# An Epoxide-Mediated Deprotection Method for Acidic Amide Auxiliary

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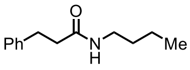
## General Information

Acids and 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline were obtained from the commercial sources or synthesized following literature procedures, and used to prepare the corresponding amides. $^{1}$H NMR was recorded on Varian Inova 500 instrument (500 MHz) or Varian Mercury Plus 400 instrument (400 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q =quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). $^{13}$C NMR spectra were recorded on Varian Inova 500 instrument (125 MHz) or Varian Mercury Plus 400 instrument (100 MHz), and were fully decoupled by broad band proton decoupling. $^{19}$F NMR spectra were recorded on Varian Mercury Plus 400 instrument (376 MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to either the center line of a triplet at 77.16 ppm of chloroform-*d* or the center line of a multiplet at 39.52 ppm of DMSO-$d^6$. LC-MS was performed on an Agilent 1260 LC with an Agilent 6230 mass spectrometer (electrospray ionization, ESI) eluting with 0.05% trifluoroacetic acid in $H_2O$ and 0.05% trifluoroacetic acid in $CH_3CN$. All starting materials and solvent were purchased from Alfa Aesar, Aldrich, Acros, TCI chemical companies or from the storehouse of Asychem Laboratories Inc. and used as received.

## Substrate Structures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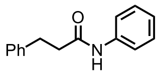
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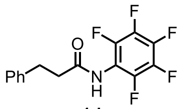
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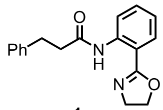
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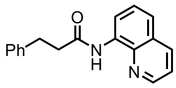
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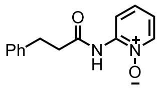
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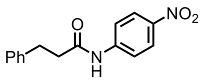
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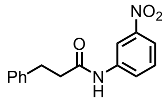
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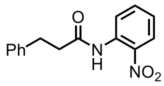
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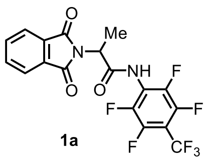
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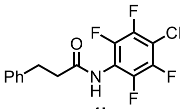
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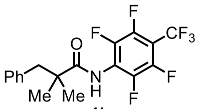
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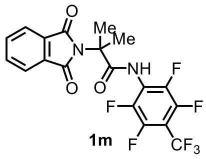
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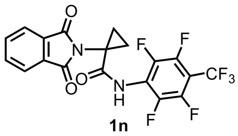
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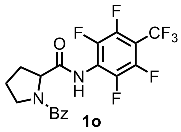
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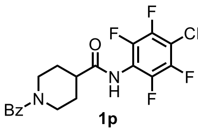
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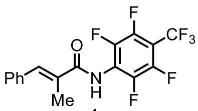
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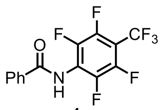
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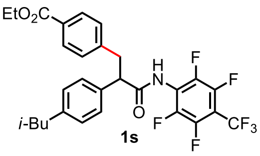
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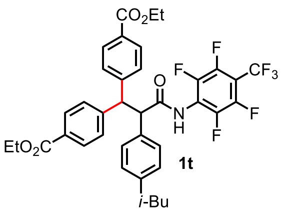
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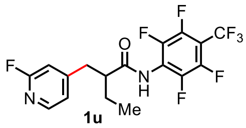
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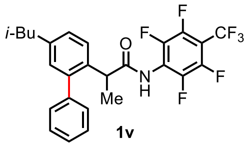
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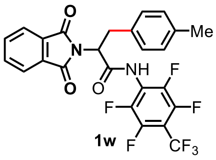
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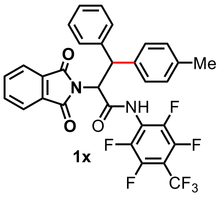
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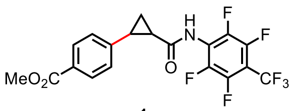
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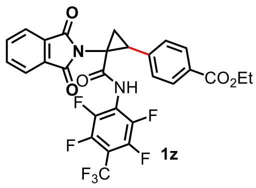
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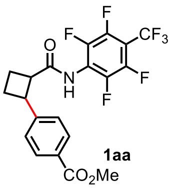
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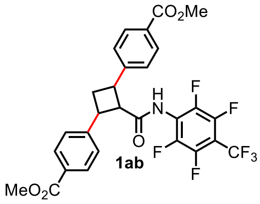
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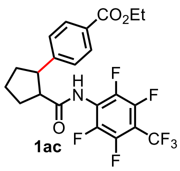
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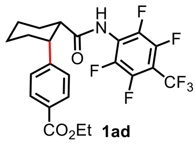
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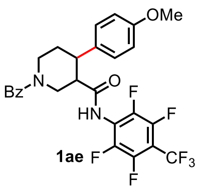
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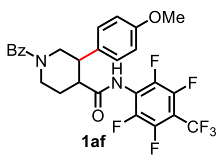
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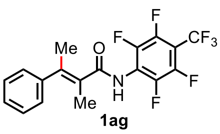
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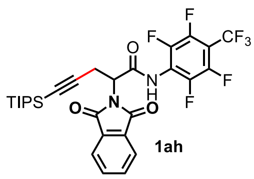
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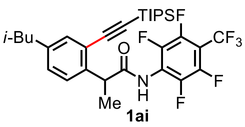
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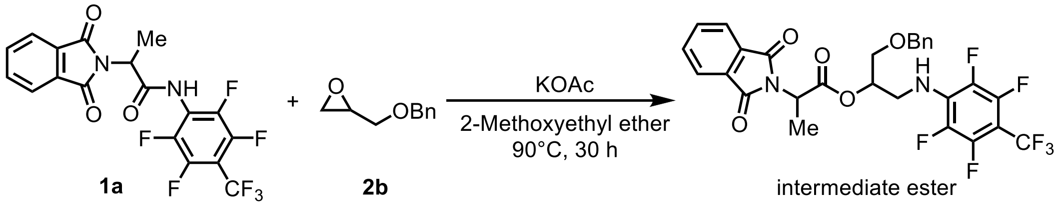
## Experimental Section

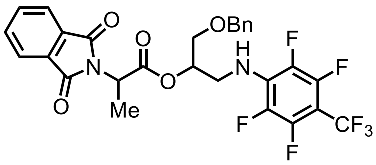
### Substrate Preparation

Substrates **1a-r** were prepared through traditional synthesis following literature procedure.[1] Substrates **1s-ai** were prepared through C−H functionalization method following literature procedure.[1, 2, 3 ,4, 5, 6]

### Synthesis Intermediate Ester and Leaving Group

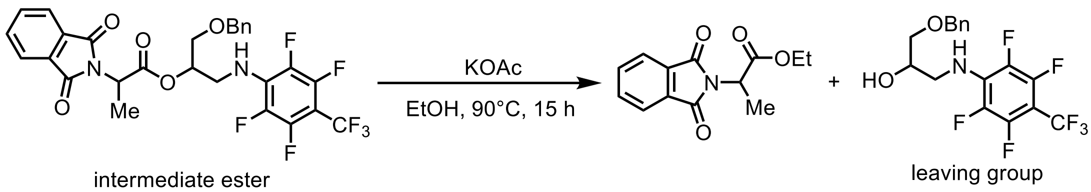



**The Procedure for the Synthesis of Intermediate Ester:** An oven-dried 25 mL Schlenk tube was charged with substrate **1a** (0.2 mmol, 86.9 mg), and then KOAc (0.2 mmol, 19.6 mg), 2-methoxyethyl ether (2 mL) and epoxide **2b** (0.6 mmol, 98.5 mg) was successively added. After inertion (vacuum/nitrogen), the reaction mixture was stirred at 90 ℃ for 30 h. Upon completion, the reaction mixture was purified by column chromatography using hexane/EtOAc (10/1) as the eluent, and the product intermediate ester was obtained as colorless oil (103.0 mg, 86%).

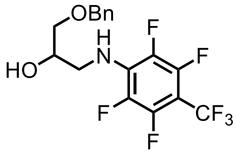


**1-(Benzyloxy)-3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenylamino)propan-2-yl 2-(1,3-dioxoisoindolin-2-yl)propanoate (intermediate ester)**

$^1$H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.83 (m, 2H), 7.78 – 7.72 (m, 2H), 7.33 – 7.27 (m, 3H), 7.21 – 7.16 (m, 2H), 5.30 – 5.21 (m, 1H), 5.00 (q, *J* = 7.0 Hz, 2H), 4.92 (br, 1H), 4.46 (s, 2H), 3.90 – 3.82 (m, 1H), 3.64 – 3.58 (m, 1H), 3.57 – 3.48 (m, 2H), 3.58 – 3.48 (m, 1H), 1.65 (d, *J* = 7.5 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.41, 167.64, 137.44, 134.56, 131.81, 128.60, 128.01, 127.62, 123.74, 73.57, 73.29, 68.98, 47.48, 46.05, 15.77. HRMS (ESI-TOF) Calcd for $C_{28}H_{22}F_7N_2O_5$ $[M+H]^+$: 599.1411, found: 599.1413.



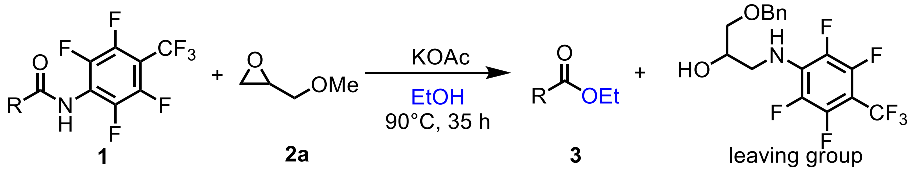

**The Procedure for the Synthesis of Leaving Group:** An oven-dried 25 mL Schlenk tube was charged with intermediate ester (0.2 mmol, 119.7 mg), and then KOAc (0.2 mmol, 19.6 mg) and EtOH (2 mL) was successively added. After inertion (vacuum/nitrogen), the reaction mixture was stirred at 90 ℃ for 15 h. Upon completion, the reaction mixture was purified by column chromatography using hexane/EtOAc (10/1) as the eluent, and the product leaving group was obtained as colorless oil.



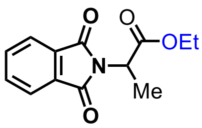

**1-(Benzyloxy)-3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenylamino)propan-2-ol (leaving group)**

$^1$H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 4.73 (s, 1H), 4.61 – 4.52 (m, 1H), 4.05 – 3.97 (m, 1H), 3.70 – 3.62 (m, 1H), 3.61 – 3.57 (m, 1H), 3.52 – 3.42 (m, 2H), 2.63 (br, 1H). HRMS (ESI-TOF) Calcd for $C_{17}H_{15}F_7NO_2$ $[M+H]^+$: 398.0986, found: 398.0986. $^{13}$C NMR (125 MHz, $CDCl_3$) δ 137.47, 128.72, 128.23, 127.98, 73.81, 71.87, 69.52, 47.73 (t, $J$ = 3.5 Hz). HRMS (ESI-TOF) Calcd for $C_{17}H_{15}FNO_2$ $[M+H]^+$: 398.0986, found: 398.0988.

