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Supplementary Information

Synthesis of 2,3-Diyne-1,4-naphthoquinone Derivatives and Evaluation of Cytotoxic Activity against Tumor Cell Lines

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Synthesis of 2,3-dibromo-1,4-naphthoquinone (**1**)

Bromine (16.0 g, 0.1 mol) was added dropwise over 5 h to a stirred solution of 1,4-naphthoquinone (7.91 g, 0.05 mol) in CH_2Cl_2 (80 mL), and during this time, hydrogen bromide was evolved. After, the solution was stirred overnight, N_2 was blown through the mixture, and the dark yellow precipitate was filtered off and washed with CH_2Cl_2. Recrystallization from CH_2Cl_2 afforded 10.27 g (65%) of the dibromo derivative, mp 220-222 °C (219-221, recrystallized from EtOAc).[1]

2,3-di(Phenylethynyl)-1,4-naphthoquinone (**2a**)

Using dichloromethane/hexane 30:70 as eluent, **2a** was obtained as a red solid (mp 151-152)[2] in 45% (51 mg, 0.143 mmol) yield; IR (KBr) ν_{max}/cm^{-1} 2198, 1667, 1591, 1534, 1490, 1370, 1328, 1309, 1258, 1159, 936, 748, 712, 682, 528; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (dd, 2H, 5.7/3.3 Hz), 7.77 (dd, 2H, 5.7 and 3.3 Hz), 7.68 (m, 4H), 7.42 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.1, 134.5, 134.2, 132.8, 132.4, 130.5, 129.0, 127.4, 122.6, 109.8, 85.4. LC-MS calcd. for $[C_{26}H_{15}O_2]^+$, 359.1072; found: 359.1111.

2,3-di(3-Hydroxy-3-methylbutynyl)-1,4-naphthoquinone (**2c**)

Using ethyl acetate/hexane 30:70 as eluent, **2c** was obtained as a dark yellow solid (mp 138-139 °C)[17] in 42% (43 mg, 0.134 mmol) yield; IR (KBr) ν_{max}/cm^{-1} 3322, 2979, 2931, 2202, 1671, 1591, 1540, 1459, 1349, 1300, 1234, 1164, 1133, 984, 951, 790, 713; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (t, 2H, 3.2 Hz), 7.73 (d, 2H, 3.2 Hz), 1.67(s, 12H), 3.74 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.6, 134.4, 134.2, 131.6, 126.9, 113.9, 76.9, 65.9, 30.9. LC-MS calcd. for $[C_{20}H_{18}O_4]^+$, 322.1205; found: 322.1271.

References

1. Crosby, I. T.; Rose, M. L.; Collis, M. P.; de Bruyn, P. J.; Keep, P. L. C.; Robertson, A. D.; *Austral. J. Chem.* **2008**, *61*, 768.
2. Romanov, V. S.; Ivanchikova, I. D.; Moroz, A. A.; Shvartsberg, M. S.; *Russ. Chem. Bull., Int. Ed.* **2005**, *54*, 1686.

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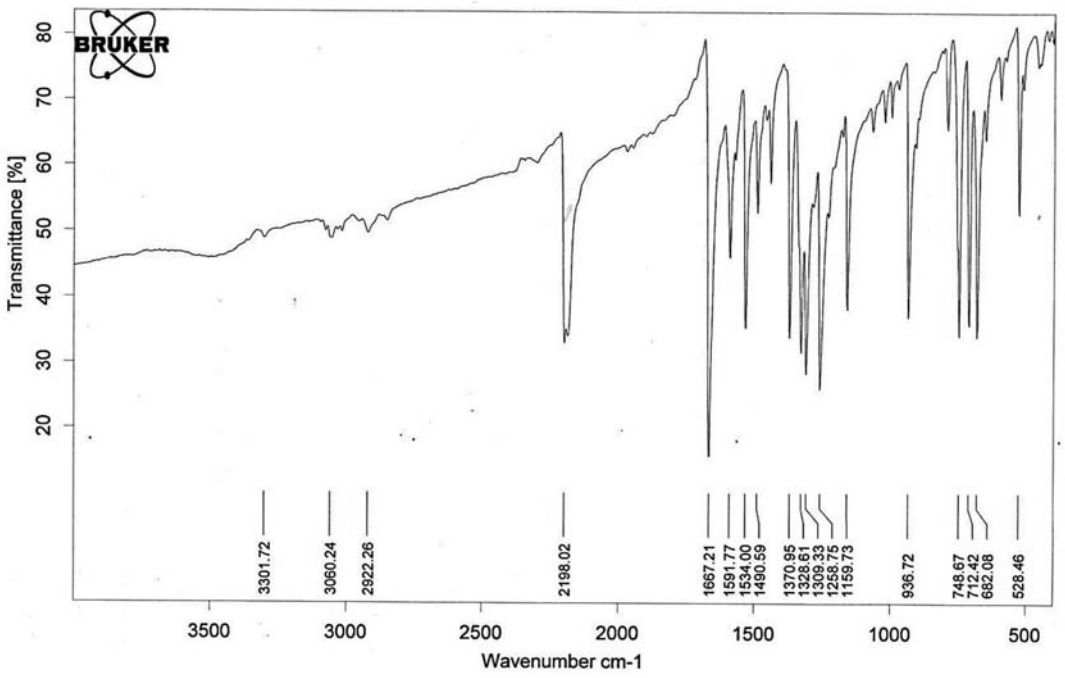

Figure S1. Infrared spectrum of **2a** (KBr).

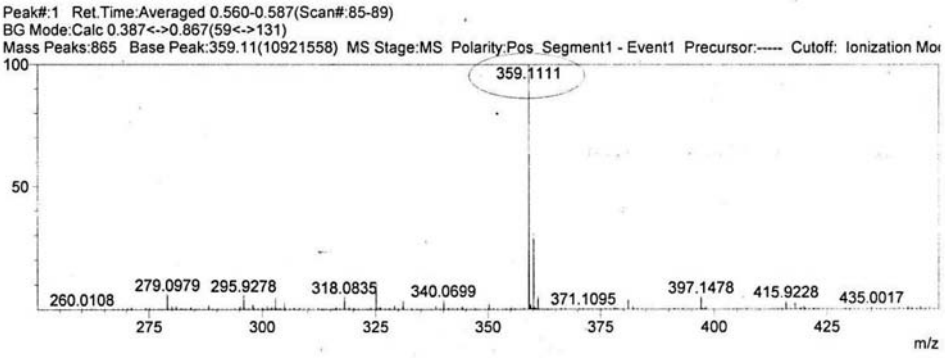

Figure S2. High resolution mass spectra (ESI-MS) of **2a**.

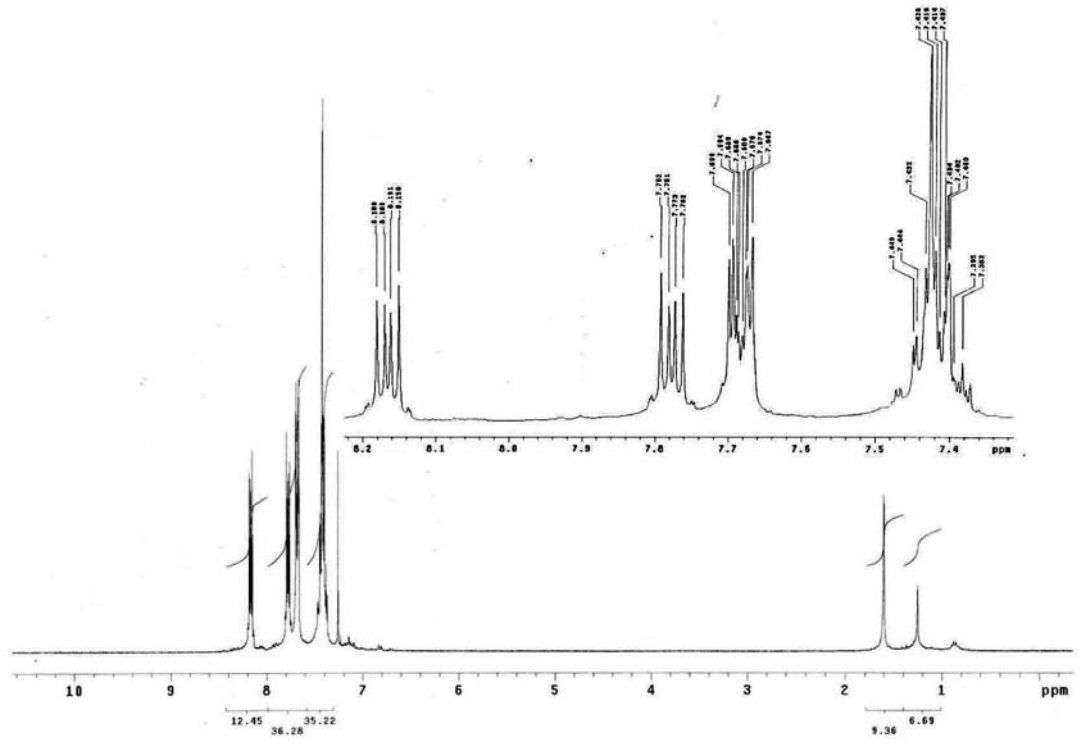

Figure S3. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2a**.

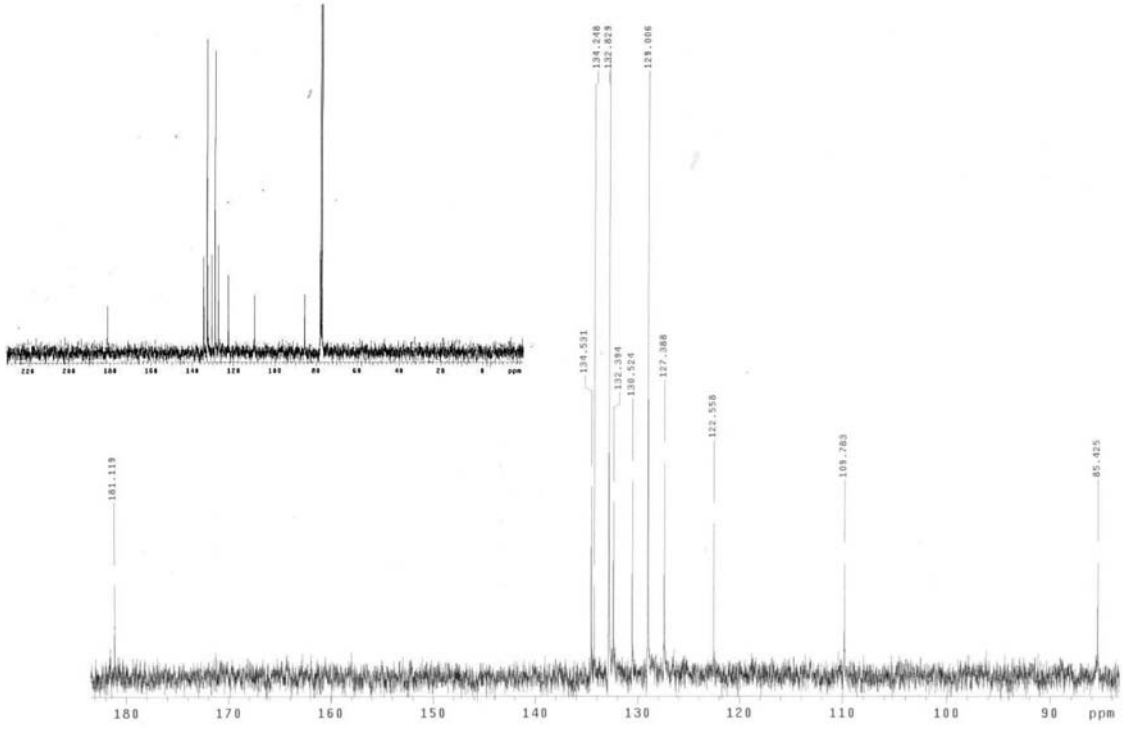

Figure S4. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2a**.

