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Synthesis of 3-(5-chloropyrazol-3-yl)propenals

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EXPERIMENTAL

The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded in $CDCl_3$ (DMSO-d_6) at room temperature on Bruker DPX-400 and AV-400 spectrometers (400.13, 100.61 и 40.56 Hz, respectively). ^{1}H, ^{13}C and ^{15}N Chemical shifts (δ in ppm) were measured with accuracy of 0.01, 0.02 and 0.1 ppm, respectively, and referred to TMS (^{1}H, ^{13}C) and nitromethane (^{15}N). The values of the δ ^{15}N were obtained through the 2D ^{1}H-^{15}N HMBC experiment. Coupling constants (*J* in Hz) values approaches to 0.1 Hz. IR spectra were recorded on a Bruker Vertex-70 instrument. MS analyses were recorded on a Shimadzu GCMS-QP5050A instrument (ionization potential 70 eV). MW activation was carried out with an Anton Paar Monowave 300 oven at the temperature control. Column and thin-layer chromatography were carried out on commercial available SiO_2(Sigma-Aldrich) with diethyl ether– hexane (1:3) mixture as eluent.

Pyrazoles **1a,b,d** and previously unknown pyrazole **1c** were prepared by described methods.[1,2] Constants of compound **1a,b,d** correspond to the literature.

5-Chloro-3-(1-chloroethyl)-1-phenyl-1H-pyrazole.

To a solution of 1,1,4-trichloropent-1-en-3-one (0.5 g, 2.7 mmol) in 1,4-dioxane (15 ml), triethylamine (0.28 g, 2.7 mmol) and phenylhydrazine (0.29 g 2.7 mmol) in 1,4-dioxane (5 ml) were added. The mixture was refluxed for 2 h. The precipitate was filtered off and the solvent was removed under reduced pressure. The product was purified by column chromatography to afford an orange oil (0.46 g, 70%). IR (microlayer, ν/cm^{-1}): 3136, 3062, 2984, 2927, 1517, 764. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.58-7.43 (m, 5H, Ph), 6.50 (s, 1H, H^4), 5.17 (q, 1H, CHCl), 1.90 (d, 3H, CH_3). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 154.8 (C^3_{Pyr}), 138.0, 129.0, 128.4, 125.1 (Ph), 127.8 (C^5_{Pyr}), 104.5 (C^4_{Pyr}), 51.8 (CHCl), 24.7 (CH_3). MS (EI, 70 eV) m/z %: 240 (M^+, 26), 205 (100), 169 (17), 143 (7), 117 (10), 102 (10), 89 (8), 77 (51), 63 (8), 51 (32). Found (%): C, 55.00; H, 4.16; Cl, 29.32; N, 11.60. Calc. for $C_{11}H_{10}Cl_2N_2$ (241.11) (%): C, 54.79; H, 4.18; Cl, 29.41; N, 11.62.

5-Chloro-3-ethenyl-1-phenyl-1H-pyrazole **1c**. A solution of 5-chloro-3-(1-chloroethyl)-1-phenyl-1*H*-pyrazole (0.31 g, 1.3 mmol) in DMF (0.47 g, 6.5 mmol) was MW irradiated at 150°C for 5 h. The product was isolated by column chromatography. Yellow oil (0.22 g, 83%). IR (microlayer, ν/cm^{-1}): 3133, 3065, 2923, 1511, 1419, 765. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.59-7.40 (m, 5H, Ph), 6.72 (dd, 1H, ^{3}J 17.6, 11.0 Hz, CH=), 6.50 (s, 1H, H^{4}), 5.78(d, 1H, ^{3}J 17.6 Hz, ^{2}J 0.7 Hz, =CH_2), 5.40 (d, 1H, ^{3}J 11.0 Hz, ^{2}J 0.7 Hz, =CH_2). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 151.1 (C^{3}_{Pyr}), 138.0, 129.0, 128.4, 125.1 (Ph), 127.8 (C^{5}_{Pyr}), 104.5 (C^{4}_{Pyr}), 51.8 (CHCl), 24.7 (CH_3). ^{15}N NMR (40.55 MHz, $CDCl_3$) δ: – 74.1 (=N-), -166.8 (NCH_3). MS (EI, 70 eV) m/z %: 204 (M^+, 100), 176 (55), 168 (78), 142 (51), 116 (60), 89 (62), 77 (94), 63 (33), 61 (90), 39 (49). Found (%): C, 64.56; H, 4.43; Cl, 17.32; N, 13.69. Calc. for $C_{11}H_9ClN_2$ (204.65) (%): C, 44.40; H, 4.41; Cl, 17.35; N, 13.72.

(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)prop-2-enal **2a** was synthesized from 5-chloro-3-ethenyl-1-methyl-1*H*-pyrazole **1a** (0.185 g, 1.3 mmol), DMF (0.556 g, 7.6 mmol), $POCl_3$ (0.766 g, 5 mmol). White powder (0.129 g, 58%). Mp 68-70 °C. IR (microlayer, ν/cm^{-1}): 3134, 2851, 2827, 1672, 1633, 1504, 974, 786. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 9.87 (d, 1H, ^{3}J 7.8 Hz, CH=O), 7.37 (d, 1H, ^{3}J 15.9 Hz, -CH=), 6.59 (dd, 1H, ^{3}J 7.8, 15.9 Hz, =C<u>H</u>-C(O)H), 6.52(c, 1H, H^{4}), 3.90 (s, 3H, NCH_3). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 193.4 (C=O), 146.9 (C^{3}), 143.4 (-CH=), 129.5 (=<u>C</u>H-C(O)H), 129.2 (C^{5}), 104.0(C^{4}), 36.6 (CH_3). ^{15}N NMR (40.55 MHz, $CDCl_3$) δ: – 66.1 (=N-), -175.6 (NCH_3). MS (EI, 70 eV) m/z %: 170 (M^+, 20), 142 (100), 141 (53), 107 (22), 81 (32), 63 (7), 52 (9), 39 (6), 28 (7). Found (%): C, 49.12; H, 4.16; Cl, 20.73; N, 16.47. Calc. for $C_7H_7ClN_2O$ (170.59) (%): C, 49.28; H, 4.14; Cl, 20.78; N, 16.42.

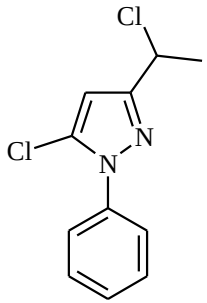
(2E)-3-[5-Chloro-1-(1-methylethyl)-1H-pyrazol-3-yl]prop-2-enal **2b** was synthesized from 5-chloro-3-ethenyl-1-(1-methylethyl)-1*H*-pyrazole **1b** (0.222 g, 1.3 mmol), DMF (0.556 g, 7.6 mmol), $POCl_3$ (0.766 g, 5 mmol). Yellow oil (0.131 g, 51%). IR (microlayer, ν/cm^{-1}): 3130, 2984, 2937,1682, 1633, 1499, 972, 785. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 9.67 (d, 1H, ^{3}J 7.9 Hz, CH=O), 7.43 (d, 1H, ^{3}J 16.1 Hz, -CH=), 6.58 (dd, 1H, ^{3}J 7.9, 16.1 Hz, =C<u>H</u>-C(O)H), 6.50 (s, 1H, H^{4}), 4.71 (m, 1H, NCH), 1.50 (d, 6H, $2CH_3$). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 193.6 (C=O), 147.0 (C^{3}), 144.2 (-CH=), 129.5 (=<u>C</u>H-C(O)H), 127.6 (C^{5}), 103.9(C^{4}), 51.0 (NCH), 22.0 (CH_3). ^{15}N NMR (40.55 MHz, $CDCl_3$) δ: – 72.1 (=N-), -152.7 (NCH). MS (EI, 70 eV) m/z %: 198 (M^+, 25), 170 (32), 155 (45), 128 (100), 93 (22), 67 (8), 52 (3), 41 (17), 27 (8). Found (%): C, 54.55; H, 5.57; Cl, 17.90; N, 14.06. Calc. for $C_9H_{11}ClN_2O$ (198.64) (%): C, 54.42; H, 5.58; Cl, 17.85; N, 14.10.

