[Supporting information]

Mechanistic Pathways in CF_3COOH-Mediated Deacetalization Reactions*

Wei, Li, * Jianchang Li, Yuchuan Wu, Nathan Fuller, and Michelle Markus

Chemical Sciences, Wyeth Research, 200 Cambridge Park Drive, Cambridge, Massachusetts, 02140, USA

weili@wyeth.com, publications.weili@gmail.com

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* Dedicated to Professor William von Eggers Doering on the occasion of his 92nd birthday.

Cyclehexan-1,4-dione (Entry 12, Table 2) **S18**

All common reagents and solvents were purchased and used without further purification. Chloroform-*d* was purchased from Cambridge Isotope Laboratories, Inc. Trifluoroacetic aced was purchased from Sigma-Aldrich. All the acetals and ketals are commercially available and were used as received after purity check. All products were characterized by ^{1}H and ^{13}C NMR. NMR spectra were recorded on Bruker-400 instruments using $CDCl_3$ or CD_2Cl_2 as the solvent for both proton and carbon NMR unless otherwise indicated. Fluorine-carbon coupling constants are also included in the ^{13}C NMR data for compounds containing fluorine substituents. The following abbreviations are used to designate the multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

General conditions for TFA-mediated deacetalization: Condition A. To a round-bottom flask containing the acetal or ketal (10 mmol) in chloroform (20 mL) was slowly added trifluoroacetic acid (6 equivalents) at ambient temperature. The resulting solution was allowed to stir for 20 hours, and then the mixture was quenched with water (20 mL) and extracted with EtOAc (3 x 30 mL). The organic layer was washed with brine (2 x 40 mL) and dried over Mg_2SO_4. The solvents were removed under reduced pressure to afford the desired aldehydes (yield as indicated).

Condition B. To a round-bottom flask containing the acetal or ketal (10 mmol) in 20 mL of chloroform was slowly added trifluoroacetic acid (20 equivalents) at ambient temperature. The resulting solution was allowed to stir for 5 hours, and then the mixture was quenched with water (30 mL) and extracted with EtOAc (3 x 40 mL). The organic

layer was washed with brine (2 x 40 mL) and dried over Mg_2SO_4. The solvents were removed under reduced pressure to afford the desired aldehydes (yield as indicated).

Condition C. To a round-bottom flask containing the acetal or ketal (10 mmol) in 20 mL of chloroform was slowly added trifluoroacetic acid (4 equivalents) at ambient temperature. The resulting solution was heated at 75 ^oC for 2 hours and then the mixture was quenched with water (20 mL) and extracted with EtOAc (3 x 30 mL). The organic layer was washed with brine (2 x 30 mL) and dried over Mg_2SO_4. The solvents were removed under reduced pressure to afford the desired aldehydes (yield as indicated).

Benzaldehyde (Entry 1, Table 2). The known benzaldehyde was obtained as a colorless oil (1.0 g, 95%) from the dimethyl acetal **10** following condition B. ^1H NMR δ (400 MHz, DMSO-d6) 10.07 (s, 1 H), 7.95 (d, *J* = 8.3 Hz, 2 H), 7.74 (t, *J* = 7.3 Hz, 1 H), 7.63 (t, *J* = 7.6 Hz, 2 H).

Benzaldehyde (Entry 2, Table 2). The known benzaldehyde was obtained as a colorless oil (0.10 g, 95%) from the diethyl acetal **11** (1.0 mmol) following condition B.

4-Chlorobenzaldehyde (Entry 3, Table 2). The known 4-chlorobenzaldehyde was obtained as a white solid (1.18 g, 84%) from the acetal **12** following condition B. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 - 7.55 (m, 2 H), 7.81 - 7.85 (m, 2 H), 9.95 - 10.04 (m, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.4, 132.0, 135.1, 141.4, 191.3.

4-n-Propylbenzaldehyde (Entry 4, Table 2). The reaction was run under both conditions A and B separately. For condition A, the diethyl acetal **13** (1.01 g, 4.5 mmol) in DCM (10 mL) was treated with TFA (3.08 g, 27 mmol) at room temperature for 20 h, and the known 4-n-propylbenzaldehyde was obtained as a colorless crystalline solid (0.554 g, 83%) after column chromatography. ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J* = 7.3 Hz, 3

H), 1.62 - 1.74 (m, 2 H), 2.64 - 2.71 (t, *J* = 7.3 Hz, 2 H), 7.33 (s, 1 H), 7.35 (s, 1 H), 7.79 - 7.80 (m, 1 H), 7.80 - 7.83 (m, 1 H), 7.82 (d, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.18, 24.62, 38.66, 129.56, 130.30, 134.85, 150.63, 192.47.

4-Methoxybenzaldehyde (Entry 5, Table 2). The reaction was run under both conditions A and B separately. For condition A, the diethyl acetal **14** (1.0 g, 4.7 mmol) in DCM (10 mL) was treated with TFA (3.25 g, 28.5 mmol) at room temperature for 20 h and the known 4-methoxybenzaldehyde was obtained as a white solid (0.560 g, 86%) after column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3 H), 6.98 - 7.04 (m, 2 H), 7.82 - 7.87 (m, 2 H), 9.89 (s, 1 H).

3, 4, 5-Trimethoxybenzaldehyde (Entry 6, Table 2). The reaction was run under both conditions A and B separately. For condition A, the dimethyl acetal **15** (1.0 g, 4.1 mmol) in DCM (10 mL) was treated with TFA (2.82 g, 24.7 mmol) at room temperature for 16 h to yield the known 3,4,5-trimethoxybenzaldehyde (white solid, 0.743 g, 92%) after column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (d, 2 H), 7.14 (s, 2 H), 9.88 (s, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.7, 60.4, 106.1, 131.1, 143.0, 153.1, 190.5.

3-Bromopropanal (Entry 7, Table 2). The reaction was run under both conditions A and B separately. For condition B, the dimethyl acetal **16** (1.83 g, 10.0 mmol) in DCM (30 mL) was treated with TFA (22.4 g, 200 mmol) at room temperature for 4 h to yield the known aldehyde (1.30 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (b, 2 H), 3.65 (b, 2H), 9.71 (b, 1 H).

2-Bromoacetaldehyde (Entry 8, Table 2). The reaction was run under both conditions A and B separately. For condition B, the diethyl acetal **17** (1.97 g, 10.0 mmol) in DCM (30 mL) was treated with TFA (22.4 g, 200 mmol) at room temperature for 6 h to yield the

known aldehyde (1.23 g, 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (b, 2 H), 8.82 (b, 1 H).