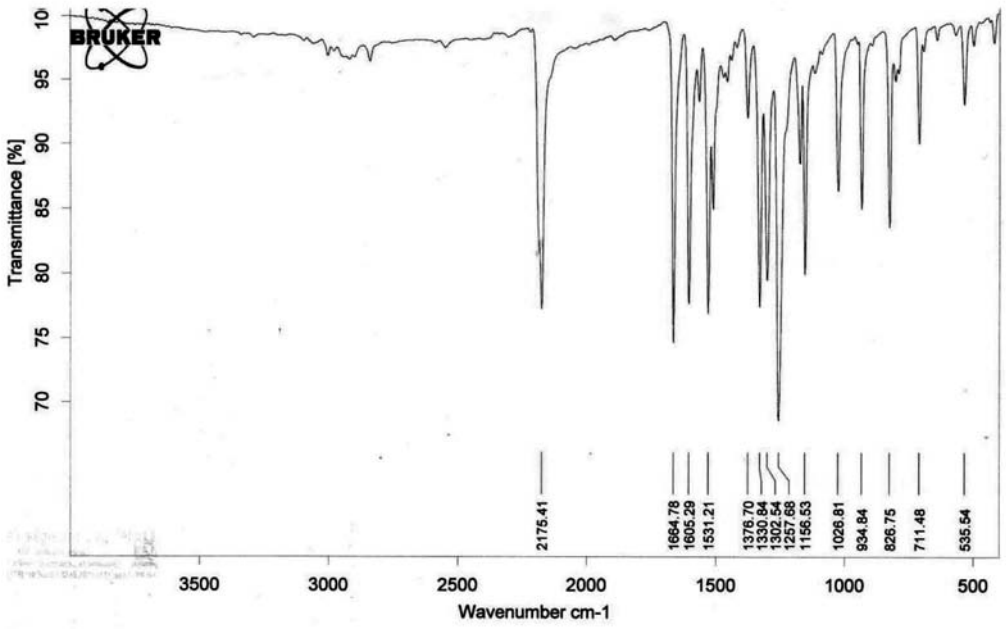

Figure S5. Infrared spectrum of **2b** (KBr).

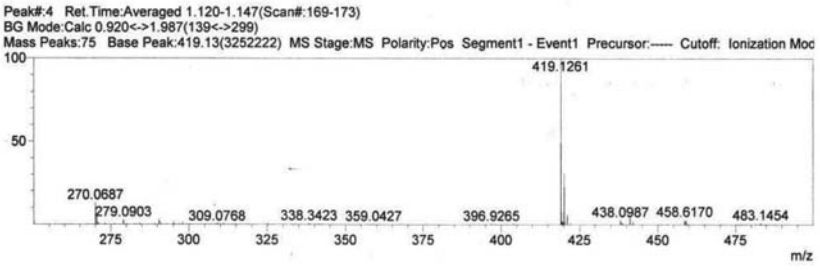

Figure S6. High resolution mass spectra (ESI-MS) of **2b**.

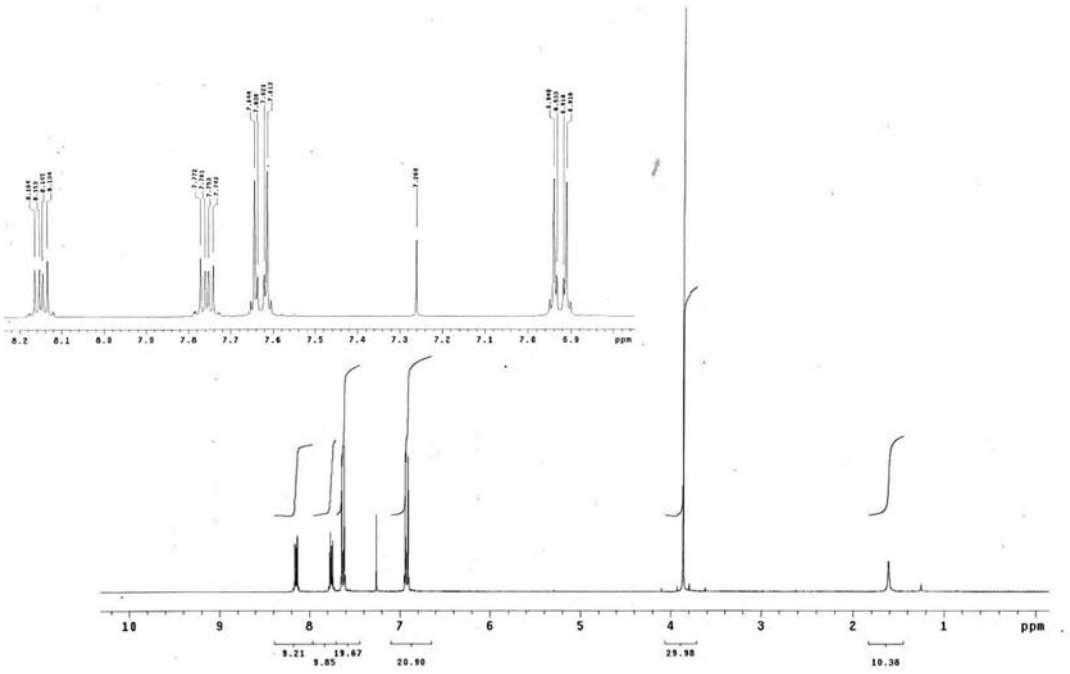

Figure S7. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2b**.

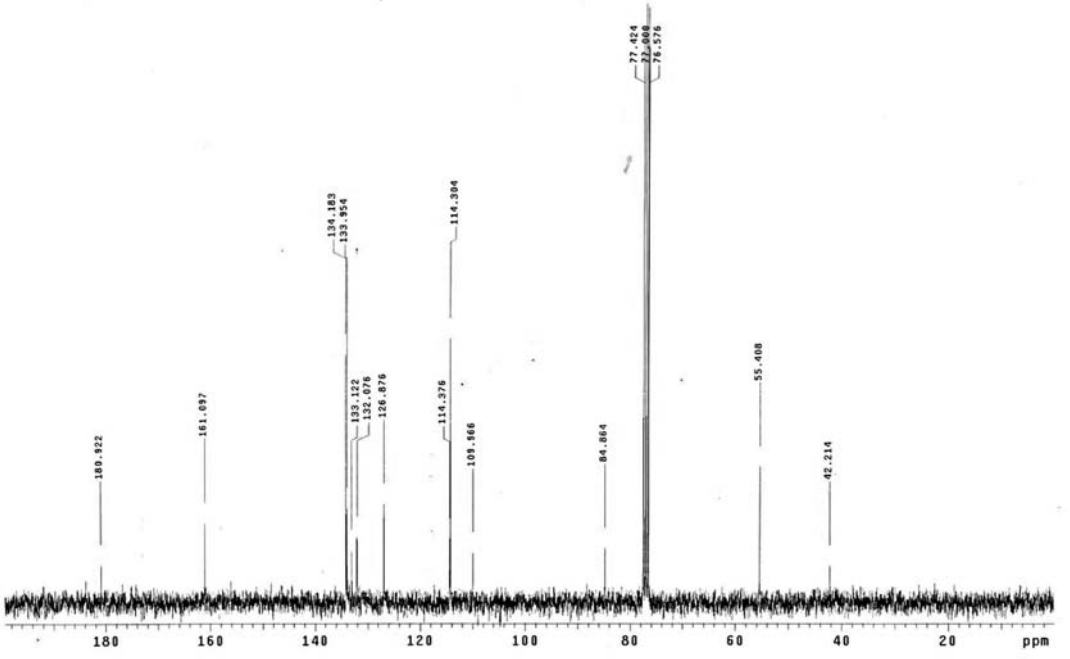

Figure S8. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2b**.

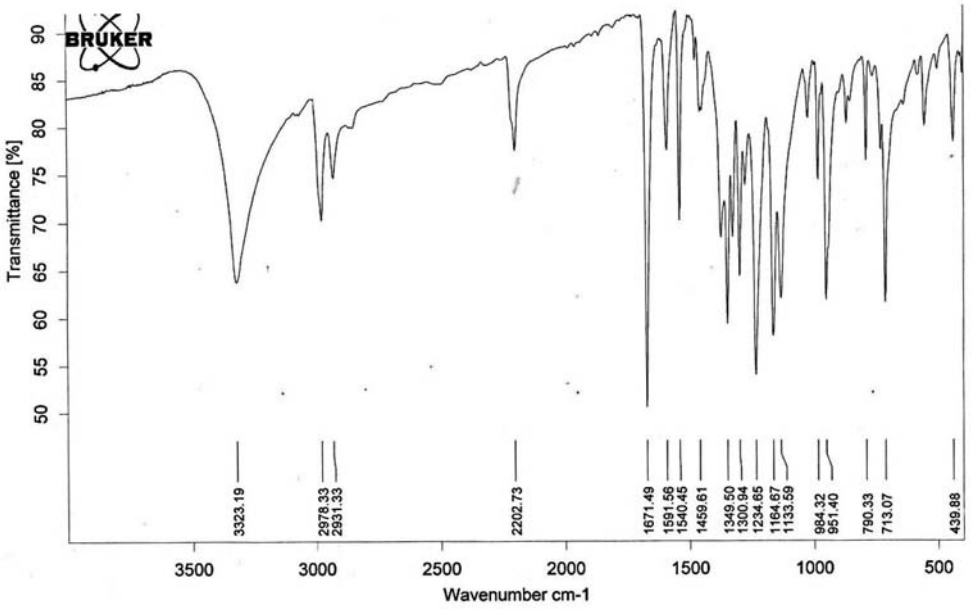

Figure S9. Infrared spectrum of **2c** (KBr).

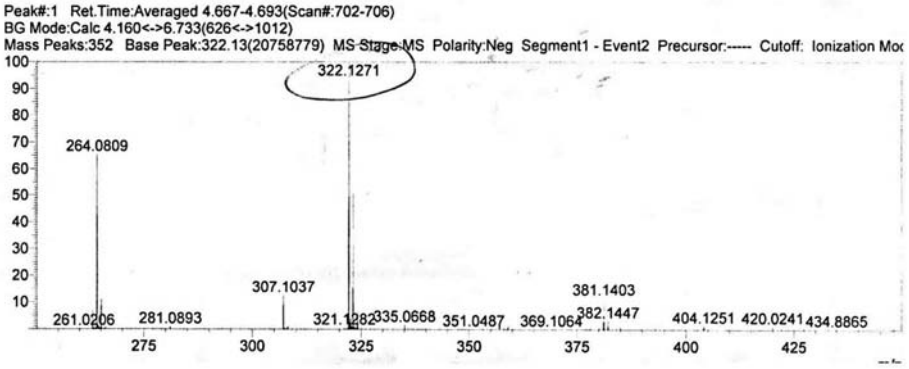

Figure S10. High resolution mass spectra (ESI-MS) of **2c**.

