

Supporting Information

A Practical Method for the Synthesis of 2-Alkynylpropenals

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2-Methylene-4-*n*-butylbut-3-yn-1-ol (7c).¹ Reaction of vinyl iodide **5** (0.799 g, 4.34 mmol), 1-hexyne (2.50 mL, 1.78 g, 21.7 mmol), (Ph₃P)₄Pd (0.225 g, 0.19 mmol), CuI (0.098 g, 0.52 mmol), and triethylamine (6.00 mL, 4.39 g, 43.4 mmol) in 75 mL of THF at rt for 26 h according to the general procedure afforded 0.984 g of a dark brown oil. This material was purified by column chromatography on 100 g of silica gel (elution with CH₂Cl₂) to provide 0.477 g (79%) of enyne **7c** as a yellow oil: IR (film) 3343, 2958, 2873, 2223, and 1618 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.43 (d, *J* = 1.5 Hz, 1H), 5.39 (app s, 1H), 4.12 (d, *J* = 5.0 Hz, 2H), 2.33 (t, *J* = 7.0 Hz, 2H), 1.72 (br s, 1H), 1.51-1.56 (m, 2H), 1.39-1.46 (m, 2H), and 0.93 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 131.8, 119.1, 92.6, 78.4, 65.9, 30.9, 22.2, 19.2, and 13.8; HRMS-EI *m/z*: [M]⁺ calcd for C₉H₁₄O, 138.1039; found, 138.1037.

2-Methylene-4-phenylbut-3-yn-1-ol (7d). Reaction of vinyl iodide **5** (1.113 g, 6.05 mmol), phenylacetylene (0.86 mL, 0.80 g, 7.86 mmol), (Ph₃P)₄Pd (0.203 g, 0.18 mmol), CuI (0.063 g, 0.33 mmol), and triethylamine (1.10 mL, 0.799 g, 7.89 mmol) in 15 mL of THF at rt for 2 h according to the general procedure afforded 1.298 g of a brown oil. This material was purified by column chromatography on 24 g of silica gel (gradient elution with 0-20% EtOAc-hexane) to provide 0.890 g of a yellow oil, which was further purified on 22 g of silica gel (gradient elution with 0-20% EtOAc-hexane) to afford 0.674 g (70%) of enyne **7d** as a pale yellow oil with spectral characteristics consistent with those reported previously.² IR (film) 3334, 3060, 2925, 2866, 2208, and 1614 cm⁻¹; ¹H

¹ Akita, M.; Yasuda, H.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 480.

² Mickelson, T. J.; Koviach, J. L.; Forsyth, C. J. *J. Org. Chem.* **1996**, *61*, 9617.

NMR (500 MHz, CDCl₃) δ 7.45-7.48 (m, 2H), 7.32-7.35 (m, 3H), 5.61 (dd, $J = 1.5, 12.0$ Hz, 2H), 4.26 (d, $J = 6.5$ Hz, 2H), and 1.80 (app t, $J = 5.5$ Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 131.9, 131.4, 128.7, 128.5, 122.9, 120.7, 91.1, 87.1, and 65.6; HRMS-EI m/z : [M]⁺ calcd for C₁₁H₁₀O, 158.0726; found, 158.0731.

2-Methylene-4-(triisopropylsilyl)but-3-ynal (1b). Reaction of a solution of the allylic alcohol **7b** (0.040 g, 0.17 mmol) in 3 mL of dichloromethane with Dess-Martin periodinane (0.089 g, 0.19 mmol) and then poly(4-vinylpyridine) (0.092 g, 0.85 mmol) according to the general procedure gave aldehyde **1b** as a yellow oil in 78% yield as determined by ¹H NMR analysis: IR (film) 2944, 2867, 2143, 1718, and 1624 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.49 (s, 1H), 6.59 (d, $J = 0.6$ Hz, 1H), 6.38 (d, $J = 0.9$ Hz, 1H), and 1.14 (apparent s, 21H); ¹³C NMR (125 MHz, CDCl₃) δ 190.0, 138.6, 133.3, 99.7, 98.5, 18.8, and 11.3.

2-Methylene-4(*n*-butyl)but-3-ynal (1c). Reaction of a solution of the allylic alcohol **7c** (0.105 g, 0.76 mmol) in 2 mL of dichloromethane with Dess-Martin periodinane (0.358 g, 0.84 mmol) and then poly(4-vinylpyridine) (0.399 g, 3.80 mmol) according to the general procedure gave aldehyde **1c** as a yellow oil in 59% yield as determined by ¹H NMR analysis: IR (film) 2958, 2932, 2234, 1706, and 1635 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.47 (s, 1H), 6.55 (d, $J = 0.5$ Hz, 1H), 6.30 (app s, 1H), 2.40 (s, 1H), 1.54-1.60 (m, 2H), 1.41-1.48 (m, 2H), and 0.93 (t, $J = 7.0$ Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 190.9, 138.5, 133.8, 97.7, 73.6, 30.6, 22.2, 19.3, and 13.8.

2-Methylene-4(phenyl)but-3-ynal (1d). Reaction of a solution of the allylic alcohol **7d** (0.093 g, 0.59 mmol) in 3 mL of dichloromethane with Dess-Martin periodinane (0.358 g, 0.84 mmol) and then poly(4-vinylpyridine) (0.312 g, 2.94 mmol)

according to the general procedure gave aldehyde **1d** as a yellow oil in 41% yield as determined by ^1H NMR analysis: IR (film) 3057, 2925, 2851, 2213, 1701, and 1628 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.57 (s, 1H), 7.53-7.55 (m, 2H), 7.35-7.37 (m, 3H), 6.70 (d, $J = 1.0$ Hz, 1H), and 6.45 (d, $J = 0.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 190.2, 138.9, 133.3, 132.1, 129.3, 128.6, 122.3, 95.7, and 82.3.

5-Hydroxy-2,2-dimethyl-6-methylene-8-(triisopropylsilyl)oct-7-yn-3-one (9b).

A solution of the lithium enolate derivative of pinacolone was generated as described in the General Procedure from the reaction of diisopropylamine (0.024 mL, 0.017 g, 0.17 mmol) and 0.67 mL of *n*-BuLi solution (2.41 M in hexane, 0.16 mmol) in 3 mL of THF followed by addition of pinacolone (0.017 mL, 0.013 g, 0.13 mmol) in 2 mL of THF. A solution of aldehyde **1b** (ca. 0.2 mmol) in 3 mL of THF was prepared as described in the General Procedure by oxidation of allylic alcohol **7b** (0.061 g, 0.26 mmol) with Dess-Martin periodinane (0.120 g, 0.28 mmol) in 5 mL of CH_2Cl_2 . Reaction of **1b** with the ketone enolate then afforded 0.070 g of a yellow oil, which was purified by column chromatography on 10 g of silica gel (gradient elution with 0-10% EtOAc-hexane) to provide 0.031 g (70%) of aldol **9b** as a pale yellow oil: IR (film) 3482, 2944, 2866, 2142, 1700, and 1616 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.69 (t, $J = 1.5$ Hz, 1H), 5.55 (t, $J = 1.5$ Hz, 1H), 4.53-4.56 (m, 1H), 3.52 (d, $J = 4.0$ Hz, 1H), 3.10 (dd, $J = 3.0, 18.0$ Hz, 1H), 2.78 (dd, $J = 8.5, 18.0$ Hz, 1H), 1.15 (s, 9H), and 1.09 (s, 21H); ^{13}C NMR (125 MHz, CDCl_3) δ 217.3, 132.9, 121.6, 105.0, 93.1, 70.1, 44.6, 42.2, 26.3, 18.8, and 11.4; HRMS-ESI m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{36}\text{O}_2\text{Si}$, 359.2377; found, 359.2376.

