Supporting Information to Accompany

Practical Synthesis of α-Aryl methyl ketones via a Transition-Metal free Meerwein Arylation

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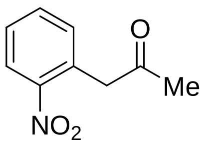
Table of contents

General Information. Unless otherwise noted, all reactions were performed under an oxygen-free atmosphere of nitrogen. All commercially available reagents were used without further purification. The diazonium tetrafluoroborate salts were either commercially available or prepared according to literature.[1] Liquid chromatography was performed using a forced flow (flash chromatography) of the indicated solvent system on silica gel (230-400 mesh).[2] ^{1}H and ^{13}C NMR spectra were recorded in deuterochloroform ($CDCl_3$), unless otherwise noted, on a 400 or 500 MHz instrument. Chemical shifts of ^{1}H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad) and coupling constant in hertz (Hz). Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77 ppm) on the δ scale. High Resolution mass spectra (HMRS) were performed on a high resolution magnetic sector mass spectrometer.

General procedure



2-nitrophenylacetone[3] **(2b)**: To a stirred solution of isopropenyl acetate (4.4 mL, 40 mmol) in acetone (13 mL) and water (7 mL) was added 0.1 mL of a solution of KOAc (200 mg, 2 mmol) in water (1 mL) followed by 2-nitrobenzenediazonium tetrafluoroborate (474 mg, 2 mmol). Then, the rest of the aqueous KOAc solution was added dropwise over 2 hours and stirred overnight. The reaction mixture was diluted with MTBE and water and the layers were separated. The aqueous layer was back-extracted with MTBE. The combined organic extracts were washed with aqueous saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude mixture purified by column chromatography on silica gel with Hexane:EtOAc (3:1) to provide 244 mg (76%) of **2b**.[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (1 H, d, *J* = 8.0 Hz), 7.61 (1 H, t, *J* = 7.0 Hz), 7.48 (1 H, t, *J* = 7.3 Hz), 7.30 (1 H, d, *J* = 7.6 Hz), 4.14 (s, 2 H), 2.34 (s, 3 H).

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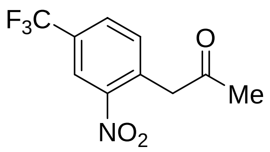
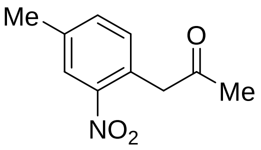
[1] Doyle, M. P.; Bryker, W. J. *J. Org. Chem.* **1979**, *44*, 1572.

[2] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

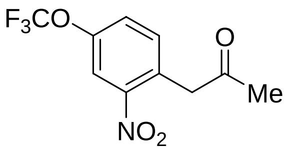
[3] Strazzolini, P.; Giumanini, A. G.; Runcio, A.; Scuccato, M. *J. Org. Chem.* **1998**, *63*, 952.



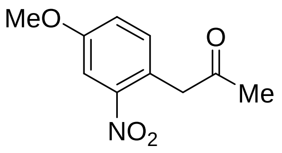
2-Nitro-4-trifluoromethylphenylacetone[4] (**2c**): The general procedure was followed. Isolated 286 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1 H, s), 7.85 (1 H, d, J = 7.6 Hz), 7.46 (1 H, d, J = 7.8 Hz), 4.25 (2 H, s), 2.36 (3 H, s).



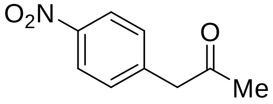
2-Nitro-4-methylphenylacetone (**2d**): The general procedure was followed. Isolated 205 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (1 H, s), 7.43 (1 H, d, *J* = 7.7 Hz), 7.18 (1 H, d, *J* = 7.7 Hz), 4.10 (2 H, s), 2.47 (3 H, s), 2.35 (3 H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 148.4, 138.9, 134.4, 133.3, 127.4, 125.6, 48.2, 29.9, 20.82; HRMS ESI (*m* / *z*): $[M + H]^+$ calcd for $C_{10}H_{12}O_3N$, 194.0810; found 194.0811.



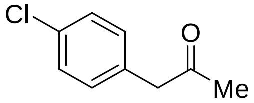
2-Nitro-4-trifluoromethoxyphenylacetone[5] (**2e**): The general procedure was followed. Isolated 162 mg (34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (1 H, d, *J* = 9.6 Hz), 7.49 (1 H, d, *J* = 8.4 Hz), 7.35 (1 H, d, *J* = 8.4 Hz), 4.17 (2 H, s), 2.35 (3 H, s).



2-Nitro-4-methoxyphenylacetone[6] (**2f**): The general procedure was followed. Isolated 50 mg (13%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (1 H, d, *J* = 2.4 Hz), 7.20-7.14 (2 H, m), 4.06 (2 H, s), 3.91 (3 H, s), 2.33 (3H, s).



4-Nitrophenylacetone[7] (**2a**): The general procedure was followed. Isolated 188 mg (58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (2 H, d, *J* = 8.5 Hz), 7.38 (2 H, d, *J* = 8.5 Hz), 3.87 (2 H, s), 2.26 (3 H, s).



4-Chlorophenylacetone[8] (**2g**): The general procedure was followed. Isolated 212 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ

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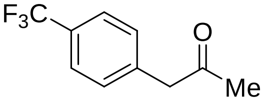
[4] Allais, A.; Meier, J.; Mathieu, J.; Nomine, G.; Peterfalvi, M.; Deraedt, R.; Chifflot, L.; Benzoni, J.; Fournex, R. *Eur. J. Med. Chem. Ther.* **1975**, *10*, 187.

[5] Wong, A.; Kuethe, J. T.; Davies, I. W. *J. Org. Chem.* **2003**, *68*, 9865.

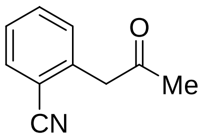
[6] Cardwell, K.; Hewitt, B.; Ladlow, M.; Magnus, P. *J. Am. Chem.* Soc. **1988**, *110,* 2242.

[7] Rafizadeh, K.; Yates, K. *J. Org. Chem.* **1984**, *49*, 1500.

7.33 (2 H, d, *J* = 8.3 Hz), 7.16 (2 H, d, *J* = 8.3 Hz), 3.70 (2 H, s), 2.19 (3 H, s).

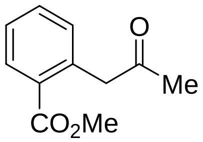


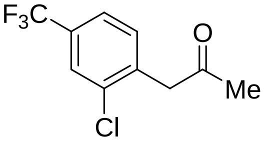
4-Trifluoromethylphenylacetone[9] (**2h**): The general procedure was followed. Isolated 257 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (2 H, d, *J* = 7.9 Hz), 7.33 (2 H, d, *J* = 7.9 Hz), 3.79 (2 H, s), 2.21 (3 H, s).



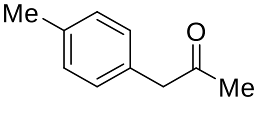
2-Cyanophenylacetone[10] (**2i**): The general procedure was followed. Isolated 207 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1 H, d, *J* = 7.8 Hz), 7.54 (1 H, t, *J* = 7.7 Hz), 7.36 (1 H, t, *J* = 7.6 Hz), 7.29 (1 H, d, *J* = 7.8 Hz), 3.97 (2 H, s), 2.27 (3 H, s).

Methyl 2-(2-oxopropyl)benzoate[11] (**2j**): The general procedure was followed. Isolated 200 mg (58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (1 H, d, *J* = 7.8 Hz), 7.49 (1 H, t, *J* = 7.5 Hz), 7.36 (1 H, t, *J* = 7.6 Hz), 7.20 (1 H, d, *J* = 7.6 Hz), 4.11 (2 H, s), 3.86 (3 H, s), 2.28 (3 H, s).





2-Chloro-4-trifluoromethylphenylacetone (**2k**): The general procedure was followed. Isolated 262 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (1 H, s), 7.49 (1 H, d, *J* = 8.0 Hz), 7.32 (1 H, d, *J* = 10.4 Hz), 3.93 (2 H, s), 2.26 (3 H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.6, 136.9, 135.0, 132.2, 131.1 (q, *J* = 33 Hz), 126.5 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 3.6 Hz), 122.2 (q, *J* = 272 Hz), 48.0, 29.9; HRMS ESI (*m* / *z*): $[M + H]^+$ calcd for $C_{10}H_9OF_3Cl$, 237.0288; found 237.0286.