## Amide Alcoholysis




**General Procedures for the Amide Alcoholysis:** An oven-dried 25 mL Schlenk tube was charged with substrate **1** (0.2 mmol), and then KOAc (0.2 mmol, 19.6 mg), EtOH (2 mL, the water content of the solvent was below 0.01wt %) and epoxide **2a** (0.6 mmol, 52.9 mg) was successively added. After inertion (vacuum/nitrogen), the reaction mixture was stirred at 90 ℃ for 35 h. Upon completion, the solvent was removed under reduced pressure. The residue was purified by column chromatography using hexane/EtOAc as the eluent (Rf value of all products is between 0.3 and 0.5 with specific eluent notified).




**Ethyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (3a)**

Substrate **1a** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3a** was obtained as a colorless oil (45.8 mg, 93%). $^1$NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.79 (m, 2H), 7.77 – 7.60 (m, 2H), 4.95 (q, $J$ = 7.5 Hz, 1H), 4.19 (td, $J$ = 7.0, 3.5 Hz, 2H), 1.69 (d, $J$ = 7.5 Hz, 3H), 1.22 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.75, 167.47, 134.20, 131.99, 123.49, 61.90, 47.66, 15.28, 14.12. HRMS (ESI-TOF) Calcd for $C_{13}H_{14}NO_4$ $[M+H]^+$: 248.0917, found: 248.0919.

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## Chromatogram and Results

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|---|---|---|---|
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| *Vial Number:* | **Vial:84** | *Injection Volume:* | **5.00** |
| *Creation operator:* | **zhangyan** | *User Name:* | **zhangyan** |
| *Instrument Method:* | **LC-052516-01-120265** | *Comment:* | |
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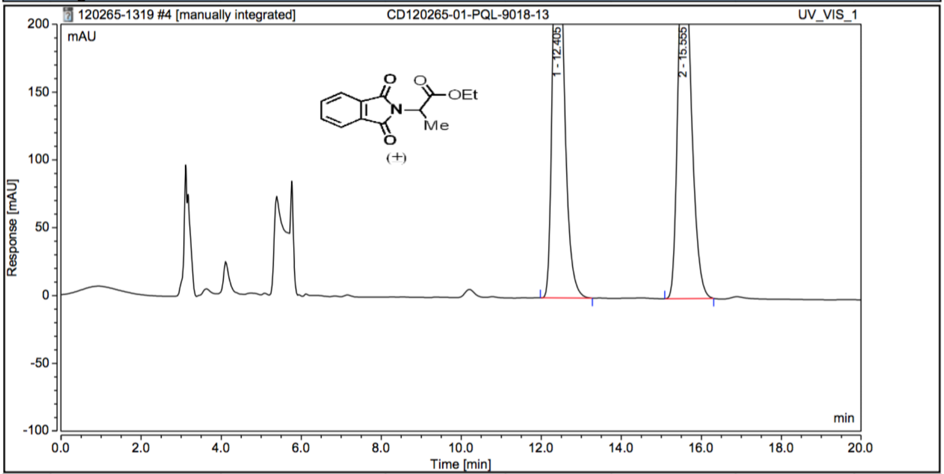
**Chromatogram**




**Integration Results**

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Amount n.a. | Plates (EP) |
|---|---|---|---|---|---|---|---|
| 1 | | 12.405 | 108.061 | 349.800 | 50.22 | n.a. | 11010 |
| 2 | | 15.555 | 107.131 | 296.907 | 49.78 | n.a. | 12286 |
| **Total:** | | | **215.192** | **646.707** | **100.00** | | |

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## Chromatogram and Results

**Injection Details**

| | | | |
|---|---|---|---|
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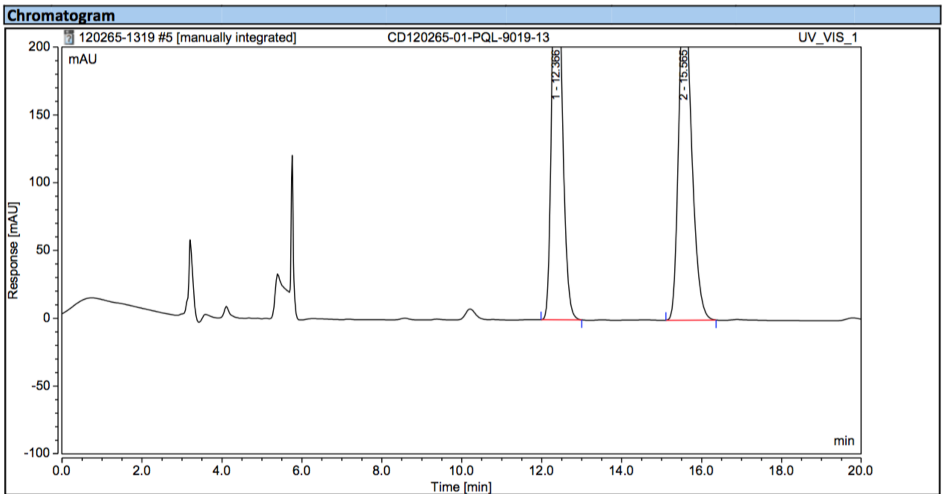
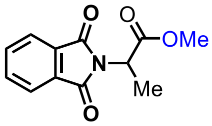
**Chromatogram**



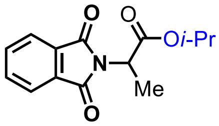

**Integration Results**

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Amount n.a. | Plates (EP) |
|---|---|---|---|---|---|---|---|
| 1 | | 12.366 | 93.680 | 337.840 | 50.25 | n.a. | 13087 |
| 2 | | 15.565 | 92.765 | 254.437 | 49.75 | n.a. | 12045 |
| **Total:** | | | **186.445** | **592.277** | **100.00** | | |



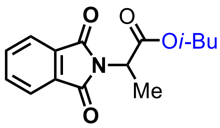

**Methyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (3a1)**

Substrate **1a** was alcoholized following the general alcoholysis procedure. MeOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3a1** was obtained as a colorless oil (42.5 mg, 91%). $^{1}$NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.75 – 7.69 (m, 2H), 4.96 (q, $J$ = 7.5 Hz, 1H), 3.72 (s, 3H), 1.68 (d, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 170.24, 167.42, 134.23, 131.94, 123.54, 52.83, 47.42, 15.33. HRMS (ESI-TOF) Calcd for $C_{12}H_{12}NO_4$ $[M+H]^+$: 234.0761, found: 234.0761.



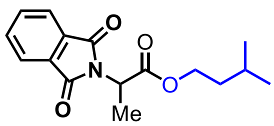

**Isopropyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (3a2)**

Substrate **1a** was alcoholized following the general alcoholysis procedure. *i*-PrOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3a2** was obtained as a colorless oil (49.5 mg, 95%). $^{1}$NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.80 (m, 2H), 7.75 – 7.69 (m, 2H), 5.11 – 4.99 (m, 1H), 4.91 (q, $J$ = 7.5 Hz, 1H), 1.66 (d, $J$ = 7.5 Hz, 3H), 1.20 (dd, $J$ = 20.0, 6.5 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.22, 167.51, 134.19, 132.01, 123.49, 47.82, 21.76, 21.68, 15.33. HRMS (ESI-TOF) Calcd for $C_{14}H_{16}NO_4$ $[M+H]^+$: 262.1074, found: 262.1081.




**Isobutyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (3a3)**

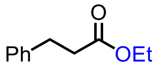
Substrate **1a** was alcoholized following the general alcoholysis procedure. *i*-BuOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3a3** was obtained as a colorless oil (50.7 mg, 92%). $^{1}$NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.79 (m, 2H), 7.75 – 7.68 (m, 2H), 4.96 (q, $J$ = 7.5 Hz, 1H), 3.96 – 3.86 (m, 2H), 1.93 – 1.79 (m, 1H), 1.69 (d, $J$ = 7.5 Hz, 3H), 0.83 (dd, $J$ = 7.0, 1.0 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.74, 167.50, 134.22, 131.96, 123.49, 71.80, 47.64, 27.66, 18.97, 18.95, 15.30. HRMS (ESI-TOF) Calcd for $C_{15}H_{18}NO_4$ $[M+H]^+$: 276.1230, found: 276.1232.




**Isopentyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (3a4)**

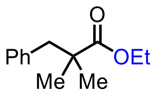
Substrate **1a** was alcoholized following the general alcoholysis procedure. *i*-AmylOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3a4** was obtained as a colorless oil (50.2 mg, 87%). $^{1}$NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.76 – 7.70 (m, 2H), 5.00 – 4.91 (m, 1H), 4.16 (t, $J$ = 7.0 Hz, 2H), 1.68

(d, $J$ = 8.0 Hz, 3H), 1.64 – 1.52 (m, 1H), 1.52 – 1.37 (m, 2H), 0.87 – 0.72 (m, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.82, 167.55, 134.23, 132.03, 123.54, 64.63, 47.70, 37.16, 25.13, 22.50, 22.41, 15.35. HRMS (ESI-TOF) Calcd for $C_{16}H_{20}NO_4$ $[M+H]^+$: 290.1387, found: 290.1387.



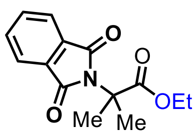
**Ethyl 3-phenylpropanoate (3b)**

Substrate **1k** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (30/1) as the eluent, **3b** was obtained as a colorless oil (34.5 mg, 97%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.24 – 7.17 (m, 3H), 4.13 (q, $J$ = 7.0 Hz, 2H), 2.96 (t, $J$ = 8.0 Hz, 2H), 2.63 (t, $J$ = 8.0 Hz, 2H), 1.24 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.98, 140.68, 128.56, 128.39, 126.31, 60.49, 36.05, 31.09, 14.30. HRMS (ESI-TOF) Calcd for $C_{11}H_{15}O_2$ $[M+H]^+$: 179.1067, found: 179.1065.



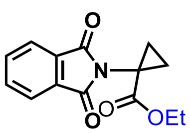
**Ethyl 2,2-dimethyl-3-phenylpropanoate (3c)**

Substrate **1l** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3c** was obtained as a colorless oil (38.8 mg, 94%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.25 – 7.20 (m, 1H), 7.13 (d, $J$ = 7.0 Hz, 2H), 4.13 (q, $J$ = 7.0 Hz, 2H), 2.87 (s, 2H), 1.25 (t, $J$ = 7.0 Hz, 3H), 1.19 (s, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 177.62, 138.10, 130.30, 128.06, 126.52, 60.52, 46.41, 43.61, 25.09, 14.31. HRMS (ESI-TOF) Calcd for $C_{13}H_{19}O_2$ $[M+H]^+$: 207.1380, found: 207.1376.



