Electronic Supporting Information

One-pot highly diastereoselective annulation to *N*-unprotected tetrasubstituted 2-pyrrolines

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General Methods

All reactions requiring dry or inert conditions were conducted in flame dried glassware under a positive pressure of nitrogen. THF and DCM were freshly distilled prior to use respectively over $LiAlH_4$ and calcium hydride and stored under nitrogen, all other solvents were dried over molecular sieves. Molecular sieves (Aldrich Molecular Sieves, 3 Å, 1.6 mm pellets) were activated under vacuum at 200°C overnight. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualised by UV light and, when necessary, by anisaldehyde spray test. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance-400 spectrometer, Bruker Avance-300 spectrometer, Bruker Avance-250 spectrometer and Bruker Avance III HD 600 spectrometer at room temperature in $CDCl_3$ as solvent. Chemical shifts for protons are reported using residual $CHCl_3$ as internal reference (δ = 7.26 ppm). Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (δ = 77.0 ppm). FTIR spectra were recorded as thin films on KBr plates using Bruker Tensor 27 spectrometer and absorption maxima are reported in wavenumber (cm^{-1}). Melting points were measured with a Stuart Model SMP 30 melting point apparatus. Petrol ether (PE) refers to light petroleum ether (boiling point 40-60 °C). Anhydrous toluene and all starting materials (unless otherwise noted) were purchased from Aldrich and used as received. Alkenes **4** were synthesized as reported in the literature.[1]

Experimental Procedures and Compounds Characterization Data

General procedure for the for the synthesis of *trans*-2-pyrrolines 6

A sample vial was charged with alkene **4** (0.10 mmol), *N*-(diphenylmethylene)glycine *tert*-butyl ester **5a** or ethyl ester **5b** (0.10 mmol) and 1,4-diazabicyclo[2.2.2]octane (2.2 mg, 0.02 mmol) in anhydrous tetrahydrofuran (0.2 mL). The reaction was stirred at room temperature for 18-40 h, monitored by TLC (eluent PE/ ethyl acetate 80:20). The hydrolysis of the imine was carried out by first diluting the reaction with THF (0.2 mL) and lowering the reaction temperature to 0 °C. Then HCl. 1N (0.5 mL) was added and the mixture was stirred for 45 min leaving the reaction vessel to reach room temperature. Dichloromethane was then added and the water layer was neutralized with saturated Na_2CO_3 solution. The water layer was separated and extracted three more times with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Products **6** were isolated by flash chromatography (eluting with PE/ ethyl acetate 90:10) in 50-96 % yield. The relative *trans*-configuration of 2-pyrrolines was confirmed on compound **6a** via NOESY experiment (see S43 of the ESI).

General procedure for the oxidation of *trans*-2-pyrrolines 6

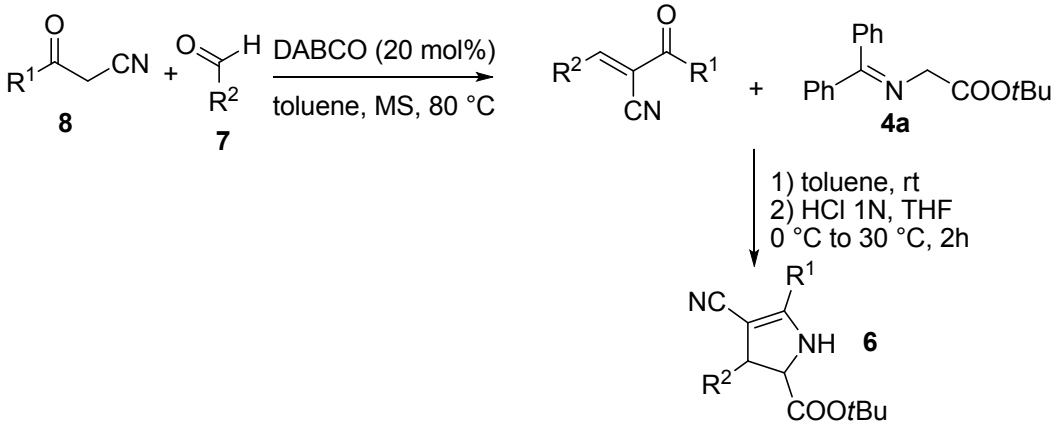
The oxidation was performed according to the literature.[2] A sample vial was charged with compound **6a** (57.2 mg, 0.17 mmol) in a mixture ethyl acetate/toluene 1:2 (0.1 mL/0.2 mL). Then 2,3-dichloro-5,6-dicyano-*p*-benzoquinone DDQ (44 mg, 0.19 mmol) was added and the reaction mixture was stirred at 70 °C for 23 h. The starting material and the product have the similar R_f but they show different red tones visualizing the TLC with anysaldehyde staining solution. The product **9** (44.1 mg, 78% yield) was isolated by flash chromatography (eluting with PE/ ethyl acetate 90:10).

General procedure for reduction of *trans*-2-pyrroline 6a

The reduction was performed according to the literature.[3] $NaBH_3CN$ (60 mg, 0.90 mmol) was added at 0 °C to a solution of acetic acid / dichlorometane 1/1 (0.7 mL / 0.7 mL) containing compound **6a** (106 mg, 0.30 mmol). The resulting mixture was stirred for 2 hours at 0 °C (TLC eluent PE/ ethyl acetate 80:20). After completion, the reaction was diluted with ethyl acetate, extracted with NaOH 1N and washed two times with water. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography (eluting from PE/ ethyl acetate 90:10 to 85:15) afforded the diastereoisomers **10** and **11** in 74% yield (77.6 mg). The diastereisomeric ratio (dr 70:30) was determined by ^1H NMR analysis of the crude reaction

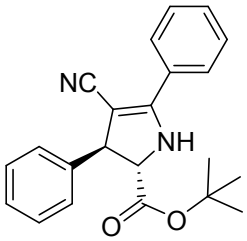
mixture. The relative configuration of the stereocentres of compound **10** and **11** was confirmed by NOESY experiments (see S44-S45 of the ESI).

One-pot sequential synthesis of *trans*-2-pyrrolines 6



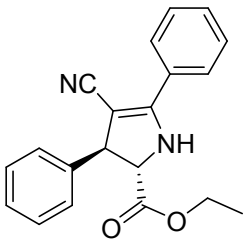
In a vial containing anhydrous toluene (0.5 mL) and molecular sieves (3 Å, ≈ 20 mg), benzoylacetonitrile **8** (0.25 mmol), benzaldehyde **7** (0.25 mmol) and 1,4-diazabicyclo[2.2.2]octane (5.6 mg, 20 mol %) were added. The reaction was stirred at 80 °C for 4-7 hours monitored by TLC till the formation of alkene **5** was complete. The reaction mixture was allowed to cool down to room temperature, then *N*-(diphenylmethylene)glycine *tert*-butyl ester **4a** (73.8 mg, 0.25 mmol) was added to the reaction mixture (for compound **6i**, additional 0.5 mL of anhydrous toluene were added to increase the solubility of the reagents). The reaction mixture was stirred at room temperature for 19-26 hours as monitored by TLC. After completion, toluene was removed, the crude diluted with THF (1 mL) and then HCl (1N) (1 mL) was added at 0 °C leaving the mixture to warm up to 30°C for 2 h. Dichloromethane was then added and the water layer was neutralized with saturated Na_2CO_3 solution. The water layer was separated and extracted three more times with dichloromethane. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by flash chromatography (eluent PE/ ethyl acetate 90:10) to give products **6** in 55-82% yield.

***tert*-Butyl-(2*S**,3*S**)-4-cyano-3,5-diphenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6a)**



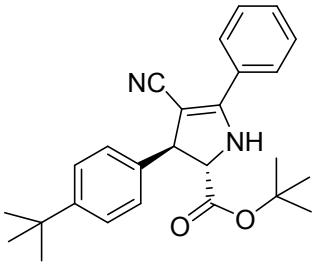
Pale yellow foam, 33.3 mg, 96 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3333, 2980, 2934, 2190, 1738, 1597, 1574, 1500, 1456, 1369, 1245, 1154, 770, 738, 698. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.85-7.82 (m, 2H), 7.51-7.27 (m, 8H), 4.90 (brs, 1H), 4.53 (d, 1H, *J*= 5.3 Hz), 4.22 (d, 1H, *J*= 5.3 Hz), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 171.1, 160.8, 141.5, 131.1, 129.2, 129.0, 128.9, 127.7, 127.2, 127.0, 118.9, 83.0, 81.0, 67.5, 53.5, 28.0. **MS** (ESI *m/z*) 369.2 [MNa^+, 100%].

Ethyl-(2*S,3*S**)-4-cyano-3,5-diphenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6b)**



Yellow wax, 23.6 mg, 74 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3326, 2981, 2928, 2190, 1738, 1596, 1574, 1498, 1456, 1437, 1295, 1236, 1200, 1096, 1029, 765, 695. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.85-7.80 (m, 2H), 7.56-7.29 (m, 8H), 4.86 (brs, 1H), 4.59 (d, 1H, *J*= 5.0 Hz), 4.35-4.21 (m, 4H), 1.35 (t, 3H, *J*= 7.1 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 172.0, 160.7, 141.2, 131.2, 129.1, 129.0, 127.9, 127.2, 127.0, 118.7, 81.7, 67.0, 62.2, 53.3, 14.2. **MS** (ESI *m/z*) 319.8 [MH^+].

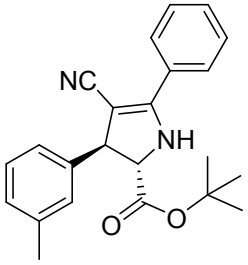
***tert*-Butyl-(2*S**,3*S**)-3-(4'-tert-butylphenyl)-4-cyano-5-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6c)**



Yellow solid, 27.4 mg, 68 % yield. **Mp** 143.5-144.5 °C. **FTIR** ν_{max} (KBr)/cm^{-1} 3322, 2966, 2905, 2191, 1735, 1500, 1459, 1369, 1245, 1155, 841, 771, 693. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.85-7.80 (m, 2H), 7.50-7.44 (m, 3H), 7.38 (d, 2H, *J*= 8.4 Hz), 7.28 (d, 2H, *J*= 8.4 Hz), 4.80 (brs, 1H), 4.51 (d, 1H, *J* = 4.9 Hz), 4.23 (dd, 1H, *J* = 4.9, 0.86 Hz), 1.53 (s, 9H), 1.32 (s, 9H). **^{13}C NMR**

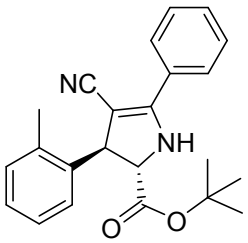
($CDCl_3$, 100 MHz): δ 171.3, 160.7, 150.6, 138.5, 131.1, 129.4, 128.9, 128.9, 127.0, 126.8, 125.9, 119.1, 83.0, 81.5, 67.5, 53.1, 34.1, 31.3, 28.0. **MS** (ESI *m/z*) 425.7 [MNa^+, 100%].

***tert*-Butyl-(2*S**,3*S**)-4-cyano-5-phenyl-3-m-tolyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6d)**



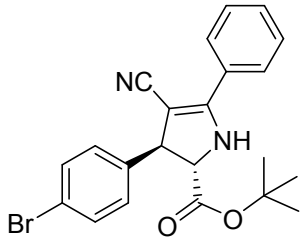
Yellow wax, 28.1 mg, 78 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3334, 2979, 2931, 2189, 1735, 1609, 1596, 1571, 1500, 1459, 1369, 1247, 1155, 845, 773, 738, 695. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.88-7.82 (m, 2H), 7.52-7.45 (m, 4H), 7.29-7.25 (m, 1H), 7.18-7.10 (m, 2H), 4.84 (brs, 1H), 4.50 (d, 1H, *J*= 5.3 Hz), 4.23 (d, 1H, *J*= 5.3 Hz), 2.37 (s, 3H), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.2, 160.7, 141.5, 138.6, 131.1, 129.3, 128.9, 128.5, 127.9, 127.0, 124.3, 119.0, 83.0, 81.3, 67.6, 53.5, 28.0, 21.5. **MS** (ESI *m/z*) 383.6 [MNa^+, 100%].

***tert*-Butyl-(2*S**,3*S**)-4-cyano-5-phenyl-3-o-tolyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6e)**



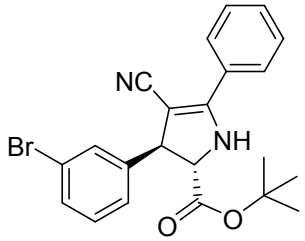
Yellow wax, 27.8 mg, 77 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3333, 2979, 2933, 2190, 1735, 1596, 1575, 1499, 1460, 1369, 1247, 1154, 844, 738, 695. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.84-7.81 (m, 2H), 7.51-7.45 (m, 3H), 7.29-7.24 (m, 1H), 7.23-7.17 (m, 3H), 4.86 (brs, 1H), 4.80 (d, 1H, *J*= 3.8 Hz), 4.14 (d, 1H, *J*= 3.8 Hz), 2.51 (s, 3H), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.4, 161.0, 139.2, 135.6, 131.1, 130.8, 129.3, 128.9, 127.5, 127.0, 126.9, 126.7, 118.9, 83.2, 81.6, 67.2, 49.2, 28.0, 19.7. **MS** (ESI *m/z*) 383.6 [MNa^+, 52%].

***tert*-Butyl-(2*S**,3*S**)-3-(4'-bromophenyl)-4-cyano-5-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6f)**



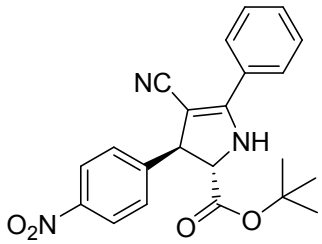
Yellow wax, 31.9 mg, 75 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3367, 2978, 2933, 2190, 1736, 1596, 1488, 1459, 1369, 1245, 1154, 1073, 1011, 841, 771, 694. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.86-7.79 (m, 2H), 7.54-7.46 (m, 5H), 7.28-7.20 (m, 2H), 4.85 (brs, 1H), 4.50 (d, 1H, *J*= 5.5 Hz), 4.17 (d, 1H, *J*= 5.5 Hz), 1.52 (s, 9H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 170.8, 161.1, 140.5, 132.2, 131.4, 129.0, 127.0, 121.7, 118.7, 83.3, 80.7, 67.4, 53.0, 28.0. **MS** (ESI *m/z*) 447.6 [MNa^+, 64%].

***tert*-Butyl-(2*S**,3*S**)-3-(3'-bromophenyl)-4-cyano-5-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6g)**



Pale yellow wax, 28.9 mg, 68 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3331, 2979, 2190, 1734, 1595, 1571, 1500, 1474, 1430, 1394, 1369, 1245, 1154, 844, 773, 739, 694. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.85-7.81 (m, 2H), 7.52-7.42 (m, 5H), 7.31-7.23 (m, 2H), 4.89 (brs, 1H), 4.50 (d, 1H, *J*= 5.3 Hz), 4.19 (d, 1H, *J*= 5.3 Hz), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 170.7, 161.2, 143.7, 131.4, 130.9, 130.6, 130.4, 129.0, 127.1, 126.0, 123.1, 118.6, 83.4, 80.3, 67.4, 53.1, 28.0. **MS** (ESI *m/z*) 447.8 [MNa^+, 55%].

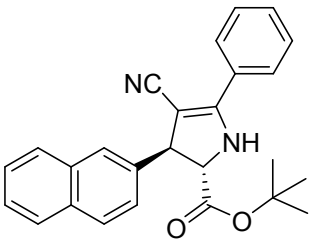
***tert*-Butyl-(2*S**,3*S**)-4-cyano-3-(4'-nitrophenyl)-5-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6h)**



Yellow foam, 31.3 mg, 80 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3345, 2980, 2933, 2190, 1735, 1596, 1571, 1521, 1458, 1369, 1348, 1246, 1154, 854, 772, 695. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.25 (d,

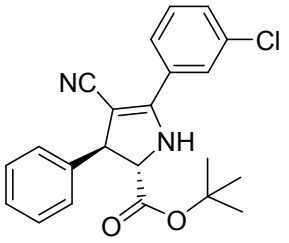
2H, *J*= 8.8 Hz), 7.86-7.80 (m, 2H), 7.56-7.47 (m, 5H), 4.93 (brs, 1H), 4.65 (d, 1H, *J*= 5.4 Hz), 4.21 (dd, 1H, *J*= 5.4, 0.82 Hz), 1.54 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 170.3, 161.6, 148.6, 147.6, 131.6, 129.1, 128.7, 128.3, 127.0, 124.4, 118.3, 83.8, 79.9, 67.1, 53.1, 28.0. **MS** (ESI *m/z*) 409.08 [MH_2O^+, 85%], 410.8 [MH_3O^+, 27%].

***tert*-Butyl-(2*S**,3*S**)-4-cyano-3-(naphthalen-2'-yl)-5-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6i)**



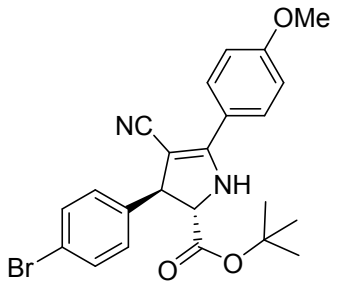
Yellow foam, 19.8 mg, 50 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3338, 3058, 2979, 2931, 2190, 1733, 1658, 1597, 1574, 1500, 1457, 1369, 1319, 1278, 1244, 1153, 845, 821, 771, 752, 704, 639. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.90-7.78 (m, 6H), 7.53-7.42 (m, 6H), 4.86 (brs, 1H), 4.71 (d, 1H, *J*= 5.3 Hz), 4.31 (d, 1H, *J*= 5.3 Hz), 1.55 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.1, 160.9, 138.8, 133.5, 133.0, 131.2, 130.0, 129.1, 129.0, 128.2, 127.9, 127.7, 127.1, 126.3, 126.1, 126.0, 125.1, 118.9, 83.2, 81.2, 67.5, 53.8, 28.0. **MS** (ESI *m/z*) 419.6 [MNa^+, 100%].

***tert*-Butyl-(2*S**,3*S**)-5-(3'-chlorophenyl)-4-cyano-3-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6j)**



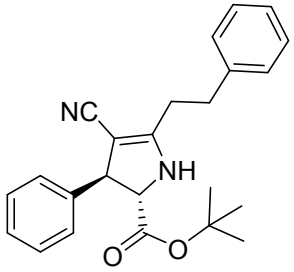
Yellow wax, 22.1 mg, 58 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3331, 2979, 2932, 2191, 1734, 1592, 1564, 1488, 1456, 1369, 1245, 1153, 1081, 843, 792, 753, 699. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.79-7.74 (m, 2H), 7.50-7.28 (m, 7H), 4.82 (brs, 1H), 4.52 (d, 1H, *J*= 5.3 Hz), 4.23 (d, 1H, *J*= 5.3 Hz), 1.53 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.0, 159.3, 141.2, 135.0, 131.2, 131.0, 130.3, 129.1, 127.9, 127.2, 126.9, 125.4, 118.3, 83.3, 82.6, 67.5, 53.6, 28.0. **MS** (ESI *m/z*) 403.6 [MNa^+, 95%].

