Oxidative Photoredox Catalysis: Mild and Selective Deprotection of PMB Ethers Mediated by Visible Light

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Supporting Information

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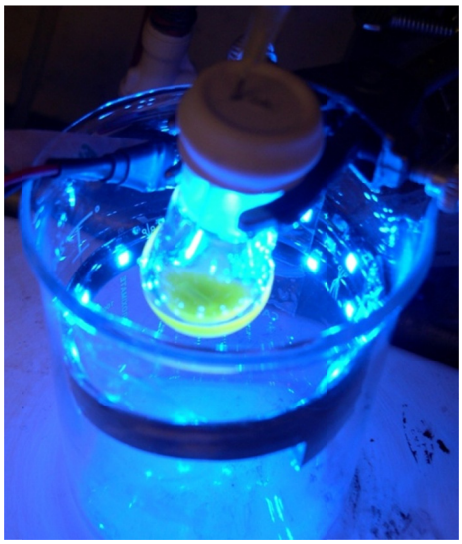
General Information:

Chemicals were either used as received or purified according to *Purification of Common Laboratory Chemicals*. All reactions were performed using common dry, inert atmosphere techniques. Reactions were monitored by TLC and visualized by a dual short wave/long wave UV lamp and stained with an ethanolic solution of potassium permanganate or p-anisaldehyde. Column flash chromatography was performed using 230-400 mesh silica gel. NMR spectra were recorded on Varian Mercury 300, Varian Unity Plus 400, and Varian Mercury 400 spectrometers. Chemical shifts for ^{1}H NMR were reported as δ, parts per million, relative to the signal of $CHCl_3$ at 7.26 ppm. Chemical shifts for ^{13}C NMR were reported as δ, parts per million, relative to the center line signal of the $CDCl_3$ triplet at 77.0 ppm. Proton and carbon assignments were established using spectral data of similar compounds. The abbreviations s, br. s, d, dd, br. d, ddd, t, q, br. q, m, and br. m stand for the resonance multiplicity singlet, broad singlet, doublet, doublet of doublets, broad doublet, doublet of doublet of doublets, triplet, quartet, broad quartet, multiplet and broad multiplet, respectively. IR spectra were recorded on an Avatar 360 FT-IR spectrometer. Mass spectra were recorded at the Mass Spectrometry Facility at the Department of Chemistry of the Boston University in Boston, MA on a Waters Q-Tof API-US with ESI high resolution mass spectrometer. Concentration refers to removal of solvent under reduced pressure (house vacuum at ca. 20 mmHg).

Reaction Apparatus:

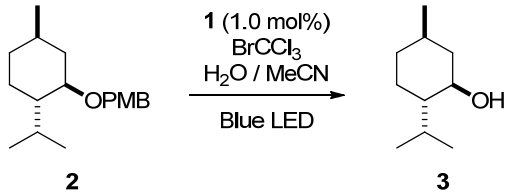
Photocatalyzed reactions were carried out under visible light irradiation by a 15 cm blue LED strip (available from http://www.creativelightings.com/, λ_{max} = 435 nm) surrounding the reaction vessel.



General Procedure A: Typical PMB Deprotection Mediated by Photoredox Catalysis

A 25 mL round bottom flask was equipped with a rubber septum and magnetic stir bar and was charged with PMB ether (1.0 mmol, 1.0 equiv), $BrCCl_3$ (2.0 mmol, 2.0 equiv), H_2O (10 mmol, 10 equiv), MeCN (10 mL), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$, **XX**, (10 μmol, 0.01 equiv). The flask was degassed (3 x freeze/pump/thaw). The heterogeneous mixture was then irradiated by a 1 W blue LED strip under an atmosphere of Ar for 6 – 24h. After the reaction was complete (as judged by TLC analysis), the mixture was poured into a separatory funnel containing 25 mL of EtOAc and 10 mL of H_2O. The layers were separated and the aqueous layer was extracted with EtOAc (2 X 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel, using the solvent system indicated, to afford the desired deprotected product.

Menthol, **3** (*Table 1, entry 1)*:



2 **3**

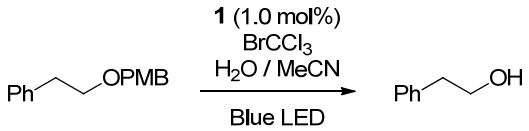
According to General Procedure A, **2**[1] (120 mg, 0.24 mmol), $BrCCl_3$ (88 µL, 0.88 mmol), and **1** (5.0 mg, 2.4 µmol), H_2O (20 µL, 2.4 mmol) in MeCN (5 mL) afforded **3** (26 mg, 69%) as a colorless solid after purification by chromatography on SiO_2 (4:1, hexanes/EtOAc) (16 h reaction time).

R_f (EtOAc/hexane 15:85): 0.28;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.40 (ddd, J = 10.7, 10.7, 4.3 Hz. 1 H), 2.17 (d sept., J = 6.8, 2.7 Hz, 1 H), 1.98 – 1.93 (m, 1 H), 1.68 – 1.58 (m, 2 H), 1.46 – 1.37 (m, 2 H) 1.14 – 1.07 (m, 1 H), 0.99 – 0.93 (m, 2 H), 0.91 (dd, J = 6.8, 6.8 Hz, 6 H), 0.81 (d, J = 6.9 Hz, 3 H).

[1] G. V. M. Sharma, C. G. Reddy and P. R. Krishna, *J. Org. Chem.*, 2003, **68**, 4574.

2-Phenylethanol, **5** (*Table 1, entry 2*):



4 **5**

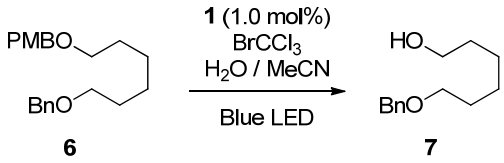
According to General Procedure A, **4**[2] (200 mg, 0.83 mmol), $BrCCl_3$ (160 µL, 1.7 mmol), **1** (9.0 mg, 8.3 µmol), and H_2O (150 µL, 8.3 mmol) in MeCN (8.3 mL) afforded **5** (87 mg, 86%) as a colorless oil after purification by chromatography on SiO_2 (85:15 to 4:1, petroleum ether/Et_2O) (12 h reaction time).

R_f (EtOAc/hexane 15:85): 0.18;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 – 7.32 (m, 2 H), 7.28 – 7.24 (m, 3 H), 3.88 (t, J = 6.6 Hz, 2 H), 2.89 (t, J = 6.6 Hz, 2 H).

[2] G. V. M. Sharma, C. G. Reddy and P. R. Krishna, *J. Org. Chem.*, 2003, **68**, 4574.

6-(Benzyloxy)hexan-1-ol,[3] **7** (*Table 1, entry 3*):



6 **7**

According to General Procedure A, **6**[4] (110 mg, 0.34 mmol), $BrCCl_3$ (68 μL, 0.68 mmol), **7** (3.8 mg, 3.4 μmol), and H_2O (61 μL, 3.4 mmol) in MeCN (3.4 mL) afforded **1** (64 mg, 92%) as a colorless oil after purification by chromatography on SiO_2 (1:3, hexanes/EtOAc) (12 h reaction time).

R_f (EtOAc/hexane 1:4): 0.13;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.29 – 7.25 (m, 3 H), 7.22 – 7.19 (m, 2 H), 4.44 (s, 2 H), 3.58 (t, J = 6.5 Hz, 2 H), 3.42 (t, J = 6.5 Hz, 2 H), 1.61 – 1.50 (m, 4 H), 1.39 – 1.31 (m, 4 H).

[3] J. E. Wilson, A. D. Casarez, D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2009, **131**, 11332.
[4] M. A. rahim, S. Matsumura, K. Toshima, *Tetrahedron Lett.* 2005, **46**, 7307.

Octan-1-ol, **11** (*Table 1, entry 4*):

8 **9**

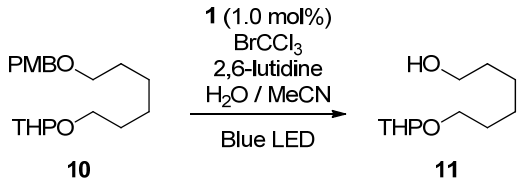
According to General Procedure A, **8**[5] (220 mg, 0.86 mmol), $BrCCl_3$ (170 µL, 1.7 mmol), **1** (9.6 mg, 8.6 µmol), and H_2O (150 µL, 8.6 mmol) in MeCN (8.6 mL) afforded **9** (92 mg, 82%) as a colorless oil after purification by chromatography on SiO_2 (7:3, petroleum ether/Et_2O) (18 h reaction time).

R_f (EtOAc/hexane 1:4): 0.31;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.34 (t, J = 7.0 Hz, 2 H), 1.60 – 1.54 (m, 2 H), 1.36 – 1.35 (m, 12 H), 0.88 (t, J = 7.0 Hz, 3 H).

[5] G. V. M. Sharma, C. G. Reddy and P. R. Krishna, *J. Org. Chem.*, 2003, **68**, 4574.

6-((Tetrahydro-2H-pyran-2-yl)oxy)hexan-1-ol,[6] **11** (*Table 1, entry 5*):



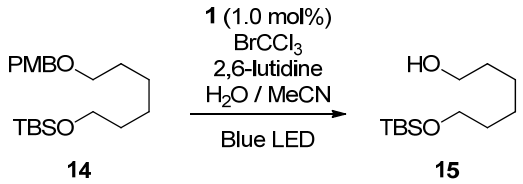
According to General Procedure A, **10**[7] (150 mg, 0.46 mmol), $BrCCl_3$ (92 μL, 0.93 mmol), 2,6-lutidine (110 μL, 0.93 mmol), **1** (5.6 mg, 4.6 μmol), and H_2O (120 μL, 4.6 mmol) in MeCN (4.5 mL) afforded **11** (75 mg, 80%) as a colorless oil after purification by chromatography on SiO_2 (1:1, hexanes/EtOAc) (12 h reaction time).

R_f (EtOAc/hexane 1:1): 0.32;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.58 (dd, J = 4.4, 2.6 Hz, 1 H), 3.88 (ddd, J = 10.7, 7.0, 2.9 Hz, 1 H), 3.76 (dt, J = 9.6, 6.6 Hz, 1 H), 3.66 (t, J = 6.6 Hz, 2 H), 3.54 – 3.50 (m, 1 H), 3.47 – 3.39 (m, 1 H), 1.88 – 1.82 (m, 1 H), 1.77 – 1.72 (m, 1 H), 1.67 – 1.52 (m, 8 H), 1.44 – 1.40 (m, 4 H).

