

Sp-sp³ C-C Bond Formation via Fe(OTf)₃/TfOH Cocatalyzed Coupling Reaction of Terminal Alkynes with Benzylic Alcohols

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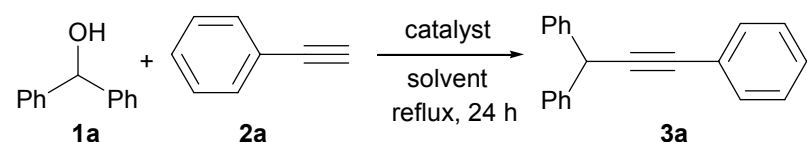
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General Remarks.

General: All reactions were carried out under N₂ atmosphere. ¹H-NMR spectra were recorded on a JEOL AL-300 or Bruker AVIII-400 spectrometers. Chemical shifts (in ppm) were referenced to tetramethylsilane ($\delta = 0$ ppm) in CDCl₃ as an internal standard. ¹³C-NMR spectra were obtained by the same NMR spectrometers and were calibrated with CDCl₃ ($\delta = 77.00$ ppm). Mass spectra were recorded by PE SCLEX QSTAR spectrometer. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. DCE, DMF, MeNO₂ were freshly distilled over CaH₂. Fe(OTf)₃ was synthesized according to literature method.¹ **1b**, **1c**, **1g**, **1h** are known compounds and prepared from the corresponding substituted ketons² by reduction with NaBH₄ in MeOH at room temperature. **2g**³ were prepared according to literature methods. Most of products **3** are not stable in air.

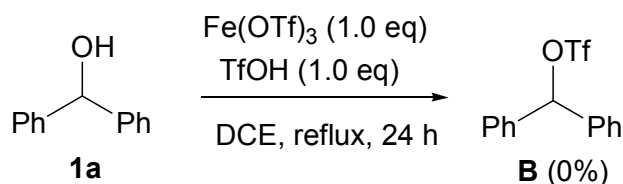
Screening with different catalysts:



entry	catalyst (%)	solvent	yield of 3aa (%) ^b
1	In(OTf) ₃ (5)	DCE	51
2	AgOTf (5)	DCE	53
3	Sc(OTf) ₃ (5)	DCE	18
4	Cu(OTf) ₂ (5)	DCE	57
5	Yb(OTf) ₃ (5)	DCE	26

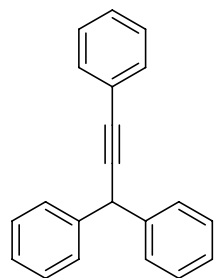
Mechanistic study

The triflate substrate can convert into the expected product as reported by Marcuzzi et. al.⁴ However, when the reaction of **1a** was carried out in the absence of alkyne, the triflate intermediate **B** was not obtained. Therefore, we consider that the reactions are more likely to occur through cationic intermediates as we described in the text. These discussions have been added in SI.



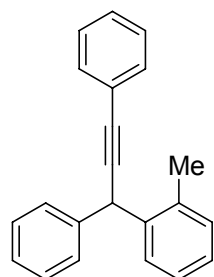
Experimental Section

1,3,3-Triphenyl-1-propyne (**3aa**)⁵



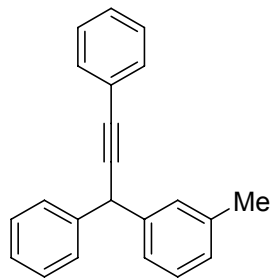
Typical procedure: TfOH (0.05 mmol, 25 μL (2 M in DMF)) was added to a solution of $\text{Fe}(\text{OTf})_3$ (11.7 mg, 0.023 mmol), benzhydrol **1a** (90.8 mg, 0.49 mmol), DCE (2.0 mL), phenylacetylene **2a** (83 μL , 0.75 mmol) in a dry Schlenck tube under N_2 . The reaction mixture was refluxed for 24 h. The solution was cooled to room temperature and evaporated under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether / dichloromethane = 40:1) to afford 101.2 mg (77%) of **3aa**: white solid; IR:(KBr) ν_{max} 1949, 1596, 1489, 756, 697, 559 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.47-7.43 (m, 6 H), 7.35-7.20 (m, 9 H), 5.21 (s, 1 H); ^{13}C NMR (75 MHz, CDCl_3): δ 141.8, 131.8, 128.7, 128.3, 128.0, 127.0, 123.5, 90.2, 84.9, 43.7; MS (70 eV): m/z (%): 268.2 (100) $[\text{M}]^+$.

1-Phenyl-3-phenyl-3-(2-methylphenyl)-1-propyne (**3ba**)⁵



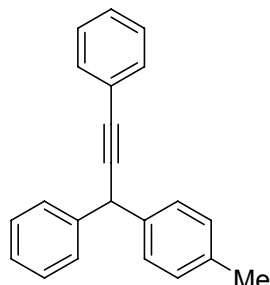
The reaction of **1b** (93.1 mg, 0.47 mmol), **2a** (83 μL , 0.75 mmol), $\text{Fe}(\text{OTf})_3$ (11.7 mg, 0.023 mmol), TfOH (0.05 mmol, 25 μL (2 M in DMF)) in DCE (2.0 mL) under N_2 afforded 113.9 mg (86%) of **3ba**: Light yellow liquid; IR:(KBr) ν_{max} 1949, 1599, 1490, 1450, 1030, 755, 694 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.52-7.16 (m, 14 H), 5.38 (s, 1 H), 2.33 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3): δ 140.8, 139.4, 136.0, 131.7, 130.7, 128.8, 128.5, 128.2, 128.0, 127.9, 127.1, 126.7, 126.3, 123.6, 90.2, 84.6, 40.8, 19.7; MS (70 eV): m/z (%): 282.3 (82) $[\text{M}]^+$, 191.2 (100).

1-Phenyl-3-phenyl-3-(3-methylphenyl)-1-propyne (3ca)



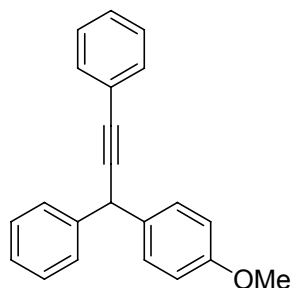
The reaction of **1c** (93.8 mg, 0.47 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (12.2 mg, 0.024 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 82.7 mg (62%) of **3ca**: Light yellow liquid; IR:(KBr) ν_{\max} 1949, 1490, 1448, 756, 695 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.49-7.43 (m, 4 H), 7.34-7.28 (m, 5 H), 7.24-7.05 (m, 4 H), 7.04 (d, J = 7.2 Hz, 1 H), 5.17 (s, 1 H), 2.33 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 141.9, 141.7, 138.3, 131.7, 128.63, 128.58, 128.5, 128.2, 127.92, 127.89, 127.7, 126.8, 125.0, 123.6, 90.4, 84.8, 43.7, 21.5; MS (70 eV): m/z (%): 282.3 (100) [M]⁺; HRMS m/z (ESI): Calcd. for C₂₂H₁₉ (M+H⁺) 283.1481, Found: 283.1478.

1-Phenyl-3-phenyl-3-(4-methylphenyl)-1-propyne (3da)



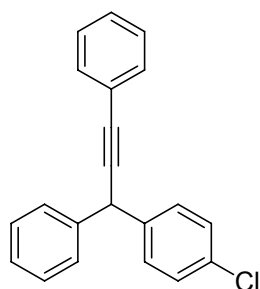
The reaction of **1d** (98.0 mg, 0.49 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (12.7 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 101.0 mg (72%) of **3da**: Light yellow liquid; IR:(KBr) ν_{\max} 1949, 1898, 1658, 1599, 1510, 1491, 1450, 756, 729, 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.41 (m, 4 H), 7.33-7.19 (m, 8 H), 7.11 (d, J = 7.6 Hz, 2 H), 5.16 (s, 1 H), 2.29 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 142.0, 138.8, 136.5, 131.7, 129.3, 128.6, 128.2, 127.9, 127.83, 127.77, 126.8, 123.6, 90.4, 84.7, 43.4, 21.0; MS (70 eV): m/z (%): 282.3 (100) [M]⁺; HRMS m/z (ESI): Calcd. for C₂₂H₁₉ (M+H⁺) 283.1481, Found: 283.1482.

1-Phenyl-3-phenyl-3-(4-methoxyphenyl)-1-propyne (3ea)⁶



The reaction of **1e** (105.9 mg, 0.49 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (11.0 mg, 0.022 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 79.4 mg (54%) of **3ea**: Light yellow liquid; IR:(KBr) ν_{\max} 1952, 1884, 1607, 1509, 1491, 1453, 1250, 1177, 1034, 757, 695 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.47-7.40 (m, 4 H), 7.35-7.20 (m, 9 H), 6.84 (d, J = 8.40, 2 H), 5.15 (s, 1 H), 3.74 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 158.5, 142.1, 133.9, 131.7, 128.9, 128.6, 128.2, 127.9, 127.8, 126.8, 123.5, 114.0, 90.5, 84.7, 55.2, 42.9; MS (70 eV): m/z (%): 298.3 (100) [M]⁺.

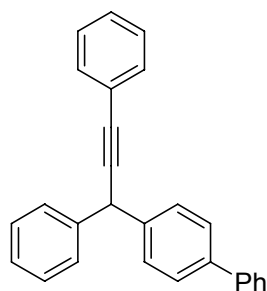
1-Phenyl-3-phenyl-3-(4-chlorophenyl)-1-propyne (3fa)⁵



The reaction of **1f** (106.5 mg, 0.49 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (12.9 mg, 0.026 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 98.0 mg (66%) of **3fa**: Light yellow liquid; IR:(KBr) ν_{\max} 1949, 1897, 1598, 1489, 1091, 755, 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.48-7.23 (m, 14 H), 5.17 (s, 1 H); ¹³C NMR (100 MHz,

CDCl₃): δ 141.3, 140.3, 132.8, 131.7, 129.3, 128.7, 128.3, 128.1, 127.8, 127.1, 123.3, 89.6, 85.3, 43.1; MS (70 eV): m/z (%): 302.2 (40) [M]⁺, 267.2 (100).

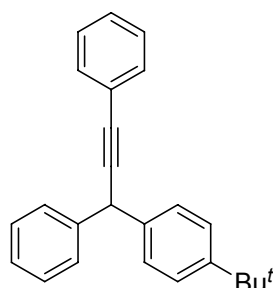
1-Phenyl-3-phenyl-3-(4-phenylphenyl)-1-propyne (**3ga**)⁷



The reaction of **1g** (120.5 mg, 0.46 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (12.5 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 122.4 mg (77%) of **3ga**: white solid; IR:(KBr) ν_{\max} 1949, 1597, 1488, 758, 696, 480 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.58-7.21 (m, 19 H), 5.25 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 141.7, 140.92, 140.87, 140.0, 131.8, 128.82, 128.77, 128.4, 128.3, 128.1, 128.0, 127.5, 127.3, 127.14, 127.06, 123.5, 90.1, 85.0, 43.4;

MS (70 eV): m/z (%): 344.3 (100) [M]⁺.

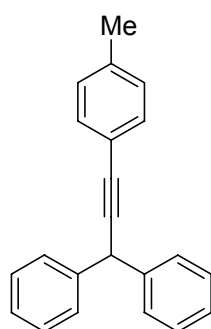
1-Phenyl-3-phenyl-3-(4-tert-butylphenyl)-1-propyne (**3ha**)



The reaction of **1h** (111.4 mg, 0.46 mmol), **2a** (83 μ L, 0.75 mmol), Fe(OTf)₃ (12.4 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 107.7 mg (72%) of **3ha**: Light yellow liquid; IR:(KBr) ν_{\max} 1948, 1599, 1509, 1491, 756, 697 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.50-7.44 (m, 4 H), 7.39-7.22 (m, 10 H), 5.19 (s, 1 H), 1.29 (s, 9 H); ¹³C NMR (75 MHz, CDCl₃): δ 149.8, 142.0, 138.8, 131.8, 128.7, 128.3, 128.0, 127.5, 126.9, 125.6, 123.6, 90.5,

84.6, 43.2, 34.3, 31.3; MS (70 eV): m/z (%): 324.3 (57) [M]⁺; 309.2 (100); HRMS m/z (ESI): Calcd. for C₂₅H₂₅ (M+H⁺) 325.1951, Found: 325.1955.

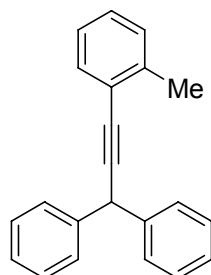
1-(4-Methylphenyl)-3,3-diphenyl-1-propyne (**3ab**)⁵



The reaction of **1a** (91.9 mg, 0.50 mmol), **2b** (95 μ L, 0.75 mmol), Fe(OTf)₃ (12.5 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 78.9 mg (56%) of **3ab**: white solid; IR:(KBr) ν_{\max} 1953, 1597, 1505, 1491, 1450, 814, 740, 700, 529 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.45-7.41 (m, 4 H), 7.36 (d, J = 8.4 Hz, 2 H), 7.32-7.28 (m, 4 H), 7.23-7.18 (m, 2 H), 7.08 (d, J = 8.0 Hz, 2H), 5.19 (s, 1 H), 2.32 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃): δ 141.9, 138.0, 131.5, 129.0, 128.6, 127.9, 126.8, 120.4, 89.4, 85.0, 43.8, 21.4; MS (70 eV): m/z (%): 282.2 (100)

[M]⁺.

