

The Scope and Limitations of Intramolecular Nicholas and Pauson-Khand Reactions for the Synthesis of Tricyclic Oxygen- and Nitrogen- Containing Heterocycles

*Kristina D. Closser, Miriam M. Quintal, and Kevin M. Shea**

Department of Chemistry, Smith College, Northampton, Massachusetts 01063

kshea@email.smith.edu

Supporting Information

Page S2 – General experimental details, materials, and compounds previously reported in the literature

Pages S2-S22 – Experimental procedures for all new compounds

Pages S23-S62 – NMR spectra of compounds **20-33**, **39-47**, **51**, and **61-62**

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General Details. All reactions were done in flame-dried glassware under nitrogen unless otherwise noted. All reaction mixtures were magnetically stirred. Removal of solvents was achieved via rotary evaporation at 10 mm Hg.

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane, diethyl ether, and tetrahydrofuran were purified using alumina drying columns. 4-Pentenal (**6**) was distilled under vacuum before use.

Compounds Previously Reported in the Literature. Compounds **5-19** and **34-35** were prepared according to Quintal, M. M.; Closser, K. D.; Shea, K. M. *Org. Lett.* **2004**, *6*, 4949-4952. Terminal alkyne **21** and the one carbon larger alkyne prepared from **29** (Scheme 7 – step #1) were prepared according to Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc.* **2002**, *124*, 2102-2103. THP-protected alcohol **22** and the one carbon larger protected alcohol prepared beginning with **29** (Scheme 7 – step #2) were prepared according to Marino, J. P.; Nguyen, H. N. *J. Org. Chem.* **2002**, *67*, 6291-6296. Compounds **58-59** were prepared according to Shea, K. M.; Closser, K. D.; Quintal, M. M. *J. Org. Chem.* **2005**, *70*, 9088-9091.

General Procedure for the Synthesis of Secondary Alcohols via Acetylide Addition to 4-Pentenal: 12-(Tetrahydro-2H-pyran-2-yloxy)dodec-1-en-6-yn-5-ol (23**).** A 100-mL two-necked flask, equipped with a rubber septum and gas inlet adapter was charged with ethyl magnesium bromide (1 M in THF, 11.5 mL, 11.5 mmol, 1.5 equiv) and cooled at 0 °C. Meanwhile, 5 mL THF was added to a 25-mL pear flask containing alkyne **22** (1.50 g, 7.61 mmol, 1.0 equiv) and the alkyne solution was transferred via cannula into the reaction flask followed by a 1 mL THF rinse. The gas inlet adapter was replaced with a reflux condenser and the reaction mixture was heated at reflux for two hours. Another

25-mL pear flask was charged with 4-pentenal (1.21 mL, 12.2 mmol, 1.6 equiv) and 15 mL THF. The reaction flask was cooled at 0 °C and the aldehyde solution was cannulated into the reaction flask. The reaction was warmed to room temperature and stirred overnight. The reaction was quenched by the addition of 10 mL saturated ammonium chloride. The aqueous layer was extracted twice with ether and the combined organic layers were washed twice with brine, dried with magnesium sulfate, filtered, and concentrated to yield 2.33 g (109%) of crude product. This was applied neat to a 175 g silica gel column eluted with 20-35% diethyl ether in petroleum ether to afford 1.65 g (77%) of **23** as a yellow oil: IR (neat) 3431, 3076, 2941, 2864, 2230, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.83 (ddt, J = 16.8, 10.2, 6.8 Hz, 1H), 5.05 (dq, J = 17.2, 1.7 Hz, 1H), 4.97 (dm, J = 10.25, 1H), 4.56 (m, 1H), 4.36 (m, 1H), 3.85 (m, 1H), 3.73 (dt, J = 9.5, 6.8 Hz, 1H), 3.49 (m, 1H), 3.38 (dt, J = 9.5, 6.6 Hz, 1H), 2.21 (m, 4H), 1.88 (br s, 1H), 1.84-1.41 (m, 13H), 1.2 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.9, 115.0, 98.8, 85.1, 81.4, 67.4, 62.2, 61.8, 37.2, 30.7, 29.6, 29.2, 28.5, 25.52, 25.47, 19.6, 18.6; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{29}\text{O}_3$ 281.2117, found 281.2131.

13-(Tetrahydro-2H-pyran-2-yloxy)tridec-1-en-6-yn-5-ol. According to the general procedure, the alkyne resulting from isomerization and THP protection of **29** (Scheme 7) (2.80 g, 13.3 mmol, 1.0 equiv) was placed in THF (8 mL) and reacted with ethyl magnesium bromide (1M in THF, 20 mL, 20 mmol, 1.5 equiv) and 4-pentenal (1.79 g, 21.3 mmol, 1.6 equiv) in 32 mL of THF to afford 4.49 g (114%) of crude product that was applied directly to a 340 g silica gel column eluted with 15-50% diethyl ether in petroleum ether. This yielded 2.08 g (53%) of the desired alcohol as a yellow oil:¹ IR (neat) 3450, 3075, 2940, 2857, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.82 (ddt, J =

17.2, 10.2, 6.6 Hz, 1H), 5.15 (dq, $J = 17.2, 1.7$ Hz, 1H), 4.97 (dm, $J = 10.2$ Hz, 1H), 4.57 (m, 1H), 4.36 (m, 1H), 3.86 (m, 1H), 3.73 (dt, $J = 9.5, 7.0$ Hz, 1H), 3.49 (m, 1H), 3.38 (dt, $J = 9.5, 6.6$ Hz, 1H), 2.20 (m, 4H), 1.88 (m, 1H), 1.74 (m, 4H), 1.55 (m, 8H), 1.38 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.9, 115.1, 98.8, 85.4, 81.3, 67.5, 62.3, 62.0, 37.2, 30.7, 29.6, 28.6, 25.8, 25.5, 19.6, 18.7; HRMS-FAB m/z $[\text{M-H}]^+$ calcd for $\text{C}_{18}\text{H}_{29}\text{O}_3$ 293.2117, found 293.2092.

General Procedure for the Synthesis of Methyl Ethers via Methylation and THP

Deprotection: 8-Methoxydodec-11-en-6-yn-1-ol (24). A 50-mL two-necked flask was equipped with a rubber septum and gas inlet adapter and charged with sodium hydride (60% in mineral oil, 0.47 g, 11.8 mmol, 3.0 equiv) and 5 mL THF. The cloudy gray suspension was cooled at 0 °C and iodomethane (1.47 mL, 23.5 mmol, 6.0 equiv) was added. To a 25-mL pear flask containing enyne **23** (1.10 g, 3.92 mmol, 1.0 equiv) was added 4 mL THF. The enyne solution was cannulated into the reaction flask followed by a 1 mL THF rinse, and the reaction mixture was warmed to room temperature. After 30 min, the reaction was quenched with 20 mL saturated sodium thiosulfate. The aqueous layer was extracted twice with ether. The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and concentrated to yield 1.08 g (94%) of the desired methyl ether as a yellow oil: IR (neat) 3076, 3932, 2860, 2228, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.80 (ddt, $J = 16.8, 10.2, 6.6$ Hz, 1H), 5.03 (dm, $J = 16.8$ Hz, 1H), 4.96 (dm, $J = 10.2$ Hz, 1H), 4.56 (m, 1H), 3.94-3.83 (m, 2H), 3.73 (dt, $J = 9.5, 6.8$ Hz, 1H), 3.48 (m, 1H), 3.38 (m, 1H), 3.38 (s, 3H), 2.25-2.16 (m, 4H), 1.84-1.42 (m, 14H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.8, 114.9, 98.7, 86.3, 78.8, 70.7, 67.3, 62.1,

56.1, 35.1, 30.7, 29.7, 29.4, 29.2, 28.6, 25.5, 19.6, 18.6; HRMS-FAB m/z $[M+H]^+$ calcd for $C_{18}H_{31}O_3$ 295.2273, found 295.2277.

To a 100-mL round-bottomed flask containing the ether synthesized in the previous step (977 mg, 3.32 mmol, 1.0 equiv) was added absolute ethanol (27 mL) and pyridinium *p*-toluenesulfonate (58 mg, 0.23 mmol, 0.1 equiv). The reaction flask was equipped with a reflux condenser and gas inlet adapter and heated at 55 °C overnight. The reaction mixture was concentrated to yield 826 mg (118%) of a yellow oil which was deposited on 1.6 g silica gel and added to a 60 g silica gel column eluted with 25% diethyl ether in petroleum ether to afford 468 mg (67%) of enyne **24** as a yellow oil: IR (neat) 3392, 3076, 2936, 2862, 2228, 1641 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.03 (dq, J = 16.8, 1.8 Hz, 1H), 4.96 (dm, J = 9.9 Hz, 1H), 3.91 (tt, J = 6.6, 1.8 Hz, 1H), 3.64 (t, J = 6.6 Hz, 2H), 3.37 (s, 3H), 2.24 (dt, J = 7.0, 1.8, 2H), 2.19 (m, 2H), 1.76 (m, 2H), 1.61-1.41 (m, 6H), 1.32 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 115.0, 86.5, 78.6, 70.8, 62.2, 56.1, 34.9, 32.1, 29.4, 28.5, 25.0, 18.6; HRMS-FAB m/z $[M+H]^+$ calcd for $C_{13}H_{23}O_2$ 211.1698, found 211.1709.

9-Methoxytridec-12-en-7-yn-1-ol (30). According to the general procedure, combination of THF (10 mL), sodium hydride (60% in mineral oil, 0.82 g, 20.5 mmol, 3.0 equiv), iodomethane (2.55 mL, 41.0 mmol, 6.0 equiv), and the enyne available in three steps from **29** (Scheme 7) (2.01 g, 6.83 mmol, 1.0 equiv) in 5 mL THF furnished 2.13 g (101%) of the target ether as a yellow oil: IR (neat) 3076, 2833, 2855, 2818, 1641 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.13 (dq, J = 17.2, 1.8 Hz, 1H), 4.96 (dm, J = 10.2 Hz, 1H), 4.56 (m, 1H), 3.92 (tt, J = 6.6, 1.8 Hz, 1H), 3.86 (m, 1H), 3.73 (dt, J = 9.5, 6.8 Hz, 1H), 3.49 (m, 1H), 3.37 (s, 3H), 2.20 (m,

4H), 1.76 (m, 5H), 1.54 (m, 8H), 1.38 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.9, 114.9, 98.8, 86.5, 78.7, 70.8, 67.5, 62.3, 56.2, 35.1, 30.8, 29.7, 29.5, 28.7, 25.8, 25.5, 19.7, 18.7; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{31}\text{O}_3$ 295.2273, found 295.2277; HRMS-FAB m/z $[\text{M}]^+$ calcd for $\text{C}_{19}\text{H}_{32}\text{O}_3$ 308.2351, found 308.2351.

Reaction of the ether prepared in the previous step (1.95 g, 6.32 mmol, 1.0 equiv), absolute ethanol (50 mL), and pyridinium *p*-toluenesulfonate (159 mg, 0.63 mmol, 0.1 equiv) yielded 1.39 g of crude product which was deposited on 3.7 g of silica gel and added to a 140 g silica gel column eluted with 30% diethyl ether in petroleum ether. This afforded 832 mg (59%) of **30** as a pale yellow oil: IR (neat) 3344, 3076, 2931, 2858, 2819, 2229, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.80 (ddt, $J = 16.8, 10.2, 6.7$ Hz, 1H), 5.03 (dm, $J = 16.8$ Hz, 1H), 4.96 (dm, $J = 10.2$ Hz, 1H), 3.92 (tm, $J = 6.6$ Hz, 1H), 3.63 (t, $J = 6.6$ Hz, 2H), 3.36 (s, 3H), 2.20 (m, 4H), 1.75 (m, 2H), 1.55 (m, 4H), 1.40 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 137.8, 114.9, 86.5, 78.6, 70.8, 62.3, 56.0, 35.0, 32.5, 29.4, 28.63, 28.59, 25.3, 18.6; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{25}\text{O}_2$ 225.1855, found 225.1871.

General Procedure for the Synthesis of Cobalt-Complexed Alkynes: 8-Methoxydodec-11-en-6-yn-1-ol dicobalt hexacarbonyl complex (25). A 25-mL pear flask containing enyne **24** (159 mg, 0.76 mmol, 1.0 equiv) was equipped with a rubber septum and gas inlet needle. Dichloromethane (2 mL) was added, followed by dicobalt octacarbonyl (310 mg, 0.907 mmol, 1.2 equiv). The reaction was stirred for 30 min, and a second portion of dicobalt octacarbonyl (103 mg, 0.302 mmol, 0.4 equiv) was added. After another 30 minutes the reaction mixture was applied directly to a 38 g silica gel column eluted with 25-50% diethyl ether in petroleum ether to afford 334 mg (89%) of

25 as a dark red oil: IR (neat) 3387, 3081, 2936, 2863, 2088, 2040, 1993, 1642 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.85 (ddt, $J = 18.5, 11.9, 6.6$ Hz, 1H), 5.08 (dd, $J = 17.0, 1.3$ Hz, 1H), 5.02 (br d, $J = 9.9$ Hz, 1H), 4.26 (dd, $J = 9.0, 3.5$ Hz, 1H), 3.68 (q, $J = 6.0$ Hz, 2H), 3.52 (s, 3H), 2.84 (m, 2H), 2.33-2.25 (m, 2H), 1.88-1.51 (m, 7H), 1.29 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 137.9, 115.4, 99.1, 98.3, 81.1, 62.7, 58.7, 37.1, 33.9, 32.5, 31.8, 30.4, 25.8.

9-Methoxytridec-12-en-7-yn-1-ol dicobalt hexacarbonyl complex (31). According to the general procedure, combination of alkyne **30** (103 mg, 0.46 mmol, 1.0 equiv), dichloromethane (1 mL), dicobalt octacarbonyl (188 mg, 0.55 mmol, 1.2 equiv then 63 mg, 0.18 mmol, 0.4 equiv) followed by direct addition to a 23 g silica gel column and elution with 25% diethyl ether in petroleum ether yielded 234 mg (100%) of **31** as a dark red oil: IR (neat) 3314, 3000, 2932, 2859, 2089, 2046, 2018 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.83 (ddt, $J = 17.0, 10.4, 6.6$ Hz, 1H), 5.05 (m, 2H), 4.26 (dd, $J = 9.1, 3.3$ Hz, 1H), 3.66 (m, 2H), 3.51 (s, 3H), 2.82 (m, 2H), 2.29 (m, 2H), 1.79 (m, 2H), 1.60 (m, 4H), 1.56 (m, 4H), 1.25 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 137.9, 115.4, 98.3, 81.1, 62.8, 62.7, 58.7, 37.1, 34.0, 32.7, 32.0, 30.3, 29.5, 25.7.

***N*-(6-methoxydec-9-en-4-ynyl)-4-methylbenzenesulfonamide dicobalt hexacarbonyl complex (39).** According to the general procedure, combination of the amine resulting from Mitsunobu reaction of alcohol **10** (92 mg, 0.28 mmol, 1.0 equiv), dichloromethane (2 mL), and dicobalt octacarbonyl (115 mg, 0.34 mmol, 1.2 equiv then 38 mg, 0.11 mmol, 0.4 equiv) followed by direct addition to an 18 g silica gel column and eluted with 25% diethyl ether in petroleum ether yielded 160 mg (90%) of **39** as a dark red oil: ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J=8.4$ Hz, 2H), 7.30 (d, $J=7.7$ Hz,

2H), 5.84 (m, 1H), 5.04 (m, 2H), 4.43 (m, 1H), 4.42 (m, 1H), 3.48 (s, 3H), 2.81 (m, 1H), 2.43 (s, 3H), 2.25 (m, 2H), 1.78 (m, 4H), 1.25 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.9, 143.7, 137.8, 136.8, 129.9, 127.2, 115.6, 98.4, 97.6, 81.1, 58.8, 43.0, 37.1, 31.8, 31.0, 30.3, 21.6.

***N*-(7-Methoxyundec-10-en-5-ynyl)-4-methylbenzenesulfonamide dicobalt**

hexacarbonyl complex (43). According to the general procedure, combination of the amine resulting from Mitsunobu reaction of alcohol **15** (100 mg, 0.286 mmol, 1.0 equiv), dichloromethane (1 mL), and dicobalt octacarbonyl (117 mg, 0.343 mmol, 1.2 equiv then 39 mg, 0.114 mmol, 0.4 equiv) followed by direct addition to an 18 g silica gel column and eluted with 25% diethyl ether in petroleum ether yielded 158 mg (87%) of **43** as a dark red oil: IR (neat) 3277, 3065, 2978, 2825, 2359, 2088, 2046, 2016, 1748, 1715, 1641, 1599 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, $J = 8.1$ Hz, 2H), 7.31 (d, $J = 8.1$ Hz, 2H), 5.89-5.79 (m, 1H), 5.09-5.01 (m, 2H), 4.40 (br s, 1H), 4.26-4.18 (m, 1H), 3.50 (s, 3H), 3.04-2.96 (m, 2H), 2.82-2.74 (m, 2H), 2.42 (s, 3H), 2.38-2.20 (m, 2H), 1.88-1.57 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.0, 143.5, 137.8, 136.9, 129.8, 127.2, 115.5, 98.3, 81.1, 58.8, 53.6, 42.9, 37.1, 33.5, 30.4, 29.6, 28.8, 21.6.

***N*-(8-methoxydodec-11-en-6-ynyl)-4-methylbenzenesulfonamide dicobalt**

hexacarbonyl complex (47). According to the general procedure, combination of the amine resulting from Mitsunobu reaction of alcohol **24** (164 mg, 0.47 mmol, 1.0 equiv), dichloromethane (1.5 mL), and dicobalt octacarbonyl (192 mg, 0.564 mmol, 1.2 equiv then 64 mg, 0.188 mmol, 0.4 equiv) followed by direct addition to a 30 g silica gel column and eluted with 25% diethyl ether in petroleum ether yielded 256 mg (84%) of **47** as a dark red oil: IR (neat) 3283, 3077, 2979, 2934, 2863, 2254, 2088, 2046, 2001, 1713,

1641, 1599 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.1$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 2H), 5.84 (m, 1H), 5.03 (m, 2H), 4.48 (br s, 1H), 4.20 (m, 2H), 3.49 (s, 3H), 2.94 (m, 2H), 2.79 (m, 2H), 2.41 (s, 3H), 2.26 (m, 2H), 1.79-1.42 (m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 143.4, 137.8, 137.1, 129.7, 127.1, 115.4, 98.9, 98.3, 81.0, 58.7, 43.1, 37.1, 33.8, 31.5, 30.3, 29.5, 26.5, 22.4, 21.5.

***N*-(9-methoxytridec-12-en-7-ynyl)-4-methylbenzenesulfonamide dicobalt**

hexacarbonyl complex (51). According to the general procedure, combination of the amine resulting from Mitsunobu reaction of alcohol **30** (157 mg, 0.43 mmol, 1.0 equiv), dichloromethane (1.5 mL), and dicobalt octacarbonyl (177 mg, 0.52 mmol, 1.2 equiv then 59 mg, 0.17 mmol, 0.4 equiv) followed by direct addition to a 28 g silica gel column and eluted with 25% diethyl ether in petroleum ether yielded 251 mg (87%) of **51** as a dark red oil: IR (neat) 3285, 3076, 2979, 2933, 2859, 2254, 2087, 2047, 2022, 1708, 1641, 1599 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 5.83 (m, 1H), 5.05 (m, 2H), 4.25 (m, 3H), 3.51 (s, 3H), 2.94 (q, $J = 6.7$ Hz, 2H), 2.79 (m, 2H), 2.42 (s, 3H), 2.28 (m, 2H), 1.78 (m, 2H), 1.59 (m, 2H), 1.47 (m, 2H), 1.44-1.18 (m, 10H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 143.4, 137.8, 137.0, 129.7, 127.2, 115.4, 99.2, 98.3, 81.0, 65.9, 58.7, 43.1, 37.1, 34.2, 33.9, 31.9, 30.3, 29.6, 29.1, 26.4, 22.4, 21.5, 15.3, 14.1.

8-Methoxydodec-11-en-6-ynoic acid dicobalt hexacarbonyl complex (61).

According to the general procedure, combination of the carboxylic acid resulting from oxidation of alcohol **24** (52 mg, 0.23 mmol, 1.0 equiv), dichloromethane (1 mL), and dicobalt octacarbonyl (95 mg, 0.28 mmol, 1.2 equiv then 31 mg, 0.09 mmol, 0.4 equiv) followed by direct addition to a 12 g silica gel column and eluted with 15-100% diethyl

ether in petroleum ether yielded 62 mg (52%) of **61** as a dark red oil: ^1H NMR (400 MHz, CDCl_3) δ 10.8 (br s, 1H), 5.85 (m, 1H), 5.05 (m, 2H), 4.27 (m, 1H), 3.48 (s, 3H), 2.86 (br s, 2H), 2.26 (m, 2H), 1.79 (m, 6H), 1.28 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 137.8, 115.5, 98.3, 81.1, 67.0, 58.8, 37.1, 33.7, 30.4, 22.4, 15.3, 14.2.

General Procedure for the Nicholas Reaction of Cobalt-Complexed Alkynes: 2-(But-3-enyl)oxon-3-yne dicobalt hexacarbonyl complex (26). A 25-mL flask containing cobalt-complexed alkyne **25** (228 mg, 0.46 mmol, 1.0 equiv) was equipped with a rubber septum and gas inlet needle. Dichloromethane (20 mL) was added, the reaction flask was cooled at 0 °C, and boron trifluoride diethyl etherate (58 μL , 0.46 mmol, 1.0 equiv) was added. The reaction was stirred for 30 min then quenched by addition of 20 mL saturated sodium bicarbonate. The organic layer was removed and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried with magnesium sulfate and added to a sintered glass funnel filled with silica gel and eluted with 10% diethyl ether in petroleum ether until the first red band was collected and concentrated to yield 91 mg (43%) of **26** as a dark red oil: IR (neat) 3080, 2934, 2859, 2088, 2045, 2014, 1642, 1609 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.87 (m, 1H), 5.04 (m, 2H), 4.40 (m, 1H), 3.97-3.46 (m, 2H), 3.28-2.89 (m, 2H), 2.40-2.20 (m, 2H), 1.93-1.53 (m, 4H), 1.32-1.18 (m, 3H), 0.87 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 138.2, 115.3, 37.8, 34.8, 31.7, 30.4, 30.1, 29.8, 29.5, 27.8, 25.9, 25.2.