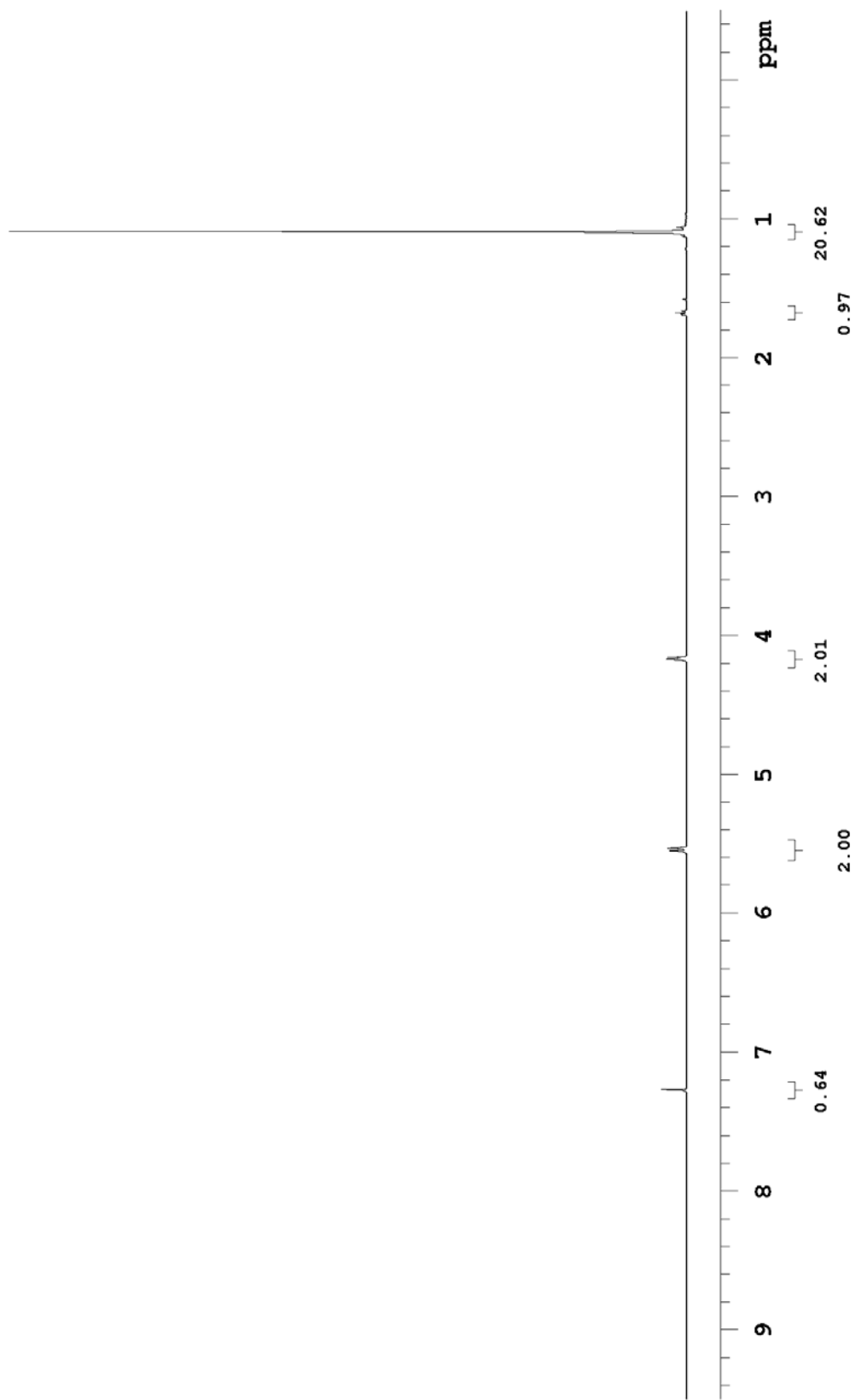
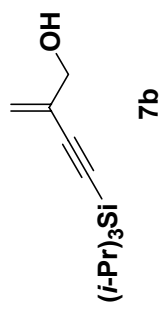
5-Hydroxy-2,2-dimethyl-6-methylene-8-(*n*-butyl)oct-7-yn-3-one (9c). A

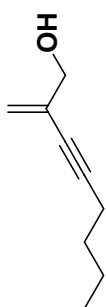
solution of the lithium enolate derivative of pinacolone was generated as described in the

General Procedure from the reaction of diisopropylamine (0.17 mL, 0.12 g, 1.2 mmol) and 0.43 mL of *n*-BuLi solution (2.35 M in hexane, 1.0 mmol) in 10 mL of THF followed by addition of pinacolone (0.105 mL, 0.085 g, 0.84 mmol) in 3 mL of THF. A solution of aldehyde **1c** (ca. 0.9 mmol) in 3 mL of THF was prepared as described in the General Procedure by oxidation of allylic alcohol **7c** (0.218 g, 1.57 mmol) with Dess-Martin periodinane (0.742 g, 1.57 mmol) in 5 mL of CH₂Cl₂. Reaction of the aldehyde with the ketone enolate then afforded 0.235 g of a yellow oil, which was purified by column chromatography on 12 g of silica gel (gradient elution with 0-10% EtOAc-hexane) to provide 0.185 g of impure **9c** as a yellow oil. This material was further purified on 18 g of silica gel (gradient elution with 0-10% EtOAc-hexane) to afford 0.140 g (70%) of **9c** as a pale yellow oil: IR (film) 3481, 2961, 2222, 1700, and 1616 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.56 (t, *J* = 1.5 Hz, 1H), 5.41 (s, 1H), 4.50-4.53 (m, 1H), 3.41 (d, *J* = 4.0 Hz, 1H), 2.99 (dd, *J* = 3.0, 17.5 Hz, 1H), 2.79 (dd, *J* = 8.5, 18.0 Hz, 1H), 2.34 (t, *J* = 7.0 Hz, 2H), 1.51-1.55 (m, 2H), 1.40-1.47 (m, 2H), 1.16 (s, 9H) and 0.93 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 197.5, 133.2, 119.9, 92.8, 78.4, 70.5, 44.7, 42.3, 30.9, 26.4, 22.2, 19.2, and 13.8; HRMS-ESI *m/z*: [M+Na]⁺ calcd for C₁₅H₂₄O₂, 259.1669; found, 259.1674.