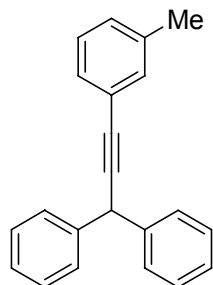
1-(2-Methylphenyl)-3,3-diphenyl-1-propyne (**3ac**)



The reaction of **1a** (91.0 mg, 0.49 mmol), **2c** (95 μ L, 0.75 mmol), Fe(OTf)₃ (12.2 mg, 0.024 mmol), TfOH (0.05 mmol, 25 μ L (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 113.4 mg (81%) of **3ac**: white solid; IR:(KBr) ν_{\max} 1954, 1596, 1489, 1453, 759, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.42 (M, 5 H), 7.32-7.28 (m, 4 H), 7.23-7.16 (m, 4 H), 7.13-7.07 (m, 1 H), 5.24 (s, 1 H), 2.44 (s,

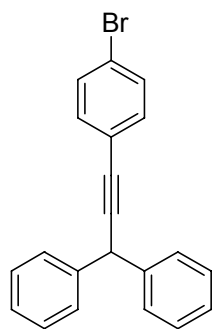
3H); ^{13}C NMR (100 MHz, CDCl_3): δ 141.9, 140.2, 132.0, 129.4, 128.6, 128.0, 127.9, 126.8, 125.5, 123.3, 94.2, 83.9, 44.0, 20.9; MS (70 eV): m/z (%): 282.3 (18) $[\text{M}]^+$, 191 (100); HRMS m/z (ESI): Calcd. for $\text{C}_{22}\text{H}_{19}$ ($\text{M}+\text{H}^+$) 283.1481, Found: 283.1491.

1-(3-Methylphenyl)-3,3-diphenyl-1-propyne (3ad)



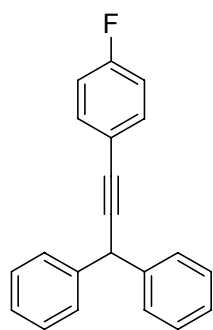
The reaction of **1a** (91.0 mg, 0.49 mmol), **2d** (95 μL , 0.75 mmol), $\text{Fe}(\text{OTf})_3$ (12.5 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μL (2 M in DMF)) in DCE (2.0 mL) under N_2 afforded 104.5 mg (75%) of **3ad**: white solid; IR:(KBr) ν_{max} 1973, 1599, 1579, 1491, 1451, 757, 697 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.44-7.41 (m, 4 H), 7.31-7.26 (m, 6 H), 7.22-7.13 (m, 3 H), 7.07 (d, $J = 7.6$ Hz, 1 H), 5.18 (s, 1 H), 2.28 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3): δ 141.8, 137.8, 132.3, 128.8, 128.7, 128.6, 128.1, 127.9, 126.8, 123.3, 89.8, 85.0, 43.7, 21.1; MS (70 eV): m/z (%): 282.2 (100) $[\text{M}]^+$; HRMS m/z (ESI): Calcd. for $\text{C}_{22}\text{H}_{19}$ ($\text{M}+\text{H}^+$) 283.1481, Found: 283.1479.

1-(4-Bromophenyl)-3,3-diphenyl-1-propyne (3ae)



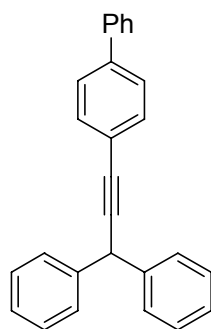
The reaction of **1a** (90.5 mg, 0.49 mmol), **2e** (129.3 mg, 0.71 mmol), $\text{Fe}(\text{OTf})_3$ (12.4 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μL (2 M in DMF)) in DCE (2.0 mL) under N_2 afforded 134.9 mg (79%) of **3ae**: white solid; IR:(KBr) ν_{max} 1953, 1597, 1581, 1484, 1450, 1070, 1010, 821, 733, 699 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.37 (m, 6 H), 7.32-7.27 (m, 6 H), 7.23-7.19 (m, 2 H), 5.17 (s, 1 H); ^{13}C NMR (100 MHz, CDCl_3): δ 141.4, 133.1, 131.4, 128.6, 127.8, 127.0, 122.4, 122.1, 91.5, 83.8, 43.7; MS (70 eV): m/z (%): 346.1 (73) $[\text{M}-1]^+$, 348.1 (74) $[\text{M}+1]^+$, 189.0 (100); HRMS m/z (ESI): Calcd. for $\text{C}_{21}\text{H}_{16}\text{Br}$ ($\text{M}+\text{H}^+$) 347.0430, Found: 347.0440.

1-(4-Fluorophenyl)-3,3-diphenyl-1-propyne (3af)



The reaction of **1a** (90.7 mg, 0.49 mmol), **2f** (90 μL , 0.75 mmol), $\text{Fe}(\text{OTf})_3$ (12.7 mg, 0.025 mmol), TfOH (0.05 mmol, 25 μL (2 M in DMF)) in DCE (2.0 mL) under N_2 afforded 112.1 mg (80%) of **3af**: Light yellow liquid; IR:(KBr) ν_{max} 1949, 1890, 1600, 1506, 1494, 1452, 1231 836, 739, 699, 530 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.46-7.40 (m, 6 H), 7.31 (t, $J = 7.6$ Hz, 4 H), 7.22 (t, $J = 6.4$ Hz, 2 H), 6.97 (t, $J = 8.8$ Hz, 2 H), 5.19 (s, 1 H); ^{13}C NMR (100 MHz, CDCl_3): δ 162.3 (d, $J = 247.0$ Hz), 141.6, 133.5 (d, $J = 8.0$ Hz), 128.6, 127.9, 126.9, 119.5 (d, $J = 4.0$ Hz), 115.4 (d, $J = 22.0$ Hz), 89.9, 83.8, 43.7; MS (70 eV): m/z (%): 286.2 (100) $[\text{M}]^+$; HRMS (ESI): Calcd. for $\text{C}_{21}\text{H}_{16}\text{F}$ ($\text{M}+\text{H}^+$) 287.1231, Found: 287.1230.

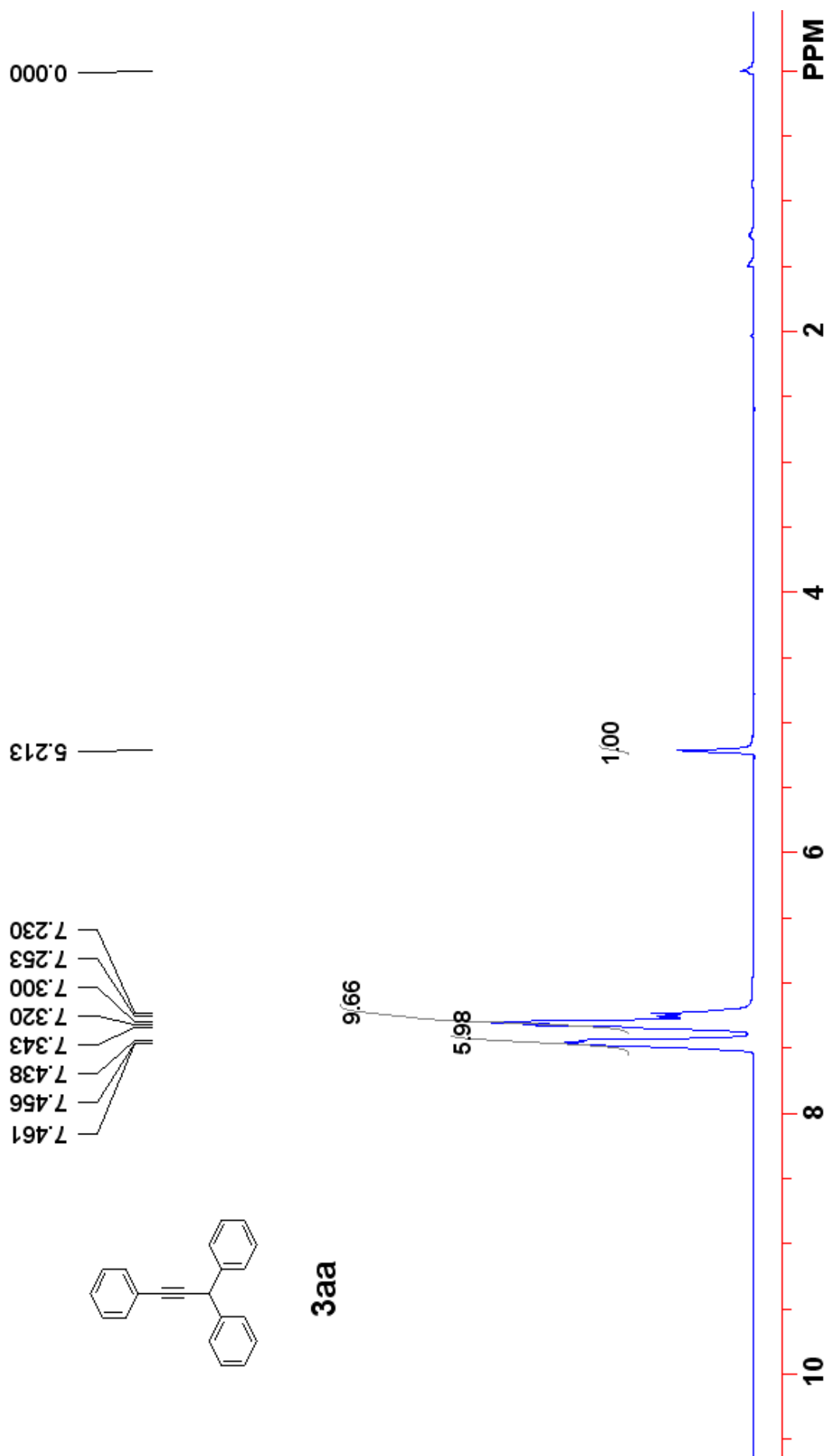
1-(4-Phenylphenyl)-3,3-diphenyl-1-propyne (**3ag**)

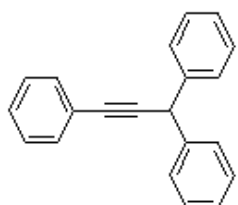
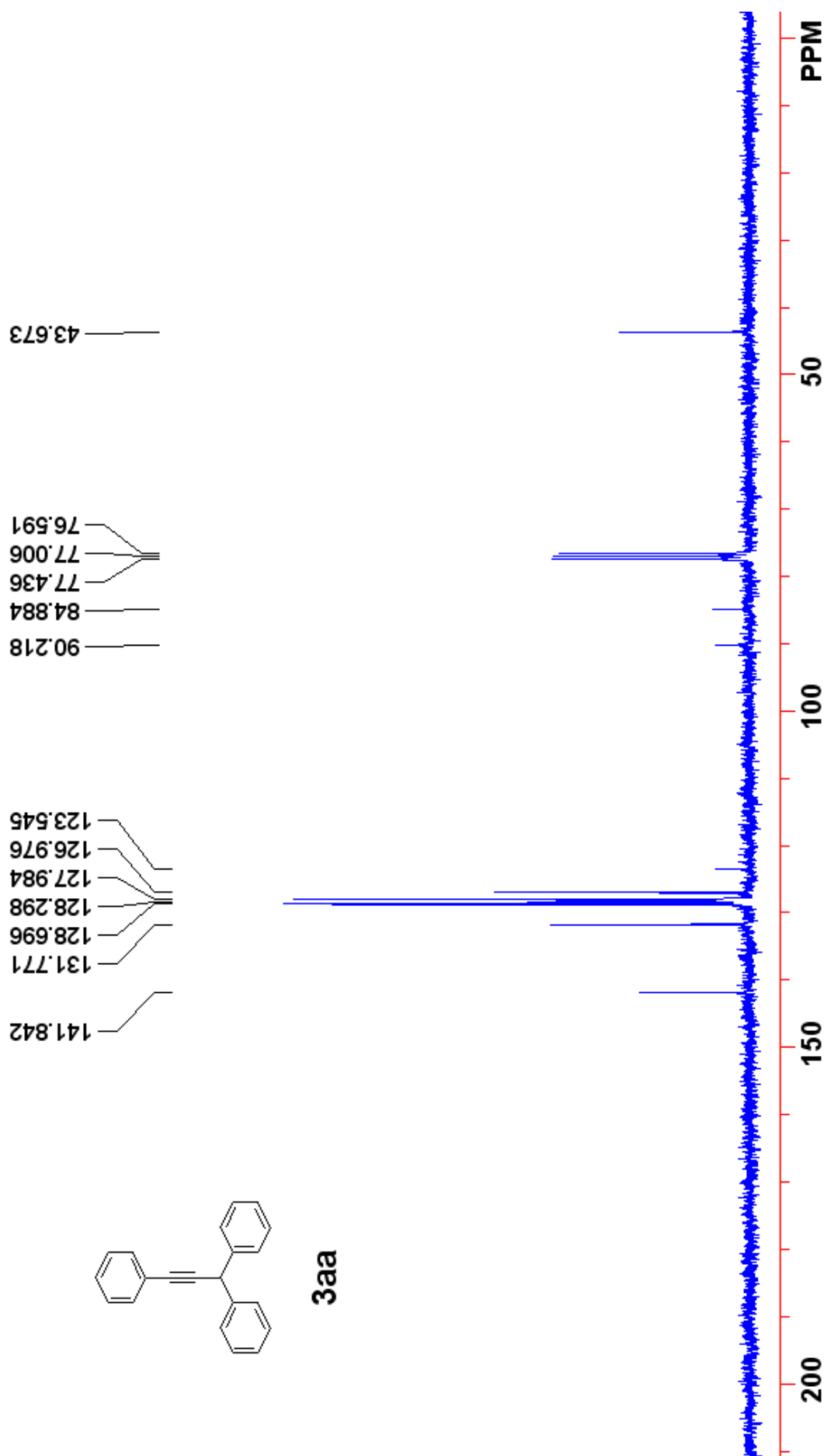


The reaction of **1a** (90.3 mg, 0.49 mmol), **2g** (129.6 mg, 0.73 mmol), Fe(OTf)₃ (12.3 mg, 0.024 mmol), TfOH (0.05 mmol, 25 μL (2 M in DMF)) in DCE (2.0 mL) under N₂ afforded 107.1 mg (63%) of **3ag**: white solid; IR:(KBr) ν_{\max} 1949, 1598, 1488, 1450, 764, 697 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.60-7.21 (m, 19 H), 5.24 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ 141.8, 140.8, 140.5, 132.2, 128.9, 128.7, 128.0, 127.6, 127.1, 127.0, 122.5, 90.9, 84.7, 43.7; MS (70 eV): m/z (%): 344.3 (100) [M]⁺; HRMS (ESI): Calcd. for C₂₇H₂₁ (M+H⁺) 345.1638, Found: 345.1642.

