A Highly Stereoselective TMSOTf-Mediated Catalytic Carbocupration of Alkynoates

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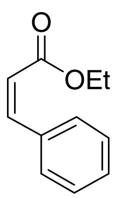
Experimental Section

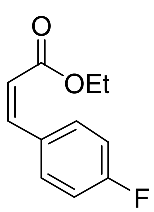
All of the reactions were performed under Ar in flame-dried glassware. Anhydrous tetrahydrofuran (THF) was obtained from a commercial source and used without purification. Copper(I) iodide (98% purity) and lithium chloride (LiCl, 99%+, ACS) were obtained from Aldrich and used without any purification. The NMR spectra were recorded with either a 360 or 500 MHz Bruker spectrometer. ^{1}H NMR spectra were obtained using $CDCl_3$ as the solvent with either tetramethylsilane (TMS: δ = 0 ppm) or chloroform ($CHCl_3$: δ = 7.26 ppm) as the internal standard. Column chromatography was performed using 60-200 μm silica gel. Analytical thin layer chromatography was performed on silica coated glass plates with F-254 indicator. Visualization was accomplished by UV light (254 nm) and $KMnO_4$.

General Experimental Procedure for the TMSOTf-Promoted Catalytic Carbocupration of 1a with PhMgBr: CuI (0.029 g, 0.15 mmol) and LiCl (0.013 g, 0.30 mmol) was placed in a 100 mL round bottom flask (flame dried under vacuum) under Ar. Dry THF (20 mL) was added to the salts, and the mixture was stirred at room temperature for a period of 0.5 h until complete dissolution had occurred. The clear, light yellow homogeneous solution was cooled to –78 °C, and **1a** (0.294 g, 3.0 mmol) was added, followed by TMSOTf (1.05 eq., 0.57 mL, 3.15 mmol). After 5 minutes at –78 °C, phenylmagnesium bromide (1.2 eq., 1.2 mL, 3.6 mmol) was added dropwise with a syringe, and the solution was stirred at –78 °C for 1 h. Trifluoroacetic acid (1.2 eq., 0.5 mL, 3.6 mmol) was added to quench the reaction at –78 °C, and the mixture was allowed to warm to room temperature and stir for 30 min. The product was extracted with sat. $NaHCO_3$, Et_2O (3 X 25 mL), and the combined organic layers were washed with deionized water followed by saturated NH_4Cl. The organic layer was separated, dried with $MgSO_4$, and concentrated in vacuo to give the crude product, which was then analyzed by ^{1}H NMR spectroscopy to determine diastereoselectivity. Column chromatography of the crude material (10% ethyl acetate in hexanes) afforded a 91% yield of the pure cinnamate product.

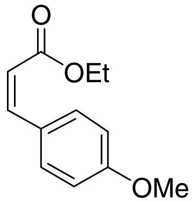
Tabulated ^{1}H NMR



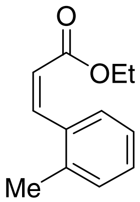
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.36 (m, 5H), 6.95 (d, *J*=12.7 Hz, 1H), 5.96 (d, *J*=12.7 Hz, 1H), 4.16 (q, *J*=7.3 Hz, 2H), 1.20 (t, *J*=7.3 Hz, 3H)[1]



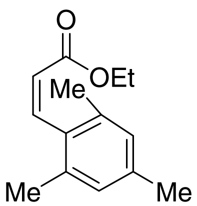
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.68 (dd, *J*=8.8, 2.9 Hz, 2H), 7.08 (dd, *J*=8.8, 8.4 Hz, 2H) 6.93 (d, *J*=12.5 Hz, 1H), 5.96 (d, *J*=12.5 Hz, 1H), 4.19 (q, *J*=7.0 Hz, 2H), 1.30 (t, *J*=7.0 Hz, 3H)[2] ^{13}C NMR (125 MHz, $CDCl_3$) 164.9 (d, *J*=249.3 Hz), 161.9, 142.0, 132.0 (d, *J*=8.8 Hz), 130.8 (d, *J*=2.8 Hz), 119.5, 114.9 (d, *J*=21.0 Hz), 60.2, 14.0[2] IR: 2983, 2361, 1719, 1601, 1509, 1159, 1031, 853 cm^{-1} HRMS (EI) calculated for $C_{11}H_{11}FO_2$ (M+): 194.0743, found: 194.0745.



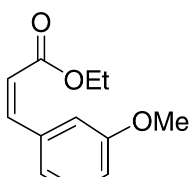
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.69 (d, *J*=8.8 Hz, 2H), 6.88 (d, *J*=8.8 Hz, 2H) 6.84 (d, *J*=12.5 Hz, 1H), 5.82 (d, *J*=12.5 Hz, 1H), 4.19 (q, *J*=7.0 Hz, 2H), 3.82 (s, 3H) 1.26 (t, *J*=7.0 Hz, 3H)[3]



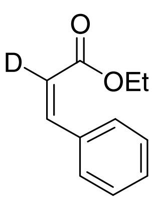
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.36 (m, 4H), 7.18 (d, *J*=12.3 Hz, 1H), 6.12 (d, *J*=12.3 Hz, 1H), 4.19 (q, *J*=7.3 Hz, 2H), 2.35 (s, 3H) 1.21 (t, *J*=7.3 Hz, 3H)[4]



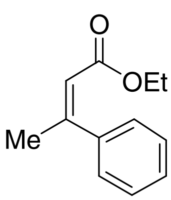
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.01 (d, *J*=11.8 Hz, 1H), 6.83 (s, 2H), 6.09 (d, *J*=11.8 Hz, 1H), 4.09 (q, *J*=7.3 Hz, 2H), 2.25 (s, 3H), 2.14 (s, 6H), 1.15 (t, *J*=7.3 Hz, 3H)[5]



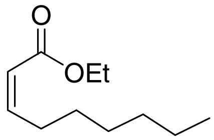
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.35 (m, 2H), 7.18 (m, 1H), 6.91 (d, *J*=12.5 Hz, 1H), 6.90 (m, 1H), 5.96 (d, *J*=12.5 Hz, 1H), 4.19 (q, *J*=7.0 Hz, 2H), 3.88 (s, 3H) 1.25 (t, *J*=7.0 Hz, 3H)[6]

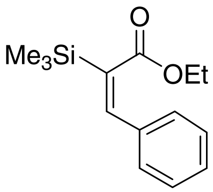


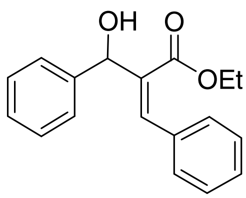
^{1}H NMR (360 MHz, $CDCl_3$) δ 7.38 (m, 5H), 6.93 (br s, 1H), 4.26 (q, *J*=7.3 Hz, 2H), 1.17 (t, J=7.3 Hz, 3H)[7]

