Supplementary Material (ESI) for Chemical Communications

Supporting Information: Part A

(Experimental Procedure and Spectral Data)

PET Imaging of Nobiletin Based on a Practical Total Synthesis

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Analysis instruments

Nuclear magnetic resonance [^{1}H NMR (270 MHz), ^{13}C NMR (68 MHz)] spectra were determined on a JEOL EX-270 instrument, [^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz)] spectra were determined on JEOL ECA-500 and JEOL α-500 instruments, and [^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz)] spectra were determined on JEOL LA-400 instruments. Chemical shifts for ^{1}H NMR were reported in parts per million downfields from tetramethylsilane (δ) as the internal standard and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the centerline of a triplet at 77.0 ppm for deuteriochloroform.

High resolution mass spectra (HRMS) were obtained on a JEOL MStation 700. Fast atom bombardment (FAB) mass spectra were obtained with 3-nitrobenzylalcohol as the matrix and a BRUKER DALTONICS micrOTOF (ESI).

Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F_{254}. Preparative TLC separations were made on 7 x 20 cm plates prepared with a 0.25 mm or 0.50 mm layer of Merck silica gel 60 F_{254}. Compounds were eluted from the adsorbent with 10% methanol in chloroform.

Column chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (spherical) 40 - 50 μm, Silica Gel 60 (spherical) 63 - 210 μm or Silica Gel 60 N (spherical, neutral) 63 - 210 μm.

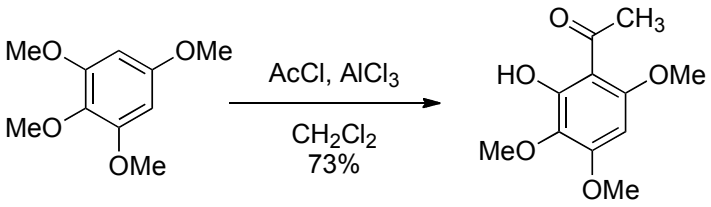
Reagents and solvents were commercial grades and were used as supplied with following exceptions:

Dichloromethane, diethylether, *n*-hexane, tetrahydrofuran toluene: dried over molecular sieves 4A.

Methanol, acetonitrile: dried over molecular sieves 3 A.

All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere.

1-(2-hydroxy-3,4,6-trimethoxyphenyl)ethanone (14)



5 **14**

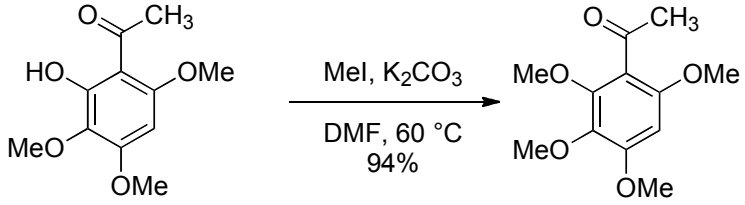
To a solution of **5** (80.2 g, 408 mmol) and AcCl (58 mL, 815 mmol, 2.0 equiv) in CH_2Cl_2 (680 mL) was added $AlCl_3$ (109 g, 815 mmol, 2.0 equiv) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 15 h. After stirring, the reaction mixture was quenched with 6 M HCl at 0 °C, and extracted with CH_2Cl_2. The organic layer was extracted with 2 M NaOH. The aqueous layer was acidified by 6 M HCl. The resulting precipitate was filtered to afford **14** (67.2g, 298 mmol, 73%) as a pale yellow crystal (mp. 114~116°C, lit. 116~118 °C).

^{1}H NMR (270 MHz, $CDCl_3$): δ 13.8 (s, 1H, OH), 5.97 (s 1H, Ar), 3.94 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.62 (s, 3H, CH_3).

Spectral data for **14** were in good agreement with those reported in reference.

D. S. Rycroft, W. J. Cole, S. Rong, *Phytochemistry*, 1998, **48**, 1351.

1-(2,3,4,6-tetramethoxyphenyl)ethanone (6)



14 **6**

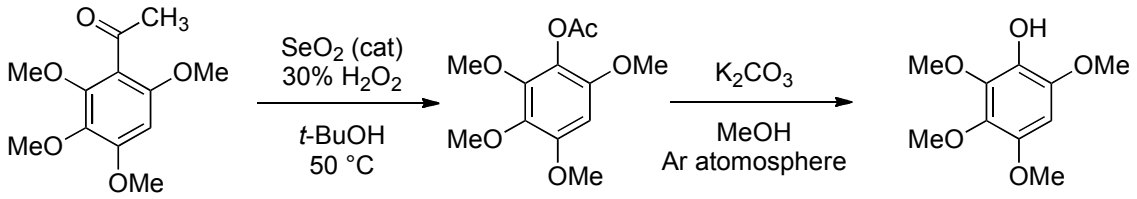
To a mixture of **14** (16.0g, 71 mmol) and K_2CO_3 (20 g, 145 mmol, 2.0 equiv) in DMF (80 mL) was added MeI (6.6 mL, 355 mmol, 5.0 equiv) under Ar atmosphere. The reaction mixture was stirred at 60 °C for 1.5 h. After cooling, the reaction mixture was poured into Et_2O, and filtered through a pad of celite. The filtrate was added to H_2O, and the reaction mixture was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give **6** (16.0 g, 66.7 mmol, 94%) as yellow syrup.

^{1}H NMR (270 MHz, $CDCl_3$): δ 6.26 (s, 1H, Ar), 3.89 (s, 6H, OCH_3), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.48 (s, 3H, CH_3).

Spectral data for **6** were in good agreement with those reported in reference.

D. S. Rycroft, W. J. Cole, S. Rong, *Phytochemistry*, 1998, **48**, 1351.

2-hydroxy-3,4,5,6-tetramethoxybenzene (15)



6 **15** **7**

To a stirred solution of **6** (21.4 g, 89.1 mmol) in *t*-BuOH (450 mL) were added SeO_2 (307 mg, 1.78 mmol, 0.02 equiv) and 30% H_2O_2 (40 mL, 350 mmol, 4.0 equiv) under Ar atmosphere at 50 °C. The reaction mixture was stirred at 50 °C for 10 h. After cooling, the reaction mixture was poured into benzene , and quenched with saturated aqueous $Na_2S_2O_5$. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **15** (15.1 g) was applied to following reaction without further purification.

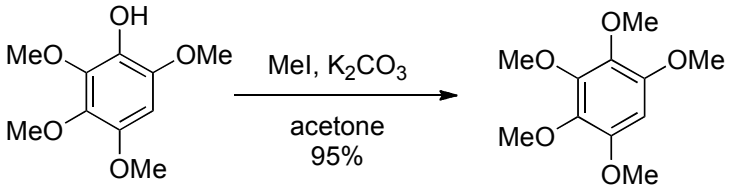
A solution of crude residue **15** (2.1 g) in MeOH (25 mL) was bubbled into Ar gas, then K_2CO_3 (13 g, 27.5 mmol) was added to the solution at room temperature. The reaction mixture was stirred at room temperature for 3 h. After stirring, the reaction mixture was acidified by 6 M HCl to pH 1 at 0 °C, and extracted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10/1, 8/1, 4/1) to afford **7** (850 mg, 3.97 mmol, 51%, 2 steps from **6**) as a pale yellow soild.

^{1}H NMR (270 MHz, $CDCl_3$): δ 6.33 (s, 1H, Ar), 5.23 (s, 1H, OH), 3.96 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3).

Spectral data for **7** were in good agreement with those reported in reference.

M. Tsukayama, E. Kusunoki, M. M. Hossain, Y. Kawamura, S. Hayashi, *Heterocycles*, 2007, **71**, 1589.

1,2,3,4,5-pentamethoxybenzene (8)



7 **8**

To a solution of **7** (900 mg, 4.20 mmol) in acetone (20 mL) were added K_2CO_3 (2.5g, 18.1 mmol, 4.2 equiv) and MeI (1.5 mL, 24.1 mmol, 5.8 equiv) under Ar atmosphere. The reaction mixture was stirred at room temperature for 9.5 h. The reaction mixture was poured into Et_2O, and filtered through a pad of celite. The crude residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 6/1) to afford **8** (910 mg, 3.99 mmol, 95%) as a white solid (mp. 60~61 °C, lit. 59~61 °C).

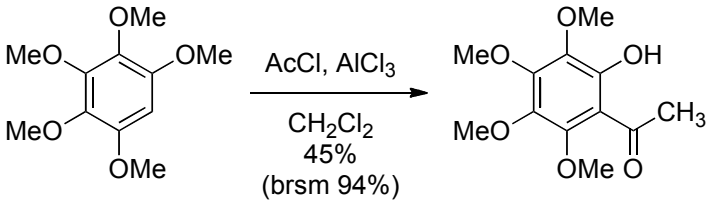
^{1}H NMR (270 MHz, $CDCl_3$): δ 6.30 (s, 1H, Ar), 3.95 (s, 3H, OCH_3), 3.85 (s, 6H, OCH_3), 3.83 (s, 6H, OCH_3).

^{13}C NMR (67.5 MHz, $CDCl_3$): δ 149.1, 147.8, 136.8, 93.8, 61.4, 61.3, 56.4.

Spectral data for **8** were in good agreement with those reported in reference.

M. A. Rahim, A. Nakajima, D. Saigusa, N. Tetsu, Y, Maruyama, M. Shibuya, H. Yamakoshi, Y. Tomioka, Y. Iwabuchi, Y. Ohizumi, T. Yamakuni, *Biochemistry*, 2009, **48**, 7713.

1-(2-hydroxy-3,4,5,6-tetramethoxyphenyl)ethanone (3)



8 **3**

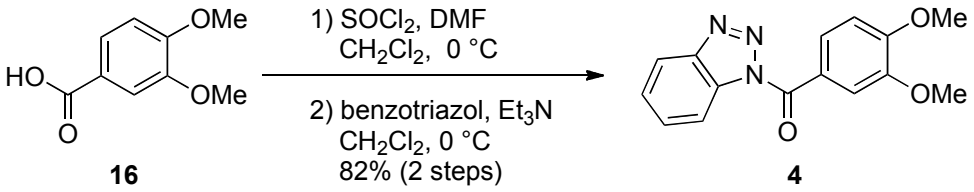
To a solution of **8** (1.0 g, 4.38 mmol) and AcCl (485 μL, 6.14 mmol, 1.4 equiv) in CH_2Cl_2 (10 mL) was added $AlCl_3$ (560 mg, 4.38 mmol, 1.0 equiv) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. The resulting mixture was poured into 2 M NaOH at 0 °C, and washed with Et_2O. The organic layer was washed with 2 M NaOH, and concentrated under reduced pressure to recover starting material (513 mg, 51%). The water layer was combined, acidified with 6 M HCl at 0 °C, and extracted with Et_2O. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford **3** (508 mg, 1.98 mmol, 45%) as a yellow oil.

^{1}H NMR (270 MHz, $CDCl_3$): δ 13.2 (s, 1H, OH), 4.08 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3) , 3.90 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3) 3.82 (s, 3H, OCH_3).2.71(s, 3H, CH_3).

Spectral data for **3** were in good agreement with those reported in reference.