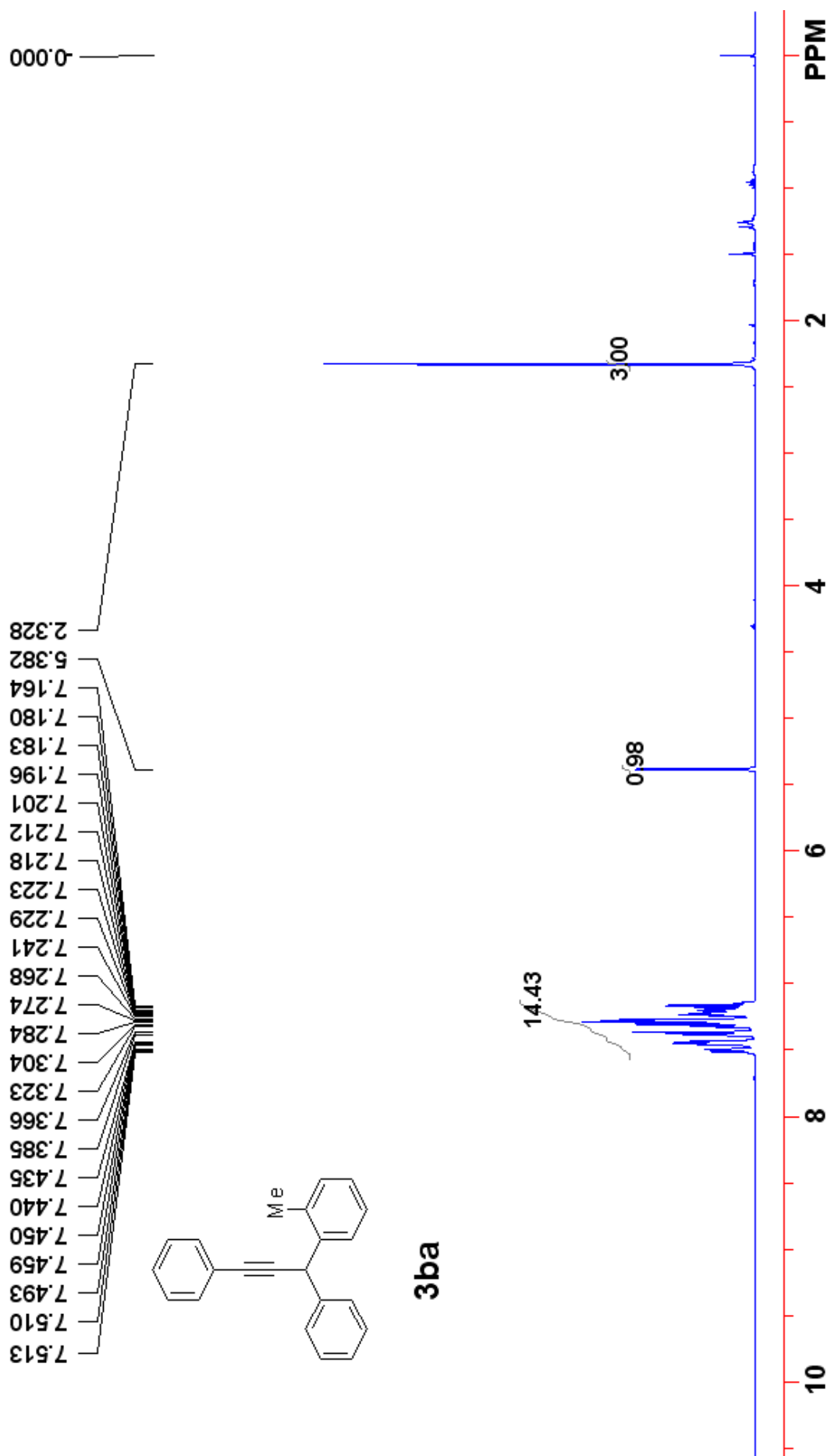
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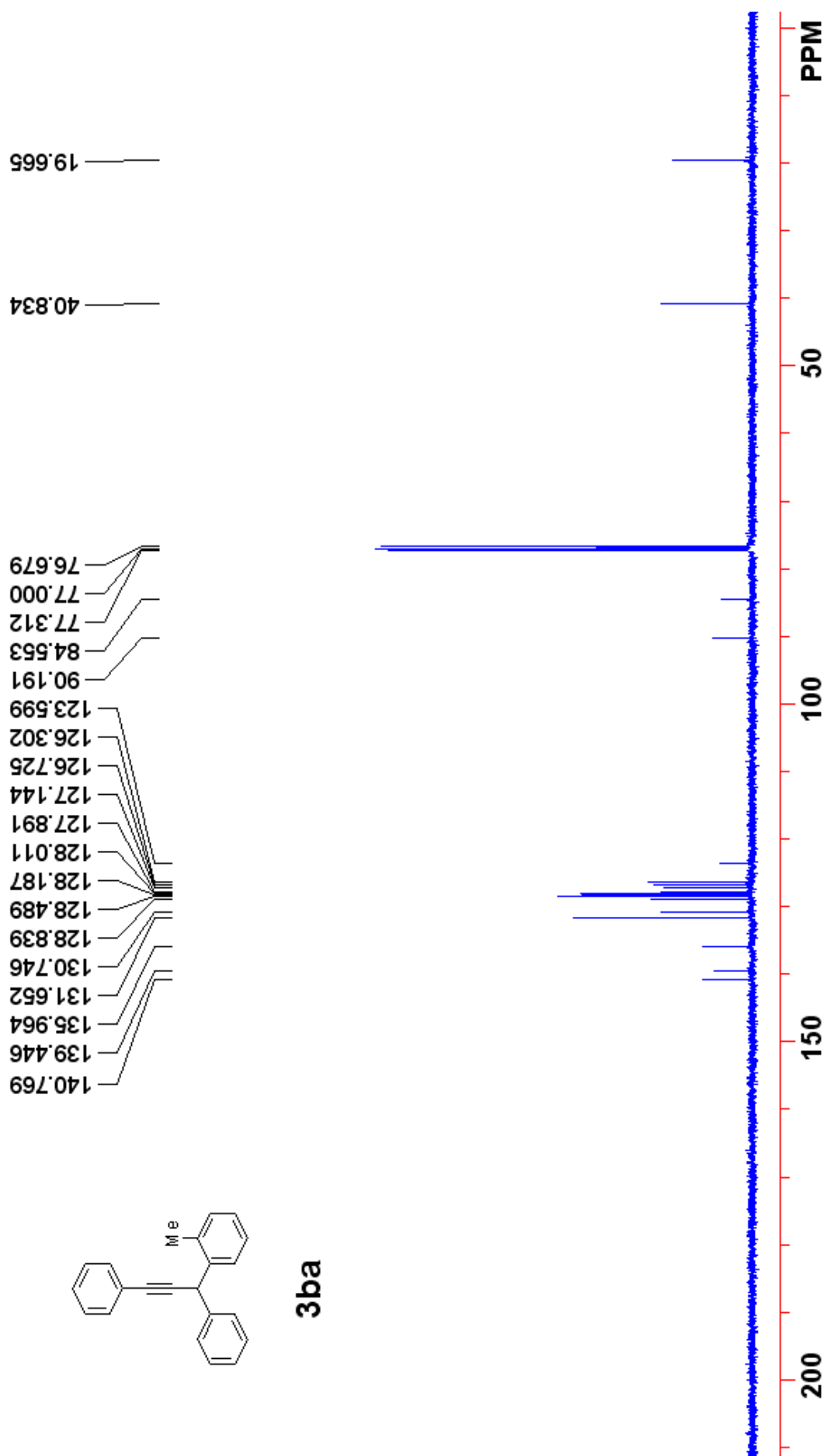
1. J. S. Haynes, J. R. Sams, R. C. Thompson, *Can. J. Chem.*, 1981, **59**, 669.
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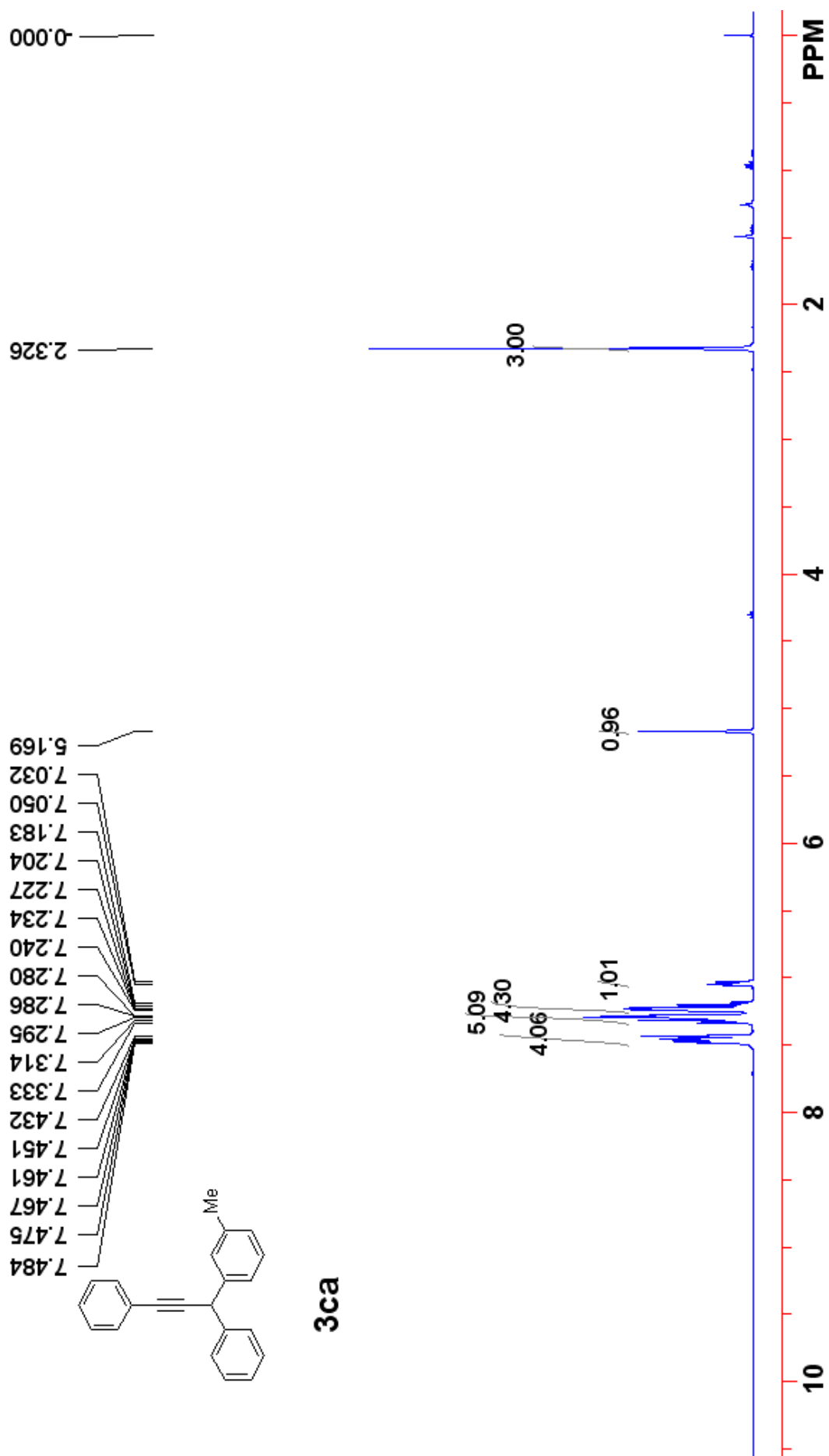