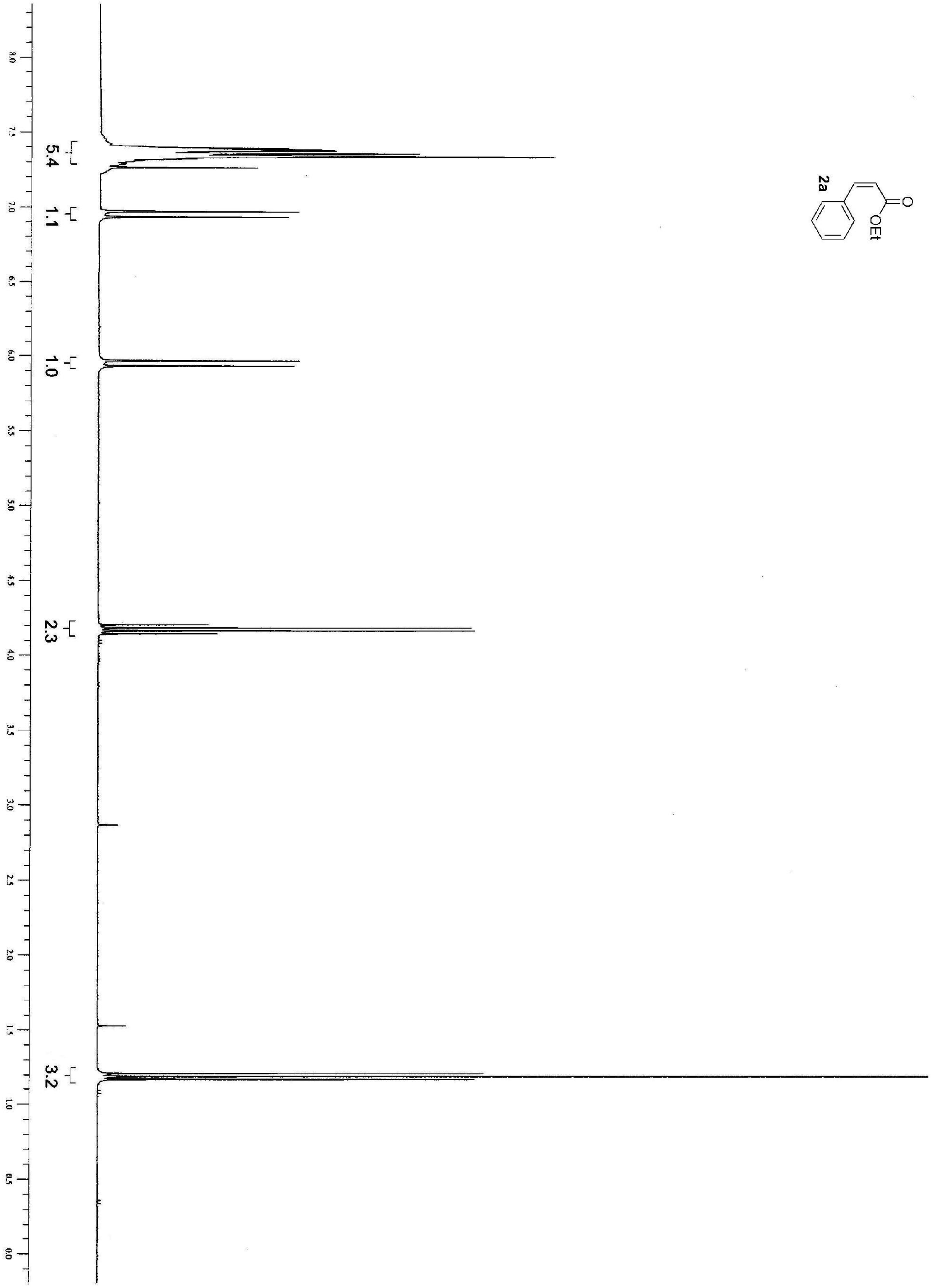


^{1}H NMR (360 MHz, $CDCl_3$) δ 7.40 (m, 4H), 7.26 (m, 1H), 5.95 (q, *J*=1.6 Hz, 1H), 4.25 (q, *J*=7.2Hz, 2H), 2.24 (d, *J*=1.6 Hz, 3H) 1.30 (t, *J*=7.2 Hz, 3H)[8]

 ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.35 (dt, *J*=11.5, 1.7, 1H), 5.77 (dt, *J*=11.6, 1.6, 1H), 4.16 (q, *J*=7.3 Hz, 2H), 2.61 (m, 2H), 1.46-1.33 (m, 8H), 1.30 (t, *J*=7.3 Hz, 3H), 0.96 (t, *J*=7.9 Hz, 3H)[9]

 ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.30 (m, 5H), 6.79 (s, 1H), 4.14 (q, *J*=7.3 Hz, 2H), 1.17 (t, *J*=7.3 Hz, 3H), 0.21 (s, 9H)[10]

 ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.35 (m, 10H), 7.01 (s, 1H), 5.66 (d, *J*=5.6 Hz, 1H), 4.08 (q, *J*=7.2 Hz, 2H), 3.20 (d, *J*=6.1 Hz, 1H), 1.04 (t, *J*=7.2 Hz, 3H)[11]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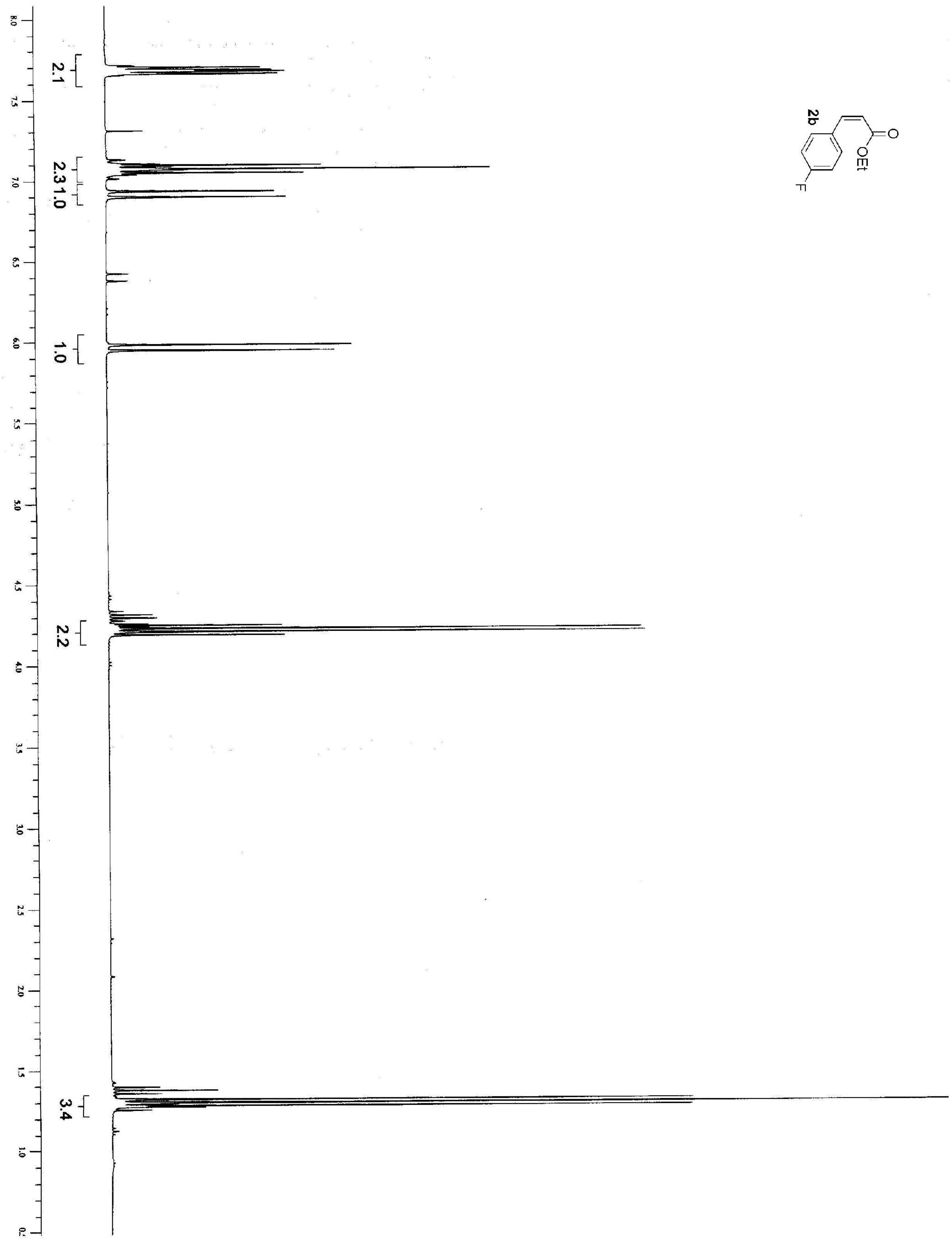
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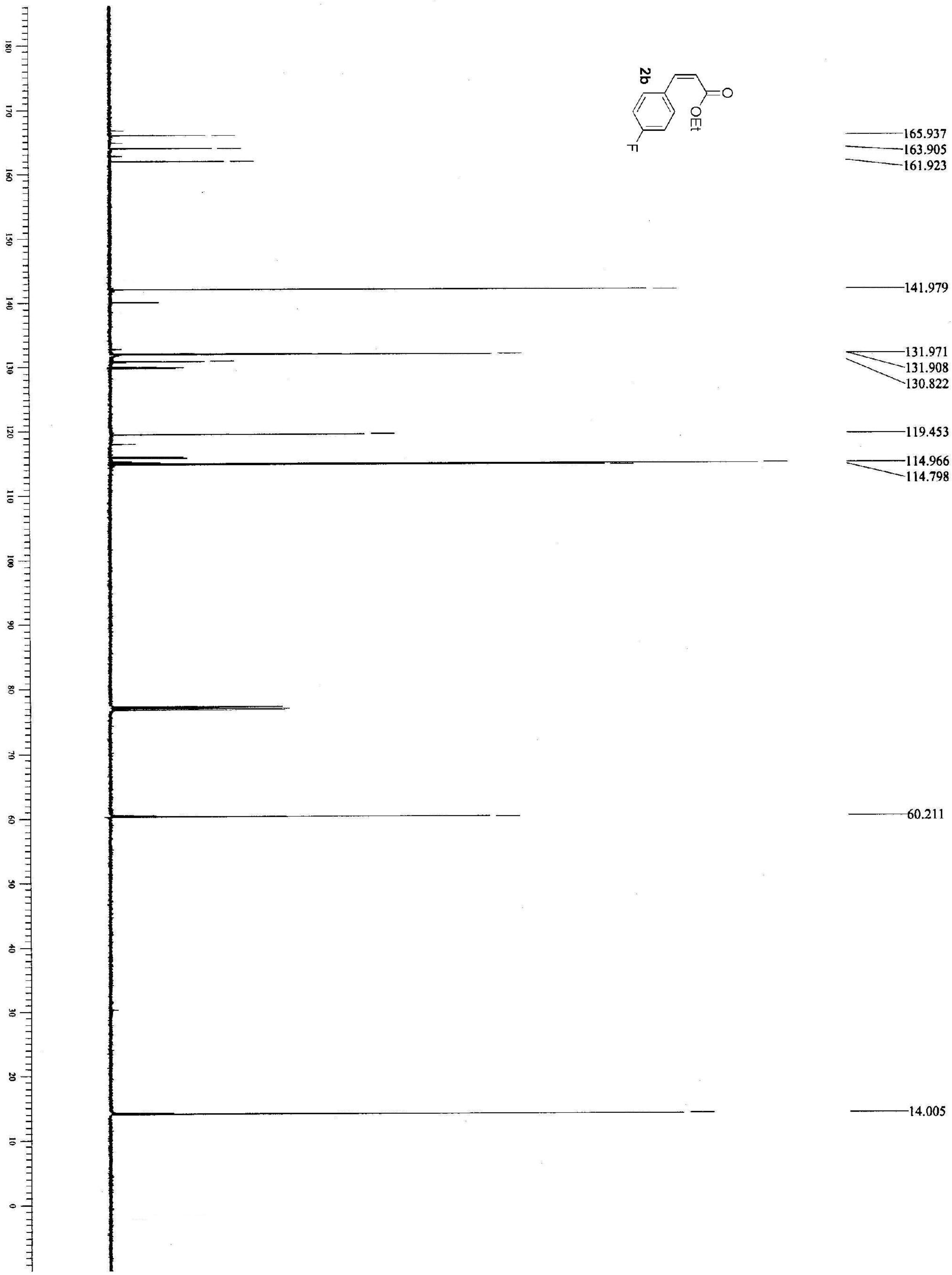
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