D. S. Rycroft, W. J. Cole, S. Rong, *Phytochemistry*, 1998, **48**, 1351.

(1*H*-benzo[*d*][1,2,3]triazol-1-yl)(3,4-dimethoxyphenyl)methanone (4)



To a solution of **16** (15.0 g, 82.3 mmol) in CH_2Cl_2 (200 mL) were added $SOCl_2$ (9.0 mL, 123 mmol, 1.5 equiv) and DMF (2.5 mL, 33 mol, 0.4 equiv) at 0 °C under Ar atmosphere. The reaction mixture was stirred at 0 °C for 1.5 h. The reaction mixture was concentrated under reduced pressure to give a crude residue including **16'**. The crude mixture was applied to following reaction without further purification.

To a solution of crude material including **16'** in CH_2Cl_2 (170 mL) were added Et_3N (11.4 mL, 82.3 mmol, 1.0 equiv) and benzotriazol (9.8 g, 82.3 mmol, 1.0 equiv) at 0 °C under Ar atmosphere. The reaction mixture was stirred at 0 °C for 30 min. After stirring, the reaction mixture was quenched with 1 M NaOH at room temperature, and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give a residue including **4**. The crude residue was purified by recrystalization from *n*-hexane/CH_2Cl_2 to afford **4** (19.1 g, 67.5 mmol, 82%, 2 steps from **16**) as a white solid (mp. 131~132 °C).

IR (film) 1691, 1271, 1047 cm^{-1}.

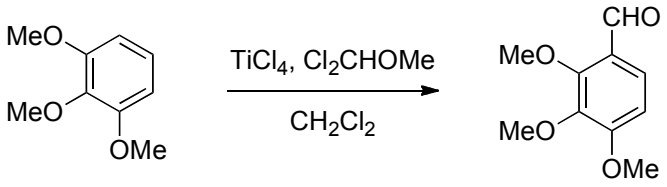
^{1}H NMR (270 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.5 Hz, 1H, Ar), 8.05(d, *J* = 8.5, 1H, Ar), 7.82 (s, 1H, Ar), 7.70 (t, *J* = 7.5 Hz, 1H, Ar), 7.55 (t, *J* = 7.5 Hz, 1H, Ar), 7.04 (d, *J* = 7.5 Hz, 1H, Ar), 4.01 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3).

^{13}C NMR (67.5 MHz, $CDCl_3$): δ 165.5, 153.9, 148.7, 145.5, 132.5, 130.2, 127.2, 126.1, 123.3, 120.0, 114.8, 113.9, 110.2, 56.1, 56.0.

MS (FAB) *m/z* 283 $(M)^+$.

HRMS (ESI) calcd for $C_{15}H_{13}N_3O_3Na^+$ $(M\text{-}Na)^+$ 306.0849, found 306.0855.

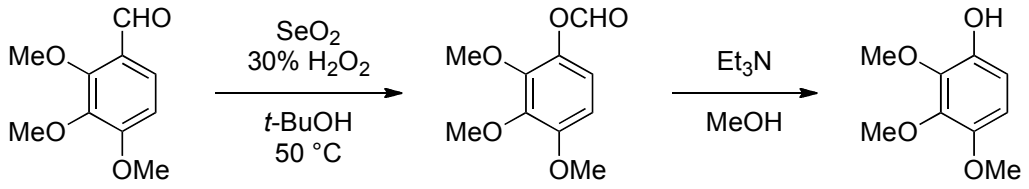
2,3,4-trimethoxybenzaldehyde (17)



9 **17**

To a stirred solution of **9** (44.7 g, 266 mmol) in CH_2Cl_2 (500 mL) were added $TiCl_4$ (58.3 mL, 532 mmol, 2.0 equiv) and Cl_2CHOMe (47 mL, 532 mmol, 2.0 equiv) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 3 h. After stirring, the reaction mixture was poured into cold water, and extracted with CH_2Cl_2. The organic layer was washed with 6 M HCl followed by saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **17** (52.7 g) was applied to following reaction without further purification.

2,3,4-trimethoxyphenol (10)

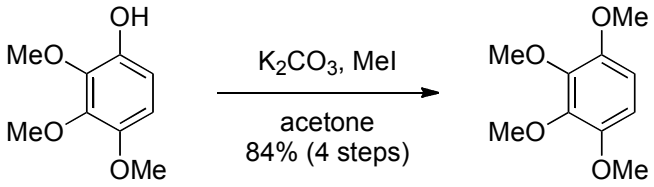


17 **18** **10**

To a solution of crude residue **17** (52.7 g) in *t*-BuOH (500 mL) were added SeO_2 (590 mg, 5.32 mmol, 0.02 equiv) and H_2O_2 (60 mL, 532 mmol, 2.0 equiv) at 50 °C. The reaction mixture was stirred at 50 °C for 1.5 h, and allowed to cool to room temperature. The resulting mixture was quenched with saturated aqueous Na_2SO_3 at 0 °C, poured into water, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **18** (53.6 g) was applied to following reaction without further purification.

To a solution of crude residue **18** (53.6 g) in MeOH (500 mL) was added Et_3N (35 mL, 253 mmol, 1.0 equiv) at 0 °C. The mixture was stirred at room temperature for 0.5 h. The reaction mixture was concentrated under reduced pressure. The crude residue was solved in CH_2Cl_2, and acidified by 2 M HCl. The organic layer was extracted with 2 M NaOH. The water layer was acidified by 6 M HCl, and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **10** (46.3 g) was applied to following reaction without further purification.

1,2,3,4-tetramethoxybenzene (11)



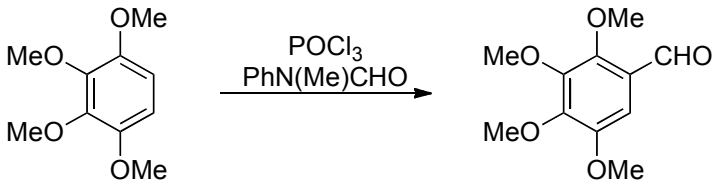
10 **11**

To a stirred solution of crude residue **10** (46.3 g) in acetone (500 mL) were added K_2CO_3 (69.5 g, 503 mmol, 1.9 equiv) and MeI (31.3 mL, 503 mmol, 1.9 equiv) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 40 h. The resulting mixture was poured into Et_2O, and filtered through a pad of celite. The filtrate was concentrated under reduced pressure. The crude residue was washed with MeOH, and filtered to afford **11** (44.3 g, 233 mmol, 84%, 4 steps from **9**) as a white solid (mp. 86~89 °C, lit. 85~88 °C).

Spectral data for **11** were in good agreement with those reported in reference.

J. W. Frost, C. A. Hansen, *US patent*, 2004, 6750049 B1

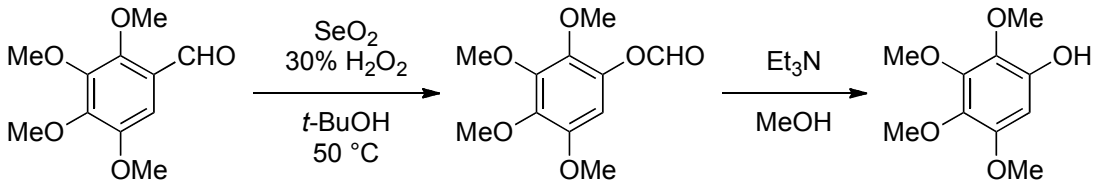
2,3,4,5-tetramethoxybenzaldehyde (19)



11 **19**

$POCl_3$ (0.73 mL, 8.07 mmol, 1.6 equiv) and *N*-methyl formanilide (0.18 g, 1.35 mmol) were stirred at room temperature for 20 min. The reaction mixture was added **11** (1.0 g, 5.04 mmol), and stirred at 60 °C for 6 h. After cooling, the reaction mixture was quenched with water at 0 °C, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **19** (1.5 g) was applied to following reaction without further purification.

2,3,4,5-tetramethoxyphenol (12)

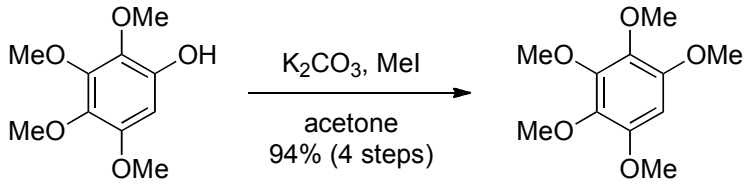


19 **20** **12**

To a solution of crude residue **19** (1.5 g) in *t*-BuOH (10 mL) were added SeO_2 (11 mg, 0.151 mmol, 0.03 equiv) and H_2O_2 (1.14 mL, 10.1 mmol, 2.0 equiv) at 50 °C. The reaction mixture was stirred at 50 °C for 2.5 h, and allowed to cool to room temperature. The resulting mixture was quenched with saturated aqueous Na_2SO_3 at 0 °C, poured into water, and extracted with EtOAc. The organic layer was washed with water followed by brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **20** (1.7 g) was applied to following reaction without further purification.

To a solution of crude residue **20** (1.7 g) in MeOH (16 mL) was added Et_3N (0.7 mL, 5.04 mmol, 1.0 equiv) at 0 °C. The mixture was stirred at room temperature for 45 min. The reaction mixture was concentrated under reduced pressure. The residue was solved in CH_2Cl_2, and acidified by 2 M HCl. The organic layer was extracted with 2 M NaOH. The water layer was acidified by 6 M HCl, and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue **12** (1.03 g) was applied to following reaction without further purification.

1,2,3,4,5-pentamethoxybenzene (8)



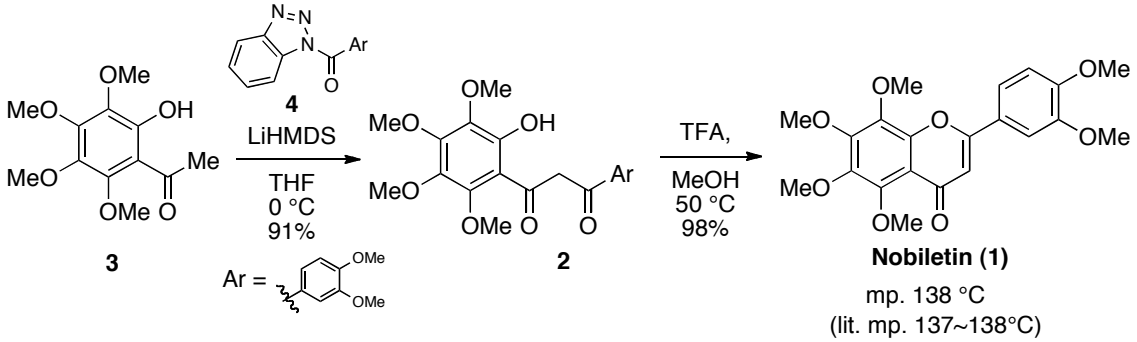
12 **8**

To a mixture of crude **12** (1.03 g) and K_2CO_3 (1.33g, 9.62 mmol, 1.9 equiv) in acetone (16 mL) was added MeI (0.6 mL, 9.62 mmol, 1.9 equiv) under Ar atmosphere. The reaction mixture was stirred at room temperature for 36 h. The resulting mixture was poured into Et_2O, and filtered through a pad of celite. The filtrate was concentrated under reduced pressure to afford **8** (1.08 g, 4.74 mmol, 94%, 4 steps from **11**) as a pale yellow solid (mp. 60~ 61°C, lit. 59~61 °C).

