Supplementary Information

Chemically Etched Silicon Powder-Supported Platinum as a Durable and Selective Catalyst for Continuous-Flow Reductive *N*-Alkylation

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Contents

1. General Information S-2
2. Characterization of ESi-Pt Catalyst S-3
3. Experimental Procedures of Continuous-Flow Reductive *N*-Alkylation S-3
4. Spectral Data of the Isolated Products S-5
5. References S-7
6. ^{1}H and ^{13}C NMR Spectra S-8

1. General Information

All reagents and solvents were obtained from commercial sources and used as received. Potassium tetrachloroplatinate(II) [K_2PtCl_4] was purchased from FUJIFILM Wako Pure Chemical Corporation. All manipulations were performed under atmospheric conditions otherwise noted. Analytical thin-layer chromatography (TLC) was performed on glass plates pre-coated silica gel (Merck: Art 5715, Kieselgel 60 F254, 0.25 mm). Column chromatography was performed with silica gel (Wakogel C-300). Visualization was accomplished by UV light (254 nm).

GC analysis was measured by an Agilent 6850 equipped with a capillary column (Agilent HP-1, 30 m, 0.32 mm i.d. or SUPELCO SLBTM-IL 60, 30 m, 0.25 mm i.d.), GC-MS was measured by Agilent 7860A/JEOL JMS-T100GC or Agilent 7890B/5977B MSD equipped with a capillary column (Agilent HP-1-MS, 30 m, 0.25 mm i.d. or DB-FFAP, 30 m, 0.32 mm i.d.). ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a JEOL JNM-ECZL500G spectrometer. Chemical shifts (δ) for ^{1}H NMR were basically reported using the residual non-deuterated chloroform as an internal standard (δ = 7.26 ppm). Chemical shifts for ^{13}C NMR were reported using $CDCl_3$ (δ = 77.0 ppm). Inductively coupled plasma mass spectrometry (ICP-MS) measurement was performed using Perkin Elmer Nexion 300D. The sample was pretreated by microwave digestion technique with high-purity nitric acid (69%, obtained from Kanto Chemical, Ultrapure-100 grade) as solvent (7 mL) using Perkin Elmer Titan MPS microwave sample preparation system. Kr adsorption isotherm measurement was performed using MicrotracBEL Bellsorp-MAX II. The adsorption/desorption was conducted at 77.36 K using liquid nitrogen. The solid sample was pretreated at 150 °C for 12 h. The specific surface area was calculated based on Brunauer-Emmett-Teller (BET) plot. SEM/EDX images were obtained on a Hitachi TS3030Plus/Bruker nanoGmbH Quantax 70. STEM imaging was performed using JEOL JEM-2100F equipped with an energy dispersive X-ray spectroscopy (EDS) detector.

XAFS measurements were performed at the BL14B2 beamline of the synchrotron SPring-8 in Japan under standard beamline conditions. The Pt L_3-edge (11.56 keV) XAFS data were corrected by transmission mode using Ar/Kr mixed gas-filled ionization chambers with the optimized gas ratio and pressure with Si (311) double-crystal monochromator. For the energy calibration of XANES spectra of Pt L_3-edge, Pt foil was used as a reference sample to set the inflection point determined by the maximum first-derivative of XANES spectra to 11563.9769 eV. Sample pellets of references and ESi-Pt catalyst were prepared with a BN dilution. XAFS data processing was carried out by using Athena and Artemis software[S1], [S2].

2. Characterization of ESi-Pt Catalyst

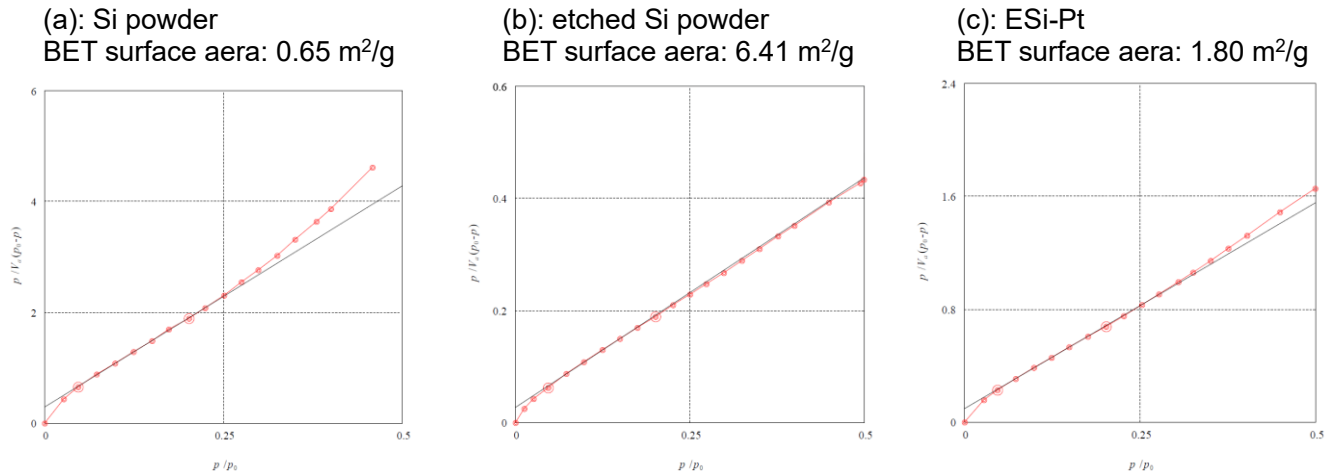


Fig. 1 Kr adsorption isotherm of (a) Si powder, (b) etched Si powder, and (c) ESi-Pt.

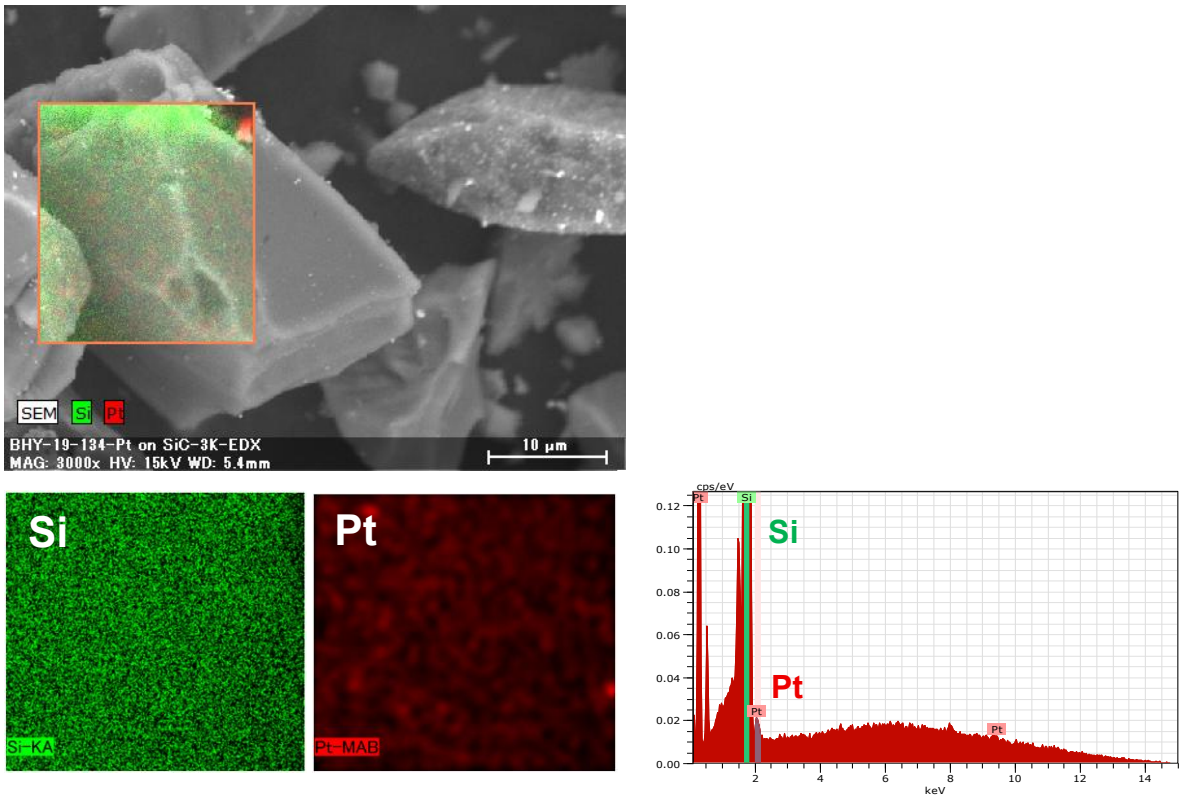


Fig. 2 SEM image of ESi-Pt and EDS mapping.