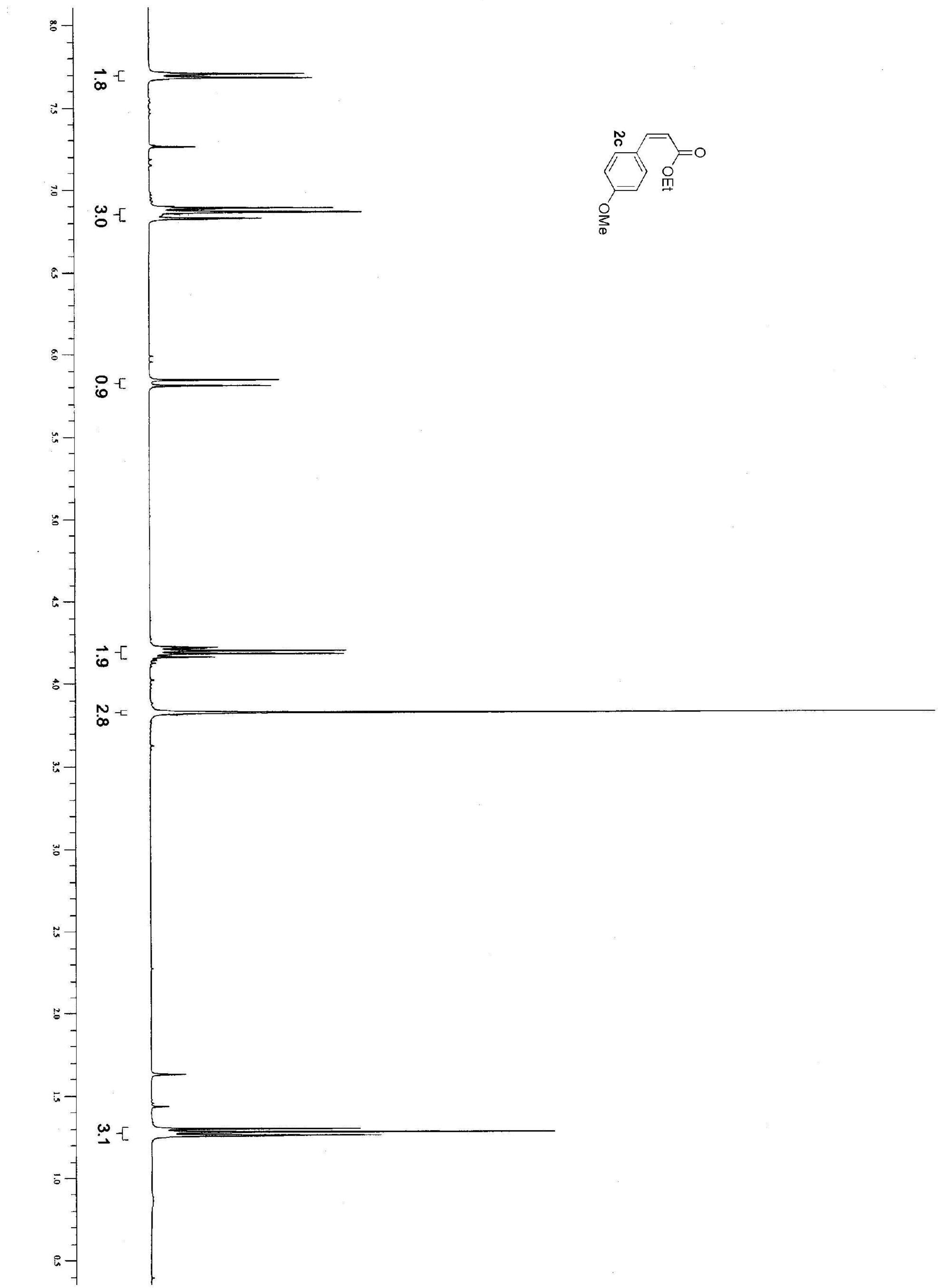
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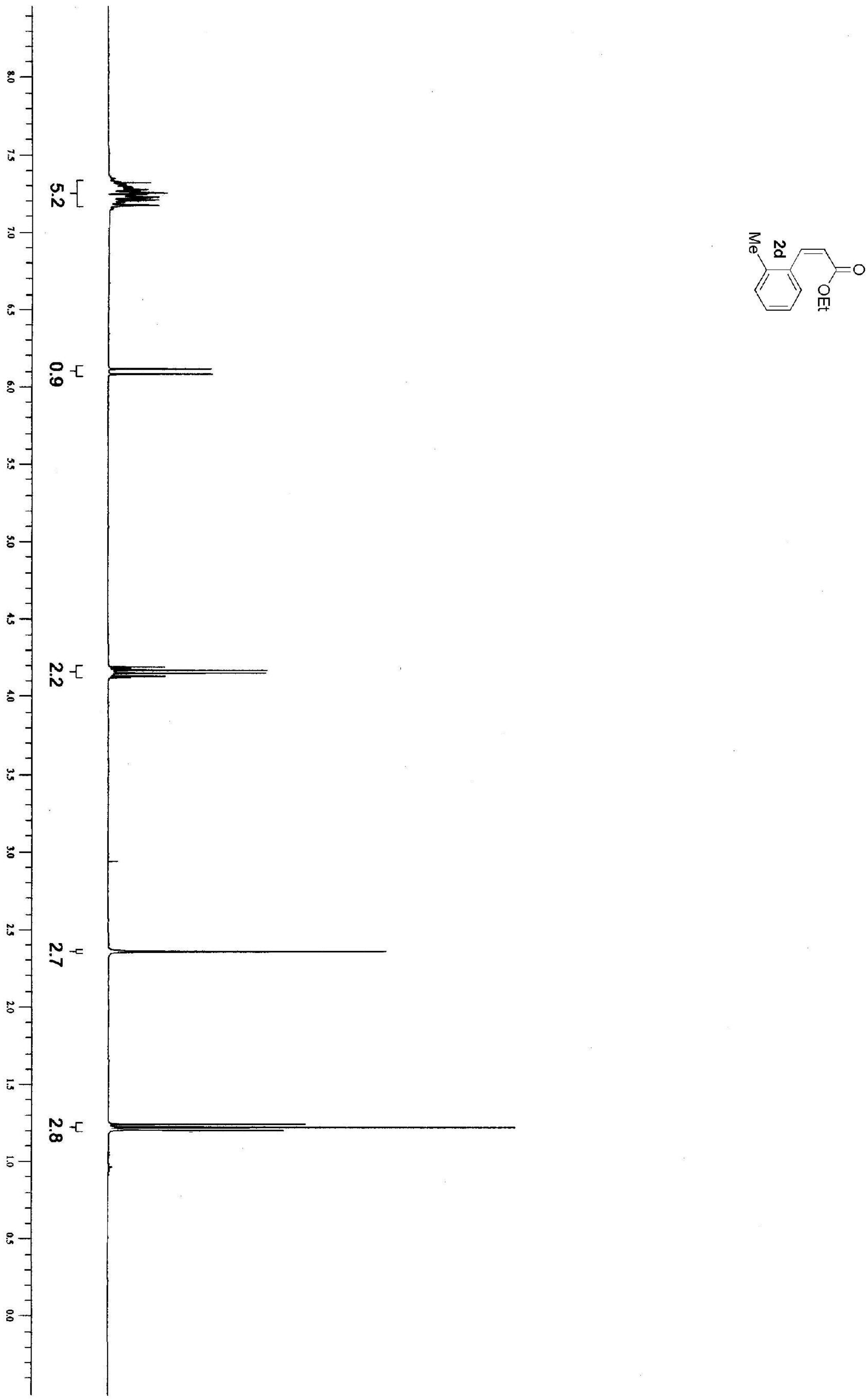
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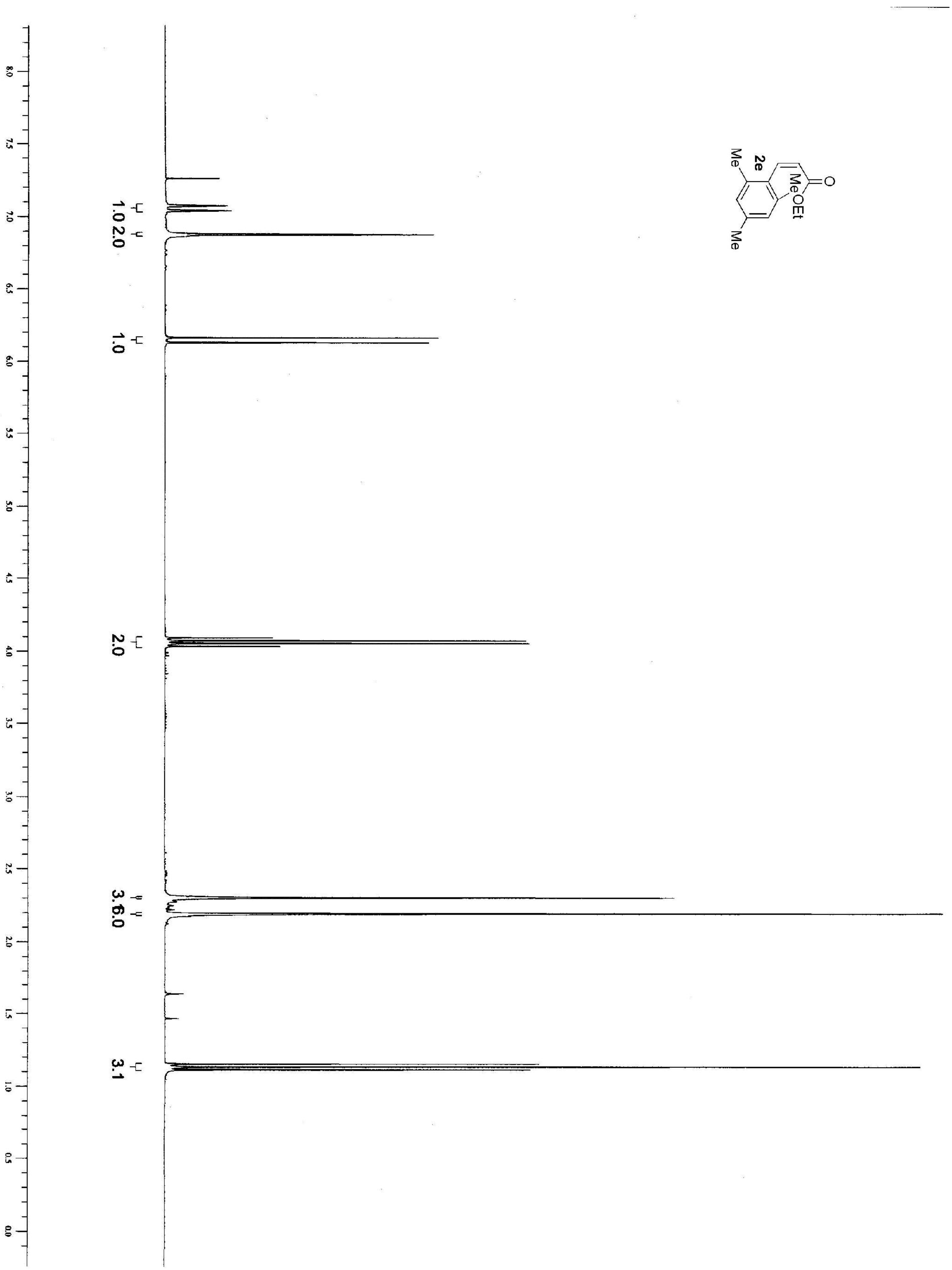