2,12-Dibut-3-enyl-1,11dioxacycloicos-3,13-diyne dicobalt hexacarbonyl complex (32). According to the general procedure, combination of cobalt-complexed alkyne **31** (234 mg, 0.46 mmol, 1.0 equiv), dichloromethane (20 mL), and boron trifluoride diethyl etherate (58 μL , 0.46 mmol, 1.0 equiv) at 0 °C for 1 h followed by the aqueous workup

and addition to a sintered glass funnel filled with silica gel and eluted with 10% diethyl ether in petroleum ether until the solution ran clear and concentration afforded 120 mg (55%) of **32** as a viscous red oil: IR (neat) 3077, 2936, 2857, 2088, 2045, 2016, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.85 (m, 1H), 5.04 (m, 2H), 4.37 (m, 1H), 3.57 (m, 2H), 2.88 (m, 2H), 2.27 (m, 2H), 1.88 (m, 2H), 1.66 (m, 4H), 1.45 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 139.2, 137.8, 117.4, 116.7, 114.0, 100.8, 100.6, 99.9, 99.7, 80.1, 79.2, 72.7, 72.6, [37.9, 36.6, 36.6, 35.8, 35.3, 34.9, 34.5, 33.6, 33.3, 33.2, 31.7, 31.5, 31.1, 30.7, 30.5, 30.3, 29.8, 29.5, 28.8, 28.1, 27.4, 26.2, 25.0, 24.8] 2 , 16.0, 14.7.

2-But-3-enyl-1-(toluene-4-sulfonyl)-3-azepyne dicobalt hexacarbonyl complex (40).

According to the general procedure, combination of cobalt-complexed alkyne **39** (135 mg, 0.22 mmol, 1.0 equiv), dichloromethane (14 mL), and boron trifluoride diethyl etherate (27 μL , 0.22 mmol, 1.0 equiv) at 0 $^\circ\text{C}$ for 1.5 h followed by the aqueous workup and addition to a sintered glass funnel filled with silica gel and eluted with 5-20% diethyl ether in petroleum ether until the solution ran clear and concentration afforded 93 mg (73%) of **40** as a dark red oil: ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 5.58 (m, 1H), 5.19 (t, J = 7.3 Hz, 1H), 4.91 (m, 2H), 4.05 (m, 1H), 3.71 (m, 1H), 3.26 (m, 1H), 2.97 (m, 1H), 2.79 (m, 1H), 2.41 (s, 3H), 2.04 (m, 2H), 1.90 (m, 1H), 1.78 (m, 1H), 1.64 (m, 1H), 1.34 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.9, 143.3, 138.8, 136.8, 129.7, 126.9, 115.7, 110.0, 98.6, 59.8, 45.3, 34.8, 34.3, 31.3, 30.1, 21.6.

2-But-3-enyl-1-(toluene-4-sulfonyl)-3-azocyne dicobalt hexacarbonyl complex (44).

According to the general procedure, combination of cobalt-complexed alkyne **43** (125 mg, 0.20 mmol, 1.0 equiv), dichloromethane (3 mL), and tetrafluoroboric acid (54% in

diethyl ether, 27 μ L, 0.20 mmol, 1.0 equiv) at 0 $^{\circ}$ C for 1 h followed by the aqueous workup and addition to a sintered glass funnel filled with silica gel and eluted with 10% diethyl ether in petroleum ether until the end of the first red band and concentration afforded 32 mg (27%) of **44** as a dark red oil: ^1H NMR (400 MHz, CDCl_3): δ 7.74 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 5.58 (m, 1H), 5.12 (m, 1H), 4.94 (m, 2H), 3.60 (d, J = 15.4 Hz, 1H), 3.15 (m, 1H), 2.94 (m, 2H), 2.42 (m, 3H), 2.42 (s, 3H), 2.26 (m, 1H), 2.01 (m, 3H), 1.64 (m, 2H), 1.28 (m, 2H).

9,18-Dibut-3-enyl-1,10-dioxacyclooctadeca-7,16-diyne-2,11-dione dicobalt

hexacarbonyl complex (62). According to the general procedure, combination of cobalt-complexed alkyne **61** (62 mg, 0.12 mmol, 1.0 equiv), dichloromethane (6 mL), and tetrafluoroboric acid (54% in diethyl ether, 17 μ L, 0.12 mmol, 1.0 equiv) at 0 $^{\circ}$ C for 1 h followed by the aqueous workup and addition to a sintered glass funnel filled with silica gel and eluted with 10% diethyl ether in petroleum ether until the solution ran clear and concentration afforded 10 mg (9%) of **62** as a dark red oil: ^1H NMR (400 MHz, CDCl_3) δ 6.03 (m, 2H), 5.84 (m, 2H), 5.03 (m, 4H), 2.80 (m, 4H), 2.55-2.19 (m, 6H), 2.01-1.54 (m, 14H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.7, 172.5, 137.1, 125.6, 115.7, 99.3, 72.8, 35.8, 34.3, 33.3, 31.5, 30.2, 25.2.

General Procedure for the Pauson-Khand Reaction of Cobalt-Complexed Alkynes: 3,4,5,6,8a,9,10,10a-Octahydro-2H-pentaleno[1,6-bc]oxonin-7(8H)-one (27 + 28).

Acetonitrile:³ To a 25-mL round-bottomed flask containing cobalt complexed alkyne **26** (132 mg, 0.28 mmol, 1.0 equiv) was added acetonitrile (27 mL). The flask was equipped with a reflux condenser, left open to the air, and heated at reflux (100 $^{\circ}$ C) for 20 min.

The reaction mixture was then cooled to room temperature, added to a sintered glass funnel containing 5 g silica gel and 5 g celite, and rinsed with ethyl acetate. The filtrate was concentrated to yield 78 mg (136%) of crude products **27** and **28**. The crude product was deposited on 150 mg silica gel and added to a 6 g silica gel column eluted with 20% diethyl ether in petroleum ether to afford 21 mg (19%) of **27** and **28** as a viscous oil with a ratio of **27:28** of 12:1.

***N*-methylmorpholine-*N*-oxide (NMO):**⁴ A 50-mL three-necked flask equipped with a rubber septum, glass stopper, and gas inlet adapter was charged with the cobalt-complexed alkyne **26** (142 mg, 0.31 mmol, 1.0 equiv) and dichloromethane (12 mL). The flask was cooled at 0 °C, NMO (108 mg, 0.92 mmol, 3.0 equiv) was added, and the reaction was warmed to room temperature. After 45 min, the reaction was again cooled at 0 °C and another portion of NMO (108 mg) was added. The reaction mixture was warmed to room temperature and stirred for 45 min. This process of cooling at 0 °C, adding NMO (108 mg) and stirring at room temperature for 45 min, was repeated a third time. TLC indicated that the reaction had gone to completion so the reaction mixture was added to a sintered glass funnel filled with celite and rinsed with dichloromethane. The filtrate was washed with water and saturated sodium bicarbonate, filtered, and concentrated to yield 70 mg (111%) of a yellow oil. The crude product was applied neat to a 7 g silica gel column eluted with 25% diethyl ether in petroleum ether to afford 17 mg (27%) of **27** as a colorless film: IR (neat) 2961, 2926, 2855, 1731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.38 (t, *J* = 7.3 Hz, 1H), 4.08 (dt, *J* = 12.4, 5.3 Hz, 1H), 3.70 (m, 1H), 3.01 (br m, 1H), 2.69 (dd, *J* = 17.8, 6.0 Hz, 1H), 2.63 (dt, *J* = 14.6, 4.4 Hz, 1H), 2.50 (m, 1H), 2.22-2.13 (m, 2H), 2.03 (dd, *J* = 17.9, 3.3 Hz, 1H), 1.89 (m, 1H), 1.73 (m, 1H),

1.65-1.51 (m, 3H), 1.40 (m, 2H), 1.01 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 211.2, 181.8, 136.0, 71.8, 65.9, 43.1, 42.1, 35.1, 29.2, 29.0, 25.2, 22.5, 19.5; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{O}_2$ 207.1391, found 207.1385.

2a,3,4,4a,6,7,8,9,10,11,13a,14,15,15a,17,18,19,20,21,22-

Icosahydrodipentaleno[1,6-bc:1',6'-lm][1,11]dioxacycloicosine-1,12(2H,13H)-dione

(33). According to the general procedure using acetonitrile, combination of Nicholas product **32** (60 mg, 0.13 mmol, 1.0 equiv) with acetonitrile (12 mL) at reflux for 20 min afforded 42 mg of crude product that was deposited on 84 mg of silica gel and added to a 4.2 g silica gel column eluted with 25% diethyl ether in petroleum ether to afford 3 mg (11%) of **33** as a colorless film: ^1H NMR (400 MHz, CDCl_3) δ 4.65 (m, 2H), 4.45 (m, 1H), 3.58 (m, 2H), 3.38 (m, 4H), 2.98 (m, 1H), 2.63 (m, 5H), 2.24 (m, 7H), 2.02 (m, 11H), 1.63-1.22 (m, 31H); ^{13}C NMR (100 MHz, CDCl_3) δ 211.5, 210.9, 179.9, 139.2, 97.2, 75.3, 73.8, 70.1, 53.5, [45-40, 32-22]²; MS-ESI m/z $[\text{M}+\text{Na}]^+$ 463.67, $[\text{M}+\text{H}]^+$ 441.87.

General Procedure of the Pauson-Khand Reaction of Cobalt-Complexed Alkynes:

1-Tosyl-1,2,3,4,6a,7,8,8a-octahydropentaleno[1,6-bc]azepin-5(6H)-one (42).

Cyclohexylamine:⁵ A 20-mL round-bottomed flask containing Nicholas product **40** (93 mg, 0.16 mmol, 1.0 equiv) was equipped with a rubber septum and gas inlet needle. 1,2-Dimethoxyethane (5.5 mL) was added followed by cyclohexylamine (27 μL , 0.24 mmol, 1.5 equiv). The rubber septum was replaced with a reflux condenser and gas inlet adapter and the reaction was heated at 60 $^\circ\text{C}$ for 3 h. The heat was removed and the reaction was allowed to stir over night. The reaction mixture was added to a sintered glass funnel filled with celite and washed with ethyl acetate (50 mL) to yield 59 mg (113%) of a

yellow oil. The crude product was applied directly to a 6 g silica gel column and eluted with 30% diethyl ether in petroleum ether to yield 51 mg (98%) of **42**.

According to the general procedure using acetonitrile, combination of Nicholas product **40** (78 mg, 0.13 mmol, 1.0 equiv) with acetonitrile (13 mL) at reflux for 25 min afforded 48 mg of crude product that was deposited on 96 mg of silica gel and added to a 4.8 g silica gel column eluted with 30% diethyl ether in petroleum ether to afford 41 mg (93%) of **2**.

According to the general procedure using NMO, combination of Nicholas product **40** (62 mg, 0.10 mmol, 1.0 equiv), dichloromethane (6 mL), and four portions of NMO (37 mg, 0.31 mmol, 3.0 equiv each) followed by stirring at room temp overnight and the standard aqueous workup yielded 43 mg of a pale yellow oil that was deposited on 80 mg of silica gel and applied to a 4.5 g silica gel column eluted with 20% diethyl ether in petroleum ether to yield 32 mg (91%) of **42** as a colorless, viscous oil: ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 5.17 (t, J = 8.4 Hz, 1H), 3.70 (dt, J = 15.4, 3.7 Hz, 1H), 2.91 (m, 1H), 2.81 (m, 1H), 2.65 (dd, J = 18.3, 6.6 Hz, 1H), 2.40 (s, 3H), 2.35-2.17 (m, 4H), 2.06 (dd, J = 18.7, 2.2 Hz, 1H), 1.88 (m, 1H), 1.71 (m, 2H), 1.26 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 209.1, 178.7, 143.5, 137.8, 135.7, 129.9, 127.1, 57.9, 43.7, 42.6, 38.9, 31.6, 29.9, 26.6, 21.6, 18.8; HRMS-FAB m/z $[\text{M}-\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_3\text{S}$ 330.1164, found 330.1153.

1-Tosyl-2,3,4,5,7a,8,9,9a-octahydro-1H-pentaleno[1,6-bc]azocin 6(7H)-one (45 + 46). According to the general procedure using acetonitrile, combination of Nicholas product **44** (23 mg, 0.038 mmol, 1.0 equiv) with acetonitrile (4 mL) at reflux for 15 min

afforded 13 mg of crude product that was added in solution to a 1.3 g silica gel column eluted with 50% diethyl ether in petroleum ether to afford 9 mg (69%) of **45** and **46**.

According to the general procedure using cyclohexylamine, combination of Nicholas product **44** (48 mg, 0.08 mmol, 1.0 equiv), 1,2-dimethoxyethane (3 mL), and cyclohexylamine (13.6 μ L, 0.12 mmol, 1.5 equiv) with heating at 60 °C over the weekend and purification on a 1.6 g silica gel column eluted with 20-40% diethyl ether in petroleum ether afforded 11 mg (41%) of **45** and **46**.

According to the general procedure using NMO, combination of Nicholas product **44** (50 mg, 0.08 mmol, 1.0 equiv), dichloromethane (5 mL), and four portions of NMO (29 mg, 0.25 mmol, 3.0 equiv each) followed by stirring at room temp overnight and the standard aqueous workup yielded 31 mg of a pale yellow oil that was deposited on 62 mg of silica gel and applied to a 3 g silica gel column eluted with 25% diethyl ether in petroleum ether to yield 12 mg (41%) of **45** and **46** as a colorless oil: IR (neat) 3048, 2955, 2925, 2856, 1706, 1671, 1597 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 5.18 (dd, J = 10.4, 4.5 Hz, 1H), 3.58 (dt, J = 15.0, 3.8 Hz, 1H), 2.75 (m, 1H), 2.63 (dd, J = 18.5, 6.4 Hz, 1H), 2.55 (m, 1H), 2.43 (s + m, 3 + 2H), 2.07 (m, 4H), 1.91 (m, 1H), 1.61 (m, 2H), 1.34 (m, 1H), 1.06 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 209.3, 117.2, 143.7, 138.1, 136.7, 129.9, 127.6, 57.2, 44.6, 42.0, 40.1, 30.4, 29.8, 29.7, 25.2, 21.6, 21.0; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_3\text{S}$ 346.1477, found 346.1460.

General Procedure for the Mitsunobu Reaction of Alcohols: *N*-(6-methoxydec-9-en-4-ynyl)-4-methylbenzenesulfonamide. A 50-mL two-necked flask equipped with a rubber septum and gas inlet adapter was charged with (fluorenyl)methyl tosylcarbamate⁷

(320 mg, 0.81 mmol, 1.5 equiv), triphenylphosphine (428 mg, 1.63 mmol, 3.0 equiv), and THF (4 mL), and cooled at 0 °C. A separate 25-mL pear flask was charged with alcohol **10** (99 mg, 0.54 mmol, 1.0 equiv) and 2 mL THF. This solution was transferred into the reaction flask via cannula followed by a 1 mL THF rinse. Diethylazodicarboxylate (232 mg, 1.36 mmol, 2.5 equiv) was added to the reaction flask, and the reaction was allowed to stir overnight. The reaction mixture was concentrated to yield 1.27 g (737%) of a yellow oil. The crude product was deposited on 4 g silica gel and added to a 35 g column eluted with 25% diethyl ether in petroleum ether to yield 206 mg (118%) of the target amine as a yellow oil, which was determined to be 90% pure based on the ¹H NMR and was used without further purification in the subsequent cobalt complexation step: IR (neat) 3283, 3073, 2822, 2976, 2249, 1748, 1640, 1598 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (dt, *J*=8.4, 1.8 Hz, 2H), 7.30 (d, *J*=8.1 Hz, 2H), 5.78 (m, 1H), 5.01 (dq, *J*=17.0, 1.7 Hz, 1H), 4.96 (dm, *J*=10.2 Hz, 1H), 4.53 (br s, 1H), 3.87 (tt, *J*=6.4, 1.9 Hz, 1H), 3.32 (s, 3H), 2.42 (s, 3H), 2.26 (td, *J*=7.0, 1.8 Hz, 2H), 2.14 (m, 2H), 1.76-1.64 (m, 3H), 1.34-1.19 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 137.8, 137.0, 130.0, 127.3, 115.2, 85.0, 80.0, 70.7, 56.3, 42.3, 34.9, 29.5, 28.5, 21.6, 16.1.

***N*-(7-Methoxy-undec-10-en-5-ynyl)-4-methyl-benzenesulfonamide** According to the general procedure, combination of (fluorenyl)methyl tosylcarbamate (902 mg, 2.29 mmol, 1.5 equiv), triphenyl phosphine (1.20 g, 4.59 mmol, 3.0 equiv), and 12 mL of THF followed by addition of alcohol **15** (300 mg, 1.53 mmol, 1.0 equiv) in 6 mL of THF then diethyl azodicarboxylate (40% in toluene, 1.73 mL, 665 mg, 3.82 mmol, 2.50 equiv) and stirring overnight at room temp yielded 3.35 g of crude product that was applied neat to a 30 g silica gel column eluted with 20-40% diethyl ether in petroleum ether to furnish 477

mg (89%) of the desired amine as a pure colorless oil: IR (neat) 3280, 3073, 2978, 2940, 2866, 2228, 1745, 1713, 1640, 1598 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 5.85-5.75 (m, 1H), 5.02 (dm, $J = 17.2$ Hz, 1H), 4.97 (dm, $J = 10.3$ Hz, 1H), 4.36 (br s, 1H), 3.89 (tt, $J = 6.6, 1.8$ Hz, 1H), 3.35 (s, 3H), 2.95 (q, $J = 6.8$ Hz, 2H), 2.42 (s, 3H), 2.22-2.14 (m, 4H), 1.81-1.67 (m, 2H), 1.62-1.47 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.4, 137.9, 136.9, 129.8, 127.2, 115.1, 85.8, 79.3, 70.8, 56.3, 42.7, 35.0, 29.5, 28.7, 25.6, 21.6, 18.2; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_3\text{S}$ 350.1790, found 350.1793.

***N*-(8-methoxydodec-11-en-6-ynyl)-4-methylbenzenesulfonamide.** According to the general procedure, combination of (fluorenyl)methyl tosylcarbamate (328 mg, 0.83 mmol, 1.5 equiv), triphenyl phosphine (438 mg, 1.67 mmol, 3.0 equiv), and 4 mL of THF followed by addition of alcohol **24** (117 mg, 0.56 mmol, 1.0 equiv) in 3 mL of THF then diethyl azodicarboxylate (40% in toluene, 595 mg, 1.39 mmol, 2.50 equiv) and stirring overnight at room temp yielded 1.24 g of crude product that was deposited on 2.4 g of silica gel and added to a 20 g silica gel column eluted with 30% diethyl ether in petroleum ether to furnish 286 mg (146%) of the desired amine as a yellow oil that was used without further purification in the subsequent cobalt complexation step: IR (neat) 3281, 3066, 2980, 2936, 2863, 2251, 1798, 1750, 1640, 1598 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.73 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 2H), 5.80 (ddt, $J = 16.8, 10.2, 6.6$ Hz, 1H), 5.02 (dq, $J = 17.0, 1.7$ Hz, 1H), 4.96 (dm, $J = 10.2$ Hz, 1H), 4.39 (m, 1H), 4.31 (q, $J = 7.2$ Hz, 1H), 3.90 (m, 1H), 3.35 (s, 3H), 2.94 (q, $J = 6.7$ Hz, 2H), 2.43 (s, 3H), 2.17 (m, 4H), 1.74 (m, 2H), 1.60 (s, 1H), 1.45-1.35 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.4, 137.9, 137.0, 129.7, 127.1, 115.1, 86.2, 78.9, 70.8, 56.3, 43.1, 35.0,

29.5, 29.1, 28.2, 25.8, 21.6, 18.6; HRMS-FAB m/z $[M+H]^+$ calcd for $C_{20}H_{30}NO_3S$ 364.1946, found 364.1963.

***N*-(9-methoxytridec-12-en-7-ynyl)-4-methylbenzenesulfonamide.** According to the general procedure, combination of (fluorenyl)methyl tosylcarbamate (394 mg, 1.00 mmol, 1.5 equiv), triphenyl phosphine (527 mg, 2.00 mmol, 3.0 equiv), and 5 mL of THF followed by addition of alcohol **30** (150 mg, 0.67 mmol, 1.0 equiv) in 4 mL of THF then diethyl azodicarboxylate (40% in toluene, 0.745 mL, 1.67 mmol, 2.50 equiv) and stirring overnight at room temp yielded 1.50 g of crude product that was deposited on 3.0 g of silica gel and added to a 24 g silica gel column eluted with 30% diethyl ether in petroleum ether to furnish 256 mg (105%) of the desired amine as a yellow oil that was used without further purification in the subsequent cobalt complexation step: IR (neat) 3286, 3075, 2979, 2936, 2860, 2250, 1798, 1748, 1713, 1641, 1598 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.80 (m, 1H), 5.02 (dq, J = 17.2, 1.6 Hz, 1H), 4.96 (dm, J = 10.2 Hz, 1H), 4.32 (m, 1H), 4.17 (m, 1H), 3.91 (m, 1H), 3.36 (s, 3H), 2.92 (q, J = 6.7 Hz, 2H), 2.42 (s, 3H), 2.18 (m, 4H), 1.73 (m, 2H), 1.57 (s, 1H), 1.46 (m, 3H), 1.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.9, 137.1, 129.7, 127.2, 115.0, 86.5, 78.8, 70.8, 56.2, 43.2, 35.0, 29.6, 29.4, 28.5, 28.3, 26.1, 21.6, 18.6; HRMS-FAB m/z $[M-H]^+$ calcd for $C_{21}H_{30}NO_3S$ 376.1946, found 376.1959.

General Procedure for the Oxidation of Alcohols to Yield Carboxylic Acids: 6-

Methoxydec-9-en-4-ynoic acid.^{8,9} A 25-mL two-necked flask equipped with a rubber septum and gas inlet adapter was charged with Dess-Martin periodinane (717 mg, 1.69 mmol, 1.2 equiv) and dichloromethane (4.5 mL). A separate 25-mL pear flask containing alcohol **10** (257 mg, 1.41 mmol, 1.0 equiv) in 1.0 mL dichloromethane was cannulated

into the reaction flask followed by a dichloromethane (0.5 mL) rinse. The reaction mixture was stirred at room temperature for 2 h, diluted with 15 mL diethyl ether, and transferred to an Erlenmeyer flask containing 15 mL of a saturated sodium bicarbonate solution and 3 g of sodium thiosulfate, and stirred for 5 min. The organic layer was washed with 50 mL of saturated sodium bicarbonate, 50 mL of water, dried with magnesium sulfate, filtered, and concentrated to yield 206 mg (81%) of the desired aldehyde as a yellow oil: IR (neat) 3077, 2980, 2932, 2823, 2728, 2247, 1726, 1640 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.80 (t, J = 1.1 Hz, 1H), 5.74-5.84 (m, 1H), 5.03 (dq, J = 17.2, 1.7 Hz, 1H), 4.96 (dm, J = 10.2 Hz, 1H), 3.90 (tt, J = 6.4, 2.0 Hz, 1H), 3.36 (s, 3H), 2.68 (tm, J = 7.1 Hz, 2H), 2.56 (tm, J = 6.8, 2H), 2.16 (m, 2H), 1.74 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.5, 137.8, 115.1, 84.3, 79.8, 70.7, 56.3, 42.7, 34.9, 29.4, 12.0; HRMS-FAB m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{17}\text{O}_2$ 181.1229, found 181.1226.

