Supporting Information

Oxidative Cross-Coupling Reaction by Scandium Catalysis for Synthesis of α-Alkyl α-Amino Acid Esters Derivatives

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Contents:

General

All reactions involving air- or moisture-sensitive reagents were carried out under an argon atmosphere. All solvents were distilled under Ar before use. All chemicals were purchased from Aldrich and J&K Chemical and used without further purification. Thin-layer chromatography (TLC) was performed using 60 mesh silica gel plates

visualized with short-wavelength UV light (254 nm). Silica gel 60 (230 - 400 mesh) was used for column chromatography. ^{1}H and ^{13}C NMR spectra were recorded using $CDCl_3$ solvent on a Bruker 400 MHz spectrometer at 298 K. The chemical shift is given indimensionless δ values and is frequency referenced relative to TMS in ^{1}H and ^{13}C NMR spectroscopy.

Experimental Section

1. Synthesis of Ethyl *N*-Aryl Glycine Esters 1a[1]

To the solution of ethyl bromoacetate (20.0 mmol) in anhydrous ethanol (3.0 mL) was added substituted benzenamine (20.0 mmol) and anhydrous NaOAc (20.0 mmol). The reaction mixture was refluxed for 6-10 h under N_2. Then, the mixture was filtered, and the filtrate was cooled at ice bath to precipitate. The precipitation was recrystallized from ethanol-hexane, giving the desired ethyl N-aryl glycine ester **1a**.

2. Synthesis of 4a[2]

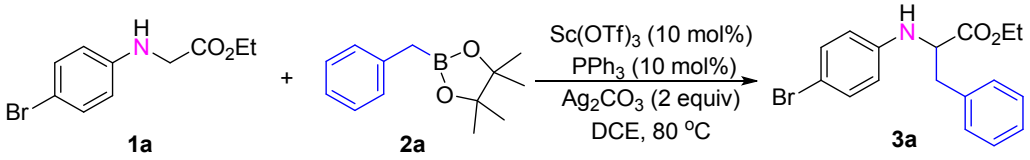
2-Bromoacetyl bromide (2.4 g, 1.2 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a mixture of $MeNH_2$ (1.0 g, 30 wt% in H_2O, 1.0 mmol) and K_2CO_3 (1.66 g, 1.2 mmol) in CH_2Cl_2/H_2O (30 mL/10 mL) at 0 °C. The mixture was then allowed to warm up to room temperature and stirred for 6 h. Then, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3*5 mL). The organic layers were combined and dried over Na_2SO_4, and CH2Cl2 was removed in vacuo. Subsequently, EtOH (5 mL), *p*-anisidine (1.23 g, 1 mmol), and NaOAc (0.84 g, 1 mmol) were added to the residue. The resulting mixture was refluxed for 6 h and was filtered. The solvent of the filtrate was removed in vacuo. Recrystallization (CH_2Cl_2/hexanes) gave the pure product 2-(4-methoxyphenylamino)-*N*-methylacetamide.

$SOCl_2$ (3.6 g, 30 mmol) was added slowly to EtOH (30mL) at 0 °C. After stirring at this temperature for 10 min, glycine (0.75 g, 10 mmol) was added to the solution. Then, the reaction was stirred at 70 °C for 3 h. EtOH was removed in vacuo. The resulting solid was then mixed with CH_2Cl_2 (30 mL) and NEt_3 (2.2 g, 22 mmol). The reaction mixture was cooled to -78 °C, and $BrCH_2COBr$ (2.0 g, 10 mmol) was added dropwise to the solution at this temperature. The solution was allowed to warm up to

1 J. Xie and Z-Z. Huang, *Angew. Chem. Int. Ed.* **2010**, *49*, 10181.
2 L. Zhao, O. Baslé and C-J. Li, *Proc. Natl. Acad. Sci. USA*, **2009**, *106*, 4107.

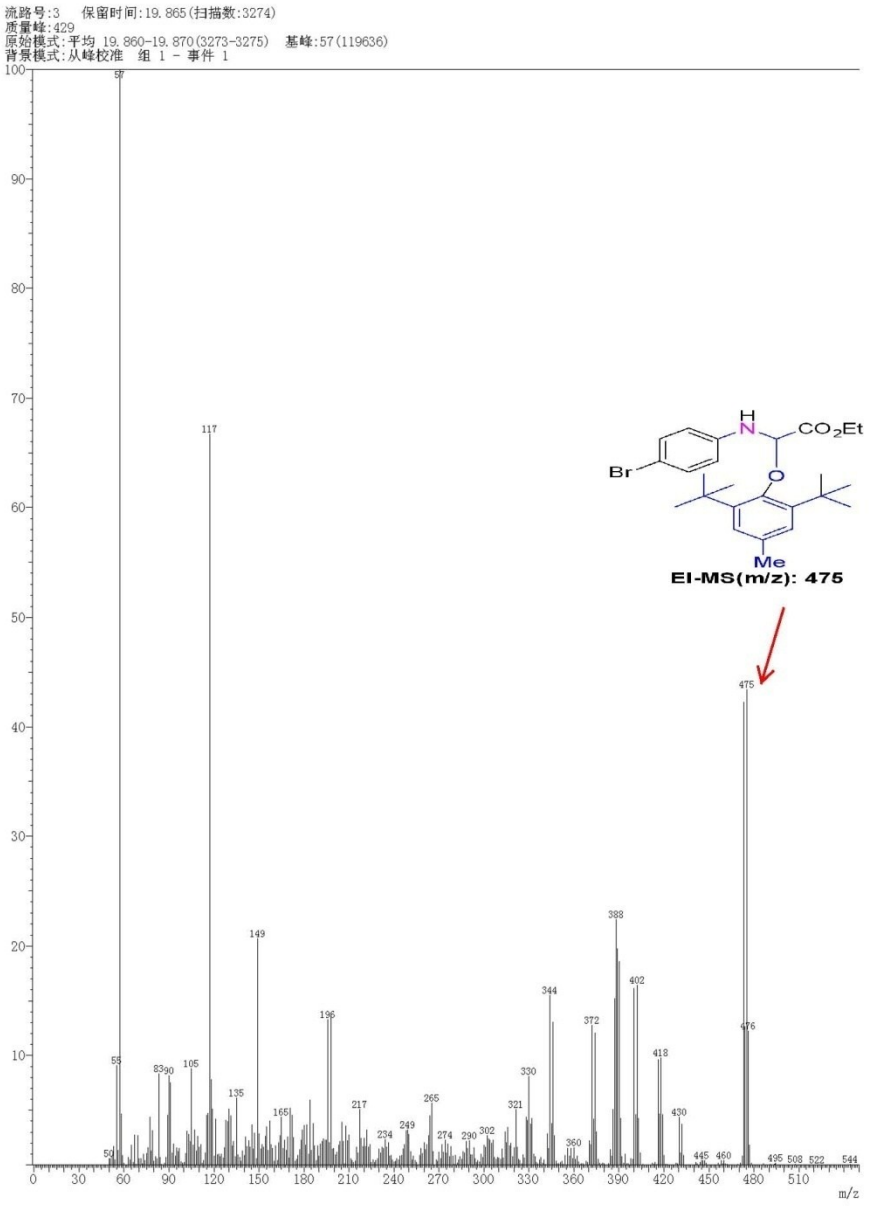
room temperature and the stirring was continued for 6 h. After that, the solution was washed with H_2O (10 mL). The organic layer was dried over Na_2SO_4, and CH_2Cl_2 was removed in vacuo to afford $BrCH_2CONHCH_2CO_2Et$ (1.8 g, 81%). NaOAc (0.50 g, 6 mmol), *p*-anisole (0.74 g, 6 mmol), and $BrCH_2CONHCH_2CO_2Et$ (1.1 g, 5 mmol) were successively added to EtOH (4 mL). The reaction tube was heated at 80 °C for 6 h. EtOH was removed in vacuo and the residue was dissolved in CH_2Cl_2 (20 mL) and washed with H_2O (5 mL). The organic layer was dried over Na_2SO_4, and CH_2Cl_2 was removed in vacuo. Flash column chromatography on silica gel by using ethyl acetate/hexanes (1:1) furnished the final product *N*-(*N*-*p*-methoxyphenylglycyl)-glycine ethyl ester.

3. General procedure for synthesis of 3a-3p, and 4aa



An oven-dried 10 mL screw-capped vial containing *N*-aryl *α*-imino ester **1a** (0.3 mmol, 1.0 equiv), Ag_2CO_3 (0.6 mmol, 2.0 equiv), $Sc(OTf)_3$ (0.03 mmol, 0.1 equiv), PPh_3 (0.03 mmol, 0.1 equiv), benzylboronic acid pinacol ester **2a** (0.36 mmol, 1.2 equiv) and purged with Ar three times. Then, DCE (2.50 mL) was added *via* syringe, and heated to 80°C in an oil bath until the starting material has disappeared for 20 hours (monitored by TLC). And then the solvent was removed in vacuo and residue was purified on a silica gel column using EA/PE as eluent to afford the desired product **3aa**.

4. key intermediate was detected by GC-MS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EI-MS(m/z): 475
m/z

质谱

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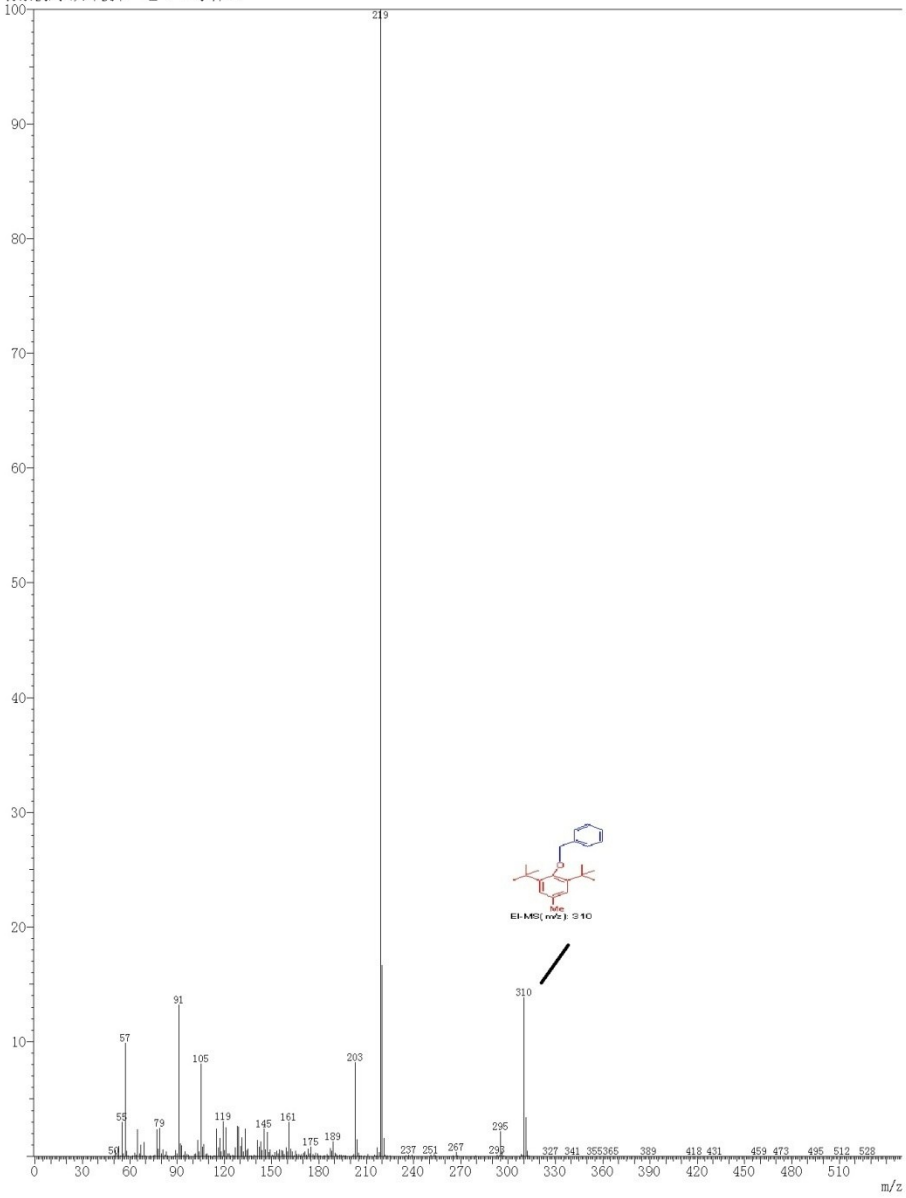
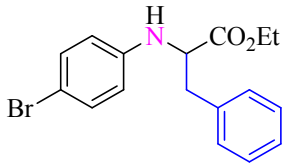
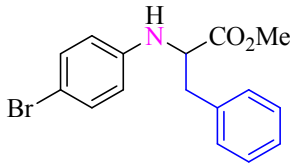


5. Analytical Data of Products



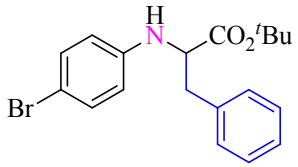
3a

Ethyl 2-((4-bromophenyl)amino)-3-phenylpropanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.18 (m, 5H), 7.14 (d, *J* = 6.8 Hz, 2H), 6.45 (d, *J* = 8.7 Hz, 2H), 4.34 – 4.16 (m, 2H), 4.16 – 4.03 (m, 2H), 3.19 – 2.98 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.67, 145.35, 136.01, 131.94, 129.19, 128.43, 126.97, 115.03, 109.89, 61.16, 57.54, 38.34, 14.05. **MS (ESI)**: found $[M+H]^+$ 348.2.



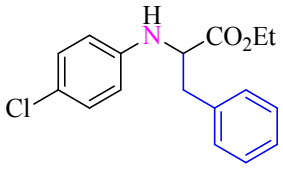
3b

Methyl 2-((4-bromophenyl)amino)-3-phenylpropanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 3H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 6.8 Hz, 2H), 6.46 (d, *J* = 8.8 Hz, 2H), 4.31 – 4.25 (m, 1H), 4.18 (d, *J* = 8.3 Hz, 1H), 3.67 (s, 3H), 3.17 – 3.05 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.19, 145.28, 135.93, 132.02, 129.15, 128.55, 127.08, 115.04, 110.03, 57.52, 52.16, 38.34. **MS (ESI)**: found $[M+H]^+$ 333.9.



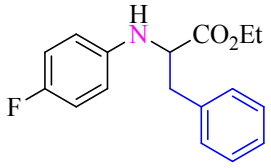
3c

tert-butyl 2-((4-bromophenyl)amino)-3-phenylpropanoate. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.21 (m, 6H), 7.19 (d, *J* = 6.6 Hz, 2H), 6.47 (d, *J* = 8.9 Hz, 2H), 4.18 (s, 2H), 3.09 (s, 2H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.86, 145.57, 136.29, 131.93, 129.42, 128.38, 126.92, 115.06, 109.74, 82.02, 57.93, 38.36, 27.90. **MS (ESI)**: found $[M+H]^+$ 376.0.



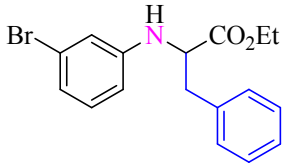
3d

Ethyl 2-((4-chlorophenyl)amino)-3-phenylpropanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 3H), 7.15 (d, *J* = 6.6 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.51 (d, *J* = 8.9 Hz, 2H), 4.29 (t, *J* = 6.2 Hz, 1H), 4.23 – 4.04 (m, 3H), 3.11 (t, *J* = 6.4 Hz, 2H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.81, 144.94, 136.05, 129.24, 129.13, 128.50, 127.03, 122.88, 114.61, 61.22, 57.70, 38.42, 14.09. **MS (ESI)**: found $[M+H]^+$ 303.8.