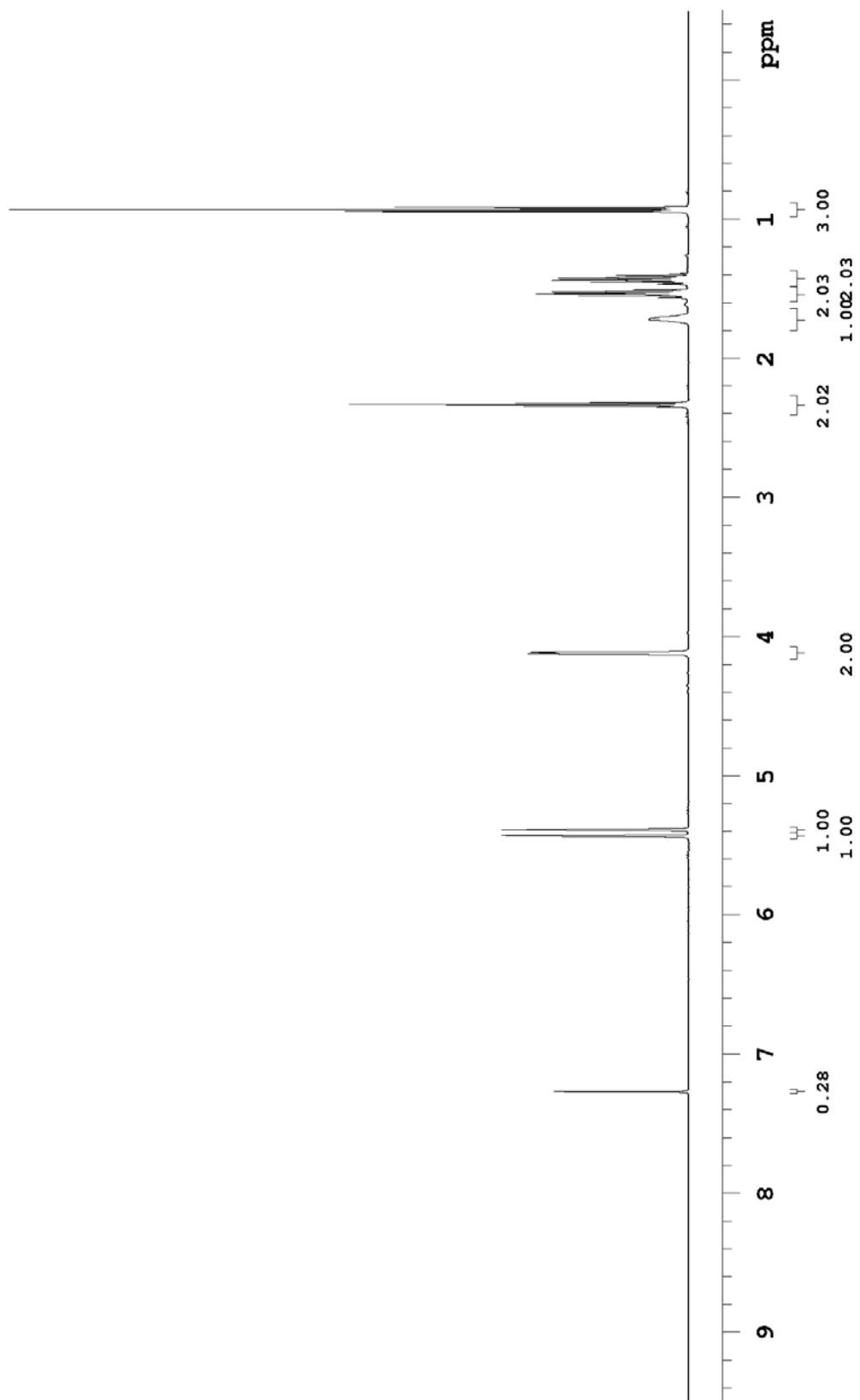
5-Hydroxy-2,2-dimethyl-6-methylene-8-(phenyl)-oct-7-yn-3-one (9d). A solution of the lithium enolate derivative of pinacolone was generated as described in the General Procedure from the reaction of diisopropylamine (0.054 mL, 0.039 g, 0.39 mmol) and 0.16 mL of *n*-BuLi solution (2.30 M in hexane, 0.36 mmol) in 4 mL of THF followed by addition of pinacolone (0.037 mL, 0.030 g, 0.30 mmol) in 2 mL of THF. A solution of aldehyde **1d** (ca. 0.3 mmol) in 2 mL of THF was prepared as described in the

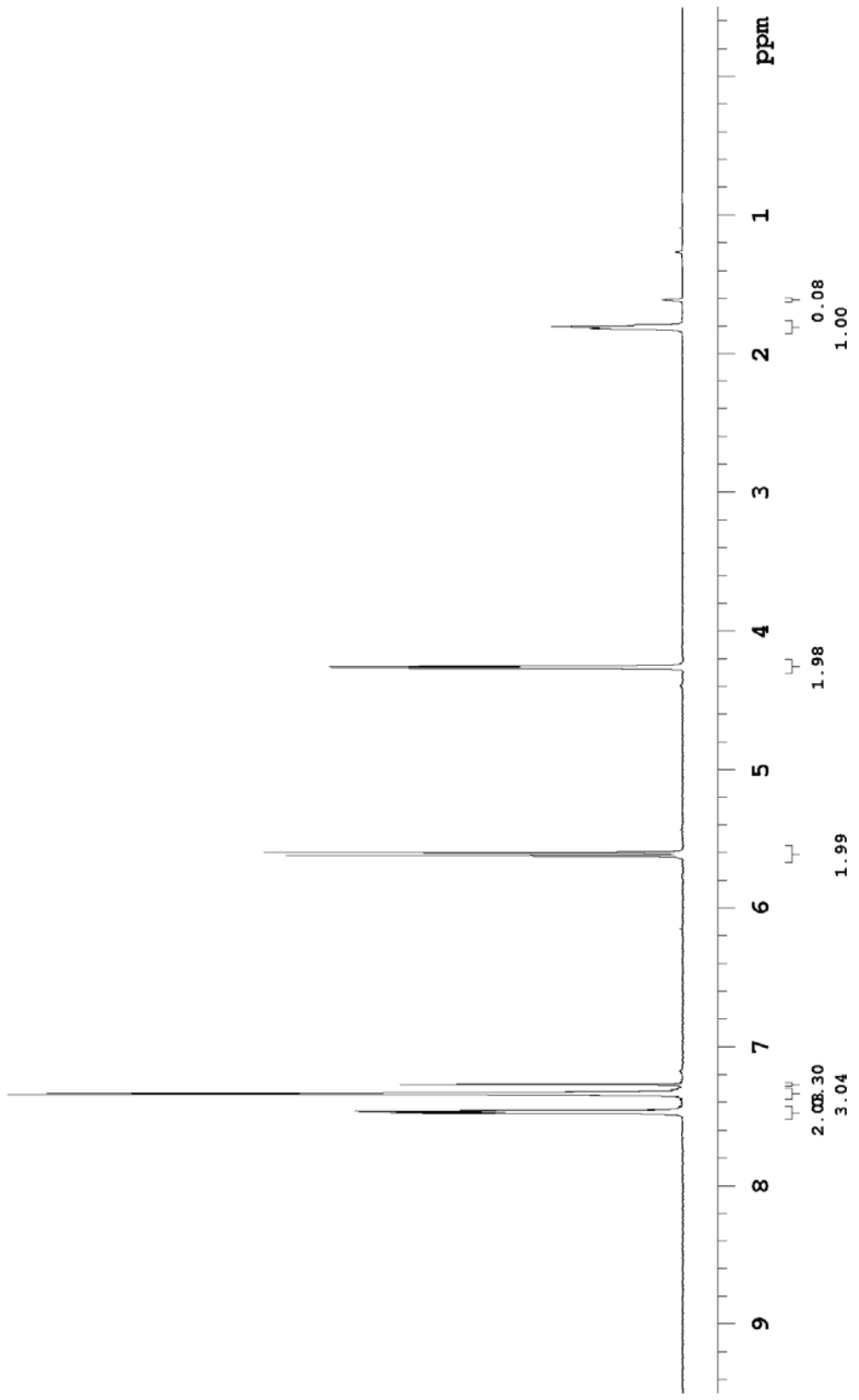
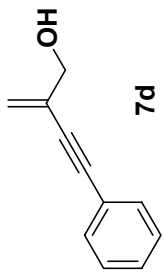
General Procedure by oxidation of allylic alcohol **7d** (0.130 g, 0.82 mmol) with Dess-Martin periodinane (0.388 g, 0.90 mmol) in 4 mL of CH₂Cl₂. Reaction of **1d** with the ketone enolate then afforded 0.097 g of a yellow oil, which was purified by column chromatography on 5 g of silica gel (gradient elution with 0-20% EtOAc-hexane) to provide 0.054 g (71%) of **9d** as a pale yellow oil: IR (film) 3462, 3057, 2970, 2201, and 1701 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.43-7.46 (m, 2H), 7.32-7.35 (m, 3H), 5.75 (t, *J* = 1.5 Hz, 1H), 5.61 (t, *J* = 1.5 Hz, 1H), 4.64-4.65 (m, 1H), 3.57 (d, *J* = 4.5 Hz, 1H), 3.06 (dd, *J* = 3.0, 18.0, 1H), 2.89 (dd, *J* = 8.5, 17.5 Hz, 1H), and 1.18 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 217.2, 132.8, 131.8, 128.7, 128.6, 123.0, 121.5, 91.5, 87.2, 70.3, 44.7, 42.2, and 26.4; HRMS-ESI *m/z*: [M+Na]⁺ calcd for C₁₇H₂₀O₂, 279.1356; found, 279.1362.