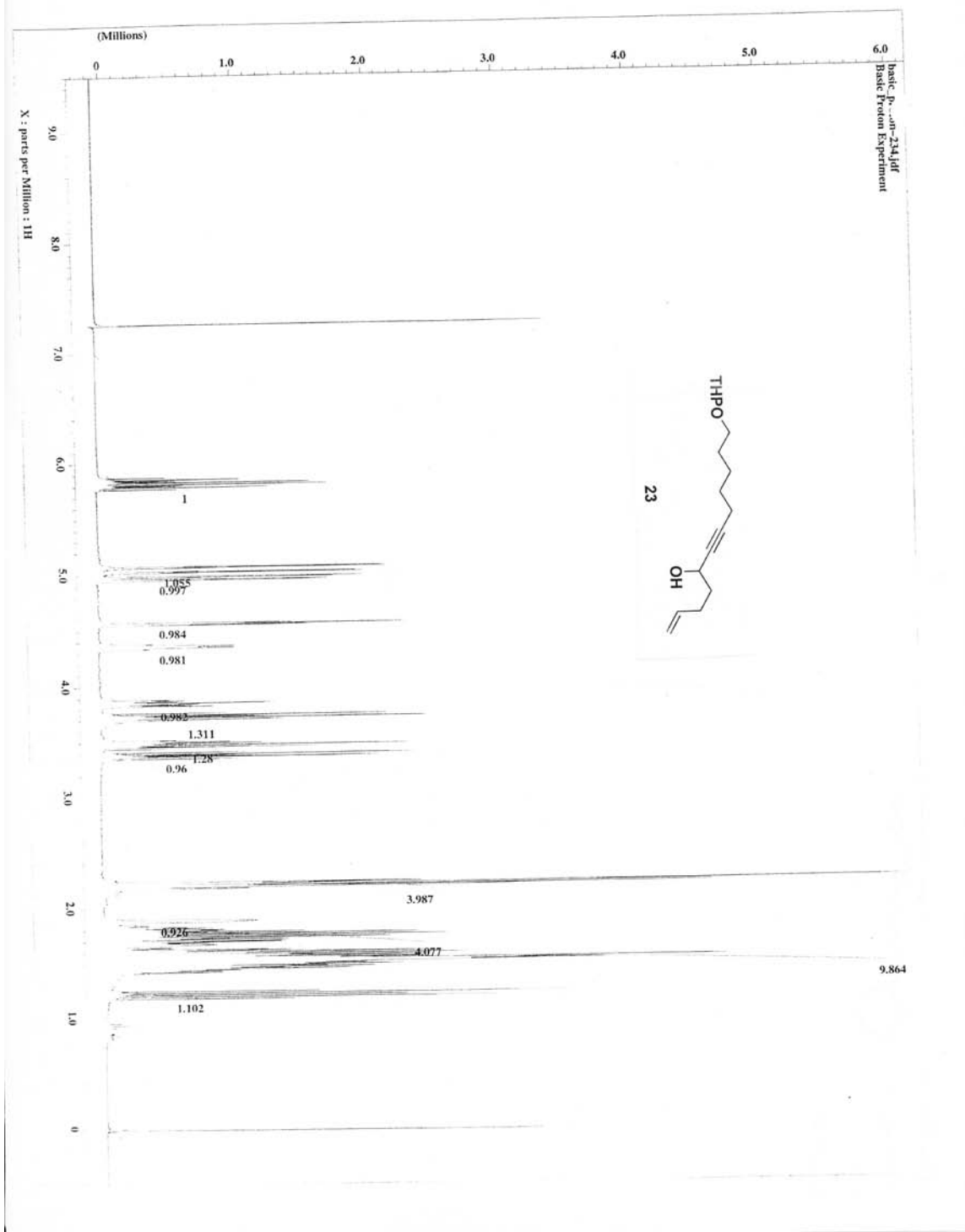
A 50-mL round-bottomed flask containing the previous prepared aldehyde (206 mg, 1.14 mmol, 1.0 equiv) was equipped with a rubber septum and gas inlet needle. Dimethylformamide (12 mL) was added followed by Oxone (703 mg, 1.14 mmol, 1.0 equiv) and the reaction was stirred at room temperature for two hours. The reaction mixture was added to a separatory funnel containing ethyl acetate (30 mL) and 1.0 M hydrochloric acid (30 mL). The aqueous layer was removed and extracted with 50 mL ethyl acetate, and the combined organic layers were washed with 1.0 M hydrochloric acid (5 x 50 mL) and brine (50 mL), dried with magnesium sulfate, filtered, and concentrated to yield 214 mg (95%) of the target carboxylic acid as a yellow oil: IR (neat) 3529-2655, 3077, 2980, 2936, 2249, 1713, 1642 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.79 (m, 1H), 5.03 (dq, J = 17.2, 1.6 Hz, 1H), 4.86 (dm, J = 10.2 Hz, 1H), 3.91 (tt, J = 6.2, 1.6 Hz, 1H),

3.37 (s, 3H), 2.92 (d, $J = 30.4$ Hz, 1H), 2.60 (m, 3H), 2.16 (m, 2H), 1.73 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.4, 137.8, 115.1, 84.4, 79.6, 70.7, 56.2, 34.8, 33.6, 29.4, 14.5; HRMS-FAB m/z $[\text{M-H}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{O}_3$ 195.1021, found 195.1017.

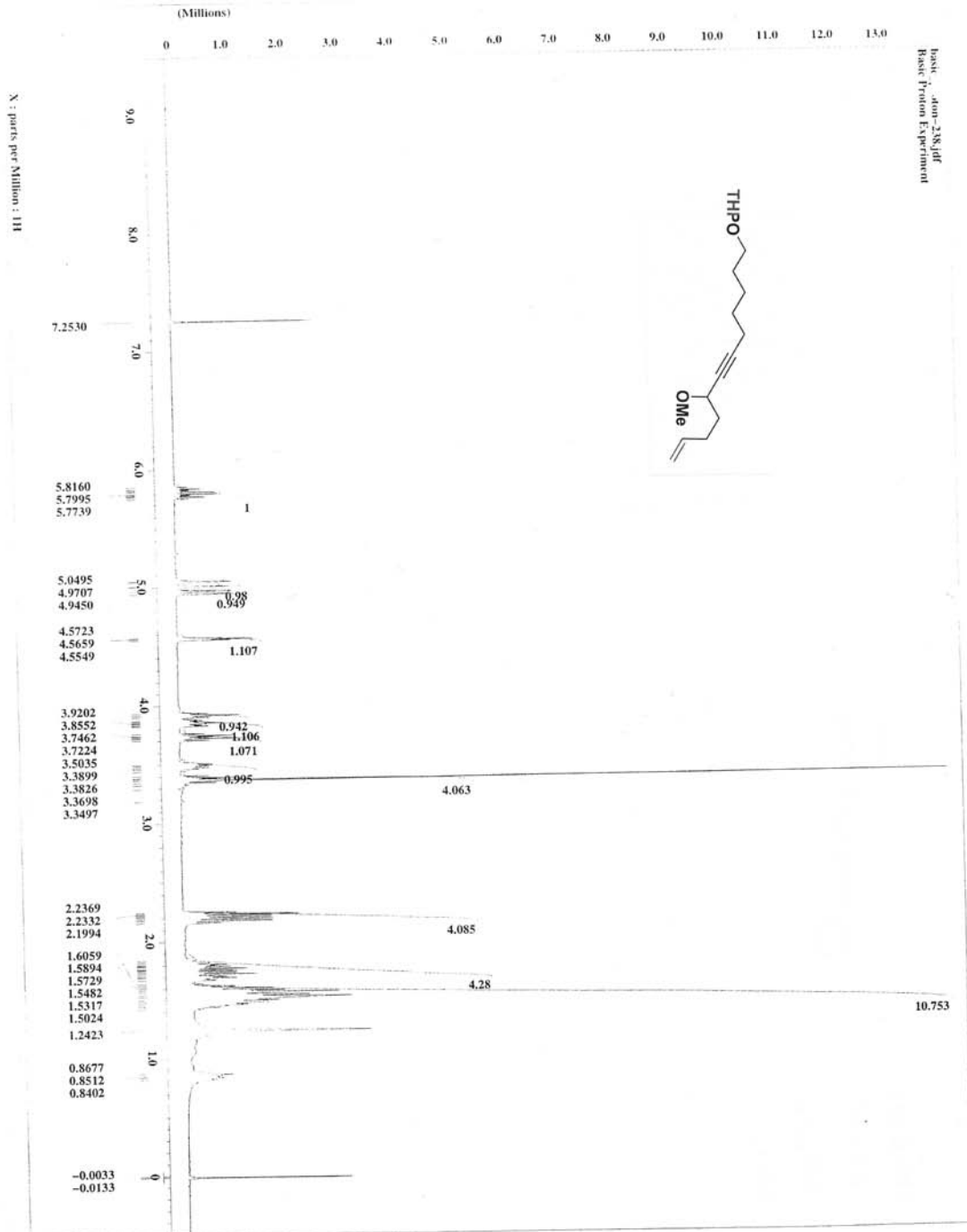
8-Methoxydodec-11-en-6-ynoic acid. According to the general procedure, combination of the Dess-Martin periodinane (520 mg, 1.23 mmol, 1.2 equiv) and dichloromethane (4.5 mL) with alcohol **24** (215 mg, 1.02 mmol, 1.0 equiv) in dichloromethane (1.0 mL) followed by stirring at room temp for 1 h and the standard aqueous workup yielded 176 mg (83%) of the desired aldehyde as a yellow oil: IR (neat) 3076, 2937, 2863, 2821, 2721, 2227, 1725, 1641 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) 9.77 (m, 1H), 5.81 (ddt, $J = 17.0, 10.4, 6.6$ Hz 1H), 5.03 (dd, $J = 17.2, 1.5$ Hz, 1H), 4.95 (dd, $J = 10.2, 1.1$ Hz, 1H), 3.92 (tt, $J = 6.6, 1.8$ Hz, 1H), 3.38 (s, 3H), 2.46 (td, $J = 7.3, 1.6$ Hz, 2H), 2.26 (td, $J = 7.0, 1.5$ Hz, 2H), 2.18 (q, $J = 7.3$ Hz, 2H), 1.76 (m, 4H), 1.56 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.3, 137.8, 115.0, 85.7, 79.2, 70.8, 56.2, 43.3, 35.0, 29.5, 28.1, 21.2, 18.5; HRMS-FAB m/z $[\text{M-H}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{O}_2$ 207.1385, found 207.1404.

According to the general procedure, combination of the previously prepared aldehyde (123 mg, 0.59 mmol, 1.0 equiv), dimethylformamide (7 mL), and Oxone (363 mg, 0.59 mmol, 1.0 equiv) and stirring at room temp for 2 h followed by the standard aqueous workup yielded 143 mg (108%) of the desired carboxylic acid as a yellow oil that was used without further purification: IR (neat) 3077, 2937, 2867, 2650, 2230, 1711, 1648, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.81 (ddt, $J = 17.2, 10.2, 6.6$ Hz, 1H), 5.04 (dq, $J = 17.0, 1.8$ Hz, 1H), 4.97 (dm, $J = 11.0$ Hz, 1H), 3.92 (tt, $J = 6.6, 1.8$ Hz, 1H), 3.38 (s, 3H), 2.94 (d, $J = 30.4$ Hz, 3H), 2.38 (t, $J = 7.5$ Hz, 2H), 2.26 (td, $J = 7.0, 1.9$ Hz, 2H), 2.20 (m,

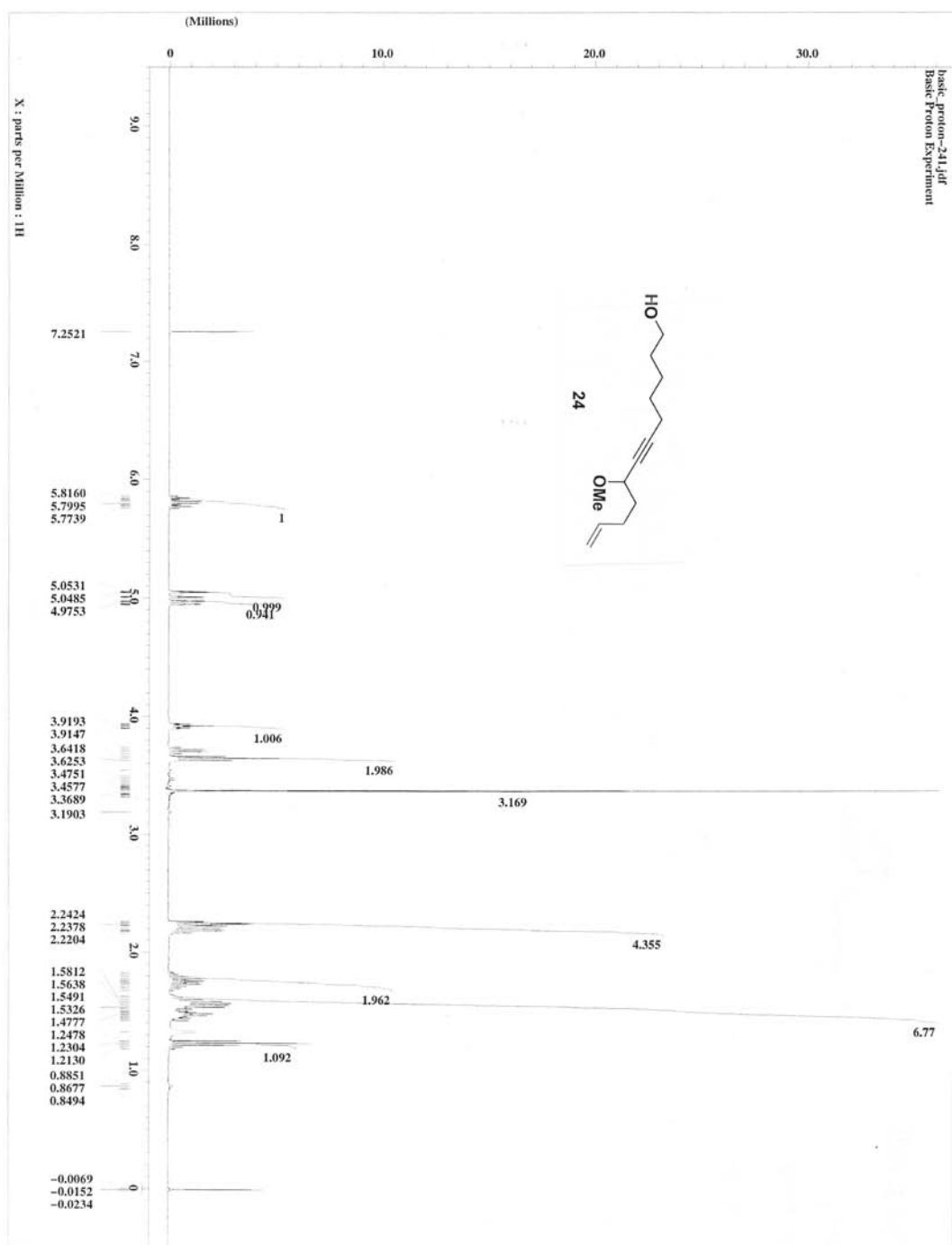
2H), 1.76 (m, 4H), 1.57 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 179.1, 137.9, 115.1, 85.9, 79.1, 70.8, 56.2, 35.0, 33.6, 29.5, 28.1, 23.9, 18.5; HRMS-FAB m/z $[\text{M-H}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{O}_3$ 223.1334, found 223.1351.



