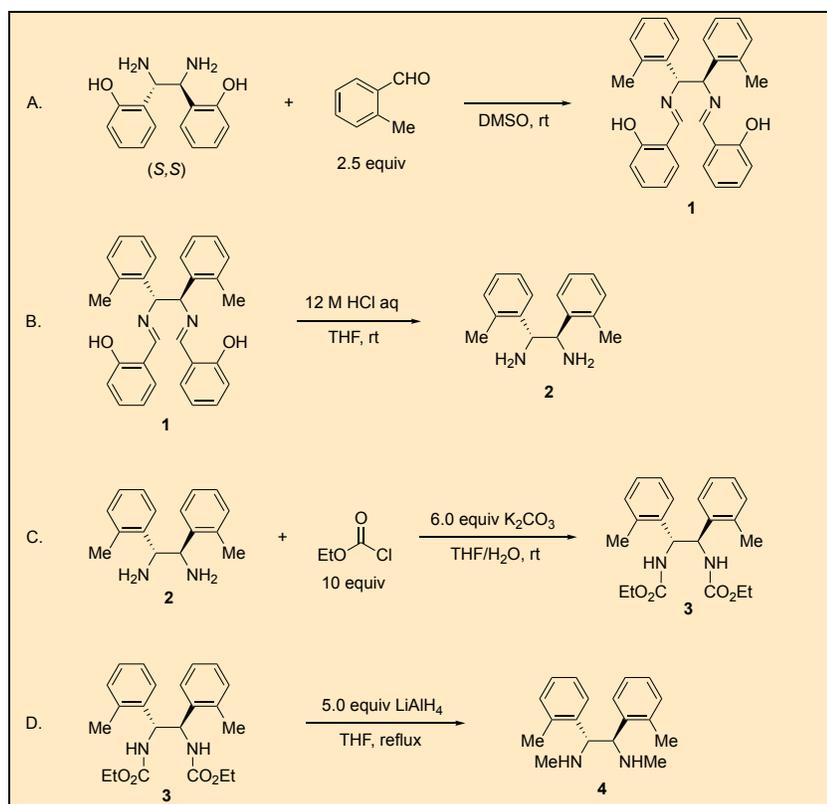


## Synthesis of Chiral Diamine Ligands for Nickel-catalyzed Asymmetric Cross-couplings of Alkylchloroboronate Esters with Alkylzincs: (1*R*,2*R*)-*N,N'*-Dimethyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane

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Checked by Skyler Mendoza and Sarah E. Reisman



**Procedure (Note 1)**

A. *(1R,2R)-N,N'-Bis(2-hydroxyphenylmethylene)-1,2-bis(2-methylphenyl)-1,2-diaminoethane (1)*. An oven-dried, 100-mL, two-necked, round-bottomed flask equipped with a magnetic stir bar (13 × 9 mm, octagon-type), a rubber septum, and a nitrogen line is evacuated under high vacuum (1.0 mmHg) and filled with nitrogen (three cycles). *(1S,2S)-1,2-Bis(2-hydroxyphenyl)-1,2-diaminoethane* (1.0 g, 4.1 mmol, 1.0 equiv) (Note 2) is added through the open neck under a positive pressure of nitrogen. The open neck is capped with a rubber septum, and then anhydrous DMSO (20 mL) (Note 3) and 2-methylbenzaldehyde (1.23 g, 10.2 mmol, 2.5 equiv) (Note 4) are added into the flask by syringe through the rubber septum. After the yellow solution (Figure 1) is stirred for 14 h at 20 °C, the reaction is quenched by the addition of distilled water (100 mL), and the mixture is extracted with Et<sub>2</sub>O (20 mL × 3). The combined organic layer is washed with water (30 mL) and a saturated aqueous solution of NaCl (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> (5 g), filtered through filter paper, and concentrated by rotary evaporation (30 mmHg, 30 °C) and under vacuum (1.0 mmHg). The product, obtained as a yellow oil as a mixture with unreacted 2-methylbenzaldehyde, is used in the next step without further purification (2.2 g, ~98% yield) (Note 5).



**Figure 1. Reaction Set-up**

B. *(1R,2R)-1,2-Bis(2-methylphenyl)-1,2-diaminoethane (2)*. An oven-dried, 100-mL, two-necked, round-bottomed flask equipped with a magnetic stir bar (13 × 9 mm, octagon-type), a rubber septum, and a nitrogen line is

evacuated under high vacuum (1.0 mmHg) and filled with nitrogen (three cycles). The solution of crude (1*R*,2*R*)-*N,N'*-bis(2-hydroxyphenylmethylene)-1,2-bis(2-methylphenyl)-1,2-diaminoethane (**1**) (1.7 g, ~3.3 mmol) in THF (50 mL) (Note 6) is added into the flask by syringe through the rubber septum, and then a 12 M HCl solution (1.5 mL) (Note 7) is added into the stirred reaction mixture by syringe over 1 min at 20 °C (Figure 2A). After the solution is stirred for 4 h (Figure 2B), Et<sub>2</sub>O (50 mL) is added to the reaction mixture, and then the diamine product is extracted with a 1 M HCl solution (10 mL × 3). The combined aqueous phase is washed with Et<sub>2</sub>O (10 mL), and then it is basified with a 2 M NaOH solution (40 mL). The resulting yellow suspension is extracted with Et<sub>2</sub>O (20 mL × 3). The combined organic layer is washed with water (30 mL) and a saturated aqueous solution of NaCl (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> (3 g), and filtered through filter paper. The volatiles are removed by rotary evaporation (30 mmHg, 30 °C) and under vacuum (1.0 mmHg) to give (1*R*,2*R*)-1,2-bis(2-methylphenyl)-1,2-diaminoethane (718 mg, 73% (2 steps)) as light brown powder (Notes 8, 9, and 10).

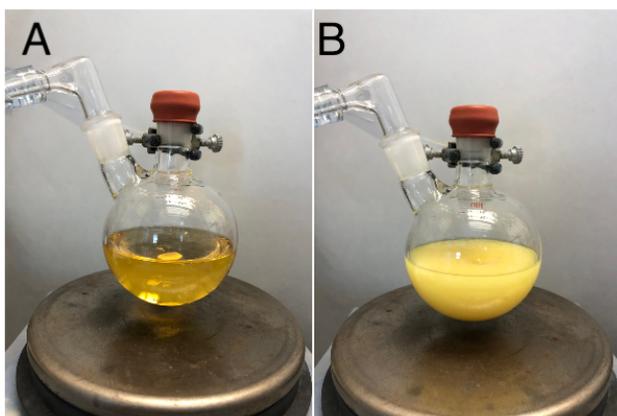


Figure 2. Reaction progression

C. (1*R*,2*R*)-*N,N'*-Diethoxycarbonyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane (**3**). An oven-dried, 100-mL, two-necked, round-bottomed flask equipped with a magnetic stir bar (13 × 9 mm, octagon-type), a rubber septum, and a nitrogen line is evacuated under high vacuum (1.0 mmHg) and filled with nitrogen (three cycles). Potassium carbonate (2.0 g, 15 mmol, 6.0 equiv) (Note 11) is added through the open neck under a positive pressure

of nitrogen. The open neck is capped by a rubber septum, and then a solution of (1*R*,2*R*)-1,2-bis(2-methylphenyl)-1,2-diaminoethane (**2**) (600 mg, 2.5 mmol, 1.0 equiv) in THF (20 mL) (Note 6) and distilled water (3 mL) are sequentially added into the flask by syringe through the rubber septum. After the resulting suspension (Figure 3A) is stirred for 10 min at 20 °C, ethyl chloroformate (2.5 mL, 2.9 g, 25 mmol, 10 equiv) (Note 12) is added dropwise into the flask by syringe over 5 min. The resulting mixture is stirred for 16 h at room temperature to give a white heterogeneous mixture (Figure 3B). This mixture is then diluted with distilled water (50 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic layer is washed with water (30 mL) and a saturated aqueous solution of NaCl (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> (5 g), filtered through filter paper, and concentrated by rotary evaporation (20 mmHg, 40 °C). The resulting yellow solid is purified by column chromatography on SiO<sub>2</sub> (wet packed in 30% EtOAc/hexanes; 3 cm diameter × 12 cm height; 50 g; eluting with 500 mL of 30% EtOAc/hexanes, 15-mL fractions) (Note 13). The desired product **3** has an R<sub>f</sub> = 0.3 (TLC analysis on SiO<sub>2</sub>; 30% EtOAc/hexanes, visualization with a 254 nm UV lamp) (Note 14). The desired product is obtained as a white solid (931 mg, 96% yield) (Notes 15 and 16).

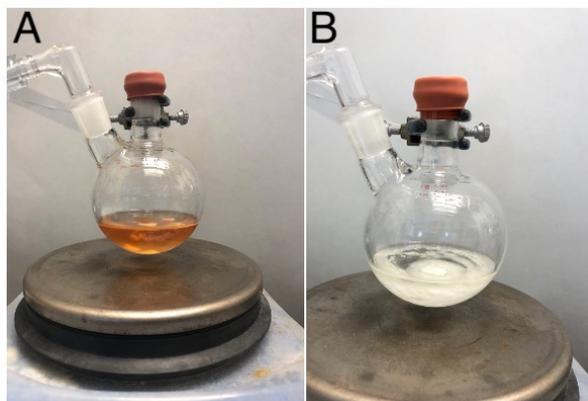


Figure 3. Reaction progression

D. (1*R*,2*R*)-*N,N'*-Dimethyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane (**4**). An oven-dried, 100-mL, two-necked, round-bottomed flask equipped with a condenser fitted with a nitrogen line, a magnetic stir bar (13 × 9 mm, octagon-type), and a rubber septum is evacuated under high vacuum (1.0 mmHg) and filled with nitrogen (three cycles). Lithium aluminum hydride (460 mg,

12 mmol, 5.0 equiv) (Note 17) is added through the open neck under a positive pressure of nitrogen. The open neck is capped by a rubber septum, and the flask is cooled by an ice/water bath. Anhydrous THF (10 mL) (Note 6) is added by syringe through the rubber septum, and the gray suspension is stirred at 0 °C for 5 min. A solution of (1*R*,2*R*)-*N,N'*-diethoxycarbonyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane (**3**) (900 mg, 2.3 mmol, 1.0 equiv) in THF (10 mL) is added dropwise by syringe through the rubber septum over 5 min (Figure 4A). The ice/water bath is replaced by an oil bath, and the reaction mixture is heated at reflux for 18 h. The mixture is cooled to 0 °C in an ice bath. Water (1 mL) is added dropwise by syringe through the septum over 10 min (Note 18), and then an aqueous solution of NaOH (3 M; 1 mL) is added in one portion. The resulting mixture is heated at reflux for 1 h until the color of the precipitate changes from gray to white (Figure 4B). The warm solution is filtered through a Büchner funnel that contains a bed of celite (1.0 cm height), and the precipitate is washed with Et<sub>2</sub>O (50 mL). The filtrate is concentrated by rotary evaporation (20 mmHg, 40 °C) and under vacuum (1 mmHg). The residue is dissolved in hexanes (50-mL) and the solution is filtered through a Büchner funnel with filter paper. The filtrate is concentrated by rotary evaporation (20 mmHg, 30 °C) and then under vacuum (1 mmHg), which yields the desired diamine ligand **4** as an off-white solid (558 mg, 88% yield, >99% *ee*) (Notes 19, 20 and 21).