3. Experimental Procedures of Continuous-Flow Reductive *N*-Alkylation

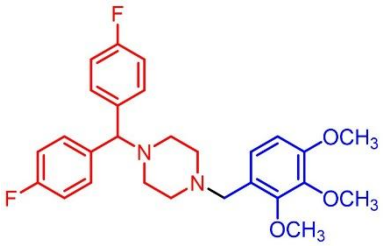
3.1 Continuous-flow synthesis of lomerizine (3aa)

ESi-Pt (0.067 mmol Pt; Pt loading: 1.09 wt%) was mixed with glass beads (1.2 g) in a vial using a vortex mixer (Vortex-Genie 2, KENIS Ltd.) at 1000 rpm for 5 min. The resulting mixture was packed into a glass column (6 mm in diameter), with PTFE filters installed at both the top and bottom of the column. The packed catalyst bed had an approximate length of 5.5 cm. The column was then placed in the heating unit of the continuous-flow reactor. 1-(Bis(4-fluorophenyl)methyl)piperazine (25 mM) and 2,3,4-trimethoxybenzaldehyde (30 mM) were separately dissolved in toluene. These solutions were supplied from two inlets at flow rates of 0.1 mL/min each and mixed in a T-shaped mixer. The liquid feed and H_2 gas (3.0–5.0 mL/min) were then introduced into a micromixer. The resulting gas–liquid mixture was preheated to 70 °C before entering the reactor. The reaction mixtures were collected in separate vials every 1 h during the reaction. The reaction was carried out at 115 °C or 140 °C, as specified in the manuscript.

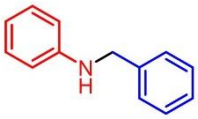
3.2 Continuous-flow synthesis of other products (a sequential process)

The reactor was used as described above. A solution containing an amine (300 mM) and a carbonyl compound (360 mM) in toluene was prepared in a 50 mL flask. MS3A (3 g) was also added into the flask. The prepared solution and H_2 gas were then injected into the flow system. The liquid feed and H_2 gas were introduced into a micromixer at flow rates of 0.1 and 7.0 mL/min, respectively. The resulting gas–liquid mixture was preheated to 70 °C before entering the reactor. The reaction mixtures were collected in separate vials every 1 h during the reaction. The reaction was carried out at 140 °C for 3 h. After completion of the reaction, the reactor was washed with clean toluene for 2 h, and the solution of the next substrate was then introduced as described in the manuscript. The products were subsequently purified by silica gel column chromatography to obtain the corresponding pure compounds.

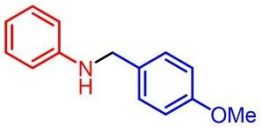
4. Spectral Data of the Isolated Products



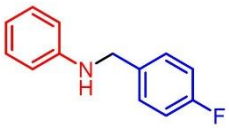
1-[Bis(4-fluorophenyl)methyl]-4-(2,3,4-trimethoxybenzyl)piperazine (lomerizine free base, **3aa**)[S2]: the products were isolated by silica gel column chromatography (hexane/EtOAc = 1:1) (pale yellow solid, 3–6 h: 197.4 mg, 94% yield; 7–10 h: 201.3 mg, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.31 (m, 4H), 6.95 (t, J = 8.5 Hz, 5H), 6.61 (d, J = 8.5 Hz, 1H), 4.19 (s, 1H), 3.87–3.84 (m, 9H), 3.48 (s, 2H); 2.28–2.37 (br, m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7 (2C) (d, $^1J_{C–F}$ = 243.1 Hz), 152.8, 152.6, 142.2., 138.4 (2C) (d, $^4J_{C–F}$ = 2.4 Hz), 129.2 (4C) (d, $^3J_{C–F}$ = 8.4 Hz), 125.2, 123.9, 115.3 (4C) (d, $^2J_{C–F}$ = 21.4 Hz), 106.9, 74.5, 61.2, 60.8, 56.4, 55.9, 53.1 (2C), 51.9 (2C).



N-Benzylaniline (**3bb**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 10:1) (colorless liquid, 877.2 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.34 (m, 4H), 7.31–7.27 (m, 1H), 7.21–7.17 (m, 2H), 6.75–6.71 (m, 1H), 6.67–6.65 (m, 2H), 4.35 (s, 2H), 4.04 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 139.4, 129.2, 128.6, 127.5, 127.2, 117.6, 112.8, 48.3.



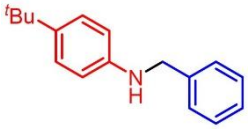
N-(4-Methoxybenzyl)aniline (**3bc**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 20:1) (pale yellow solid, 1062.5 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.5 Hz, 2H), 7.17 (t, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.71 (t, J = 7.5 Hz, 1H), 6.64 (d, J = 8.5 Hz, 2H), 4.25 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 148.2, 131.4, 129.2, 128.8, 117.5, 114.0, 112.8, 55.3, 47.8.



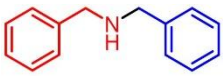
N-(4-Fluorobenzyl)aniline (**3bd**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 20:1) (light yellow liquid, 834.5 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.33 (m, 2H), 7.20–7.17 (m, 2H), 7.03 (t, J = 8.5 Hz, 2H), 6.74 (t, J = 7.5 Hz, 1H), 6.63 (d, J = 8.5 Hz, 2H), 4.31 (s, 2H), 4.03 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0 (d, $^1J_{C–F}$ = 243.9 Hz), 147.9, 135.1 (d, $^4J_{C–F}$ = 3.0 Hz), 129.3, 129.0 (d, $^3J_{C–F}$ = 8.0 Hz), 117.7, 115.4 (d, $^2J_{C–F}$ = 21.1 Hz), 112.8, 47.6.



N-(4-Chlorobenzyl)aniline (**3be**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 30:1) (light yellow liquid, 977.6 mg, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (s, 4H), 7.20–7.16 (m, 2H), 6.74 (t, J = 7.5 Hz, 1H), 6.63–6.60 (m, 2H), 4.32 (s, 2H), 4.06 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 138.0, 132.8, 129.3, 128.7, 128.7, 117.8, 112.8, 47.6.



N-Benzyl-4-(*tert*-butyl)aniline (**3cb**)[S5]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 20:1) (light yellow liquid, 1135.8 mg, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.32 (m, 4H), 7.23 (d, *J* = 7.0 Hz, 1H), 7.20 (d, *J* = 9.5 Hz, 2H), 4.31 (s, 2H), 3.93 (brs, 1H), 1.27 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.8, 140.3, 139.7, 128.6, 127.5, 127.2, 126.0, 112.5, 48.6, 33.8, 31.5.



N, *N*-Dibenzylamine (**3db**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 20:1) (colorless liquid, 850.8 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.25 (m, 10H), 3.81 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 128.4, 128.1, 126.9, 53.1.



N-Benzyl-*N*-3-phenylpropylamine (**3eb**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 1:1) (light yellow liquid, 1023.4 mg, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.18 (m, 7H), 7.19 (t, *J* = 4.5 Hz, 3H), 3.79 (s, 2H), 2.68 (q, *J* = 7.5 Hz, 4H), 1.85 (quint, *J* = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 140.4, 128.4, 128.3, 128.1, 126.9, 125.7, 54.0, 48.9, 33.6, 31.7.



