

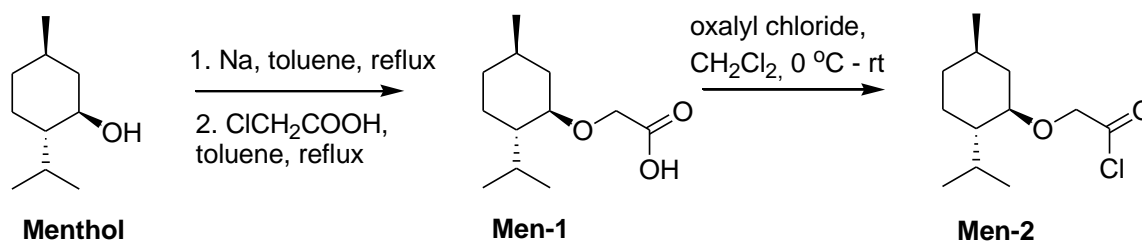
Supporting Information

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1. Preparation of menthol and thymol intermediates used in synthesis of ciprofloxacin conjugates.

1.1. Synthesis of menthol ether derivatives



Scheme 1. Synthesis of menthol ether derivative **Men-2**.

1.1.1. (1R,2S,5R)-(2-Isopropyl-5-methyl-cyclohexyloxy)-acetic acid (**Men-1**)

To 100 ml round bottom flask (-)-menthol (10.0 g, 0.064 mol) and anhydrous toluene (25 mL) were added. To magnetically stirred solution sodium (3.5 g, 0.152 mol) was added and the mixture was refluxed with stirring for 20 h. After cooling to 80 °C the solution of sodium mentholate was decanted, residual sodium was washed with anhydrous toluene (2 mL) and to hot toluene solution was dropped solution of chloracetic acid (2.36 g, 0.025 mol) in anhydrous toluene (20 mL). The resulting mixture was refluxed with stirring for 28 h. After cooling to 40 °C to resulting orange paste toluene (25 mL) and water (25 mL) were added and after mixing the phases were separated. The organic phase was additionally extracted with water (2x25 mL). The combined water phases were acidified with 20% HCl_{aq} (20 mL) and extracted with

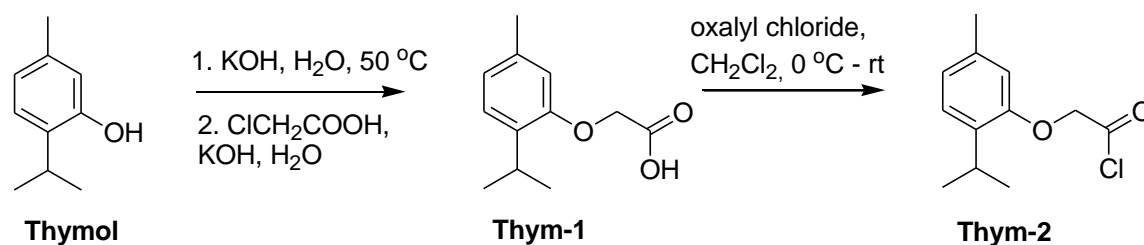
toluene (3x50 mL). The organic phase was dried with anhydrous MgSO_4 and concentrated under reduced pressure. Distillation of residual oil under reduced pressure to gave product as colorless oil; 4.55g (85%), b.p. = 138.5-140.0 °C/ 3.0-3.5 mbar (114-116 °C/ 0.35 mmHg)¹.

^1H NMR (CDCl_3 , 300 MHz) δ (ppm): 0.79 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 7.8 Hz, 3H), 0.93 (d, J = 5.4 Hz, 3H), 0.79-1.01 (m, 3H), 1.27-1.39 (m, 2H), 1.62-1.69 (m, 2H), 2.03-2.10 (m, 1H), 2.17-2.228 (m, 1H), 3.31 (dt, J = 10.8 Hz, 1H), 4.15 (q, J = 16.8 Hz, 2H), 9.93 bs (1H).
 ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 16.1, 20.9, 22.2, 23.2, 25.6, 31.5, 34.3, 39.9, 47.9, 65.4, 80.6, 175.0.

1.1.2. (1*R*,2*S*,5*R*)-(2-Isopropyl-5-methyl-cyclohexyloxy)-acetic acid chloride (Men-2)

To magnetically stirred at 0-2 °C solution of Men-1 (0.30g, 1.40 mmol) in CH_2Cl_2 (4 mL) oxalyl chloride (0.24 mL, 2.80 mmol) was dropped. The resulting solution was stirred at 0-2 °C for 30 min and then the cooling bath was removed and reaction mixture was stirred and room temperature for 3.5 h. Solvent was evaporated under reduced pressure and the product was used to the next step without further purification.

1.2. Synthesis of thymol ether derivatives



Scheme 2. Synthesis of thymol eter derivative **Thym-2**.

1.2.1. (2-Isopropyl-5-methyl-phenoxy)-acetic acid (Thym-1)

To 50 ml round bottom flask thymol (2.0g, 13.3 mmol), water (15 mL) and solid KOH (1 g, 0.018 mol) were added. This mixture was warmed on a water-bath at 50 °C until complete solution took place. In the second flask chloracetic acid (1.36 g, 14.3 mmol) was dissolved in water (10 mL) and 2 drops of phenolphthalein was added. Next, to this solution 10% KOH_{aq} solution was added until a permanent pink color was obtained. The two previously obtained

solution were then mixed and refluxed for 20 min. The hot mixture was filtered, the filtrate was cooled and acidified with concentrated hydrochloric acid (3 mL). After few seconds beige solid was precipitated. The solvent was decanted, solid was washed with water (3x10 mL) and solid was dried by toluene addition (100 mL) and evaporation this solvent under reduced pressure. The residual solid was washed with hot hexane (15 mL) and dried under reduced pressure. The product was obtained as white solid, 0.60g (22%), mp = 150.1-151.1 °C (142-144 °C)².

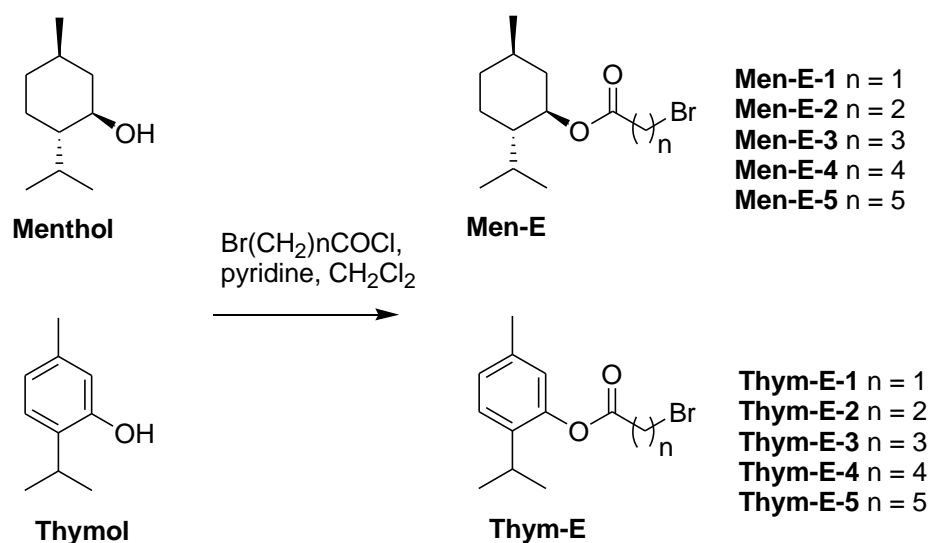
¹H NMR (CDCl₃, 300 MHz) δ (ppm): 1.22 (d, *J* = 6.9 Hz, 6H), 2.31 (s, 3H), 3.27-3.41 (m, 1H), 4.69 (s, 2H), 6.59 (bs, 1H), 6.79-6.83 (m, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 10.43 (bs, 1H).

¹³C NMR (CDCl₃, 75 MHz) δ (ppm): 21.3, 22.8 (2xC), 26.6, 65.2, 112.4, 122.7, 126.4, 134.6, 136.5, 154.6, 174.8.

1.2.2. (2-Isopropyl-5-methyl-phenoxy)-acetic acid chloride (Thym-2)

To magnetically stirred at 0-2 °C solution of Thym-1 (0.20g, 0.96 mmol) in CH₂Cl₂ (4 mL) oxalyl chloride (0.16 mL, 1.92 mmol) was dropped. The resulting solution was stirred at 0-2 °C for 30 min and then the cooling bath was removed and reaction mixture was stirred and room temperature for 6 h. Solvent was evaporated under reduced pressure and the product was used to the next step without further purification.

1.3. Synthesis of menthol and thymol ester derivatives



Scheme 3. Synthesis of menthol and thymol ester derivatives.

General procedure for the synthesis of menthol and thymol esters

To a magnetically stirred at 0-2 °C solution of thymol (0.90 g, 6.00 mmol) in CH₂Cl₂ (40 mL) pyridine (0.73 mL, 9.00 mmol) was added and next solution of appropriate bromoacyl chloride (9.00 mmol) in CH₂Cl₂ (20 mL) was added dropwise. After 45 min the cooling bath was removed and the solution was stirred at room temperature for 4 h. The reaction mixture was washed with water (50 mL), 1% HCl_{aq} solution (50 mL), water (50 mL) and dried over anhydrous Na₂SO₄. After evaporation of the solvent the product was isolated by column chromatography on silica gel (230-400 mesh) using hexane as mobile phase.

1.3.1. Menthyl bromoacetate (Men-E-1)

Colorless oil, 70%.³

¹H NMR (CDCl₃, 300 MHz) δ (ppm): 0.77 (d, J = 6.9 Hz, 3H), 0.85-0.96 (m, 1H), 0.90 (d, J = 3.6 Hz, 3H), 0.92 (d, J = 3.6 Hz, 3H), 1.00-1.12 (m, 2H), 1.38-1.50 (m, 2H), 1.65-1.73 (m, 2H), 1.85-1.92 (m, 1H), 1.98-2.05 (m, 1H), 3.80 (d, J = 1.5 Hz, 2H), 4.73 (dt, J = 4.5 Hz, 10.8 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ (ppm): 16.2, 20.7, 22.0, 23.4, 26.2, 26.3, 31.4, 34.1, 40.5, 47.0, 76.4, 166.9.

1.3.2. Menthyl 3-bromopropionate (Men-E-2)

Colorless oil, 80%.

¹H NMR (CDCl₃, 500 MHz) δ (ppm): 0.76 (d, J = 7.0 Hz, 3H), 0.83-0.86 (m, 1H), 0.90 (d, J = 6.5 Hz, 3H), 0.92 (d, J = 6.0 Hz, 3H), 0.96-1.10 (m, 2H), 1.36-1.42 (m, 1H), 1.45-1.55 (m, 1H), 1.66-1.70 (m, 2H), 1.86-1.92 (m, 1H), 1.99-2.03 (m, 1H), 2.90 (t, J = 7.0 Hz, 2H), 3.80 (dt, J = 1.5 Hz, 7.0 Hz, 2H), 4.74 (dt, J = 4.5 Hz, 10.5 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ (ppm): 16.3, 20.8, 22.0, 23.4, 26.3 (2xC), 31.4, 34.2, 38.1, 40.9, 47.0, 75.1, 166.9.

1.3.3. Menthyl 4-bromobutyrate (Men-E-3)

Colorless oil, 79%.⁴

¹H NMR (CDCl₃, 500 MHz) δ (ppm): 0.76 (d, J = 7.0 Hz, 3H), 0.83-0.89 (m, 1H), 0.90 (d, J = 4.5 Hz, 3H), 0.91 (d, J = 4.0 Hz, 3H), 0.94-1.10 (m, 2H), 1.34-1.40 (m, 1H), 1.44-1.51 (m, 1H), 1.65-1.70 (m, 2H), 1.82-1.88 (m, 1H), 1.96-2.00 (m, 1H), 2.14-2.20 (m, 2H), 2.48 (dt, J = 1.5 Hz, 7.5 Hz, 2H), 3.46 (dt, J = 1.0 Hz, 6.5 Hz, 2H), 4.74 (dt, J = 4.5 Hz, 10.5 Hz, 1H). ¹³C NMR (CDCl₃, 125 MHz) δ (ppm): 16.3, 20.8, 22.0, 23.4, 26.3, 27.9, 31.4, 32.7, 32.9, 34.2, 40.9, 47.0, 74.4, 172.1.

1.3.4. Menthyl 5-bromopentanoate (Men-E-4)

Colorless oil, 87%.

^1H NMR (CDCl_3 , 500 MHz) δ (ppm): 0.76 (d, $J = 7.0$ Hz, 3H), 0.83-0.88 (m, 1H), 0.89 (d, $J = 4.0$ Hz, 3H), 0.91 (d, $J = 3.5$ Hz, 3H), 0.93-1.10 (m, 2H), 1.34-1.40 (m, 1H), 1.44-1.54 (m, 1H), 1.65-1.70 (m, 2H), 1.75-1.81 (m, 2H), 1.82-1.87 (m, 1H), 1.87-1.93 (m, 2H), 1.96-2.00 (m, 1H), 2.32 (t, $J = 7.0$ Hz, 2H), 3.42 (t, $J = 6.5$ Hz, 2H), 4.68 (dt, $J = 4.5$ Hz, 11.0 Hz, 1H). ^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm): 16.3, 20.8, 22.0, 23.4, 23.7, 26.3, 31.4, 32.0, 33.1, 33.7, 34.3, 41.0, 47.0, 74.2, 172.7.

1.3.5. Menthyl 6-bromohexanoate (Men-E-5)

Colorless oil, 94%.

^1H NMR (CDCl_3 , 500 MHz) δ (ppm): 0.76 (d, $J = 7.0$ Hz, 3H), 0.82-0.88 (m, 1H), 0.89 (d, $J = 4.0$ Hz, 3H), 0.91 (d, $J = 3.5$ Hz, 3H), 0.92-1.00 (m, 1H), 1.01-1.10 (m, 1H), 1.34-1.40 (m, 1H), 1.44-1.54 (m, 3H), 1.63-1.70 (m, 4H), 1.83-1.91 (m, 3H), 1.96-2.00 (m, 1H), 2.30 (t, $J = 7.0$ Hz, 2H), 3.41 (t, $J = 6.5$ Hz, 2H), 4.68 (dt, $J = 4.5$ Hz, 11.0 Hz, 1H). ^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm): 16.3, 20.8, 22.0, 23.4, 24.3, 26.3, 27.7, 31.4, 32.4, 33.5, 34.3, 34.5, 41.0, 47.0, 74.1, 173.0.

1.3.6. Thymol bromoacetate (Thym-E-1)

Colorless oil, 82%.

^1H NMR (CDCl_3 , 300 MHz) δ (ppm): 1.20 (d, $J = 7.5$ Hz, 6H), 2.32 (s, 3H), 2.96-3.01 (m, 1H), 4.05 (s, 2H), 6.83 (bs, 1H), 7.03-7.07 (m, 1H), 7.21 (d, $J = 7.8$ Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 20.8, 23.0 (2xC), 25.3, 26.9, 122.1, 126.6, 127.7, 136.8, 137.0, 147.5, 166.1.

1.3.7. Thymol 3-bromopropionate (Thym-E-2)

Colorless oil, 62%.

