SI supporting information

Selective cleavage of 3,5-bis-(trifluoromethyl) benzylcarbamate by $SmI_2/Et_3N/H_2O$

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General All reactions were performed under nitrogen atmosphere (using standard Schlenk technique or glove-box). All commercial reagents were used as received. Phosgene solution was commercial and used as received. Mono protected diamines were commercial and used as received. Tetrahydrofuran was distilled from benzophenone/sodium and stored over sodium in a glovebox. NMR spectra were recorded at 400 MHz in deuterated chloroform.

Gas chromatography/mass spectrometry analyses were performed on a DB-5 equivalent capillary column (length 30m, i.d. 25 μm) using helium as carrier gas. Injector temperature 300 °C. Temperature program: 40 to 330 °C (12 °C/min) with 4 minutes hold time. The MS detector consisted of an ion trap with 70 eV ionization.

Preparation of SmI_2 in THF Diiodoethane (12 mmol, 3.37 g) was added to THF (100 ml). To this was added samarium metal (19 mmol, 2.85 g, powder). The mixture was allowed to stir at room temperature under a nitrogen atmosphere for one hour. This yields a deep-blue 0.12 M solution of SmI_2.

General procedure for protection To a 3,5-bis-trifluoromethylbenzylalcohol solution in dry THF (2 mmol in 5 mL, 0.4 M) was added a phosgene solution (4 mmol, 20% solution in toluene) under nitrogen. The contents were allowed to stir for 24 hours and evaporated to remove solvent and remaining phosgene (CAUTION!). The resulting chloroformate was dissolved in acetone (5 mL) and added to a solution of the amine (2.0 mmol) and $NaHCO_3$ in acetone/water (9:1, 10 mL). After the reaction was complete (as judged by TLC or GC/MS analysis) the contents was evaporated and partitioned between water and ethyl acetate. The organic phase was washed with water twice and last with saturated ammonium chloride, dried over sodium sulphate and evaporated to yield the crude carbamate. Purification by passing through a short silica plug using dichloromethane is usually enough to recover the pure product in almost quantitative yield, but some derivatives demanded proper flash chromatography.

Compound **1**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H ^{1}H: 7.81 (s, 1H), 7.78 (s, 2H), 5.14 (s, 2H), 4.70 (s, 1H), 2.09 (s, 3H), 1.94 (s, 6H), 1.67 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ_c 139.6, 132.0, 131.6, 127.5, 124.5, 121.8, 51.1, 41.7, 36.2, 29.5. HRMS (ESI-MS) [M+H$^+$] calcd for $C_{20}H_{22}F_6NO_2$: 422.1555. Found: 422.1554

Compound **4a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.83 (1H, s), 7.80 (2H, s), 5.23 (2H, s), 3.95 (1H, m), 3.65 (2H, m), 3.46-3.43 (2H, m), 1.72 (2H, m), 1.55 (2H, m), 0.90 (9H, s), 0.07 (6H, s). ^{13}C

NMR (100 MHz, $CDCl_3$): δ_c 157.3, 142.4, 134.5 (q, J=33Hz), 130.3, 125.8 (q, J=273 Hz), 124.5 (m), 69.1, 67.9, 43.3, 36.8, 36.5, 28.4, 20.7, -2.13. HRMS (ESI-MS) $[M+H]^+$, calcd for $C_{21}H_{30}F_6NO_3Si$: 486.1899 Found: 486.1885.

Compound **4b**: Identical with the commercially available material.

Compound **5a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.82 (1H, s), 7.79 (2H,s), 5.14 (2H, s), 4.71 (1H, bs), 2.10 (3H, m), 1.96 (6H, m), 1.68 (6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_c 154.5, 139.2, 131.9 (q, J=33.7 Hz), 127.8, 124.5, 123.1 (q, J=273 Hz), 122.1, 80.3, 65.6, 43.7, 28.4, 28.3. HRMS (ESI-MS) calcd $C_{19}H_{23}F_6N_2O_4$: 457.1562 Found: 457.1562.

Compound **5b**: Spectral properties identical with the commercially available material.

Compound **6a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.83 (1H), 7.80 (2H), 7.32 (5H), 5.19 (2H, s), 4.79 (1H, br s), 3.53 (3H), 2.84 (2H, m), 2.15 (2H, m), 1.94 (2H, m), 1.55 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ_c 154.1, 139.3, 138.3, 131.8 (q, J=33.8 Hz), 129.1, 128.2, 127.7, 127.0, 123.1 (q, J=274 Hz), 121.9 m, J=3.5 Hz), 64.8, 63.0, 52.1, 48.5.

HRMS (ESI-MS) calcd for $C_{22}H_{23}F_6N_2O_2$: 461.1664 Found: 461.1657.

Compound **6b**: Identical with the commercially available material.

Compound **7a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.77 (s, 1H), 7.73 (s, 2H), 7.32-7.24 (m, 5H), 5.17 (s, 2H), 5.08 (s, 2H), 3.44 (br s, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_c 155.1, 154.5, 139.1, 136.3, 132.0 (q, J=34 Hz), 128.5, 128.2, 128.0, 127.9, 123.1 (q, J=274 Hz), 122.1 (q, J=3.5 Hz) 67.5, 65.7, 43.7, 26.5.HRMS (ESI-MS) calcd for $C_{22}H_{21}F_6N_2O_4$: 491.1406. Found: 491.1401

Compound **7b**: Identical with the commercially available material.

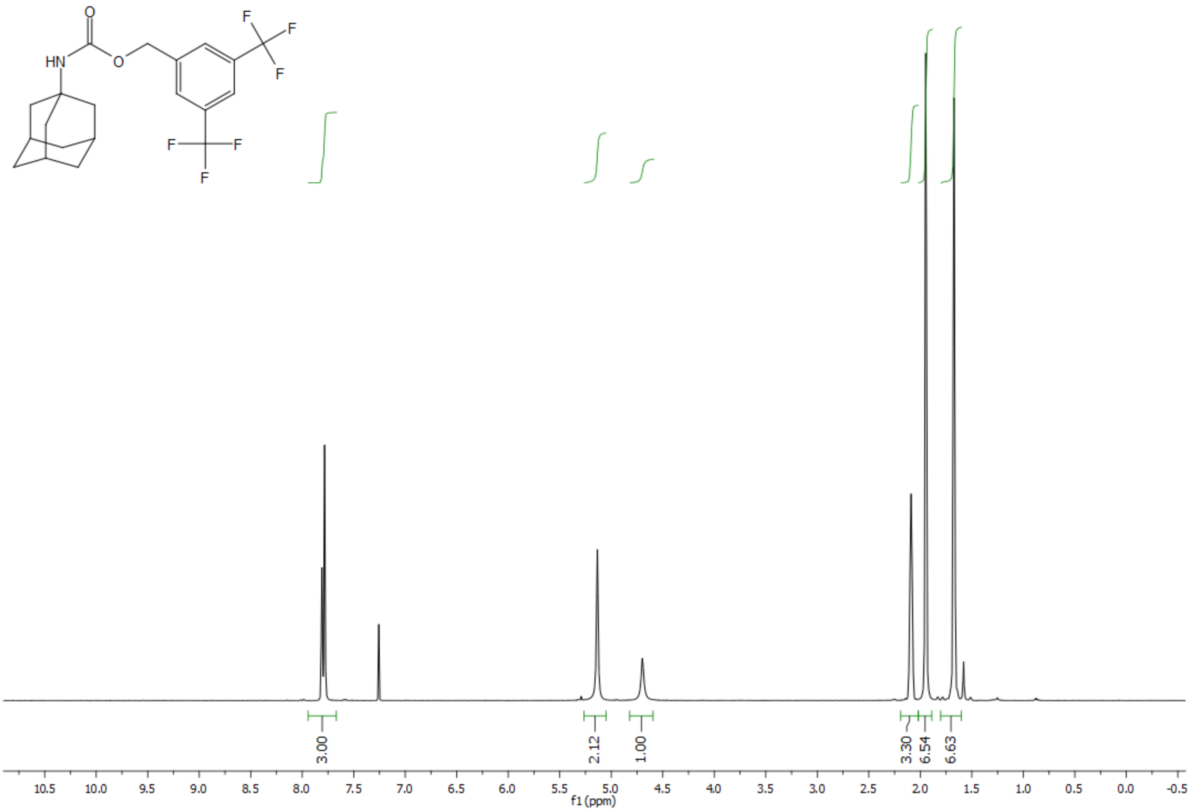
Compound **7c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.75 (s, 1H), 7.73 (s, 2H), 5.16 (s, 2H), 3.44 (m, 4H), 2.80 (s, 4H), 2.45 (s, NH) ^{13}C NMR (100 MHz, $CDCl_3$): δ_c 154.6, 139.4, 131.8 (^2J=33.5 Hz), 127.7 (q), 123.1 (q, ^1J=272.4 Hz), 121.9 (q, J=3.8 Hz), 65.4, 45.6, 44.8.