N-Benzyl-*N*-octylamine (**3fb**)[S4]: the product was isolated by silica gel column chromatography (hexane/EtOAc = 1:1) (light yellow liquid, 898.7 mg, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.23 (m, 5H), 3.79 (s, 2H), 2.62 (t, *J* = 7.5 Hz, 2H), 1.51 (quint, *J* = 7.5 Hz, 2H), 1.32–1.26 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 128.4, 128.1, 126.8, 54.1, 49.5, 31.8, 30.1, 29.5, 29.3, 27.4, 22.6, 14.1.

5. References

[S1] Newville, M. IFEFFIT: interactive XAFS analysis and FEFF fitting. *J. Synchrotron Rad.* **8**, 322–324 (2001).

[S2] Ravel, B., Newville, M. ATHENA, ARTEMIS, HEPHAESTUS: data analysis for X-ray absorption spectroscopy using IFEFFIT. *J. Synchrotron Rad.* **12**, 537–541 (2005).

[S3] Narsaiah, A. V., Kumar, J. K. A simple and efficient synthesis of the antimigraine drug lomerizine. *Synthesis* **12** 1989−1991 (2010).

[S4] Zhang, Z., Baek, H., Soliman, E., Ohno, A., Yamada, Y. M. A. Durable etched silicon powder-supported palladium catalyst for continuous flow hydrogenation and reductive alkylation. *Chem.-Methods* **5**, e202500050 (2025).

[S5] He, R., Toy, P. H., Lam, Y. Polymer-supported Hantzsch 1,4-dihydropyridine ester: an Efficient biomimetic hydrogen source. *Adv. Synth. Catal.* **350**, 54–60 (2008).

6. ^{1}H and ^{13}C NMR Spectra

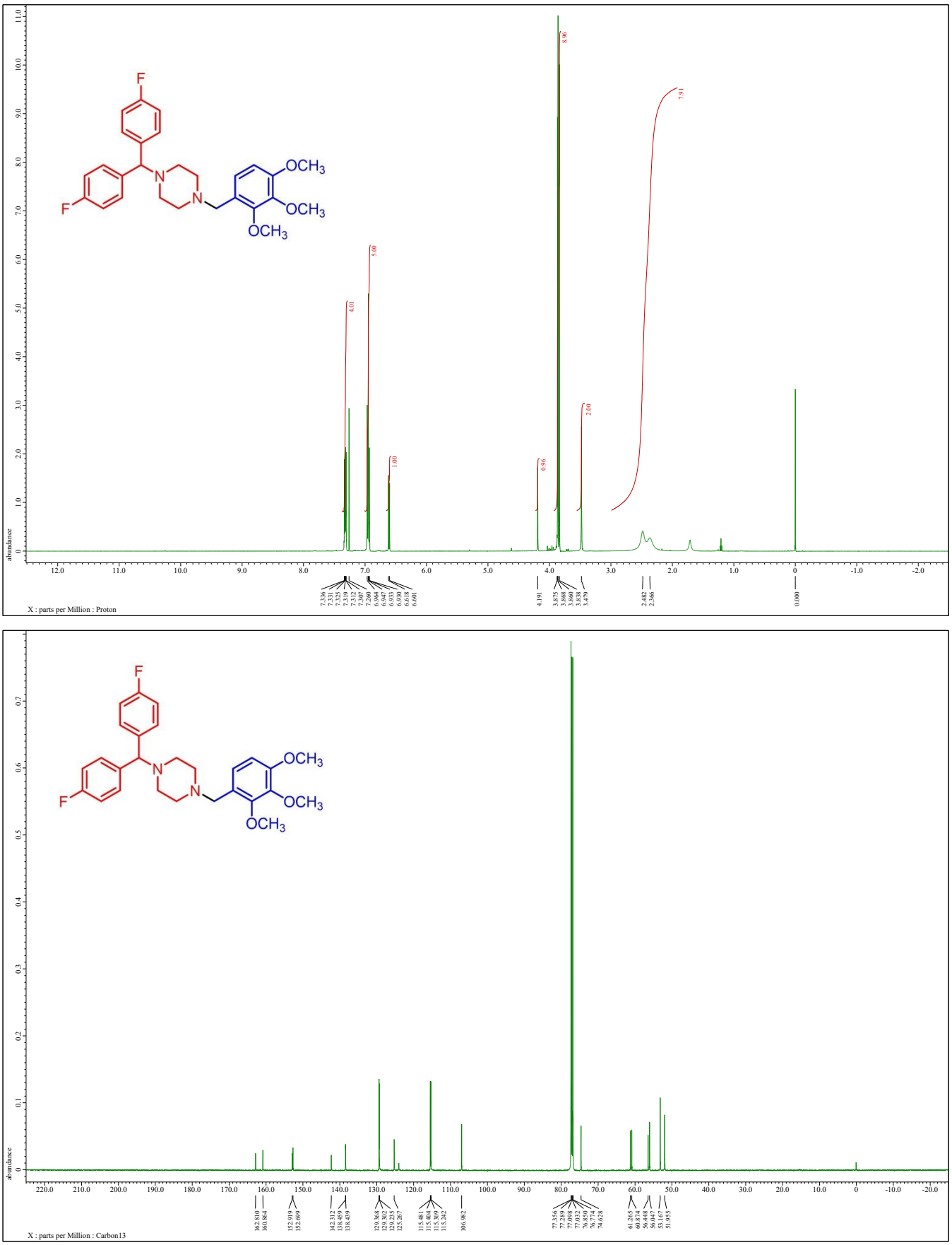


Fig. 3 ^{1}H and ^{13}C NMR spectra of product **3aa**.