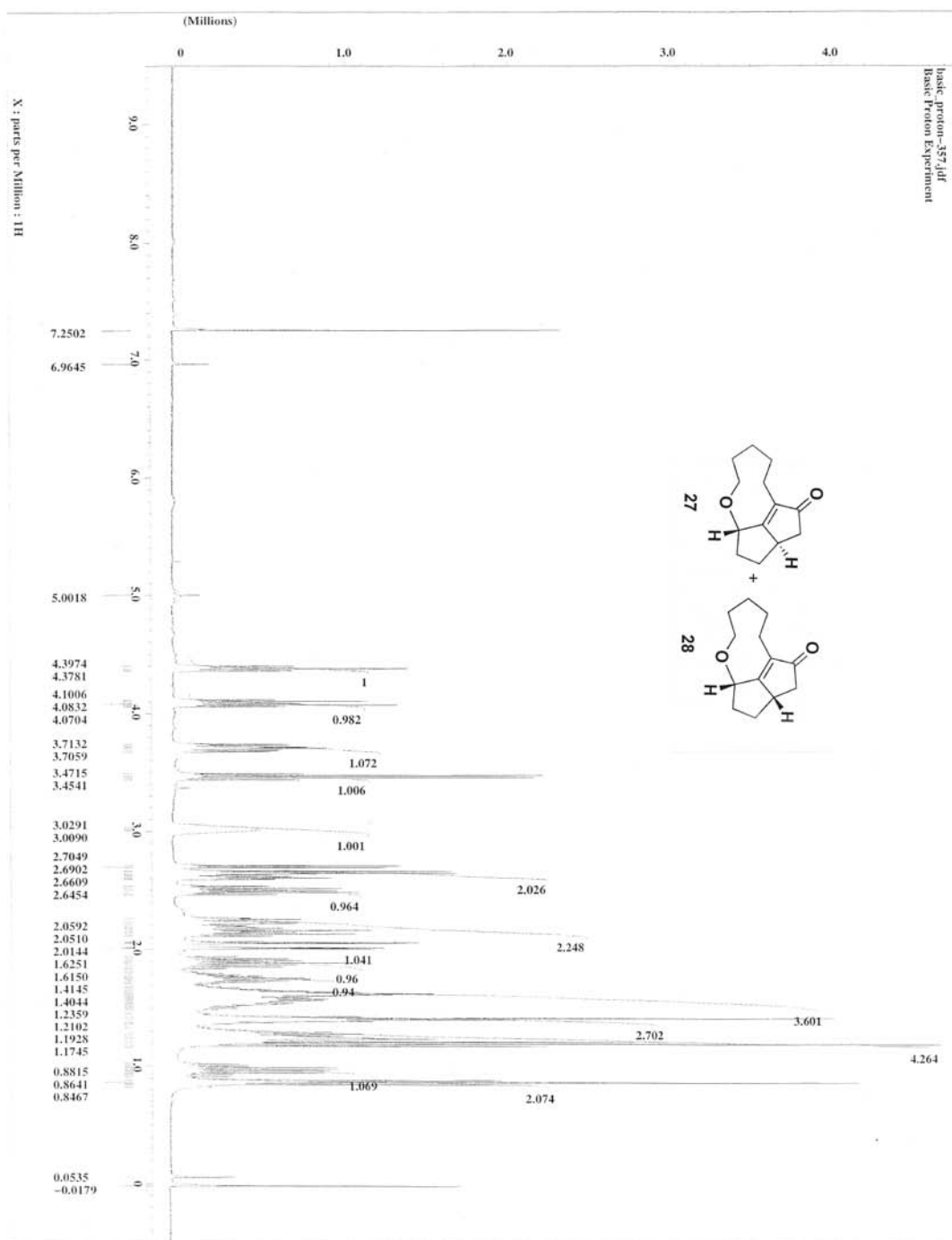
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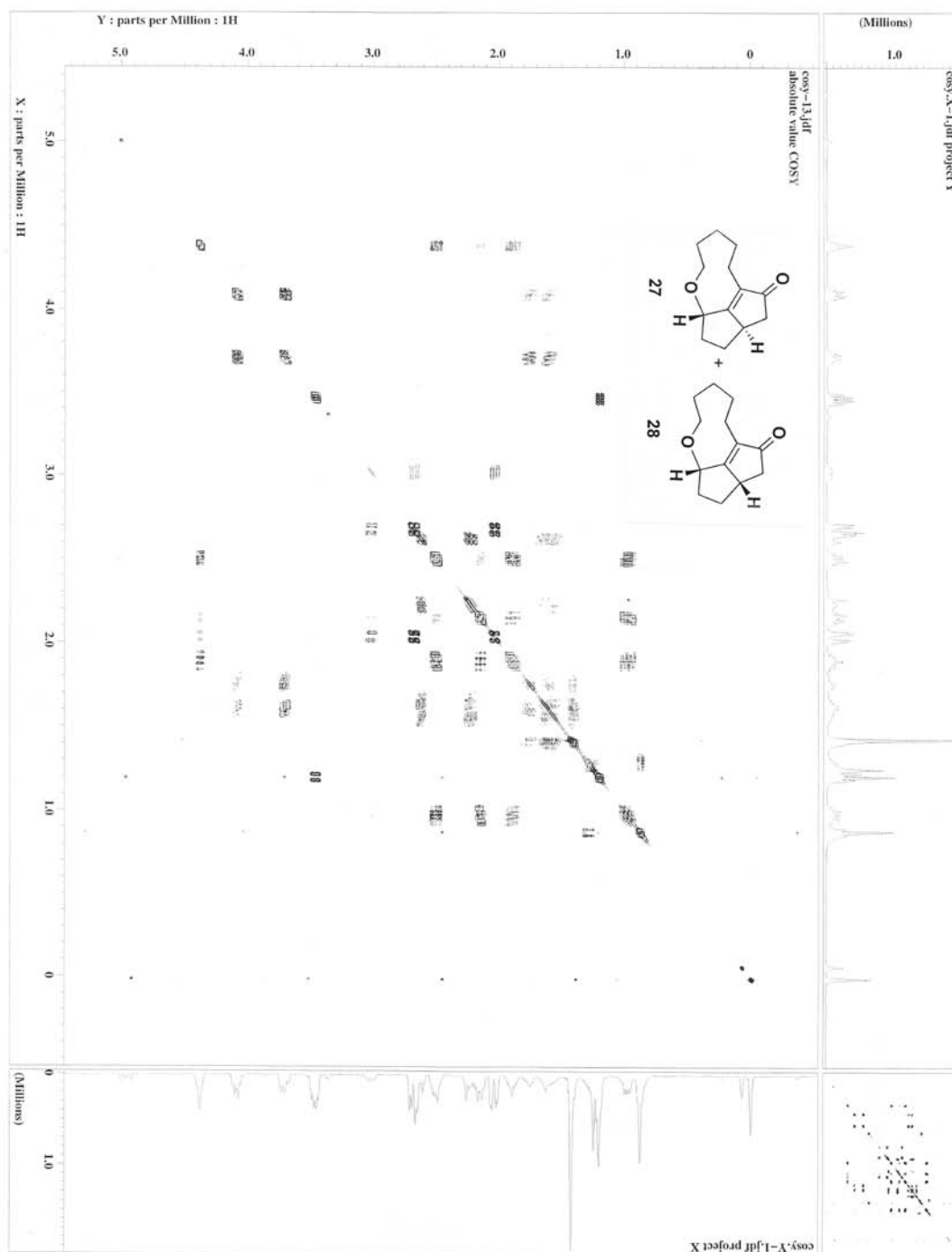
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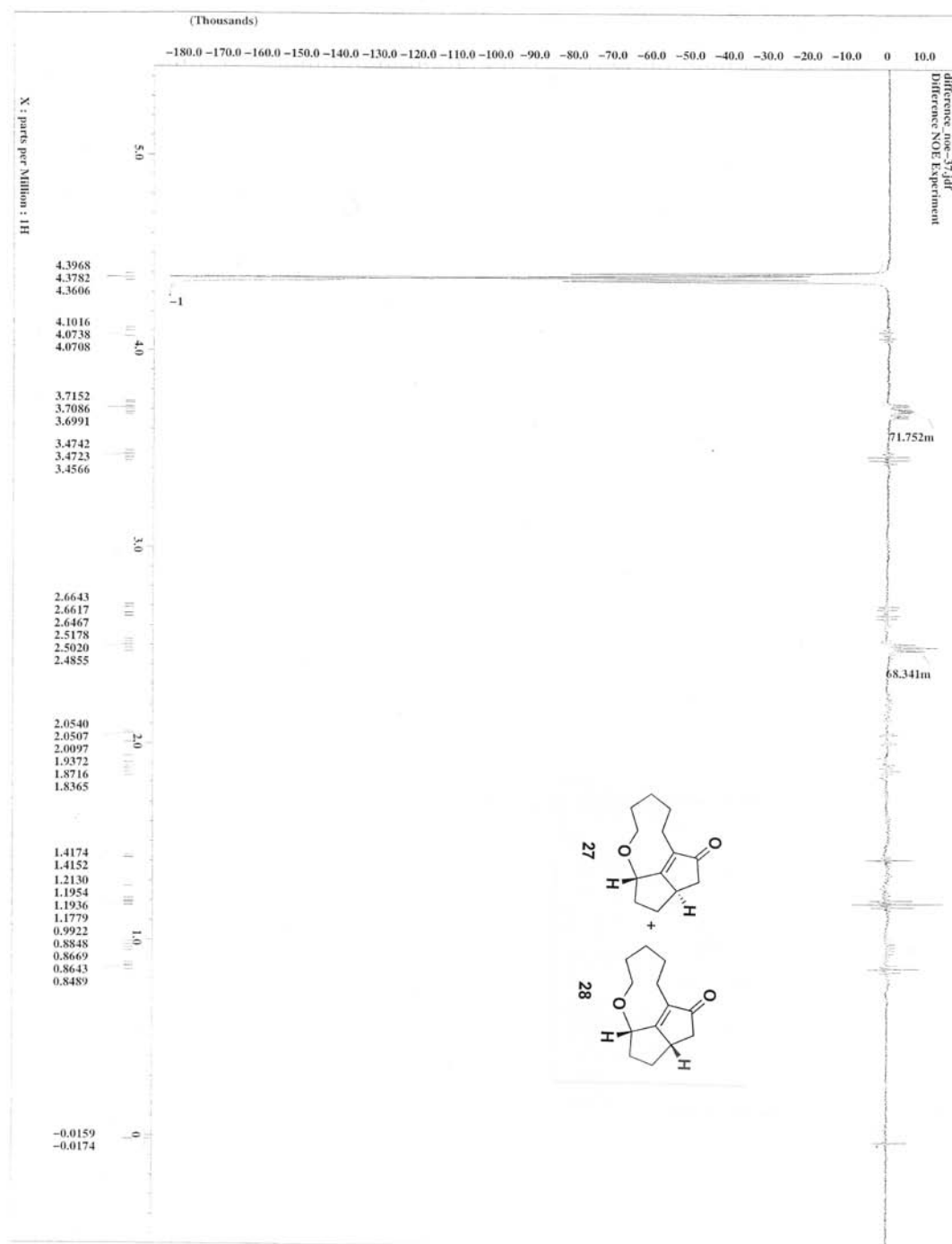
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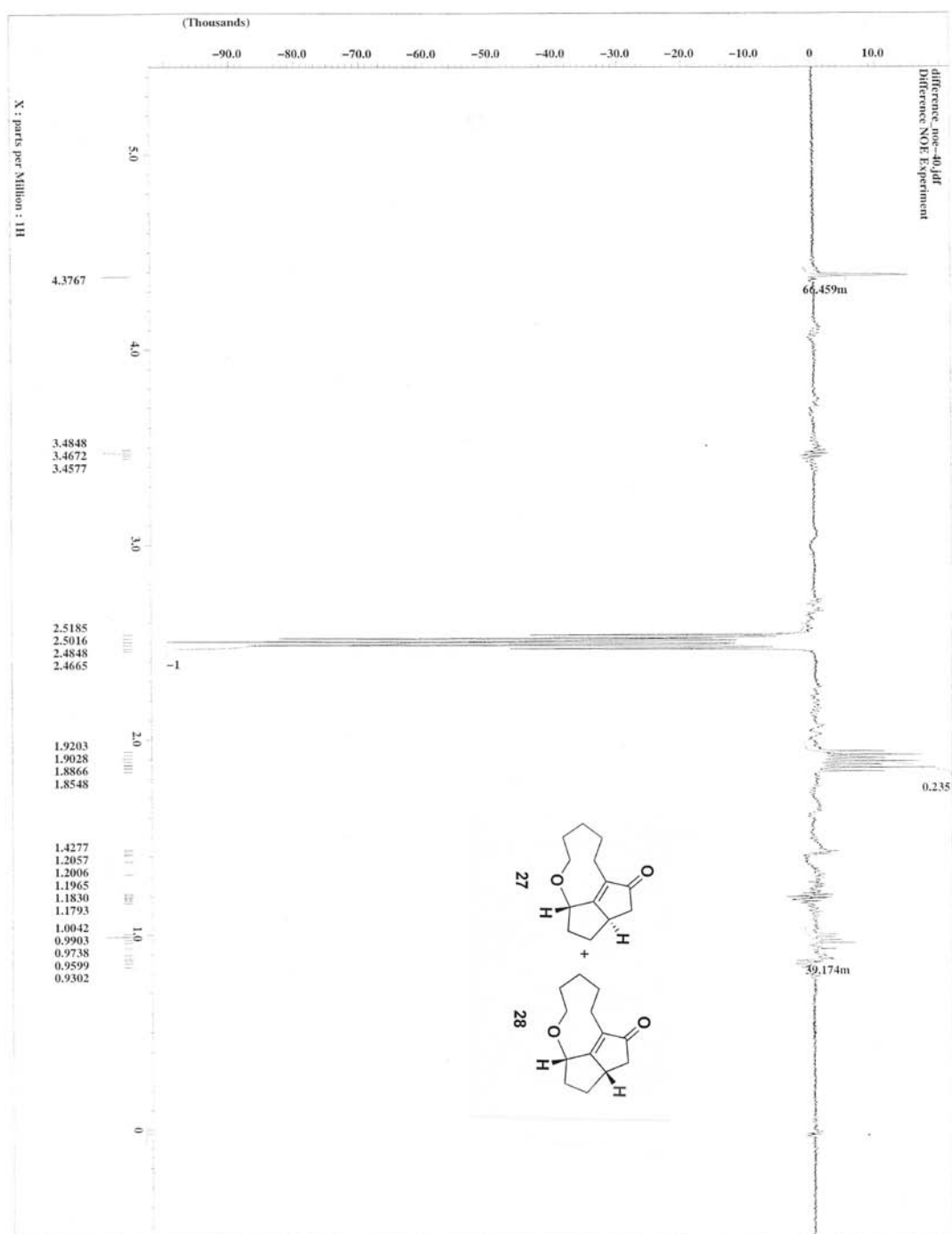
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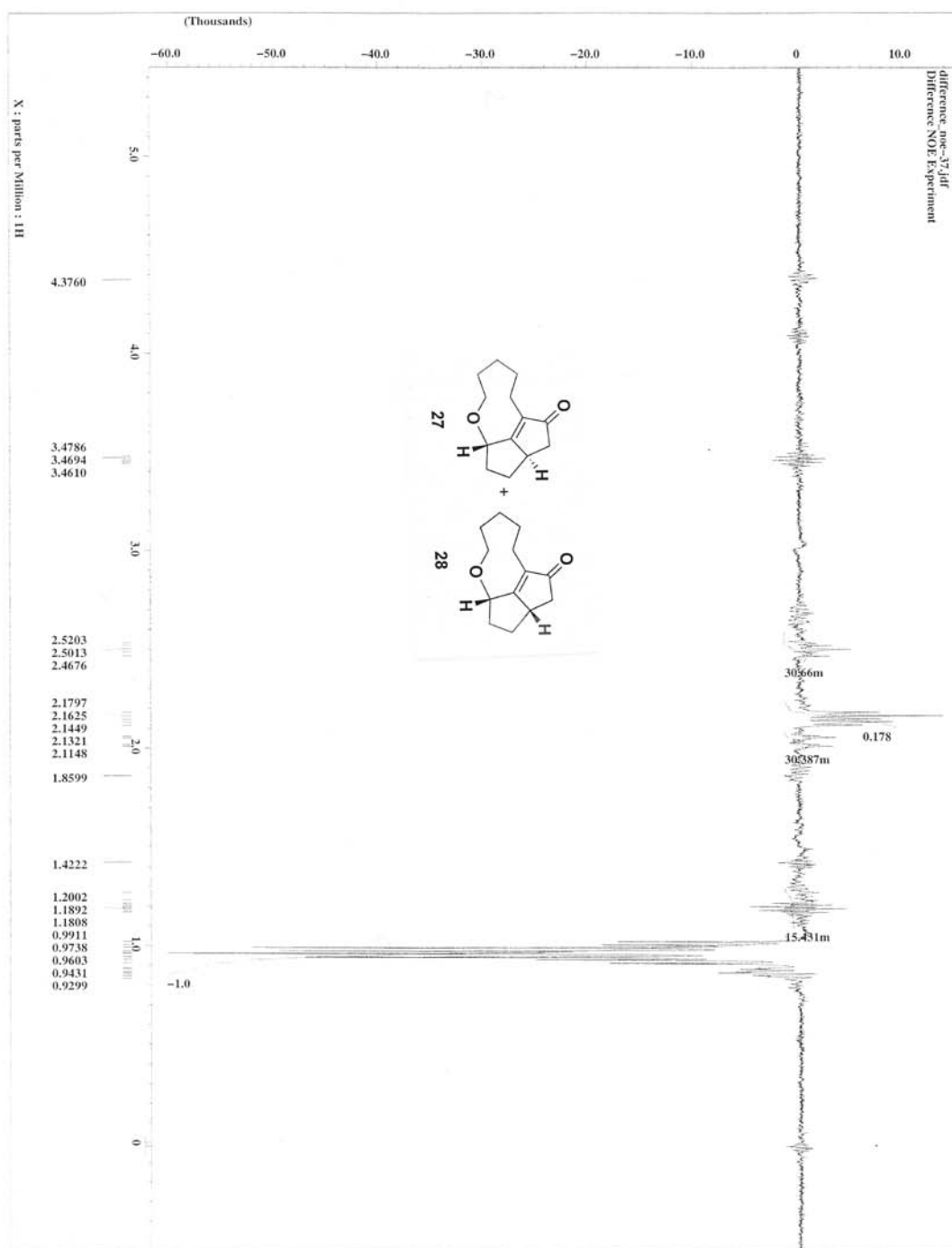
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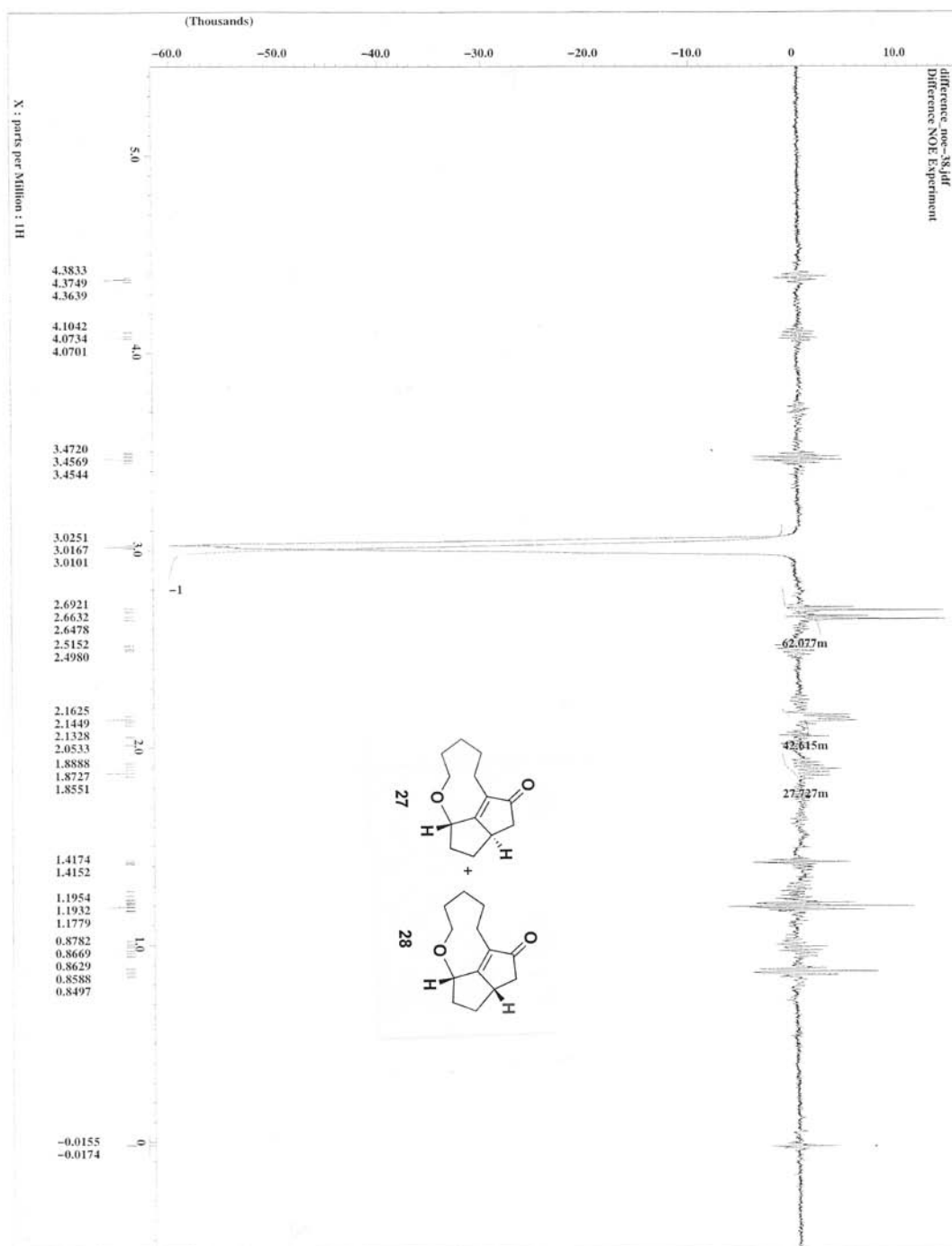
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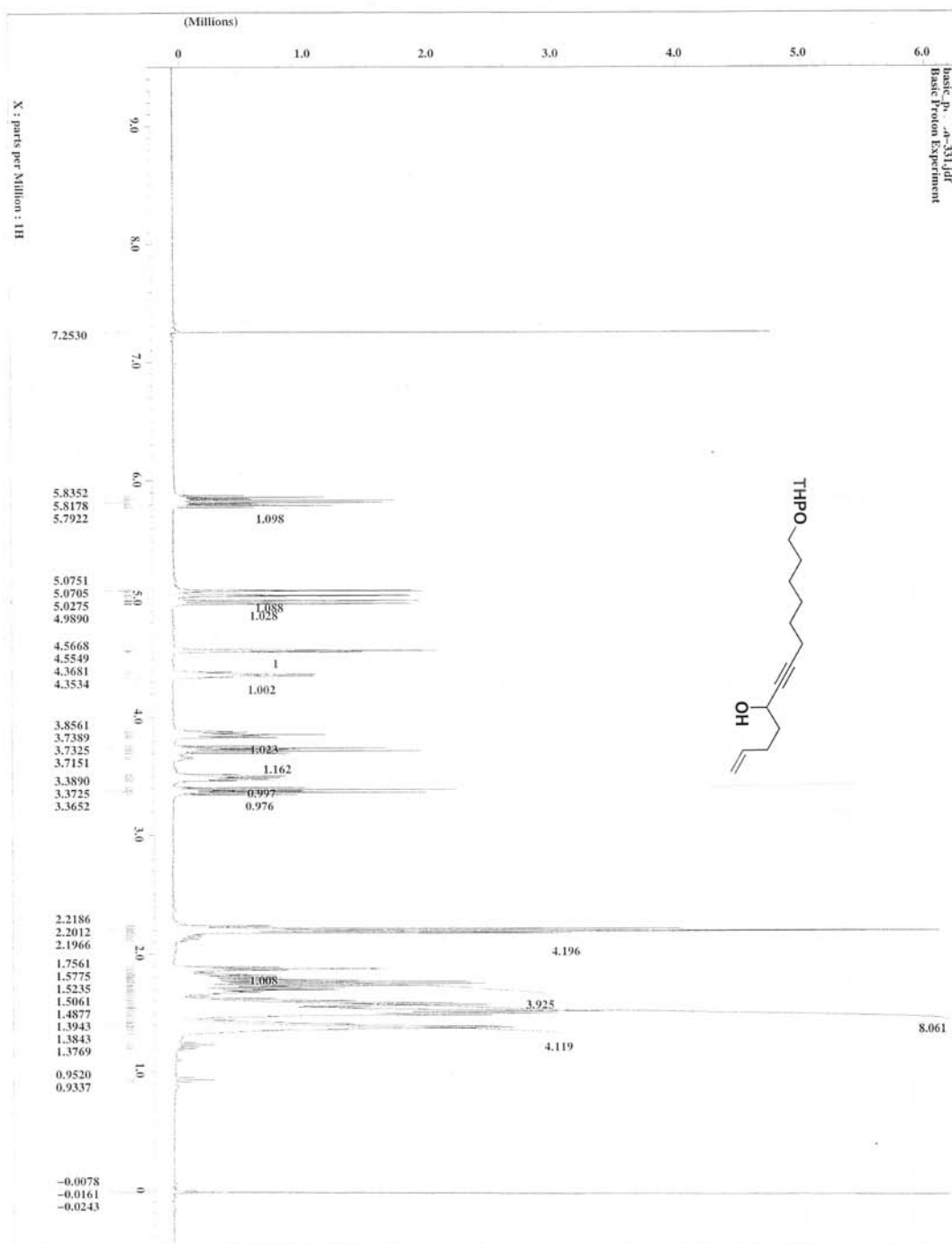
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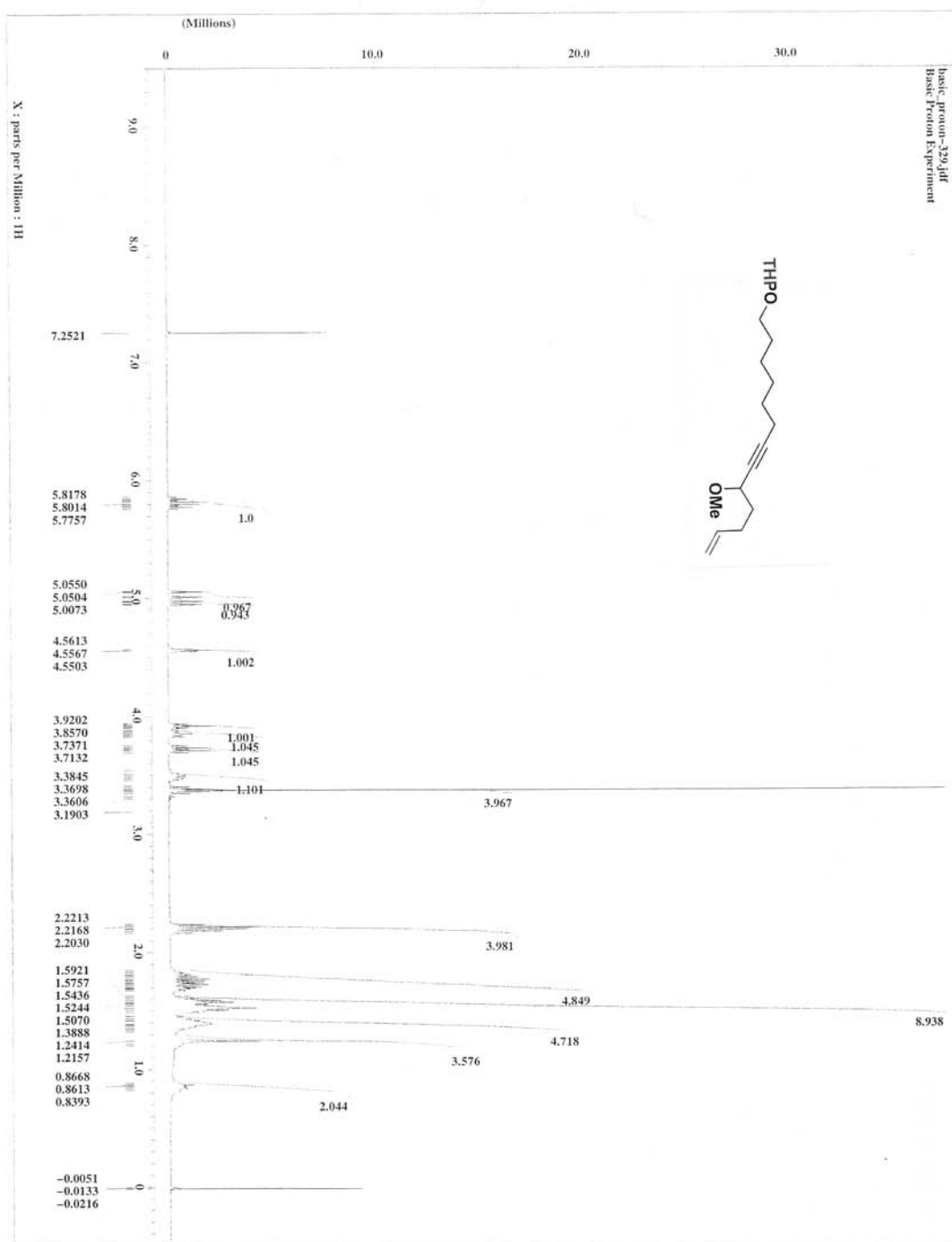
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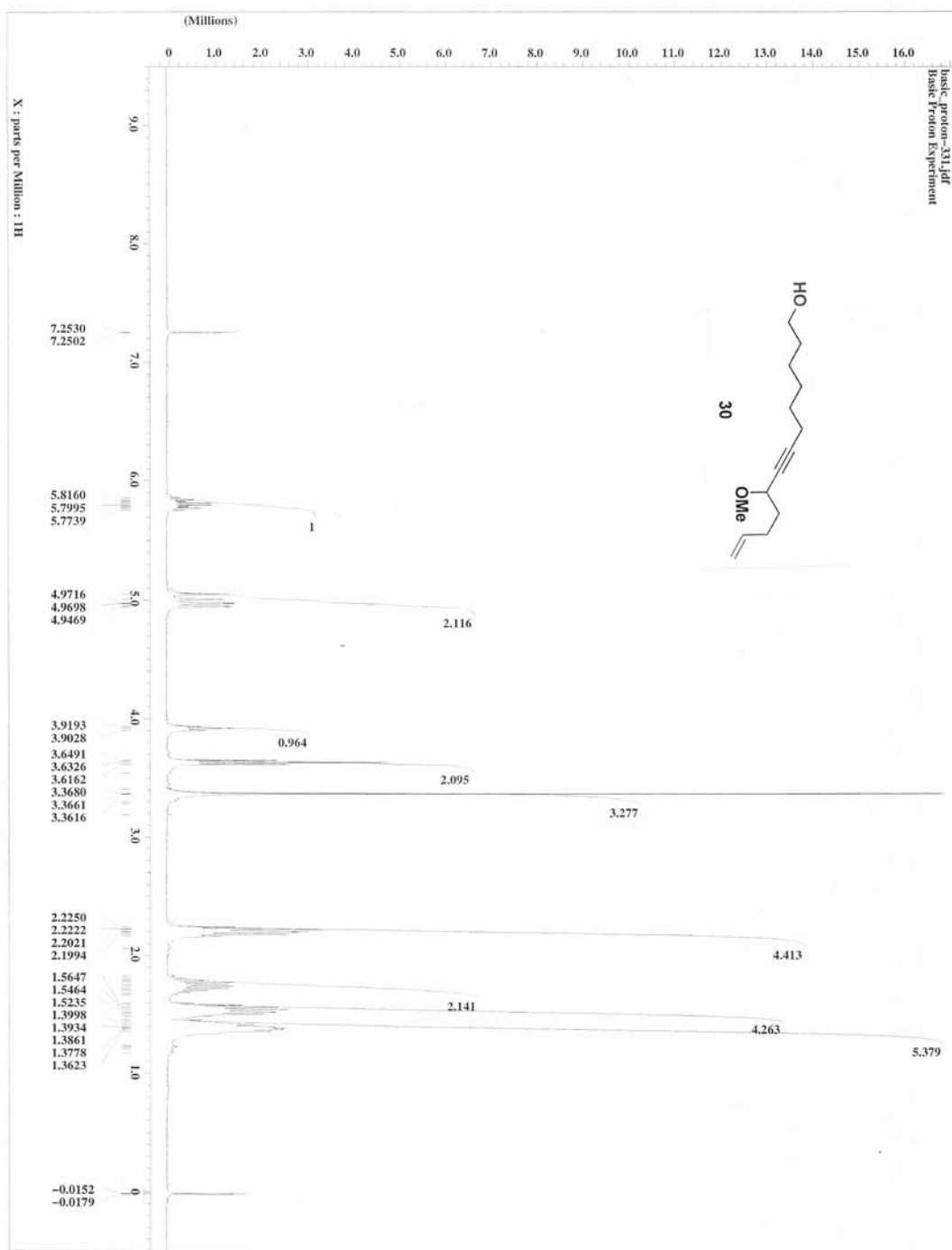
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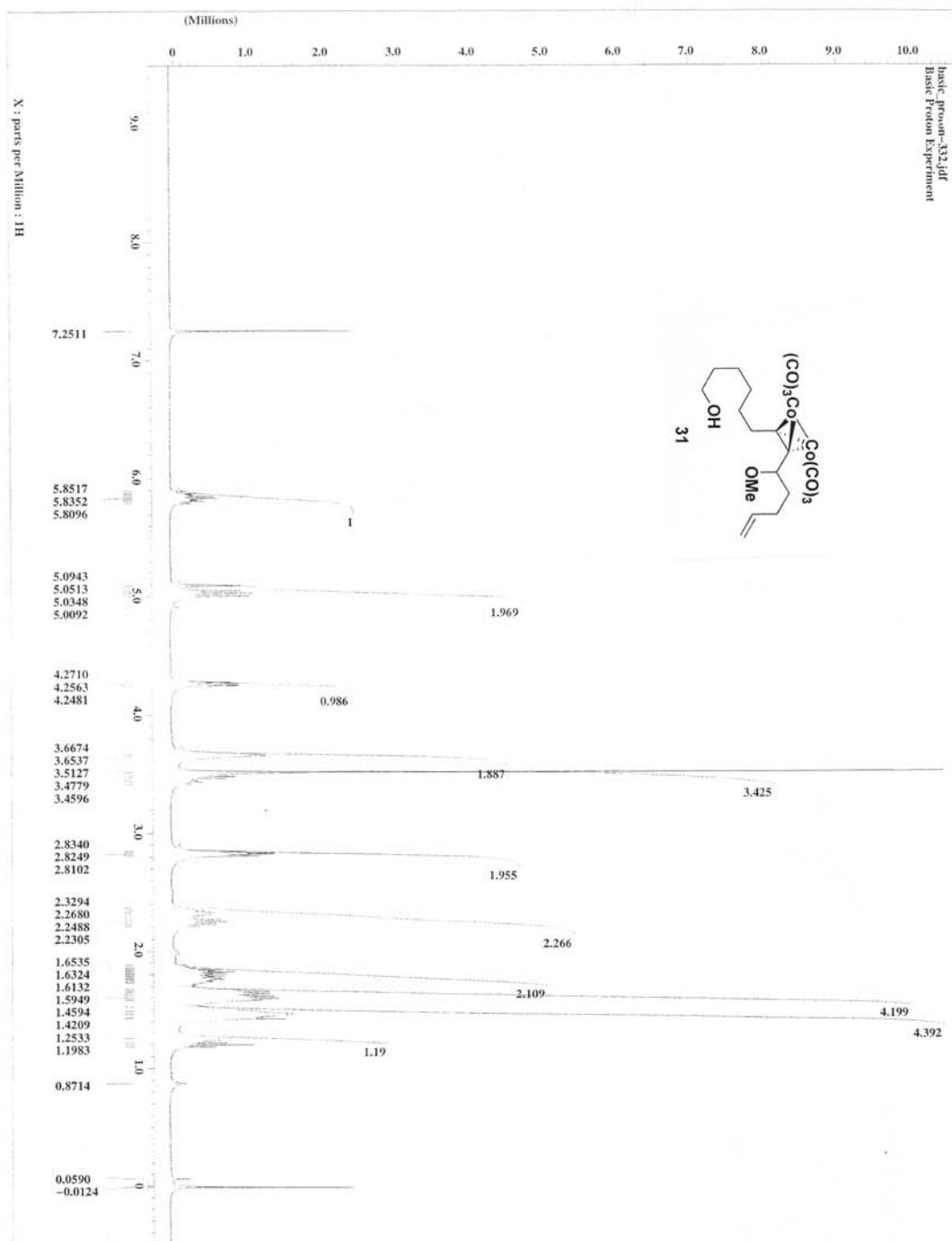
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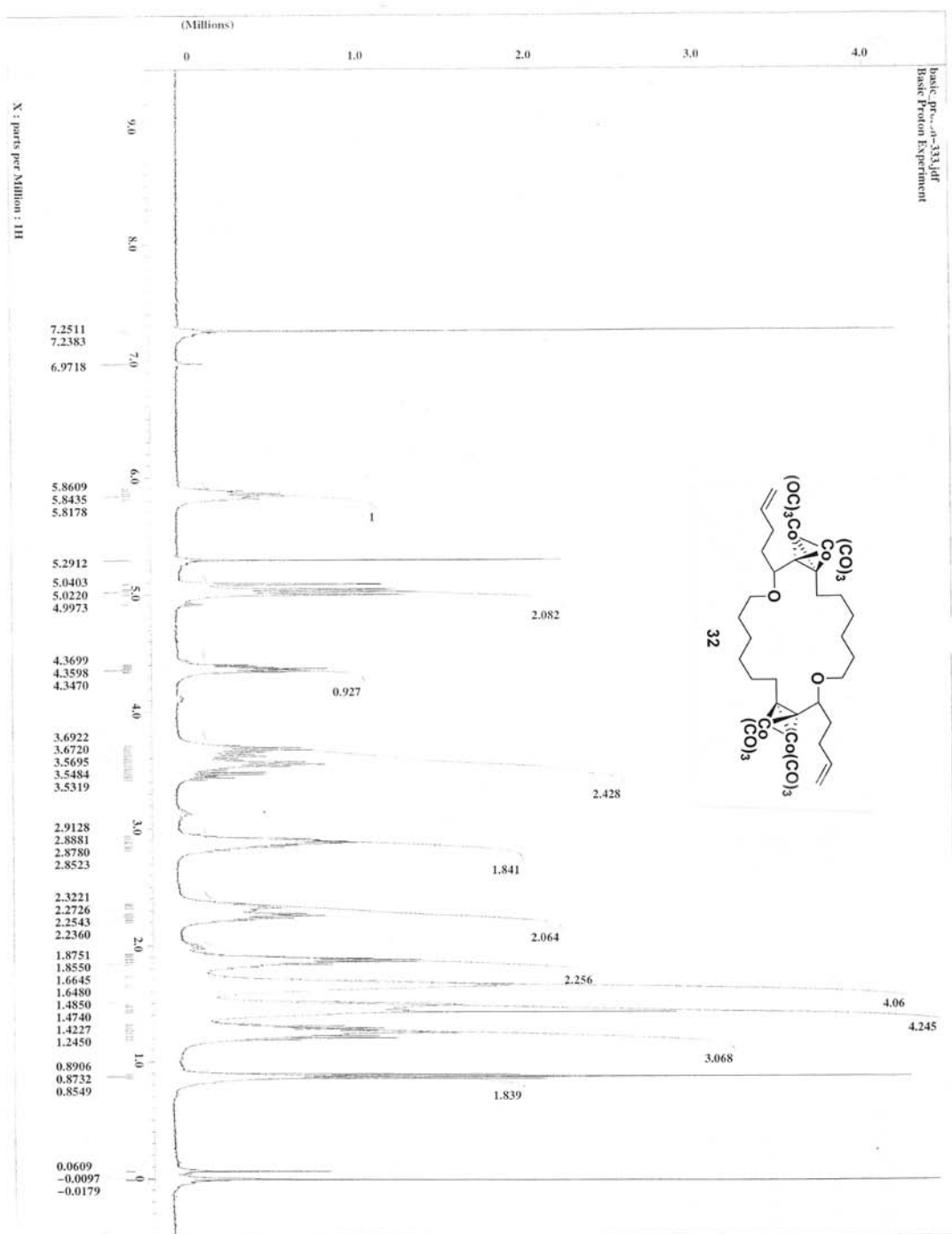
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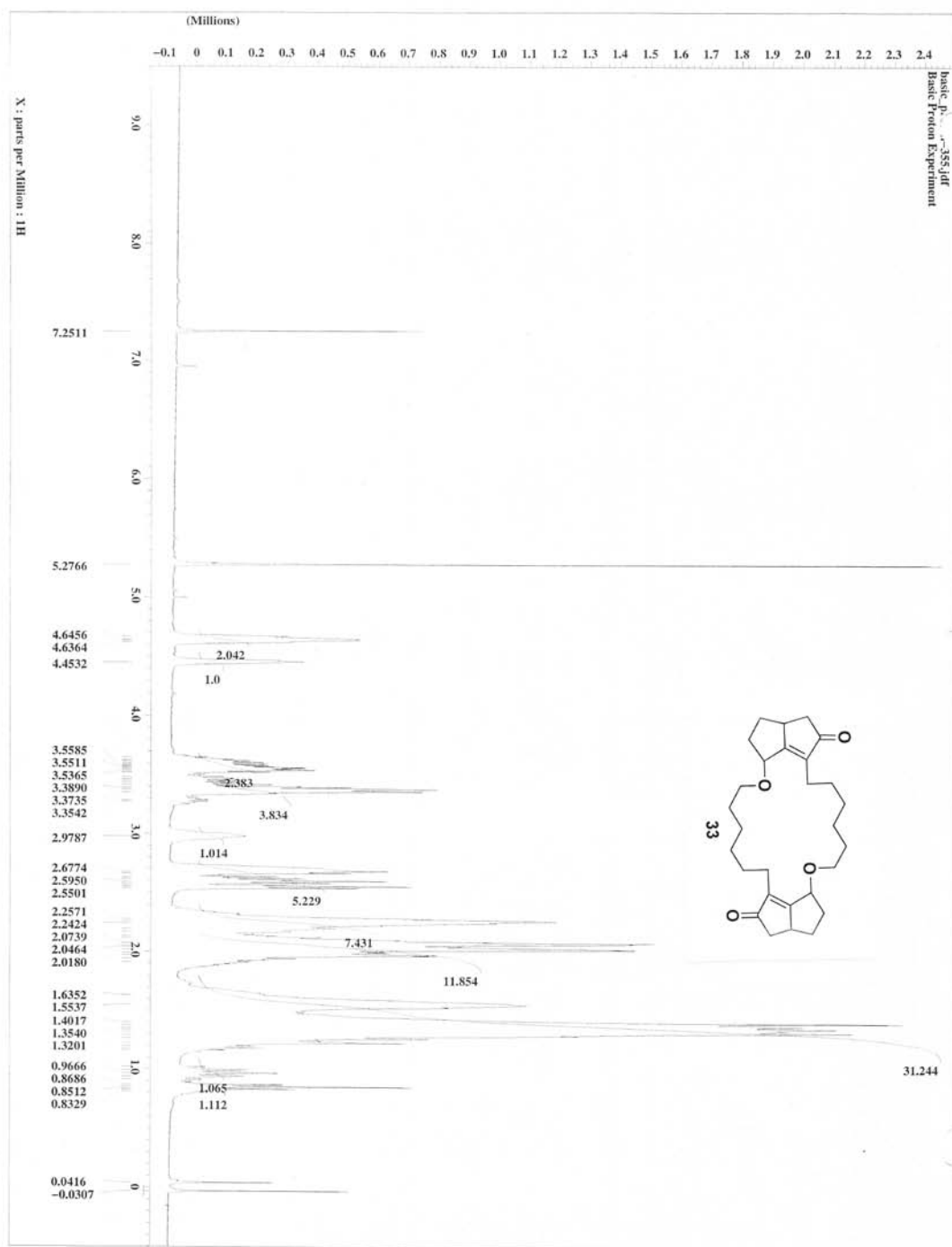
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Spectrometer Frequency: 400 MHz
Solvent: CDCl₃



