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Variations in Site of Lithiation of N-(2-(4-Methoxyphenyl)ethyl)pivalamide; Use in Ring Substitution

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Keywords:	lithium, metalation, lithiation, electrophilic aromatic substitution , aldehydes
Abstract:	Lithiation of N-(2-(4-methoxyphenyl)ethyl)pivalamide at -20 to 0 °C with three mole equivalents of n-BuLi in anhydrous THF, followed by reactions with various electrophiles, gives high yields of products involving ring substitution ortho- the pivaloylaminoethyl group, which was unexpected in view of earlier results reported with t-BuLi.

Variations in Site of Lithiation of *N*-(2-(4-Methoxyphenyl)ethyl)pivalamide; Use in Ring Substitution

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Abstract: Lithiation of *N*-(2-(4-methoxyphenyl)ethyl)pivalamide at –20 to 0 °C with three mole equivalents of *n*-BuLi in anhydrous THF, followed by reactions with various electrophiles, gives high yields of products involving ring substitution *ortho*- to the pivaloylaminoethyl group, which was unexpected in view of earlier results reported with *t*-BuLi.

Key words: *N*-(2-(4-methoxyphenyl)ethyl)pivalamide, directed lithiation, synthesis, electrophile, dilithium intermediate

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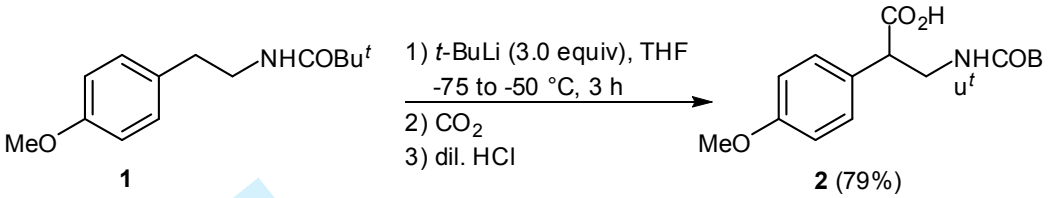
Phenylethylamine derivatives, especially ones containing oxygen substituents on the phenyl ring (which includes many biologically active compounds such as dopamine, adrenaline and mescaline), represent a hugely important class of chemicals of interest to both industry and academe, and selective methods for their synthesis are of considerable interest. Organolithium reagents play an important role in the development of clean and environmentally friendly processes for the regioselective production of specific products.[2,3] For example, lithiation of aromatic compounds often takes place proximal to a directing metalating group (DMG), which typically possess an oxygen or nitrogen atom.[4] Use of such

DMGs to facilitate lithiation, followed by reactions of the organolithium intermediates obtained *in-situ* with electrophiles, has found wide application in a variety of synthetic transformations to produce substituted aromatics or heterocycles.[5,6] This approach is one of the most efficient for synthesis of substituted and/or modified derivatives, which sometimes might be difficult to produce by other routes.[5,6]

In connection with other work on the use of lithium reagents in organic synthesis,[7] we have recently reported a detailed study for the regioselective lithiation and substitution of various substituted benzylamines.[8,9] Sometimes different products were formed, depending on the nature of the lithiating agent or reaction conditions. We found, for example, that treatment of *N*-(2-methoxybenzyl)pivalamide with *t*-BuLi in THF at −78 °C, followed by reaction with an electrophile, gave substitution *ortho*- to the methoxy group selectively,[8] in sharp contrast with results reported by Simig and Schlosser, who showed that lithiation of this substrate using *n*-BuLi at 0 °C, followed by treatment with carbon dioxide, resulted in carboxylation *ortho*- to the pivaloylaminomethyl group in 64% yield.[10]

Recently, we have been interested in regioselective lithiation and substitution of phenethylamine derivatives and found that direct lithiation of ring-unsubstituted acyl derivatives occurred at the α-position.[11] Simig and Schlosser also reported that lithiation of *N*-2-((4-methoxyphenyl)ethyl)pivalamide (**1**) using *t*-BuLi at −75 to −50 °C, followed by treatment with carbon dioxide, resulted in carboxylation at the CH_2 next to the 4-methoxyphenyl ring (α-lithiation) to give **2** in 79% yield (Scheme 1).[12] We wished to investigate the possibility of ring lithiation of *N*-(2-(4-methoxyphenyl)ethyl)pivalamide (**1**), notwithstanding that lithiation at this site was not reported at all under the conditions used by Simig and Schlosser.[12] We have therefore investigated lithiation under other conditions and

now report that we have been able to establish conditions for a high-yielding and general ring-substitution process.



Scheme 1. Lithiation of **1** followed by reaction with CO_2 as reported by Schlosser[12]

Initially, **1** was lithiated with *t*-BuLi (three molar equivalents) under conditions similar to those used by Schlosser,[12] followed by reaction with benzophenone (1.4 molar equivalents). The crude product was purified by column chromatography to give residual **1** (30%) and a new product, *N*-(3-hydroxy-2-(4-methoxyphenyl)-3,3-diphenylpropyl)pivalamide (**3**; Figure 1), obtained in 58% yield. Compound **3** was clearly obtained *via* the intermediacy of dilithium species **4** (Figure 1), which was in accord with the results reported by Schlosser.[12]

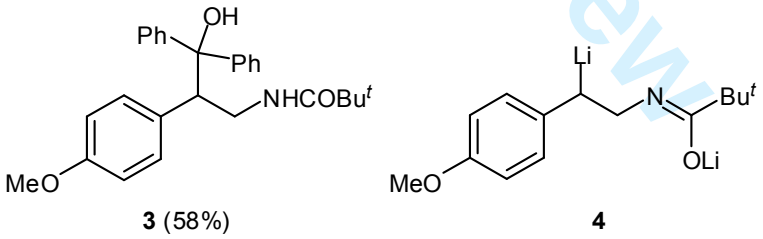
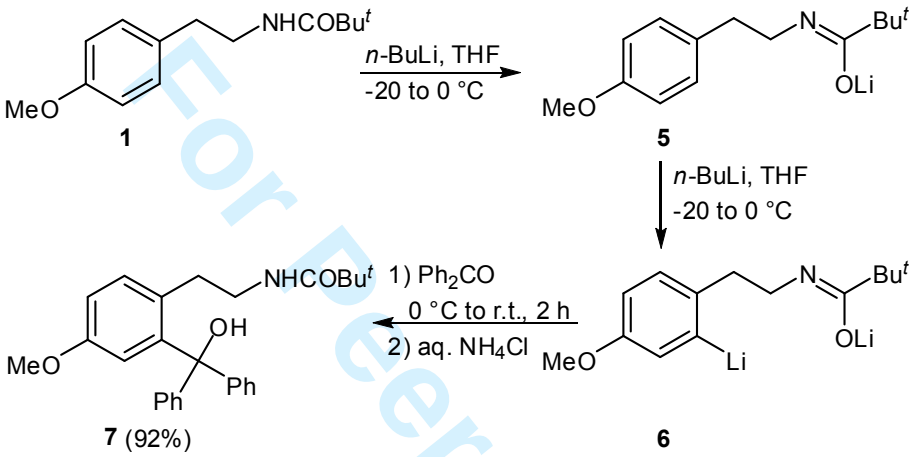


Figure 1 Structures of compound **3** and dilithium intermediate **4**

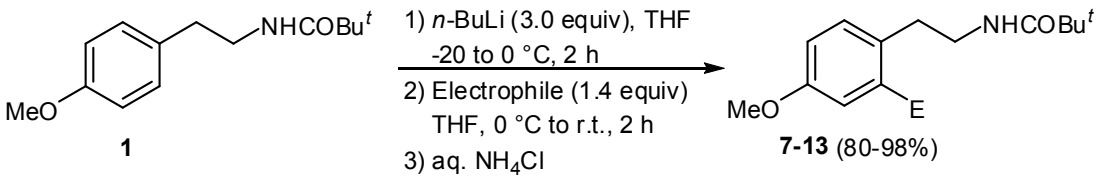
A reaction carried out with *n*-BuLi under the same conditions as were used with *t*-BuLi resulted in the starting material **1** being recovered quantitatively, indicating that no *C*-lithiation had taken place, but lithiation of **1** with *n*-BuLi (3.0 molar equivalents) at –20 to 0

°C over 2 h, followed by treatment with benzophenone gave a new compound, shown by its spectral properties[13,14] to be **7** (Scheme 2), isolated in 92% yield. This suggested that lithiation took place on the ring and that lithium reagents **5** and **6** were produced *in-situ* (Scheme 2).



Scheme 2 Lithiation of **1** with *n*-BuLi followed by reactions with benzophenone

The latter reaction clearly had potential as a synthetic method and therefore the same lithiation procedure was used for reactions with a range of different electrophiles (Scheme 3). Following work-up of the reaction mixtures the crude products were purified by column chromatography (silica gel; Et_2O–hexane, 1:1) to give the corresponding substituted products **7**–**13** in 80–98% yields (Table 1).



Scheme 3 Lithiation of **1** with *n*-BuLi followed by reactions with electrophiles

Table 1 Synthesis of Products **7**–**13** According to Scheme 3

Product	Electrophile	E	Yield (%)[a]
7	Ph_2CO	$Ph_2C(OH)$	92
8	$(CH_2)_5CO$	$(CH_2)_5C(OH)$	88
9	EtCOMe	EtC(OH)Me	95
10	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CH(OH)$	80
11	4-$Me_2NC_6H_4CHO$	4-$Me_2NC_6H_4CH(OH)$	90
12	Me_2NCHO	CHO	98
13	I_2	I	89

[a] Yield of isolated product after purification by flash column chromatography.

Clearly, the procedure outlined in Scheme 3 represents a simple, efficient and high yielding route for substitution of *N*-(2-(4-methoxyphenyl)ethyl)pivalamide (**1**) *ortho*- to the pivaloylaminoethyl group. However, it was not clear why lithiation of **1** with *t*-BuLi at −75 to −50 °C gave side-chain substitution, while lithiation with *n*-BuLi at −20 to 0 °C gave ring substitution. One possibility was that at low temperature the lithiation step was under kinetic control, leading to the intermediate **4**, with only the *t*-BuLi sufficiently reactive to effect the lithiation under such conditions, but that at higher temperature the organolithium intermediate **4** was capable of isomerization to **6**, so that reactions conducted at the higher temperature were under thermodynamic control. In order to test this possibility, the reaction of **1** was initially carried out at −75 to −50 °C with *t*-BuLi (3.0 molar equivalents) for 3 h (conditions previously shown to produce **4**), and the mixture was then warmed to 0 °C and maintained for a further 2 h, after which benzophenone (1.4 molar equivalents) was added. The cooling bath was removed and the mixture was stirred for 2 h while warming to room temperature. Purification of the crude product by column chromatography gave **7** in 82% yield along with

residual **1** (14%). This finding clearly indicated that the dilithium reagent **6** (Scheme 2) is thermodynamically more stable than the dilithium reagent **4** (Figure 1) at higher temperature.

In conclusion, *N*-(2-(4-methoxyphenyl)ethyl)pivalamide (**1**) undergoes lithiation with *n*-BuLi at 0 ºC, followed by treatment with various electrophiles, to give high yields of the corresponding substituted products having the substituent *ortho*- to the pivaloylaminoethyl group. This contrasts sharply with earlier results using *t*-BuLi at lower temperature, which gave α-substitution. The variation arises because the dilithium reagent **4**, formed at low temperature with *t*-BuLi, is less stable than dilithium reagent **6**, to which it isomerises at 0 ºC.

Acknowledgments

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References and Notes

(1) Permanent address: G. A. El-Hiti, Department of Chemistry, Faculty of Science, Tanta University, Tanta 31527, Egypt.

(2) See for example: (a) Clayden, J. *Organolithiums: Selectivity for Synthesis*, Pergamon: Oxford, **2002**. (b) Schlosser, M. *Organometallics in Synthesis*, 2nd ed.; Wiley: Chichester, **2002**; pp. 1–352. (c) Capriati, V.; Florio, S.; Salomone, A. *Topics in Stereochemistry*. **2010**, *26*, 135. (d) Coldham, I.; Sheikh, N. S. *Topics in Stereochemistry*. **2010**, *26*, 253.

(3) See for example: (a) Beak, P.; Snieckus, V. *Acc. Chem. Res.*, **1982**, *15*, 306. (b) Nájera, C.; Sansano, J. M.; Yus, M. *Tetrahedron* **2003**, *59*, 9255. (c) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 2206. (d) Chadwick, S. T.; Ramirez, A.; Gupta, L.; Collum, D. B. *J. Am. Chem. Soc.* **2007**, *129*, 2259. (e) Dyke, A. M.; Gill, D. M.; Harvey, J. N.; Hester, A. J.; Lloyd-Jones, G. C.; Muñoz, M. P.; Shepperson I. R. *Angew.*

Chem. Int. Ed. **2008**, *47*, 5067. (f) Coldham, I.; Raimbault, S.; Chovatia, P. T.; Patel, J. J.; Leonori, D.; Sheikh, N. S.; Whittaker, D. T. E. *Chem. Commun*. **2008**, 4174. (g) Coldham, I.; Leonori, D.; Beng, T. K.; Gawley, R. E. *Chem. Commun*. **2009**, 5239. (h) Coldham, I.; Raimbault, S.; Whittaker, D. T. E.; Chovatia, P. T.; Leonori, D.; Patel, J. J.; Sheikh, N. S. *Chem.-A Eur. J*. **2010**, *16*, 4082. (i) Robinson, S. P.; Sheikh, N. S.; Baxter, Carl A.; Coldham, I. *Tetrahedron Lett*. **2010**, *51*, 3642. (j) Guerrand, H. D. S.; Adams, H.; Coldham, I. *Org. Biomol. Chem*. **2011**, *9*, 7921. (k) Thompson, M. J.; Louth, J. C.; Little, S. M.; Jackson, M. P.; Boursereau, Y.; Chen, B.; Coldham, I. *ChemMedChem* **2012**, *7*, 578. (l) Sheikh, N. S.; Leonori, D.; Barker, G.; Firth, J. D.; Campos, K. R.; Meijer, A. J. H. M.; O'Brien, P.; Coldham, I. *J. Am. Chem. Soc*. **2012**, *134*, 5300.

(4) See for example: (a) Beak, P.; Zajdel, W. J.; Reitz, D. B. *Chem. Rev.* **1984**, *84*, 471. (b) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. (c) El-Hiti, G. A. *Heterocycles* **2000**, *53*, 1839. (d) Turck, A.; Plé, N.; Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4489. (e) Anctil, E. J.-G.; Snieckus, V. *J. Organomet. Chem.* **2002**, *653*, 150. (f) Smith, K.; El-Hiti, G. A. *Curr. Org. Synth.* **2004**, *1*, 253. (g) Chinchilla, R.; Nájera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667. (h) Schlosser, M. *Angew. Chem. Int. Ed*. **2005**, *44*, 376. (i) Foubelo, F.; Yus, M. *Curr. Org. Chem*. **2005**, *9*, 459. (j) Rathman, T. L.; Bailey, W. F. *Org. Process Res. Dev.* **2009**, *13*, 144. (k) Houlden, C. E.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Org. Lett*. **2010**, *12*, 3090. (l) Houlden, C. E.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Org. Lett*. **2010**, *12*, 3090. (m) Page, A.; Clayden, J. *Beilstein J. Org. Chem.* **2011**, *7*, 1327. (n) El-Hiti, G. A.; Hegazy, A. S.; Alotaibi, M. H.; Ajarim, M. D. *ARKIVOC* **2012**, *(vii)*, 35.

(5) Examples for substituted benzenes: (a) Clayden, J.; Turner, H.; Pickworth, M.; Adler, T. *Org. Lett*. **2005**, *7*, 3147. (b) Clayden, J.; Dufour, J. *Tetrahedron Lett*. **2006**, *47*, 6945. (c) Burgos, P. O.; Fernández, I.; Iglesias, M. J.; García-Granda, S.; Ortiz, F. L. *Org. Lett*. **2008**, *10*, 537. (d) Castanet, A.-S.; Tilly, D.; Véron, J.-B.; Samanta, S. S.; De, A.; Ganguly, T.;

Mortier, J. *Tetrahedron* **2008**, *64*, 3331. (e) Michon, C.; Murai, M.; Nakatsu, M.; Uenishi, J.; Uemura M. *Tetrahedron*, **2009**, *65*, 752. (f) Tilly, D.; Fu, J.-M.; Zhao, B.-P.; Alessi, M.; Catanet, A.-S.; Snieckus, V.; Mortier, J. *Org. Lett*. **2010**, *12*, 68. (g) Slocum, D. W.; Wang, S.; White, C. B.; Whitley, P. E. *Tetrahedron* **2010**, *66*, 4939. (h) Cho, I.; Meimetis, L.; Belding, L.; Katz, M. J.; Dudding, T.; Britton, R. *Beilstein J. Org. Chem*. **2011**, *7*, 1315. (i) Schmid, M.; Waldner, B.; Schnürch, M.; Mihovilovic, M. D.; Stanetty, P. *Tetrahedron* **2011**, *67*, 2895. (j) Volz, N.; Clayden, J. *Angew. Chem. Int. Ed*. **2011**, *50*, 12148.

(6) Examples for substituted heterocycles: (a) Robert, N.; Bonneau, A.-L.; Hoarau, C.; Marsais, F. *Org. Lett*. **2006**, *8*, 6071. (b) Comoy, C.; Banaszak, E.; Fort, Y. *Tetrahedron* **2006**, *62*, 6036. (c) Luisi, R.; Capriati, V.; Florio, S.; Musio, B. *Org. Lett*. **2007**, *9*, 1263. (d) Clayden, J.; Hennecke, U. *Org. Lett*. **2008**, *10*, 3567. (e) McLaughlin, M.; Marcantonio, K.; Chen, C.; Davies, I. W. *J. Org. Chem*. **2008**, *73*, 4309. (f) Capriati, V.; Florio, S.; Luisi, R.; Mazzanti, A.; Musio, B. *J. Org. Chem*. **2008**, *73*, 3197. (g) Affortunato, F.; Florio, S.; Luisi, R.; Musio B. *J. Org. Chem.* **2008**, *73*, 9214. (h) Musio, B.; Clarkson, G. J.; Shipman, M.; Florio, S.; Luisi, R. *Org. Lett*. **2009**, *11*, 325. (i) Clayton, J.; Clayden, J. *Tetrahedron Lett*. **2011**, *52*, 2436. (j) Ibrahim, N.; Chevot, F.; Legraverend, M. *Tetrahedron Lett*. **2011**, *52*, 305.

(7) See for example: (a) Smith, K.; El-Hiti, G. A.; Abdo, M. A.; Abdel-Megeed M. F. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1029. (b) Smith, K.; El-Hiti, G. A.; Abdel-Megeed, M. F.; Abdo, M. A. *J. Org. Chem.* **1996**, *61*, 647. (c) Smith, K.; El-Hiti, G. A.; Abdel-Megeed, M. F.; Abdo, M. A. *J. Org. Chem.* **1996**, *61*, 656. (d) Smith, K.; El-Hiti, G. A.; Pritchard, G. J.; Hamilton, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2299. (e) Smith, K.; El-Hiti, G. A.; Shukla, A. P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2305. (f) Smith, K.; El-Hiti, G. A.; Hawes, A. C. *Synthesis* **2003**, 2047. (g) Smith, K.; El-Hiti, G. A.; Mahgoub, S. A. *Synthesis* **2003**, 2345. (h) El-Hiti, G. A. *Synthesis* **2003**, 2799 (i) Smith, K.; El-Hiti, G. A.; Abdel-Megeed, M. F. *Synthesis* **2004**, 2121. (j) El-Hiti, G. A. *Synthesis* **2004**, 363. (k) Smith, K.; El-

Hiti, G. A.; Hegazy, A. S. *Synthesis* **2005**, 2951. (l) Smith, K.; Barratt, M. L. *J. Org. Chem.* **2007**, *72*, 1031.

(8) (a) Smith, K.; El-Hiti, G. A.; Hegazy, A. S. *Synlett*, **2009**, 2242. (b) Smith, K.; El-Hiti, G. A.; Hegazy, A. S.; Fekri, A.; Kariuki, B. M. *ARKIVOC* **2009**, *(xiv)*, 266.

(9) (a) Smith, K.; El-Hiti, G. A.; Hegazy, A. S. *Chem. Commun*. **2010**, *46*, 2790. (b) Smith, K.; El-Hiti, G. A.; Hegazy, A. S.; Fekri, A. *Heterocycles* **2010**, *80*, 941. (c) Smith, K.; El-Hiti, G. A.; Hegazy, A. S. *Synthesis* **2010**, 1371. (d) Smith, K.; El-Hiti, G. A.; Hegazy, A. S.; Kariuki, B. *Beilstein J. Org. Chem.* **2011**, *7,* 1219.

(10) Simig, G.; Schlosser, M. *Tetrahedron Lett.* **1988**, *29*, 4277.

(11) Smith, K.; El-Hiti, G. A.; Alshammari, M. B. *Synthesis* **2012**, *44*, 2013.

(12) Simig, G.; Schlosser, M. *Tetrahedron Lett.* **1991**, *32*, 1963.

(13) Assignments of signals are based on integration values, coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged.