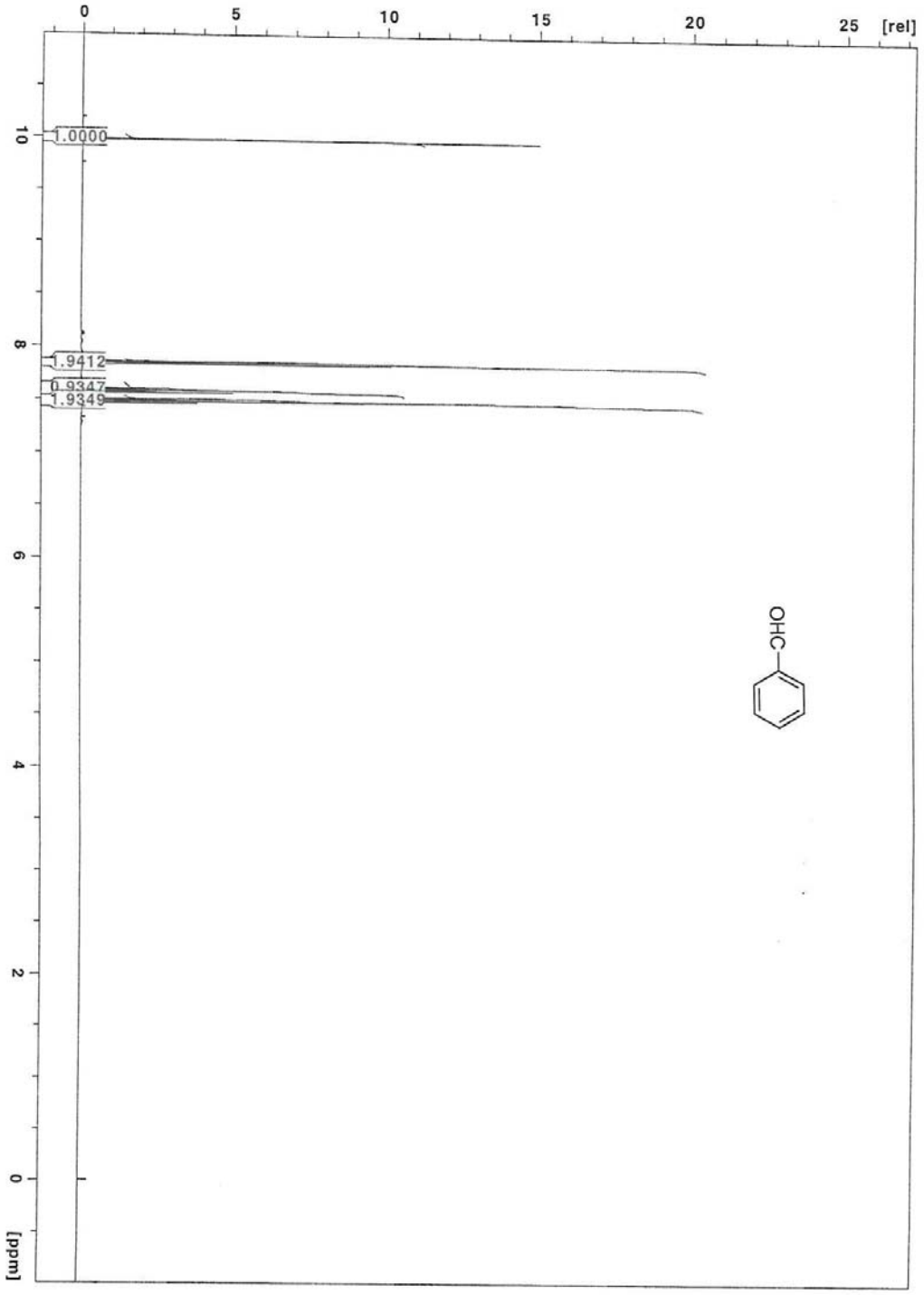
Benzaldehyde (Entry 9, Table 2). The reaction was run under both conditions A and B separately. For condition B, the cyclic acetal **18** (1.50 g, 10.0 mmol) in DCM (20 mL) was treated with TFA (22.4 g, 200 mmol) at room temperature for 10 h to yield 1.0 g (95%) of the known benzaldehyde (for analytical data, see Entry 1 & 2).

4-Bromobenzaldehyde (Entry 10, Table 2). The reaction was run under both conditions A and B separately. For condition A, the cyclic acetal **19** (1.04 g, 4.5 mmol) in DCM (10 mL) was treated with TFA (3.0 g, 26 mmol) at room temperature for 20 h, and the known 4-bromobenzaldehyde was obtained as a white solid (0.730 g, 91%) after chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 - 7.72 (m, 2 H), 7.73 - 7.79 (m, 2 H), 9.98 (s, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 128.8, 130.0, 131.5, 134.1, 190.1.

2-Bromobenzaldehyde (Entry 11, Table 2). The reaction was run under both conditions B and C separately. For condition C, The cyclic acetal **20** (1.03 g, 4.5 mmol) in DCM (15 mL) was treated with TFA (10.2 g, 90 mmol) at 75 ^{o}C for 4 h and the known 2-bromobenzaldehyde was obtained as a white solid (0.732 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.48 (m, 2 H), 7.64 - 7.68 (m, 1 H), 7.90 - 7.94 (m, 1 H), 10.37 (s, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 127.1 , 127.9, 129.9, 133.5, 133.9, 135.4, 191.9.

Cyclohexane-1,4-dione (Entry 12, Table 2). The reaction was run under both conditions A and B separately. For condition B, the cyclic ketal **21** (1.56 g, 10.0 mmol) in DCM (20 mL) was treated with TFA (22.8 g, 200 mmol) at room temperature for 12 h and the known cyclohexane-1,4-dione was obtained as a white solid (1.01 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72 (s, 8 H).

Benzaldehyde (Entry1 & 2, Table 2)