[6] Y. Hayashi, H. Gotoh, T. Tamura, H. Yamaguchi, R. Masui and M. Shoji, *J. Am. Chem. Soc.*, 2005, **127**, 16028.
[7] G. V. M. Sharma, C. G. Reddy and P. R. Krishna, *J. Org. Chem.*, 2003, **68**, 4574.

6-((Tert-butyldimethylsilyl)oxy)hexan-1-ol,[8] **6** (*Table 1, entry 6*):



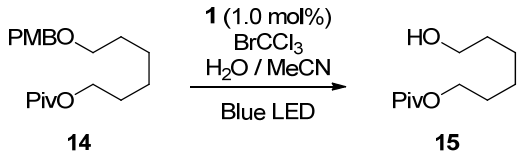
According to General Procedure A, **14**[9] (200 mg, 0.51 mmol), $BrCCl_3$ (100 μL, 1.0 mmol), 2,6-lutidine (120 μL, 1.0 mmol), **1** (5.6 mg, 5.0 μmol), and H_2O (92 μL, 5.1 mmol) in MeCN (7 mL) afforded **15** (96 mg, 81%) as a colorless oil after purification by chromatography on SiO_2 (15:85, hexanes/EtOAc) (14 h reaction time).

R_f (EtOAc/hexane 1:3): 0.27;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.64 (t, J = 6.4 Hz, 2 H), 3.61 (t, J = 6.8 Hz, 2 H), 1.59 – 1.43 (m, 4 H), 1.37 – 1.35 (m, 4 H), 0.99 (s, 9 H), 0.04 (s, 6 H).

[8] F. Kaiser, L. Schwink, J. Velder and H. G. Schmalz, *J. Org. Chem.*, 2002, **67**, 9248.
[9] P. R. Krishan, B. Lavanya, A. K. Mahalingam, V. V. R. Reddy and G. V. M. Sharma, *Lett. Org. Chem.*, 2005, **2**, 360.

6-Hydroxyhexyl pivalate,[10] **15** (*Table 1, entry 7*):



14 **15**

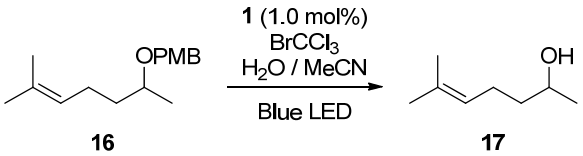
According to General Procedure A, **14** (250 mg, 0.75 mmol), $BrCCl_3$ (150 μL, 1.5 mmol), **1** (8.4 mg, 7.5 μmol), and H_2O (140 μL, 7.5 mmol) in MeCN (7.5 mL) afforded **15** (110 mg, 75%) as a colorless oil after purification by chromatography on SiO_2 (3:1, hexanes/EtOAc) (12 h reaction time).

R_f (EtOAc/hexane 1:4): 0.15;

^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.05 (t, J = 6.5 Hz, 2 H), 3.64 (t, J = 6.5 Hz, 2 H), 1.67 – 1.61 (m, 3 H), 1.59 – 1.55 (m, 2 H), 1.41 – 1.37 (m, 4 H), 1.19 (s, 9 H).

[10] G. Koza, C. Theunissen, J. R. Al Dulayymi and M. S. Baird, *Tetrahedron*, 2009, **65**, 10214.

6-Methylhept-5-en-2-ol, **17** (*Table 1, entry 9*):

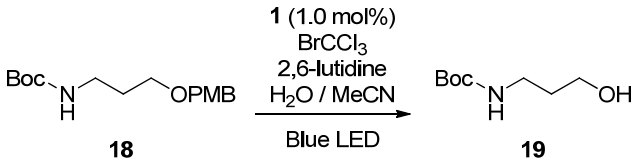


According to General Procedure A, **16** (130 mg, 0.52 mmol), $BrCCl_3$ (100 µL, 1.1 mmol), **1** (5.6 mg, 5.2 µmol), and H_2O (94µL, 5.2 mmol) in MeCN (7 mL) afforded **17** (55 mg, 84%) as a colorless oil after purification by chromatography on SiO_2 (7:3 petroleum ether/Et_2O) (12 h reaction time).

R_f (EtOAc/hexane 1:4): 0.33;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.17 – 5.15 (m, 1 H), 3.84 – 3.76 (m, 1 H), 2.13 – 2.02 (m, 2 H), 1.69 (s, 3 H), 1.62 (s, 3 H), 1.51 – 1.45 (m, 3 H), 1.19 (d, J = 6.2 Hz, 3 H).

tert-Butyl (3-hydroxypropyl)carbamate,[11] **19** (*Table 1, entry 9*):



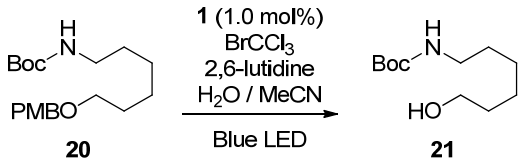
According to General Procedure A, **18** (90 mg, 0.31 mmol), $BrCCl_3$ (60 µL, 0.62 mmol), 2,6-lutidine (71 µL, 0.62 mmol), **1** (3.4 mg, 3.1 µmol), and H_2O (56 µL, 3.1 mmol) in MeCN (3 mL) afforded **19** (39 mg, 71%) as a colorless oil after purification by chromatography on SiO_2 (1:19, MeOH/DCM) (12 h reaction time).

R_f (MeOH/DCM 1:19): 0.38;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.75 (br. s, 1 H), 3.65 (br. t, J = 3.6 Hz, 2 H), 3.29 (q, J = 6.0 Hz, 2 H), 2.89 (br. s, 1 H), 1.69 – 1.63 (m, 2 H), 1.44 (s, 9 H).

[11] S. Priet, I. Zlatev, I. Barvik, Jr., K. Geerts, P. Leyssen, J. Neyts, H. Dutartre, B. Canard, J. –J. Vasseurt, F. Morvan and K. Alvarez, *J. Med. Chem.*, 2010, **53**, 6608.

Tert-butyl (6-hydroxyhexyl)carbamate,[12] **21** (*Table 1, entry 10*):



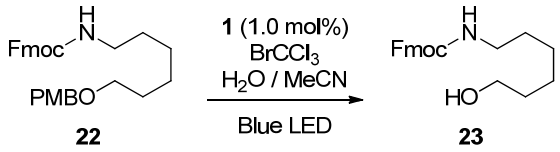
According to General Procedure A, **20** (100 mg, 0.29 mmol), $BrCCl_3$ (58 µL, 0.59 mmol), 2,6-lutidine (69 µL, 0.59 mmol), **1** (3.2 mg, 2.9 µmol), and H_2O (52 µL, 5.9 mmol) in MeCN (3 mL) afforded **21** (49 mg, 79%) as a colorless solid after purification by chromatography on SiO_2 (1:49, MeOH/DCM) (12 h reaction time).

R_f (MeOH/DCM 1:19): 0.42;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.51 (br. s, 1 H), 3.63 (dt, J = 11.5, 6.2 Hz, 2 H), 3.12 (dt, J = 12.9, 6.7 Hz, 2 H), 1.62 – 1.52 (m, 3 H), 1.50 – 1.32 (m, 14 H).

[12] A. Arduini, R. Bussolati, A. Credi, G. Faimani, S. Caraudée, A. Pochini, A. Secchi, M. Semeraro, S. Silvi and M. Venturi, *Chem. Eur. J.*, 2009, **15**, 3230.

(9H-Fluoren-9-yl)methyl (6-hydroxyhexyl)carbamate,[13] **23** (*Table X, entry X*):



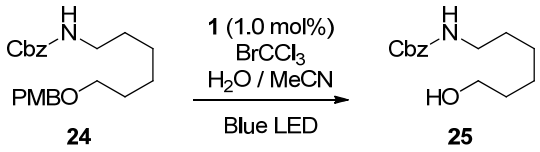
According to General Procedure A, **22** (100 mg, 0.23 mmol), $BrCCl_3$ (45 μL, 0.46 mmol), **1** (2.6 mg, 2.3 μmol), and H_2O (23 μL, 2.3 mmol) in MeCN (3 mL) afforded **23** (59 mg, 76%) as a colorless solid after purification by chromatography on SiO_2 (1:19, MeOH/DCM) (12 h reaction time).

R_f (MeOH/DCM 1:19): 0.35;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (d, J = 7.4 Hz, 2 H), 7.59 (d, J = 7.4 Hz, 1 H), 7.40 (t, J = 7.4 Hz, 2 H), 7.32 (t, J = 7.4 Hz, 2 H), 4.73 (br. s, 1 H), 4.41 (d, J = 6.8 Hz, 2 H), 4.22 (t, J = 6.8 Hz, 1 H), 3.19 (t, J = 7.0 Hz, 4 H), 1.86 – 1.79 (m, 2 H), 1.55 – 1.49 (m, 2 H), 1.43 – 1.34 (m, 4 H).

[13] M. Quintanar-Audelo, A. Fernández-Carvajal, W. Van Den Nest, C. Carreño, A. Ferrer-Montiel and F. Albericio, *J. Med. Chem.*, 2007, **50**, 6133.

Benzyl (6-hydroxyhexyl)carbamate,[14] **25** (*Table 1, entry 12*):



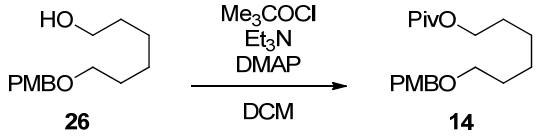
According to General Procedure A, **24** (180 mg, 0.48 mmol), $BrCCl_3$ (96 µL, 0.96 mmol), **1** (5.4 mg, 4.8 µmol), and H_2O (86 µL, 4.8 mmol) in MeCN (6 mL) afforded **25** (110 mg, 91%) as a colorless solid after purification by chromatography on SiO_2 (1:19, MeOH/DCM) (18 h reaction time).

R_f (MeOH/DCM 1:19): 0.37;

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 – 7.31 (m, 5 H), 5.09 (s, 2 H), 4.73 (br. s, 1 H), 3.63 (br. t, J = 6.0 Hz, 2 H), 3.20 (q, J = 6.8 Hz, 2 H), 1.57 – 1.48 (m, 5 H), 1.40 – 1.32 (m, 4 H).