HRMS (ESI-MS) calcd for $C_{14}H_{15}F_6N_2O_2$: 357.1038. Found: 357.1044

Deprotection using Mg/MeOH To a solution of the carbamate (0.06 mmol in 3 mL dry MeOH, 0.02 M) and dodecane (0.06 mmol, 13.6 µl, 0.02M) was added magnesium powder (50 mg, approx. 30 eq). The solution was stirred under nitrogen over night. The reaction mixture was filtered and and 10 ml K_2CO_3/potassium-sodium tartrate solution was added followed by 10 mL Et_2O. The organic phase was analyzed using GC. The conversion was calculated based on the reduction in starting material and appearance of 3,5-bis-trifluoromethyltoluene.

Competitive experiments using SmI_2 or Mg Equimolar amounts of CBz-protected adamantylamine, **1** and dodecane (as internal standard) was subjected to either a $SmI_2/Et_3N/H_2O$ solution in THF or a suspension of magnesium powder in dry methanol. Samples were withdrawn and analysed using gas chromatography and the decrease of carbamate (as well as increase of 3,5-bis-trifluorotoluene) was plotted against time.

Stability experiments In 0.5-1 ml of solvent (see table) was dissolved 0.05 mmol **1** and 0.05 mmol dodecane (as internal standard). A sample was taken, and the reagent was added to make approx. 1 mL. At 10 min, one hour and 24 hours samples were withdrawn and analysed using gas chromatography. A decrease in carbamate concentration was taken as evidence of breakdown.