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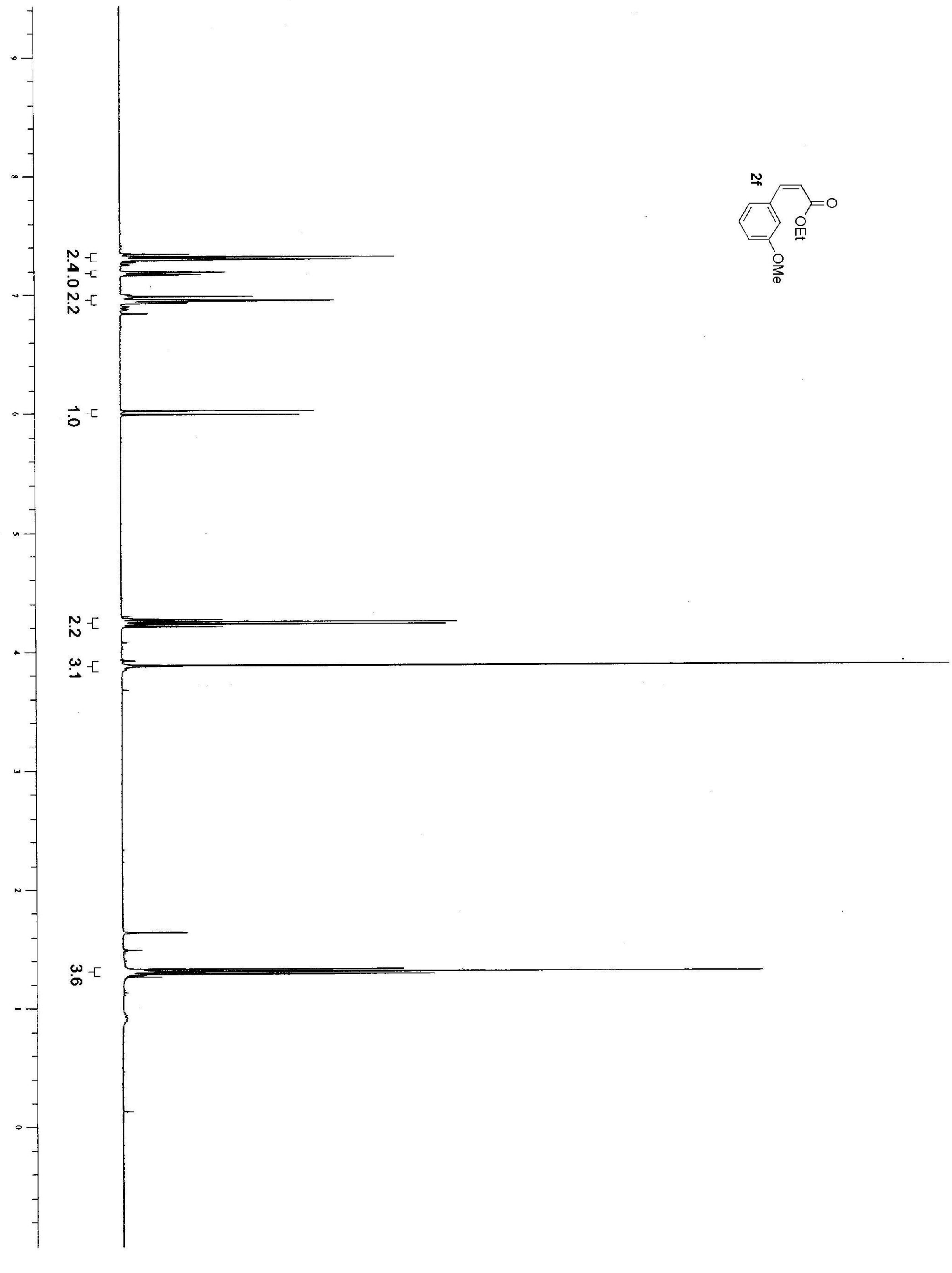
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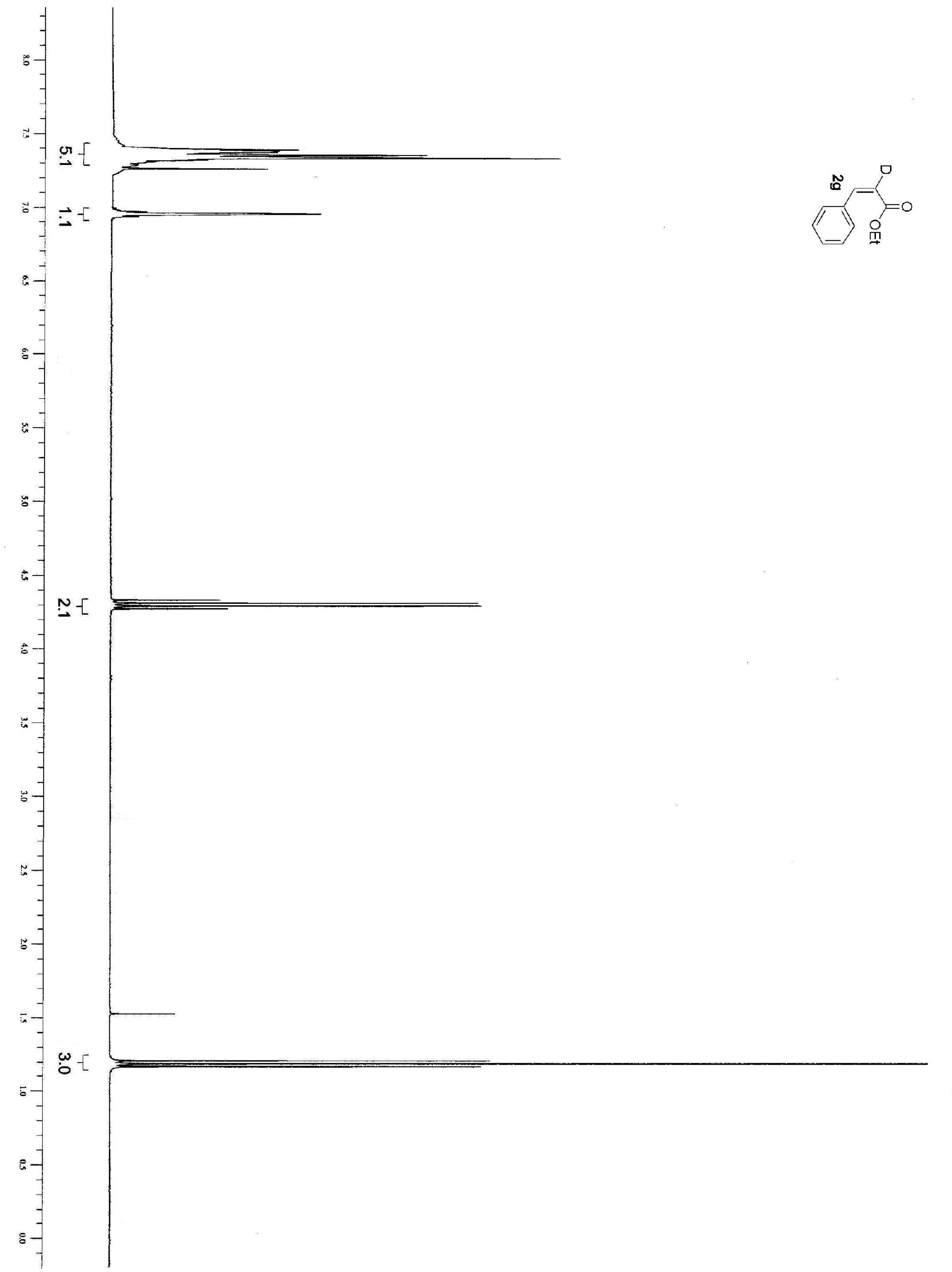