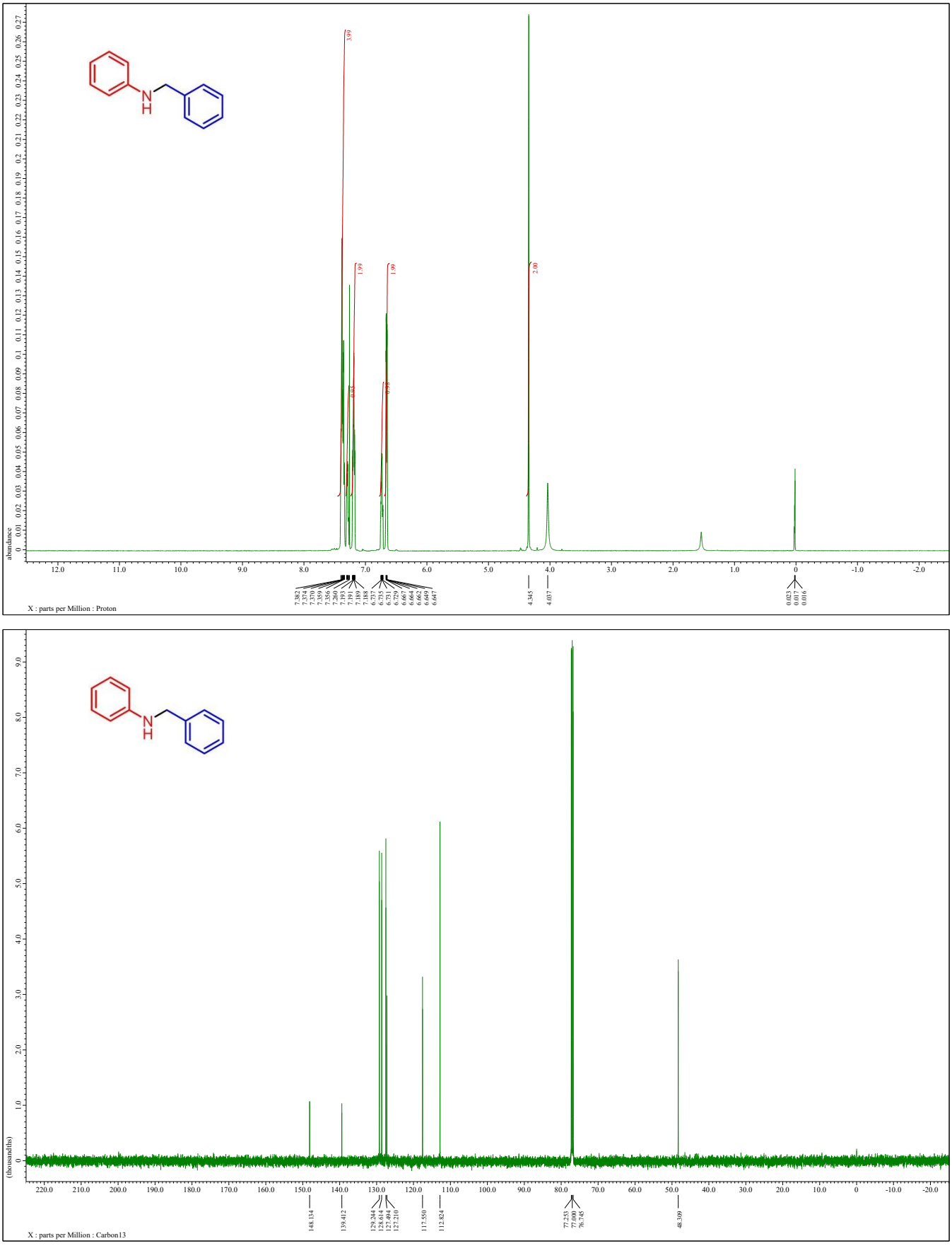
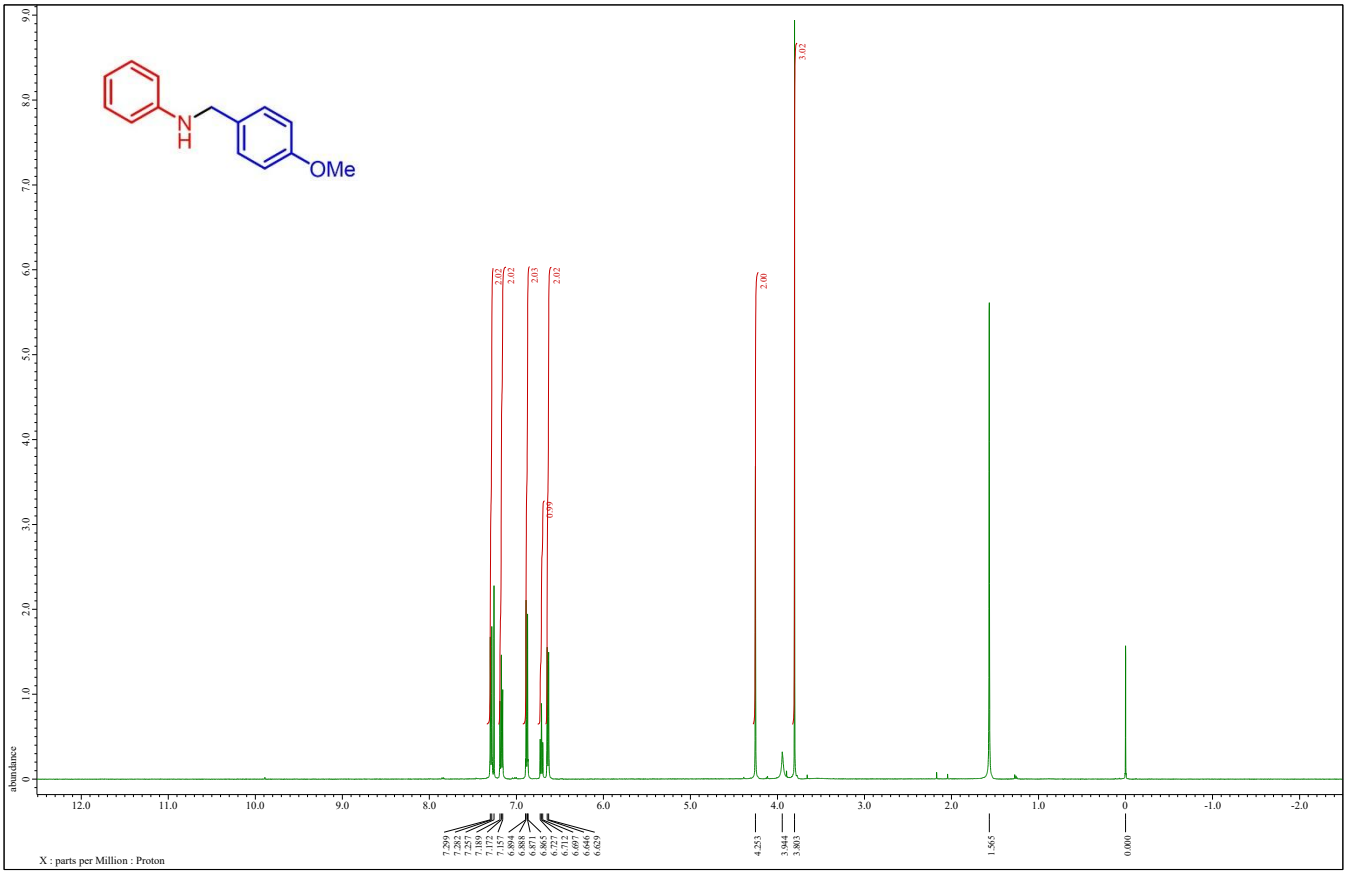


Fig. 4 ^{1}H and ^{13}C NMR spectra of product **3bb**.



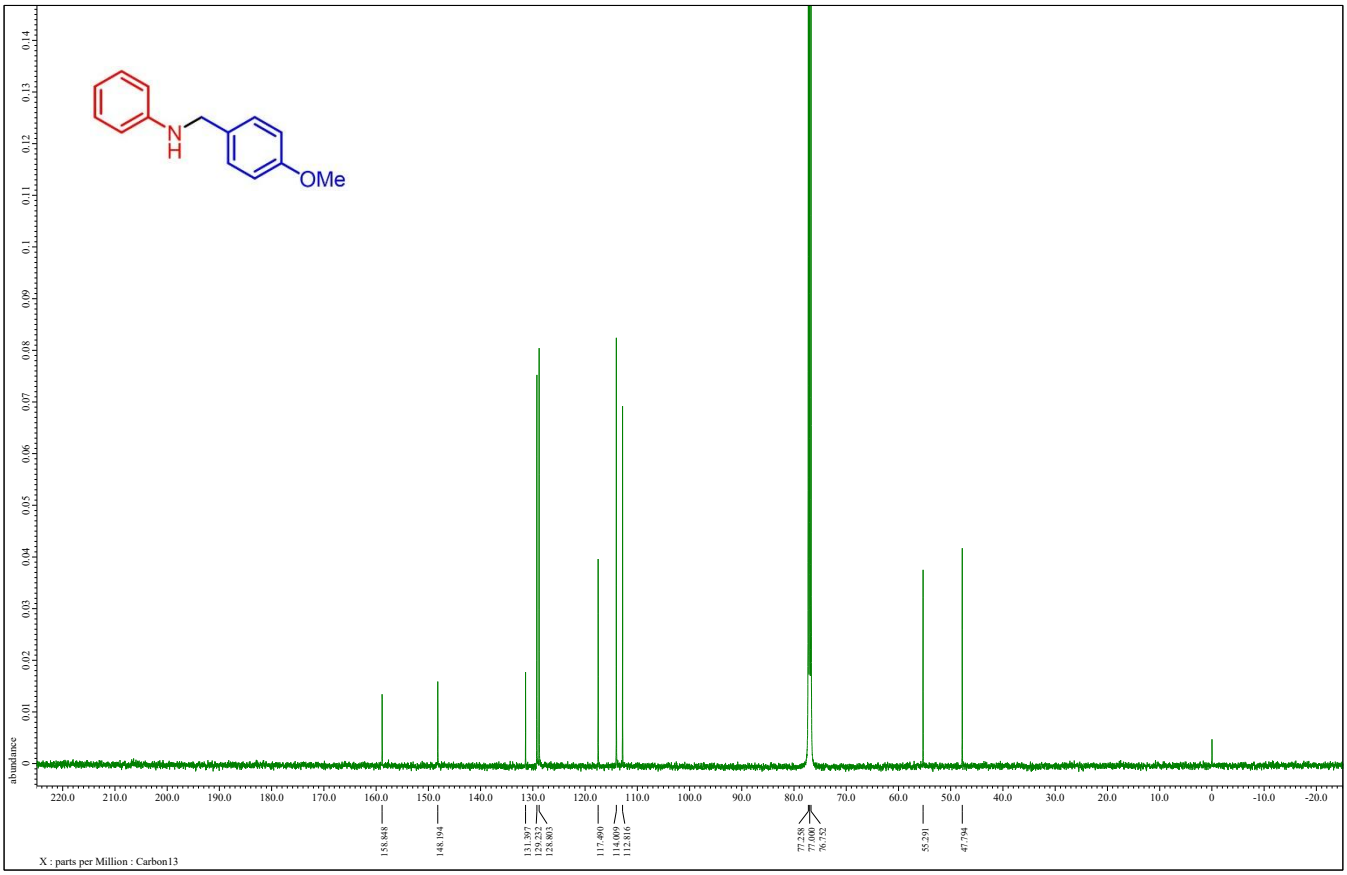


Fig. 5 ^{1}H and ^{13}C NMR spectra of product **3bc**.

