

Supporting Information

One-pot sequential alkynylation and cycloaddition:

Regioselective construction and biological
evaluation of novel benzoxazole-triazole derivatives

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2-(3-Benzyl-5-phenyl-3H-[1,2,3]triazol-4-yl)-benzooxazole 4{I,I,I}:

¹H NMR (CDCl₃, 300MHz): δ 7.75-7.71 (m, 3H), 7.39-7.34 (m, 4H), 7.33-7.25 (m, 4H), 7.20-7.15 (m, 3H), 6.06 (s, 2H); ¹³C NMR (CDCl₃, 75 MHz): δ 153.05, 149.97, 149.09, 141.01, 134.98, 130.00, 129.05, 128.85, 128.73, 128.37, 128.12, 126.33, 125.21, 121.65, 120.57, 110.92, 53.80; HRMS (ESI): calcd for C₂₂H₁₆N₄O [M+Na]⁺ 375.1216, found 375.1214.

4-(5-Benzooxazol-2-yl-4-phenyl-[1,2,3]triazol-1-ylmethyl)-benzonitrile 4{I,I,3}:

¹H NMR (CDCl₃, 300MHz): δ 7.82-7.79 (m, 3H), 7.60 (d, J=8.1 Hz, 2H), 7.52 (s, 2H), 7.48-7.46 (m, 4H), 7.42 (d, J=4.2 Hz, 2H), 6.23 (s, 2H); ¹³C NMR (CDCl₃, 75 MHz): δ 152.66, 148.64, 145.11, 140.92, 140.12, 134.27, 132.56, 130.90, 129.28, 128.97, 128.78, 128.40, 126.59, 126.05, 125.40, 120.49, 115.38, 110.99, 53.19; HRMS (ESI): calcd for C₂₃H₁₅N₅O [M+H]⁺ 378.1349, found 378.1350.

2-[3-(4-Nitro-benzyl)-5-phenyl-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{I,I,4}:

¹H NMR (CDCl₃, 300MHz): δ 8.17 (d, J=8.7 Hz, 2H), 7.83-7.80 (m, 3H), 7.58 (d, J=8.7 Hz, 2H), 7.50-7.47 (m, 4H), 7.46-7.40 (m, 2H), 6.29 (s, 2H); ¹³C NMR (CDCl₃, 75 MHz): δ 150.36, 149.88, 147.94, 142.02, 140.89, 129.70, 129.30, 129.01, 128.41, 126.61, 125.43, 125.09, 123.98, 122.81, 121.57, 120.50, 111.00, 52.98; HRMS (ESI): calcd for C₂₂H₁₅N₅O₃ [M+H]⁺ 398.1248, found 398.1256.

2-[3-Benzyl-5-(4-methoxy-phenyl)-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{I,2,I}:

¹H NMR (CDCl₃, 300 MHz): δ 7.75 (t, J=4.8 Hz, 1H), 7.69 (d, J=8.7 Hz, 2H), 7.43-7.40 (m, 2H), 7.33 (t, J=4.5 Hz, 2H), 7.28 (t, J= 4.8 Hz, 3H), 7.16 (s, 1H), 6.92 (s, 1H), 6.88 (s, 1H), 6.06 (s, 2H), 3.78 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz): δ 160.30, 153.22, 149.92, 148.97, 141.02, 135.05, 130.20, 128.70, 128.32, 128.10, 126.23, 125.17, 122.45, 121.05, 120.52, 113.83, 110.89; HRMS (ESI): calcd for C₂₃H₁₈N₄O₂ [M+Na]⁺ 405.1322, found 405.1325.

2-[3-(2,5-Difluoro-benzyl)-5-(4-methoxy-phenyl)-3H-[1,2,3]triazol-4-yl]-benzooxazole

4{1,2,2}:

¹H NMR (CDCl₃, 300 MHz): δ 7.84 (d, J=8.4 Hz, 3H), 7.53 (s, 1H), 7.43 (s, 2H), 7.02 (d, J=8.1 Hz, 3H), 6.97–6.88 (m, 2H), 6.19 (s, 2H), 3.89 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz): δ 160.43, 160.29, 157.87, 157.07, 154.59, 152.93, 149.98, 148.90, 140.96, 130.27, 126.36, 125.25, 122.19, 121.32, 120.61, 116.11, 115.77, 110.92, 55.33, 47.46; HRMS (ESI): calcd for C₂₃H₁₆N₄O₂ [M+H]⁺ 419.1314, found 419.1323.

4-[5-Benzooxazol-2-yl-4-(4-methoxy-phenyl)-[1,2,3]triazol-1-ylmethyl]-benzonitrile

4{1,2,3}:

¹H NMR (CDCl₃, 300MHz): δ 7.74-7.68 (m, 3H), 7.52 (d, J=8.4, 2H), 7.42 (d, J=6.6Hz, 3H), 7.35-7.32 (m, 2H), 6.93 (d, J=8.7 Hz, 2H), 6.15 (s, 2H), 3.82 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz): δ 160.56, 152.96, 149.92, 147.66, 141.10, 140.23, 132.55, 132.49, 130.43, 130.34, 128.76, 126.49, 125.37, 120.44, 118.08, 113.87, 113.57, 110.97, 55.35, 53.20; HRMS (ESI): calcd for C₂₄H₁₇N₅O₂ [M+Na]⁺ 430.1274, found 430.1293.

2-[5-(4-Methoxy-phenyl)-3-(4-nitro-benzyl)-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{1,2,4}:

¹H NMR (CDCl₃, 300MHz): δ 8.16 (d, J=8.7 Hz, 2H), 7.78 (d, J=8.7 Hz, 3H), 7.56 (d, J=8.4 Hz, 2H), 7.50-7.46 (m, 1H), 7.43-7.40 (m, 2H), 7.01 (d, J=8.7 Hz, 2H), 6.27 (s, 2H), 3.88 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz): δ 160.58, 149.86, 149.12, 140.83, 140.24, 132.62, 130.31, 128.91, 126.51, 125.38, 122.12, 121.10, 120.45, 119.59, 118.44, 113.98, 110.97, 55.35, 53.22; HRMS (ESI): calcd for C₂₃H₁₇N₅O₄ [M+H]⁺ 428.1353, found 428.1353.

2-[3-(4-Fluoro-benzyl)-5-(4-methoxy-phenyl)-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{1,2,5}:

¹H NMR (CDCl₃, 300 MHz): δ 7.77-7.67 (m, 3H), 7.44-7.28 (m, 5H), 6.92-6.85 (m, 4H), 6.03 (s, 2H), 3.67 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz): δ 160.34, 153.36, 149.88, 141.01, 130.85,

130.21, 128.45, 126.32, 125.24, 122.34, 120.96, 120.51, 116.13, 115.79, 115.52, 113.84, 110.92, 55.42, 53.01; HRMS (ESI): calcd for $C_{23}H_{17}N_4O_2$ $[M+Na]^+$ 423.1228, found 423.1262.

2-[3-(2,5-Difluoro-benzyl)-5-p-tolyl-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{1,3,2}:

1H NMR ($CDCl_3$, 300 MHz): δ 7.76-7.74 (m, 1H), 7.63 (d, $J=7.8$ Hz, 2H), 7.43-7.38 (m, 2H), 7.34-7.32 (m, 3H), 7.29-7.26 (m, 3H), 7.17 (s, 2H), 6.06 (s, 2H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.13, 153.07, 149.86, 149.07, 140.93, 138.93, 134.92, 129.00, 128.60, 128.23, 128.02, 126.98, 126.14, 125.06, 121.26, 120.43, 110.83, 53.67, 21.31. HRMS (ESI): calcd for $C_{23}H_{18}N_4O$ $[M+H]^+$ 367.1553, found 367.1536.

2-[3-Benzyl-5-(2-bromo-phenyl)-3H-[1,2,3]triazol-4-yl]-benzooxazole 4{1,4,1}:

1H NMR ($CDCl_3$, 300 MHz): δ 7.71 (s, 1H), 7.58 (d, $J=8.4$ Hz, 2H), 7.51 (d, $J=6$ Hz, 1H), 7.36 (s, 6H), 7.26-7.19 (m, 3H), 6.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.86, 149.94, 141.01, 135.10, 132.81, 131.79, 130.59, 128.75, 128.34, 128.17, 127.22, 126.17, 125.08, 125.77, 124.16, 123.59, 121.52, 120.52, 110.89, 53.75; HRMS (ESI): calcd for $C_{22}H_{15}BrN_4O$ $[M+H]^+$ 431.0502, found 431.0482.

2-[3-Benzyl-5-(4-methoxy-phenyl)-3H-[1,2,3]triazol-4-yl]-5-methyl-benzooxazole 4{2,2,1}:

1H NMR ($CDCl_3$, 300 MHz): δ 7.68 (d, $J=8.7$ Hz, 2H), 7.53 (s, 1H), 7.28-7.25 (m, 4H), 7.18-7.11 (m, 2H), 6.89 (d, $J=8.7$ Hz, 2H), 6.04 (s, 2H), 3.78 (s, 3H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.26, 153.24, 148.80, 148.21, 141.24, 135.14, 130.16, 128.88, 128.79, 128.69, 128.10, 127.40, 122.51, 121.18, 120.34, 113.96, 110.23, 55.30, 53.75, 21.46; HRMS (ESI): calcd for $C_{24}H_{20}N_4O_2$ $[M+H]^+$ 397.1659, found 397.1650.

2-[3-(2,5-Difluoro-benzyl)-5-(4-methoxy-phenyl)-3H-[1,2,3]triazol-4-yl]-5-methyl-benzooxazole 4{2,2,2}:

^1H NMR (CDCl_3 , 300 MHz): δ 7.74 (d, $J=8.7$ Hz, 2H), 7.50 (s, 1H), 7.31 (d, $J=8.4$ Hz, 1H), 7.16 (d, $J=9$ Hz, 2H), 7.01-6.74 (m, 4H), 6.08 (s, 2H), 3.79 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 160.39, 157.86, 157.06, 154.56, 152.94, 148.74, 148.26, 141.18, 135.25, 130.24, 128.80, 127.54, 122.26, 121.45, 120.41, 116.09, 115.76, 113.86, 110.26, 55.32, 47.41, 21.44. HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{18}\text{F}_2\text{N}_4\text{O}_2$ $[\text{M}+\text{H}]^+$ 433.1471, found 433.1470.

4-[4-(4-Methoxy-phenyl)-5-(5-methyl-benzooxazol-2-yl)-[1,2,3]triazol-1-ylmethyl]-benzonitrile 4{2,2,3}:

^1H NMR (CDCl_3 , 300MHz): δ 7.69 (d, $J=8.4$ Hz, 2H), 7.52 (d, $J=6.6$ Hz, 3H), 7.41 (d, $J=8.1$ Hz, 2H), 7.28 (d, $J=8.4$ Hz, 1H), 7.14 (d, $J=8.4$ Hz, 1H), 6.92 (d, $J=8.7$ Hz, 2H), 6.13 (s, 2H), 3.80 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 160.44, 152.94, 148.93, 148.09, 141.04, 140.35, 135.39, 132.53, 130.32, 128.77, 127.69, 122.19, 121.25, 120.27, 118.35, 113.86, 112.28, 110.32, 55.33, 53.19, 21.48; HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{19}\text{N}_5\text{O}_2$ $[\text{M}+\text{H}]^+$ 422.1612, found 422.1611.

2-[5-(4-Methoxy-phenyl)-3-(4-nitro-benzyl)-3H-[1,2,3]triazol-4-yl]-5-methyl-benzooxazole 4{2,2,4}:

^1H NMR (CDCl_3 , 300MHz): δ 8.16 (d, $J=8.7$ Hz, 2H), 7.77 (d, $J=8.7$ Hz, 2H), 7.327-7.256 (m, 4H), 7.35 (d, $J=8.4$ Hz, 1H), 7.21 (d, $J=8.4$ Hz, 1H), 6.99 (d, $J=8.7$ Hz, 2H), 6.25 (s, 2H), 3.88 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 160.45, 152.96, 152.03, 151.56, 149.01, 148.08, 142.22, 141.02, 135.43, 130.36, 128.97, 127.73, 123.97, 122.14, 120.27, 113.87, 110.35, 55.36, 52.98, 21.50; HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{19}\text{N}_5\text{O}_4$ $[\text{M}+\text{H}]^+$ 442.1510, found 442.1511.

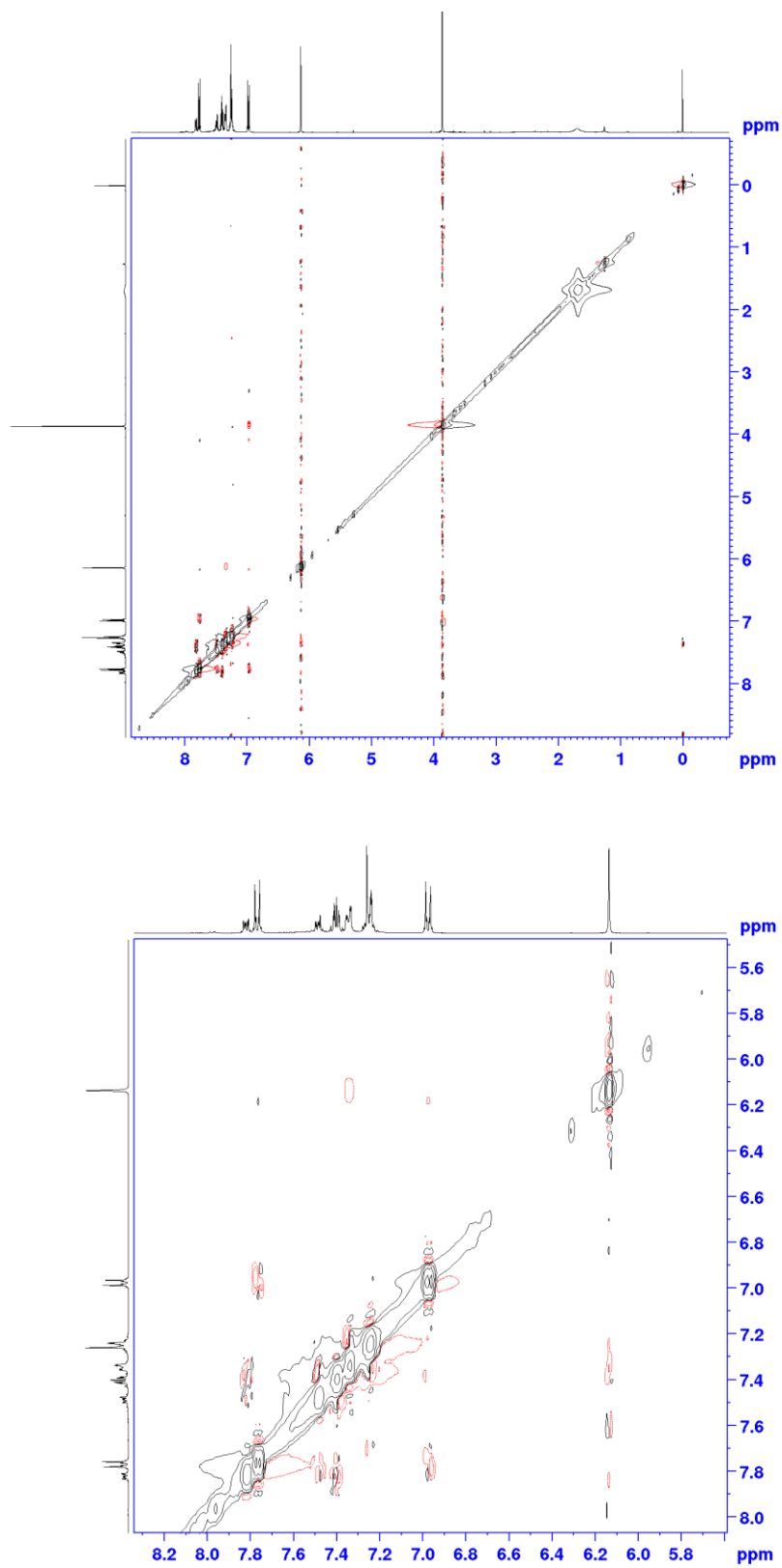


Figure S1. NOESY ^1H NMR spectrum of **4{1,2,1}**.

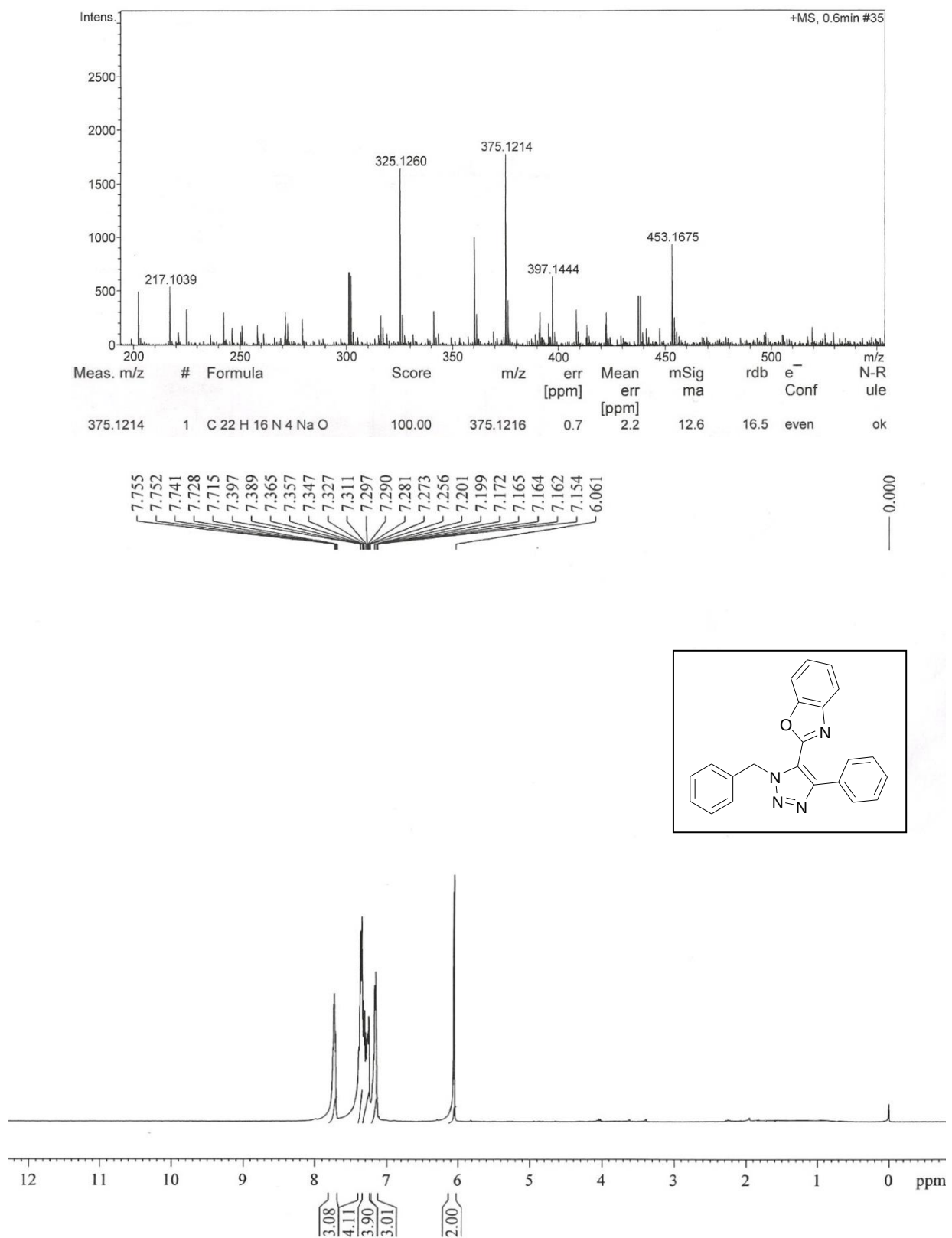


Figure S2. Mass & ¹H NMR spectra of **4{1,1,1}**.

