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**Supporting informations**
**for**

# Synthesis and medicinal chemical characterisation of antiproliferative *O,N*-functionalised isopulegol derivatives

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# Contents

## 1. General methods

Commercially available solvents were used as obtained from suppliers (Molar Chemicals Ltd, Halásztelek, Hungary; Merck Ltd., Budapest, Hungary and VWR International Ltd., Debrecen, Hungary), while applied solvents were dried according to standard procedures. Optical rotations were measured in MeOH at 20 °C with a Perkin-Elmer 341 polarimeter (PerkinElmer Inc., Shelton, CT, USA). Chromatographic separations and monitoring of reactions were carried out on Merck Kieselgel 60 (Merck Ltd., Budapest, Hungary). Elemental analyses for all prepared compounds were performed on a Perkin-Elmer 2400 Elemental Analyzer (PerkinElmer Inc., Waltham, MA, USA). GC measurements for direct separation of commercially available enantiomers of isopulegol to determine the enantiomeric purity of starting material **1** and separation of *O*-acetyl derivatives of enantiomers were performed on a Chirasil-DEX CB column (2500 × 0.25 mm I.D.) on a Perkin-Elmer Autosystem XL GC consisting of a Flame Ionization Detector (Perkin-Elmer Corporation, Norwalk, CT, USA) and a Turbochrom Workstation data system (Perkin-Elmer Corp., Norwalk, CT, USA). Melting points were determined on a Kofler apparatus (Nagema, Dresden, Germany) and are uncorrected. $^{1}$H- and $^{13}$C JMOD NMR were recorded on Brucker Avance DRX 500 spectrometer [500 MHz ($^{1}$H) and 125 MHz ($^{13}$C), δ = 0 (TMS)]. Chemical shifts are expressed in ppm (δ) relative to TMS as the internal reference. *J* values are given by Hz.

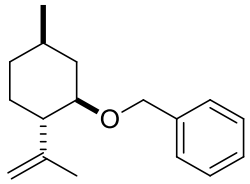
(–)-Isopulegol **1** is available commercially from Merck Co with *ee* = 95%. Diol **27** were prepared according to literature procedures, and all spectroscopic data were similar to those described therein.[1]

## 2. Experimental section and compound characterisations

### 2.1. General procedure for benzylation

A suspension of NaH (60% purity, 6.6 mmol) in dry THF (10 mL) was added to a solution of alcohol (6.6 mmol) in dry THF (20 mL). The reaction mixture was stirred at 25 °C for 30 min before substituted benzyl bromide and KI (6.6 mmol) were added to the mixture. Stirring was continued for 12−72 h at 60 °C. When the reaction was complete, the mixture was poured into a saturated $NH_4Cl$ solution (30 mL) and extracted with EtOAc (3 × 50 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated in vacuo, and the crude product was purified by column chromatography (silica gel, *n*-hexane:EtOAc = 19:1 to 9:1 as eluent) to provide **2a–c** or **30a–c**.

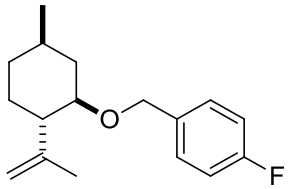
**((((1*R*,2*S*,5*R*)-5-Methyl-2-(prop-1-en-2-yl)cyclohexyl)oxy)methyl)benzene (2a)**




**2a**

Prepared with **1** and benzyl bromide (9.9 mmol) at reflux temperature for 12 h. Yield: 70%, colourless oil. All physical properties and spectroscopic data of compound **2a** were consistent with the literature data.[2]

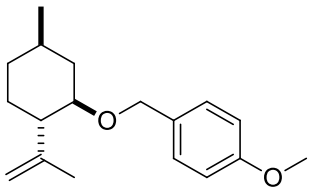
**1-Fluoro-4-((((1*R*,2*S*,5*R*)-5-methyl-2-(prop-1-en-2-yl)cyclohexyl)oxy)methyl)benzene (2b)**




**2b**

Prepared with **1** and *p*-fluorobenzyl bromide (9.9 mmol) at reflux temperature for 12 h. Yield: 88%, colourless oil. $[\alpha]_D^{20}$ = -50.54 (c 0.26, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.97-1.00 (2H, m), 0.95 (3H, d, *J* = 6.6 Hz), 1.25-1.46 (2H, m), 1.64 (2H, d, *J* = 11.8 Hz), 1.68 (3H, s), 2.07 (1H, td, *J* = 9.7, 3.1 Hz), 2.14 (1H, d, *J* = 12.2 Hz), 3.29 (1H, td, *J* = 10.5, 4.1 Hz), 4.38 (1H, d, *J* = 11.5 Hz), 4.57 (1H, d, *J* = 11.5 Hz), 4.79 (2H, s), 6.98 (2H, t, *J* = 8.6 Hz), 7.27 (2H, td, *J* = 7.9, 1.9 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 20.2, 22.4, 31.2, 31.7, 34.6, 40.4, 51.9, 69.8, 79.4, 111.2, 115.1 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 129.4 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 135.0 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 148.0, 163.3 (d, $^1J_{C\text{-}F}$ = 243.4 Hz). HR-MS (ESI): *m/z* calcd for $C_{17}H_{24}FO$ $[M+H]^+$: 263.18112; found: 263.17968.

**1-Methoxy-4-((((1*R*,2*S*,5*R*)-5-methyl-2-(prop-1-en-2-yl)cyclohexyl)oxy)methyl)benzene (2c)**

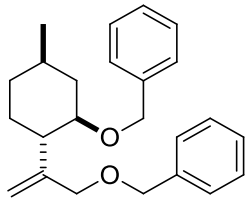



**2c**

Prepared with **1** and *p*-methoxybenzyl bromide (9.9 mmol) at reflux temperature for 12 h. Yield: 78%, colourless oil. $[\alpha]_D^{20}$ = +55.04 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-0.99 (2H, m), 0.94 (3H, d, *J* =

6.6 Hz), 1.26-1.45 (2H, m), 1.61-1.66 (2H, m), 1.68 (3H, s), 2.06 (1H, td, *J* = 9.4, 3.4 Hz), 2.14 (1H, d, *J* = 12.3 Hz), 3.27 (1H, td, *J* = 10.5, 4.1 Hz), 3.79 (3H, s), 4.37 (1H, d, *J* = 11.2 Hz), 4.53 (1H, d, *J* = 11.3 Hz), 4.79 (2H, s), 6.84 (2H, d, *J* = 8.5 Hz), 7.24 (2H, d, *J* = 7.1 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 20.2, 22.5, 31.3, 31.7, 34.6, 40.4, 51.9, 55.4, 70.1, 78.9, 111.1, 113.8, 129.3, 131.4, 148.1, 159.1. HR-MS (ESI): *m/z* calcd for $C_{18}H_{27}O_2$ $[M+H]^+$: 275.20111; found: 275.19957.

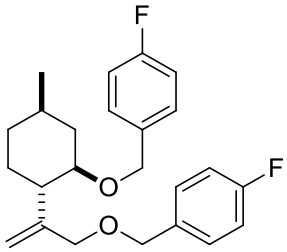
**(((2-((1*S*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)allyl)oxy)methyl)benzene (30a)**



**30a**

Prepared with **29** and benzyl bromide (19.8 mmol) at reflux temperature for 48 h and eluted by *n*-hexane:EtOAc = 19:1. Yield: 60%, colourless oil. All physical properties and spectroscopic data of compound **30a** were consistent with the literature data.[3]

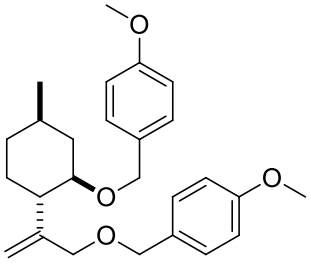
**1-Fluoro-4-(((2-((1S,2R,4R)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)allyl)oxy)methyl)benzene (30b)**



**30b**

Prepared with **29** and *p*-fluorobenzyl bromide (19.8 mmol) at reflux temperature for 24 h. Yield: 88%, colourless oil. $[\alpha]_D^{20}$ = -128.10 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-0.98 (2H, m), 0.95 (3H, d, *J* = 6.6 Hz), 1.32-1.47 (2H, m), 1.64-1.67 (1H, m), 1.72-1.78 (1H, m), 2.00-2.05 (1H, m), 2.13-2.17 (1H, m), 3.32 (1H, td, *J* = 10.5, 4.1 Hz), 3.95 (1H, d, *J* = 13.0 Hz), 4.03 (1H, d, *J* = 13.0 Hz), 4.32 (1H, d, *J* = 11.4 Hz), 4.42 (2H, q, *J* = 11.8 Hz), 4.55 (1H, d, *J* = 11.4 Hz), 5.00 (1H, s), 5.15 (1H, d, *J* = 1.2 Hz), 6.94-7.01 (4H, m), 7.20-7.28 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.4, 31.6, 31.9, 34.7, 40.7, 47.6, 70.1, 71.4, 73.5, 81.3, 111.1, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 115.2 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 129.4 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.5 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 134.5 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 134.9 ($^4J_{C\text{-}F}$ = 3.3 Hz, 149.0, 163.3 (d, $^1J_{C\text{-}F}$ = 243.7 Hz), 163.4 (d, $^1J_{C\text{-}F}$ = 243.4 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{29}F_2O_2$ $[M+H]^+$: 387.21356; found: 387.21288.

**1-Methoxy-4-(((2-((1*S*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)allyl)oxy)methyl)benzene (30c)**



**30c**

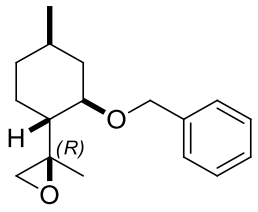
Prepared with **29** and *p*-methoxybenzyl bromide (19.8 mmol) at reflux temperature for 72 h. Yield: 67%, colourless oil. $[\alpha]_D^{20}$ = +14.25 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.97 (2H, m), 0.93 (3H, d, *J* =

6.5 Hz), 1.32-1.46 (2H, m), 1.63 (1H, d, *J* = 12.8 Hz), 1.71-1.76 (1H, m), 1.99-2.05 (1H, m), 2.11-2.17 (1H, m), 3.31 (1H, td, *J* = 10.5, 4.1 Hz), 3.76 (3H, s), 3.78 (3H, s), 3.94 (1H, d, *J* = 13.1 Hz), 4.03 (1H, d, *J* = 13.1 Hz), 4.30 (1H, d, *J* = 11.2 Hz), 4.40 (2H, q, *J* = 11.5 Hz), 4.50 (1H, d, *J* = 11.2 Hz), 4.98 (1H, s), 5.14 (1H, d, *J* = 1.3 Hz), 6.81 (2H, d, *J* = 8.6 Hz), 6.84 (2H, d, *J* = 8.6 Hz), 7.17 (2H, d, *J* = 8.5 Hz), 7.23 (1H, d, *J* = 8.6 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.4, 31.6, 32.0, 34.8, 40.8, 47.8, 55.4, 70.5, 71.8, 73.2, 80.9, 110.8, 113.8, 113.9, 129.3, 131.0, 131.4, 149.2, 159.2, 159.3. HR-MS (ESI): *m/z* calcd for $C_{26}H_{35}O_4$ $[M+Na]^+$: 433.23548; found: 433.23629.

### 2.2. General procedure of epoxidation

To the solution of allylic alcohol derivatives (11.9 mmol) in $CH_2Cl_2$ (50 mL), $Na_2HPO_4 \cdot 12H_2O$ (35.7 mmol) in water (130 mL) and *m*-chloroperbenzoic acid (70% purity, 23.8 mmol) was added at 0 °C then the mixture was stirred at room temperature. When the reaction was complete (2 h), the mixture was separated and the aqueous phase was extracted with $CH_2Cl_2$ (100 mL). The organic layer was washed with 5% KOH solution (3 × 50 mL), dried ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by column chromatography on silica gel with a mixture of *n*-hexane:EtOAc = 19:1 (compound **2a–b**, **30a–b**) or *n*-hexane:EtOAc = 9:1 (compound **2c**, **30c**) as eluent to afford epoxides.

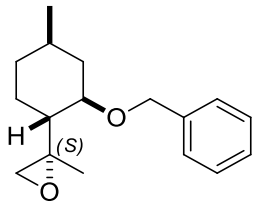
**(*R*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-2-methyloxirane (3a)**




**3a**

Prepared with **2a**. Yield: 43%, colourless oil. All physical properties and spectroscopic data of compound **3a** were consistent with the literature data.[3]

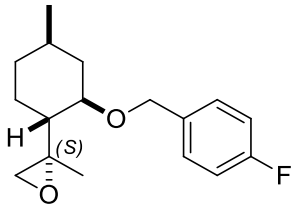
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-2-methyloxirane (3b)**




**3b**

Prepared with **2a**. Yield: 25%, colourless oil. All physical properties and spectroscopic data of compound **3b** were consistent with the literature data.[3]

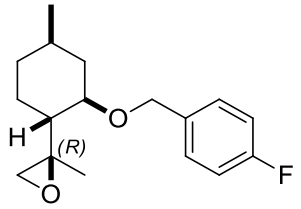
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-2-methyloxirane (4a)**




**4a**

Prepared with **2b**. Yield: 44%, colourless oil. $[\alpha]_D^{20}$ = -10.26 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.99 (2H, m), 0.95 (3H, d, *J* = 6.4 Hz), 1.16-1.30 (2H, m), 1.25 (3H, s), 1.66-1.76 (2H, m), 2.19 (1H, d, *J* = 12.2 Hz), 2.50 (2H, s), 3.31 (1H, td, *J* = 10.4, 4.0 Hz), 4.41 (1H, d, *J* = 11.4 Hz), 4.68 (1H, d, *J* = 11.4 Hz), 7.01 (2H, t, *J* = 8.5 Hz), 7.38 (1H, dd, *J* = 7.6, 6.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 18.7, 22.3, 28.0, 31.4, 34.2, 39.7, 49.4, 52.1, 58.4, 69.1, 78.5, 115.1 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 129.4 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 134.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 163.3 (d, d, $^1J_{C\text{-}F}$ = 243.3 Hz. HR-MS (ESI): *m/z* calcd for $C_{17}H_{23}FNaO_2$: 301.15798; found: 301.15695.

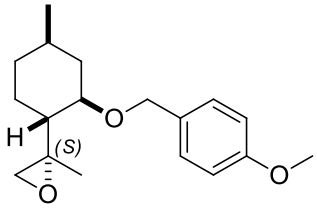
**(*R*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-2-methyloxirane (4b)**




**4b**

Prepared with **2b**. Yield: 31%, colourless oil. $[\alpha]_D^{20}$ = -23.26 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-0.93 (2H, m), 0.95 (3H, d, *J* = 6.5 Hz), 1.08-1.13 (1H, m), 1.14 (3H, s), 1.24-1.30 (1H, m), 1.37-1.46 (1H, m), 1.69 (1H, d, *J* = 13.0 Hz), 1.87-1.90 (1H, m), 2.19 (1H, d, *J* = 12.2 Hz), 2.66 (1H, d, *J* = 5.0 Hz), 2.74 (1H, d, *J* = 5.0 Hz), 3.25 (1H, td, *J* = 10.6, 4.1 Hz), 4.36 (1H, d, *J* = 11.5 Hz), 4.63 (1H, d, *J* = 11.5 Hz), 7.02 (2H, t, *J* = 8.6 Hz), 7.27 (1H, dd, *J* = 7.7, 6.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 16.8, 22.3, 26.5, 31.5, 33.9, 40.0, 50.7, 56.7, 57.9, 69.6, 78.9, 115.2 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 129.2 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 134.8, 163.3 (d, $^1J_{C\text{-}F}$ = 245.7 Hz). HR-MS (ESI): *m/z* calcd for $C_{17}H_{24}FO_2$ $[M+H]^+$: 279.17603; found: 279.17510.

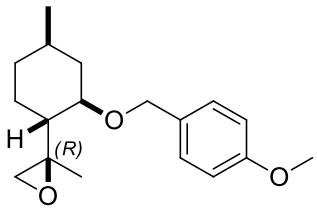
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Methoxybenzyl)oxy)-4-methylcyclohexyl)-2-methyloxirane (5a)**




**5a**

Prepared with **2c**. Yield: 42%, colourless oil. $[\alpha]_D^{20}$ = +83.24 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.97 (2H, m), 0.95 (3H, d, *J* = 6.6 Hz), 1.10-1.20 (1H, m), 1.24 (3H, s), 1.26-1.39 (2H, m), 1.66 (1H, d, *J* = 12.9 Hz), 1.71-1.75 (1H, m), 2.20 (1H, d, *J* = 12.2 Hz), 2.49 (2H, q, *J* = 4.9 Hz), 3.26 (1H, td, *J* = 10.5, 4.0 Hz), 3.79 (3H, s), 4.38 (1H, d, *J* = 11.2 Hz), 4.64 (1H, d, *J* = 11.2 Hz), 6.87 (2H, d, *J* = 8.3 Hz), 7.33 (1H, d, *J* = 8.3 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 18.9, 22.2, 27.8, 31.2, 34.1, 39.6, 49.0, 51.9, 55.3, 58.3, 69.3, 77.3, 77.9, 113.7, 129.2, 131.0, 159.0. HR-MS (ESI): *m/z* calcd for $C_{18}H_{26}NaO_3$ $[M+Na]^+$: 313.17796; found: 313.17697.

**(*R*)-2-((1*R*,2*R*,4*R*)-2-((4-Methoxybenzyl)oxy)-4-methylcyclohexyl)-2-methyloxirane (5b)**

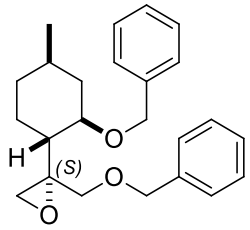



**5b**

Prepared with **2c**. Yield: 28%, colourless oil. $[\alpha]_D^{20}$ = +76.75 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-0.93 (2H, m), 0.94 (3H, d, *J* = 6.5 Hz), 1.06-1.11 (1H, m), 1.12 (3H, s), 1.23-1.41 (2H, m), 1.68 (1H, d, *J* = 12.9 Hz), 1.85-1.89 (1H, m), 2.20 (1H, d, *J* = 12.1 Hz), 2.66 (1H, d, *J* = 4.9 Hz), 2.75 (1H, d, *J* = 4.9 Hz), 3.23 (1H,

td, *J* = 10.6, 4.1 Hz), 3.80 (3H, s), 4.34 (1H, d, *J* = 11.3 Hz), 4.59 (1H, d, *J* = 11.3 Hz), 6.87 (2H, d, *J* = 8.3 Hz), 7.23 (2H, t, *J* = 8.2 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 16.7, 22.3, 26.5, 31.5, 34.0, 40.0, 50.8, 55.4, 56.9, 58.0, 69.9, 78.4, 113.9, 129.2, 131.2, 159.2. HR-MS (ESI): *m/z* calcd for $C_{18}H_{26}NaO_3$ [M+Na]$^+$: 313.17796; found: 313.17686.

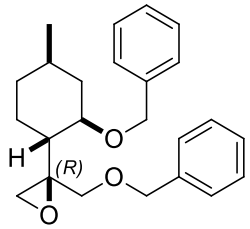
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-2-((benzyloxy)methyl)oxirane (31a)**




**31a**

Prepared with **30a**. Yield: 38%, colourless oil. All physical properties and spectroscopic data of compound **31a** were consistent with the literature data.[3]

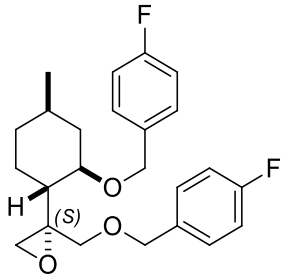
**(*R*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-2-((benzyloxy)methyl)oxirane (31b)**




**31b**

Prepared with **30b**. Yield: 28%, colourless oil. All physical properties and spectroscopic data of compound **31b** were consistent with the literature data.[3]

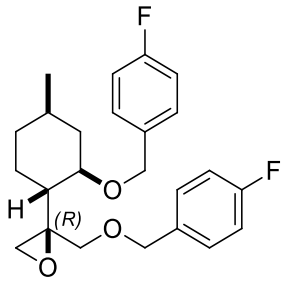
**(*S*)-2-((1*R*,2*R*,4R)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-2-(((4-fluorobenzyl)oxy)methyl)oxirane (32a)**




**32a**

Prepared with **30b**. Yield: 32%, colourless oil. $[\alpha]_D^{20}$ = -149.40 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.89-0.89 (2H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.25-1.42 (3H, m), 1.67 (1H, d, *J* = 12.9 Hz), 1.91 (1H, d, *J* = 12.3 Hz), 2.17 (1H, d, *J* = 12.2 Hz), 2.74 (1H, d, *J* = 5.1 Hz), 2.88 (1H, d, *J* = 5.1 Hz), 3.39 (1H, td, *J* = 10.4, 4.0 Hz), 3.55 (3H, t, *J* = 12.3 Hz), 4.30 (1H, d, *J* = 11.3 Hz), 4.43 (2H, s), 4.57 (1H, d, *J* = 11.3 Hz), 6.99 (4H, t, *J* = 8.5 Hz), 7.20-7.27 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 27.1, 31.4, 34.2, 40.4, 48.6, 52.7, 59.3, 69.7, 70.6, 72.8, 78.6, 115.2 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 115.3 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 129.3 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.5 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 134.0 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 134.8 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 163.3 (d, $^1J_{C\text{-}F}$ = 243.7 Hz), 163.4 (d, $^1J_{C\text{-}F}$ = 244.0 Hz. HR-MS (ESI): *m/z* calcd for $C_{18}H_{26}NaO_3$ [M+Na]$^+$: 403.20848; found: 403.20833.

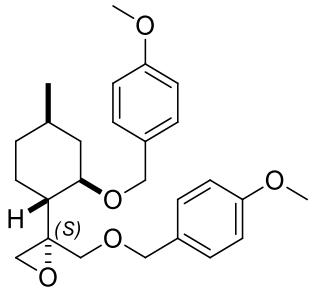
**(*R*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-2-(((4-fluorobenzyl)oxy)methyl)oxirane (32b)**




**32b**

Prepared with **30b**. Yield: 32%, colourless oil. $[\alpha]_D^{20}$ = -113.33 (c 0.30, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-0.97 (2H, m), 0.94 (3H, d, *J* = 6.5 Hz), 1.11-1.20 (1H, m), 1.33-1.38 (1H, m), 1.55 (2H, s), 1.63-1.69 (2H, m), 1.75-1.80 (1H, m), 2.18 (1H, d, *J* = 12.5 Hz), 2.57 (1H, d, *J* = 4.8 Hz), 2.75 (1H, d, *J* = 4.8 Hz), 3.22 (1H, td, *J* = 10.6, 4.0 Hz), 3.60 (2H, dd, *J* = 15.6, 11.1 Hz), 4.29 (1H, d, *J* = 11.5 Hz), 4.40 (1H, d, *J* = 11.8 Hz), 4.47 (1H, d, *J* = 11.8 Hz), 4.62 (1H, d, *J* = 11.5 Hz), 6.97-7.01 (4H, m), 7.23-7.29 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.9, 31.3, 34.2, 39.9, 44.9, 48.4, 59.9, 69.1, 71.9, 72.7, 79.0, 115.2 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 129.4 (d, $^3J_{C\text{-}F}$ = 7.5 Hz), 129.5 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 134.1 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 134.7 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 163.3 (d, $^1J_{C\text{-}F}$ = 243.7 Hz), 163.4 (d, $^1J_{C\text{-}F}$ = 243.9 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{28}F_2NaO_3$ $[M+Na]^+$: 425.19042; found: 425.18963.

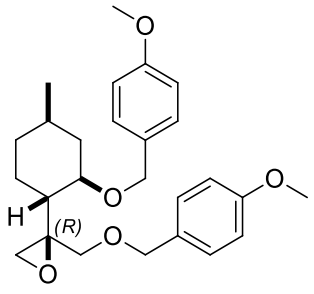
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Methoxybenzyl)oxy)-4-methylcyclohexyl)-2-(((4-methoxybenzyl)oxy)methyl)oxirane (33a)**




**33a**

Prepared with **30c**. Yield: 38%, colourless oil. $[\alpha]_D^{20}$ = +10.63 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.80-0.98 (3H, m), 0.92 (3H, d, *J* = 6.5 Hz), 1.25-1.31 (1H, m), 1.34-1.45 (2H, m), 1.65 (1H, d, *J* = 12.2 Hz), 1.88-1.93 (1H, m), 2.14-2.20 (1H, m), 2.73 (1H, d, *J* = 5.1 Hz), 2.89 (1H, d, *J* = 5.1 Hz), 3.38 (1H, td, *J* = 10.6, 4.2 Hz), 3.50 (1H, d, *J* = 11.2 Hz), 3.57 (1H, d, *J* = 11.2 Hz), 3.75-3.82 (1H, m), 3.79 (6H, s), 4.28 (1H, d, *J* = 11.0 Hz), 4.39 (1H, d, *J* = 11.7 . $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 27.1, 31.4, 34.3, 40.5, 49.0, 52.9, 55.4, 59.4, 70.1, 73.1, 78.3, 113.8, 113.9, 129.2, 129.4, 130.4, 131.3, 159.2, 159.3. HR-MS (ESI): *m/z* calcd for $C_{26}H_{35}O_5$ $[M+Na]^+$: 449.23039; found: 449.23067.

**(*R*)-2-((1*R*,2*R*,4*R*)-2-((4-Methoxybenzyl)oxy)-4-methylcyclohexyl)-2-(((4-methoxybenzyl)oxy)methyl)oxirane (33b)**



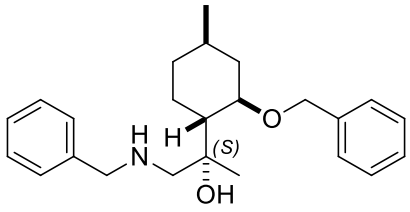
**33b**

Prepared with **30c**. Yield: 29%, colourless oil. $[\alpha]_D^{20}$ = +3.04 (c 0.25, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-0.95 (3H, m), 0.93 (3H, d, *J* = 6.5 . $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.8, 31.3, 34.3, 39.9, 44.6, 48.5, 55.4, 60.0, 69.4, 71.8, 73.0, 78.5, 113.8, 129.4, 130.5, 131.1, 159.2. HR-MS (ESI): *m/z* calcd for $C_{26}H_{35}O_5$ $[M+Na]^+$: 449.23039; found: 449.23118.

### 2.3. General procedure for ring-opening of epoxide with primary amines

A solution of epoxides (2.9 mmol) in MeCN (30 mL) was added to the appropriate amines (5.8 mmol) in MeCN (10 mL) and $LiClO_4$ (2.9 mmol). The mixture was kept at reflux temperature for 8–20 h. When the reaction completed (indicated by TLC), the mixture was evaporated to dryness, and the residue was again dissolved in water (15 mL) and extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic phase was dried ($Na_2SO_4$), filtered and concentrated. The crude product was purified by column chromatography on silica gel, using $CHCl_3$:MeOH = 19:1 as the eluent to furnish aminodiol and aminotriol derivatives, respectively.

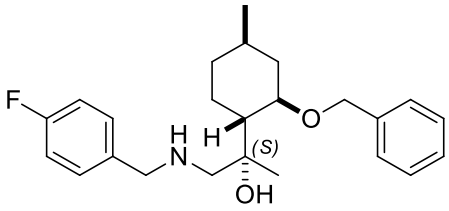
**(*S*)-1-(Benzylamino)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (6a)**



**6a**

Prepared with **3a** with benzylamine at reflux temperature for 20 h. Yield: 72%, white crystals. All physical properties and spectroscopic data of compound **6a** were consistent with literature data.[3]

**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((4-fluorobenzyl)amino)propan-2-ol (7a)**

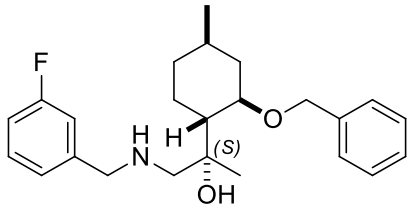


**7a**

Prepared with **3a** with *p*-fluorobenzylamine at reflux temperature for 20 h. Yield: 67%, colourless oil. $[\alpha]_D^{20}$ = -41.63 (c 0.19, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.81-0.87 (1H, m), 0.96 (3H, d, *J* = 6.5 Hz), 0.99-1.05 (1H, m), 1.06 (3H, s), 1.35-1.45 (1H, m), 1.60-1.80 (3H, m), 1.90-1.95 (1H, m), 2.26 (1H, d, *J* = 12.1 Hz), 2.44 (2H, dd, *J* = 17.2, 11.5 Hz), 3.61 (1H, td, *J* = 10.6, 3.7 Hz), 6.65 (1H, d, *J* = 13.4 Hz), 3.79 (1H, d, *J* = 13.4 Hz), 4.41 (1H, d, *J* = 10.9 Hz), 4.70 (1H, d, *J* = 10.9 Hz), 5.10 (1H, brs), 6.96 (2H, t, *J* = 8.5 Hz), 7.25-7.35 (7H, m). $^{13}$C NMR (125

MHz, $CDCl_3$): δ = 22.3, 26.8, 31.5, 34.5, 39.7, 48.2, 53.5, 57.8, 70.3, 75.2, 81.0, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 128.1, 128.3, 128.7, 129.6 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 136.8 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 137.6, 162.9 (d, $^1J_{C\text{-}F}$ = 242.7 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{33}FNO_2$ $[M+H]^+$: 386.24953; found: 386.24816.

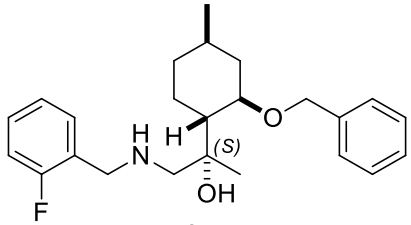
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((3-fluorobenzyl)amino)propan-2-ol (8a)**




**8a**

Prepared with **3a** with *m*-fluorobenzylamine at reflux temperature for 20 h. Yield: 54%, colourless oil. $[\alpha]_D^{20}$ = -6.78 (c 0.28, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.80-0.88 (1H, m), 0.92-1.03 (3H, m), 0.96 (3H, d, *J* = 6.5 Hz), 1.06 (3H, s), 1.35-1.45 (1H, m), 1.62-1.69 (3H, m), 1.94 (1H, td, *J* = 12.0, 3.1 Hz), 2.24 (1H, d, *J* = 10.5 Hz), 2.45 (2H, d, *J* = 11.4 Hz), 3.60 (1H, td, *J* = 10.6, 3.9 Hz), 3.68 (1H, d, *J* = 13.9 Hz), 3.83 (1H, d, *J* = 13.9 Hz), 4.41 (1H, d, *J* = 10.9 Hz), 4.71 (1H, d, *J* = 10.9 Hz), 5.12 (1H, brs), 6.89 (1H, td, *J* = 8.6, 2.2 Hz), 7.05 (1H, s), 7.08 (1H, d, *J* = 7.1Hz), 7.21-7.34 (6H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.8, 31.6, 34.5, 39.7, 48.2, 53.7, 57.9, 70.3, 72.8, 75.2, 80.0, 110.0, 113.5 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 114.9 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 123.6 (d, $^4J_{C\text{-}F}$ = 2.6 Hz), 128.1, 128.3, 128.7, 129.7 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 137.6. HR-MS (ESI): *m/z* calcd for $C_{24}H_{33}FNO_2$ $[M+H]^+$: 386.24953; found: 386.24959.

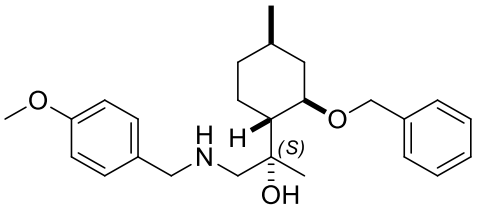
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((2-fluorobenzyl)amino)propan-2-ol (9a)**




**9a**

Prepared with **3a** with *o*-fluorobenzylamine at reflux temperature for 20 h. Yield: 66%, colourless oil. $[\alpha]_D^{20}$ = -41.65 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.82-0.89 (1H, m), 0.95 (3H, d, *J* = 6.5 Hz), 0.97-1.05 (1H, m), 1.07 (3H, s), 1.34-1.42 (1H, m), 1.57-1.72 (5H, m), 1.87-1.95 (1H, m), 2.25 (1H, d, *J* = 11.9 Hz), 2.48 (2H, t, *J* = 12.2 Hz), 3.59 (1H, td, *J* = 10.6, 3.5 Hz), 3.81 (1H, q, *J* = 14.1 Hz), 4.41 (1H, d, *J* = 11.0 Hz), 4.69 (1H, d, *J* = 11.0 Hz), 5.02 (1H, s), 6.95-7.38 (9H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.9, 31.6, 34.6, 39.8, 47.2, 47.3, 48.3, 57.9, 70.3, 75.2, 81.1, 115.2 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 124.0 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 128.1, 128.2, 128.3, 128.7, 130.3 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 137.8, 162.3 (d, $^1J_{C\text{-}F}$ = 243.9 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{33}FNO_2$ $[M+H]^+$: 386.24953; found: 386.24813.

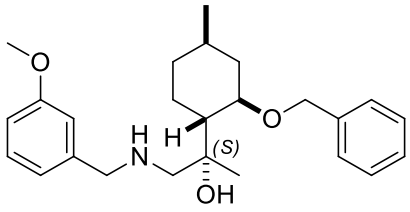
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((4-methoxybenzyl)amino)propan-2-ol (10a)**



**10a**

Prepared with **3a** with *p*-methoxybenzylamine at reflux temperature for 20 h. Yield: 67%, colourless oil. $[\alpha]_D^{20}$ = -28.47 (c 0.17, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-0.96 (2H, m), 0.96 (3H, d, *J* = 6.4 Hz), 1.00-1.07 (2H, m), 1.12 (3H, s), 1.25-1.44 (2H, m), 1.64-1.75 (3H, m), 2.27 (1H, d, *J* = 12.0 Hz), 2.80 (2H, dd, *J* = 20.3, 11.8 Hz), 3.60 (1H, td, *J* = 10.4, 3.5 Hz), 4.00 (1H, d, *J* = 13.1 Hz), 4.09 (1H, d, *J* = 13.1 Hz), 4.38 (1H, d, *J* = 10.9 Hz), 4.70 (1H, d, *J* = 10.9 Hz), 6.90 (2H, d, *J* = 8.2 Hz), 7.25-7.37 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.7, 22.1, 26.6, 31.3, 33.9, 39.4, 48.6, 53.0, 55.5, 56.1, 70.3, 73.6, 80.5, 114.6, 128.4, 128.5, 128.9, 130.8, 137.1. HR-MS (ESI): *m/z* calcd for $C_{25}H_{36}NO_3$ $[M+H]^+$: 398.26952; found: 398.26842.

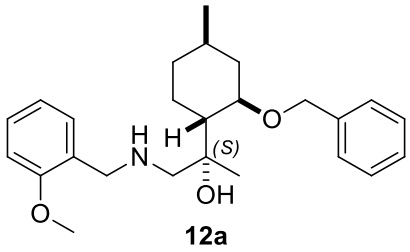
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((3-methoxybenzyl)amino)propan-2-ol (11a)**



**11a**

Prepared with **3a** with *m*-methoxybenzylamine at reflux temperature for 20 h. Yield: 65%, colourless oil. $[\alpha]_D^{20}$ = +1.41 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.79-0.88 (6H, m), 0.96 (3H, d, *J* = 6.6 Hz), 0.98-1.04 (2H, m), 1.06 (3H, s), 1.37-1.41 (1H, m), 1.62 (1H, d, *J* = 13.0 Hz), 1.70-1.73 (3H, m), 1.94 (1H, td, *J* = 12.3, 3.4 Hz), 2.26 (1H, dd, *J* = 12.1, 1.5 Hz), 2.46 (2H q, *J* = 11.4 Hz), 3.60 (1H, td, *J* = 10.6, 3.9 Hz), 3.67 (1H, d, *J* = 13.6 Hz), 3.79 (3H, s), 3.83 (1H, d, *J* = 13.6 Hz), 5.09 (1H, brs), 6.76 (1H, dd, *J* = 8.1, 2.1 Hz), 6.89 (1H, s), 6.91 (1H, d, *J* = 2.4 Hz), 7.19 (1H, t, *J* = 7.8 Hz), 7.26-7.35 (5H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.8, 31.5, 34.5, 39.7, 48.2, 54.2, 55.3, 57.9, 70.2, 75.2, 81.0, 112.5, 113.4, 120.5, 128.1, 128.3, 128.7, 129.2, 137.7, 142.9, 159.8. HR-MS (ESI): *m/z* calcd for $C_{25}H_{36}NO_3$ $[M+H]^+$: 398.26952; found: 398.26906.

**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((2-methoxybenzyl)amino)propan-2-ol (12a)**

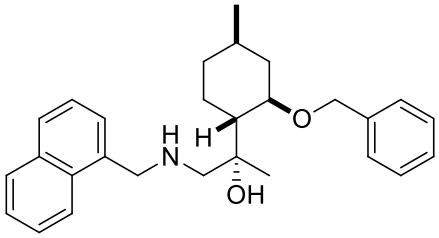


**12a**

Prepared with **3a** with *o*-methoxybenzylamine at reflux temperature for 20 h. Yield: 46%, colourless oil. $[\alpha]_D^{20}$ = -25.70 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.90-1.00 (1H, m), 0.95 (3H, d, *J* = 6.6 Hz), 0.97-1.08 (2H, m), 1.14 (3H, s), 1.35-1.45 (1H, m), 1.60-1.75 (3H, m), 2.25 (1H, d, *J* = 12.1 Hz), 2.89 (2H, dd, *J* = 18.6, 11.9 Hz), 3.60 (1H, td, *J* = 10.4, 3.5 Hz), 3.82 (3H, s), 4.28 (2H, t, *J* = 14.3 Hz), 4.39 (1H, d, *J* = 11.0 Hz), 4.70 (1H, d, *J* = 11.0 Hz), 6.90 (1H, d, *J* = 8.2 Hz), 6.98 (1H, t, *J* = 7.4 Hz), 7.28-7.39 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ =

21.3, 22.0, 26.6, 31.3, 33.8, 39.4, 48.9, 49.9, 55.4, 55.7, 70.3, 73.0, 80.4, 110.9, 121.5, 128.5, 128.8, 131.3, 131.9, 137.1, 157.8. HR-MS (ESI): *m/z* calcd for $C_{25}H_{36}NO_3$ $[M+H]^+$: 398.26952; found: 398.26928.

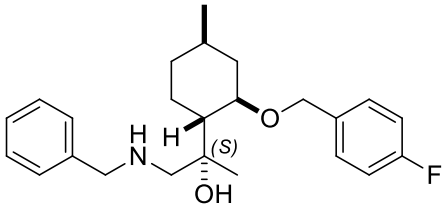
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-((naphthalen-1-ylmethyl)amino)propan-2-ol (13a)**



**13a**

Prepared with **3a** with 1-naphthylmethylamine at reflux temperature for 20 h. Yield: 93%, colourless oil. $[\alpha]_D^{20}$ = -44.05 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.73-0.85 (2H, m), 0.92 (3H, d, *J* = 6.5 Hz), 0.94-1.01 (1H, m), 1.06 (3H, s), 1.30-1.42 (1H, m), 1.52 (1H, d, *J* = 12.8 Hz), 1.61 (1H, dd, *J* = 12.1, 2.7 Hz), 1.93 (1H, td, *J* = 12.0, 3.1 Hz), 2.22 (1H, d, *J* = 12.1 Hz), 2.58 (2H, s), 3.56 (1H, td, *J* = 10.5, 3.6 Hz), 4.13 (1H, d, *J* = 13.2 Hz), 4.26 (1H, d, *J* = 13.2 Hz), 4.38 (1H, d, *J* = 10.9 Hz), 4.68 (1H, d, *J* = 11.0 Hz), 5.07 (1H, brs), 7.25-7.48 (9H, m), 7.72 (1H, d, *J* = 8.1 Hz), 7.81 (1H, d, *J* = 7.6 Hz), 8.24 (1H, d, *J* = 8.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 22.3, 26.9, 31.5, 34.3, 39.7, 48.0, 52.3, 58.2, 70.2, 75.3, 81.0, 124.6, 125.4, 125.5, 125.7, 126.1, 127.6, 128.0, 128.2, 128.5, 128.7, 132.3, 133.9, 136.5, 137.7. HR-MS (ESI): *m/z* calcd for $C_{28}H_{36}NO_2$ $[M+H]^+$: 418.27460; found: 418.27330.

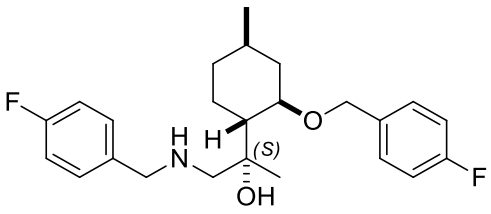
**(*S*)-1-(Benzylamino)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (16a)**



**16a**

Prepared with **4a** with benzylamine at reflux temperature for 20 h. Yield: 74%, colourless oil. $[\alpha]_D^{20}$ = -3.00 (c 0.25, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.87 (1H, m), 0.92-1.04 (2H, m), 0.95 (3H, d, *J* = 6.5 Hz), 1.06 (3H, s), 1.35-1.45 (1H, m), 1.60-1.73 (2H, m), 1.93 (H, td, *J* = 12.5, 3.1 Hz), 2.24 (1H, d, *J* = 12.0 Hz), 2.46 (2H, dd, *J* = 16.7, 11.5 Hz), 3.59 (1H, td, *J* = 10.6, 3.8 Hz), 3.70 (1H, d, *J* = 13.5 Hz), 3.83 (1H, d, *J* = 13.5 Hz), 4.37 (1H, d, *J* = 10.9 Hz), 4.67 (1H, d, *J* = 10.9 Hz), 5.02 (1H, s), 7.01 (2H, t, *J* = 8.5 Hz), 7.20-7.32 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 2.4, 31.6, 34.5, 39.7, 48.1, 54.3, 57.9, 69.5, 75.3, 81.1, 115.6 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 126.7, 128.1, 128.3, 130.0 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 133.5 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 141.2, 163.6 (d, $^1J_{C\text{-}F}$ = 244.7 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{33}FNO_2$ $[M+H]^+$: 386.24953; found: 386.24874.

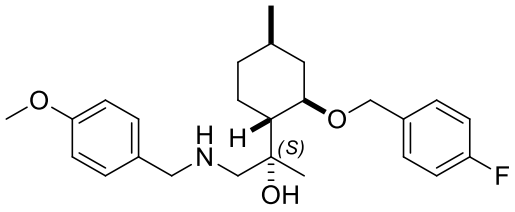
**(*S*)-1-((4-Fluorobenzyl)amino)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (17a)**



**17a**

Prepared with **4a** with *p*-fluorobenzylamine at reflux temperature for 20 h. Yield: 83%, colourless oil. $[\alpha]_D^{20}$ = -8.07 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.79-0.89 (2H, m), 0.96 (3H, d, *J* = 6.4 Hz), 0.96-1.03 (1H, m), 1.06 (3H, s), 1.25-1.45 (3H, m), 1.60-1.70 (4H, m), 1.89-1.95 (1H, m), 2.24 (H, d, *J* = 12.0 Hz), 2.44 (1H, dd, *J* = 17.1, 11.5 Hz), 3.59 (1H, td, *J* = 10.6, 3.6 Hz), 3.65 (1H, d, *J* = 13.4 Hz), 3.79 (1H, d, *J* = 13.4 Hz), 4.37 (1H, d, *J* = 10.8 Hz), 4.67 (1H, d, *J* = 10.8 Hz), 5.03 (1H, s), 6.94-7.03 (4H, m), 7.25-7.30 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 22.3, 26.8, 31.5, 34.5, 39.7, 48.1, 53.5, 57.8, 69.5, 75.2, 81.0, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz, 115.5 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 29.6 (d, $^3J_{C\text{-}F}$ = 7.6 Hz), 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 133.5 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 136.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 162.9 (d, $^1J_{C\text{-}F}$ = 242.4 Hz), 163.6 (d, $^1J_{C\text{-}F}$ = 244.8 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{32}F_2NO_2$ $[M+H]^+$: 404.24011; found: 404.23842.

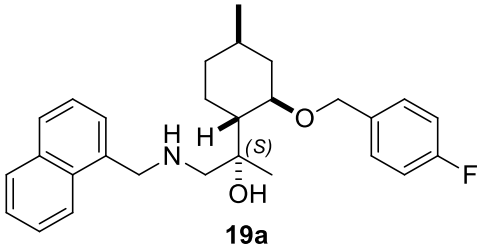
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-1-((4-methoxybenzyl)amino)propan-2-ol (18a)**




**18a**

Prepared with **4a** with *p*-methoxybenzylamine at reflux temperature for 20 h. Yield: 86%, colourless oil. $[\alpha]_D^{20}$ = -3.83 (c 0.29, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.79-0.87 (1H, m), 0.96 (3H, d, *J* = 6.3 Hz), 0.95-1.05 (1H, m), 1.06 (3H, s), 1.35-1.45 (1H, s), 1.61-1.69 (2H, m), 1.87-1.95(3H, m), 2.24 (1H, d, *J* = 12.0 Hz), 2.48 (2H, dd, *J* = 19.1, 11.5 Hz), 3.58 (1H, td, *J* = 10.5, 3.6 Hz), 3.67 (1H, d, *J* = 13.2 Hz), 3.78 (3H, s), 3.80 (1H, d, *J* = 13.2 Hz), 4.36 (1H, d, *J* = 10.9 Hz), 4.66 (1H, d, *J* = 10.8 Hz), 5.06 (1H, brs), 6.83 (2H, d, *J* = 8.0 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 7.22-7.30 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 22.3, 26.8, 31.5, 34.4, 39.7, 48.2, 53.6, 55.4, 57.6, 69.5, 75.1, 81.0, 113.8, 115.6 (d, $^2J_{C\text{-}F}$ = 21.2 Hz, 129.4, 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 132.5, 133.5 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 158.7, 163.6 (d, $^1J_{C\text{-}F}$ = 244.9 Hz). HR-MS (ESI): *m/z* calcd for $C_{25}H_{35}FNO_3$ $[M+H]^+$: 416.26010; found: 416.25837.

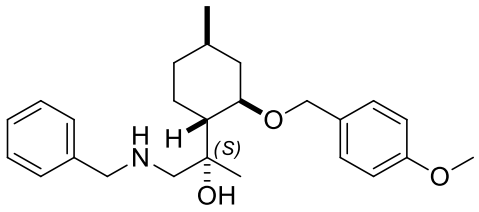
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-1-((naphthalen-1-ylmethyl)amino)propan-2-ol (19a)**




**19a**

Prepared with **4a** with 1-naphthylmethylamine at reflux temperature for 20 h. Yield: 90%, colourless oil. $[\alpha]_D^{20}$ = -3.87 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.90 (2H, m), 0.93 (3H, d, *J* = 6.5 Hz), 0.96-1.04 (1H, m), 1.06 (3H, s), 1.30-1.40 (1H, m), 1.52 (1H, d, *J* = 12.9 Hz), 1.57-1.70 (3H, m), 1.90-1.97 (1H, m), 2.21 (1H, d, *J* = 12.0 Hz), 2.58 (2H, s), 3.56 (1H, td, *J* = 10.6, 3.7 Hz), 4.13 (1H, d, *J* = 13.2 Hz), 4.26 (1H, d, *J* = 13.2 Hz), 4.35 (1H, d, *J* = 10.9 Hz), 4.65 (1H, d, *J* = 10.9 Hz), 5.00 (1H, s), 7.00 (2H, d, *J* = 8.5 Hz), 7.25-7.46 (7H, m), 7.73 (1H, d, *J* = 8.1 Hz), 7.82 (1H, d, *J* = 7.6 Hz), 8.24 (1H, d, *J* = 8.1 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 22.4, 26.9, 31.5, 34.3, 39.7, 48.0, 52.4, 58.2, 69.5, 75.3, 81.1, 115.5 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 124.6, 125.4, 125.6, 125.7, 126.1, 127.6, 128.5, 130.0 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 132.3, 133.5 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 134.0, 136.6, 163.6 (d, $^1J_{C\text{-}F}$ = 244.8 Hz). HR-MS (ESI): *m/z* calcd for $C_{28}H_{35}FNO_2$ $[M+H]^+$: 436.26518; found: 436.26425.

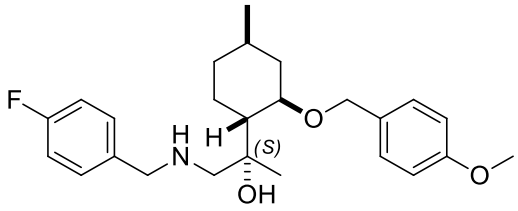
**(*S*)-1-(Benzylamino)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (22a)**



**22a**

Prepared with **5a** with benzylamine at reflux temperature for 20 h. Yield: 88%, colourless oil. $[\alpha]_D^{20}$ = +79.96 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.86 (1H, m), 0.92-1.02 (2H, m), 0.96 (3H, d, *J* = 6.4 Hz), 1.05 (3H, s), 1.30-1.45 (1H, m), 1.60-1.70 (4H, m), 1.89-1.95 (1H, m), 2.25 (1H, d, *J* = 12.0 Hz), 2.45 (2H, dd, *J* = 18.1, 11.5 Hz), 3.57 (1H, td, *J* = 10.6, 3.7 Hz), 3.69 (1H, d, *J* = 13.5 Hz), 3.78 (3H, s), 3.83 (1H, d, *J* = 13.6 Hz), 4.34 (1H, d, *J* = 10.6 Hz), 4.63 (1H, d, *J* = 10.6 Hz), 5.13 (1H, brs), 6.86 (2H, d, *J* = 8.4 Hz), 7.18-7.32 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.8, 31.5, 34.5, 39.7, 48.1, 54.2, 55.4, 57.9, 69.8, 75.2, 80.6, 114.1, 126.7, 128.1, 128.3, 129.8, 129.9, 141.2, 159.5. HR-MS (ESI): *m/z* calcd for $C_{25}H_{36}NO_3$ $[M+H]^+$: 398.26952; found: 398.26859.

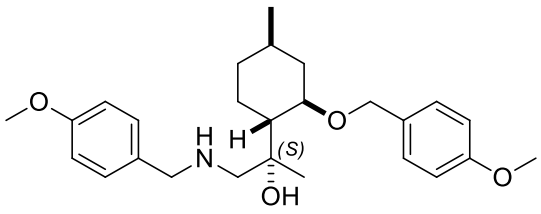
**(*S*)-1-((4-Fluorobenzyl)amino)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (23a)**



**23a**

Prepared with **5a** with *p*-fluorobenzylamine at reflux temperature for 20 h. Yield: 71%, colourless oil. $[\alpha]_D^{20}$ = +91.35 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.89 (1H, m), 0.96 (3H, d, *J* = 6.4 Hz), 0.97-1.03 (1H, m), 1.05 (3H, s), 1.35-1.45 (1H, m), 1.60-1.67 (2H, m), 1.87-1.92 (1H, m), 2.26 (1H, d, *J* = 12.0 Hz), 2.44 (2H, q, *J* = 11.4 Hz), 3.57 (1H td, *J* = 10.5, 3.6 Hz), 3.66 (1H, d, *J* = 13.4 Hz), 3.78 (3H, s), 3.79 (1H, d, *J* = 13.4 Hz), 4.33 (1H, d, *J* = 10.6 Hz), 4.64 (1H, d, *J* = 10.6 Hz), 5.17 (1H, brs), 6.86 (2H, d, *J* = 8.1 Hz), 6.96 (2H, t, *J* = 8.4 Hz), 7.23-7.29 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.8, 31.5, 34.5, 39.7, 48.1, 53.4, 55.4, 57.7, 69.8, 75.1, 80.6, 114.1, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 129.6 (d, $^3J_{C\text{-}F}$ = 7.6 Hz), 129.8, 129.9, 136.6, 159.6, 162.9 (d, $^1J_{C\text{-}F}$ = 242.5 Hz). HR-MS (ESI): *m/z* calcd for $C_{25}H_{35}FNO_3$ $[M+H]^+$: 416.26010; found: 416.25914.

**(*S*)-1-((4-Methoxybenzyl)amino)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (24a)**

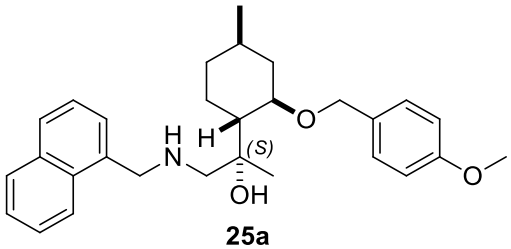


**24a**

Prepared with **5a** with *p*-methoxybenzylamine at reflux temperature for 20 h. Yield: 55%, colourless oil. $[\alpha]_D^{20}$ = +114.00 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-0.92 (1H, m), 0.95 (3H, d, *J* = 6.5 Hz), 0.97-1.05 (2H, m), 1.09 (3H, s), 1.35-1.45 (1H, m), 1.63 (1H, d, *J* = 10.3 Hz), 1.73 (1H, td, *J* = 12.2, 2.4 Hz), 2.25 (1H, d, *J* = 12.0 Hz), 2.72 (2H, dd, *J* = 17.5, 11.8 Hz), 3.56 (1H, td, *J* = 10.4, 3.6 Hz), 3.78 (3H, s), 3.79 (3H, s), 3.92 (1H, d, *J* =

13.2 Hz), 4.03 (1H, d, *J* = 13.2 Hz), 4.31 (1H, d, *J* = 10.6 Hz), 4.62 (1H, d, *J* = 10.6 Hz), 6.87 (4H, t, *J* = 7.9 Hz), 7.21-7.31 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.8, 22.1, 26.6, 31.3, 34.0, 39.4, 48.5, 52.9, 55.4, 56.1, 69.8, 73.8, 80.2, 114.2, 114.4, 127.0, 129.3, 130.1, 130.6, 159.7, 159.8. HR-MS (ESI): *m/z* calcd for $C_{26}H_{38}NO_4$ $[M+H]^+$: 428.28008; found:428.27901.

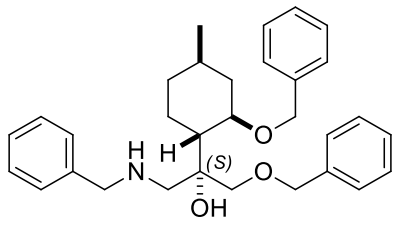
**(*S*)-2-((1*R*,2*R*,4*R*)-2-((4-Methoxybenzyl)oxy)-4-methylcyclohexyl)-1-((naphthalen-1-ylmethyl)amino)propan-2-ol (25a)**




**25a**

Prepared with **5a** with 1-naphthylmethylamine at reflux temperature for 20 h. Yield: 87%, colourless oil. $[\alpha]_D^{20}$ = +97.26 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.90 (2H, m), 0.93 (3H, d, *J* = 6.5 Hz), 0.96-1.02 (1H, m), 1.05 (3H, s), 1.30-1.40 (1H, m), 1.50-1.70 (6H, m), 1.89-1.95 (1H, m), 2.22 (1H, d, *J* = 11.9 Hz), 2.57 (2H, s), 3.55 (1H, td, *J* = 10.5, 3.6 Hz), 3.78 (3H, s), 4.13 (1H, d, *J* = 13.3 Hz), 4.26 (1H, d, *J* = 13.2 Hz), 4.32 (1H, d, *J* = 10.6 Hz), 4.62 (1H, d, *J* = 10.7 Hz), 5.11 (1H, s), 6.85 (2H, d, *J* = 8.2 Hz), 7.23 (2H, d, *J* = 8.2 Hz), 7.36-7.47 (4H, m), 7.72 (1H, d, *J* = 8.1 Hz), 7.82 (1H, d, *J* = 7.7 Hz), 8.23 (1H, d, *J* = 7.9 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 22.4, 26.9, 31.5, 34.4, 39.7, 47.9, 52.3, 55.4, 58.3, 69.8, 75.3, 80.6, 114.1, 124.6, 125.4, 125.5, 125.7, 126.0, 127.6, 128.5, 129.8, 129.9, 132.3, 133.9, 136.6, 159.5. HR-MS (ESI): *m/z* calcd for $C_{29}H_{38}NO_3$ $[M+H]^+$: 448.28517; found: 448.28409.

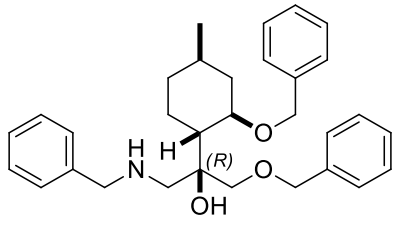
**(*S*)-1-(Benzylamino)-3-(benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (34a)**




**34a**

Prepared with **31a** and benzylamine at reflux temperature for 8 h. Yield: 62%, colourless oil. All physical properties and spectroscopic data of compound **34a** were consistent with the literature data.[3]

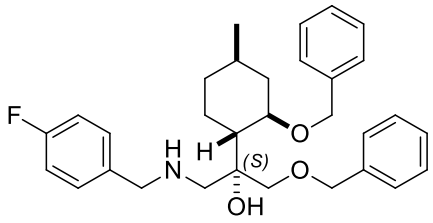
**(*R*)-1-(Benzylamino)-3-(benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (34b)**




**34b**

Prepared with **31b** and benzylamine at reflux temperature for 8 h. Yield: 62%, colourless oil. All physical properties and spectroscopic data of compound **34b** were consistent with the literature data.[3]

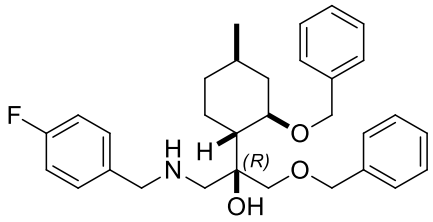
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((4-fluorobenzyl)amino)propan-2-ol (35a)**



**35a**

Prepared with **31a** and *p*-fluorobenzylamine at reflux temperature for 8 h. Yield: 60%, colourless oil. $[\alpha]_D^{20}$ = -9.05 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-1.02 (3H, m), 0.95 (3H, d, *J* = 6.2 Hz), 1.42-1.77 (10H, m), 2.33 (1H, d, *J* = 12.3 Hz), 3.30 (1H, d, *J* = 12.1 Hz), 3.37 (1H, d, *J* = 12.1 Hz), 3.53 (1H, d, *J* = 9.4 Hz), 3.68 (1H, td, *J* = 10.1, 3.6 Hz), 3.80 (2H, dd, *J* = 12.6, 8.9 Hz), 4.10 (1H, d, *J* = 12.8 Hz), 4.43-4.50 (3H, m), 4.68 (1H, d, *J* =10.9 Hz), 6.88 (2H, t, *J* = 8.3 Hz), 6.99 (2H, t, *J* = 7.6 Hz), 7.33-7.40 (10H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.0, 25.8, 31.0, 34.1, 39.8, 48.3, 52.0, 53.8, 70.0, 74.7, 79.2, 116.6 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 128.4, 128.7, 128.8, 128.9, 129.0, 131.6 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 137.4. HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29076.

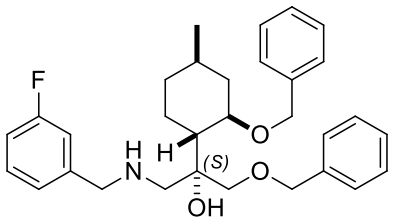
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((4-fluorobenzyl)amino)propan-2-ol (35b)**



**35b**

Prepared with **31b** and *p*-flourobenzylamine at reflux temperature for 8 h. Yield: 92%, colourless oil. $[\alpha]_D^{20}$ = -60.69 (c 0.26, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-0.98 (2H, m), 0.94 (3H, d, *J* = 6.2 Hz), 1.16-1.25 (1H, m), 1.35-1.45 (1H, m), 1.62 (1H, d, *J* = 12.9 Hz), 1.68 (1H, dd, *J* = 13.1, 2.8 Hz), 1.86 (1H, t, *J* = 10.2 Hz), 2.20 (1H, d, *J* = 12.1 Hz), 2.61 (2H, s), 3.45 (2H, s), 3.63-3.70 (2H, m), 3.77 (1H, d, *J* = 13.4 Hz), 4.18 (1H, d, *J* = 10.8 Hz), 4.42 (1H, d, *J* = 12.0 Hz), 4.49 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 10.8 Hz), 6.95 (2H, t, *J* = 8.4 Hz), 7.22-7.34 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.9, 40.2, 48.4, 53.5, 54.1, 70.1, 73.8, 74.3, 76.1, 81.1, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 127.9, 128.1, 128.2, 128.4, 128.6, 129.7 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 137.9, 138.5, 162.9 (d, $^1J_{C\text{-}F}$ = 242.3 Hz). HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29062.

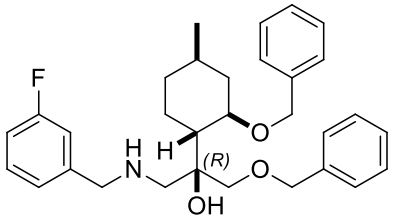
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((3-fluorobenzyl)amino)propan-2-ol (36a)**



**36a**

Prepared with **31a** and *m*-fluorobenzylamine at reflux temperature for 8 h. Yield: 74%, colourless oil. $[\alpha]_D^{20}$ = -18.25 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-1.01 (3H, m), 0.93 (3H, d, *J* = 6.6 Hz), 1.34-1.40 (1H, m), 1.61 (1H, d, *J* = 12.4 Hz), 1.77-1.81 (1H, m), 1.94 (1H, td, *J* = 11.7, 3.1 Hz), 2.22 (1H, dd, *J* = 12.3, 1.6 Hz), 2.58 (2H, dd, *J* = 15.6, 11.5 Hz), 3.41 (1H, d, *J* = 10.1 Hz), 3.53 (1H, d, *J* = 10.1 Hz), 3.64 (1H, td, *J* = 10.6, 4.0 Hz), 3.67 (2H, d, *J* = 1.5 Hz), 4.26 (1H, d, *J* = 11.1 Hz), 4.46 (1H, d, *J* = 12.2 Hz), 4.62 (2H, d, *J* = 11.9 Hz), 6.89 (1H, td, *J* = 8.4, 2.2 Hz), 6.98-7.03 (2H, m), 7.19-7.31 (11H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.6, 34.8, 40.3, 48.1, 53.5, 54.1, 70.1, 73.7, 75.0, 76.6, 80.4, 113.7 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, 114.9 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 123.6 (d, $^4J_{C\text{-}F}$ = 2.6 Hz), 127.6, 127.8, 128.0, 128.2, 128.4, 128.6, 129.8 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 138.0, 138.9, 164.2 (d, $^1J_{C\text{-}F}$ = 243.9 Hz). HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29301.

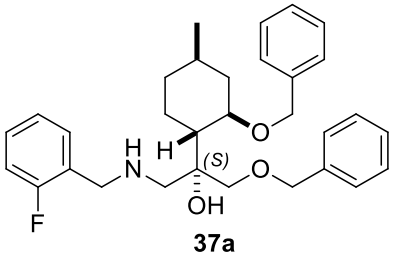
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((3-fluorobenzyl)amino)propan-2-ol (36b)**




**36b**

Prepared with **31b** and *m*-flourobenzylamine at reflux temperature for 8 h. Yield: 89%, colourless oil. $[\alpha]_D^{20}$ = -20.40 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.89-0.90 (2H, m), 0.94 (3H, d, *J* = 6.45 Hz), 1.18-1.26 (1H, m), 1.33-1.43 (1H, m), 1.63 (1H, d, *J* = 13.0 Hz), 1.67-1.72 (1H, m), 1.88 (1H, td, *J* = 13.2, 3.3 Hz), 2.20 (1H, d, *J* = 11.6 Hz), 2.62 (2H, s), 3.45 (2H, dd, *J* = 11.1, 9.5 Hz), 3.67 (1H, td, *J* = 10.7, 3.9 Hz), 3.71 (1H, d, *J* = 13.9 Hz), 3.80 (1H, d, *J* = 13.9 Hz), 4.19 (1H, d, *J* = 10.9 Hz), 4.42 (1H, d, *J* = 12.0 Hz), 4.50 (1H, d, *J* = 12.0 Hz), 4.56 (1H, d, *J* = 10.9 Hz), 6.88 (1H, td, *J* = 8.8, 2.1 Hz), 7.03-7.06 (2H, m), 7.19-7.33 (11H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.5, 31.6, 34.9, 40.3, 48.5, 53.8, 54.3, 70.2, 73.9, 74.3, 76.2, 81.2, 113.6 (d, $^2J_{C\text{-}F}$ = 21.2 Hz),, 114.9 (d, $^2J_{C\text{-}F}$ = 20.9 Hz), 115.0, 123.6 ((d, $^4J_{C\text{-}F}$ = 2.5 Hz),, 127.7, 127.9, 128.1, 128.2, 128.5, 128.6, 129.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz),. HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29062.

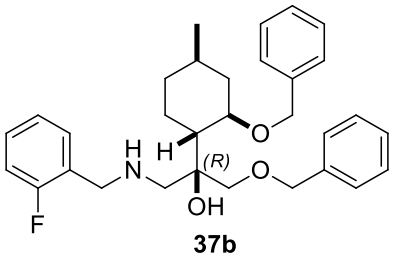
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((2-fluorobenzyl)amino)propan-2-ol (37a)**




**37a**

Prepared with **31a** and *o*-fluorobenzylamine at reflux temperature for 8 h. Yield: 74%, colourless oil. $[\alpha]_D^{20}$ = -50.10 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.87-1.00 (4H, m), 0.93 (3H, d, *J* = 6.4 Hz), 1.30-1.43 (1H, m), 1.61 (1H, d, *J* = 12.3 Hz), 1.78 (1H, d, *J* = 12.8 Hz), 1.95 (1H, t, *J* = 10.6 Hz), 2.21 (1H, d, *J* = 12.1 Hz), 2.60 (2H, s), 3.42 (1H, d, *J* = 10.1 Hz), 3.53 (1H, d, *J* = 10.1 Hz), 3.61 (1H, td, *J* = 10.6, 3.6 Hz), 3.76 (2H, s), 4.19 (1H, d, *J* = 10.9 Hz), 4.45 (1H, d, *J* = 12.2 Hz), 4.58 (1H, d, *J* = 10.9 Hz), 4.63 (1H, d, *J* = 12.2 Hz), 6.97-7.05 (2H, m), 7.18-7.31 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.5, 34.7, 40.1, 47.6, 47.9, 53.2, 70.1, 73.6, 74.8, 76.6, 80.4, 115.2 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 124.0 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 127.5, 127.8, 128.1, 128.4, 128.6, 130.3 (d, $^3J_{C\text{-}F}$ = 4.6 Hz), 137.8, 138.9, 162.3 (d, $^1J_{C\text{-}F}$ = 244.0 Hz),. HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29081.

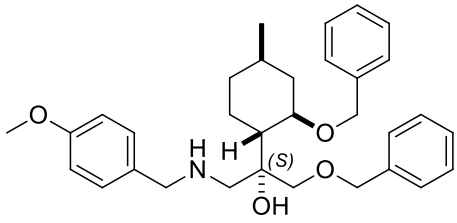
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((2-fluorobenzyl)amino)propan-2-ol (37b)**



**37b**

Prepared with **31b** and *o*-flourobenzylamine at reflux temperature for 8 h. Yield: 74%, colourless oil. $[\alpha]_D^{20}$ = -67.30 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-0.97 (2H, m), 0.93 (3H, d, *J* = 6.2 Hz), 1.20-1.30 (1H, m), 1.33-1.43 (1H, m), 1.60-1.74 (4H, m), 1.86 (1H, td. *J* = 12.6, 2.4 Hz), 2.19 (1H, d, *J* = 12.0 Hz), 2.64 (2H, s), 3.45 (2H, t, *J* = 10.7 Hz), 3.65 (1H, td, *J* = 10.5, 3.4 Hz), 3.82 (2H, t, *J* = 14.8 Hz), 4.17 (1H, d, *J* = 10.8 Hz), 4.42 (1H, d, *J* = 11.9 Hz), 4.50 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 10.8 Hz), 6.98 (1H, t, *J* = 9.0 Hz), 7.06 (1H, t, *J* = 7.4 Hz), 7.16-7.36 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.9, 40.2, 47.3, 48.4, 54.2, 70.1, 73.8, 74.3, 76.1, 81.2, 115.2 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 123.9 (d, $^4J_{C\text{-}F}$ = 3.2 Hz),, 124.0, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.6, 130.2 (d, $^3J_{C\text{-}F}$ = 5.0 Hz), 138.0, 138.6, 162.3 (d, $^1J_{C\text{-}F}$ = 244.0 Hz). HR-MS (ESI): *m/z* calcd for $C_{31}H_{39}FNO_3$ $[M+H]^+$: 492.29140; found: 492.29055.

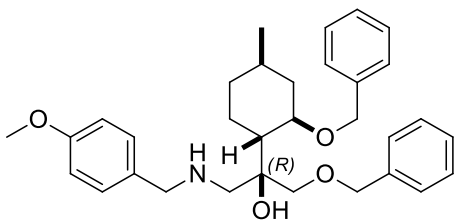
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((4-methoxybenzyl)amino)propan-2-ol (38a)**



**38a**

Prepared with **31a** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 54%, colourless oil. $[\alpha]_D^{20}$ = -47.15 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-1.00 (3H, m), 0.93 (3H, d, *J* = 6.3 Hz), 1.37 (1H, s), 1.63 (1H, d, *J* = 12.1 Hz), 1.80 (1H, d, *J* = 13.6 Hz), 1.88 (1H, d, *J* = 10.3 Hz), 2.23 (1H, d, *J* = 12.2 Hz), 2.76 (1H, d, *J* = 11.3 Hz), 3.42 (1H, d, *J* = 9.9 Hz), 3.57 (1H, d, *J* = 9.9 Hz), 3.63-3.80 (4H, m), 3.76 (3H, s), 4.27 (1H, d, *J* = 10.9 Hz), 4.46 (1H, d, *J* = 11.9 Hz), 4.58 (1H, d, *J* = 10.9 Hz) 4.61 (1H, d, *J* = 12.0 Hz), 6.79 (2H, d, *J* = 7.7 Hz), 7.12 (2H, d, *J* = 7.9 Hz), 7.22-7.32 (10H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.4, 31.5, 34.6, 40.2, 48.2, 53.6, 55.4, 70.1, 73.9, 75.5, 80.2, 114.1, 127.8, 128.0, 128.3, 128.5, 128.6, 129.8, 137.9. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31052.

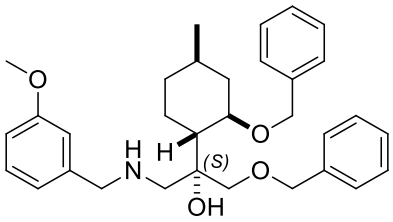
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((4-methoxybenzyl)amino)propan-2-ol (38b)**



**38b**

Prepared with **31b** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 73%, colourless oil. $[\alpha]_D^{20}$ = -56.30 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.98 (2H, m), 0.93 (3H, d, *J* = 6.3 Hz), 1.17-1.26 (1H, m), 1.36 (1h, brs), 1.61 (1H, d, *J* = 12.8 Hz), 1.71 (1H, d, *J* = 13.0 Hz), 1.87 (1H, td, *J* = 10.4, 2.6 Hz), 2.19 (1H, d, *J* = 11.8 Hz), 2.61 (2H, s), 3.45 (2H, s), 3.63-3.75 (3H, m), 3.77 (3H, s), 4.19 (1H, d, *J* = 10.9 Hz), 4.42 (1H, d, *J* = 12.0 Hz), 4.49 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 10.8 Hz), 5.08 (1H, brs), 6.81 (2H, d, *J* = 8.2 Hz), 7.19-7.31 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.6, 35.0, 40.3, 48.4, 53.8, 54.3, 55.4, 70.1, 73.9, 74.5, 76.2, 81.2, 113.8, 127.7, 127.9, 128.1, 128.4, 128.6, 129.3, 133.4, 138.1, 138.8, 158.6. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31073.

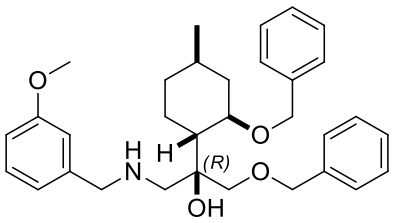
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((3-methoxybenzyl)amino)propan-2-ol (39a)**




**39a**

Prepared with **31a** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 73%, colourless oil. $[\alpha]_D^{20}$ = -5.08 (c 0.25, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-1.01 (3H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.33-1.40 (1H, m), 1.61 (1H, d, *J* = 12.9 Hz), 1.79 (1H, dd, *J* = 12.8, 3.2 Hz), 1.94 (1H, td, *J* = 11.6, 3.1 Hz), 2.21 (1H, d, *J* = 13.6 Hz), 2.60 (2H, q, *J* = 11.5 Hz), 3.41 (1H, d, *J* = 10.2 Hz), 3.54 (1H, d, *J* = 10.2 Hz), 3.64 (1H, td, *J* = 10.6, 3.9 Hz), 3.67 (2H, s), 3.75 (3H, s), 4.24 (1H, d, *J* = 11.0 Hz), 4.45 (1H, d, *J* = 12.2 Hz), 4.59 (1H, d, *J* = 11.1 Hz), 4.63 (1H, d, *J* = 12.2 Hz), 6.76 (1H, dd, *J* = 8.0, 1.8 Hz), 6.85 (2H, s), 7.16-7.31 (11H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.6, 34.8, 40.3, 48.0, 53.5, 54.5, 55.3, 70.1, 73.7, 75.0, 80.4, 112.5, 113.8, 120.6, 127.8, 128.2, 128.4, 128.6, 138.0, 159.9. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31148.

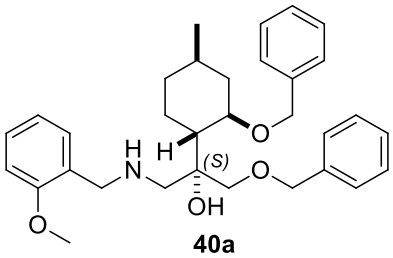
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((3-methoxybenzyl)amino)propan-2-ol (39b)**




**39b**

Prepared with **31b** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 87%, colourless oil. $[\alpha]_D^{20}$ = -6.43 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.98 (2H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.20-1.26 (1H, m), 1.34-1.40 (1H, m), 1.61 (1H, d, *J* = 12.8 Hz), 1.72-1.75 (1H, m), 1.88 (1H, td, *J* = 12.4, 3.4 Hz), 2.19 (1H, d, *J* = 12.2 Hz), 2.62 (2H, dd, *J* = 13.8, 11.6 Hz), 3.46 (2H, s), 3.67 (1H, td, *J* = 10.6, 3.9 Hz), .3.69 (1H, d, *J* = 13.6 Hz), 3.77 (3H, s), 3.79 (1H, d, *J* = 13.6 Hz), 4.19 (1H, d, *J* = 10.9 Hz), 4.42 (1H, d, *J* = 12.0 Hz), 4.49 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 10.9 Hz), 6.74 (1H, dd, *J* = 7.5, 2.3 Hz), 6.88 (2H, d, *J* = 7.5 Hz), 7.16-7.33 (11H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.5, 31.6, 35.0, 40.3, 48.4, 54.3, 54.4, 55.3, 70.2, 73.9, 74.5, 76.3, 81.2, 112.5, 113.6, 120.5, 127.9, 128.1, 128.2, 128.4, 128.6, 138.1, 138.7. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31156.

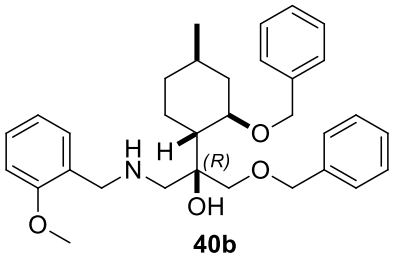
**(*S*)-1-(Benzyloxy)-2-((1R,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((2-methoxybenzyl)amino)propan-2-ol (40a)**



**40a**

Prepared with **31a** and *o*-methoxybenzylamine at reflux temperature for 8 h. Yield: 77%, colourless oil. $[\alpha]_D^{20}$ = -21.75 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.94 (4H, m), 0.86 (3H, d, *J* = 6.4 Hz), 1.28-1.37 (1H, m), 1.56-1.71 (3H, m), 2.19 (1H, d, *J* = 9.9 Hz), 3.05 (1H, d, *J* = 12.2 Hz), 3.37 (2H, d, *J* = 9.9 Hz), 3.48 (1H, td, *J* = 10.3, 3.7 Hz), 3.59 (3H, s), 3.63 (1H, d, *J* = 9.6 Hz), 4.07 (2H, s), 4.19 (1H, d, *J* = 11.1 Hz), 4.41 (1H, d, *J* = 11.8 Hz), 4.49 (1H, d, *J* = 11.8 Hz), 4.54 (1H, d, *J* = 11.1 Hz), 6.71 (1H, d, *J* = 8.2 Hz), 6.87 (1H, t, *J* = 7.4 Hz), 7.13-7.29 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.0, 25.8, 31.0, 34.2, 39.8, 48.5, 49.6, 53.4, 55.6, 69.8, 73.8, 74.2, 76.4, 79.4, 110.8, 121.6, 128.1, 128.3, 128.4, 128.7, 128.8, 131.5, 132.0, 137.5, 157.7. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31070.

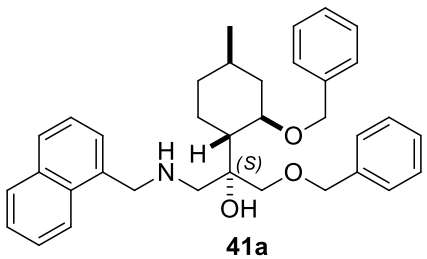
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((2-methoxybenzyl)amino)propan-2-ol (40b)**



**40b**

Prepared with **31b** and *o*-methoxybenzylamine at reflux temperature for 8 h. Yield: 85%, colourless oil. $[\alpha]_D^{20}$ = -36.10 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-0.97 (2H, m), 0.93 (1H, d, *J* = 6.4 Hz), 1.07-1.15 (1H, m), 1.36 (1h, brs), 1.65-1.70 (3H, m), 2.21 (1H, d, *J* = 12.1 Hz), 2.84 (1H, d, *J* = 11.9 Hz), 3.33 (1H, d, *J* = 10.5 Hz), 3.40 (1H, d, *J* = 9.6 Hz), 3.45-3.50 (1H, m), 3.58 (1H, d, *J* = 9.6 Hz), 3.76 (3H, s), 4.13-4.23 (3H, m), 4.45 (1H, d, *J* = 12.0 Hz), 4.58 (2H, t, *J* = 10.4 Hz), 6.85 (1H, d, *J* = 7.7 Hz), 6.96 (1H, t, *J* = 7.4 Hz), 7.20-7.35 (12H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 25.9, 31.1, 34.2, 39.7, 49.5, 49.7, 51.2, 55.6, 70.1, 73.9, 80.3, 110.7, 121.3, 128.2, 128.5, 128.6, 128.8, 137.2. HR-MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_4$ $[M+H]^+$: 504.31138; found: 504.31069.

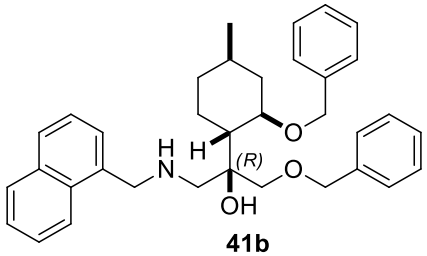
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (41a)**



**41a**

Prepared with **31a** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 70%, colourless oil. $[\alpha]_D^{20}$ = -53.00 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-1.03 (3H, m), 0.92 (3H, d, *J* = 6.3 Hz), 1.25-1.35 (1H, m), 1.59 (1H, d, *J* = 11.2 Hz), 1.75 (1H, d, *J* = 11.3 Hz), 1.92 (1H, d, *J* = 10.1 Hz), 2.15 (1H, d, *J* = 12.0 Hz), 2.70 (1H, dd, *J* = 17.0, 11.5 Hz), 3.40 (1H, d, *J* = 10.1 Hz), 3.52 (1H, d, *J* = 10.1 Hz), 3.64 (1H, td, *J* = 10.6, 3.5 Hz), 4.04 (1H, d, *J* = 10.9 Hz), 4.13 (2H, s), 4.43 (1H, d, *J* = 12.2 Hz), 4.49 (1H, d, *J* = 10.9 Hz), 4.61 (1H, d, *J* = 12.2 Hz), 7.07 (2H, d, *J* = 4.1 Hz), 7.22-7.48 (12H, m), 7.74 (1H, d, *J* = 7.8 Hz), 7.83 (1H, dd, *J* = 8.1, 2.8 Hz), 8.11 (1H, d, *J* = 8.3 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.5, 34.7, 40.1, 47.9, 52.4, 53.8, 69.9, 73.6, 74.9, 76.7, 80.4, 124.3, 125.4, 125.9, 126.1, 127.5, 127.8, 128.1, 128.4, 128.5, 128.7, 132.1, 134.0, 137.8, 138.8. HR-MS (ESI): *m/z* calcd for $C_{35}H_{42}NO_3$ $[M+H]^+$: 524.31647; found: 524.31563.

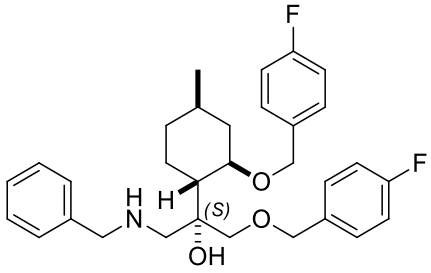
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (41b)**




**41b**

Prepared with **31b** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 64%, colourless oil. $[\alpha]_D^{20}$ = -59.00 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.77-0.94 (2H, m), 0.91 (3H, d, *J* = 6.7 Hz), 1.15-1.23 (1H, m), 1.34 (1H, brs), 1.53-1.68 (4H, m), 1.89 (1H, t, *J* = 10.1 Hz), 2.17 (1H, d, *J* = 12.0 Hz), 2.75 (2H, s), 3.44 (2H, t, *J* = 10.5 Hz), 3.63 (1H, td, *J* = 10.5, 3.4 Hz), 4.17 (2H, dd, *J* = 10.8, 6.2 Hz), 4.24 (1H, d, *J* = 13.2 Hz), 4.39 (1H, d, *J* = 12.0 Hz), 4.47 (1H, d, *J* = 12.0 Hz), 4.51 (1H, d, *J* = 10.9 Hz), 5.09 (1H, brs), 7.20-7.46 (14H, m), 7.72 (1H, d, *J* = 8.1 Hz), 7.82 (1H, d, *J* = 7.9 Hz), 8.21 (1H, d, *J* = 8.2 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 26.5, 31.5, 34.8, 40.2, 48.2, 52.4, 54.6, 70.1, 73.8, 74.3, 76.3, 81.1, 124.5, 125.4, 125.5, 125.7, 126.1, 127.7, 128.0, 128.1, 128.4, 128.5, 128.6, 132.3, 134.0, 138.0, 138.6. HR-MS (ESI): *m/z* calcd for $C_{35}H_{42}NO_3$ $[M+H]^+$: 524.31647; found: 524.31571.

**(*S*)-1-(Benzylamino)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (44a)**

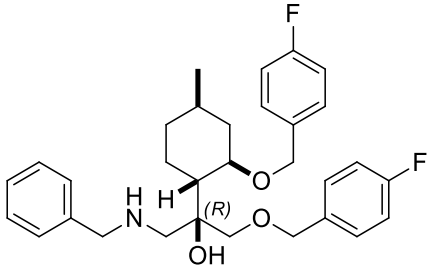



**44a**

Prepared with **32a** and benzylamine at reflux temperature for 8 h. Yield: 87%, colourless oil. $[\alpha]_D^{20}$ = -128.17 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.99 (3H, m), 0.93 (3H, d, *J* = 6.6 Hz), 1.36 (1H, brs), 1.50-1.65 (4H, m), 1.74 (1H, dd, *J* = 12.6, 2.6 Hz), 1.93 (1H, t, *J* = 9.7 Hz), 2.19 (1H, d, *J* = 12.0 Hz), 2.58 (2H, q, *J* = 11.4 Hz), 3.39 (1H, d, *J* = 10.1 Hz), 3.51 (1H, t, *J* = 10.2 Hz), 3.64 (1H, td, *J* = 10.7, 3.8 Hz), 3.71 (2H, q, *J* = 13.4 Hz), 4.15 (1H, d, *J* = 10.8 Hz), 4.41 (1H, d, *J* = 12.0 Hz), 4.54 (1H, d, *J* = 10.8 Hz), 4.58 (1H, d, *J* = 12.0 Hz), 6.94-7.00 (4H, m), 7.12 (2H, t, *J* = 7.4 Hz), 7.22-7.31 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.5, 34.6, 40.2, 47.7, 53.3, 54.6, 69.3, 72.9, 74.7, 76.7, 115.2 (d, $^2J_{C-F}$ = 21.1 Hz), 115.4 (d, $^2J_{C-F}$ = 21.2 Hz), 115.5, 127.0,

128.2, 128.4, 129.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 129.8 (d, $^{4}J_{C\text{-}F}$ = 7.9 Hz), 133.7 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 134.5 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 163.3, 163.5. HR-MS (ESI): *m/z* calcd for $C_{31}H_{38}F_2NO_3$ $[M+H]^+$: 510.28198; found: 510.28108.

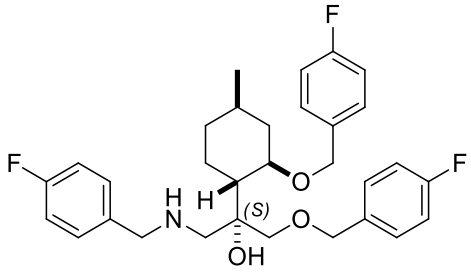
**(*R*)-1-(Benzylamino)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (44b)**




**44b**

Prepared with **32b** and benzylamine at reflux temperature for 8 h. Yield: 79%, colourless oil. $[\alpha]_D^{20}$ = -130.75 (c 0.24, MeOH). $^{1}$H NMR (500 MHz, $CDCl_3$): δ = 0.87-0.98 (2H, m), 1.12-1.19 (1H, m), 1.36 (1H, brs), 1.50-1.75 (5H, m), 1.88 (1H, t, *J* = 10.2 Hz), 2.18 (1H, d, *J* = 14.2 Hz), 2.59 (2H, s), 3.44 (2H, dd, *J* = 14.4, 9.6 Hz), 3.66 (1H, td, *J* = 10.5, 3.4 Hz), 3.72 (1H, d, *J* = 13.5 Hz), 3.80 (1H, d, *J* = 13.5 Hz), 4.14 (1H, d, *J* = 10.7 Hz), 4.42 (2H, q, *J* = 11.8 Hz), 4.53 (1H, d, *J* = 10.7 Hz), 5.13 (1H, brs), 6.96-7.01 (4H, q, *J* = 8.6 Hz), 7.17-7.29 (9H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.8, 40.2, 48.2, 54.2, 54.3, 69.4, 73.1, 74.3, 76.2, 81.3, 115.4 (t, $^{2}J_{C\text{-}F}$ = 21.5 Hz), 126.8, 128.2, 128.3, 129.7 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 129.8 (d, $^{4}J_{C\text{-}F}$ = 8.1 Hz), 133.8 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 134.3 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 163.4 (d, $^{1}J_{C\text{-}F}$ = 243.9 Hz), 163.5 (d, $^{1}J_{C\text{-}F}$ = 244.7 Hz),. HR-MS (ESI): *m/z* calcd for $C_{31}H_{38}F_2NO_3$ $[M+H]^+$: 510.28198; found: 510.28113.

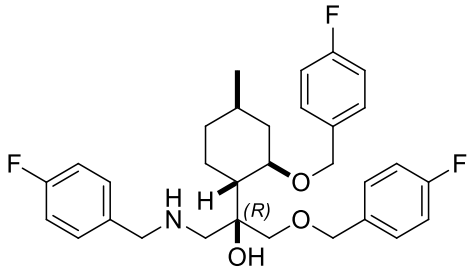
**(*S*)-1-((4-Fluorobenzyl)amino)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (45a)**




**45a**

Prepared with **32a** and *p*-fluorobenzylamine at reflux temperature for 8 h. Yield: 79%, colourless oil. $[\alpha]_D^{20}$ = -113.52 (c 0.27, MeOH). $^{1}$H NMR (500 MHz, $CDCl_3$): δ = 0.86-1.00 (3H, m), 0.94 (3H, d, *J* = 6.5 Hz), 1.36 (1H, brs), 1.62 (1H, d, *J* = 12.5 Hz), 1.74 (1H, d, *J* = 12.6 Hz), 1.92 (1H, td, *J* = 10.5, 2.5 Hz), 2.20 (1H, d, *J* = 12.1 Hz), 2.54 (2H, t, *J* = 13.0 Hz), 3.38 (1H, d, *J* = 10.1 Hz), 3.52 (1H, d, *J* = 10.1 Hz), 3.62 (1H, td, *J* = 10.5, 3.5 Hz), 3.65 (2H, s), 4.18 (1H, d, *J* = 10.9 Hz), 4.41 (1H, d, *J* = 12.0 Hz), 4.58 (2H, d, *J* = 11.4 Hz), 6.97 (6H, quin, *J* = 8.4 Hz), 7.14-7.28 (6H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.5, 34.6, 40.1, 69.3, 72.9, 74.7, 76.6, 80.4, 115.1 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 115.3 (d, $^{2}J_{C\text{-}F}$ = 21.1 Hz), 115.6 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 129.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 129.6 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 129.8 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 133.7 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 134.5 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 162.9 (d, $^{1}J_{C\text{-}F}$ = 242.7 Hz), 163.4 (d, $^{1}J_{C\text{-}F}$ = 243.9 Hz), 163.5 (d, $^{1}J_{C\text{-}F}$ = 244.5 Hz),. HR-MS (ESI): *m/z* calcd for $_{31}H_{37}F_3NO_3$ M+H]$^+$: 528.27255; found: 528.27161.

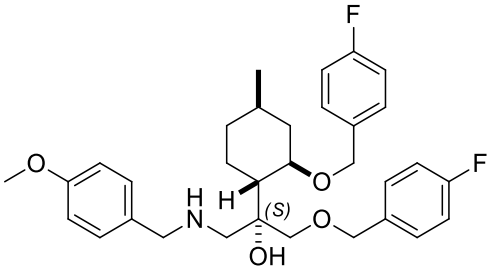
**(*R*)-1-((4-Fluorobenzyl)amino)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (45b)**



**45b**

Prepared with **32b** and *p*-fluorobenzylamine at reflux temperature for 8 h. Yield: 79%, colourless oil. $[\alpha]_D^{20}$ = -131.37 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-0.98 (2H, m), 0.94 (3H, d, *J* = 6.7 Hz), 112-1.20 (1H, m), 1.36 91H, brs), 1.50-1.70 (5H, m), 1.87 (1H, t, *J* = 10.1 Hz), 2.19 (1H, d, *J* = 12.1 Hz), 2.57 (2H, s), 3.43 (1H, dd, *J* = 16.0, 9.5 Hz), 3.63-3.69 (2H, m), 3.76 (1H, d, *J* = 13.4 Hz), 4.14 (1H, d, *J* = 10.7 Hz), 4.42 (2H, q, *J* = 11.8 Hz), 4.53 (1H, d, *J* = 10.7 Hz), 5.13 (1H, brs), 7.00 (6H, quin, *J* = 9.6 Hz), 7.19 (2H, t, *J* = 7.2 Hz), 7.24-7.27 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.8, 40.2, 48.2, 53.4, 54.1, 69.4, 73.1, 74.2, 76.2, 81.3, 115.1 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 115.2 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 115.5 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 129.6 (d, $^3J_{C\text{-}F}$ = 7.7 Hz), 129.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.8 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 133.7 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 134.3 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 136.7, 162.9 (d, $^1J_{C\text{-}F}$ = 242.9 Hz), 163.4 (d, $^1J_{C\text{-}F}$ = 244.1 Hz), 163.5 (d, $^1J_{C\text{-}F}$ = 245.0 Hz),. HR-MS (ESI): *m/z* calcd for $C_{31}H_{37}F_3NO_3$ $[M+H]^+$: 528.27255; found: 528.27187.

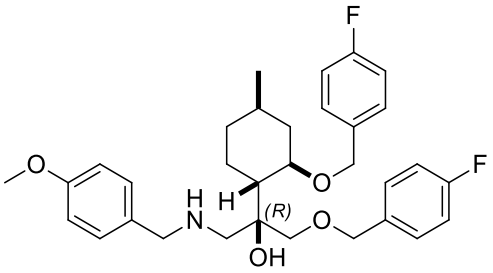
**(*S*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-((4-methoxybenzyl)amino)propan-2-ol (46a)**



**46a**

Prepared with **32a** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 89%, colourless oil. $[\alpha]_D^{20}$ = -204.12 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.86-1.00 (3H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.32-1.42 (1H, m), 1.62 (1H, d, *J* = 12.6 Hz), 1.75 (1H, dd, *J* = 12.7, 2.8 Hz), 1.91 (1H, t, *J* =9.8 Hz), 2.19 (1H, d, *J* = 12.1 Hz), 2.61 (2H, q, *J* = 11.5 Hz), 3.38 (1H, d, *J* = 10.1 Hz), 3.51 (1H, d, *J* = 10.1 Hz), 3.61-3.68 (3H, m), 3.77 (3H, s), 4.17 (1H, d, *J* = 10.8 Hz), 4.41 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 10.8 Hz), 4.57 (1H, d, *J* = 11.9 Hz), 6.82 (2H, d, *J* = 8.2 Hz), 6.98 (4H, q, *J* = 8.7 Hz), 7.12-7.18 (4H, m), 7.25-7.30 (2H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.5, 31.5, 34.6, 40.1, 47.8, 53.2, 53.8, 55.4, 69.3, 72.9, 74.8, 76.4, 80.5, 113.9, 115.2 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 129.5 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.9 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 133.7 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 134.5 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 158.8, 163.4 (d, $^1J_{C\text{-}F}$ = 243.8 Hz), 163.5 (d, $^1J_{C\text{-}F}$ = 244.6 Hz). HR-MS (ESI): *m/z* calcd for $C_{32}H_{40}F_2NO_4$ $[M+H]^+$: 540.29254; found: 540.29186.

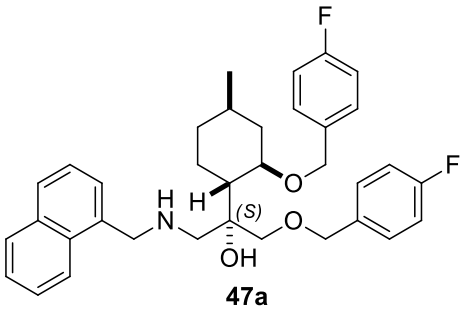
**(*R*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-((4-methoxybenzyl)amino)propan-2-ol (46b)**



**46b**

Prepared with **32b** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 92%, colourless oil. $[\alpha]_D^{20}$ = -111.18 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.87-0.97 (2H, m), 0.93 (3H, d, *J* = 6.7 Hz), 1.11-1.19 (1H, m), 1.36 (1H, brs), 1.62 (1H, d, *J* = 12.7 Hz), 1.69 (1H, dd, *J* = 10.6, 2.4 Hz), 1.86 (1H, t, *J* = 10.1 Hz), 2.18 (1H, d, *J* = 12.2 Hz), 2.59 (2H, t, *J* = 14.0 Hz), 3.43 (2H, s), 3.63-3.68 (2H, m), 3.74 (1H, d, *J* = 11.2 Hz), 3.78 (3H, s), 4.14 (1H, d, *J* = 10.7 Hz), 4.42 (2H, q, *J* = 11.8 Hz), 4.53 (1H, d, *J* = 10.8 Hz), 6.82 (2H, d, *J* = 7.9 Hz), 6.99 (4H, q, *J* = 8.5 Hz), 7.17-7.26 (6H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.8, 40.2, 48.3, 53.6, 54.1, 55.4, 69.4, 73.1, 74.3, 76.1, 81.3, 113.8, 115.4 (t, $^2J_{C\text{-}F}$ = 22.0 Hz), 129.3, 129.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.8 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 133.8 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 134.3 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 158.6, 163.4 (d, $^1J_{C\text{-}F}$ = 244.4 Hz), 163.5 (d, $^1J_{C\text{-}F}$ = 244.4 Hz). HR-MS (ESI): *m/z* calcd for $C_{32}H_{40}F_2NO_4$ $[M+H]^+$: 540.29254; found: 540.29200.

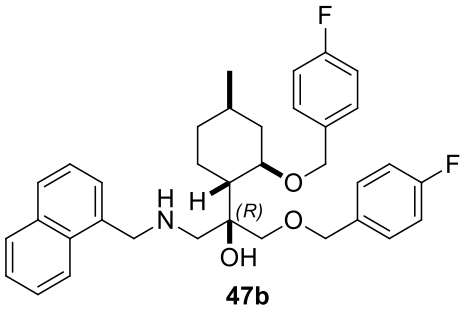
**(*S*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (47a)**



**47a**

Prepared with **32a** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 86%, colourless oil. $[\alpha]_D^{20}$ = -119.77 (c 0.26, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-1.05 (3H, m), 0.92 (3H, d, *J* = 6.1 Hz), 1.31 (1H, brs), 1.50-1.60 (4H, m), 1.75 (1H, dd, *J* = 10.2, 2.6 Hz), 1.87 (1H, t, *J* = 10.7 Hz), 2.12 (1H, d, *J* = 12.1 Hz), 2.70 (2H, q, *J* = 11.5 Hz), 3.38 (1H, d, *J* = 10.1 Hz), 3.48 (1H, d, *J* = 10.0 Hz), 3.63 (1H, td, *J* = 10.6, 3.4 Hz), 3.95 (1H, d, *J* = 10.8 Hz), 4.15 (2H, s), 4.41 (1H, t, *J* = 10.4 Hz), 4.55 (1H, d, *J* = 12.0 Hz), 6.86 (2H, t, *J* = 8.5 Hz), 6.93-7.00 (4H, m), 7.20-7.27 (2H, m), 7.35-7.42 (2H, m), 7.48 (2H, t, *J* = 3.6 Hz)), 7.74 (1H, d, *J* = 7.4 Hz), 7.83 (1H, t, *J* = 5.1 Hz), 8.12 (1H, d, *J* = 6.1 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.7, 31.5, 34.7, 40.3, 48.0, 52.5, 53.8, 69.3, 73.0, 75.1, 76.7, 80.6, 115.3 (t, $^2J_{C\text{-}F}$ = 20.6 Hz),, 125.4, 125.8, 126.0, 128.8, 129.5 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.8 (d, $^4J_{C\text{-}F}$ = 8.1 Hz), 132.1, 133.7 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 134.1, 134.6 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 163.5. HR-MS (ESI): *m/z* calcd for $C_{35}H_{40}F_2NO_3$ $[M+H]^+$: 560.29763; found: 560.29689.

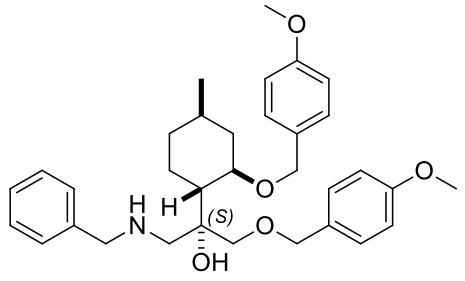
**(*R*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (47b)**




**47b**

Prepared with **32b** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 72%, colourless oil. $[\alpha]_D^{20}$ = -102.35 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.77-0.94 (2H, m), 0.91 (3H, d, *J* = 6.2 Hz), 1.10-1.18 (1H, m), 1.30-1.40 (1H, m), 1.54 (1H, d, *J* = 12.8 Hz), 1.65 (1H, dd, *J* = 12.9, 2.6 Hz), 1.88 (1H, td, *J* = 12.5, 2.5 Hz), 2.16 (1H, d, *J* = 12.0 Hz), 2.17 (2H, d, *J* = 13.9 Hz), 3.42 (1H, dd, *J* = 15.5, 9.4 Hz), 3.63 (1H, td, *J* = 10.5, 3.4 Hz), 4.12 (1H, d, *J* = 10.8 Hz), 4.20 (2H, q, *J* = 13.2 Hz), 4.21 (2H, q, *J* = 11.8 Hz), 4.50 (1H, d, *J* = 10.7 Hz), 5.07 (1H, brs), 6.97 (4H, q, *J* = 9.0 Hz), 7.16 (2H, t, *J* = 7.5 Hz), 7.22 (2H, t, *J* = 7.4 Hz), 7.37 (1H, t, *J* = 7.6 Hz), 7.42-7.49 (3H, m), 7.73 (1H, d, *J* = 8.0 Hz), 7.82 (1H, t, *J* = 8.5 Hz), 8.21 (1H, d, *J* = 8.6 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.7, 40.2, 48.1, 52.4, 54.5, 69.3, 73.1, 74.3, 76.3, 81.2, 115.2 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 115.4 (d, $^2J_{C\text{-}F}$ = 21.5 Hz) , 124.5, 125.4, 125.6, 125.8, 126.1, 127.7, 128.6, 129.6 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.8 (d, $^2J_{C\text{-}F}$ = 8.1 Hz), 132.2, 133.7 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 134.0, 134.3 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 136.5, 163.4 (d, $^1J_{C\text{-}F}$ = 244.4 Hz), 163.5 (d, $^1J_{C\text{-}F}$ = 244.5 Hz). HR-MS (ESI): *m/z* calcd for $C_{35}H_{40}F_2NO_3$ $[M+H]^+$: 560.29763; found: 560.29686.

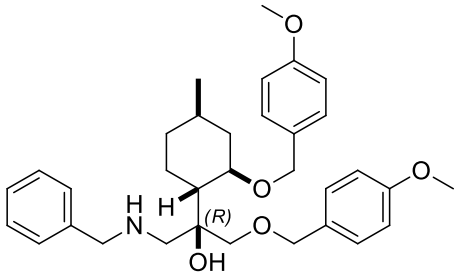
**(*S*)-1-(Benzylamino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (50a)**




**50a**

Prepared with **33a** and benzylamine at reflux temperature for 8 h. Yield: 80%, colourless oil. $[\alpha]_D^{20}$ = +1.74 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-0.98 (4H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.30-1.40 (1H, m), 1.60 (1H, d, *J* = 11.9 Hz), 1.76 (1H, dd, *J* = 12.4, 2.7 hz), 1.88 (1H, td, *J* = 10.8, 3.2 Hz), 2.21 (1H, d, *J* = 13.5 Hz), 2.64 (2H, t, *J* = 12.5 Hz), 3.37 (1H, d, *J* = 10.0 Hz), 3.51 (1H, d, *J* = 10.0 Hz), 3.60 (1H, td, *J* = 10.7, 4.0 Hz), 3.70 (2H, t, *J* = 15.3 Hz), 3.78 (3H, s), 3.79 (3H, s), 4.16 (1H, d, *J* = 10.7 Hz), 4.37 (1H, d, *J* = 11.6 Hz), 4.53 (2H, d, *J* = 10.8 Hz), 6.83 (4H, t, *J* = 9.0 Hz), 7.12 (2H, d, *J* = 8.5 Hz), 7.21-7.28 (7H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.5, 29.8, 31.6, 34.7, 40.3, 48.2, 53.7, 54.3, 55.4, 69.7, 73.3, 74.6, 76.3, 80.0, 113.9, 114.1, 127.1, 128.3, 128.5, 129.4, 129.8, 130.2, 131.0, 159.3, 159.5. HR-MS (ESI): *m/z* calcd for $C_{33}H_{44}NO_5$ $[M+H]^+$: 534.32195; found: 534.32300.

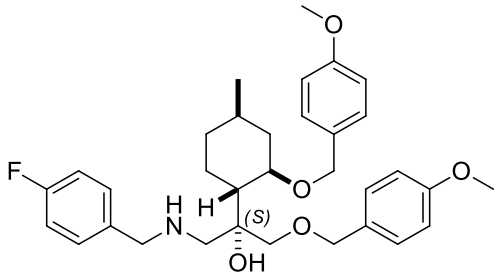
**(*R*)-1-(Benzylamino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (50b)**



**50b**

Prepared with **33b** and benzylamine at reflux temperature for 8 h. Yield: 64%, colourless oil. $[\alpha]_D^{20}$ = +0.50 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.85-0.96 (3H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.14-1.27 (1H, m), 1.30-1.40 (1H, m), 1.60 (1H, d, *J* = 12.5 Hz), 1.69 (1H, dd, *J* = 13.1, 3.2 Hz), 1.85 (1H, td, *J* = 12.8, 3.2 Hz), 2.19 (1H, d, *J* = 13.5 Hz), 2.61 (2H, s), 3.41 (2H, s), 3.63 (1H, td, *J* = 10.5, 3.9 Hz), 3.72 (1H, d, *J* = 13.6 Hz), 3.75-3.82 (2H, m), 3.78 (3H, s), 3.79 (3H, s), 4.12 (1H, d, *J* = 10.5 Hz), 4.35 (1H, d, *J* = 11.6 Hz), 4.42 (1H, d, *J* = 11.6 Hz), 4.49 (1H, d, *J* = 10.5 Hz), 6.84 (4H, q, *J* = 8.6 Hz), 7.16 (2H, d, *J* = 8.5 Hz), 7.22 (2H, d, *J* = 8.5 Hz), 7.29 (4H, t, *J* = 6.8 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.9, 40.2, 48.3, 54.2, 55.4, 69.7, 73.4, 74.1, 76.2, 80.9, 113.8, 114.0, 126.8, 128.2, 128.3, 129.6, 129.8. HR-MS (ESI): *m/z* calcd for $C_{33}H_{44}NO_5$ $[M+H]^+$: 534.32195; found: 534.32316.

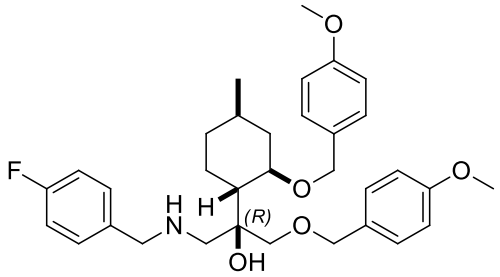
**(*S*)-1-((4-Fluorobenzyl)amino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (51a)**



**51a**

Prepared with **33a** and *p*-fluorobenzylamine at reflux temperature for 8 h. Yield: 78%, colourless oil. $[\alpha]_D^{20}$ = +10.00 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.81-0.99 (4H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.30-1.40 (1H, m), 1.60 (1H, d, *J* = 12.5 Hz), 1.76 (1H, dd, *J* = 12.5, 2.8 Hz), 1.89 (1H, td, *J* = 11.3, 3.0 Hz), 2.21 (1H, d, *J* = 12.2 Hz), 2.54 (2H, s), 3.36 (1H, d, *J* = 10.1 Hz), 3.48 (1H, t, *J* = 5.4 Hz), 3.58-3.66 (3H, m), 3.78 (3H, s), 3.79 (3H, s), 4.18 (1H, d, *J* = 10.8 Hz), 4.37 (1H, d, *J* = 11.8 Hz), 4.54 (1H, d *J* = 11.8 Hz), 4.56 (1H, d, *J* = 10.8 Hz), 6.83 (4H, t, *J* = 7.7 Hz), 6.95 (2H, t, *J* = 8.7 Hz), 7.13 (2H, d, *J* = 8.5 Hz), 7.21 (4H, t, *J* = 8.4 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.6, 31.6, 34.8, 40.3, 48.1, 53.5, 53.8, 55.4, 69.6, 73.3, 74.6, 80.0, 113.9, 114.0, 115.2 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 129.4, 129.6 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 129.7, 130.2. HR-MS (ESI): *m/z* calcd for $C_{33}H_{43}FNO_5$ $[M+H]^+$: 552.31253; found: 552.31319.

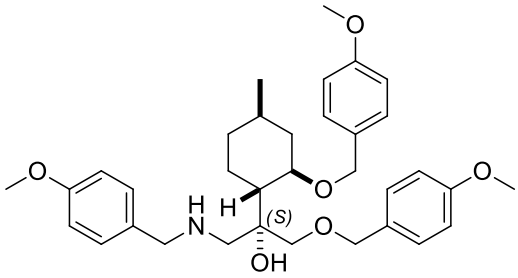
**(*R*)-1-((4-Fluorobenzyl)amino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (51b)**



**51b**

Prepared with **33b** and *p*-fluorobenzylamine at reflux temperature for 8 h. Yield: 78%, colourless oil. $[\alpha]_D^{20}$ = -12.37 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-0.96 (4H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.14-1.25 (1H, m), 1.30-1.45 (1H, m), 1.65 (1H, dd, *J* = 13.1, 3.3 Hz), 1.84 (1H, td, *J* = 12.7, 3.2 Hz), 2.18 (1H, d, *J* = 12.3 Hz), 2.58 (2H, s), 3.62 (1H, td, *J* = 10.7, 3.9 Hz), 3.67 (1H, d, *J* = 13.5 Hz), 3.76 (1H, d, *J* = 13.4 Hz), 3.78 (3H, s), 3.79 (3H, s), 3.80 (1H, d, *J* = 11.3 Hz), 4.12 (1H, d, *J* = 10.5 Hz), 4.35 (1H, d, *J* = 11.6 Hz), 4.42 (1H, d, *J* = 11.6 Hz), 4.49 (1H, d, *J* = 10.5 Hz), 6.82-6.87 (4H, m), 6.95 (2H, t, *J* = 8.7 Hz), 7.16 (2H, d, *J* = 8.5 Hz), 7.21-7.26 (4H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.9, 40.2, 48.3, 53.5, 54.2, 55.4, 69.7, 73.4, 73.9, 76.2, 80.8, 113.8, 114.0, 115.0 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 129.6, 129.7, 129.8, 130.1, 130.7, 159.3. HR-MS (ESI): *m/z* calcd for $C_{33}H_{43}FNO_5$ $[M+H]^+$: 552.31253; found: 552.31392.

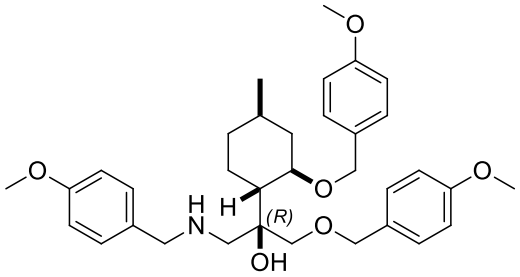
**(*S*)-1-((4-Methoxybenzyl)amino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (52a)**



**52a**

Prepared with **33a** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 89%, colourless oil. $[\alpha]_D^{20}$ = +14.17 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-0.98 (5H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.18-1.22 (1H, m), 1.31-1.36 (1H, m), 1.60 (1H, d, *J* = 12.6 Hz), 1.77 (1H, dd, *J* = 12.7, 3.1 Hz), 1.87 (1H, td, *J* = 10.7, 8.6 Hz), 2.12-2.31 (4H, m), 2.59 (2H, q, *J* = 11.5 Hz), 3.36 (1H, d, *J* = 10.1 Hz), 3.48 (1H, d, *J* = 10.1 Hz), 3.58-3.63 (3H, m), 3.76 (3H, s), 3.77 (3H, s), 3.78 (3H, s), 4.16 (1H, d, *J* = 10.7 Hz), 4.37 (1H, d, *J* = 11.8 Hz), 4.52 (1H, d, *J* = 2.0 Hz), 4.54 (1H, d, *J* = 3.2 Hz), 6.80-6.85 (6H, m), 7.12 (2H, d, *J* = 8.5 Hz), 7.16 (2H, d, *J* = 8.5 Hz), 7.21 (2H, d, *J* = 8.5 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.5, 29.8, 31.6, 34.8, 40.3, 48.1, 53.5, 53.9, 55.4, 76.4, 80.1, 113.9, 113.9, 114.1, 129.4, 129.5, 129.8, 130.2, 131.1. HR-MS (ESI): *m/z* calcd for $C_{34}H_{46}NO_6$ $[M+H]^+$: 564.33251; found: 564.33265.

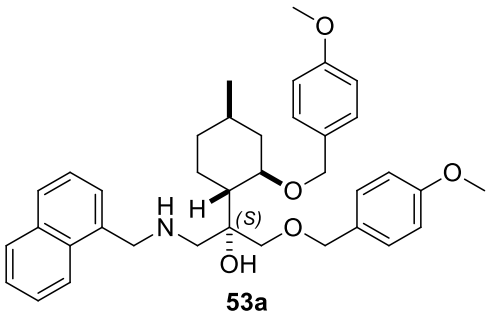
**(*R*)-1-((4-Methoxybenzyl)amino)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (52b)**



**52b**

Prepared with **33b** and *p*-methoxybenzylamine at reflux temperature for 8 h. Yield: 92%, colourless oil. $[\alpha]_D^{20}$ = +18.72 (c 0.25, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.79-0.95 (7H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.13-1.37 (4H, m), 1.60 (1H, d, *J* = 12.9 Hz), 1.68-1.82 (1H, m), 1.79-1.85 (1H, m), 2.16-2.31 (2H, m), 2.62 (2H, s), 3.42 (2H, q, *J* = 9.6 Hz), 3.62 (1H, td, *J* = 10.5, 3.9 Hz), 3.70 (2H, q, *J* = 13.2 Hz), 3.77 (6H, d), 3.78 (3H, s), 4.13 (1H, d, *J* = 10.5 Hz), 4.35 (1H, d, *J* = 11.6 Hz), 4.41 (1H, d, *J* = 11.6 Hz), 4.49 (1H, d, *J* = 10.5 Hz), 6.80-6.86 (6H, m), 7.14-7.22 (6H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.4, 31.5, 34.9, 40.3, 48.4, 53.6, 54.1, 55.4, 69.8, 73.4, 74.3, 76.0, 80.8, 129.4, 129.6, 129.8, 130.2, 130.8, 158.8, 159.4, 159.5. HR-MS (ESI): *m/z* calcd for $C_{34}H_{46}NO_6$ $[M+H]^+$: 564.33251; found: 564.33269.

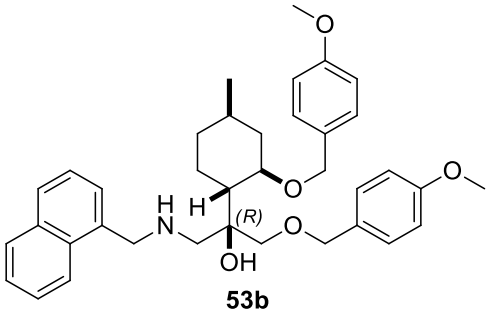
**(*S*)-1-((4-Methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (53a)**



**53a**

Prepared with **33a** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 88%, colourless oil. $[\alpha]_D^{20}$ = +20.65 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.83-1.00 (3H, m), 0.91 (3H, d, *J* = 6.5 Hz), 1.25-1.34 (1H, m), 1.58 (1H, d, *J* = 12.5 Hz), 1.73 (1H, dd, *J* = 12.7, 3.0 Hz), 1.88 (1H, td, *J* = 11.6, 2.9 Hz), 2.15 (1H, dd, *J* = 16.0, 4.3 Hz), 2.68 (2H, s), 3.36 (1H, d, *J* = 10.1 Hz), 3.47 (1H, d, *J* = 10.2 Hz), 3.60 (1H, td, *J* = 10.6, 3.8 Hz), 3.73 (3H, s), 3.78 (3H, s), 3.97 (1H, d, *J* = 10.6 Hz), 4.13 (2H, s), 4.35 (1H, d, *J* = 11.8 Hz), 4.43 (1H, d, *J* = 10.7 Hz), 4.53 (1H, d, *J* = 11.8 Hz), 6.72 (2H, d, *J* = 8.5 Hz), 6.82 (2H, d, *J* = 8.5 Hz), 6.96 (2H, d, *J* = 8.5 Hz), 7.20 (2H, d, *J* = 8.5 Hz), 7.37-7.42 (2H, m), 7.45-7.50 (2H, m), 7.74 (1H, d, *J* = 7.8 Hz), 7.84 (1H, dd, *J* = 6.9, 3.0 Hz). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.6, 31.5, 34.7, 40.2, 47.9, 52.3, 53.8, 55.3, 55.4, 69.5, 73.2, 74.5, 80.0, 113.8, 113.9, 124.2, 125.4, 125.7, 126.0, 128.8, 129.4, 129.8, 130.0, 134.0, 159.2, 159.4. HR-MS (ESI): *m/z* calcd for $C_{37}H_{46}NO_5$ $[M+H]^+$: 584.33760; found: 584.33873.