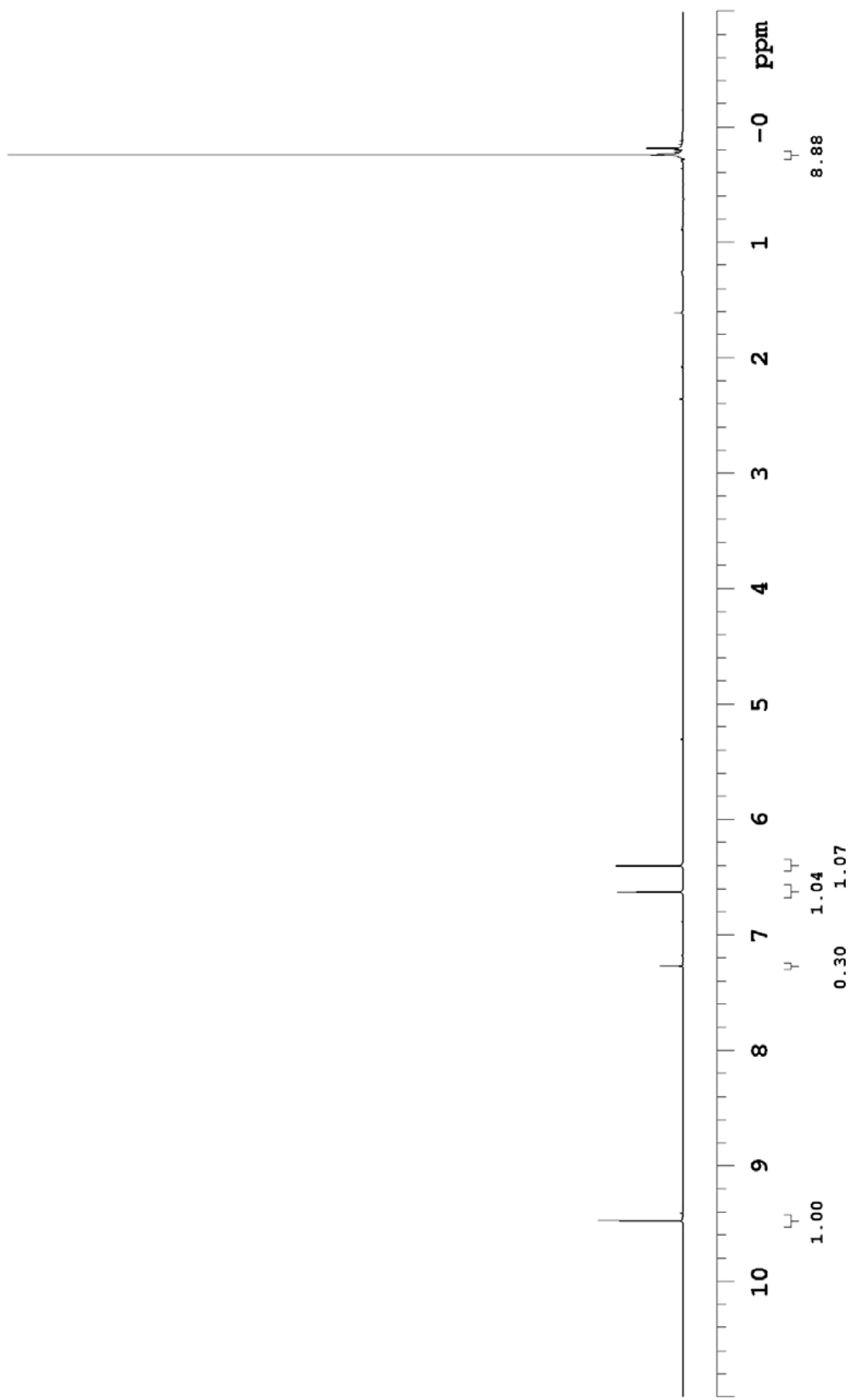
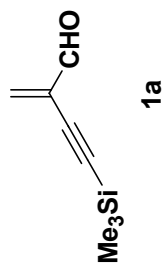


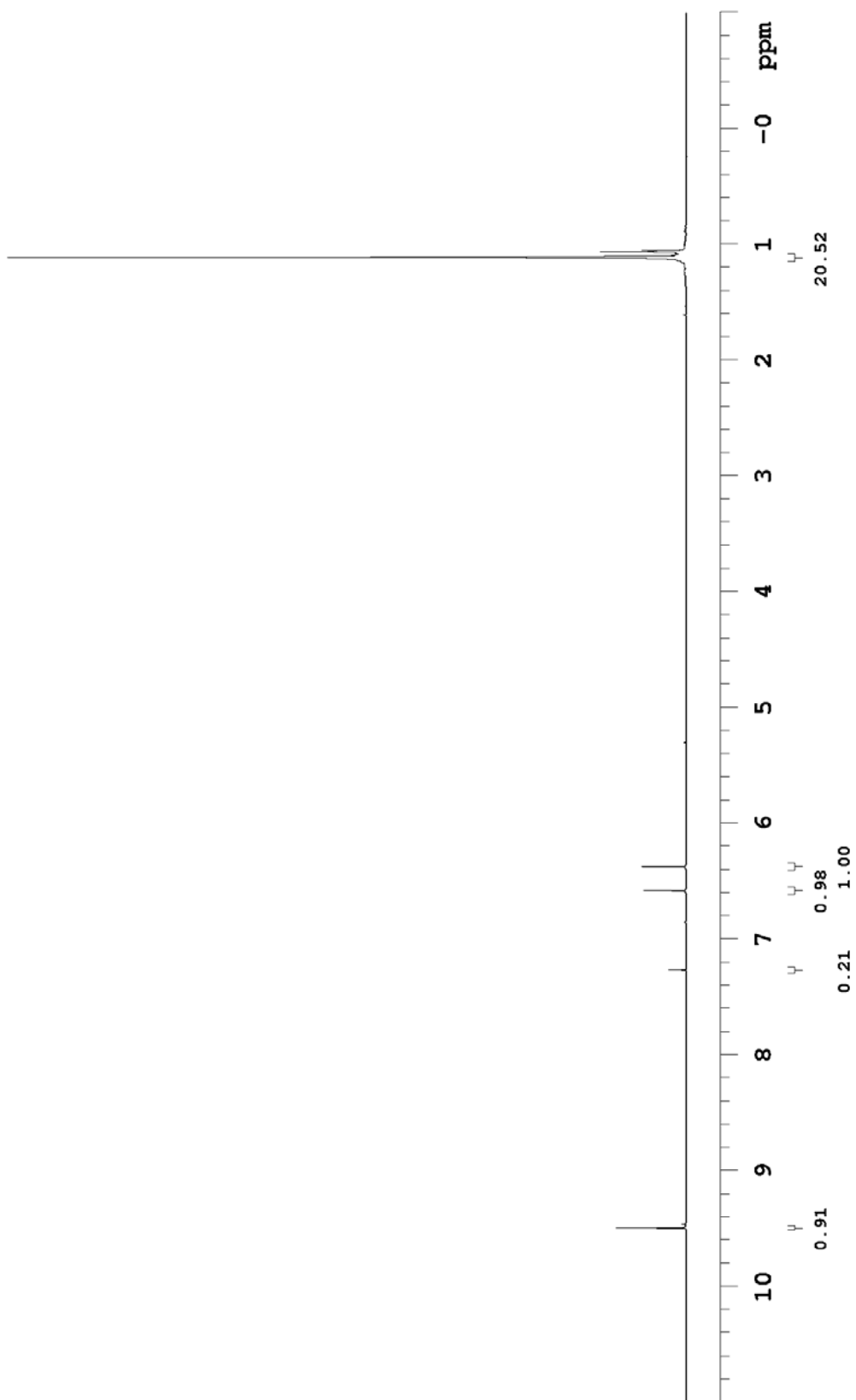
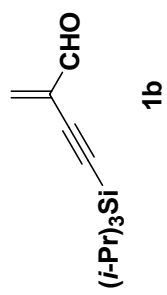