(2E)-3-(5-Chloro-1-phenyl-1H-pyrazol-3-yl)prop-2-enal **2c** was synthesized from 5-chloro-3-ethenyl-1-phenyl-1*H*-pyrazole **1c** (0.266 g, 1.3 mmol), DMF (0.556 g, 7.6 mmol), $POCl_3$ (0.766 g, 5 mmol). White powder (0.139 g, 46%). Mp 114-116 °C. IR (microlayer, ν / cm^{-1}): 3127, 3059, 2924, 2843, 2740, 1681, 1633, 1506, 969,792. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 9.72 (d, 1H, ^3J 7.8 Hz, CH=O), 7.59 (d, 1H, ^3J 7.3 Hz, *o*-H_{Ph}), 7.53 (dd, ^3J 7.3, 6.5 Hz, 2H, *m*-H_{Ph}), 7.49 (t, 2H, ^3J 6.5 Hz, *p*-H_{Ph}), 7.47 (d, 1H, ^3J 16.2 Hz, -CH=), 6.71 (s, 1H, H^4), 6.68 (dd, 1H, ^3J 16.2, 7.8 Hz, =C<u>H</u>-C(O)H). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 193.2 (C=O), 148.4 (C^3), 143.0 (-CH=), 137.7 (C^i_{Ph}), 130.51 (=<u>C</u>H-C(O)H), 129.2 (H^5, C^m_{Ph}), 129.0 (C^p_{Ph}), 125.0 (C^o_{Ph}), 105.7 (C^4). ^{15}N NMR (40.55 MHz, $CDCl_3$) δ: – 58.2 (=N-), -152.9 (NPh). MS (EI, 70 eV) m/z %: 232 (M^+, 26), 204 (100), 168 (39), 143 (29), 116 (24), 89 (16), 77 (99), 63 (6), 51 (67). Found (%): C, 61.83; H, 3.88; Cl, 15.27; N, 12.08. Cal. for $C_{12}H_9ClN_2O$ (232.66) (%): C, 61.95; H, 3.90; Cl, 15.24; N, 12.04.

(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)-2-methylprop-2-enal **2d** was synthesized from 5-chloro-1-methyl-3-[(1*E*)-prop-1-en-1-yl]-1*H*-pyrazole **1d** (0.204 g, 1.3 mmol), DMF (0.556 g, 7.6 mmol), $POCl_3$ (0.766 g, 5 mmol). Yellow oil (0.127 g, 53%). IR (microlayer, ν / cm^{-1}): 3132, 2852, 2735, 1692, 1515, 974, 798. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 9.69 (s, 1H, CH=O), 6.58 (s, 2H, H^4, -CH=), 3.70 (s, 3H, NCH_3), 1.77 (d, 3H, ^4J 3.7 Hz, CH_3). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 182.7 (C=O), 149.8 (C^3), 133.2 (H^5), 131.8 (-CH=), 120.1 (=C), 114.5 (C^4), 35.8 (NCH_3), 18.3 (CH_3). ^{15}N NMR (40.55 MHz, $CDCl_3$) δ: – 79.6 (=N-), -178.9 (NCH_3). MS (EI, 70 eV) m/z %: 184 (M^+, 100), 169 (100), 156 (41), 149 (51), 132 (11), 121 (32), 108 (39), 80 (31), 66 (10), 51 (15), 39 (20). Found (%): C, 51.87; H, 4.93; Cl, 19.14; N, 15.19. Calc. for $C_8H_9ClN_2O$ (184.62) (%): C, 52.04; H, 4.91; Cl, 19.20; N, 15.17.

(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)prop-2-enoic acid **3.** Mp 163-165 °C. IR (KBr, ν/cm^{-1}): 3115, 2954, 1683, 1638, 1495, 994, 803. ^{1}H NMR (400.13 MHz, DMSO-d_6) δ: 7.31 (d, 1H, ^3J 16.1 Hz, -CH=), 6.93 (s, 1H, H^4), 6.41 (d, 1H, ^3J 16.1 Hz, -C<u>H</u>-COOH), 3.81 (s, 3H, CH_3). ^{13}C NMR (100.62 MHz, DMSO-d_6) δ: 167.3 (COOH), 146.7 (C^3), 135.2 (-CH=), 127.2 (C^5), 120.6 (=<u>C</u>H-COOH), 103.9(C^4), 36.4 (CH_3). Found (%): C, 45.18; H, 3.80; Cl, 18.97; N, 14.98. Calc. for $C_7H_7ClN_2O_2$ (186.59) (%): C, 45.06; H, 3.78; Cl, 19.00; N, 15.01.

5-Chloro-3-(1-chloroethyl)-1-phenyl-1H-pyrazole



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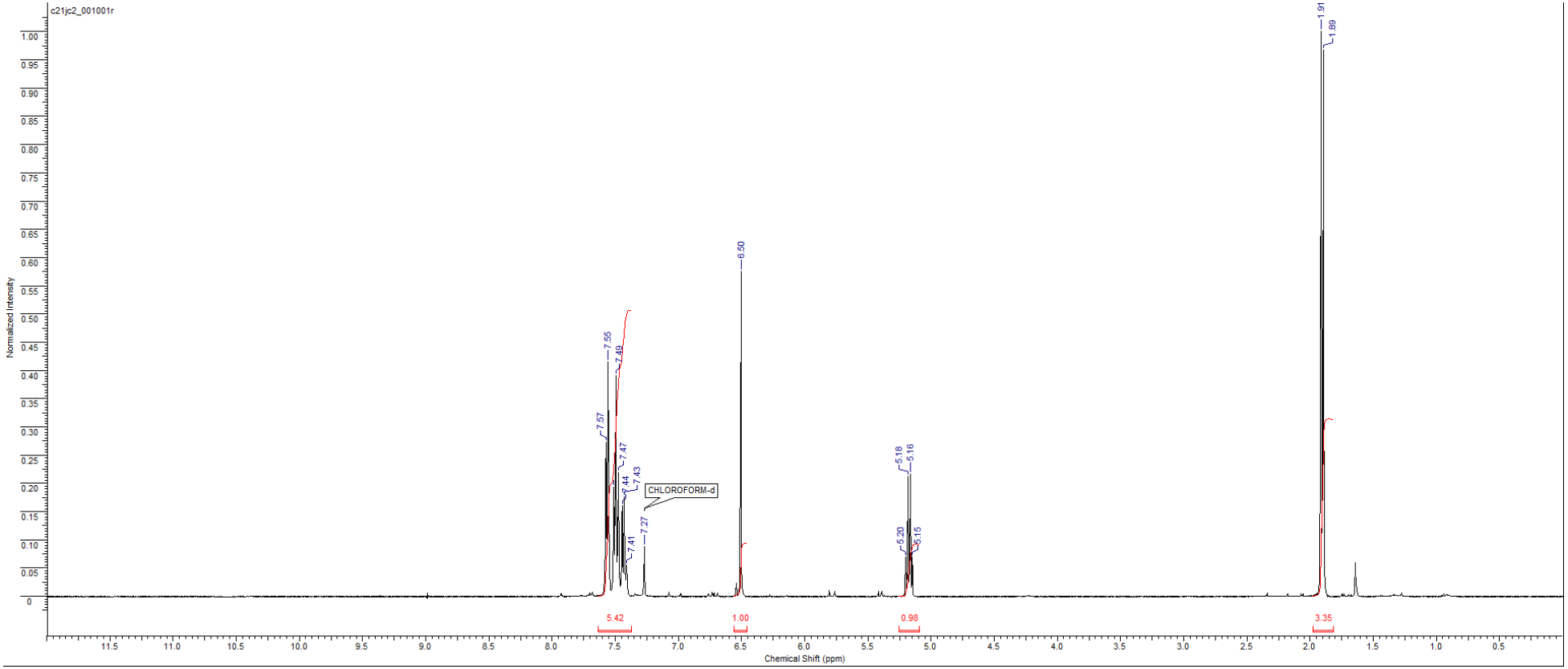
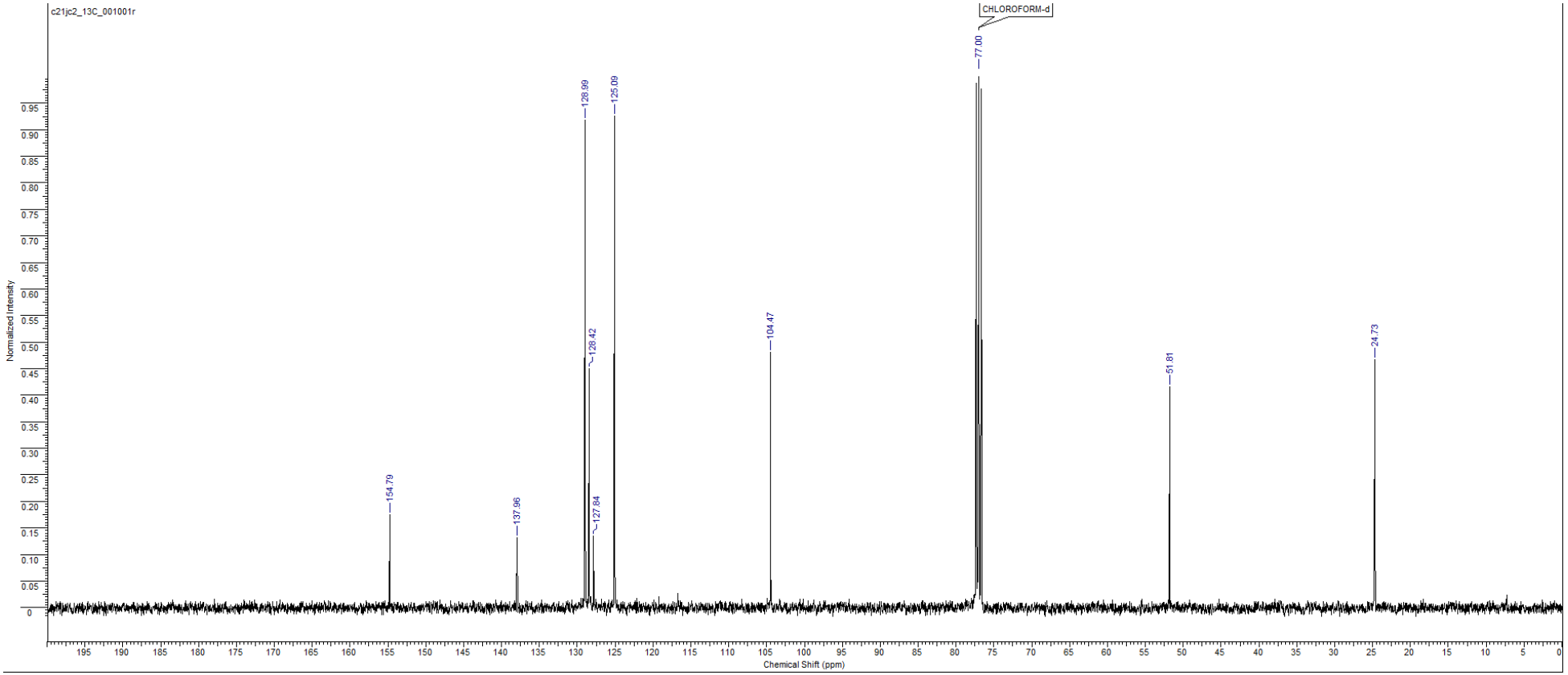