4-Methylphenylacetone[7] (**2l**): The general procedure was followed. Isolated 104 mg (39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (2 H, d, *J* = 8.0 Hz), 7.14 (2 H, d, *J* = 8.0 Hz), 3.69 (2 H, s), 2.38 (3 H, s), 2.18 (3 H, s).

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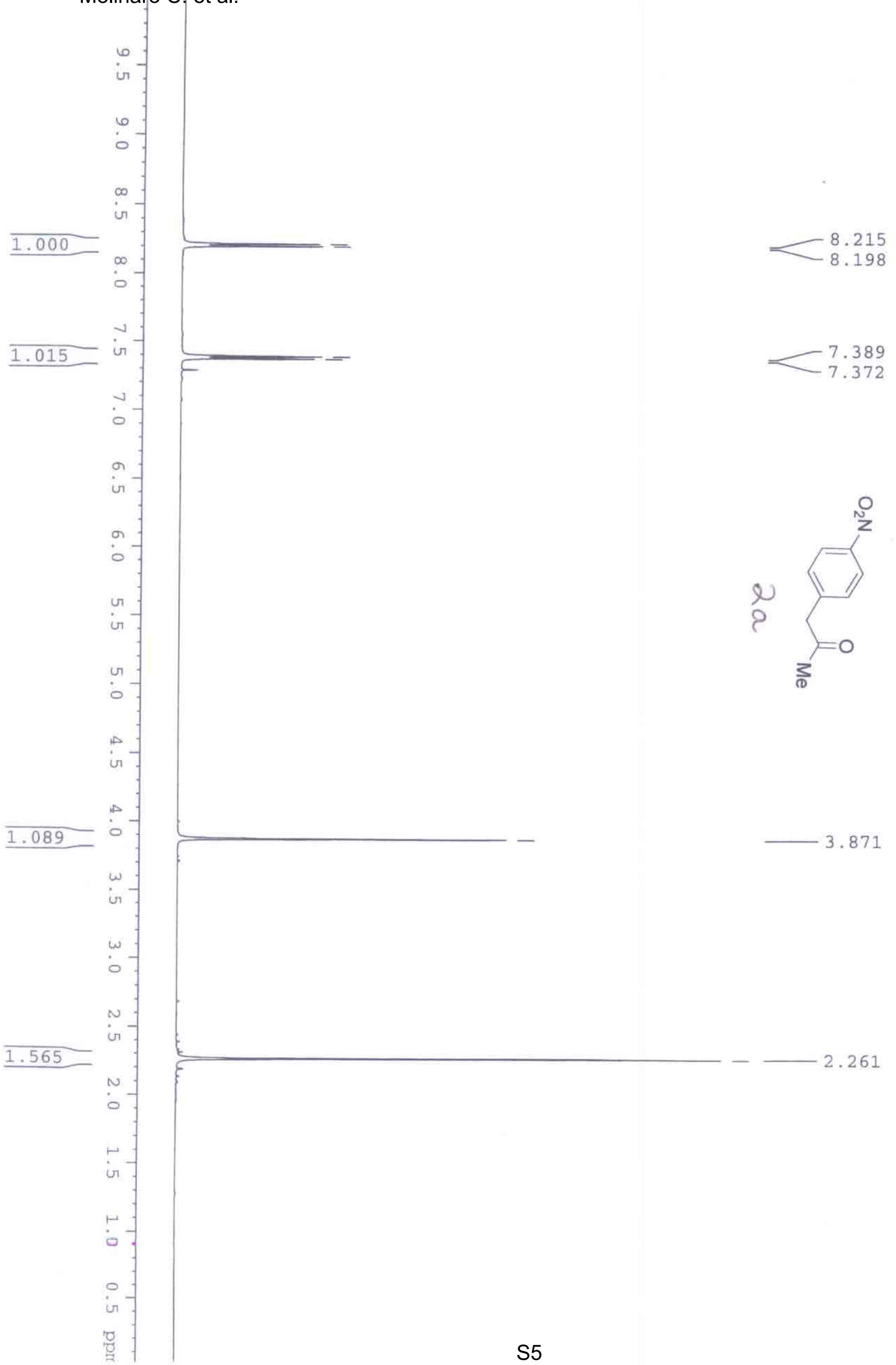
