

Facile Synthesis and Platinum complexes of 4',5,5''-Trisubstituted- 2,2':6',2''-terpyridines

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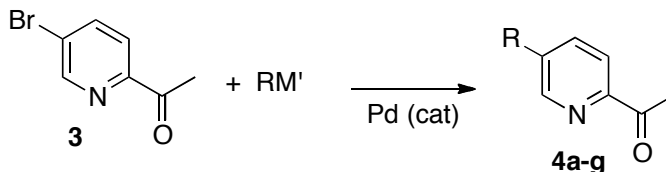
Page 2-5: Experimental for **4a-g**

Page 6-49: NMR spectra

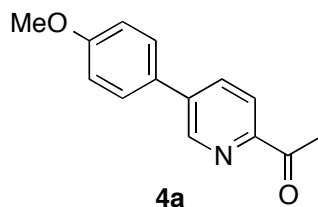
Experimental

All reactions were performed under an Argon atmosphere and solvents were purified prior to use. NMR spectra were recorded on a Bruker ARX400 MHz Bruker Spectrometer. Mass Spectra were recorded on a Voyager-DE PRO MALDI-TOF mass spectrometer. Fourier transform infrared spectra were recorded in pressed KBr pellets on a Perkin Elmer 1000 FTIR spectrometer. UV-visible absorption spectra were recorded on a Perkin Elmer Lambda 950 UV/vis spectrometer.

Synthetic procedures for the formation of 4a-g from 3 as illustrated below.

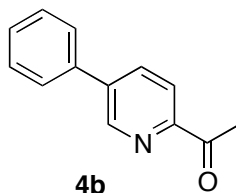


1-(5-(4-methoxyphenyl)pyridin-2-yl)ethanone:



A suspension of (4-methoxyphenyl)boronic acid (71 mg, 0.47 mmol), **3** (78 mg, 0.39 mmol), K_2CO_3 (108 mg, 0.78 mmol), $Pd(PPh_3)_4$ (10 mg, 0.008 mmol) in toluene/ H_2O (5:1) was heated to 105 °C for 15 h. The reaction was cooled to RT and extracted with EtOAc (20 mL x 3), dried $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel (5:1 cyclohexane/EtOAc) afforded 1-(5-(4-methoxyphenyl)pyridin-2-yl)ethanone **4a** (62 mg, 90%) as a white solid. 1H NMR (400 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.07 (d, $J=8.2$ Hz, 1H), 7.94 (d, $J=8.2$ Hz, 1H), 7.57 (d, $J=8.5$ Hz, 2H), 7.02 (d, $J=8.5$ Hz, 2H), 3.86 (s, 3H), 2.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.7, 160.3, 151.6, 146.9, 139.3, 134.2, 129.1, 128.4, 121.8, 114.7, 55.4, 25.8. This data matched as described in reference.

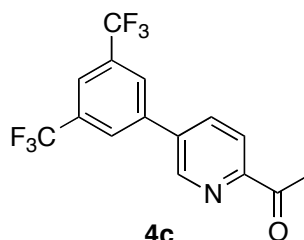
1-(5-phenylpyridin-2-yl)ethanone (4b):



A suspension of phenylboronic acid (256 mg, 2.1 mmol), **3** (350 mg, 1.75 mmol), K_2CO_3 (483 mg, 3.5 mmol), $Pd(PPh_3)_4$ (10 mg, 0.008 mmol) in toluene/ H_2O (5:1) was heated to 105 °C for 15 h. The reaction was cooled to RT and extracted with EtOAc (20 mL x 3), dried $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography on silica gel (5:1 cyclohexane/EtOAc)

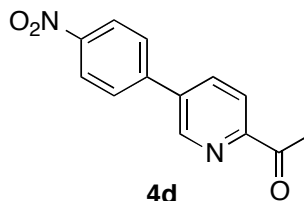
afforded 1-(5-phenylpyridin-2-yl)ethanone **4b** (280 mg, 81%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.91(d, $J=2.2$ Hz, 1H), 8.12 (d, $J=8.1$ Hz, 1H), 8.01 (dd, $J=8.1$, 2.2 Hz, 1H), 7.63 (d, $J=7.1$ Hz, 2H), 7.50 (m, 3H), 2.77(s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 199.7, 152.2, 147.4, 139.8, 136.8, 134.9, 129.2, 128.8, 127.3, 121.8, 25.8.

1-(5-(3,5-bis(trifluoromethyl)phenyl)pyridin-2-yl)ethanone (4c):



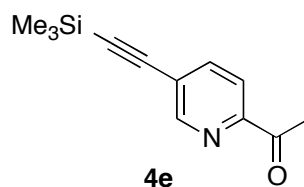
Potassium 3,5-Bis(trifluoromethyl)phenyltrifluoroborate (183 mg, 0.57 mmol), **3** (114 mg, 0.57 mmol), K_2CO_3 (157 mg, 1.14 mmol), and $\text{Pd}(\text{PPh}_3)_4$ (10 mg, 0.008 mmol) were added to a solution of toluene/ H_2O (5:1, 20 mL) and refluxed for 12 h. The mixture was cooled to RT, diluted with CH_2Cl_2 (50 mL) and washed once with H_2O (20 mL) and then brine (20 mL). The organic layer was dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography on silica gel, (3:1 cyclohexane/EtOAc) afforded **4c** (160 mg, 85%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.94(d, $J=2.0$ Hz, 1H), 8.18 (d, $J=8.9$ Hz, 1H), 8.10 (d, $J=2.0$ Hz, 1H), 8.07 (s, 2H), 7.97 (s, 1H), 2.77 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ =199.4, 153.4, 147.4, 139.2, 136.9, 135.4, 127.4, 124.4, 122.4, 121.7, 25.8. IR (KBr) 1696, 1379, 699 cm^{-1} . HRMS (m/z) calculated for 334.0667 ($\text{M}+\text{H}$) $\text{C}_{15}\text{H}_{10}\text{F}_6\text{NO}$, found 334.0528 ($\text{M}+\text{H}$) $^+$.

1-(5-(4-nitrophenyl)pyridin-2-yl)ethanone (4d):



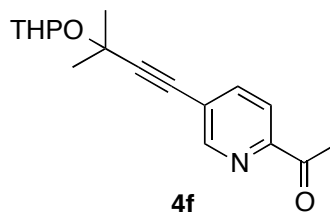
A suspension of (4-nitrophenyl)boronic acid (125 mg, 0.75 mmol), **3** (150 mg, 0.75 mmol), K_2CO_3 (207 mg, 1.5 mmol), $\text{Pd}(\text{PPh}_3)_4$ (10 mg, 0.008 mmol) in toluene/ H_2O (5:1) was heated to 120 $^\circ\text{C}$ for 15 h. The reaction was cooled to RT and extracted with EtOAc (20 mL x 3), dried MgSO_4 , filtered and concentrated *in vacuo*. Flash chromatography on silica gel, (5:1 cyclohexane/EtOAc) afforded **4d** (100 mg, 55%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.96(d, $J=2.3$ Hz, 1H), 8.40 (d, $J=8.7$ Hz, 2H), 8.20 (d, $J=8.0$ Hz, 1H), 8.09 (dd, $J=8.0$, 2.3 Hz, 1H), 7.80 (d, $J=8.7$ Hz, 2H), 2.79 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ =199.5, 153.3, 148.0, 147.6, 143.2, 137.5, 135.5, 128.2, 124.5, 121.9, 25.9. IR (KBr) 1690, 1522, 1345 cm^{-1} HRMS (m/z) calculated for 243.0770 ($\text{M}+\text{H}$) $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}_3$, found 243.0776 ($\text{M}+\text{H}$) $^+$.

1-(5-((trimethylsilyl)ethynyl)pyridin-2-yl)ethanone (4e):



A solution of **3** (407 mg, 2.03 mmol), trimethylsilylacetylene (0.6 mL, 4.07 mmol), $\text{PdCl}_2(\text{PhCN})_2$ (39 mg, 0.10 mmol), PPh_3 (53 mg, 0.20 mmol), and Cu(II)acetate (20 mg, 0.10 mmol) in diisopropylamine (20 mL) was heated at 80 °C for 4h. The reaction was cooled to r.t. and filtered to remove the precipitate of diisopropylamine hydrobromide salts. The solvent was removed and the residue was taken up in CH_2Cl_2 . Extraction with H_2O (20 mL x 2), dried MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (3:1 cyclohexane/EtOAc) afforded **4e** (365 mg, 84%) as a brown oil. ^1H NMR (400 MHz, CDCl_3): δ 8.71 (s, 1H), 7.98 (d, $J=2.3$ Hz, 1H), 7.86 (d, $J=2.3$ Hz, 1H), 2.72 (s, 3H), 0.29 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ =199.4, 151.7, 139.6, 123.7, 120.8, 101.6, 100.9, 25.8, -0.29. IR (KBr) 1700, 1219, 862 cm^{-1} . HRMS (m/z) calculated for 218.1001 ($\text{M}+\text{H}$) $\text{C}_{12}\text{H}_{16}\text{NOSi}$, found 218.1055 ($\text{M}+\text{H}$) $^+$.

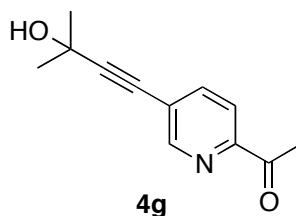
1-(5-(3-methyl-3-(THP-2-yloxy)but-1-ynyl)pyridin-2-yl)ethanone (4f):



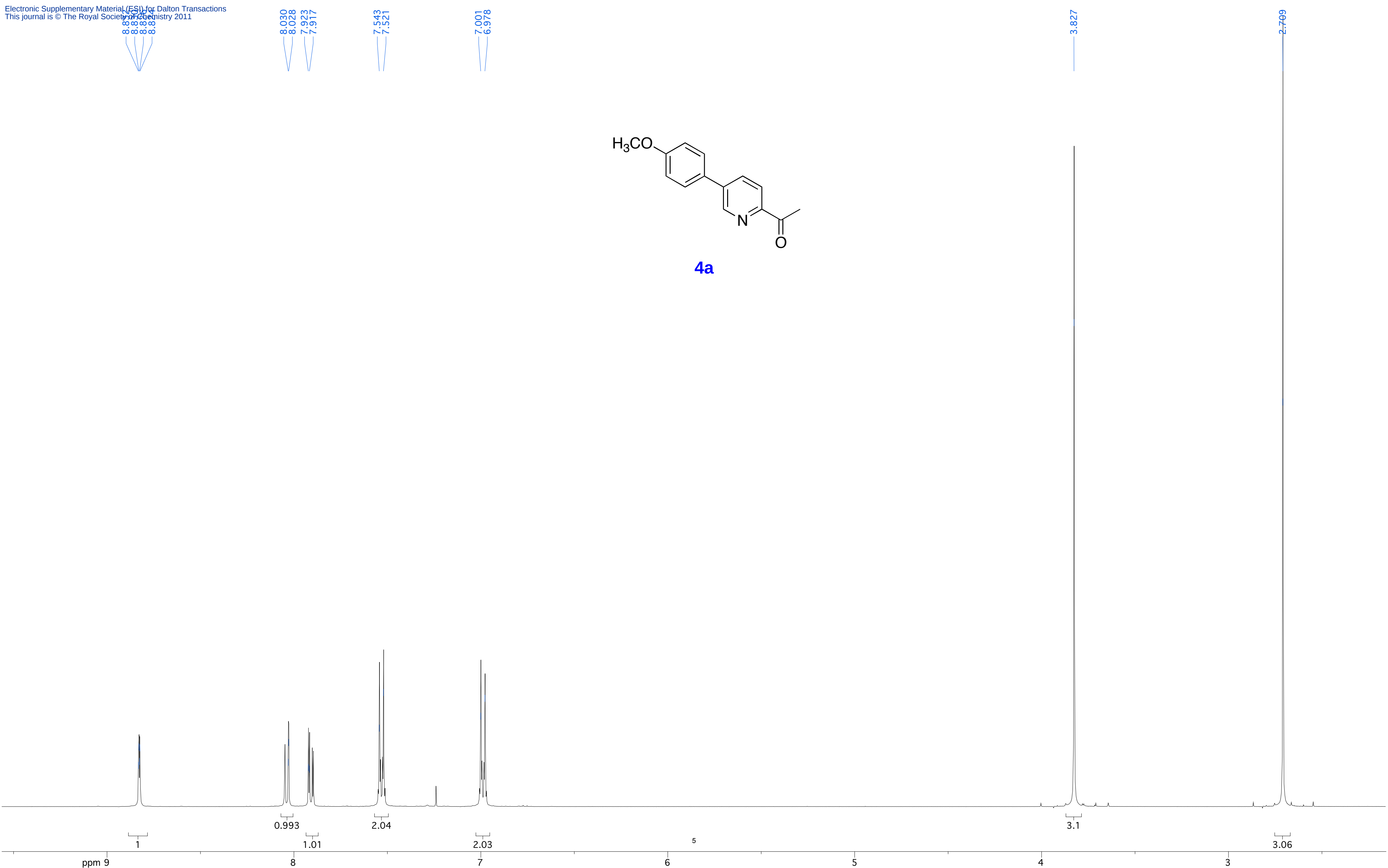
A mixture of **3** (104 mg, 0.52 mmol), 2-((2-methylbut-3-yn-2-yl)oxy)tetrahydro-2H-pyran (352 mg, 2.0 mmol), $\text{Pd(PPh}_3)_4$ (10 mg, 0.008 mmol), CuI (50 mg, 0.26 mmol) in diisopropylamine (20 mL) was heated at 50 °C for 10h. The reaction was cooled to r.t. and filtered to remove the precipitate of diisopropylamine hydrobromide salts. The solvent was removed and the residue was taken up in CH_2Cl_2 . Extraction with H_2O (20 mL x 2), dried (MgSO_4), filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (3:1 cyclohexane/EtOAc) afforded **4f** (140 mg, 94%) as an oil. ^1H NMR (400 MHz, CDCl_3): δ 8.63 (s, 1H), 7.94 (d, $J=2.3$ Hz, 1H), 7.78 (d, $J=2.3$ Hz, 1H), 5.07 (s, 1H), 3.94 (m, 1H), 3.48 (m, 1H), 1.84~1.37 (m, 12H). ^{13}C NMR (100 MHz, CDCl_3): δ =199.2, 151.6, 151.3, 139.2, 123.5, 120.8, 98.2, 96.1, 80.3, 71.2, 63.2, 31.8, 30.2, 29.7, 25.7, 25.3, 20.3. IR (KBr) 3310, 1560, 855 cm^{-1} . HRMS (m/z) calculated for 288.1600 ($\text{M}+\text{H}$) $\text{C}_{17}\text{H}_{22}\text{NO}_3$, found 288.1621 ($\text{M}+\text{H}$) $^+$.

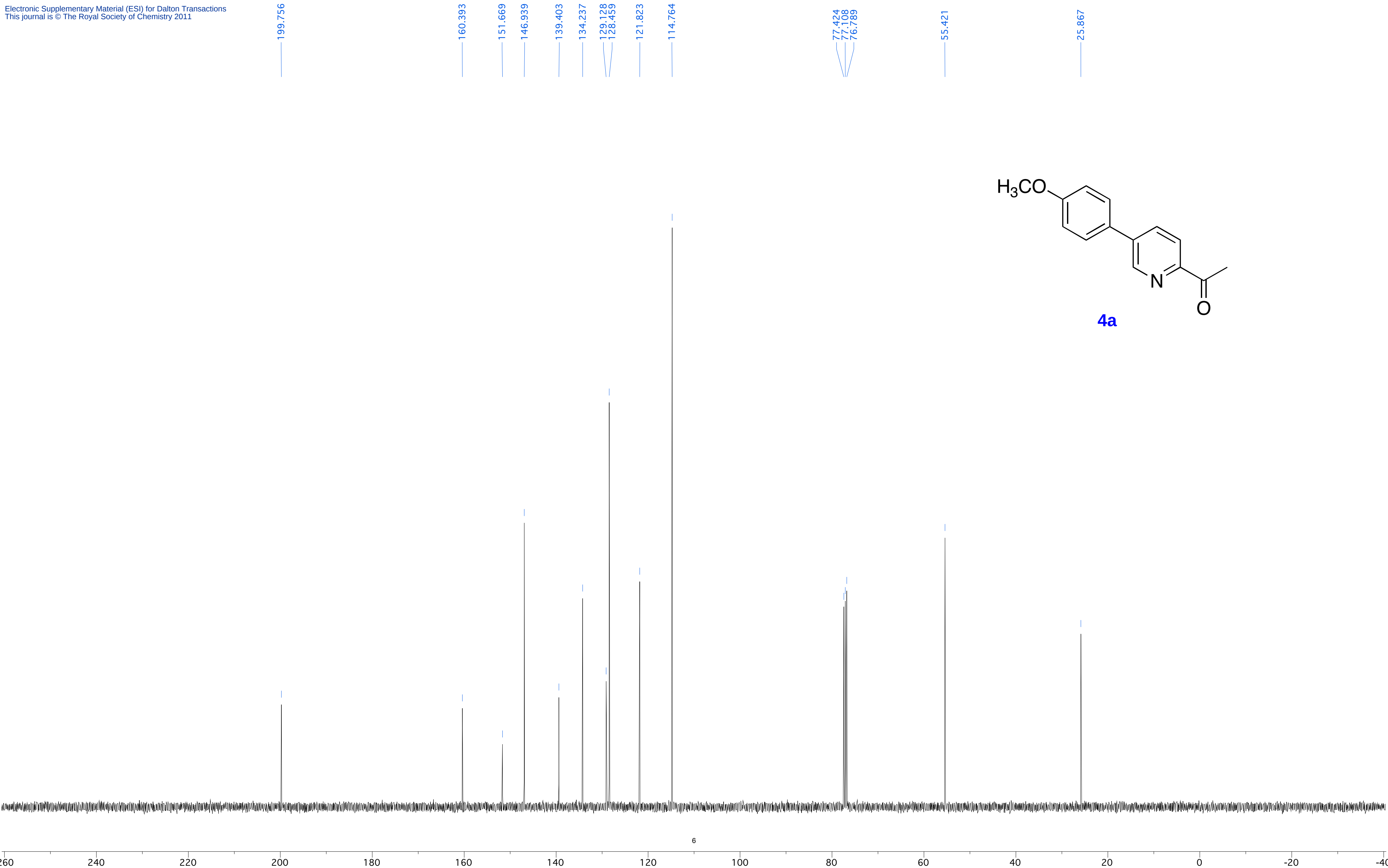
2-((2-methylbut-3-yn-2-yl)oxy)tetrahydro-2H-pyran was synthesized via the published procedure of: Cowie, J.S.; Landor, P. D.; Landor, S.R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 3807.

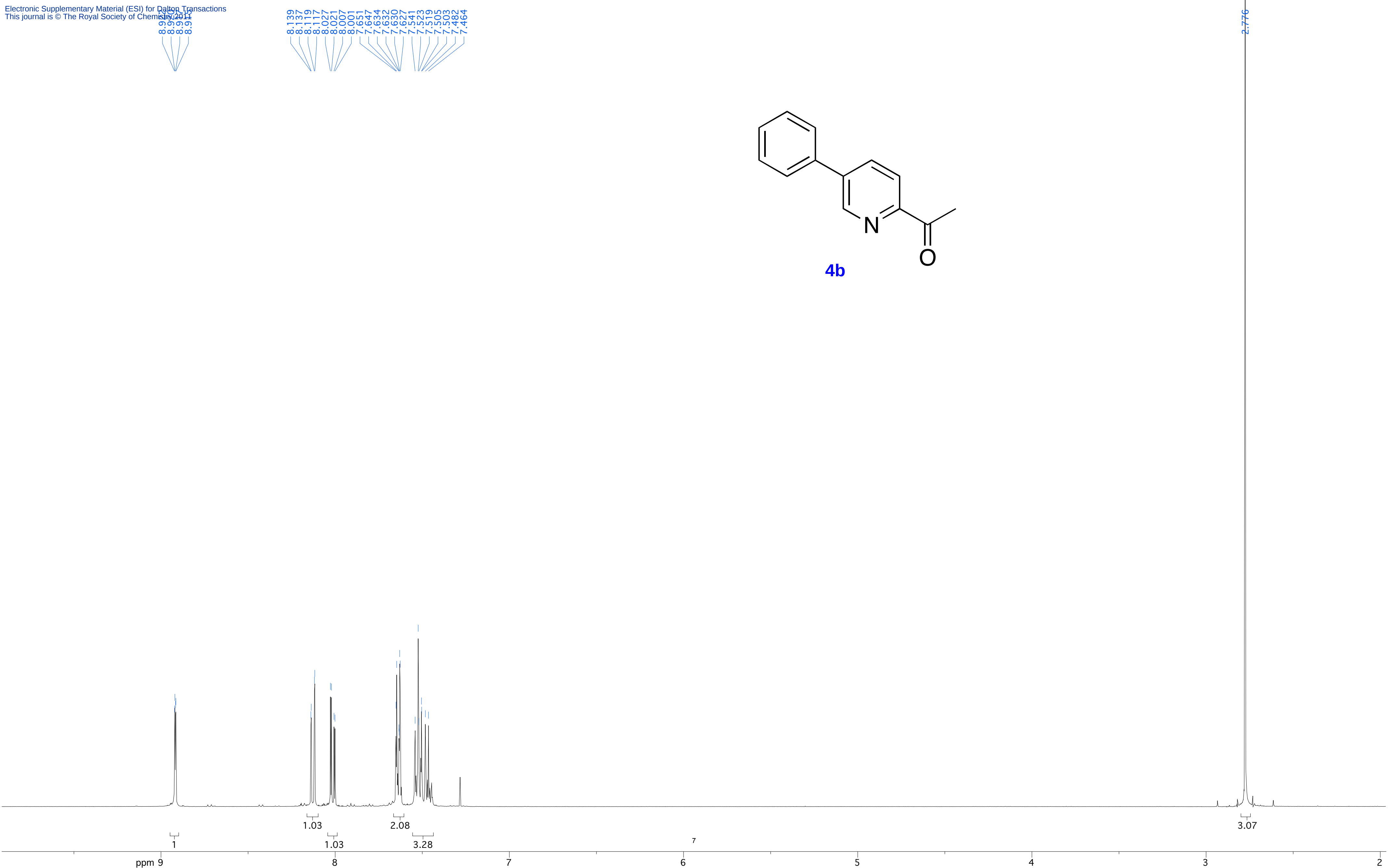
1-(5-(2-methyl-3-butyn-2-ol)pyridin-2-yl)ethanone (4g):