Spectral data for **8** were in good agreement with those reported in reference.

M. A. Rahim, A. Nakajima, D. Saigusa, N. Tetsu, Y, Maruyama, M. Shibuya, H. Yamakoshi, Y. Tomioka, Y. Iwabuchi, Y. Ohizumi, T. Yamakuni, *Biochemistry*, 2009, **48**, 7713.

Nobiletin (1)



To a mixture of **3** (5.2 g, 0.69 mmol) and **4** (6.3 g, 0.76 mmol, 1.1 equiv) in THF (40 mL) was added LHMDS (81 mL, 81 mmol, 4.0 equiv, 1 M sol. in THF) under Ar atmosphere at -30 °C. The reaction mixture was stirred at 0 °C for 2 h. The resulting mixture was quenched with saturated aqueous NH_4Cl at 0 °C, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give a residue including **21**. The residue was purified by recrystallization from EtOAc/n-Hexane to afford **21** (7.8 g, ca 91%) as a yellow solid. The crude solid was applied to following reaction without further purification.

To a solution of crude solid including **21** (3.1 g) in MeOH (30 mL) was added TFA (3 mL) at room temperature. The reaction mixture was stirred at 50 °C for 24 h. After stirring, the reaction mixture was concentrated under reduced pressure to give a residue including **1**. The residue was purified by recrystallization from hot MeOH to afford **1** (2.9 g, 98%) as a pale yellow solid (mp. 138 °C, lit 137~138 °C).

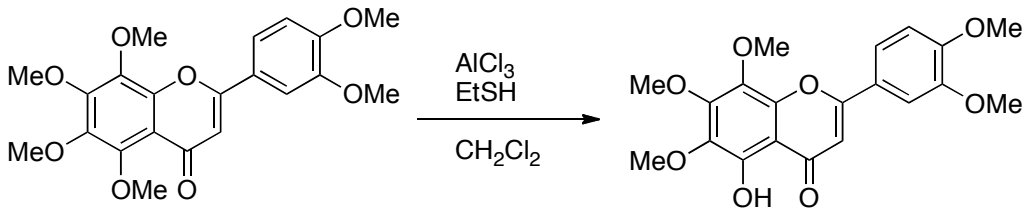
^{1}H NMR (270 MHz, $CDCl_3$): δ 7.57 (d, J_1 = 8.6 Hz, J_2 = 2.1 Hz, 1H, Ar), 7.42 (d, J = 2.1 Hz, 1H, Ar), 7.00 (d, J = 8.6 Hz, 1H, Ar), 6.62 (d, 1H, CH), 4.11 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.00-3.95 (m, 12H, OCH_3).

Spectral data for **1** were in good agreement with those reported in reference.

W. Dandana, W. Jian, H. Xuehui, T. Ying, N. Kunyi, *J. Pharm. Biomed. Anal.,* 2007, **44**, 63.

a

5-desmethylnobiletin (13)



1 **13**

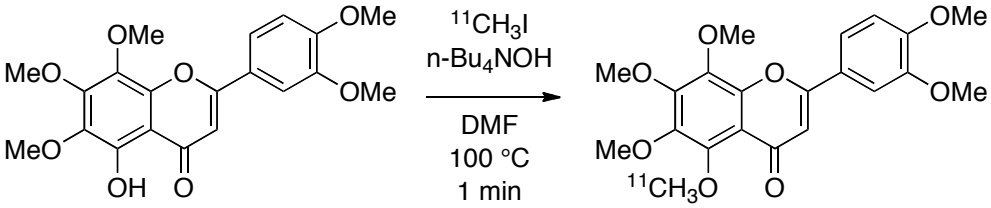
To a solution of **1** (50 mg, 0.13 mmol) in CH_2Cl_2 (40 mL) was added $AlCl_3$ (33 mg, 0.26 mmol, 2.0 equiv) in EtSH (0.66 mL) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. The resulting mixture was quenched with 6 M HCl at 0 °C, and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 2/1-1/1) to afford **13** (36 mg, 76%) as yellow needles (mp. 145 °C, lit. 146~147 °C).

^{1}H NMR (270 MHz, $CDCl_3$): δ 12.5(s, 1H, ArOH), 7.59 (dd, J_1 = 8.1 Hz, J_2 = 2.7 Hz, 1H, Ar), 7.42 (d, J = 2.7 Hz, 1H, Ar), 7.00 (d, J = 8.1 Hz, 1H, Ar), 6.62 (d, 1H, CH), 4.11 (s, 3H, OCH_3), 4.00-3.95 (m, 12H, OCH_3).

Spectral data for **1** were in good agreement with those reported in reference.

X. Wang, F. Li, H. Zhang, Y. Geng, J. Yuan, T. Jiang. *J. Chromatogr. A,* 2005, **1090**, 188.

5-[^{11}C]-Nobiletin ([^{11}C]-1)



13 **[^{11}C]-1**

Radioactive ^{11}C was generated by the ^{14}N(p, α)^{11}C nuclear reaction using the cyclotron. Preparation of [^{11}C]CH_3I and subsequent ^{11}C-methylation of **13** to **[^{11}C]-1** were achieved automatically using specially designed equipment. The [^{11}C] CH_3I prepared was trapped in anhydrous DMF containing **13** (1.0 mg) and 10% aqueous tetrabutylammonium hydroxide. The reaction vessel was heated at 100°C and kept there for 1 min. The radioactive mixture containing **[^{11}C]-1** was quenched by addition of an HPLC mobile phase (0.5 mL) and then applied to a column (Inertsil ODS3 (7.6*250 mm)). The column was eluted with CH_3CN/H_2O (400/600) at a flow rate of 6.0 mL/min, and a radioactive fraction having a retention time of 11 min was collected in a flask. After evaporation of the solvents from the flask under reduced pressure, the pure **[^{11}C]-1** was recovered by saline containing 0.1% Tween80.

2.3. Radiochemical purity and specific activity determinations

Radiochemical purity was assayed by analytical HPLC (column: Inertsil ODS3 (4.6*150 mm, 5u), UV at 250 nm, mobile phase: CH_3CN/H_2O = 500:500). The retention time was 3.6 min for **[^{11}C]-1** at a flow rate of 2.0 mL/min. Confirmation of the identity of **[^{11}C]-1** was achieved by co-injection with the authentic **1.** For the determination of specific activity, mass (μmol) of **[^{11}C]-1** with a known radioactivity (GBq) was determined by HPLC comparison of UV absorbance at 250 nm of the radioligand with those of known concentrations of non- radioactive nobiletin **1.**

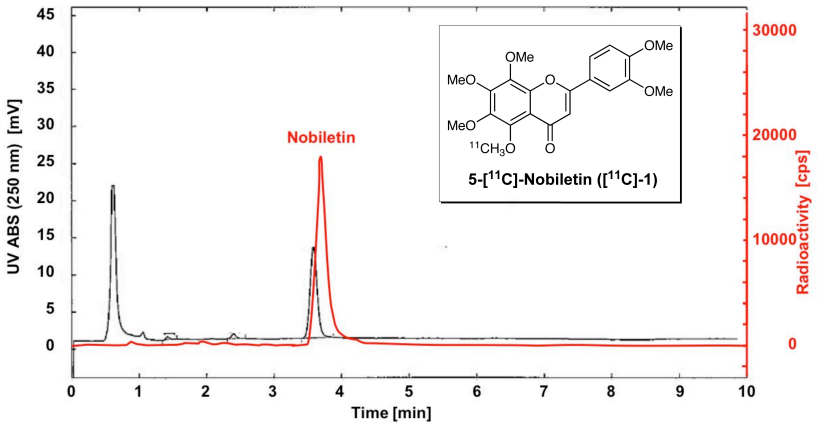


Figure 1. HPLC chromatogram of [^{11}C]-nobiletin (**[^{11}C]-1**) (after purification).

*2.4. PET study**

The distribution of **[^{11}C]-1** was determined with a small-animal PET system (Clairvivo PET, Shimadzu Corporation, Kyoto, Japan). Before PET analysis, an 8-month-old SD rat (Japan SLC Inc., Shizuoka, Japan) anesthetized with chloral hydrate was placed on the animal CT to obtain CT image. Purified **[^{11}C]-1** was diluted with saline containing 0.1% Tween80 to adjust the radioactivity at a dose of 10 MBq for injection (10 MBq/rat). Then, the **[^{11}C]-1** solution was intravenously injected into the rat via the tail vein, and PET scan was started immediately and continued for 60 min. The radioactivity in the form of coincident gamma photons was measured and converted to Bq/cm^3 of tissue volume by calibration after correction for decay and attenuation. A time activity curve was obtained from the mean voxel radioactivity in the region of interest of the PET images and analyzed by using software *ImageJ*.

*2.5 Biodistribution of [^{11}C]Nobiletin**

SD male rats (n=4) were injected with **[^{11}C]-1** solution (10 MBq/rat) via the tail vein. At 5 min after the injection, the rats were sacrificed, and the blood and organs (heart, lungs, liver, spleen, kidneys, and brain) were removed. The radioactivity of blood and each organ was measured by using an auto gamma counter (1480 Wizard 3, Perkin Elmer, USA).

*Animal care and experiments were performed in accordance with the Guidelines for the Care and Use of Laboratory Animals of the University of Shizuoka.