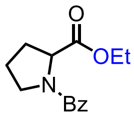
**Ethyl 2-(1,3-dioxoisoindolin-2-yl)-2-methylpropanoate (3d)**

Substrate **1m** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3d** was obtained as a colorless oil (47.1 mg, 90%). $^1$NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.76 (m, 2H), 7.73 – 7.65 (m, 2H), 4.20 (q, $J$ = 7.0 Hz, 2H), 1.81 (s, 6H), 1.22 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.97, 168.40, 134.12, 131.96, 123.19, 61.72, 60.46, 29.79, 24.51, 14.14. HRMS (ESI-TOF) Calcd for $C_{14}H_{16}NO_4$ $[M+H]^+$: 262.1074, found: 262.1073.



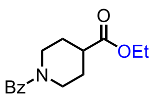
**Ethyl 1-(1,3-dioxoisoindolin-2-yl)cyclopropanecarboxylate (3e)**

Substrate **1n** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3e** was obtained as a colorless oil (47.6 mg, 92%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.79 – 7.68 (m, 2H), 4.11 (dd, *J* = 14.0, 7.0 Hz, 2H), 1.83 (dd, *J* = 8.5, 5.0 Hz, 2H), 1.44 (dd, *J* = 8.5, 5.0 Hz, 2H), 1.16 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 170.59, 168.16, 134.34, 131.76, 123.57, 61.93, 31.75, 16.27, 14.17. HRMS (ESI-TOF) Calcd for $C_{14}H_{14}NO_4$ $[M+H]^+$: 260.0917, found: 260.0918.



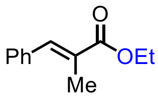

**Ethyl 1-benzoylpyrrolidine-2-carboxylate (3f)**

Substrate **1o** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3f** was obtained as a colorless oil (43.9 mg, 89%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.5 Hz, 2H), 7.43 – 7.35 (m, 3H), 4.69 – 4.59 (m, 1H), 4.22 (q, *J* = 7.0 Hz, 2H), 3.64 (dt, *J* = 14.0, 7.0 Hz, 1H), 3.56 – 3.47 (m, 1H), 2.31 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.04 – 1.97 (m, 2H), 1.92 – 1.82 (m, 1H), 1.29 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 172.36, 169.73, 136.38, 130.23, 128.33, 127.33, 61.22, 59.37, 50.03, 29.51, 25.47, 14.30. HRMS (ESI-TOF) Calcd for $C_{14}H_{18}NO_3$ $[M+H]^+$: 248.1281, found: 248.1286.



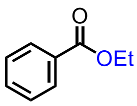

**Ethyl 1-benzoylpiperidine-4-carboxylate (3g)[7]**

Substrate **1p** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (5/1) as the eluent, **3g** was obtained as a colorless oil (47.6 mg, 91%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.33 (m, 5H), 4.66 – 4.37 (m, 1H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.84 – 3.55 (m, 1H), 3.16 – 3.93 (m, 2H), 2.61 – 2.52 (m, 1H), 2.11 – 1.70 (m, 4H), 1.25 (d, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.29, 170.57, 136.13, 129.74, 128.61, 126.94, 60.79, 47.12, 41.64, 41.21, 29.83, 14.32. Calcd for $C_{15}H_{20}NO_3$ $[M+H]^+$: 262.1438, found: 262.1420.



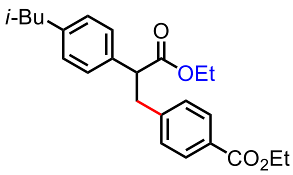

**Ethyl 2-methyl-3-phenylacrylate (3h)**

Substrate **1q** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3h** was obtained as a colorless oil (34.7 mg, 91%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.43 – 7.36 (m, 4H), 7.35 – 7.29 (m, 1H), 4.28 (q, *J* = 7.0 Hz, 2H), 2.13 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.81, 138.76, 136.09, 129.75, 128.76, 128.47, 128.35, 61.00, 14.46, 14.18. HRMS (ESI-TOF) Calcd for $C_{12}H_{15}O_2$ $[M+H]^+$: 191.1067, found: 191.1065.



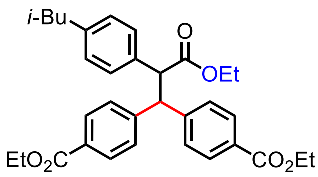

**Ethyl benzoate (3i)**

Substrate **1r** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (30/1) as the eluent, **3i** was obtained as a colorless oil (18.5 mg, 62%). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.11 – 8.01 (m, 2H), 7.59 – 7.52 (m, 1H), 7.48 – 7.40 (m, 2H), 4.38 (q, *J* = 7.0 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.75, 132.91, 130.61, 129.64, 128.42, 61.07, 14.46. HRMS (ESI-TOF) Calcd for $C_9H_{11}O_2$ $[M+H]^+$: 151.0754, found: 151.0739.



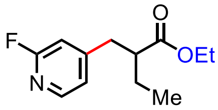

**Ethyl 4-(3-ethoxy-2-(4-isobutylphenyl)-3-oxopropyl)benzoate (3j)**

Substrate **1s** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (25/1) as the eluent, **3j** was obtained as a colorless oil (72.4 mg, 95%). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.21 – 7.17 (m, 4H), 7.08 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 4.15 – 3.96 (m, 2H), 3.83 – 3.76 (m, 1H), 3.46 – 3.41 (m, 1H), 3.08 – 3.03 (m, 1H), 2.44 (d, *J* = 8.0 Hz, 2H), 1.89 – 1.79 (m, 1H), 1.38 (t, *J* = 8.0 Hz, 3H), 1.12 (t, *J* = 8.0 Hz, 3H), 0.89 (d, *J* = 8.0 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 173.30, 166.65, 144.65, 141.00, 135.66, 129.63, 129.47, 129.08, 128.70, 127.65, 60.91, 53.05, 45.11, 39.95, 30.26, 22.44, 14.42, 14.14. HRMS (ESI-TOF) Calcd for $C_{24}H_{31}O_4$ $[M+H]^+$: 383.2217, found: 383.2216.



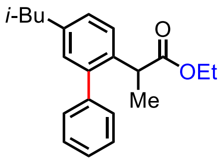

**Diethyl 4,4'-(3-ethoxy-2-(4-isobutylphenyl)-3-oxopropane-1,1-diyl) dibenzoate (3k)**

Substrate **1t** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (25/1) as the eluent, **3k** was obtained as a colorless oil (101.5 mg, 96%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.40 – 4.33 (m, 3H), 4.27 (q, *J* = 7.0 Hz, 2H), 4.02 – 3.96 (m, 1H), 3.94 – 3.88 (m, 1H), 2.35 (d, *J* = 7.0 Hz, 2H), 1.79 – 1.73 (m, 1H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.01 (t, *J* = 7.0 Hz, 3H), 0.82 – 0.80 (m, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.47, 166.47, 166.43, 147.42, 146.29, 141.21, 133.58, 130.12, 129.67, 129.42, 128.49, 128.28, 127.95, 61.07, 60.95, 56.16, 55.00, 45.07, 30.20, 22.41, 22.38, 14.47, 14.40, 14.05. HRMS (ESI-TOF) Calcd for $C_{33}H_{39}O_6$ $[M+H]^+$: 531.2741, found: 531.2739.



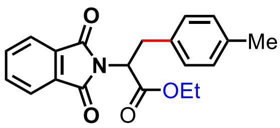

**Ethyl 2-((2-fluoropyridin-4-yl)methyl)butanoate (3l)**

Substrate **1u** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3l** was obtained as a colorless oil (42.4 mg, 94%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 5.0 Hz, 1H), 6.99 (d, *J* = 5.0 Hz, 1H), 6.74 (s, 1H), 4.15 – 4.01 (m, 2H), 2.96 (dd, *J* = 14.0, 9.5 Hz, 1H), 2.77 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.65 – 2.55 (m, 1H), 1.72 – 1.65 (m, 1H), 1.63 – 1.53 (m, 1H), 1.16 (t, *J* = 7.0 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.66, 164.15 (d, *J* = 237.5 Hz), 154.76 (d, *J* = 7.5 Hz), 147.57 (d, *J* = 15.0 Hz), 122.07 (d, *J* = 3.8 Hz), 109.75 (d, *J* = 36.3 Hz), 60.65, 48.01, 37.14 (d, *J* = 2.5 Hz), 25.63, 14.33, 11.66. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -69.29 (S). HRMS (ESI-TOF) Calcd for $C_{12}H_{17}FNO_2$ $[M+H]^+$: 226.1238, found: 226.1238.



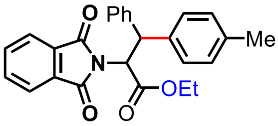

**Ehyl 2-(5-isobutylbiphenyl-2-yl)propanoate (3m)**

Substrate **1v** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (50/1) as the eluent, **3m** was obtained as a colorless oil (59.8 mg, 96%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.36 (m, 4H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.04 (s, 1H), 4.17 – 4.05 (m, 2H), 3.87 (q, *J* = 7.0 Hz, 1H), 2.49 (d, *J* = 7.0 Hz, 2H), 1.94 – 1.86 (m, 1H), 1.37 (d, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.21, 141.65, 141.51, 140.05, 136.04, 130.96, 129.59, 128.68, 128.16, 127.04, 126.62, 60.63, 45.12, 41.02, 30.23, 22.57, 22.55, 19.39, 14.20. HRMS (ESI-TOF) Calcd for $C_{21}H_{27}O_2$ $[M+H]^+$: 311.2006, found: 311.2006.



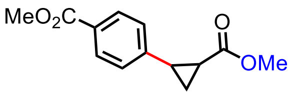

**Ethyl 2-(1,3-dioxoisoindolin-2-yl)-3-p-tolylpropanoate (3n)**

Substrate **1w** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (15/1) as the eluent, **3n** was obtained as a colorless oil (63.1 mg, 93%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.74 (m, 2H), 7.71 – 7.63 (m, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 5.15 – 5.08 (m, 1H), 4.27 – 4.20 (m, 2H), 3.58 – 3.46 (m, 2H), 2.22 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 169.02, 167.65, 136.40, 134.15, 133.79, 131.77, 129.35, 128.80, 123.56, 62.12, 53.68, 34.33, 21.13, 14.25. HRMS (ESI-TOF) Calcd for $C_{20}H_{20}NO_4$ $[M+H]^+$: 338.1387, found: 338.1388.



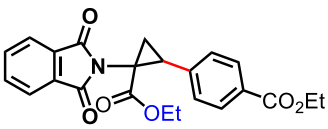

**Ethyl 2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-3-p-tolylpropanoate (3o)**

Substrate **1x** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3o** was obtained as a colorless oil (62.2 mg, 75%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.69 (m, 2H), 7.69 – 7.62 (m, 2H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 9.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 0.5H), 7.17 (t, *J* = 7.0 Hz, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 0.5H), 6.93 (d, *J* = 7.5 Hz, 1H), 5.78 – 5.71 (m, 1H), 5.33 – 5.23 (m, 1H), 4.13 – 3.98 (m, 2H), 2.32 (s, 1.5H), 2.13 (s, 1.5H), 1.06 – 0.98 (m, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.43, 168.37, 167.49, 167.44, 142.03, 140.84, 138.75, 137.61, 136.46, 136.44, 134.11, 131.52, 131.45, 129.47, 129.32, 128.73, 128.57, 127.98, 127.83, 127.81, 127.70, 126.85, 123.50, 123.45, 77.41, 77.16, 76.91, 61.75, 61.71, 55.40, 55.26, 50.33, 50.29, 29.81, 21.14, 20.99, 13.83. HRMS (ESI-TOF) Calcd for $C_{26}H_{24}NO_4$ $[M+H]^+$: 414.1700, found: 414.1703.