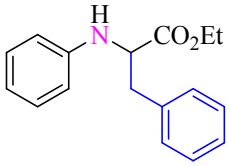
3e

Ethyl 2-((4-fluorophenyl)amino)-3-phenylpropanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (dt, *J* = 7.0, 5.1 Hz, 3H), 7.20 (d, *J* = 6.6 Hz, 2H), 6.90 (t, *J* = 8.7 Hz, 2H), 6.61 – 6.52 (m, 2H), 4.29 (t, *J* = 6.4 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.15-3.13 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.13, 156.24 (d, *J* = 236.1 Hz), 142.73, 142.71, 136.24, 129.24, 128.49, 126.99, 115.74 (d, *J* = 22.4 Hz), 114.62 (d, *J* = 7.5 Hz), 61.13, 58.47, 38.68, 14.09. **MS (ESI)**: found $[M+H]^+$ 287.8.



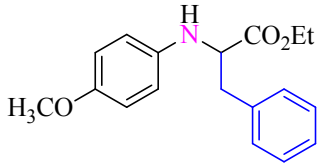
3f

Ethyl 2-((3-bromophenyl)amino)-3-phenylpropanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 3H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 6.6 Hz, 1H), 6.73 (s, 1H), 6.50 (d, *J* = 8.2 Hz, 1H), 4.33 – 4.24 (m, 2H), 4.20 – 4.09 (m, 2H), 3.17 – 3.06 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.62, 147.62, 135.97, 130.56, 129.26, 128.52, 127.07, 123.24, 121.05, 116.05, 112.12, 61.30, 57.31, 38.40, 14.12. **MS (ESI)**: found $[M+H]^+$ 348.0.



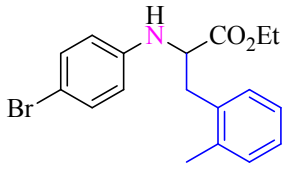
3g

Ethyl 3-phenyl-2-(phenylamino)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 7.17 (t, *J* = 7.8 Hz, 4H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 2H), 4.35 (t, *J* = 6.3 Hz, 1H), 4.26 – 3.95 (m, 3H), 3.16 – 3.08 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.11, 146.32, 136.31, 129.30, 129.28, 128.45, 126.93, 118.31, 113.52, 61.09, 57.66, 38.59, 14.10. **MS (ESI)**: found $[M+H]^+$ 269.8.



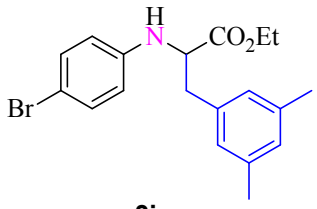
3h

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 1H), 7.18 (d, *J* = 6.7 Hz, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.57 (d, *J* = 8.9 Hz, 2H), 4.25 (t, *J* = 6.4 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 3.10 (d, *J* = 6.4 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.42, 152.77, 140.54, 136.54, 129.27, 128.43, 126.88, 115.25, 114.85, 77.32, 77.00, 76.68, 60.95, 59.01, 55.67, 38.90, 14.09. **MS (ESI)**: found $[M+H]^+$ 299.7.



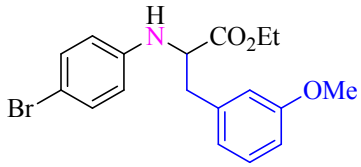
3i

Ethyl 2-((4-bromophenyl)amino)-3-(o-tolyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.9 Hz, 2H), 7.16 – 7.14 (m, 2H), 7.12 – 7.10 (m, 2H), 6.44 (d, *J* = 8.9 Hz, 1H), 4.24 (t, *J* = 7.0 Hz, 0H), 4.14 – 4.04 (m, 1H), 3.11 – 3.09 (m, 1H), 2.34 (s, 1H), 1.13 (t, *J* = 7.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.30, 145.63, 136.49, 134.62, 131.97, 130.52, 129.76, 127.14, 126.03, 115.11, 110.13, 61.21, 57.13, 36.48, 19.51, 14.01. **MS (ESI)**: found $[M+H]^+$ 361.9.



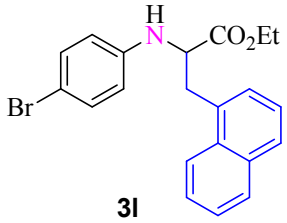
3j

Ethyl 2-((4-bromophenyl)amino)-3-(3,5-dimethylphenyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.9 Hz, 2H), 6.88 (s, 1H), 6.76 (s, 2H), 6.47 (d, *J* = 9.9 Hz, 2H), 4.25 (t, *J* = 5.9 Hz, 1H), 4.13 (d, 7.1 Hz, 3H), 3.11 – 2.93 (m, 2H), 2.27 (s, 6H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.92, 145.51, 137.97, 135.82, 131.97, 128.68, 127.03, 115.14, 109.95, 61.16, 57.68, 38.35, 21.23, 14.12. **MS (ESI)**: found $[M+H]^+$ 376.0.



3k

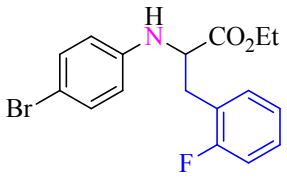
Ethyl 2-((4-bromophenyl)amino)-3-(3-methoxyphenyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.9 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.9 Hz, 1H), 6.74 (d, *J* = 8.9 Hz, 1H), 6.69 (s, 1H), 6.47 (d, *J* = 8.9 Hz, 2H), 4.28 (s, 1H), 4.21 (s, 1H), 4.16 – 4.11 (m, 2H), 3.76 (s, 3H), 3.14 – 3.03 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ172.69, 159.61, 145.38, 137.55, 131.98, 129.48, 121.55, 115.09, 112.27, 109.95, 61.24, 57.50, 55.09, 38.36, 14.10. **MS (ESI)**: found $[M+H]^+$ 469.0.



3l

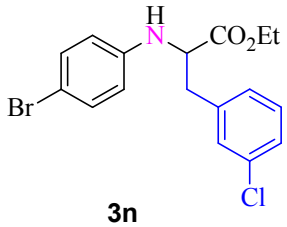
Ethyl 2-((4-bromophenyl)amino)-3-(naphthalen-2-yl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.41 – 7.35 (m, 1H), 7.32 (d, *J* = 6.7 Hz, 1H), 7.22 – 7.16 (m, 2H), 6.46 – 6.34 (m, 2H), 4.42 (t, *J* = 6.7 Hz, 1H), 4.23 (s, 1H), 4.11 – 3.91 (m, 2H), 3.63-3.48 (m, 2H), 1.05 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.17, 145.50, 133.87, 132.40, 131.95, 128.96, 127.94, 127.58, 126.28, 125.73, 125.30, 123.26,

115.09, 110.11, 61.26, 57.45, 36.10, 13.95. **MS (ESI)**: found $[M+H]^+$ 398.2.



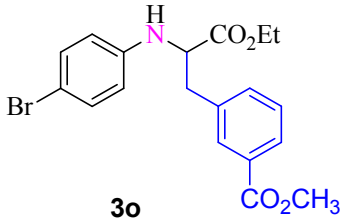
3m

Ethyl 2-((4-bromophenyl)amino)-3-(2-fluorophenyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 2H), 6.49 (d, *J* = 8.9 Hz, 2H), 4.34 – 4.24 (m, 2H), 4.15 – 4.07 (m, 2H), 3.24 – 3.04 (m, 2H), 1.16 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.72, 145.35, 132.03, 131.57, 131.52, 128.94 (d, *J* = 8.2 Hz), 124.11 (d, *J* = 3.5 Hz), 123.35 (d, *J* = 15.9 Hz), 115.35 (d, *J* = 22.1 Hz), 115.07, 110.04, 61.35, 56.72, 32.30, 14.00. ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.68, 161.22 (d, *J* = 245.2 Hz), 145.22, 131.93, 131.49 (d, *J* = 4.5 Hz), 128.87 (d, *J* = 8.2 Hz), 124.04 (d, *J* = 3.5 Hz), 123.21 (d, *J* = 15.9 Hz), 115.26 (d, *J* = 22.1 Hz), 114.93, 109.88, 61.30, 56.51, 32.14, 13.95. **MS (ESI)**: found $[M+H]^+$ 366.1.



3n

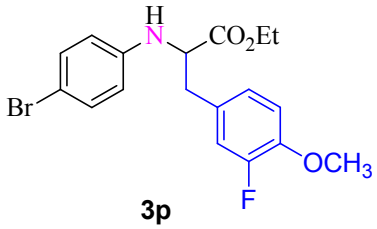
Ethyl 2-((4-bromophenyl)amino)-3-(3-chlorophenyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.18 (m, 4H), 7.15 (s, 1H), 7.03 (d, *J* = 6.7 Hz, 1H), 6.49 (d, *J* = 8.9 Hz, 2H), 4.35 – 4.17 (m, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.15 – 2.99 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.37, 145.12, 138.11, 134.21, 132.08, 129.70, 129.40, 127.46, 127.22, 115.13, 110.19, 61.43, 57.37, 37.94, 14.11. **MS (ESI)**: found $[M+H]^+$ 382.9.



3o

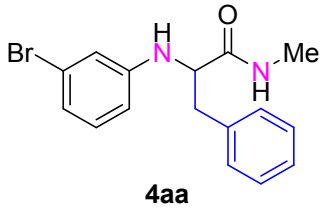
Methyl 3-(2-((4-bromophenyl)amino)-3-ethoxy-3-oxopropyl)benzoate. **^{1}H NMR** (400

MHz, $CDCl_3$) δ 7.92 (d, *J* = 6.3 Hz, 1H), 7.85 (s, 1H), 7.39 – 7.30 (m, 2H), 7.25 (d, *J* = 8.9 Hz, 2H), 6.48 (d, *J* = 8.9 Hz, 2H), 4.33 – 4.23 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 3.21 – 3.10 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.40, 166.82, 145.17, 136.51, 133.87, 132.03, 130.36, 130.29, 128.51, 128.25, 115.14, 110.11, 61.40, 57.46, 52.12, 38.07, 14.07. **MS (ESI)**: found $[M+H]^+$ 406.2.



3p

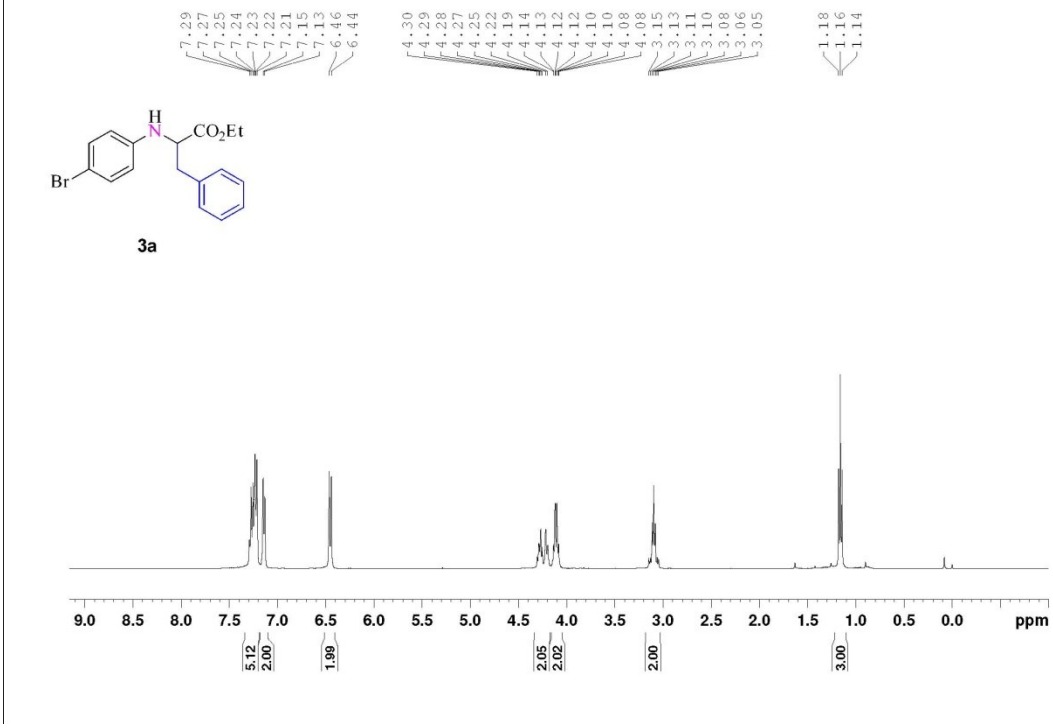
Ethyl 2-((4-bromophenyl)amino)-3-(3-fluoro-4-methoxyphenyl)propanoate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 1H), 6.93 – 6.80 (m, 1H), 6.48 (d, *J* = 8.8 Hz, 1H), 4.24 (t, *J* = 5.9 Hz, 1H), 4.19-4.11 (m, 3H), 3.87 (s, 1H), 3.10-2.99 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.49, 151.95 (d, *J* = 245.8 Hz), 146.53 (d, *J* = 10.6 Hz), 145.14, 132.01, 128.74 (d, *J* = 6.2 Hz), 124.98 (d, *J* = 3.5 Hz), 116.87 (d, *J* = 18.2 Hz), 115.03, 113.07, 113.05, 110.00, 77.32, 77.00, 76.68, 61.37, 57.34, 56.10, 37.16, 14.15. **MS (ESI)**: found $[M+H]^+$ 396.2.



4aa

2-((3-bromophenyl)amino)-N-methyl-3-phenylpropanamide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 3H), 7.20 (d, *J* = 7.0 Hz, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.90 (t, *J* = 8.5 Hz, 1H), 6.68 (s, 1H), 6.55 (s, 1H), 6.43 (d, *J* = 8.1, 1H), 4.03 – 3.90 (m, 2H), 3.33 – 3.01 (m, 2H), 2.79 (d, *J* = 5.0 Hz, 3H), 1.31 – 1.20 (d, *J* = 7.8 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.64, 147.79, 136.26, 130.65, 128.96, 128.94, 127.29, 123.22, 122.09, 116.69, 112.23, 59.71, 38.73, 26.09. **MS (ESI)**: found $[M+H]^+$ 333.0.