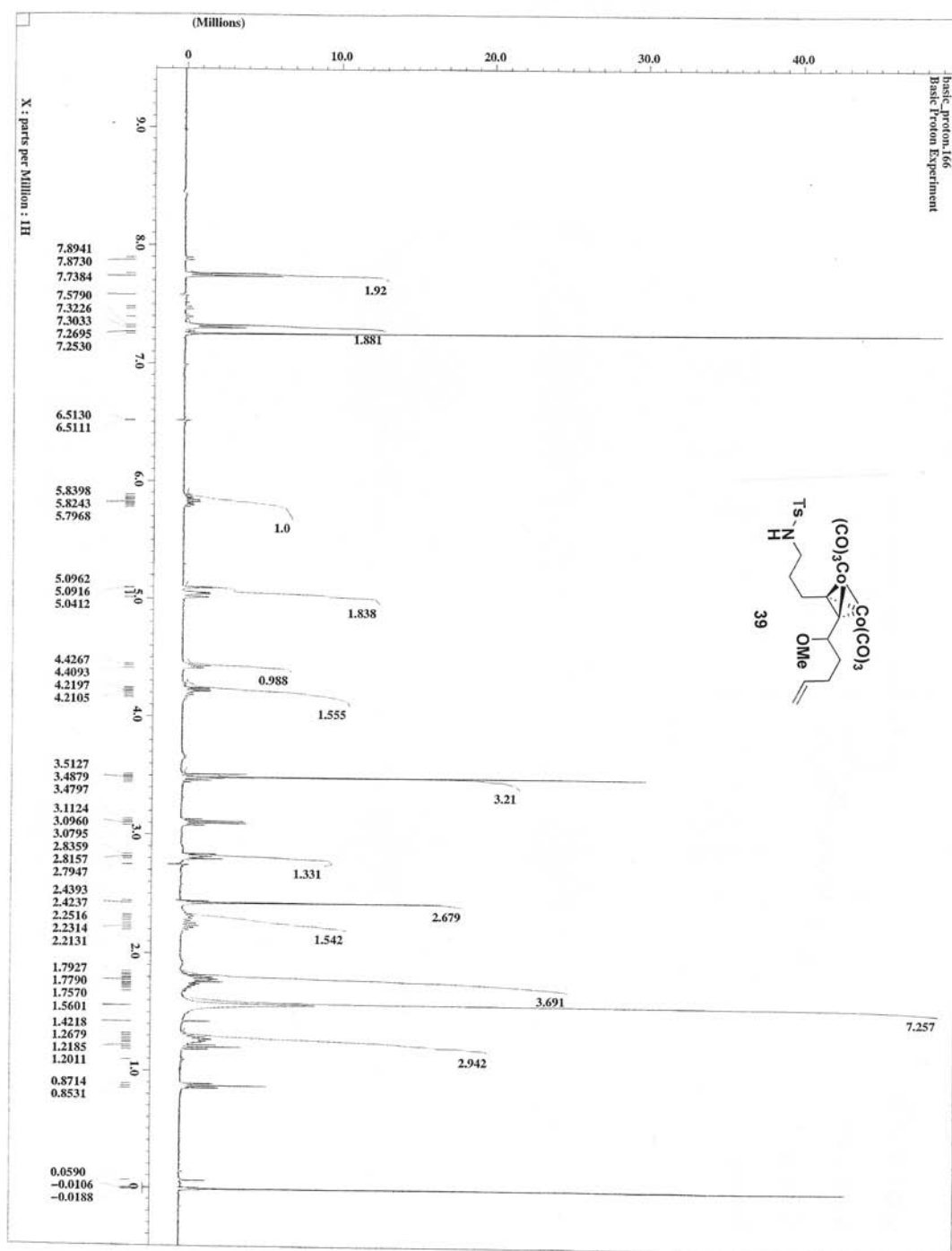
Spectrometer Frequency: 400 MHz
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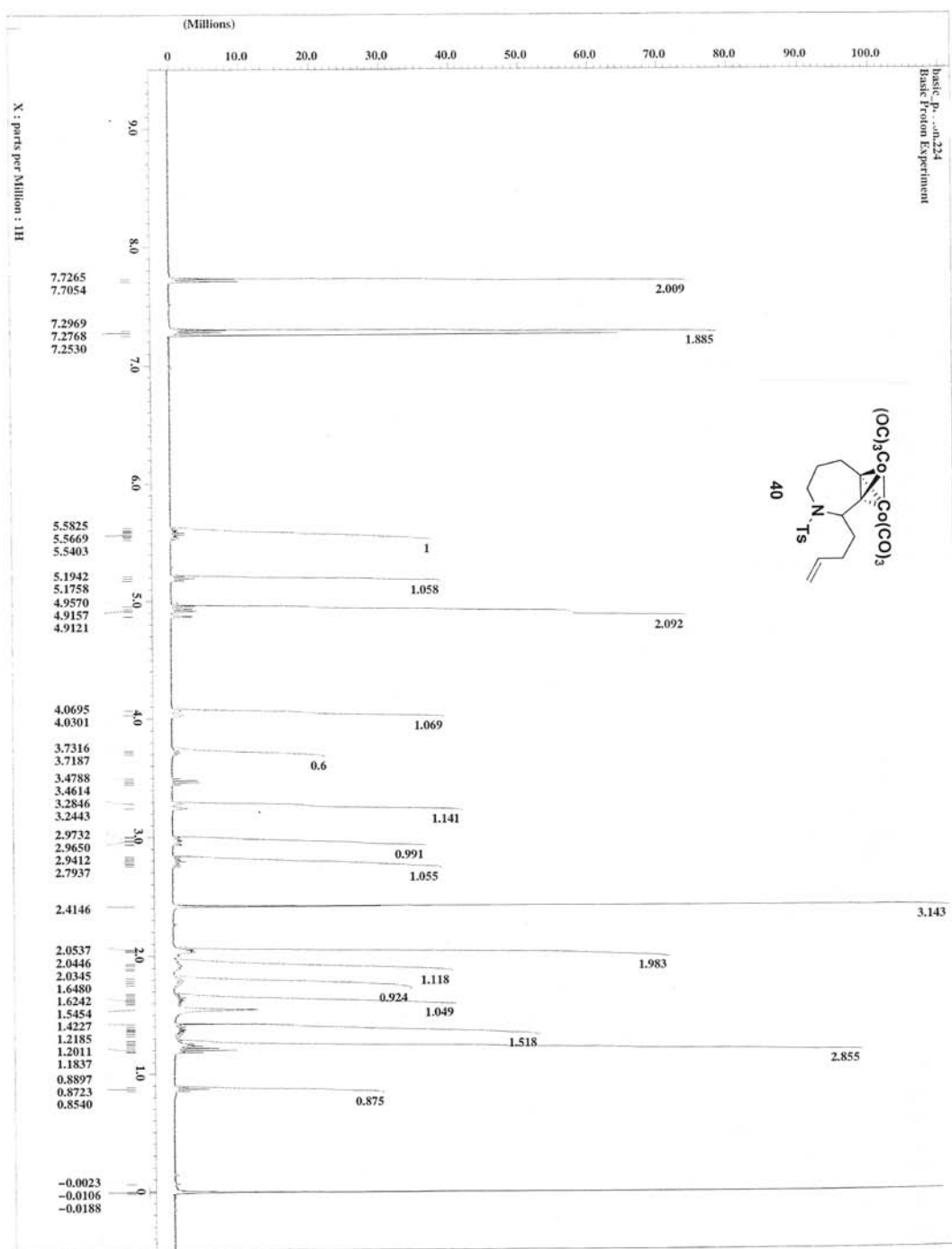
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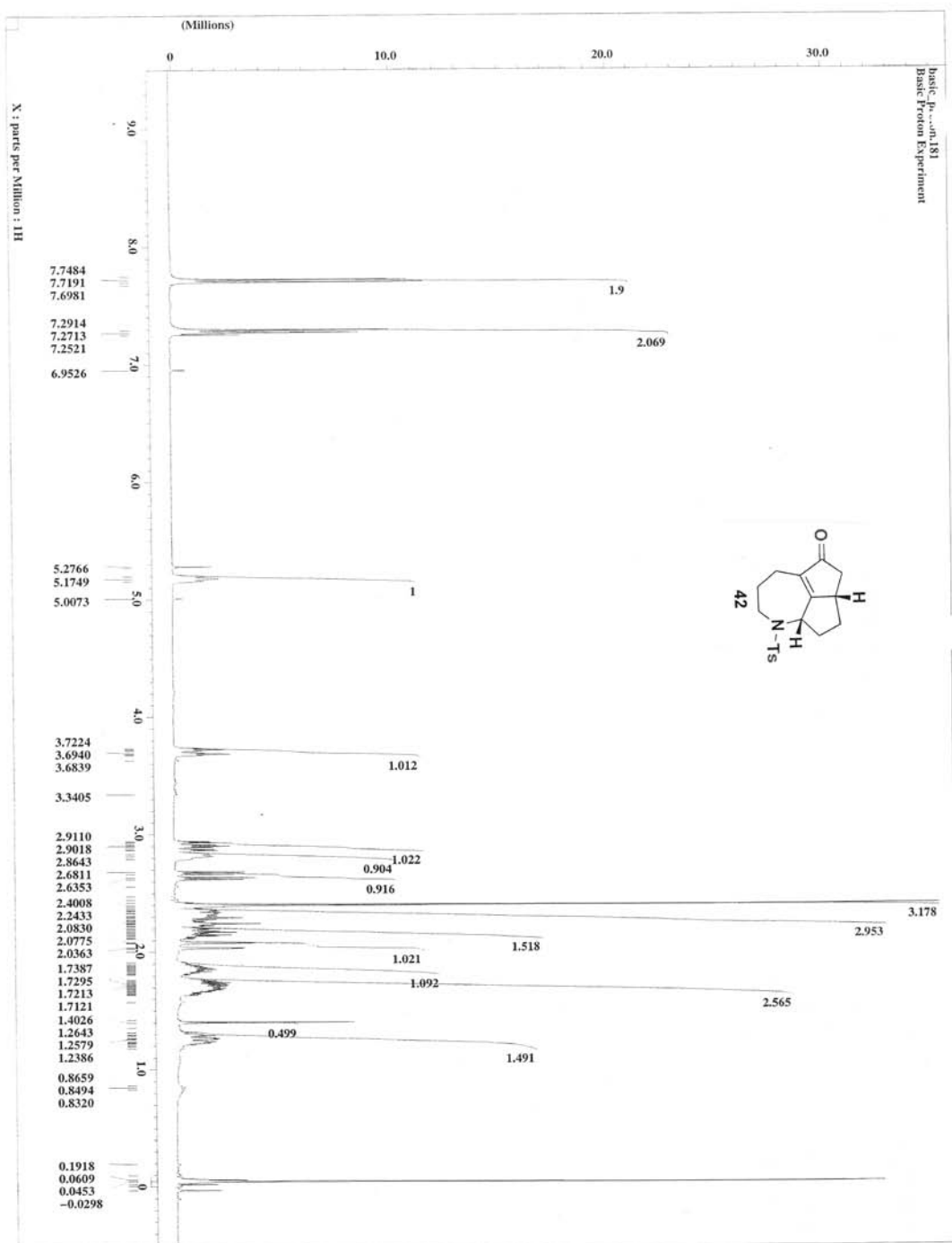