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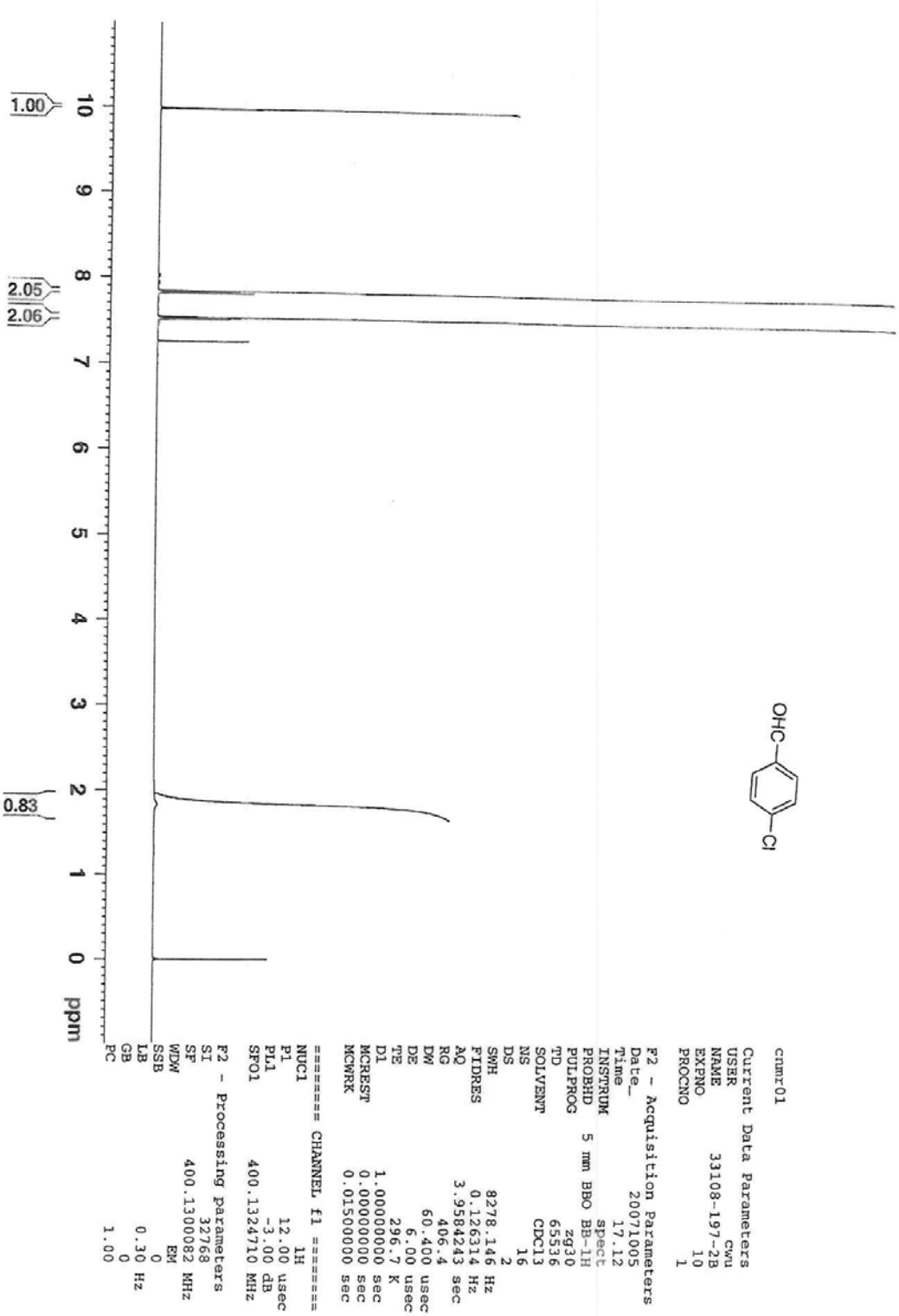

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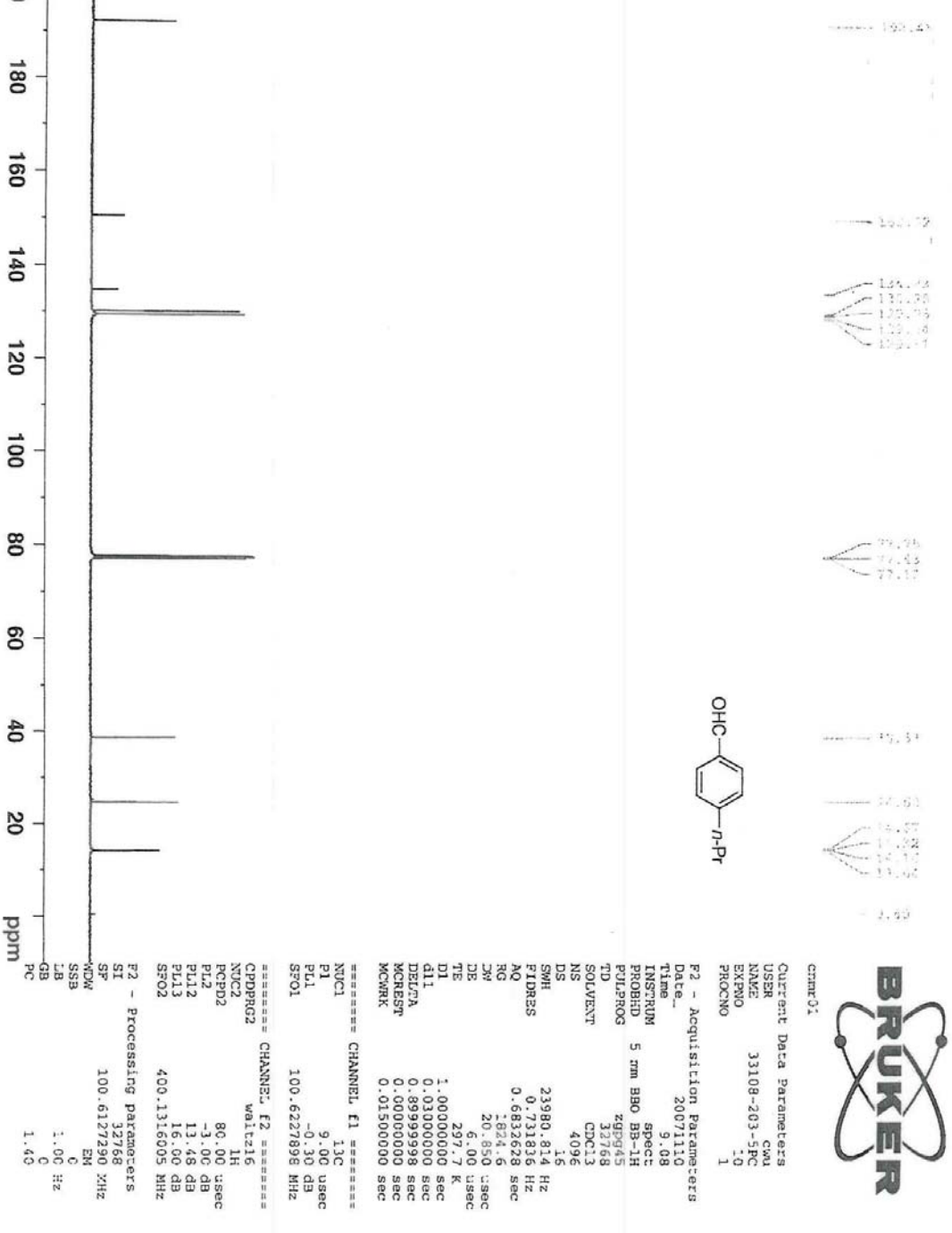