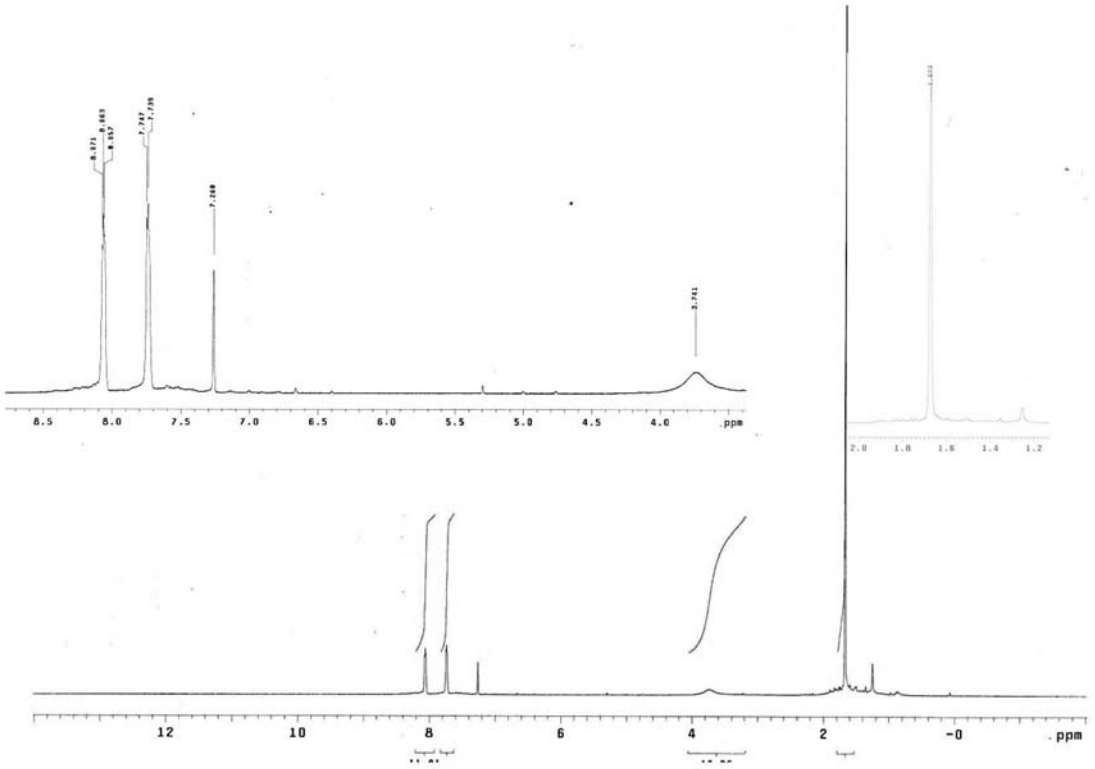

Figure S 11. ^{1}H NMR spectrum (400 MHz**,** $CDCl_3$) of **2c.**

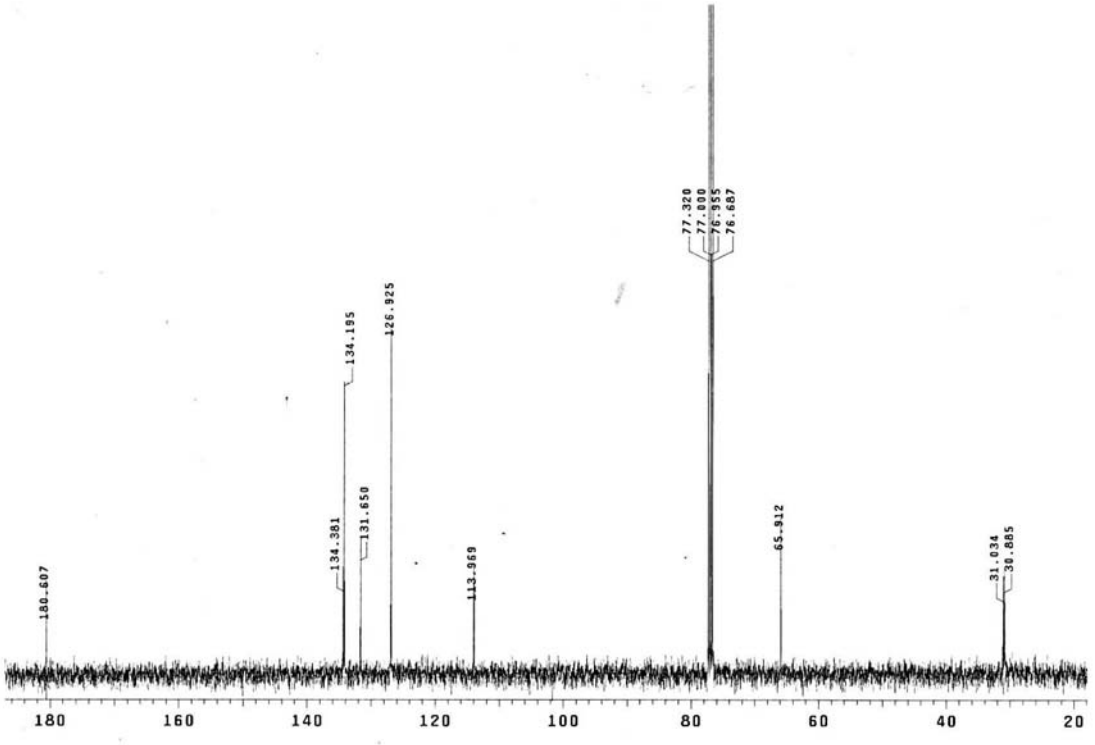

Figure S12. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **2c**.

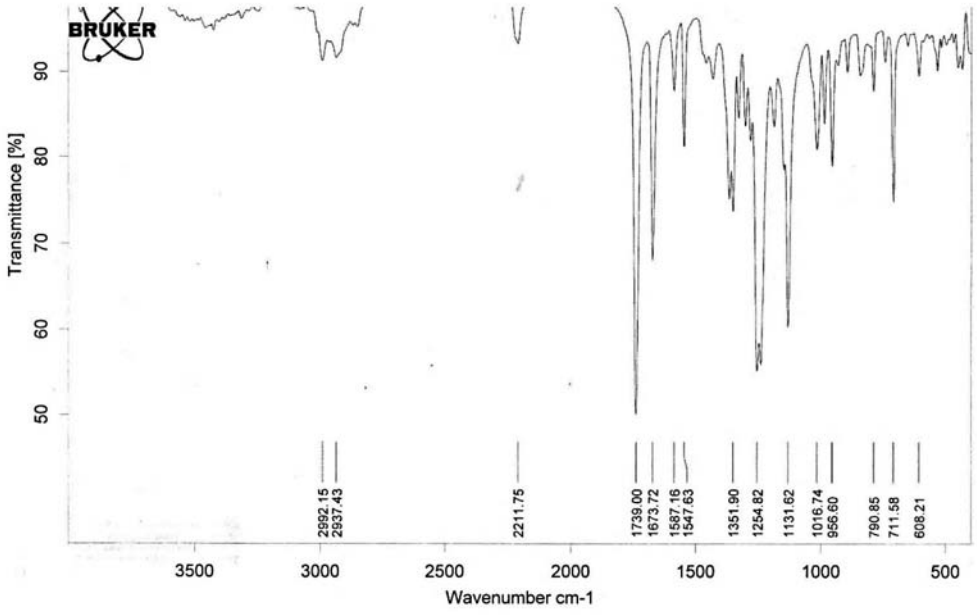

Figure S13. Infrared spectrum of **2c'** (KBr).

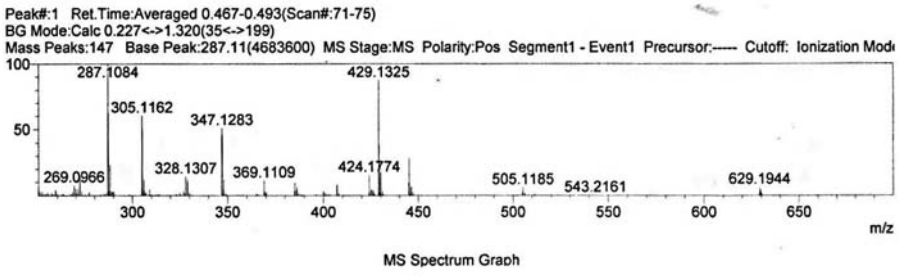

Figure S14. High resolution mass spectra (ESI-MS) of **2c'**.

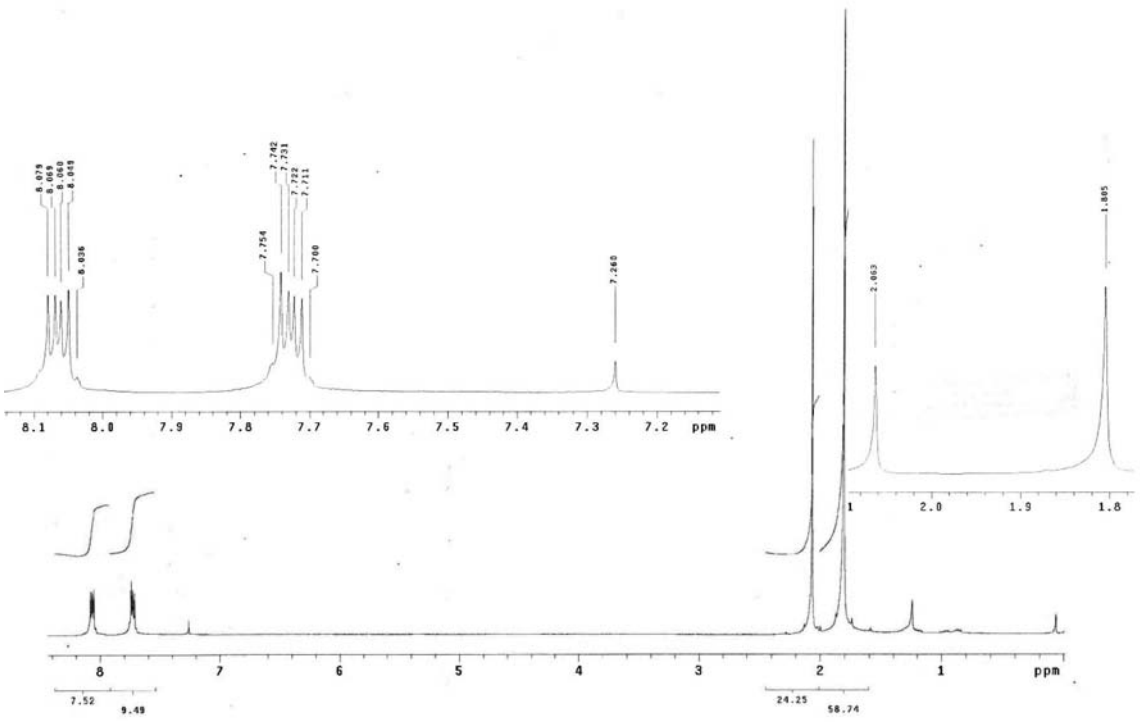

Figure S15. ^{1}H NMR spectrum (300 MHz**,** $CDCl_3$) of **2c'**.

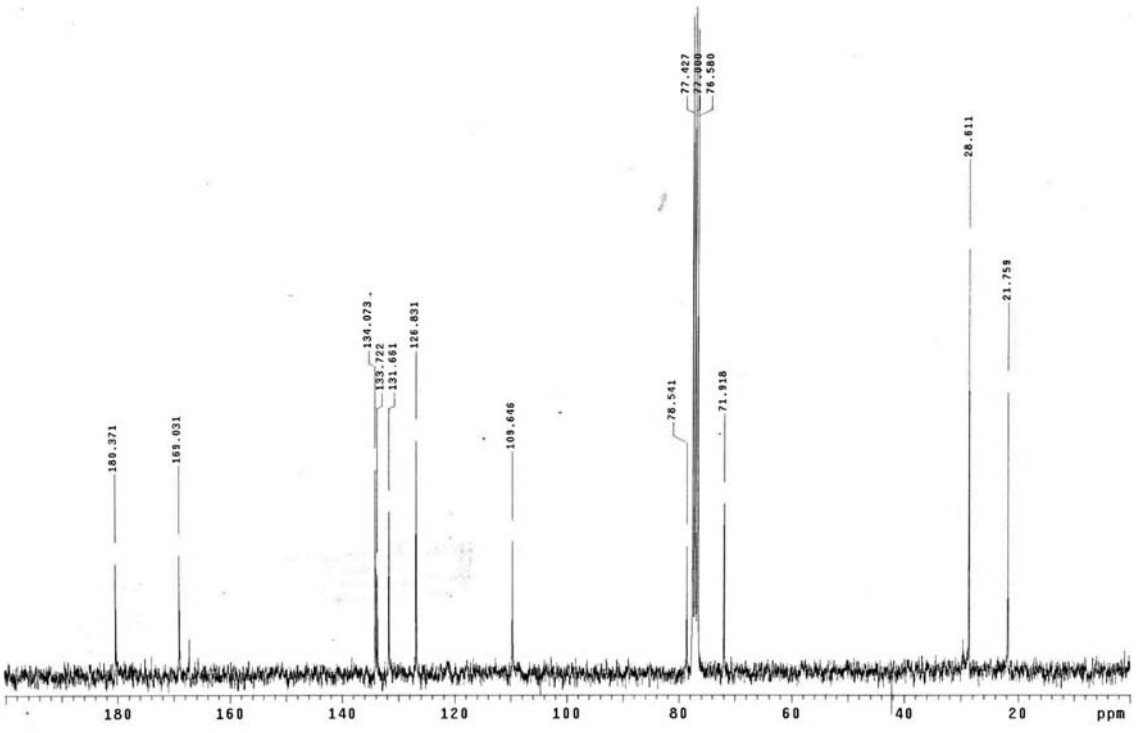

Figure S16. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2c'**.

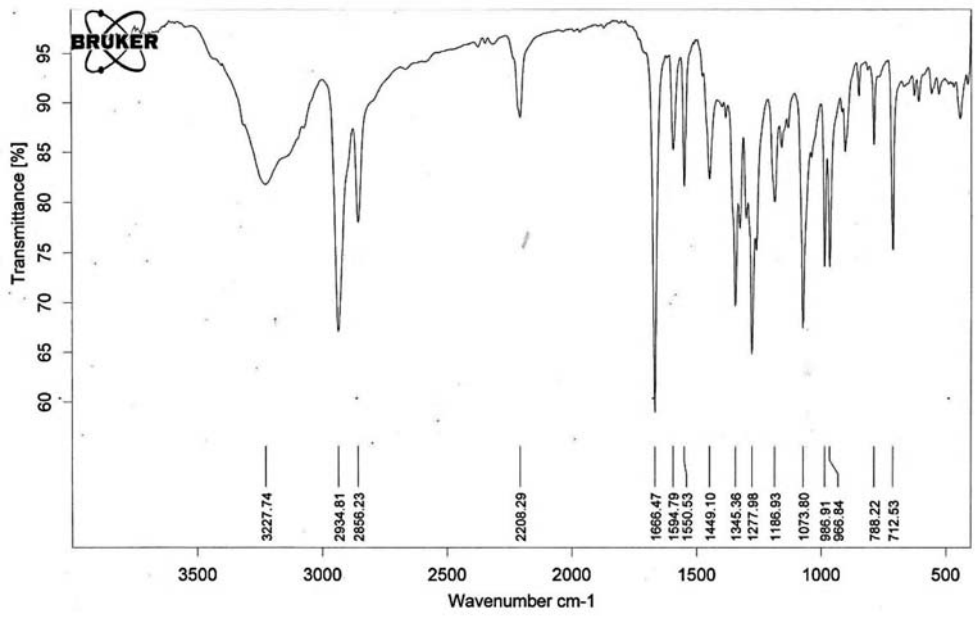

Figure S17. Infrared spectrum of **2d** (KBr).