^1H NMR (CDCl_3 , 300 MHz) δ (ppm): 1.19 (d, $J = 7.2$ Hz, 6H), 2.31 (s, 3H), 2.93-3.06 (m, 1H), 3.19 (t, $J = 6.6$ Hz, 2H), 3.70 (t, $J = 6.6$ Hz, 2H), 6.82 (bs, 1H), 7.02-7.05 (m, 1H), 7.21 (d, $J = 7.8$ Hz, 1H). ^{13}C NMR (CDCl_3 , 75 MHz) δ (ppm): 20.8, 23.1 (2xC), 25.7, 27.0, 37.8, 122.5, 126.5, 127.4, 136.6, 137.0, 147.6, 169.3.

1.3.8. Thymol 4-bromobutyrate (Thym-E-3)

Colorless oil, 88%.

^1H NMR (CDCl_3 , 500 MHz) δ (ppm): 1.19 (d, $J = 7.0$ Hz, 6H), 2.27-2.33 (m, 2H), 2.31 (s, 3H), 2.80 (t, $J = 7.0$ Hz, 2H), 2.92-2.98 (m, 1H), 3.55 (t, $J = 6.5$ Hz, 2H), 6.80 (bs, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 7.19 (d, $J = 8.0$ Hz, 1H). ^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm): 20.8, 23.0 (2xC), 27.2, 27.6, 32.4, 32.5, 122.6, 126.5, 127.2, 136.6, 136.9, 147.7, 171.3.

1.3.9. Thymol 5-bromopentanoate (Thym-E-4)

Colorless oil, 88%.

^1H NMR (CDCl_3 , 500 MHz) δ (ppm): 1.19 (d, $J = 7.0$ Hz, 6H), 1.92-2.02 (m, 4H), 2.31 (s, 3H), 2.62 (t, $J = 7.0$ Hz, 2H), 2.92-2.98 (m, 1H), 3.46 (t, $J = 6.5$ Hz, 2H), 6.80 (bs, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 1H). ^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm): 20.8, 23.0 (2xC), 23.6, 27.1, 32.0, 32.9, 33.4, 122.7, 126.4, 127.2, 136.6, 136.9, 147.8, 171.8.

1.3.10. Thymol 6-bromohexanoate (Thym-E-5)

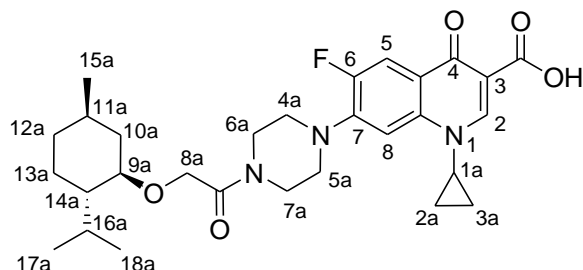
Colorless oil, 82%.

^1H NMR (CDCl_3 , 500 MHz) δ (ppm): 1.19 (d, $J = 6.5$ Hz, 6H), 1.55-1.61 (m, 2H), 1.77-1.84 (m, 2H), 1.91-1.96 (m, 2H), 2.31 (s, 3H), 2.60 (t, $J = 7.5$ Hz, 2H), 2.93-2.98 (m, 1H), 3.44 (t, $J = 7.0$ Hz, 2H), 6.79 (bs, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 7.19 (d, $J = 7.5$ Hz, 1H). ^{13}C NMR (CDCl_3 , 125 MHz) δ (ppm): 20.8, 23.0 (2xC), 24.2, 27.1, 27.7, 32.4, 33.4, 34.1, 122.7, 126.4, 127.1, 136.6, 137.0, 147.8, 172.1.

1. Galpin, D.R., Huitric, A.C., J. Org. Chem., 1968, 33, 2, 921-923.
2. Pawełczyk, A., Sowa-Kasprzyk, A., Olender, D., Zaprutko, L., Molecules, 2018, 23, 2360.
3. Singh, R., Gosh, S. K, Tetrahedron: Asymmetry, 2014, 25, 57-62.
4. Ha, T. H., Suh, K-H., Lee G. S., Bull. Korean Chem. Soc., 2013, 34, 549-552.

2. Numbering of signals in ^1H NMR for selected ciprofloxacin conjugates.

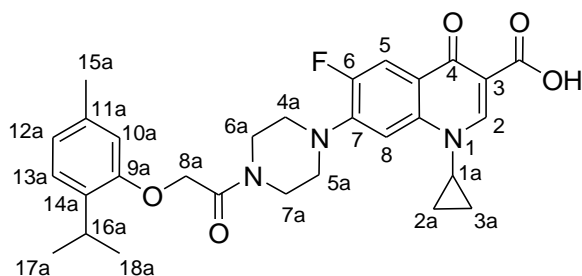
1-cyclopropyl-6-fluoro-7-{4-[2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyloxy)-acetyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (1)



White solid. Yield 92%. Mp = 185.7-189.6 °C.

^1H NMR (CDCl_3 , 300 MHz) δ (ppm): 0.72 (d, J = 6.6 Hz, 3H-15a), 0.89-0.93 (m, 3H-17a, 3H-18a, 1H-10a, 1H-12a, 1H-13a), 1.15-1.34 (m, 2H-2a, 2H-3a, 1H-11a, 1H-14a), 1.53-1.61 (m, 1H-12a, 1H-13a), 2.06-2.17 (m, 1H-10a, 1H-16a), 3.01-3.18 (m, 1H-9a), 3.27-3.30 (m, 4H-6a, 7a), 3.51 (bs, 1H-1a), 3.71-3.81 (m, 4H-4a, 5a), 4.05-4.24 (m, 2H-8a), 7.29 (d, J = 7.2 Hz, 1H-8), 7.85 (d, J = 12.9 Hz, 1H-5), 8.60 (s, 1H-2), 14.81 (s, 1H-OH).

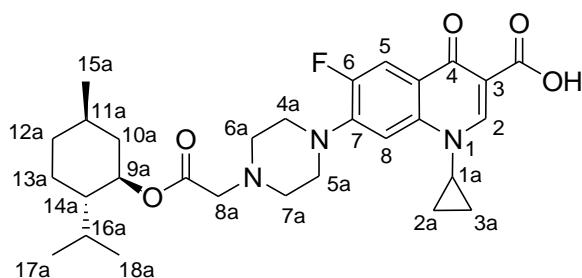
1-cyclopropyl-6-fluoro-7-{4-[2-(2-isopropyl-5-methylphenoxy)acetyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (9)



White solid. Yield 81%. Mp = 232.8-234.0 °C.

^1H NMR ($\text{CDCl}_3/\text{CD}_3\text{OD}$, 9:1 mixture, 300 MHz) δ (ppm): 1.18-1.20 (m, 2H-2a), 1.21 (d, J = 7.0 Hz, 6H-17a, 18a), 1.39-1.43 (m, 2H-3a), 2.33 (s, 3H-15a), 3.37-3.93 (m, 4H-6a, 7a, 1H-16a), 3.54-3.61 (m, 1H-1a), 3.90 (t, J = 5.1 Hz, 4H-4a, 5a), 4.76 (s, 2H-8a), 6.72 (bs, 1H-10a), 6.82 (d, J = 7.8 Hz, 1H-12a), 7.14 (d, J = 7.5 Hz, 1H-13a), 7.39 (d, J = 6.9 Hz, 1H-8), 8.04 (d, J = 12.9 Hz, 1H-5), 8.79 (s, 1H-2).

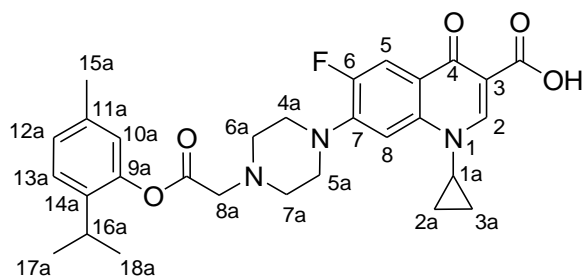
1-cyclopropyl-6-fluoro-7-{4-[2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyloxy)-2-oxoethyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (2)



White solid. Yield 63%. Mp = 214.5-215.4 °C.

¹H NMR (CDCl₃, 300 MHz) δ (ppm): 0.78 (d, *J* = 6.9 Hz, 3H-15a), 0.84-0.96 (m, 1H-12a), 0.90 (d, *J* = 2.4 Hz, 3H-17a), 0.92 (d, *J* = 2.1 Hz, 3H-18a), 0.96-1.14 (m, 1H-10a, 1H-13a), 1.18-1.23 (m, 2H-2a), 1.37-1.55 (m, 2H-3a, 1H-11a, 1H-14a), 1.69-1.72 (m, 1H-12a, 1H-13a), 1.82-1.89 (m, 1H-10a), 1.99-2.04 (m, 1H-16a), 2.84 (bs, 4H-6a,7a), 3.30(d, *J* = 2.7 Hz, 2H-8a), 3.41 (t, *J* = 4.5 Hz, 4H-4a, 5a), 3.51-3.61 (m, 1H-1a), 4.77(dt, *J* = 4.5 Hz, 10.8 Hz, 1H-9a), 7.37 (d, *J* = 7.2 Hz, 1H-8), 7.95 (d, *J* = 12.9 Hz, 1H-5), 8.72 (s, 1H-2), 15.00 (s, 1H-OH).

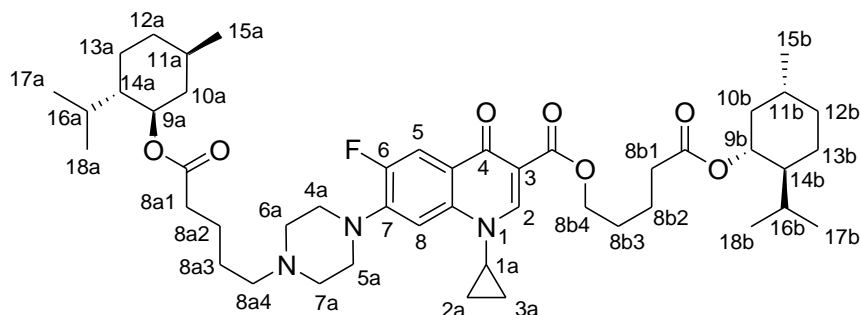
1-cyclopropyl-6-fluoro-7-{4-[2-(2-isopropyl-5-methylphenoxy)acetyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (10)



Pale beige solid. Yield 65%. Mp = 240.2-241.8 °C.

¹H NMR (CDCl₃/CD₃OD, 9:1 mixture, 500 MHz) δ (ppm): 1.18-1.20 (m, 2H-2a), 1.21 (d, *J* = 7.0 Hz, 6H-17a, 18a), 1.39-1.43 (m, 2H-3a), 2.33 (s, 3H-15a), 2.95 (t, *J* = 4.0 Hz, 4H-6a, 7a), 3.38-3.40 (m, 1H-16a), 3.45 (t, *J* = 4.5 Hz, 4H-4a, 5a), 3.56-3.60 (m, 1H-1a), 3.63 (s, 2H-8a), 6.83 (bs, 1H-10a), 7.04-7.06 (m, 1H-12a), 7.22 (d, *J* = 8.0 Hz, 1H-13a), 7.40 (d, *J* = 7.0 Hz, 1H-8), 7.98 (d, *J* = 13.0 Hz, 1H-5), 8.76 (s, 1H-2).

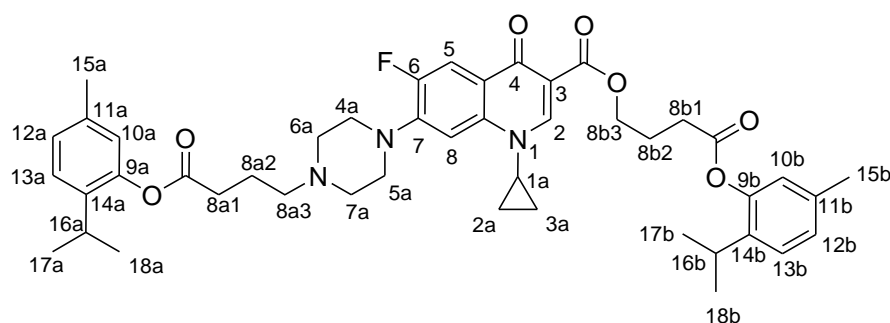
5-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyloxy)-5-oxopentyl-1-cyclopropyl-6-fluoro-7-{4-[5-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyloxy)-5-oxopentyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylate (**7**)



Solidifying oil. Yield 7%.

¹H NMR (CDCl₃, 300 MHz) δ (ppm): 0.75 (d, *J* = 4.8 Hz, 3H-15b), 0.77 (d, *J* = 4.8 Hz, 3H-15a), 0.84-0.92 (m, 12H-17a, 18a, 17b, 18b, 1H-12a, 1H-12b), 0.95-1.16 (m, 2H-2a, 1H-13a, 1H-13b, 1H-10a, 1H-10b), 1.28-1.51 (m, 2H-3a, 1H-14a, 1H-14b, 1H-11a, 1H-11b), 1.64-1.72 (m, 4H-8a3, 8b3, 1H-12a, 1H-12b, 1H-13a, 1H-13b), 1.78-1.90 (m, 4H-8a2, 8b2, 1H-10a, 1H-10b), 1.94-2.02 (m, 2H-16a, 16b), 2.31-2.39 (m, 4H-8a1, 8b1), 2.45 (t, *J* = 4.2 Hz, 2H-8a4), 2.65 (t, *J* = 4.8 Hz, 4H-6a, 7a), 3.29 (t, *J* = 4.8 Hz, 4H-4a, 5a), 3.38-3.46 (m, 1H-1a), 4.32 (t, *J* = 6.0 Hz, 2H-8b4), 4.63-4.74 (m, 2H-9a, 9b), 7.27 (d, *J* = 7.2 Hz, 1H-8), 8.04 (d, *J* = 13.5 Hz, 1H-5), 8.52 (s, 1H-2).