[14] E. Boseggia, M. Gatos, L. Lucatello, F. Mancin, S. Moro, M. Palumbo, C. Sissi, P. Tecilla, U. Tonellato and G. Zagotto, *J. Am. Chem. Soc.*, 2004, **126**, 4543.

6-((4-Methoxybenzyl)oxy)hexyl pivalate, **14**:



A flame dried 25 mL round bottom flask, equipped with a magnetic stir bar was charged with **26** (640 mg, 2.7 mmol), Et_3N (810 mg, 8.0 mmol), DMAP (33 mg, 0.27 mmol), and dry DCM (15 mL). The mixture was then treated with trimethylacetyl chloride (390 mg, 3.22 mmol) and stirred at room temperature for 2 hours. The mixture was poured into a separatory funnel containing 25 mL of DCM and 25 mL of H_2O. The layers were separated and the aqueous layer was extracted with DCM (2 x 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (9:1, hexanes/EtOAc) to afford **14** (630 mg, 73%) as a colorless oil (2 h reaction time).

R_f (EtOAc/hexane 1:9): 0.29;

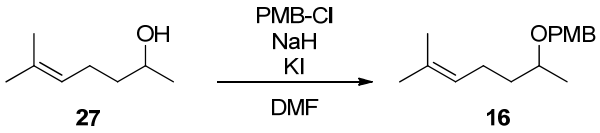
IR (neat): 2936, 2860, 1723, 1612, 1513, 1480, 1286, 1247, 1161, 1095, 910, 732 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.26 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 4.43 (s, 2 H), 4.04 (t, J = 6.5 Hz, 2 H), 3.80 (s, 3 H), 3.43 (t, J = 7.0 Hz, 2 H), 1.65 – 1.57 (m, 4 H), 1.43 – 1.31 (m, 4 H), 1.19 (s, 9 H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 178.3, 158.9, 130.5, 129.0, 113.5, 72.3, 69.7, 64.1, 55.0, 38.5, 29.5, 28.4, 27.0, 25.7, 25.6;

HRMS (ESI) *m/z* calculated for $C_{19}H_{30}NaO_4^+$ ($[M+Na]^+$) 345.4042, found 345.2033.

1-Methoxy-4-(((6-methylhept-5-en-2-yl)oxy)methyl)benzene, **16**:



A flame dried 50 mL round bottom flask, equipped with a magnetic stir bar was charged with **27** (400 mg, 3.1 mmol), KI (27 mg, 0.16 mmol) and dry DMF (30 mL) and cooled to 0 ºC. The mixture was then treated with a 60% dispersion of NaH in mineral oil (140 mg, 3.4 mmol) and stirred at room temperature for 30 minutes. PMB-Cl (540 mg, 3.43 mmol) was then added dropwise and the mixture stirred at room temperature for 12 hours. The mixture was poured into a separatory funnel containing 25 mL of EtOAc and 25 mL of H_2O. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (19:1, hexanes/EtOAc) to afford **16** (640 mg, 82%) as a colorless oil (12 h reaction time).

R_f (EtOAc/hexane 1:19): 0.60;

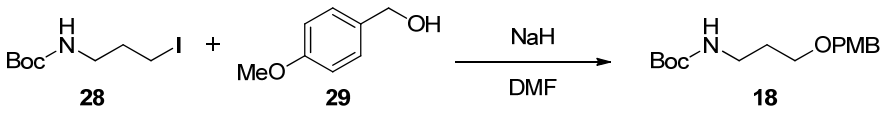
IR (neat): 2966, 2927, 2858, 1613, 1512, 1454, 1374, 1245, 1171, 1079, 1037, 820 cm^{-1};

^1H NMR ($CDCl_3$, 400 MHz): δ 7.27 (d, J = 8.8 Hz, 2 H), 6.87 (d, J = 8.8 Hz, 2 H), 5.10 (br. t, J = 7.2 Hz, 1 H), 4.49 (d, J = 11.2 Hz, 1 H), 4.38 (d, J = 11.2 Hz, 1 H), 3.80 (s, 3 H), 3.53 – 3.46 (m, 1 H), 2.06 (q, J = 7.6 Hz, 1 H), 1.68 (s, 3 H), 1.66 – 1.59 (m, 1 H), 1.61 (s, 3 H), 1.45 – 1.40 (m, 1 H), 1.18 (d, J = 6.0 Hz, 3 H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.9, 131.2, 131.1, 129.0, 124.3, 113.5, 74.0, 69.8, 55.0, 36.6, 25.5, 24.0, 19.5, 17.5;

HRMS (ESI) *m/z* calculated for $C_{16}H_{24}NaO_2^+$ ($[M+Na]^+$) 271.1674, found 271.1508.

tert-Butyl (3-((4-methoxybenzyl)oxy)propyl)carbamate, **18**:



A flame dried 50 mL round bottom flask, equipped with a magnetic stir bar was charged with **29** (290 mg, 2.1 mmol), and dry DMF (15 mL) and cooled to 0 ºC. The mixture was then treated with a 60% dispersion of NaH in mineral oil (93 mg, 2.3 mmol) and stirred at room temperature for 30 minutes. **28**[15] (550 mg, 1.9 mmol) in DMF (5 mL) was then added dropwise and the mixture stirred at room temperature for 18 hours. The mixture was poured into a separatory funnel containing 25 mL of EtOAc and 25 mL of H_2O. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (85:15, hexanes/EtOAc) to afford **18** (320 mg, 57%) as a colorless oil (18 h reaction time).

R_f (EtOAc/hexane 15:85): 0.37;

IR (neat): 3350, 2975, 2933, 2864, 1697, 1612, 1512, 1365, 1245, 1171, 1096, 1035, 820, 617 cm^{-1};

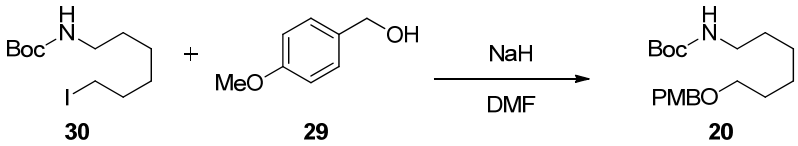
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.25 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.5 Hz, 2 H), 4.87 (br. s, 1 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.51 (t, J = 6.0 Hz, 2 H), 3.23 (br. q, J = 6.0 Hz, 2 H), 1.80 – 1.75 (m, 2 H), 1.43 (s, 9 H);

^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.1, 155.9, 130.3, 129.1, 113.7, 78.8, 72.6, 68.2, 55.1, 38.6, 29.5, 28.3;

HRMS (ESI) *m/z* calculated for $C_{16}H_{25}NNaO_4^+$ ($[M+Na]^+$) 318.1681, found 318.1675.

[15] K. T. Ziebart, S. M. Dixon, B. Avila, M. H. El-Badri, K. G. Guggenheim, M. J. Kurth and M. D. Toney, *J. Med. Chem.*, 2010, **53**, 3718.

tert-Butyl (6-((4-methoxybenzyl)oxy)hexyl)carbamate, **20**:



30 **29** **20**

A flame dried 50 mL round bottom flask, equipped with a magnetic stir bar was charged with **29** (2.5 g, 19 mmol) and dry DMF (120 mL) and cooled to 0 ºC. The mixture was then treated with a 60% dispersion of NaH in mineral oil (810 mg, 20 mmol) and stirred at room temperature for 30 minutes. **30**[16] (5.5 g, 17 mmol) in DMF (40 mL) was then added dropwise and the mixture stirred at room temperature for 12 hours. The mixture was poured into a separatory funnel containing 50 mL of EtOAc and 50 mL of H_2O. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 75 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (4:1, hexanes/EtOAc) to afford **20** (3.6 g, 63%) as a colorless oil (12 h reaction time).

R_f (EtOAc/hexane 1:3): 0.42;

IR (neat): 3350, 2934, 2859, 1700, 1612, 1512, 1365, 1246, 1171, 1094, 908, 729 cm^{-1};

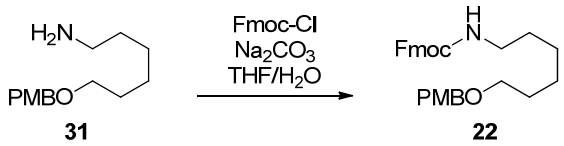
^1H NMR ($CDCl_3$, 400 MHz): δ 7.25 (d, J = 8.0 Hz, 2 H), 6.87 (d, J = 8.0 Hz, 2 H), 4.48 (br. s, 1 H), 4.23 (s, 2 H), 3.80 (s, 3 H), 3.43 (t, J = 6.4 Hz, 2 H), 3.10 (br. q, J = 6.0 Hz, 2 H), 1.63 – 1.56 (m, 2 H), 1.50 – 1.41 (m, 2 H), 1.44 (s, 9 H), 1.39 – 1.29 (m, 4 H);

^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.1, 155.9, 130.7, 129.2, 113.7, 72.5, 70.0, 55.2, 40.5, 30.0, 29.7, 28.4, 26.6, 25.9;

HRMS (ESI) *m/z* calculated for $C_{19}H_{31}NNaO_4^+$ ($[M+Na]^+$) 360.2151, found 360.2145.

[16] S. Isomura, P. Wirsching and K. D. Janda, *J. Org. Chem.*, 2001, **66**, 4115.

(9H-Fluoren-9-yl)methyl (6-((4-methoxybenzyl)oxy)hexyl)carbamate, **22**:



A 25 mL round bottom flask, equipped with a magnetic stir bar was charged with **31** (450 mg, 1.9 mmol), Na_2CO_3 (200 mg, 1.9 mmol), THF (8 mL) and H_2O (2 mL) and treated with Fmoc-Cl (490 mg, 1.9 mmol). The mixture was stirred at room temperature for 2 hours. The mixture was poured into a separatory funnel containing 50 mL of EtOAc and 50 mL of H_2O. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (3:1, hexanes/EtOAc) to afford **22** (770 mg, 89%) as a colorless oil (12 h reaction time).