(14) Analytical data for **7**: white solid (0.32 g, 92%); mp 179–181 °C. IR (FT): ν_{max} = 3321, 2958, 1627, 1575, 1292, 1243 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.35–7.26 (m, 11 H, OH and 2 C_6H_5), 7.16 (d, *J* = 8.3 Hz, 1 H, H-6 of 4-$MeOC_6H_3$), 6.79 (dd, *J* = 2.8, 8.3 Hz, 1 H, H-5 of 4-$MeOC_6H_3$), 6.24 (d, *J* = 2.8 Hz, 1 H, H-3 of 4-$MeOC_6H_3$), 6.15 (br, exch., 1 H, NH), 3.63 (s, 3 H, OCH_3), 3.37 (app. q, *J* = 7 Hz, 2 H, CH_2NH), 2.60 (t, *J* = 7.2 Hz, 2 H, CH_2), 1.11 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ = 178.8 (s, C=O), 156.9 (s, C-4 of 4-$MeOC_6H_3$), 147.1 (s, C-1 of 2 C_6H_5), 146.6 (s, C-2 of 4-$MeOC_6H_3$), 132.8 (d, C-6 of 4-$MeOC_6H_3$), 130.7 (s, C-1 of 4-$MeOC_6H_3$), 127.9 (d, C-3/C-5 of 2 C_6H_5), 127.7 (d, C-2/C-6 of 2 C_6H_5), 127.2 (d, C-4 of 2 C_6H_5), 117.1 (d, C-3 of 4-$MeOC_6H_3$), 111.9 (d, C-5 of 4-$MeOC_6H_3$), 83.0 (s, C–OH), 55.0 (q, OCH_3), 41.1 (t, CH_2NH), 38.4 [s, $C(CH_3)_3$], 32.5 (t,

$ArCH_2$), 27.5 [q, $C(CH_3)_3$] ppm. MS (EI): *m/z* (%) = 399 (77, $[M - H_2O]^+$), 298 (99), 285 (90), 261 (33), 239 (10), 222 (26), 209 (31), 193 (73), 165 (53), 152 (13), 105 (48), 83 (100). HRMS (EI): *m/z* calcd for $C_{27}H_{29}NO_2$ ($[M - H_2O]^+$): 399.2198; found: 399.2187.

Electronic Supplementary Information (ESI)

Variations in Site of Lithiation of *N*-(2-(4-Methoxyphenyl)ethyl)pivalamide; Use in Ring Substitution

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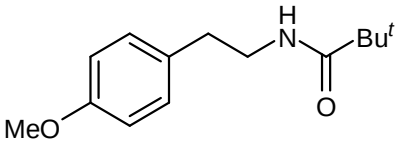
Instrumentation and Chemicals

General. Melting point determinations were performed by the open capillary method using a Gallenkamp melting point apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV500 spectrometer operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C measurements. Chemical shifts δ are reported (for compounds **3** and **7** in the main manuscript) in parts per million (ppm) relative to TMS and coupling constants *J* are in Hz, reported to the nearest 1 Hz. ^{13}C multiplicities were revealed by DEPT signals. Assignments of signals are based on integration values, coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged. The proton multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Low-resolution mass spectra were recorded on a Waters GCT Premier spectrometer and high-resolution mass spectra were recorded on a Waters LCT Premier XE instrument. IR spectra were recorded on a Jasco FT/IR-660 plus instrument by dissolving the product in chloroform, applying droplets on a NaCl plate and allowing evaporation of the solvent. Column chromatography was carried out using Fischer Scientific silica 60A (35-70 micron). Alkyllithiums were obtained from Aldrich Chemical Company and were estimated prior to use by the method of Watson and Eastham.[1] Other chemicals were obtained from Aldrich Chemical Company and used without further purification.

Synthesis of *N*-(2-(4-Methoxyphenyl)ethyl)pivalamide (1)

The synthesis of **1** was not previously reported, although use of the compound has been reported.[2] A mixture of 2-(4-methoxyphenyl)ethanamine (5.00 g, 33.1 mmol), pivaloyl chloride (4.40 g, 36.4 mmol) and triethylamine (4.60 g, 45.5 mmol) in DCM (50 mL) was stirred for 1 h at room temperature. The mixture was washed with H_2O (2 × 25 mL). The organic layer was dried ($MgSO_4$) and removed under reduced pressure. The solid obtained was purified by crystallization from hexane to give pure **1** (7.09 g, 30.1 mmol; 91%) as a white crystalline solid, mp: 71–73 °C.



IR (FT): ν_{max} 3350, 2959, 1655, 1534, 1365 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.03 (d, *J* = 9 Hz, 2 H, H-2/H-6 of 4-$CH_3OC_6H_4$), 6.78 (d, *J* = 9 Hz, 2 H, H-3/H-5 of 4-$CH_3OC_6H_4$), 5.60 (br., exch., 1 H, NH), 3.72 (s, 3 H, OCH_3), 3.39 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.68 (t, *J* = 7 Hz, 2 H, CH_2), 1.07 [s, 9 H, C(CH_3)$_3$].

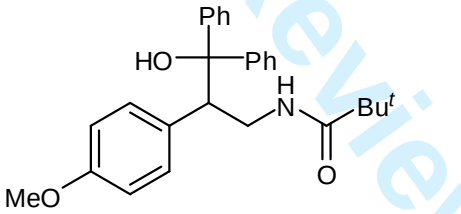
^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.3 (s, C=O), 158.3 (s, C-4 of 4-$CH_3OC_6H_4$), 131.0 (s, C-1 of 4-$CH_3OC_6H_4$), 129.7 (d, C-2/C-6 of 4-$CH_3OC_6H_4$), 114.0 (d, C-3/C-5 of 4-$CH_3OC_6H_4$), 55.3 (q, OCH_3), 40.8 (t, CH_2NH), 38.6 [s, *C*$(CH_3)_3$], 34.7 (t, CH_2), 27.5 [q, C(*C*$H_3)_3$].

MS (EI): *m/z* (%) = 235 (8, $[M]^+$), 220 (4), 192 (7), 134 (100), 121 (30), 105 (8), 91 (14), 77 (10), 65 (4), 57 (10).

HRMS (EI): *m/z* [M^+]calcd for $C_{14}H_{21}NO_2$: 235.1572; found: 235.1571.

Synthesis of *N*-(3-Hydroxy-2-(4-methoxyphenyl)-3,3-diphenylpropyl)pivalamide (3)

A solution of *t*-BuLi in pentane (1.45 mL, 1.9 M, 2.8 mmol) was added to a cold (–75 °C), stirred solution of *N*-(2-(4-methoxyphenyl)ethyl)pivalamide (**1**; 0.20 g, 0.85 mmol) in anhydrous THF (15 mL) under N_2. The mixture was stirred for 3 h at –50 °C after which a solution of benzophenone (0.255 g, 1.40 mmol) in anhydrous THF (5 mL) was added. The cooling bath was removed and the reaction mixture was stirred for 2 h. The reaction mixture was quenched with aqueous saturated NH_4Cl (20 mL) and diluted with diethyl ether (20 mL). The organic layer was separated, washed with H_2O (2 × 20 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue obtained was purified by column chromatography (silica gel; hexane: Et_2O, 1:1 by volume) to give pure **3** (0.20 g, 58%) as a white solid; mp 157–160 °C.



IR (FT): ν_{max} 3399, 2960, 1641, 1511, 1301, 1248 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 9 Hz, 2 H, H-2/H-6 of 4-$CH_3OC_6H_4$), 7.28 (app. t, *J* = 7 Hz, 2 H, H-3/H-5 of one C_6H_5), 7.22 (d, *J* = 7 Hz, 2 H, H-2/H-6 of one C_6H_5), 7.13 (t, *J* = 7 Hz, 1 H, H-4 of one C_6H_5), 7.06 (d, *J* = 7 Hz, 2 H, H-2/H-6 of other C_6H_5), 7.00 (app. t, *J* = 7 Hz, 2 H, H-3/H-5 of other C_6H_5), 6.90 (t, *J* = 7 Hz, 1 H, H-4 of other C_6H_5), 6.61 (d, *J* = 9 Hz, 2 H, H-3/H-5 of 4-$CH_3OC_6H_4$), 5.39 (br., exch., 1 H, NH), 4.08 (app. t, *J* = 7 Hz, 1 H, CH), 3.81 (app. dt, *J* = 14, 7 Hz, 1 H, C*H*$_a$H$_b$), 3.64 (s, 3 H, OCH_3), 3.34 (m, 1 H, CH$_a$*H*$_b$), 0.85 [s, 9 H, C$(CH_3)_3$].

^{13}C NMR (125 MHz, $CDCl_3$): *δ* 179.1 (s, C=O), 158.3 (s, C-4 of 4-$CH_3OC_6H_4$), 146.5, 146.1 (2 s, C-1 of 2 C_6H_5), 131.0 (d, C-3/C-5 of one C_6H_5), 130.8 (s, C-1 of 4-$CH_3OC_6H_4$), 128.4 (d, C-3/C-5 of other C_6H_5), 127.6 (d, C-2/C-6 of 4-$CH_3OC_6H_4$), 126.8, 126.0 (2 d, C-4 of 2 C_6H_5), 125.9, 125.7

(2 d, C-2/C-6 of 2 C_6H_5), 113.5 (d, C-3/C-5 of 4-$CH_3OC_6H_4$), 79.7 (s, C–OH), 55.1 (q, OCH_3), 51.6 (d, CH), 41.2 (t, CH_2), 38.5 [s, *C*$(CH_3)_3$], 27.3 [q, C(*C*$H_3)_3$].

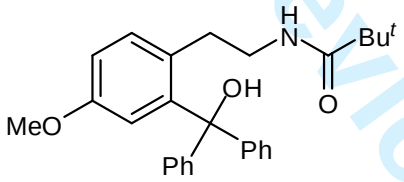
MS (ES^-): *m/z* (%) = 454 (32, [M + $^{37}Cl]^-$), 452 (100, [M + $^{35}Cl]^-$), 339 (5).

HRMS (ES^-): *m/z* [M + $^{35}Cl]^-$ calcd for $C_{27}H_{31}NO_3Cl$: 452.1992; found: 452.2008.

General Procedure for Lithiation and Substitution of 1: Synthesis of 3-Substituted Derivatives 7–12

A solution of *n*-BuLi in hexane (1.75 mL, 1.60 M, 2.80 mmol) was added to a cold (–20 °C), stirred solution of **1** (0.20 g, 0.85 mmol) in anhydrous THF (15 mL) under N_2. The mixture was stirred for 2 h while it was allowed to warm up to 0 °C, after which an electrophile (1.40 mmol), in anhydrous THF (5 mL) if solid, neat otherwise, was added. The cooling bath was removed and the reaction mixture was stirred for 2 h. The reaction mixture was quenched with aqueous saturated NH_4Cl (20 mL) and diluted with diethyl ether (20 mL). The organic layer was separated, washed with H_2O (2 × 20 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue obtained was purified by column chromatography (silica gel; hexane: Et_2O in 1:1 by volume) to give the pure products **7–12**.

N-(2-(2-(Hydroxydiphenylmethyl)-4-methoxyphenyl)ethyl)pivalamide (7)



White solid (0.32 g, 92%); mp 179–181 °C.

IR (FT): ν_{max} 3321, 2958, 1627, 1575, 1292, 1243 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 11 H, OH and 2 C_6H_5), 7.16 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 6.79 (dd, *J* = 3, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.24 (d, *J* = 3 Hz, 1 H, H-3 of 4-$CH_3OC_6H_3$), 6.15 (br., exch., 1 H, NH), 3.63 (s, 3 H, OCH_3), 3.37 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.60 (t, *J* = 7 Hz, 2 H, CH_2), 1.11 [s, 9 H, C$(CH_3)_3$].

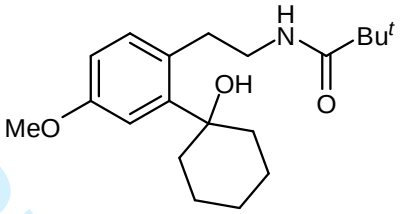
^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.8 (s, C=O), 156.9 (s, C-4 of 4-$CH_3OC_6H_3$), 147.1 (s, C-1 of 2 C_6H_5), 146.6 (s, C-2 of 4-$CH_3OC_6H_3$), 132.8 (d, C-6 of 4-$CH_3OC_6H_3$), 130.7 (s, C-1 of 4-$CH_3OC_6H_3$), 127.9 (d, C-3/C-5 of 2 C_6H_5), 127.7 (d, C-2/C-6 of 2 C_6H_5), 127.2 (d, C-4 of 2

C_6H_5), 117.1 (d, C-3 of 4-$CH_3OC_6H_3$), 111.9 (d, C-5 of 4-$CH_3OC_6H_3$), 83.0 (s, C–OH), 55.0 (q, OCH_3), 41.1 (t, CH_2NH), 38.4 [s, *C*$(CH_3)_3$], 32.5 (t, CH_2), 27.5 [q, C(*C*$H_3)_3$].

MS (EI): *m/z* (%) 399 (77, $[M - H_2O]^+$), 298 (99), 285 (90), 261 (33), 239 (10), 222 (26), 209 (31), 193 (73), 165 (53), 152 (13), 105 (48), 83 (100).

HRMS (EI): *m/z* ($[M - H_2O]^+$) calcd for $C_{27}H_{29}NO_2$: 399.2198; found: 399.2187.

N-(2-(2-(1-Hydroxycyclohexyl)-4-methoxyphenyl)ethyl)pivalamide (8)



Oil (0.24 g, 88%).

IR (FT): ν_{max} 3369, 2931, 1645, 1529, 1365, 1238 cm^{-1}.

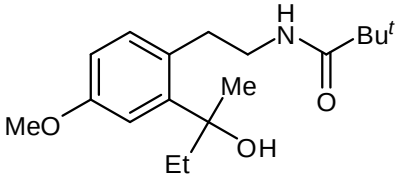
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.07 (d, *J* = 2 Hz, 1 H, H-3 of 4-$CH_3OC_6H_3$), 6.97 (dd, *J* = 2, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.80 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 6.69 (br. s, exch., 1 H, OH), 5.54 (br., exch., 1 H, NH), 3.81 (s, 3 H, OCH_3), 3.38 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.68 (t, *J* = 7 Hz, 2 H, CH_2), 1.95–1.50 (m, 10 H, *c*-Hex), 1.08 [s, 9 H, C$(CH_3)_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.5 (s, C=O), 156.0 (s, C-4 of 4-$CH_3OC_6H_3$), 140.0 (s, C-2 of 4-$CH_3OC_6H_3$), 126.3 (d, C-6 of 4-$CH_3OC_6H_3$), 126.0 (s, C-1), 111.5 (d, C-3 of 4-$CH_3OC_6H_3$), 111.0 (d, C-5 of 4-$CH_3OC_6H_3$), 73.0 (s, C–OH), 55.4 (q, OCH_3), 40.9 (t, CH_2NH), 38.6 [s, *C*$(CH_3)_3$], 36.7 (d, C-2/C-6 of *c*-Hex), 35.1 (t, CH_2), 27.5 [q, C(*C*$H_3)_3$], 25.9 (d, C-4 of *c*-Hex), 21.9 (d, C-3/C-5 of *c*-Hex).

MS (ES^+): *m/z* (%) = 356 (100, $[M + Na]^+$), 316 (5), 299 (10), 158 (3).

HRMS (ES^+): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{31}NO_3{}^{23}Na$: 356.2202; found: 356.2215.

N-(2-(2-(2-Hydroxybutan-2-yl)-4-methoxyphenyl)ethyl)pivalamide (9)



Oil (0.24 g, 95%).

IR (FT): ν_{max} 3348, 2964, 1639, 1531, 1355, 1240 cm^{-1}.

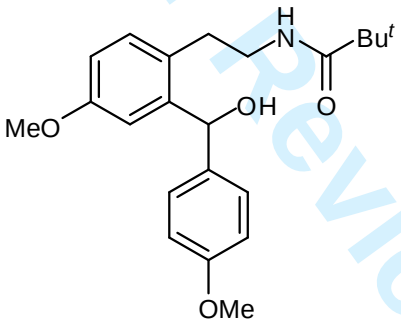
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.03 (d, *J* = 2 Hz, 1 H, H-3 of 4-$CH_3OC_6H_3$), 6.98 (dd, *J* = 2, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.79 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 5.56 (br., exch., 1 H, NH), 3.88 (br. s, exch., 1 H, OH), 3.80 (s, 3 H, OCH_3), 3.40 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.68 (t, *J* = 7 Hz, 2 H, CH_2), 1.92–1.75 (m, 2 H, CH_3CH_2), 1.47 (s, 3 H, C*H*$_3$C–OH), 1.07 [s, 9 H, $C(CH_3)_3$], 0.73 (t, *J* = 7 Hz, 3H, C*H*$_3$$CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.3 (s, C=O), 155.6 (s, C-4 of 4-$CH_3OC_6H_3$), 135.0 (s, C-2 of 4-$CH_3OC_6H_3$), 131.1 (s, C-1 of 4-$CH_3OC_6H_3$), 127.4 (d, C-6 of 4-$CH_3OC_6H_3$), 113.8 (d, C-3 of 4-$CH_3OC_6H_3$), 111.6 (d, C-5 of 4-$CH_3OC_6H_3$), 75.3 (s, C–OH), 55.4 (q, OCH_3), 40.8 (t, CH_2NH), 38.6 [s, *C*$(CH_3)_3$], 35.0 (t, CH_3CH_2), 34.7 (t, CH_2), 27.5 [q, C(*C*H_3)$_3$], 26.7 (q, *C*H_3C–OH), 8.8 (q, *C*H_3CH_2).

MS (AP^+): *m/z* (%) = 290 (100, $[M - H_2O]^+$), 222 (3), 189 (2), 153 (3), 124 (3).

HRMS (AP^+): *m/z* $[M - H_2O]^+$ calcd for $C_{18}H_{28}NO_2$: 290.2120; found: 290.2119.

N-(2-(2-(Hydroxy(4-methoxyphenyl)methyl)-4-methoxyphenyl)ethyl)pivalamide (10)



Oil (0.25 g, 81%).

IR (FT): ν_{max} 3349, 2927, 1610, 1511, 1368, 1246 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.14 (d, *J* = 9 Hz, 2 H, H-2/H-6 of 4-$CH_3OC_6H_4$), 7.05 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 6.78 (dd, *J* = 3, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.76 (d, *J* = 9 Hz, 2 H, H-3/H-5 of 4-$CH_3OC_6H_4$), 6.73 (d, *J* = 3 Hz, 1 H, H-3 of 4-$CH_3OC_6H_3$), 5.63 (d, *J* = 1 Hz, 1 H, CH), 5.36 (br., exch., 1 H, NH), 5.05 (d, exch., *J* = 1 Hz, 1 H, OH), 3.74 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.40 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.44 (t, *J* = 7 Hz, 2 H, CH_2), 1.03 [s, 9 H, $C(CH_3)_3$].

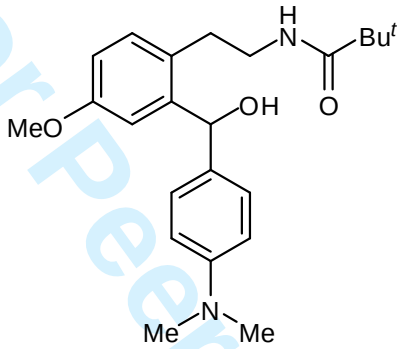
^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.2 (s, C=O), 159.4 (s, C-4 of 4-$CH_3OC_6H_3$), 158.0 (s, C-4 of 4-$CH_3OC_6H_4$), 142.9 (s, C-1 of 4-$CH_3OC_6H_4$), 132.9 (s, C-2 of 4-$CH_3OC_6H_3$), 130.7 (d, C-6 of

4-$CH_3OC_6H_3$), 128.8 (s, C-1 of 4-$CH_3OC_6H_3$), 127.6 (d, C-2/C-6 of 4-$CH_3OC_6H_4$), 115.9 (d, C-3 of 4-$CH_3OC_6H_3$), 113.8 (d, C-3/C-5 of 4-$CH_3OC_6H_4$), 113.0 (d, C-5 of 4-$CH_3OC_6H_3$), 72.2 (d, CH), 55.33 (q, OCH_3), 55.31 (q, OCH_3), 40.1 (t, CH_2NH), 38.6 [s, $C(CH_3)_3$], 32.3 (t, CH_2), 27.6 [q, $C(CH_3)_3$].

MS (EI): *m/z* (%) = 353 (30, $[M - H_2O]^+$), 308 (32), 281 (40), 264 (25), 165 (100), 134 (92), 120 (54), 105 (81), 84 (99).

HRMS (EI): *m/z* $[M - H_2O]^+$ calcd for $C_{22}H_{27}NO_3$: 353.1991; found: 353.1999.

N-(2-(2-((4-(Dimethylamino)phenyl)(hydroxy)methyl)-4-methoxyphenyl)ethyl)-pivalamide (11)



Oil (0.29 g, 90%).

IR (FT): ν_{max} 3343, 2956, 1612, 1520, 1350, 1249 cm^{-1}.

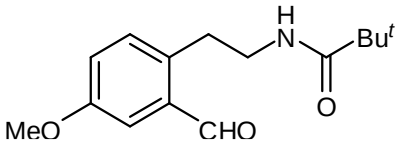
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 (d, *J* = 9 Hz, 2 H, H-2/H-6 of 4-$Me_2NC_6H_4$), 7.02 (d, *J* = 3 Hz, 1 H, H-3 of 4-$CH_3OC_6H_3$), 6.96 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 6.69 (dd, *J* = 3, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.61 (d, *J* = 9 Hz, 2 H, H-3/H-5 of 4-$Me_2NC_6H_4$), 5.91 (s, exch., 1 H, OH), 5.65 (br., exch., 1 H, NH), 3.71 (s, 3 H, OCH_3), 3.30 (m, 1 H, H_aH_b of CH_2NH), 3.22 (m, 1 H, H_aH_b of CH_2NH), 2.86 [s, 6 H, $N(CH_3)_2$], 2.78 (m, 1 H, H_aH_b of CH_2), 2.57 (m, 1 H, H_aH_b of CH_2), 1.03 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.5 (s, C=O), 159.1 (s, C-4 of 4-$CH_3OC_6H_3$), 150.1 (s, C-4 of 4-$Me_2NC_6H_4$), 143.5 (s, C-2 of 4-$CH_3OC_6H_3$), 141.2 (s, C-1 of 4-$Me_2NC_6H_4$), 128.3 (s, C-1 of 4-$CH_3OC_6H_3$), 127.9 (d, C-2/C-6 of 4-$Me_2NC_6H_4$), 126.7 (d, C-6 of 4-$CH_3OC_6H_3$), 113.0 (d, C-3 of 4-$CH_3OC_6H_3$), 112.6 (d, C-5 of 4-$CH_3OC_6H_3$), 112.4 (d, C-3/C-5 of 4-$Me_2NC_6H_4$), 72.8 (s, C–OH), 55.3 (q, OCH_3), 40.6 [q, $N(CH_3)_2$], 40.1 (t, CH_2NH), 38.5 [s, $C(CH_3)_3$], 31.5 (t, CH_2), 27.5 [q, $C(CH_3)_3$].