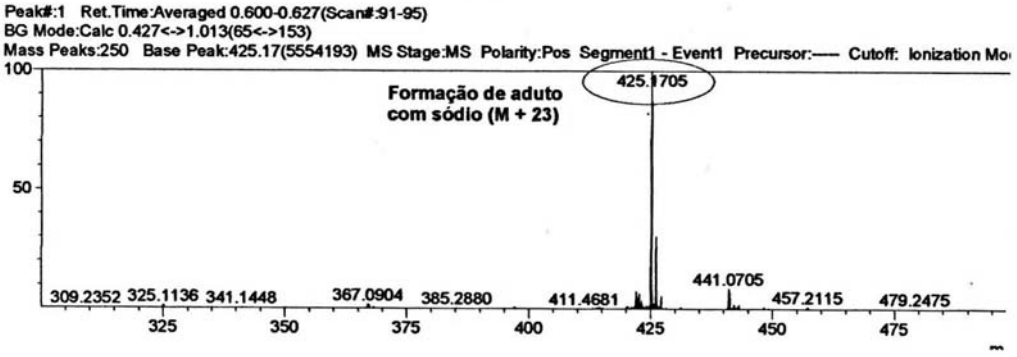

Figure S18. High resolution mass spectra (ESI-MS) of **2d**.

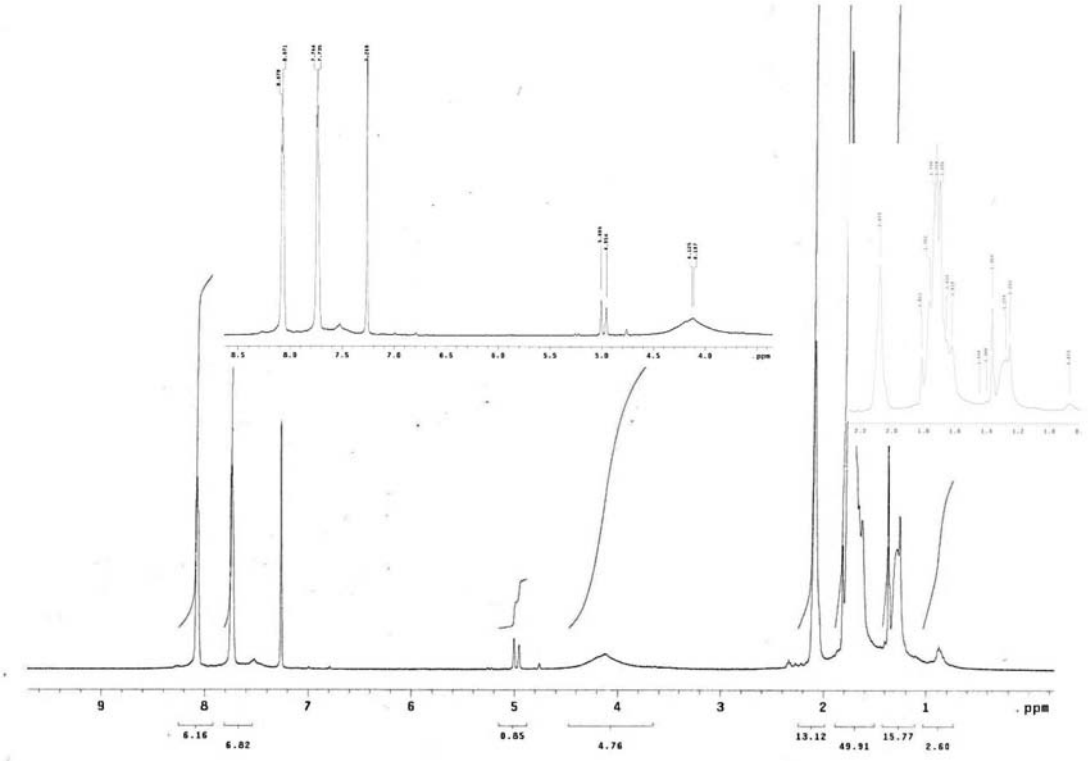

Figure S19. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **2d**.

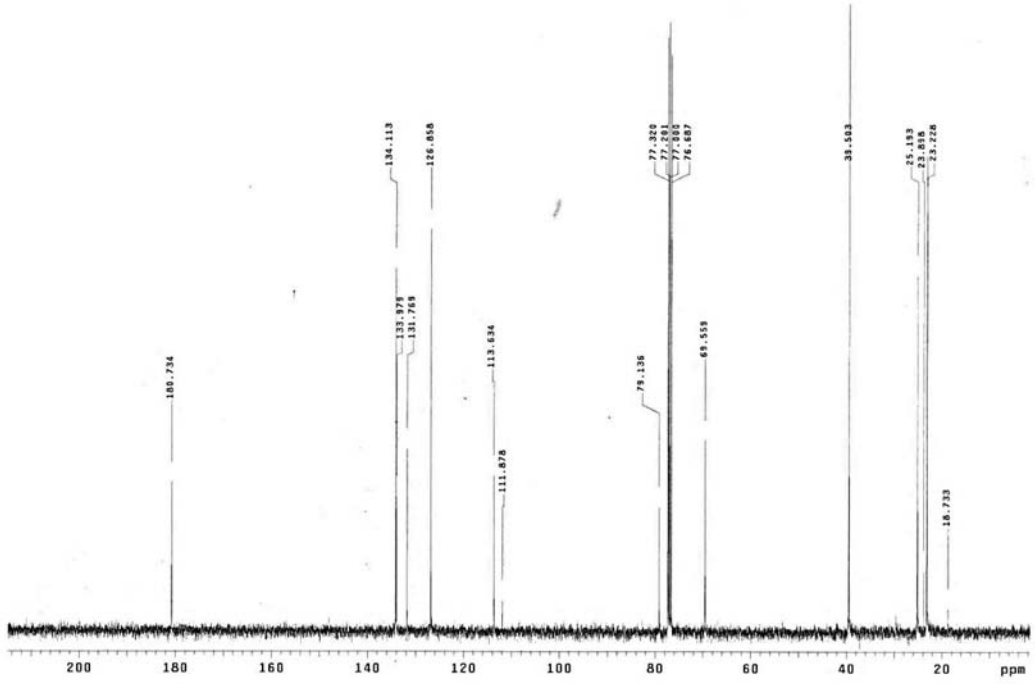

Figure S 20. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **2d**.

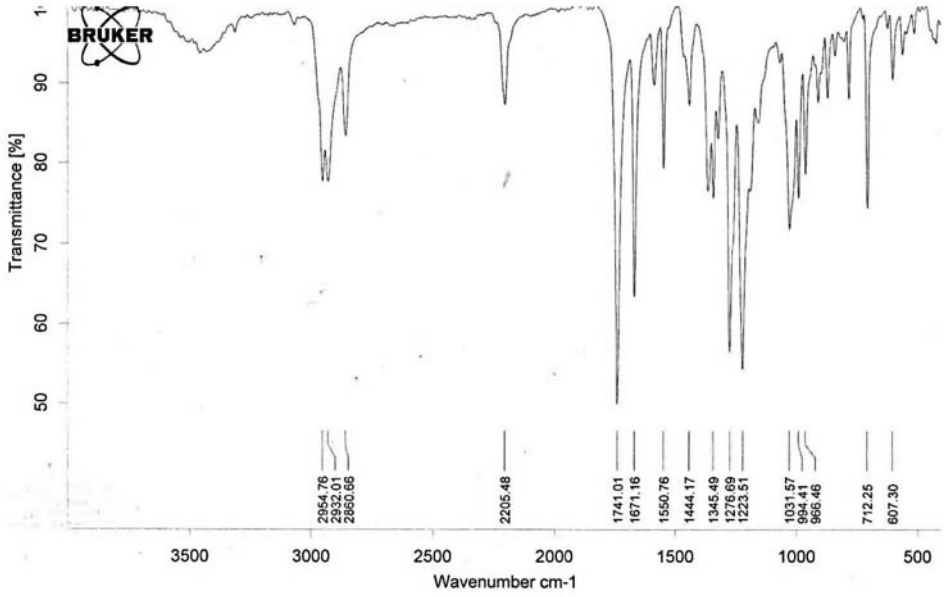

Figure S21. Infrared spectrum of **2d'** (KBr).

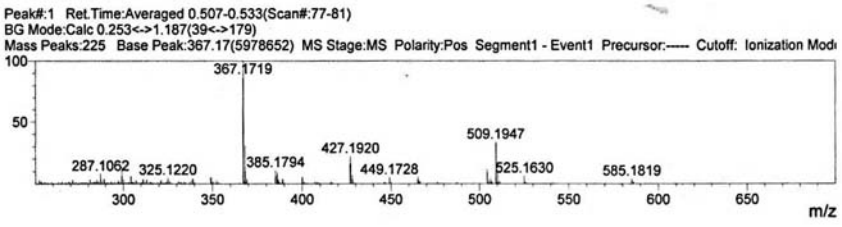

Figure S22. High resolution mass spectra (ESI-MS) of **2d'**.

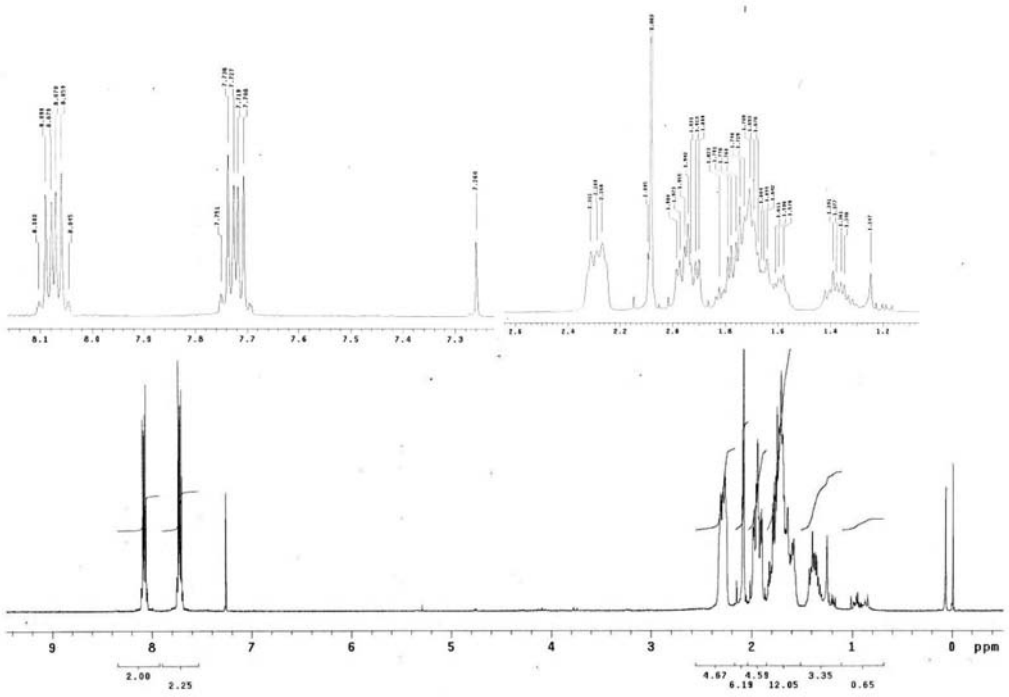

Figure S23. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2d'.**

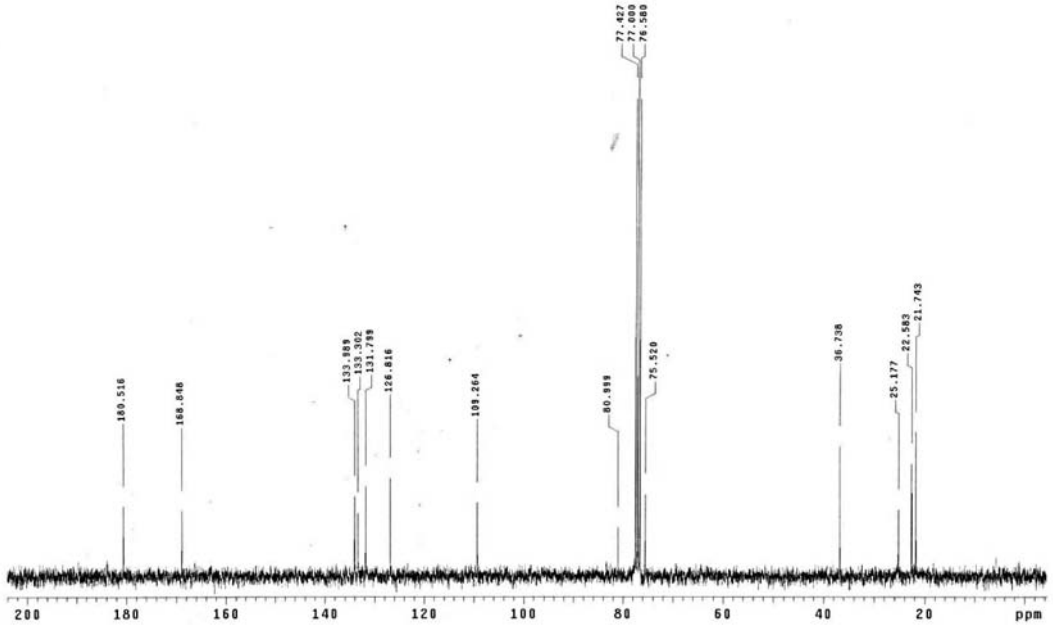

Figure S24. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2d'**.