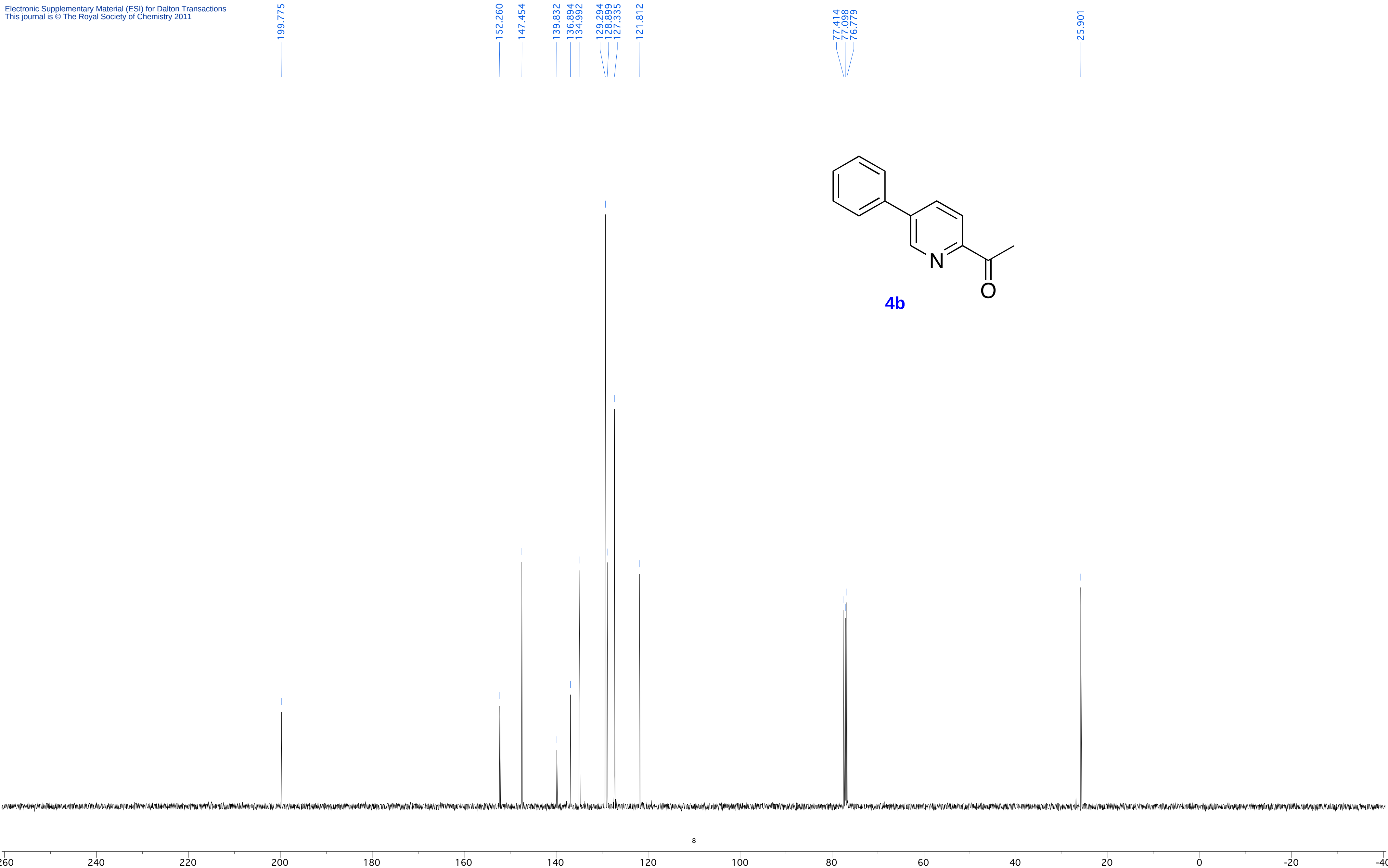


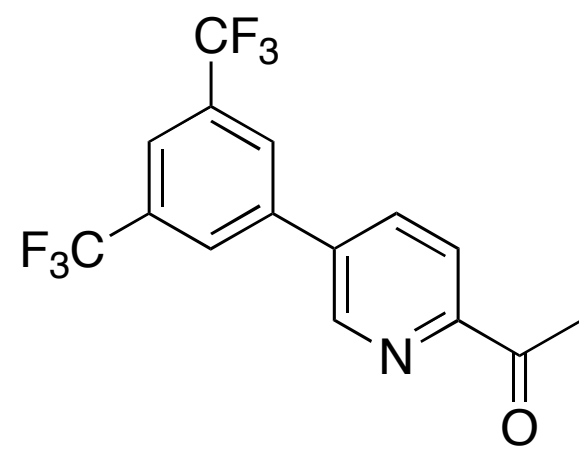
A mixture of **3** (120 mg, 0.6 mmol), 2-methyl-3-butyn-2-ol (0.4, 1.2 mmol), Pd(PPh₃)₄ (10 mg, 0.008 mmol), CuI (50 mg, 0.26 mmol) in diisopropylamine (20 mL) was heated at 50 °C for 10h. The reaction was cooled to r.t. and filtered to remove the precipitate of diisopropylamine hydrobromide salts. The solvent was removed and the residue was taken up in CH₂Cl₂. Extraction with H₂O (20 mL x 2), dried (MgSO₄), filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (3:1 cyclohexane/EtOAc) afforded **4g** (100 mg, 83%) as an oil. ¹H NMR (400 MHz, CDCl₃): δ 8.70 (s, 1H), 8.00 (d, *J*=8.5 Hz, 1H), 7.83 (d, *J*=8.5 Hz, 1H), 2.73 (s, 3H), 1.65 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ=199.4, 151.3, 139.4, 121.0, 100.2, 65.6, 65.4, 31.2, 31.0, 25.9. IR (KBr) 3210, 1697, 953 cm⁻¹. HRMS (*m/z*) calculated for 204.1025 C₁₂H₁₄NO₂, found 204.1001 (M+H)⁺.



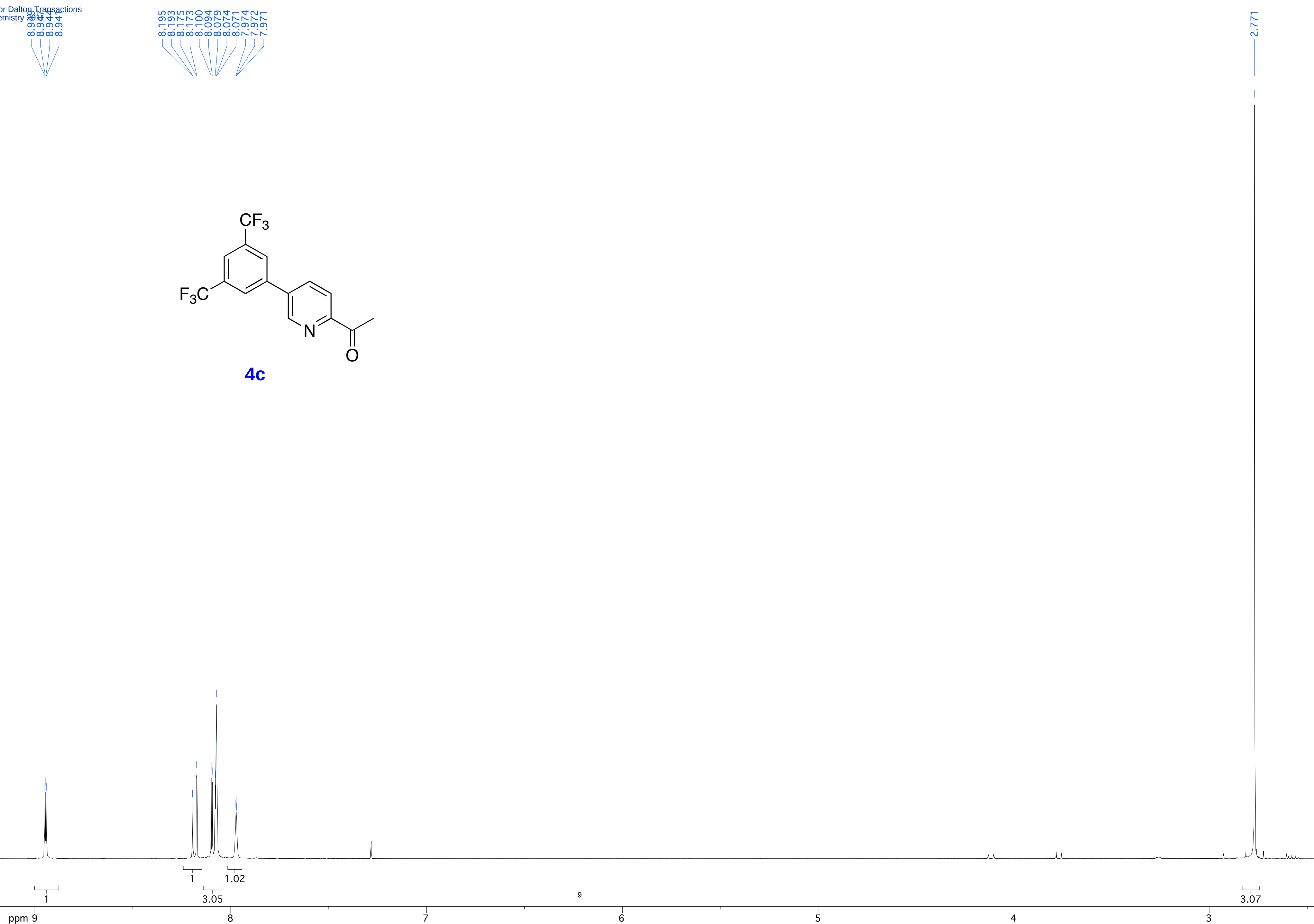


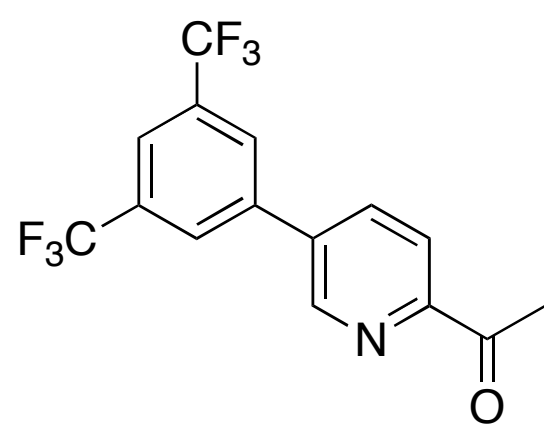




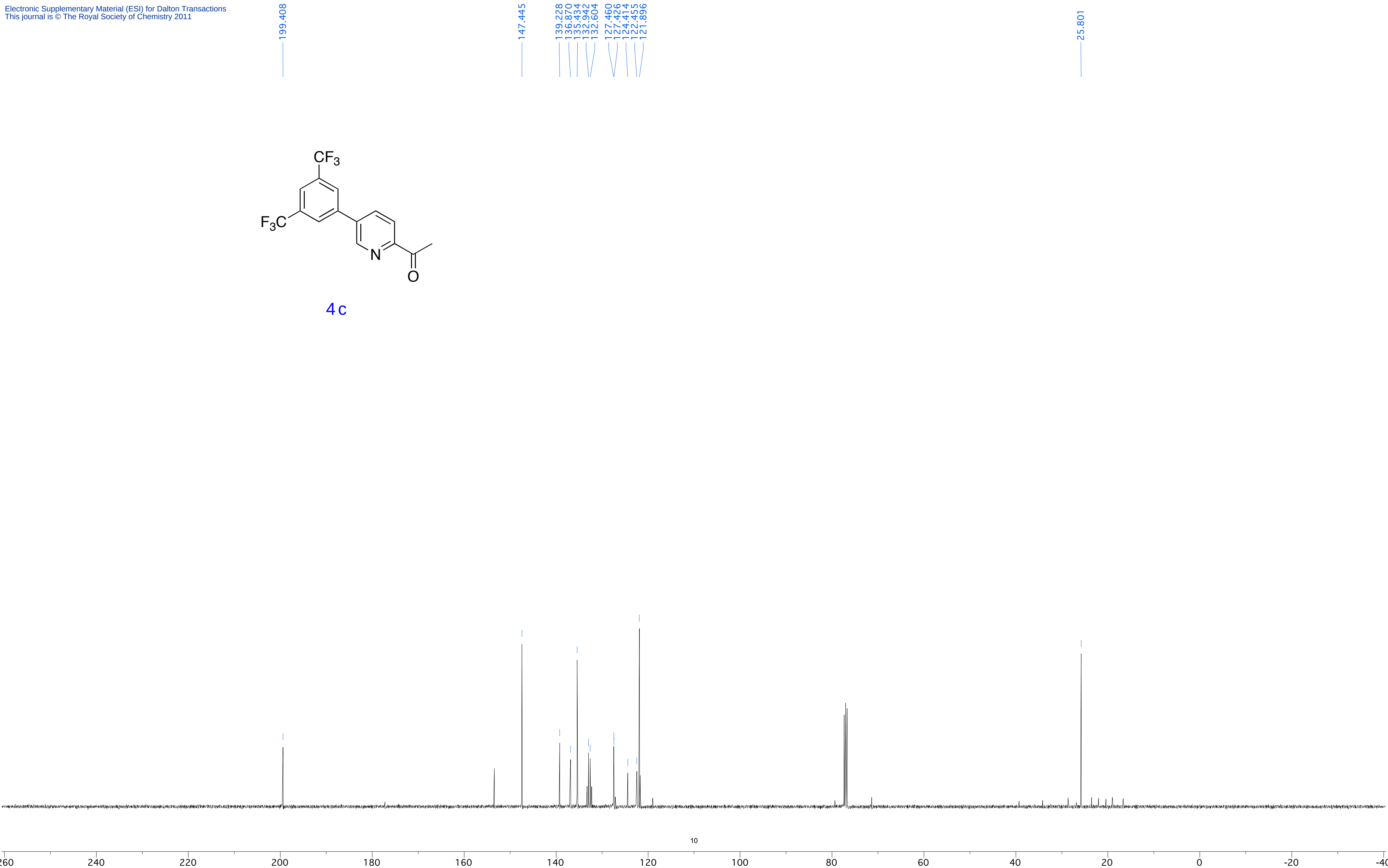


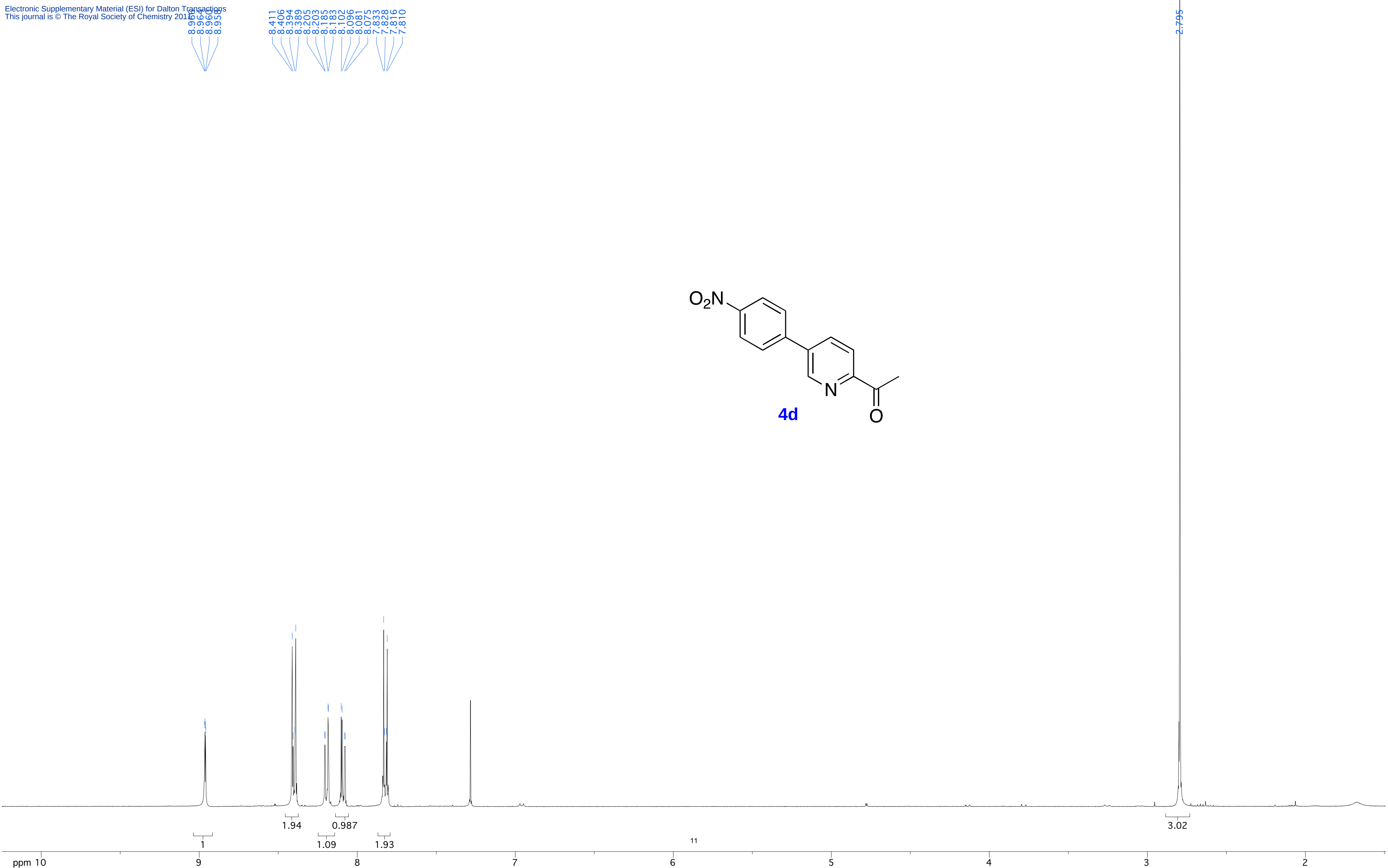
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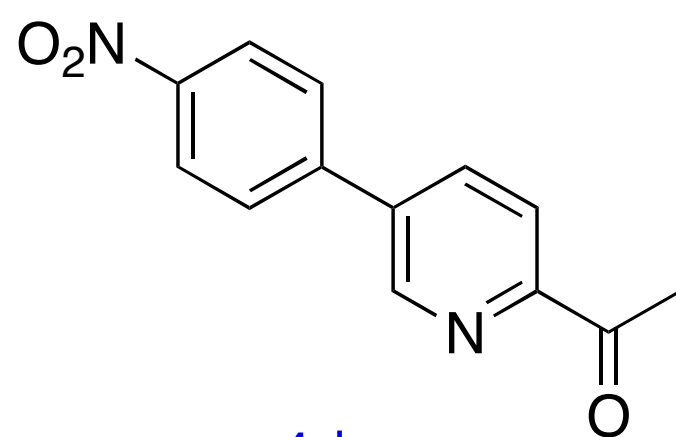




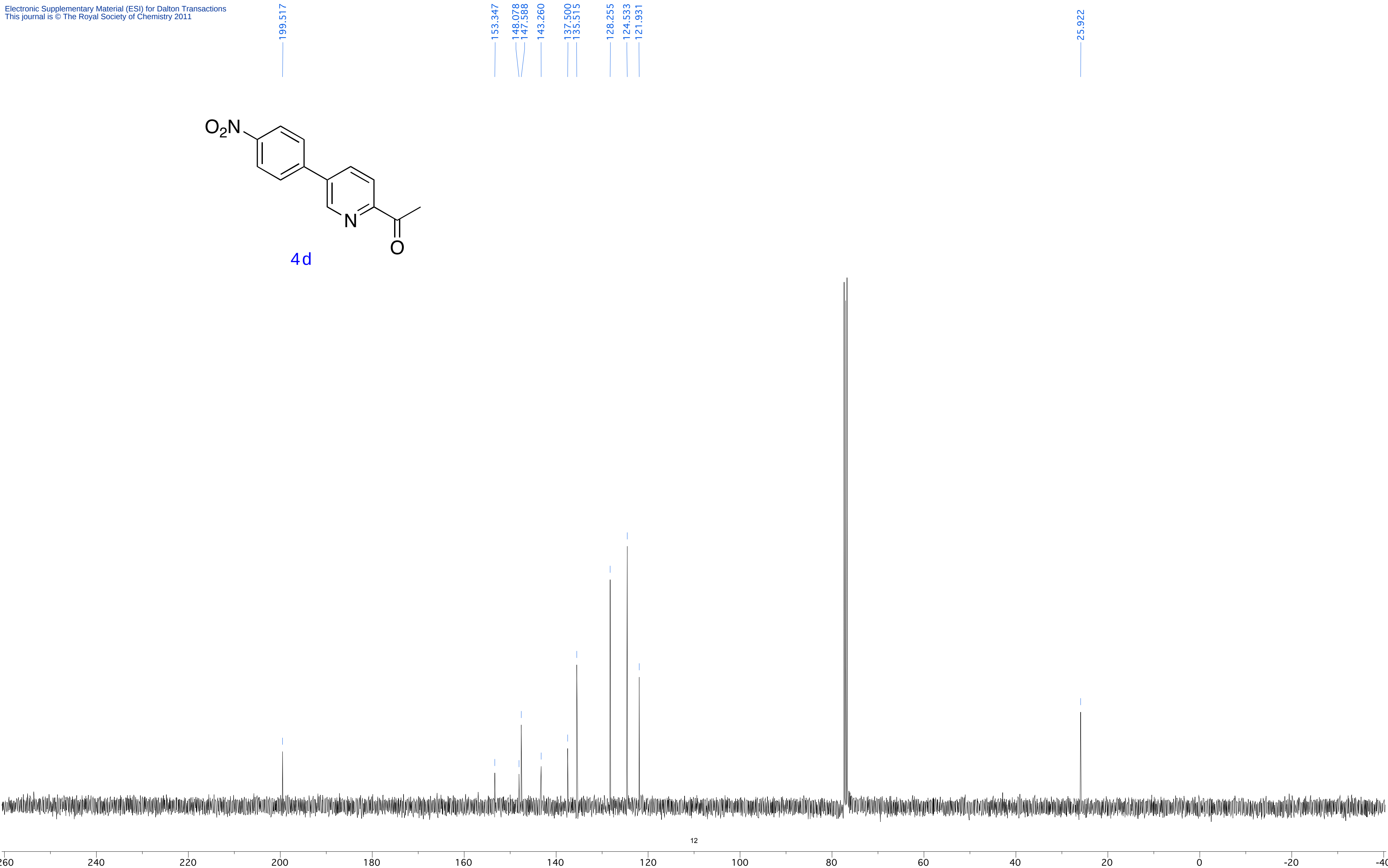
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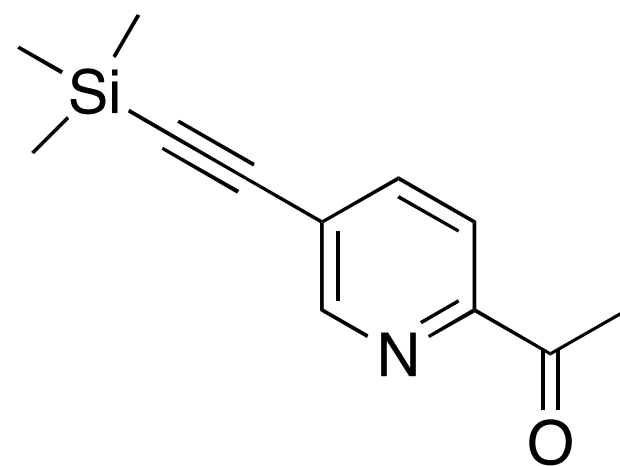