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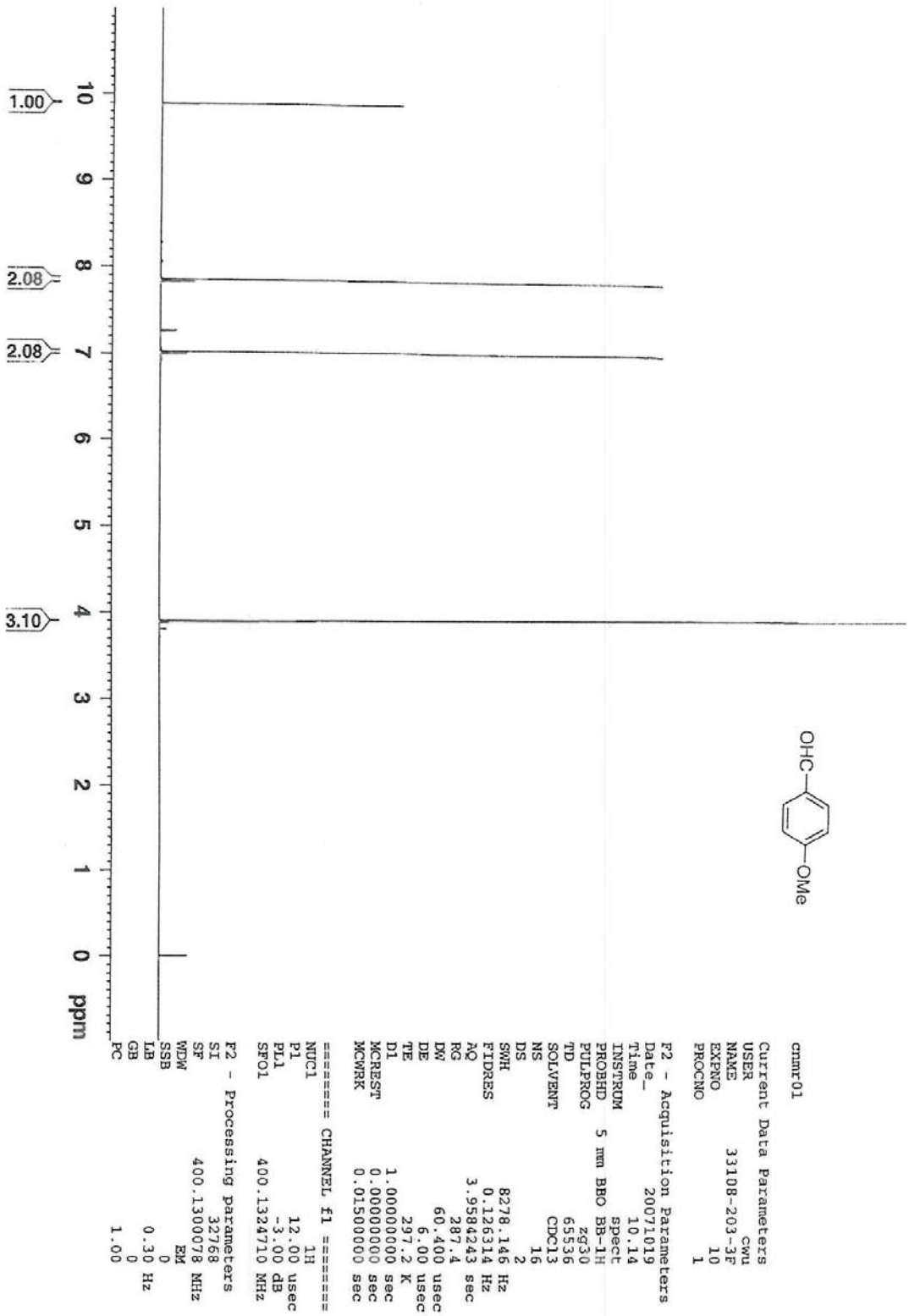