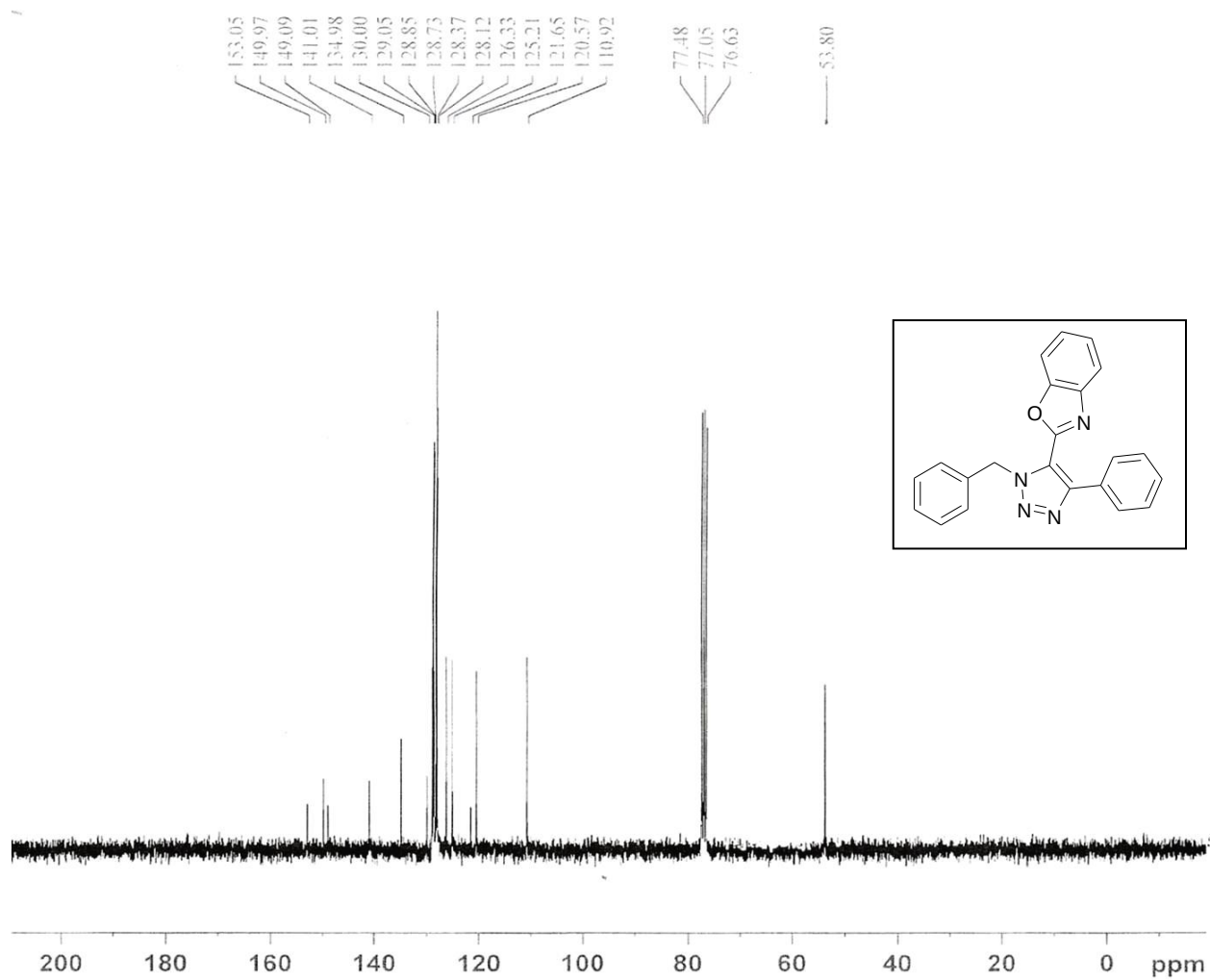


Figure S3. ^{13}C NMR spectrum of **4{1,1,1}**.

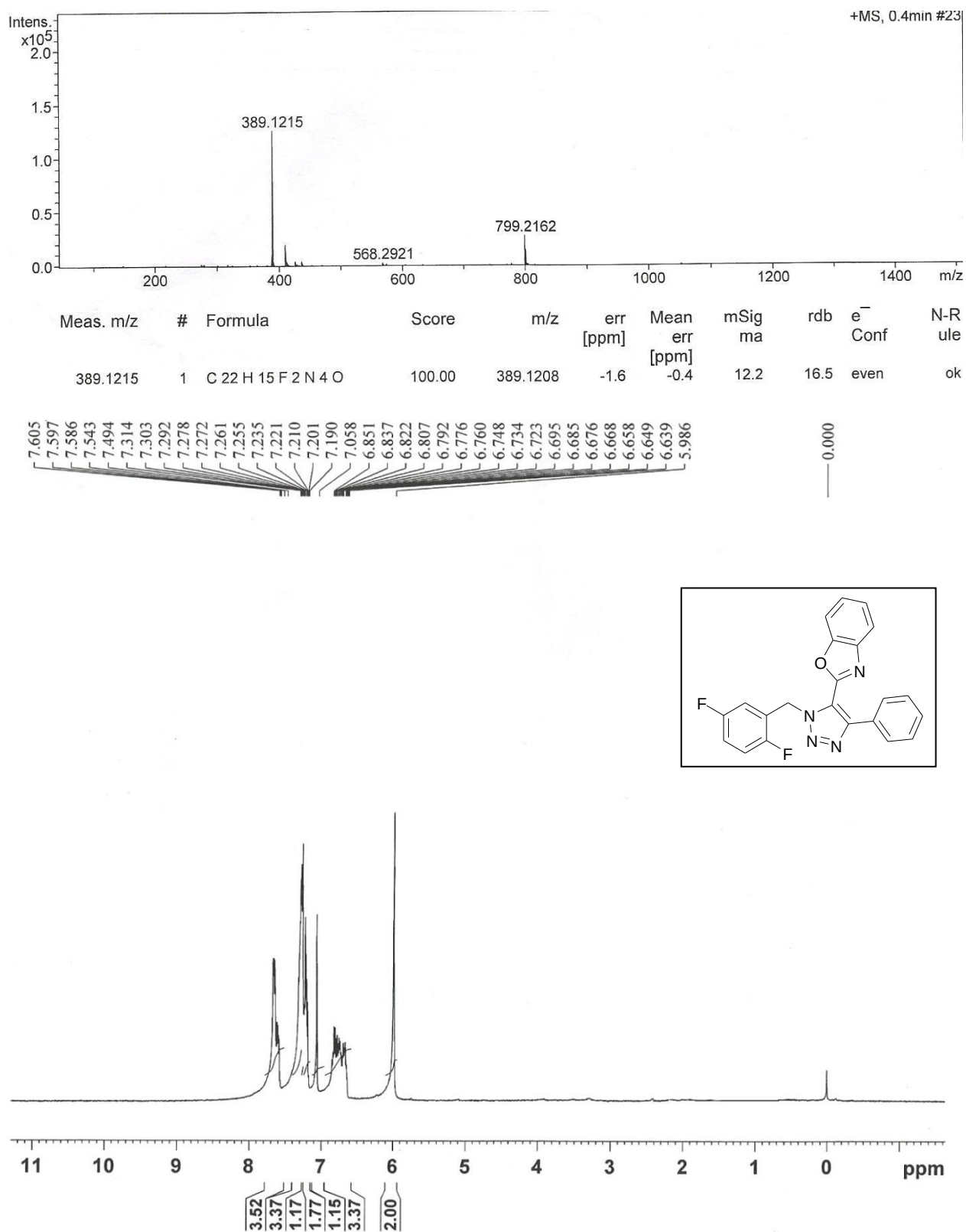


Figure S4. Mass & ¹H NMR spectra of **4{1,1,2}**.

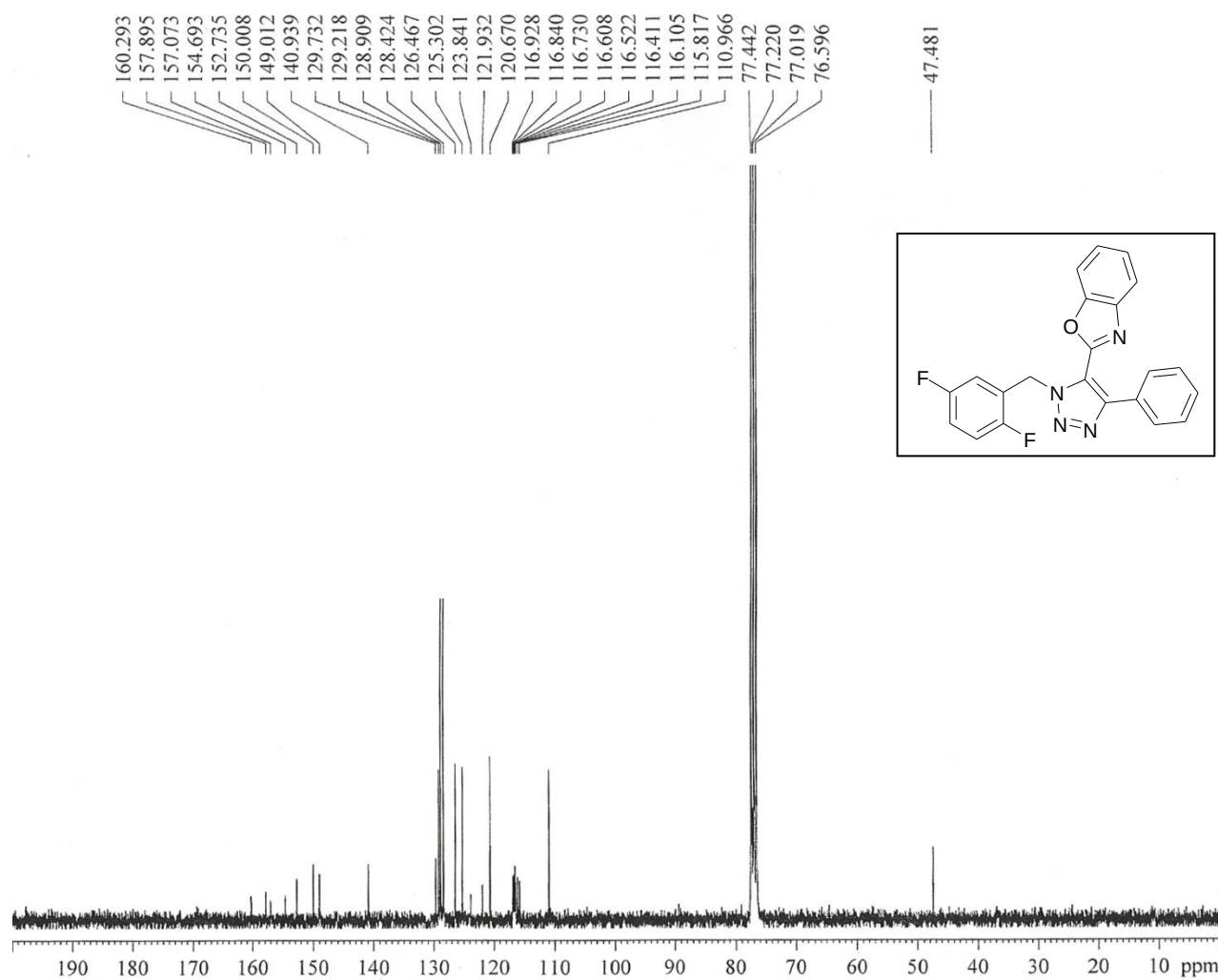


Figure S5. ^{13}C NMR spectrum of 4{1,1,2}.

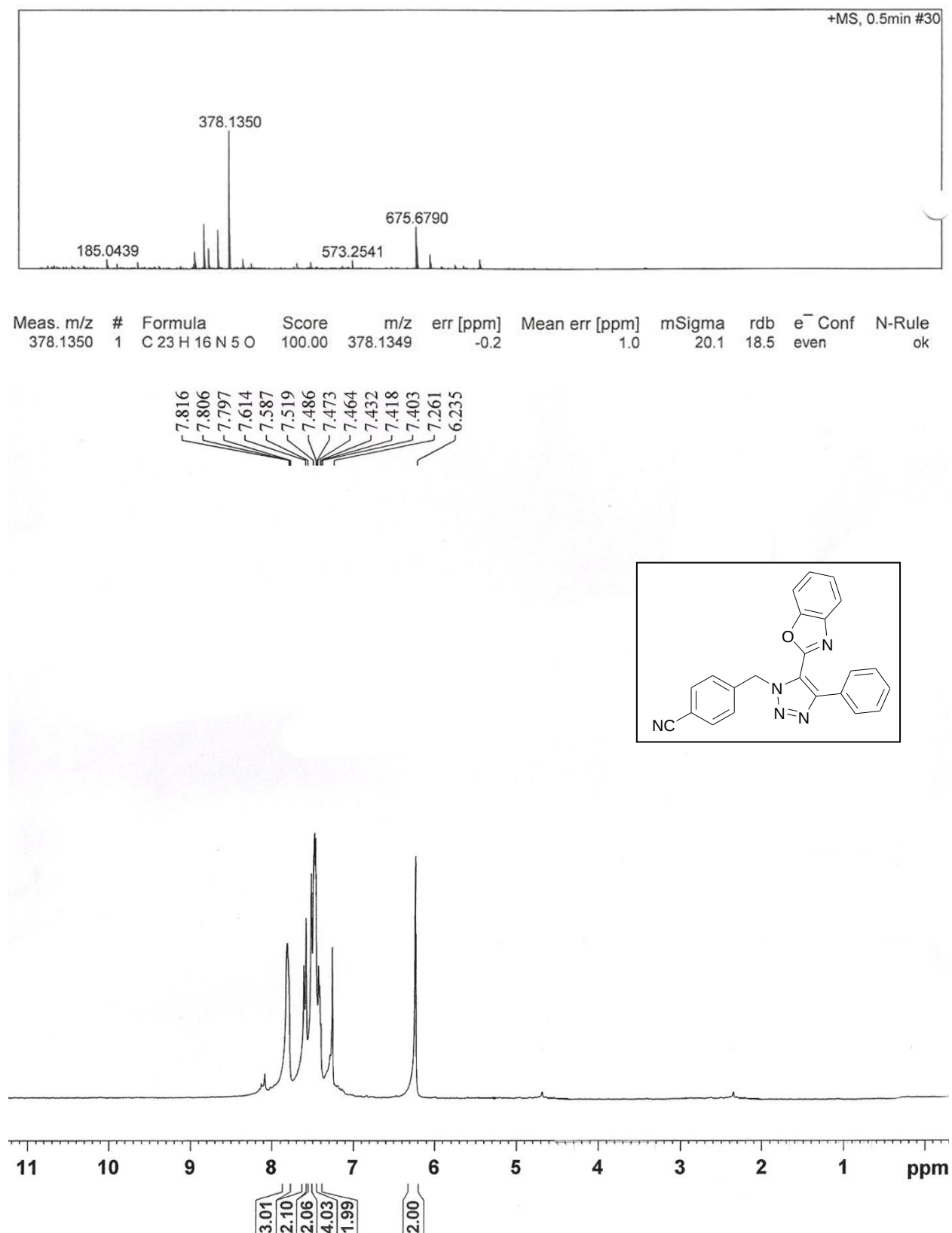


Figure S6. Mass & ^1H NMR spectra of **4{1,1,3}**.

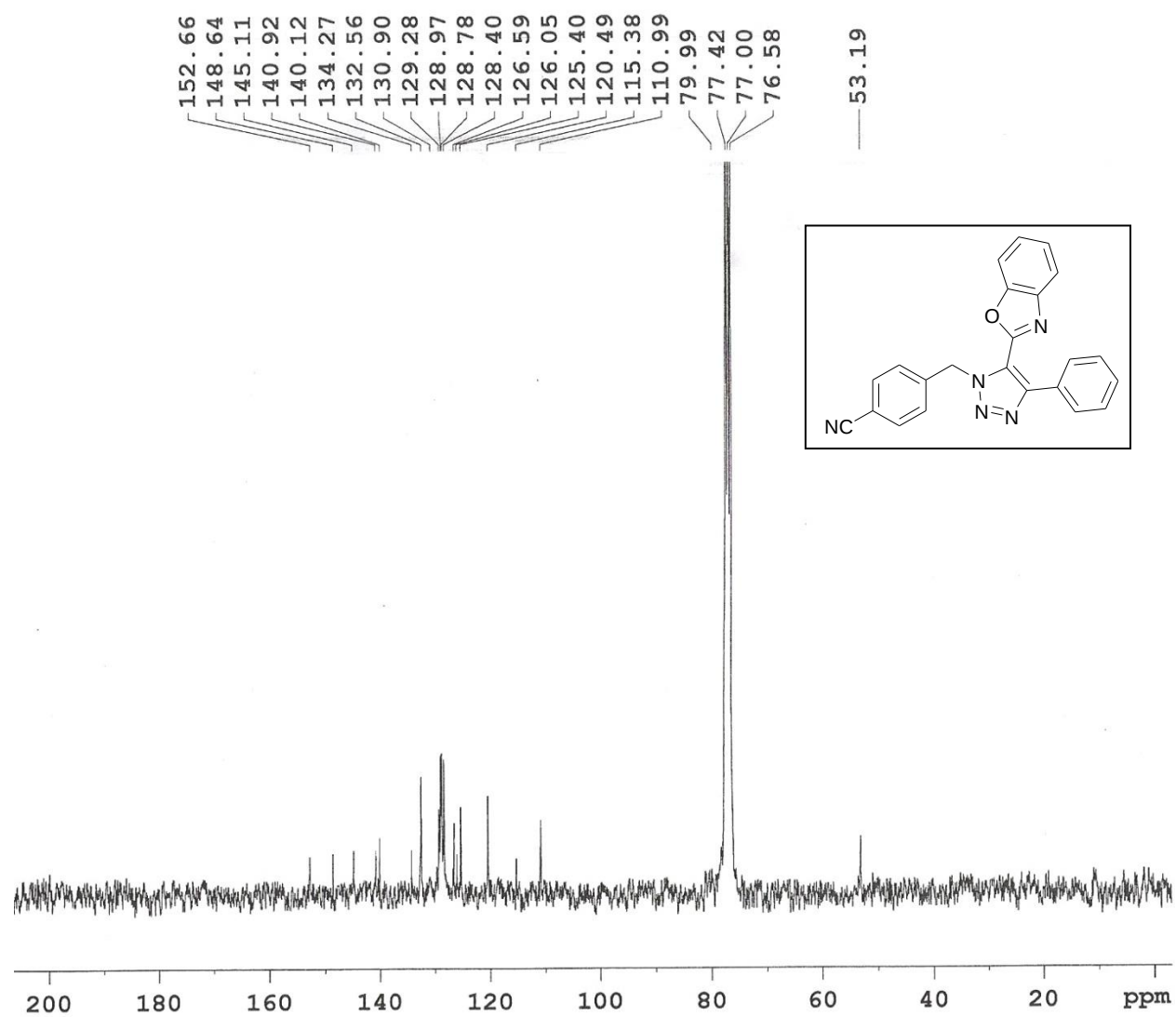


Figure S7. ^{13}C NMR spectrum of 4{1,1,3}.