***tert*-Butyl-(2*S**,3*S**)-3-(4'-bromophenyl)-4-cyano-5-(4'-methoxyphenyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (6k)**



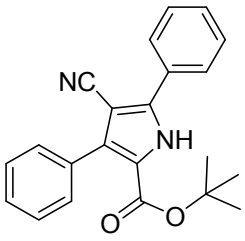
Pale yellow foam, 34.2 mg, 75 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3331, 2978, 2931, 2190, 1735, 1596, 1574, 1499, 1456, 1369, 1245, 1154, 844, 769, 740, 697. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.79 (d, 2H, *J*= 8.8 Hz), 7.50 (d, 2H, *J*= 8.4 Hz), 7.23 (d, 2H, *J*= 8.4 Hz), 6.98 (d, 2H, *J*= 8.8 Hz), 4.75 (brs, 1H), 4.48 (d, 1H, *J*= 5.3 Hz), 4.14 (d, 1H, *J*= 5.3 Hz), 3.87 (s, 3H), 1.52 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 170.9, 161.9, 160.7, 140.7, 132.1, 129.0, 128.7, 121.6, 121.4, 119.1, 114.3, 83.2, 79.1, 67.4, 55.4, 53.0, 28.0. **MS** (ESI *m/z*) 479.8 [MNa$^+$, 100%].

***tert*-Butyl-(2*S**,3*S**)-4-cyano-5-phenethyl-3-phenyl-2,3-dihydro-1H-pyrrole-2-carboxylate (6l)**



Yellow wax, 32.6 mg, 87 % yield. **FTIR** ν_{max} (KBr)/cm^{-1} 3359, 3055, 2983, 2929, 2196, 1737, 1604, 1497, 1456, 1370, 1266, 1154, 739, 702. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.36-7.25 (m, 8H), 7.14-7.10 (m, 2H), 4.47 (brs, 1H), 4.31 (d, 1H, *J*= 5.0 Hz), 4.02 (d, 1H, *J*= 5.0 Hz), 3.06-2.94 (m, 2H), 2.93-2.84 (m, 1H), 2.81-2.73 (m, 1H), 1.51 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.1, 164.8, 141.6, 139.5, 128.9, 128.6, 128.4, 127.5, 127.0, 126.6, 118.2, 82.9, 81.9, 68.2, 52.1, 33.3, 29.5, 28.0. **MS** (ESI *m/z*) 397.2 [MNa$^+$, 20%].

***tert*-Butyl 4-cyano-3,5-diphenyl-1H-pyrrole-2-carboxylate (9)**

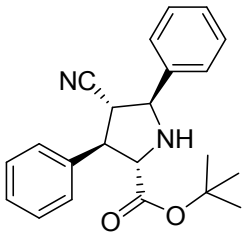


White solid, 26.9 mg, 78 % yield. **Mp** 169 °C (Decomp.). **FTIR** ν_{max} (KBr)/cm^{-1} 3270, 2980, 2931, 2224, 1691, 1496, 1466, 1447, 1425, 1369, 1304, 1251, 1210, 1153, 846, 770, 737, 696. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.79 (brs, 1H), 7.80 (d, 2H, *J*= 7.0 Hz), 7.52-7.35 (m, 8H), 1.34 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 160.0, 140.6, 134.6, 131.7, 130.0, 129.8, 129.4, 128.7, 128.1, 127.8, 126.5, 121.0, 116.0, 93.9, 82.6, 28.0. **MS** (ESI *m/z*) 367.6 [MNa^+, 100%].

***tert*-Butyl 4-cyano-3,5-diphenylpyrrolidine-2-carboxylate**

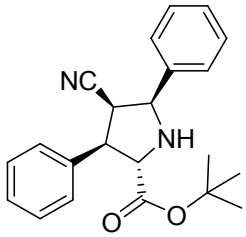
77.6 mg, 74% yield. The diastereoisomeric ratio was found to be 70:30 by ^{1}H-NMR analysis. **FTIR** ν_{max} (KBr)/cm^{-1} 3336, 2979, 2932, 2245, 1728, 1497, 1457, 1369, 1251, 1158, 1132, 841, 750, 700.

Major diast.: *tert*-(2*S,3*R**,4*S**,5*S**)-butyl 4-cyano-3,5-diphenylpyrrolidine-2-carboxylate (10)**



White solid, 44.6 mg. **Mp** 82.5- 84.1 °C. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.60-7.56 (m, 2H), 7.42-7.29 (m, 8H), 4.63 (d, 1H, *J*= 10.0 Hz), 4.00 (d, 1H, *J*= 6.6 Hz), 3.68 (dd, 1H, *J*= 10.0, 6.6 Hz), 2.94 (dd, 1H, *J*= 10.0, 10.0 Hz), 2.88 (brs, 1H), 1.44 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 172.6, 139.3, 139.2, 129.0, 128.8, 128.5, 127.9, 127.3, 126.5, 119.0, 82.3, 66.3, 65.8, 54.2, 47.2, 27.9. **MS** (ESI *m/z*) 349.7 [MH^+, 11%].

Minor diast.: (2*S,3*R**,4*R**,5*S**)-*tert*-butyl 4-cyano-3,5-diphenylpyrrolidine-2-carboxylate (11)**

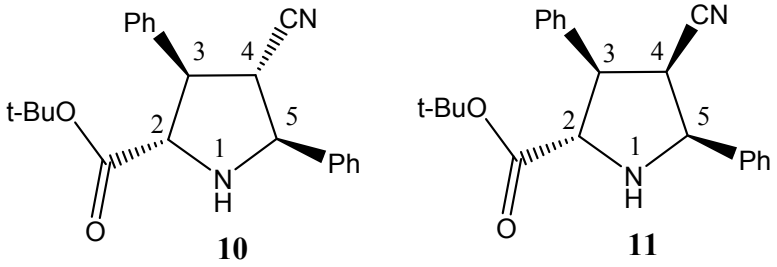


White solid, 33 mg. **Mp** 152-153 °C. **^{1}H NMR** ($CDCl_3$, 600 MHz): δ 7.57-7.55 (m, 2H), 7.48-7.46 (m, 2H), 7.42-7.37 (m, 4H), 7.35-7.30 (m, 2H), 4.81 (d, 1H, *J*= 5.0 Hz), 4.32 (d, 1H, *J*= 8.5 Hz), 3.76 (dd, 1H, *J* = 8.5, 6.8 Hz), 3.51 (dd, 1H, *J*= 6.8, 5.0 Hz), 2.81 (brs, 1H), 1.33 (s, 9H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 173.2, 138.0, 136.5, 128.6, 128.5, 128.4, 128.0, 127.1, 117.1, 82.0, 64.4, 63.4, 52.7, 43.6, 27.8. **MS** (ESI *m/z*) 349.7 [MH^+, 33%], 371.8 [MNa^+, 28%].

Computational Details

Conformational searches for the reactant **6a** and for the products **10** and **11** were performed by using the MMFF force field and the Spartan software.[4] Geometry optimizations and second derivative computations needed to ascertain the nature of the located stationary points were carried out at the DFT level, by using the M06-2X functional in conjunction with the 6-31+G(d,p) basis set; solvation effects (acetic acid) were included by means of the polarizable continuum model (PCM).[5] NMR computations were carried out by following the procedure of ref 6: the minimum energy configurations and the energetics needed for the Boltzmann weighting of the shielding tensors were taken from PCM($CHCl_3$)/M06-2X/6-31+G(d,p) calculations, while shielding tensors were evaluated by using the B3LYP functional in conjunction with the extended 6-311+G(2d,p) basis set and the PCM, see Table 1. All DFT calculations were carried out by using the "ultrafine" integration grid implemented in the Gaussian program.[7]

Table 1. ^{1}H-NMR computed and observed chemical shifts (ppm, vs TMS) of products **10** and **11**.



	δ_2	δ_3	δ_4	δ_5
10				
Theor.	4.1	3.6	2.8	4.6
Sper.	4.0	3.7	2.9	4.6
11				
Theor.	4.5	3.7	3.3	5.0
Sper.	4.4	3.8	3.5	4.8

^{1}H-NMR spectrum of major diastereoisomer **10** is in agreement with structurally similar diethyl (2*R*,3*S*,4*R*,5*R*)-3,5-diphenylpyrrolidine-2,4-dicarboxylate.[8]

References

1. (a) J. S. Yadav, B. V. Subba Reddy, A. K. Basak, B. Visali, A. V. Narsaiah and K. Nagaiah, *Eur. J. Org. Chem*., 2004, 546; (b) P. K. Amancha, Y.-C. Lai, I.-C. Chen, H.-J. Liu and J.-L. Zhu, *Tetrahedron*, 2010, **66**, 871.
2. (a) R. P. Wurz and A. B. Charette, *Org. Lett*., 2005, **7**, 2313 and references therein. (b) S. R. Cheruku, M. P. Padmanilayam and J. L. Vennerstrom, *Tetrahedron Lett.*, 2003, **44**, 3701.
3. G. W. Gribble and J. H. Hoffman, *Synthesis*, 1977, 859.
4. Spartan'04, Wavefunction, Inc. Irvine, CA, 2004.
5. S. Miertuš, E. Scrocco and J. Tomasi, *Chem. Phys.*, 1981, **55**, 117.
6. P. H. Willoughby, M. J. Jansma and T. R. Hoye, *Nat. Protoc.*, 2014, **9**, 643.
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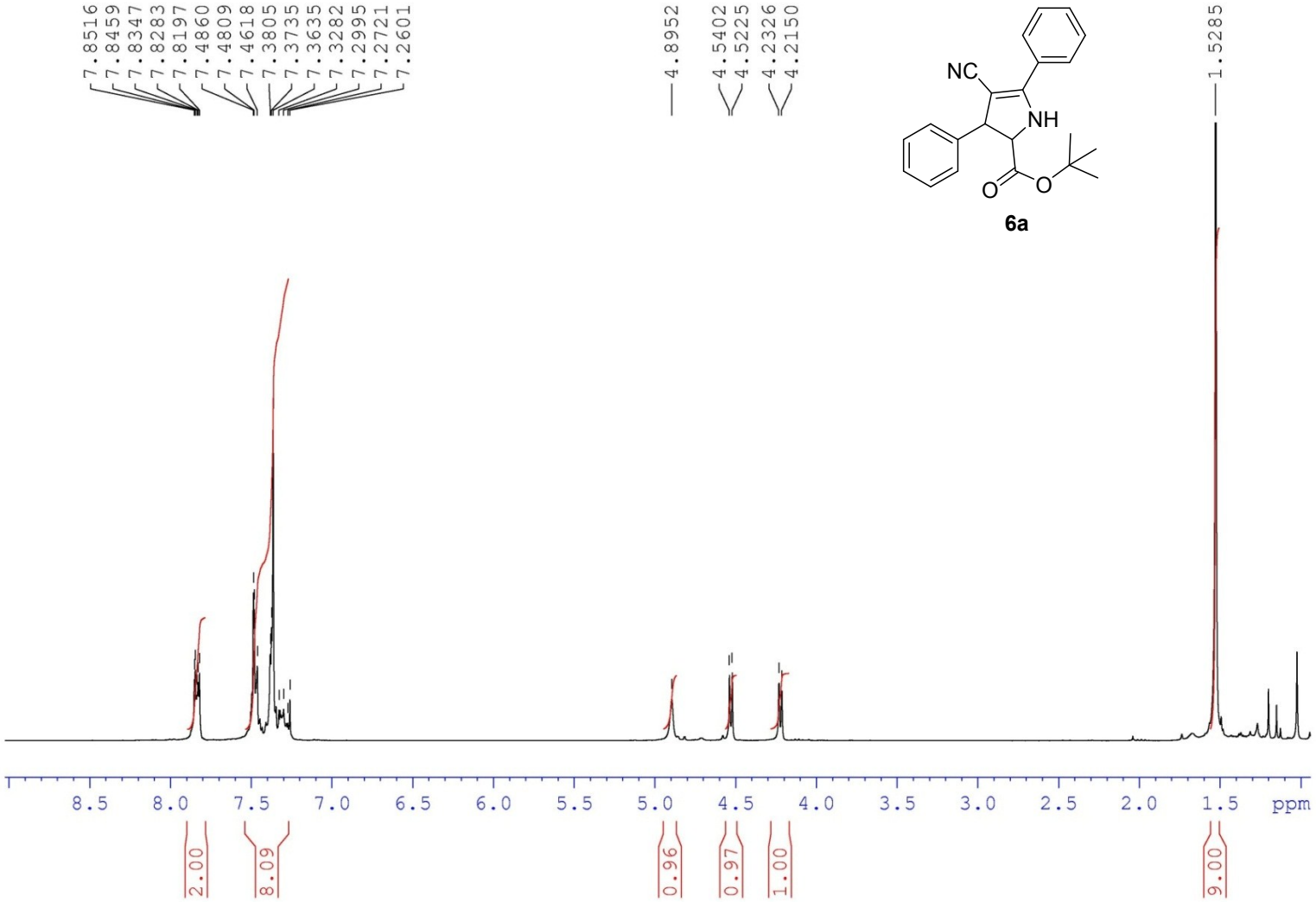
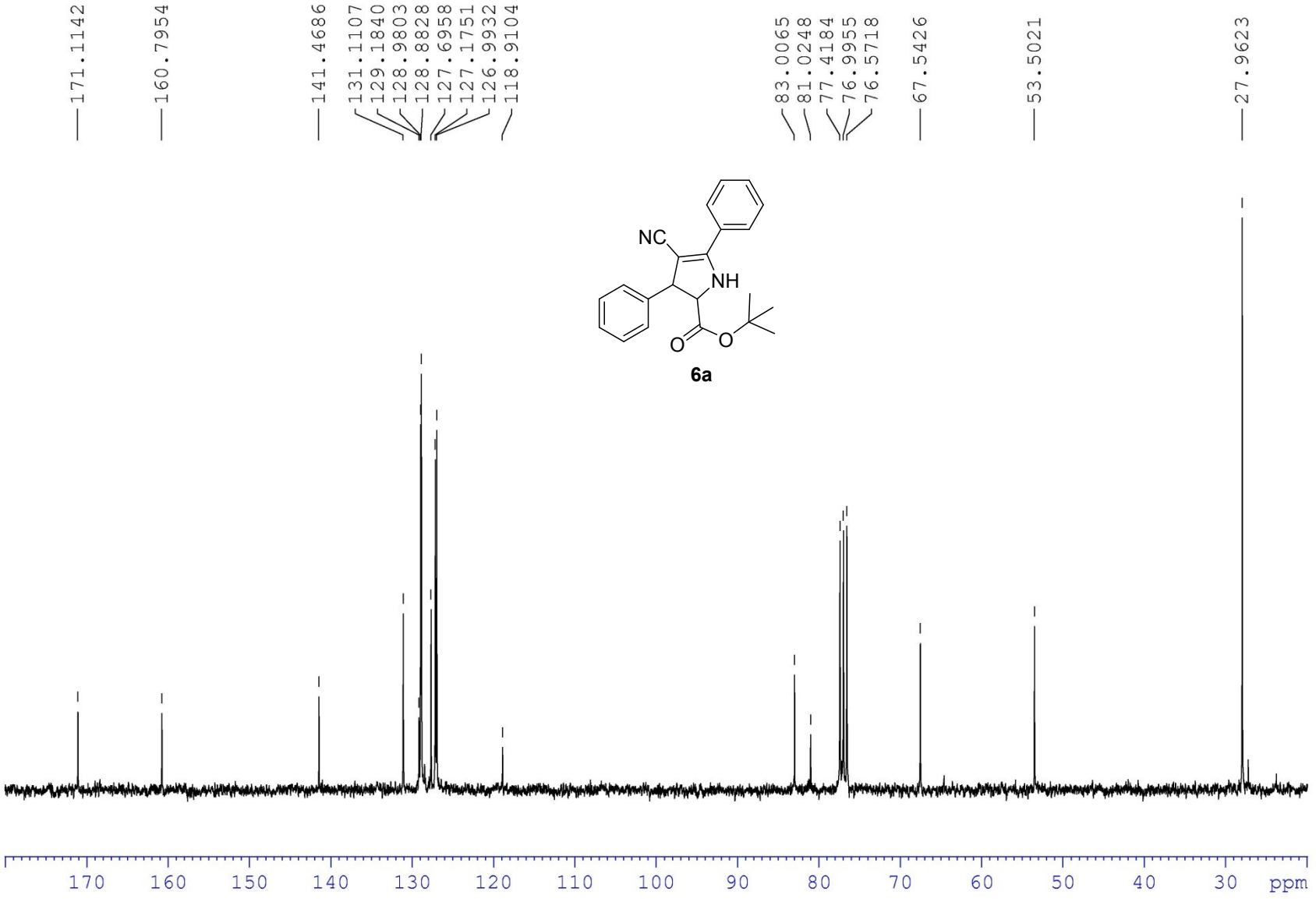
8. I. Merino, S. Laxmi Y. R., J. Flórez, J. Barluenga, J. Ezquerra and C. Pedregal, *J. Org. Chem.*, 2002, **67**, 648.