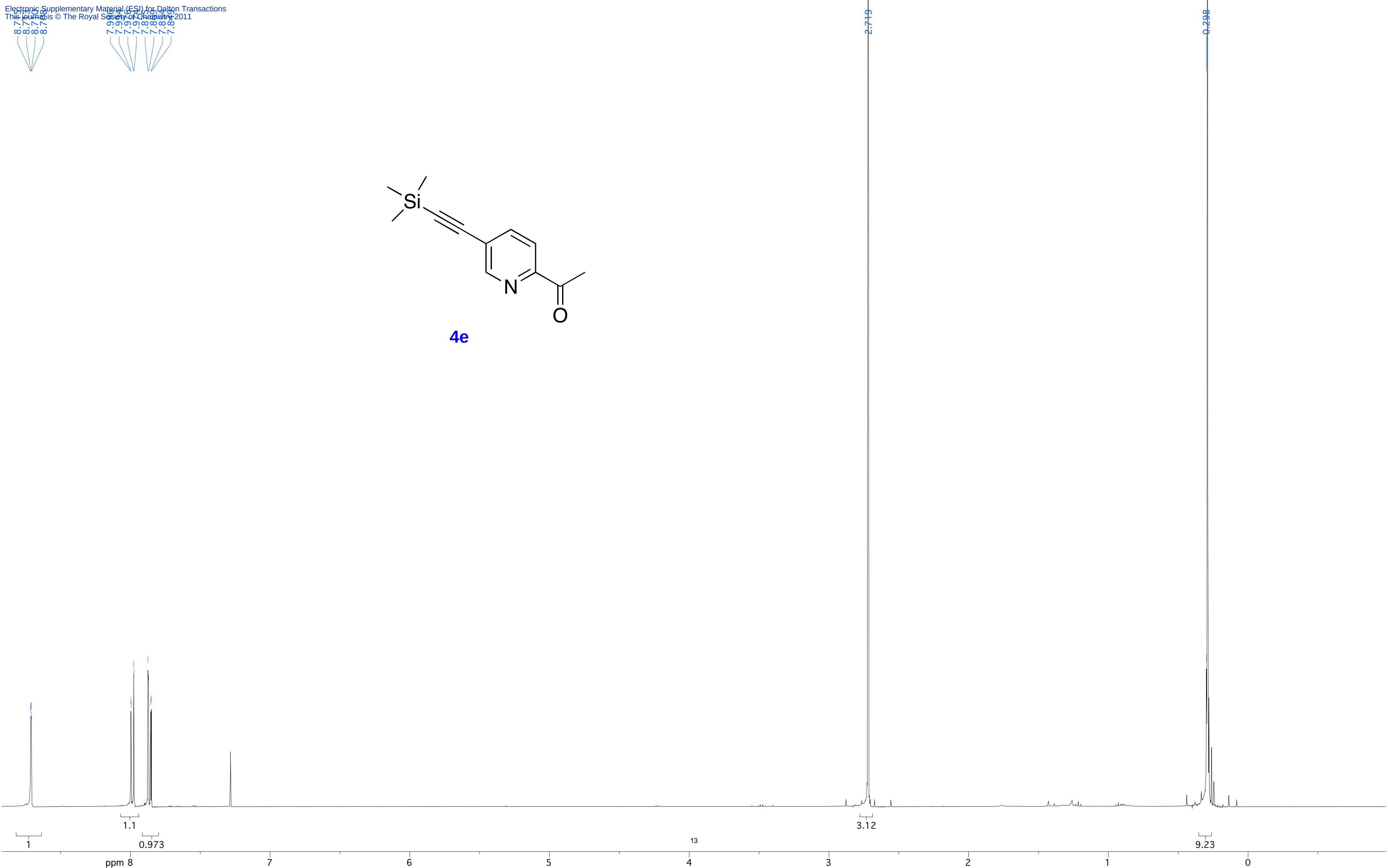


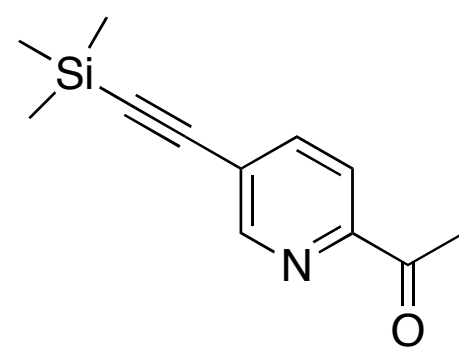
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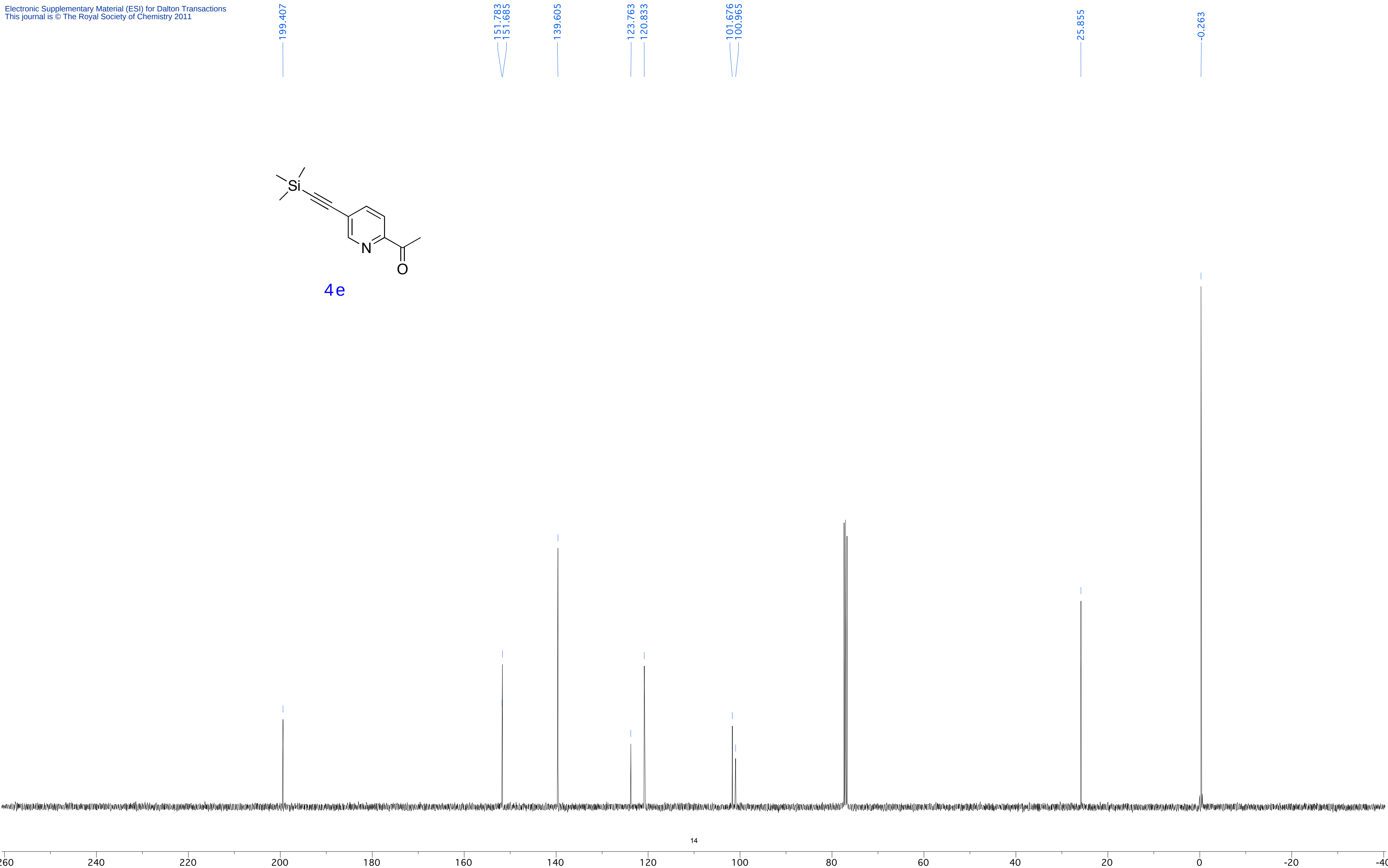


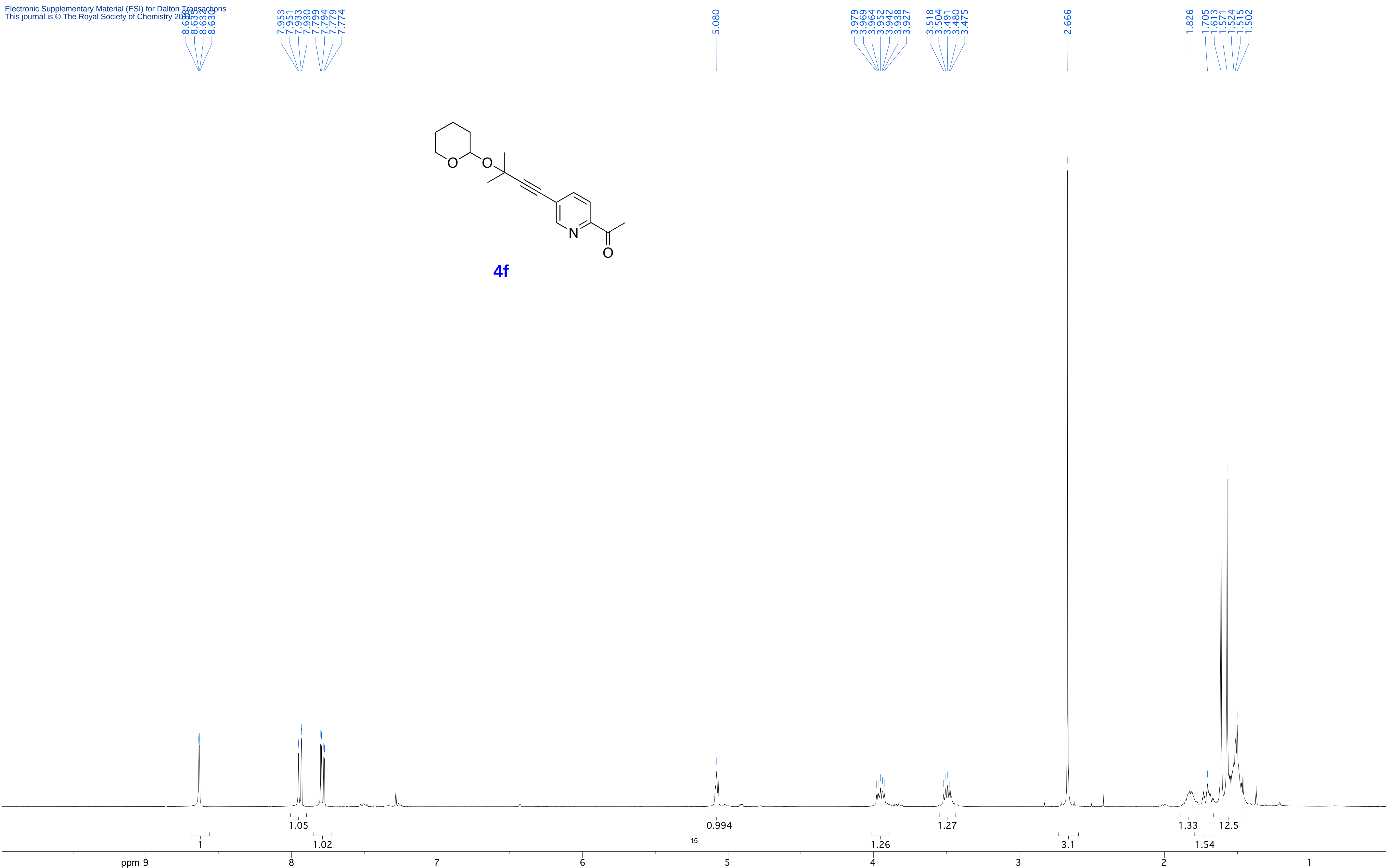
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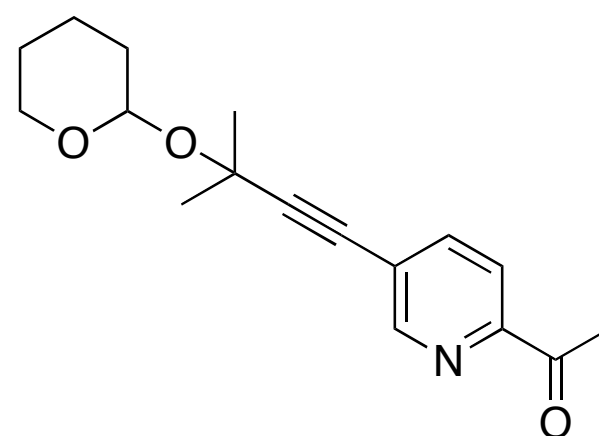




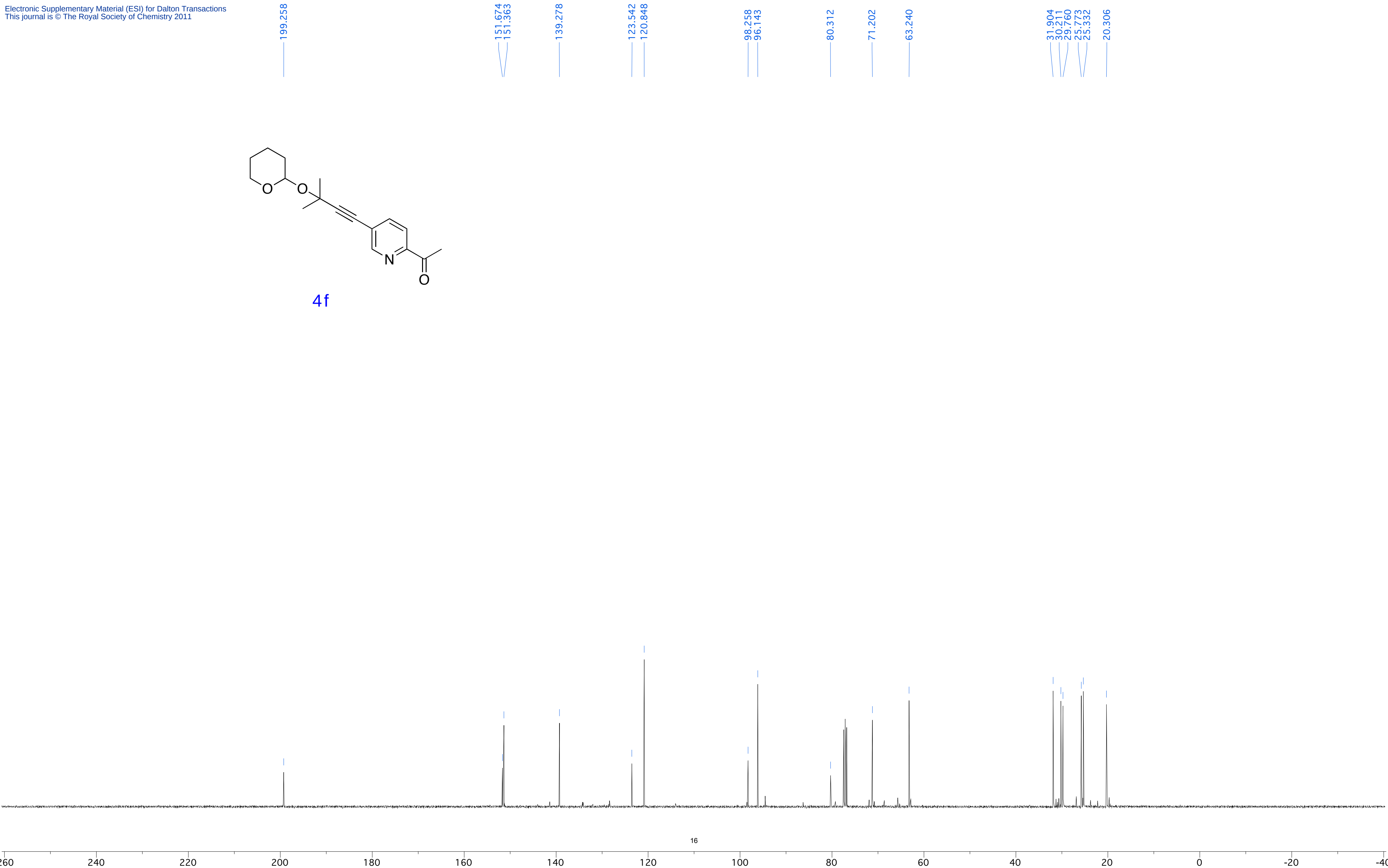
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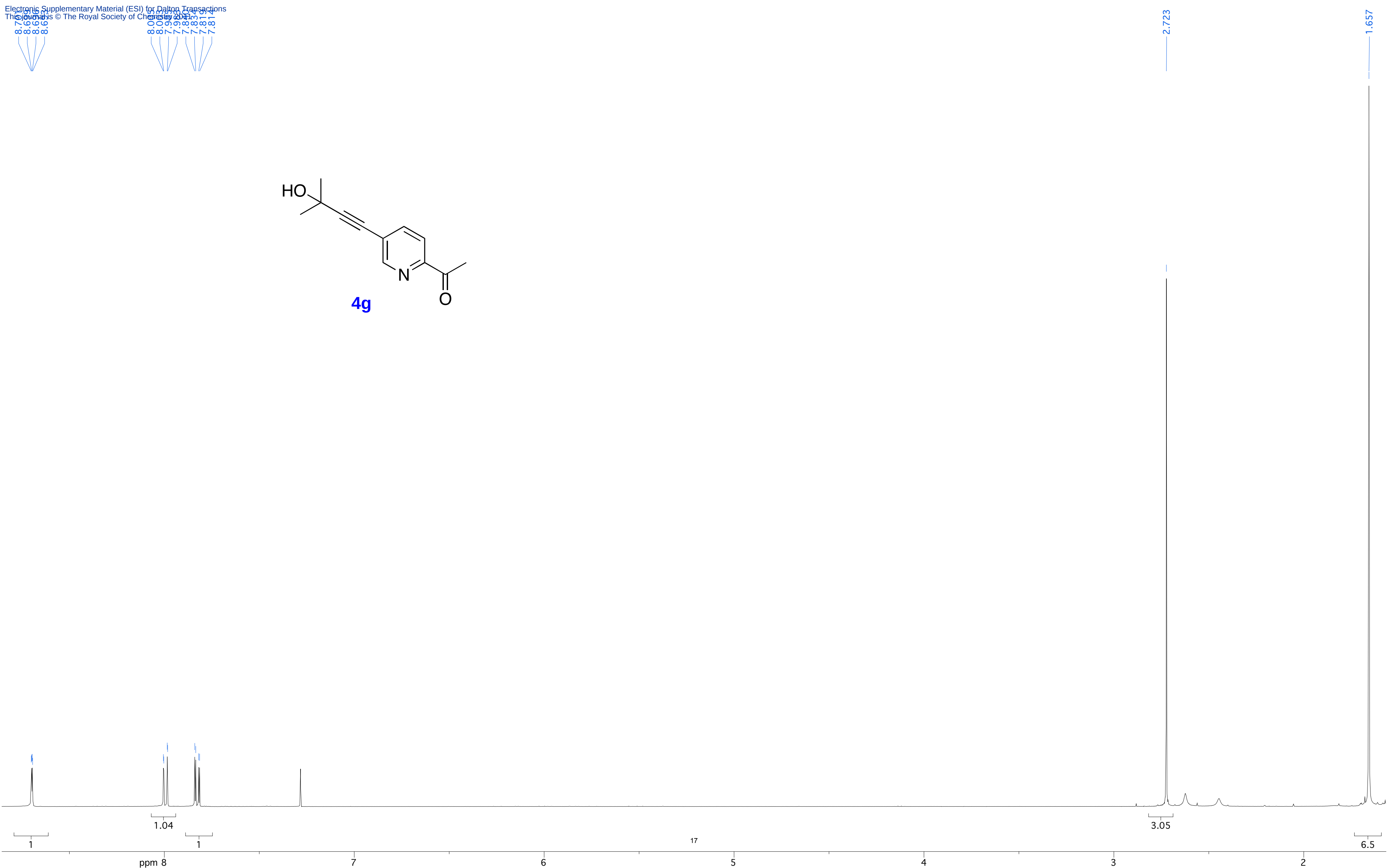
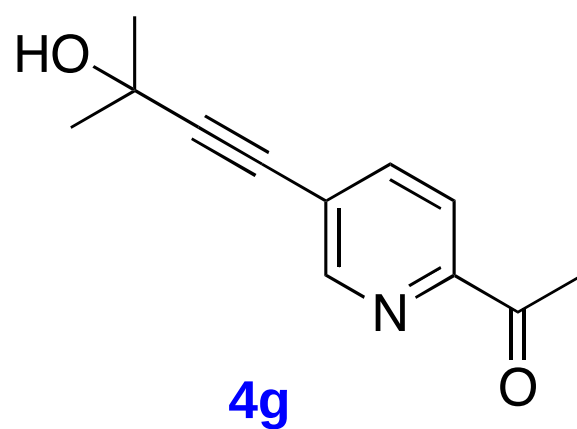


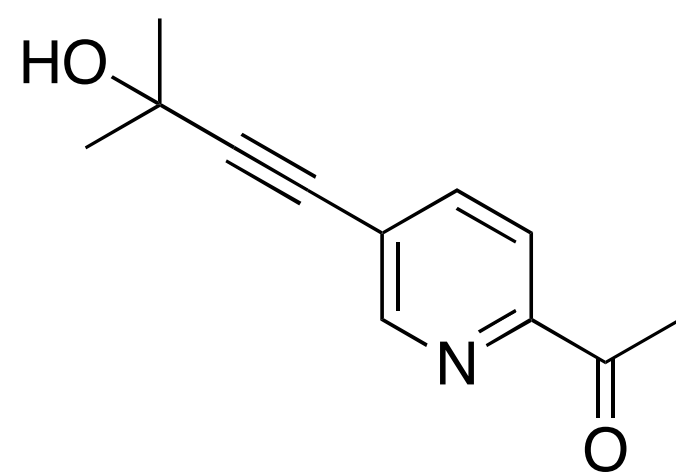




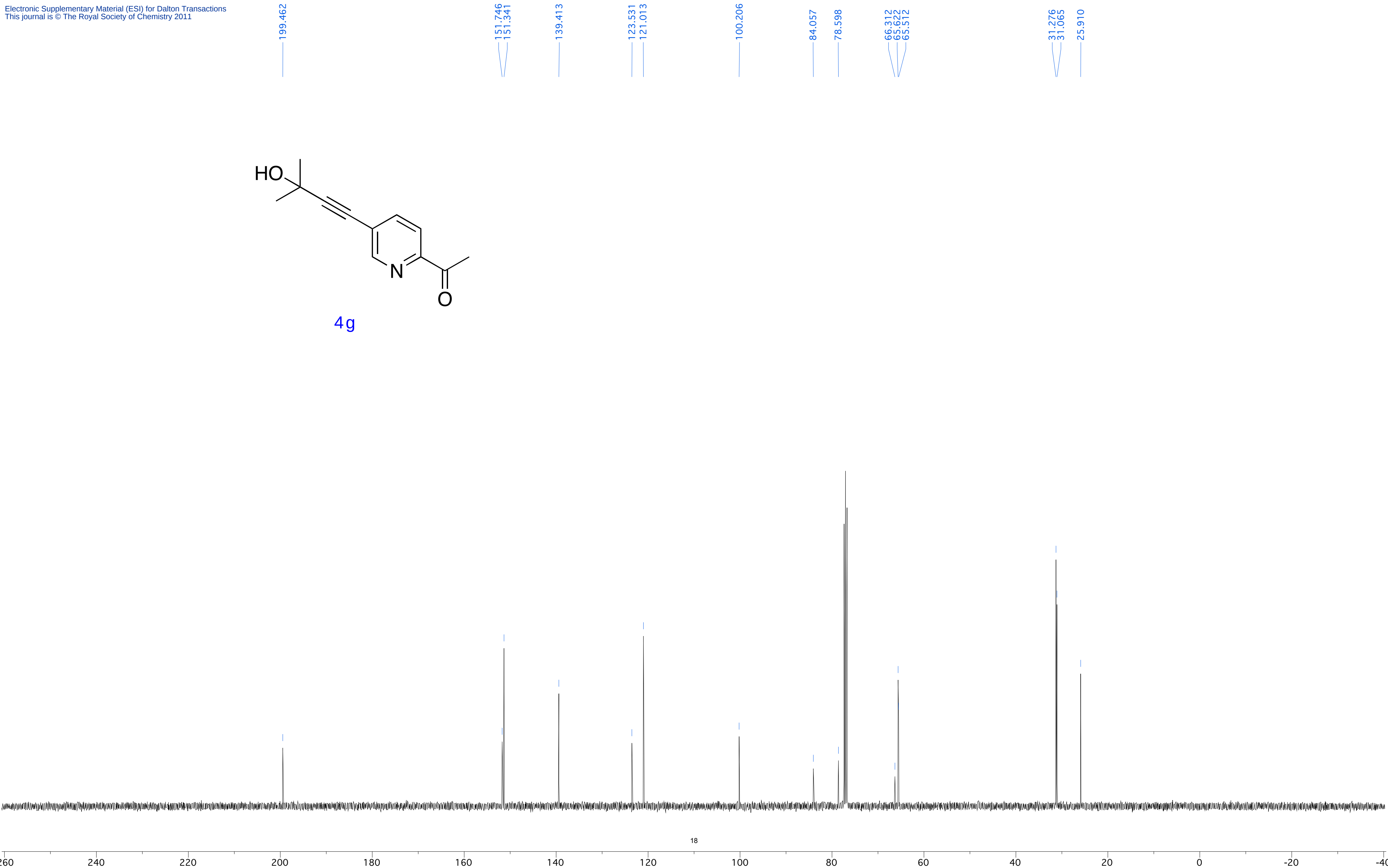
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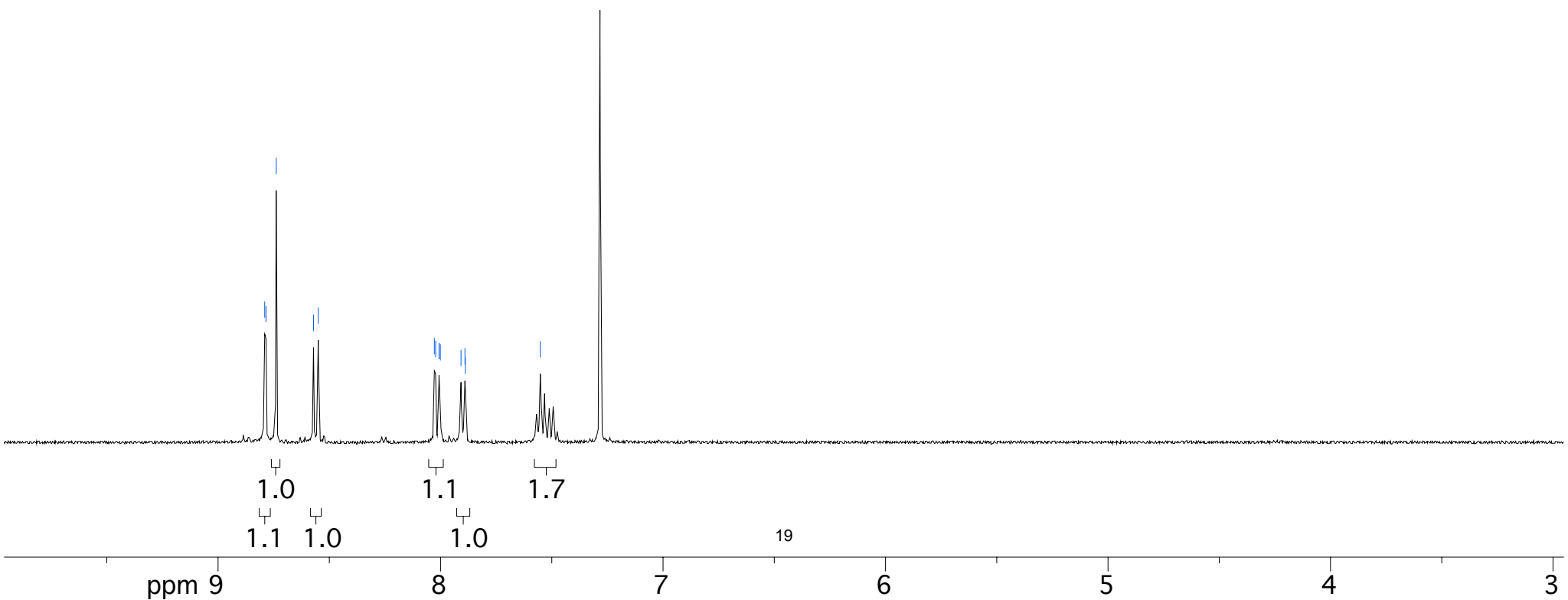
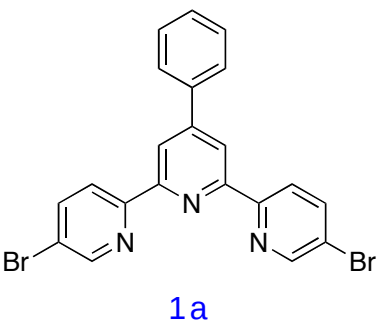
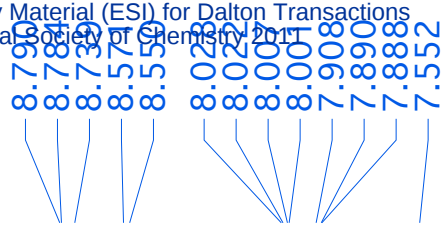