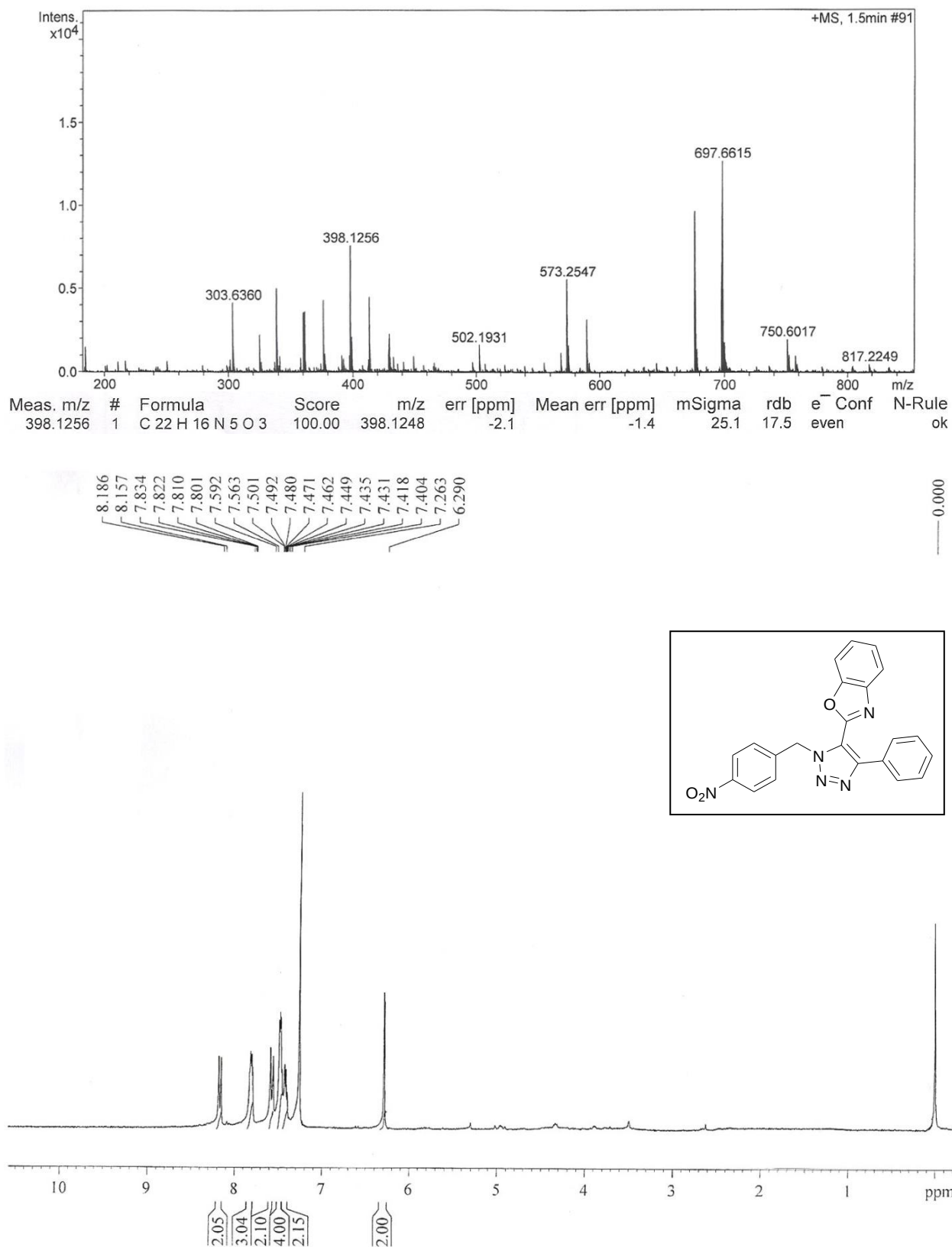


Figure S8. Mass & ¹H NMR spectra of **4{1,1,4}**.

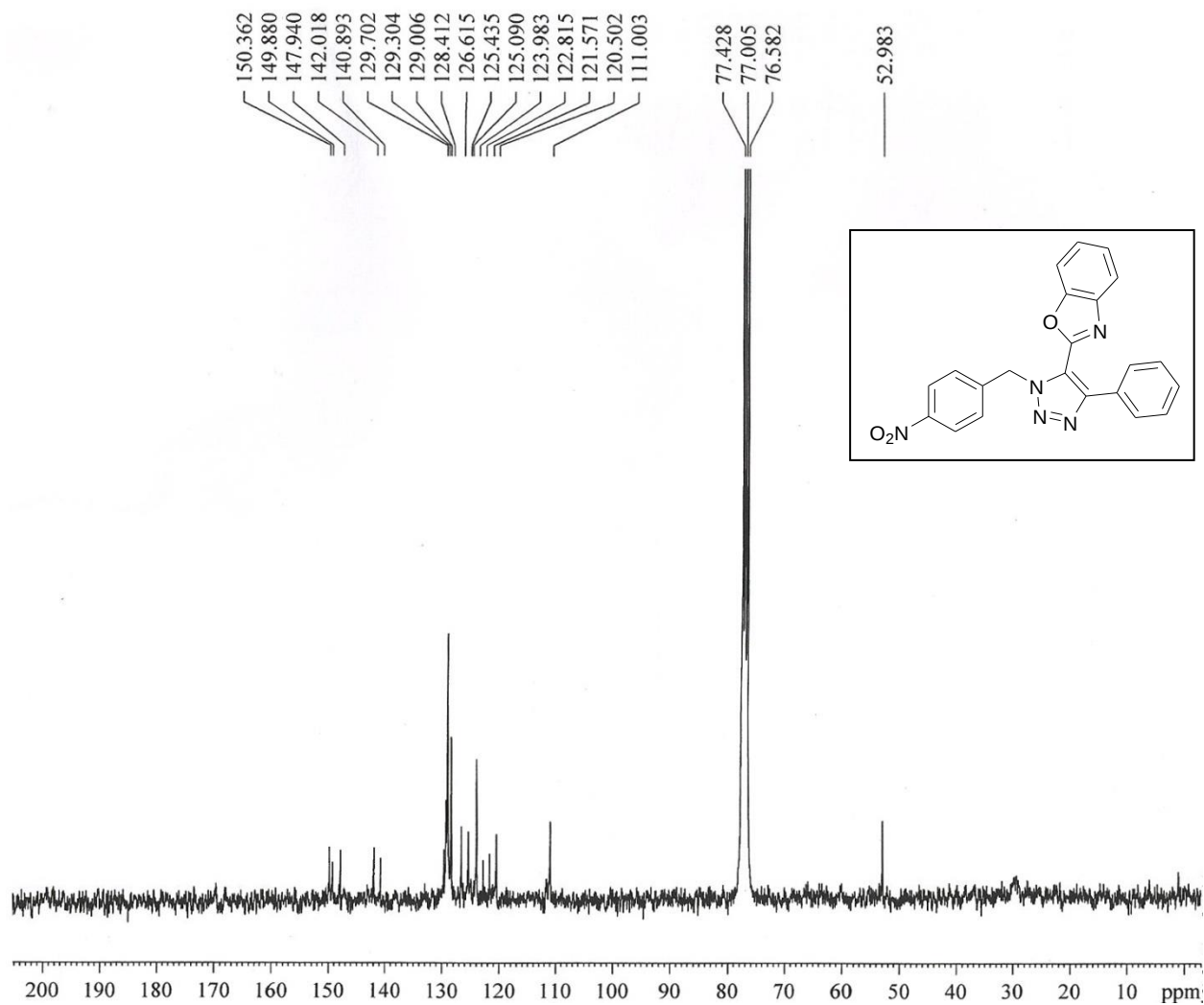


Figure S9. ¹³C NMR spectrum of 4{1,1,4}.

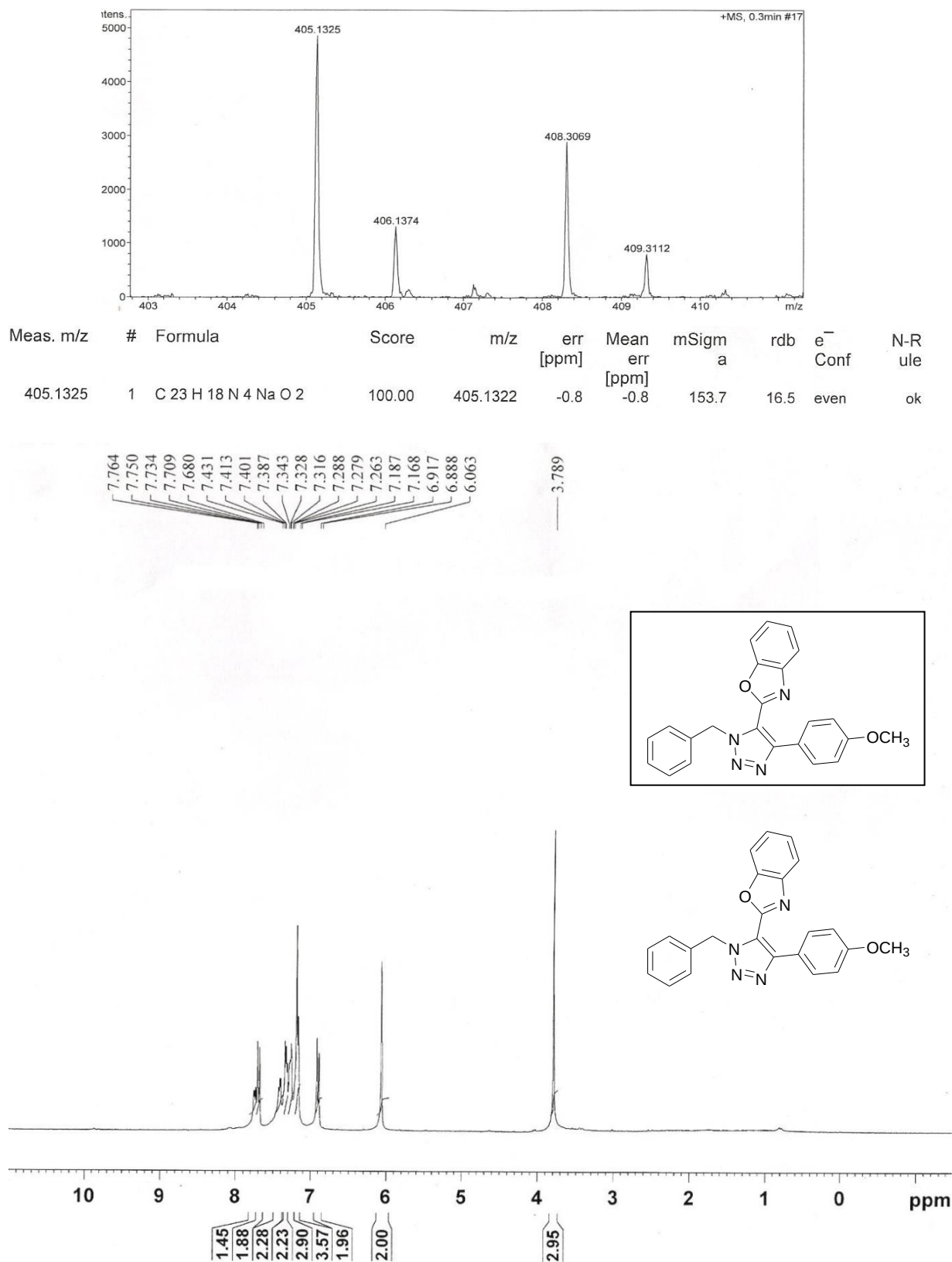


Figure S10. Mass & ¹H NMR spectra of **4{1,2,1}**.

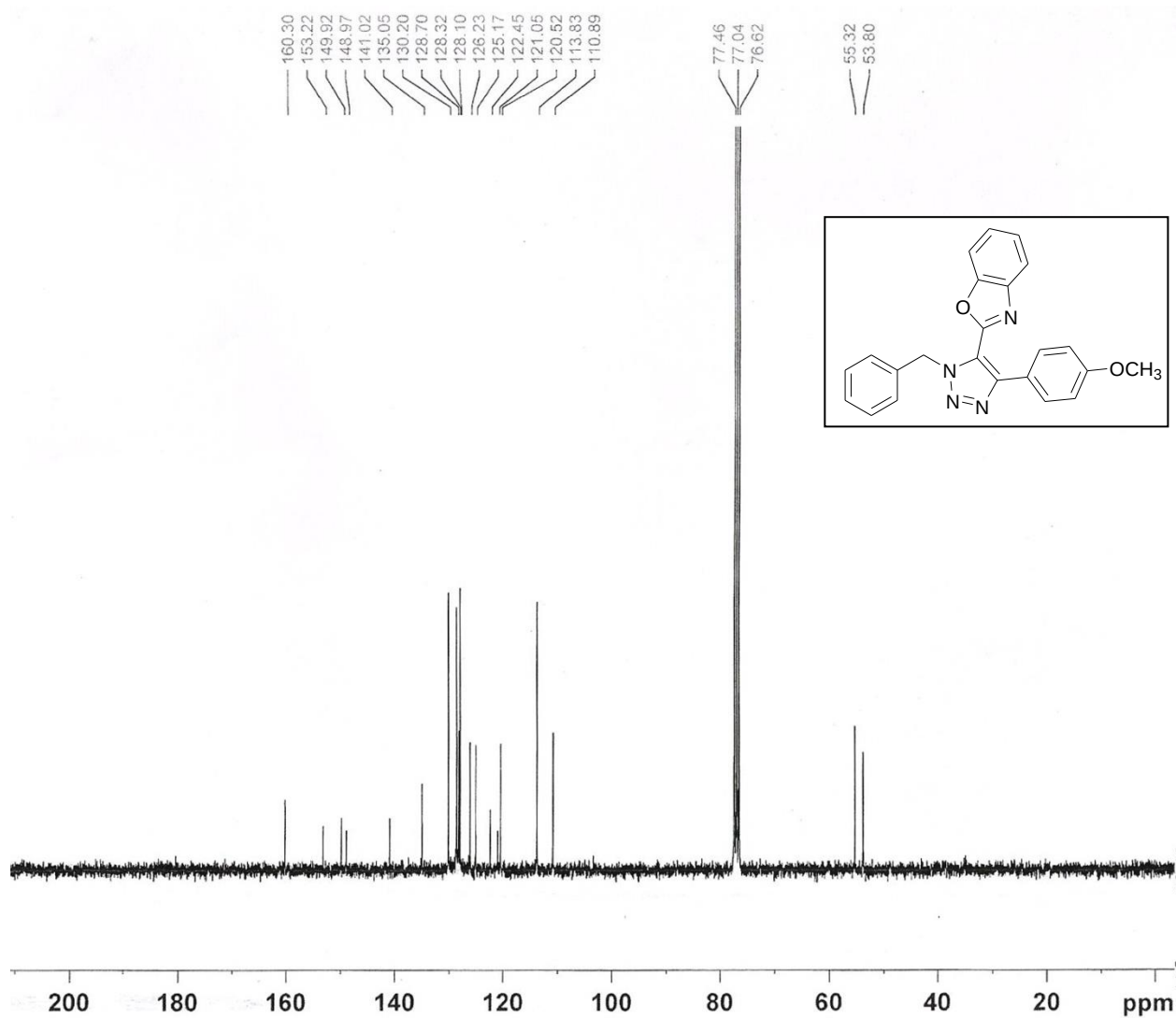


Figure S11. ^{13}C NMR spectrum of **4{1,2,1}**.

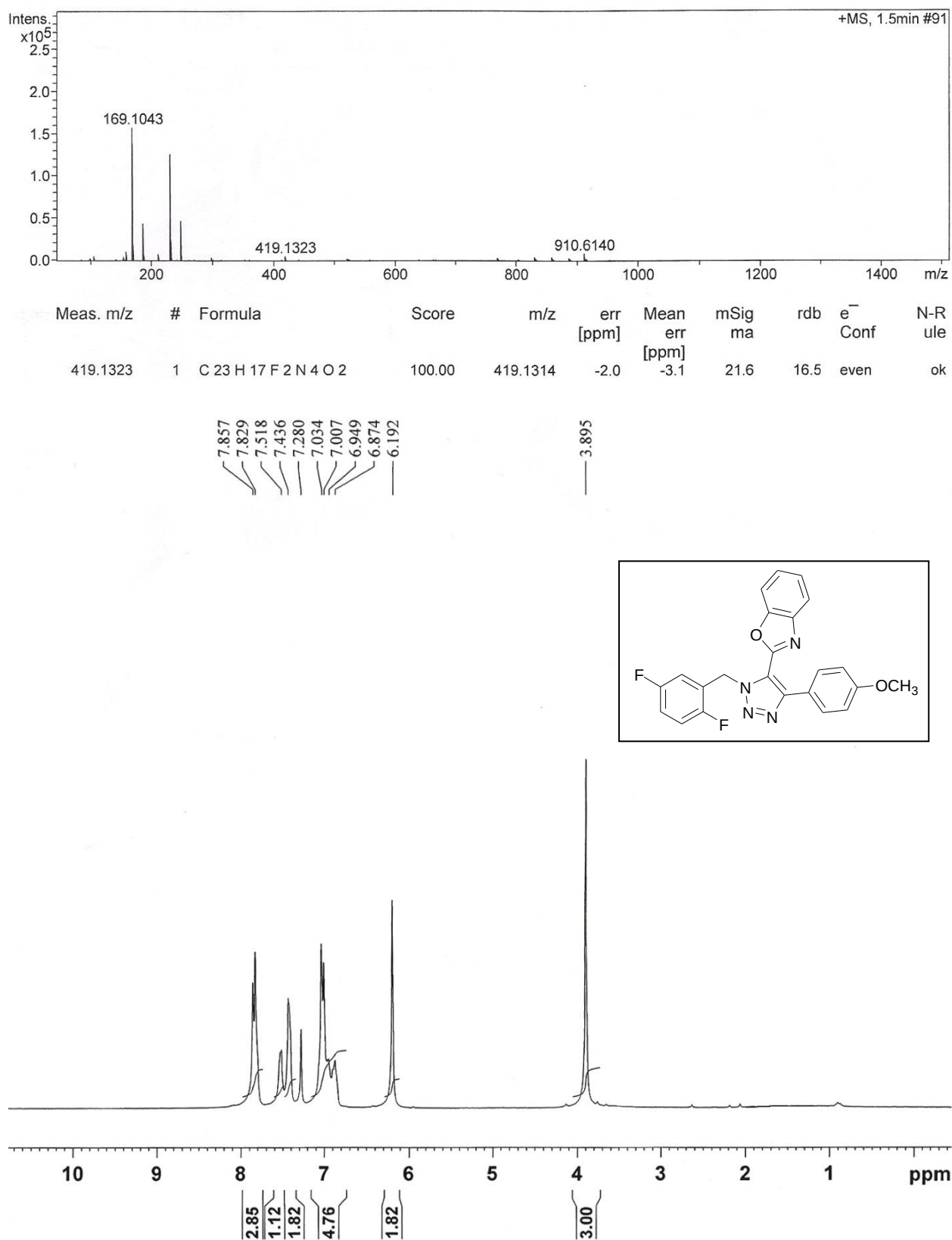


Figure S12. Mass & ¹H NMR spectra of **4{1,2,2}**.