Supplementary Material (ESI) for Chemical Communications

Supporting Information: Part B

(^{1}H and ^{13}C Spectral Data)

PET Imaging of Nobiletin Based on a Practical Total Synthesis

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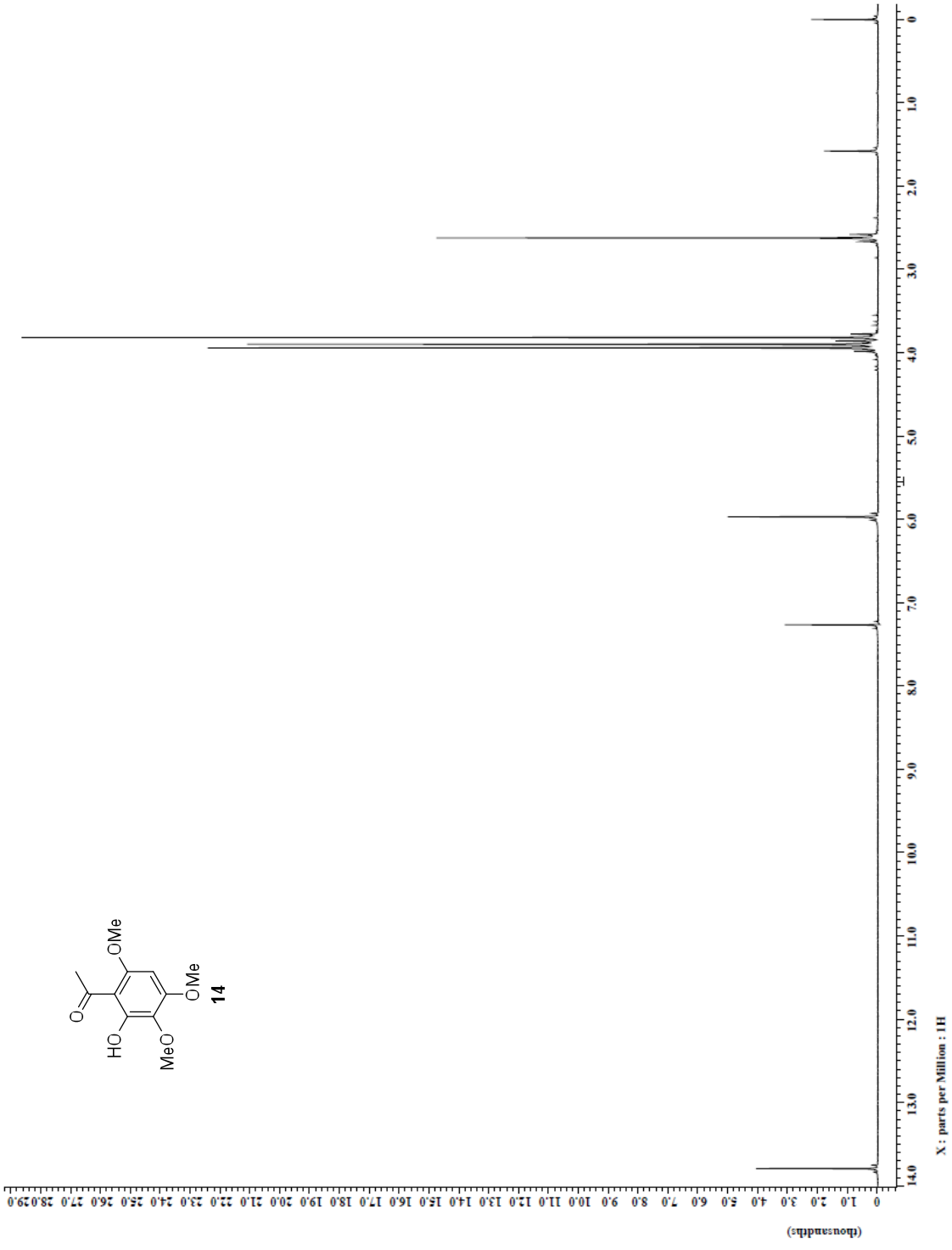
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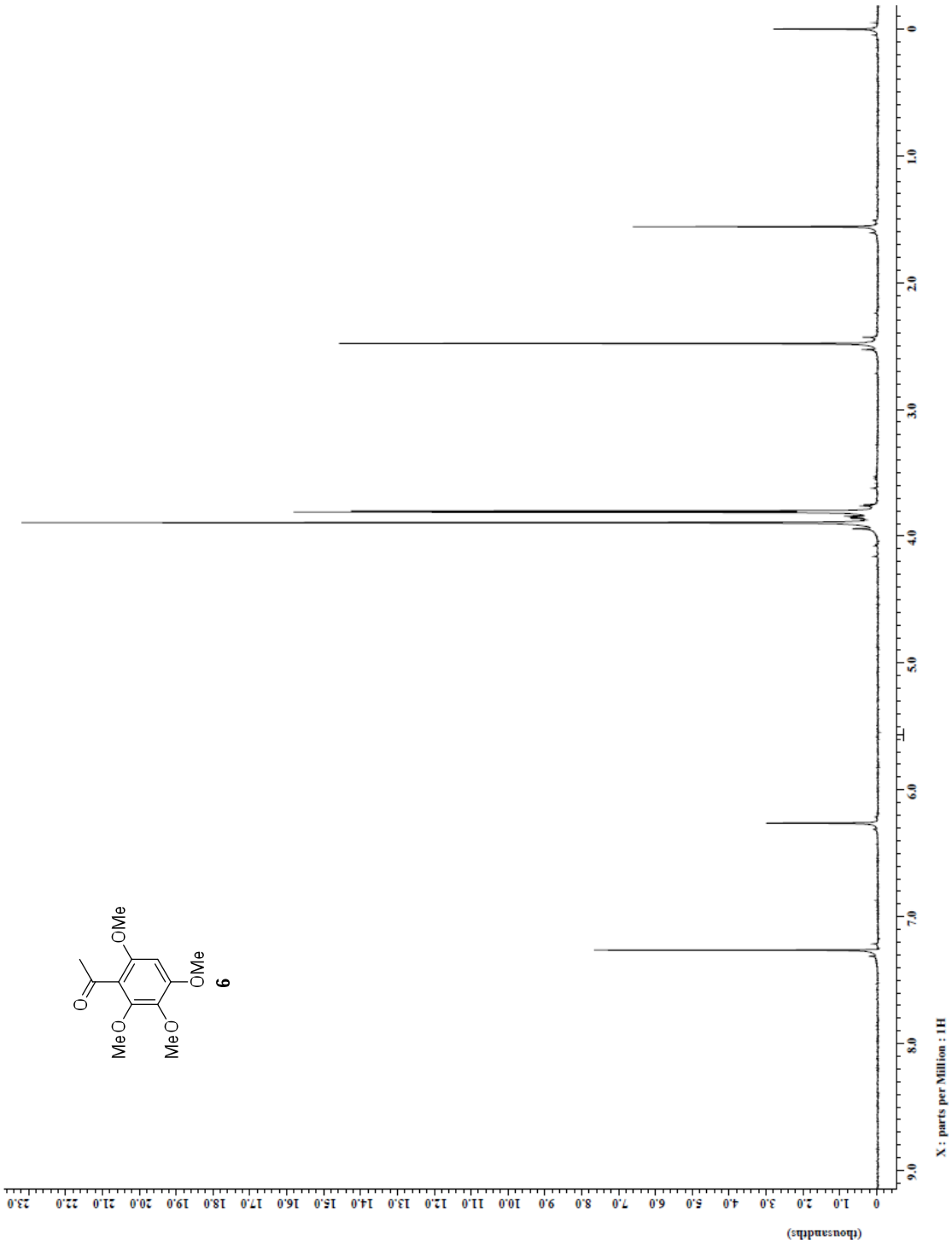
HO
MeO
14
X : parts per Million : 1H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O