^{1}H and ^{13}C NMR spectra of Products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4.27
4.25
4.22
4.19
4.14
4.13
4.12
4.12
4.10
4.10
4.08
4.08
3.15
3.13
3.11
3.10
3.08
3.06
3.05
1.18
1.16
1.14
H
N
CO2Et
Br
3a
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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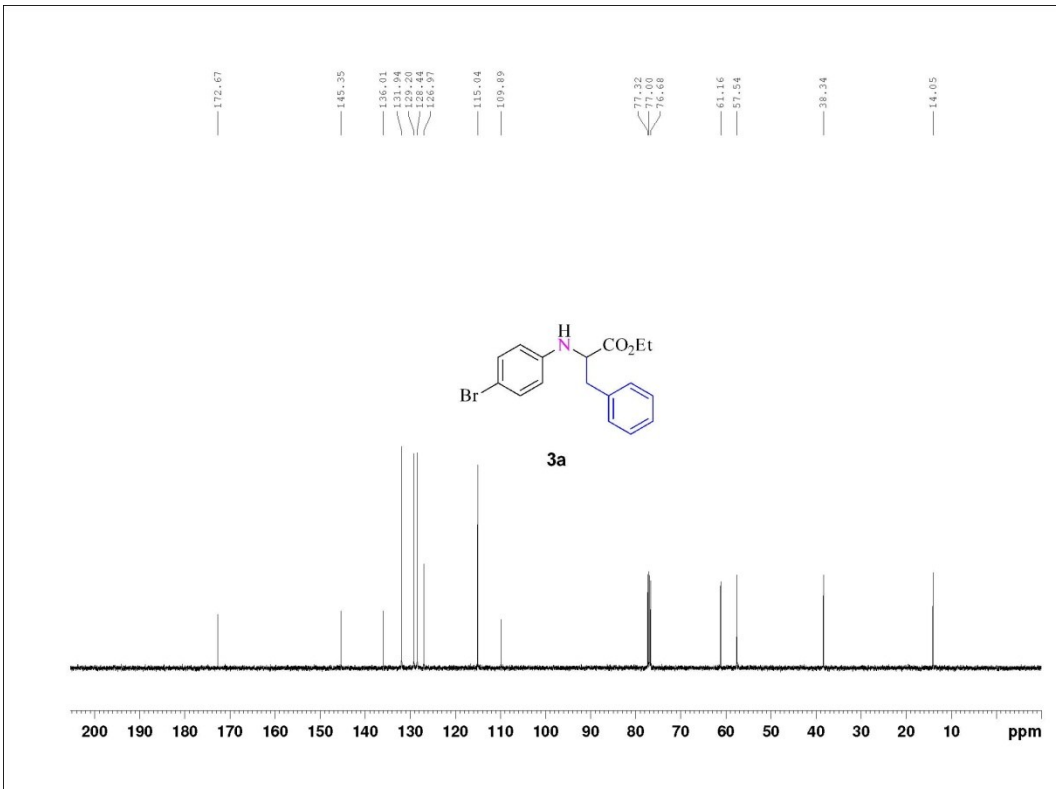
1.99
2.05
2.02
2.00
3.00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77.00
76.68
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14.05
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N
CO2Et
Br
3a
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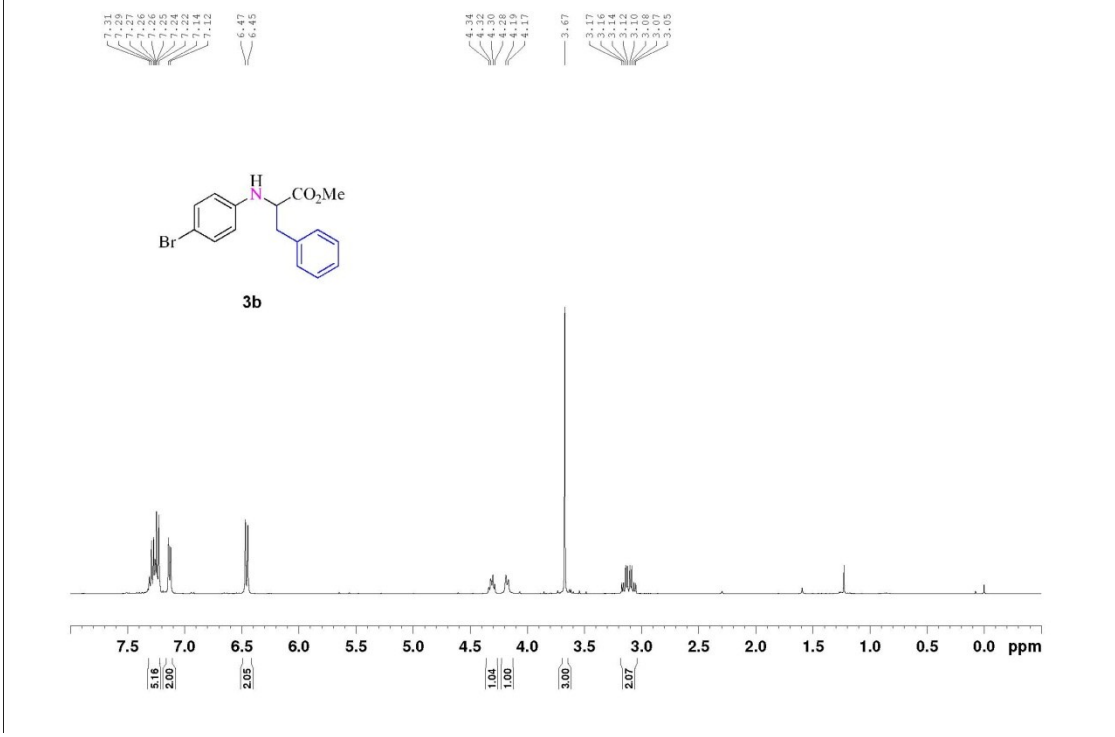
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4.28
4.19
4.17
3.67
3.17
3.16
3.14
3.12
3.10
3.08
3.07
3.05
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CO2Me
Br
3b
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6.0
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5.0
4.5
4.0
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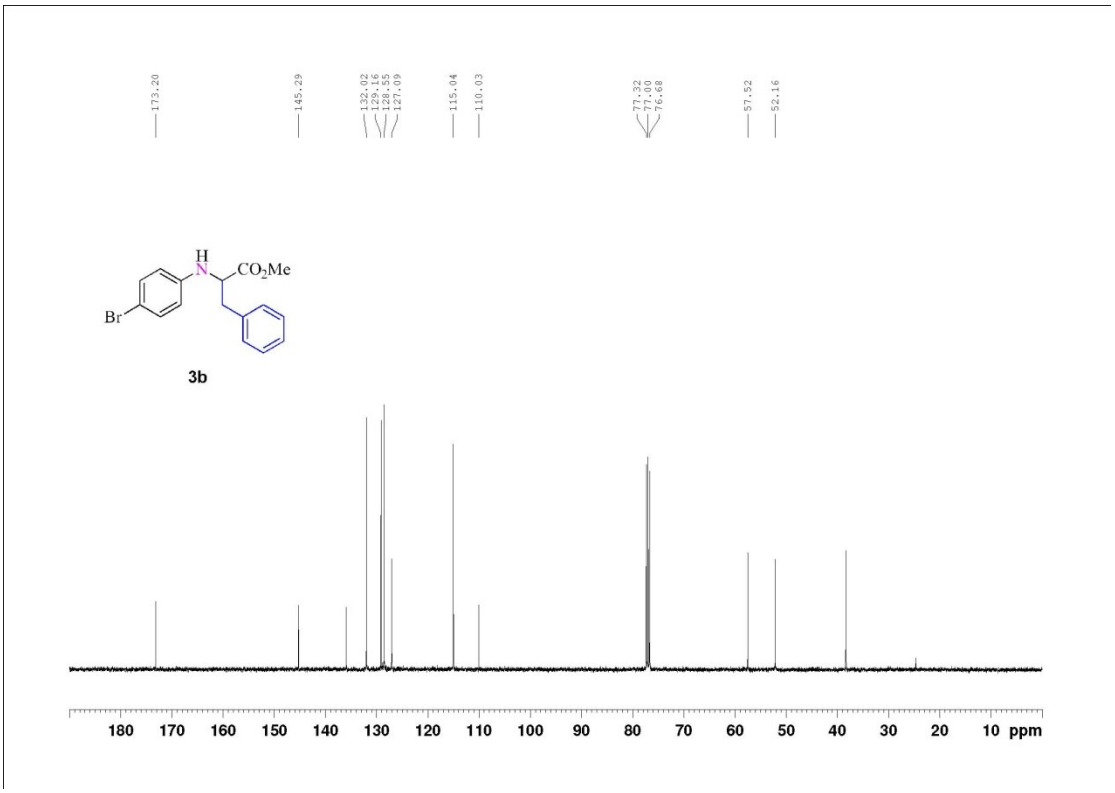
3.00
2.07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52.16
H
N
CO2Me
Br
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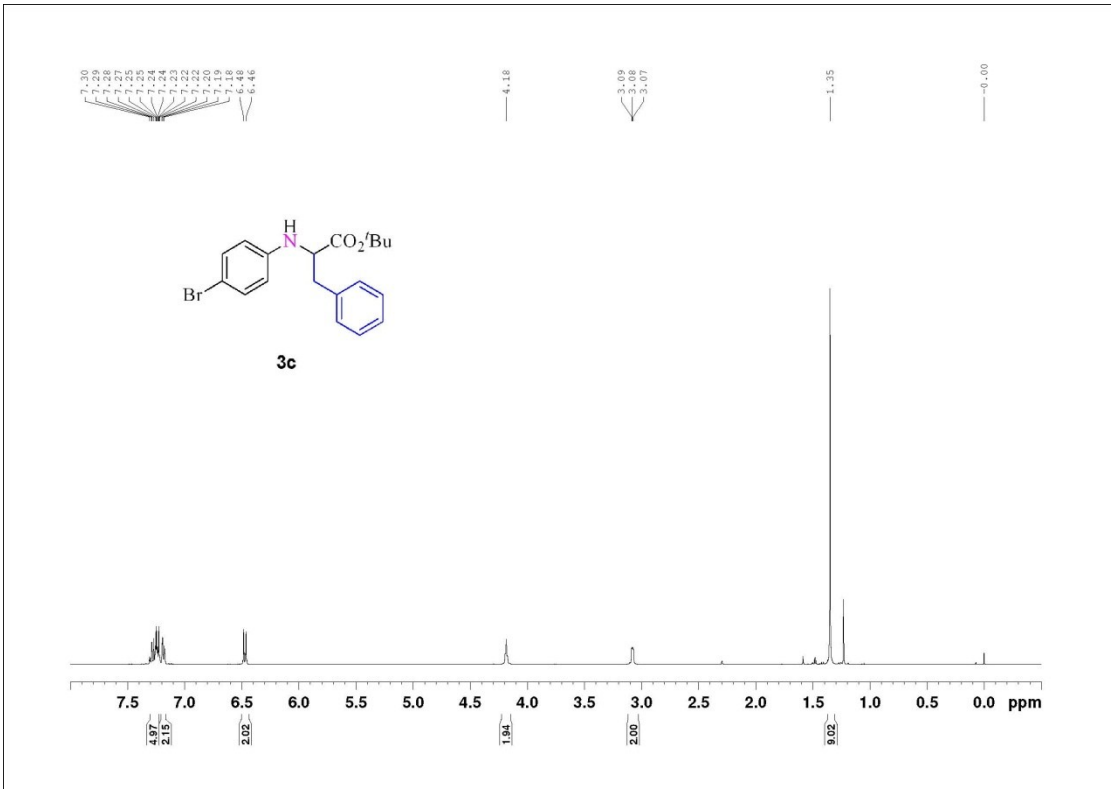
40
30
20
10
ppm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6.46
4.18
3.09
3.08
3.07
1.35
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H
N
CO2tBu
Br
3c
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6.5
6.0
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5.0
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4.0
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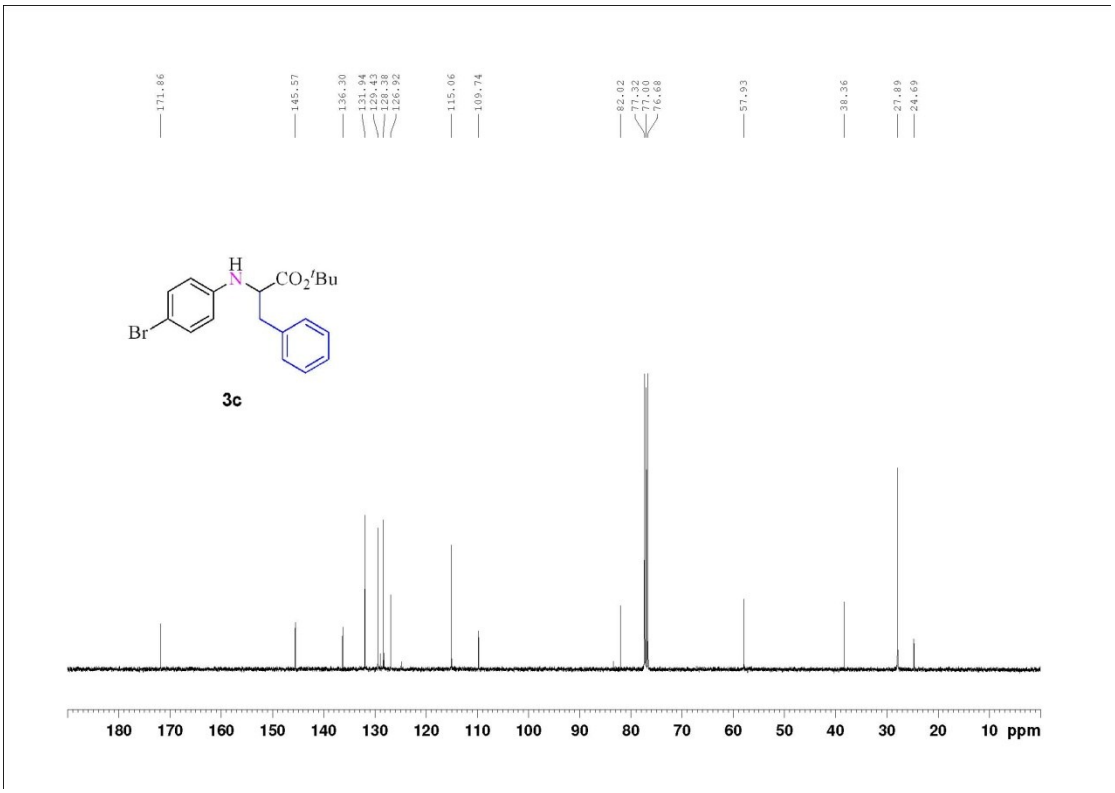
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57.93