[8] Kurz, M. E.; Baru, V.; Nguyen, P-N. *J. Org. Chem.* **1984**, *49*, 1603.
[9] Owen, J. R.; Saunders, W. H. Jr. *J. Am. Chem. Soc.* **1966**, 88, 5809.
[10] Schubert, T.; Kula, M.-R.; Müller, M. *Synthesis* **1999**, 2045.
[11] Korte, D. E.; Hegedus, L. S.; Wirth, R. K. *J. Org. Chem.* **1977**, *42*, 1329.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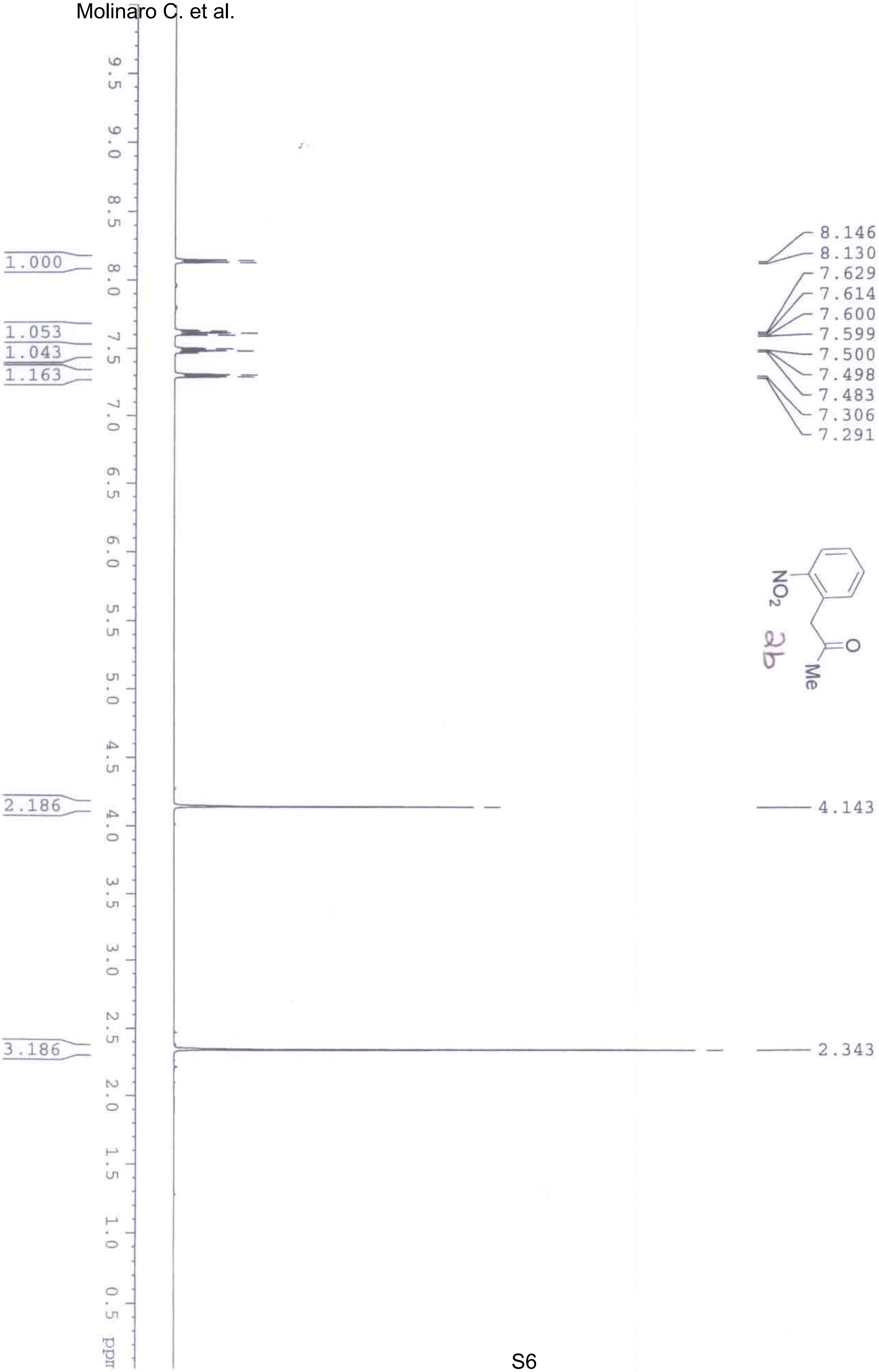
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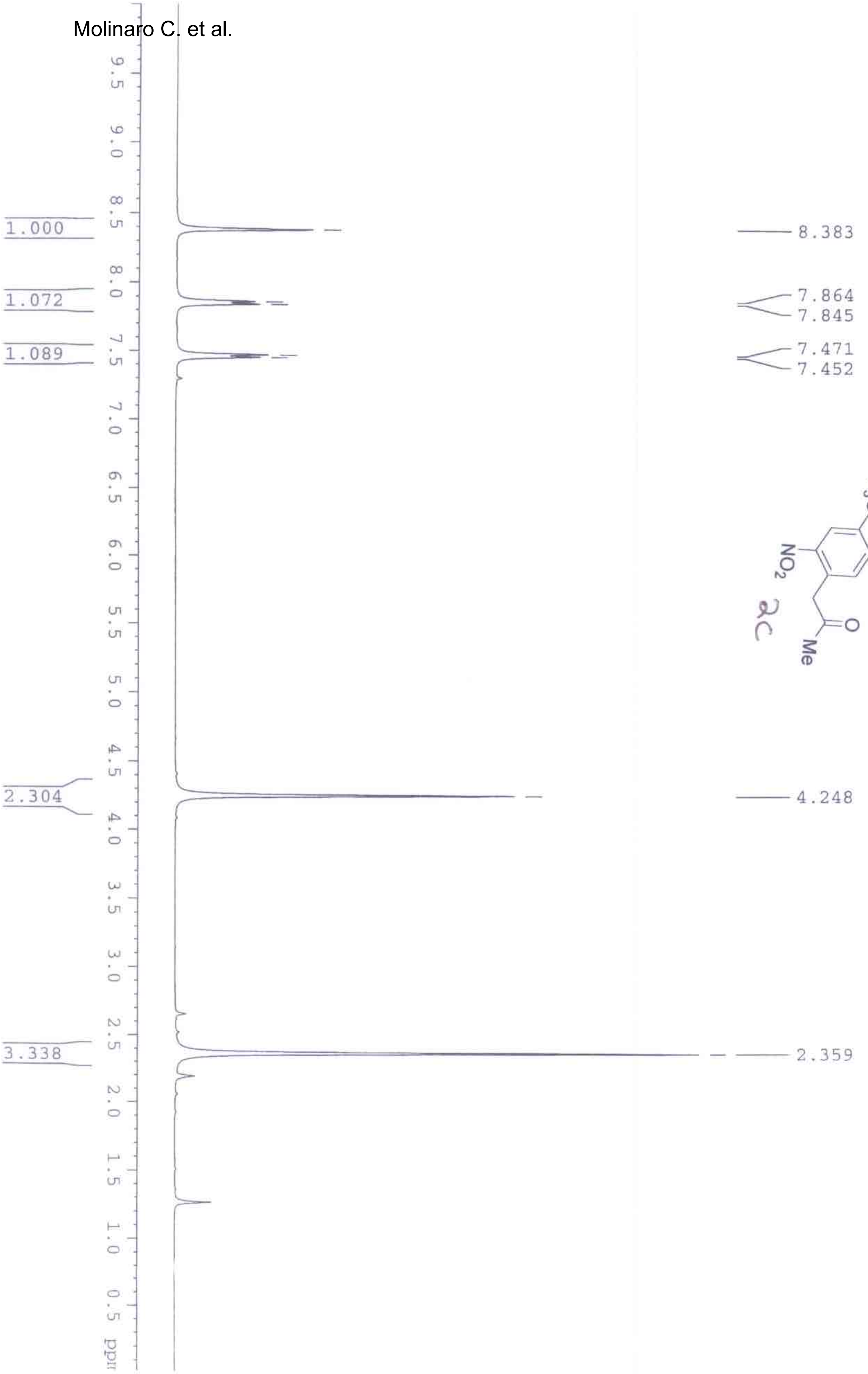
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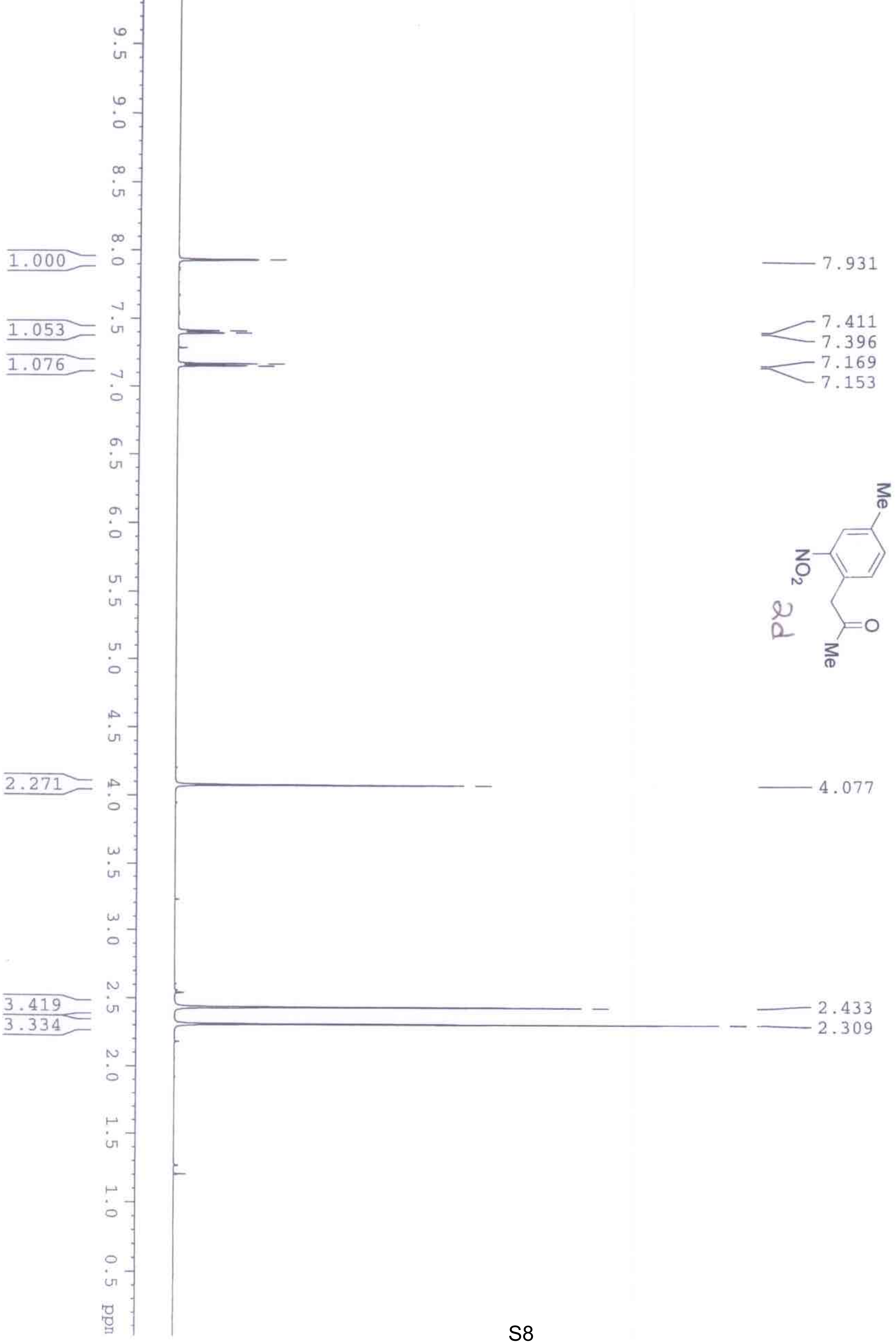