2-(2-isopropyl-5-methylphenoxy)-2-oxoethyl-1-cyclopropyl-6-fluoro-7-{4-[2-(2-isopropyl-5-methylphenoxy)-2-oxoethyl]piperazin-1-yl}-4-oxo-1,4-dihydroquinoline-3-carboxylate (**15**)

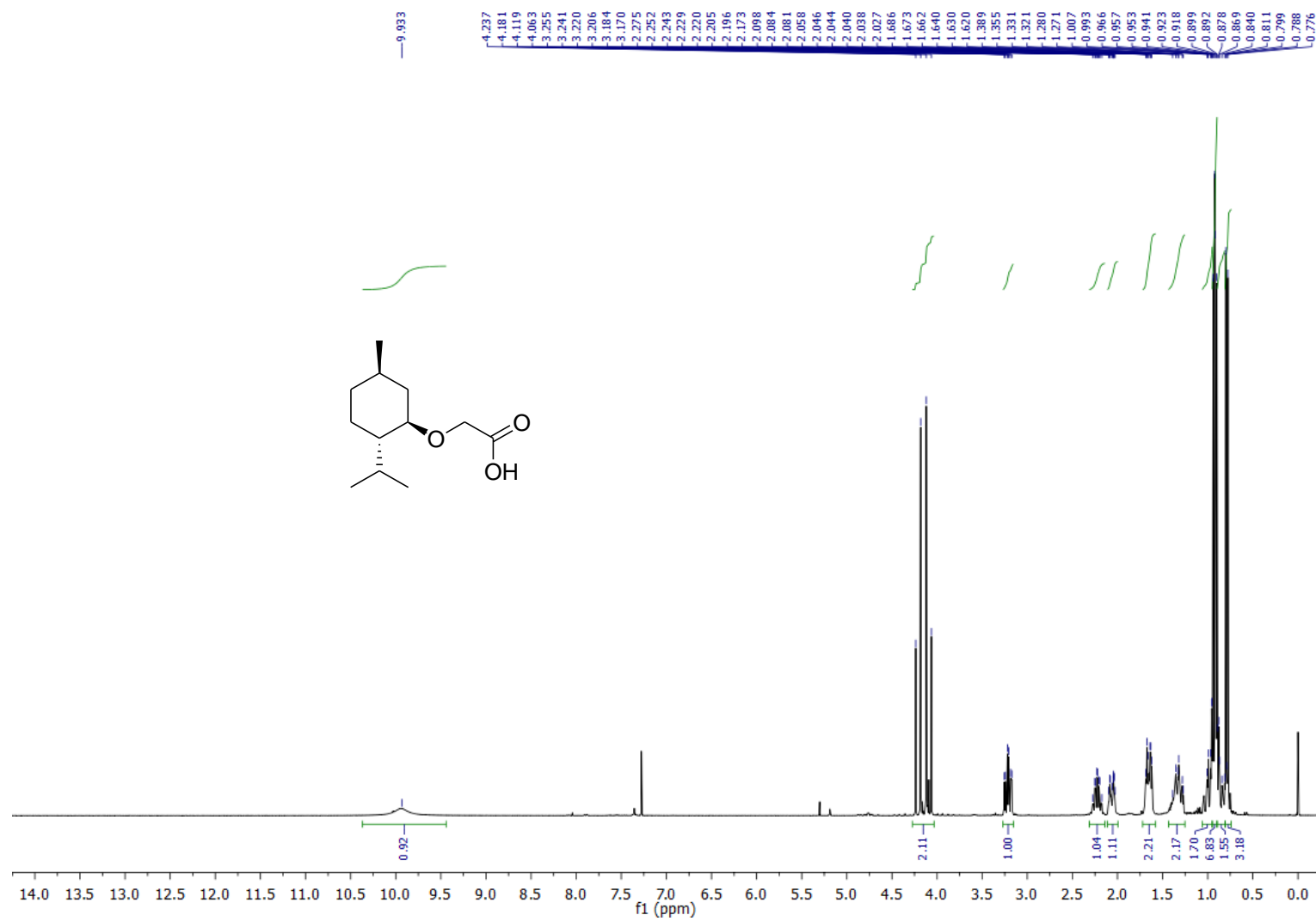


White solid. Yield 21%. Mp = 105.5-107.2 °C.

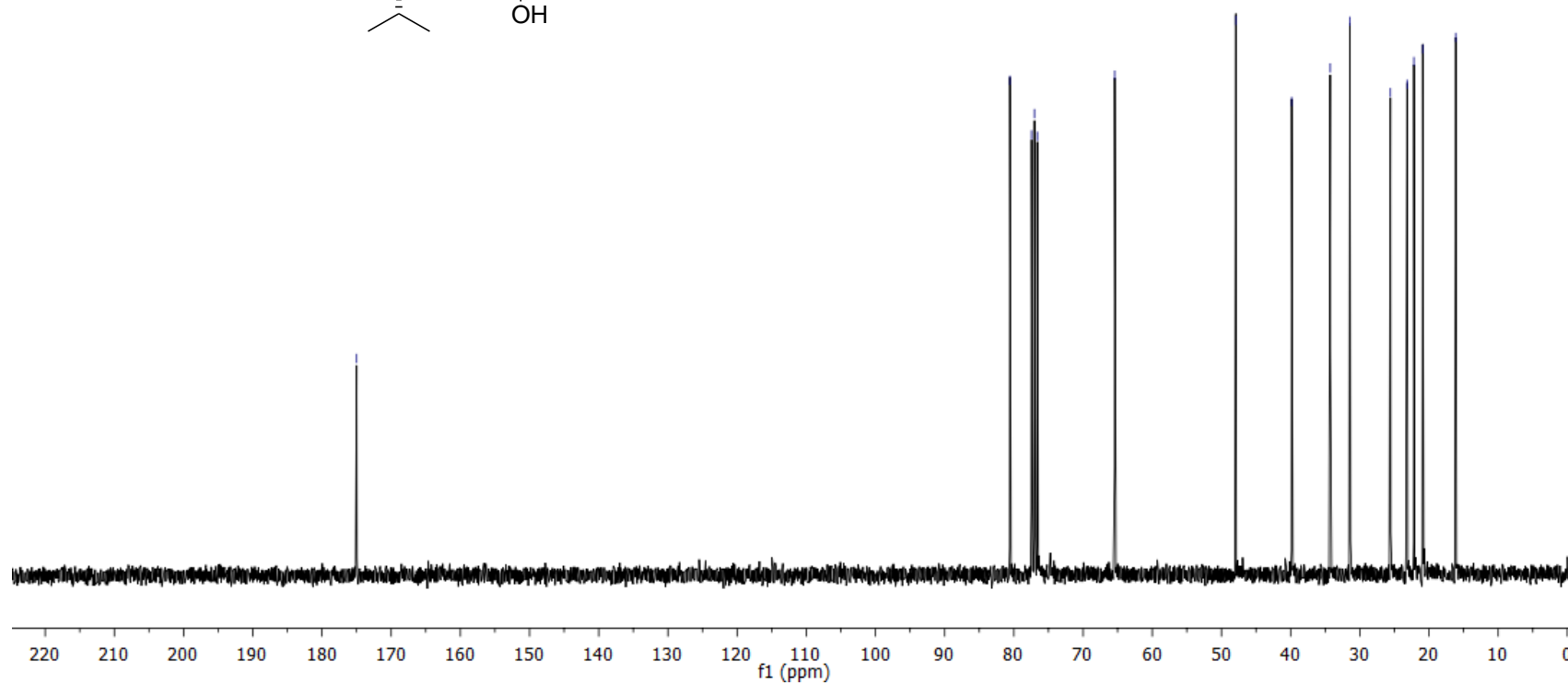
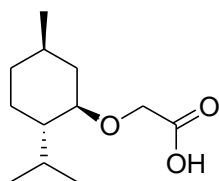
¹H NMR (CDCl₃, 500 MHz) δ (ppm): 1.06-1.09 (m, 2H-2a), 1.16 (d, *J* = 7.0 Hz, 6H-17a, 18a), 1.20 (d, *J* = 7.0 Hz, 6H-17b, 18b), 1.24-1.28 (m, 2H-3a), 1.98-2.04 (m, 2H-8a2), 2.23 (s, 3H-15a), 2.24-2.28 (m, 2H-8b2), 2.31 (s, 3H-15b), 2.56 (t, *J* = 7.0 Hz, 2H-8a1), 2.68 (t, *J* =

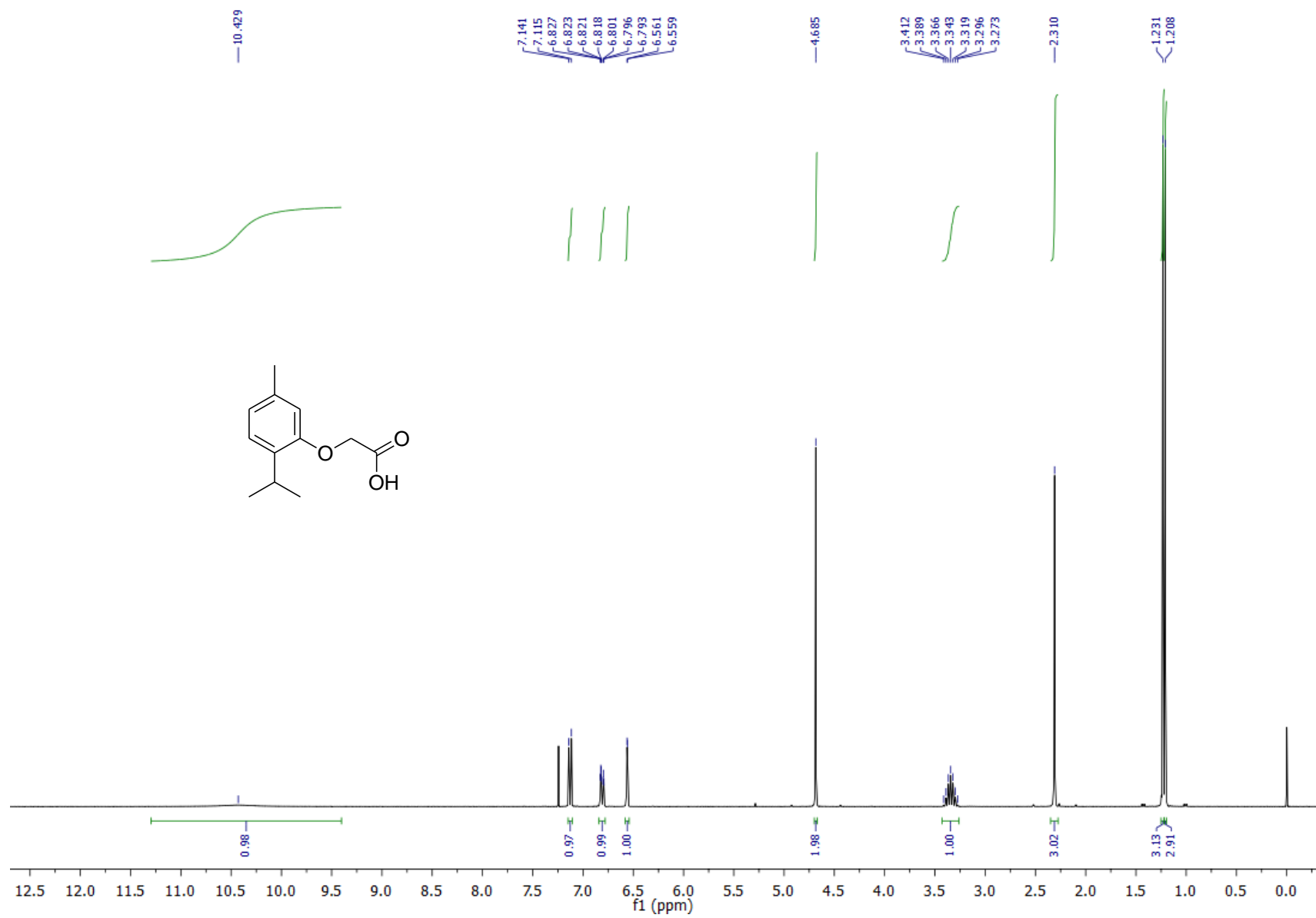
7.0 Hz, 2H-8b1), 2.71 (t, $J = 4.0$ Hz, 4H-6a, 7a), 2.83 (t, $J = 7.5$ Hz, 2H-8a1), 2.93-3.01 (m, 2H-16a, 16b), 3.30 (t, $J = 4.5$ Hz, 4H-4a, 5a), 3.33-3.38 (m, 1H-1a), 4.43 (t, $J = 6.5$ Hz, 2H-8b3), 6.78 (s, 1H-10b), 6.82 (s, 1H-10a), 6.99 (d, $J = 8.0$ Hz, 1H-12b), 7.02 (d, $J = 7.5$ Hz, 1H-12a), 7.17 (d, $J = 7.5$ Hz, 1H-13b), 7.20 (d, $J = 8.0$ Hz, 1H-13a), 7.26 (d, $J = 7.5$ Hz, 1H-8), 8.02 (d, $J = 13.5$ Hz, 1H-5), 8.48 (s, 1H-2).

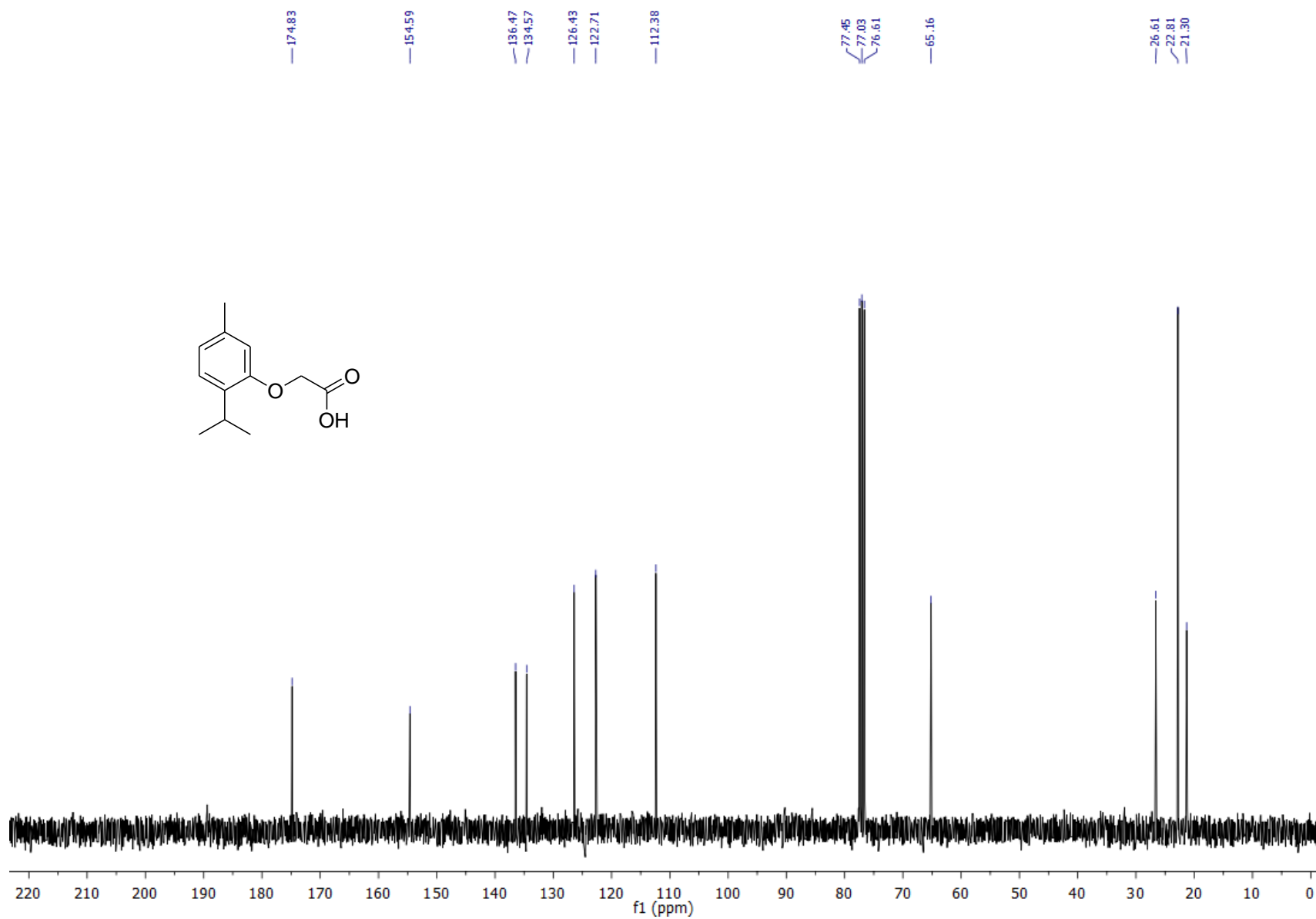
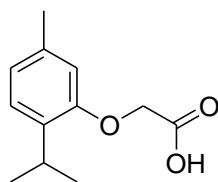
3. The NMR spectra of menhtol and thymol intermediates.

