

Supporting Information

Iron(II)/Persulfate Mediated Newman-Kwart Rearrangement

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1. Organic Chemistry

1.1. General considerations

Commercially available starting materials were purchased from Sigma-Aldrich, Alfa Aesar, TCI Europe, and Apollo Scientific and were used without further purification. Ammonium persulfate was purchased as for molecular biology and for electrophoresis (>98%) grade and the purity was checked by ICPMS (*vide infra*). Oxygen-18 enriched water (min 98%) was purchased from Rotem Industries Ltd. Solvents were obtained from Sigma-Aldrich; unless stated otherwise, reagent grade solvents were used for reactions and column chromatography and analytical grade solvents were used for recrystallizations. "Petrol" refers to petroleum ether having boiling point in the range of 40-60 °C. Reactions were heated using either a heating mantle or an oil bath; temperature was controlled with two independent thermocouples which calibration had been cross-checked with a mercury thermometer. Reaction progress was monitored by thin layer chromatography (TLC) on aluminium sheets coated with silica gel 60 F₂₅₄ (Merck Millipore) and detection was carried out using UV light (325 nm and 254 nm) and/or chemical solutions. Crude reaction mixtures were purified either by recrystallization, by manual flash column chromatography on silica gel 60 (230-400 mesh, 0.040-0.063 mm; Merck Millipore), or by automated flash column chromatography (Biotage Isolera One).

¹H, ¹³C, and ¹⁹F Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance 300, 400, 600 or 700 at room temperature. ¹³C NMR experiments were proton decoupled. ¹H and ¹³C NMR spectra are reported relative to the internal reference of the relative deuterated solvent. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hertz (Hz). Multiplicity is described with (s): singlet, (d): doublet, (t): triplet and (q): quadruplet. Full NMR assignment was performed with the aid of multidimensional and long-range experiments. Carbon multiplicities were assigned by Distortionless Enhancement by Polarization Transfer (DEPT) experiments and are reported as follows, (C): quaternary carbon, (CH₂): secondary carbon, (CH₃): methyl group.

High resolution mass spectrometry data were recorded on a Thermo Finnigan MAT900xp (CI, EI), Agilent 6510 QTOF (ESI), Waters LCT Premier spectrometers (ESI), or Thermo Exactive mass spectrometer with an Orbitrap (ESI, APCI). For the MS/MS experiments (ESI, APCI) an LTQ XL ion trap from Thermo Fisher was used. Inductively coupled plasma mass spectrometry was recorded on a PerkinElmer Nexion 350D. Melting points were taken either on a Gallenkamp or a Stuart SMP20 heating block and are uncorrected; when measured after recrystallization, the solvent is mentioned in brackets.

1.2. General procedures

1.2.1. General Procedure 1 for the synthesis of *O*-aryl carbamothioates using sodium hydride as the base

Into a flame-dried three-neck round-bottom flask, equipped with an argon inlet and a condenser, were added the phenol derivative (1 equiv.) and the anhydrous solvent (tetrahydrofuran or dimethylformamide, as indicated) (reaction concentration = 0.4 mol.L⁻¹). The reaction vessel was degassed with argon and the solution cooled to 0 °C. Sodium hydride (60% w/w in mineral oil, 1.2 equiv.) was subsequently added portion-wise. Once all the dihydrogen was released, the solution was allowed to warm at room temperature and dimethylthiocarbamoyl chloride (1.1 equiv.) was added. The resulting suspension was heated at 70 °C under argon for the indicated time. The reaction was subsequently cooled to room temperature before a saturated aqueous solution of ammonium chloride was added. The resulting mixture was extracted with ethyl acetate. If no base-sensitive functionalities were present on the molecule, the combined organic layers were washed with a 1 M aqueous solution of sodium hydroxide to remove unreacted phenol, otherwise brine was used. The combined organic layers were dried over magnesium sulfate and solvents were removed under reduced pressure. The residue was purified using the indicated method.

1.2.2. General Procedure 2 for the synthesis of *O*-aryl carbamothioates using DABCO as the base

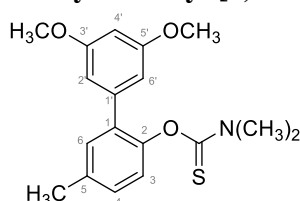
Into a flame-dried round-bottom flask, equipped with an argon inlet and a condenser, were added the phenol derivative (1 equiv.) and anhydrous THF (reaction concentration = 0.5 mol.L⁻¹). To this were added 1,4-diazabicyclo[2.2.2]octane (DABCO, 1.3 equiv.) and dimethylthiocarbamoyl chloride (1.3 equiv.). The resulting solution was heated at 50 °C under argon for the indicated time. The reaction was subsequently cooled to room temperature before most of the THF was removed under reduced pressure. The resulting mixture was diluted with a saturated aqueous solution of ammonium chloride and extracted with ethyl acetate. If no base-sensitive functionalities were present on the molecule, the combined organic layers were washed with a 1 M aqueous solution of sodium hydroxide to remove unreacted phenol, else brine was used. The combined organic layers were dried over magnesium sulfate and solvents were removed under reduced pressure. The residue was purified using the indicated method.

1.2.3. General Procedure 3 for the synthesis of *S*-aryl carbamothioates *via* the Iron(II)/APS-mediated NKR

A screw-cap vial (14 mL) was charged with the *O*-aryl carbamothioate (1 equiv.), ammonium persulfate (1 equiv.), Mohr's salt (5 mol%), and CH₃CN/H₂O (3:1, reaction concentration = 0.083-0.17 mol.L⁻¹). The vial was capped and the reaction was heated at the indicated temperature under maximum stirring (1200 rpm) for the indicated time. After cooling to room temperature, the crude reaction mixture was diluted with brine and then extracted with chloroform. The combined organic phases were dried over magnesium sulfate and evaporated under reduced pressure. The residue was purified using the indicated method.

1.3. Synthesis of *O*-aryl carbamothioates 1a-m

O-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate (1a)



Appearance: White solid
Chemical Formula: C₁₈H₂₁NO₃S
Molecular Weight: 331.43
Yield: 89%

3',5'-Dimethoxy-5-methyl-[1,1'-biphenyl]-2-ol (2.00 g, 8.20 mmol) was treated according to general procedure 1 using THF as solvent (reaction time = 16 h). Purification by automated flash column chromatography (SiO₂ Biotage SNAP 100 g; 0%→30% EtOAc in petrol) afforded the title compound as a white solid (2.41 g, 89%).

Note: the 3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-ol starting material was synthesized according to previously published procedure.¹

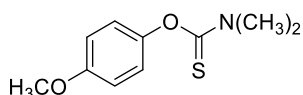
¹H NMR (700 MHz, CDCl₃) δ (ppm): 7.21 (d, ⁴J = 1.8 Hz, 1H, Ph-H6), 7.19 (dd, ³J = 8.0 Hz, ⁴J = 1.8 Hz, 1H, Ph-H4), 7.05 (d, ³J = 8.0 Hz, 1H, Ph-H3), 6.64 (d, ⁴J = 2.0 Hz, 2H, Ph'-H2'&H6'), 6.44 (t, ⁴J = 2.0 Hz, 1H, Ph'-H4'), 3.78 (s, 6H, Ph'-OCH₃), 3.36 (s, 3H, -N(CH₃)₂), 3.12 (s, 3H, -N(CH₃)₂), 2.40 (s, 3H, Ph-CH₃)
¹³C NMR (176 MHz, CDCl₃) δ (ppm): 188.1 (C=S), 160.5 (Ph'-COCH₃), 148.8 (Ph-C2), 139.9 (Ph'-C1'), 136.0 (Ph-C5), 134.8 (Ph-C1), 131.3 (Ph-C6), 129.0 (Ph-C4), 124.4 (Ph-C3), 107.2 (Ph'-C2'&C6'), 100.1 (Ph'-C4'), 55.6 (Ph'-OCH₃), 43.3 (-N(CH₃)₂), 38.7 (-N(CH₃)₂), 21.2 (Ph-CH₃)

m.p.: 87-88 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₈H₂₂NO₃S m/z 332.1320, found m/z 332.1321

Analytical data are in accordance with literature.¹

***O*-(4-methoxyphenyl) dimethylcarbamothioate (1b)**



Appearance: White solid
Chemical Formula: C₁₀H₁₃NO₂S
Molecular Weight: 211.28
Yield: 81%

4-Methoxyphenol (2.483 g, 20.0 mmol) was treated according to general procedure 1 using THF as solvent (reaction time = 18 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 80 g; 12 CV 5%→35% EtOAc in petrol) afforded the title compound as a white solid (3.44 g, 81%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.97 (d, ³J = 9.0 Hz, 2H, Ph-*H*_{2,6}), 6.89 (d, ³J = 9.0 Hz, 2H, Ph-*H*_{3,5}), 3.80 (s, 3H, Ph-OCH₃), 3.45 (s, 3H, -N(CH₃)₂), 3.33 (s, 3H, -N(CH₃)₂)

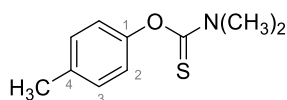
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 188.5 (C=S), 157.4 (C), 147.8 (C), 123.5 (CH), 114.2 (CH), 55.6 (CH₃), 43.37 (-N(CH₃)₂), 38.72 (-N(CH₃)₂)

m.p.: 84 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₀H₁₄NO₂S m/z 212.0740, found m/z 212.0740

Analytical data are in accordance with literature.²

***O*-(4-methylphenyl) dimethylcarbamothioate (1c)**



Appearance: White solid
Chemical Formula: C₁₀H₁₃NOS
Molecular Weight: 195.28
Yield: 80%

4-Methylphenol (554 mg, 5.12 mmol) was treated according to general procedure 1 using DMF as solvent (reaction time = 16 h). Purification by flash column chromatography (SiO₂, 20%→60% CH₂Cl₂ in petrol) afforded the title compound as a white solid (801 mg, 80%).

¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.19 (d, ³J = 8.0 Hz, 2H, Ph-*H*₃), 6.95 (d, ³J = 8.0 Hz, 2H, Ph-*H*₂), 3.46 (s, 3H, -N(CH₃)₂), 3.34 (s, 3H, -N(CH₃)₂), 2.36 (s, 3H, Ph-CH₃)

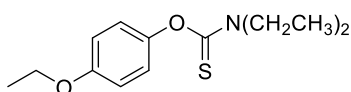
¹³C NMR (150 MHz, CDCl₃) δ (ppm): 188.3 (C=S), 152.0 (C), 135.7 (C), 129.9 (CH), 122.5 (CH), 43.4 (-N(CH₃)₂), 38.8 (-N(CH₃)₂), 21.1 (Ph-CH₃)

m.p.: 90-92°C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₀H₁₄NOS m/z 196.0791, found m/z 196.0793

Analytical data are in accordance with literature.²

***O*-(4-ethoxyphenyl) diethylcarbamothioate (1d)**



Appearance: White solid
Chemical Formula: C₁₃H₁₉NO₂S
Molecular Weight: 253.36
Yield: 58%

A dry round-bottom flask was charge with 4-ethoxyphenol (1.38 g, 10 mmol) and anhydrous DMF (20 mL). The resulting solution was cooled to 0 °C in an ice bath and sodium hydride (60% in mineral oil, 440 mg, 11 mmol) was added portionwise under a strong flow of nitrogen. The resulting suspension was stirred for 30 min at 0 °C and then allowed to warm to room temperature, after which diethylthiocarbamoyl chloride (1.96 g, 13 mmol) was added. The reaction was then heated to 40 °C for 15 h under an inert atmosphere and vigorous stirring. The reaction was subsequently allowed to cool to room temperature after which the reaction was quenched with water (50 mL) and then extracted with diethyl ether (300 mL). The organic layer was separated and washed successively with water (50 mL), 1M aqueous sodium hydroxide (2×50 mL), water (50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate and evaporated to dryness to give a yellow oil. Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 10%→25% EtOAc in petrol) afforded the title compound as a white solid (1.47 g, 58%).

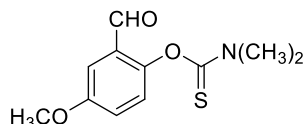
¹H NMR (700 MHz, CDCl₃) δ (ppm): 6.96 (d, ³J = 9.1 Hz, 2H, ArH), 6.88 (d, ³J = 9.1 Hz, 2H, ArH), 4.02 (q, ³J = 7.1 Hz, 2H, -CH₂CH₃), 3.90 (q, ³J = 7.1 Hz, 2H, -CH₂CH₃), 3.68 (q, ³J = 7.1 Hz, 2H, -CH₂CH₃), 1.41 (t, ³J = 7.1 Hz, 3H, -CH₂CH₃), 1.21 (2×t, ³J = 7.1 Hz, 2×3H, -CH₂CH₃)
¹³C NMR (176 MHz, CDCl₃) δ (ppm): 187.6 (C=S), 156.8 (C), 147.6 (C), 123.6 (CH), 114.8 (CH), 63.9 (CH₂), 48.6 (CH₂), 44.3 (CH₂), 15.0 (CH₃), 13.7 (CH₃), 12.0 (CH₃)

m.p.: 67-69 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₂₀NO₂S m/z 254.1209, found m/z 254.1199

Analytical data are in accordance with literature.³

***O*-(2-formyl-4-methoxyphenyl) dimethylcarbamothioate (1e)**



Appearance: Colourless solid

Chemical Formula: C₁₁H₁₃NO₃S

Molecular Weight: 239.29

Yield: 84%

2-Hydroxy-5-methoxybenzaldehyde (1.52 g, 10 mmol) was treated according to general procedure 2 using DMF as solvent (reaction time = 22 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 20%→45% EtOAc in petrol) afforded the title compound as a colourless solid (2.01 g, 84%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 10.04 (s, 1H, -CHO), 7.39 (d, ⁴J = 3.1 Hz, 1H, Ph-H3), 7.18 (dd, ³J = 8.9 Hz, ⁴J = 3.1 Hz, 1H, Ph-H5), 7.06 (d, ³J = 8.9 Hz, 1H, Ph-H6), 3.88 (s, 3H, -OCH₃), 3.49 (s, 3H, -N(CH₃)₂), 3.43 (s, 3H, -N(CH₃)₂)

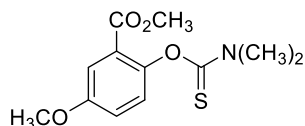
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 188.1 (-CHO), 187.8 (C=S), 157.6 (C), 149.6 (C), 129.6 (C), 125.4 (CH), 121.9 (CH), 111.4 (CH), 55.8 (-OCH₃), 43.6 (-N(CH₃)₂), 38.9 (-N(CH₃)₂)

m.p.: 87 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₁H₁₄NO₃S m/z 240.0689, found m/z 240.0682

Analytical data are in accordance with literature.⁴

Methyl 2-((dimethylcarbamothioyl)oxy)-5-methoxybenzoate (1f)



Appearance: Pale yellow solid

Chemical Formula: C₁₂H₁₅NO₄S

Molecular Weight: 269.32

Yield: 57%

Methyl 2-hydroxy-5-methoxybenzoate (1.82 g, 10.0 mmol) was treated according to general procedure 2 using DMF as solvent (reaction time = 19 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 25%→45% EtOAc in petrol) afforded the title compound as a pale yellow solid (1.54 g, 57%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.51 (d, ⁴J = 3.1 Hz, 1H, Ph-H3), 7.11 (dd, ³J = 8.7 Hz, ⁴J = 3.1 Hz, 1H, Ph-H5), 7.05 (d, ³J = 8.7 Hz, 1H, Ph-H6), 3.86 (s, 3H, -CO₂CH₃), 3.85 (s, 3H, -OCH₃), 3.48 (s, 3H, -N(CH₃)₂), 3.40 (s, 3H, -N(CH₃)₂)

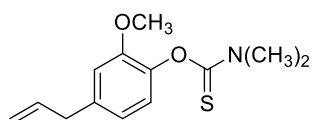
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 188.0 (C=S), 164.7 (C=O), 157.0 (C), 147.3 (C), 125.8 (CH), 124.3 (C), 119.4 (CH), 115.5 (CH), 55.8 (-OCH₃), 52.1 (-CO₂CH₃), 43.3 (-N(CH₃)₂), 38.8 (-N(CH₃)₂)

m.p.: 104-105 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₂H₁₆NO₄S m/z 270.0795, found m/z 270.0788

Analytical data are in accordance with literature.⁵

***O*-(4-allyl-2-methoxyphenyl) dimethylcarbamothioate (1g)**



Appearance: White solid
Chemical Formula: C₁₃H₁₇NO₂S
Molecular Weight: 251.34
Yield: 83%

4-Allyl-2-methoxyphenol (2.00 g, 12.1 mmol) was treated according to general procedure 1 using DMF as solvent (reaction time = 16 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 0%→15% EtOAc in hexane) afforded the title compound as a white solid (2.51 g, 83%).

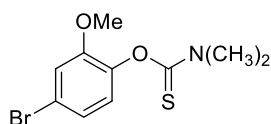
¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.98 (d, ³J = 8.2 Hz, 1H, Ph-*H*₆), 6.82 (bs, 1H, Ph-*H*₃), 6.82 (d, ³J = 8.2 Hz, 1H, Ph-*H*₅), 6.01 (ddt, ³J = 17 Hz, 10.1 Hz, 6.8 Hz, 1H, H₂C-*HC*=CH₂), 5.18-5.08 (m, 2H, H₂C-*HC*=CH₂), 3.84 (s, 3H, -OCH₃), 3.48 (s, 3H, -N(CH₃)₂), 3.42 (d, ³J = 6.8 Hz, 2H, H₂C-*HC*=CH₂), 3.37 (s, 3H, -N(CH₃)₂)
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 188.1 (C=S), 151.3 (C), 141.3 (C), 138.9 (C), 137.1 (CH), 123.7 (CH), 116.2 (CH₂), 120.5 (CH), 113.0 (CH), 56.0 (-OCH₃), 43.4 (-N(CH₃)₂), 40.2 (CH₂), 38.7 (-N(CH₃)₂)

m.p.: 70 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₁₈NO₂S m/z 252.1053, found m/z 252.1043

Analytical data are in accordance with literature.⁶

***O*-(4-bromo-2-methoxyphenyl) dimethylcarbamothioate (1h)**



Appearance: Colourless solid
Chemical Formula: C₁₀H₁₂BrNO₂S
Molecular Weight: 290.18
Yield: 76%

4-Bromo-2-methoxyphenol (2.03 g, 10.0 mmol) was treated according to general procedure 2 using DMF as solvent (reaction time = 18 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 20%→45% EtOAc in petrol) afforded the title compound as a colourless solid (2.20 g, 76%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.14-7.09 (m, 2H, Ar*H*), 6.95-6.90 (m, 1H, Ar*H*), 3.84 (s, 3H, -OCH₃), 3.47 (s, 3H, -N(CH₃)₂), 3.36 (s, 3H, -N(CH₃)₂)

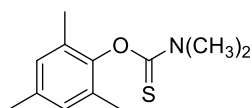
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 187.4 (C=S), 152.3 (C), 142.1 (C), 125.3 (CH), 123.6 (CH), 119.4 (C), 116.2 (CH), 56.2 (-OCH₃), 43.5 (-N(CH₃)₂), 38.8 (-N(CH₃)₂)

m.p.: 87-88 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₀H₁₃BrNO₂S m/z 289.9845, found m/z 289.9839

Analytical data are in accordance with literature.⁶

***O*-mesityl dimethylcarbamothioate (1i)**



Appearance: Colourless solid
Chemical Formula: C₁₂H₁₇NOS
Molecular Weight: 223.33
Yield: 81%

2,4,6-Trimethylphenol (1.36 g, 10.0 mmol) was treated according to general procedure 1 using DMF as solvent (reaction time = 3.5 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 0%→5% EtOAc in petrol) afforded the title compound as a colourless solid (1.81 g, 81%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.91 (s, 2H, Ar*H*), 3.51 (s, 3H, -N(CH₃)₂), 3.40 (s, 3H, -N(CH₃)₂), 2.31 (s, 3H, Ar-*CH*₃), 2.16 (s, 6H, Ar-*CH*₃)

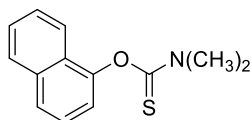
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 186.6 (C=S), 149.0 (C), 135.3 (C), 130.4 (C), 129.2 (CH), 43.3 (-N(CH₃)₂), 38.4 (-N(CH₃)₂), 20.9 (CH₃), 16.5 (CH₃)

m.p.: 66-67 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₂H₁₈NOS m/z 224.1104, found m/z 224.1098

Analytical data are in accordance with literature.⁶

***O*-(naphthalen-1-yl) dimethylcarbamothioate (1j)**



Appearance: White solid
 Chemical Formula: C₁₃H₁₃NOS
 Molecular Weight: 231.31
 Yield: 70%

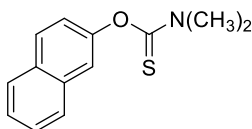
Naphthalen-1-ol (1.44 g, 10.0 mmol) was treated according to general procedure 2 using DMF as solvent (reaction time = 20 h). At the end of the reaction, the crude mixture was poured in into crushed ice (50 g). This resulting yellow precipitate was rinsed with water (3 × 25 mL) and then dried under high vacuum. Purification of this material by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 5%→20% EtOAc in petrol) afforded the title compound as a white solid (1.63 g, 70%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.94-7.89 (m, 1H, ArH), 7.88-7.83 (m, 1H, ArH), 7.80 (d, ³J = 8.2 Hz, 1H, ArH), 7.57-7.49 (m, 3H, ArH), 7.25 (d, ³J = 7.5 Hz, 1H, ArH), 3.56 (s, 3H, -N(CH₃)₂), 3.53 (s, 3H, -N(CH₃)₂)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 188.0 (C=S), 150.0 (C), 134.6 (C), 128.2 (CH), 127.5 (C), 126.5 (CH), 126.4 (CH), 126.1 (CH), 125.3 (CH), 121.6 (CH), 119.6 (CH), 43.5 (-N(CH₃)₂), 38.9 (-N(CH₃)₂)
m.p.: 123-124 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₁₄NOS m/z 232.0791, found m/z 232.0791
 Analytical data are in accordance with literature.⁶

O-(naphthalen-2-yl) dimethylcarbamothioate (1k)



Appearance: Colourless solid
 Chemical Formula: C₁₃H₁₃NOS
 Molecular Weight: 231.31
 Yield: 75%

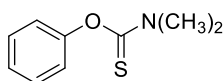
Naphthalen-2-ol (1.20 g, 8.32 mmol) was treated according to general procedure 2 using DMF as solvent (reaction time = 14 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 20%→30% EtOAc in petrol) afforded the title compound as a colourless solid (1.44 g, 75%).

¹H NMR (700 MHz, CDCl₃) δ (ppm): 7.87-7.84 (m, 2H, ArH), 7.82-7.79 (m, 1H, ArH), 7.51-7.44 (m, 3H, ArH), 7.27-7.24 (m, 1H, ArH), 3.49 (s, 3H, -N(CH₃)₂), 3.40 (s, 3H, -N(CH₃)₂)

¹³C NMR (176 MHz, CDCl₃) δ (ppm): 188.1 (C=S), 151.8 (C), 133.8 (C), 131.7 (C), 129.1 (CH), 128.0 (CH), 127.9 (CH), 126.6 (CH), 125.9 (CH), 122.6 (CH), 119.6 (CH), 43.5 (-N(CH₃)₂), 38.9 (-N(CH₃)₂)
m.p.: 88-89 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₁₄NOS m/z 232.0791, found m/z 232.0793
 Analytical data are in accordance with literature.²

O-phenyl dimethylcarbamothioate (1l)



Appearance: Pale yellow oil
 Chemical Formula: C₉H₁₁NOS
 Molecular Weight: 181.25
 Yield: 42%

A dry round-bottom flask was charged with sodium phenolate (2.00 g, 17.2 mmol) and anhydrous tetrahydrofuran (40 mL) and the resulting solution was cooled to 0 °C. Dimethylthiocarbamoyl chloride (2.55 g, 20.6 mmol) was subsequently added and the reaction was warmed to 70 °C and stirred at this temperature for 18 h under inert atmosphere. The reaction was subsequently allowed to cool to room temperature after which the reaction was quenched with water (50 mL) and then extracted with diethyl ether (200 mL). The organic layer was separated and washed successively with water (50 mL), 1M aqueous sodium hydroxide (2×50 mL), water (50 mL), and brine (50 mL). The organic layer was dried over magnesium sulfate and solvents were evaporated under reduced pressure. The residue was purified by automated flash column chromatography (SiO₂ Büchi FlashPure 80 g; 10%→30% EtOAc in petrol) to afford the title compound as a clear oil (1.30 g, 42%).

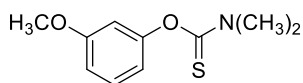
¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.43-7.37 (m, 2H, *m*-PhH), 7.29-7.23 (m, 1H, *p*-PhH), 7.10-7.05 (m, 2H, *o*-PhH), 3.45 (s, 3H, -N(CH₃)₂), 3.33 (s, 3H, -N(CH₃)₂)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 187.9 (C=S), 154.2 (C), 129.3 (CH), 126.0 (CH), 122.9 (CH), 43.3 (-N(CH₃)₂), 38.8 (-N(CH₃)₂)

HRMS (APCI): [M+H]⁺ Calcd. m/z for C₉H₁₂NOS 182.0634, found m/z 182.0631

Analytical data are in accordance with literature.²

O-(3-methoxyphenyl) dimethylcarbamothioate (1m)



Appearance: Pale-yellow oil

Chemical Formula: C₁₀H₁₃NO₂S

Molecular Weight: 211.28

Yield: 90%

3-Methoxyphenol (870 mg, 7.0 mmol) was treated according to general procedure 2 using THF as solvent (reaction time = 16 h). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 80 g; solvent A: 10% EtOAc in CHCl₃, solvent B: petrol; 2 CV 10% A in B, 5 CV 10%→52% A in B, 3 CV 52% A in B) afforded the title compound as a pale-yellow oil (1.33 g, 90%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.28 (t, ³J = 8.0 Hz, 1H, Ph-*H*₅), 6.80 (ddd, ³J = 8.4 Hz, ⁴J = 2.3, 0.7 Hz, 1H, Ph-*H*₆), 6.67 (ddd, ³J = 8.4 Hz, ⁴J = 2.3, 0.7 Hz, 1H, Ph-*H*₄), 6.63 (t, ⁴J = 2.3 Hz, 1H, Ph-*H*₂), 3.80 (s, 3H, Ph-OCH₃), 3.46 (s, 3H, -N(CH₃)₂), 3.34 (s, 3H, -N(CH₃)₂)

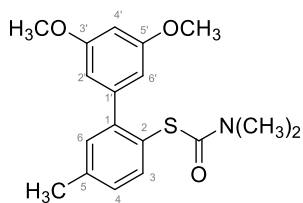
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 187.7 (C=S), 160.4 (C), 155.0 (C), 129.5 (CH), 115.1 (CH), 111.8 (CH), 108.9 (CH), 55.5 (Ph-OCH₃), 43.3 (-N(CH₃)₂), 38.8 (-N(CH₃)₂)

HRMS (ESI): [M+H]⁺ Calcd. for C₁₀H₁₄NO₂S m/z 212.0740, found m/z 212.0742

Analytical data are in accordance with literature.²

1.4.Synthesis of *S*-aryl carbamothioates 2a-m

S-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate (2a)



Appearance: Pale orange solid
Chemical Formula: C₁₈H₂₁NO₃S
Molecular Weight: 331.43
Yield: 75% (81% on 10 mmol scale)

O-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate **1a** (331 mg, 1 mmol) was treated according to general procedure 3 (reaction time = 2 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 40 g; 20%→60% diethyl ether in petrol) afforded the title compound as a pale orange solid (250 mg, 75%).

10 mmol scale synthesis

A 250 mL round-bottomed flask was charged with *O*-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate **1a** (3.31 g, 10.0 mmol), ammonium persulfate electrophoresis grade (>98%) (3.28 g, 14.0 mmol), Mohr's salt (196 mg, 5 mol%) and acetonitrile/water (3:1, 120 mL). The reaction was heated at 65 °C for 4.5 h under vigorous stirring. The reaction was subsequently allowed to cool to room temperature and the acetonitrile was removed under reduced pressure. The resulting aqueous layer was extracted with chloroform (3×100 mL). Combined organic layers were dried over magnesium sulfate and the solvent was removed under reduced pressure. Purification of the yellow residue by automated flash column chromatography (SiO₂ Büchi FlashPure 80 g; 20%→80% diethyl ether in petrol) afforded the title compound as a pale orange solid (2.70 g, 81%).

¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.50 (d, ³J = 7.6 Hz, 1H, Ph-*H*3), 7.21 (d, ⁴J = 2.0 Hz, 1H, Ph-*H*6), 7.20 (dd, ³J = 8.0 Hz, ⁴J = 2.0 Hz, 1H, Ph-*H*4), 6.52 (d, ⁴J = 2.3 Hz, 2H, Ph'-*H*2'&*H*6'), 6.46 (t, ⁴J = 2.3 Hz, 1H, Ph'-*H*4'), 3.79 (s, 6H, Ph'-OCH₃), 2.97 (s, 6H, -N(CH₃)₂), 2.40 (s, 3H, Ph-CH₃)

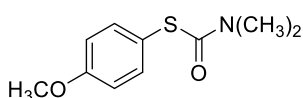
¹³C NMR (150 MHz, CDCl₃) δ (ppm): 167.8 (C=O), 160.1 (Ph'-COCH₃), 146.9 (Ph-C1), 143.5 (Ph'-C1'), 139.9 (Ph-C5), 138.1 (Ph-C3), 131.3 (Ph-C6), 129.0 (Ph-C4), 123.8 (Ph-C2), 107.6 (Ph'-C2'&C6'), 100.0 (Ph'-C4'), 55.5 (Ph'-OCH₃), 37.1 (-N(CH₃)₂), 21.4 (Ph-CH₃)

m.p.: 70-72 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₈H₂₂NO₃S m/z 332.1320, found m/z 332.1318

Analytical data are in accordance with literature.¹

S-(4-methoxyphenyl) dimethylcarbamothioate (2b)



Appearance: Colourless solid
Chemical Formula: C₁₀H₁₃NO₂S
Molecular Weight: 211.28
Yield: 95%

O-(4-methoxyphenyl) dimethylcarbamothioate **1b** (105 mg, 0.50 mmol) was treated according to general procedure 3 (reaction time = 1 h, temperature = 45 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 2×4 g; 10%→25% EtOAc in *n*-hexane) afforded the title compound as a colourless solid (100 mg, 95%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.42 (d, ³J = 8.9 Hz, 2H, Ar*H*), 6.94 (d, ³J = 8.9 Hz, 2H, Ar*H*), 3.84 (s, 3H, -OCH₃), 3.07 (bs, 6H, -N(CH₃)₂)

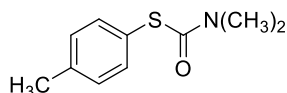
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 167.7 (C=O), 160.6 (C), 137.3 (CH), 119.5 (C), 114.6 (CH), 55.4 (-OCH₃), 36.9 (-N(CH₃)₂)

m.p.: 87-88 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₀H₁₄NO₂S m/z 212.0740, found m/z 212:0740

Analytical data are in accordance with literature.²

S-(*p*-tolyl) dimethylcarbamothioate (**2c**)



Appearance: Colourless oil
Chemical Formula: C₁₀H₁₃NOS
Molecular Weight: 195.28
Yield: 95%

O-(4-methylphenyl) dimethylcarbamothioate **1c** (195 mg, 1.00 mmol) was treated according to general procedure 3 (reaction time = 1.5 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 5%→20% EtOAc in petrol) afforded the title compound as a colourless oil (185 mg, 95%).

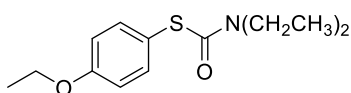
¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.30 (d, ³*J* = 8.0 Hz, 2H, Ar*H*), 7.12 (d, ³*J* = 8.0 Hz, 2H, Ar*H*), 3.05-2.90 (2×bs, 6H, -N(CH₃)₂), 2.29 (s, 3H, -CH₃)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 167.3 (C=O), 139.4 (C), 135.7 (CH), 129.8 (CH), 125.2 (C), 36.9 (-N(CH₃)₂), 21.3 (CH₃)

HRMS (ESI): [M+H]⁺ Calcd. for C₁₀H₁₄NOS m/z 196.0791, found m/z 196.0793

Analytical data are in accordance with literature.²

S-(4-ethoxyphenyl) diethylcarbamothioate (**2d**)



Appearance: Clear oil
Chemical Formula: C₁₃H₁₉NO₂S
Molecular Weight: 253.36
Yield: 87%

O-(4-ethoxyphenyl) diethylcarbamothioate **1d** (183 mg, 0.72 mmol) was treated according to general procedure 3 (reaction time = 1 h, temperature = 45 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 0%→2% EtOAc in CH₂Cl₂) afforded the title compound as a clear colourless oil (158 mg, 87%).

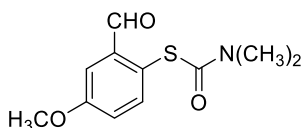
¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.42 (d, ³*J* = 8.8 Hz, 2H, Ar*H*), 6.92 (d, ³*J* = 8.8 Hz, 2H, Ar*H*), 4.06 (q, ³*J* = 7.0 Hz, 2H, -OCH₂CH₃), 3.45 (q, ³*J* = 7.1 Hz, 4H, -NCH₂CH₃), 1.43 (t, ³*J* = 7.0 Hz, 3H, -OCH₂CH₃), 1.28 (bs, 3H, -NCH₂CH₃), 1.19 (bs, 3H, -NCH₂CH₃)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 166.5 (C=O), 159.9 (C), 137.4 (CH), 119.3 (C), 115.1 (CH), 63.6 (CH₂), 42.3 (CH₂), 14.8 (CH₃), 13.8 (CH₃), 13.2 (CH₃)

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₂₀NO₂S m/z 254.1209, found m/z 254.1210

Analytical data are in accordance with literature.³

S-(2-formyl-4-methoxyphenyl) dimethylcarbamothioate (**2e**)



Appearance: Colourless solid
Chemical Formula: C₁₁H₁₃NO₃S
Molecular Weight: 239.29
Yield: 95%

O-(2-formyl-4-methoxyphenyl) dimethylcarbamothioate **1e** (239 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 1 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 24 g; 15%→30% EtOAc in petrol) afforded the title compound as a colourless solid (227 mg, 95%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 10.33 (s, 1H, -CHO), 7.53 (d, ⁴*J* = 3.0 Hz, 1H, Ph-*H*3), 7.46 (d, ³*J* = 8.5 Hz, 1H, Ph-*H*6), 7.13 (dd, ³*J* = 8.5 Hz, ⁴*J* = 3.0 Hz, 1H, Ph-*H*5), 3.87 (s, 3H, -OCH₃), 3.16 (s, 3H, -N(CH₃)₂), 3.02 (s, 3H, -N(CH₃)₂)

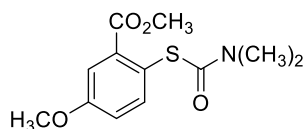
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 191.3 (-CHO), 166.0 (C=O), 161.1 (C), 139.0 (C), 138.9 (CH), 123.5 (C), 121.2 (CH), 112.1 (CH), 55.7 (-OCH₃), 37.1 (-N(CH₃)₂)

m.p.: 90 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₁H₁₄NO₃S m/z 240.0689, found m/z 240.0685

Analytical data are in accordance with literature.⁴

Methyl 2-((dimethylcarbamoyl)thio)-5-methoxybenzoate (**2f**)



Appearance: Colourless oil
Chemical Formula: C₁₂H₁₅NO₄S
Molecular Weight: 269.32
Yield: 93%

Methyl 2-((dimethylcarbamothioyl)oxy)-5-methoxybenzoate **1f** (269 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 1 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 24 g; 25%→45% EtOAc in petrol) afforded the title compound as a colourless oil (250 mg, 93%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.49 (d, ³J = 8.6 Hz, 1H, Ph-*H*₆), 7.41 (d, ⁴J = 3.0 Hz, 1H, Ph-*H*₃), 7.02 (dd, ³J = 8.6 Hz, ⁴J = 3.0 Hz, 1H, Ph-*H*₅), 3.88 (s, 3H, -OCH₃), 3.84 (s, 3H, -OCH₃), 3.06 (bs, 6H, -N(CH₃)₂)

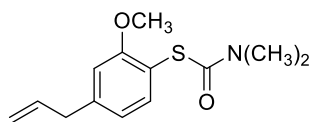
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 166.93 (C), 166.88 (C), 160.1 (C), 139.2 (CH), 136.7 (C), 120.1 (C), 117.4 (CH), 116.0 (CH), 55.6 (-OCH₃), 52.3 (-CO₂CH₃), 37.0 (-N(CH₃)₂)

m.p.: 104-105 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₂H₁₆NO₄S m/z 270.0795, found m/z 270.0789

Analytical data are in accordance with literature.⁵

S-(4-allyl-2-methoxyphenyl) dimethylcarbamothioate (**2g**)



Appearance: Colourless solid
Chemical Formula: C₁₃H₁₇NO₂S
Molecular Weight: 251.34
Yield: 86%

O-(4-allyl-2-methoxyphenyl) dimethylcarbamothioate **1g** (251 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 1.5 h, temperature = 45 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 12 g; 10%→25% EtOAc in petrol) afforded the title compound as a colourless solid (215 mg, 86%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.39 (d, ³J = 7.7 Hz, 1H, Ph-*H*₆), 6.83 (d, ³J = 7.7 Hz, 1H, Ph-*H*₅), 6.81 (bs, 1H, Ph-*H*₃), 5.98 (ddt, ³J = 17 Hz, 10.1 Hz, 6.7 Hz, 1H, -H₂C-HC=CH₂), 5.18-5.08 (m, 2H, -H₂C-HC=CH₂), 3.88 (s, 3H, -OCH₃), 3.42 (d, ³J = 6.7 Hz, 2H, -H₂C-HC=CH₂), 3.14 (bs, 3H, -N(CH₃)₂), 3.02 (bs, 3H, -N(CH₃)₂)

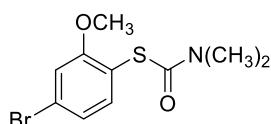
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 166.6 (C=O), 160.1 (C), 144.2 (C), 138.1 (CH), 136.7 (CH), 121.3 (CH), 116.4 (CH₂), 114.1 (C), 111.9 (CH), 56.1 (-OCH₃), 40.4 (CH₂), 37.0 (-N(CH₃)₂)

m.p.: 70 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₁₈NO₂S m/z 252.1053, found m/z 252.1044

Analytical data are in accordance with literature.⁶

S-(4-bromo-2-methoxyphenyl) dimethylcarbamothioate (2h)



Appearance: Colourless solid
Chemical Formula: C₁₀H₁₂BrNO₂S
Molecular Weight: 290.18
Yield: 86%

O-(2-bromo-4-methoxyphenyl) dimethylcarbamothioate **1h** (290 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 1 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 24 g; 5%→25% EtOAc in petrol) afforded the title compound as a colourless solid (251 mg, 86%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.33-7.29 (m, 1H, ArH), 7.14-7.07 (m, 2H, ArH), 3.86 (s, 3H, -OCH₃), 3.11 (bs, 3H, -N(CH₃)₂), 3.02 (s, 3H, -N(CH₃)₂)

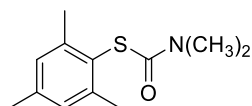
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.6 (C=O), 160.6 (C), 138.9 (CH), 125.2 (C), 124.1 (CH), 116.2 (C), 115.2 (CH), 56.4 (-OCH₃), 37.0 (-N(CH₃)₂)

m.p.: 111-112 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₀H₁₃BrNO₂S m/z 289.9845, found m/z 289.9837

Analytical data are in accordance with literature.⁶

S-mesityl dimethylcarbamothioate (2i)



Appearance: Colourless solid
Chemical Formula: C₁₂H₁₇NOS
Molecular Weight: 223.33
Yield: 72%

S-mesityl dimethylcarbamothioate **1i** (446 mg, 2.0 mmol) was treated according to general procedure 3 (reaction time = 1.5 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 0%→25% EtOAc in petrol) afforded the title compound as a colourless solid (321 mg, 72%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 6.99 (s, 2H, ArH), 3.17 (bs, 3H, -N(CH₃)₂), 3.05 (bs, 3H, -N(CH₃)₂), 2.40 (s, 3H, Ar-CH₃), 2.30 (s, 6H, Ar-CH₃)

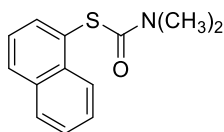
¹³C NMR (100 MHz, CDCl₃) δ (ppm): 166.3 (C=O), 143.4 (C), 139.5 (C), 129.1 (CH), 124.7 (C), 37.0 (-N(CH₃)₂), 21.9 (CH₃), 21.2 (CH₃)

m.p.: 72-73 °C

HRMS (APCI): [M+H]⁺ Calcd. for C₁₂H₁₈NOS m/z 224.1104, found m/z 224.1099

Analytical data are in accordance with literature.⁶

S-(naphthalen-1-yl) dimethylcarbamothioate (2j)



Appearance: Orange oil
Chemical Formula: C₁₃H₁₃NOS
Molecular Weight: 231.31
Yield: 85%

O-(naphthalen-1-yl) dimethylcarbamothioate **1j** (231 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 2 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 10%→20% EtOAc in petrol) afforded the title compound as an orange oil (195 mg, 85%).