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Br
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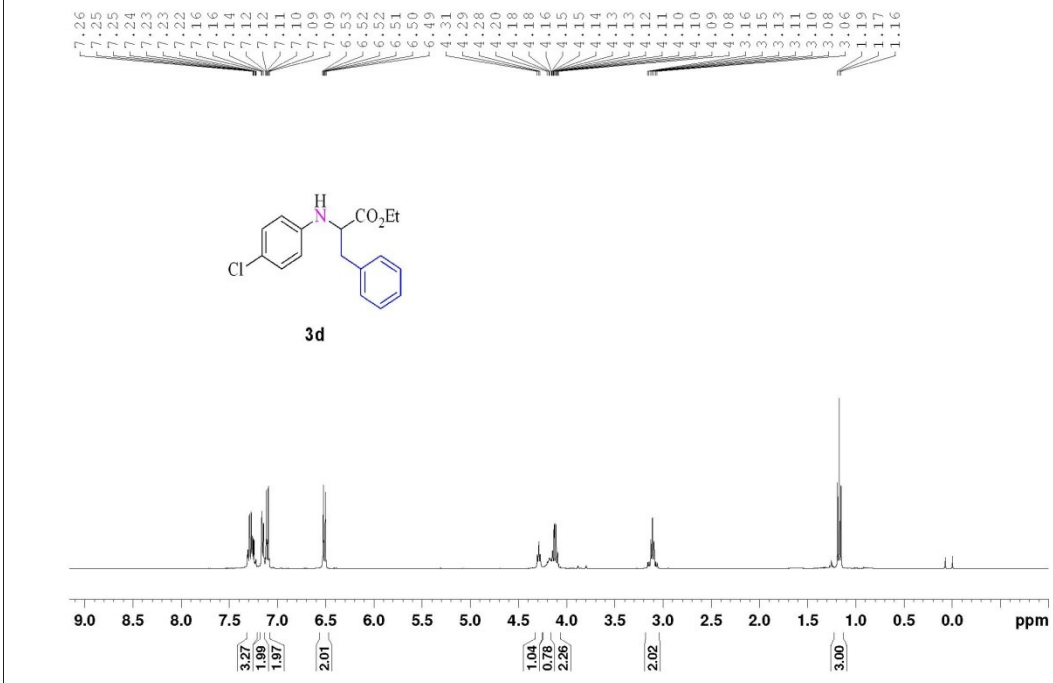
ppm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7.10
7.09
7.09
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6.51
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4.12
4.11
4.10
4.10
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4.08
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3.15
3.13
3.11
3.10
3.08
3.06
1.19
1.17
1.16
H
N
CO2Et
Cl
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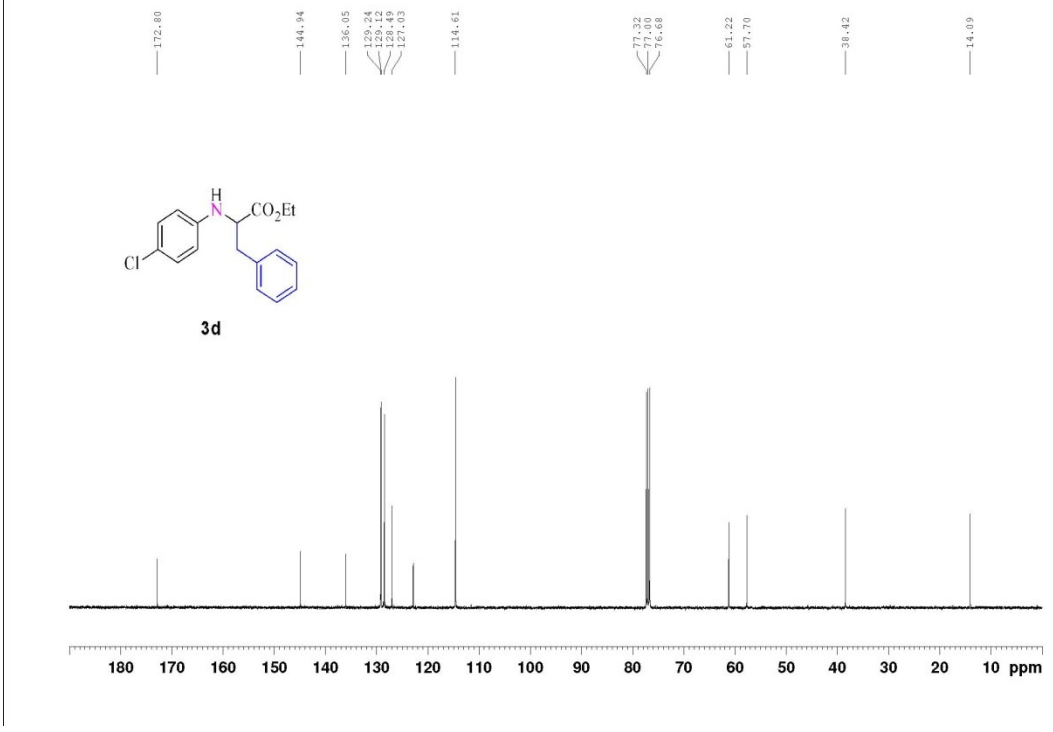
3.00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CO2Et
Cl
3d
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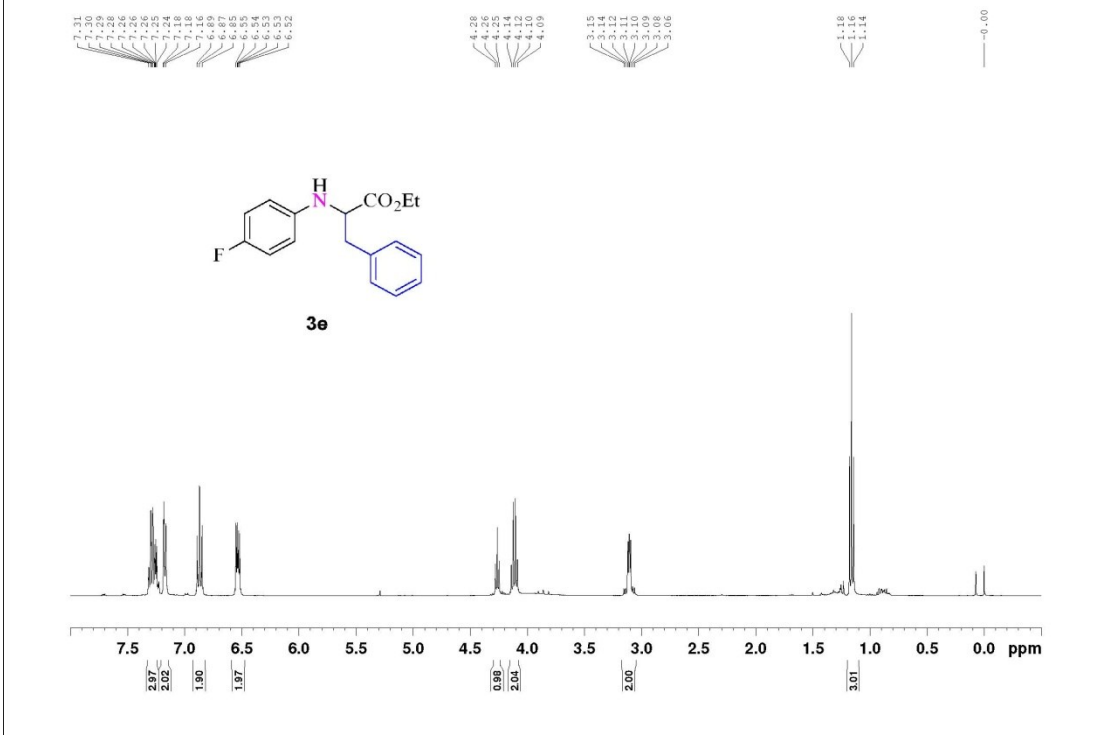
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6.52
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4.25
4.14
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4.09
3.15
3.14
3.12
3.11
3.10
3.09
3.08
3.06
1.18
1.16
1.14
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N
CO2Et
F
3e
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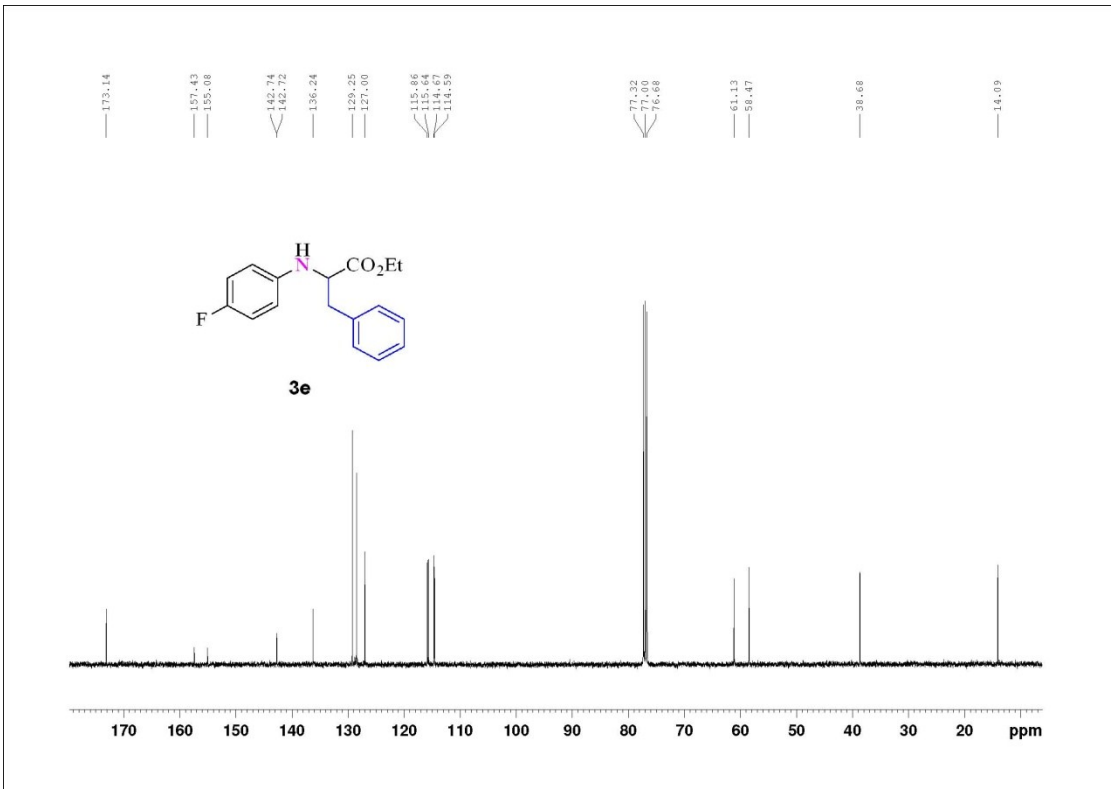
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N
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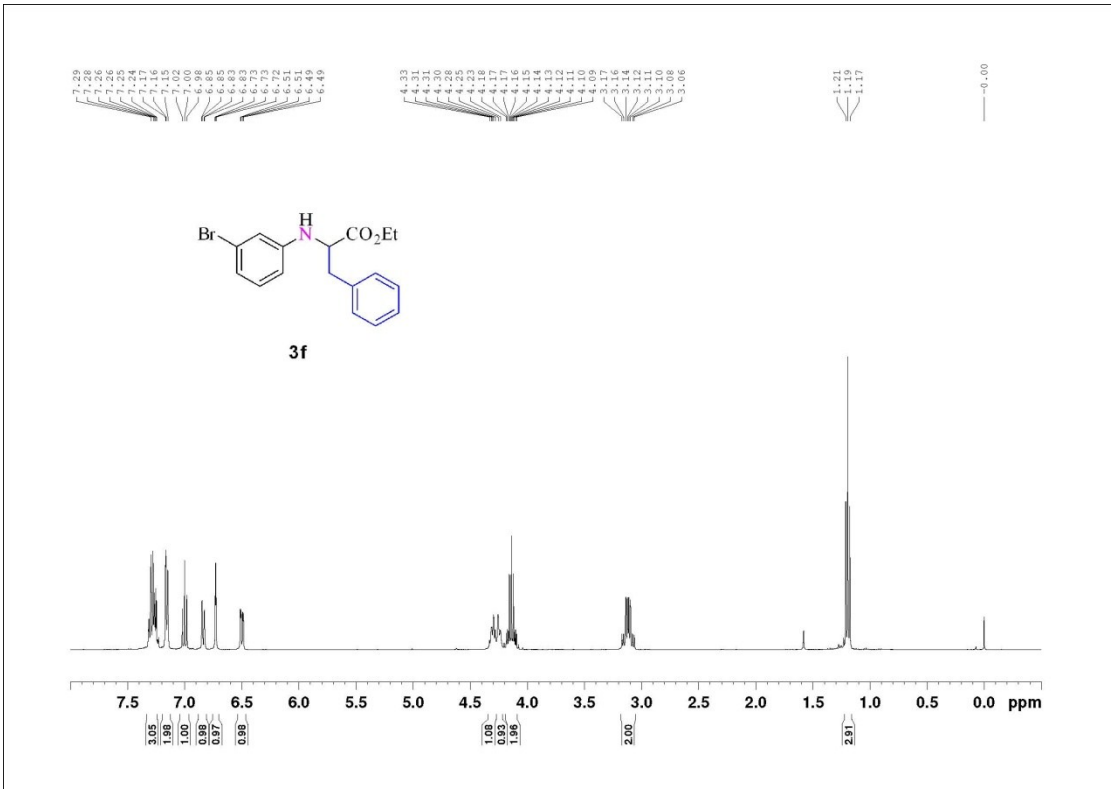
ppm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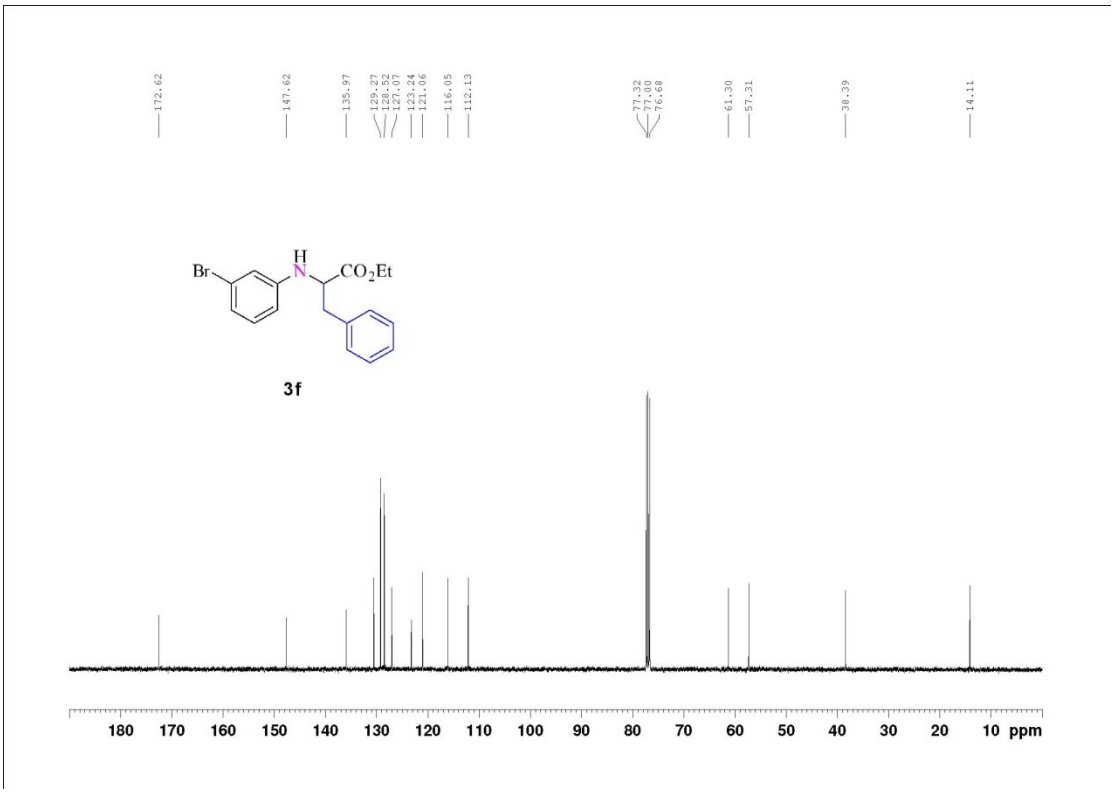
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CO2Et
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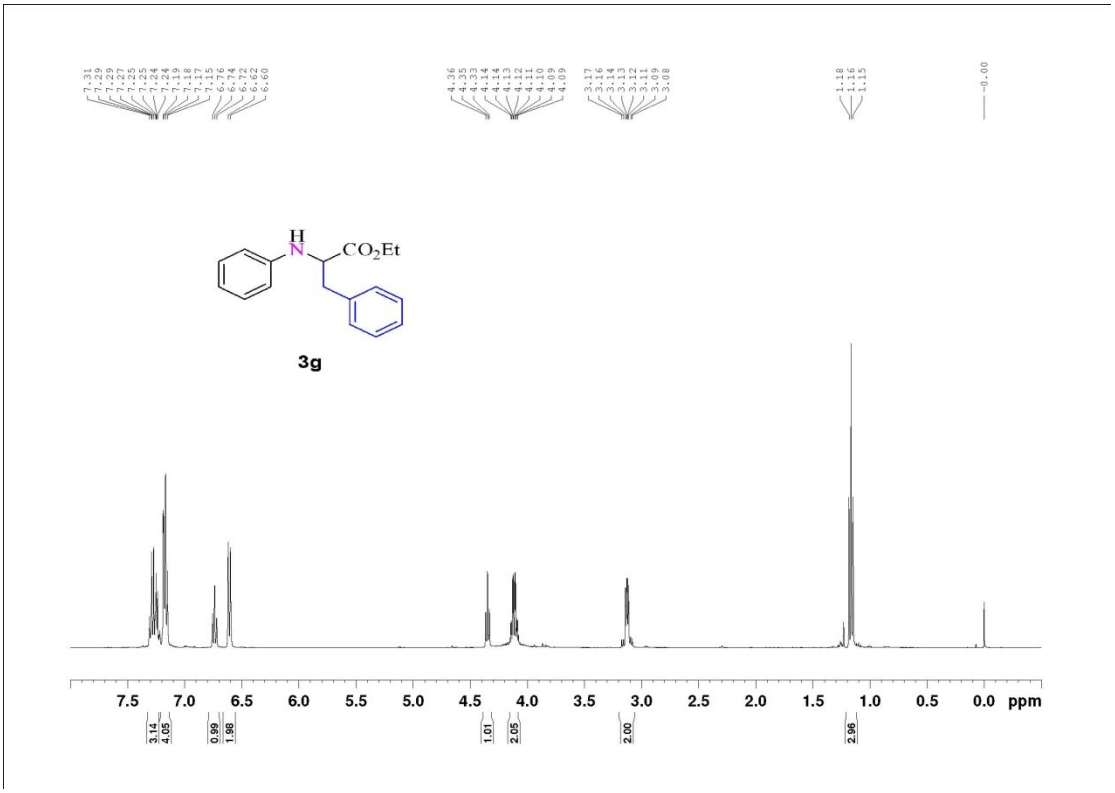
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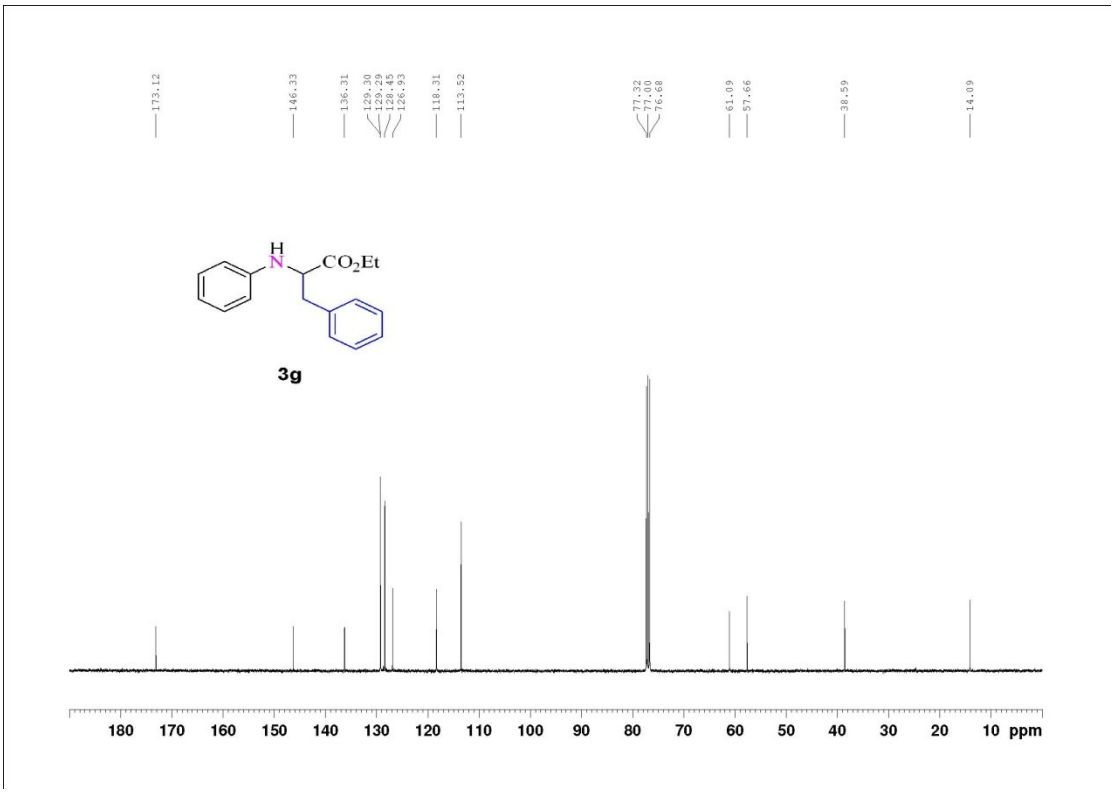
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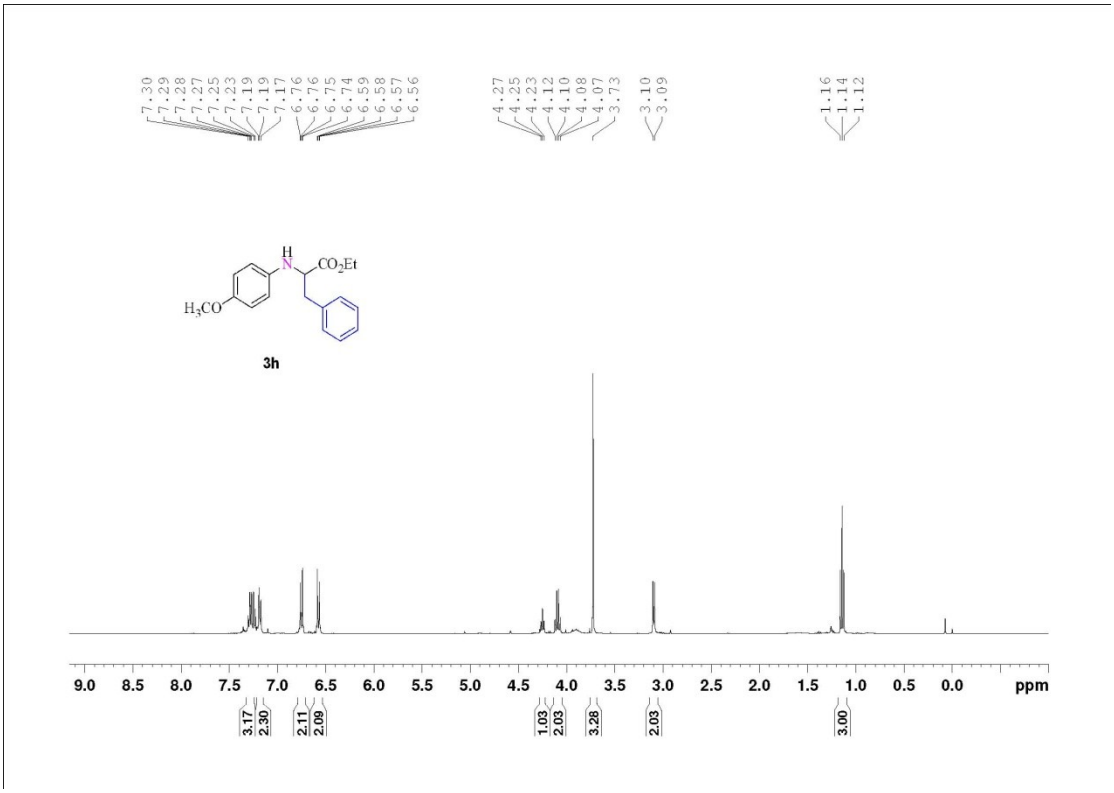