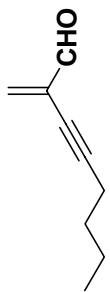
7c



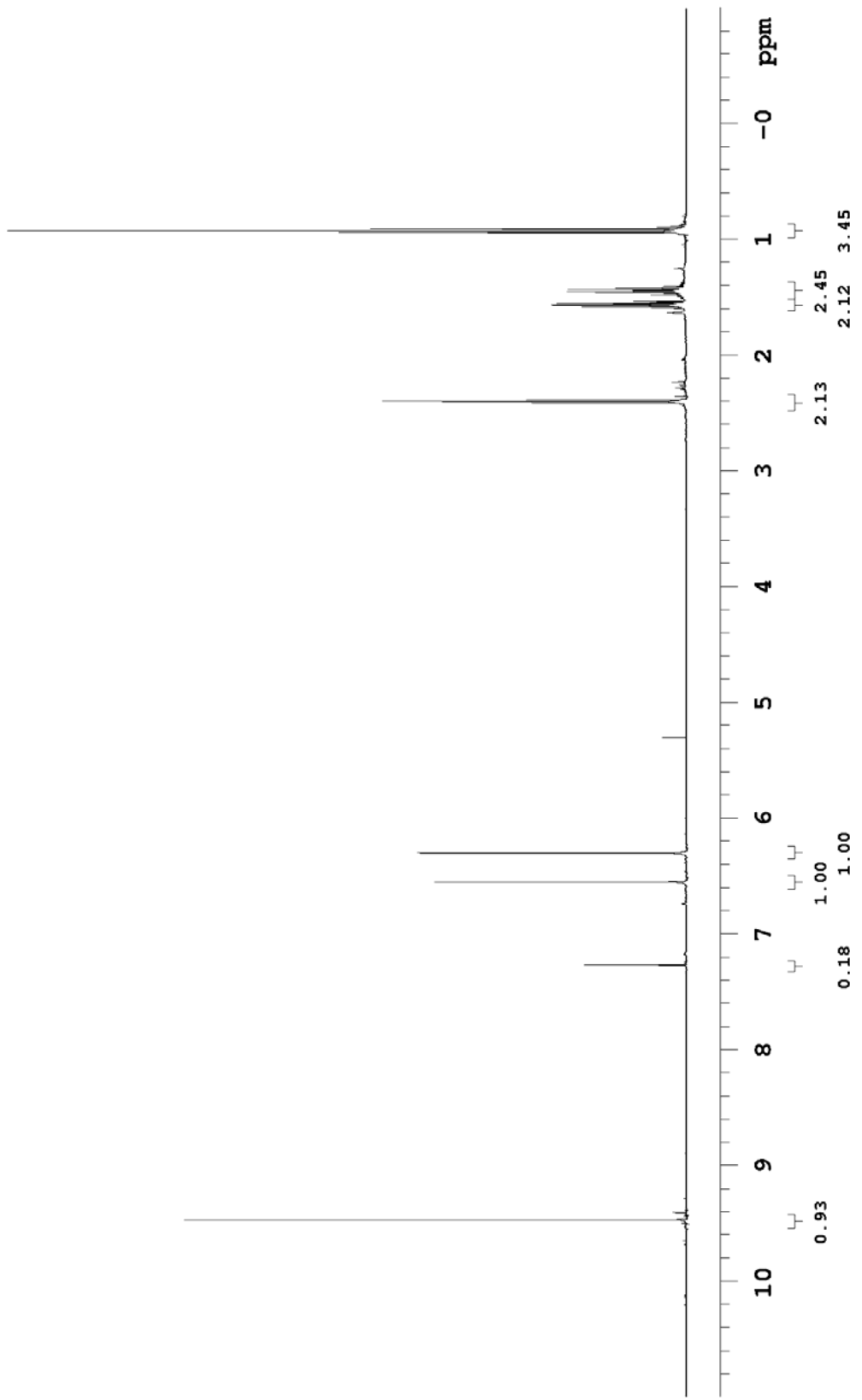


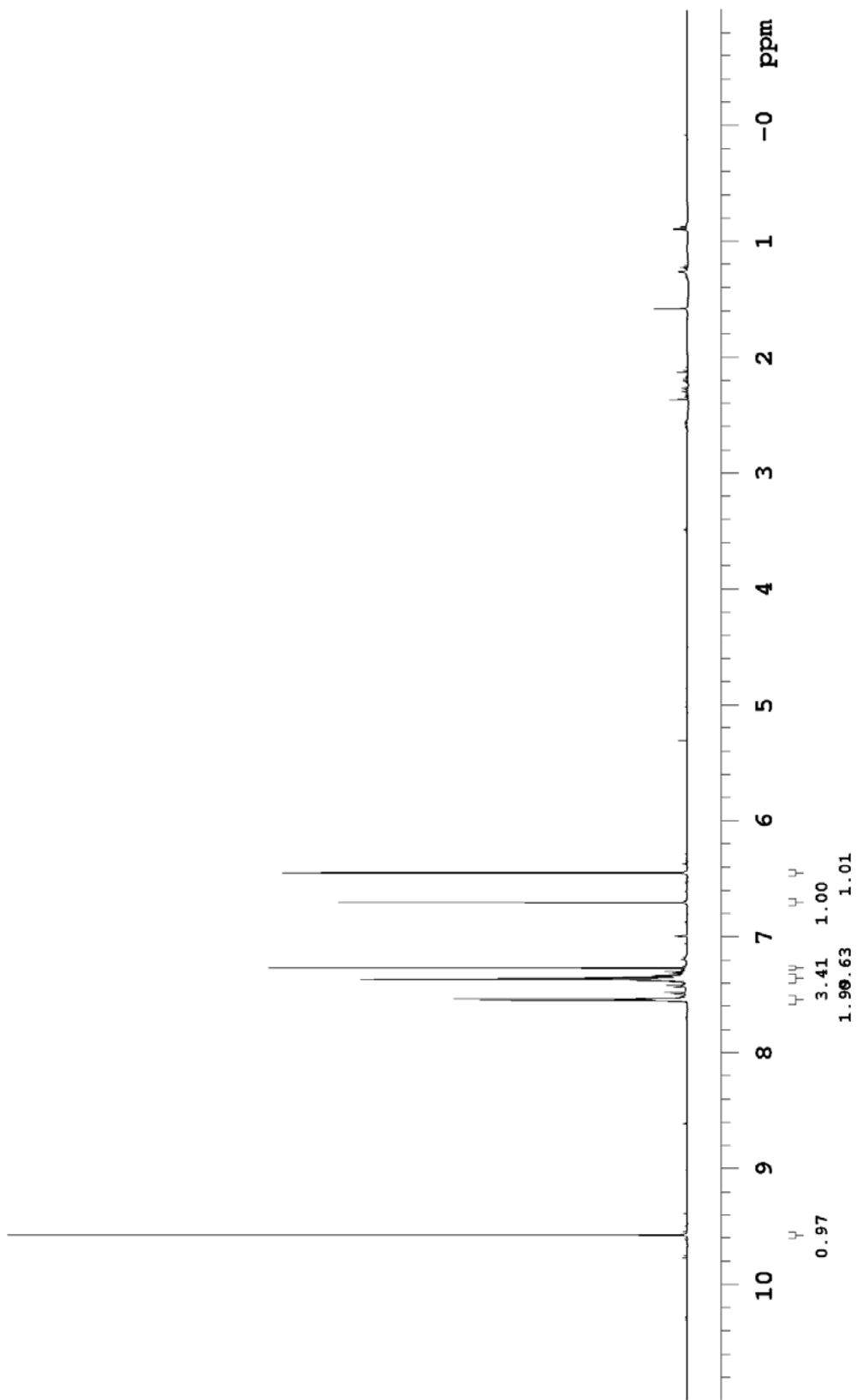
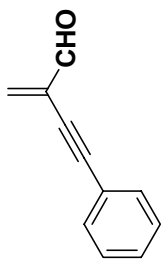