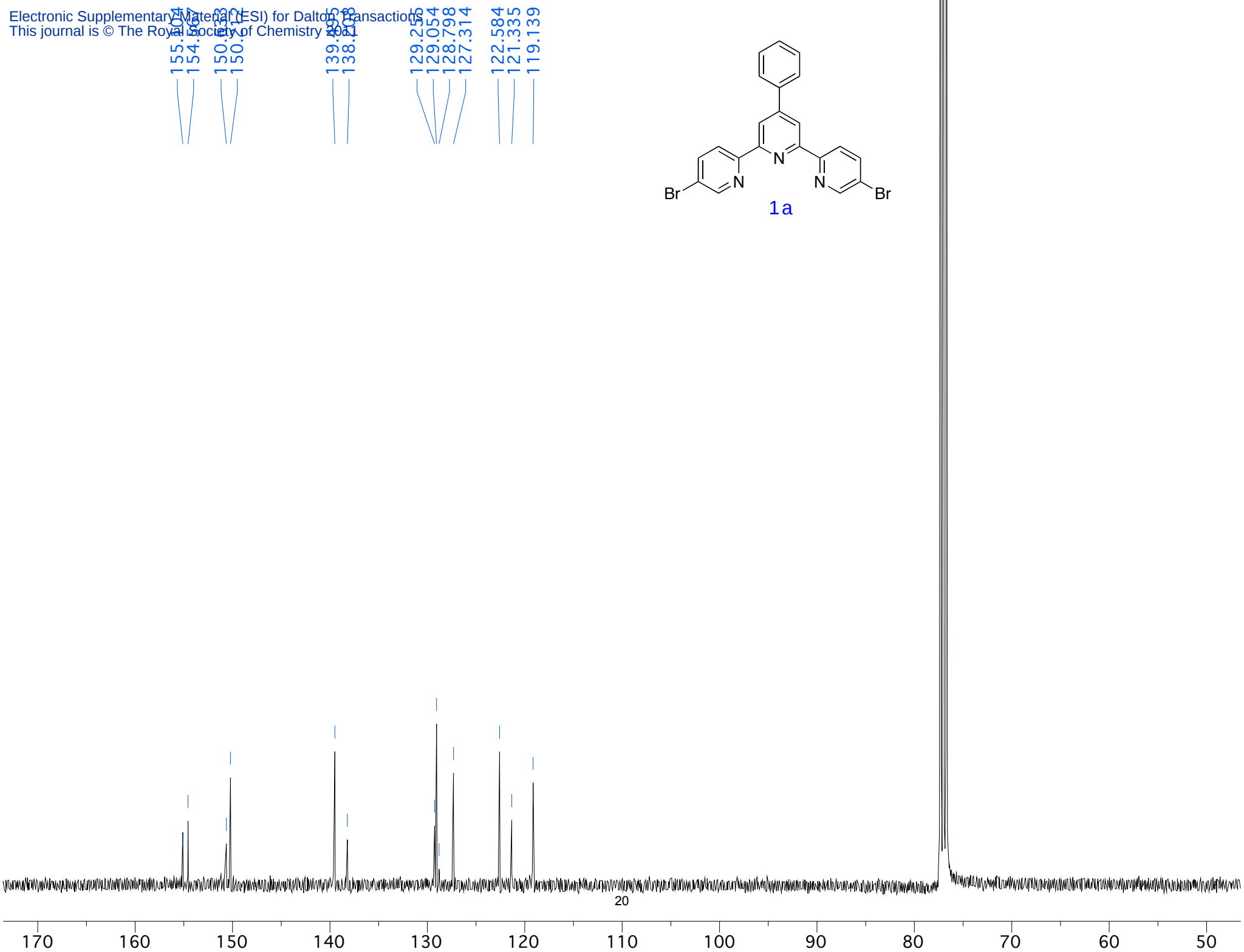
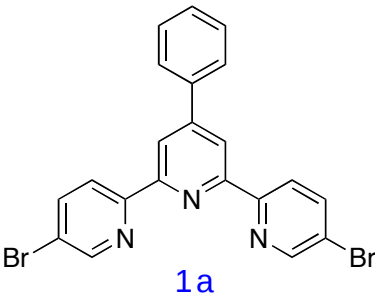


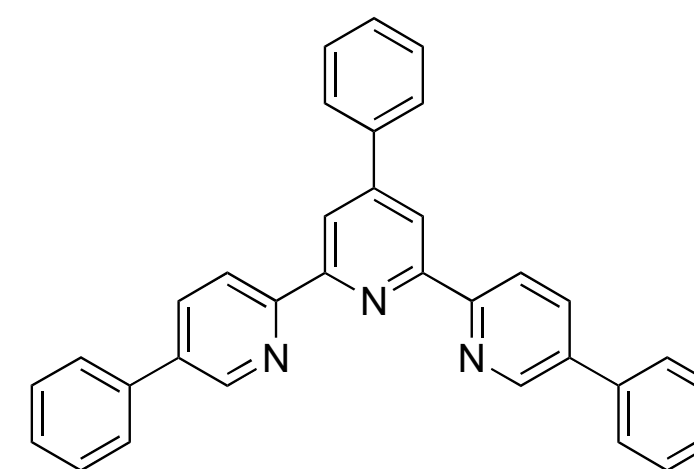
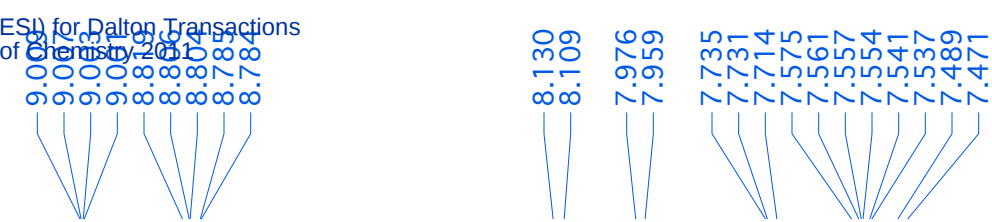


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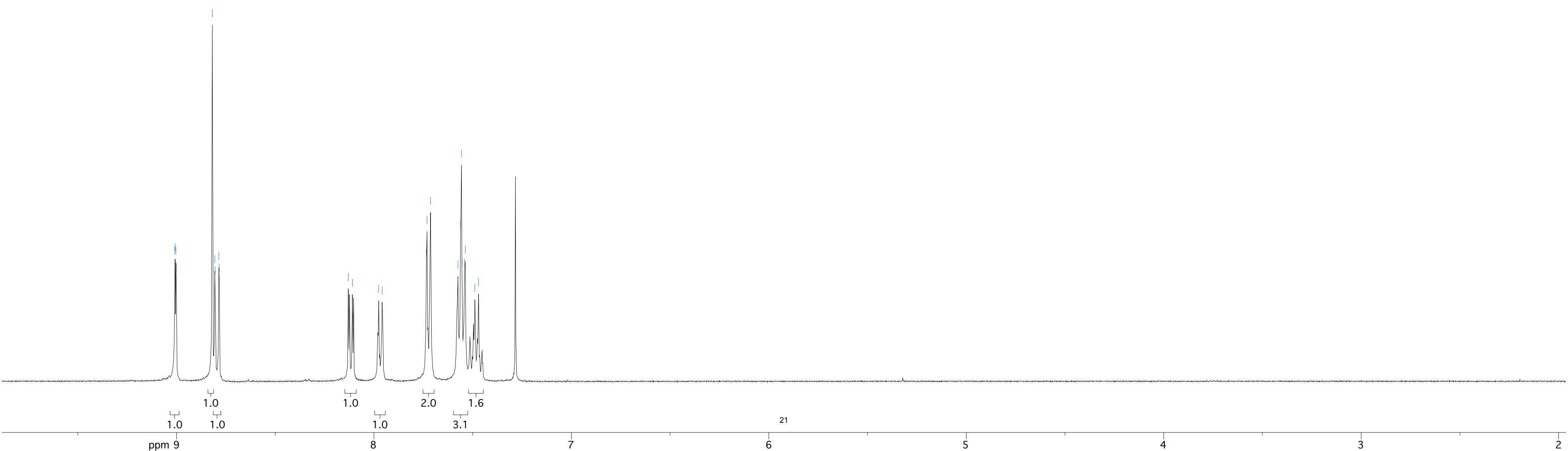


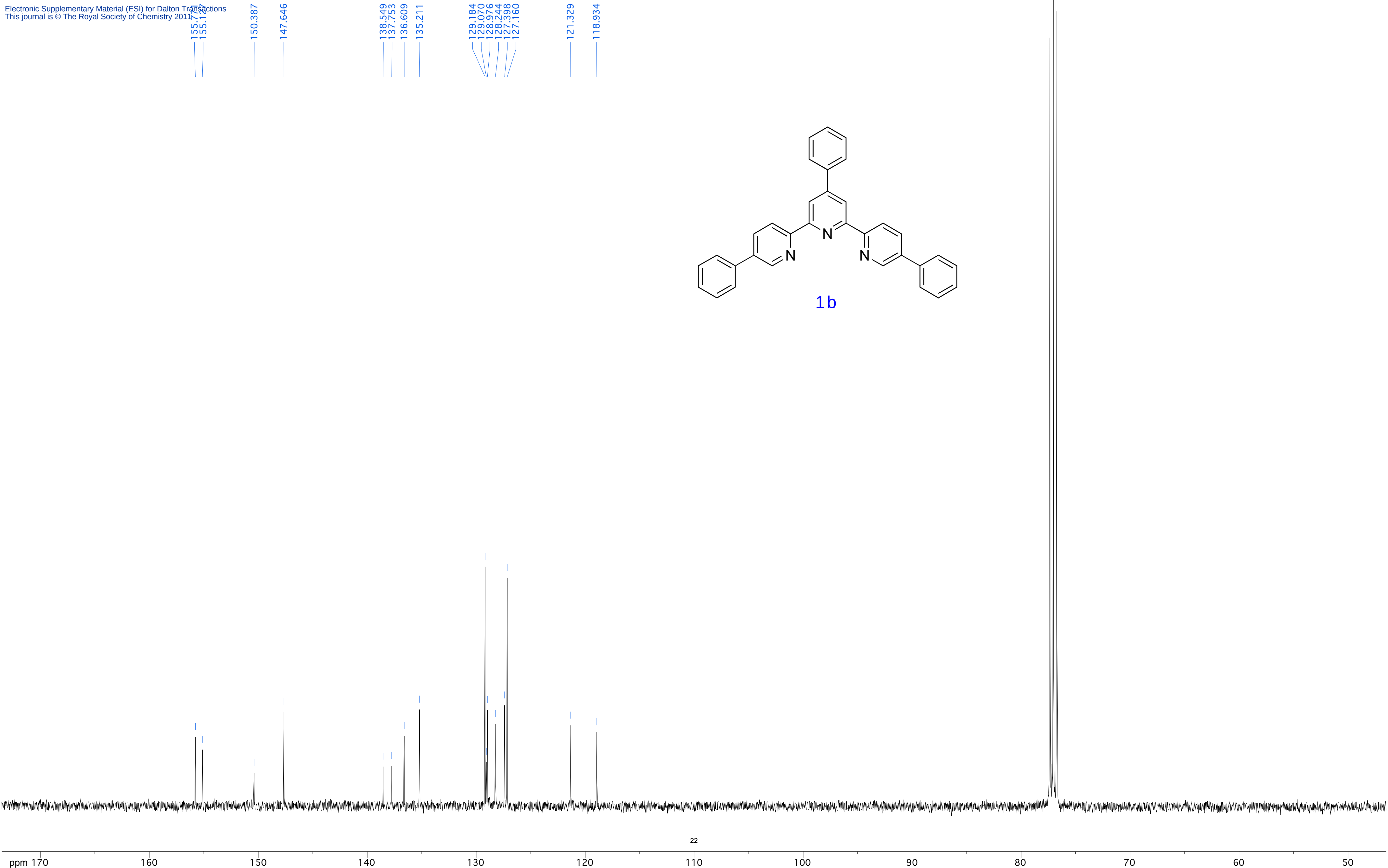


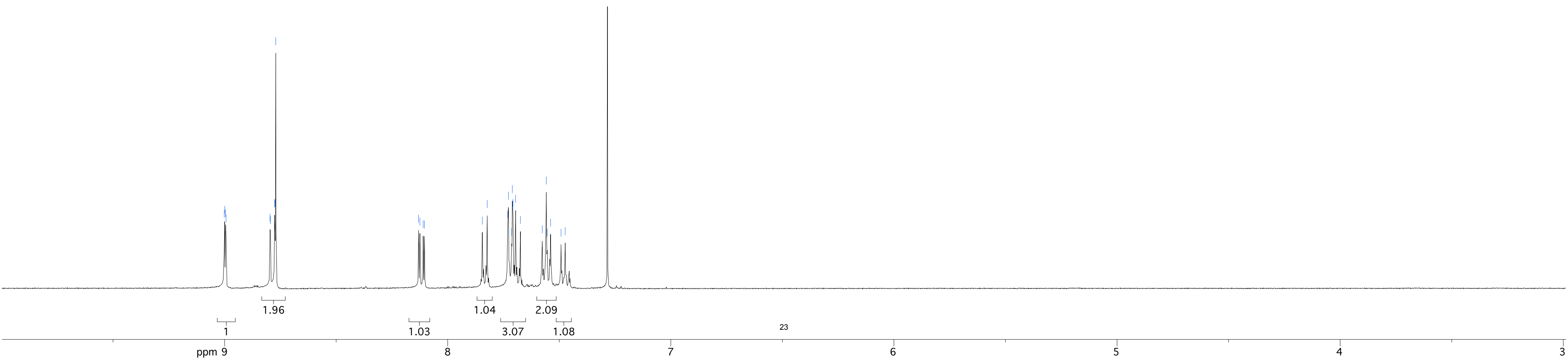
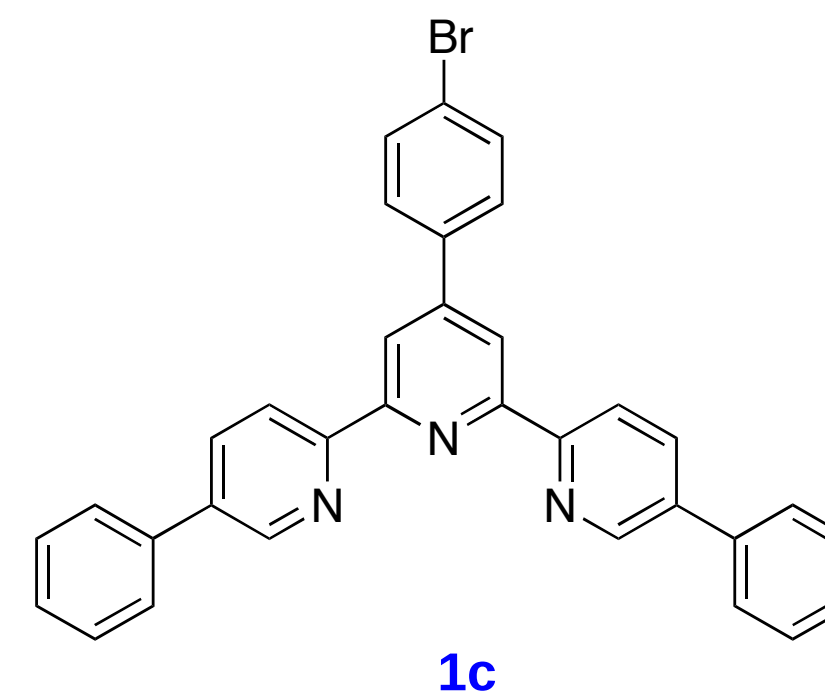
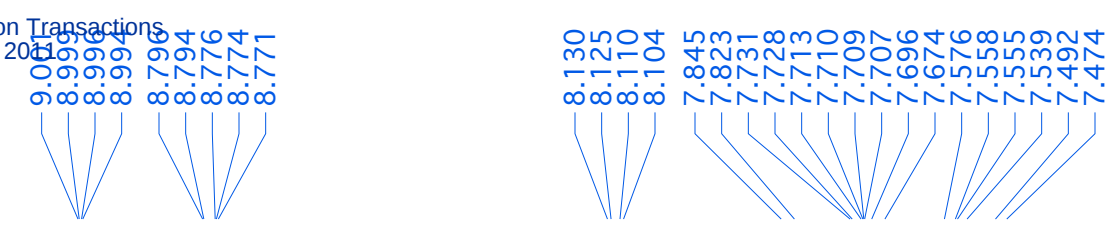