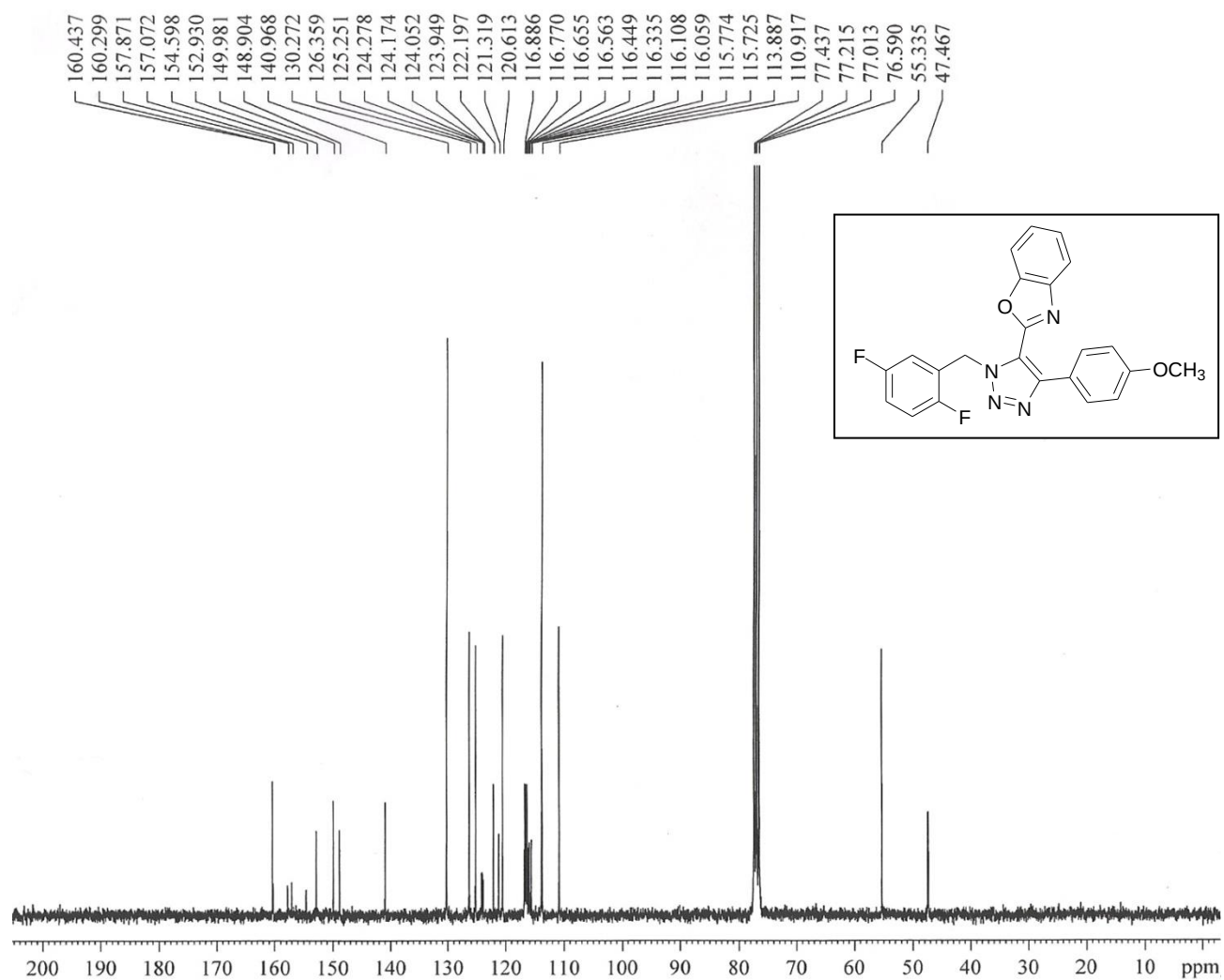


Figure S13. ^{13}C NMR spectrum of **4{1,2,2}**.

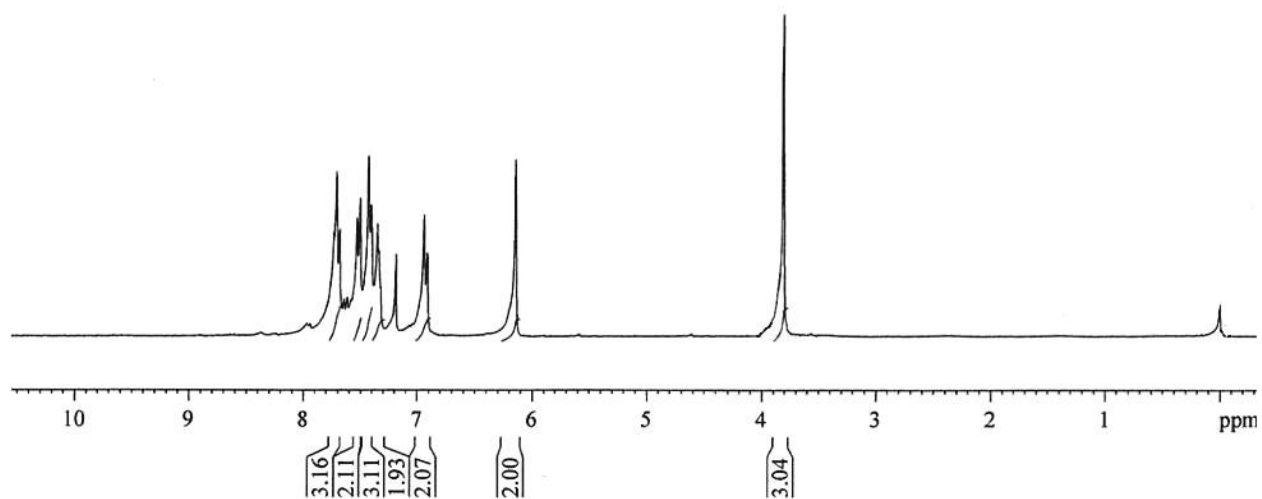
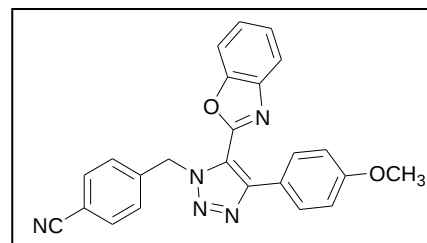
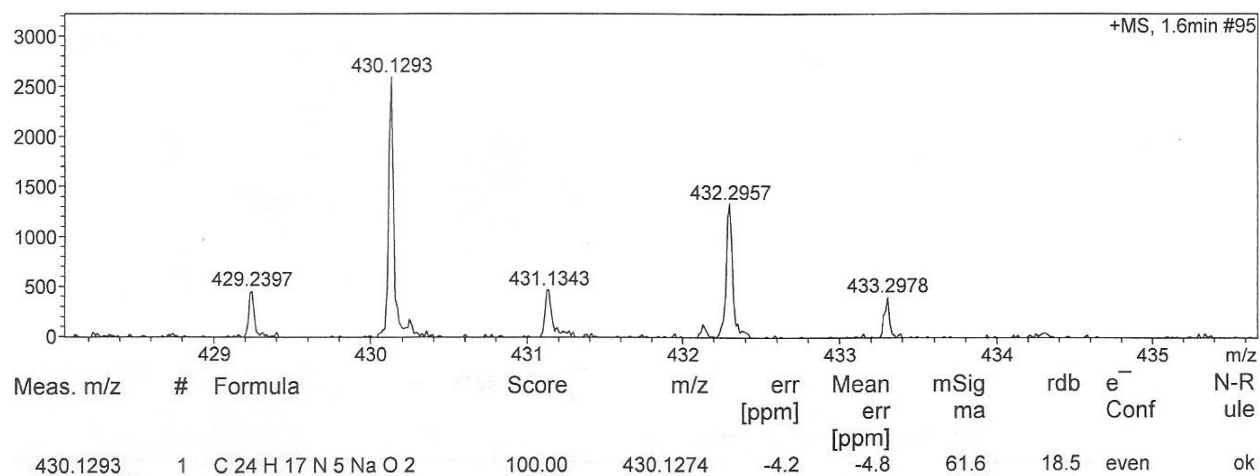


Figure S14. Mass & ¹H NMR spectra of **4{1,2,3}**.

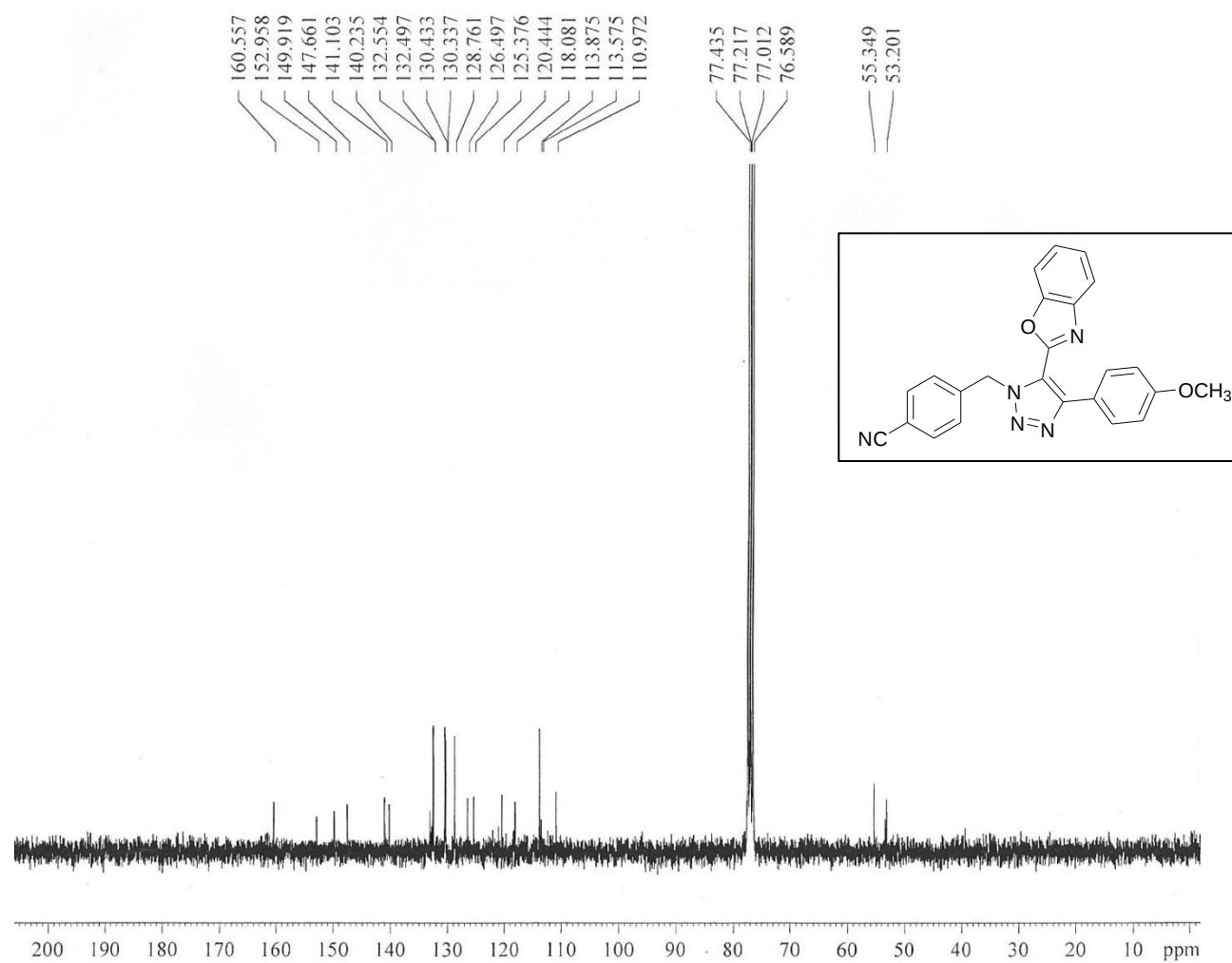


Figure S15. ¹³C NMR spectrum of **4{1,2,3}**.

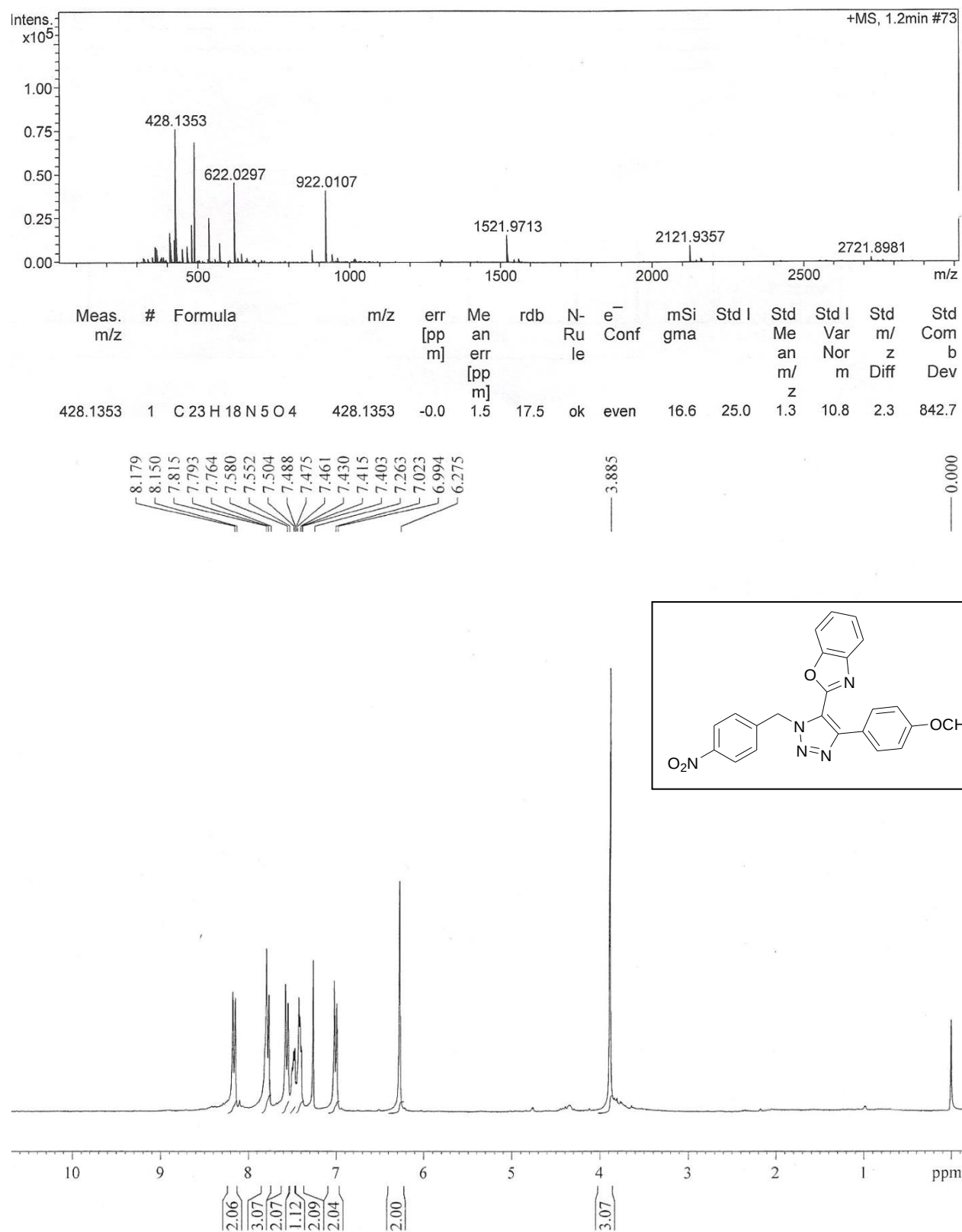


Figure S16. Mass & ¹H NMR spectra of **4{1,2,4}**.

