 131.49, 130.11, 124.73, 122.78, 104.58 (q, $J = 2.2$ Hz), 61.31. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -61.78.³



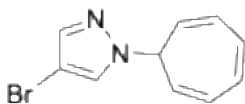
3-Phenyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7c). With a reaction time of 20 min the product was obtained as a yellow oil (0.199g, 85%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.89 – 7.82 (m, 2H), 7.52 (d, $J = 2.4$ Hz, 1H), 7.45 – 7.36 (m, 2H), 7.34 – 7.26 (m, 1H), 6.77 (dd, $J = 3.7, 2.7$ Hz, 2H), 6.61 (d, $J = 2.3$ Hz, 1H), 6.29 (dddd, $J = 9.2, 4.0, 2.6, 1.6$ Hz, 2H), 5.82 – 5.73 (m, 2H), 4.31 (tt, $J = 5.1, 1.6$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 151.93, 133.78, 131.42, 129.97, 128.71, 127.72, 125.83, 124.12, 124.05, 103.10, 61.03.³



4-Methyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7d). With a reaction time of 20 min, the product was obtained as a clear oil (0.158, 92%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.40 (s, 1H), 7.28 – 7.23 (m, 1H), 6.79 – 6.68 (m, 2H), 6.25 (dddd, $J = 9.2, 3.9, 2.6, 1.6$ Hz, 2H), 5.67 (ddt, $J = 9.4, 5.1, 0.9$ Hz, 2H), 4.19 (tt, $J = 5.0, 1.5$ Hz, 1H), 2.10 (d, $J = 0.7$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 140.23, 131.36, 127.44, 123.99, 123.97, 116.33, 60.57, 9.04.³

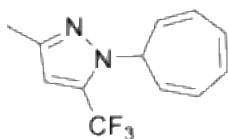


4-Chloro-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7e). With a reaction time of 20 min the product was obtained as a yellow solid (0.168g, 87%). **Melting point** 65-67°C. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.48 (dd, $J = 18.4, 0.7$ Hz, 2H), 6.75 (dd, $J = 3.7, 2.7$ Hz, 2H), 6.30 (dddd, $J = 9.3, 3.9, 2.6, 1.4$ Hz, 2H), 5.67 (ddt, $J = 9.4, 5.3, 0.9$ Hz, 2H), 4.29 (tt, $J = 5.3, 1.4$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 138.20, 131.48, 126.77, 124.73, 122.95, 110.20, 61.11.³



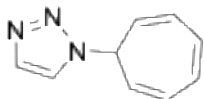
4-Bromo-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7f). With a reaction time of 20 min the product was obtained as a yellow oil (0.237g, 78%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.49 (dd, $J = 18.5, 0.7$ Hz, 2H), 6.80 – 6.70 (m, 2H), 6.30 (dddd, $J = 9.2, 4.0, 2.6, 1.4$ Hz, 2H), 5.67 (ddt, $J = 9.3, 5.2, 0.9$ Hz, 2H), 4.29 (tt, $J = 5.2, 1.4$

Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 138.20, 131.49, 126.78, 124.73, 122.95, 110.20, 61.11.⁴



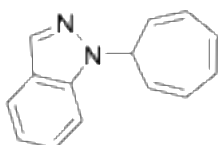
1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g).

With a reaction time of 20 min the product was obtained as a pale-yellow oil (0.204g, 85%). ^1H NMR (400 MHz, CDCl_3) δ 6.83 – 6.73 (m, 2H), 6.34 (s, 1H), 6.27 (dddd, J = 9.2, 4.0, 2.6, 1.7 Hz, 2H), 5.71 – 5.63 (m, 2H), 4.08 (tt, J = 4.8, 1.7 Hz, 1H), 2.22 (d, J = 0.8 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 141.76 (q, J = 37.9 Hz), 140.08, 131.48, 123.85, 123.30, 104.19 (q, J = 2.1 Hz), 58.27, 11.05. ^{19}F NMR (376 MHz, CDCl_3) δ -61.94.³



1-(Cyclohepta-2,4,6-trien-1-yl)-1H-1,2,3-triazole (7h).

With a reaction time of 20 min the product was obtained as a yellow oil (0.120g, 75%). ^1H NMR (400 MHz, CDCl_3) δ 7.69 (s, 2H), 6.83 – 6.73 (m, 2H), 6.30 (dddd, J = 9.2, 3.9, 2.5, 1.6 Hz, 2H), 5.77 (dd, J = 9.5, 4.9 Hz, 2H), 4.61 (tt, J = 4.9, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 134.54, 131.69, 131.56, 125.43, 124.03, 122.56, 122.34, 63.75.³



1-Cyclohepta-2,4,6-trienyl-1H-indazole (7k).

With a reaction time of 20 min the product was isolated as a white solid (0.179g, 86% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.11 (s, 1H), 7.78 (dt, J = 8.1, 1.1 Hz, 1H), 7.44 – 7.30 (m, 2H), 7.17 (ddd, J = 8.0, 4.8, 2.9 Hz, 1H), 6.87 – 6.77 (m, 2H), 6.37 – 6.24 (m, 2H), 5.79 (dd, J = 9.4, 4.8 Hz, 2H), 4.56 (tt, J = 4.8, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 139.44, 133.67, 131.51, 126.33, 124.60, 124.09, 123.95, 121.37, 120.96, 109.45, 58.17.⁵

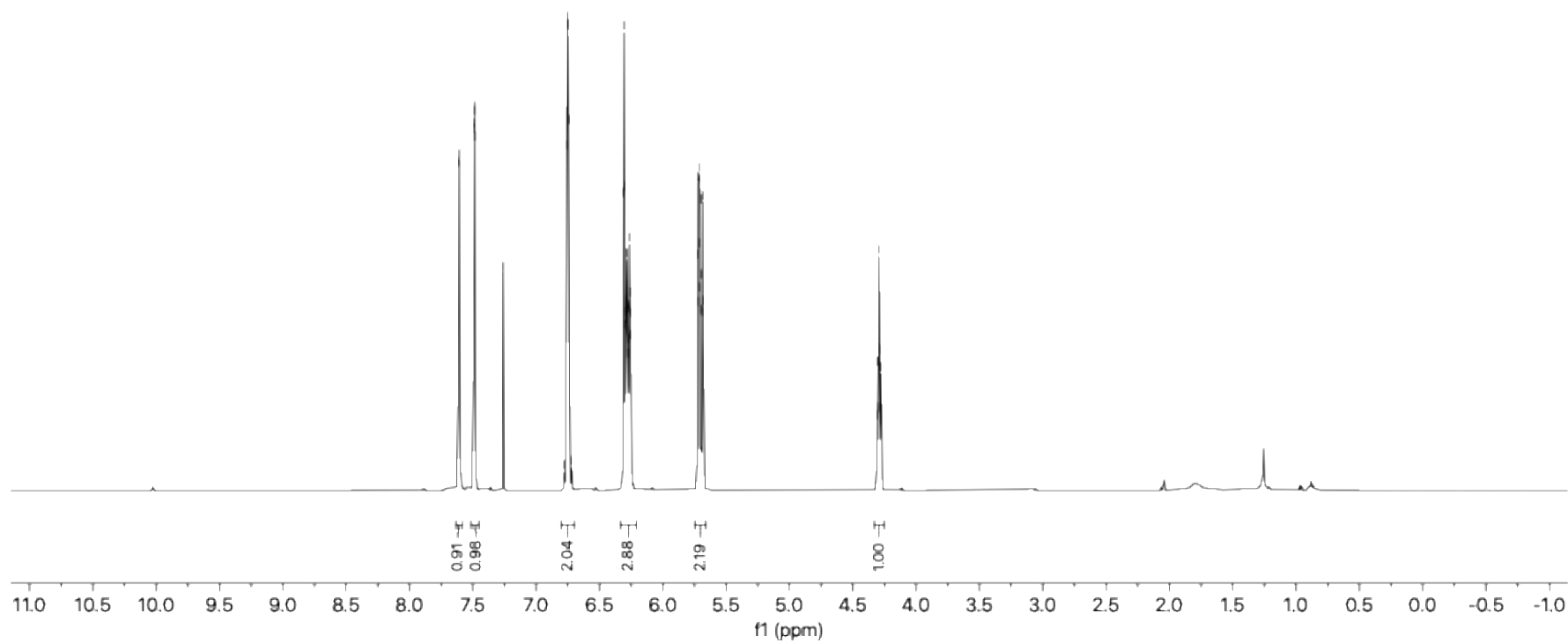
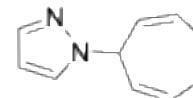
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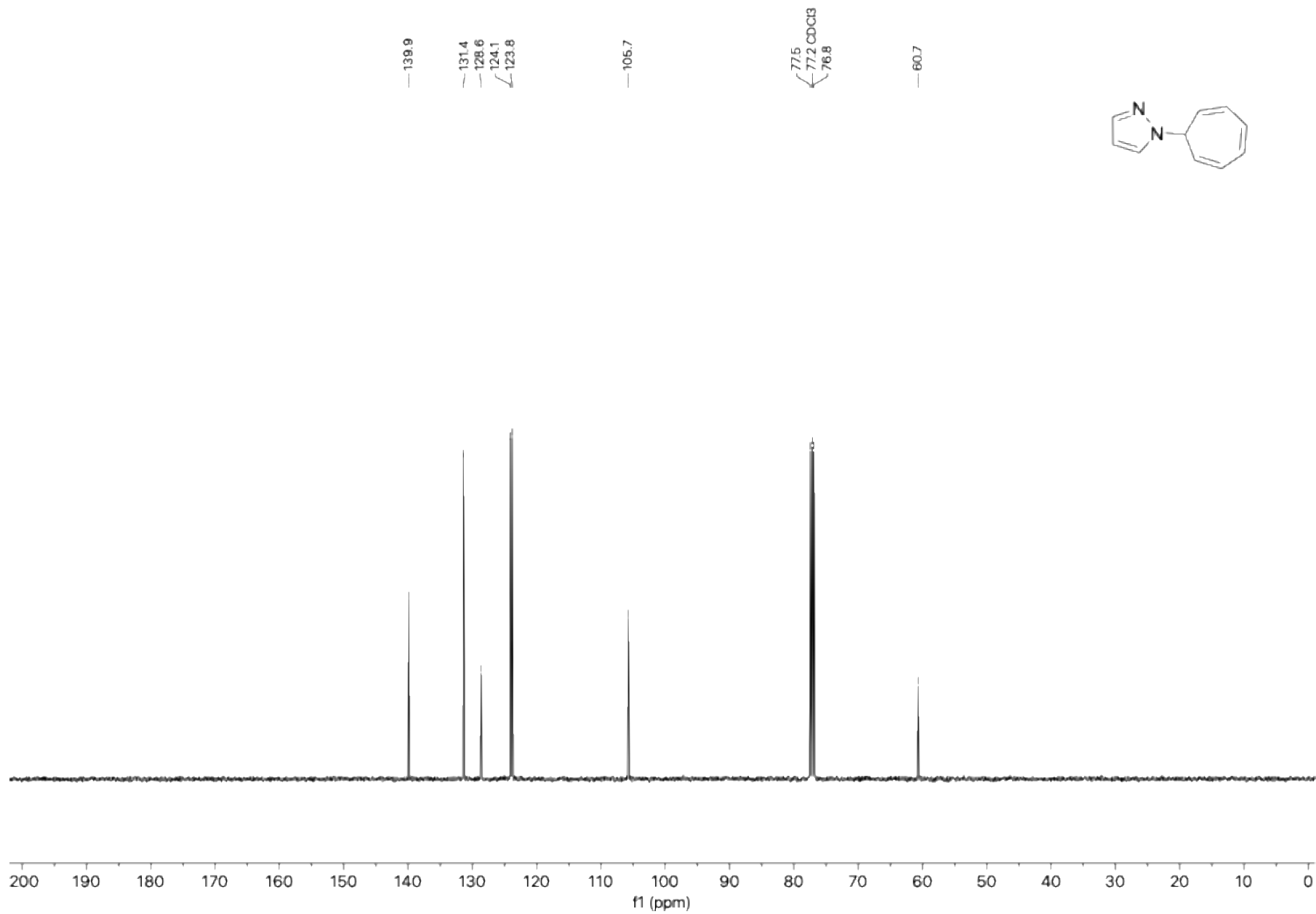
^1H -, ^{13}C -NMR Spectra of Synthesized Compounds