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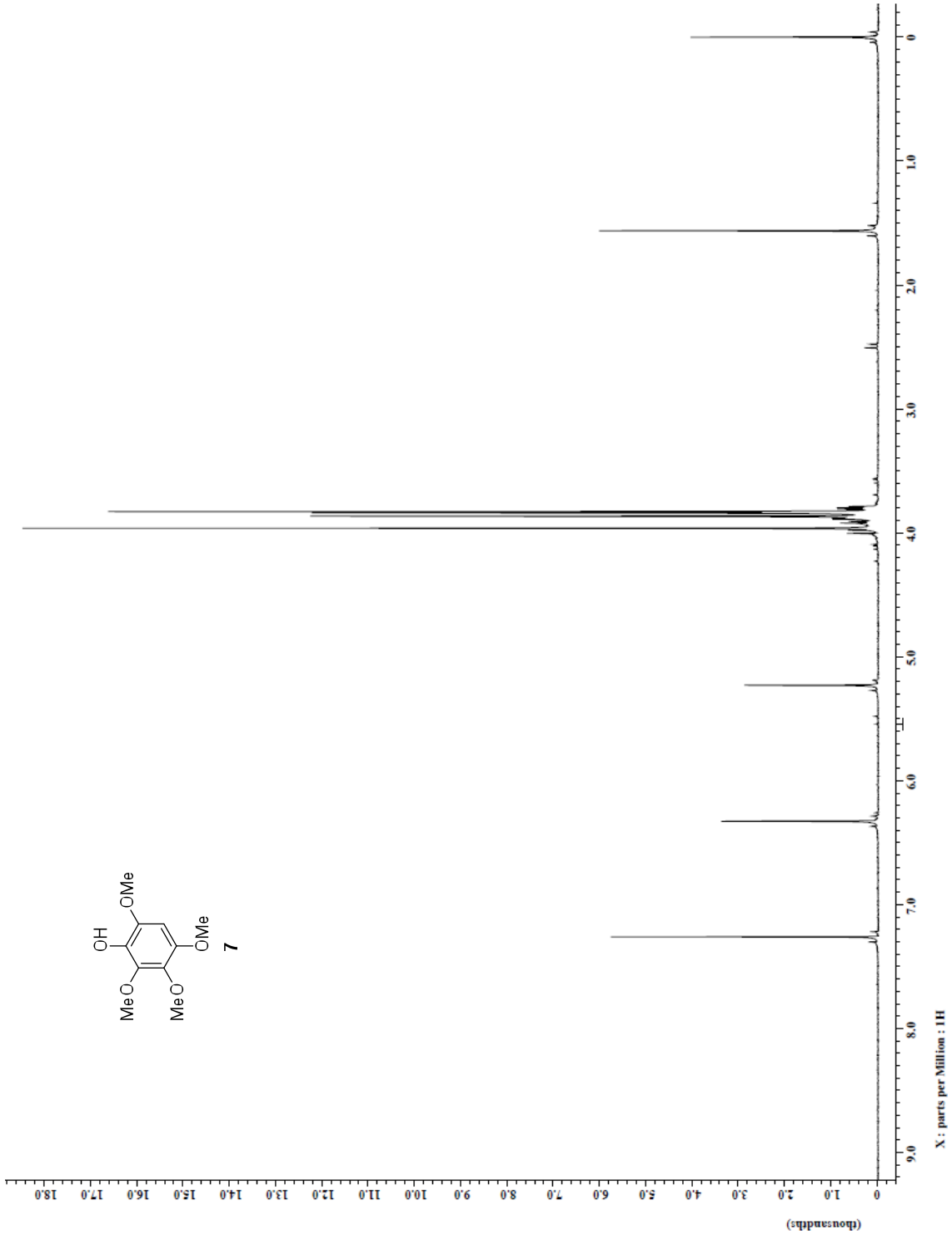
(thousandths)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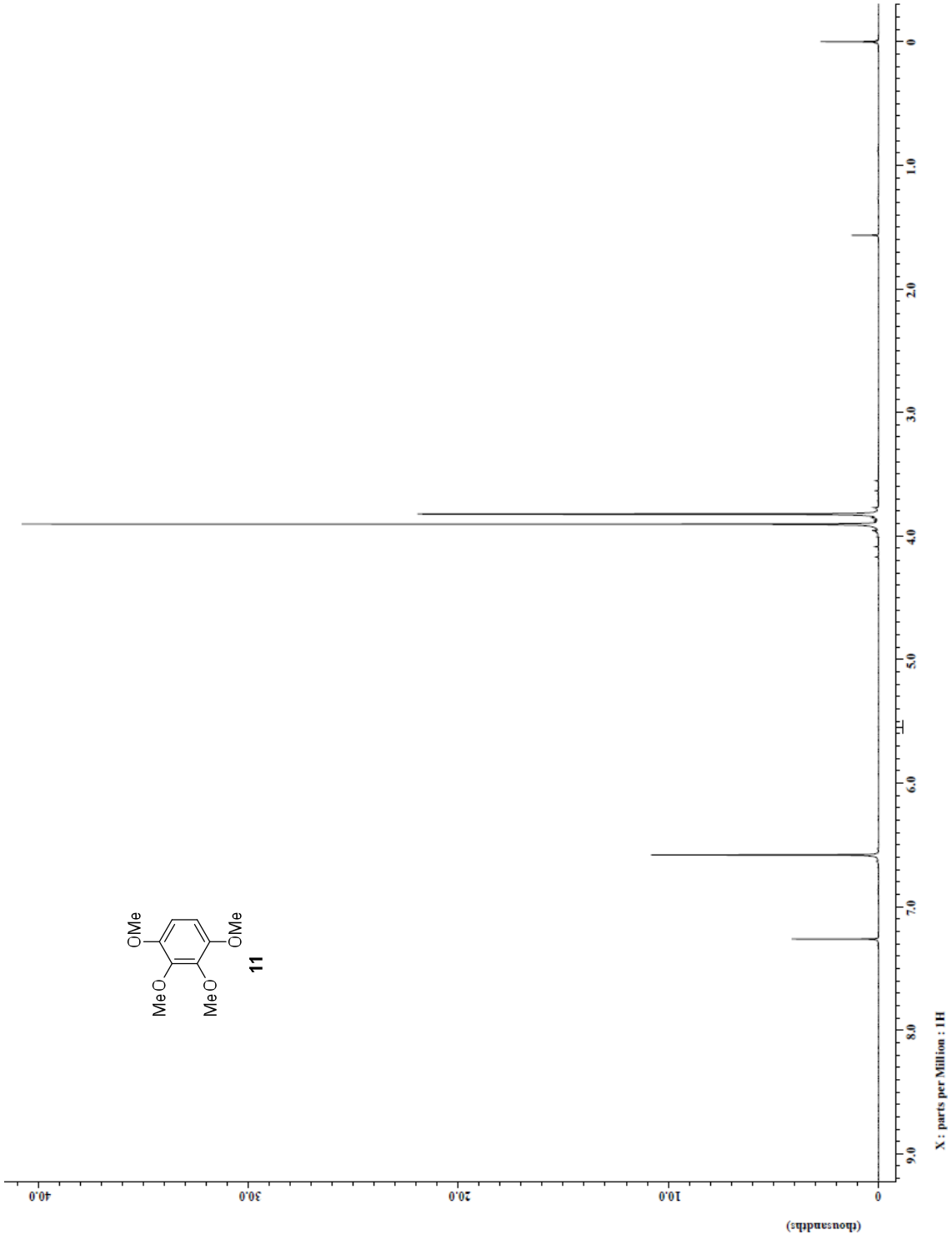
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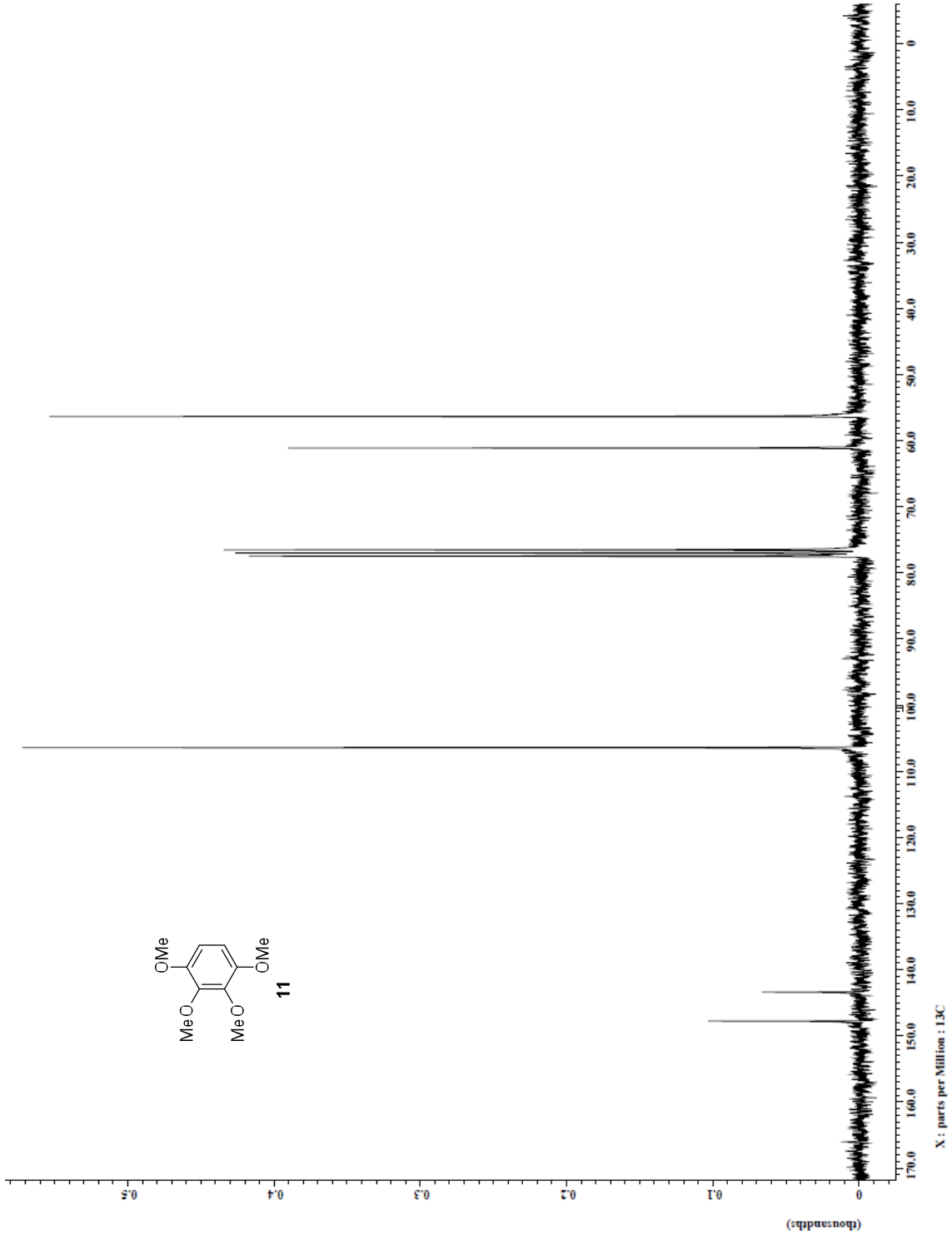
(thousandths)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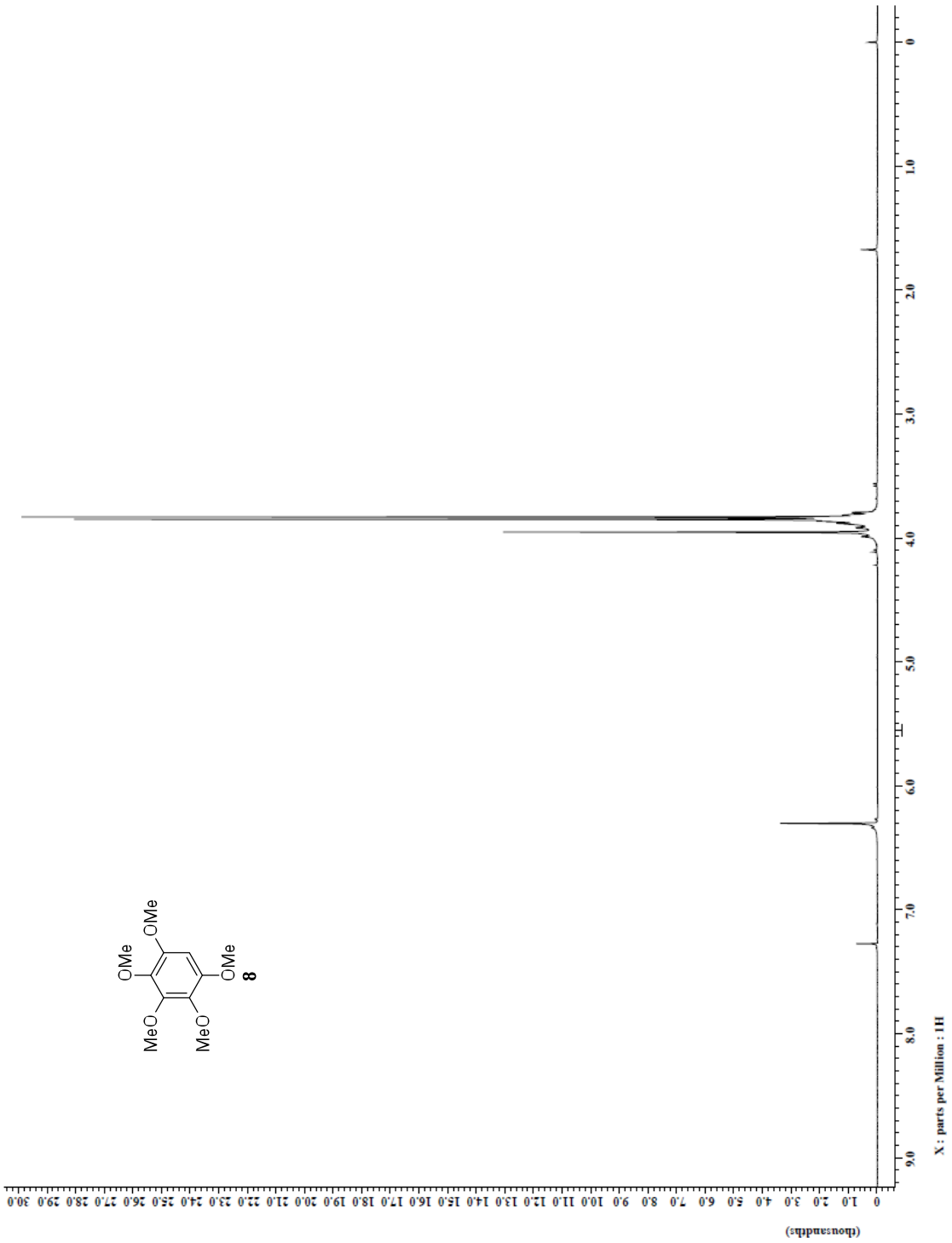
(thousandths)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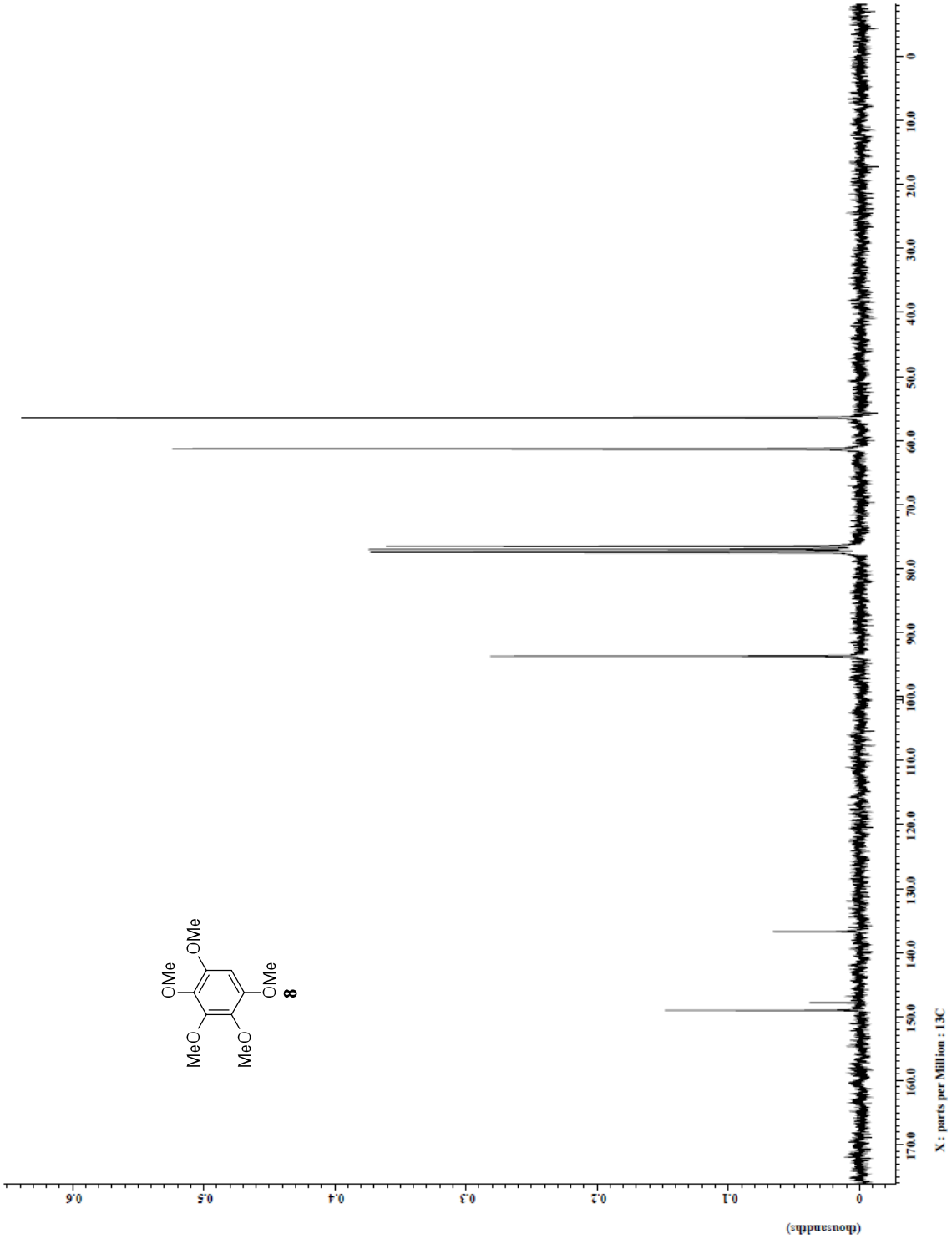