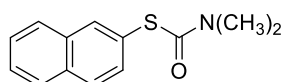
¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.26 (d, ³J = 8.4 Hz, 1H, ArH), 7.97 (d, ³J = 8.0 Hz, 1H, ArH), 7.90 (d, ³J = 8.0 Hz, 1H, ArH), 7.82 (dd, ³J = 8.4 Hz, ⁴J = 1.0 Hz, 1H, ArH), 7.63-7.57 (m, 1H, ArH), 7.57-7.48 (m, 2H, ArH), 3.26 (bs, 3H, -N(CH₃)₂), 3.05 (bs, 3H, -N(CH₃)₂)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 166.6 (C=O), 136.2 (CH), 135.2 (C), 134.2 (C), 130.8 (CH), 128.6 (CH), 127.0 (CH), 126.22 (CH), 126.18 (C), 125.8 (CH), 125.6 (CH), 37.1 (-N(CH₃)₂)

HRMS (ESI): [M+H]⁺ Calcd. for C₁₃H₁₄NOS m/z 232.0791, found m/z 232.0792

Analytical data are in accordance with literature.⁶

S-(naphthalen-2-yl) dimethylcarbamothioate (2k)



Appearance: Colourless solid
Chemical Formula: C₁₃H₁₃NOS
Molecular Weight: 231.31
Yield: 84%

O-(naphthalen-2-yl) dimethylcarbamothioate **1k** (231 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 2 h, temperature = 65 °C). Purification by automated flash column chromatography (SiO₂ Büchi FlashPure 24 g; 20%→100% Et₂O in petrol) followed by recrystallization in diethyl ether afforded the title compound as a colourless solid (194 mg, 84%).

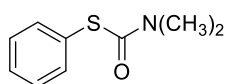
¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.02 (s, 1H, ArH), 7.88-7.80 (m, 3H, ArH), 7.50-7.45 (m, 3H, ArH), 3.13 (bs, 3H, -N(CH₃)₂), 3.05 (bs, 3H, -N(CH₃)₂)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 167.0 (C=O), 135.3 (C), 133.5 (C), 133.3 (CH), 132.3 (CH), 128.5 (CH), 128.0 (CH), 127.7 (CH), 126.9 (CH), 126.3 (CH), 126.1 (C), 37.0 (-N(CH₃)₂)

m.p.: 111 °C

HRMS (APCI): [M+H]⁺ Calcd. m/z for C₁₃H₁₄NOS 232.0791, found m/z 232.0785

S-phenyl dimethylcarbamothioate (2l)



Appearance: *Not isolated*
Chemical Formula: C₉H₁₁NOS
Molecular Weight: 181.25
Conversion (NMR): <10%

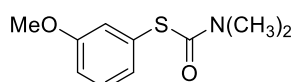
O-phenyl dimethylcarbamothioate **1l** (181 mg, 1.0 mmol) was treated according to general procedure 3 (reaction time = 1.5 h, temperature = 65 °C). The residue obtained after work-up was analysed by LCMS and NMR to determine the conversion; the mixture was composed of starting material (70%) carbamate side-product (20%) and the title compound (<10%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.54-7.49 (m, 2H, ArH), 7.43-7.35 (m, 3H, ArH), 3.11 (bs, 3H, -N(CH₃)₂), 3.02 (bs, 3H, -N(CH₃)₂)

LCMS (ESI): [M+H]⁺: m/z 182.0

Analytical data are in accordance with literature.²

S-(3-methoxyphenyl) dimethylcarbamothioate (2m)



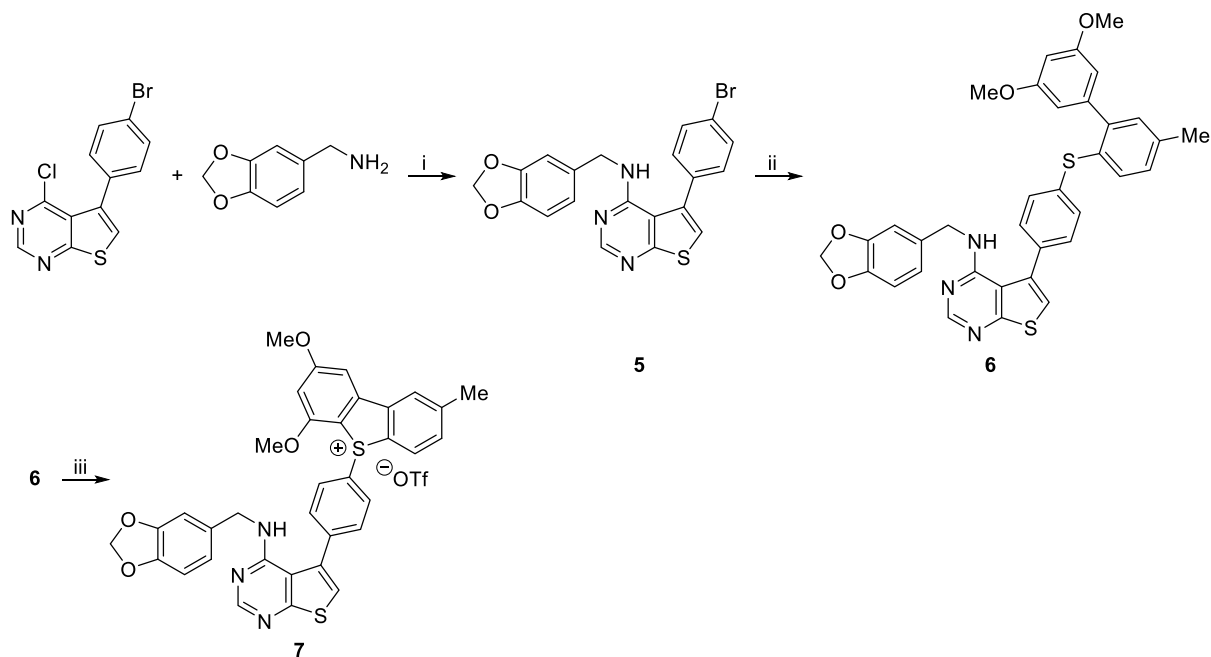
Appearance: *Not isolated*
Chemical Formula: C₁₀H₁₃NO₂S
Molecular Weight: 211.28
Conversion (NMR): 17%

O-(3-methoxyphenyl) dimethylcarbamothioate **1m** (211 mg, 1 mmol) was treated according to general procedure 3 (reaction time = 2 h, temperature = 65 °C). The residue obtained after work-up was analysed by NMR to determine the conversion; the mixture was composed of starting material (60%), carbamate side-product (23%) and the title compound (17%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.29 (t, ³J = 7.8 Hz, 1H, ArH), 7.09 (ddd, ³J = 7.8 Hz, ⁴J = 1.5 Hz, 0.9 Hz, 1H, ArH), 7.05 (dd, ⁴J = 2.5 Hz, 1.5 Hz, 1H, ArH), 6.93 (ddd, ³J = 7.8 Hz, ⁴J = 2.5 Hz, 0.9 Hz, 1H, ArH), 3.81 (s, 3H, Ph-OCH₃), 3.10 (bs, 3H, -N(CH₃)₂), 3.01 (bs, 3H, -N(CH₃)₂)

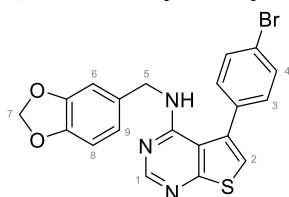
Analytical data are in accordance with literature.²

1.5.Synthesis of ¹⁸F-AEM1 labeling precursor 7



Scheme S1: Synthetic route to ¹⁸F-AEM1 labeling precursor 7. Conditions: (i) diisopropylethylamine, anhydrous dimethylformamide, 50 °C, 24 h, 79% yield; (ii) **2a**, *t*BuOK, Pd₂(dba)₃, DPEPhos, toluene, reflux, 56% yield; (iii) Ca(OCl)₂, acetate buffer pH 4, acetonitrile, 3 °C, 15 min, 72% yield.

N-(benzo[*d*][1,3]dioxol-5-ylmethyl)-5-(4-bromophenyl)thieno[2,3-*d*]pyrimidin-4-amine (**5**)



Appearance: Pale yellow solid

Chemical Formula: C₂₀H₁₄BrN₃O₂S

Molecular Weight: 440.32

Yield: 79%

A dry round-bottom flask was charged with 5-(4-bromophenyl)-4-chlorothieno[2,3-*d*]pyrimidine (990 mg, 3.04 mmol), benzo[*d*][1,3]dioxol-5-ylmethanamine (551 mg, 3.64 mmol), diisopropylethylamine (635 μL, 3.64 mmol) and anhydrous dimethylformamide (15 mL). The resulting solution was stirred at 50 °C under inert atmosphere for 24 h. The reaction mixture was subsequently allowed to cool to room temperature, and quenched with water (50 mL). The product was extracted with diethyl ether (3×100 mL). The combined organic layers were washed with a saturated aqueous solution of potassium carbonate (50 mL), water (2×50 mL) and brine (50 mL). After drying over magnesium sulfate, the solvents were removed under reduced pressure. Purification of the residue by automated flash column chromatography (SiO₂ GraceRESOLV™ 80 g; 12 CV 5%→40% ethyl acetate in petrol) afforded the title compound as a pale yellow solid (1.06 g, 79%).

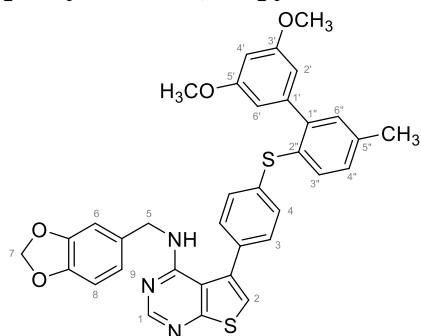
¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.52 (s, 1H, *H*1), 7.52 (d, ³*J* = 8.3 Hz, 2H, *H*3 or *H*4), 7.26 (d, ³*J* = 8.3 Hz, 2H, *H*4 or *H*3), 7.07 (s, 1H, *H*2), 6.73 (d, ³*J* = 7.9 Hz, 1H, *H*8), 6.63 (d, ⁴*J* = 1.8 Hz, 1H, *H*6), 6.58 (dd, ³*J* = 7.9 Hz, ⁴*J* = 1.8 Hz, 1H, *H*9), 5.97 (s, 2H, *H*7), 5.01 (t, ³*J* = 5.1 Hz, 1H, -NH), 4.50 (d, ³*J* = 5.1 Hz, 2H, *H*5)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 167.2 (C), 157.1 (C), 154.3 (CH), 148.0 (C), 147.1 (C), 134.9 (C), 133.4 (C), 132.1 (CH), 131.7 (C), 130.8 (CH), 123.1 (C), 120.83 (CH), 120.7 (CH), 114.0 (C), 108.4 (CH), 108.1 (CH), 101.2 (CH₂), 44.8 (CH₂)

m.p.: 149-152 °C

HRMS (ESI): [M+H]⁺ Calcd. for C₂₀H₁₅BrN₃O₂S m/z 440.0063, found m/z 440.0073

***N*-(benzo[*d*][1,3]dioxol-5-ylmethyl)-5-(4-((3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)thio)phenyl)thieno[2,3-*d*]pyrimidin-4-amine (6)**



Appearance: Golden coloured sticky solid

Chemical Formula: C₃₅H₂₉N₃O₄S₂

Molecular Weight: 619.75

Yield: 56%

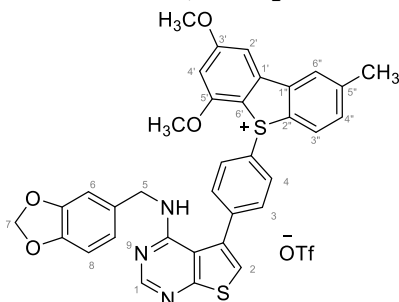
An oven-dried round-bottom flask was charged with bromoaryl **5** (660 mg, 1.50 mmol), *S*-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate **2a** (522 mg, 1.57 mmol), DPEPhos (97 mg, 0.18 mmol), tris(dibenzylideneacetone)dipalladium(0) (83 mg, 0.091 mmol) and potassium *tert*-butoxide (505 mg, 4.50 mmol). The flask was evacuated and refilled with argon (three times). Anhydrous toluene (15 mL) was injected after which the flask was sealed and the reaction was stirred at 120 °C for 2 h under argon. The reaction mixture was subsequently allowed to cool to room temperature and diluted with ethyl acetate (75 mL). The organic layer was washed with water (2×10 mL) and brine (10 mL), and was then dried over magnesium sulfate. The dried organic layer was filtered over Celite® before the solvents were removed under reduced pressure. Purification by automated flash column chromatography (SiO₂ GraceRESOLV™ 40 g; 16 CV 0%→35% ethyl acetate in petrol) afforded the title compound as a golden coloured viscous oil (520 mg, 56%).

¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.51 (s, 1H, *H*1), 7.27 (d, ³*J* = 7.9 Hz, 1H, *H*3''), 7.22 (d, ³*J* = 8.6 Hz, 2H, *H*3 or *H*4), 7.21 (d, ⁴*J* = 2.4 Hz, 1H, *H*6''), 7.15 (d, ³*J* = 8.6 Hz, 2H, *H*4 or *H*3), 7.12 (dd, ³*J* = 7.9 Hz, ⁴*J* = 2.4 Hz, 1H, *H*4''), 7.02 (s, 1H, *H*2), 6.66 (d, ³*J* = 7.8 Hz, 1H, *H*8), 6.63 (d, ⁴*J* = 1.6 Hz, 1H, *H*6), 6.58 (dd, ³*J* = 7.8 Hz, ⁴*J* = 1.6 Hz, 1H, *H*9), 6.47-6.42 (m, 3H, *H*2'-4'-6'), 5.98 (s, 2H, *H*7), 5.17 (t, ³*J* = 5.3 Hz, 1H, -NH), 4.51 (d, ³*J* = 5.3 Hz, 2H, *H*5), 3.74 (s, 6H, -OCH₃), 2.40 (s, 3H, -CH₃)

¹³C NMR (100 MHz, CDCl₃) δ (ppm): 167.2 (C), 160.3 (C), 157.2 (C), 154.2 (CH), 147.9 (C), 147.0 (C), 144.7 (C), 142.7 (C), 139.1 (C), 138.3 (C), 134.1 (C), 133.8 (CH), 133.6 (C), 131.8 (C), 131.6 (CH), 129.9 (CH), 129.6 (CH), 129.3 (CH), 129.0 (C), 120.8 (CH), 120.4 (CH), 114.0 (C), 108.3 (CH), 108.1 (CH), 107.6 (CH), 101.1 (CH₂), 99.6 (CH), 55.4 (-OCH₃), 44.7 (CH₂), 21.2 (CH₃)

HRMS (EI): [M]⁺ Calcd. for C₃₅H₂₉N₃O₄S₂ m/z 619.1594, found m/z 619.1593

5-(4-(4-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)thieno[2,3-d]pyrimidin-5-yl)phenyl)-2,4-dimethoxy-8-methyl-5H-dibenzo[b,d]thiophen-5-ium trifluoromethanesulfonate (7)



Appearance: Off-white amorphous powder

Chemical Formula: $C_{36}H_{28}F_3N_3O_7S_3$

Molecular Weight: 767.81

Yield: 72%

Biaryl thioether **6** (124 mg, 0.20 mmol) and sodium trifluoromethanesulfonate (69 mg, 0.40 mmol) were dissolved in acetonitrile (6 mL) and the resulting solution was cooled to 0 °C. Into a separate vial, calcium hypochlorite (technical grade 65% wt., 31 mg, 0.14 mmol) and 1M aqueous acetate buffer (4 mL, pH 4.2) were added and briefly stirred at room temperature until full solubilization. The resulting solution was added dropwise over 10 min into the round-bottomed flask at 0 °C under vigorous stirring. At the end of the addition, the reaction was allowed to warm to room temperature and was stirred for a further 5 min at room temperature. The reaction was subsequently diluted with 1M aqueous solution of sodium hydroxide (9 mL). The resulting crude reaction mixture was extracted with dichloromethane (3×35 mL) and the combined organic layers were washed with a 1M aqueous solution of sodium triflate (10 mL). The combined organic layers were dried over magnesium sulfate and the solvents removed *in vacuo*. The residue was taken up in dichloromethane (2 mL) and added dropwise to a stirred solution of diethyl ether (7 mL); an off-white precipitate immediately formed. The precipitate was allowed to settle and the supernatant was discarded. The remaining powder was subsequently triturated twice in diethyl ether (2×5 mL) to afford the title compound as a pure off-white amorphous powder (110 mg, 72%).

1H NMR (400 MHz, DMSO- d_6) δ (ppm): 8.43 (s, 1H, H1), 8.42 (bs, 1H, H6"), 8.15 (d, $^3J = 8.2$ Hz, 1H, H3"), 7.76 (d, $^4J = 2.0$ Hz, 1H, H2'), 7.71 (d, $^3J = 8.6$ Hz, 2H, H3 or H4), 7.65 (d, $^3J = 8.6$ Hz, 2H, H4 or H3), 7.65 (s, 1H, H2), 7.59 (dd, $^3J = 8.2$ Hz, $^4J = 1.1$ Hz, 1H, H4"), 6.96 (d, $^4J = 2.0$ Hz, 1H, H4'), 6.80 (d, $^4J = 1.7$ Hz, 1H, H6), 6.74 (d, $^3J = 7.9$ Hz, 1H, H8), 6.67 (dd, $^3J = 7.9$ Hz, $^4J = 1.7$ Hz, 1H, H9), 6.07 (t, $^3J = 5.5$ Hz, 1H, -NH), 6.00 (s, 2H, H7), 4.54-4.42 (m, 2H, H5), 4.02 (s, 3H, -OCH₃), 3.90 (s, 3H, -OCH₃), 2.55 (s, 3H, -CH₃)

^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm): 167.1 (C), 167.0 (C), 158.2 (C), 156.7 (C), 153.7 (CH), 147.2 (C), 146.1 (C), 144.8 (C), 142.2 (C), 140.9 (C), 139.1 (C), 132.7 (C), 132.6 (CH), 132.3 (C), 131.5 (CH), 130.4 (C), 129.6 (CH), 127.9 (CH), 126.7 (C), 125.5 (CH), 123.6 (CH), 120.8 (q, $^1J_{C-F} = 321$ Hz, Triflate), 120.4 (CH), 112.7 (C), 108.03 (CH), 107.99 (CH), 107.8 (C), 102.2 (CH), 100.9 (2 signals: CH & CH₂), 57.4 (-OCH₃), 56.8 (-OCH₃), 43.7 (CH₂), 21.3 (CH₃)

^{19}F NMR (282 MHz, DMSO- d_6) δ (ppm): -77.8 (Triflate)

m.p.: 157-158 °C

HRMS (ESI): [M+H]⁺ Calcd. for $C_{35}H_{28}N_3O_4S_2$ m/z 618.1521, found m/z 618.1531

1.6. ICP-MS analysis of APS

Table S1: Concentration of metals by ICP-MS in different commercial batches of ammonium persulfate (APS)

	Metal content ($\mu\text{g/L}$)				
	Ag-107	Cr-52	Cu-65	Fe 56	Mn 55
①, electrophoresis grade (>98%)	1.404	0.130	0.144	1.074	0.021
②, ACS grade (98%)	0.446	2.176	0.105	13.184	0.188
③, ACS grade (98%)	73.645	0.290	0.264	0.850	0.120
Blank	0.0170	0.005	0.006	0.209	0.002

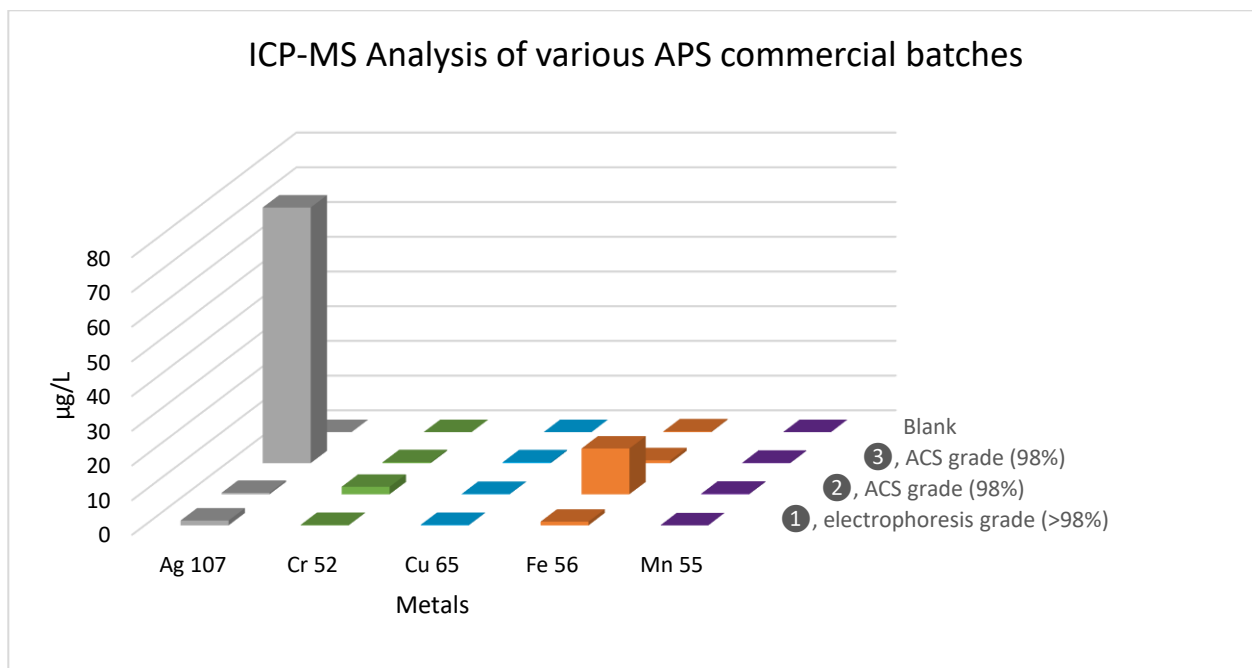
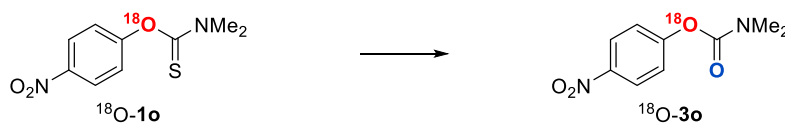


Figure S1: ICP-MS analysis of various APS commercial batches.

Batch ②, contaminated in iron, mediated NKR rearrangement in the absence of any added metal. All experiments described in the article and Supporting Information were carried-out using batch ①, electrophoresis grade (> 98%), which did not react unless a metal catalyst was added.

1.7. Mechanistic investigation using ^{18}O -labelled reagents



Scheme S2: Reaction of ^{18}O -labelled ^{18}O -**1o** under the described NKR conditions.

A J. Young flask (25 mL) was charged with ^{18}O -labelled *O*-aryl carbamothioate ^{18}O -**1o** (228 mg, 1.0 mmol), ammonium persulfate (456 mg, 2 mmol), Mohr's salt (20 mg, 5 mol%). The flask was evacuated and refilled with nitrogen (three times). Anhydrous and degassed acetonitrile (12 mL) was injected after which the flask was sealed and allowed to stir (1200 rpm) at 65 °C for 1 h. The reaction was cooled to room temperature, and then diluted with brine (5 mL) and extracted with chloroform (3×50 mL). The combined organic phases were dried over magnesium sulfate and evaporated under reduced pressure. The residue was purified by automated flash column chromatography (SiO₂ Büchi FlashPure 25 g; 5%→100% [5% EtOAc in CHCl₃] in petrol) to afford ^{18}O -**1o** as a white solid (137 mg, 65%) which was analysed by ¹H & ¹³C NMR spectroscopy and Tandem mass spectrometry MS-MS (Figure S2).

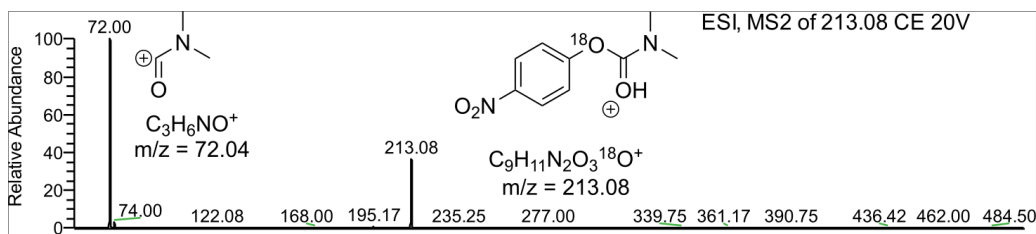
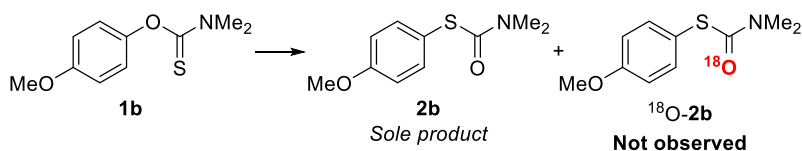


Figure S2: MS-MS analysis of isolated product ^{18}O -**1o**.



Scheme S3: NKR of **1b** using $[^{18}\text{O}]\text{H}_2\text{O}$ as solvent.

A screw-cap vial (14 mL) was charged with *O*-aryl carbamothioate **1b** (105 mg, 0.5 mmol), ammonium persulfate (114 mg, 0.5 mmol), Mohr's salt (10 mg, 5 mol%), and $\text{CH}_3\text{CN}/[^{18}\text{O}]\text{H}_2\text{O}$ (3:1, 6 mL). The vial was capped and the reaction was heated at 45 °C under maximum stirring (1200 rpm) for 1 h. After cooling to room temperature, the crude reaction mixture was diluted with brine (5 mL) and then extracted with chloroform (3×10 mL). The combined organic phases were dried over magnesium sulfate and evaporated under reduced pressure. The residue was purified by automated flash column chromatography (SiO_2 Büchi FlashPure 2×8 g; 10%→25% EtOAc in petrol) to afford **2b** as a white solid (100 mg, 95%). Analysis by ^1H NMR and HRMS confirmed the isolated product was not labelled with ^{18}O (Figure S3 & S4).

133446_190812172149
1 in 2 dilution of submitted sample

08/12/19 17:21:49

RPKCL245

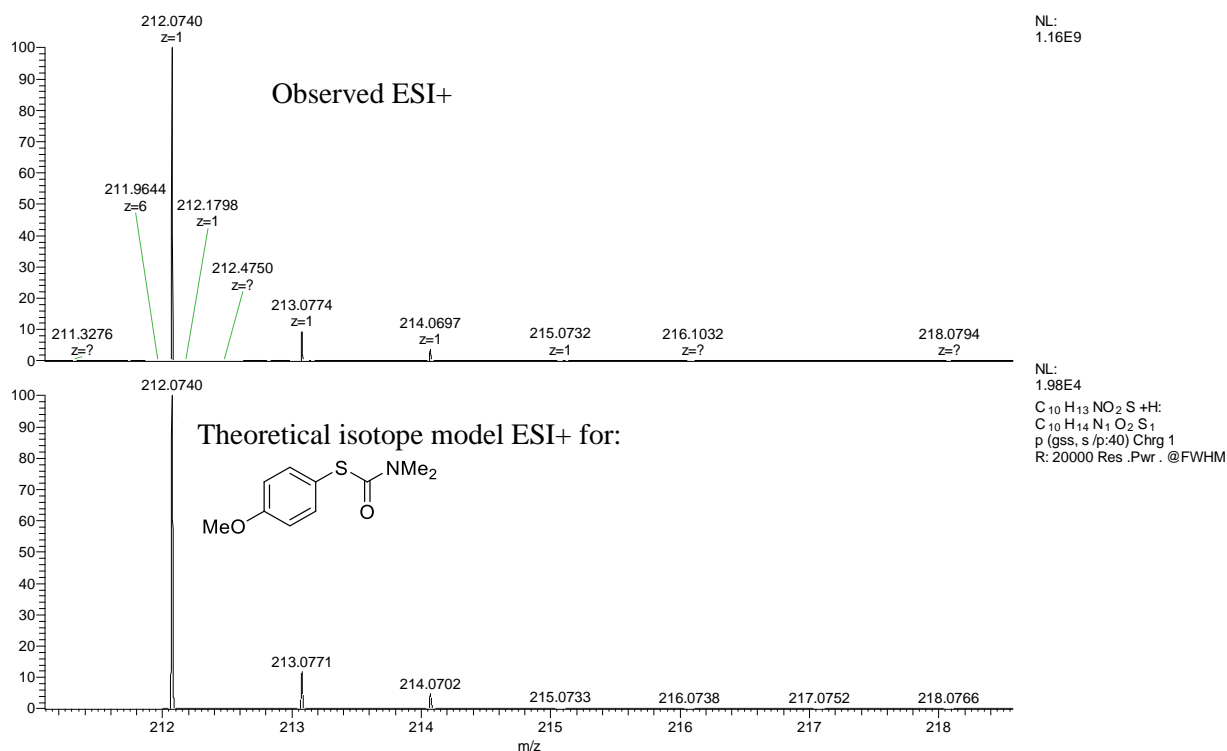


Figure S3: HRMS analysis of the isolated material following NKR of **1b** using $[^{18}\text{O}]\text{H}_2\text{O}$ as solvent (top) compared to the theoretical isotope model (ESI+) of **2b** (bottom).

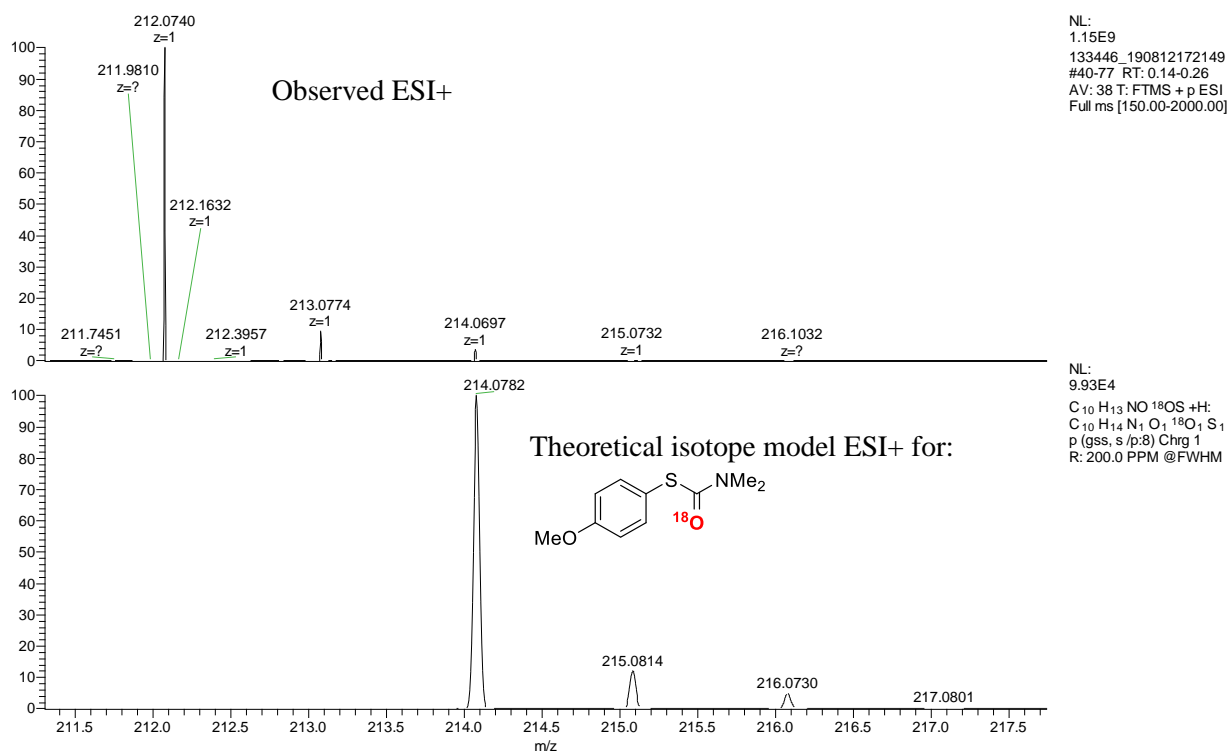
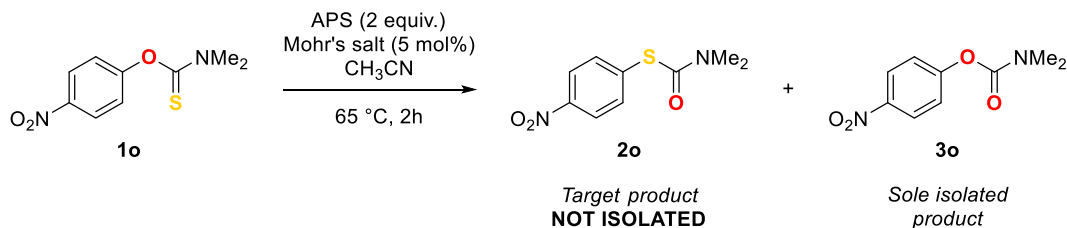


Figure S4: HMRs analysis of the isolated material following NKR of **1b** using [^{18}O] H_2O as solvent (top) compared to the theoretical isotope model (ESI+) of ^{18}O -**2b** (bottom).

1.8. Confirmation of carbamate formation



Scheme S4: Attempted NKR on *O*-aryl carbamothioate **1o**.

A screw-cap vial (14 mL) was charged with **1o** (226 mg, 1.0 mmol), ammonium persulfate (456 mg, 2.0 mmol), Mohr's salt (20 mg, 5 mol%), and CH_3CN (12 mL). The vial was capped and the reaction was heated at 65°C under maximum stirring (1200 rpm) for 2 h. After cooling to room temperature, most of the acetonitrile was removed under reduced pressure. The residue was diluted with brine (10 mL) and then extracted with chloroform (3×10 mL). The combined organic phases were dried over magnesium sulfate and evaporated under reduced pressure. The residue was purified by automated flash column chromatography (SiO_2 Büchi FlashPure 12 g; 15% \rightarrow 50% EtOAc in petrol). The isolated pure fraction (185 mg) was analysed by NMR (Figure S5 & S6, bottom back line) and the resulting spectra were compared to those of an authentic standard of 4-nitrophenyl dimethylcarbamate **3o** synthesized by a previously published procedure (Figure S5 & S6, top green line).⁷ This confirmed the isolated fraction to be 4-nitrophenyl dimethylcarbamate (185 mg, 88%).

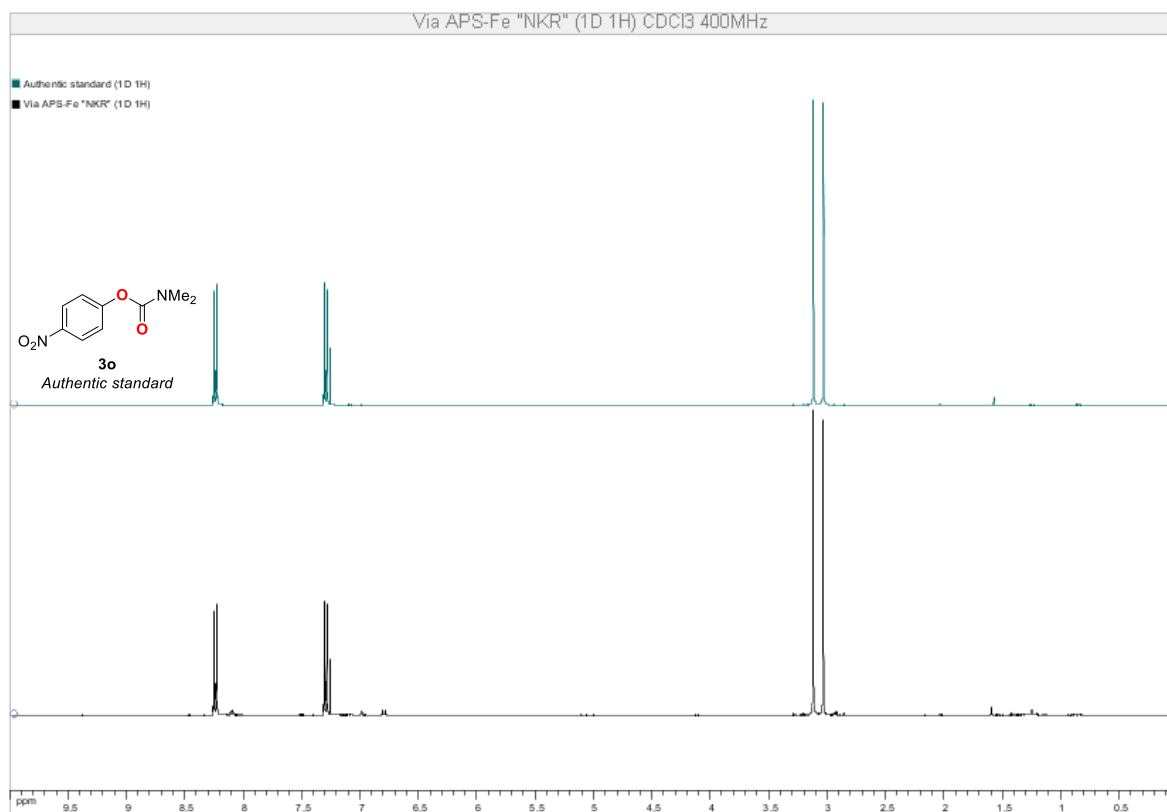


Figure S5: ¹H NMR (CDCl₃, 400 MHz) spectrum of the isolated fraction (black line) and the authentic standard of 4-nitrophenyl dimethylcarbamate **3o** (green line).