**(*R*)-1-((4-Methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)-3-((naphthalen-1-ylmethyl)amino)propan-2-ol (53b)**



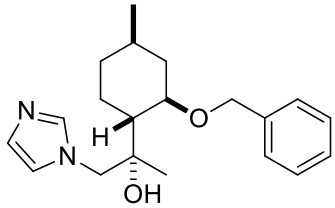
**53b**

Prepared with **33b** and 1-naphthylmethylamine at reflux temperature for 8 h. Yield: 73%, colourless oil. $[\alpha]_D^{20}$ = +1.78 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.78-0.93 (2H, m), 0.91 (3H, d, *J* = 6.5 Hz), 1.15-1.21 (1H, m), 1.30-1.36 (1H, m), 1.64-1.68 (1H, m), 1.86 (1H, td, *J* = 12.7, 3.2 Hz), 2.15-2.20 (1H, m), 2.73 (2H, s), 3.41 (2H, s), 3.62 (1H, td, *J* = 10.7, 3.9 Hz), 3.76 (3H, s), 3.78 (3H, s), 4.12 (1H, d, *J* = 10.5 Hz), 4.16 (1H, d, *J* = 13.1 Hz), 4.23 (1H, d, *J* = 13.2 Hz), 4.33 (1H, d, *J* = 11.6 Hz), 4.40 (1H, d, *J* = 11.6 Hz), 4.47 (1H, d, *J* = 10.5 Hz), 6.80-6.85 (4H, m), 7.13 (2H, d, *J* = 8.6 Hz), 7.19 (2H, d, *J* = 8.5 Hz), 7.37 (1H, t, *J* = 8.0 Hz), 7.42-7.47 (3H, m), 7.72 (1H, d, *J* = 8.1 Hz), 7.80-7.83 (1H, m), 8.19-8.22 (1H, m). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.3, 26.5, 31.5, 34.9, 40.3, 48.3, 52.4, 54.7, 55.4, 69.8, 73.4, 74.2, 80.9, 113.9, 114.1, 124.6, 125.4, 125.6, 125.8, 127.6, 128.6, 129.5, 129.7, 134.0. HR-MS (ESI): *m/z* calcd for $C_{37}H_{46}NO_5$ $[M+H]^+$: 584.33760; found: 584.33901.

## 2.4. General procedure for ring-opening of epoxide with azoles

A solution of epoxides (2.9 mmol) in dry DMF (30 mL) was added to the azoles (8.7 mmol) in dry DMF (10 mL) and $K_2CO_3$ (14.5 mmol). The mixture was kept at reflux temperature for 48–96 h. When the reaction was completed (indicated by TLC), the mixture was dissolved in water (15 mL) and extracted with EtOAc (3 × 50 mL). The combined organic phase was again extracted with saturated NaCl solution (3 × 50 mL), then dried ($Na_2SO_4$), filtered and concentrated. The crude product was purified by column chromatography on silica gel with $CHCl_3$:MeOH = 19:1, resulting in *O*-benzyl derivatives.

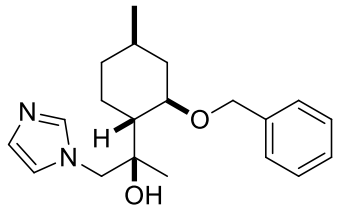
**(*S*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-(1*H*-imidazol-1-yl)propan-2-ol (14a)**



**14a**

Prepared with **3a** and imidazole at reflux temperature for 96 h. Yield: 58%, white crystal. All physical properties and spectroscopic data of compound **14a** were consistent with the literature data.[4]

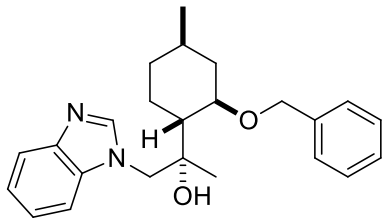
**(*R*)-2-((1*R*,2*R*,4*R*)-2-(Benzyloxy)-4-methylcyclohexyl)-1-(1*H*-imidazol-1-yl)propan-2-ol (14b)**




**14b**

Prepared with **3b** and imidazole at reflux temperature for 96 h. Yield: 38%, colourless oil. All physical properties and spectroscopic data of compound **14b** were consistent with the literature data.[4]

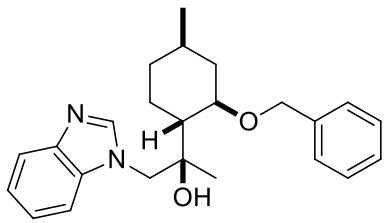
**(*S*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (15a)**




**15a**

Prepared with **3a** with benzimidazole at reflux temperature for 96 h. Yield: 71%, colourless oil. $[\alpha]_D^{20}$ = -20.13 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.75-0.80 (1H, m), 0.91 (3H, d, *J* = 6.4 Hz), 0.92-0.97 (1H, m), 1.02-1.14 (1H, m), 1.12 (3H, s), 1.35-1.47 (1H, m), 1.50-1.55 (1H, m), 1.60-1.70 (2H, m), 1.84 (1H, dd, *J* = 13.0, 2.8 Hz), 2.24 (1H, d, *J* = 12.2 Hz), 3.61 (1H, td, *J* = 10.4, 3.5 Hz), 4.03 (1H, d, *J* = 14.3 Hz), 4.11 (1H, d, *J* = 14.3 Hz), 4.39 (1H, d, *J* = 11.1 Hz), 4.67 (1H, d, *J* = 11.1 Hz), 5.50 (1H, s), 7.23-7.40 (8H, m), 7.79 (1H, d, *J* = 7.5 Hz), 8.19 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.5, 22.0, 27.5, 31.4, 34.0, 39.5, 48.0, 53.2, 70.2, 75.4, 80.3, 110.1, 120.3, 121.7, 122.6, 128.4, 128.8, 135.2, 137.1, 143.3, 145.2. HR-MS (ESI): *m/z* calcd for $C_{24}H_{31}N_2O_2$ $[M+H]^+$: 379.23855; found:379.23728.

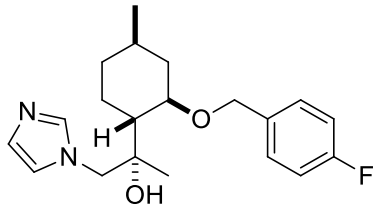
**(*R*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (15b)**




**15b**

Prepared with **3b** with benzimidazole at reflux temperature for 96 h. Yield: 28%, colourless oil. $[\alpha]_D^{20}$ = -45.89 (c 0.19, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.92 (3H, s), 0.99 (3H, d, *J* = 6.4 Hz), 0.97-1.06 (2H, m), 1.13-1.23 (1H, m), 1.40-1.52 (1H, m), 1.67 (1H, brs), 1.73-1.82 (2H, m), 1.97 (1H, dd, *J* = 12.9, 2.9 Hz), 2.32 (1H, d, *J* = 12.1 Hz), 3.53 (1H, td, *J* = 10.5, 3.5 Hz), 3.99 (1H, d, *J* = 14.3 Hz), 4.11 (1H, d, *J* = 14.3 Hz), 4.25 (1H, d, *J* = 11.1 Hz), 4.75 (1H, d, *J* = 11.1 Hz), 4.80 (1H, s), 7.16-7.40 (8H, m), 7.77 (1H, d, *J* = 7.8 Hz), 7.89 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 24.3, 27.2, 31.5, 34.6, 39.2, 51.5, 51.7, 70.2, 75.5, 80.5, 110.3, 120.3, 121.8, 122.8, 128.5, 128.6, 129.0, 135.1, 137.3, 143.4, 144.9. HR-MS (ESI): *m/z* calcd for $C_{24}H_{31}N_2O_2$ $[M+H]^+$: 379.23855; found: 379.23700.

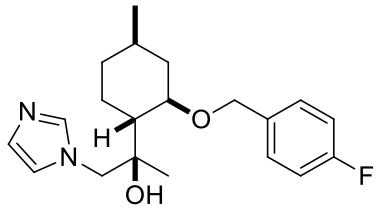
**(*S*)-2-((1R,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-1-(1*H*-imidazol-1-yl)propan-2-ol (20a)**



**20a**

Prepared with **4a** with imidazole at reflux temperature for 96 h. Yield: 58%, colourless oil. $[\alpha]_D^{20}$ = +12.76 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.83-0.90 (1H, m), 0.93 (3H, d, *J* = 6.3 Hz), 0.95-1.06 (2H, m), 1.09 (3H, s), 1.32-1.42 (2H, m), 1.66 (1H, d, *J* = 13.1 Hz), 1.75 (1H, dd, *J* = 13.0, 2.8 Hz), 2.22 (1H, d, *J* = 12.2 Hz), 3.58 (1H, td, *J* = 10.4, 3.6 Hz), 3.79 (1H, d, *J* = 14.2 Hz), 3.90 (1H, d, *J* = 14.2 Hz), 4.36 (1H, d, *J* = 11.0 Hz), 4.64 (1H, d, *J* = 11.0 Hz), 5.40 (1H, s), 7.00-7.07 (4H, m), 7.26-7.29 (2H, m), 7.54 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.6, 22.0, 27.4, 31.4, 33.9, 39.5, 47.1, 55.4, 69.5, 74.8, 80.4, 115.7 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 121.0, 128.5, 130.2 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 133.0 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 138.7, 163.7. HR-MS (ESI): *m/z* calcd for $C_{20}H_{28}FN_2O_2$ $[M+H]^+$: 347.21348; found: 347.21229.

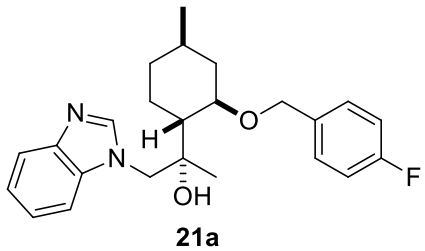
**(*R*)-2-((1*R*,2*R*,4*R*)-2-((4-Fluorobenzyl)oxy)-4-methylcyclohexyl)-1-(1*H*-imidazol-1-yl)propan-2-ol (20b)**



**20b**

Prepared with **4b** with imidazole at reflux temperature for 96 h. Yield: 25%, colourless oil. $[\alpha]_D^{20}$ = +53.38 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.93-1.01 (1H, m), 0.96 (3H, s), 0.97 (3H, d, *J* = 6.2 Hz), 1.03-1.15 (1H, m), 1.37-1.49 (1H, m), 1.65-1.75 (2H, m), 0.89 (1H, dd, *J* = 12.9, 3.0 Hz), 2.26 (1H, d, *J* = 12.2 Hz), 3.35 (1H, td, *J* = 10.5, 3.6 Hz), 3.85 (1H, d, *J* = 14.0 Hz), 3.91 (1H, d, *J* = 13.9 Hz), 4.22 (1H, d, *J* = 11.0 Hz), 4.66 (1H, d, *J* = 11.0 Hz), 6.96 (1H, s), 7.05 (3H, t, *J* = 8.4 Hz), 7.29-7.33 (2H, m), 7.52 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 24.4, 27.1, 31.5, 34.5, 39.9, 51.3, 54.2, 69.4, 74.7, 80.5, 115.8 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 121.1, 128.3, 130.1 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 133.2 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 138.4, 163.7 (d, $^1J_{C\text{-}F}$ = 245.7 Hz). HR-MS (ESI): *m/z* calcd for $C_{20}H_{28}FN_2O_2$ $[M+H]^+$: 347.21348; found: 347.21223.

**(*S*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (21a)**

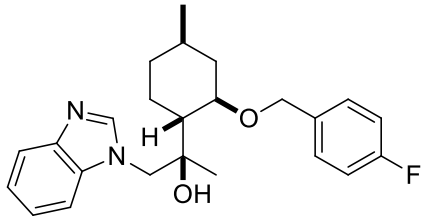


**21a**

Prepared with **4a** with benzimidazole at reflux temperature for 96 h. Yield: 71%, colourless oil. $[\alpha]_D^{20}$ = +30.84 (c 0.25, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.72-0.82 (1H, m), 0.91 (3H, d, *J* = 6.6 Hz), 0.90-0.97 (1H, m),

1.06-1.15 (1H, m), 1.12 (3H, s), 1.38-1.47 (1H, m), 1.49-1.55 (1H, m), 1.60-1.68 (2H, m), 1.85 (1H, dd, *J* = 13.0, 3.0 Hz), 2.22 (1H, d, *J* = 12.1 Hz), 3.60 (1H, td, *J* = 10.5, 3.8 Hz), 4.03 (1H, d, *J* = 14.3 Hz), 4.11 (1H, d, *J* = 14.3 Hz), 4.36 (1H, d, *J* = 11.0 Hz), 4.63 (1H, d, *J* = 11.0 Hz), 5.44 (1H, s), 7.02 (2H, t, *J* = 8.5 Hz), 7.22-7.27 (4H, m), 7.39 (1H, d, *J* = 7.6 Hz), 7.79 (1H, d, *J* = 7.2 Hz), 8.18 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.6, 22.0, 27.5, 31.4, 34.0, 39.5, 47.9, 53.2, 69.4, 75.5, 80.4, 110.1, 115.7 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 120.3, 121.8, 122.7, 130.2 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 132.9 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 135.2, 143.3, 145.2, 163.7. HR-MS (ESI): *m/z* calcd for $C_{24}H_{30}FN_2O_2$ $[M+H]^+$: 397.22913; found: 379.22798.

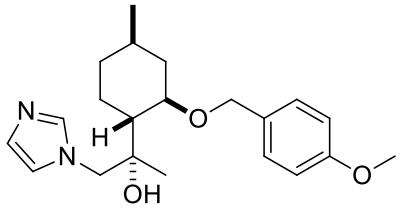
**(*R*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (21b)**




**21b**

Prepared with **4b** with benzimidazole at reflux temperature for 96 h. Yield: 36%, colourless oil. $[\alpha]_D^{20}$ = +4.67 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.95-1.03 (2H, m), 0.98 (3H, s), 0.99 (3H, d, *J* = 4.2 Hz), 1.16-1.25 (1H, m), 1.40-1.50 (1H, m), 1.65 (1H, brs, 1.72-1.79 (2H, m), 1.98 (1H, dd, *J* = 13.0, 3.0 Hz), 2.27 (1H, d, *J* = 12.0 Hz), 3.47 (1H, td, *J* = 10.5, 3.6 Hz), 4.09-4.17 (3H, m), 4.65 (1H, d, *J* = 10.9 Hz), 4.78 (1H, s), 7.06 (2H, t, *J* = 8.5 Hz), 7.18-7.31 (5H, m), 7.78 (1H, d, *J* = 7.7 Hz), 7.97 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 24.6, 27.2, 31.5, 34.6, 39.9, 51.6, 51.7, 69.4, 75.6, 80.8, 110.4, 115.8 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 120.4, 121.9, 122.8, 130.1 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 133.2 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 135.2, 143.4, 144.8, 163.7 (d, $^1J_{C\text{-}F}$ = 245.8 Hz). HR-MS (ESI): *m/z* calcd for $C_{24}H_{30}FN_2O_2$ $[M+H]^+$: 397.22913; found: 397.22779.

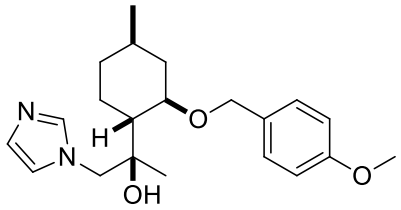
**(*S*)-1-(1*H*-Imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (26a)**




**26a**

Prepared with **5a** with imidazole at reflux temperature for 96 h. Yield: 50%, colourless oil. $[\alpha]_D^{20}$ = +133.40 (c 0.20 MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.72-0.80 (1H, m), 0.85 (3H, d, *J* = 6.7 Hz), 0.88-0.98 (1H, m), 0.99 (3H, s), 1.22-1.34 (2H, m), 1.58 (1H, d, *J* = 12.9 Hz), 1.65 (1H, dd, *J* = 13.0, 2.8 Hz), 2.16 (1H, d, *J* = 12.3 Hz), 3.49 (1H, td, *J* = 10.4, 3.6 Hz), 3.71 (1H, d, *J* = 14.2 Hz), 3.72 (3H, s), 3.81 (1H, d, *J* = 14.2 Hz), 4.25 (1H, d, *J* = 10.8 Hz), 4.54 (1H, d, *J* = 10.8 Hz), 5.45 (1H, brs), 6.80 (2H, d, *J* = 8.2 Hz), 6.93 (1H, s), 6.98 (1H, s), 7.15 (2H, d, *J* = 8.2 Hz), 7.48 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.5, 22.0, 27.4, 31.4, 33.9, 39.4, 47.0, 55.4, 55.5, 69.7, 74.8, 79.8, 114.2, 121.0, 128.3, 129.2, 130.1, 138.6, 159.7. HR-MS (ESI): *m/z* calcd for $C_{21}H_{31}N_2O_3$ $[M+H]^+$: 359.23347; found: 359.23230.

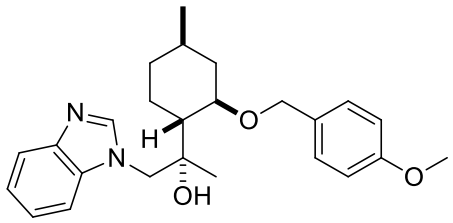
**(*R*)-1-(1*H*-Imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (26b)**



**26b**

Prepared with **5b** with imidazole at reflux temperature for 96 h. Yield: 25%, colourless oil. $[\alpha]_D^{20}$ = +100.52 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.92 (3H, s), 0.92-0.95 (1H, m), 0.97 (3H, d, *J* = 6.7 Hz), 0.95-1.05 (2H, m), 1.37-1.49 (1H, m), 1.64-1.74 (2H, m), 1.87 (1H, dd, *J* = 12.8, 3.2 Hz), 3.28 (1H, d, *J* = 12.2 Hz), 3.39 (1H, td, *J* = 10.5, 3.7 Hz), 3.78 (3H, s), 3.79 (2H, s), 4.24 (1H, d, *J* = 10.9 Hz), 4.66 (1H, d, *J* = 11.0 Hz), 6.89 (2H, d, *J* = 8.4 Hz), 6.94 (1H, s), 7.02 (1H, s), 7.28 (2H, d, *J* = 8.7 Hz), 7.47 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 24.2, 27.1, 31.5, 34.6, 39.9, 51.4, 54.0, 55.5, 69.6, 74.7, 79.7, 114.3, 121.1, 128.1, 129.3, 130.1, 138.5, 159.8. HR-MS (ESI): *m/z* calcd for $C_{21}H_{31}N_2O_3$ $[M+H]^+$: 359.23347; found: 359.23226.

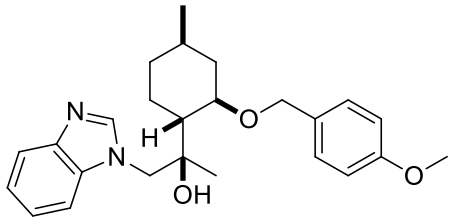
**(*S*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (27a)**



**27a**

Prepared with **5a** with benzimidazole at reflux temperature for 96 h. Yield: 43%, colourless oil. $[\alpha]_D^{20}$ = +124.00 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.82-0.80 (1H, m), 0.88-0.96 (1H, m), 0.91 (3H, d, *J* = 6.3 Hz), 1.06-1.14 (1H, m), 1.10 (3H, s), 1.35-1.45 (1H, m), 1.48-1.53 (1H, m), 1.60-1.70 (2H, m), 1.83 (1H, dd, *J* = 13.0, 2.7 Hz), 2.23 (1H, d, *J* = 12.0 Hz), 3.58 (1H, td, *J* = 10.4, 3.6 Hz), 3.79 (3H, s), 4.02 (1H, d, *J* = 14.3 Hz), 4.10 (1H, d, *J* = 14.3 Hz), 4.32 (1H, d, *J* = 10.8 Hz), 4.60 (1H, d, *J* = 10.8 Hz), 5.55 (1H, s), 6.86 (2H, d, *J* = 8.2 Hz), 7.20-7.26 (4H, m), 7.38 (1H, d, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 7.3 Hz), 8.19 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 21.5, 22.0, 27.5, 31.4, 34.0, 39.5, 48.0, 53.2, 55.4, 69.7, 75.4, 79.9, 110.1, 114.2, 120.3, 121.7, 122.6, 129.2, 130.1, 135.2, 143.3, 145.2, 159.7. HR-MS (ESI): *m/z* calcd for $C_{25}H_{33}N_2O_3$ $[M+H]^+$: 409.24912; found:409.24803.

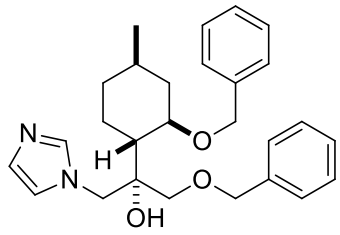
**(*R*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (27b)**



**27b**

Prepared with **5b** with benzimidazole at reflux temperature for 96 h. Yield: 28%, colourless oil. $[\alpha]_D^{20}$ = +109.23 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.92 (3H, s), 0.94-1.05 (2H, m), 0.99 (3H, d, *J* = 6.6 Hz), 1.13-1.21 (1H, m), 1.40-1.55 (1H, m), 1.64 (1H, s), 1.71-1.79 (2H, m), 1.96 (1H, dd, *J* = 12.9, 2.9 Hz), 2.32 (1H, d, *J* = 11.9 Hz), 3.51 (1h, td, *J* = 10.5, 3.5 Hz), 3.77 (3H, s), 4.99 (1H, d, *J* = 14.3 Hz), 4.10 (1H, d, *J* = 14.3 Hz), 4.19 (1H, d, *J* = 10.9 Hz), 4.69 (1H, d, *J* = 10.9 Hz), 4.87 (1H,s), 6.90 (2H, d, *J* = 8.3 Hz), 7.19-7.29 (5H, m), 7.77 (1H, d, *J* = 7.4 Hz), 7.95 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 24.3, 27.3, 31.5, 34.6, 39.9, 51.4, 51.7, 55.5, 69.7, 80.0, 110.3, 114.3, 120.3, 121.8, 122.7, 129.4, 130.1, 135.1, 143.4, 144.9, 159.9. HR-MS (ESI): *m/z* calcd for $C_{25}H_{33}N_2O_3$ $[M+H]^+$: 409.24912; found:409.24790.

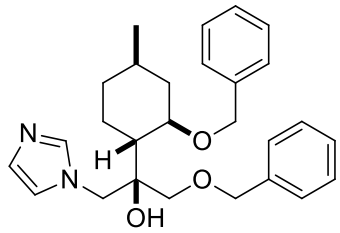
**(*S*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-(1*H*-imidazol-1-yl)propan-2-ol (42a)**




**42a**

Prepared with **31a** and imidazole at reflux temperature for 48 h. Yield: 67%, colourless oil. All physical properties and spectroscopic data of compound **42a** were consistent with the literature data.[4]

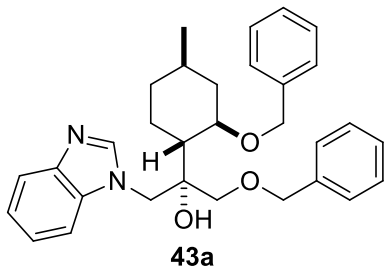
**(*R*)-1-(Benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)-3-(1*H*-imidazol-1-yl)propan-2-ol (42b)**




**42b**

Prepared with **31b** and imidazole at reflux temperature for 48 h. Yield: 83%, colourless oil. All physical properties and spectroscopic data of compound **42b** was consistent with literature data.[4]

**(*S*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-3-(benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (43a)**

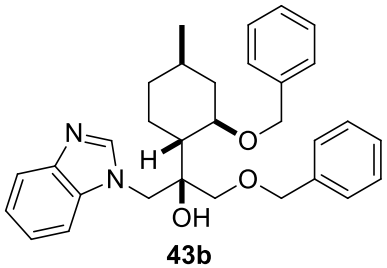



**43a**

Prepared with **31a** and benzimidazole at reflux temperature for 48 h. Yield: 45%, colourless oil. $[\alpha]_D^{20}$ = -32.54 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.84-1.05 (3H, m), 0.98 (3H, d, *J* = 6.3 Hz), 1.16-1.25 (1H, m),

1.40-1.45 (1H, m), 1.73 (1H, d, *J* = 12.8 Hz), 1.92 (1H, td, *J* = 10.3, 2.6 Hz), 2.10 (1H, d, *J* = 13.2 Hz), 2.31 (1H, d, *J* = 12.2 Hz), 3.10 (1H, d, *J* = 9.7 Hz), 3.20 (1H, d, *J* = 9.6 Hz), 3.52 (1H, td, *J* = 10.5, 3.4 Hz), 4.04 (1H, d, *J* = 14.4 Hz), 4.18 (1H, d, *J* = 10.9 Hz), 4.22 (1H, d, *J* = 11.8 Hz), 4.33 (1H, d, *J* = 14.4 Hz), 4.37 (1H, d, *J* = 11.7 Hz), 4.73 (1H, d, *J* = 10.9 Hz), 4.08 (1H, s), 7.06-7.38 (13H, m), 7.75 (1H, d, *J* = 8.0 Hz), 7.91 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.4, 34.7, 40.0, 49.0, 49.3, 70.3, 73.5, 73.6, 76.5, 80.2, 110.8, 120.0, 122.7, 127.9, 128.0, 128.5, 128.9, 135.2, 137.4, 137.8, 143.2, 145.1. HR-MS (ESI): *m/z* calcd for $C_{31}H_{37}N_2O_3$ $[M+H]^+$: 485.28042; found:485.27971.

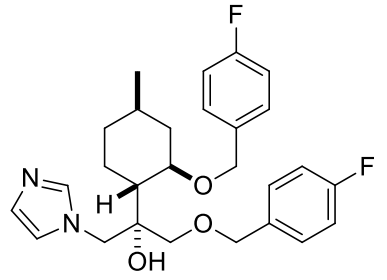
**(*R*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-3-(benzyloxy)-2-((1*R*,2*R*,4*R*)-2-(benzyloxy)-4-methylcyclohexyl)propan-2-ol (43b)**




**43b**

Prepared with **31b** and benzimidazole at reflux temperature for 48 h. Yield: 75%, colourless oil. $[\alpha]_D^{20}$ = -86.15 (c 0.20, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.84 (1H, m), 0.87-0.97 (1H, m), 0.94 (3H, d, *J* = 6.6 Hz), 1.27 (1H, d, *J* = 12.8 Hz), 1.37-1.47 (1H, m), 1.56-1.68 (3H, m), 1.84 (1H, dd, *J* = 12.8, 2.4 Hz), 2.22 (1H, d, *J* = 12.1 Hz), 3.06 (1H, d, *J* = 9.6 Hz), 3.28 (1H, d, *J* = 9.6 Hz), 3.56 (1H, td, *J* = 10.3, 3.6 Hz), 4.10 (2H, d, *J* = 11.8 Hz), 4.22 (1H, d, *J* = 11.7 Hz), 4.43 (1H, d, *J* = 7.1 Hz), 4.46 (1H, d, *J* = 4.5 Hz), 4.54 (1H, d, *J* = 11.0 Hz), 5.03 (1H, s), 7.17-7.45 (13H, m), 7.77 (1H, d, *J* = 8.0 Hz), 8.05 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.3, 34.7, 39.8, 49.5, 49.6, 70.1, 71.6, 73.5, 75.4, 80.5, 110.4, 120.1, 128.1, 128.2, 128.3, 128.4, 128.6, 128.7, 135.4, 137.2, 137.9, 143.3, 145.4. HR-MS (ESI): *m/z* calcd for $C_{31}H_{37}N_2O_3$ $[M+H]^+$: 485.28042; found:485.27975.

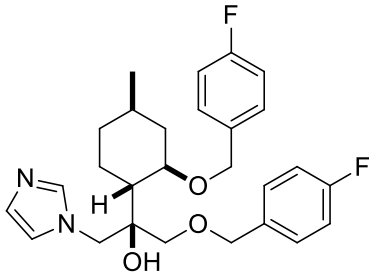
**(*S*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-(1*H*-imidazol-1-yl)propan-2-ol (48a)**




**48a**

Prepared with **32a** and imidazole at reflux temperature for 48 h. Yield: 84%, colourless oil. $[\alpha]_D^{20}$ = -179.71 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.87-1.12 (3H, m), 0.96 (3H, d, *J* = 6.3 Hz), 1.35-1.45 (1H, m), 1.57 (1H, brs), 1.70 (1H, d, *J* = 12.7 Hz), 1.83 (1H, t, *J* = 11.0 Hz), 1.99 (1H, d, *J* = 12.8 Hz), 2.25 (1H, d, *J* = 11.8 Hz), 3.14 (2H, t, *J* = 10.6 Hz), 3.34 (1H, td, *J* = 10.4, 3.3 Hz), 3.89 (1H, d, *J* = 14.0 Hz), 4.06 (1H, d, *J* = 14.0 Hz), 4.19 (1H, d, *J* = 10.9 Hz), 4.31 (1H, d, *J* = 11.7 Hz), 4.40 (1H, d, *J* = 11.7 Hz), 4.63 (1H, d, *J* = 10.9 Hz), 4.84 (1H, s), 6.93 (1H, s), 7.00-7.06 (5H, m), 7.22-7.29 (4H, m), 7.42 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 26.6, 31.4, 34.6, 40.1, 48.8, 51.1, 69.4, 73.0, 73.9, 75.9, 80.1, 115.4 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 121.1, 129.6 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 138.4. HR-MS (ESI): *m/z* calcd for $C_{27}H_{33}F_2N_2O_3$ $[M+H]^+$: 471.24592; found: 471.24490.

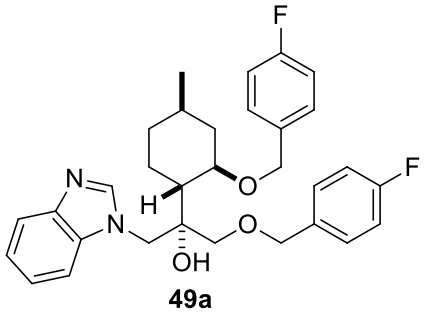
**(*R*)-1-((4-Fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)-3-(1*H*-imidazol-1-yl)propan-2-ol (48b)**




**48b**

Prepared with **32b** and imidazole at reflux temperature for 48 h. Yield: 59%, colourless oil. $[\alpha]_D^{20}$ = -126.73 (c 0.26, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.93 (2H, m), 0.93 (3H, d, *J* = 6.3 Hz), 1.36-1.49 (3H, m), 1.66 (1H, d, *J* = 12.6 Hz), 1.74 (1H, d, *J* = 12.7 Hz), 2.18 (1H, d, *J* = 12.2 Hz), 3.15 (1H, d, *J* = 9.6 Hz), 3.30 (1H, d, *J* = 9.6 Hz), 3.56 (1H, td, *J* = 10.0, 3.4 Hz), 3.95 (1H, d, *J* = 14.1 Hz), 4.09 (1H, d, *J* = 14.1 Hz), 4.16 (1H, d, *J* = 11.0 Hz), 4.33 (1H, d, *J* = 11.8 Hz), 4.46 (1H, d, *J* = 11.8 Hz), 4.54 (1H, d, *J* = 11.0 Hz), 5.14 (1H, s), 7.00-7.06 (6H, m), 7.18 (2H, t, *J* = 6.6 Hz), 7.27 (2H, t, *J* = 6.5 Hz), 7.50 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 20.1, 26.8, 31.5, 34.6, 39.9, 69.4, 72.4, 73.1, 75.5, 80.7, 115.5 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 115.7 (d, $^2J_{C\text{-}F}$ = 20.9 Hz), 121.2, 128.6, 129.8 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 133.1 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 133.7 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 138.9, 163.6 (d, $^1J_{C\text{-}F}$ = 244.9 Hz), 163.7 (d, $^1J_{C\text{-}F}$ = 245.3 Hz). HR-MS (ESI): *m/z* calcd for $C_{27}H_{33}F_2N_2O_3$ $[M+H]^+$: 471.24592; found: 471.24500.

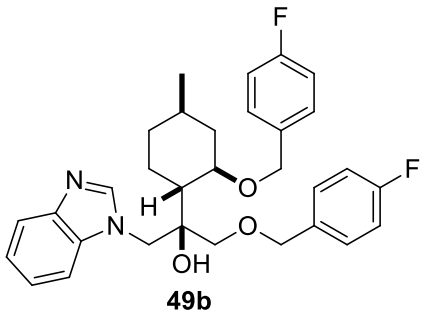
**(*S*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (49a)**




**49a**

Prepared with **32a** and benzimidazole at reflux temperature for 48 h. Yield: 75%, colourless oil. $[\alpha]_D^{20}$ = -141.73 (c 0.22, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.90-1.03 (2H, m), 0.97 (3H, d, *J* = 6.6 Hz), 1.17-1.26 (1H, m), 1.36-1.46 (1H, m), 1.52 (2H, s), 1.74 (1H, d, *J* = 12.8 Hz), 1.91 (1H, t, *J* = 12.6 Hz), 2.08 (1H, dd, *J* = 13.1, 2.6 Hz), 2.27 (1H, d, *J* = 11.0 Hz), 3.12 (1H, d, *J* = 9.7 Hz), 3.22 (1H, d, *J* = 9.7 Hz), 3.47 (1H, d, *J* = 10.4, 3.8 Hz), 4.09 (1H, d, *J* = 10.6 Hz), 4.11 (1H, d, *J* = 14.1 Hz), 4.21 (1H, d, *J* = 11.7 Hz), 4.33 (1H, d, *J* = 5.1 Hz), 4.34 (1H, d, *J* = 10.5 Hz), 4.64 (1H, d, *J* = 10.8 Hz), 4.78 (1H, s), 6.97-7.28 (11H, m), 7.76 (1H, d, *J* = 8.0 Hz), 7.97 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 26.7, 31.4, 34.7, 40.2, 49.1, 49.2, 69.5, 73.0, 73.8, 76.6, 80.4, 110.7, 115.4 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 120.3, 121.9, 122.7, 129.7 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 135.3, 143.5, 145.0. HR-MS (ESI): *m/z* calcd for $C_{31}H_{35}F_2N_2O_3$ $[M+H]^+$: 521.26157; found: 521.26065.

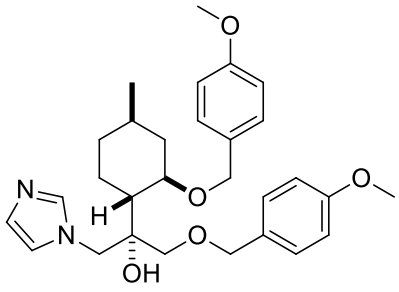
**(*R*)-1-(1*H*-Benzo[*d*]imidazol-1-yl)-3-((4-fluorobenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-fluorobenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (49b)**




**49b**

Prepared with **32b** and benzimidazole at reflux temperature for 48 h. Yield: 65%, colourless oil. $[\alpha]_D^{20}$ = -137.58 (c 0.24, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.83 (1H, m), 0.90-0.97 (1H, m), 0.94 (3H, d, *J* = 6.7 Hz), 0.35-0.45 (1H, m), 1.50-1.60 (2H, m), 1.67 (1H, t, *J* = 12.2 Hz), 1.86 (1H, d, *J* = 13.1 Hz), 2.20 (1H, d, *J* = 12.1 Hz), 3.09 (1H, d, *J* = 9.6 Hz), 3.27 (1H, d, *J* = 9.6 Hz), 3.58 (1H, td, *J* = 10.3, 3.5 Hz), 4.11 (1H, d, *J* = 12.1 Hz), 4.13 (1H, d, *J* = 10.4 Hz), 4.22 (1H, d, *J* = 11.7 Hz), 4.40 (2H, d, *J* = 12.6 Hz), 4.53 (1H, d, *J* = 11.0 Hz), 5.04 (H, s), 6.96-7.26 (10H, m), 7.41 (1H, d, *J* = 7.8 Hz), 7.77 (1H, d, *J* = 7.1 Hz), 8.05 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 26.7, 31.4, 34.7, 39.9, 49.2, 49.7, 69.4, 72.0, 75.7, 80.7, 110.3, 115.6 (t, $^2J_{C\text{-}F}$ = 21.1 Hz), 120.3, 121.8, 122.6, 129.9 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 130.1 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 133.1 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 133.7 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 135.4, 143.5, 145.4. HR-MS (ESI): *m/z* calcd for $C_{31}H_{35}F_2N_2O_3$ $[M+H]^+$: 521.26157; found: 521.26098.

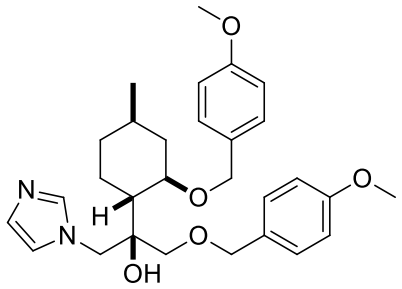
**(*S*)-1-(1*H*-Imidazol-1-yl)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (54a)**




**54a**

Prepared with **33a** and imidazole at reflux temperature for 48 h. Yield: 52%, colourless oil. $[\alpha]_D^{20}$ = +22.66 (c 0.21, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-1.04 (4H, m), 0.95 (3H, d, *J* = 6.6 Hz), 1.35-1.45 (1H, m), 1.60-1.73 (9H, m), 1.79 (1H, td, *J* = 12.6, 3.2 Hz), 1.95-2.02 (1H, m), 2.27 (1H, d, *J* = 11.3 Hz), 3.08 (2H, dd, *J* = 13.5, 9.7 Hz), 3.37 (1H, td, *J* = 10.6, 3.8 Hz), 3.77-3.80 (1H, m), 3.78 (3H, s), 3.80 (3H, s), 4.02 (1H, d, *J* = 14.0 Hz), 4.18 (1H, d, *J* = 10.9 Hz), 4.25 (1H, d, *J* = 11.4 Hz), 4.36 (1H, d, *J* = 11.5 Hz), 4.63 (1H, d, *J* = 10.8 Hz), 4.91 (1H, brs), 6.85-6.91 (5H, m), 6.99 (1H, s), 7.19 (2H, d, *J* = 8.5 Hz), 7.23 (2H, d, *J* = 8.5 Hz), 7.41 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.5, 31.3, 34.6, 40.0, 49.0, 51.0, 55.4, 55.5, 69.6, 73.1, 73.4, 75.7, 79.4, 113.9, 114.3, 129.4, 129.5, 130.1, . HR-MS (ESI): *m/z* calcd for $C_{29}H_{39}N_2O_5$ $[M+H]^+$: 495.28590; found: 495.28616.

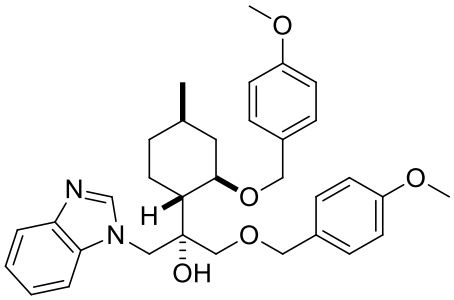
**(*R*)-1-(1*H*-Imidazol-1-yl)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (54b)**



**54b**

Prepared with **33b** and imidazole at reflux temperature for 48 h. Yield: 52%, colourless oil. $[\alpha]_D^{20}$ = +3.52 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.93 (2H, m), 0.92 (3H, d, *J* = 6.5 Hz), 1.36-1.46 (3H, m), 1.62-1.72 (6H, m), 2.19 (1H, dd, *J* = 12.1, 5.2 Hz), 3.08 (1H, d, *J* = 9.6 Hz), 3.28 (1H, d, *J* = 9.6 Hz), 3.52 (1H, td, *J* = 10.1, 3.7 Hz), 3.79 (3H, s), 3.81 (3H, s), 3.93 (1H, d, *J* = 14.1 Hz), 4.08 (1H, d, *J* = 13.4 Hz), 4.11 (1H, d, *J* = 10.4 Hz), 4.28 (1H, d, *J* = 11.6 Hz), 4.42 (1H, d, *J* = 11.6 Hz), 4.50 (1H, d, *J* = 10.8 Hz), 5.20 (1H, s), 6.85 (2H, d, *J* = 8.5 Hz), 6.89 (2H, d, *J* = 8.5 Hz), 6.99 (2H, s), 7.14 (2H, d, *J* = 8.5 Hz), 7.23 (2H, d, *J* = 8.5 Hz), 7.50 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.1, 26.8, 31.4, 34.6, 39.9, 48.0, 52.1, 55.4, 55.5, 69.7, 71.9, 13.2, 75.4, 80.2, 114.0, 114.1, 121.3, 128.4, 129.4, 129.7, 130.0, 130.1, 159.7. HR-MS (ESI): *m/z* calcd for $C_{29}H_{39}N_2O_5$ $[M+H]^+$: 495.28590; found: 495.28611

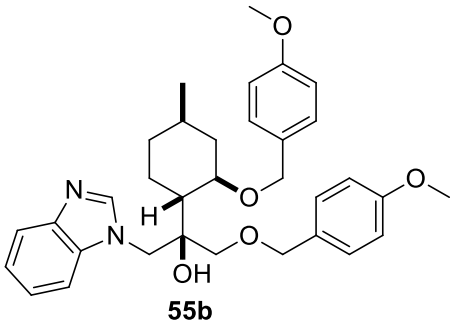
**(*S*)-1-(1*H*-Benzo[d]imidazol-1-yl)-3-((4-methoxybenzyl)oxy)-2-((1R,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (55a)**



**55a**

Prepared with **32a** and benzimidazole at reflux temperature for 48 h. Yield: 78%, colourless oil. $[\alpha]_D^{20}$ = -35.13 (c 0.23, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88-1.03 (2H, m), 0.97 (3H, d, *J* = 6.5 Hz), 1.12-1.20 (1H, m), 1.35-1.45 (1H, m), 1.62 (3H, brs), 1.72 (1H, d, *J* = 12.6 Hz), 1.88 (1H, td, *J* = 12.8, 3.1 Hz), 2.06 (1H, dd, *J* = 13.2, 3.2 Hz), 2.30 (1H, d, *J* = 12.1 Hz), 3.06 (1H, d, *J* = 9.6 Hz), 3.15 (1H, d, *J* = 9.6 Hz), 3.49 (1H, td, *J* = 10.6, 3.8 Hz), 3.78 (3H, s), 3.80 (3H, s), 4.02 (1H, d, *J* = 14.4 Hz), 4.13 (1H, d, *J* = 11.1 Hz), 4.15 (1H, d, *J* = 12.5 Hz), 4.29 (1H, s), 4.31 (1H, d, *J* = 3.7 Hz), 4.67 (1H, d, *J* = 10.7 Hz), 4.84 (1H, s), 6.84 (2H, d, *J* = 8.5 Hz), 6.89 (2H, d, *J* = 8.5 Hz), 7.11-7.24 (6H, m), 7.75 (1H, d, *J* = 8.0 Hz), 7.96 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.4, 34.7, 40.0, 49.0, 49.3, 55.4, 55.5, 69.8, 73.2, 73.3, 76.5, 79.8, 110.9, 113.9, 1144.3, 120.0, 121.8, 122.6, 129.5, 129.6, 130.0, 130.1, 143.3, 145.1, 159.4, 159.8. HR-MS (ESI): *m/z* calcd for $C_{33}H_{41}N_2O_5$ $[M+H]^+$: 545.30155; found: 545.30411.

**(*R*)-1-(1*H*-Benzo[d]imidazol-1-yl)-3-((4-methoxybenzyl)oxy)-2-((1*R*,2*R*,4*R*)-2-((4-methoxybenzyl)oxy)-4-methylcyclohexyl)propan-2-ol (55b)**



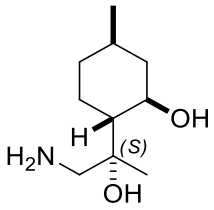
**55b**

Prepared with **33b** and benzimidazole at reflux temperature for 48 h. Yield: 88%, colourless oil. $[\alpha]_D^{20}$ = -12.63 (c 0.27, MeOH). $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.76-0.81 (1H, m), 0.88-0.96 (1H, m), 0.93 (3H, d, *J* = 6.5 Hz), 1.35-1.45 (1H, m), 1.52-1.67 (7H, m), 1.81 (1H, dd, *J* = 12.7, 2.8 Hz), 2.21 (1H, d, *J* = 11.6 Hz), 3.02 (1H, d, *J* = 9.6 Hz), 3.15 (1H, d, *J* = 9.6 Hz), 3.53 (1H, td, *J* = 10.5, 3.8 Hz), 3.77 (3H, s), 3.81 (3H, s), 4.05 (1H, d, *J* = 10.6 Hz), 4.08 (1H, d, *J* = 14.0 Hz), 4.16 (1H, d, *J* = 11.4 Hz), 4.38 (1H, d, *J* = 11.5 Hz), 4.42 (1H, d, *J* = 14.3 Hz), 4.49 (1H, d, *J* = 10.8 Hz), 5.07 (1H, s), 6.82 (2H, d, *J* = 8.5 Hz), 6.90 (2H, d, *J* = 8.5 Hz), 7.11 (2H, d, *J* = 8.5 Hz), 7.21-7.23 (4H, m), 7.43-7.45 (1H, m), 7.76-7.78 (1H, m), 8.05 (1H, s). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 22.2, 26.6, 31.4, 34.7, 39.9, 49.4, 49.7, 55.4, 55.5, 69.7, 71.4, 73.1, 75.4, 80.2, 110.4, 114.0, 114.1, 120.1, 121.7, 122.6, 129.4, 129.8, 130.0, 130.1, 135.4, 143.3, 145.4, 159.5, 159.6. HR-MS (ESI): *m/z* calcd for $C_{33}H_{41}N_2O_5$ $[M+H]^+$: 545.30155; found:545.30328.

### 2.4. General procedure for debenzylation

A suspension of palladium-on-carbon (5% Pd, 0.22 g) in MeOH (50 mL) was added to isopulegol-based benzyl derivatives (14.0 mmol) in MeOH (100 mL), and the mixture was stirred under an $H_2$ atmosphere (1 atm) at room temperature. After completion of the reaction (as monitored by TLC, 24 h), the mixture was filtered through a Celite pad, and the solution was evaporated to dryness. The crude products were recrystallised in diethyl ether, resulting in primary aminodiol **28a** and aminotriols **56a–b**.

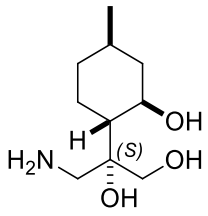
**(1*R*,2*R*,5*R*)-2-((*S*)-1-Amino-2-hydroxypropan-2-yl)-5-methylcyclohexanol (28a)**



**28a**

Prepared with **6a**, **16a** or **22a**. Yield: 85% (with **6a**), 87% (with **16a**), 67% (with **22a**), white crystals. All physical properties and spectroscopic data of compound **28a** were consistent with the literature data.[3]

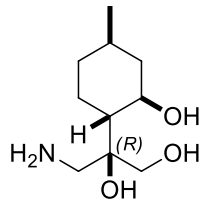
**(*S*)-3-Amino-2-((1*R*,2*R*,4*R*)-2-hydroxy-4-methylcyclohexyl)propane-1,2-diol (56a)**




**56a**

Prepared with **34a**, **44a** or **50a**. Yield: 87% (with **34a**), 82% (with **44a**), 75% (with **50a**), white crystals. All physical properties and spectroscopic data of compound **56a** were consistent with the literature data.[3]

**(*R*)-3-Amino-2-((1*R*,2*R*,4*R*)-2-hydroxy-4-methylcyclohexyl)propane-1,2-diol (56b)**




**56b**

Prepared with **34b**, **44b** or **50b**. Yield: 90% (with **31b**), 87% (with **44b**), 93% (with **39b**), white crystals. All physical properties and spectroscopic data of compound **56b** were consistent with the literature data.[3]

## 3. Antiproliferative effect of *O*-benzyl derivatives

During our antiproliferative work we intended to use a practical investigational approach, therefore, we focused on the present treatment guidelines of gynecological cancers to choose a long time available, well-characterised positive control molecule which is recommended for the therapy of all cancer types included in our experiment (namely, breast, cervical and ovarian cancer). According to the online available guidelines of the European Society of Medical Oncology (ESMO) platinum compounds, like cisplatin, are effective in the clinical treatment of different gynecological cancers.

Platinum-based therapy is still the first-line treatment option in local cervical cancer and it can be beneficial in combination with paclitaxel or topotecan in the therapy of advanced/metastatic cervical cancer.[5] Moreover, patients suffering from either primary (early stage or epithelial form) or recurrent ovarian cancer can be treated with platinum derivatives, in most cases as part of combination chemotherapy.[6] Among numerous different types of breast cancer according to their pathophysiological or developmental origin, for most triple negative breast cancer (defined by the absence of expression of estrogen and progesterone receptors and of overexpression of HER2 or amplification of HER2neu) chemotherapy included platinum derivatives remains the standard treatment.[7] MDA-MB-231 cell line used in our work is an experimentally applicable triple negative breast cancer cell line.

**Table 1.** Antiproliferative activities of the *O,N*-functionalized (−)-isopulegol analogs against cancer cells.

| **Compounds** | Conc. (μM) | Growth inhibition (%) ± SEM [calculated $IC_{50}$ (μM)] | | | |
|---|---|---|---|---|---|
| | | HeLa | MCF7 | MDA-MB-231 | A2780 |
| **2a** | 10 | 35.97 ± 1.04 | - | 21.85 ± 2.86 | - |
| | 30 | 59.57 ± 0.51 | 31.63 ± 2.29 | 86.99 ± 1.44 | 42.94 ± 2.68 |
| **2b** | 10 | - | - | - | - |
| | 30 | - | - | - | - |
| **2c** | 10 | - | - | - | - |
| | 30 | 54.02 ± 2.48 | 37.72 ± 0.91 | - | 28.40 ± 2.78 |
| **6a** | 10 | 97.71 ± 0.29 | 97.61 ± 0.85 | 76.83 ± 1.01 | 91.59 ± 0.40 |
| | 30 | 98.11 ± 0.31 | 98.03 ± 0.46 | 78.91 ± 0.86 | 94.28 ± 0.34 |
| | | **2.84** | **2.30** | **3.42** | **2.62** |
| **7a** | 10 | - | - | - | - |
| | 30 | 60.08 ± 1.04 | 73.75 ± 2.69 | - | 29.83 ± 3.50 |
| | | **24.28** | **20.29** | | |
| **8a** | 10 | 72.48 ± 2.41 | 72.71 ± 1.69 | 41.52 ± 1.43 | 30.63 ± 0.80 |
| | 30 | 98.76 ± 0.32 | 95.61 ± 0.25 | 96.07 ± 0.60 | 98.82 ± 0.59 |
| | | **5.20** | **3.54** | **9.94** | **9.31** |
| **9a** | 10 | 63.73 ± 2.68 | 39.03 ± 1.33 | - | - |
| | 30 | 90.39 ± 1.02 | 89.63 ± 0.72 | 44.06 ± 2.87 | 98.07 ± 0.27 |
| | | **6.51** | **8.57** | | |
| **10a** | 10 | 75.79 ± 1.70 | 92.40 ± 0.86 | 45.67 ± 0.73 | 42.90 ± 2.70 |
| | 30 | 98.88 ± 0.49 | 96.98 ± 1.10 | 83.54 ± 0.96 | 93.87 ± 0.90 |
| | | **4.32** | **1.93** | **5.73** | **7.25** |
| **11a** | 10 | 65.35 ± 2.30 | 76.77 ± 0.93 | 35.98 ± 2.12 | 32.90 ± 1.83 |
| | 30 | 97.90 ± 0.42 | 95.86 ± 1.09 | 95.35 ± 0.33 | 95.34 ± 0.68 |
| | | **6.29** | **1.95** | **11.67** | **12.51** |
| **12a** | 10 | 81.76 ± 1.80 | 46.87 ± 1.33 | - | 58.46 ± 2.64 |
| | 30 | 82.42 ± 0.72 | 98.13 ± 1.01 | 87.58 ± 1.35 | 99.92 ± 0.67 |
| | | **4.59** | **4.20** | **12.78** | **7.39** |
| **13a** | 10 | 67.83 ± 0.99 | 61.46 ± 1.67 | - | 28.27 ± 1.89 |

| | | | | | |
|---|---|---|---|---|---|
| | 30 | 86.85 ± 0.23 | 92.19 ± 0.75 | 60.95 ± 1.76 | 94.20 ± 0.39 |
| | | **5.42** | **4.26** | **24.97** | **13.73** |
| **14a** | 10 | - | - | - | - |
| | 30 | 59.74 ± 1.72 | 34.65 ± 2.39 | - | 39.55 ± 2.33 |
| | | **24.54** | | | |
| **14b** | 10 | - | - | - | - |
| | 30 | 70.80 ± 0.86 | 55.99 ± 3.07 | - | 49.51 ± 1.24 |
| | | **23.20** | | | |
| **15a** | 10 | 32.09 ± 1.25 | 51.01 ± 1.64 | - | 35.21 ± 0.19 |
| | 30 | 89.02 ± 1.63 | 98.28 ± 0.47 | 83.21 ± 2.57 | 98.30 ± 0.15 |
| | | **11.63** | **7.02** | **16.71** | **12.25** |
| **15b** | 10 | 61.57 ± 0.36 | 55.18 ± 0.97 | - | 44.30 ± 1.82 |
| | 30 | 86.34 ± 0.80 | 94.78 ± 1.16 | 80.01 ± 1.34 | 99.15 ± 0.41 |
| | | **6.46** | **9.41** | **27.64** | **10.88** |
| **30a** | 10 | 40.35 ± 0.80 | - | - | - |
| | 30 | 44.53 ± 1.24 | 40.28 ± 1.27 | 28.05 ± 1.92 | 29.67 ± 0.98 |
| **30b** | 10 | 32.83 ± 3.15 | - | - | 24.03 ± 2.30 |
| | 30 | 61.46 ± 1.42 | 46.19 ± 1.04 | 25.03 ± 1.36 | 52.02 ± 2.06 |
| **30c** | 10 | 39.25 ± 0.86 | - | - | - |
| | 30 | 60.57 ± 1.03 | 23.99 ± 1.45 | - | 27.39 ± 3.56 |
| | | **24.74** | | | |
| **34a** | 10 | 99.10 ± 0.14 | 84.11 ± 0.17 | 97.83 ± 0.32 | 90.40 ± 0.17 |
| | 30 | 98.65 ± 0.20 | 83.18 ± 0.19 | 99.31 ± 0.25 | 91.08 ± 0.18 |
| | | **2.57** | **1.99** | **3.98** | **4.06** |
| **34b** | 10 | 97.38 ± 1.07 | 94.76 ± 0.19 | 95.52 ± 0.31 | 99.05 ± 0.23 |
| | 30 | 98.23 ± 0.72 | 96.43 ± 0.39 | 96.96 ± 0.46 | 99.13 ± 0.74 |
| | | **2.27** | **3.69** | **3.40** | **3.26** |
| **35a** | 10 | 53.73 ± 0.81 | 30.16 ± 3.58 | - | 33.67 ± 1.39 |
| | 30 | 98.89 ± 0.08 | 98.59 ± 0.26 | 94.40 ± 0.56 | 99.89 ± 0.61 |
| | | **7.15** | **10.43** | **15.38** | **11.85** |
| **35b** | 10 | 97.65 ± 0.21 | 82.87 ± 0.33 | 94.81 ± 1.14 | 93.37 ± 0.22 |
| | 30 | 97.84 ± 0.20 | 83.56 ± 0.50 | 98.39 ± 0.17 | 93.96 ± 0.34 |
| | | **2.50** | **2.56** | **3.78** | **4.28** |
| **36a** | 10 | 96.68 ± 0.20 | 95.34 ± 0.54 | 95.38 ± 0.59 | 95.02 ± 0.54 |
| | 30 | 96.63 ± 0.12 | 96.18 ± 0.39 | 96.08 ± 0.59 | 95.40 ± 0.54 |
| | | **2.78** | **1.10** | **3.93** | **1.41** |
| **36b** | 10 | 98.73 ± 0.38 | 95.69 ± 0.31 | 93.67 ± 0.66 | 95.15 ± 0.84 |
| | 30 | 98.07 ± 0.59 | 96.80 ± 0.37 | 97.13 ± 0.30 | 95.30 ± 0.35 |
| | | **2.32** | **0.74** | **4.17** | **0.91** |
| **37a** | 10 | 98.17 ± 0.33 | 97.36 ± 0.24 | 94.40 ± 0.50 | 98.97 ± 0.33 |
| | 30 | 98.89 ± 0.24 | 98.43 ± 0.21 | 93.76 ± 0.95 | 100.20 ± 0.45 |
| | | **2.38** | **1.80** | **2.94** | **3.02** |
| **37b** | 10 | 83.04 ± 0.31 | 83.71 ± 1.36 | 83.85 ± 1.22 | 95.32 ± 0.31 |
| | 30 | 96.20 ± 0.55 | 91.93 ± 0.90 | 92.49 ± 0.96 | 99.37 ± 0.26 |
| | | **2.60** | **5.07** | **6.00** | **4.01** |
| **38a** | 10 | 97.66 ± 0.16 | 84.07 ± 0.28 | 97.93 ± 0.51 | 92.77 ± 0.22 |
| | 30 | 97.43 ± 1.57 | 84.48 ± 0.23 | 100.10 ± 0.83 | 93.37 ± 0.43 |
| | | **2.37** | **1.50** | **3.21** | **2.51** |
| **38b** | 10 | 95.78 ± 0.29 | 93.34 ± 0.44 | 96.48 ± 0.59 | 99.05 ± 0.26 |
| | 30 | 95.36 ± 1.10 | 93.86 ± 0.55 | 96.64 ± 0.46 | 99.24 ± 0.23 |
| | | **2.38** | **2.12** | **3.15** | **3.79** |
| **39a** | 10 | 99.39 ± 0.38 | 95.74 ± 0.24 | 96.52 ± 0.88 | 94.92 ± 0.94 |
| | 30 | 99.16 ± 0.56 | 95.08 ± 0.30 | 95.10 ± 0.69 | 99.09 ± 0.66 |

| | | | | | |
|---|---|---|---|---|---|
| | | **1.57** | **0.68** | **1.89** | **0.85** |
| **39b** | 10 | 80.28 ± 0.90 | 72.10 ± 1.52 | - | 84.12 ± 1.47 |
| | 30 | 100.80 ± 0.70 | 95.30 ± 0.33 | 94.46 ± 0.52 | 95.10 ± 0.58 |
| | | **4.63** | **1.48** | **16.75** | **1.37** |
| **40a** | 10 | 98.11 ± 0.16 | 84.87 ± 0.89 | 95.70 ± 0.33 | 90.12 ± 0.18 |
| | 30 | 97.57 ± 0.36 | 84.49 ± 0.64 | 96.78 ± 0.45 | 90.20 ± 0.22 |
| **40b** | | **2.05** | **1.78** | **2.45** | **2.19** |
| | 10 | 95.61 ± 0.95 | 93.41 ± 0.38 | 95.04 ± 0.89 | 98.98 ± 0.42 |
| | 30 | 98.31 ± 0.18 | 94.76 ± 2.80 | 98.40 ± 1.38 | 99.12 ± 0.80 |
| | | **2.63** | **1.63** | **2.00** | **1.99** |
| **41a** | 10 | 97.06 ± 0.49 | 81.09 ± 1.23 | 96.82 ± 0.54 | 90.66 ± 0.48 |
| | 30 | 97.26 ± 0.52 | 87.71 ± 0.66 | 97.98 ± 0.80 | 90.70 ± 0.30 |
| | | **2.56** | **5.93** | **3.57** | **5.00** |
| **41b** | 10 | 81.43 ± 0.55 | 82.93 ± 0.42 | 83.05 ± 0.40 | 97.06 ± 0.73 |
| | 30 | 98.99 ± 0.10 | 90.69 ± 0.69 | 91.21 ± 0.71 | 98.50 ± 0.39 |
| | | **2.52** | **5.67** | **2.59** | **4.06** |
| **43a** | 10 | 68.78 ± 0.39 | 67.47 ± 1.29 | 30.83 ± 3.06 | 82.97 ± 0.25 |
| | 30 | 99.10 ± 0.14 | 86.38 ± 1.29 | 98.30 ± 0.69 | 90.42 ± 0.42 |
| **43b** | | **6.85** | **7.45** | **12.36** | **5.34** |
| | 10 | 97.81 ± 0.33 | 84.33 ± 1.00 | 84.65 ± 1.11 | 98.33 ± 0.26 |
| | 30 | 95.36 ± 1.31 | 95.73 ± 1.16 | 95.86 ± 1.10 | 98.84 ± 0.20 |
| | | **3.98** | **5.68** | **5.02** | **4.32** |
| **44a** | 10 | 98.18 ± 0.25 | 95.66 ± 0.88 | 93.76 ± 2.40 | 95.20 ± 0.55 |
| | 30 | 98.78 ± 0.26 | 100.20 ± 0.58 | 101.10 ± 0.83 | 97.28 ± 0.26 |
| | | **1.34** | **0.88** | **1.46** | **2.23** |
| **44b** | 10 | 95.99 ± 0.12 | 96.15 ± 0.48 | 97.92 ± 0.27 | 95.60 ± 0.33 |
| | 30 | 96.40 ± 0.13 | 100.30 ± 0.12 | 98.81 ± 0.18 | 98.48 ± 0.14 |
| | | **2.95** | **0.96** | **2.71** | **2.10** |
| **45a** | 10 | 93.74 ± 0.50 | 93.74 ± 0.40 | 88.90 ± 2.42 | 93.76 ± 0.89 |
| | 30 | 96.82 ± 0.09 | 97.23 ± 0.52 | 95.04 ± 1.04 | 95.28 ± 0.34 |
| | | **2.88** | **0.84** | **1.79** | **2.26** |
| **45b** | 10 | 93.38 ± 0.29 | 96.39 ± 1.26 | 94.71 ± 2.86 | 94.16 ± 0.09 |
| | 30 | 94.47 ± 0.26 | 99.67 ± 1.08 | 99.30 ± 0.84 | 95.68 ± 0.19 |
| | | **2.72** | **0.91** | **1.91** | **1.41** |
| **46a** | 10 | 93.38 ± 0.37 | 97.67 ± 0.87 | 99.62 ± 1.54 | 93.84 ± 0.43 |
| | 30 | 95.54 ± 0.27 | 98.43 ± 0.30 | 99.43 ± 0.82 | 95.36 ± 0.20 |
| | | **2.45** | **0.90** | **1.91** | **1.52** |
| **46b** | 10 | 94.25 ± 0.35 | 98.31 ± 0.48 | 98.52 ± 0.23 | 95.12 ± 0.38 |
| | 30 | 95.78 ± 0.37 | 98.96 ± 0.25 | 98.96 ± 0.18 | 95.76 ± 0.16 |
| | | **1.58** | **0.90** | **1.76** | **1.39** |
| **50a** | 10 | 93.80 ± 0.26 | 96.18 ± 0.81 | 99.45 ± 0.87 | 98.01 ± 0.51 |
| | 30 | 97.41 ± 0.59 | 101.90 ± 0.76 | 101.30 ± 0.78 | 100.20 ± 0.62 |
| | | **3.67** | **1.43** | **2.19** | **1.64** |
| **50b** | 10 | 98.90 ± 0.33 | 97.45 ± 0.38 | 97.46 ± 2.33 | 100.10 ± 0.09 |
| | 30 | 98.58 ± 0.26 | 98.95 ± 0.18 | 101.30 ± 0.98 | 100.60 ± 0.28 |
| | | **3.09** | **1.49** | **2.13** | **0.93** |
| **51a** | 10 | 95.05 ± 0.81 | 94.52 ± 0.76 | 91.65 ± 1.32 | 94.12 ± 0.92 |
| | 30 | 99.14 ± 0.14 | 100.70 ± 0.88 | 99.20 ± 0.90 | 100.00 ± 0.35 |
| | | **2.84** | **1.64** | **1.91** | **1.48** |
| **51b** | 10 | 97.25 ± 0.27 | 98.03 ± 0.73 | 95.82 ± 1.22 | 93.94 ± 0.97 |
| | 30 | 99.14 ± 0.14 | 101.50 ± 1.09 | 100.10 ± 0.81 | 100.30 ± 0.37 |
| | | **3.62** | **1.32** | **3.18** | **1.92** |
| **52a** | 10 | 96.86 ± 0.71 | 100.70 ± 0.03 | 96.78 ± 0.31 | 98.65 ± 2.06 |

| | | | | | |
|---|---|---|---|---|---|
| | 30 | 97.57 ± 0.41 | 100.80 ± 1.73 | 98.82 ± 0.20 | 99.72 ± 1.59 |
| | | **1.95** | **1.42** | **1.65** | **1.33** |
| **52b** | 10 | 99.21 ± 0.12 | 96.55 ± 0.50 | 97.12 ± 0.33 | 97.34 ± 0.44 |
| | 30 | 99.37 ± 0.09 | 98.95 ± 0.18 | 98.82 ± 0.20 | 100.90 ± 0.63 |
| | | **3.52** | **1.60** | **2.84** | **1.50** |
| **Cisplatin** | 10 | 42.61 ± 2.33 | 53.03 ± 2.29 | 67.51 ± 1.01 | 83.57 ± 1.21 |
| | 30 | 99.93 ± 0.26 | 86.90 ± 1.24 | 87.75 ± 1.10 | 95.02 ± 0.28 |
| | | **12.43** | **5.78** | **3.74** | **1.30** |

# 4. Reference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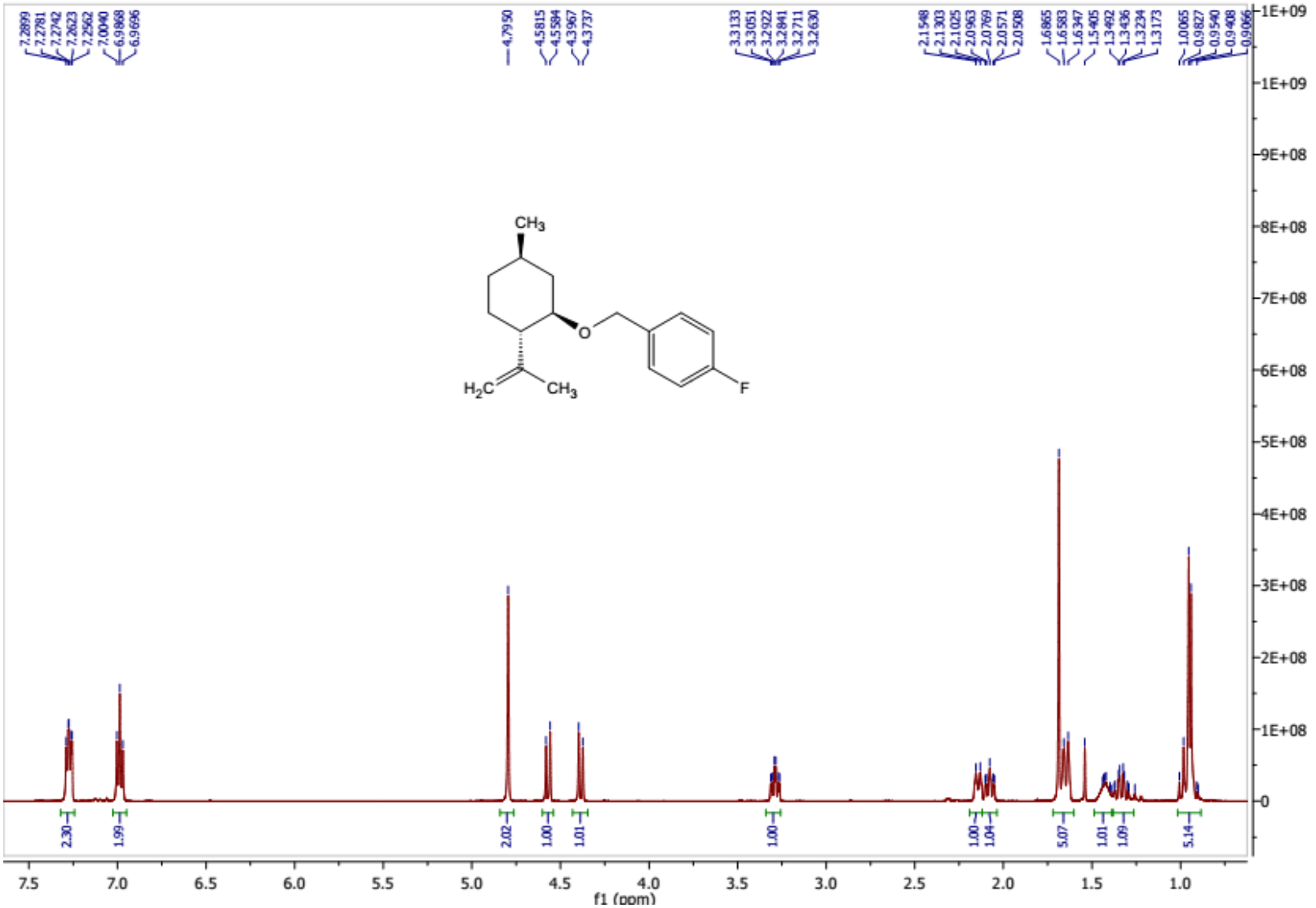
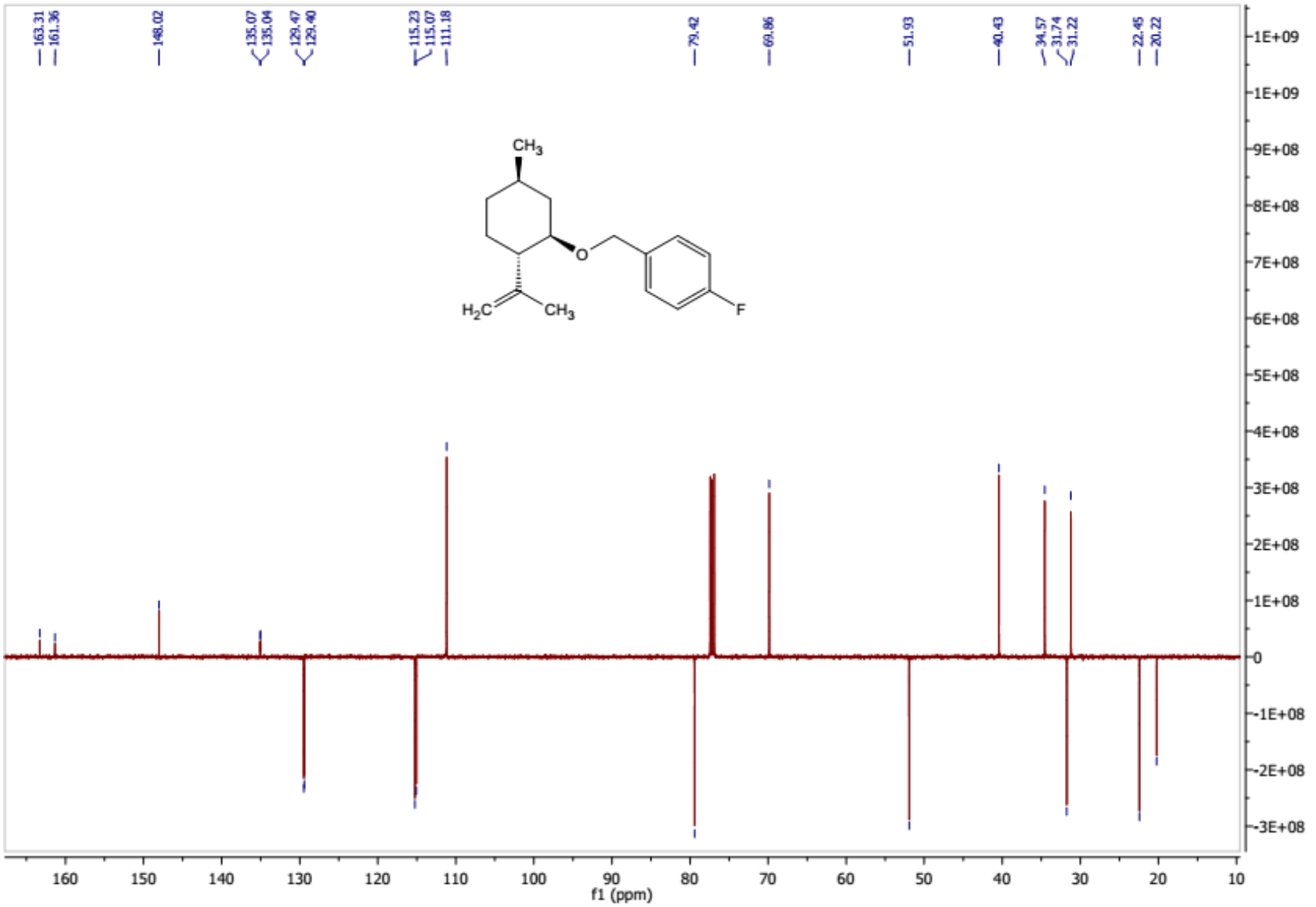
## 5. $^{1}$H- and $^{13}$C-NMR spectra of new compounds