R_f (EtOAc/hexane 1:3): 0.23;

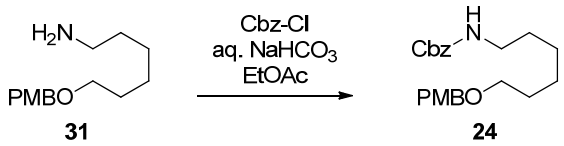
IR (neat): 3337, 3066, 2935, 2858, 1708, 1512, 1449, 1245, 1034, 907, 272, 647 cm^{-1};

^1H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J* = 7.0 Hz, 2 H), 7.59 (d, *J* = 7.0 Hz, 2 H), 7.40 (t, *J*= 7.0 Hz, 2 H), 7.31 (dt, *J* = 7.0, 1.0 Hz, 2 H), 7.26 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 4.73 (br. s, 1 H), 4.43 (s, 3 H), 4.40 (d, *J* = 6.8 Hz, 2 H), 4.22 (t, *J* = 6.8 Hz, 1 H), 3.80 (s, 3 H), 3.43 (t, *J*= 6.5 Hz, 2 H), 3.18 (q, *J* = 6.5 Hz, 2 H), 1.63 – 1.57 (m, 2 H), 1.54 – 1.48 (m, 2 H), 1.41 – 1.30 (m, 4 H);

^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.0, 156.3, 144.0, 141.2, 130.6, 129.2, 127.6, 127.0, 125.0, 119.9, 113.7, 72.5, 69.9, 66.4, 55.2, 47.2, 40.9, 29.8, 29.6, 26.5, 25.8;

HRMS (ESI) *m/z* calculated for $C_{29}H_{33}NNaO_4^+$ ($[M+Na]^+$) 482.2307, found 482.2292.

Benzyl (6-((4-methoxybenzyl)oxy)hexyl)carbamate, **24**:



31 **24**

A 50 mL round bottom flask, equipped with a magnetic stir bar was charged with **XX** (290 mg, 1.2 mmol), sat. aq. $NaHCO_3$ (16 mL), EtOAc (29 mL) and cooled to 0 ºC. The biphasic mixture was treated with benzyl chloroformate (450 mg, 2.7 mmol) and stirred at 0 ºC for 1.5 hours and warmed to room temperature for 5 hours. The layers were then separated. The aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (3:7, hexanes/EtOAc) to afford **24** (340 mg, 76%) as a colorless oil (6.5 h reaction time).

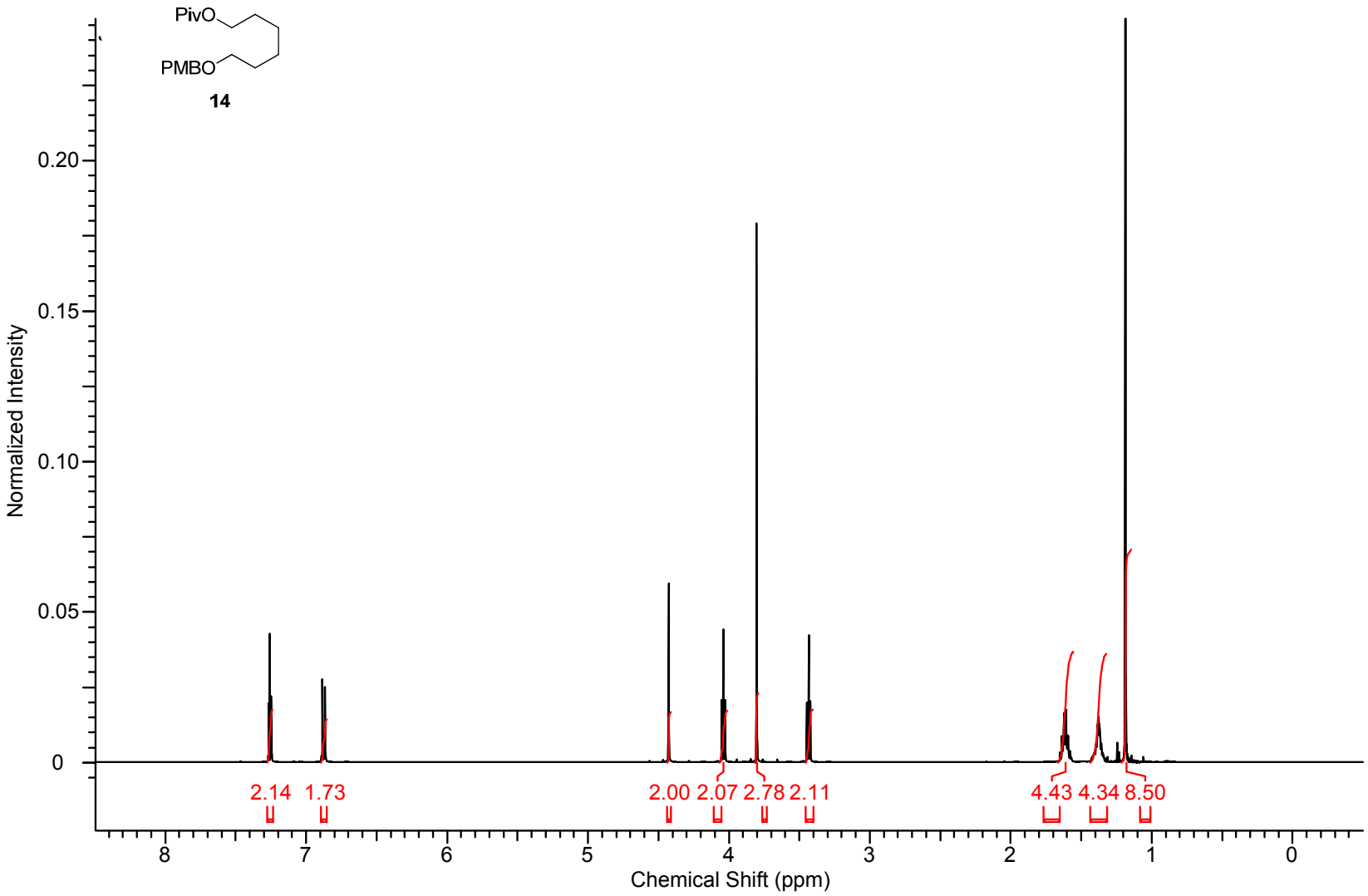
R_f (EtOAc/hexane 1:3): 0.35;

IR (neat): 3326, 2934, 2857, 1700, 1611, 1512, 1454, 1245, 1094, 1033, 822, 697 cm^{-1};

^1H NMR ($CDCl_3$, 400 MHz): δ 7.36 – 7.31 (m, 5 H), 7.26 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 5.09 (s, 2 H), 4.73 (br. s, 1 H), 4.42 (s, 2 H), 3.80 (s, 3 H), 3.42 (t, *J* = 6.4 Hz, 2 H), 3.18 (q, *J* = 6.4 Hz, 2 H), 1.63 – 1.56 (m, 2 H), 1.53 – 1.46 (m, 2 H), 1.41 – 1.30 (m, 4 H),

^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.0, 156.3, 136.6, 130.6, 129.2, 128.4, 128.0, 128.0, 113.7, 72.5, 69.9, 66.5, 55.2, 40.9, 29.8, 29.6, 26.5, 25.8;

HRMS (ESI) *m/z* calculated for $C_{22}H_{29}NNaO_4^+$ ($[M+Na]^+$) 394.1994, found 394.2012.


PivO
PMBO
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0.10
0.05
0
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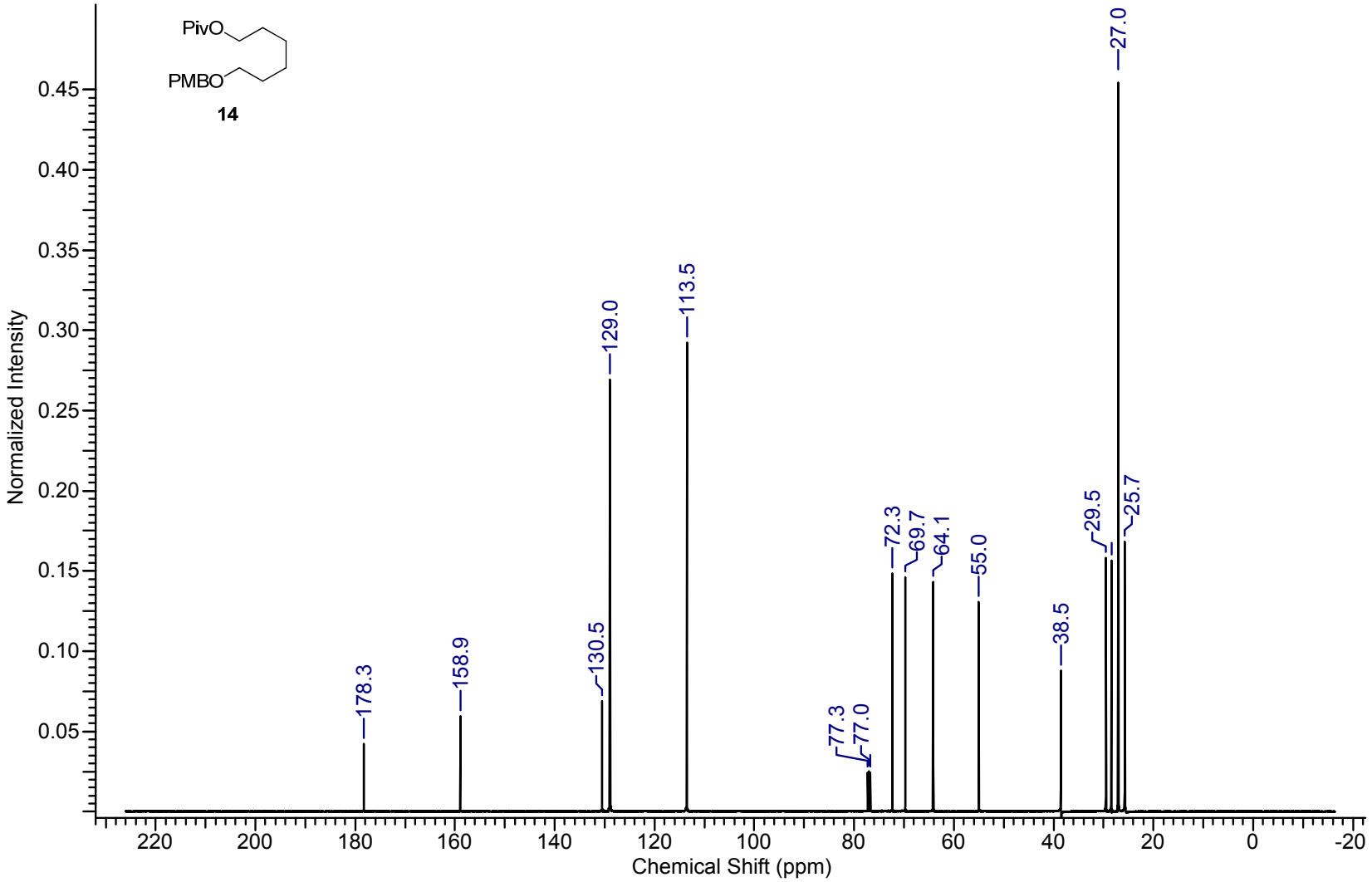
1.73
2.00
2.07
2.78
2.11
4.43
4.34
8.50
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