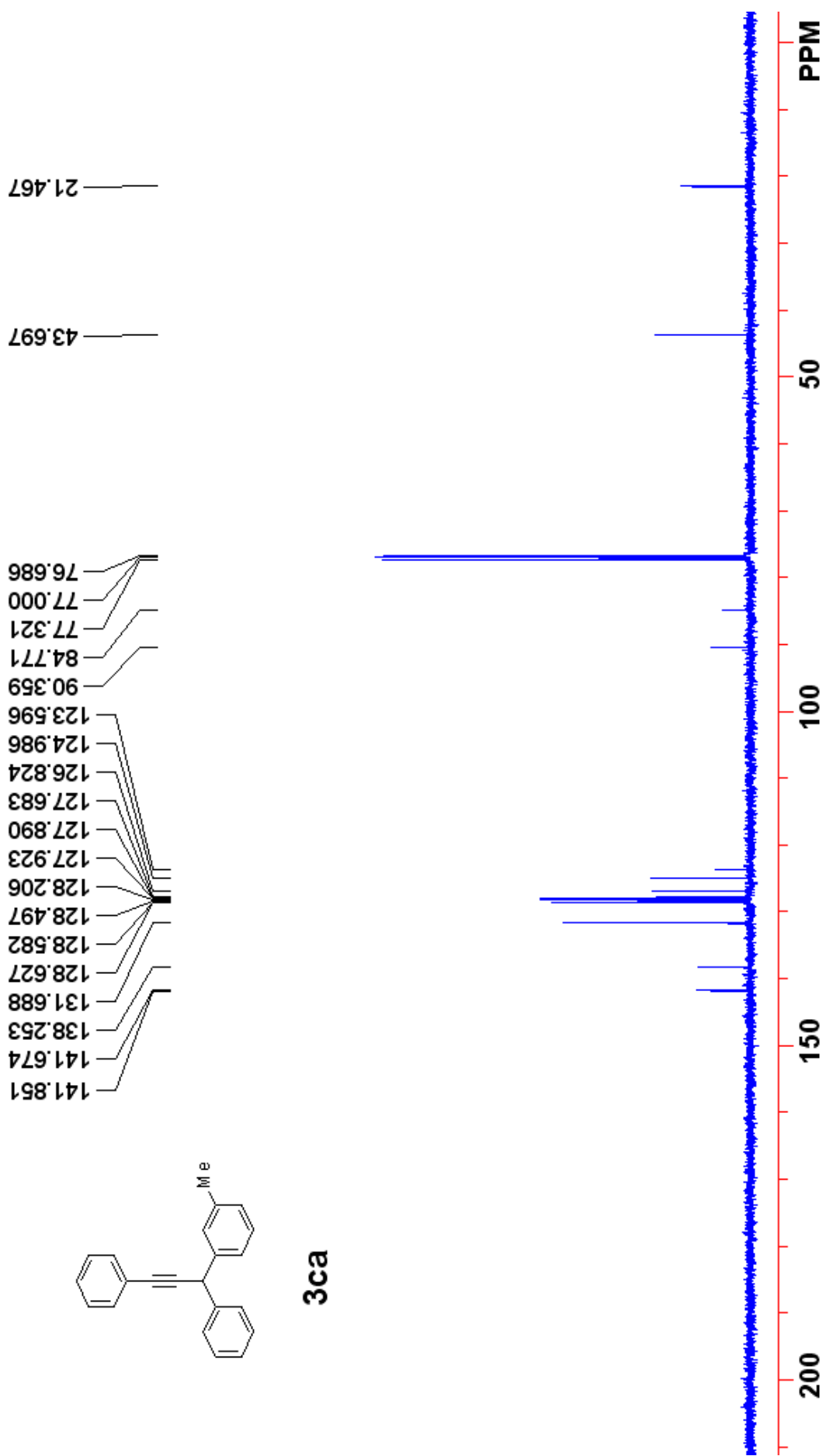


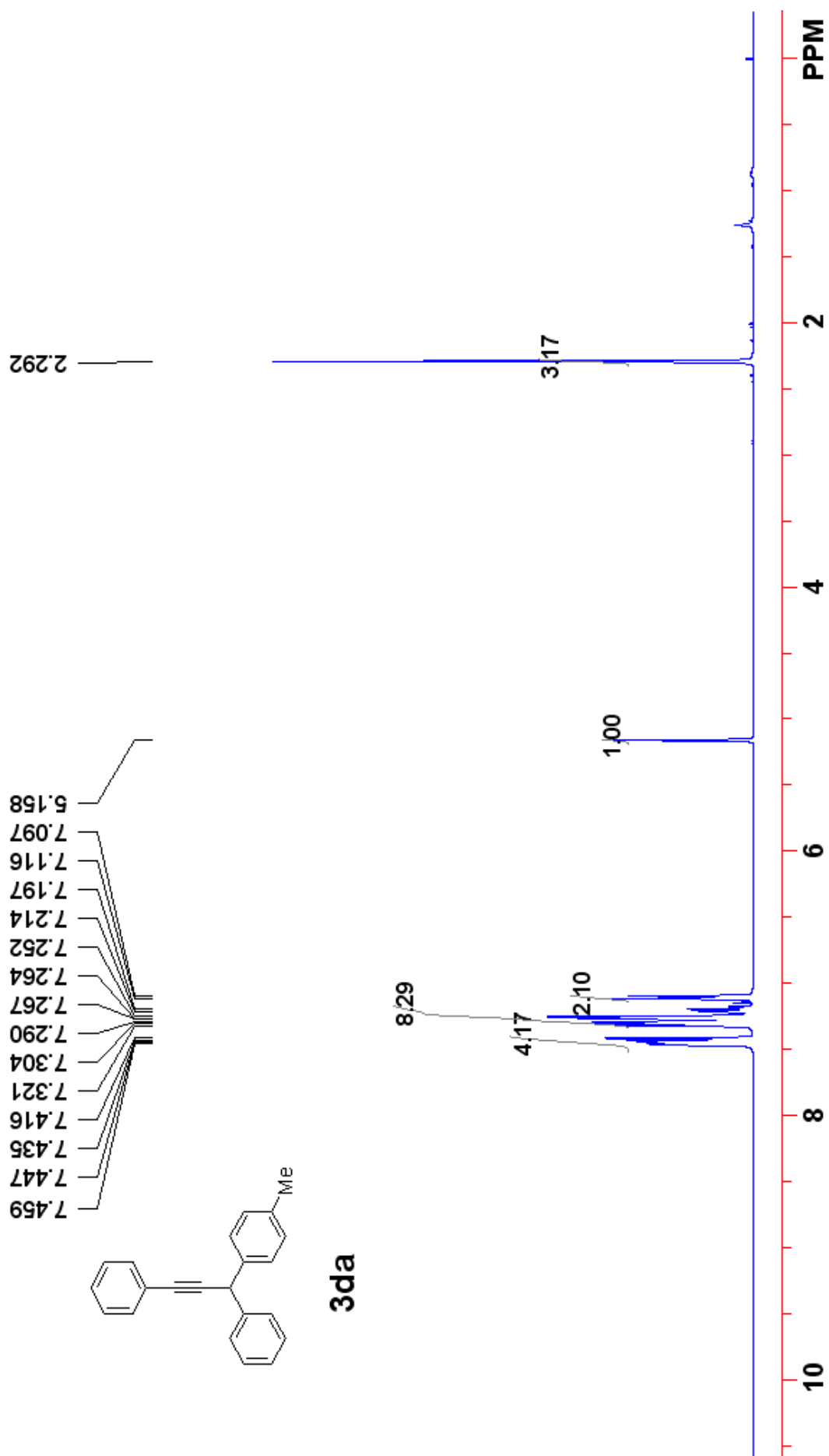
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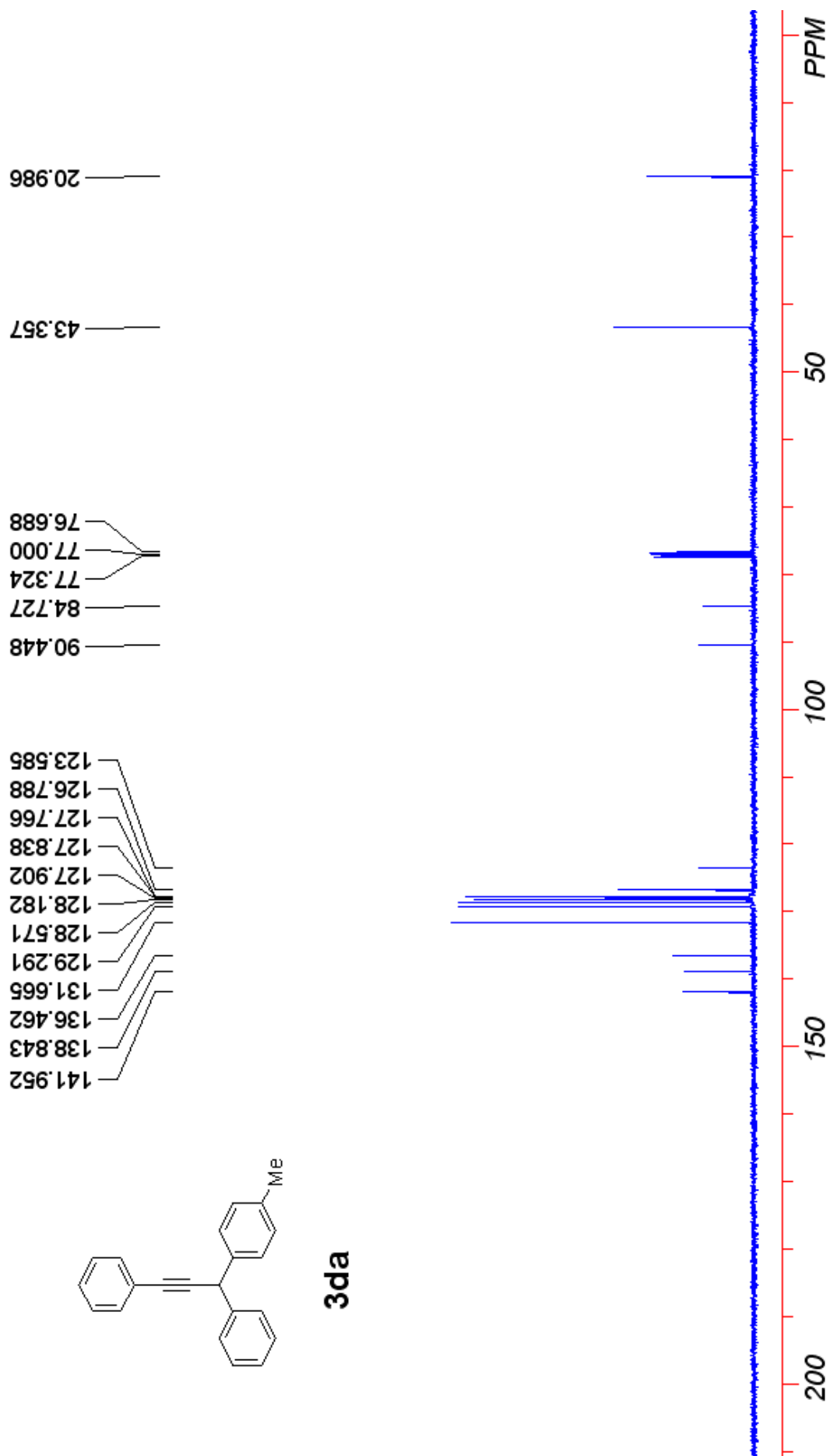