MS (ES^-): *m/z* (%) = 419 (100, $[M + Cl]^-$), 383 (15), 374 (20), 327 (34), 292 (35), 291 (98), 283 (14), 220 (5).

HRMS (EI): *m/z* $[M + Cl]^-$ calcd for $C_{23}H_{32}N_2O_3{}^{35}Cl$: 419.2101; found: 419.2093.

N-(2-(2-Formyl-4-methoxyphenyl)ethyl)pivalamide (12)



Oil (0.22 g, 98%).

IR (FT): ν_{max} 3380, 2928,1662, 1639, 1528, 1360, 1246 cm^{-1}.

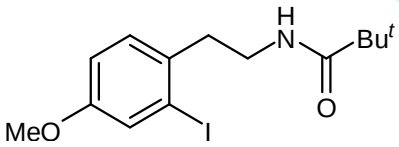
^1H NMR (500 MHz, $CDCl_3$): δ = 10.38 (s, 1 H, CHO), 7.57 (d, *J* = 2 Hz , 1 H, H-3 of 4-$CH_3OC_6H_3$), 7.33 (dd, *J* = 2, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 6.89 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 5.59 (br., exch., 1 H, NH), 3.85 (s, 3 H, OCH_3), 3.40 (app. q, *J* = 7 Hz, 2 H, C*H*$_2$NH), 2.72 (t, *J* = 7 Hz, 2 H, CH_2), 1.07 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.6 (d, CHO), 178.4 (s, C=O), 160.6 (s, C-4 of 4-$CH_3OC_6H_3$), 141.0 (s, C-2 of 4-$CH_3OC_6H_3$), 138.5 (s, C-1 of 4-$CH_3OC_6H_3$), 136.3 (d, C-6 of 4-$CH_3OC_6H_3$), 128.4 (d, C-5 of 4-$CH_3OC_6H_3$), 112.0 (d, C-3 of 4-$CH_3OC_6H_3$), 55.8 (q, OCH_3), 40.9 (t, CH_2NH), 38.6 [s, *C*$(CH_3)_3$], 34.6 (t, CH_2), 27.4 [q, C(*C*$H_3)_3$].

MS (EI): *m/z* (%) = 263 (54, $[M]^+$), 231 (15), 162 (100), 144 (90), 135 (83), 116 (28), 105 (31), 83 (99).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{15}H_{21}NO_3$: 263.1521; found: 263.1524.

N-(2-(2-Iodo-4-methoxyphenyl)ethyl) pivalamide (13)



Oil (0.27 g, 89%).

IR (FT): ν_{max} 3351, 2957, 1641, 1511, 1365, 1246 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 3 Hz , 1 H, H-3 of 4-$CH_3OC_6H_3$), 7.02 (d, *J* = 8 Hz, 1 H, H-6 of 4-$CH_3OC_6H_3$), 6.78 (dd, *J* = 3, 8 Hz, 1 H, H-5 of 4-$CH_3OC_6H_3$), 5.62 (br., exch., 1 H, NH), 3.69 (s, 3 H, OCH_3), 3.40 (app. q, *J* = 7 Hz, 2H, C*H*$_2$NH), 2.83 (t, *J* = 7 Hz, 2 H, CH_2), 1.09 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.4 (s, C=O), 158.5 (s, C-4 of 4-$CH_3OC_6H_3$), 133.7 (s, C-1 of 4-$CH_3OC_6H_3$), 130.2 (d, C-6 of 4-$CH_3OC_6H_3$), 124.6 (d, C-3 of 4-$CH_3OC_6H_3$), 114.5 (d, C-5 of

4-$CH_3OC_6H_3$), 100.3 (s, C-2 of 4-$CH_3OC_6H_3$), 55.5 (q, OCH_3), 39.7 (t, CH_2NH), 39.0 (t, CH_2), 38.7 [s, *C*$(CH_3)_3$], 27.6 [q, C(*C*$H_3)_3$].

MS (EI): *m/z* (%) = 361 (15, $[M]^+$), 259 (100), 246 (98), 234 (69), 148 (48), 134 (99), 121 (74), 83 (92).

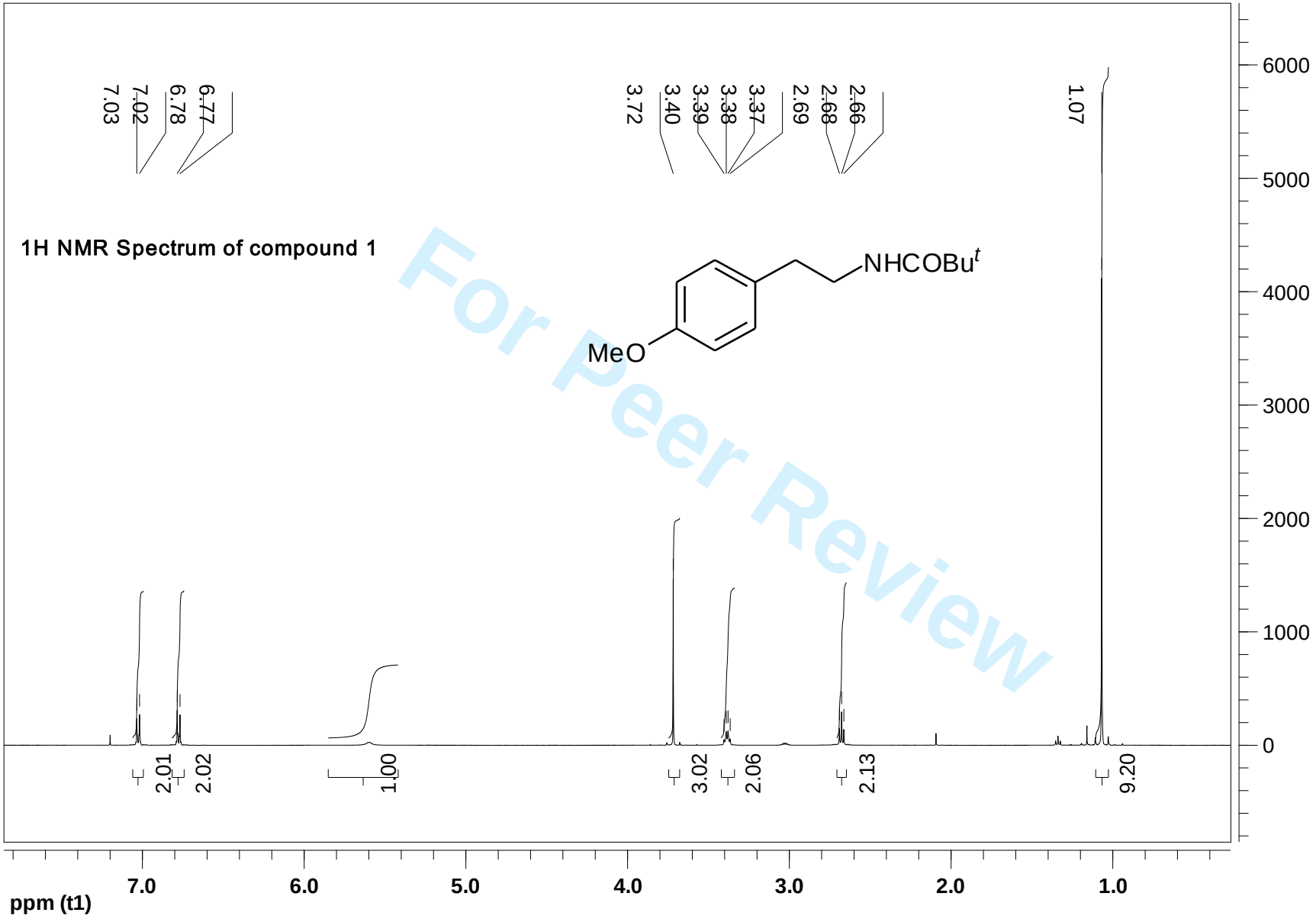
HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{20}NO_2I$: 361.0539; found: 361.0533.

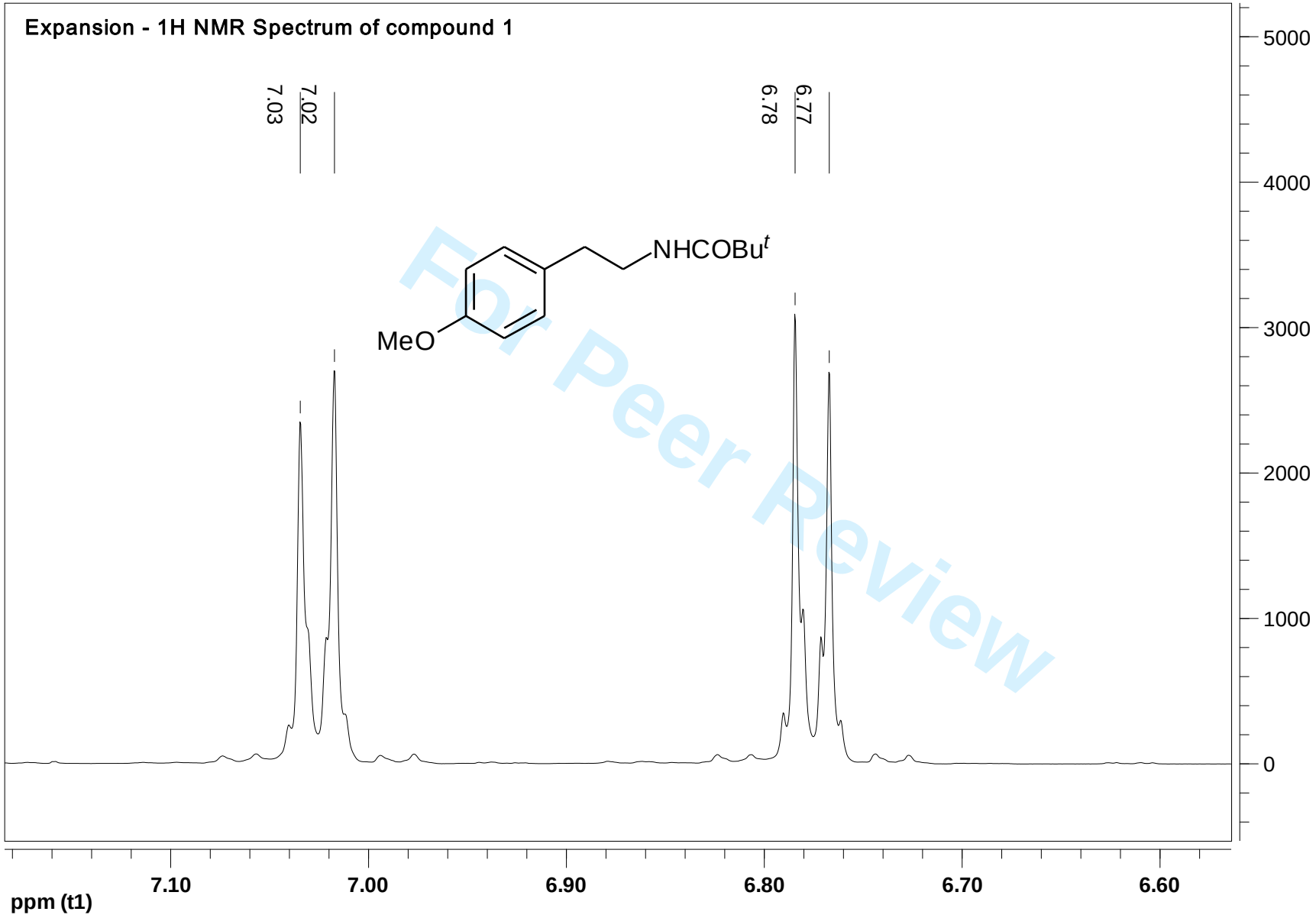
References

1 Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

2 Simig, G.; Schlosser, M. *Tetrahedron Lett.* **1991**, *32*, 1963.

NMR Spectra for Some of the Synthesised Compounds





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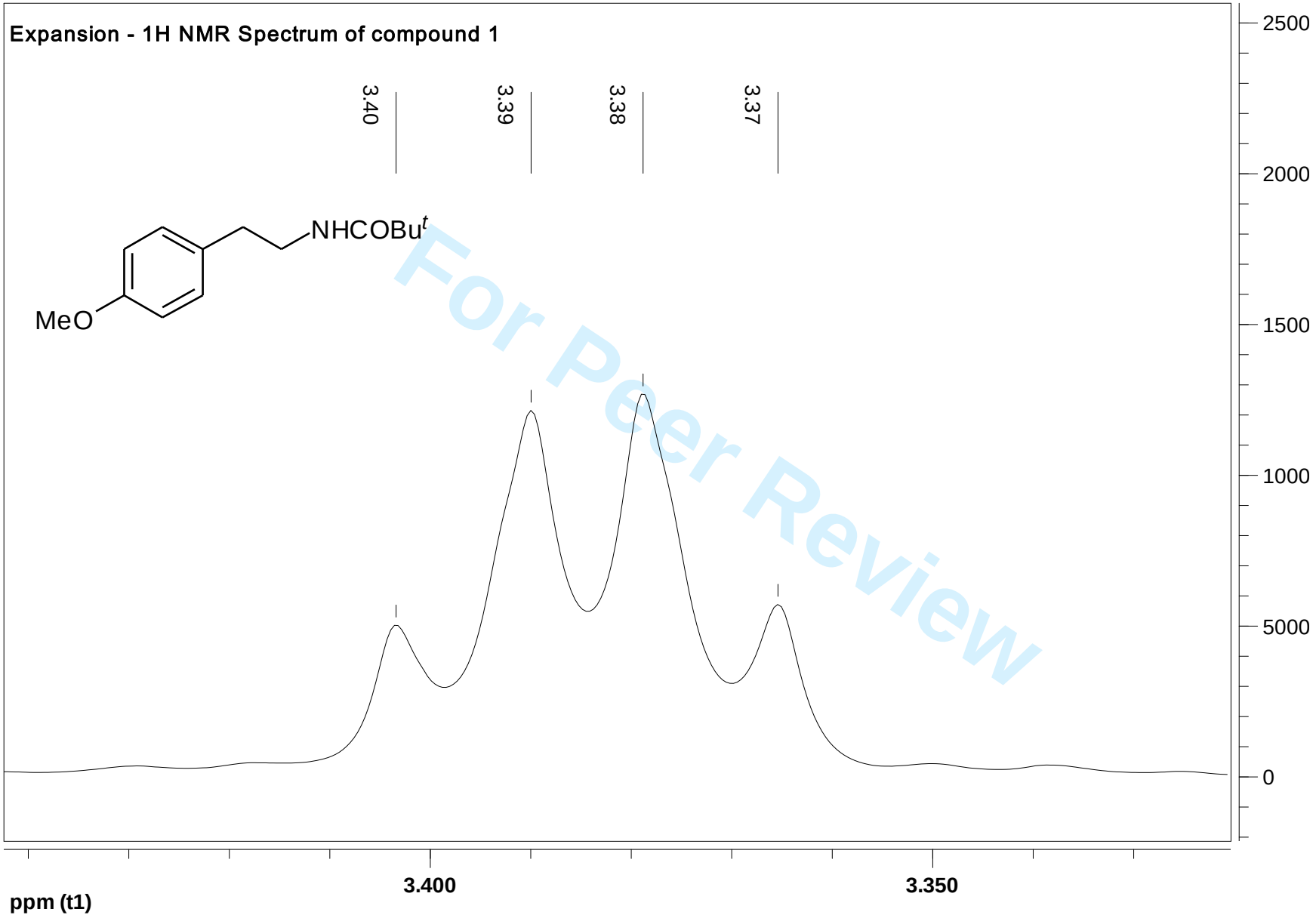

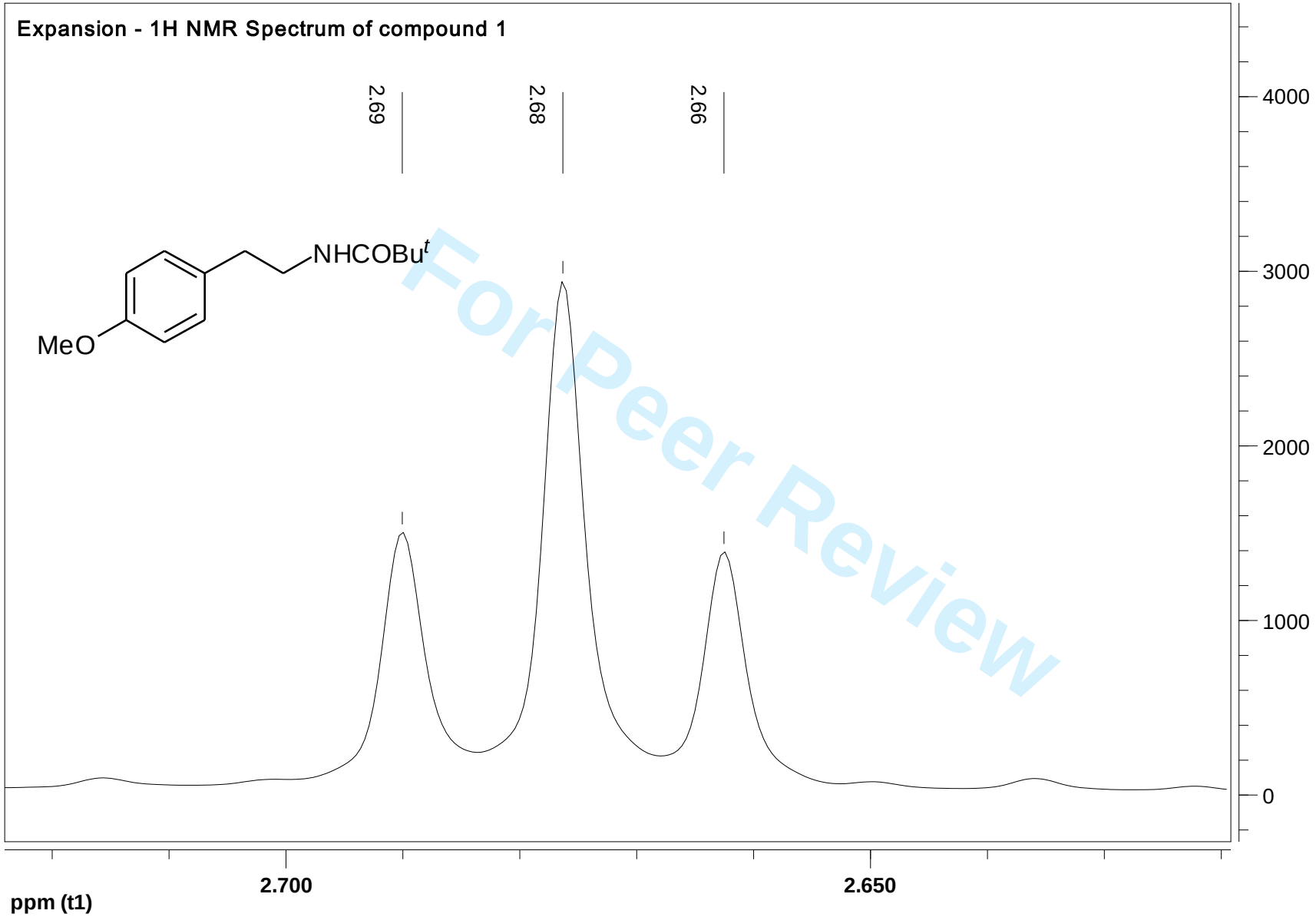

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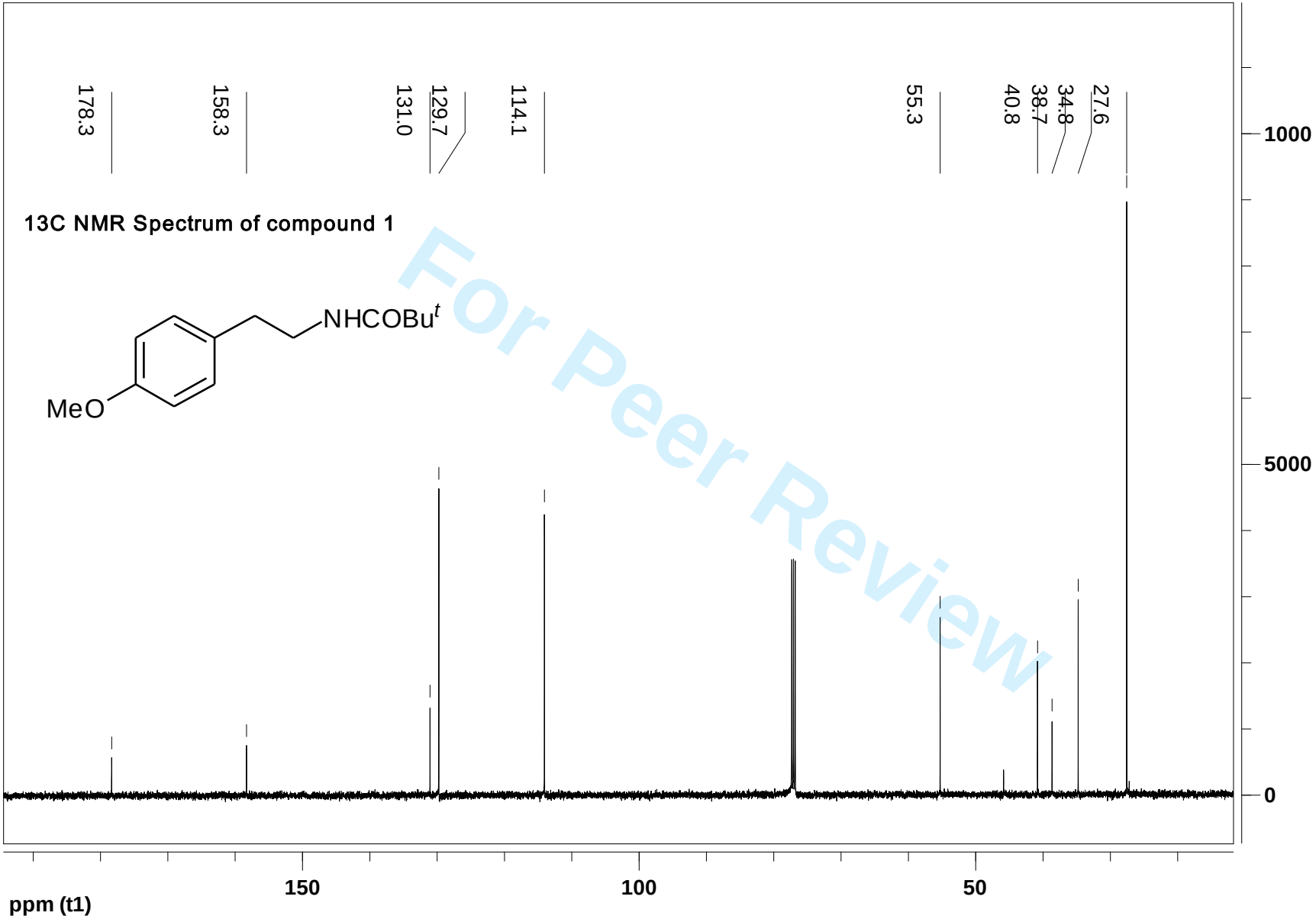