^1H -NMR (400 MHz CDCl_3) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7a)

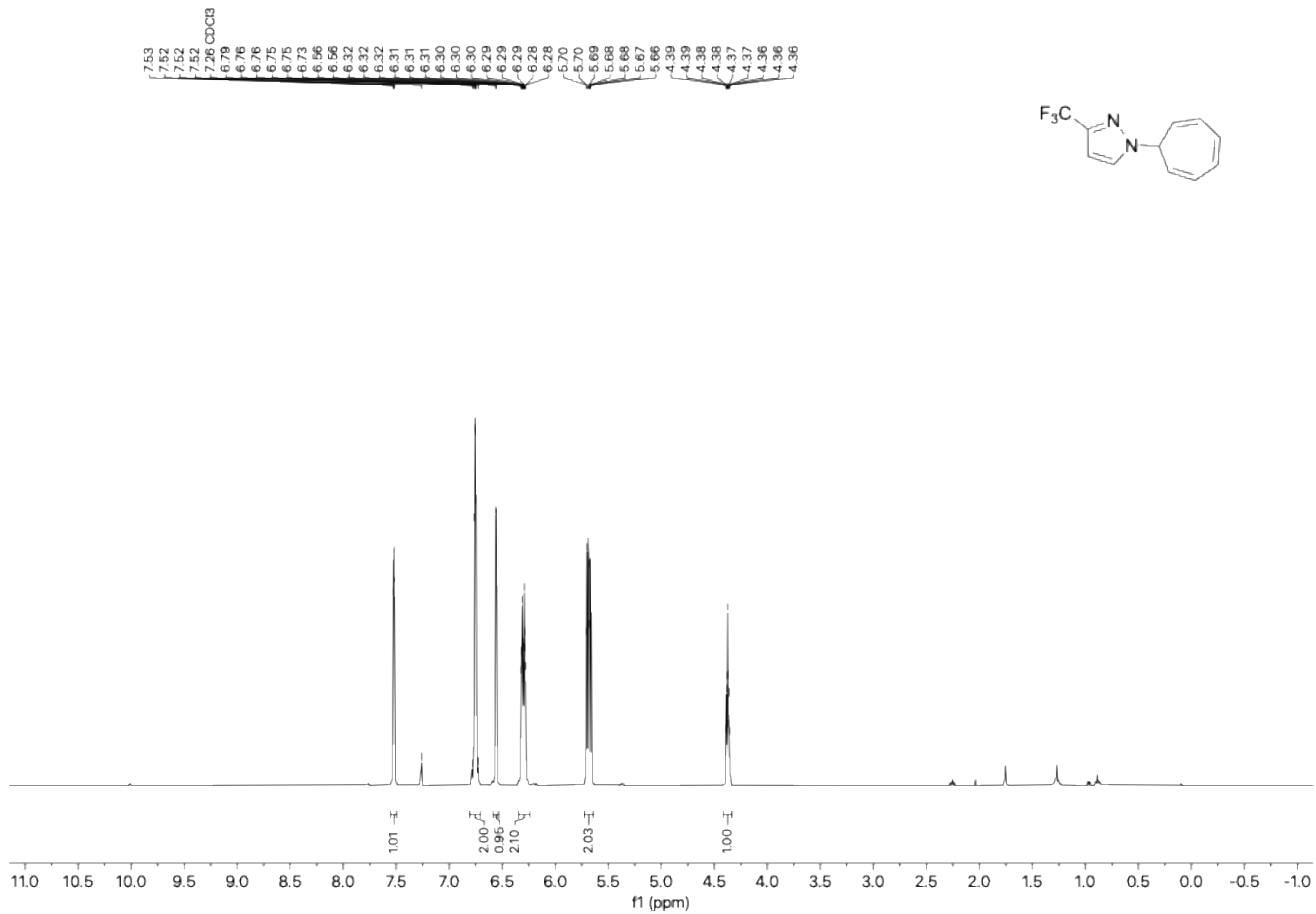
7.61, 7.49, 7.49, 7.48, 7.26 CDCl_3 , 6.78, 6.76, 6.75, 6.75, 6.74, 6.72, 6.31, 6.31, 6.30, 6.29, 6.29, 6.29, 6.28, 6.28, 6.27, 6.27, 6.27, 6.26, 6.26, 6.26, 6.25, 5.72, 5.72, 5.71, 5.71, 5.71, 5.70, 5.70, 5.70, 5.69, 5.69, 5.68, 4.31, 4.30, 4.30, 4.29, 4.29, 4.29, 4.28, 4.28, 4.27



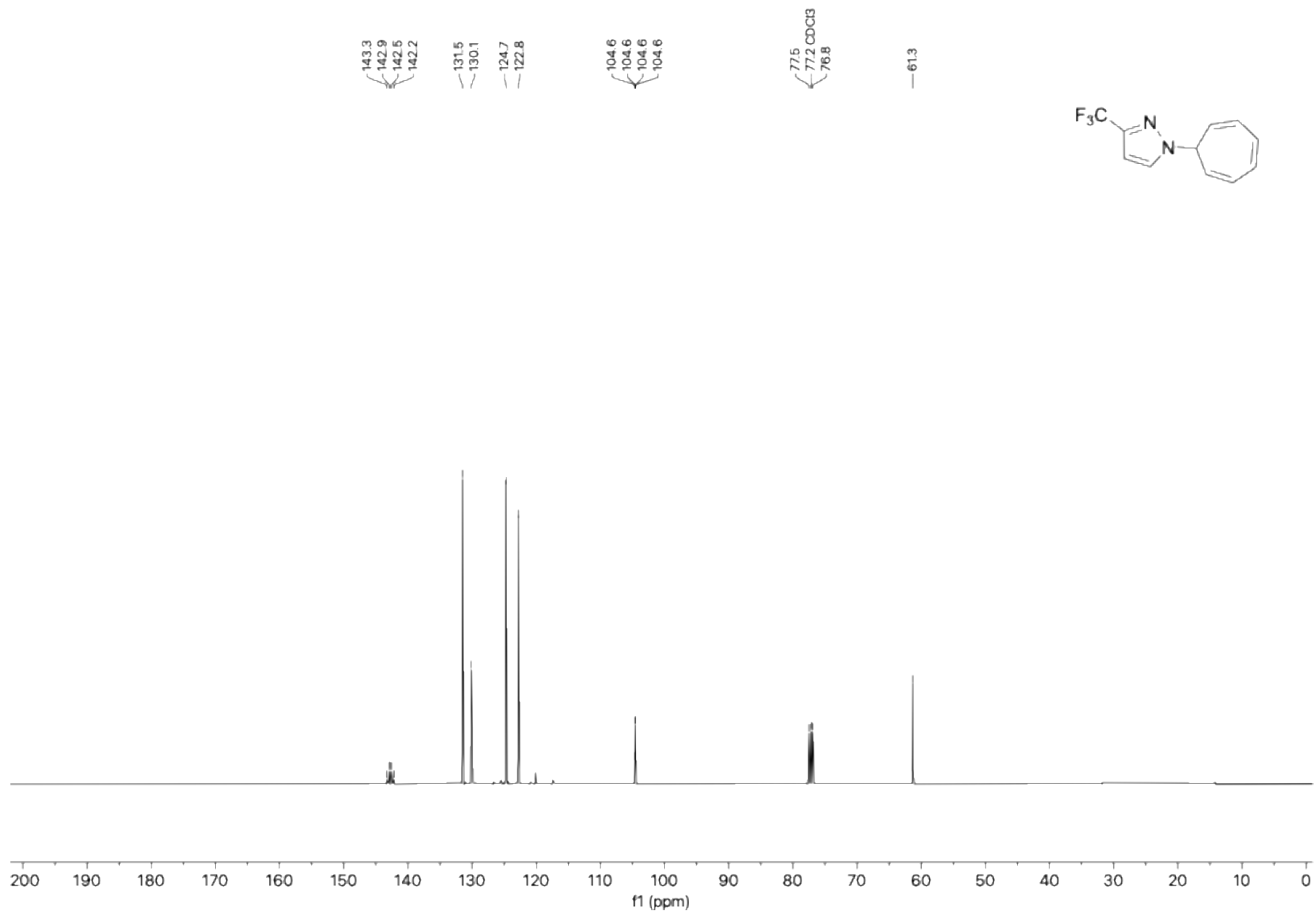
^{13}C -NMR (101 MHz CDCl_3) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7a)



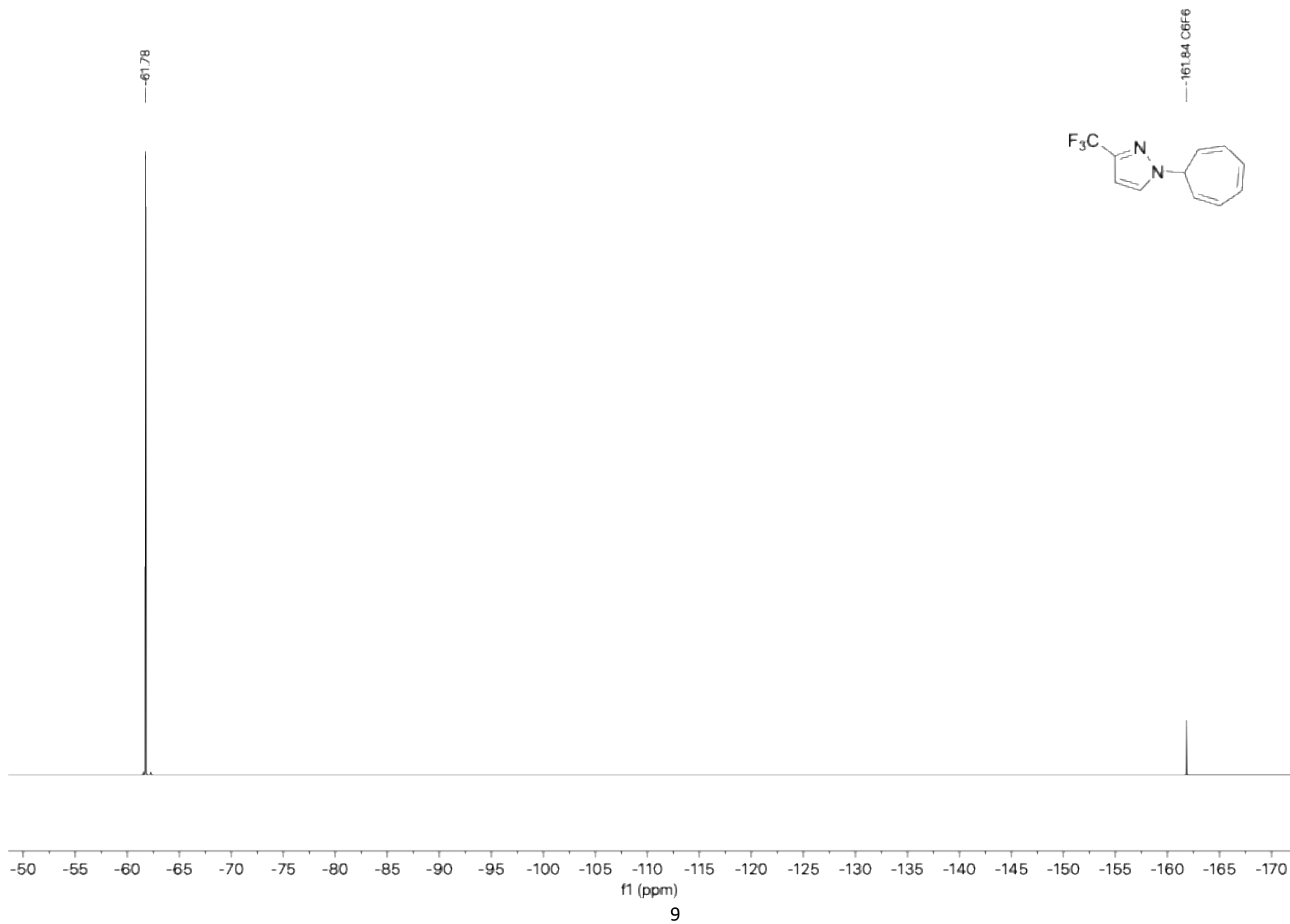
¹H-NMR (400 MHz CDCl₃) 3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b)