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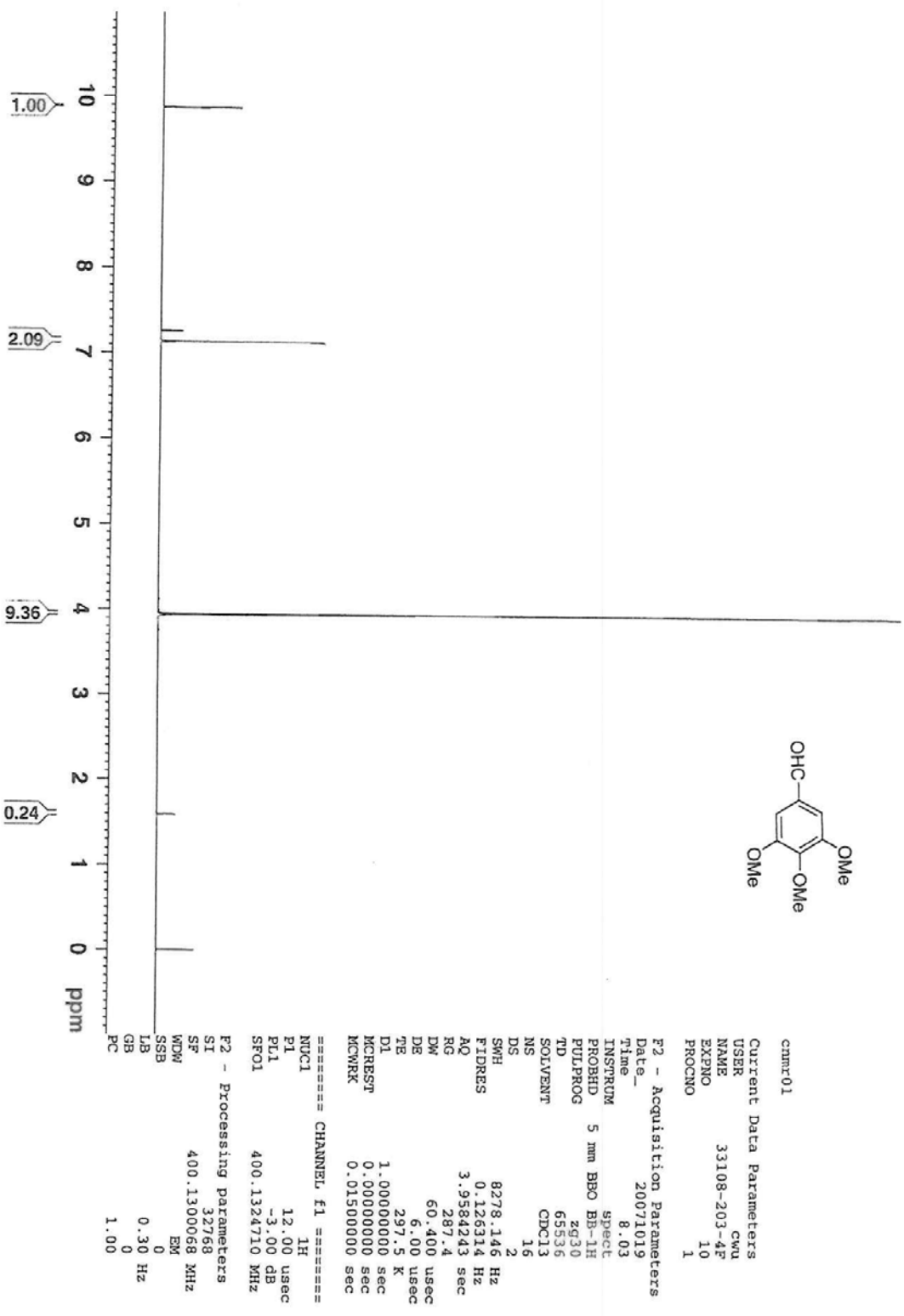
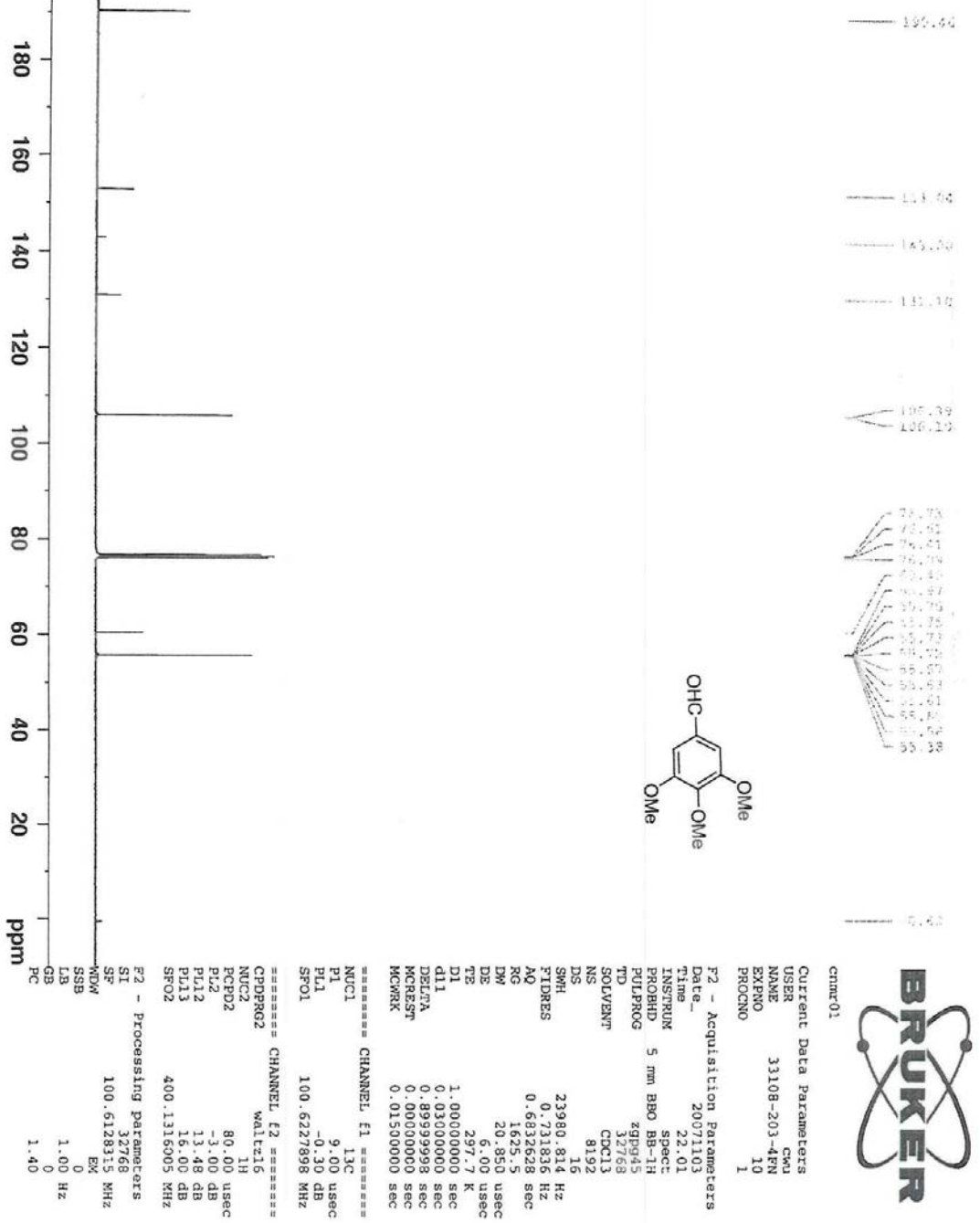


3,4,5-Trimethoxybenzaldehyde (Entry 6, Table 2)



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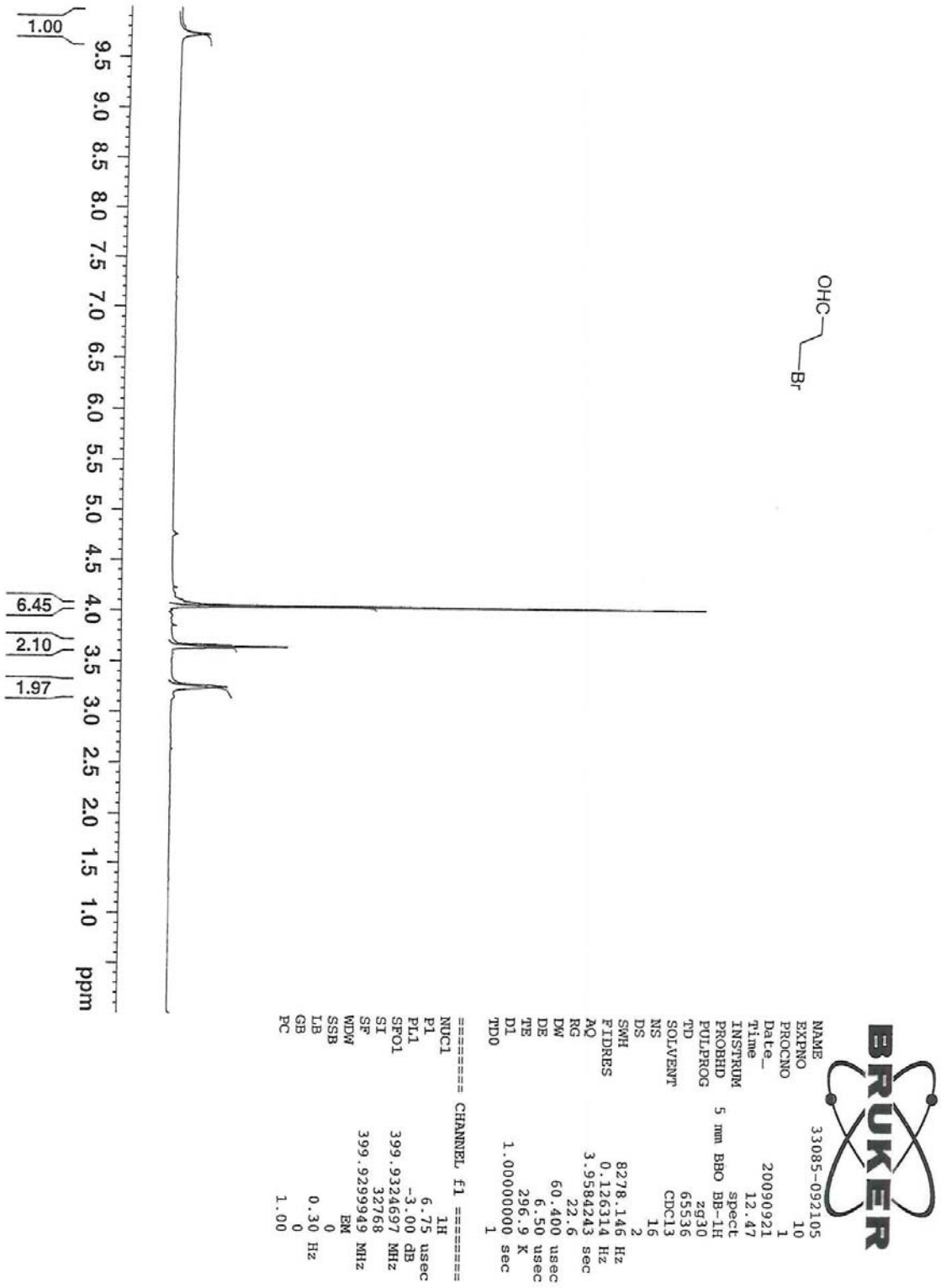