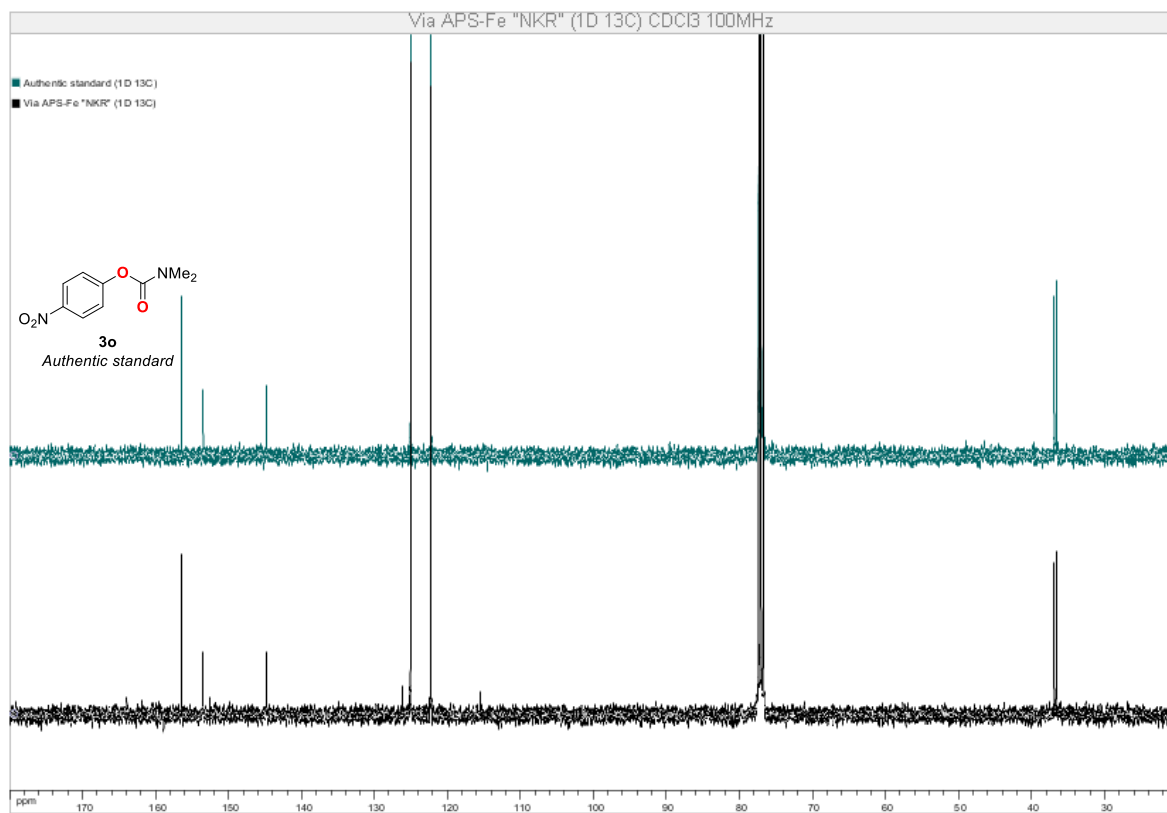
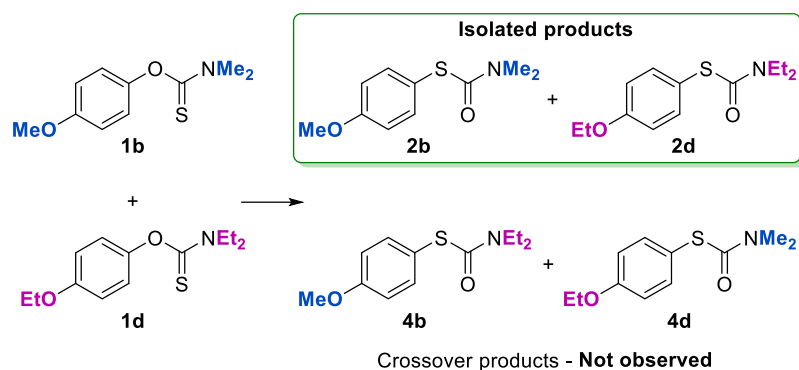


Figure S6: ¹³C NMR (CDCl₃, 100 MHz) spectrum of the isolated fraction (black line) and the authentic standard of 4-nitrophenyl dimethylcarbamate **3o** (green line).

1.9. Crossover experiment



Scheme S5: Crossover experiment.

A screw-cap vial (14 mL) was charged with **1b** (106 mg, 0.5 mmol), **1d** (126 mg, 0.5 mmol), ammonium persulfate (228 mg, 1.0 mmol), Mohr's salt (20 mg, 5 mol%), and CH₃CN/H₂O (3:1, 12 mL). The vial was capped and the reaction was heated at 45 °C under maximum stirring (1 200 rpm) for 1 h. After cooling to room temperature, the crude reaction mixture was diluted with brine (5 mL) and then extracted with chloroform (3 × 50 mL). The combined organic phases were dried over magnesium sulfate and evaporated under reduced pressure to give a yellow oil (0.221 g) which was analysed *via* ¹H NMR spectroscopy (Figure S7) and HRMS.

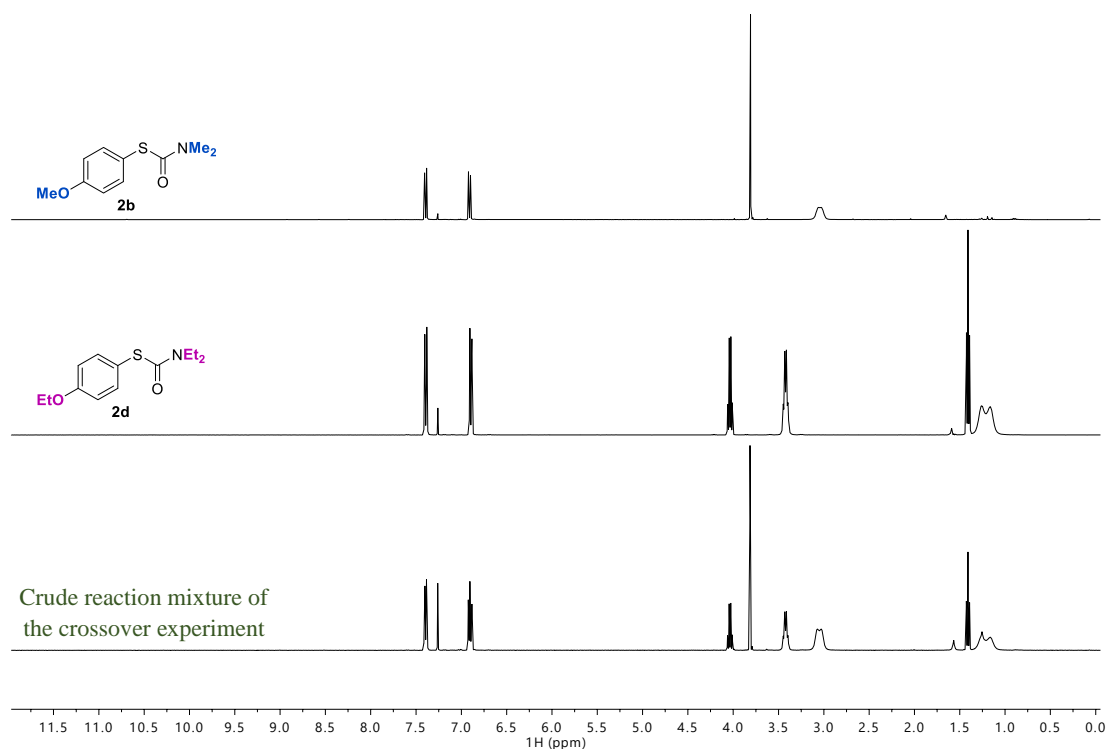


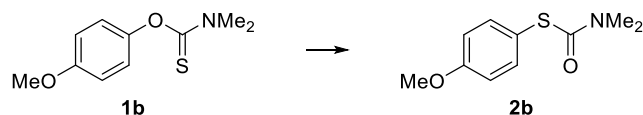
Figure S7: ¹H NMR analysis of the crossover experiment (bottom) overlapped with the ¹H NMR of authentic standards **2b** (top) and **2d** (bottom); all NMRs in CDCl₃, recorded at 400 MHz.

HRMS (ESI) m/z [M+H]⁺: calc. for C₁₀H₁₄NO₂S: 212.0740 (**2b**) and C₁₃H₂₀NO₂S (**2d**): 254.1209

Found in crossover reaction mixture: 212.0741 & 254.1210

No peaks were observed for m/z matching **4b** and **4d**.

1.10. Kinetic profile



Scheme S6: Prototypical reaction used for the kinetic study.

A screw-cap vial (14 mL) was charged with **1b** (106 mg, 0.5 mmol), ammonium persulfate (114 mg, 0.5 mmol), Mohr's salt (10 mg, 5 mol%), and CH₃CN/H₂O (3:1, 6 mL, pre-warmed to 45 °C). The vial was capped and the reaction was heated at 45 °C under maximum stirring (1 200 rpm). At the desired time-point, the reaction was cooled to -78 °C in a dry ice/acetone bath. A sample of the reaction mixture (1.0 mL) was added to water (0.2 mL) in a screw-cap vial (14 mL). To this was added CHCl₃ (10 mL) and mixed well. This mixture was dried over MgSO₄ and then filtered through a cotton plug in a syringe (20 mL). The organic solvents were removed under reduced pressure and the residue was dried under high-vacuum before ¹H NMR spectroscopy analysis. This protocol was repeated for each timepoint.

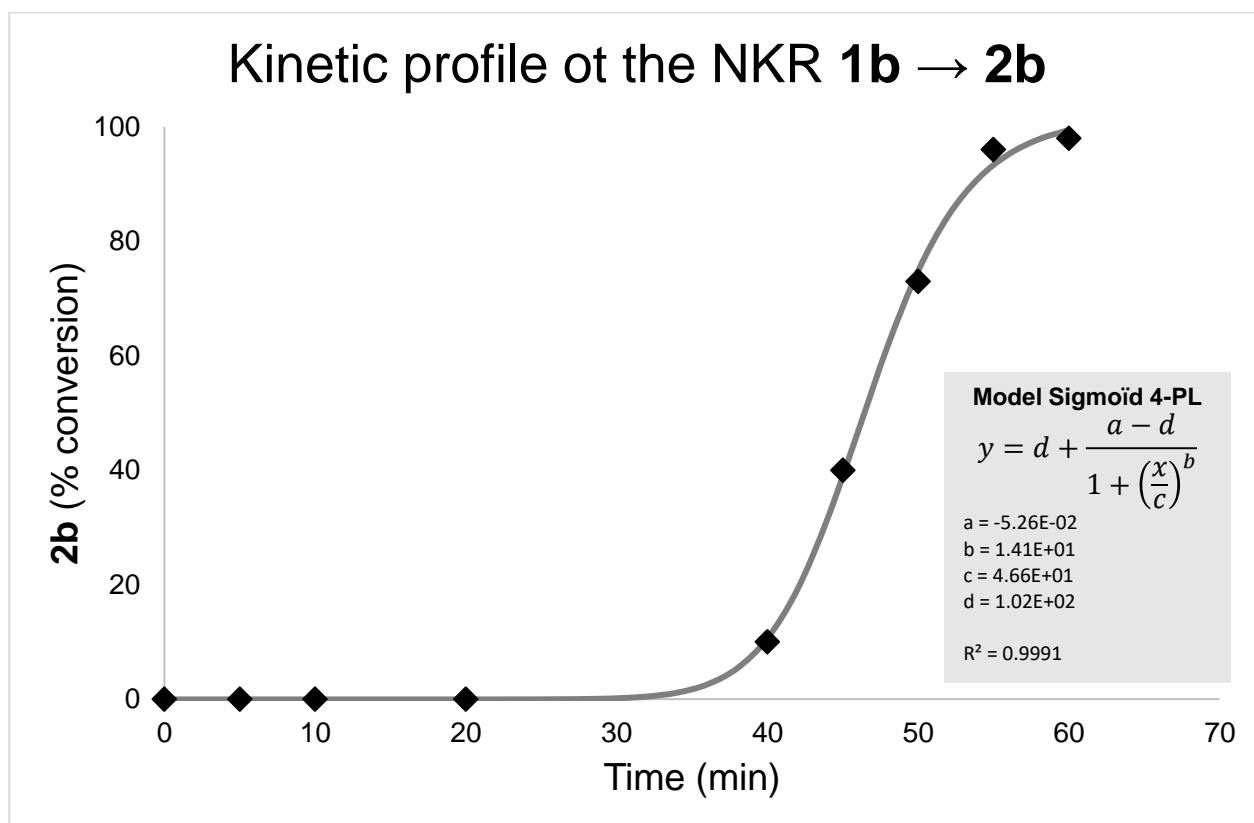


Figure S8: Kinetic profile of the rearrangement of **1b** to **2b**.

2. Radiolabeling experiments

2.1. Definitions and general considerations

All labeling reactions were performed manually using [^{18}F]fluoride in [^{18}O]H $_2\text{O}$ (50-1500 MBq). Radio-HPLC were performed with an Agilent 1200 HPLC system equipped with a 1200 Series Diode Array Detector and a GABI Star NaI(Tl) scintillation detector (energy window 400-700 keV). The system was used for purification as well as characterization of radiotracers. Columns and conditions used for purification and quality controls (QC) are indicated in the protocol or next to the corresponding chromatogram.

Radiochemical yields were calculated as follows:

- Analytical radiochemical yields (ARCY) were determined using radio-HPLC chromatograms of the quenched crude labeling mixture and refer to the area under the curve (AUC) of the radioactive peak of interest divided by the summed AUC of all other radioactive peaks ([^{18}F]fluoride and potential side-products).
- Isolated radiochemical yields (RCY) refer to the activity of the pure tracer isolated after HPLC divided by the initial activity of [^{18}F]fluoride in [^{18}O]H $_2\text{O}$ used for the labeling; no corrections were made for losses during transfer, cartridges trapping and release.

2.2. Cartridge conditioning and cryptand mixture preparation

Various Solid Phase Extraction (SPE) cartridges were used in the radiolabeling experiments described hereafter. These cartridges were conditioned as follows:

Sep-Pak Accell Plus QMA Plus Light Cartridge (130 mg, Waters Cat. no. WAT023525) was flushed successively with aqueous sodium hydroxide (1M, 5 mL), HPLC water (10 mL), aqueous potassium **carbonate** (1M, 1 mL), HPLC water (10 mL) and air-dried (10 mL).

Sep-Pak Alumina N Plus Light Cartridge (280 mg, Waters Cat. no. WAT023561) was flushed with HPLC water (1 mL) and air-dried (5 mL).

Sep-Pak tC18 Plus Light Cartridge (145 mg, Waters Cat. no. WAT036805) was flushed with methanol (5 mL), HPLC water (10 mL) and air-dried (10 mL).

Unless otherwise stated, all radiolabeling experiments were carried-out with a cryptand mixture composed of Kryptofix 222 (30 mM) and potassium **bicarbonate** (30 mM) in acetonitrile/water (85:15). Typically, a solution of potassium **bicarbonate** (19 mg) in HPLC water (1 mL) was added to a previously prepared solution of Kryptofix 222 (71 mg) in acetonitrile (5.5 mL). To elute [^{18}F]fluoride from the QMA, 0.5 mL of the resulting solution was used for each labeling experiment.

2.3. Radiolabeling of ^{18}F -AEM1 (non-optimized protocol)

^{18}F Fluoride in ^{18}O -water (300-1500 MBq) was trapped on a Sep-Pak® QMA cartridge, released with a solution (0.5 mL) of Kryptofix 222 (30 mM) and potassium bicarbonate (30 mM) dissolved in acetonitrile/water (85:15). After removing the solvent by heating at 92 °C (heating mantle) under a stream of nitrogen, anhydrous acetonitrile (0.5 mL) was added, and the distillation was continued at 92 °C. This procedure was repeated once and the reaction vial was subsequently capped. The labeling precursor **7** (2.5 mg) dissolved in anhydrous dimethylsulfoxide (0.5 mL) was added and the mixture was stirred at 125 °C for 25 min. After cooling, the reaction was diluted with a 20% ethanol in water solution (1.5 mL) and purified by HPLC using a Zorbax® 300SB-C18 column (250 × 9.4 mm) using water and methanol as solvents at 3.50 mL.min⁻¹. A gradient elution [0-13 min, 50→79% MeOH/H₂O; 13-16 min, hold at 79% MeOH/H₂O; 16-18 min, 79→95% MeOH/H₂O; 18-22 min hold at 95% MeOH/H₂O; 22-25 min, 95→50% MeOH/H₂O] allowed for isolation of the radioactive product (Figure S9, Rt ≈ 16.5 min). The isolated fraction was diluted to 20 mL with water and passed through a Sep-Pak Alumina N cartridge followed by a Sep-Pak tC18 cartridge. The pure ^{18}F -AEM1 was eluted from the Sep-Pak tC18 cartridge with ethanol (0.5 mL). The isolated decay-corrected RCY was 15 ± 4% (*n* = 4) at the end of HPLC purification and the radiochemical purity was > 98%. The identity of the radiochemical product was confirmed by co-elution with the non-radioactive analogue (Figure S10).

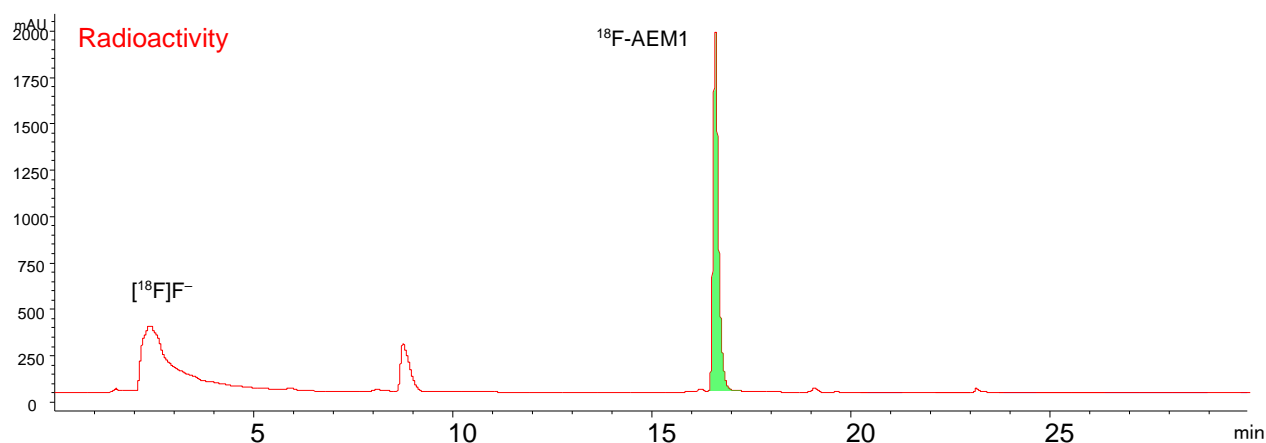


Figure S9. Preparative HPLC chromatogram of ^{18}F -AEM1

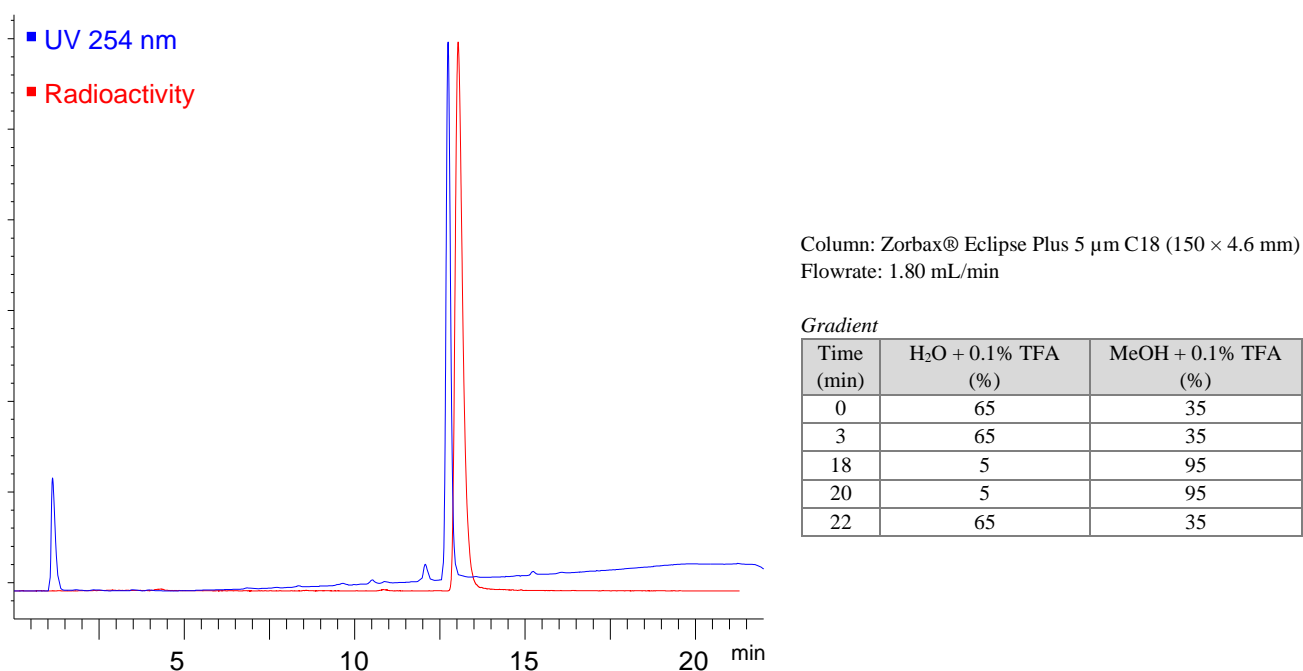
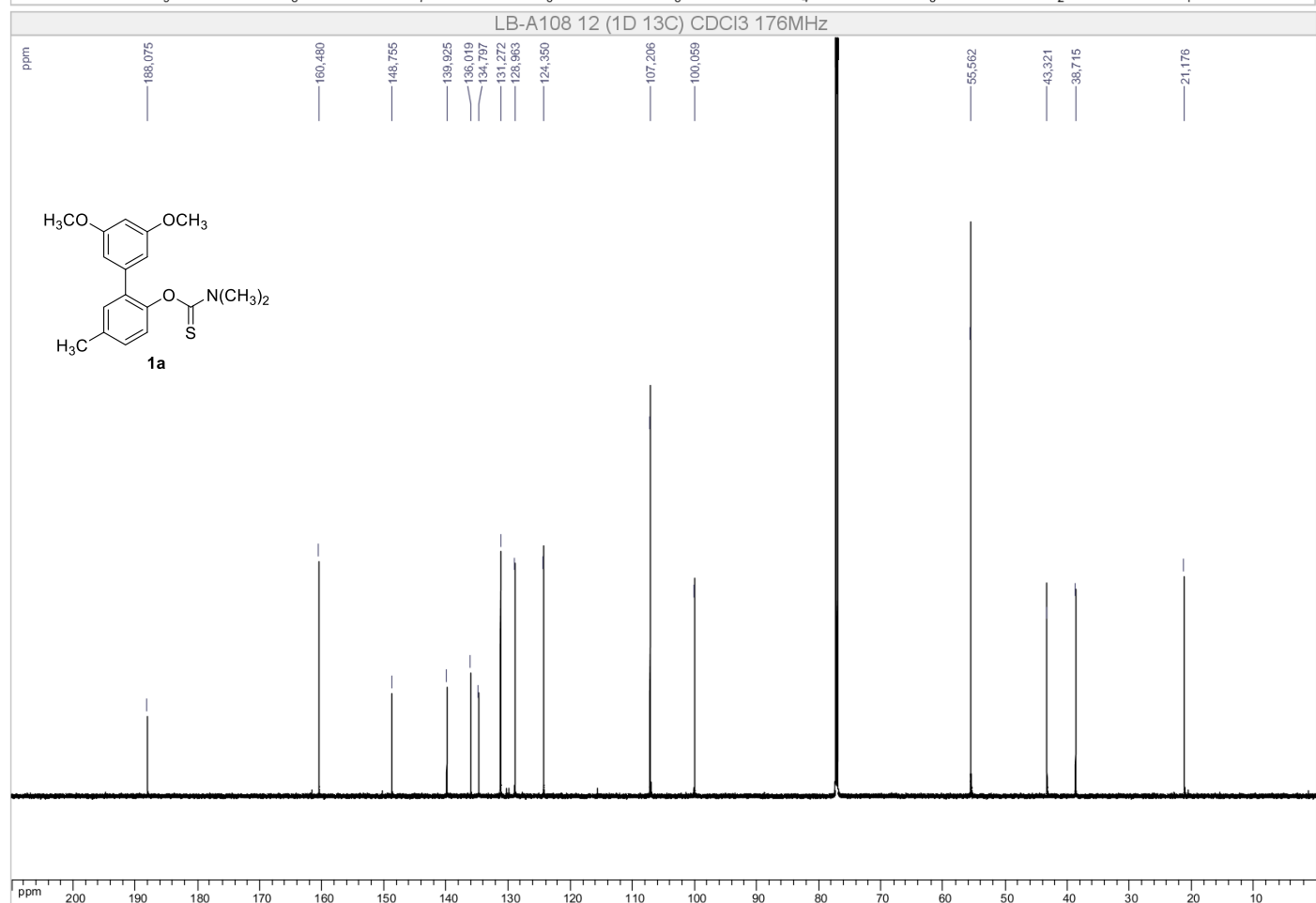
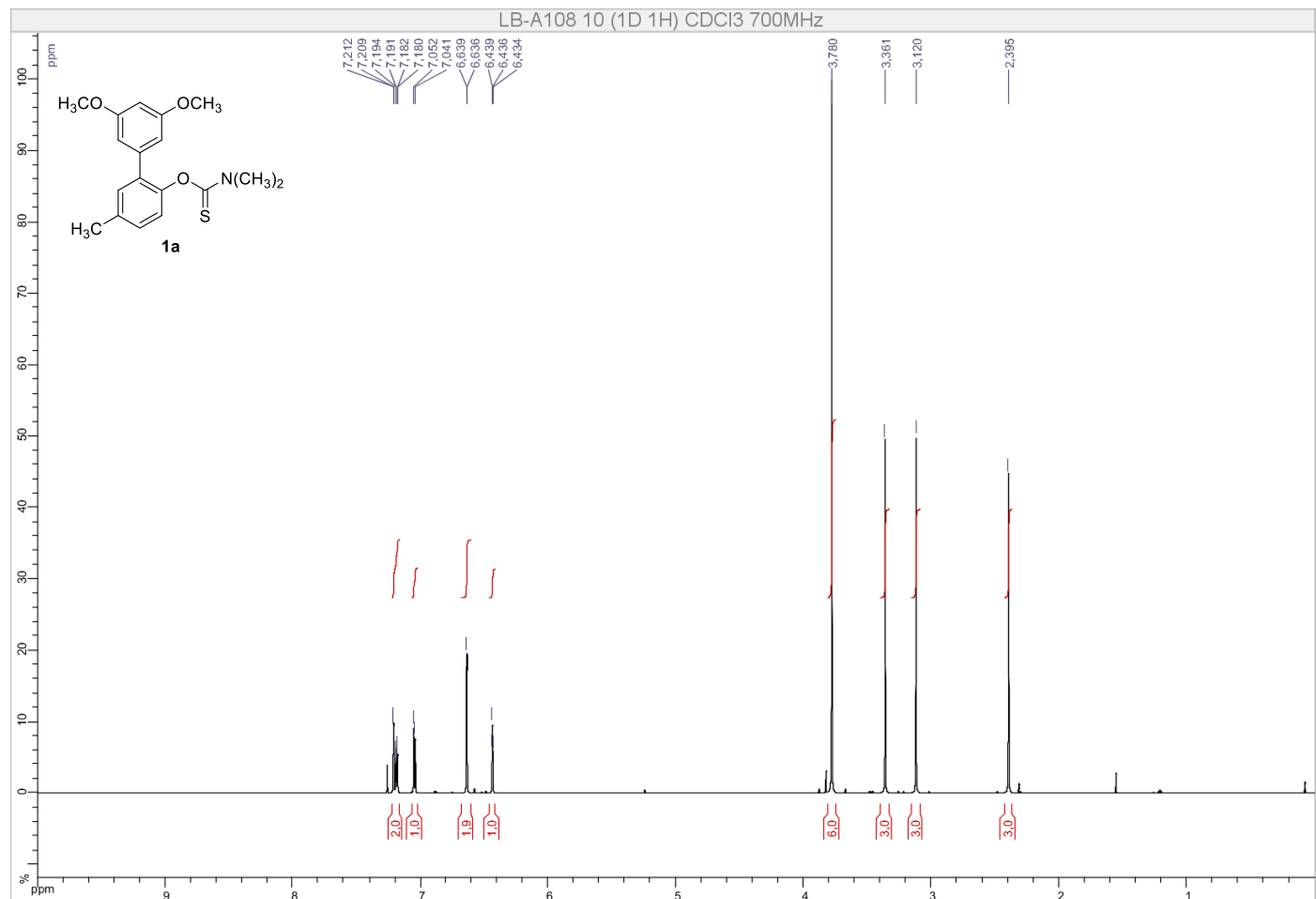


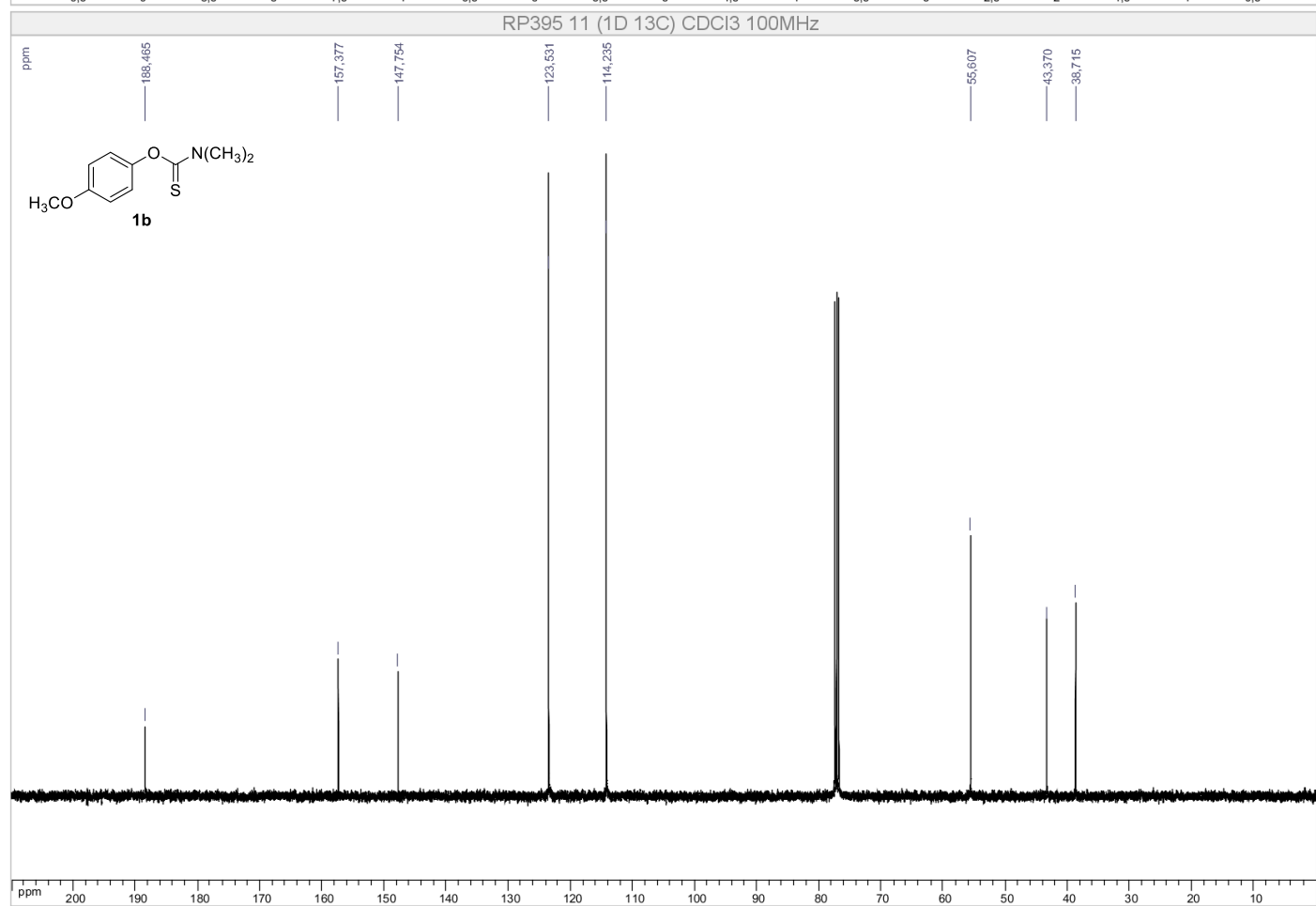
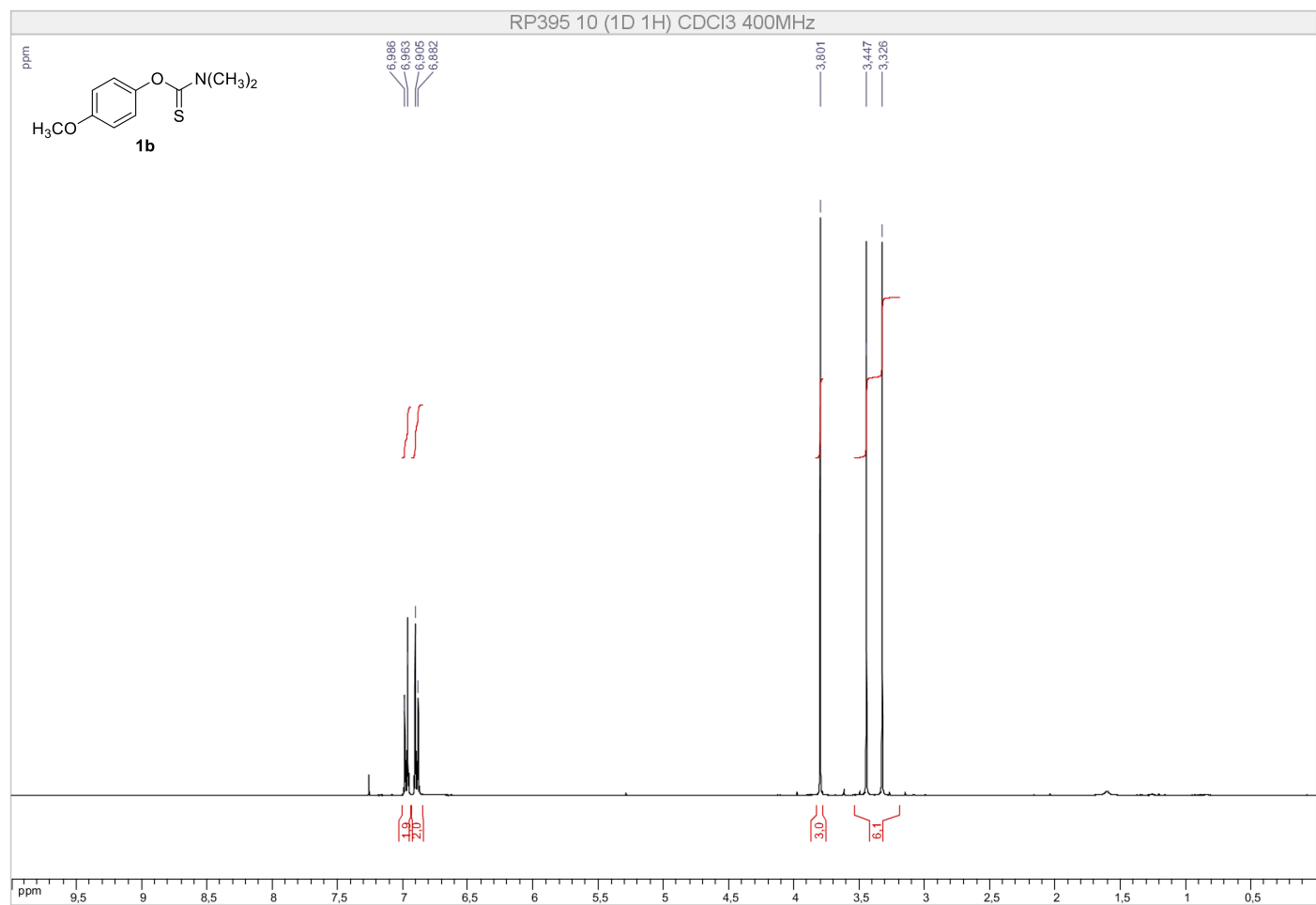
Figure S10. HPLC chromatogram of the isolated radiochemical product ^{18}F -AEM1, co-injected with the non-radioactive AEM1 reference