^{13}C NMR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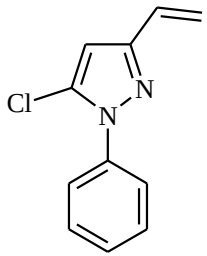
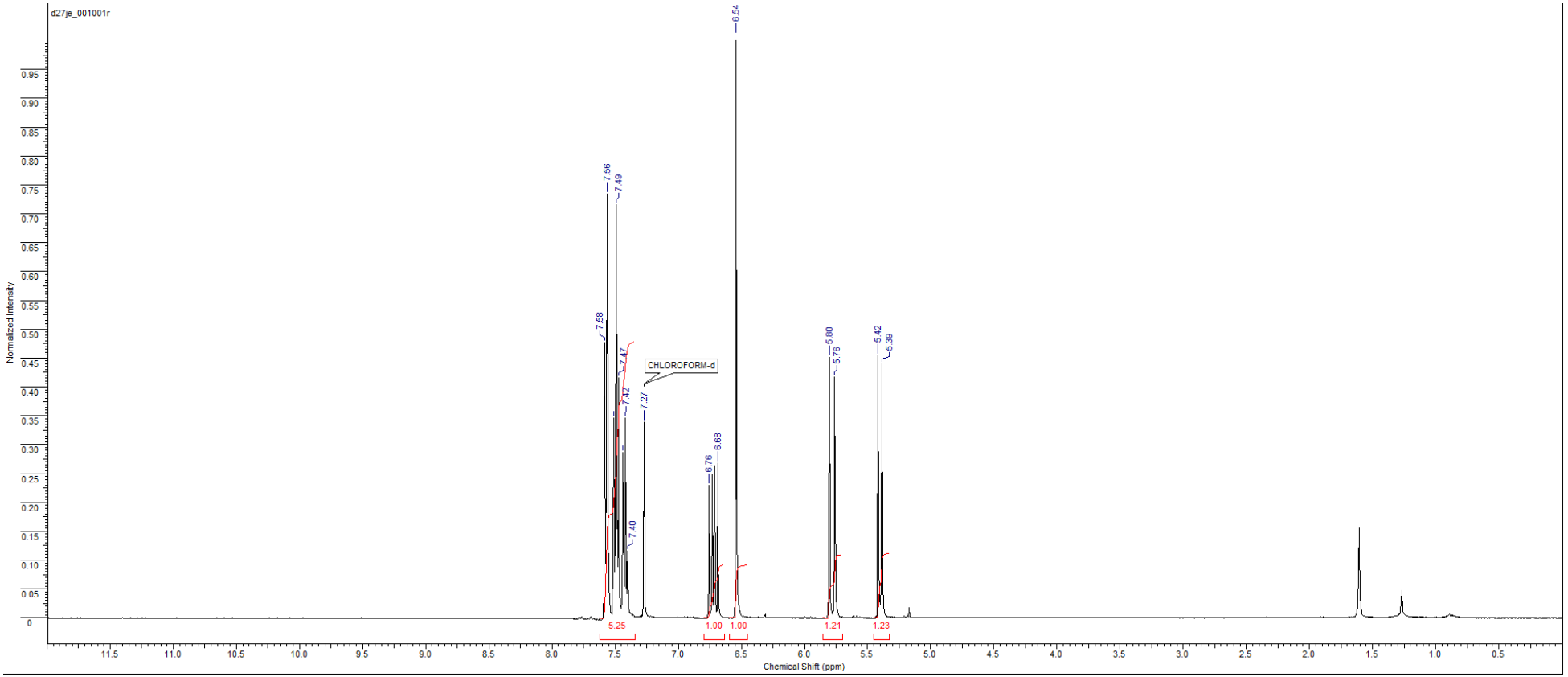
51.81
24.73
Normalized Intensity
Chemical Shift (ppm)