(thousandths)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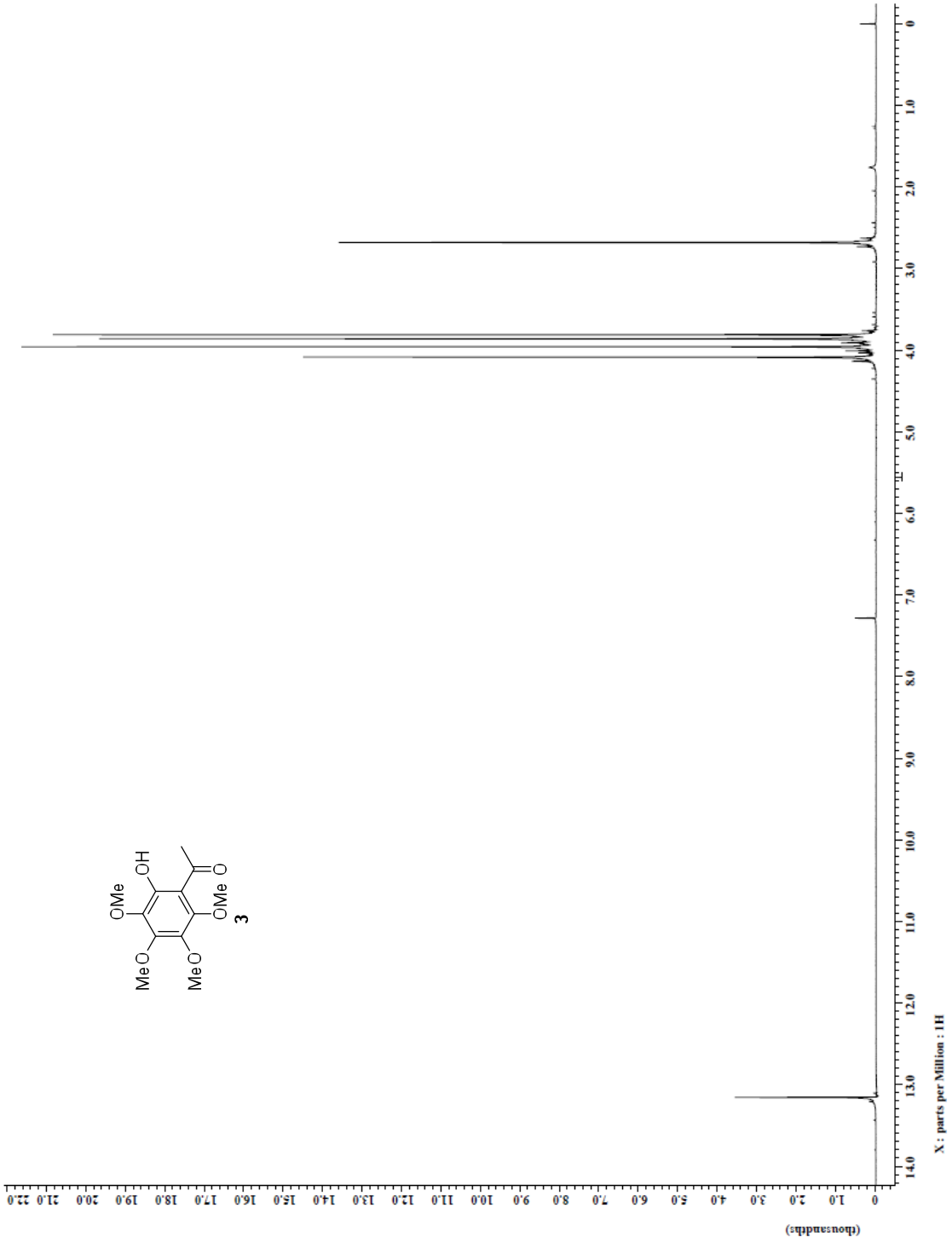
(thousandths)
X : parts per Million : 13C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MeO
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O
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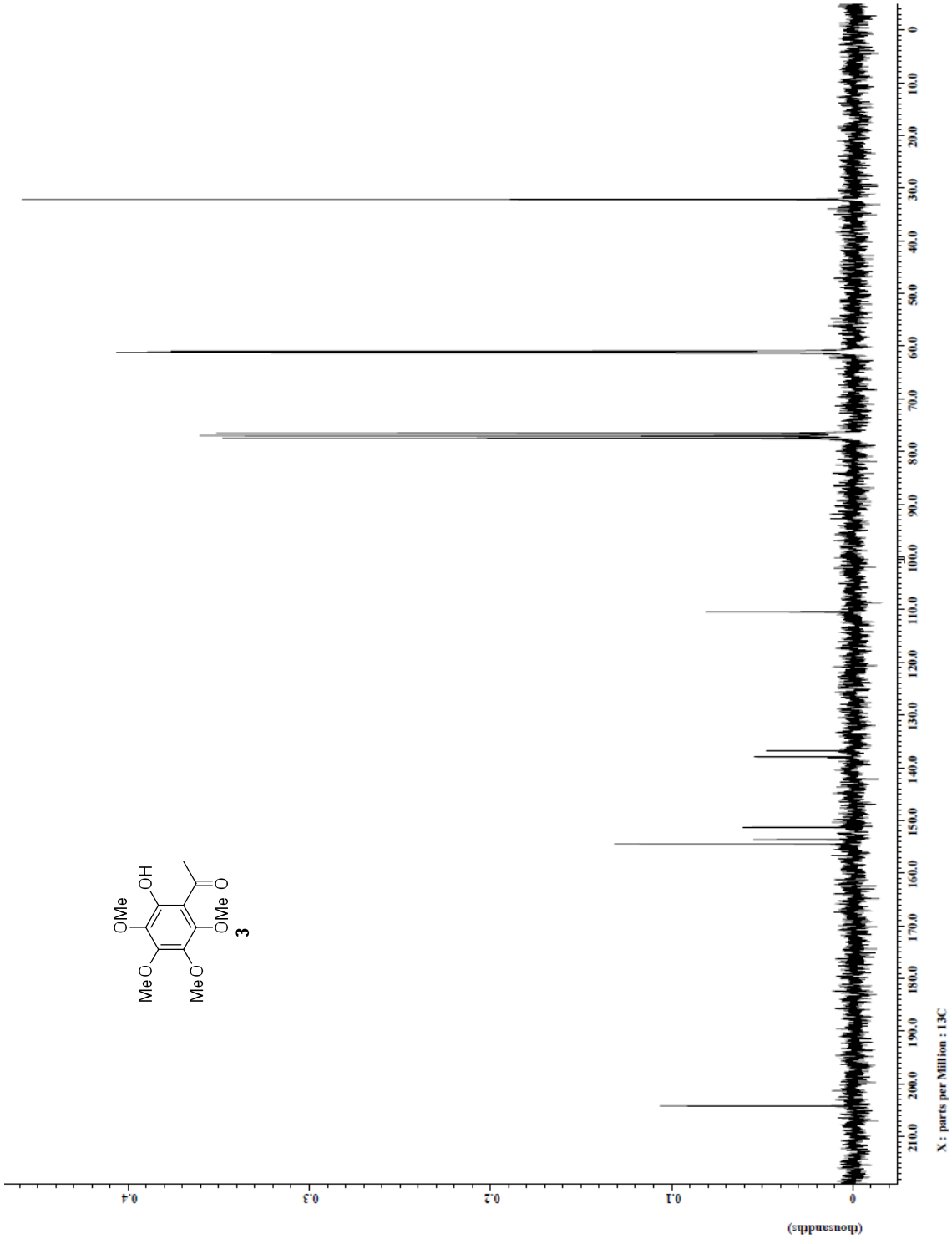
X : parts per Million : 1H
(thousandths)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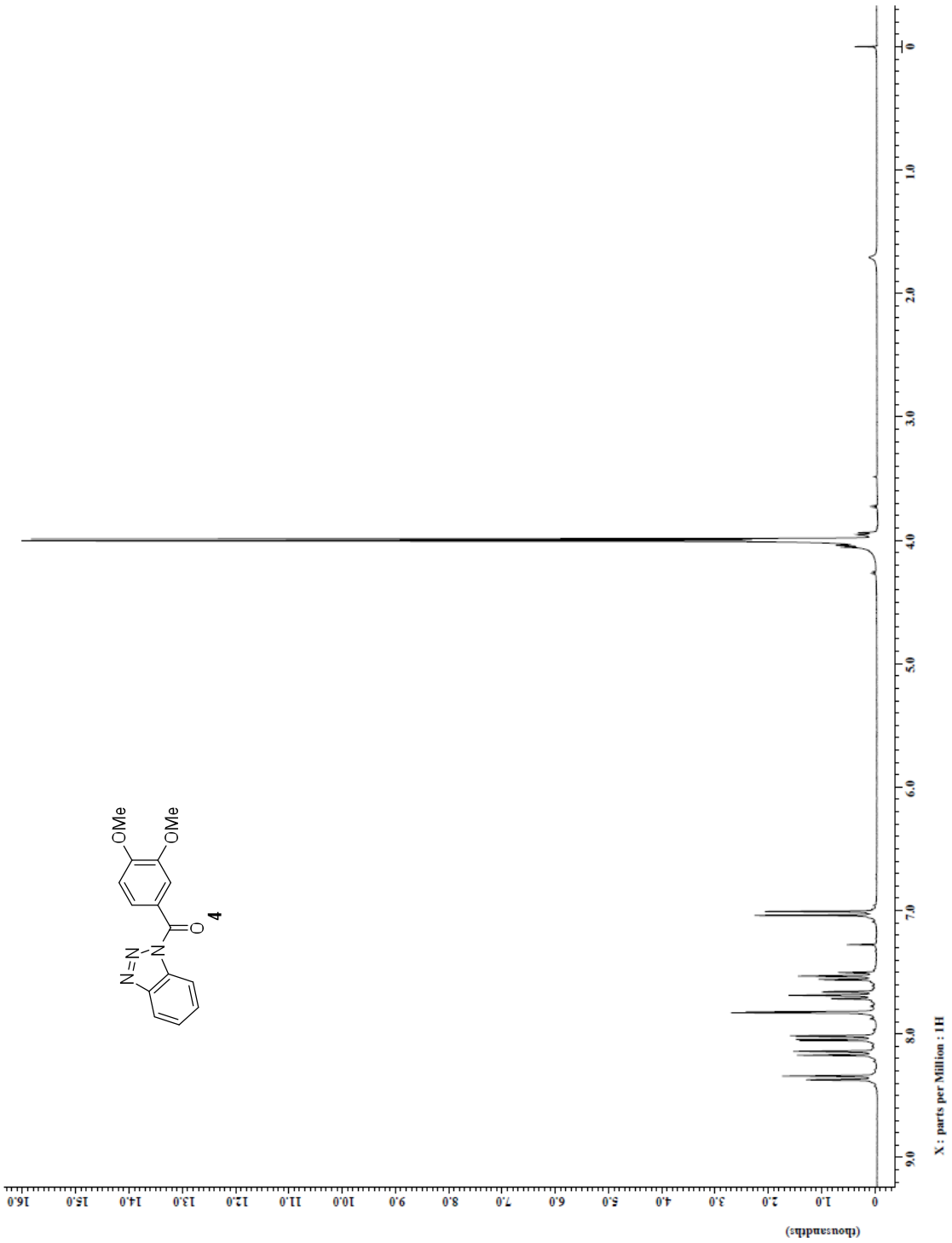