Appendix

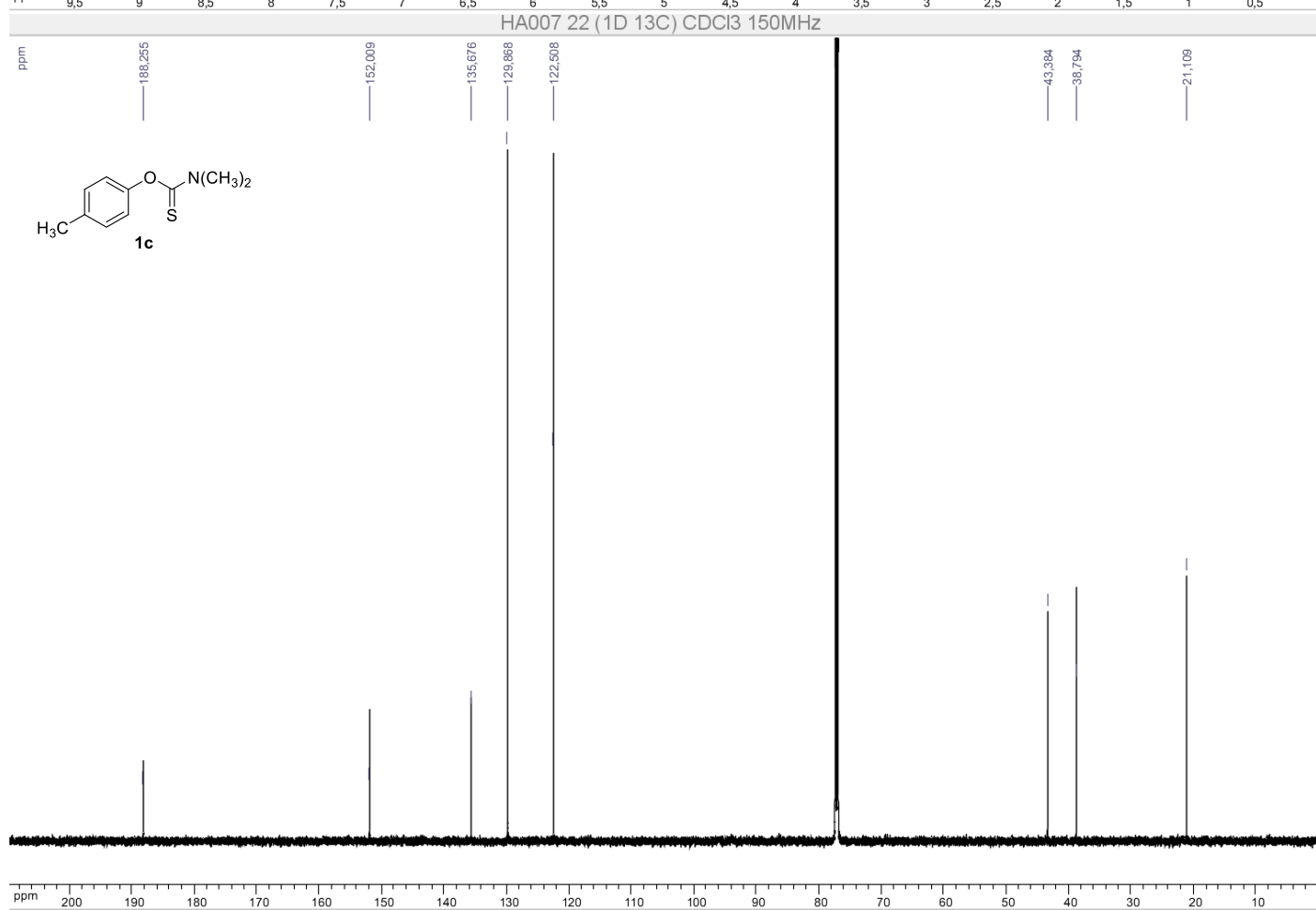
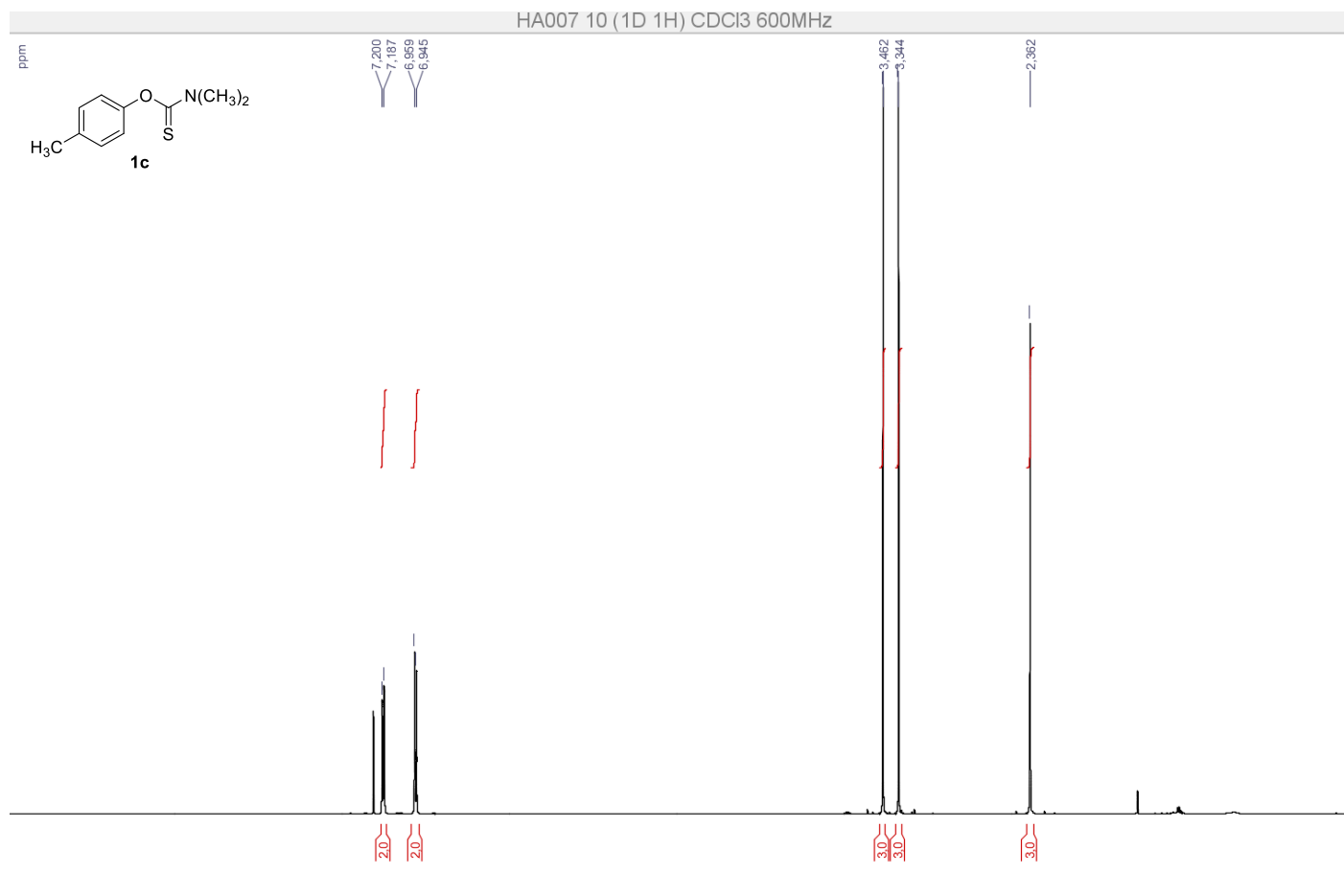
O-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate (**1a**)



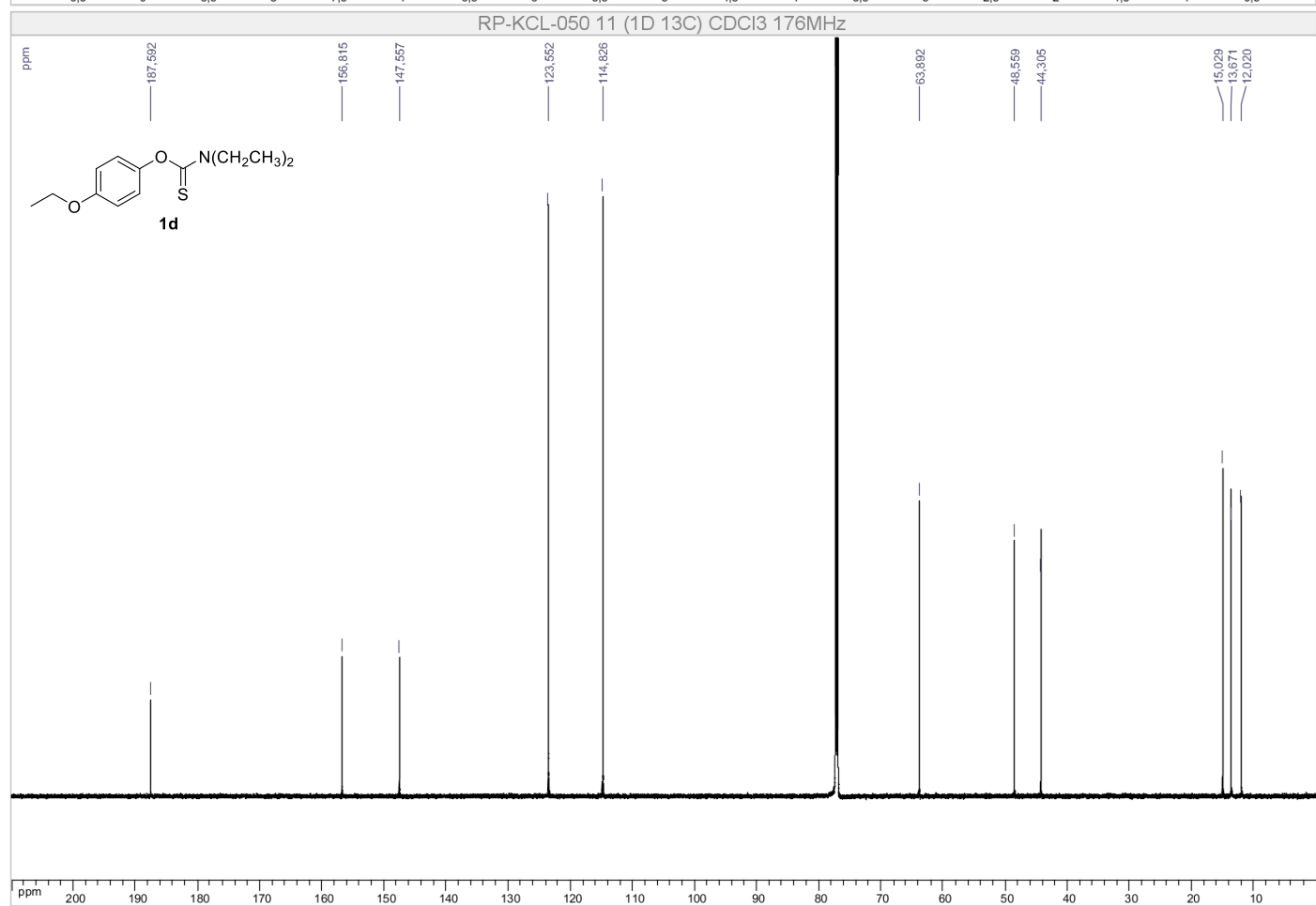
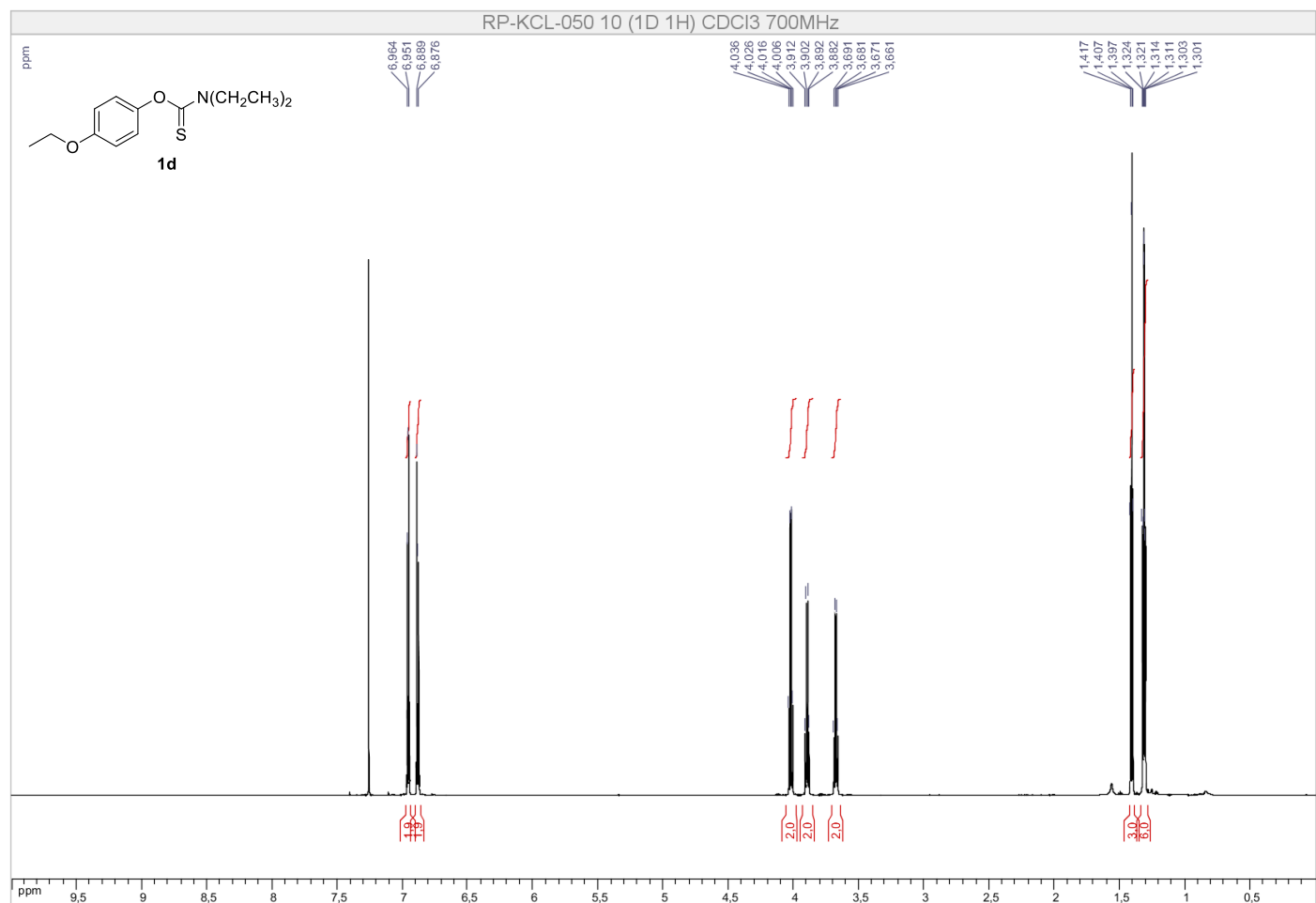
O-(4-methoxyphenyl) dimethylcarbamothioate (**1b**)



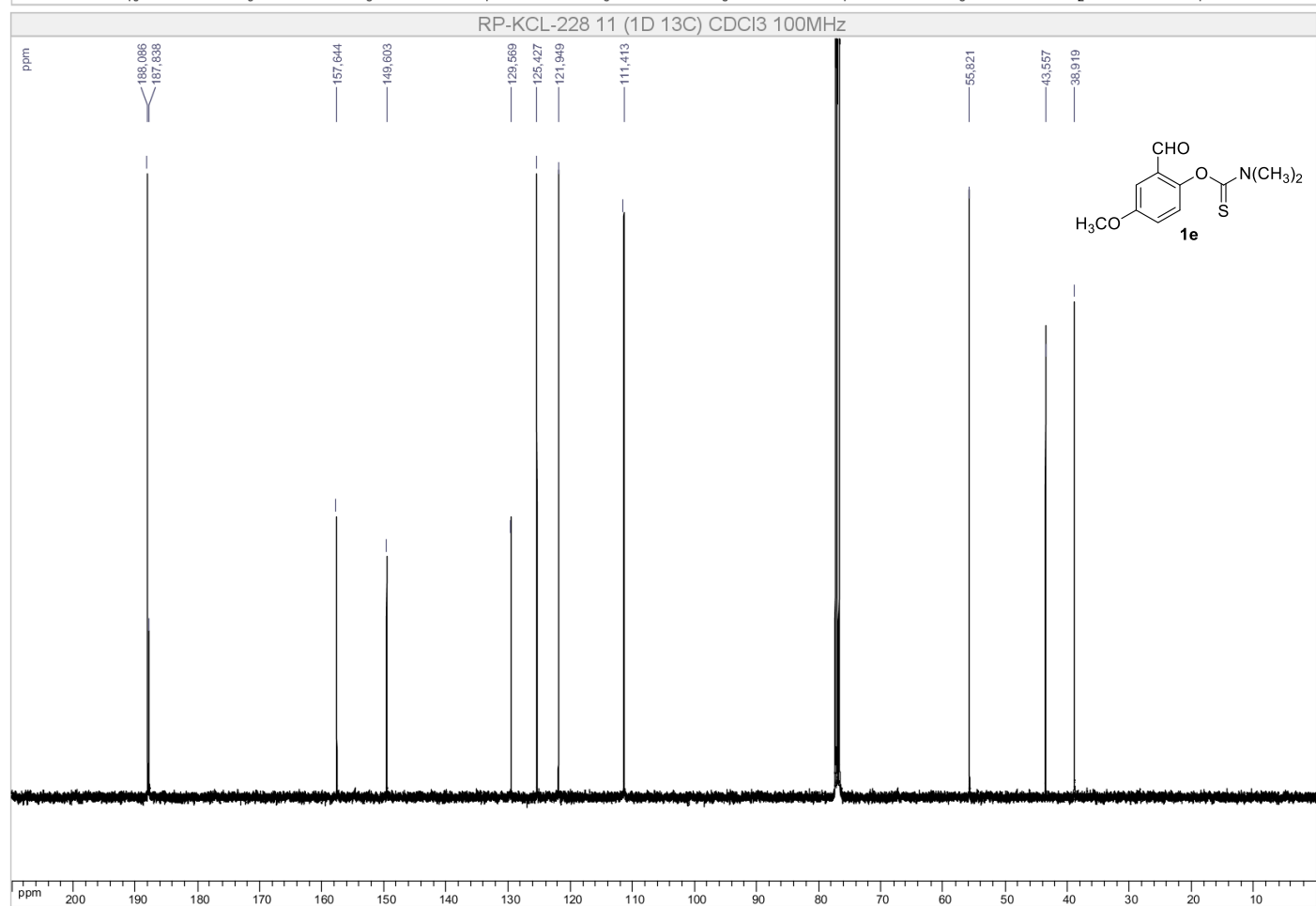
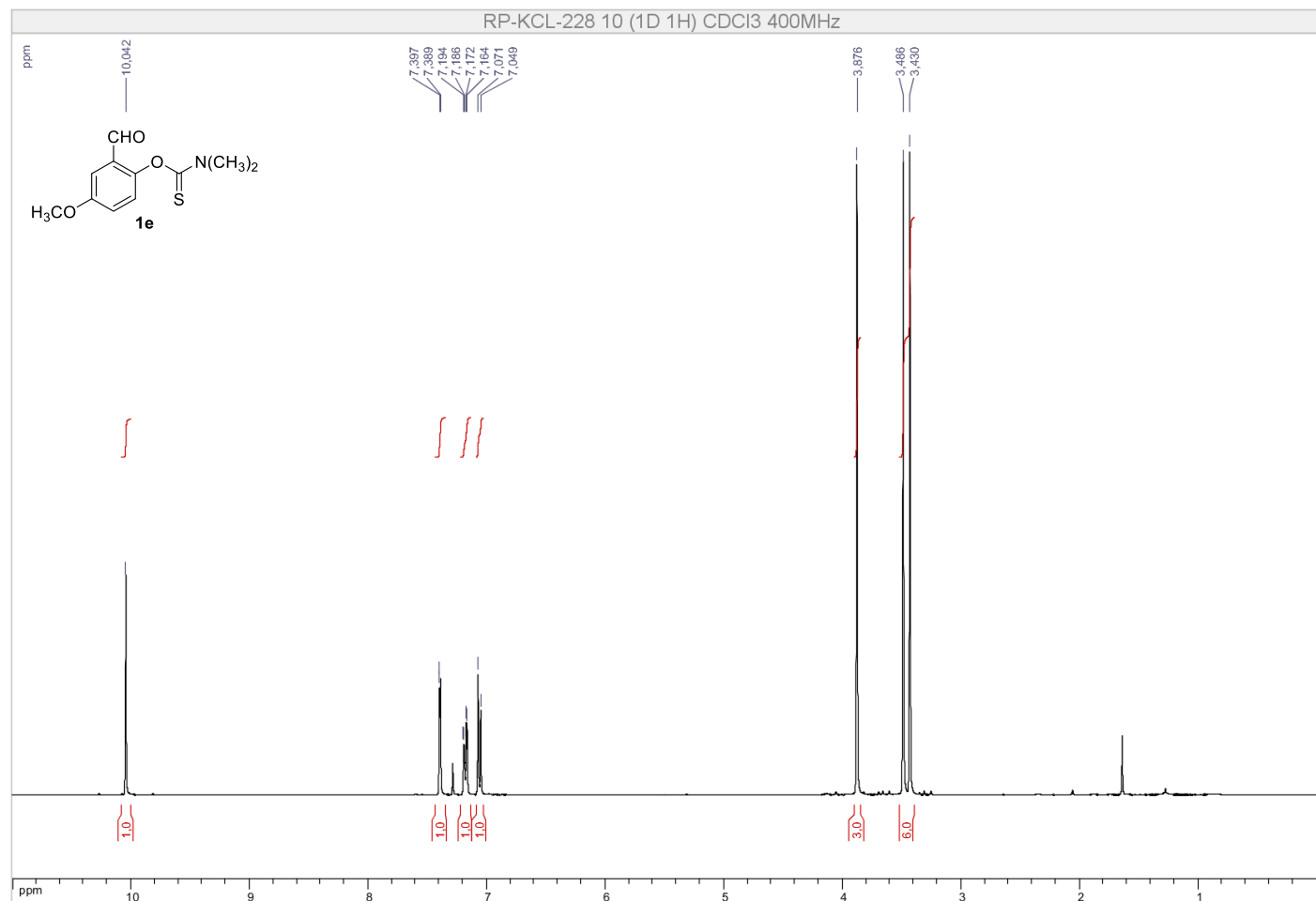
O-(4-methylphenyl) dimethylcarbamothioate (**1c**)



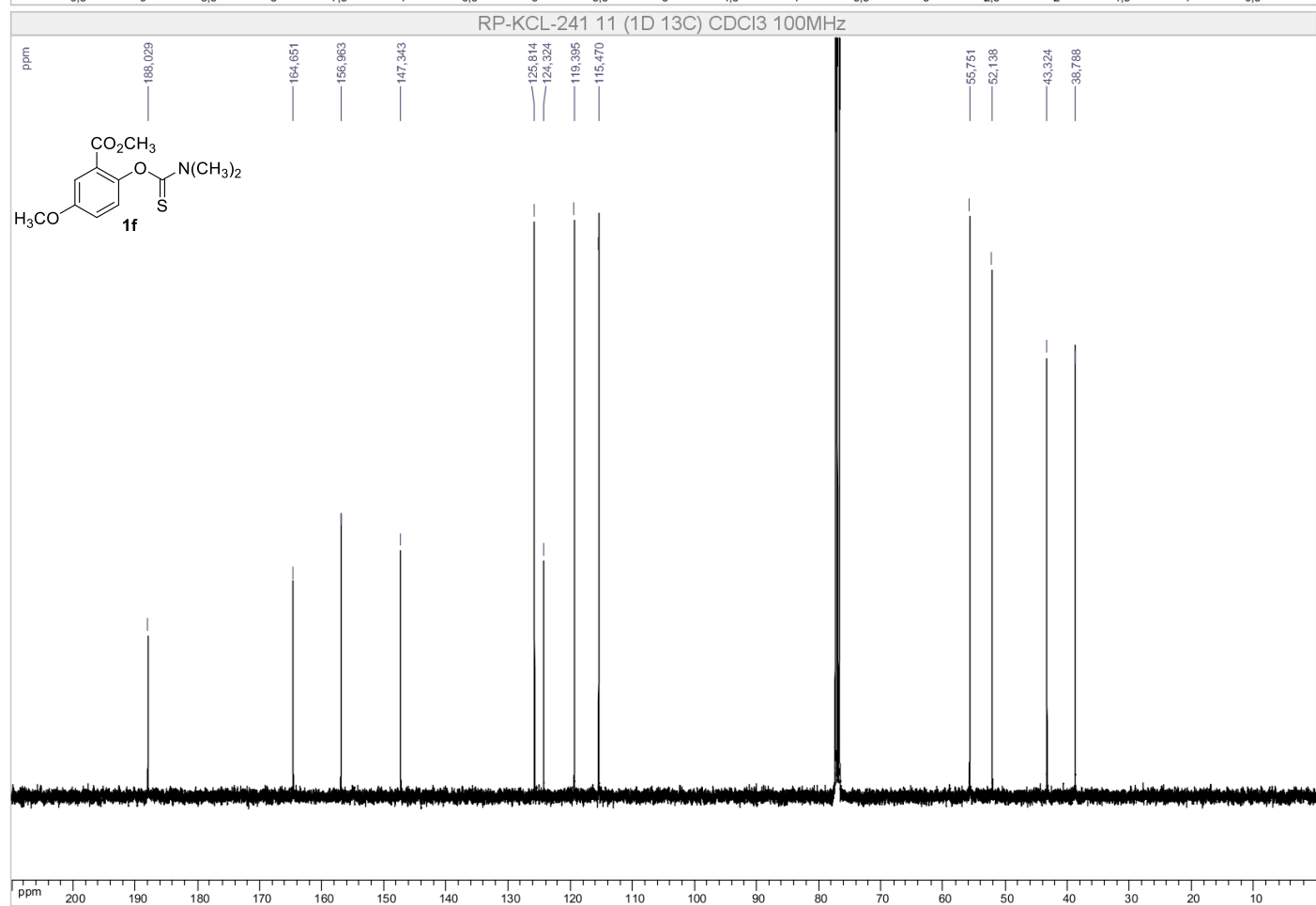
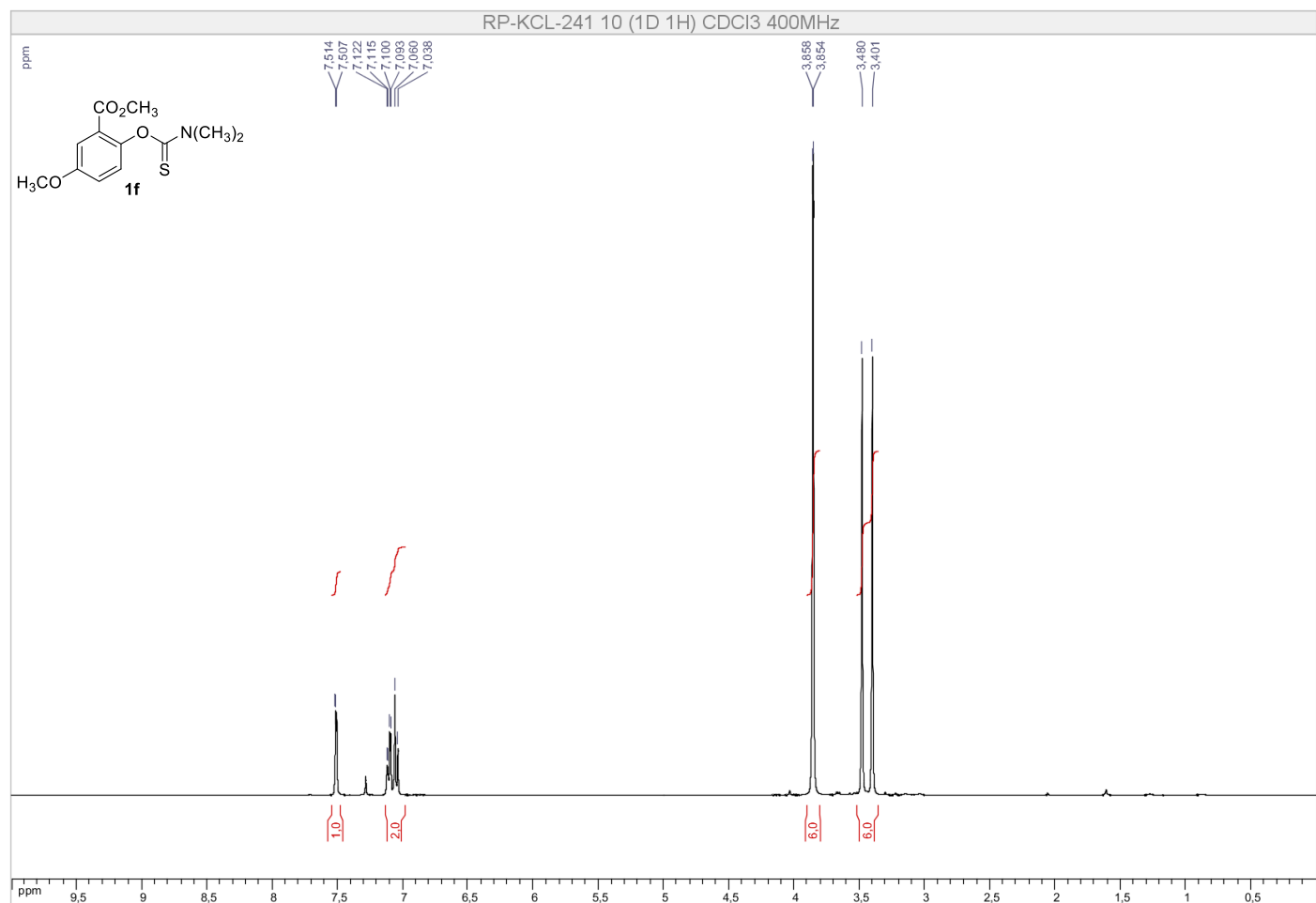
O-(4-ethoxyphenyl) diethylcarbamothioate (**1d**)



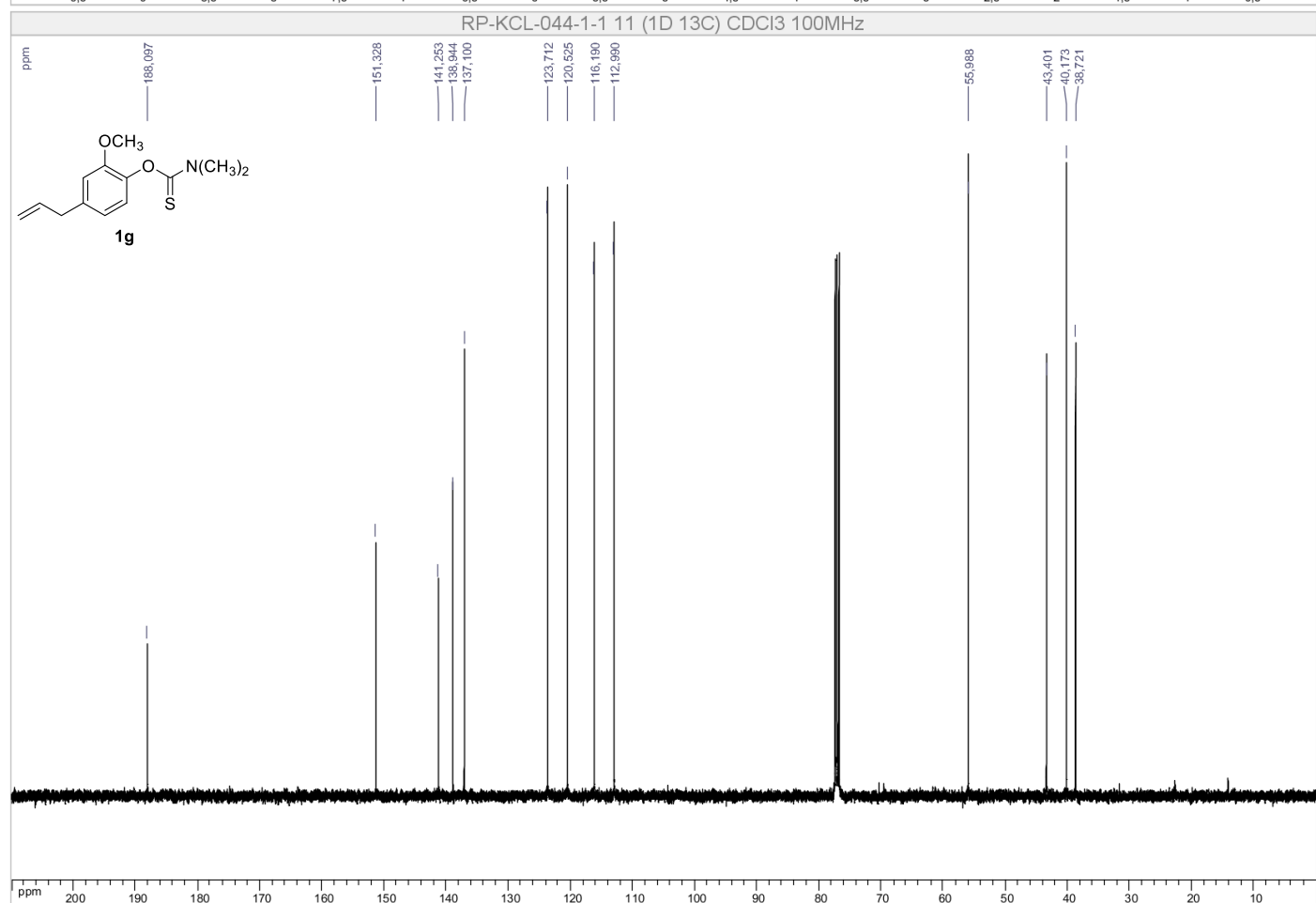
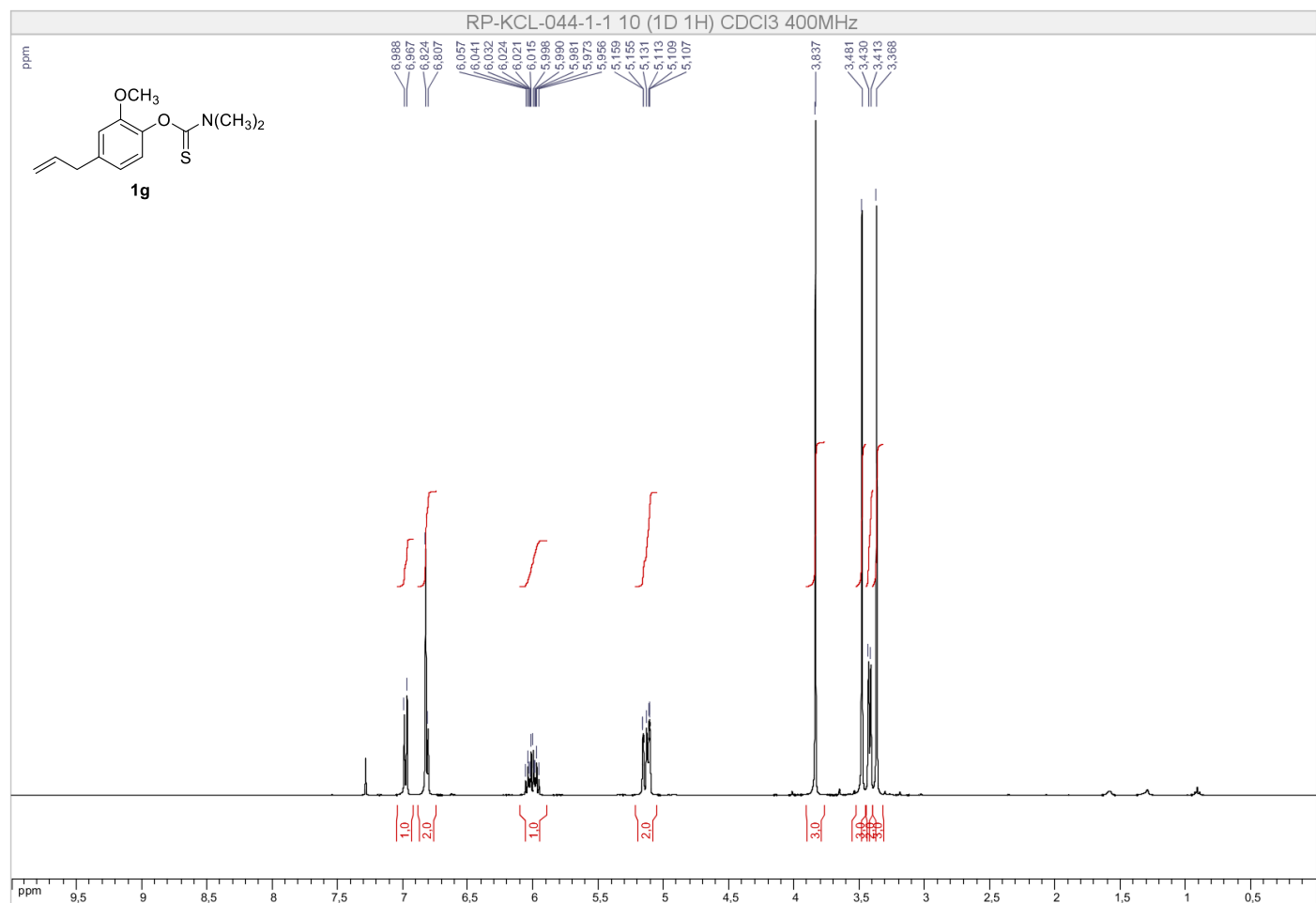
O-(2-formyl-4-methoxyphenyl) dimethylcarbamothioate (**1e**)