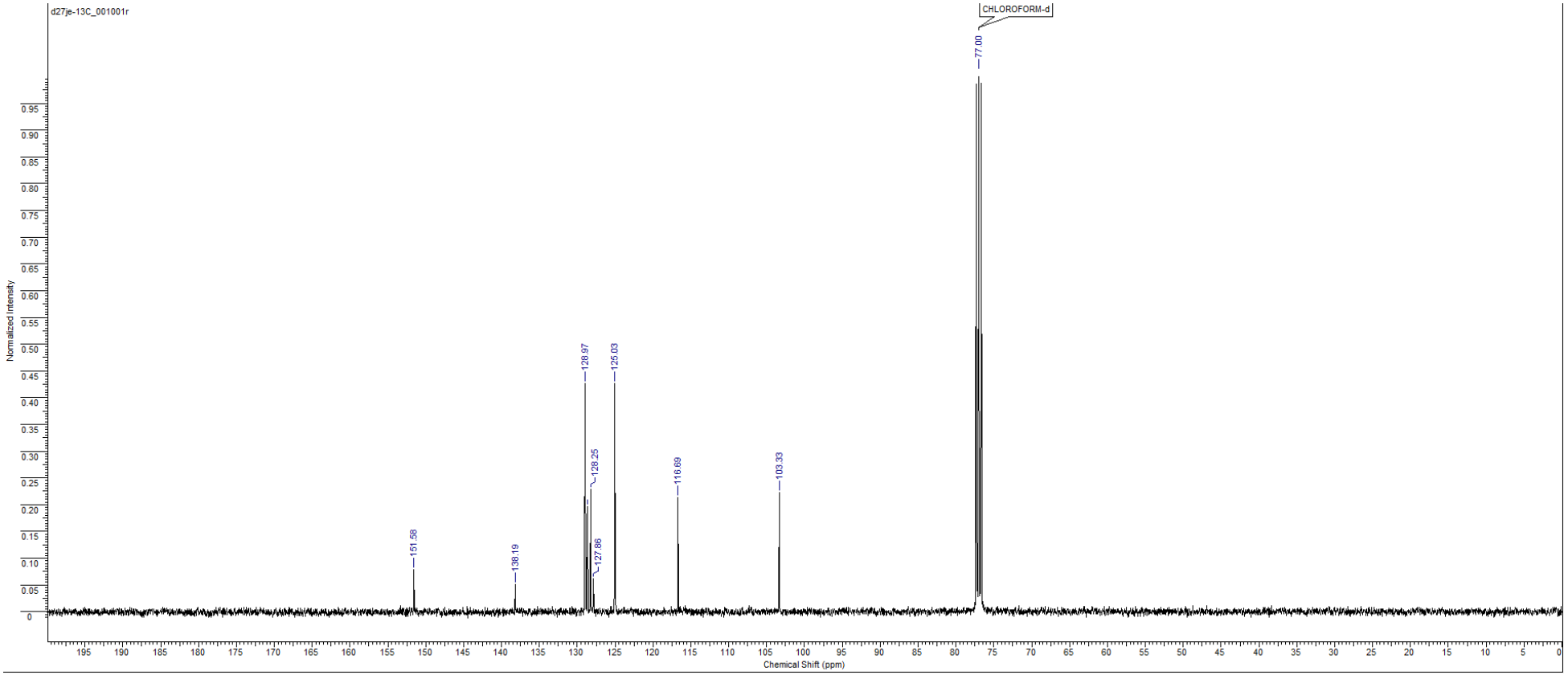
5-Chloro-3-ethenyl-1-phenyl-1H-pyrazole **1c**.



^{1}H NMR



^{13}C NMR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CHLOROFORM-d
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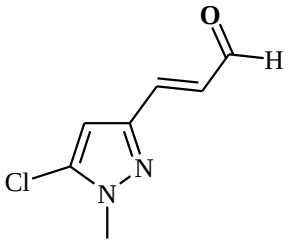
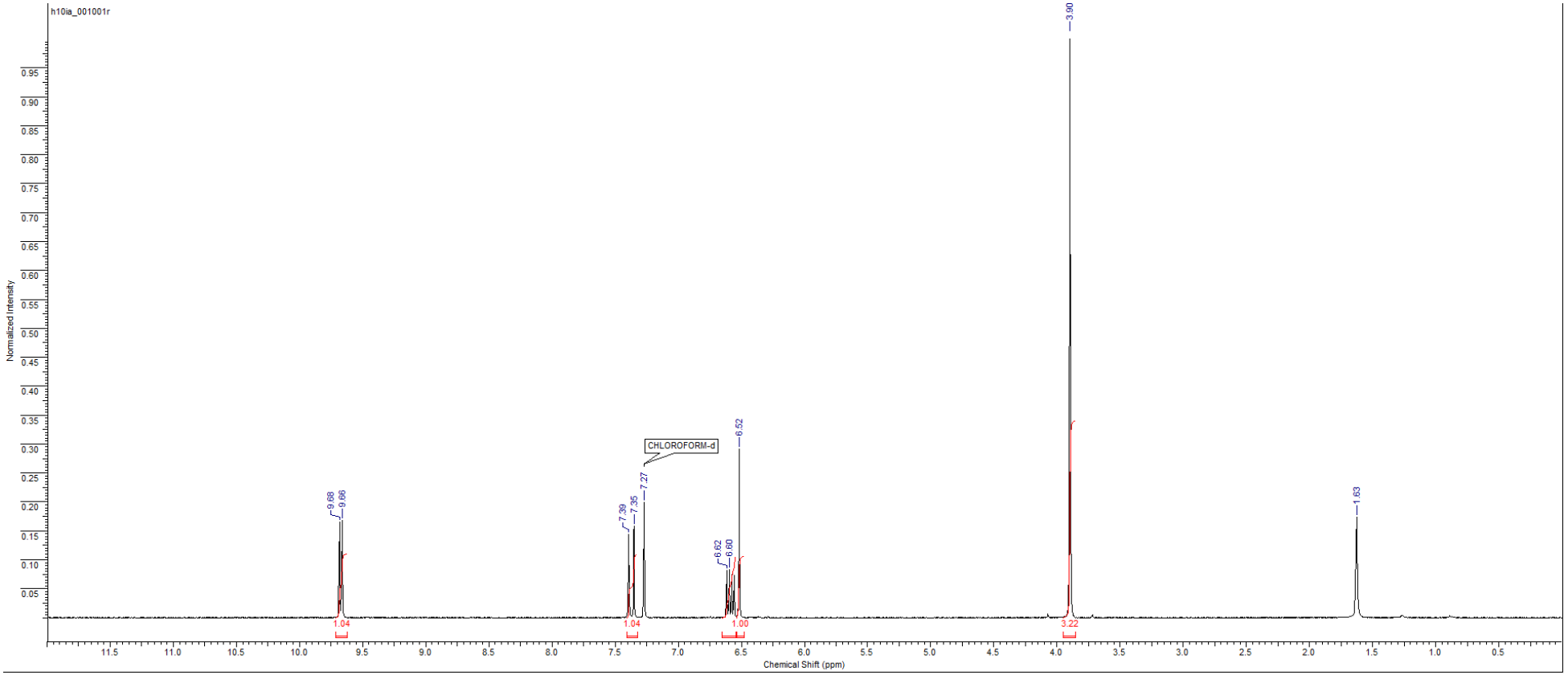
128.97
125.03
128.25
127.86
116.69
103.33
151.58
138.19
Normalized Intensity
Chemical Shift (ppm)