NMR Spectra

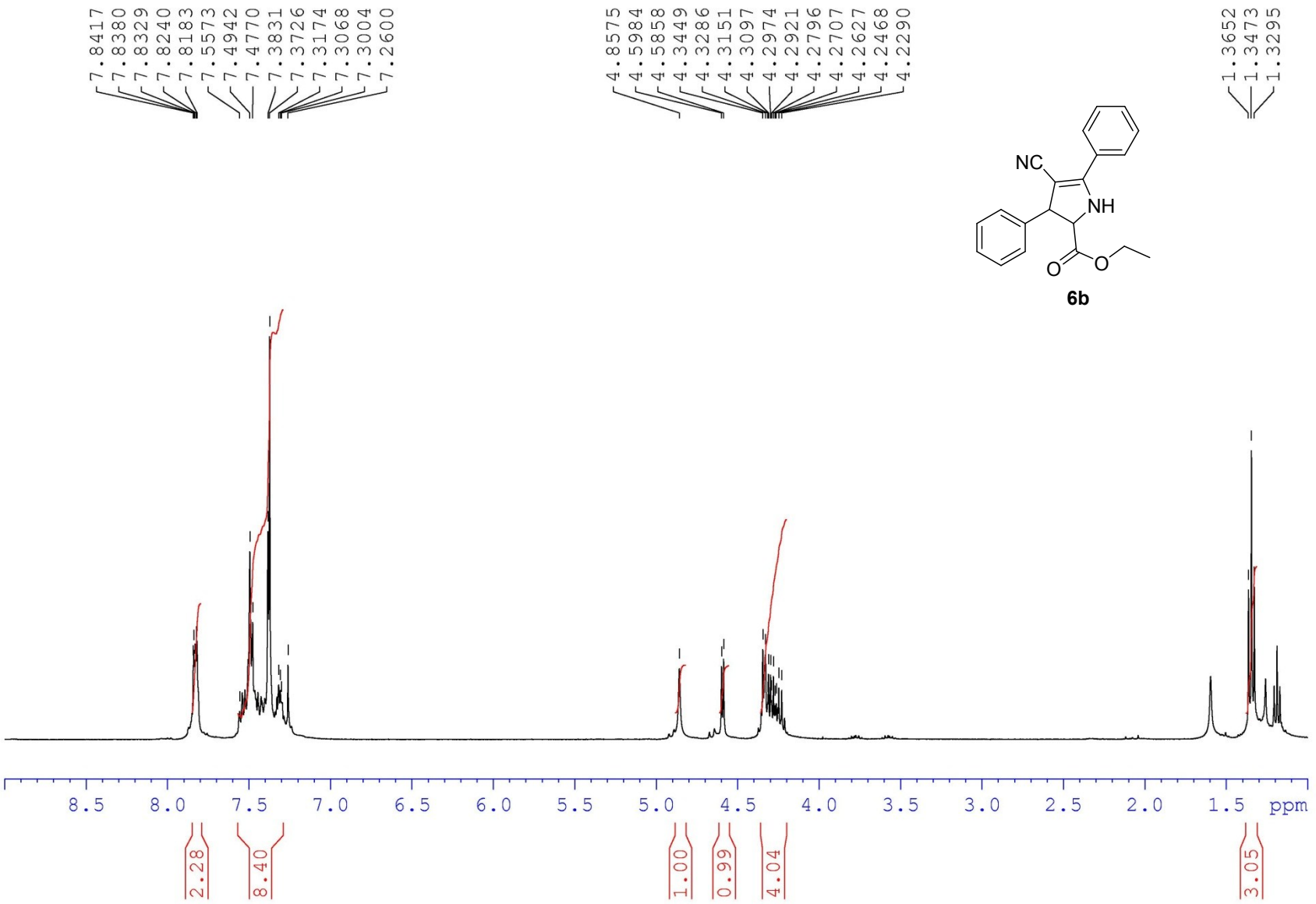
^{1}H NMR in $CDCl_3$ (300 MHz)



^{13}C NMR in $CDCl_3$ (75 MHz)

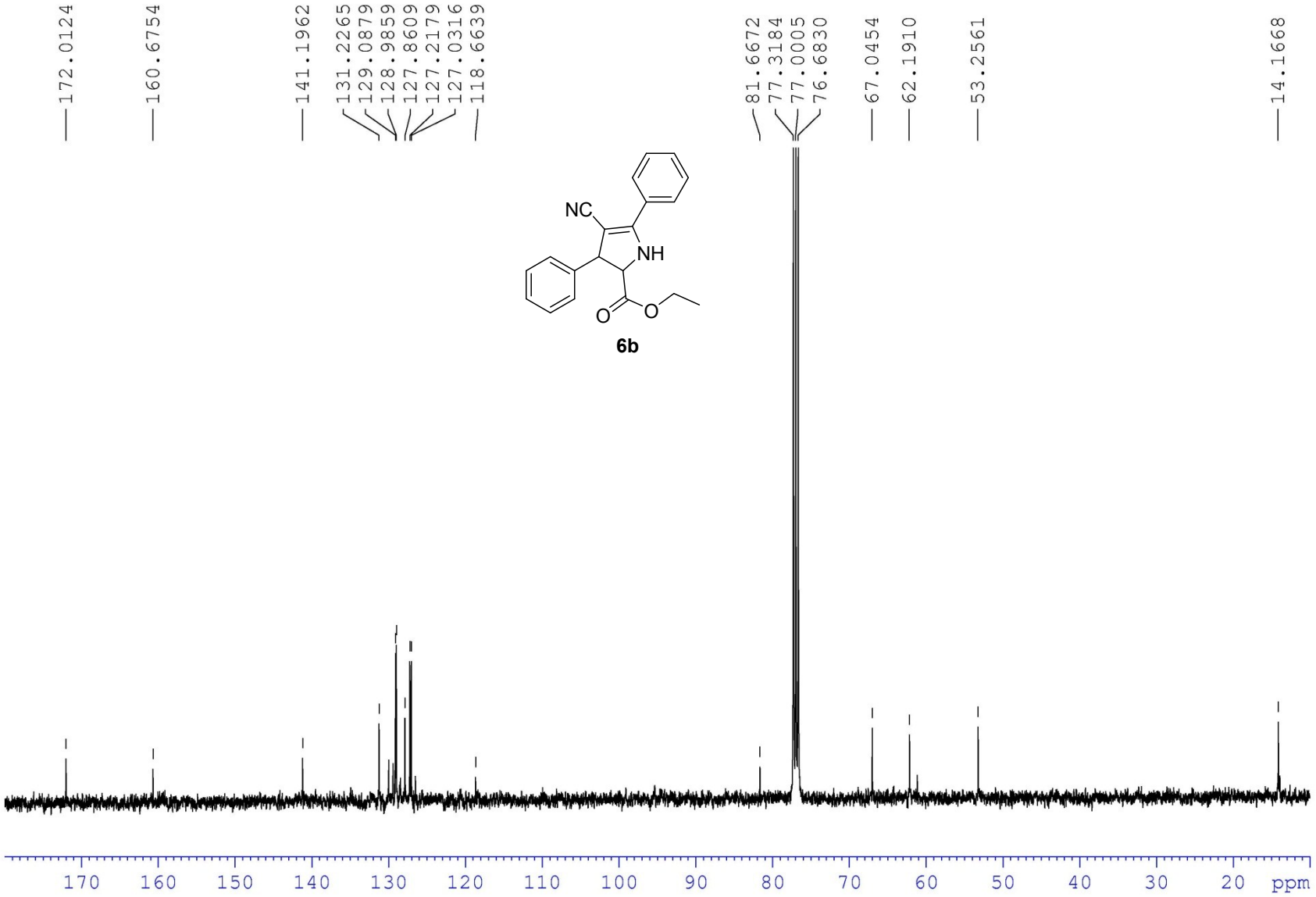


^{1}H NMR in $CDCl_3$ (400 MHz)

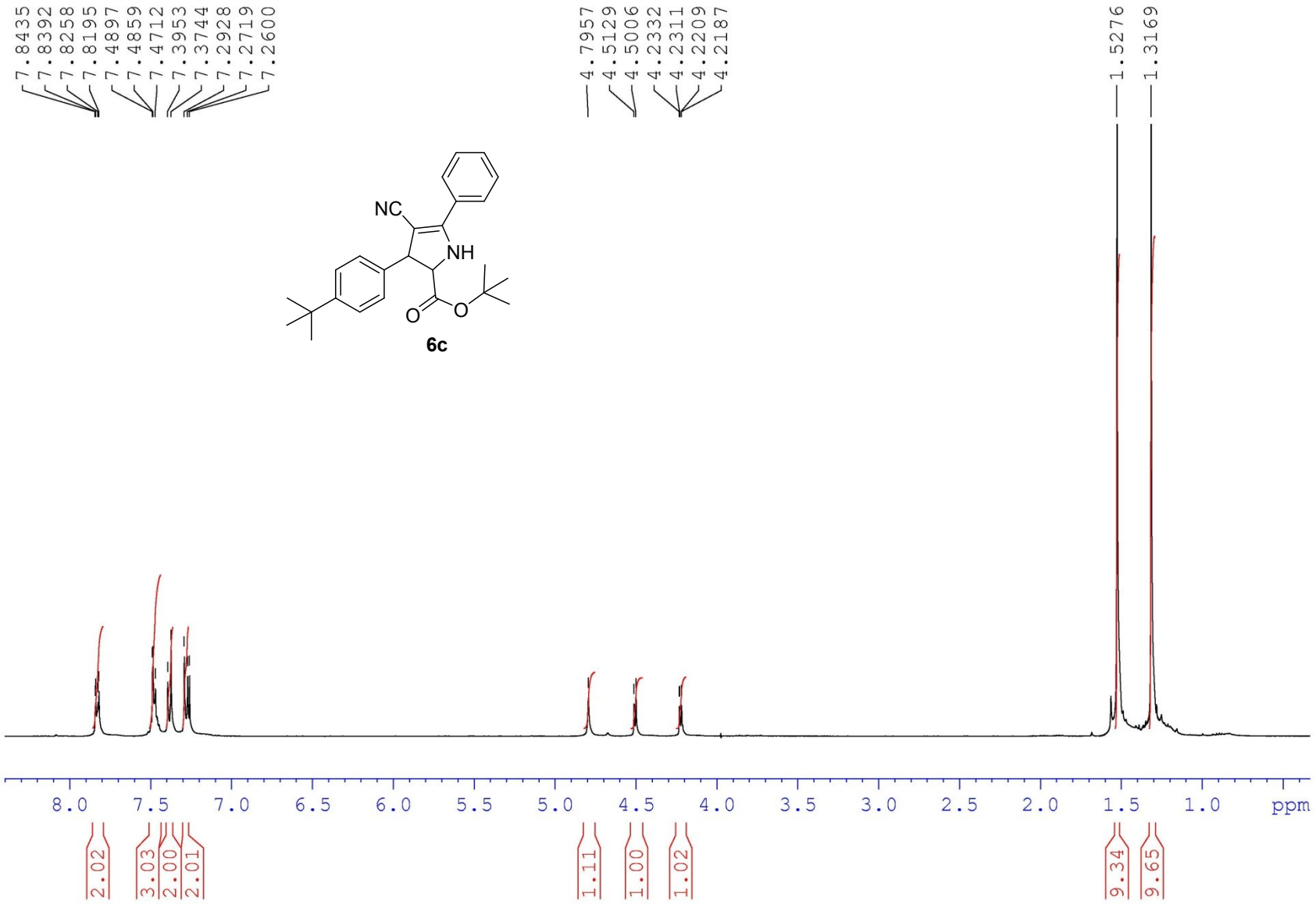


6b

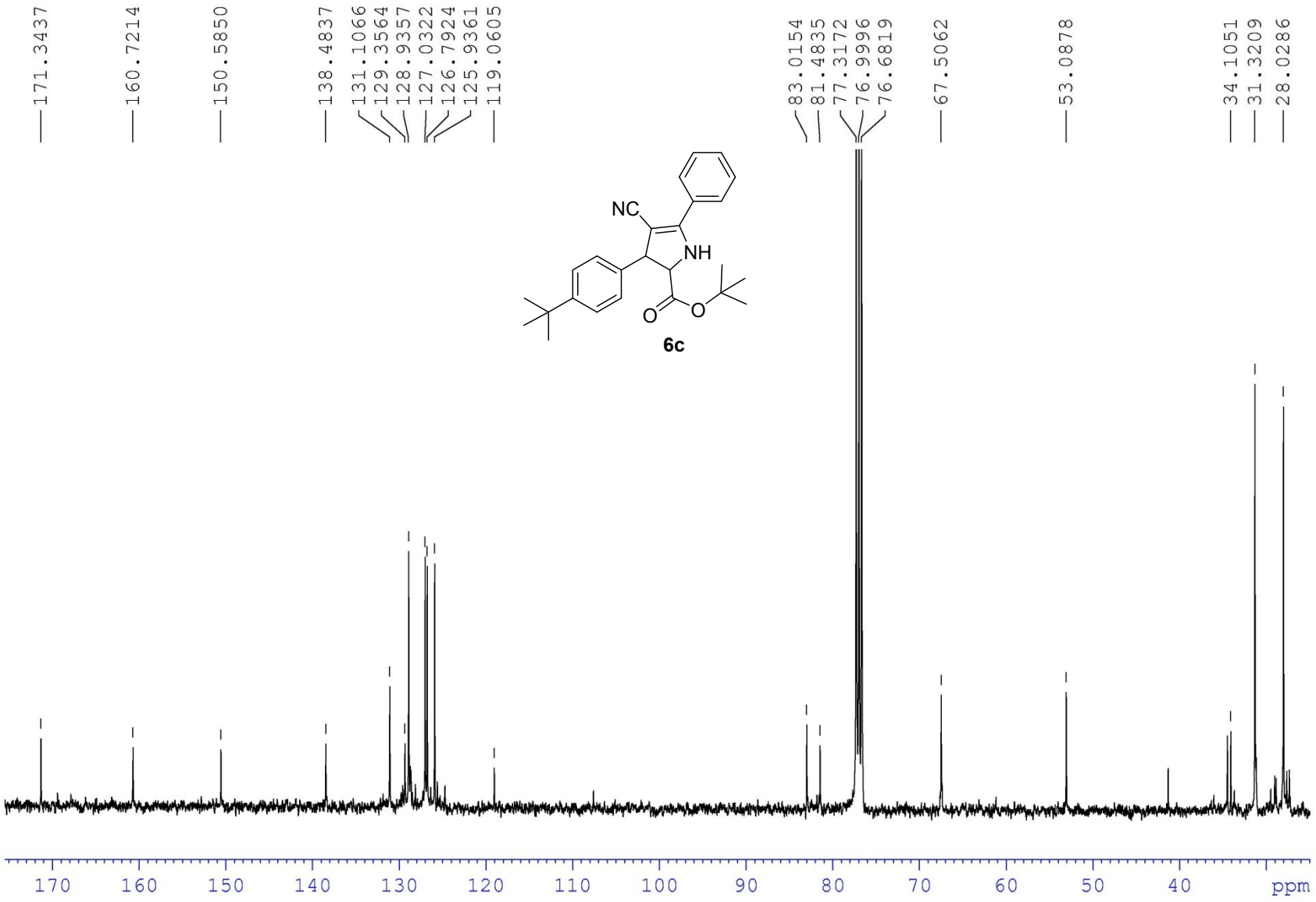
^{13}C NMR in $CDCl_3$ (100 MHz)



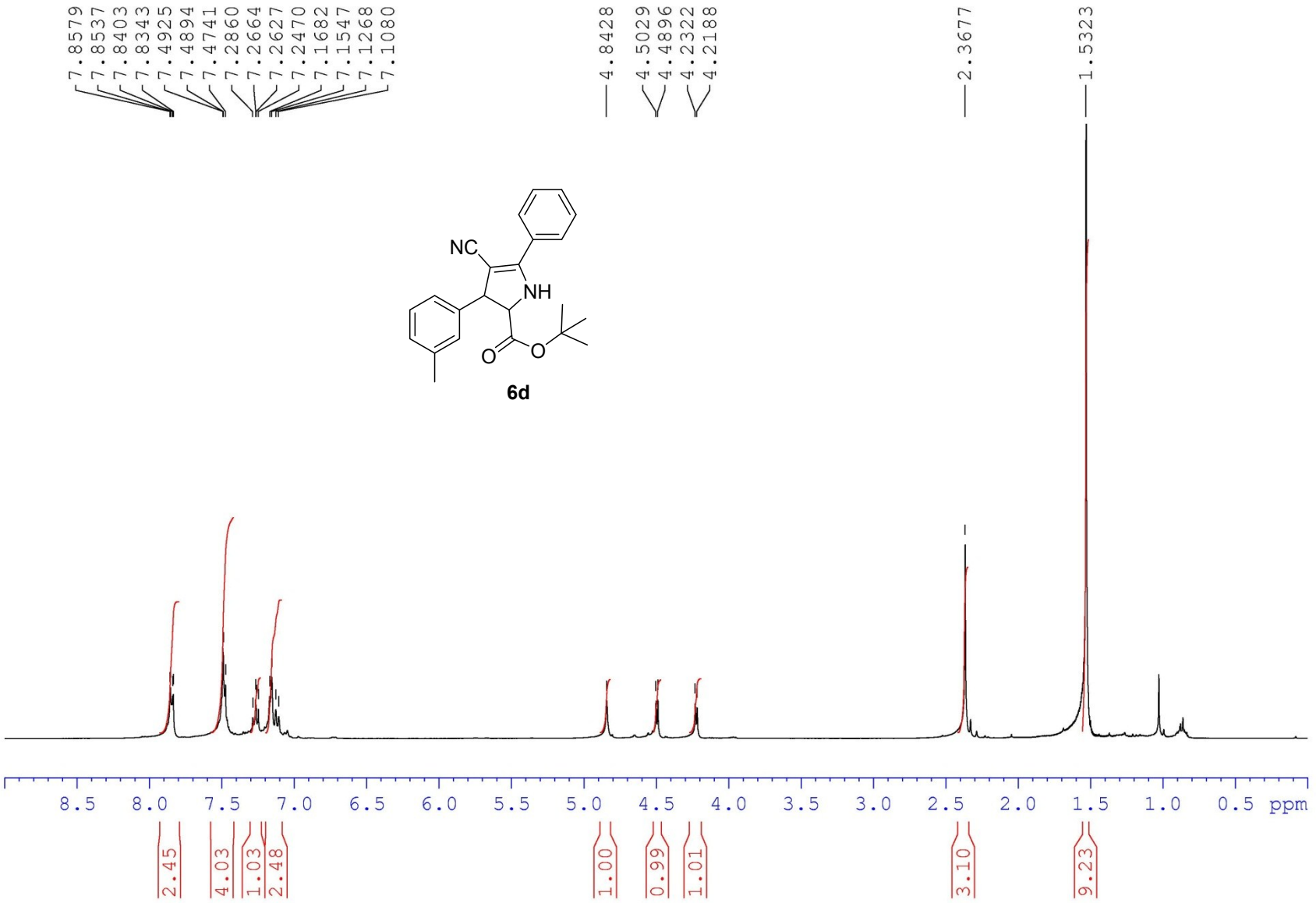
^{1}H NMR in $CDCl_3$ (400 MHz)



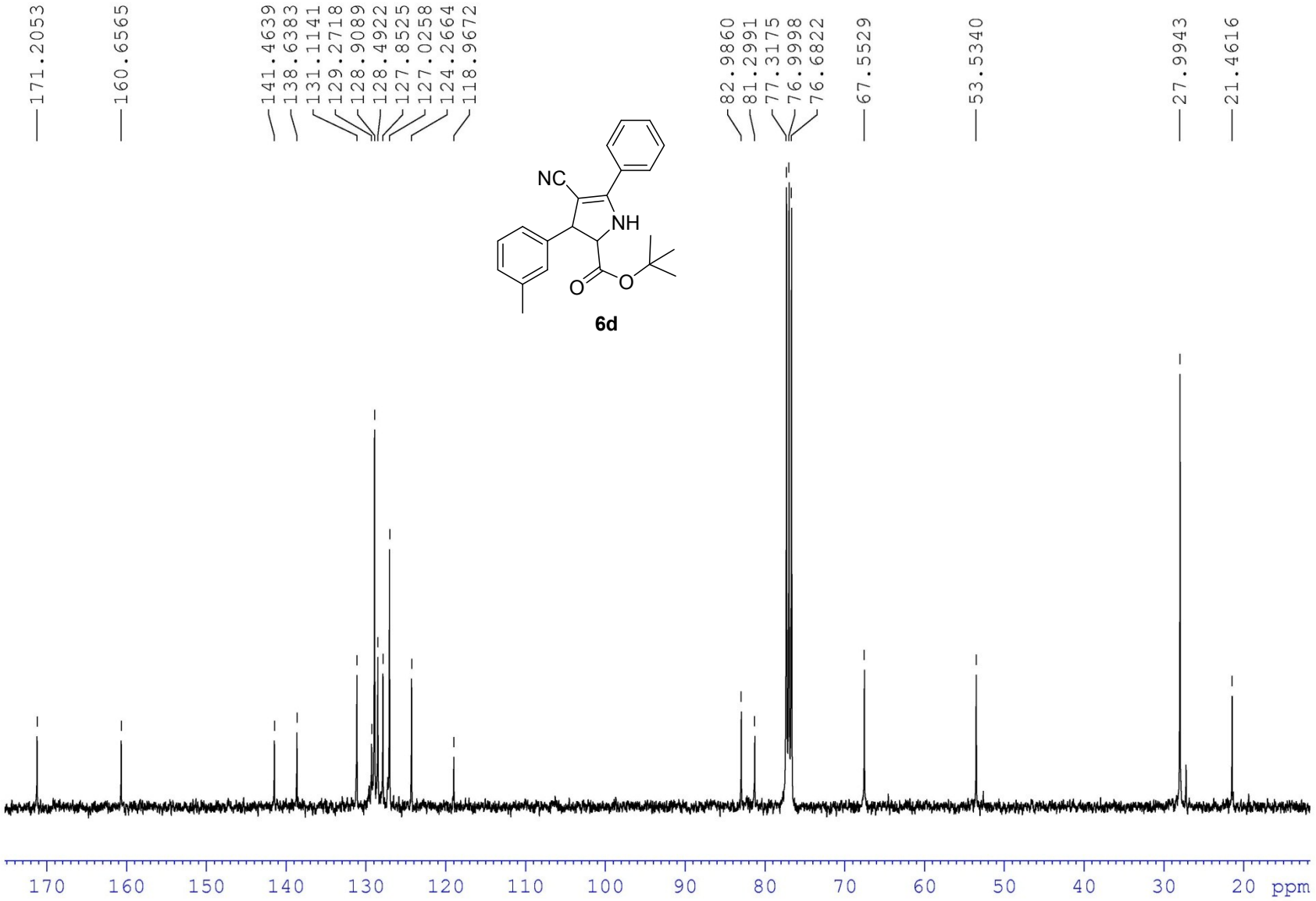
^{13}C NMR in $CDCl_3$ (100 MHz)