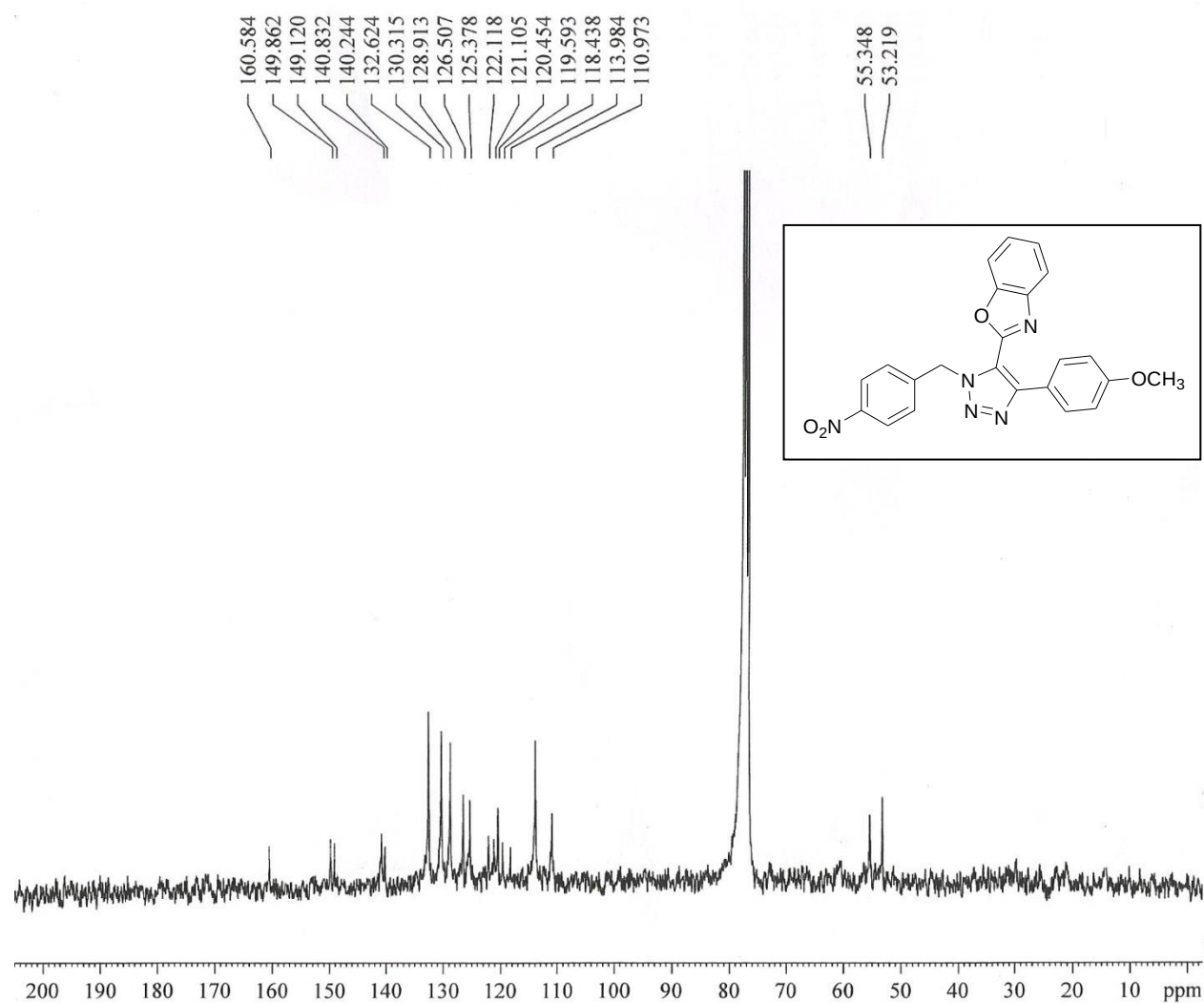


Figure S17. ^{13}C NMR spectrum of **4{1,2,4}**.

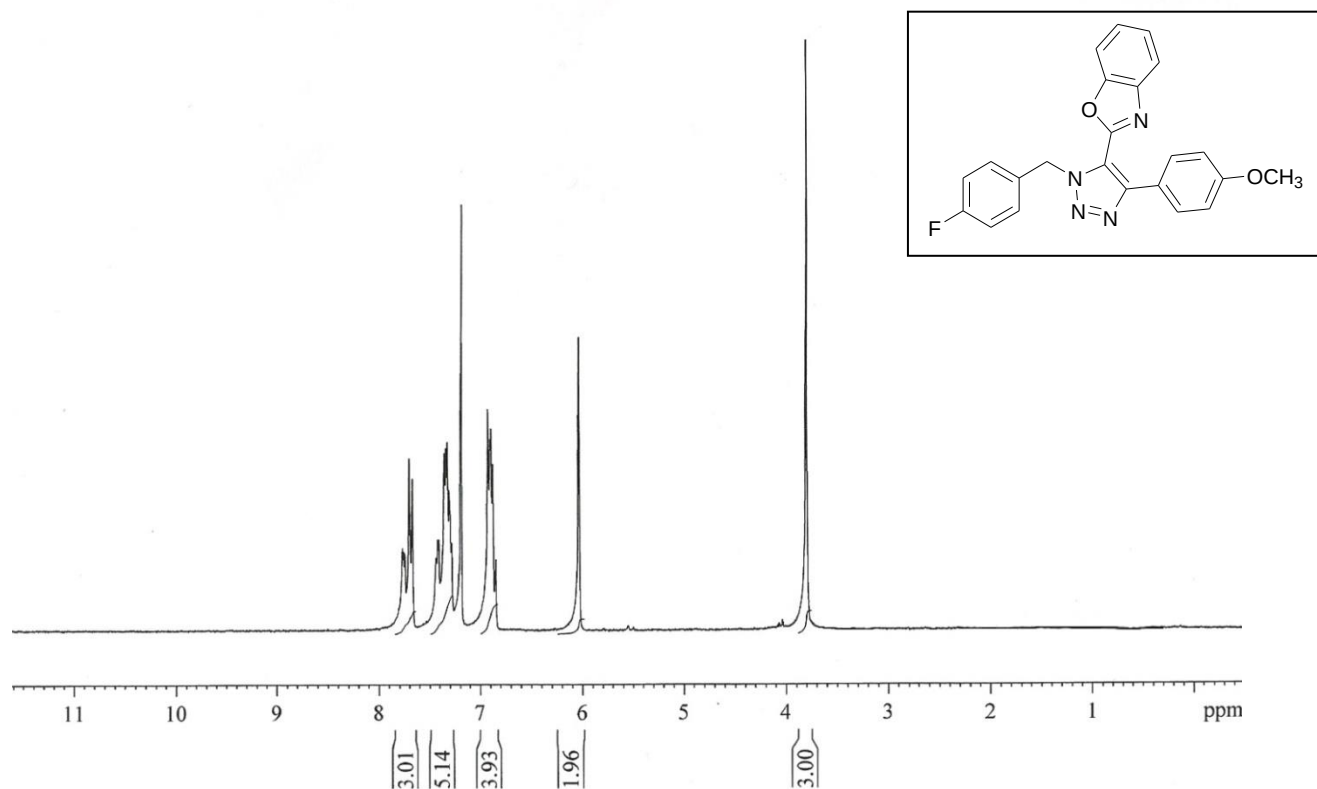
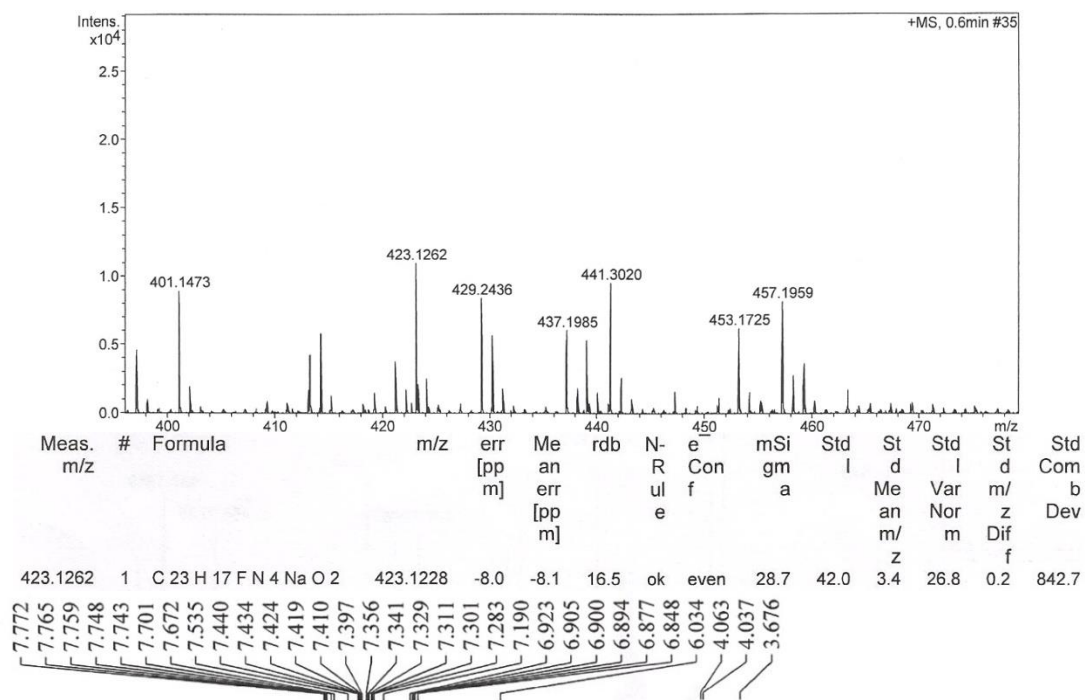


Figure S18. Mass & ¹H NMR spectra of 4{1,2,5}.

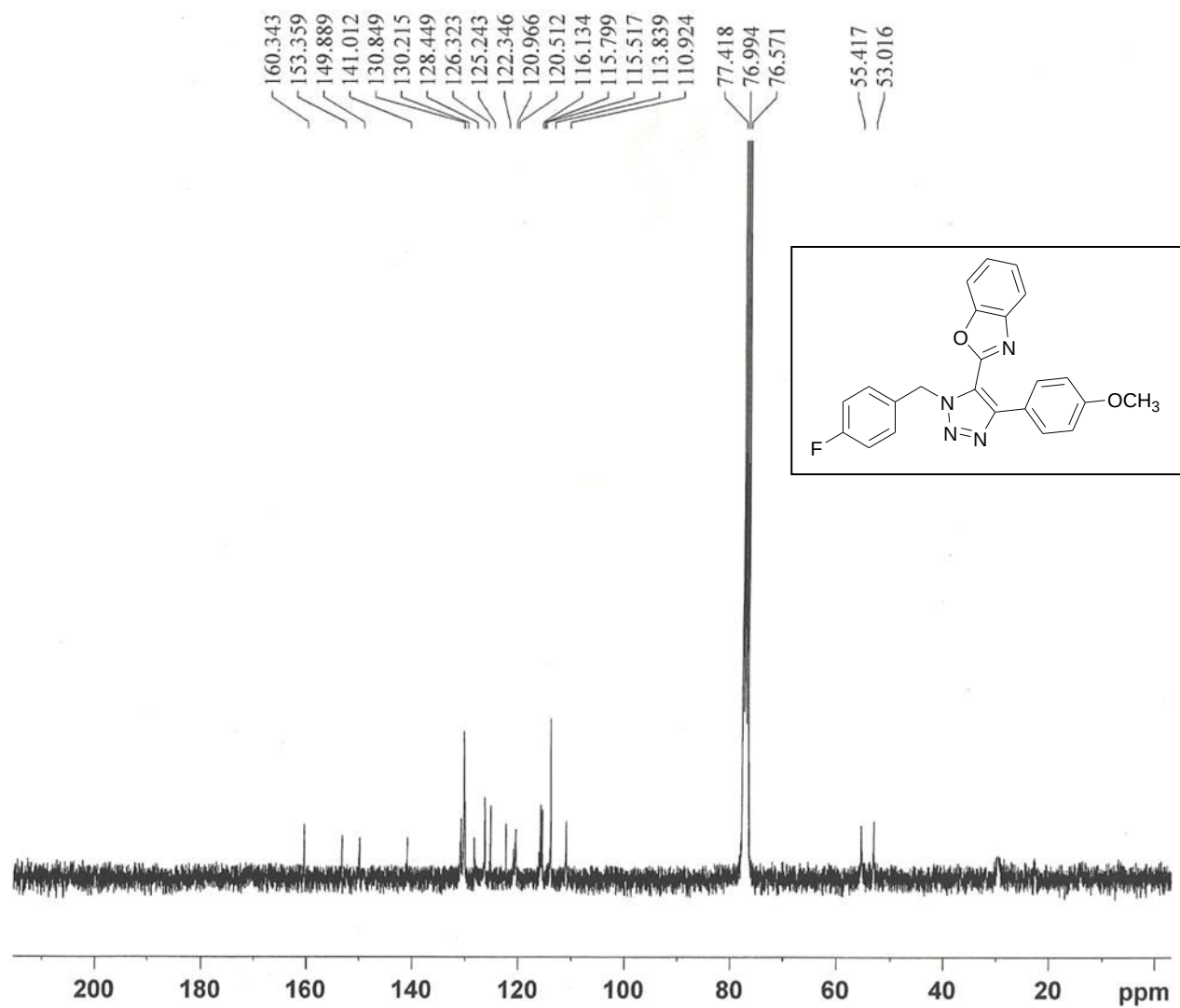
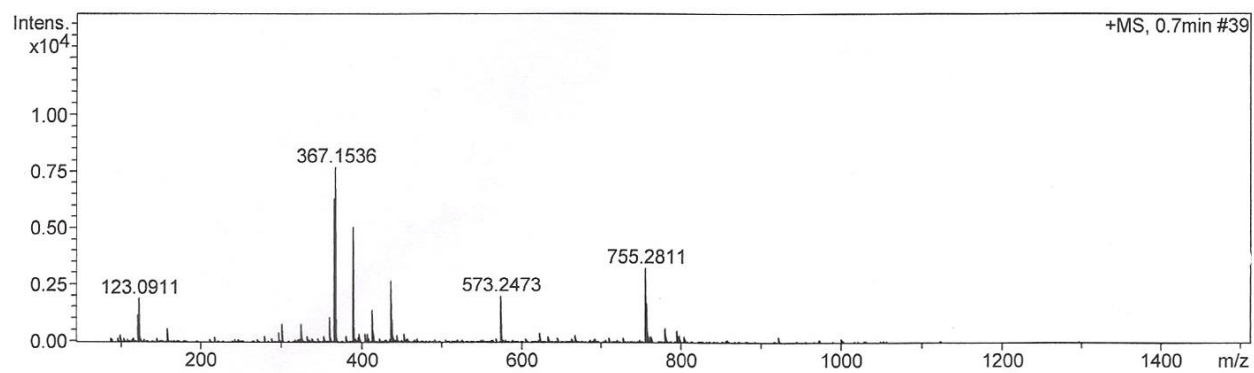


Figure S19. ^{13}C NMR spectrum of 4{1,2,5}.



Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e ⁻ Conf	N-Rule
367.1536	1	C ₂₃ H ₁₉ N ₄ O	100.00	367.1553	4.8	5.9	20.0	16.5	even	ok

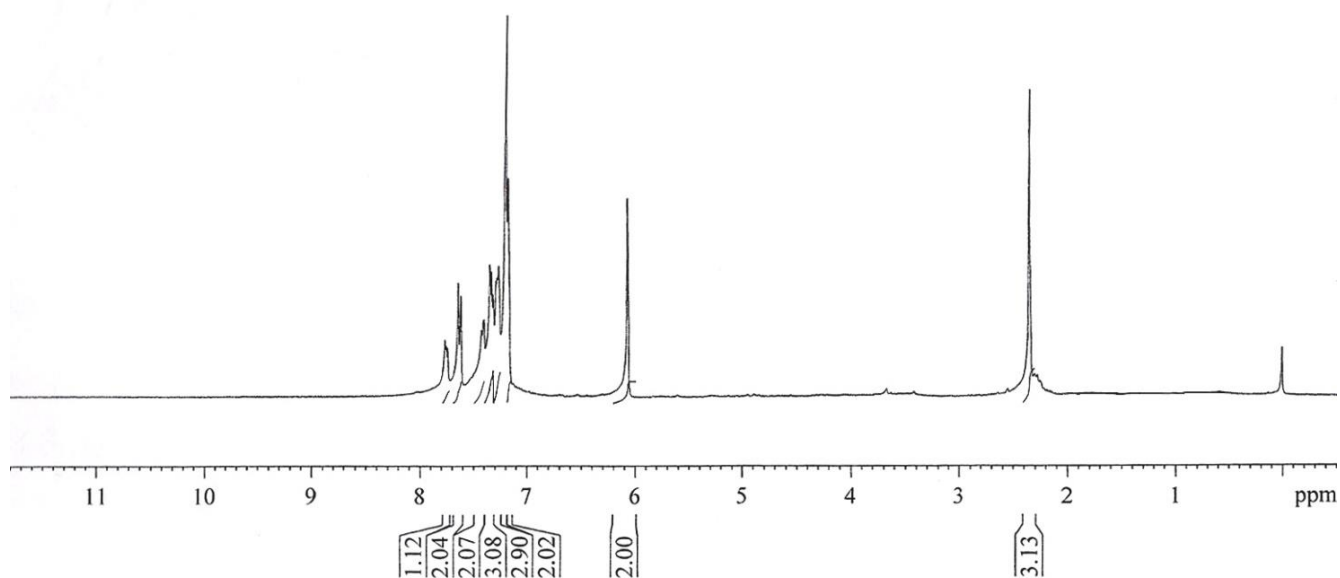
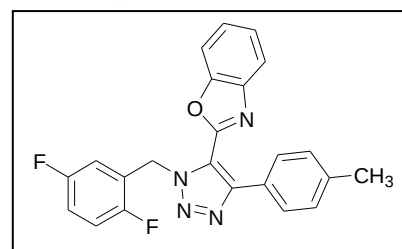
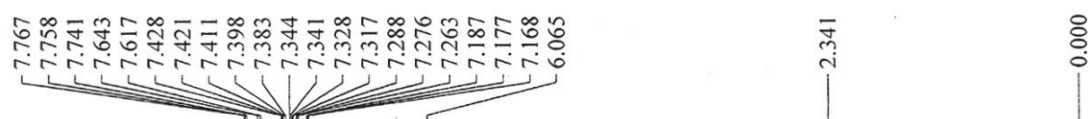


Figure S20. Mass & ¹H NMR spectra of 4{1,3,2}.