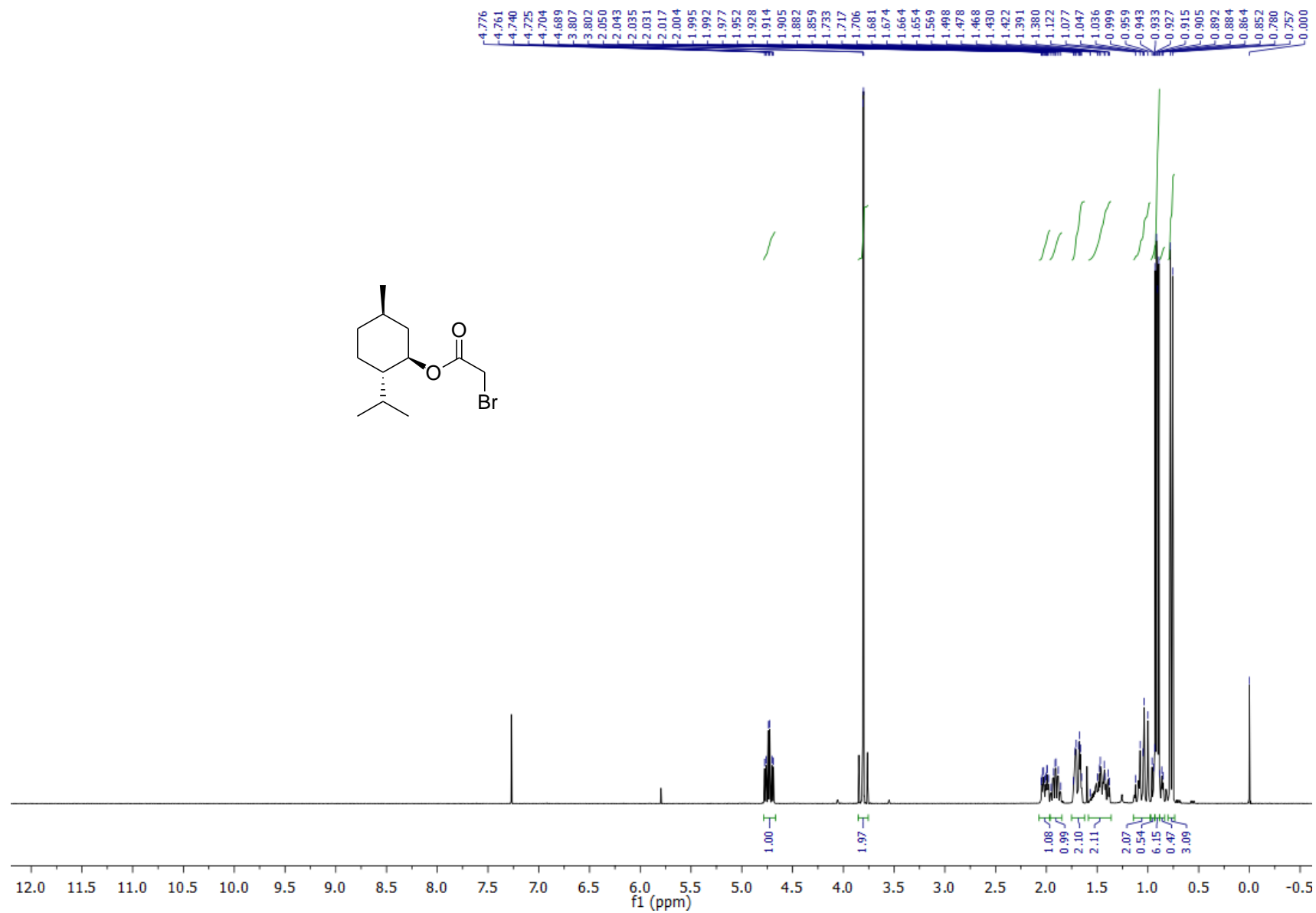


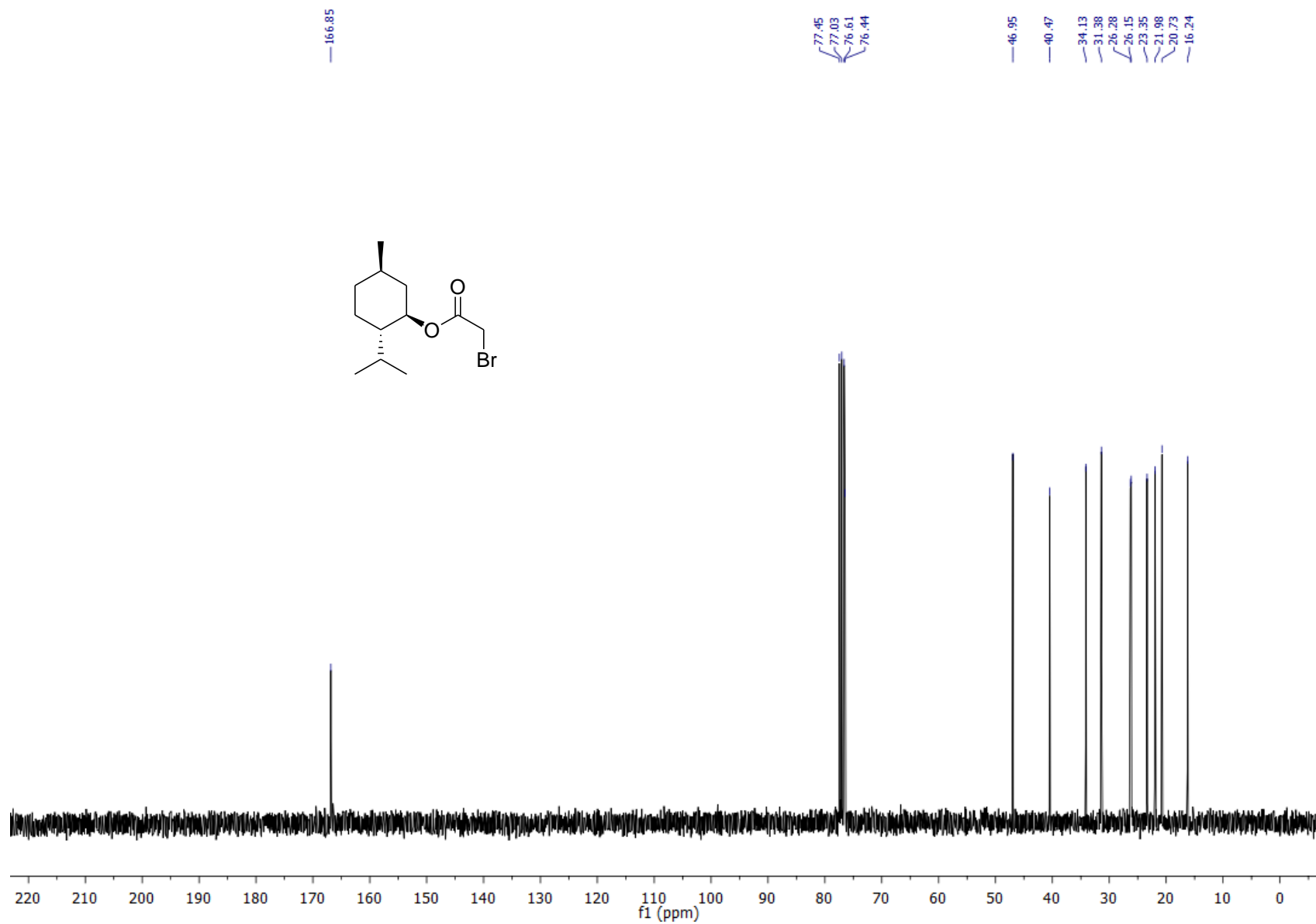
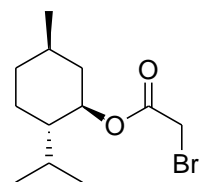
174.99
 80.57
 77.45
 77.03
 76.61
 65.42
 47.92
 39.85
 34.27
 31.45
 25.58
 23.17
 22.19
 20.91
 16.14