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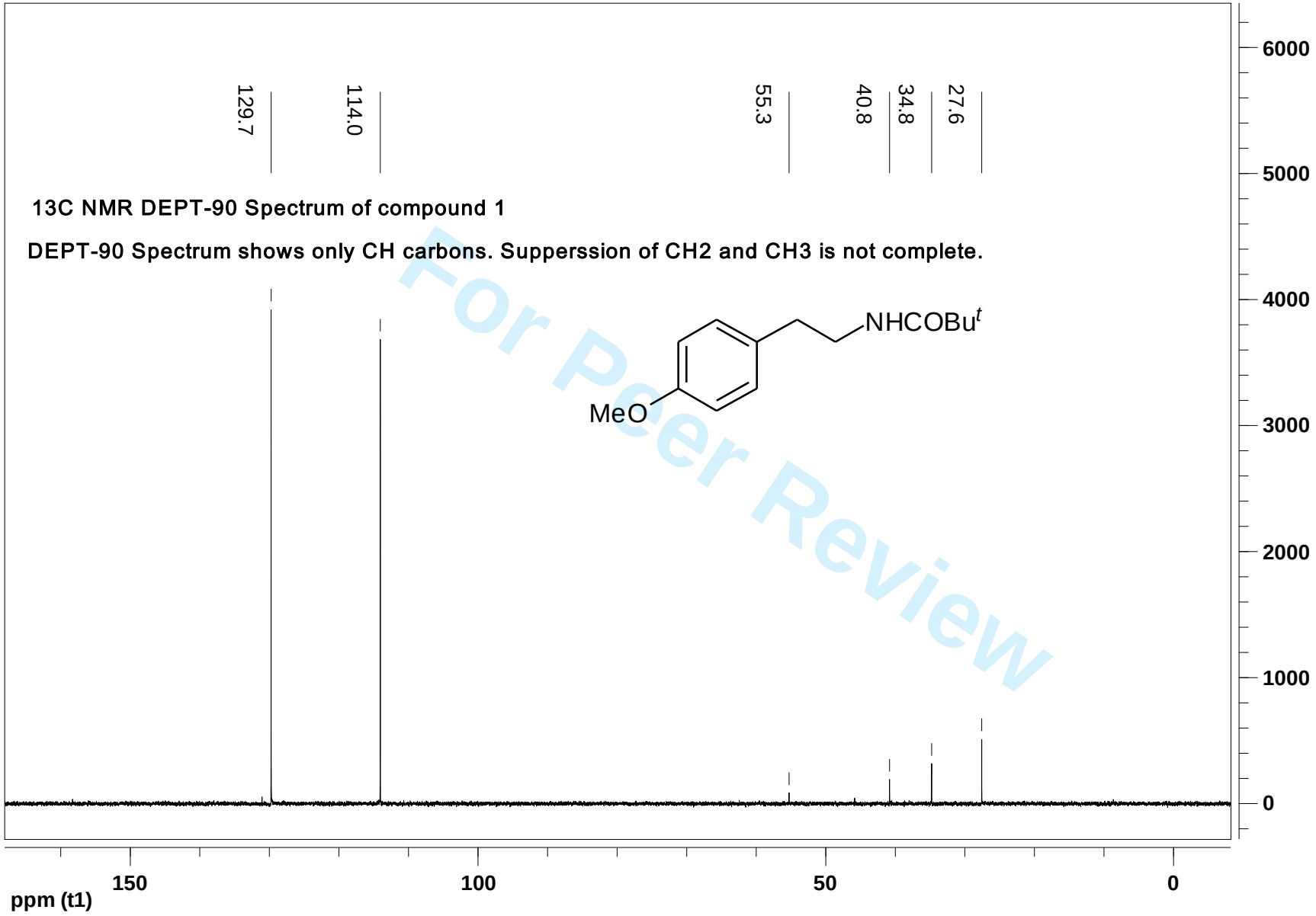

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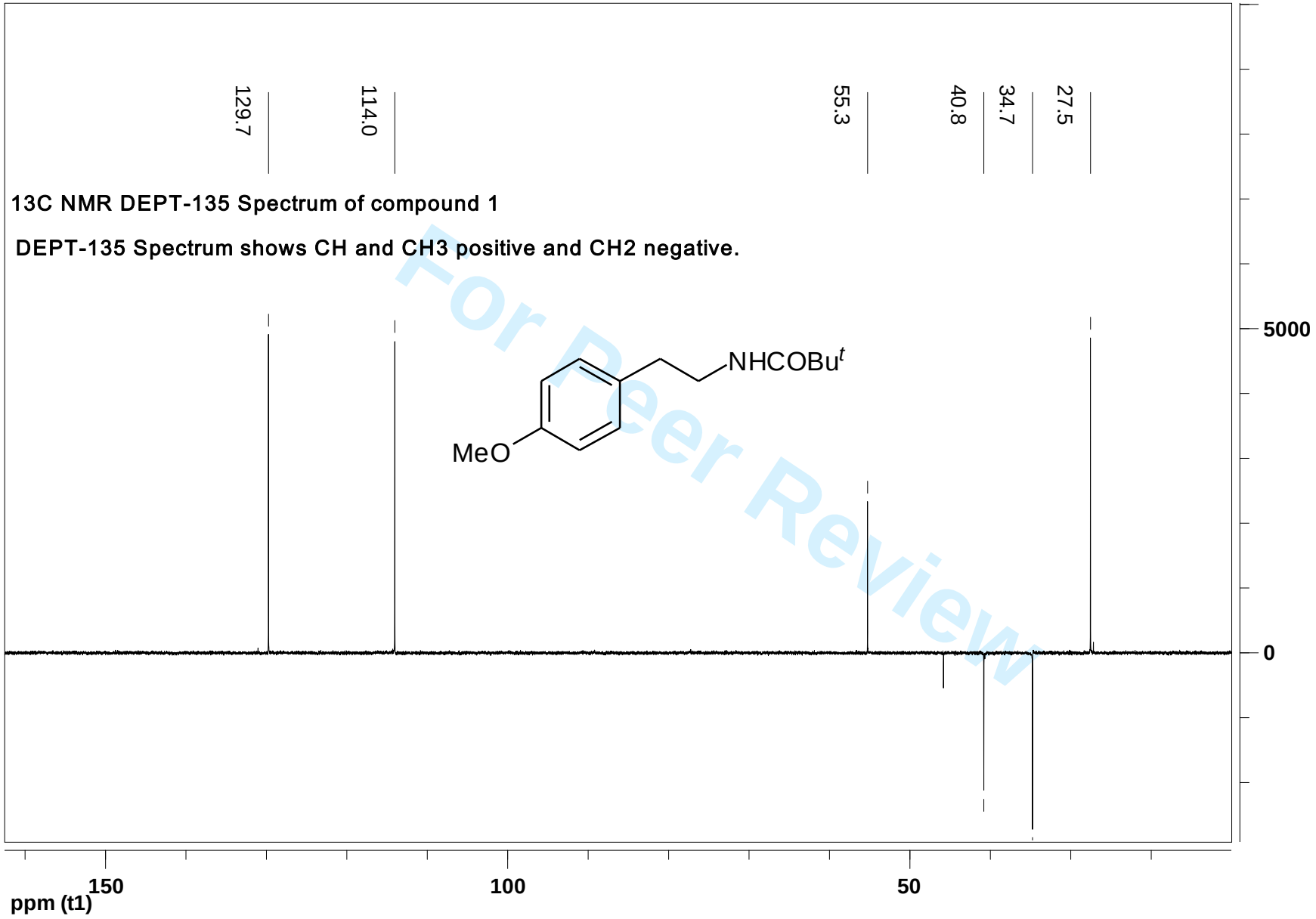

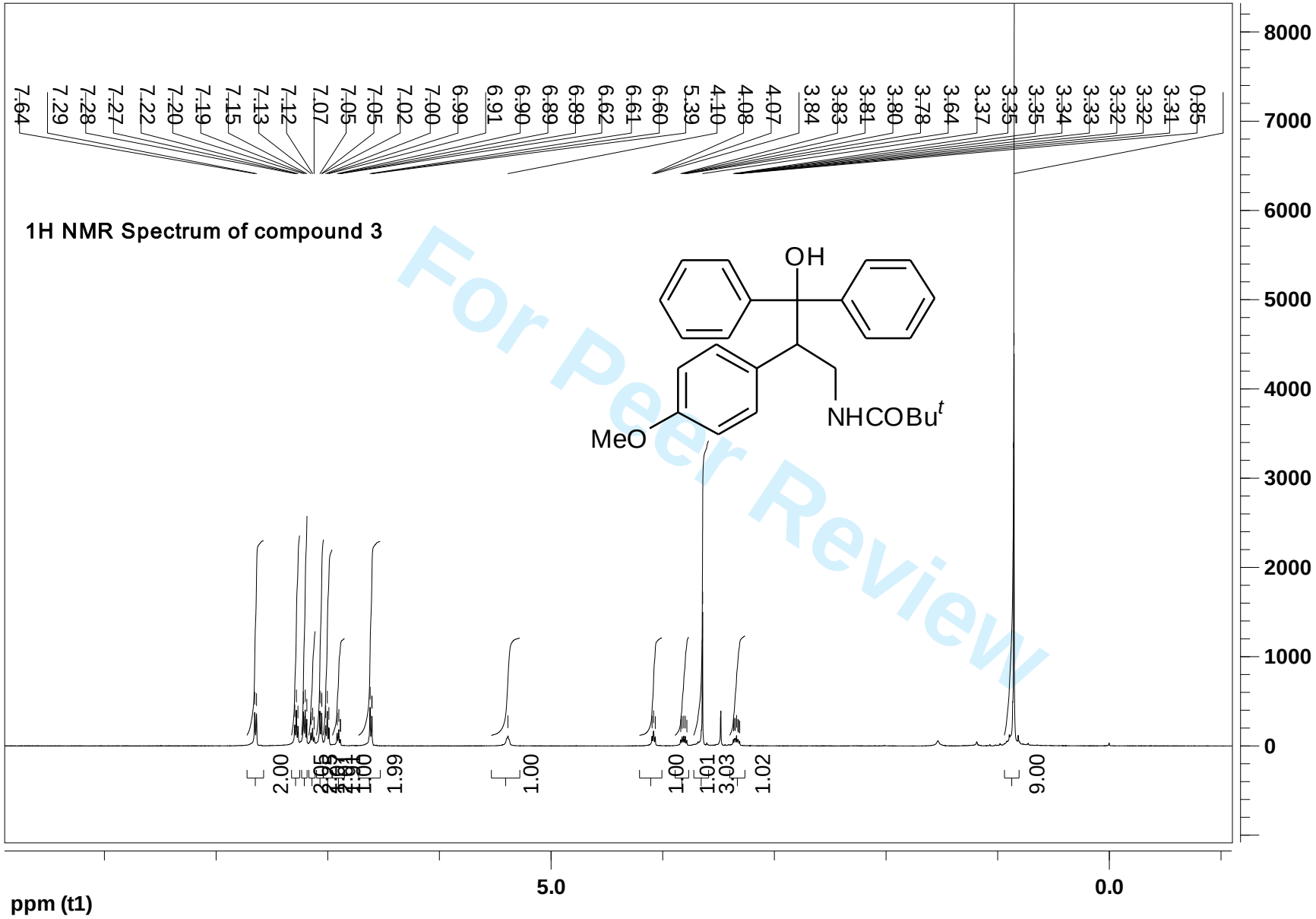

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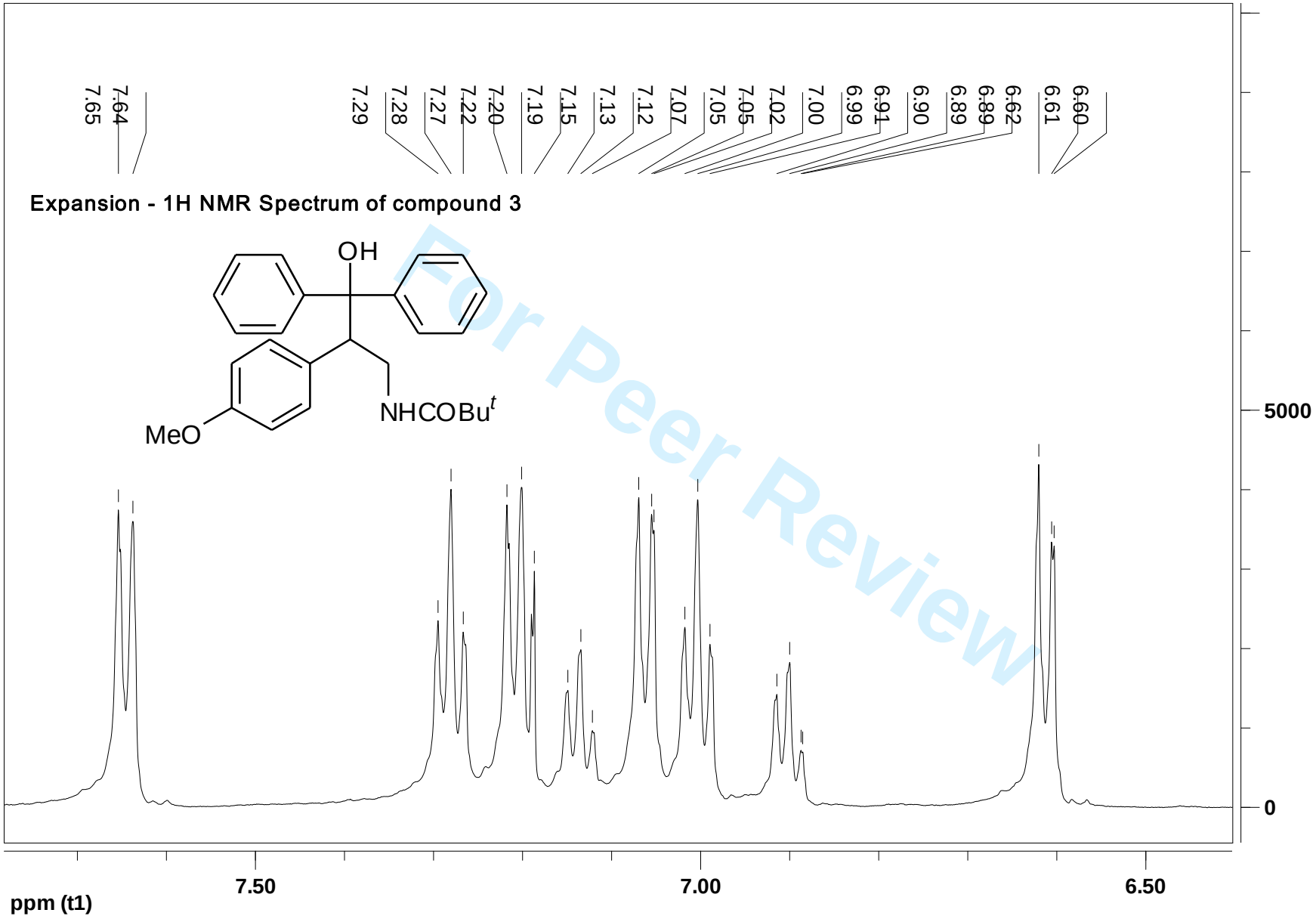