(thousandths)
X : parts per Million : 13C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N
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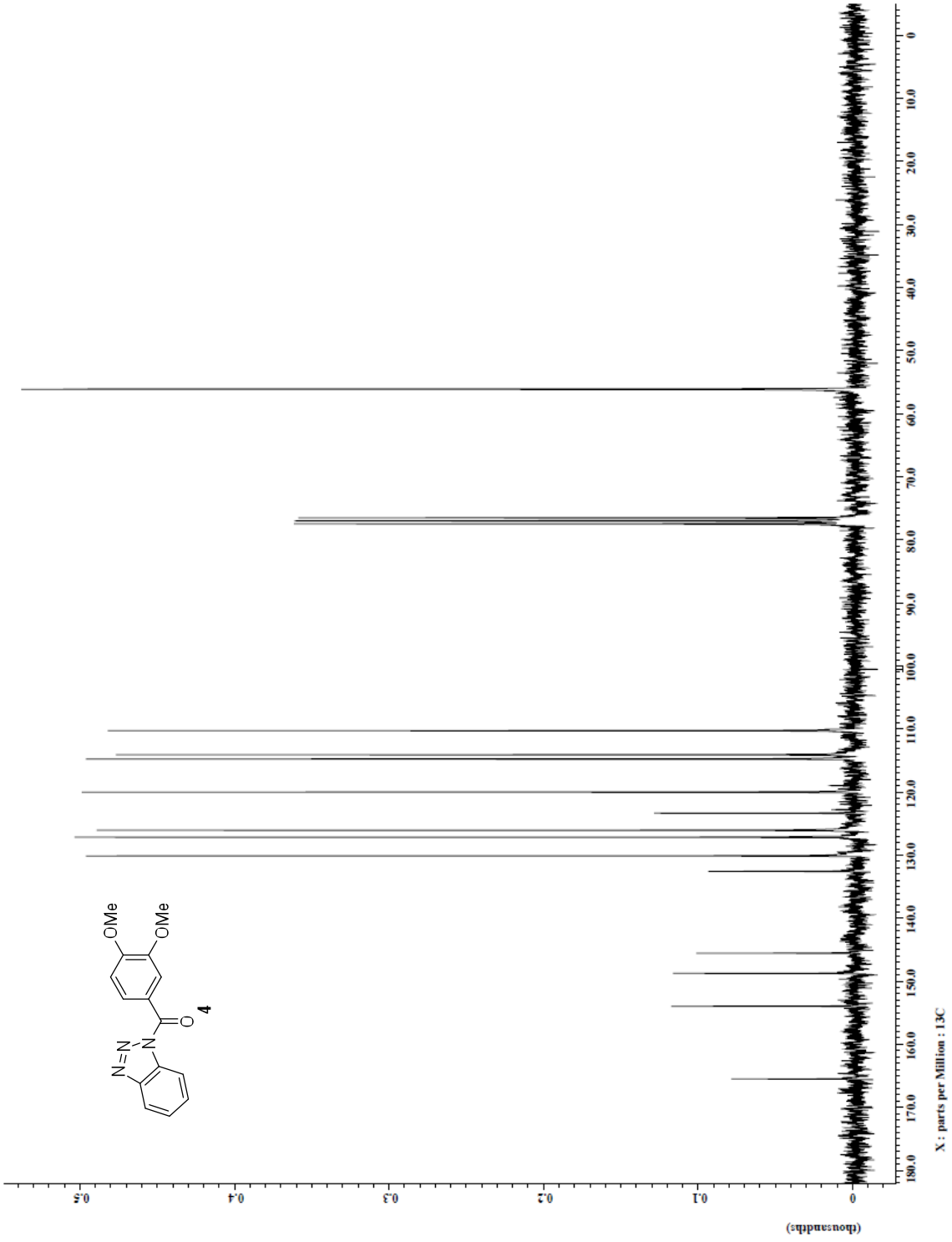
(thousandths)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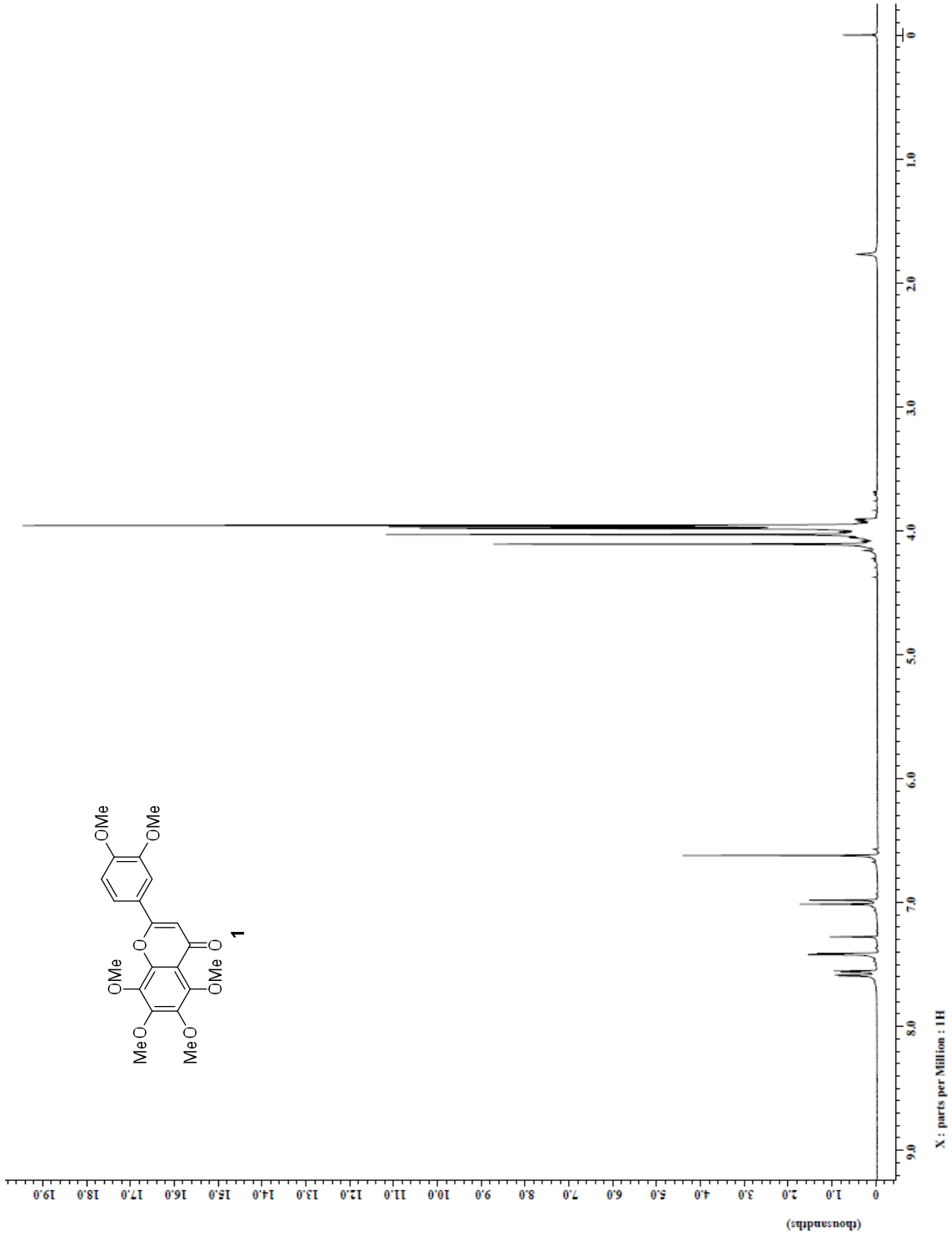
X : parts per Million : 13C
(thousandths)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MeO
MeO
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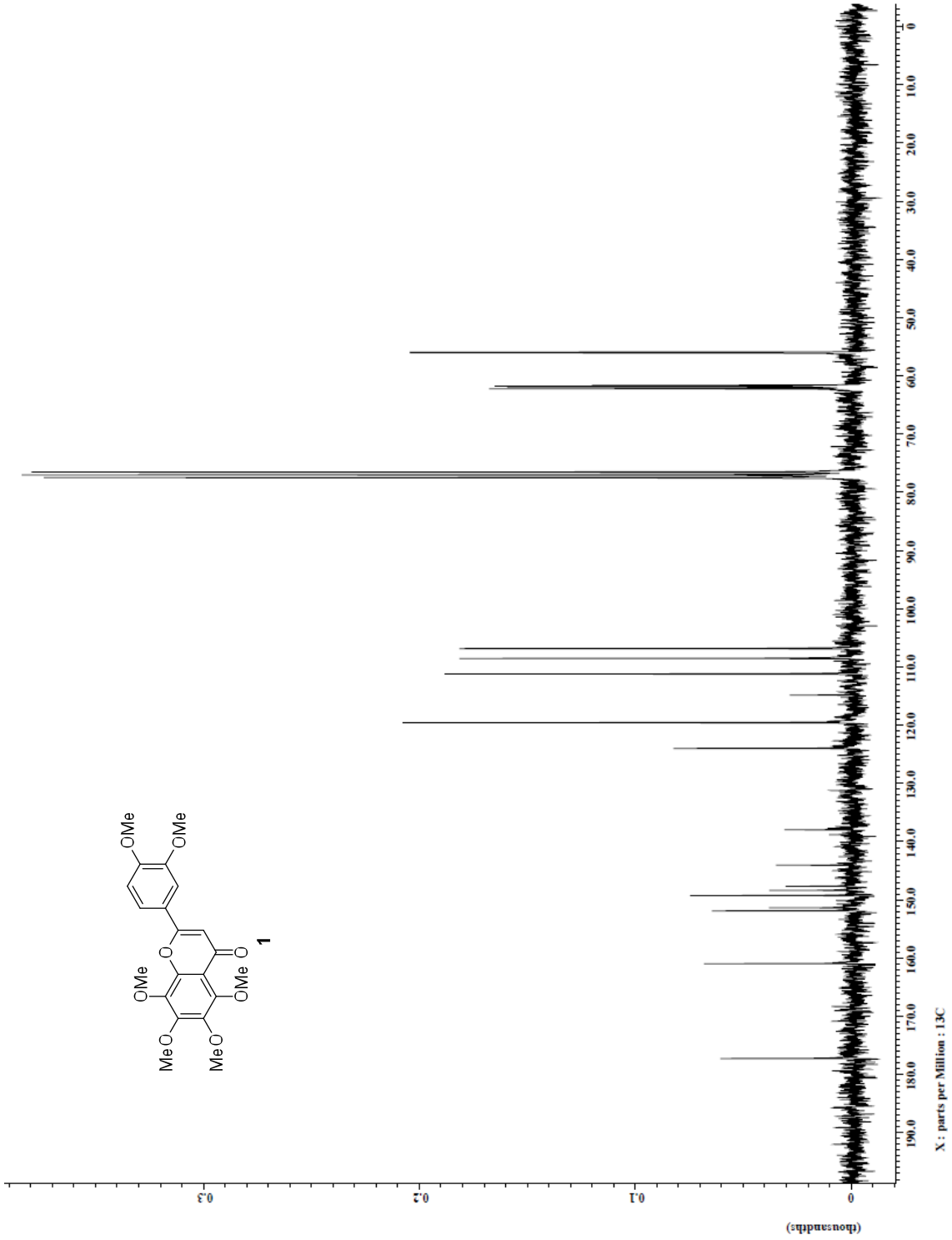