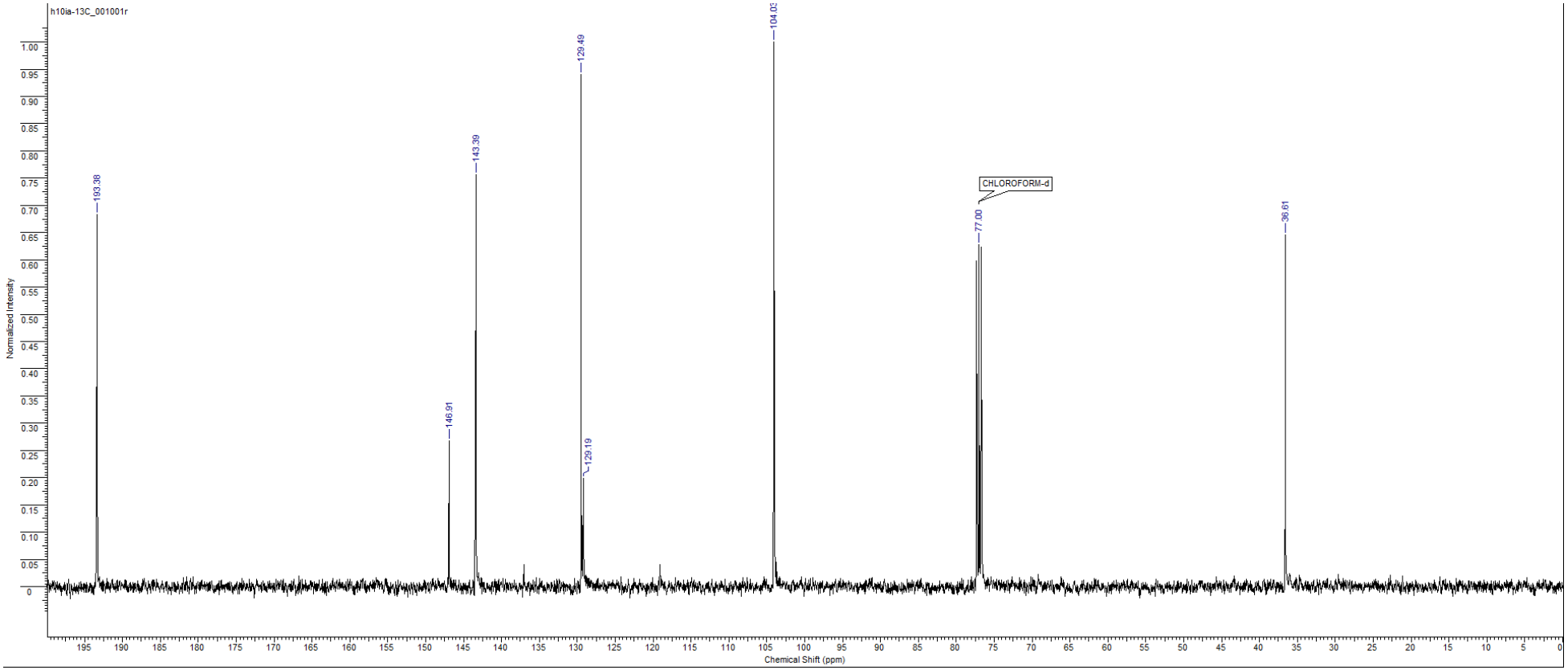
(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)prop-2-enal **2a**.



^{1}H NMR



^{13}C NMR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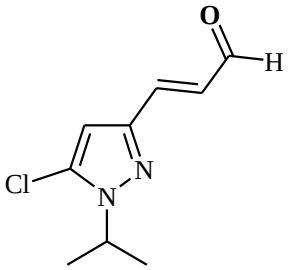
146.91
143.39
129.49
129.19
104.03
CHLOROFORM-d
77.00
36.61
Normalized Intensity
Chemical Shift (ppm)

(2E)-3-[5-Chloro-1-(1-methylethyl)-1H-pyrazol-3-yl]prop-2-enal **2b.**



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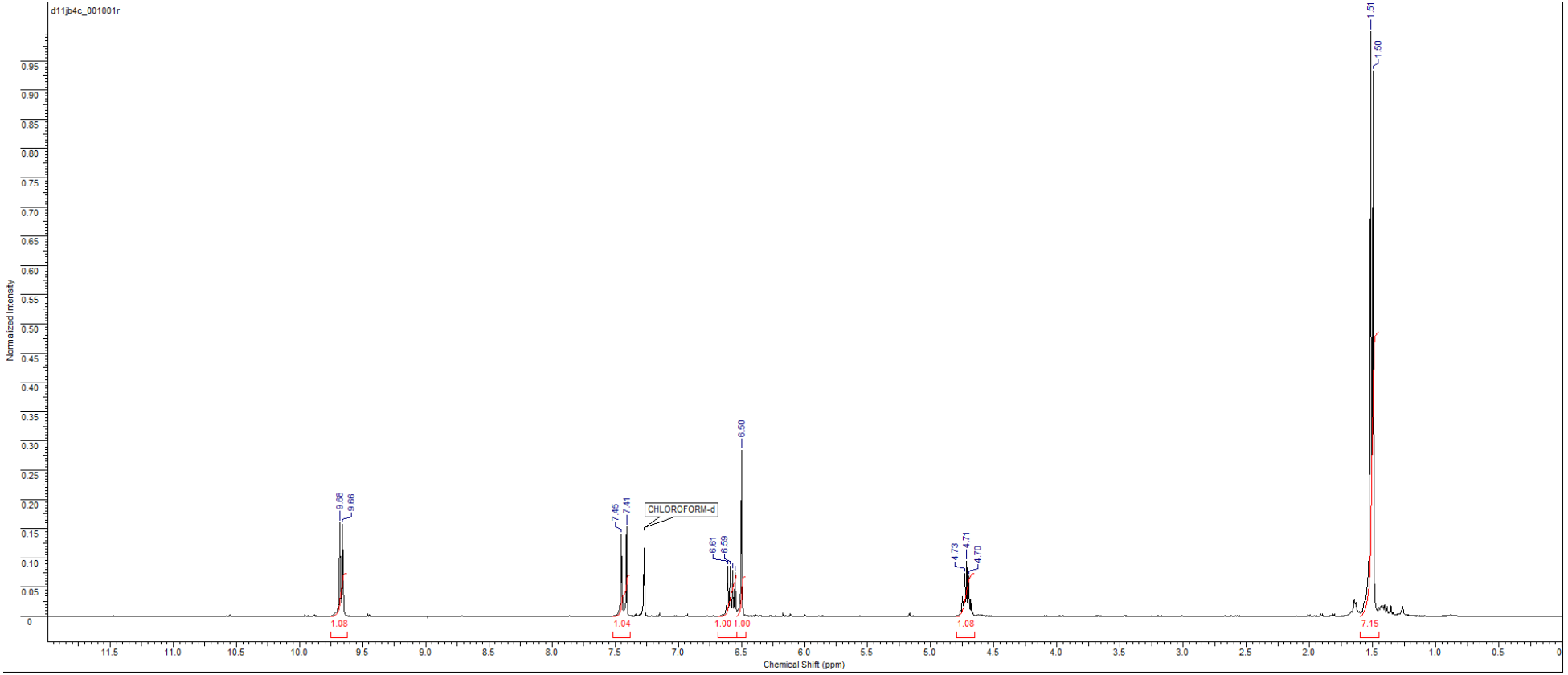