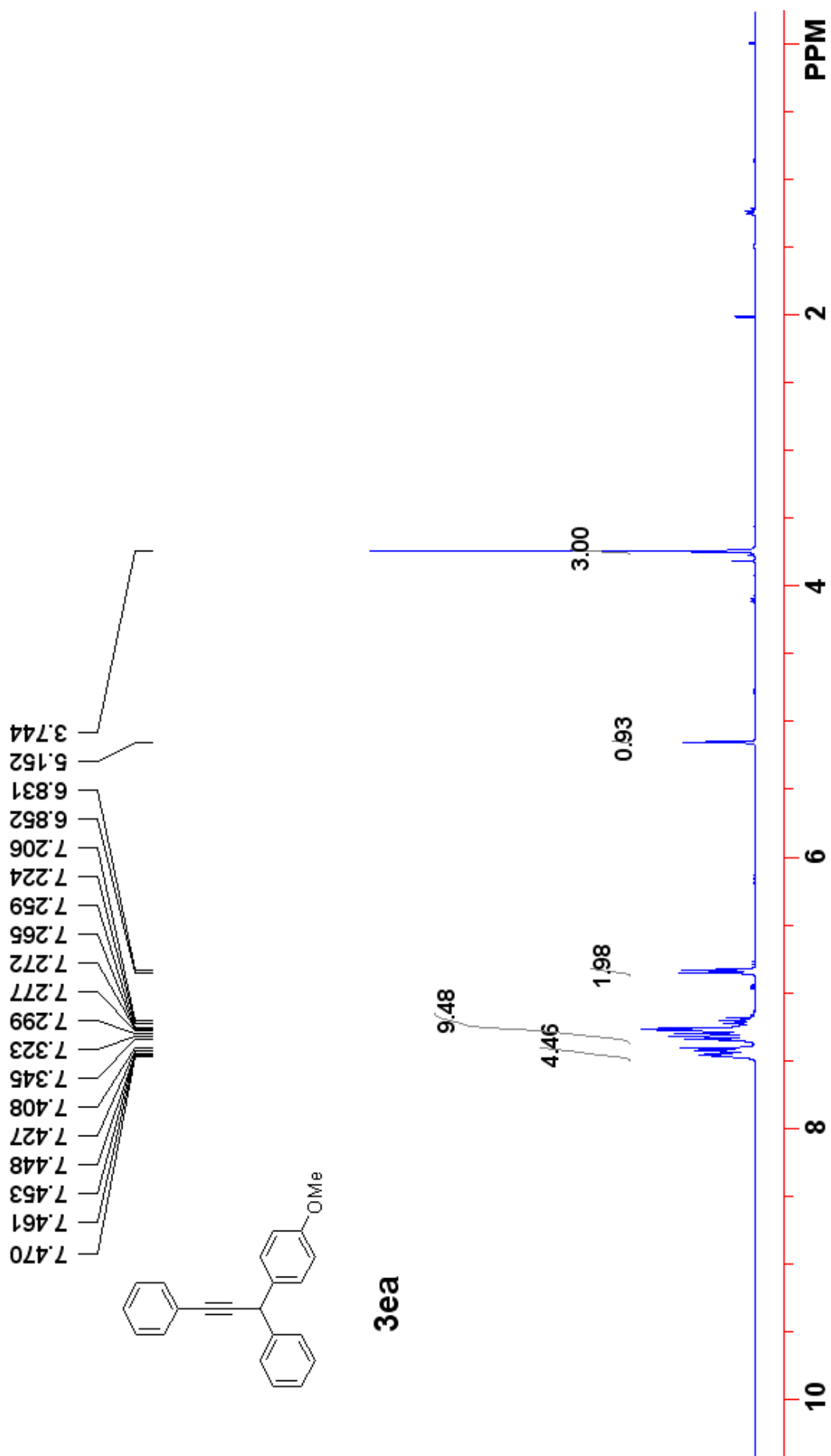


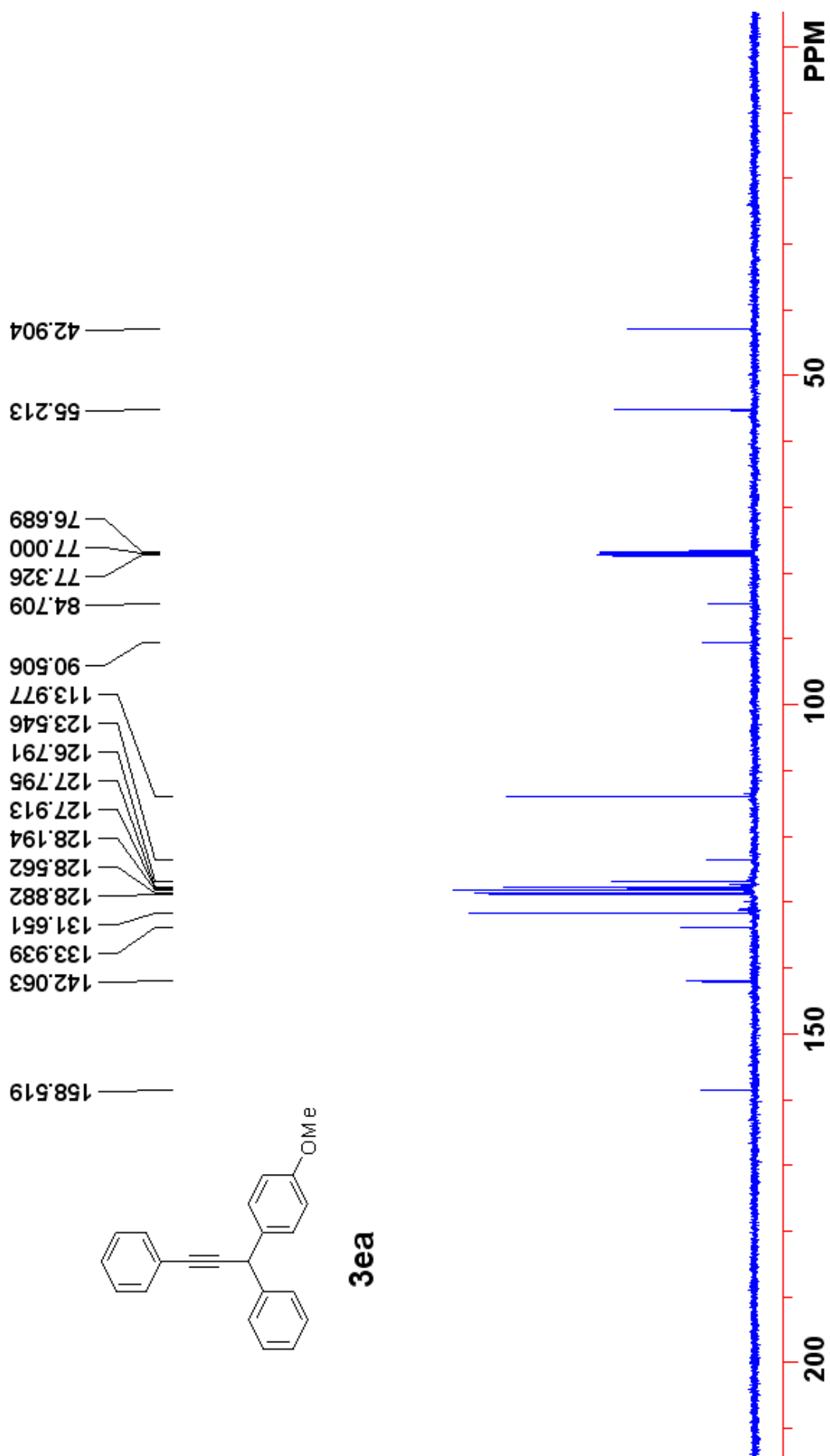


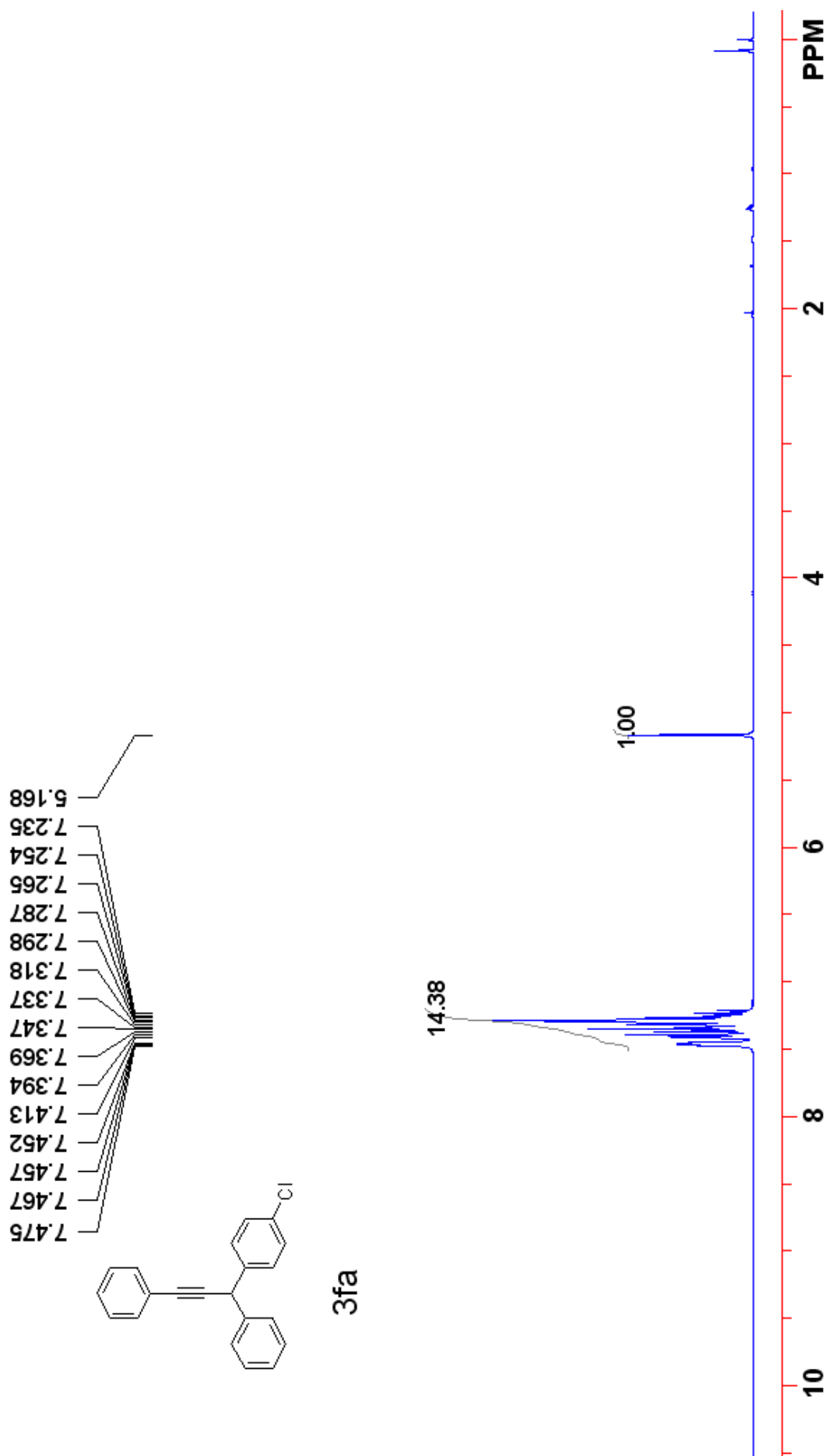


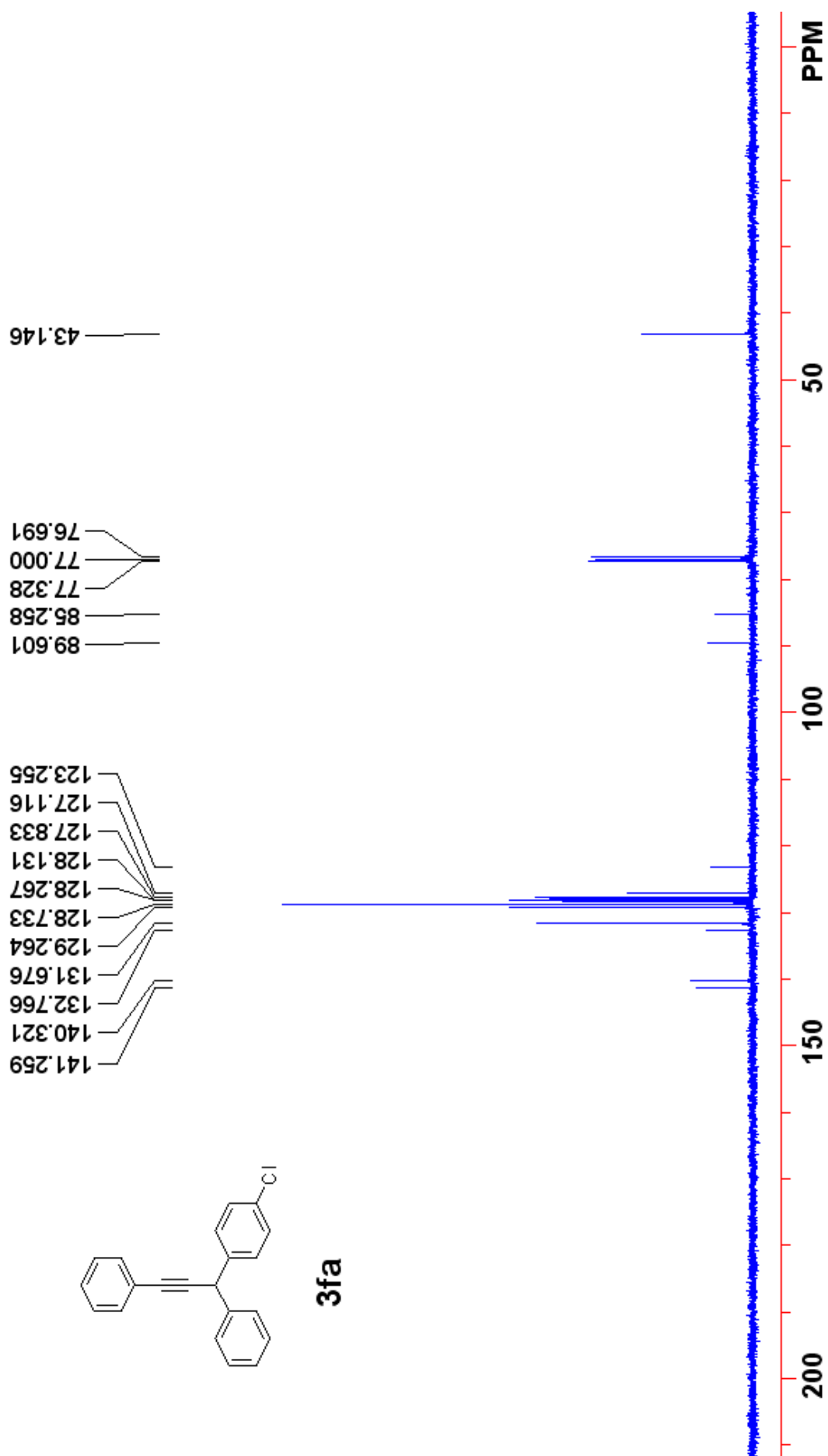