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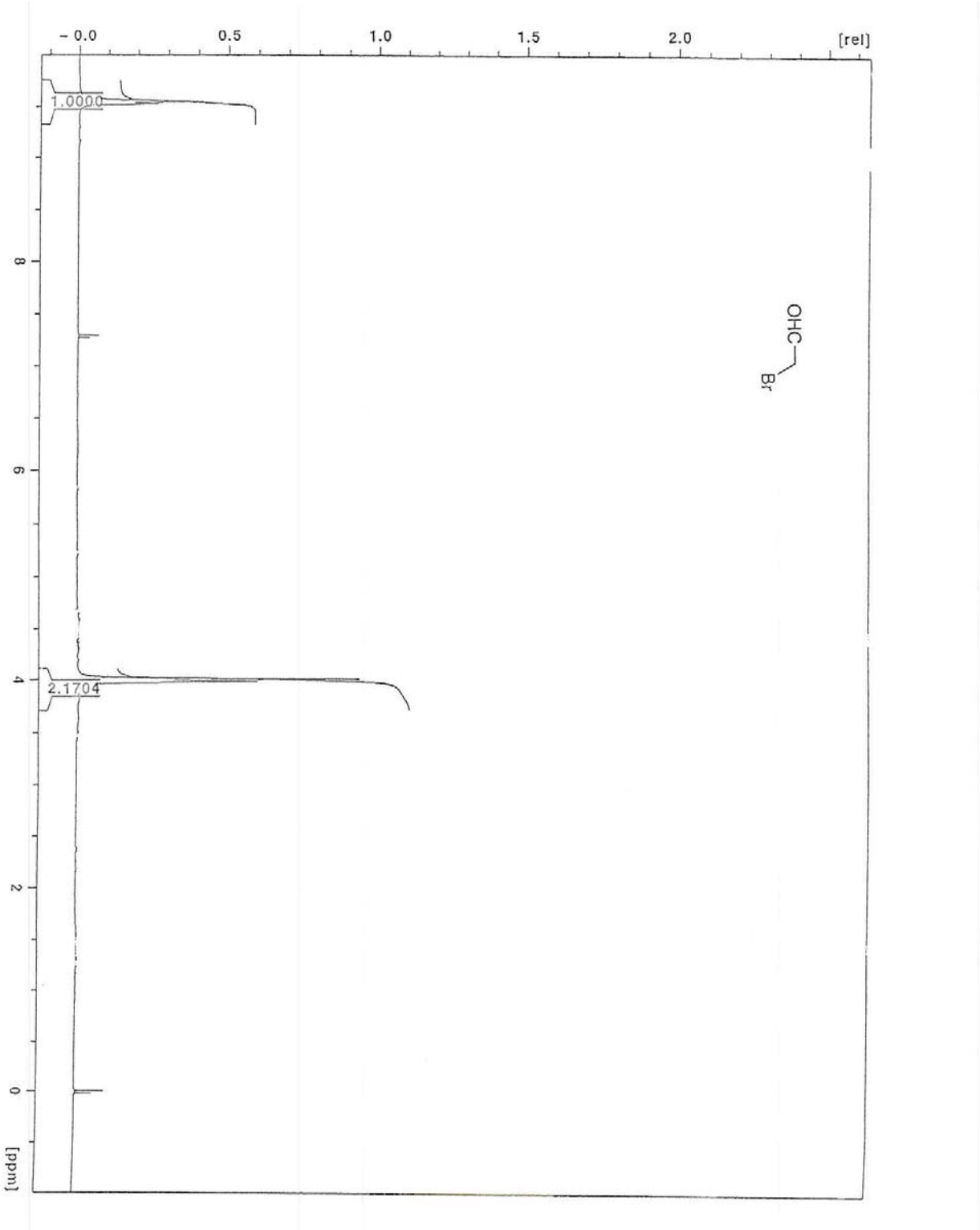
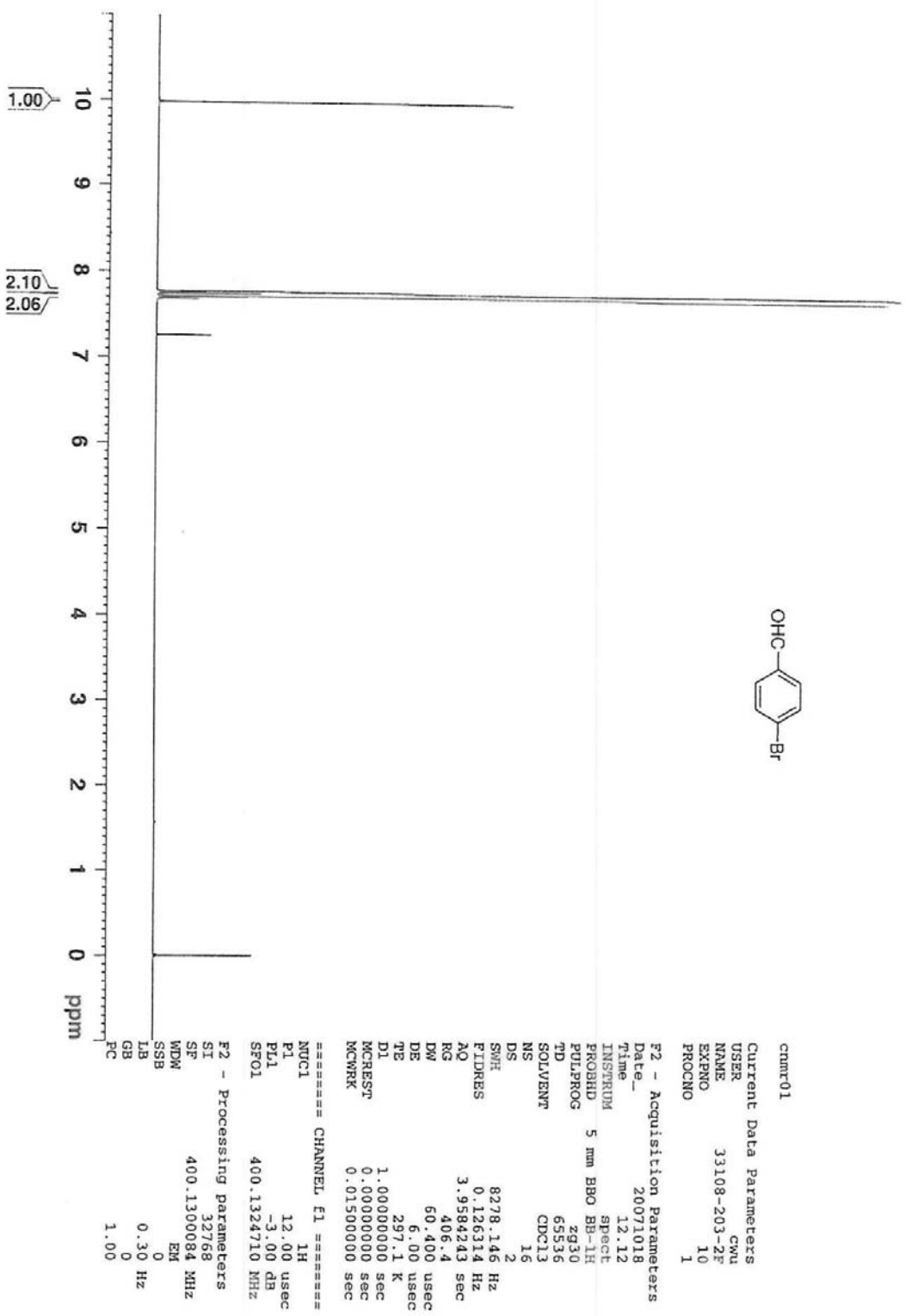