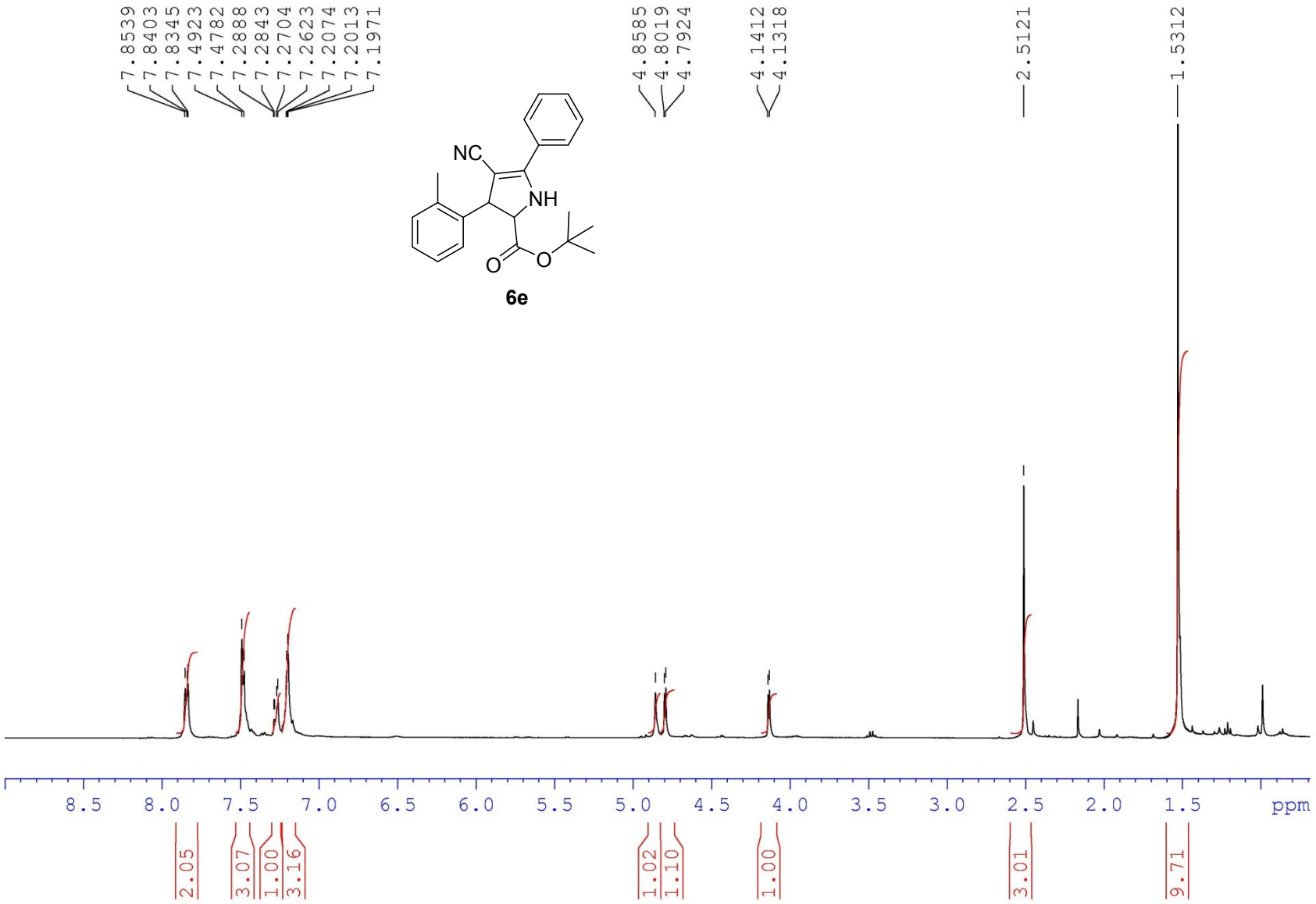
^{1}H NMR in $CDCl_3$ (400 MHz)



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

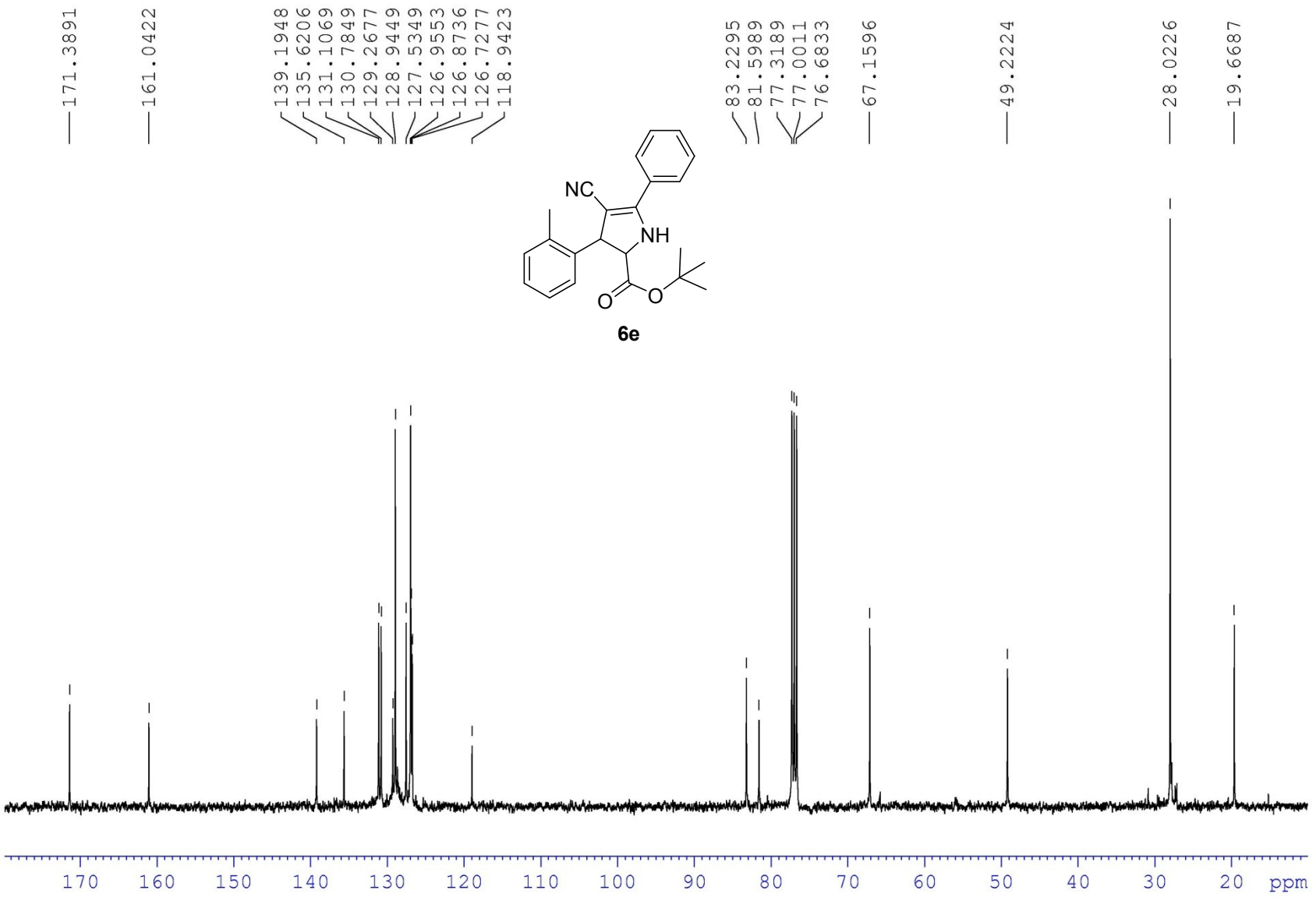


^{1}H NMR in $CDCl_3$ (400 MHz)

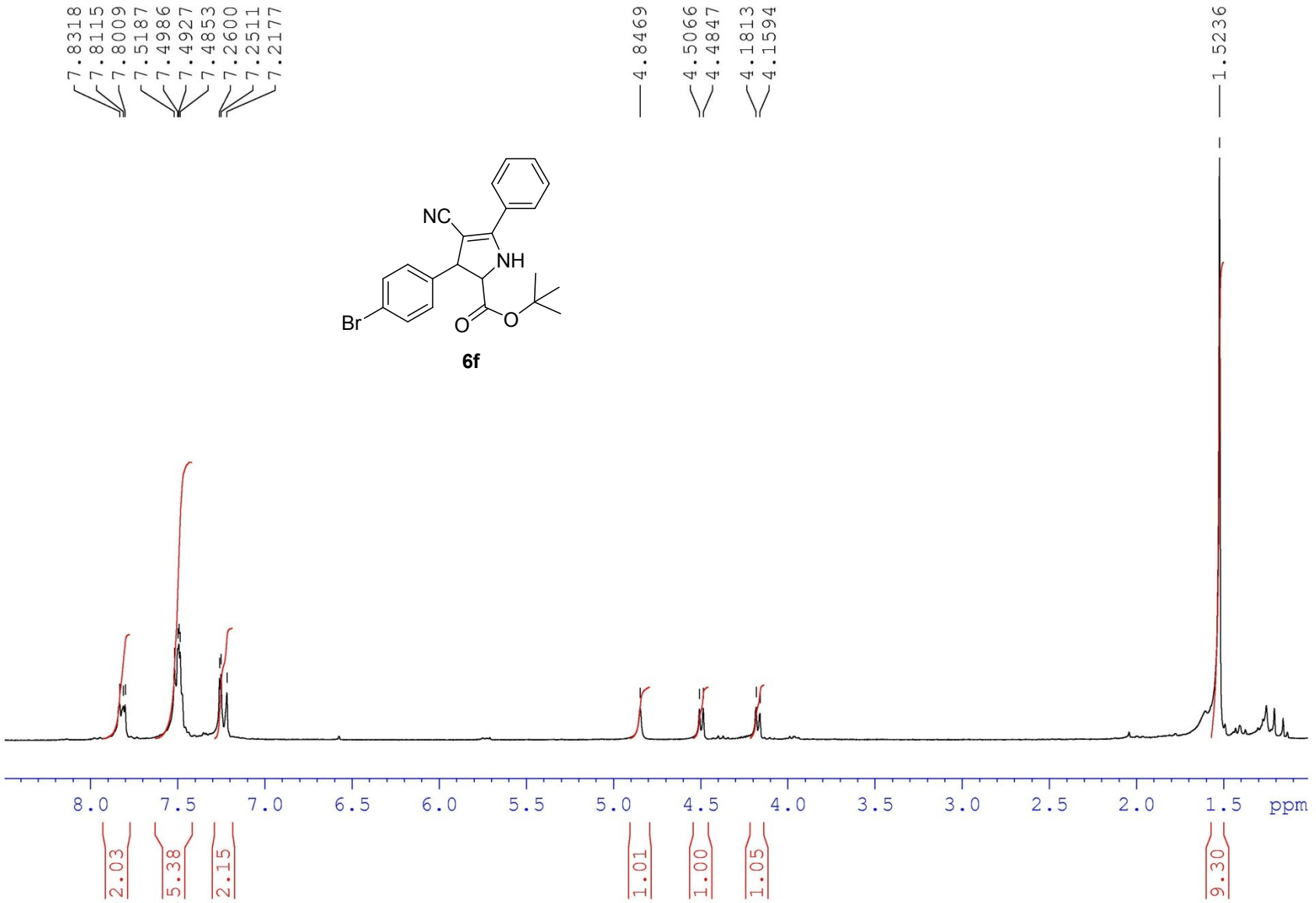


6e

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

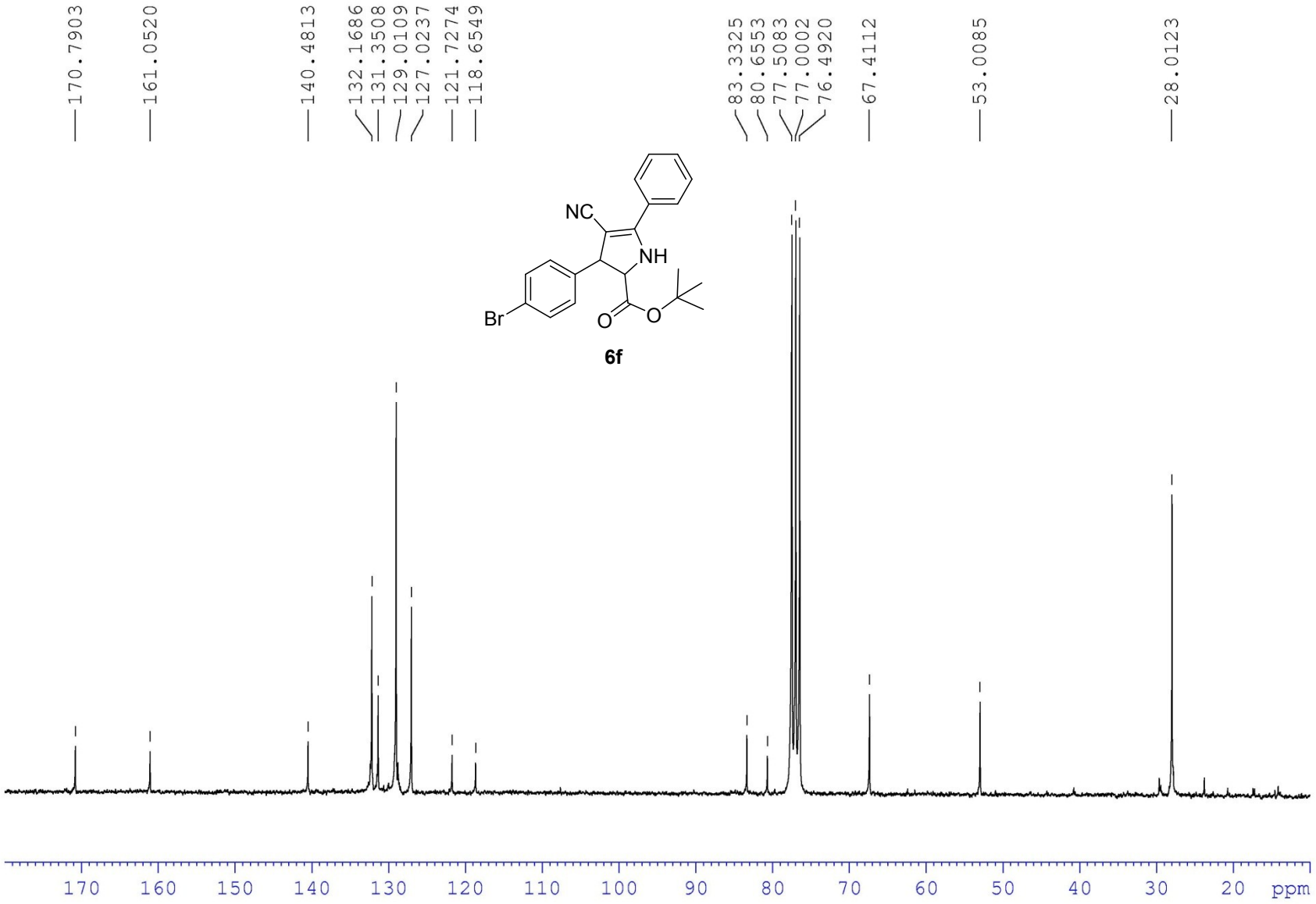


^{1}H NMR in $CDCl_3$ (250 MHz)