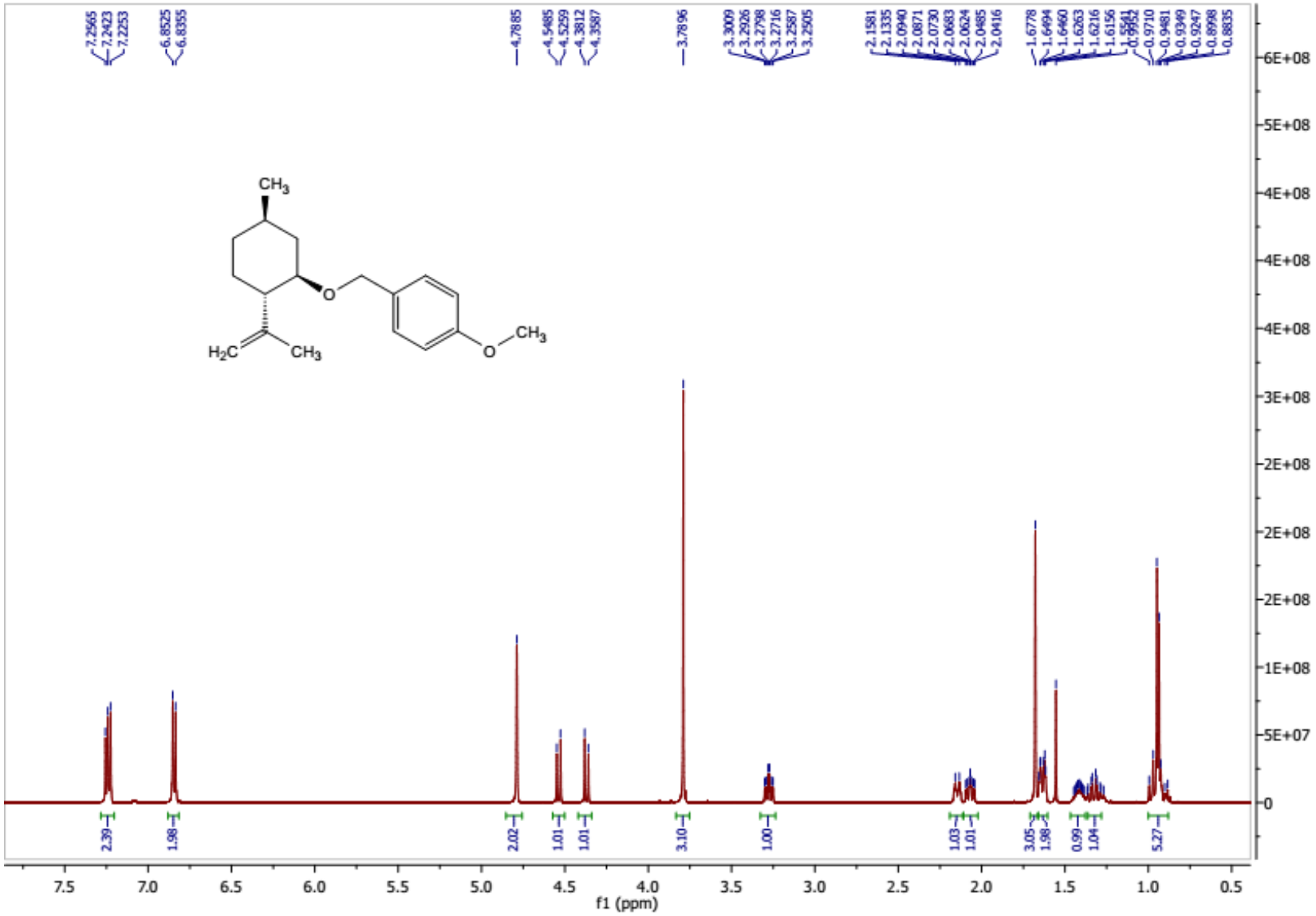
$^{1}$H-NMR of compound **2b**



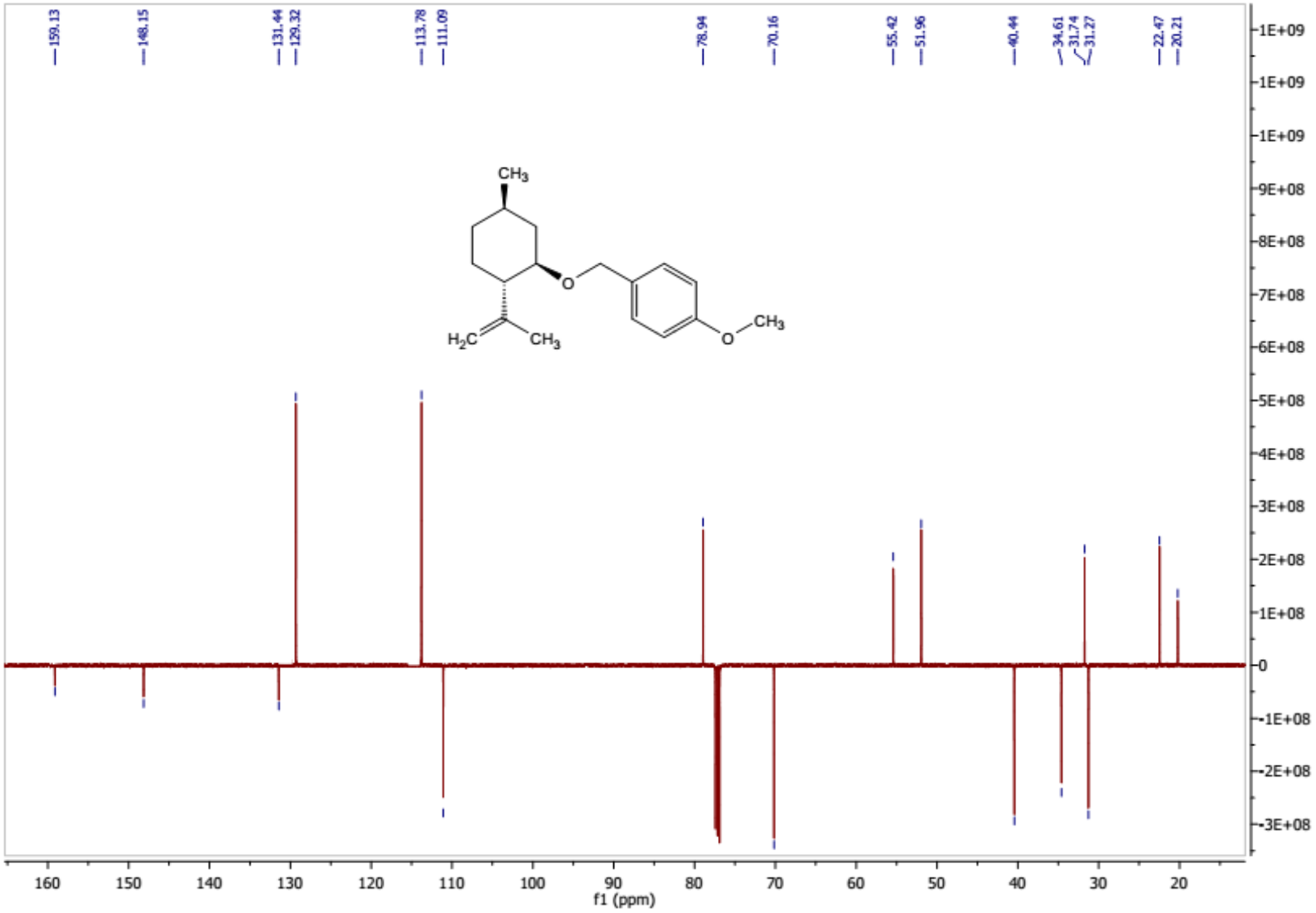
$^{13}$C-NMR of compound **2b**



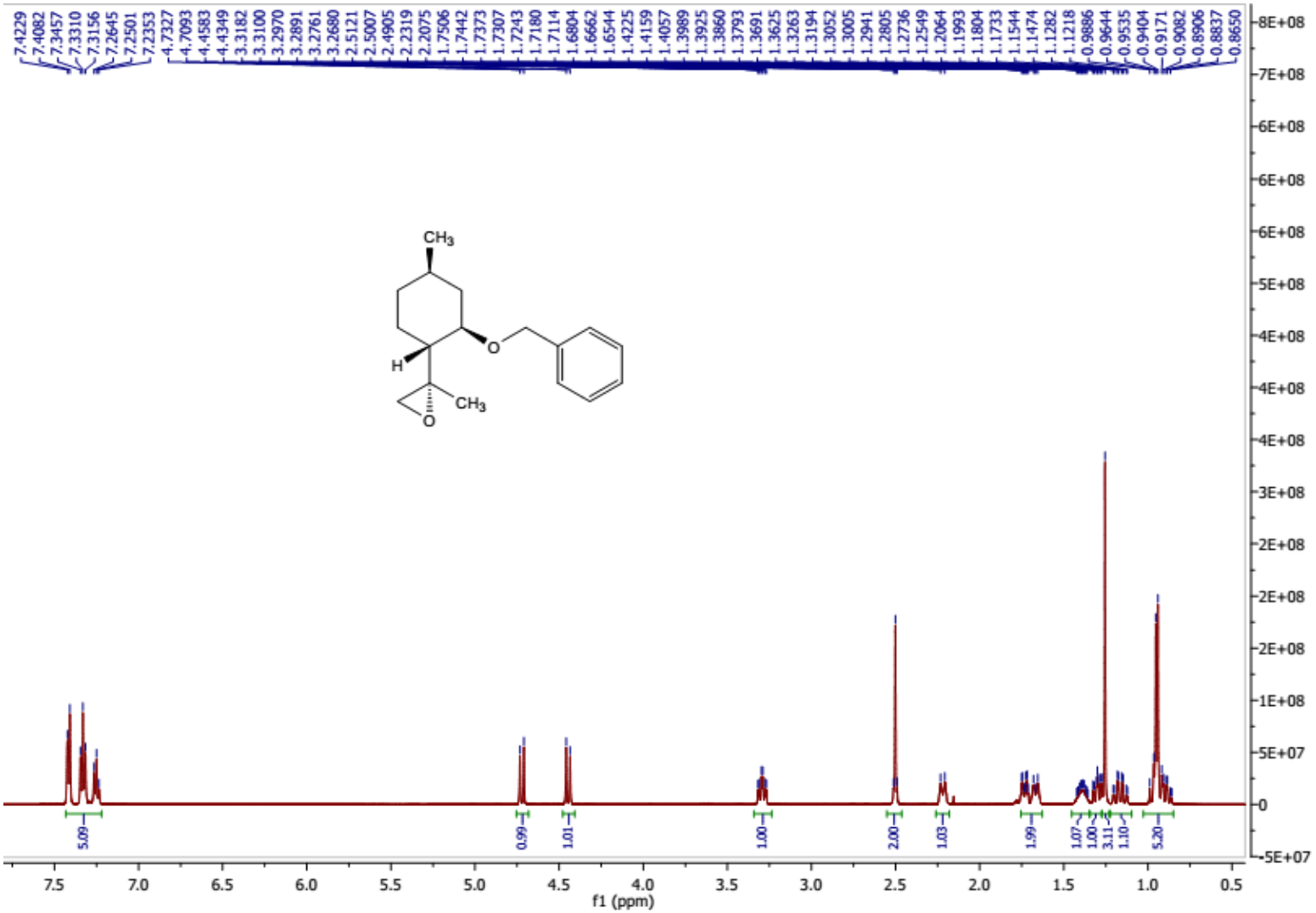
$^{1}$H-NMR of compound **2c**



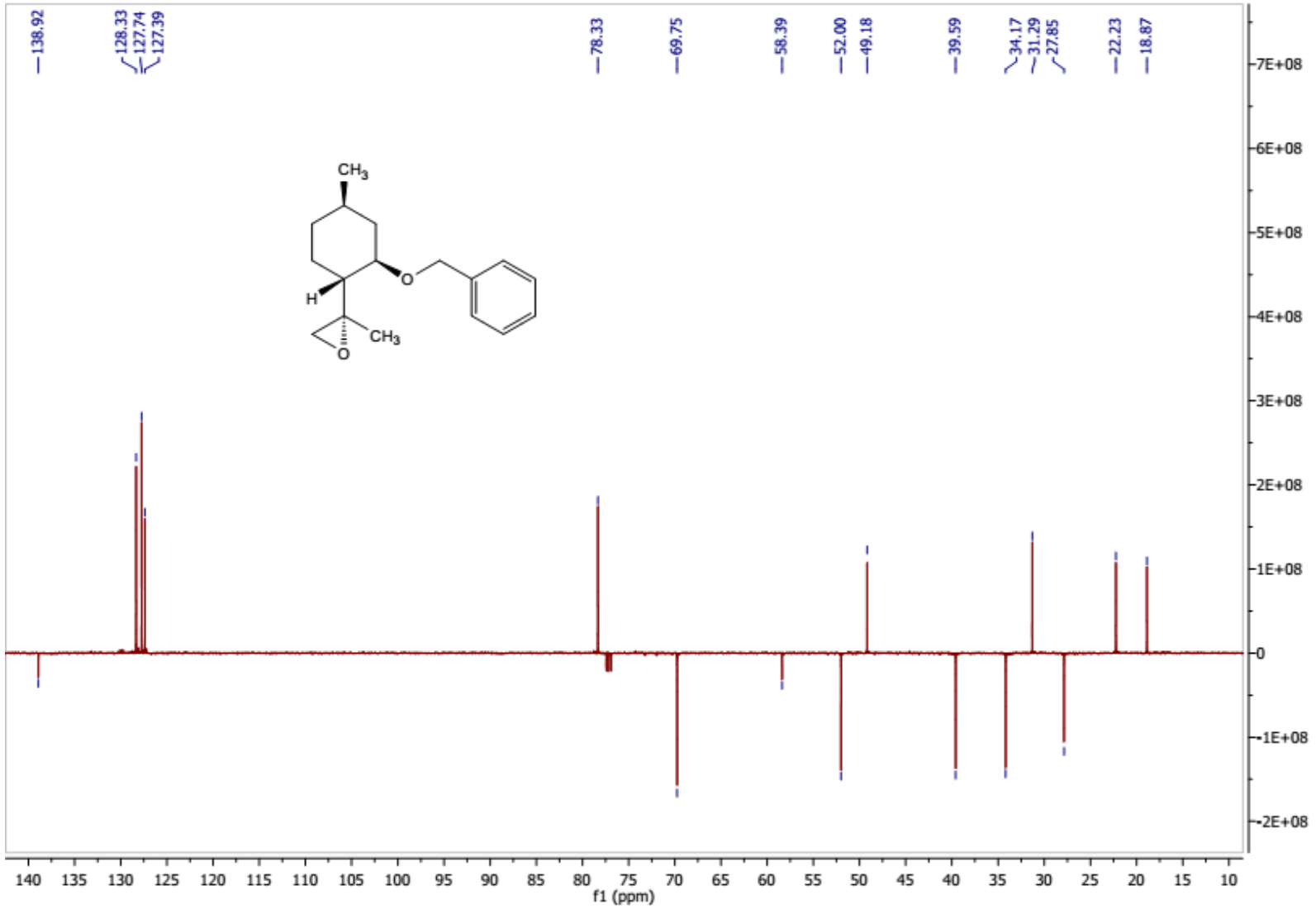
$^{13}$C-NMR of compound **2c**



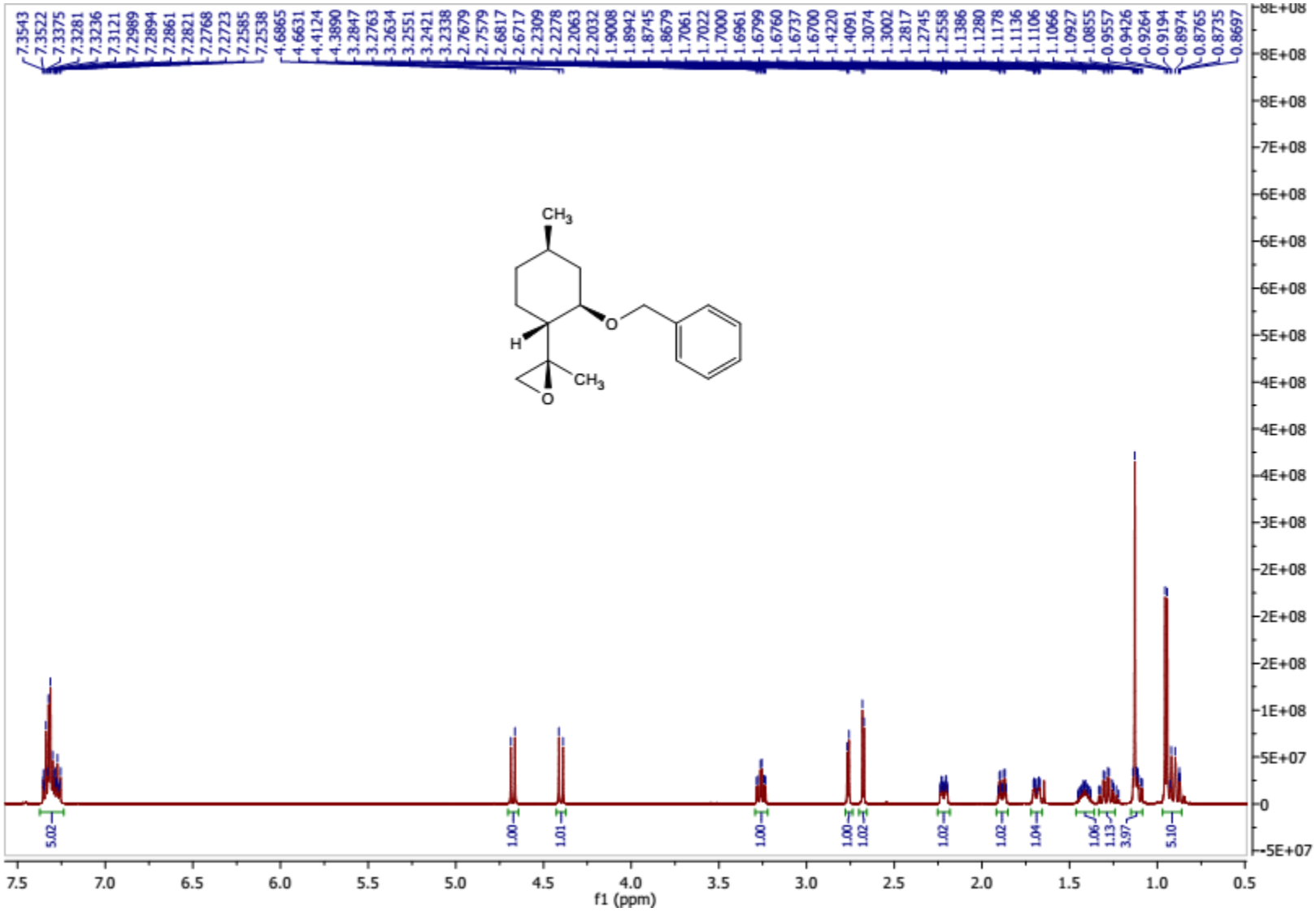
[1]H-NMR of compound **3a**



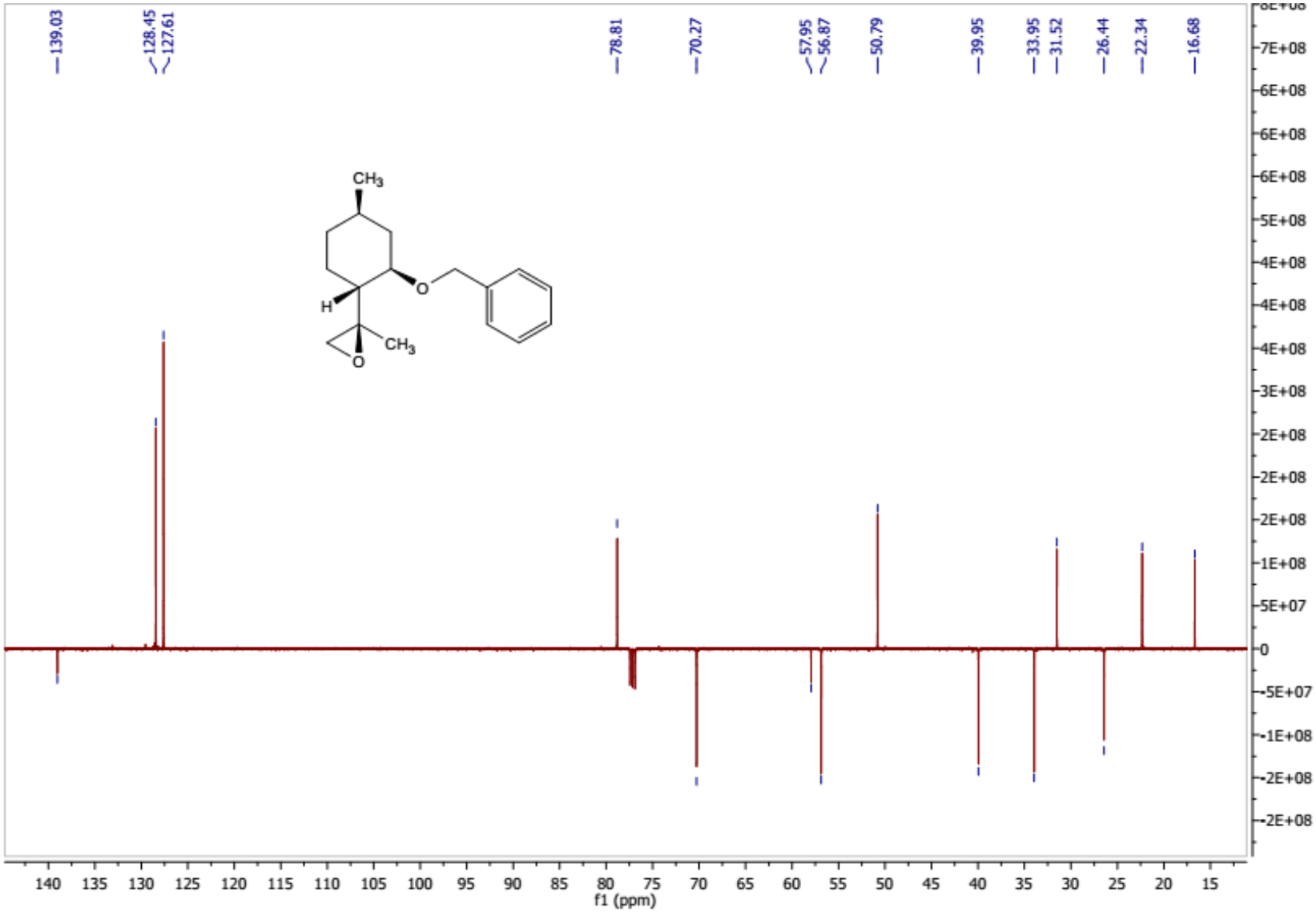
$^{13}$C-NMR of compound **3a**



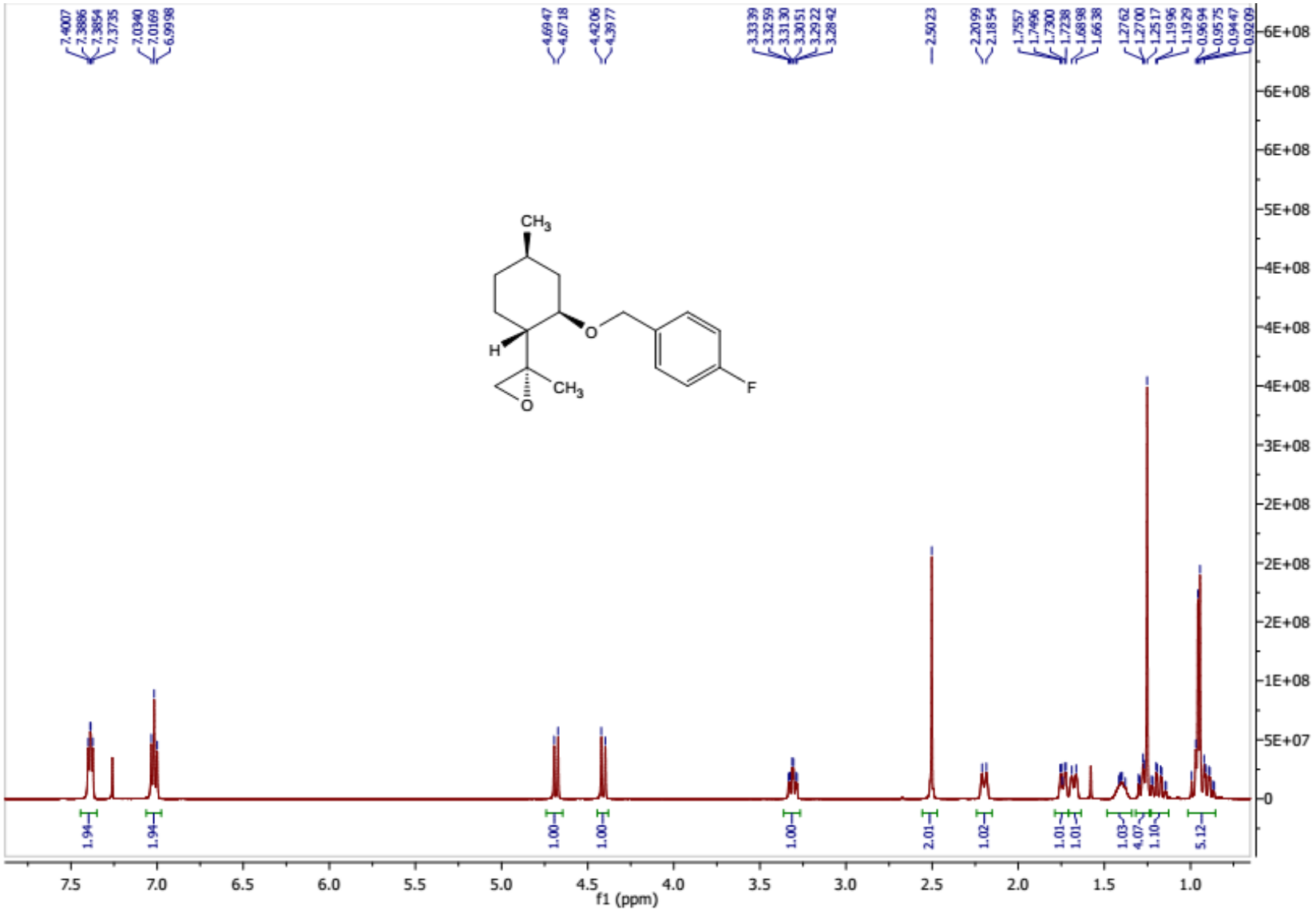
[1]H-NMR of compound **3b**



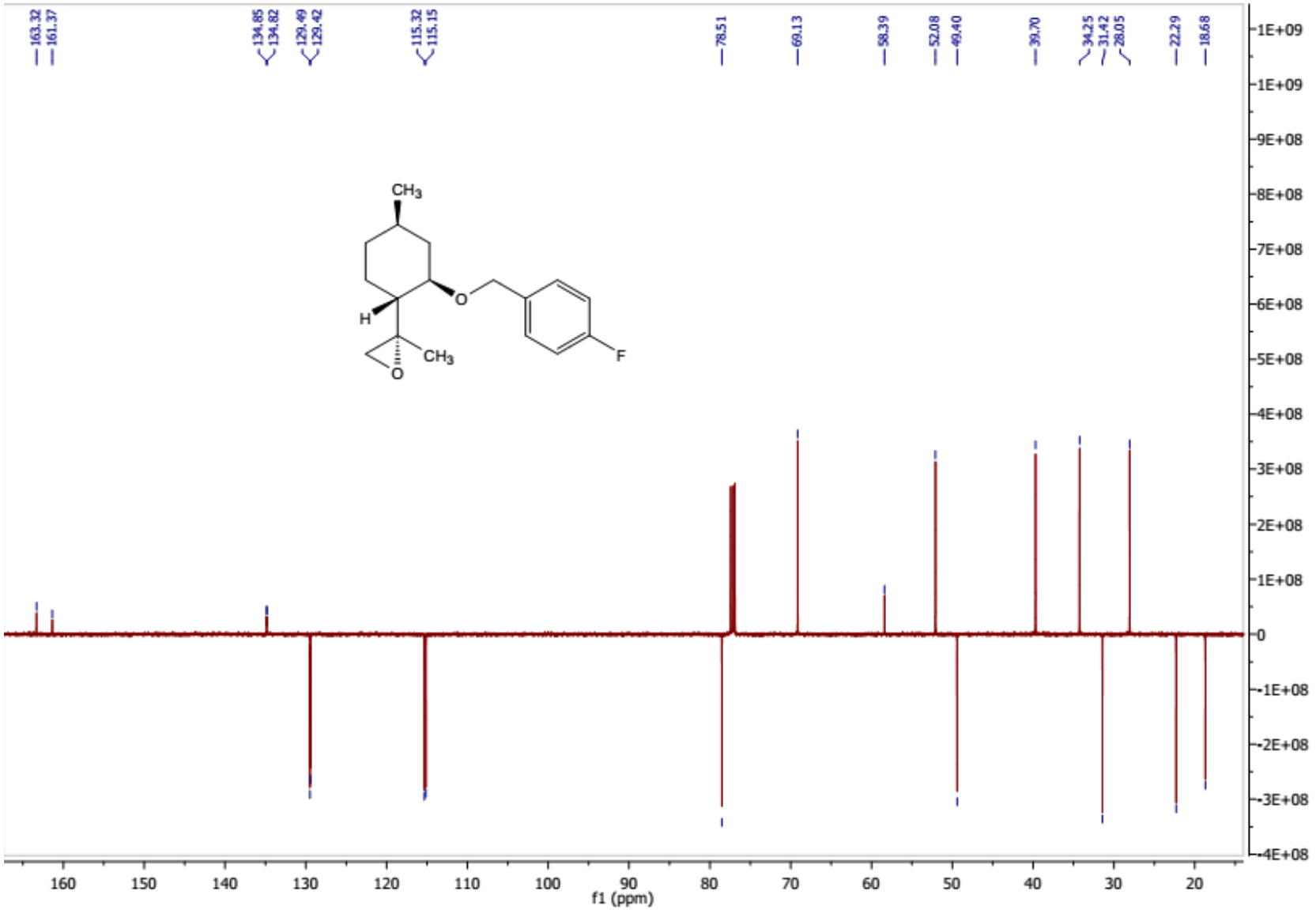
$^{13}$C-NMR of compound **3b**



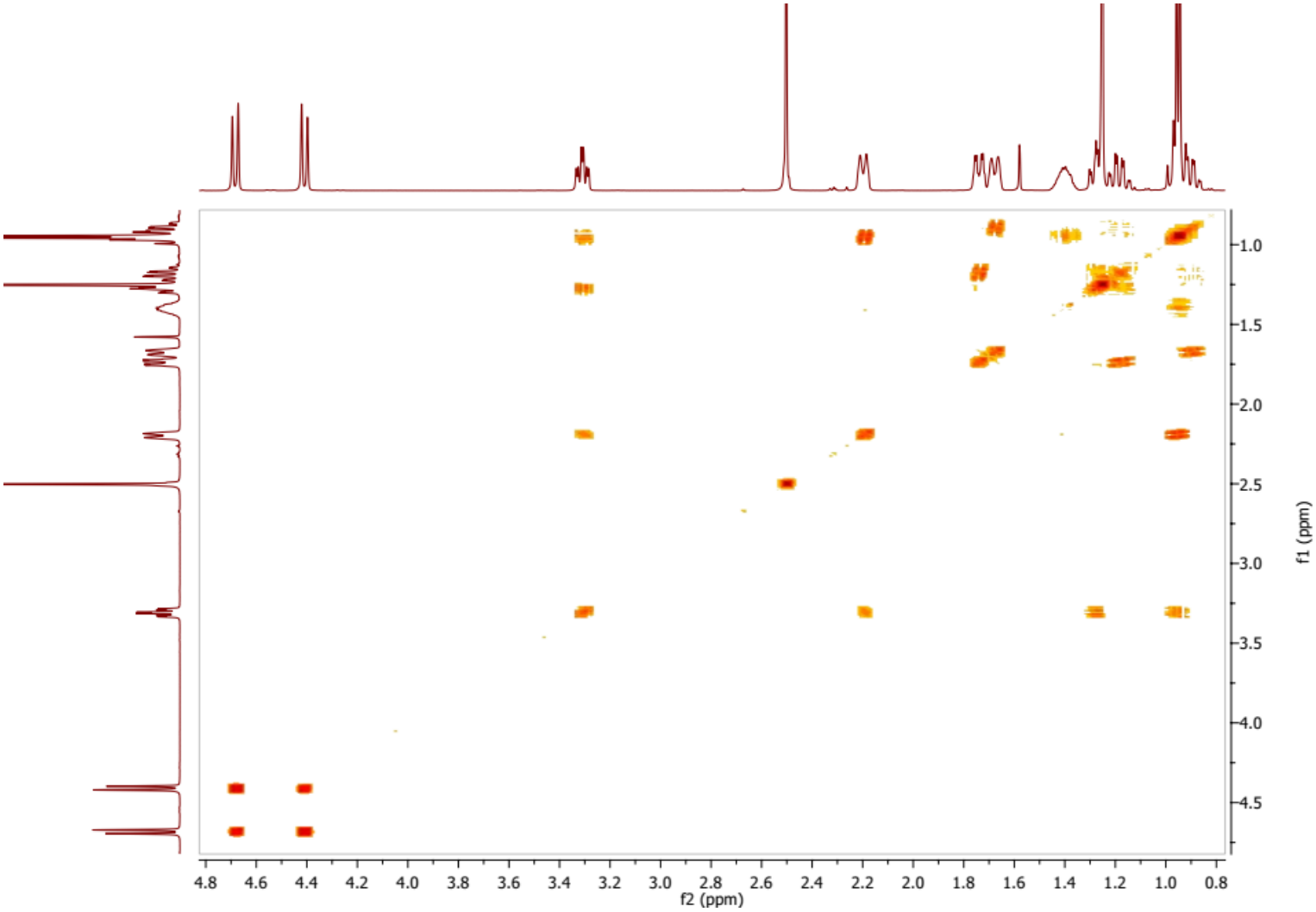
[1]H-NMR of compound **4a**



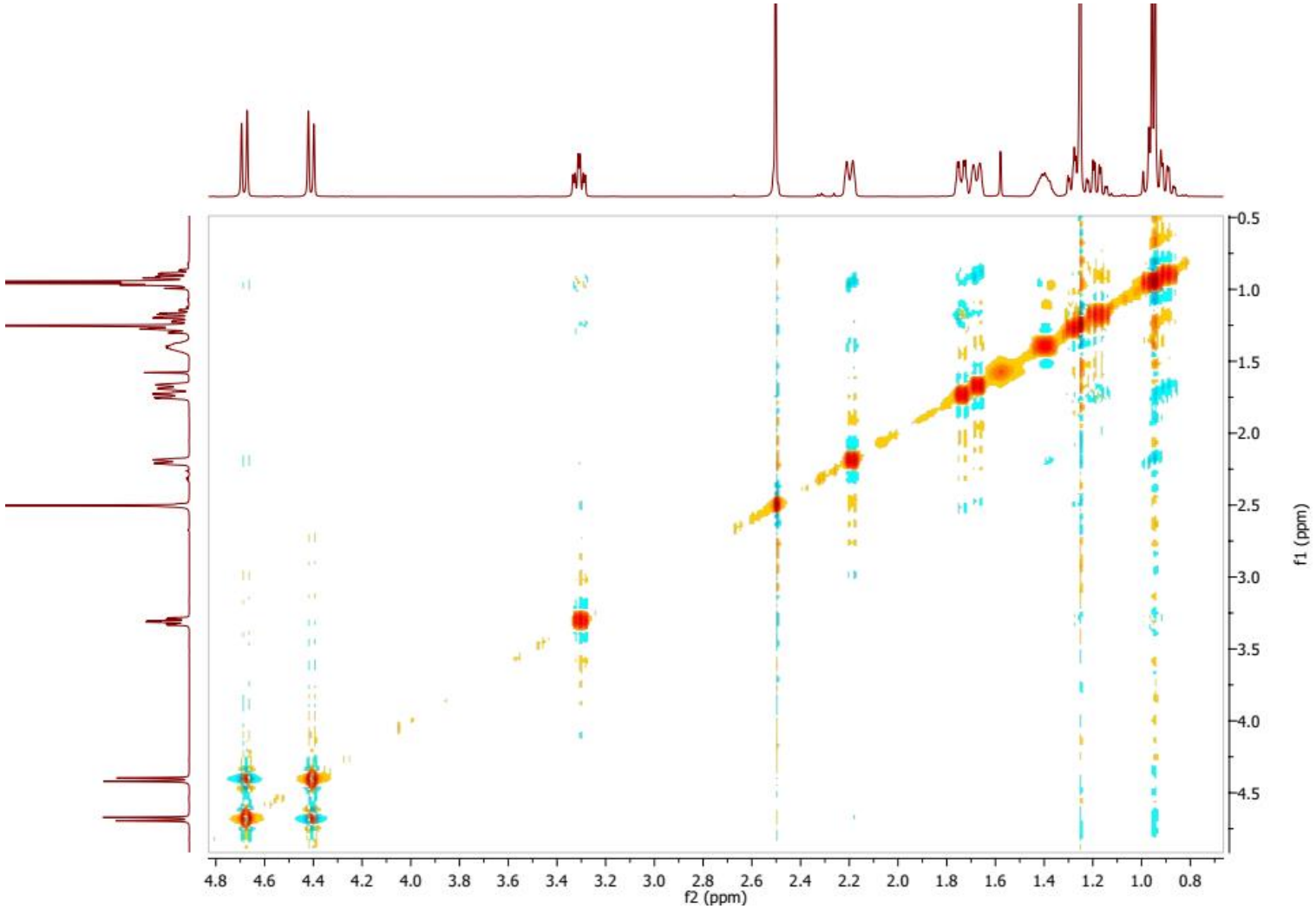
$^{13}$C-NMR of compound **4a**



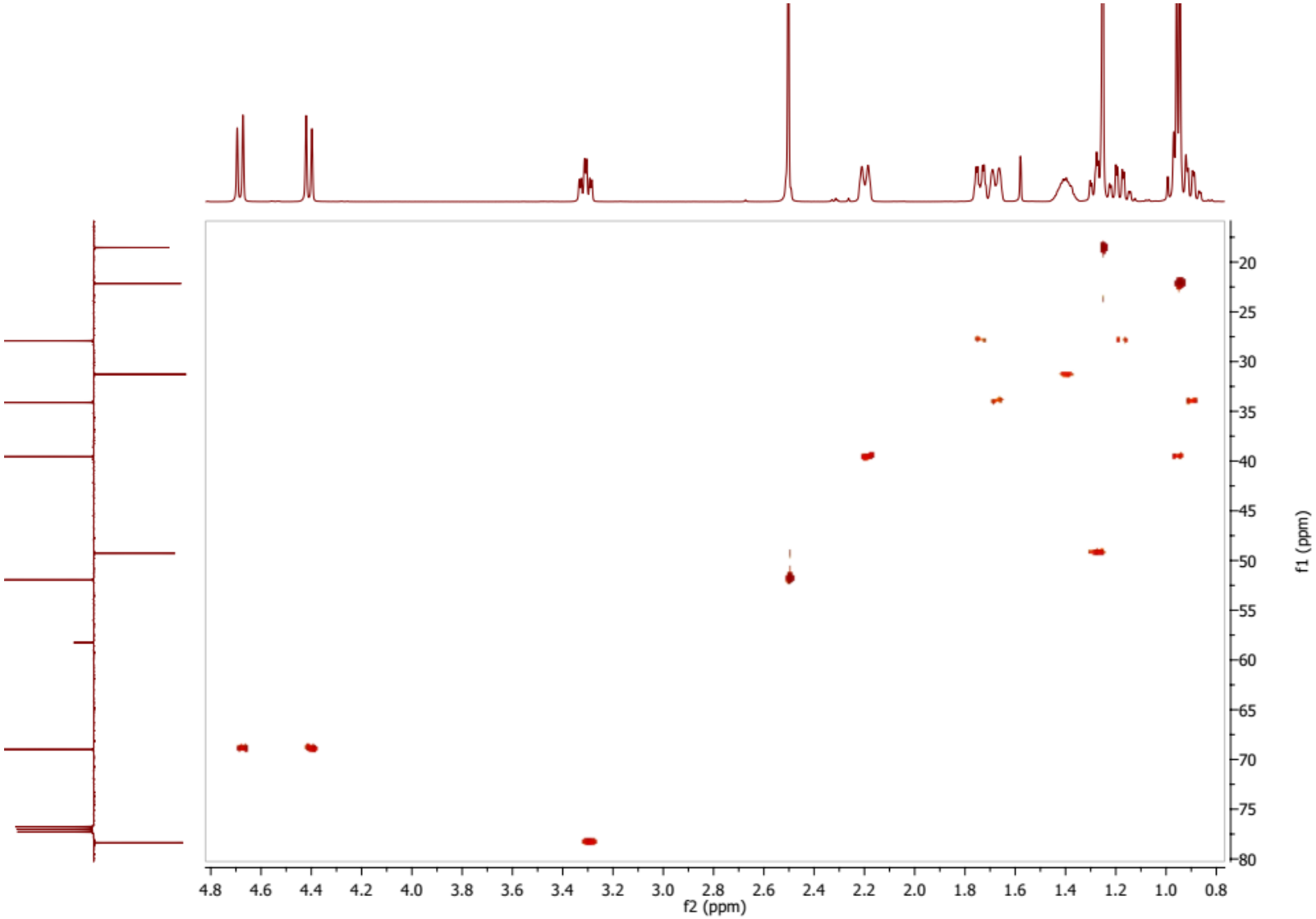
COSY spectrum of compound **4a**



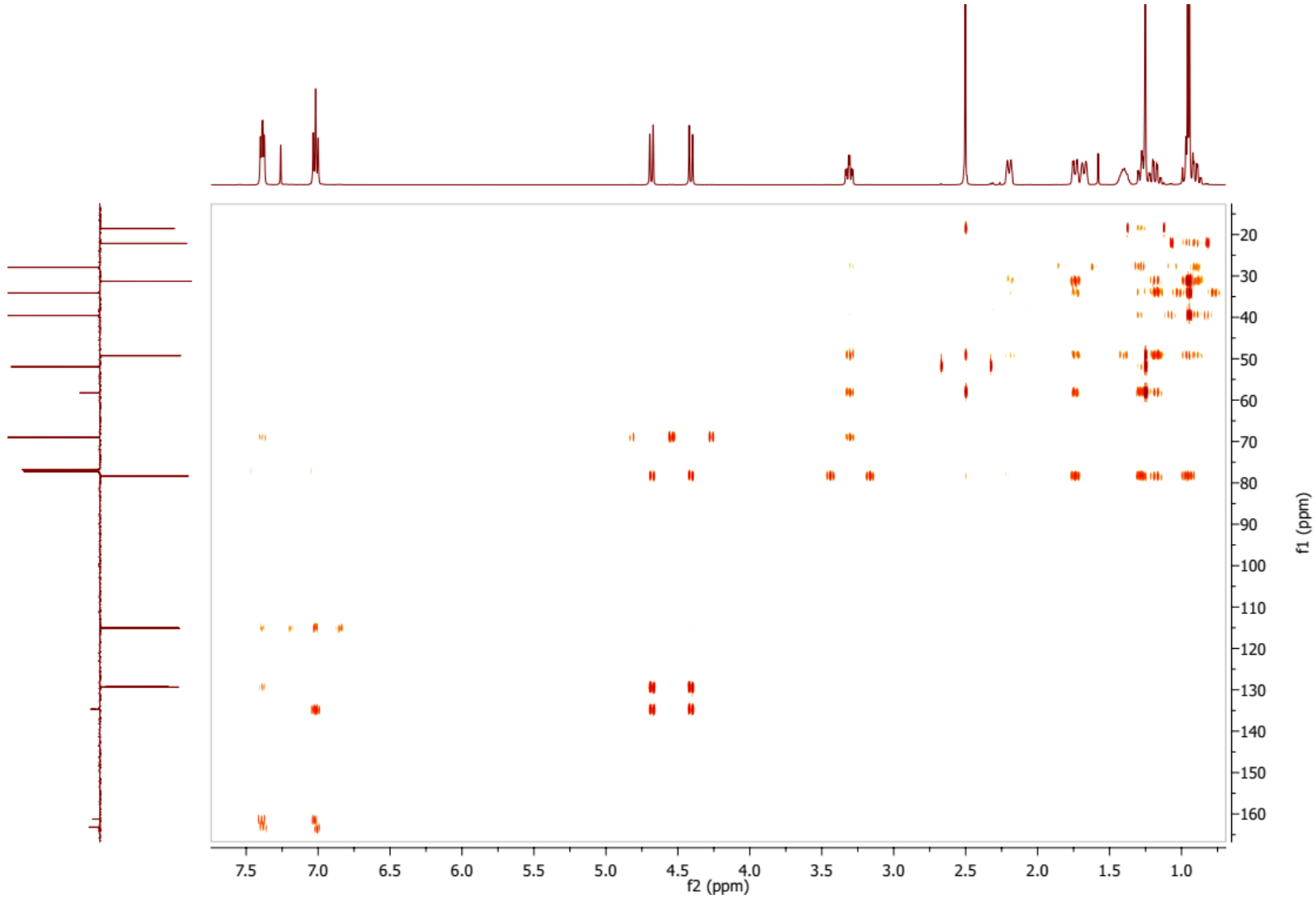
NOESY spectrum of compound **4a**



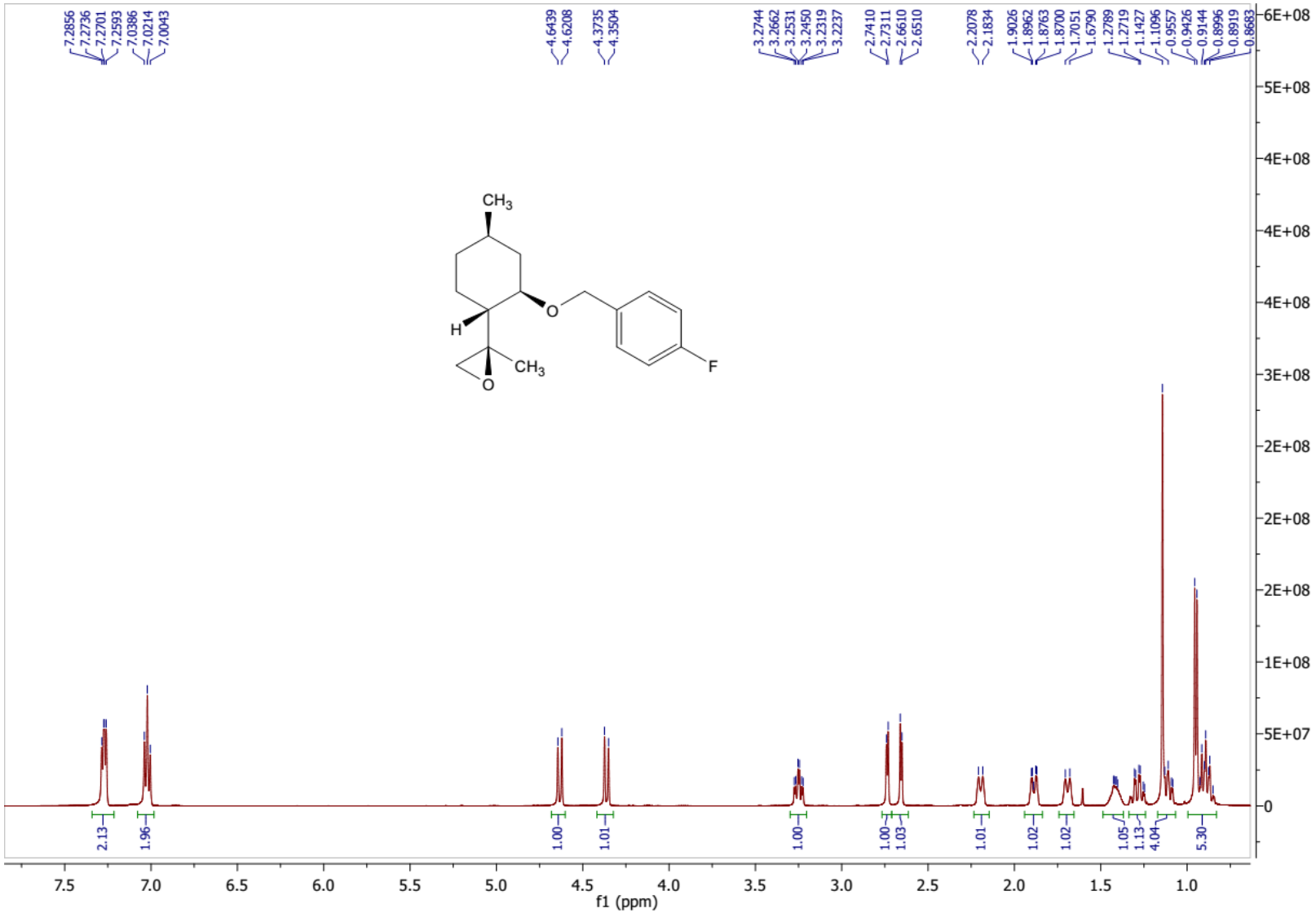
HSQC spectrum of compound **4a**



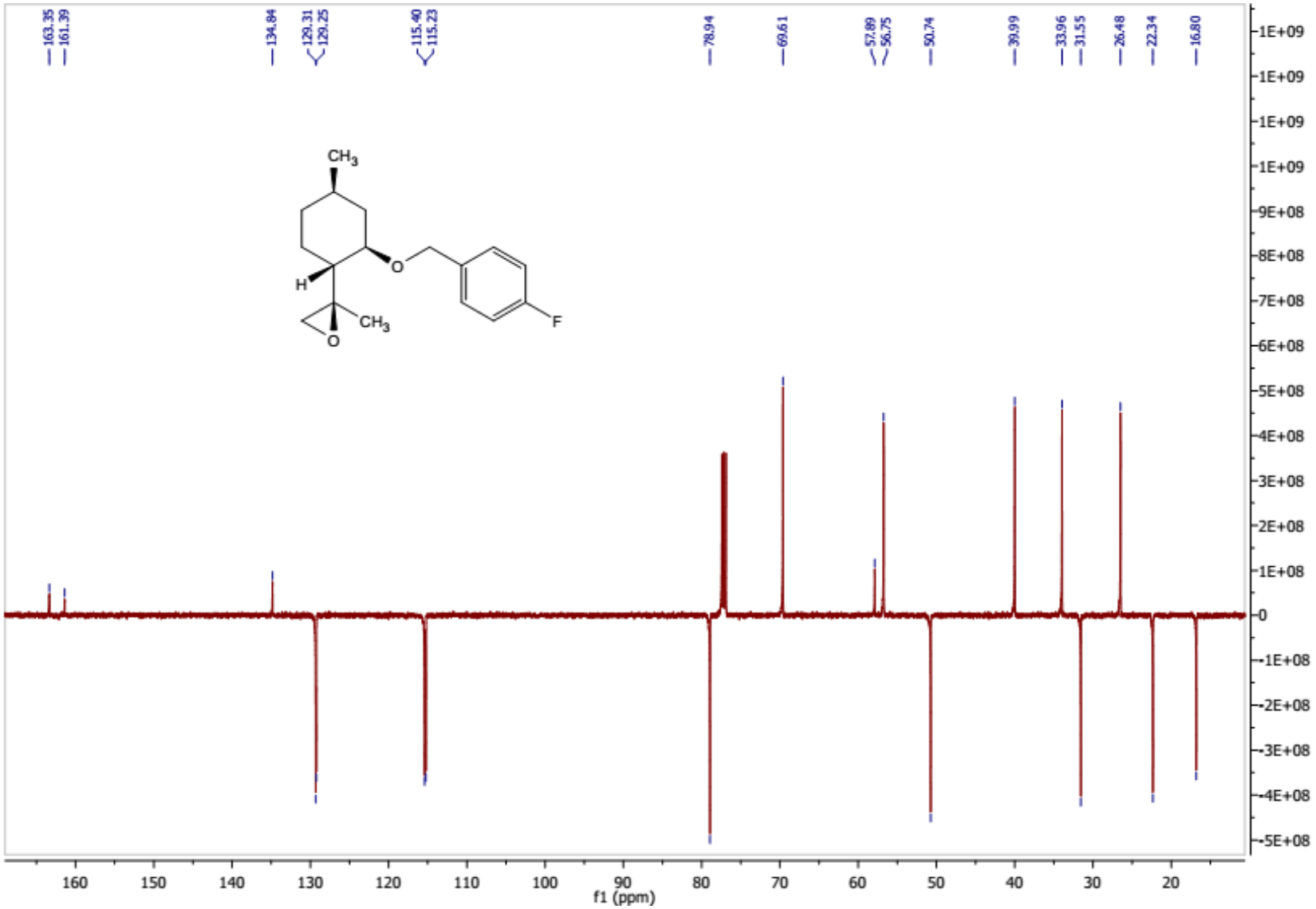
HMBC spectrum of compound **4a**



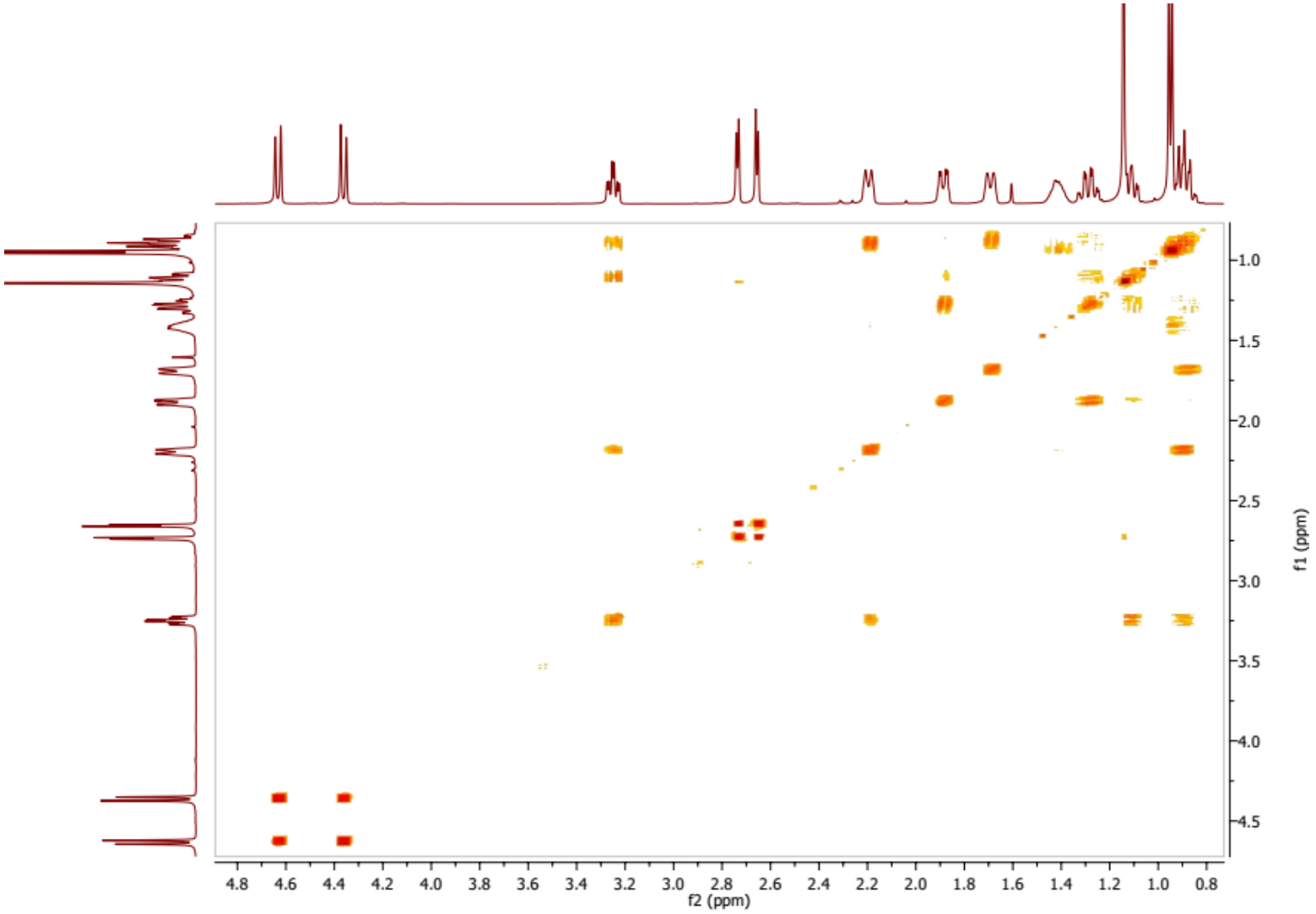
[1]H-NMR of compound **4b**



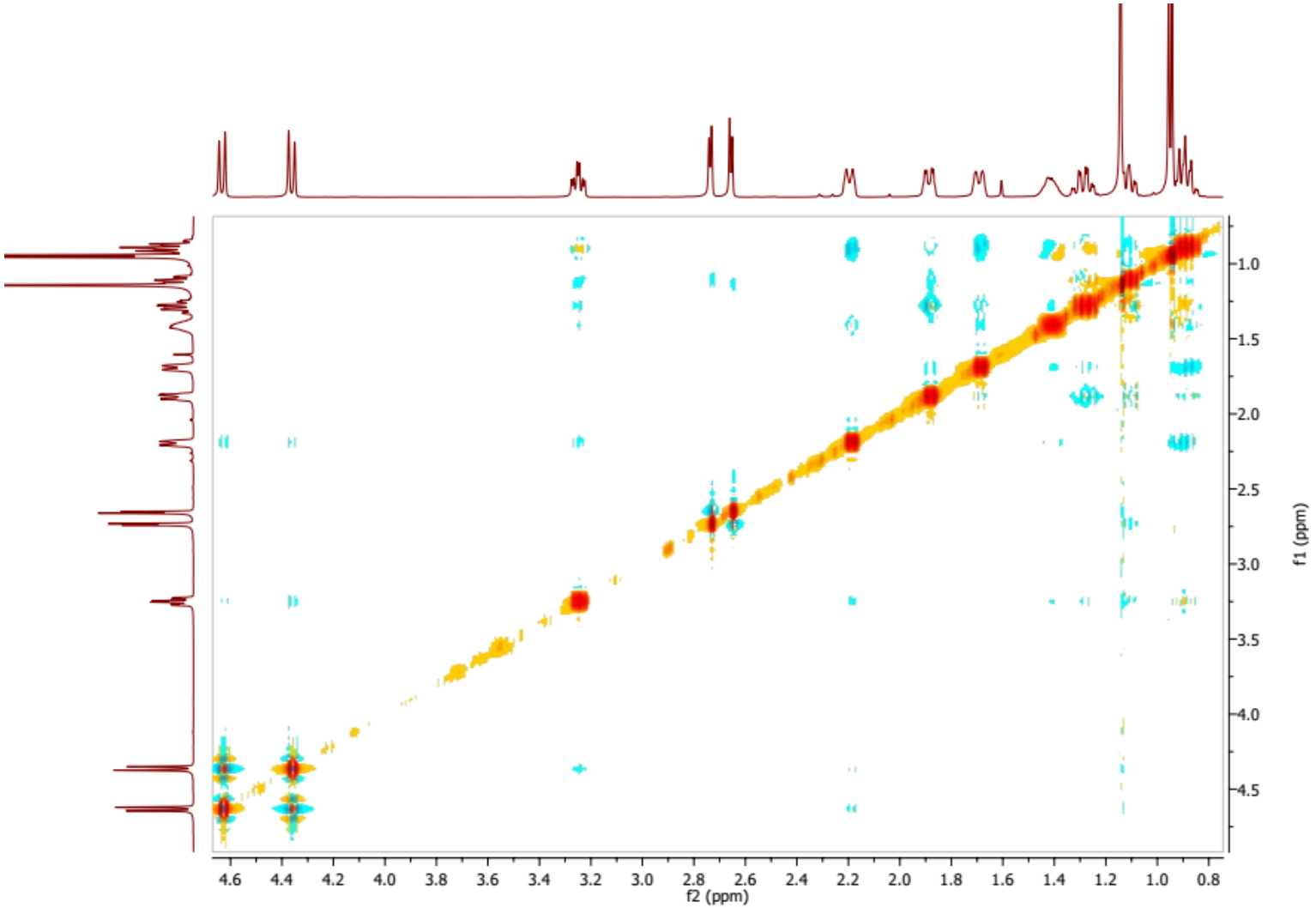
$^{13}$C-NMR of compound **4b**



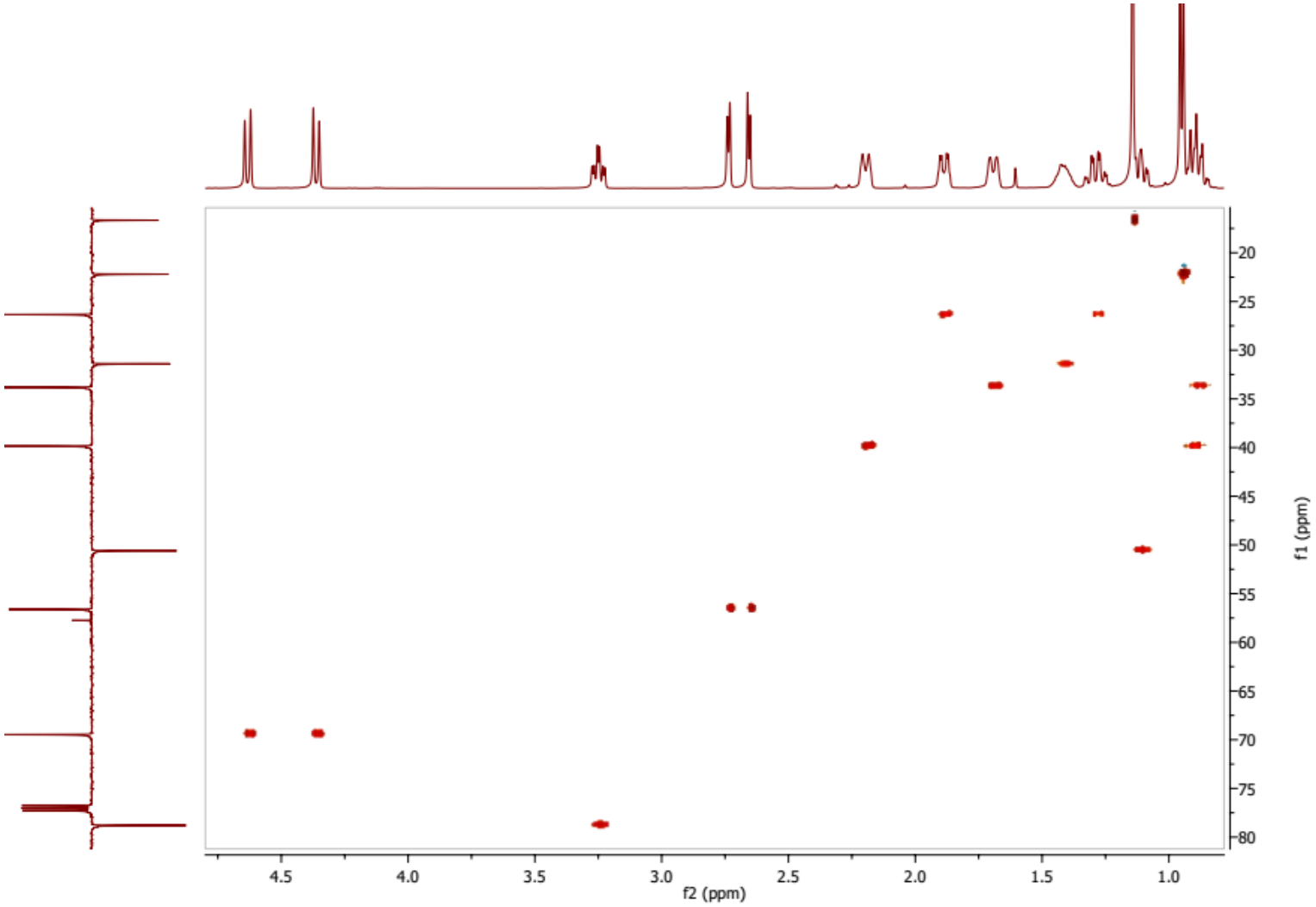
COSY spectrum of compound **4b**



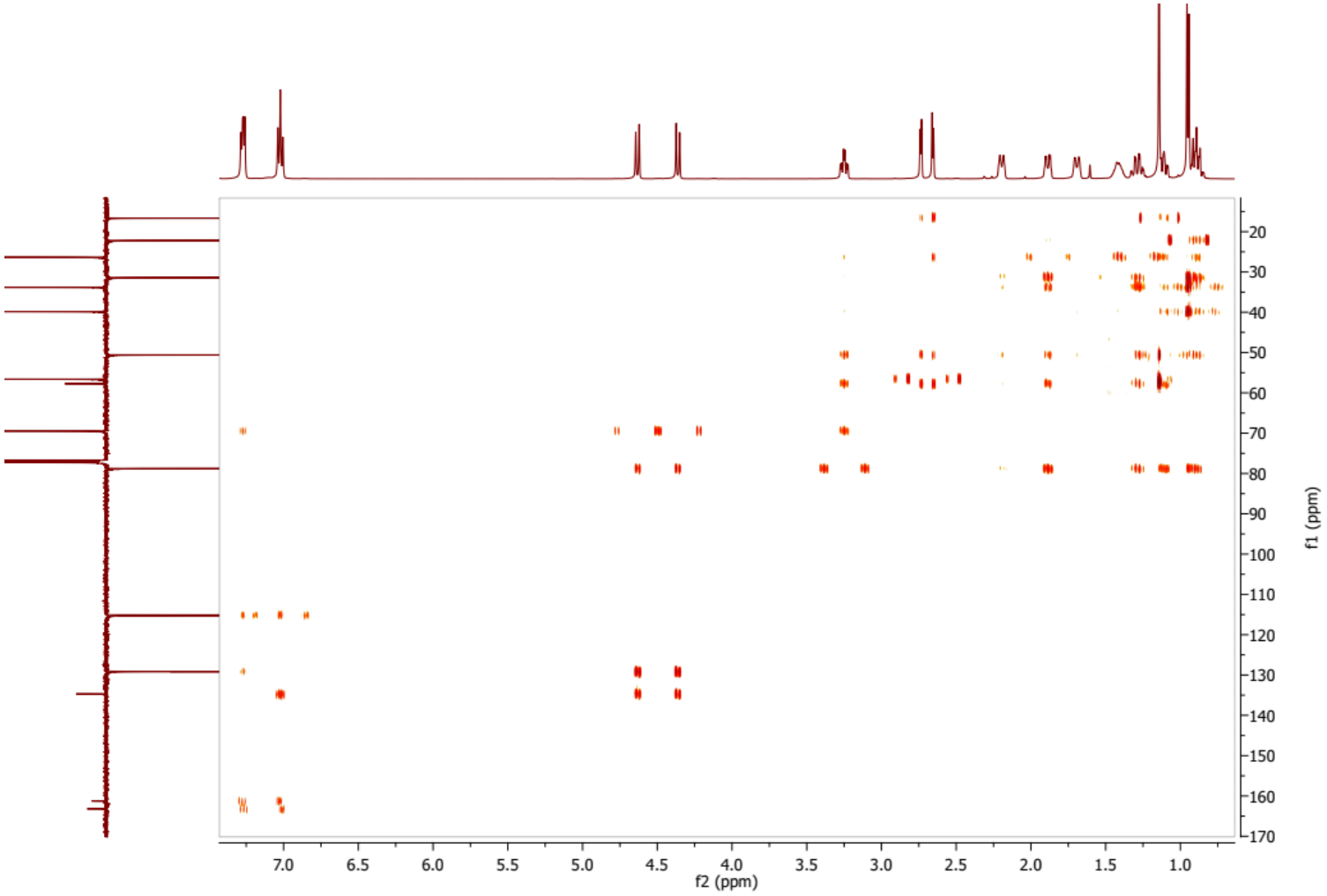
NOESY spectrum of compound **4b**



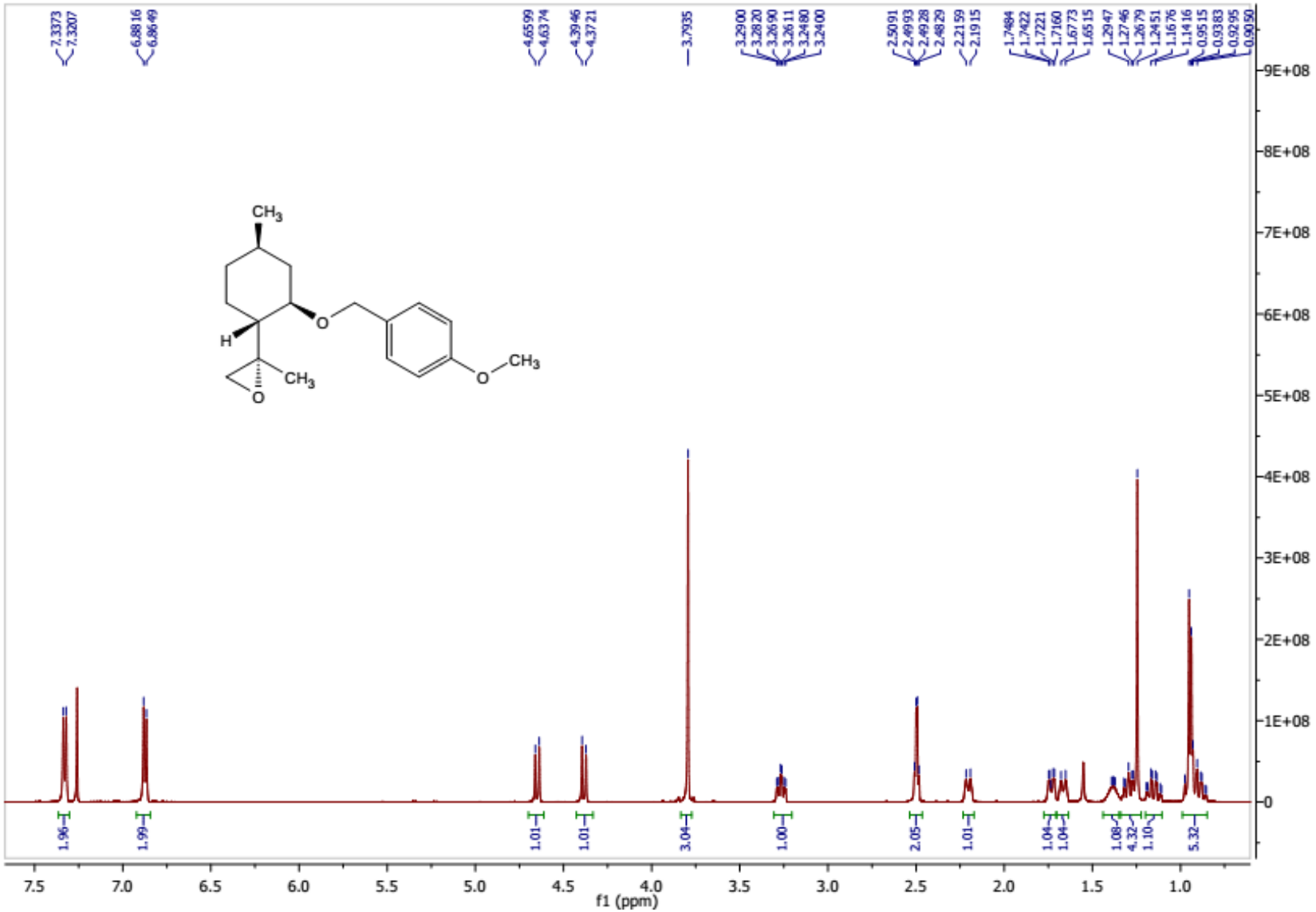
HSQC spectrum of compound **4b**



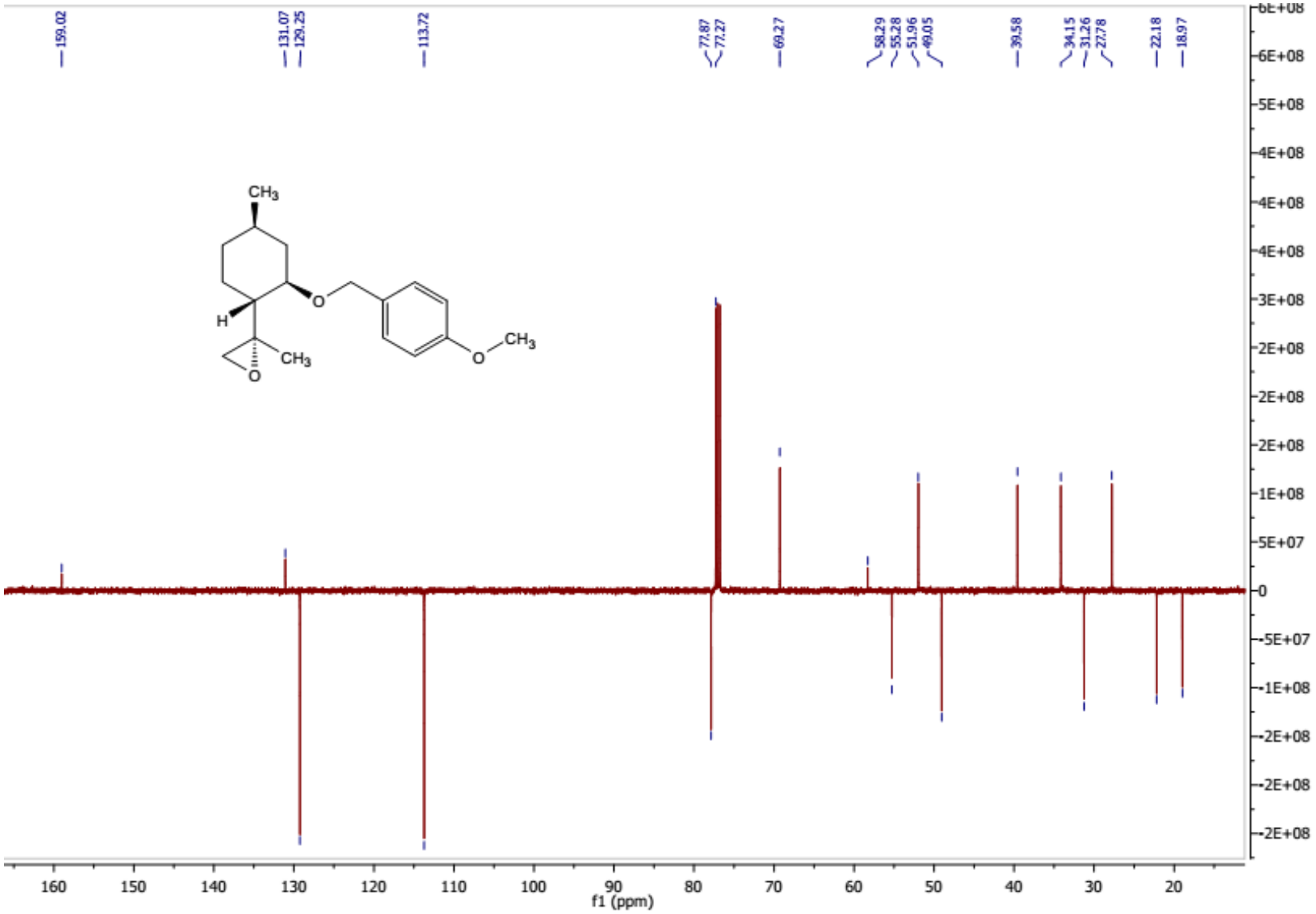
HMBC spectrum of compound **4b**



[1]H-NMR of compound **5a**



$^{13}$C-NMR of compound **5a**



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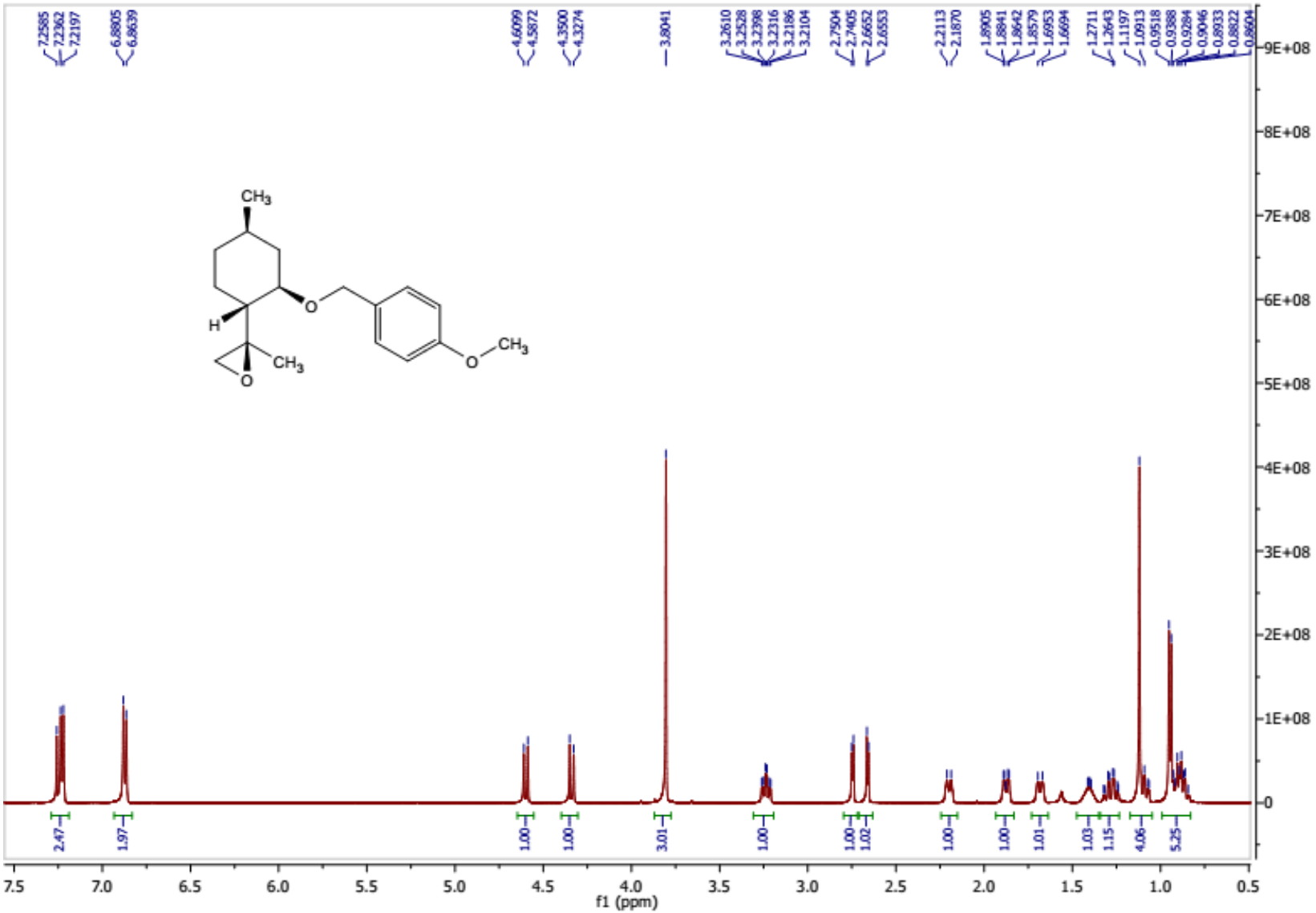

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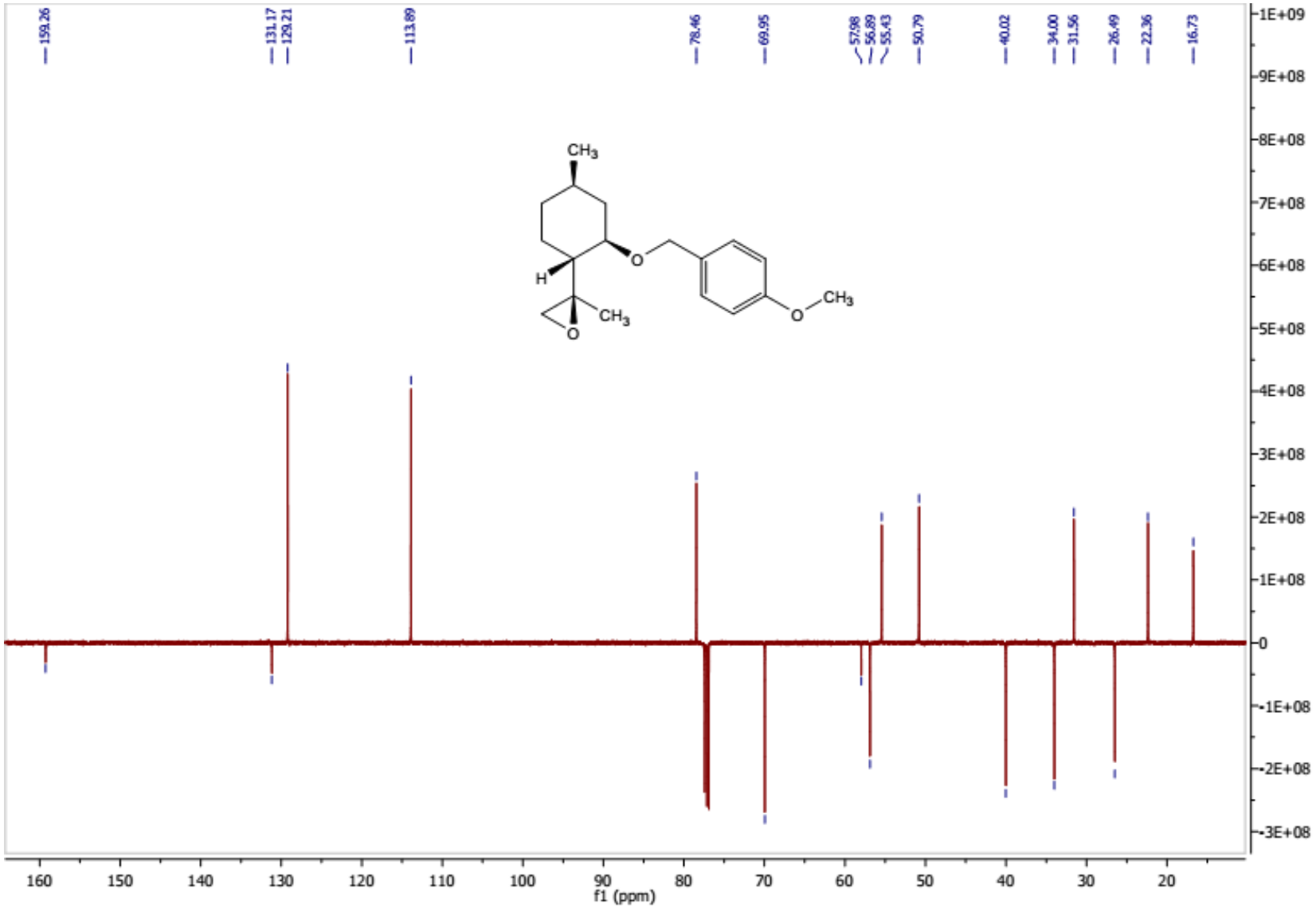
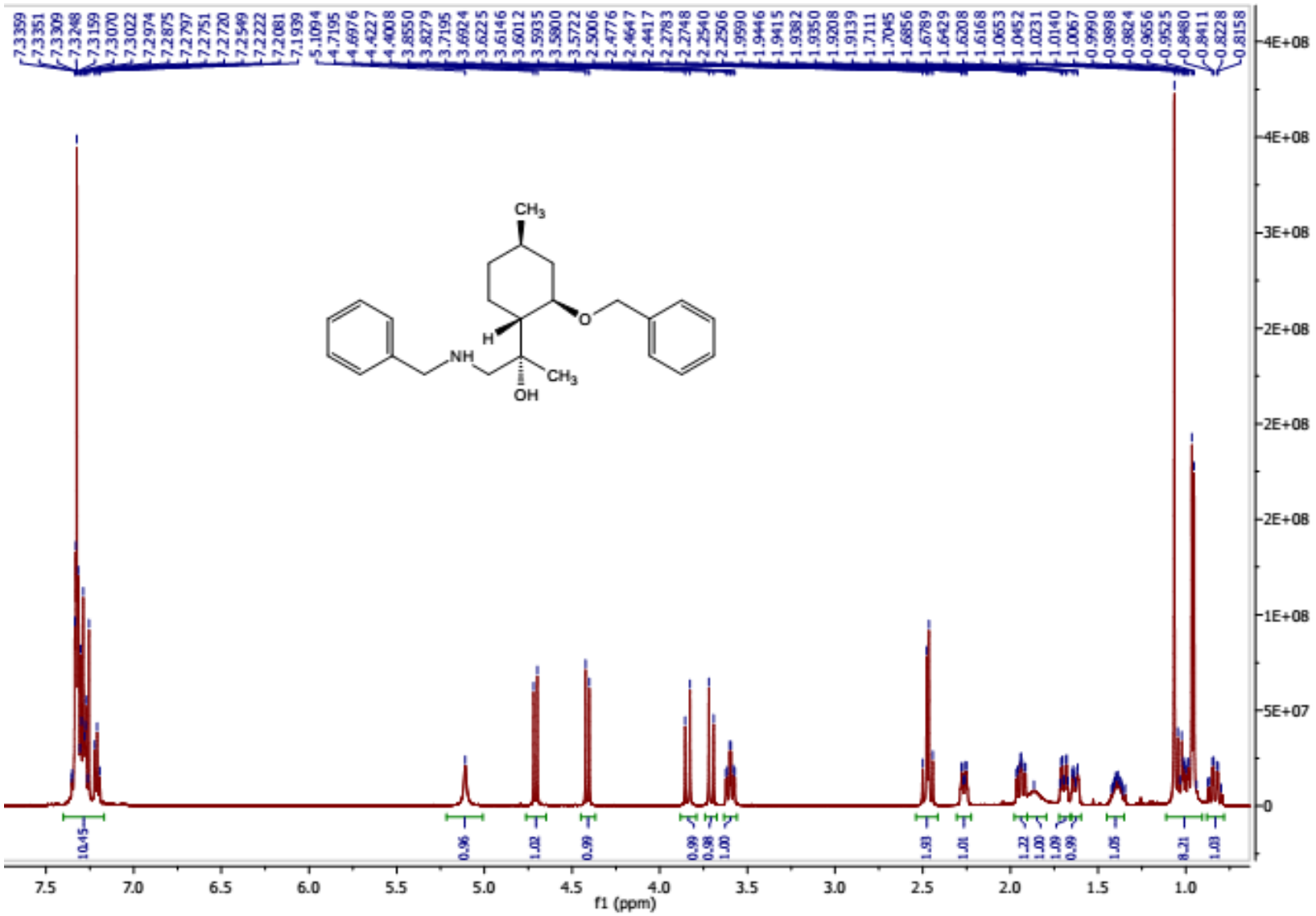
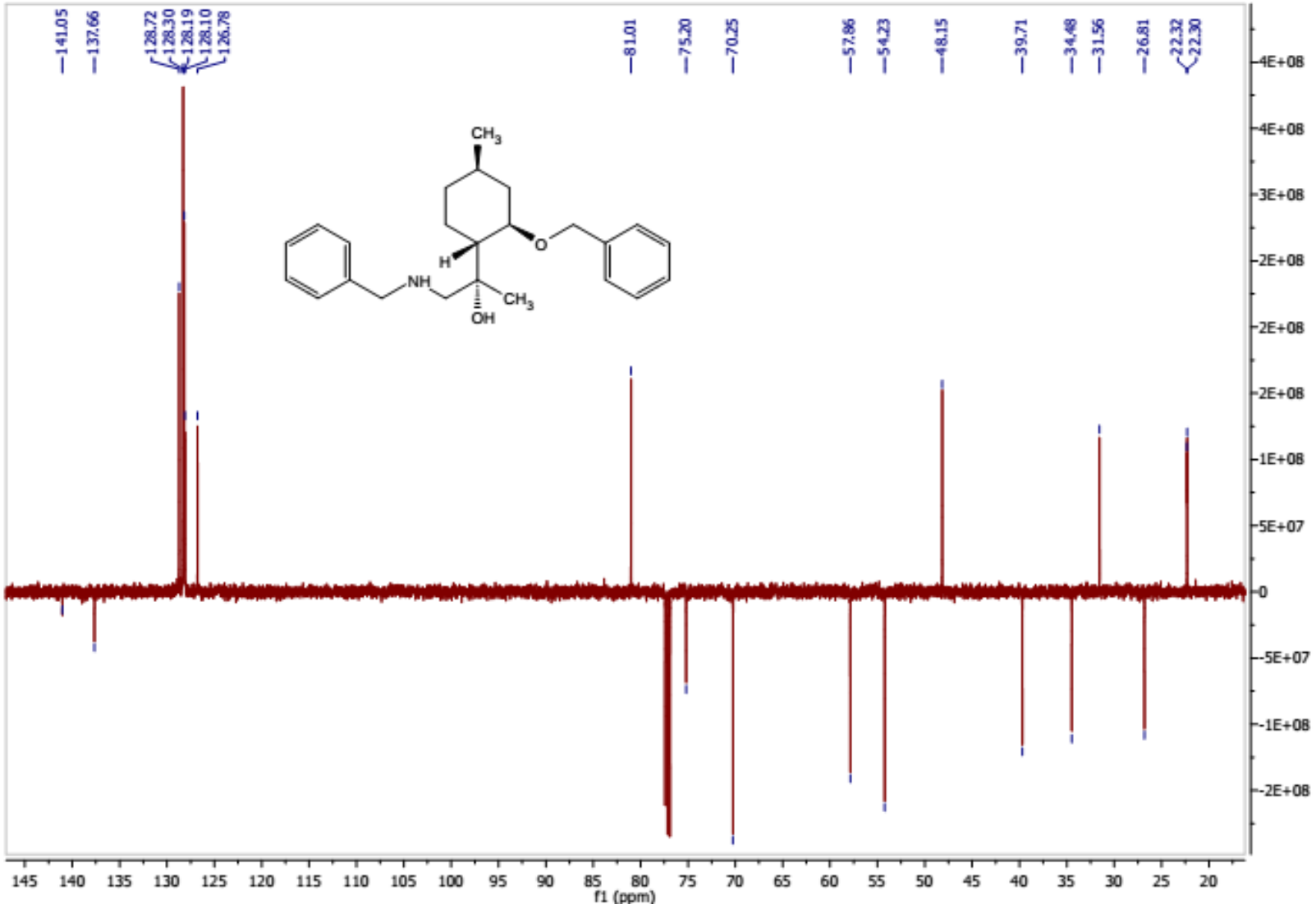


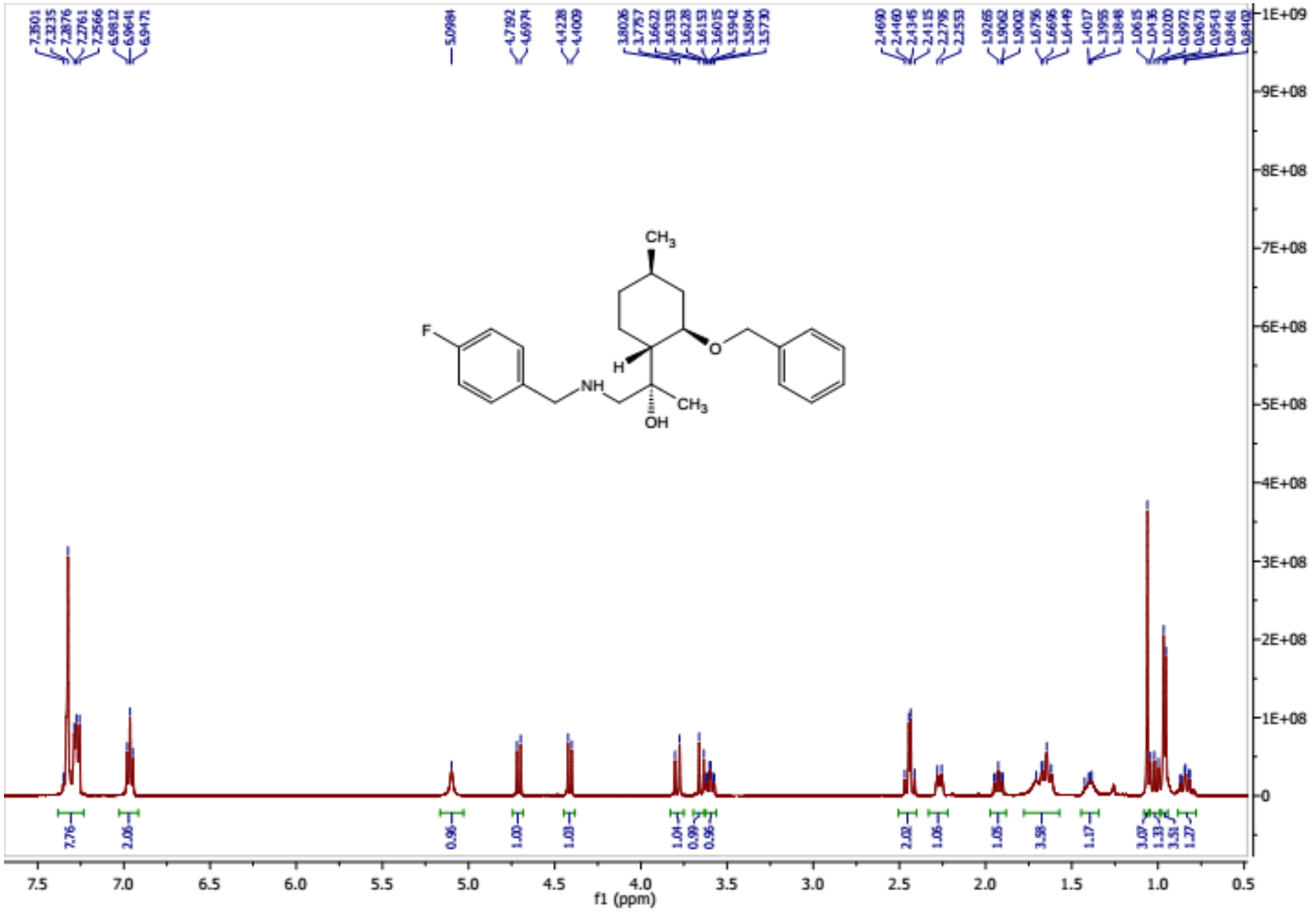
[1]H-NMR of compound **6a**



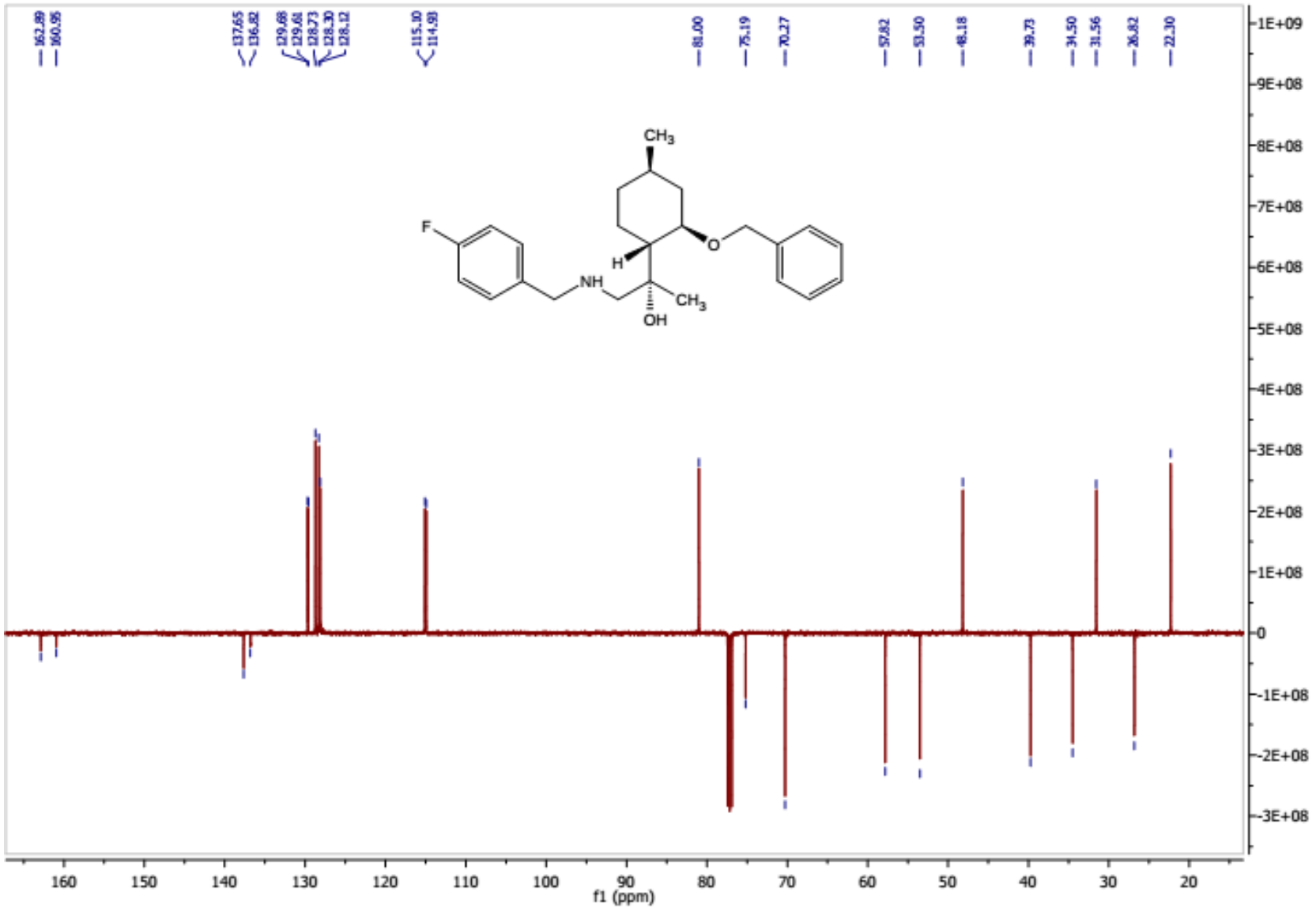
$^{13}$C-NMR of compound **6a**



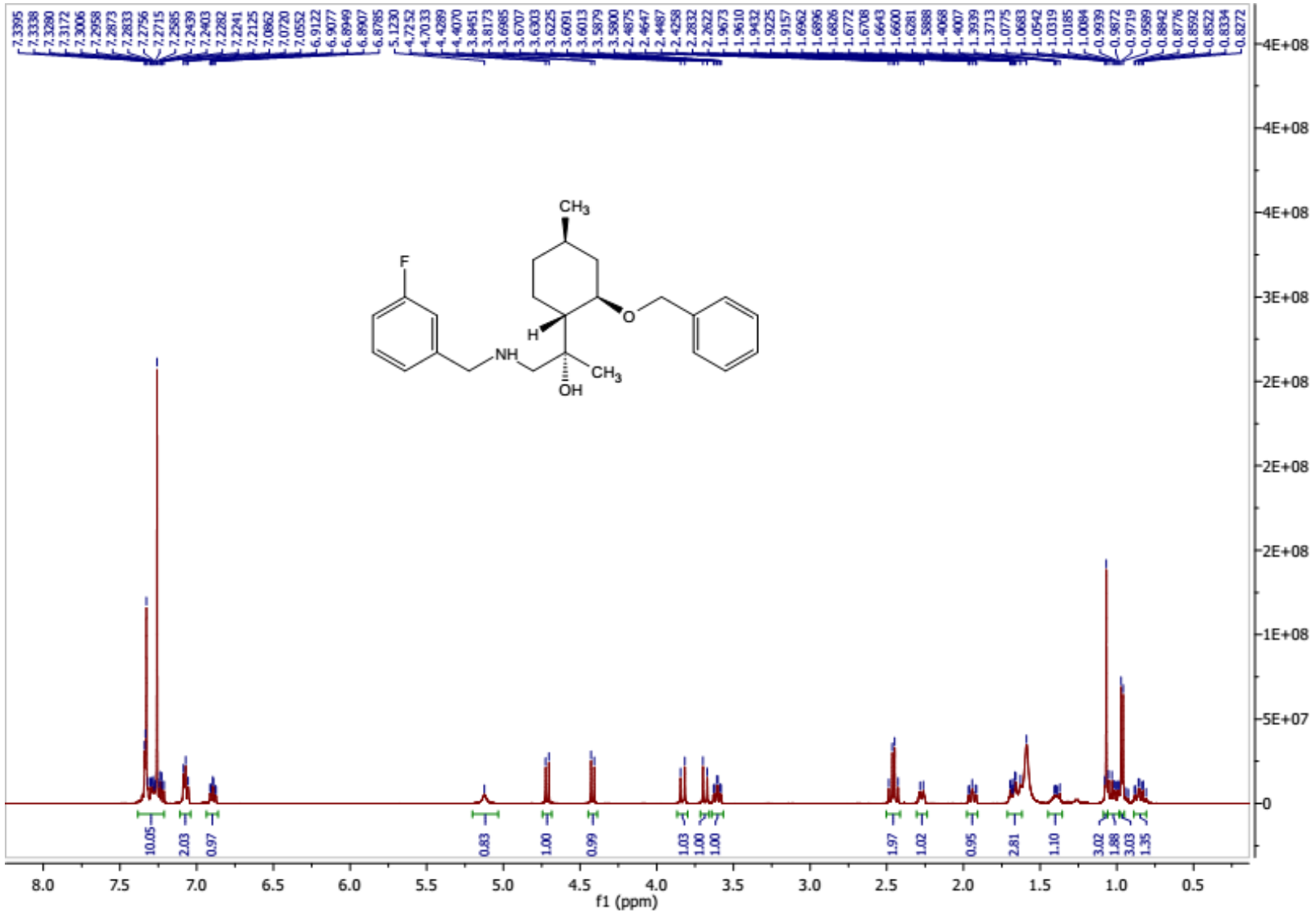
[1]H-NMR of compound **7a**



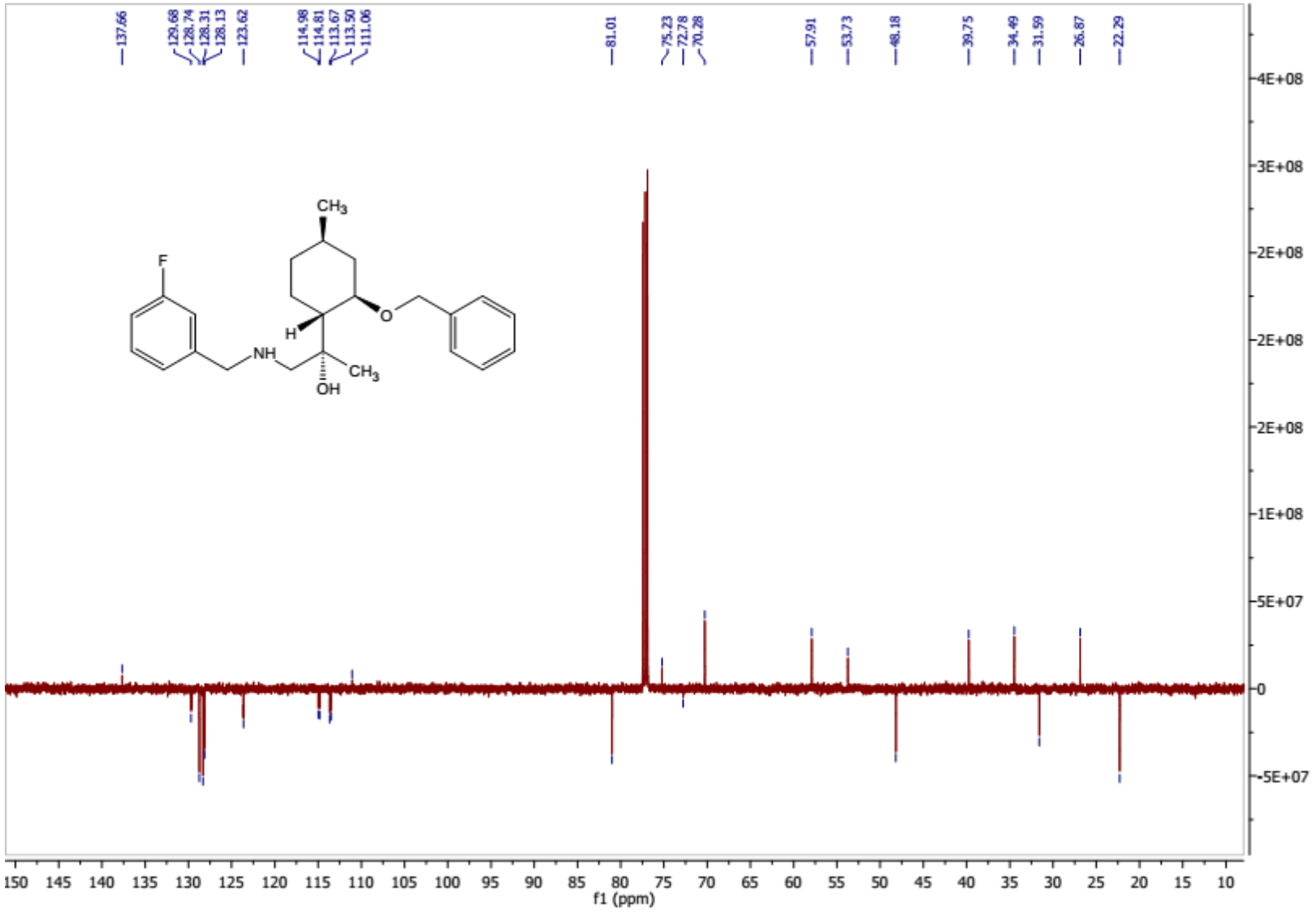
$^{13}$C-NMR of compound **7a**



[1]H-NMR of compound **8a**



$^{13}$C-NMR of compound **8a**



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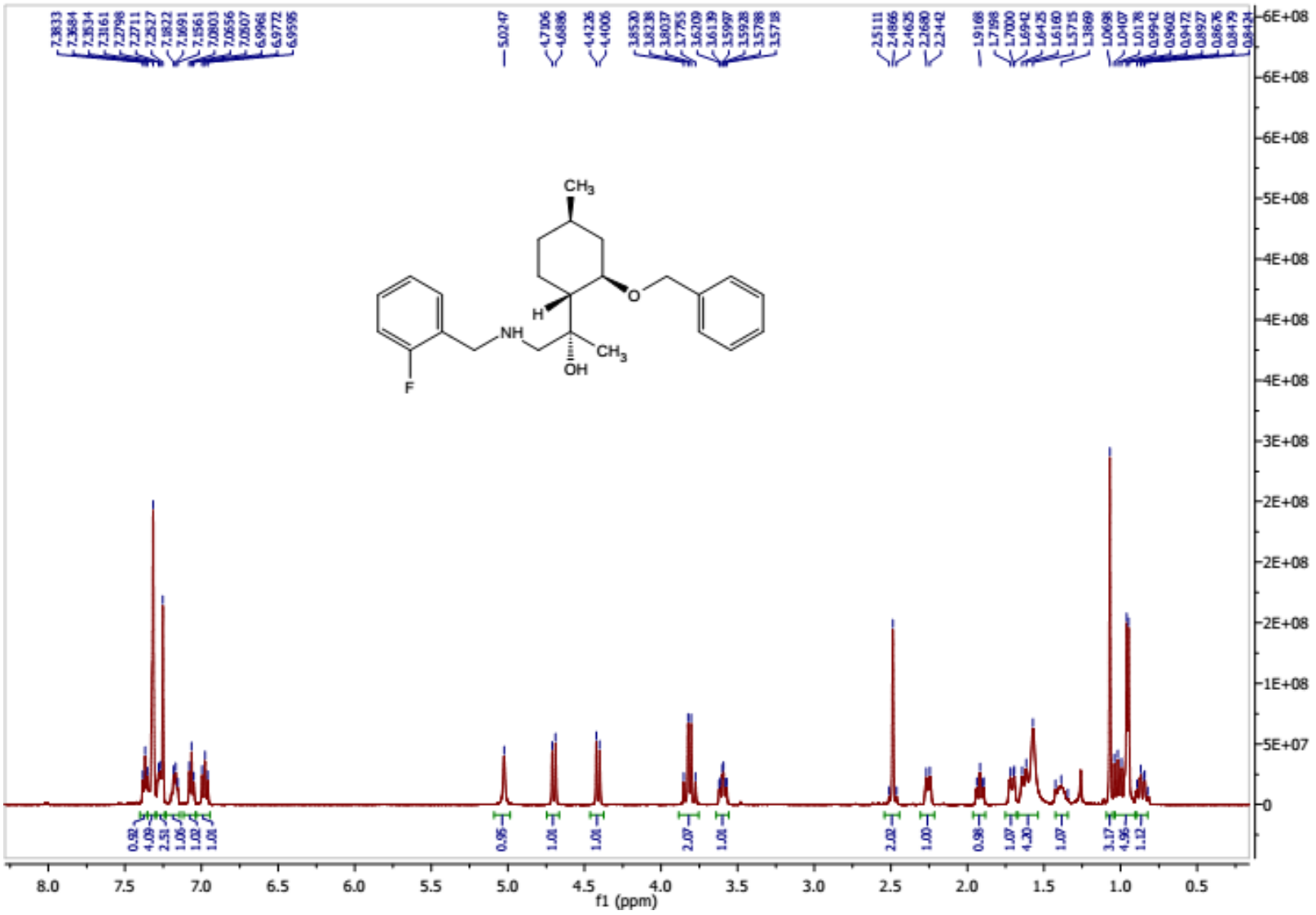

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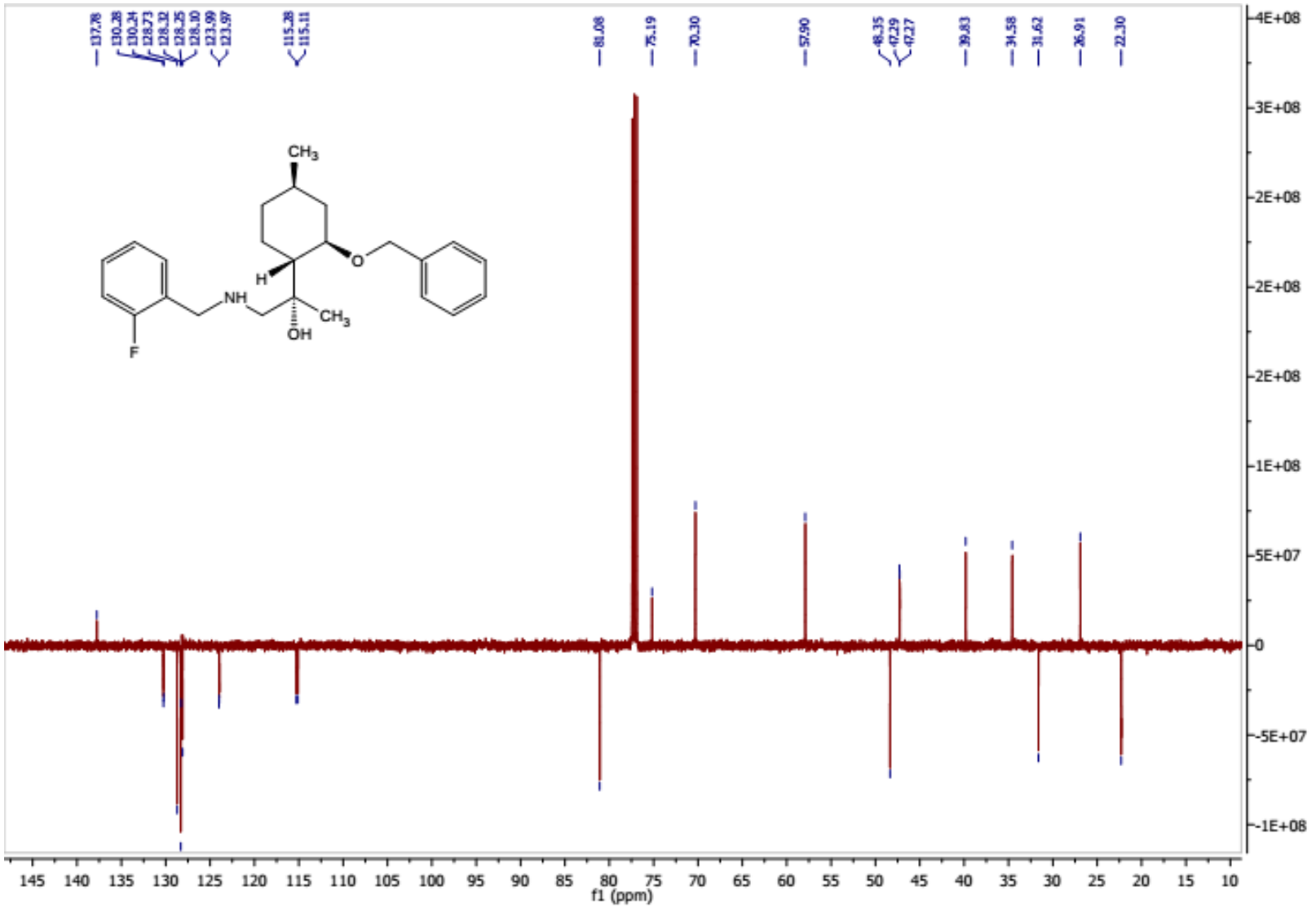

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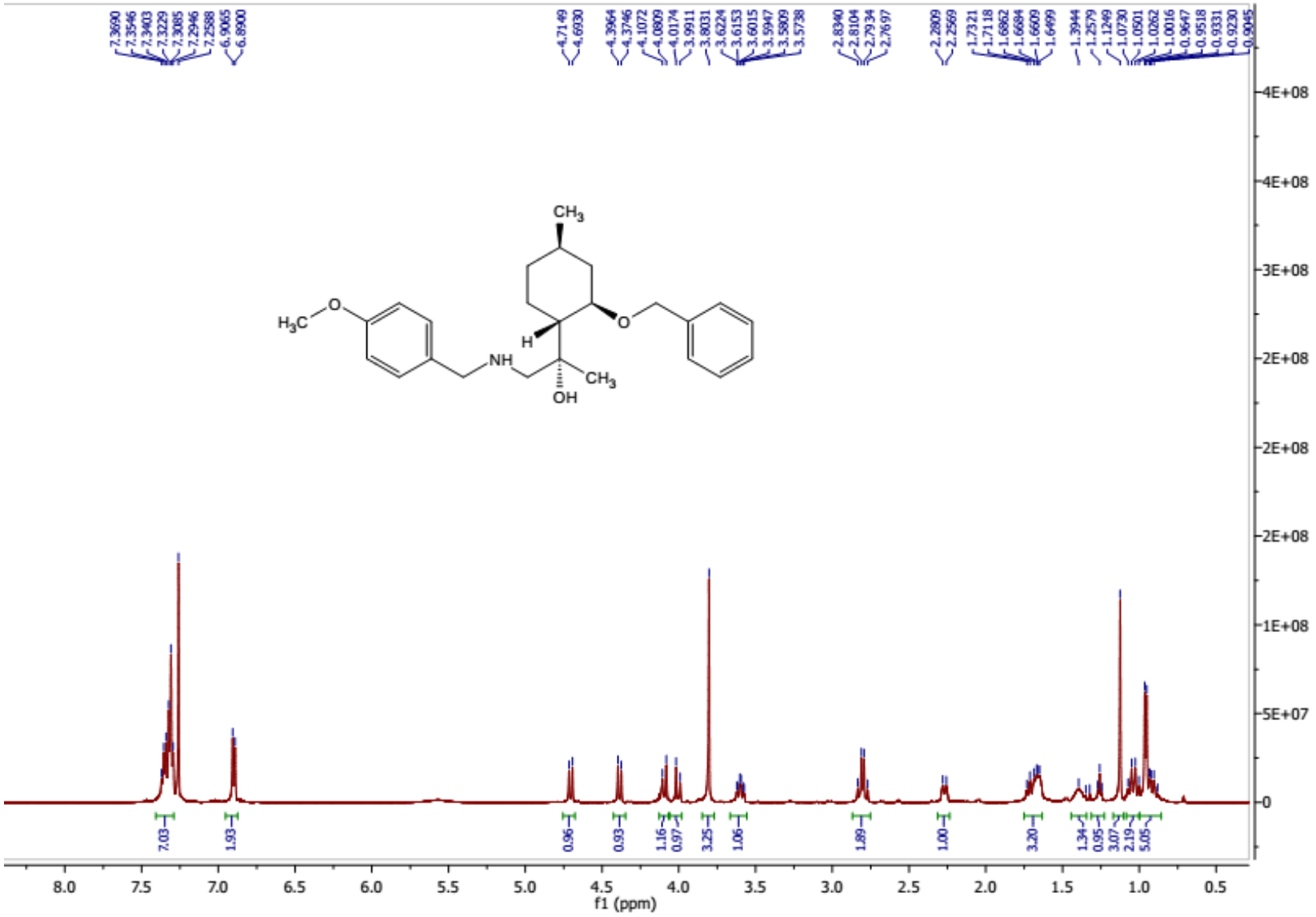

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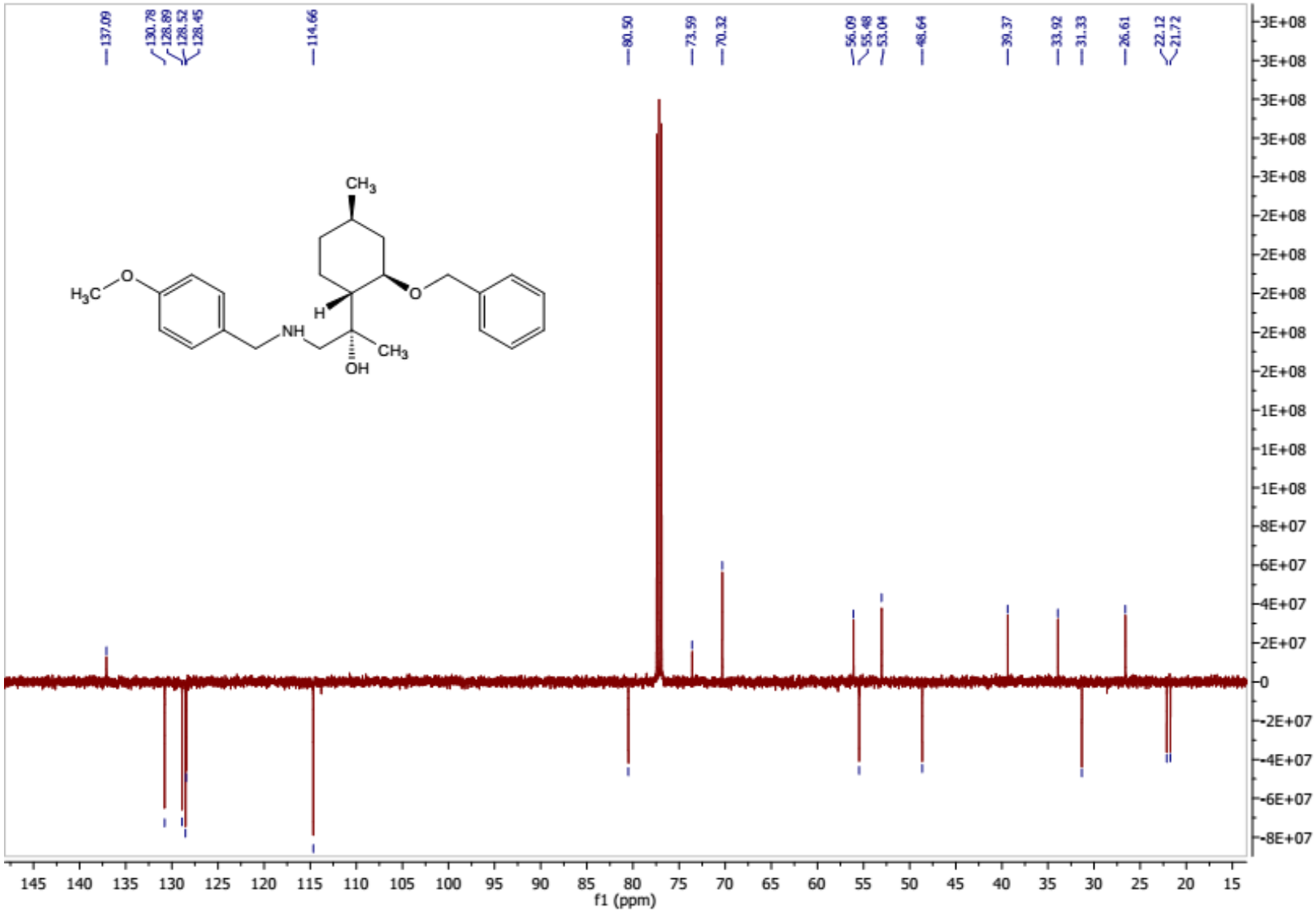

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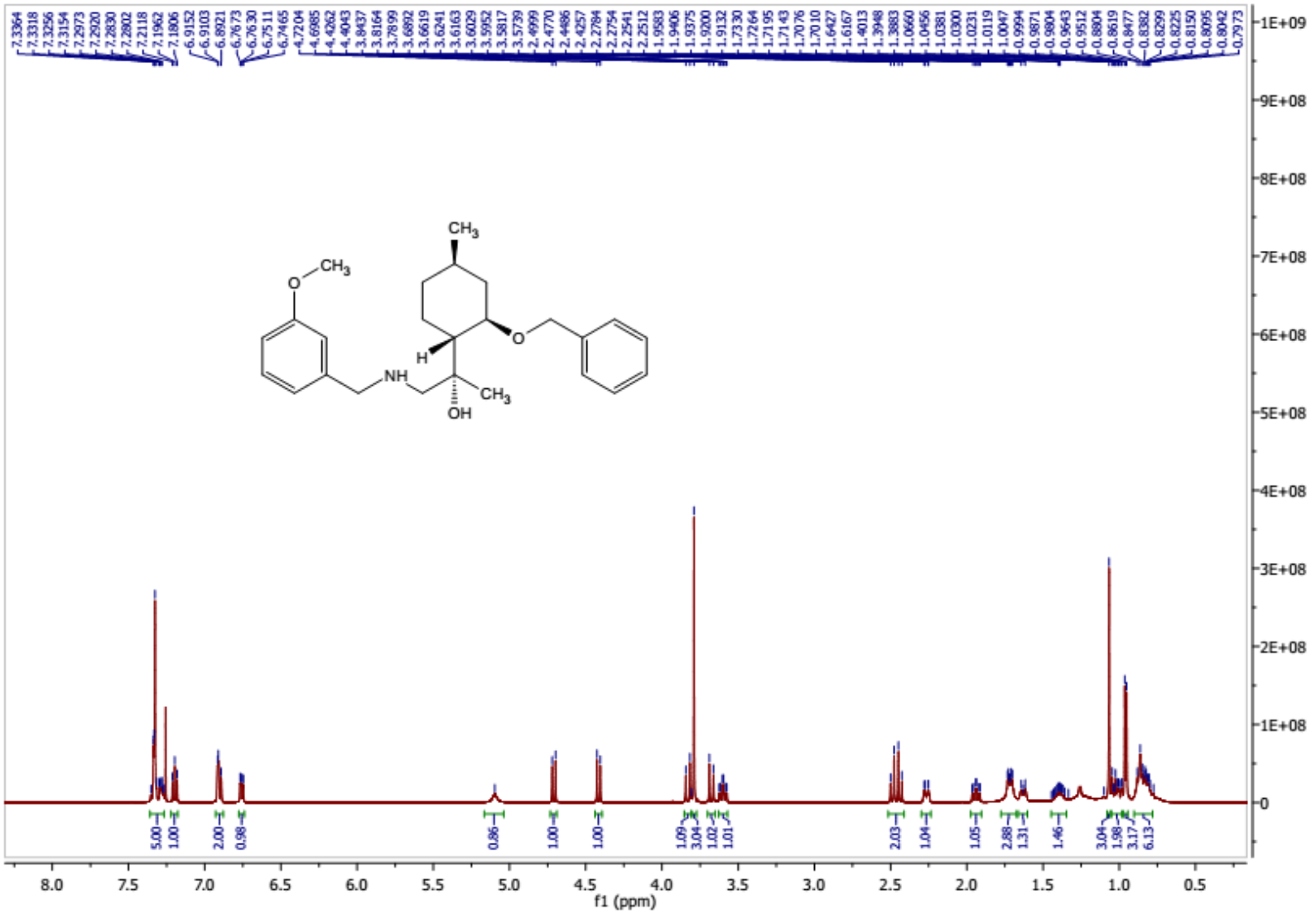

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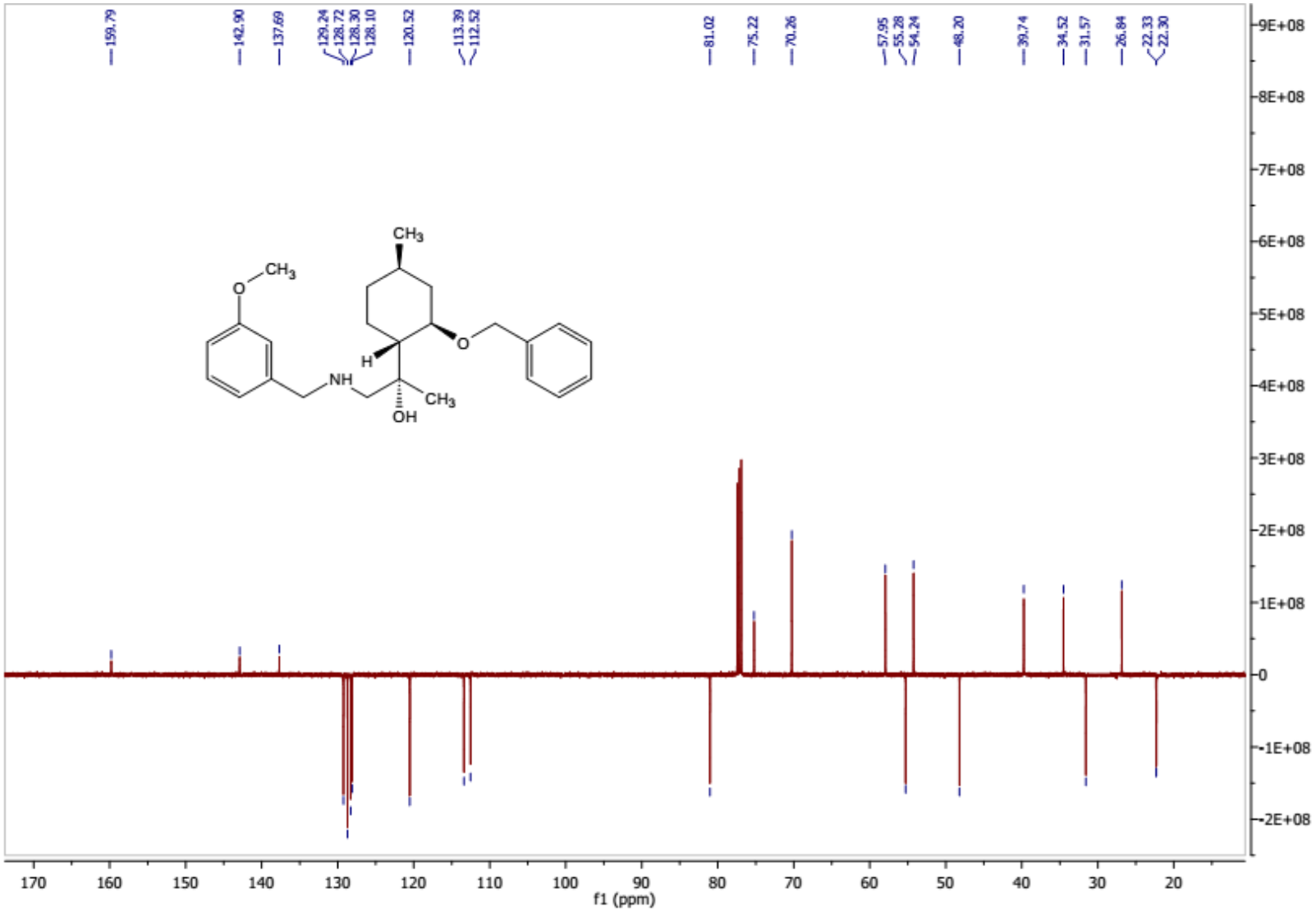

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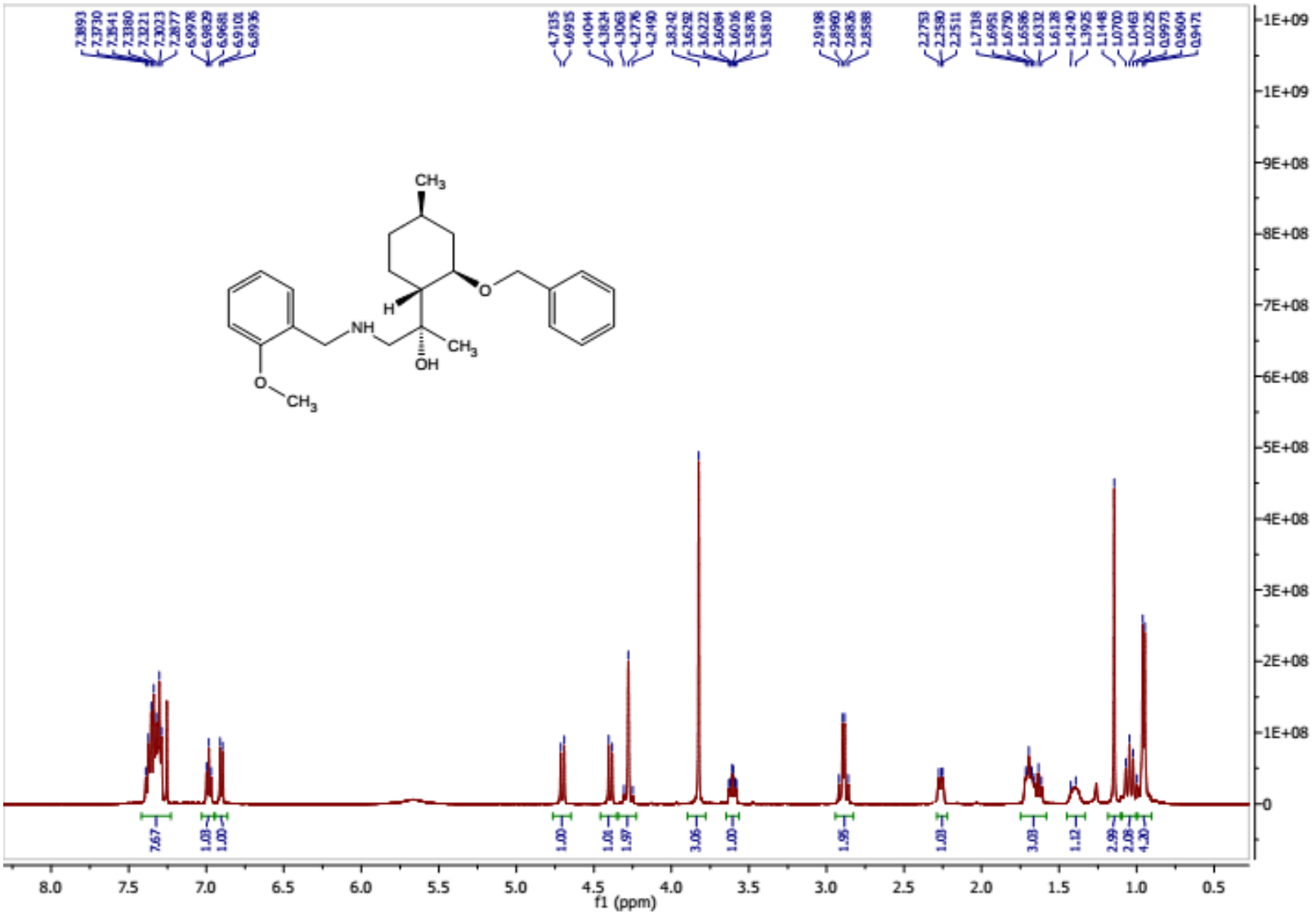

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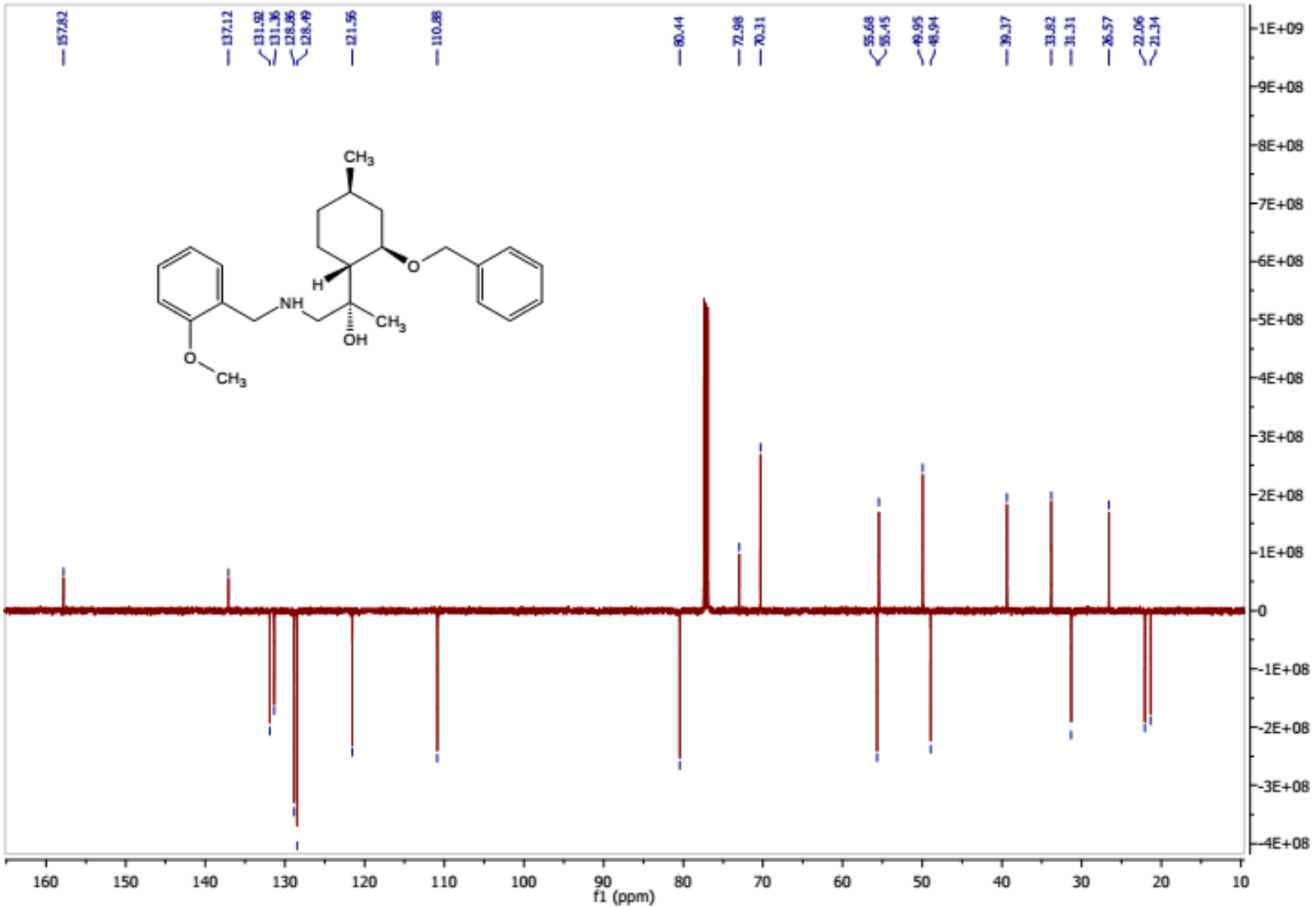

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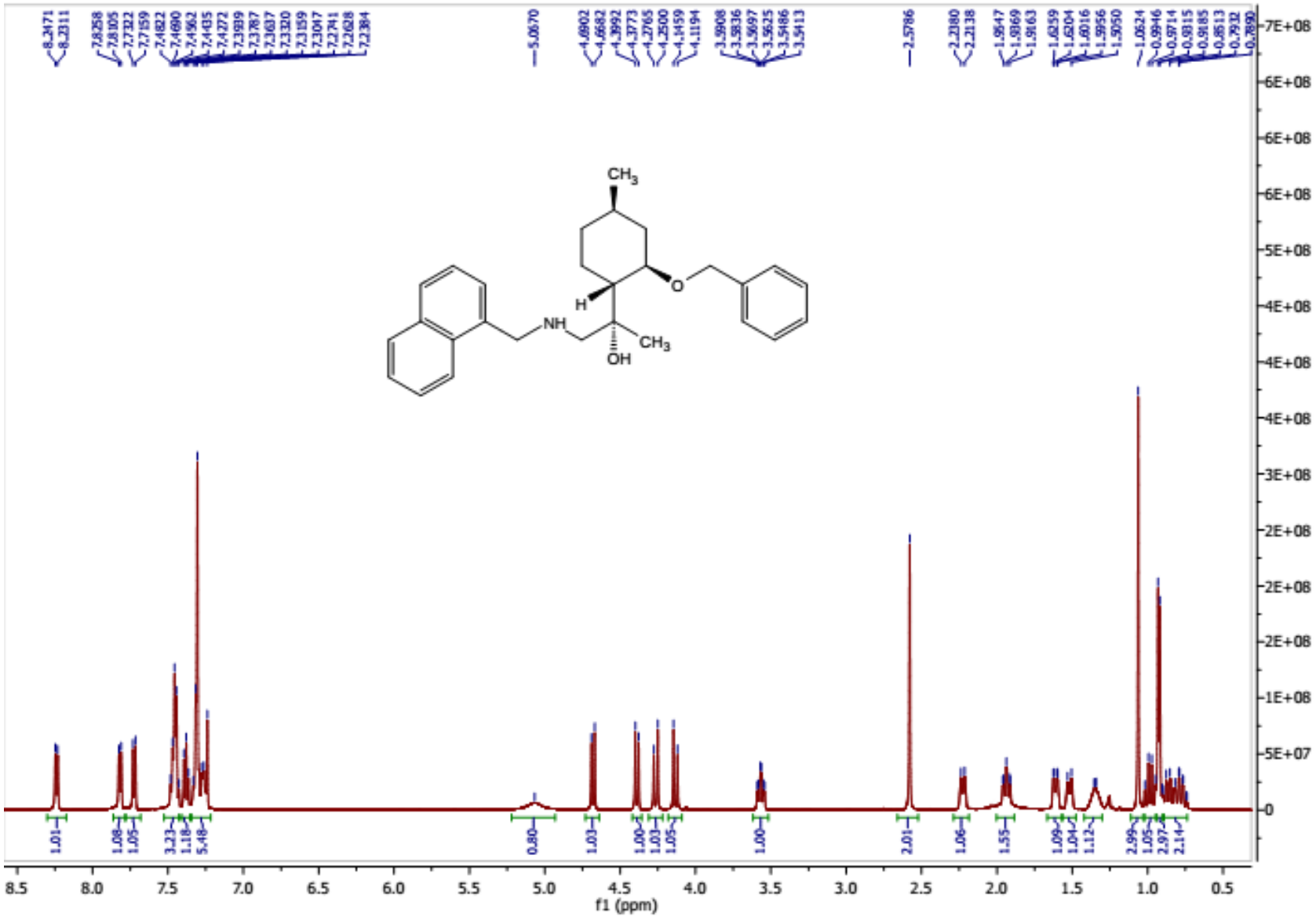

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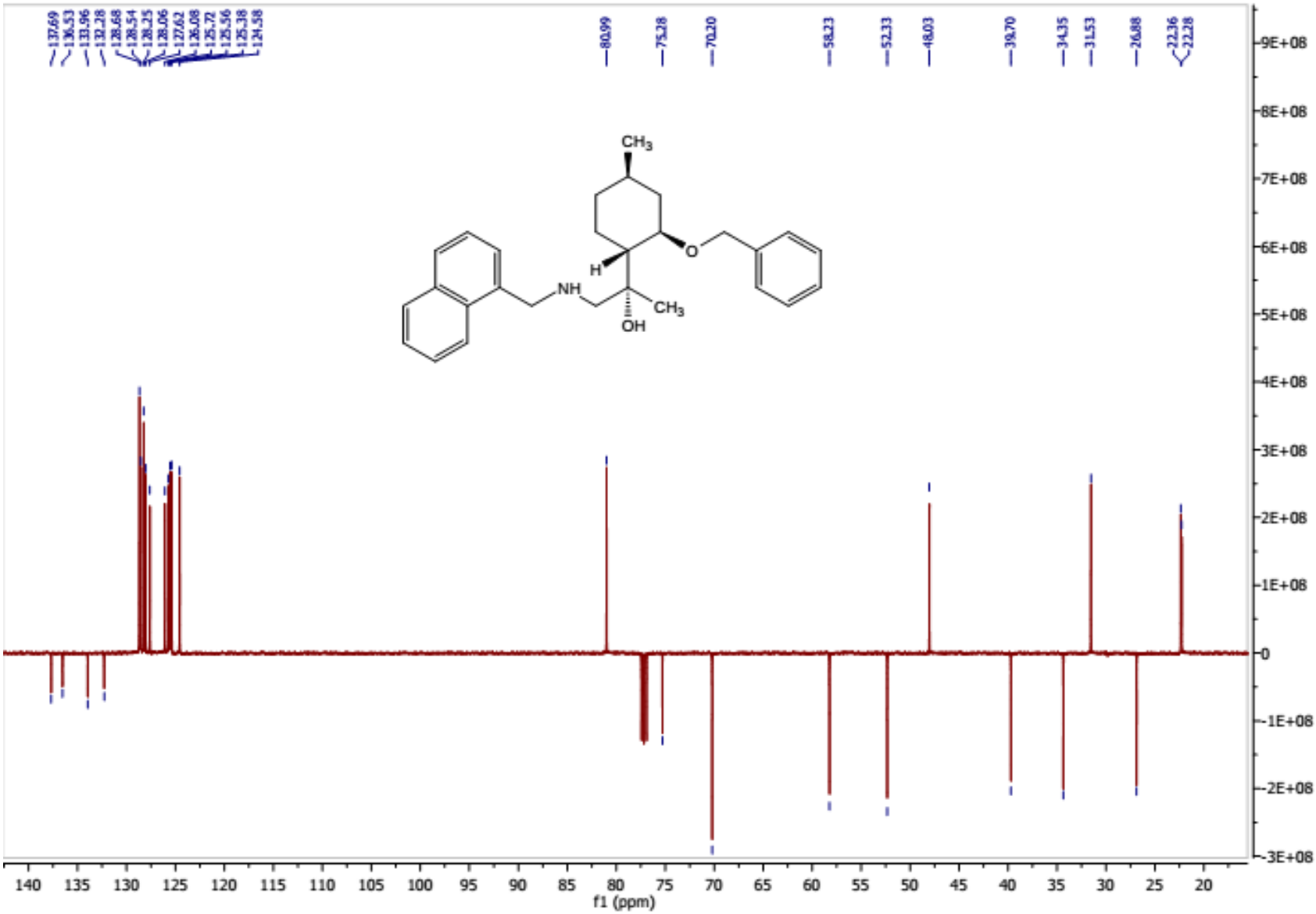
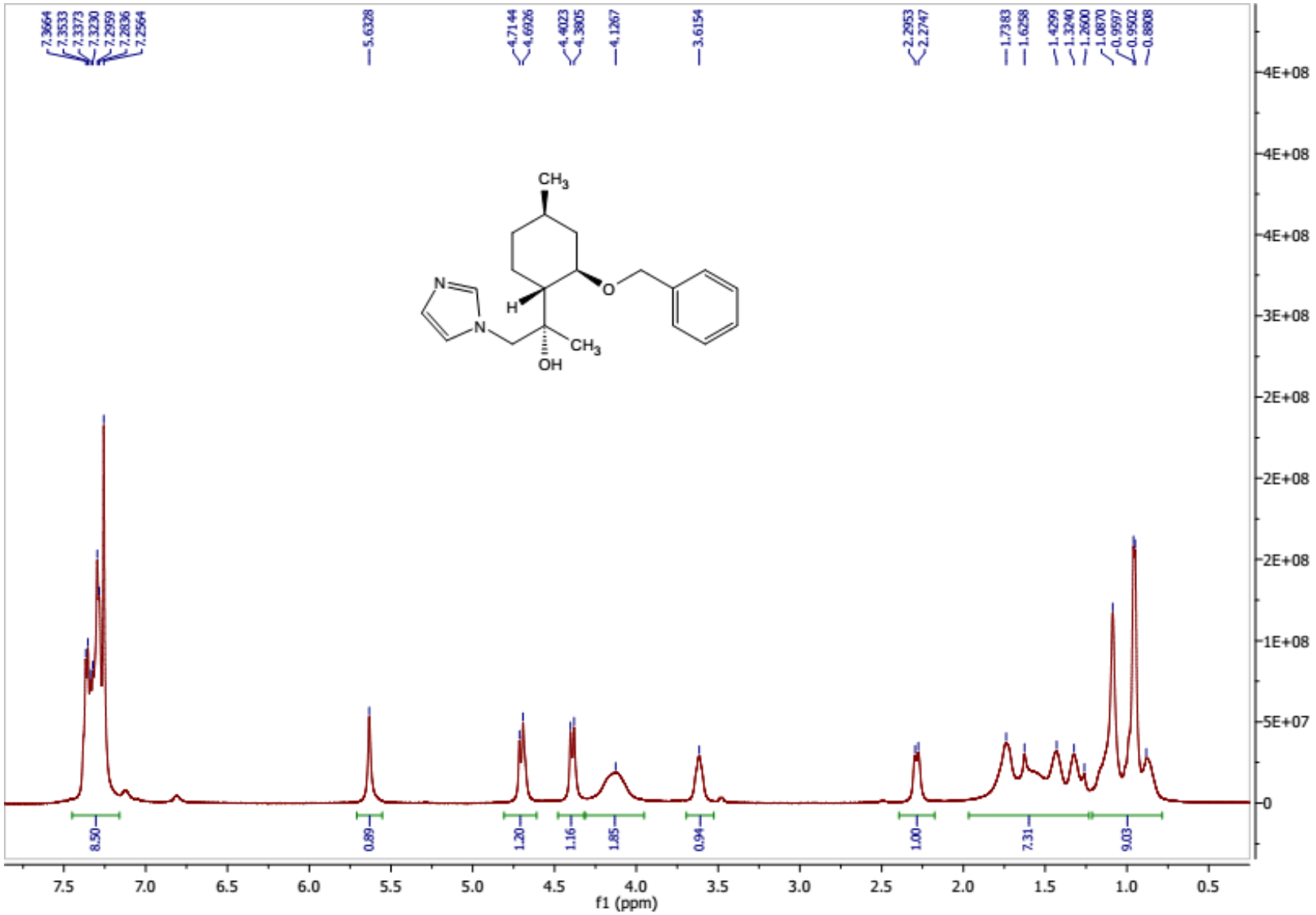
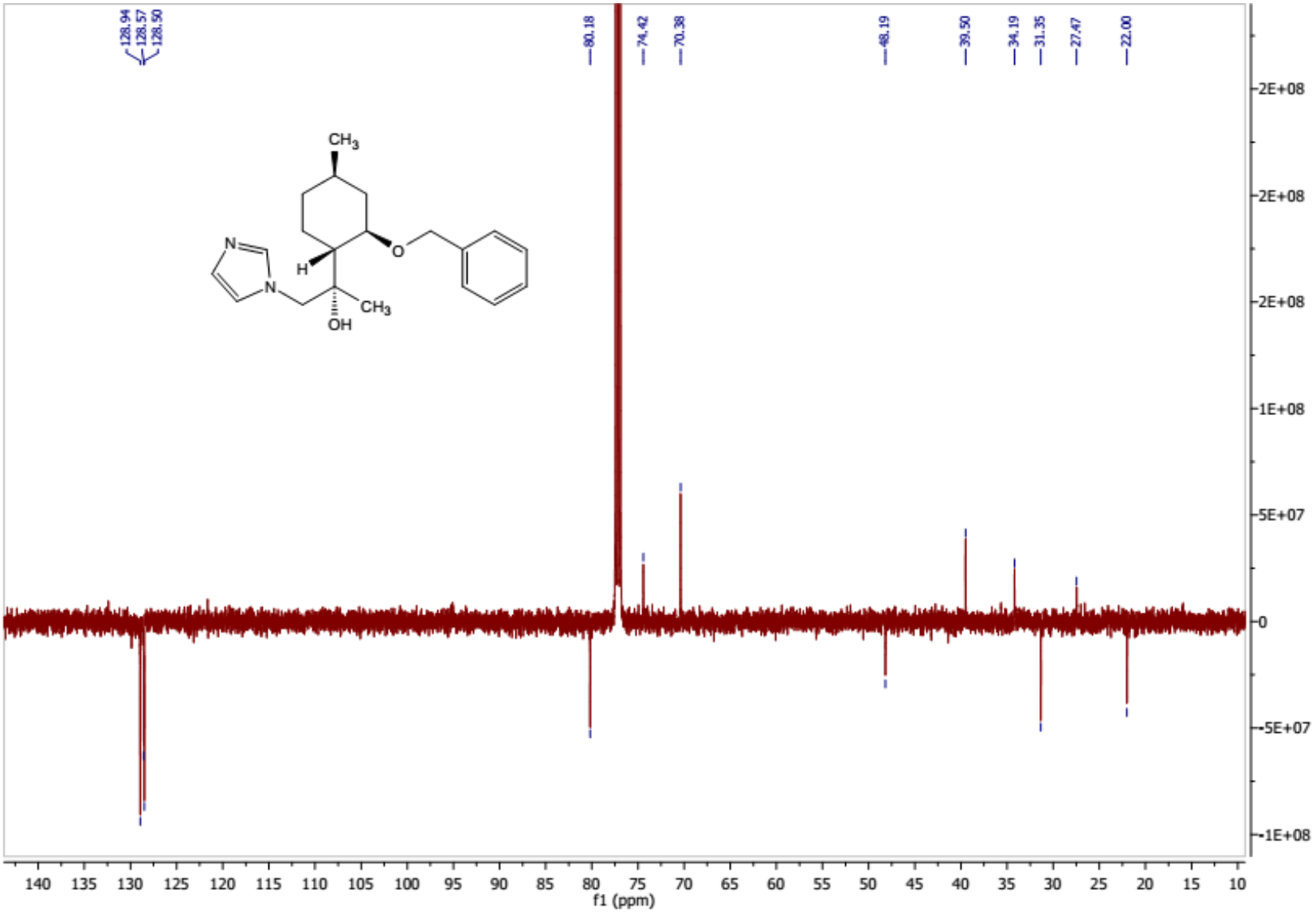