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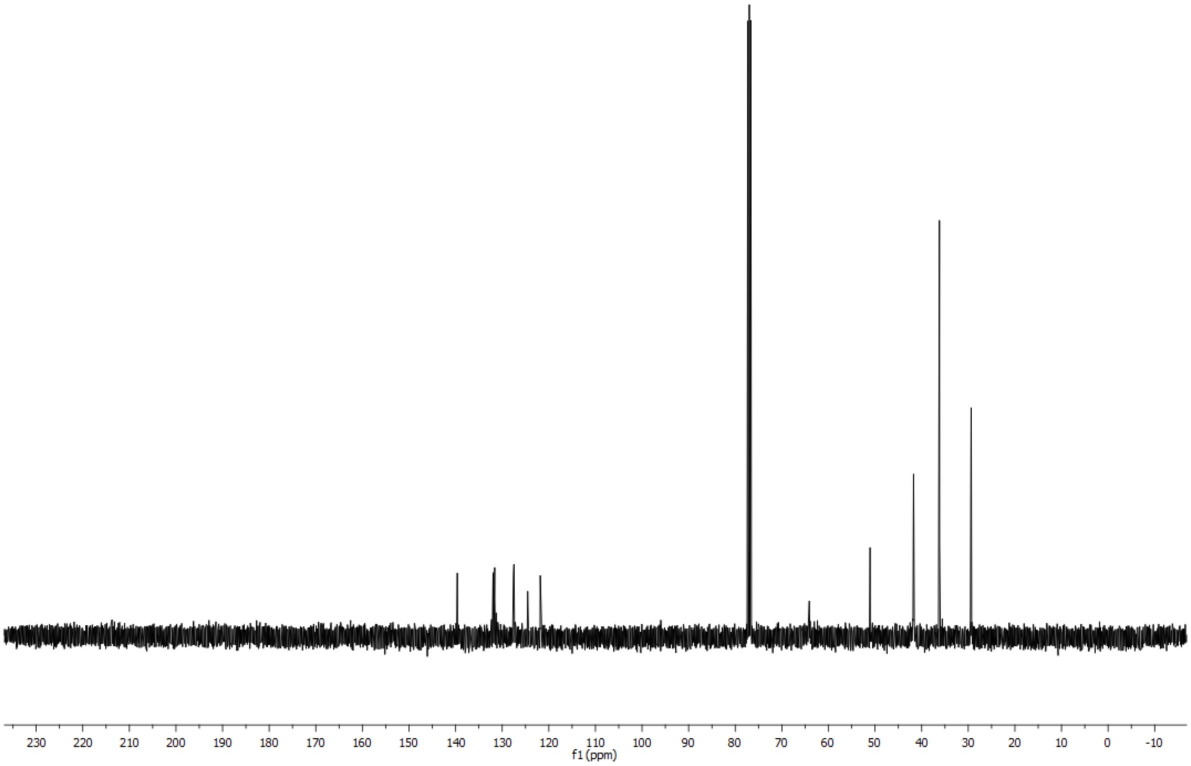
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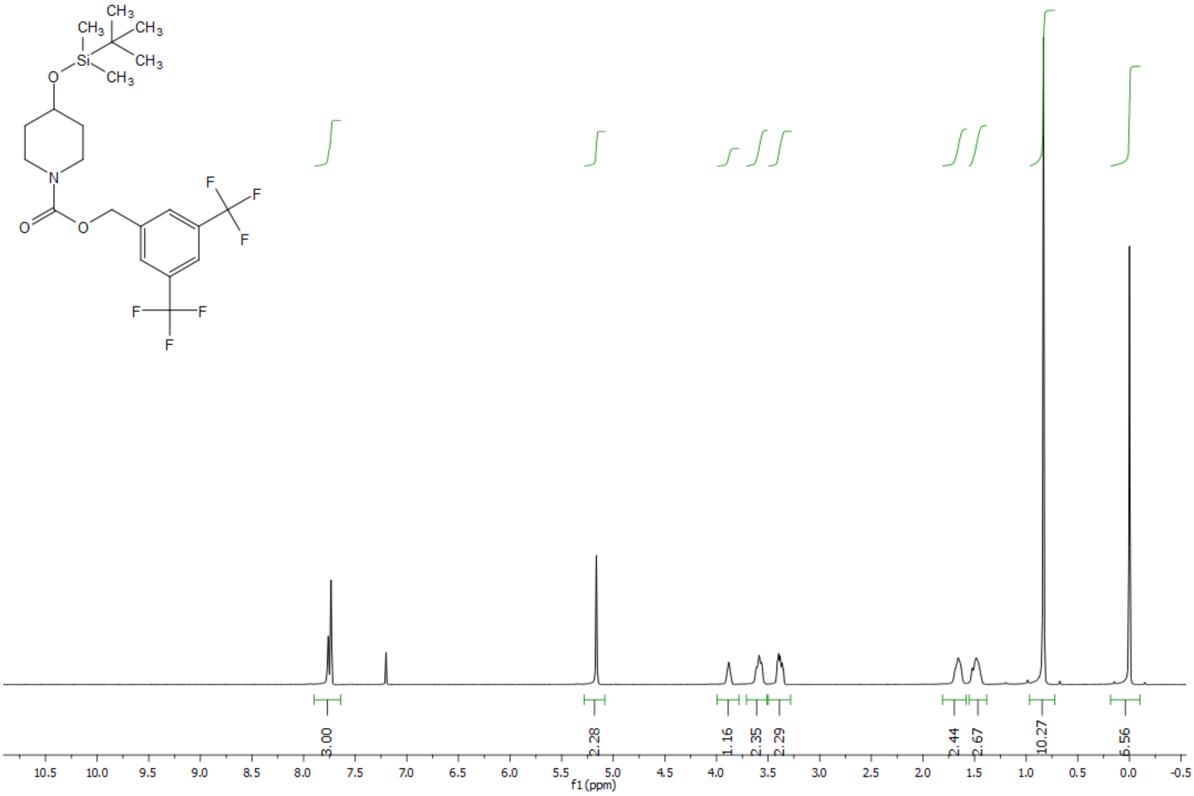
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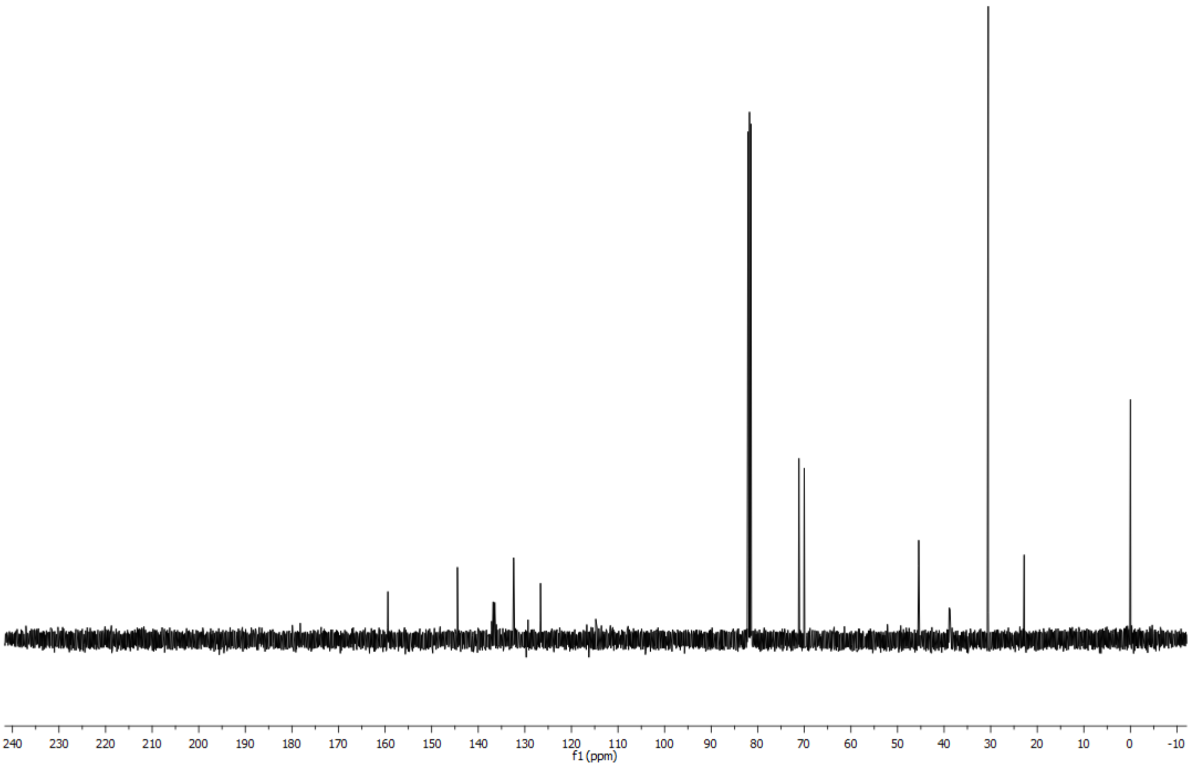
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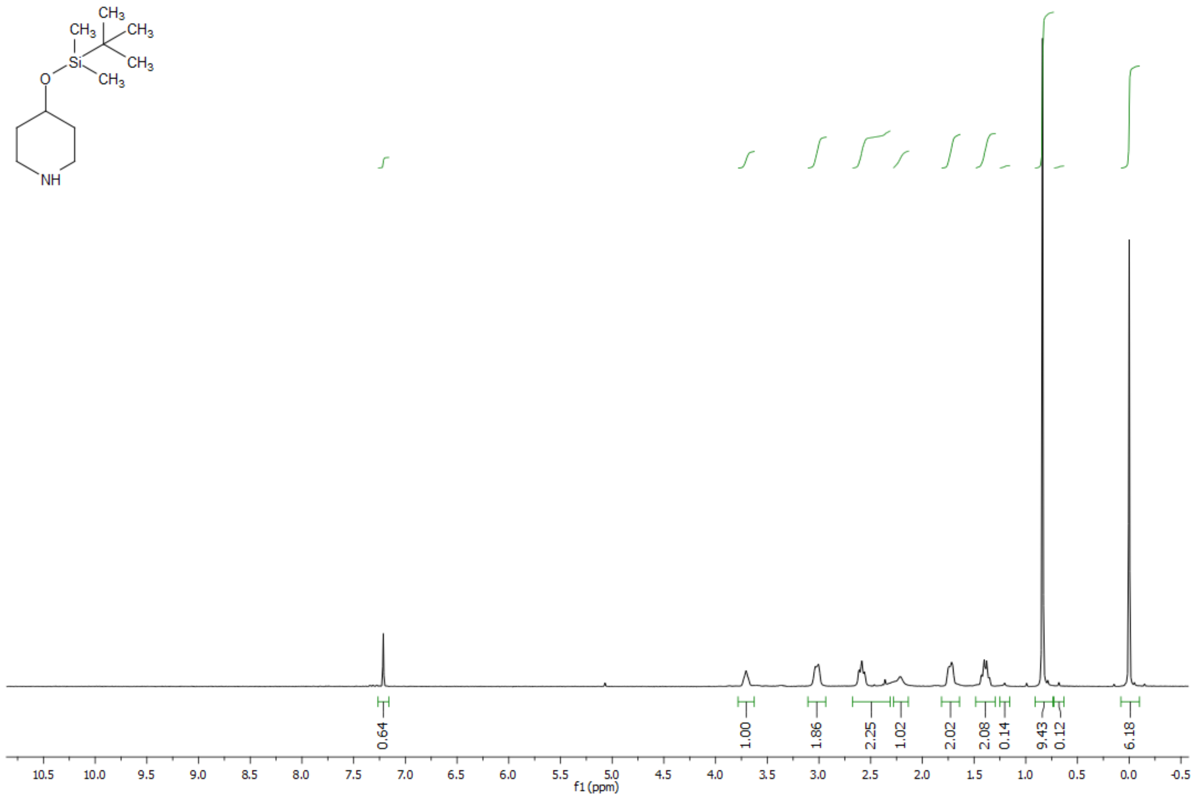
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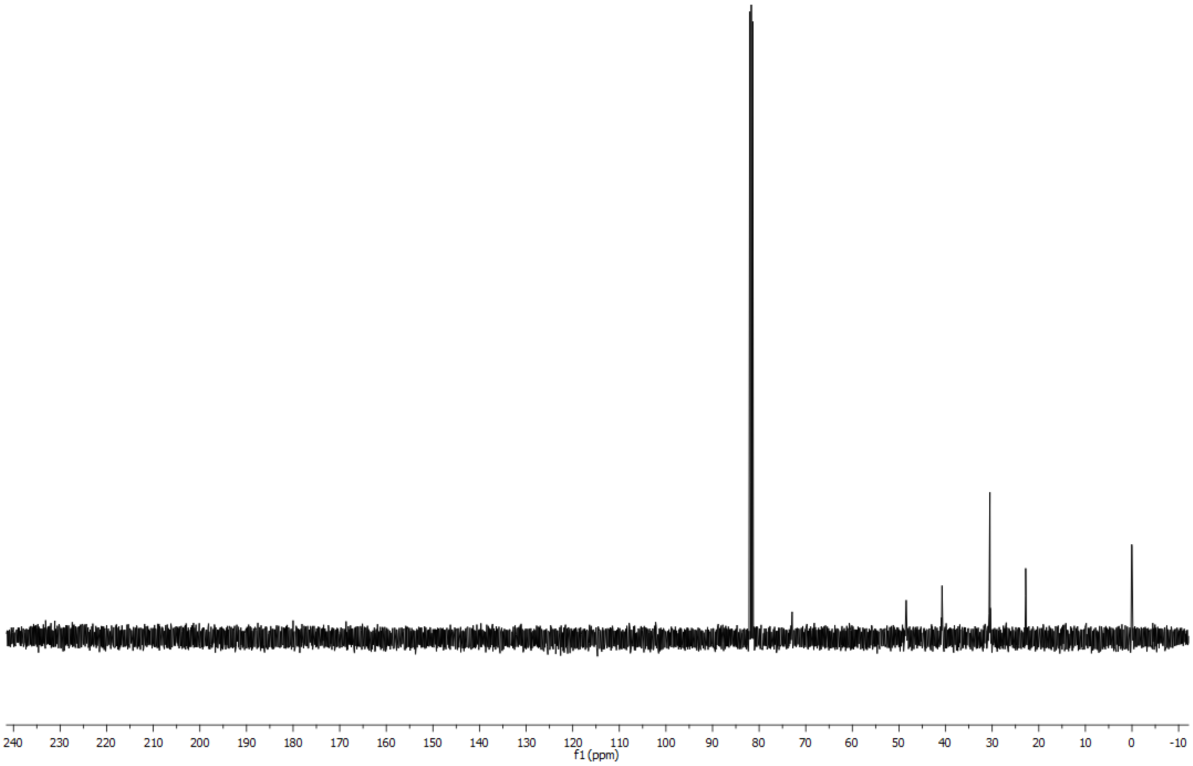