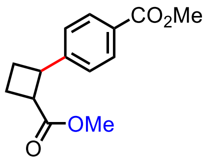

**Methyl 4-(2-(methoxycarbonyl)cyclopropyl)benzoate (3p)**

Substrate **1y** was alcoholized following the general alcoholysis procedure. MeOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, **3p** was obtained as a colorless oil (43.2 mg, 92%). $^{1}$NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 3.43 (s, 3H), 2.60 (q, *J* = 8.0 Hz, 1H), 2.18 – 2.13 (m, 1H), 1.77 – 1.72 (m, 1H), 1.43 – 1.37 (m, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 171.20, 167.14, 142.09, 129.36, 128.66, 52.15, 51.71, 25.60, 22.16, 11.75. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}O_4$ $[M+H]^+$: 235.0965, found: 235.0966.



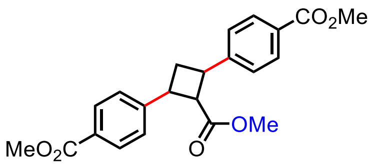

**Ethyl 4-(2-(1,3-dioxoisoindolin-2-yl)-2-(ethoxycarbonyl)cyclopropyl) benzoate (3q)**

Substrate **1z** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, **3q** was obtained as a colorless oil (73.9 mg, 91%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 2H), 7.92 – 7.91 (m, 2H), 7.79 – 7.77 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 4.38 (q, *J* = 7.0 Hz, 2H), 3.84 – 3.76 (m, 2H), 3.17 (t, *J* = 9.5 Hz, 1H), 2.51 (dd, *J* = 9.0, 6.5 Hz, 1H), 1.94 (dd, *J* = 9.0, 6.5 Hz, 1H), 1.40 (t, *J* = 7.0 Hz, 3H), 0.78 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.22, 167.65, 166.66, 140.20, 134.56, 131.87, 129.91, 129.46, 123.76, 61.74, 61.07, 38.21, 33.48, 19.24, 14.50, 13.84. HRMS (ESI-TOF) Calcd for $C_{23}H_{22}NO_6$ $[M+H]^+$: 408.1442, found: 408.1442.



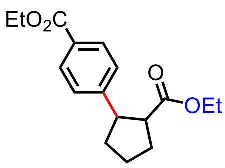

**Methyl 4-(2-(methoxycarbonyl)cyclobutyl)benzoate (3r)**

Substrate **1aa** was alcoholized following the general alcoholysis procedure. MeOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, **3r** was obtained as a colorless oil (46.3 mg, 93%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.91 (s, 3H), 3.88 – 3.81 (m, 1H), 3.71 (s, 3H), 3.22 (q, *J* = 8.0 Hz, 1H), 2.38 – 2.31 (m, 2H), 2.29 – 2.12 (m, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.66, 167.13, 148.93, 129.86, 128.39, 126.50, 52.16, 51.94, 45.07, 43.10, 25.33, 21.90. HRMS (ESI-TOF) Calcd for $C_{14}H_{17}O_4$[M+H]$^+$: 249.1121, found: 249.1128



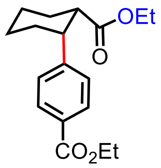

**Dimethyl 4,4'-(2-(methoxycarbonyl)cyclobutane-1,3-diyl)dibenzoate (3s)**

Substrate **1ab** was alcoholized following the general alcoholysis procedure. MeOH was used as the solvent. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, **3s** was obtained as a colorless oil (72.4 mg, 95%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 4H), 7.34 (d, *J* = 8.0 Hz, 4H), 3.91 (s, 6H), 3.84 (q, *J* = 8.0 Hz, 2H), 3.75 (s, 3H), 3.32 – 3.28 (m, 1H), 2.87 – 2.81 (m, 1H), 2.34 – 2.26 (m, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 173.61, 167.04, 147.96, 130.01, 128.73, 126.67, 52.26, 52.23, 51.98, 39.53, 32.49, 29.85. HRMS (ESI-TOF) Calcd for $C_{22}H_{23}O_6$ [M+H]$^+$: 383.1489, found: 383.1458.



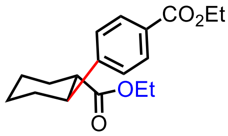

**Ethyl 4-(2-(ethoxycarbonyl)cyclopentyl)benzoate (3t)**

Substrate **1ac** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, **3t** was obtained as a colorless oil (53.6 mg, 92%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.96 (t, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 7.0 Hz, 2H), 4.05 (q, *J* = 7.0 Hz, 2H), 3.37 (q, *J* = 9.0 Hz, 1H), 2.81 (q, *J* = 9.0 Hz, 1H), 2.24 – 2.10 (m, 2H), 2.02 – 1.93 (m, 1H), 1.91 – 1.79 (m, 2H), 1.79 – 1.69 (m, 1H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.54, 166.67, 149.47, 129.83, 128.74, 127.34, 60.90, 60.50, 52.18, 49.86, 35.08, 30.84, 25.16, 14.47, 14.31. HRMS (ESI-TOF) Calcd for $C_{17}H_{23}O_4$ [M+H]$^+$: 291.1591, found: 291.1591.

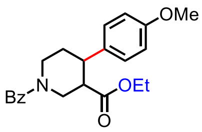



**cis-Ethyl 4-(2-(ethoxycarbonyl)cyclohexyl)benzoate (cis-3u)**

Substrate **1ad** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (10/1) as the eluent, ***cis*-3u** was obtained as colorless oil (50.5 mg, 83%) and t***rans*-3u** was obtained as colorless oil (4.0 mg, 6%). The configuration of ***cis*-3n** was assigned as cis- based on the $^{1}$H spectrum data of ***cis*-3u** match those of the reported compound cis- N-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenyl)-2-p-tolylcyclohexanecarboxamide.[4] $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 7.0 Hz, 2H), 3.90 – 3.80 (m, 2H), 2.89 – 2.76 (m, 1H), 2.63 – 2.53 (m, 1H), 2.08 – 1.99 (m, 1H), 1.92 – 1.78 (m, 3H), 1.62 – 1.56 (m, 1H), 1.50 – 1.42 (m, 2H), 1.42 – 1.34 (m, 4H), 0.94 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.95, 166.72, 150.21, 129.75, 128.74, 127.49, 60.90, 60.09, 49.97, 46.82, 34.18, 30.17, 26.19, 25.42, 14.47, 14.10. HRMS (ESI-TOF) Calcd for $C_{18}H_{25}O_4$ $[M+H]^+$: 305.1747, found: 305.1749.

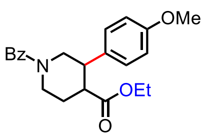



***trans*-Ethyl 4-(2-(ethoxycarbonyl)cyclohexyl)benzoate (*trans*-3u):** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.40 – 4.31 (m, 2H), 3.93 – 3.80 (m, 2H), 3.02 – 2.90 (m, 2H), 2.40 – 2.32 (m, 1H), 2.11 – 2.05 (m, 1H), 1.94 – 1.88 (m, 1H), 1.84 – 1.71 (m, 3H), 1.62 – 1.53 (m, 2H), 1.38 (t, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.0 Hz, 3H). HRMS (ESI-TOF) Calcd for $C_{18}H_{25}O_4$ $[M+H]^+$: 305.1747, found: 305.1747.

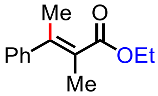



**Ethyl 1-benzoyl-4-(4-methoxyphenyl)piperidine-3-carboxylate (3v)**

Substrate **1ae** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3v** was obtained as a colorless oil (69.2 mg, 94%). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 5H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.08 – 4.76 (m, 1H), 4.00 – 3.78 (m, 3H), 3.77 (s, 3H), 3.31 – 2.56 (m, 4H), 1.90 – 1.56 (m, 2H), 1.00 – 0.77 (m, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 170.60, 158.65, 135.74, 134.33, 129.97, 128.67, 128.38, 127.09, 114.01, 60.53, 55.35, 29.78, 14.00. HRMS (ESI-TOF) Calcd for $C_{22}H_{26}NO_3$ $[M+H]^+$: 368.1856, found: 368.1838.

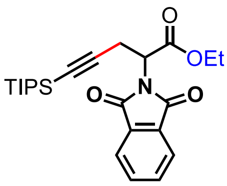


**Ethyl 1-benzoyl-3-(4-methoxyphenyl)piperidine-4-carboxylate (3w)** Substrate **1af** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3w** was obtained as a colorless oil (66.1 mg, 90%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.32 (m, 5H), 7.20 – 6.95 (m, 2H), 6.93 – 6.70 (m, 2H), 4.99 – 4.68 (m, 1H), 3.93 (dd, *J* = 14.0, 7.0 Hz, 2H), 3.77 (s, 3H), 3.17 – 2.68 (m, 4H), 2.19 – 1.53 (m, 4H), 1.01 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 173.65, 170.56, 158.86, 129.89, 128.68, 127.00, 114.11, 60.56, 55.48, 55.36, 48.78, 29.85, 14.13. HRMS (ESI-TOF) Calcd for $C_{22}H_{26}NO_3$ $[M+H]^+$: 368.1856, found: 368.1834.



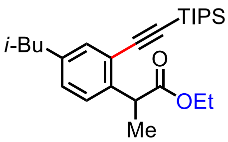

**(E)-ethyl 2-methyl-3-phenylbut-2-enoate (3x)**[8]

Substrate **1ag** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (30/1) as the eluent, **3x** was obtained as a colorless oil (38.7 mg, 95%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.32 – 7.28 (m, 1H), 7.17 (d, *J* = 7.0 Hz, 2H), 4.34 – 4.24 (m, 2H), 2.28 (d, *J* = 1.5 Hz, 3H), 1.78 (d, *J* = 1.5 Hz, 3H), 1.38 (t, *J* = 7.0 Hz, 3H). The $^1$H NMR spectral data matches that of previously reported: *Org. Lett.* **2002**, *4*, 189-191. HRMS (ESI-TOF) Calcd for $C_{13}H_{17}O_2$ $[M+H]^+$: 205.1223, found: 205.1223.