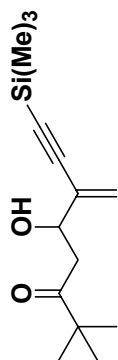




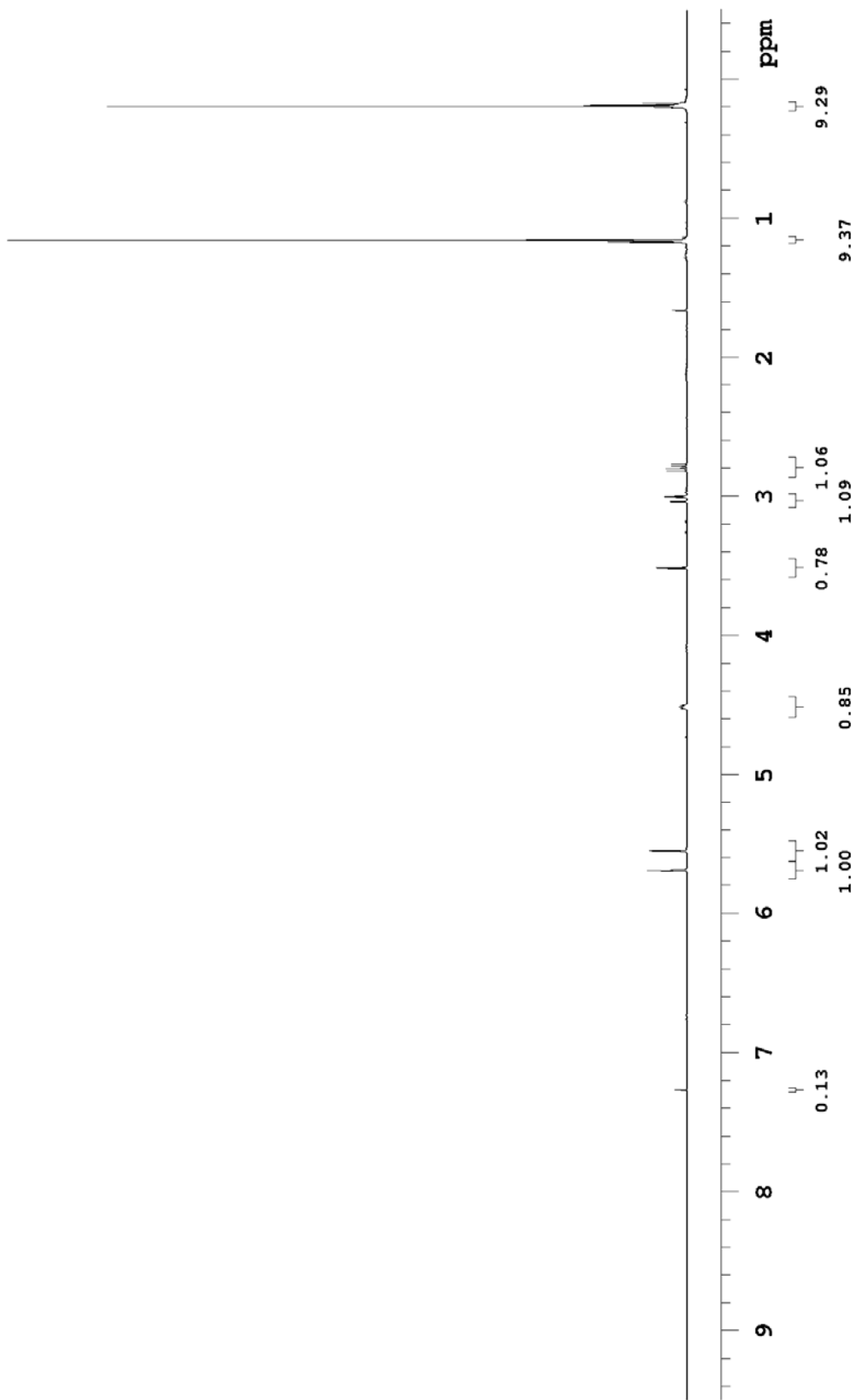
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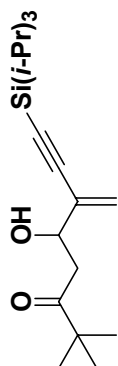