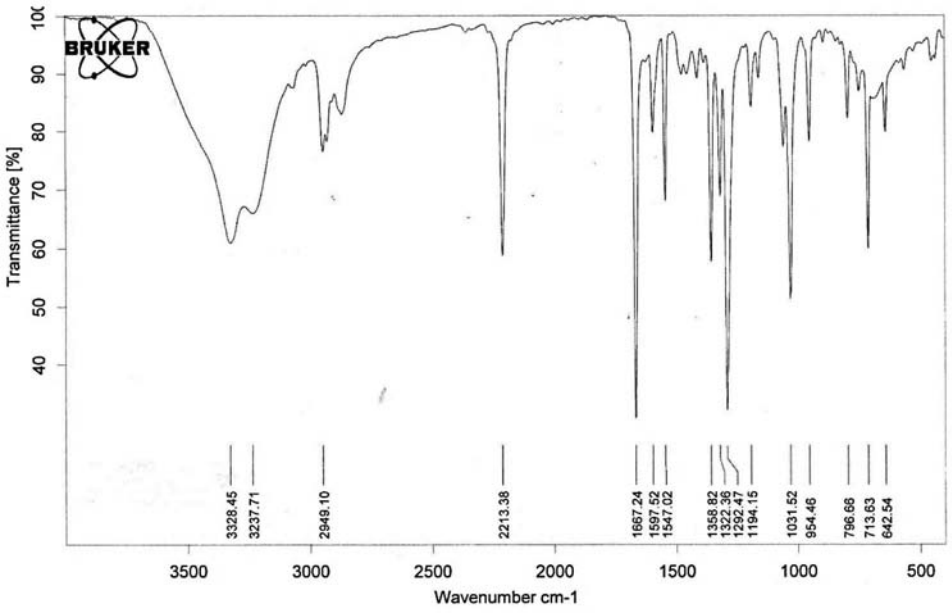

Figure S25. Infrared spectrum of **2e** (KBr).

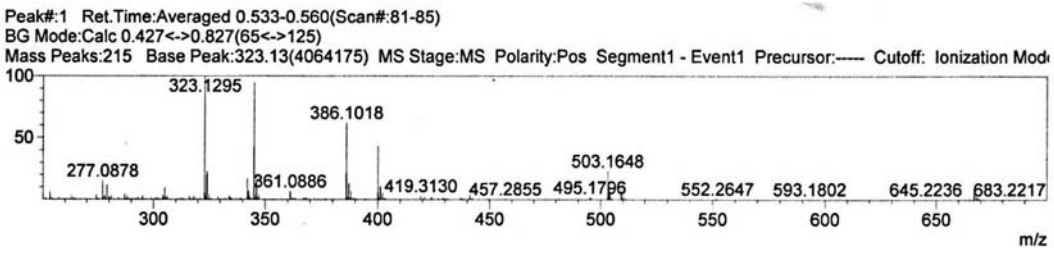

Figure S26. High resolution mass spectra (ESI-MS) of **2e**.

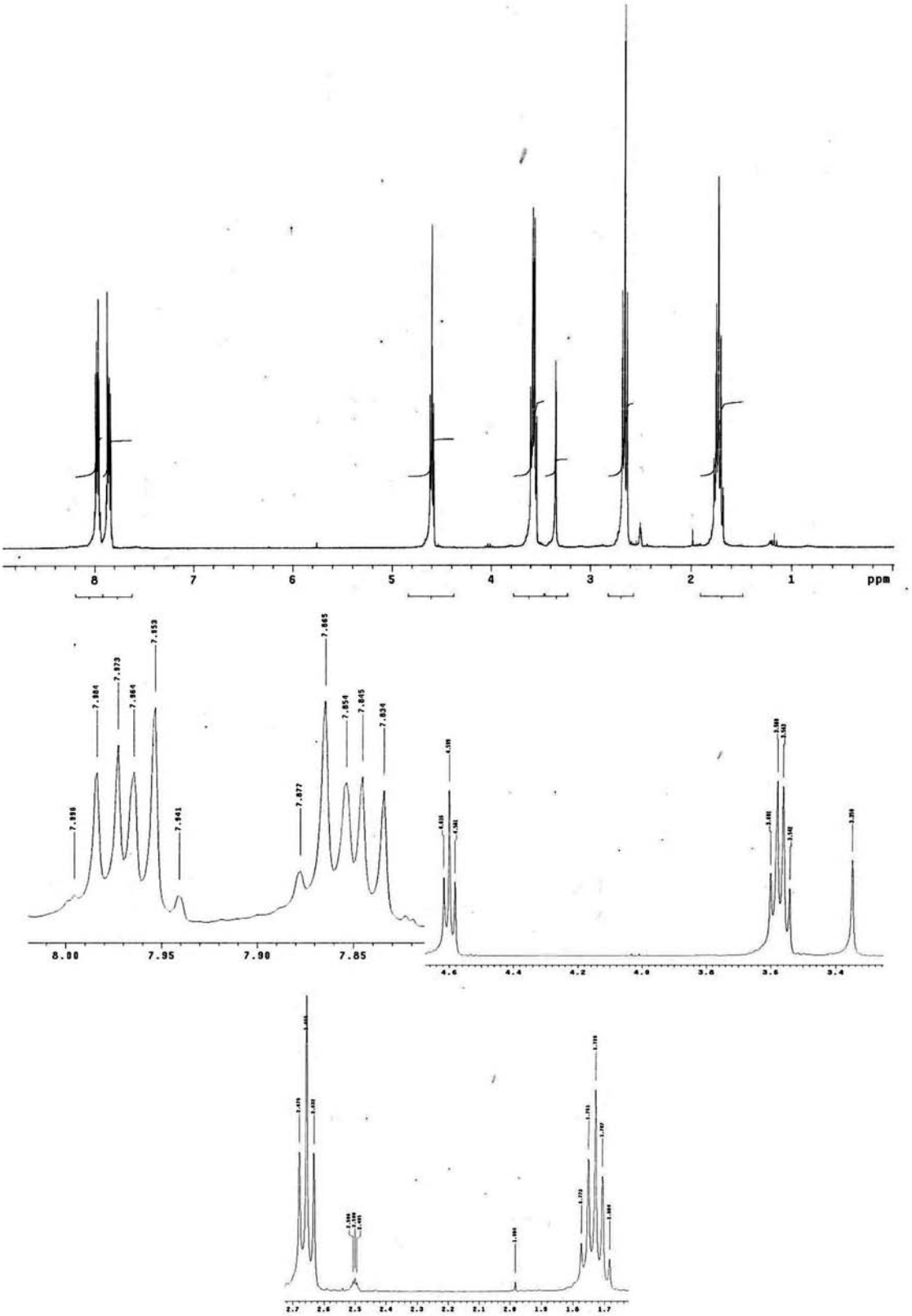

Figure S27. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of **2e**.

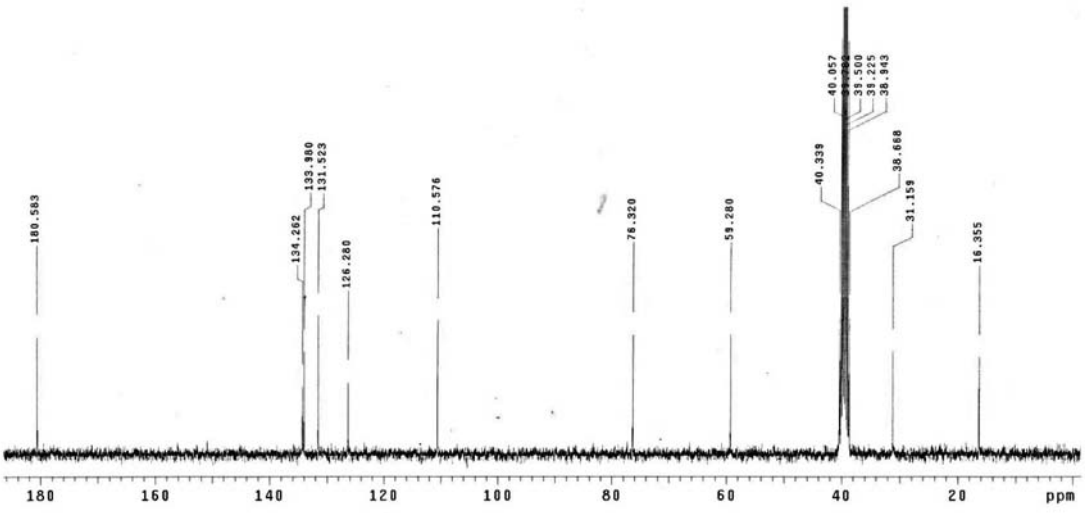

Figure S28. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **2e**.

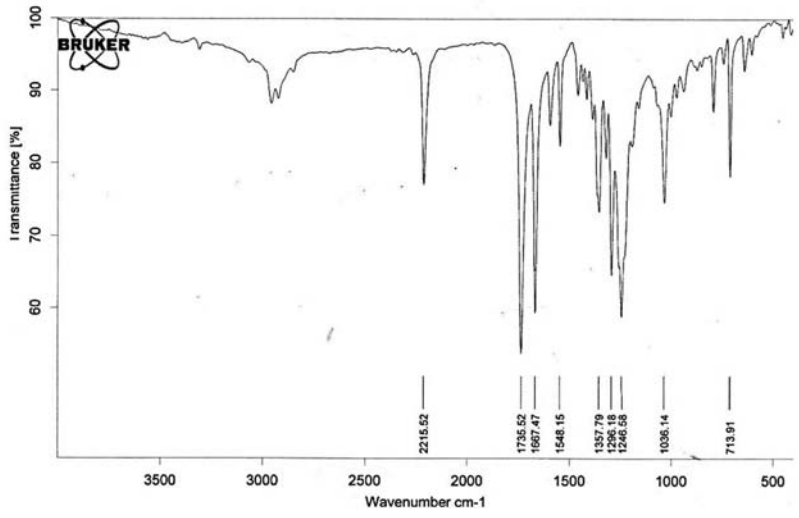

Figure S29. Infrared spectrum of **2e'** (KBr).

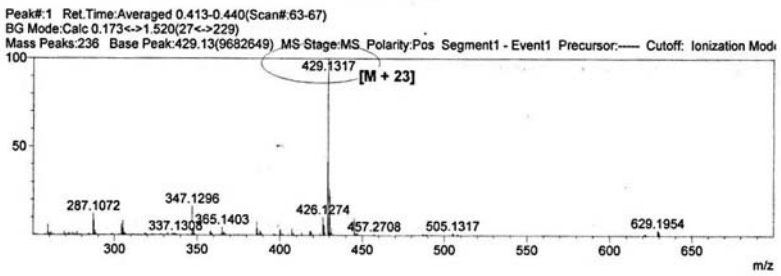

Figure S30. High resolution mass spectra (ESI-MS) of **2e'**.