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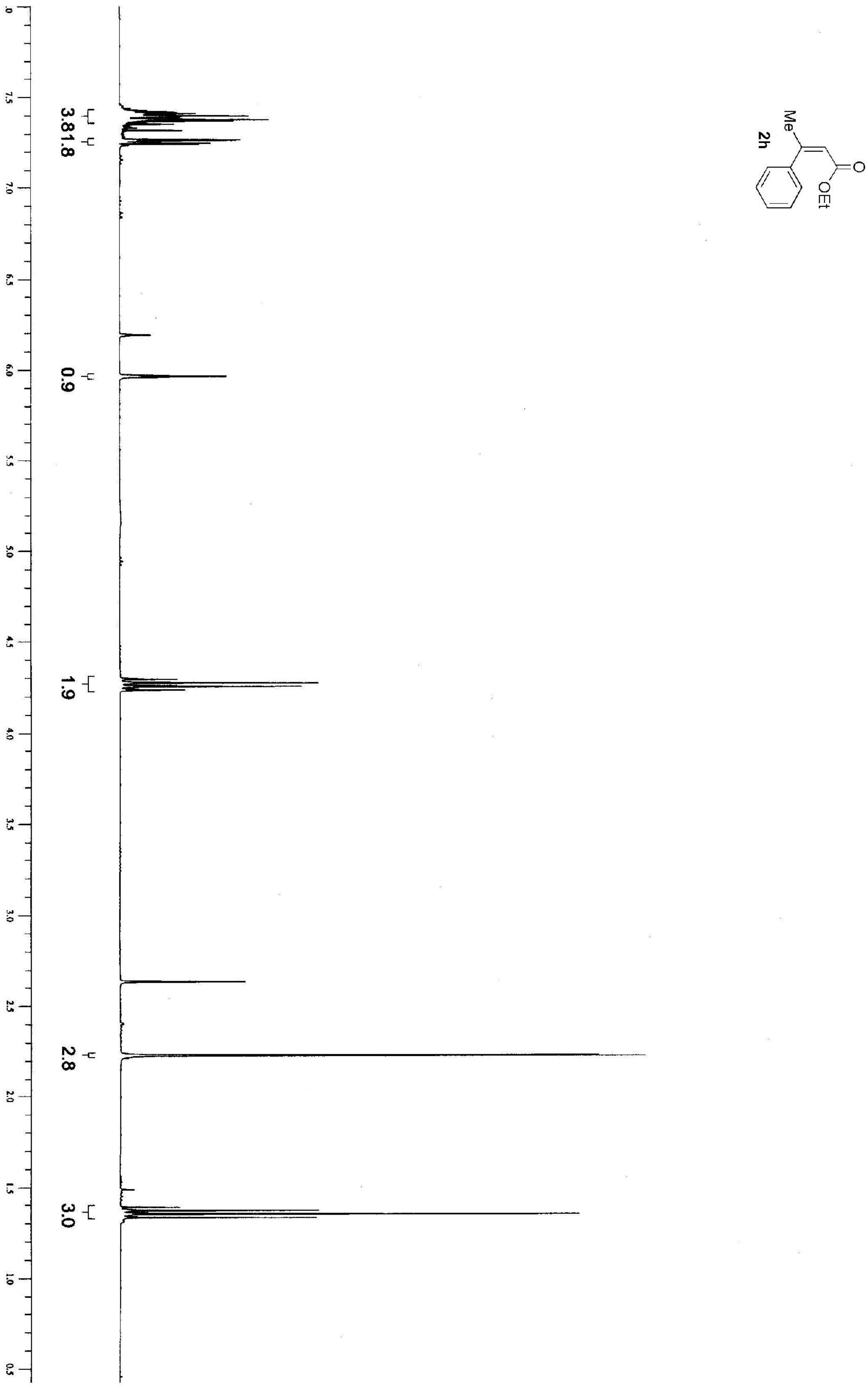