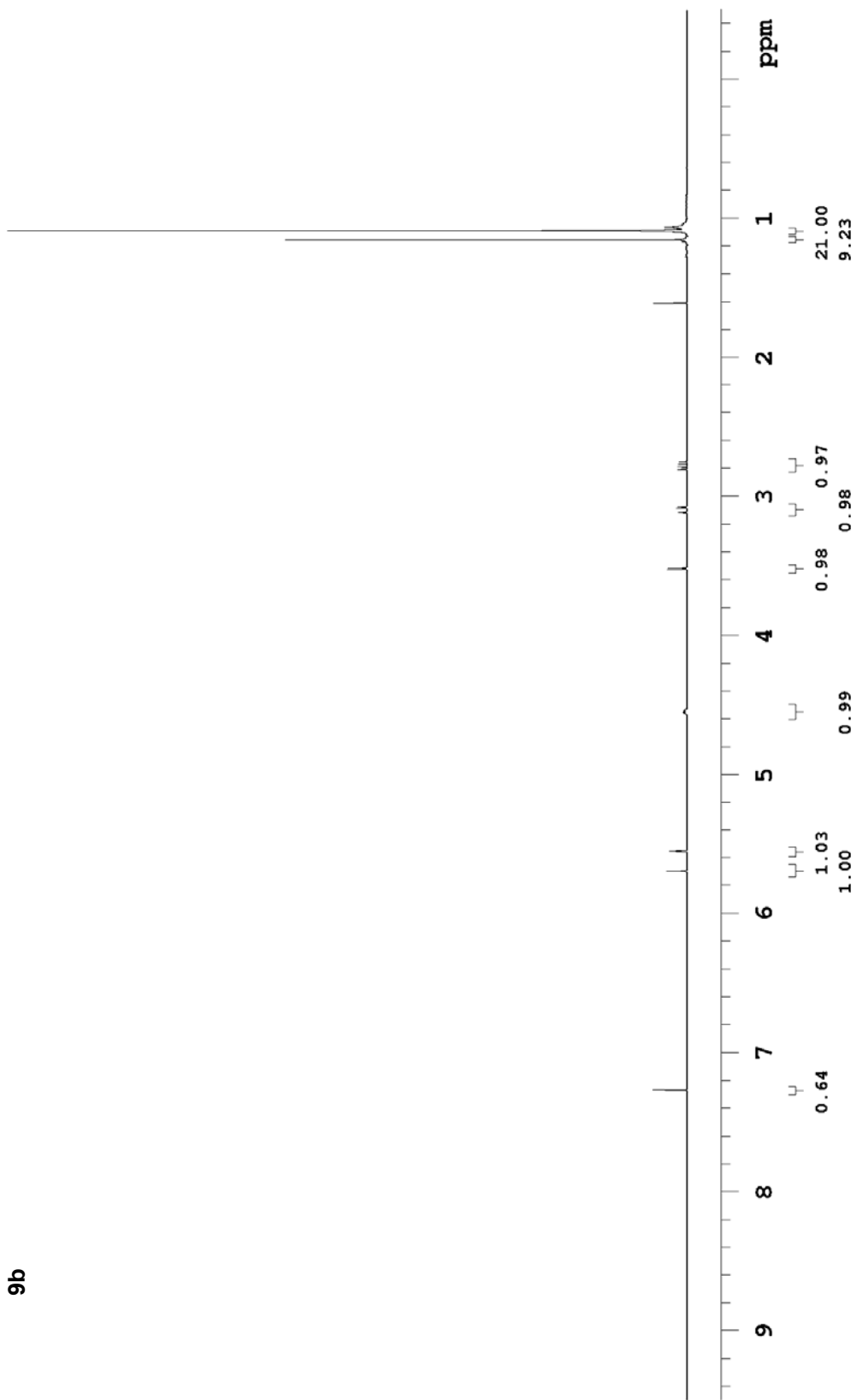


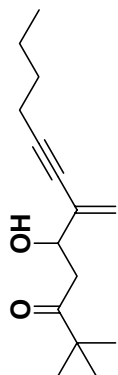
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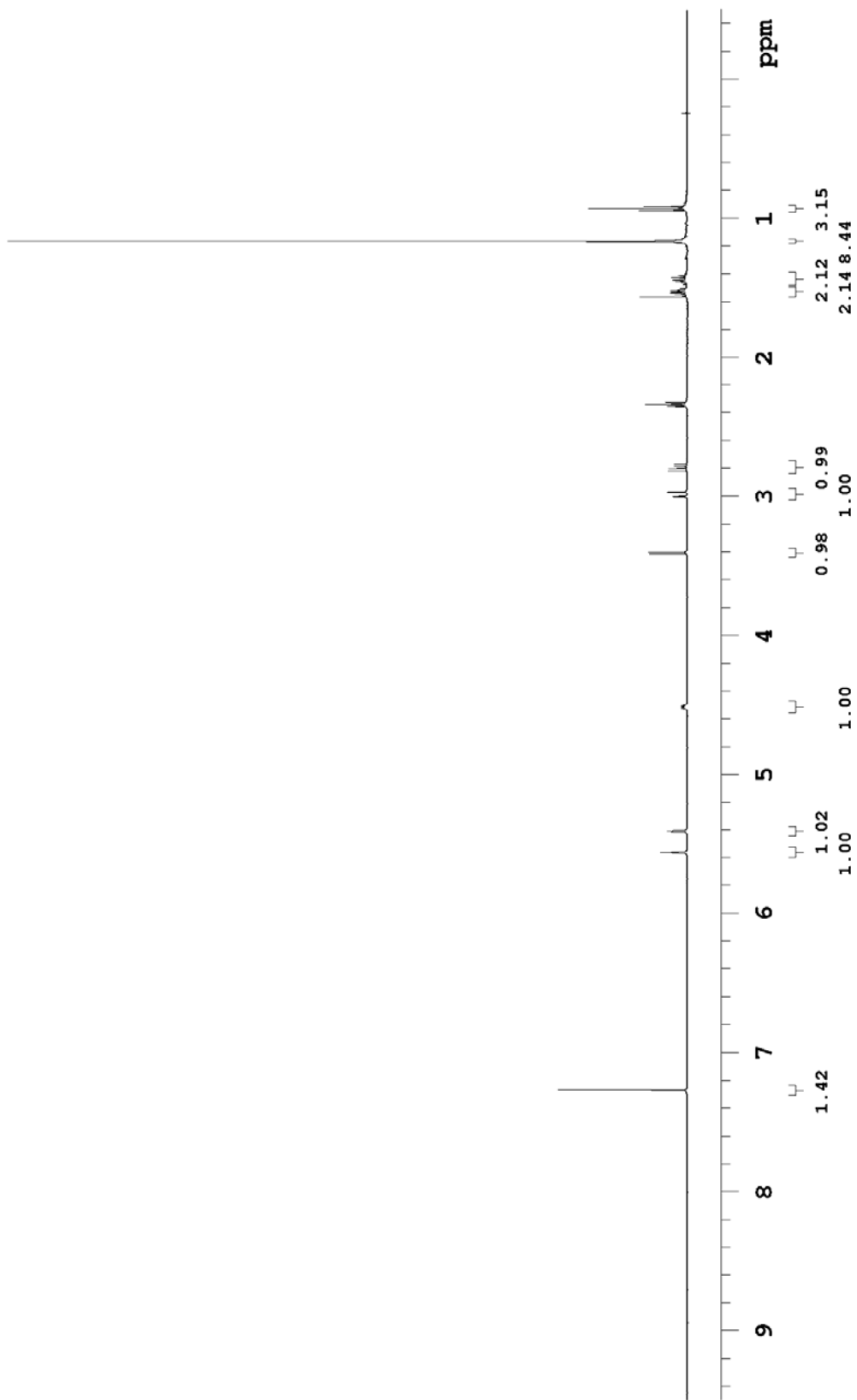