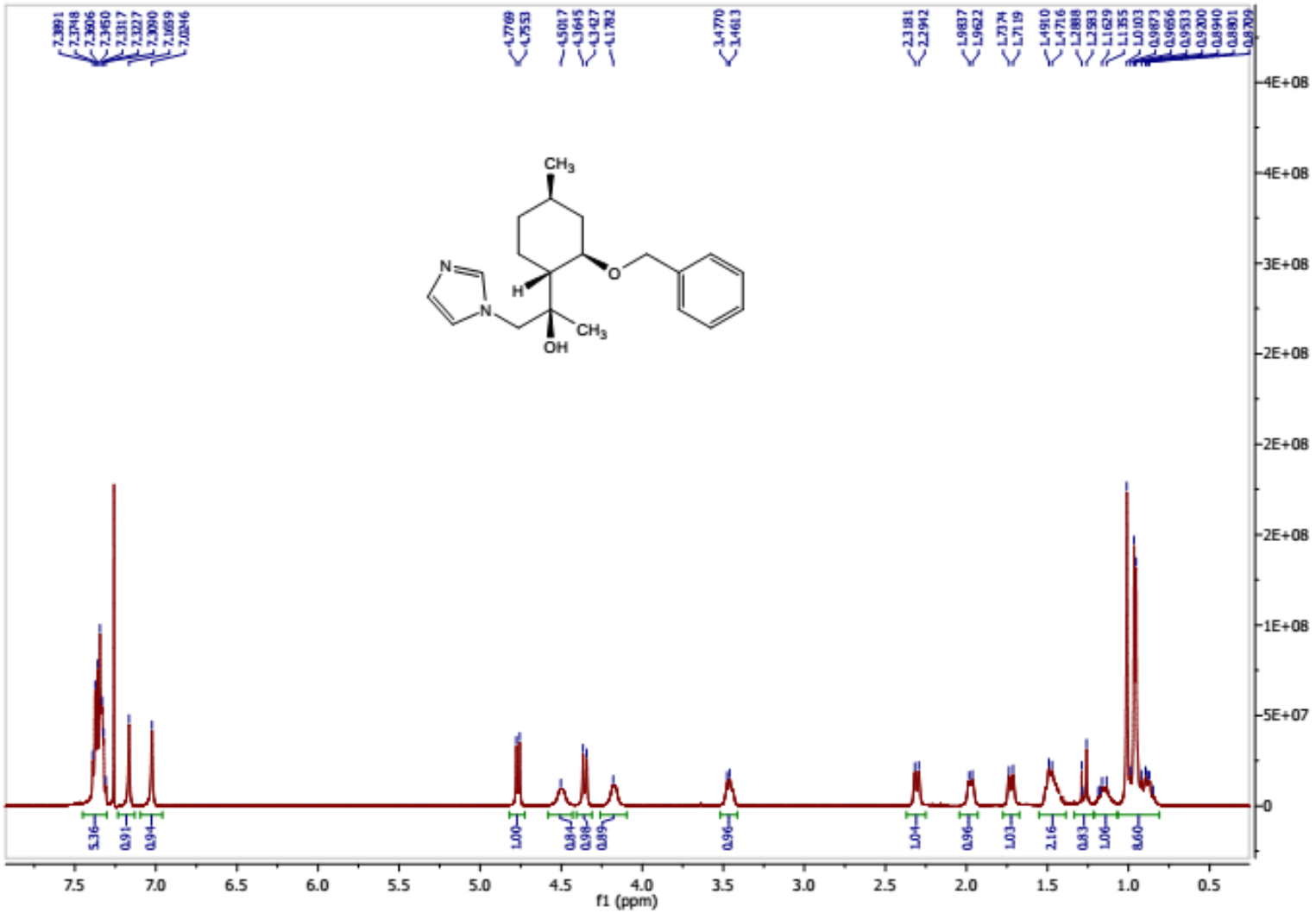
[1]H-NMR of compound **14a**



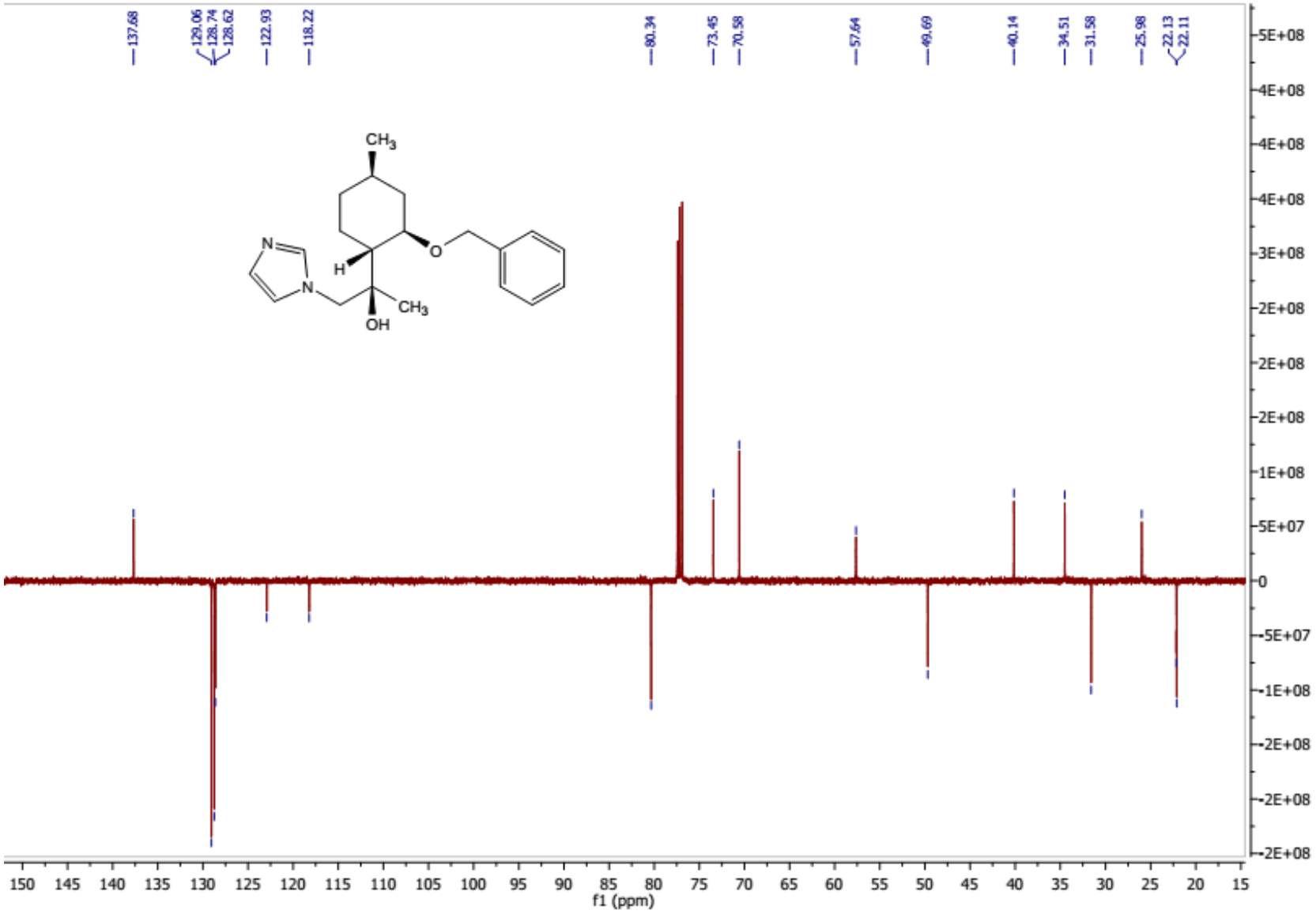
$^{13}$C-NMR of compound **14a**



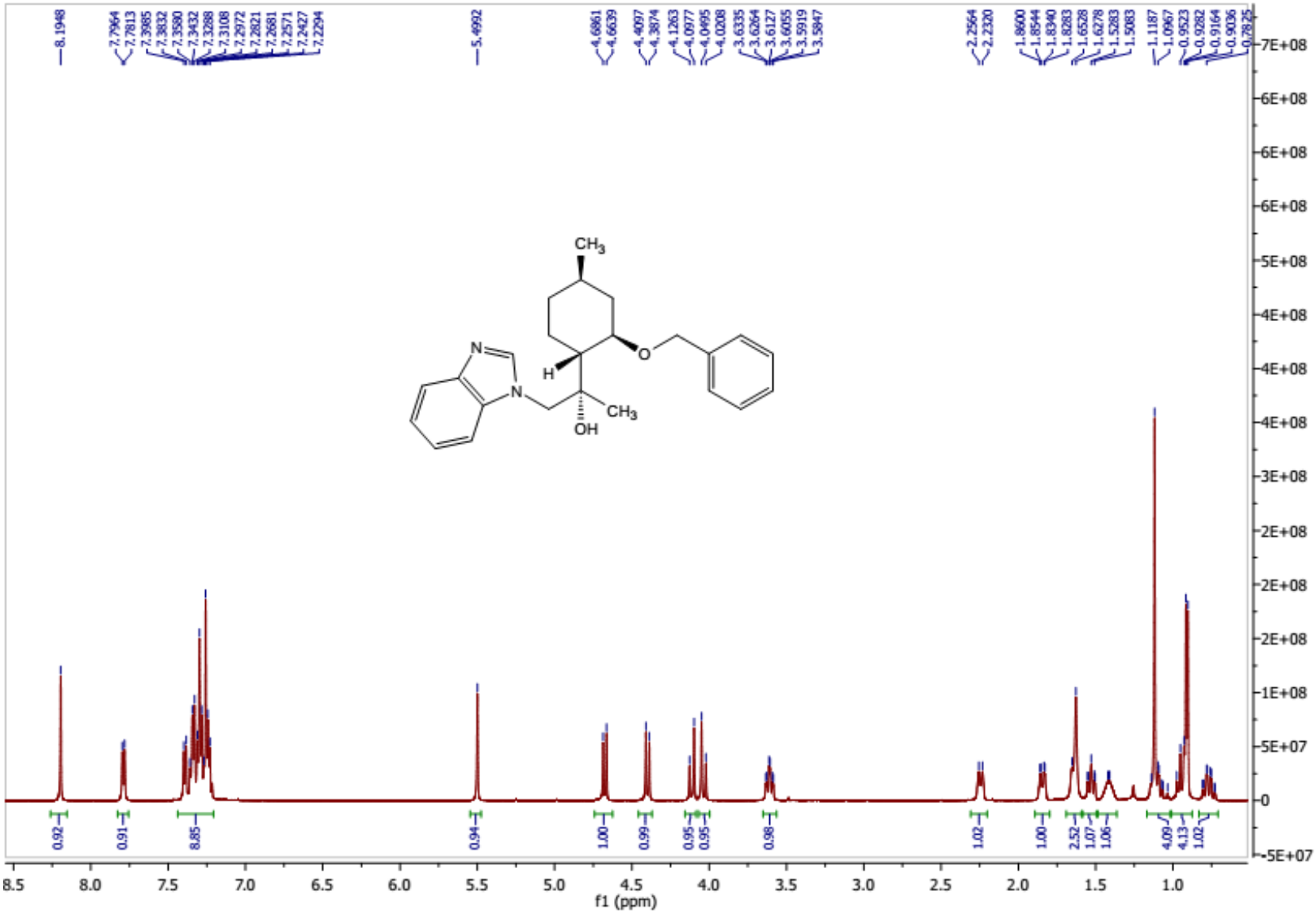
[1]H-NMR of compound **14b**



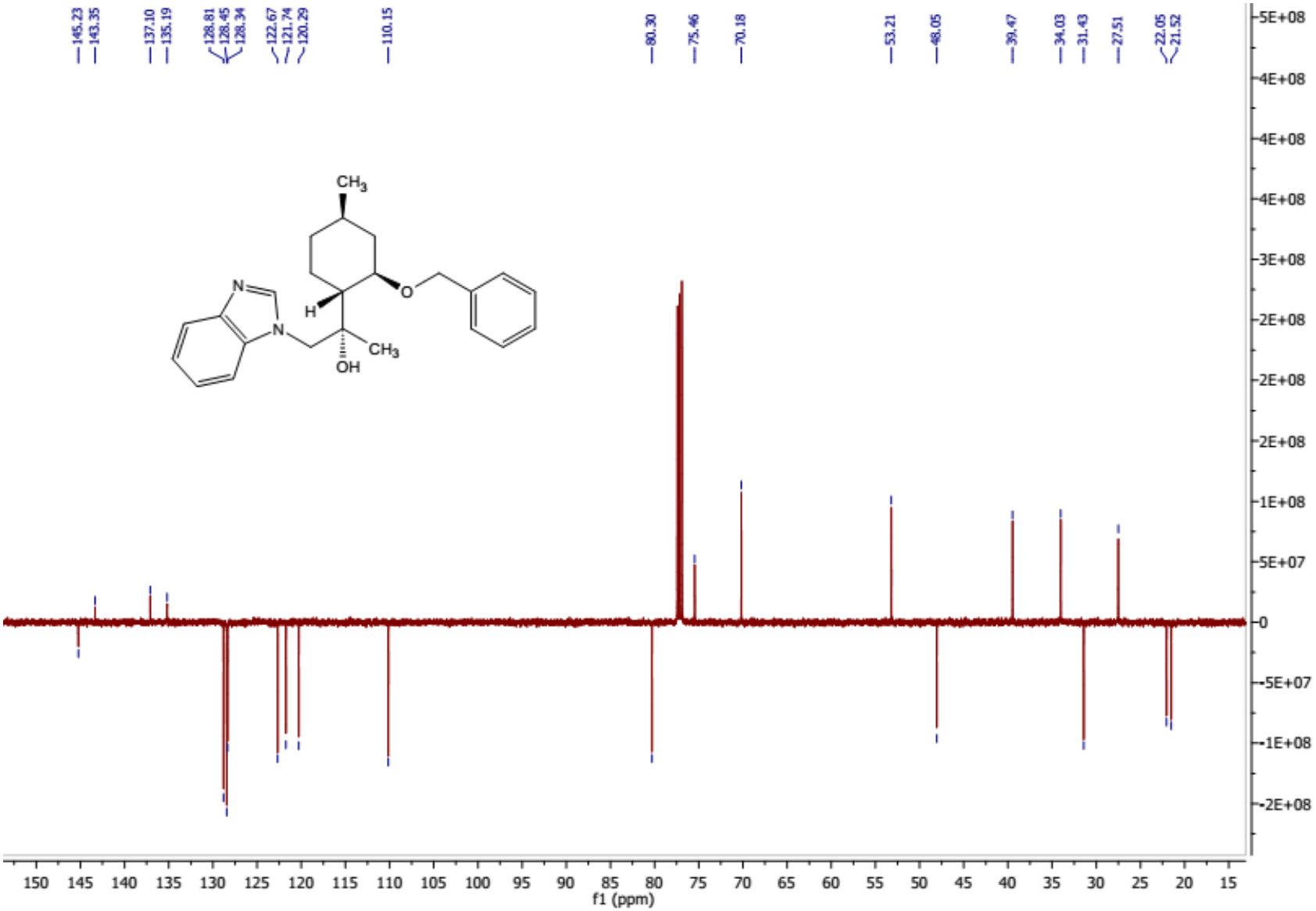
$^{13}$C-NMR of compound **14b**



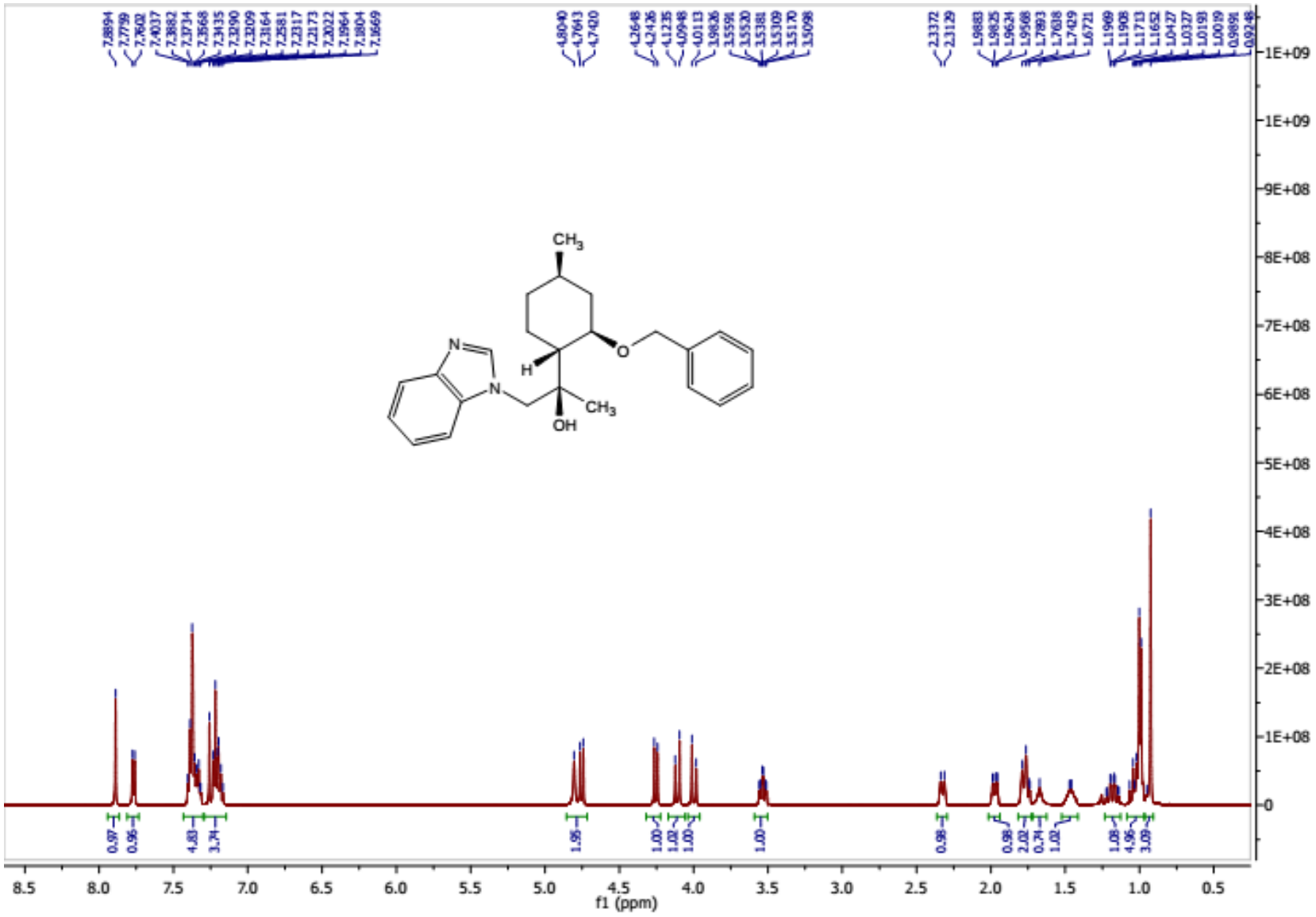
[1]H-NMR of compound **15a**



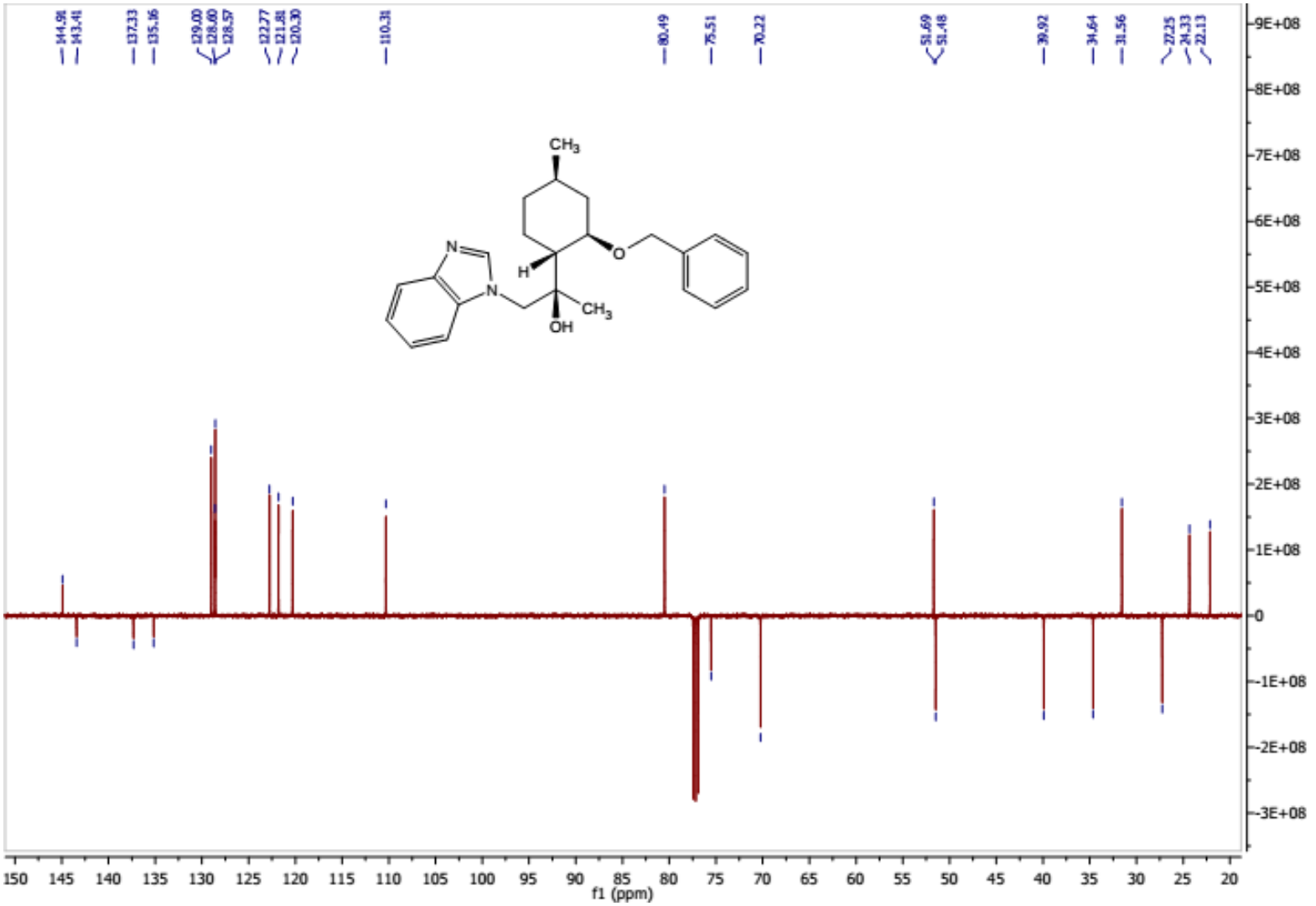
$^{13}$C-NMR of compound **15a**



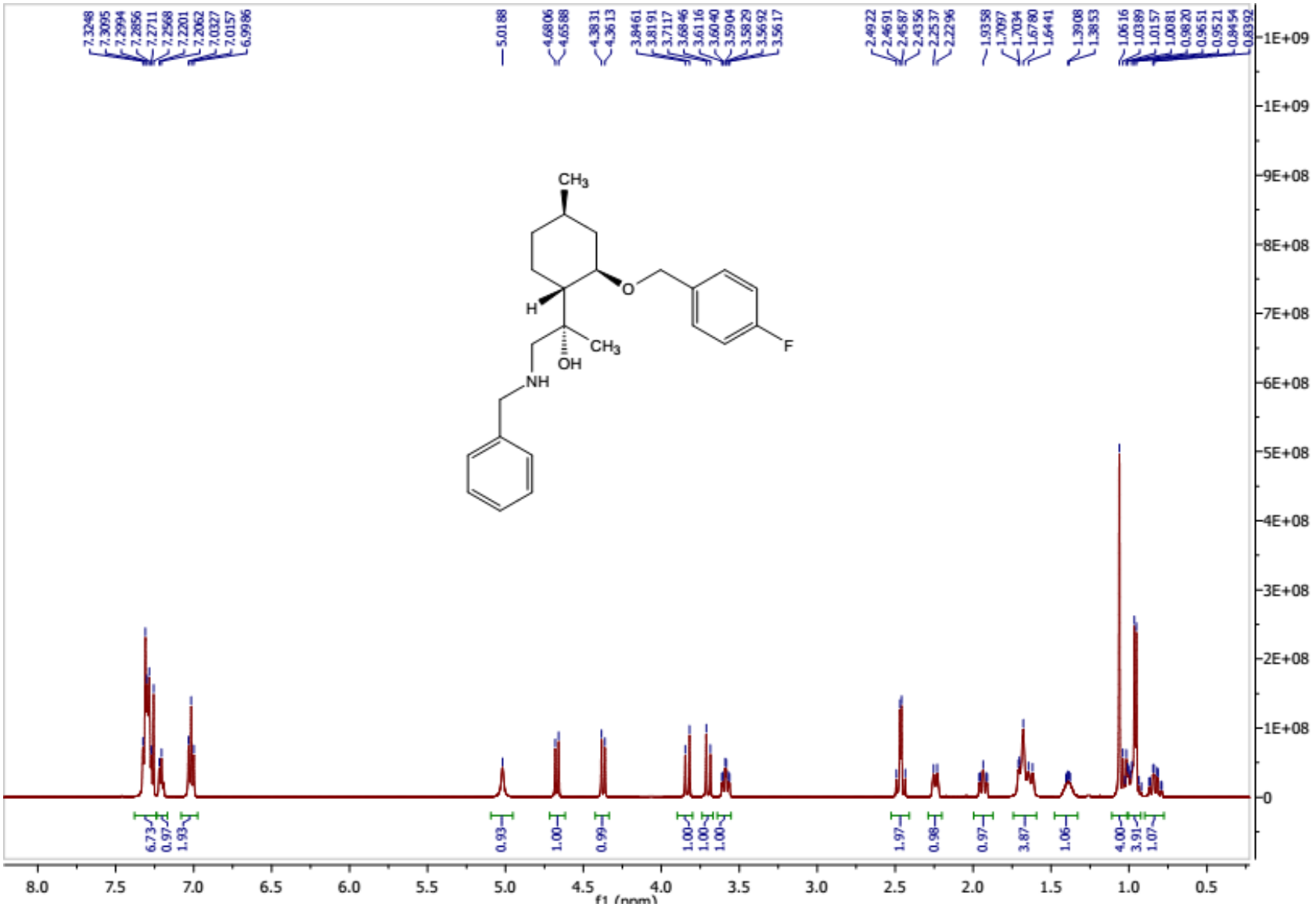
[1]H-NMR of compound **15b**



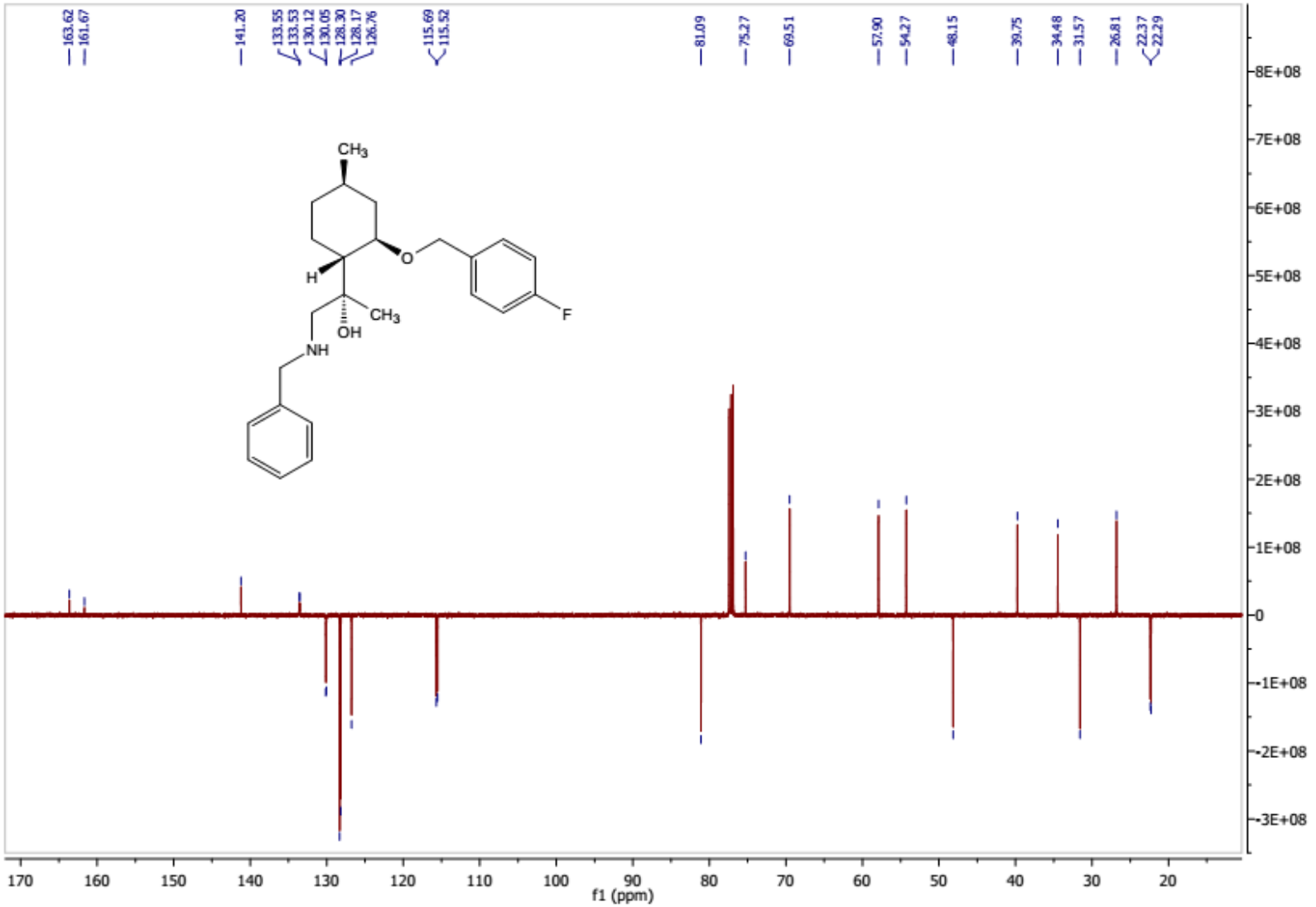
$^{13}$C-NMR of compound **15b**



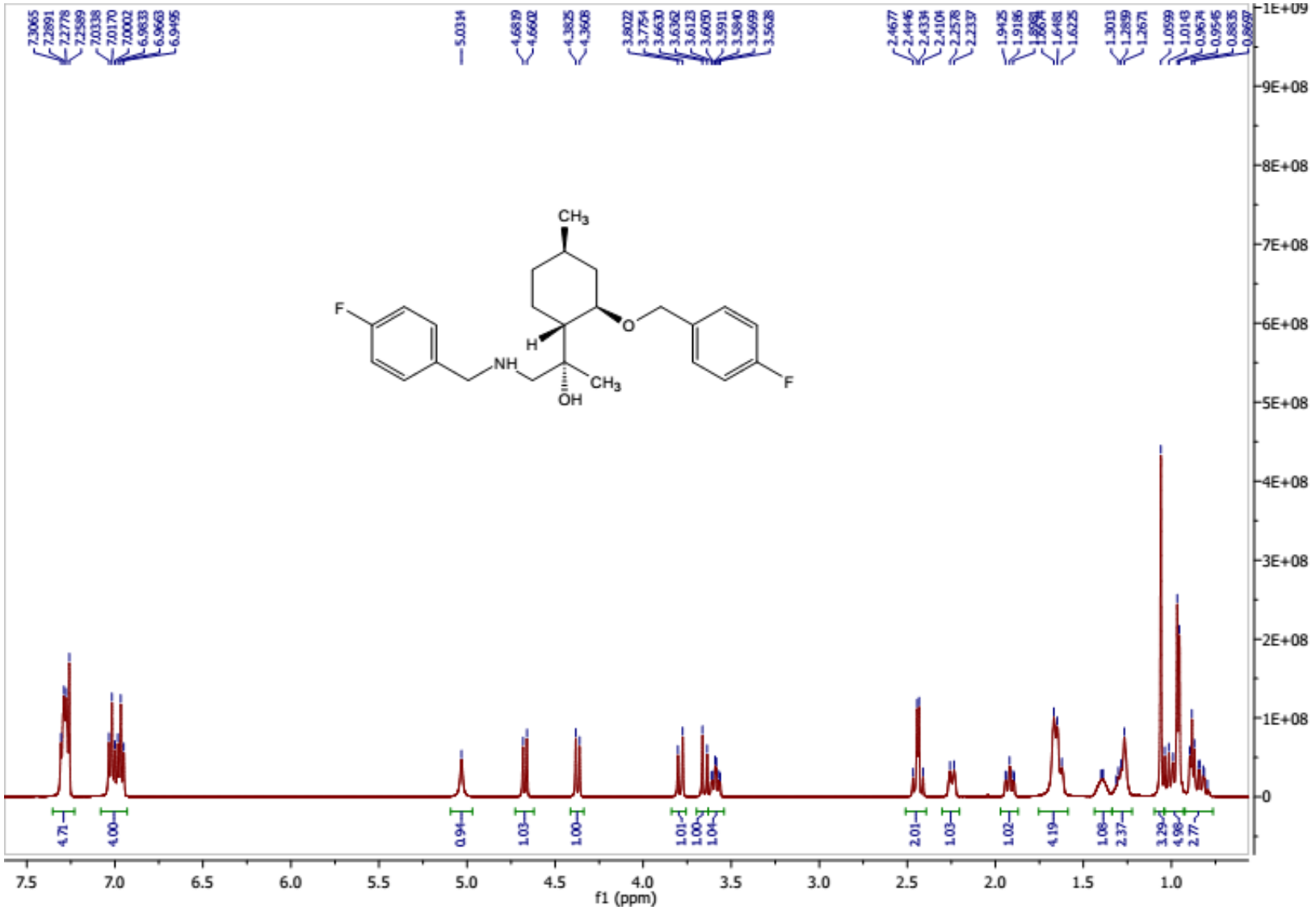
[1]H-NMR of compound **16a**



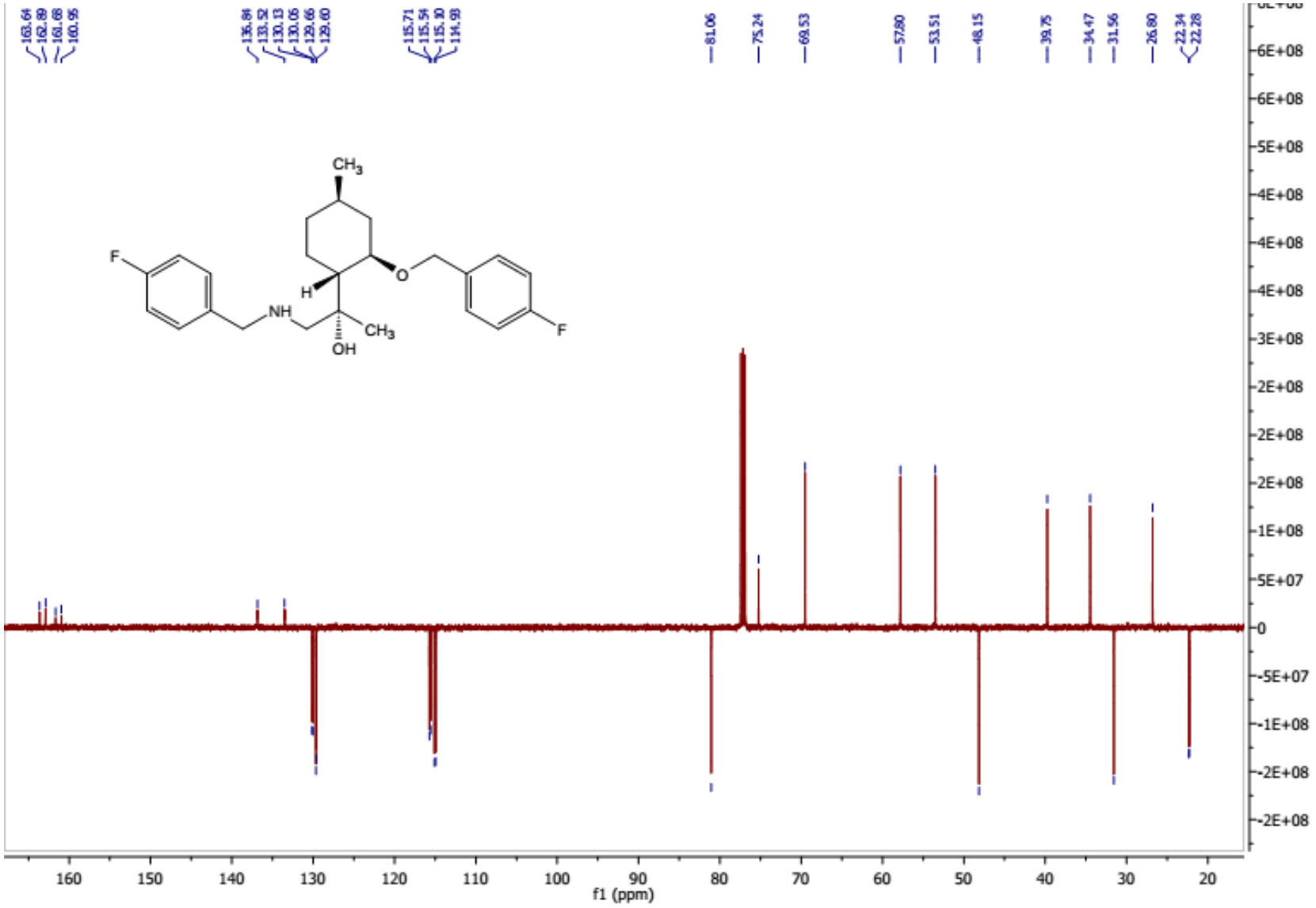
$^{13}$C-NMR of compound **16a**



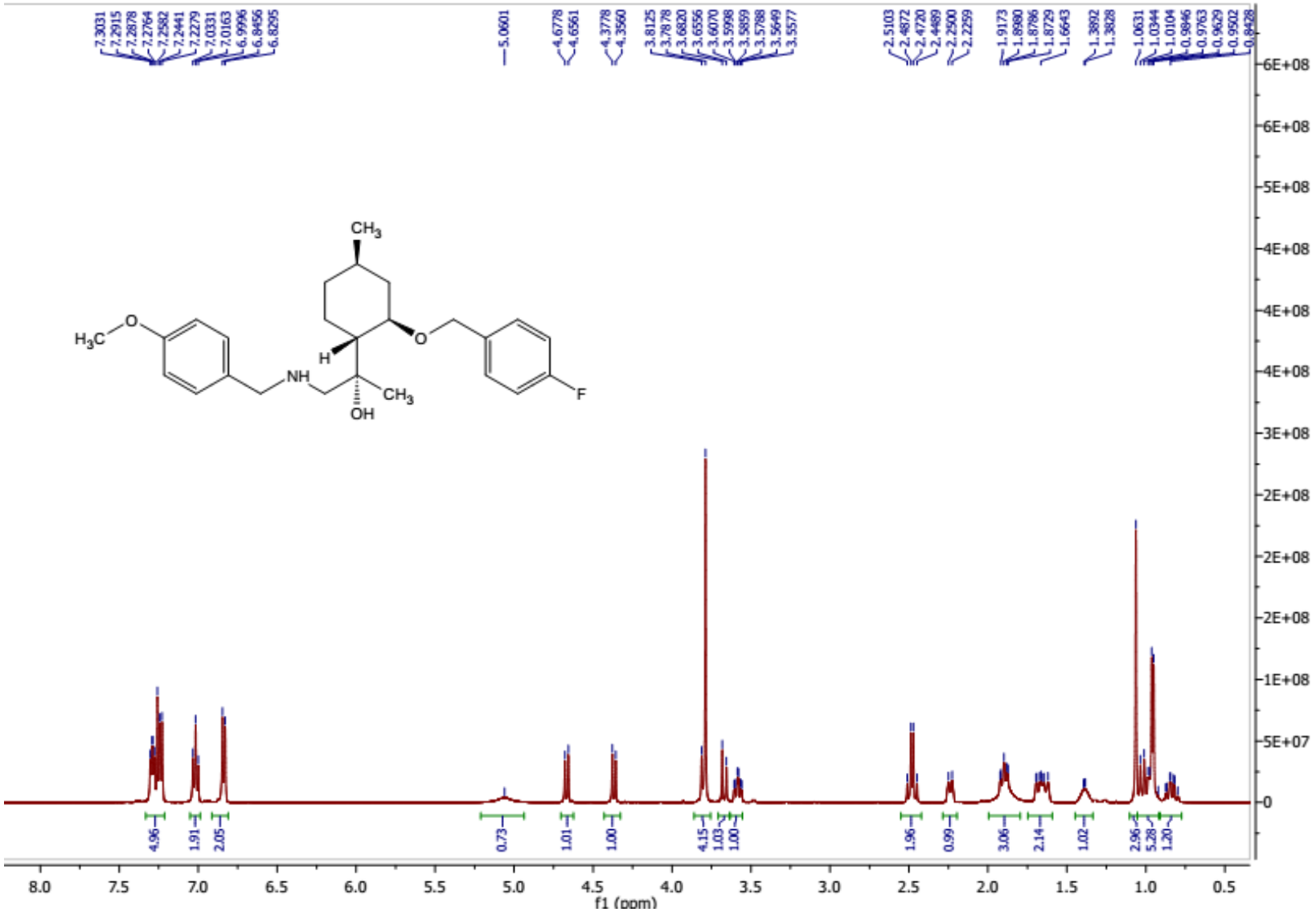
[1]H-NMR of compound **17a**



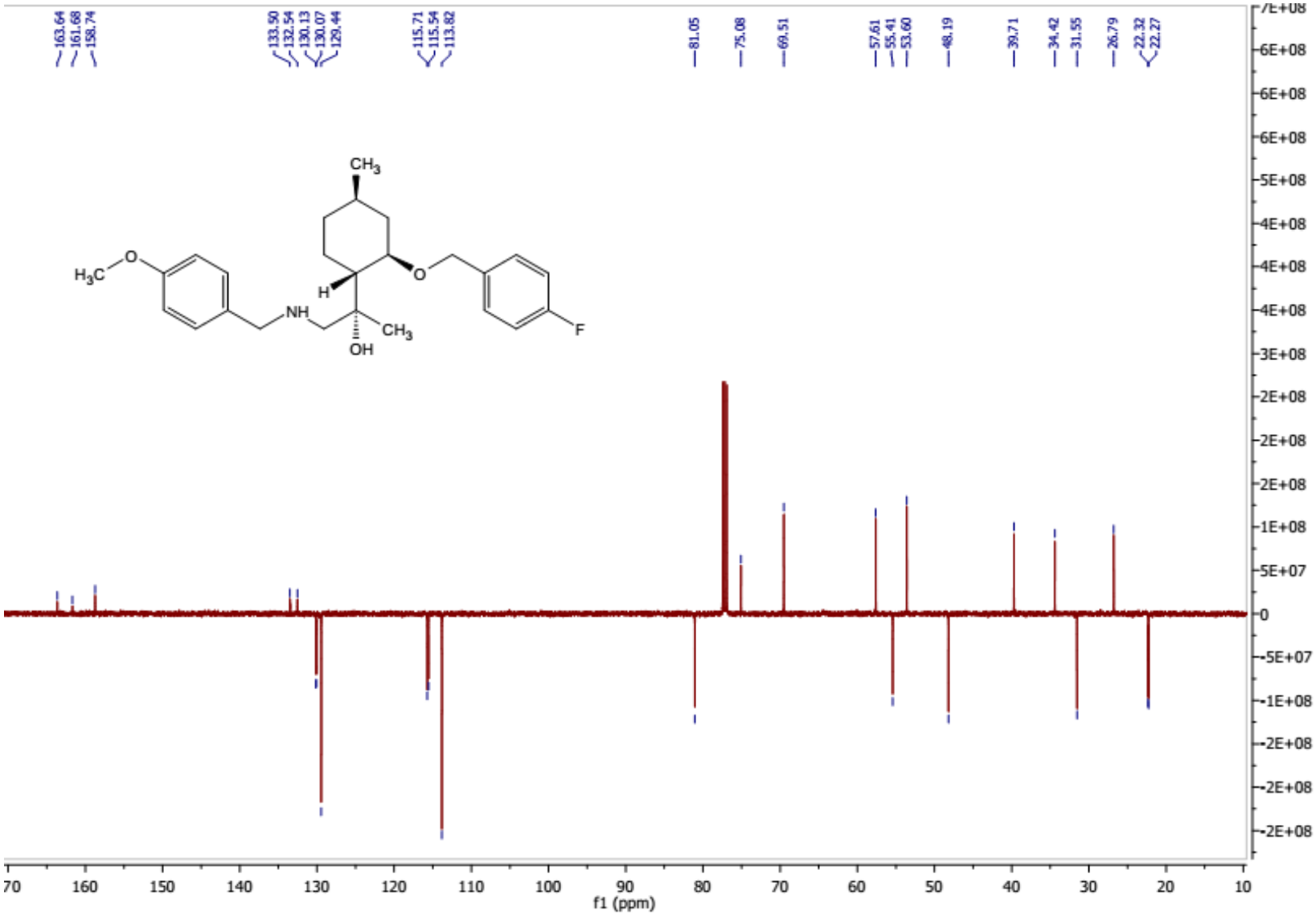
$^{13}$C-NMR of compound **17a**



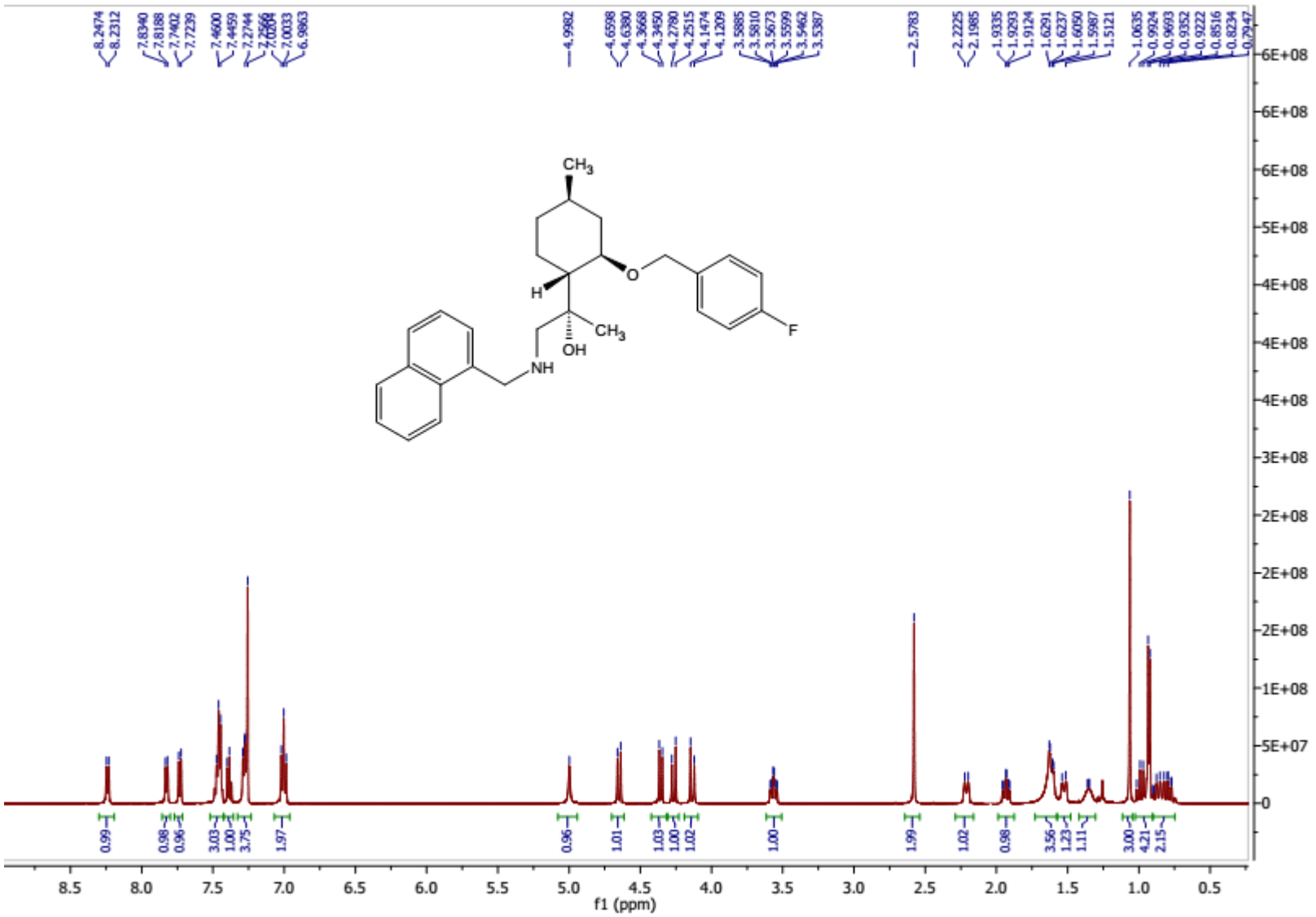
[1]H-NMR of compound **18a**



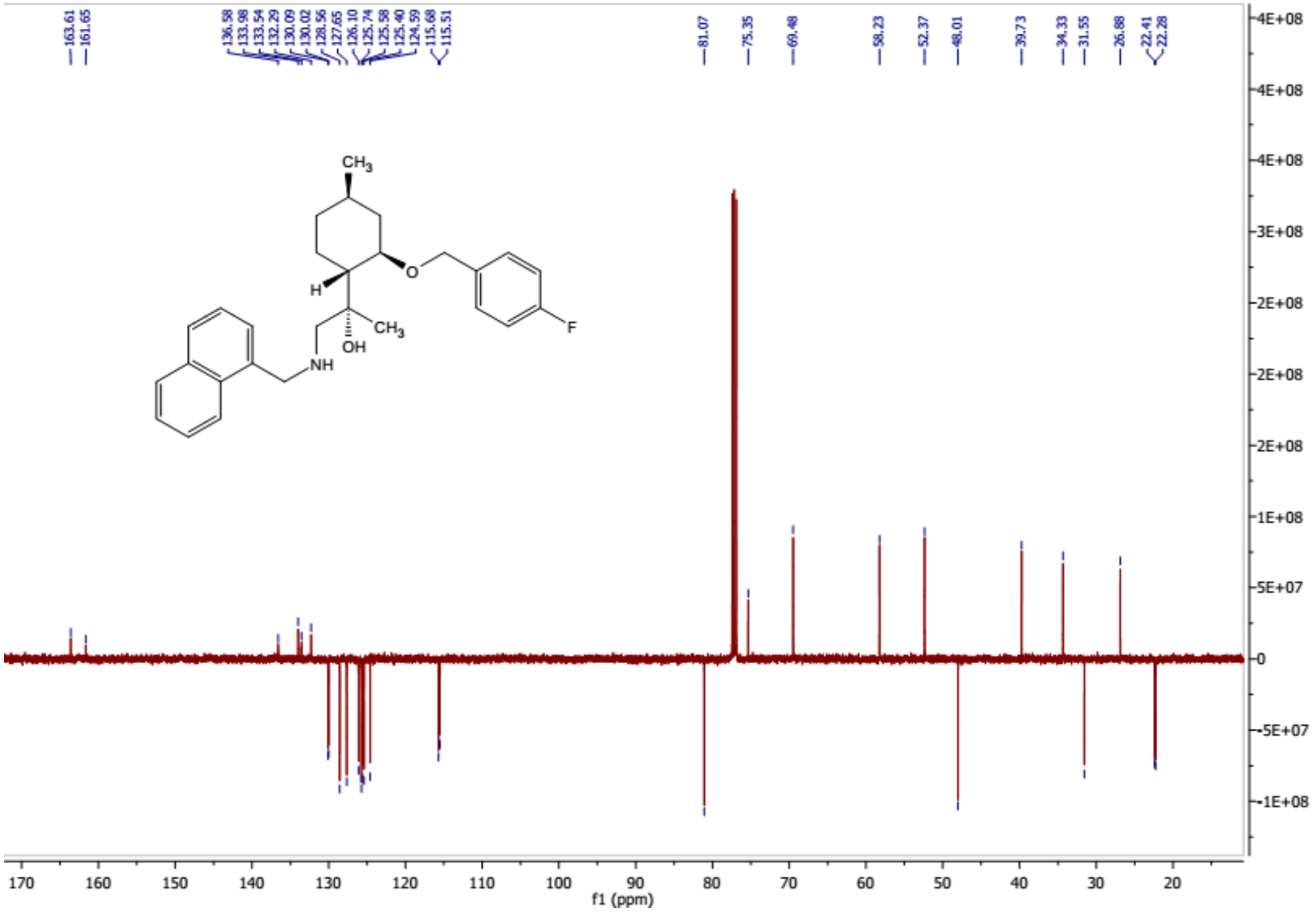
$^{13}$C-NMR of compound **18a**



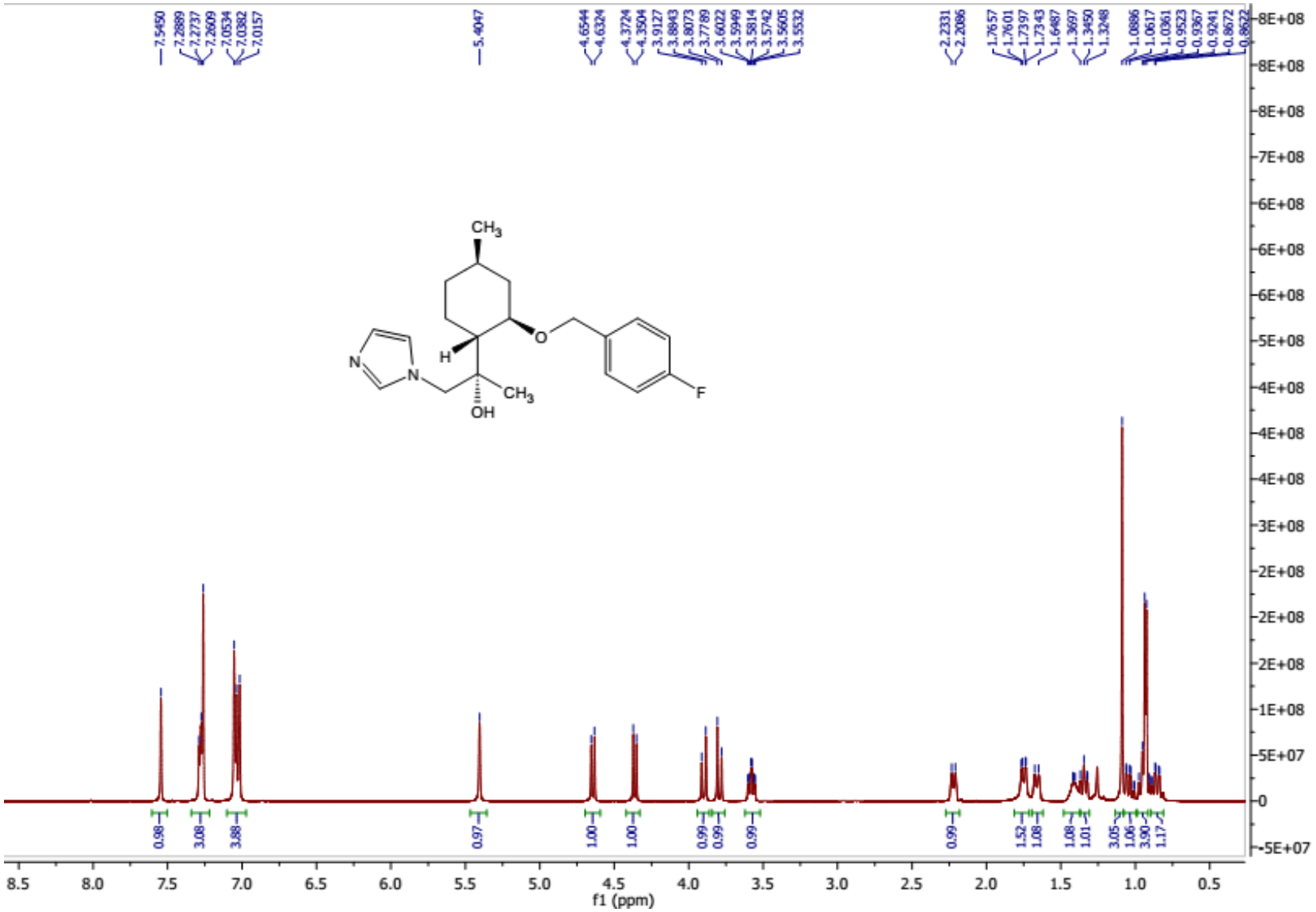
[1]H-NMR of compound **19a**



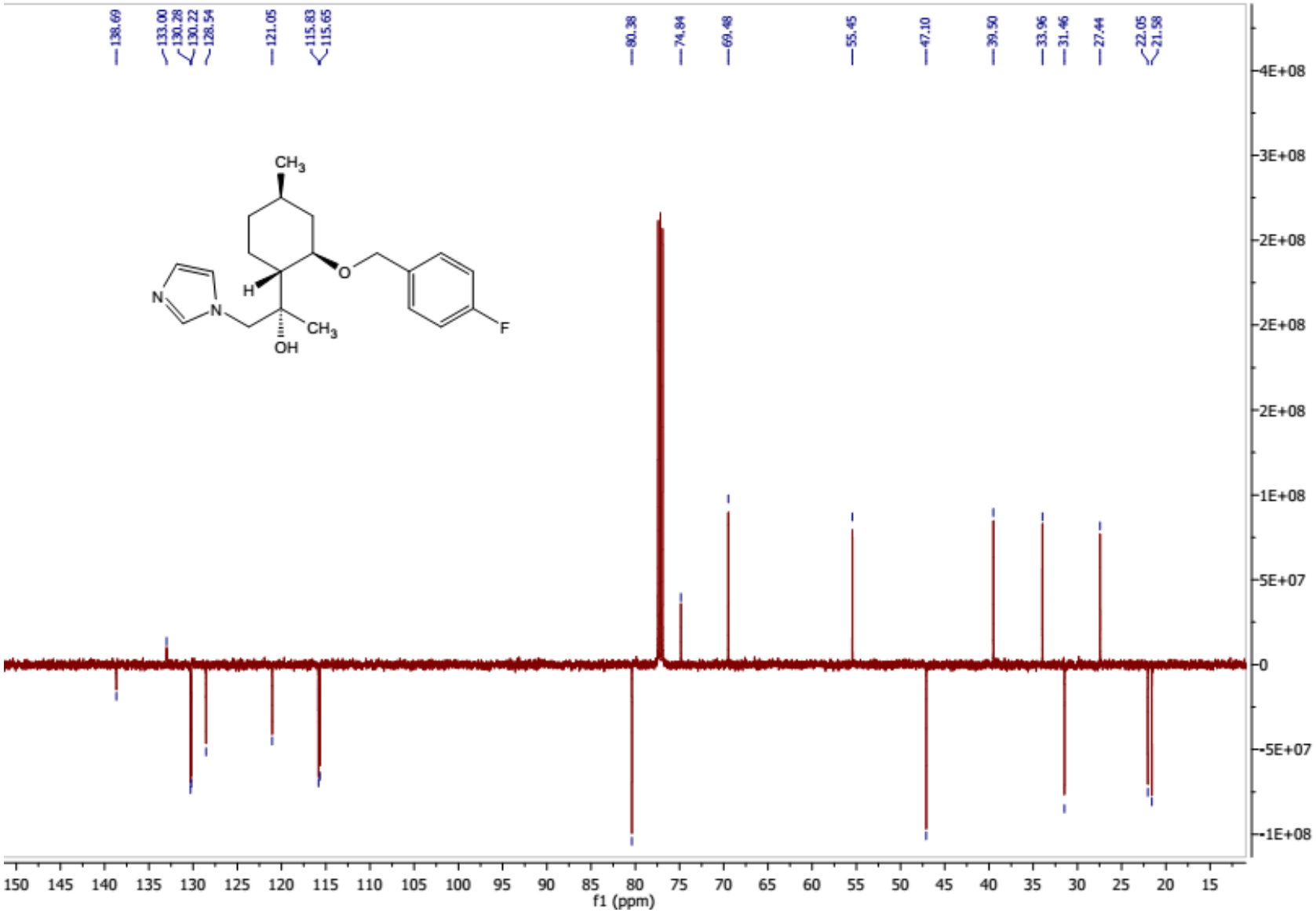
$^{13}$C-NMR of compound **19a**



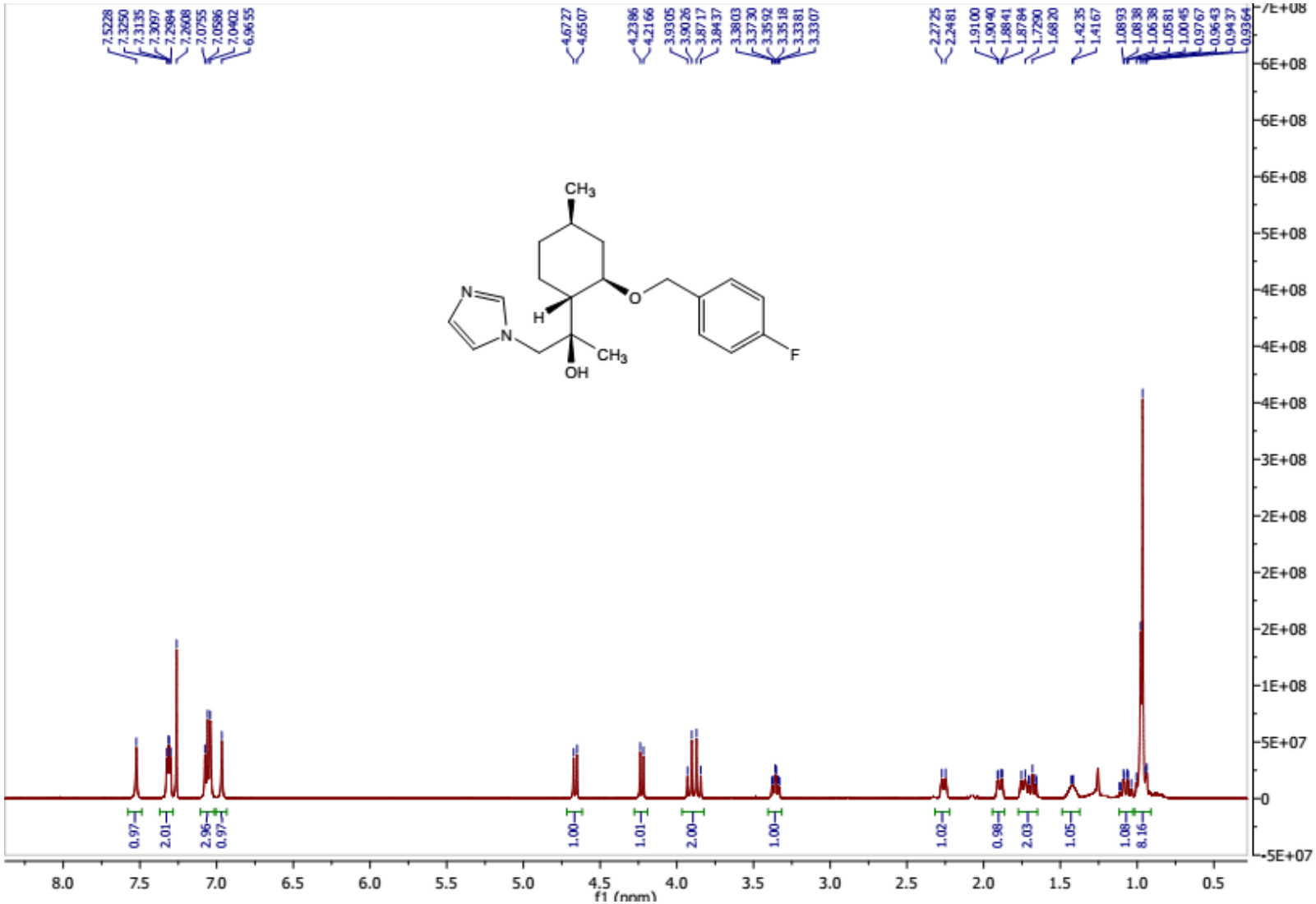
[1]H-NMR of compound **20a**



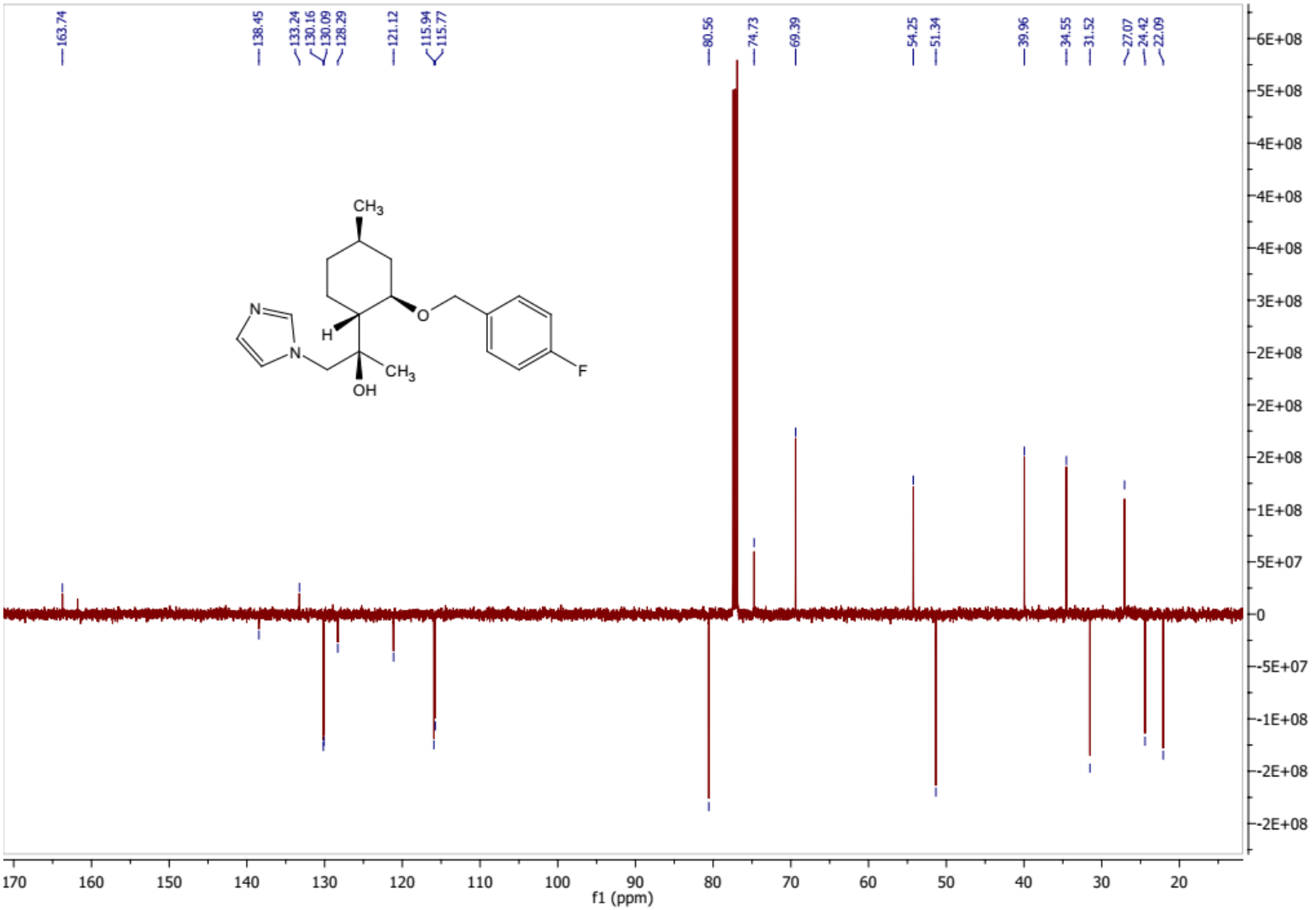
$^{13}$C-NMR of compound **20a**



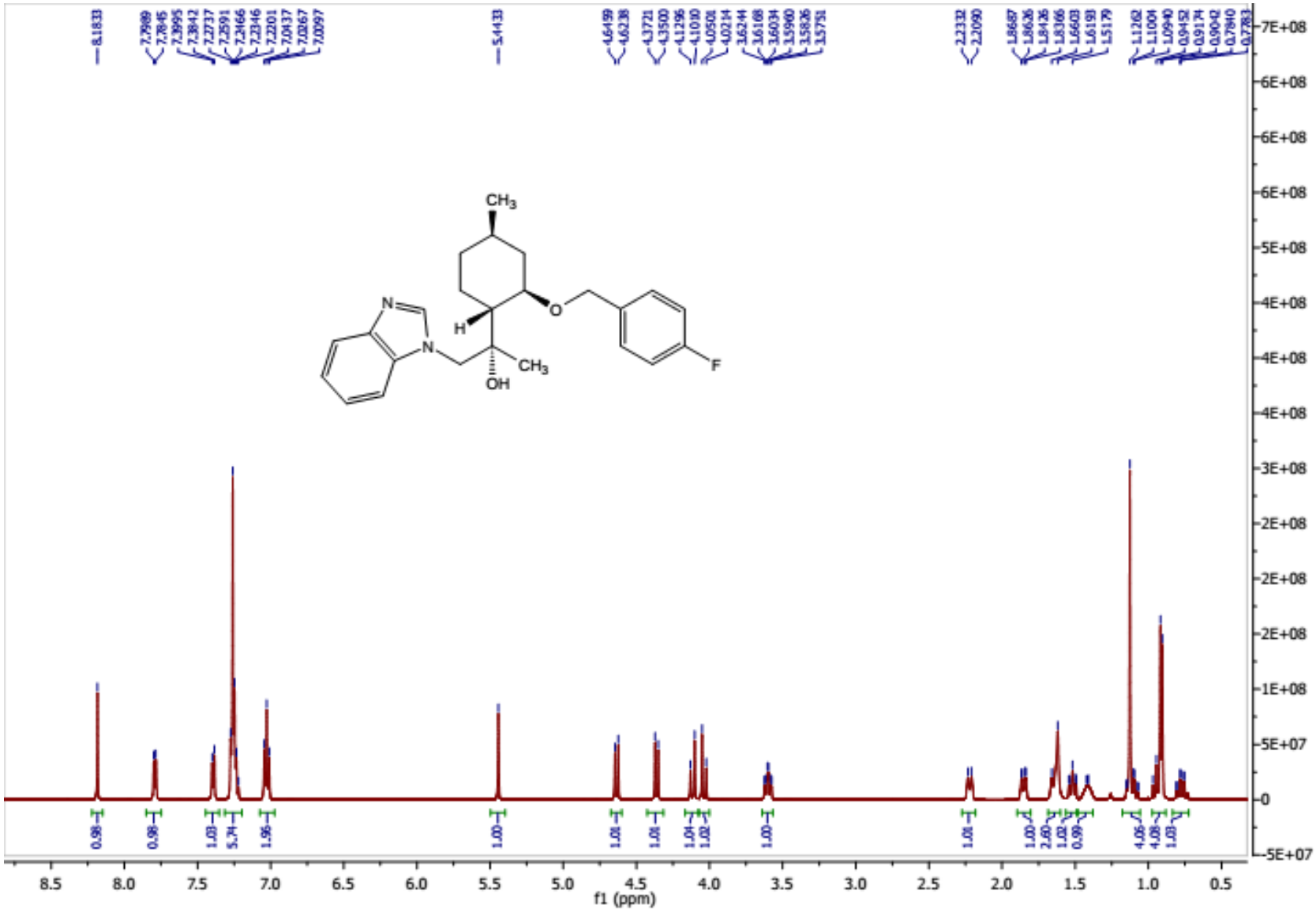
[1]H-NMR of compound **20b**



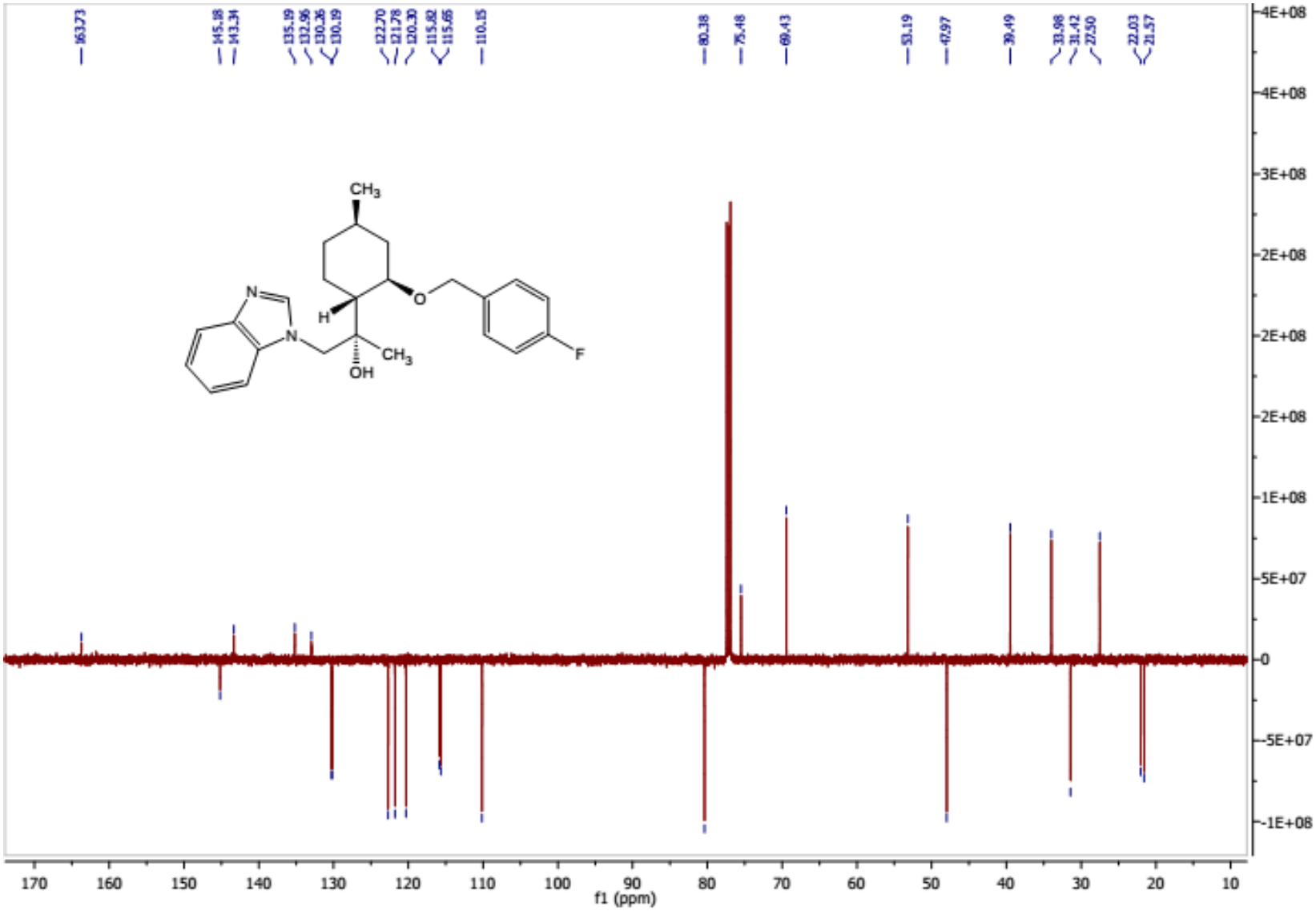
$^{13}$C-NMR of compound **20b**



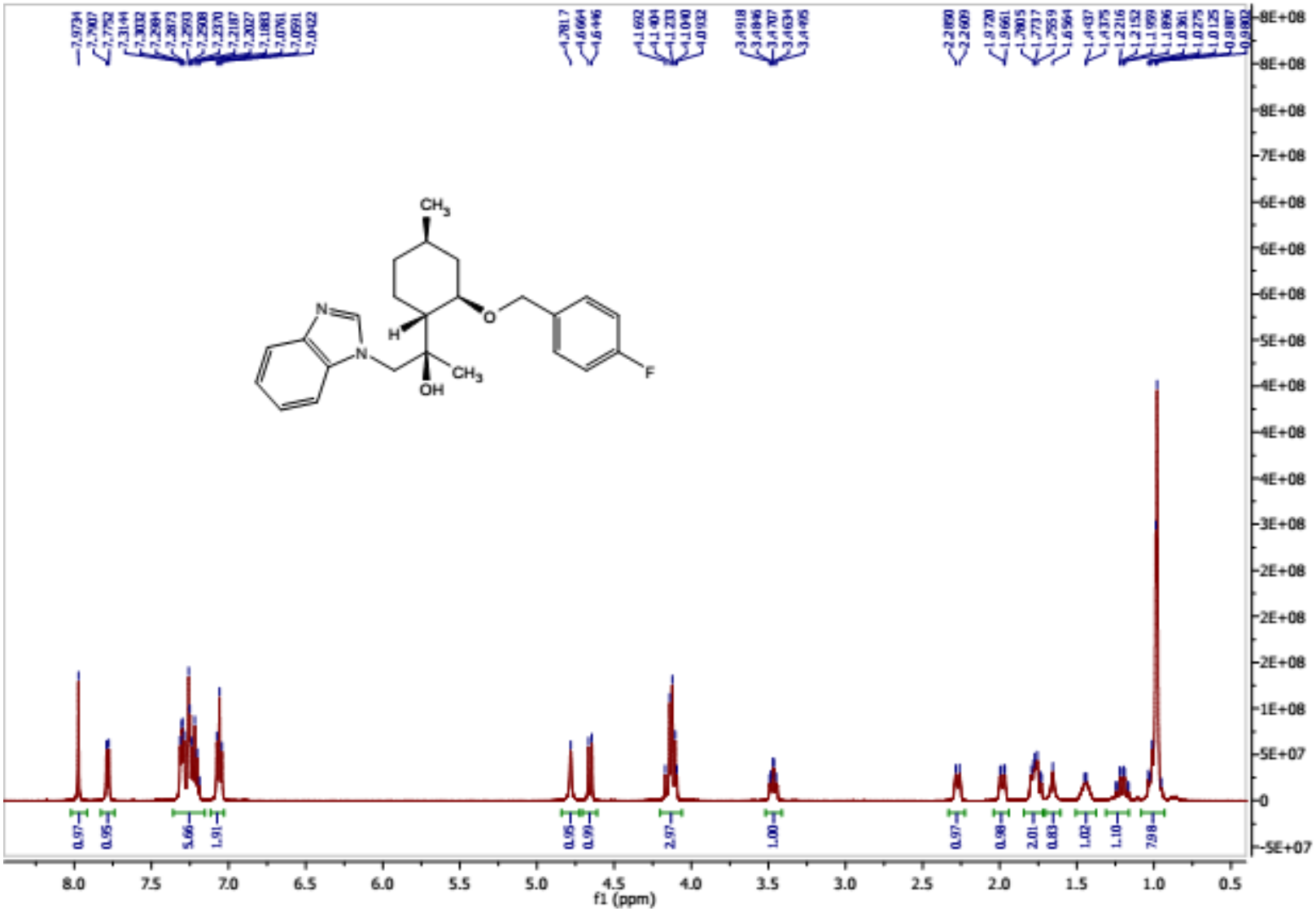
[1]H-NMR of compound **21a**



$^{13}$C-NMR of compound **21a**

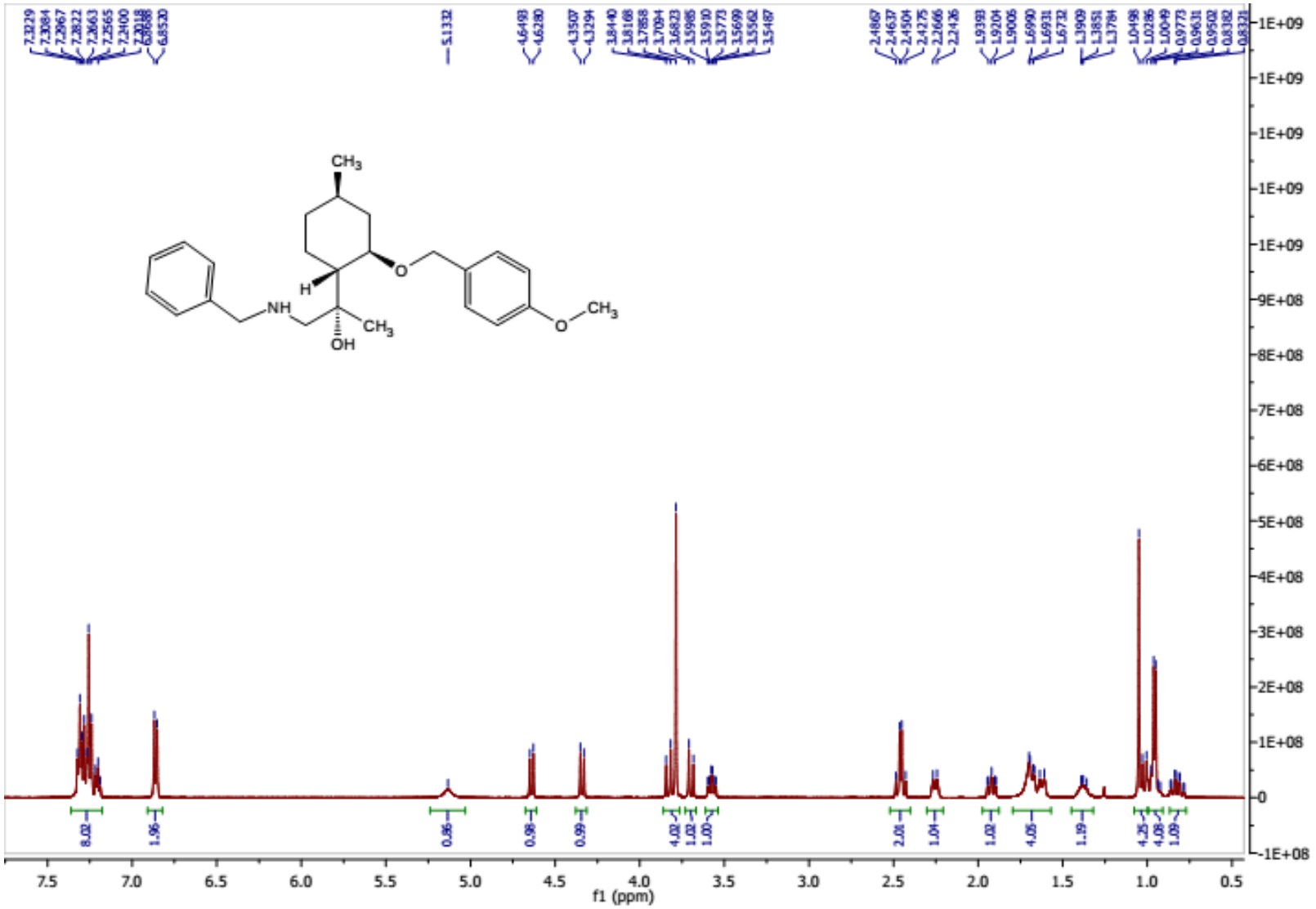


[1]H-NMR of compound **21b**



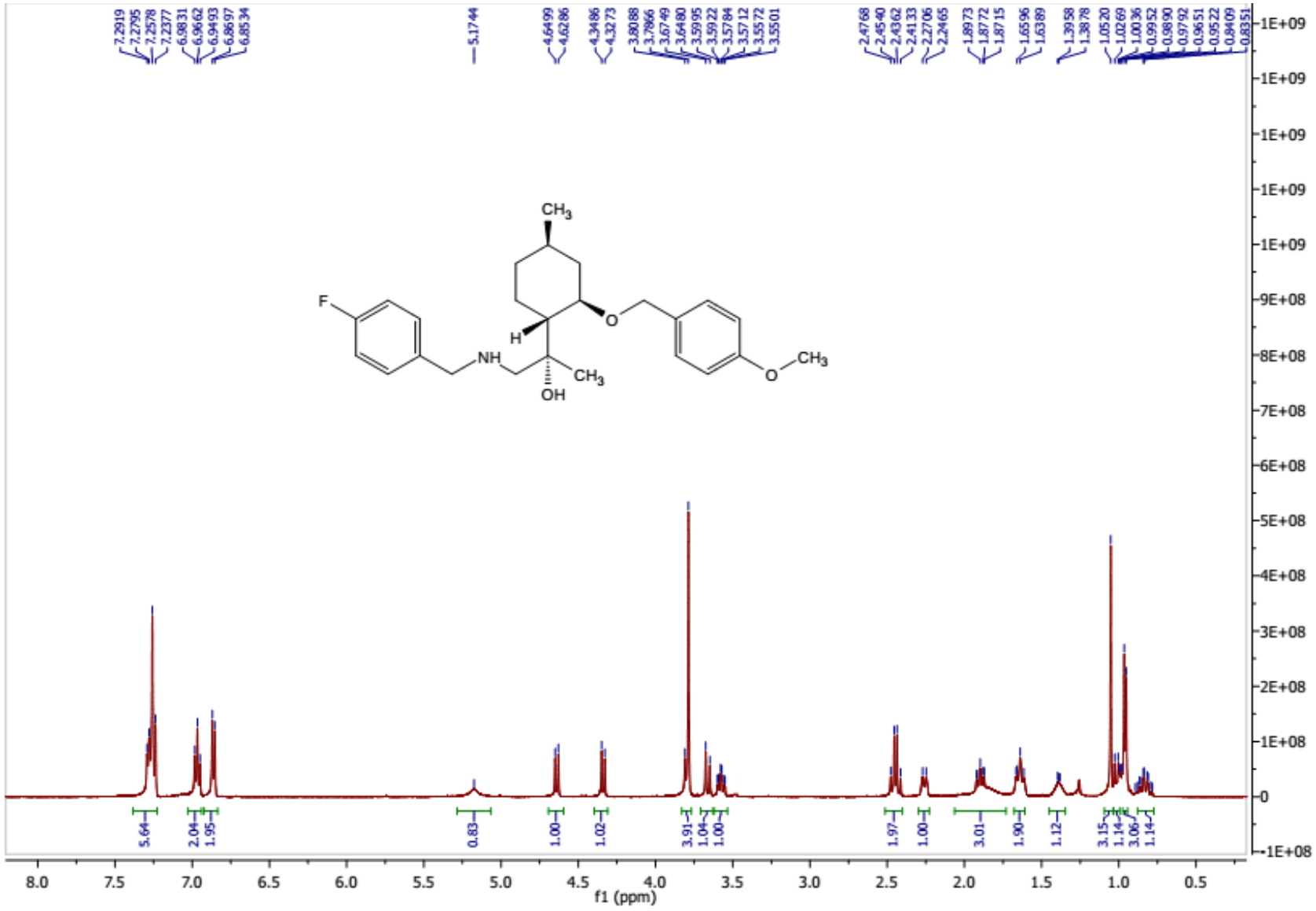
$^{13}$C-NMR of compound **21b**

[1]H-NMR of compound **22a**



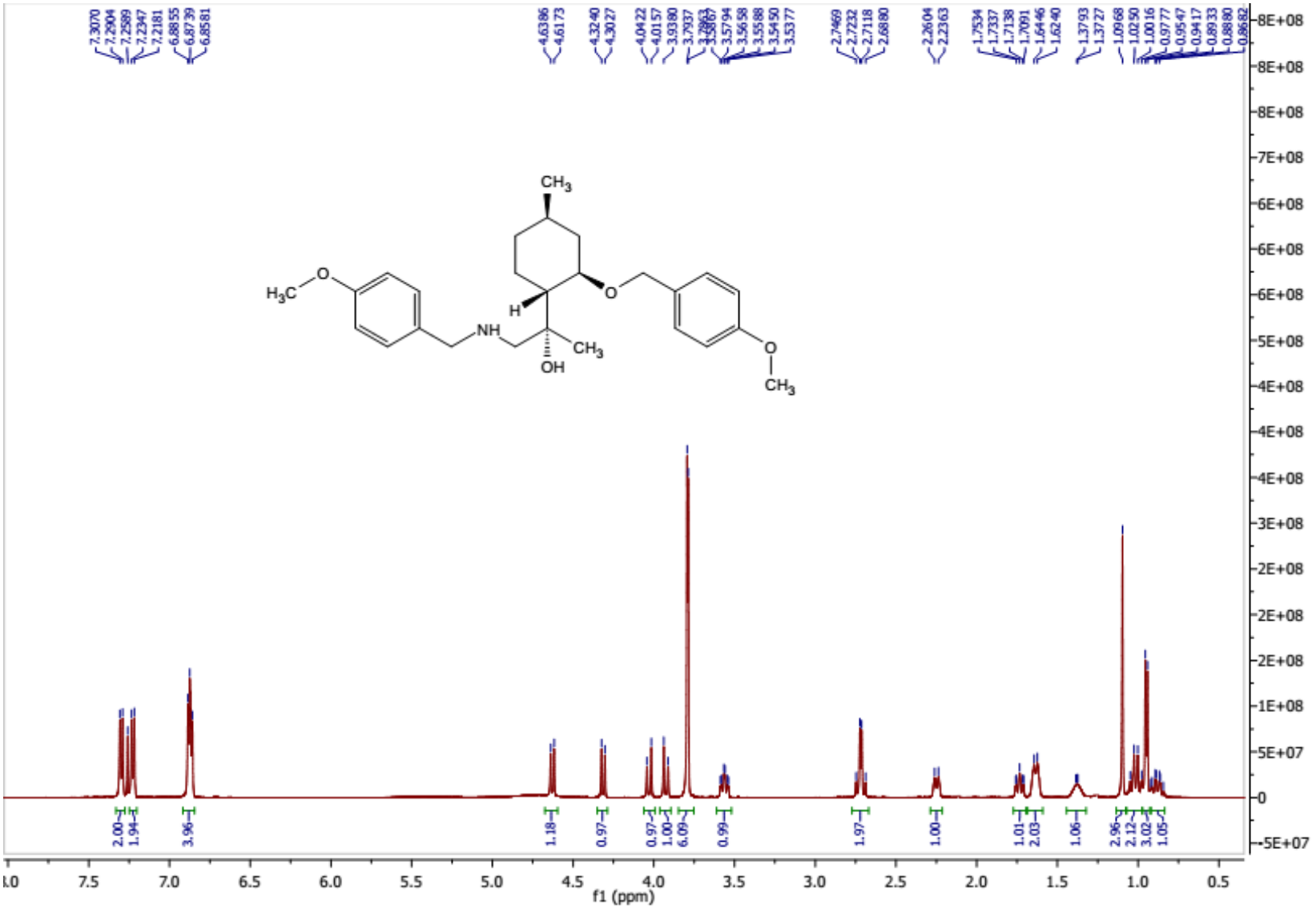
$^{13}$C-NMR of compound **22a**

[1]H-NMR of compound **23a**

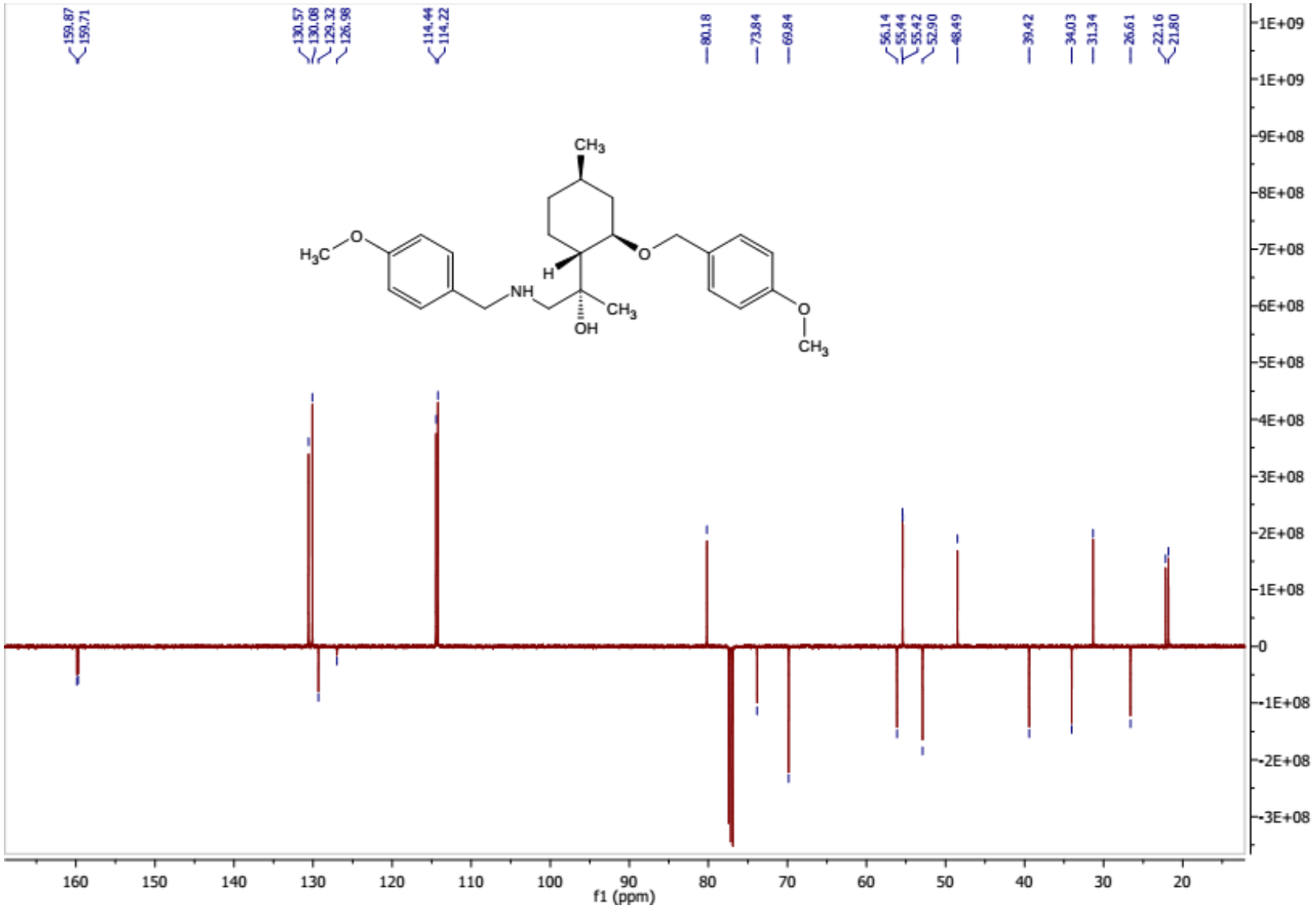


$^{13}$C-NMR of compound **23a**

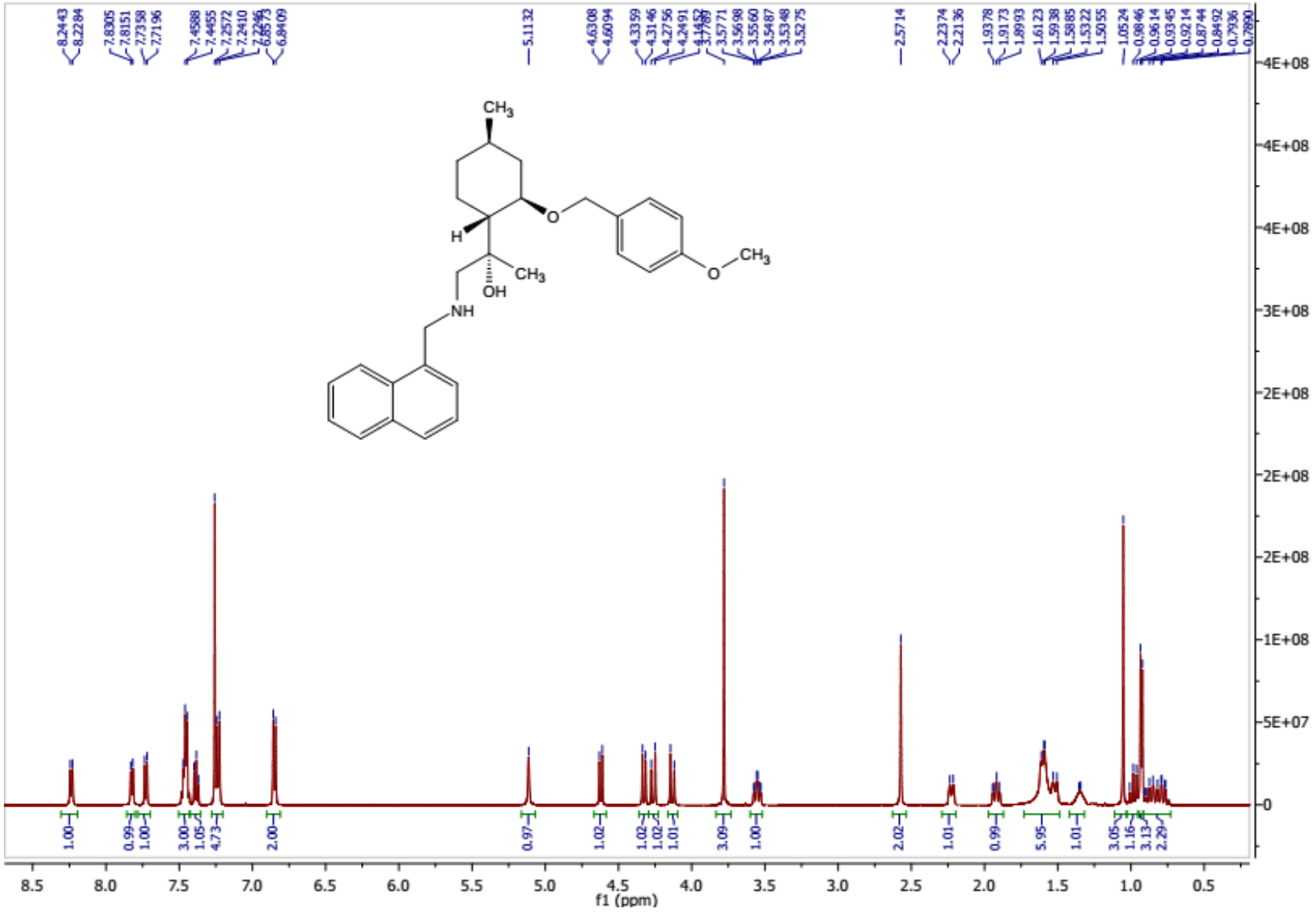
[1]H-NMR of compound **24a**



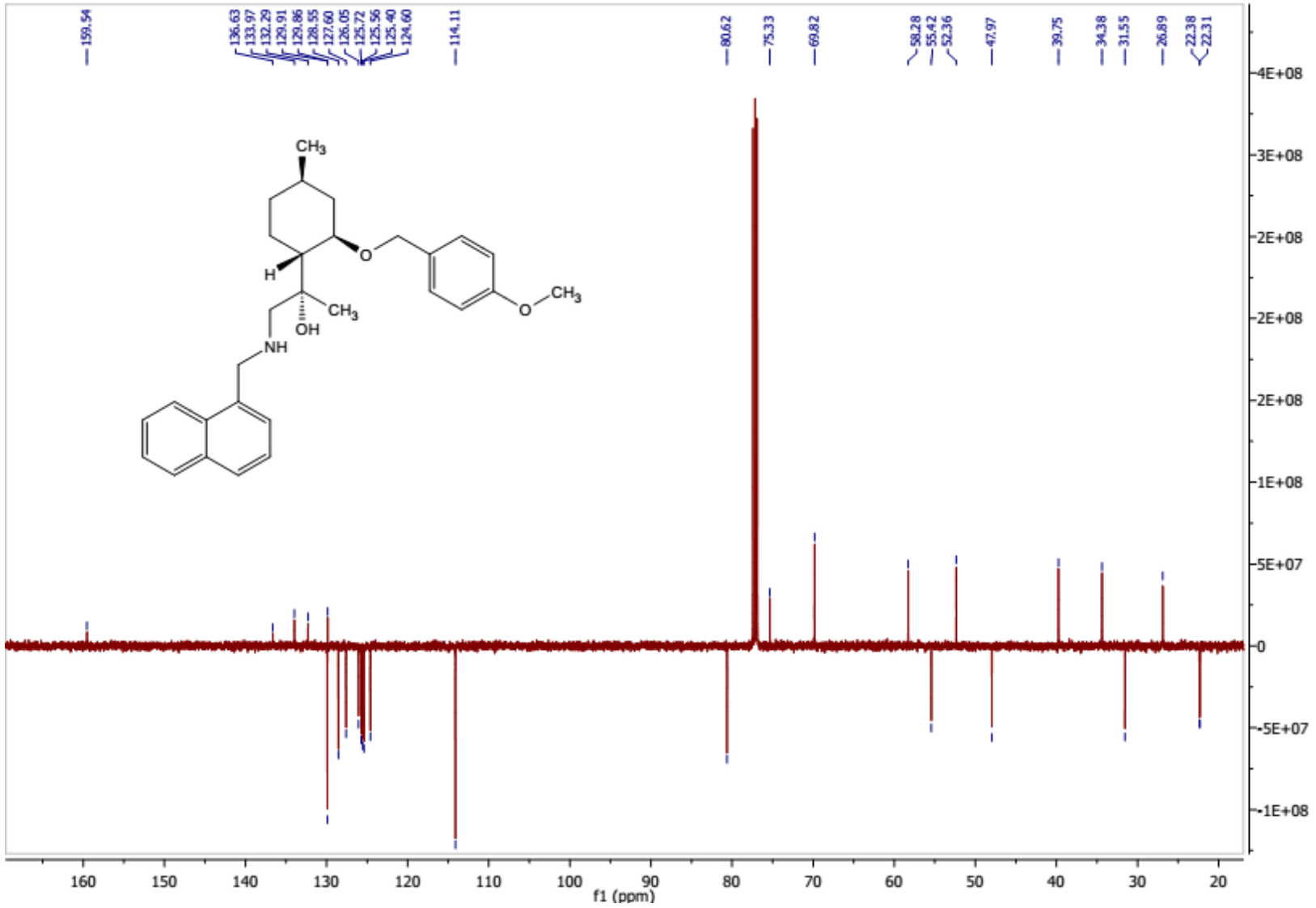
$^{13}$C-NMR of compound **24a**



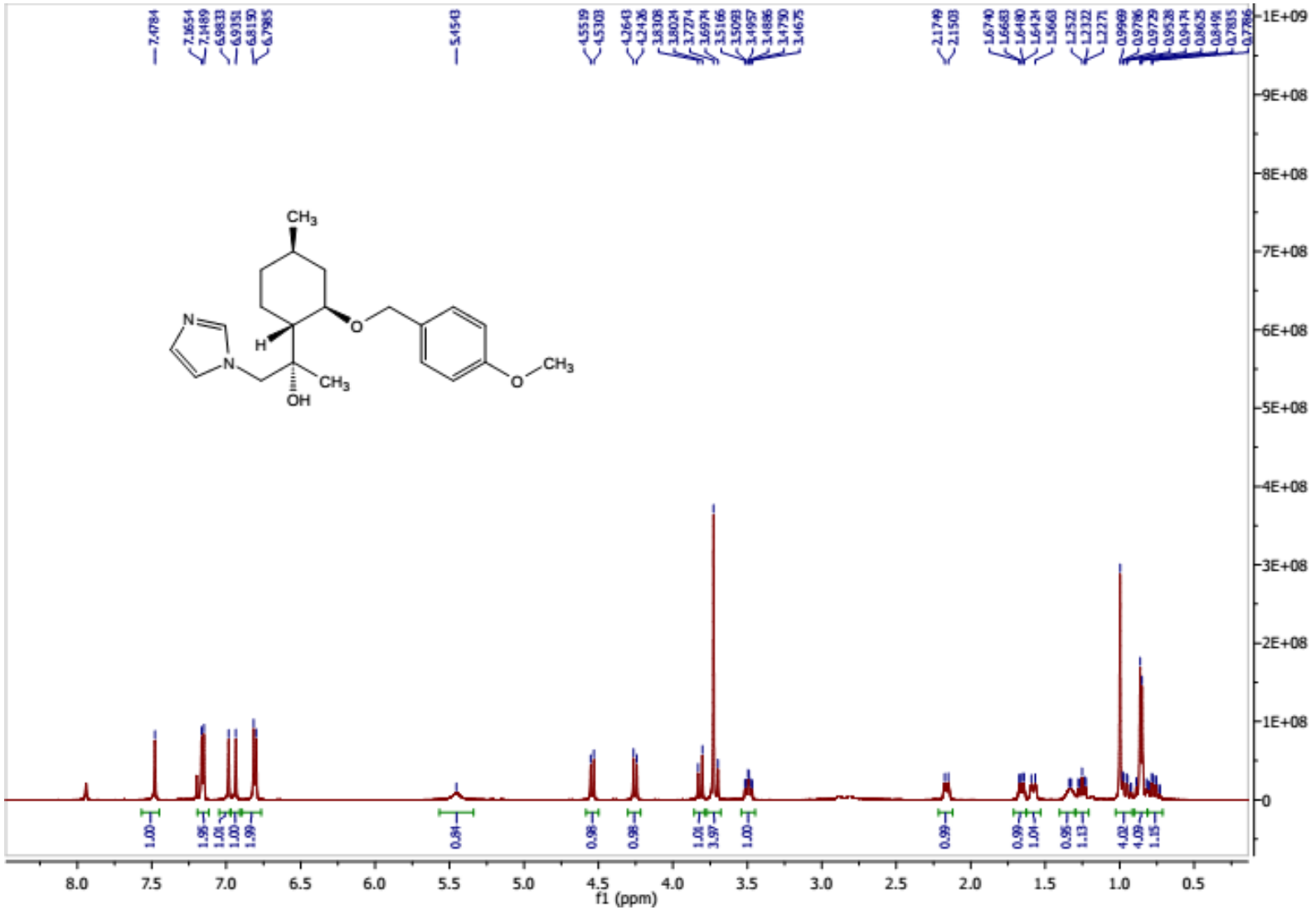
[1]H-NMR of compound **25a**



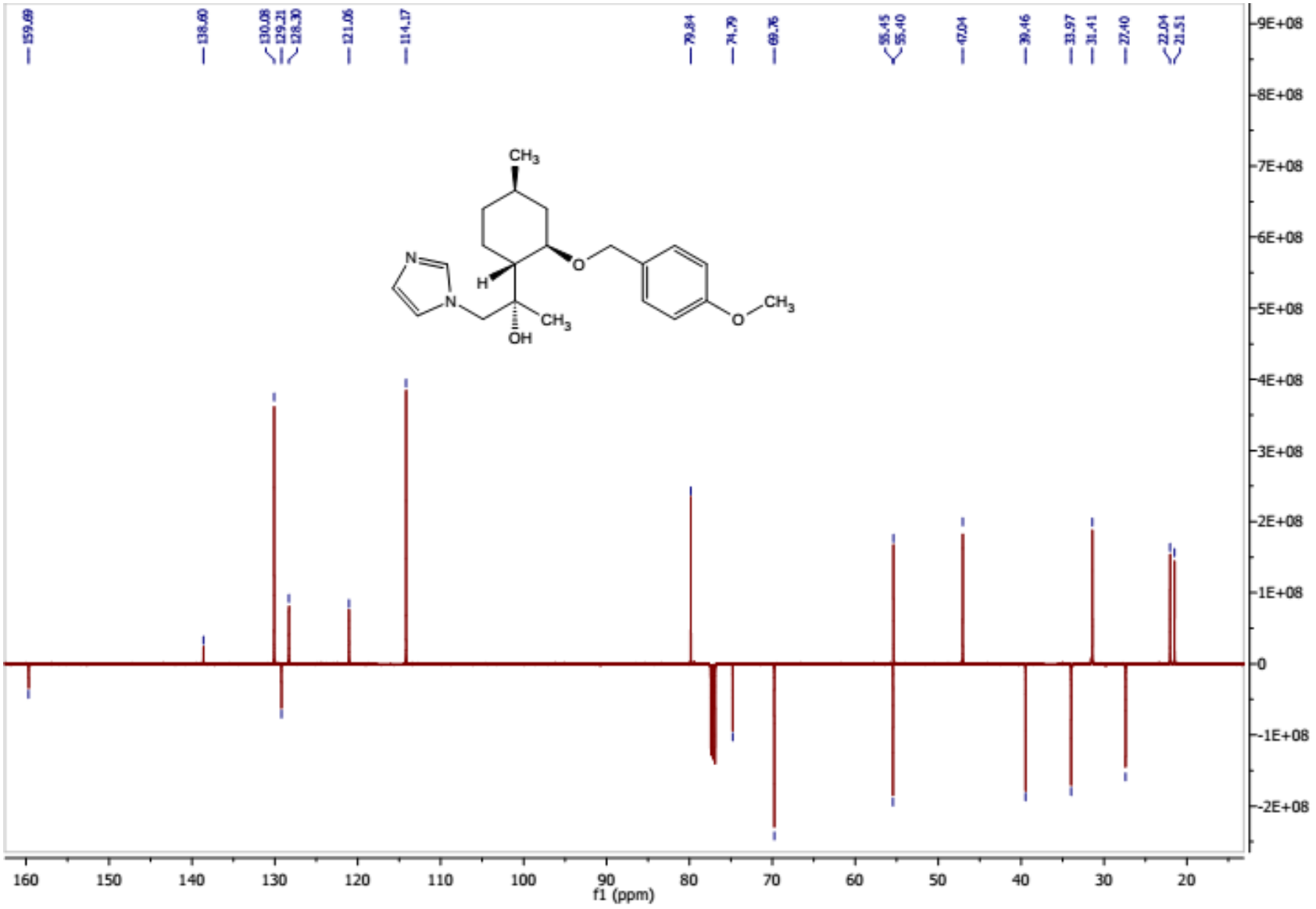
$^{13}$C-NMR of compound **25a**



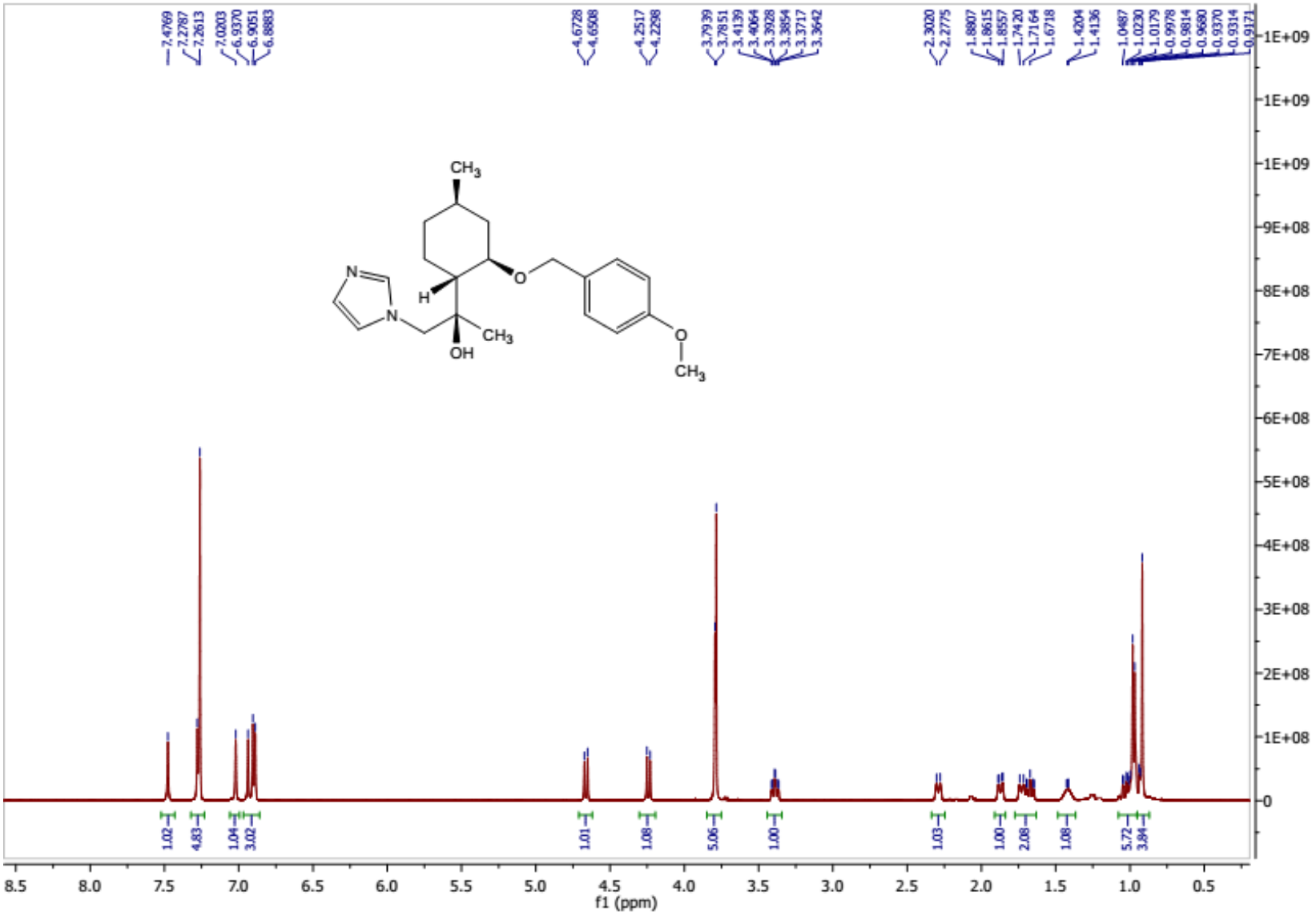
[1]H-NMR of compound **26a**



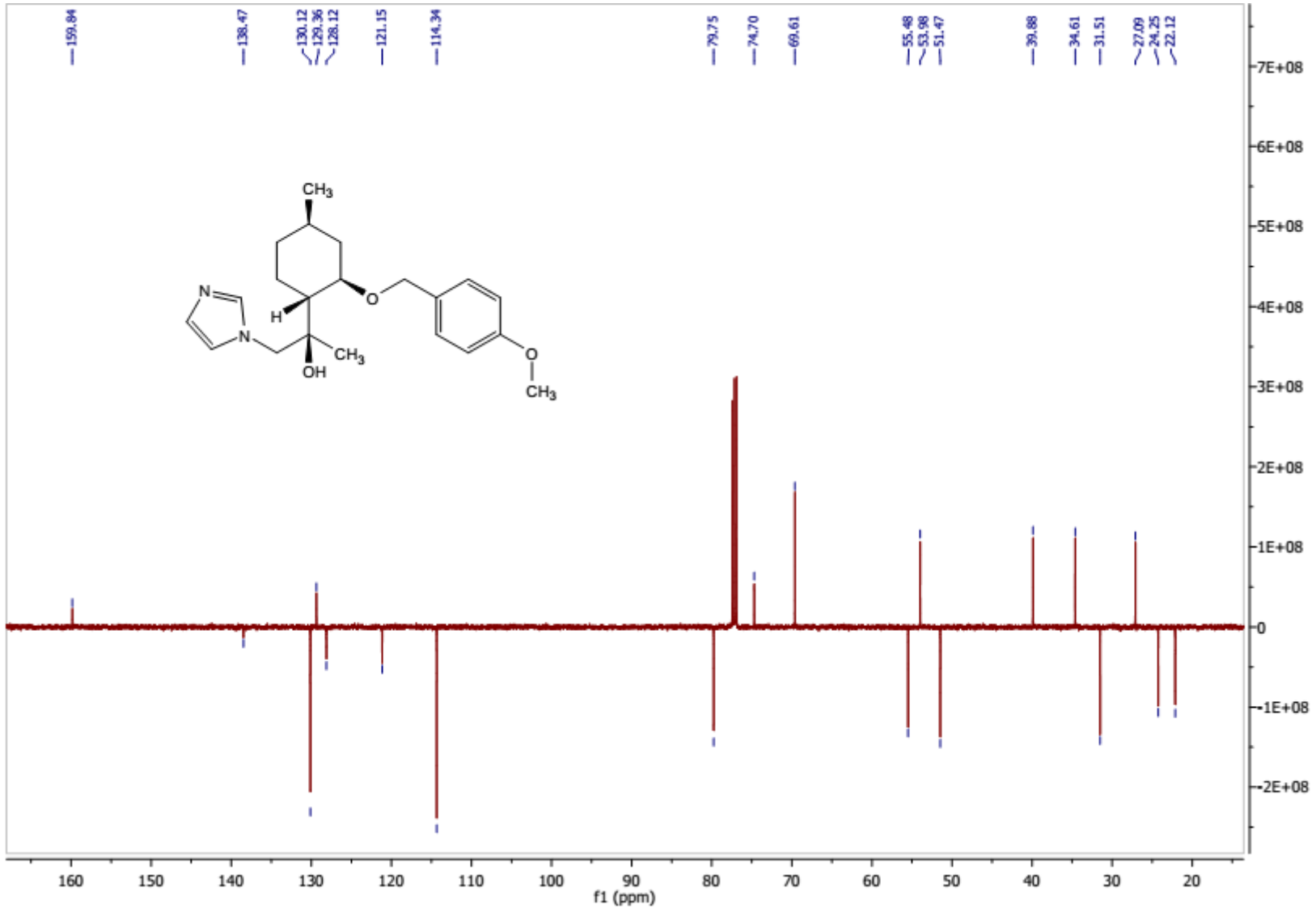
$^{13}$C-NMR of compound **26a**



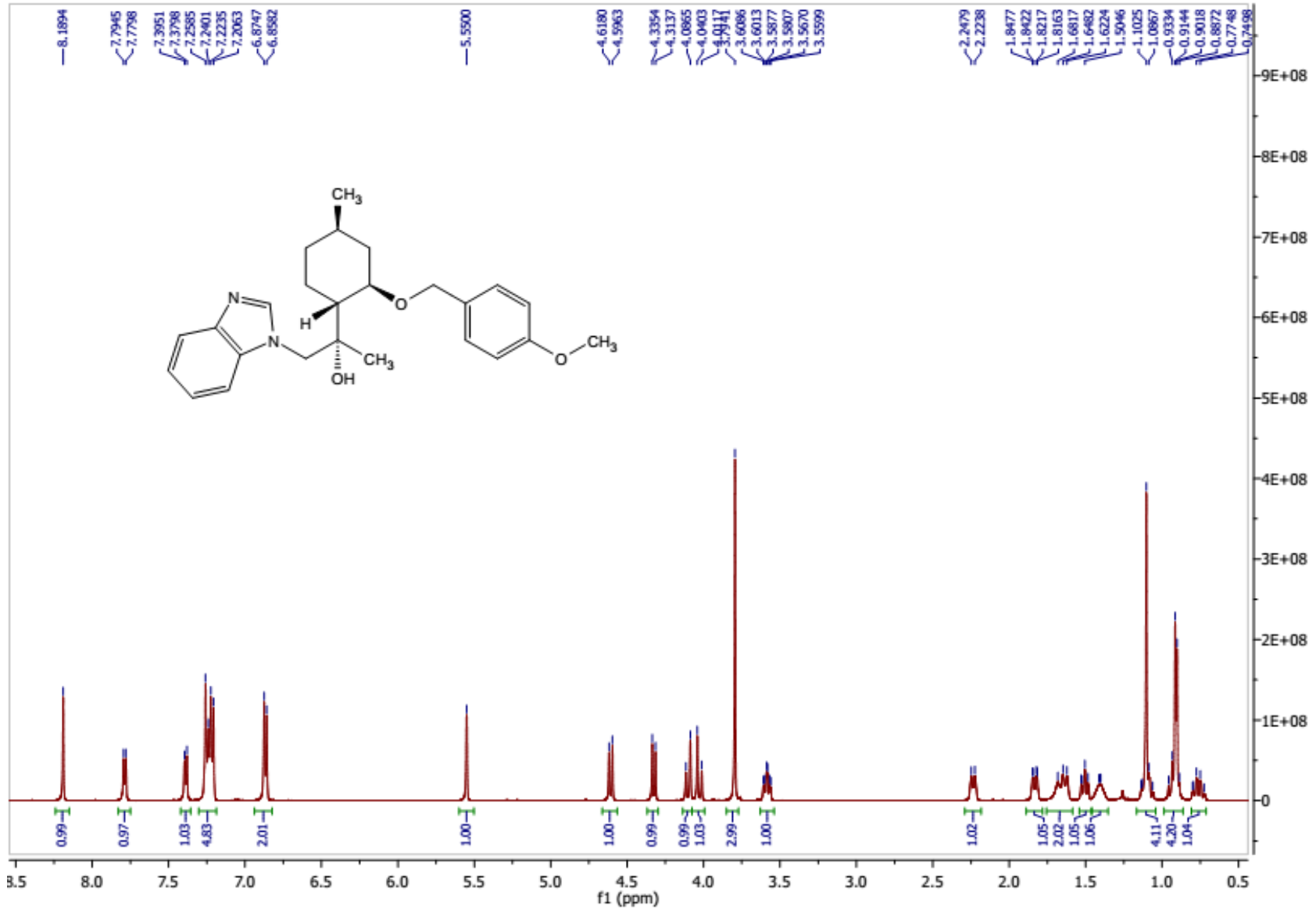
[1]H-NMR of compound **26b**



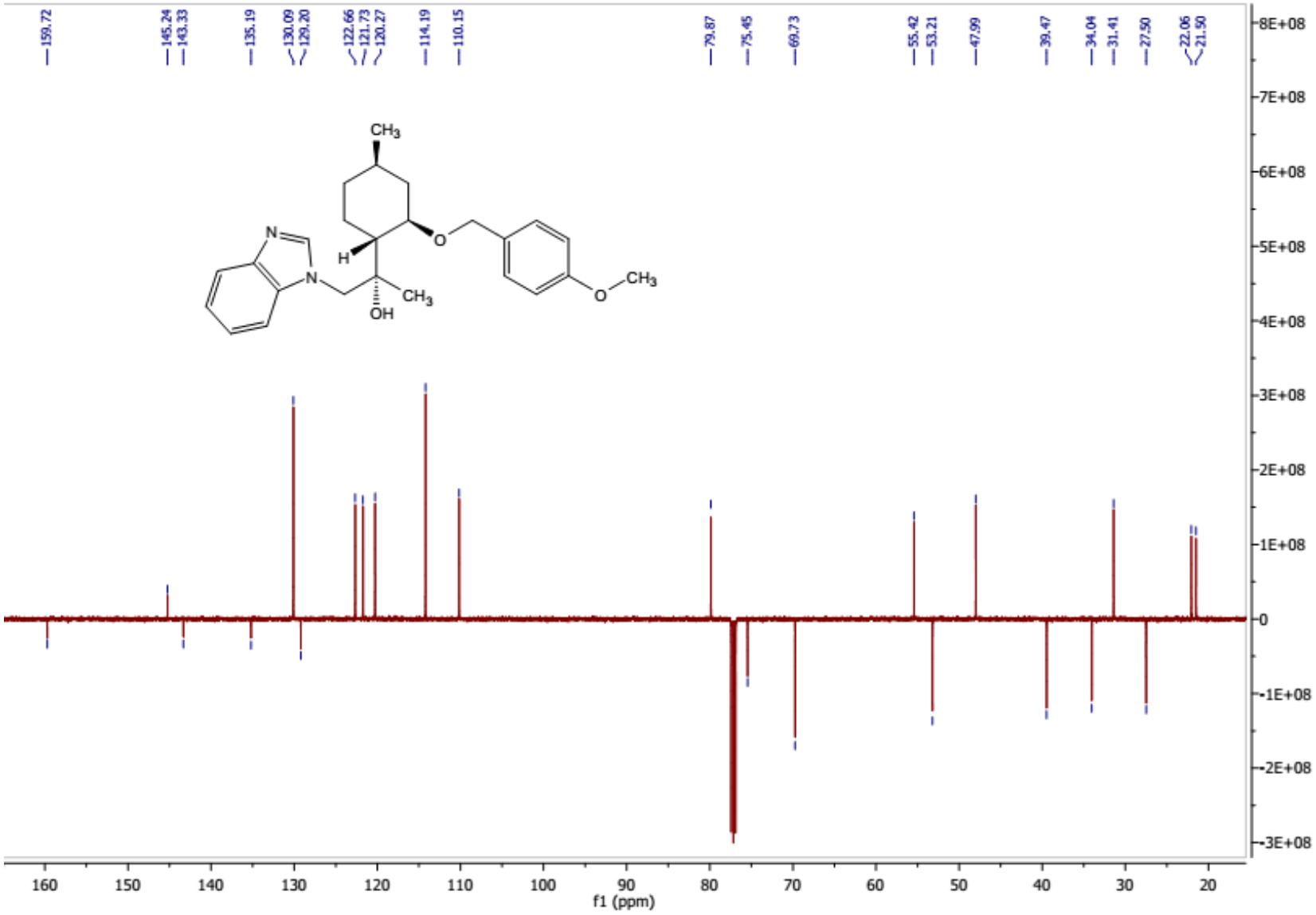