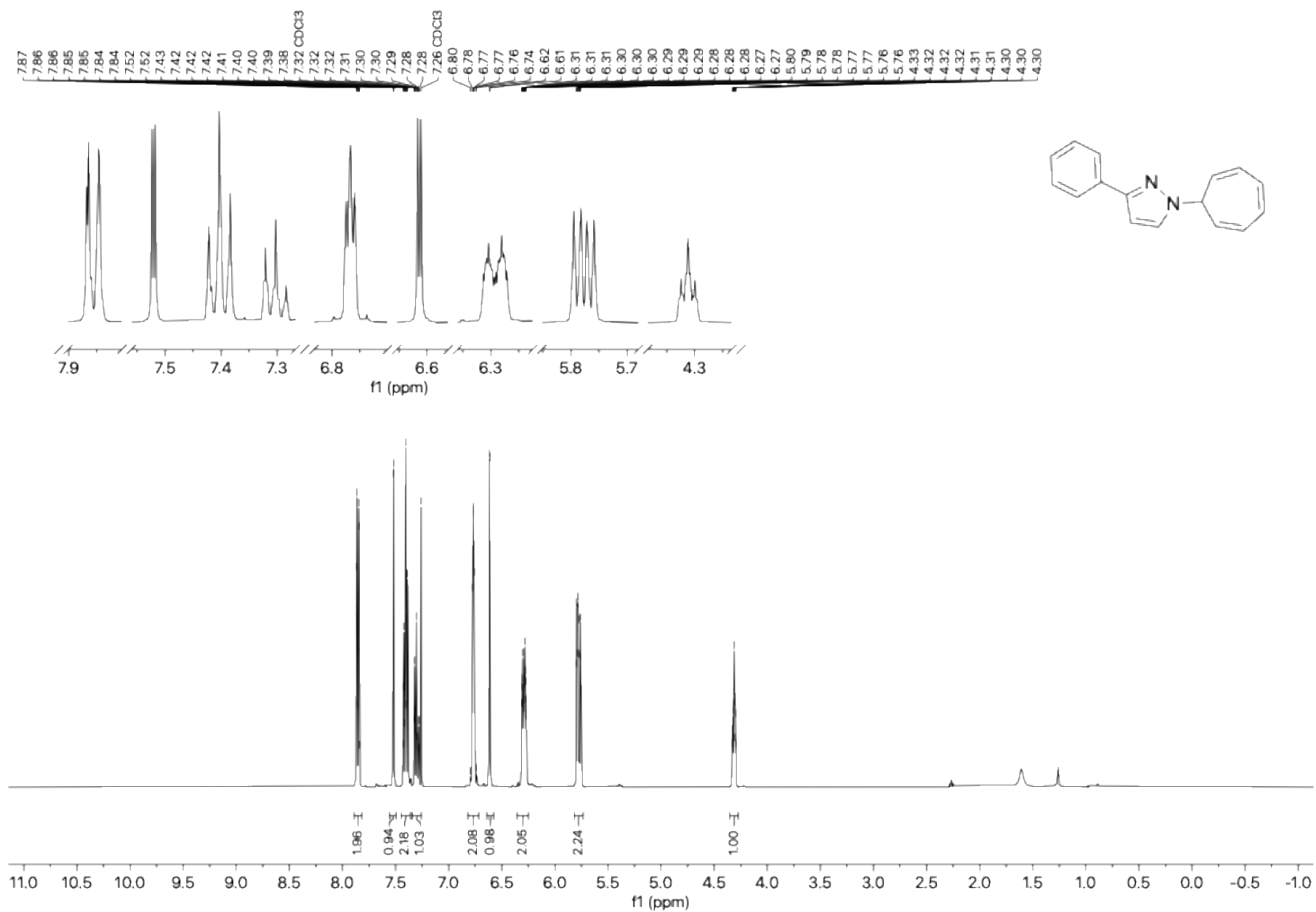
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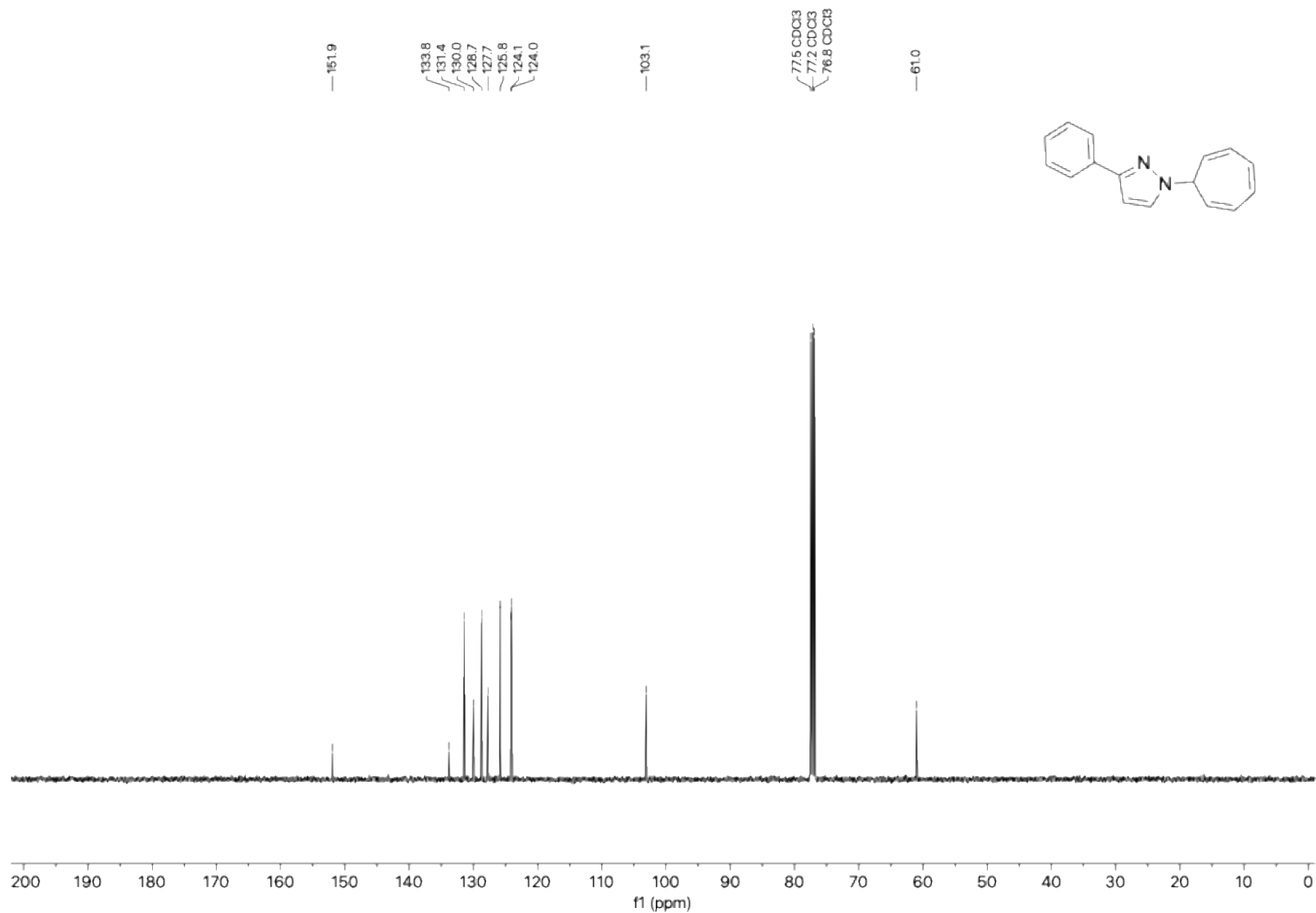
¹⁹F-NMR (376 MHz CDCl₃) 3-Trifluoromethyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7b)



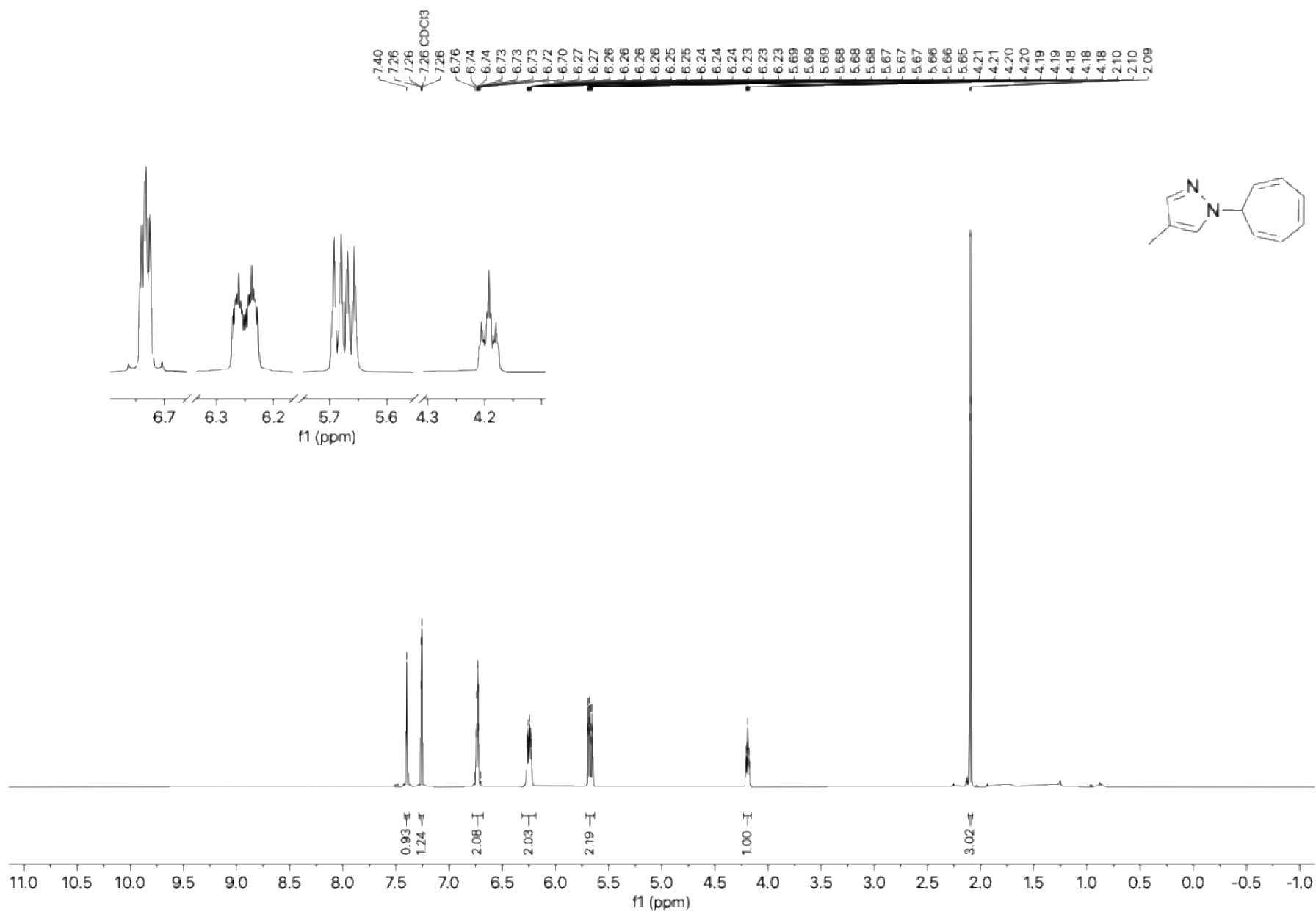
¹H-NMR (400 MHz CDCl₃) 3-Phenyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7c)