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4.08
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3.09
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1.14
1.12
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N
CO2Et
H3CO
3h
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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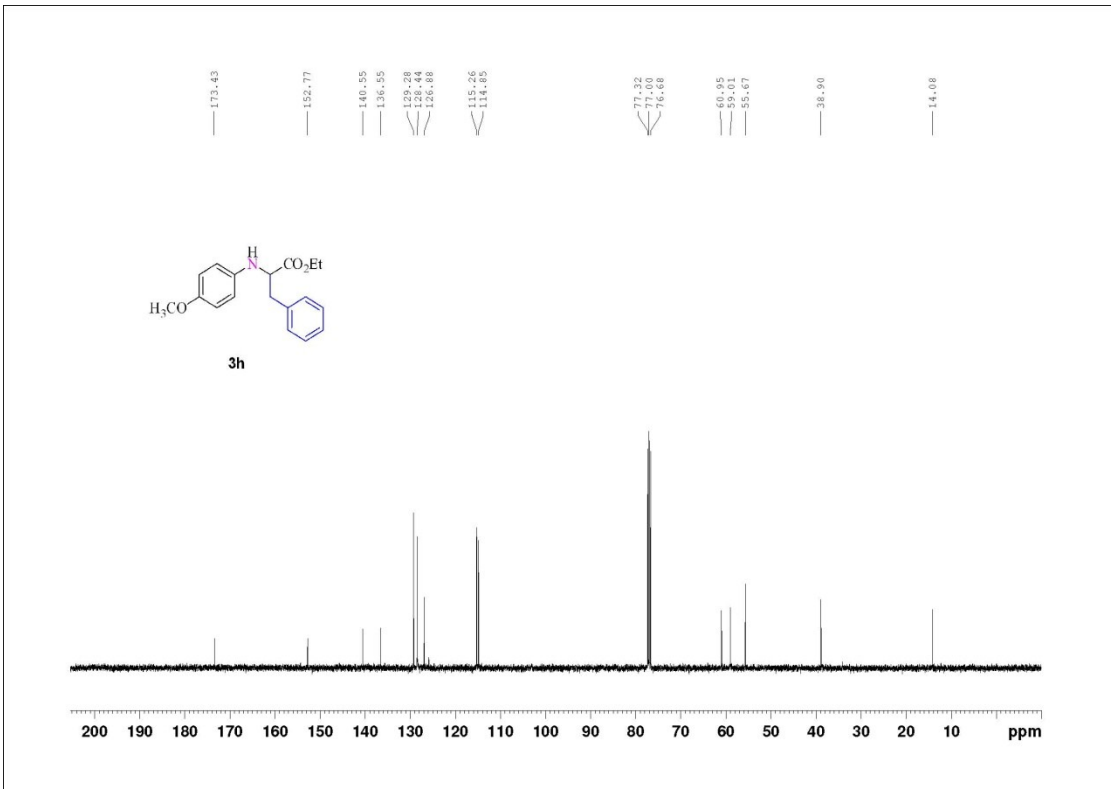
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CO2Et
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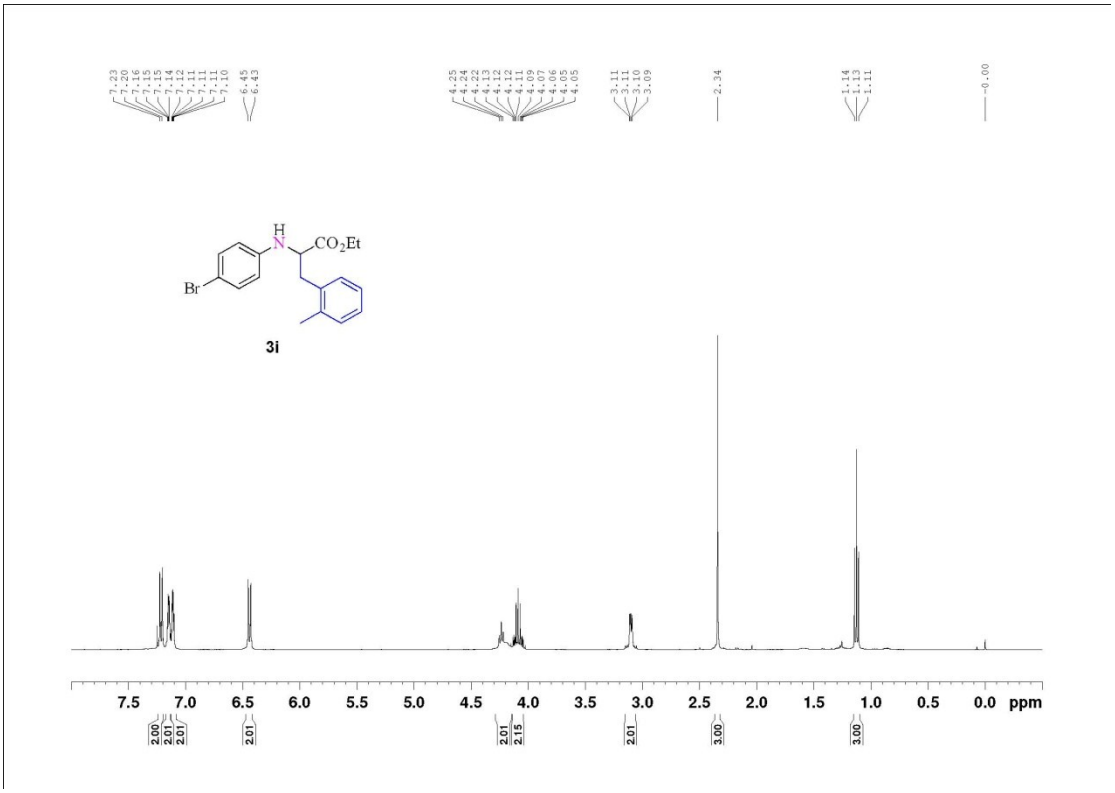
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4.11
4.09
4.07
4.06
4.05
4.05
3.11
3.11
3.10
3.09
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1.14
1.13
1.11
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N
CO2Et
Br
3i
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6.0
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5.0
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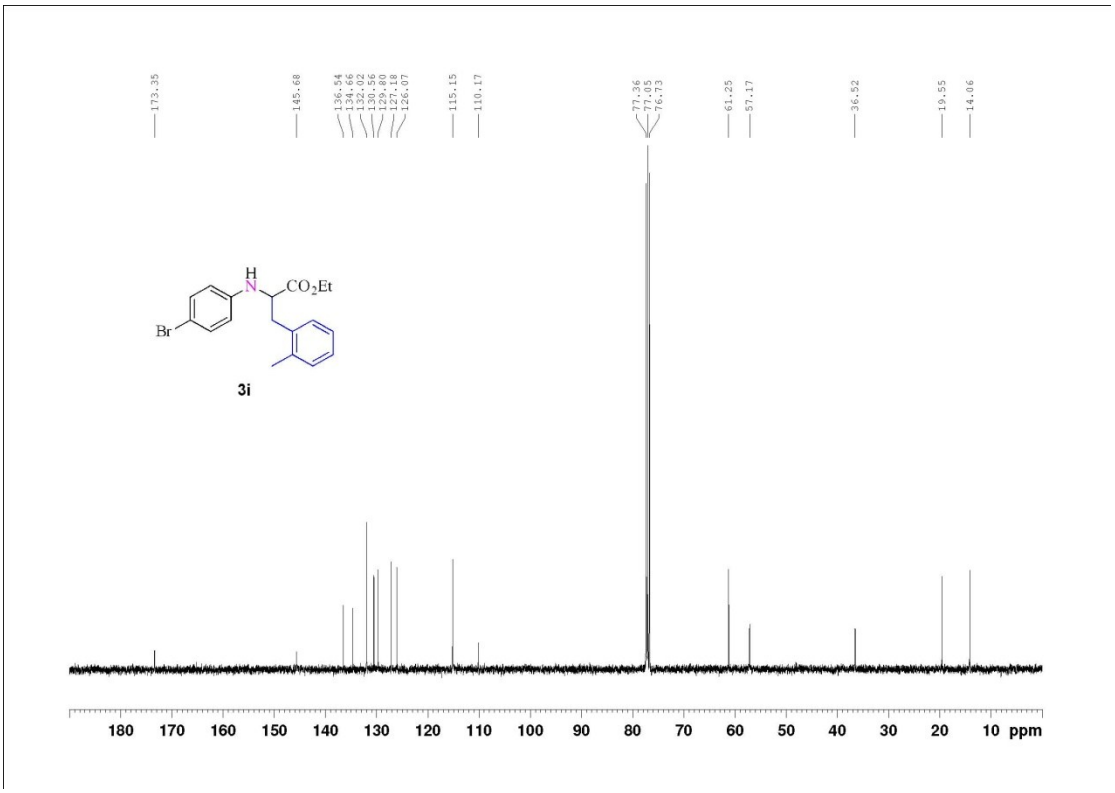
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126.07
115.15
110.17
77.36
77.05
76.73
61.25
57.17
36.52
19.55
14.06
H
N
CO2Et
Br
3i
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10
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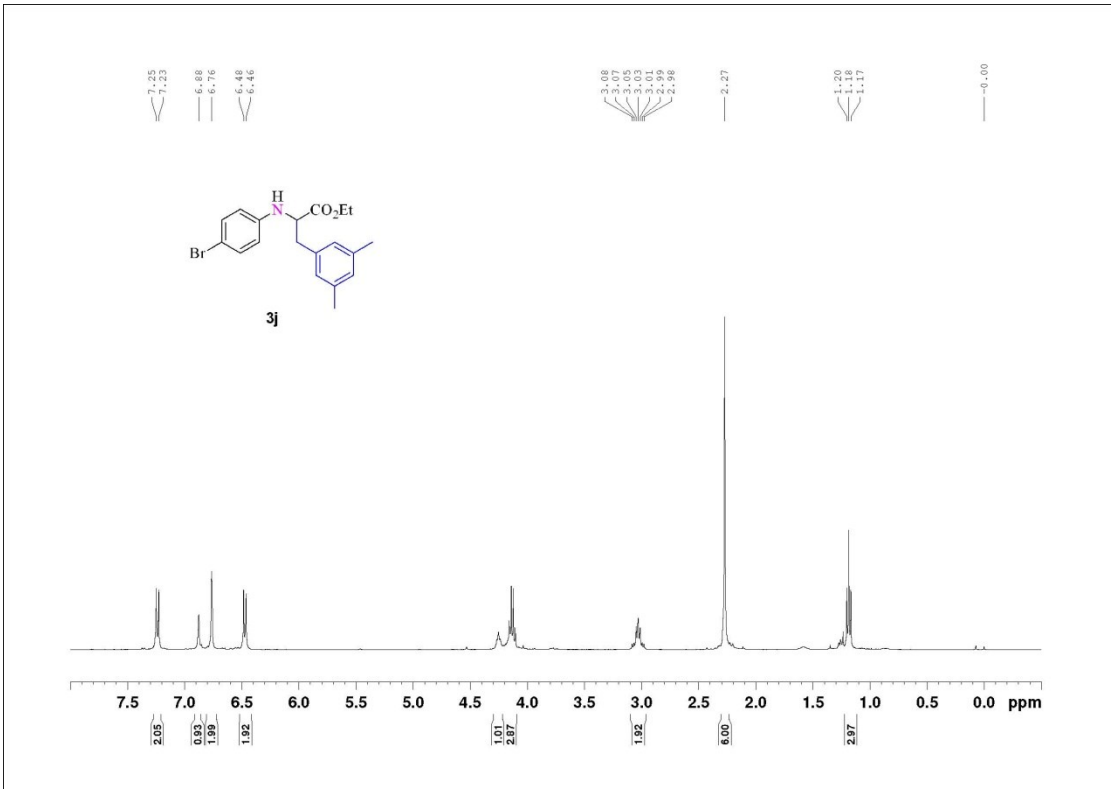
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2.98
2.27
1.20
1.18
1.17
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N
CO2Et
Br
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6.0
5.5
5.0
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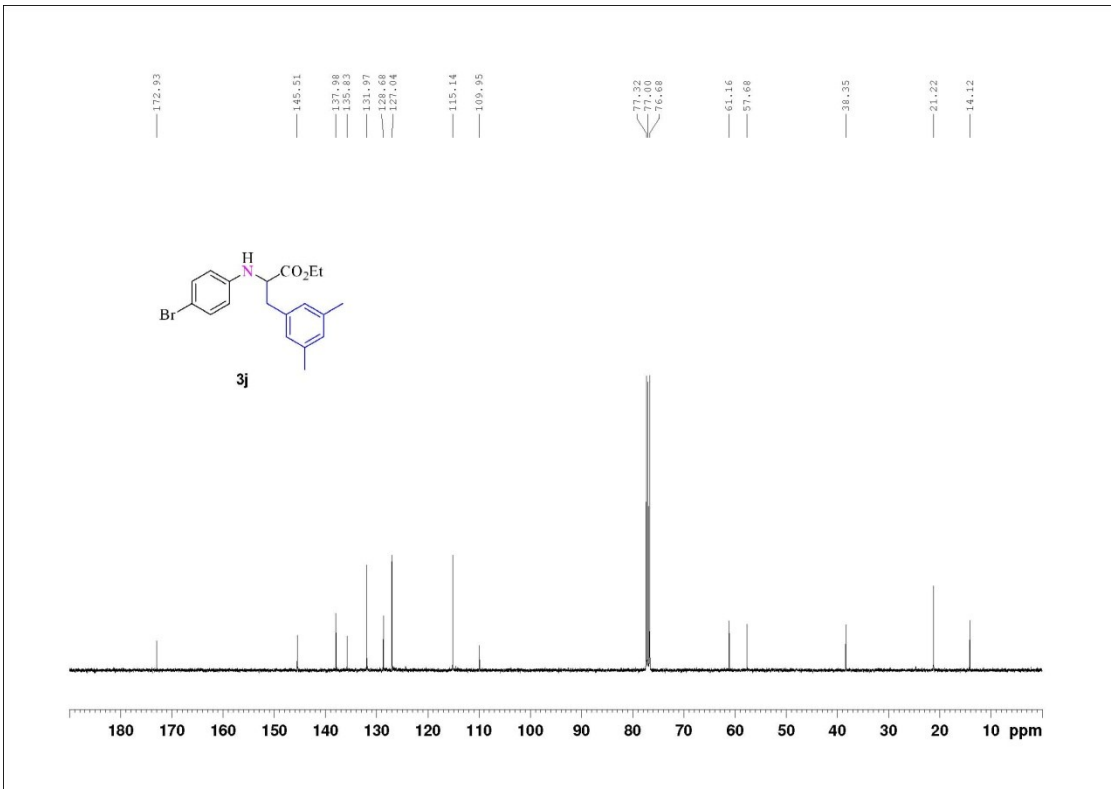
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.05
0.93
1.99
1.92
1.01
2.07
1.92
6.00