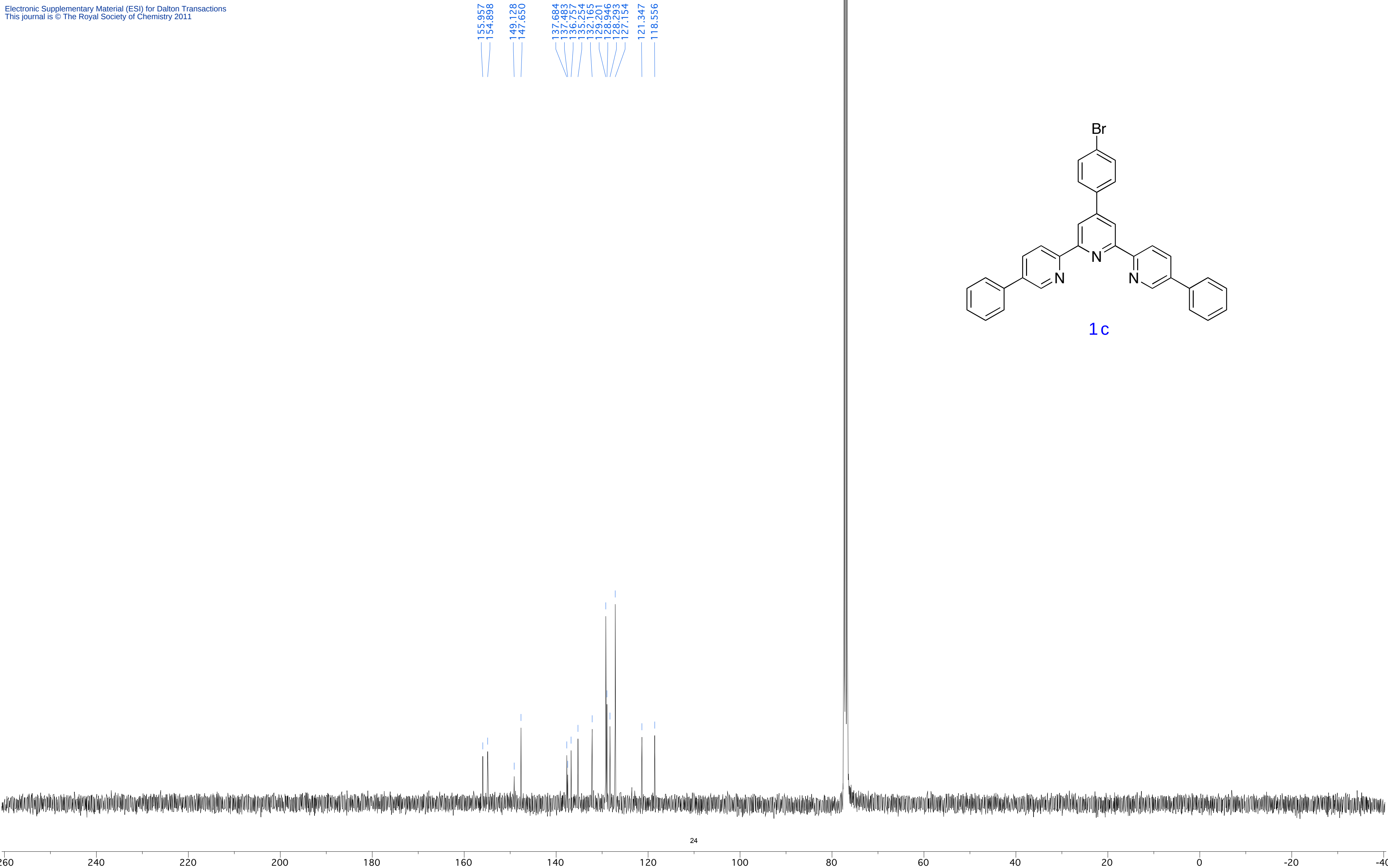


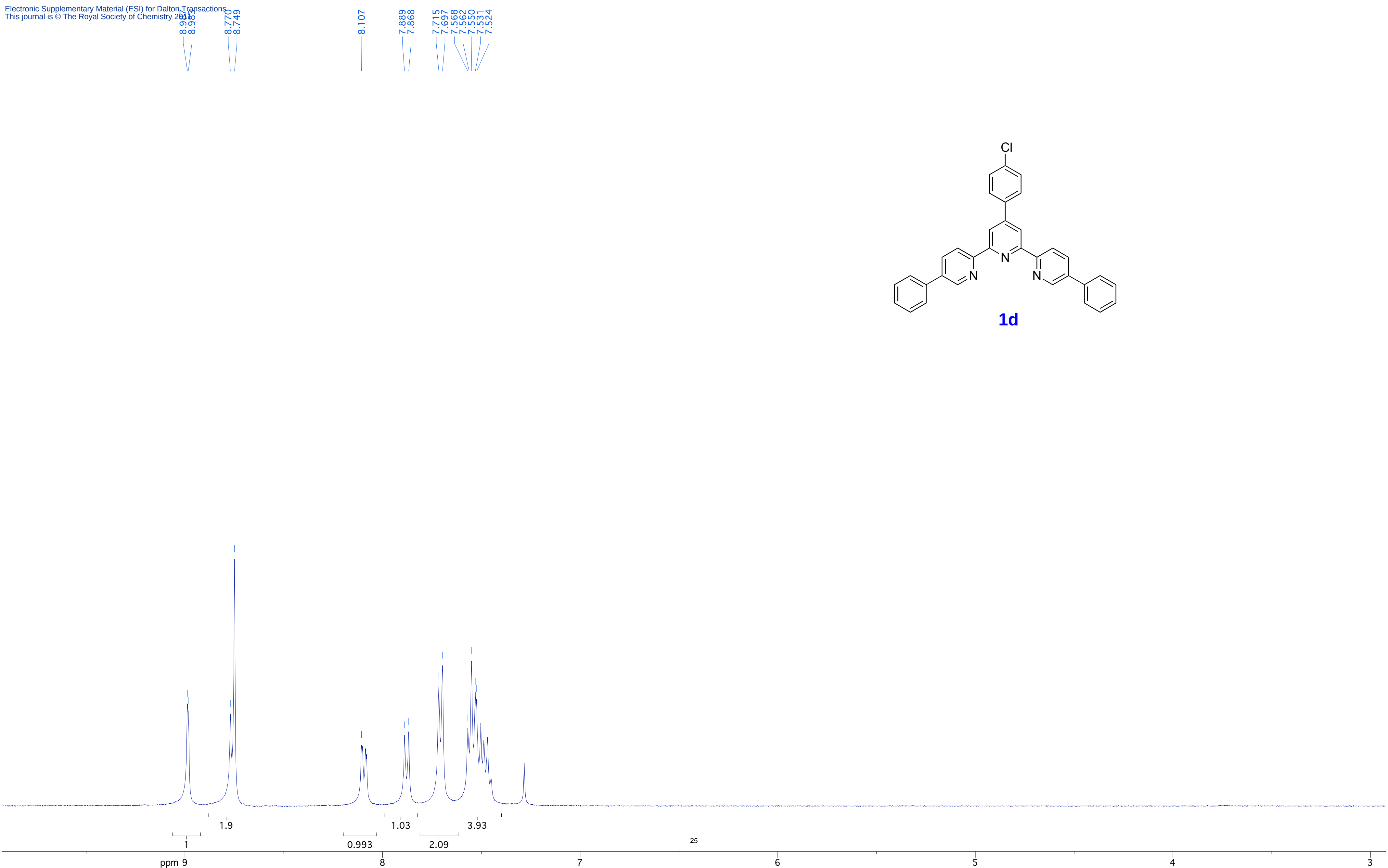
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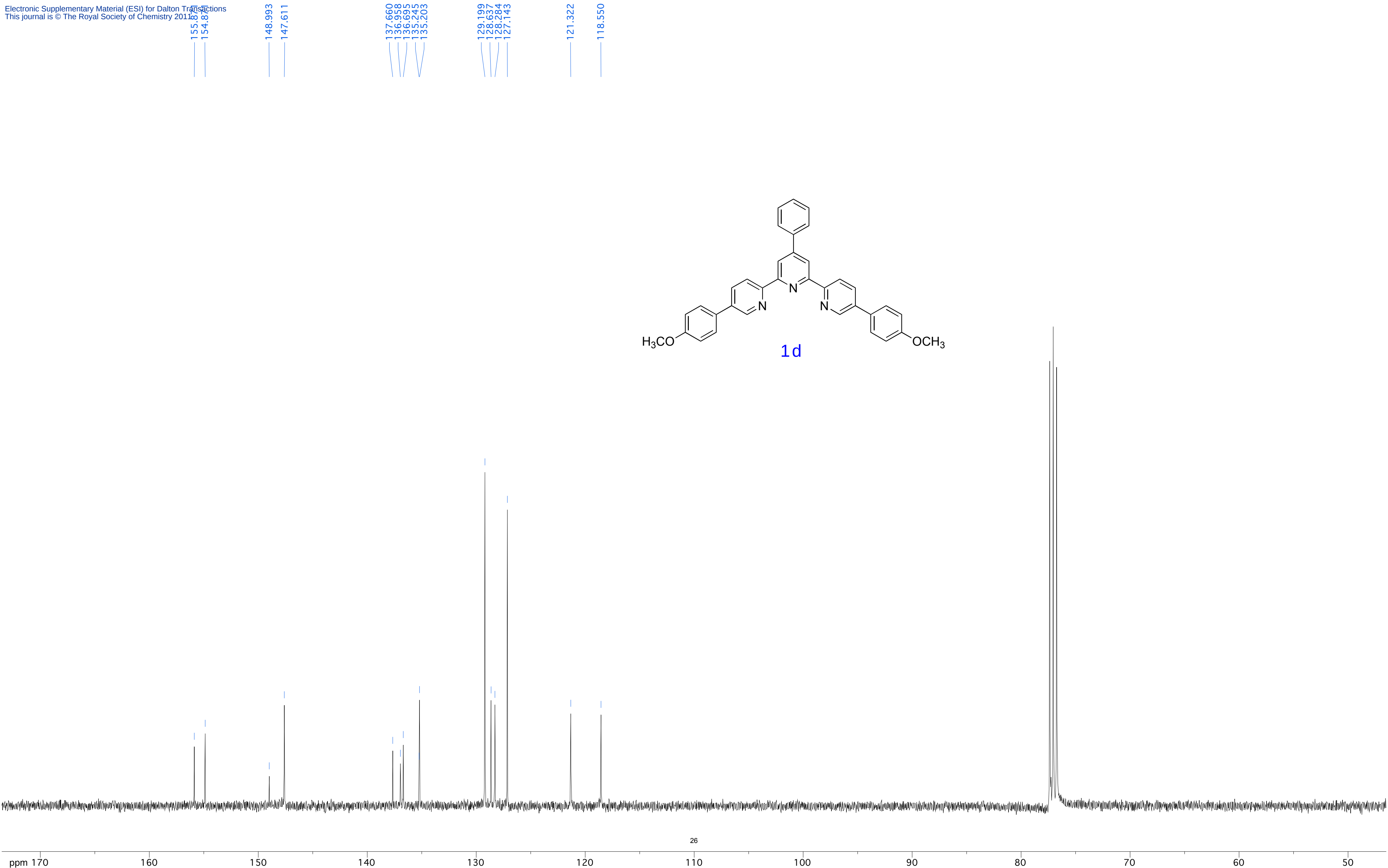