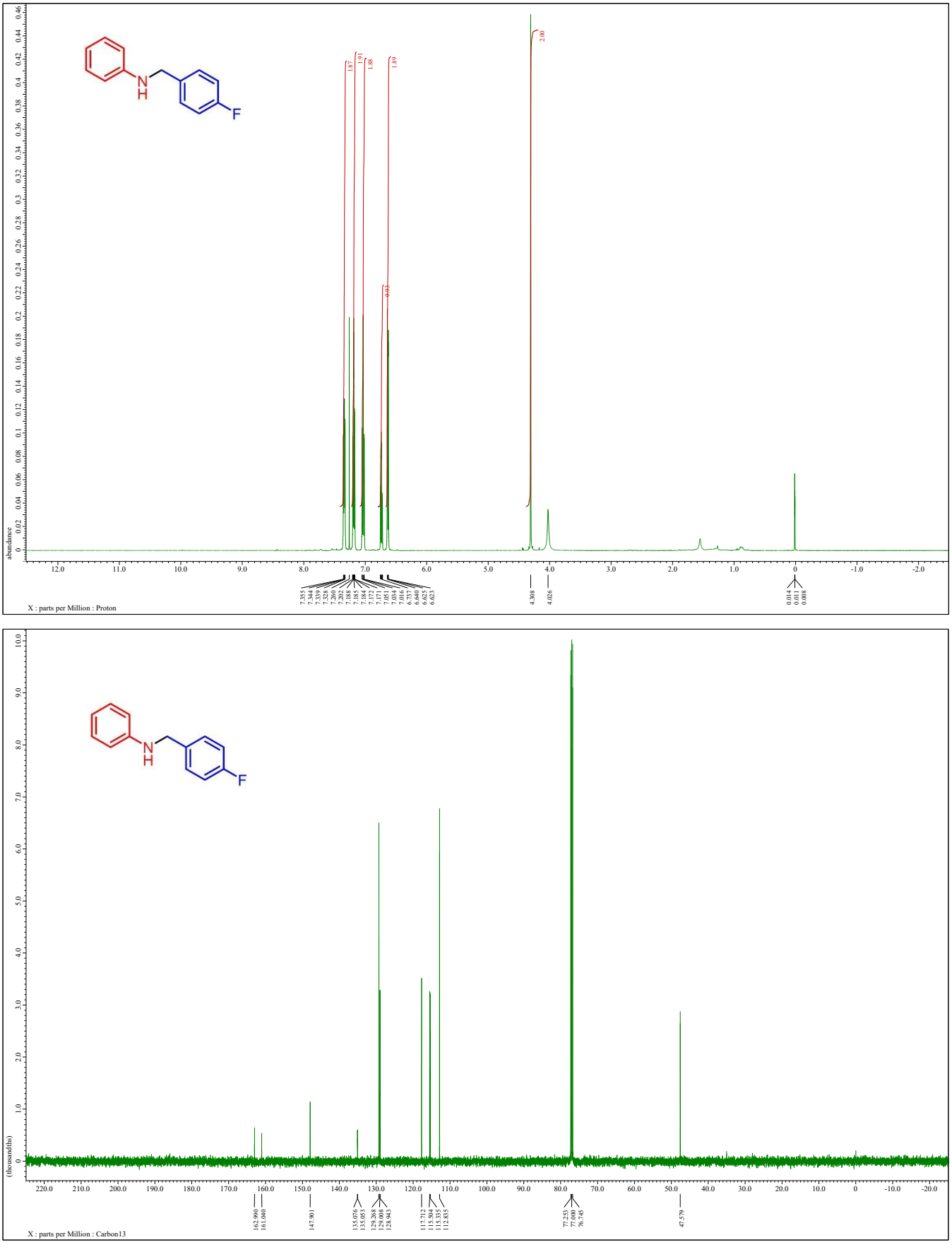
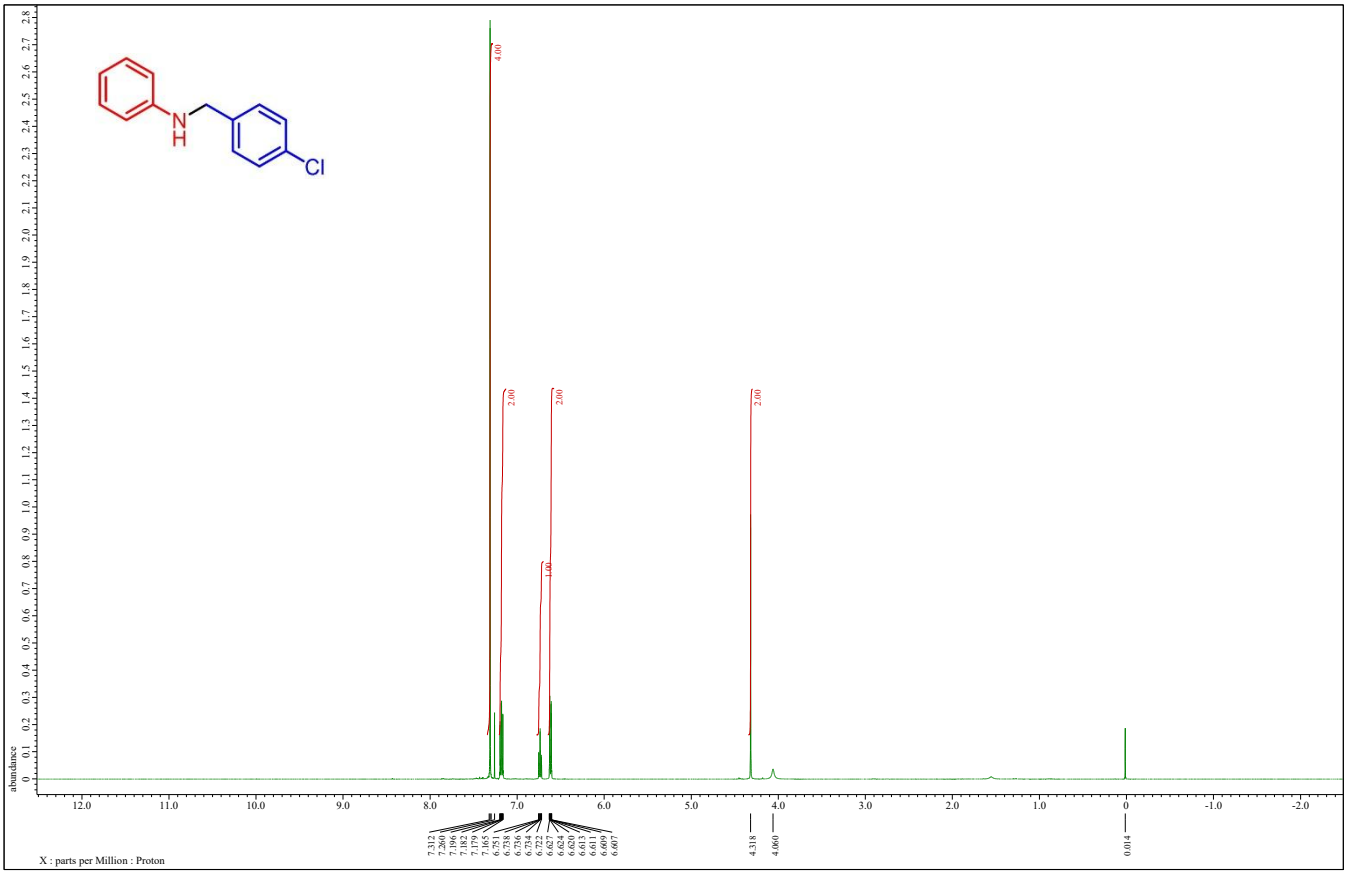


Fig. 6 ^{1}H and ^{13}C NMR spectra of product **3bd**.