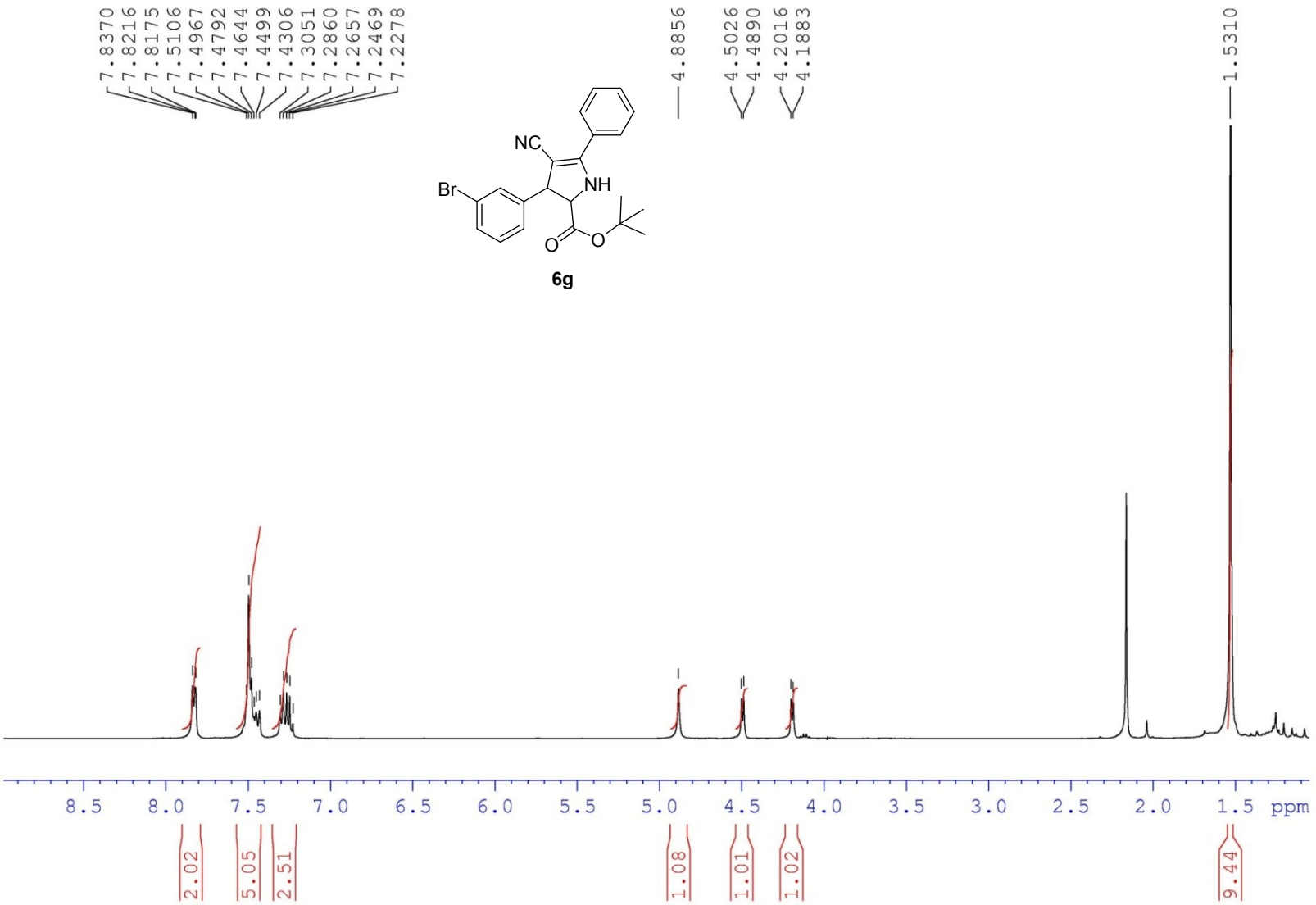


6f

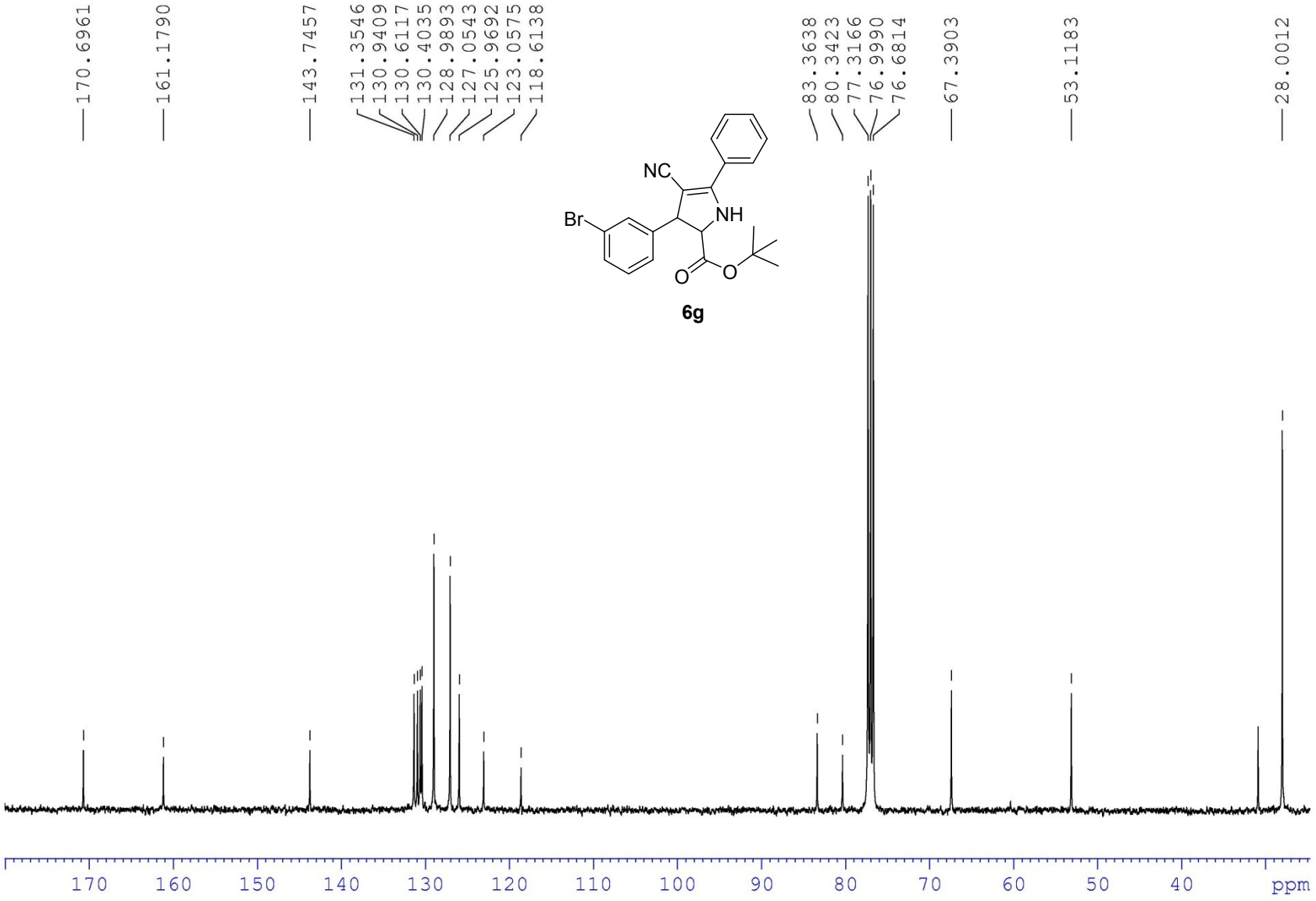
^{13}C NMR in $CDCl_3$ (62.5 MHz)



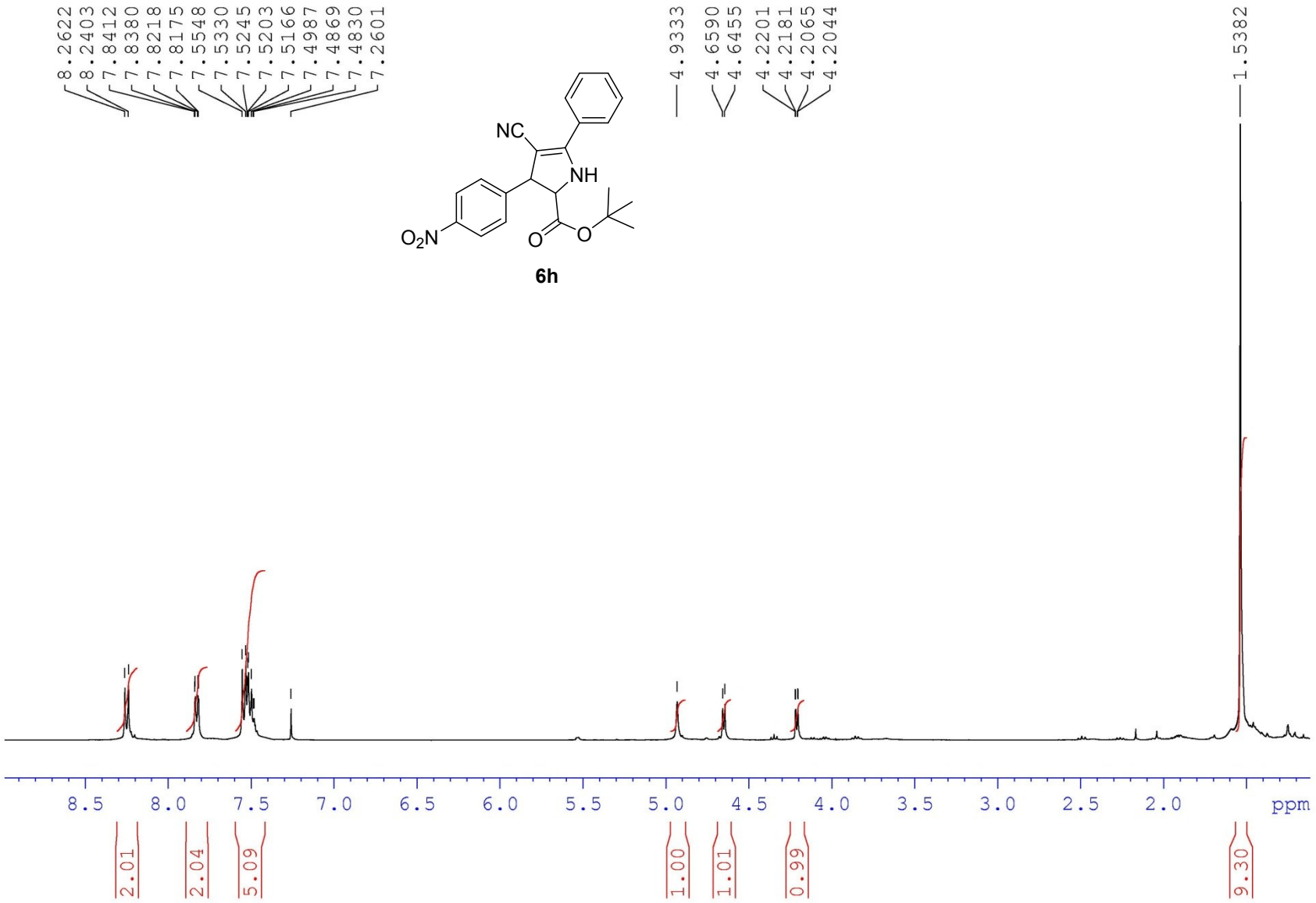
^{1}H NMR in $CDCl_3$ (400 MHz)



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

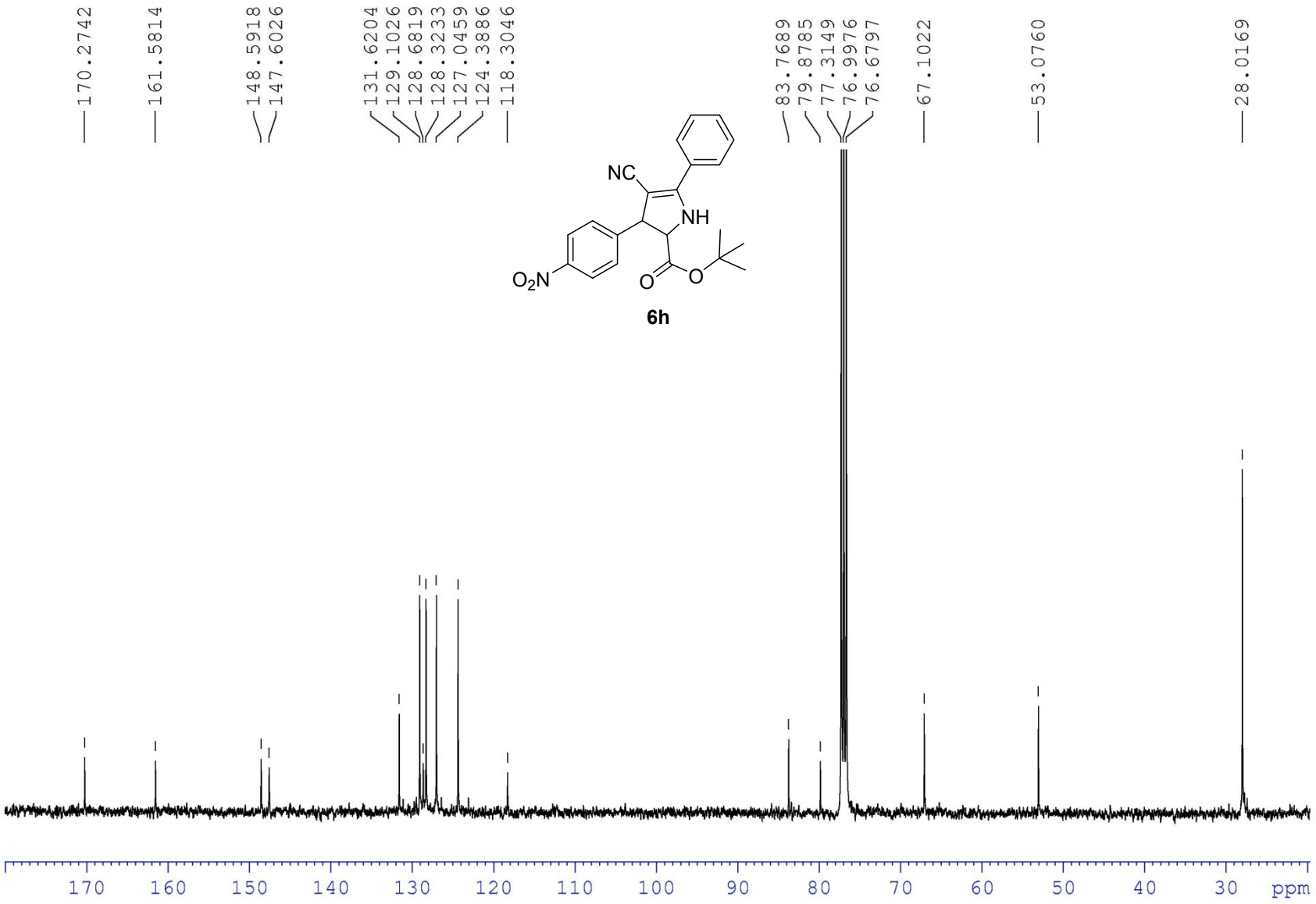


^{1}H NMR in $CDCl_3$ (400 MHz)

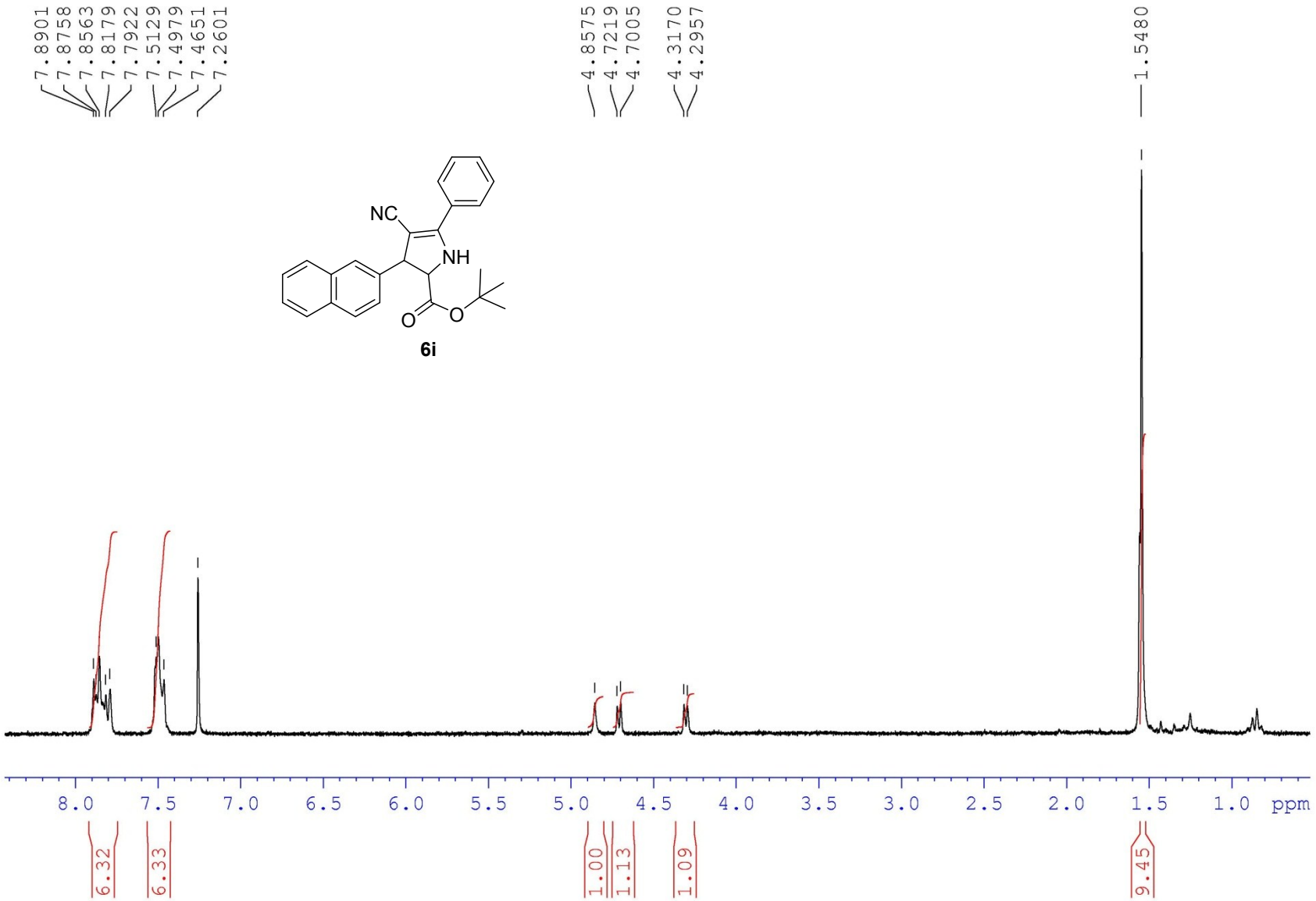


6h

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



^{1}H NMR in $CDCl_3$ (250 MHz)