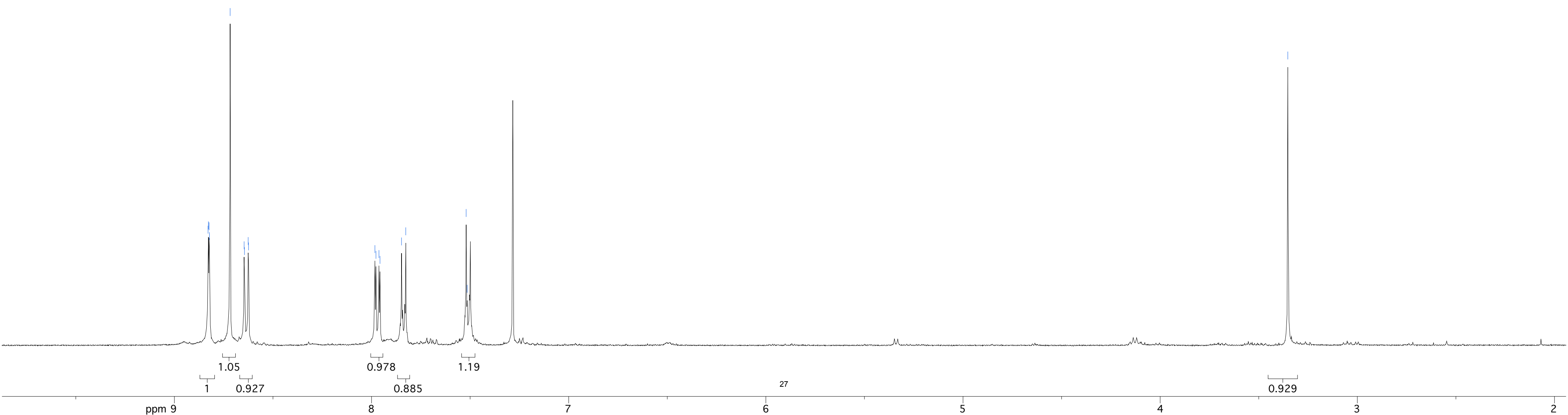


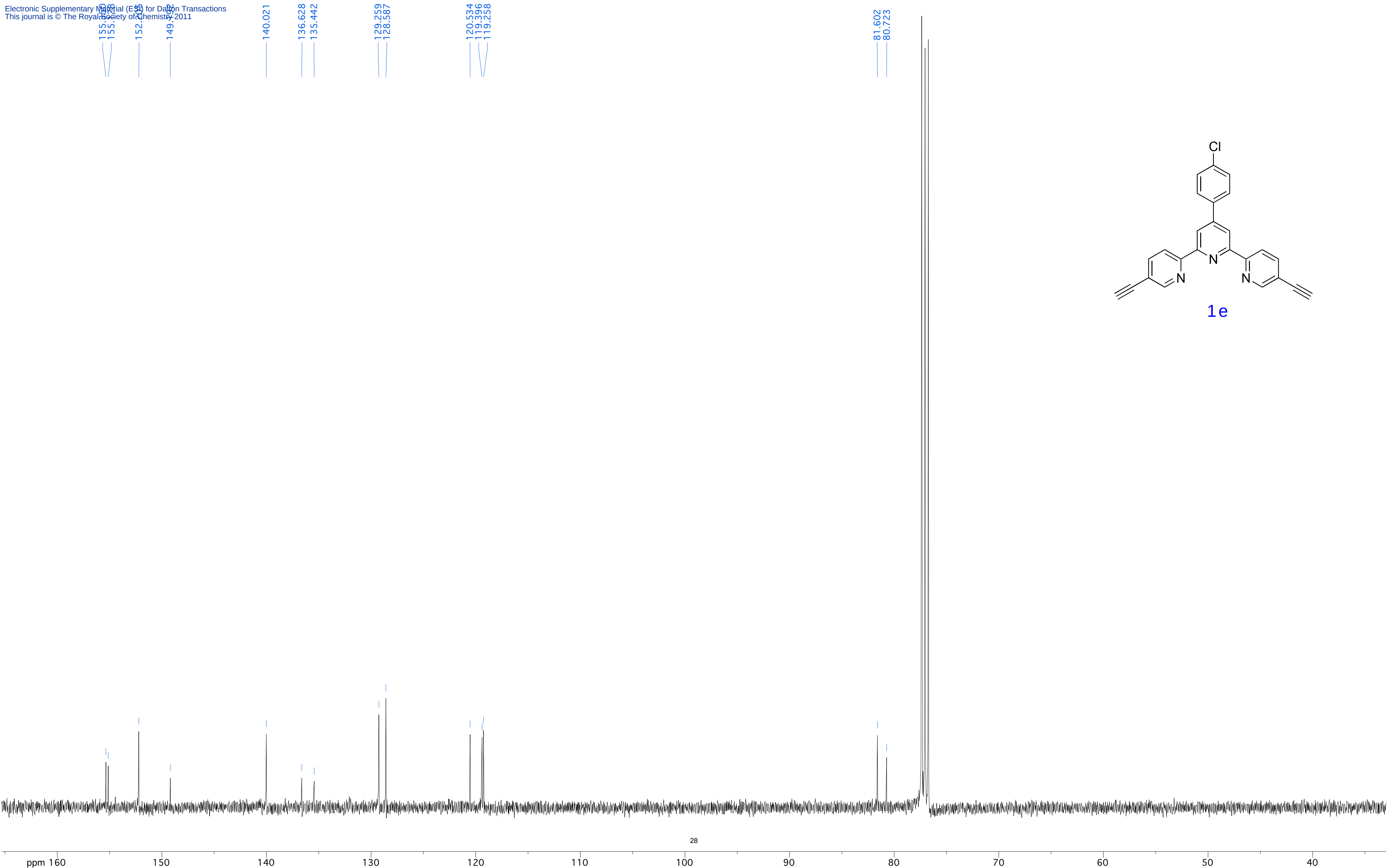


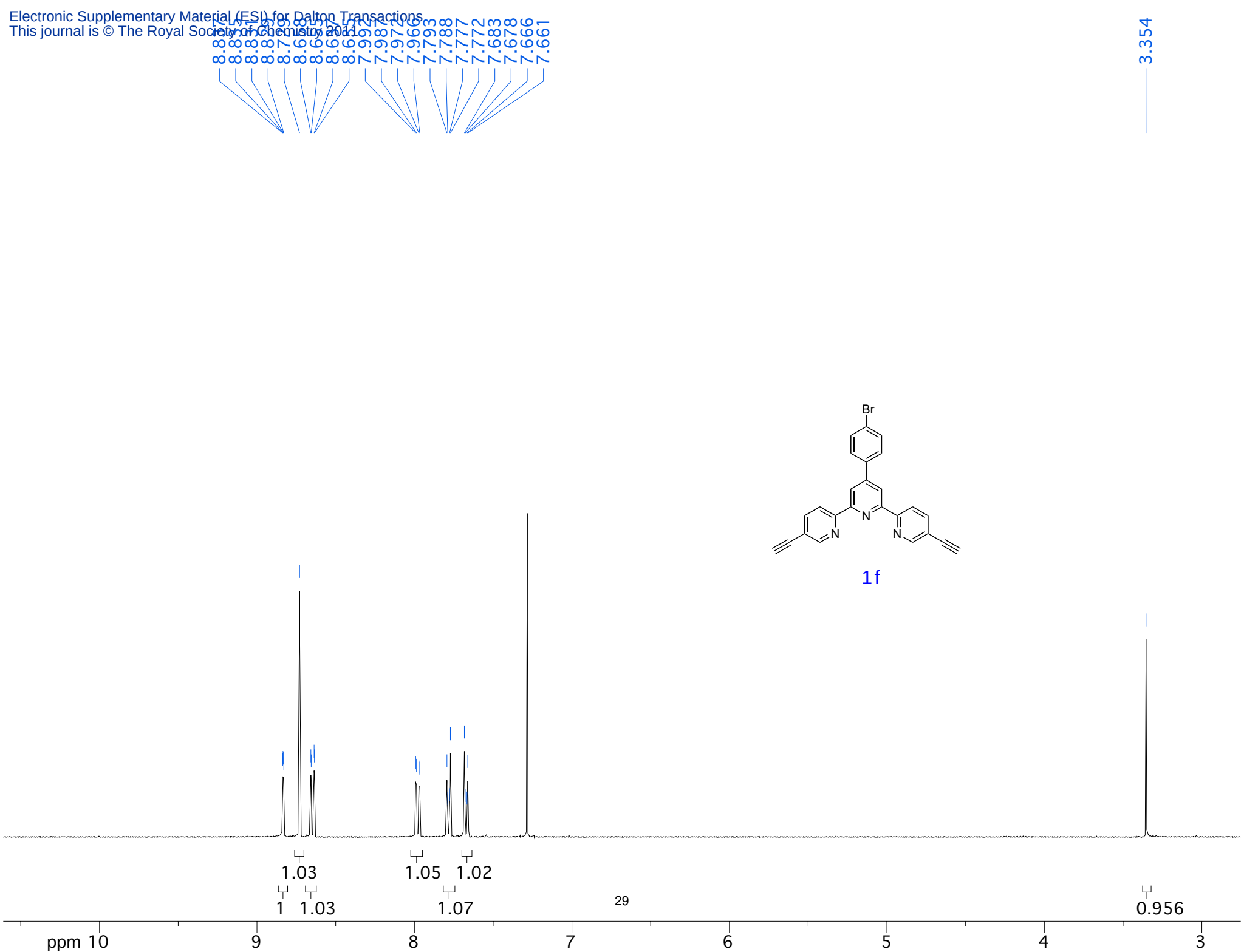


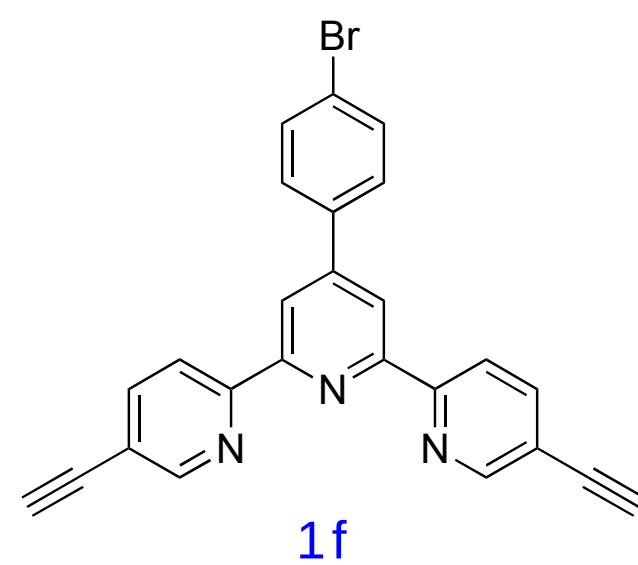


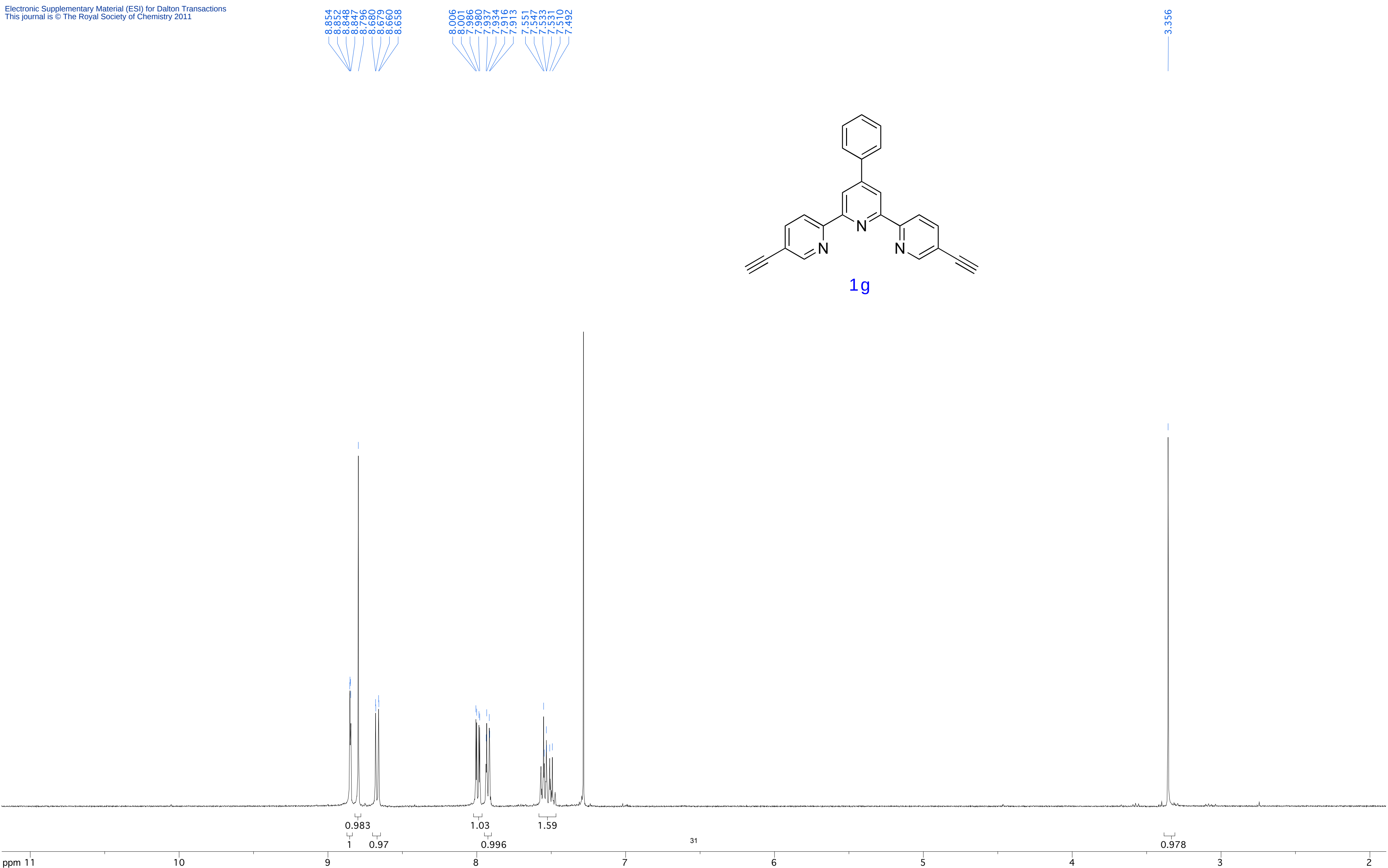


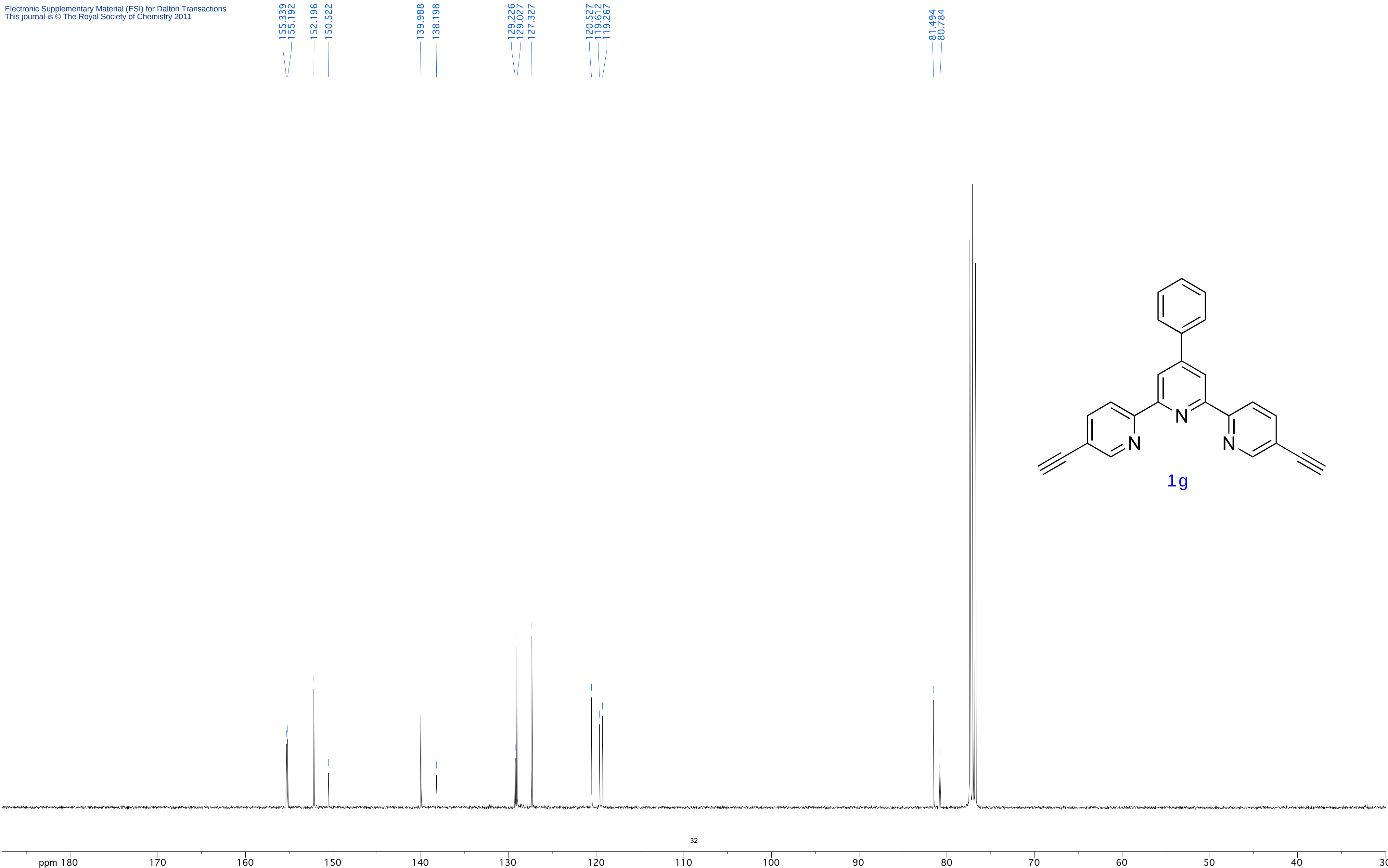


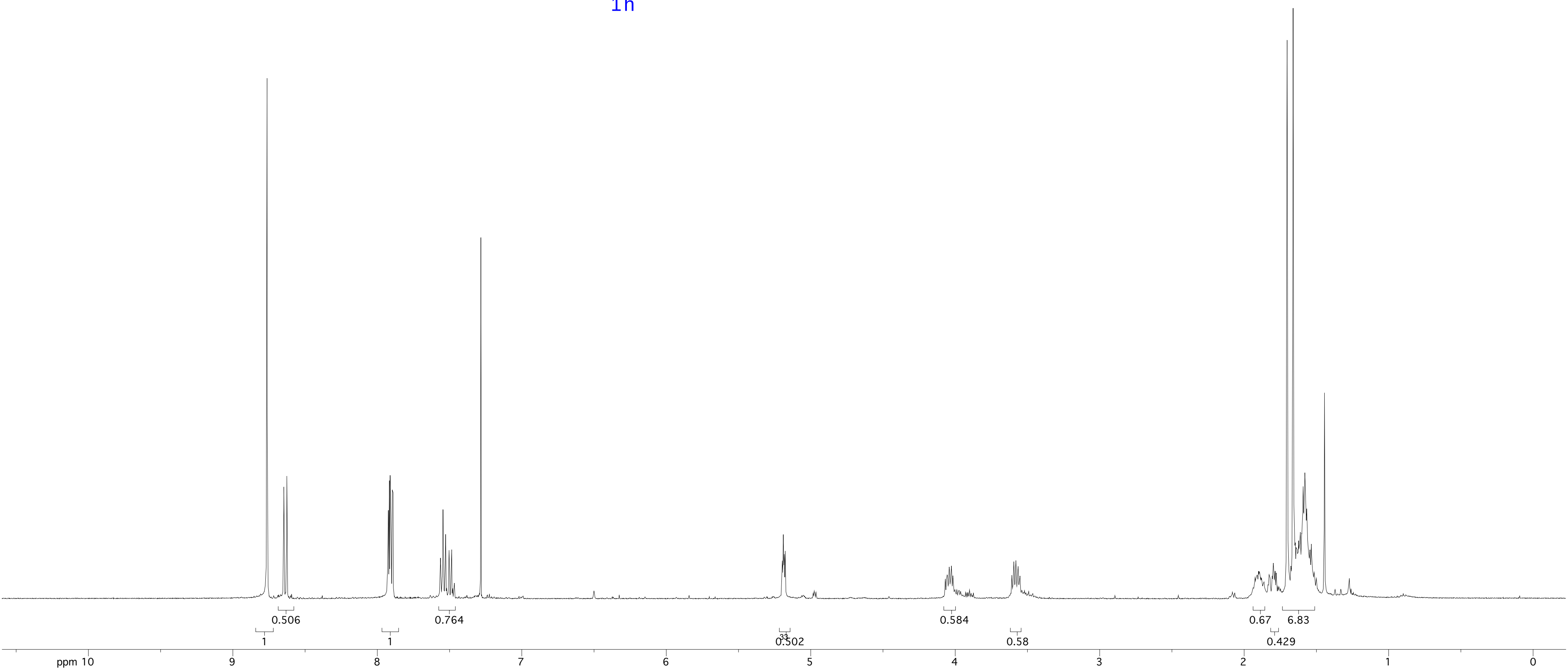
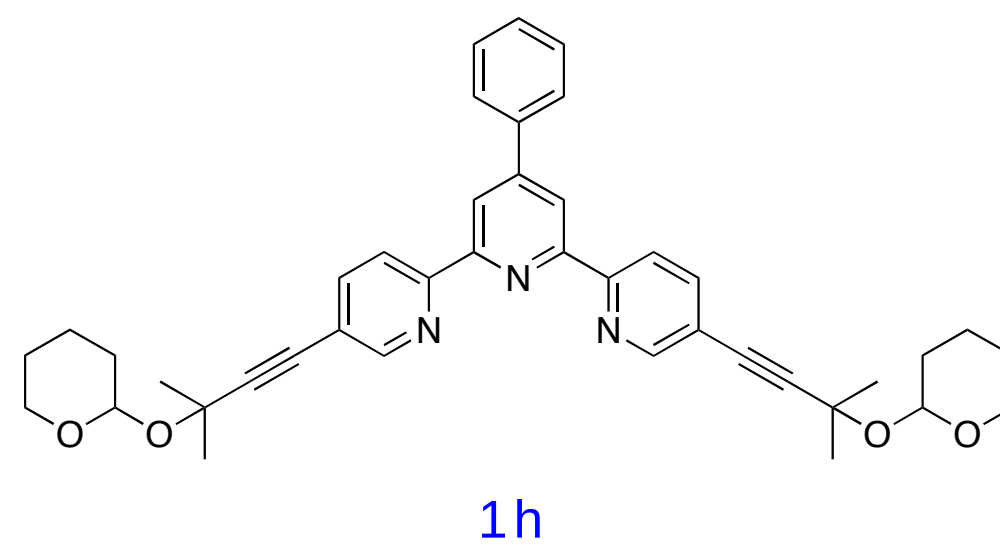


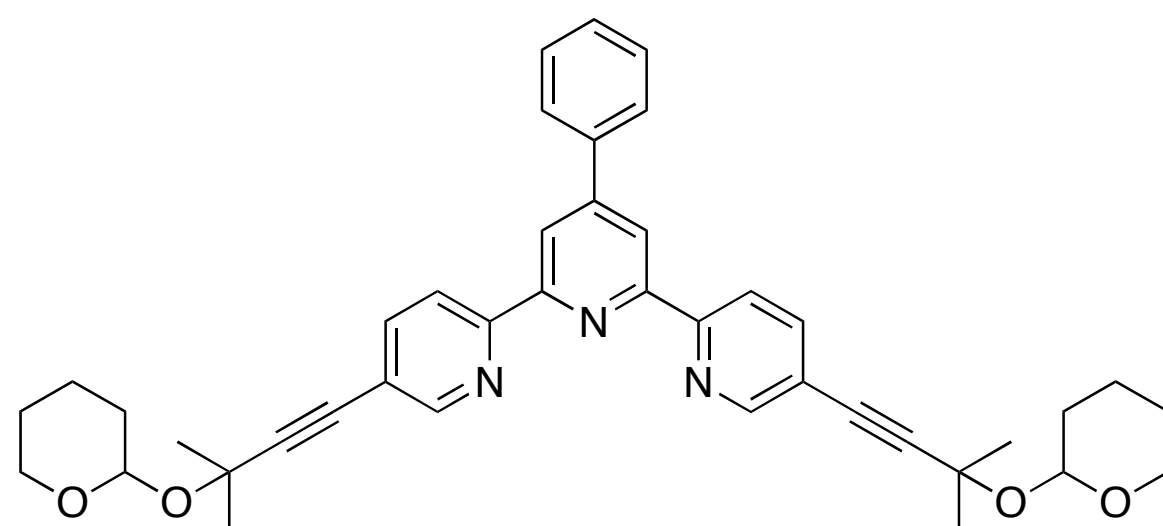




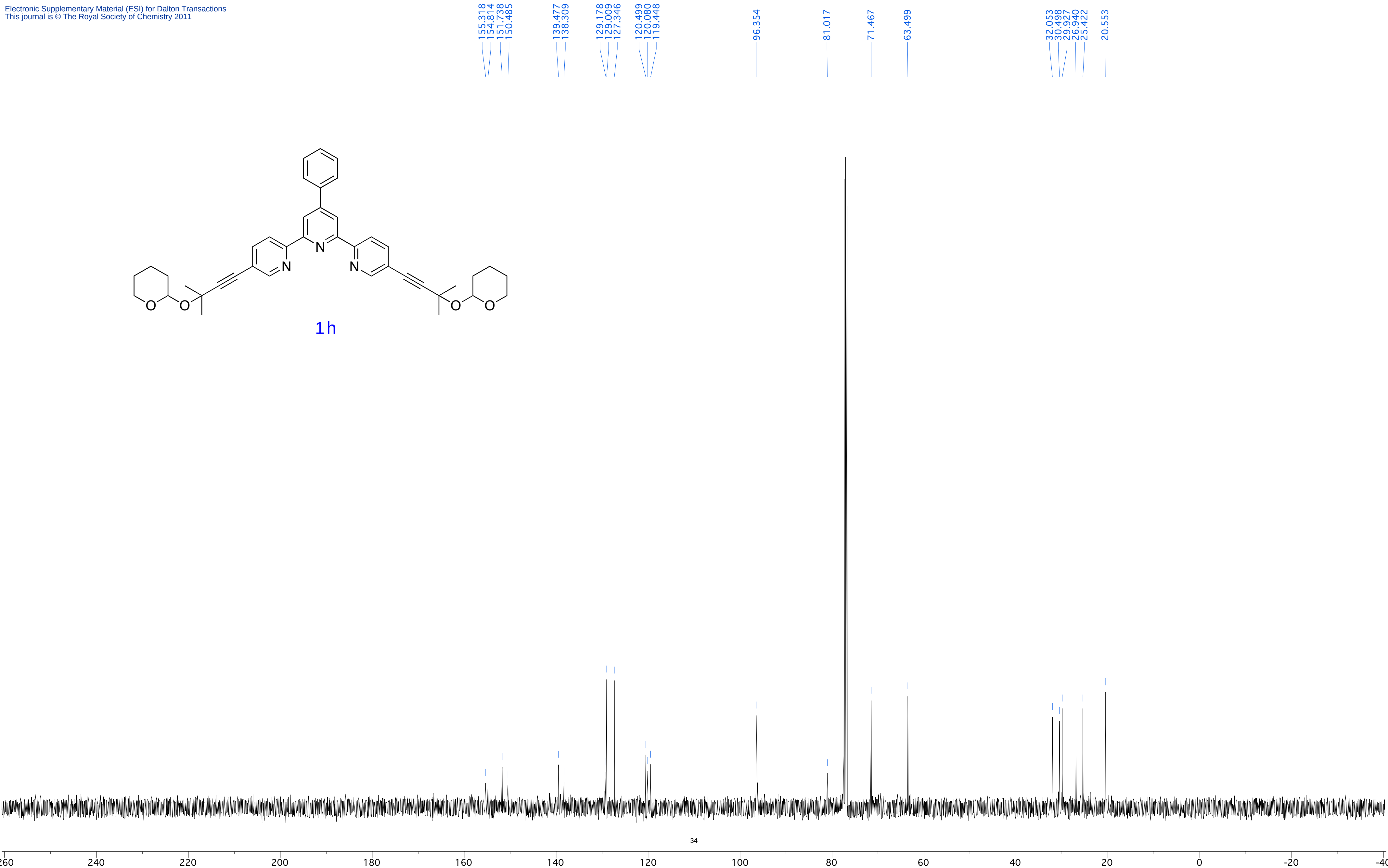


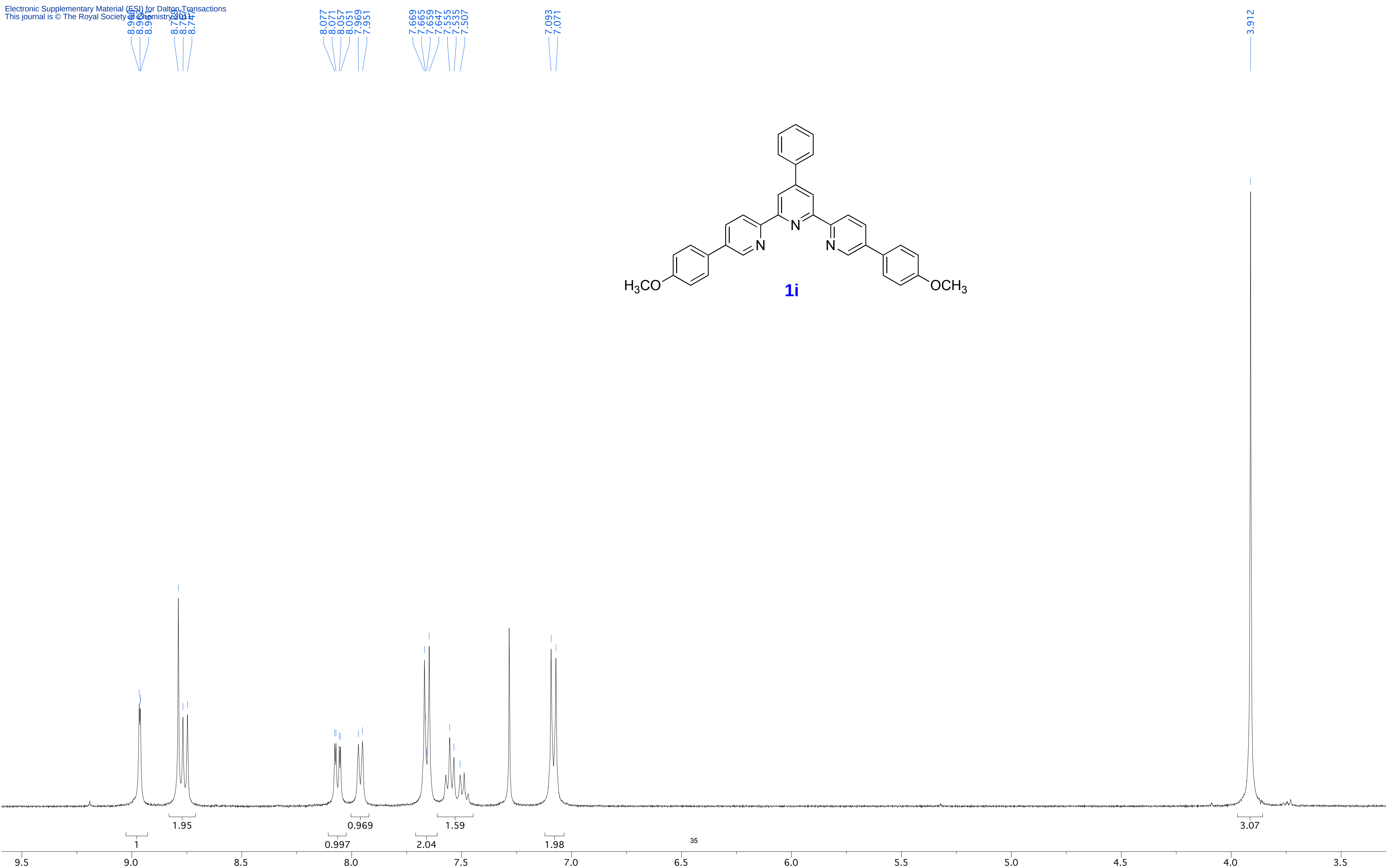
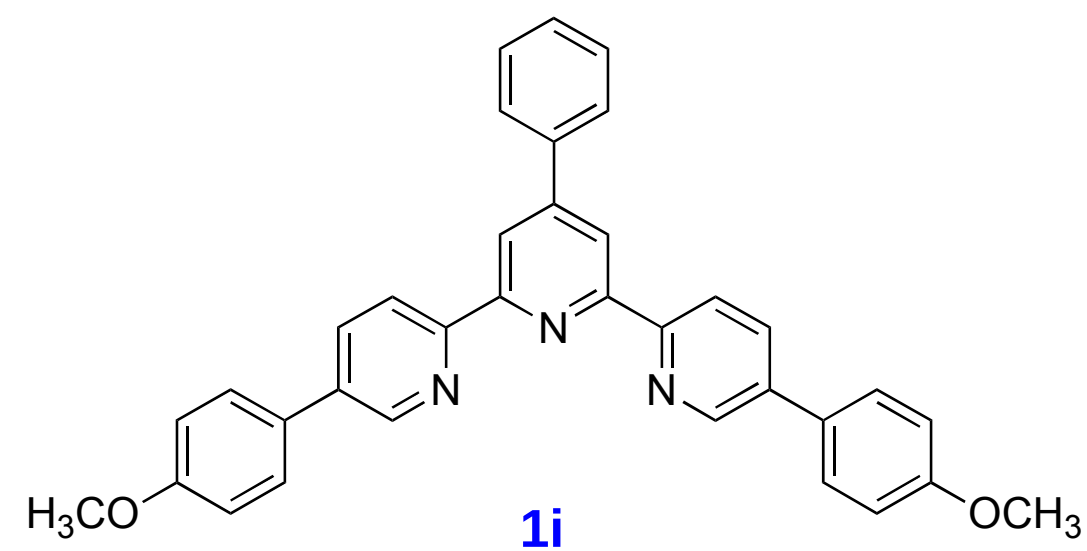


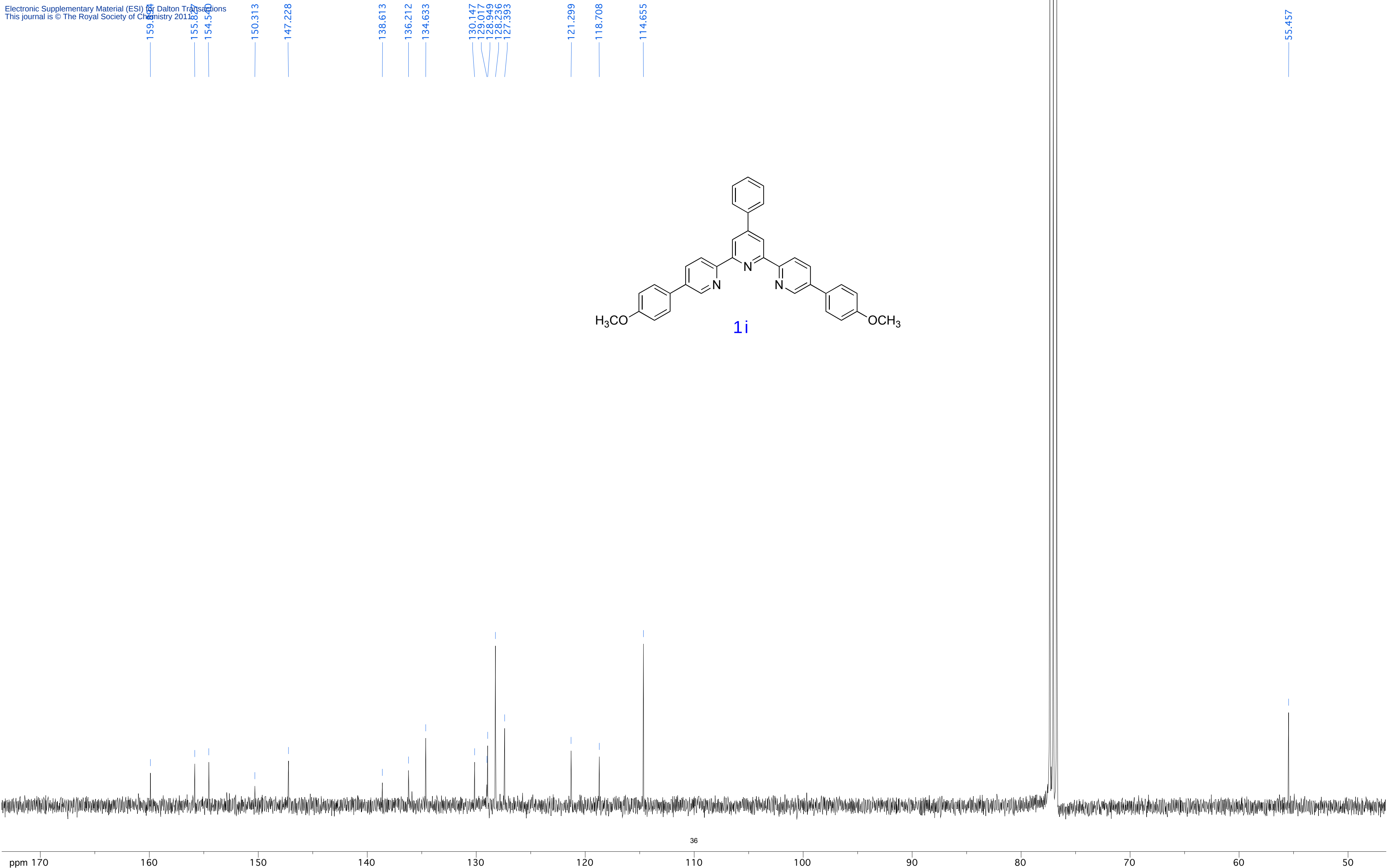
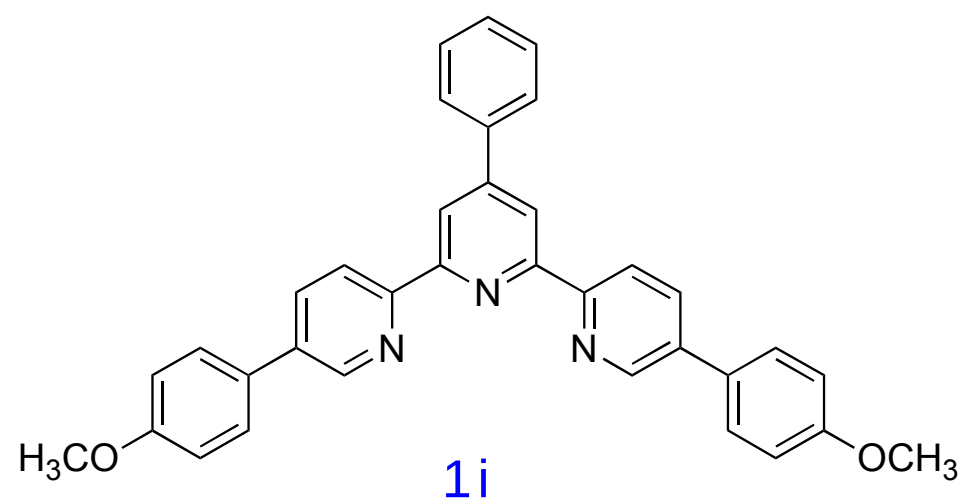