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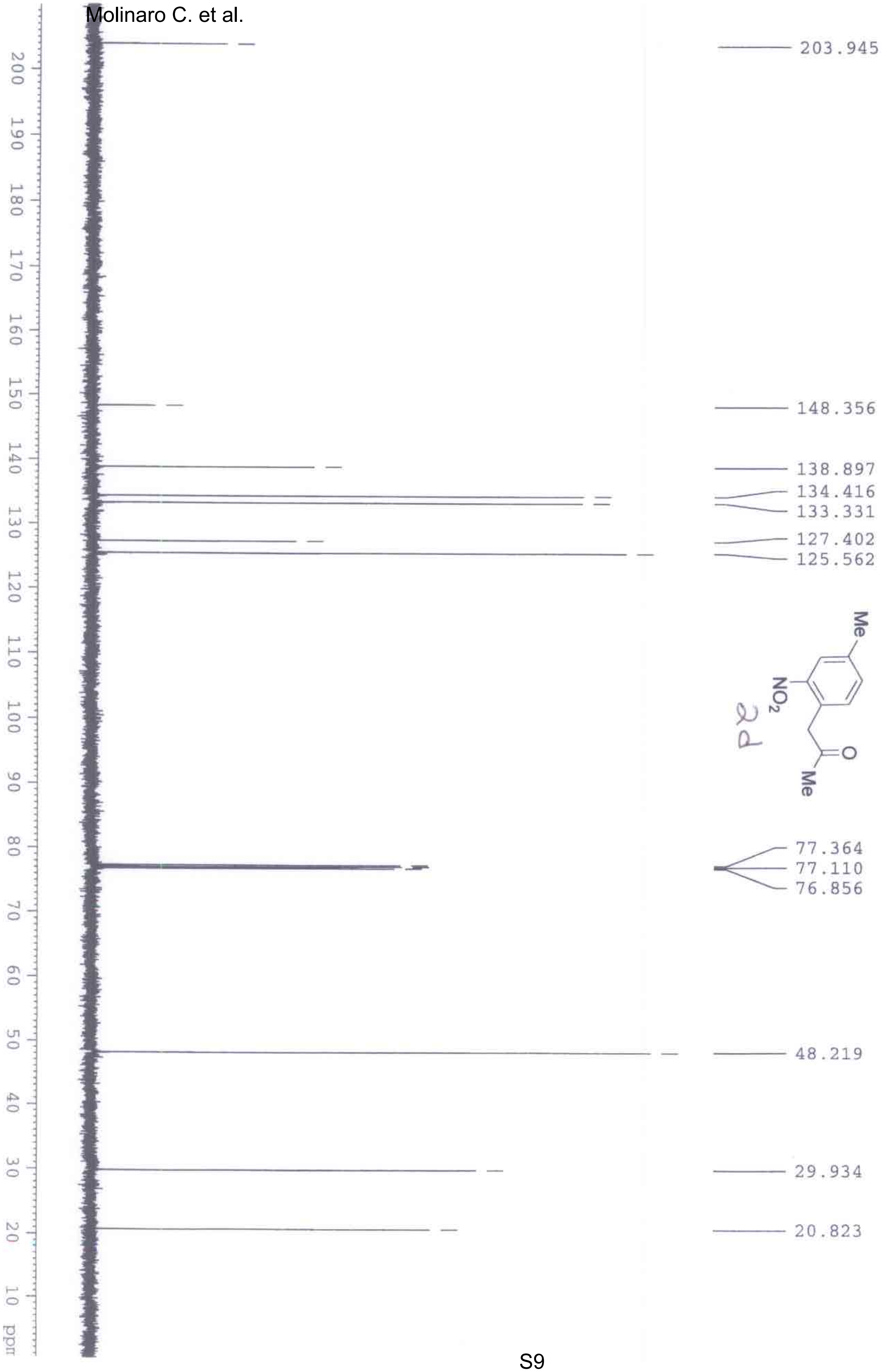
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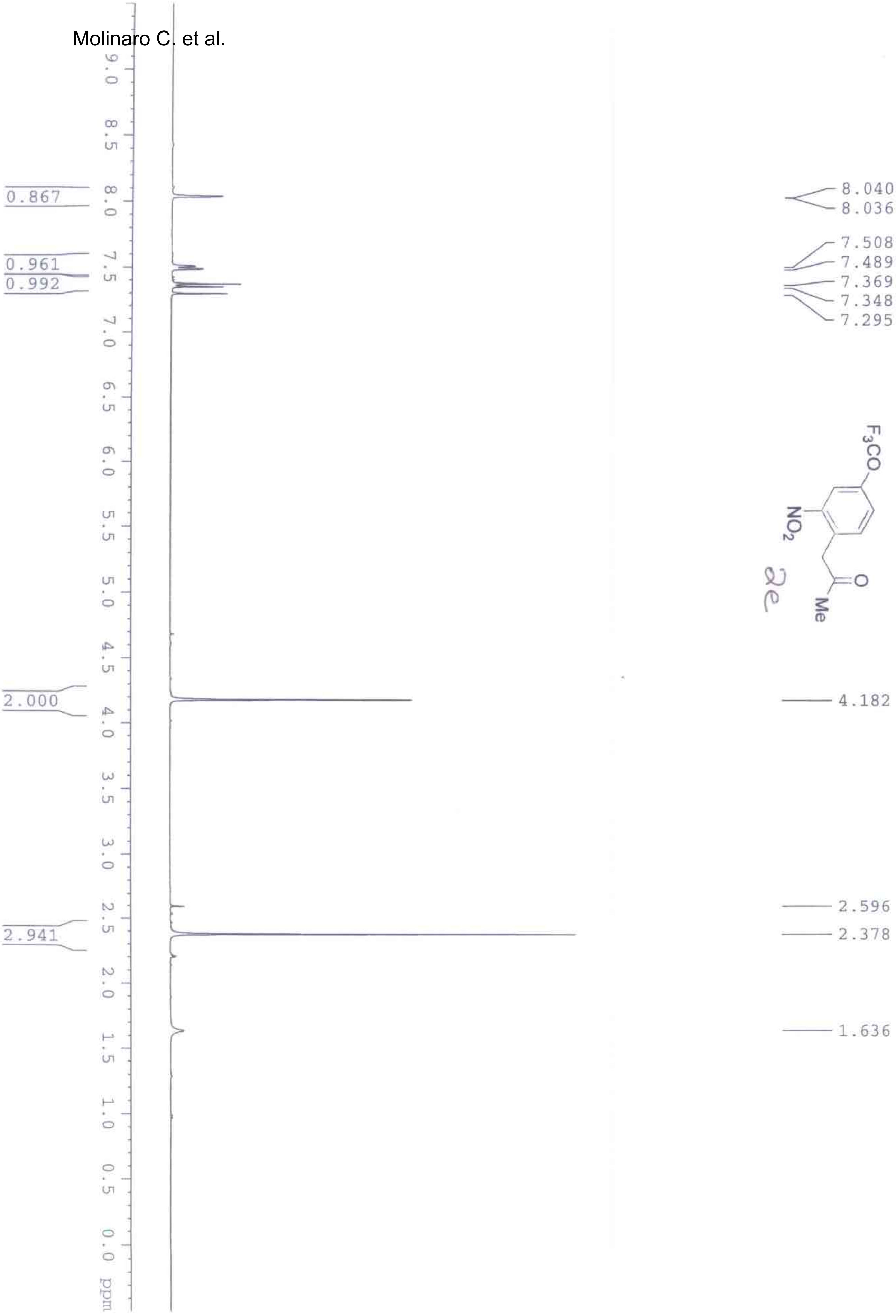
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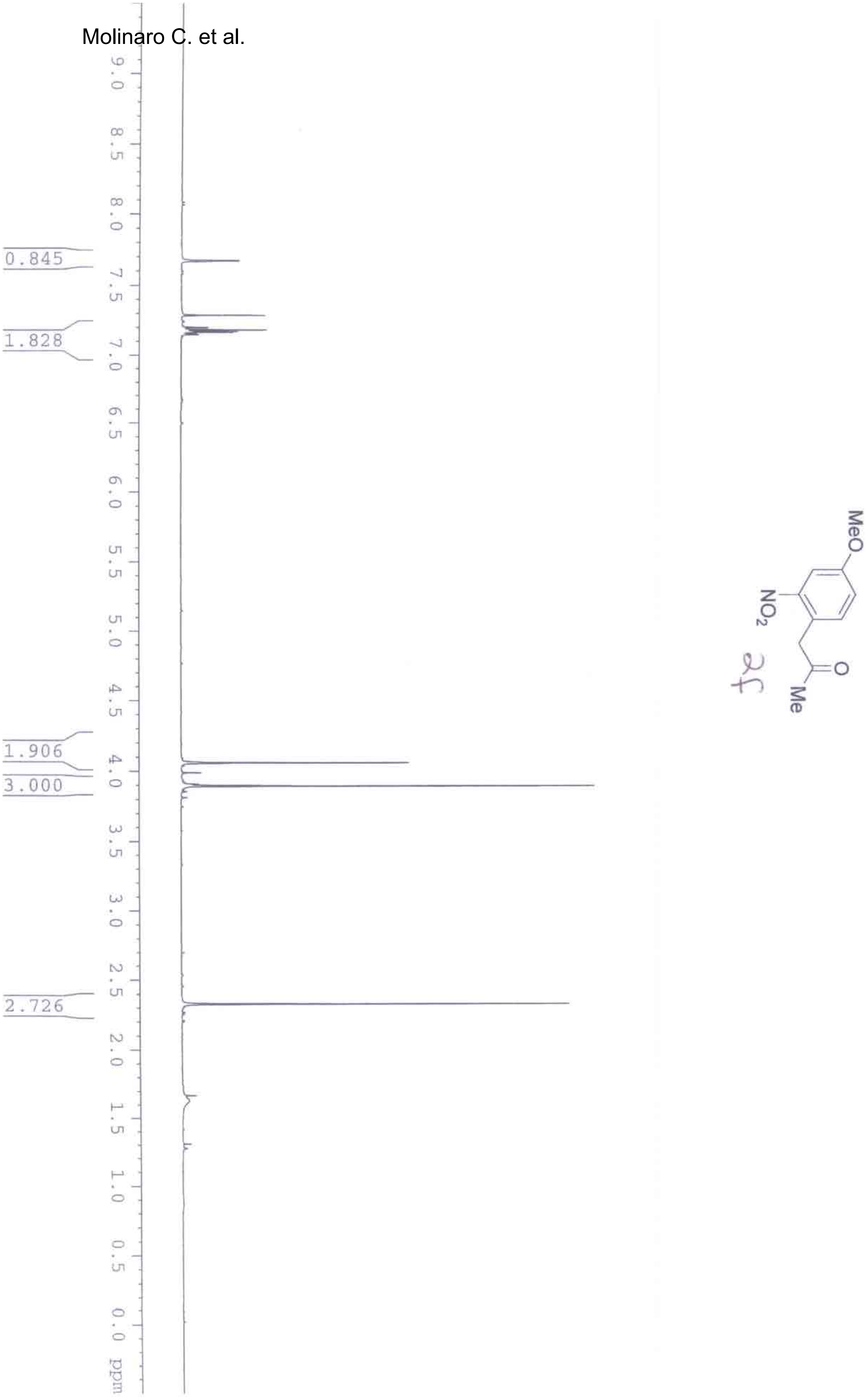
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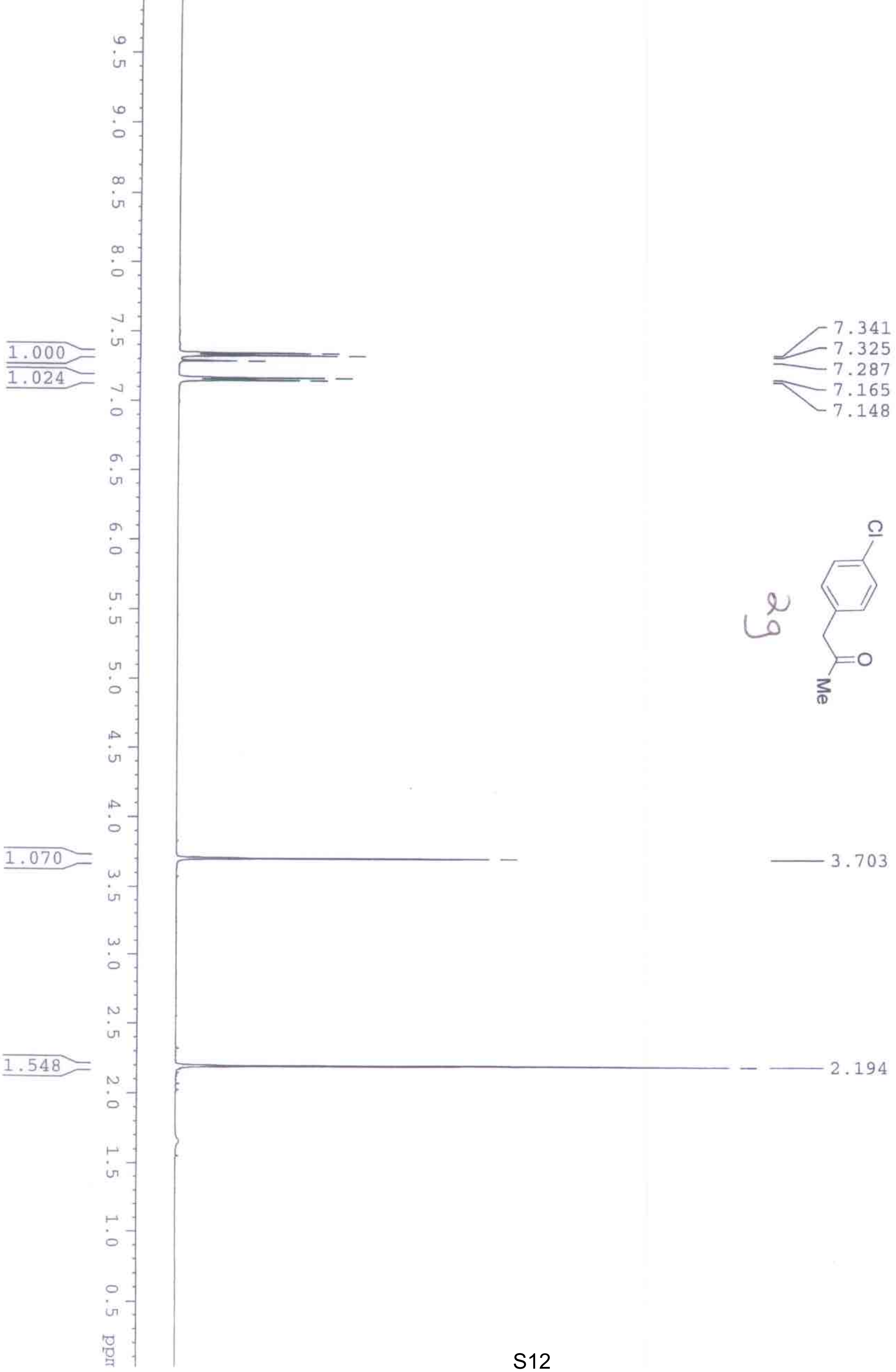