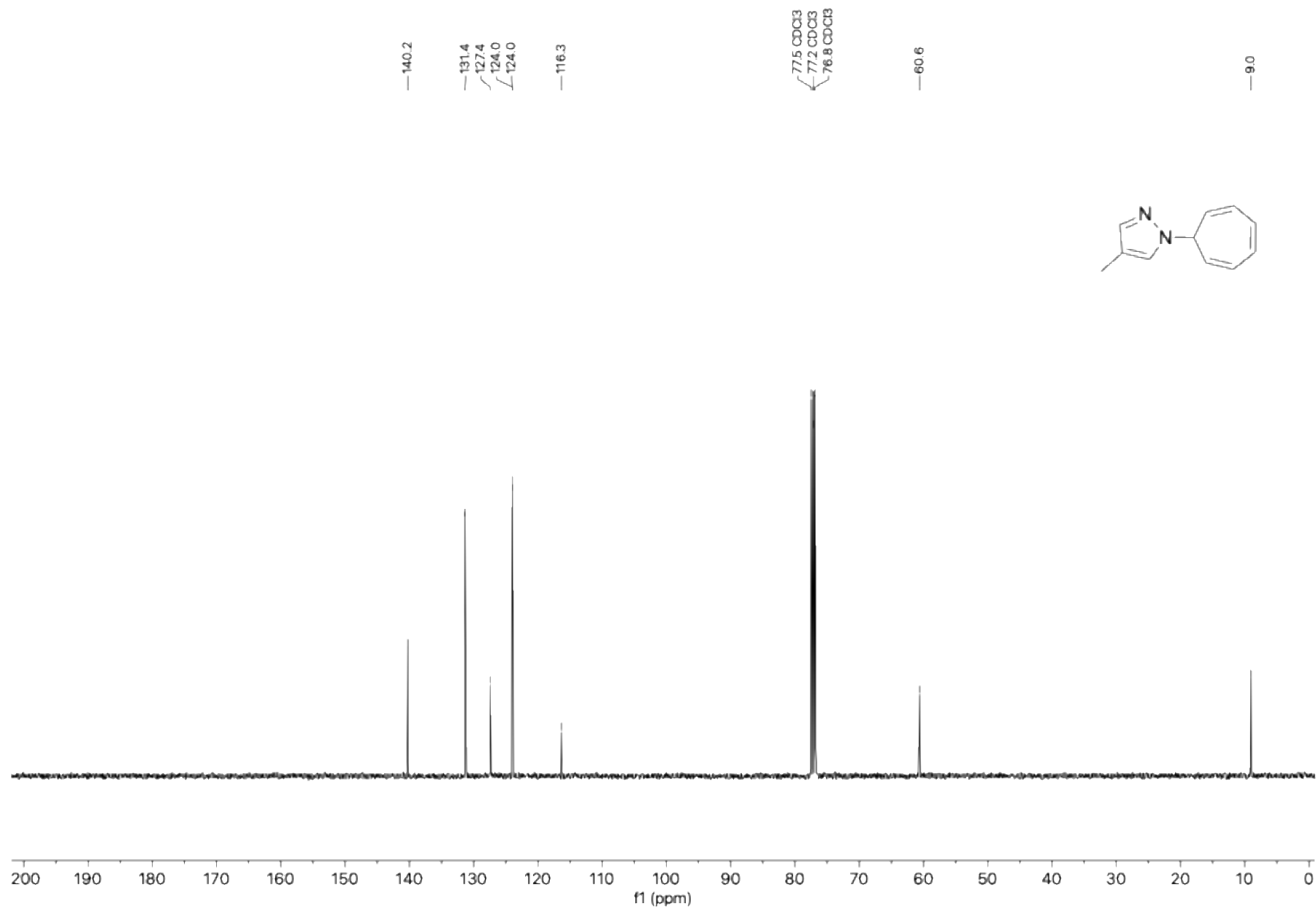
¹³C-NMR (101 MHz CDCl₃) 3-Phenyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7c)



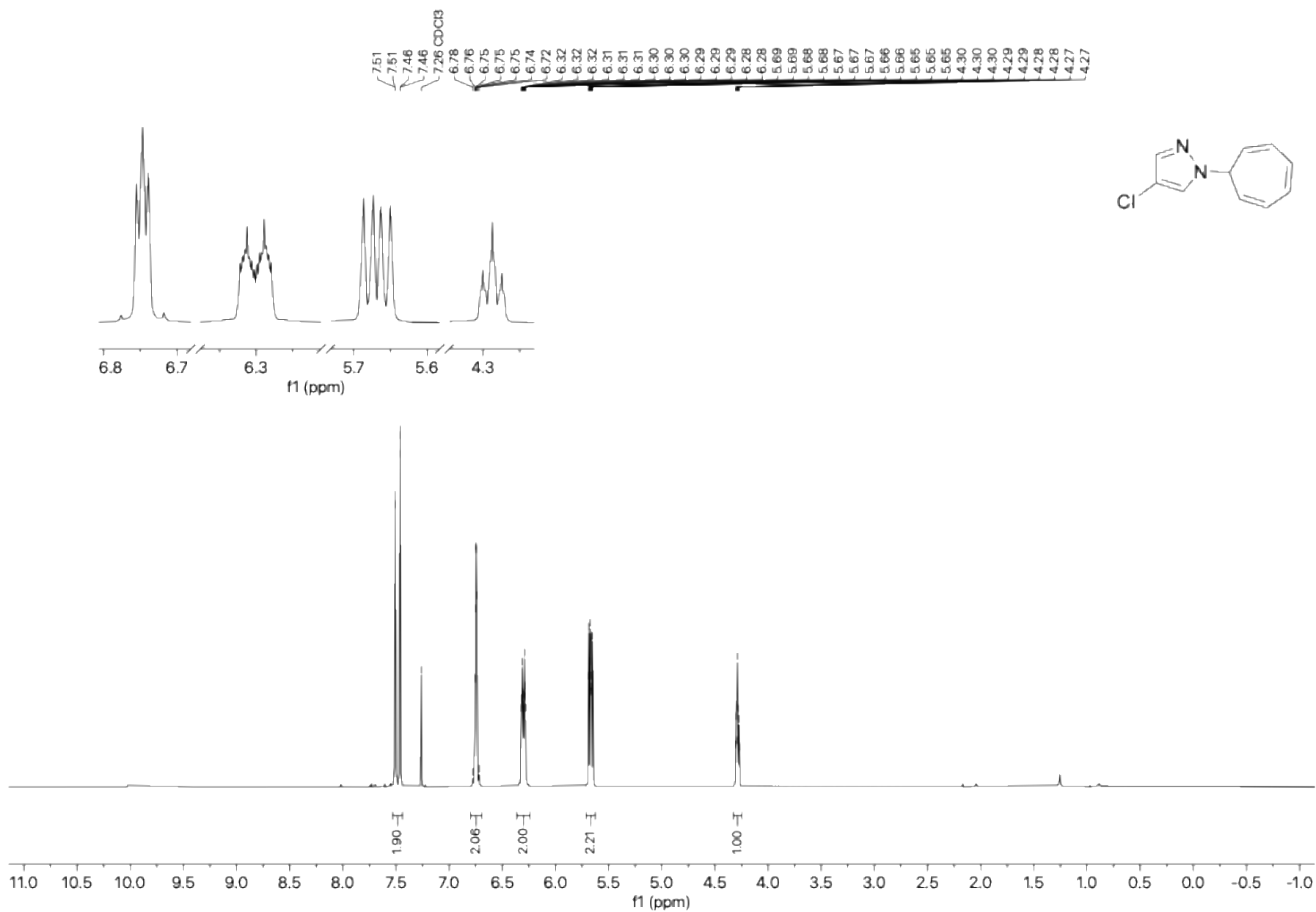
¹H-NMR (400 MHz CDCl₃) 4-Methyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7d)



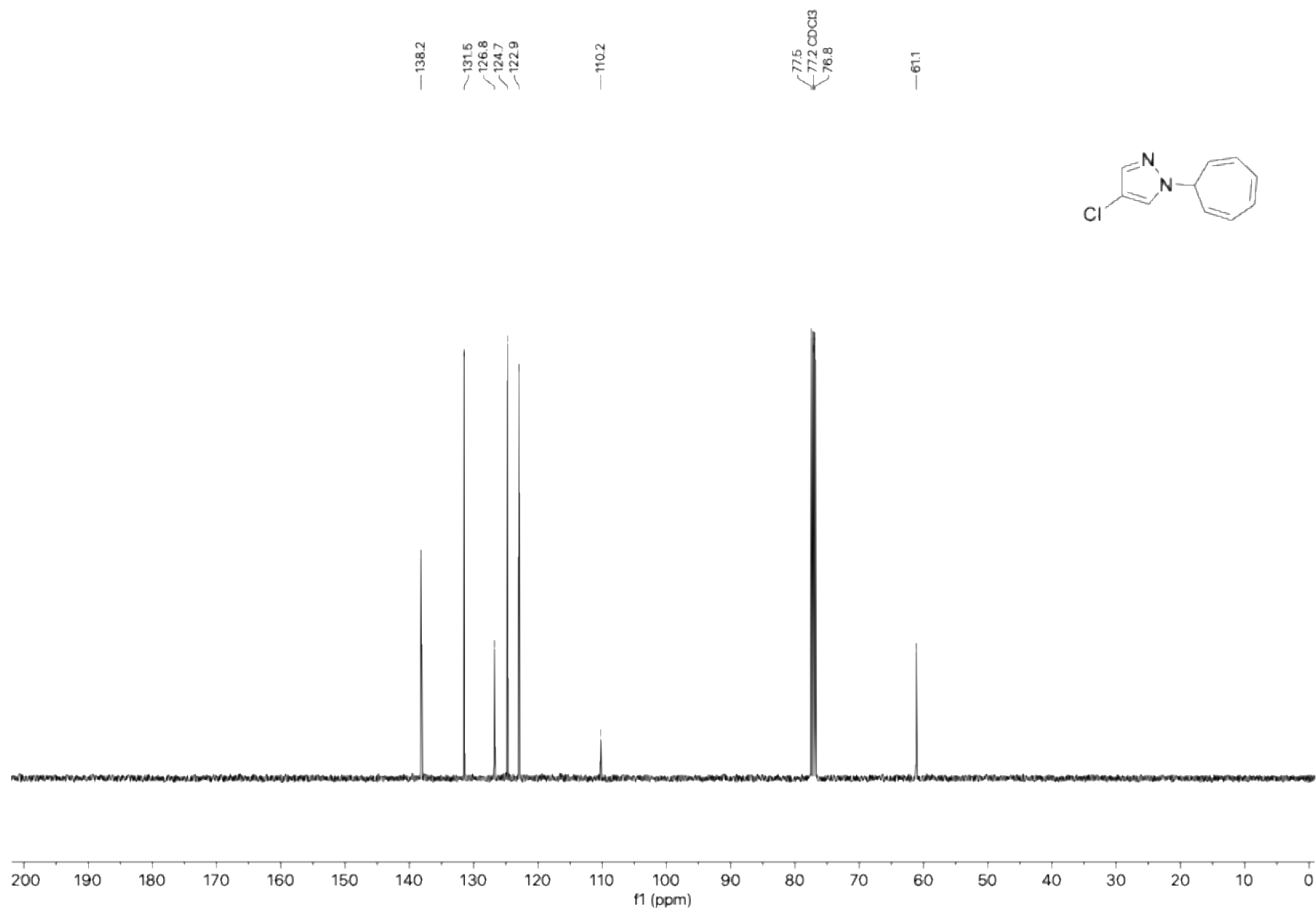
¹³C-NMR (101 MHz CDCl₃) 4-Methyl-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7d)