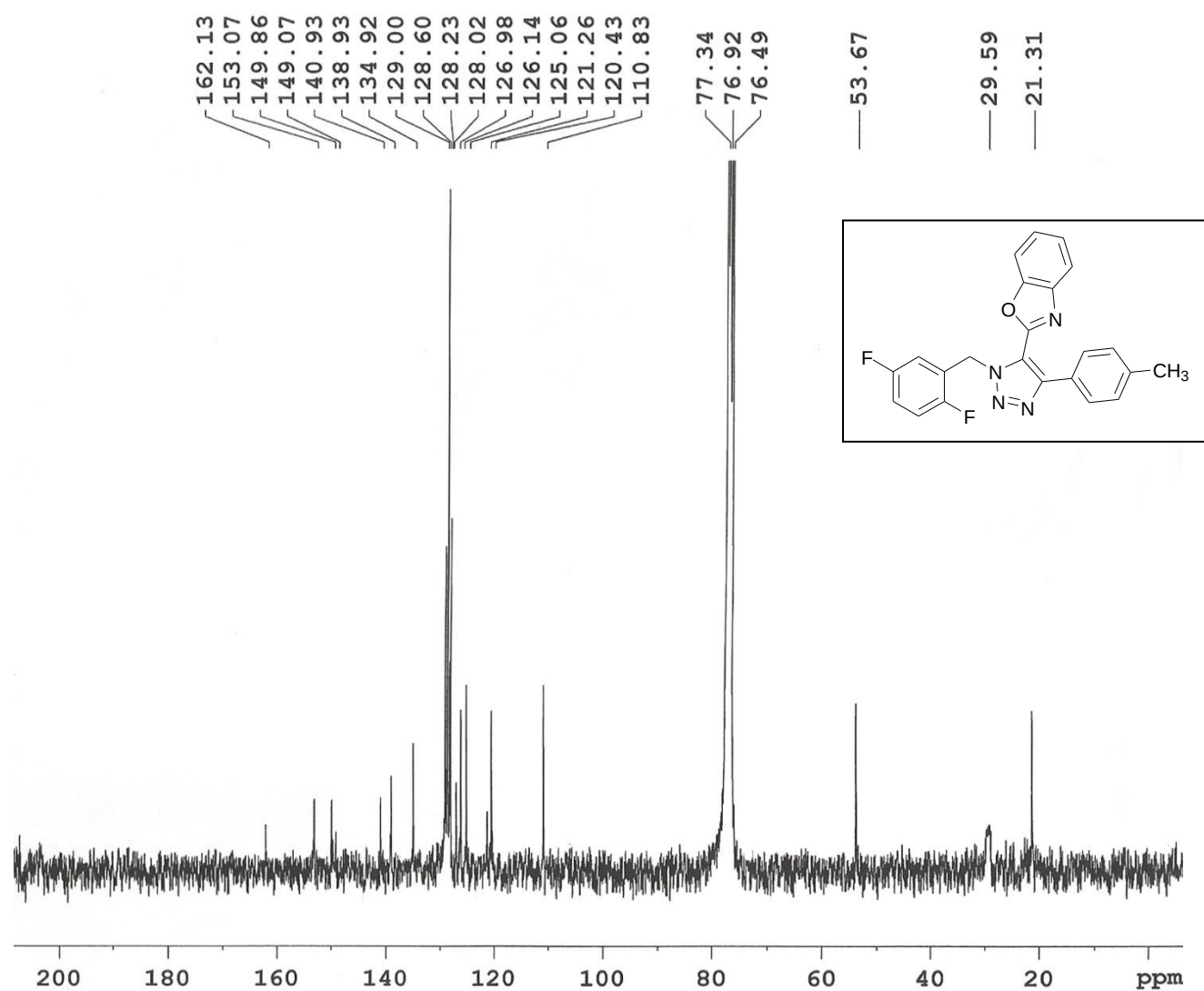
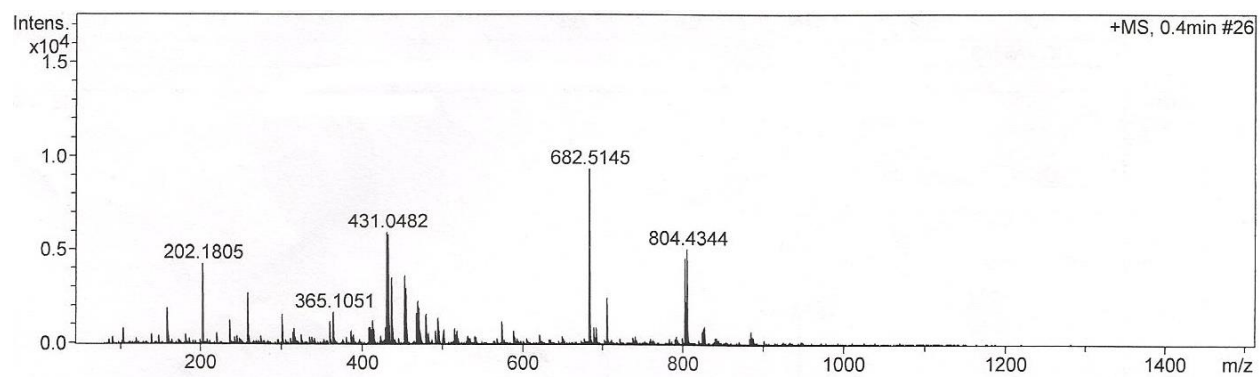


Figure S21. ^{13}C NMR spectrum of 4{1,3,2}.



Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e ⁻ Conf	N-Rule
431.0482	1	C ₂₂ H ₁₆ BrN ₄ O	100.00	431.0502	4.6	3.3	19.2	16.5	even	ok

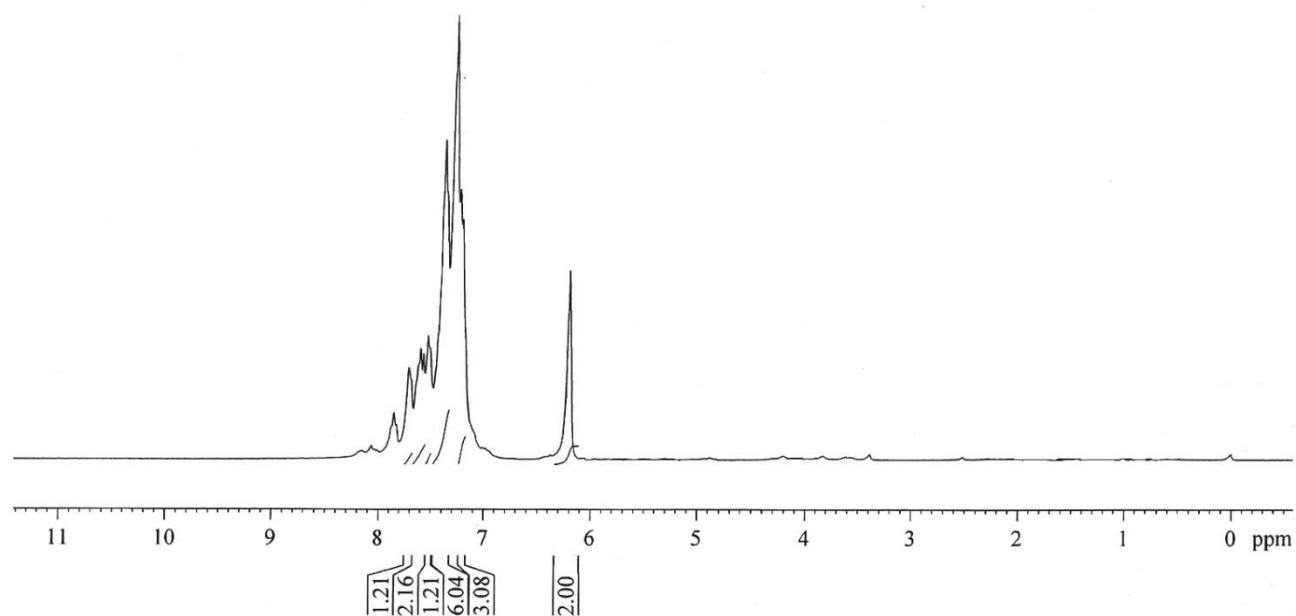
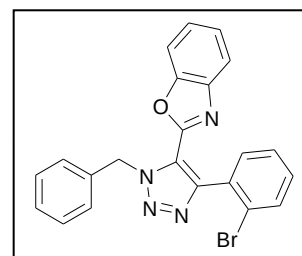
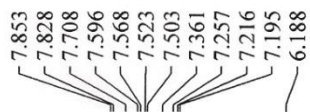


Figure S22. Mass & ¹H NMR spectra of 4{1,4,1}.

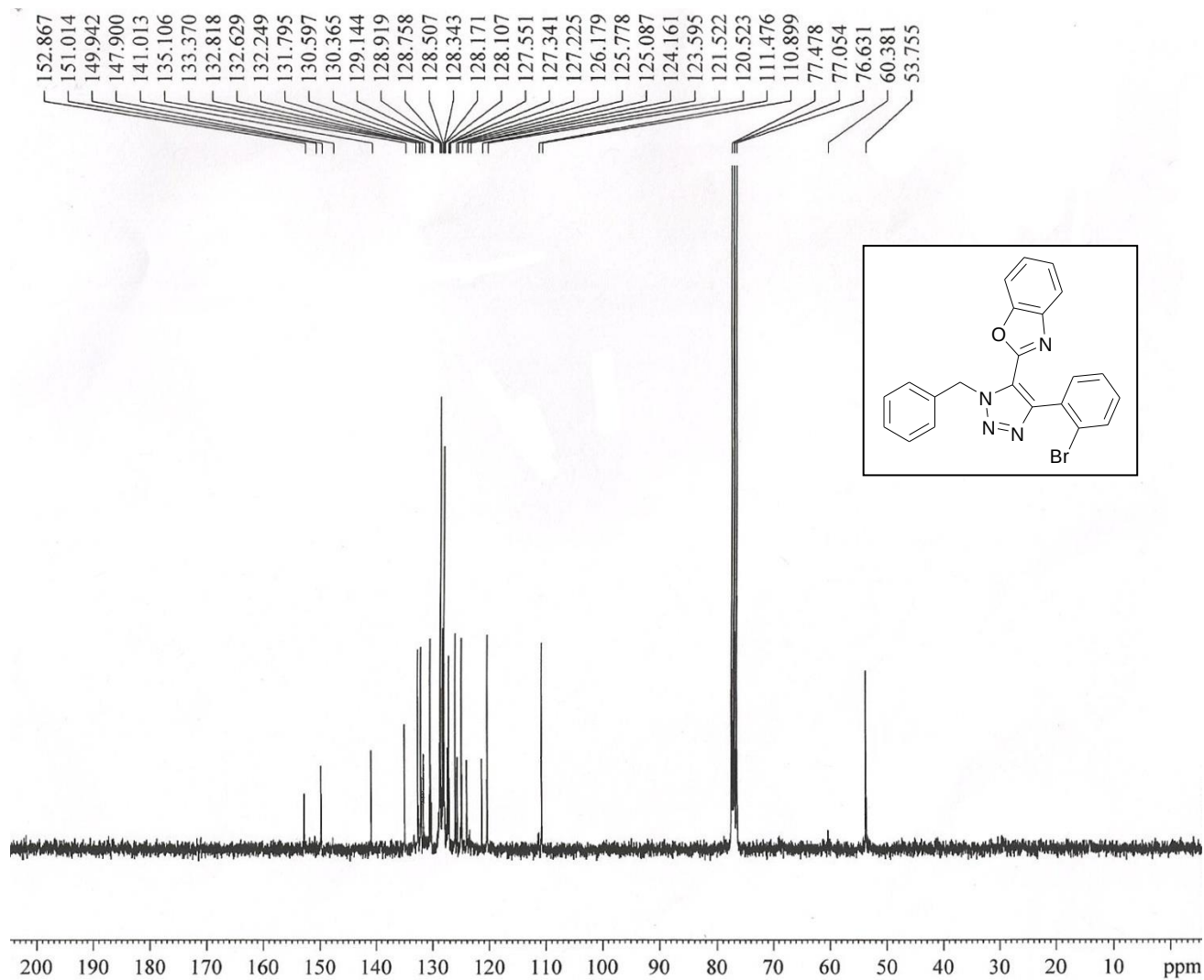


Figure S23. ^{13}C NMR spectrum of **4{1,4,1}**.

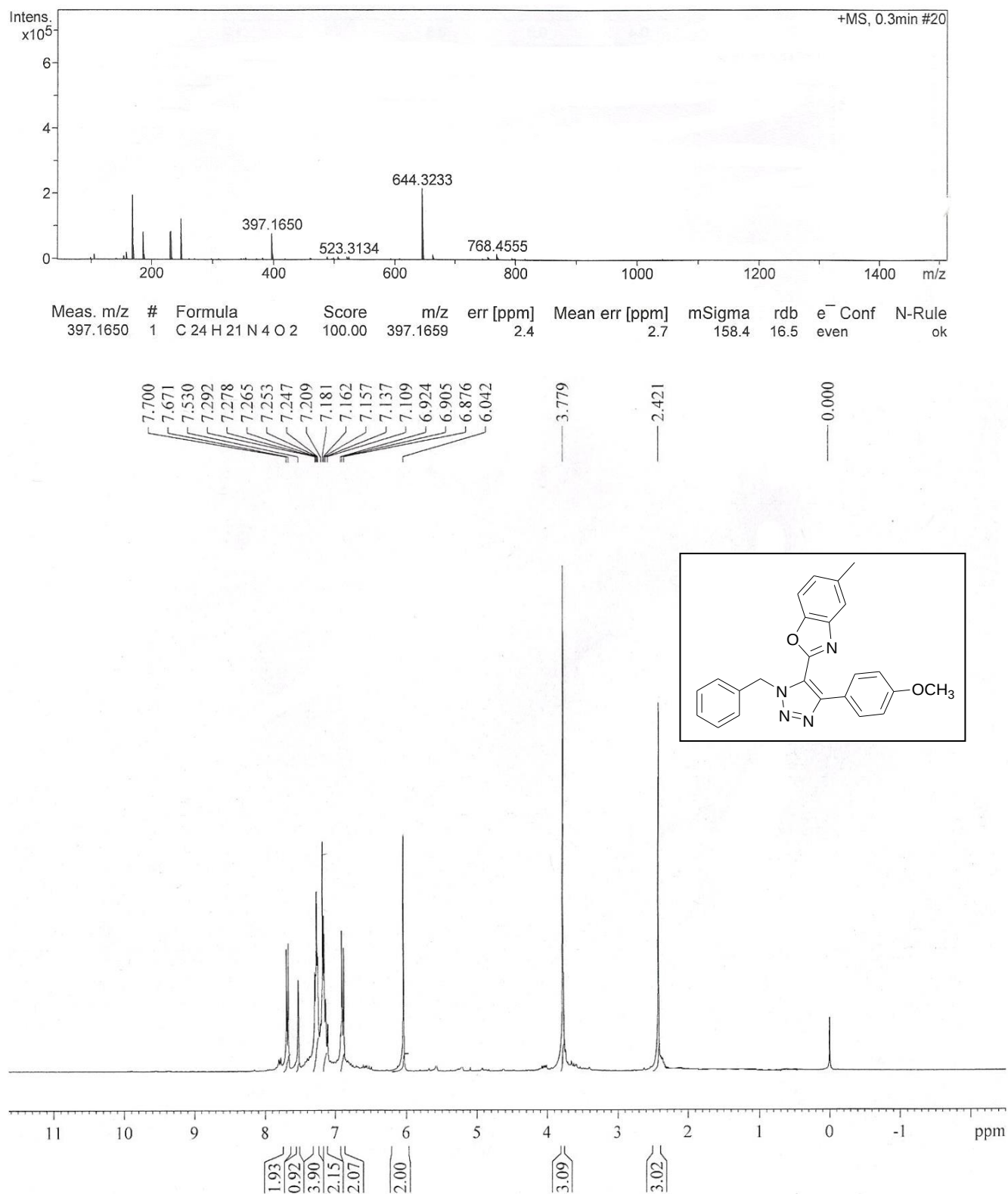


Figure S24. Mass & ¹H NMR spectra of **4{2,2,1}**.

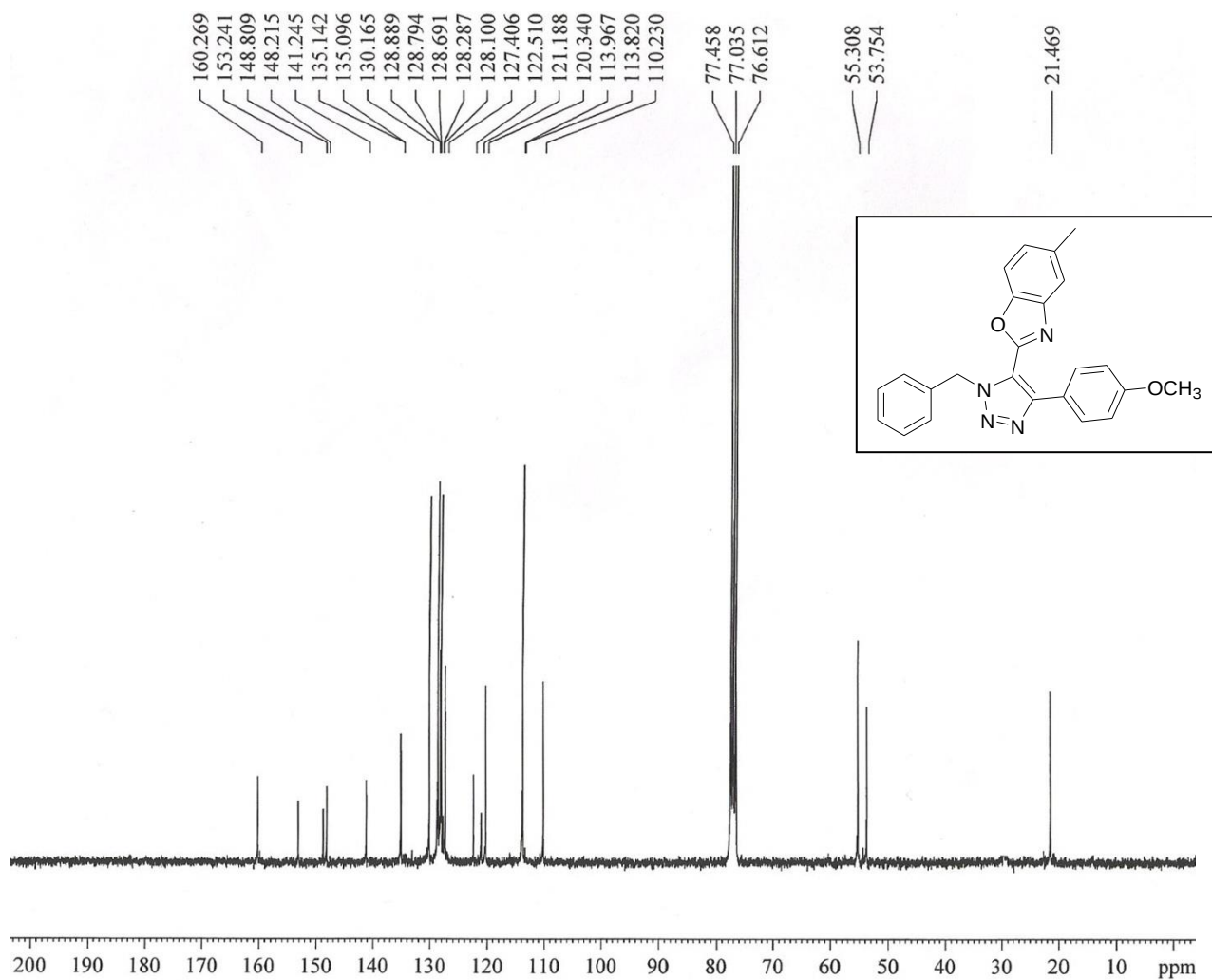


Figure S25. ^{13}C NMR spectrum of 4{2,2,1}.