PivO
PMBO
14
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0.30
0.25
0.20
0.15
0.10
0.05
178.3
158.9
130.5
129.0
113.5
77.3
77.0
72.3
69.7
64.1
55.0
38.5
29.5
27.0
25.7
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200
180
160
140
120
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80
60
40
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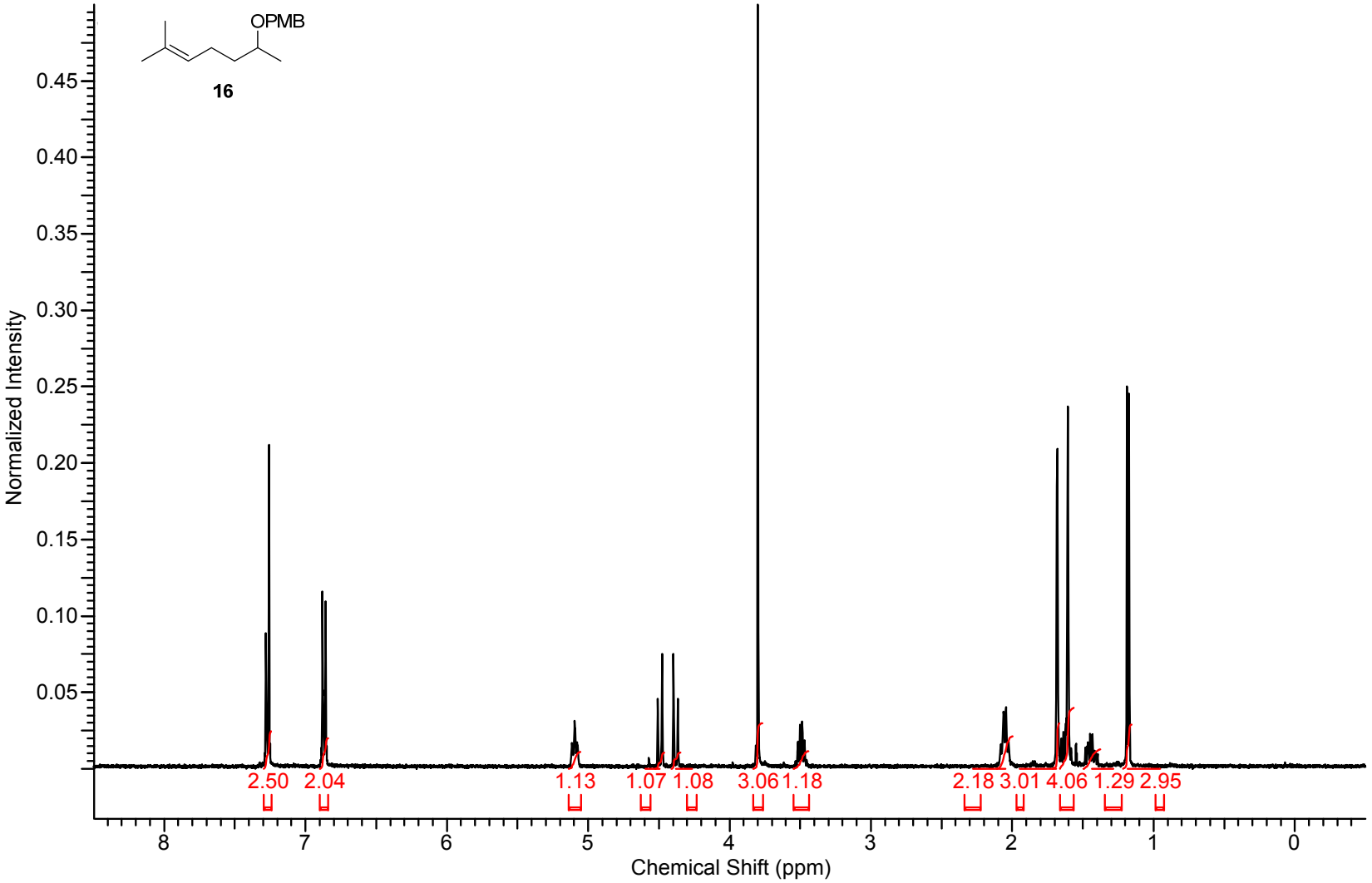
0
-20
Chemical Shift (ppm)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2.50
2.04
1.13
1.07
1.08
3.06
1.18
2.18
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4.06
1.29
2.95
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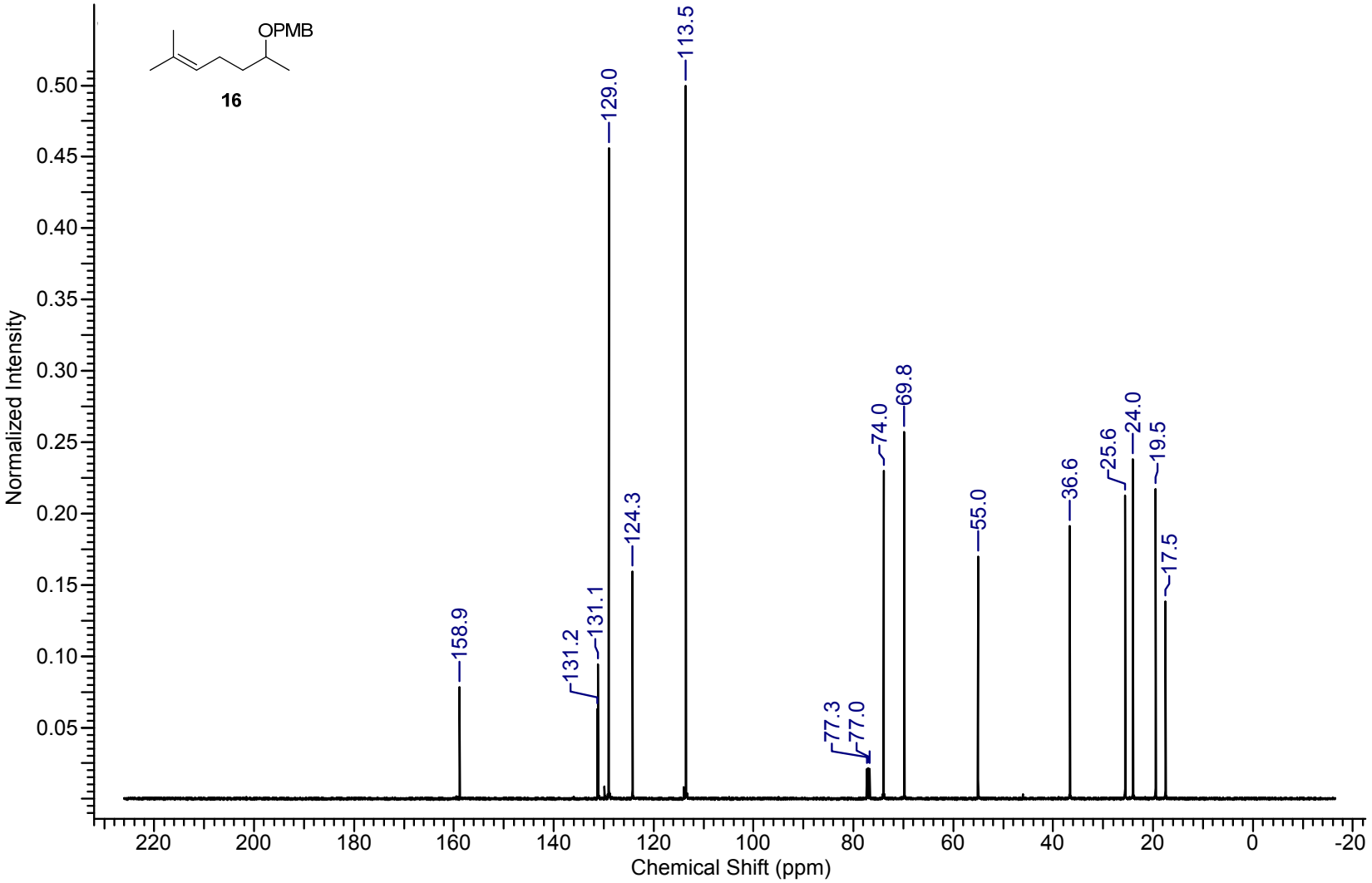
5
4
3
2
1
0
Chemical Shift (ppm)