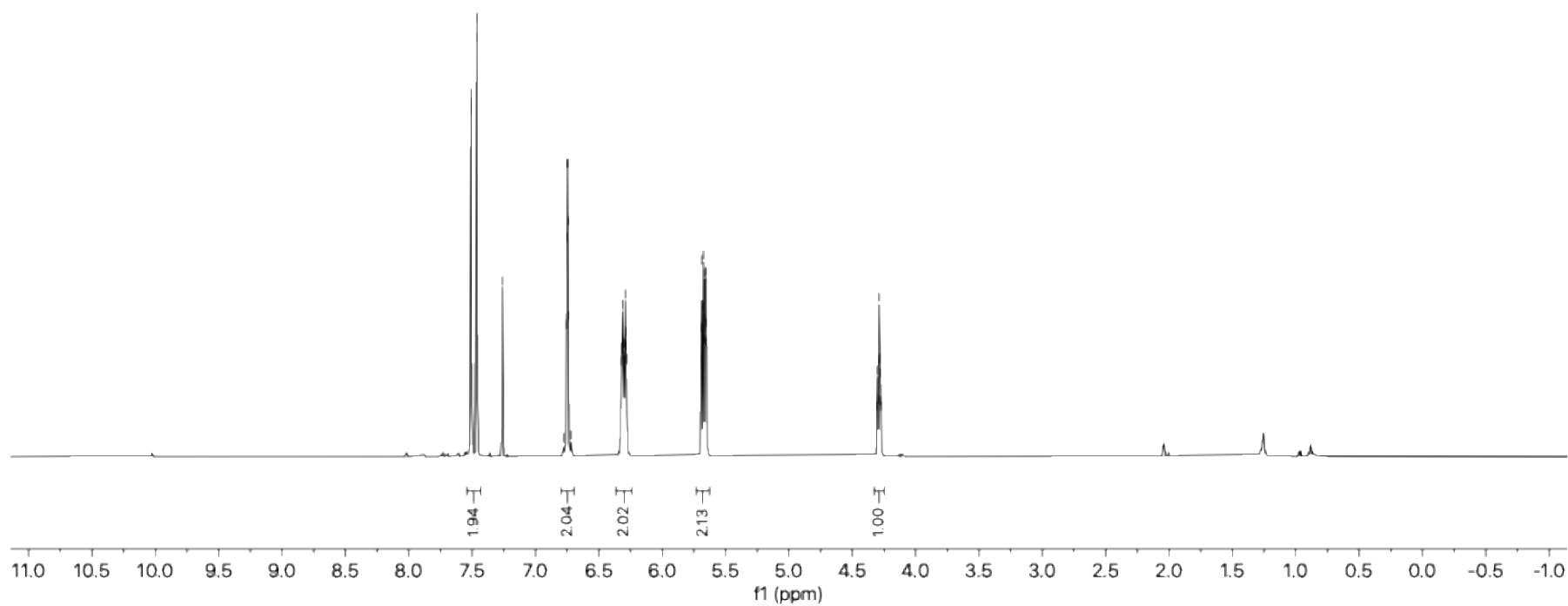
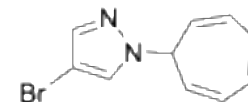
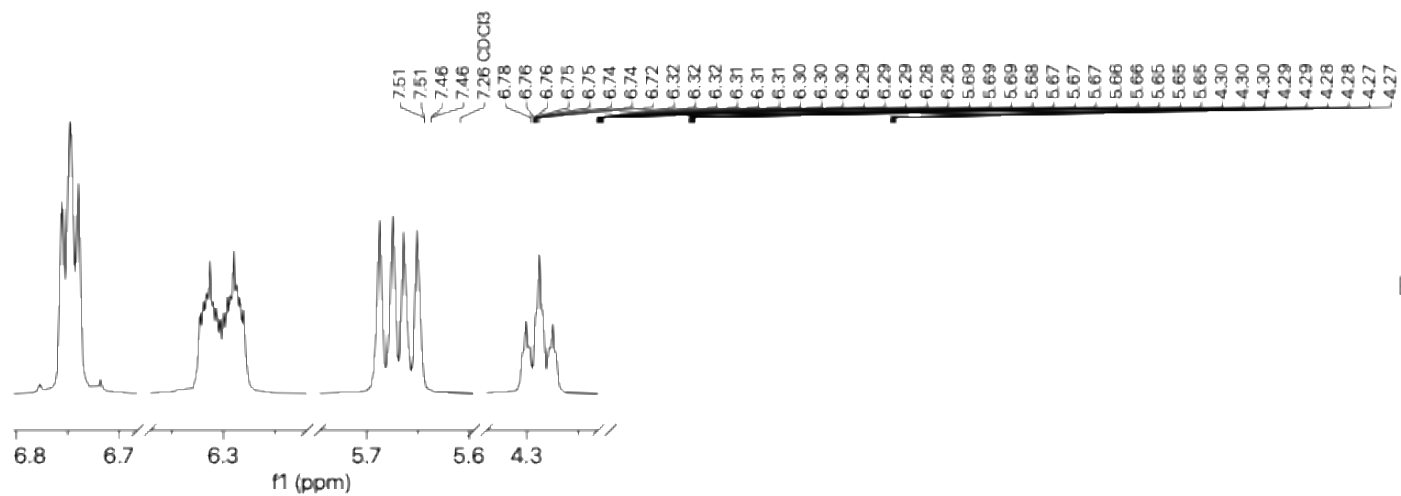
¹H-NMR (400 MHz CDCl₃) 4-Chloro-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7e)



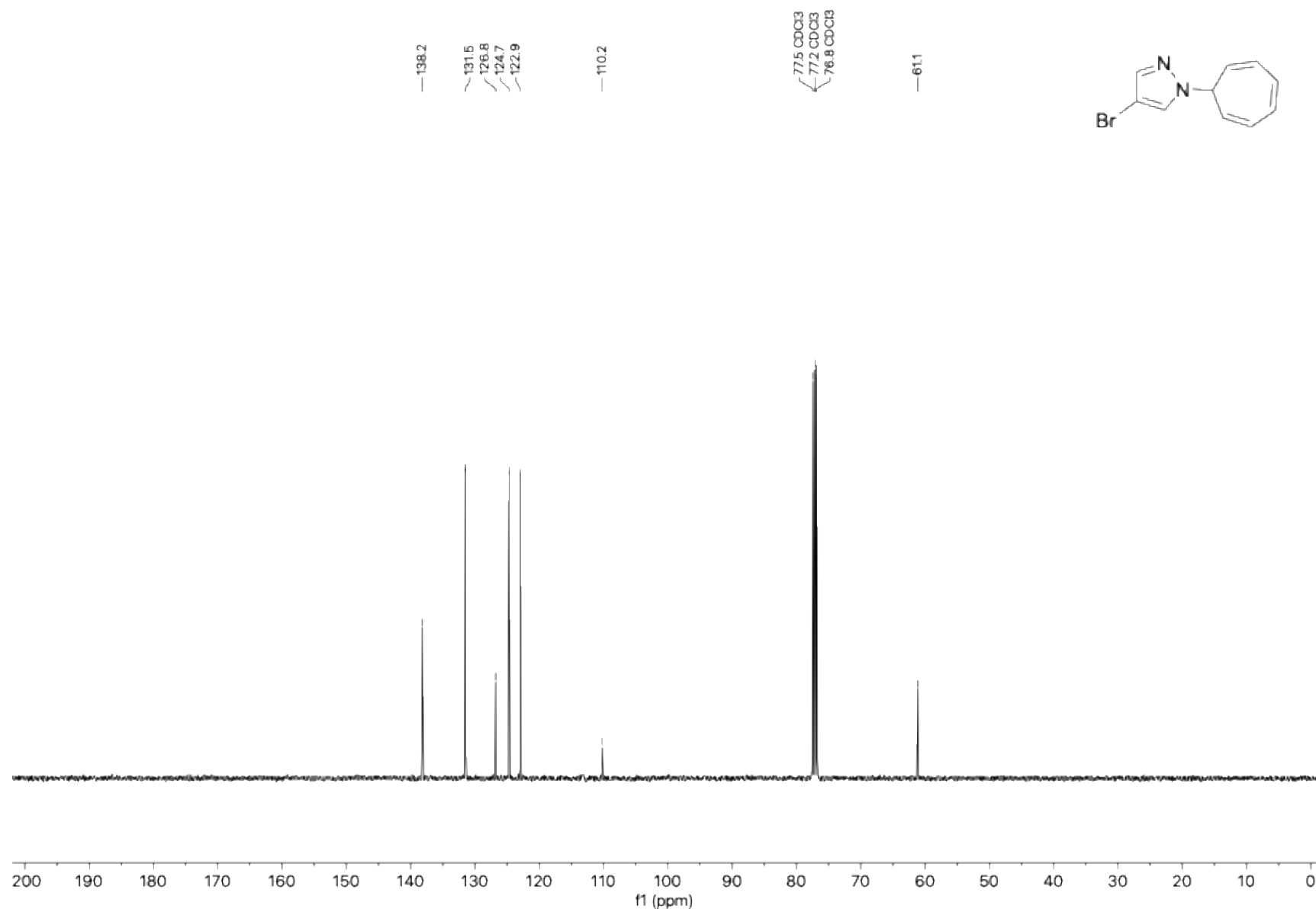
^{13}C -NMR (101 MHz CDCl_3) 4-Chloro-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7e)