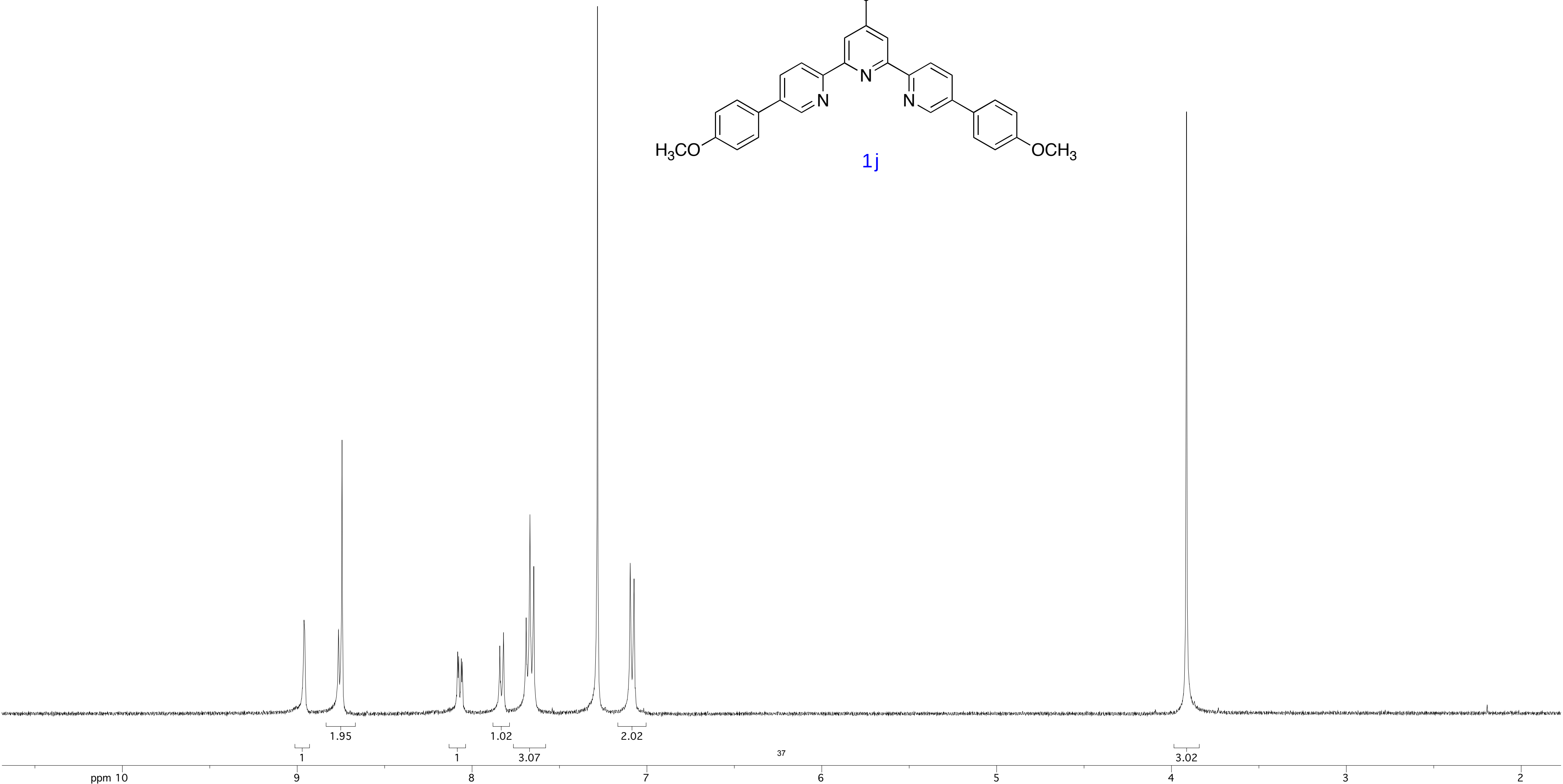
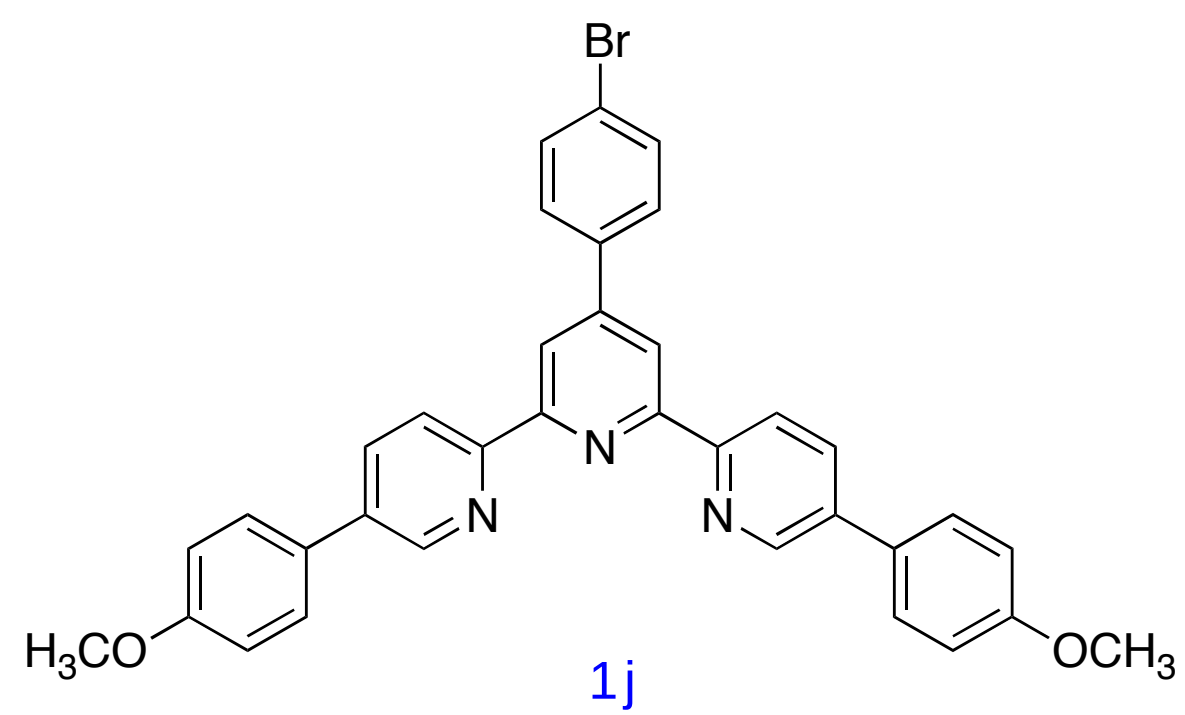


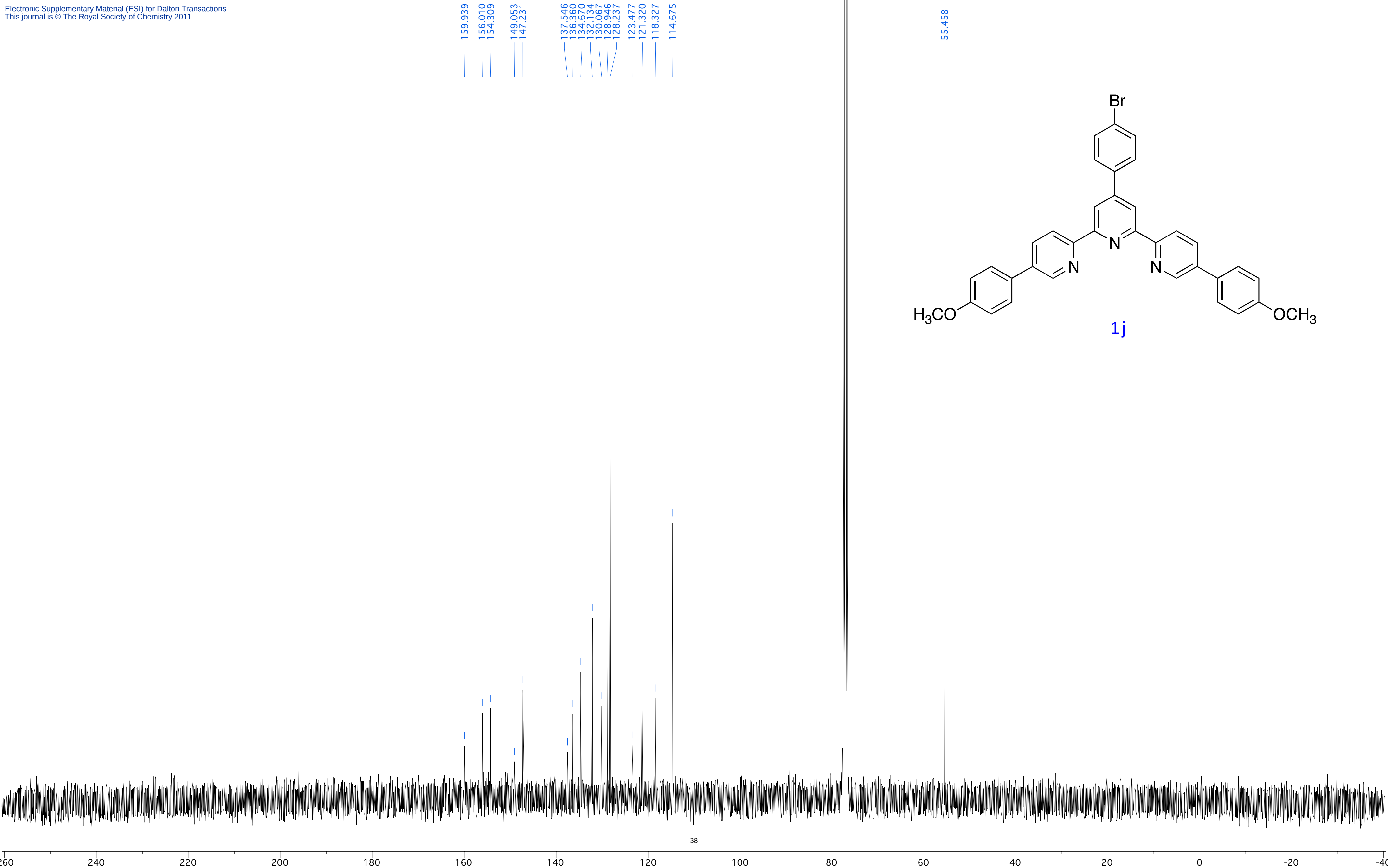
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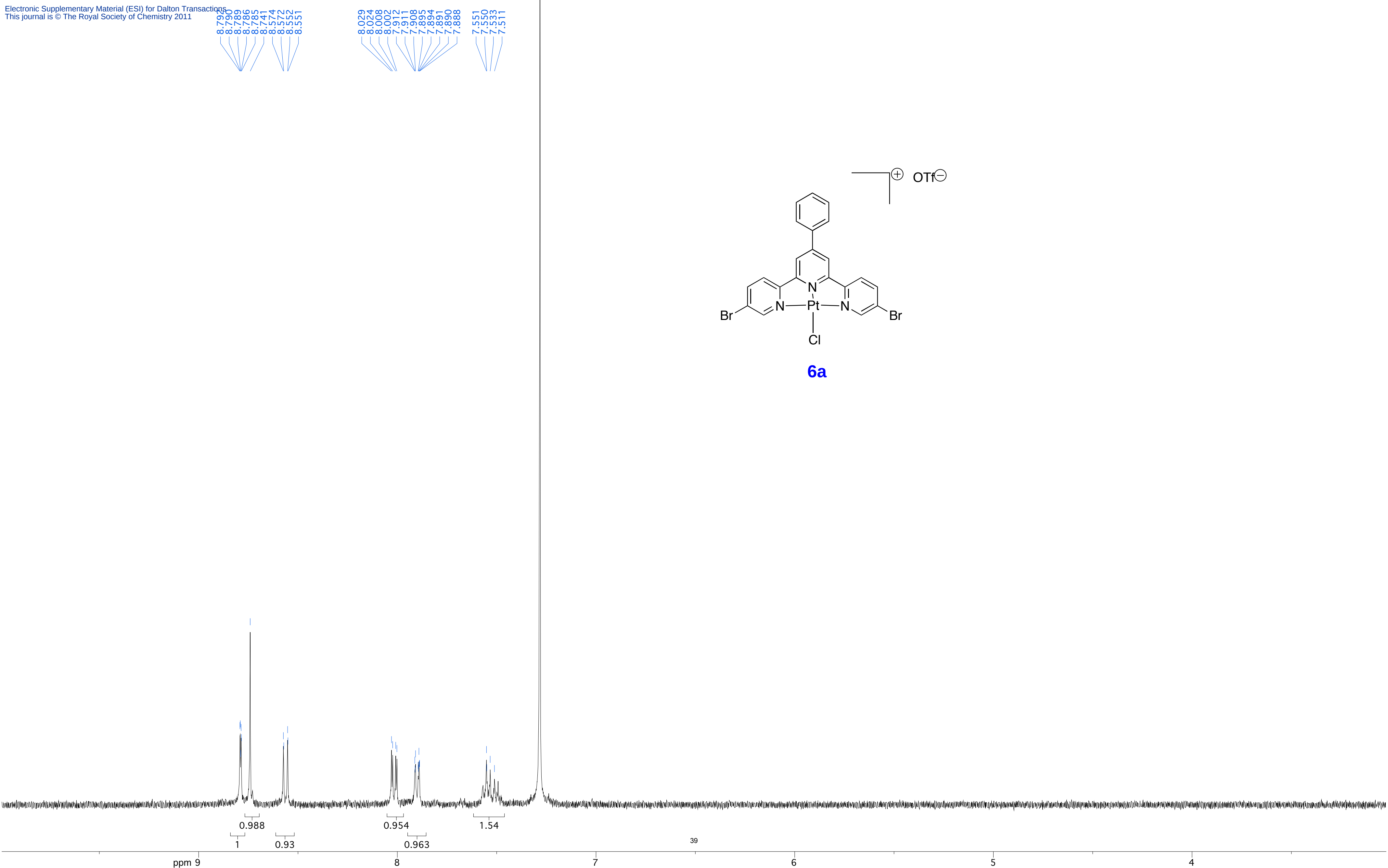