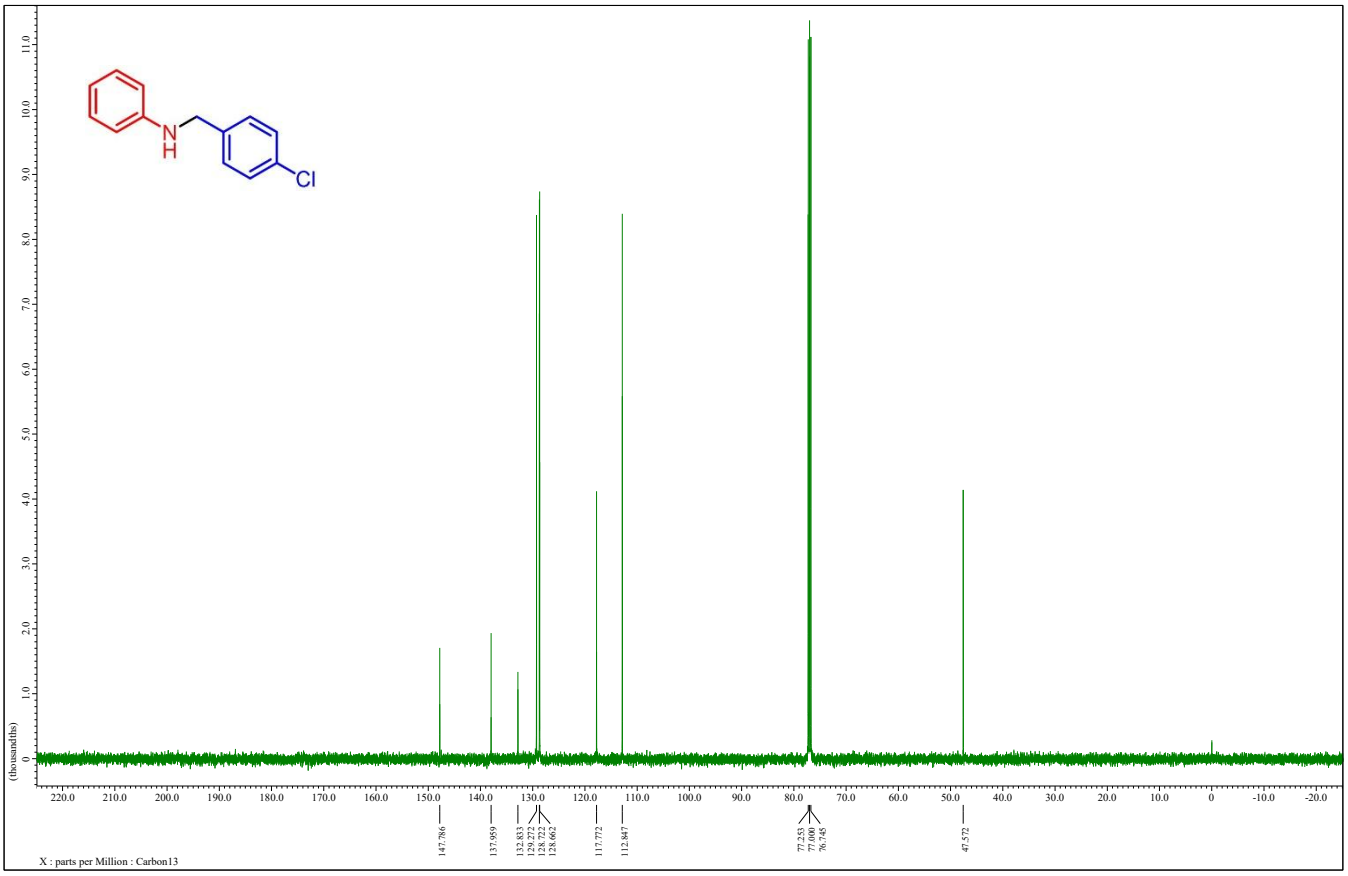


Fig. 7 ^{1}H and ^{13}C NMR spectra of product **3bf**.

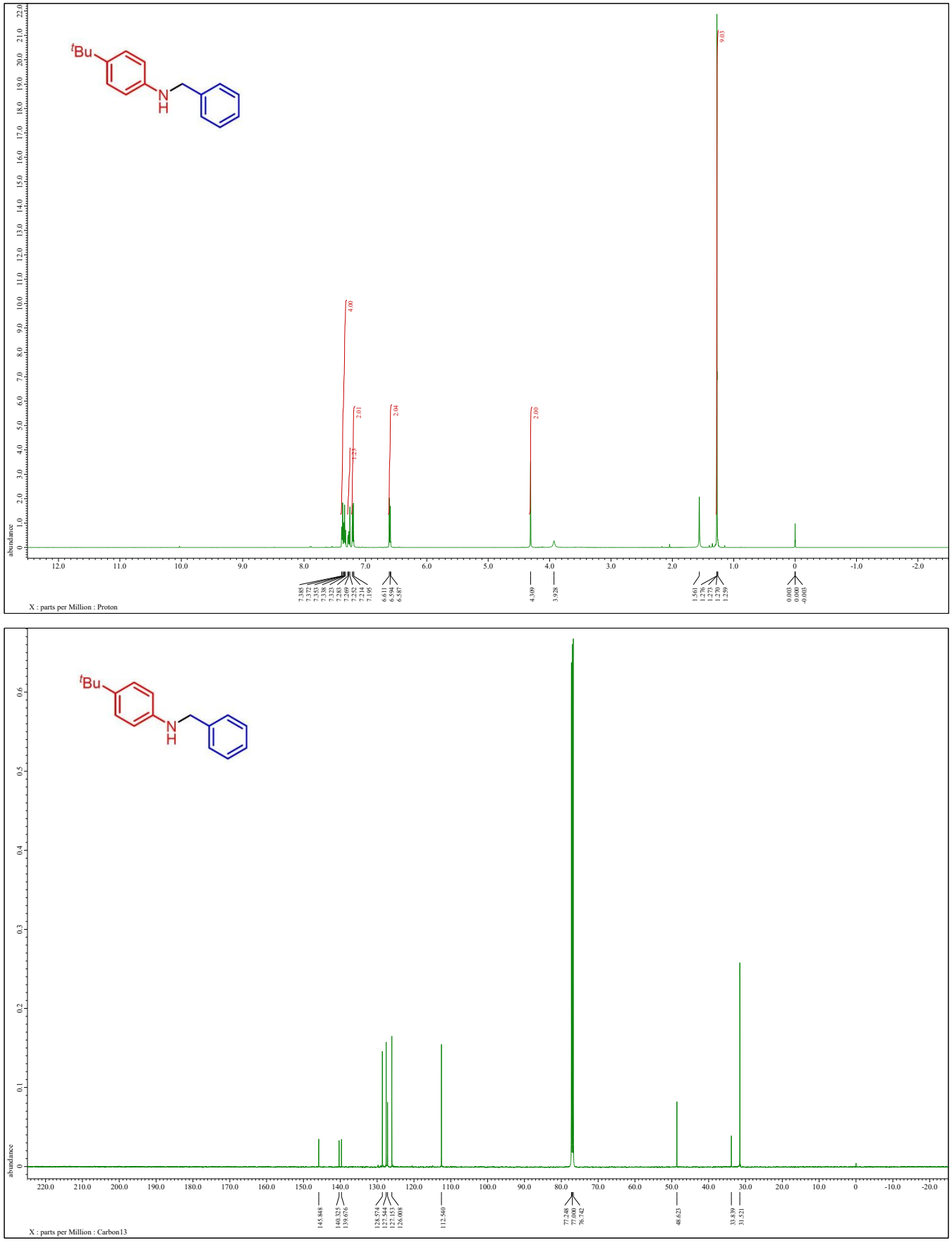


Fig. 8 ^{1}H and ^{13}C NMR spectra of product **3cb**.