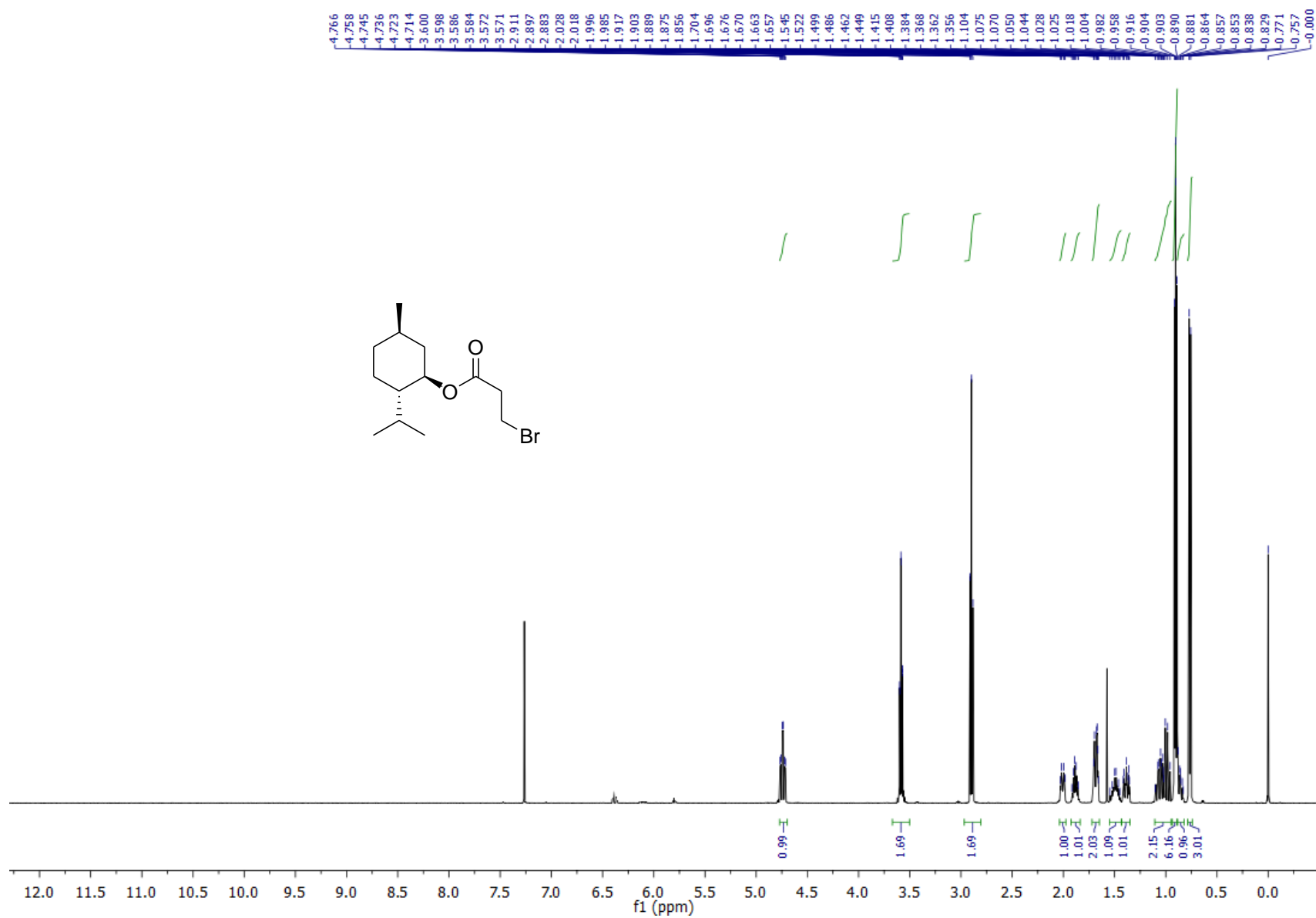


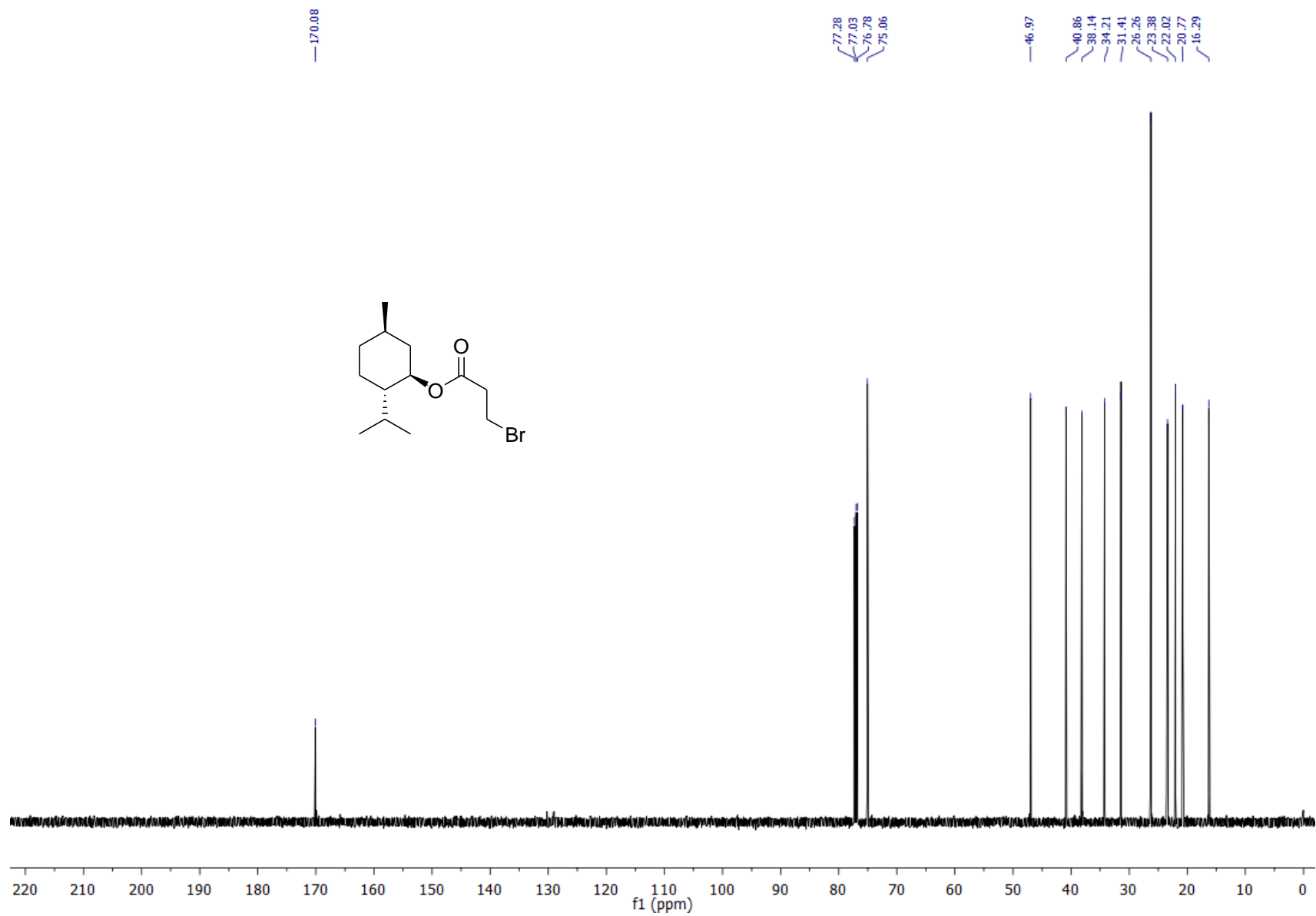


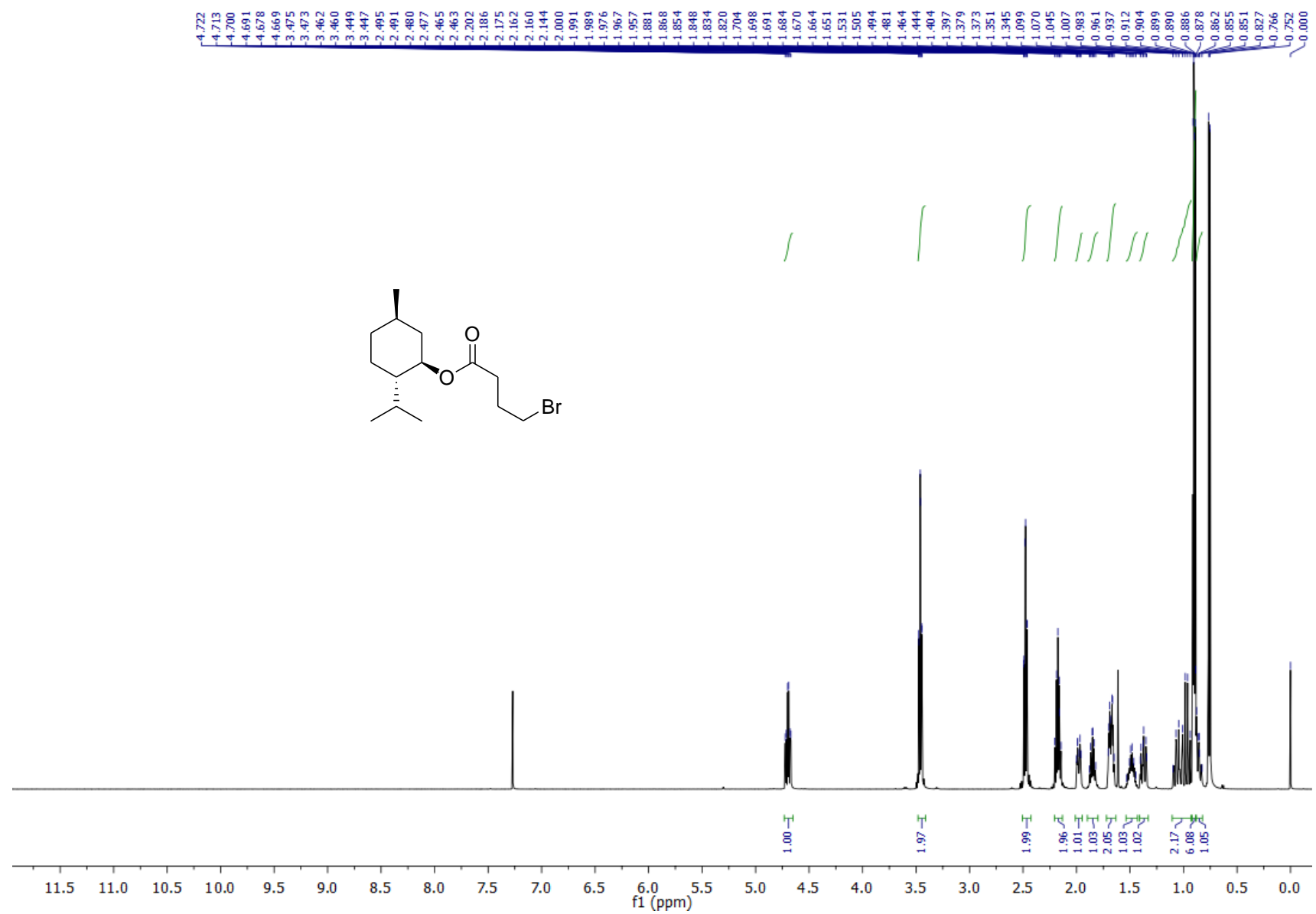


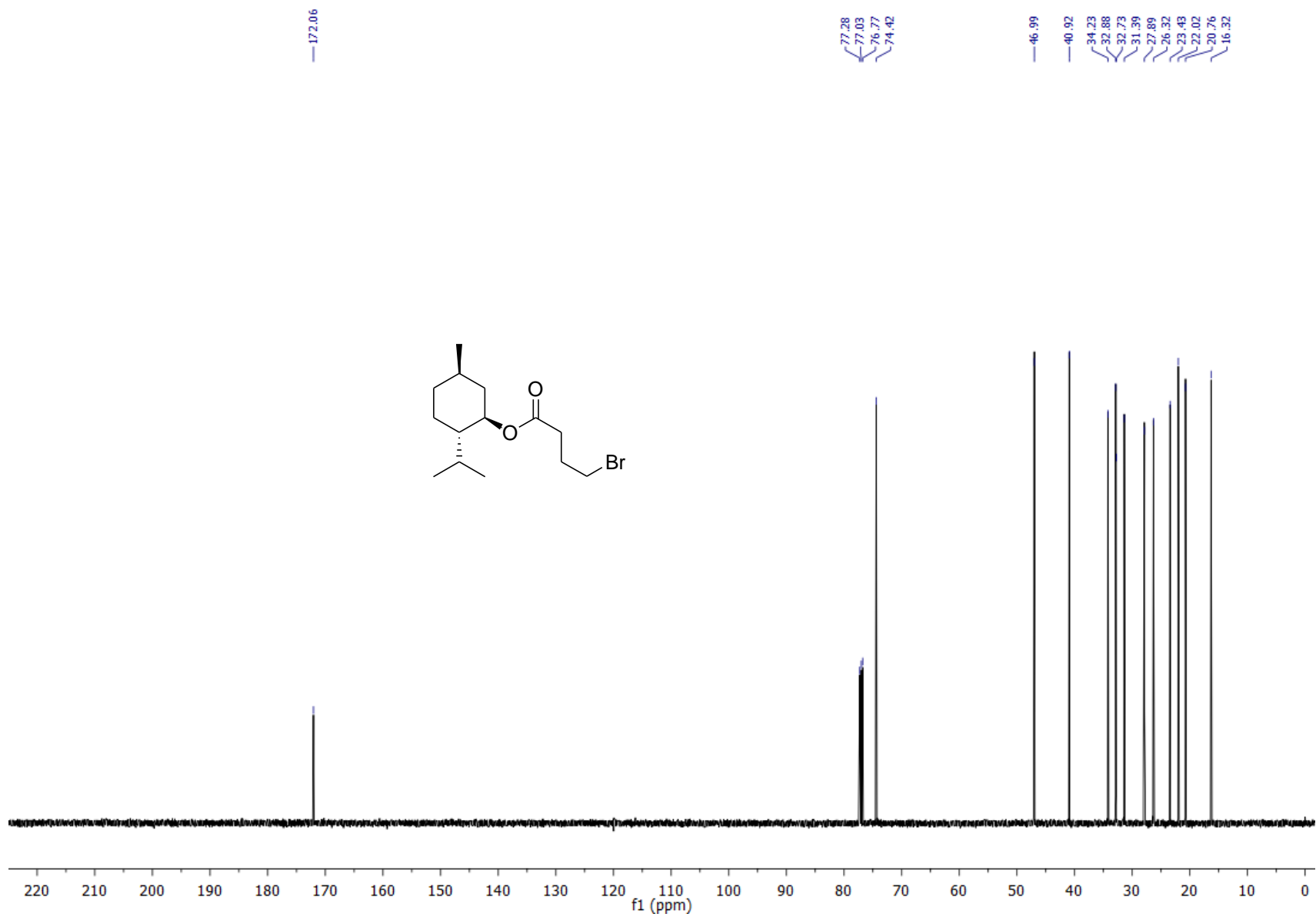
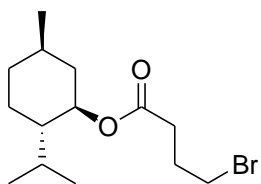