**Ethyl 2-(1,3-dioxoisoindolin-2-yl)-5-(triisopropylsilyl)pent-4-ynoate (3y)**

Substrate **1ah** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (20/1) as the eluent, **3y** was obtained as a colorless oil (72.5 mg, 85%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.76 – 7.69 (m, 2H), 5.08 (dd, *J* = 12.0, 5.0 Hz, 1H), 4.29 – 4.15 (m, 2H), 3.36 (dd, *J* = 17.5, 12.0 Hz, 1H), 3.11 (dd, *J* = 17.5, 5.0 Hz, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 0.88 – 0.76 (m, 21H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.05, 167.31, 134.21, 132.02, 123.59, 102.79, 83.66, 62.28, 50.91, 20.86, 18.43, 18.42, 14.19, 11.11. HRMS (ESI-TOF) Calcd for $C_{24}H_{34}NO_4Si$ $[M+H]^+$: 428.2252, found: 428.2250.

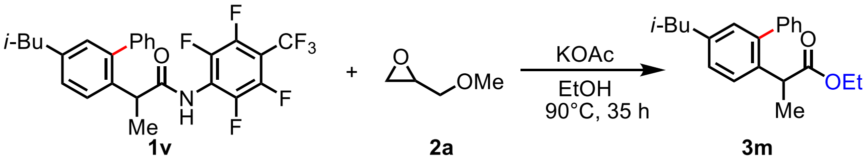



**Ethyl 2-(4-isobutyl-2-((triisopropylsilyl)ethynyl)phenyl)propanoate (3z)**

Substrate **1ai** was alcoholized following the general alcoholysis procedure. After purification by column chromatography using hexane/EtOAc (50/1) as the eluent, **3z** was obtained as a colorless oil (77.5 mg, 93%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.25 (m, 1H), 7.21 (d, *J* =

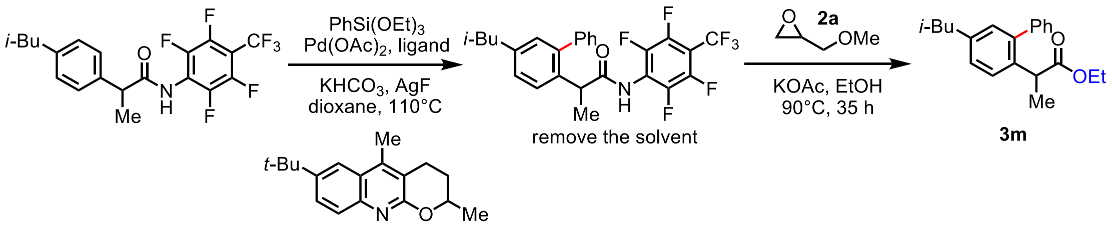
8.0 Hz, 1H), 7.11 – 7.04 (m, 1H), 4.37 (q, $J$ = 7.0 Hz, 1H), 4.21 – 4.03 (m, 2H), 2.41 (d, $J$ = 7.0 Hz, 2H), 1.85 (dp, $J$ = 14.0, 7.0 Hz, 1H), 1.47 (d, $J$ = 7.0 Hz, 3H), 1.20 (t, $J$ = 7.0 Hz, 3H), 1.14 (s, 18H), 0.90 (d, $J$ = 7.0 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 174.82, 140.59, 140.27, 133.38, 129.90, 126.21, 122.75, 105.43, 94.54, 60.74, 44.90, 42.85, 30.18, 22.53, 22.52, 18.83, 18.66, 14.25, 11.53. HRMS (ESI-TOF) Calcd for $C_{26}H_{43}O_2Si$ $[M+H]^+$: 415.3027, found: 415.3024.

**Procedure for scale up synthesis of 3m**




An oven-dried 250 mL Schlenk tube was charged with substrate **1v** (2.032 mmol, 1.011g), and then KOAc (2.032 mmol, 199 mg), EtOH (20 mL, the water content of the solvent was 0.01wt %) and epoxide **2a** (6.096 mmol, 537 mg) was successively added. After inertion (vacuum/nitrogen), the reaction mixture was stirred at 90 ℃ for 35 h. Upon completion, the solvent was removed under reduced pressure. The residue was purified by column chromatography using hexane/EtOAc(50/1) as the eluent, **3m** was obtained as a colorless oil (600 mg, 95%).

**Procedure for one-pot synthesis of 3m[3]**




An oven-dried 250 mL Schlenk tube was charged with amide substrate (2.374 mmol, 1.000 g), $Pd(OAc)_2$ (0.237 mmol, 53 mg), 7-(tert-butyl)-2,5-dimethyl-3,4-dihydro- 2H-pyrano[2,3-b]-quinoline (0.475 mmol, 128 mg), AgF (7.122 mmol, 903 mg), and $KHCO_3$ (4.748 mmol, 475 mg). Triethoxyphenylsilane (4.748 mmol, 1.141 g) and 1,4-dioxane (24 mL) were added. The reaction mixture was first stirred at room temperature for 10 min and then heated to 110 ℃ for 8 hours with vigorous stirring. After cooling down the reaction vessel, the second batch of the triethoxyphenylsilane (4.748 mmol, 1.141 g) and AgF (7.122 mmol, 903 mg) were added, and the mixture was then heated to 110 ℃ for another 10 hours with vigorous stirring. Upon completion, the solvent was removed under reduced pressure. To the residue was added KOAc (2.374 mmol, 233 mg), EtOH (24 mL, the water content of the solvent was 0.01wt %) and epoxide **2a** (7.122 mmol, 627 mg). After inertion (vacuum/nitrogen), the reaction mixture was stirred at 90 ℃ for 35 h. Upon completion, the solvent was removed under reduced pressure. The residue was purified by column chromatography using hexane/EtOAc(50/1) as the eluent, **3m** was obtained as a colorless oil (470 mg, 64%).

**Ehyl 2-(5-isobutylbiphenyl-2-yl)propanoate (3m)** $^1$H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.36 (m, 4H), 7.15 (d, $J$ = 8.0 Hz, 1H), 7.04 (s, 1H), 4.17 – 4.05 (m, 2H), 3.87 (q, $J$ = 7.0 Hz, 1H), 2.49 (d, $J$ = 7.0 Hz, 2H), 1.94 – 1.86 (m, 1H), 1.37 (d, $J$ = 7.0 Hz, 3H), 1.20 (t, $J$ = 7.0 Hz, 3H), 0.94 (d, $J$ = 6.5 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 175.21, 141.65, 141.51, 140.05, 136.04, 130.96, 129.59, 128.68, 128.16, 127.04, 126.62, 60.63, 45.12, 41.02, 30.23, 22.57, 22.55, 19.39, 14.20. HRMS (ESI-TOF) Calcd for $C_{21}H_{27}O_2$ $[M+H]^+$: 311.2006, found: 311.2006.