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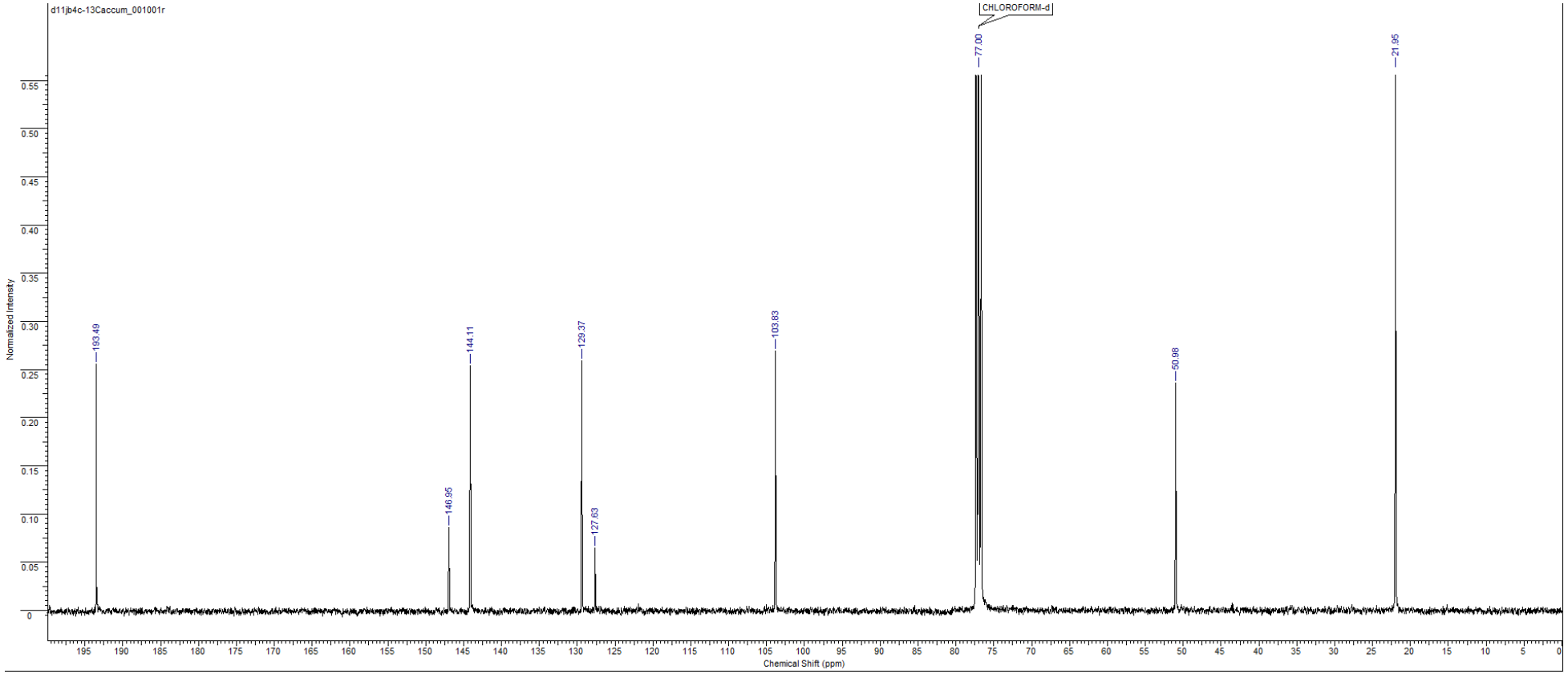
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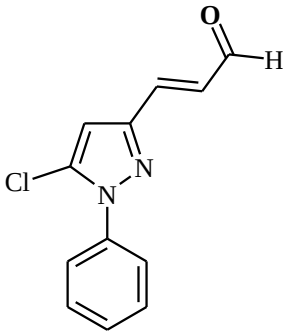
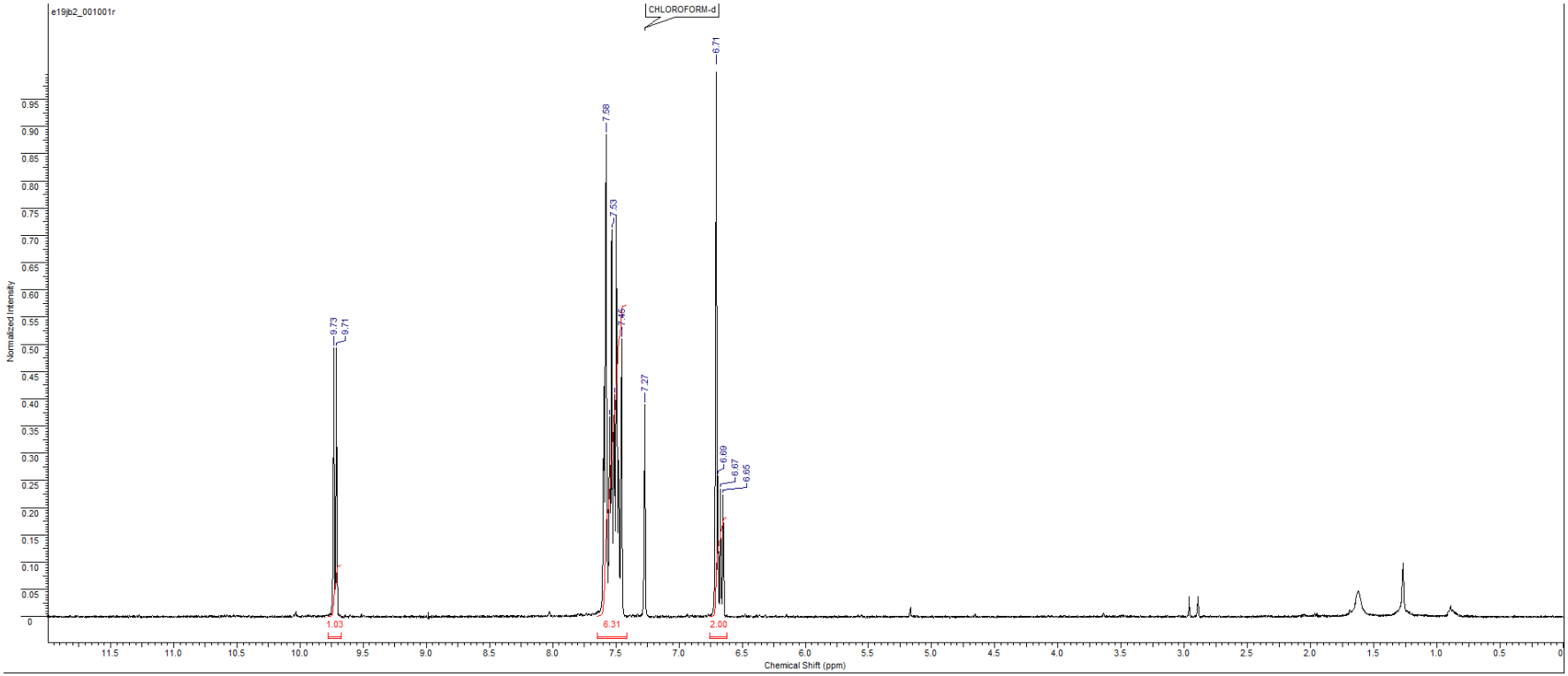
193.49
146.95
144.11
129.37
127.63
103.83
50.98
Normalized Intensity
Chemical Shift (ppm)

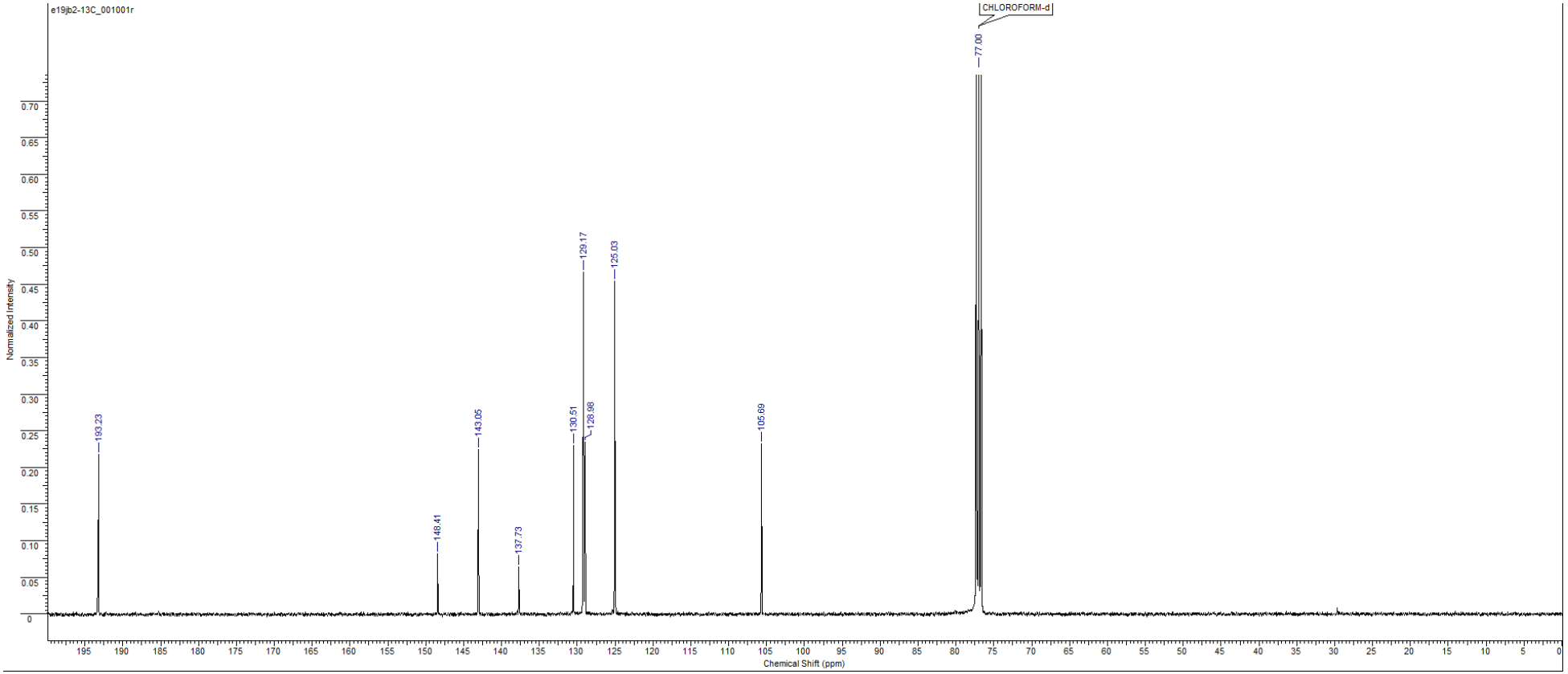
(2E)-3-(5-Chloro-1-phenyl-1H-pyrazol-3-yl)prop-2-enal **2c**.