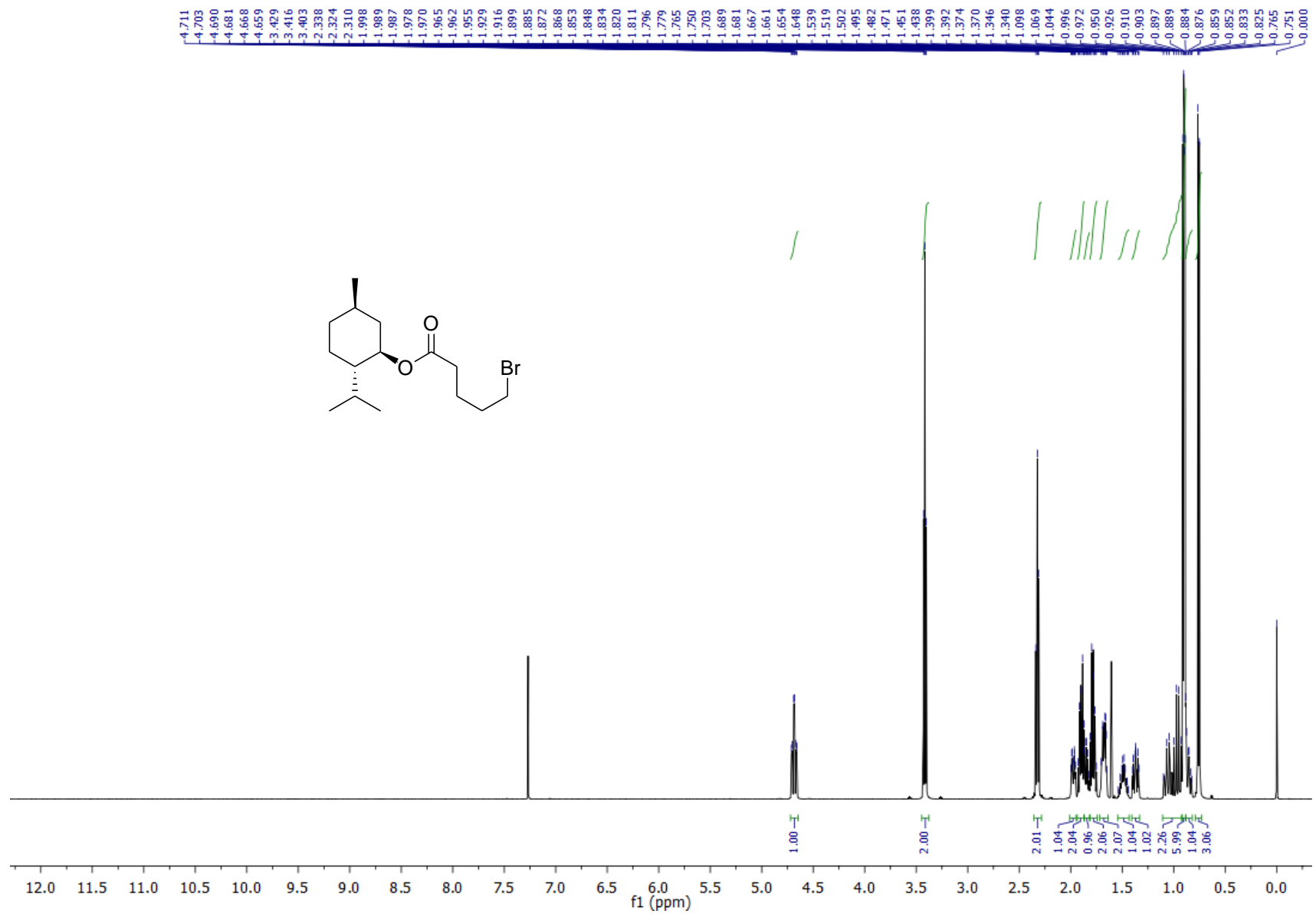


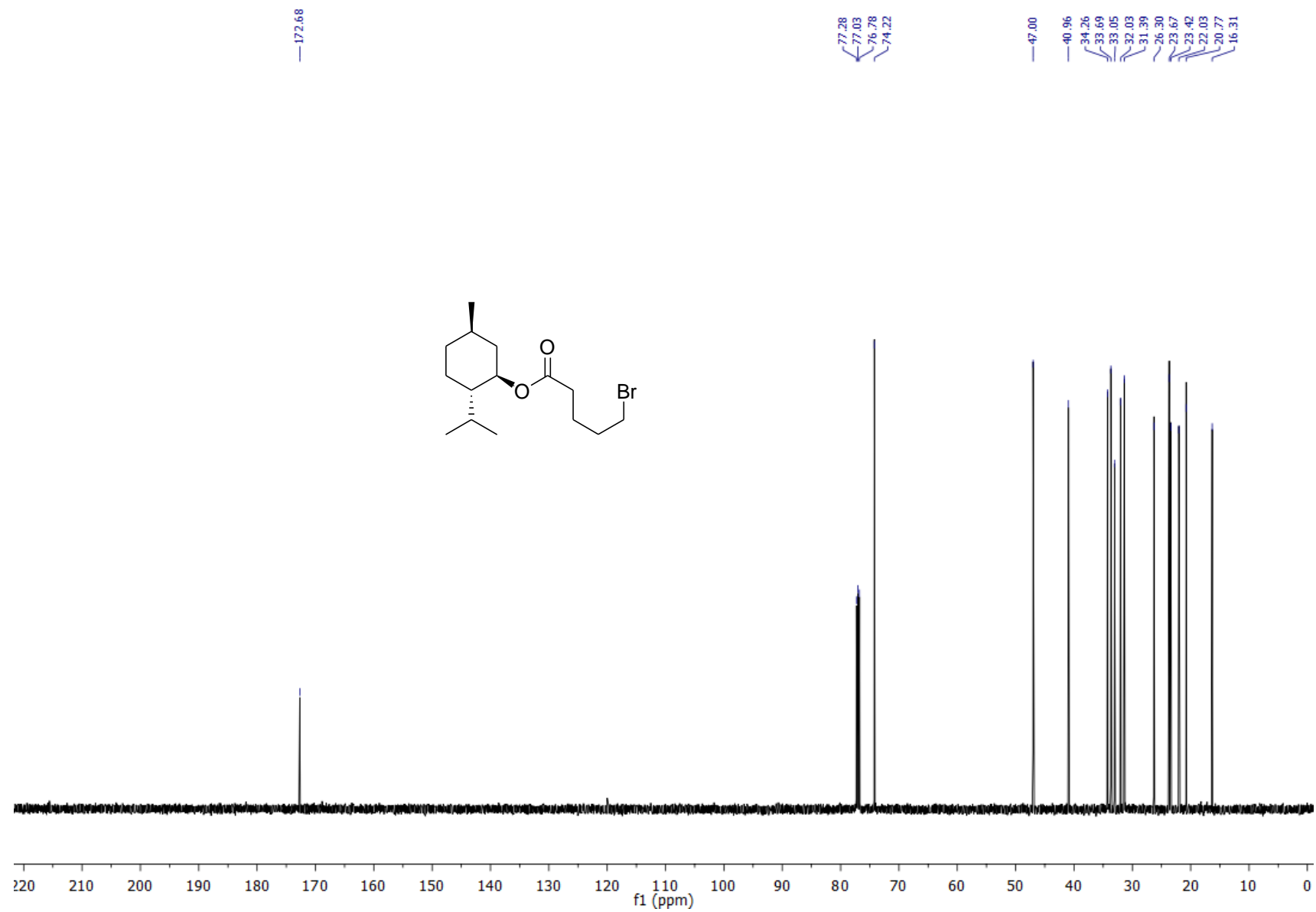


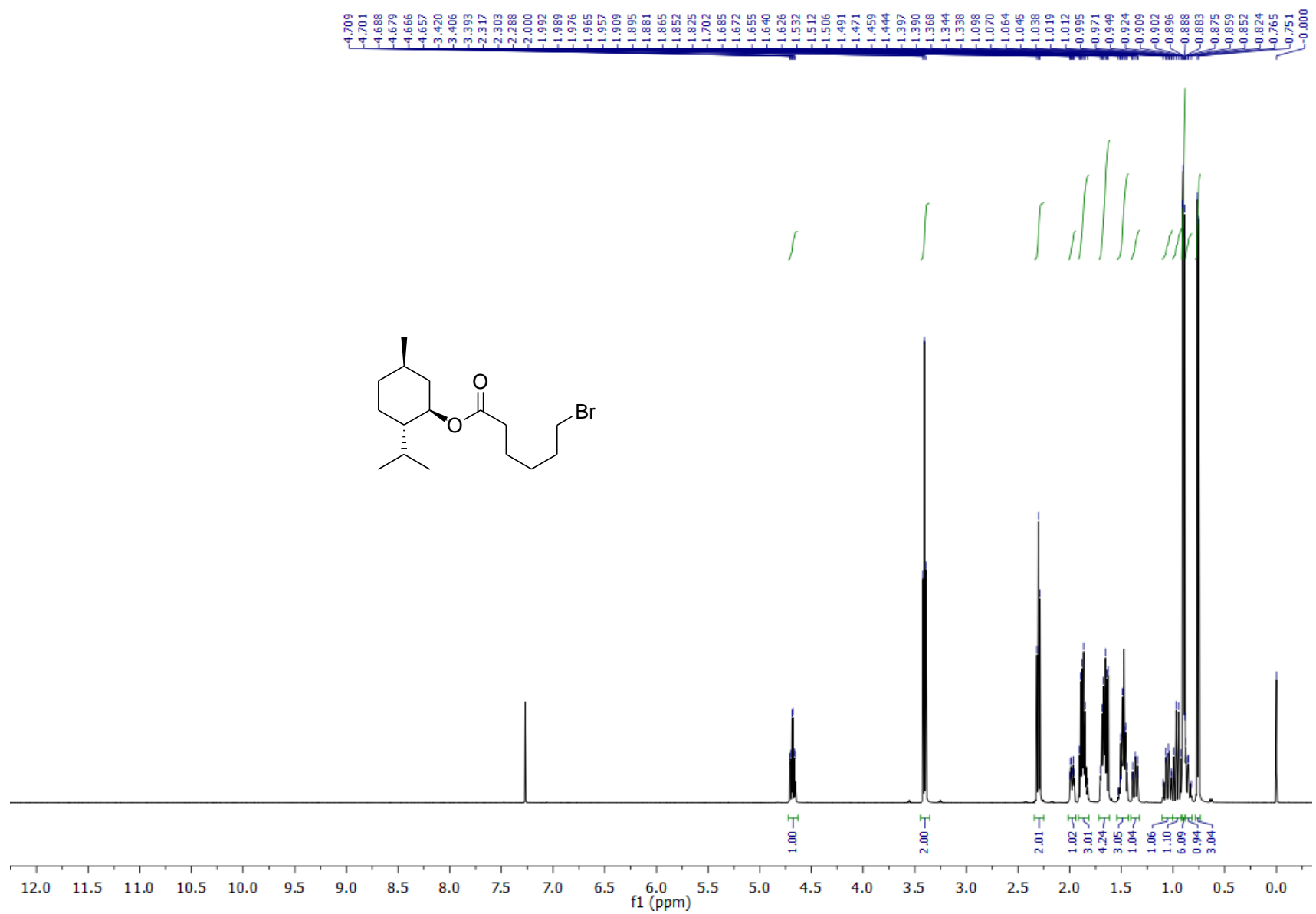


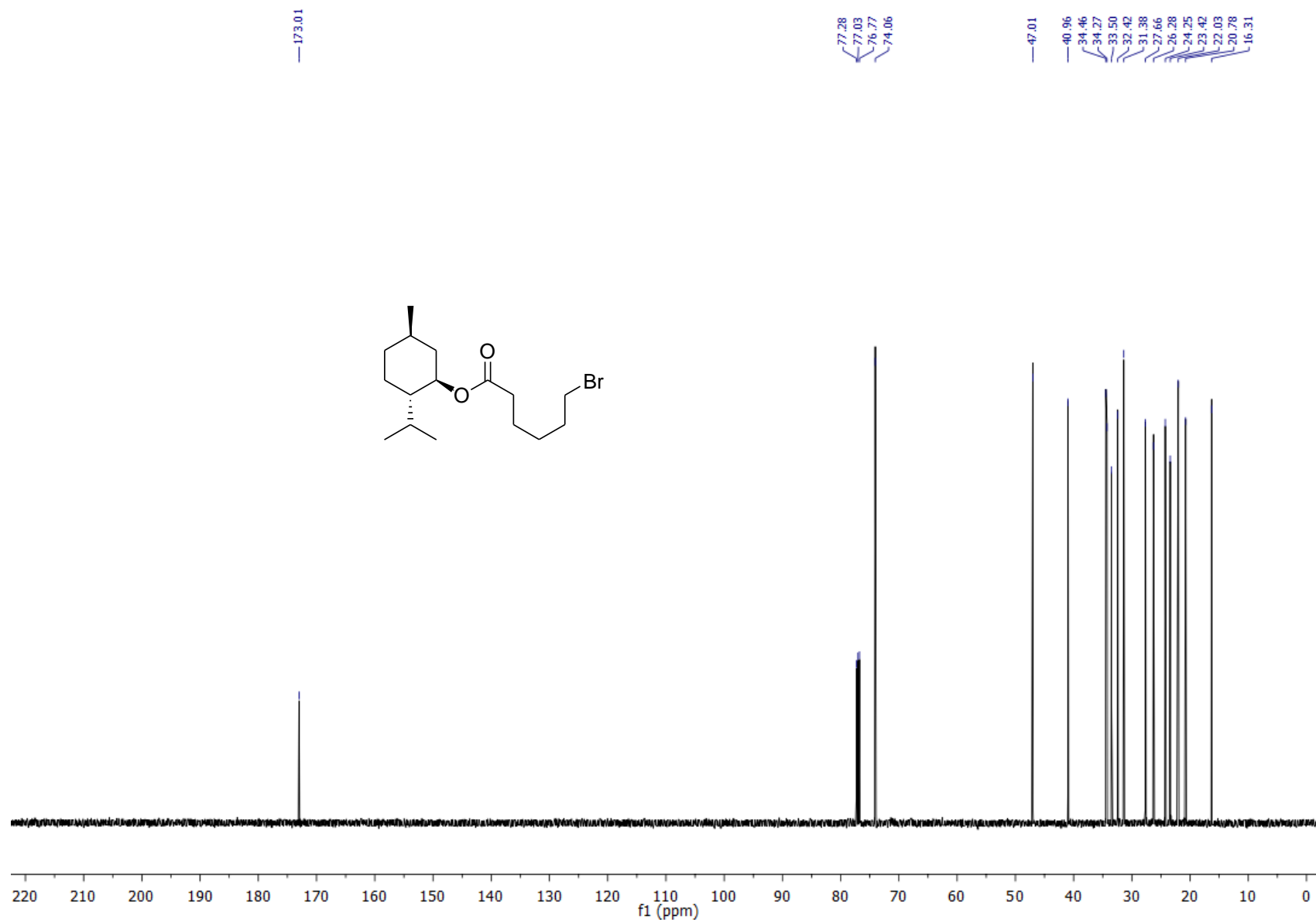
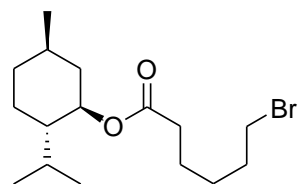


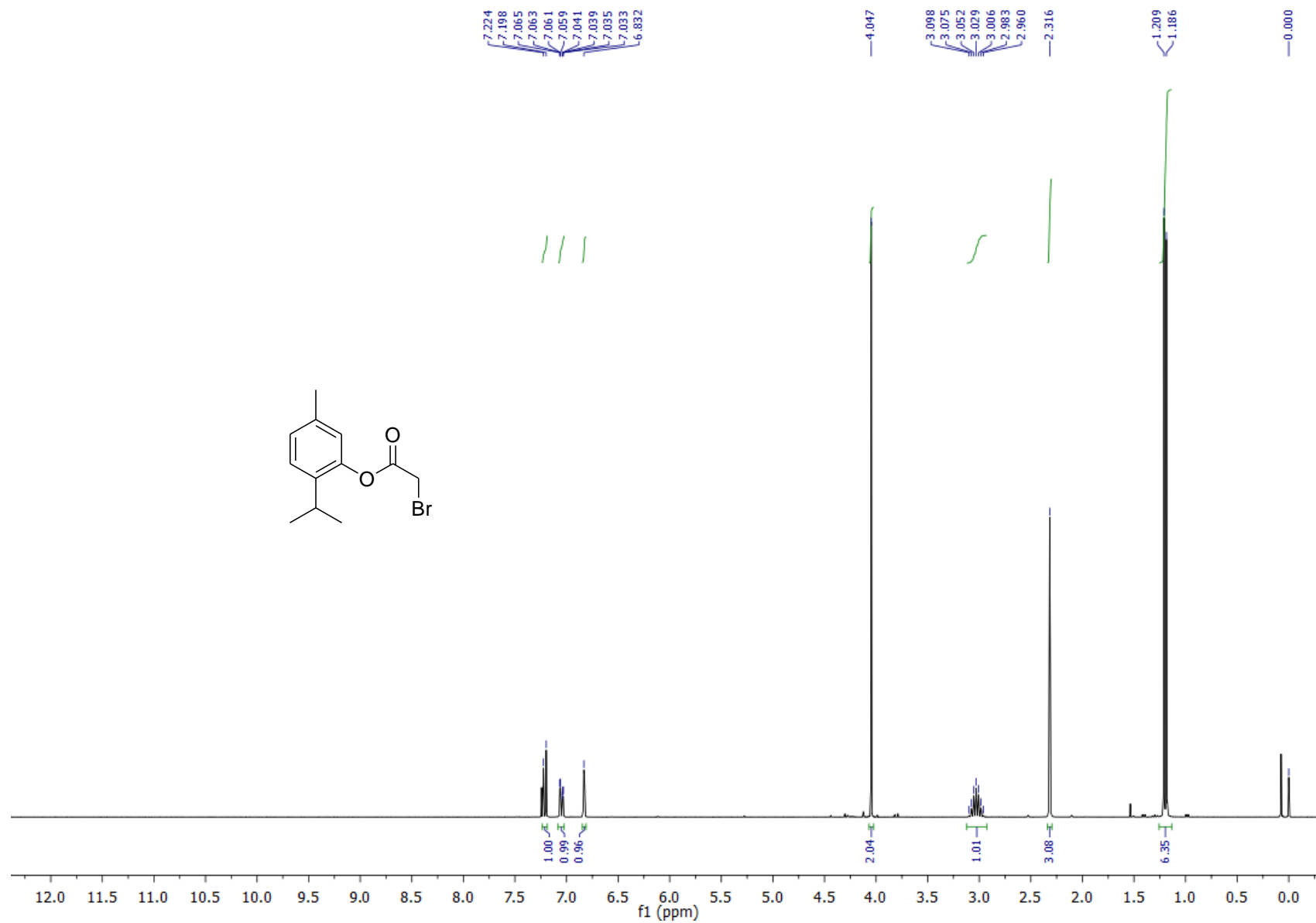
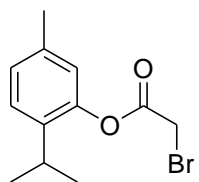


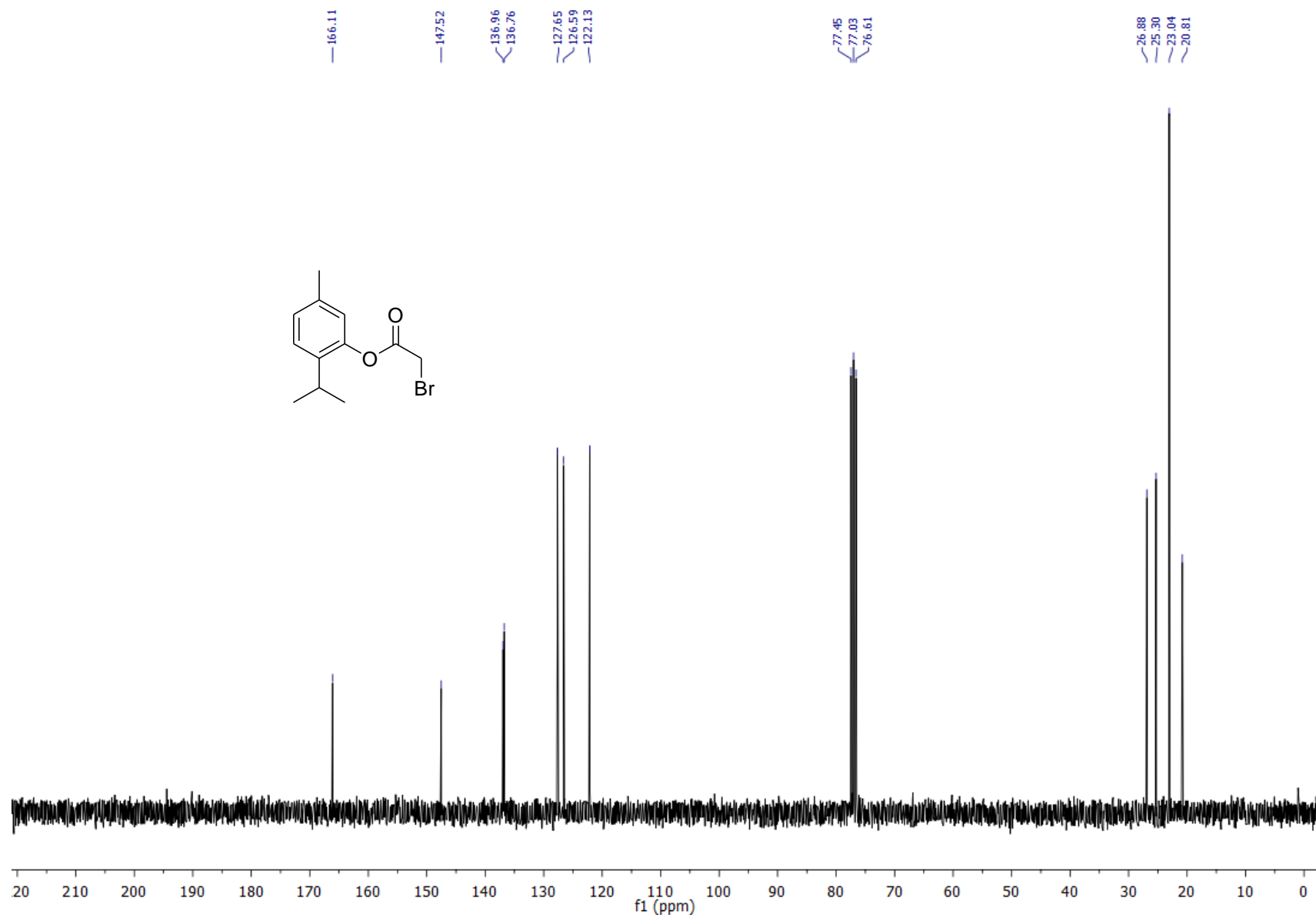
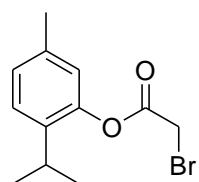