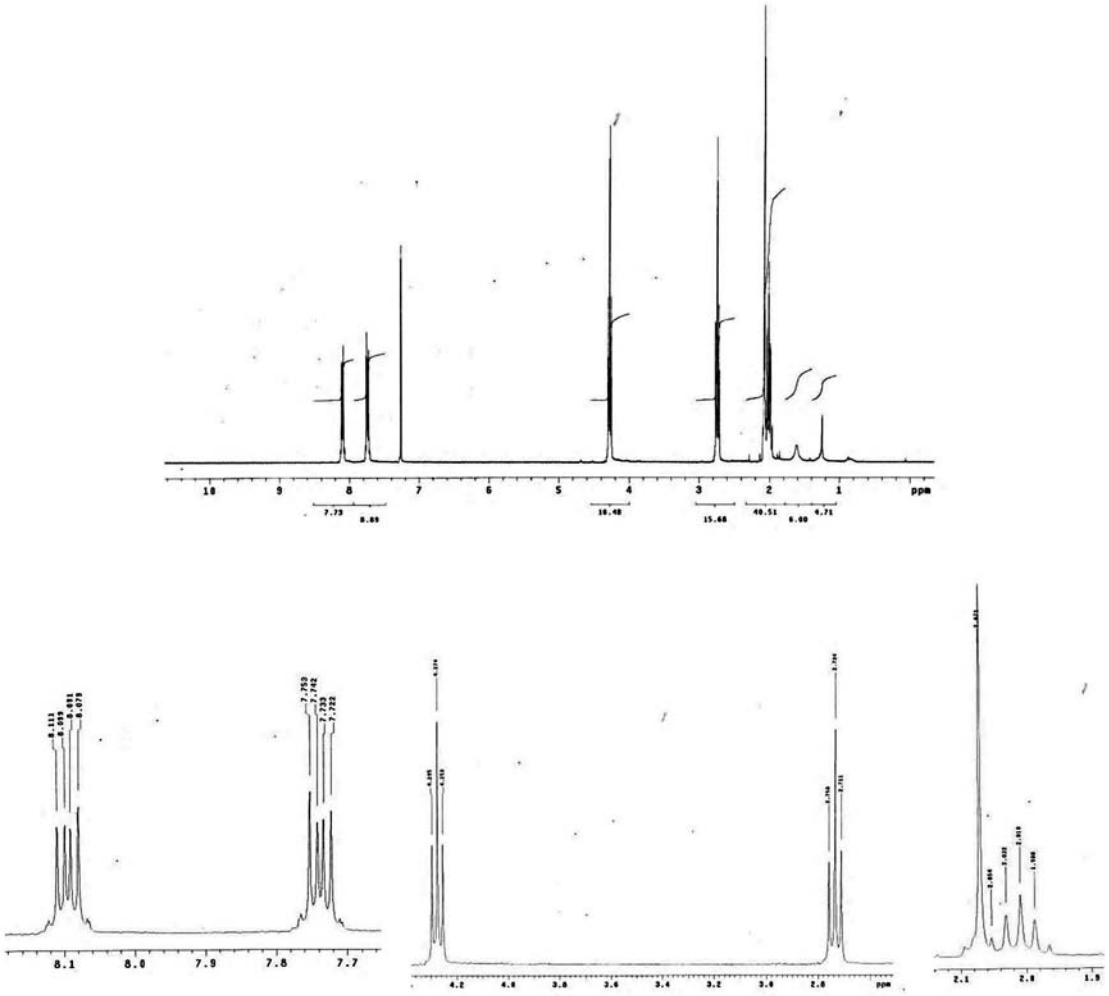

Figure S31. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2e'**.

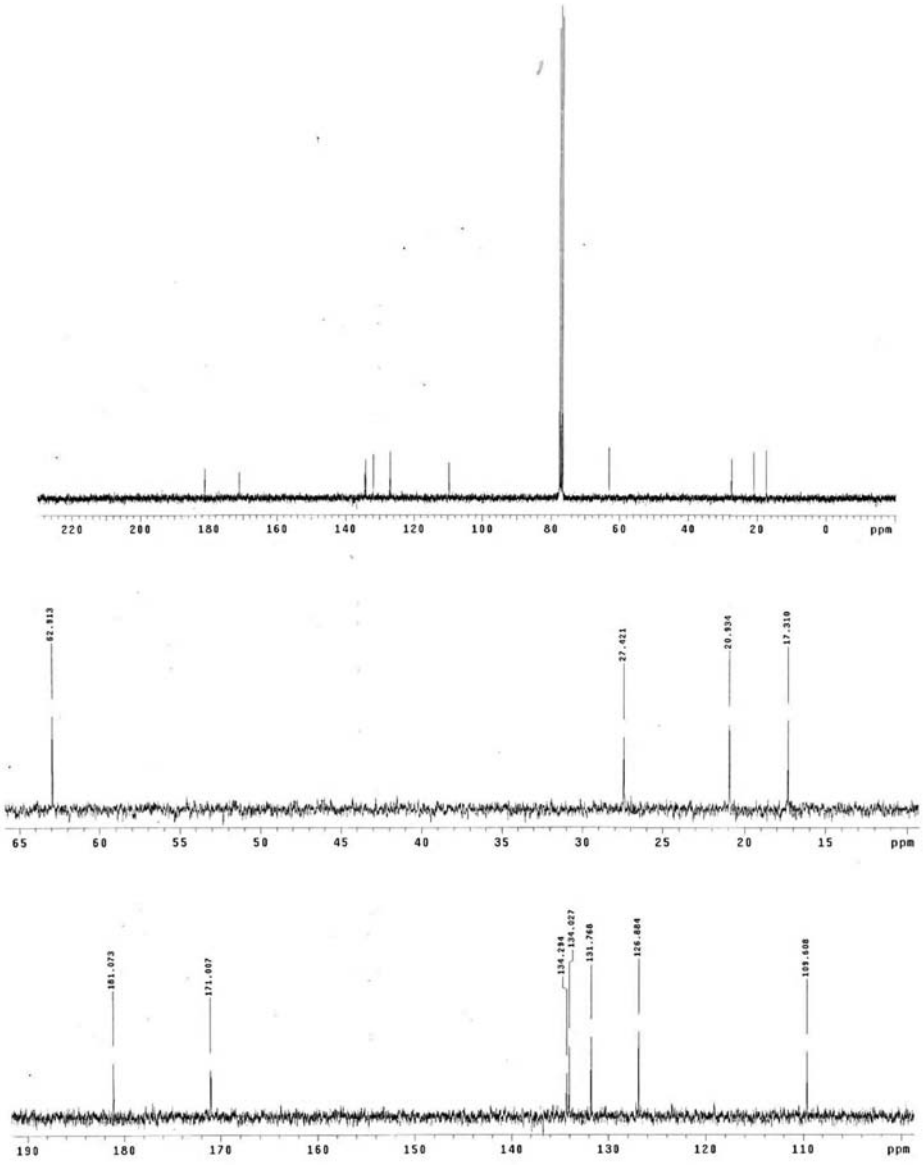

Figure S32. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2e'**.

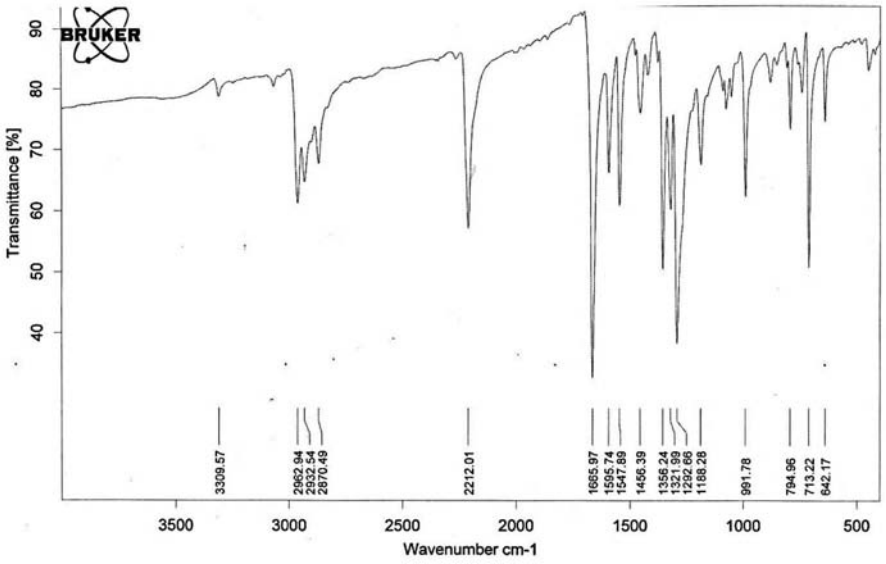

Figure S33. Infrared spectrum of **2f** (KBr).

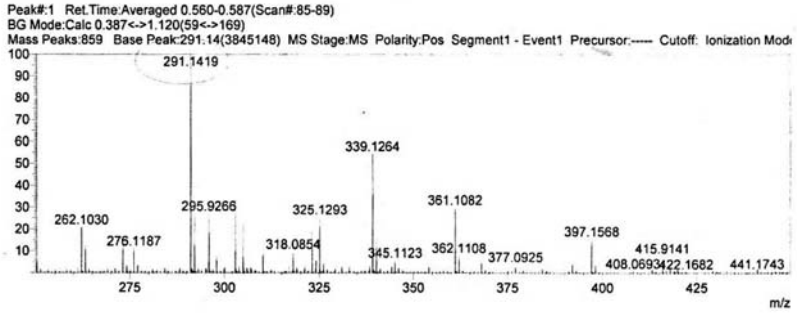

Figure S34. High resolution mass spectra (ESI-MS) of **2f**.

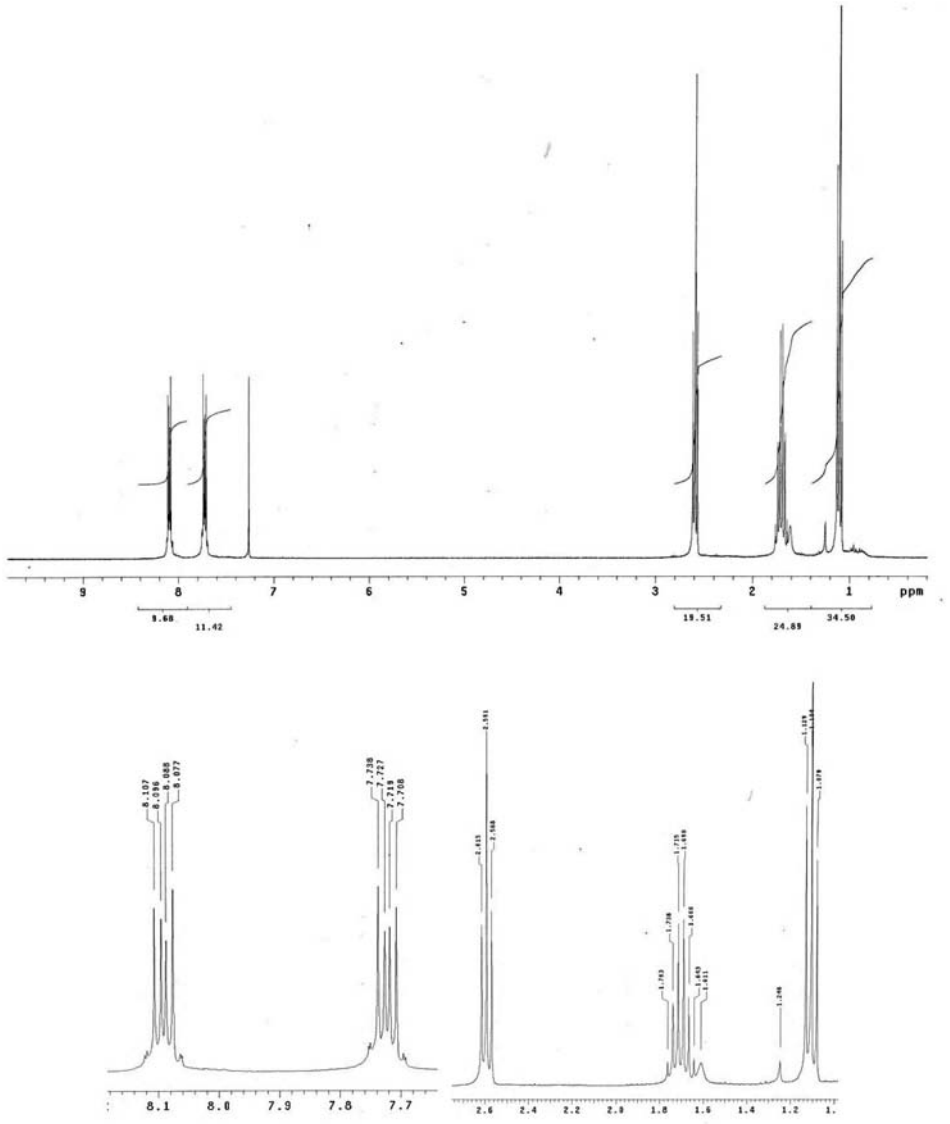

Figure S35. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2f**.