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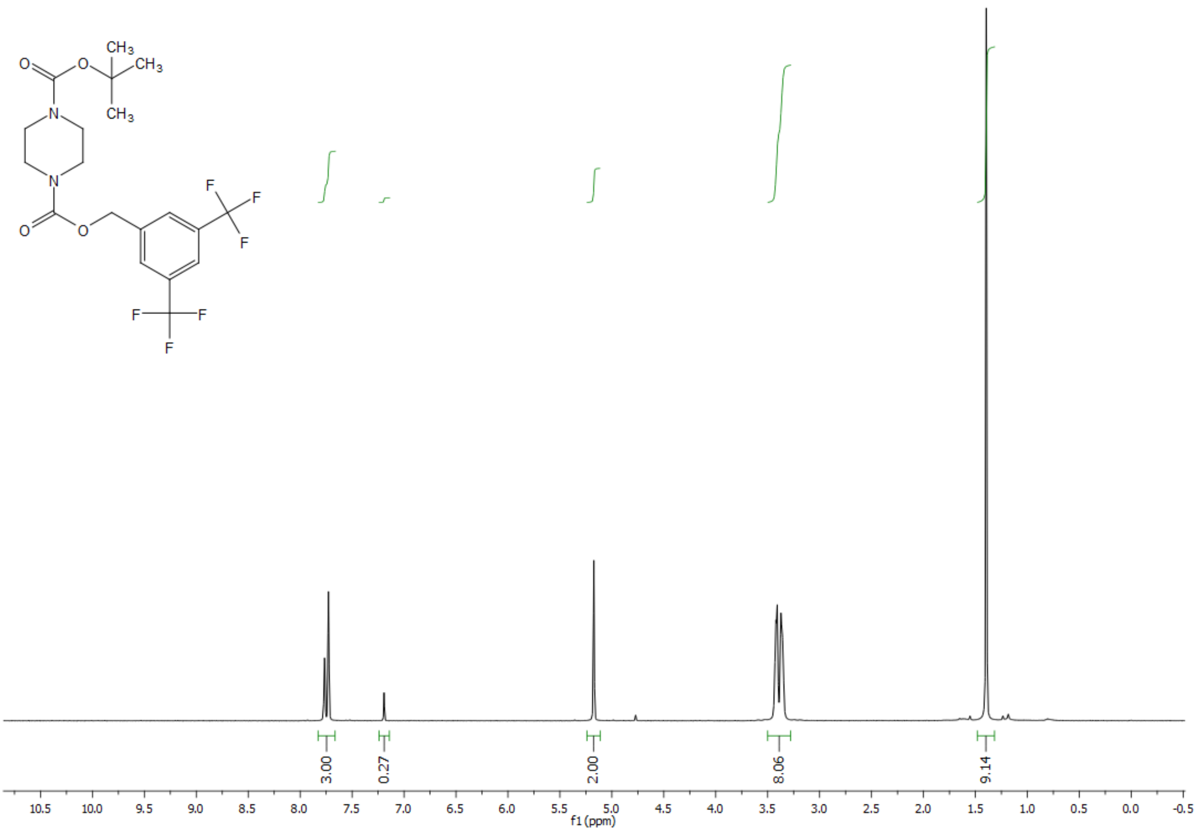
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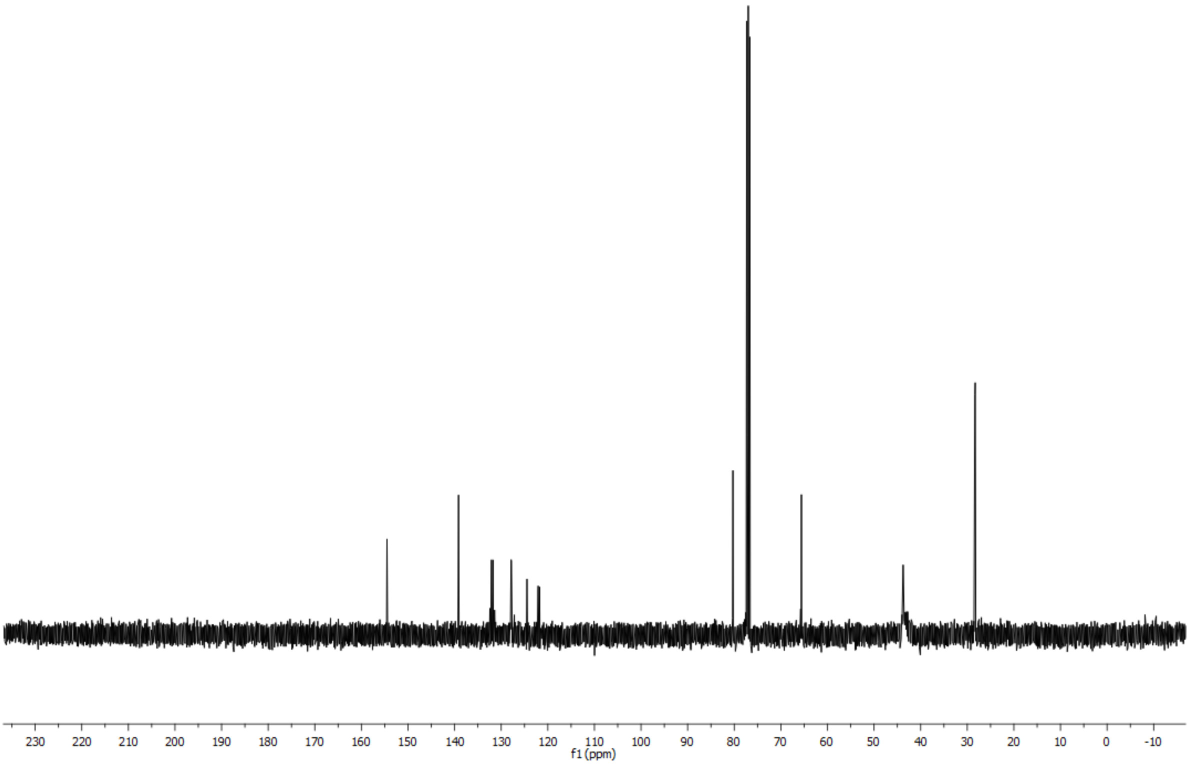
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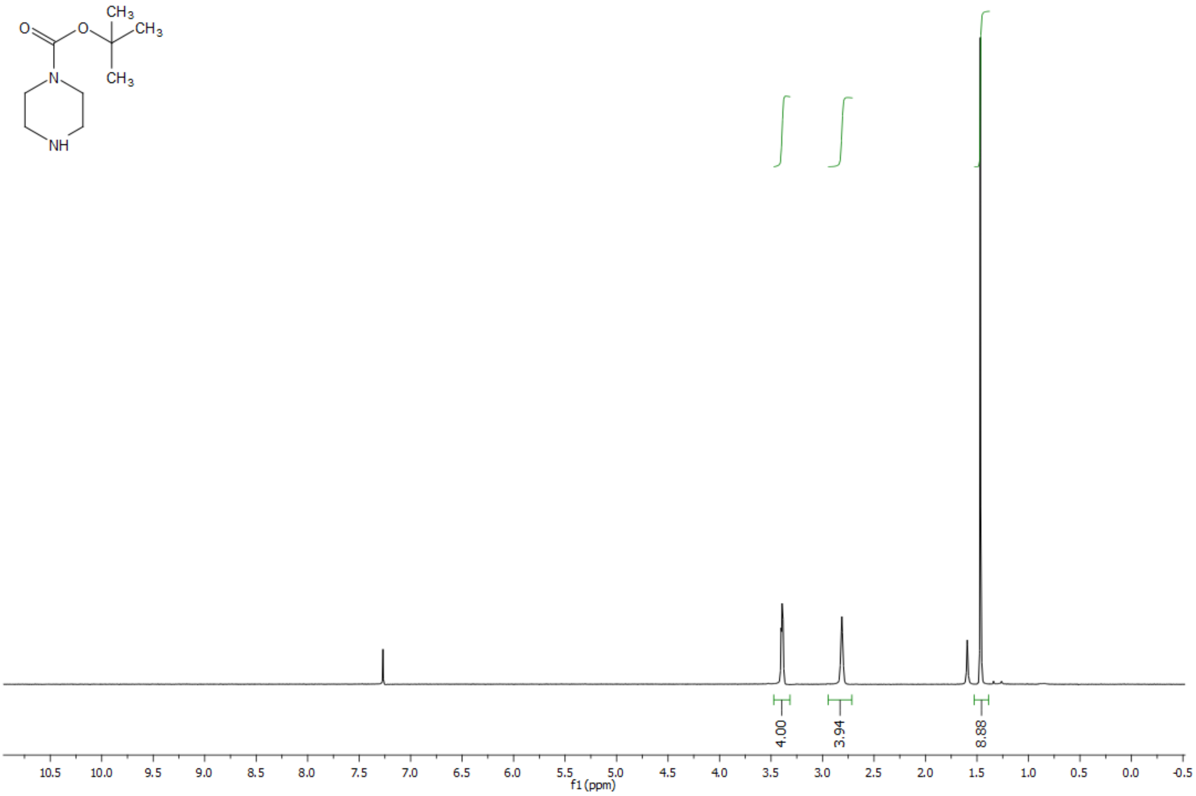
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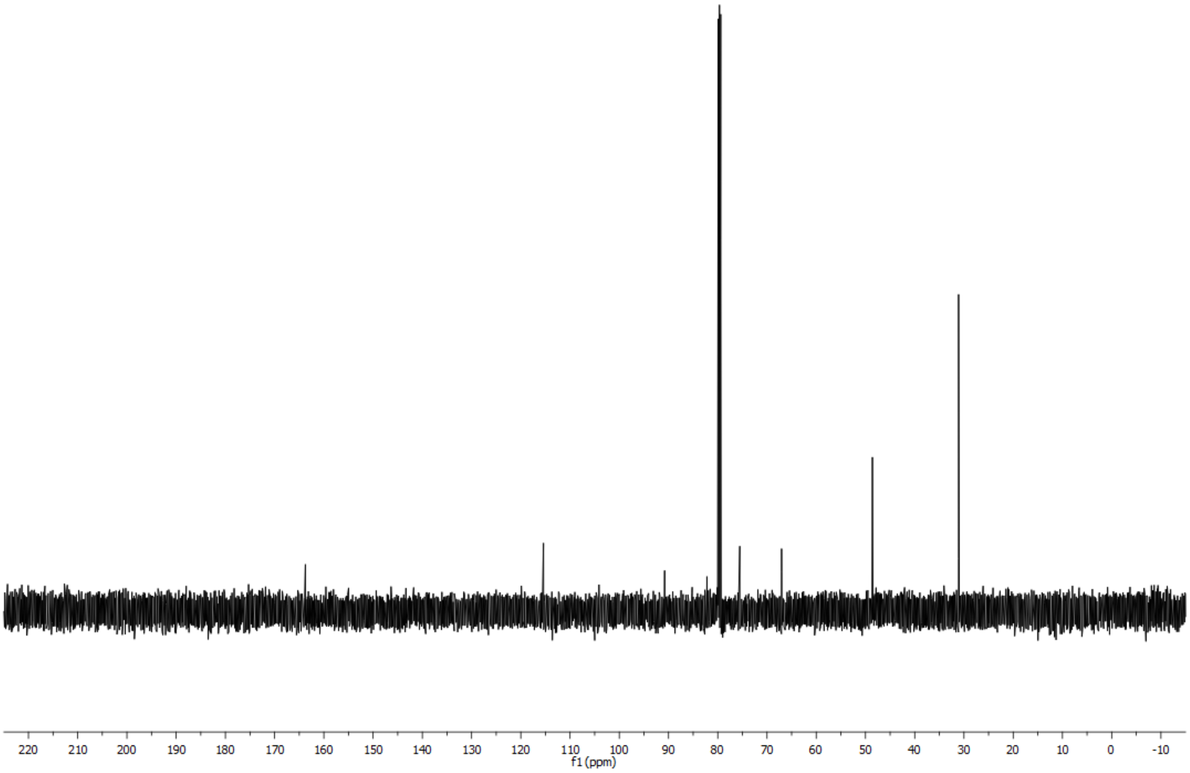
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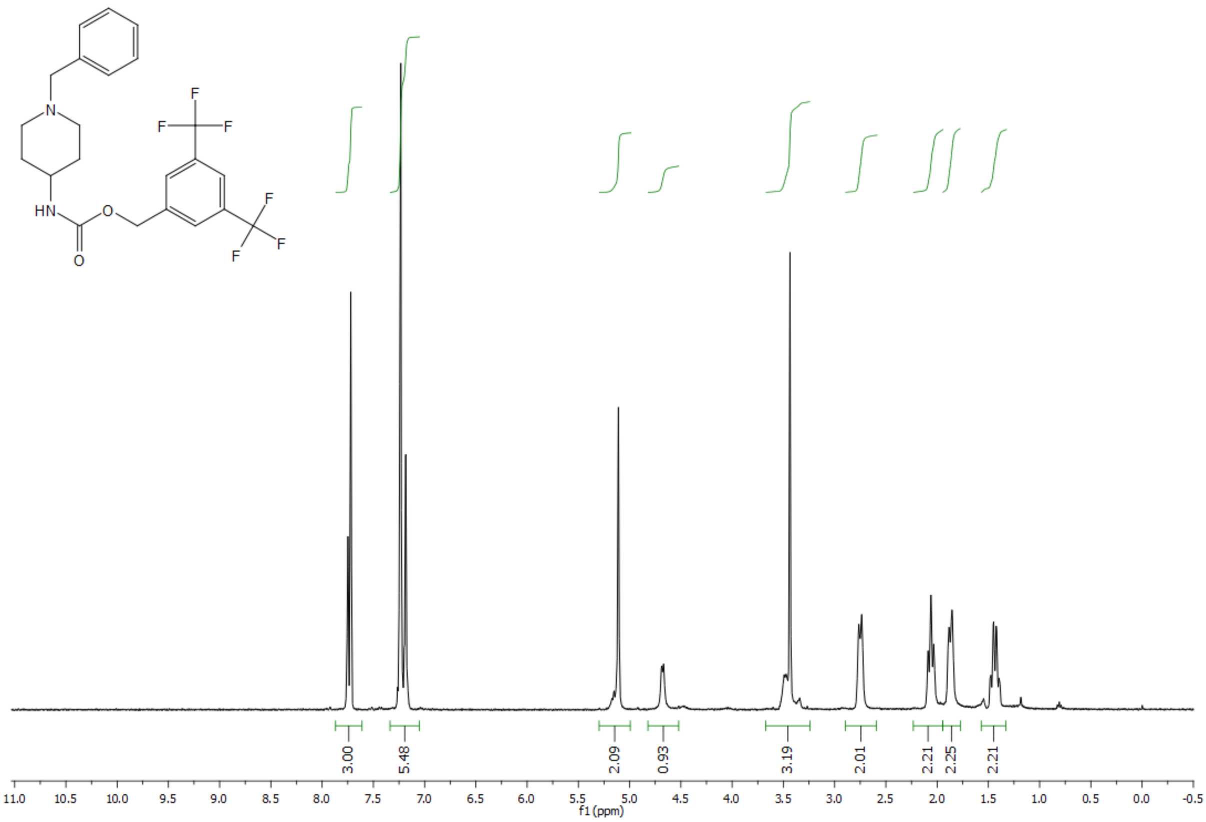