2.97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77.00
76.68
61.16
57.68
38.35
21.22
14.12
H
N
CO2Et
Br
3j
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150
140
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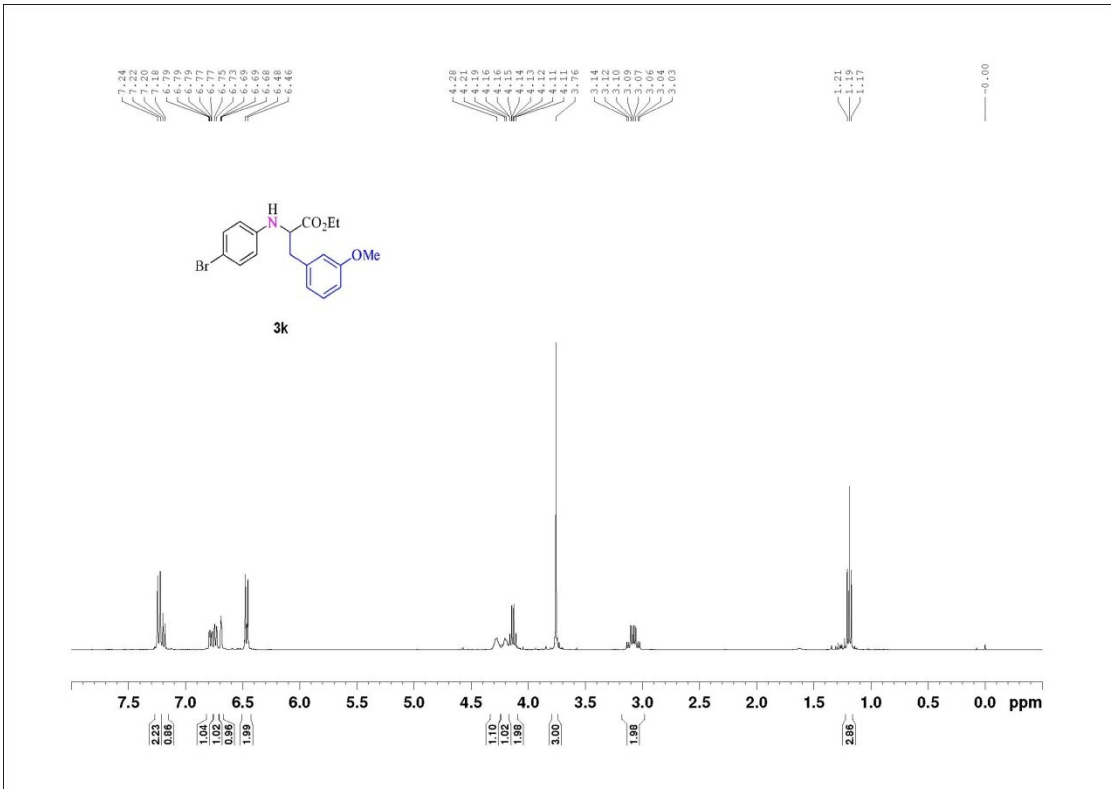
20
10
ppm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6.68
6.48
6.46
4.28
4.21
4.19
4.18
4.16
4.15
4.14
4.13
4.12
4.11
4.11
3.96
3.14
3.12
3.10
3.09
3.07
3.06
3.04
3.03
1.21
1.19
1.17
0.00
H
N
CO2Et
Br
OMe
3k
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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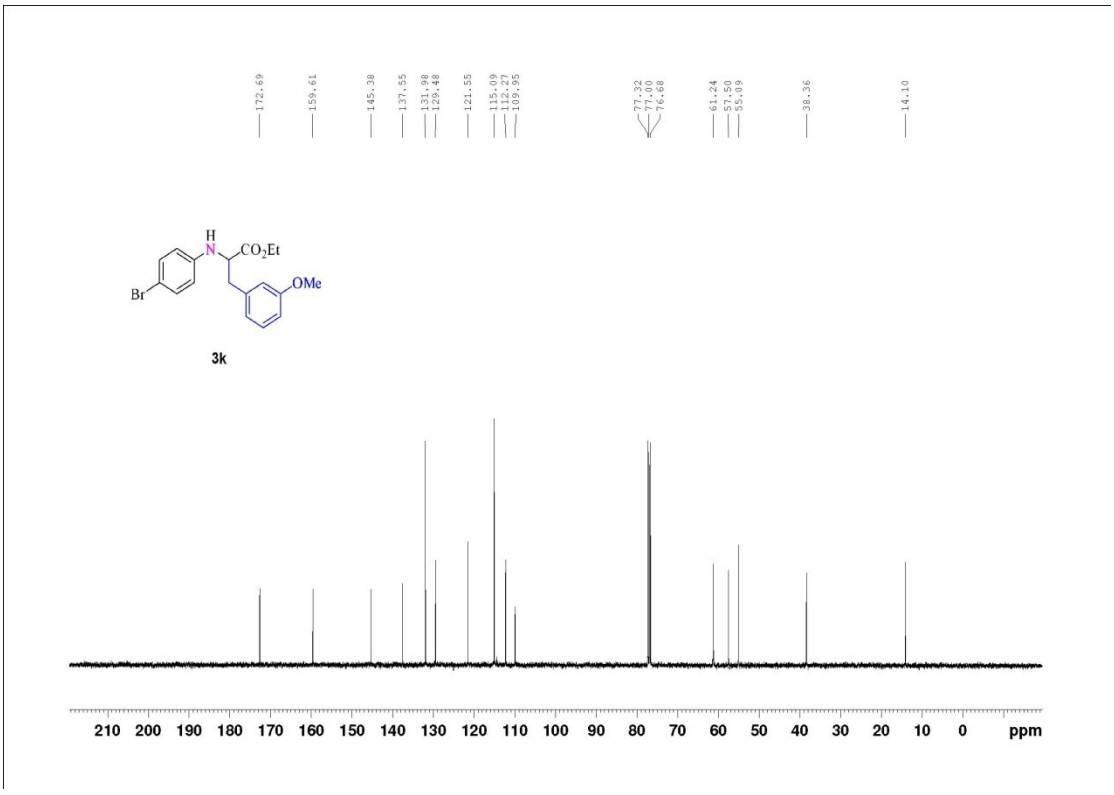
1.04
1.02
0.96
1.99
1.10
1.02
1.98
3.00
1.98
2.86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77.00
76.68
61.24
57.50
55.09
38.36
14.10
H
N
CO2Et
Br
OMe
3k
210
200
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20
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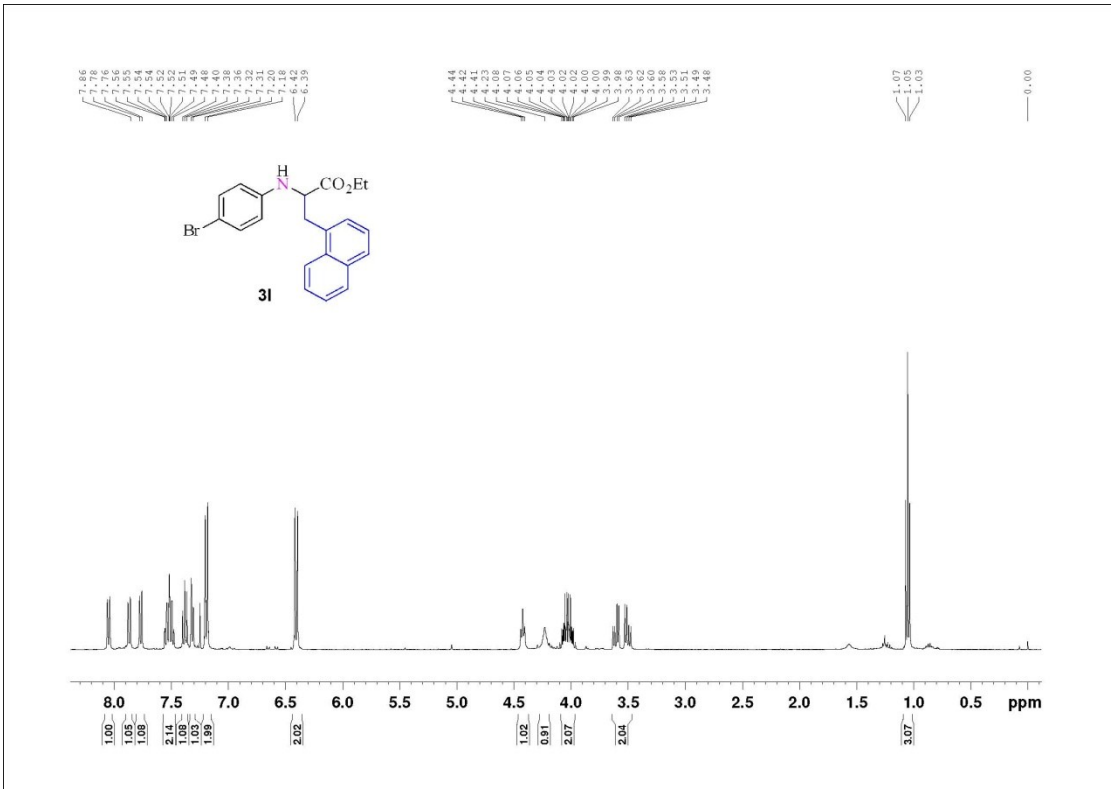
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7.38
7.36
7.32
7.31
7.20
7.18
6.42
6.39
4.44
4.42
4.41
4.23
4.08
4.07
4.06
4.05
4.04
4.03
4.02
4.02
4.00
4.00
3.99
3.98
3.63
3.62
3.60
3.58
3.53
3.51
3.49
3.48
1.07
1.05
1.03
0.00
H
N
CO2Et
Br
3l
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
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1.08
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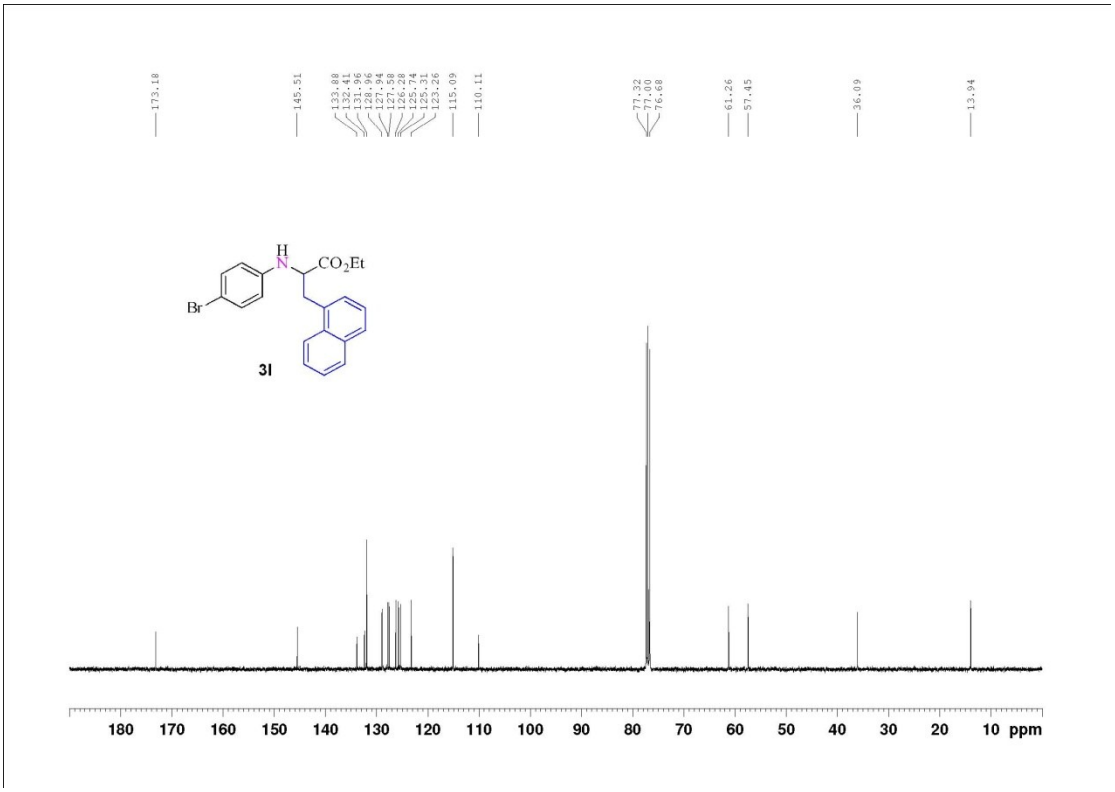
1.99
2.02
1.02
0.91
2.07
2.04
3.07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123.26
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110.11
77.32
77.00
76.68
61.26
57.45
36.09
13.94
H
N
CO2Et
Br
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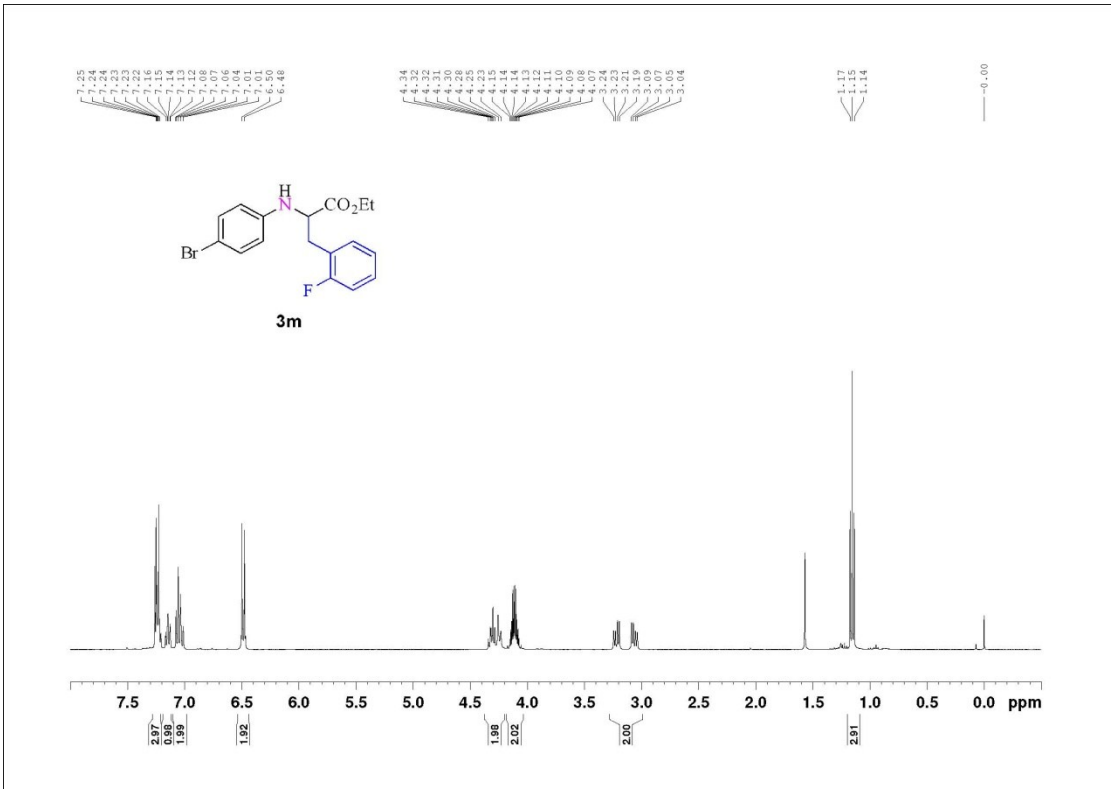
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7.15