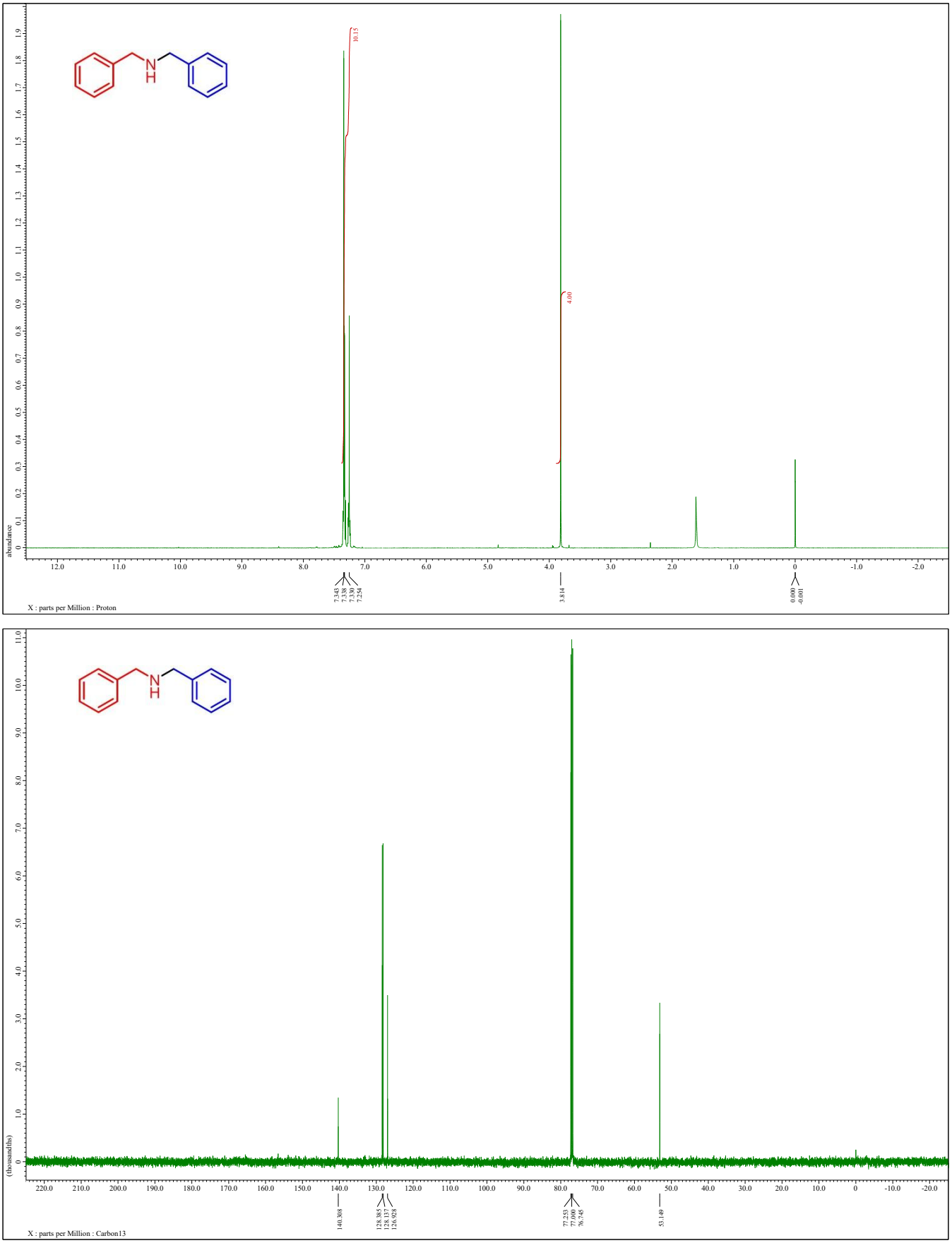


Fig. 9 ^{1}H and ^{13}C NMR spectra of product **3db**.