$^{13}$C-NMR of compound **26b**



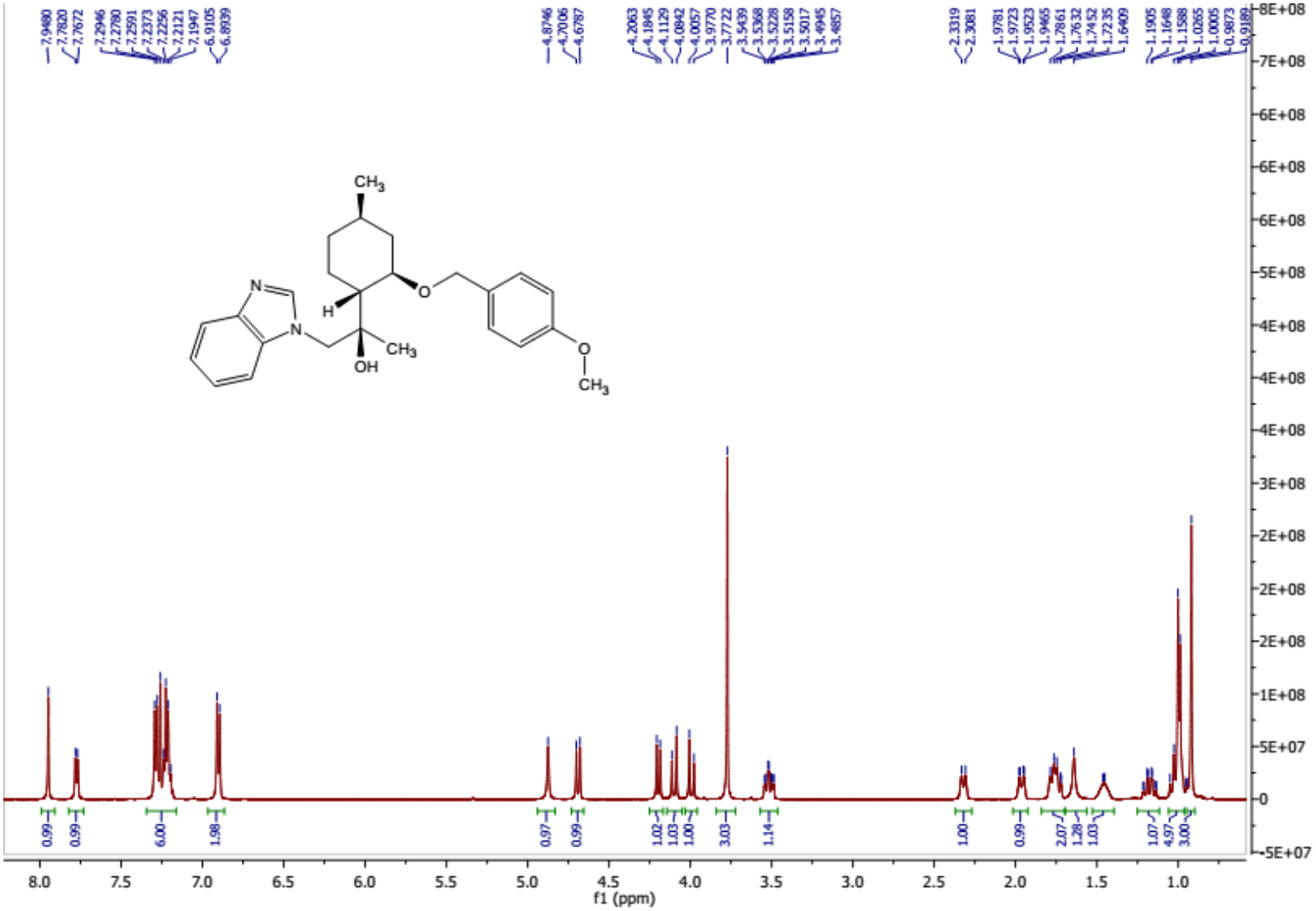
[1]H-NMR of compound **27a**



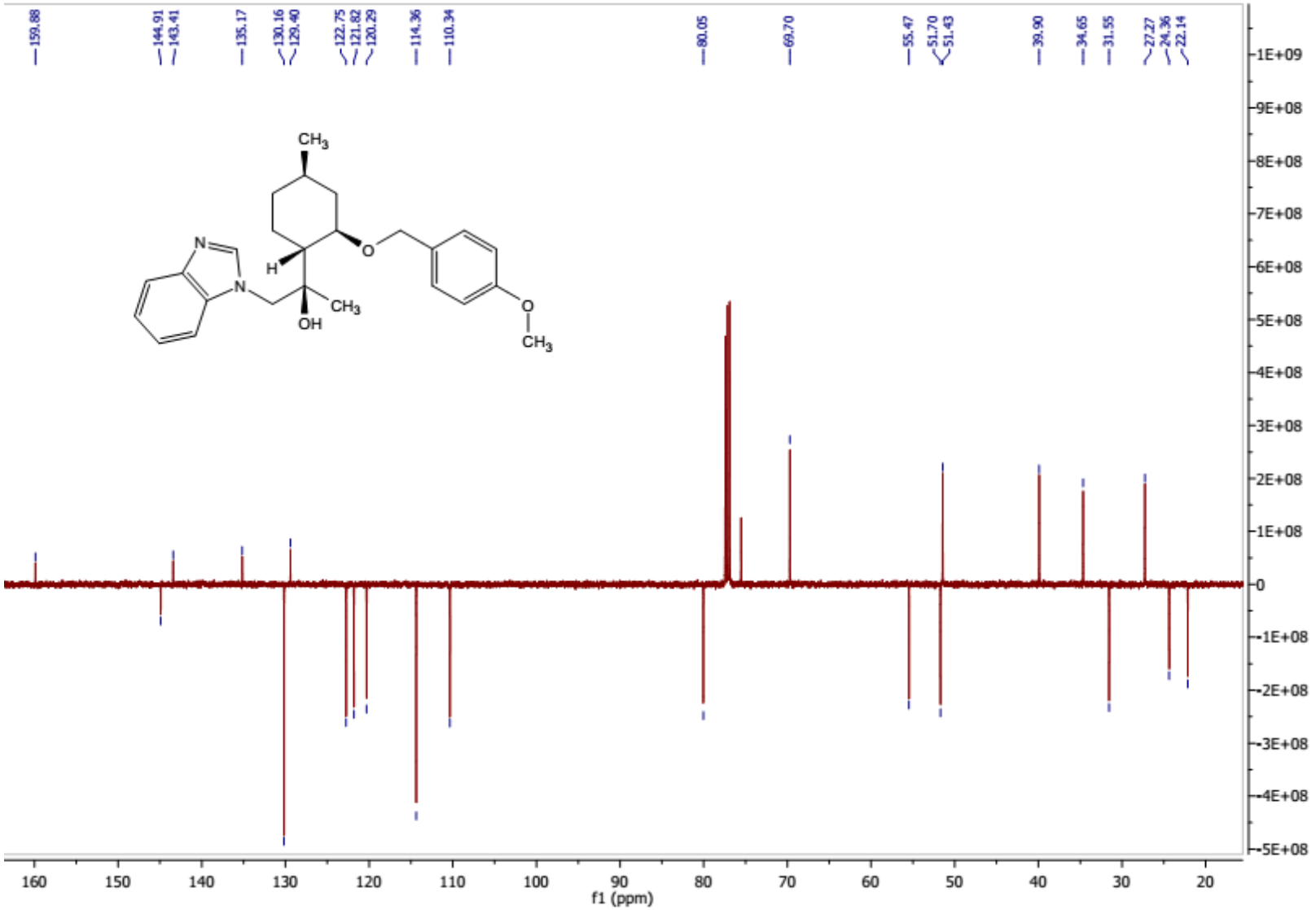
$^{13}$C-NMR of compound **27a**



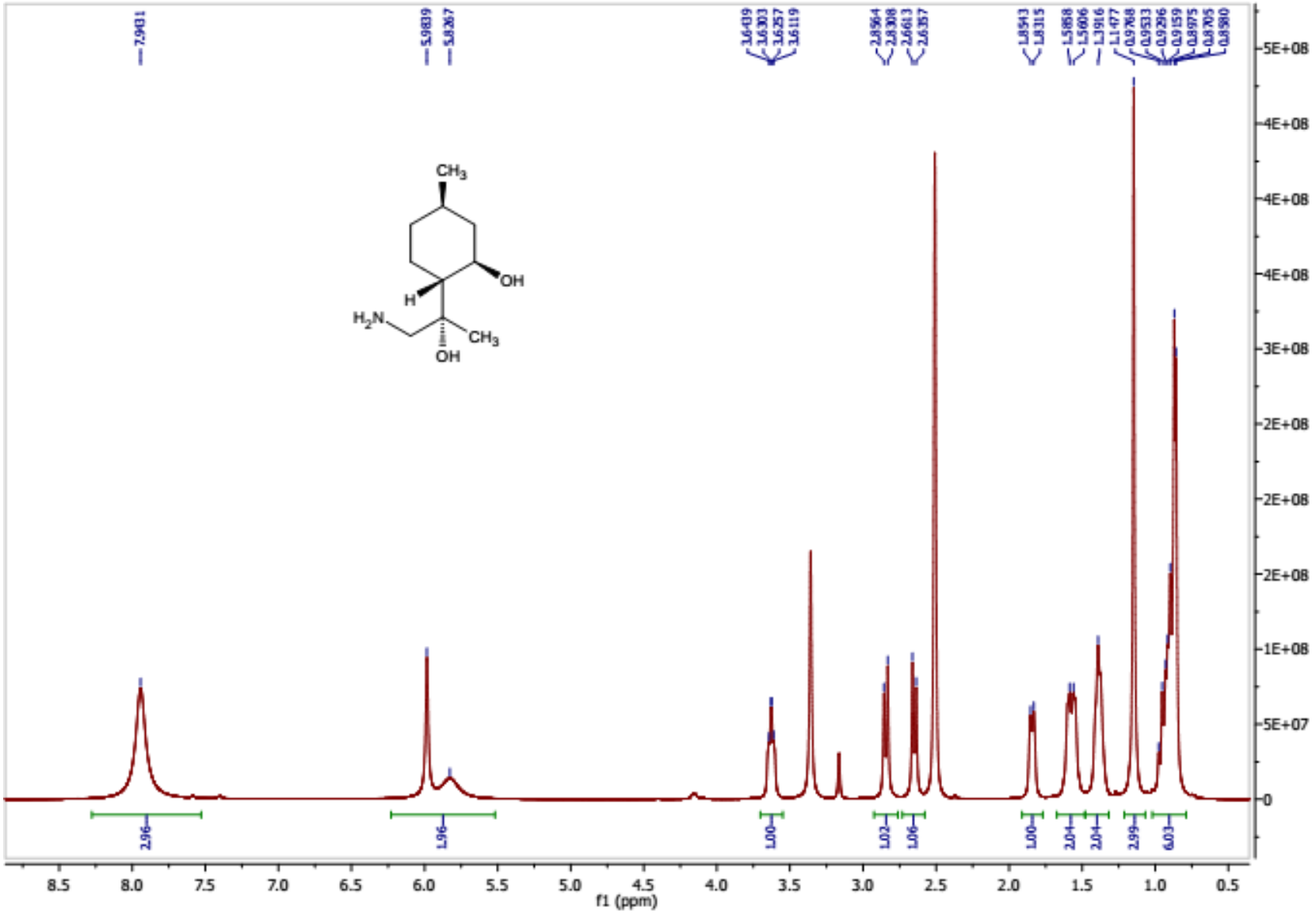
[1]H-NMR of compound **27b**



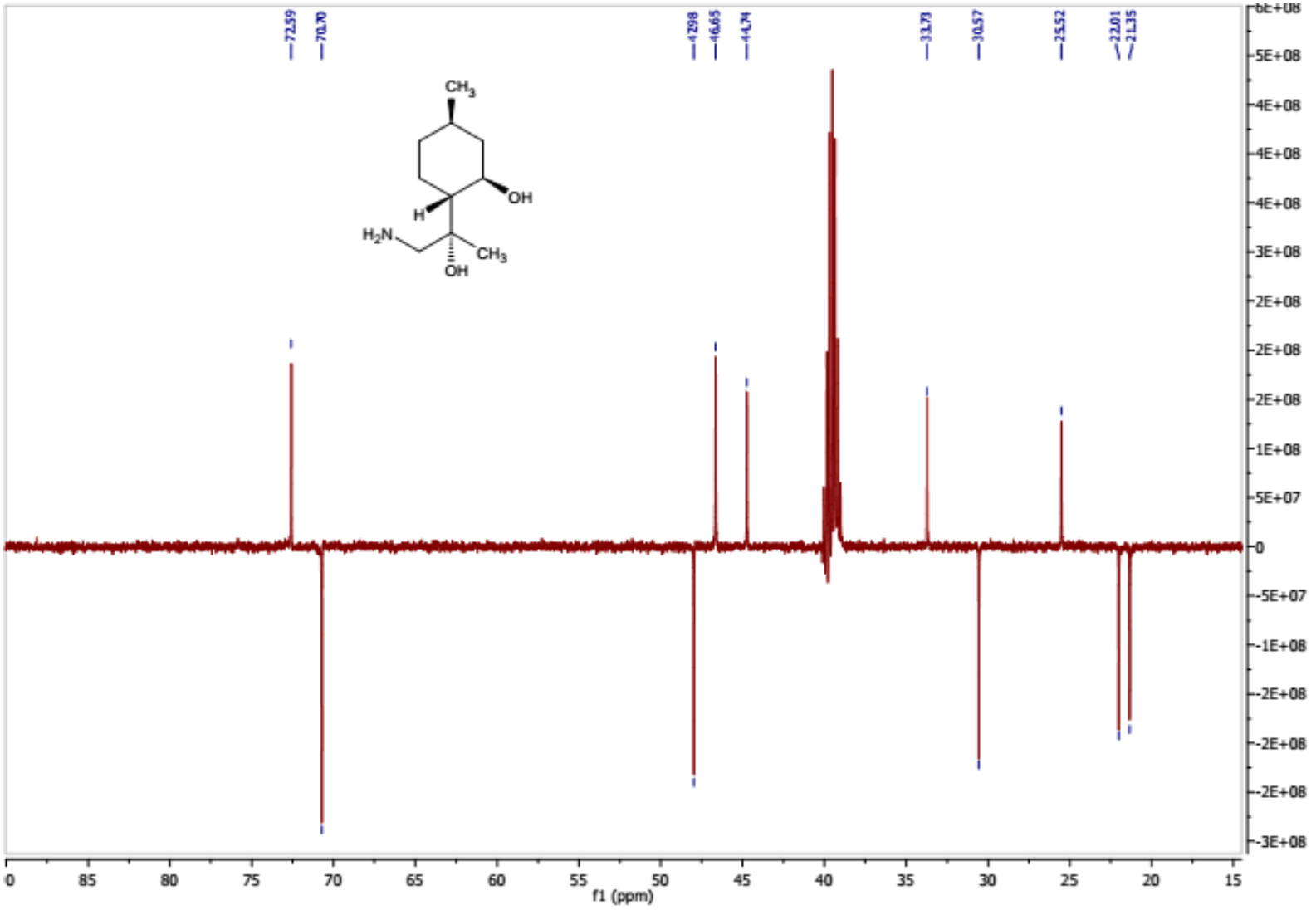
$^{13}$C-NMR of compound **27b**



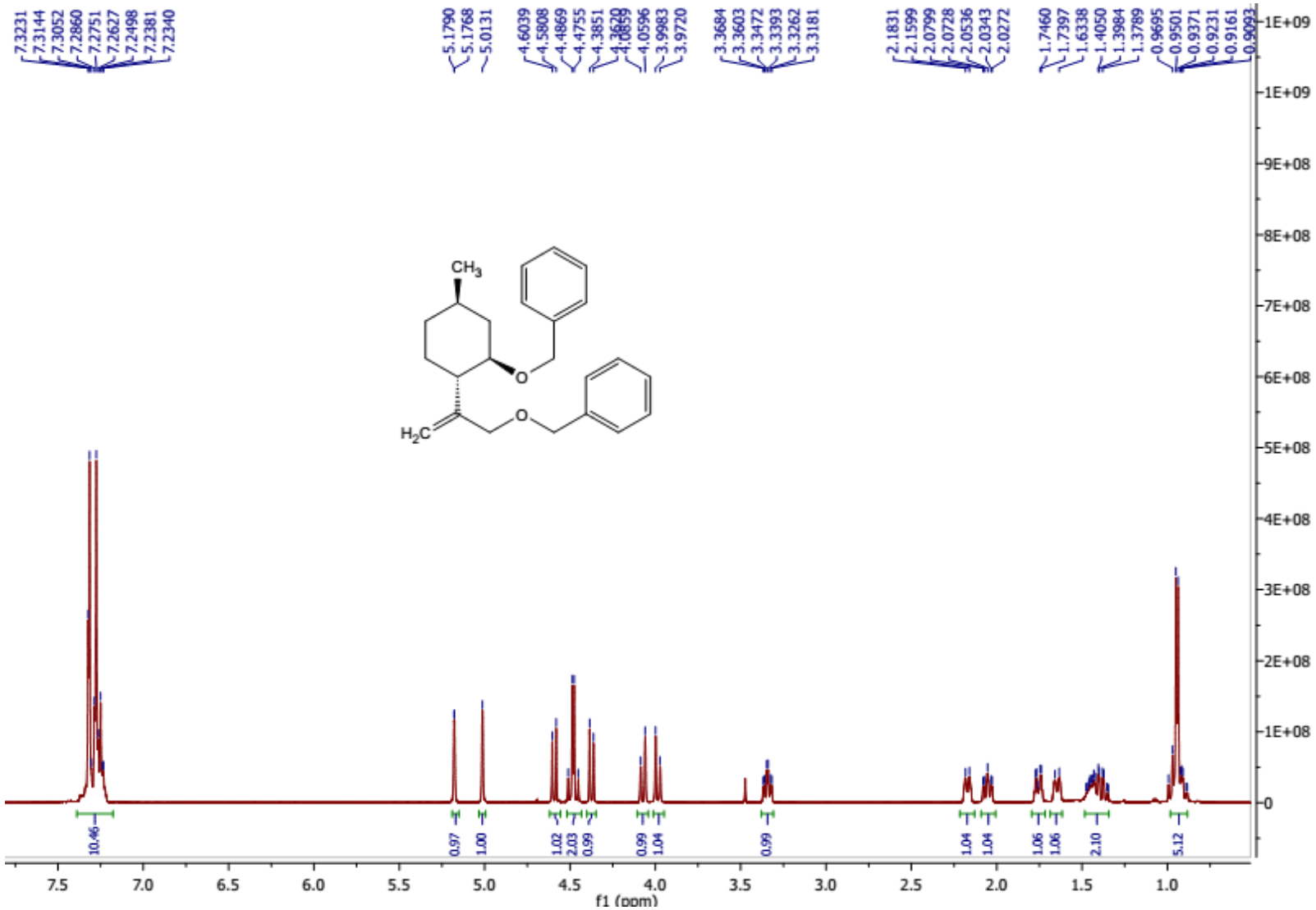
[1]H-NMR of compound **28a**



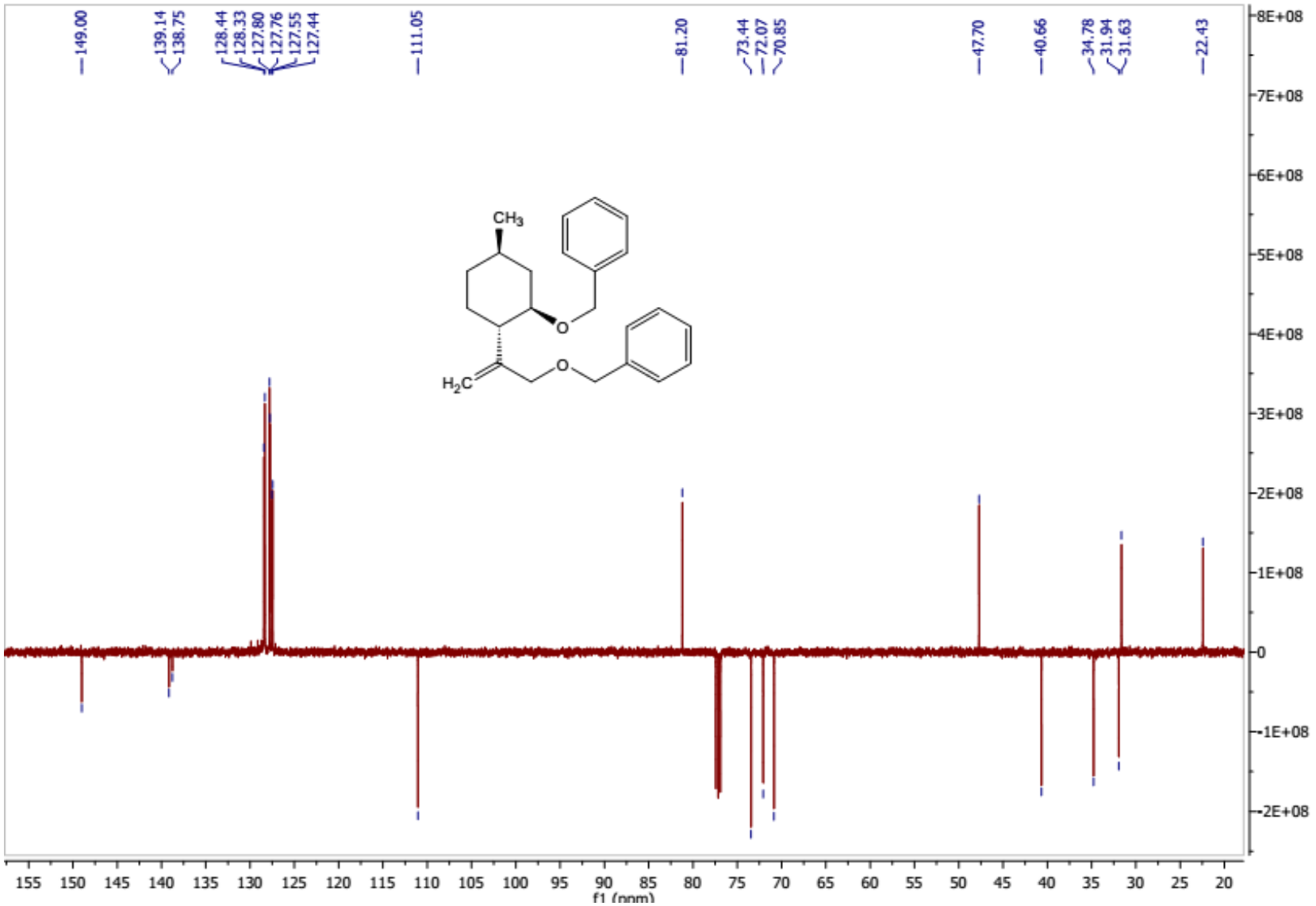
$^{13}$C-NMR of compound **28a**



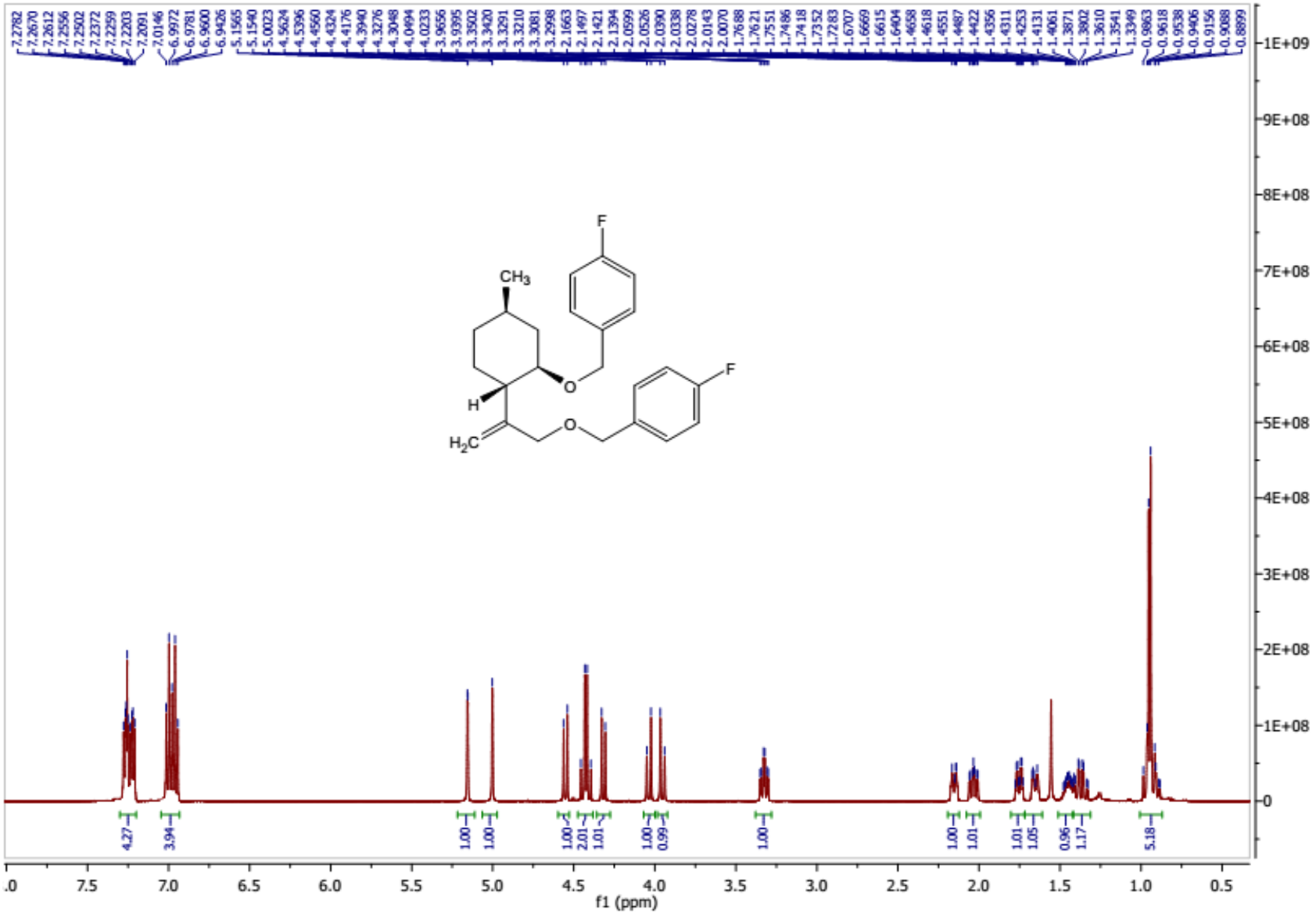
[1]H-NMR of compound **30a**



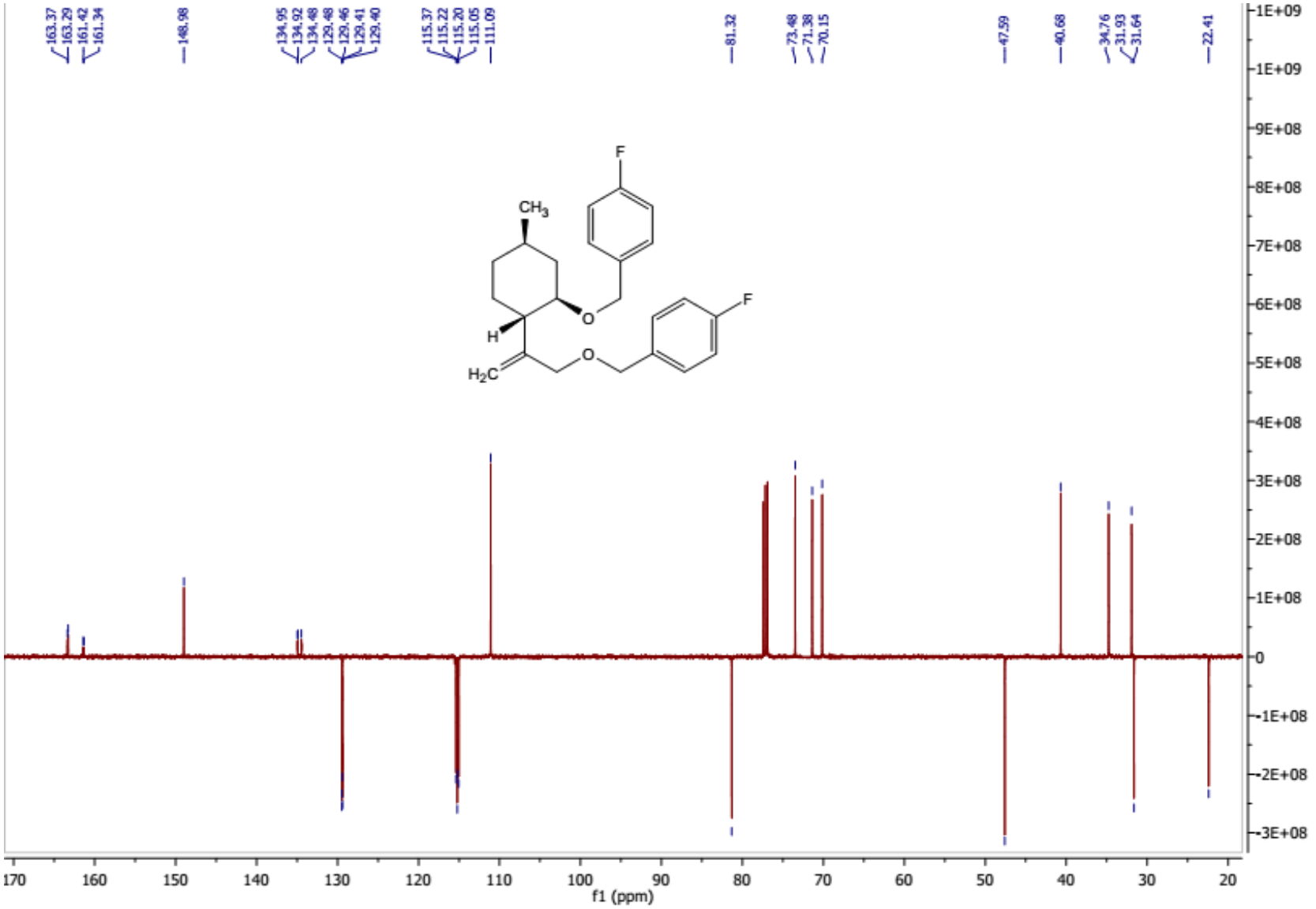
$^{13}$C-NMR of compound **30a**



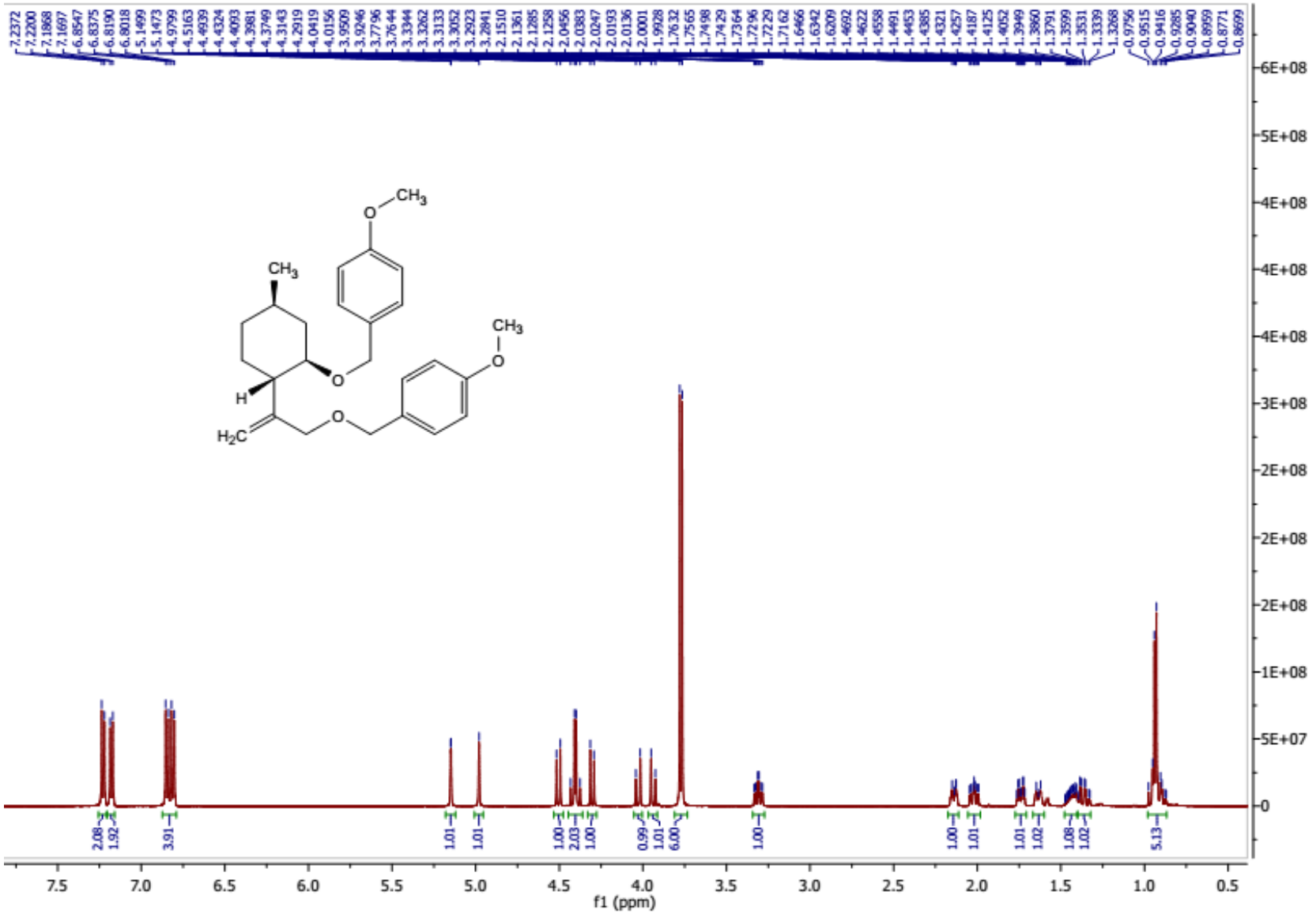
[1]H-NMR of compound **30b**



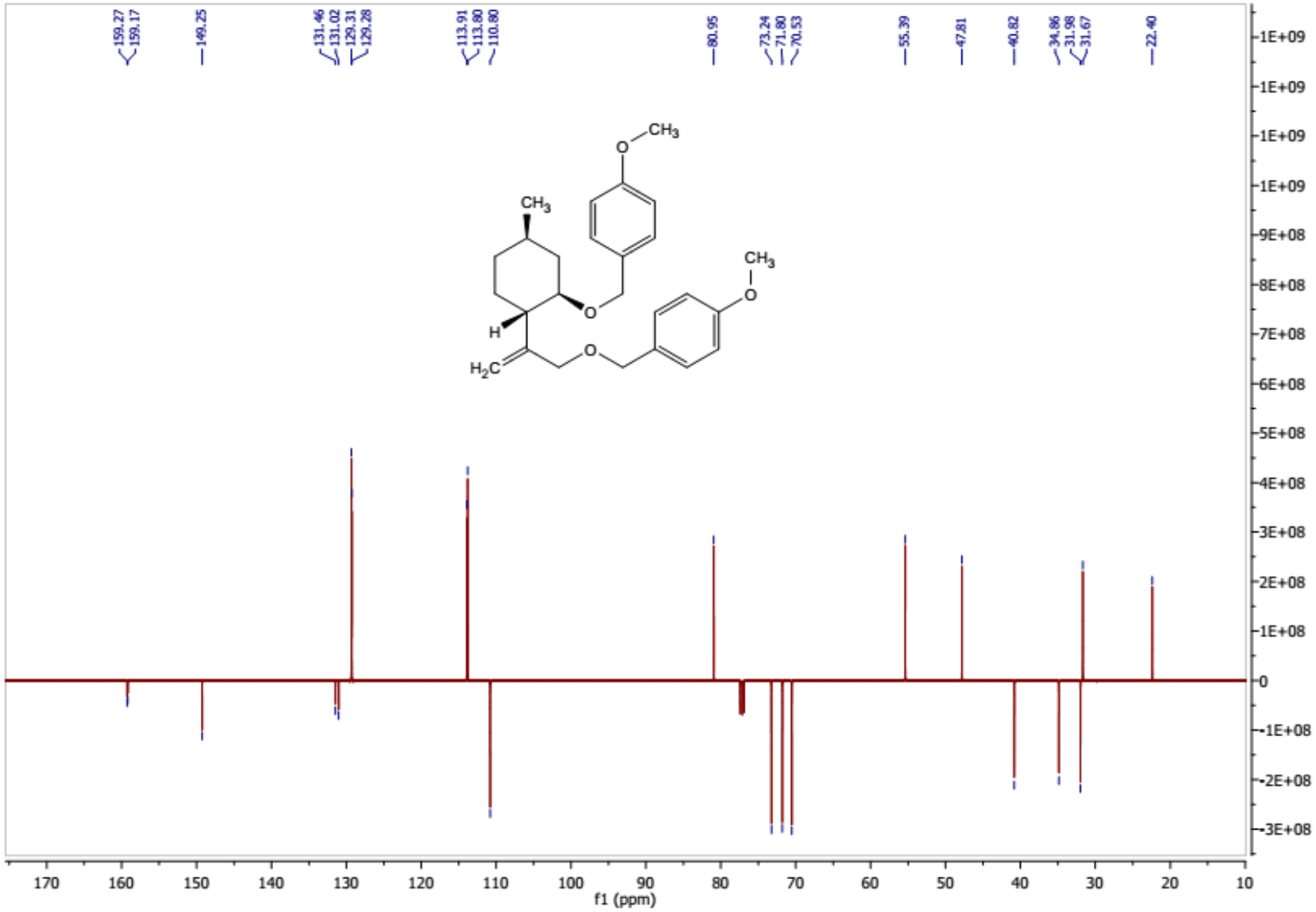
$^{13}$C-NMR of compound **30b**



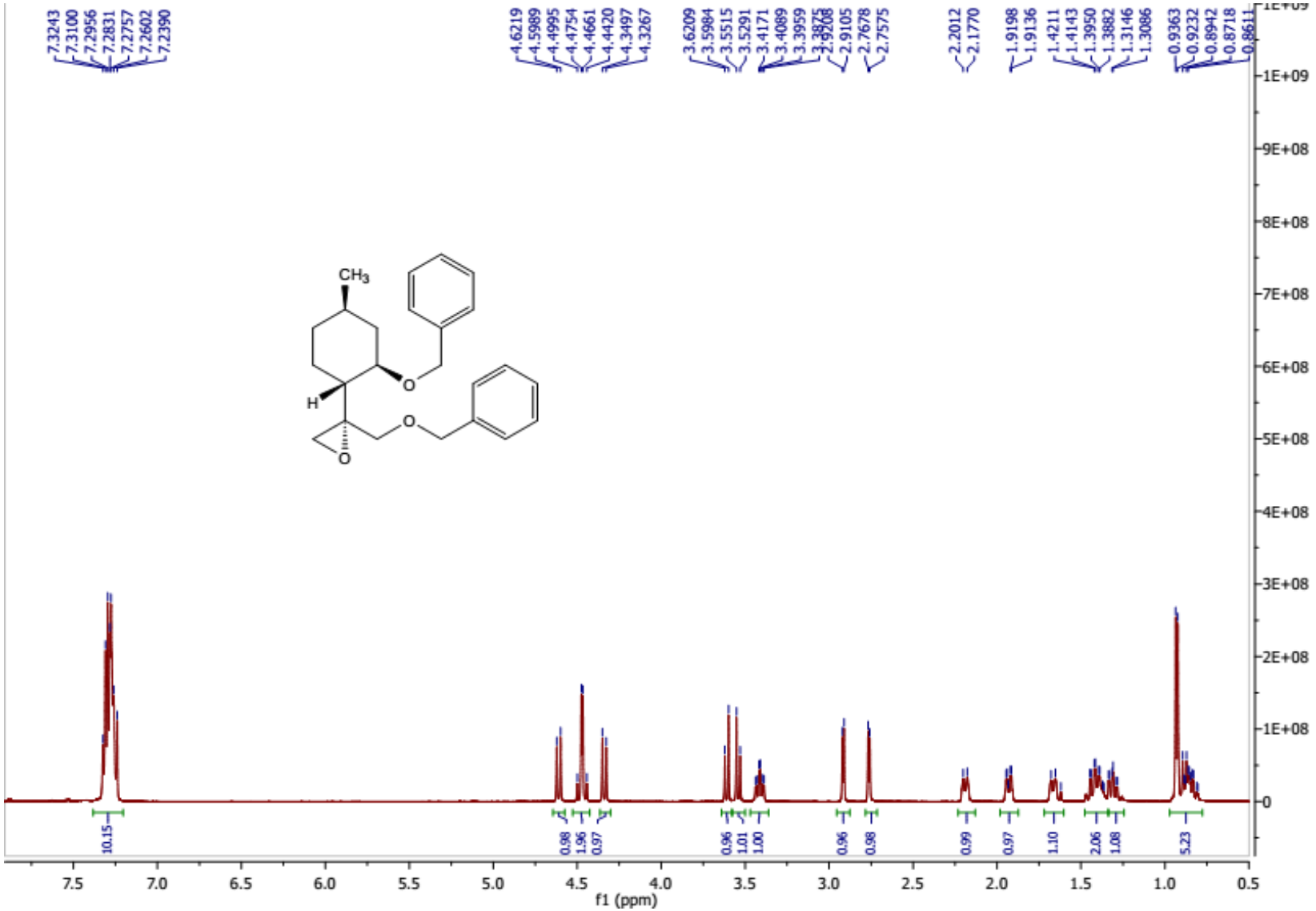
[1]H-NMR of compound **30c**



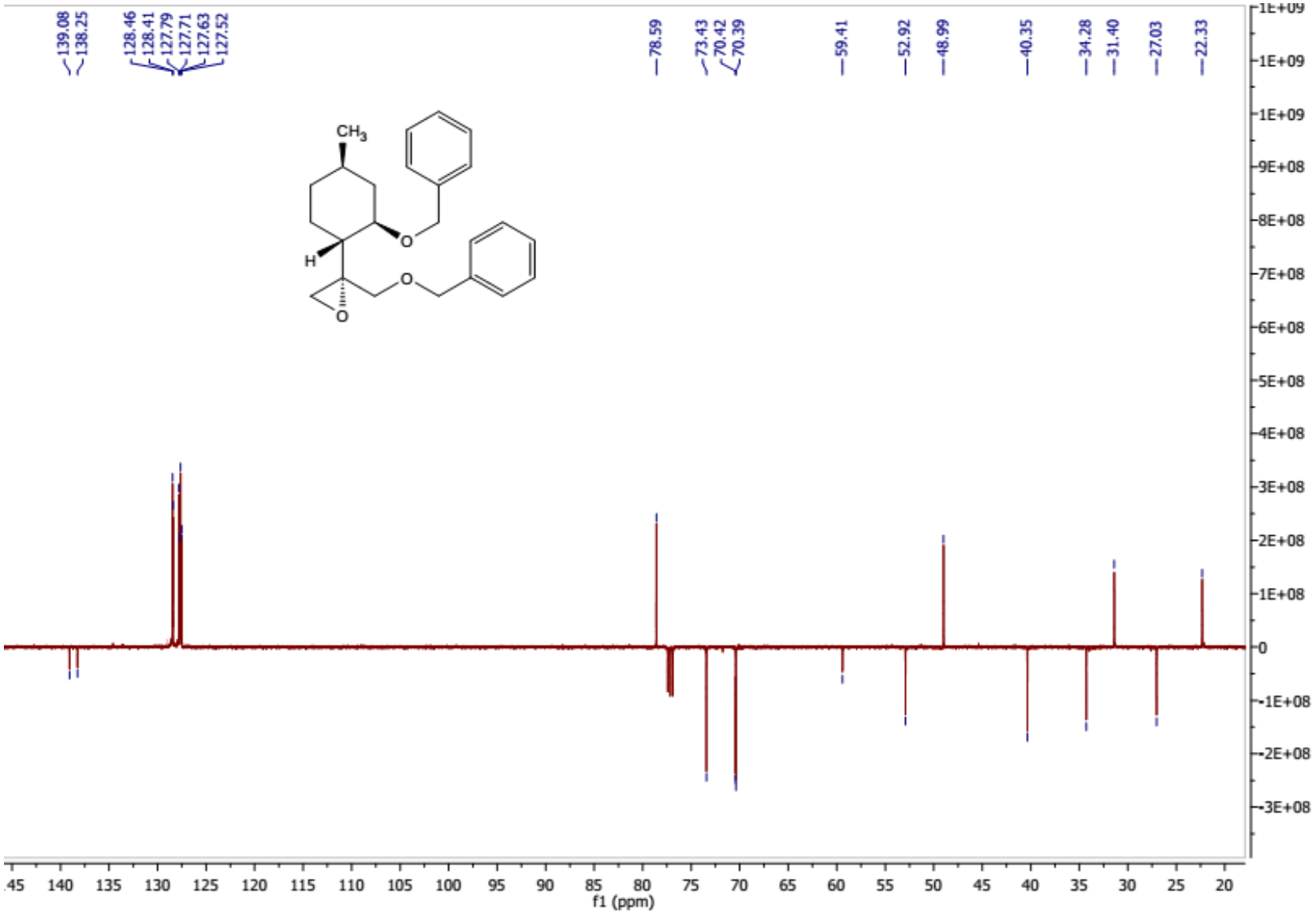
$^{13}$C-NMR of compound **30c**



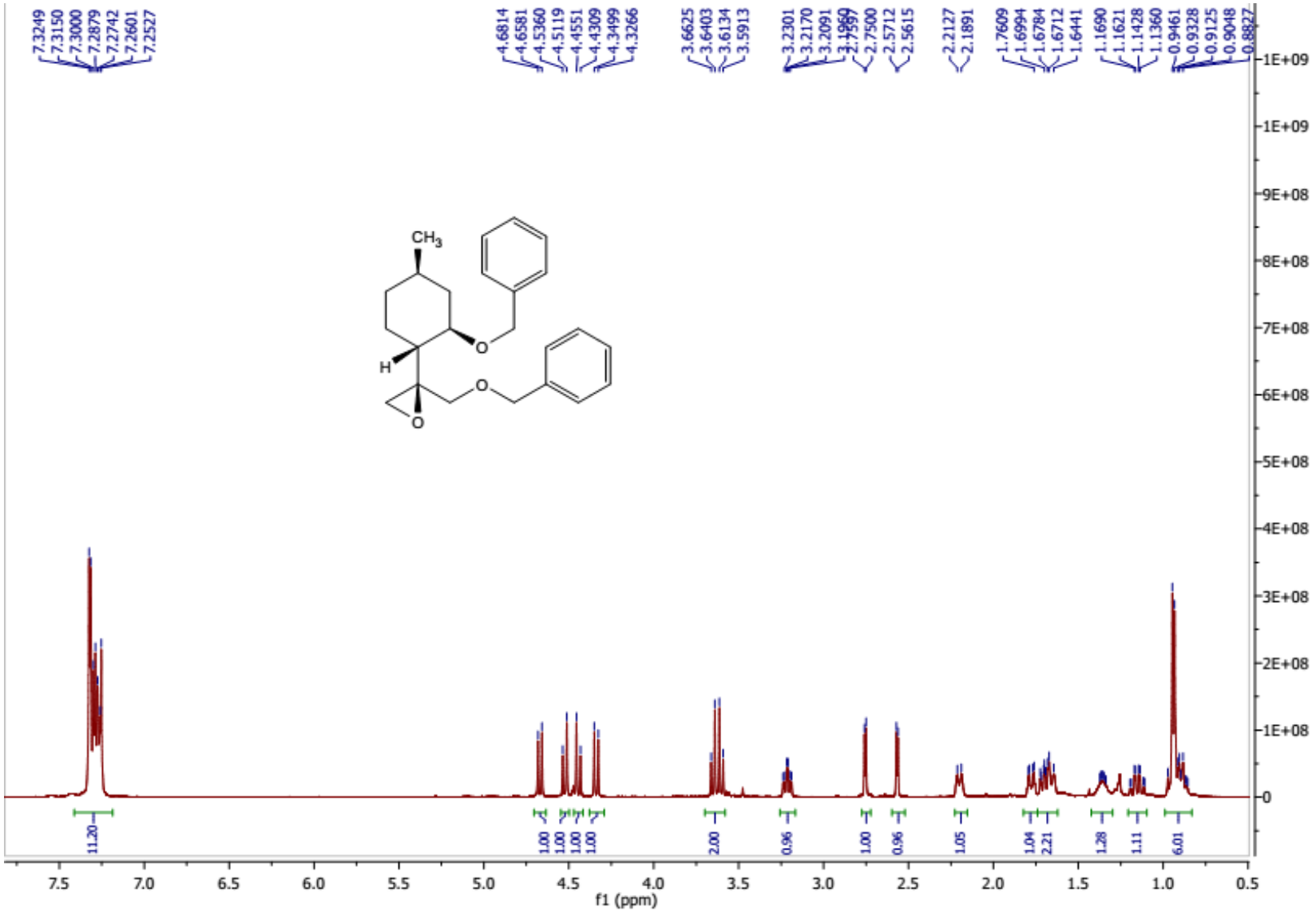
[1]H-NMR of compound **31a**



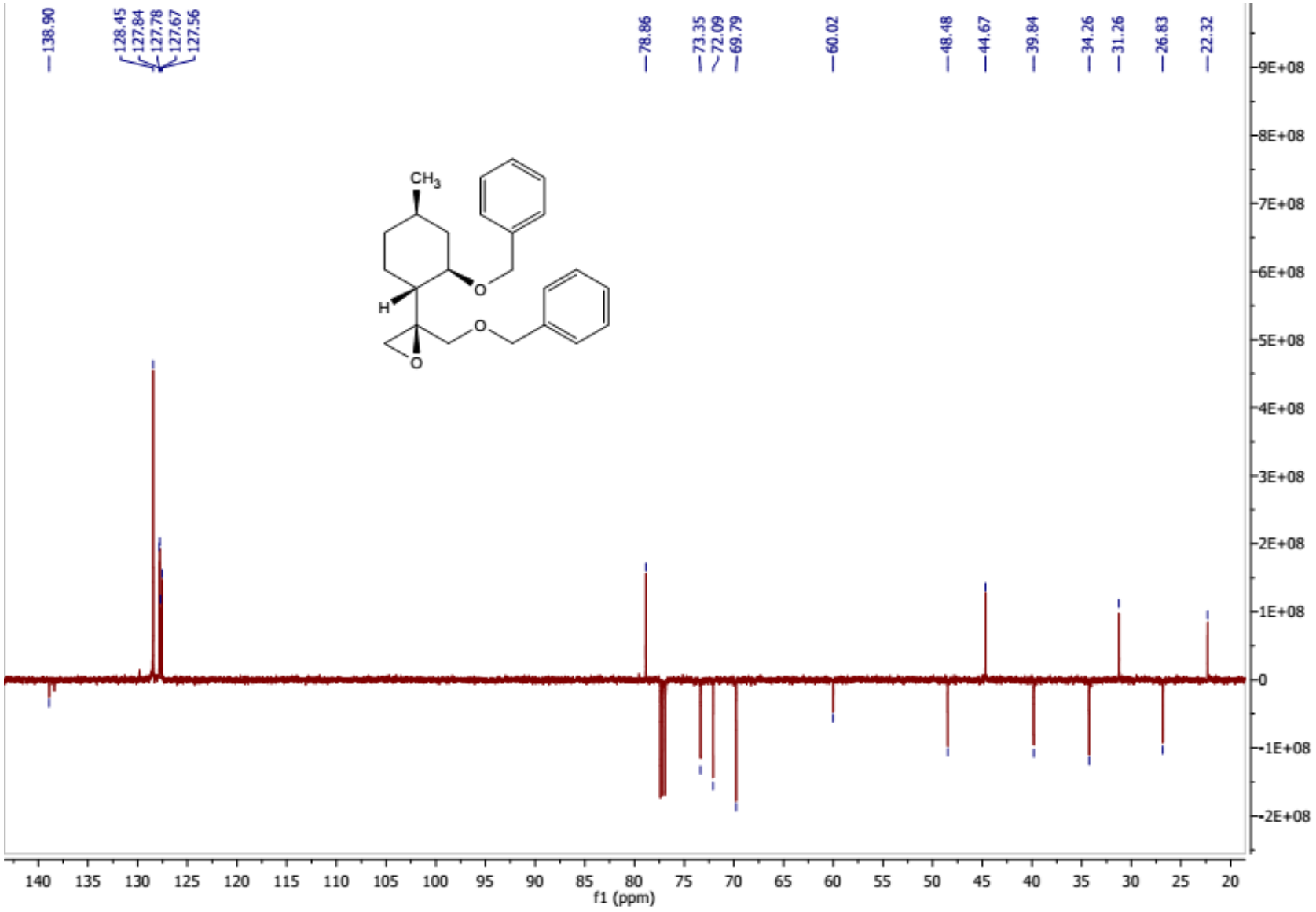
$^{13}$C-NMR of compound **31a**



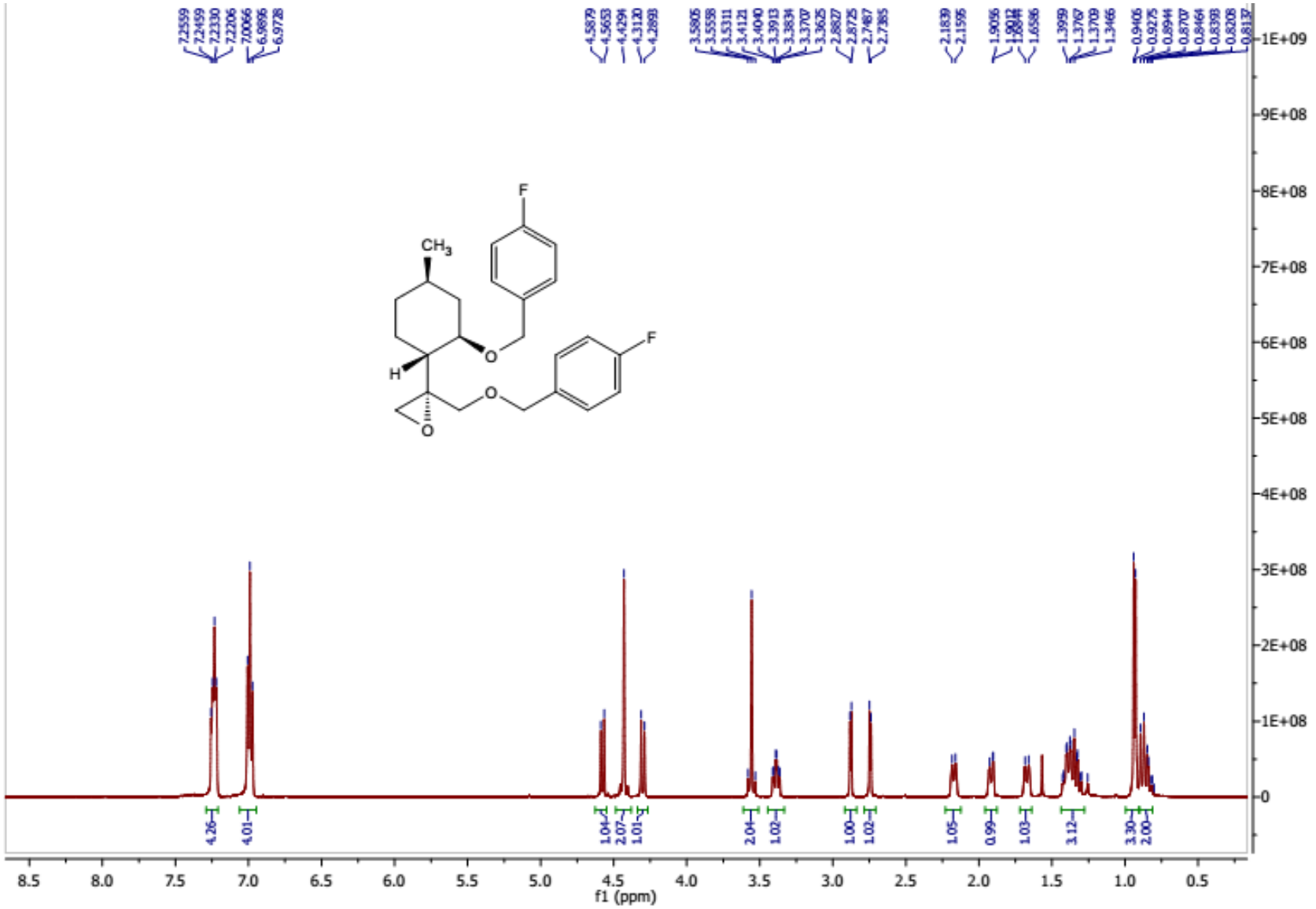
[1]H-NMR of compound **31b**



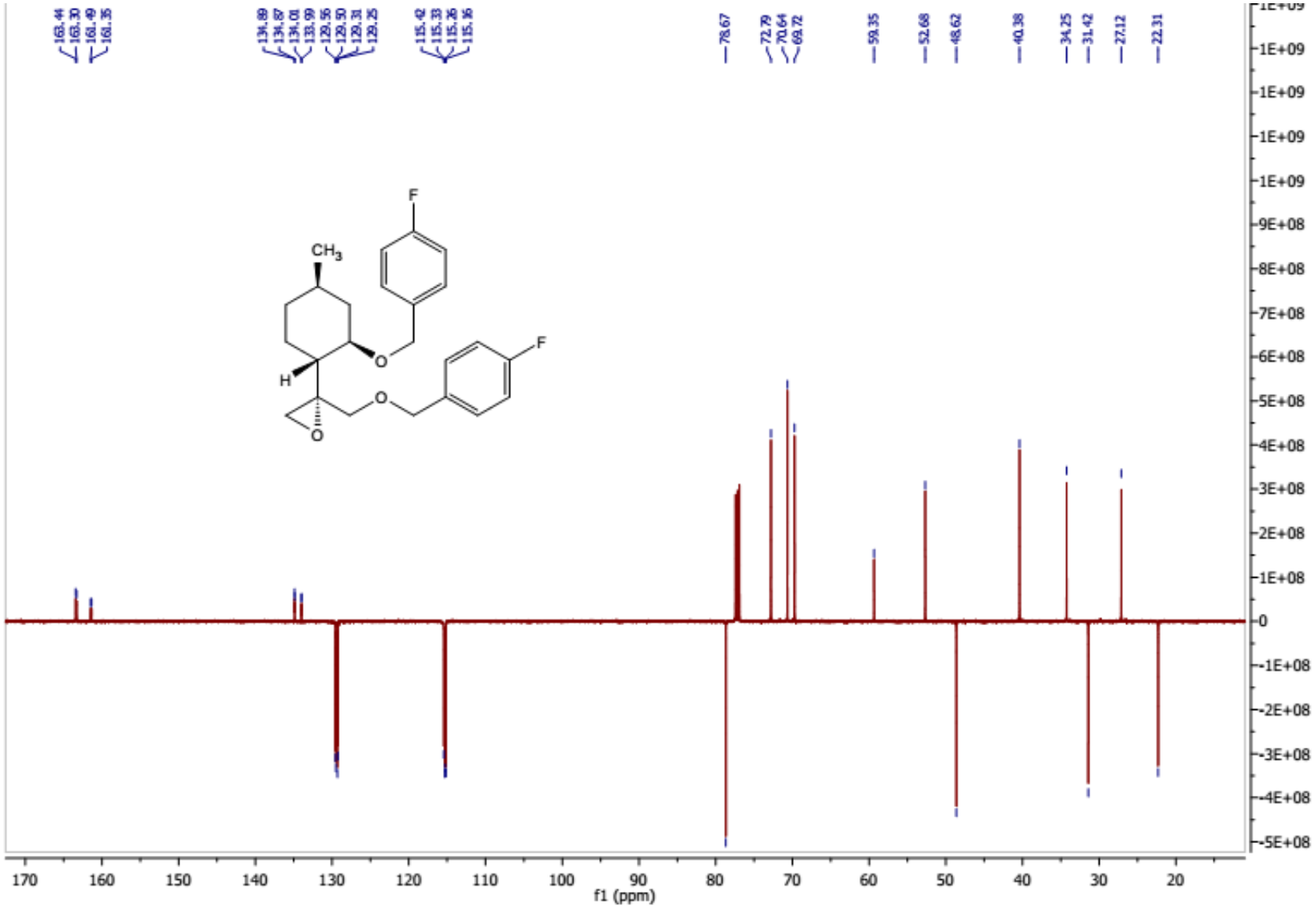
$^{13}$C-NMR of compound **31b**



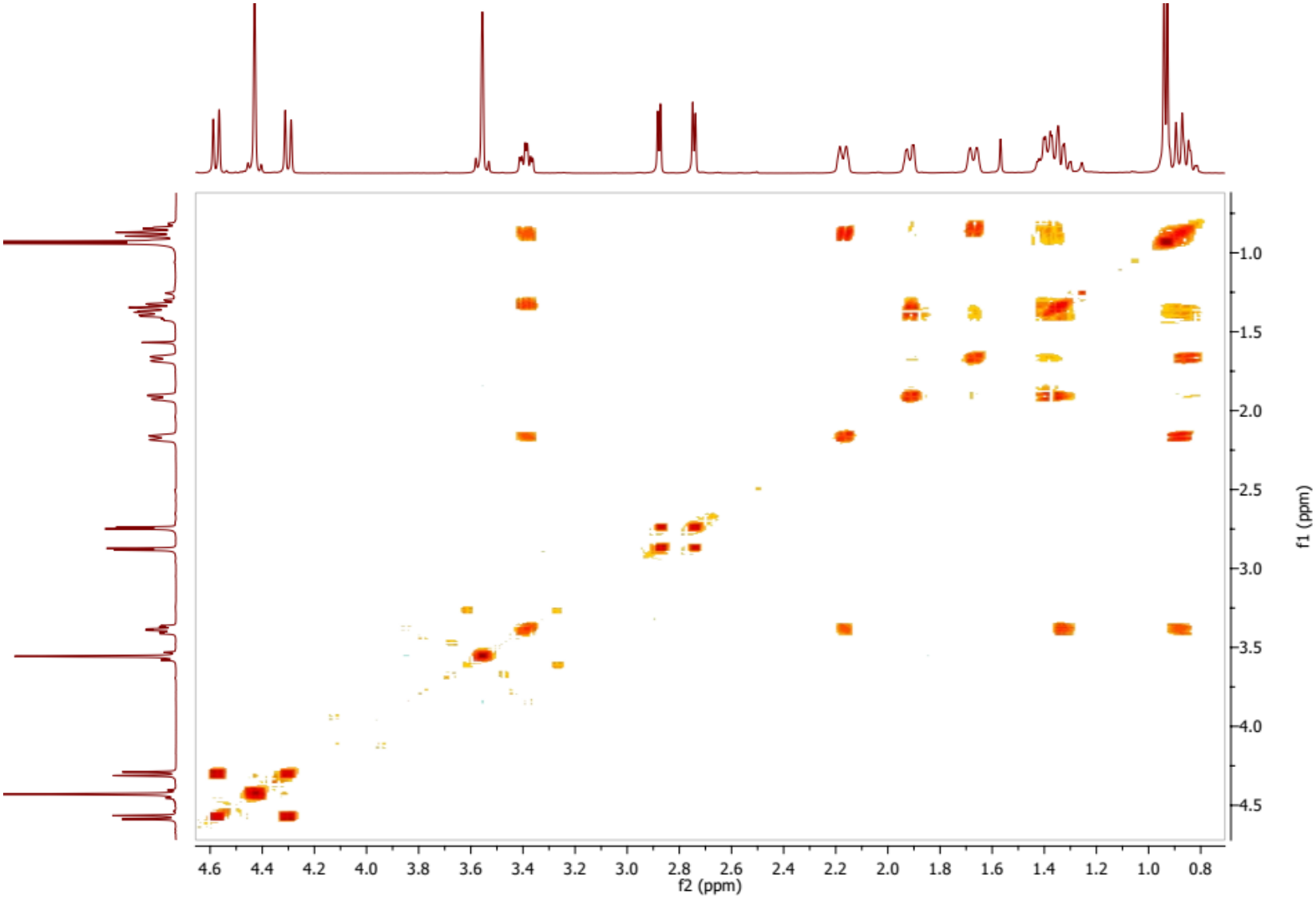
[1]H-NMR of compound **32a**



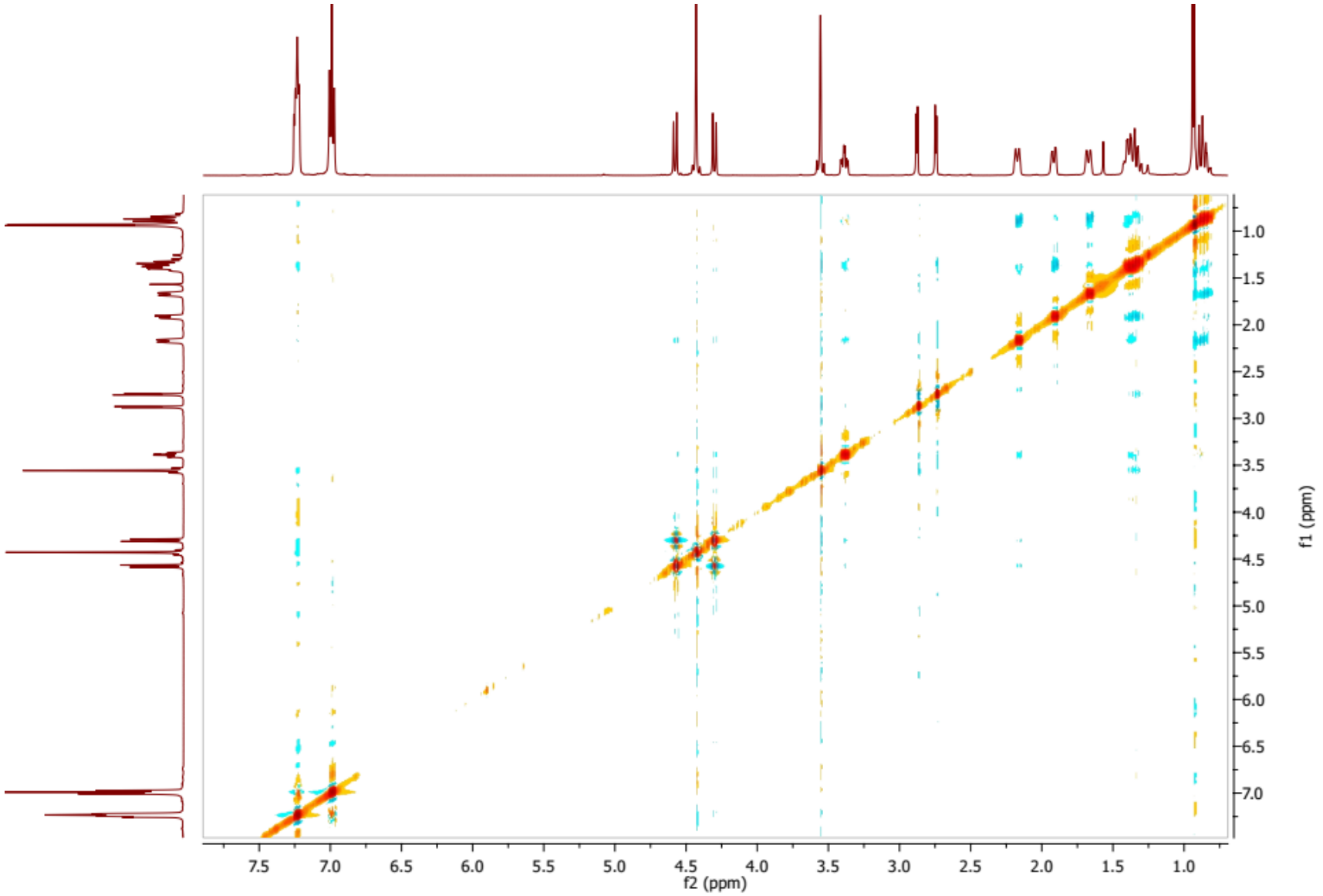
$^{13}$C-NMR of compound **32a**



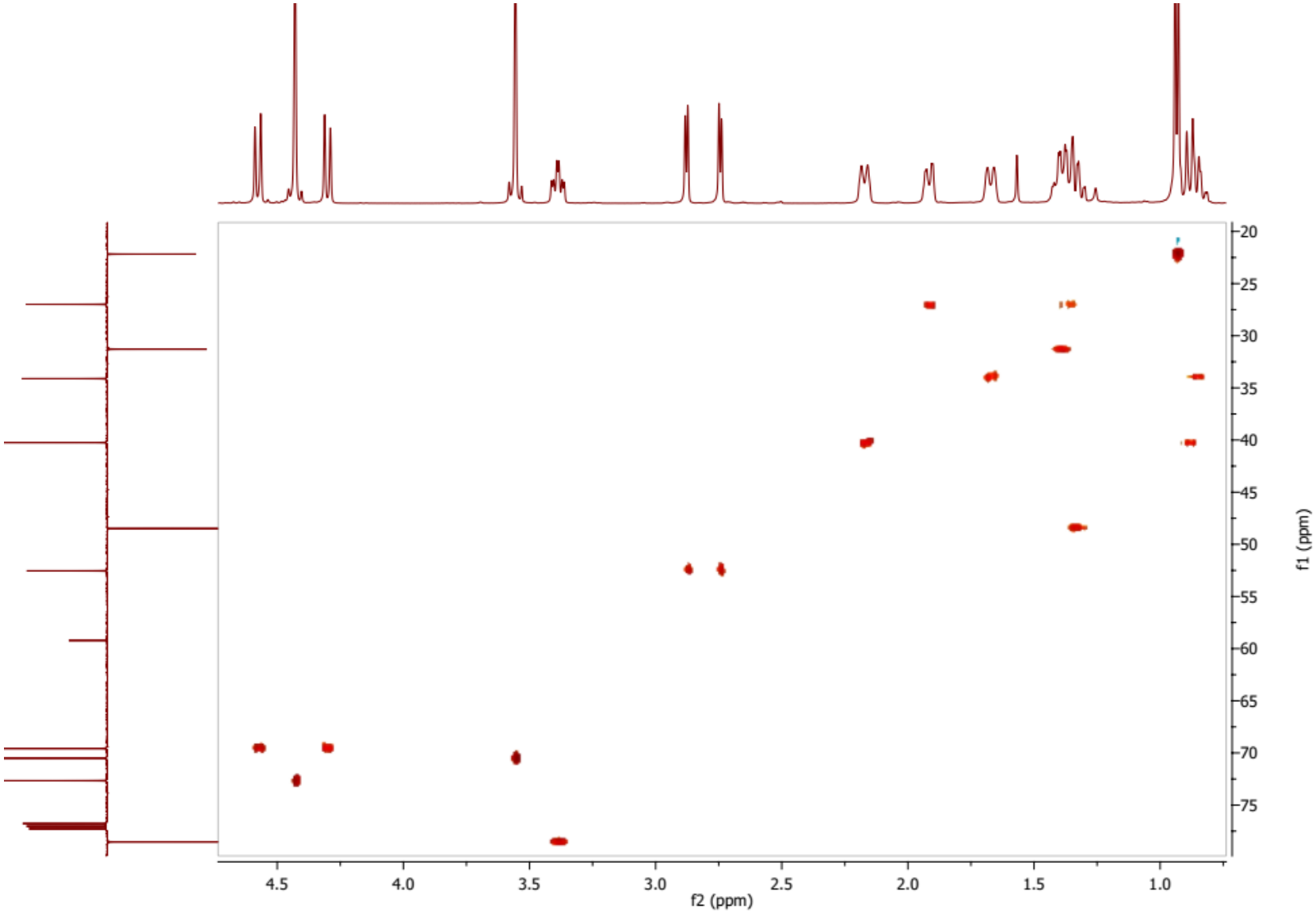
COSY spectrum of compound **32a**



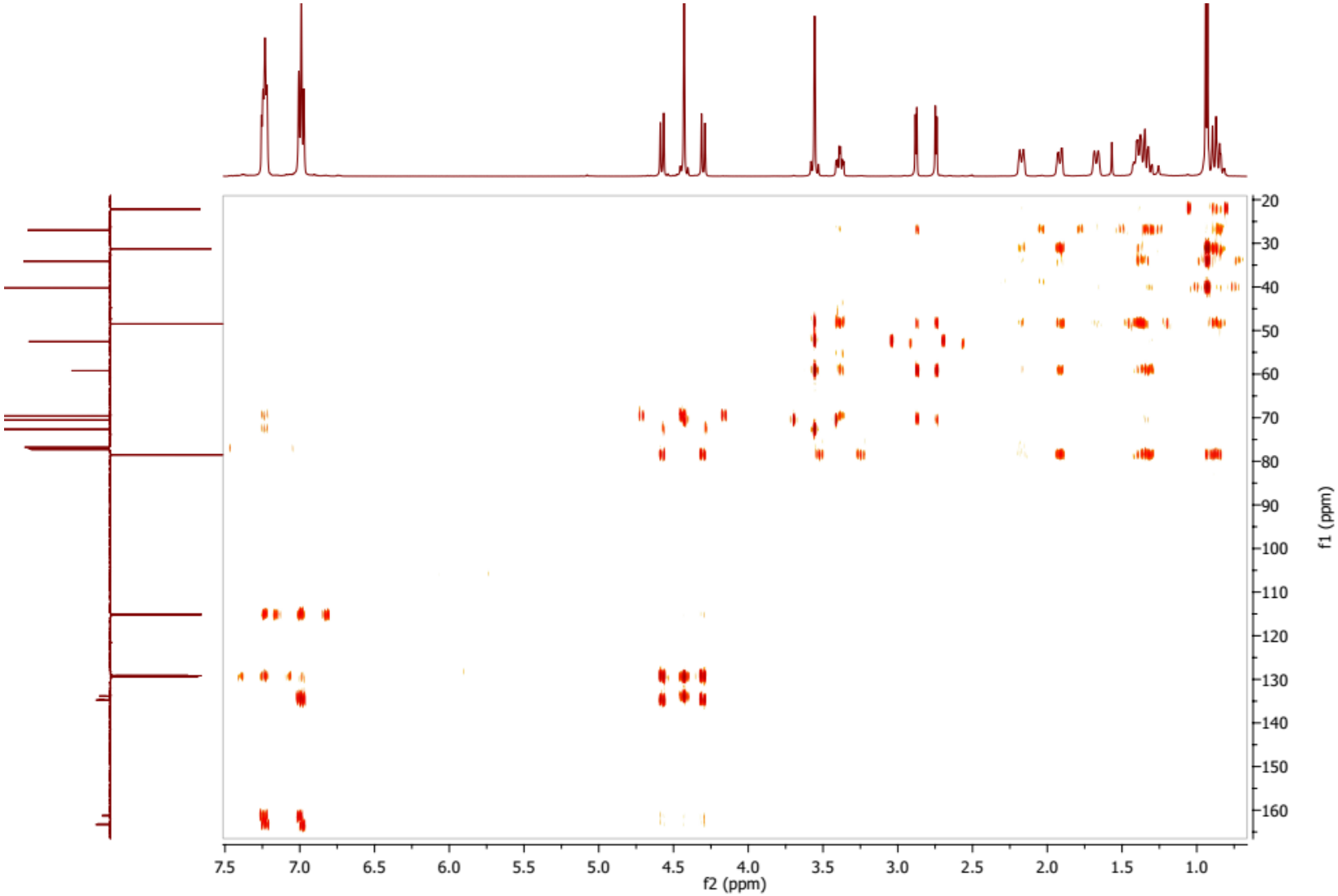
NOESY spectrum of compound **32a**



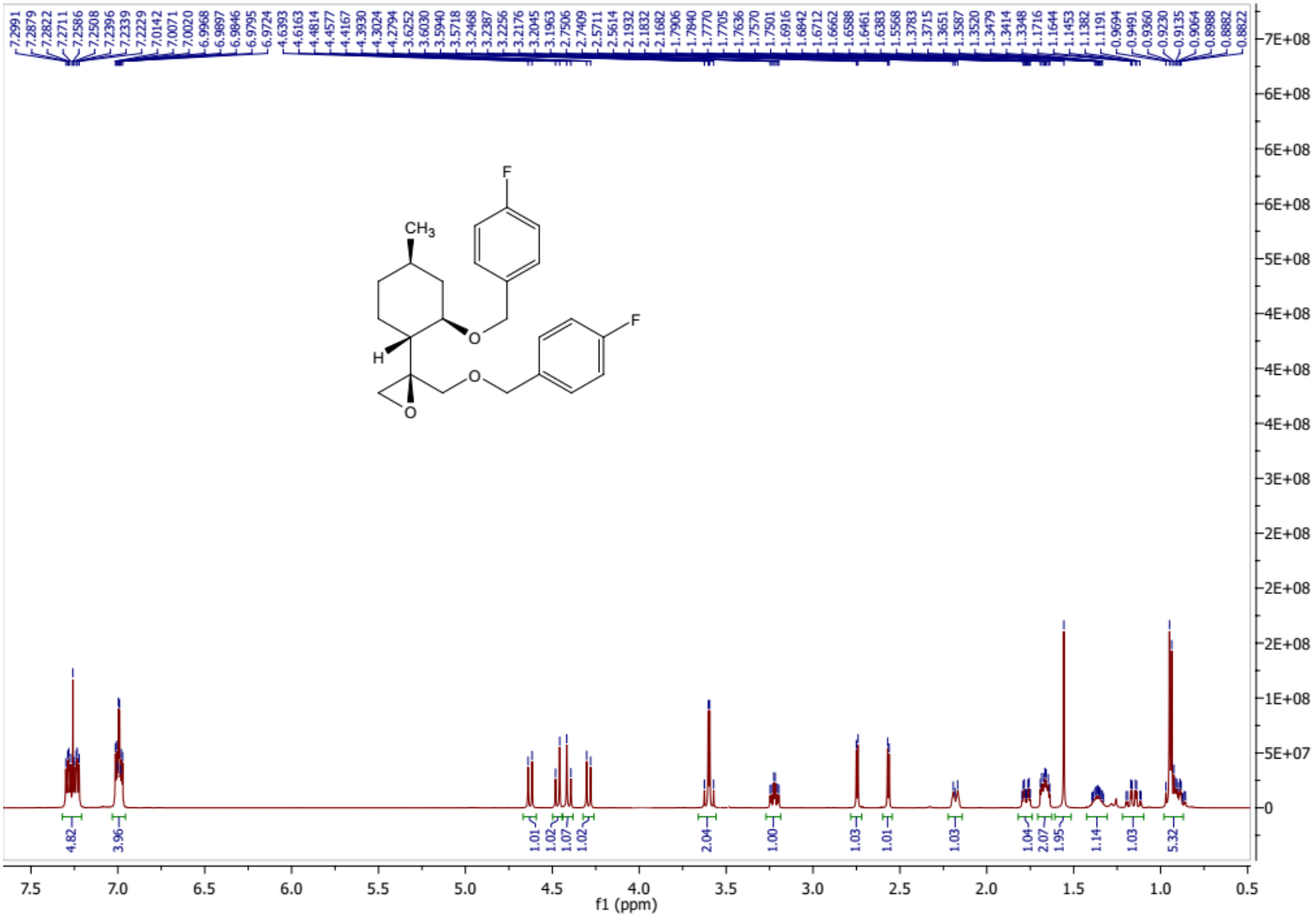
HSQC spectrum of compound **32a**



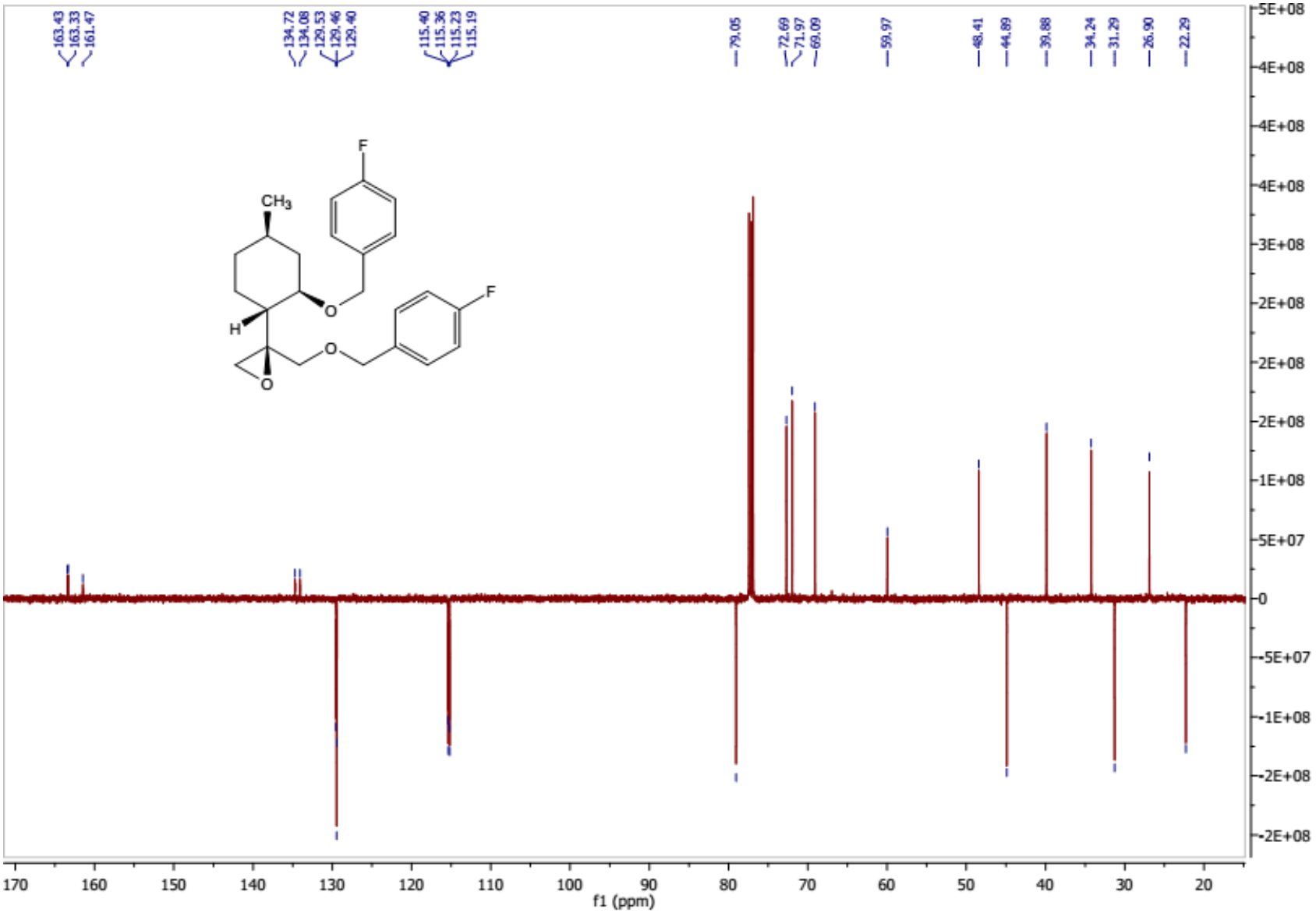
HMBC spectrum of compound **32a**



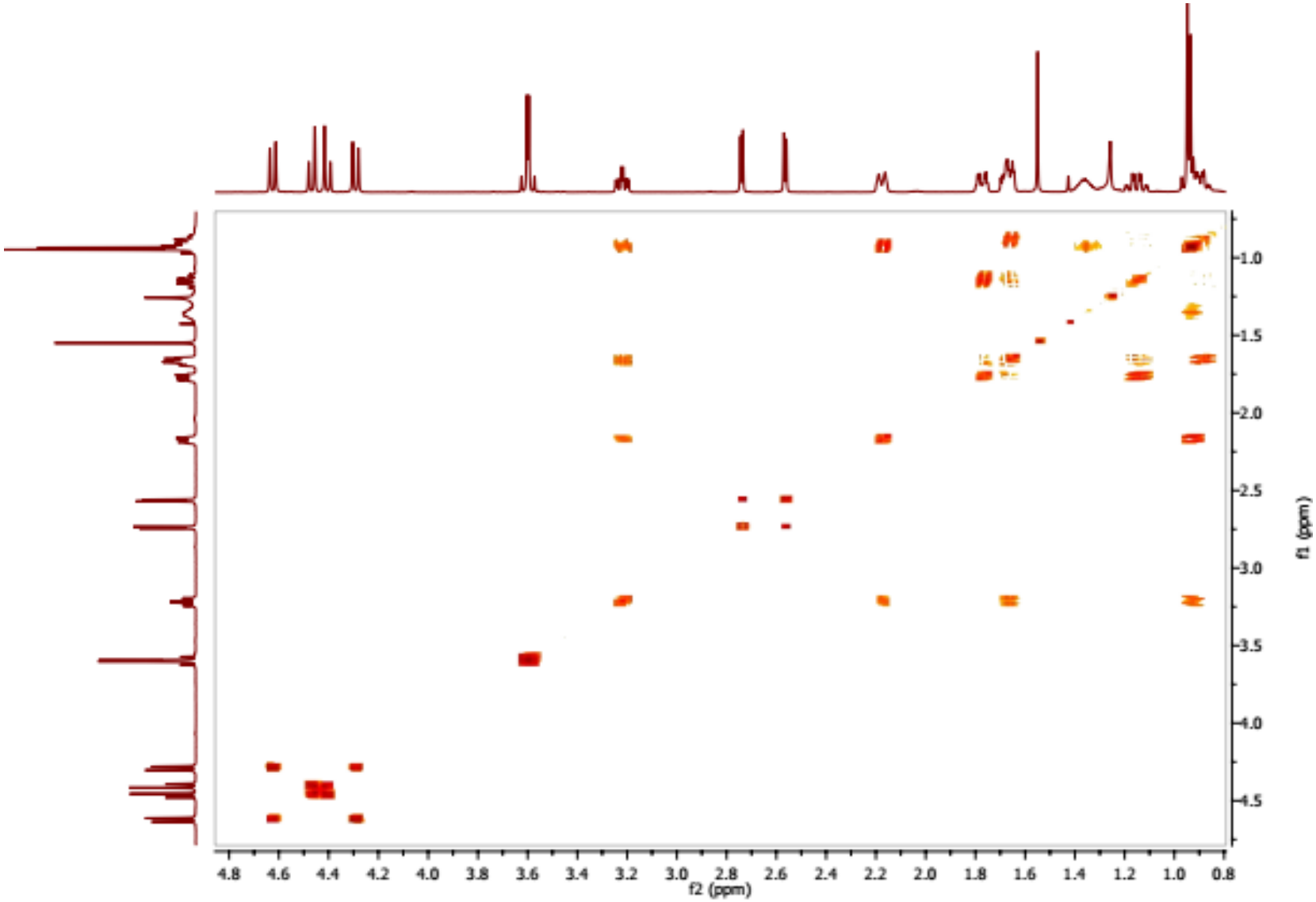
[1]H-NMR of compound **32b**



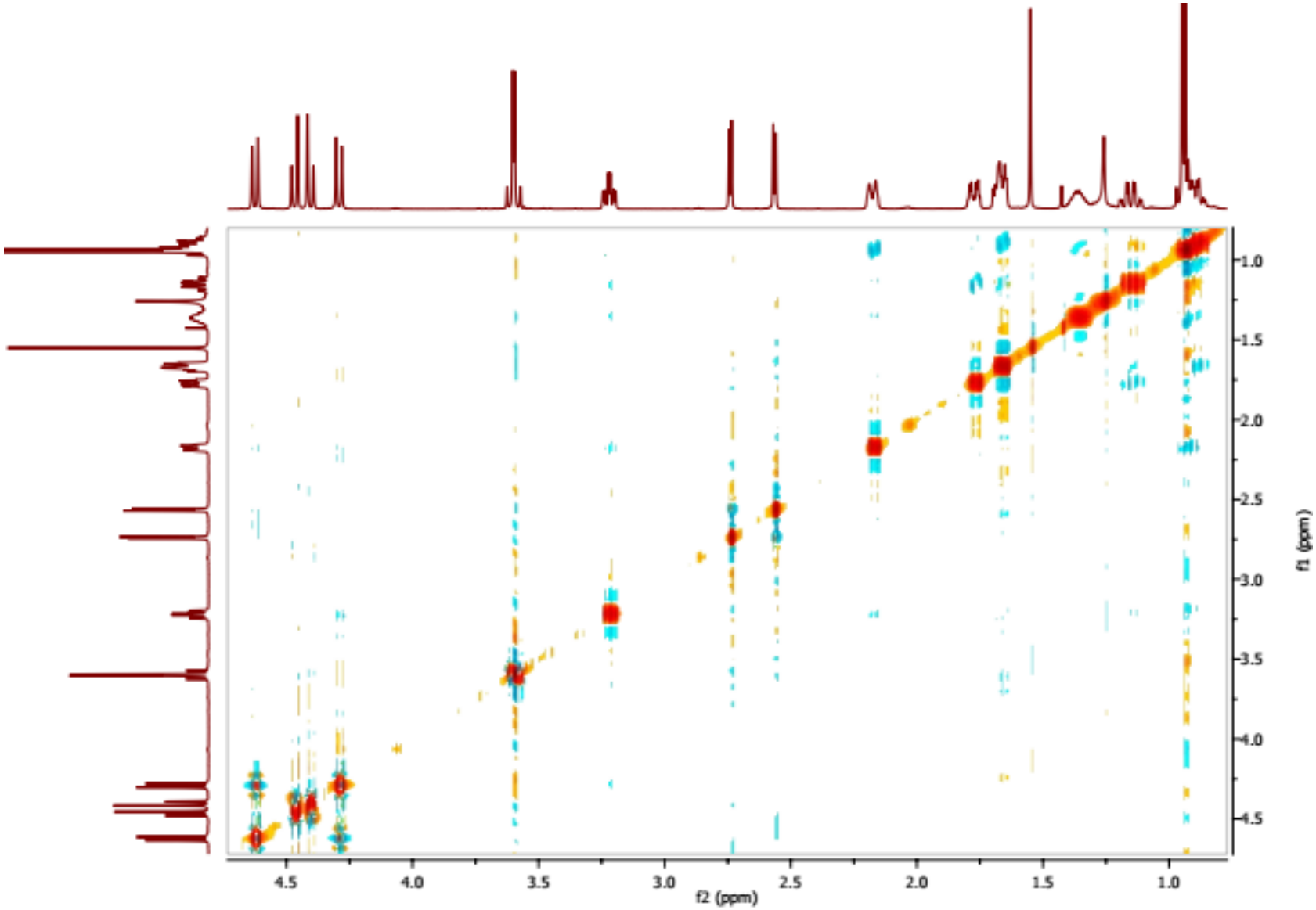
$^{13}$C-NMR of compound **32b**



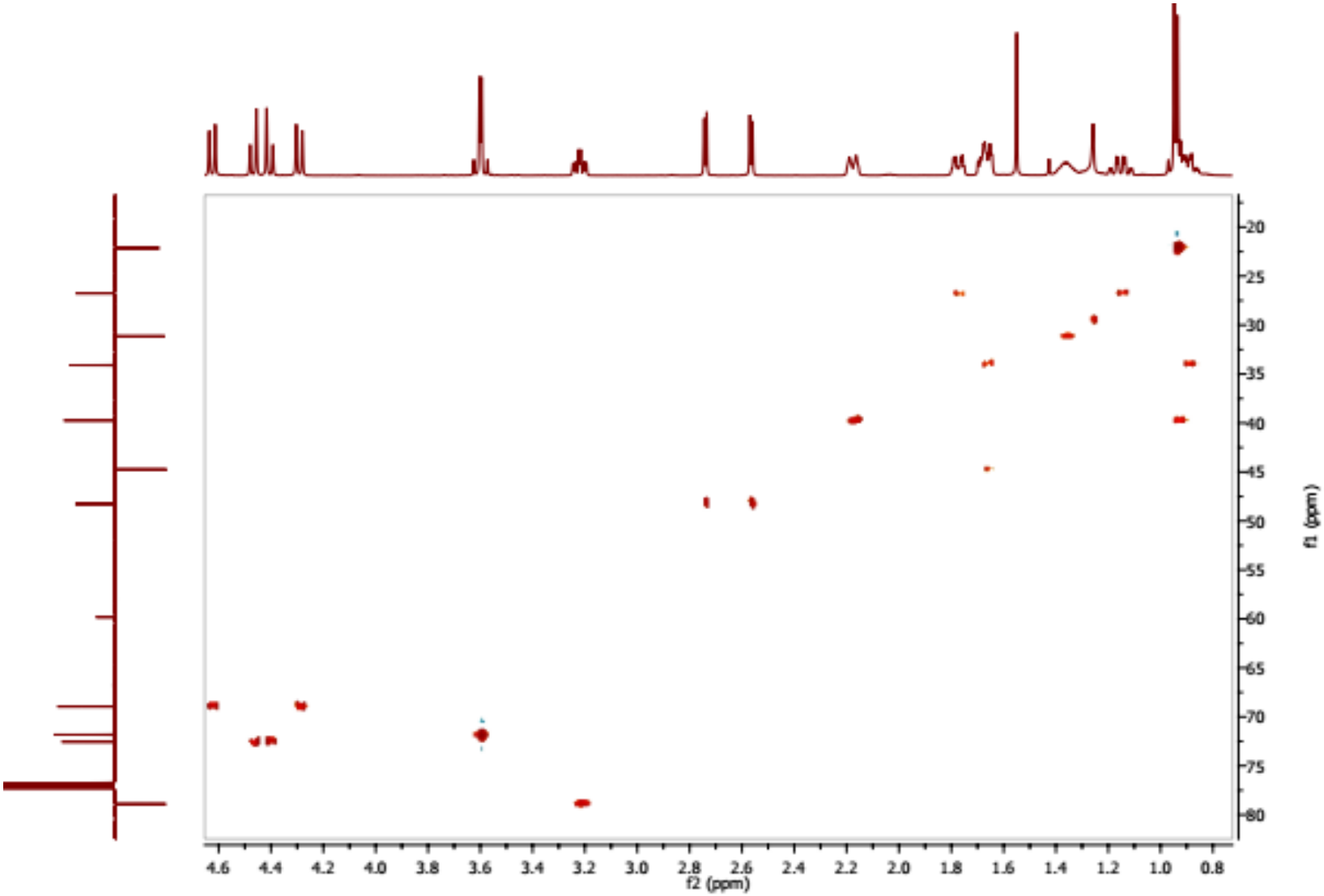
COSY spectrum of compound **32a**



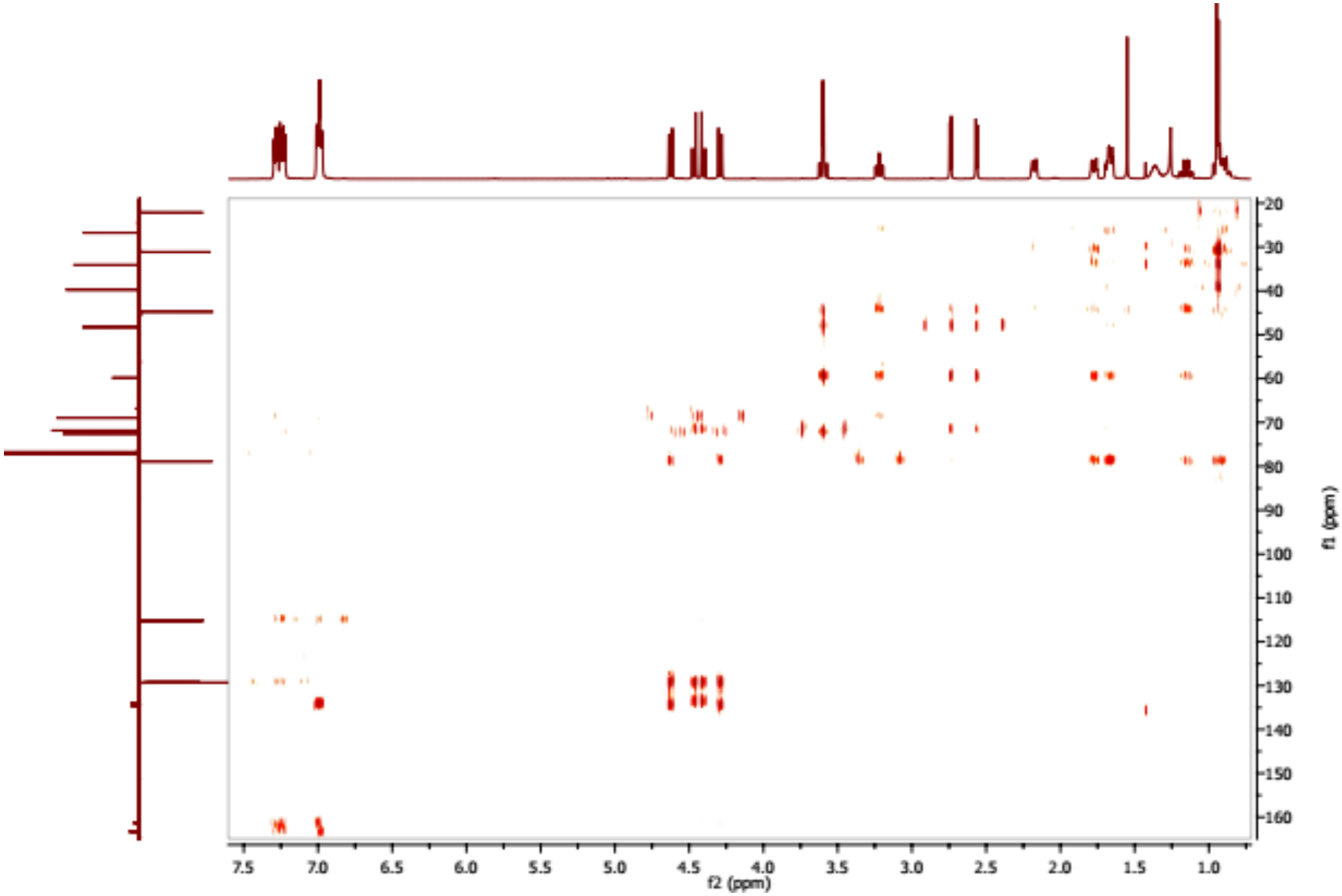
NOESY spectrum of compound **32a**



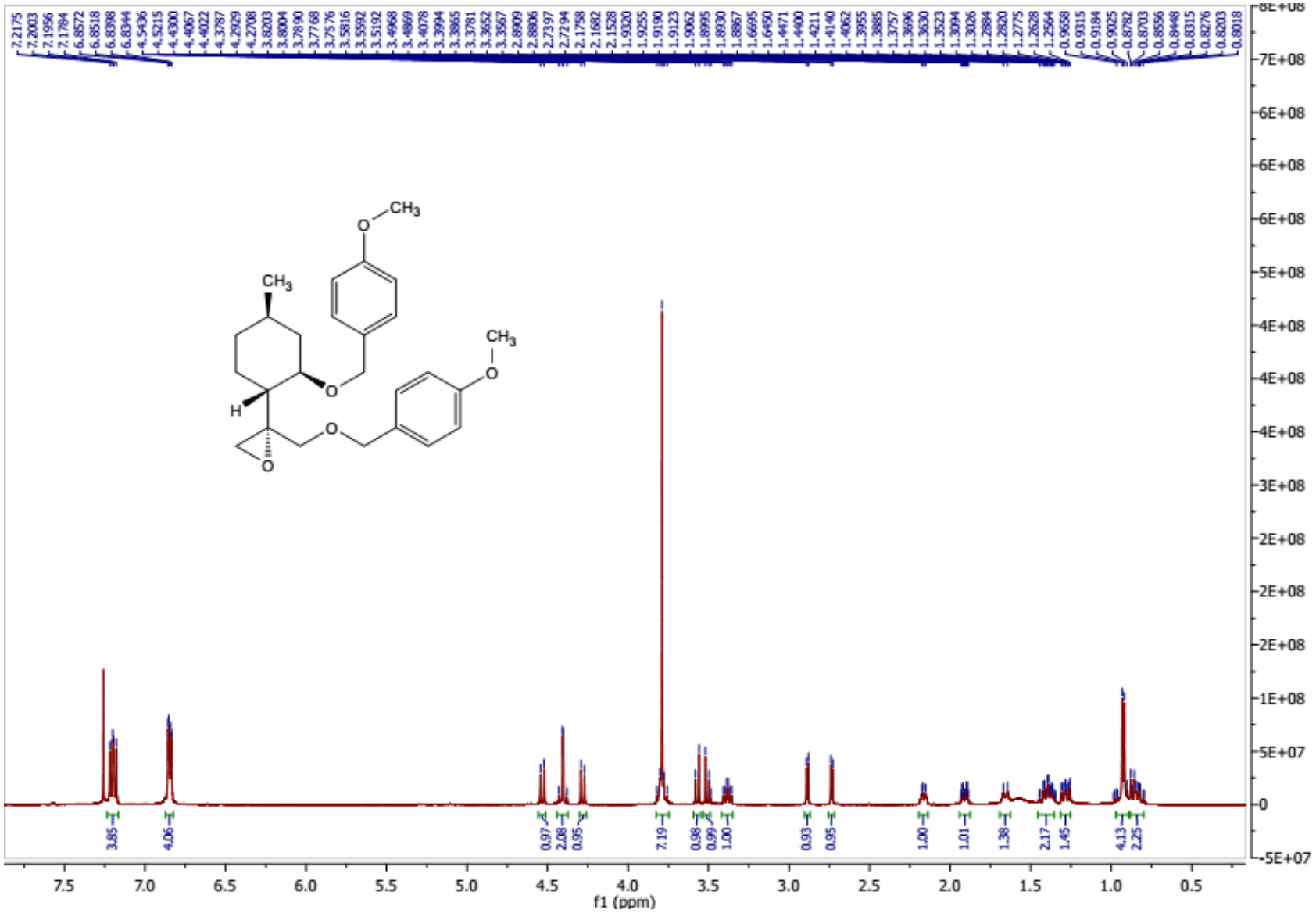
HSQC spectrum of compound **32a**



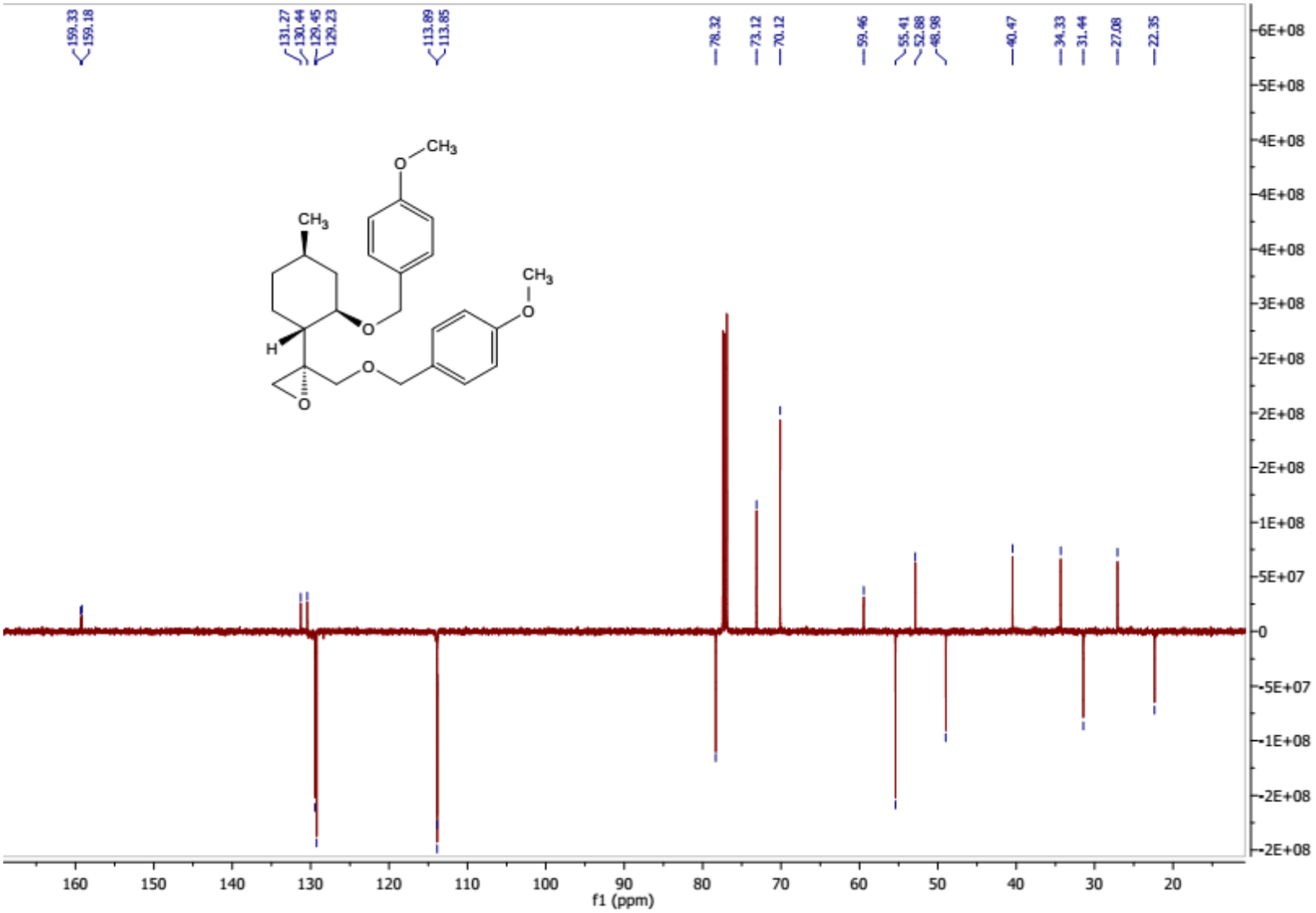
HMBC spectrum of compound **32a**



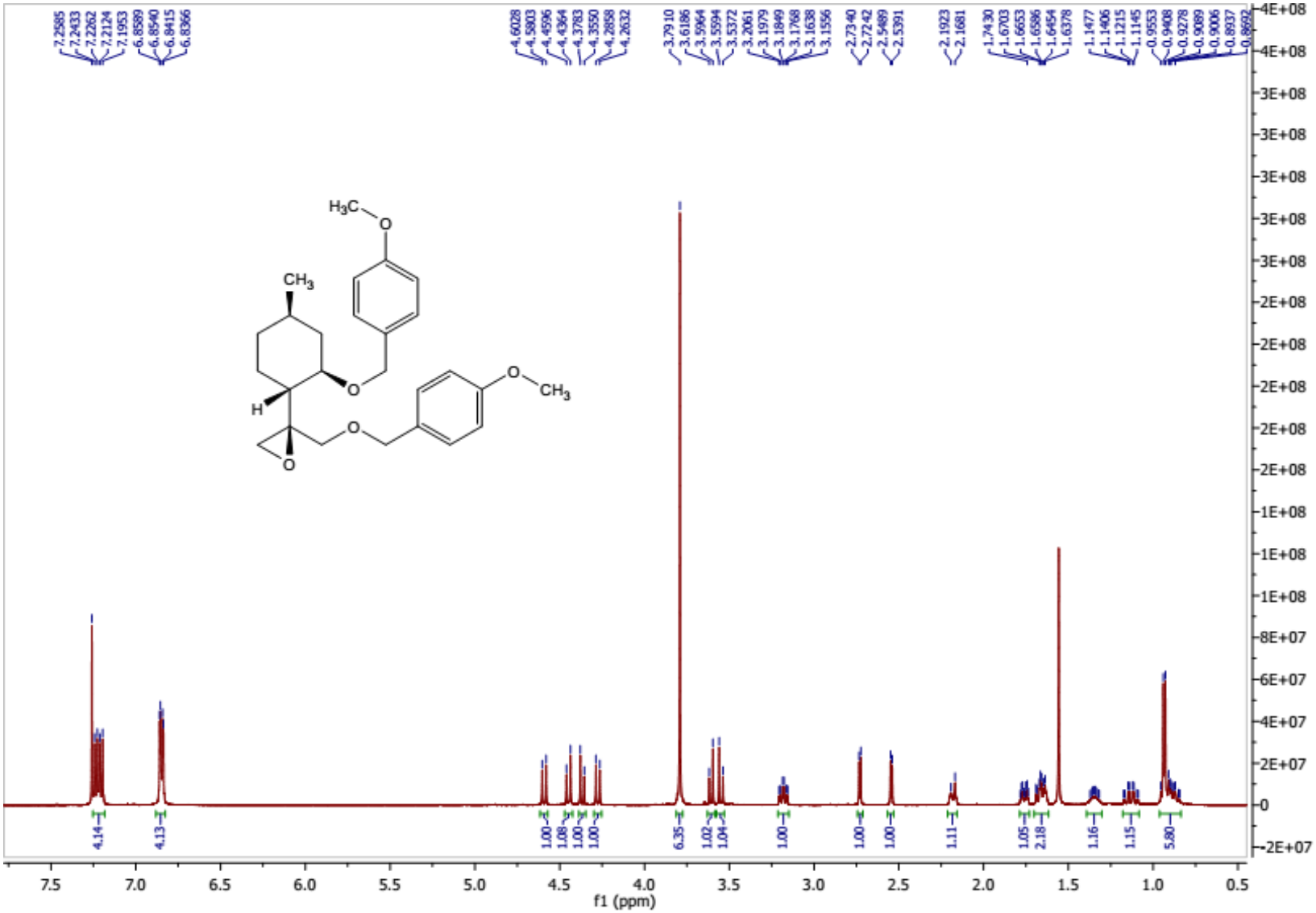
[1]H-NMR of compound **33a**



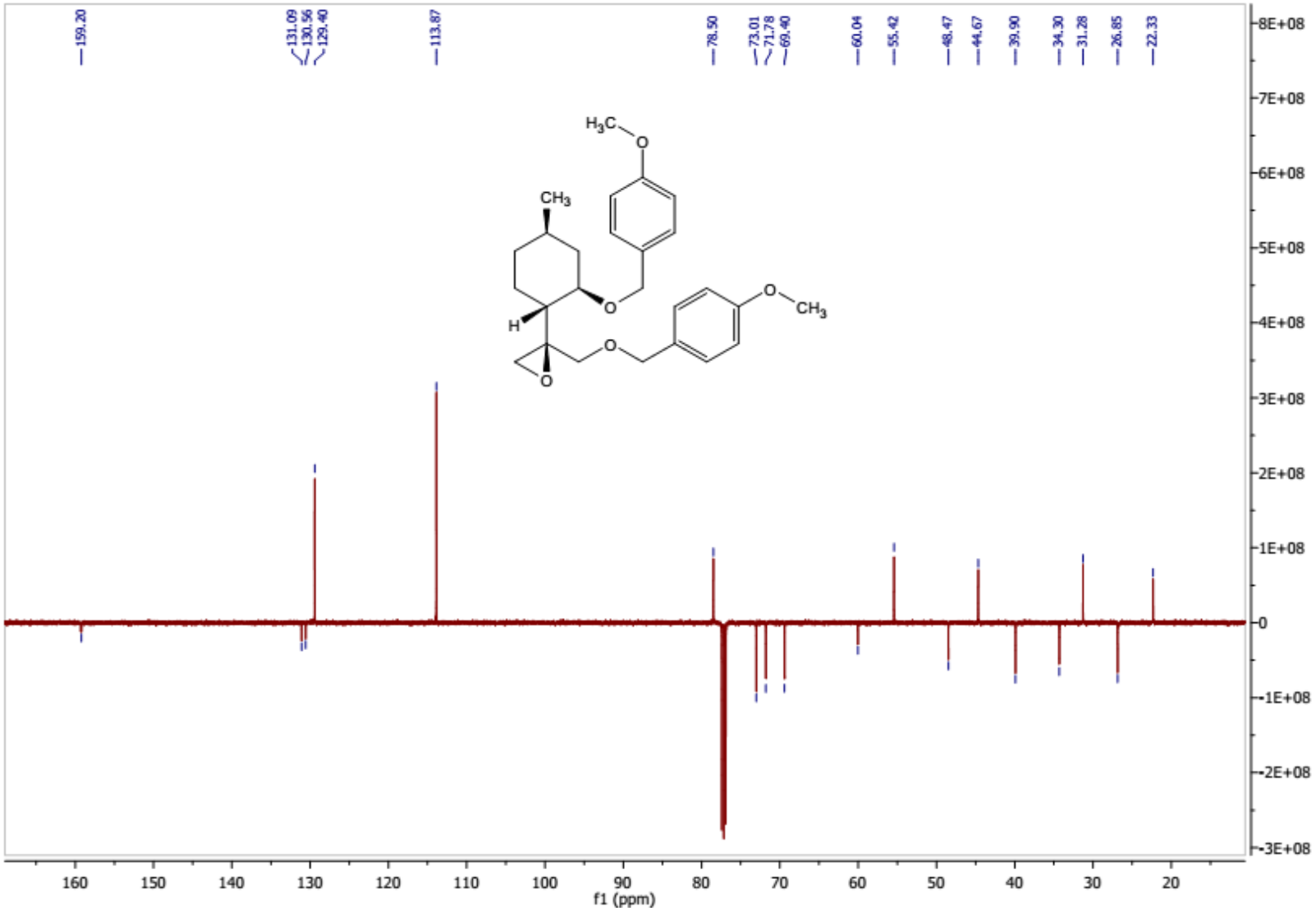
$^{13}$C-NMR of compound **33a**



[1]H-NMR of compound **33b**



$^{13}$C-NMR of compound **33b**



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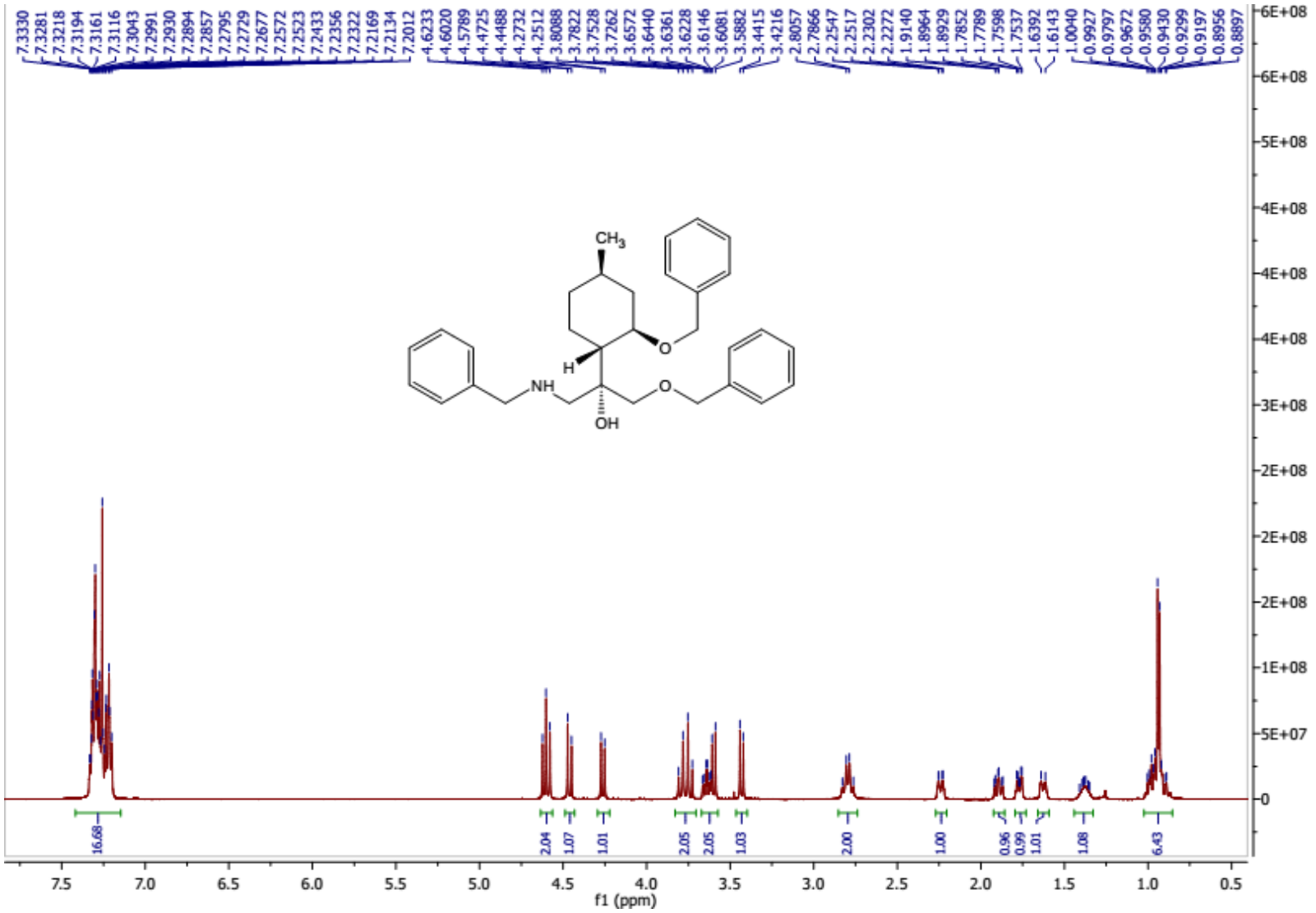
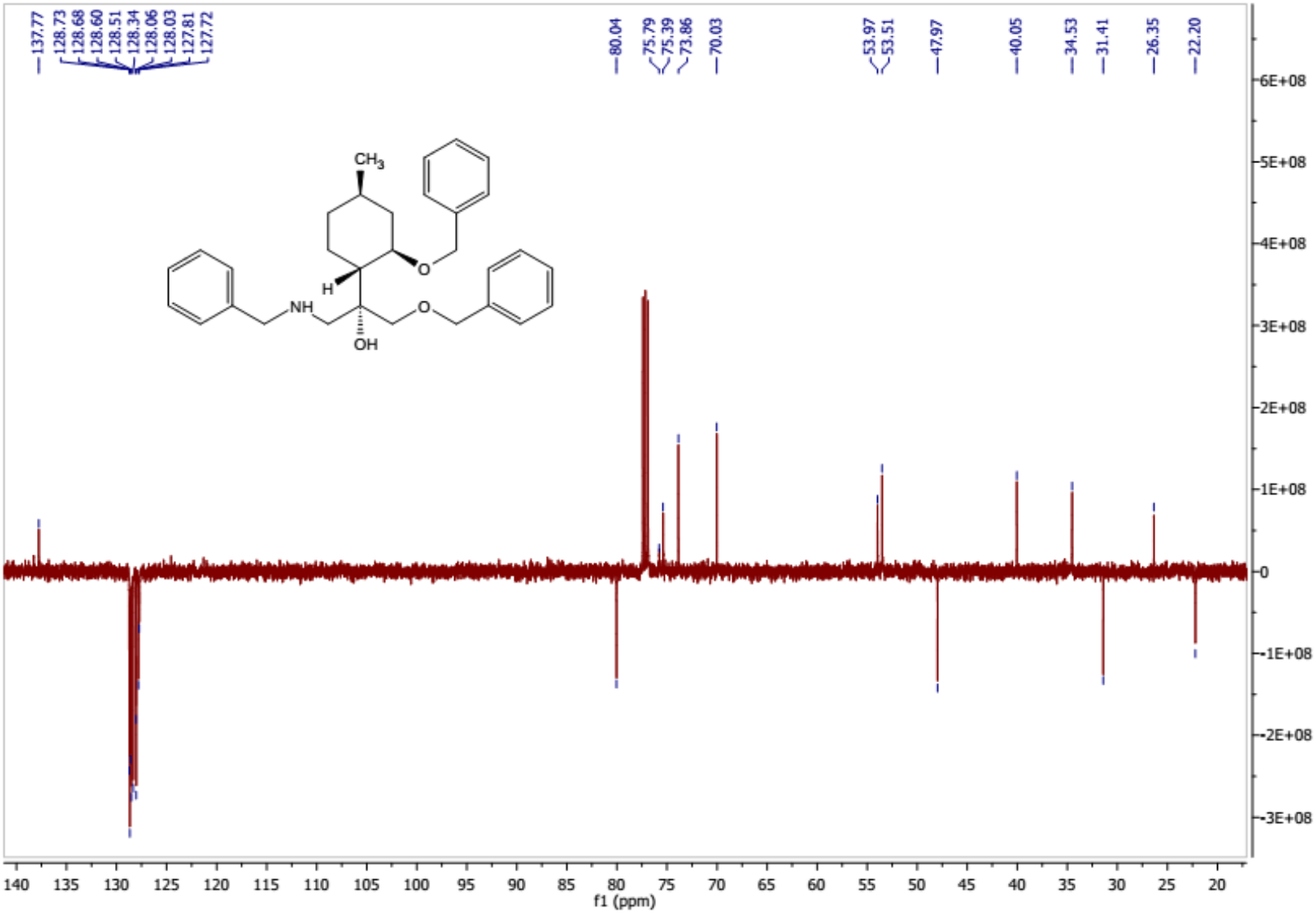