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7.13
7.12
7.08
7.07
7.06
7.04
7.01
7.01
6.50
6.48
4.34
4.32
4.32
4.31
4.30
4.28
4.25
4.23
4.15
4.14
4.14
4.13
4.12
4.11
4.10
4.09
4.08
4.07
3.24
3.23
3.21
3.19
3.09
3.07
3.05
3.04
1.17
1.15
1.14
0.00
H
N
CO2Et
Br
F
3m
7.5
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.0
ppm
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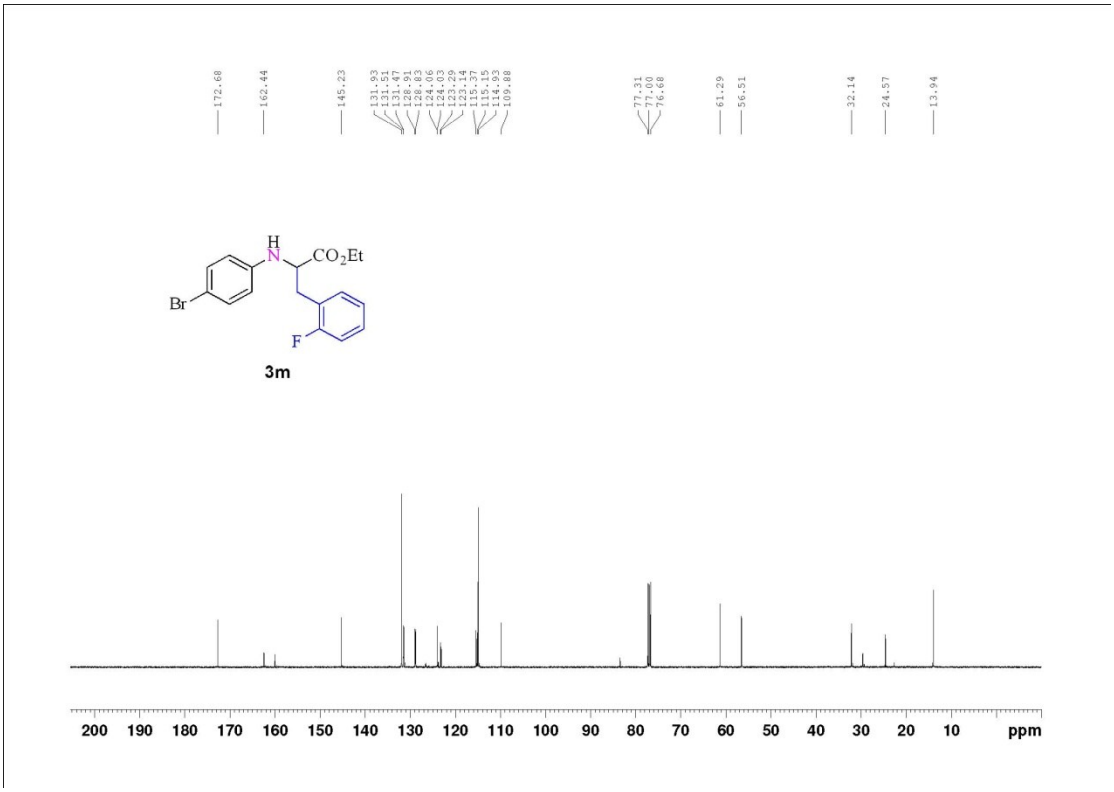
1.92
1.98
2.02
2.00
2.91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128.83
124.06
124.03
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123.14
115.37
115.15
114.93
109.88
77.31
77.00
76.68
61.29
56.51
32.14
24.57
13.94
H
N
CO2Et
Br
F
3m
200
190
180
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160
150
140
130
120
110
100
90
80
70
60
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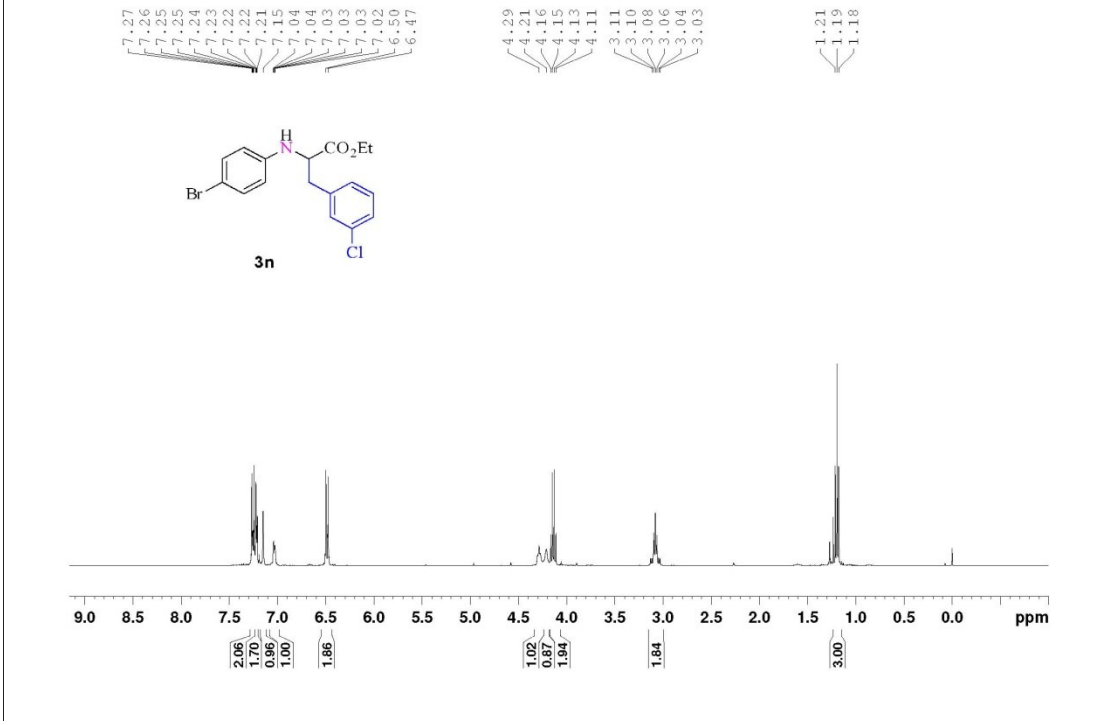
30
20
10
ppm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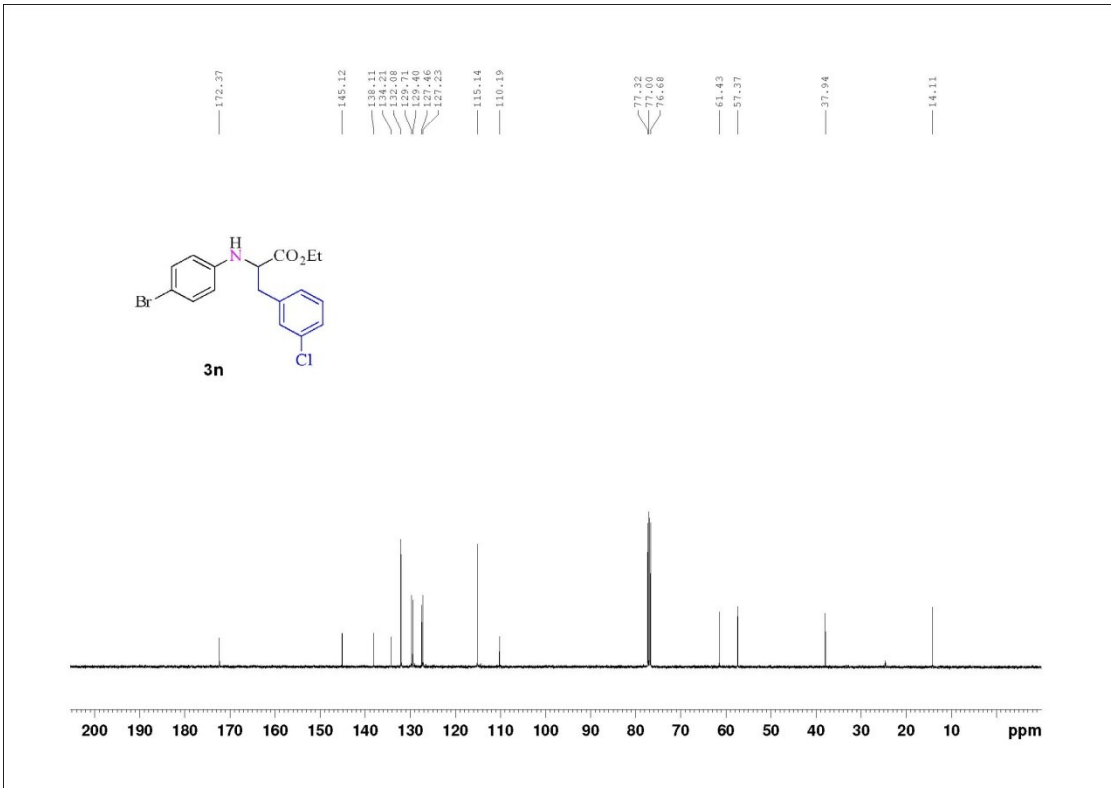
7.23
7.22
7.22
7.21
7.15
7.04
7.04
7.03
7.03
7.03
7.02
6.50
6.47
4.29
4.21
4.16
4.15
4.13
4.11
3.11
3.10
3.08
3.06
3.04
3.03
1.21
1.19
1.18
H
N
CO2Et
Br
Cl
3n
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.06
1.70
0.96
1.00
1.86
1.02
0.87
1.94
1.84
3.00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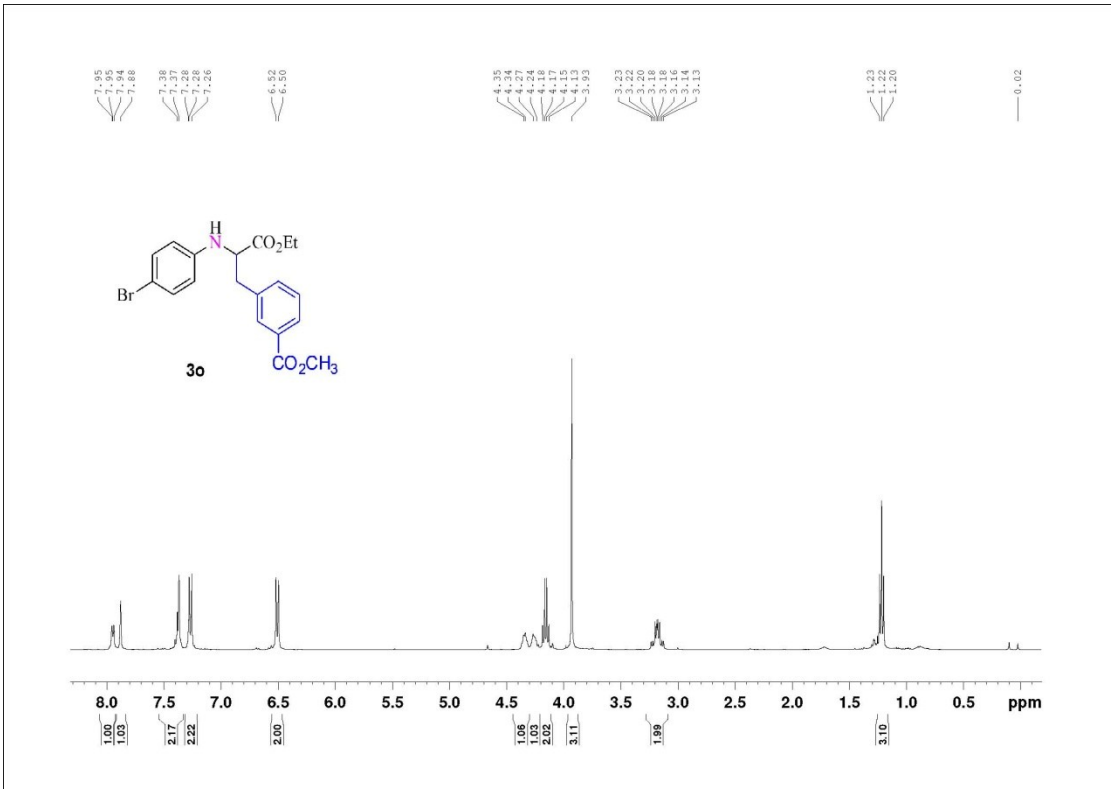
127.46
127.23
115.14
110.19
77.32
77.00
76.68
61.43
57.37
37.94
14.11
H
N
CO2Et
Br
Cl
3n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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6.50
4.35
4.34
4.27
4.24
4.18
4.17
4.15
4.13
3.93
3.23
3.22
3.20
3.18
3.16
3.14
3.13
1.23
1.22
1.20
0.02
H
N
CO2Et
Br
CO2CH3
3o