Benzaldehyde (Entry 9, Table 2, see Entry 1, Table 2)

4-bromobenzaldehyde (Entry 10, Table 2)



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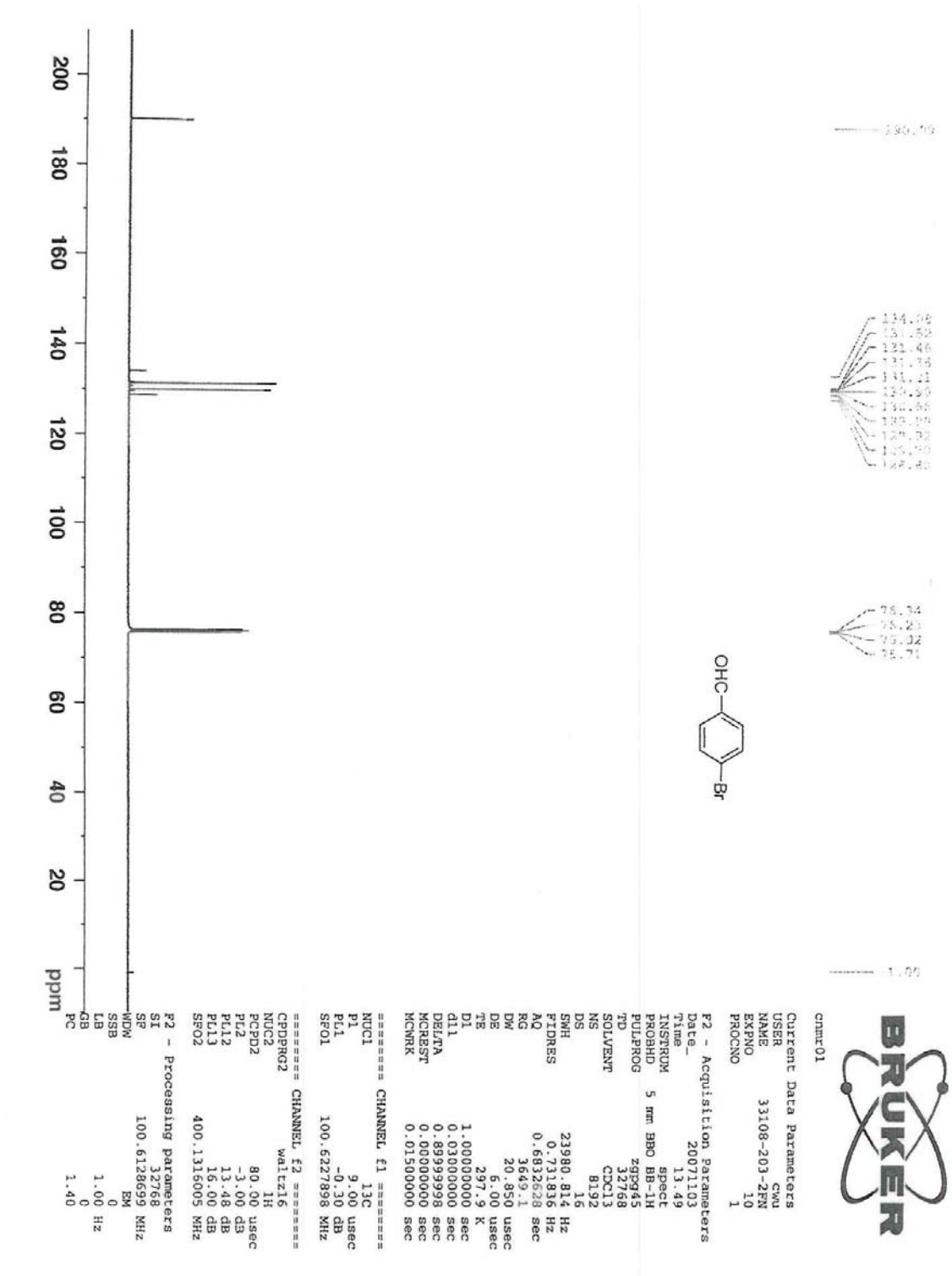