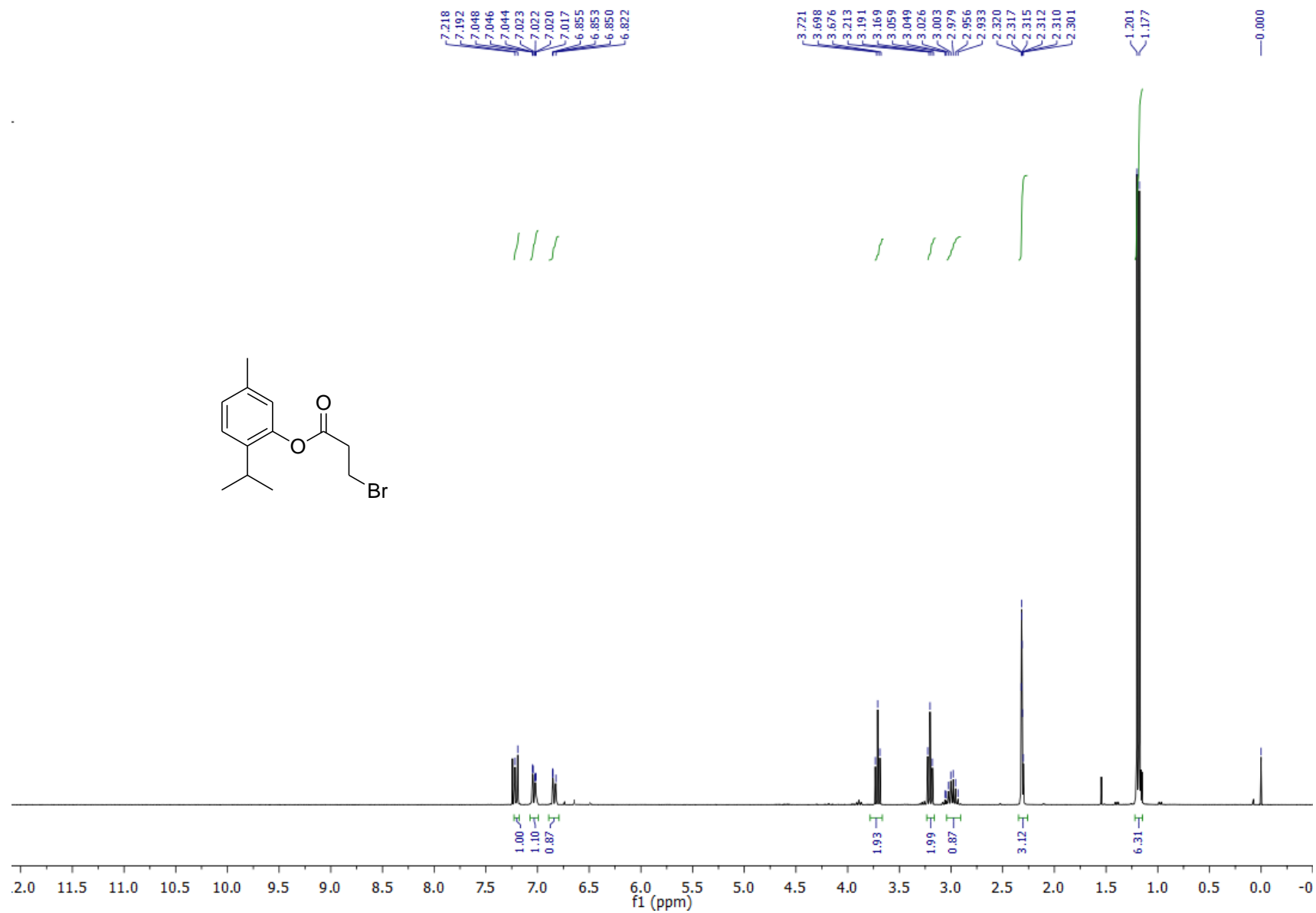
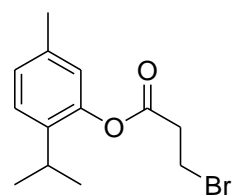


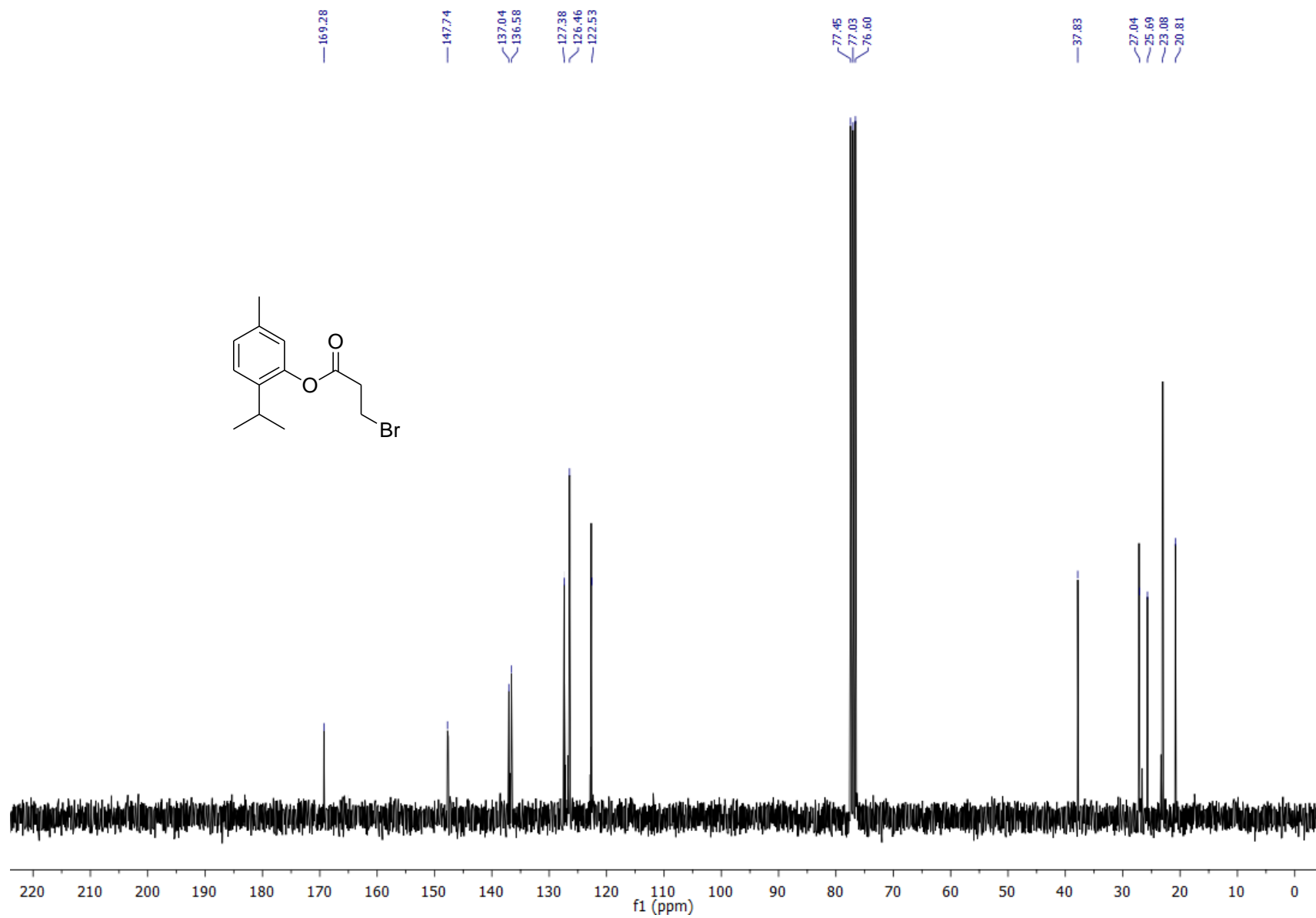
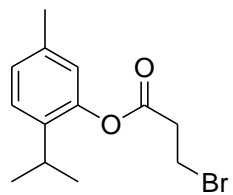


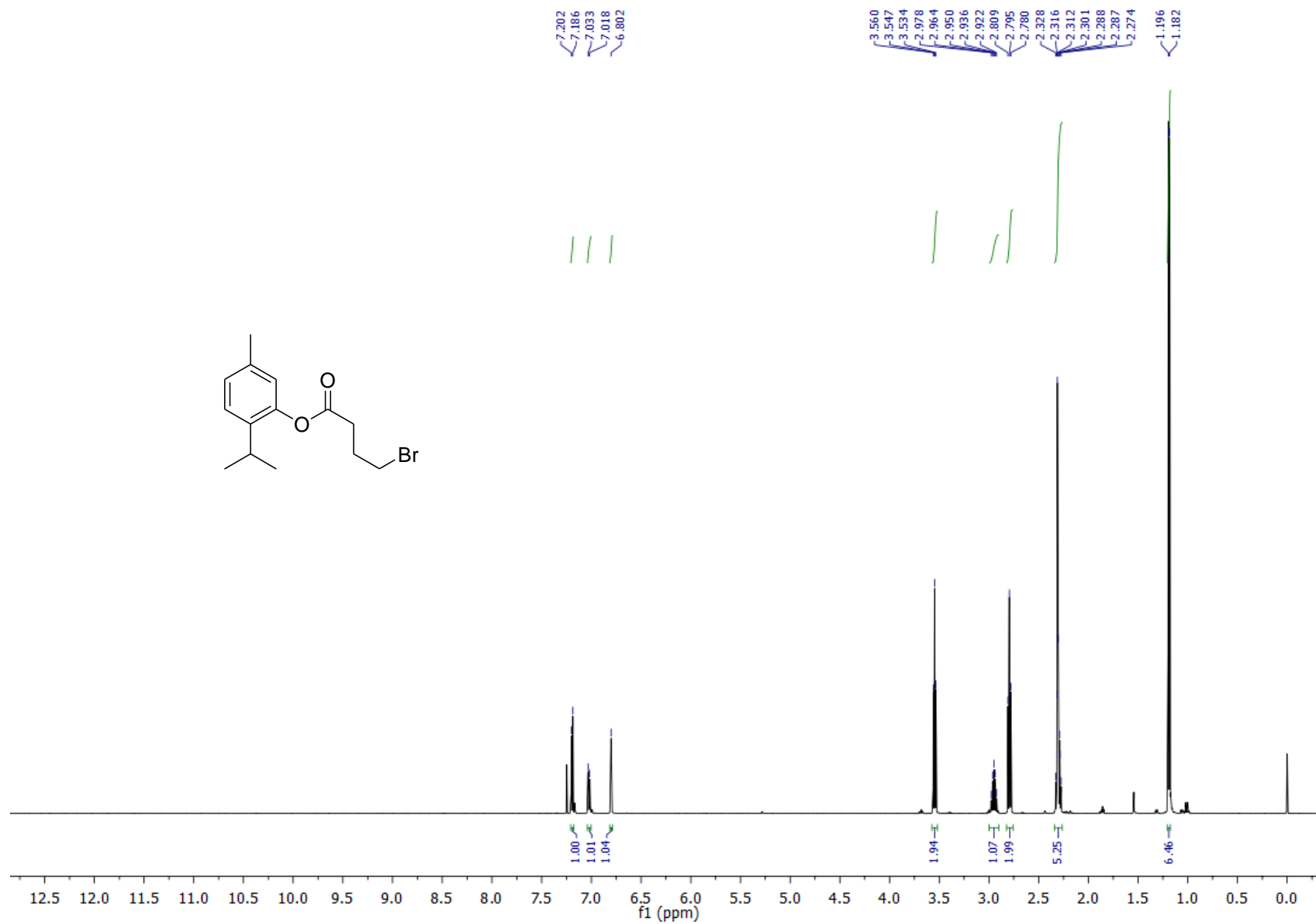
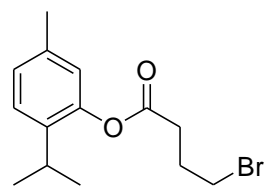