$^{13}$C-NMR of compound **34a**



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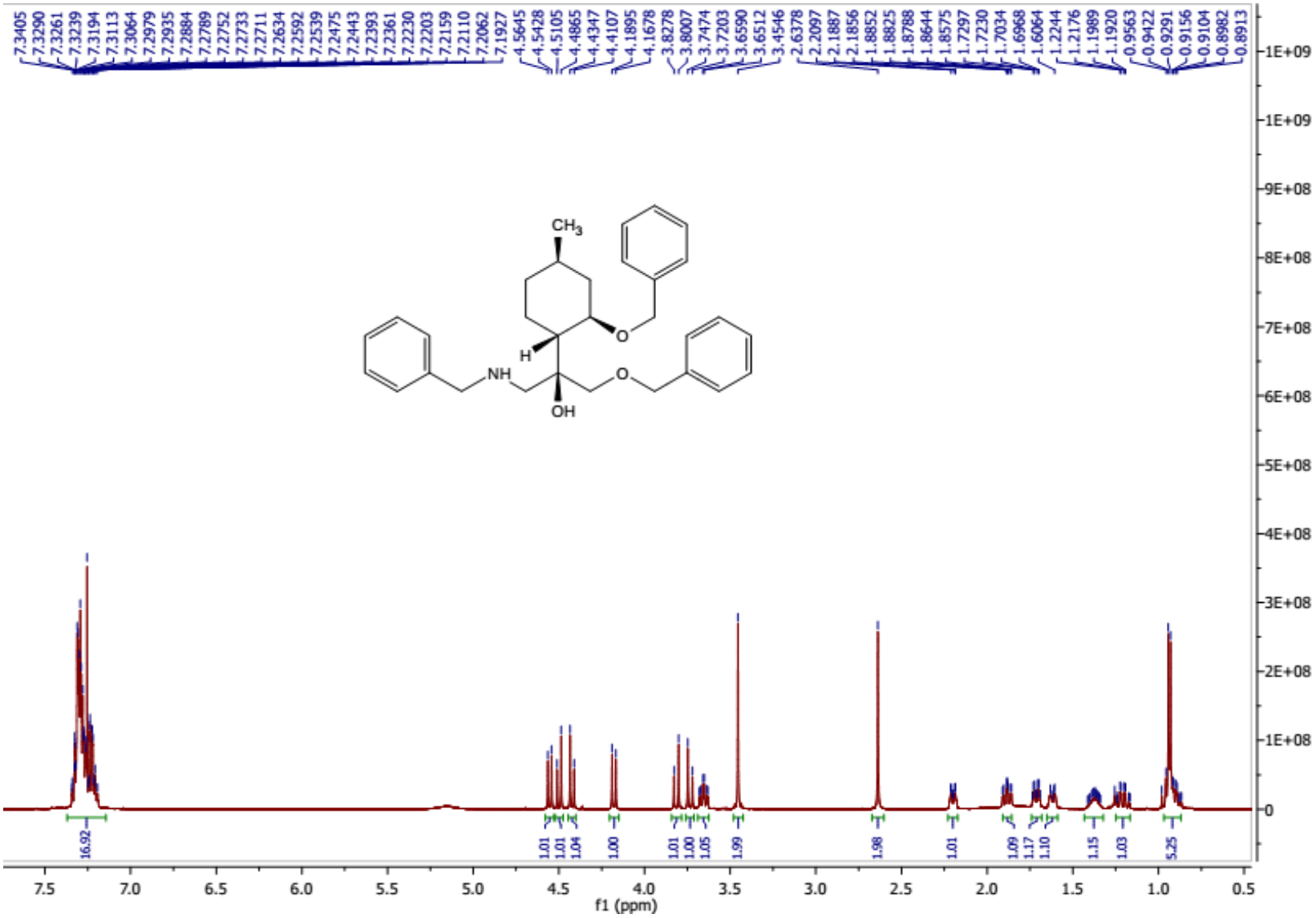
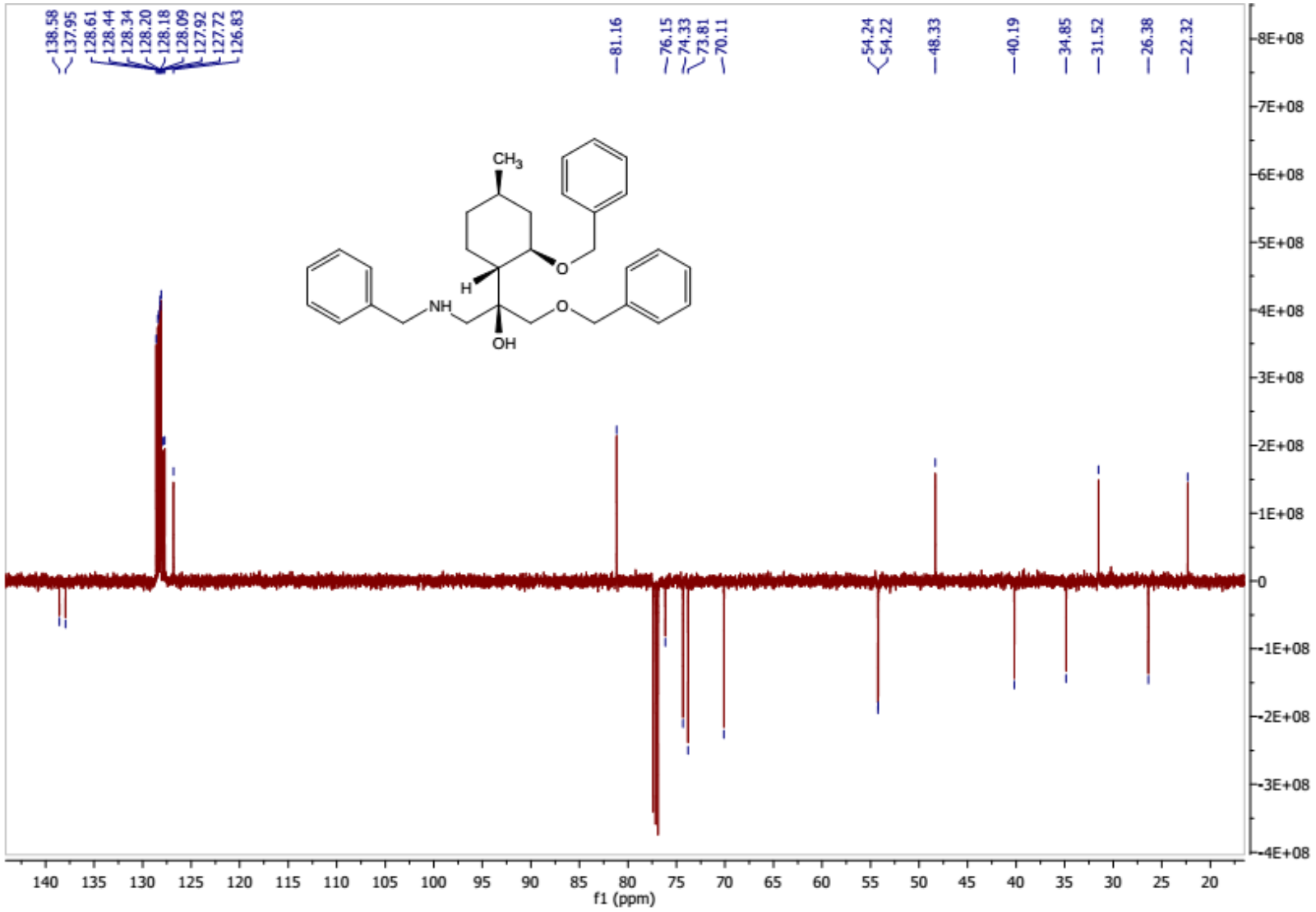


$^{13}$C-NMR of compound **34b**



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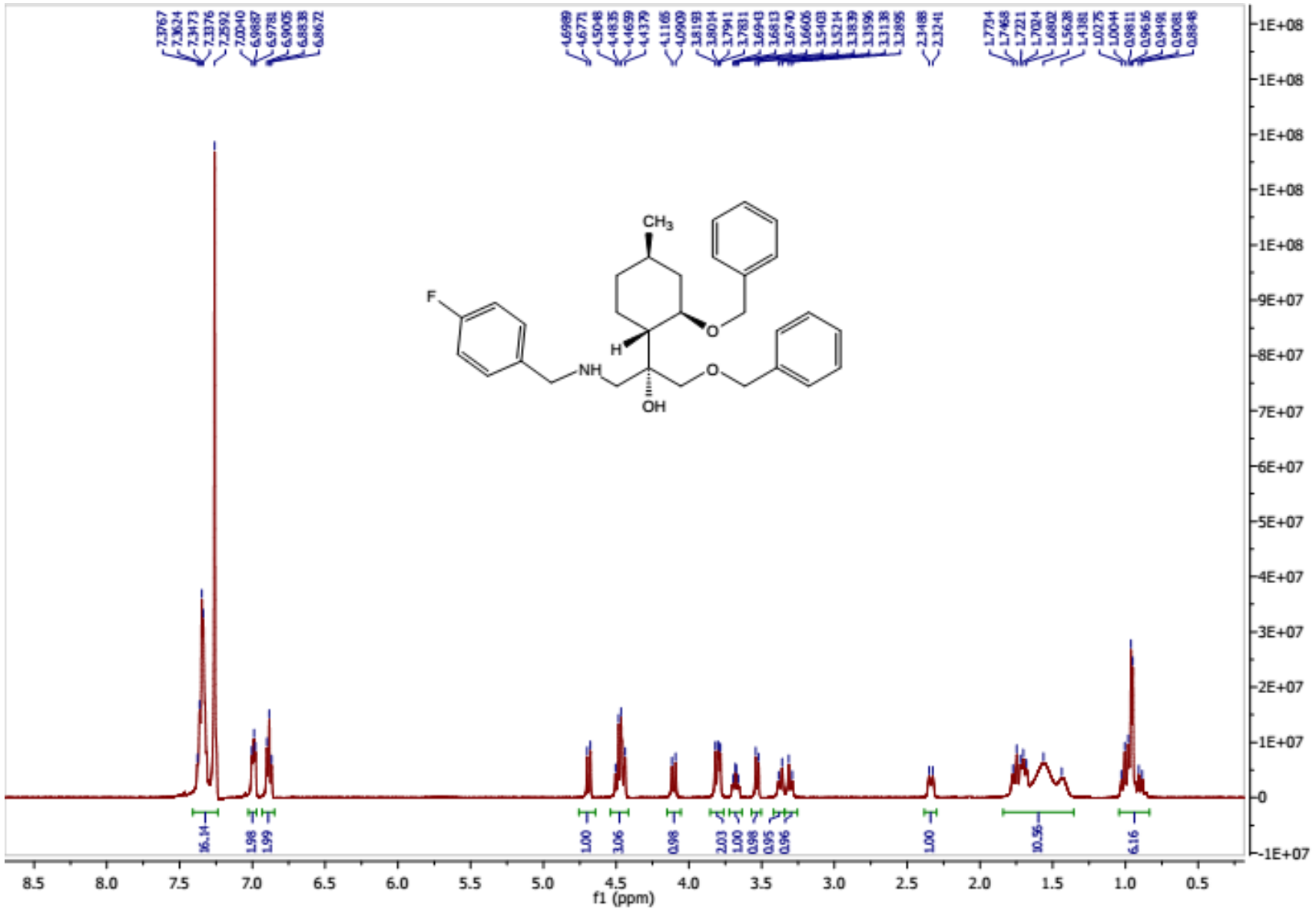
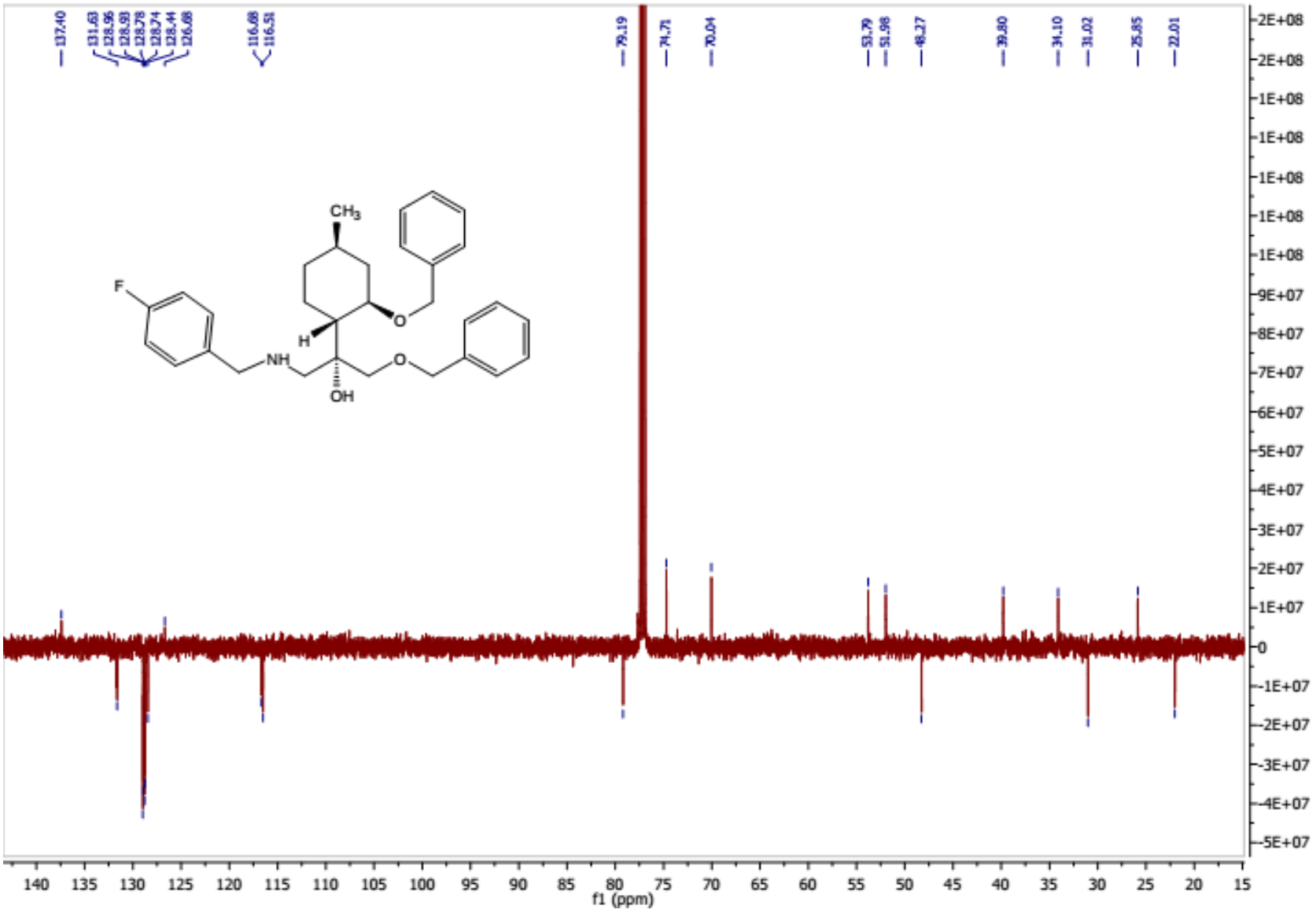


$^{13}$C-NMR of compound **35a**



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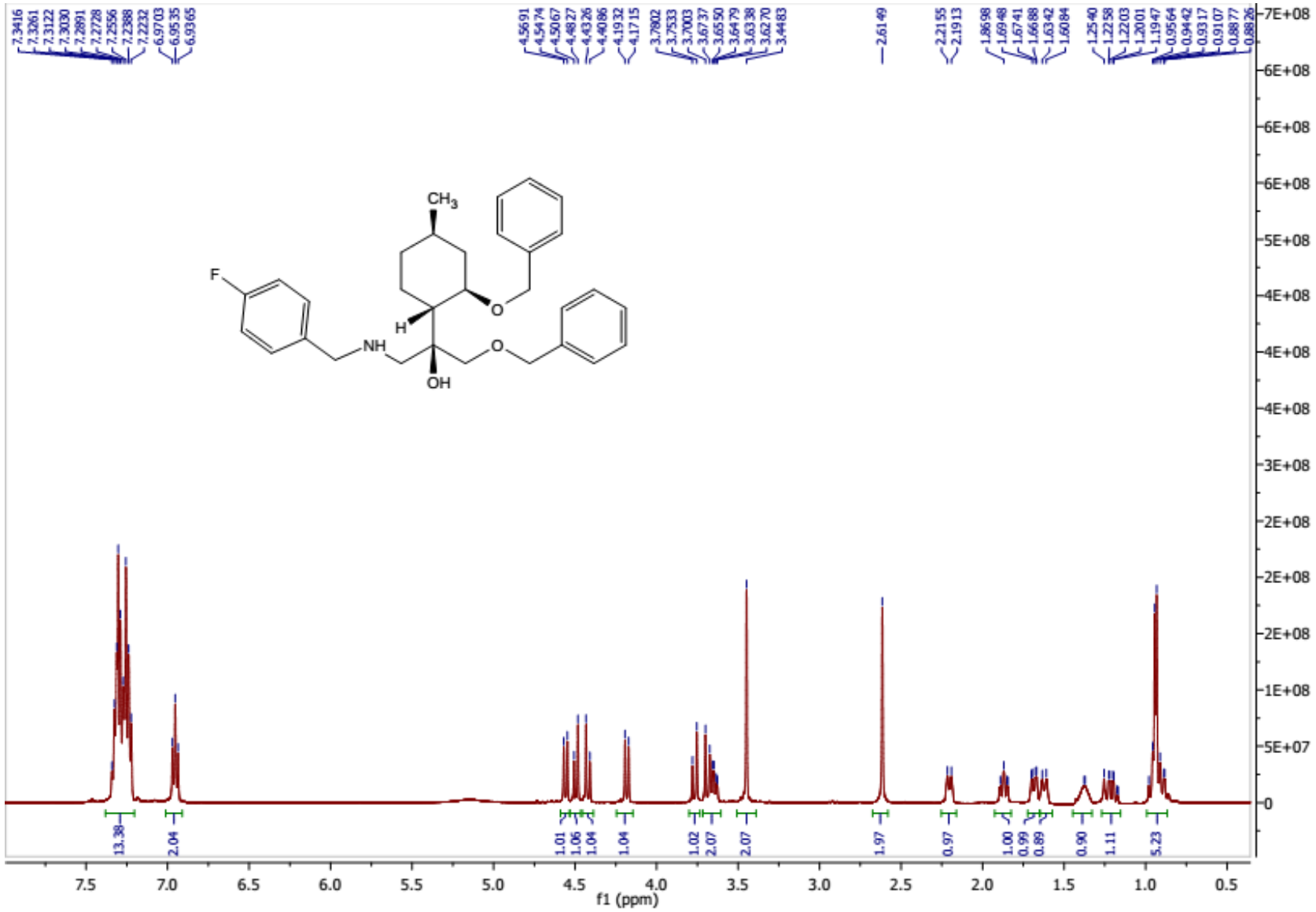
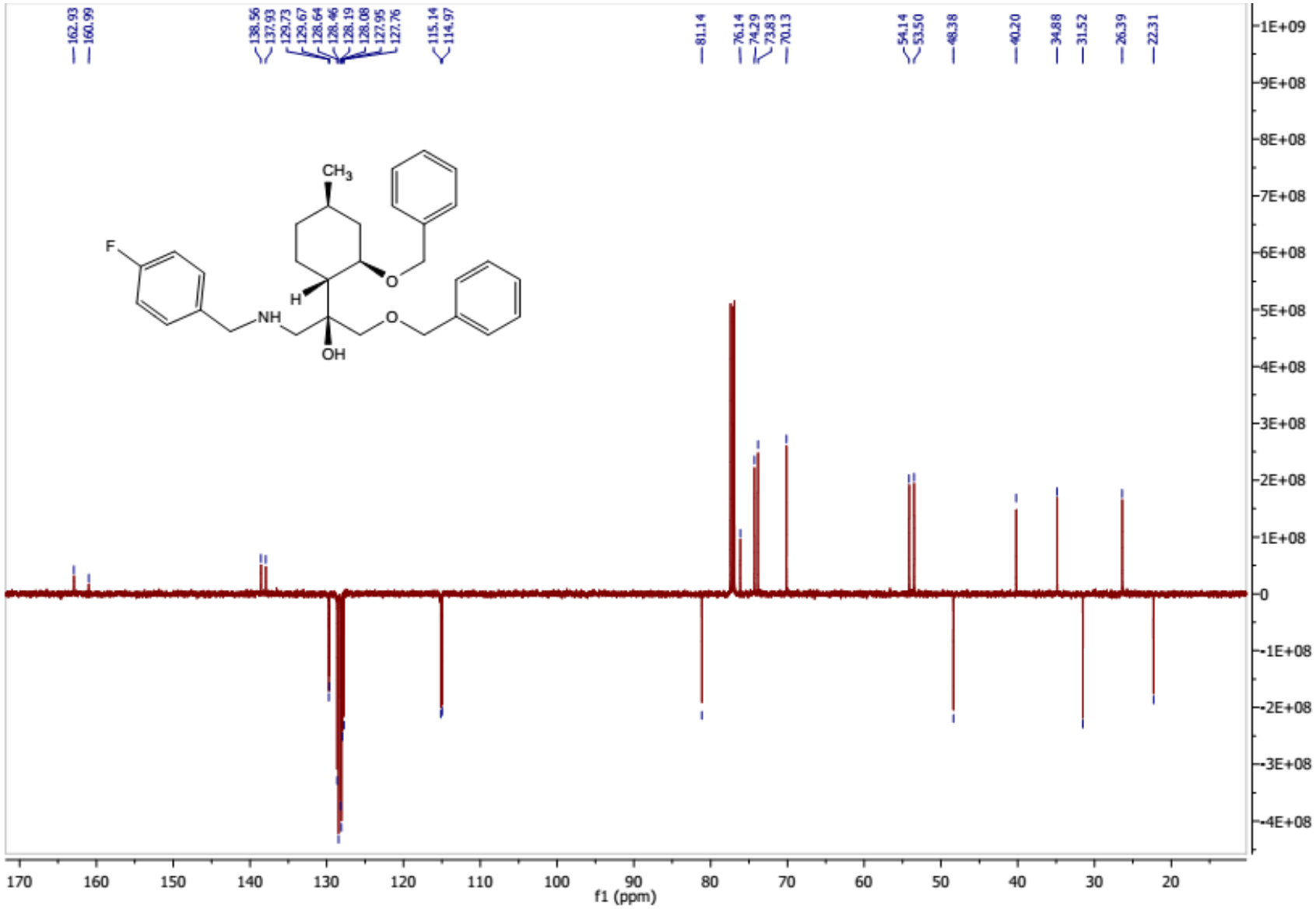
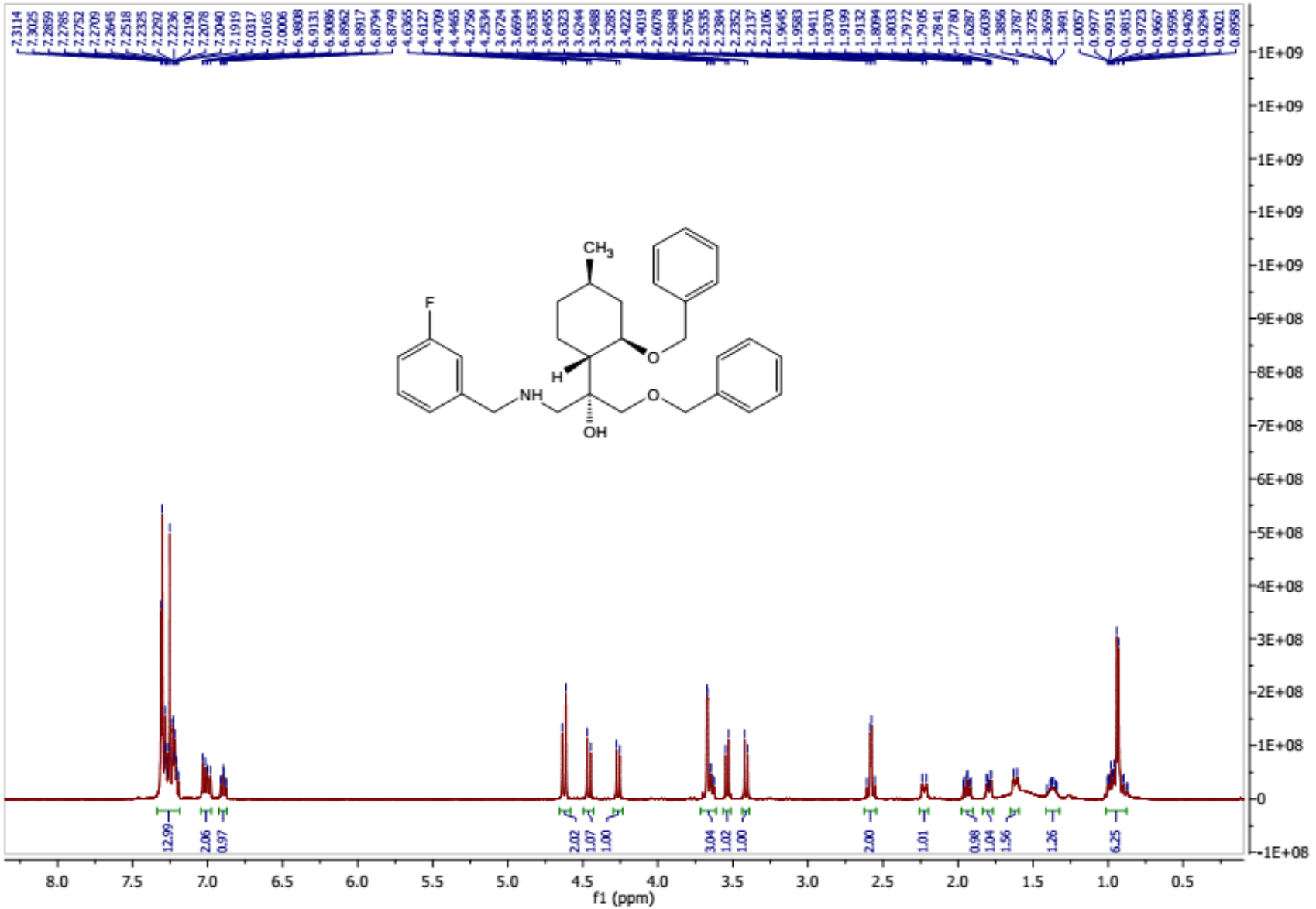


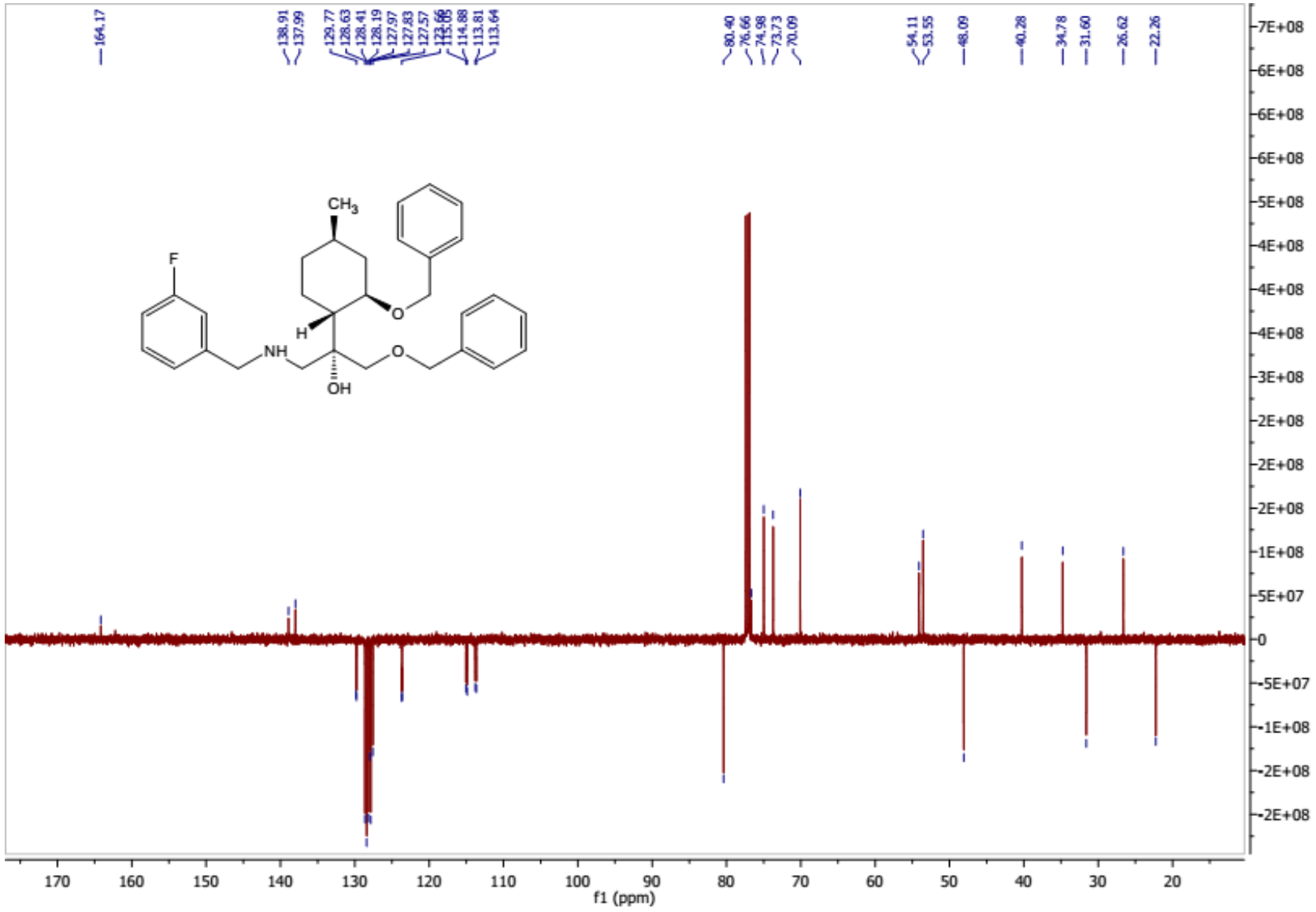
$^{13}$C-NMR of compound **35b**



[1]H-NMR of compound **36a**



$^{13}$C-NMR of compound **36a**



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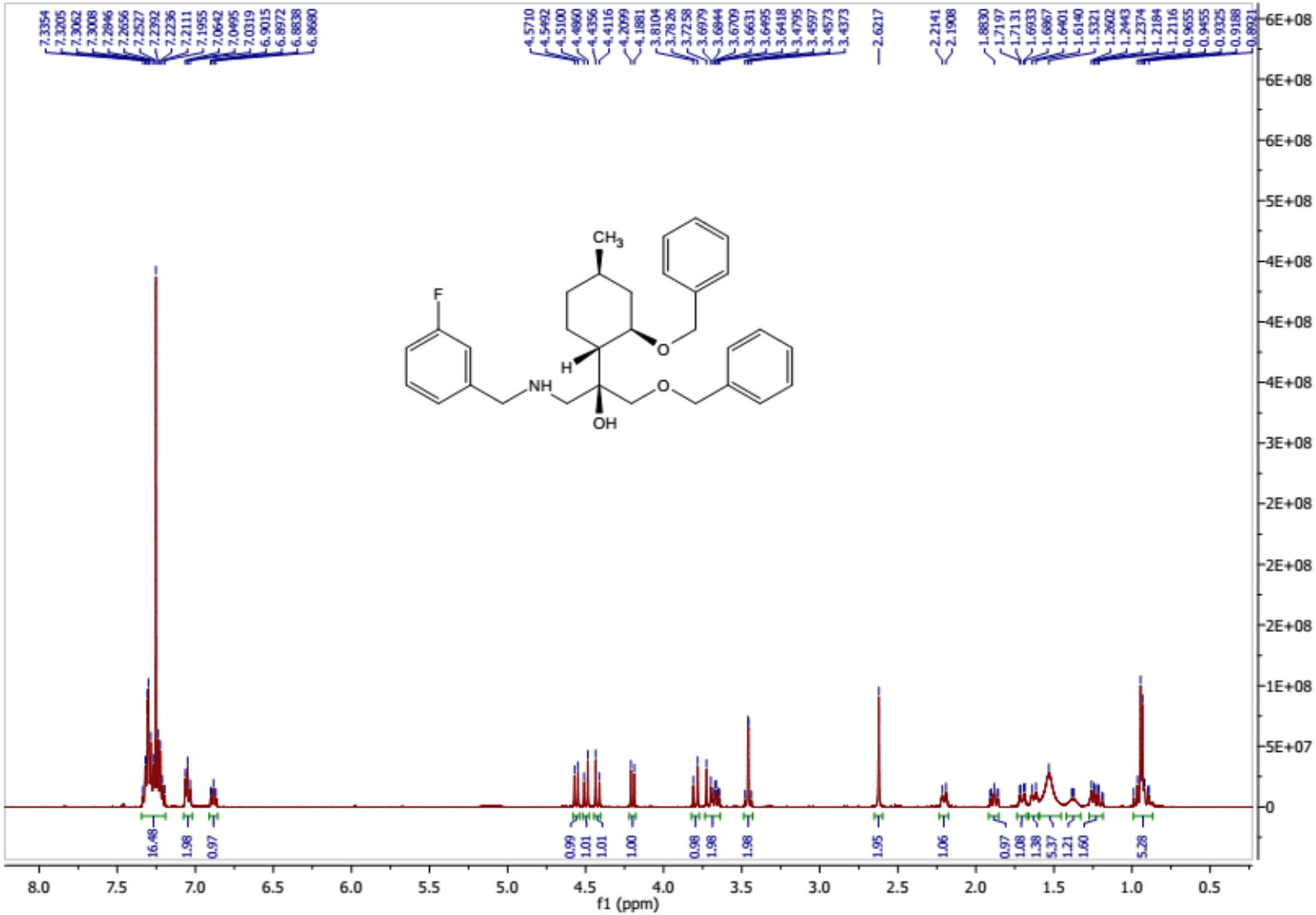
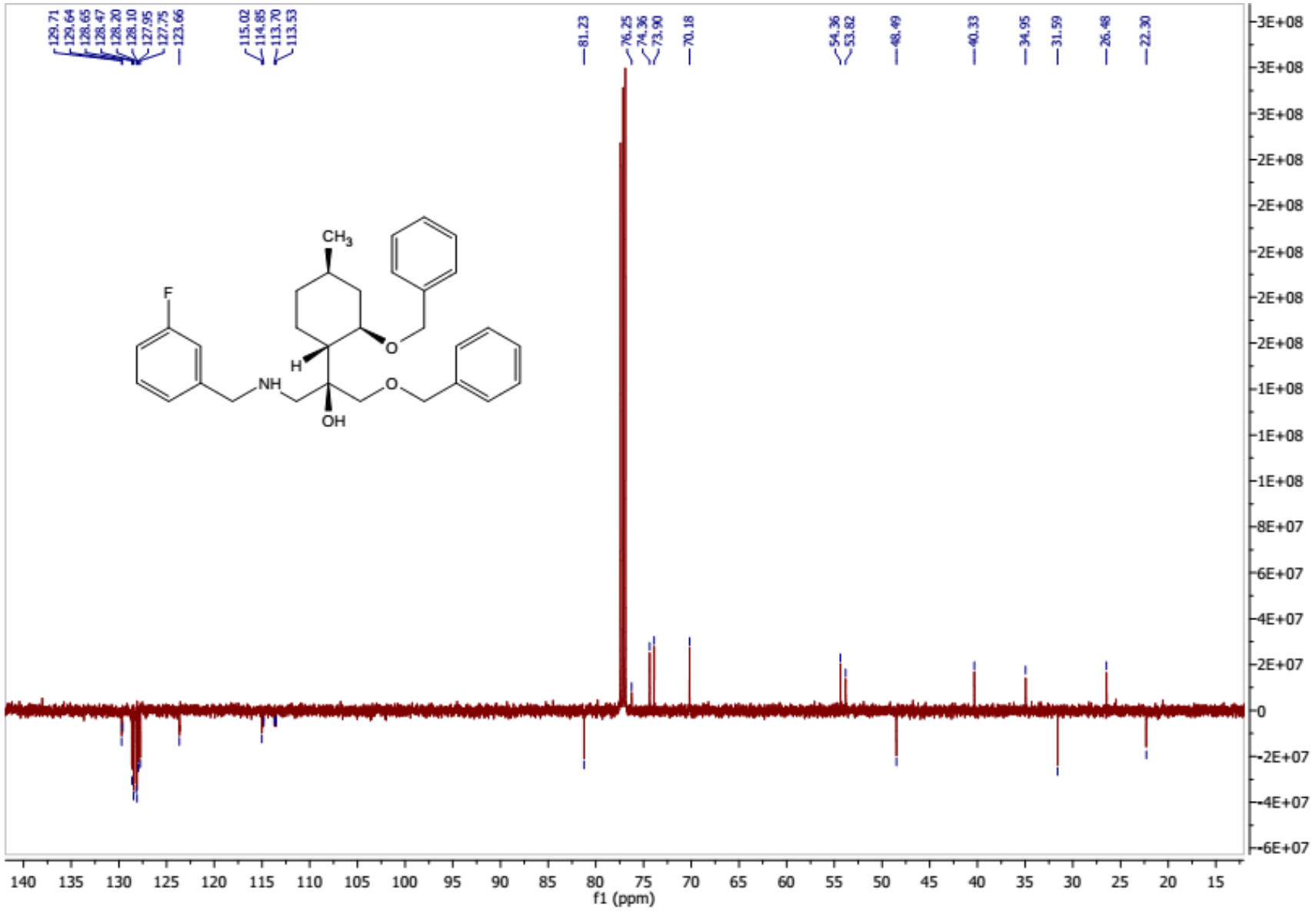


$^{13}$C-NMR of compound **36b**



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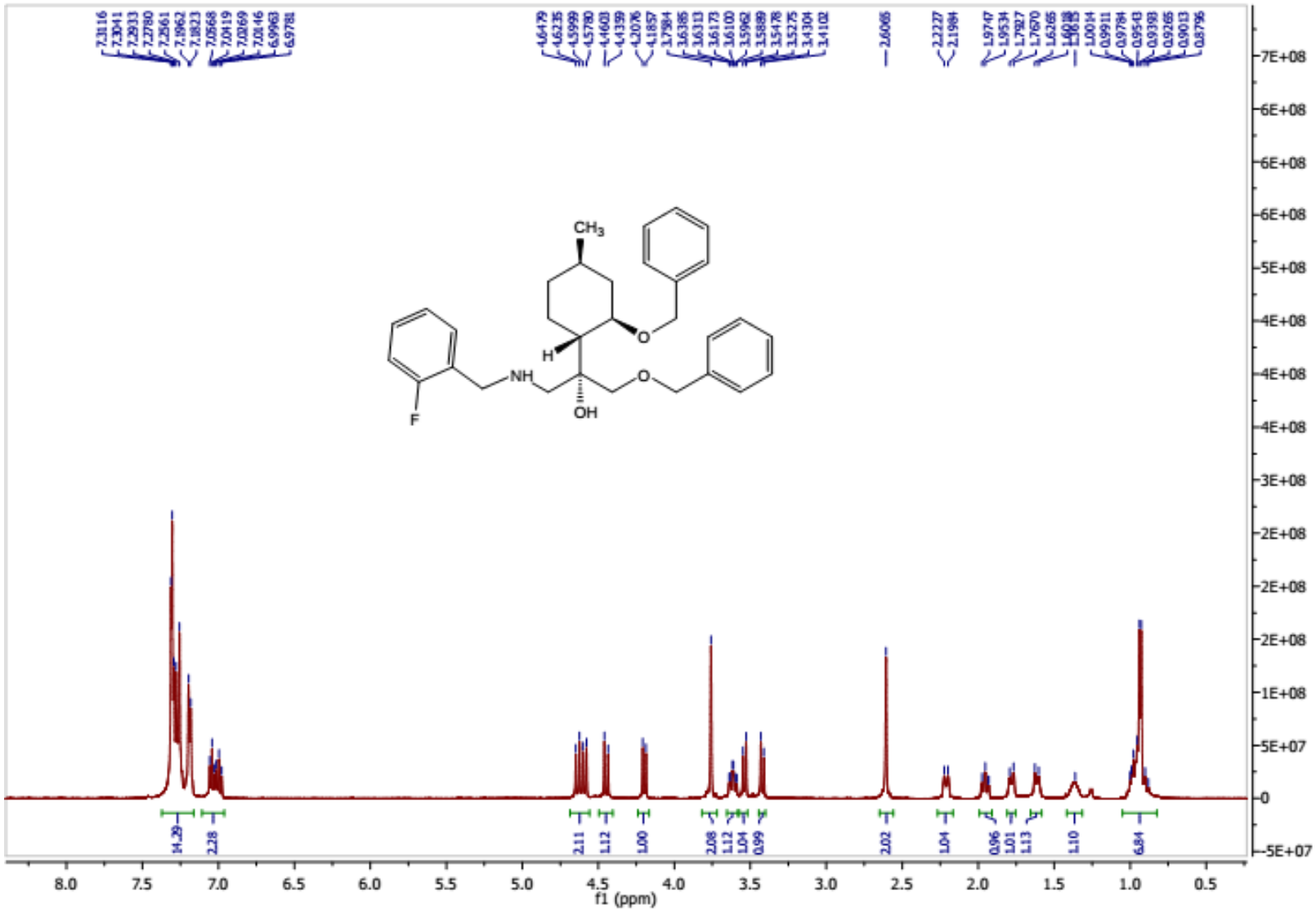
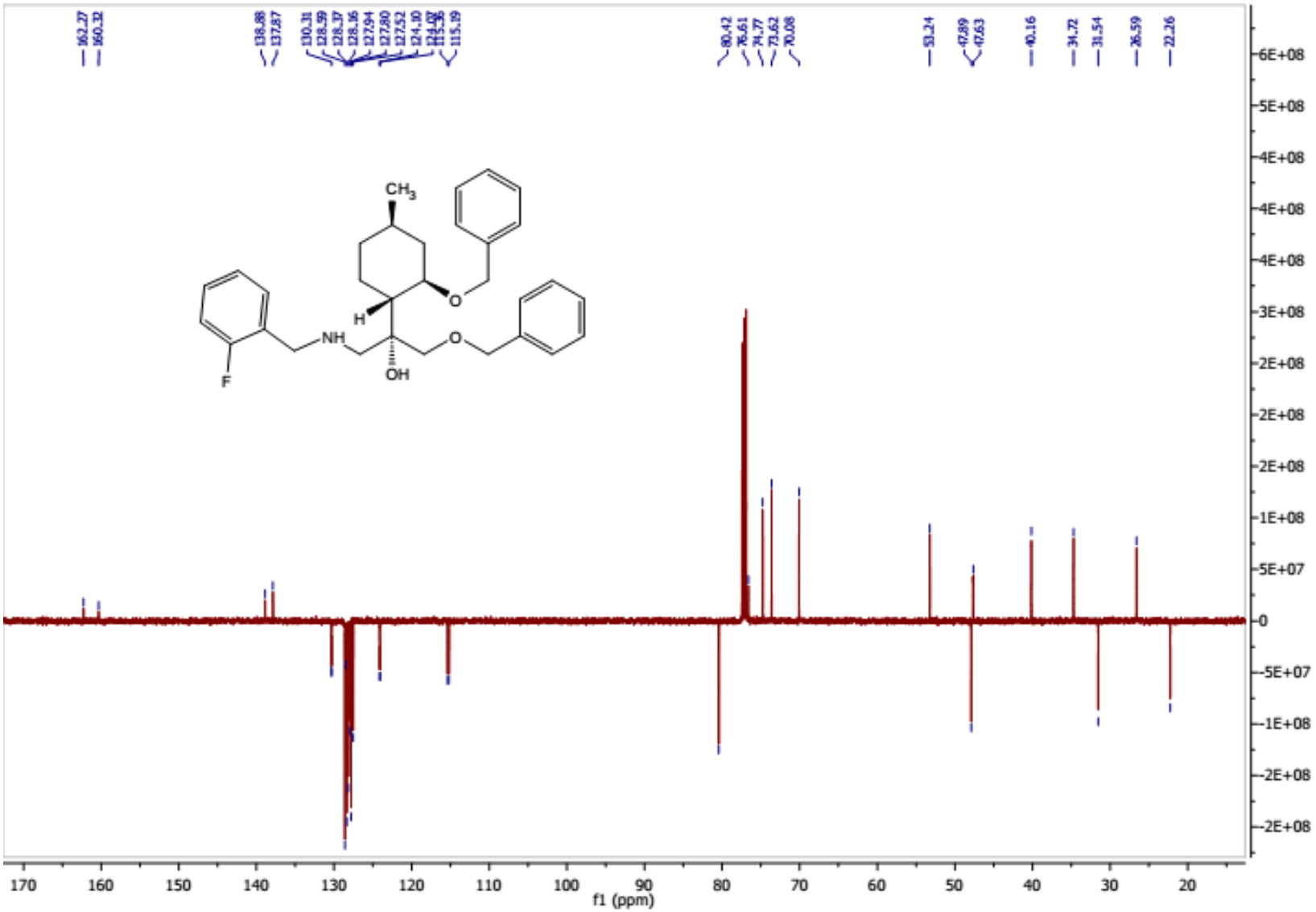


$^{13}$C-NMR of compound **37a**



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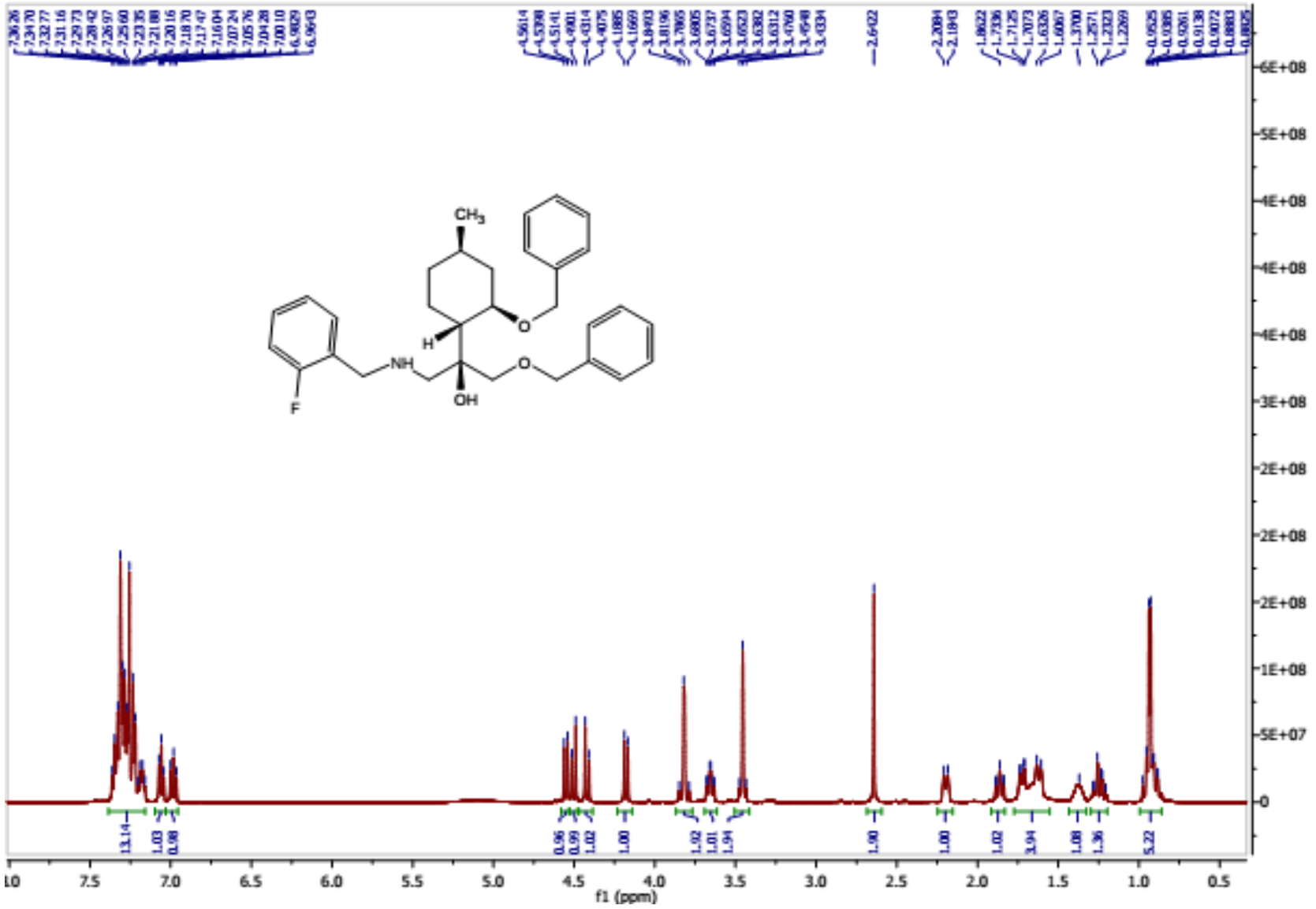

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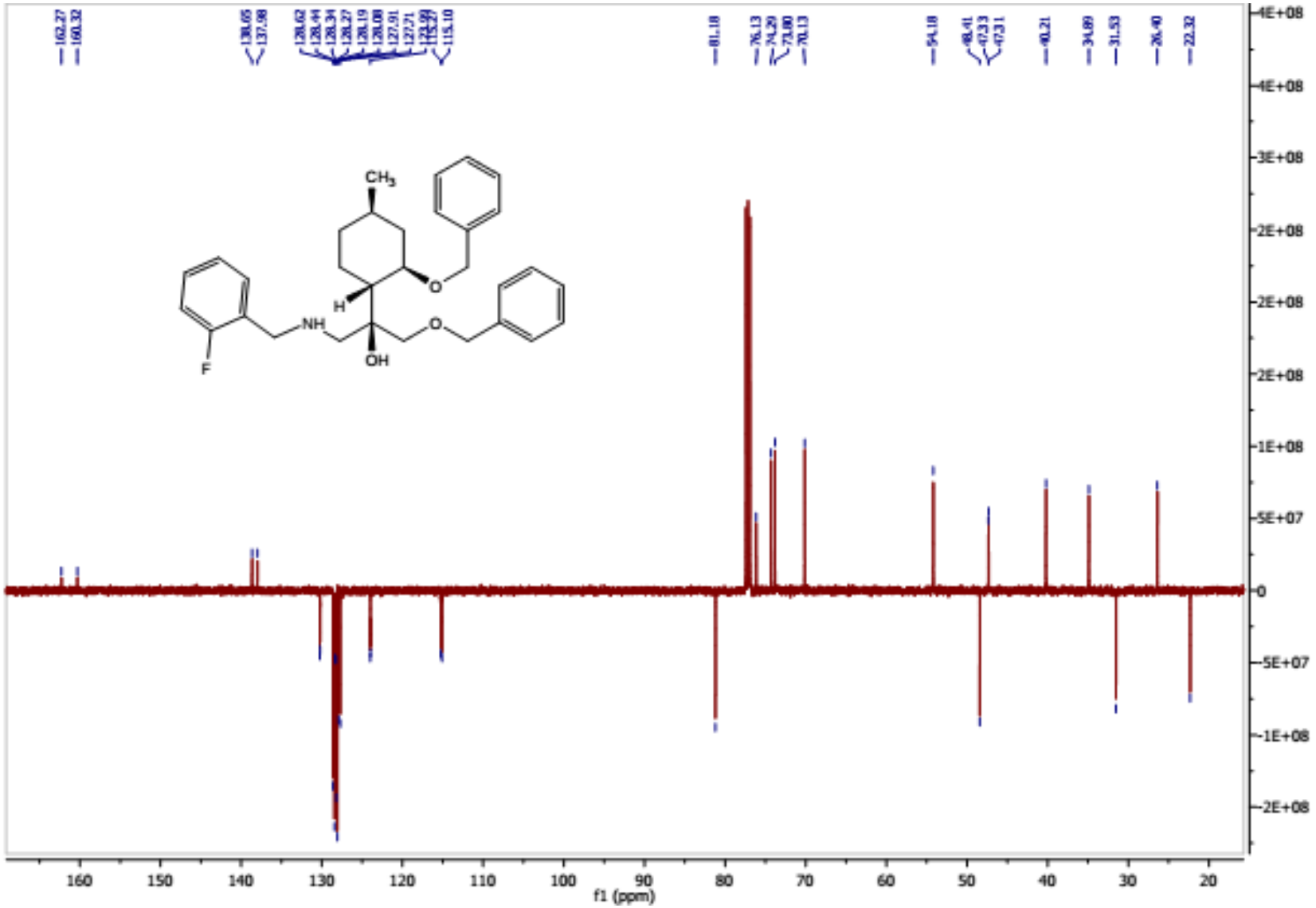
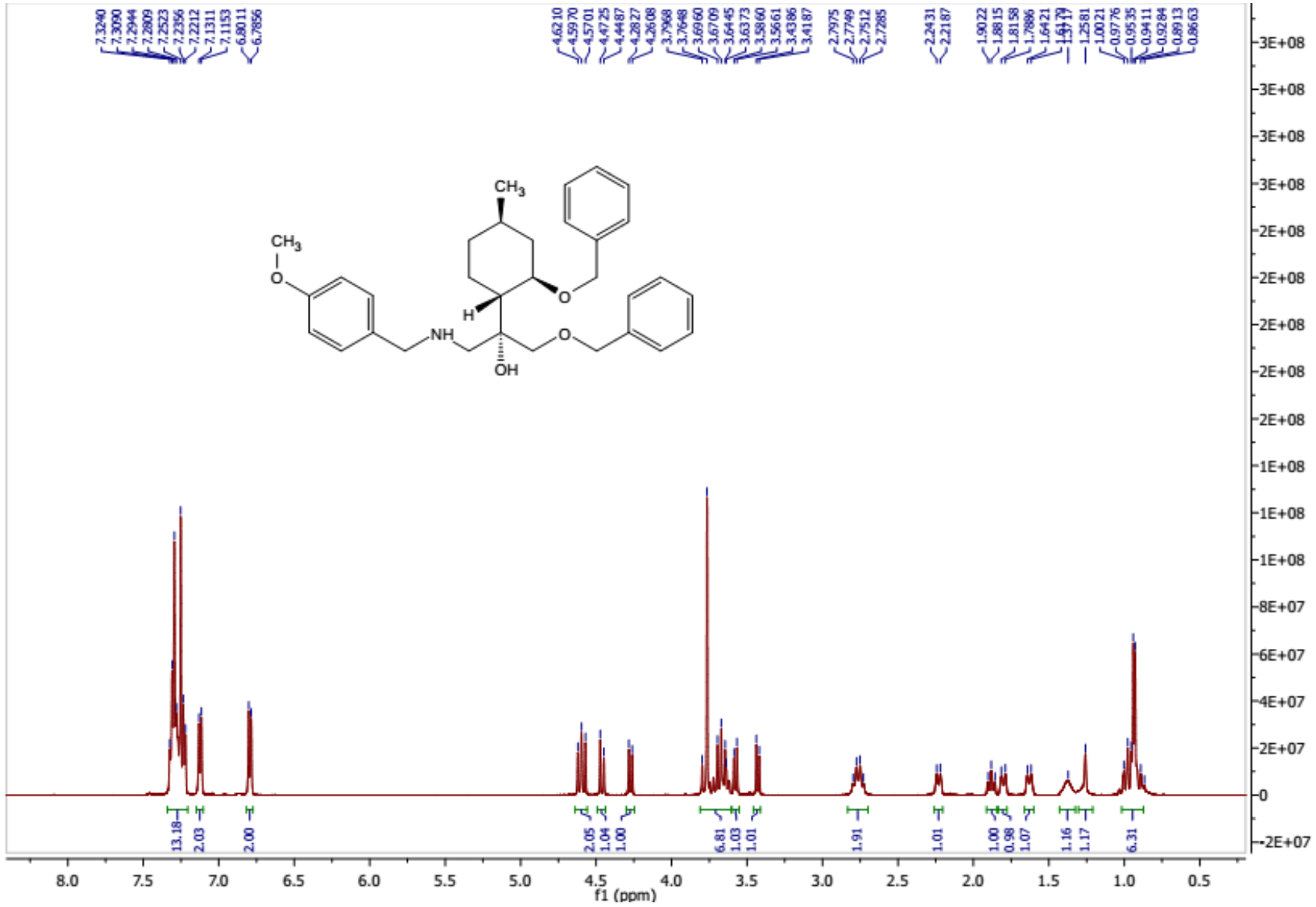
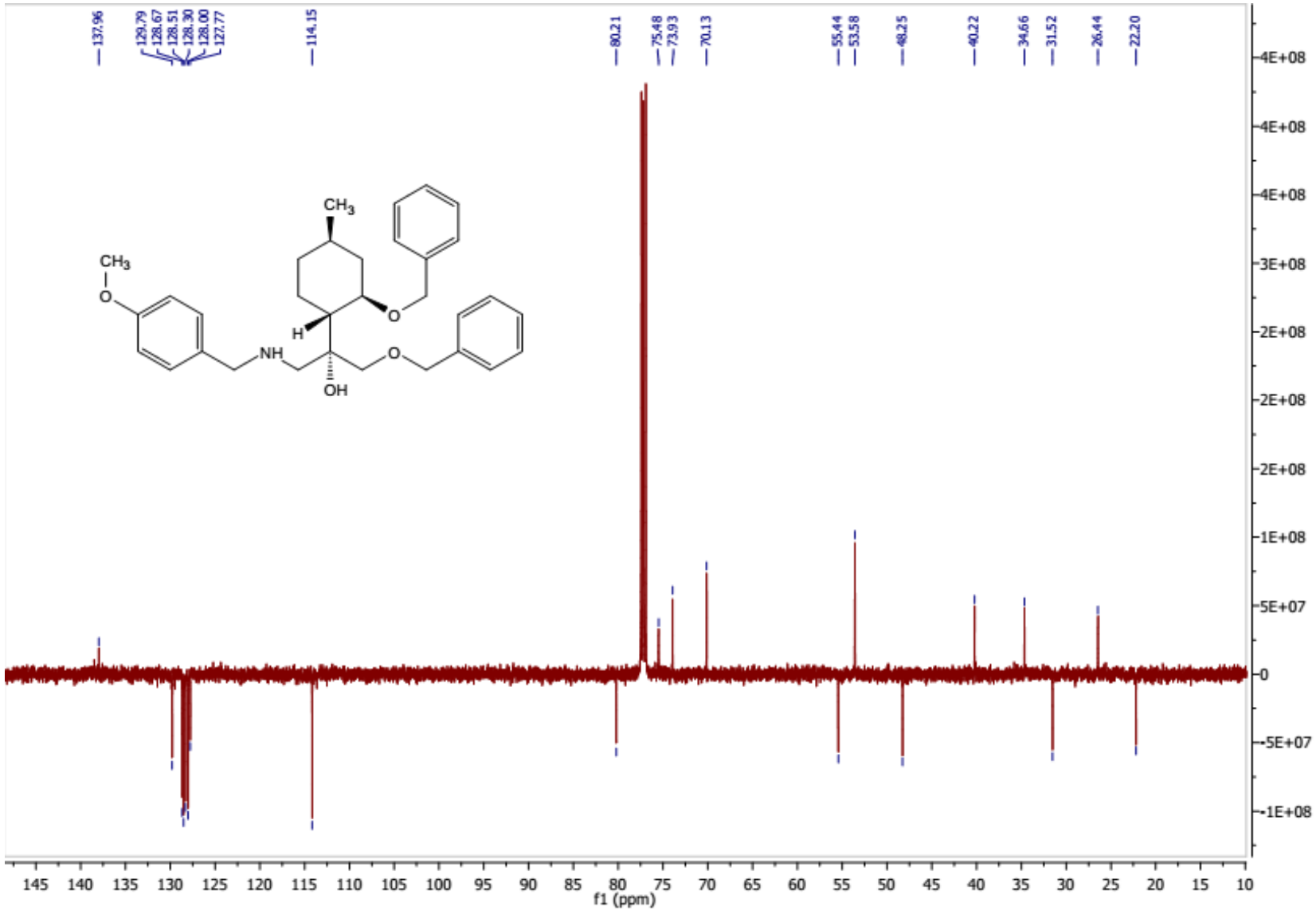


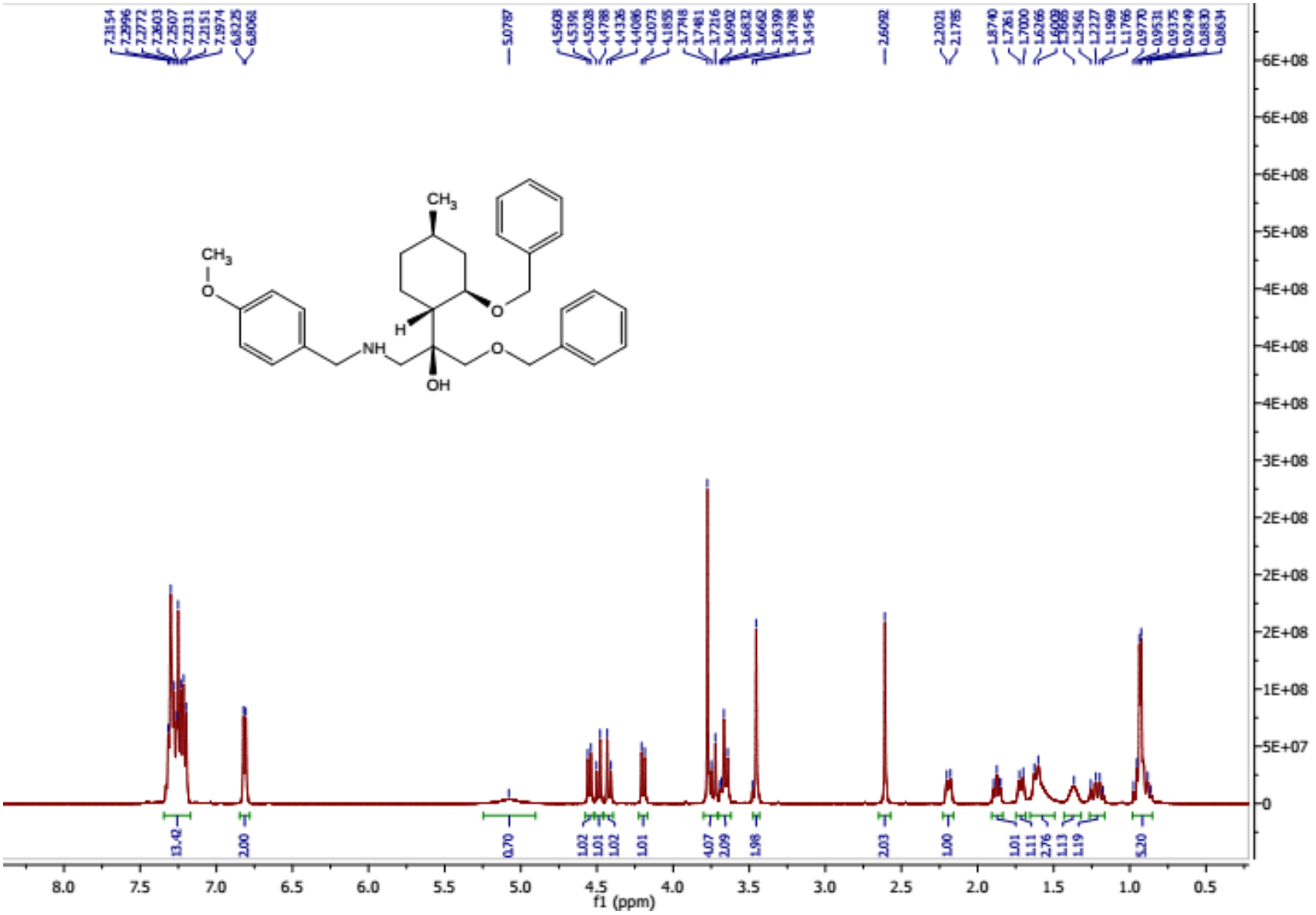
[1]H-NMR of compound **38a**



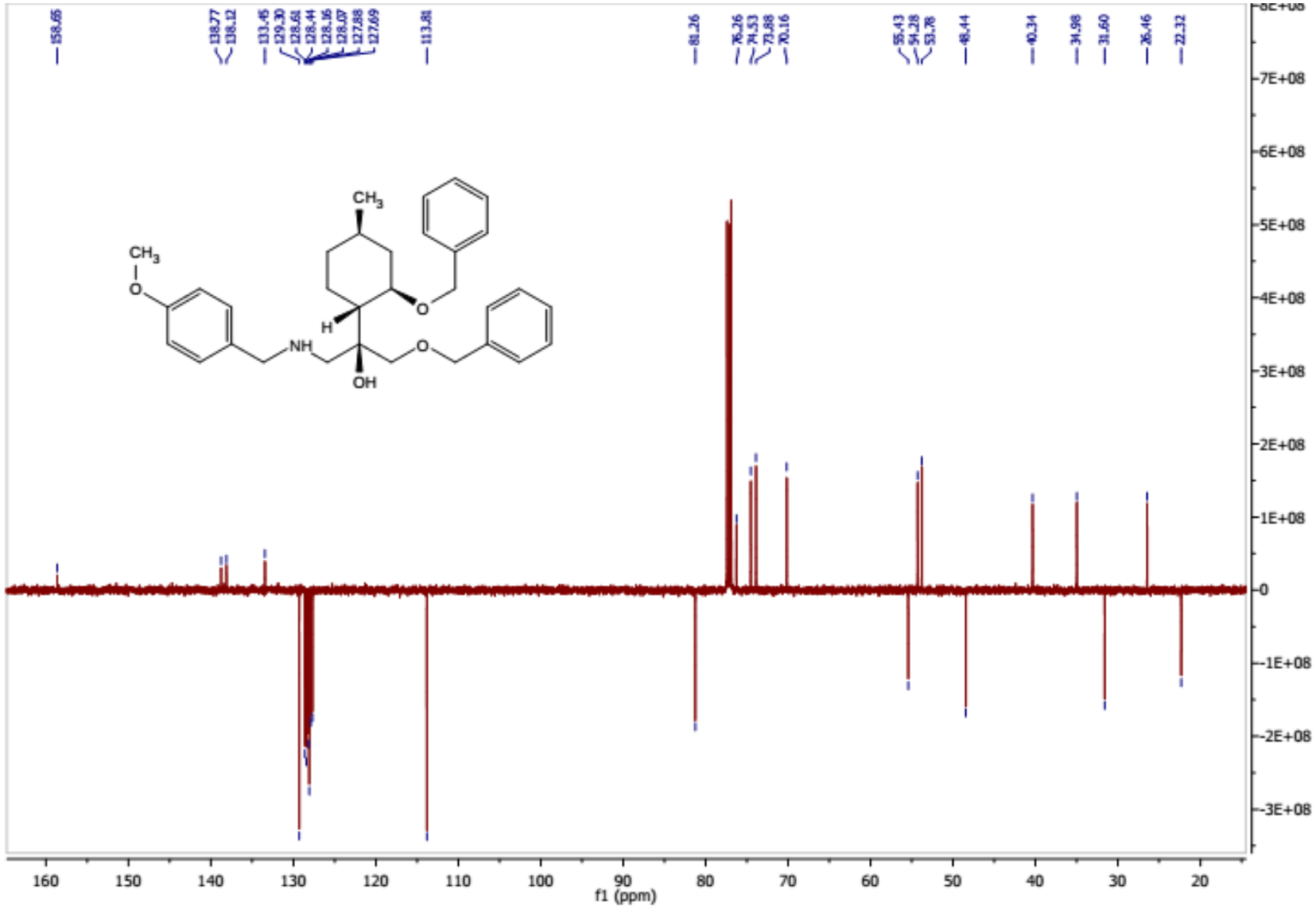
$^{13}$C-NMR of compound **38a**



[1]H-NMR of compound **38b**



$^{13}$C-NMR of compound **38b**



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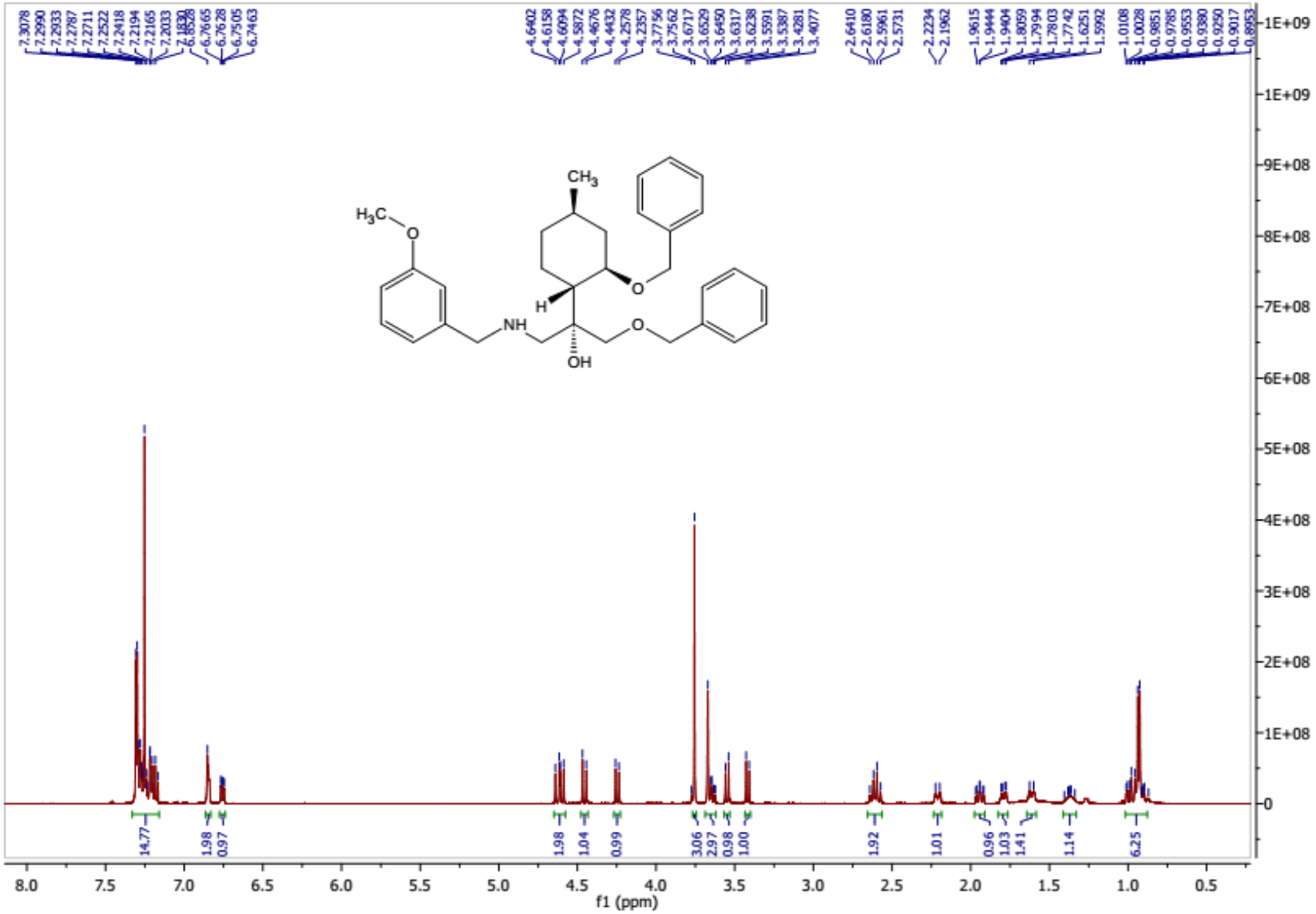

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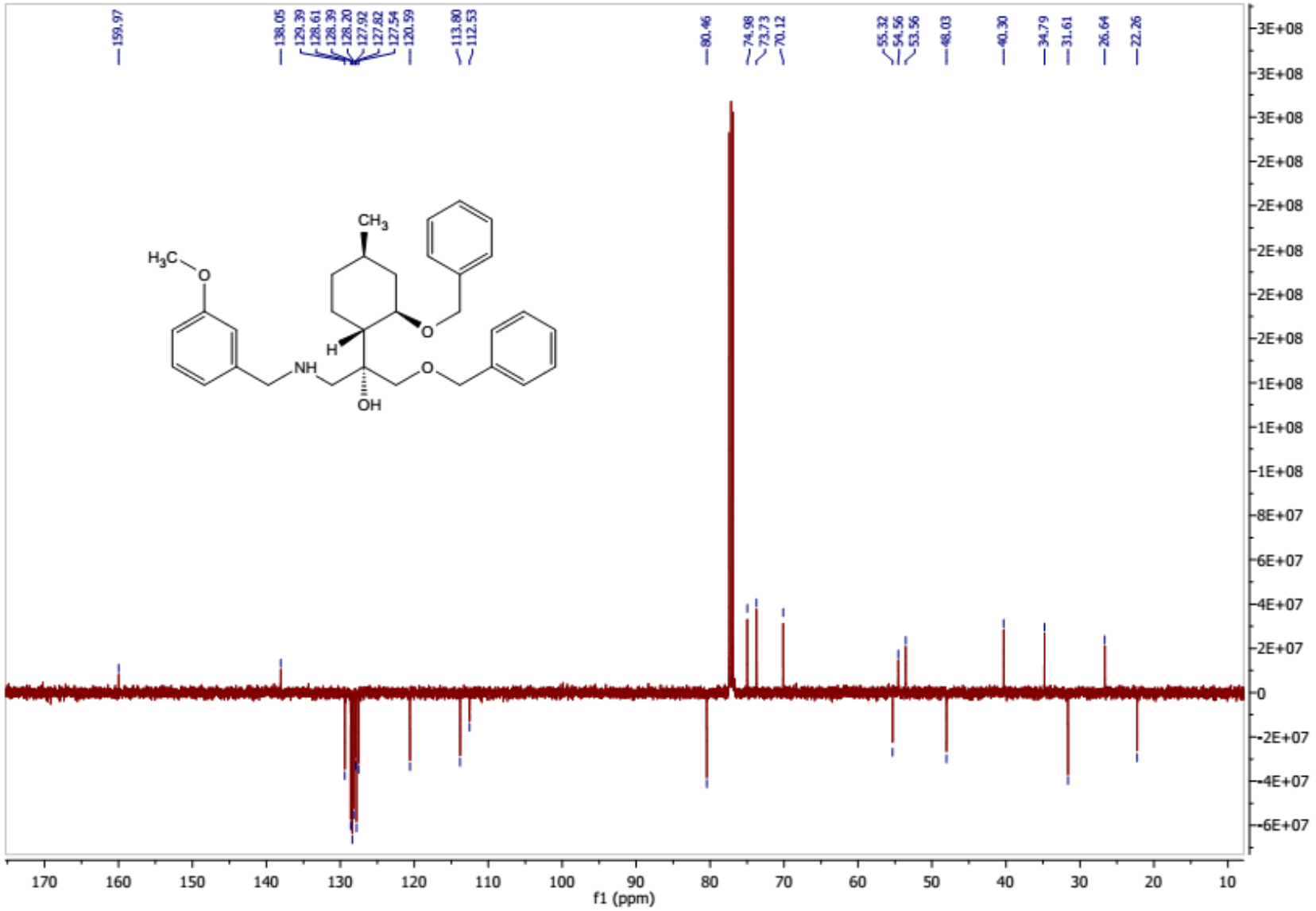

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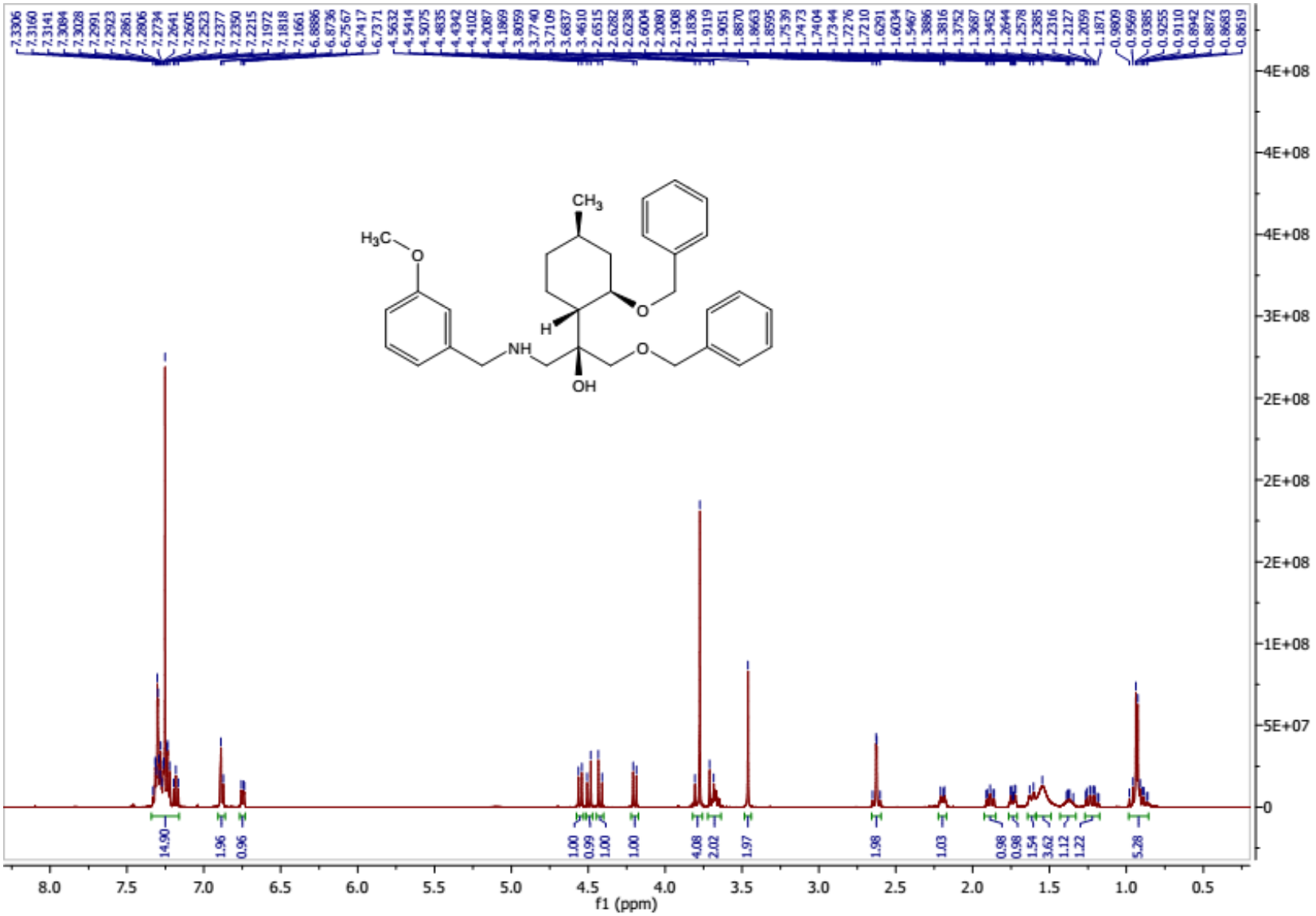

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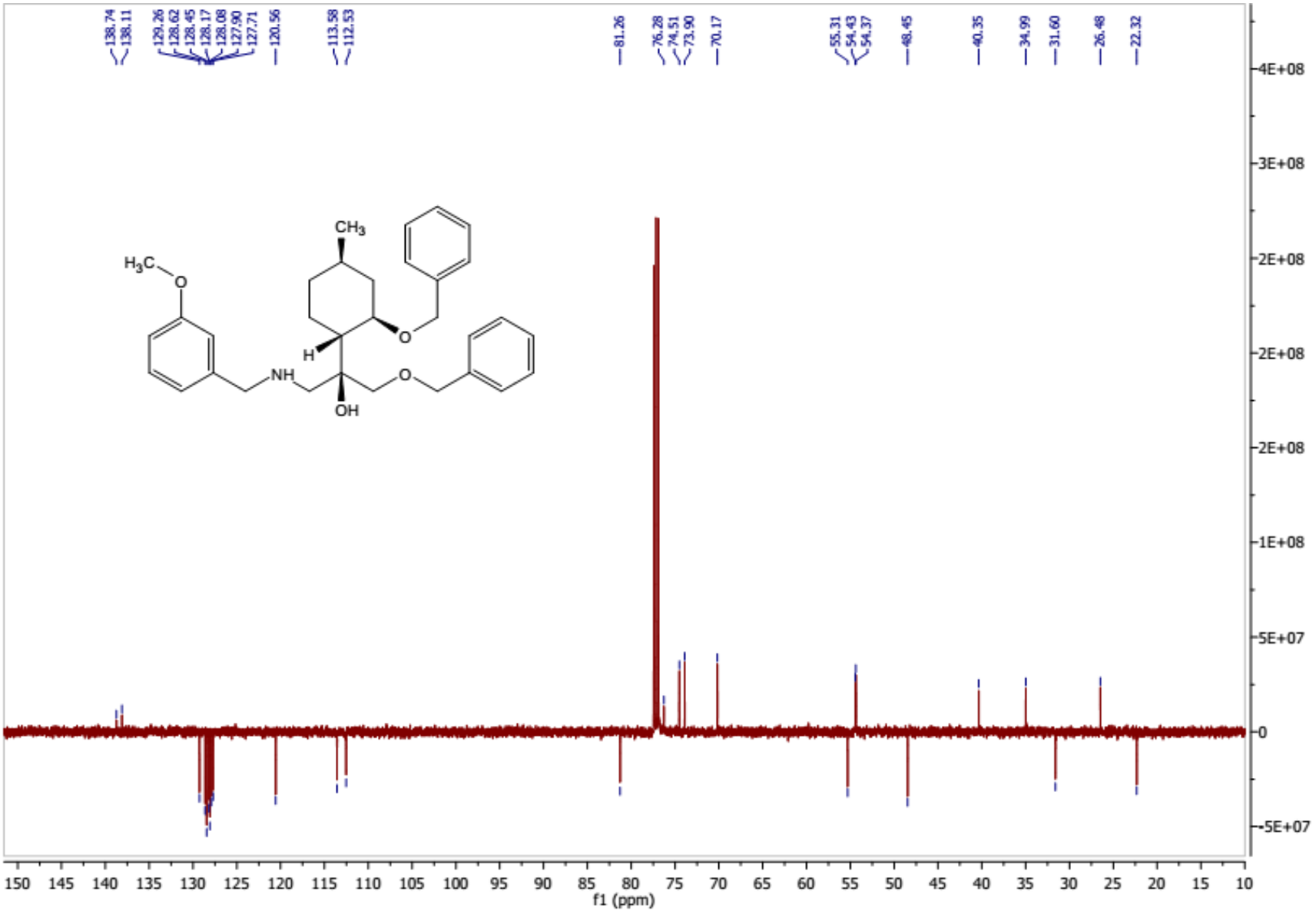
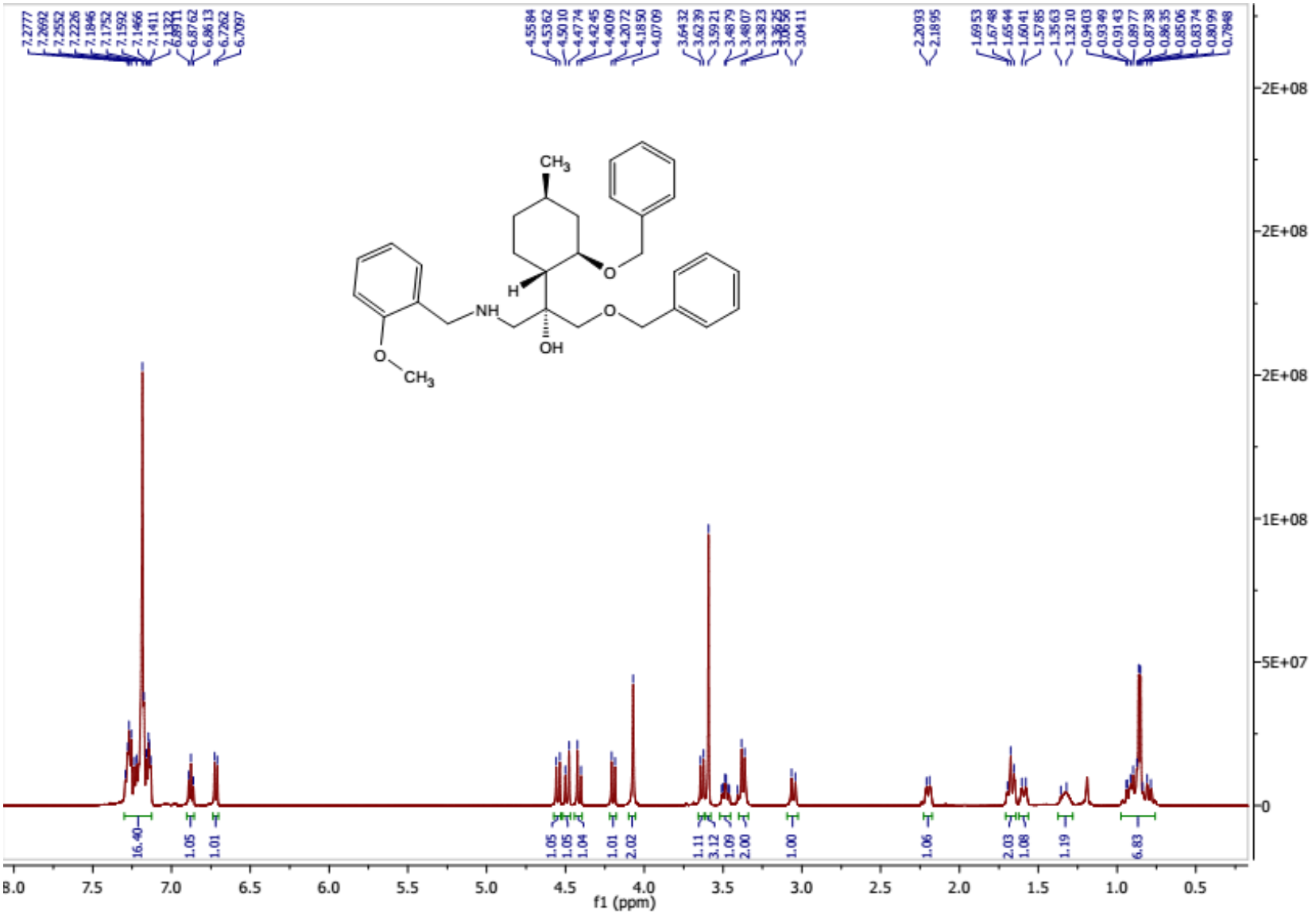
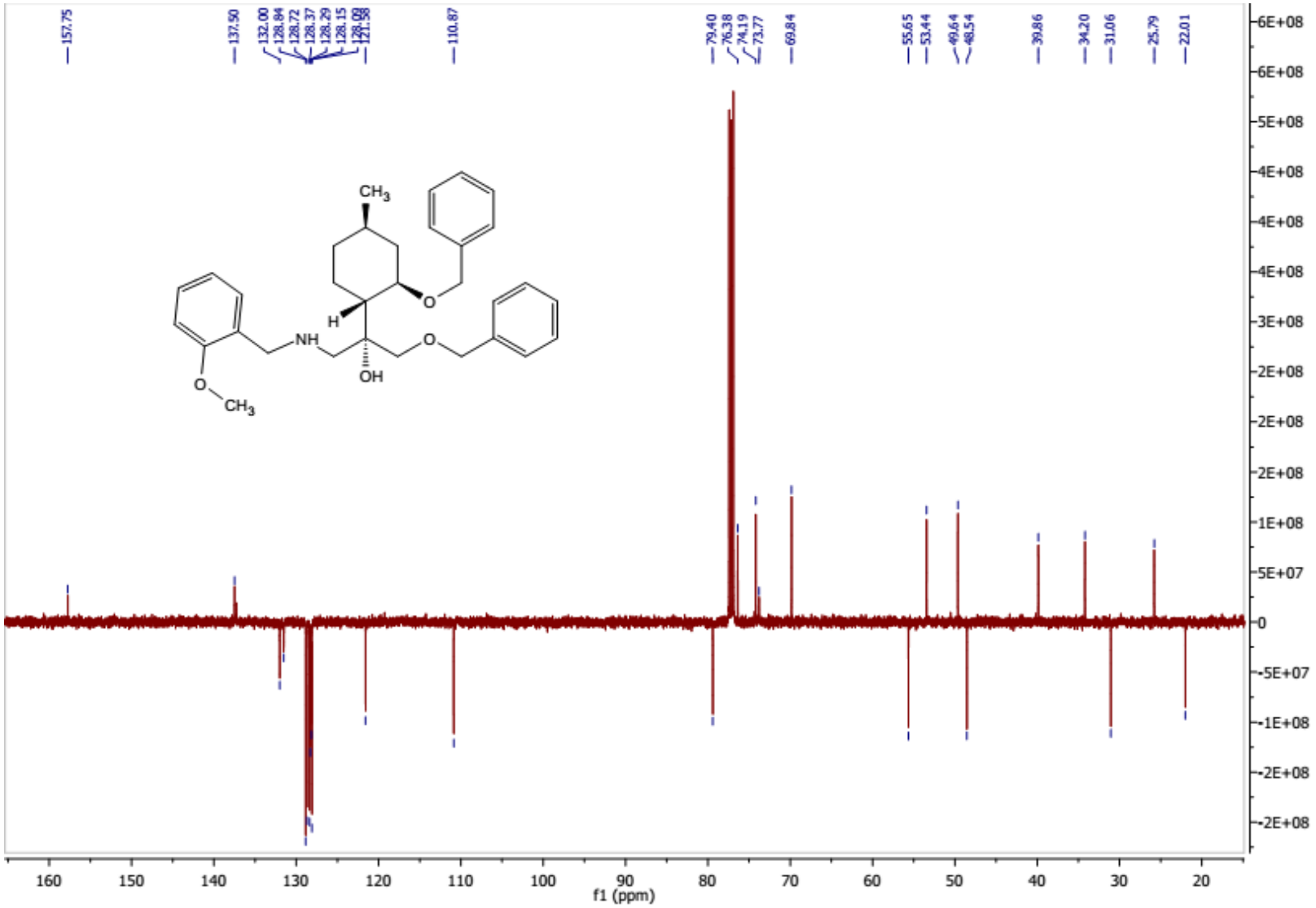


$^{1}$H-NMR of compound **40a**



$^{13}$C-NMR of compound **40a**



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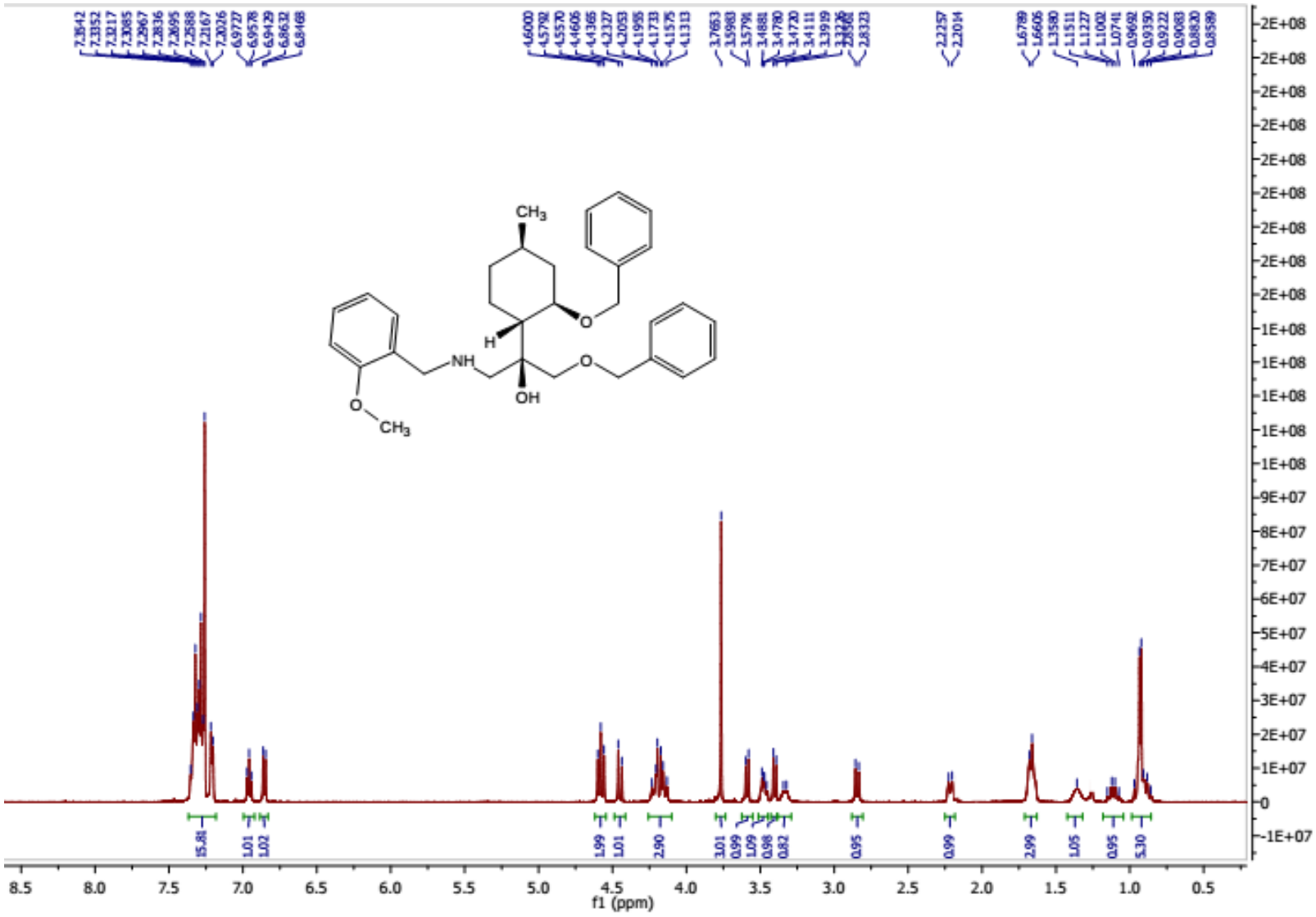
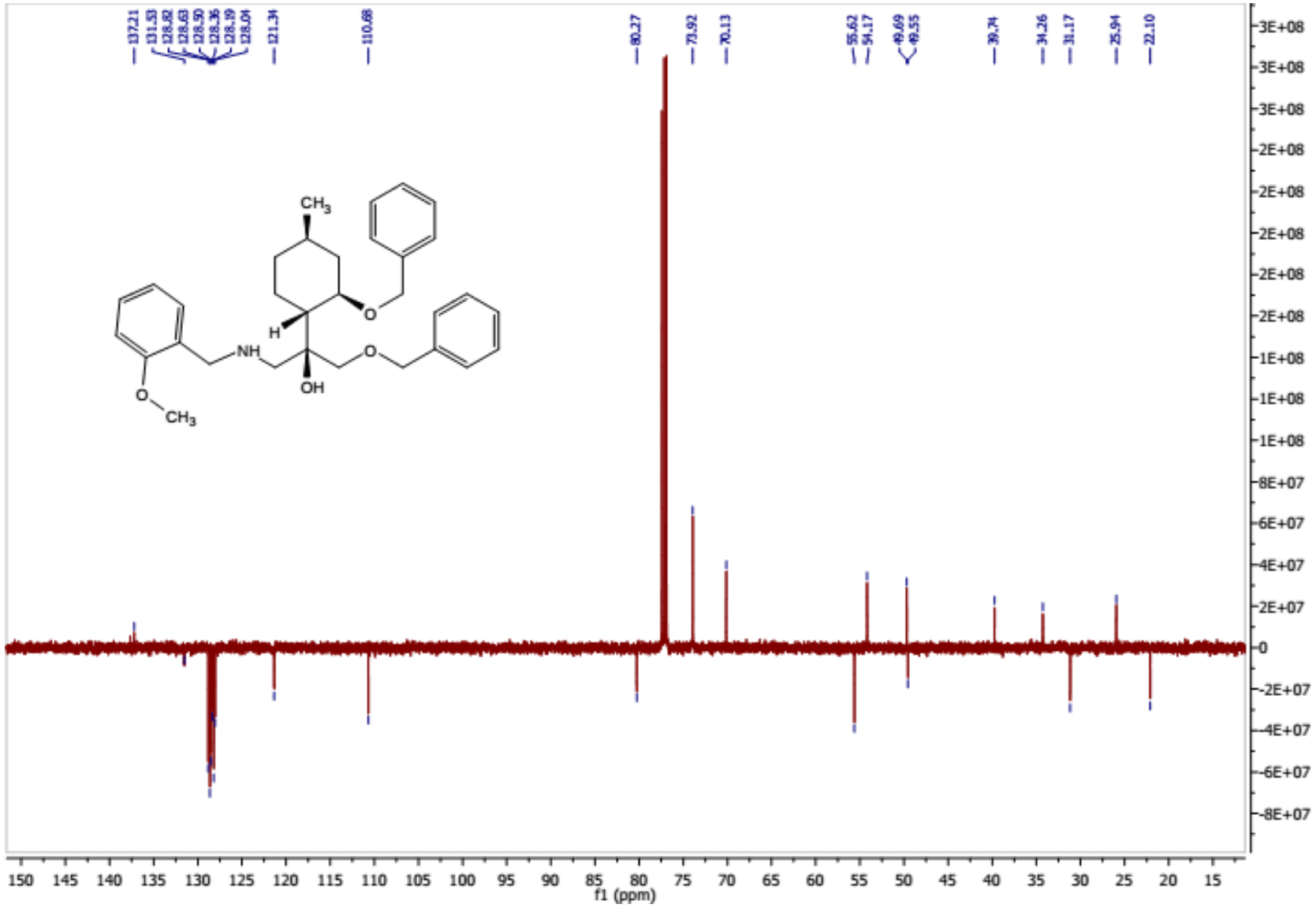


$^{13}$C-NMR of compound **40b**



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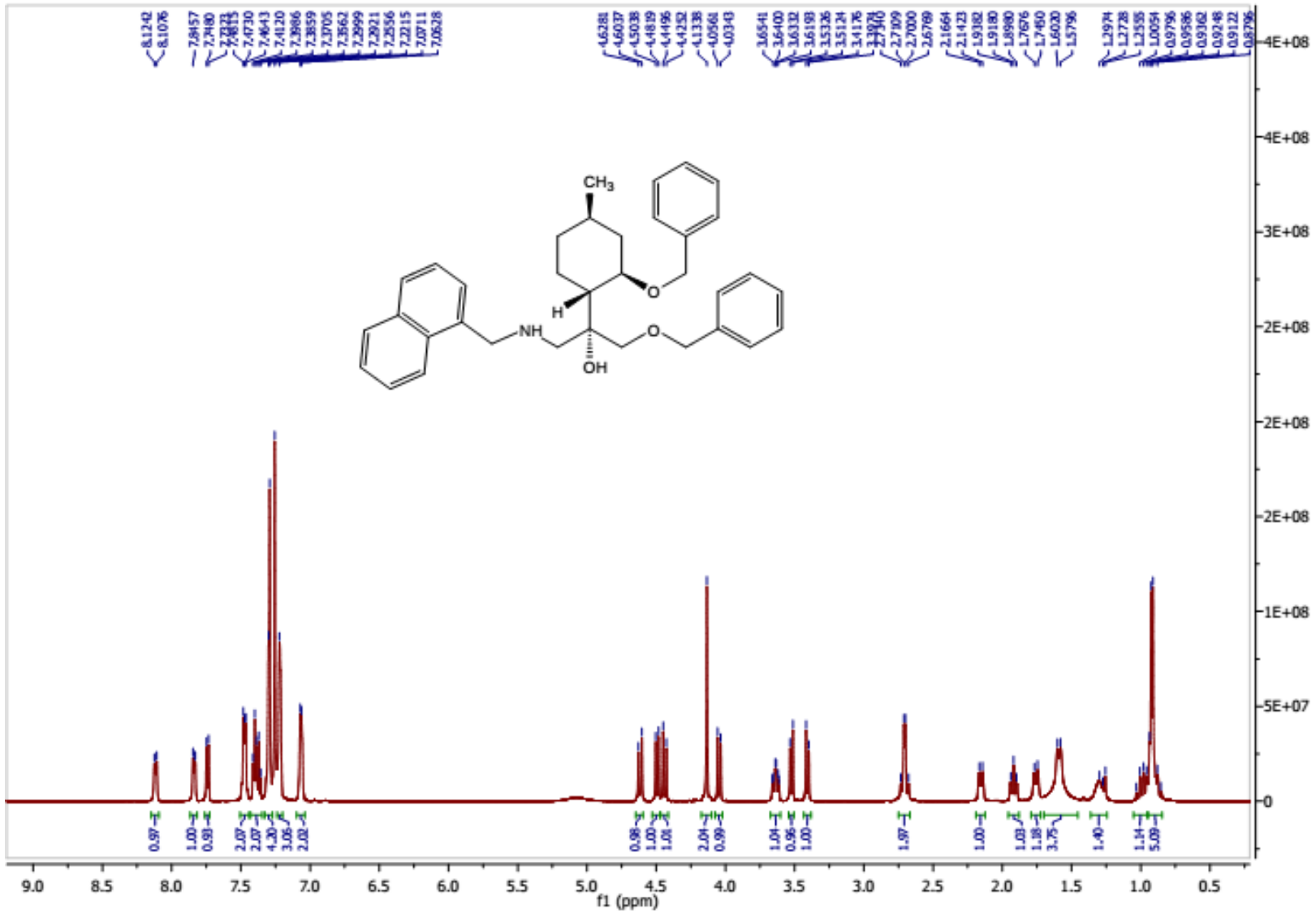
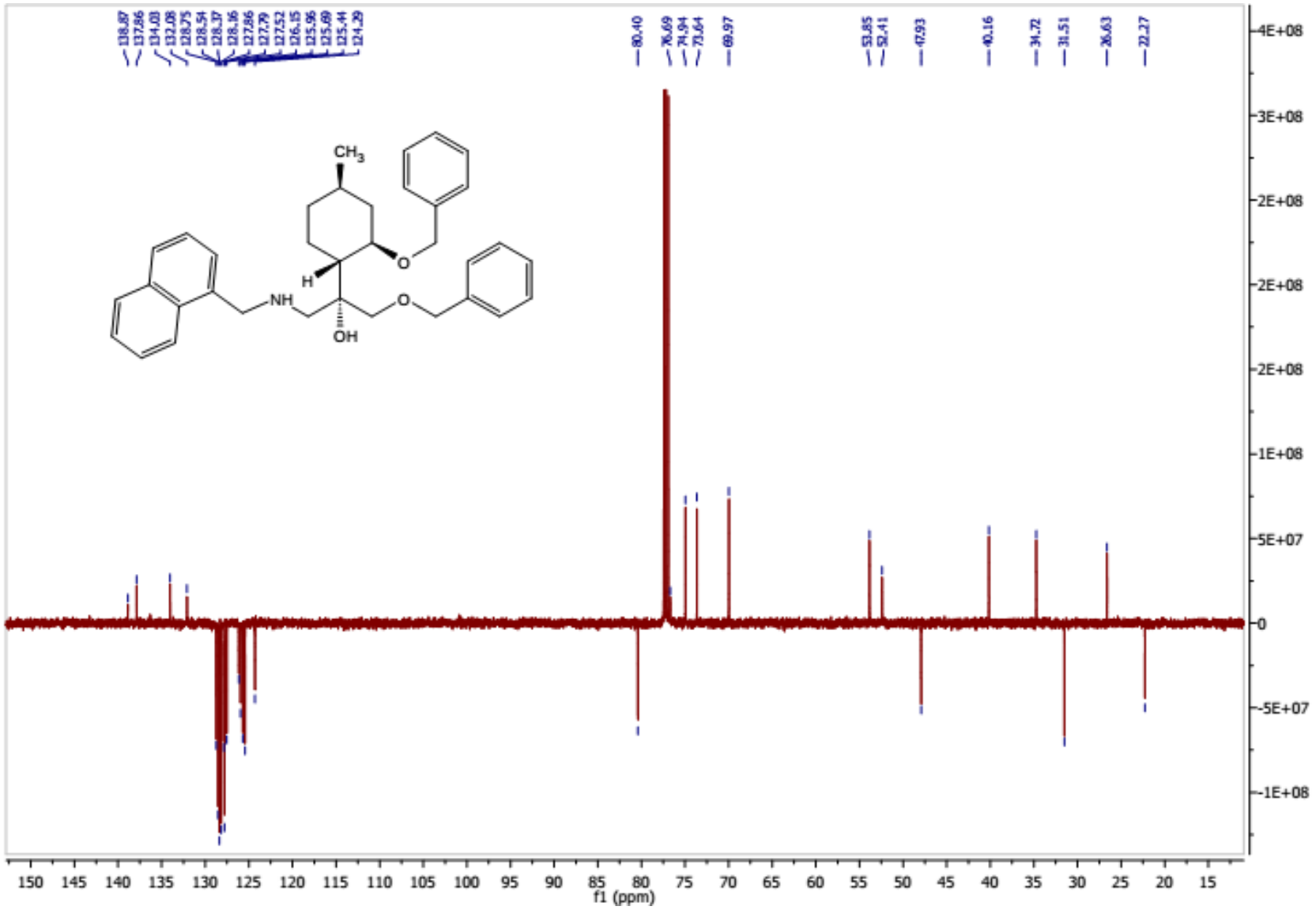