^{1}H NMR



^{13}C NMR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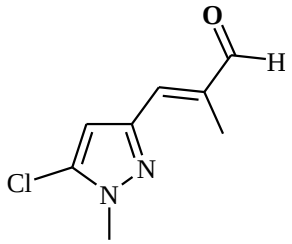
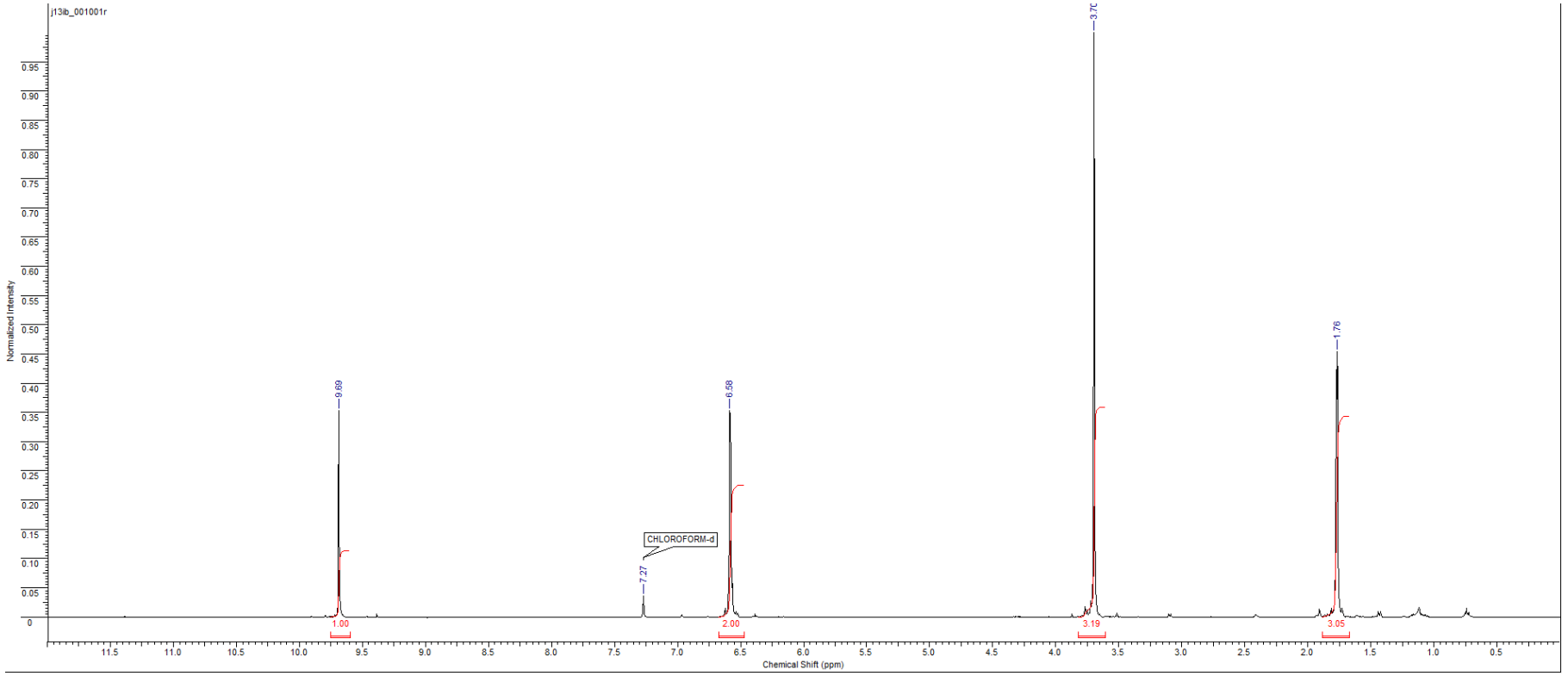
193.23
148.41
143.05
137.73
130.51
129.17
128.98
125.03
105.69
Normalized Intensity
Chemical Shift (ppm)

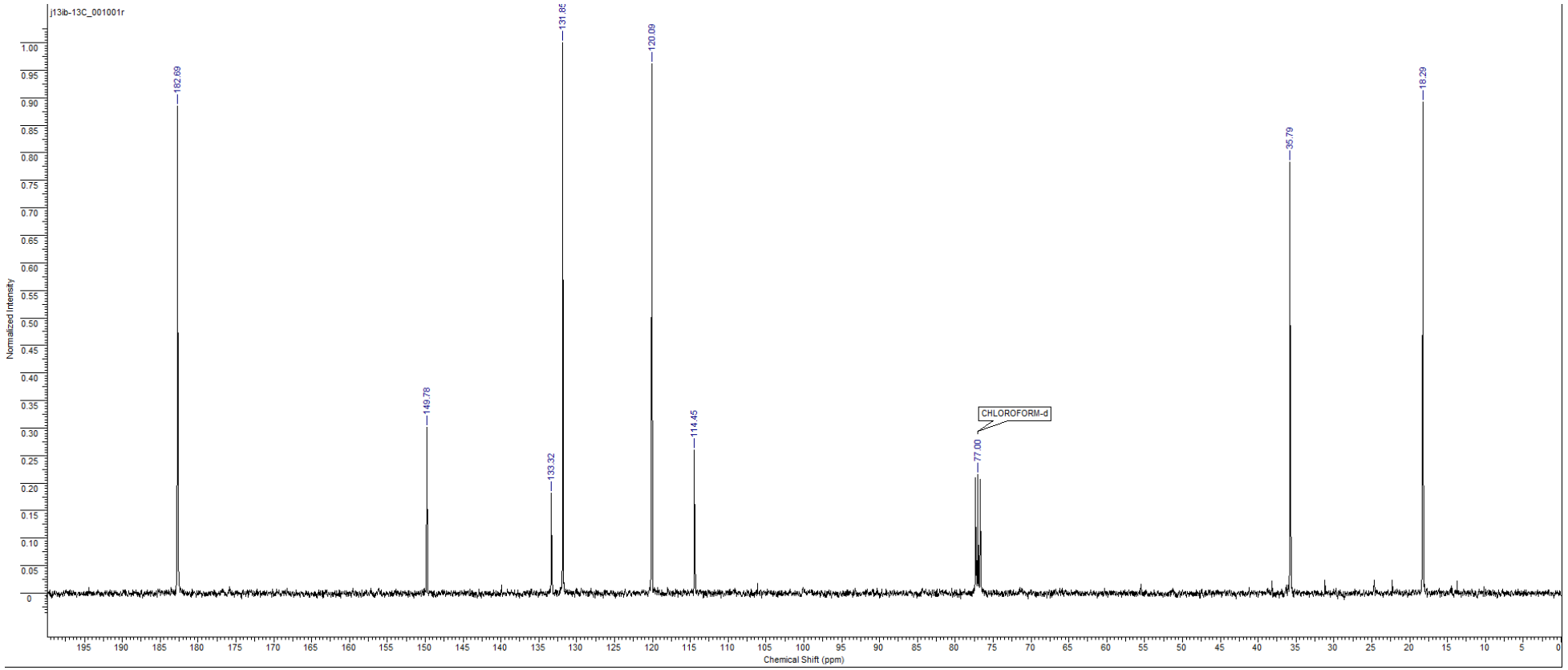
(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)-2-methylprop-2-enal **2d.**