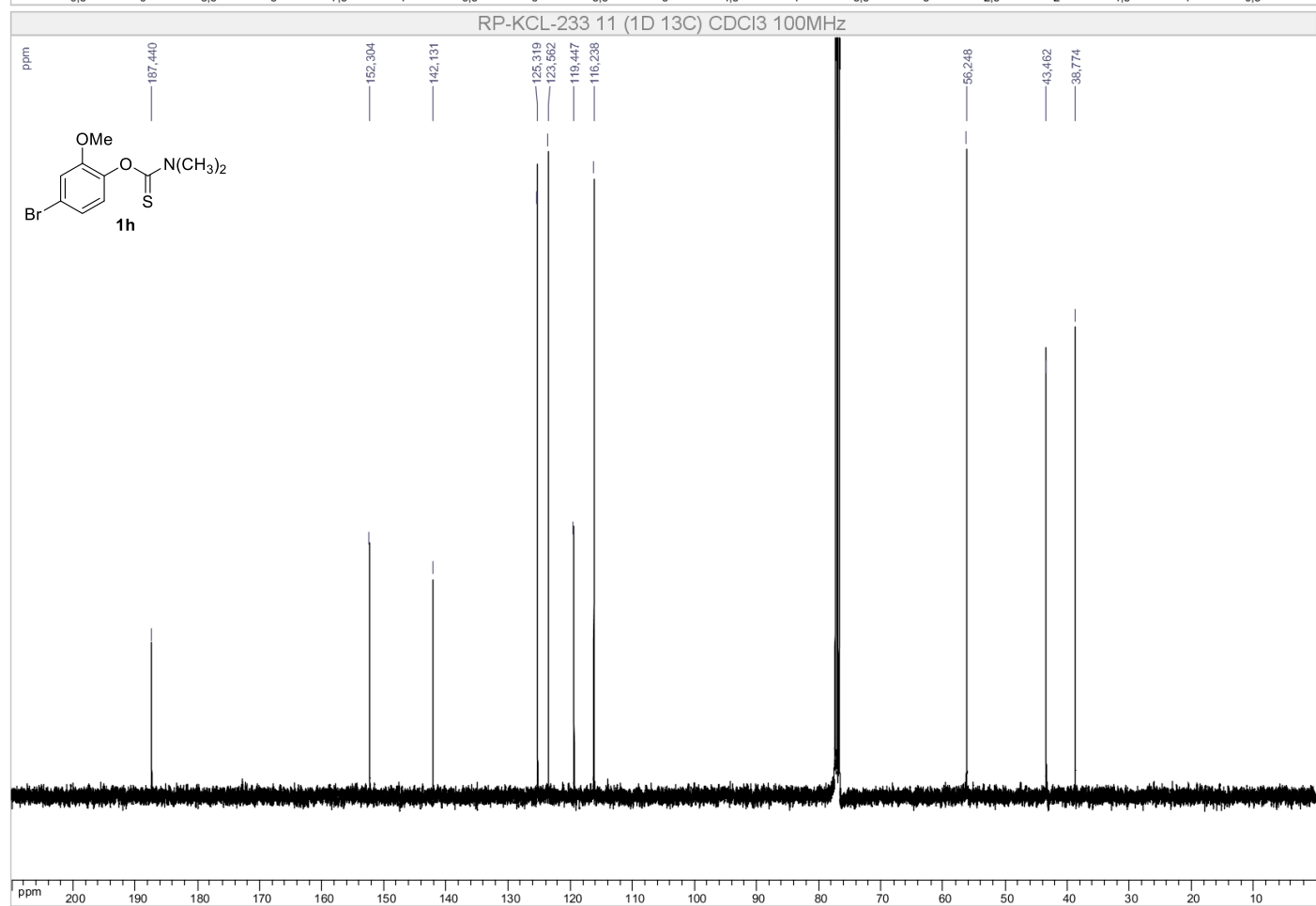
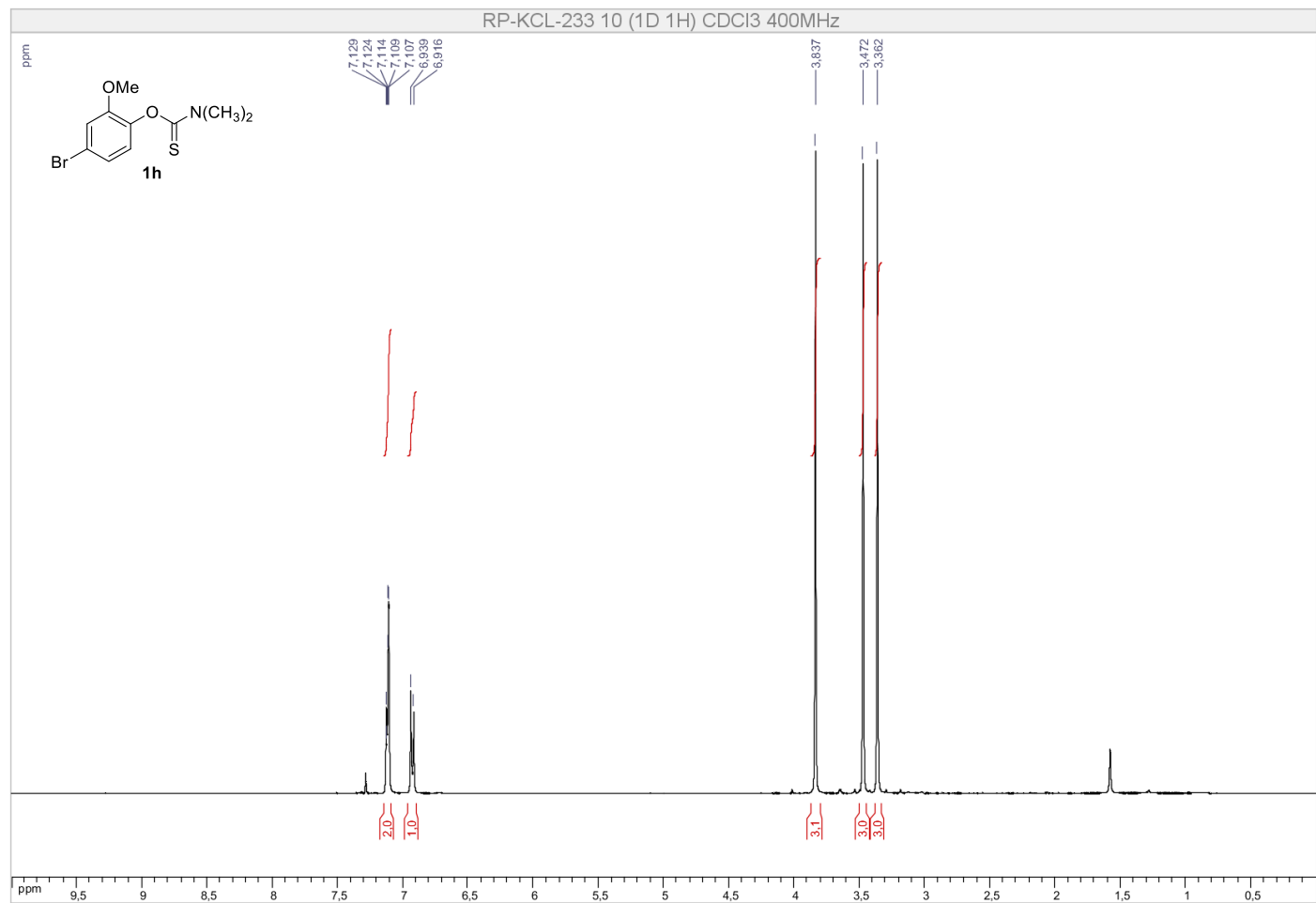
Methyl 2-((dimethylcarbamothioyl)oxy)-5-methoxybenzoate (**1f**)



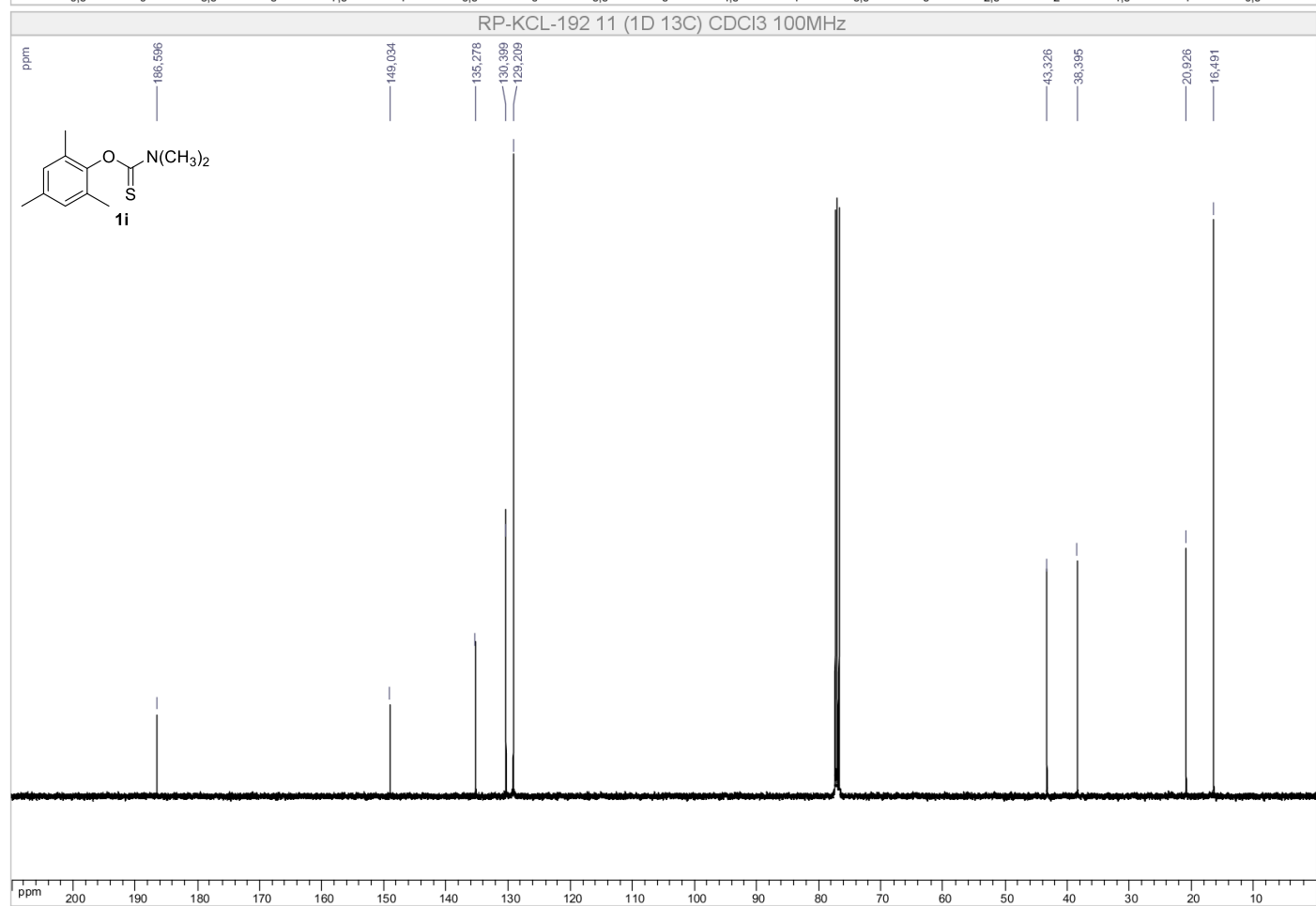
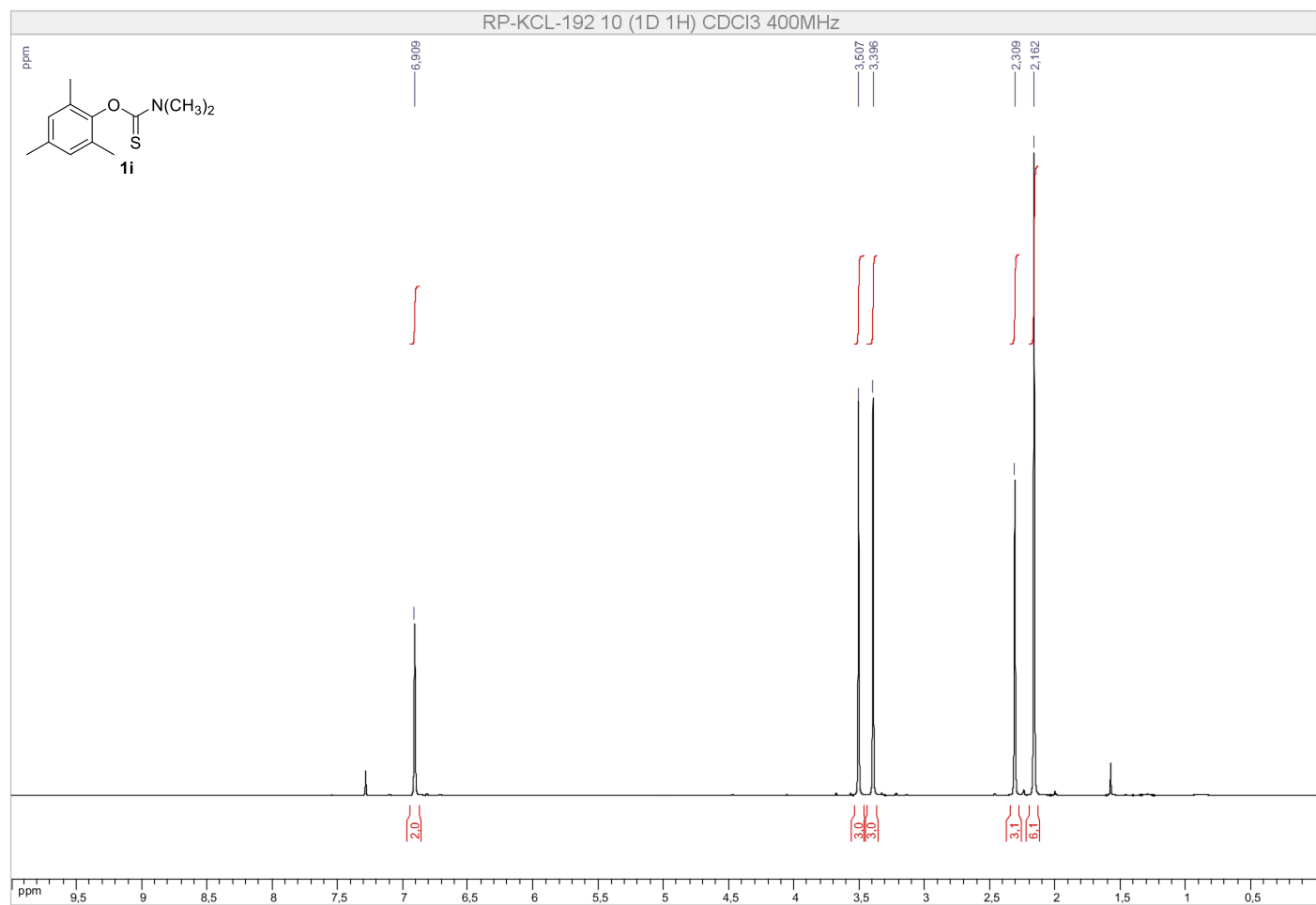
O-(4-allyl-2-methoxyphenyl) dimethylcarbamothioate (**1g**)



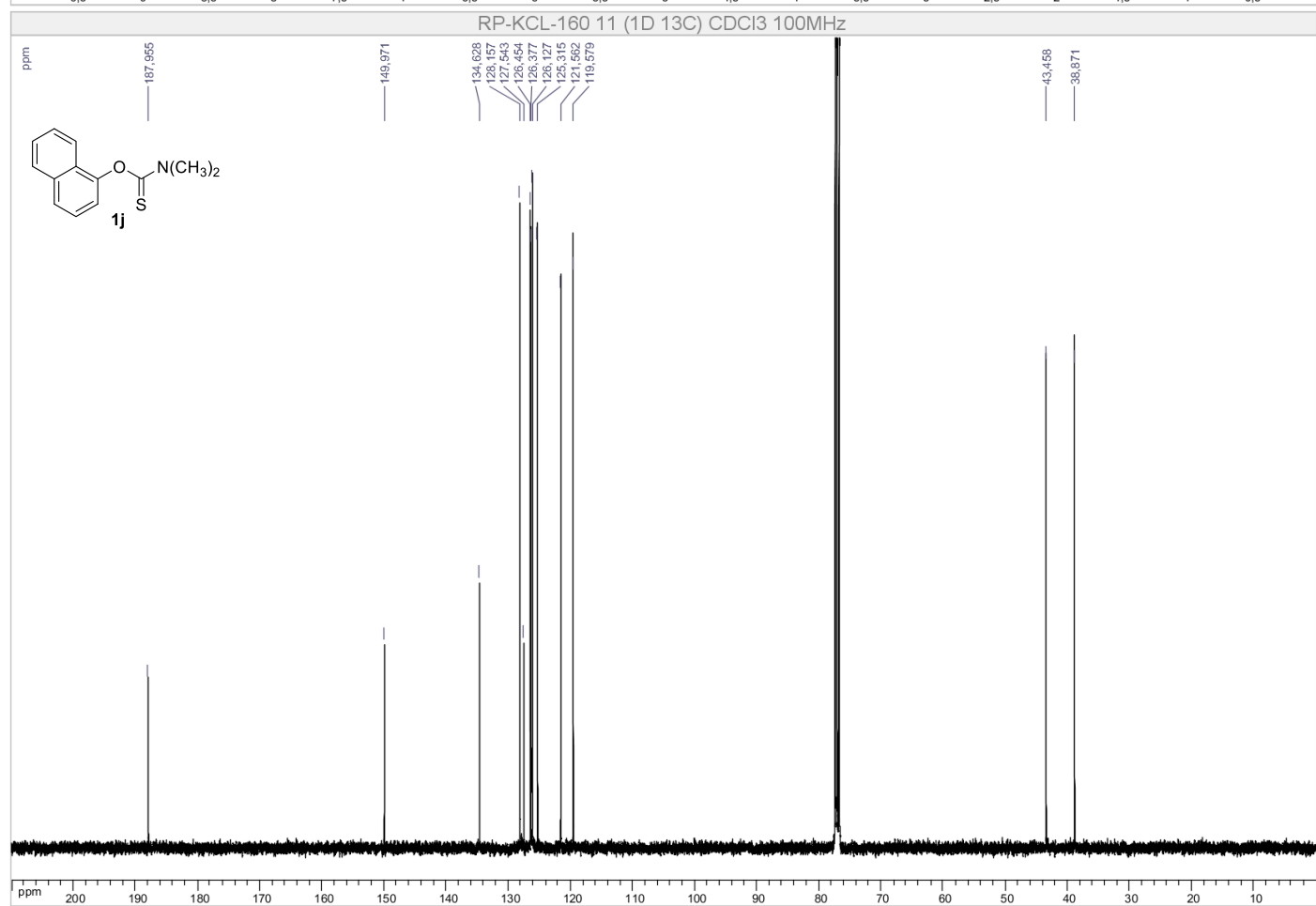
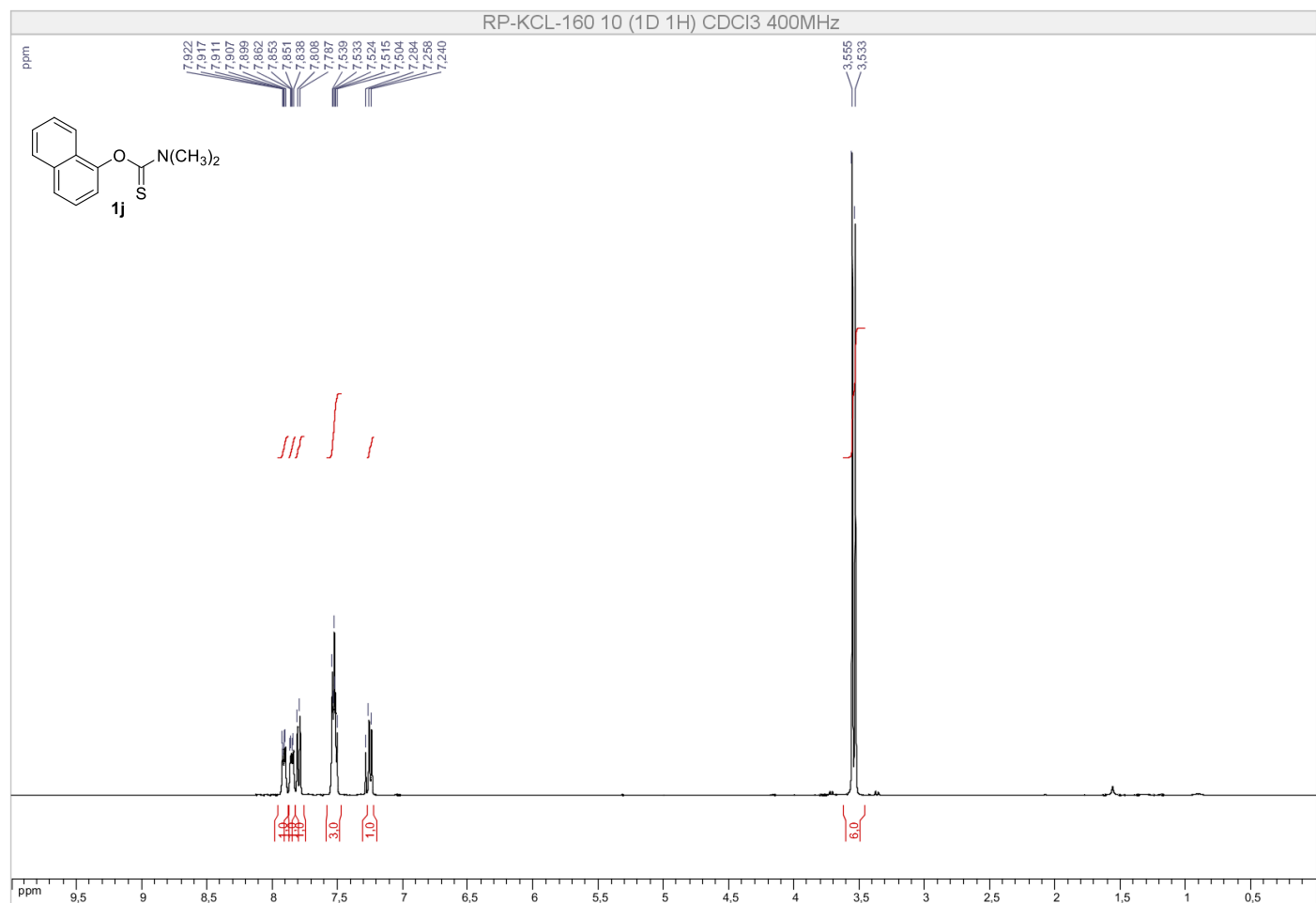
O-(4-bromo-2-methoxyphenyl) dimethylcarbamothioate (**1h**)



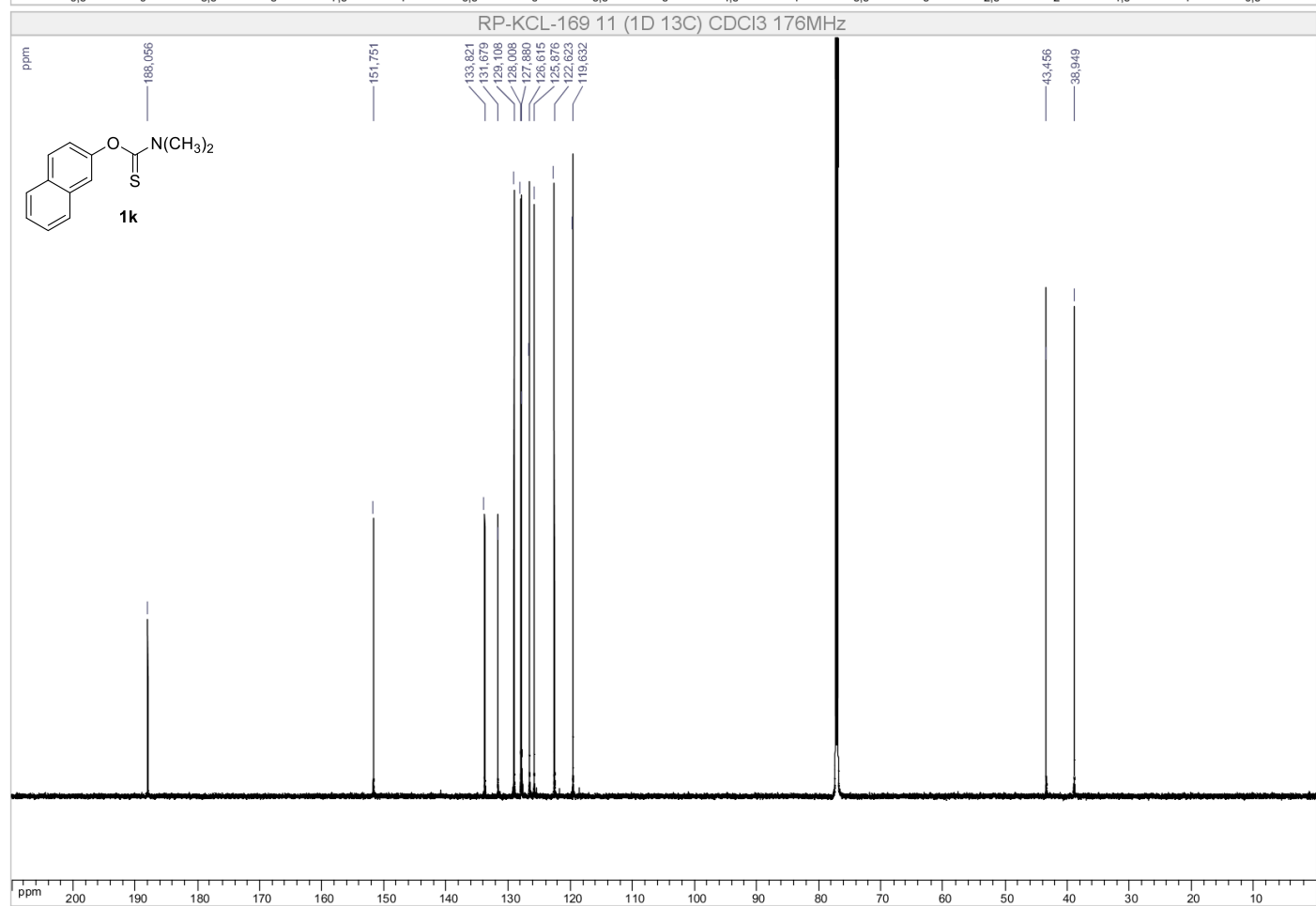
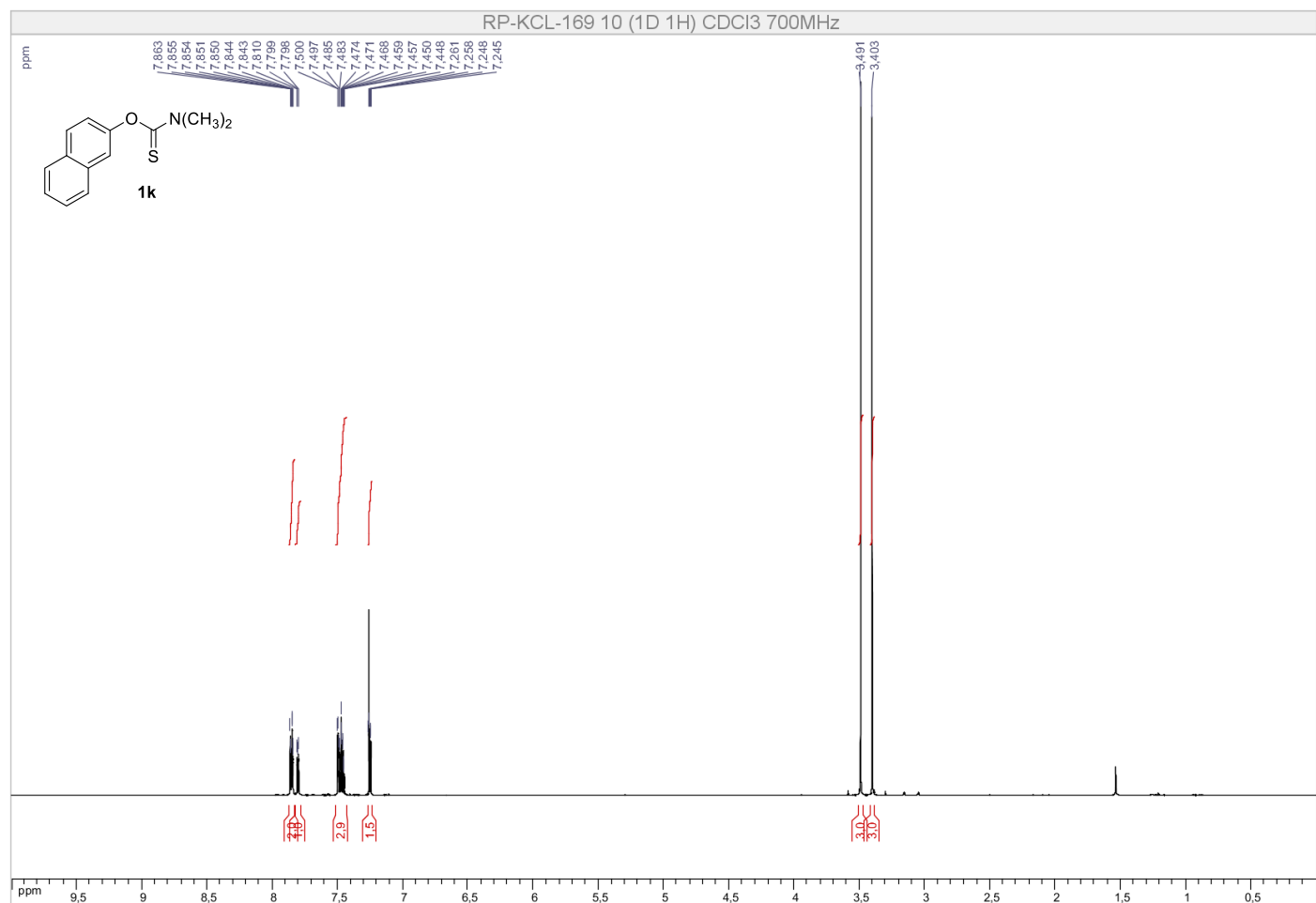
O-mesityl dimethylcarbamothioate (**1i**)



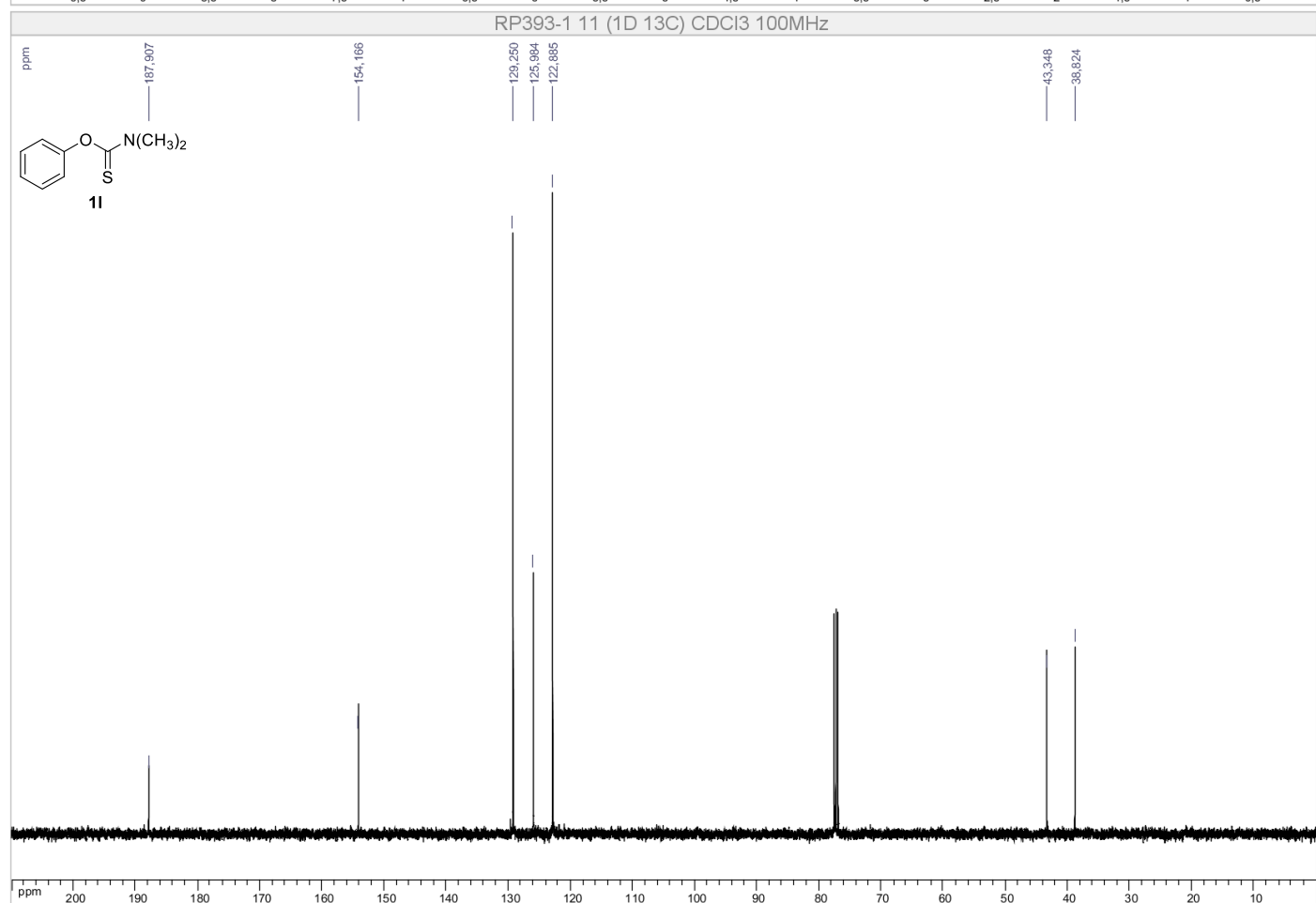
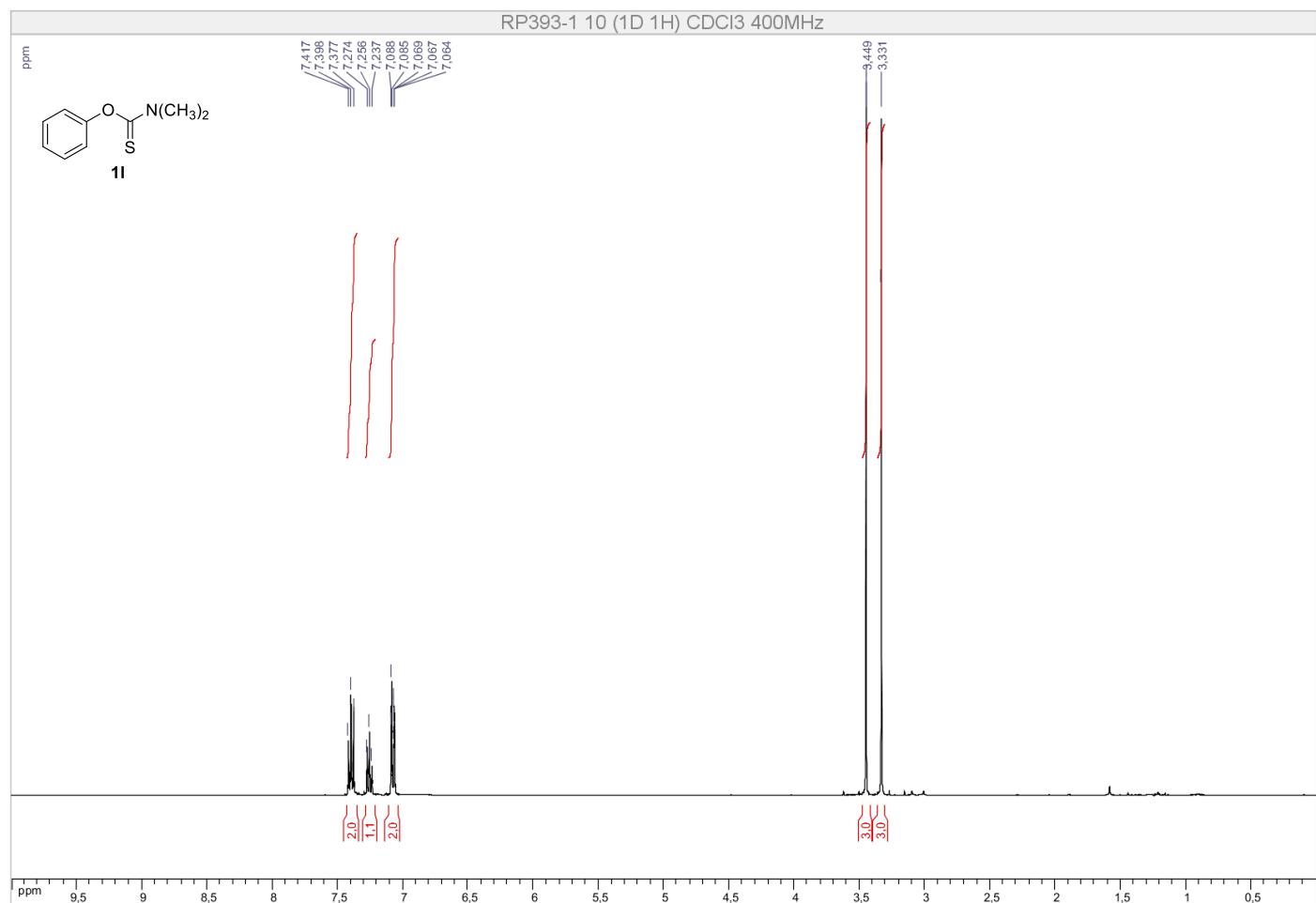
O-(naphthalen-1-yl) dimethylcarbamothioate (**1j**)