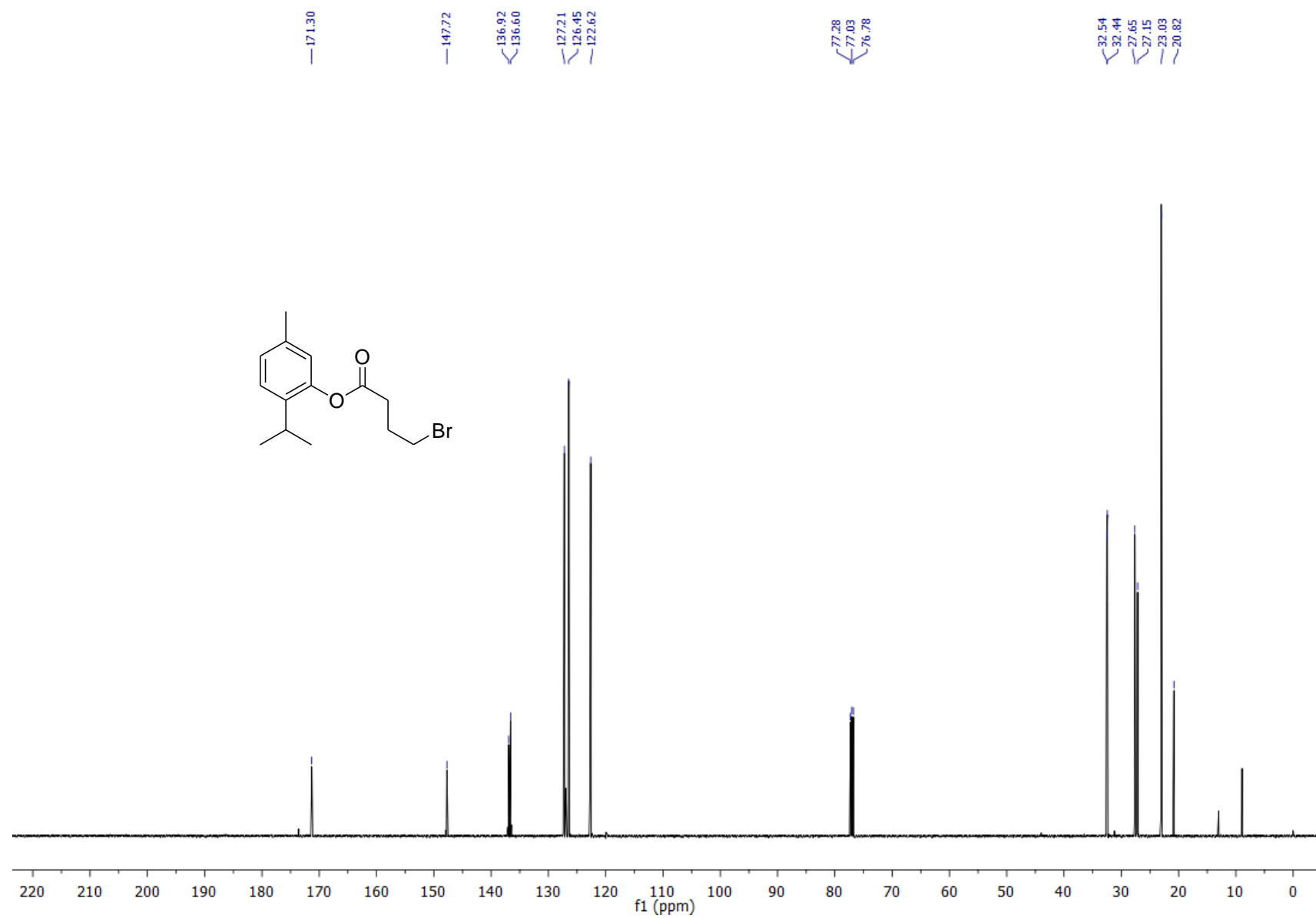


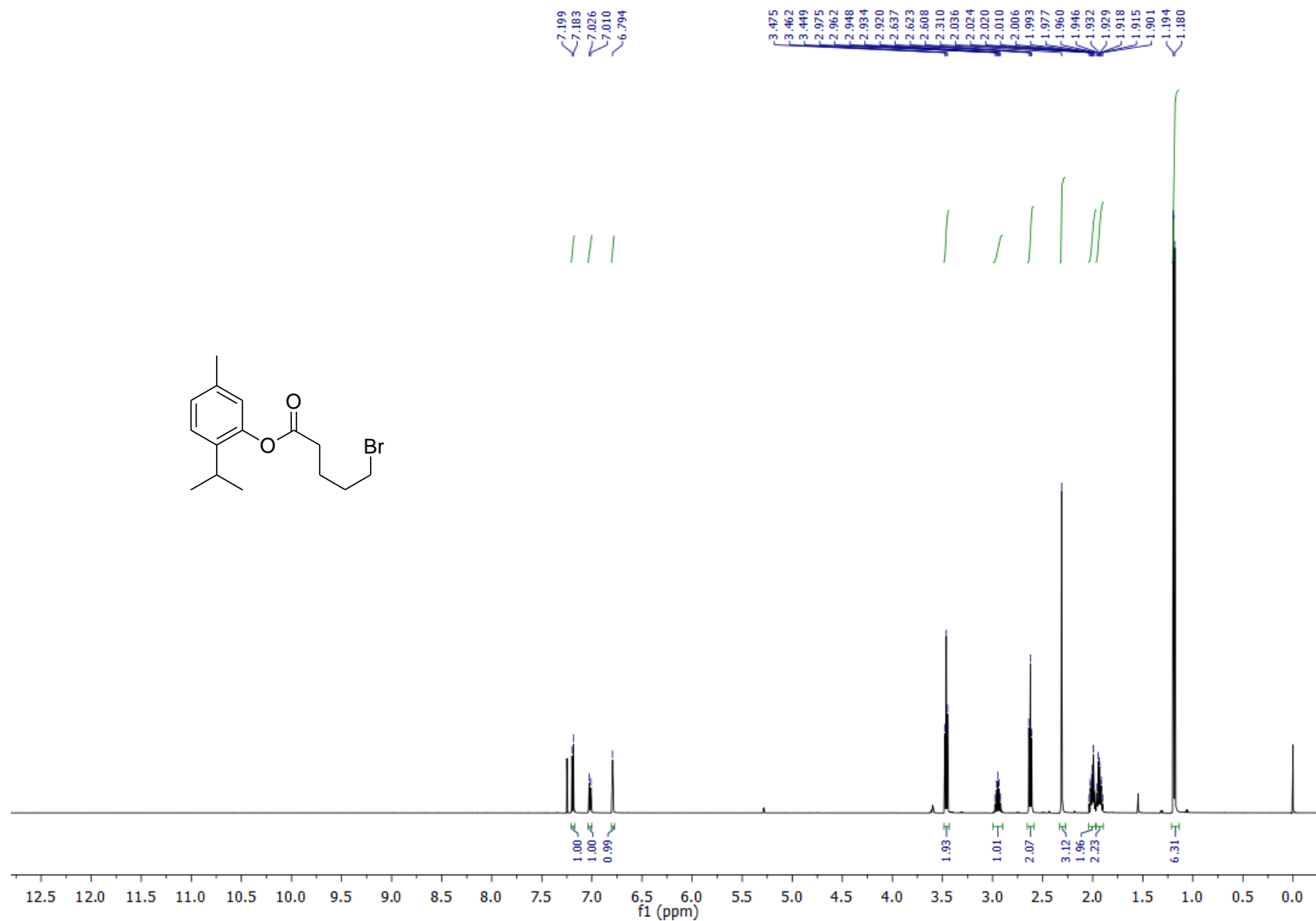
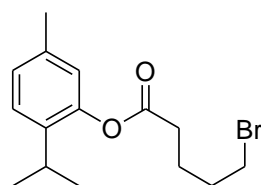


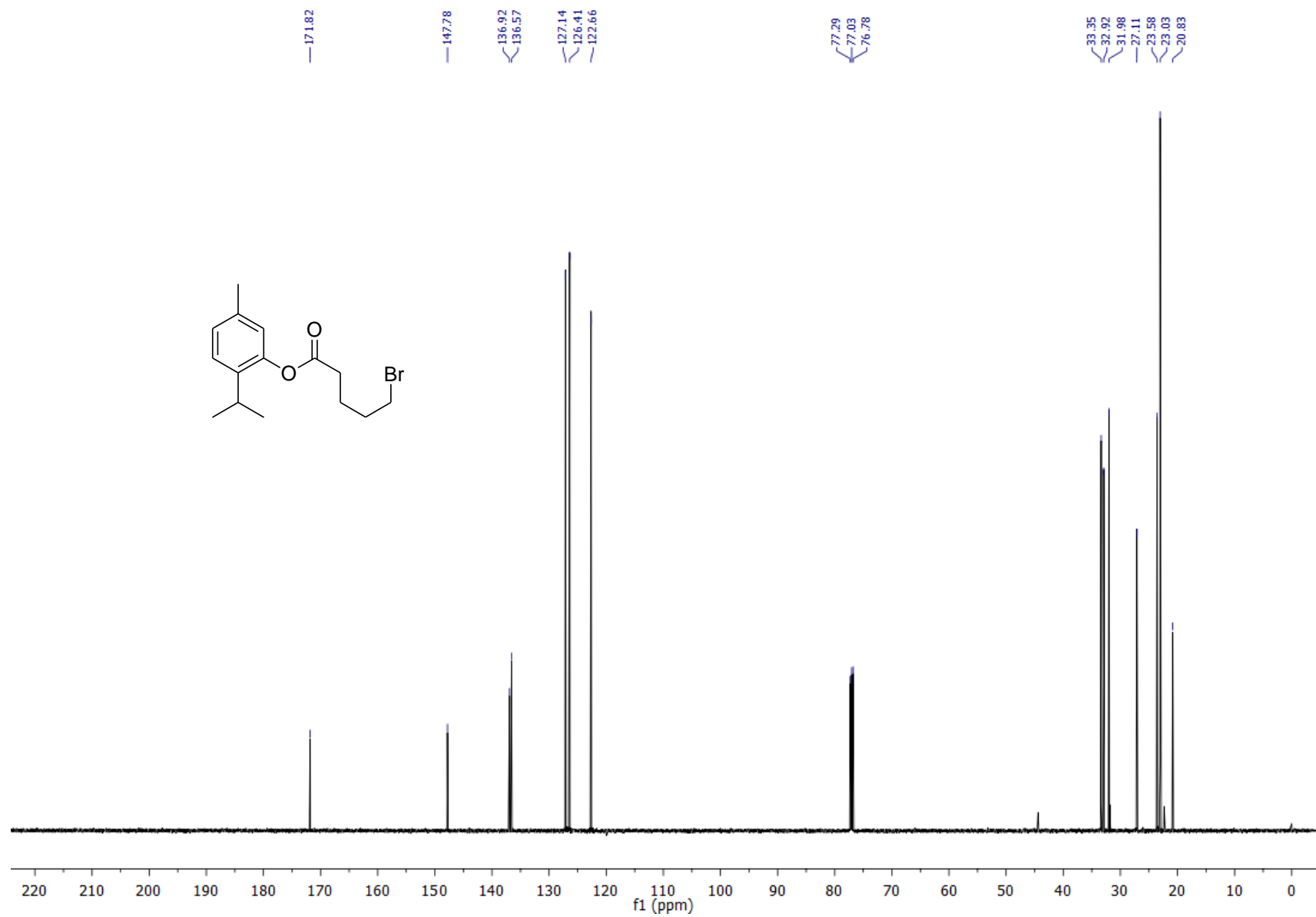


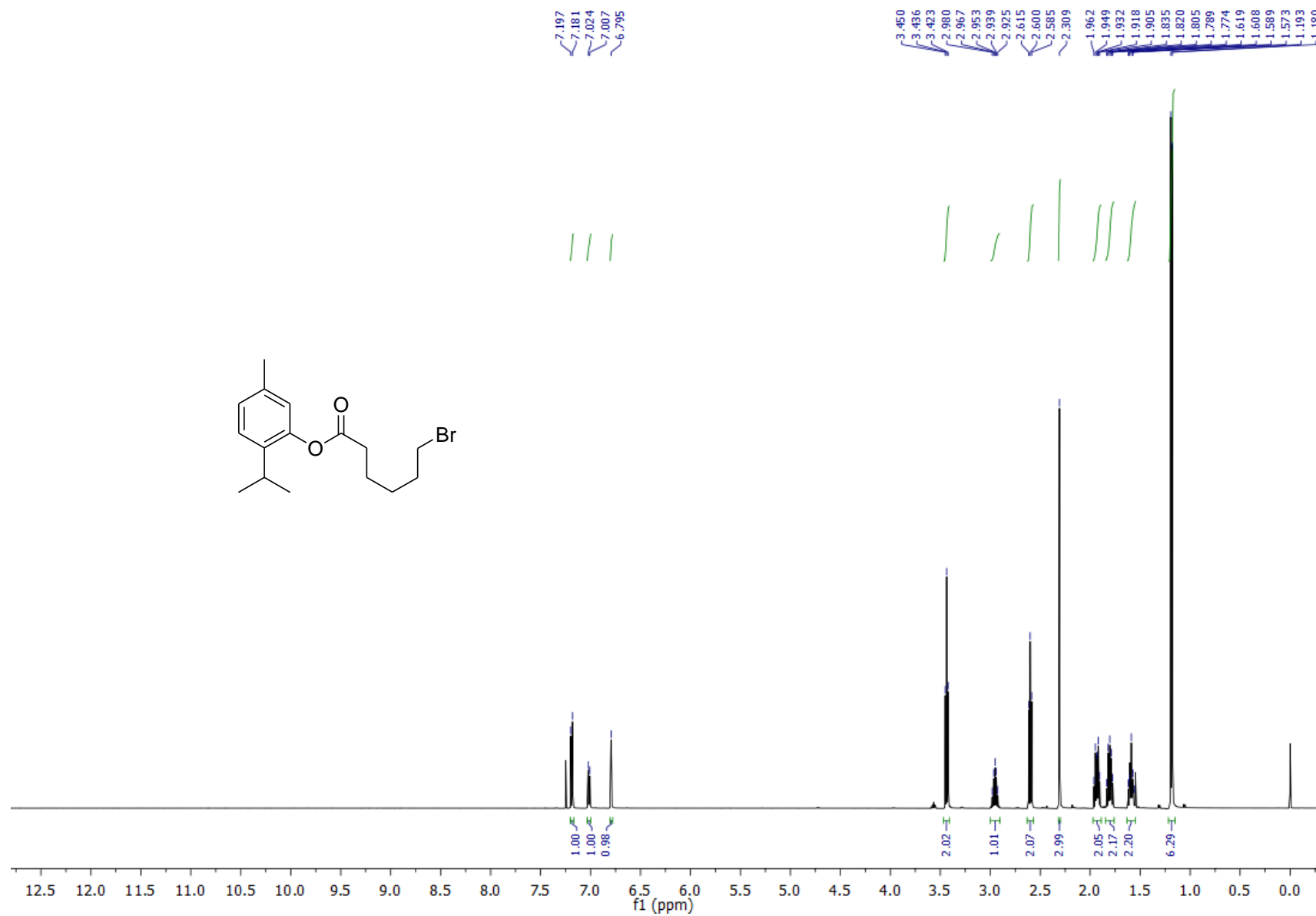
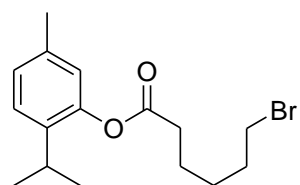


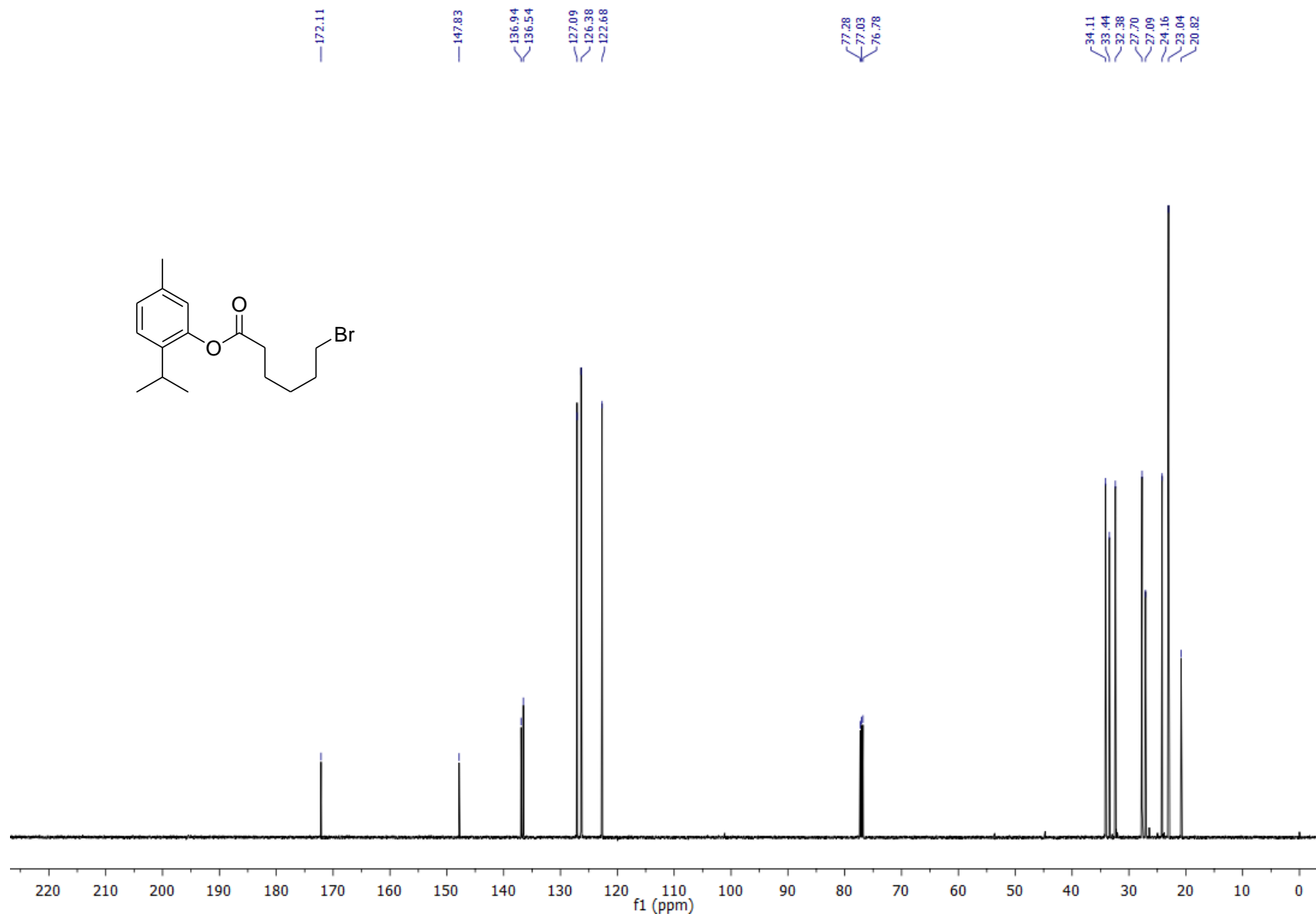












4. The NMR spectra of ciprofloxacin conjugates in order: **1, 9; 2-6; 10-14; 7-8; 15-16.**