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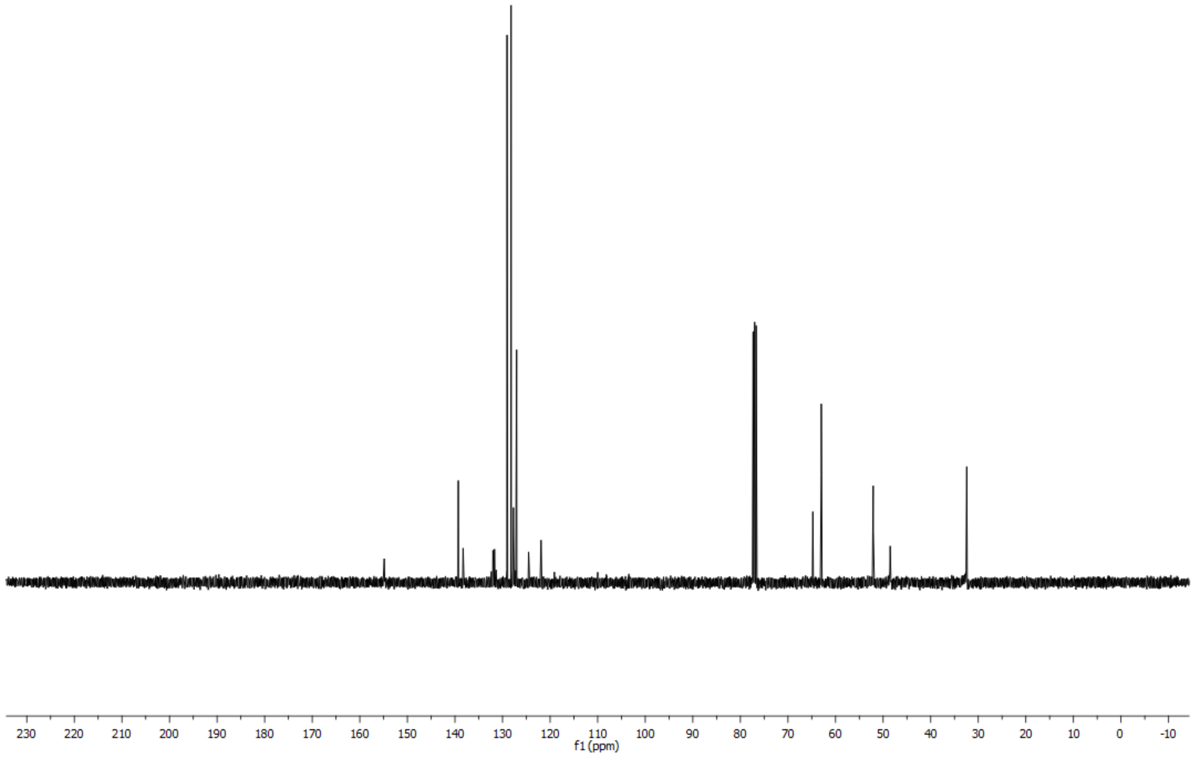
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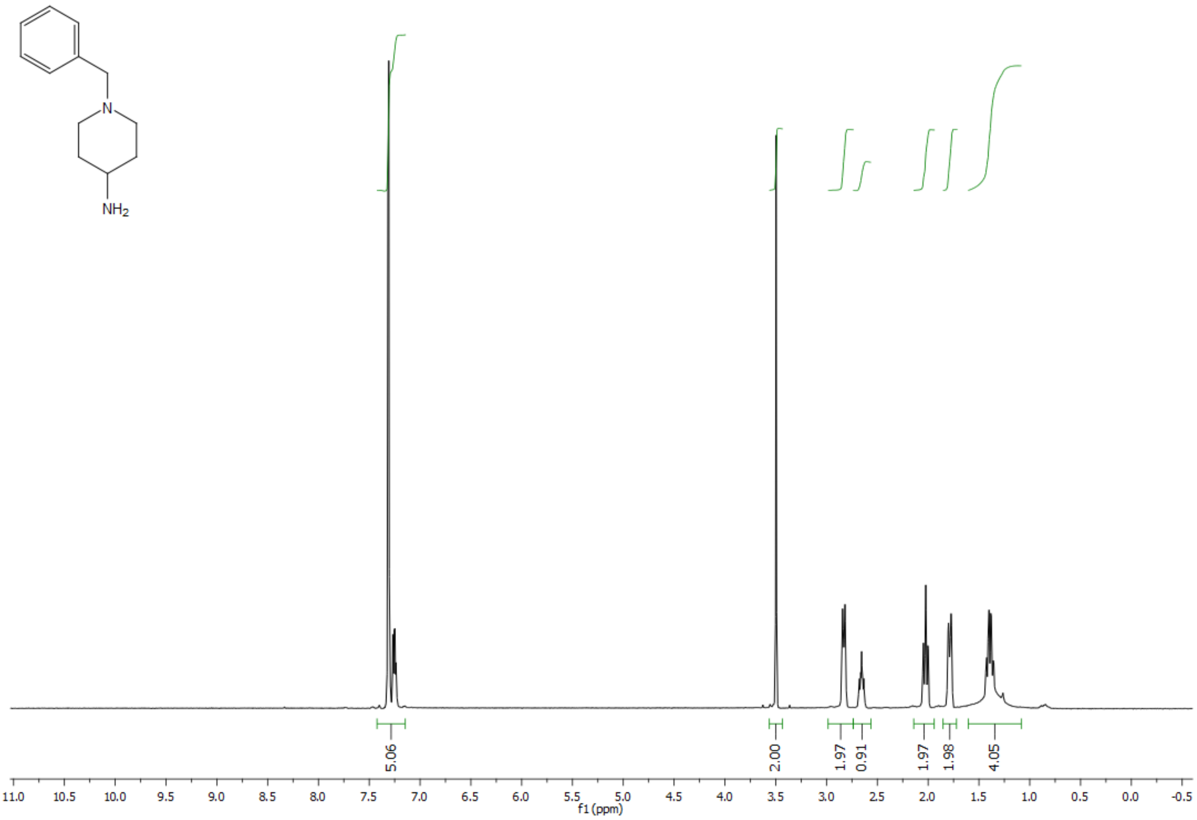
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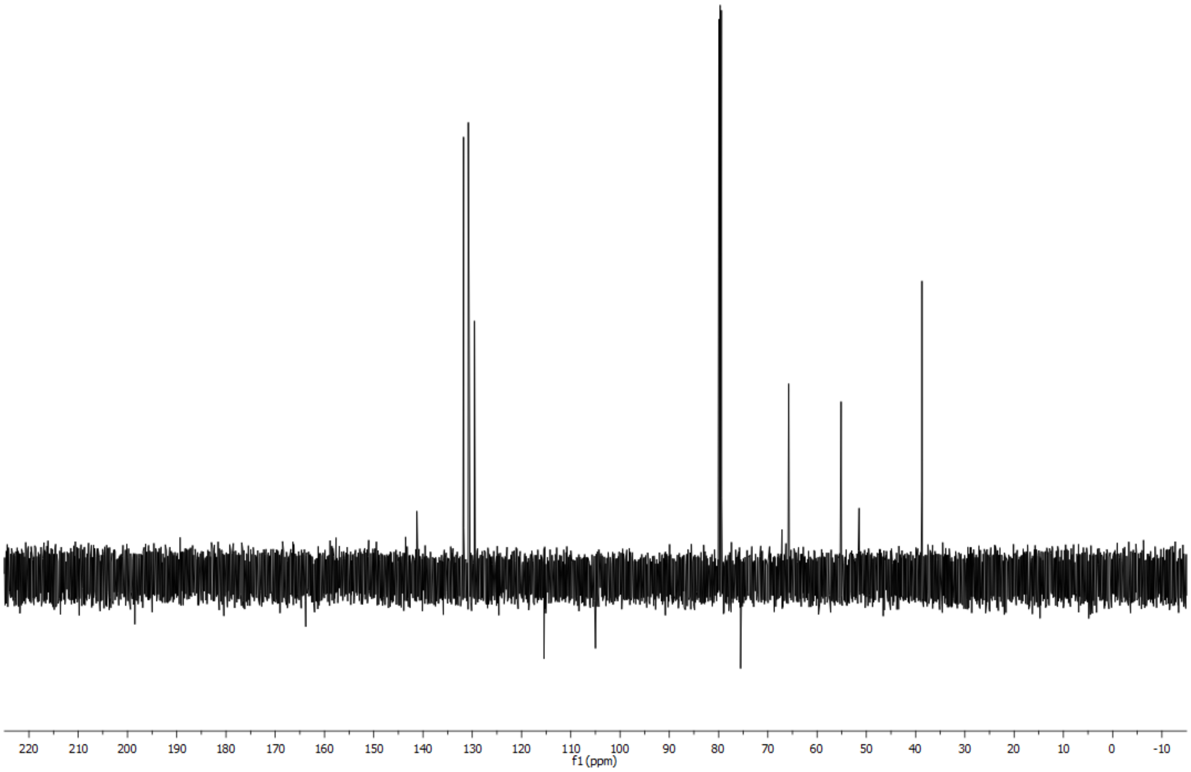
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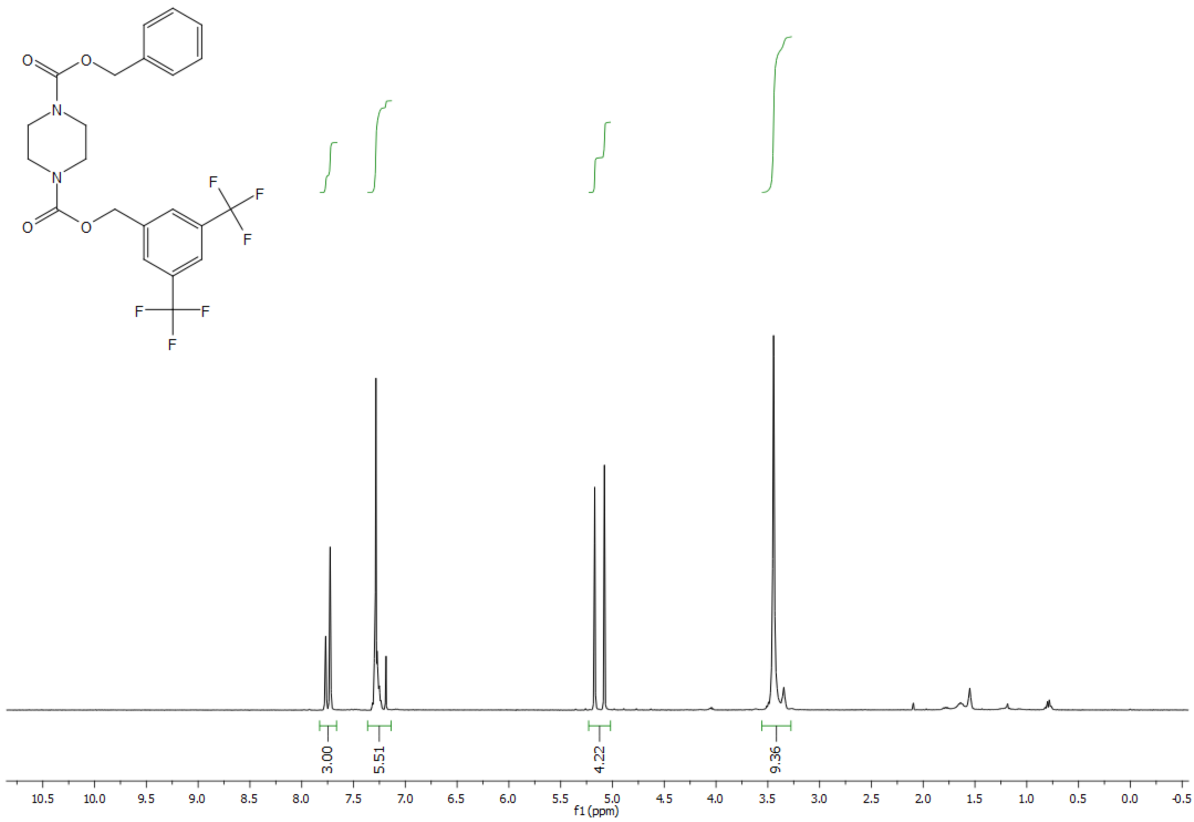
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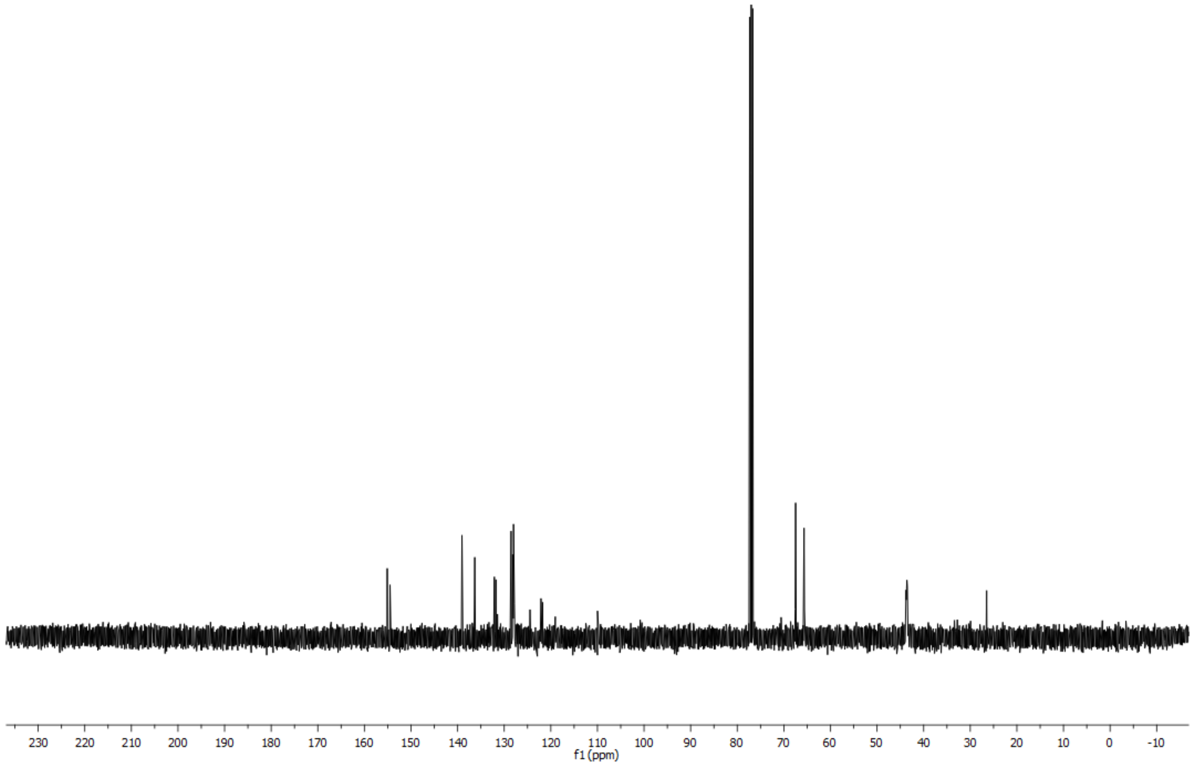