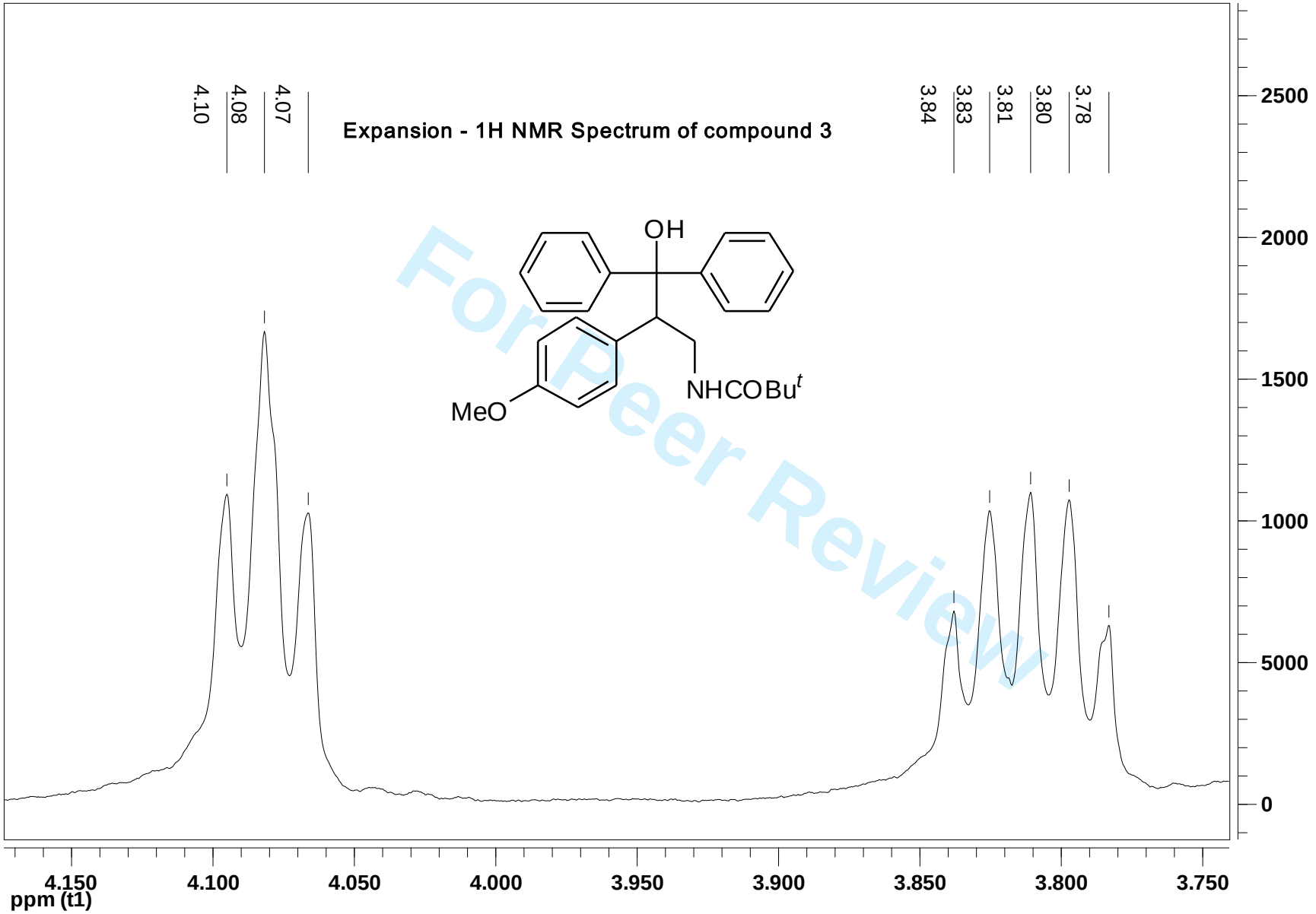

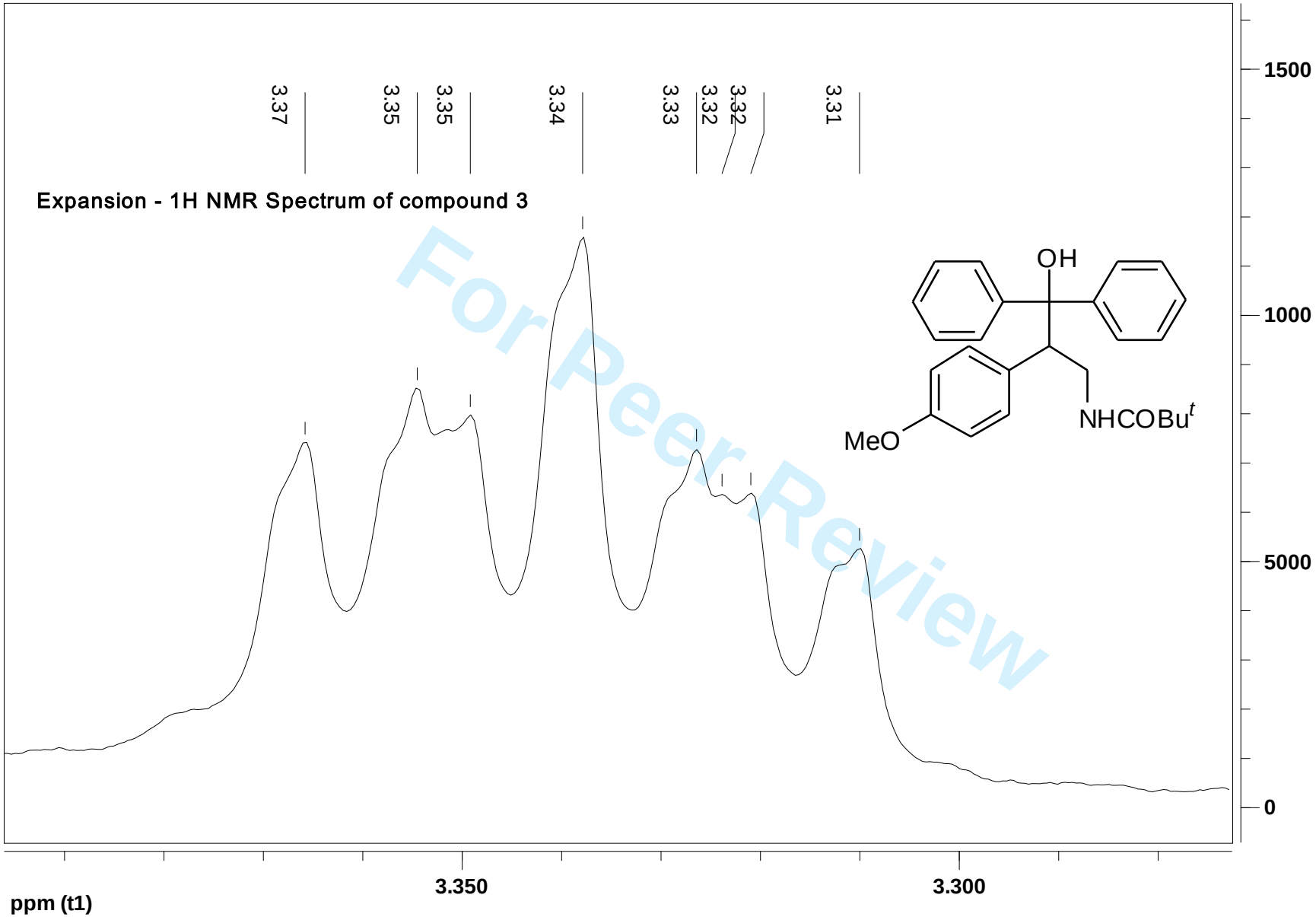

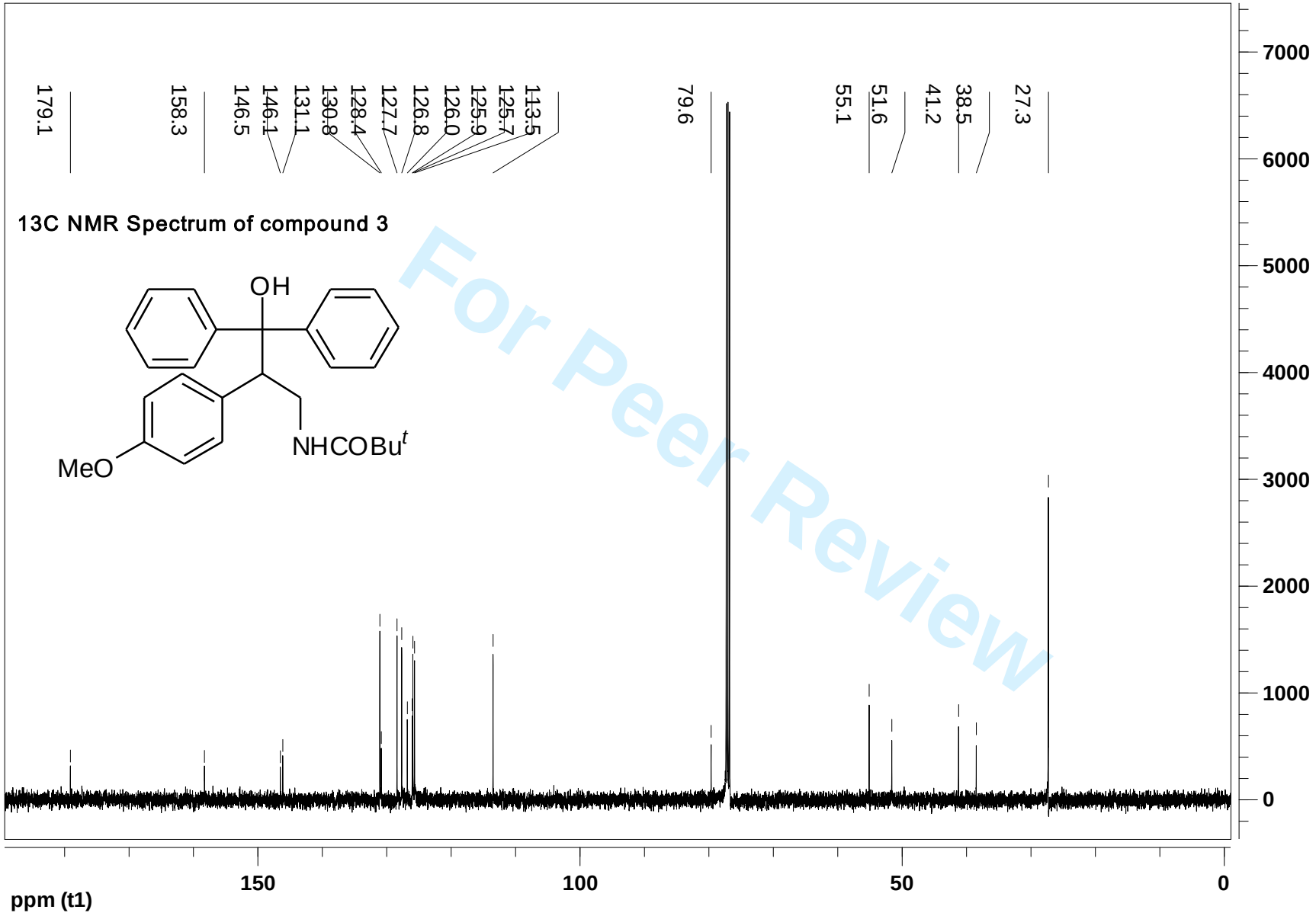

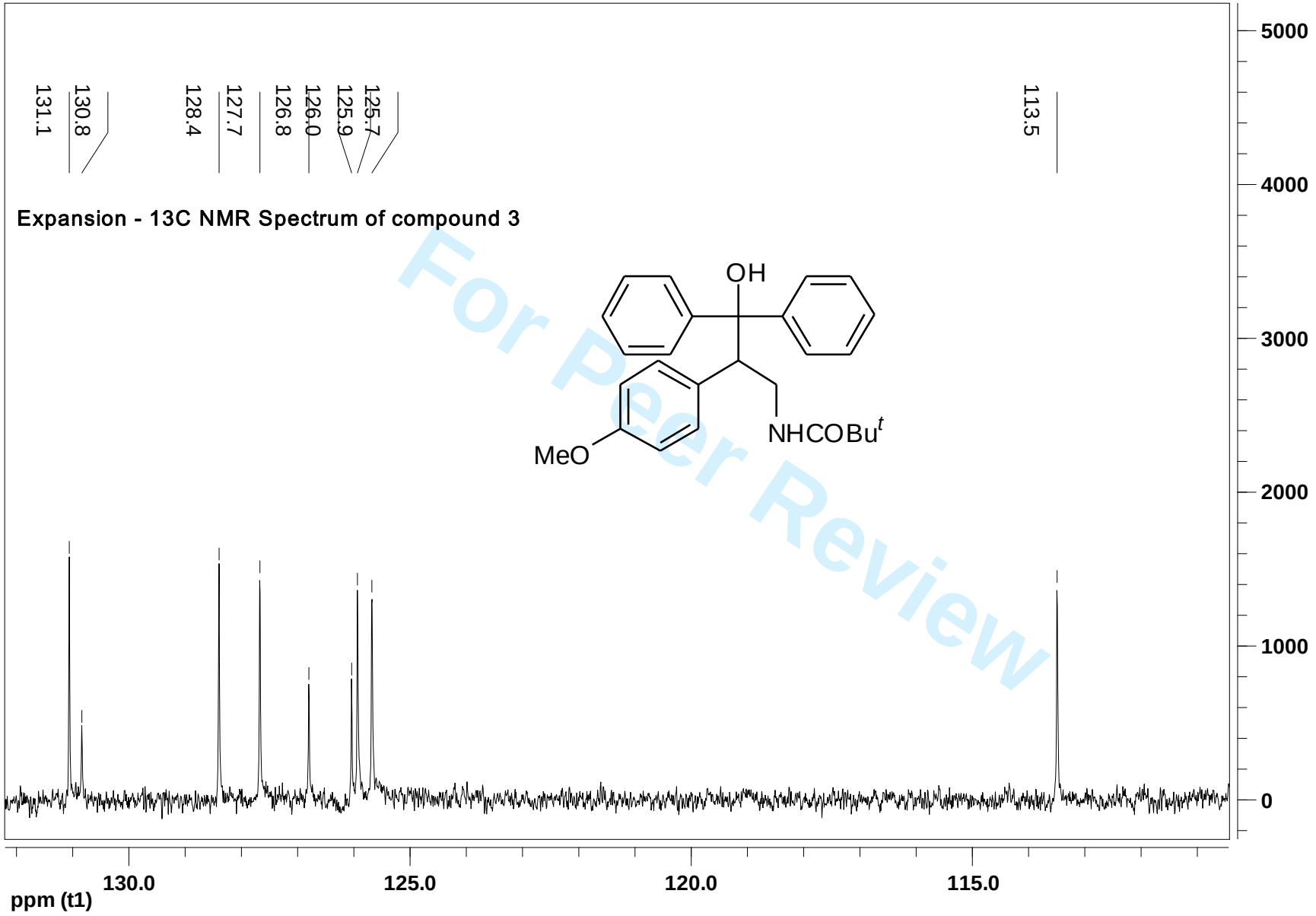

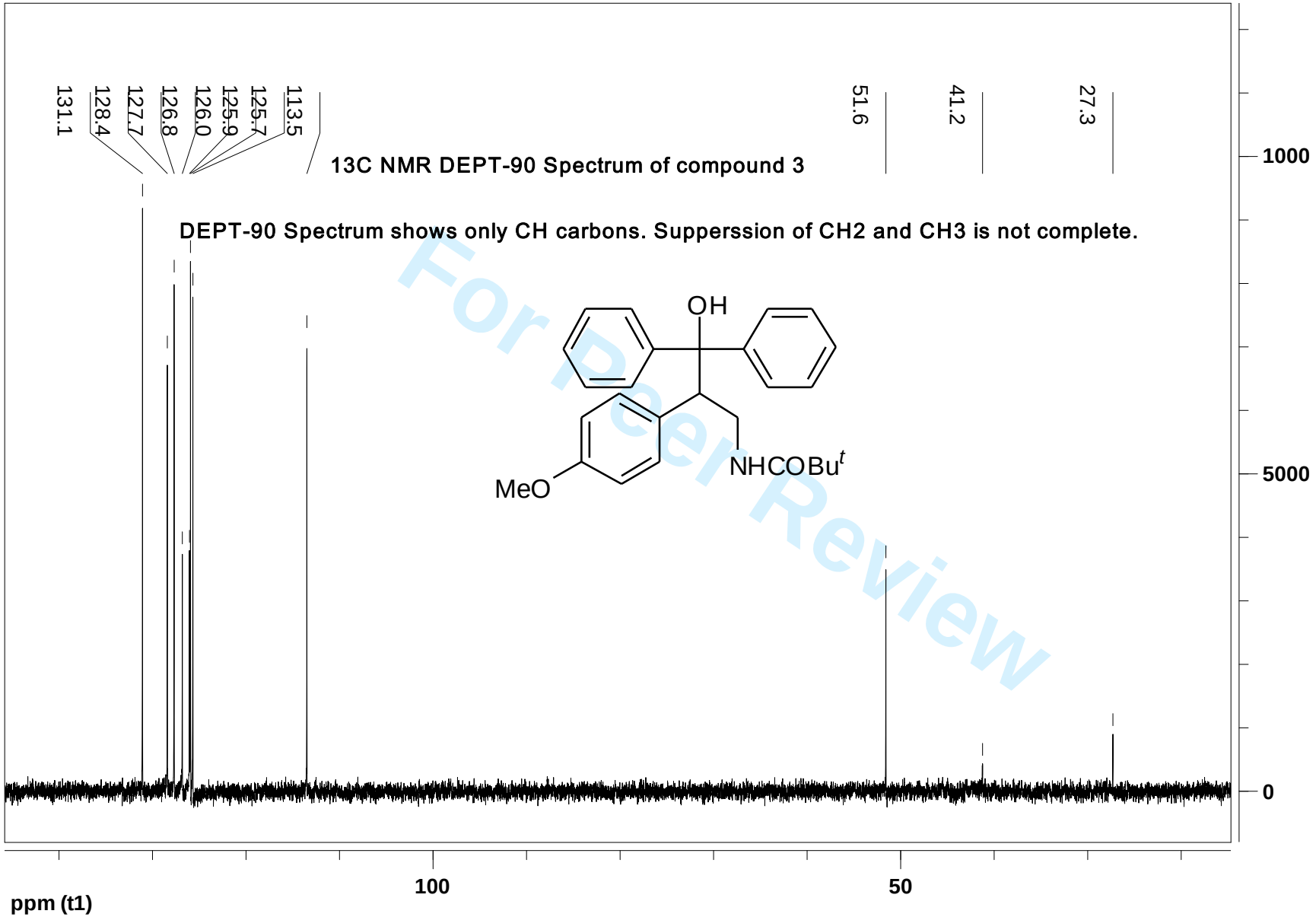

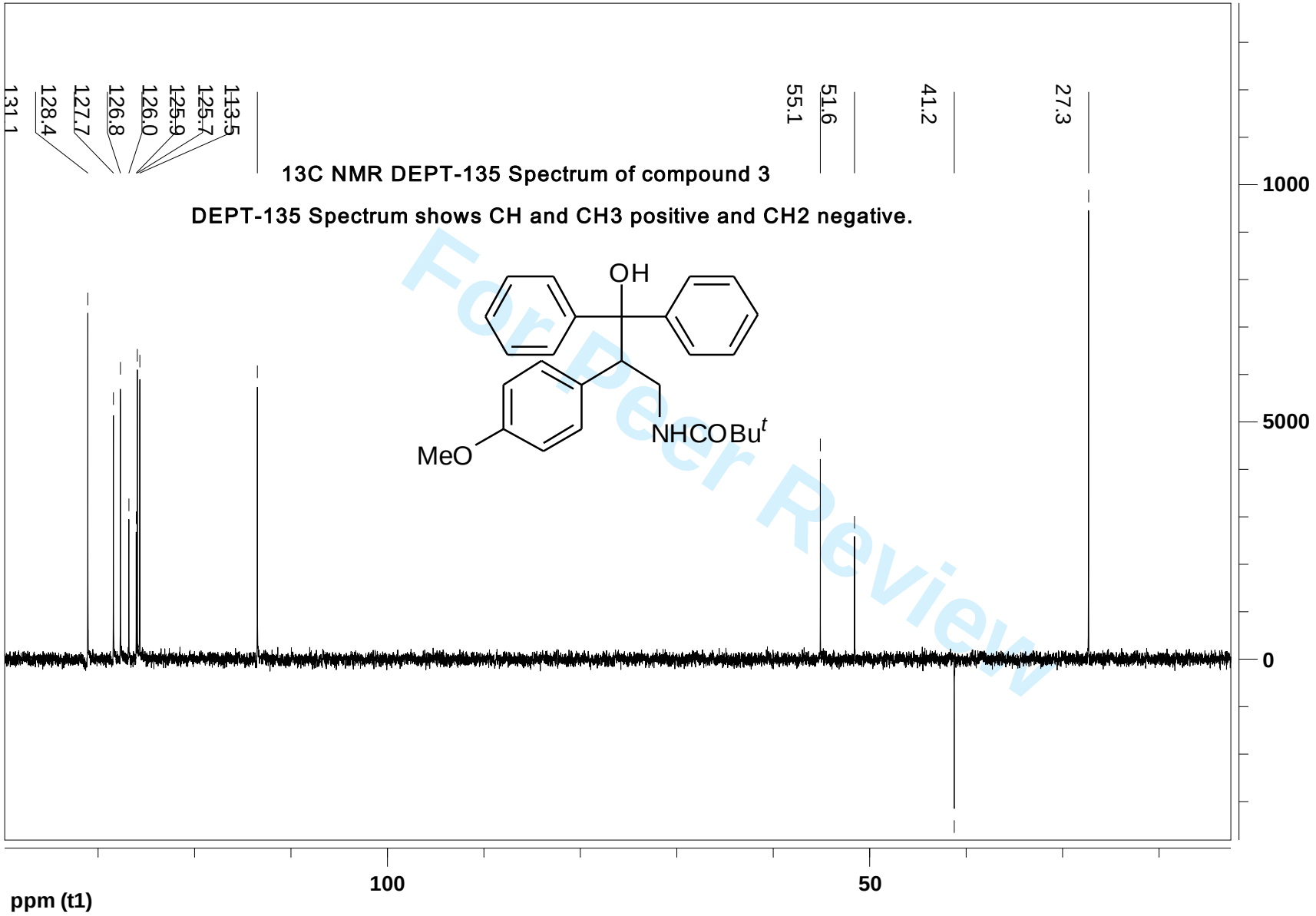

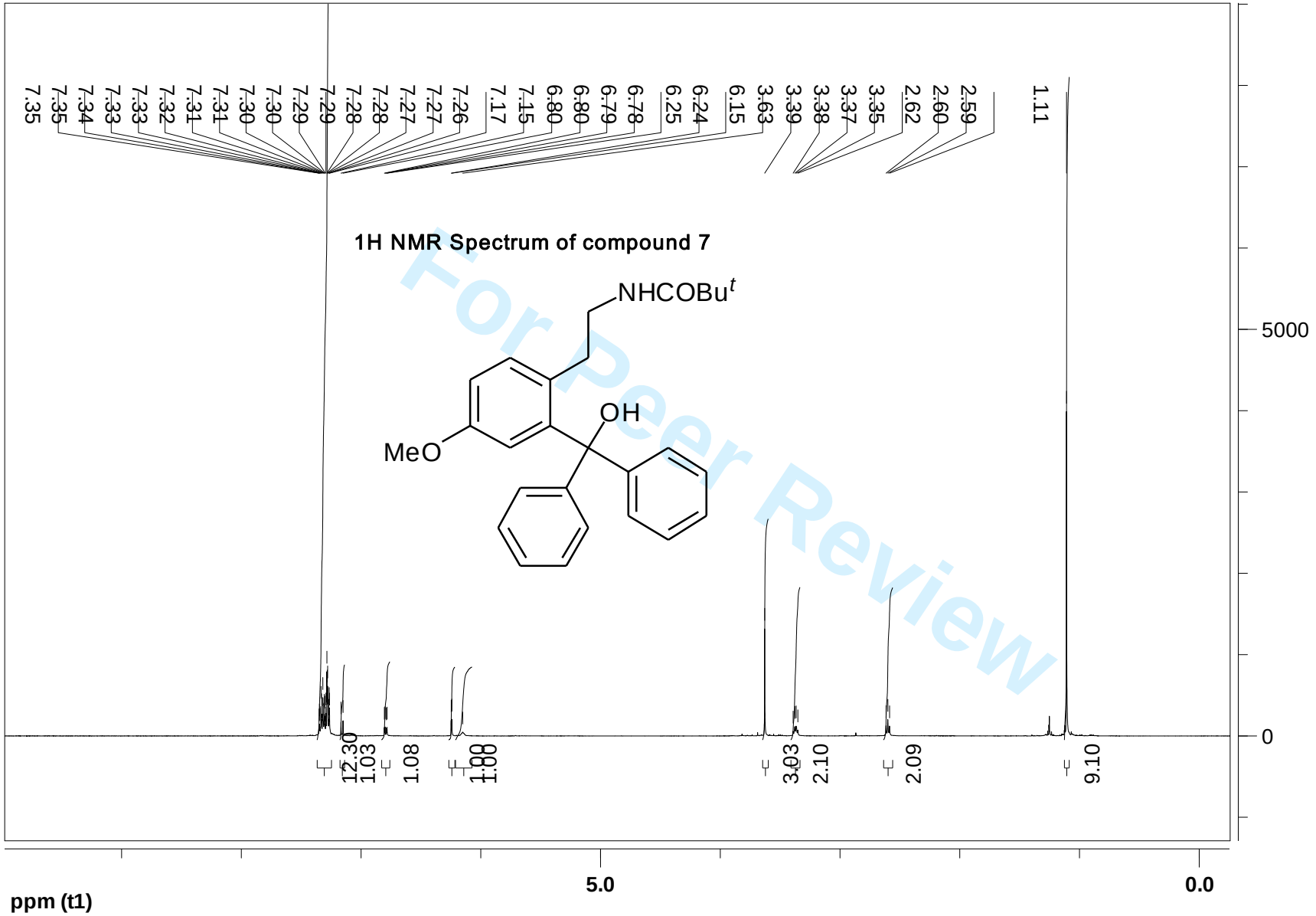