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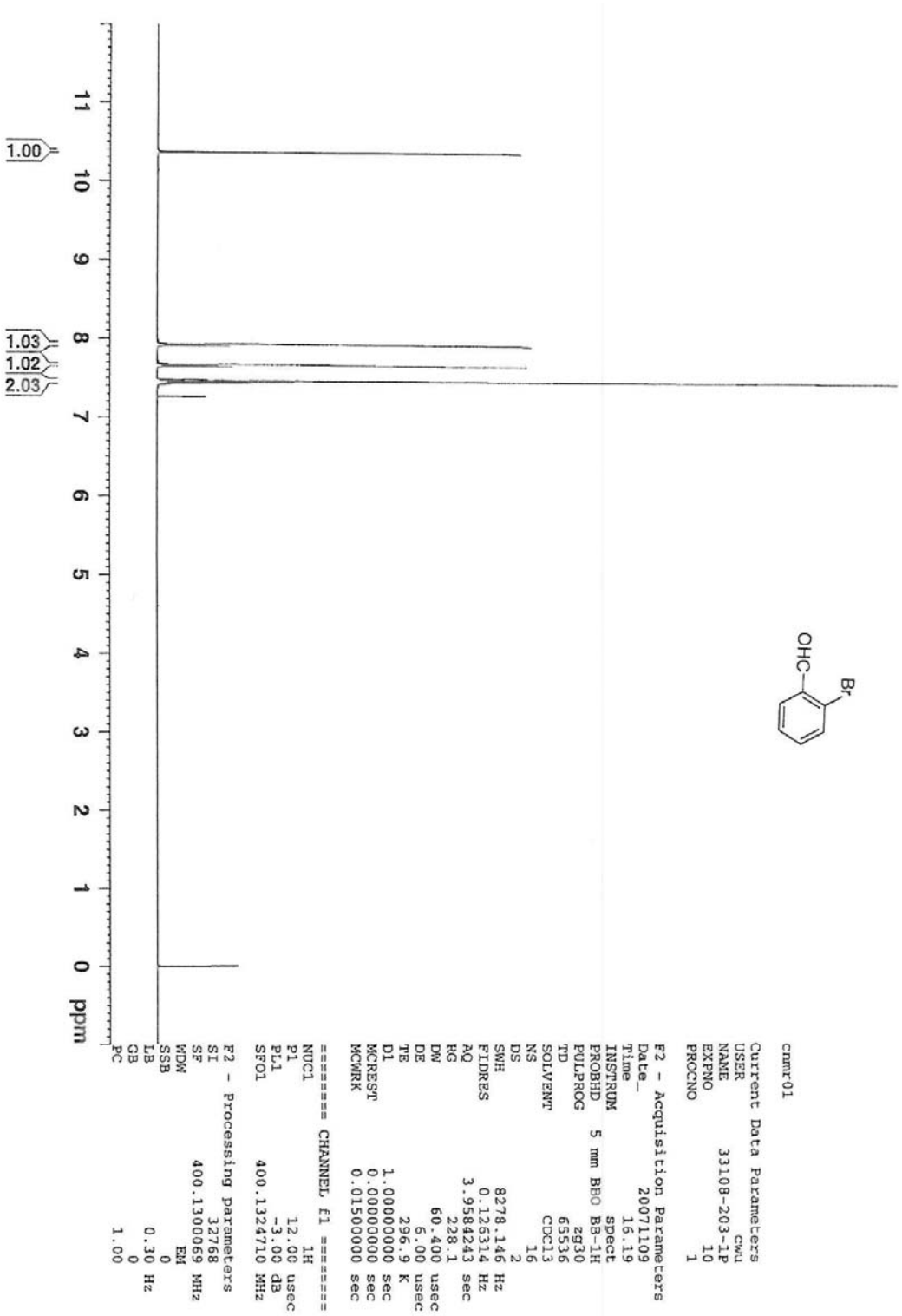

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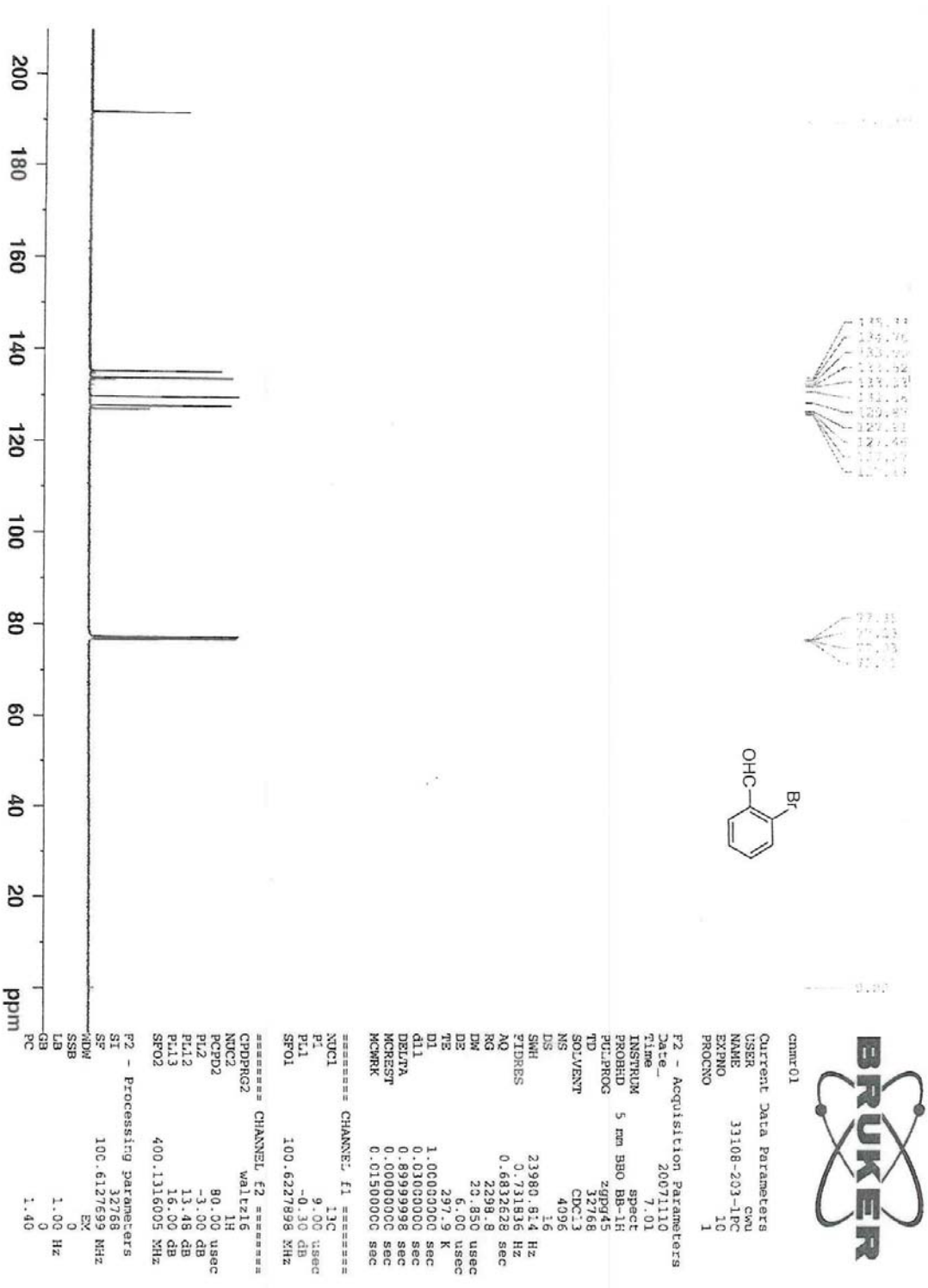

Cyclohexane-1,4-dione (Entry 12, Table 2)