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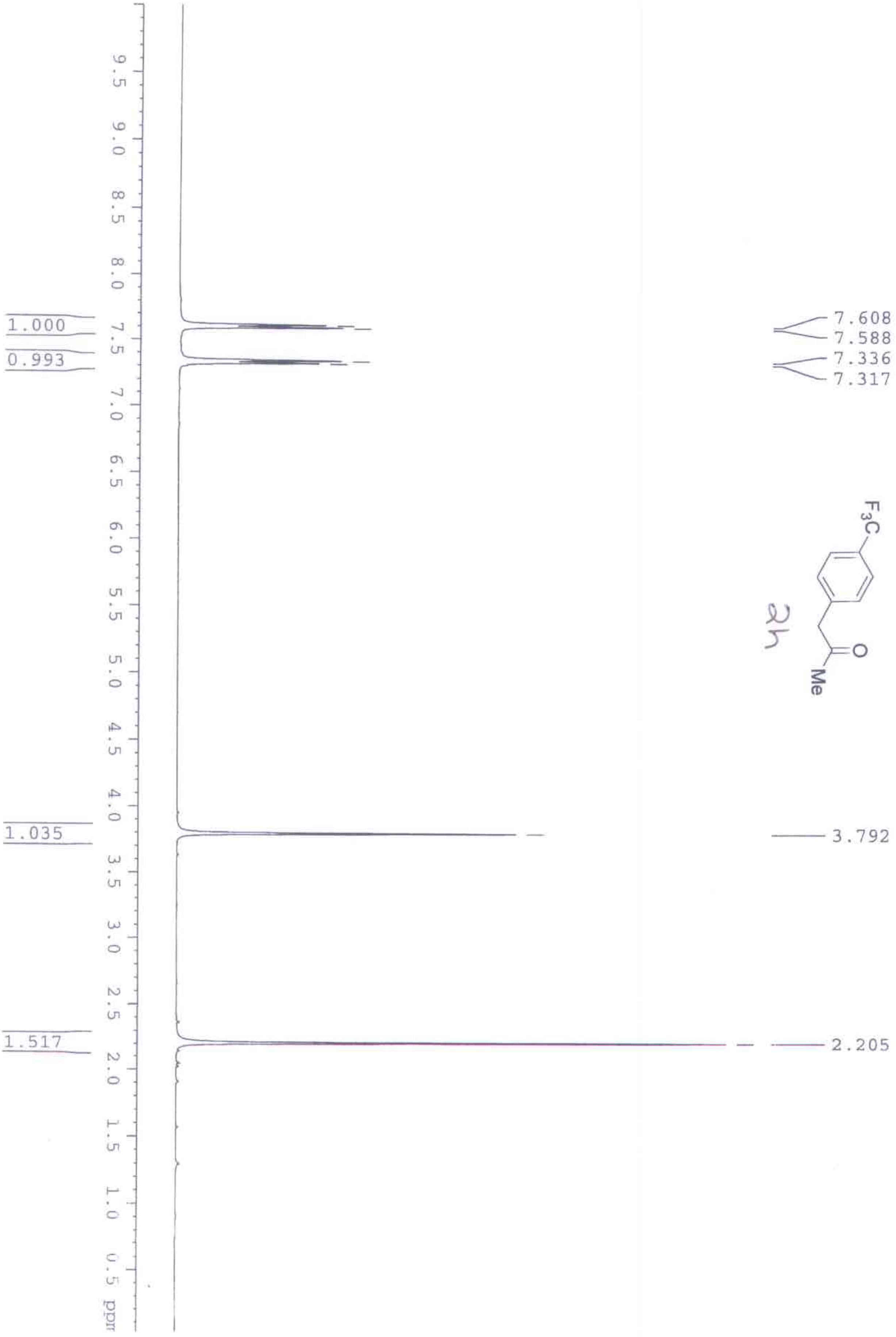
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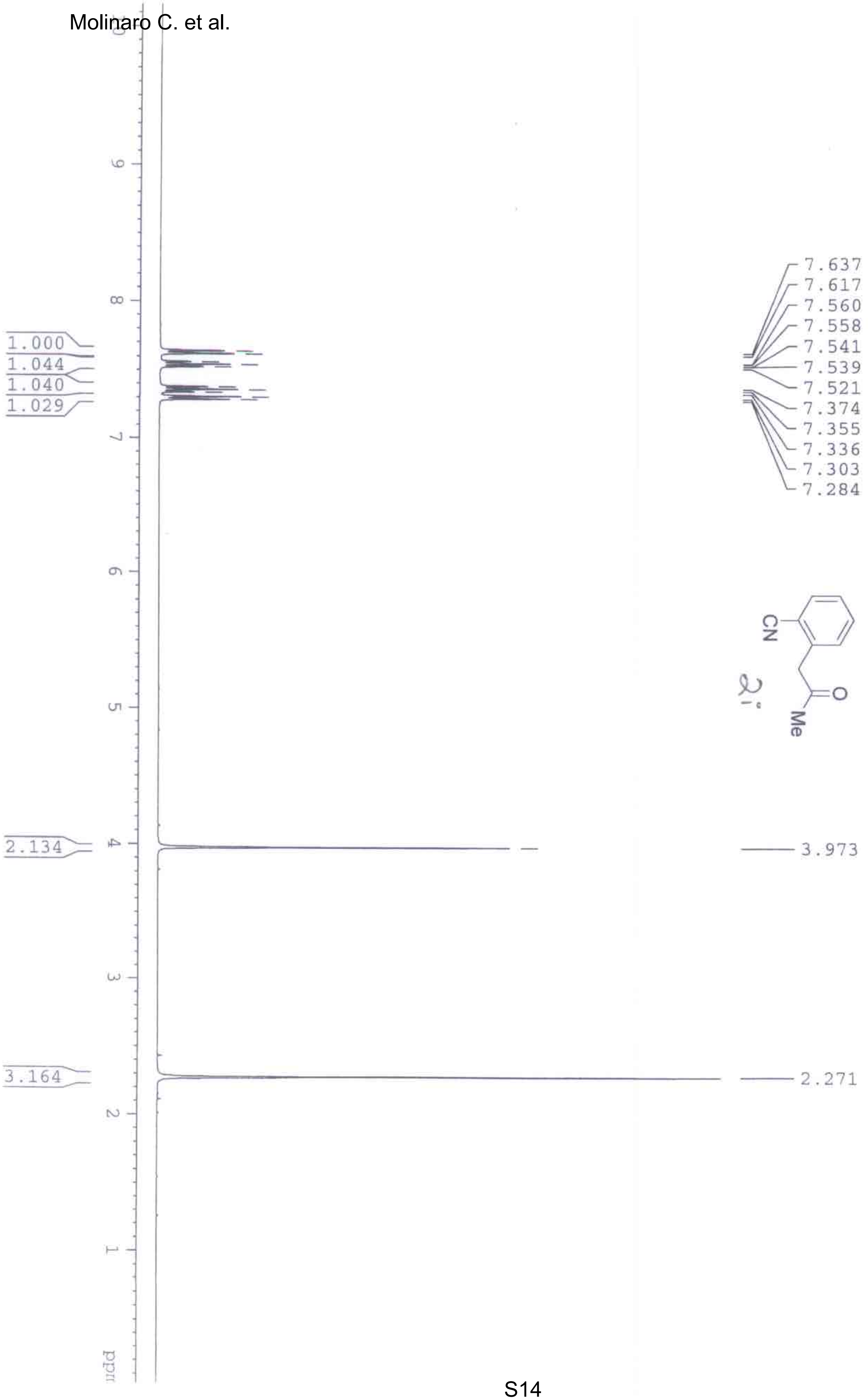
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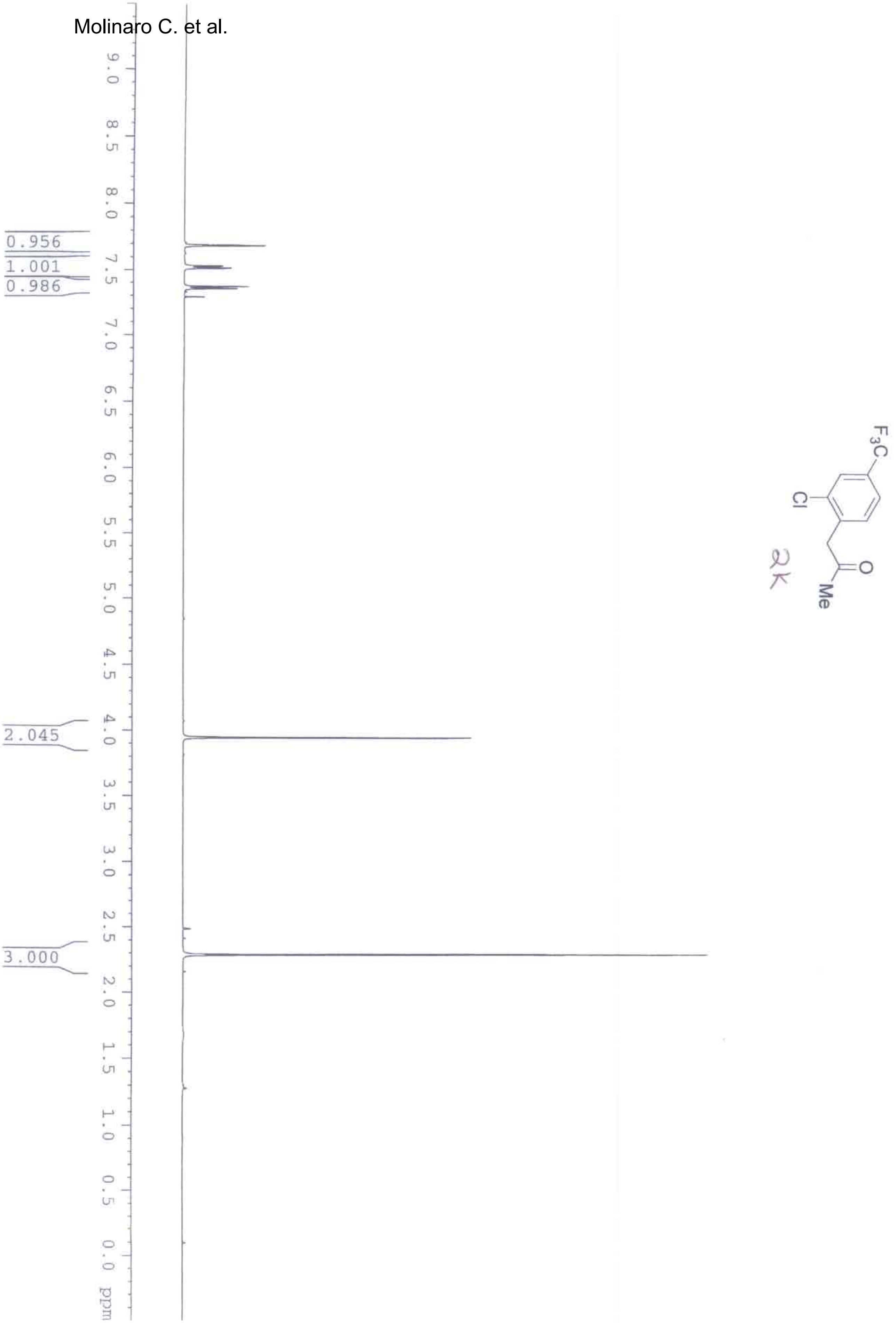