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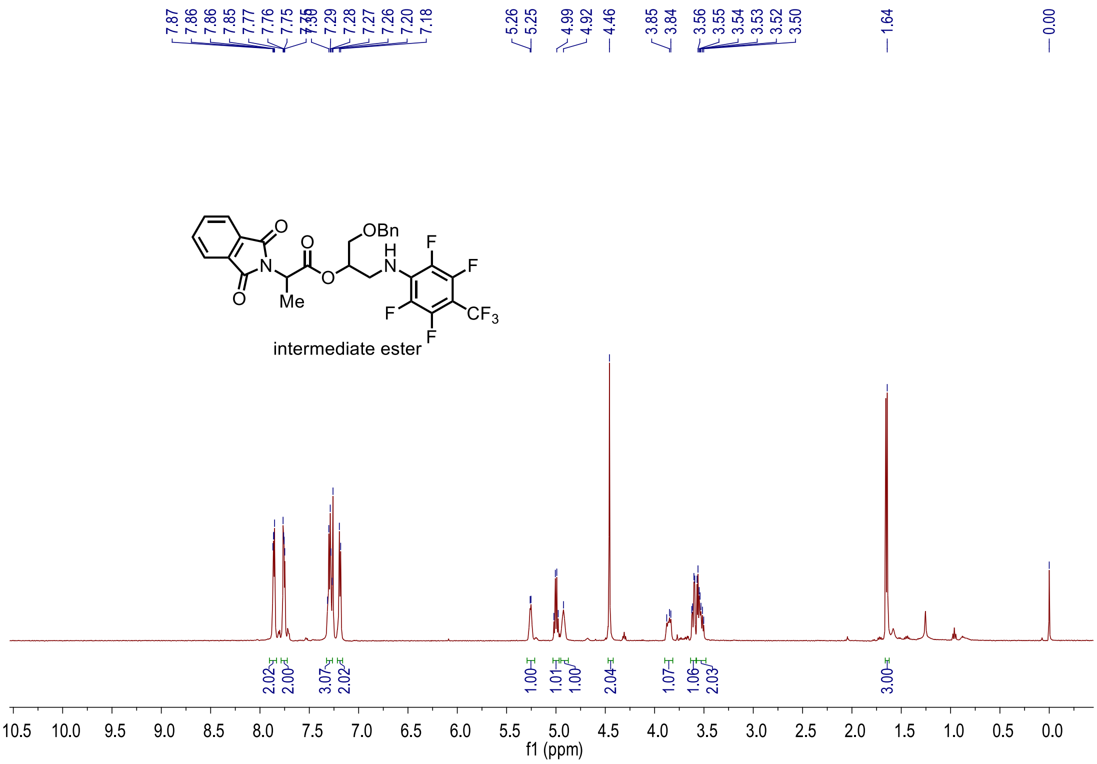
## $^1$H and $^{13}$C NMR Spectra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5.26
5.25
4.99
4.92
4.46
3.85
3.84
3.56
3.55
3.54
3.53
3.52
3.50
1.64
0.00
OBn
H
N
F
O
Me
CF$_3$
intermediate ester
2.02
2.00
3.07
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1.00
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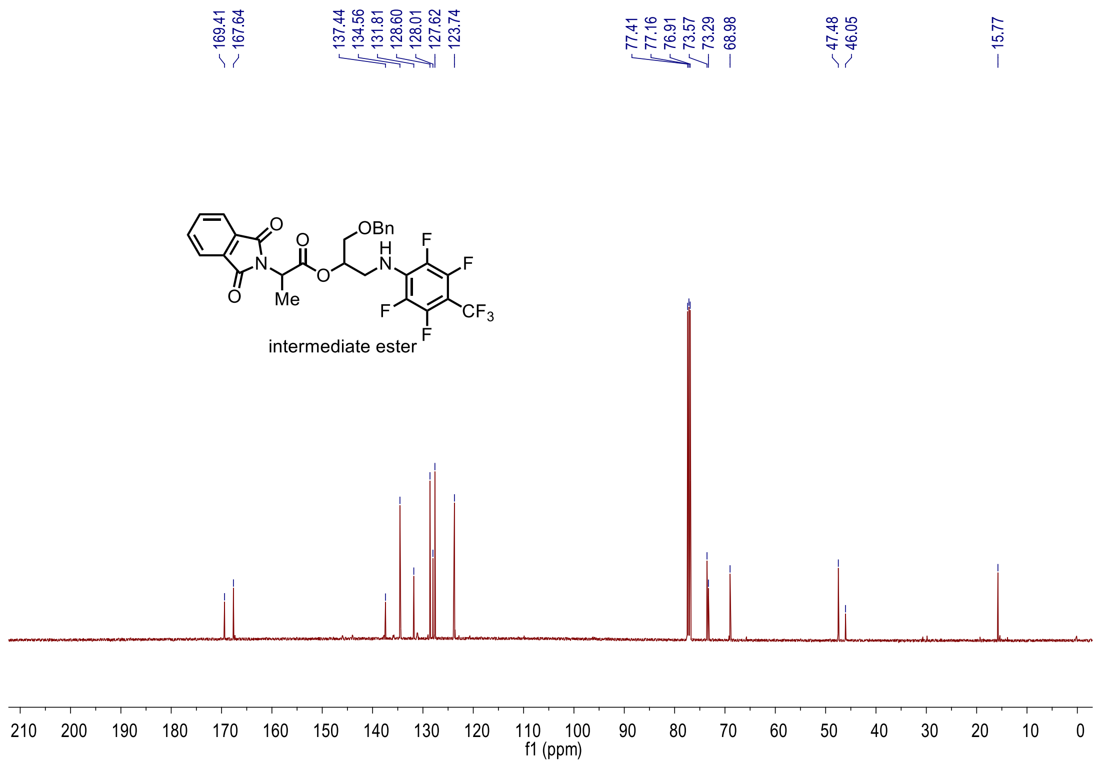
2.03
3.00
f1 (ppm)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N
F
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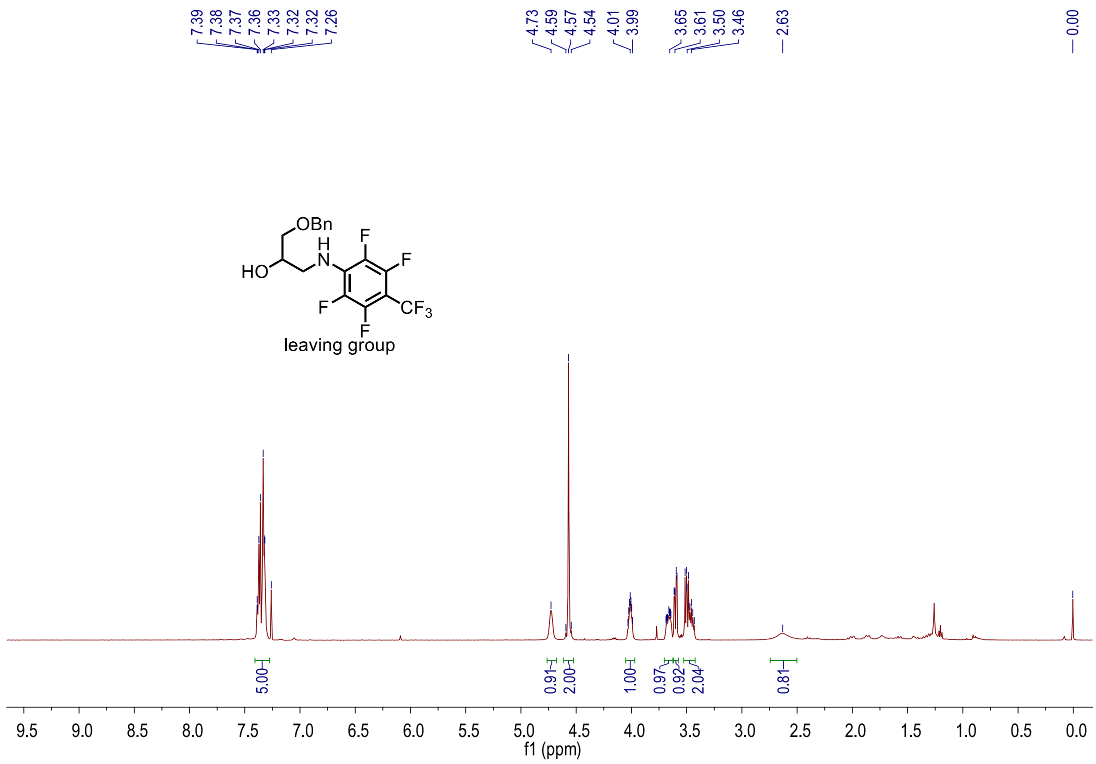
Me
CF$_3$
intermediate ester
f1 (ppm)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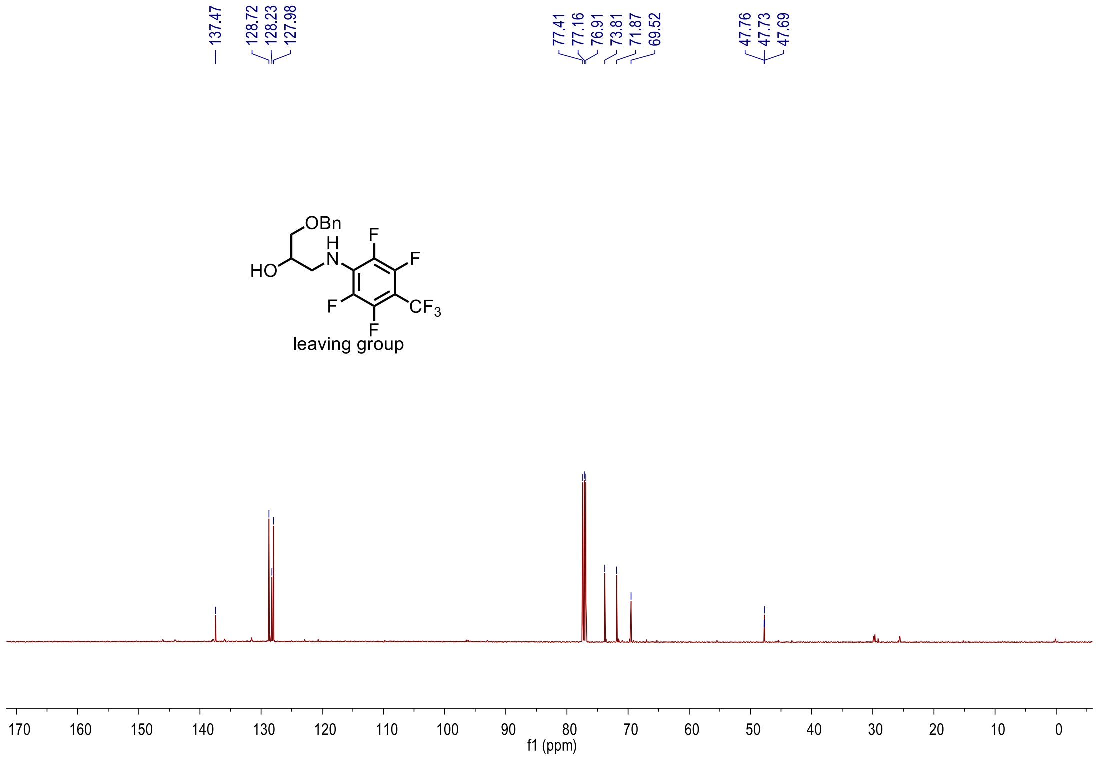
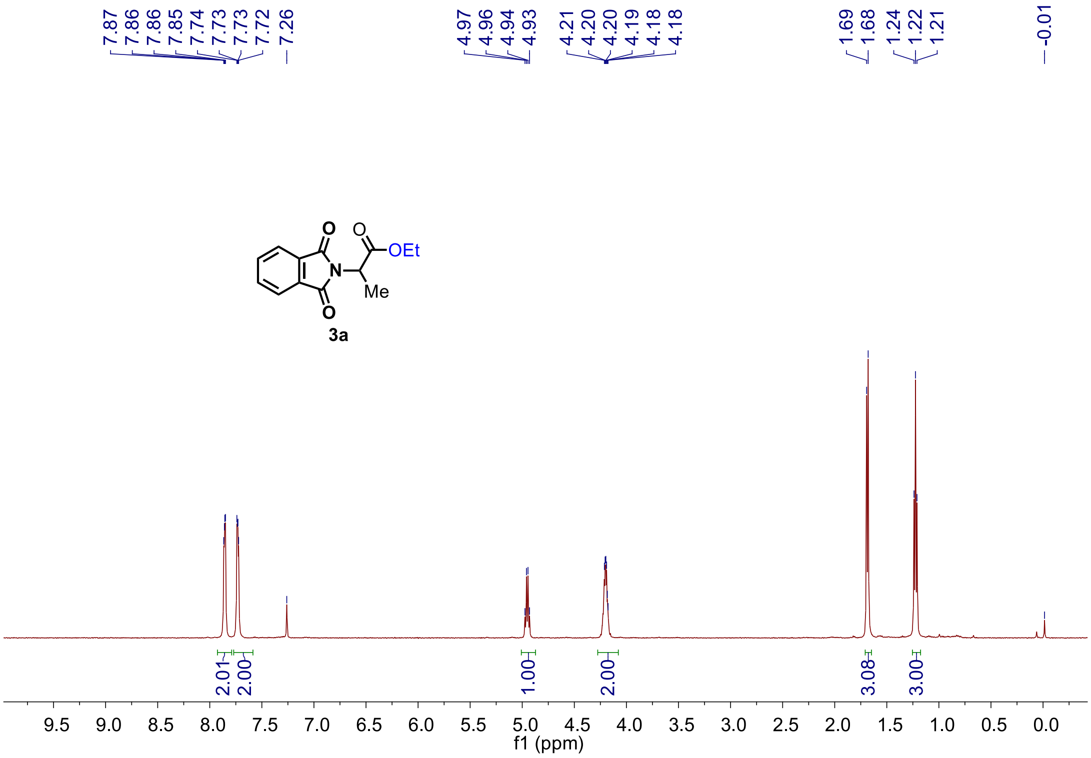
0.00
OBn
H
N
F
F
HO
F
CF3
F
leaving group
5.00
0.91 2.00
1.00
0.97 0.92 2.04
0.81
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