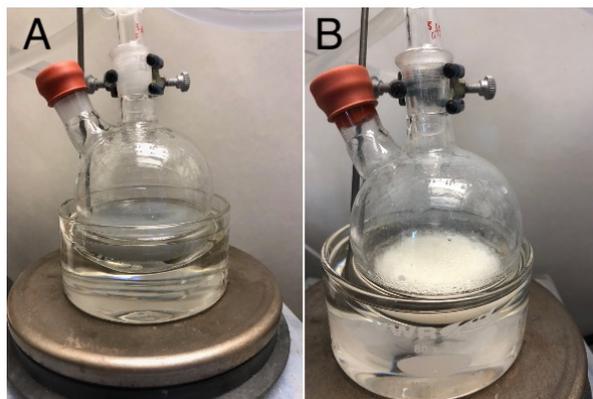


Figure 4. (A) Reaction set-up; (B) Quenched reaction

## Notes

1. Prior to performing each reaction, a thorough hazard analysis and risk assessment should be carried out with regard to each chemical substance and experimental operation on the scale planned and in the context of the laboratory where the procedures will be carried out. Guidelines for carrying out risk assessments and for analyzing the hazards associated with chemicals can be found in references such as Chapter 4 of "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at <https://www.nap.edu/catalog/12654/prudent-practices-in-the-laboratory-handling-and-management-of-chemical>. See also "Identifying and Evaluating Hazards in Research Laboratories" (American Chemical Society, 2015) which is available via the associated website "Hazard Assessment in Research Laboratories" at <https://www.acs.org/content/acs/en/about/governance/committees/chemicalsafety/hazard-assessment.html>. In the case of this procedure, the risk assessment should include (but not necessarily be limited to) an evaluation of the potential hazards associated with (1*S*,2*S*)-1,2-bis(2-hydroxyphenyl)-1,2-diaminoethane, dimethylsulfoxide, 2-methylbenzaldehyde, diethyl ether, sodium chloride, nitrogen, sodium sulfate, tetrahydrofuran, hydrochloric acid, sodium hydroxide, potassium carbonate, ethyl chloroformate, ethyl acetate, silica gel, hexanes, lithium aluminum hydride, and celite. Warning: Lithium aluminium hydride is pyrophoric and reacts violently with water.
2. (1*S*,2*S*)-1,2-Bis(2-hydroxyphenyl)-1,2-diaminoethane (min. 97%) was purchased from Strem and used as received.
3. Anhydrous DMSO (99.8+%) was purchased from Alfa-Aesar and used as received.
4. 2-Methylbenzaldehyde (97%) was purchased from Combi-Blocks and distilled (15 mmHg, 100 °C) before use to remove carboxylic acid.
5. The checkers did not purify the material prior to use in the next step, although the checkers report that compound **1** can be purified by column chromatography on SiO<sub>2</sub>, eluting with 10% EtOAc/hexanes:  $R_f = 0.35$  (10% EtOAc/hexanes, visualization with a 254 nm UV lamp). Compound **1**, when purified in this way, is obtained as a yellow solid, which has the following properties: mp 161–162 °C;  $[\alpha]_D^{23} +0.09$  (c 0.415, CHCl<sub>3</sub>); IR (film) 3466, 2924, 1660, 1627, 1581, 1490, 1460, 1277, 1151, 755,

- 733  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.07 (s, 6H), 5.13 (s, 2H), 6.80 (td,  $J = 7.4, 1.1$  Hz, 2H), 6.91 – 7.00 (m, 4H), 7.09 (td,  $J = 7.4, 1.4$  Hz, 2H), 7.14 – 7.20 (m, 4H), 7.26 (ddd,  $J = 8.3, 7.3, 1.7$  Hz, 2H), 7.62 (dd,  $J = 7.8, 1.4$  Hz, 2H), 8.33 (s, 2H), 13.34 (s, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 19.7, 74.9, 117.0, 118.7, 118.9, 126.3, 127.6, 128.9, 130.6, 131.9, 132.8, 135.53, 137.6, 161.1, 166.1. HRMS (DI-ESI)  $m/z$  calcd. for  $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ) 449.2224; found 449.2219. Following chromatography, the purity of compound **1** (97%) was determined by quantitative  $^1\text{H}$  NMR analysis using 1,1,2,2-tetrachlorethane as an internal standard.
- Anhydrous THF (99+%) was purchased from J.T. Baker (water content: 24 ppm) and purified by passage through activated alumina under argon.
  - A solution of 12 M HCl was purchased from Fisher Scientific and used as received.
  - Submitters reported the product to be a yellow oil while checkers found the product to be a light brown powder.
  - A second reaction performed on the same scale provided 708 mg (72% for two steps) of the product (**2**).
  - Compound **2** has the following properties: mp: 80–82 °C;  $[\alpha]_{\text{D}}^{22} +22.5$  (c 0.955,  $\text{CHCl}_3$ ); IR (neat) 3367, 3021, 2930, 1582, 1488, 1462, 1358, 1317, 1050, 897, 730 ( $\text{cm}^{-1}$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 1.65 (s, 4H), 2.12 (s, 6H), 4.34 (s, 2H), 7.02 (dd,  $J = 7.6, 1.6$  Hz, 2H), 7.10 (td,  $J = 7.4, 1.4$  Hz, 2H), 7.20 (td,  $J = 7.5, 1.5$  Hz, 2H), 7.59 (dd,  $J = 7.8, 1.4$  Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 19.7, 55.9, 126.1, 126.9 (2C), 130.4, 135.3, 141.8. HRMS (DI-ESI)  $m/z$  calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_2$  ( $[\text{M}+\text{H}]^+$ ) 241.1699; found 241.1695. The purity of compound **2** (97%) was determined by quantitative  $^1\text{H}$  NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.
  - Potassium carbonate (anhydrous, 99%) was purchased from Alfa-Aesar and used as received.
  - Ethyl chloroformate (97%) was purchased from Aldrich and used as received.
  - Column chromatography was performed on Silicycle 60 Å silica gel.
  - Analytical thin-layer chromatography was performed using EMD 0.25 mm silica gel 60-F<sub>254</sub> plates. The checkers used Merck 0.25 mm TLC silica gel 60-F<sub>254</sub> plates.
  - A second reaction performed on the same scale provided 921 mg (95%) of the product (**3**).
  - Compound **3** has the following properties: mp (dec.) 90–103 °C;  $[\alpha]_{\text{D}}^{23} -44.1$  (c 0.96,  $\text{CHCl}_3$ ); IR (film) 3320, 2978, 1687, 1534, 1258, 1051,

- 910, 769, 732 (cm<sup>-1</sup>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ : 1.24 (t, *J* = 7.1 Hz, 6H), 1.95 (s, 6H), 3.97 – 4.24 (m, 4H), 5.25 – 5.36 (m, 2H), 5.50 – 5.65 (m, 2H), 6.93 (d, *J* = 7.5 Hz, 2H), 7.07 (td, *J* = 7.5, 1.4 Hz, 2H), 7.17 (td, *J* = 7.5, 1.5 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 2H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ: 14.7, 19.4, 56.5, 61.2, 126.4, 126.7, 127.8, 130.6, 136.3, 137.8, 157.4; HRMS (DI-ESI) *m/z* calcd. for C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub> ([M+H]<sup>+</sup>) 385.2122; found 385.2121. The purity of compound **3** (98%) was determined by quantitative <sup>1</sup>H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.
17. Lithium aluminum hydride (powder, 95%) was purchased from Strem and used as received.
18. Quenching excess lithium aluminum hydride with water is a highly exothermic process that produces H<sub>2</sub>. Dropwise addition of water is recommended, and care should be taken to efficiently cool and stir the reaction mixture.
19. A second reaction performed on the same scale provided 551 mg (85%) of the product (**4**).
20. Compound **4** has the following properties: mp 100–102 °C; [α]<sub>D</sub><sup>23</sup> +7.2 (c 0.96, CHCl<sub>3</sub>); IR (film) 3296, 3234, 2918, 2862, 2783, 1488, 1463, 1426, 1339, 1175, 1140, 1106, 900, 864, 768, 731 (cm<sup>-1</sup>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ: 1.91 (s, 6H), 2.24 (s, 6H), 2.61 (s, 2H), 3.94 (s, 2H), 6.86 (ddt, *J* = 7.7, 1.4, 0.7 Hz, 2H), 7.01 (td, *J* = 7.4, 1.4 Hz, 2H), 7.18 – 7.11 (m, 2H), 7.50 (dd, *J* = 7.7, 1.4 Hz, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 101 MHz) δ: 19.5, 34.2, 65.2, 125.8, 126.6, 126.7, 129.9, 137.0, 139.6; HRMS (DI-ESI) *m/z* calcd. for C<sub>18</sub>H<sub>24</sub>N<sub>2</sub> ([M+H]<sup>+</sup>) 269.2012; found 269.2006. The purity of compound **4** (97%) was determined by quantitative <sup>1</sup>H NMR analysis using ethylene carbonate as an internal standard.
21. Compound **4** is converted to the acetylated amide for *ee* determination as follows: An oven-dried 8-mL vial equipped with a magnetic stir bar is charged with compound **4** (54 mg, 0.20 mmol, 1.0 equiv), and then it is capped with a PTFE-lined pierceable cap. The vial is evacuated and backfilled with nitrogen (three cycles). Dichloromethane (2 mL) is added by syringe. The solution is stirred at room temperature for 5 min, then acetyl chloride (47 mg, 0.60 mmol, 3.0 equiv) (Note 22) and triethylamine (61 mg, 0.60 mmol, 3.0 equiv) (Note 23) are sequentially added by syringe. The resulting solution is stirred for 16 h. The reaction is quenched by water (5 mL), and the reaction mixture is extracted with ethyl acetate (10 mL × 3). The combined organic layer is washed with water (10 mL) and a saturated aqueous solution of NaCl (10 mL), dried