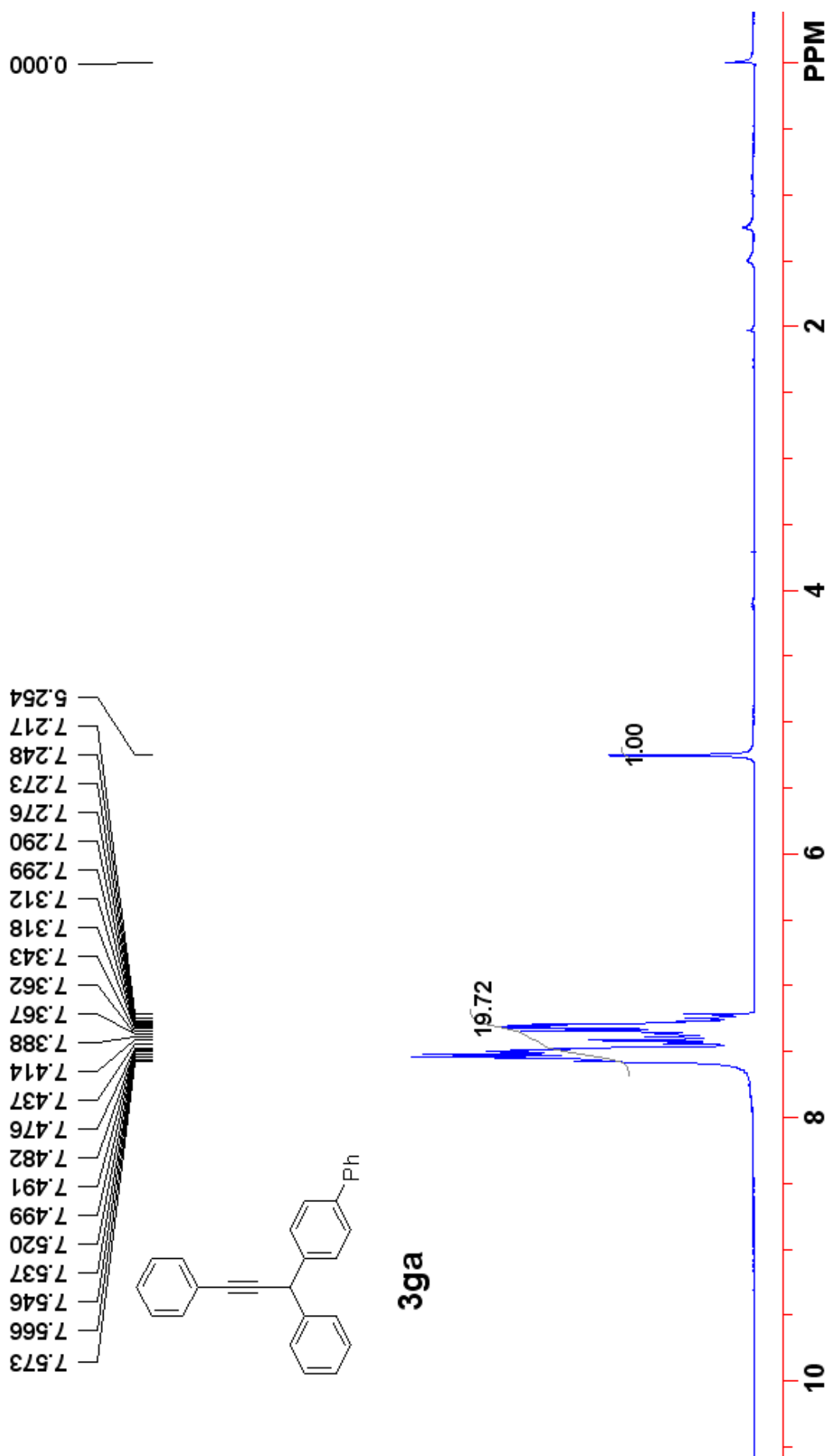


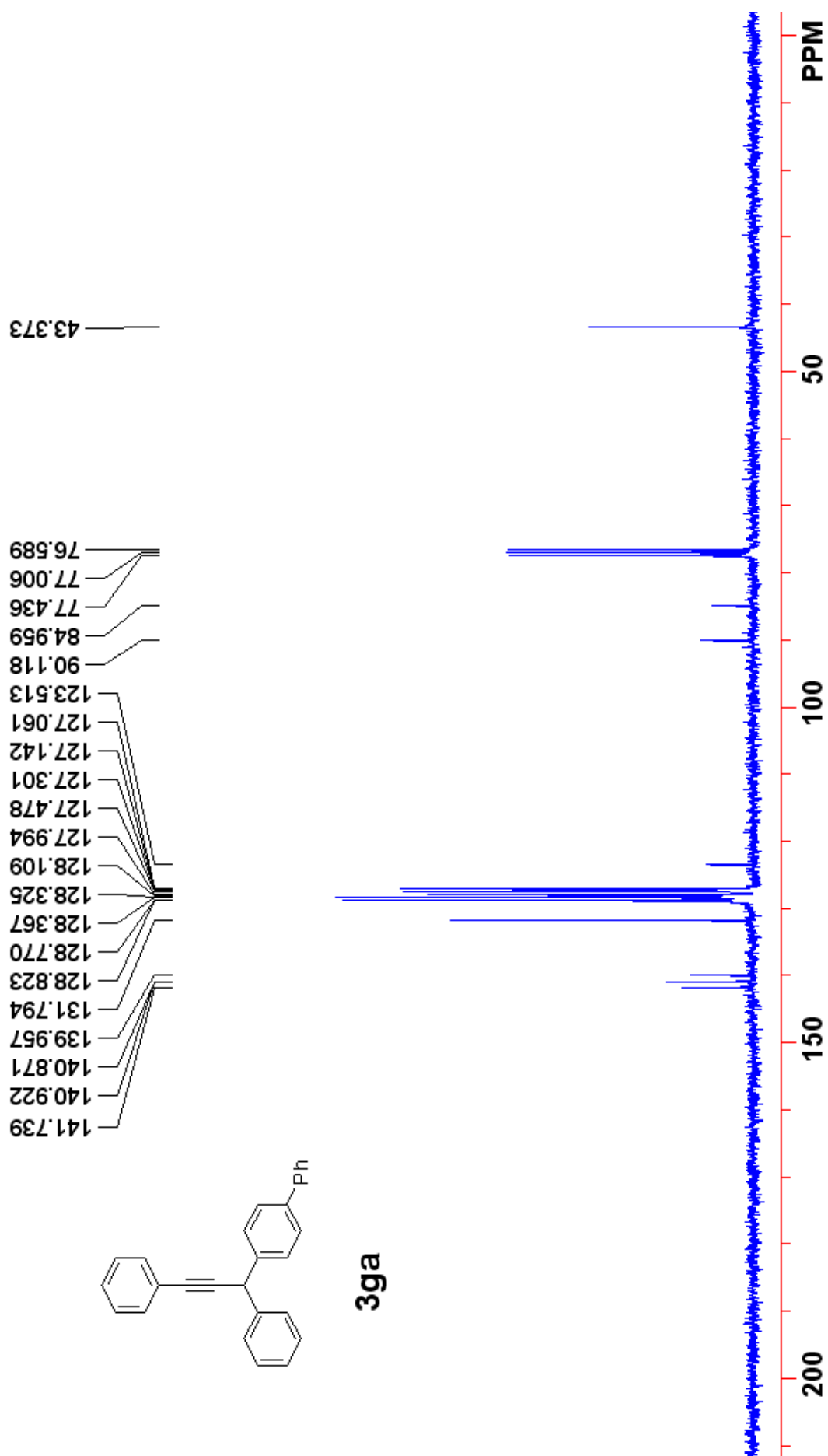


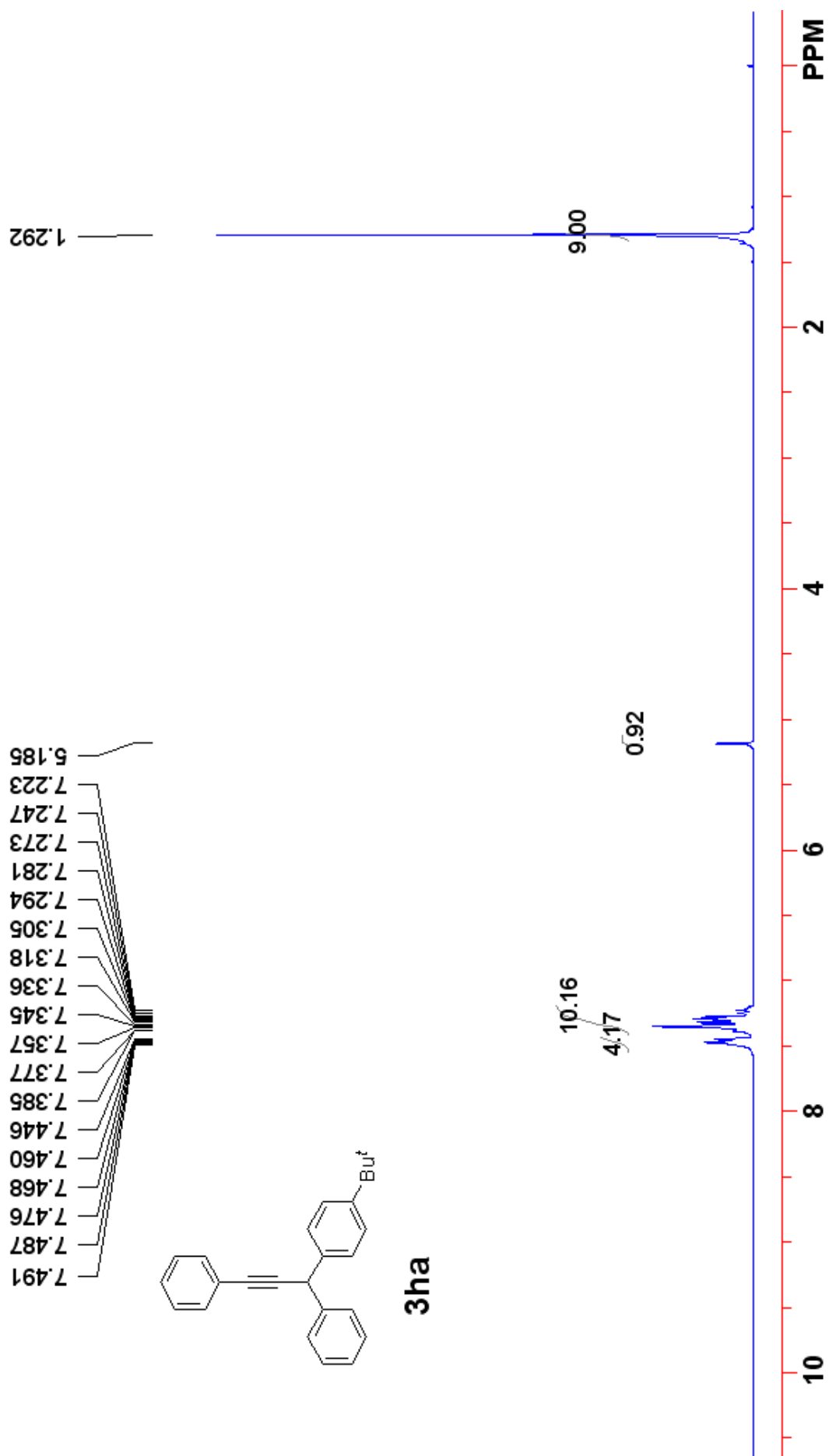


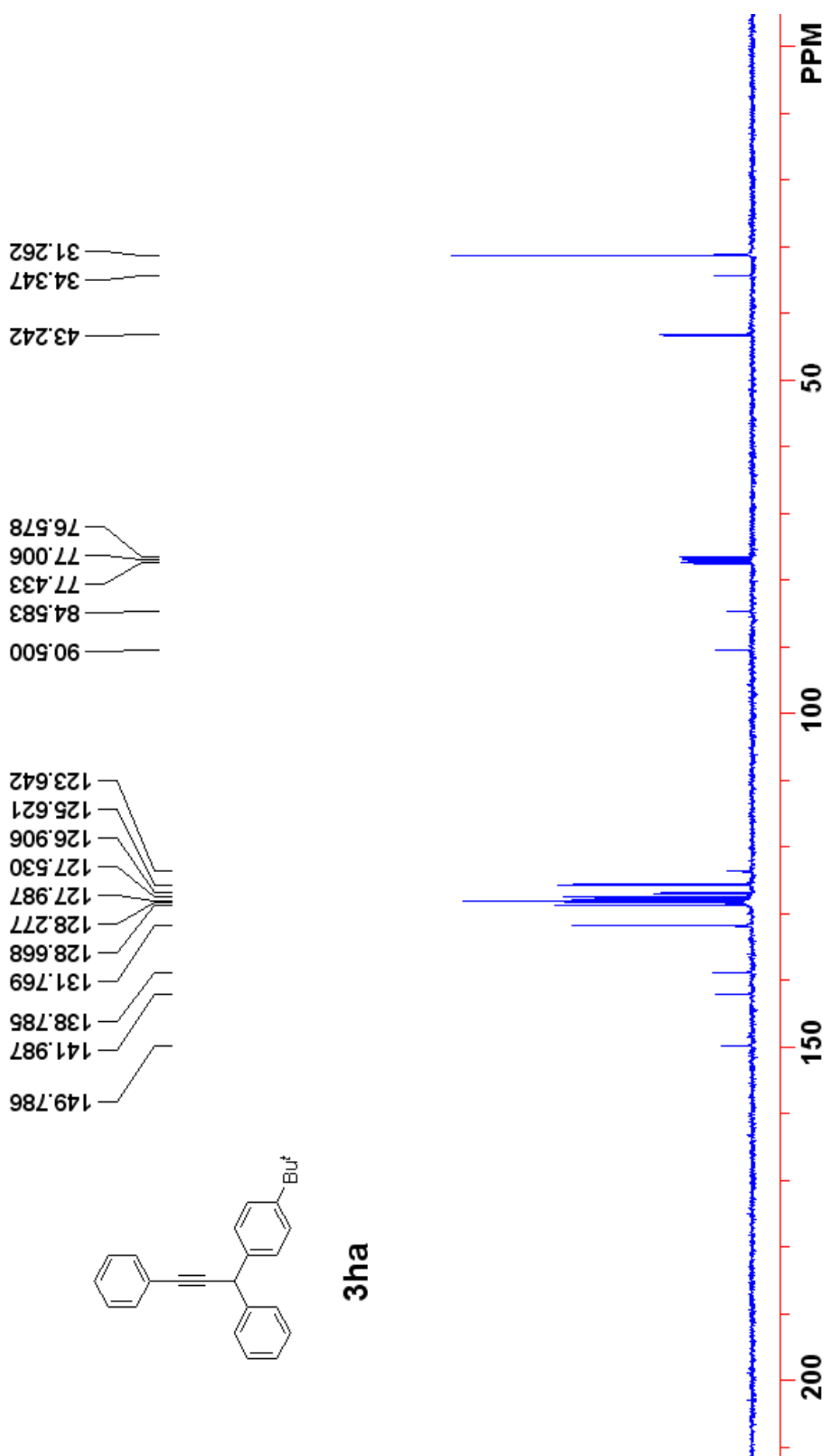