$^{13}$C-NMR of compound **41a**



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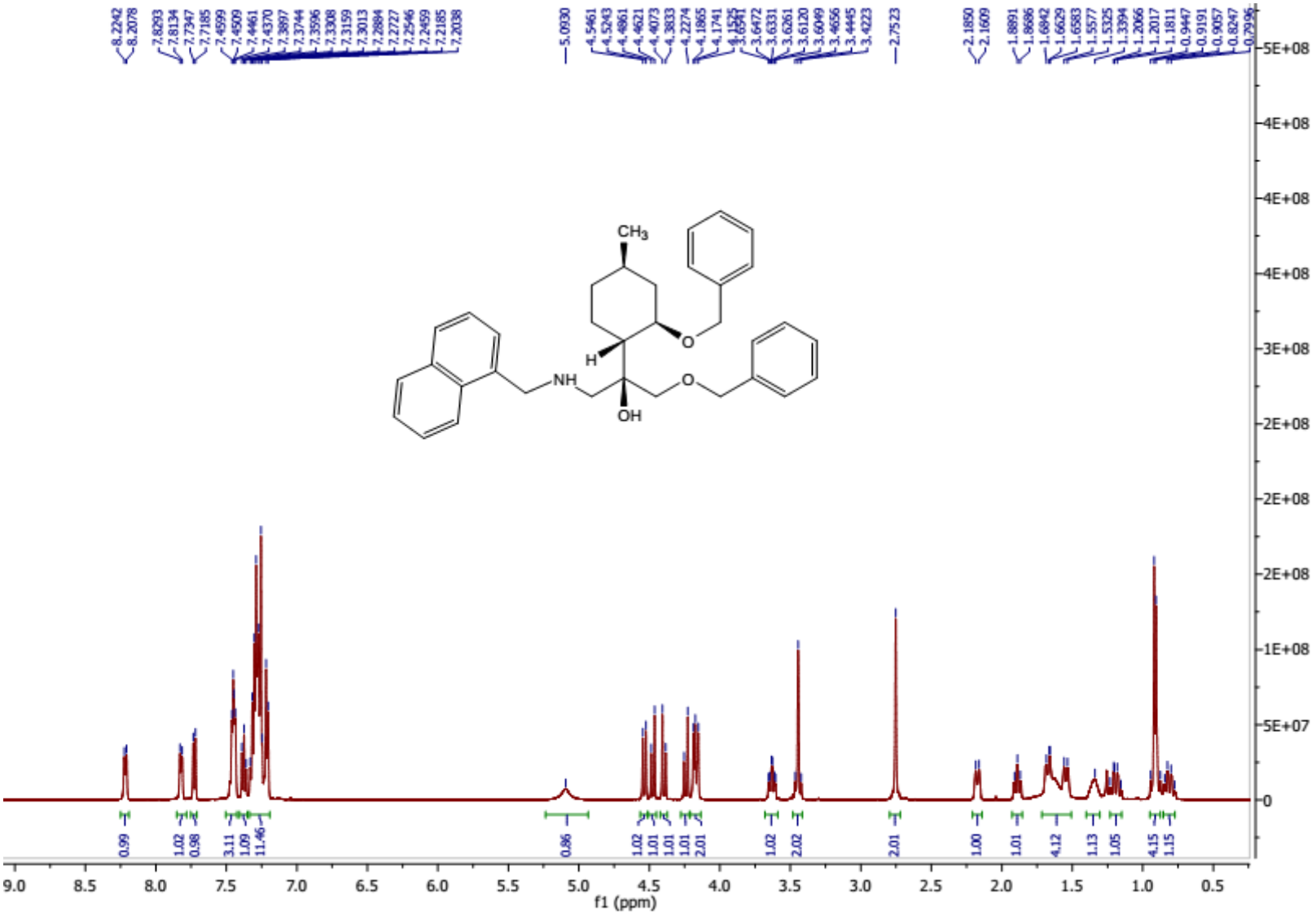
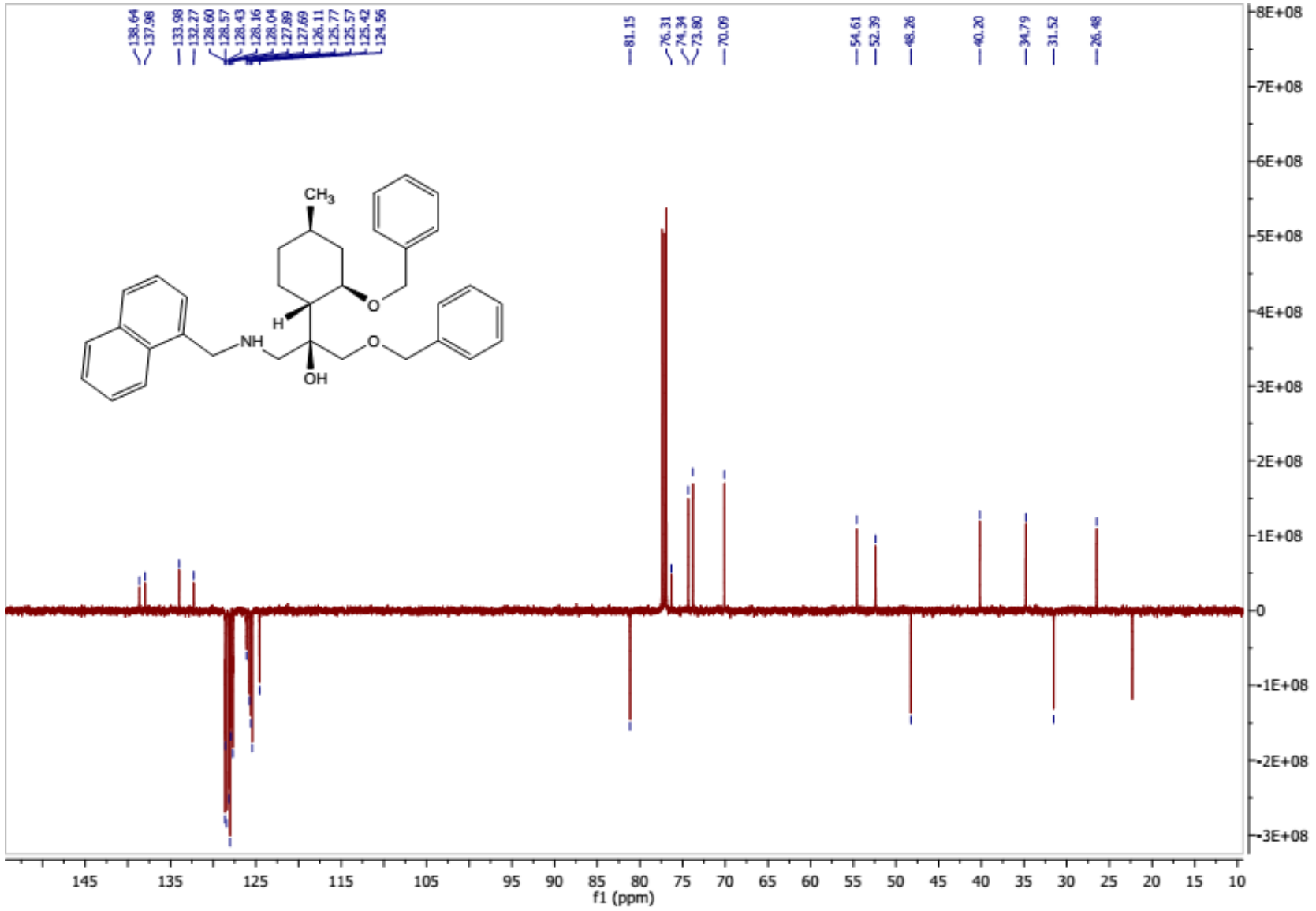
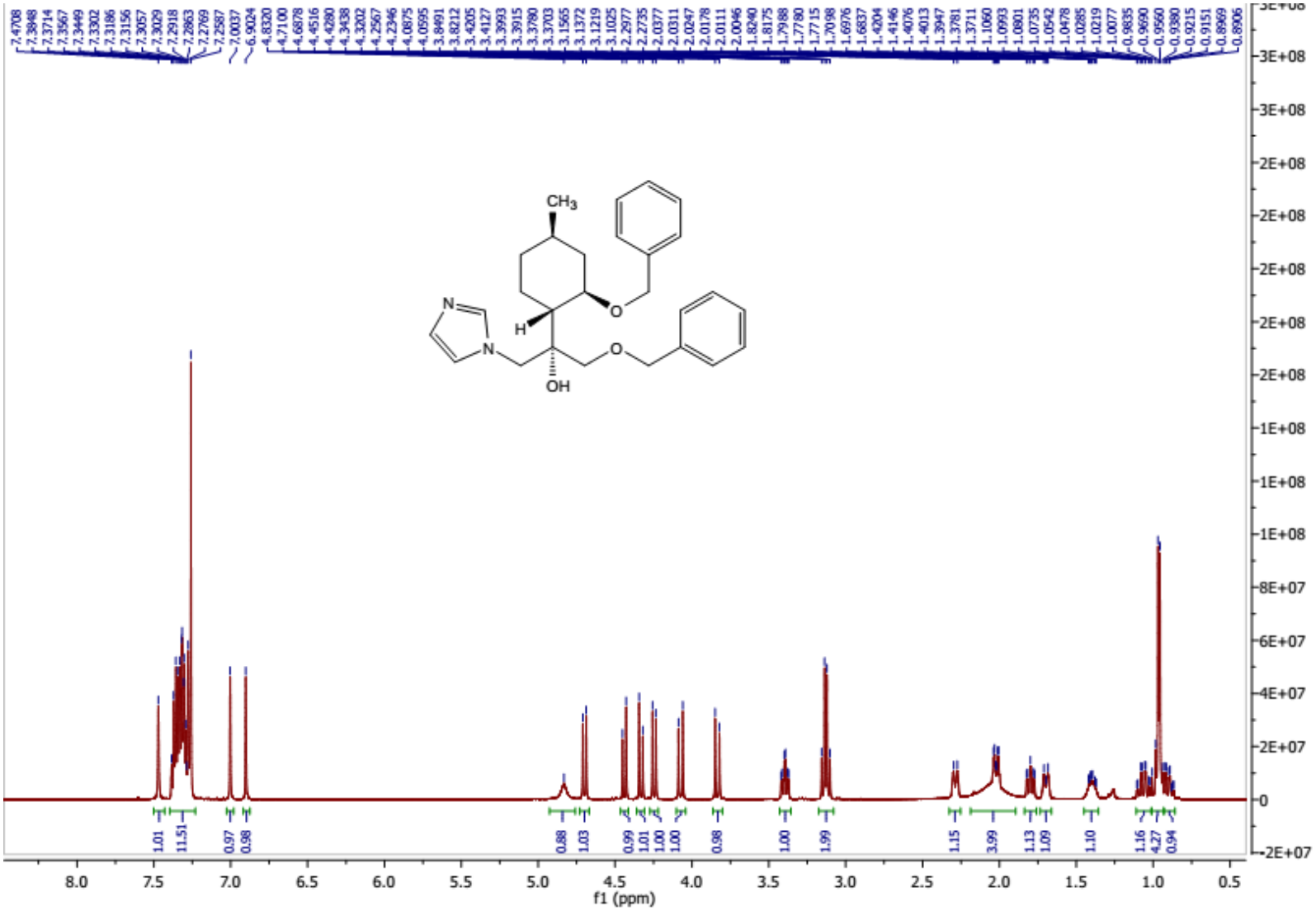


$^{13}$C-NMR of compound **41b**



[1]H-NMR of compound **42a**



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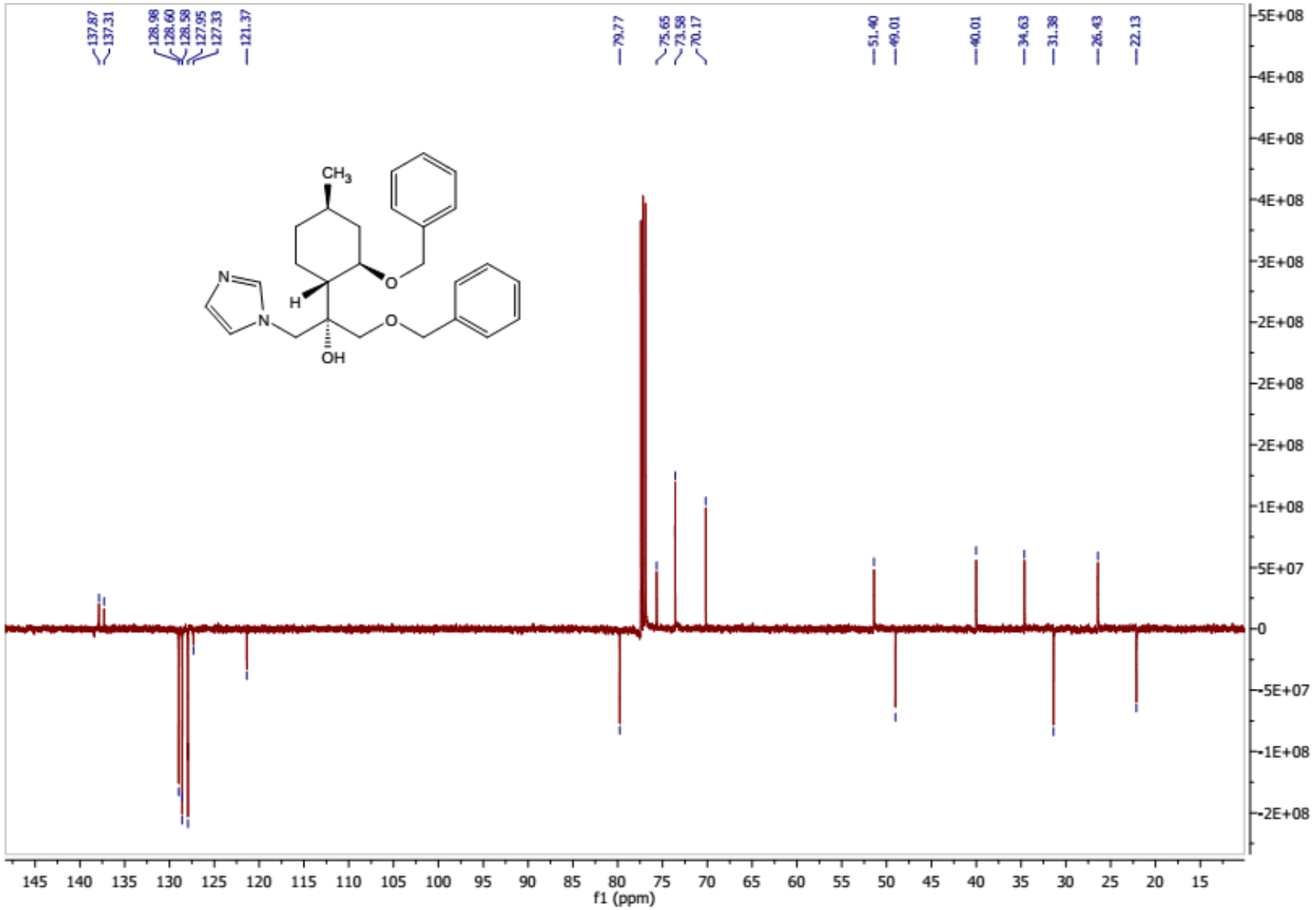

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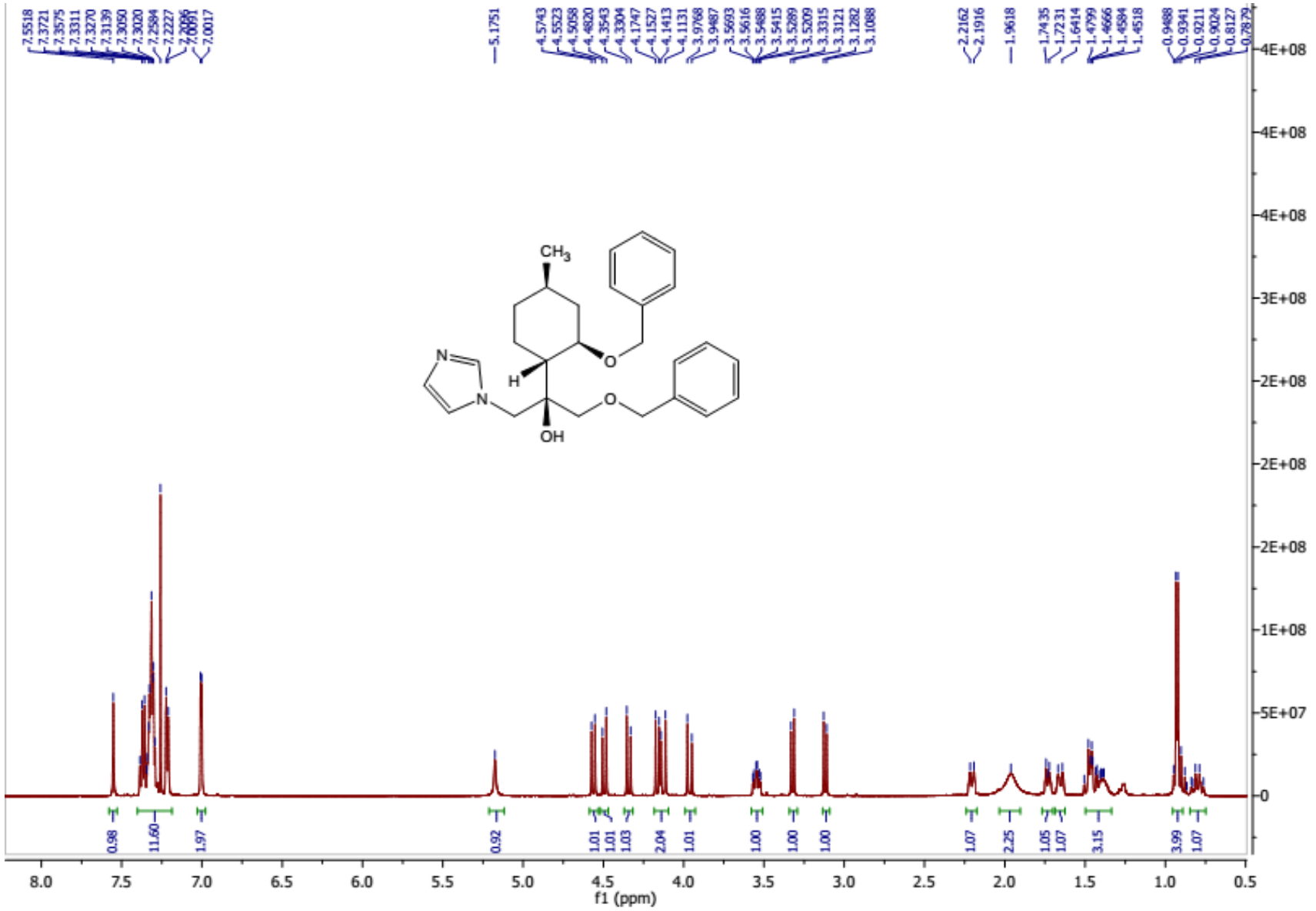

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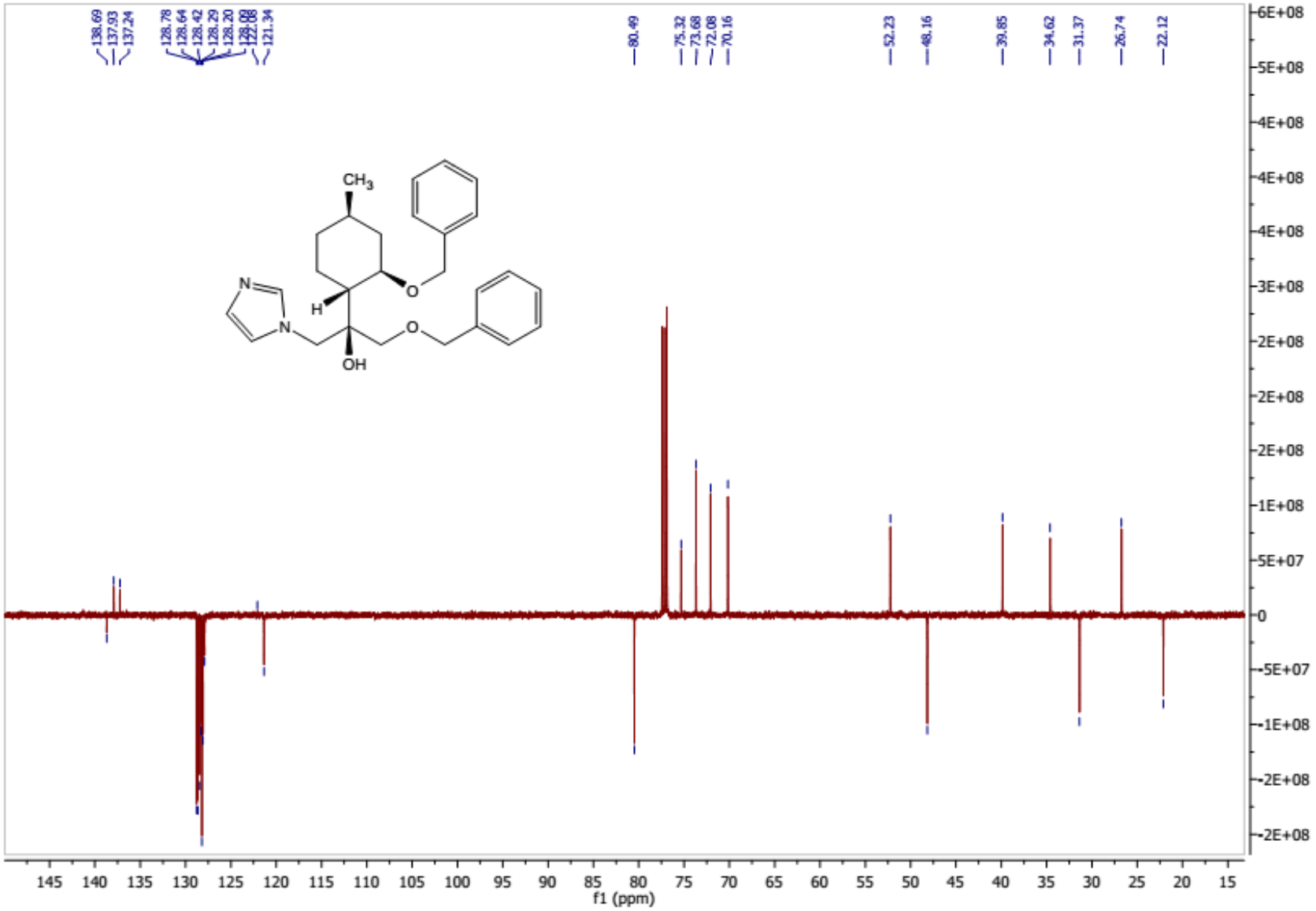
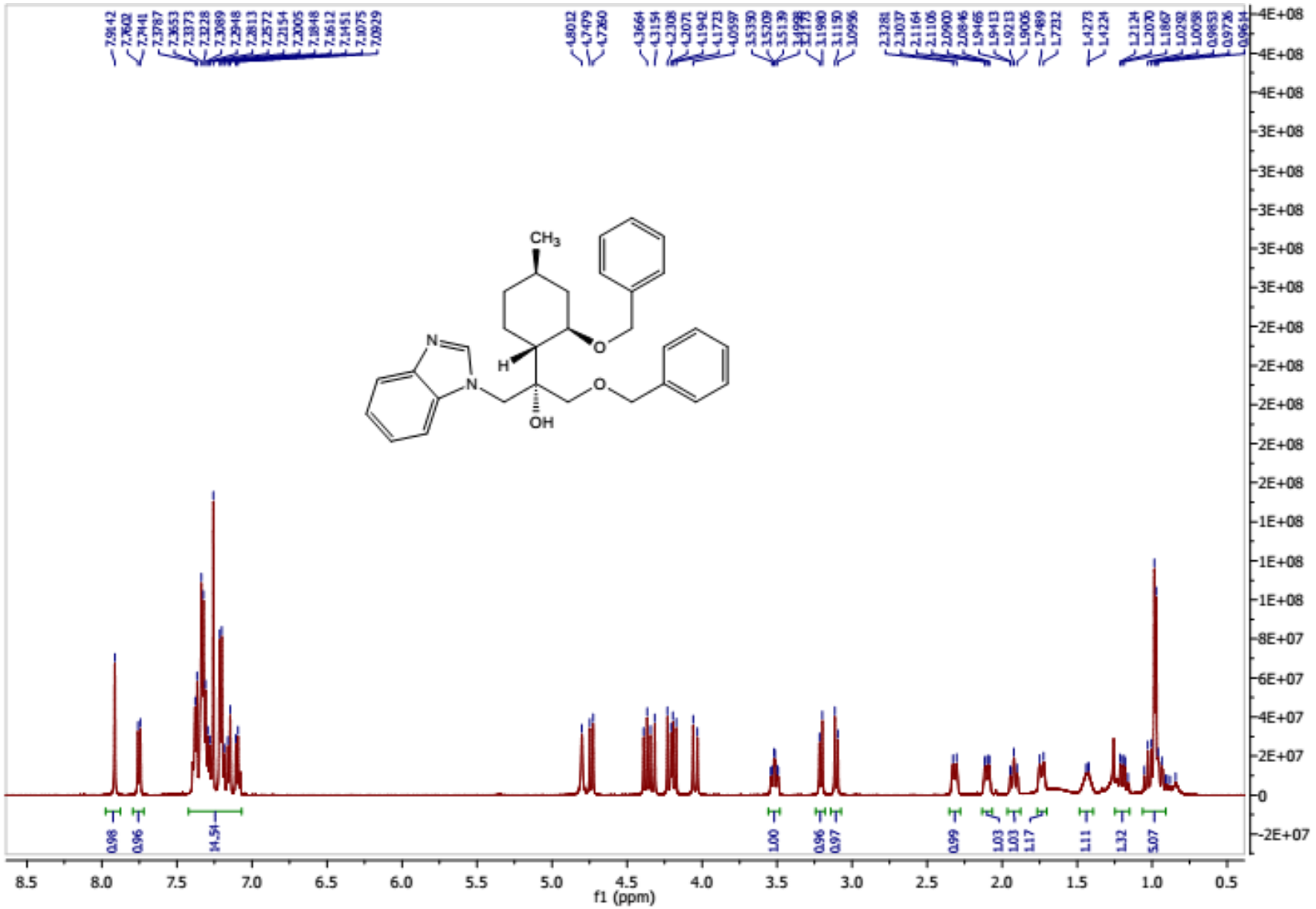


[1]H-NMR of compound **43a**



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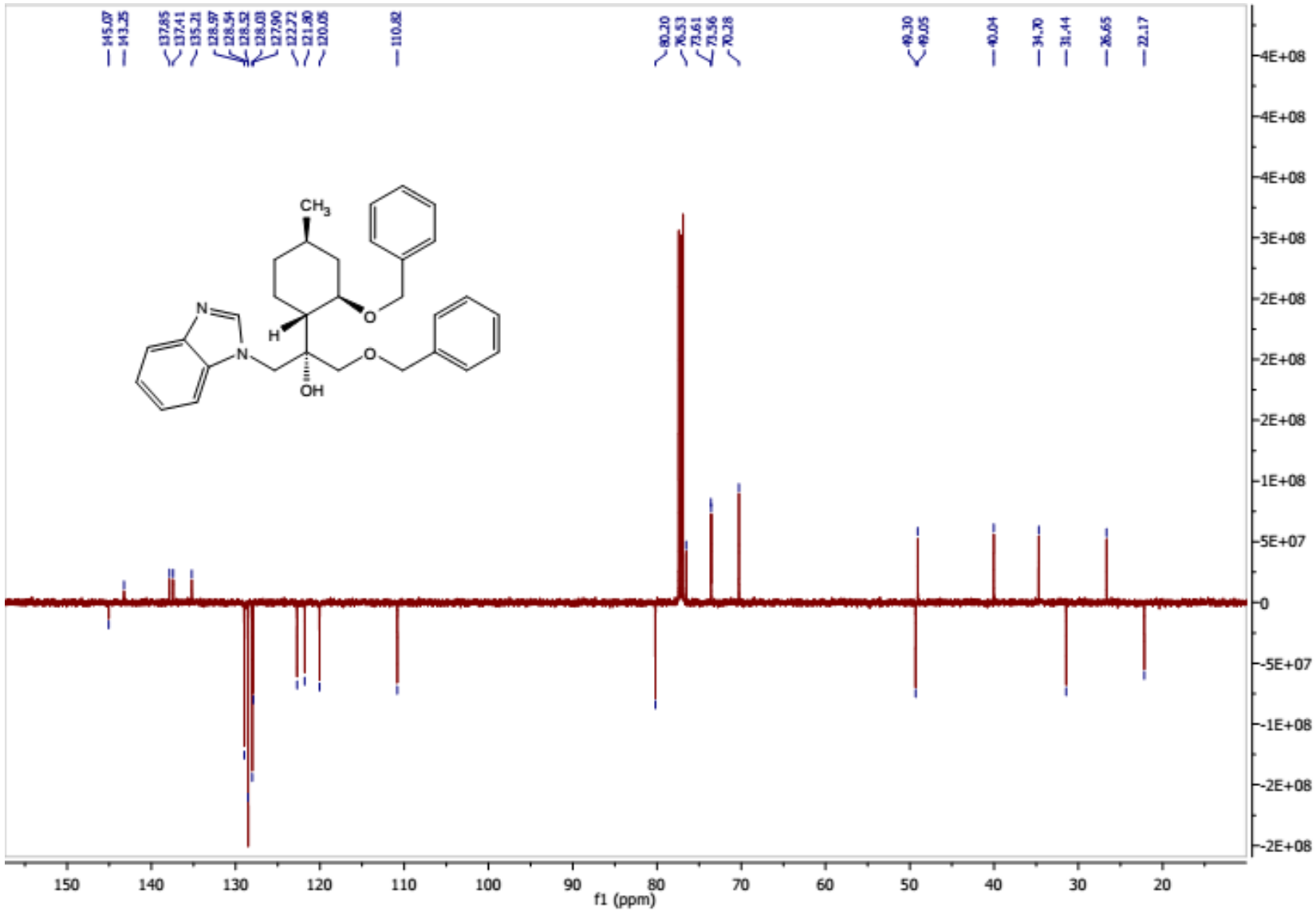

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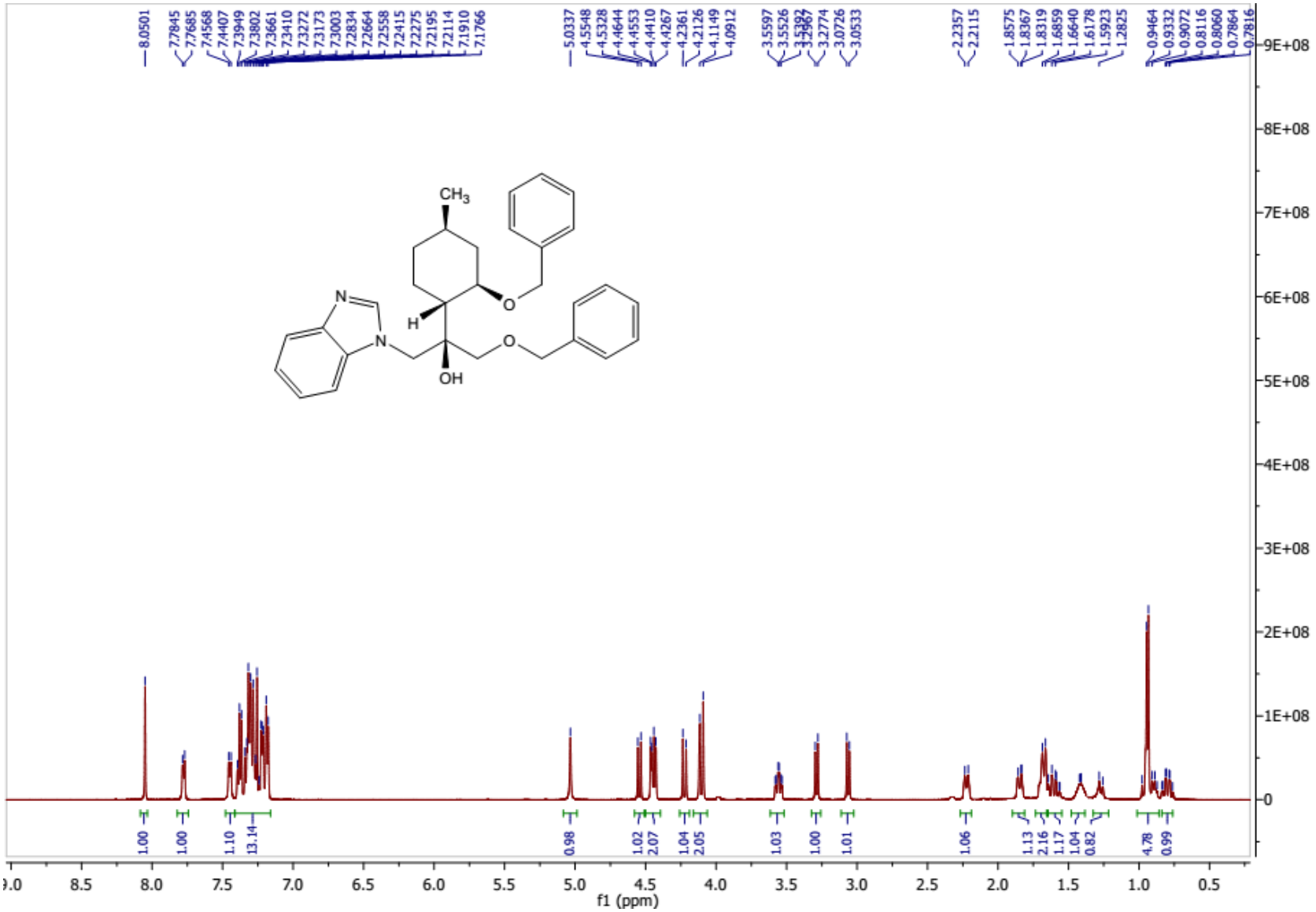
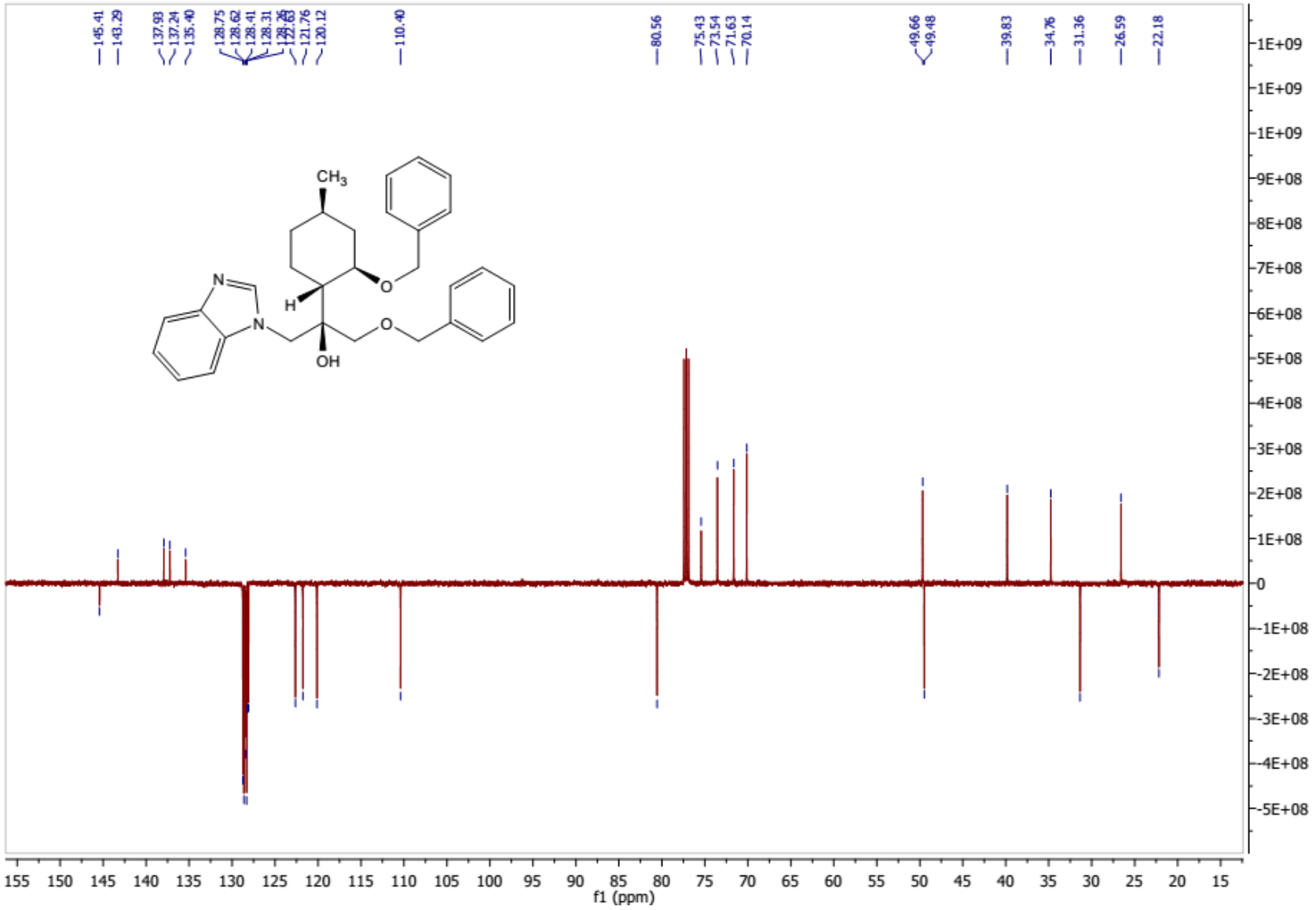
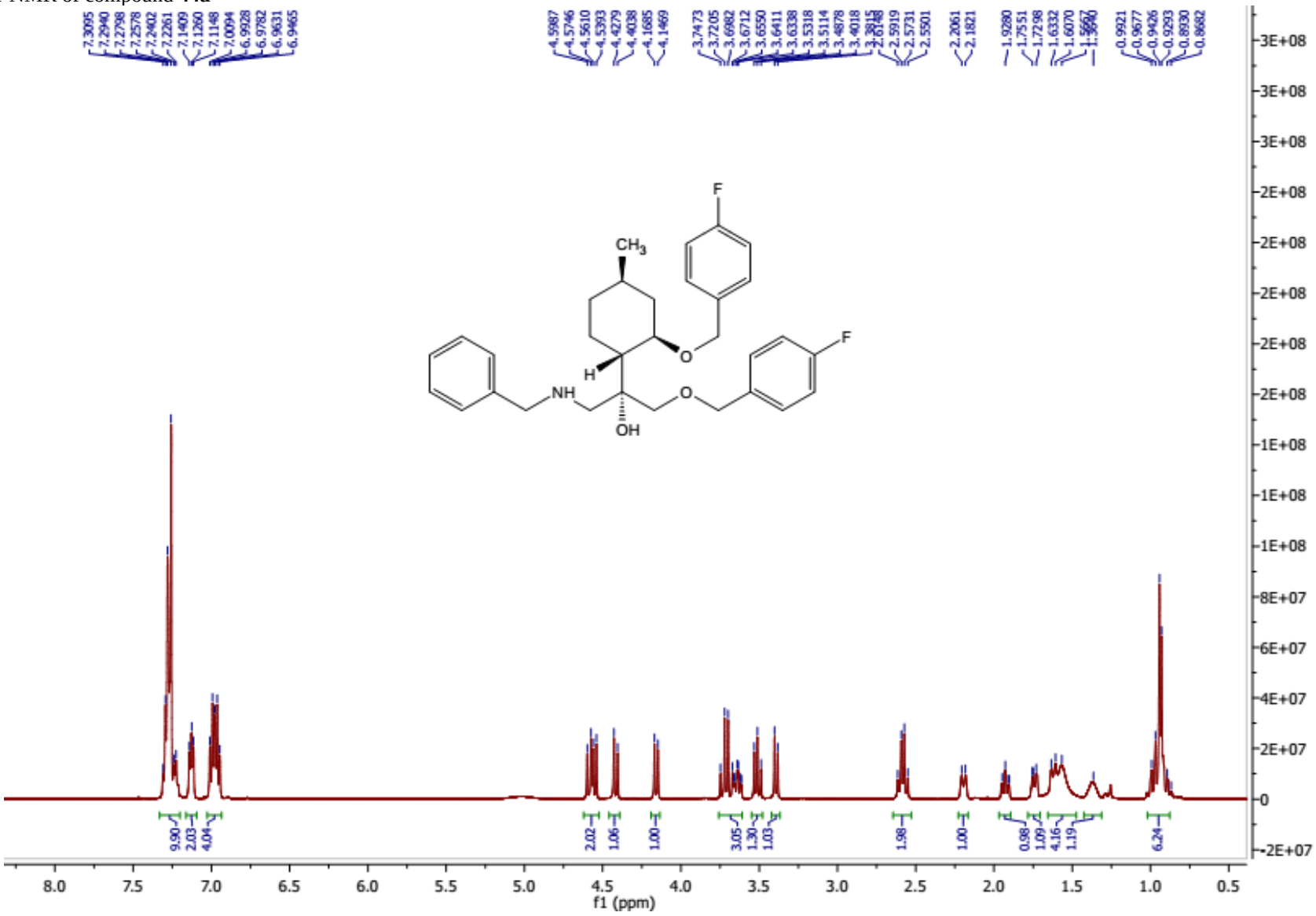


$^{13}$C-NMR of compound **43b**



[1]H-NMR of compound **44a**



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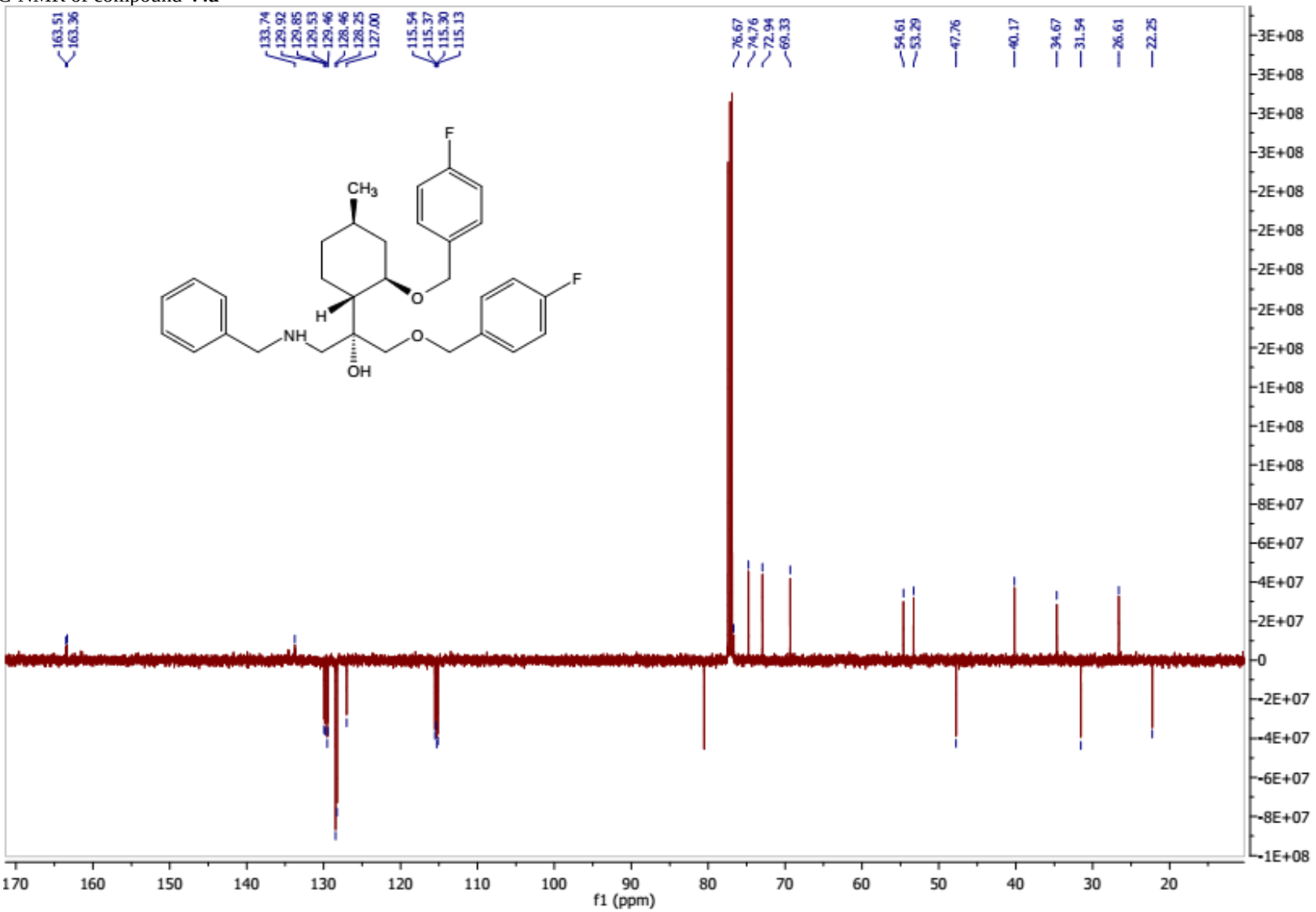
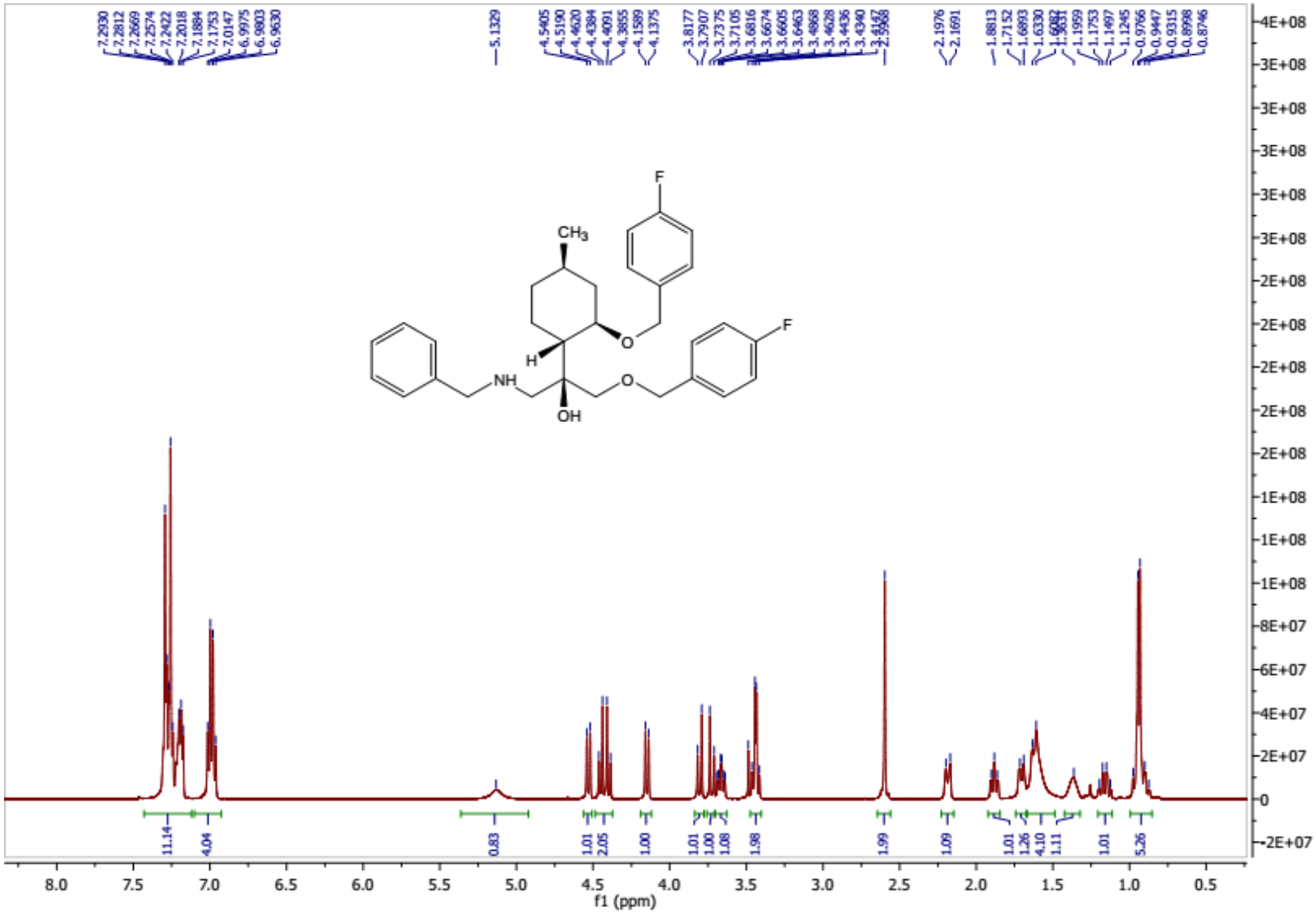
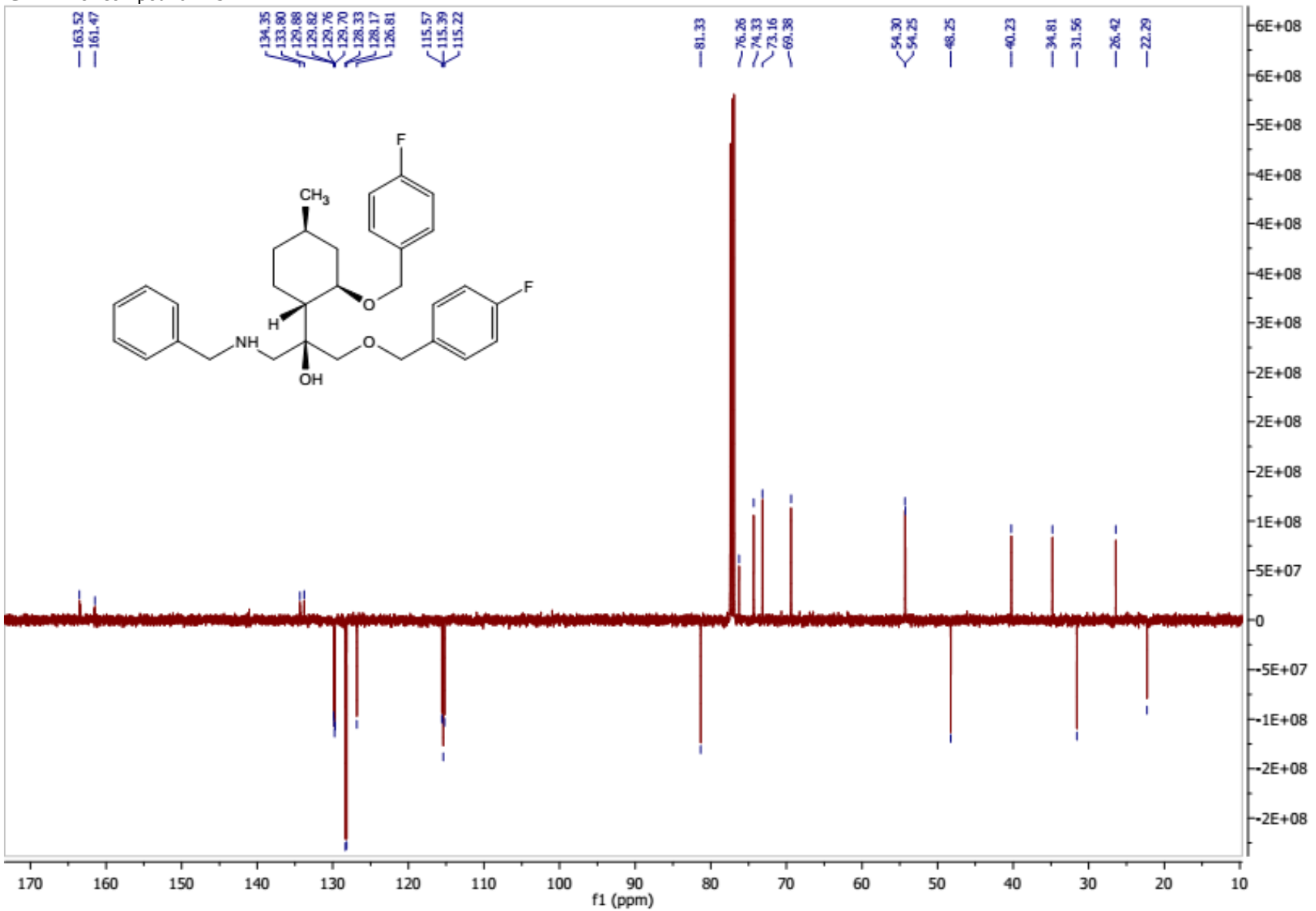


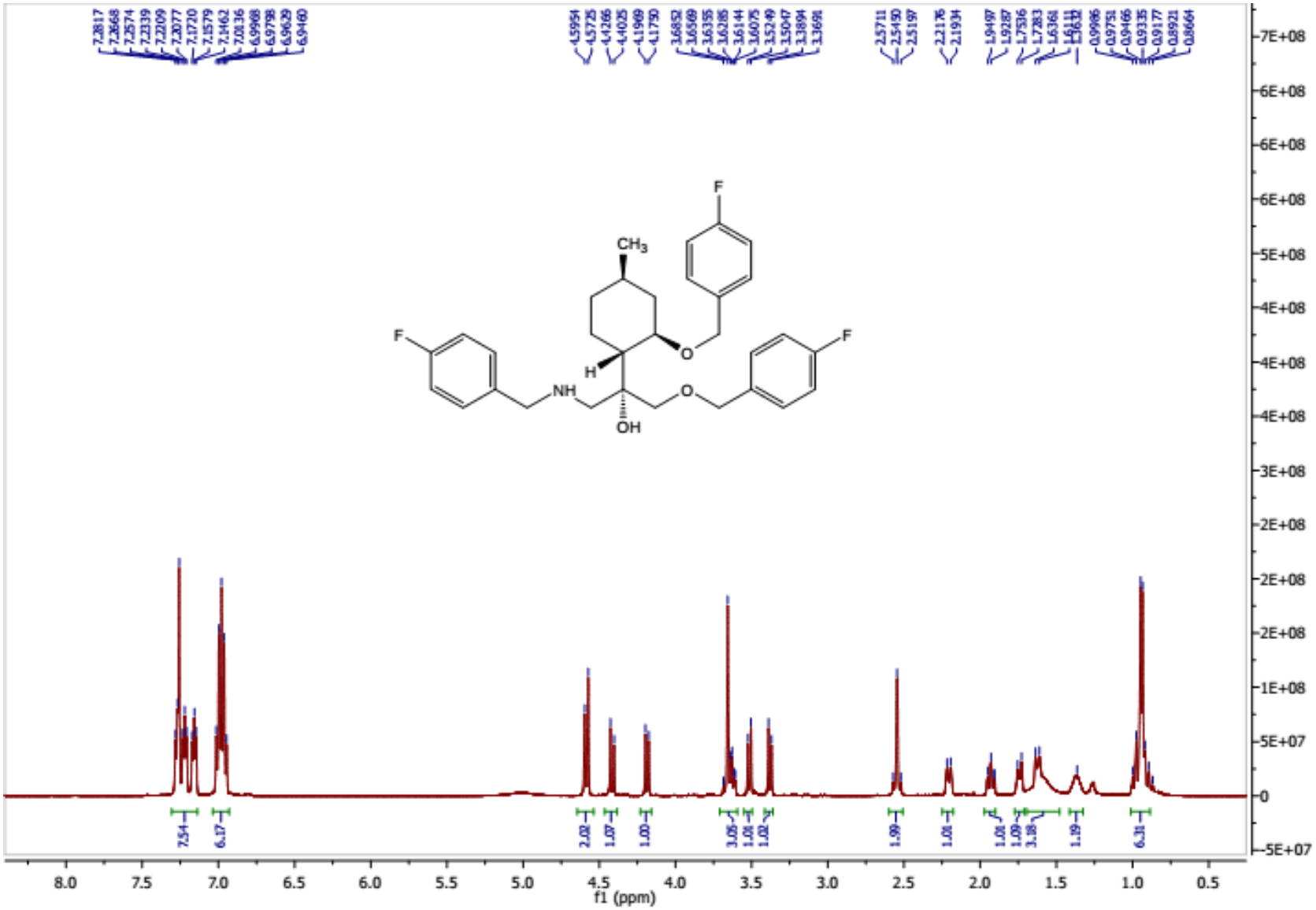
[1]H-NMR of compound **44b**



$^{13}$C-NMR of compound **44b**



[1]H-NMR of compound **45a**



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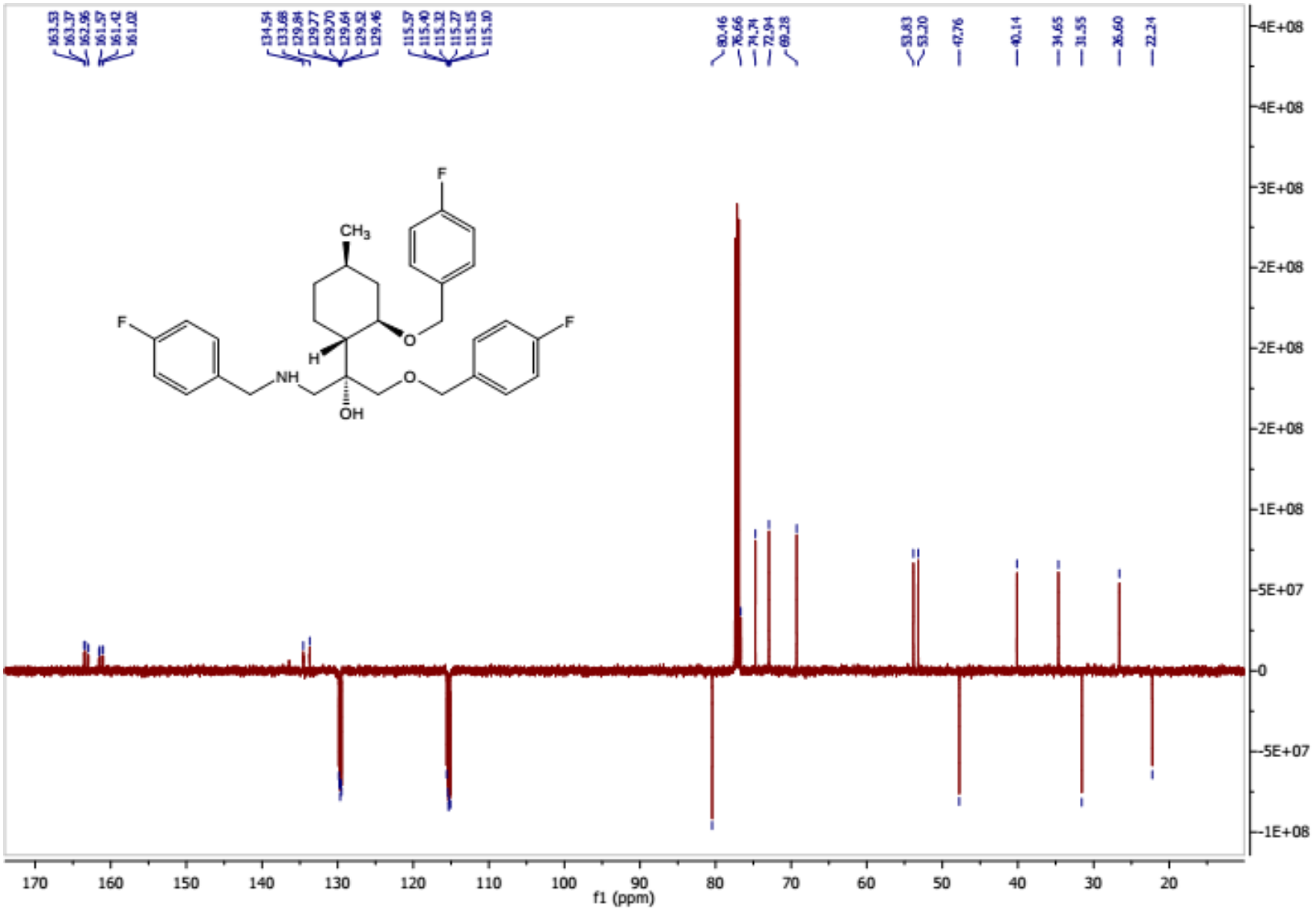

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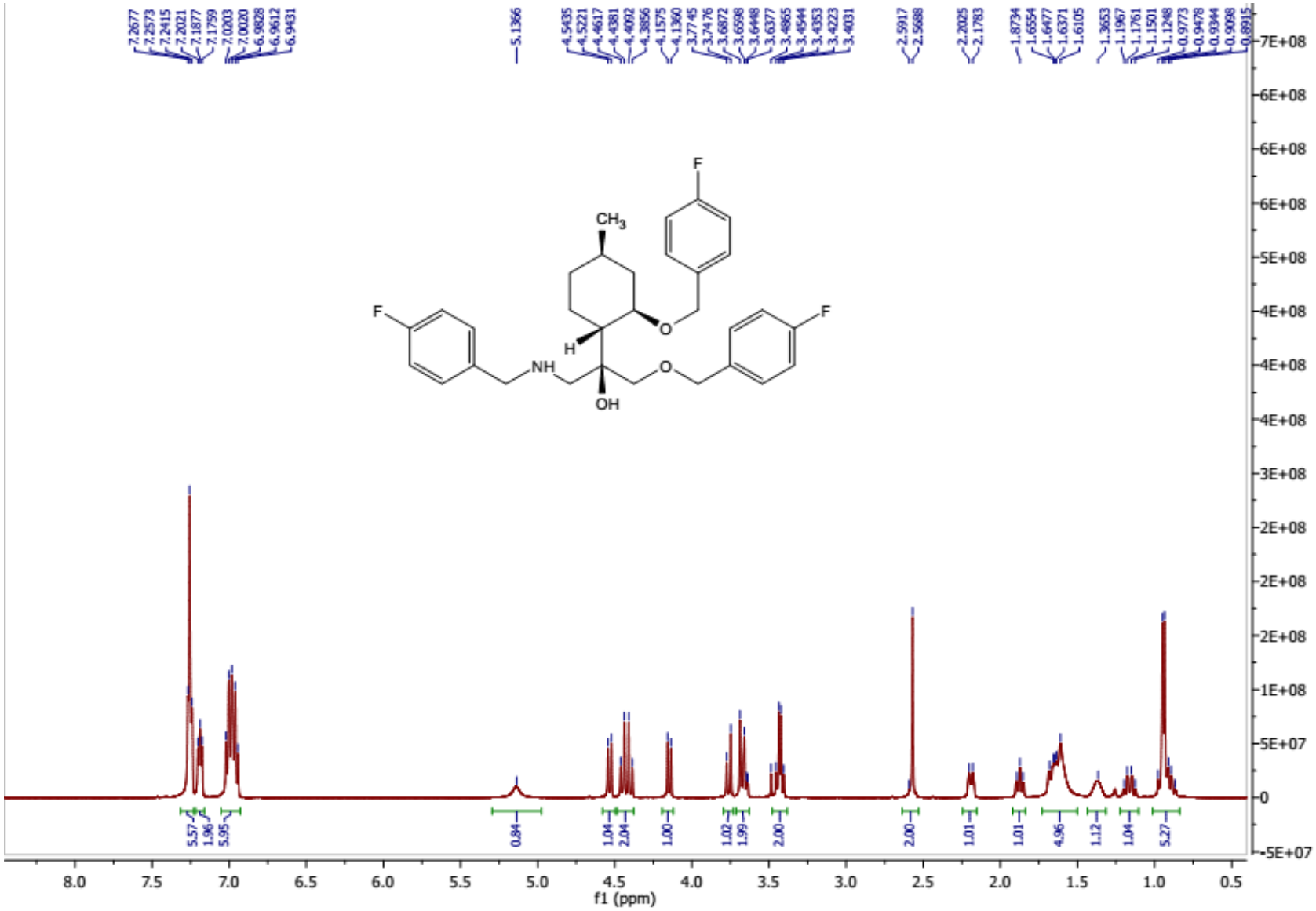

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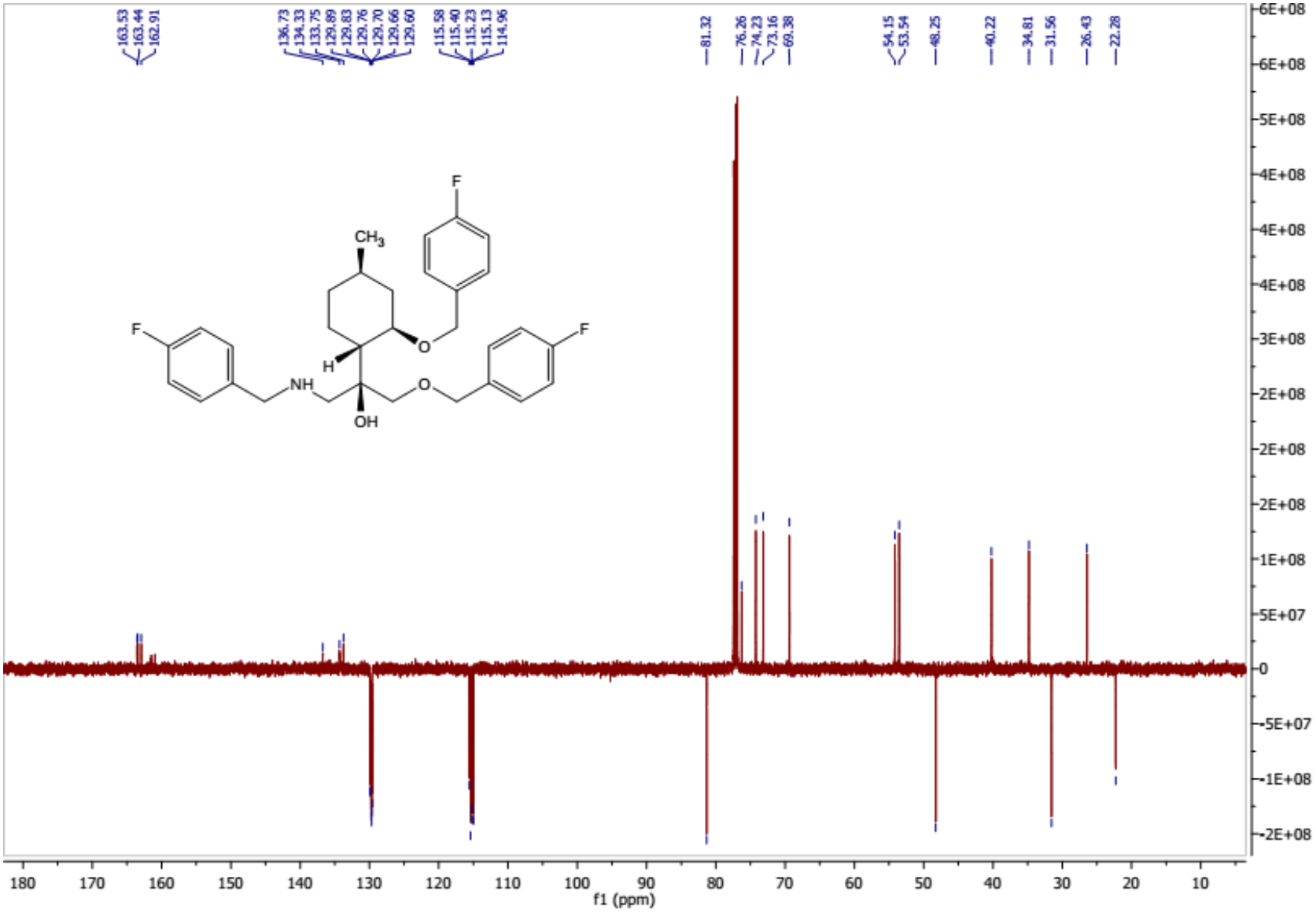
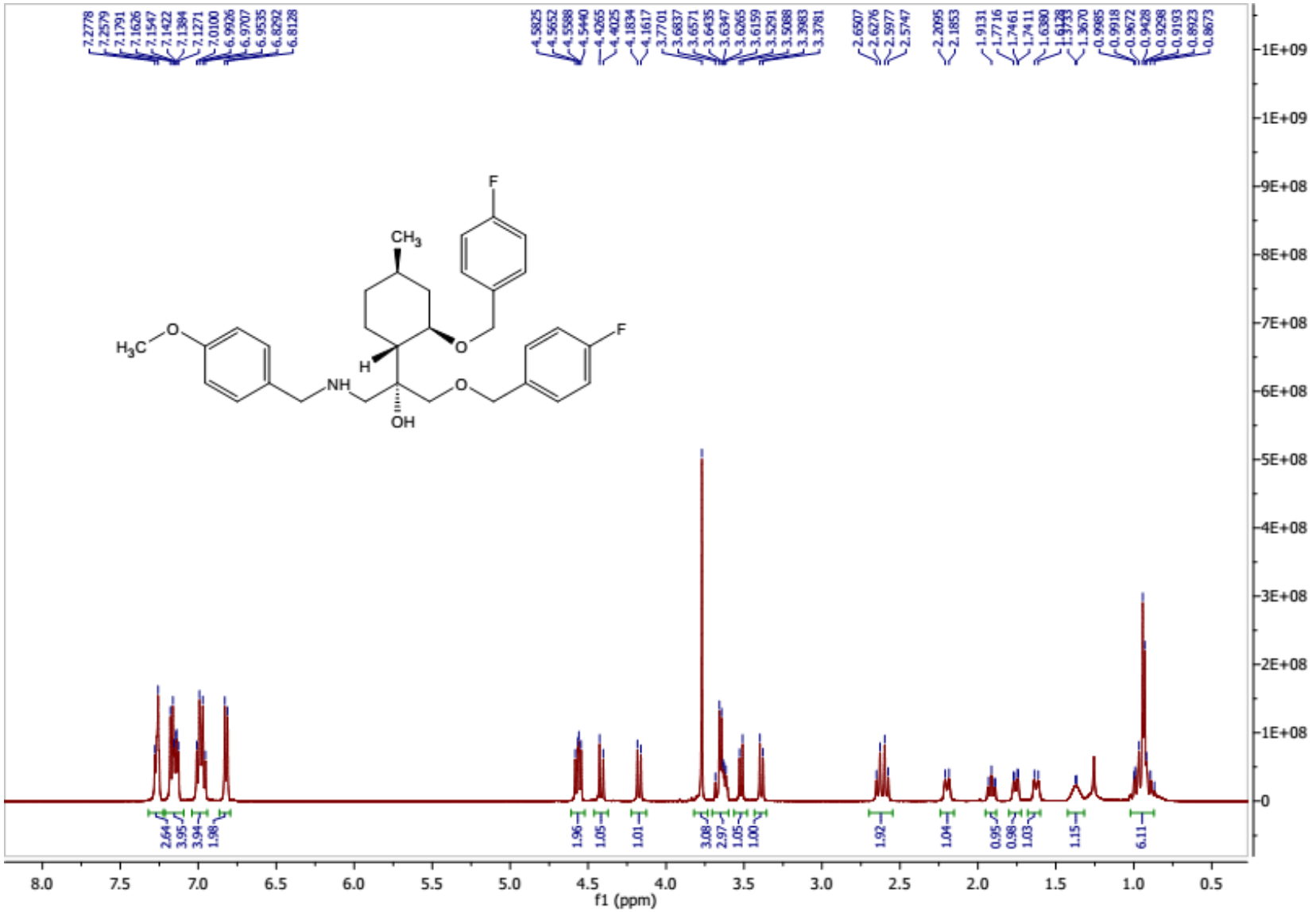
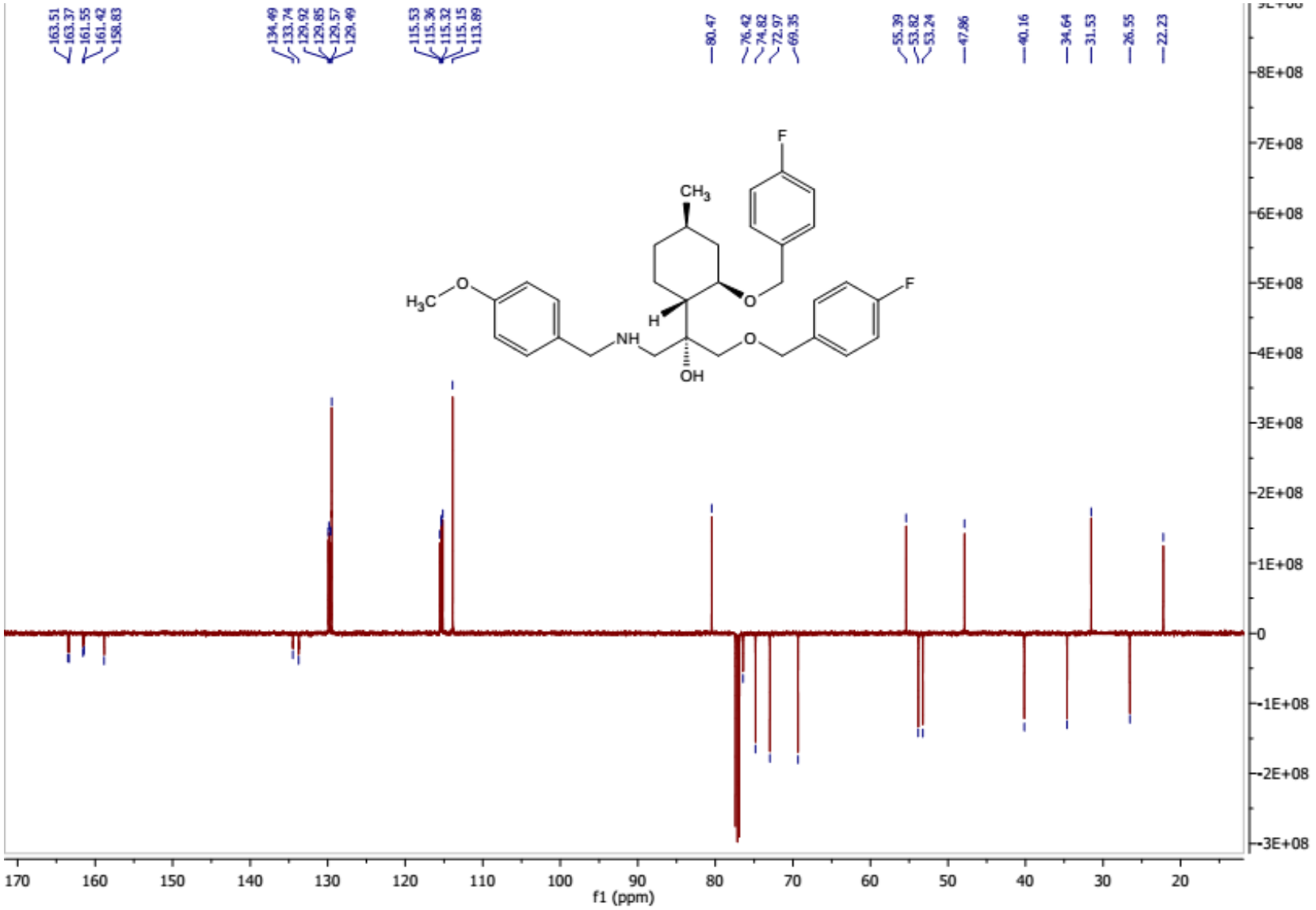