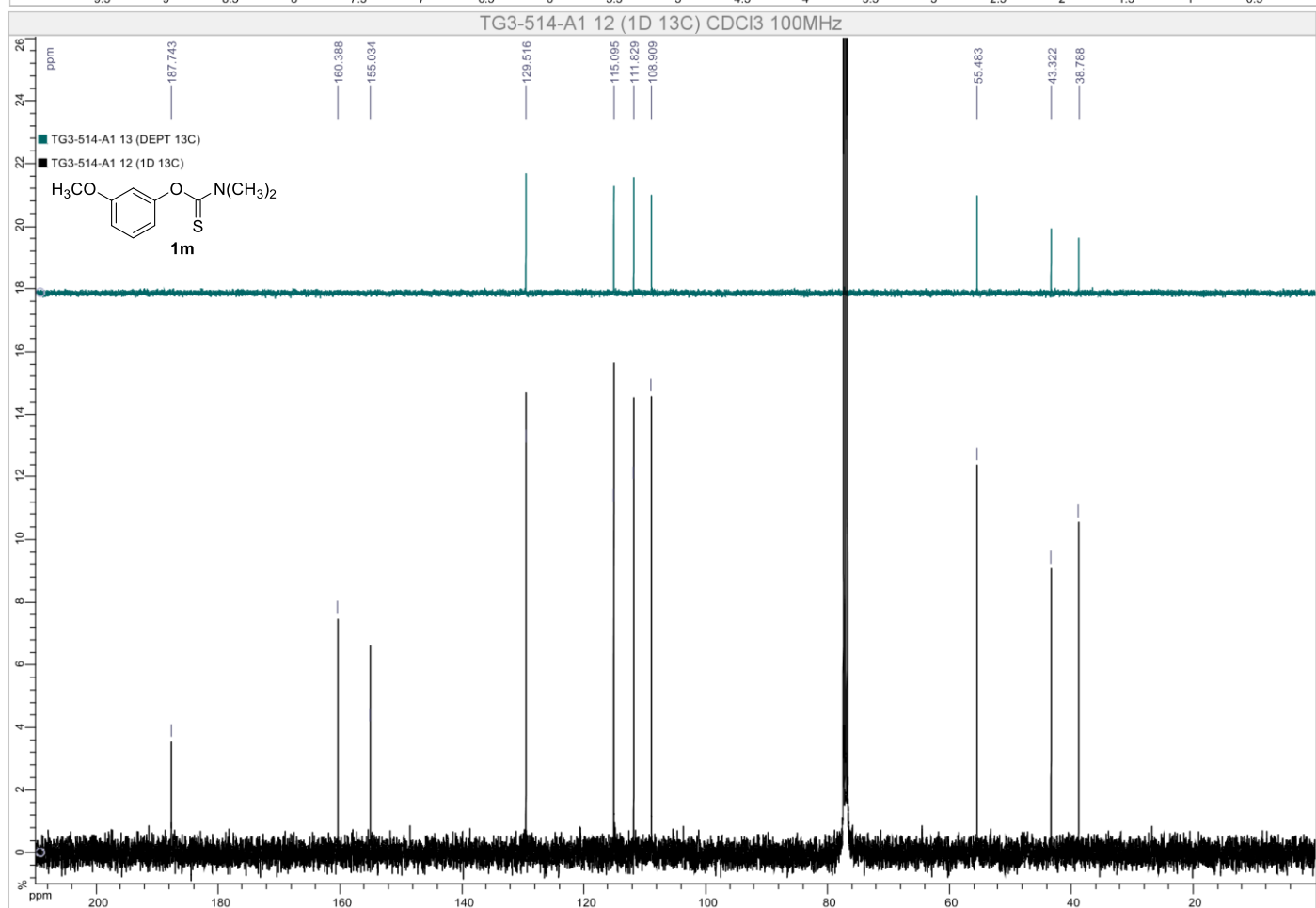
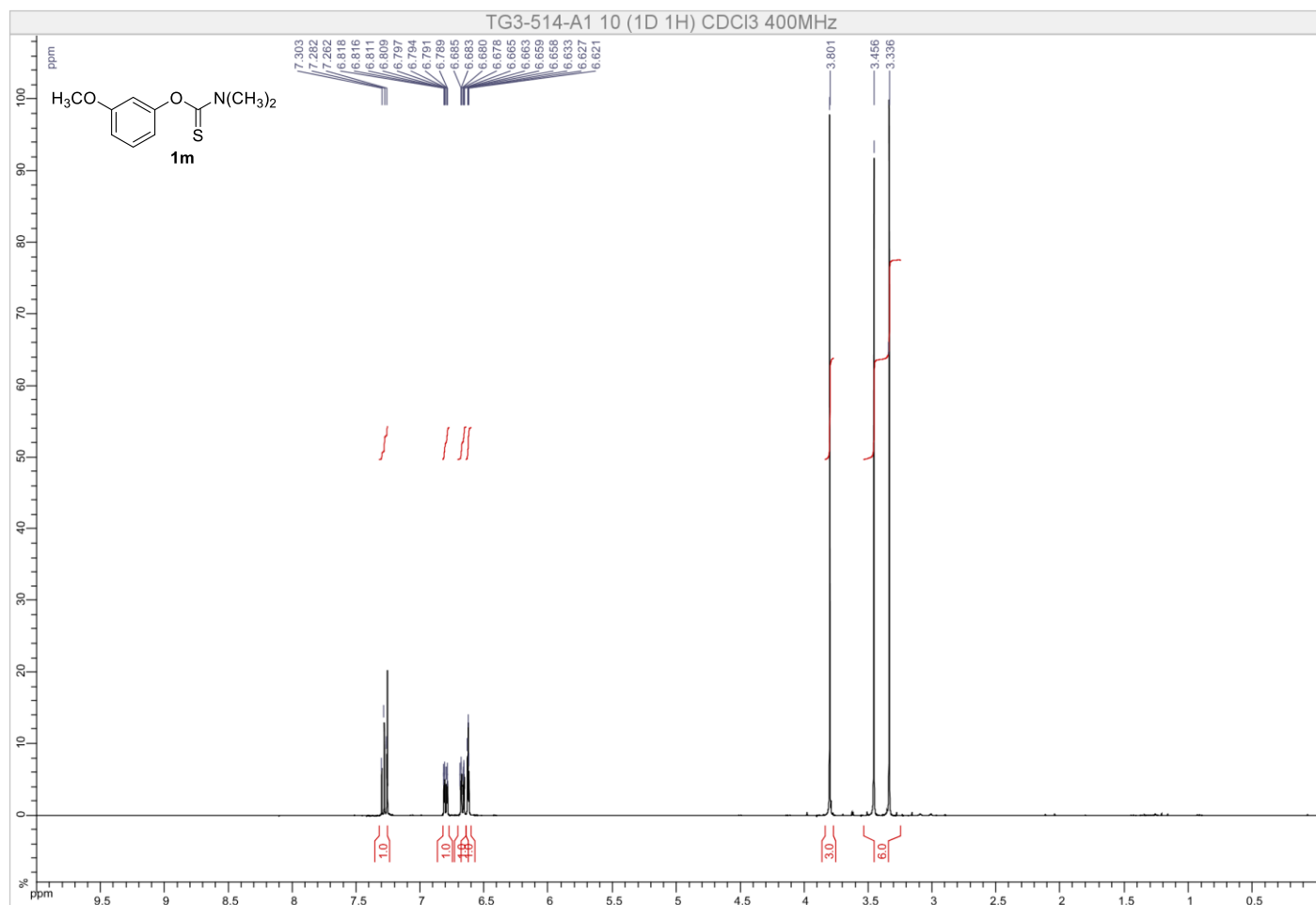
O-(naphthalen-2-yl) dimethylcarbamothioate (**1k**)



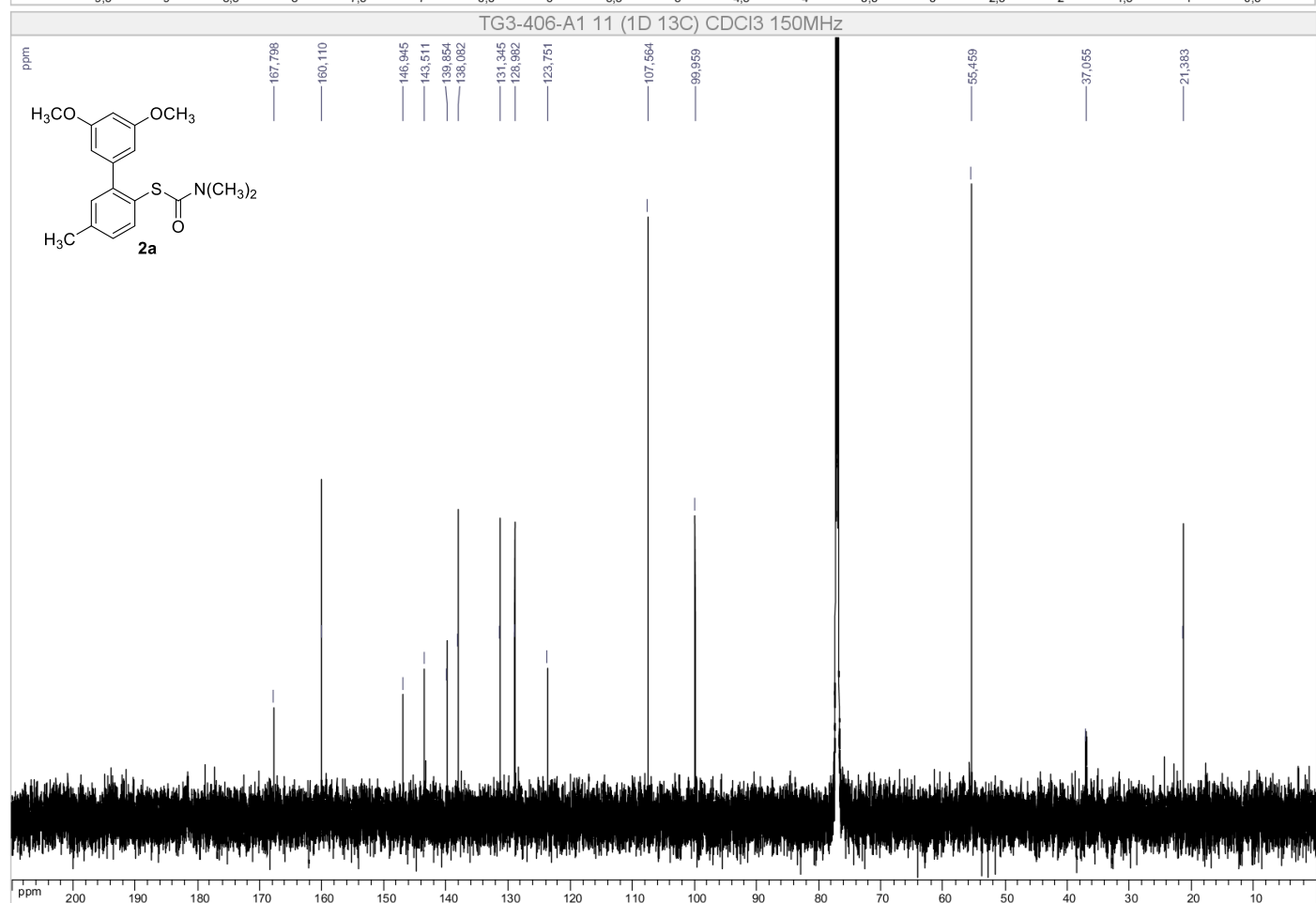
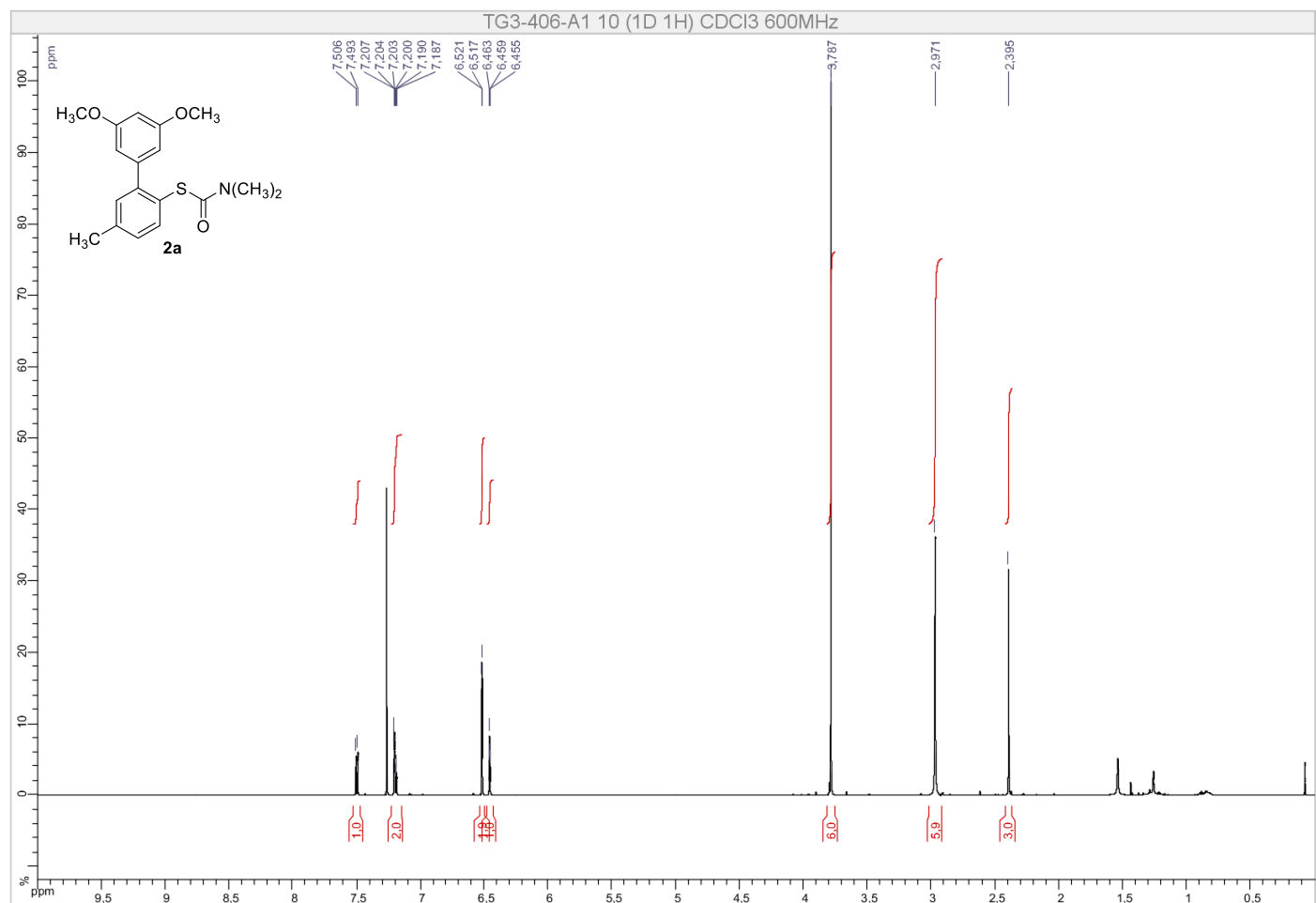
O-phenyl dimethylcarbamothioate (**11**)



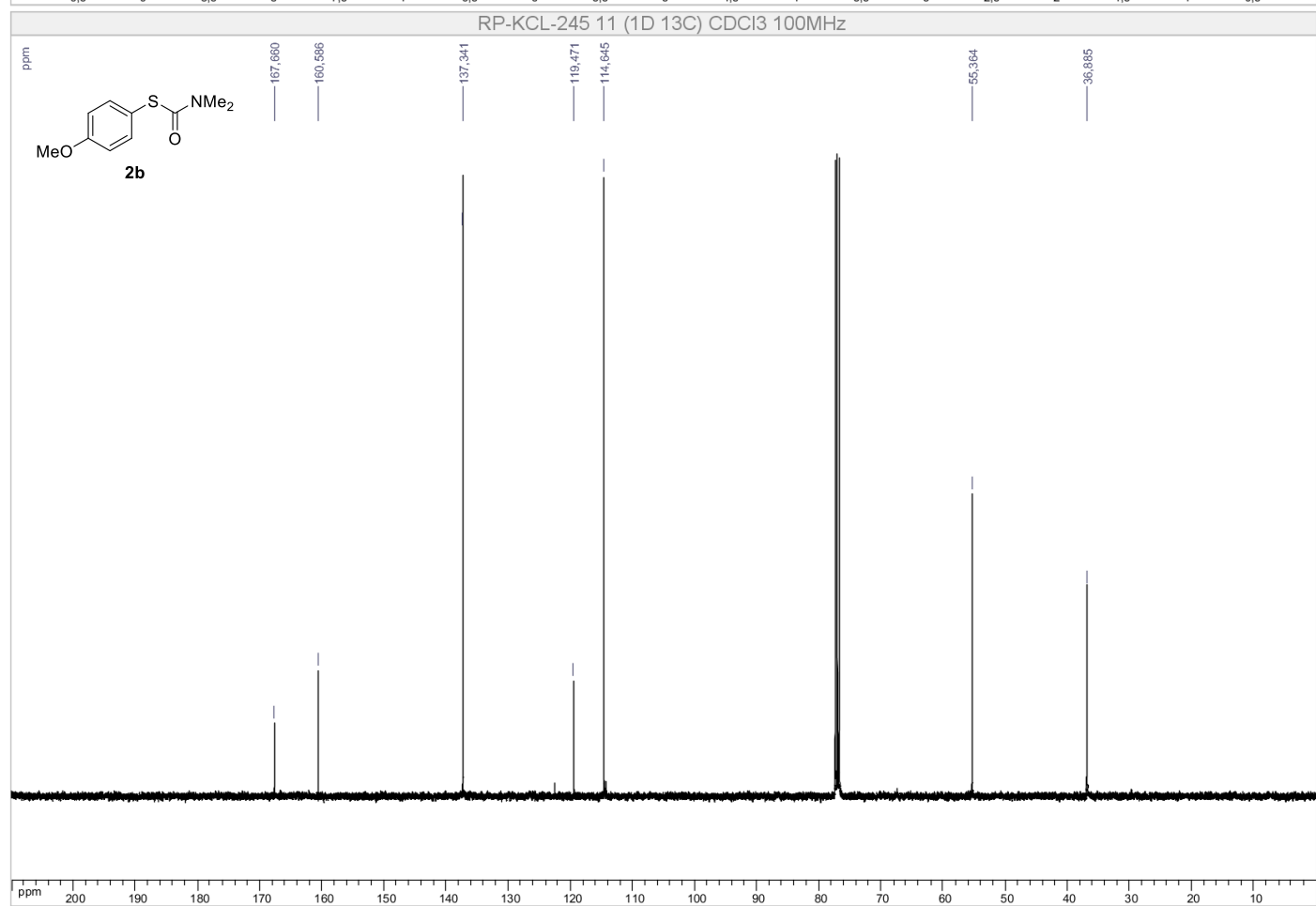
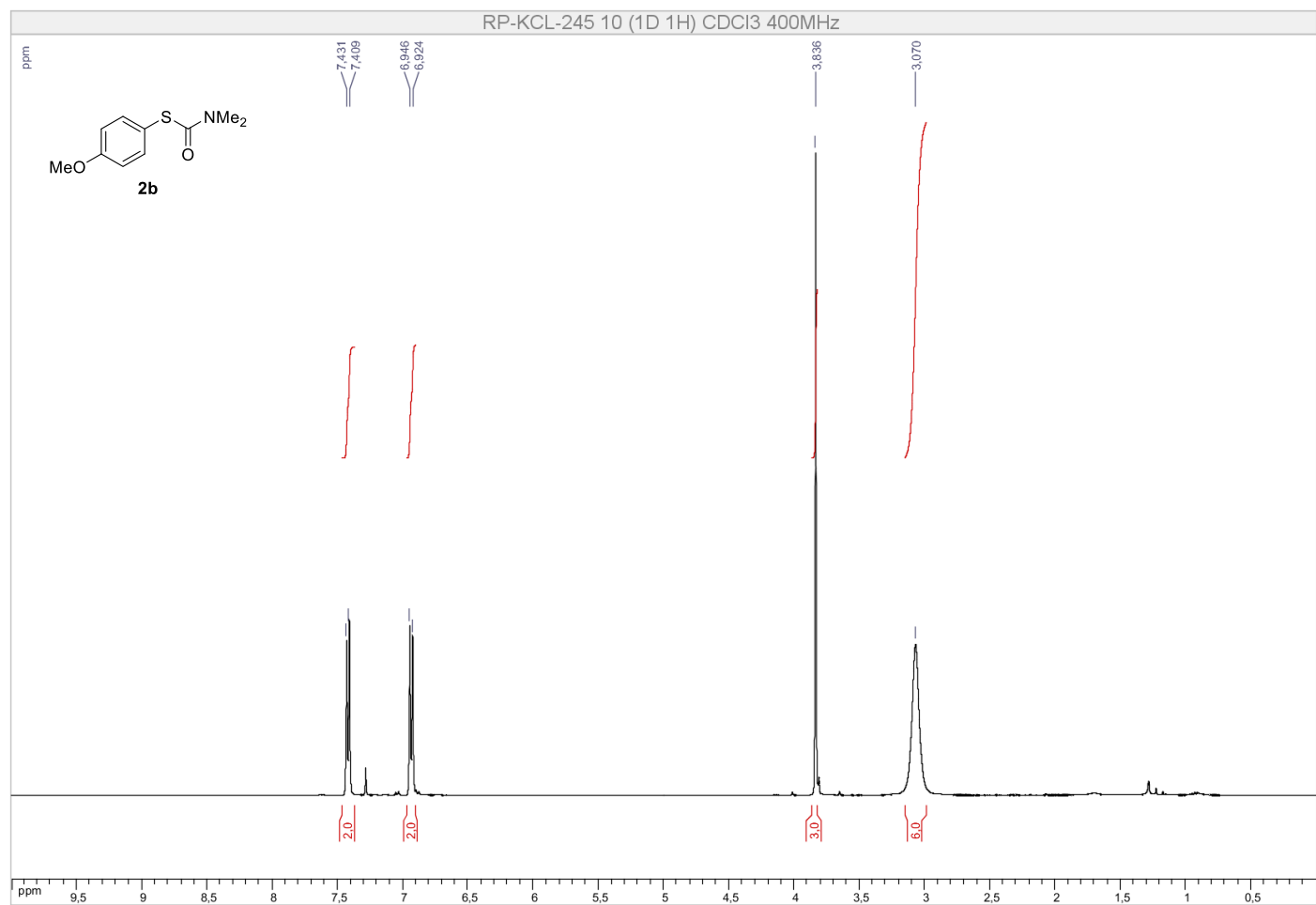
O-(3-methoxyphenyl) dimethylcarbamothioate (**1m**)



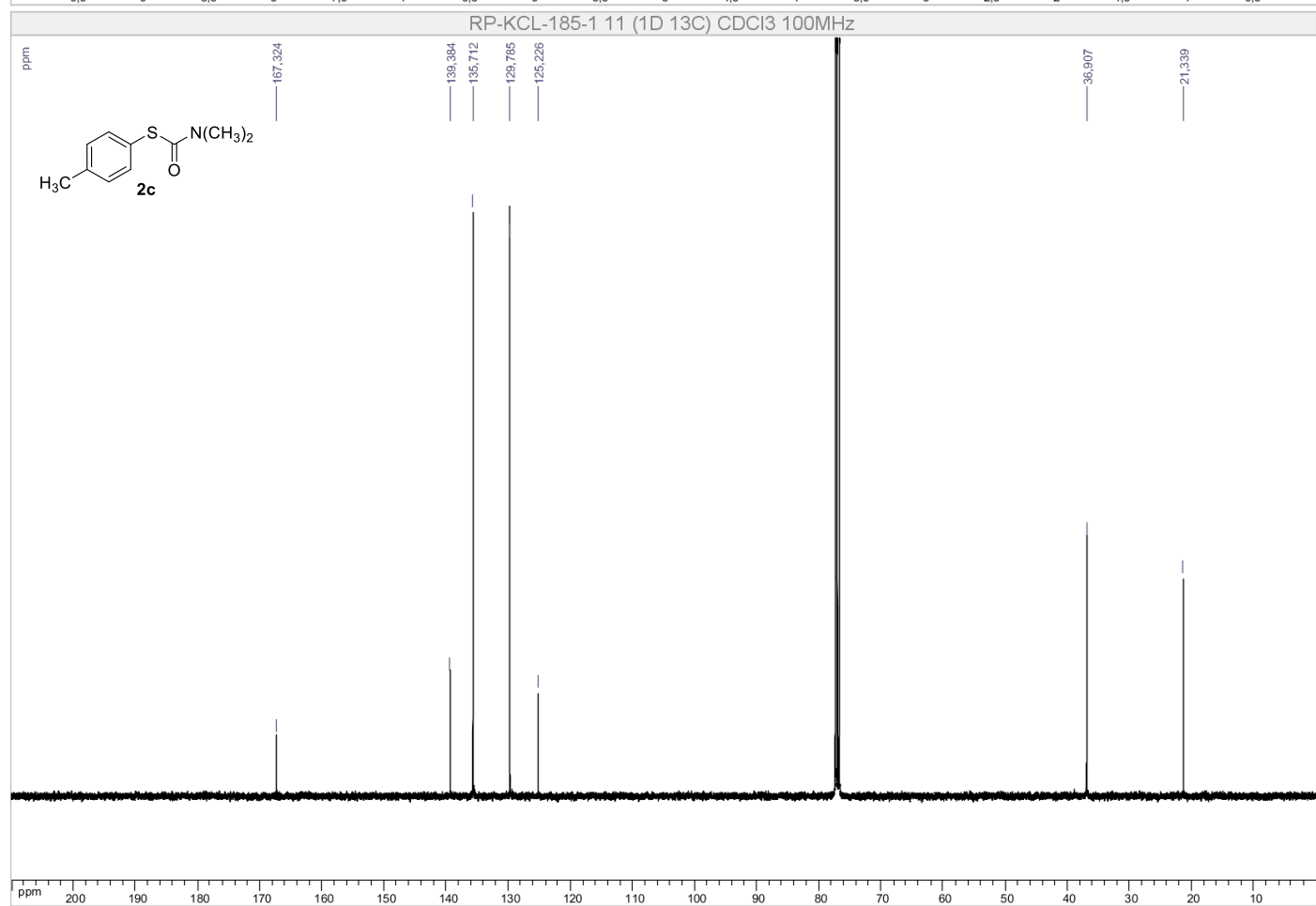
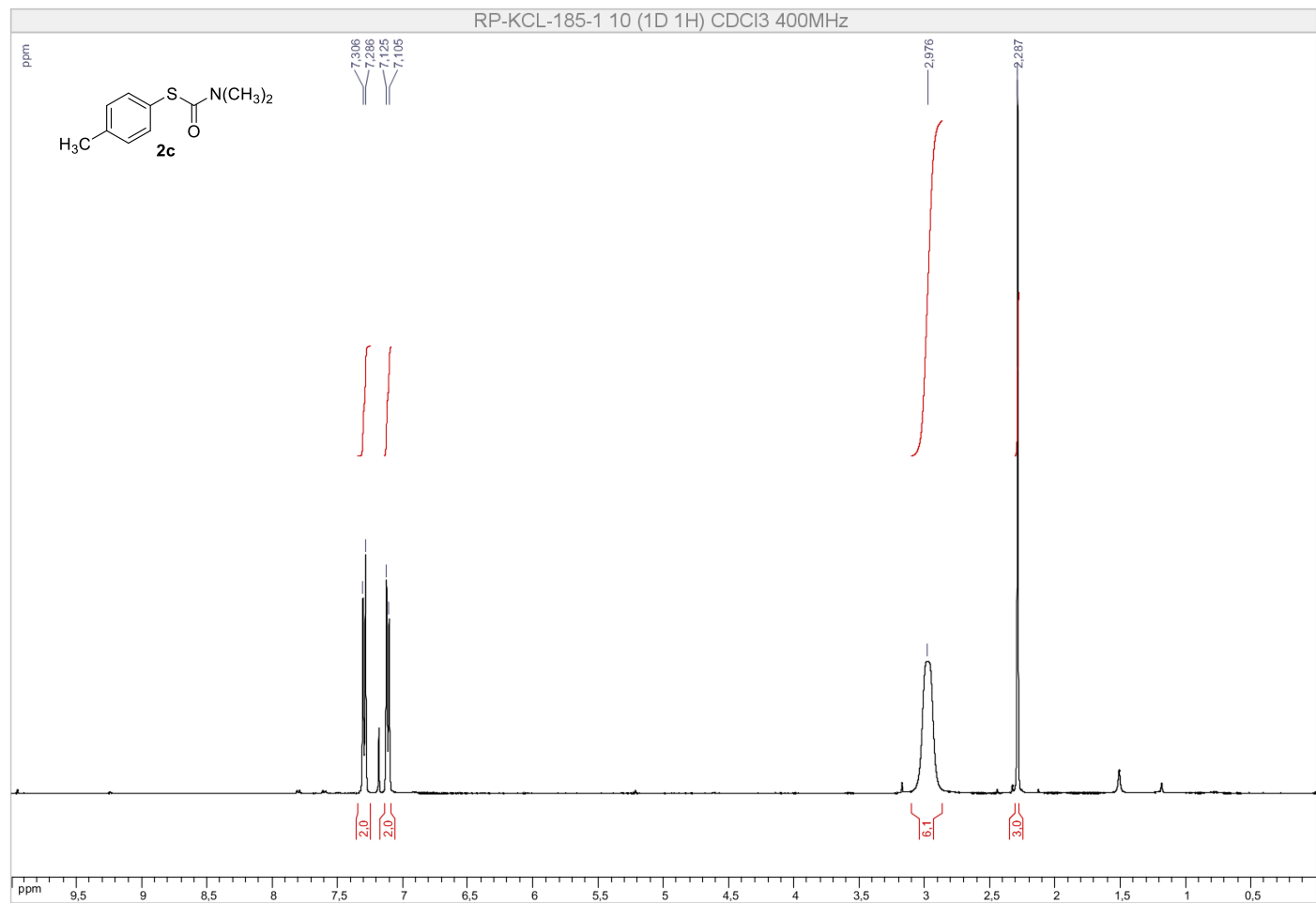
S-(3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl) dimethylcarbamothioate (**2a**)



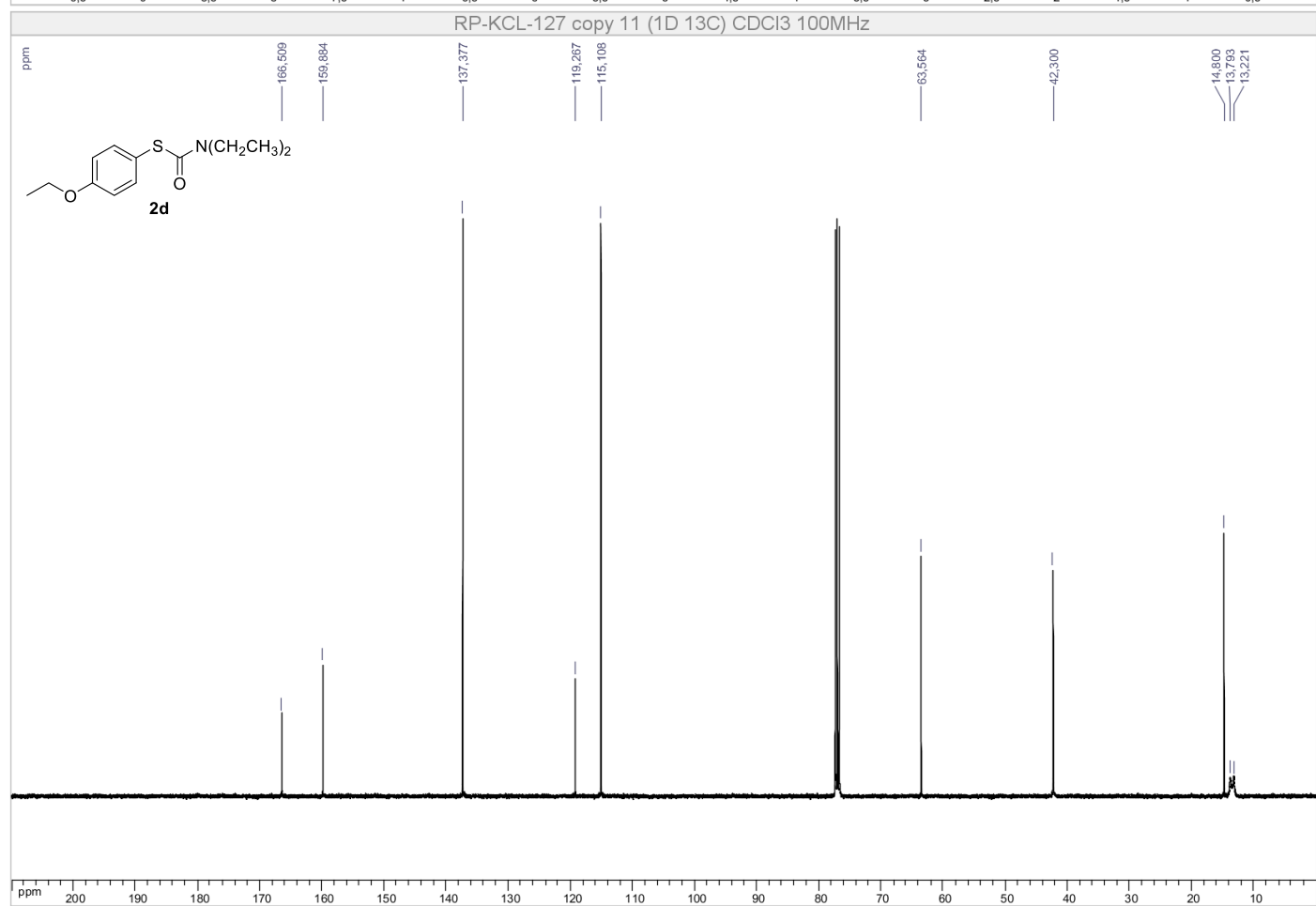
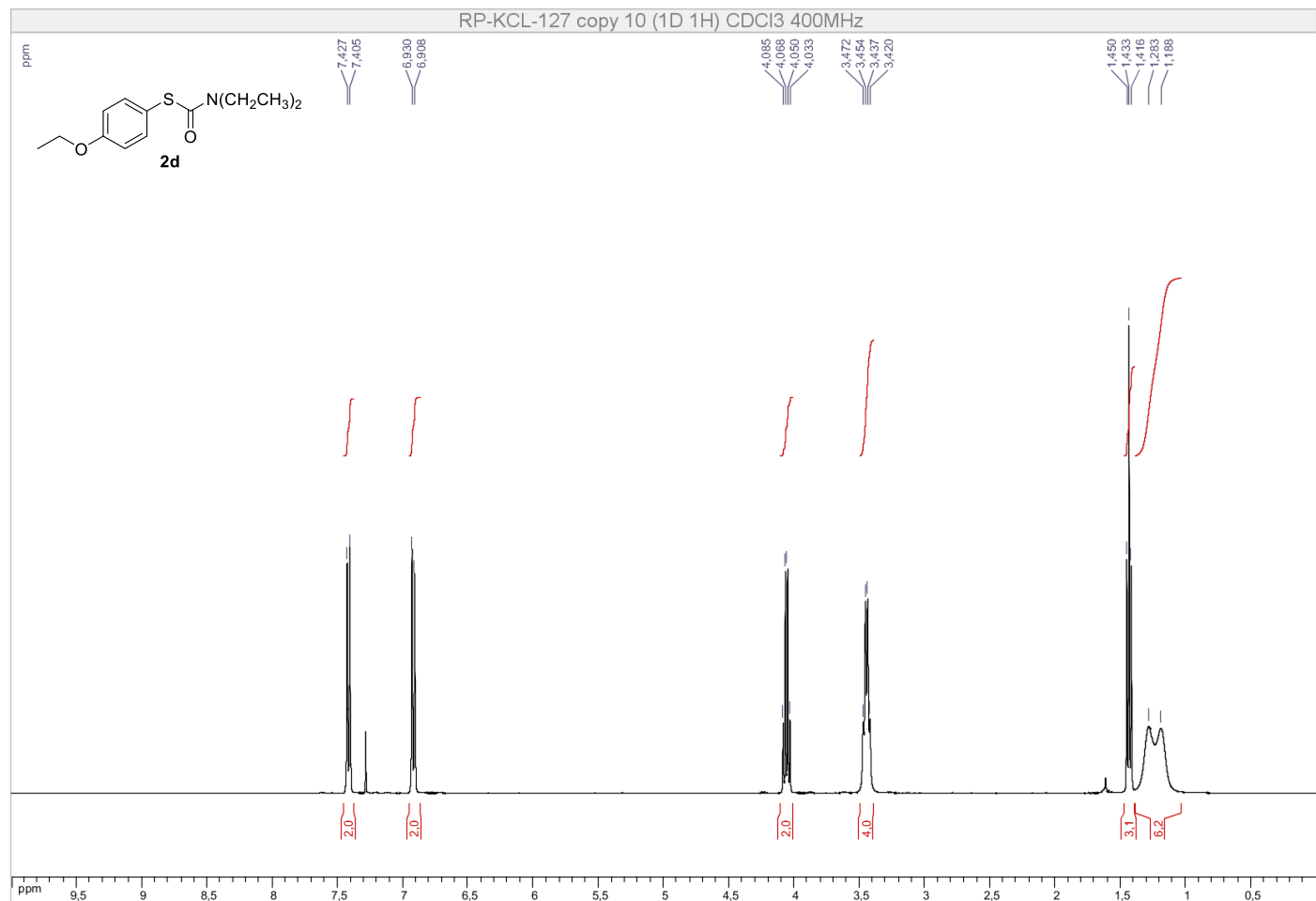
S-(4-methoxyphenyl) dimethylcarbamothioate (**2b**)



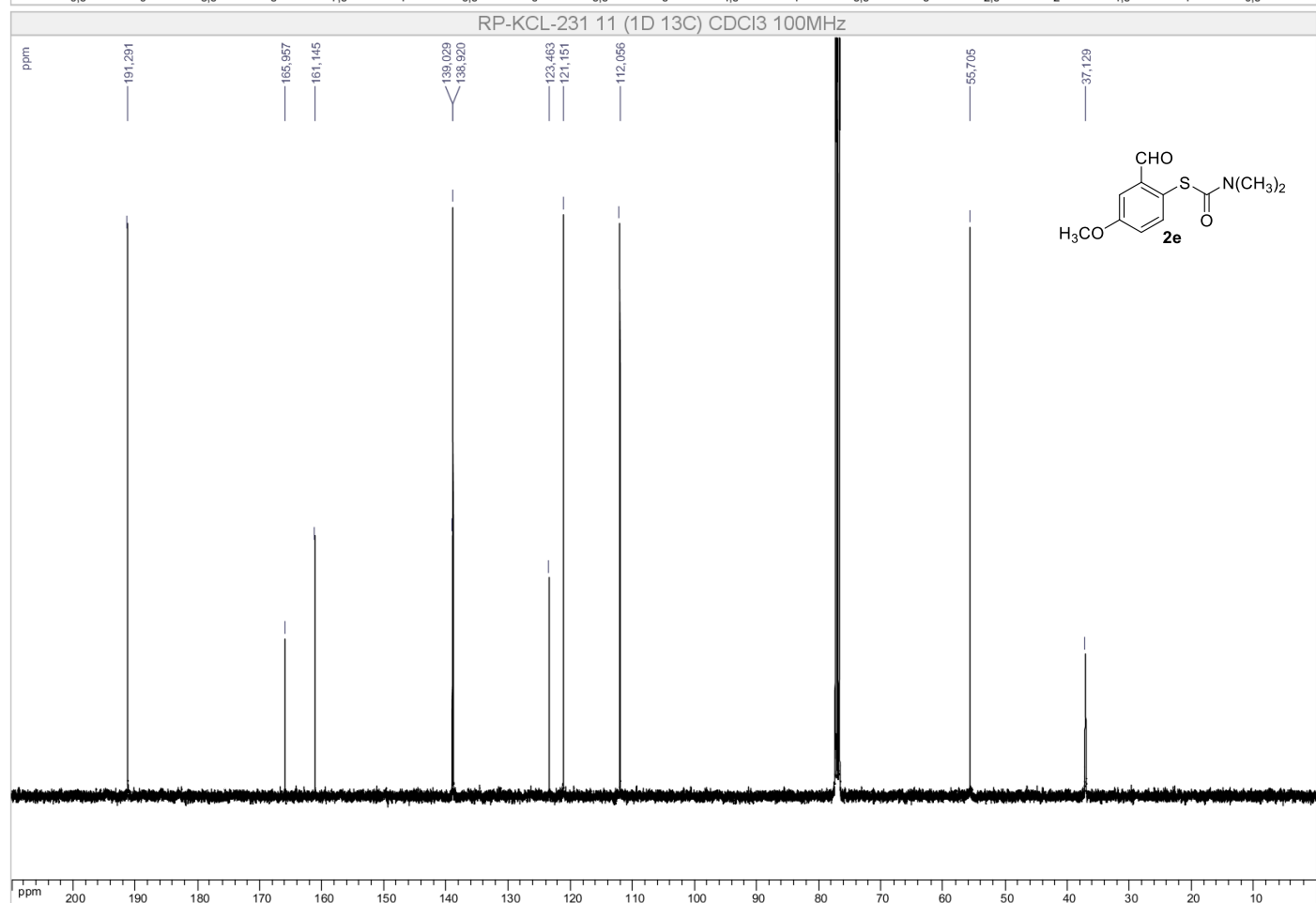
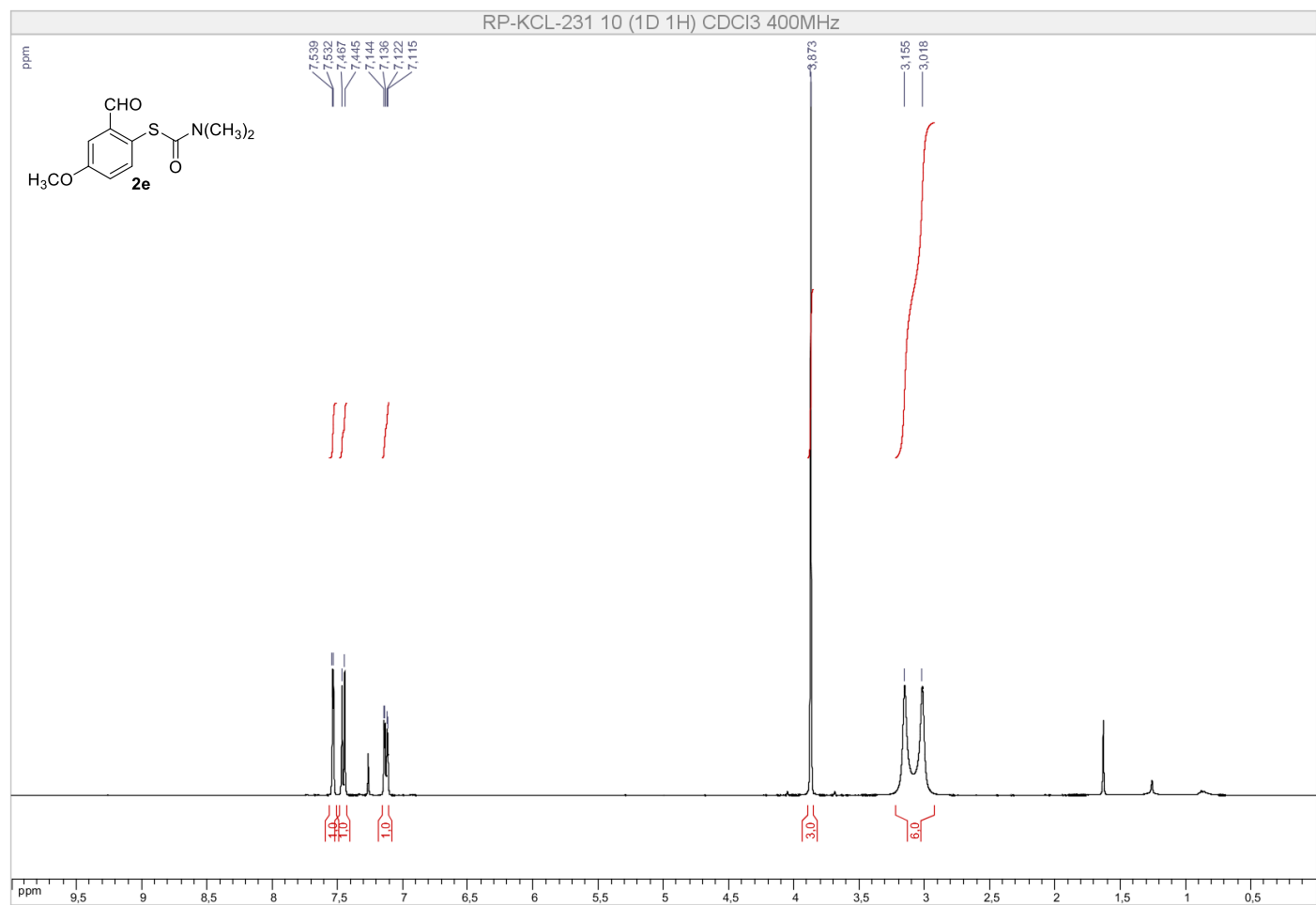
S-(*p*-tolyl) dimethylcarbamothioate (**2c**)