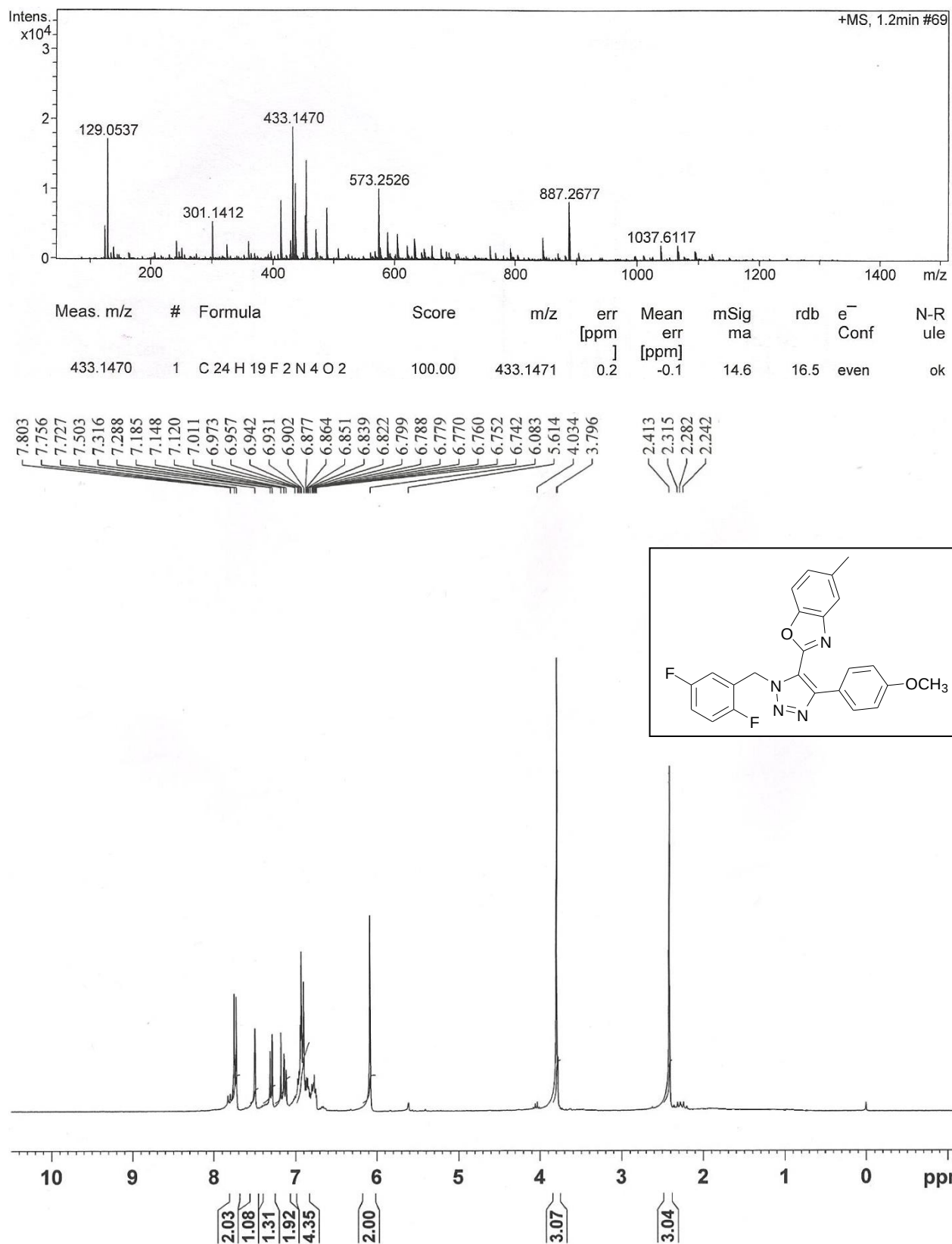


Figure S26. Mass & ¹H NMR spectra of 4{2,2,2}.

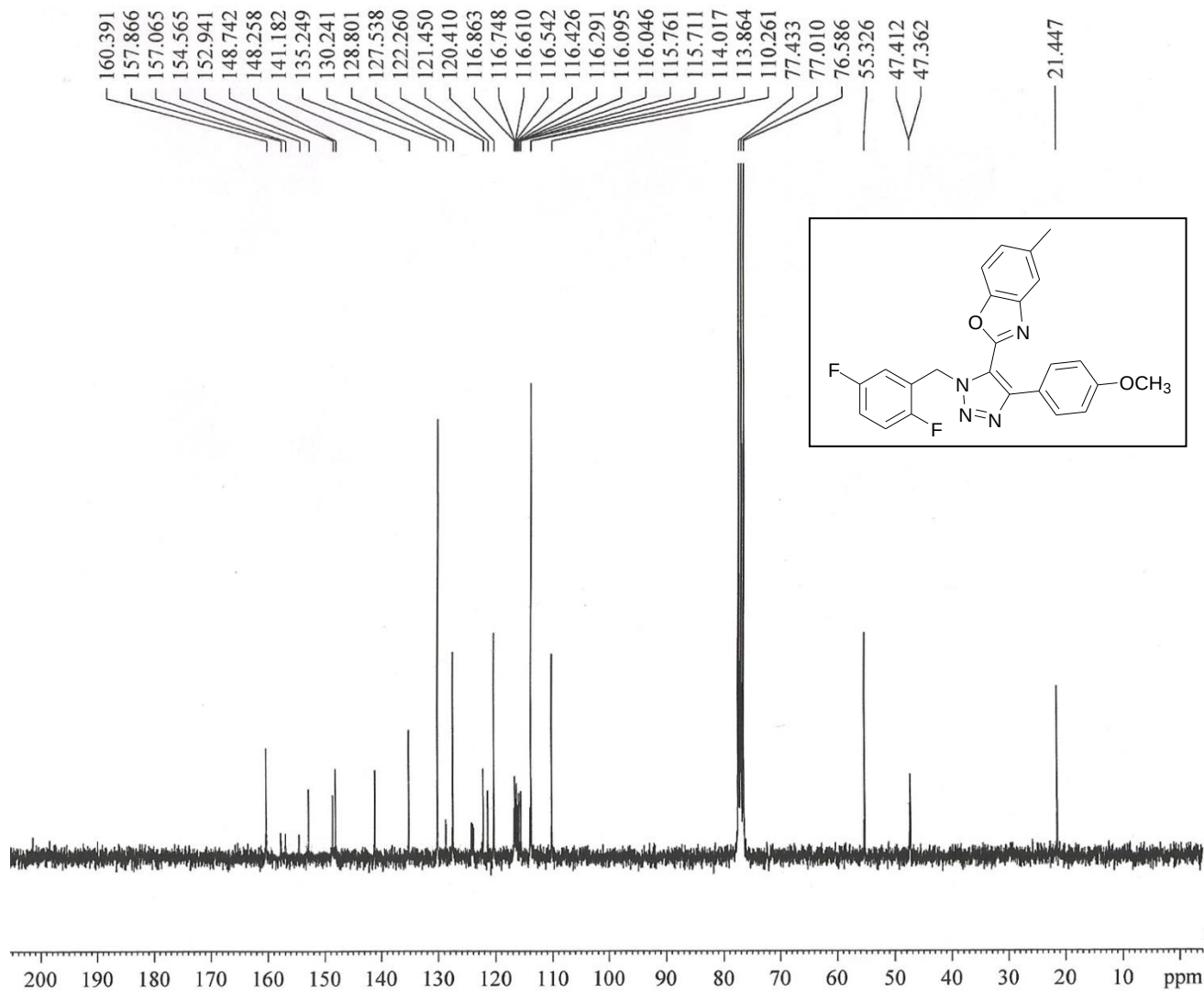


Figure S27. ^{13}C NMR spectrum of **4{2,2,2}**.

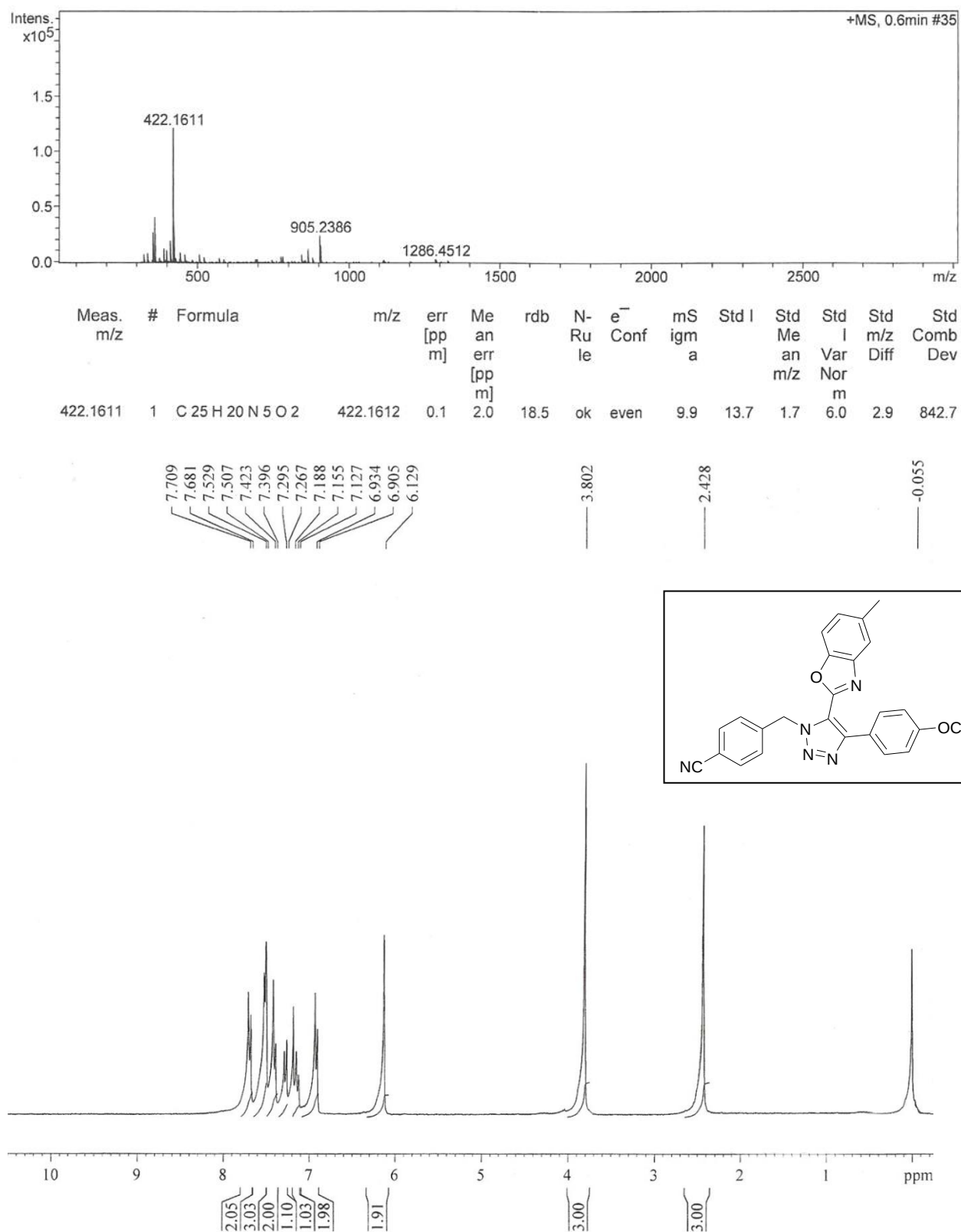


Figure S28. Mass & ¹H NMR spectra of 4{2,2,3}.

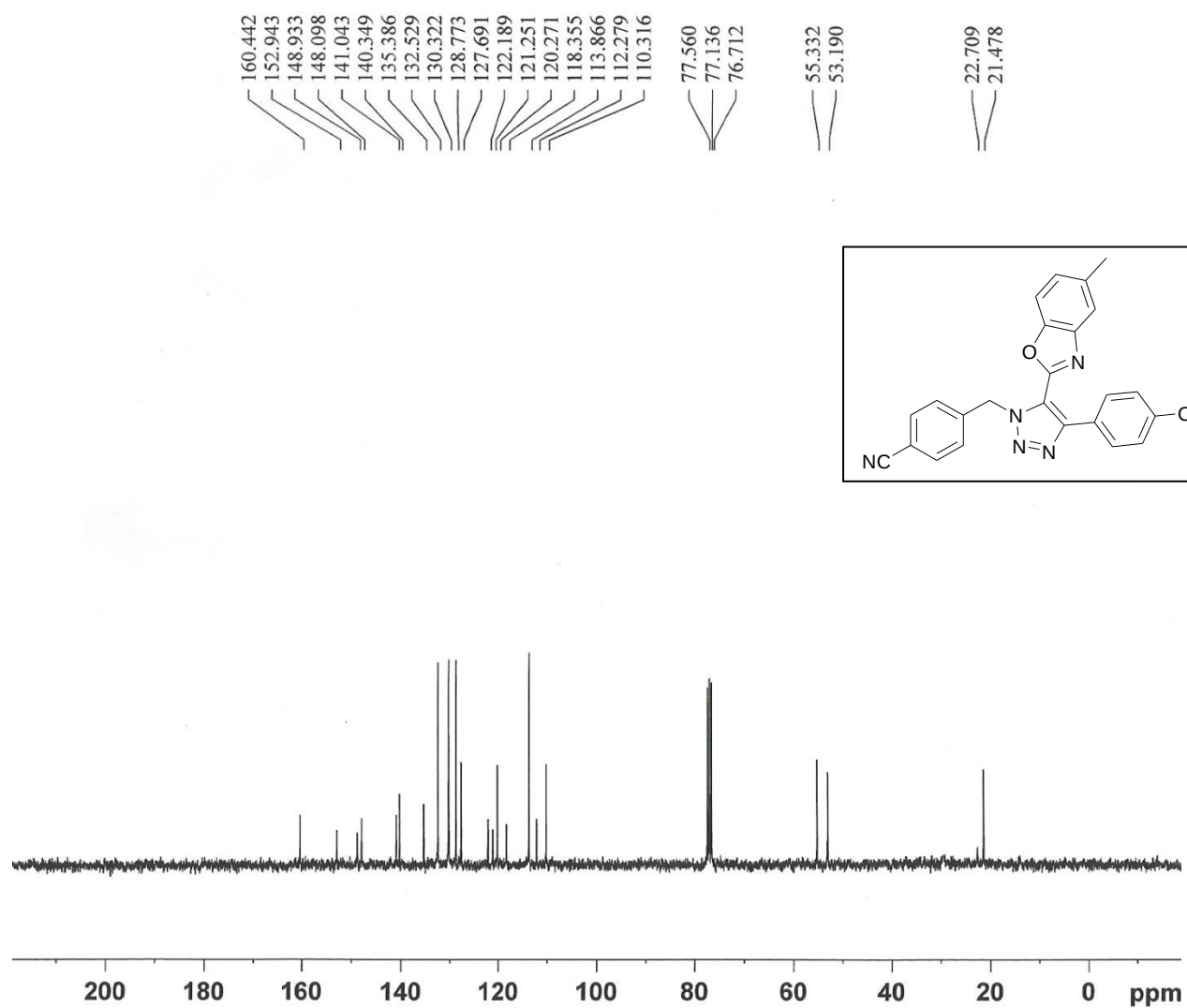


Figure S29. ^{13}C NMR spectrum of 4{2,2,3}.

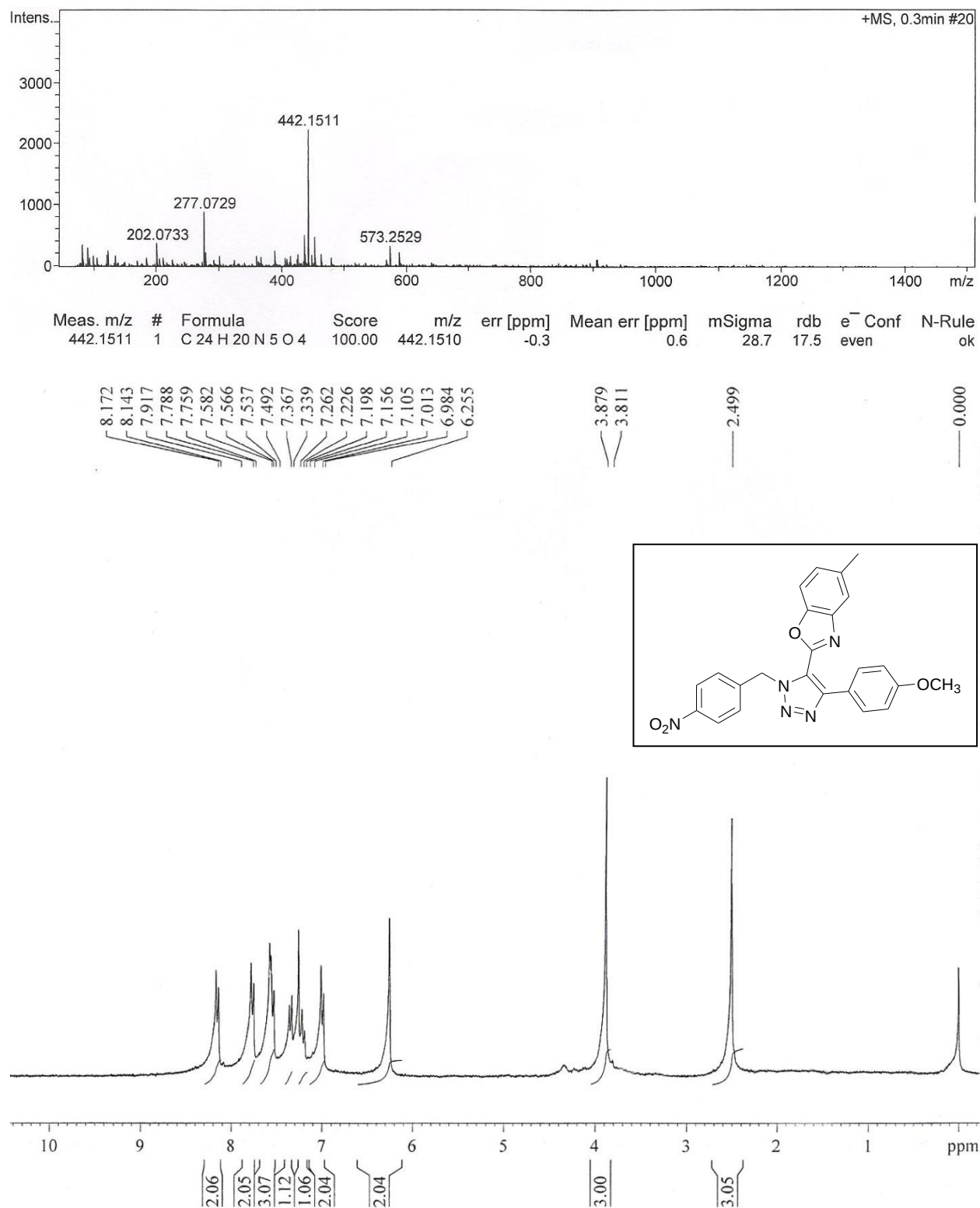


Figure S30. Mass & ¹H NMR spectra of 4{2,2,4}.