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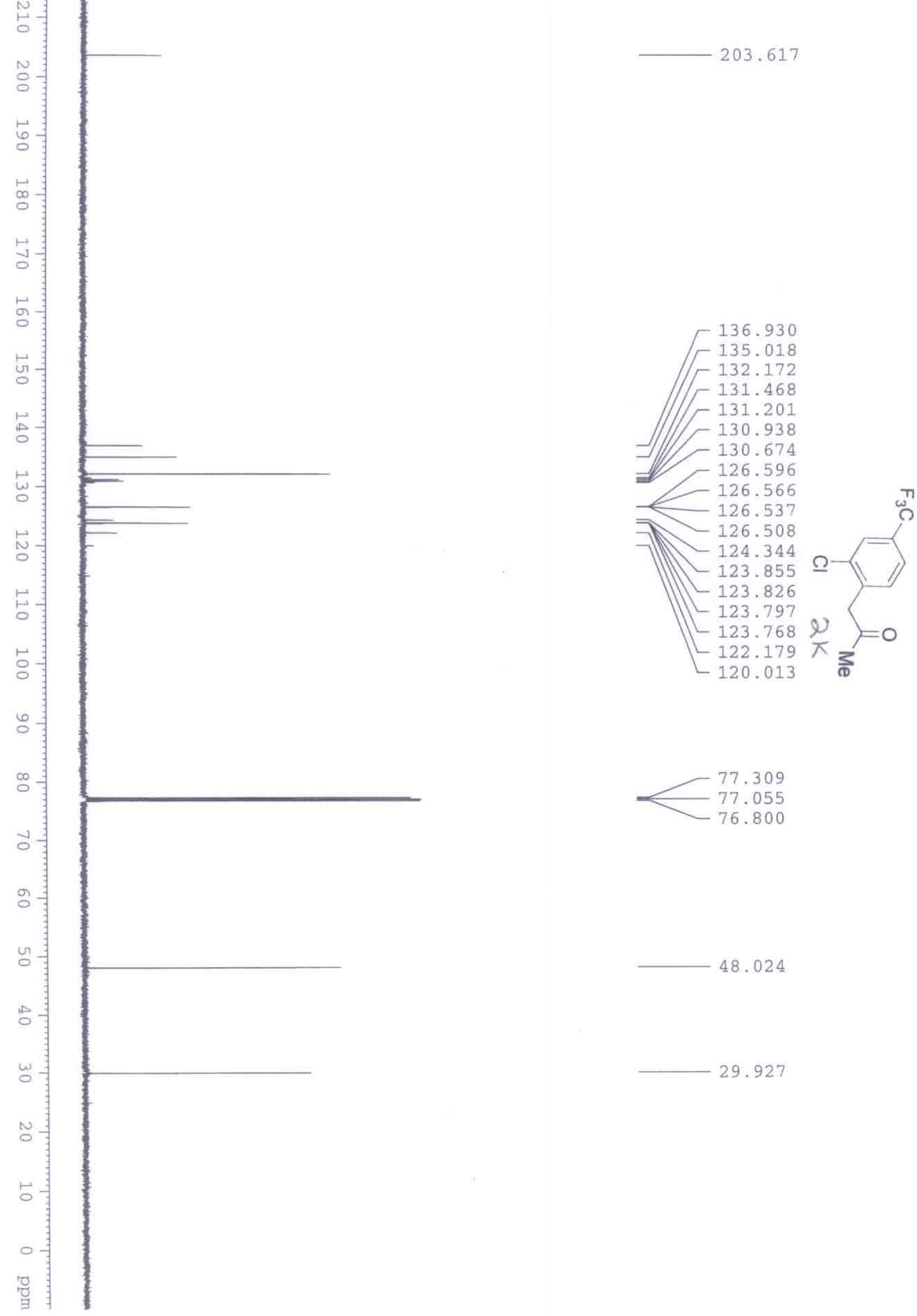
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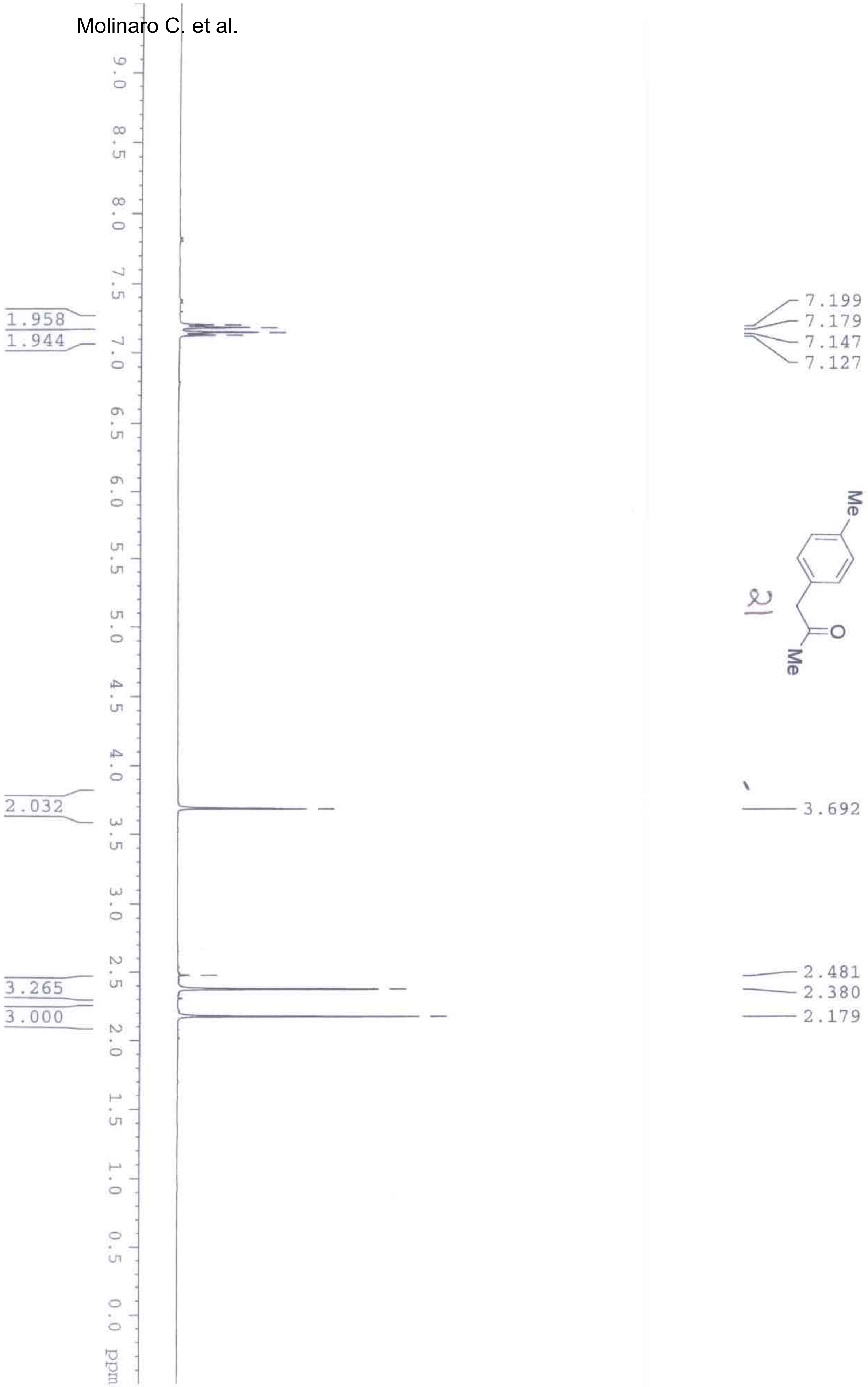
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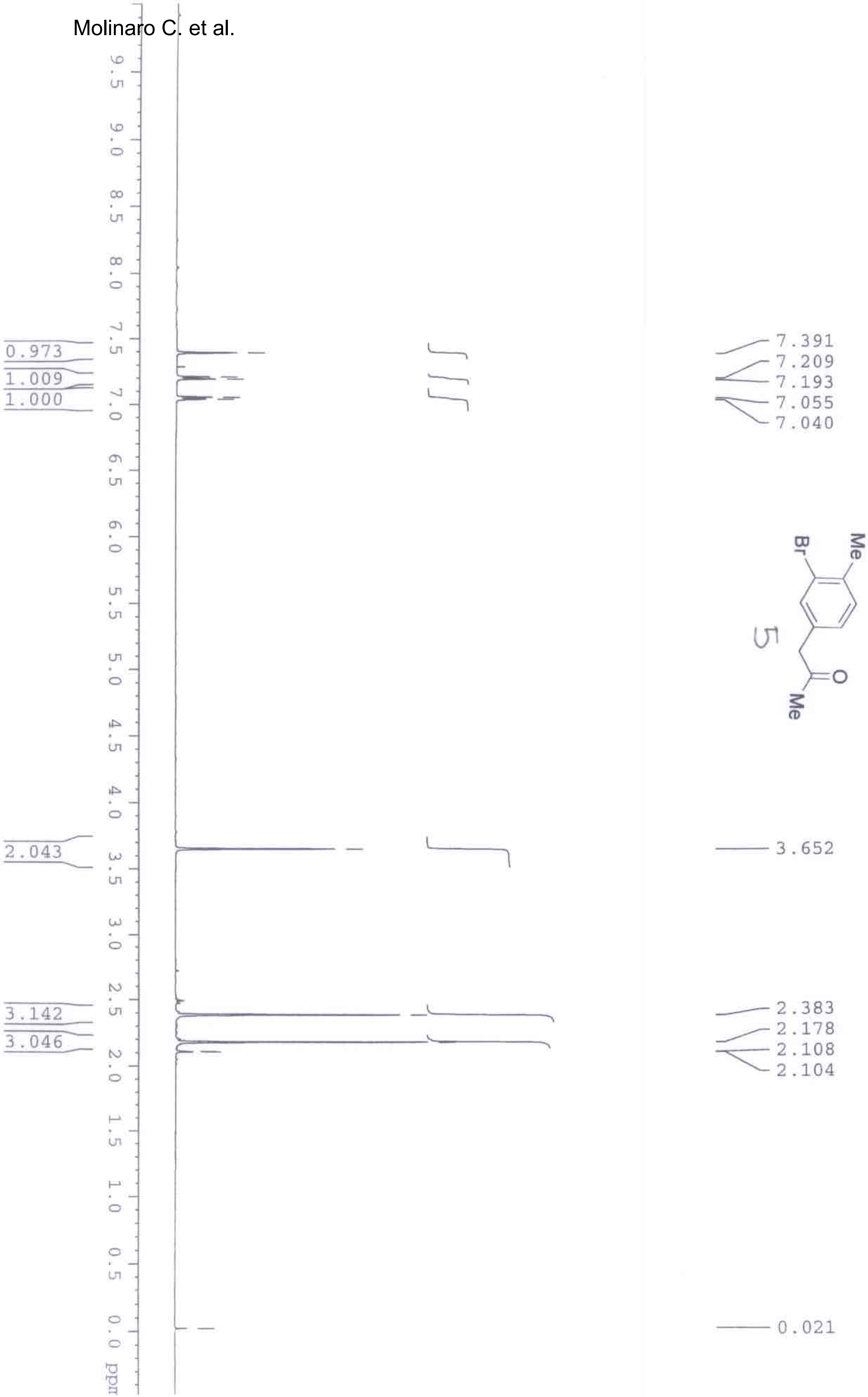
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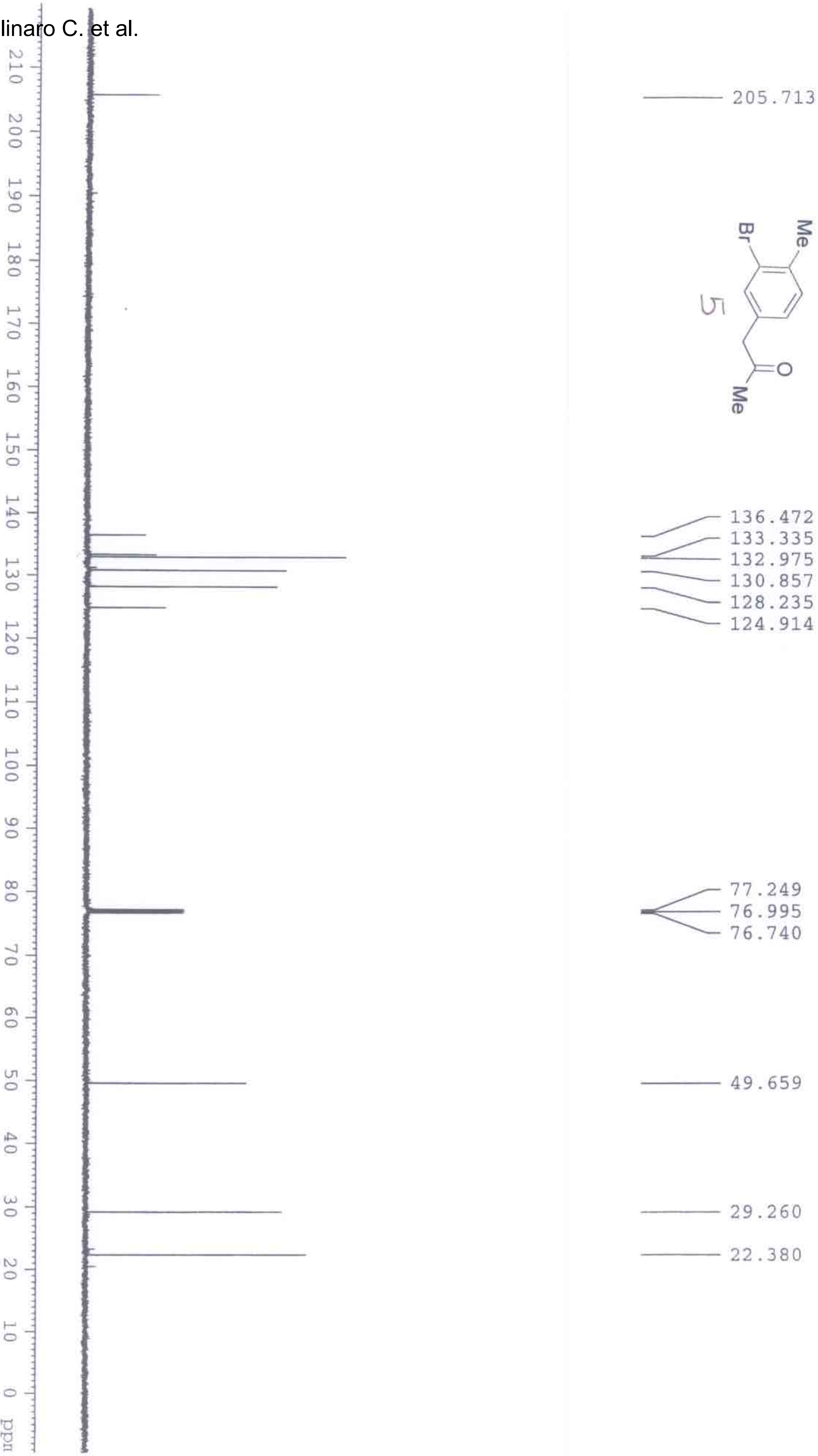
205.713
Br
Me
5
O
Me
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124.914
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76.740
49.659
29.260
22.380
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
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20
10
0
ppm