OPMB
16
Normalized Intensity
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0.20
0.15
0.10
0.05
158.9
131.2
131.1
129.0
124.3
113.5
77.3
77.0
74.0
69.8
55.0
36.6
25.6
24.0
19.5
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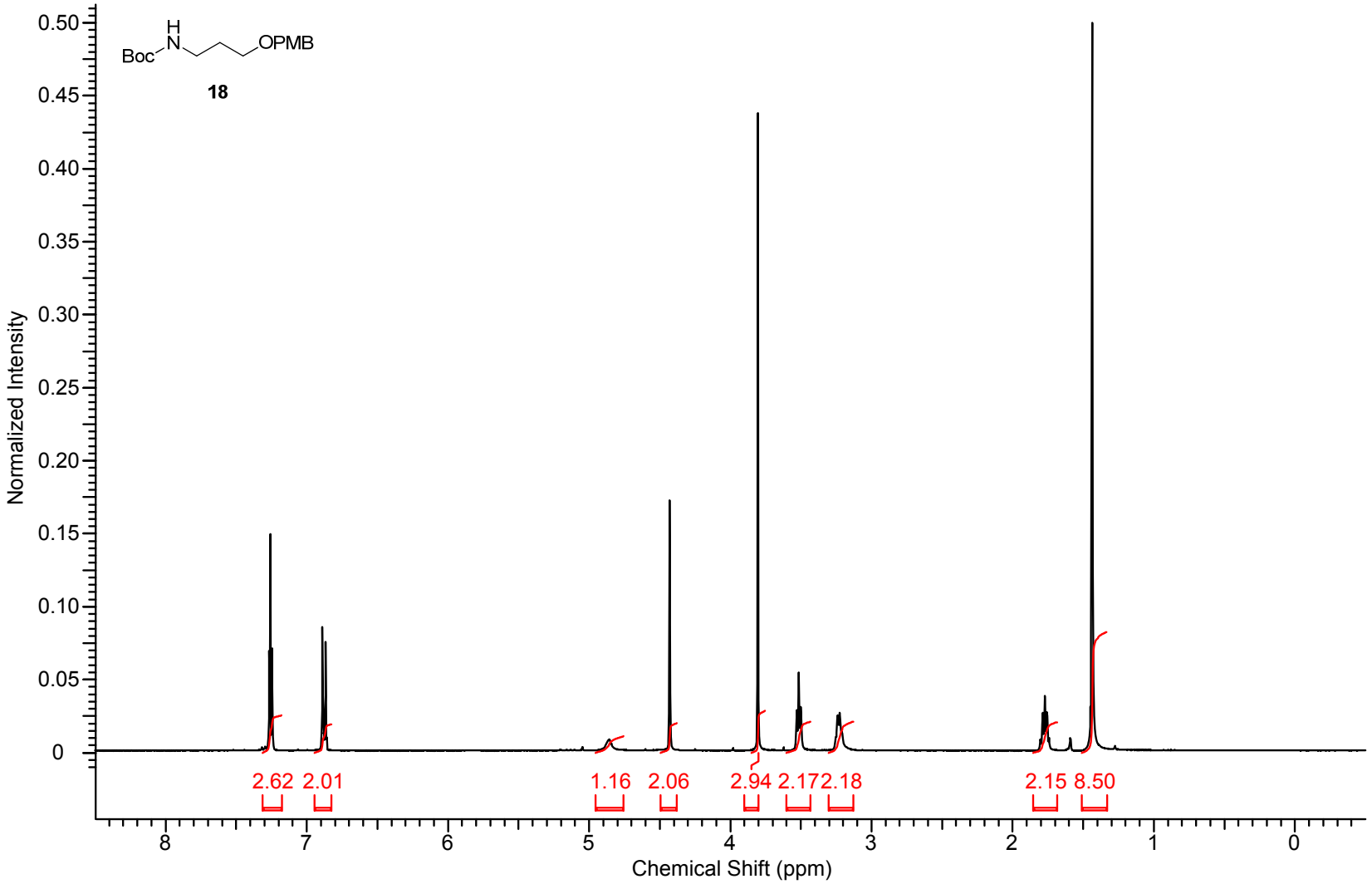
80
60
40
20
0
-20
Chemical Shift (ppm)