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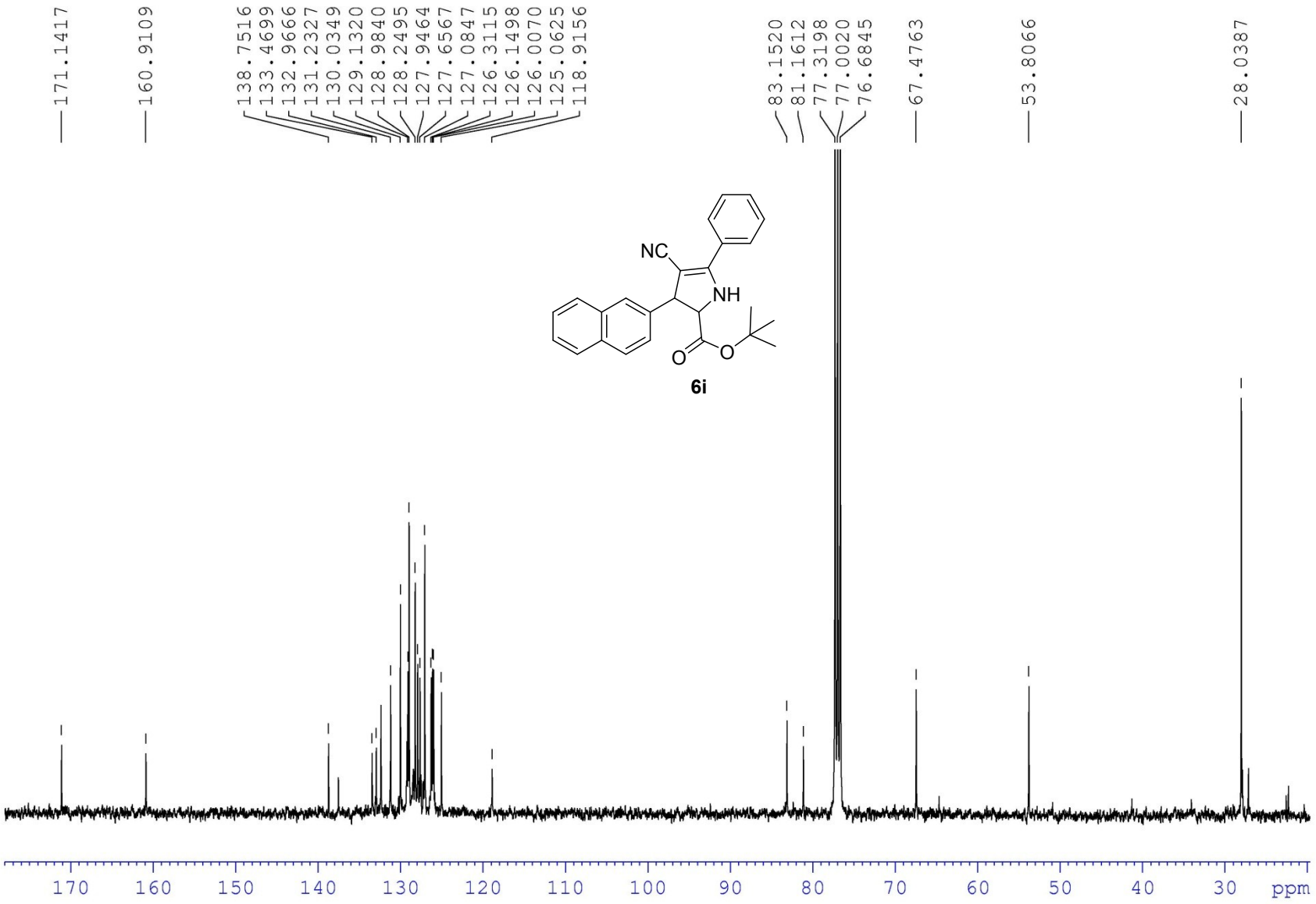

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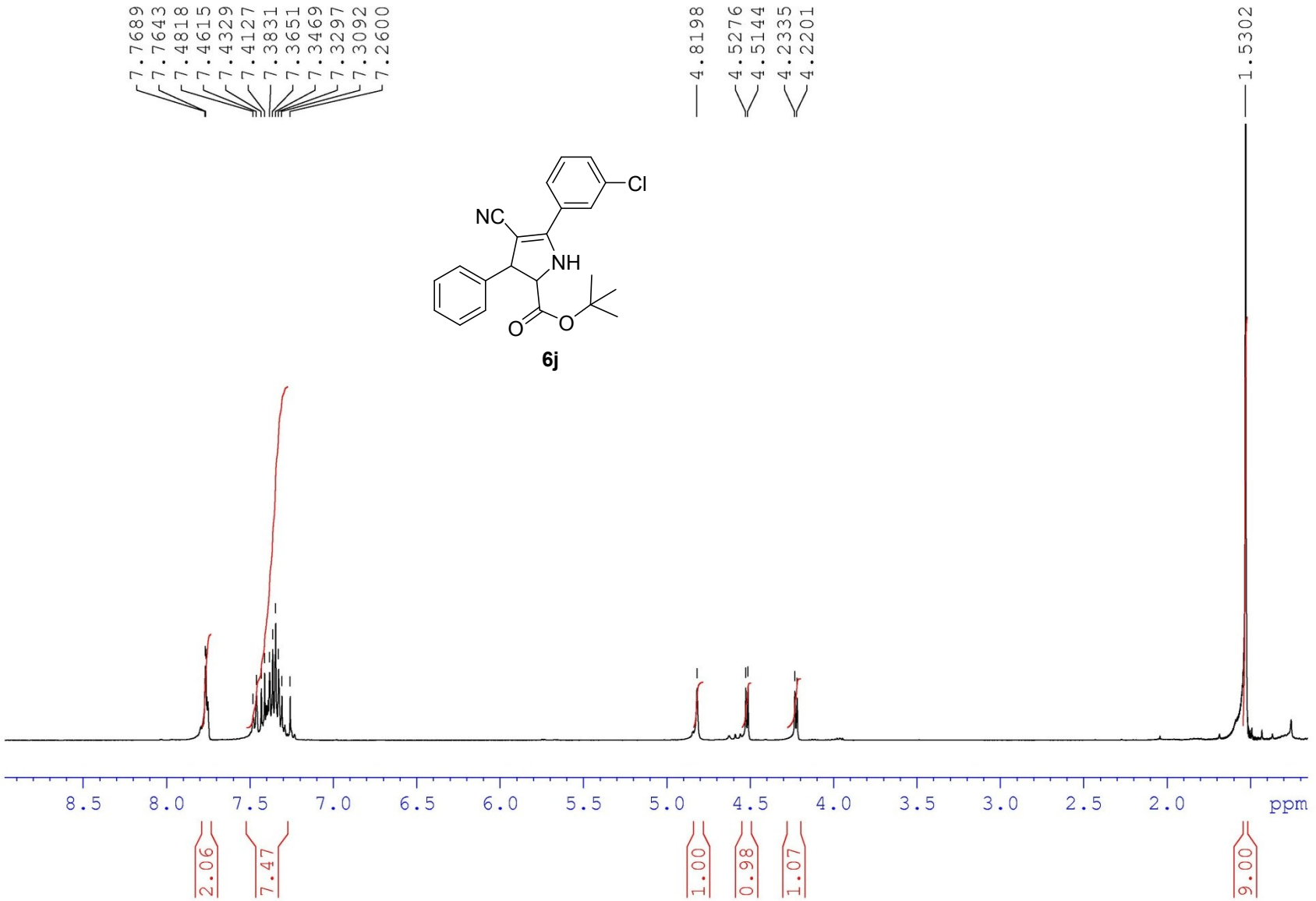
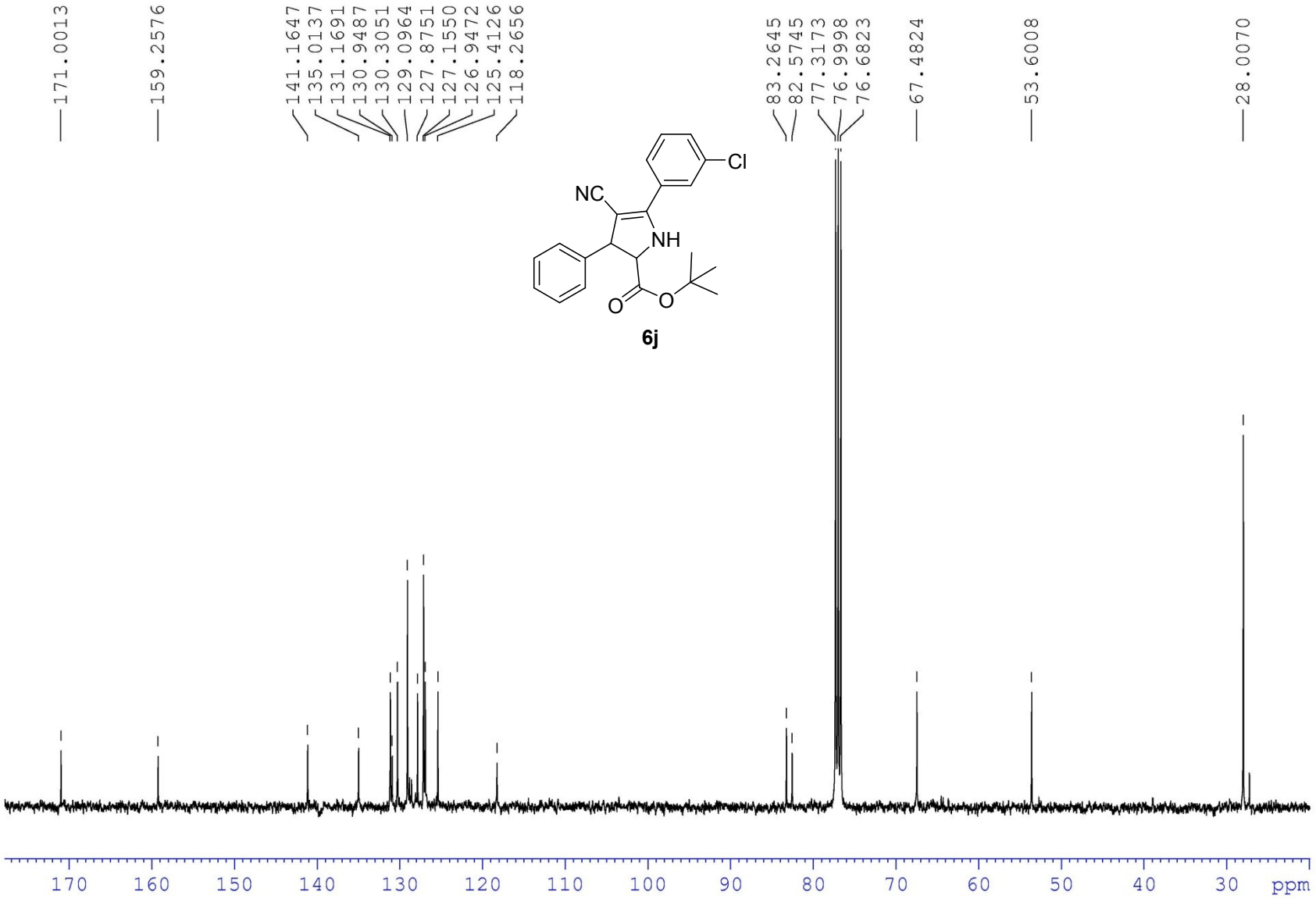
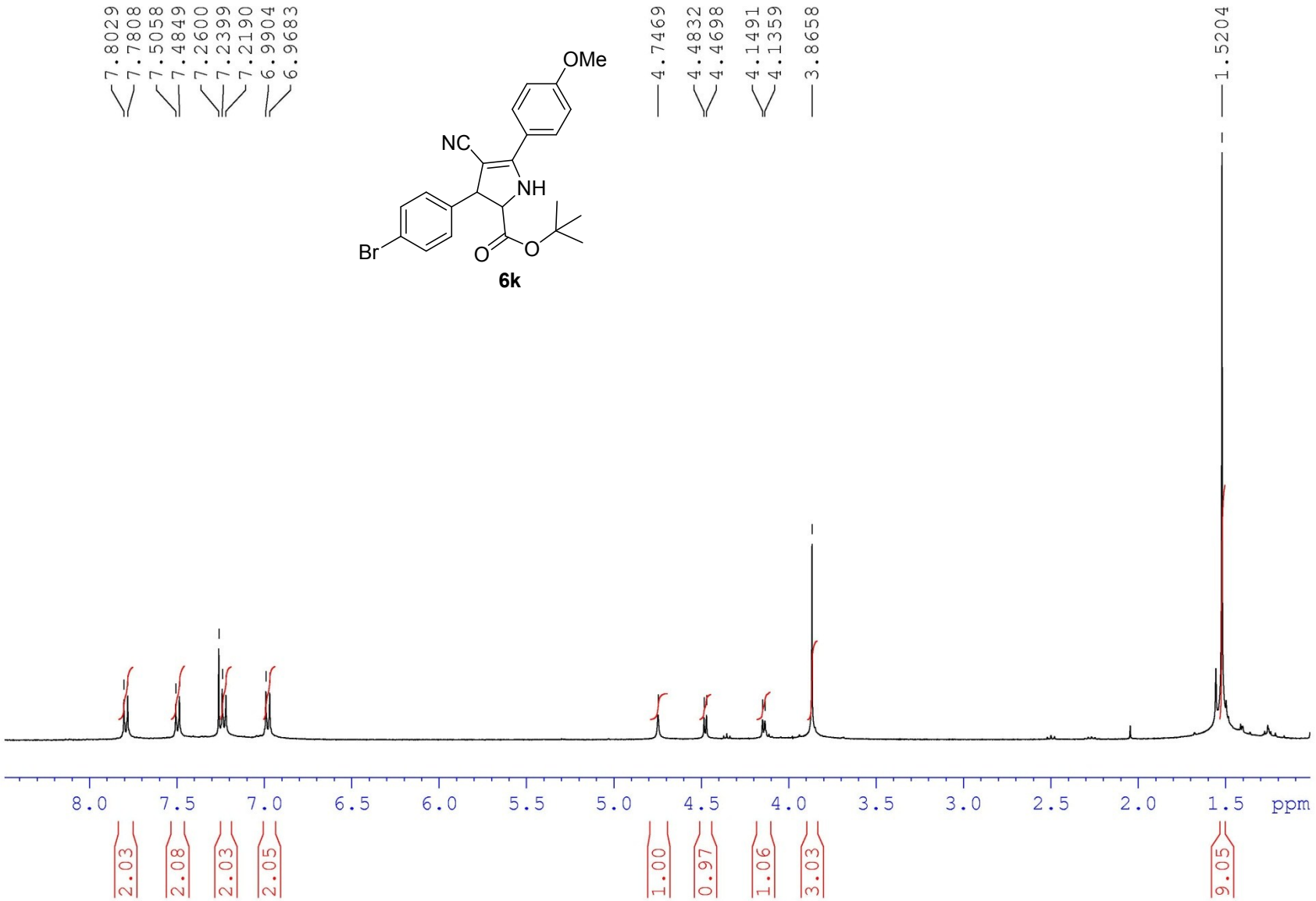


6j

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



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



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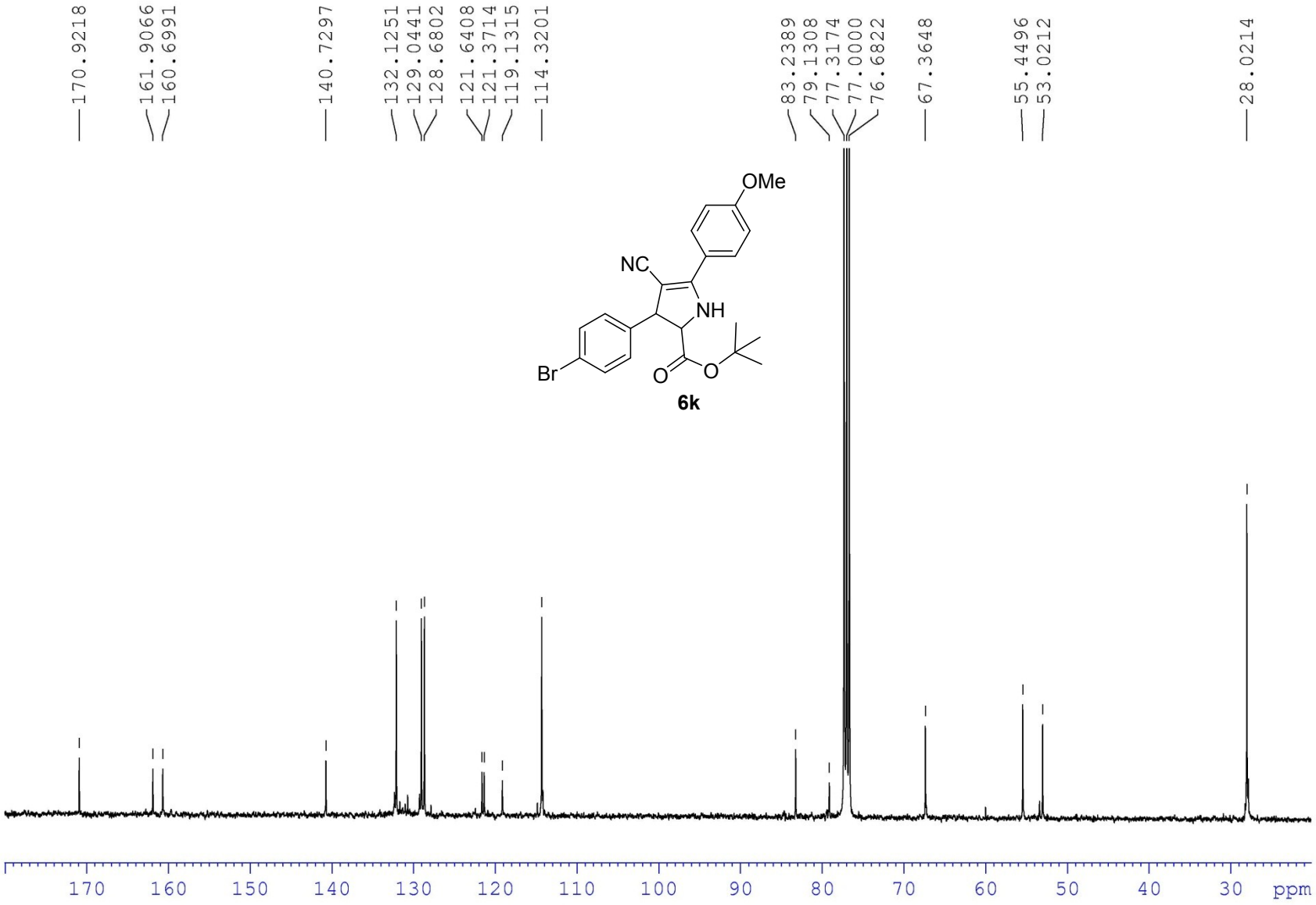
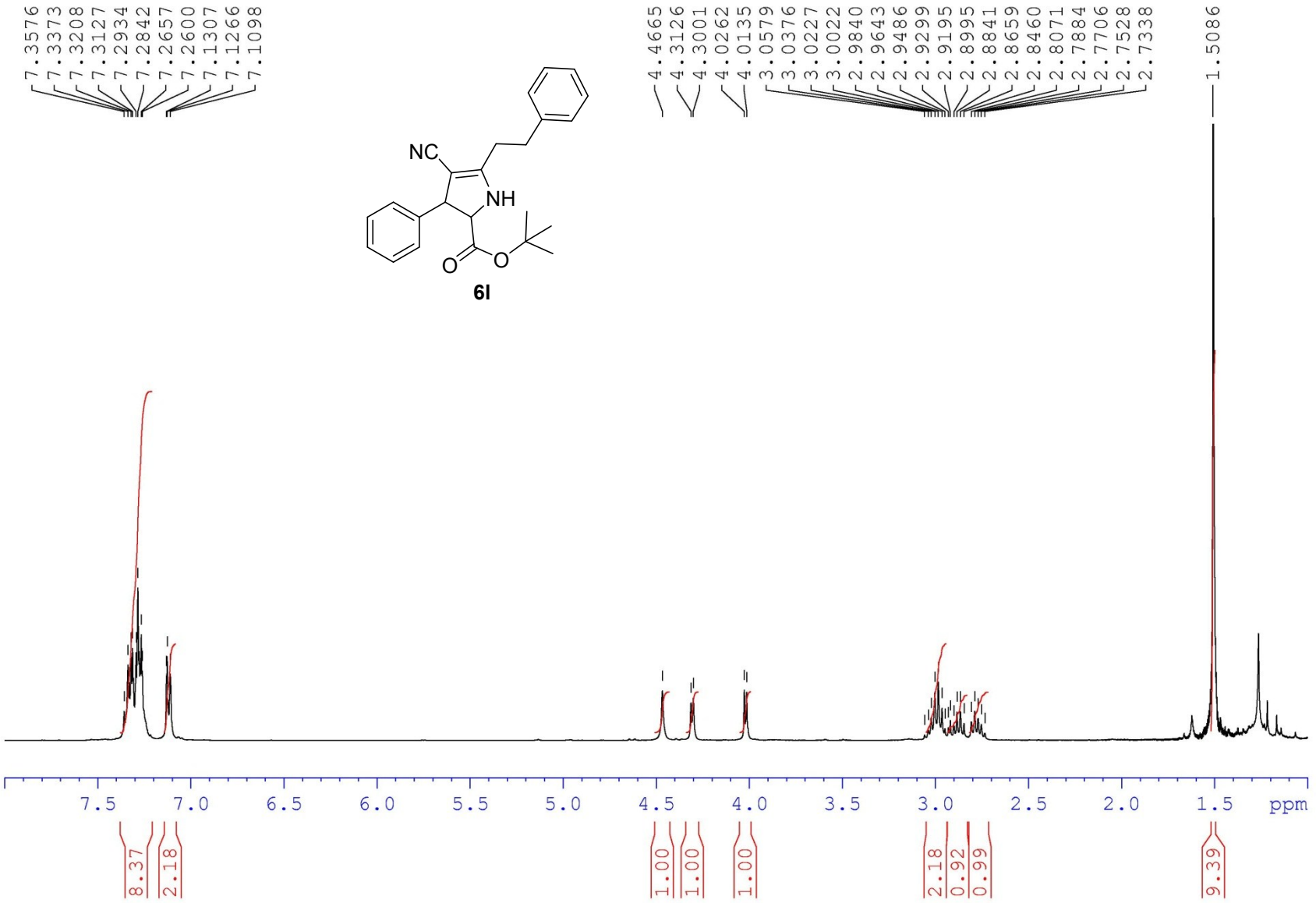
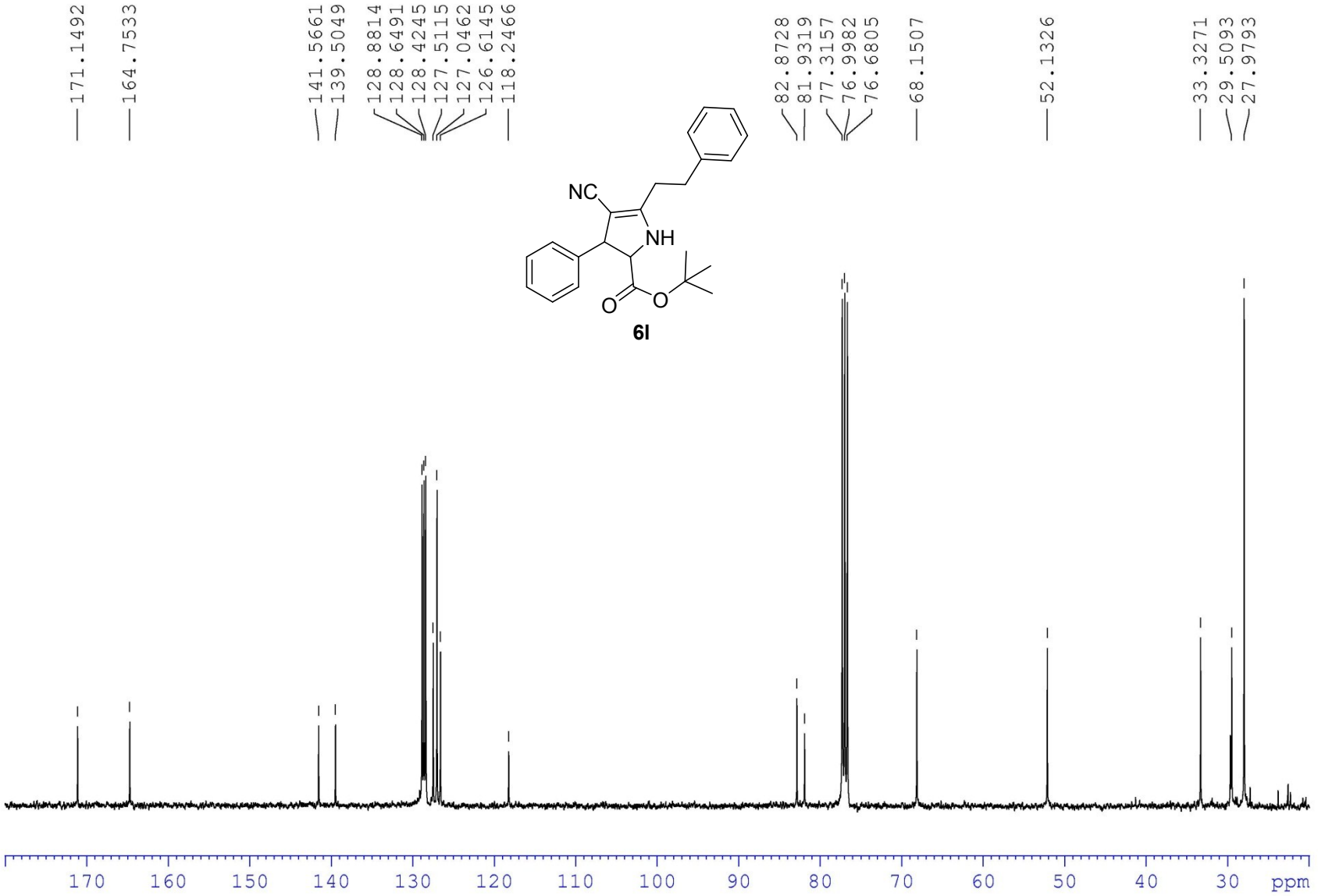