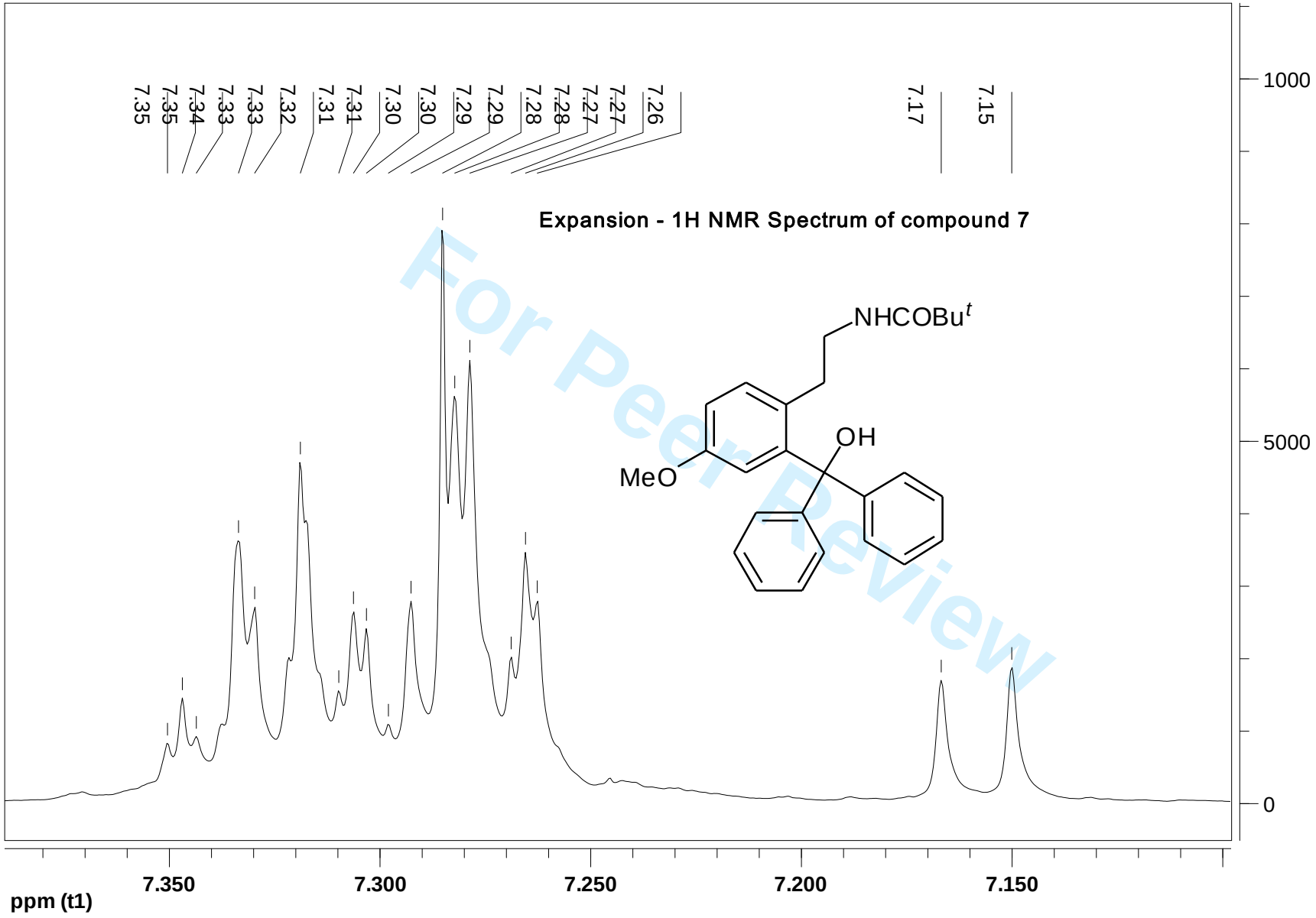

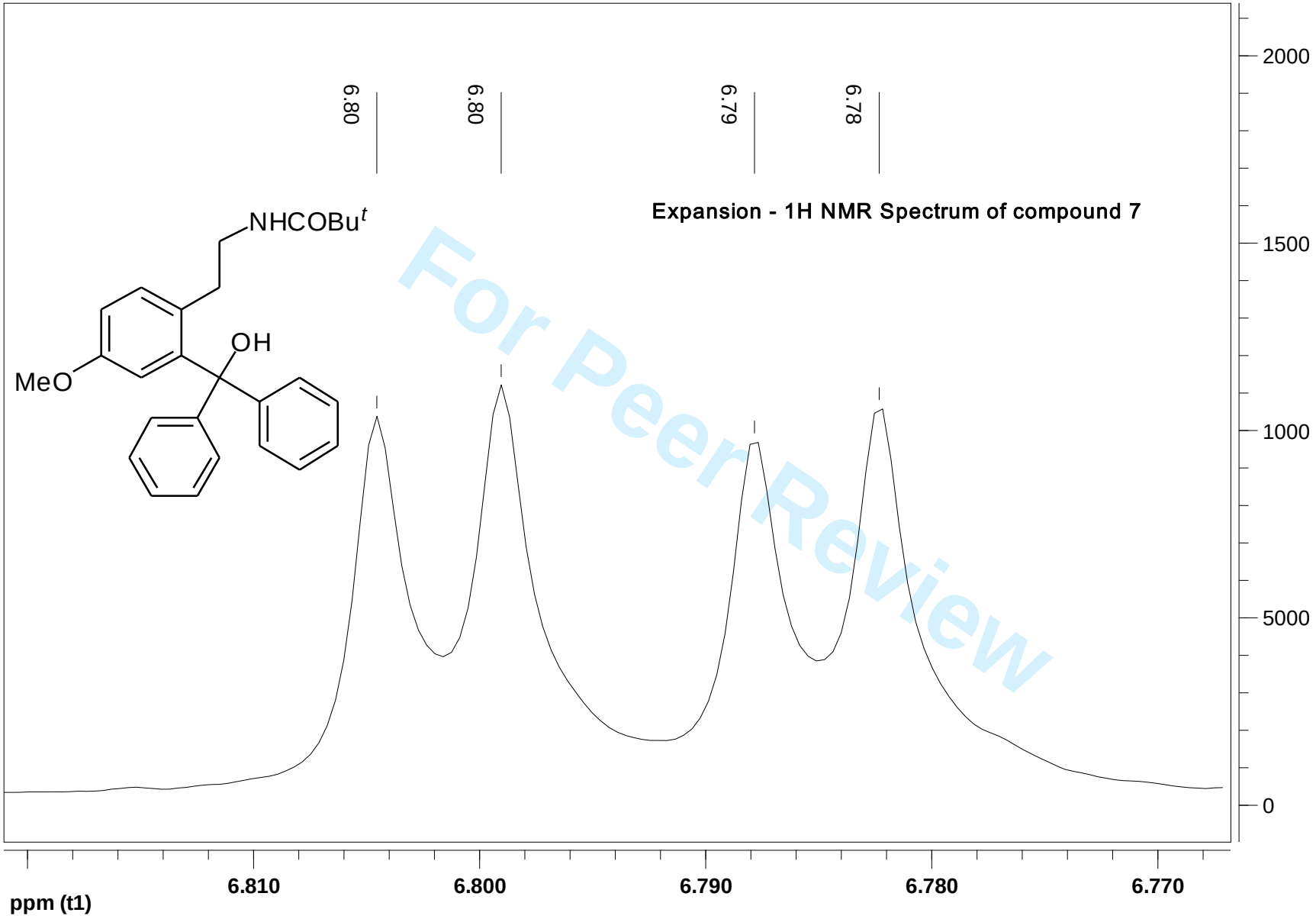

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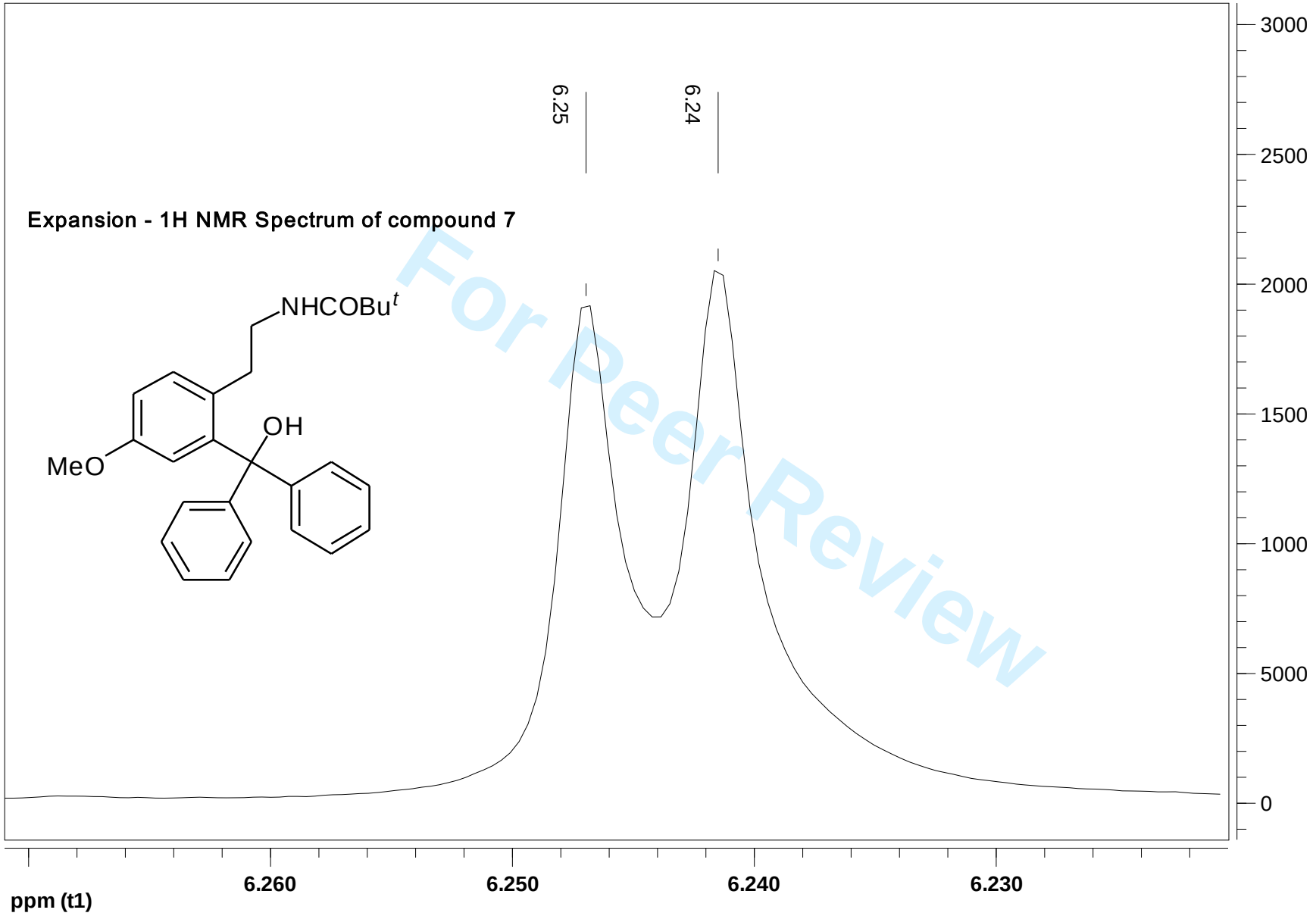

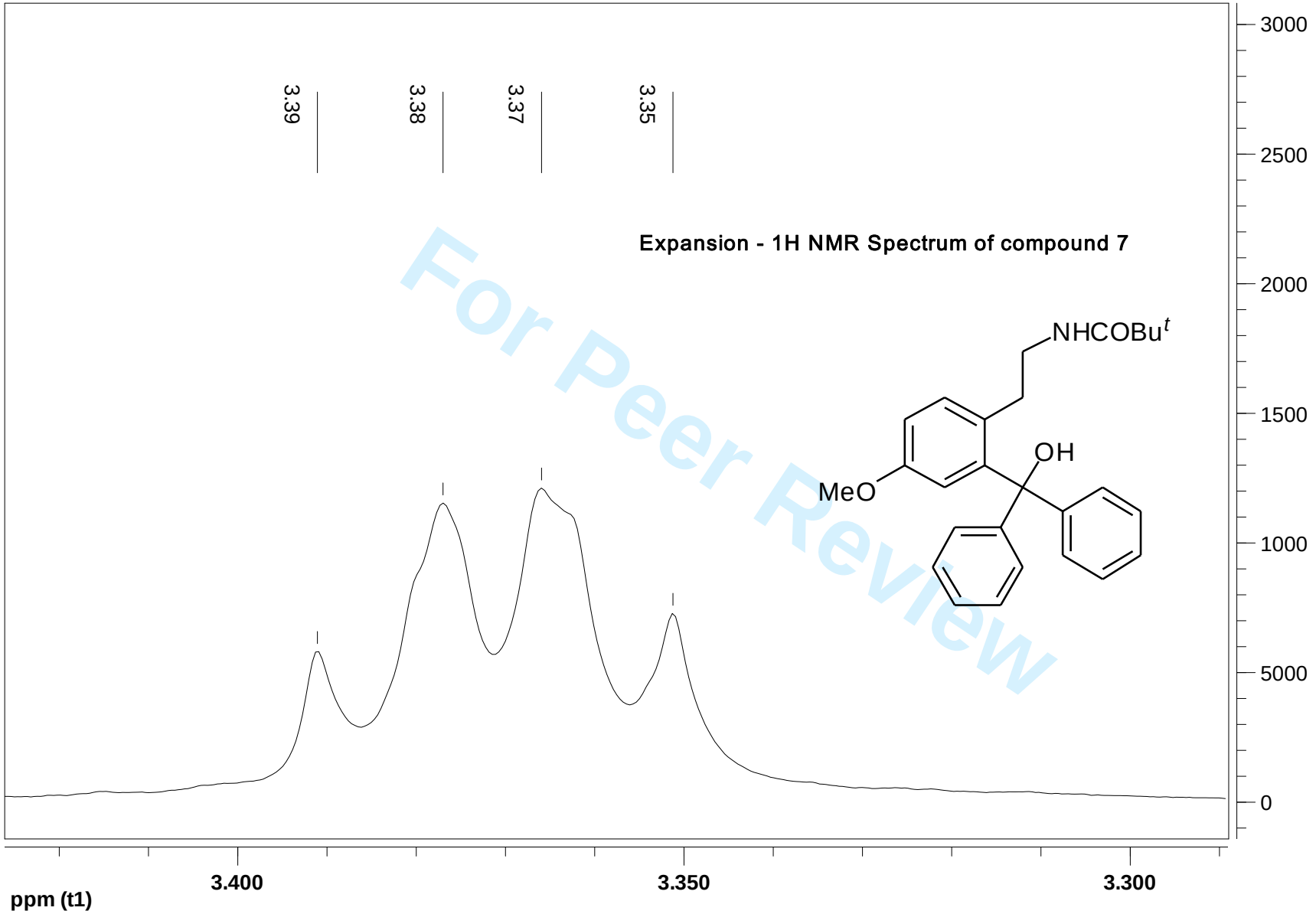

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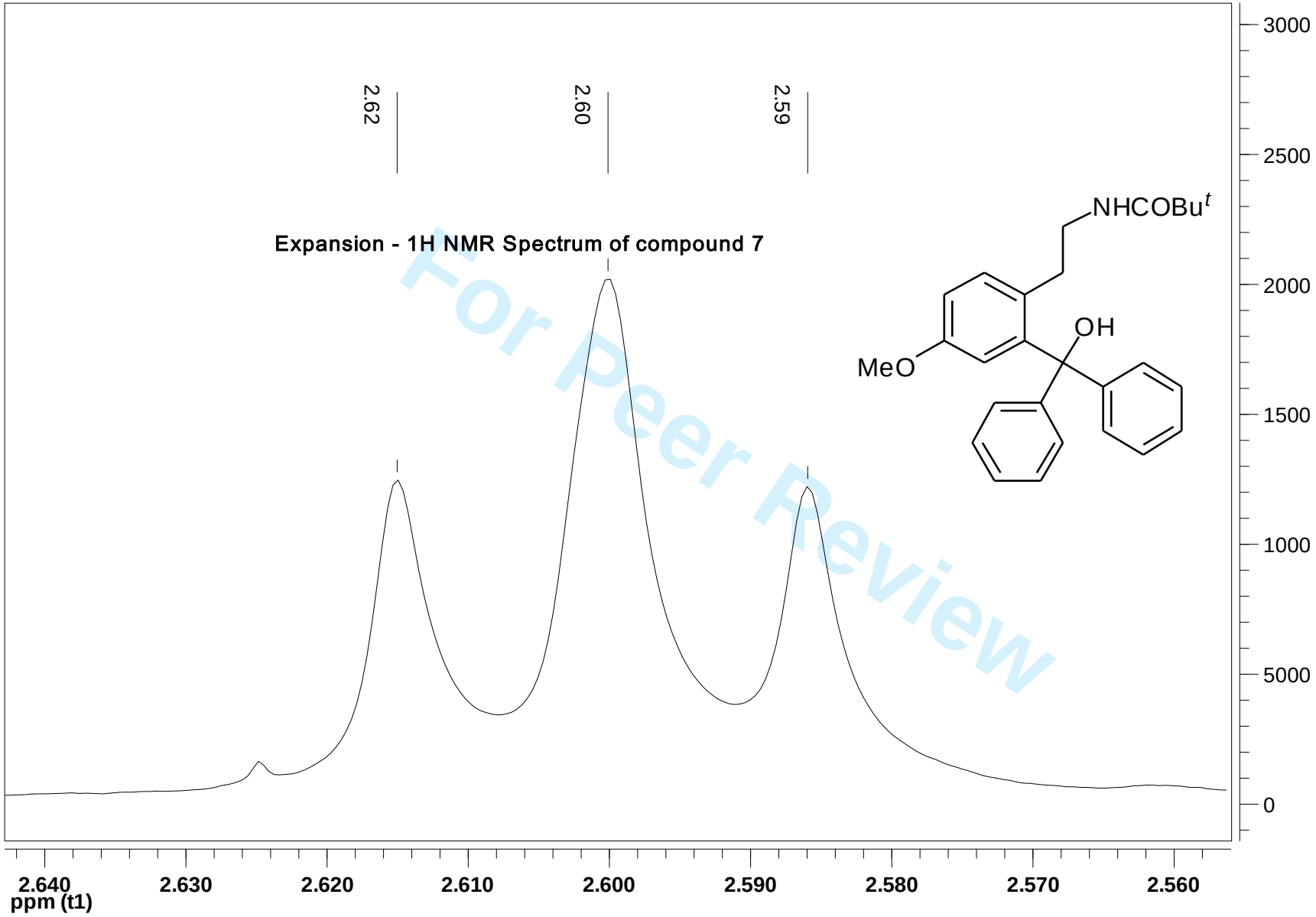