S40

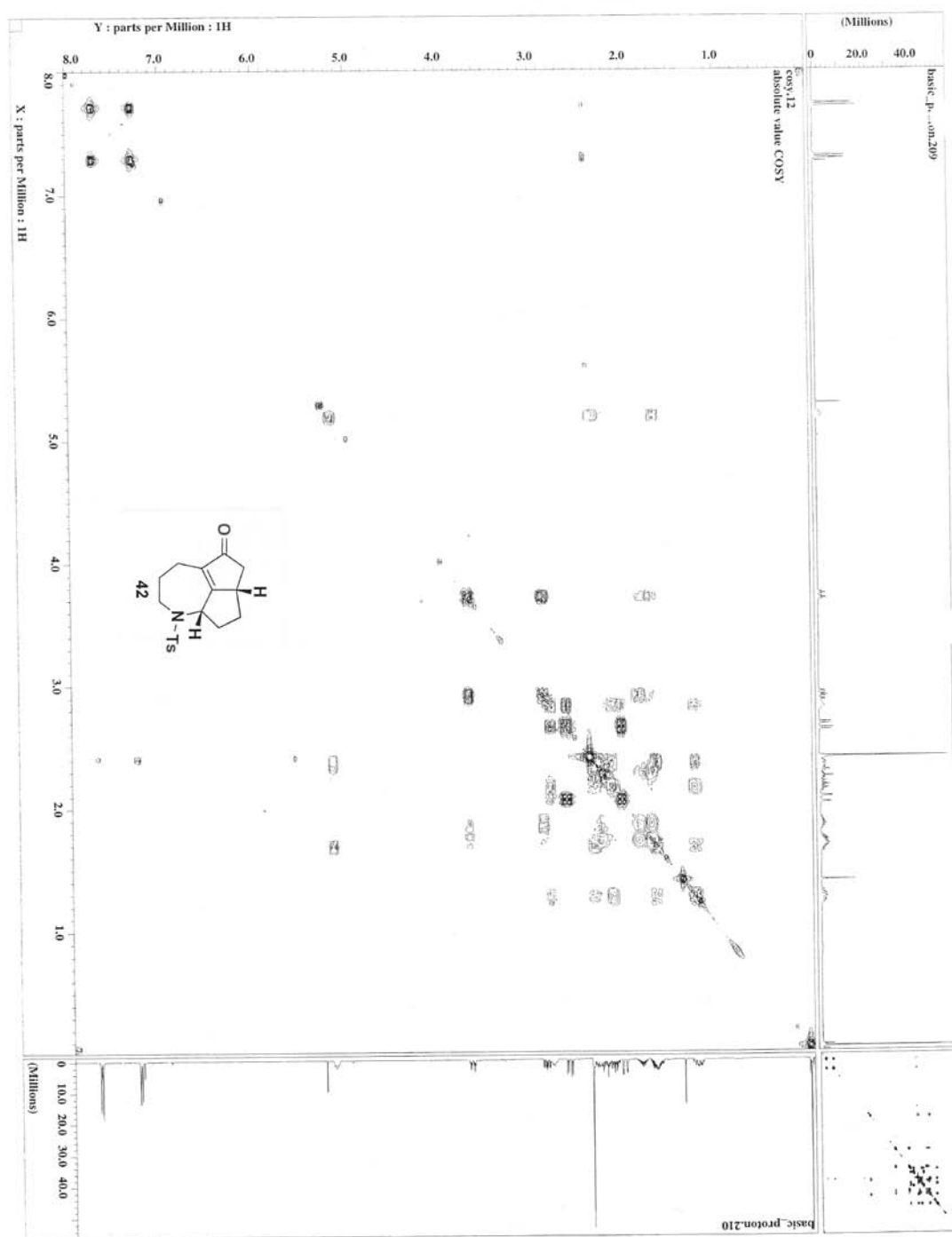


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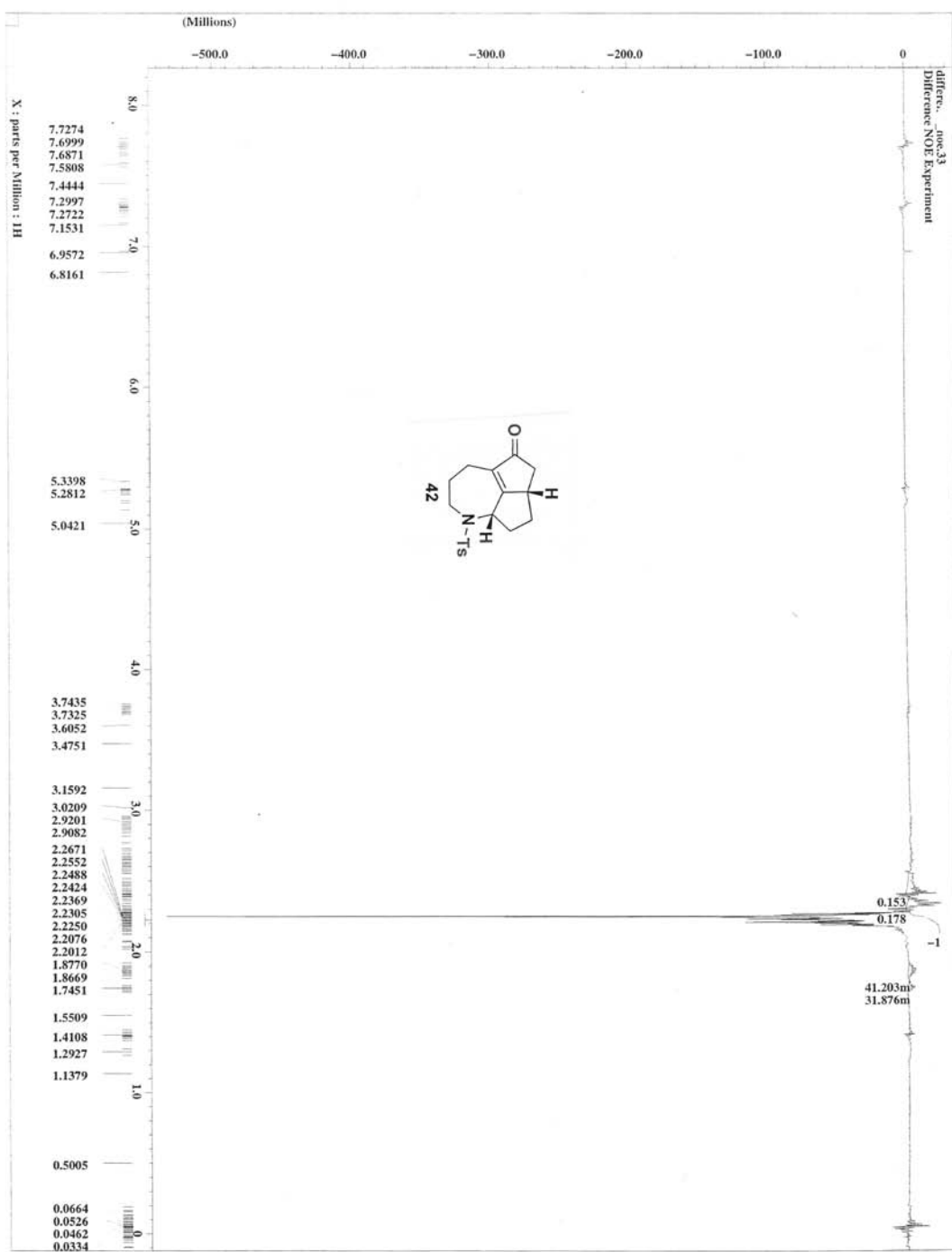