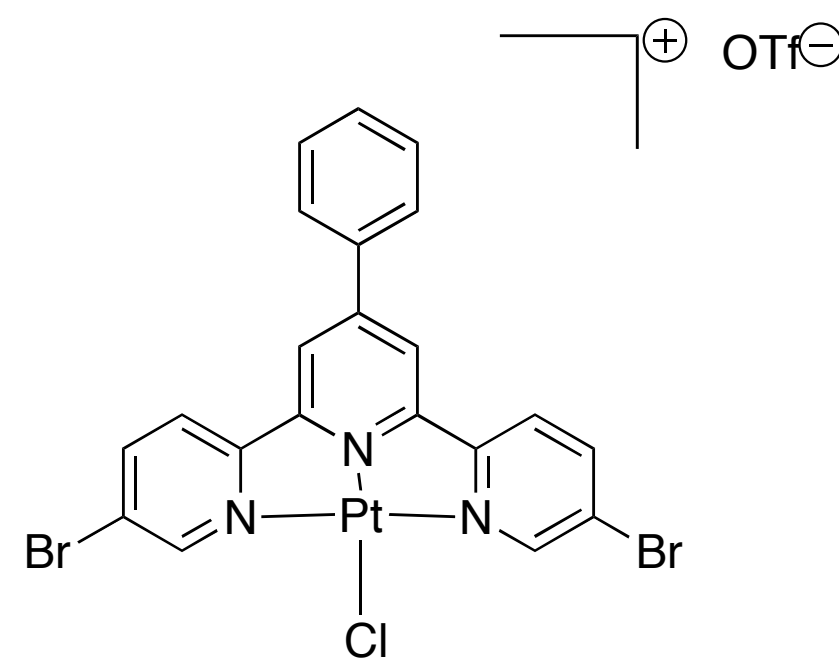




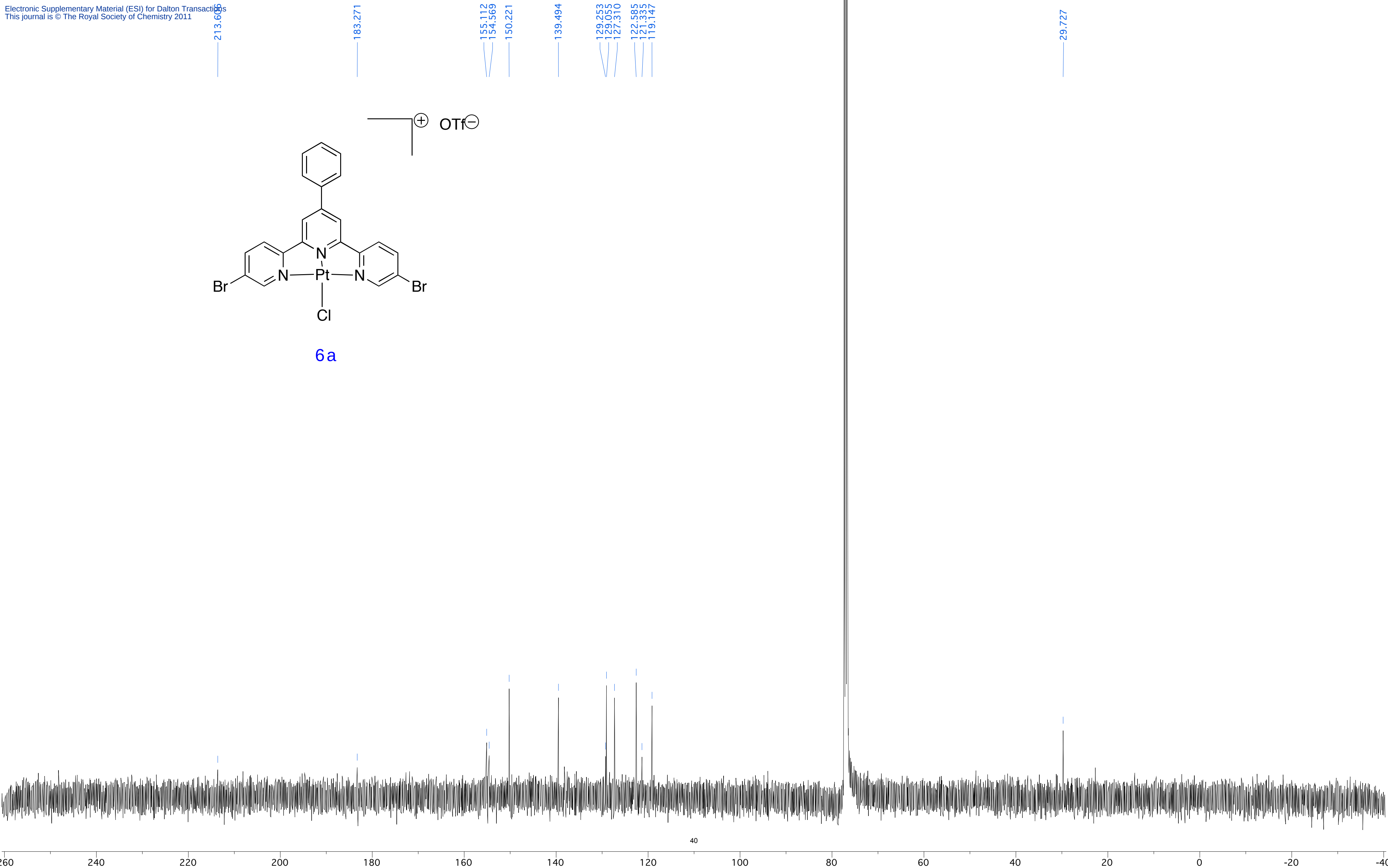


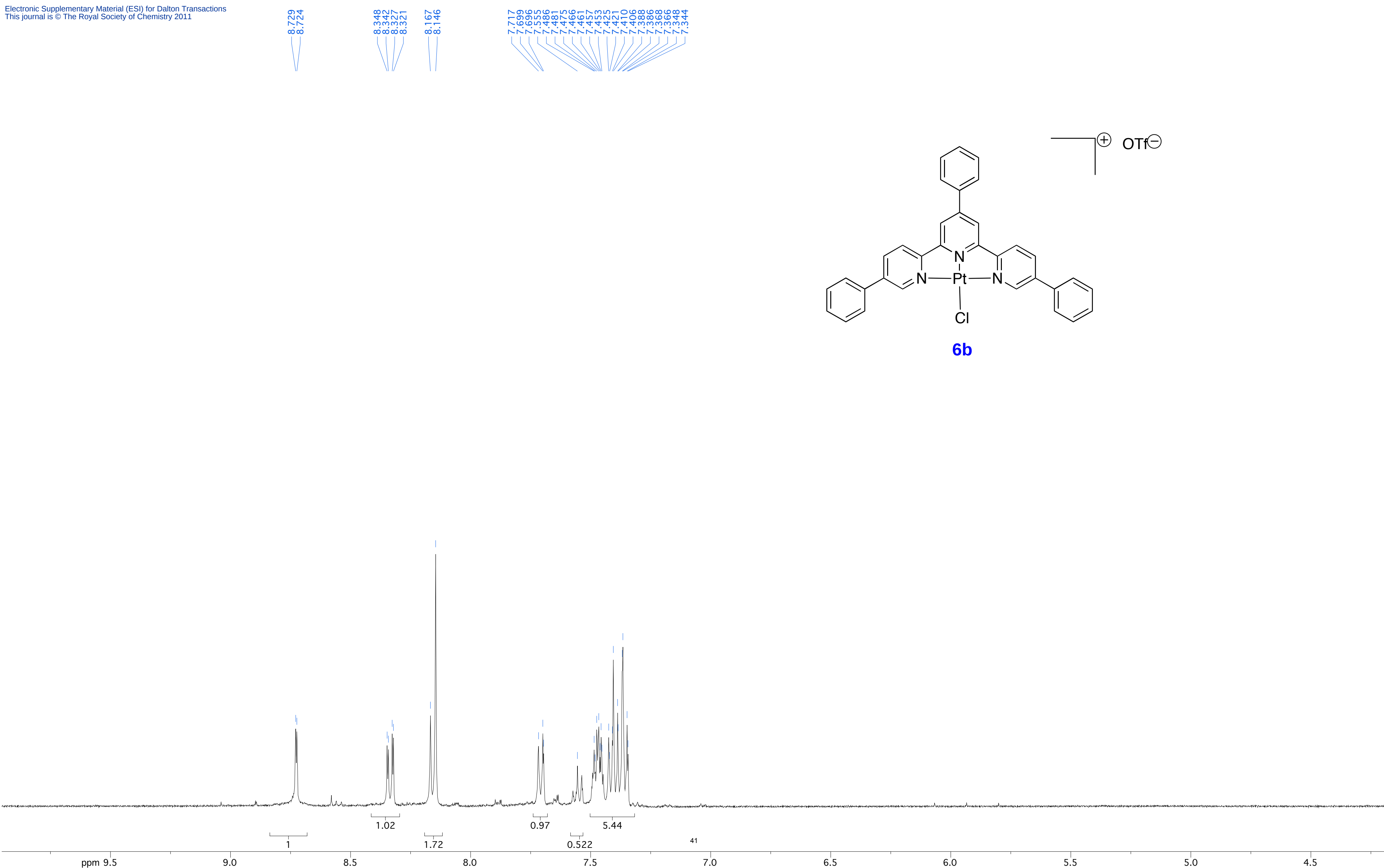


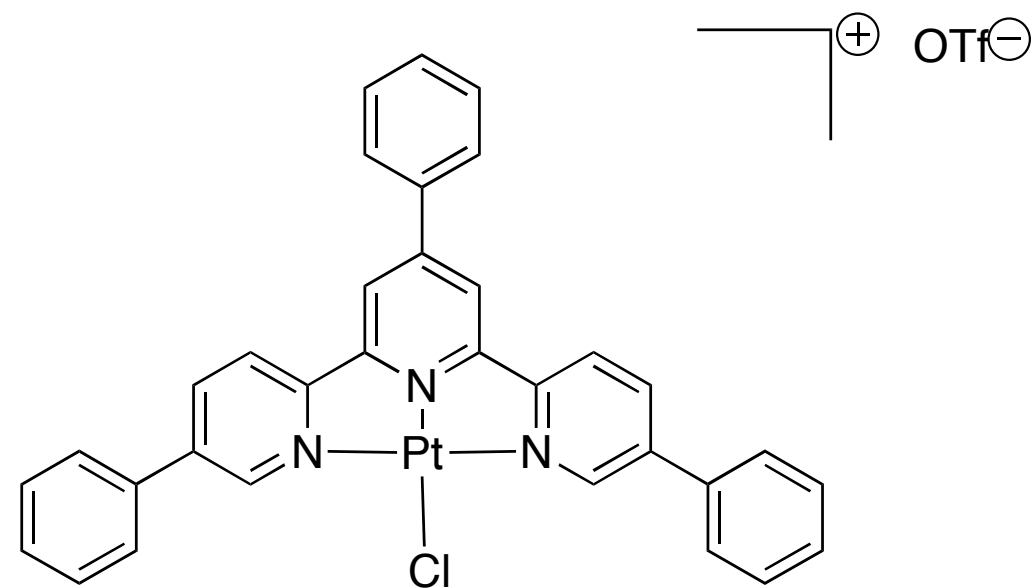




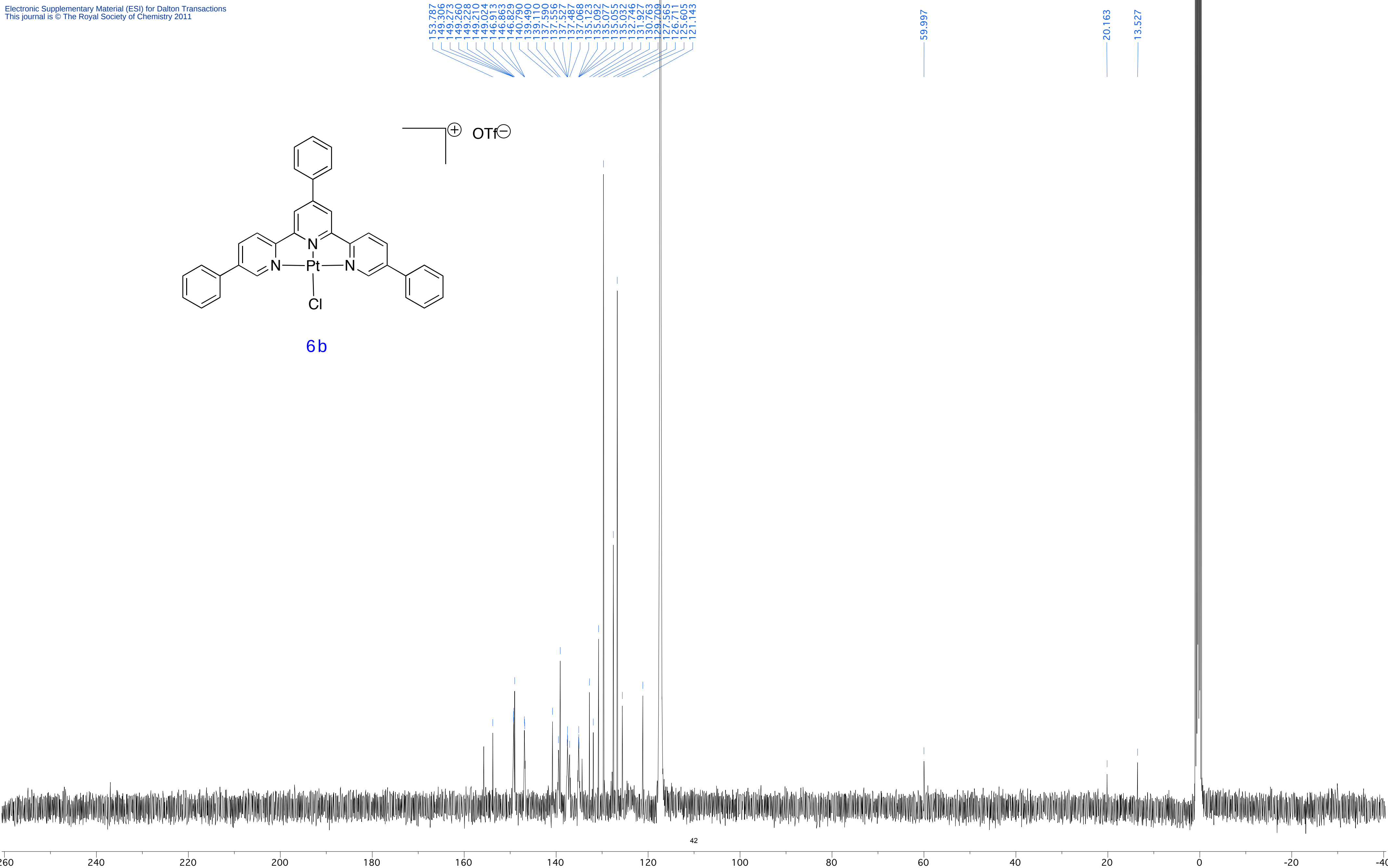
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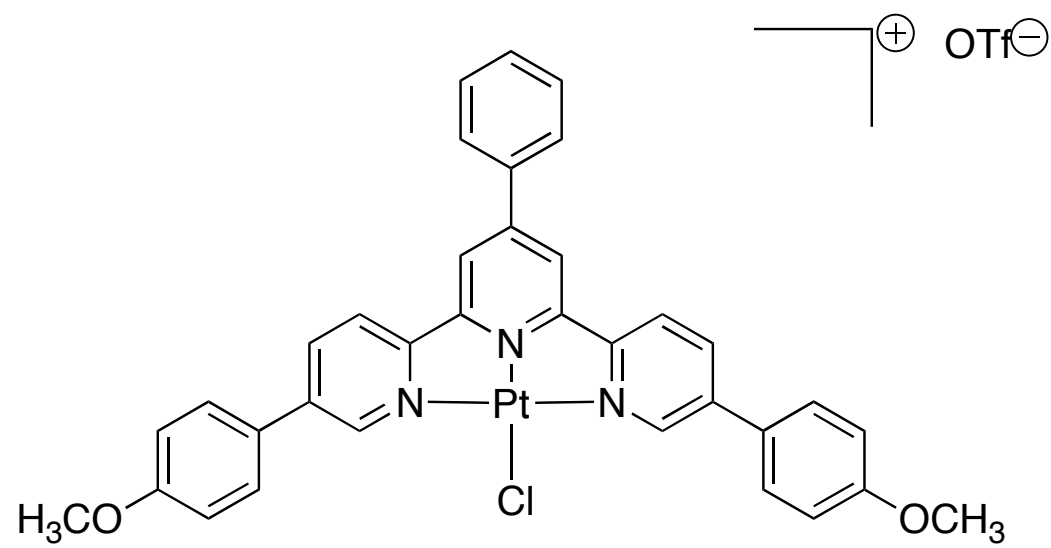




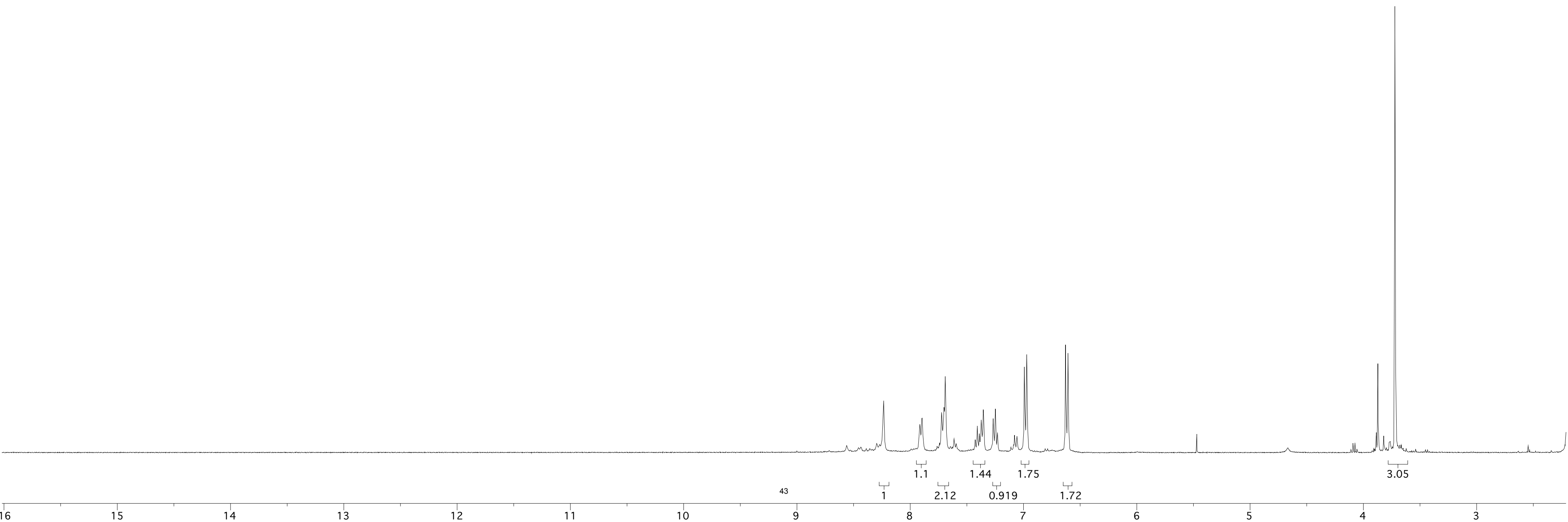


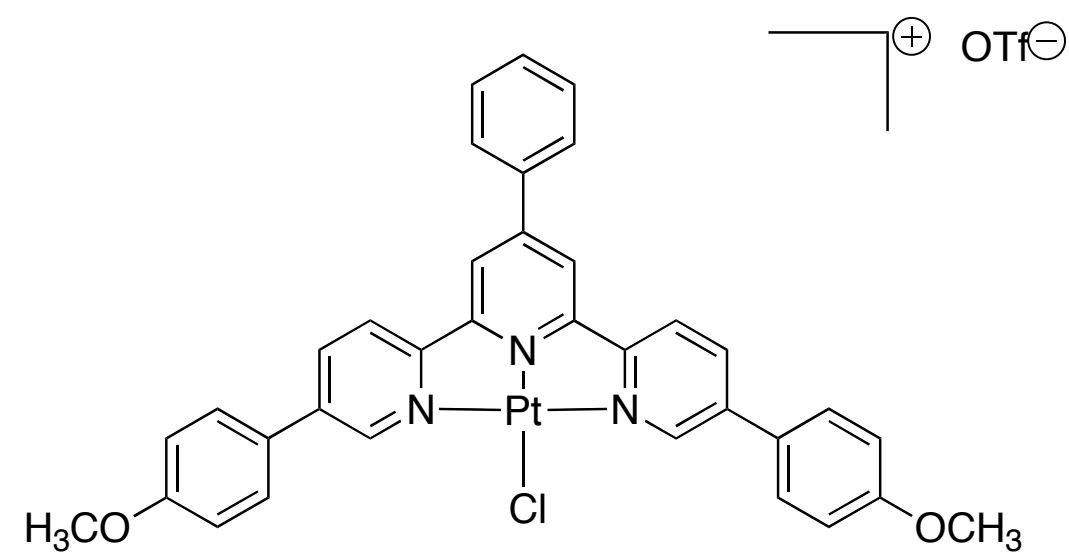
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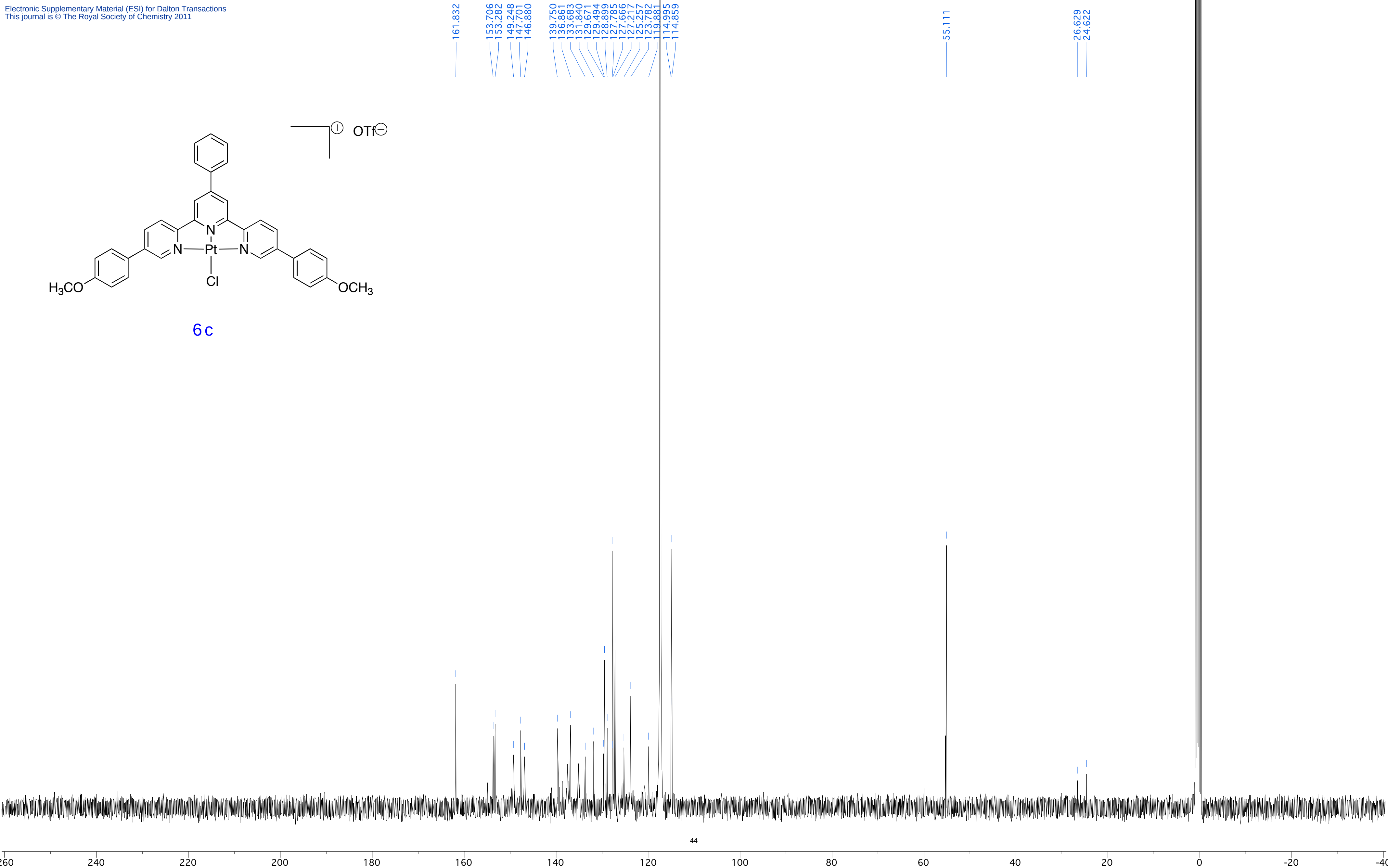


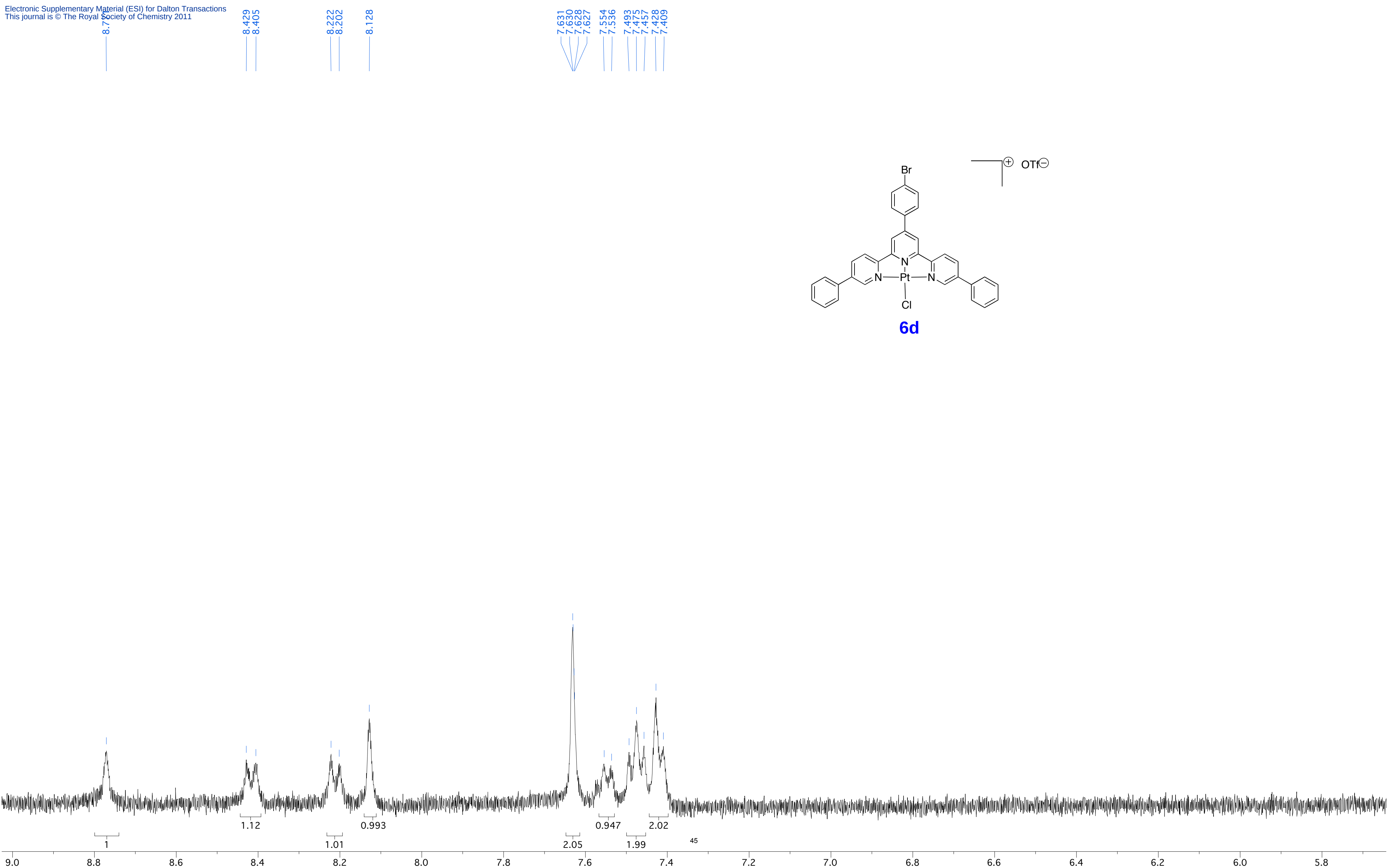
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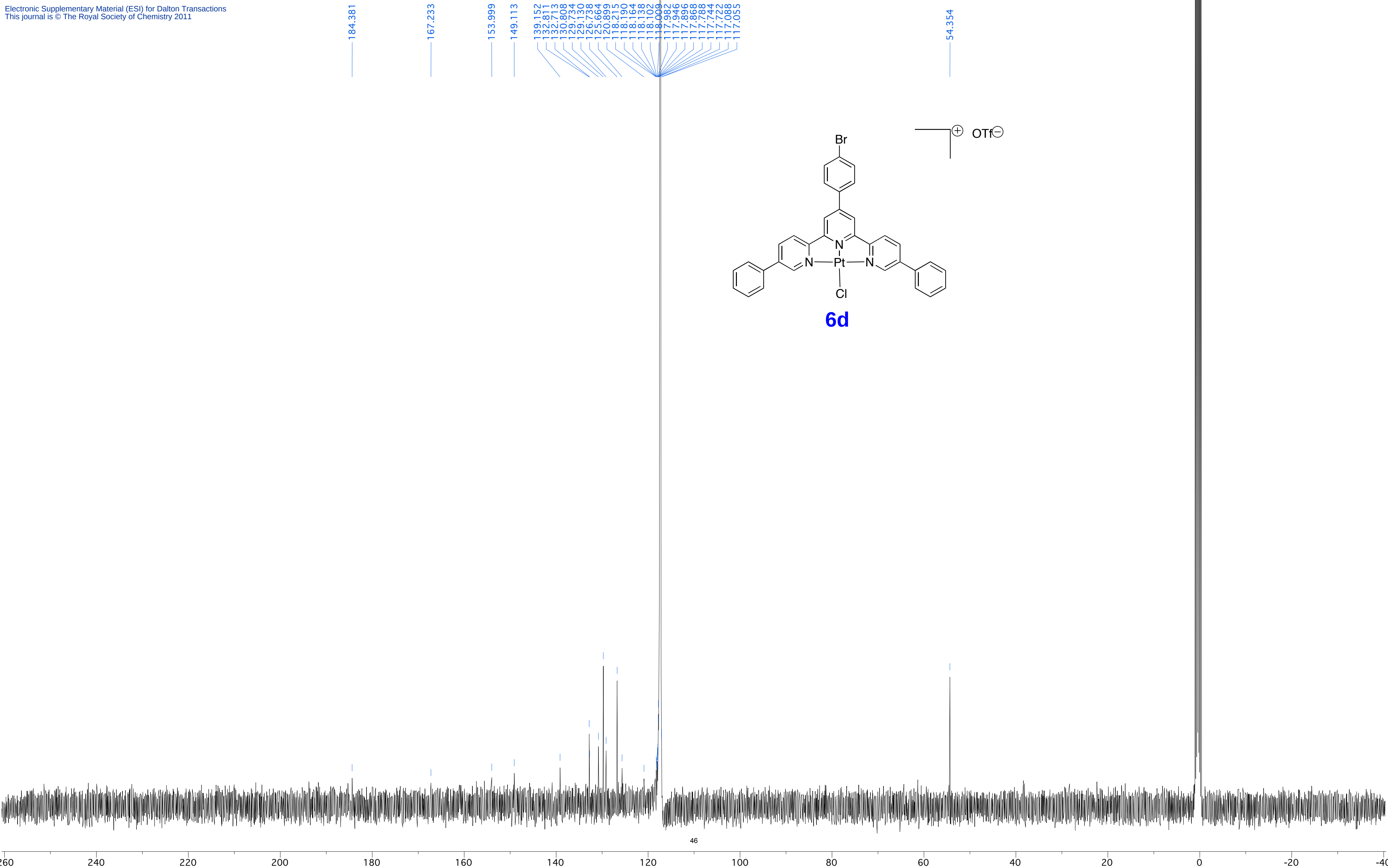




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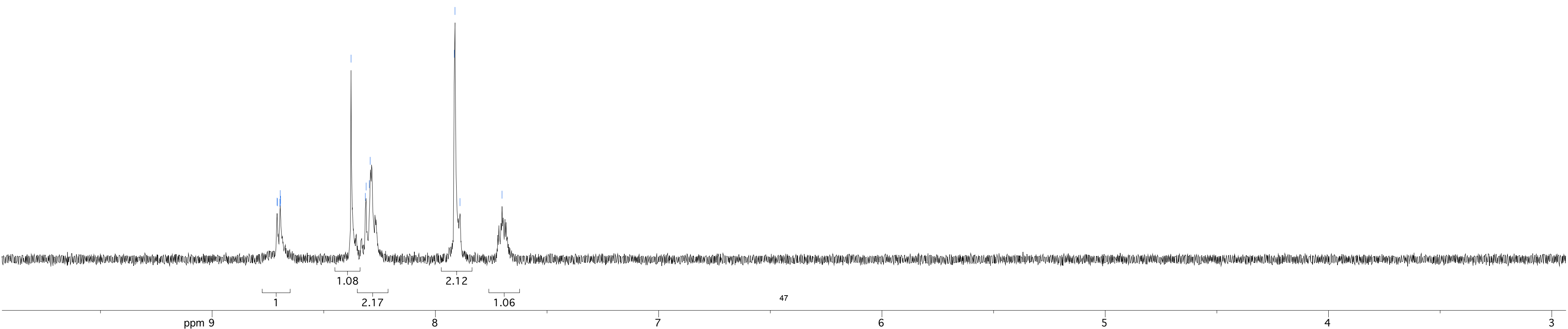
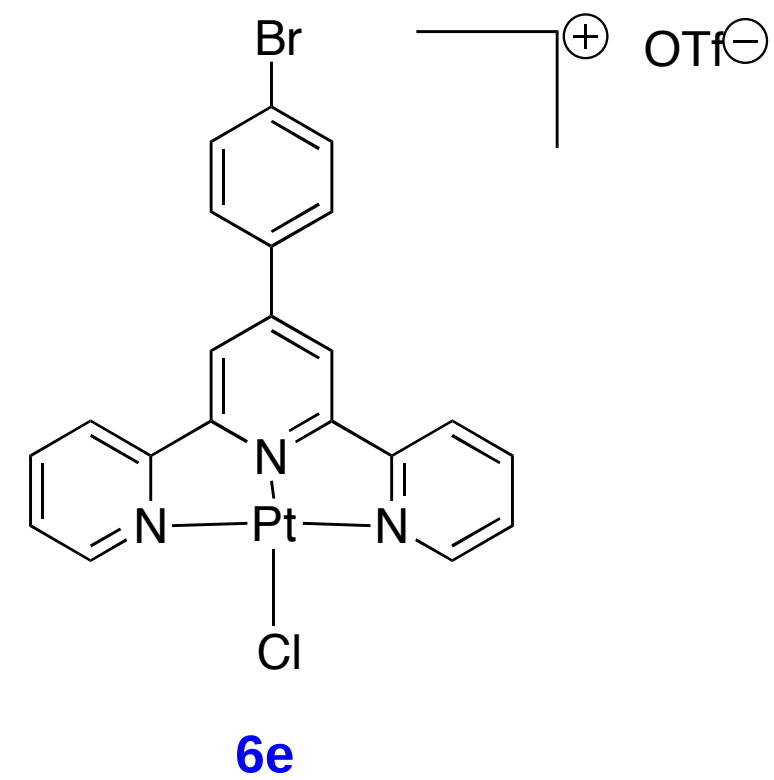


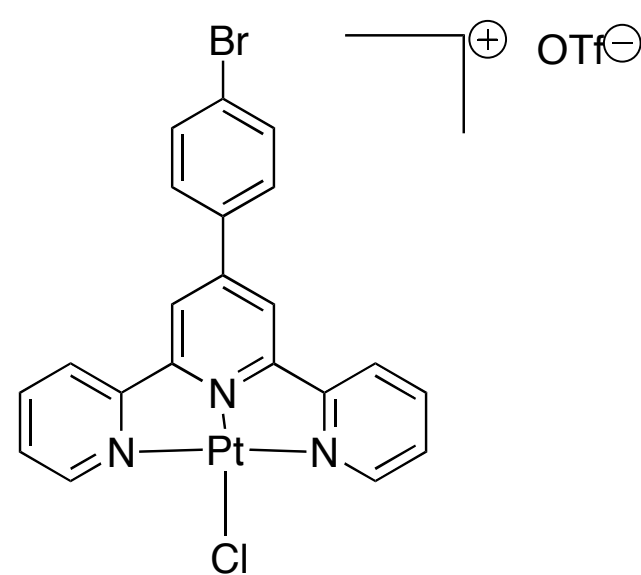
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8.292

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7.912
7.890

7.702





6e