- over anhydrous  $\text{Na}_2\text{SO}_4$  (1 g), filtered through filter paper, and concentrated by rotary evaporation (20 mmHg, 40 °C) and under vacuum (1 mmHg). The resulting yellow oil is purified by preparative thin-layer chromatography (Note 24) with EtOAc as the eluent ( $R_f = 0.2$ ), which gives (1*R*,2*R*)-*N,N'*-diacetyl-*N,N'*-dimethyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane as a white solid.
22. The acetylated product has the following properties: mp 31–32 °C;  $[\alpha]_D^{23} -2.8$  (c 0.350,  $\text{CHCl}_3$ ); IR (film) 3065, 3019, 2928, 2853, 1651, 1461, 1396, 1313, 1143, 1010, 739  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.08 (s, 6H), 2.36 (s, 5H), 2.68 (s, 6H), 6.58 (s, 2H), 6.86–6.94 (m, 4H), 7.06 (ddd,  $J = 7.5, 6.2, 2.4$  Hz, 2H), 7.15 (dq,  $J = 8.2, 0.7$  Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 19.9, 22.5, 32.6, 51.3, 125.4, 127.6, 129.3, 131.0, 135.0, 138.0, 170.8; HRMS (DI-ESI)  $m/z$  calcd. for  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ) 353.2224; found 353.2229. The purity of the compound (99%) was determined by quantitative  $^1\text{H}$  NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The *ee* (> 99%) was determined by HPLC analysis with an Agilent 1100 Series HPLC system equipped with a CHIRALPAK OD-H column (length 250 mm, I.D. 4.6 mm) (hexanes/2-propanol 90:10, 1.0 mL/min) with  $t_r$  (major) = 6.3 min,  $t_r$  (minor) = 7.7 min. The peak areas were measured at  $\lambda = 230$  nm.
23. Acetyl chloride (98%) was purchased from Sigma-Aldrich and used as received.
24. Triethylamine (>99%) was purchased from Sigma-Aldrich and used as received.

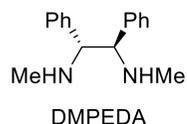
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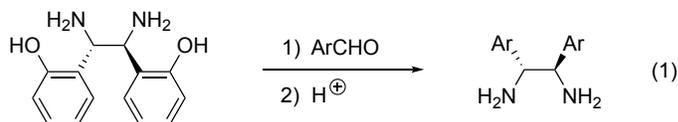
## Discussion

Chiral *N,N'*-dimethyl-1,2-diphenylethylene-1,2-diamine (DMPEDA) and its derivatives are used as chiral ligands for metal-catalyzed asymmetric reactions. Rhodium and iridium/DMPEDA complexes catalyze asymmetric hydrogen transfer reactions with high enantioselectivity.<sup>2</sup>



We found that a nickel/diamine catalyst is effective for alkyl-alkyl cross-coupling reactions.<sup>3</sup> Furthermore, the use of chiral DMPEDA-type ligands enables the enantioconvergent cross-coupling of racemic alkyl halides with various organometallic compounds.<sup>4</sup> For the Negishi coupling of alkylchloroboronate esters with alkylzincs, (1*R*,2*R*)-*N,N'*-dimethyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane **4** is the best ligand in terms of yield and enantioselectivity.<sup>5</sup> Herein, we report a procedure for the synthesis of diamine ligand **4**.

The procedure for the synthesis of 1,2-bis(2-methylphenyl)-1,2-diaminoethane **2** is based on the method reported by Chin and co-workers.<sup>6</sup> A series of diphenylethylenediamine derivatives is synthesized from a single diamine (1,2-bis-(2-hydroxyphenyl)-1,2-diaminoethane) with this method. (Eq 1)



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## Appendix

## Chemical Abstracts Nomenclature (Registry Number)

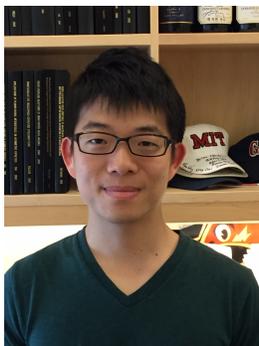
- (1S,2S)-1,2-Bis(2-hydroxyphenyl)-1,2-diaminoethane: Phenol, 2,2'-[(1S,2S)-1,2-diamino-1,2-ethanediyl]bis-; (870991-68-7)  
2-Methylbenzaldehyde: Benzaldehyde, 2-methyl-; (529-20-4)  
(1R,2R)-N,N'-Bis(2-hydroxyphenylmethylene)-1,2-bis(2-methylphenyl)-1,2-diaminoethane: Phenol, 2,2'-[[(1R,2R)-1,2-bis(2-methylphenyl)-1,2-ethanediyl]bis[(E)-nitrilomethylidyne]]bis-; (1055301-46-6)  
(1R,2R)-1,2-Bis(2-methylphenyl)-1,2-diaminoethane: 1,2-Ethanediamine, 1,2-bis(2-methylphenyl)-, (1R,2R)-; (872595-04-5)  
Ethyl chloroformate: Carbonochloridic acid, ethyl ester; (541-41-3)  
Potassium carbonate: Carbonic acid, potassium salt (1:2); (584-08-7)

Lithium aluminum hydride: Aluminate(1-), tetrahydro-, lithium (1:1), (T-4)-;  
(16853-85-3)

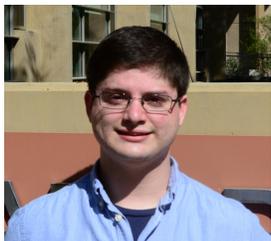
(1R,2R)-N,N'-Dimethyl-1,2-bis(2-methylphenyl)-1,2-diaminoethane: 1,2-  
Ethanedi-amine, N<sup>1</sup>,N<sup>2</sup>-dimethyl-1,2-bis(2-methylphenyl)-, (1R,2R)-;  
(2055363-47-6)



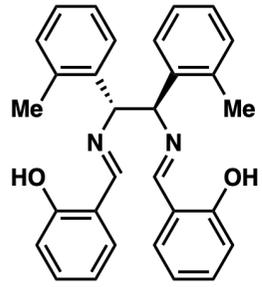
Prof. Greg Fu received a B.S. degree in 1985 from MIT, where he worked in the laboratory of Prof. K. Barry Sharpless. After earning a Ph.D. from Harvard in 1991 under the guidance of Prof. David A. Evans, Prof. Fu spent two years as a postdoctoral fellow with Prof. Robert H. Grubbs at Caltech. In 1993, he returned to MIT, where he served as a member of the faculty from 1993–2012. In 2012, he was appointed the Altair Professor of Chemistry at Caltech. Prof. Fu is currently the Norman Chandler Professor of Chemistry at Caltech. Prof. Fu received the Corey Award of the American Chemical Society (ACS) in 2004, the Mukaiyama Award of the Society of Synthetic Organic Chemistry of Japan in 2006, the Award for Creative Work in Synthetic Organic Chemistry of the ACS in 2012, and the H. C. Brown Award of the ACS in 2018. He is a member of the American Academy of Arts and Sciences (2007) and of the National Academy of Sciences (2014). Prof. Fu serves as an associate editor of the *Journal of the American Chemical Society*.



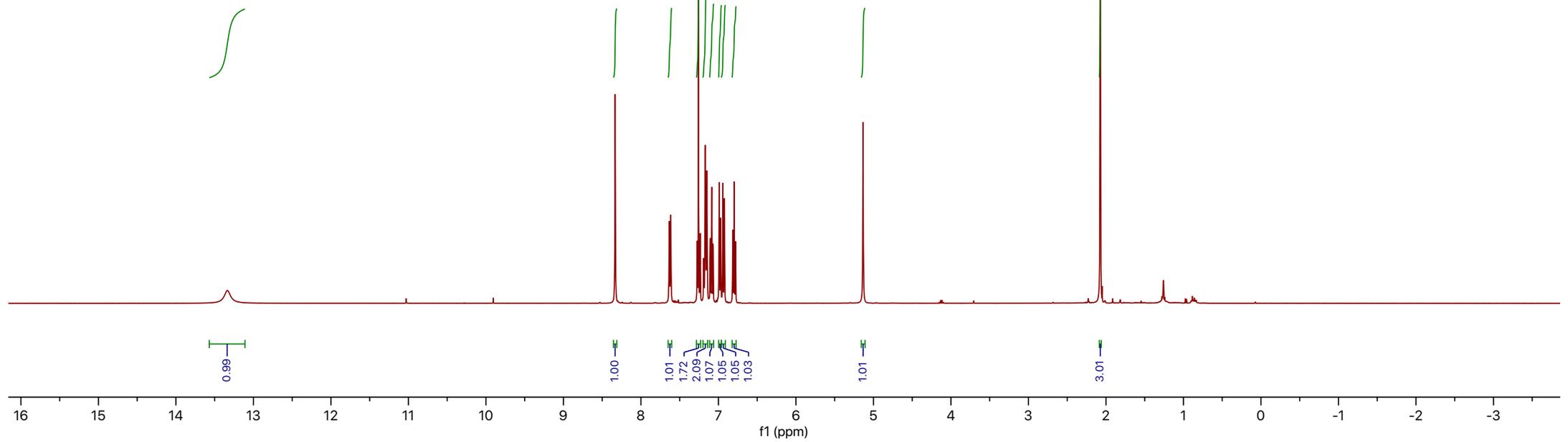
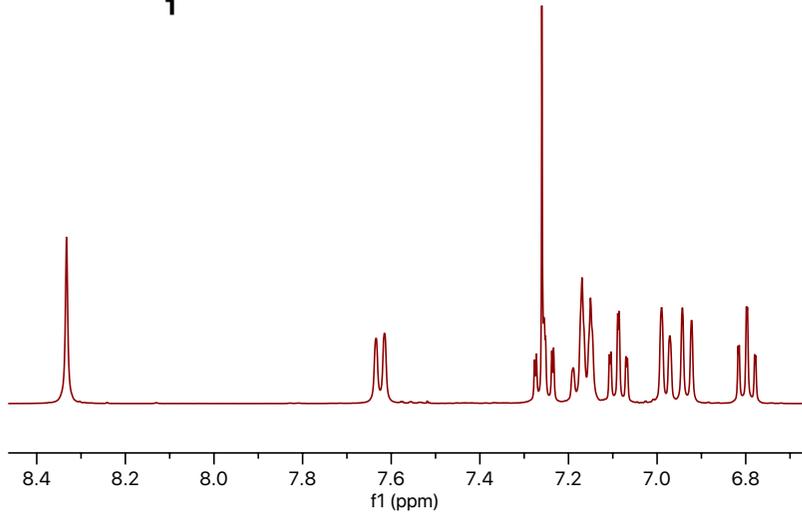
Yusuke Masuda was born in Osaka, Japan, in 1990. He received a B.S. degree in 2012 from Kyoto University, and he obtained a Ph.D. degree in 2017 from Kyoto University under the direction of Professor Masahiro Murakami. In 2017, he joined the group of Professor Greg Fu at Caltech as a postdoctoral fellow, where he worked on the development of transition metal-catalyzed enantioselective cross-coupling reactions. He is currently an assistant professor in the lab of Professor Masahiro Murakami at Kyoto University. His research focused on transition metal-catalyzed and photo-induced reactions.

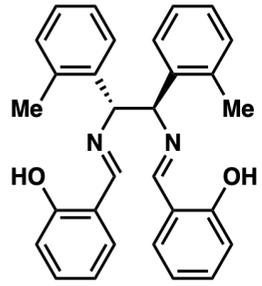


Skyler Mendoza was born in Kennewick, WA in 1994. He received a B.S. degree in 2016 from the University of Washington, where he conducted research in the lab of Professor Gregory Horwitz focused on the development of new methods for detecting and quantifying neutralizing antibodies. He is currently pursuing his Ph.D. in the lab of Professor Sarah E. Reisman where his graduate research focuses on the synthesis of complex natural products.

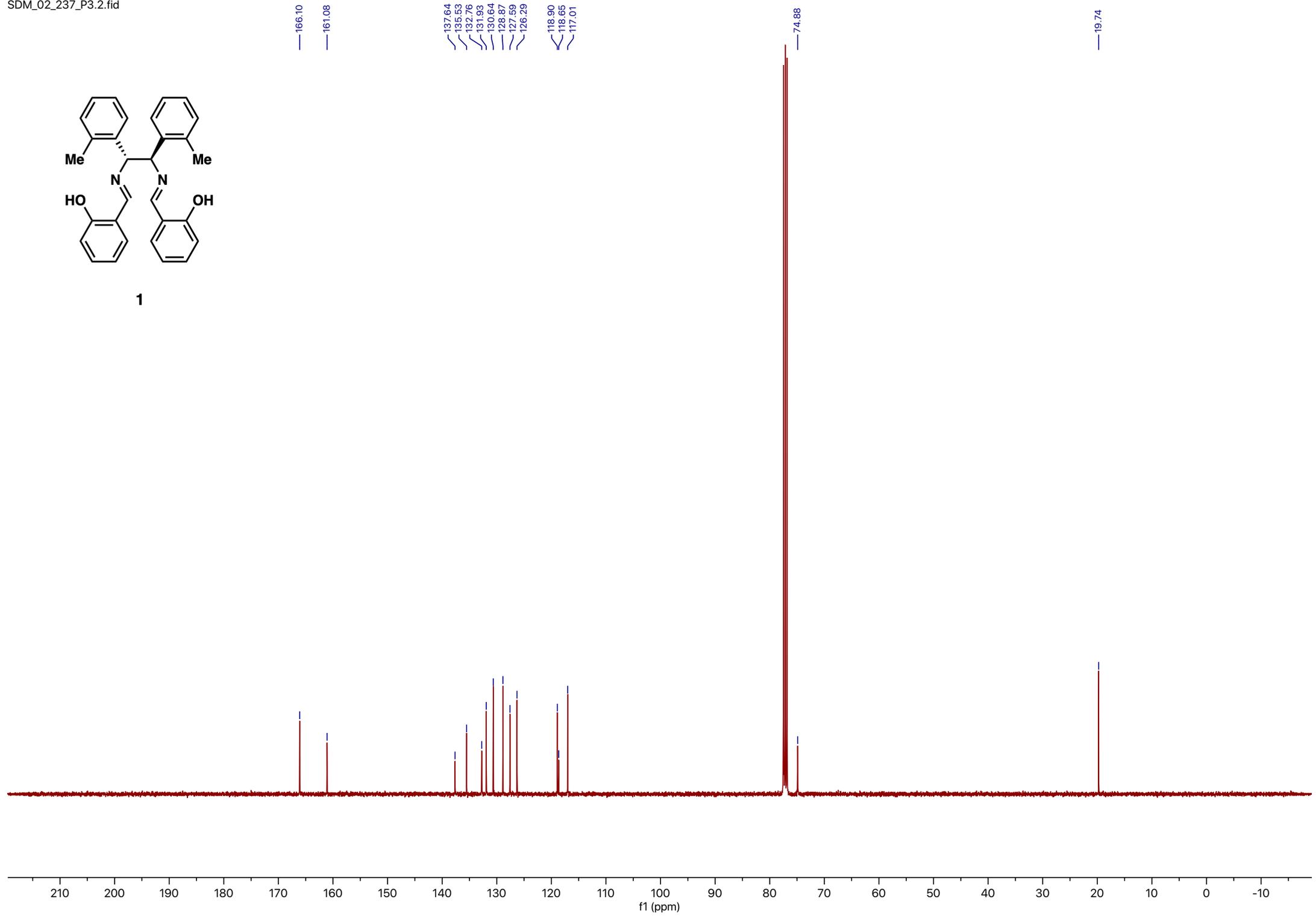


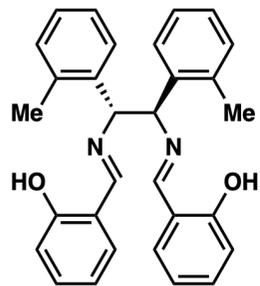
1





1

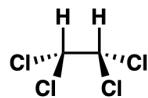




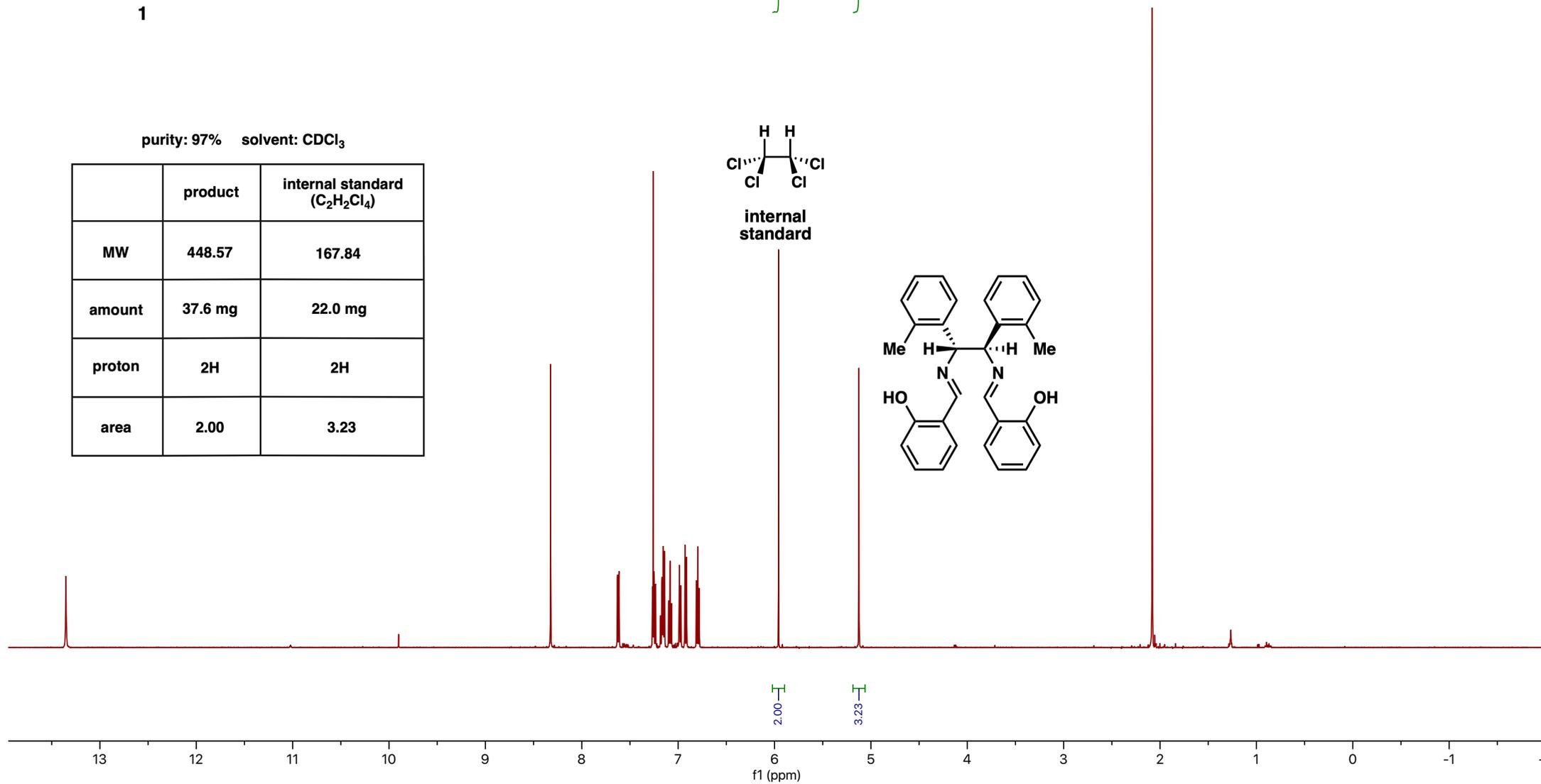
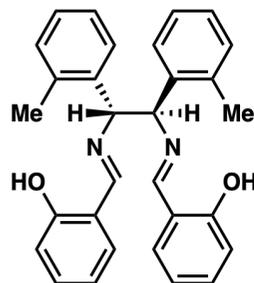
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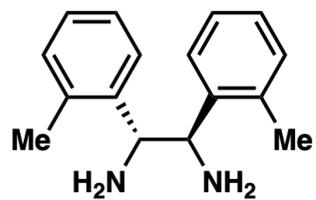
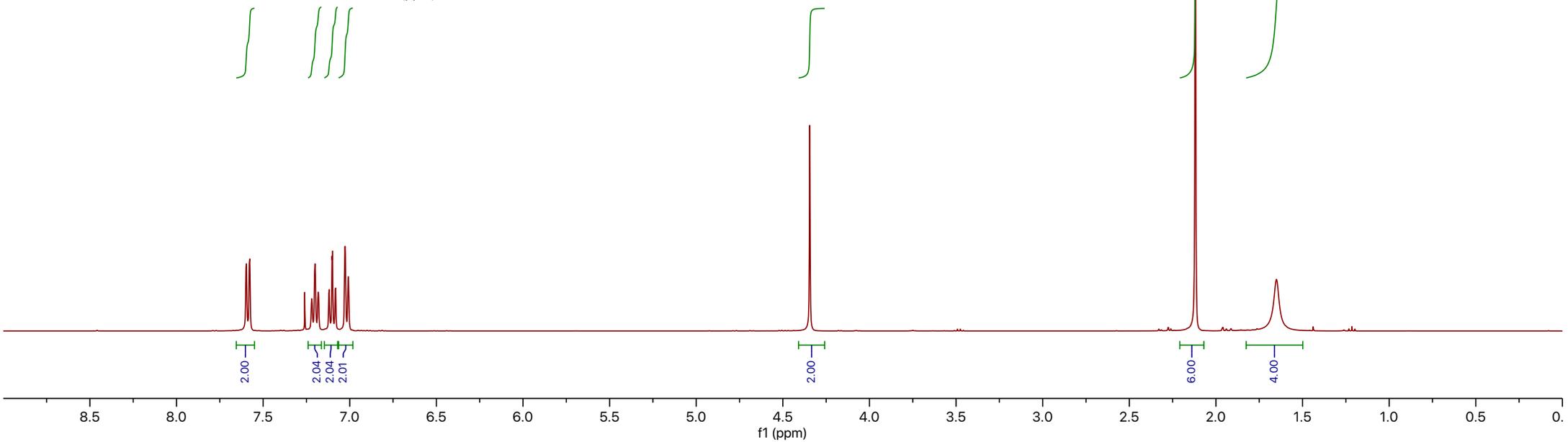
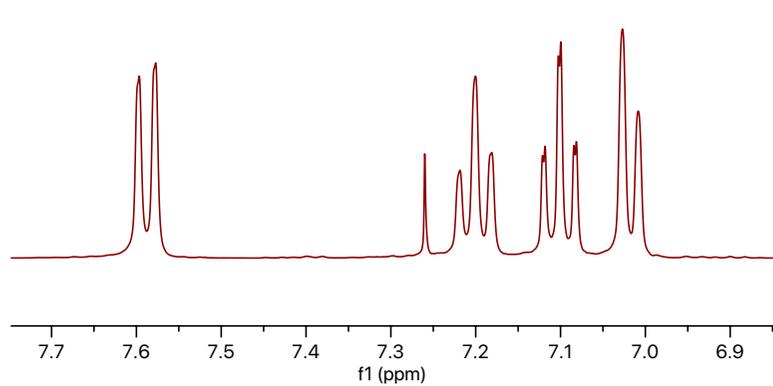
purity: 97% solvent: CDCl<sub>3</sub>

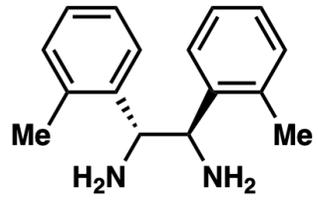
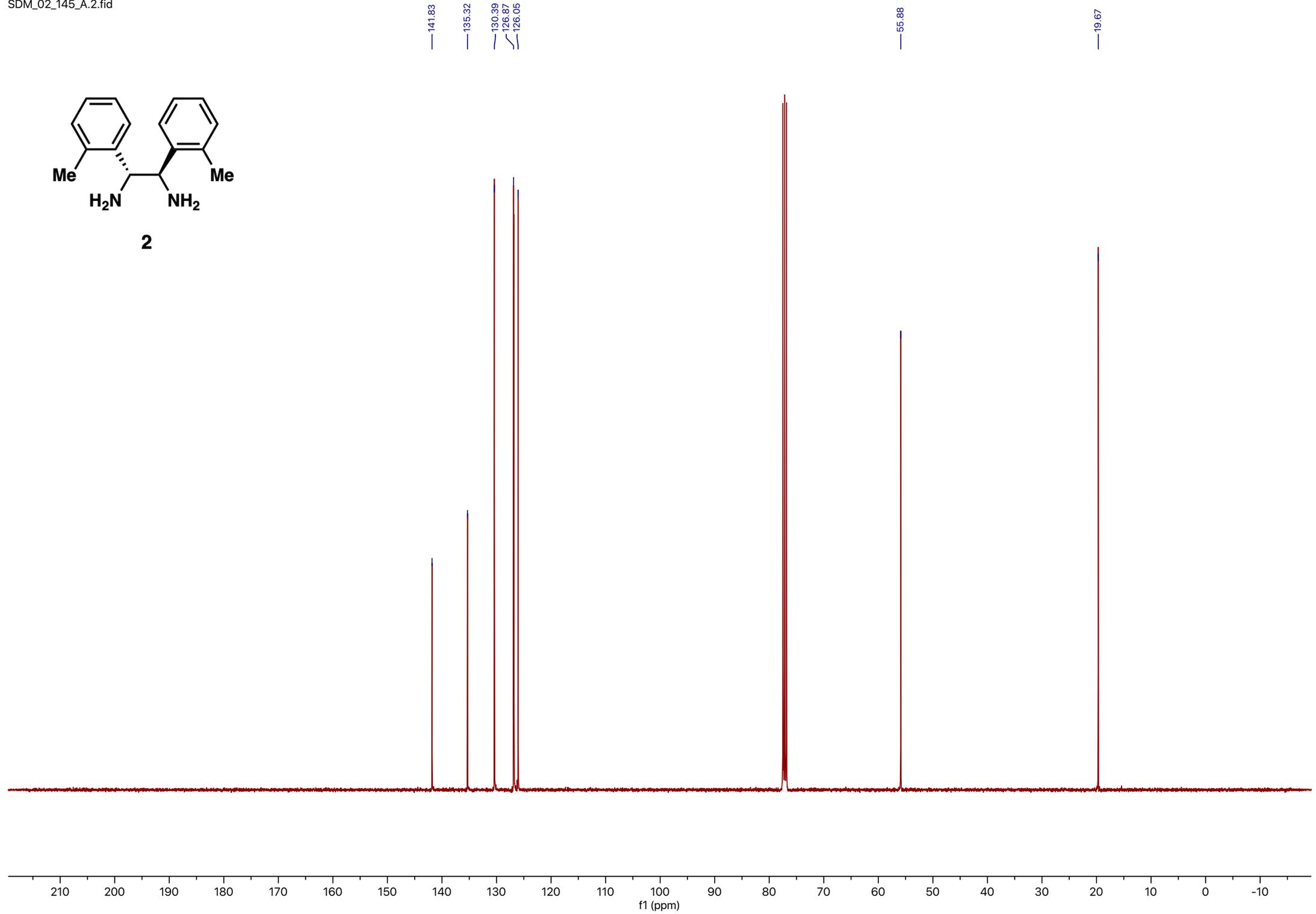
	product	internal standard (C <sub>2</sub> H <sub>2</sub> Cl <sub>4</sub> )
MW	448.57	167.84
amount	37.6 mg	22.0 mg
proton	2H	2H
area	2.00	3.23



internal  
standard



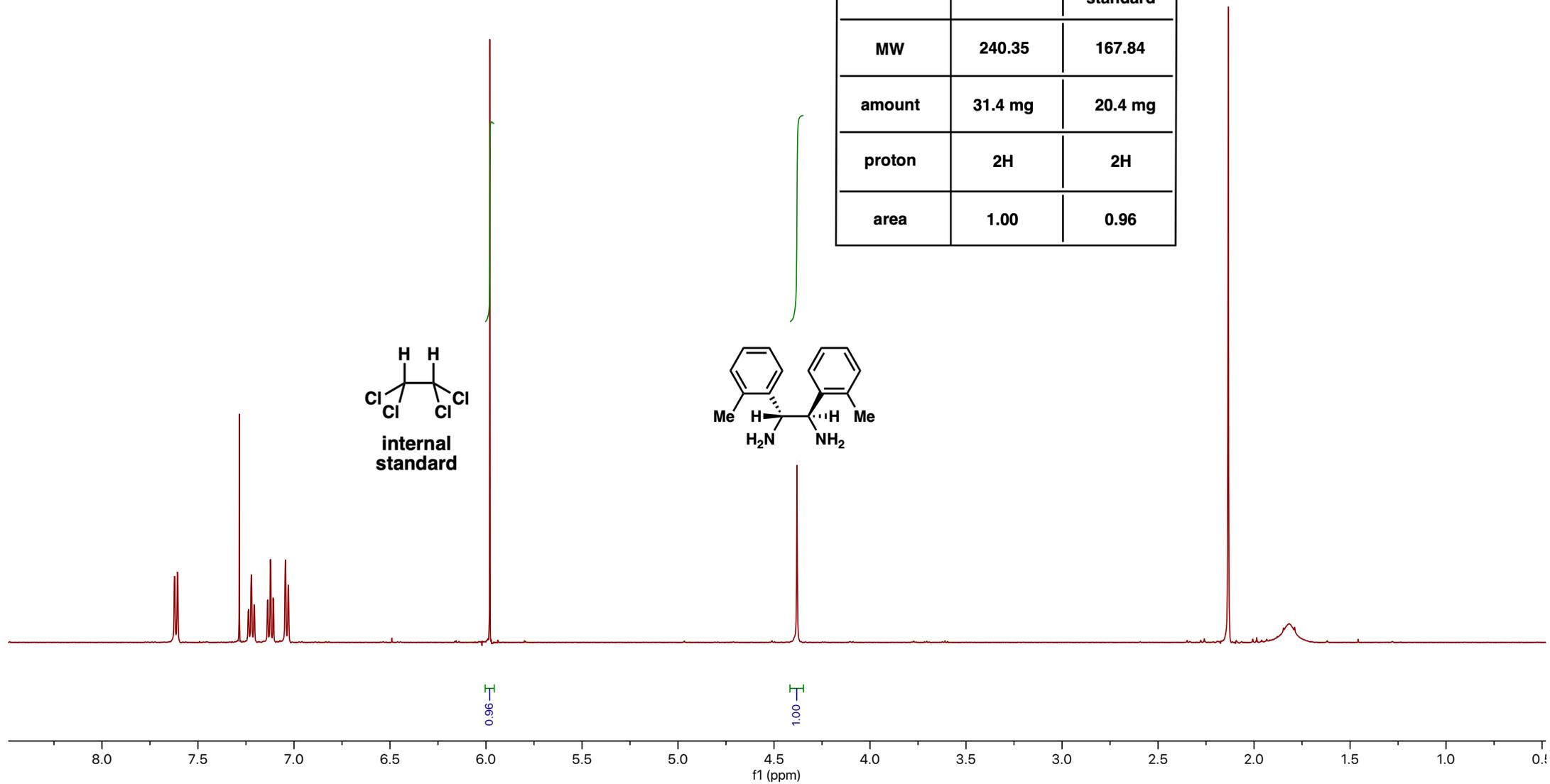
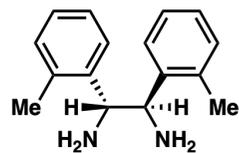
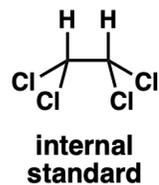
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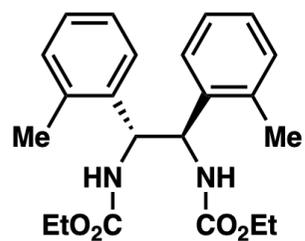
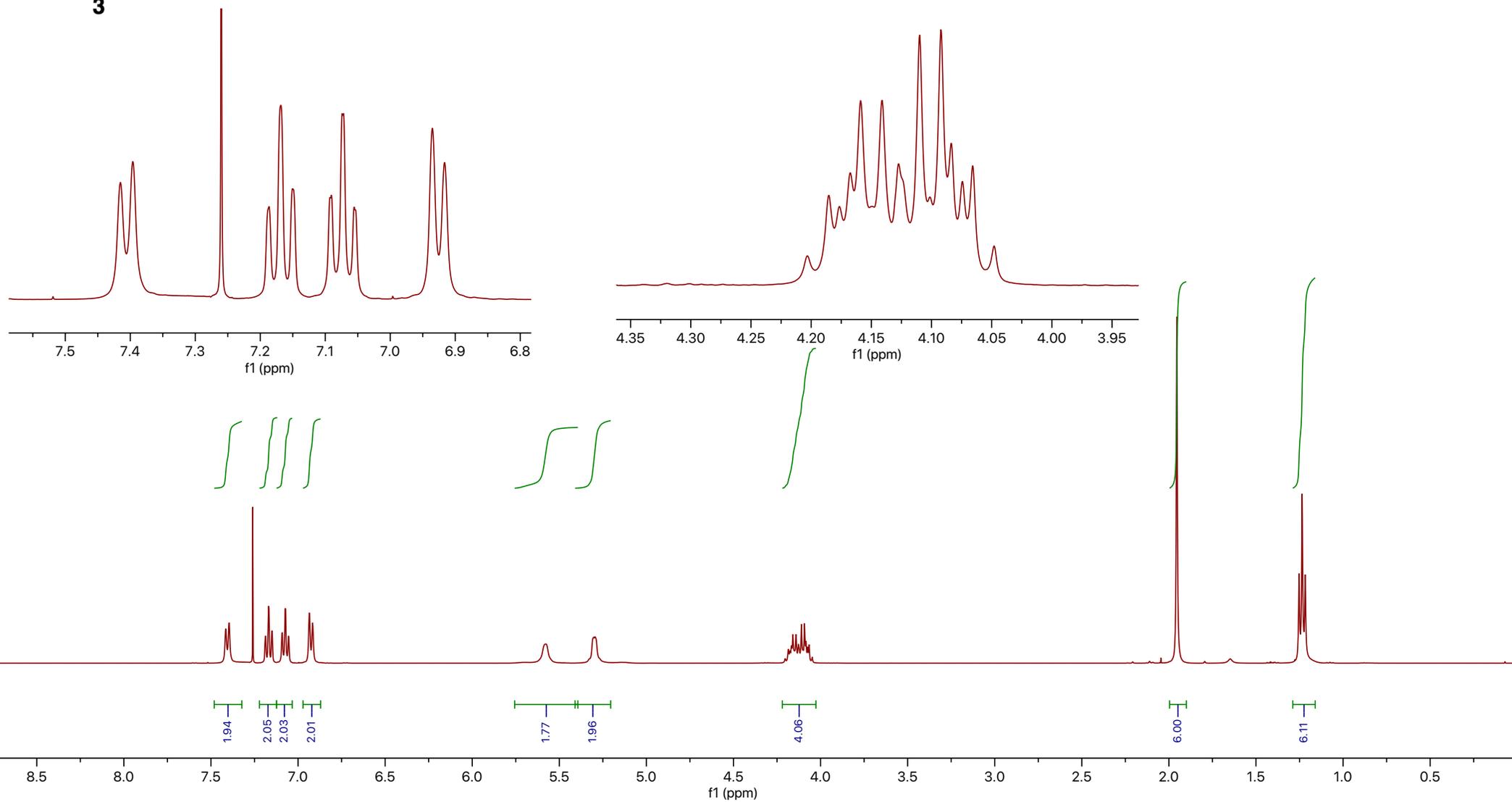
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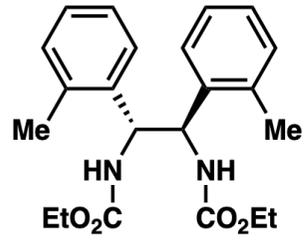
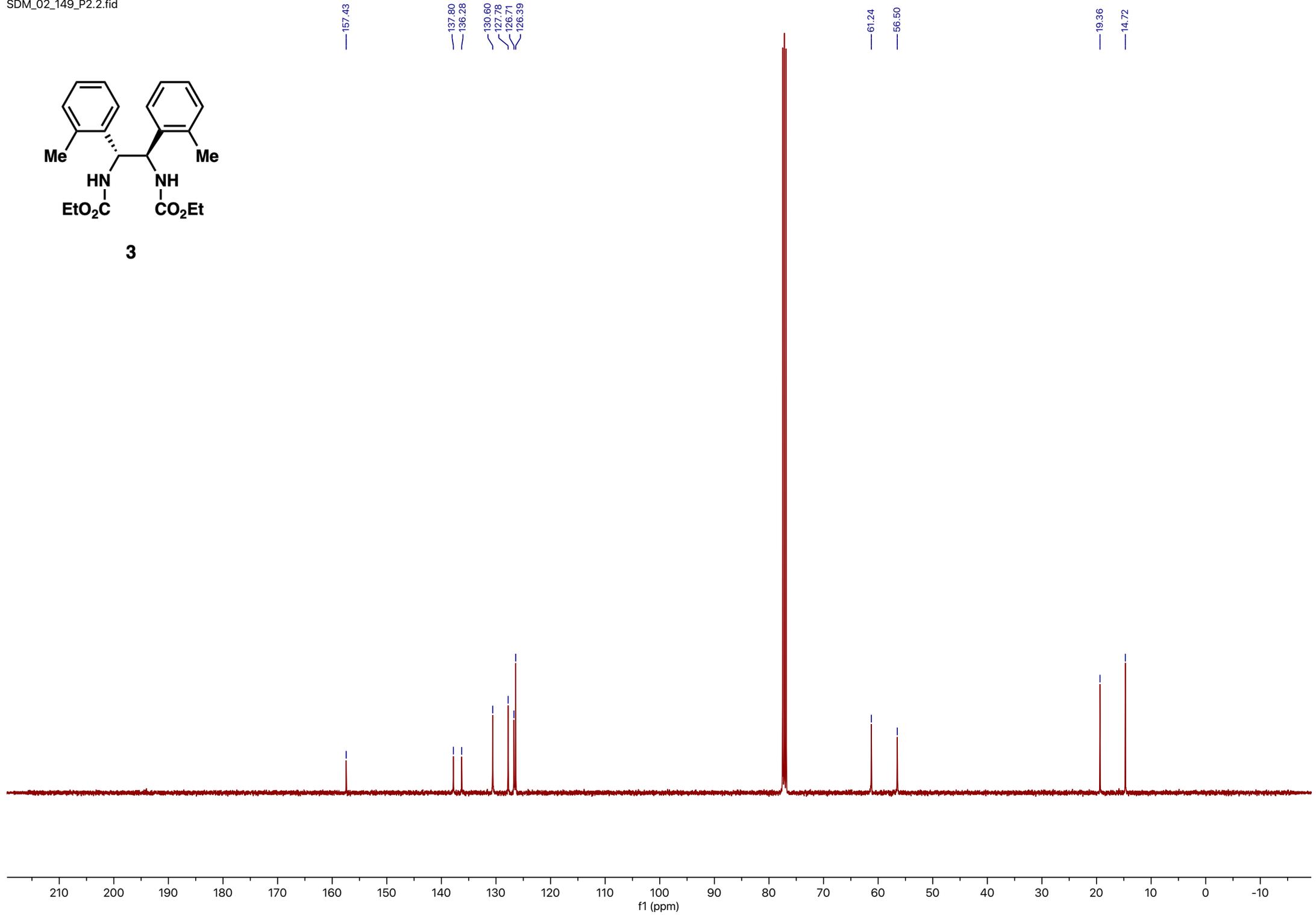
purity: 97%

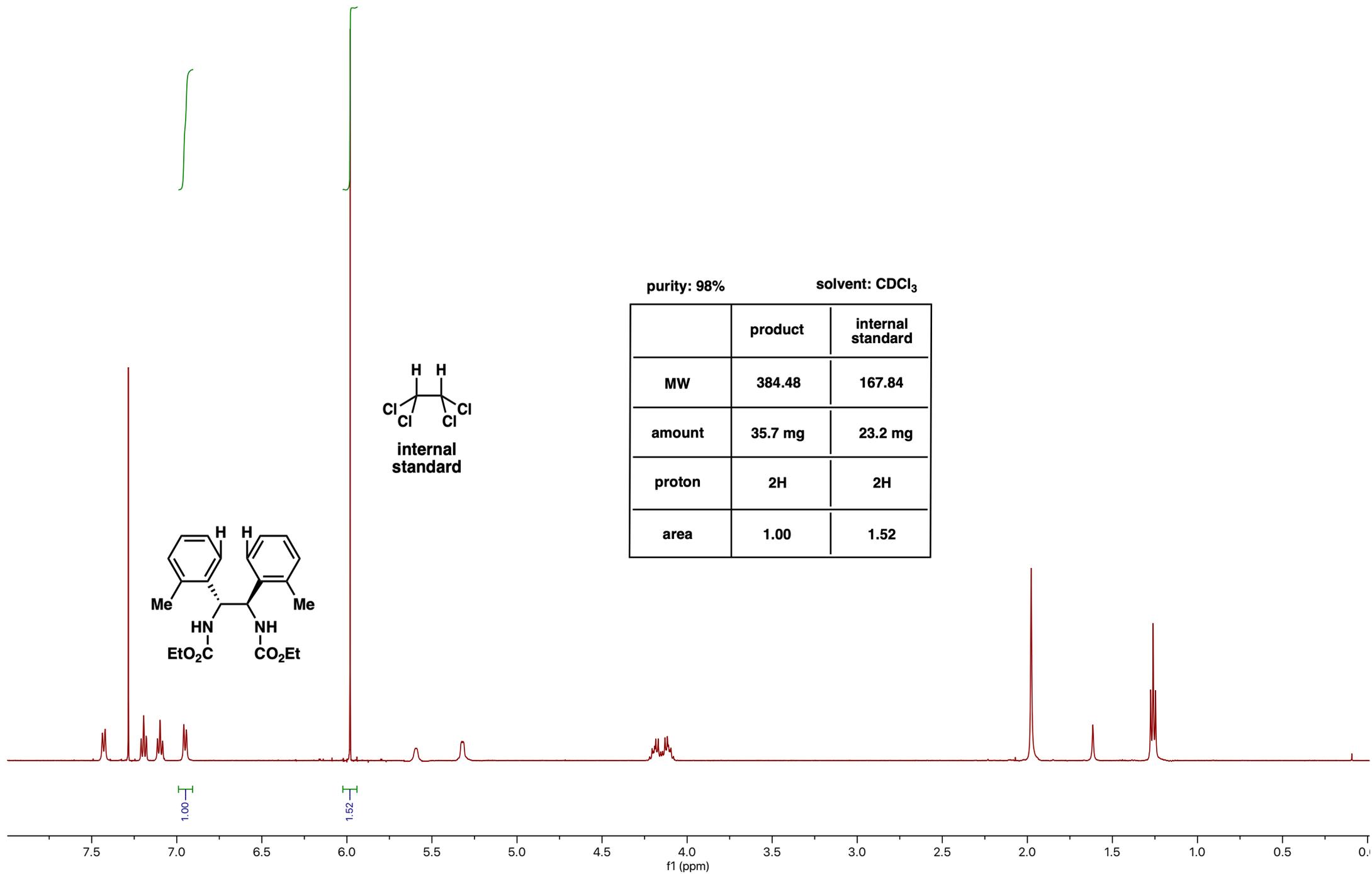
solvent: CDCl<sub>3</sub>

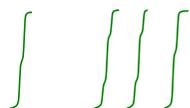
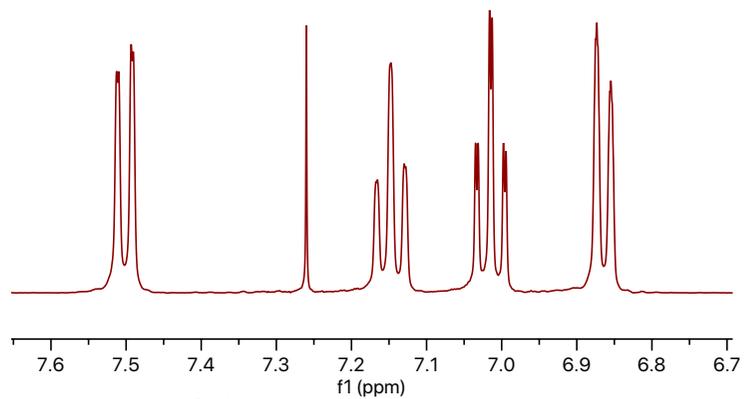
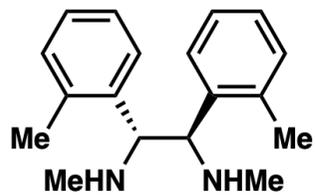
	product	internal standard
MW	240.35	167.84
amount	31.4 mg	20.4 mg
proton	2H	2H
area	1.00	0.96



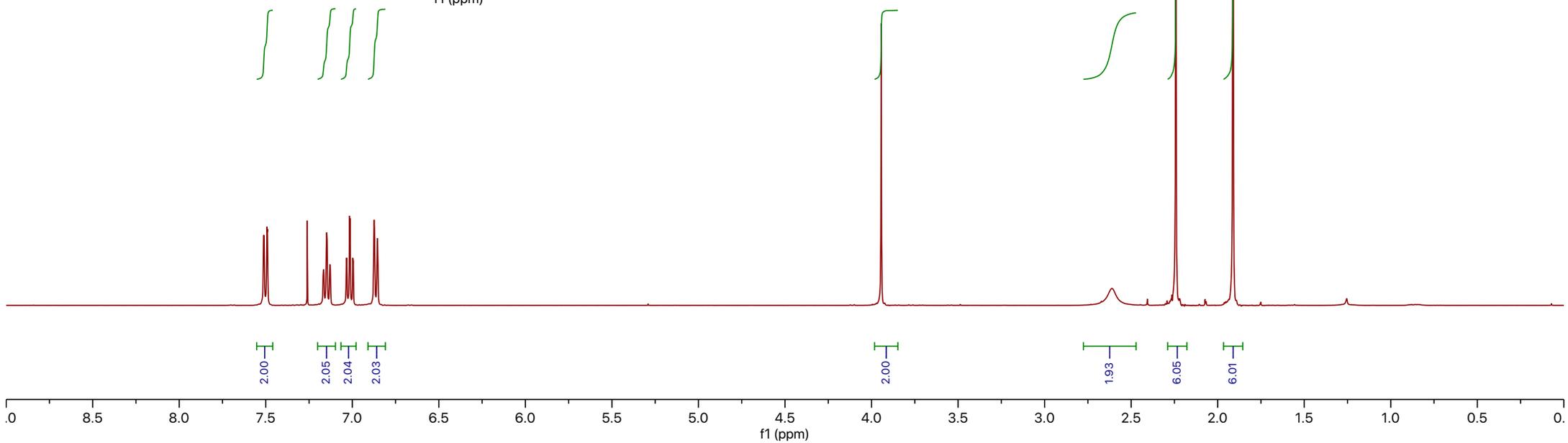
**3**

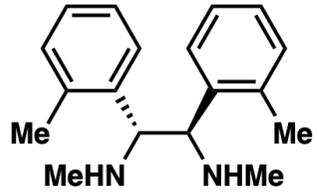
**3**





2.00  
2.05  
2.04  
2.03



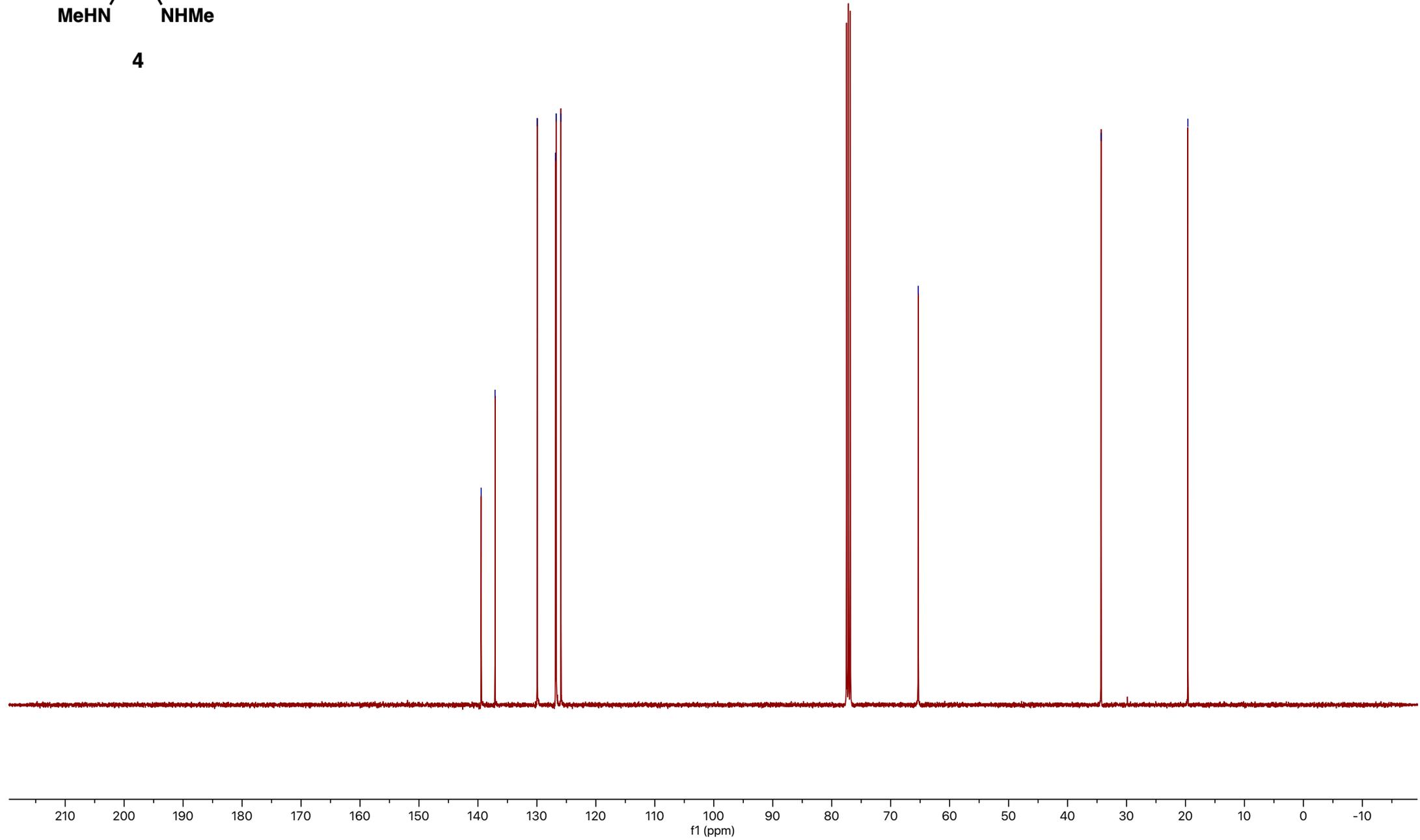


139.45  
137.10  
129.96  
126.85  
126.74  
125.92

65.33

34.31

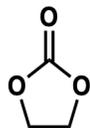
19.59



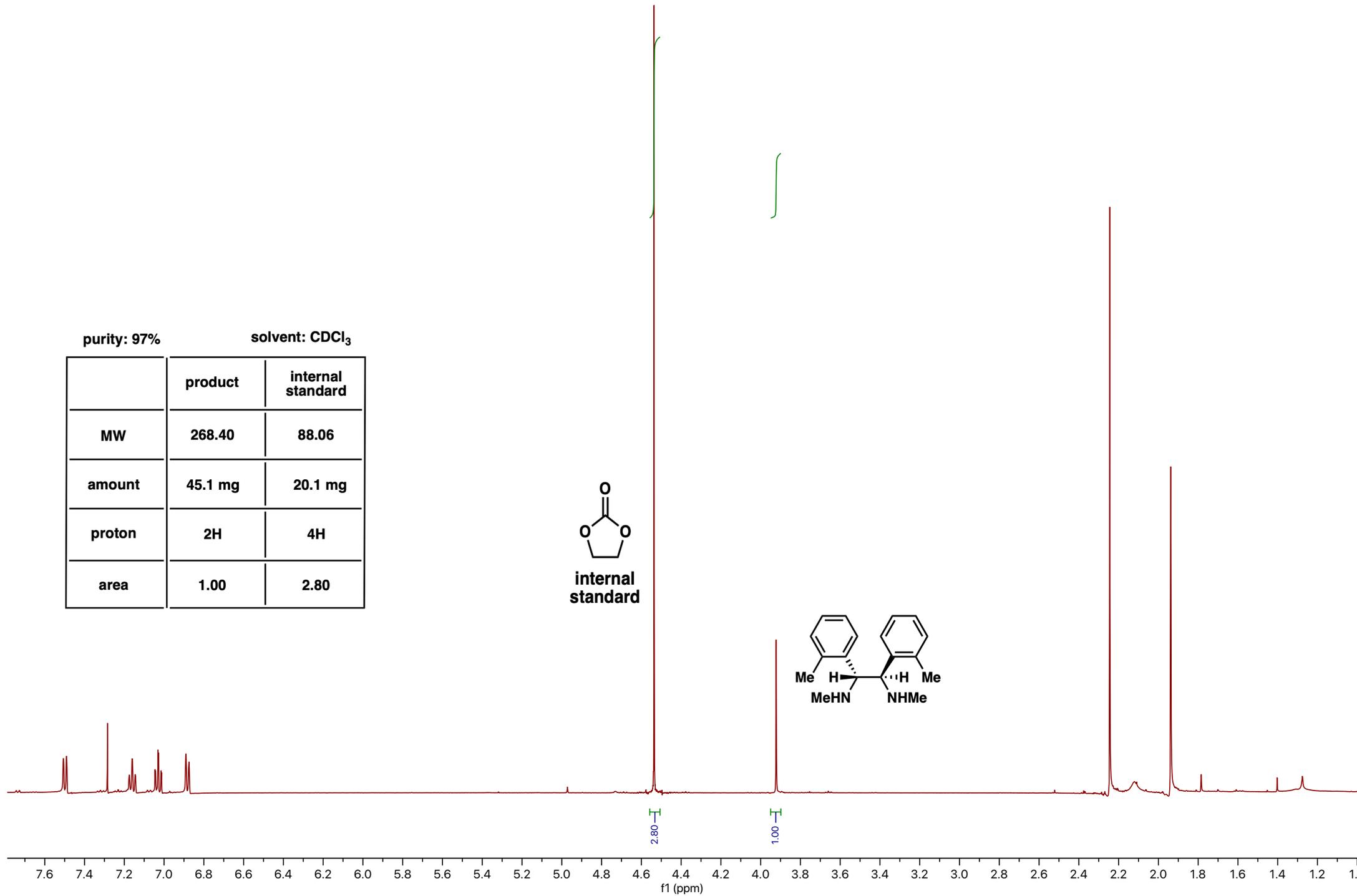
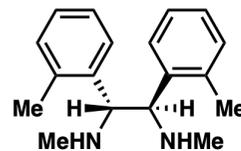
purity: 97%

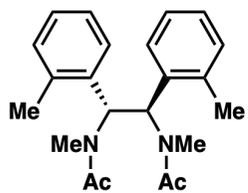
solvent: CDCl<sub>3</sub>

	product	internal standard
MW	268.40	88.06
amount	45.1 mg	20.1 mg
proton	2H	4H
area	1.00	2.80

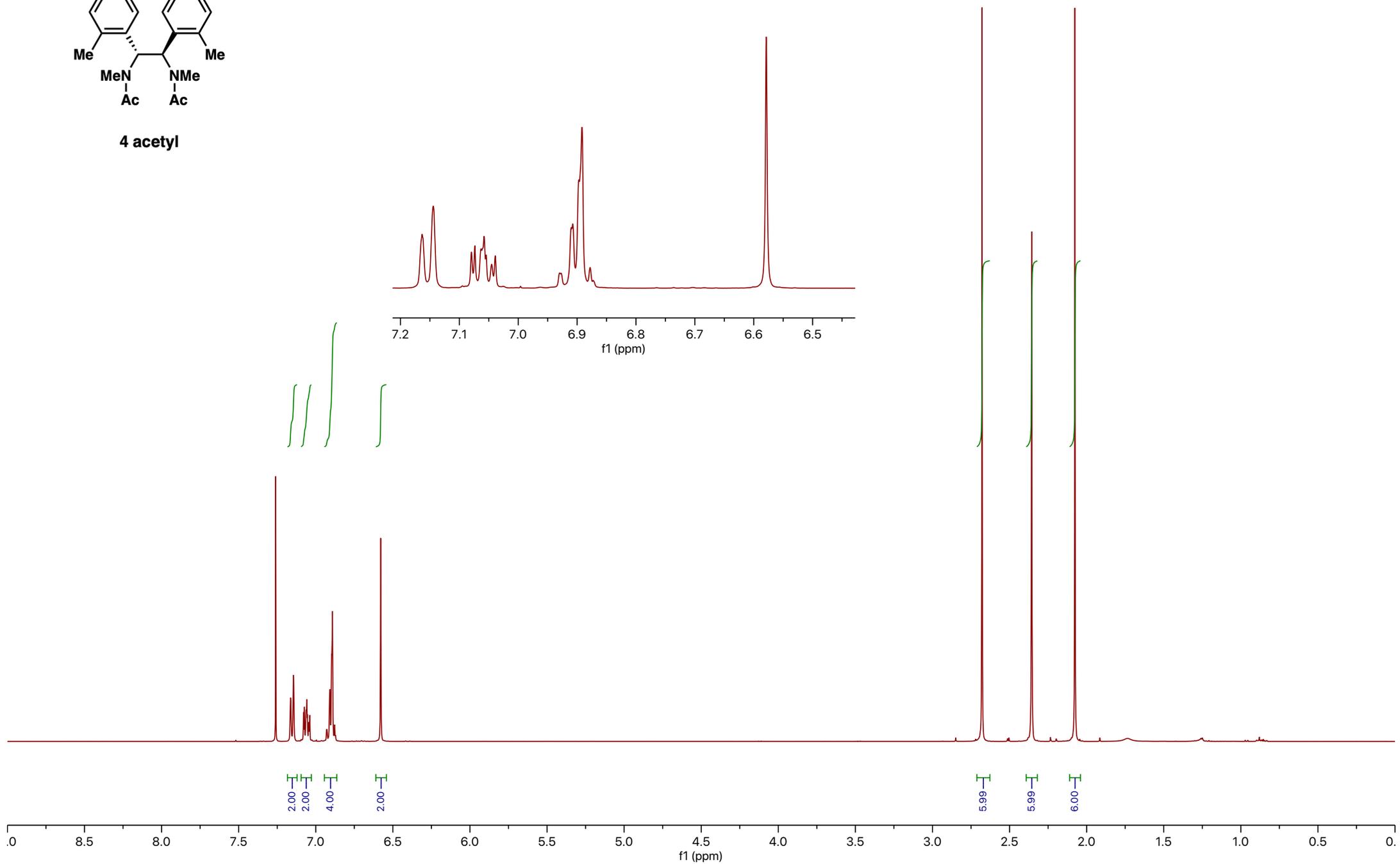


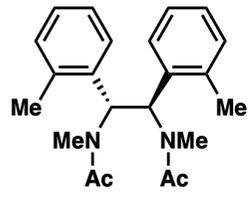
internal standard



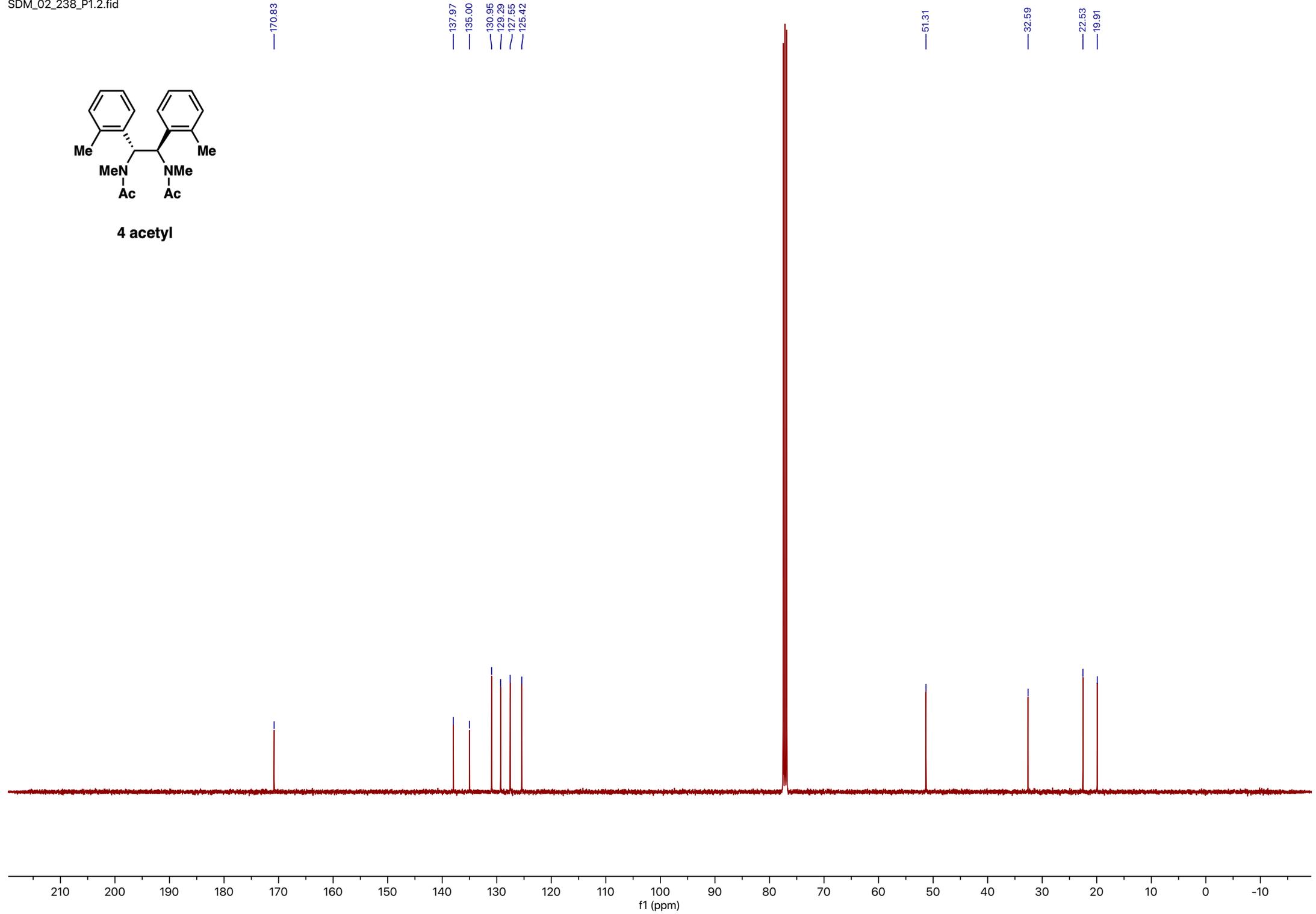


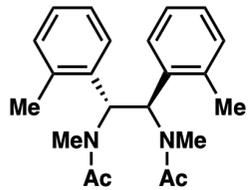
4 acetyl





4 acetyl





4 acetyl

purity: 99% solvent: CDCl<sub>3</sub>

	product	internal standard (C <sub>2</sub> H <sub>2</sub> Cl <sub>4</sub> )
MW	352.48	167.84
amount	32.3 mg	11.1 mg
proton	2H	2H
area	2.00	1.46