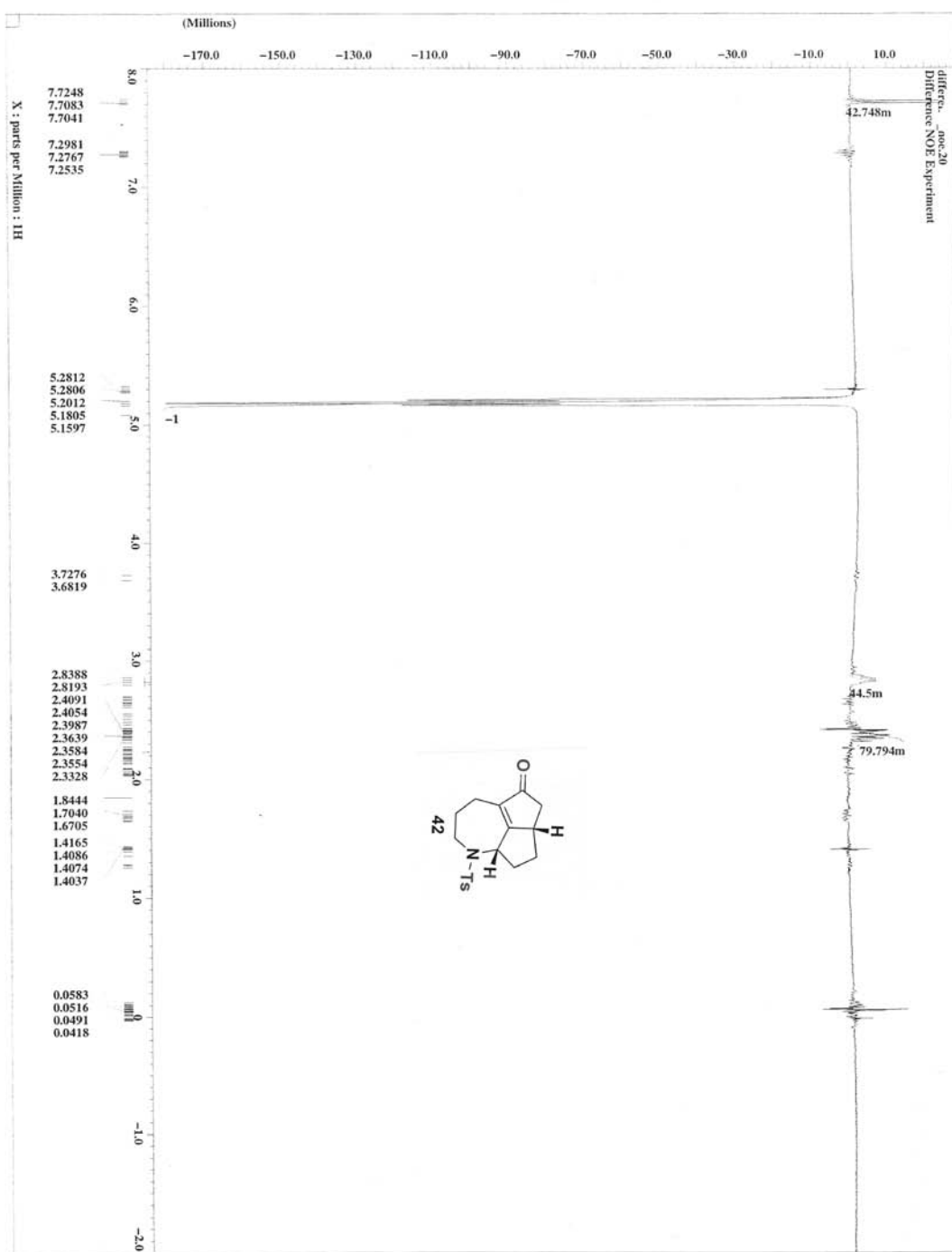
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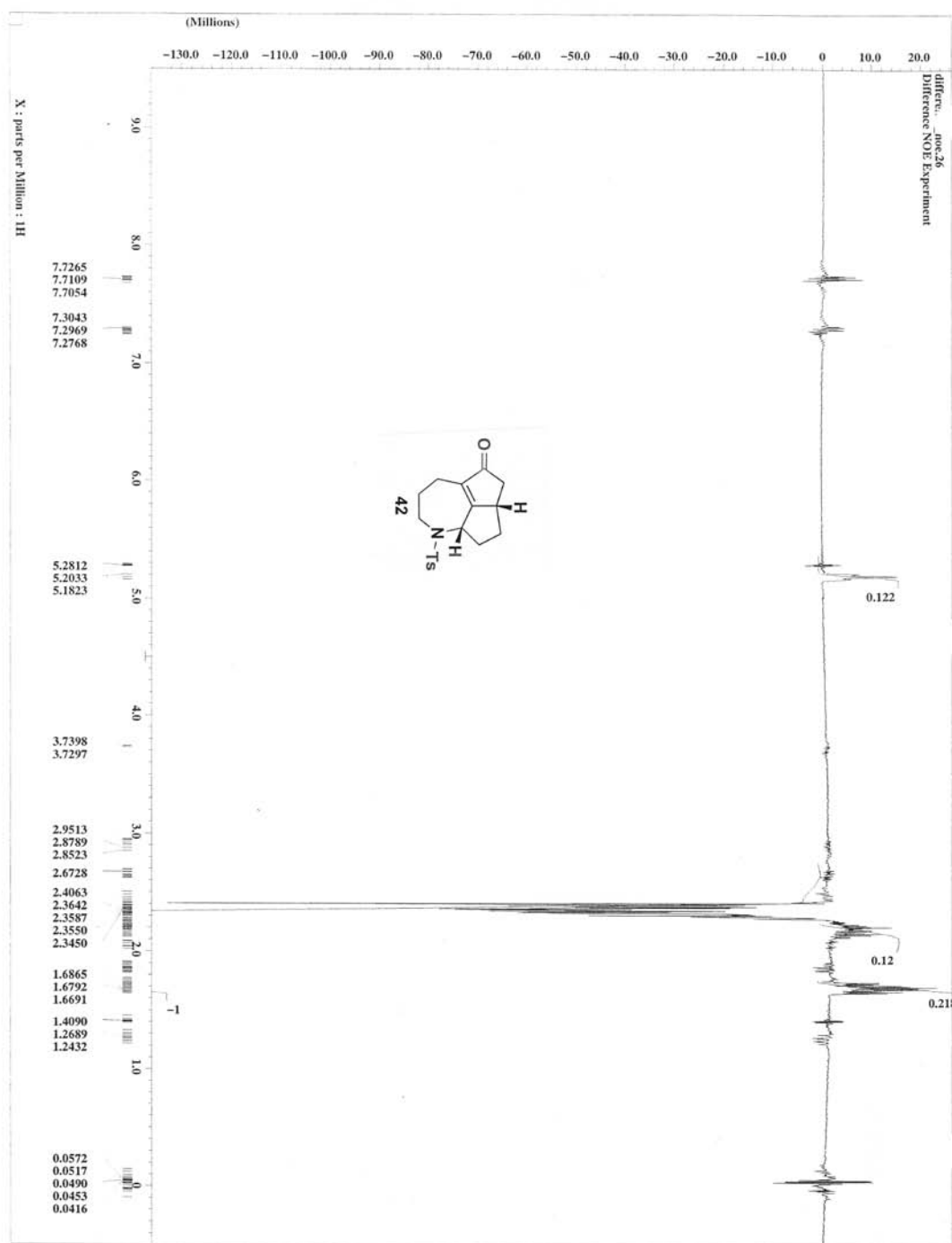
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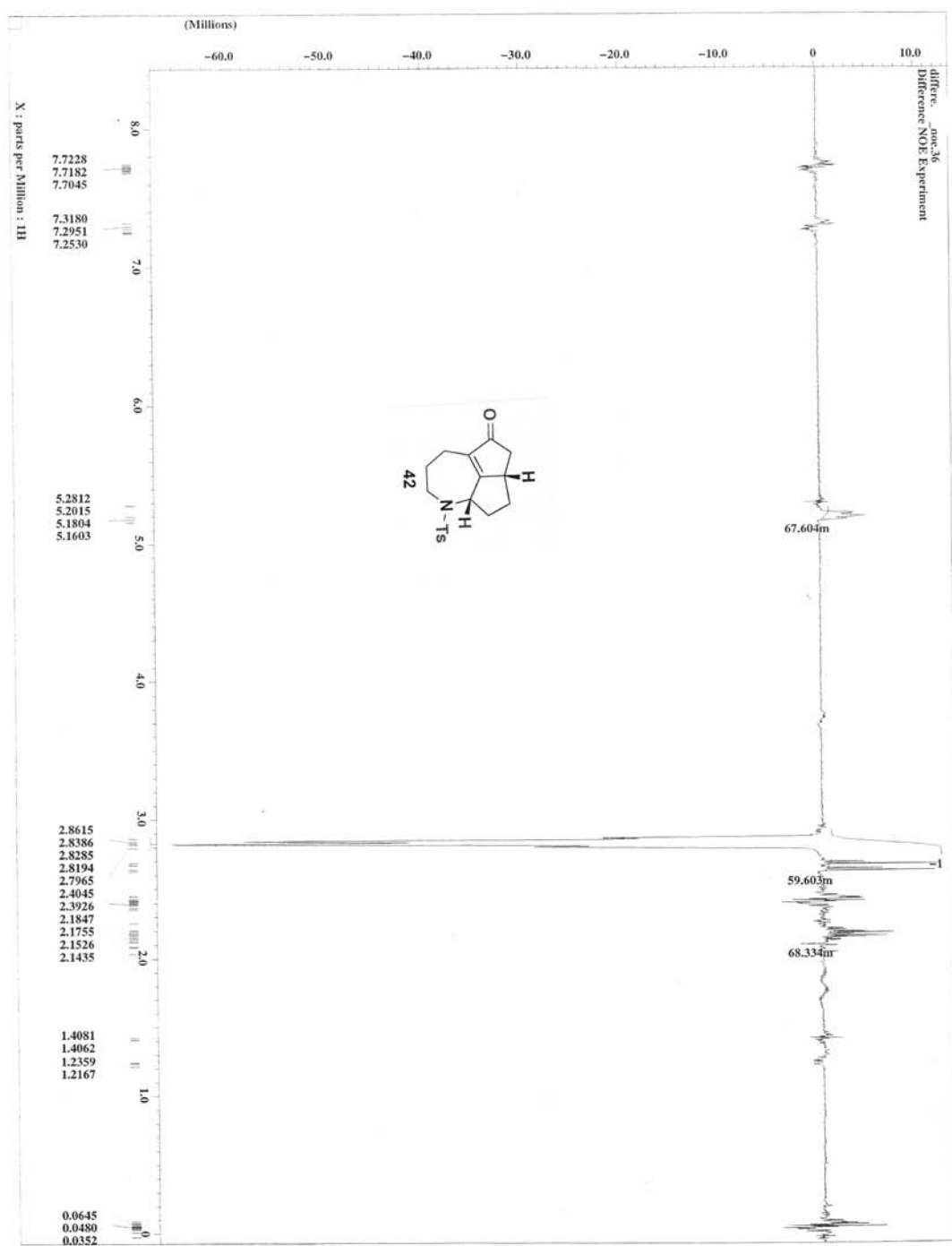
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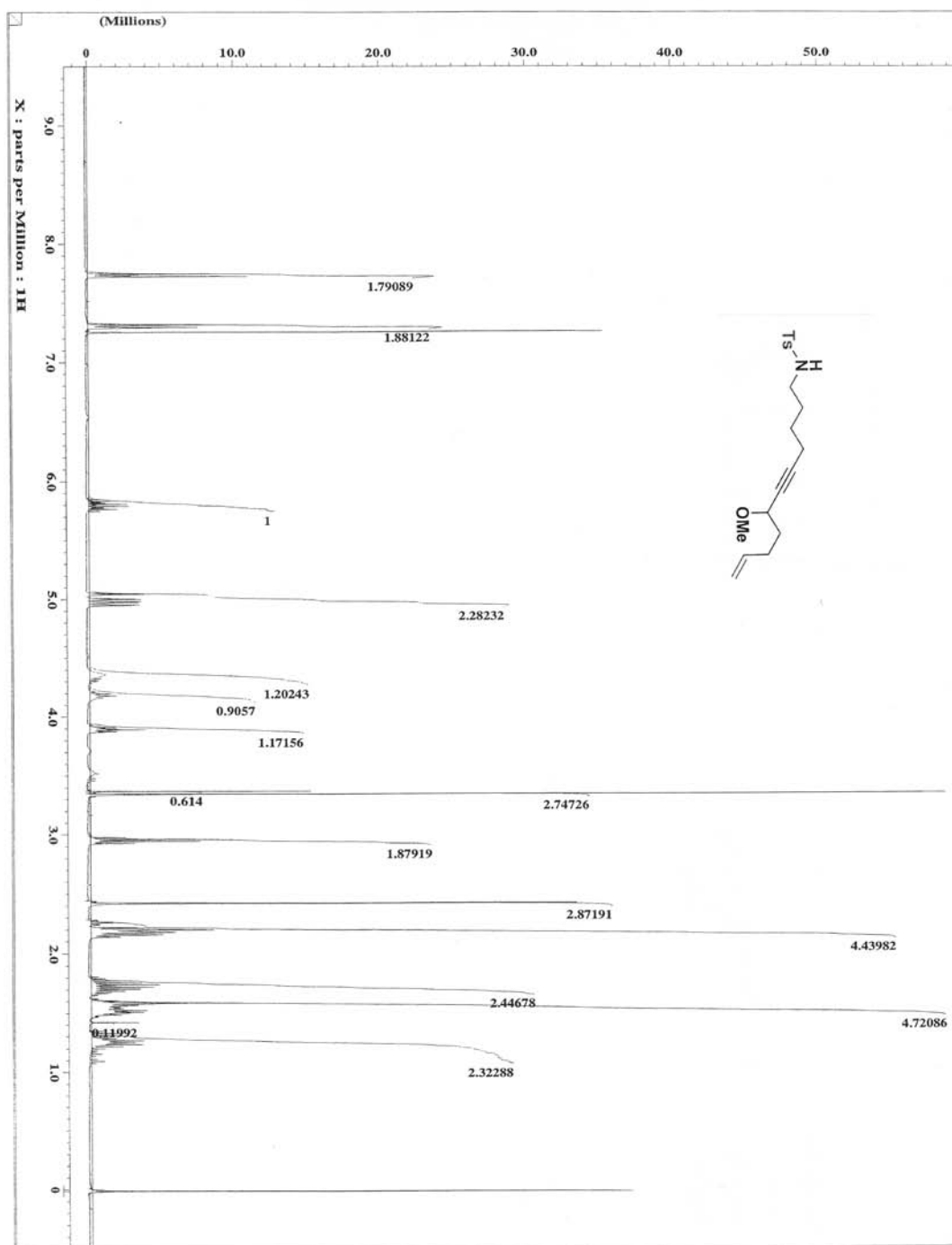
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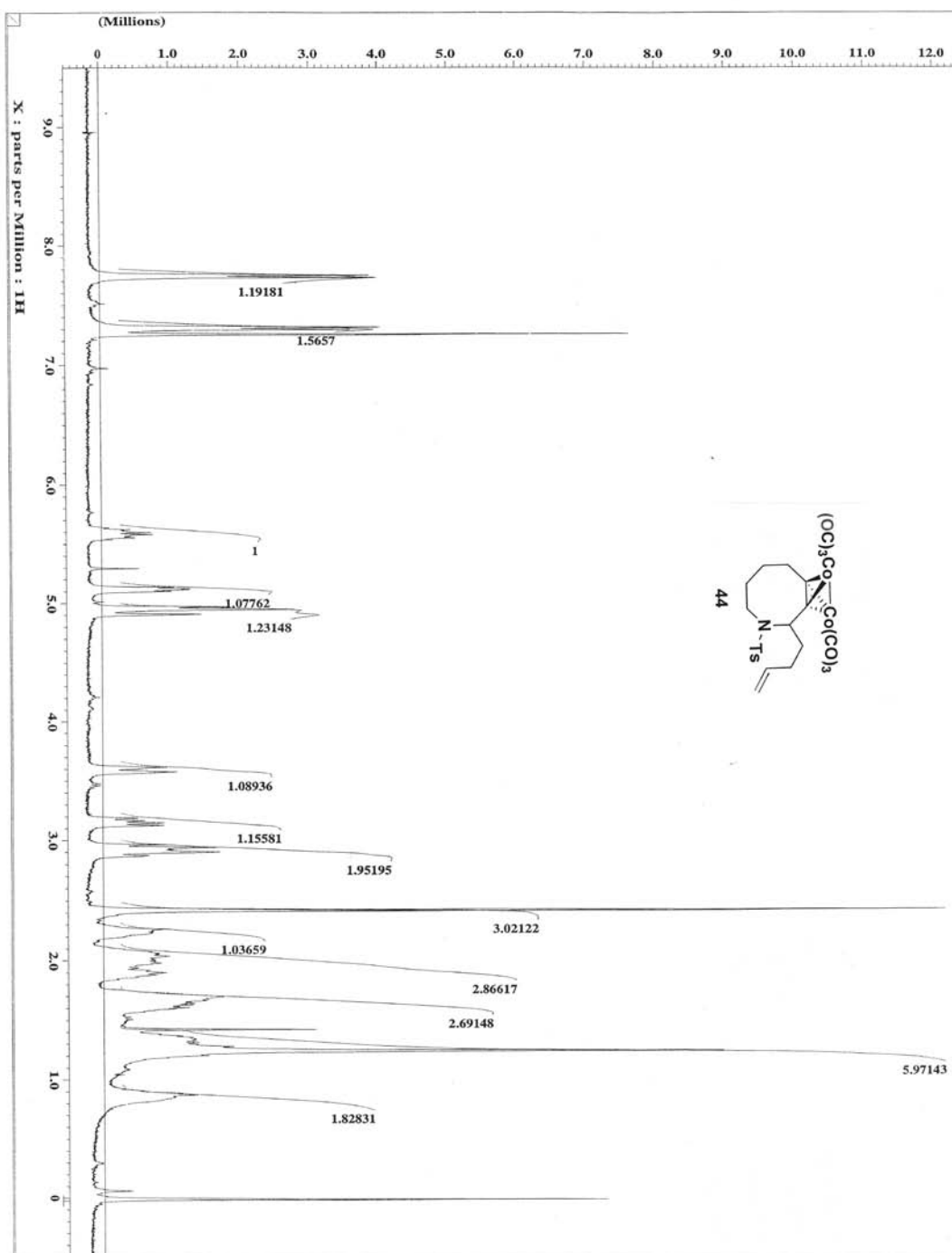
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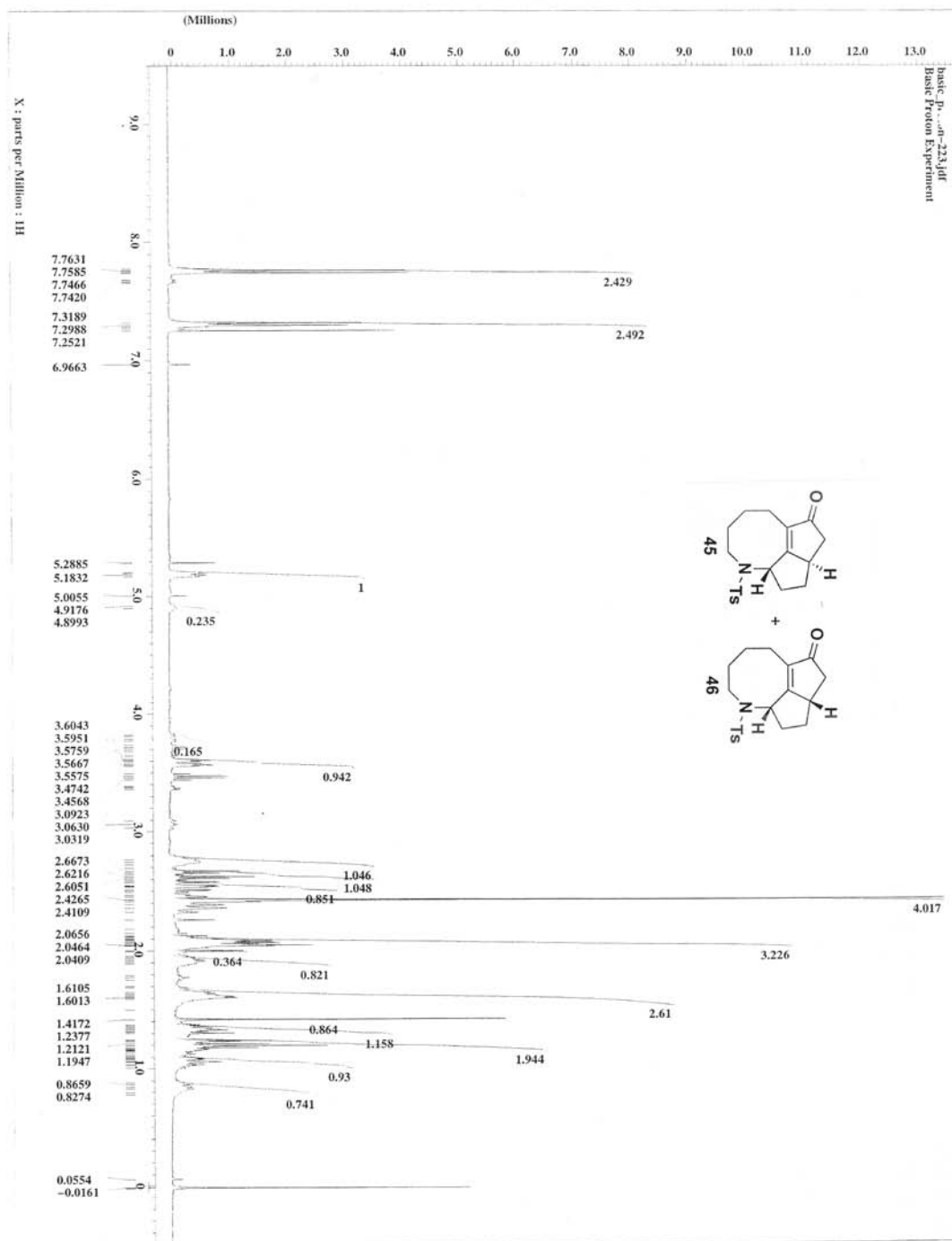
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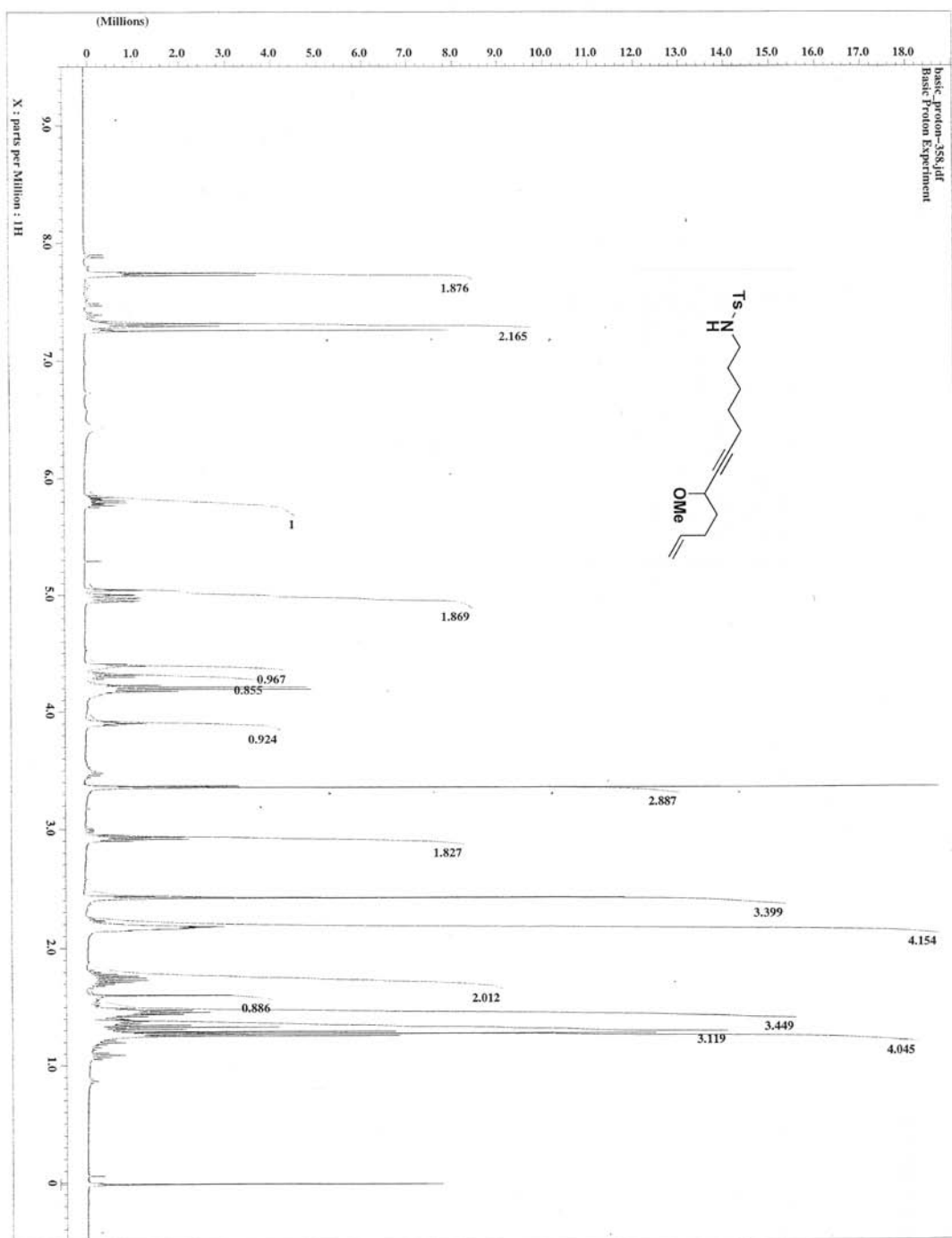
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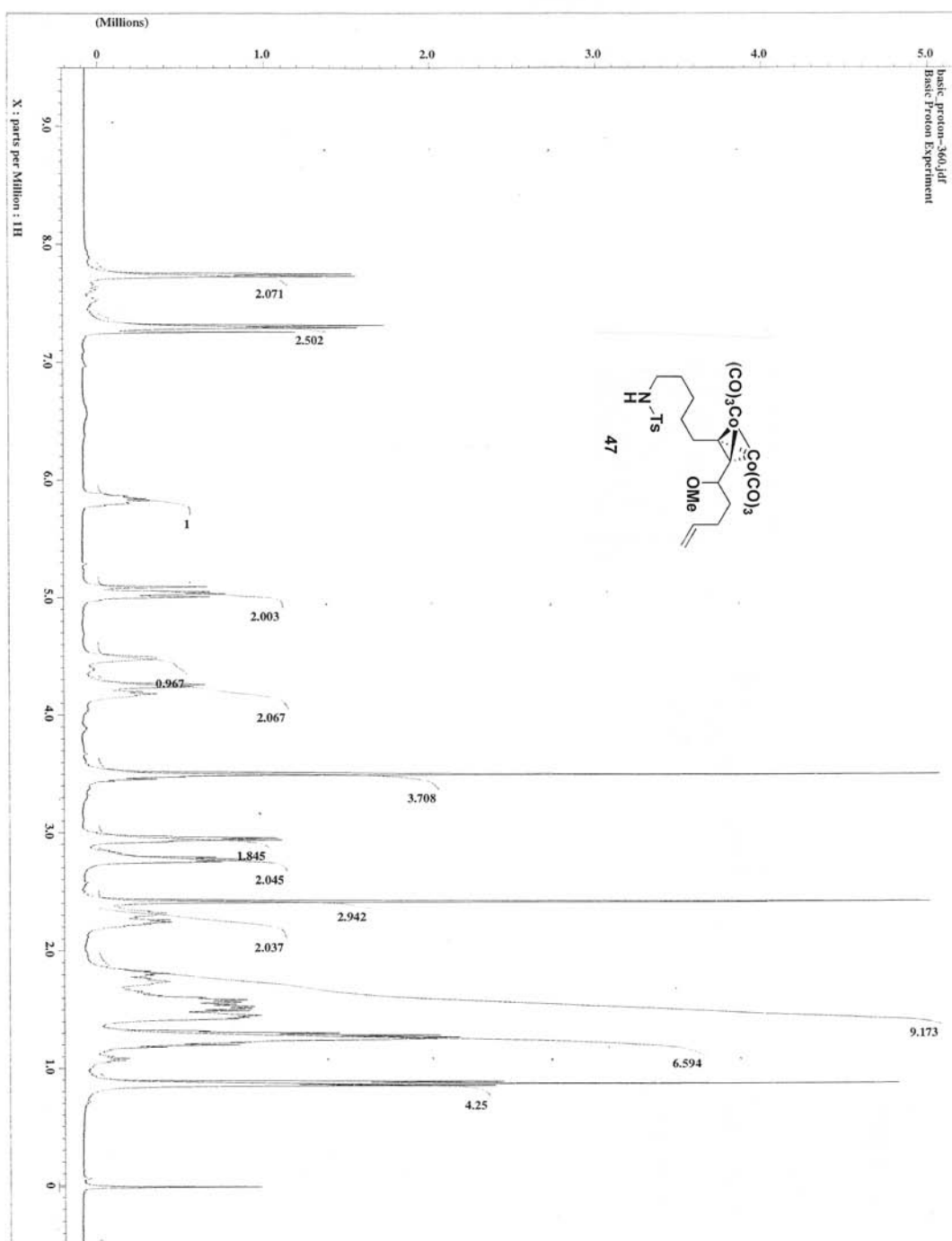
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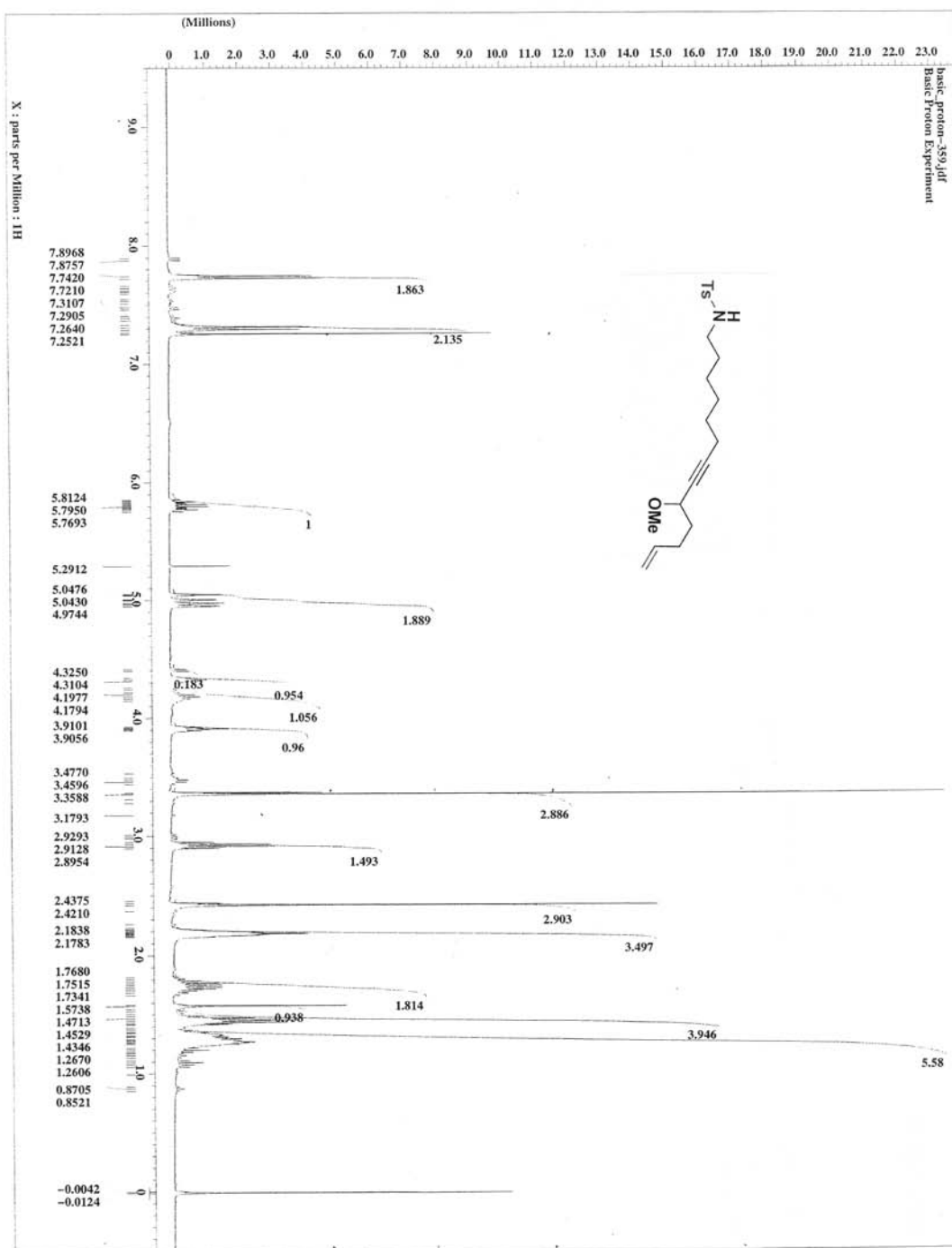
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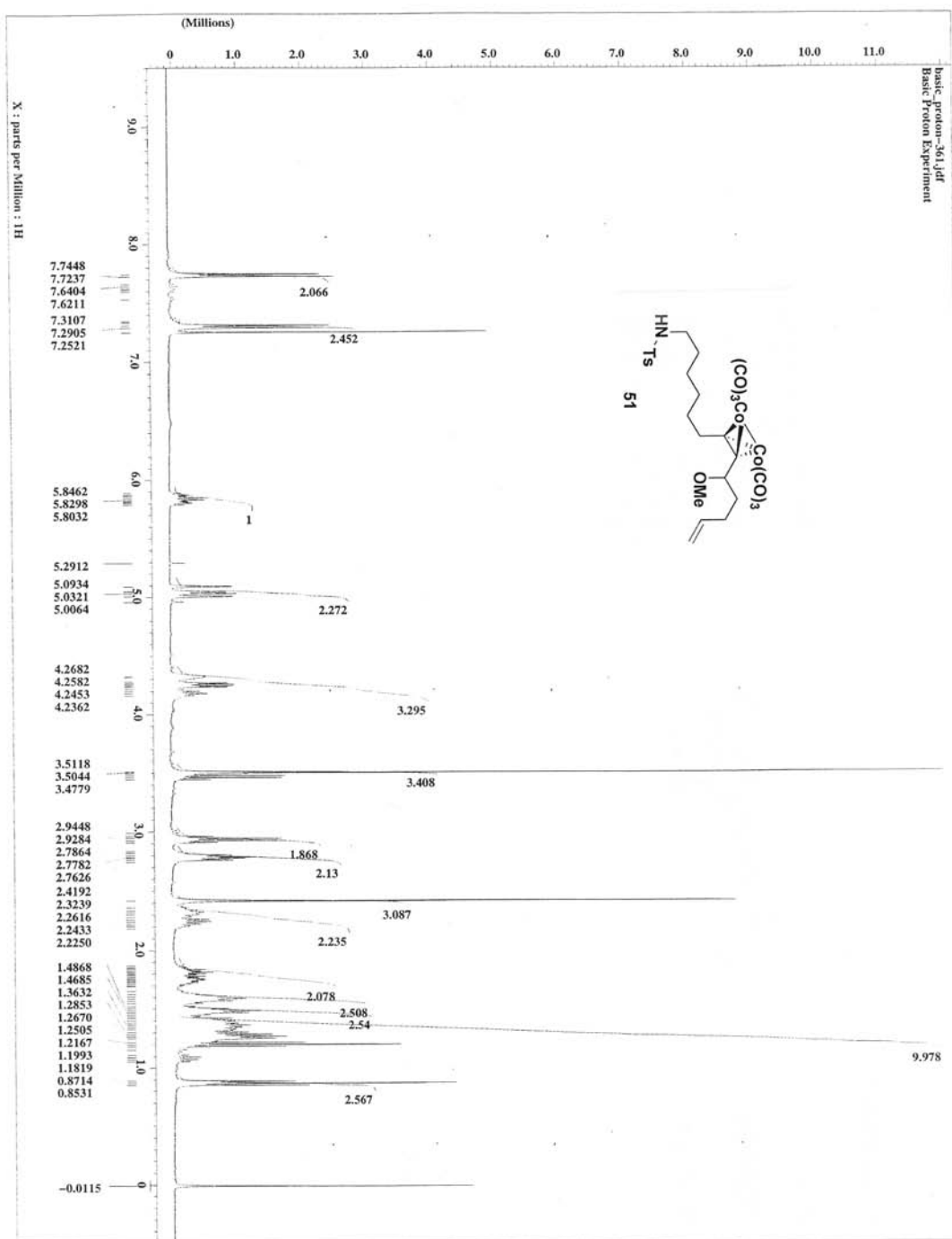
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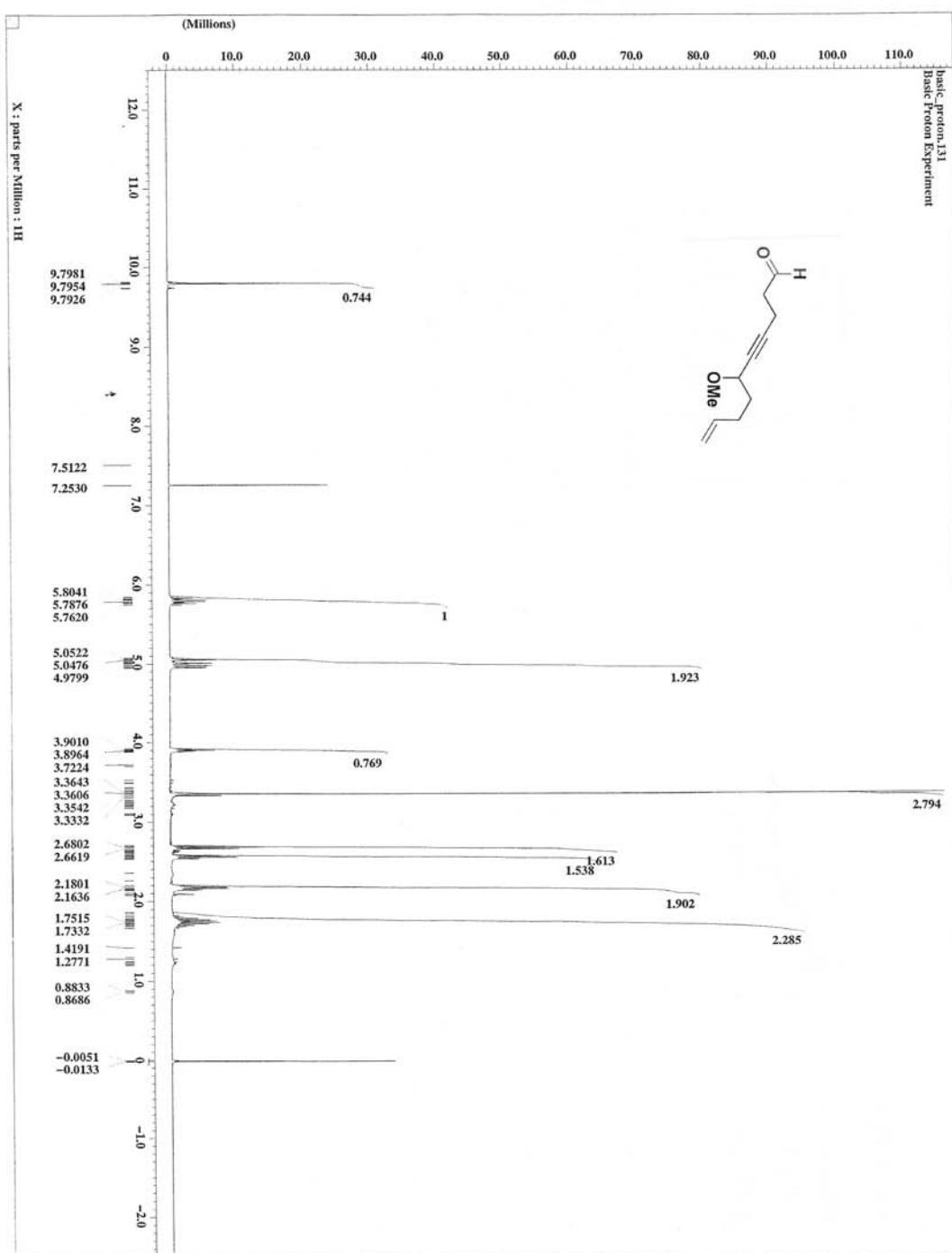
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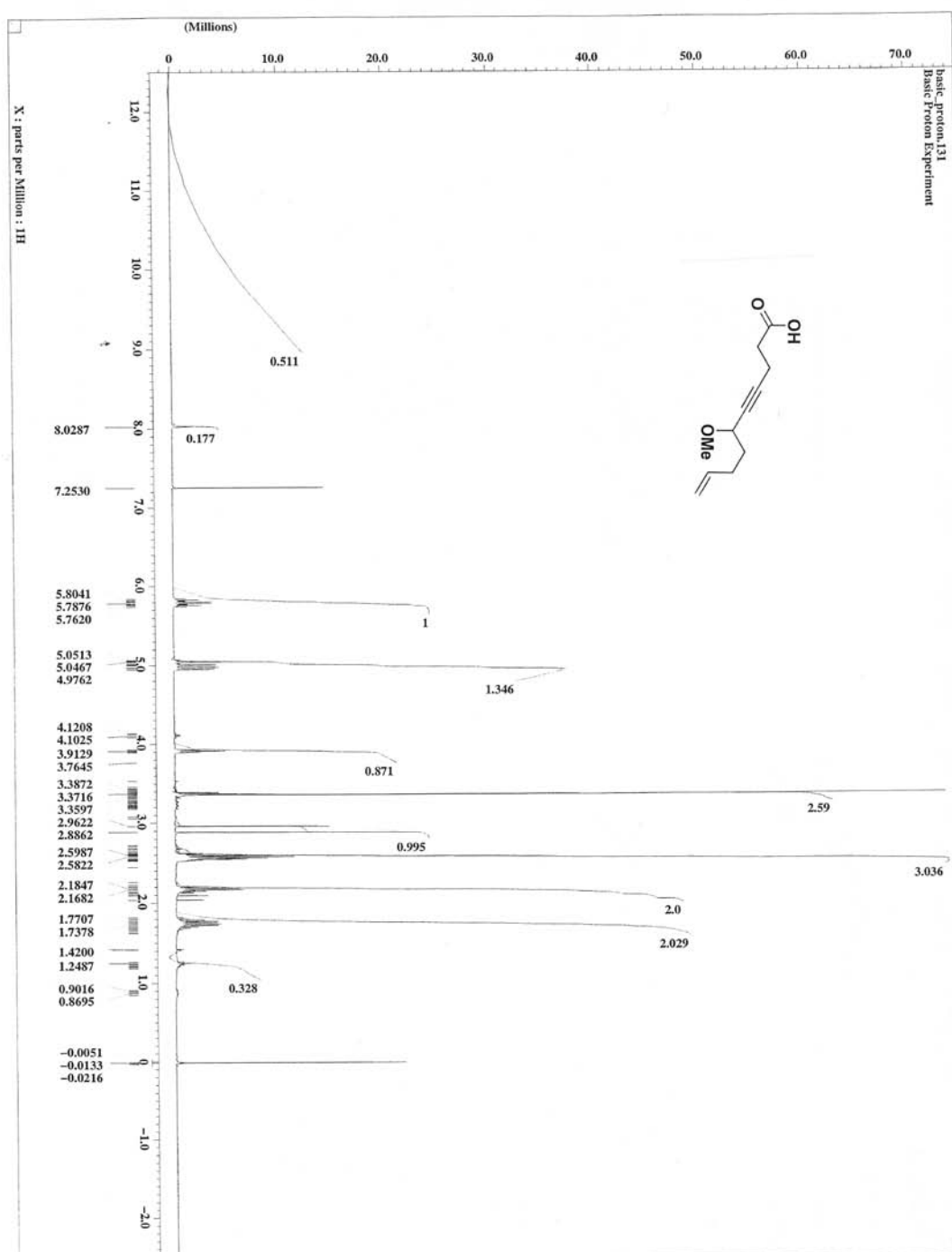
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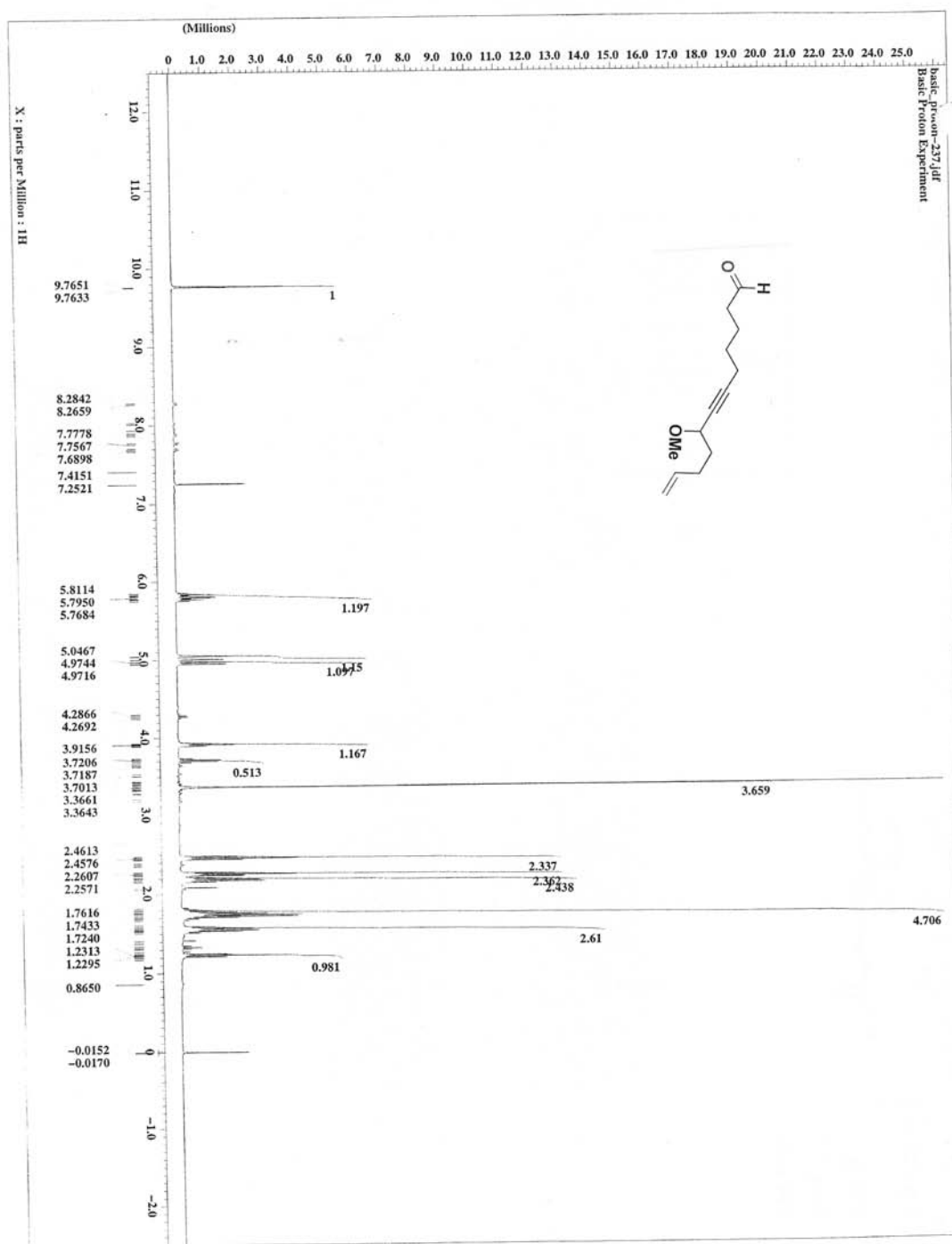