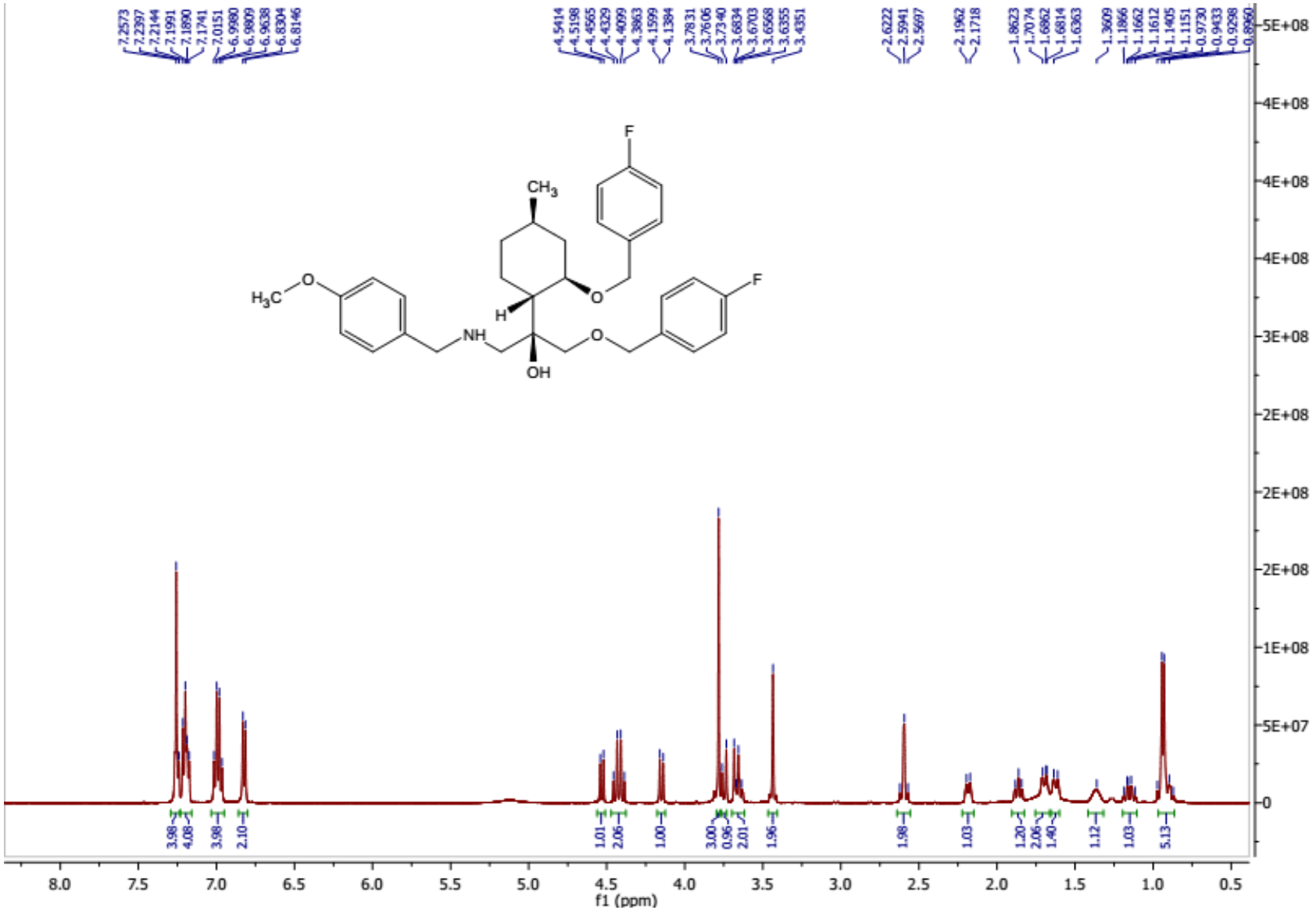
[1]H-NMR of compound **46a**



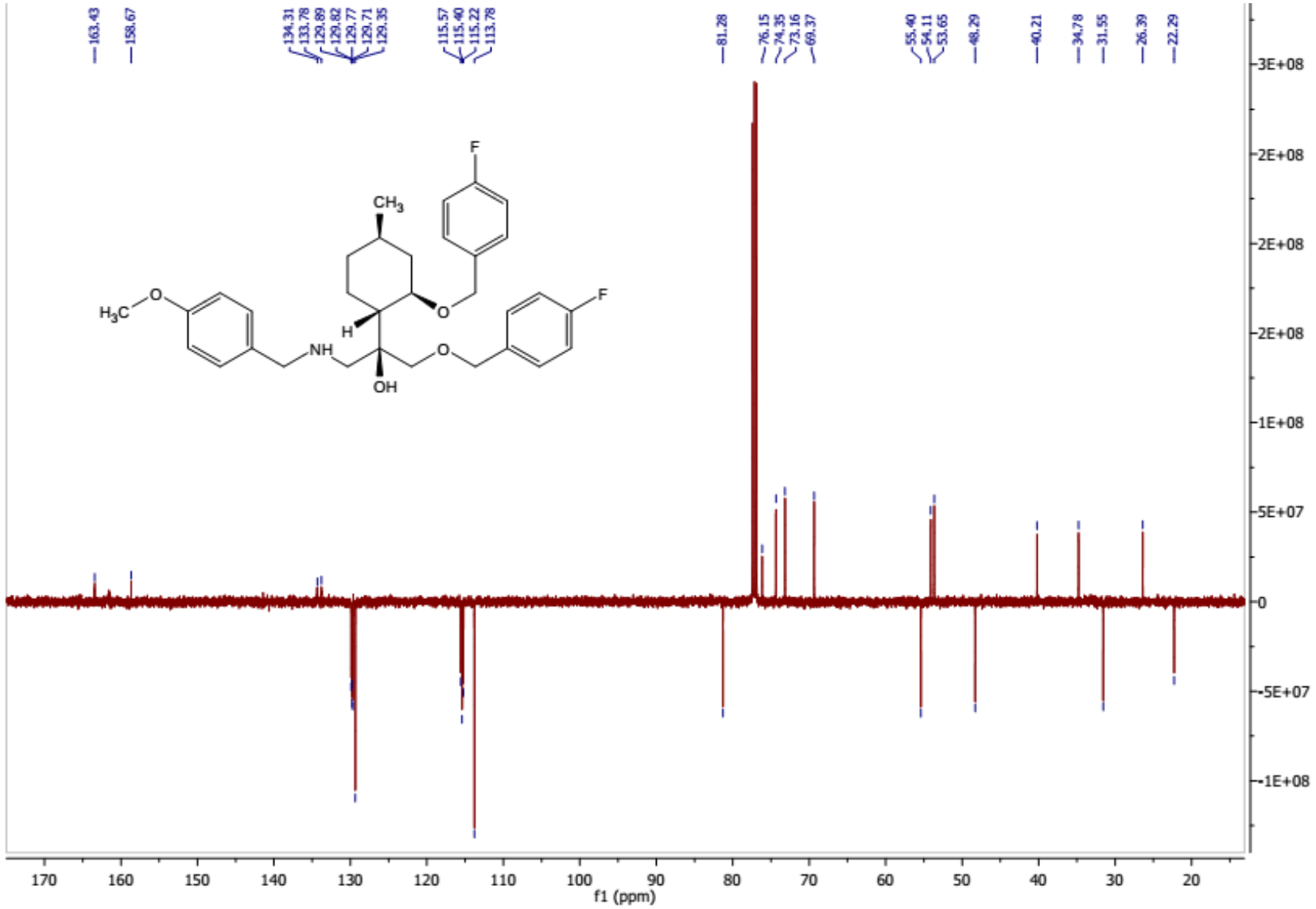
$^{13}$C-NMR of compound **46a**



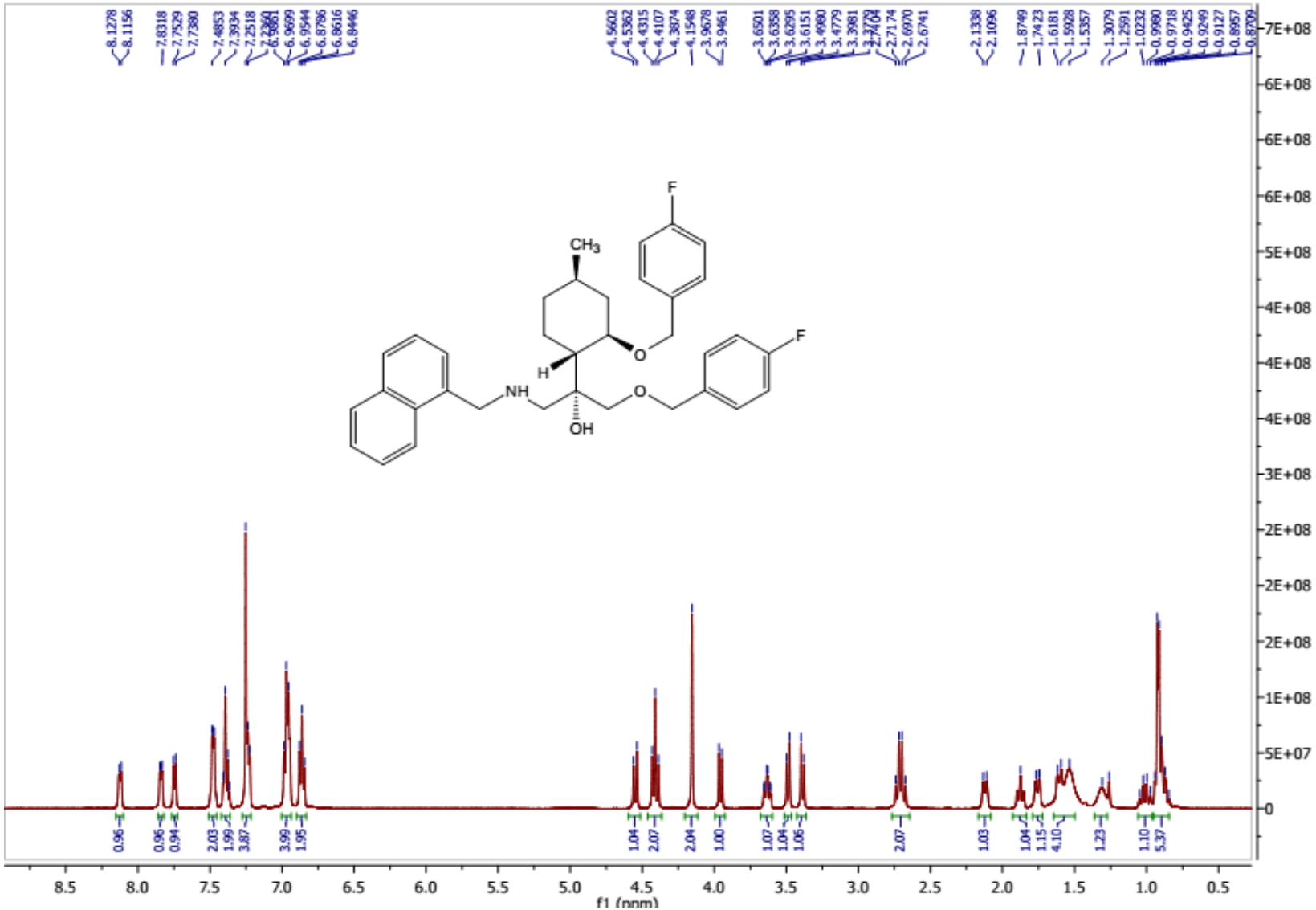
[1]H-NMR of compound **46b**



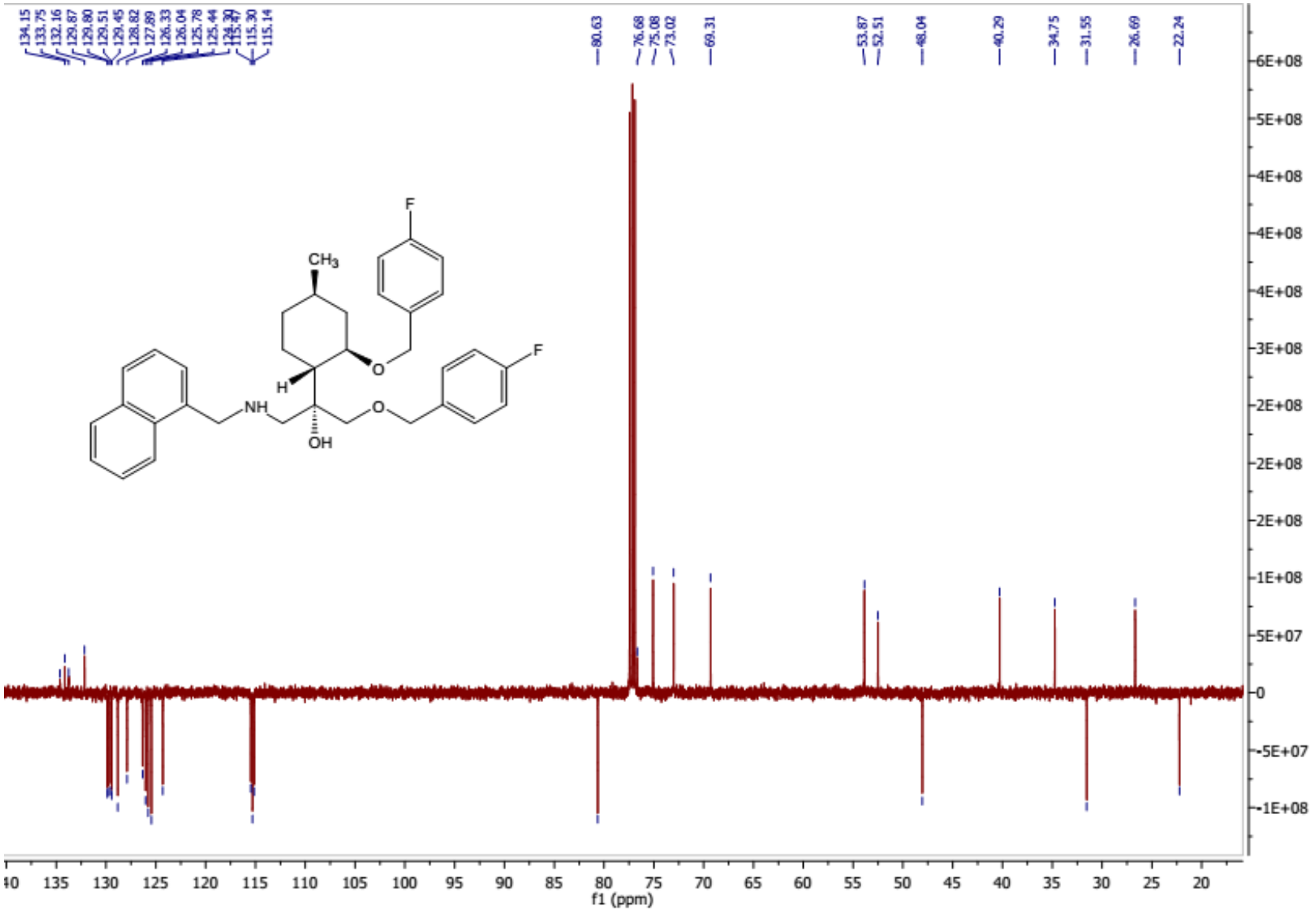
$^{13}$C-NMR of compound **46b**



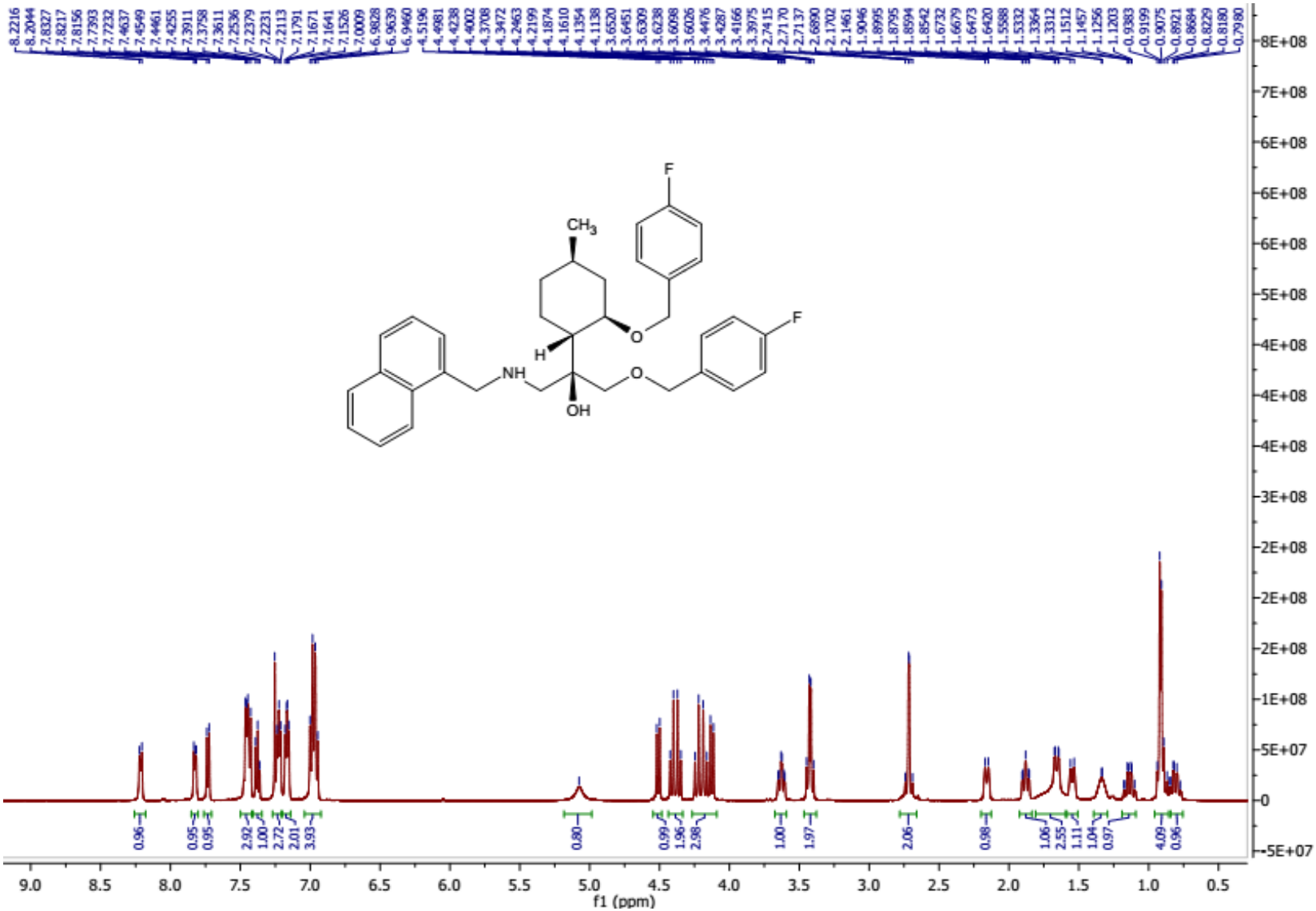
[1]H-NMR of compound **47a**



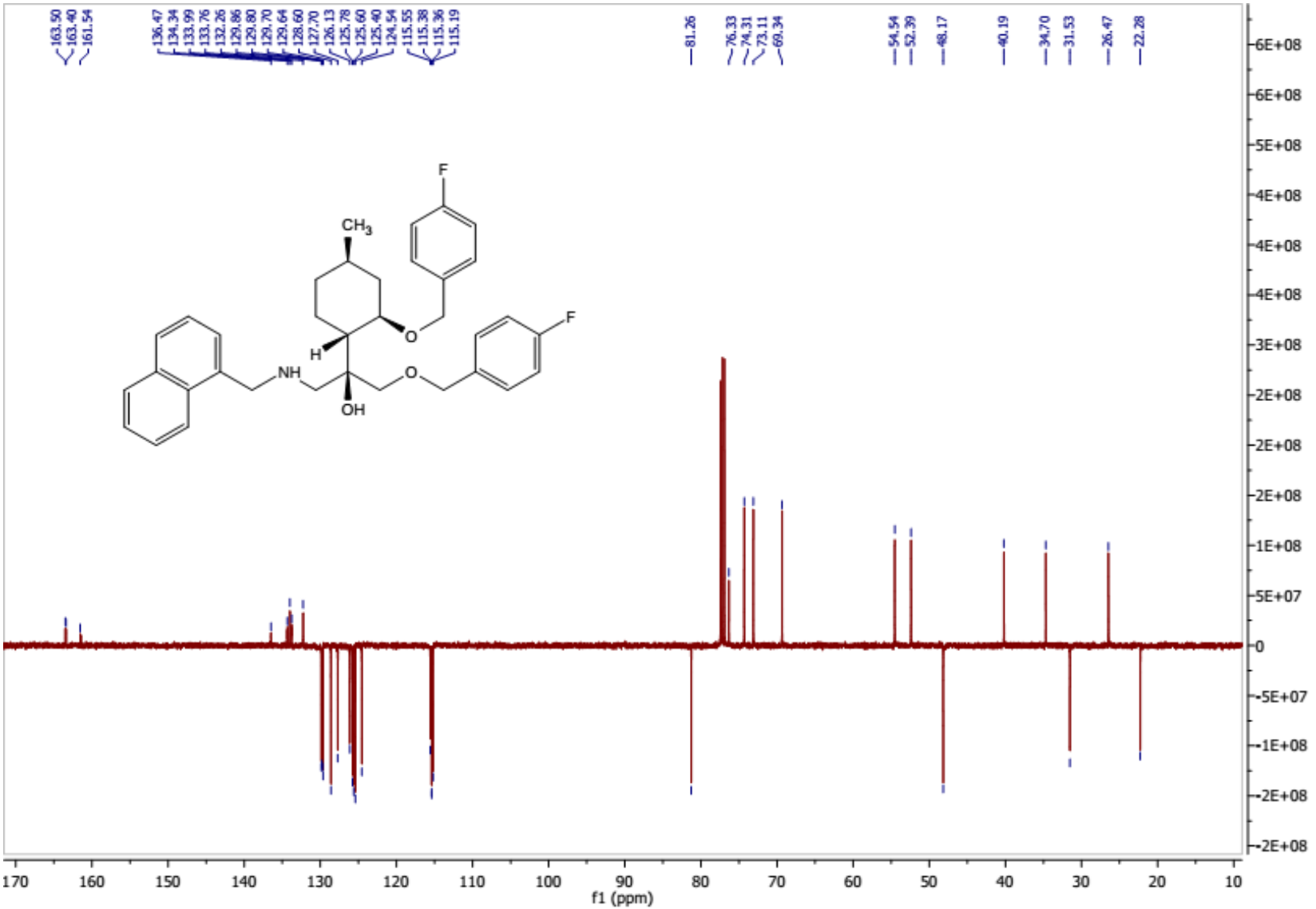
$^{13}$C-NMR of compound **47a**



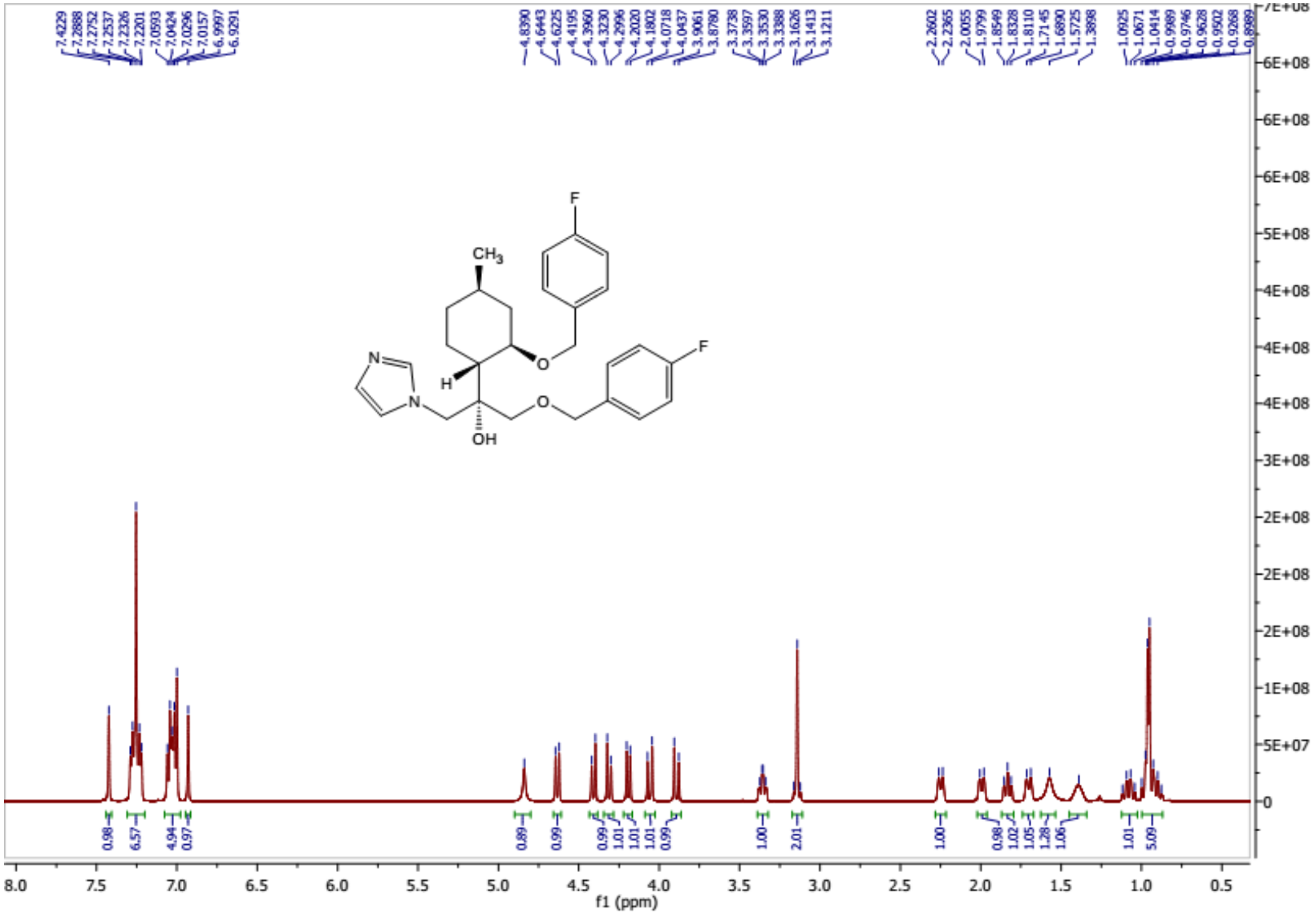
[1]H-NMR of compound **47b**



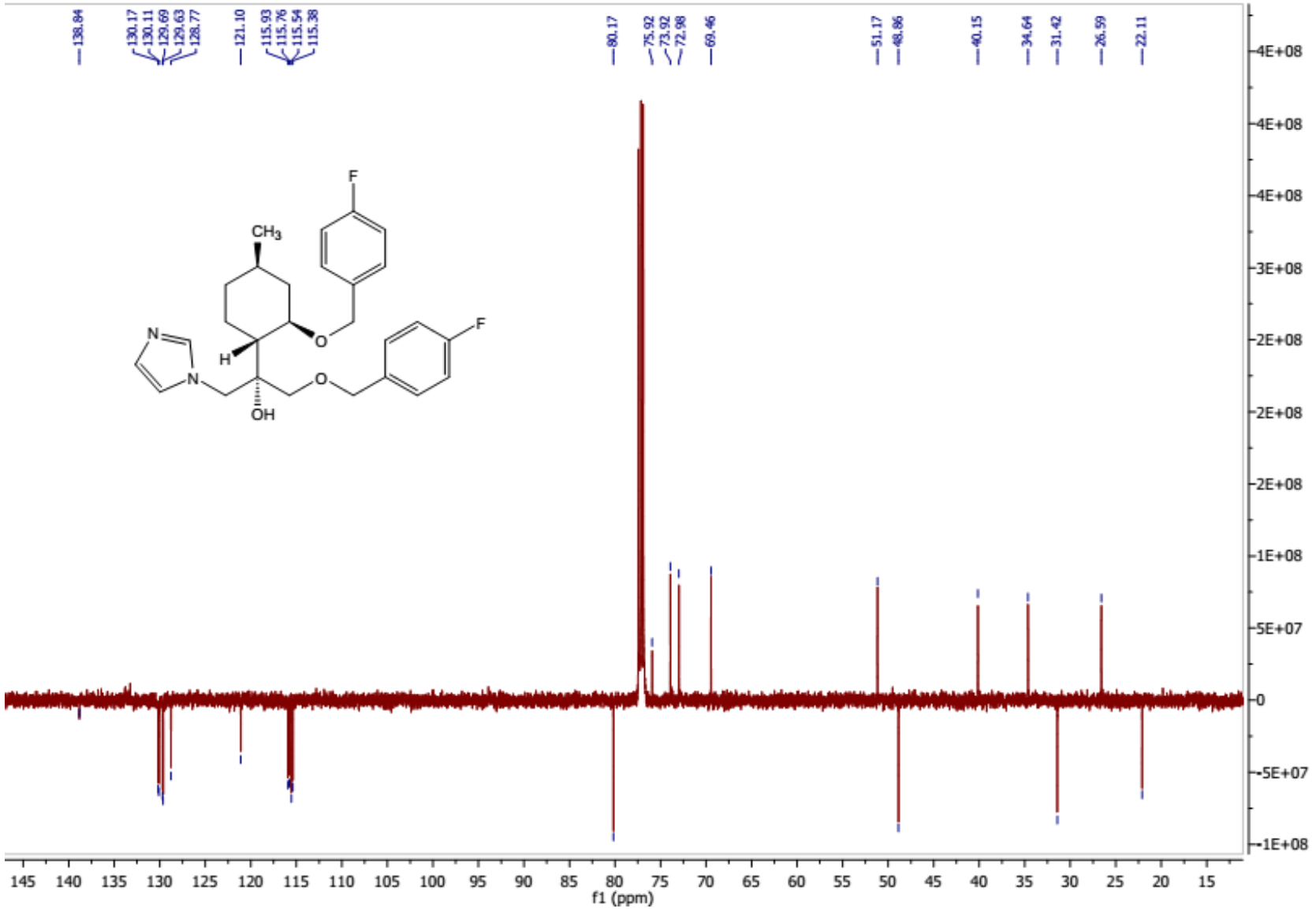
$^{13}$C-NMR of compound **47b**



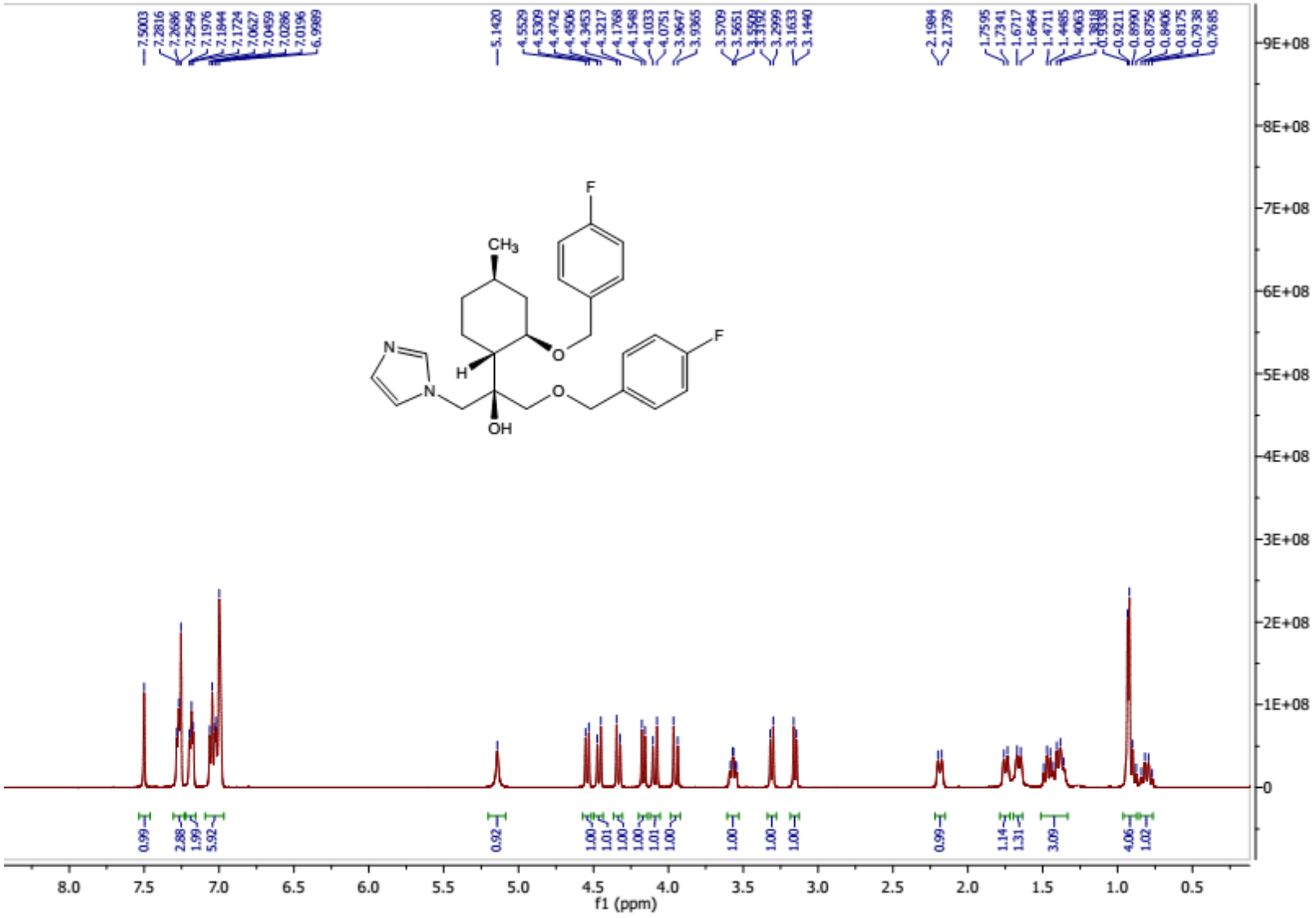
[1]H-NMR of compound **48a**



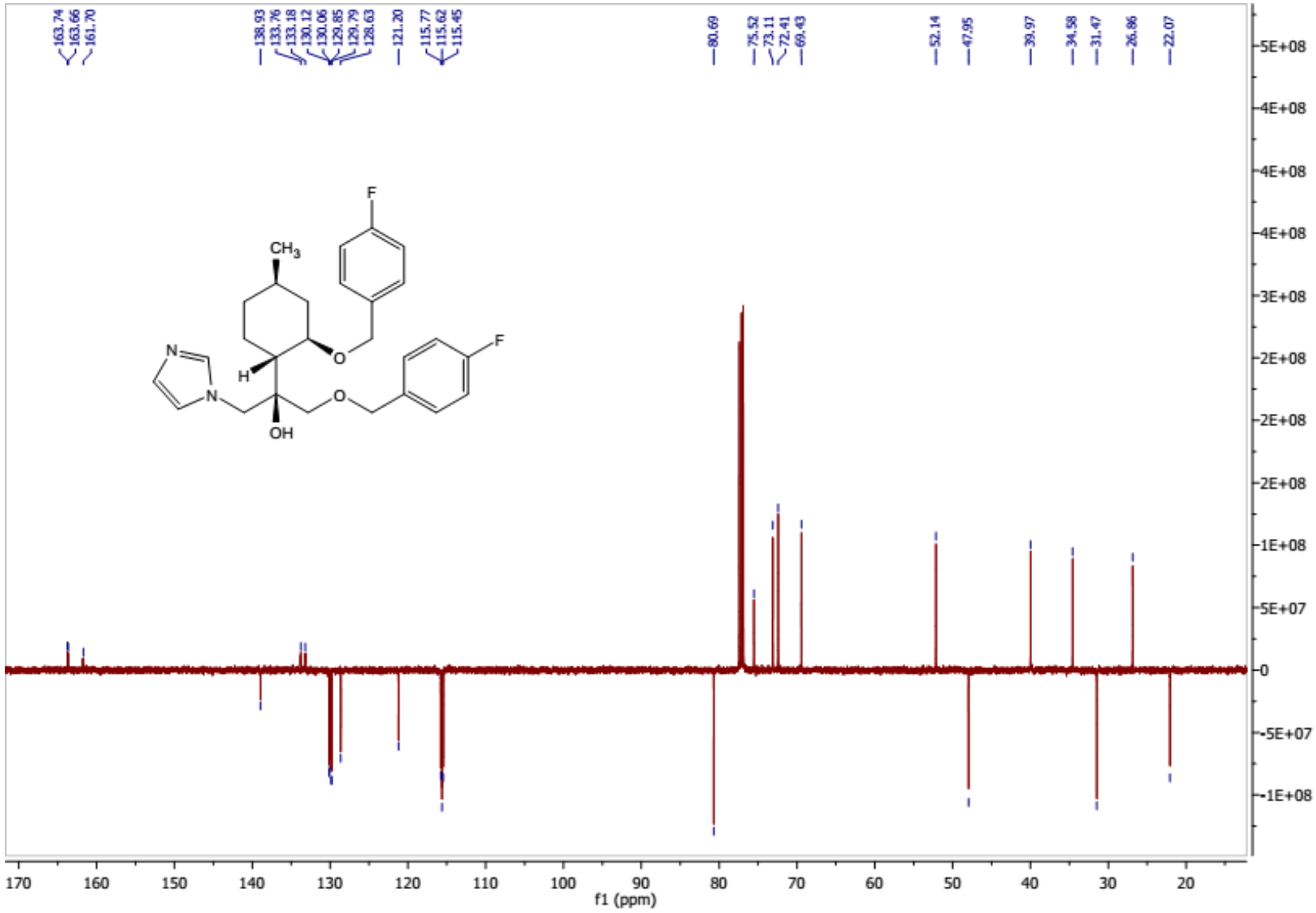
$^{13}$C-NMR of compound **48a**



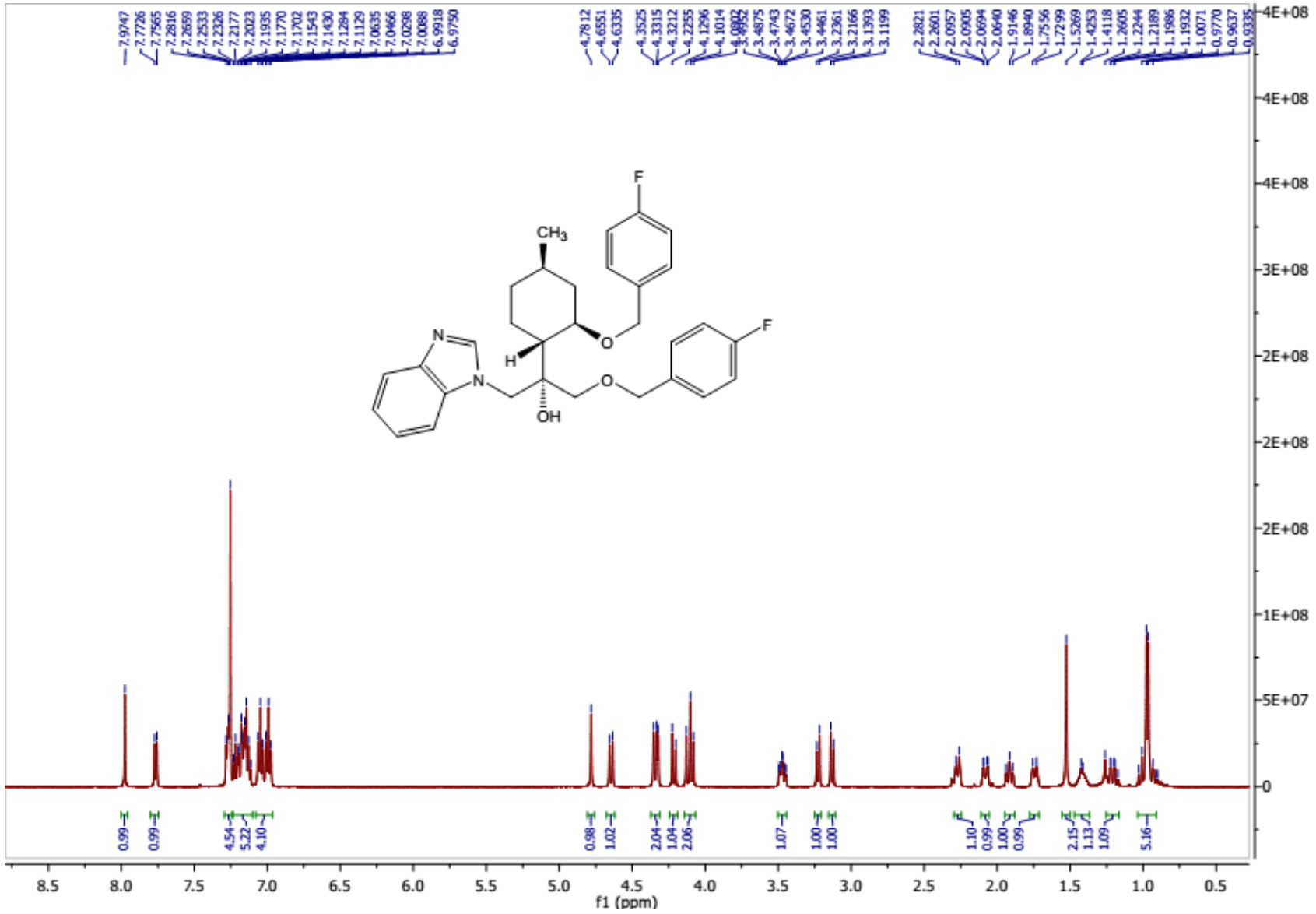
[1]H-NMR of compound **48b**



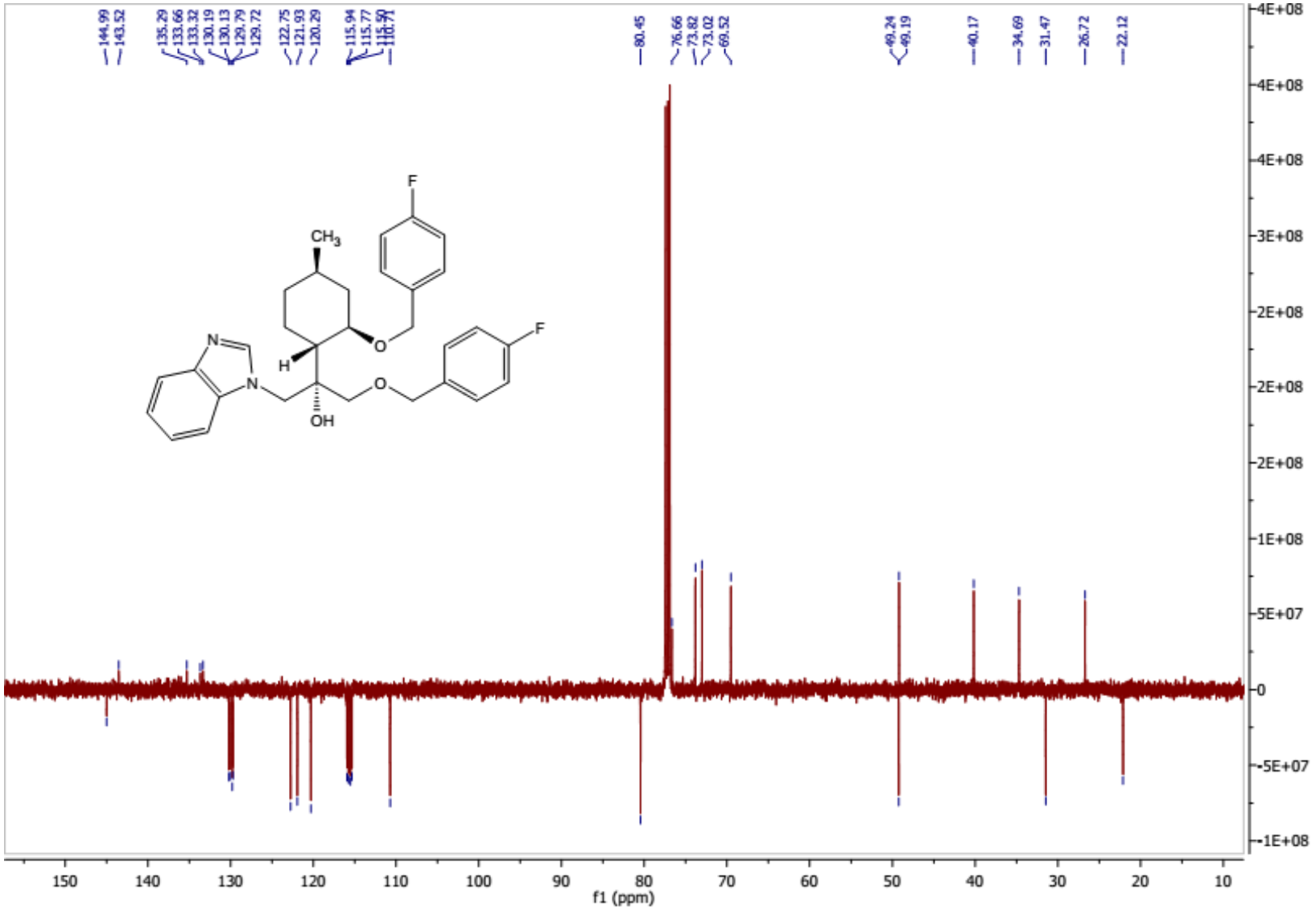
$^{13}$C-NMR of compound **48b**



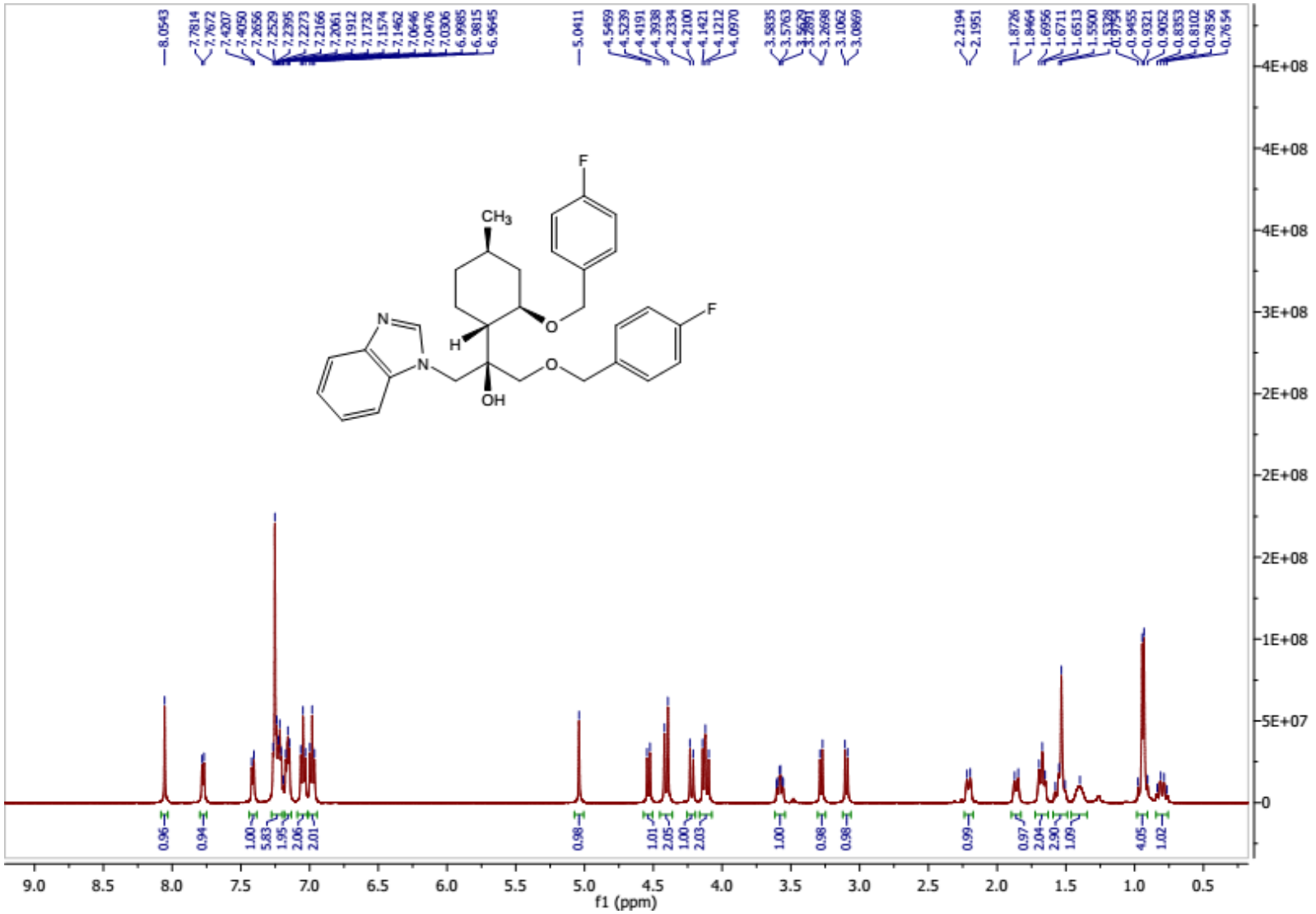
[1]H-NMR of compound **49a**



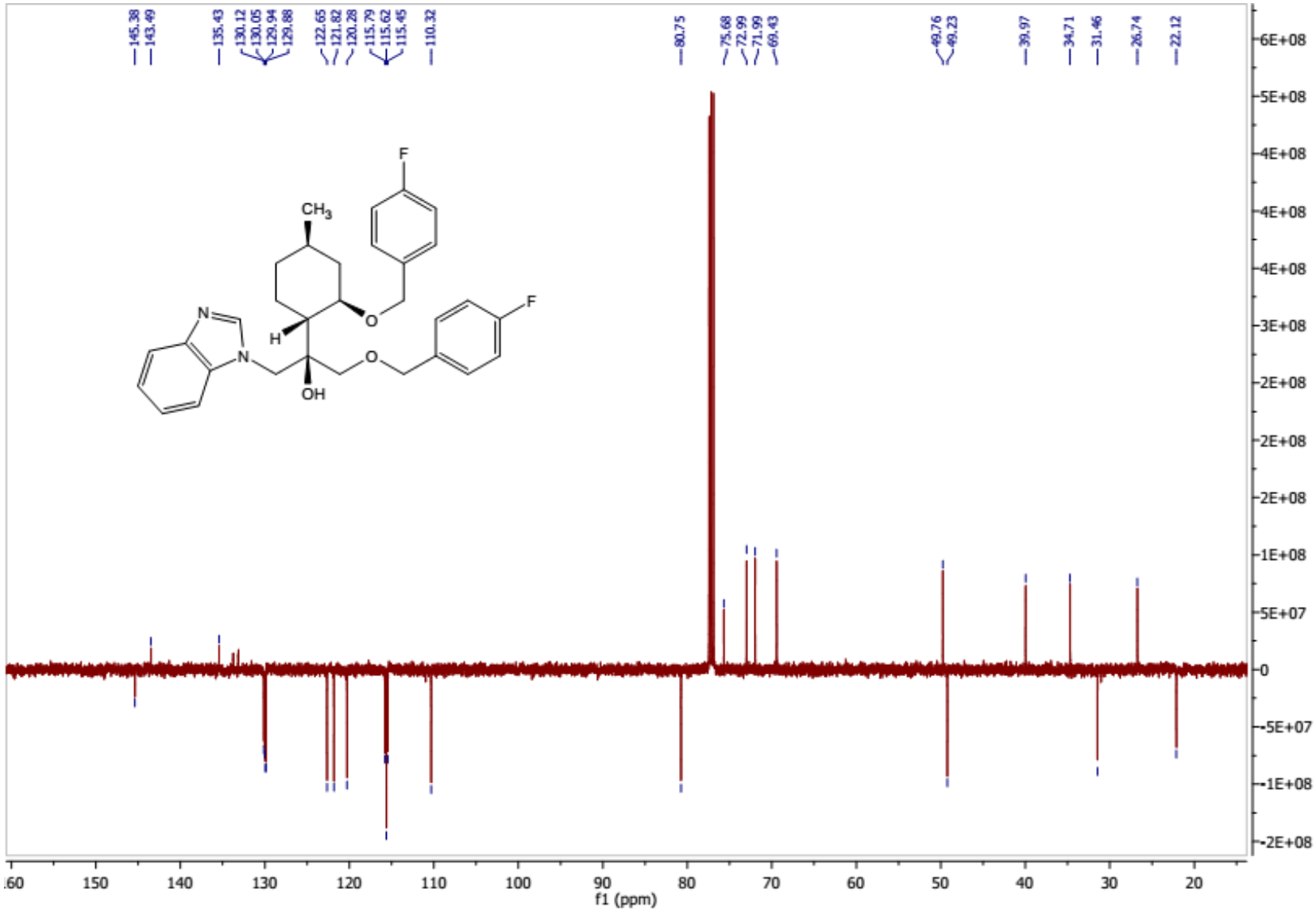
$^{13}$C-NMR of compound **49a**



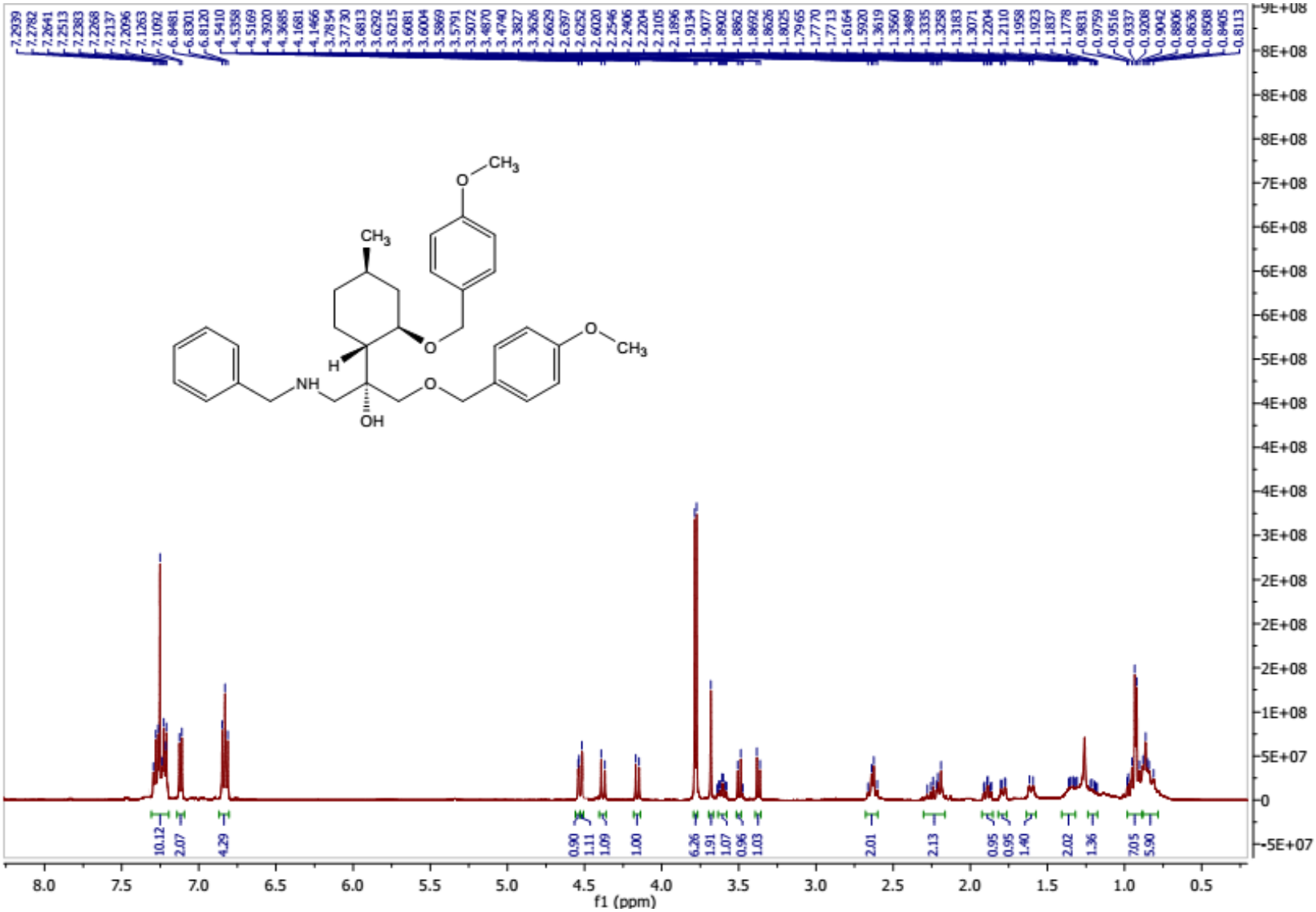
[1]H-NMR of compound **49b**



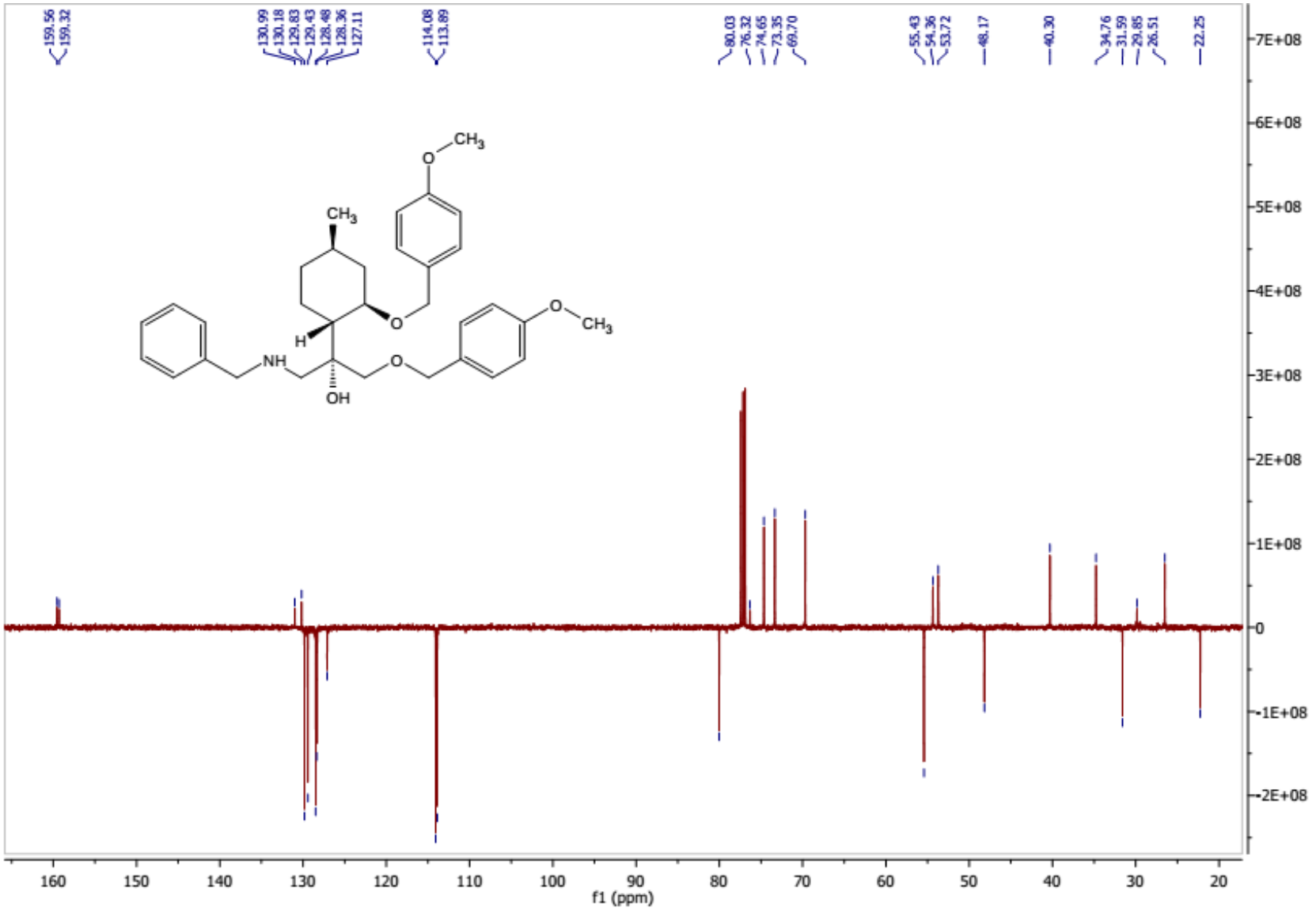
$^{13}$C-NMR of compound **49b**



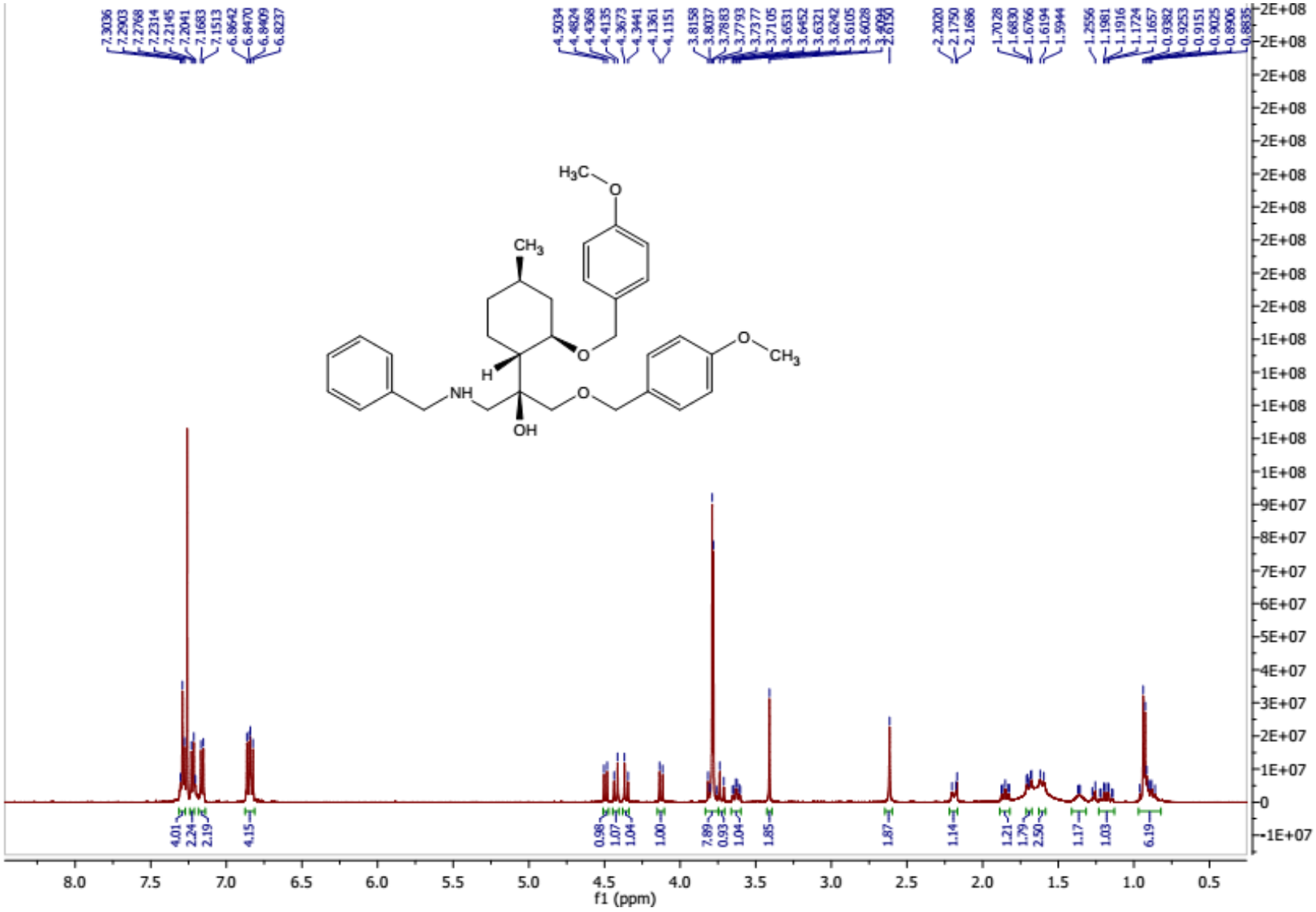
[1]H-NMR of compound **50a**



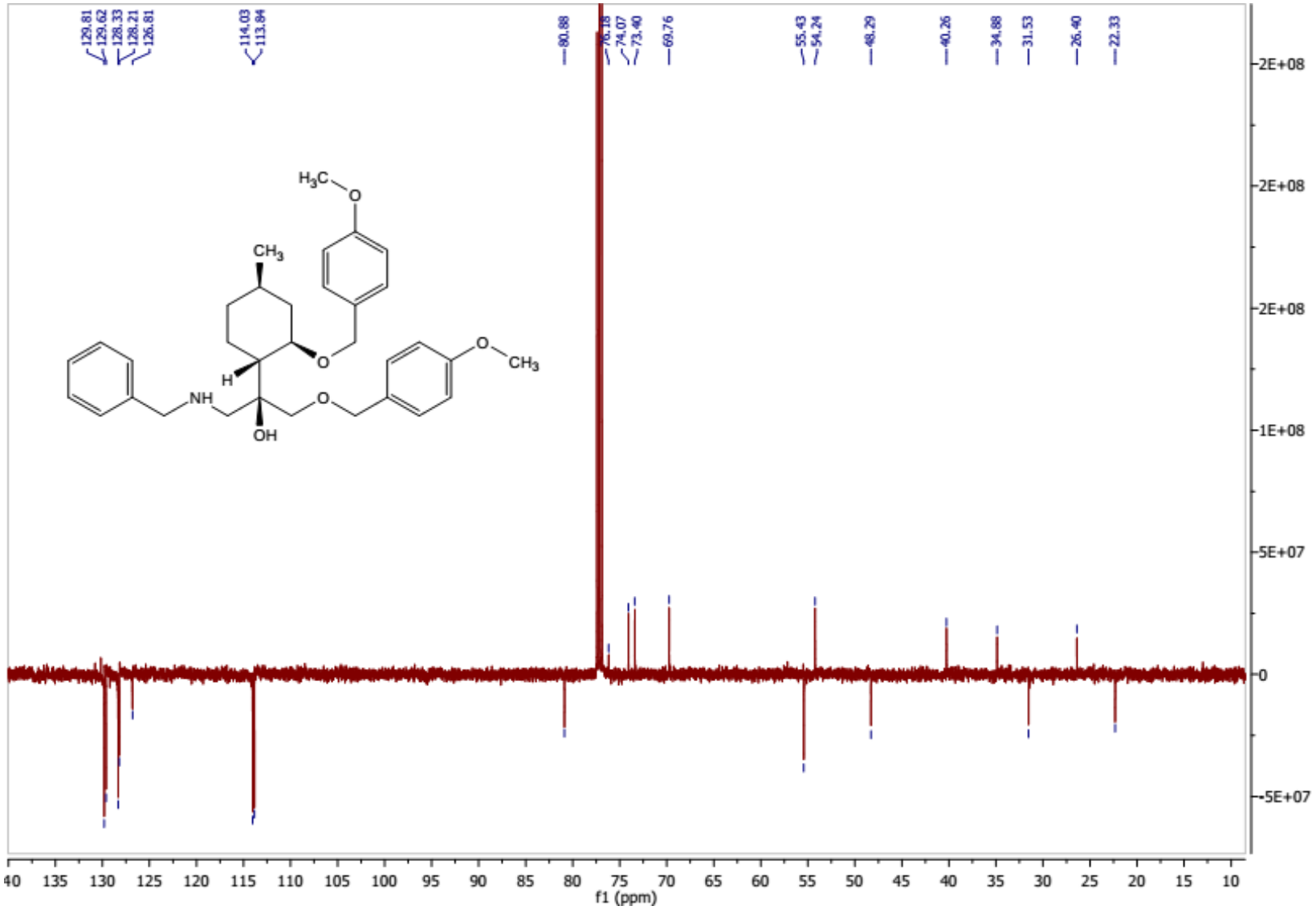
$^{13}$C-NMR of compound **50a**



[1]H-NMR of compound **50b**



$^{13}$C-NMR of compound **50b**



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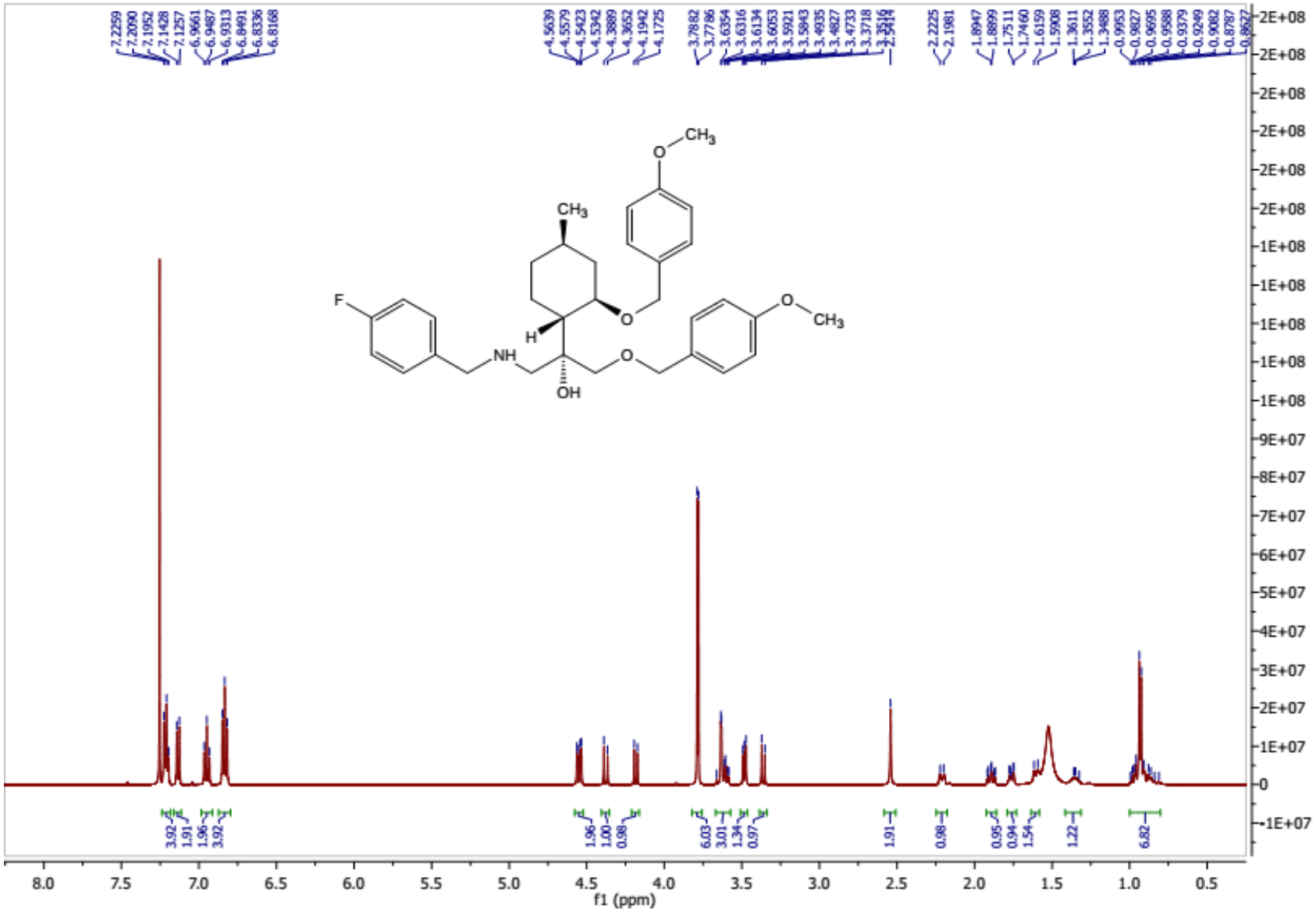
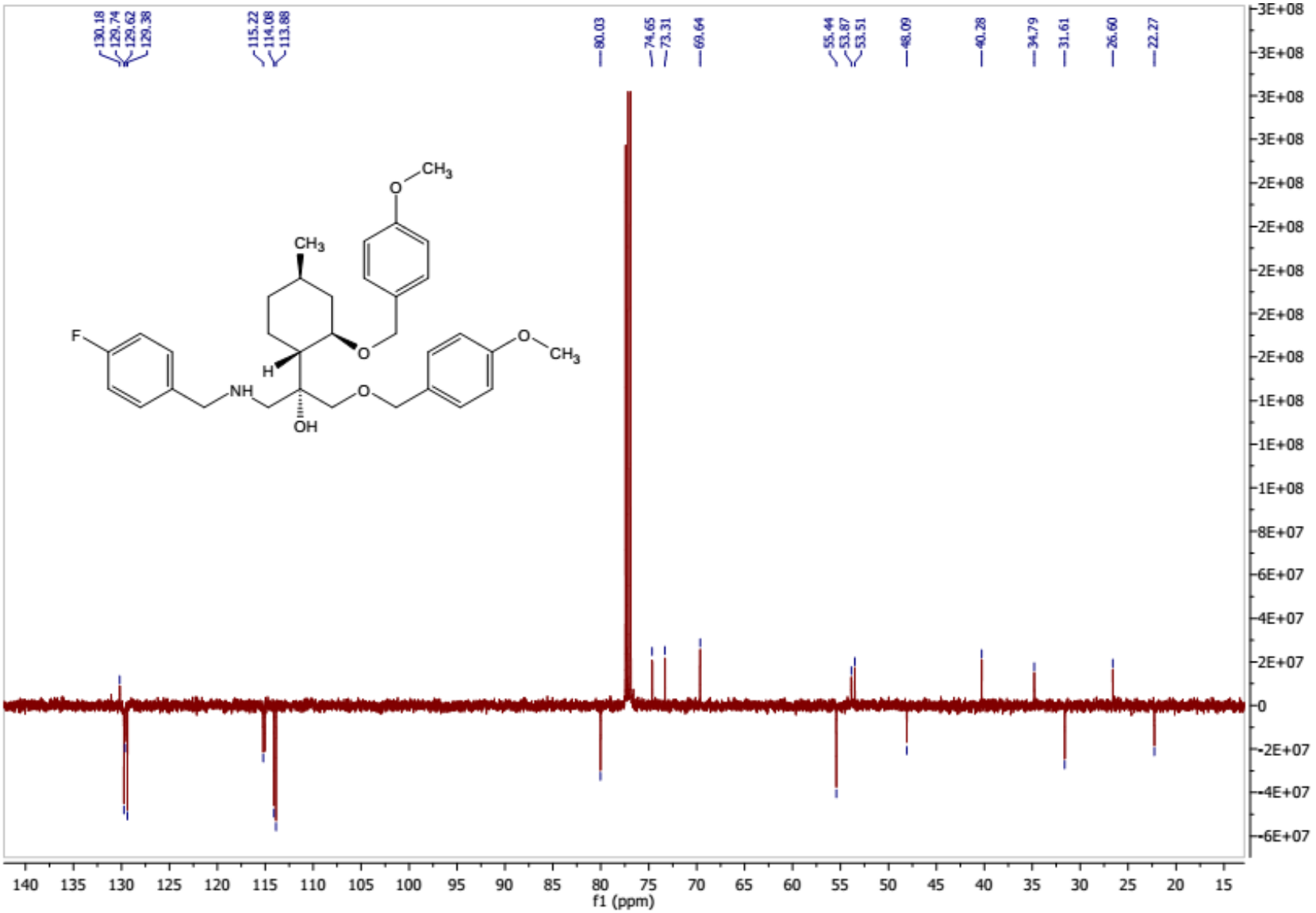


$^{13}$C-NMR of compound **51a**



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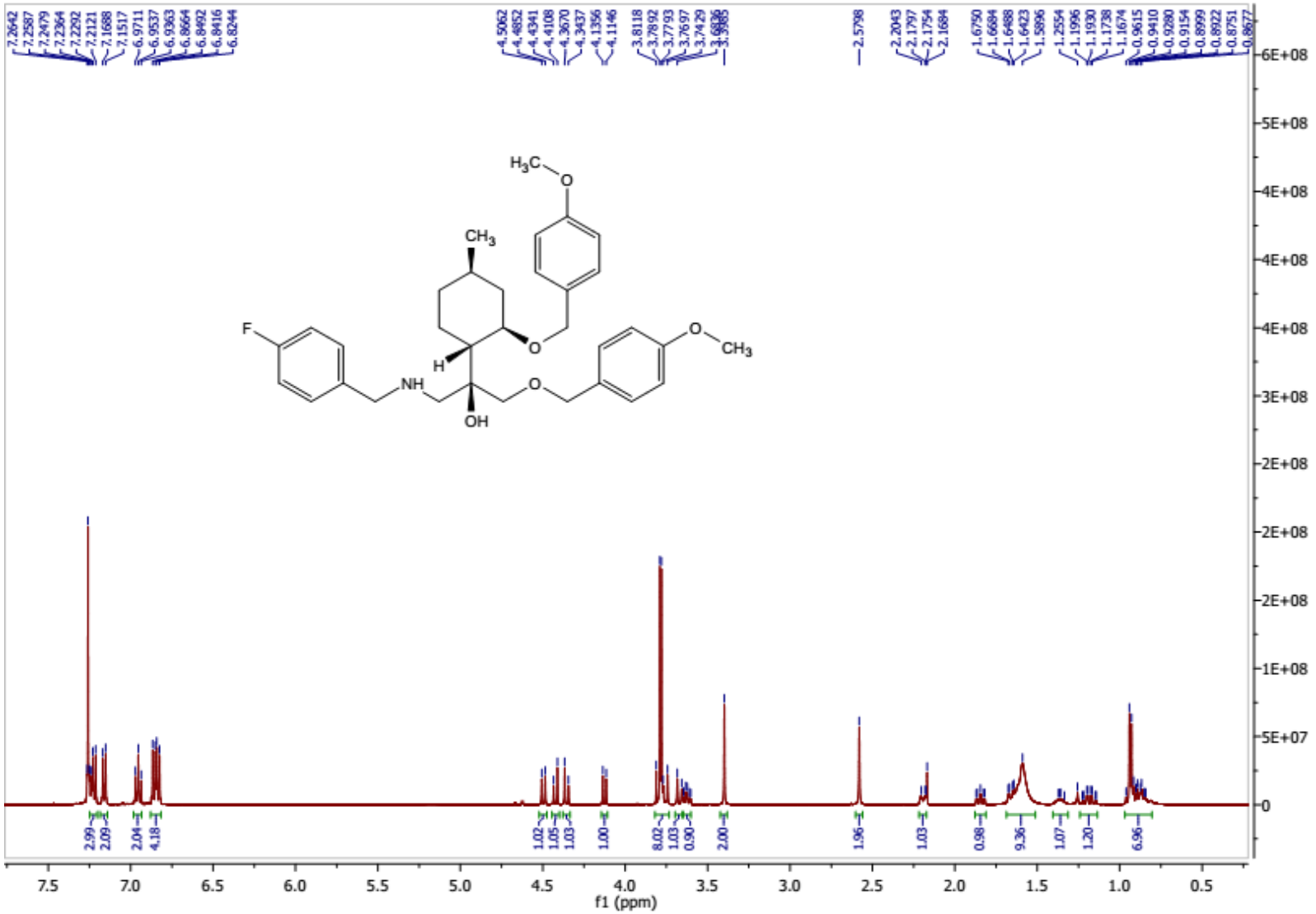
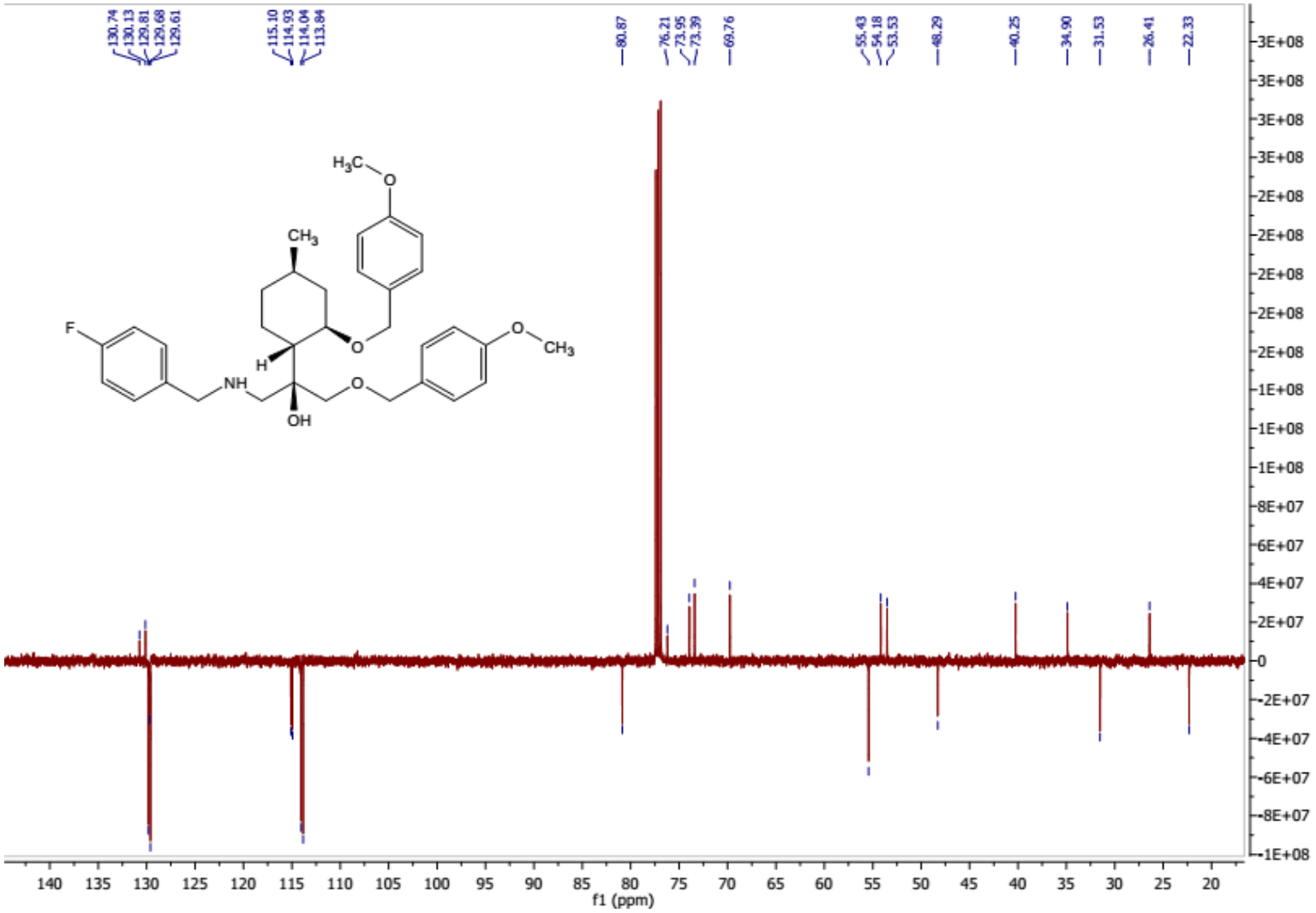


$^{13}$C-NMR of compound **51b**



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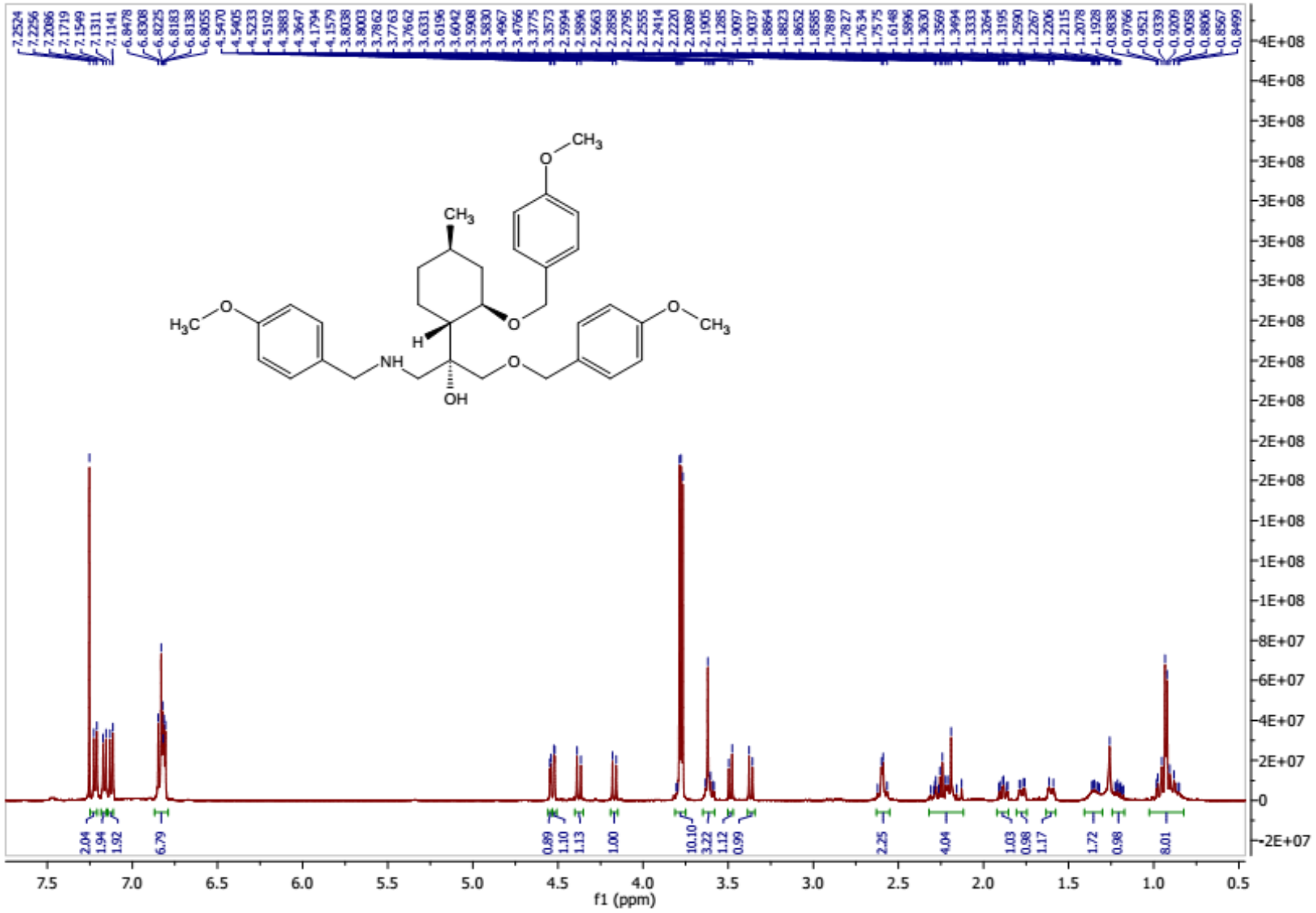
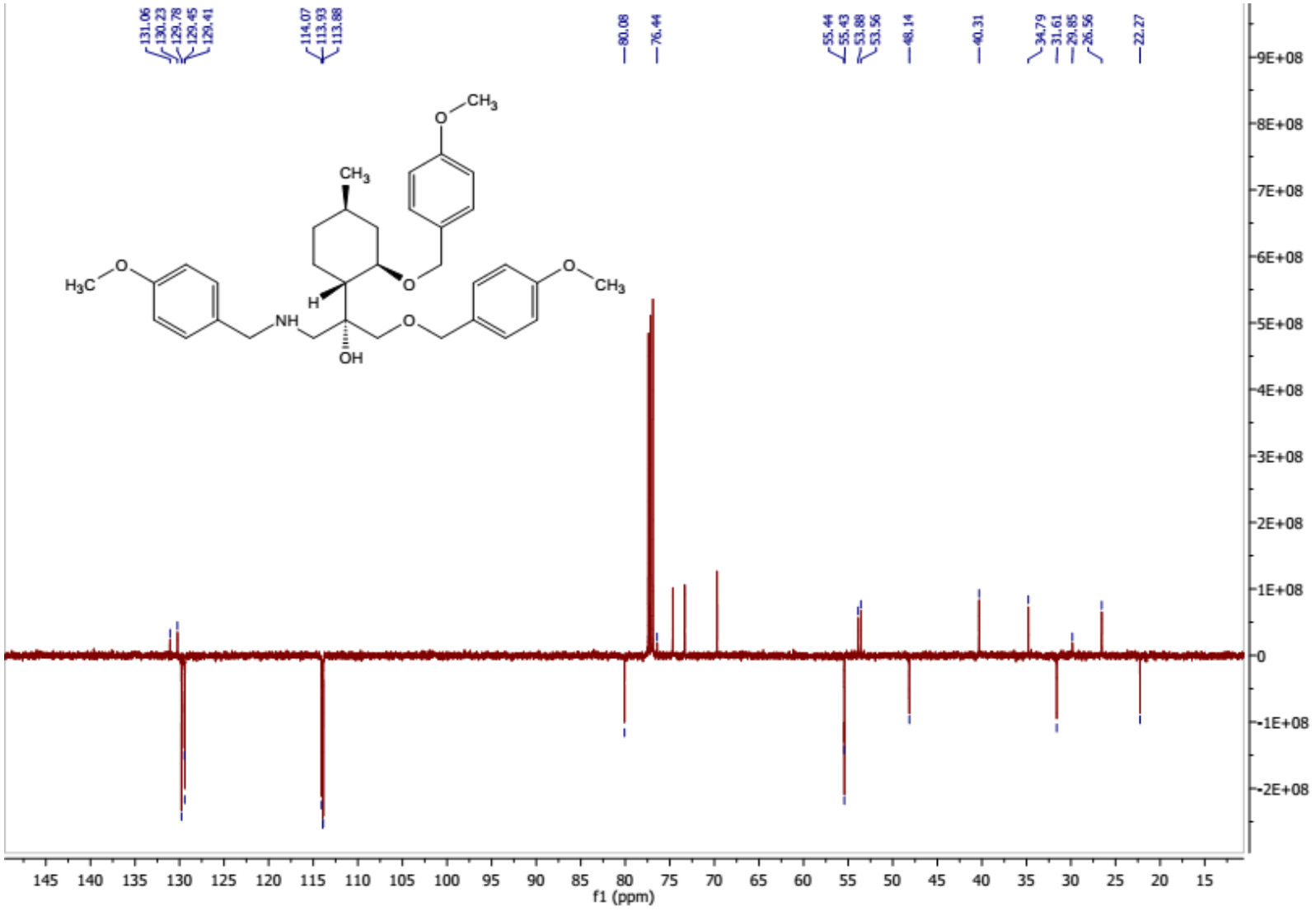
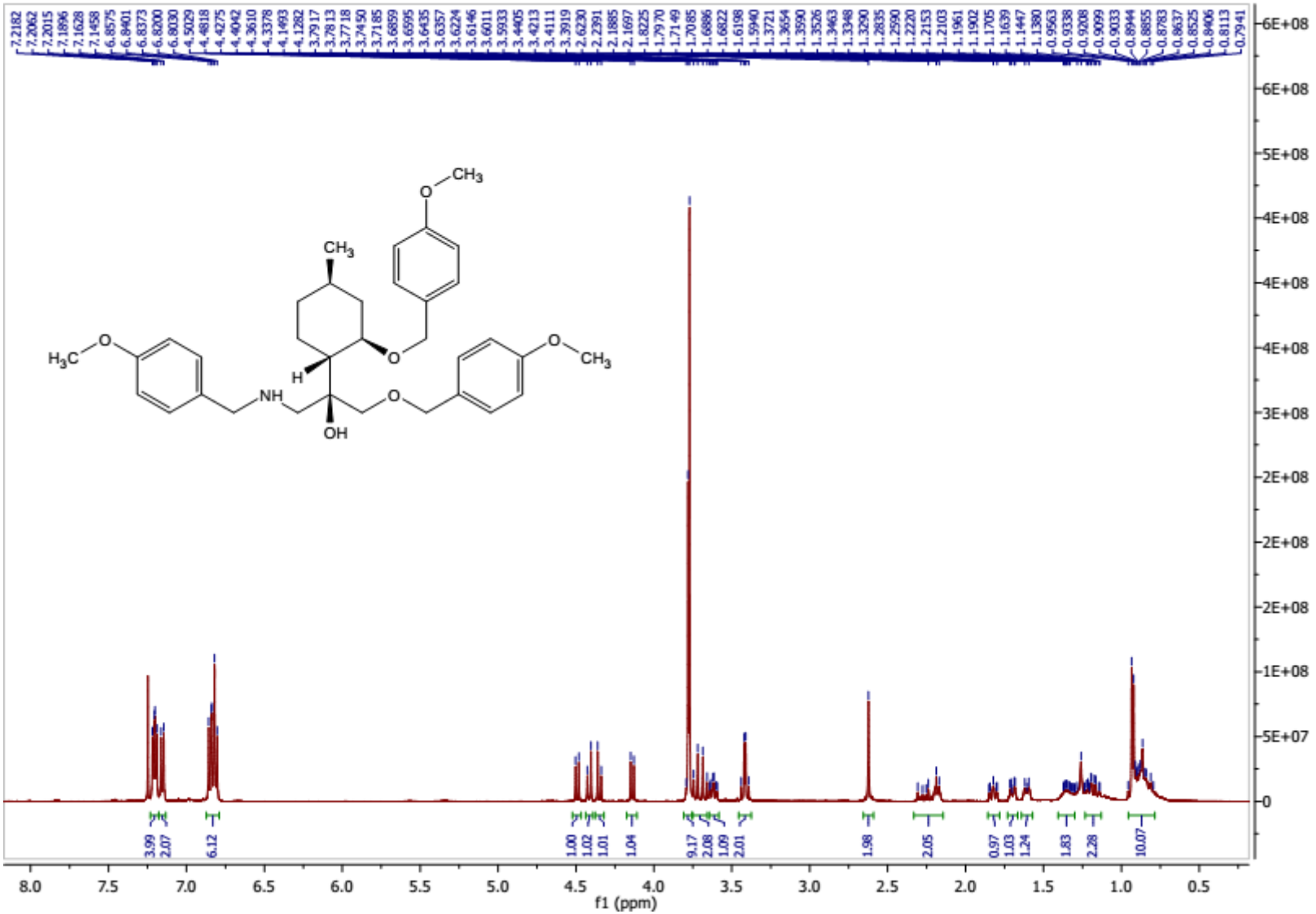


$^{13}$C-NMR of compound **52a**



[1]H-NMR of compound **52b**



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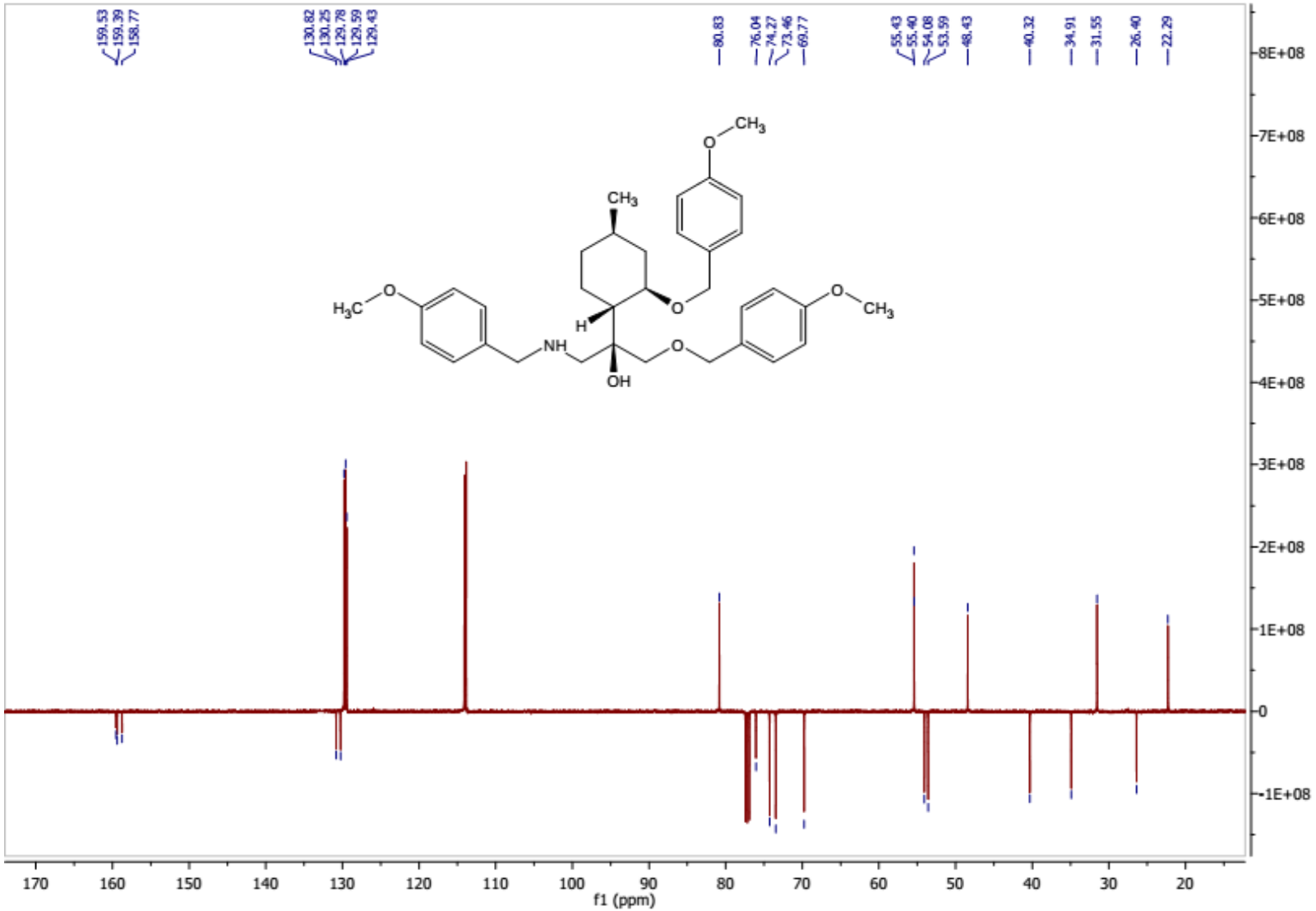

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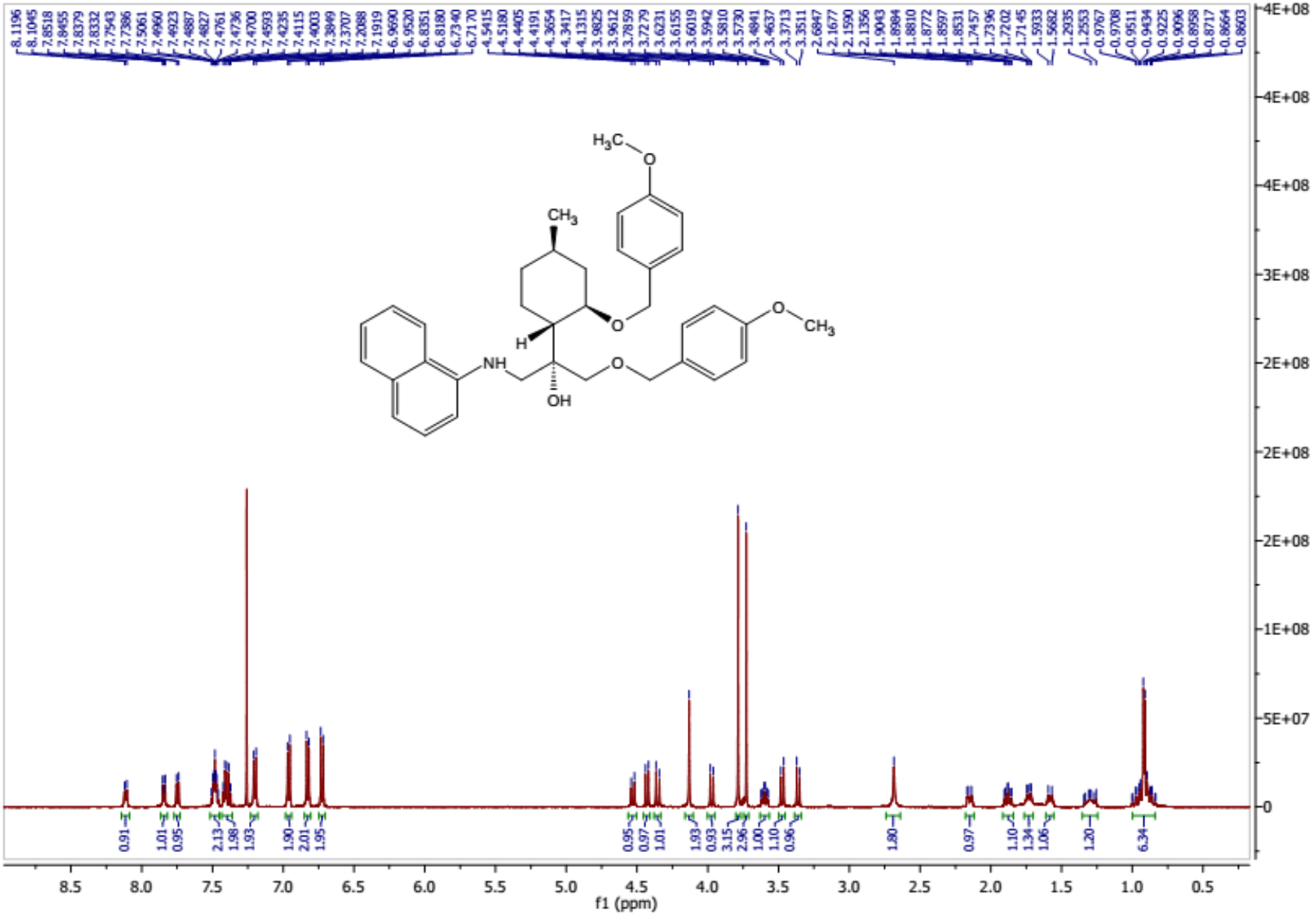

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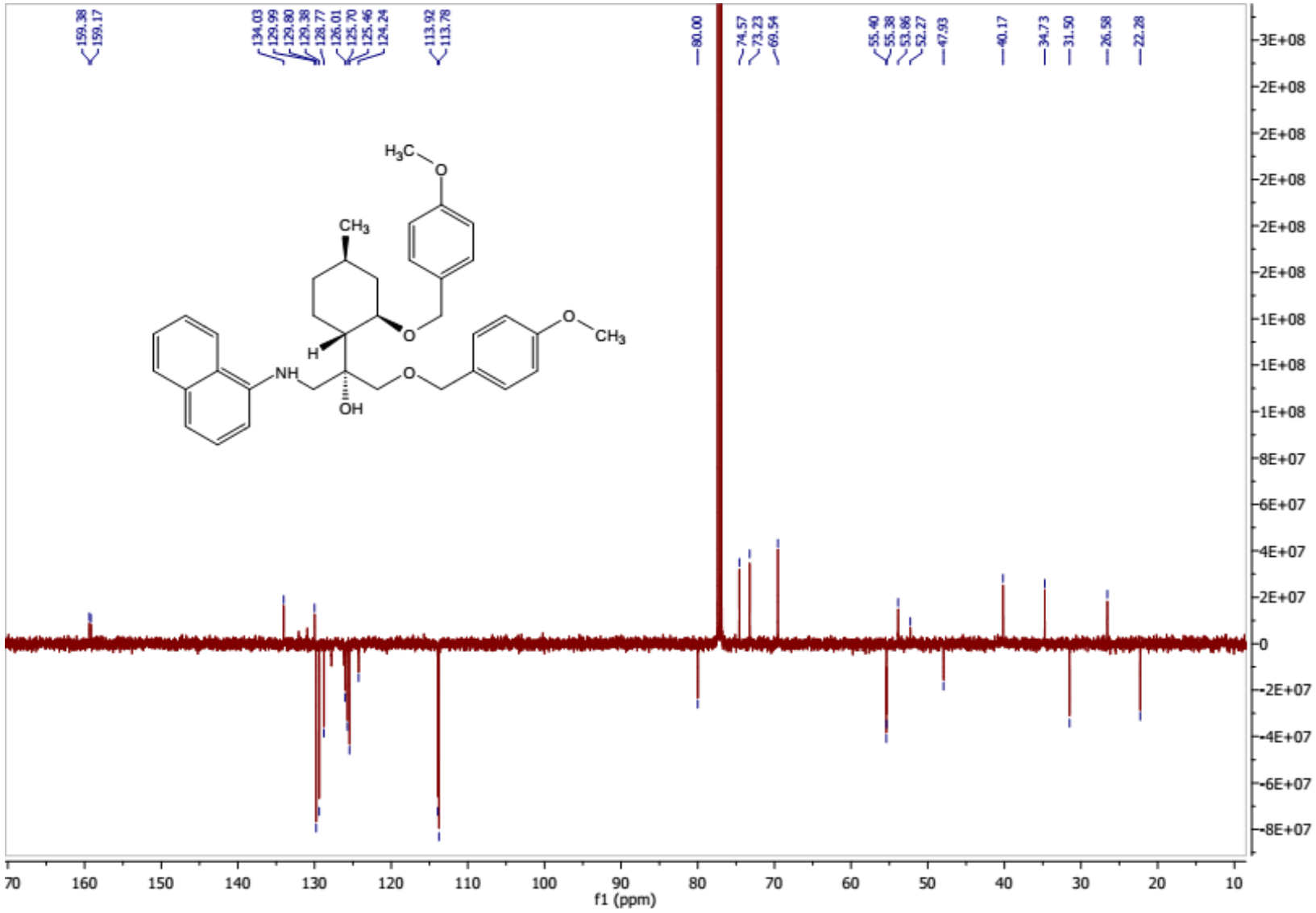

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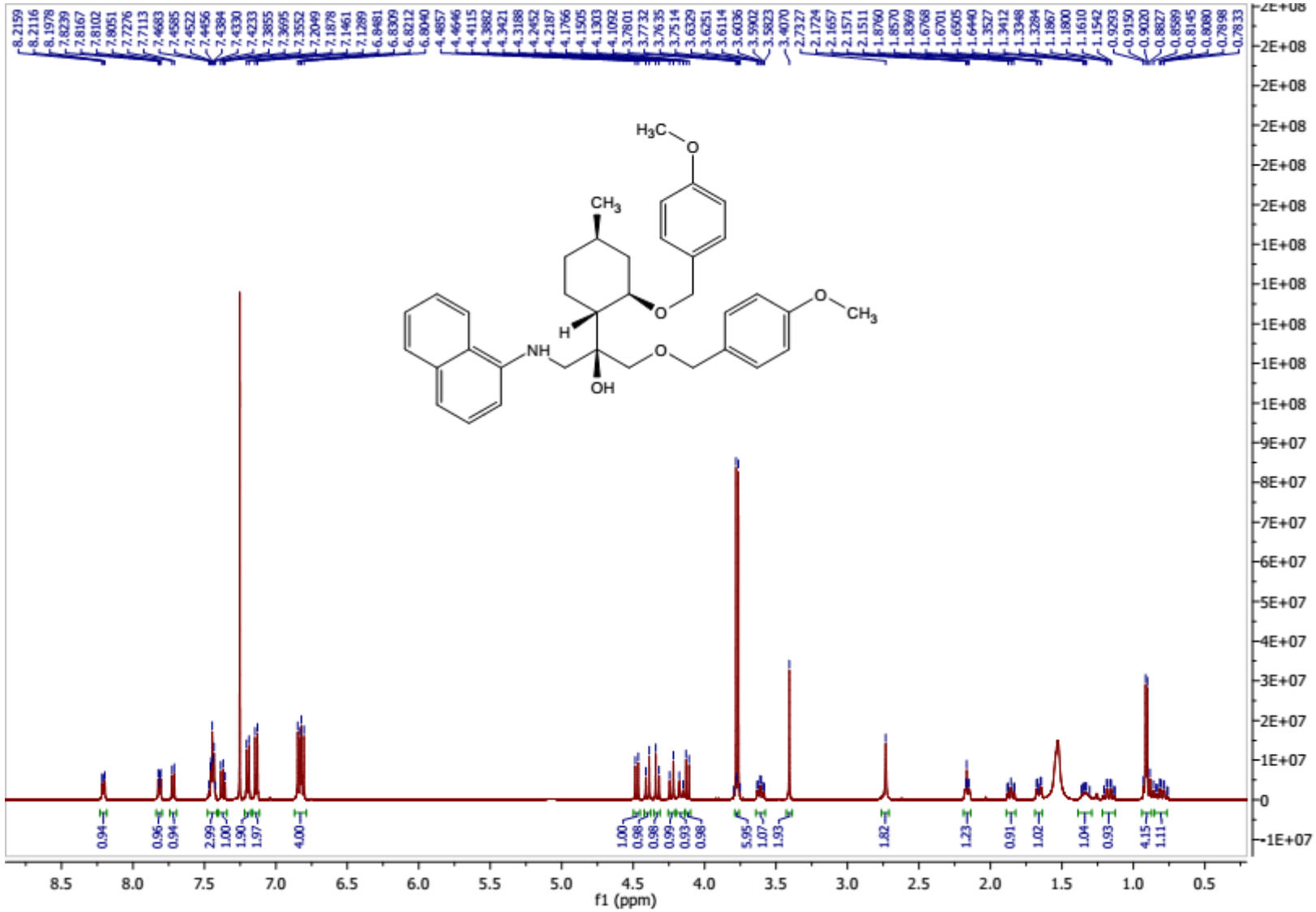
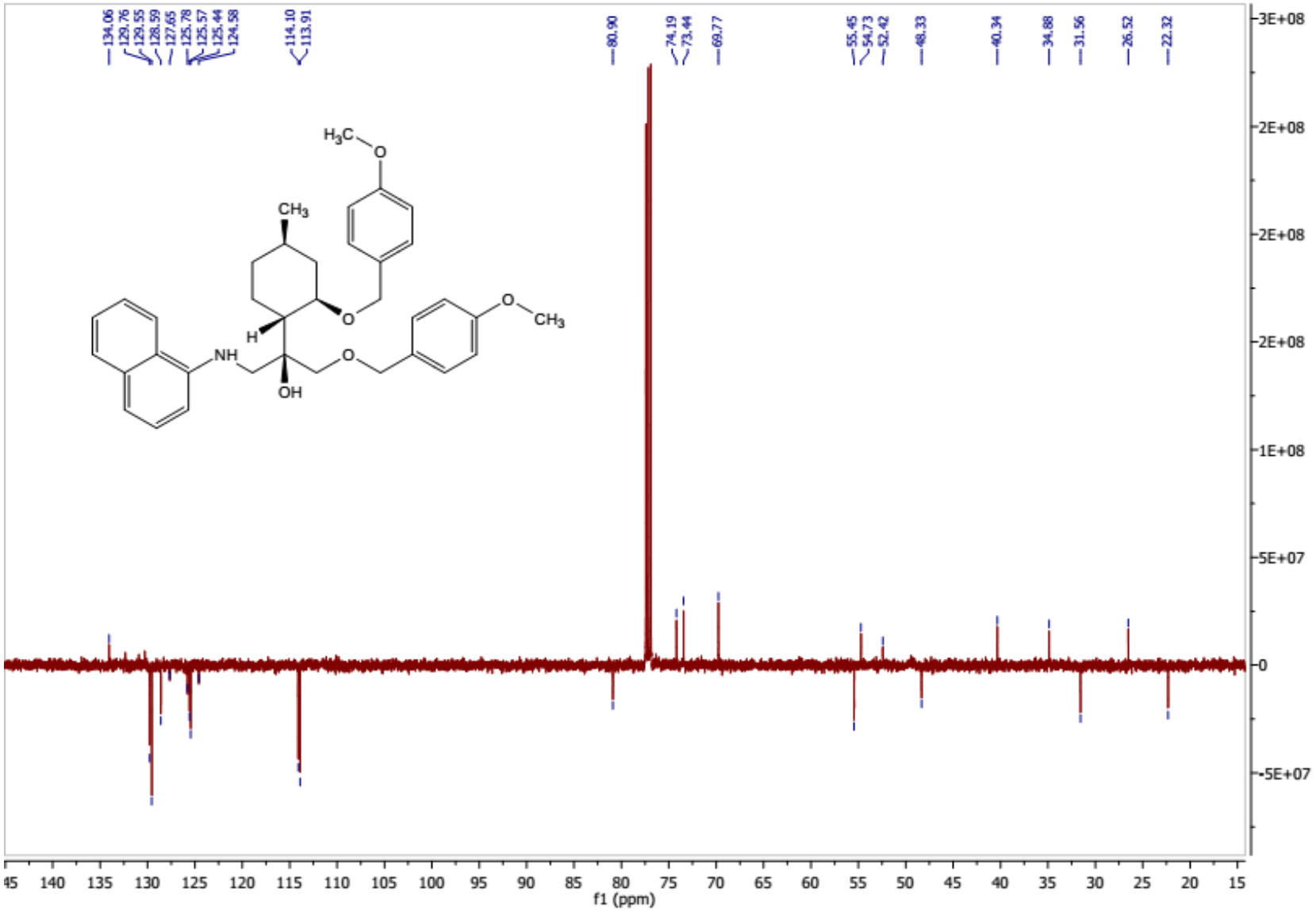


$^{13}$C-NMR of compound **53b**



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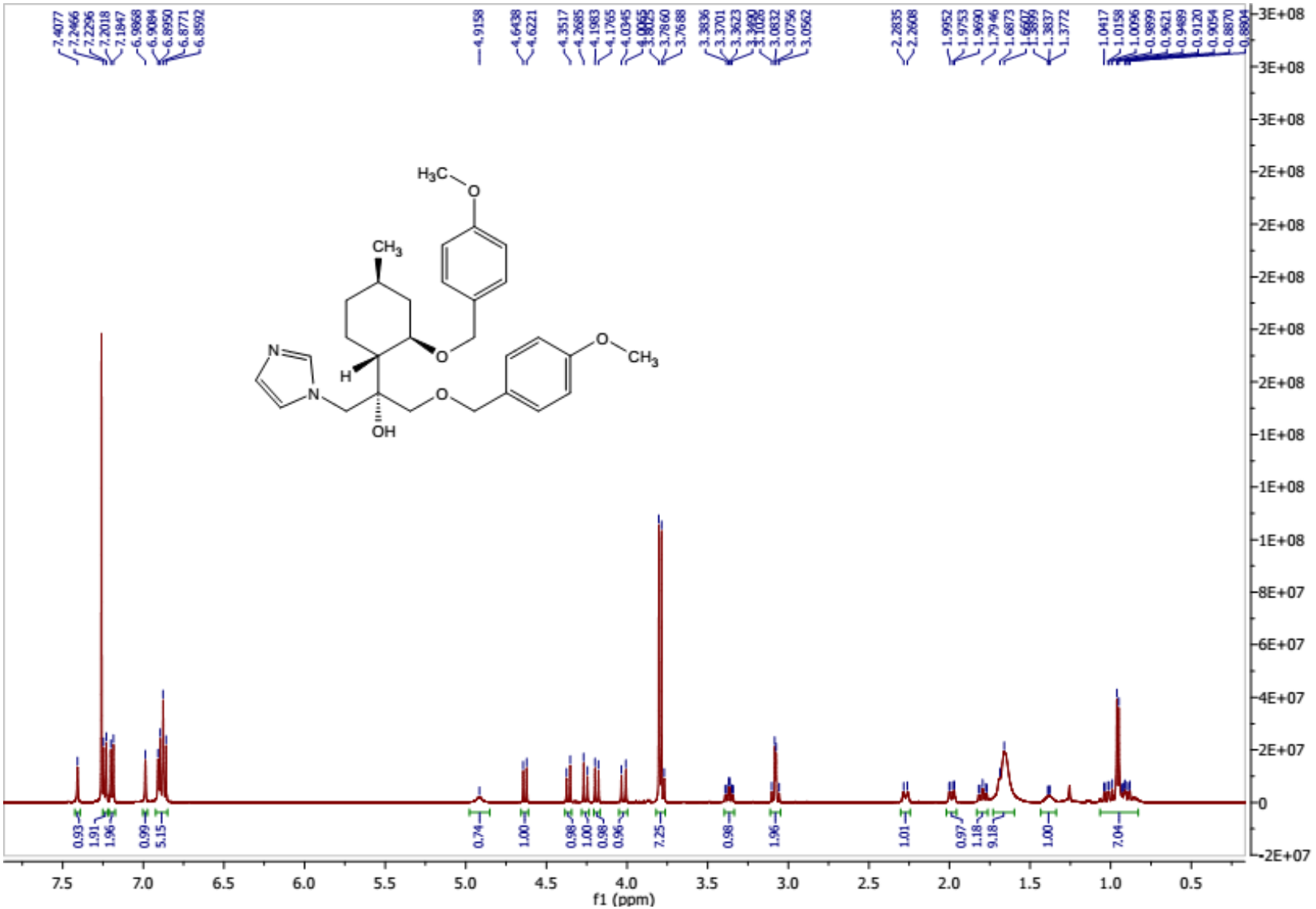

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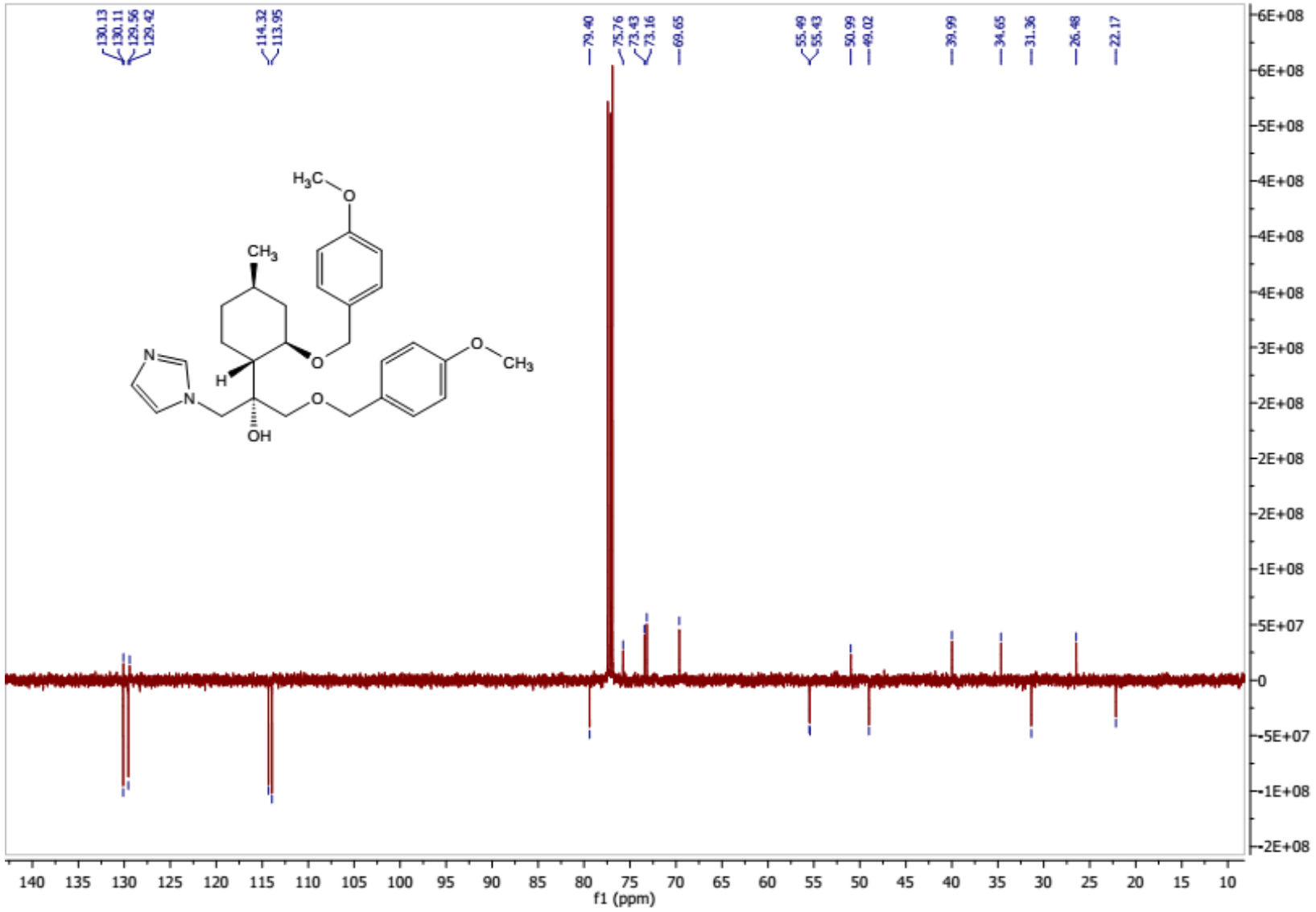
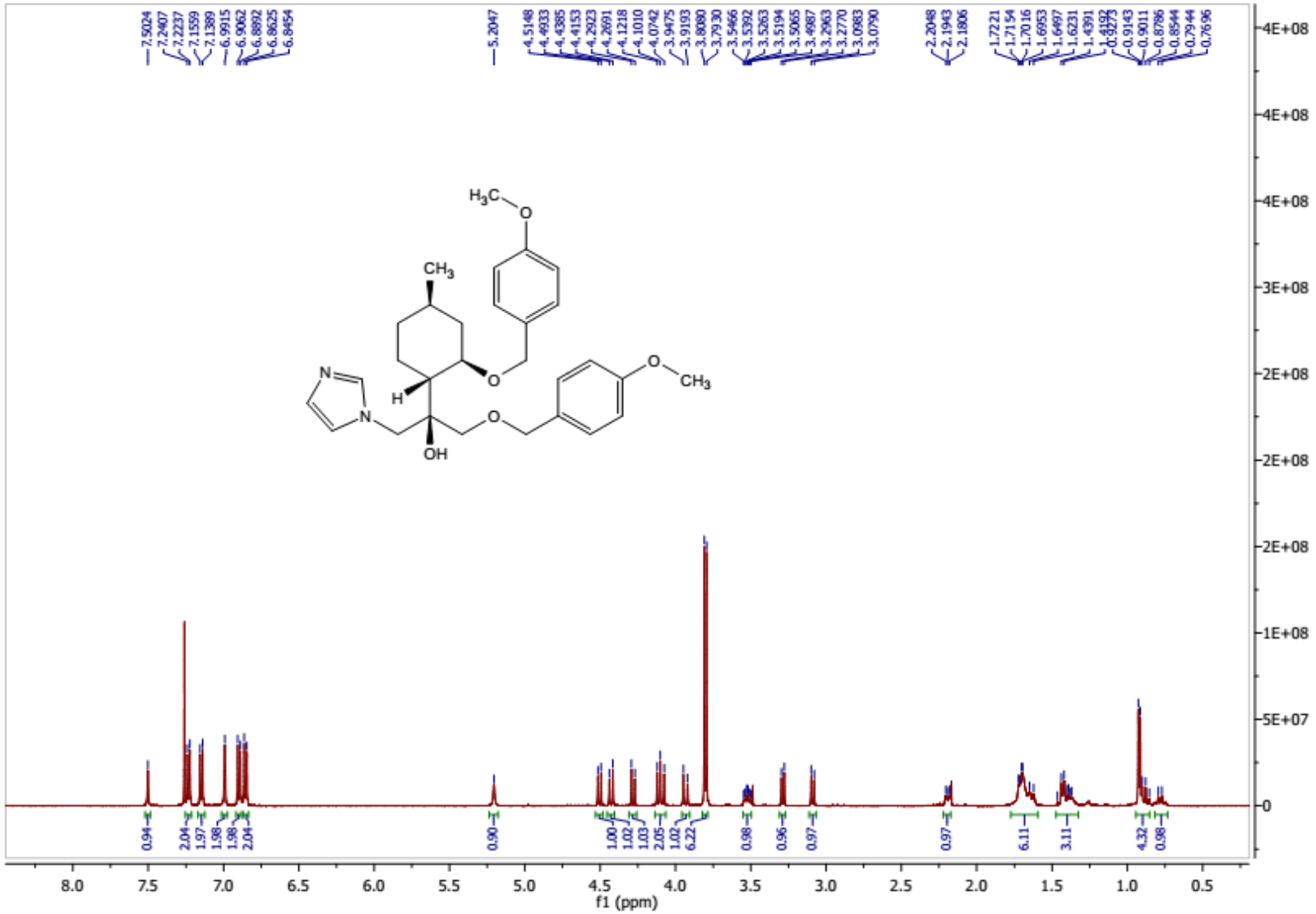


$^{1}$H-NMR of compound **54b**



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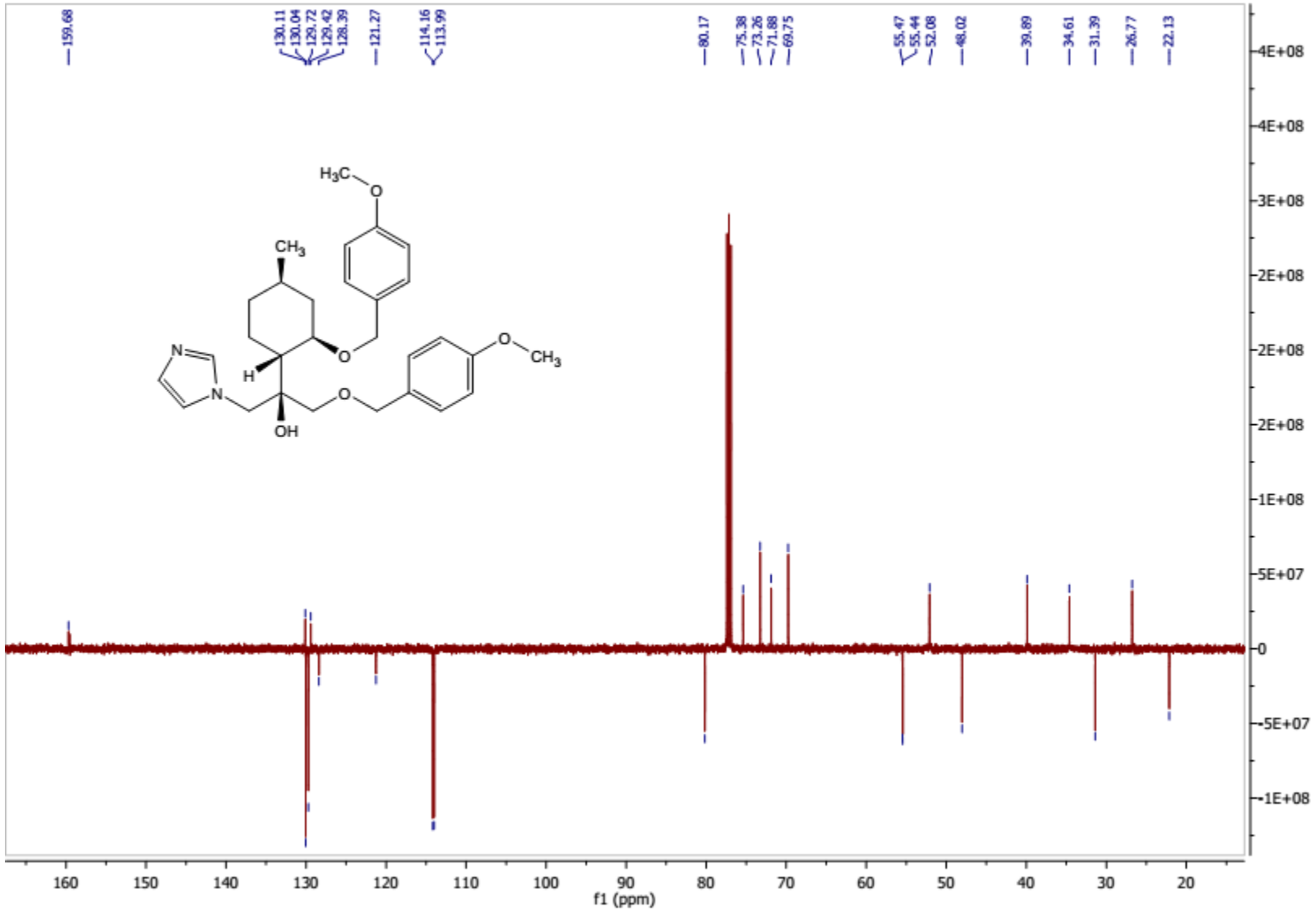

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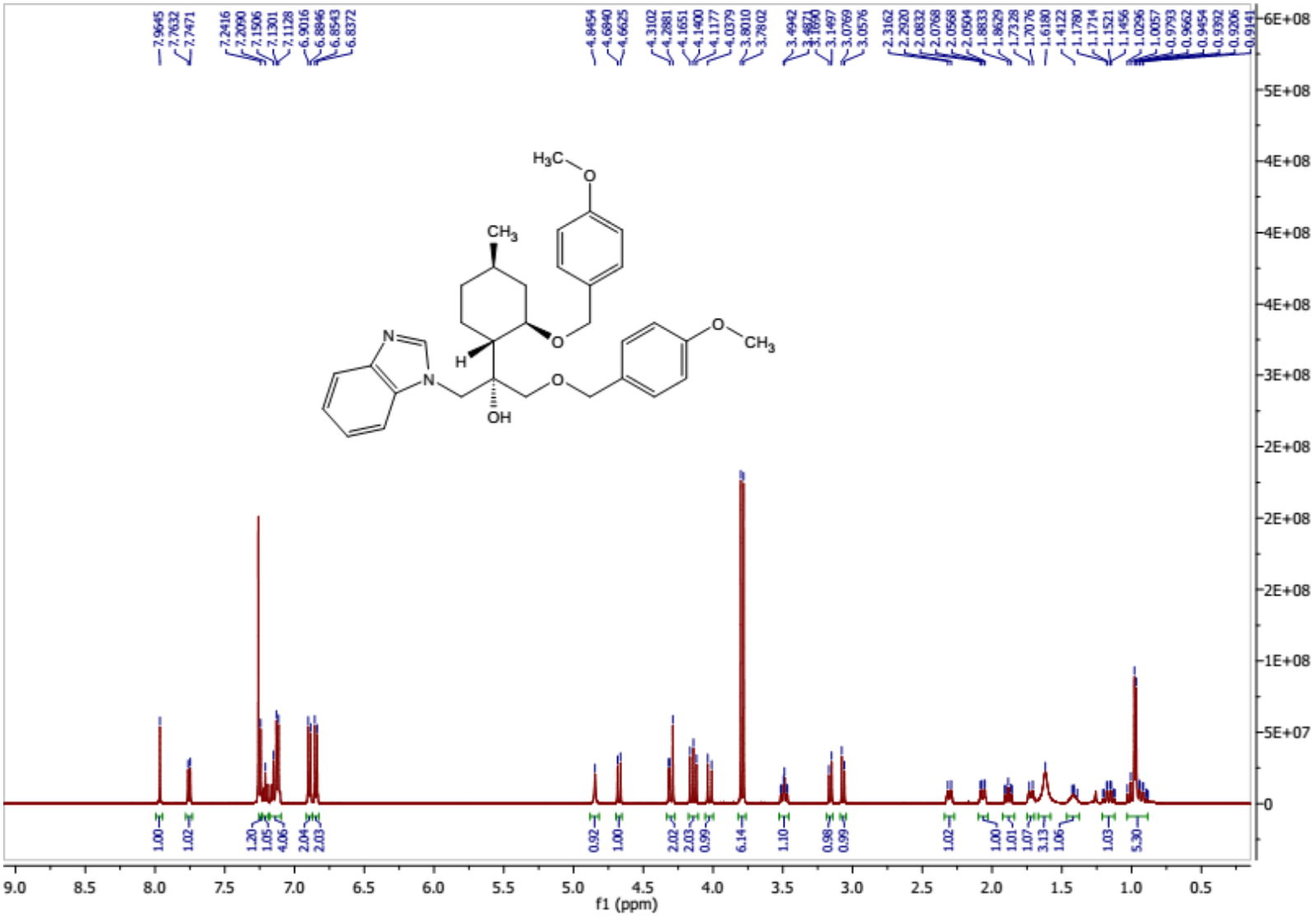
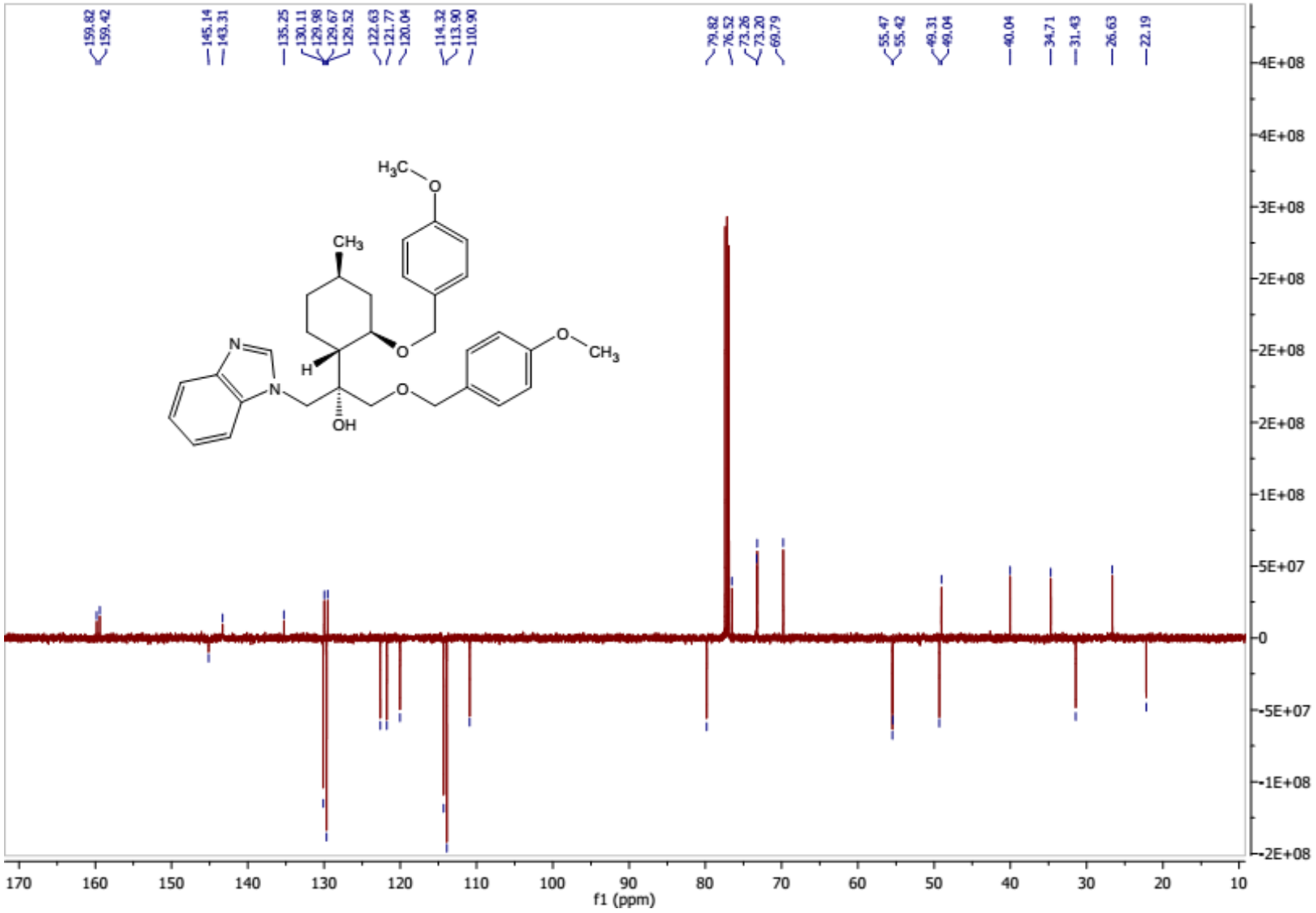
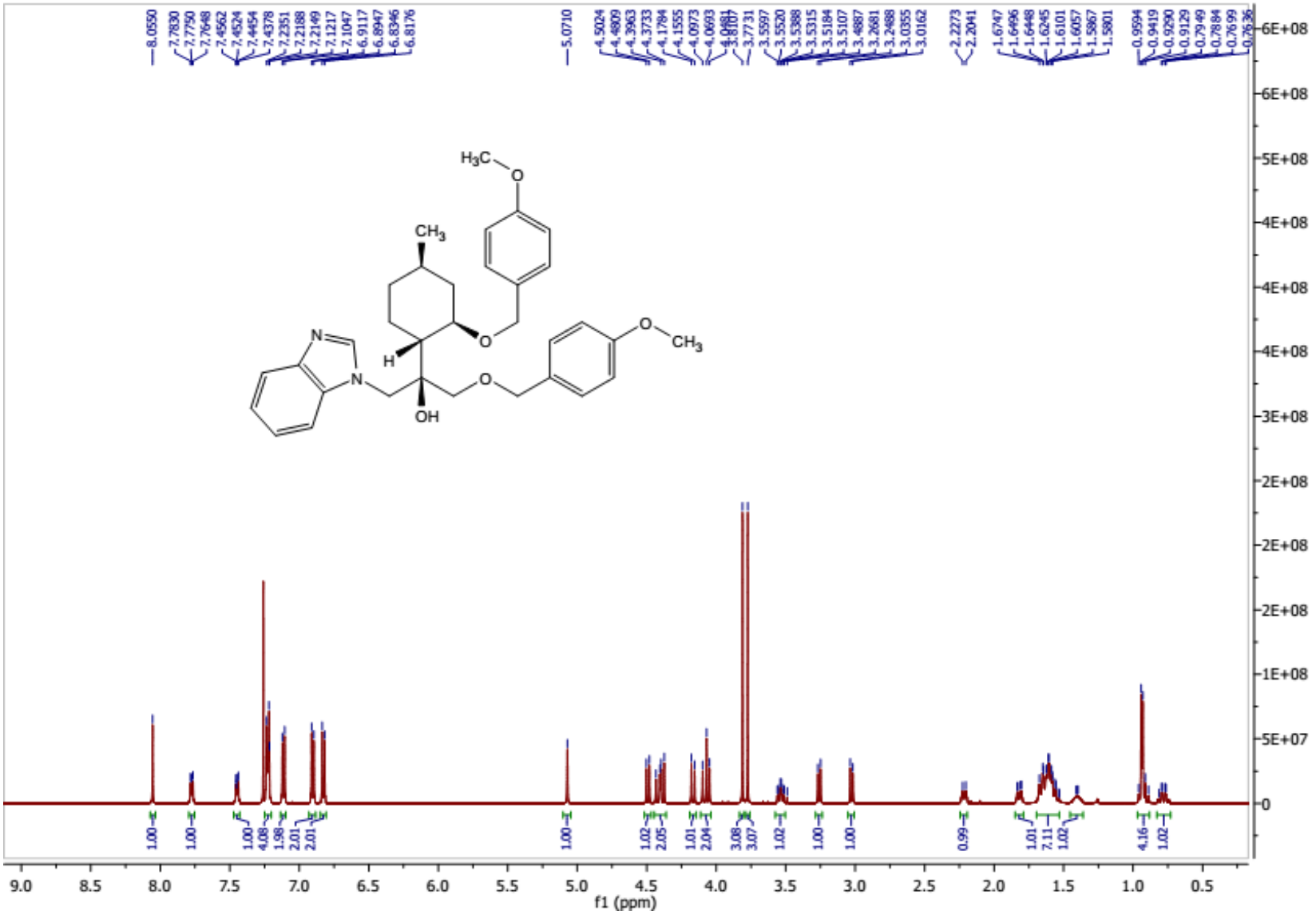


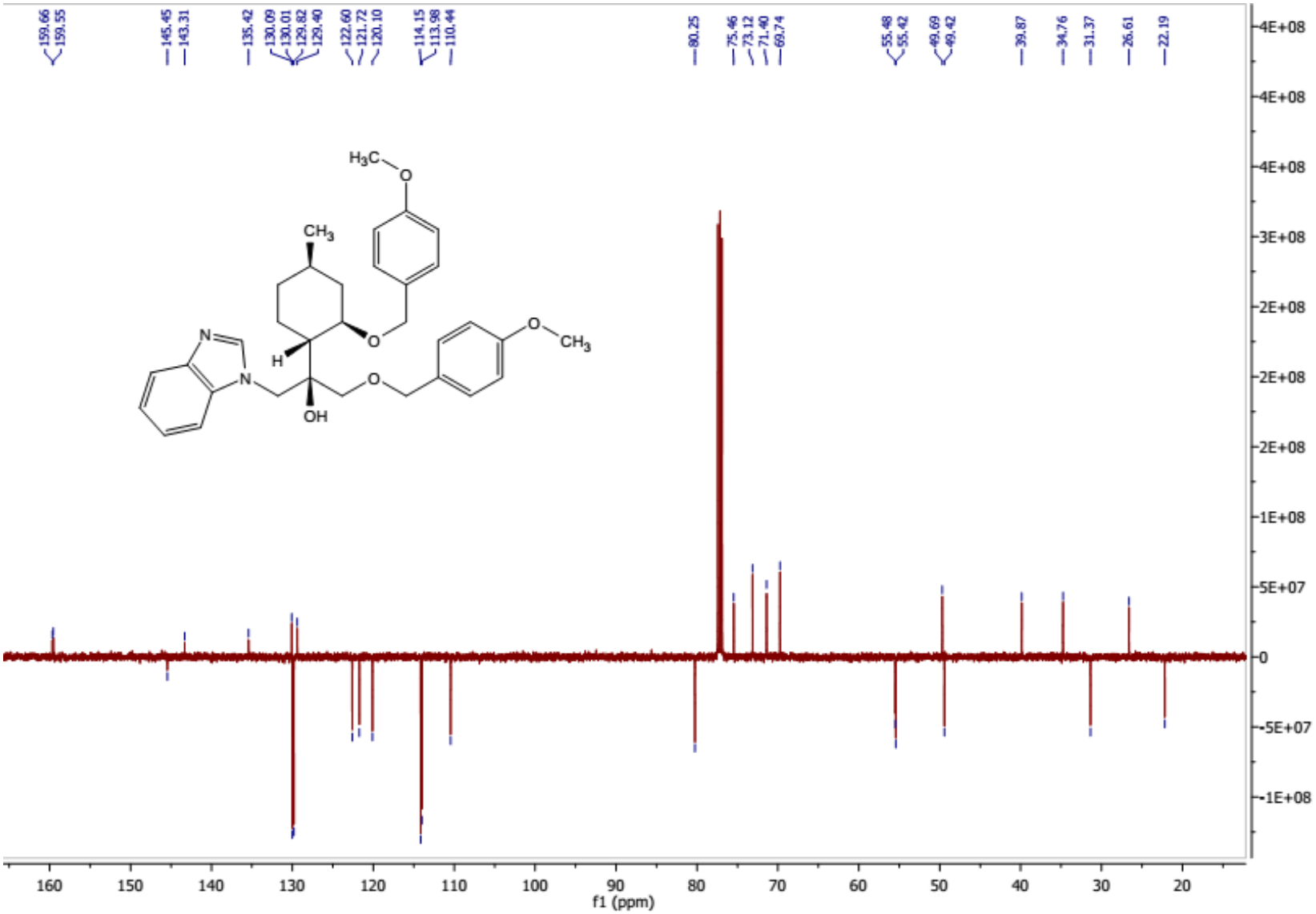
$^{13}$C-NMR of compound **55a**



[1]H-NMR of compound **55b**



$^{13}$C-NMR of compound **55b**



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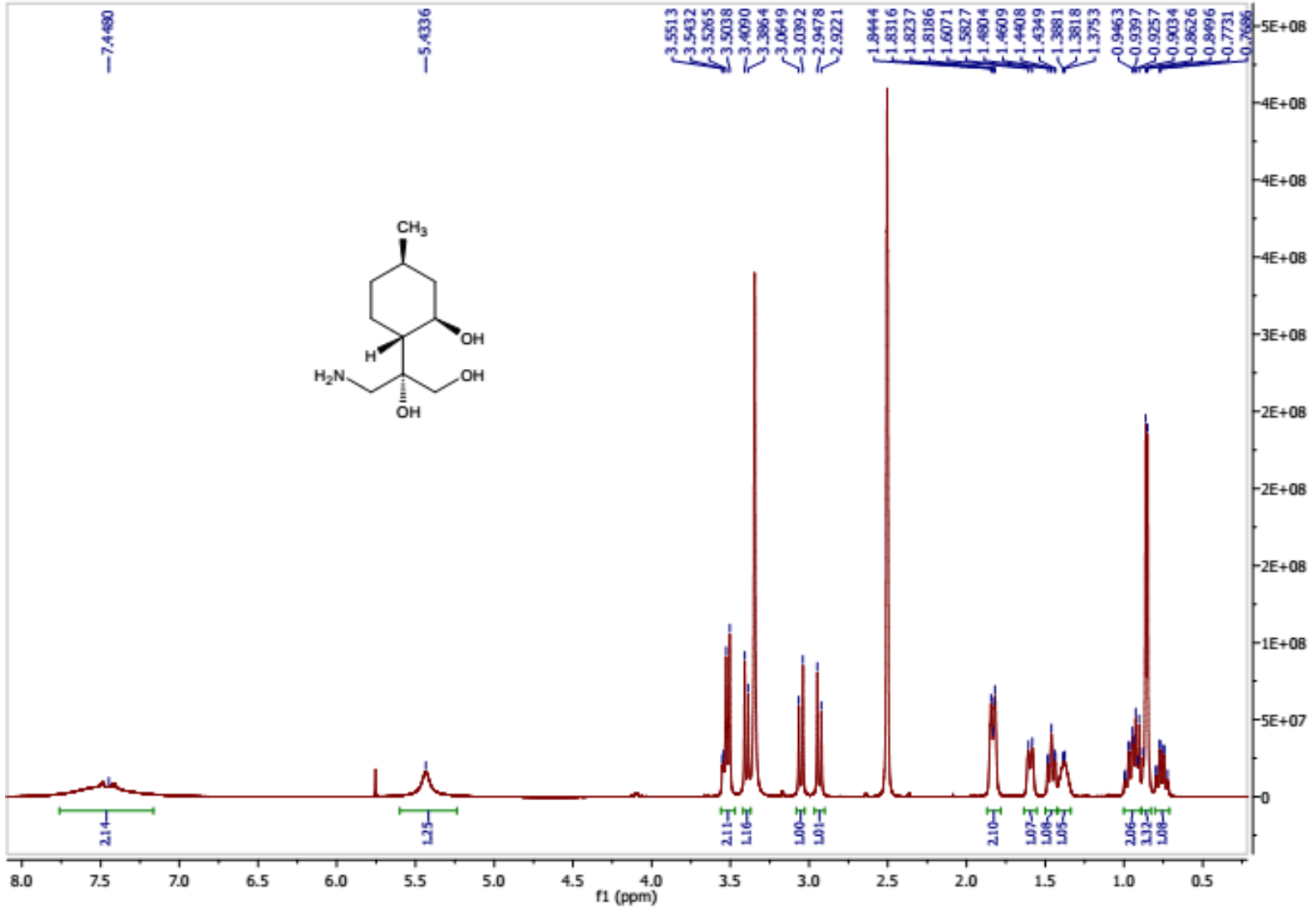
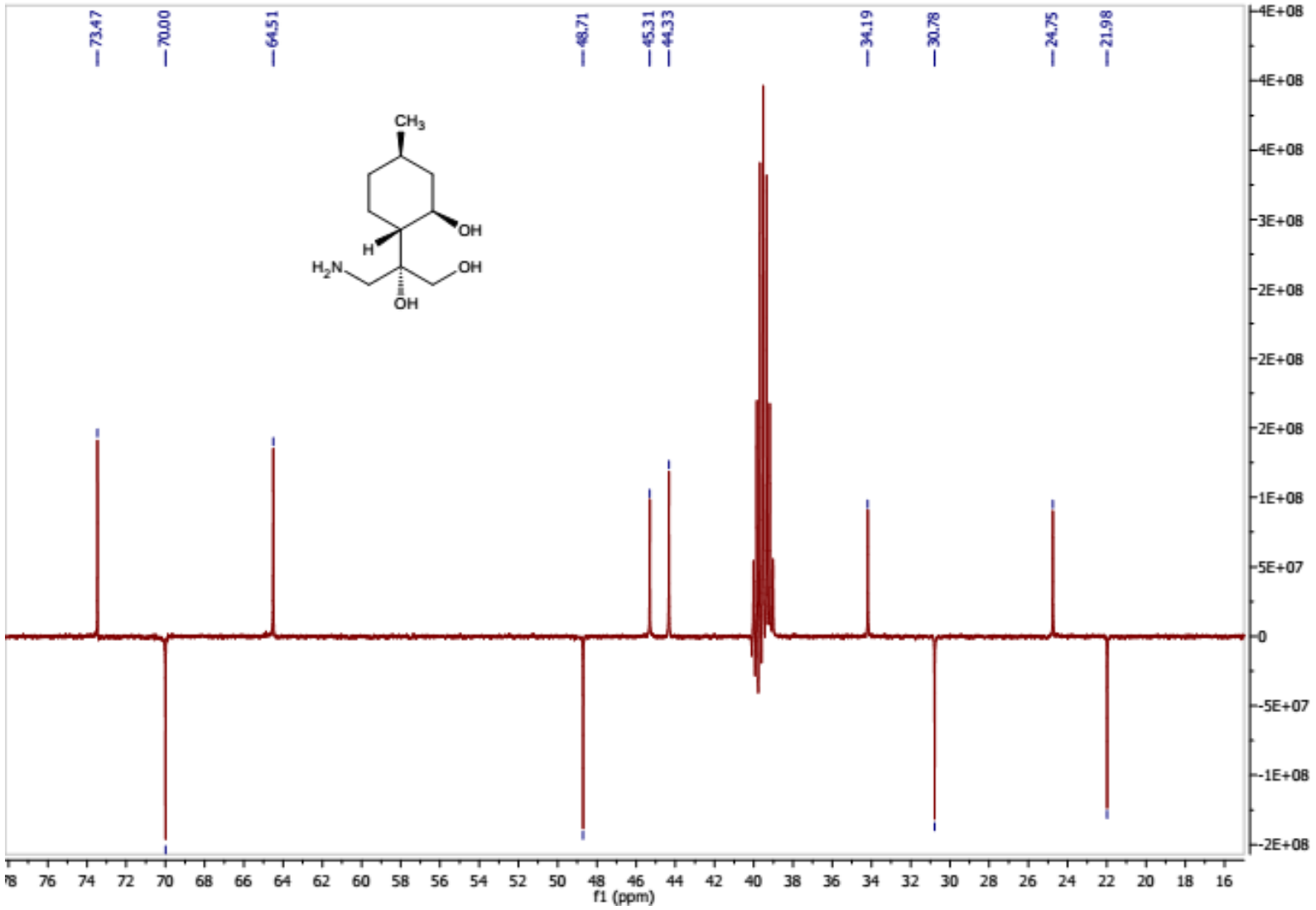


$^{13}$C-NMR of compound **56a**



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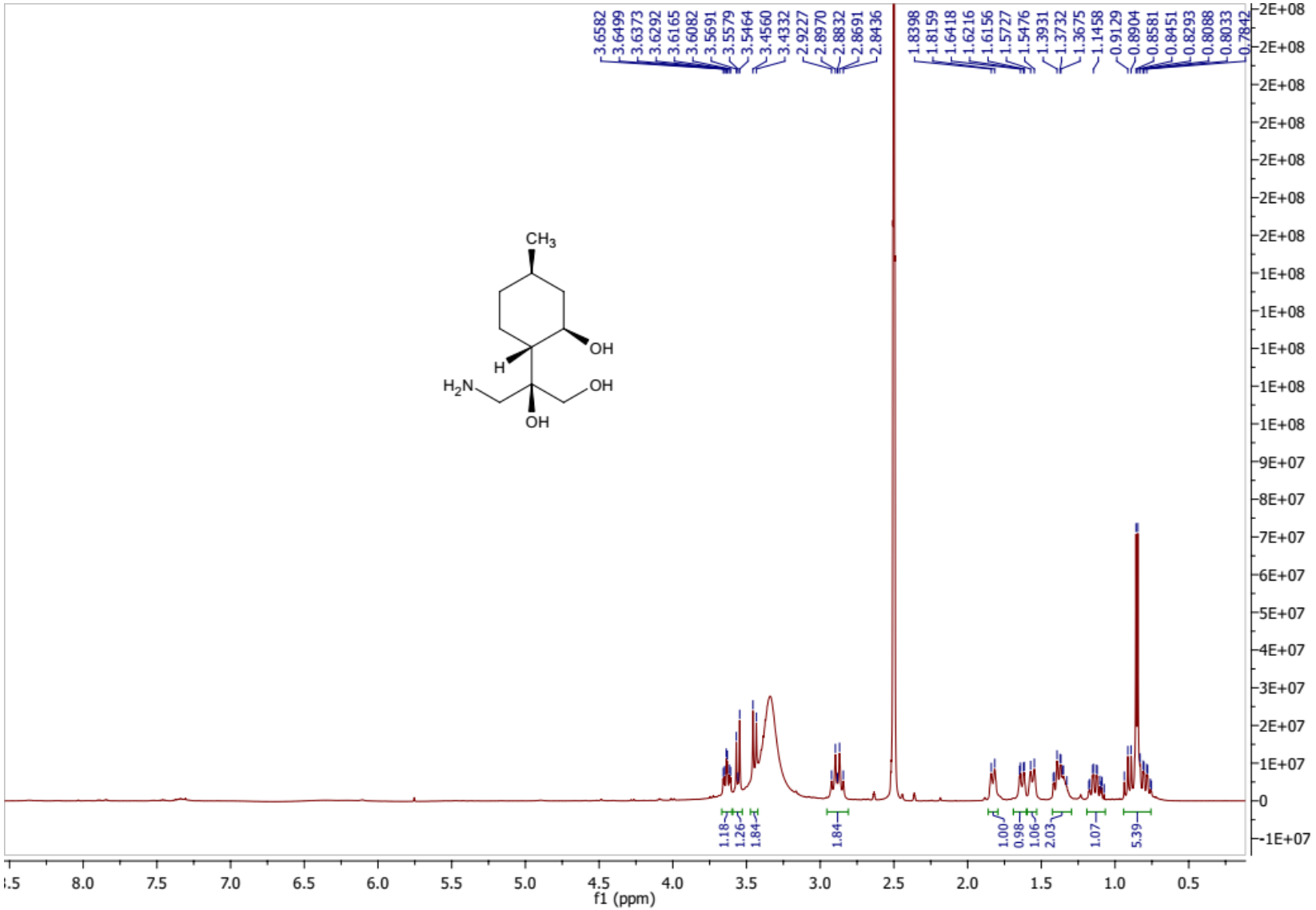

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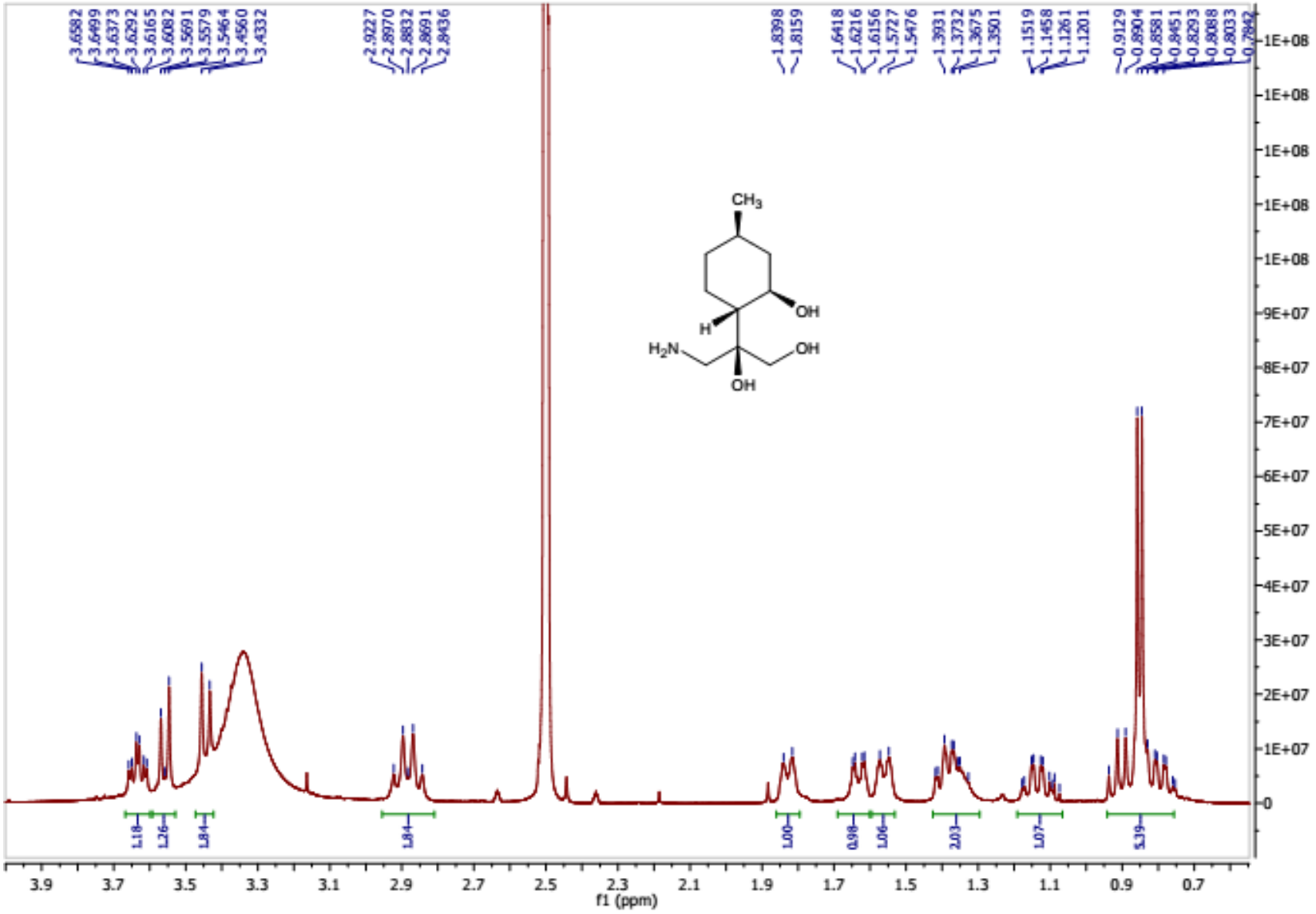

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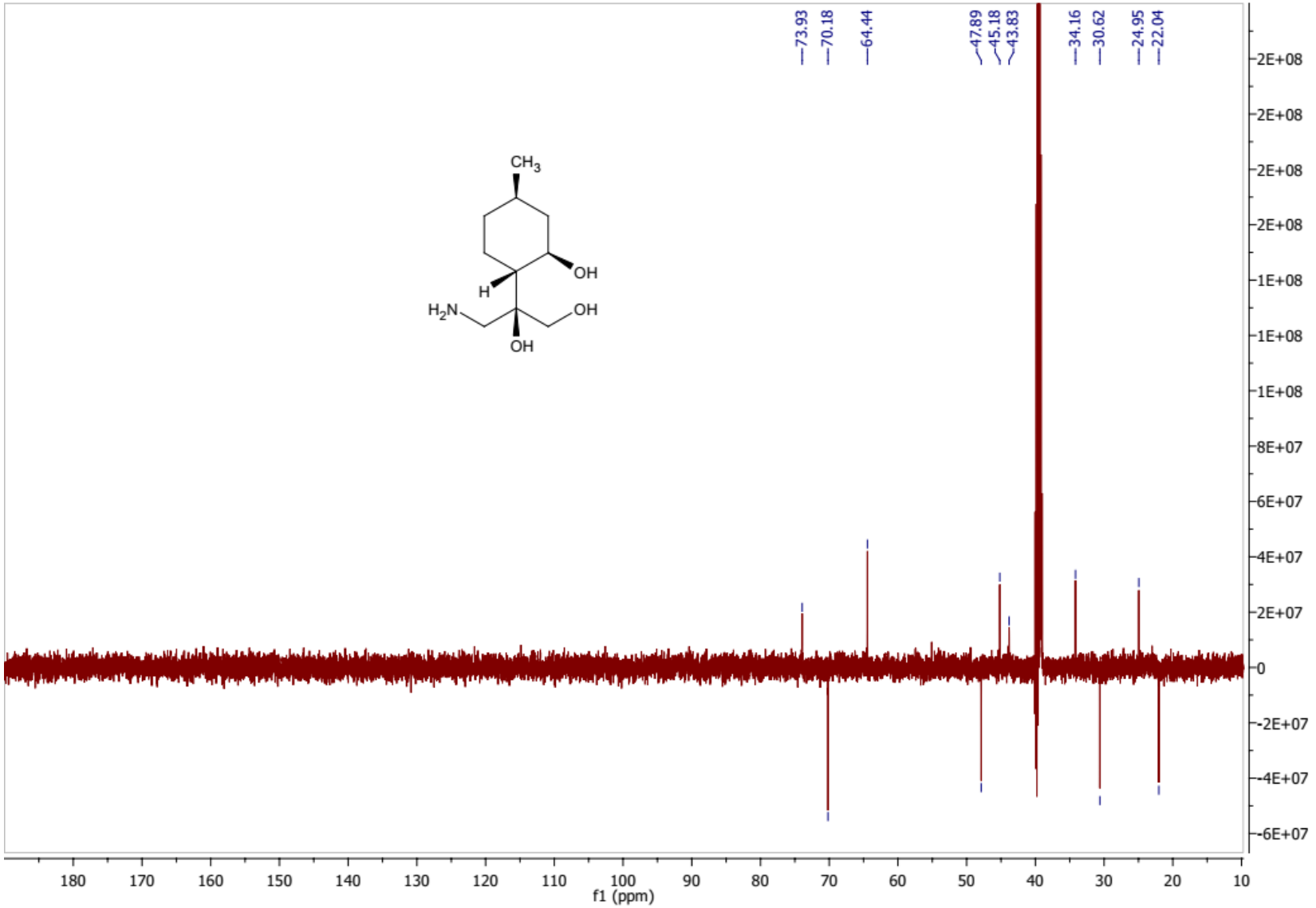

$^{13}$C-NMR of compound **56b**