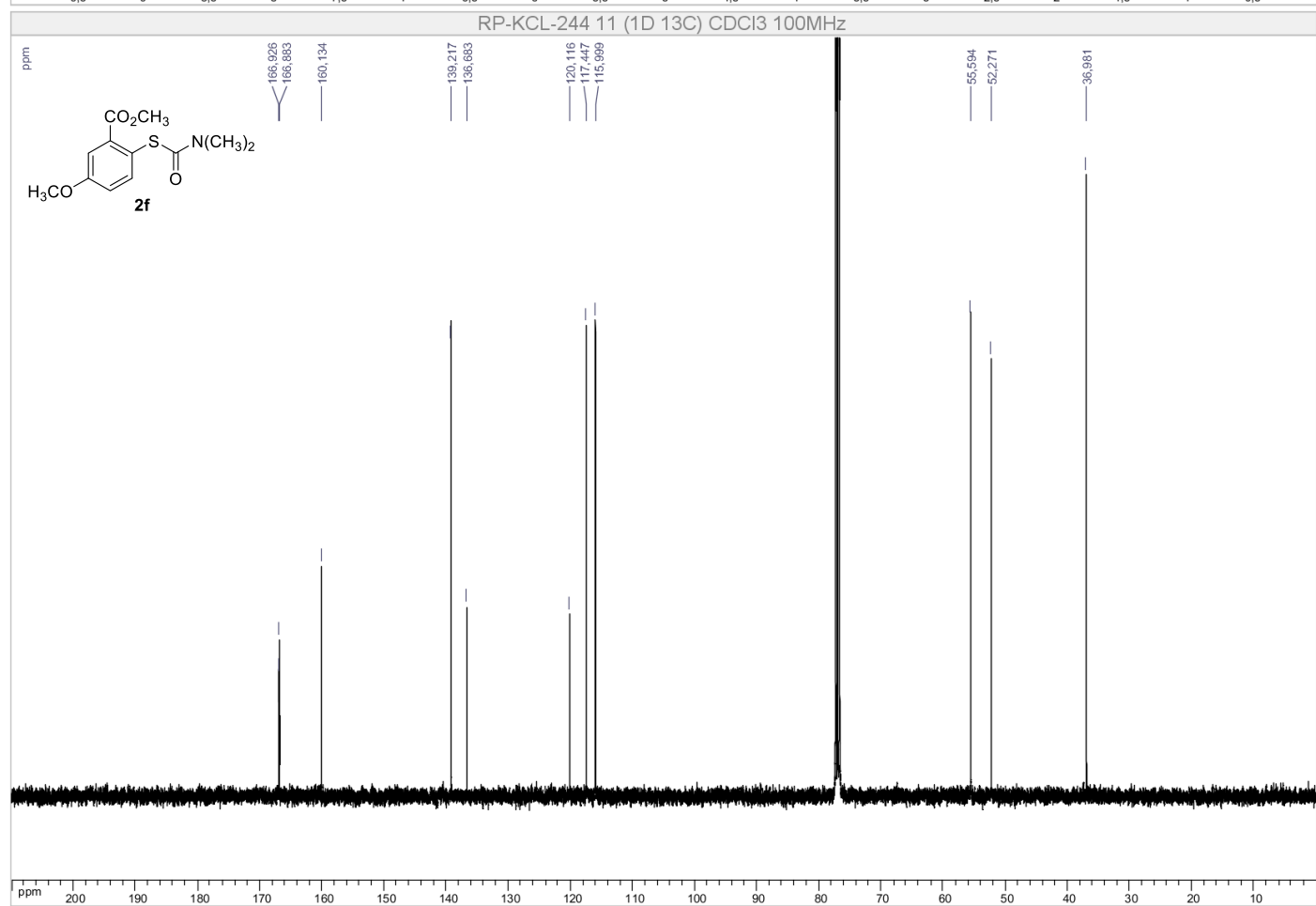
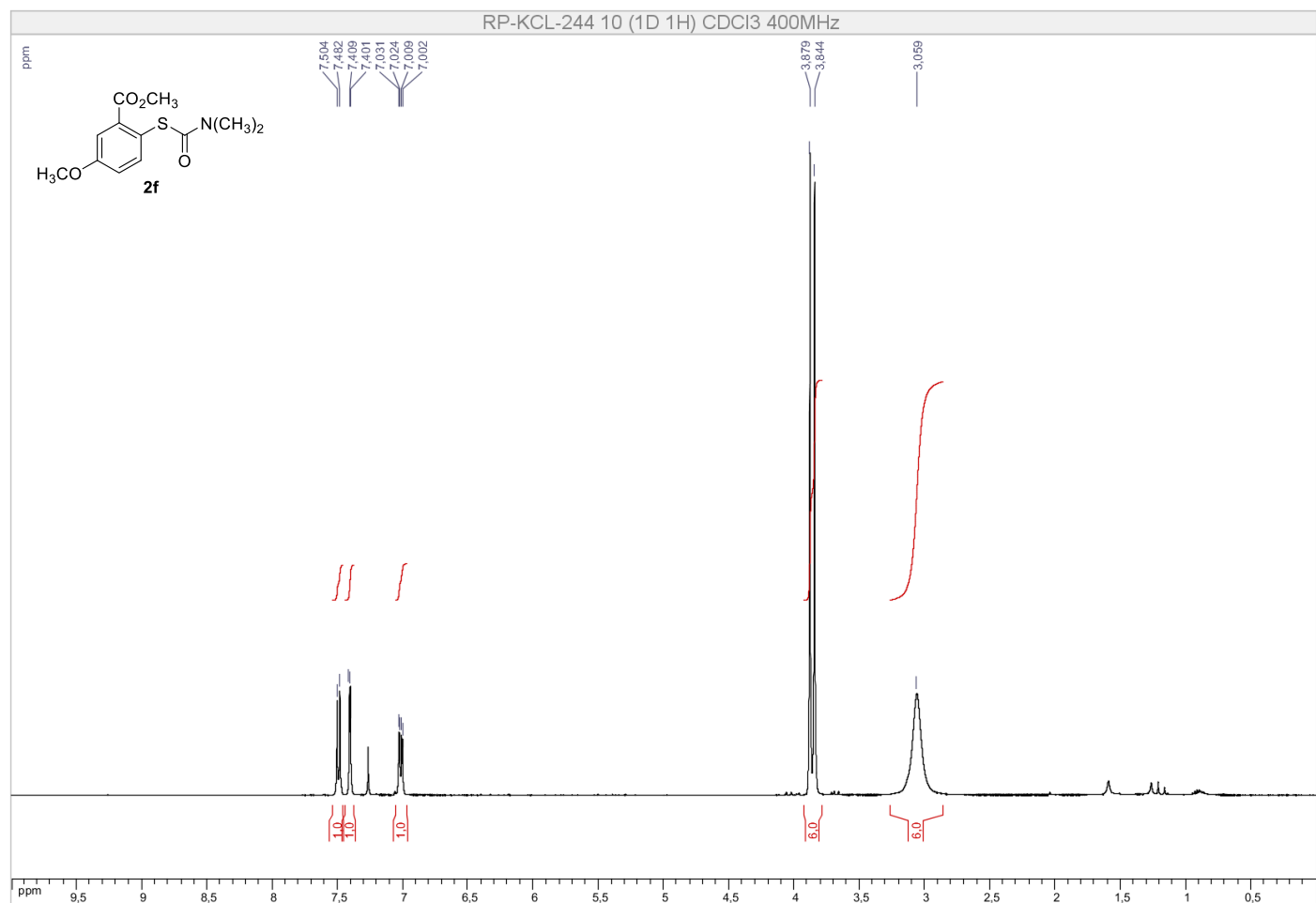
S-(4-ethoxyphenyl) diethylcarbamothioate (**2d**)



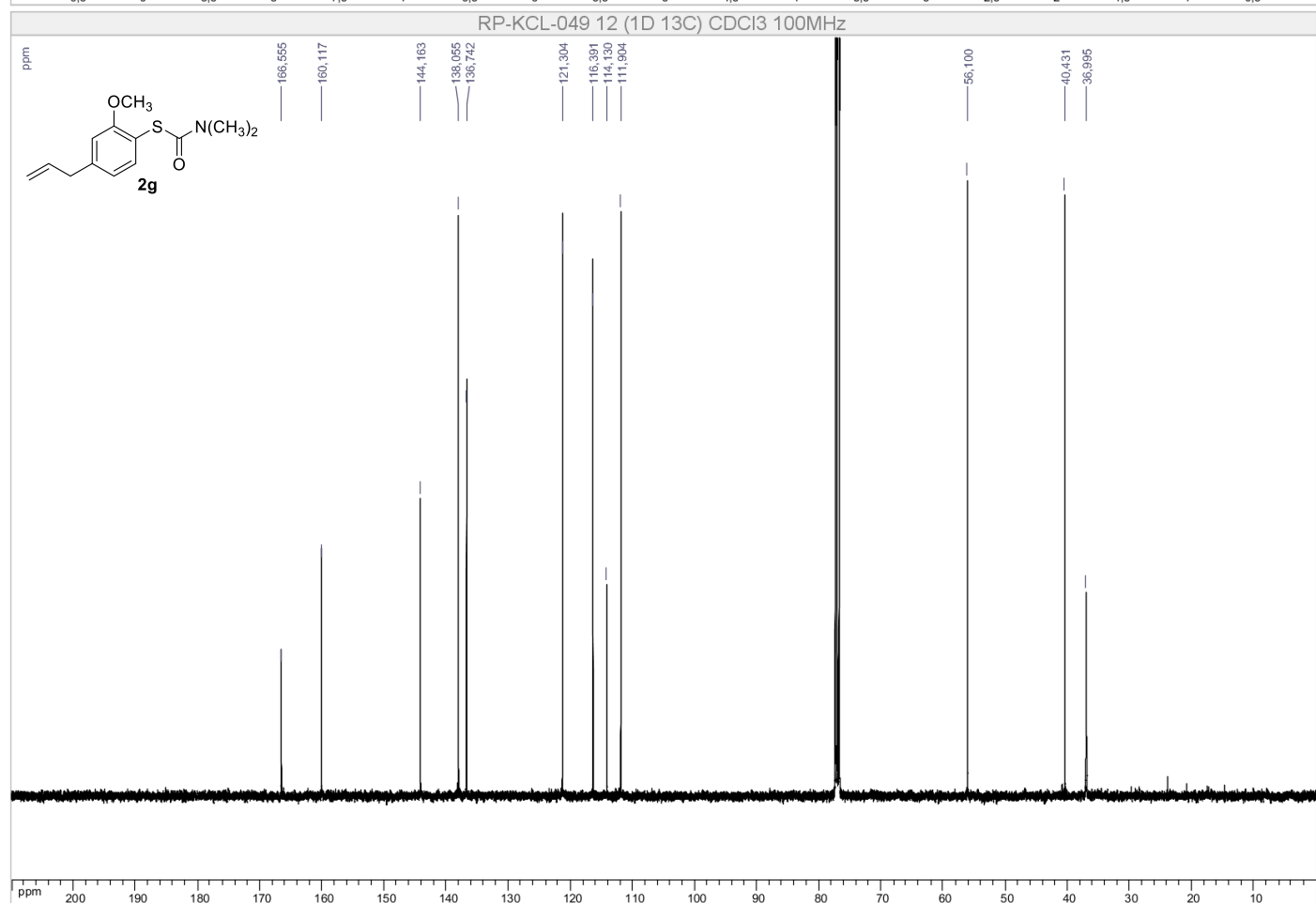
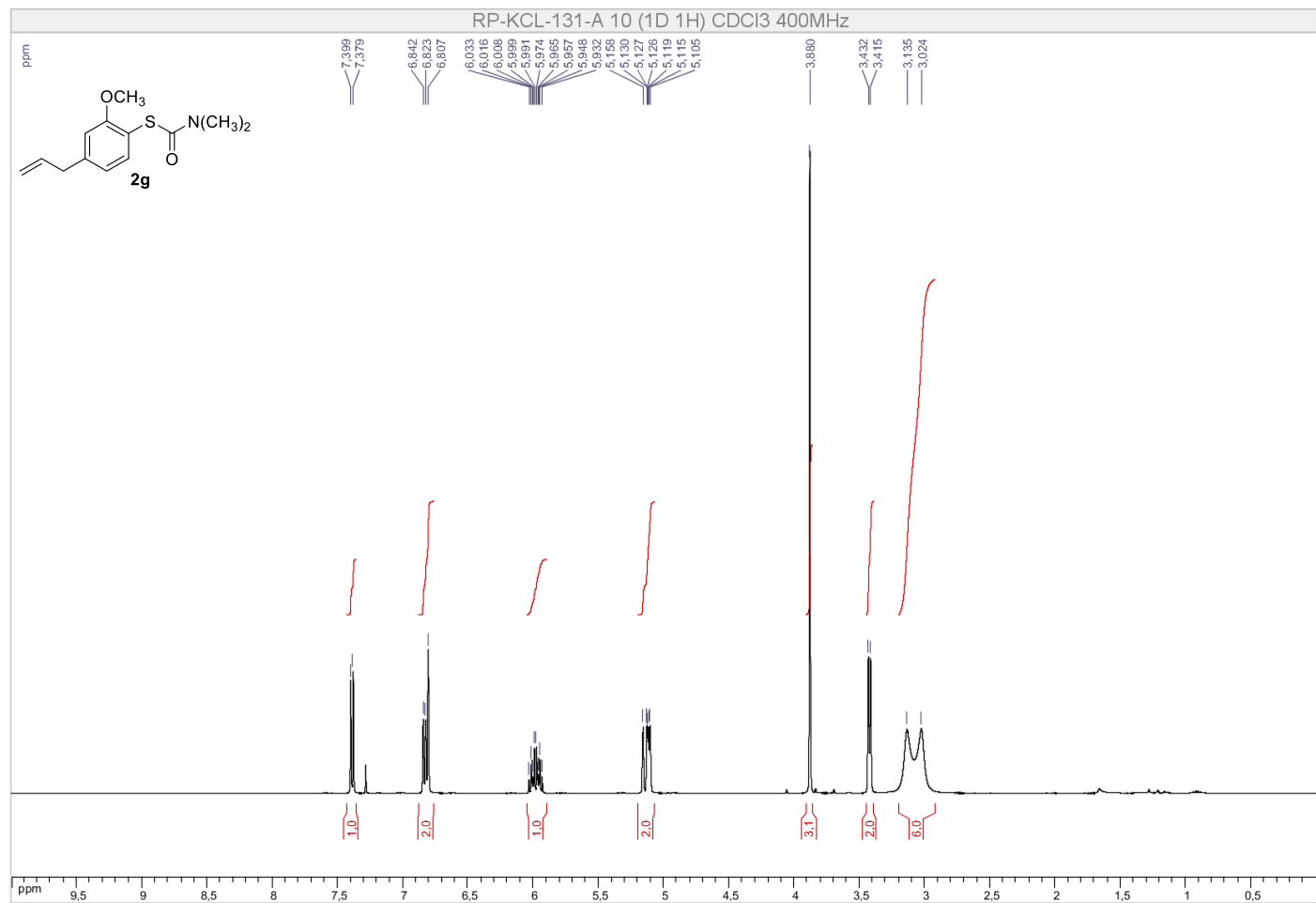
S-(2-formyl-4-methoxyphenyl) dimethylcarbamothioate (**2e**)



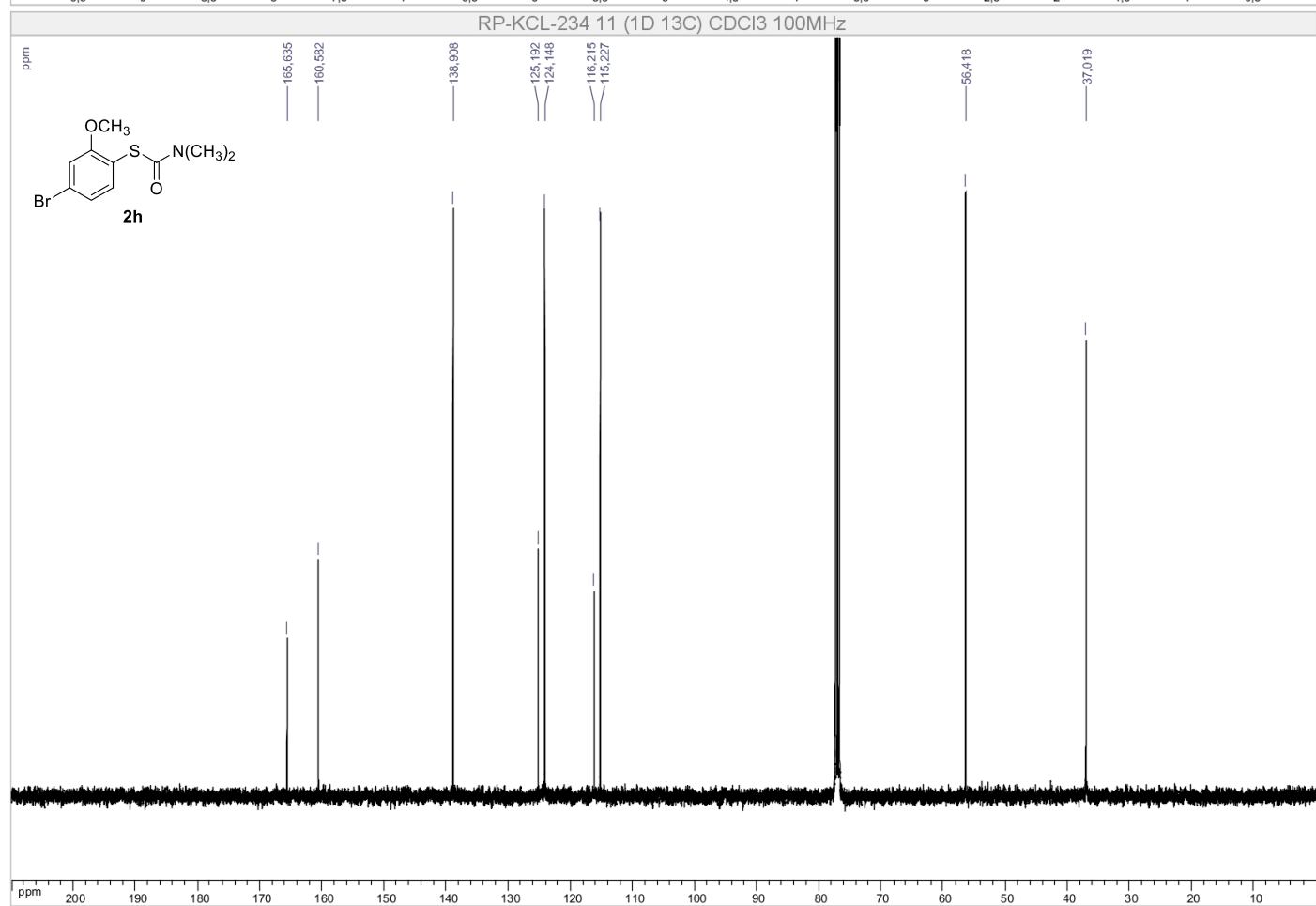
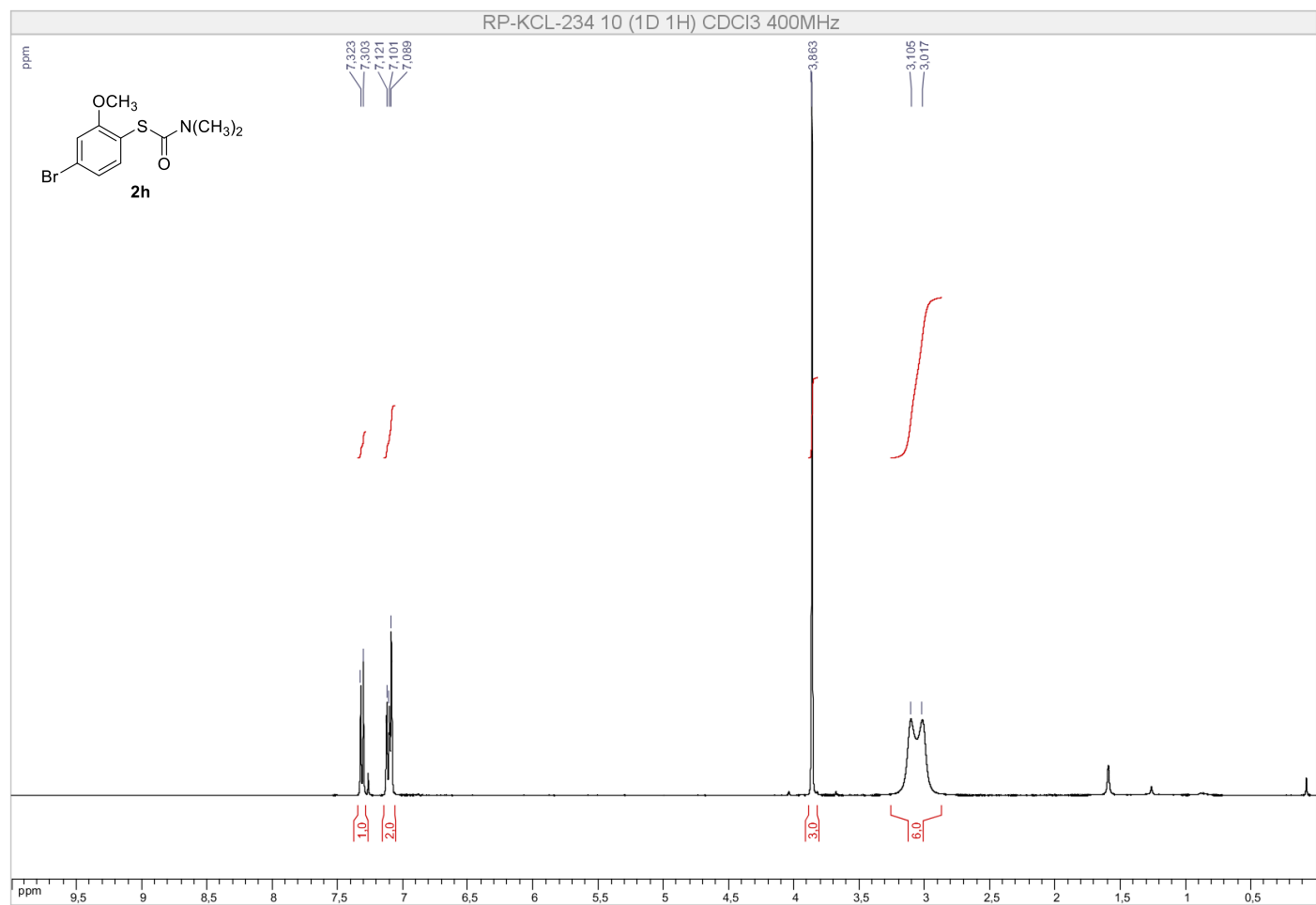
Methyl 2-((dimethylcarbamoyl)thio)-5-methoxybenzoate (**2f**)



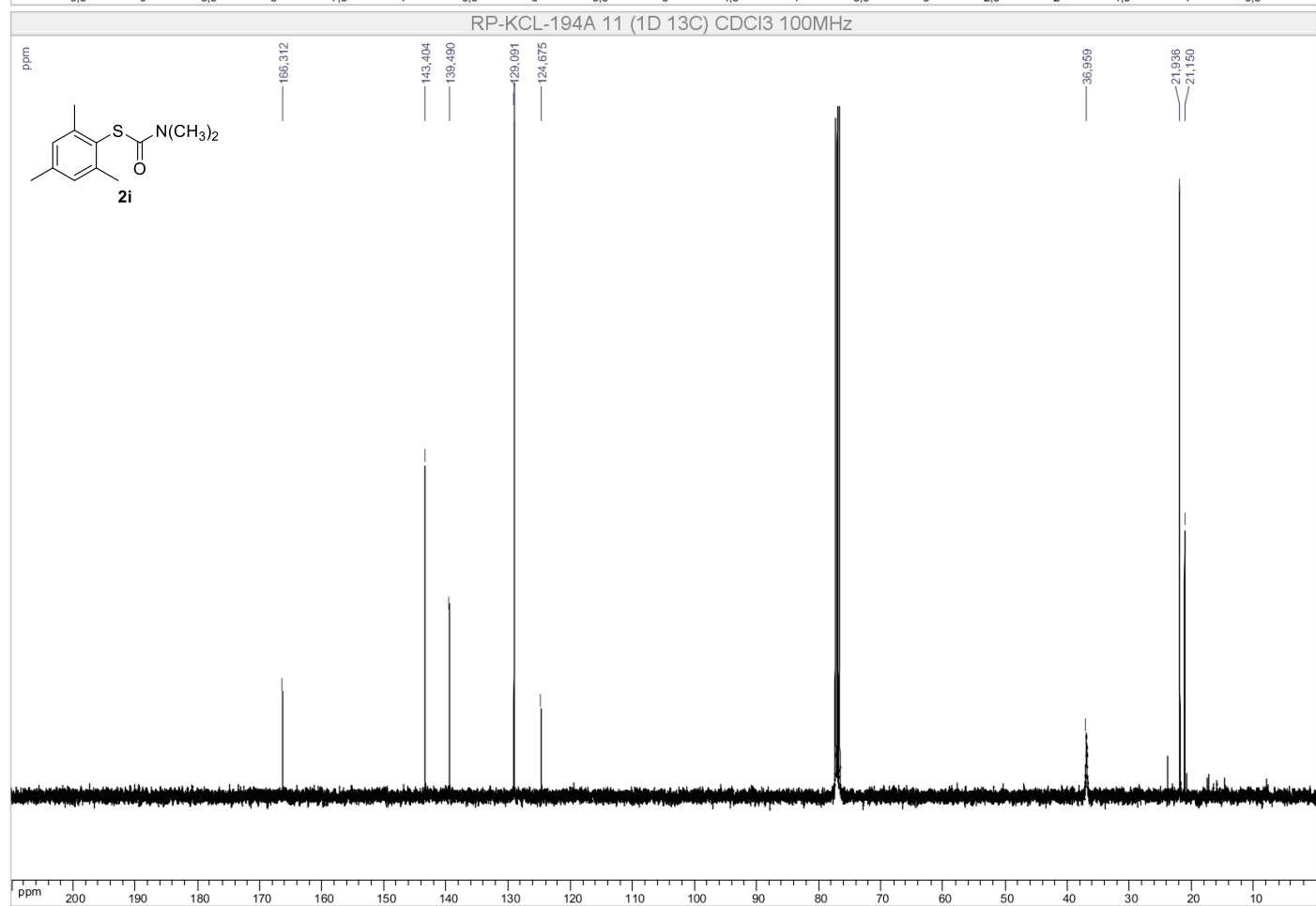
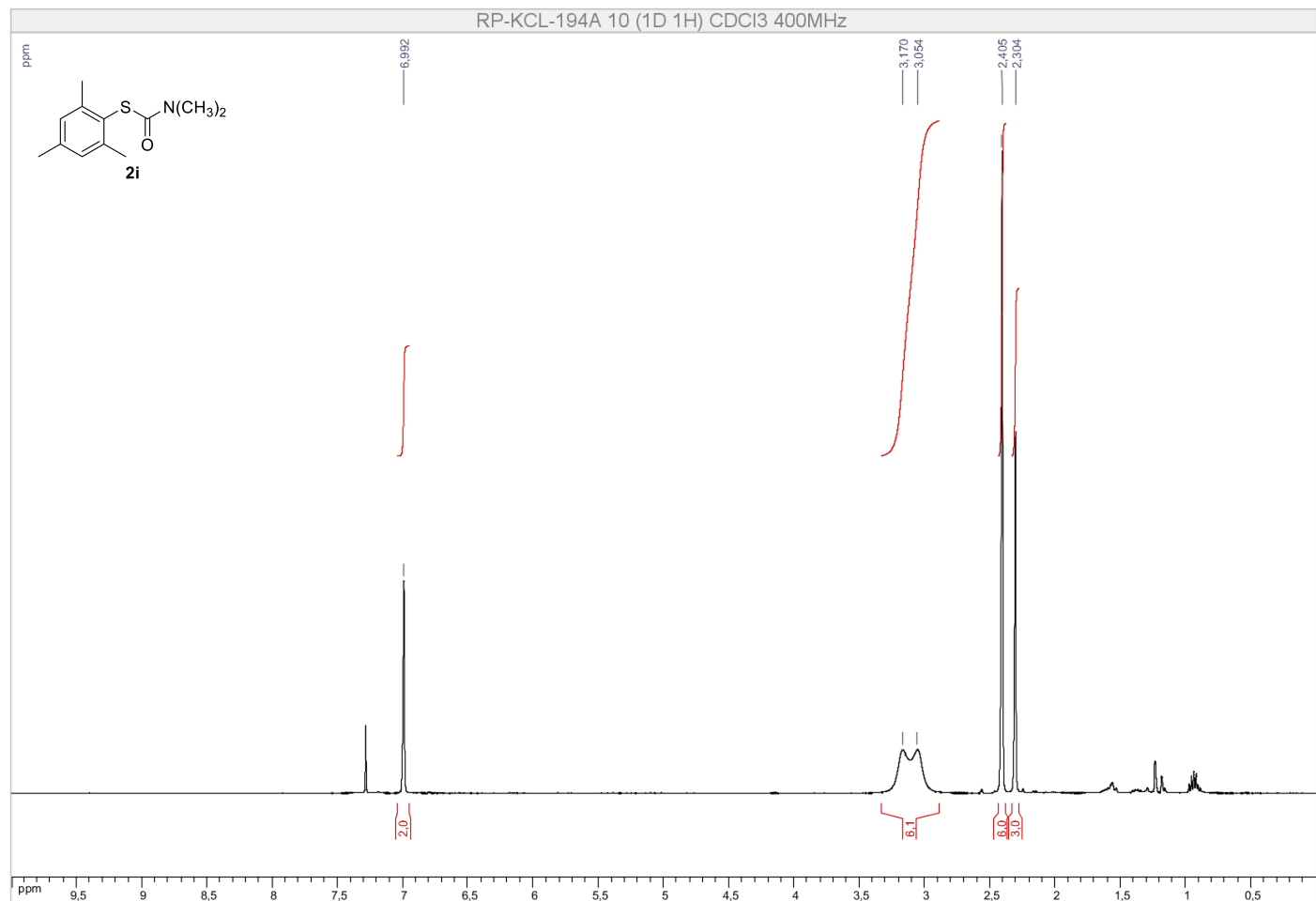
S-(4-allyl-2-methoxyphenyl) dimethylcarbamothioate (**2g**)



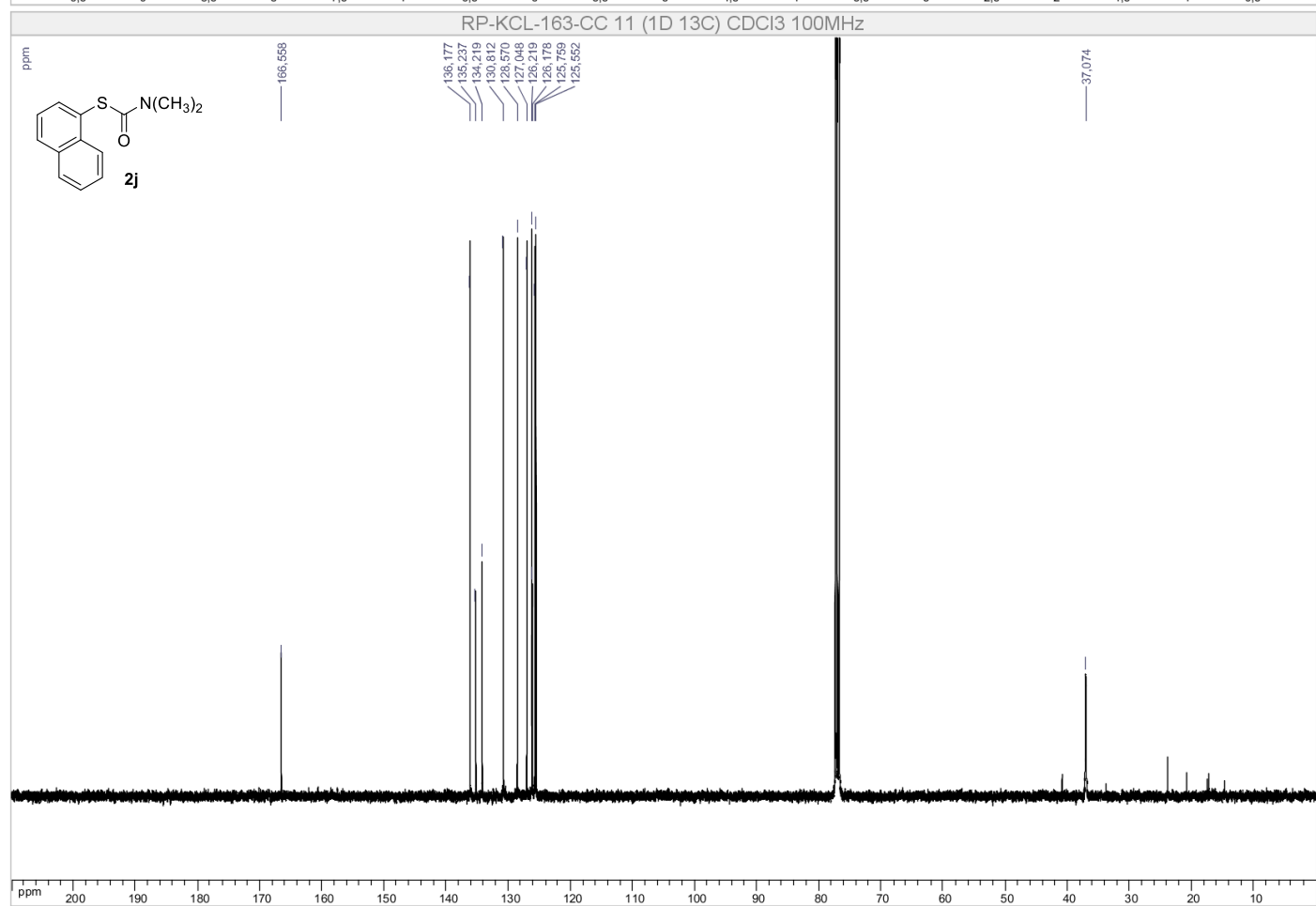
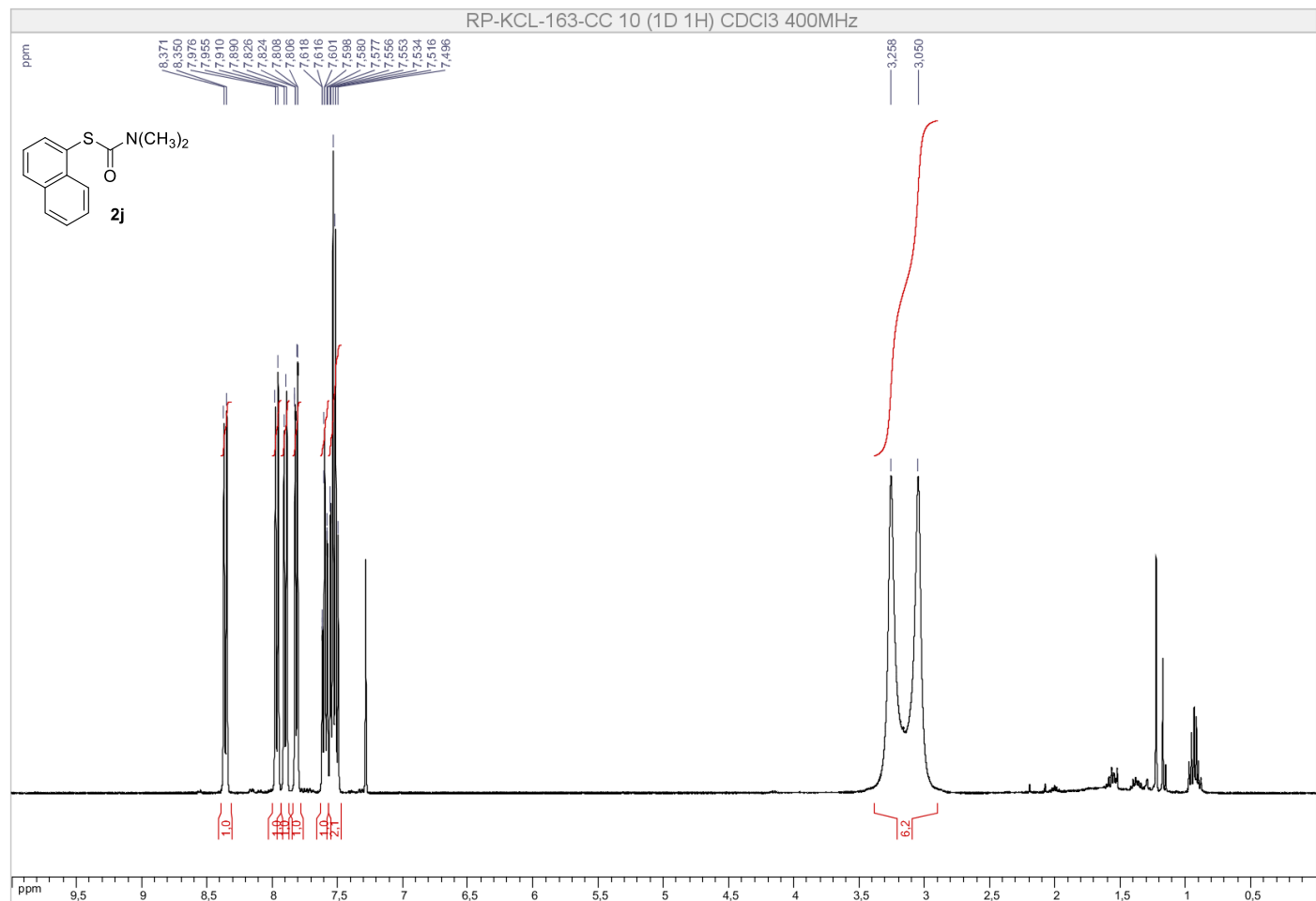
S-(4-bromo-2-methoxyphenyl) dimethylcarbamothioate (**2h**)