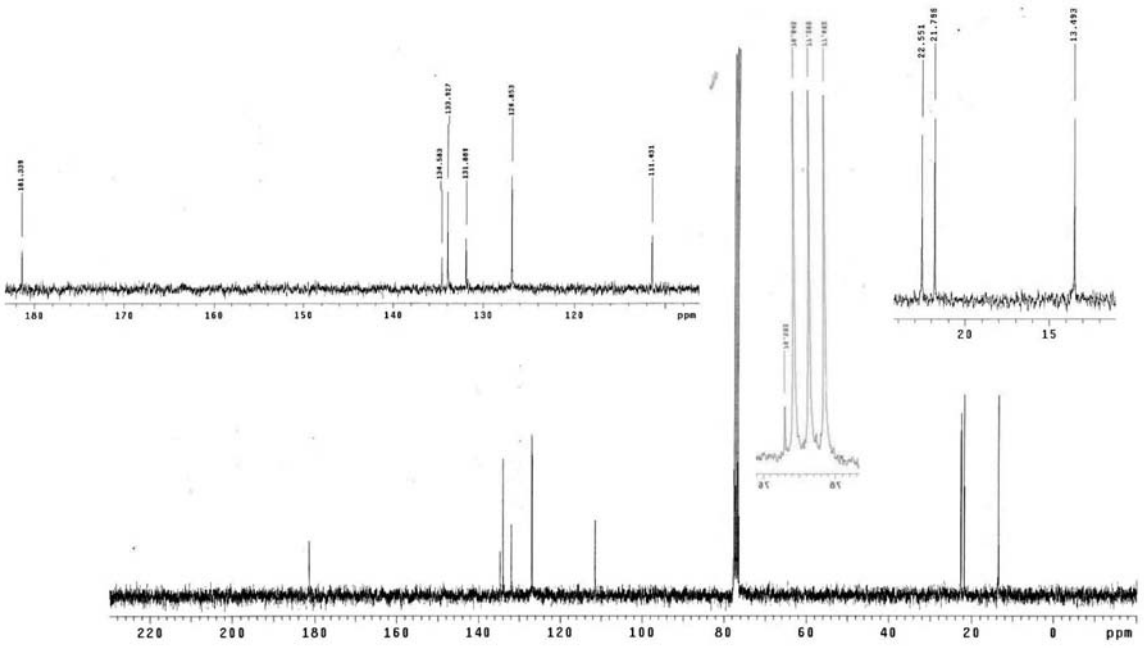

Figure S36. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2f**.

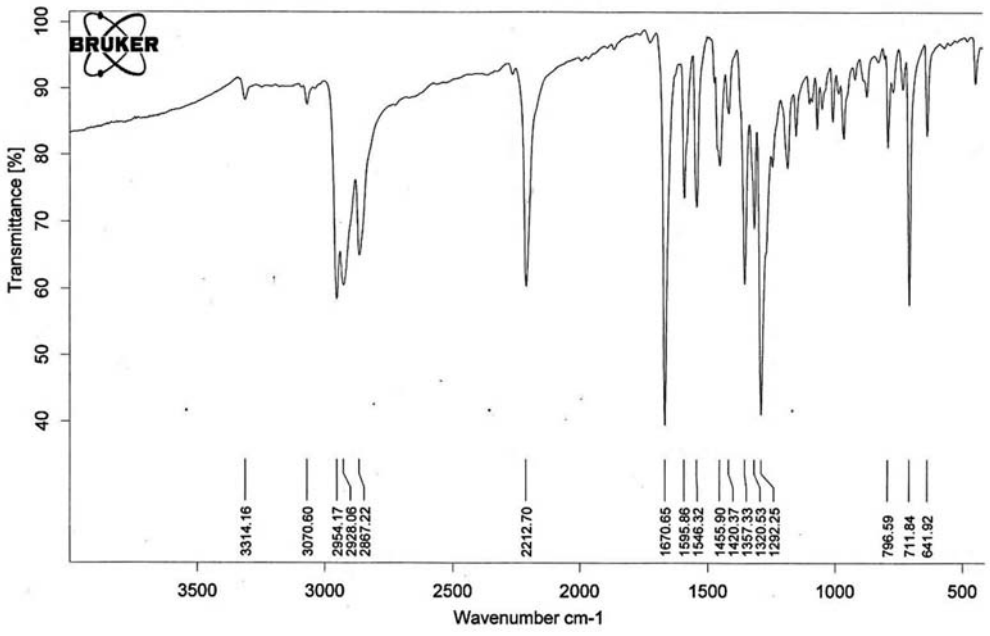

Figure S37. Infrared spectrum of **2g** (KBr).

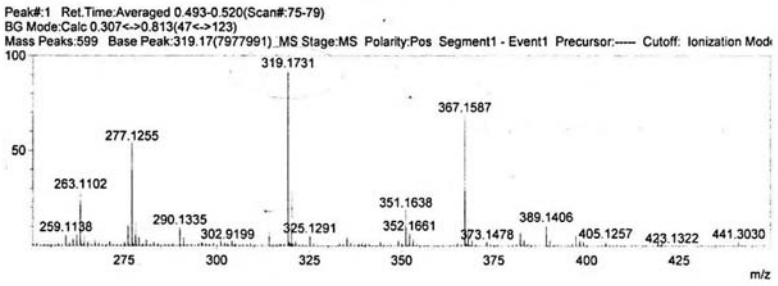

Figure S38. High resolution mass spectra (ESI-MS) of **2g**.

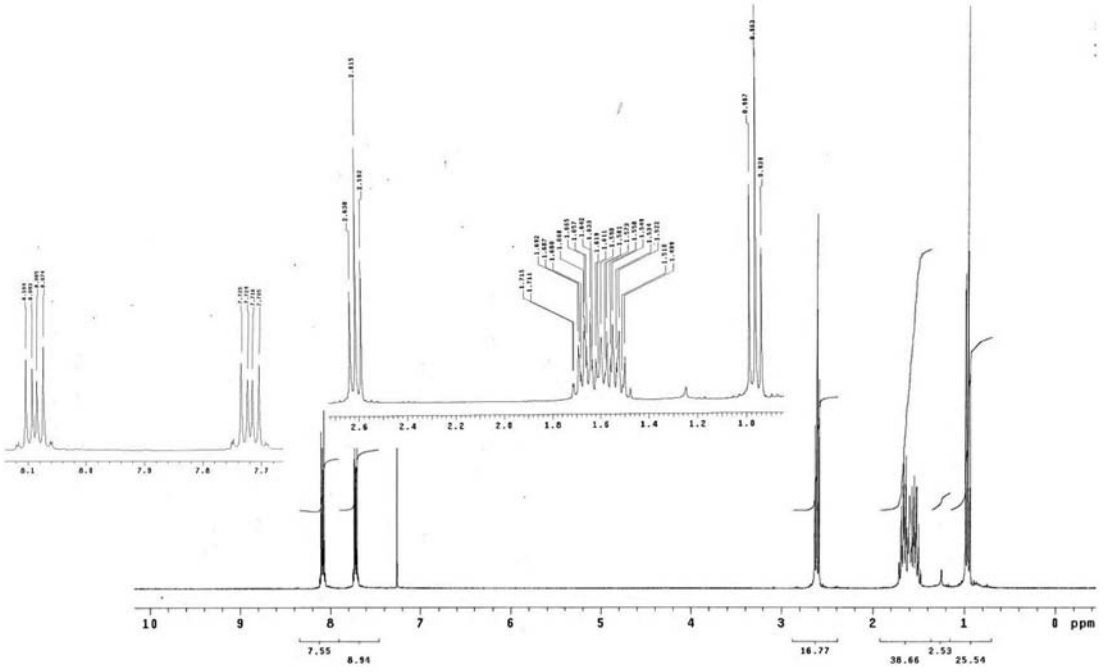

Figure S39. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2g**.

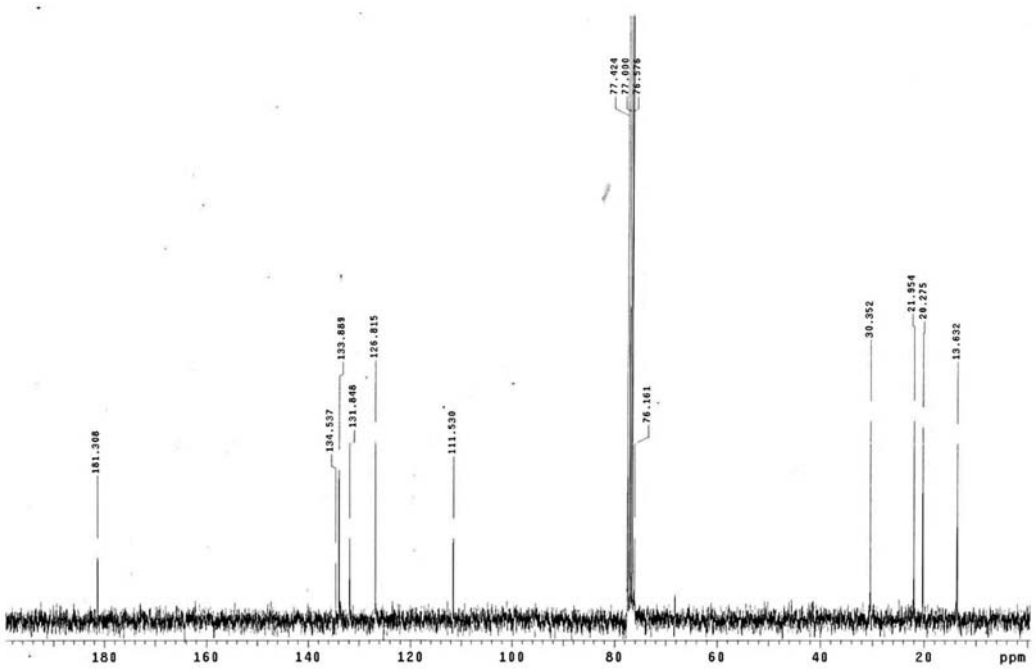

Figure S40. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2g**.

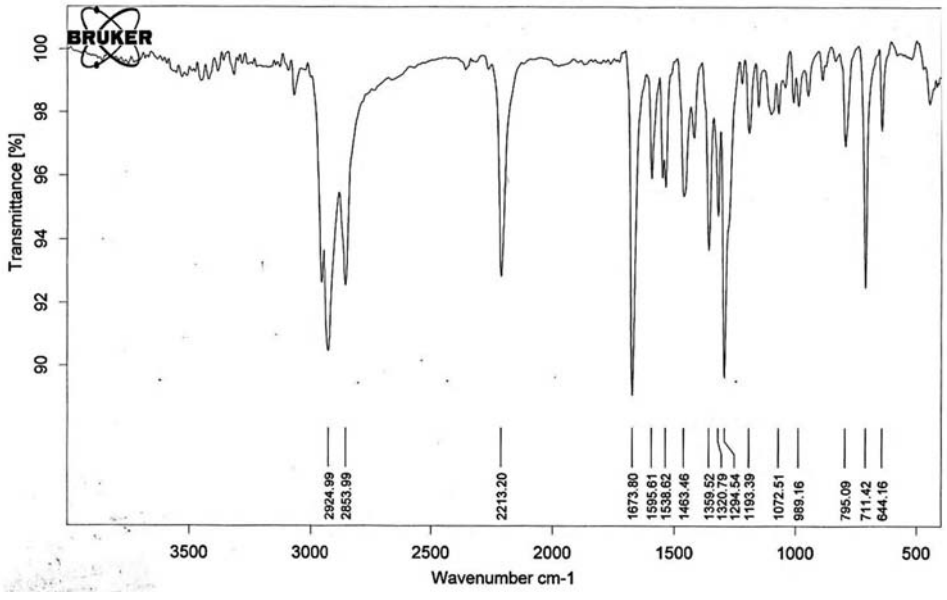

Figure S41. Infrared spectrum of **2h** (KBr).

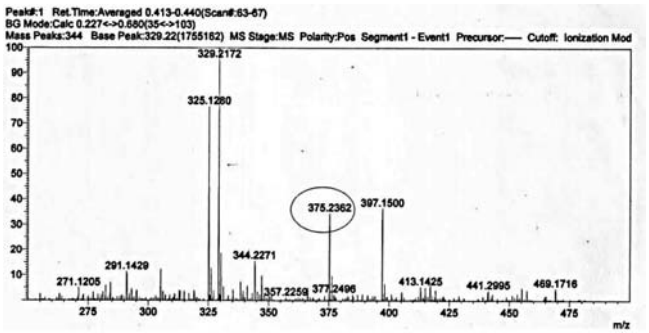

Figure S42. High resolution mass spectra (ESI-MS) of **2h**.