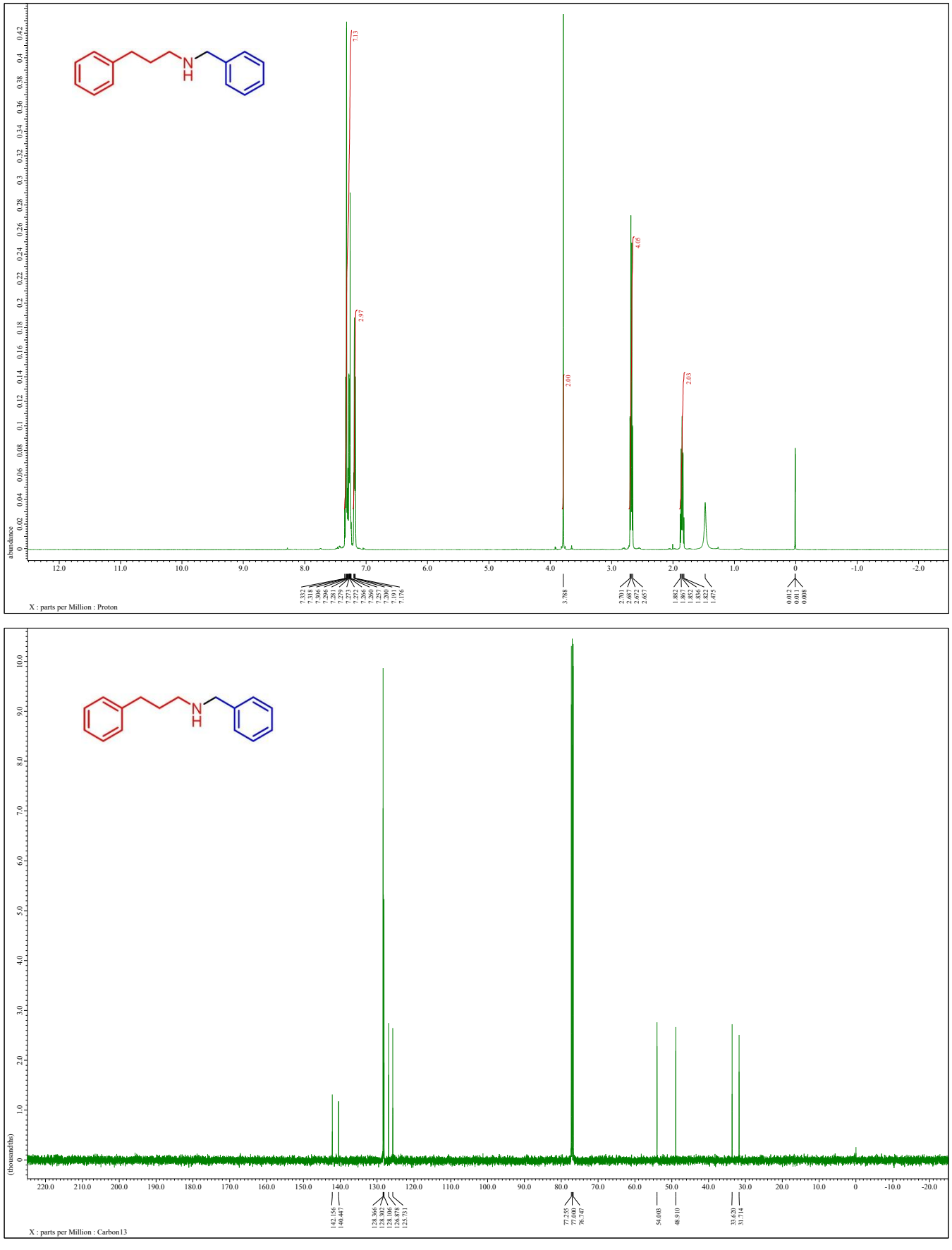
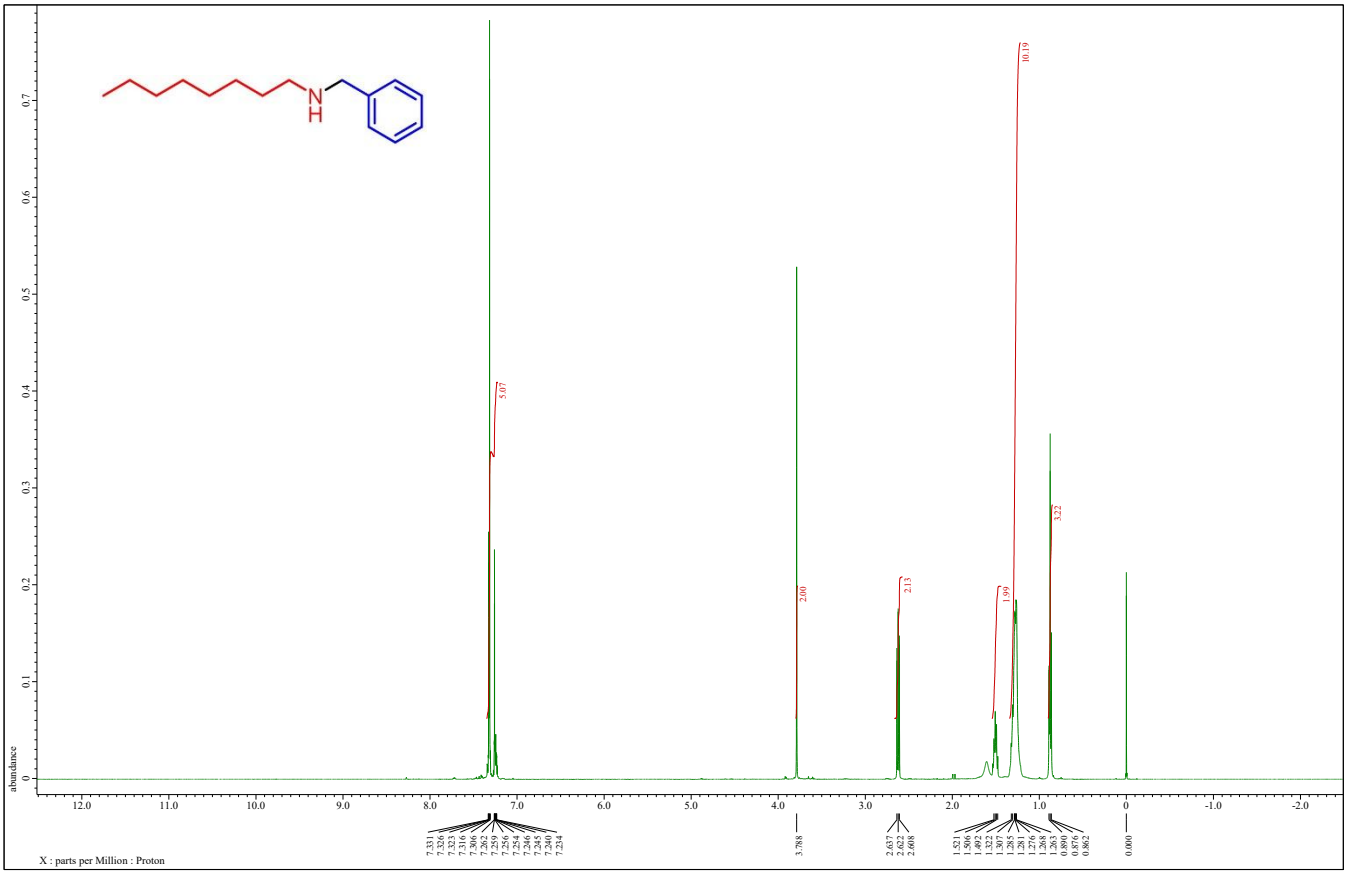


Fig. 10 ^{1}H and ^{13}C NMR spectra of product **3eb**.



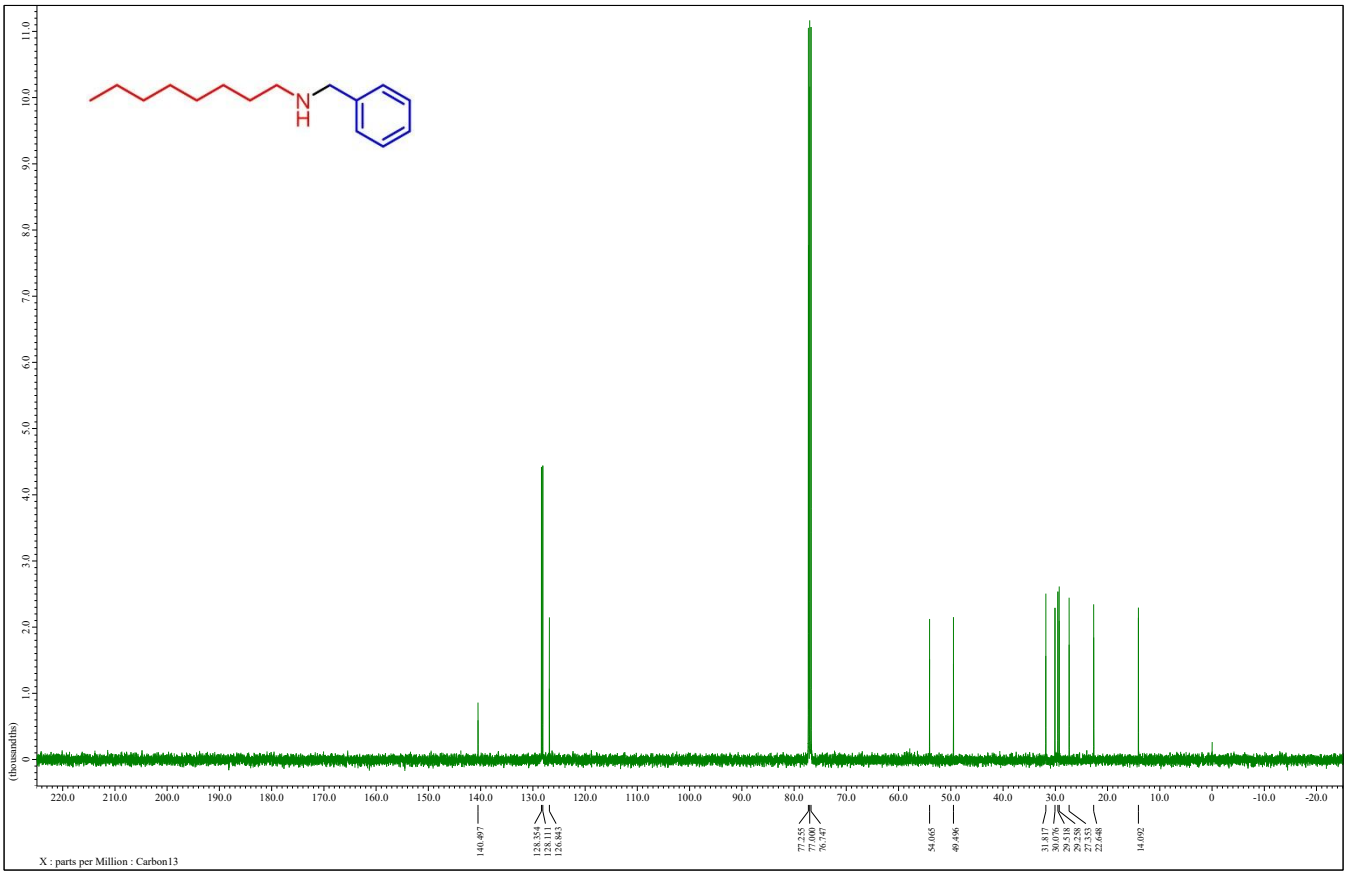


Fig. 11 ^{1}H and ^{13}C NMR spectra of product **3fb**.