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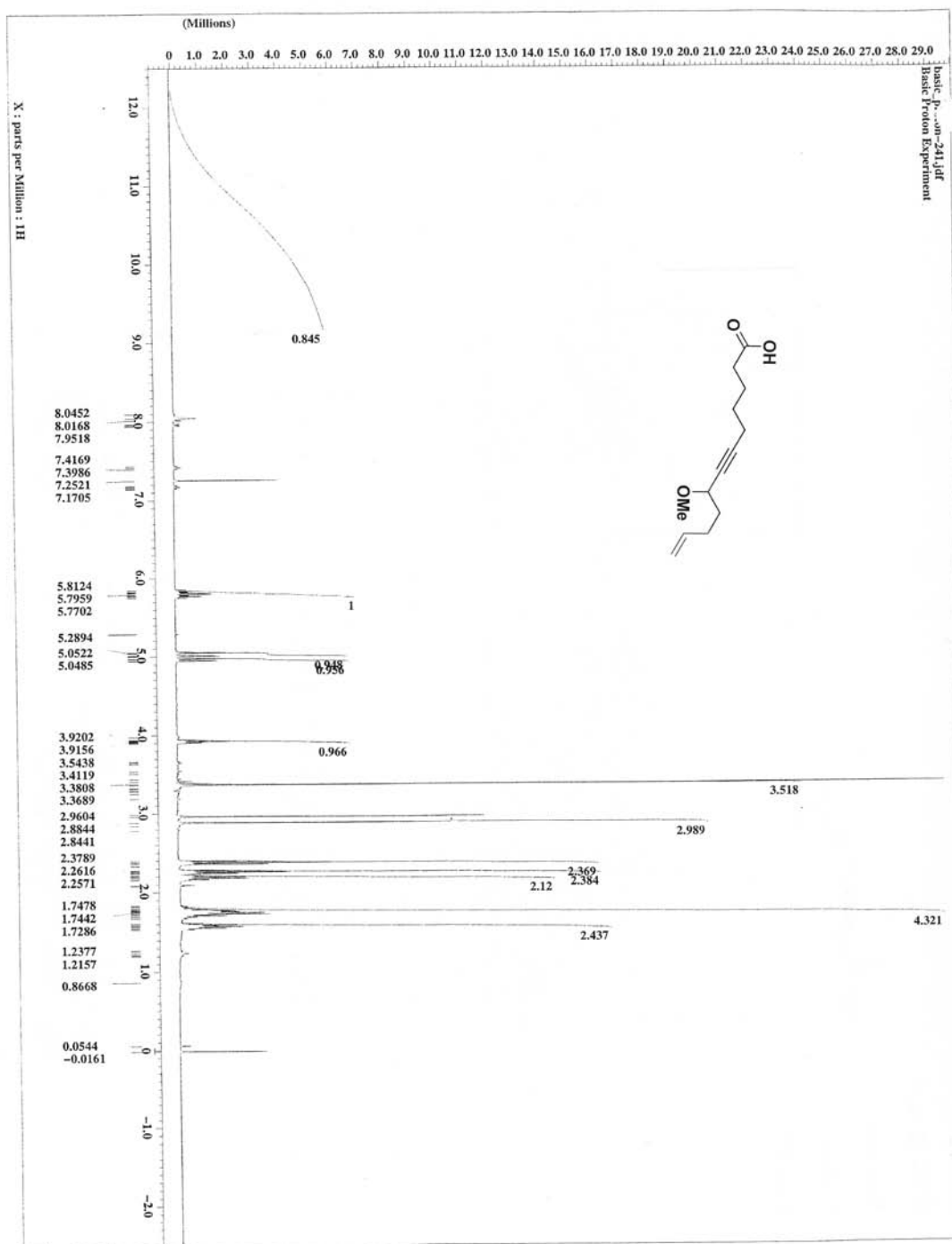
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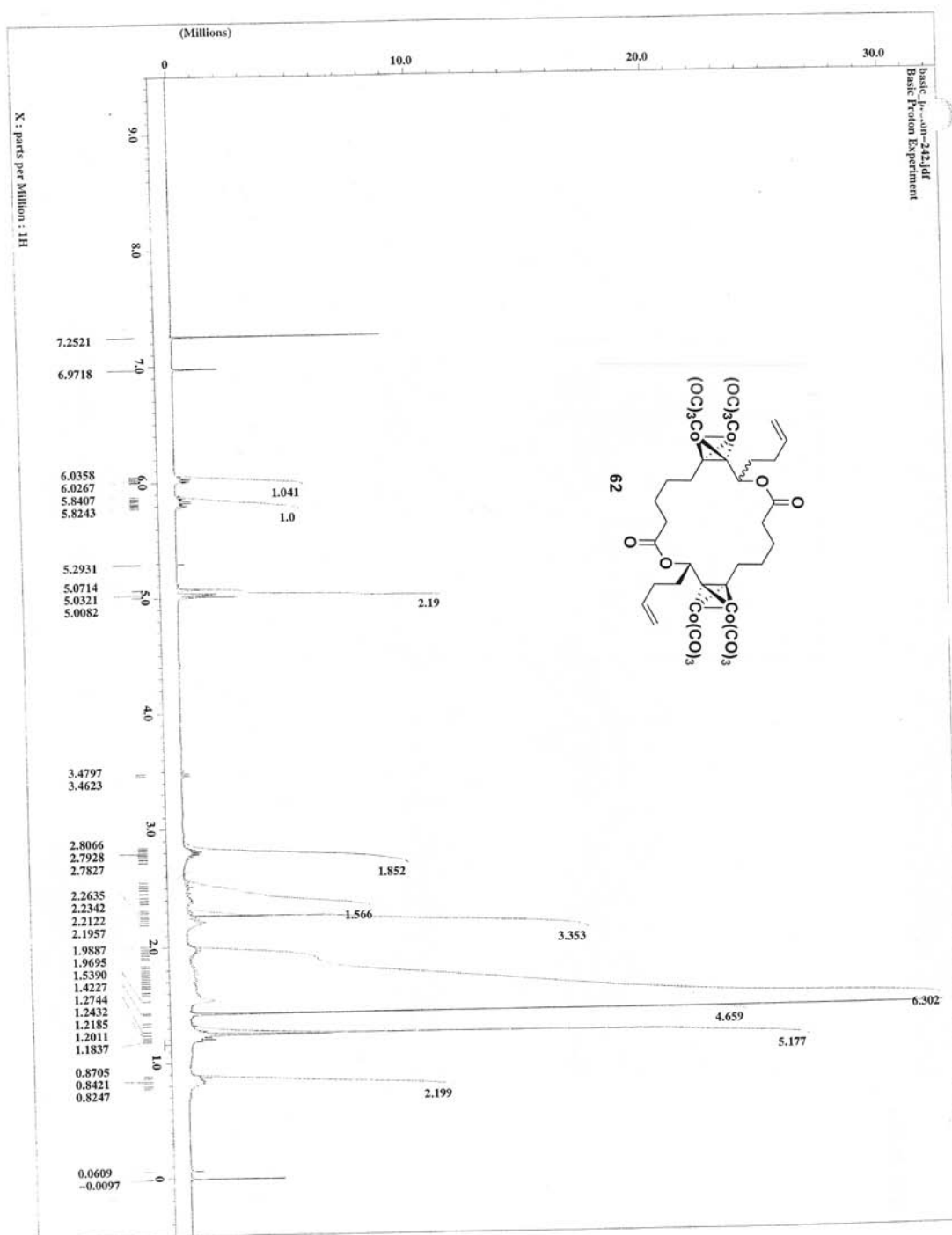
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Spectrometer Frequency: 400 MHz
Solvent: CDCl₃



Spectrometer Frequency: 400 MHz
Solvent: CDCl₃



Spectrometer Frequency: 400 MHz
Solvent: CDCl₃

References.

- ¹ An additional 1.36 g of product was collected that was 50% pure by ¹H NMR for an approximate yield of 70%.
- ² Compound **33** is a mixture of diastereomers; thus, the ¹³C peaks appear split and there are many in this range.
- ³ a) Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4353-4363. b) Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 5505-5506.
- ⁴ Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289-5292.
- ⁵ Sugihara, T.; Yamada, M.; Ban, H.; Yamaguchi, M.; Kaneko, C. *Angew. Chem. Int. Ed.* **1997**, *36*, 2801-2804.
- ⁶ NMR data for cis isomer **46** only.
- ⁷ Bach, T.; Kather, K. *J. Org. Chem.* **1996**, *61*, 7642-7643.
- ⁸ Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277-7287.
- ⁹ Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031-1034.