137.47
128.72 128.23 127.98
77.41 77.16 76.91 73.81 71.87 69.52
47.76 47.73 47.69
OBn
H
N
F
F
HO
F
CF3
F
leaving group
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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4.93
4.21
4.20
4.20
4.19
4.18
4.18
1.69
1.68
1.24
1.22
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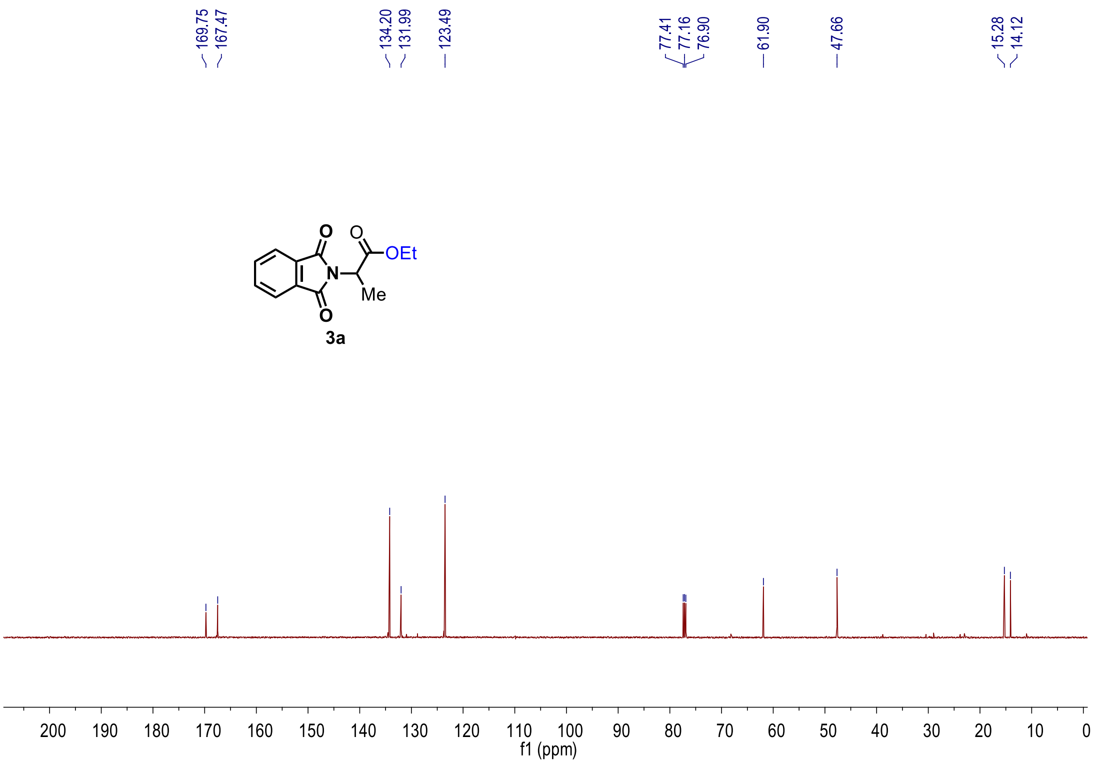
OEt
Me
3a
2.01
2.00
1.00
2.00
3.08
3.00
f1 (ppm)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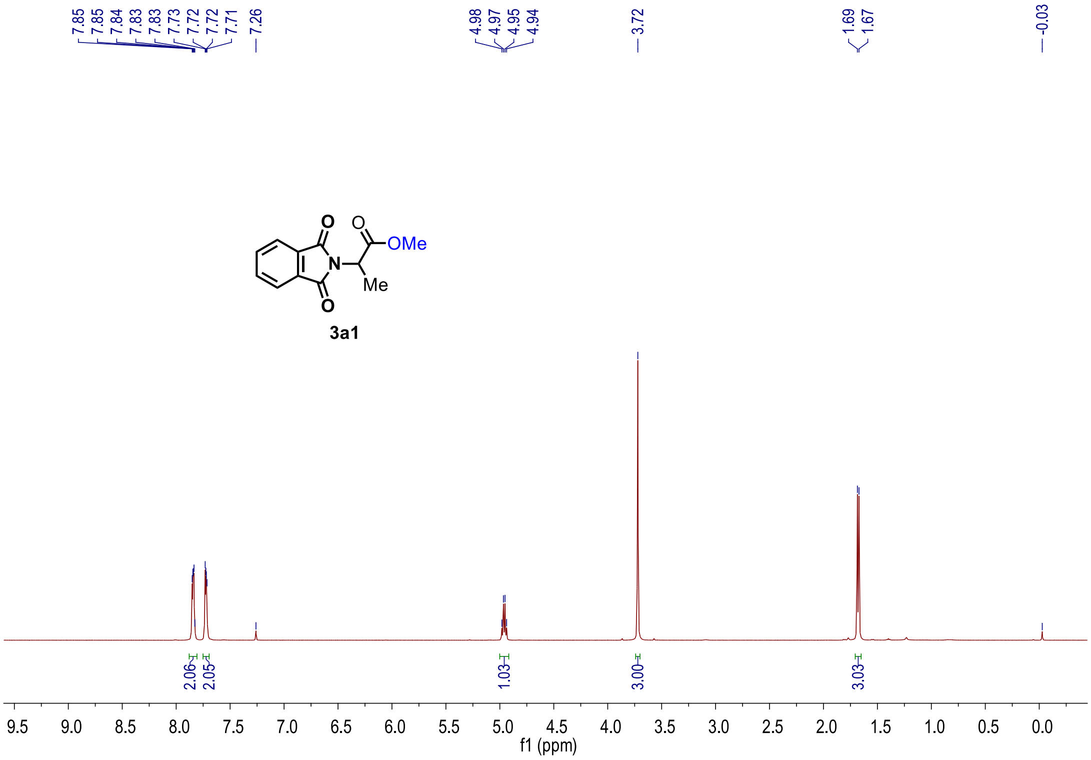
Me
3a
f1 (ppm)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7.26
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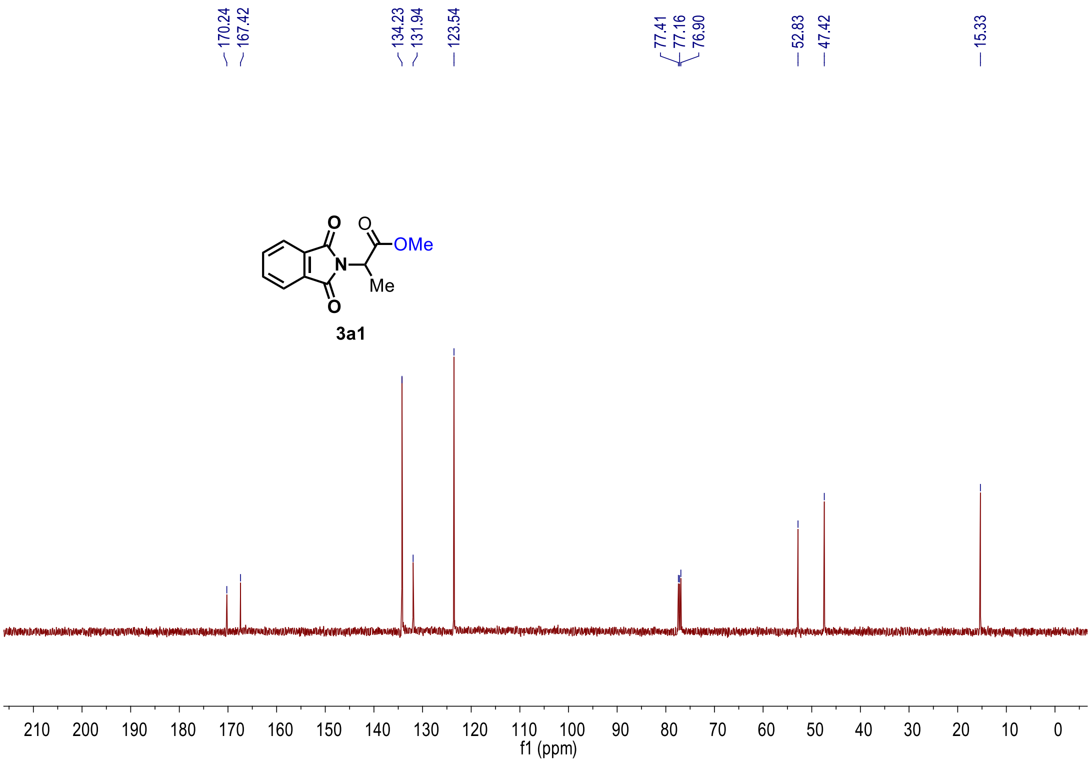
4.95
4.94
3.72
1.69
1.67
-0.03
OMe
Me
3a1
2.06
2.05
1.03
3.00
3.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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OMe
Me
3a1
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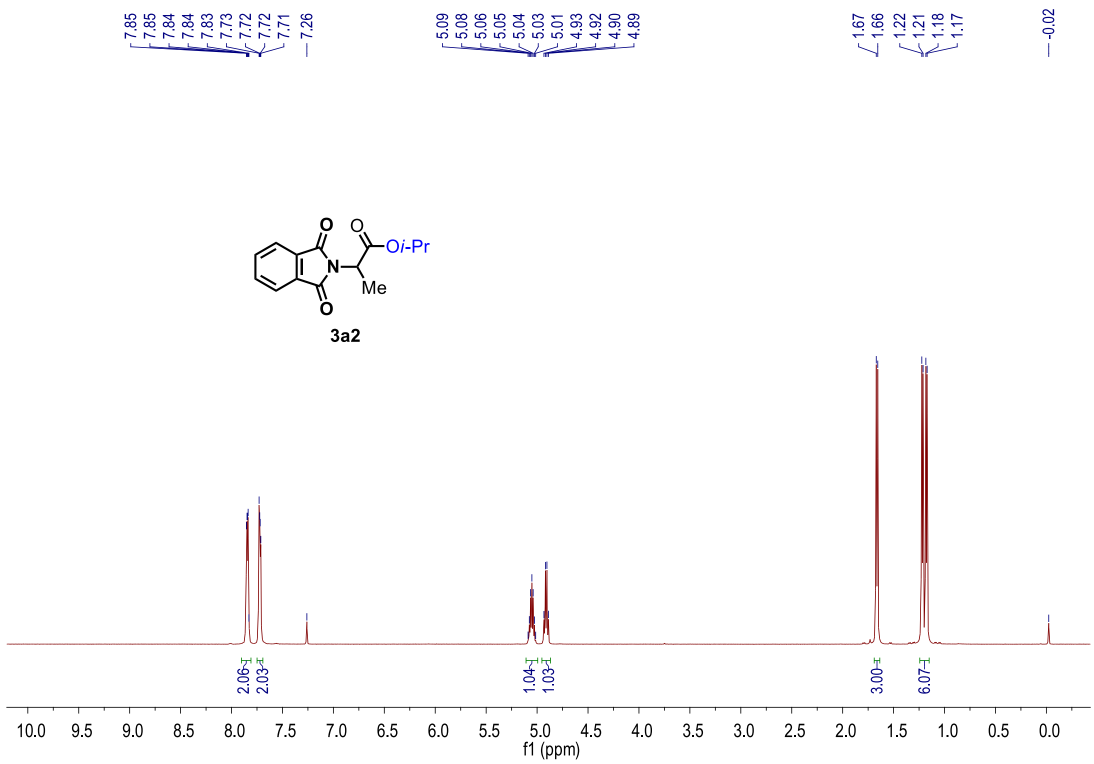