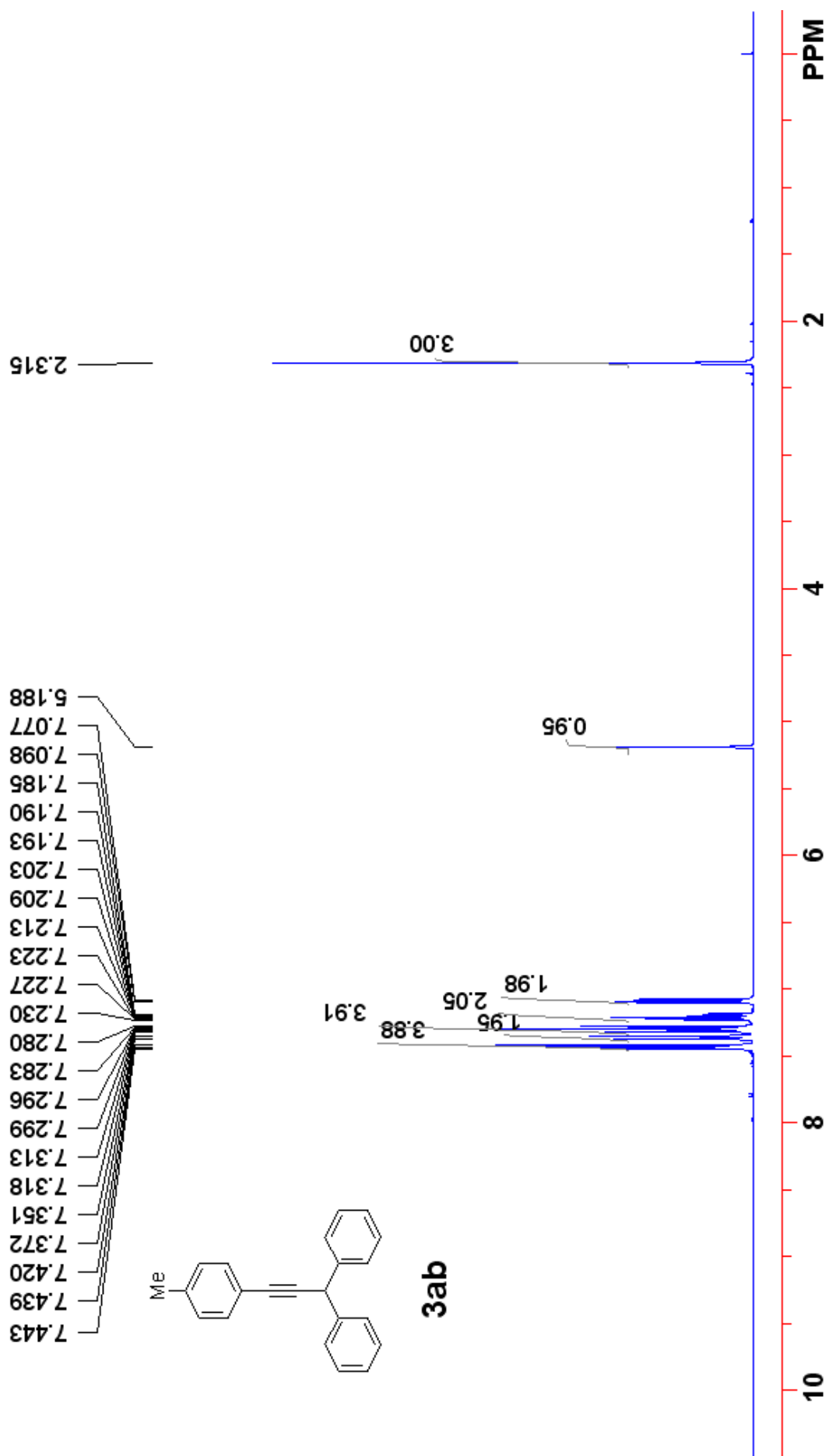


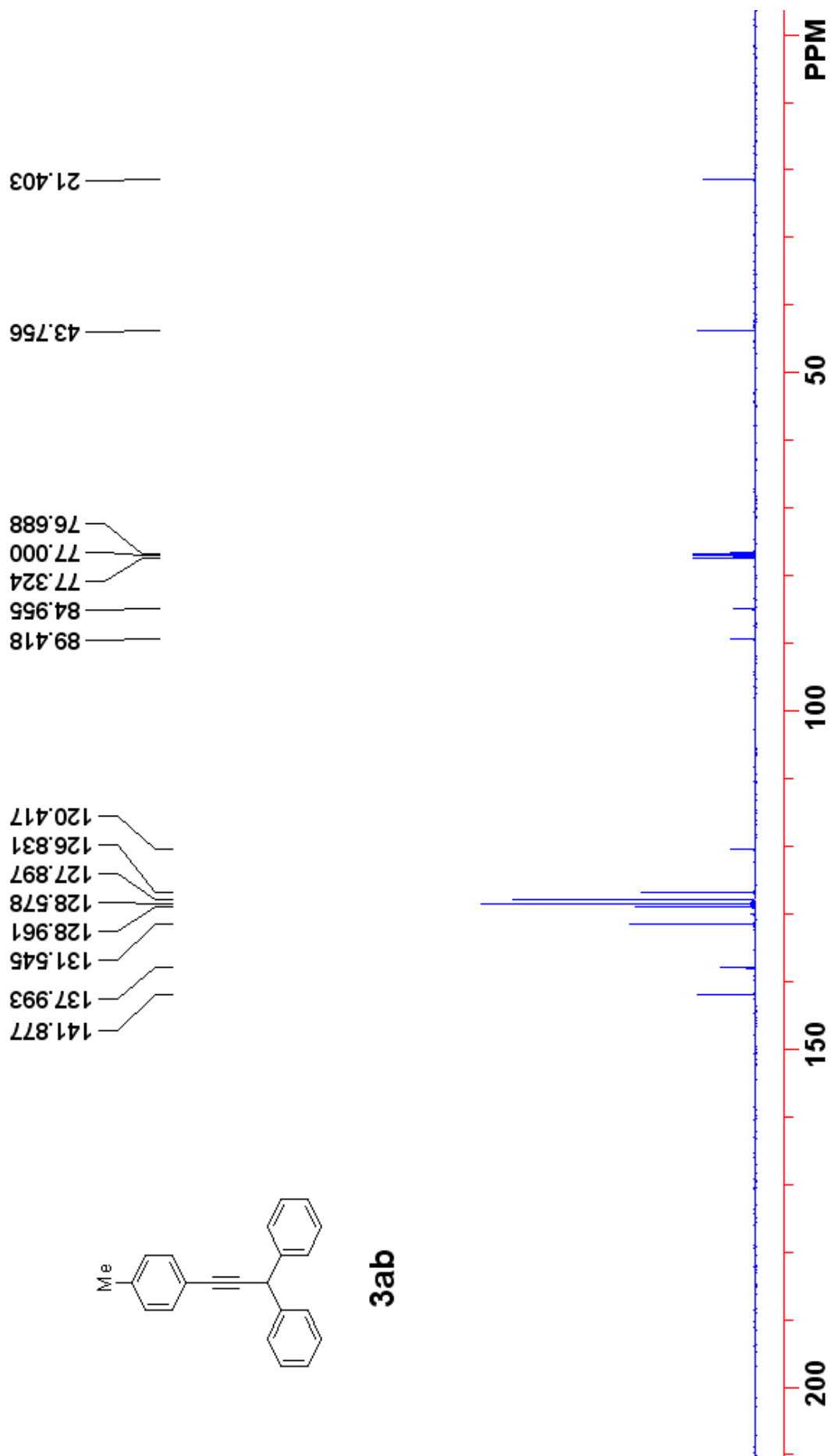


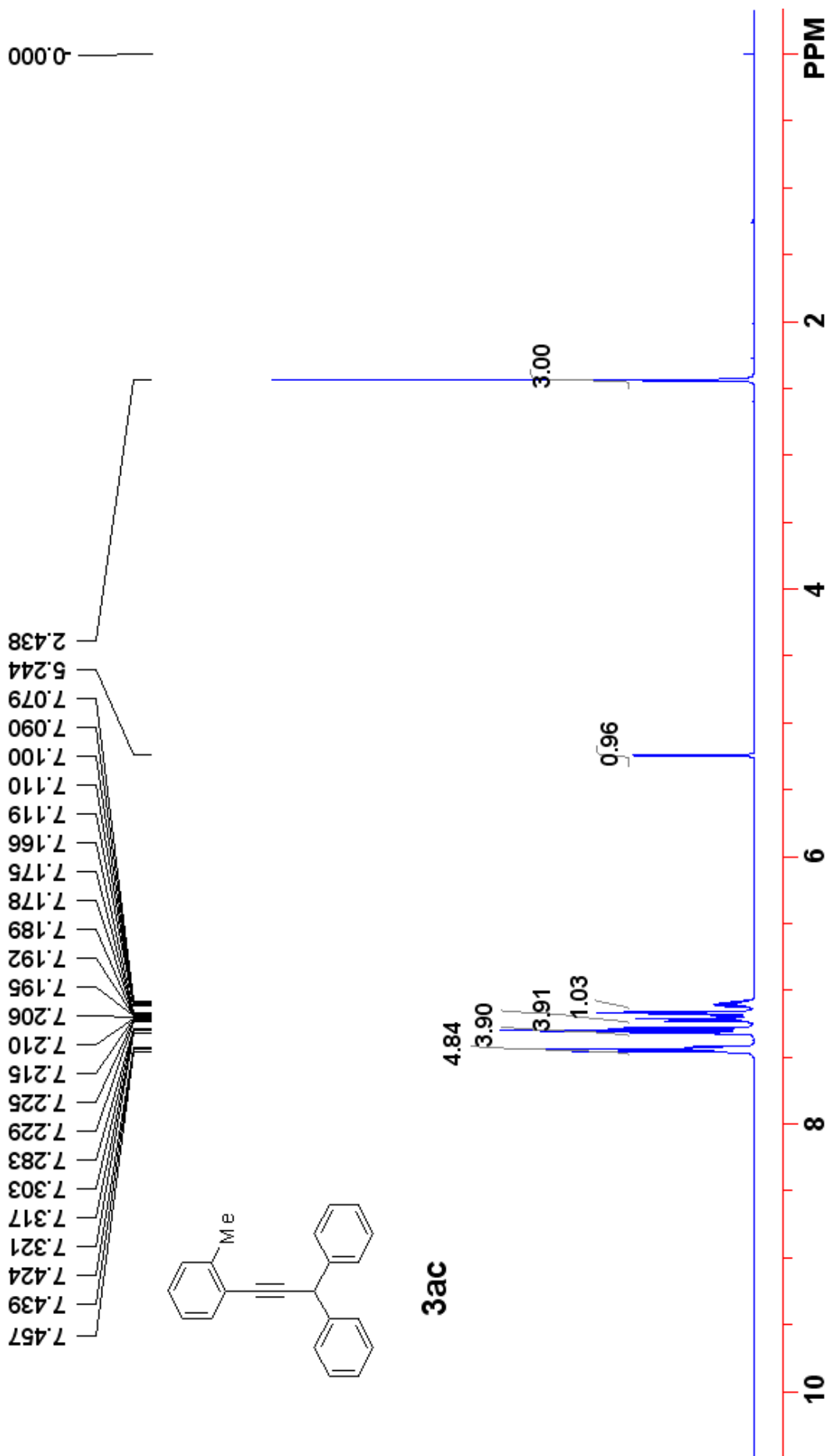


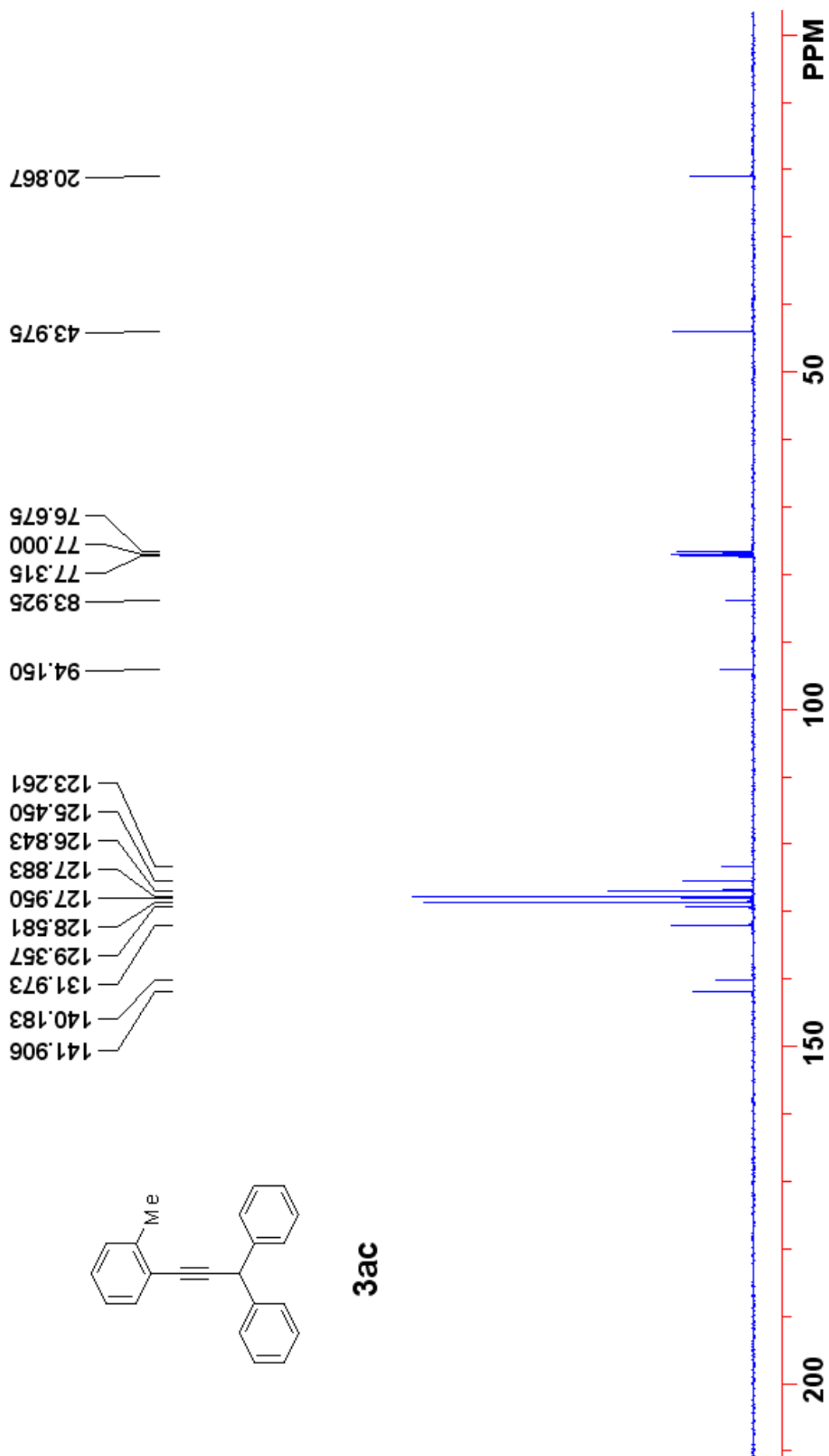