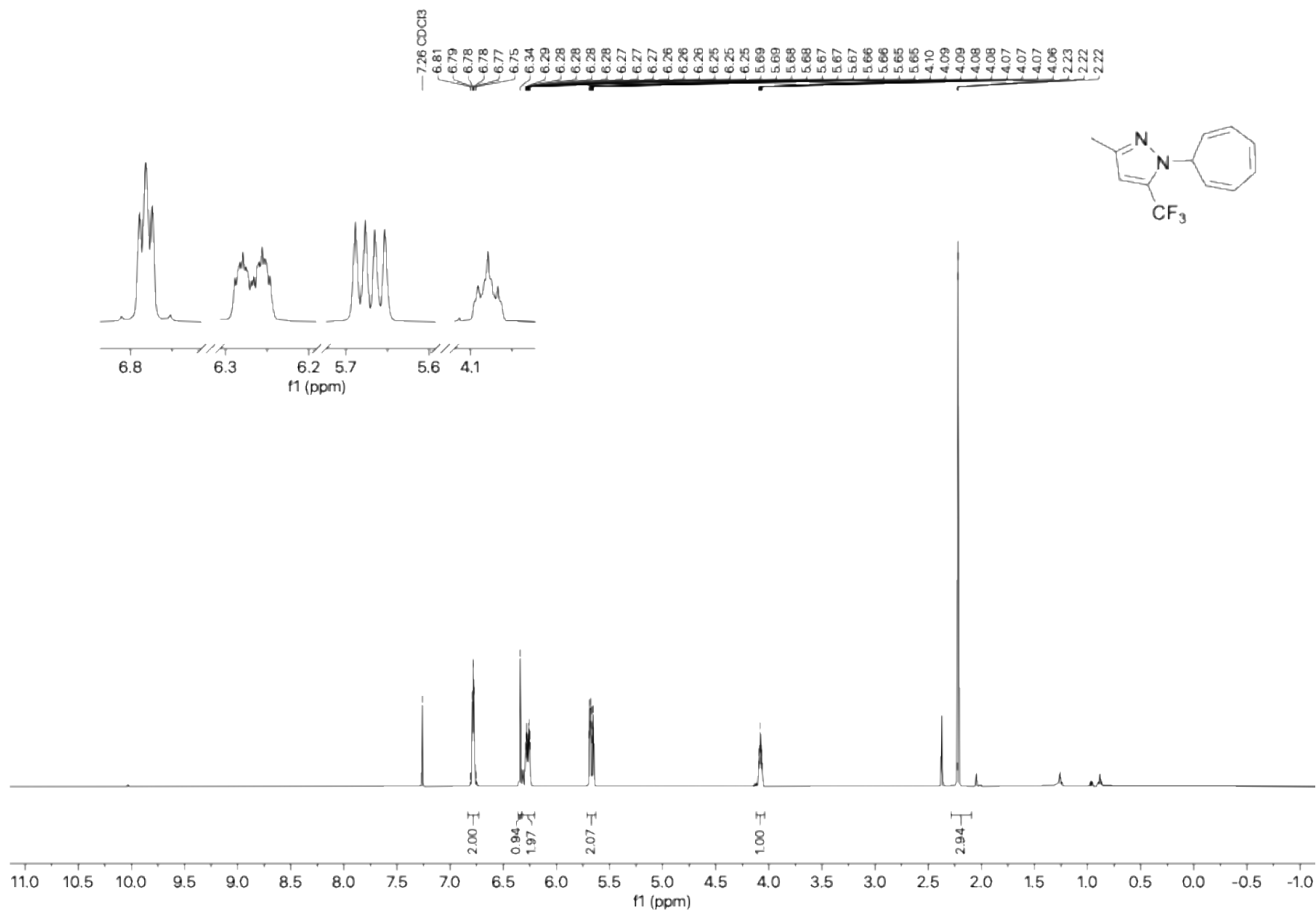
¹H-NMR (400 MHz CDCl₃) 4-Bromo-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7f)



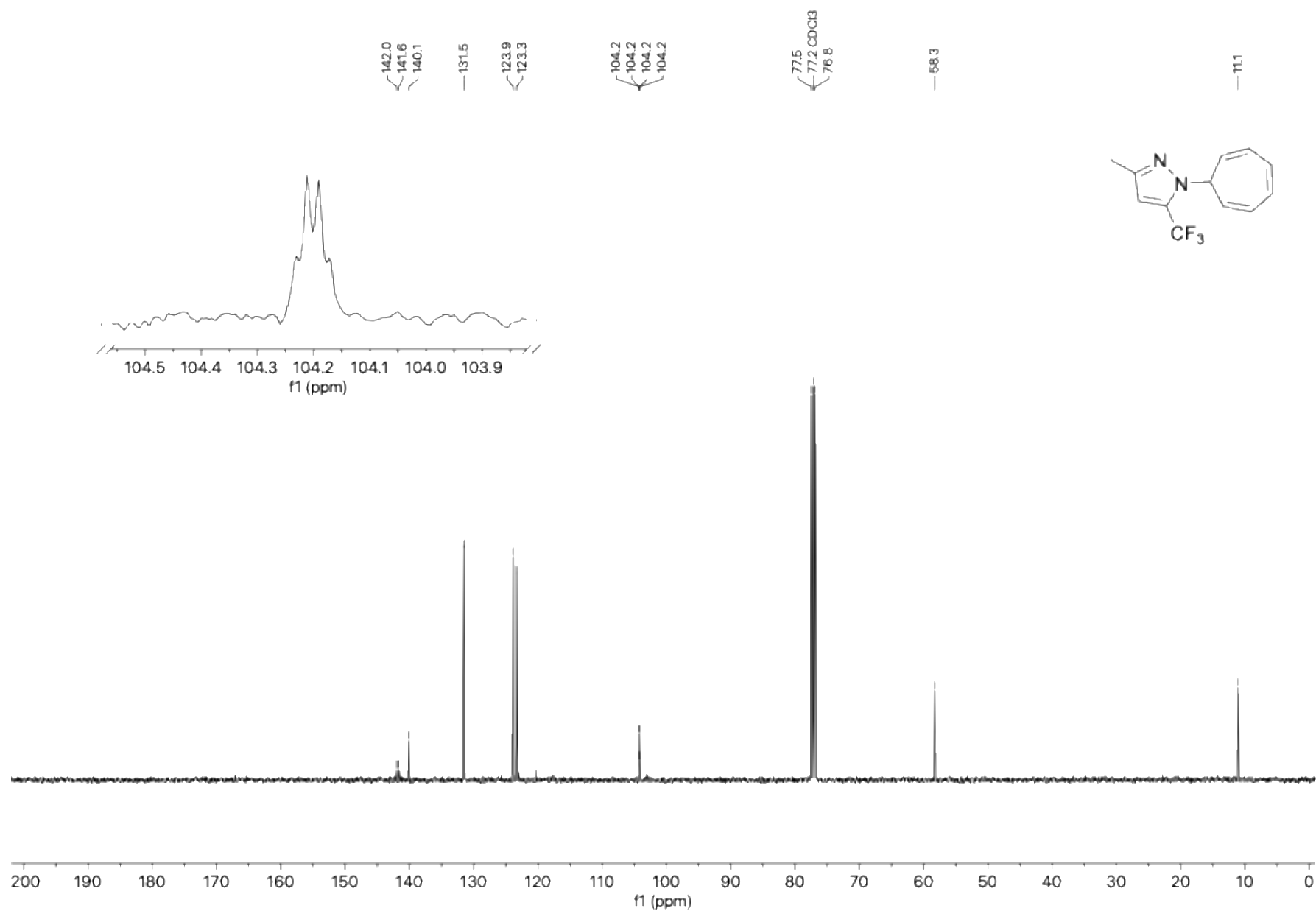
^{13}C -NMR (101 MHz CDCl_3) 4-Bromo-1-(cyclohepta-2,4,6-trien-1-yl)-1H-pyrazole (7f)



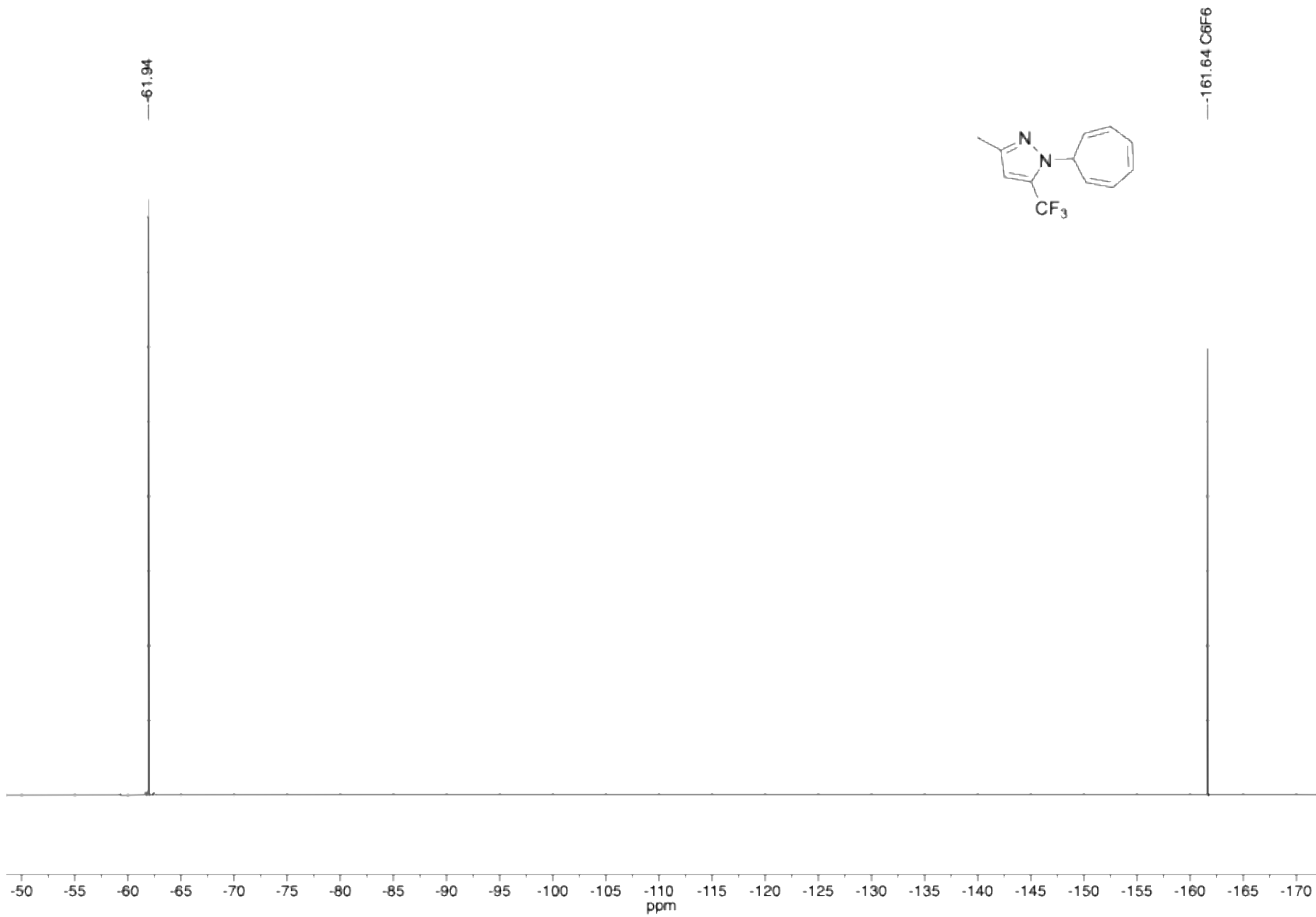
¹H-NMR (400 MHz CDCl₃) **1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)**