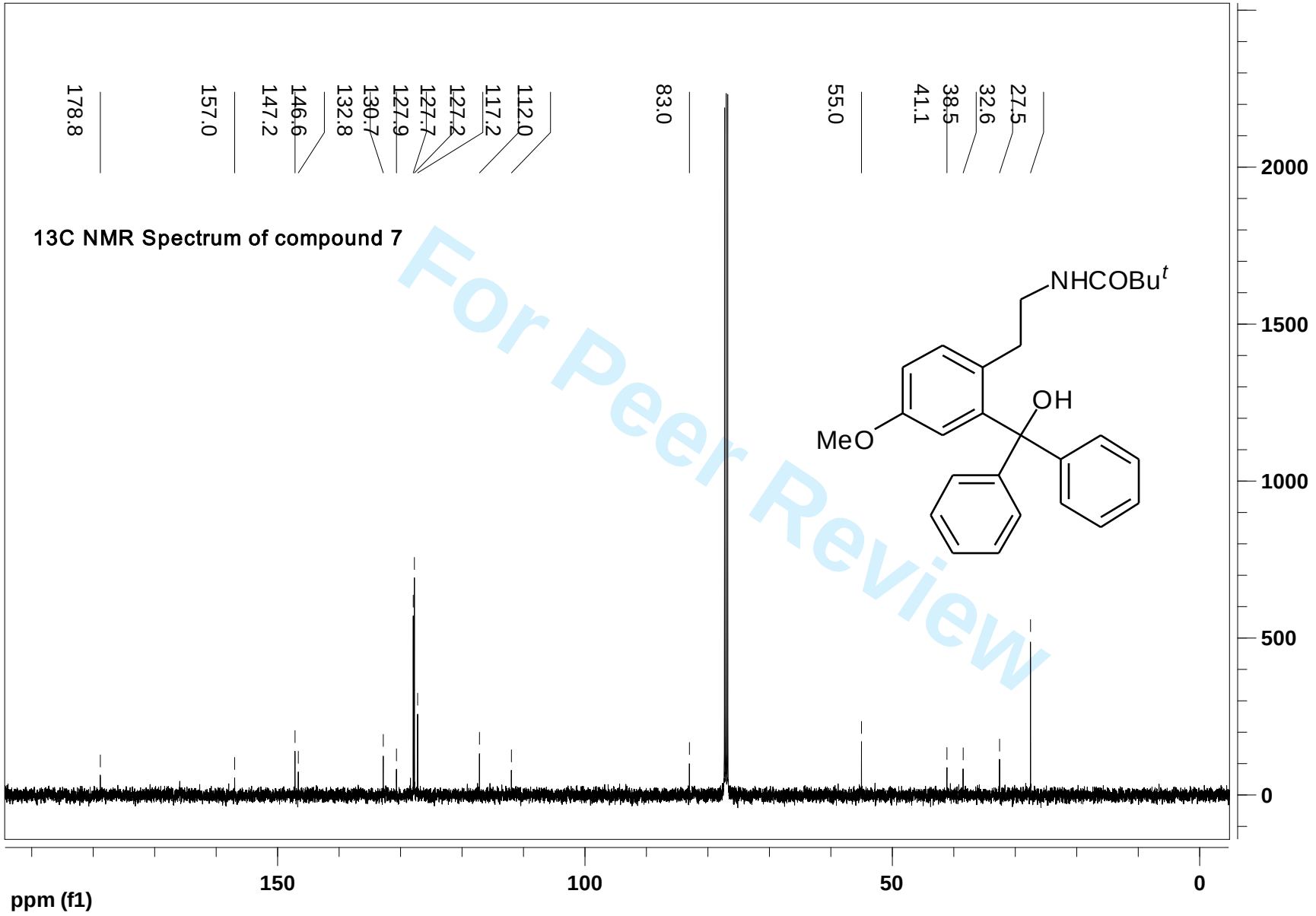

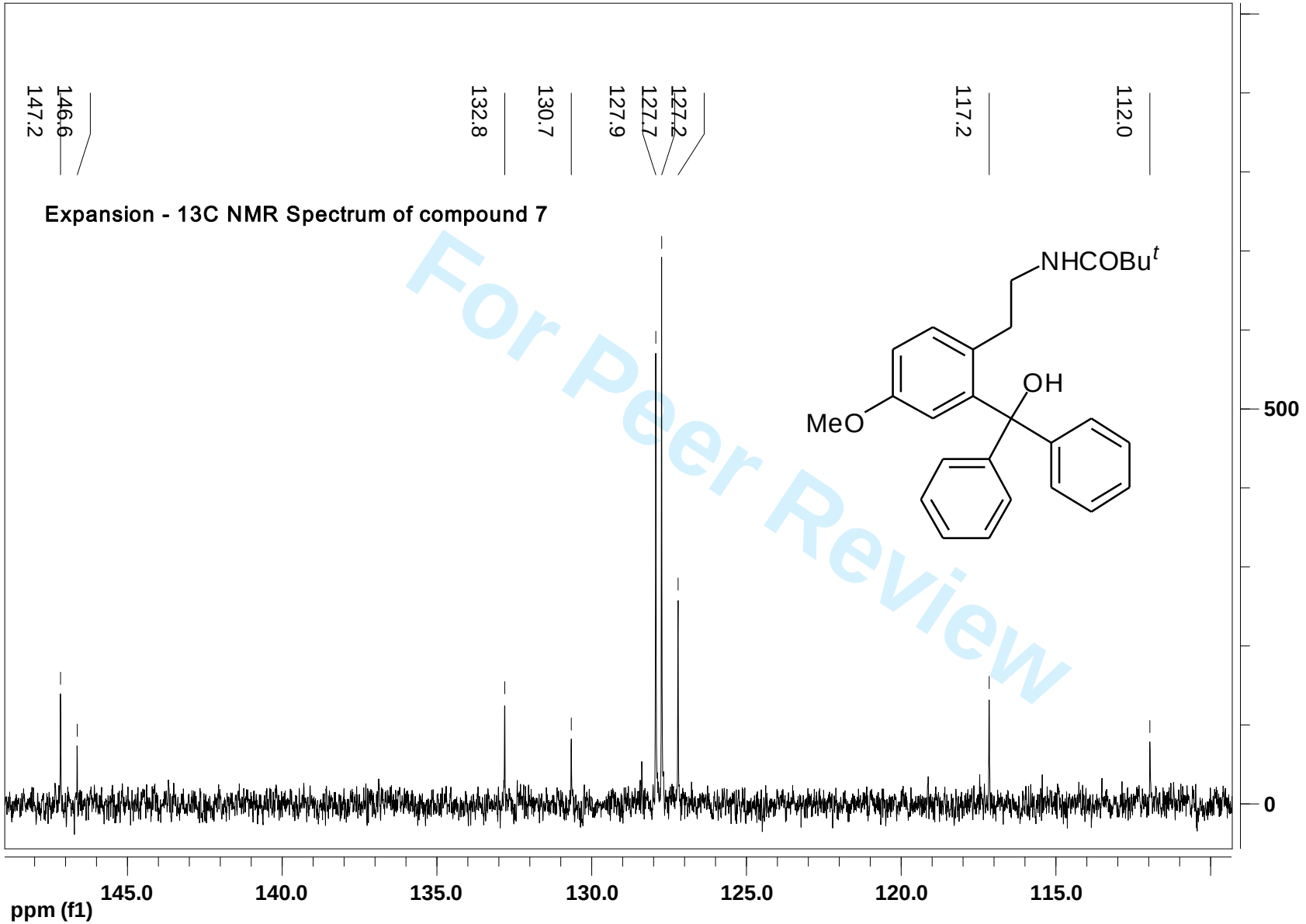

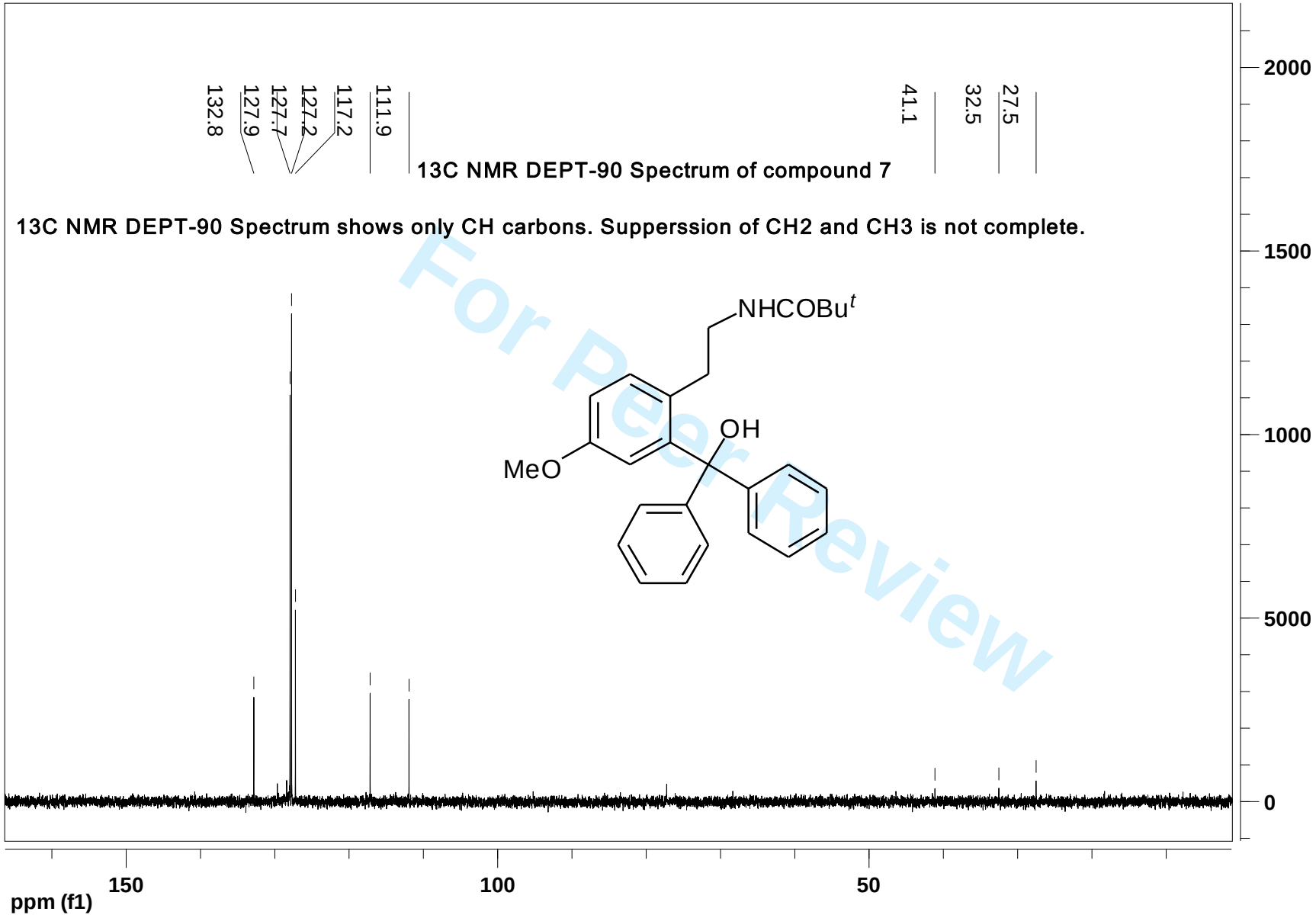

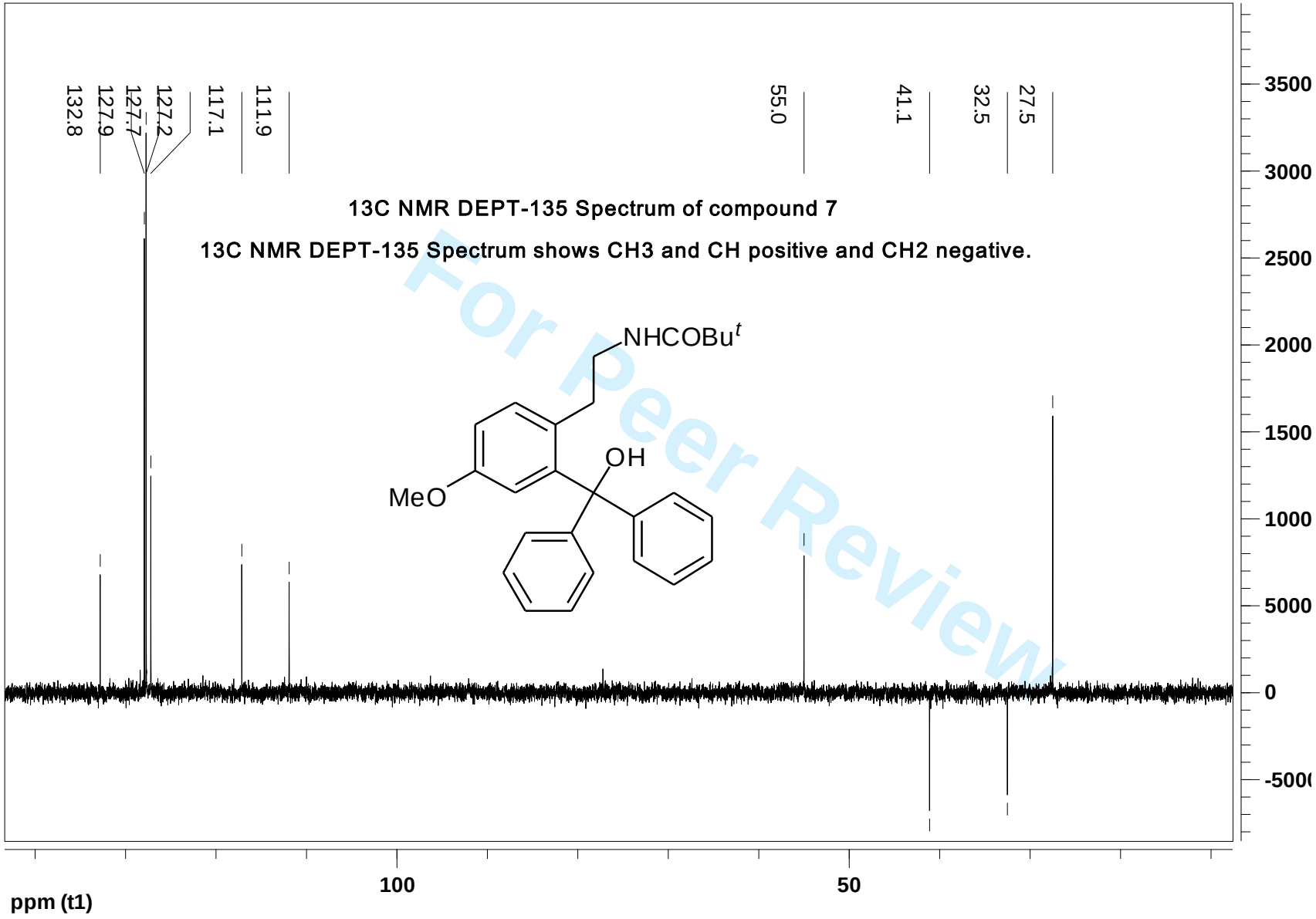

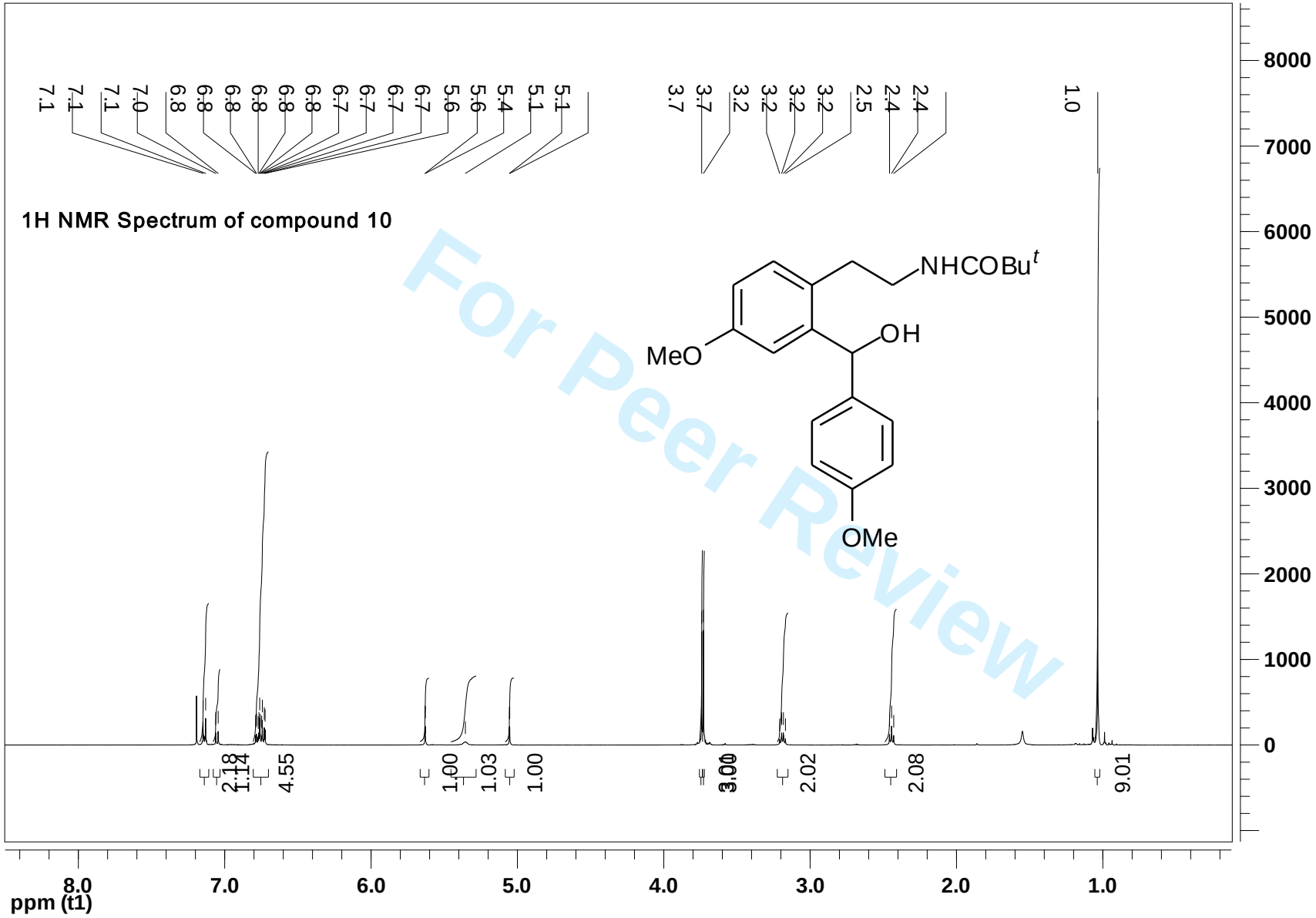

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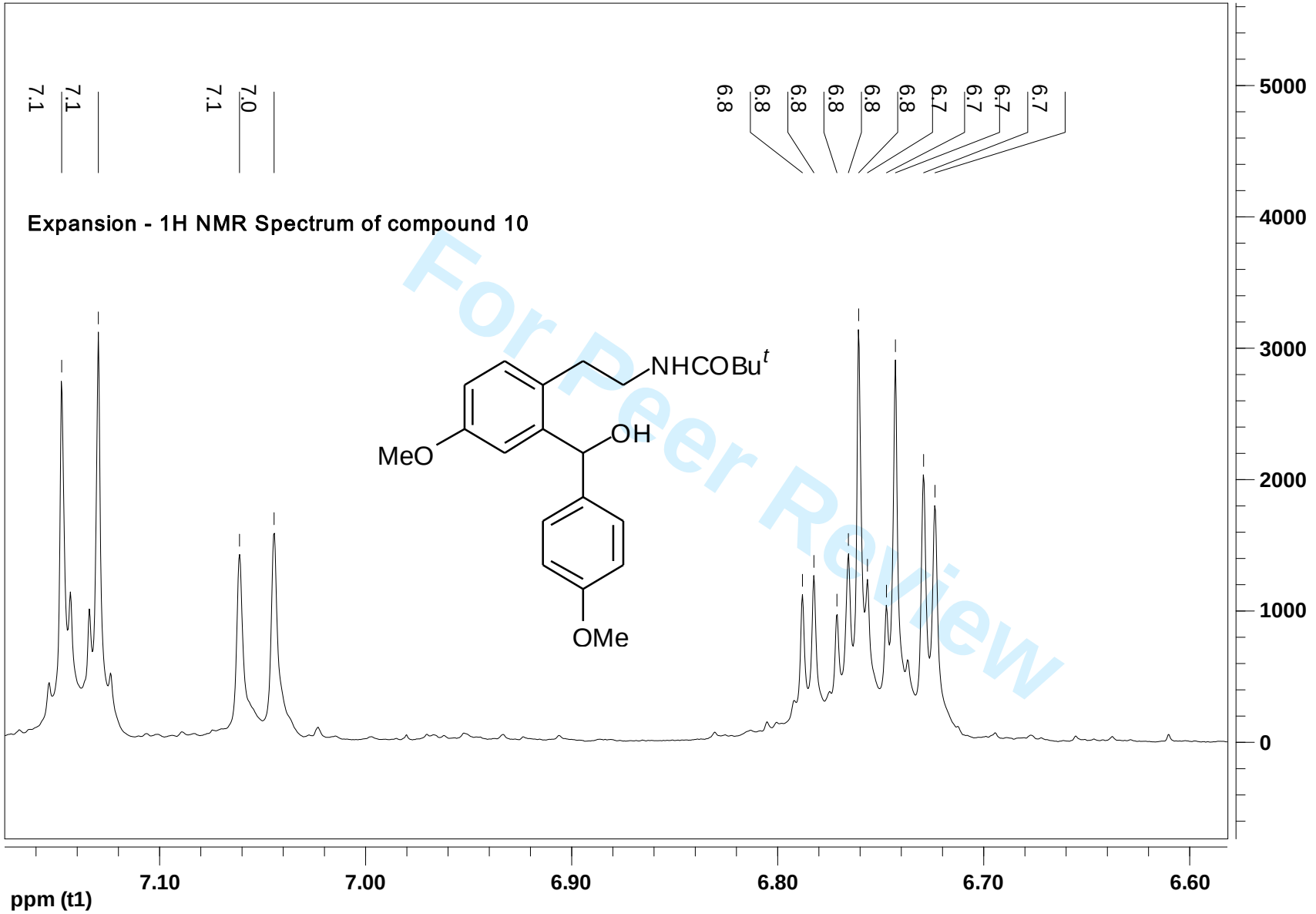

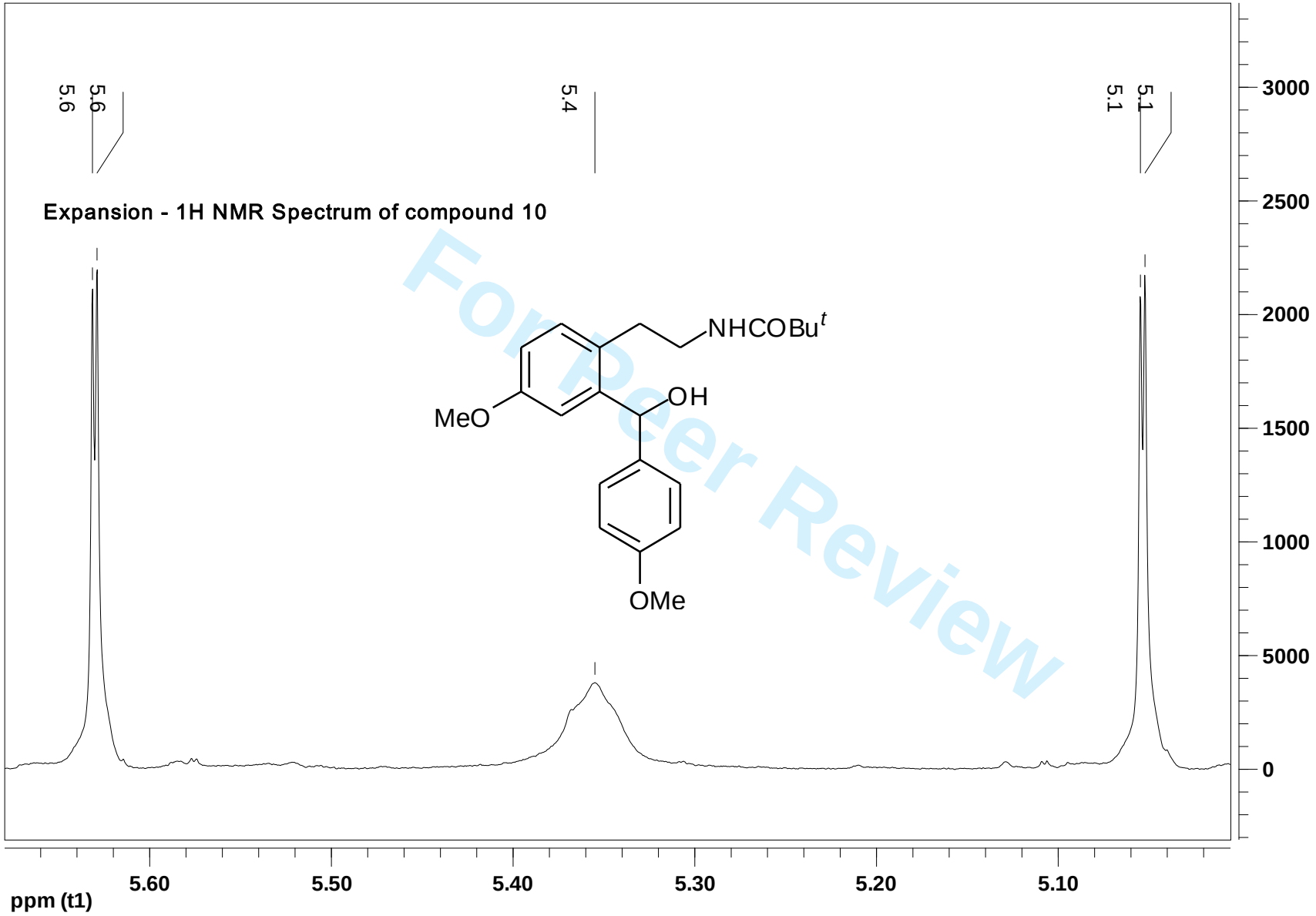

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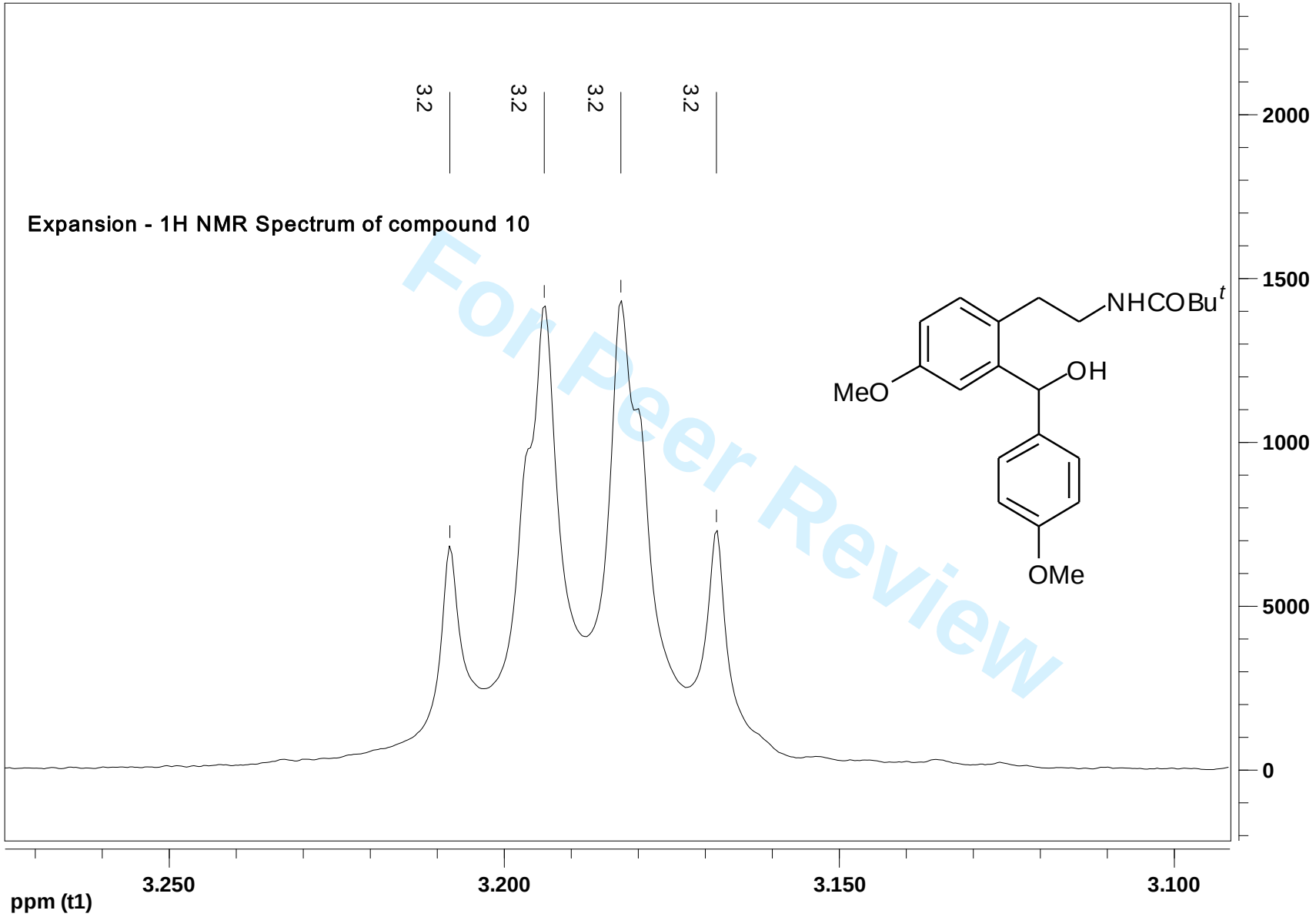