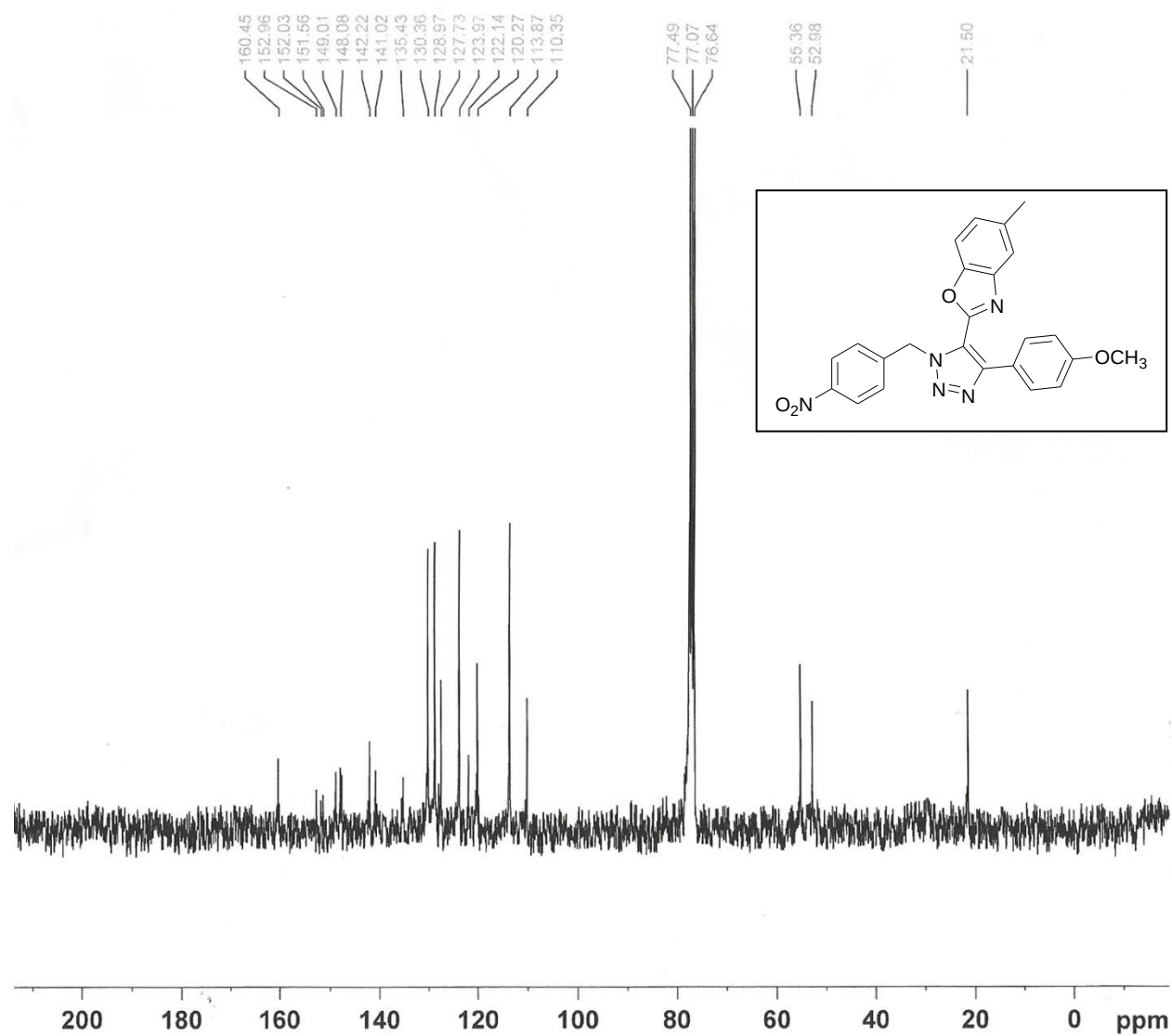


Figure S31. ¹³C NMR spectrum of **4{2,2,4}**.

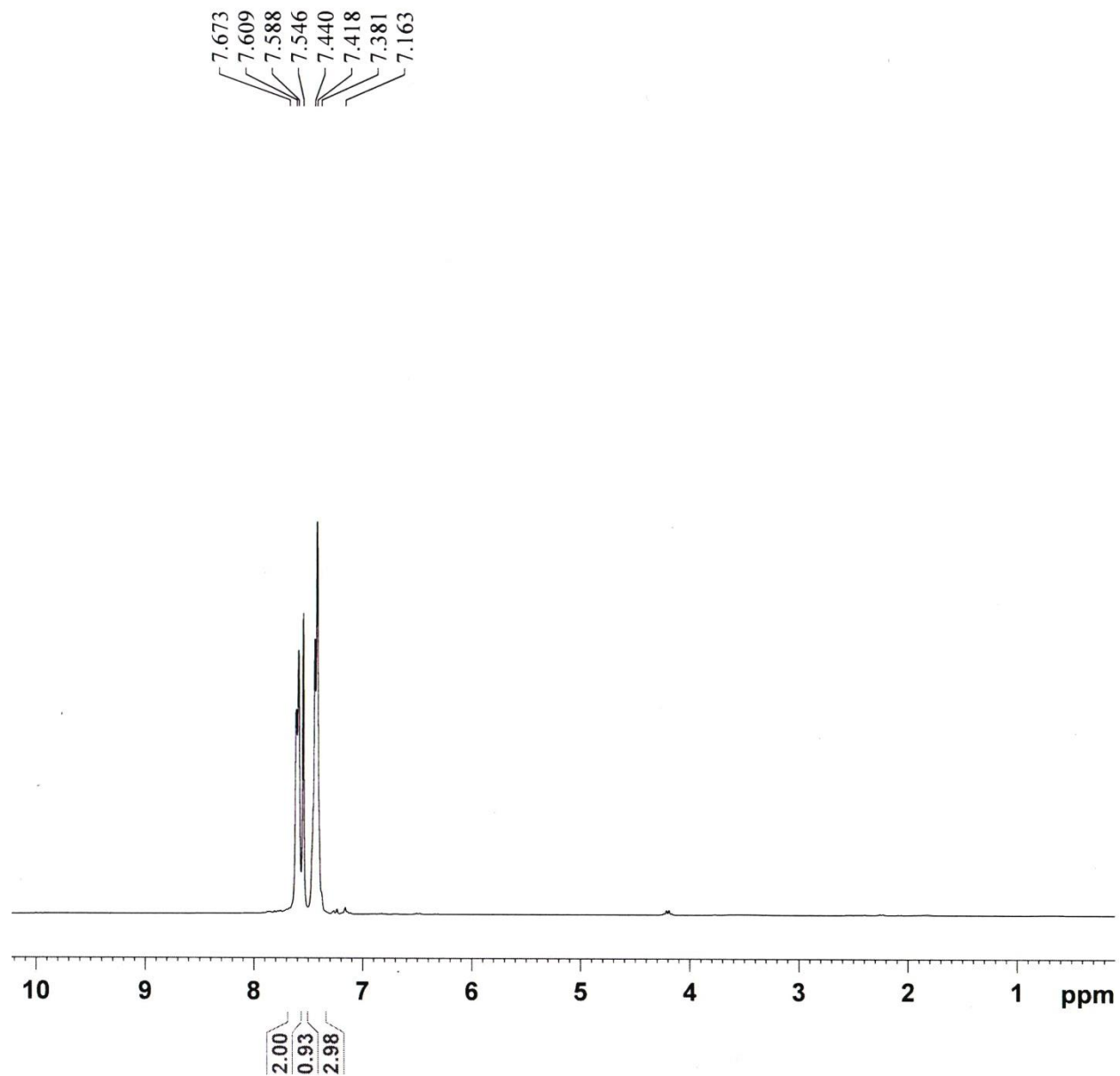


Figure S32. ^1H NMR spectrum of **2{1}**.

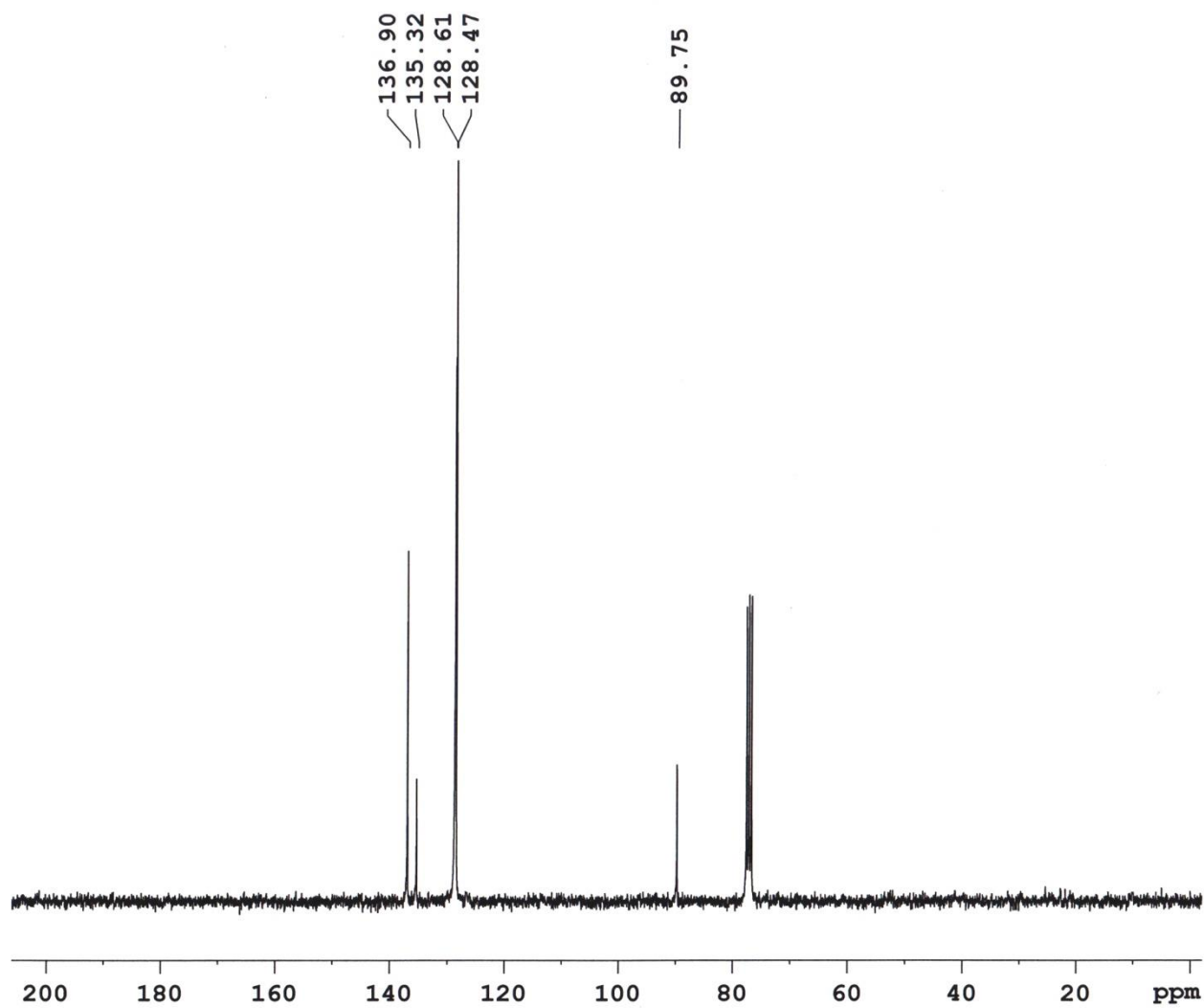


Figure S33. ^{13}C NMR spectrum of **2{1}**.

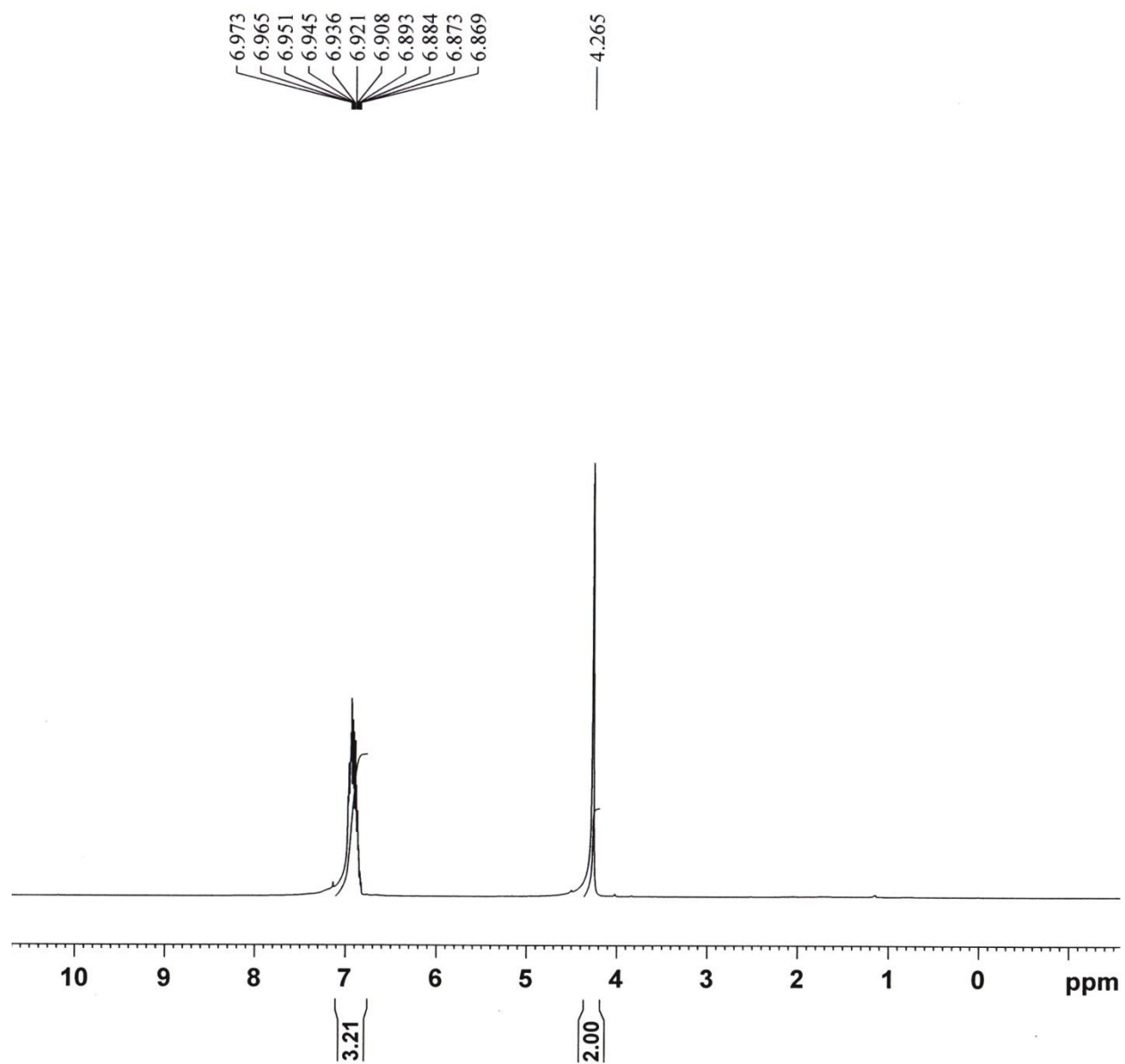


Figure S34. ^1H NMR spectrum of **3{2}**.

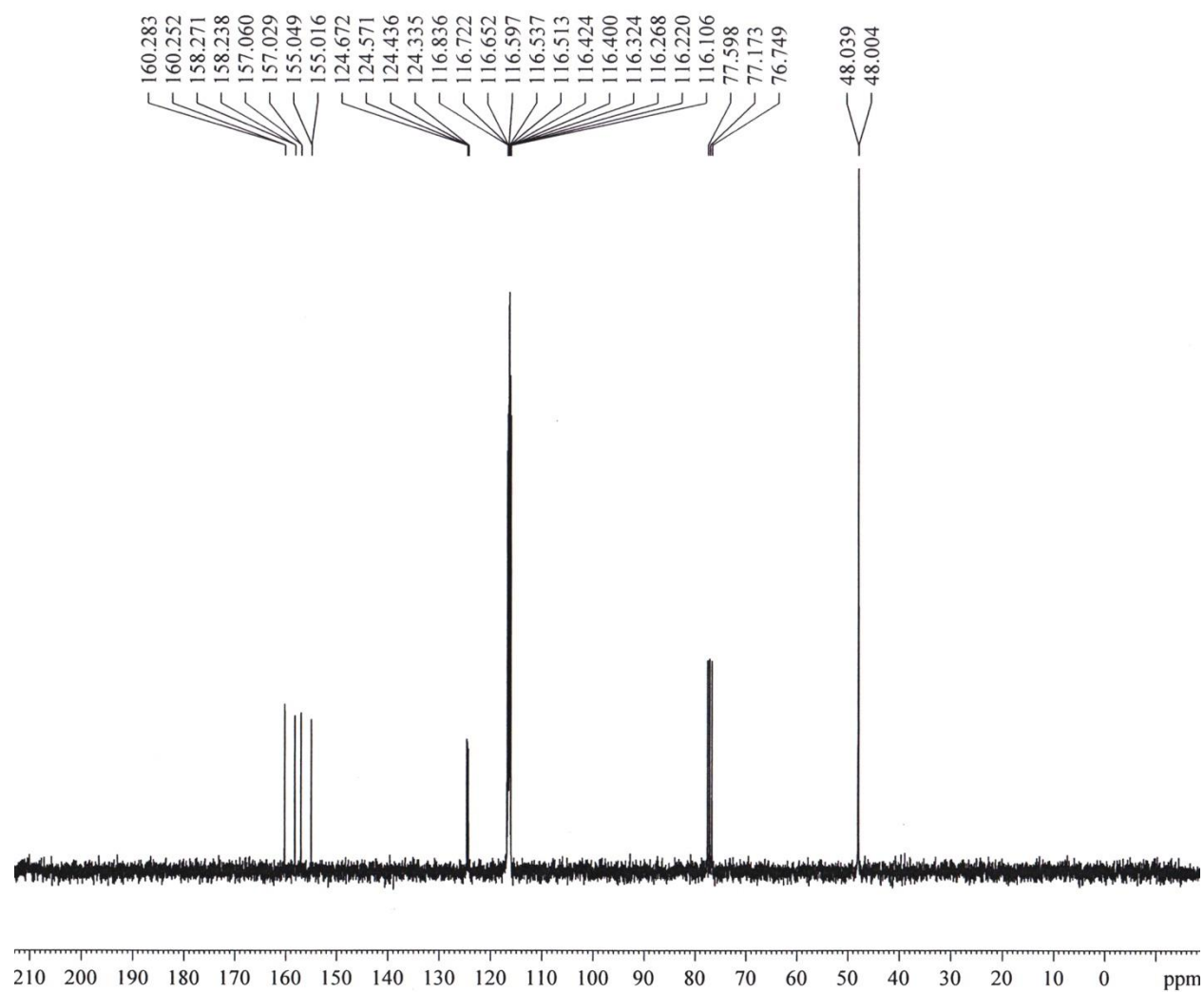


Figure S35. ¹³C NMR spectrum of 3{2}.