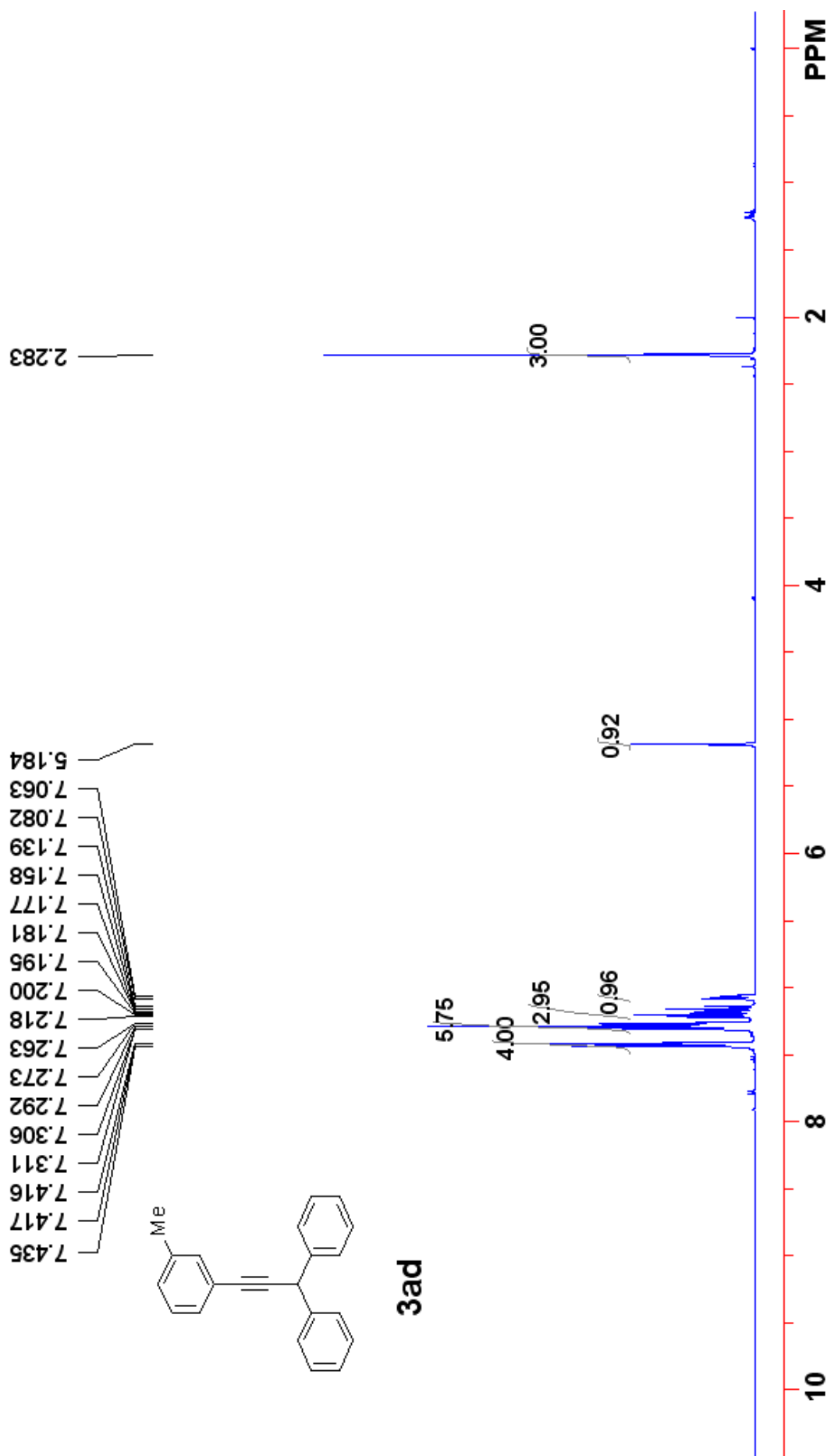


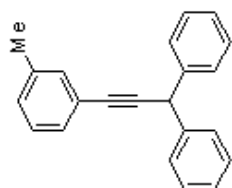
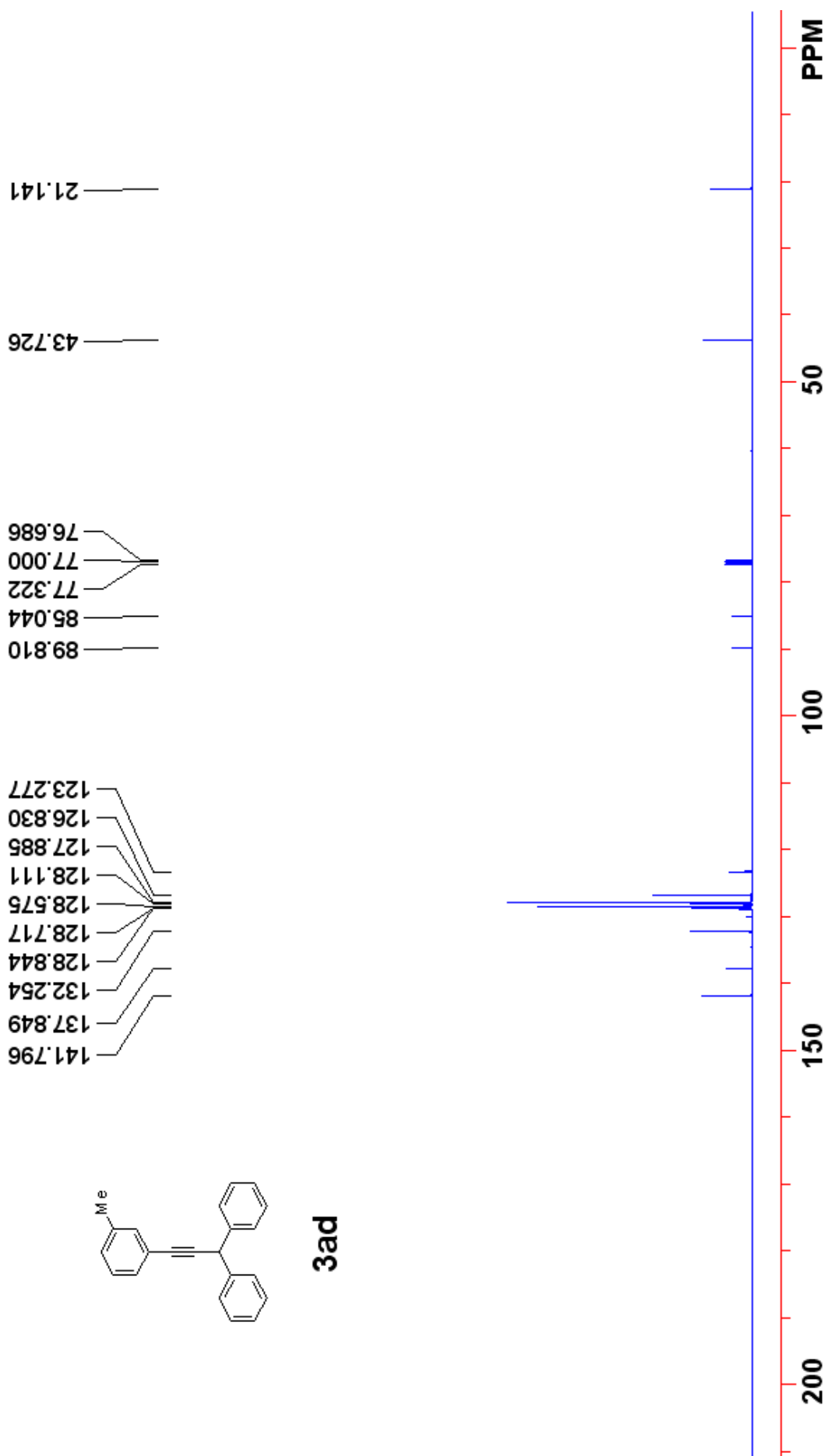












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