^{1}H NMR in $CDCl_3$ (400 MHz)

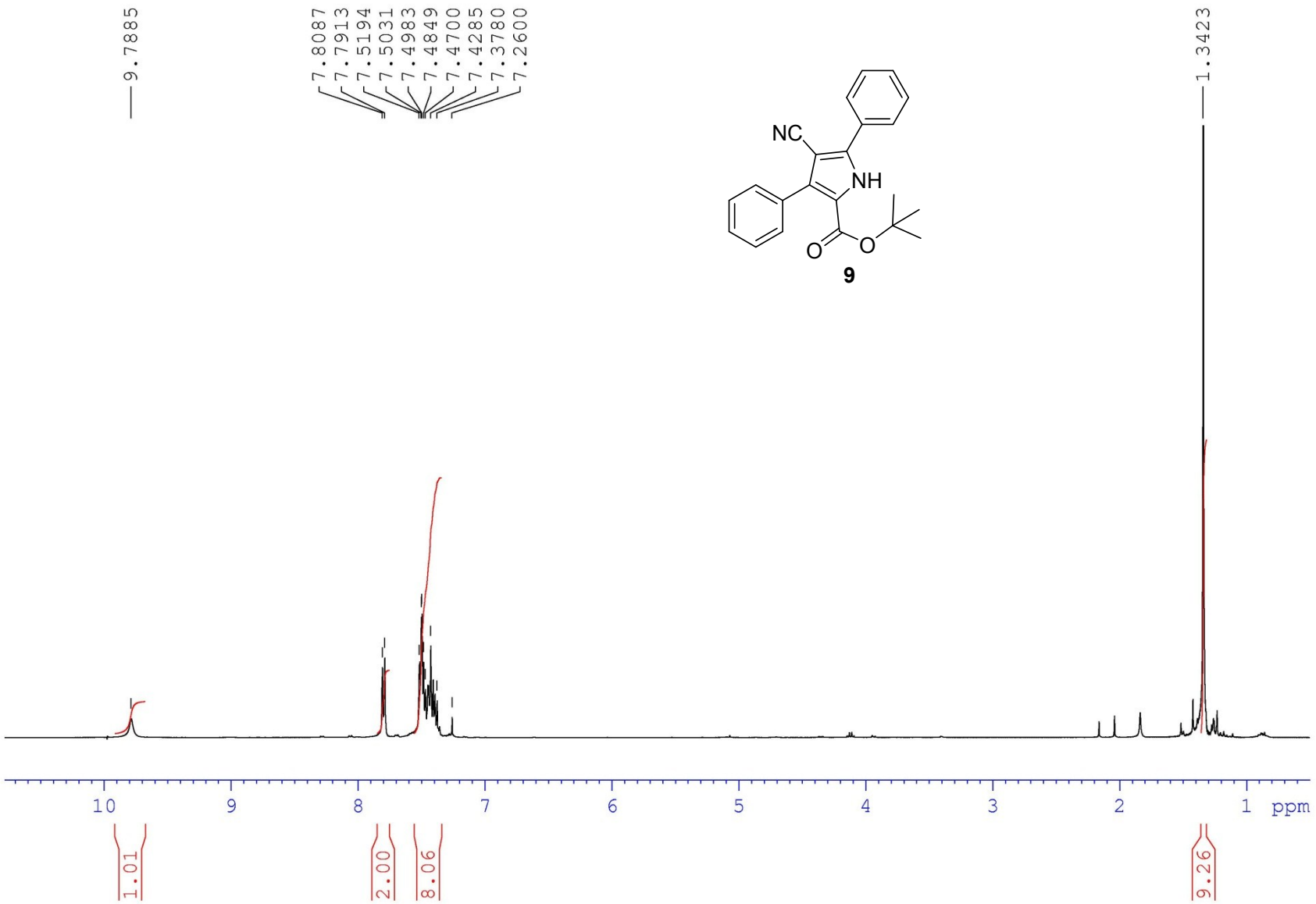


6l

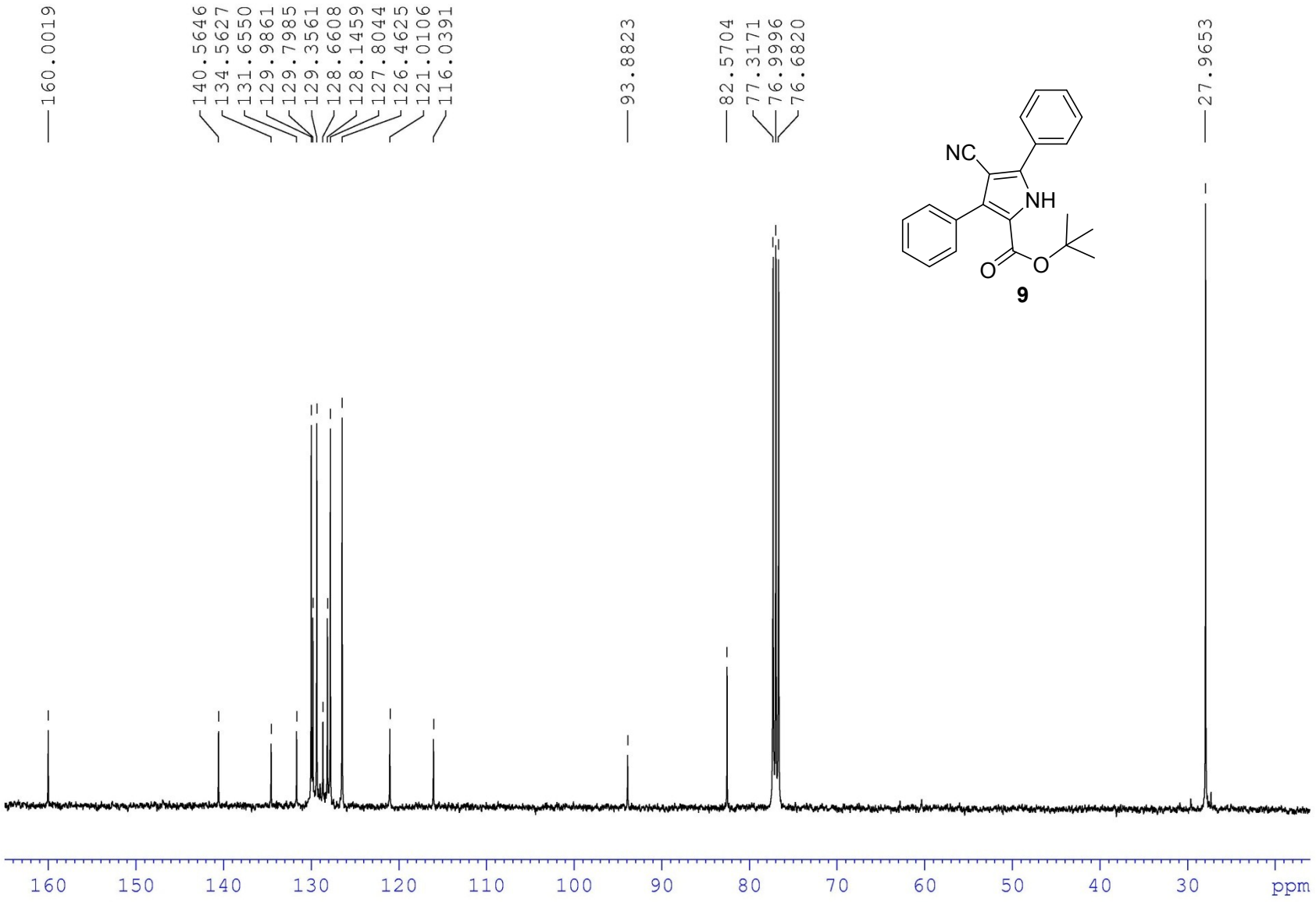
^{13}C NMR in $CDCl_3$ (100 MHz)



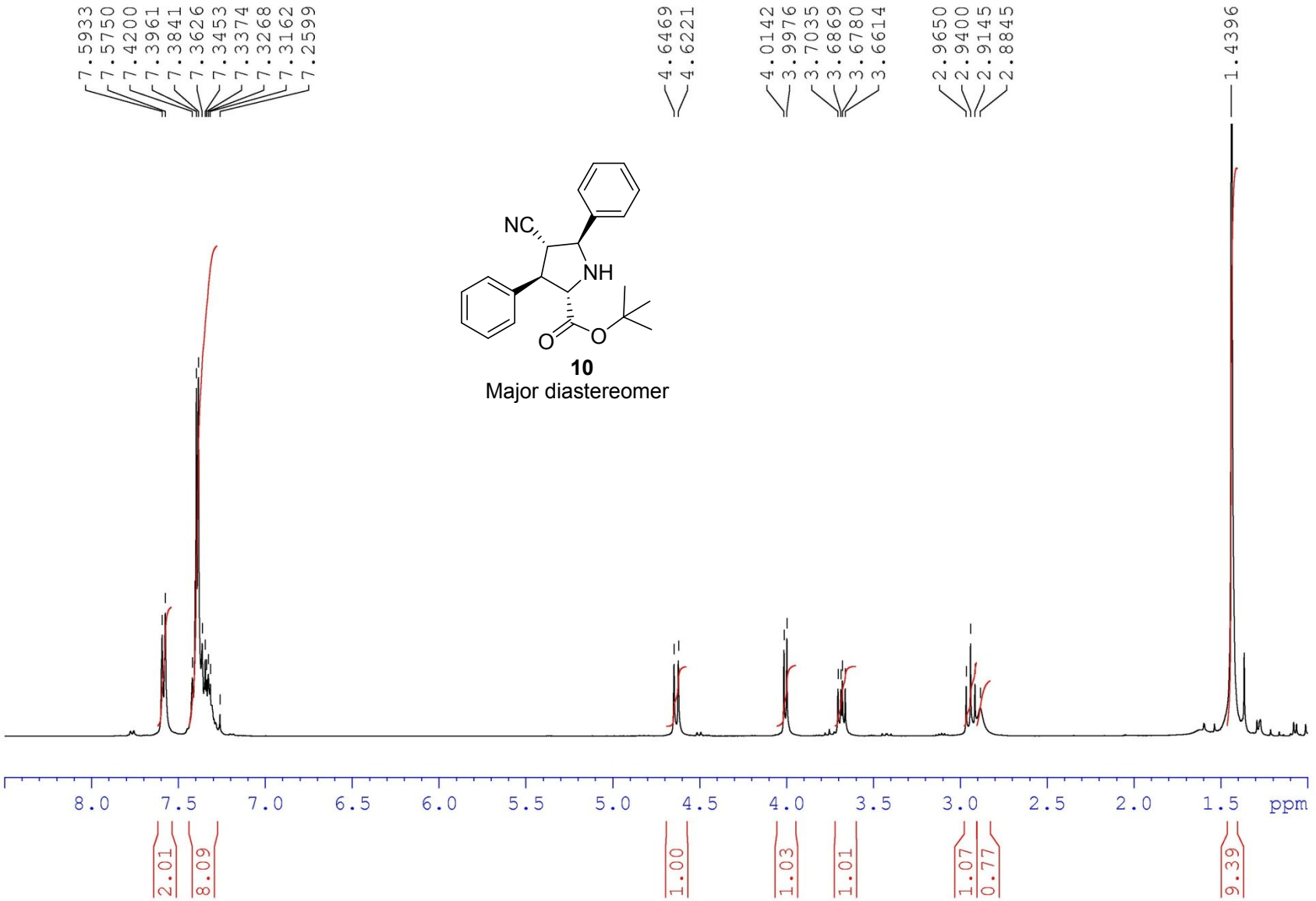
^{1}H NMR in $CDCl_3$ (400 MHz)



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



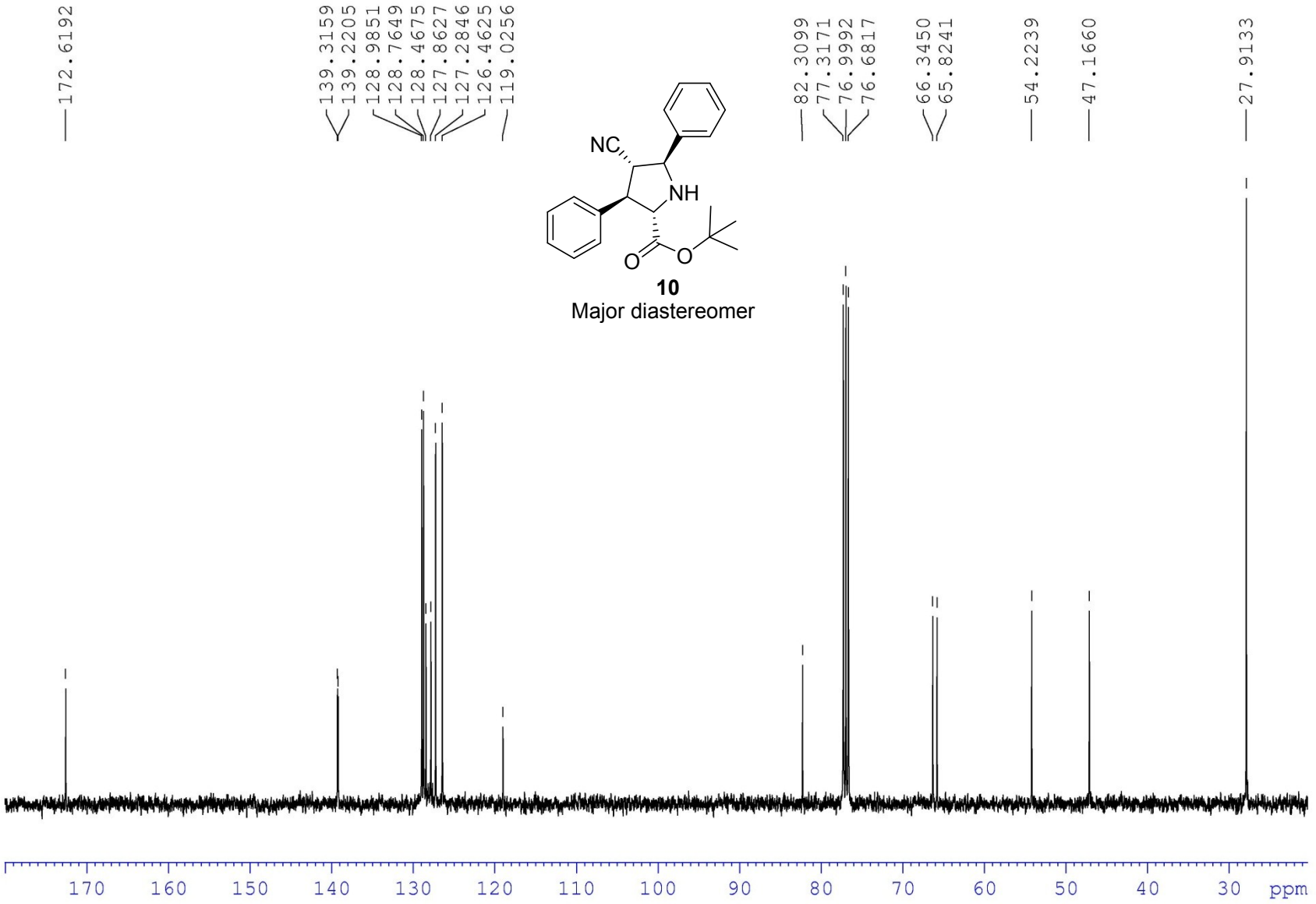
^{1}H NMR in $CDCl_3$ (400 MHz)