Boc
H
N
OPMB
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0.15
0.10
0.05
0
2.62
2.01
1.16
2.06
2.94
2.17
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2.15
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8
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5
4
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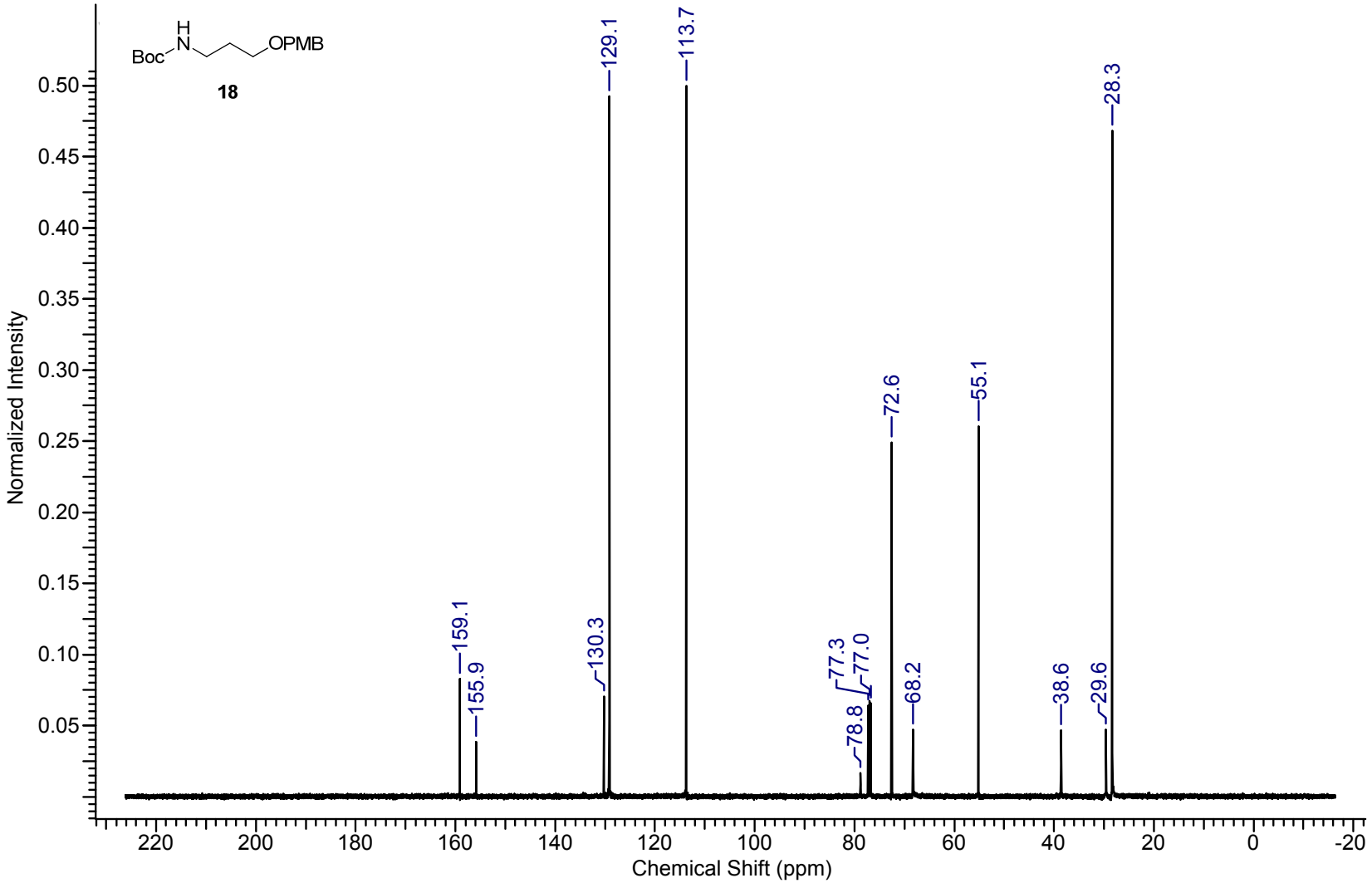
Chemical Shift (ppm)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H
N
OPMB
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0.25
0.20
0.15
0.10
0.05
159.1
155.9
130.3
129.1
113.7
77.3
77.0
78.8
72.6
68.2
55.1
38.6
29.6
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200
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140
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80
60
40
20
0
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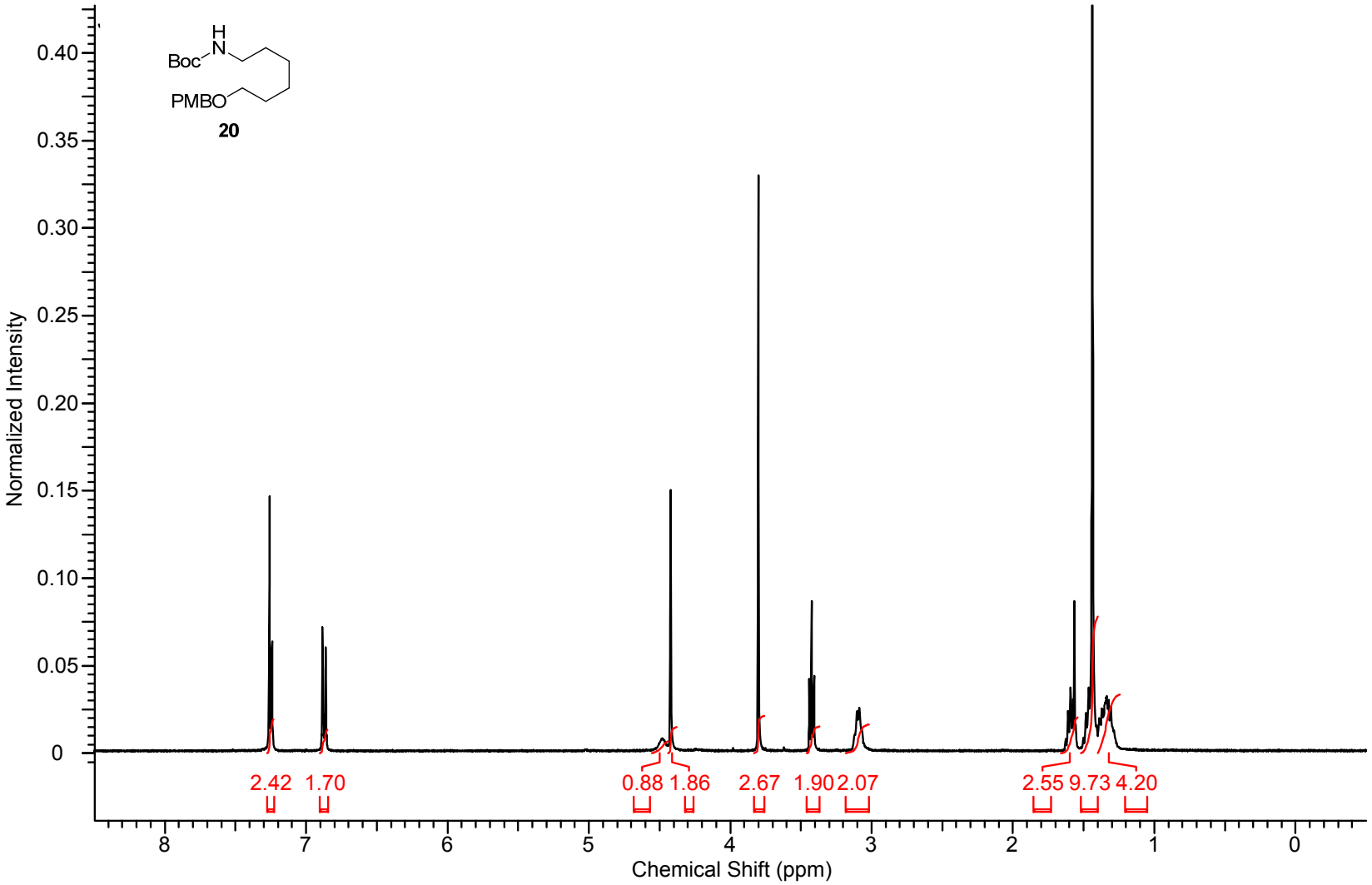
Chemical Shift (ppm)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Boc
PMBO
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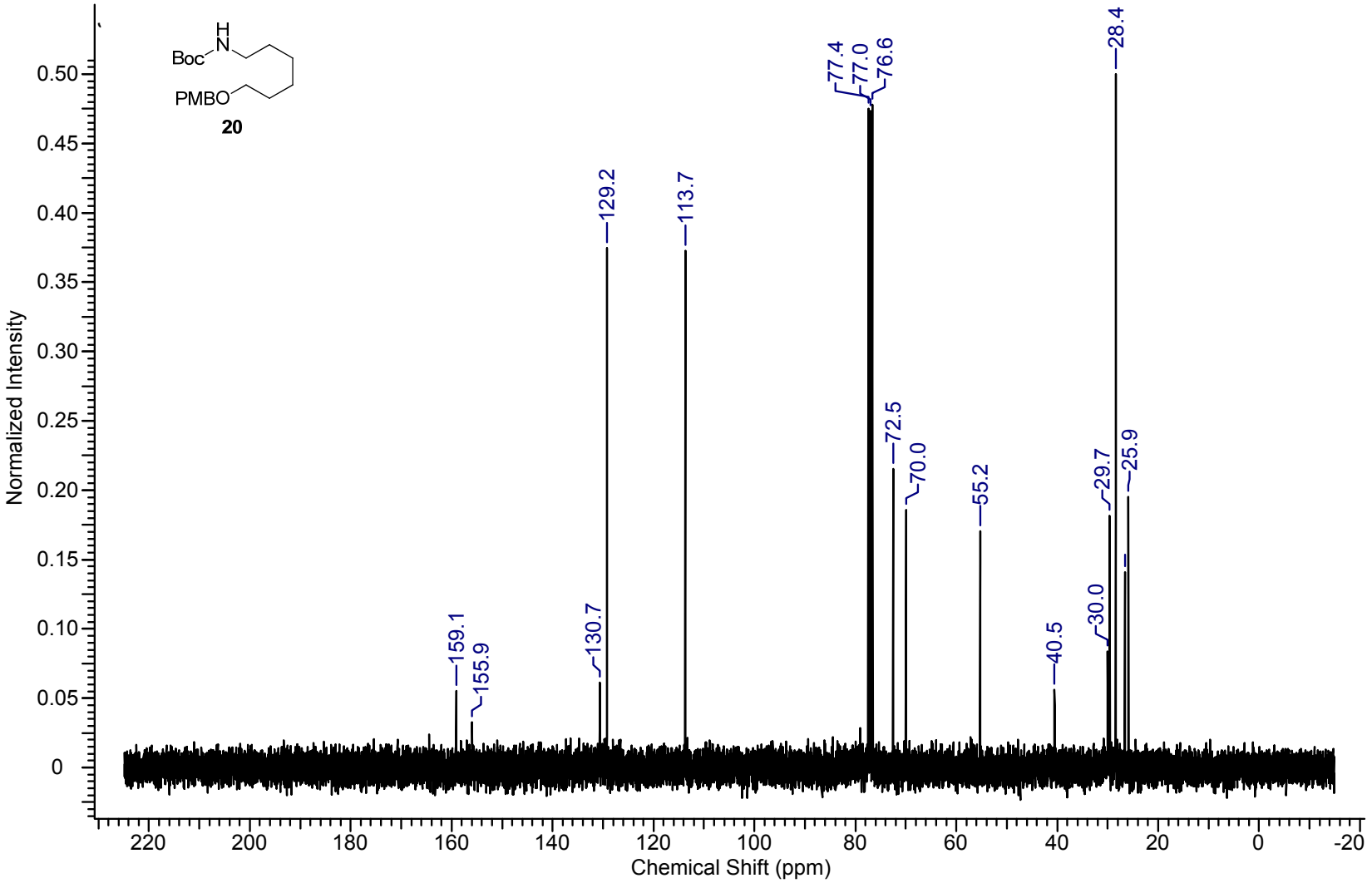
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PMBO
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0.10
0.05
0
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200
180
160
140
120
100
80
60
40
20
0
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Chemical Shift (ppm)
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155.9
130.7
129.2
113.7
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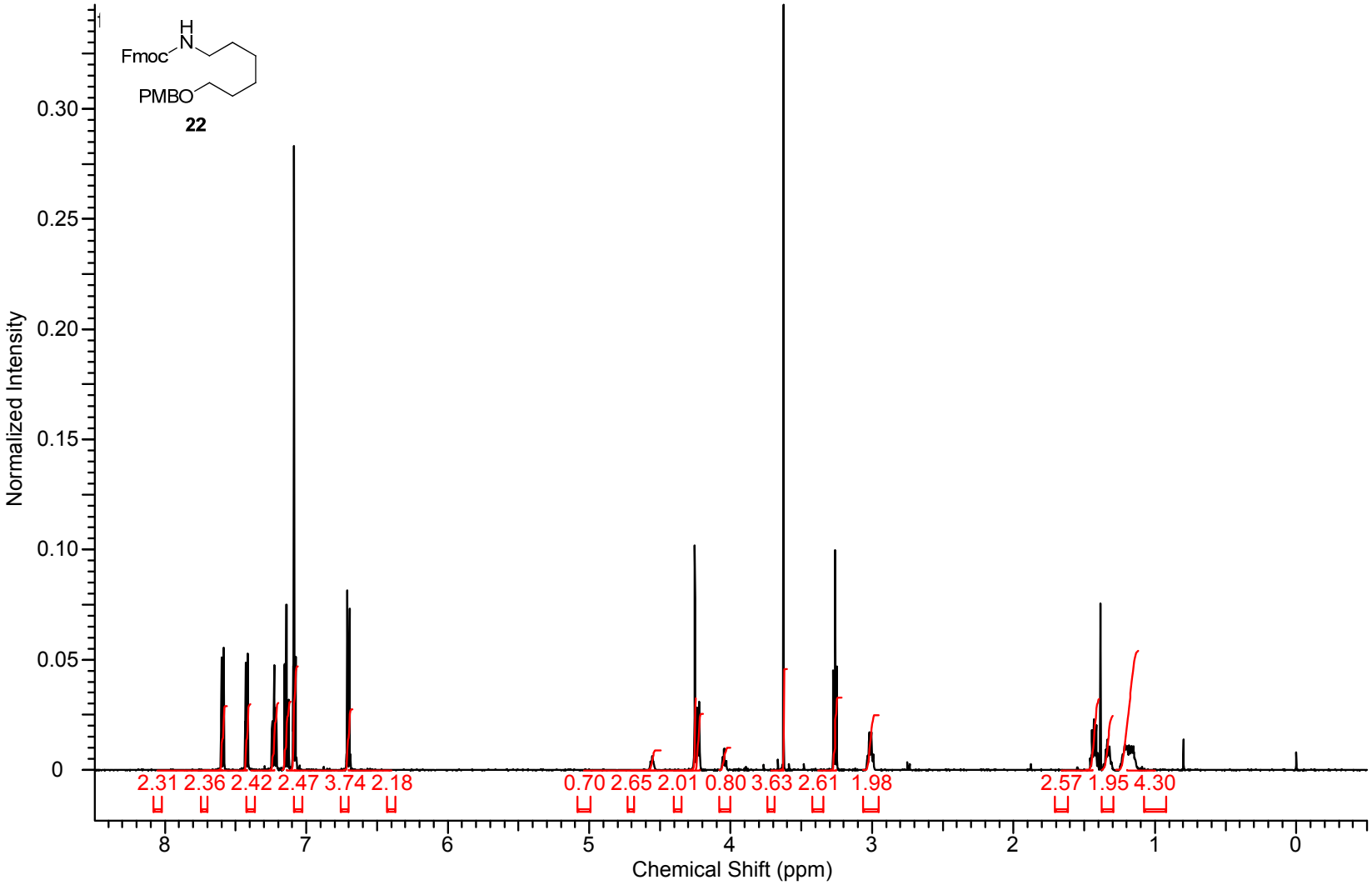
40.5
30.0
29.7
28.4
25.9