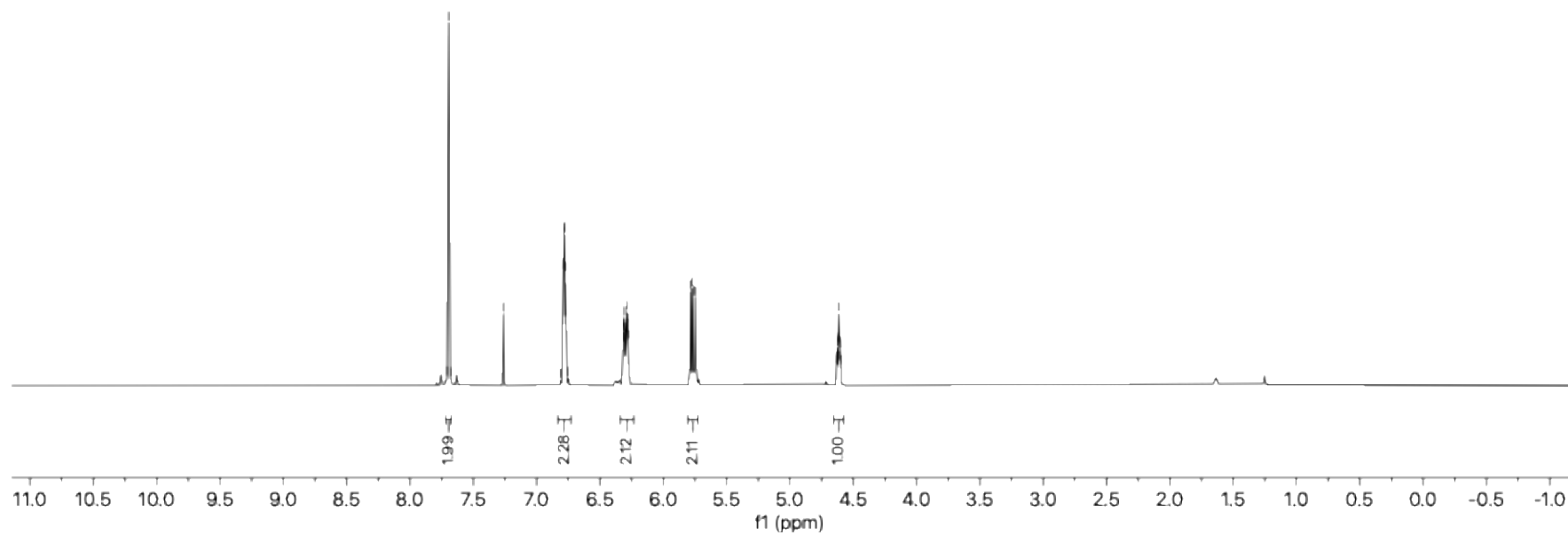
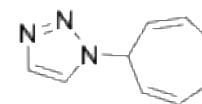
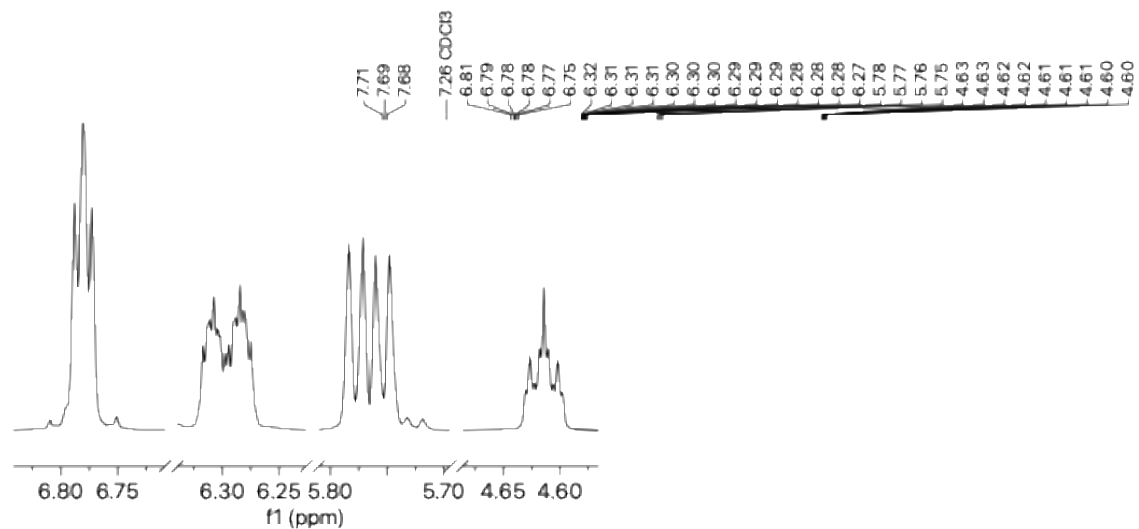
¹³C-NMR (101 MHz CDCl₃) **1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)**



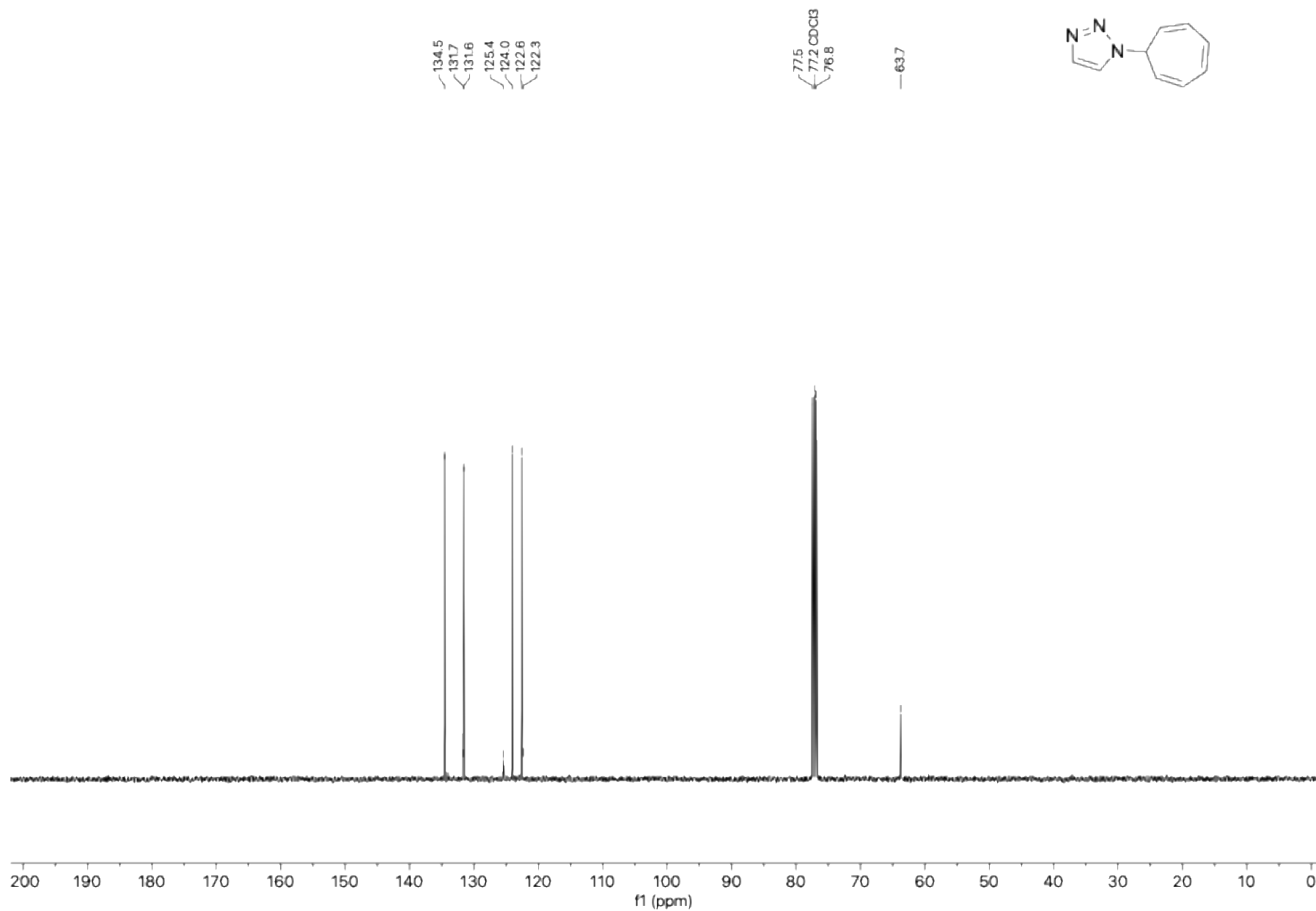
¹⁹F-NMR (376 MHz CDCl₃) **1-(Cyclohepta-2,4,6-trien-1-yl)-3-methyl-5-(trifluoromethyl)-1H-pyrazole (7g)**



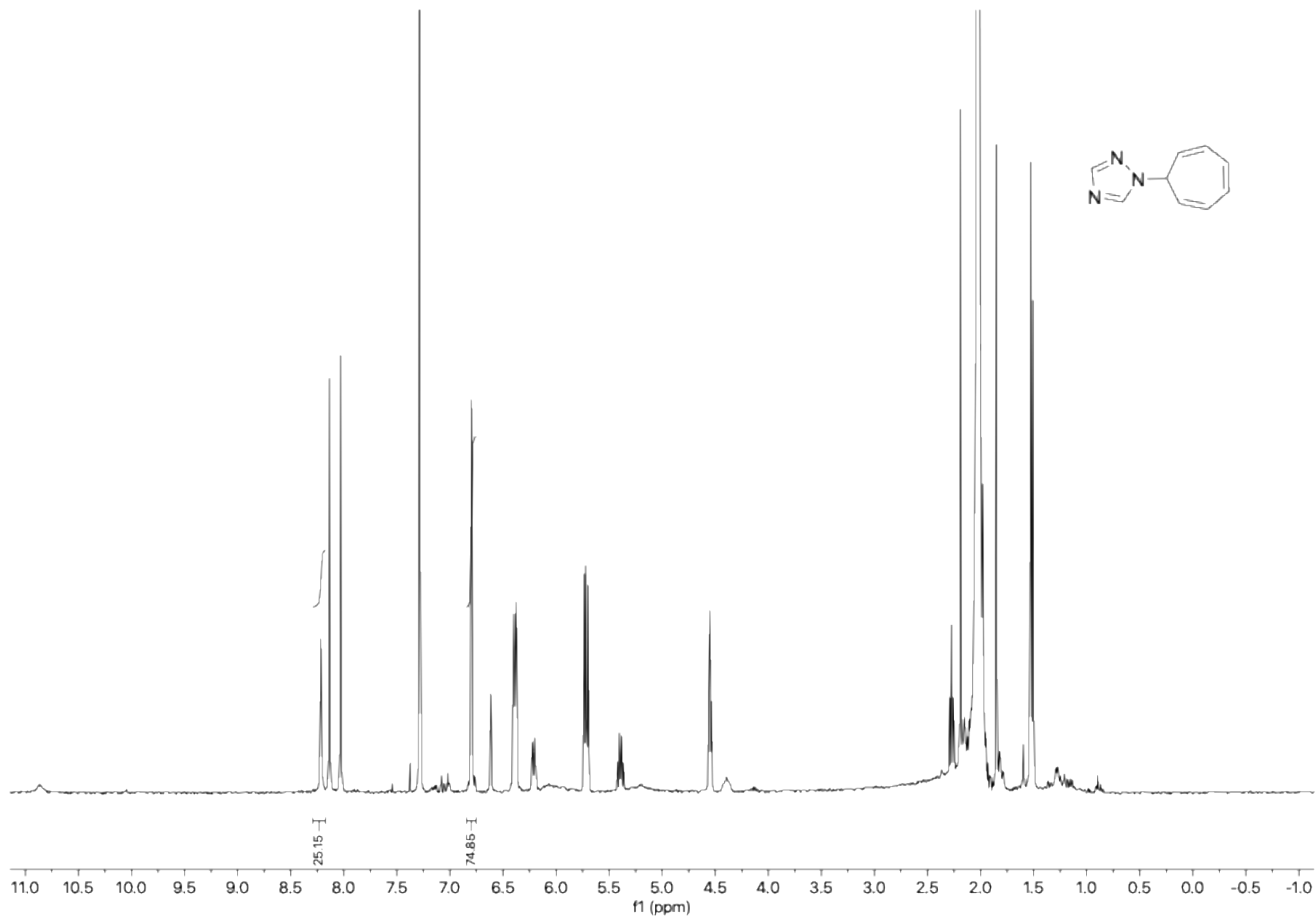
¹H-NMR (400 MHz CDCl₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-1,2,3-triazole (7h)