^{1}H NMR



^{13}C NMR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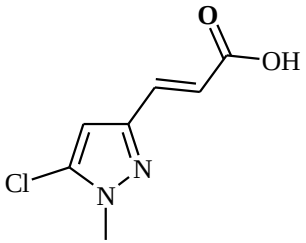
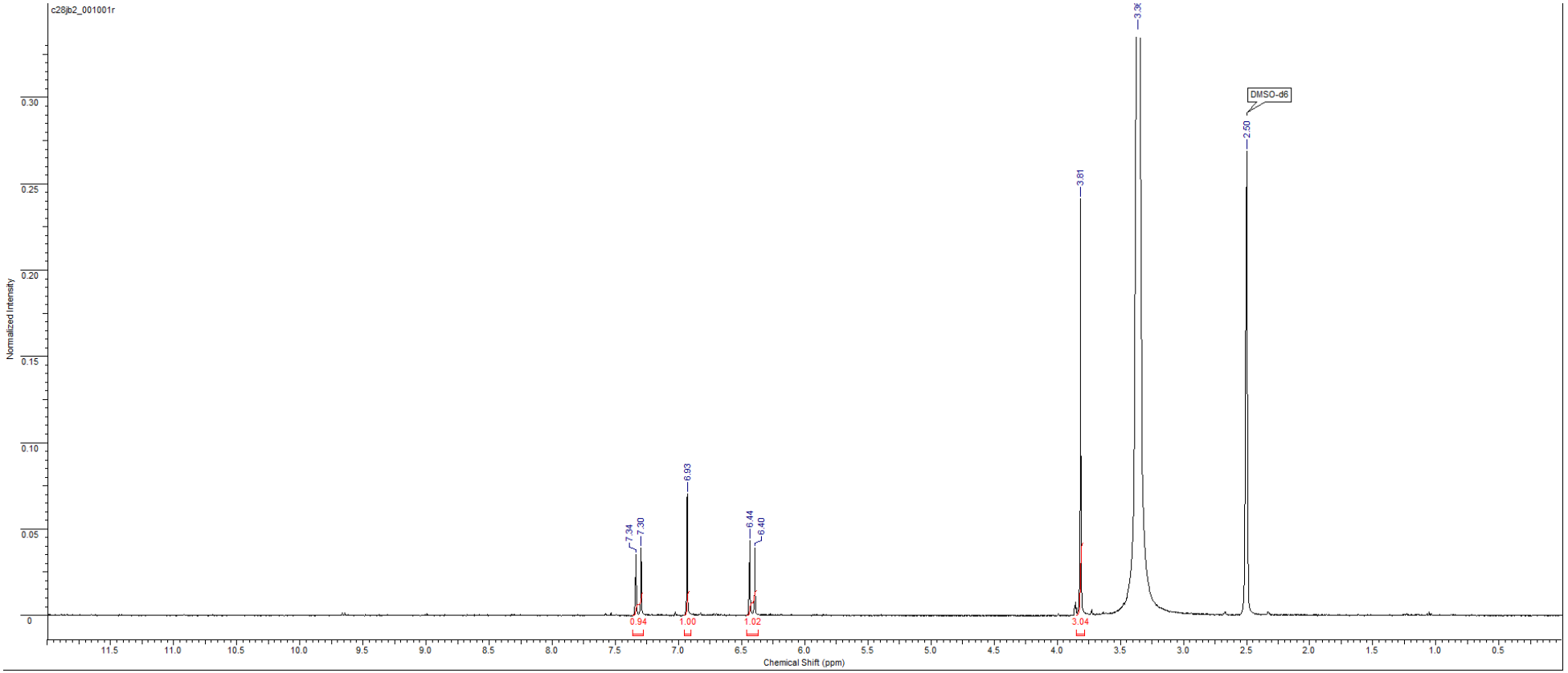
Normalized Intensity
Chemical Shift (ppm)
182.69
149.78
133.32
131.85
120.09
114.45
77.00
CHLOROFORM-d
35.79
18.29

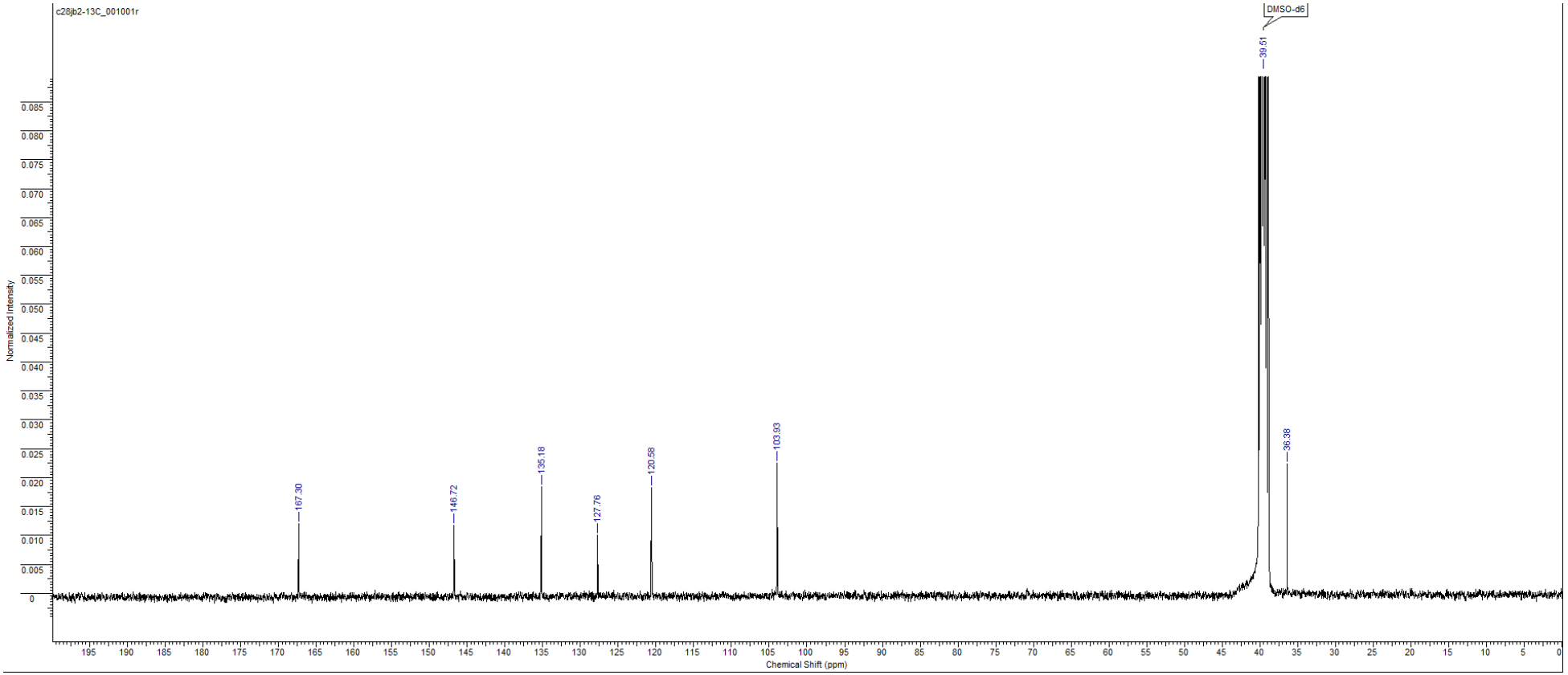
(2E)-3-(5-Chloro-1-methyl-1H-pyrazol-3-yl)prop-2-enoic acid **3.**



^{1}H NMR



^{13}C NMR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DMSO-d6
39.51
36.38
167.30
146.72
135.18
127.76
120.58
103.93
Normalized Intensity
Chemical Shift (ppm)

References

1 G. G. Levkovskaya, V. A. Kobelevskaya, E. V. Rudyakova, K. Q. Ha, D. O. Samultsev and I. B. Rozentsveig, *Tetrahedron*, 2011, **67**, 1844.

2 G. G. Levkovskaya, E. V. Rudyakova, V. A. Kobelevskaya, A. V. Popov and I. B. Rozentsveig, *Arkivoc*, 2016, **iii**, 82.