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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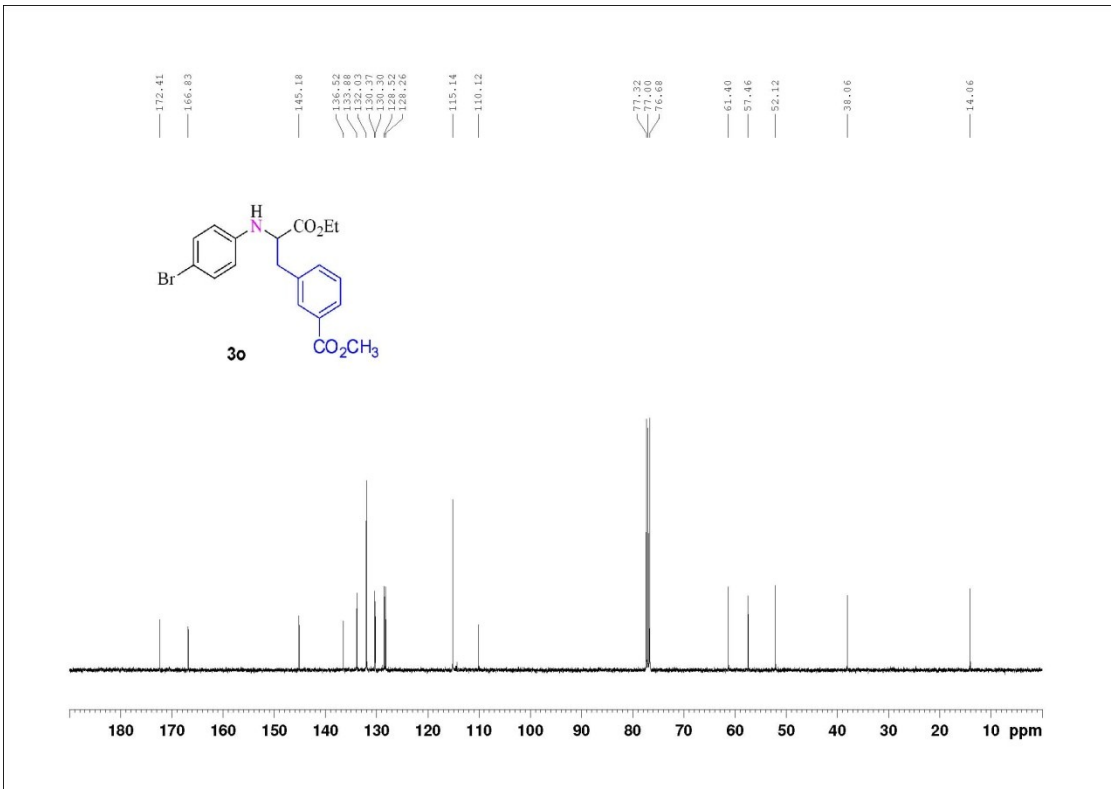
1.03
2.17
2.22
2.00
1.06
1.03
2.02
3.11
1.99
3.10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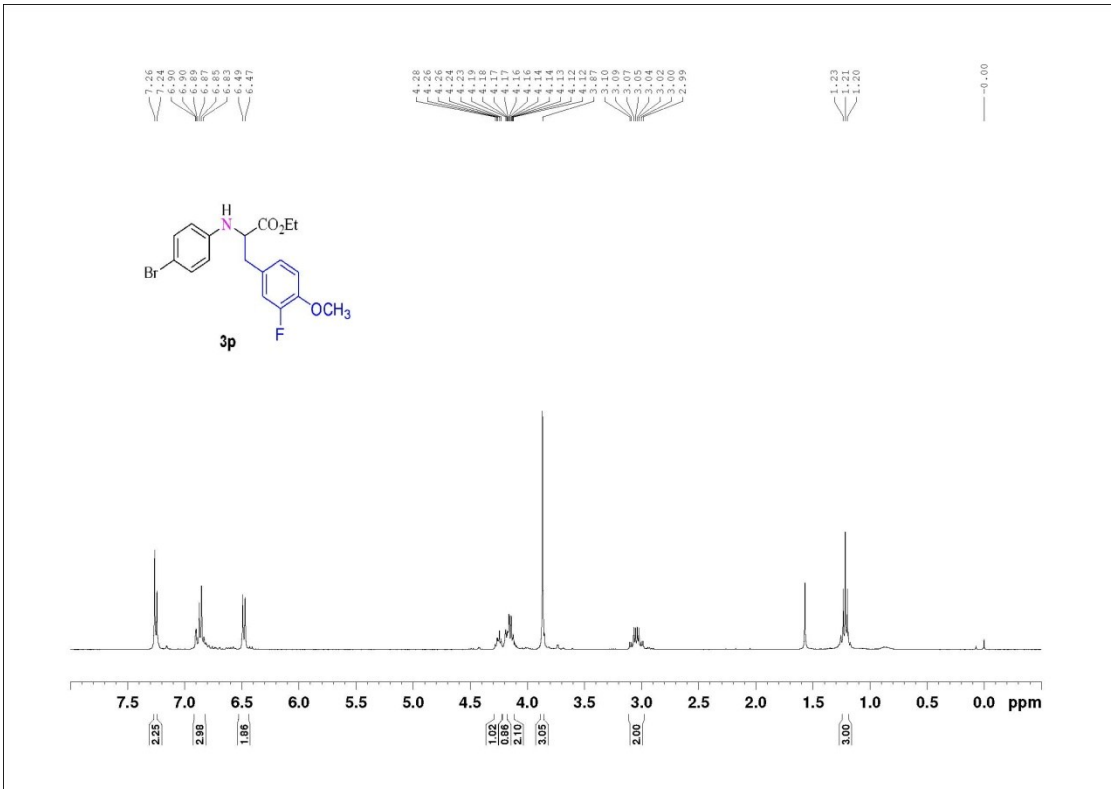
128.52
126.26
115.14
110.12
77.32
77.00
76.68
61.40
57.46
52.12
38.06
14.06
H
N
CO2Et
Br
CO2CH3
3o
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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6.47
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4.26
4.26
4.24
4.23
4.21
4.19
4.18
4.17
4.17
4.16
4.16
4.14
4.13
4.12
4.12
3.87
3.10
3.09
3.07
3.05
3.04
3.02
3.00
2.99
1.23
1.21
1.20
0.00
H
N
CO2Et
Br
OCH3
F
3p
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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ppm
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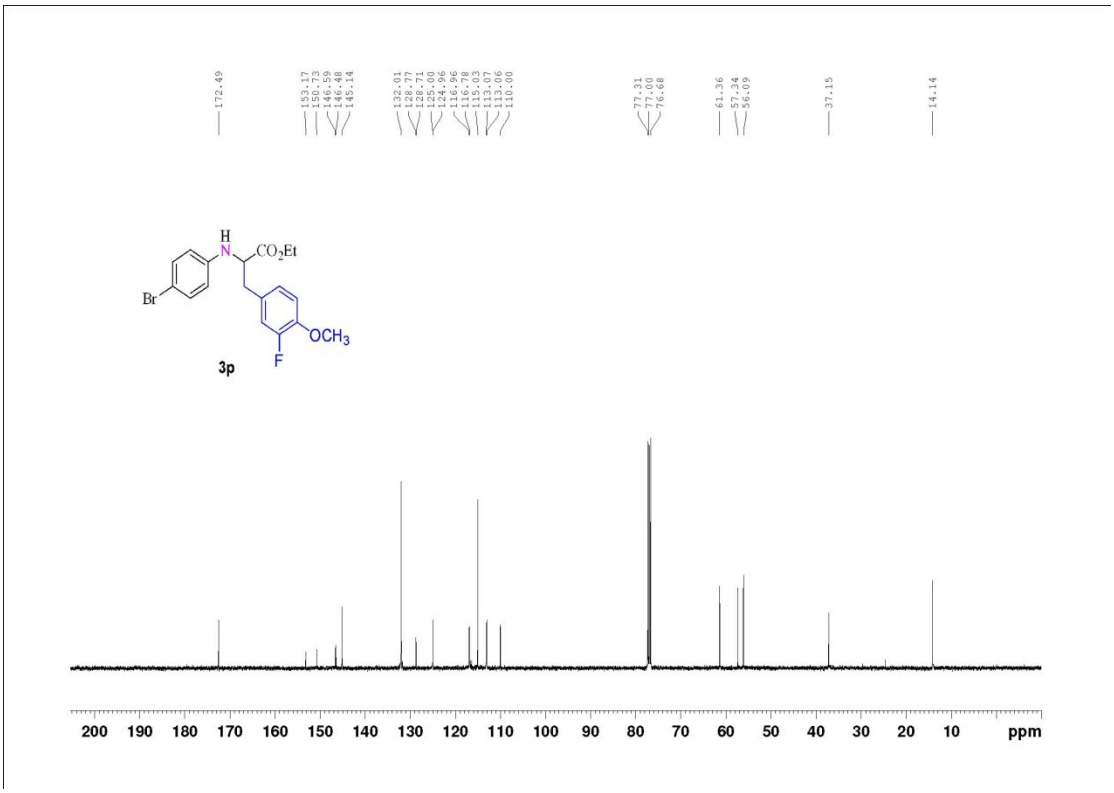
1.02
0.86
2.10
3.05
2.00
3.00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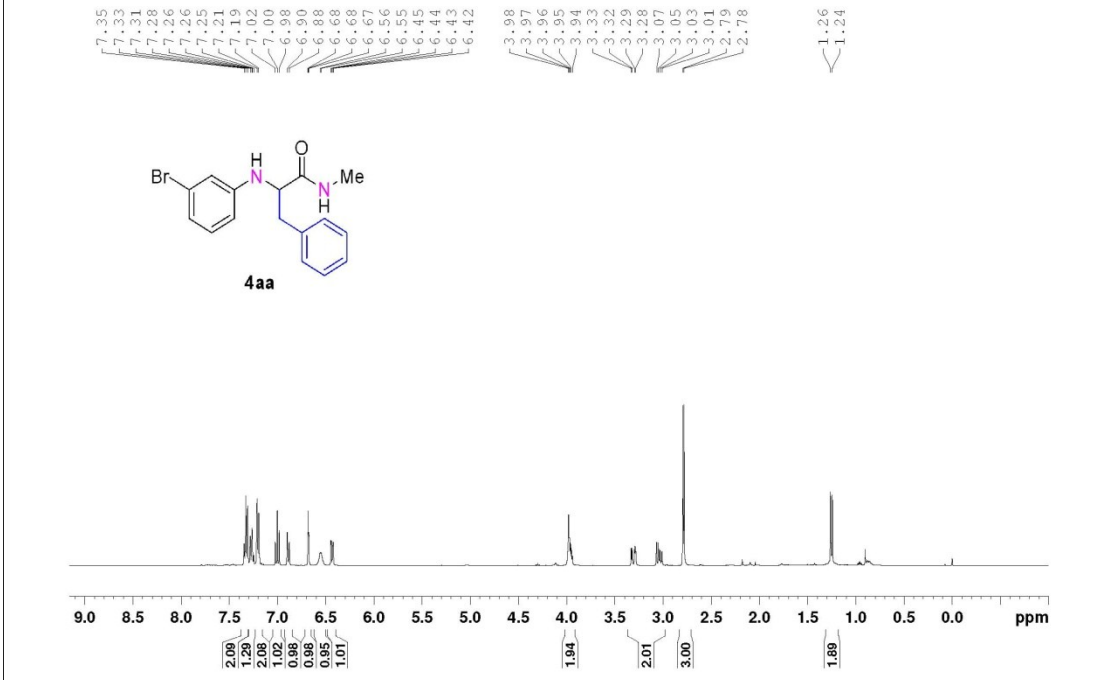
124.96
116.96
116.78
115.03
113.07
113.06
110.00
77.31
77.00
76.68
61.36
57.34
56.09
37.15
14.14
H
N
CO2Et
Br
OCH3
F
3p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.25
7.21
7.19
7.02
7.00
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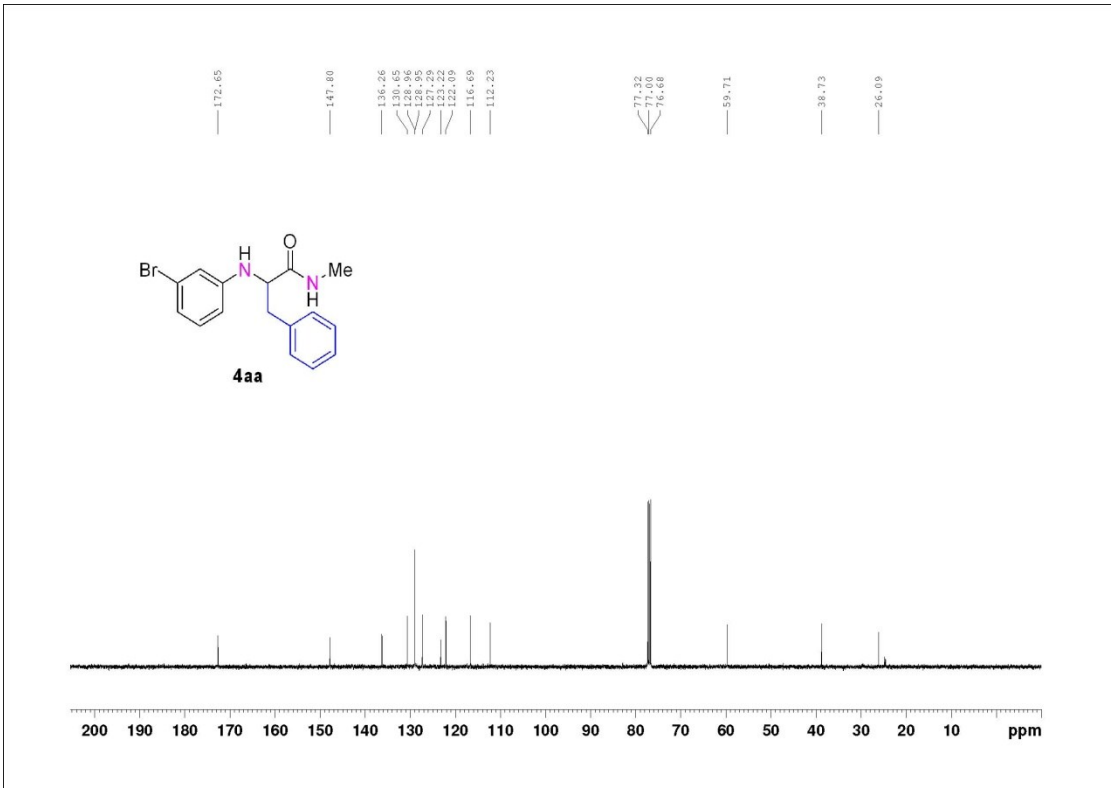
6.67
6.56
6.55
6.45
6.44
6.43
6.42
3.98
3.97
3.96
3.95
3.94
3.33
3.32
3.29
3.28
3.07
3.05
3.03
3.01
2.79
2.78
1.26
1.24
Br
H
N
O
N
Me
H
4aa
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.09
1.29
2.08
1.02
0.98
0.98
0.95
1.01
1.94
2.01
3.00
1.89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130.65
128.96
128.95
127.20
123.22
122.09
116.69
112.23
77.32
77.00
76.68
59.71
38.73
26.09
Br
H
N
O
N
Me
H
4aa
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm