

SUPPORTING INFORMATION

Hydrogen-Bonded *Helical* Self-Assembly of Sterically-Hindered Benzyl Alcohols: Rare Isostructurality and Synthons Equivalence Between Alcohols and Acids

Jarugu Narasimha Moorthy*[†] and Susovan Mandal[†] and Paloth Venugopalan[¶]

[†]*Department of Chemistry, Indian Institute of Technology, Kanpur 208016, INDIA*

[¶]*Department of Chemistry, Panjab University, Chandigarh 160014, INDIA*

moorthy@iitk.ac.in

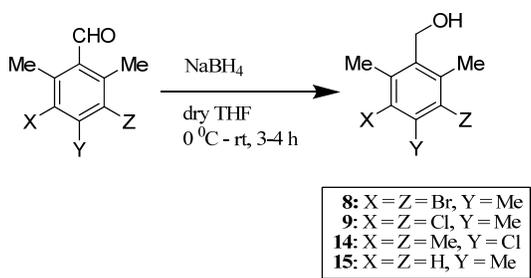
Table of Contents

1	General aspects, experimental procedures and Characterization data of 8-15	S2-S5
2	¹ H spectrum of 3,5-dibromo-2,4,6-trimethylbenzyl alcohol 8 in CDCl ₃	S6
3	¹³ C spectrum of 3,5-dibromo-2,4,6-trimethylbenzyl alcohol 8 in DMSO- <i>d</i> ₆	S7
4	¹ H spectrum of 3,5-dichloro-2,4,6-trimethylbenzyl alcohol 9 in CDCl ₃	S8
5	¹³ C spectrum of 3,5-dichloro-2,4,6-trimethylbenzyl alcohol 9 in CDCl ₃	S9
6	¹ H spectrum of 3-bromo-2,4,5,6-tetramethylbenzyl alcohol 10 in CDCl ₃	S10
7	¹³ C spectrum of 3-bromo-2,4,5,6-tetramethylbenzyl alcohol 10 in CDCl ₃	S11
8	¹ H spectrum of 3-chloro-2,4,5,6-tetramethylbenzyl alcohol 11 in CDCl ₃	S12
9	¹³ C spectrum of 3-chloro-2,4,5,6-tetramethylbenzyl alcohol 11 in CDCl ₃	S13
10	¹ H spectrum of 4-bromo-2,3,5,6-tetramethylbenzyl alcohol 12 in CDCl ₃	S14
11	¹³ C spectrum of 4-bromo-2,3,5,6-tetramethylbenzyl alcohol 12 in CDCl ₃	S15
12	¹ H spectrum of 4-chloro-2,3,5,6-tetramethylbenzyl alcohol 13 in CDCl ₃	S16
13	¹³ C spectrum of 4-chloro-2,3,5,6-tetramethylbenzyl alcohol 13 in CDCl ₃	S17
14	¹ H spectrum of 2,3,4,5,6-pentamethylbenzyl alcohol 14 in CDCl ₃	S18
15	¹³ C spectrum of 2,3,4,5,6-pentamethylbenzyl alcohol 14 in CDCl ₃	S19
16	¹ H spectrum of 2,4,6-trimethylbenzyl alcohol 15 in CDCl ₃	S20
17	¹³ C spectrum of 2,4,6-trimethylbenzyl alcohol 15 in CDCl ₃	S21

General Aspects. Anhyd tetrahydrofuran (THF) was freshly distilled over sodium prior to use and purged with nitrogen gas. All other solvents were distilled before use. Column chromatography was conducted with silica gel of 60-120 μ mesh.

General Procedure for the Reduction of Substituted Aldehydes: In a 50 mL dry two-necked round bottomed flask was taken substituted benzaldehyde (2.50 mmol) dissolved in dry THF (20 mL) under a N₂ gas atmosphere and cooled to 0 °C in an ice bath. After 15 min, NaBH₄ (3.00 mmol) was introduced in small portions. The reaction mixture was gradually allowed to attain room temperature and stirred for 3-4 h. It was then quenched with dil HCl at ice cold conditions. The THF was removed and the residue was extracted with EtOAc. The organic extract was further washed with brine, dried over anhyd Na₂SO₄, filtered and the solvent removed to yield the crude product, which was purified by silica-gel column chromatography to obtain pure substituted benzyl alcohols (**8**, **9**, **14** and **15**) in good yields (88-92%).

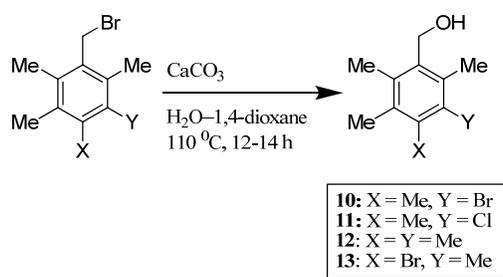
Scheme S1



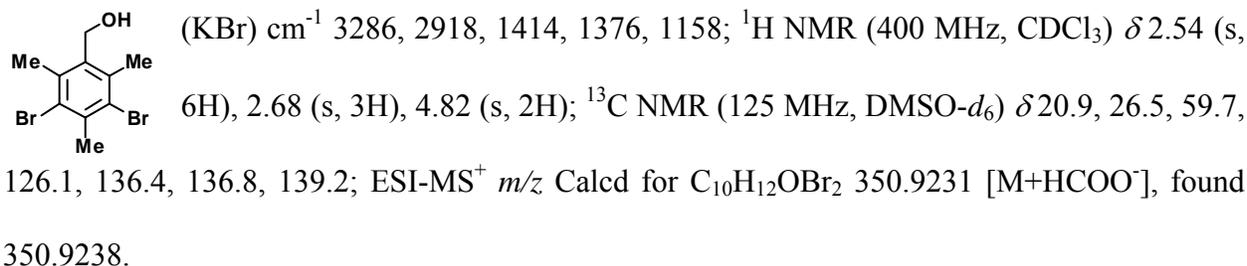
General Procedure for the Hydrolysis of Substituted Benzyl Bromides: In a 100 mL two-necked round bottomed flask was taken substituted benzyl bromide (5.00 mmol) along with CaCO₃ (25.00 mmol) in a 1:1 solvent mixture of 1,4-dioxane and H₂O (30 mL). The reaction

mixture was heated at reflux for 12-14 h. It was then cooled to room temperature and acidified with Conc HCl to yield white precipitate of benzyl alcohol. It was then extracted with EtOAc and washed with brine. The organic extract was dried over anhyd Na₂SO₄, filtered and the solvent removed to afford the crude product, which was purified by silica-gel column chromatography in a good yield (80-95%).

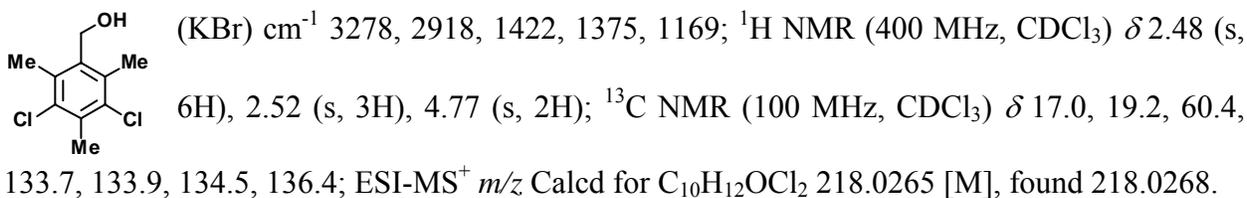
Scheme S2



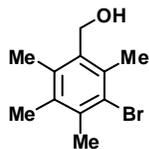
3,5-Dibromo-2,4,6-trimethylbenzyl Alcohol 8: Colorless solid, yield 89%; mp 191-193 °C; IR



3,5-Dichloro-2,4,6-trimethylbenzyl Alcohol 9: Colorless solid, yield 92%; mp 174-177 °C; IR



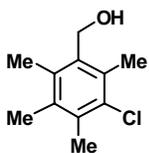
3-Bromo-2,4,5,6-tetramethylbenzyl Alcohol 10: Colorless solid, yield 80%; mp 160-162 °C;



IR (KBr) cm^{-1} 3287, 2919, 1413, 1205, 998; ^1H NMR (400 MHz, CDCl_3) δ 2.27 (s, 3H), 2.33 (s, 3H), 2.46 (s, 3H), 2.55 (s, 3H), 4.79 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 16.2, 17.5, 20.6, 21.6, 60.6, 127.2, 134.5, 134.7, 134.8, 135.4, 136.4; EI-

MS^+ m/z Calcd for $\text{C}_{11}\text{H}_{15}\text{OBr}$ 242.0306 [M], found 242.0307.

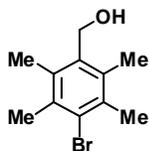
3-Chloro-2,4,5,6-tetramethylbenzyl Alcohol 11: Colorless solid, yield 92%; mp 151-153 °C;



IR (KBr) cm^{-1} 3278, 2920, 1417, 1211, 999; ^1H NMR (500 MHz, CDCl_3) δ 2.24 (s, 3H), 2.35 (s, 3H), 2.39 (s, 3H), 2.49 (s, 3H), 4.78 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 16.2, 17.1, 18.0, 60.3, 132.5, 133.3, 134.1, 134.5, 134.6, 135.3; EI- MS^+

m/z Calcd for $\text{C}_{11}\text{H}_{15}\text{OCl}$ 198.0811 [M], found 198.0810.

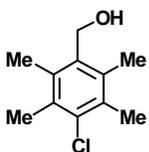
4-Bromo-2,3,5,6-tetramethylbenzyl Alcohol 12: Colorless solid, yield 95%; mp 164-165 °C;



IR (KBr) cm^{-1} 3251, 2920, 1446, 1423, 1382, 989; ^1H NMR (400 MHz, CDCl_3) δ 2.40 (s, 6H), 2.44 (s, 6H), 4.76 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 17.0, 21.3,

59.9, 129.6, 134.3, 134.7, 135.4; ESI- MS^+ m/z Calcd for $\text{C}_{11}\text{H}_{15}\text{OBr}$ 265.0204 [M+Na⁺], found 265.0207.

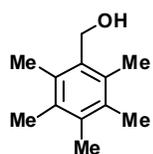
4-Chloro-2,3,5,6-tetramethylbenzyl Alcohol 13: Colorless solid, yield 84%; mp 144-147 °C;



IR (KBr) cm^{-1} 3257, 2920, 1446, 1382, 1308, 993; ^1H NMR (400 MHz, CDCl_3) δ

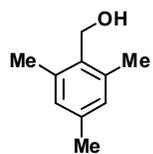
2.37 (s, 12H), 4.77 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 16.5, 17.7, 59.8, 132.4, 134.6, 134.7, 135.4; EI-MS $^+$ m/z Calcd for $\text{C}_{11}\text{H}_{15}\text{OCl}$ 198.0811 [M], found 198.0812.

2,3,4,5,6-Pentamethylbenzyl Alcohol 14: Colorless solid, yield 88%; mp 143-146 °C; IR (KBr)



cm^{-1} 3269, 2916, 1444, 1383, 1306, 991; ^1H NMR (500 MHz, CDCl_3) δ 2.24 (s, 6H), 2.25 (s, 3H), 2.37 (s, 6H), 4.79 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 16.2, 16.7, 16.9, 60.1, 132.8, 132.9, 133.9, 135.2; ESI-MS $^+$ m/z Calcd for $\text{C}_{12}\text{H}_{18}\text{O}$ 161.1330 [M+H-H $_2\text{O}$], found 161.1341.

2,4,6-Trimethylbenzyl Alcohol 15: Colorless solid, yield 91%; mp 67-69 °C; IR (KBr) cm^{-1}



3269, 2916, 1444, 1383, 1306, 991; ^1H NMR (500 MHz, CDCl_3) δ 2.24 (s, 6H), 2.25 (s, 3H), 2.37 (s, 6H), 4.79 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 16.2, 16.7, 16.9, 60.1, 132.8, 132.9, 133.9, 135.2; ESI-MS $^+$ m/z Calcd for $\text{C}_{10}\text{H}_{14}\text{O}$ 151.1123 [M+H], found 151.1127.

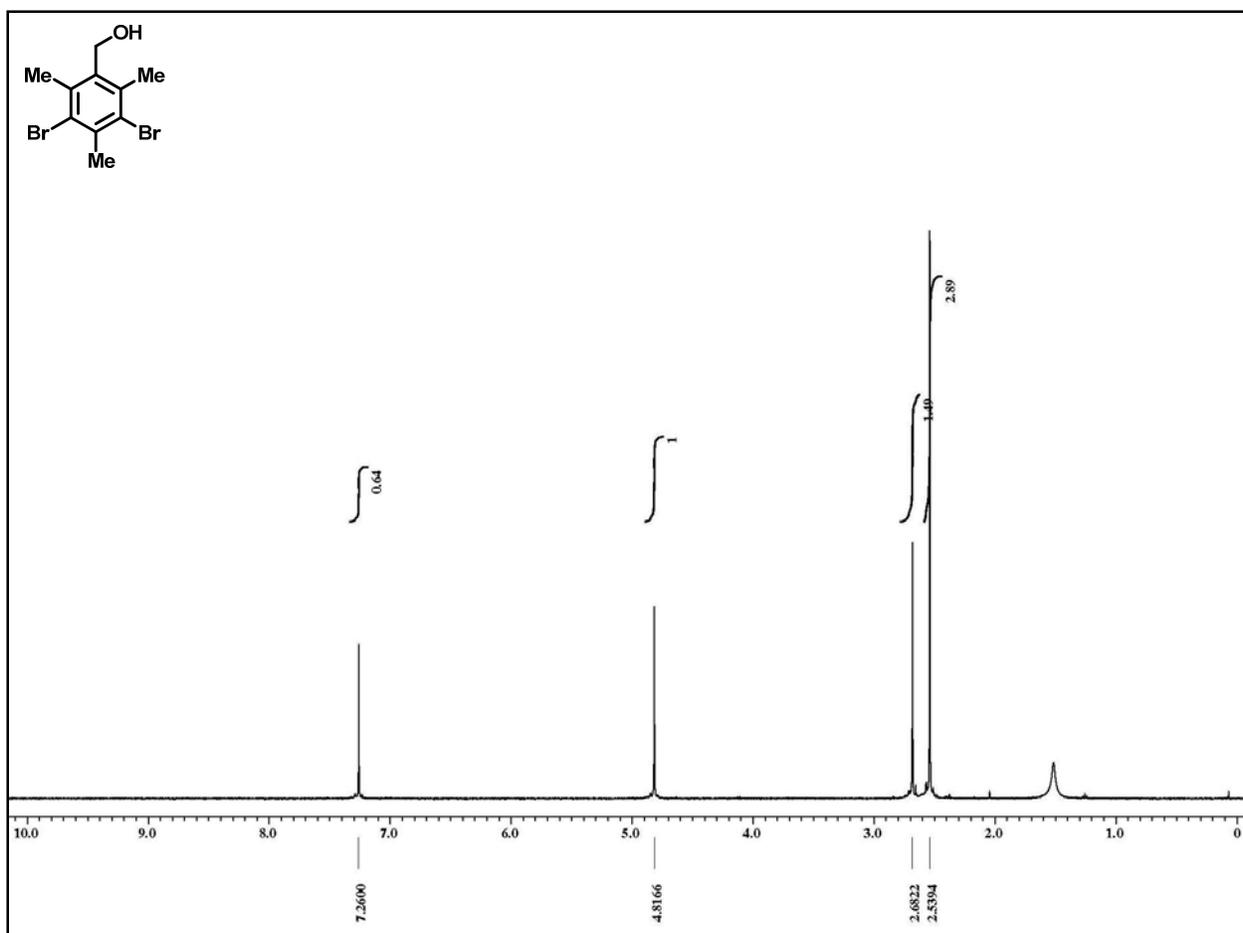


Figure S1. ¹H NMR (400 MHz) spectrum of 3,5-dibromo-2,4,6-trimethylbenzyl alcohol **8** in CDCl₃.

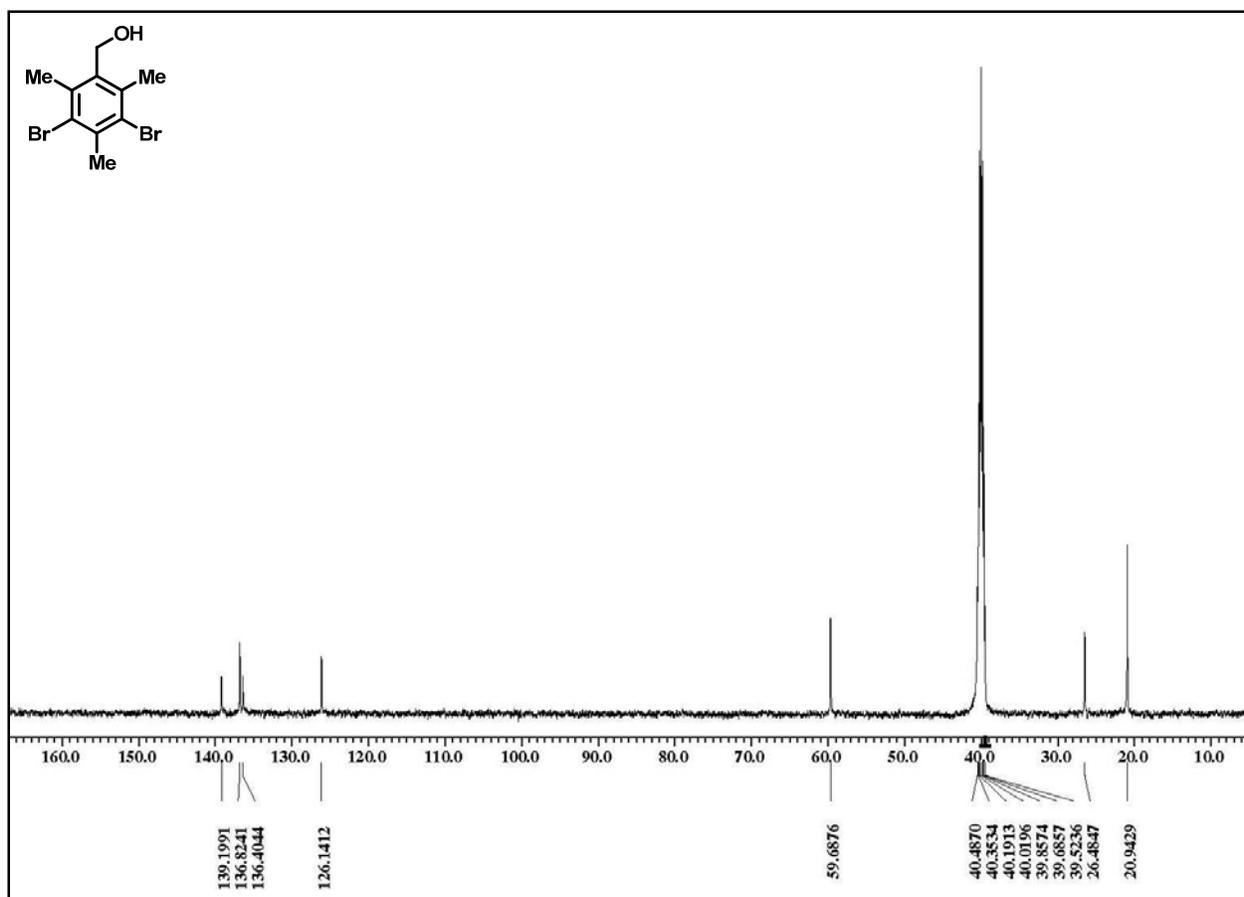


Figure S2. ¹³C NMR (125 MHz) spectrum of 3,5-dibromo-2,4,6-trimethylbenzyl alcohol **8** in DMSO-*d*₆.

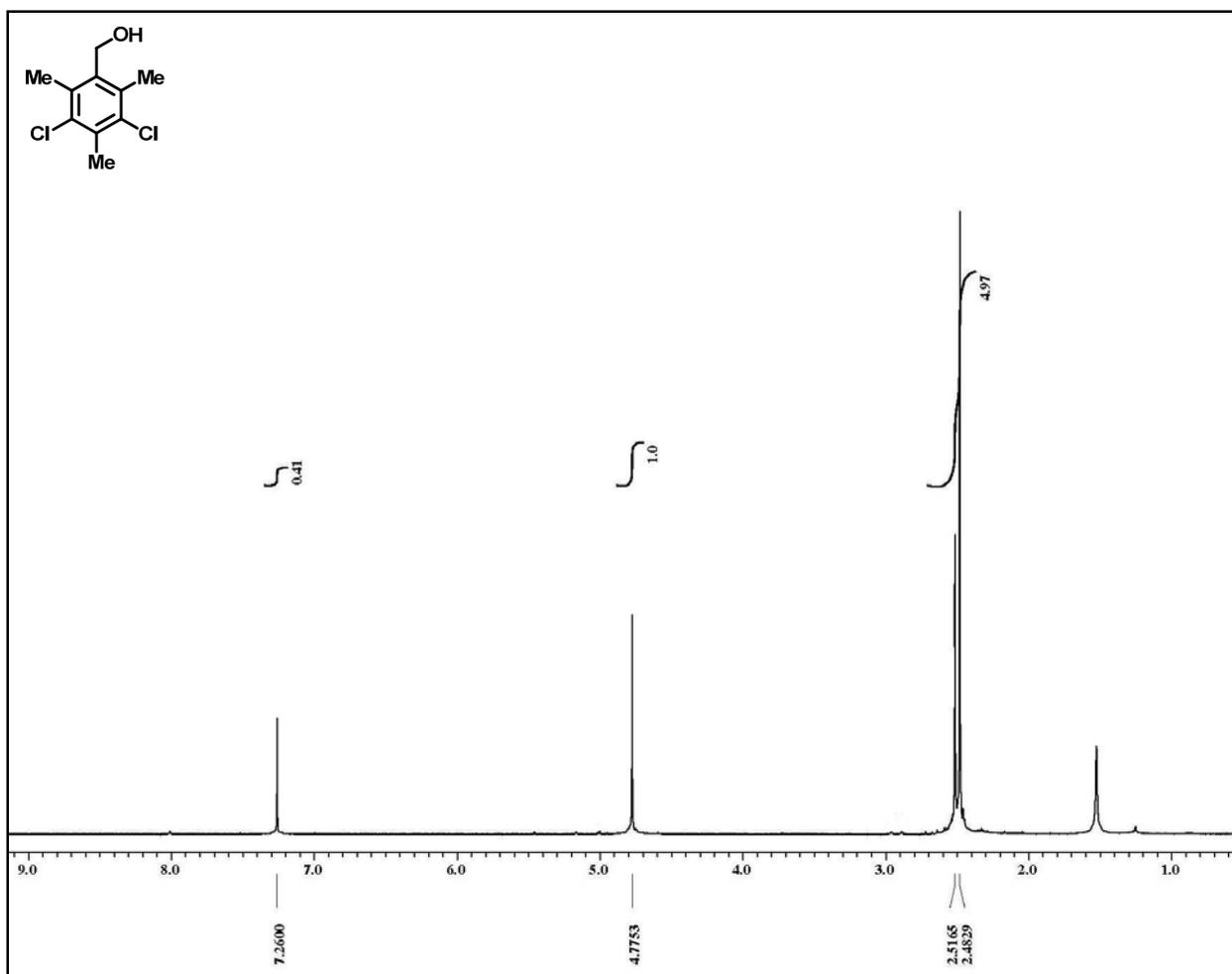


Figure S3. ¹H NMR (400 MHz) spectrum of 3,5-dichloro-2,4,6-trimethylbenzyl alcohol **9** in CDCl₃.

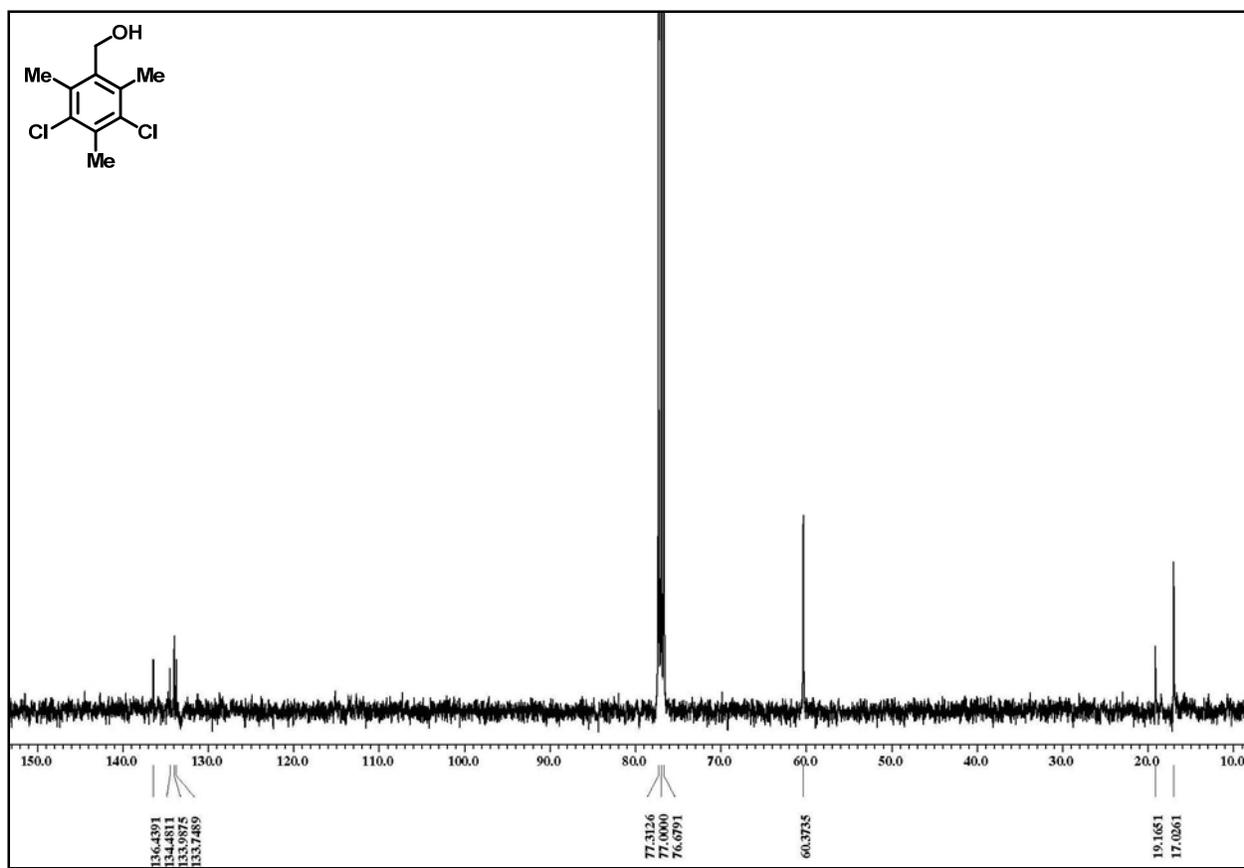


Figure S4. ¹³C NMR (100 MHz) spectrum of 3,5-dichloro-2,4,6-trimethylbenzyl alcohol **9** in CDCl₃.

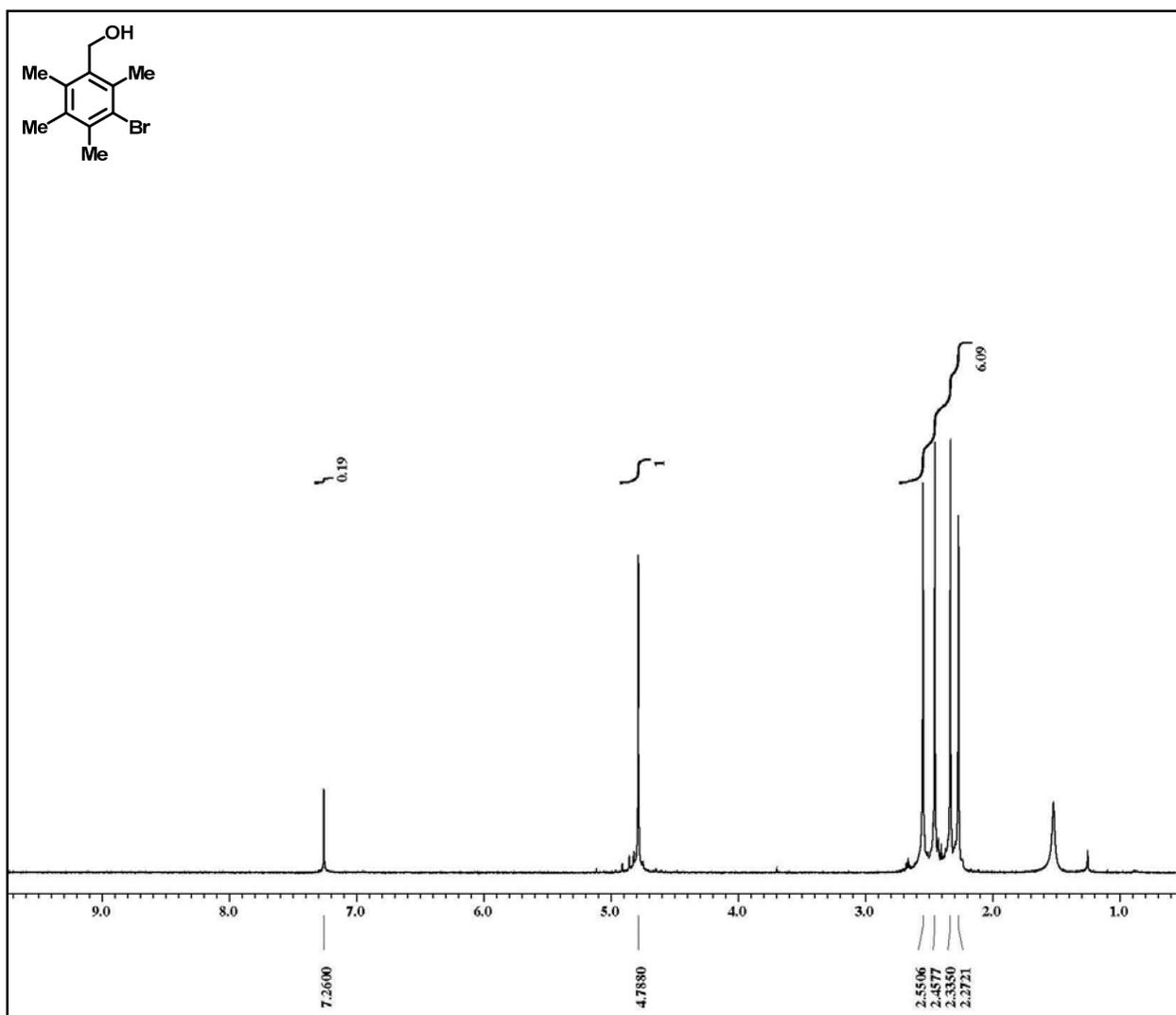


Figure S5. ¹H NMR (400 MHz) spectrum of 3-bromo-2,4,5,6-tetramethylbenzyl alcohol **10** in CDCl₃.

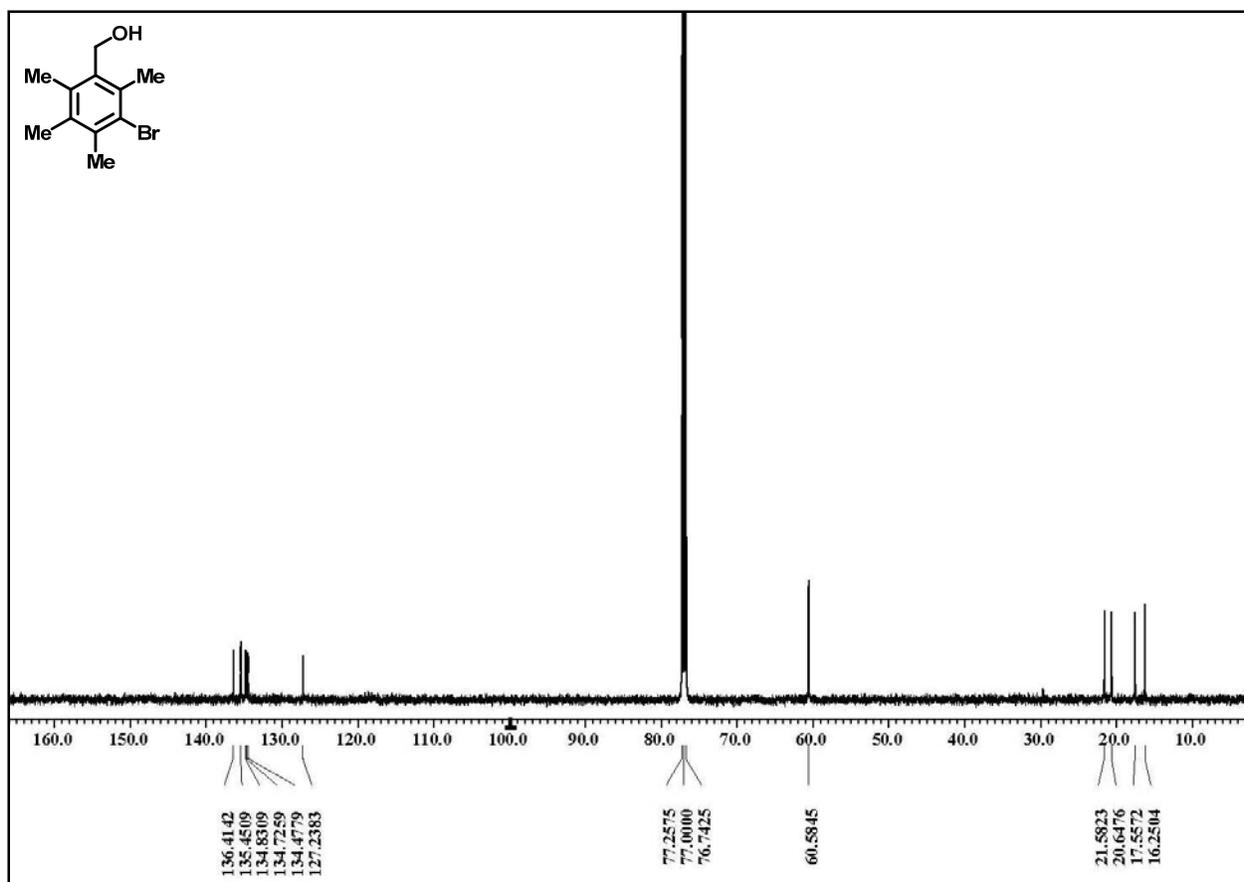


Figure S6. ¹³C NMR (125 MHz) spectrum of 3-bromo-2,4,5,6-tetramethylbenzyl alcohol **10** in CDCl₃.

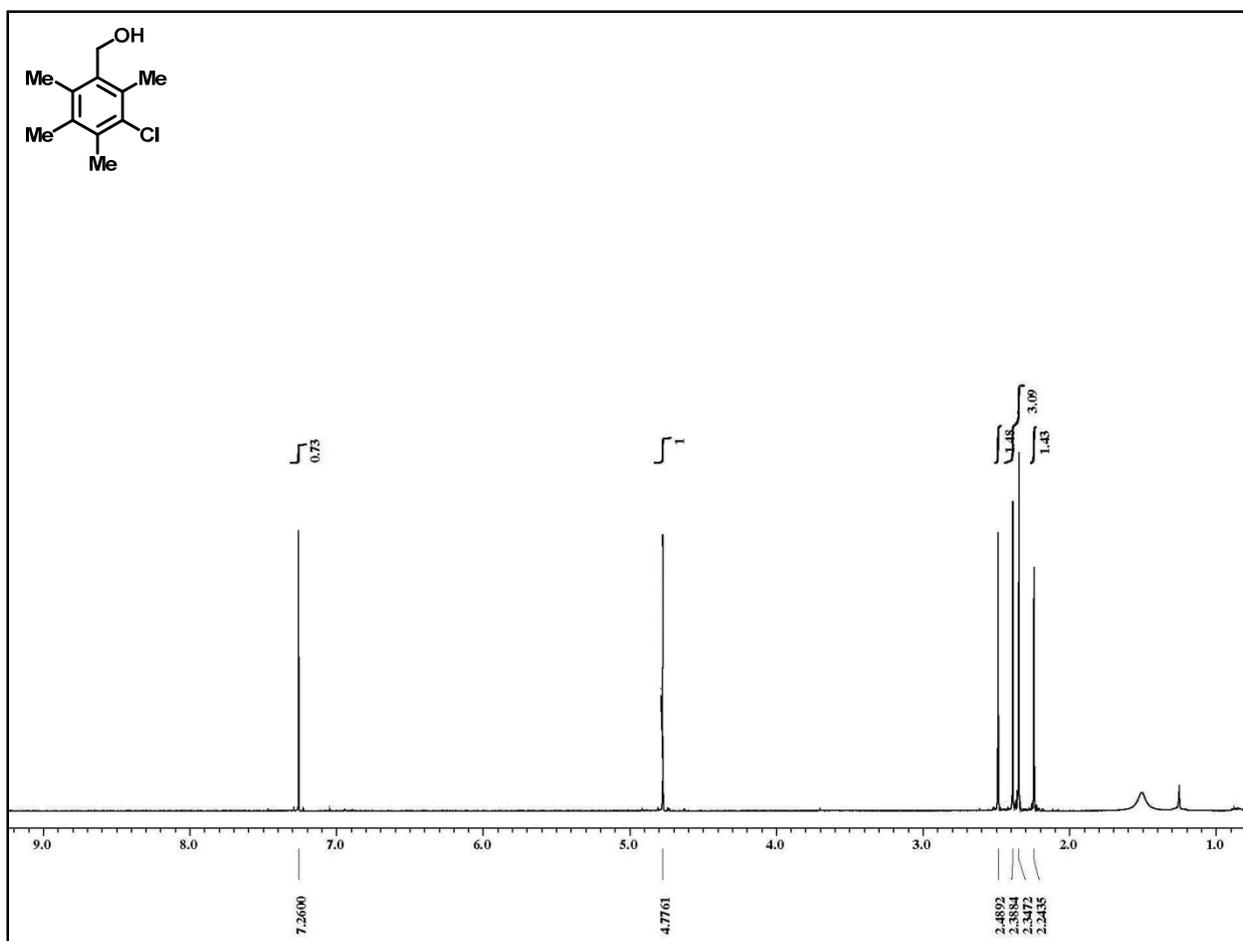


Figure S7. ¹H NMR (500 MHz) spectrum of 3-chloro-2,4,5,6-tetramethylbenzyl alcohol **11** in CDCl₃.

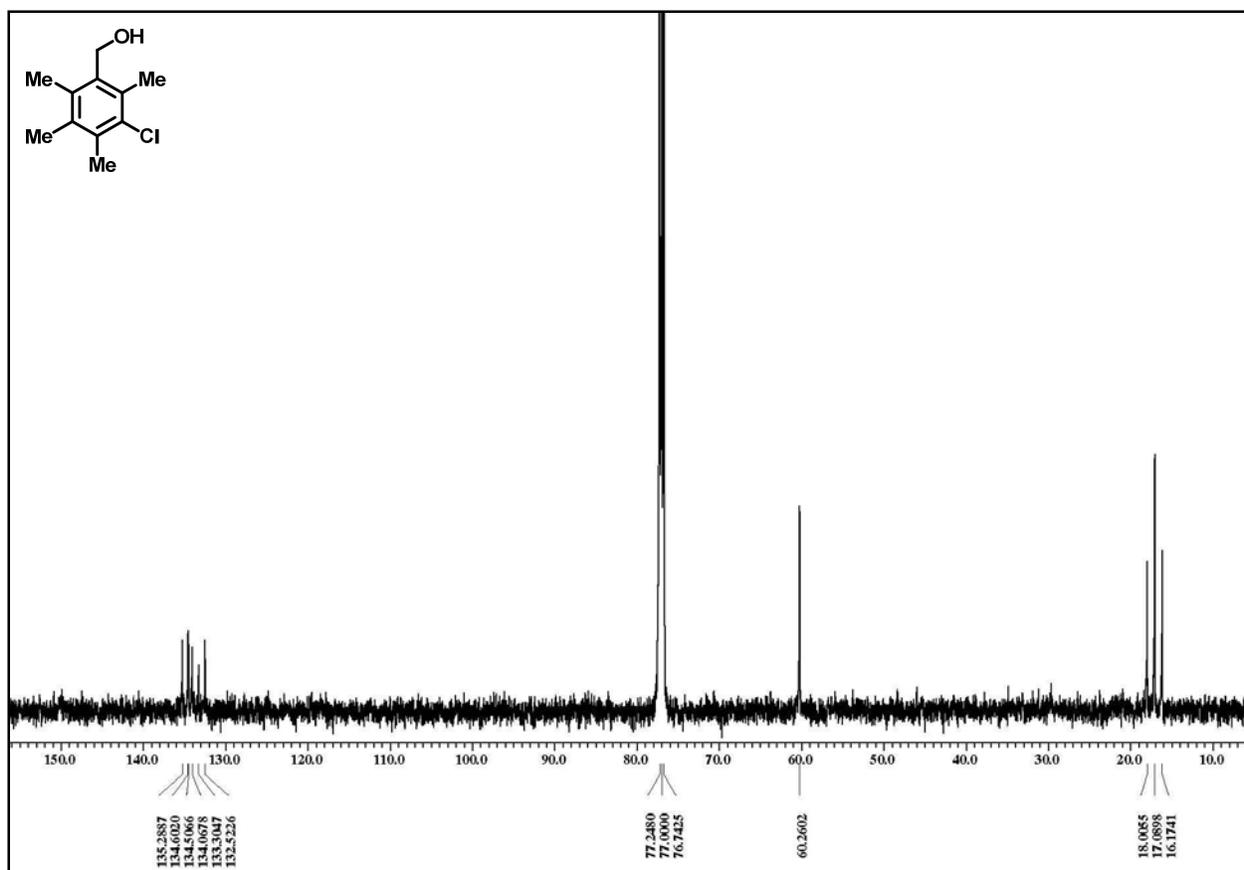


Figure S8. ¹³C NMR (125 MHz) spectrum of 3-chloro-2,4,5,6-tetramethylbenzyl alcohol **11** in CDCl₃.

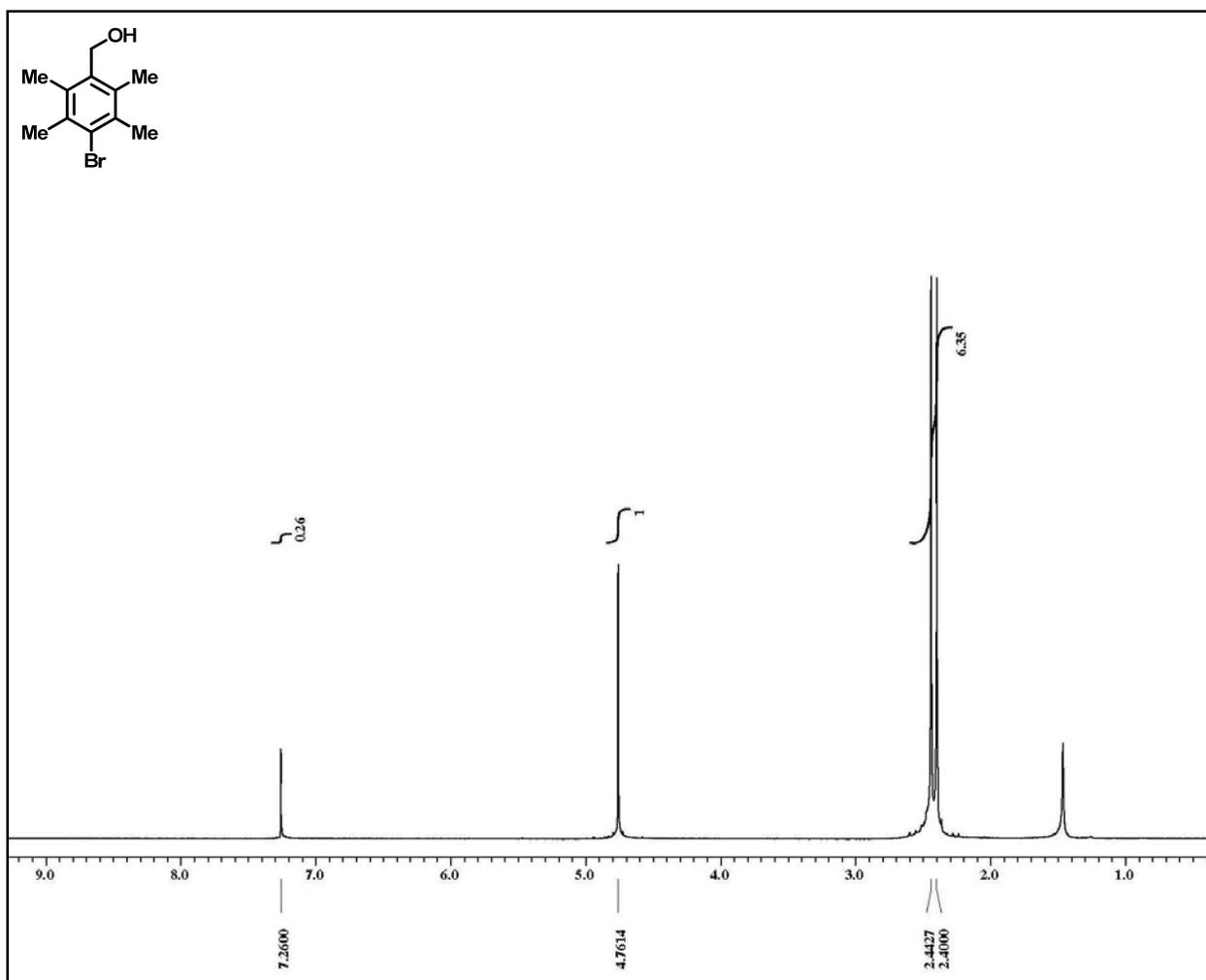


Figure S9. ¹H NMR (400 MHz) spectrum of 4-bromo-2,3,5,6-tetramethylbenzyl alcohol **12** in CDCl₃.

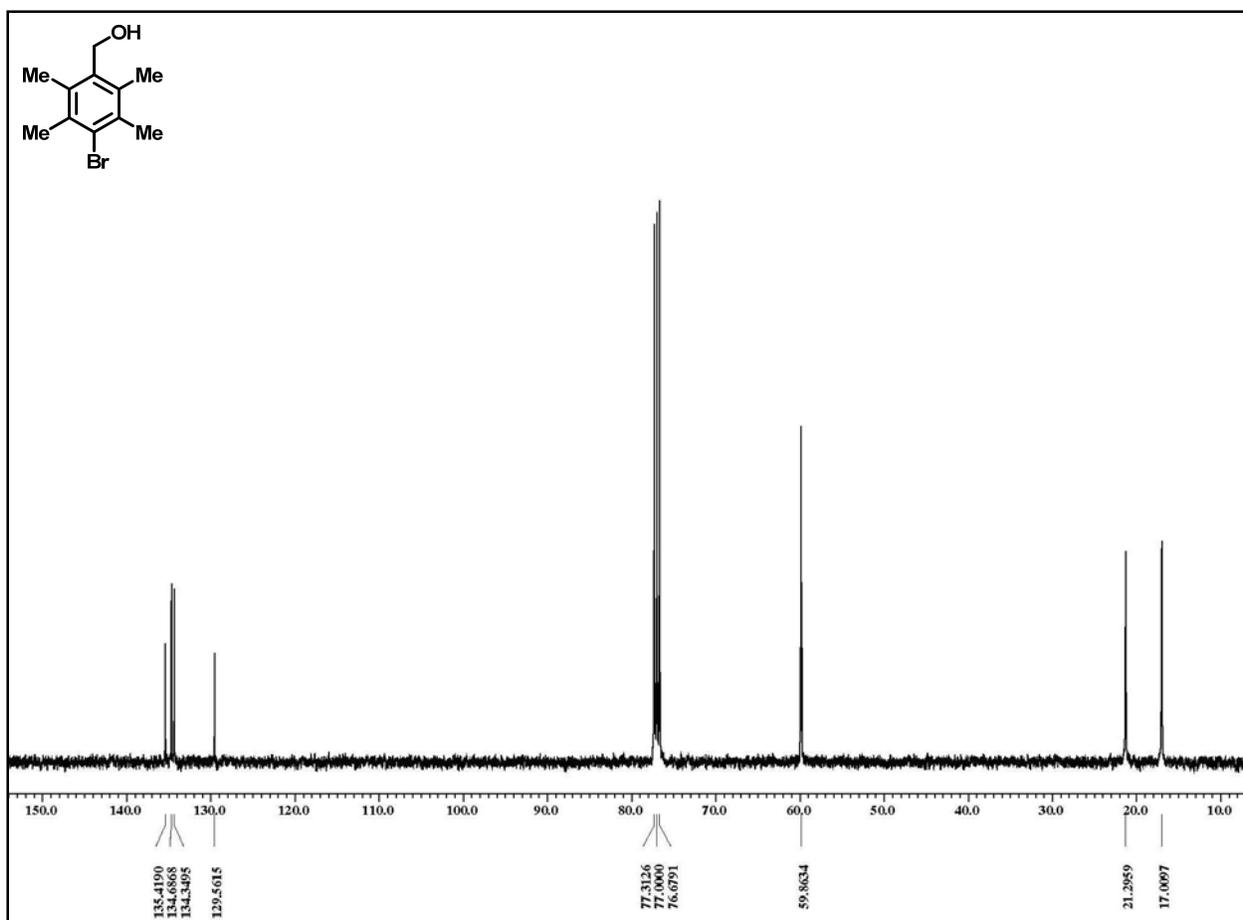


Figure S10. ¹³C NMR (100 MHz) spectrum of 4-bromo-2,3,5,6-tetramethylbenzyl alcohol **12** in CDCl₃.

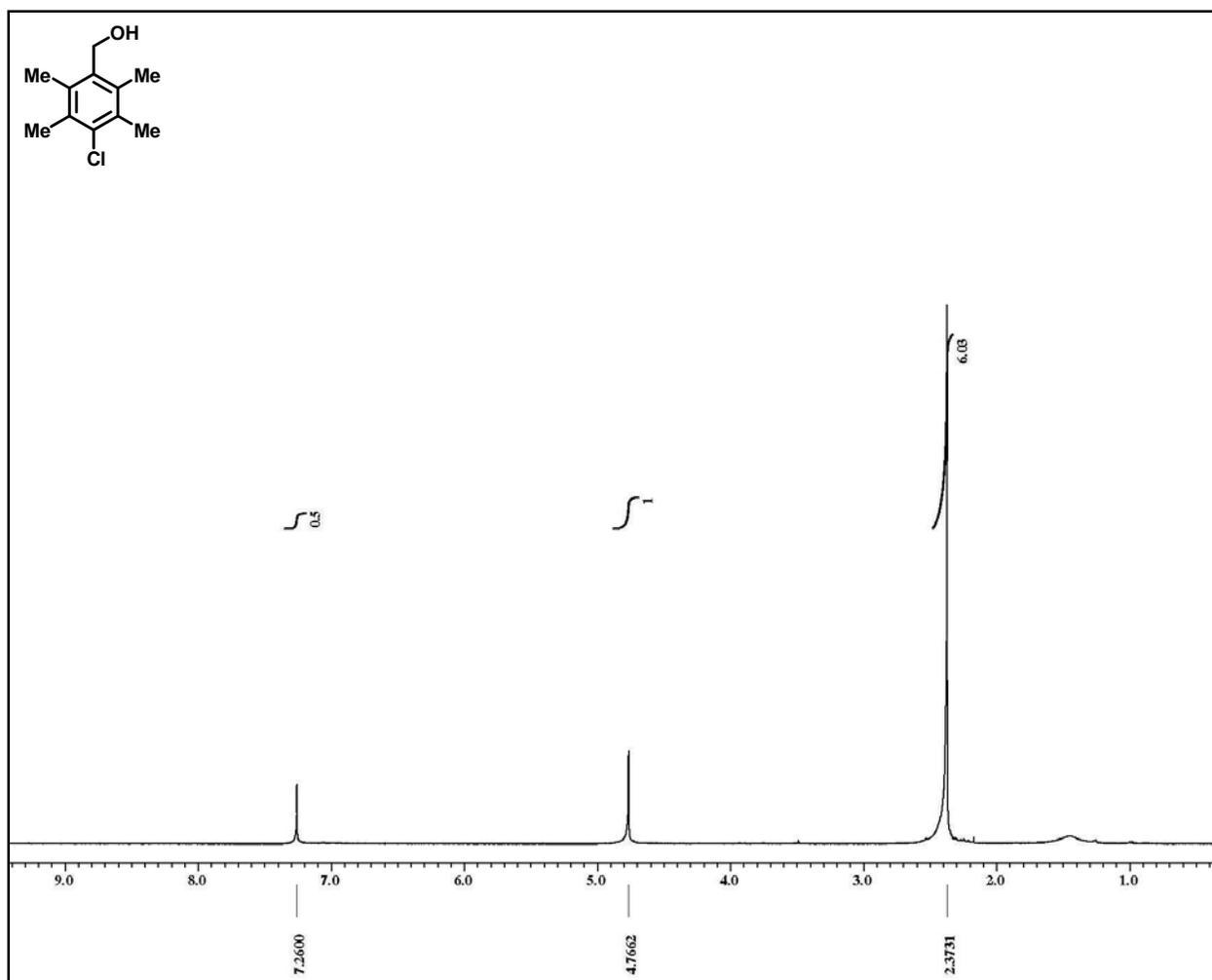


Figure S11. ^1H NMR (400 MHz) spectrum of 4-chloro-2,3,5,6-tetramethylbenzyl alcohol **13** in CDCl_3 .

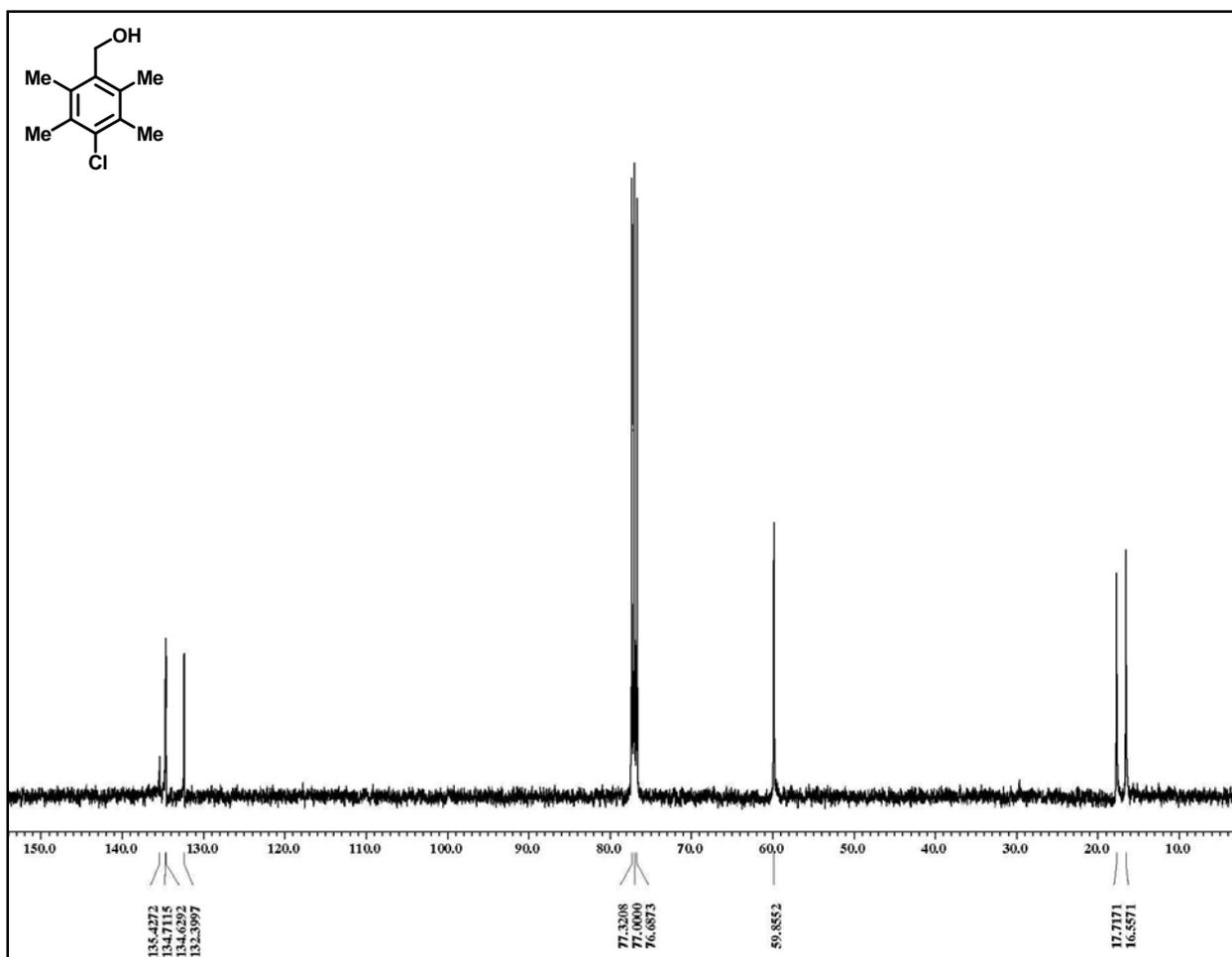


Figure S12. ¹³C NMR (100 MHz) spectrum of 4-chloro-2,3,5,6-tetramethylbenzyl alcohol **13** in CDCl₃.

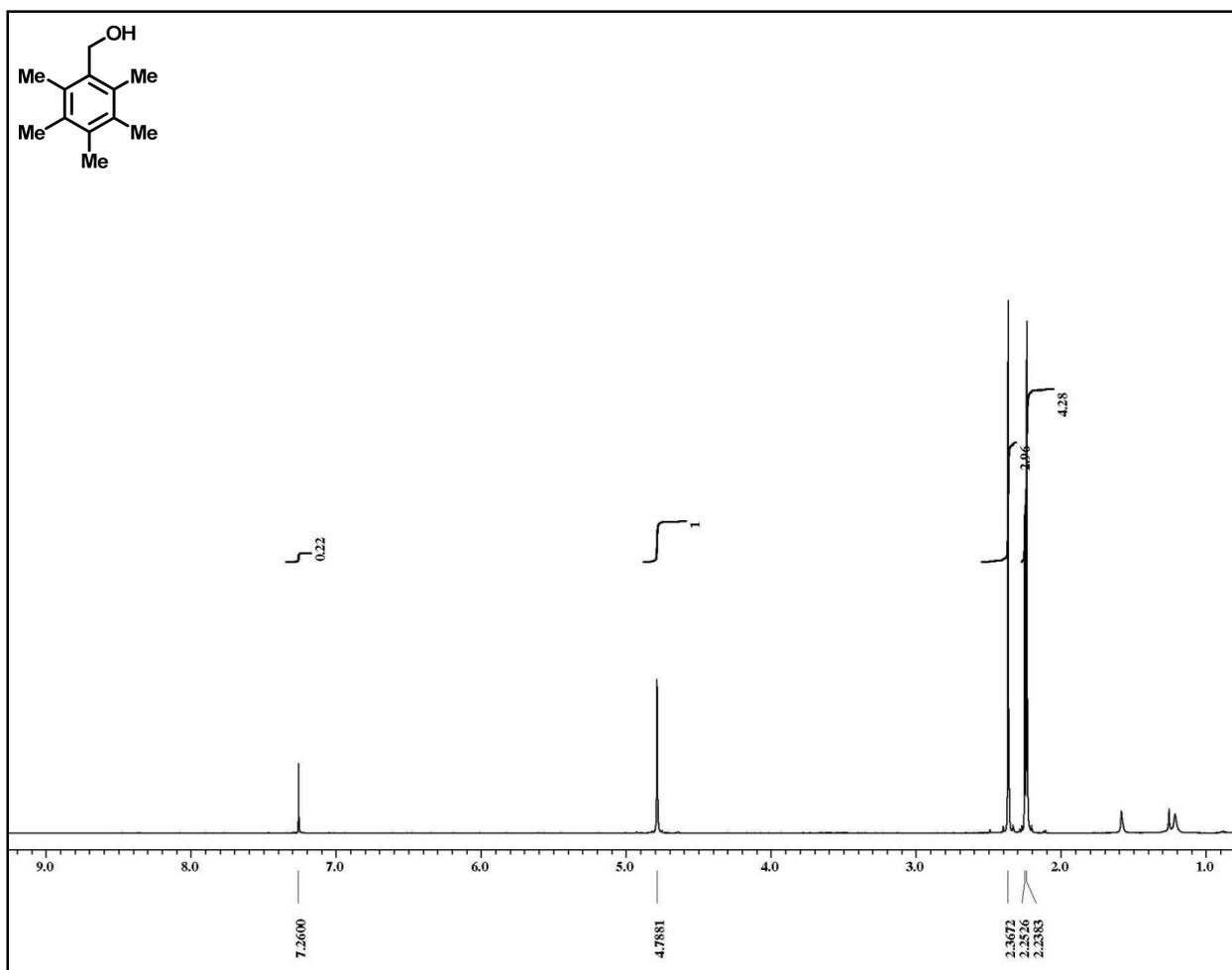


Figure S13. ¹H NMR (500 MHz) spectrum of 2,3,4,5,6-pentamethylbenzyl alcohol **14** in CDCl₃.

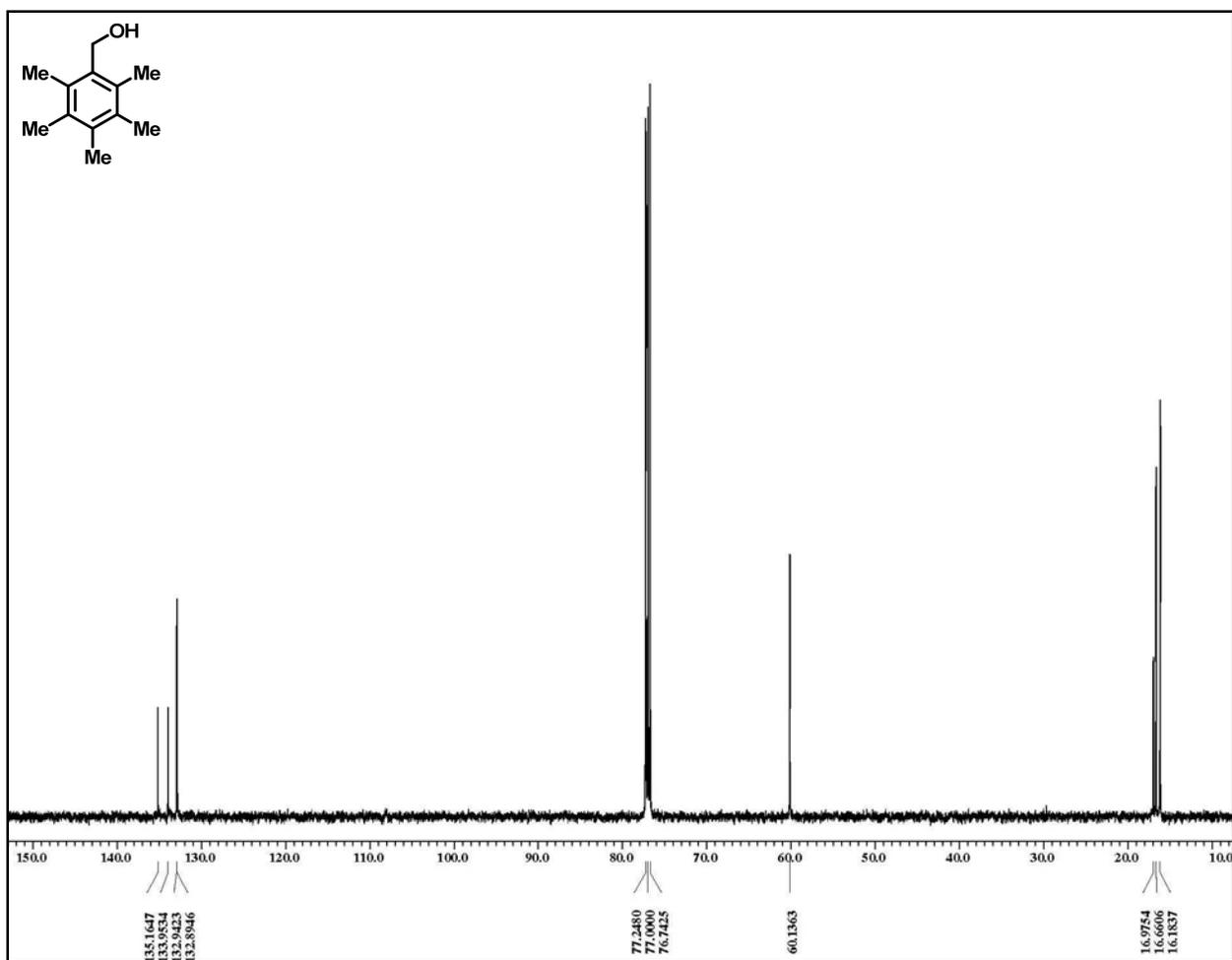


Figure S14. ¹³C NMR (125 MHz) spectrum of 2,3,4,5,6-pentamethylbenzyl alcohol **14** in CDCl₃.

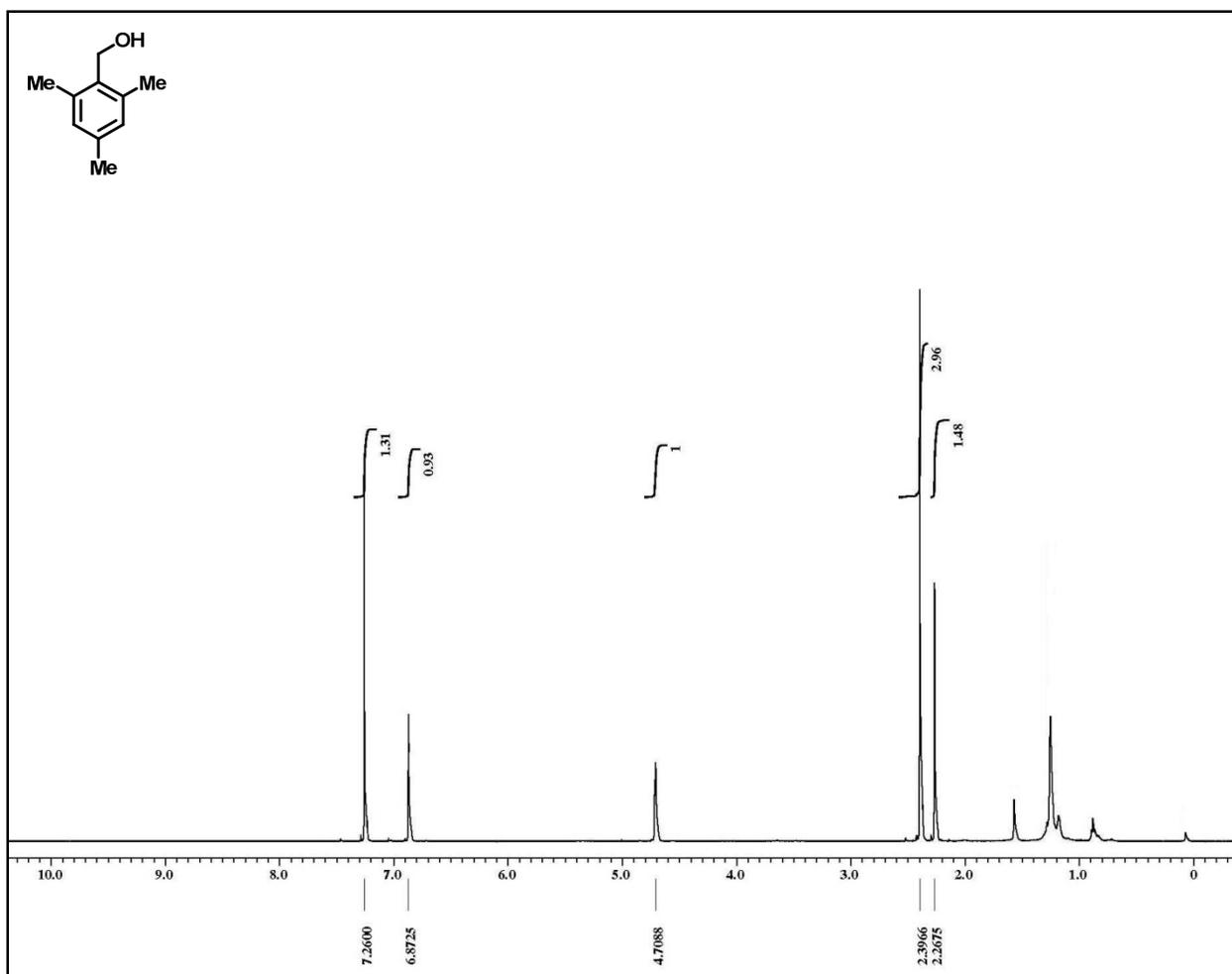


Figure S15. ¹H NMR (500 MHz) spectrum of 2,4,6-trimethylbenzyl alcohol **15** in CDCl₃.

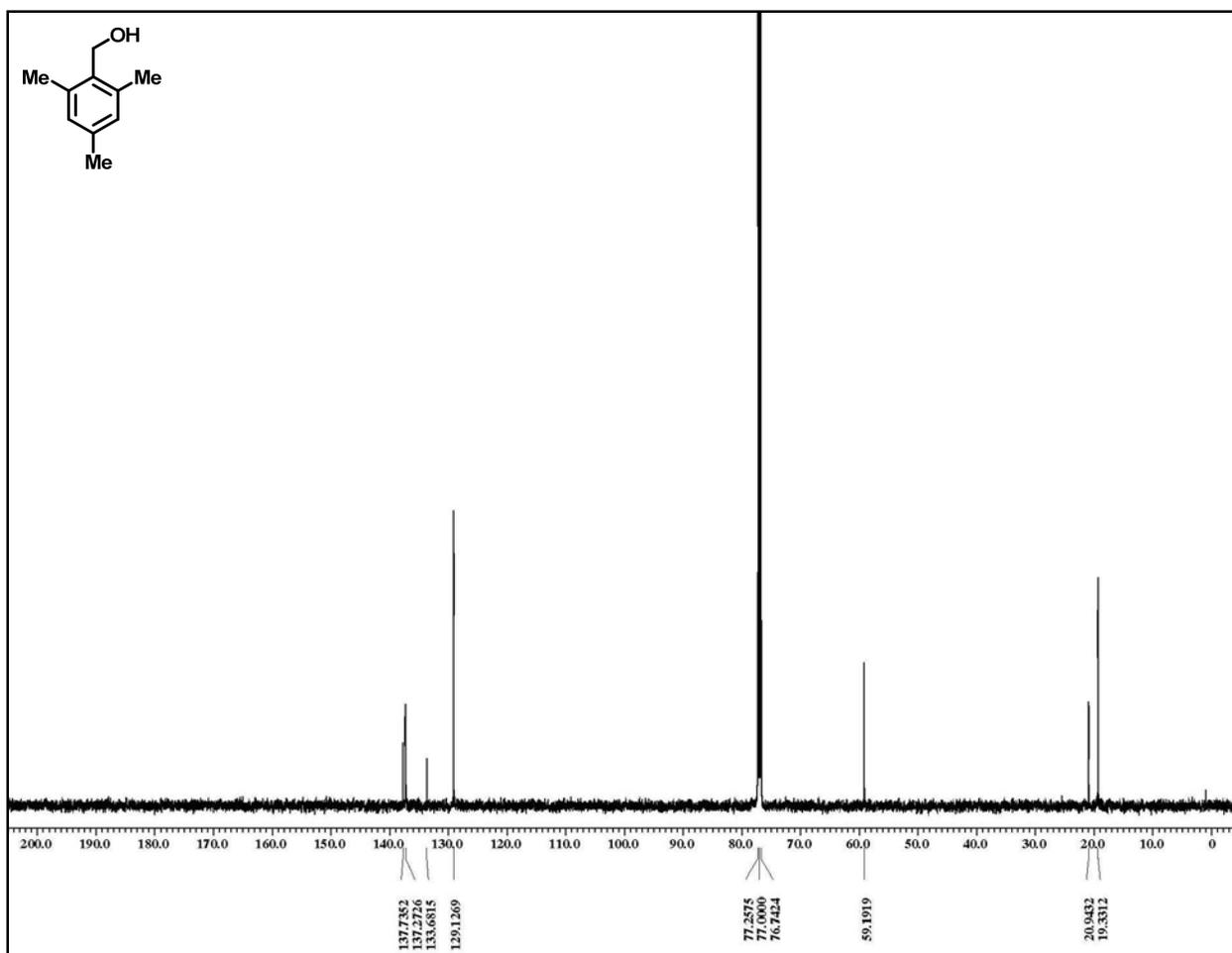


Figure S16. ¹³C NMR (125 MHz) spectrum of 2,4,6-trimethylbenzyl alcohol **15** in CDCl₃.