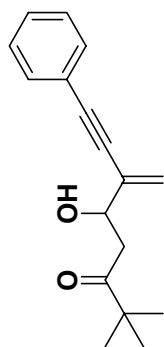
9b



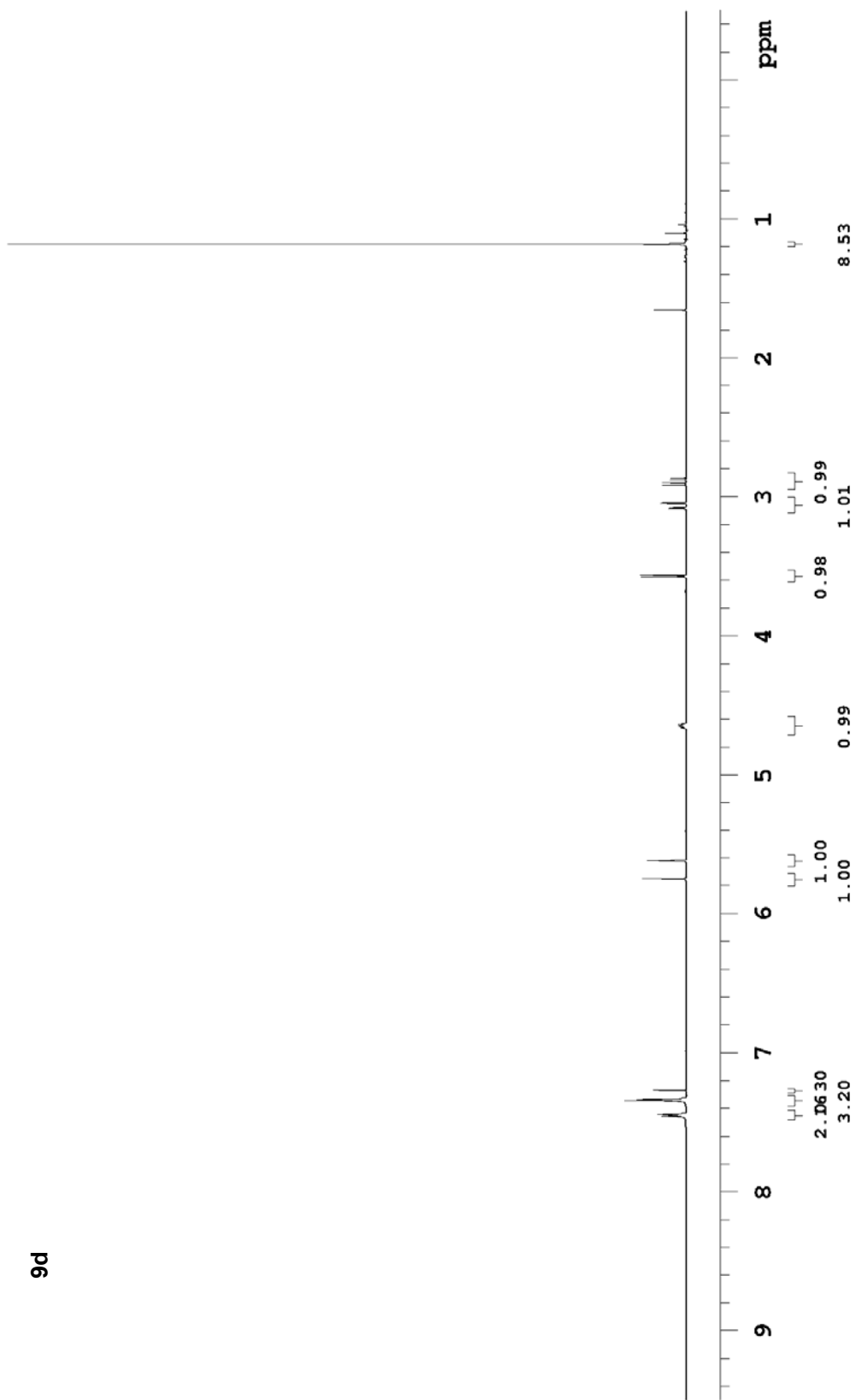


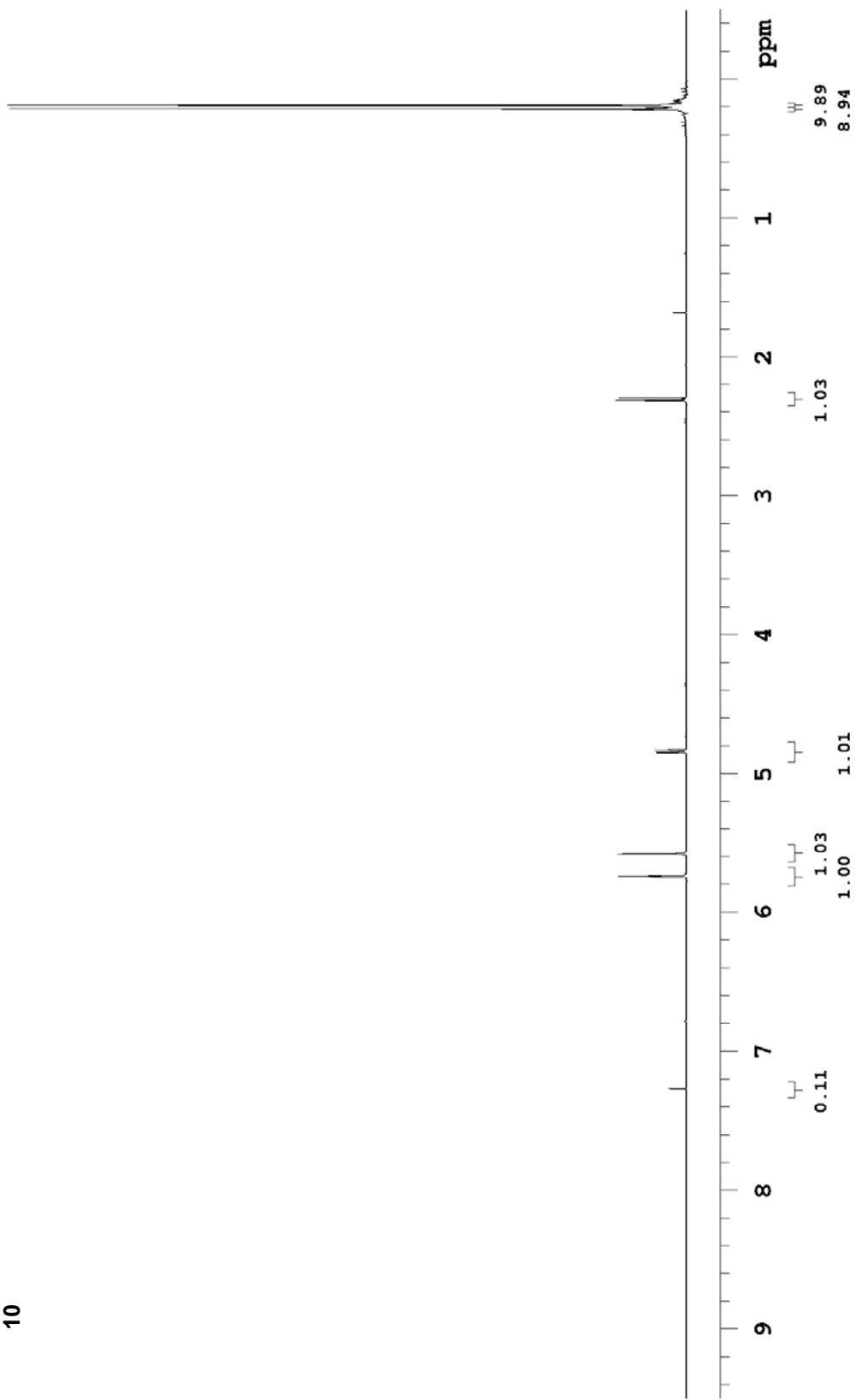
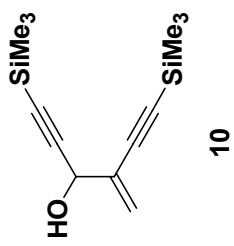
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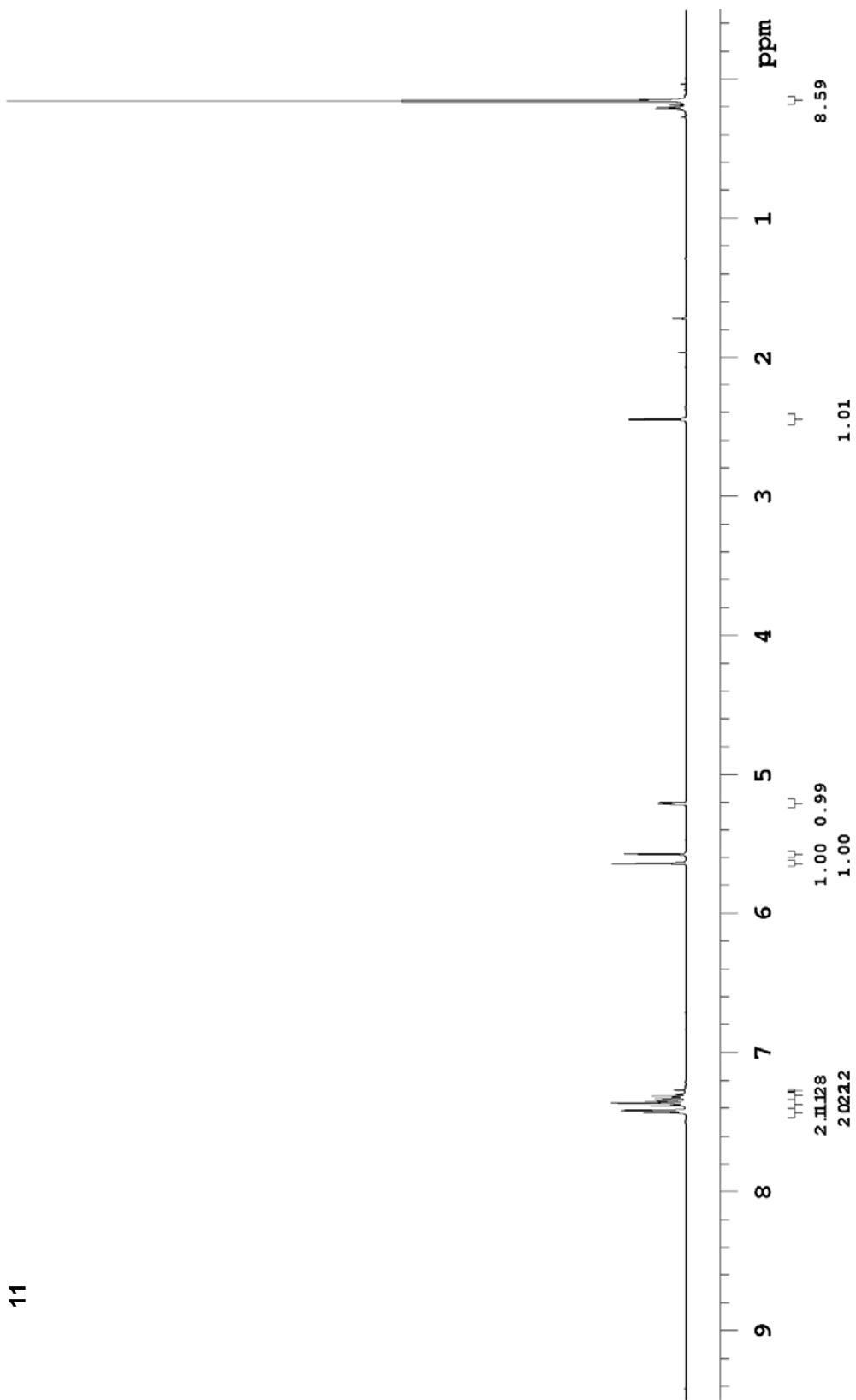
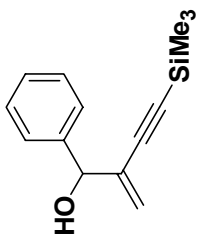


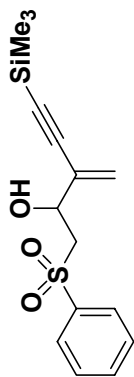


9d









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