(thousandths)
X : parts per Million : 1H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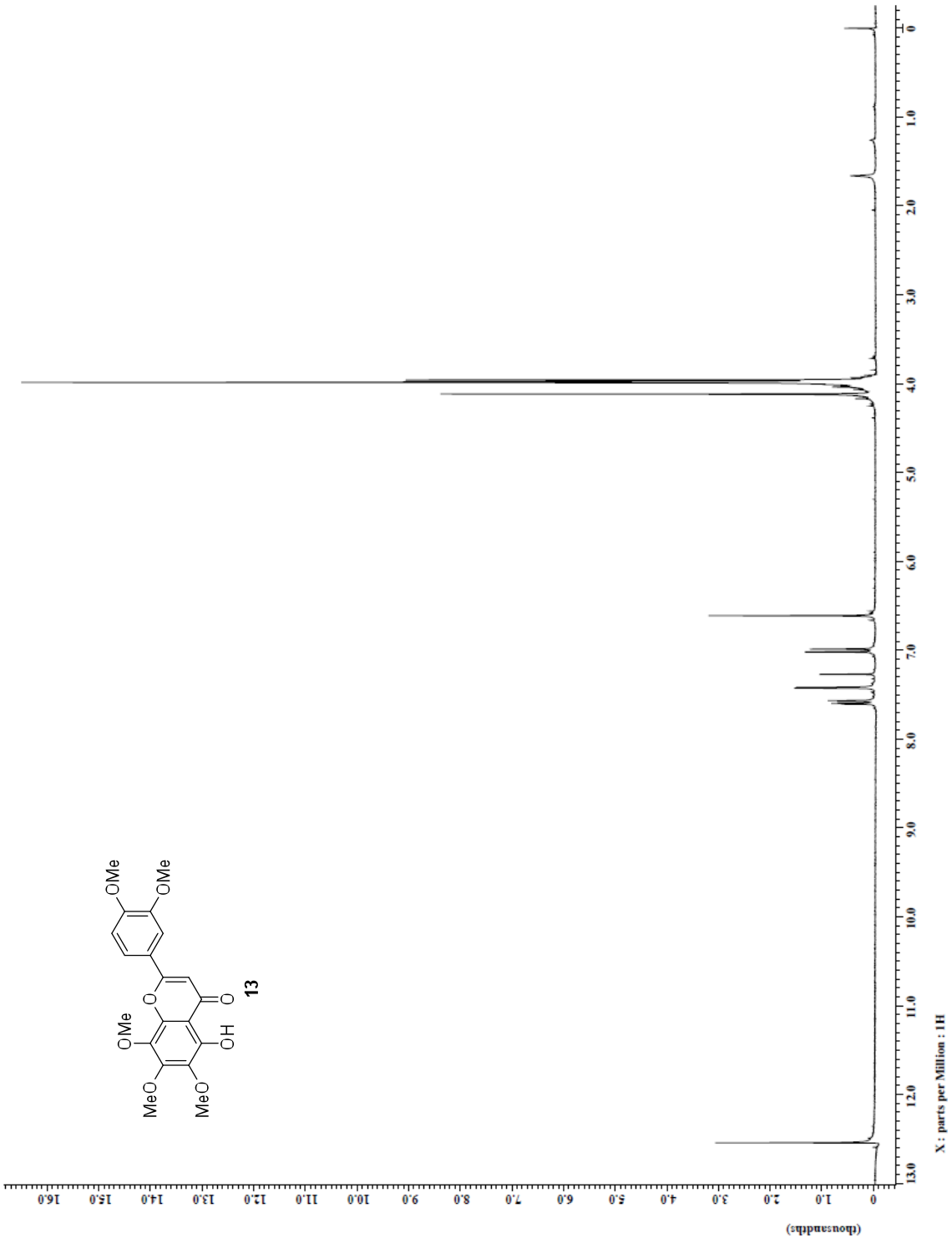
X : parts per Million : 13C
(thousandths)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OMe
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MeO
HO
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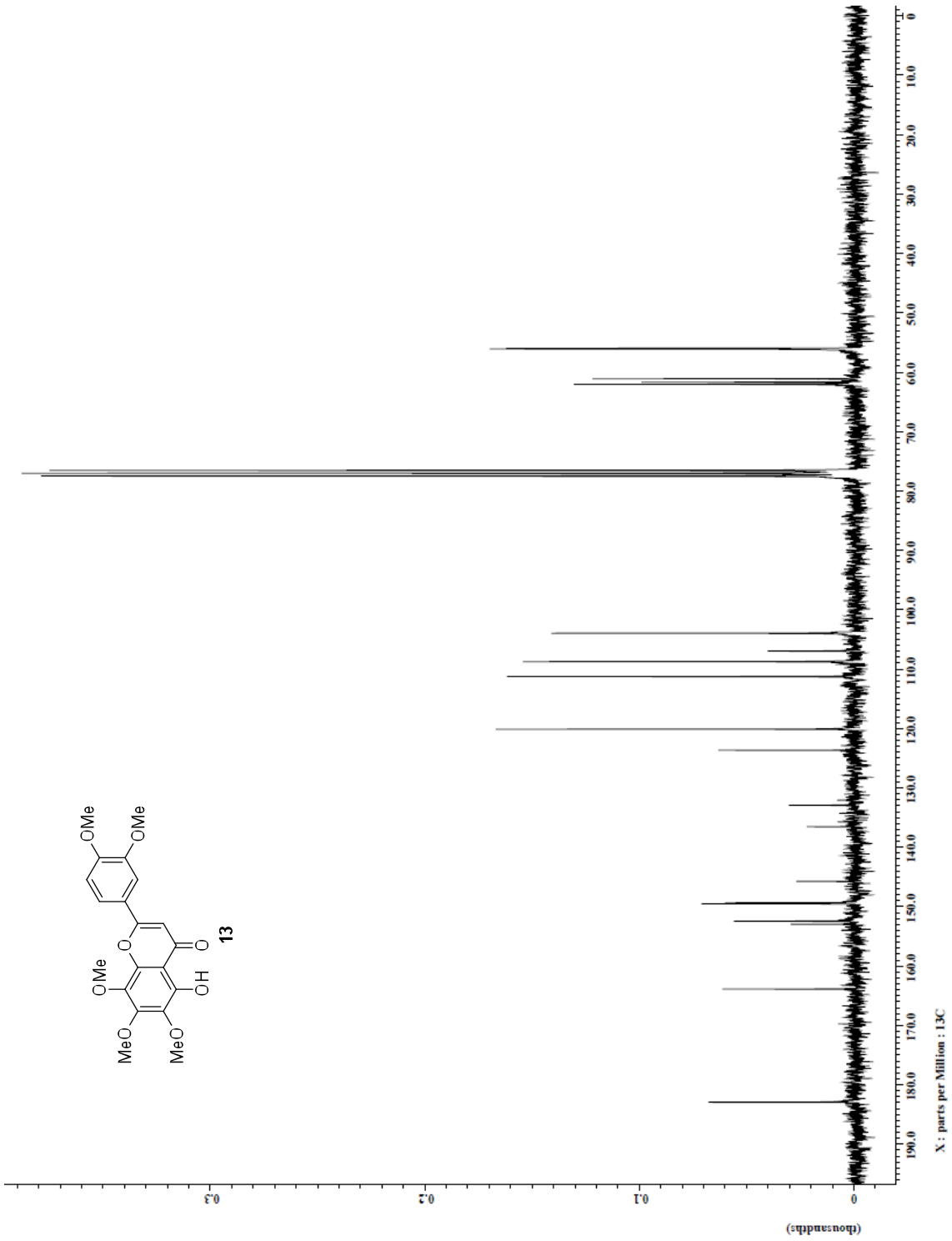
X : parts per Million : 1H
(thousandths)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(thousandths)