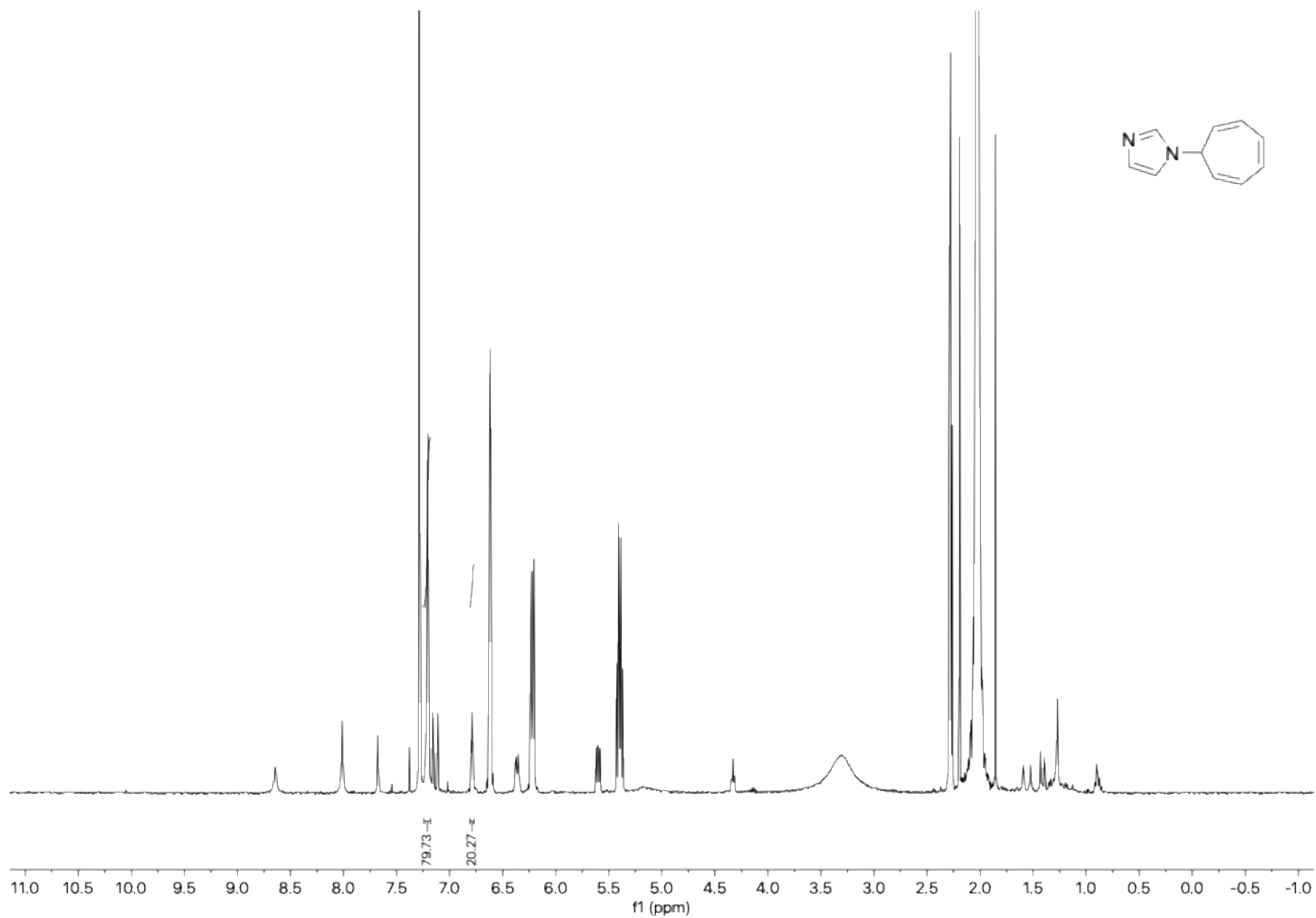
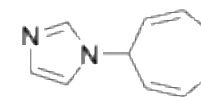
¹³C-NMR (101 MHz CDCl₃) 1-(Cyclohepta-2,4,6-trien-1-yl)-1H-1,2,3-triazole (7h)



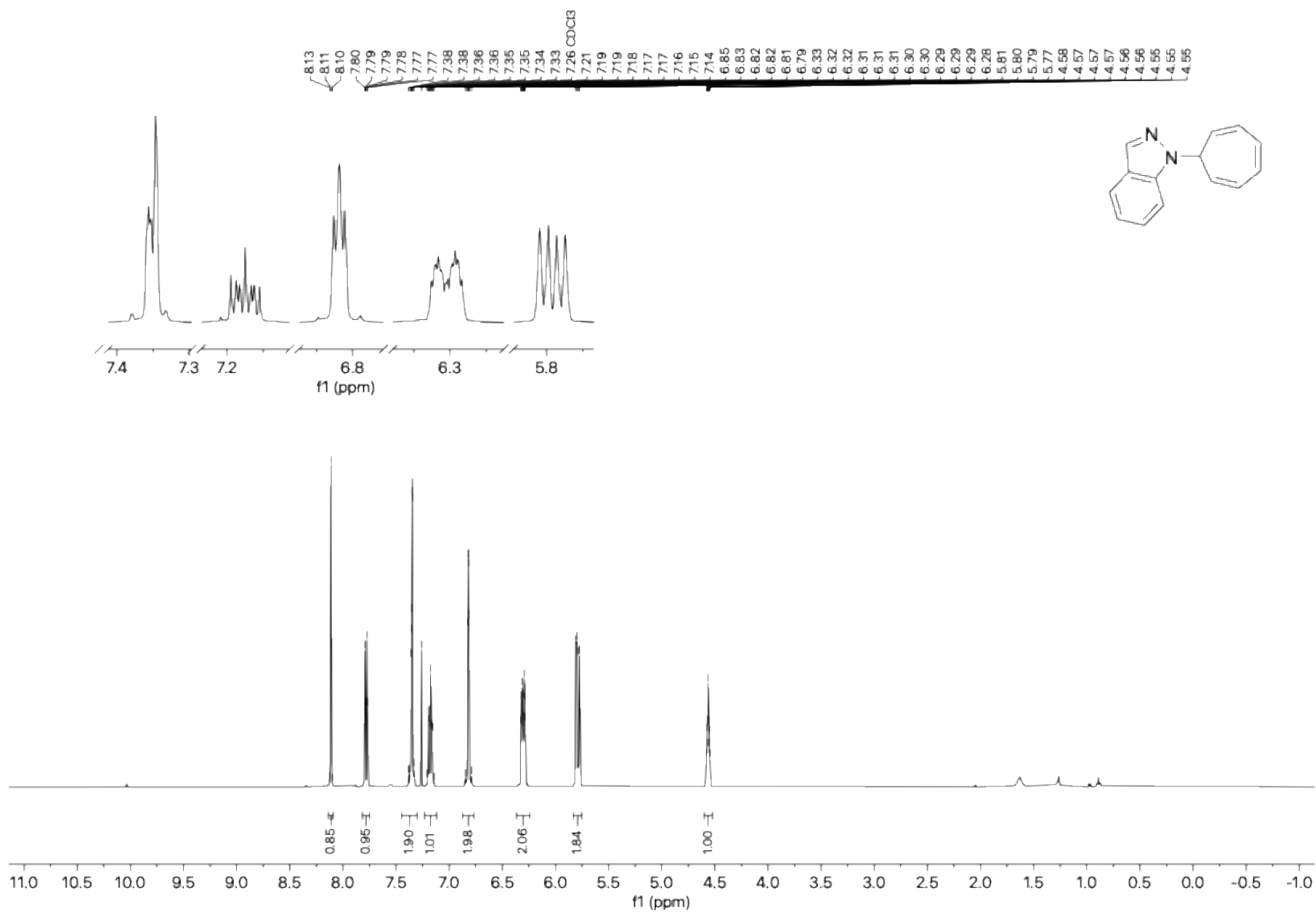
¹H-NMR (400 MHz CDCl₃) Crude NMR of 1-(Cyclohepta-2,4,6-trienyl-1-yl)-1H-1,2,4-triazole (7i)



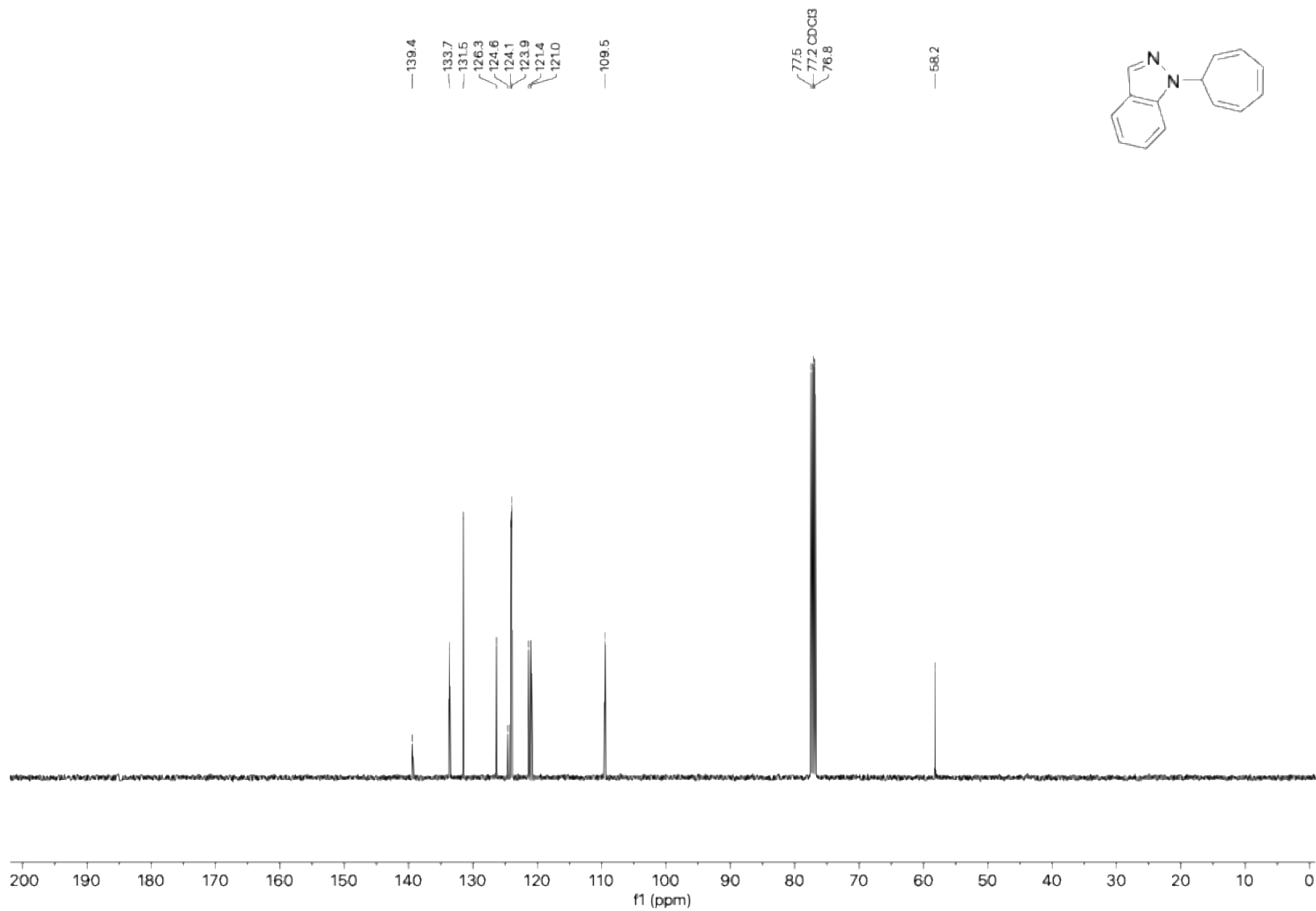
¹H-NMR (400 MHz CDCl₃) Crude NMR of 1-(Cyclohepta-2,4,6-trienyl-1-yl)-1H-imidazole (7j)



¹H-NMR (400 MHz CDCl₃) 1-Cyclohepta-2,4,6-trienyl-1H-indazole (7k)



^{13}C -NMR (101 MHz CDCl_3) 1-Cyclohepta-2,4,6-trienyl-1H-indazole (7k)



¹H-NMR (400 MHz CDCl₃) Crude NMR of 7-phenylthiocycloheptatriene(7I)