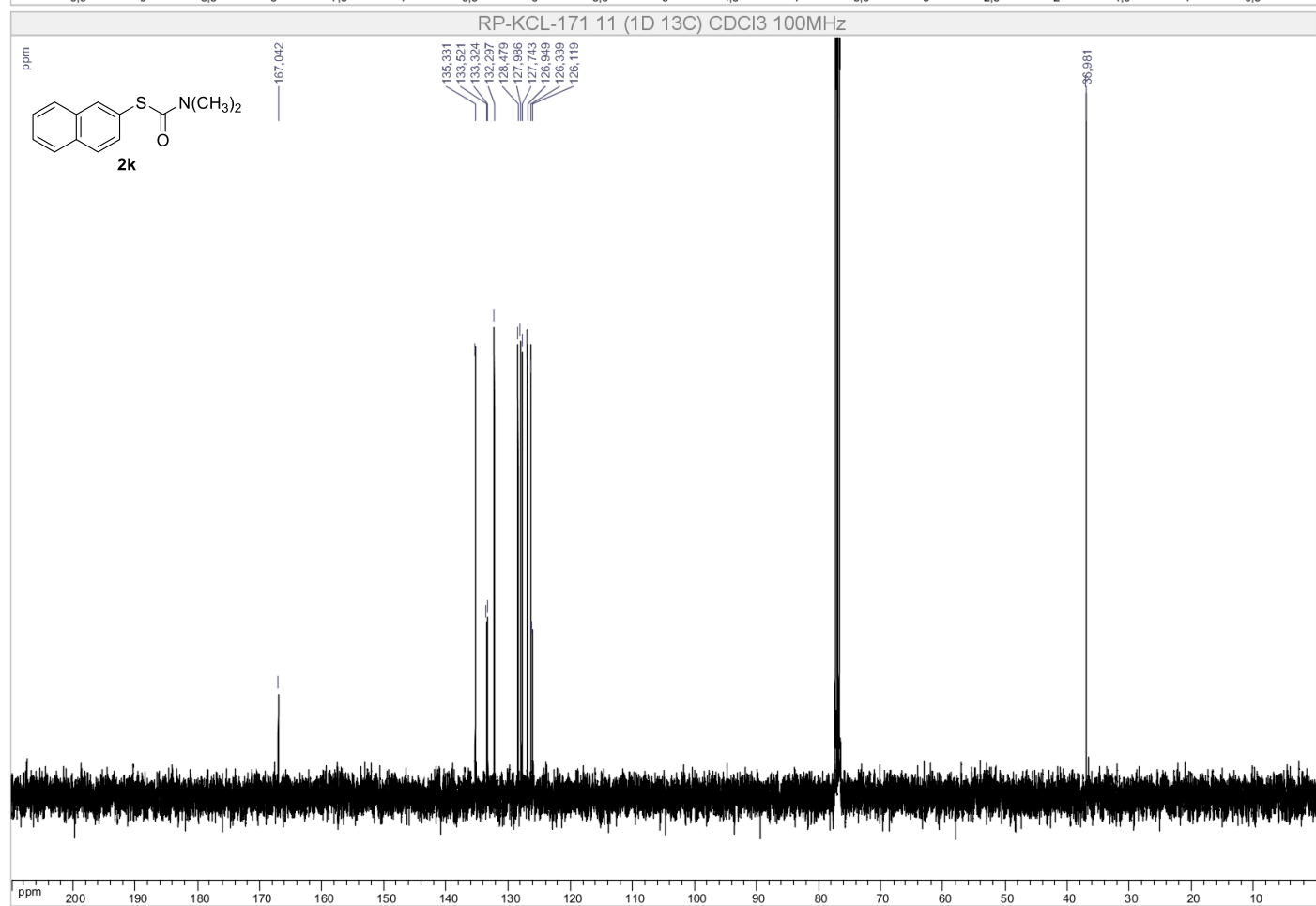
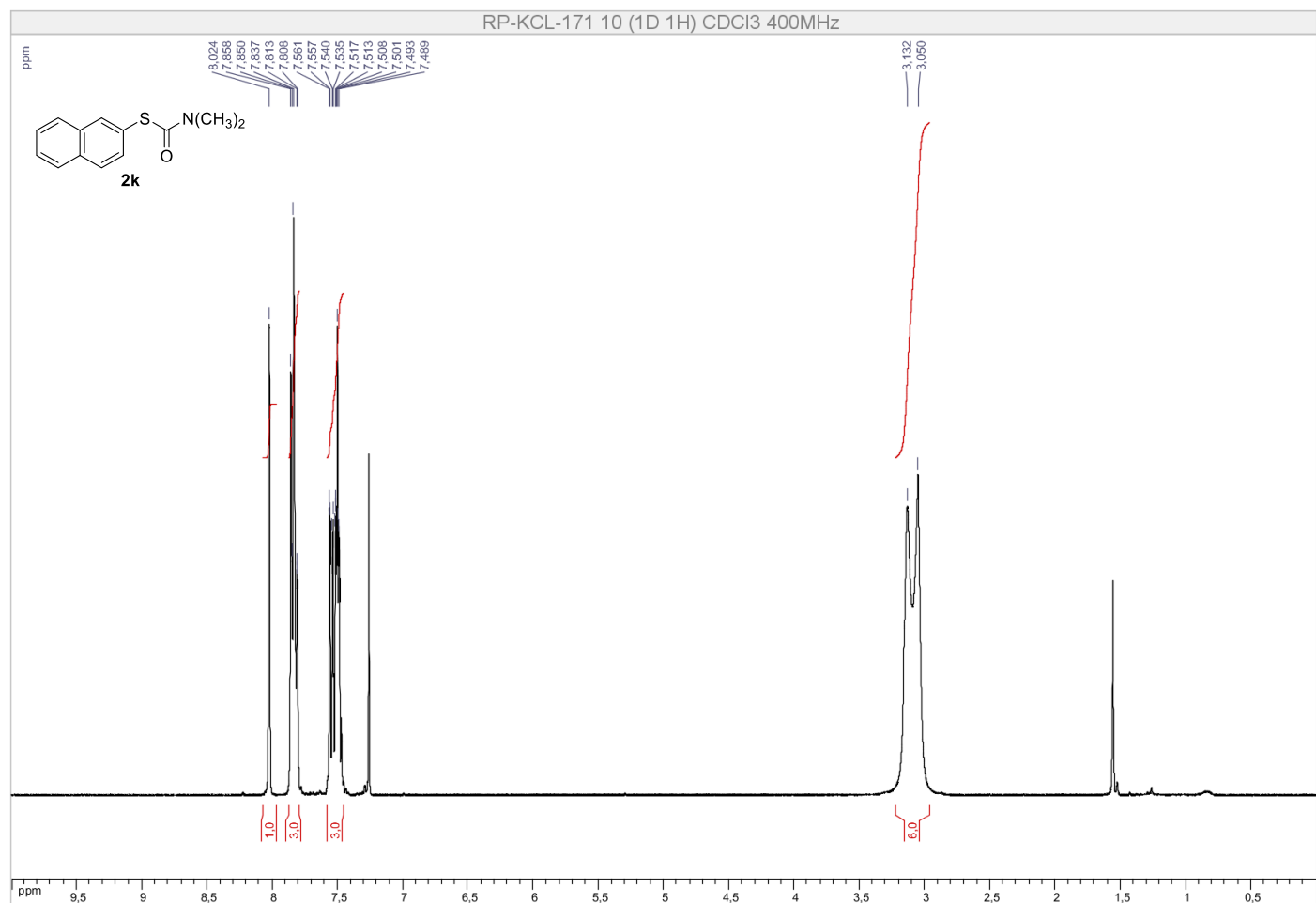
S-mesityl dimethylcarbamothioate (**2i**)



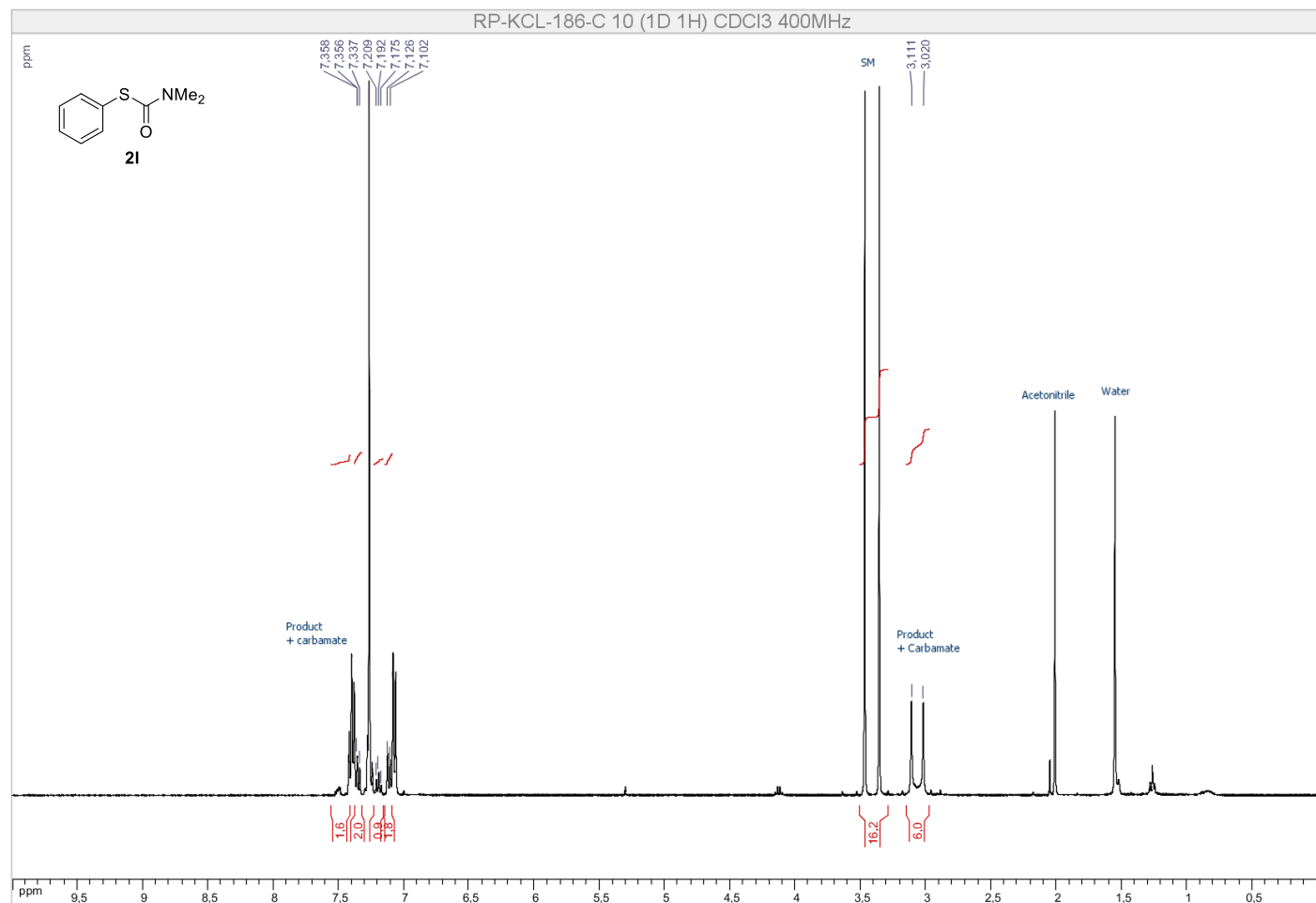
S-(naphthalen-1-yl) dimethylcarbamothioate (**2j**)



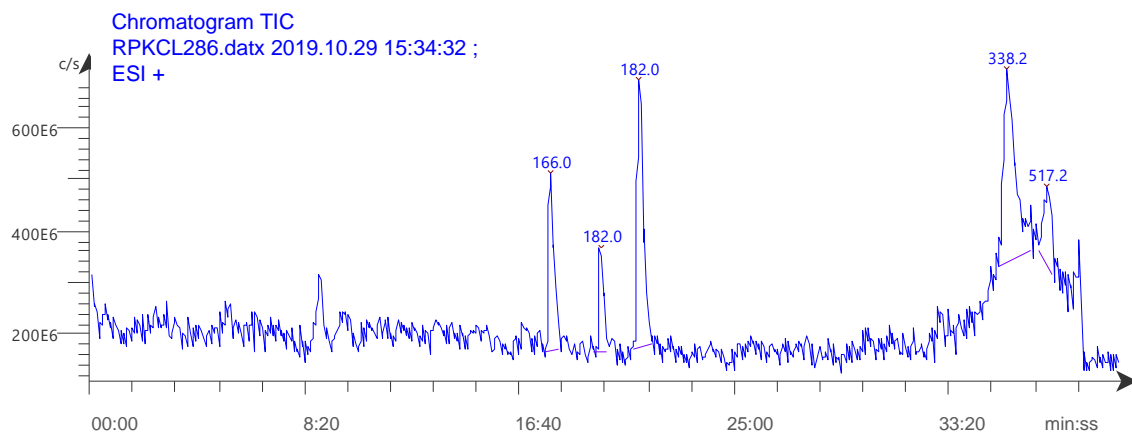
S-(naphthalen-2-yl) dimethylcarbamothioate (**2k**)



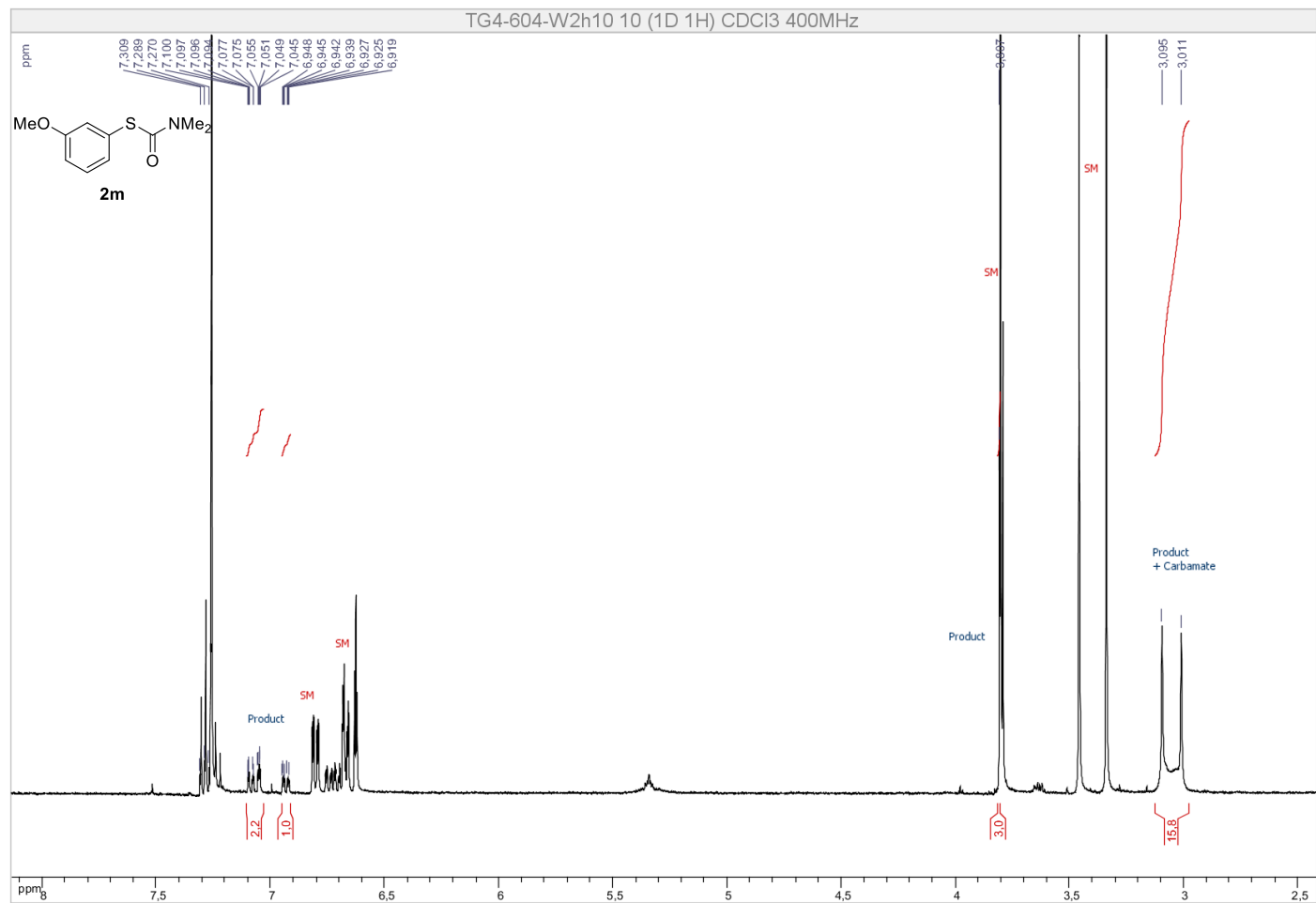
S-phenyl dimethylcarbamothioate (**21**) – NMR of the crude reaction mixture



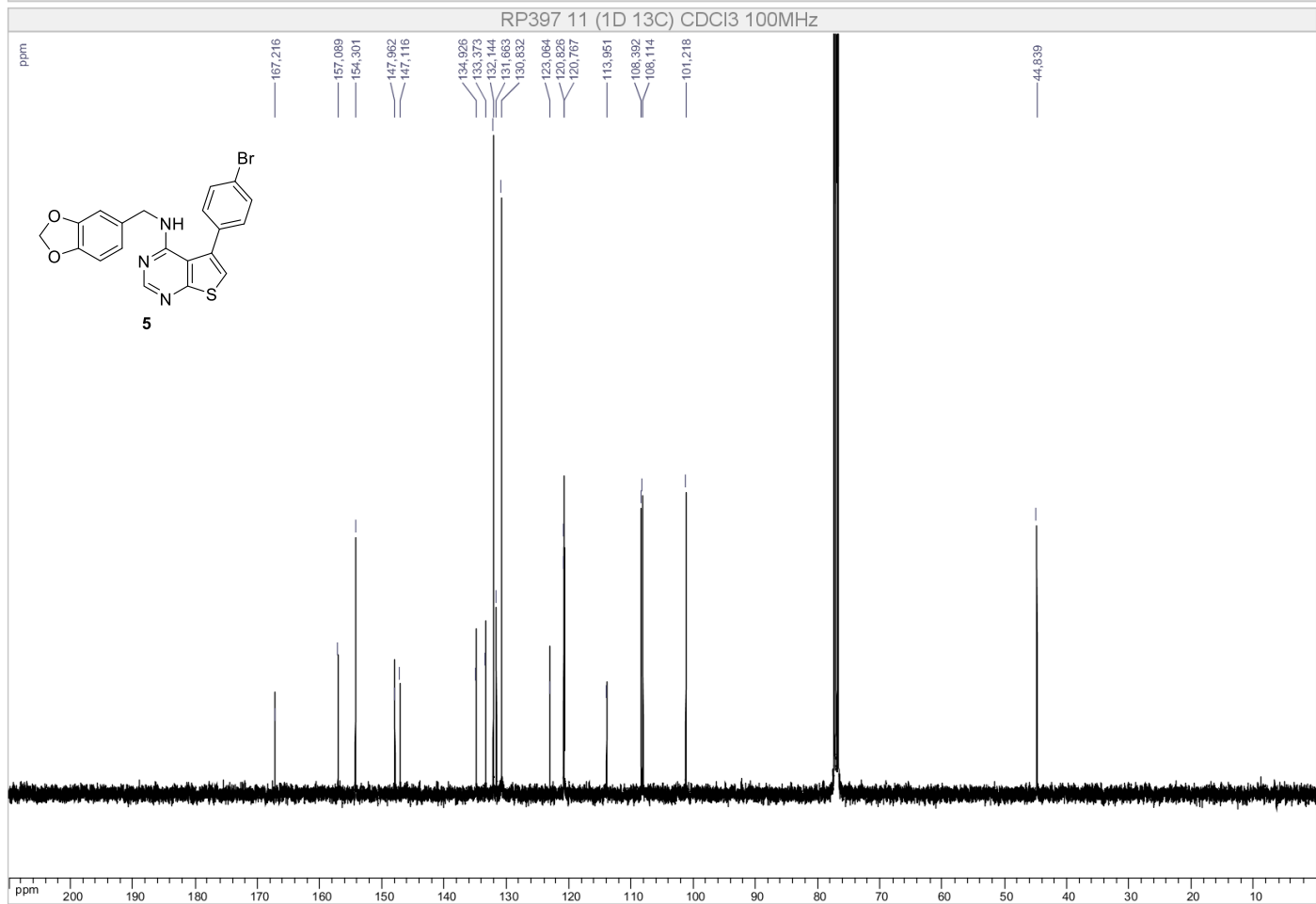
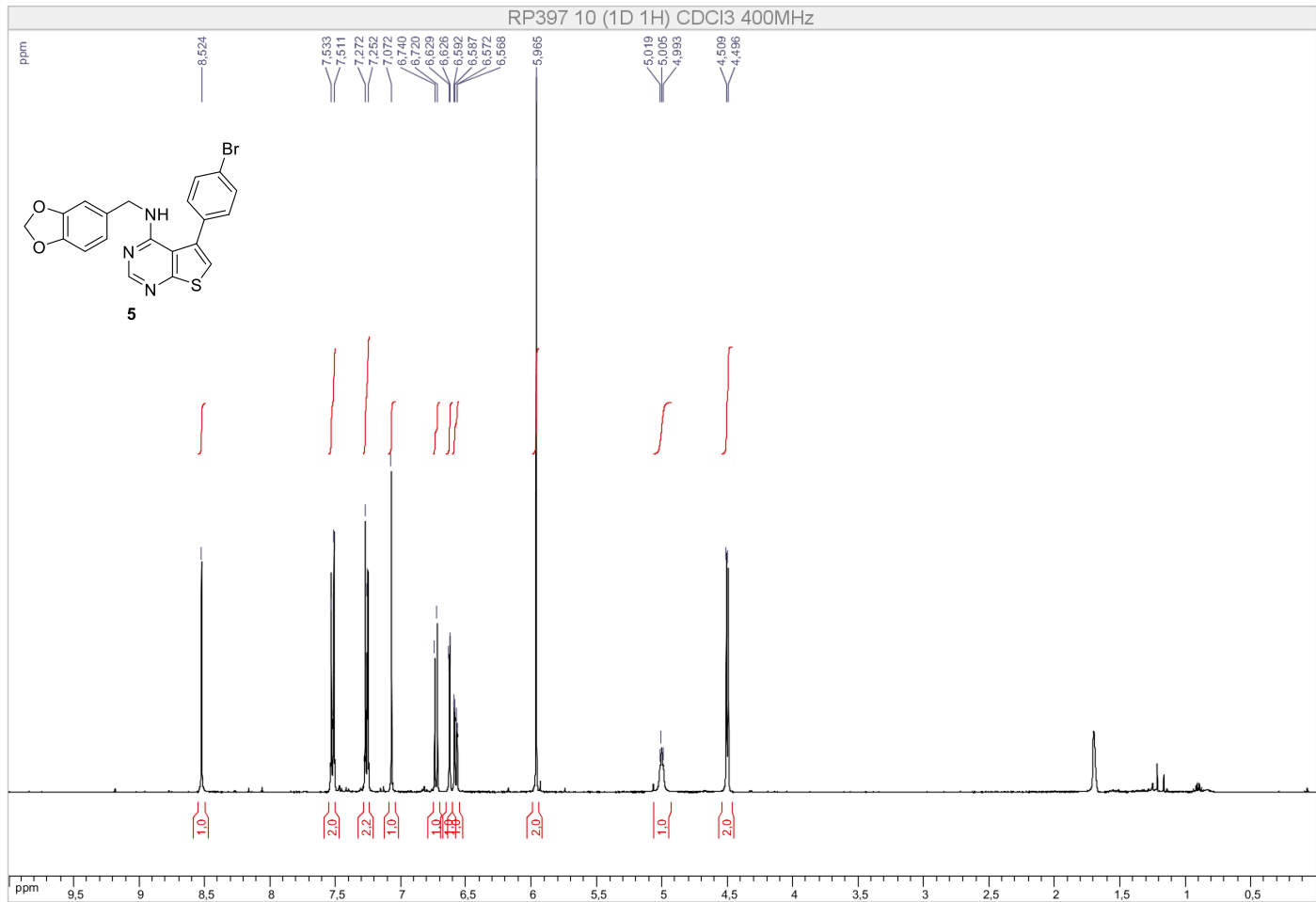
S-phenyl dimethylcarbamothioate (**21**) – LCMS of the crude reaction mixture



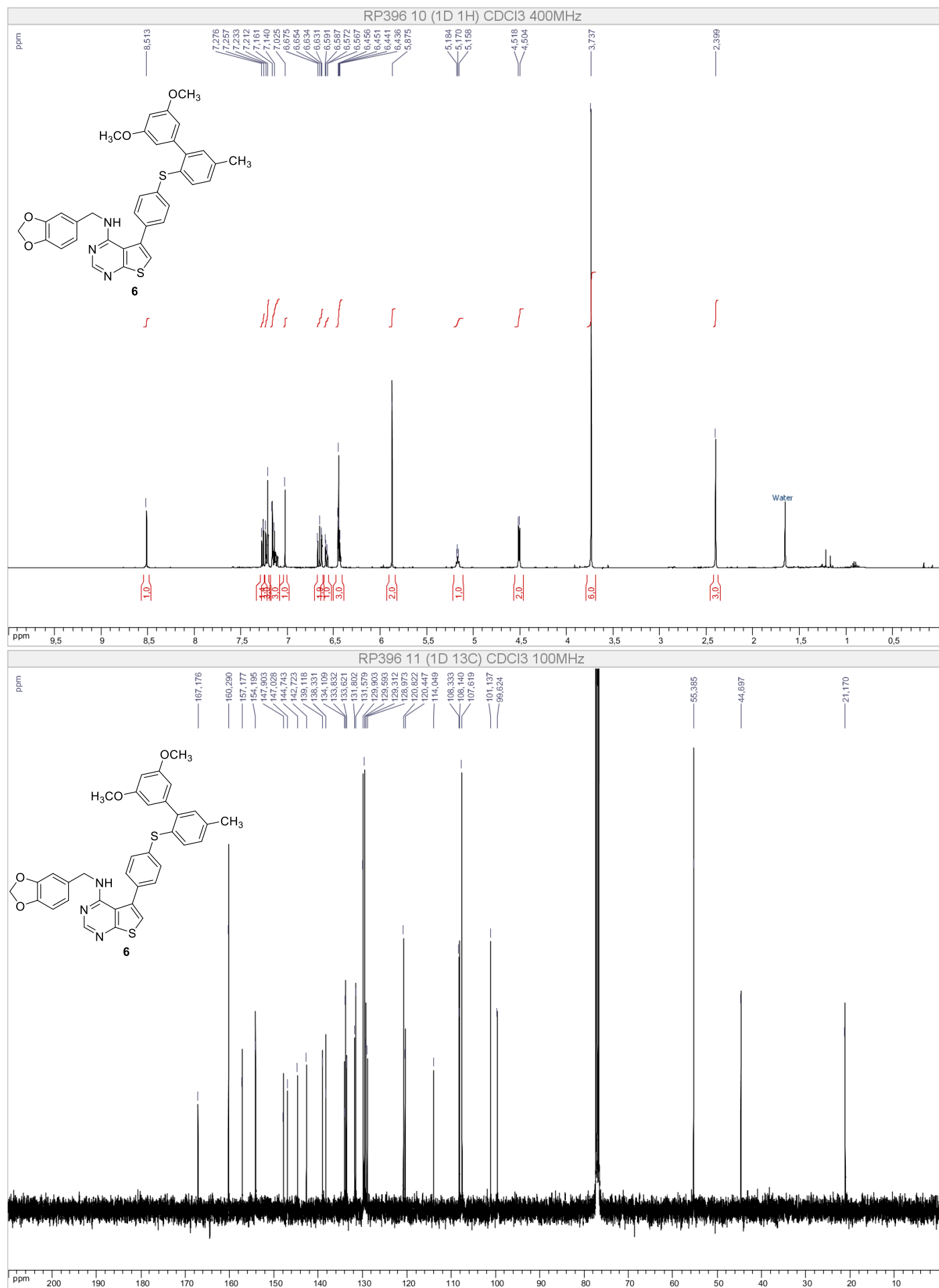
S-(3-methoxyphenyl) dimethylcarbamothioate (**2m**) – NMR of the crude reaction mixture



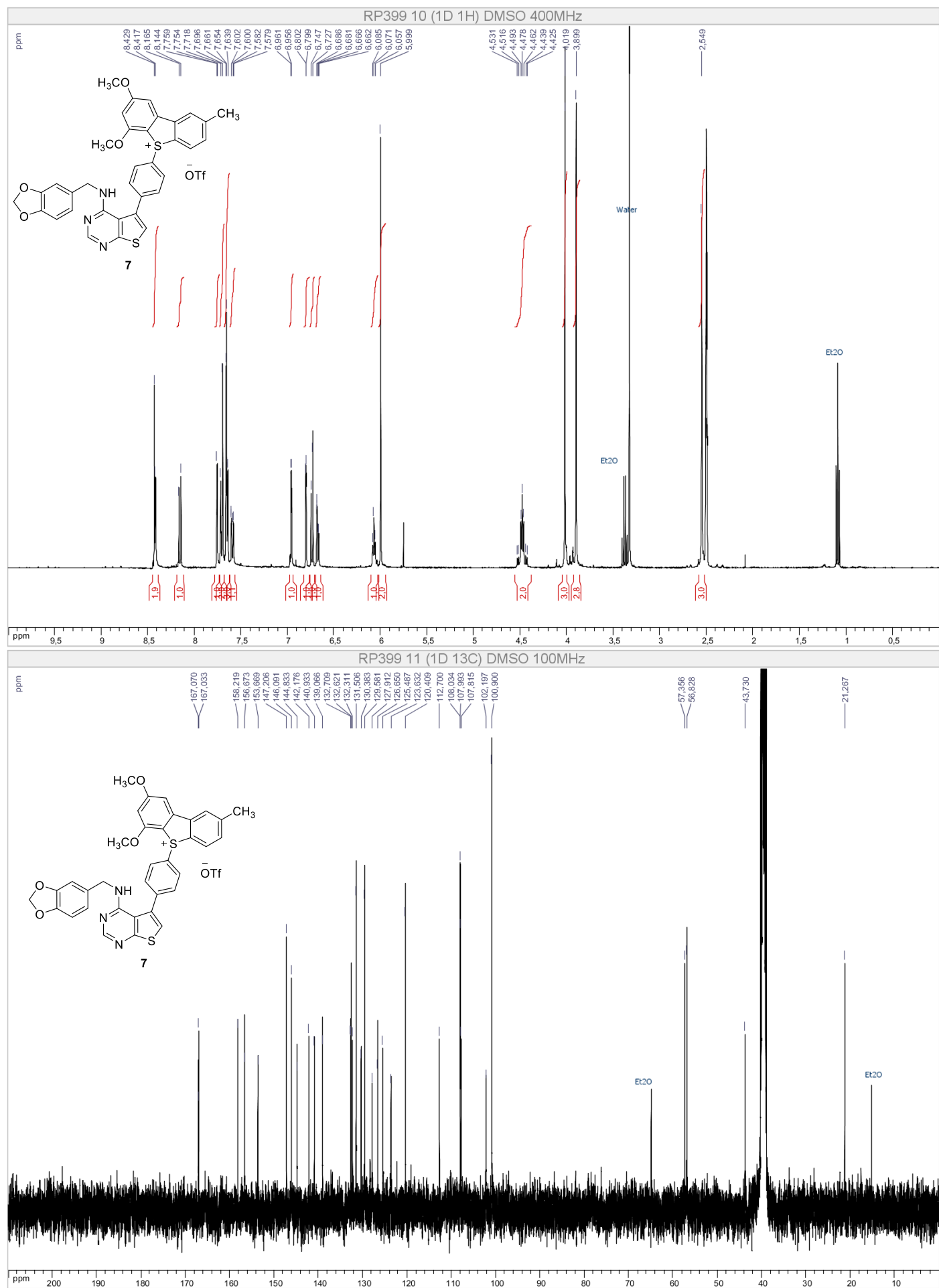
N-(benzo[d][1,3]dioxol-5-ylmethyl)-5-(4-bromophenyl)thieno[2,3-*d*]pyrimidin-4-amine (**5**)



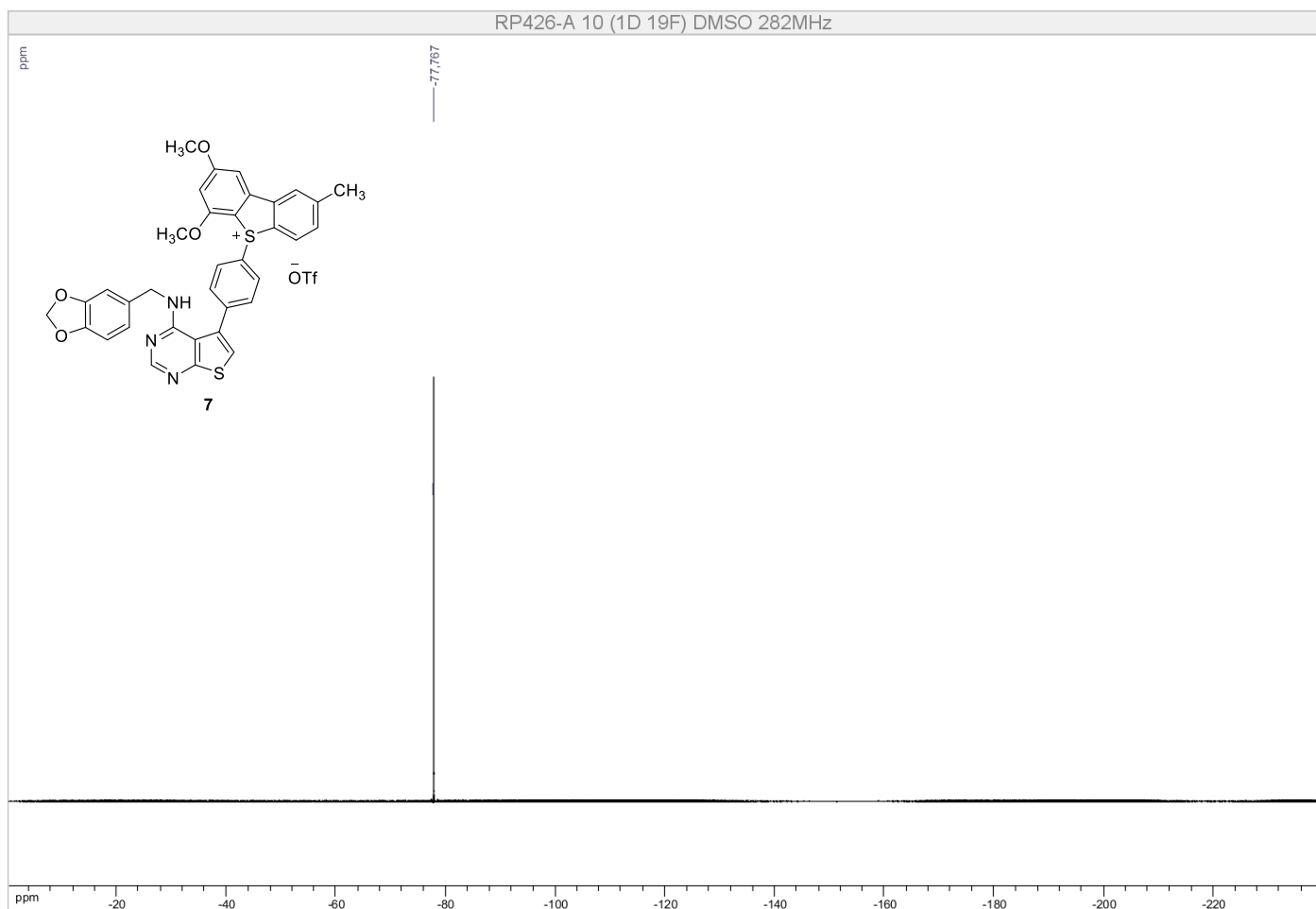
N-(benzo[*d*][1,3]dioxol-5-ylmethyl)-5-(4-((3',5'-dimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)thio)phenyl)thieno[2,3-*d*]pyrimidin-4-amine (**6**)



5-(4-(4-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)thieno[2,3-d]pyrimidin-5-yl)phenyl)-2,4-dimethoxy-8-methyl-5H-dibenzo[b,d]thiophen-5-ium trifluoromethanesulfonate (**7**)



5-(4-(4-((Benzo[d][1,3]dioxol-5-ylmethyl)amino)thieno[2,3-d]pyrimidin-5-yl)phenyl)-2,4-dimethoxy-8-methyl-5H-dibenzo[b,d]thiophen-5-ium trifluoromethanesulfonate (**7**)



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- (2) J. D. Moseley, R. F. Sankey, O. N. Tang and J. P. Gilday, *Tetrahedron*, 2006, **62**, 4685–4689.
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- (6) A. J. Perkowski, C. L. Cruz and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2015, **137**, 15684–15687.
- (7) A. John and K. M. Nicholas, *J. Org. Chem.*, 2012, **77**, 5600–5605.