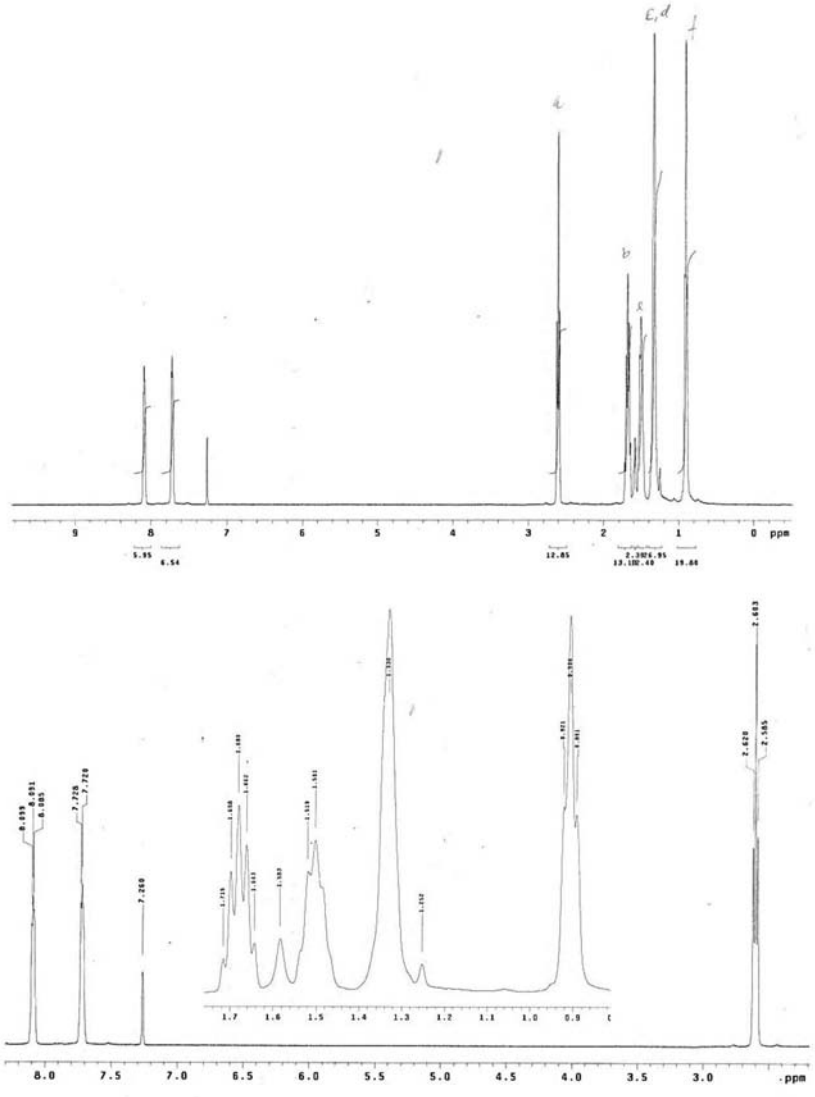

Figure S43. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **2h**.

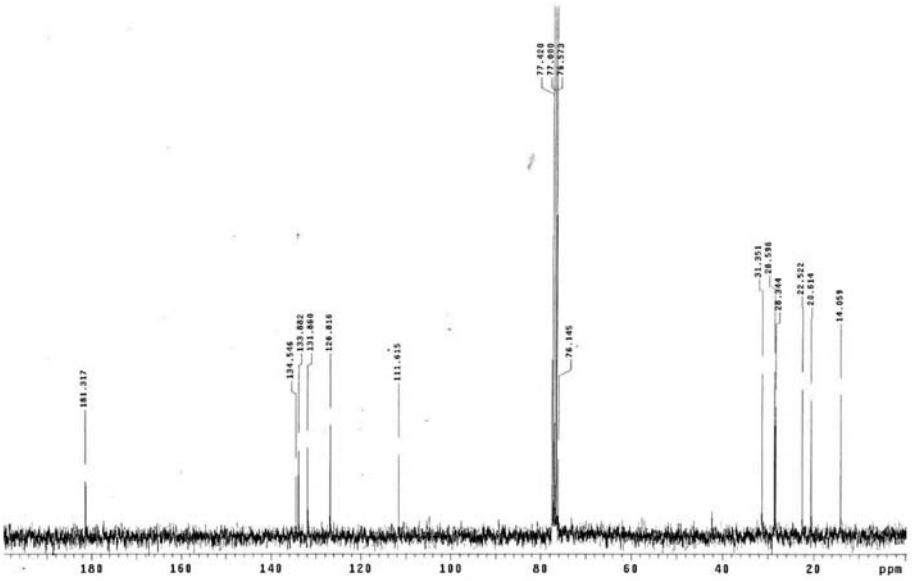

Figure S44. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of **2h**.

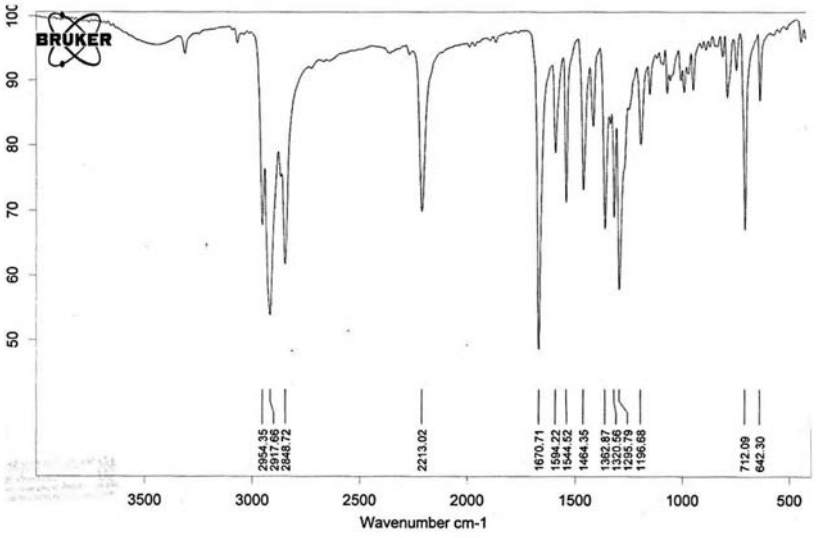

Figure S45. Infrared spectrum of **2i** (KBr).

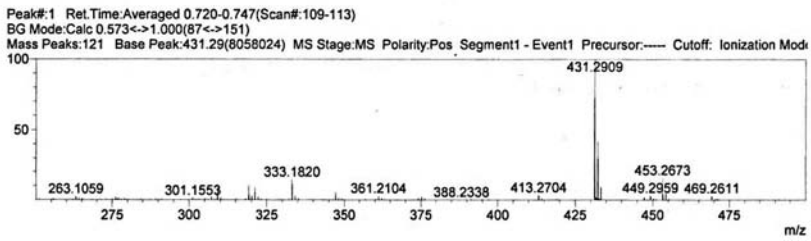

Figure S46. High resolution mass spectra (ESI-MS) of **2i**.

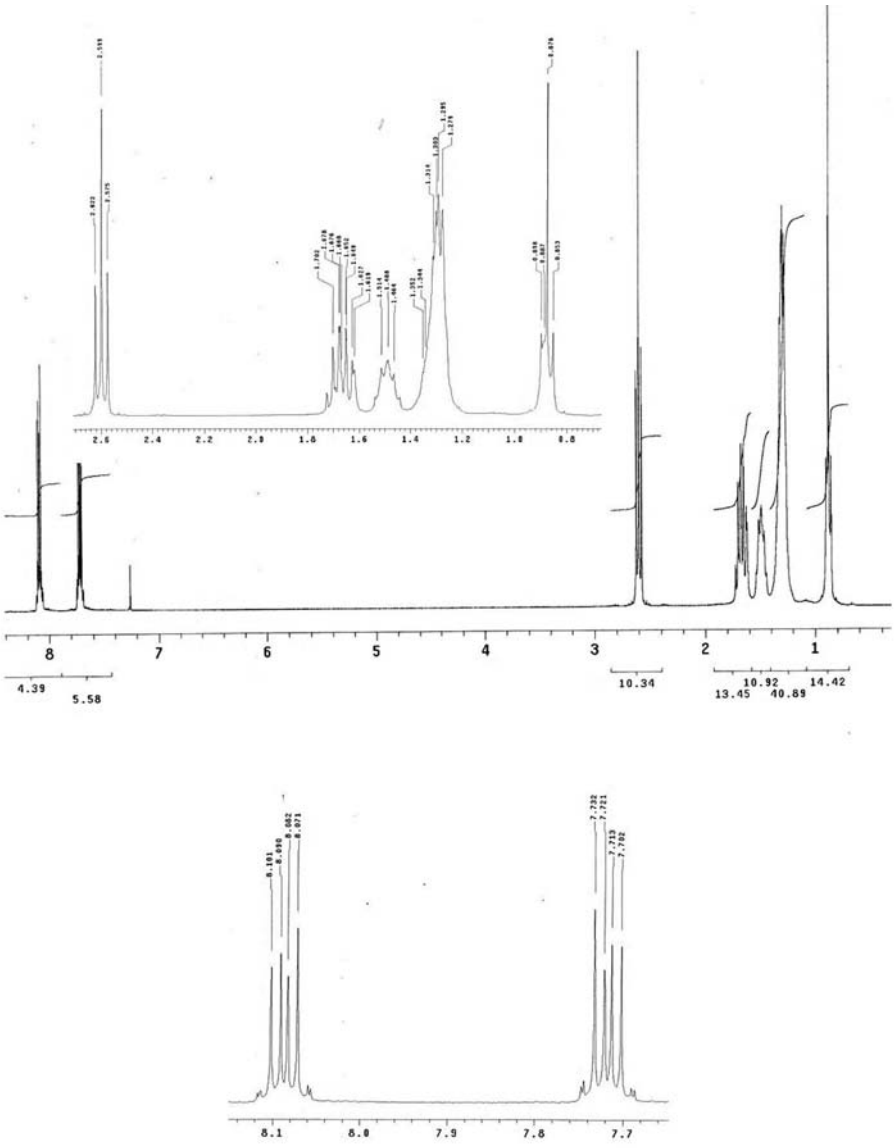

Figure S47. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **2i**.

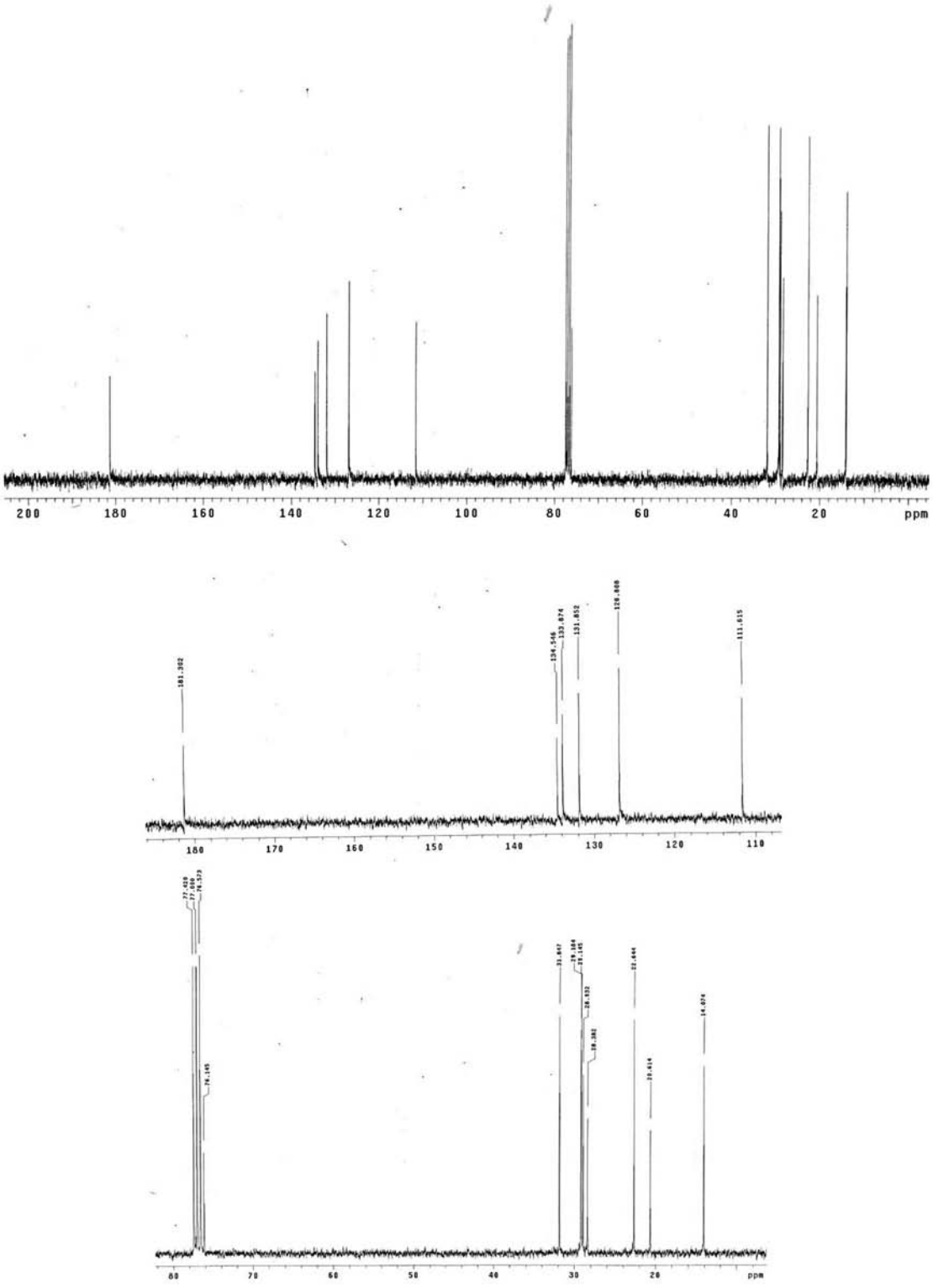

Figure S48. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **2i**.