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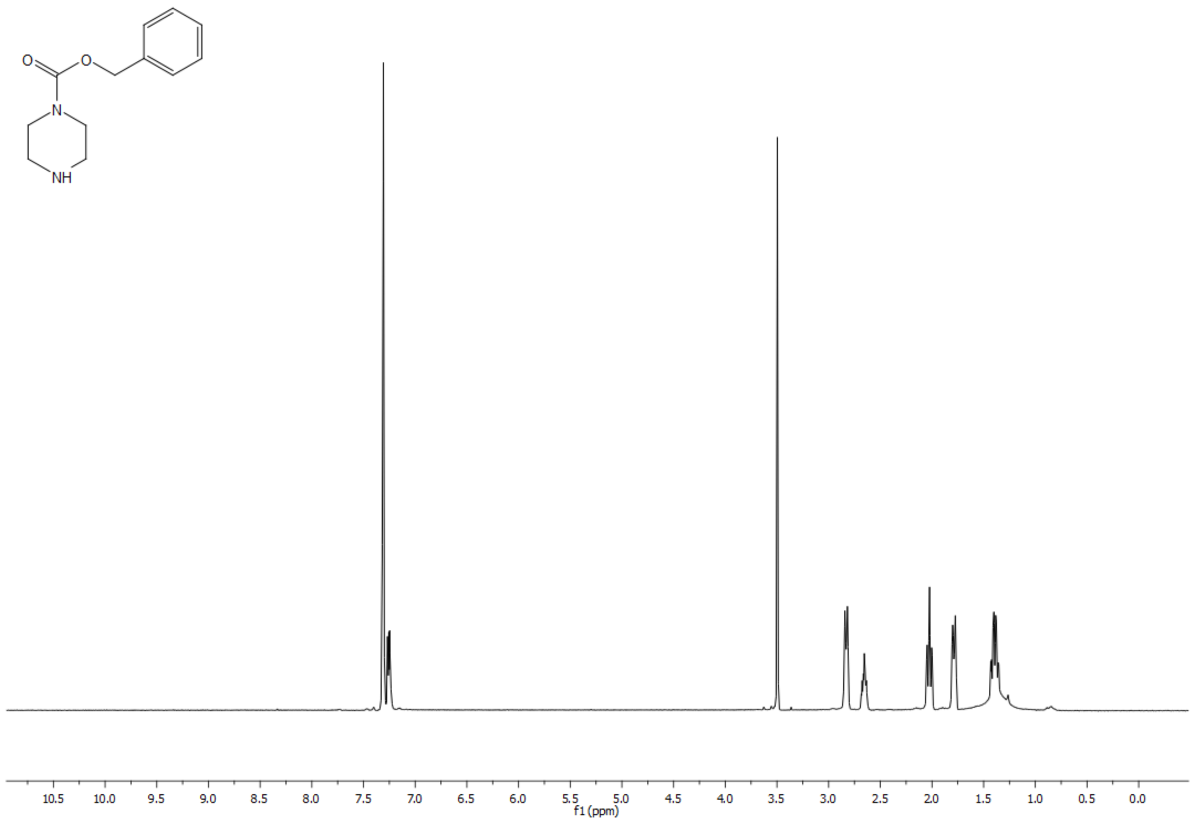
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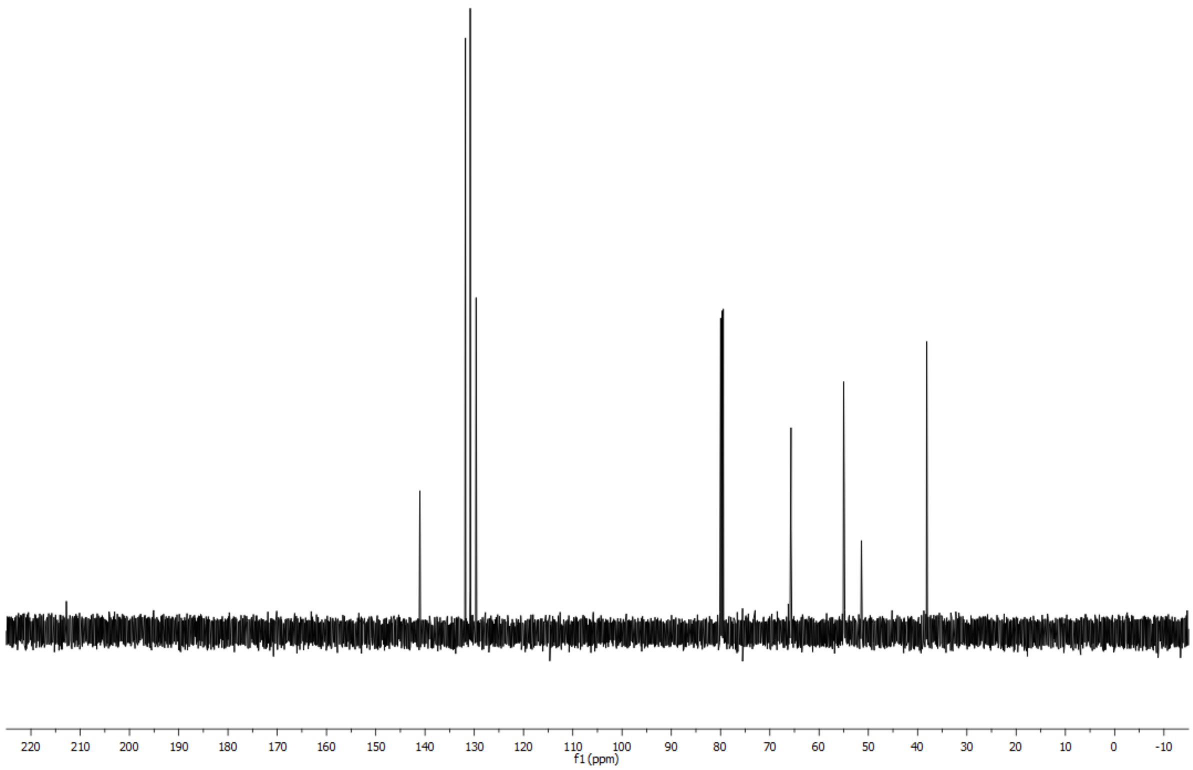
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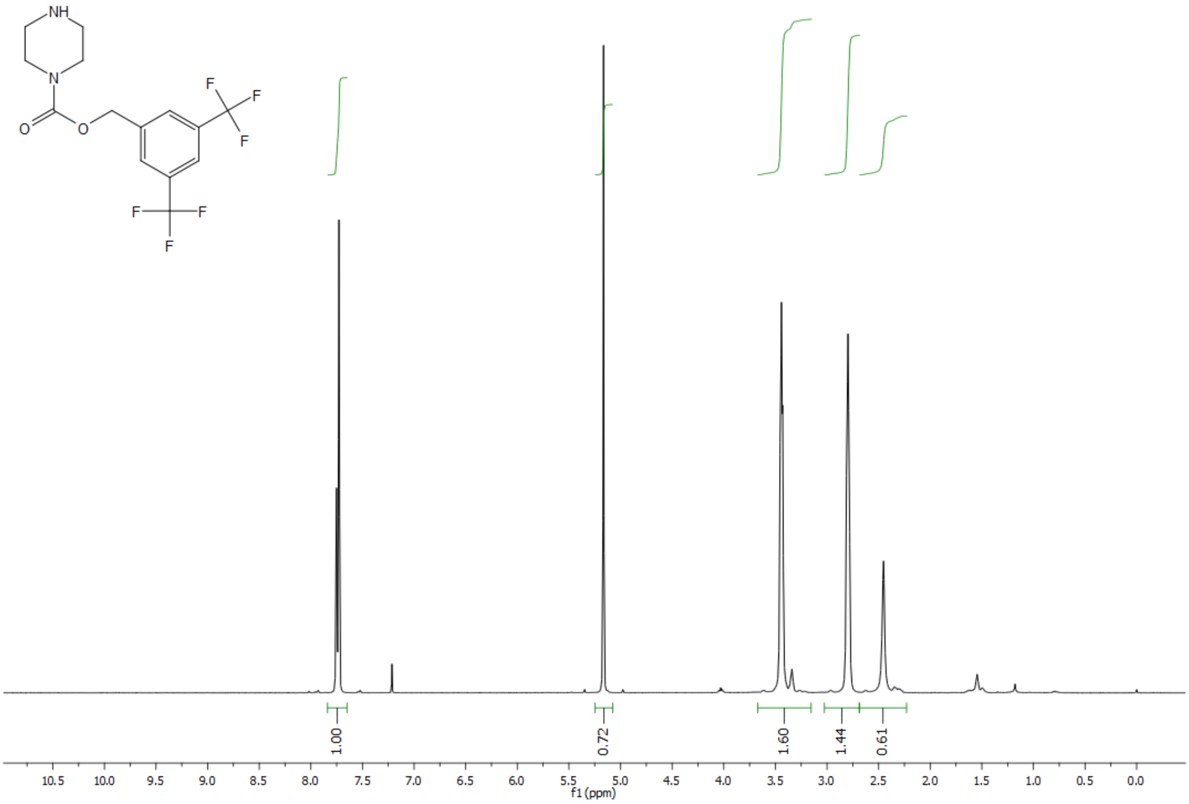
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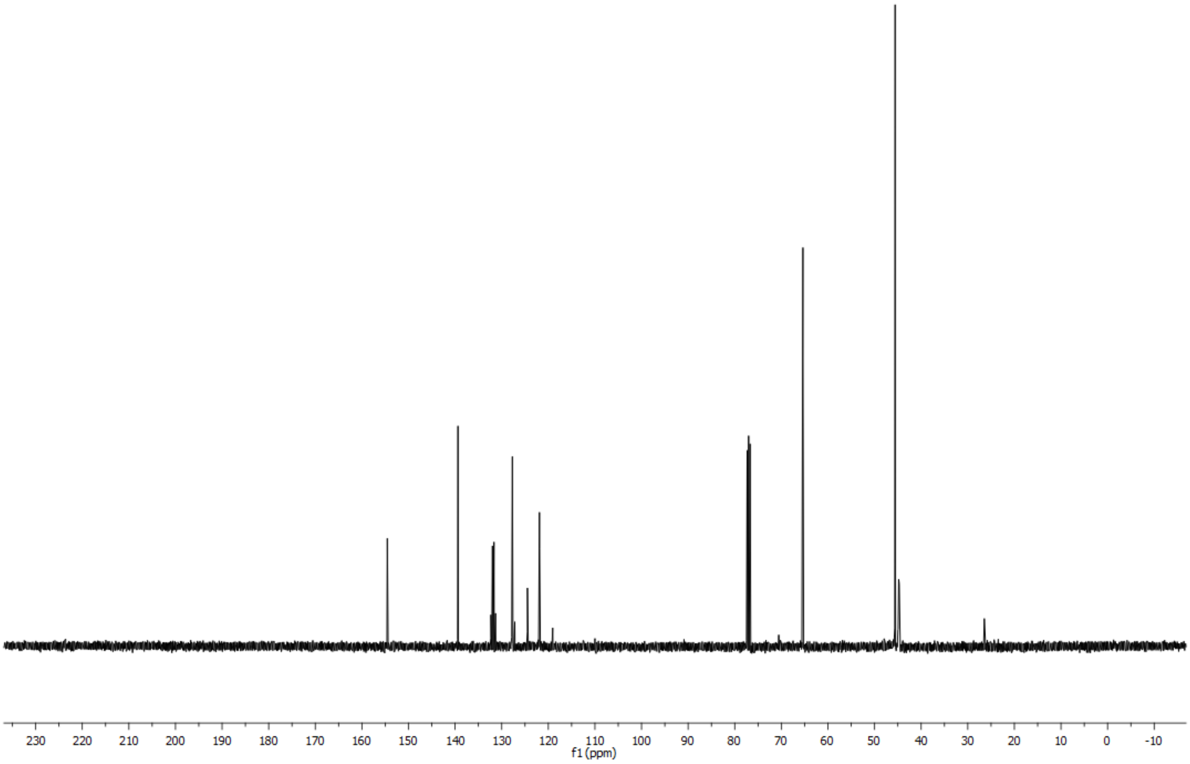
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