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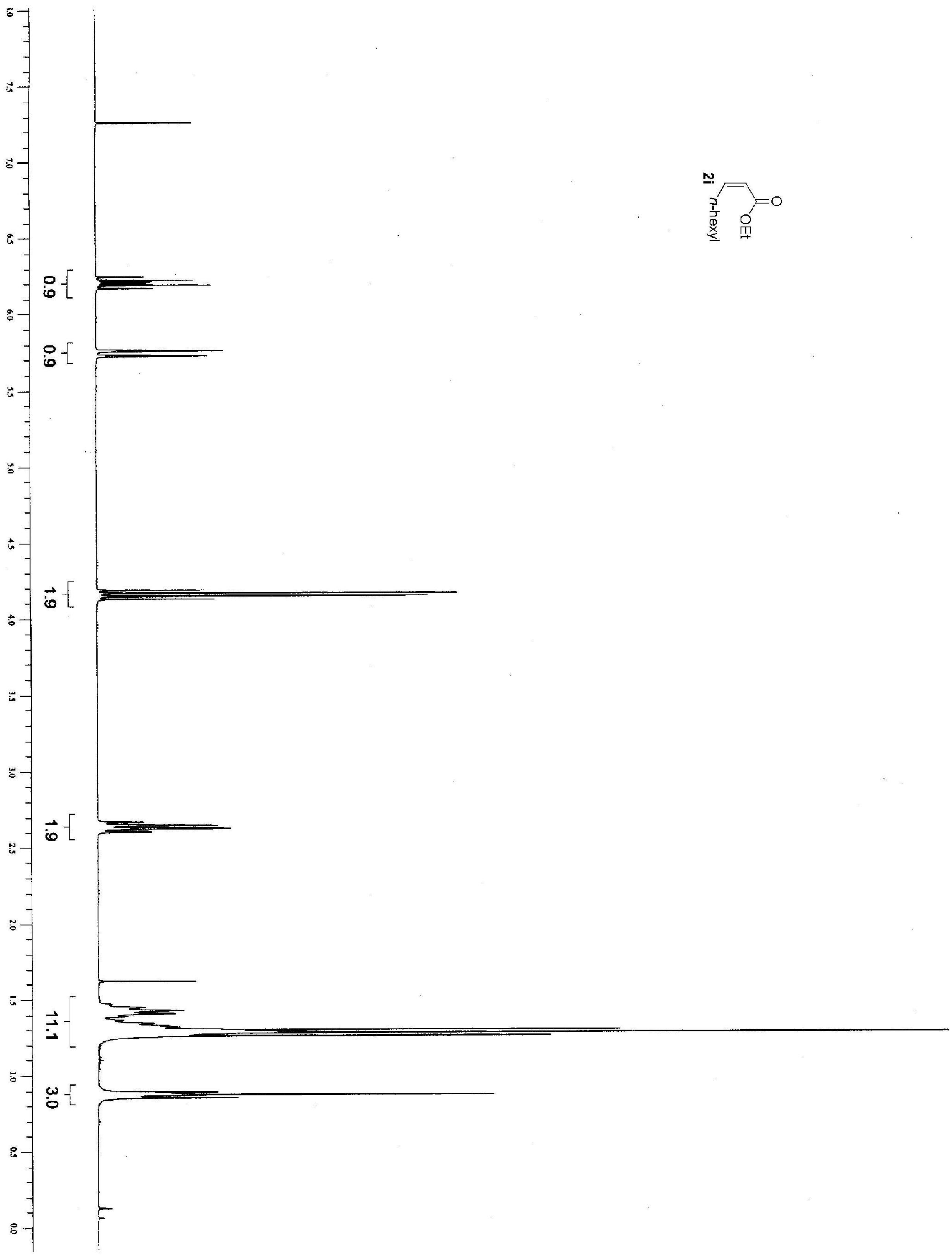
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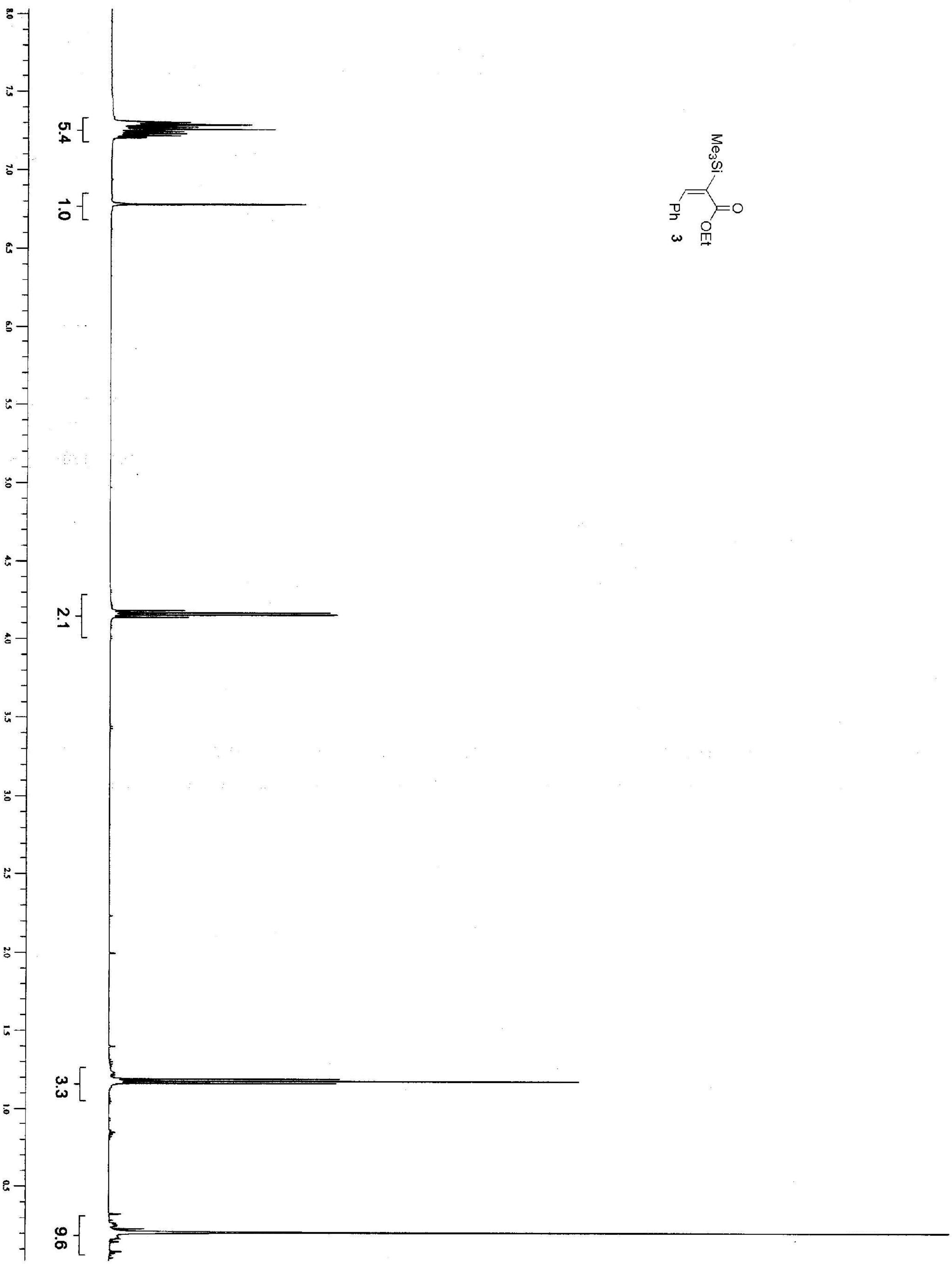
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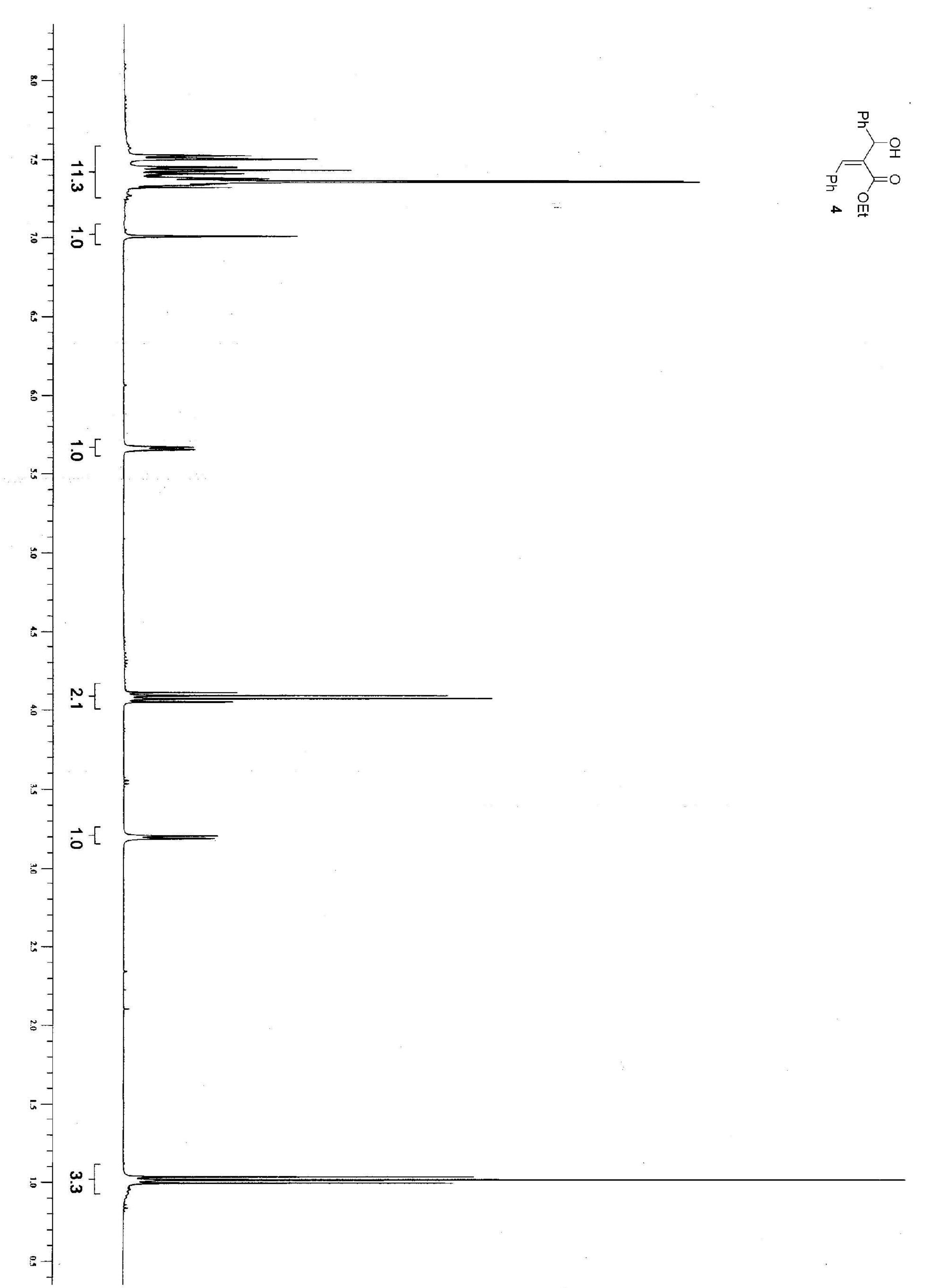

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6.0
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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

References:

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