Fmoc
H
N
PMBO
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Normalized Intensity
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0.10
0.05
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0.70 2.65 2.01 0.80 3.63 2.61 1.98
2.57 1.95 4.30
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5
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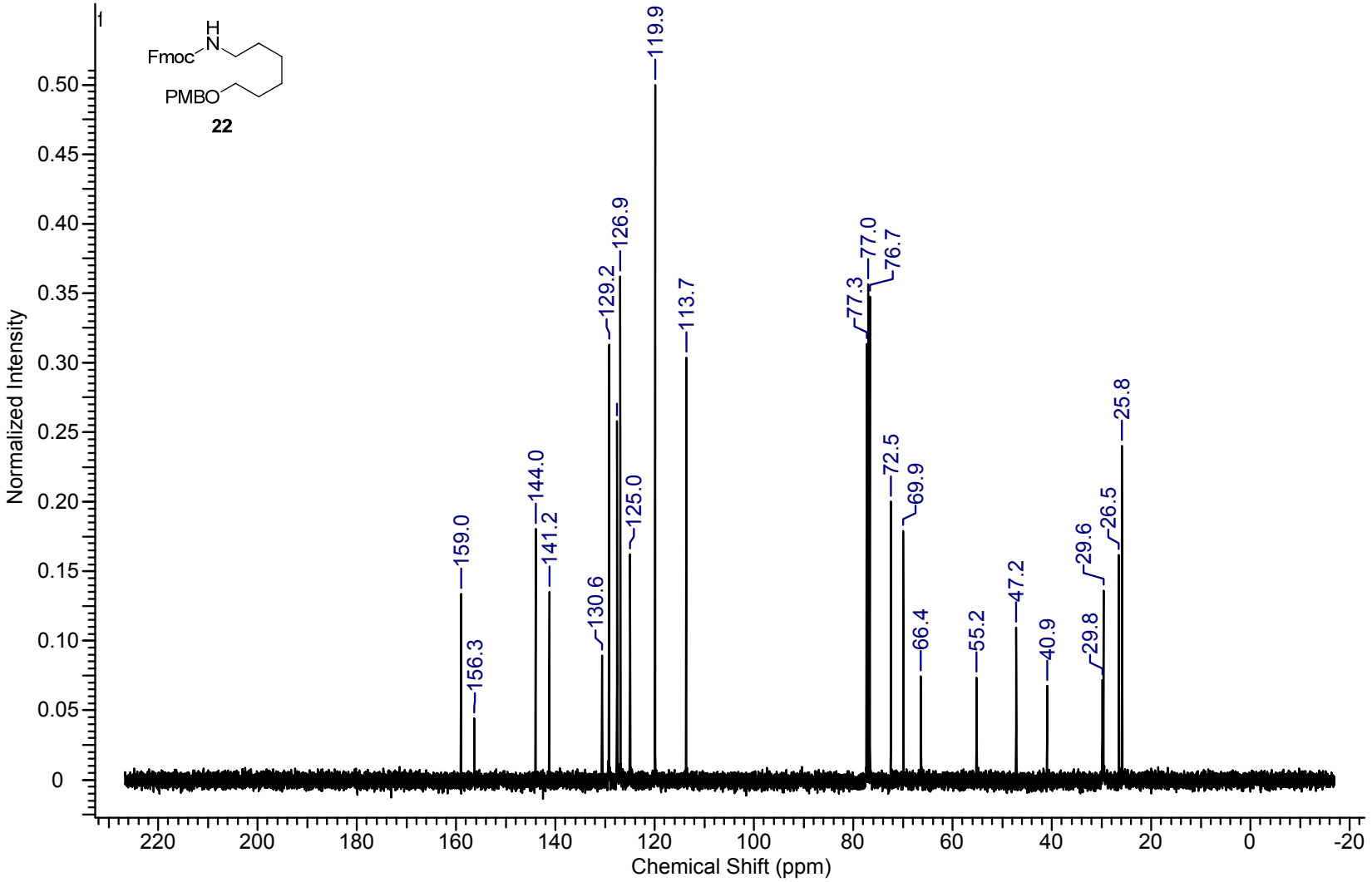
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PMBO
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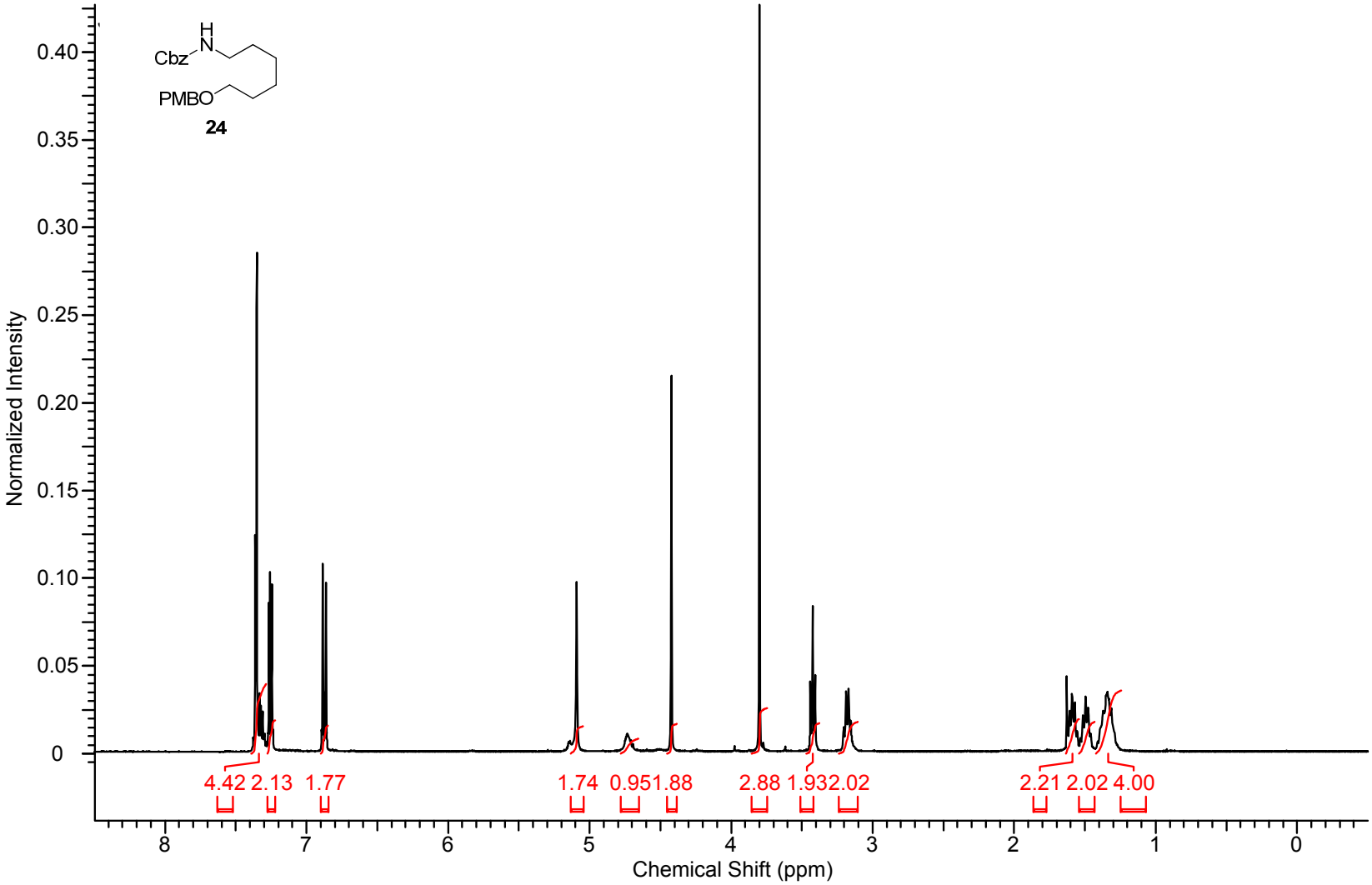
25.8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0.05
0
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1.74 0.95 1.88
2.88 1.93 2.02
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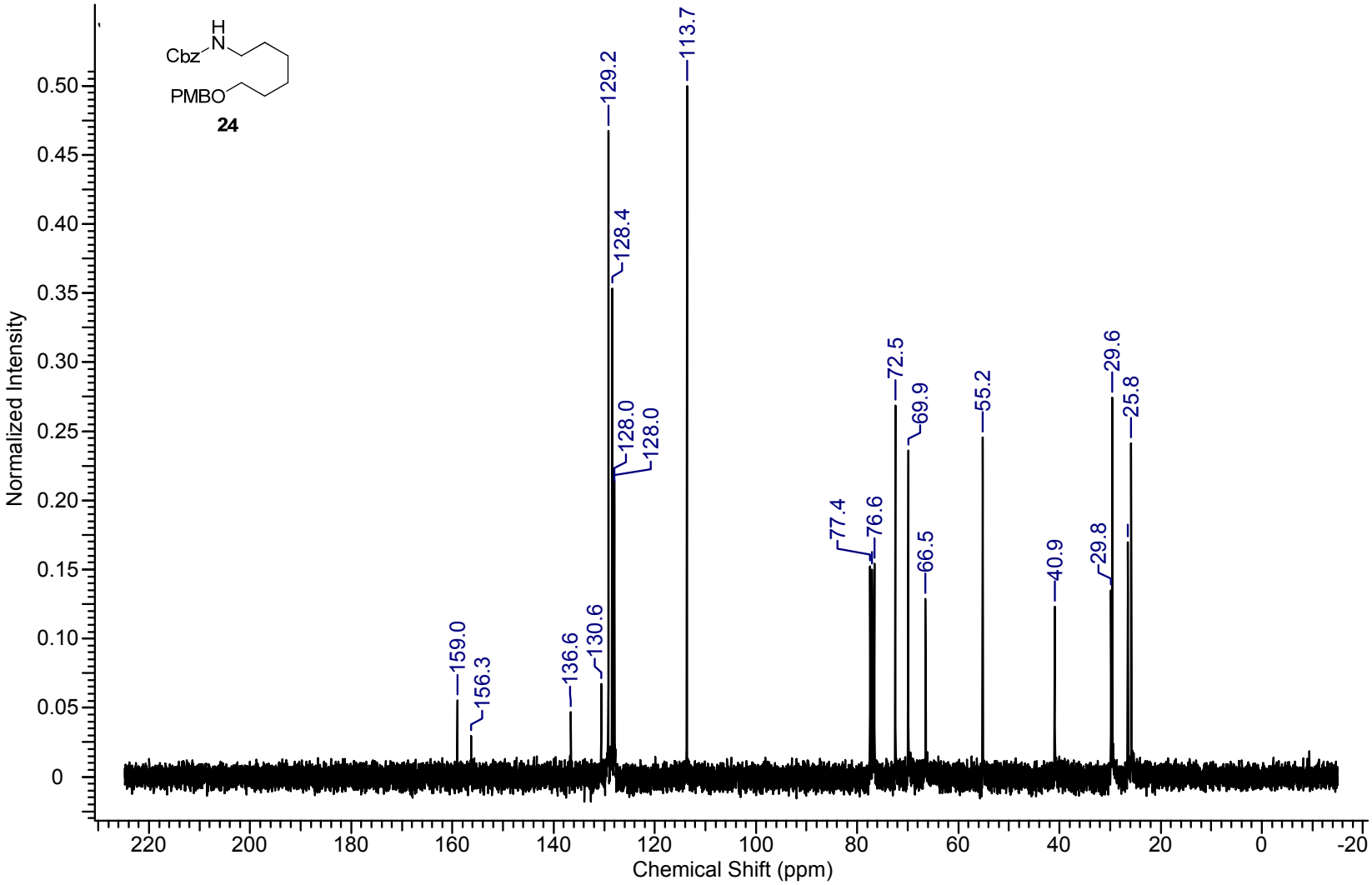
Cbz
N
H
PMBO
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Normalized Intensity
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0.10
0.05
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220
200
180
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120
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60
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-20
Chemical Shift (ppm)
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72.5
69.9
66.5
55.2
40.9
29.8
29.6
25.8