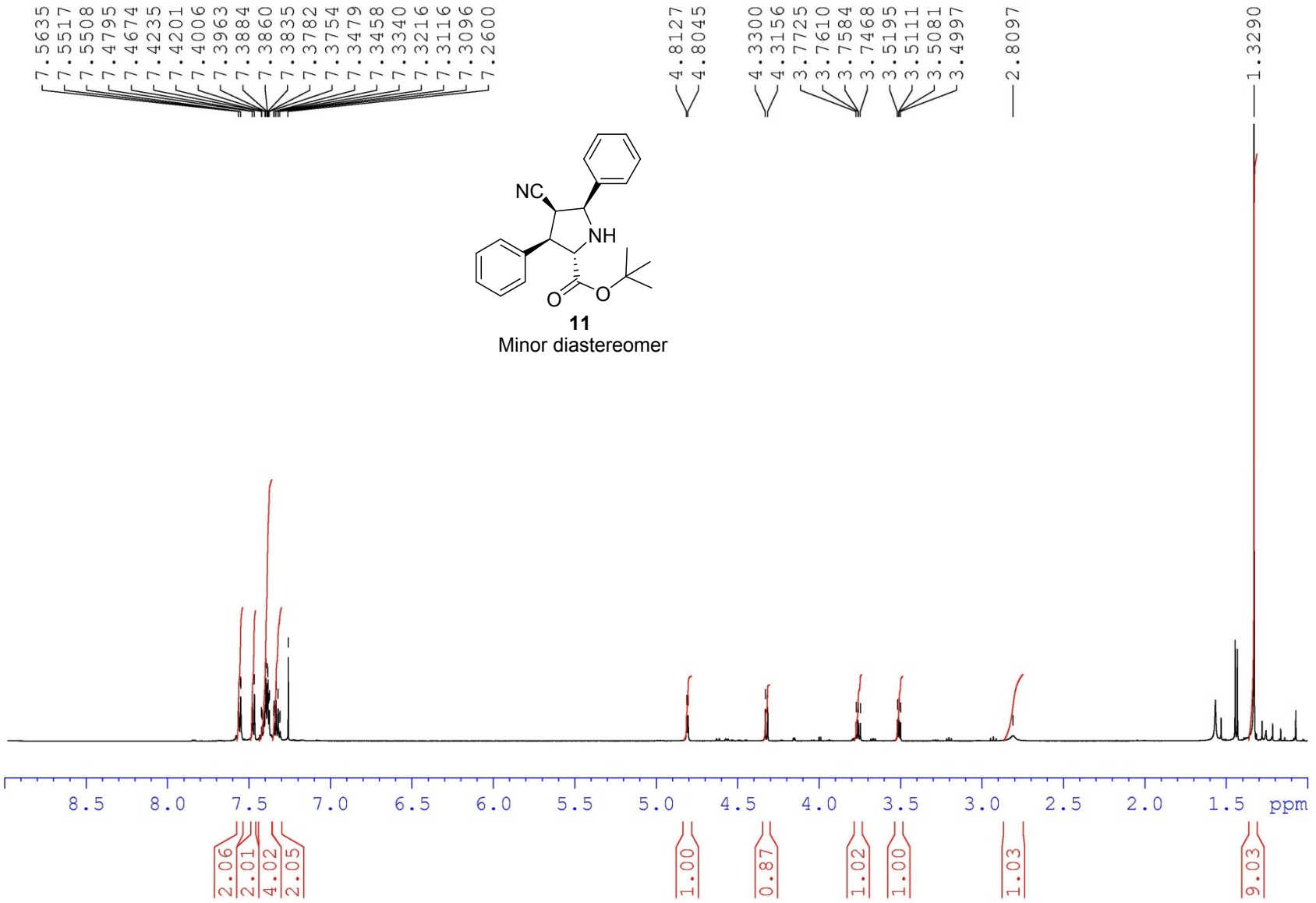
10

Major diastereomer

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

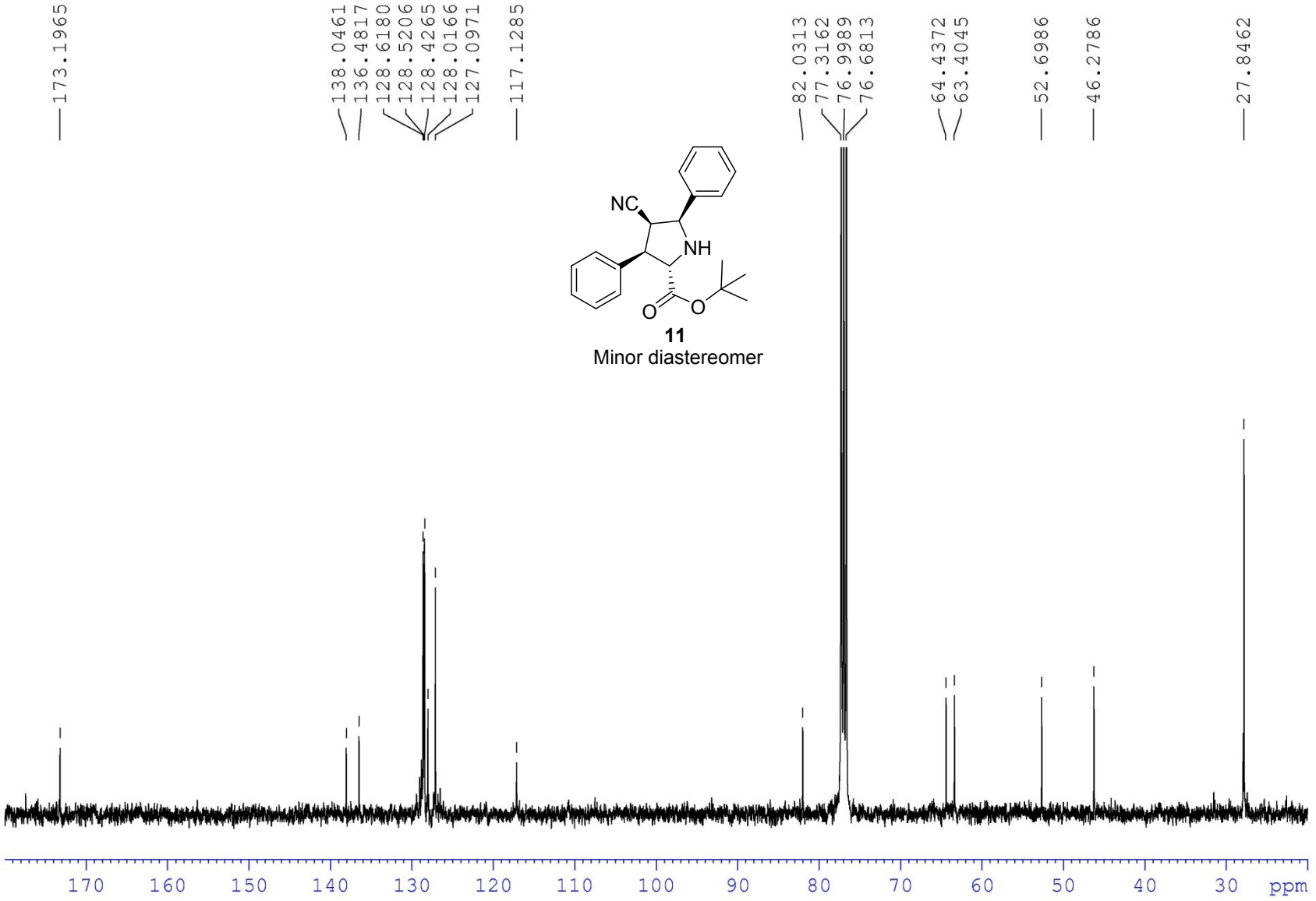


^{1}H NMR in $CDCl_3$ (600 MHz)



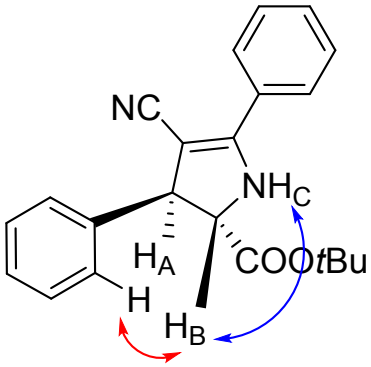
11
Minor diastereomer

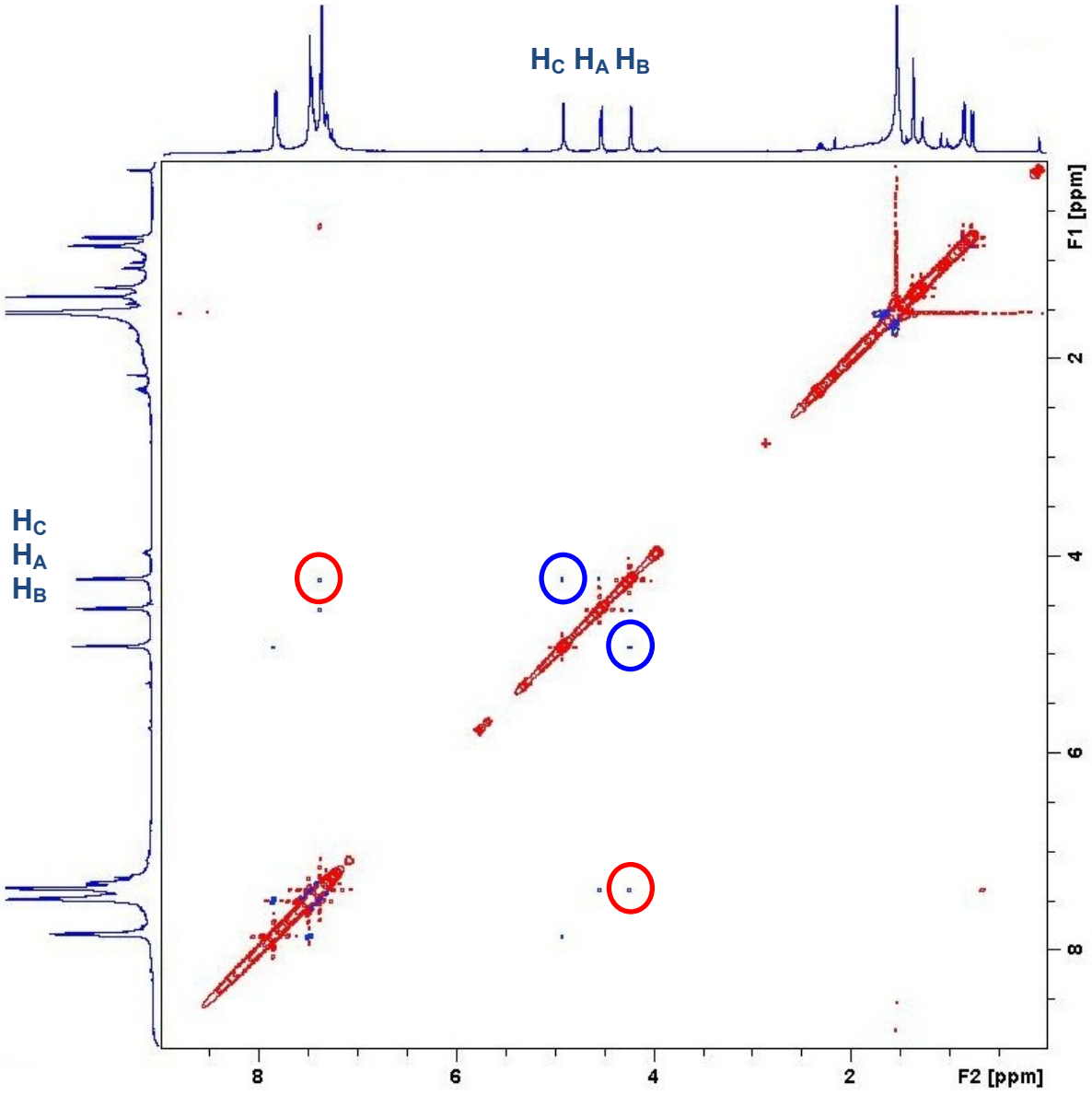
^{13}C NMR in $CDCl_3$ (100 MHz)



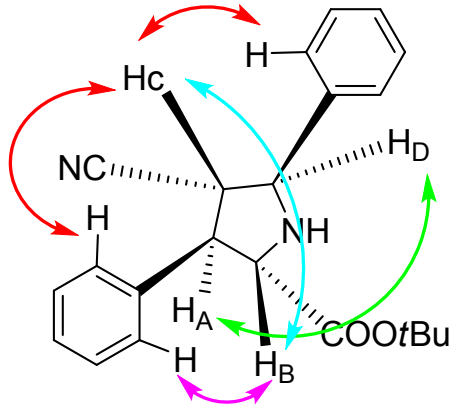
11
Minor diastereomer

Confirmation of the relative configuration of compound 6a by NOESY
(400 MHz, $CDCl_3$)

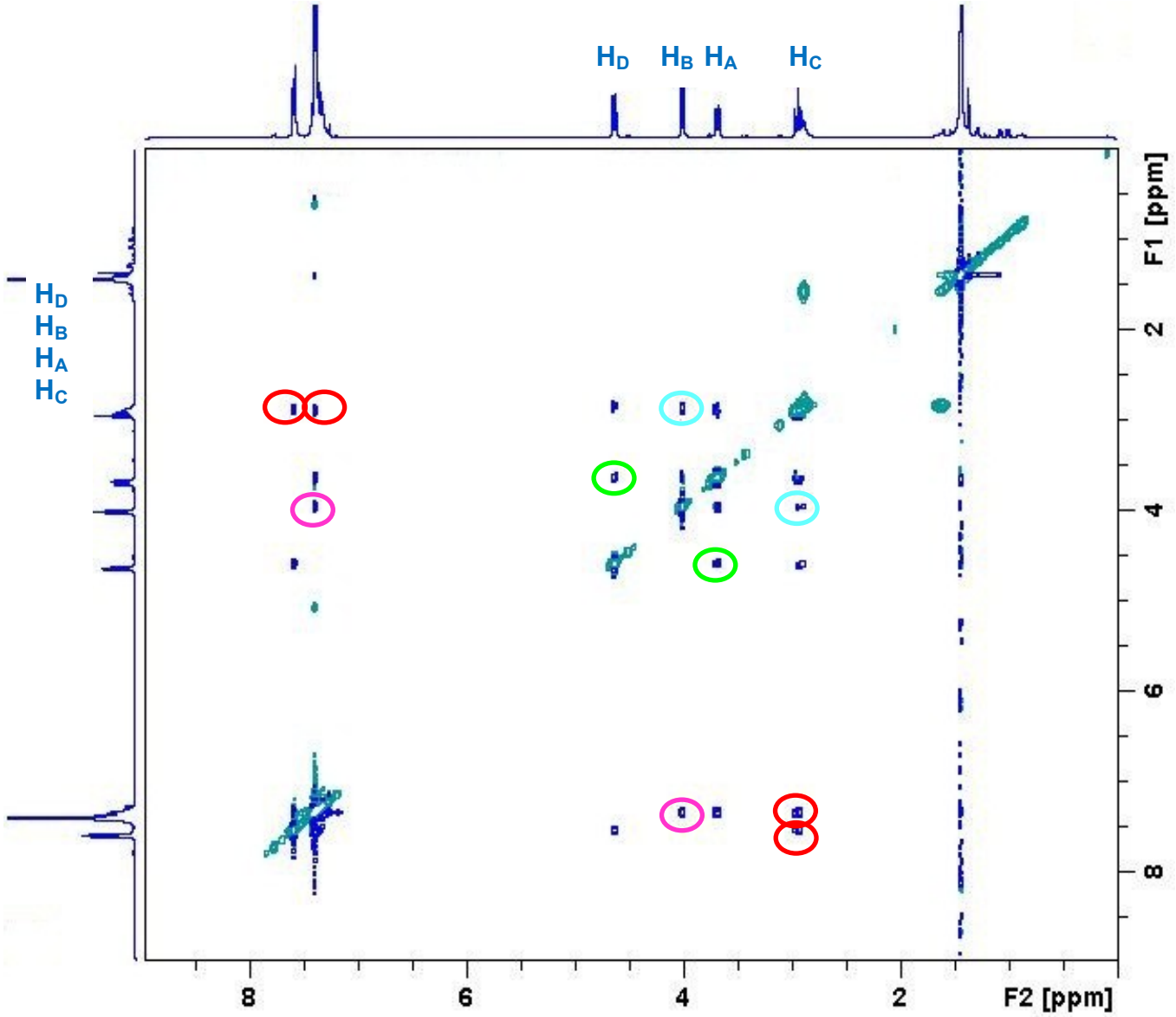




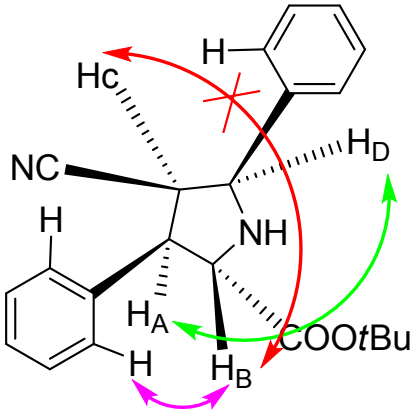
Confirmation of the relative configuration of compound 10 by NOESY
(400 MHz, $CDCl_3$)



Major diastereomer



Confirmation of the relative configuration of compound 11 by NOESY
(600 MHz, $CDCl_3$)



Minor diastereomer