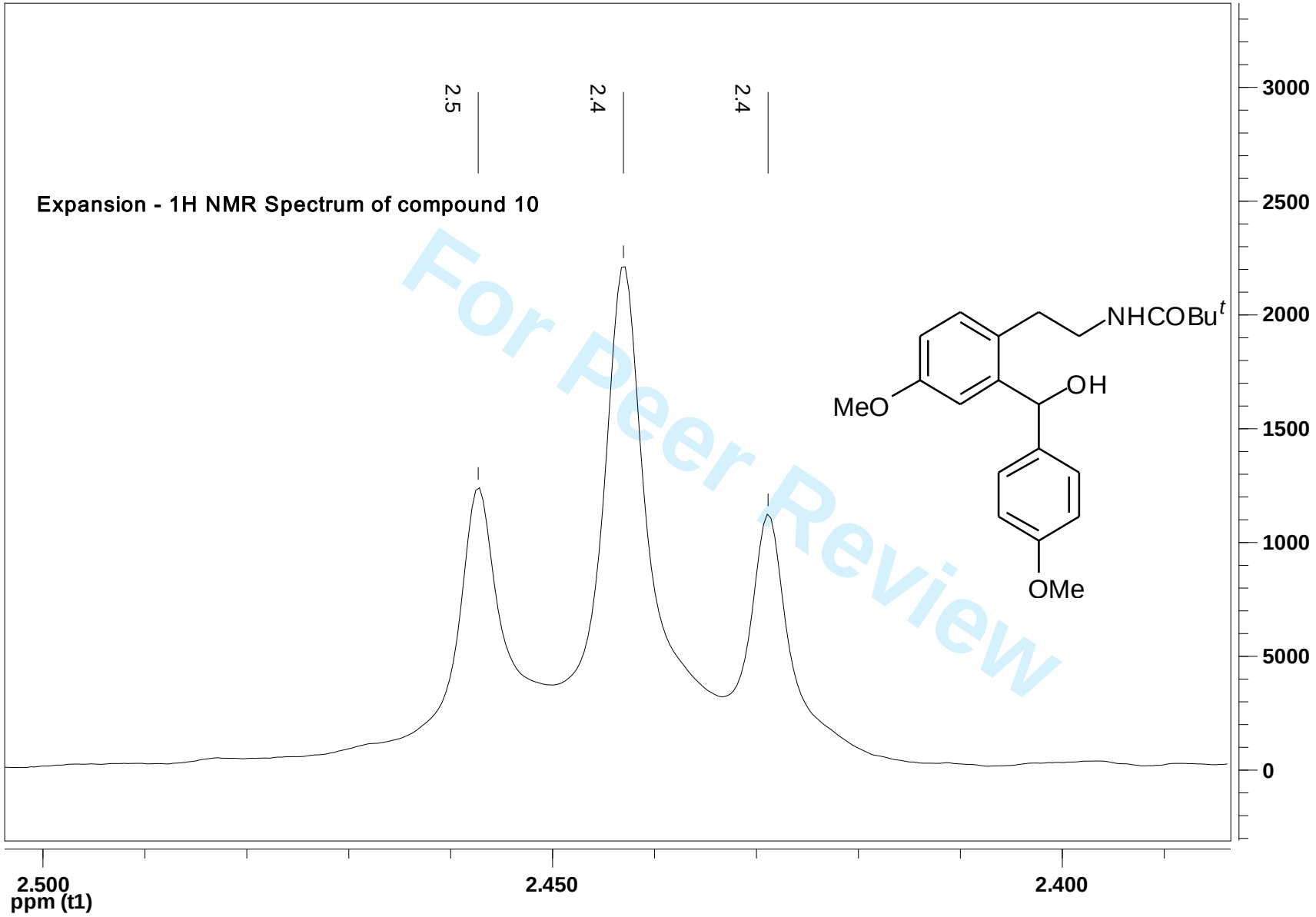

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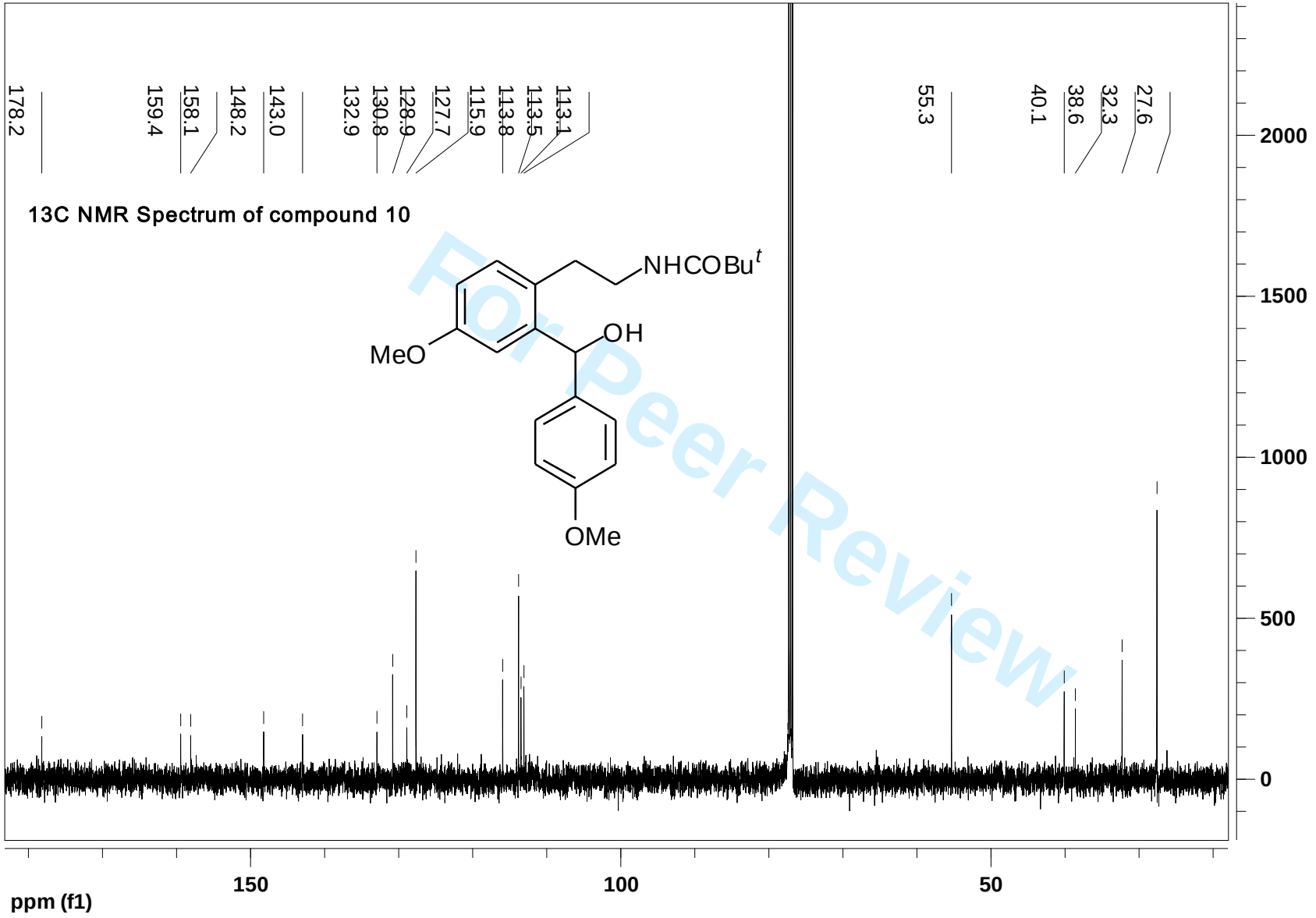

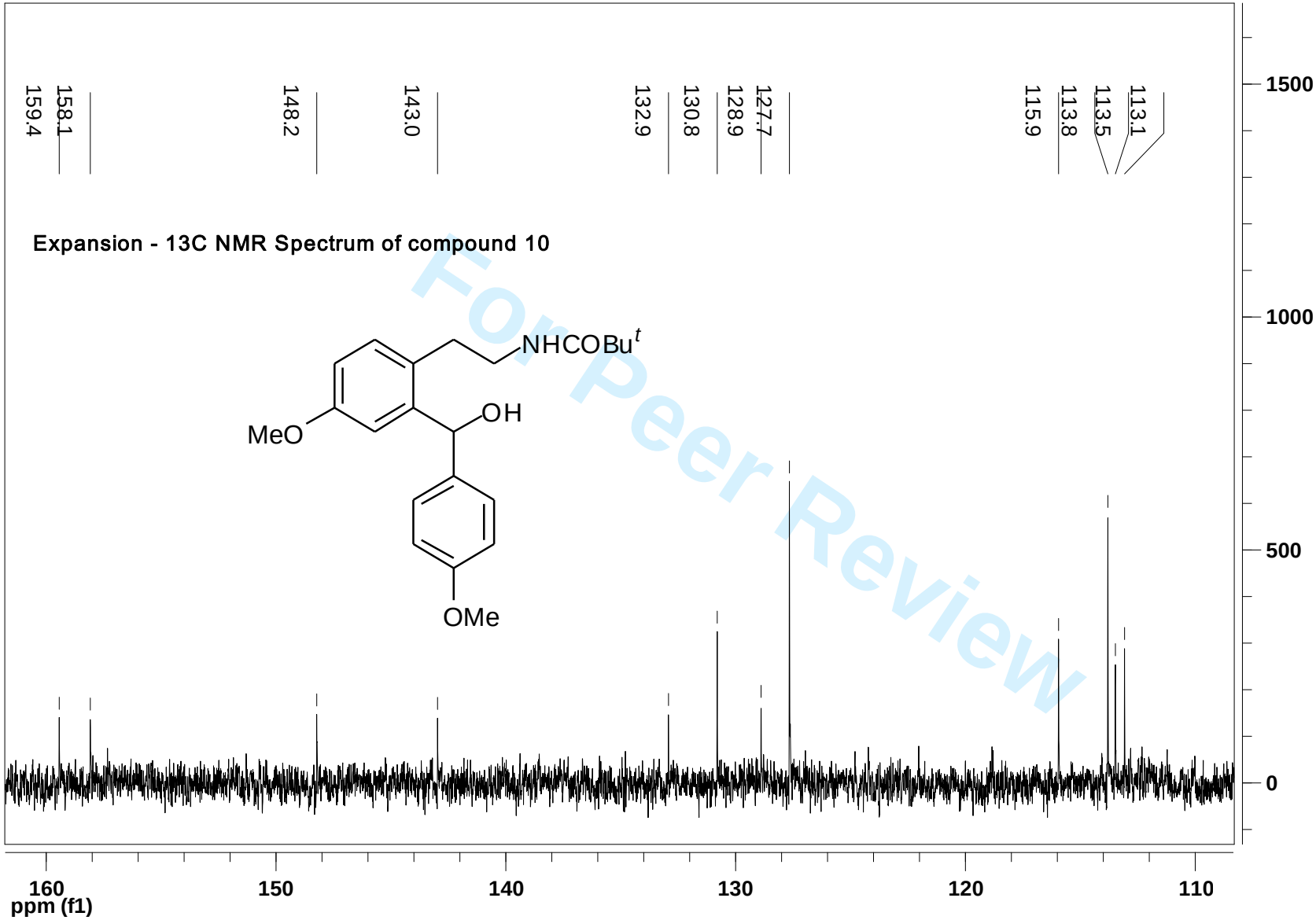

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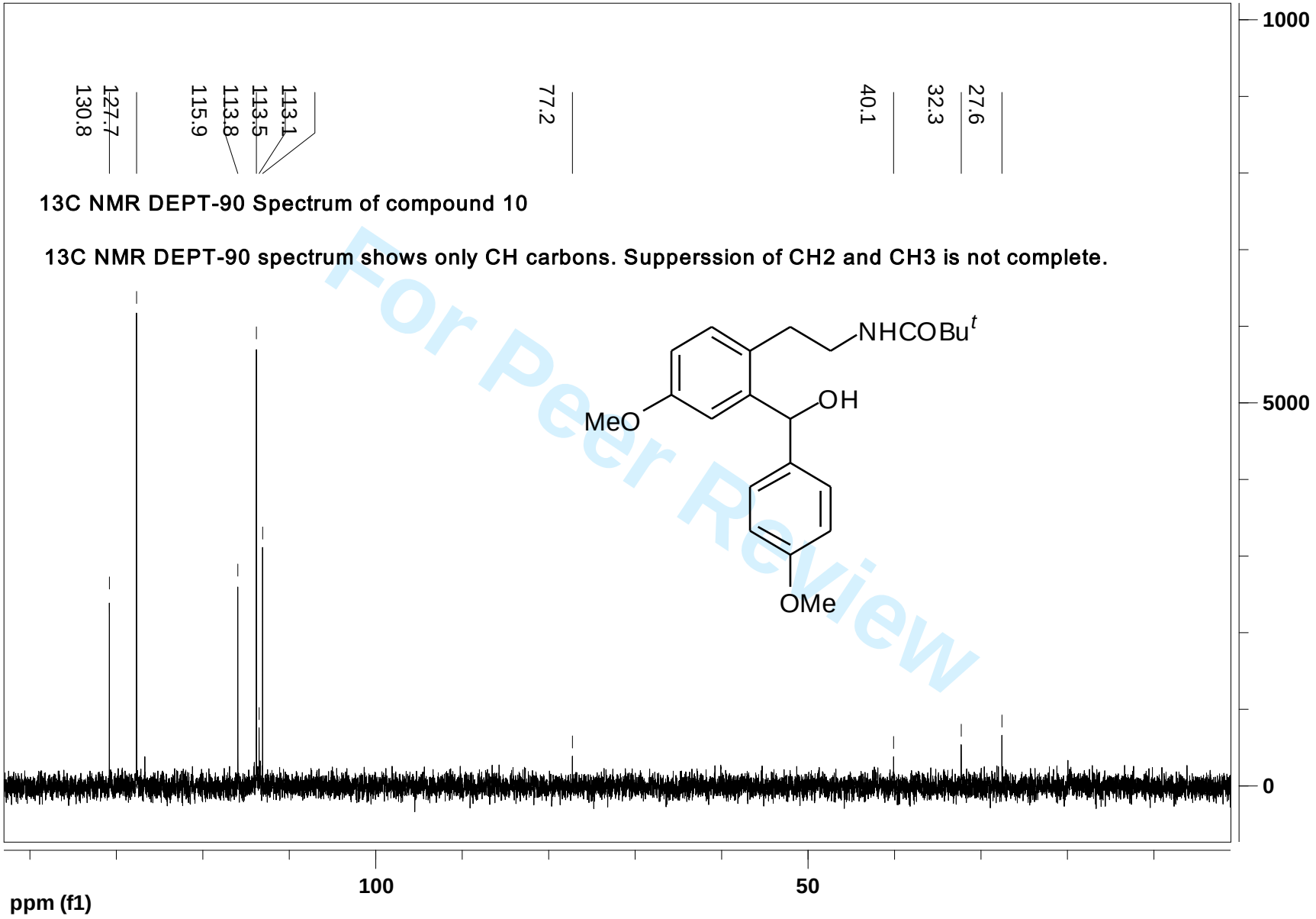
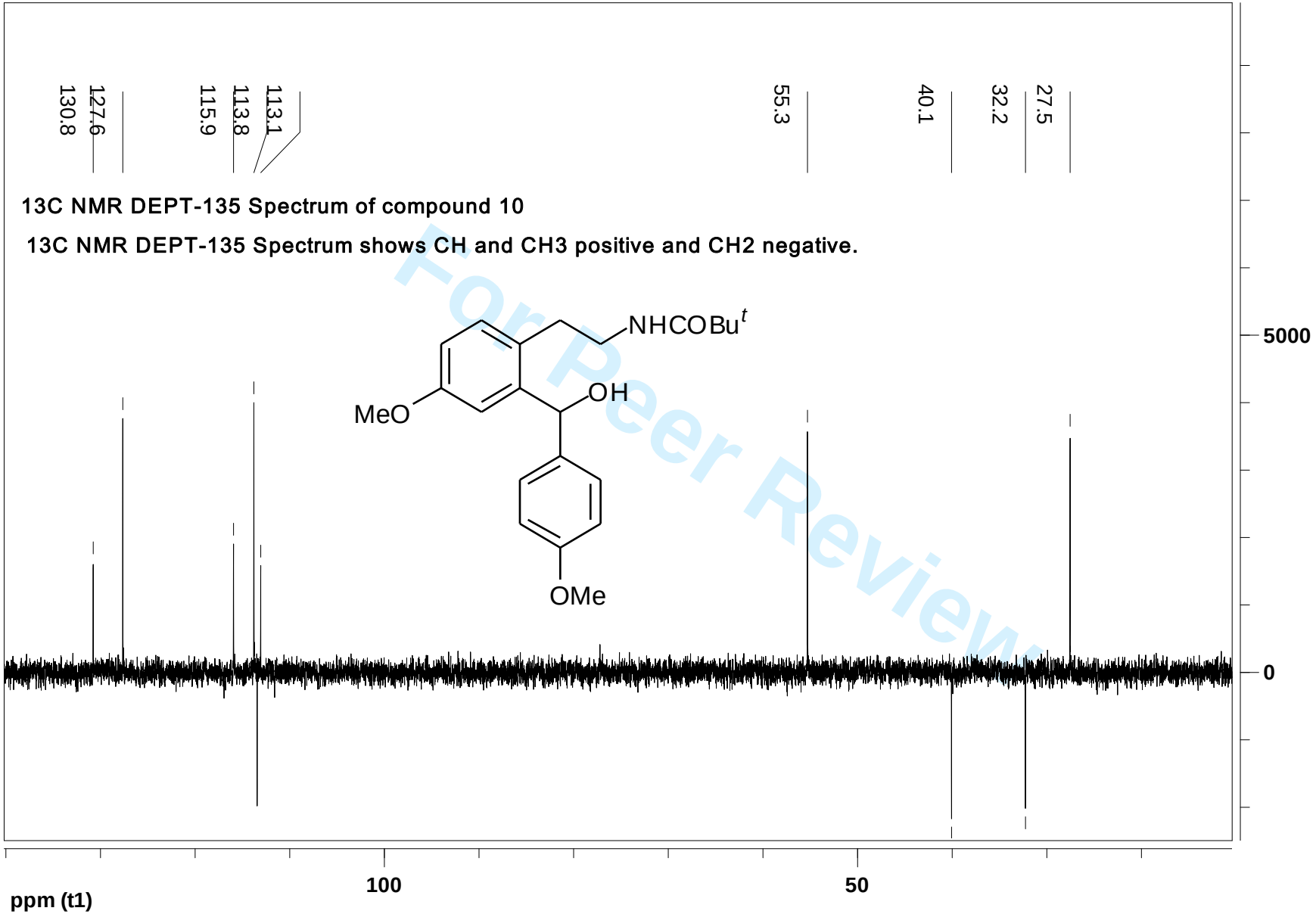


13C NMR DEPT-90 Spectrum of compound 10

13C NMR DEPT-90 spectrum shows only CH carbons. Supperssion of CH2 and CH3 is not complete.



13C NMR DEPT-135 Spectrum of compound 10

13C NMR DEPT-135 Spectrum shows CH and CH3 positive and CH2 negative.

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