f1 (ppm)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5.06
5.05
5.04
5.03
5.01
4.93
4.92
4.90
4.89
1.67
1.66
1.22
1.21
1.18
1.17
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Me
N
O
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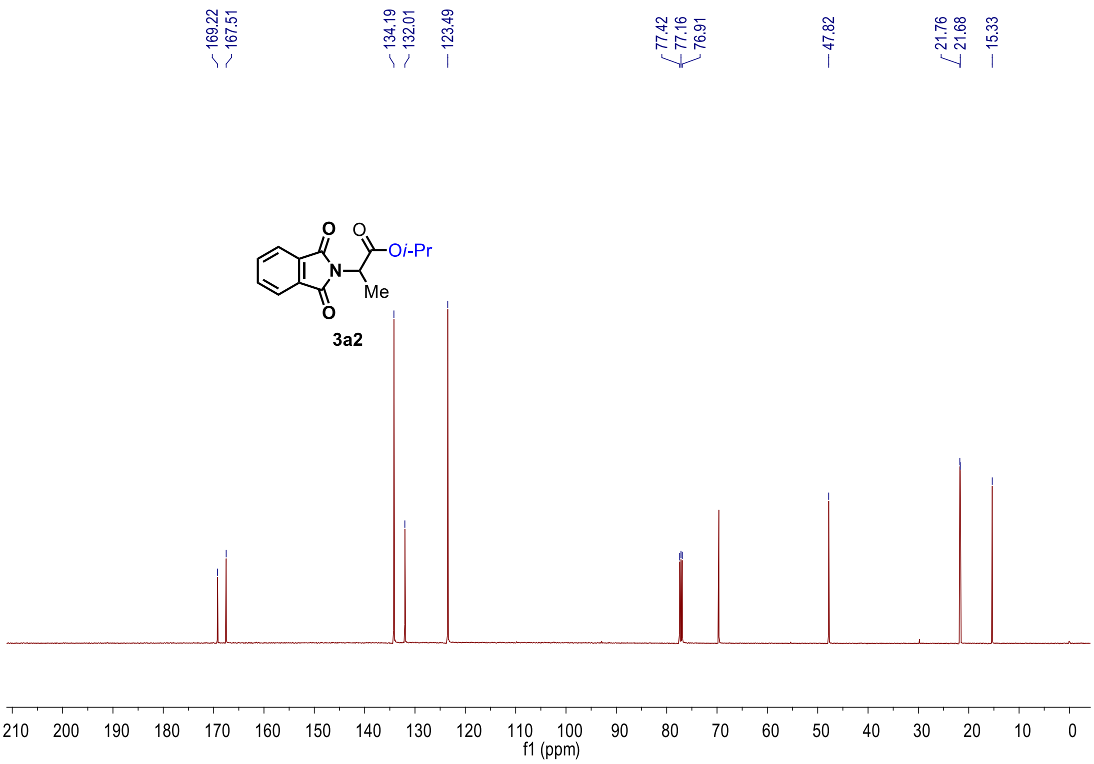
1.04
1.03
3.00
6.07
f1 (ppm)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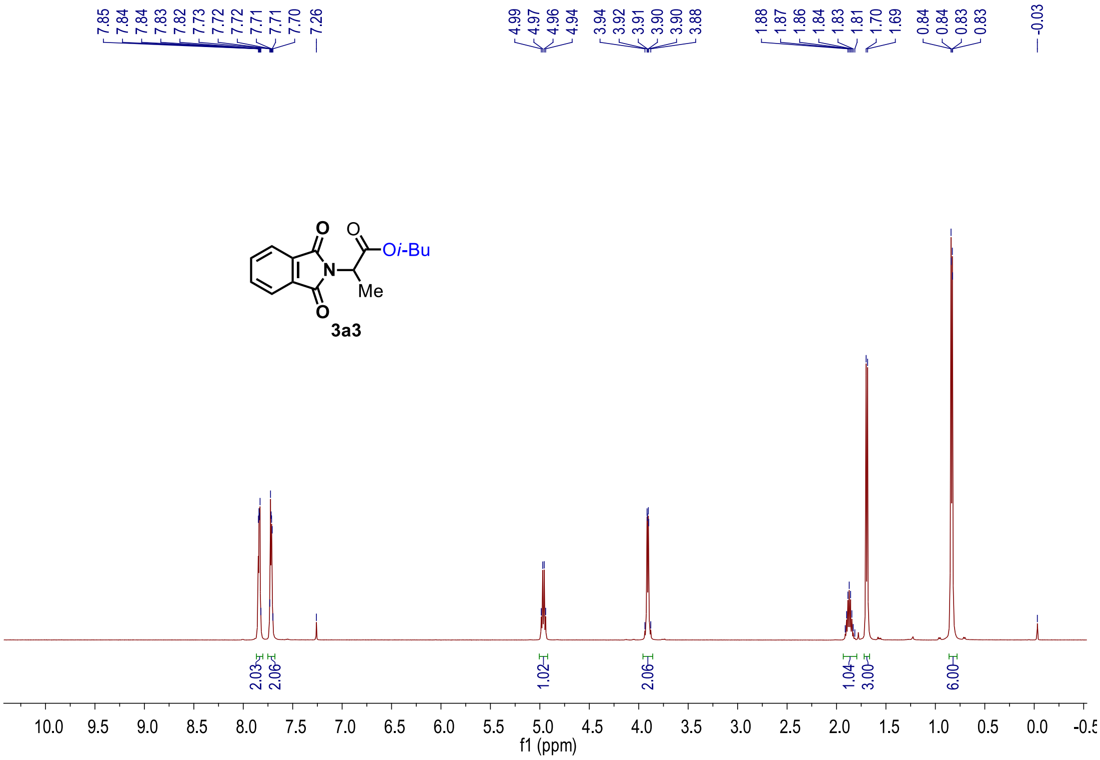
O
3a2
f1 (ppm)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7.72
7.71
7.71
7.70
7.26
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4.97
4.96
4.94
3.94
3.92
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3.90
3.88
1.88
1.87
1.86
1.84
1.83
1.81
1.70
1.69
0.84
0.84
0.83
0.83
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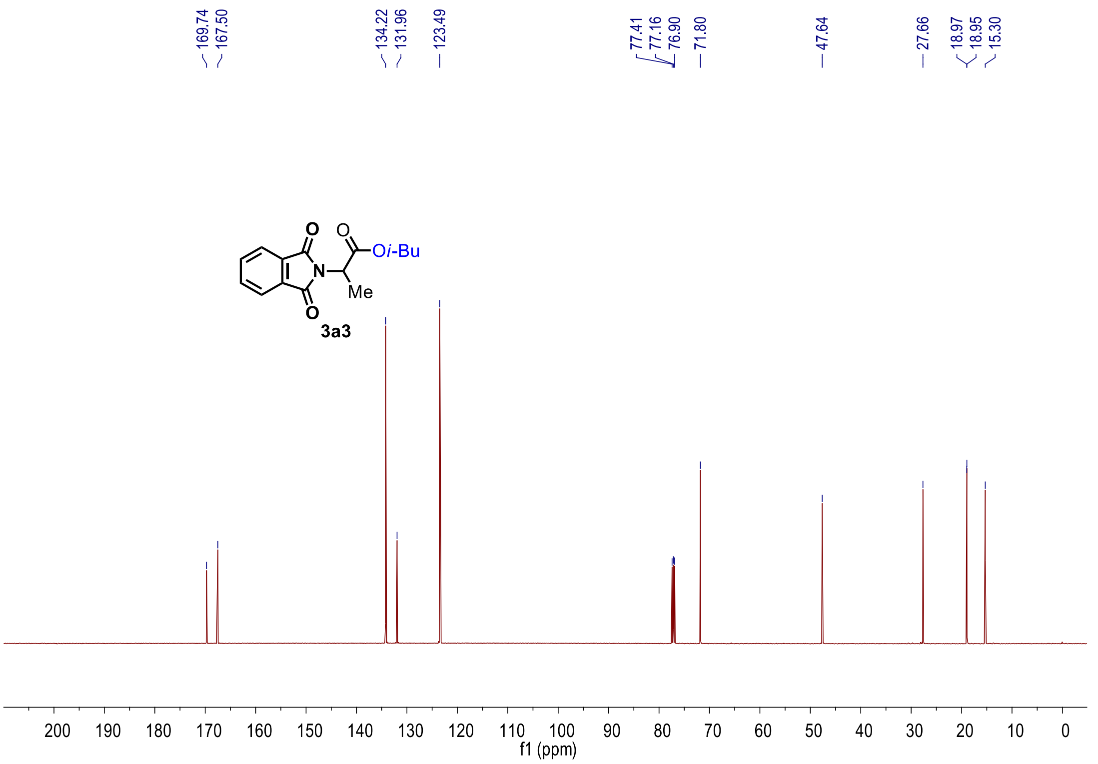
Oi-Bu
Me
3a3
2.03
2.06
1.02
2.06
1.04
3.00
6.00
f1 (ppm)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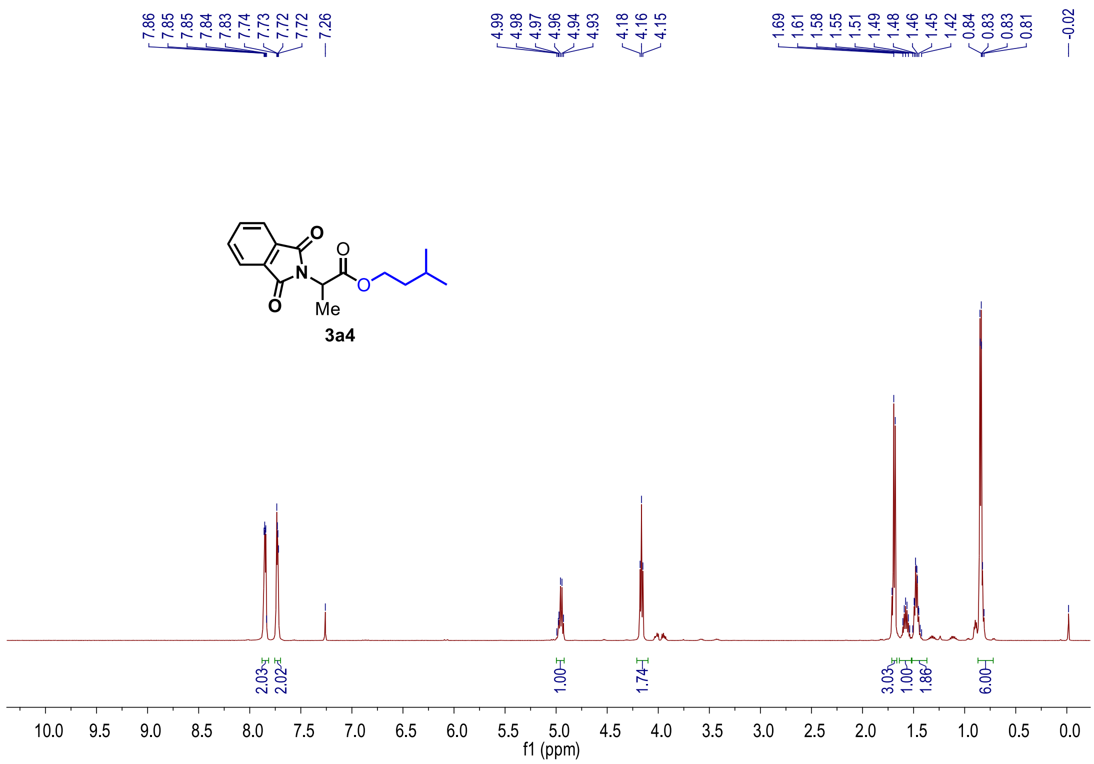
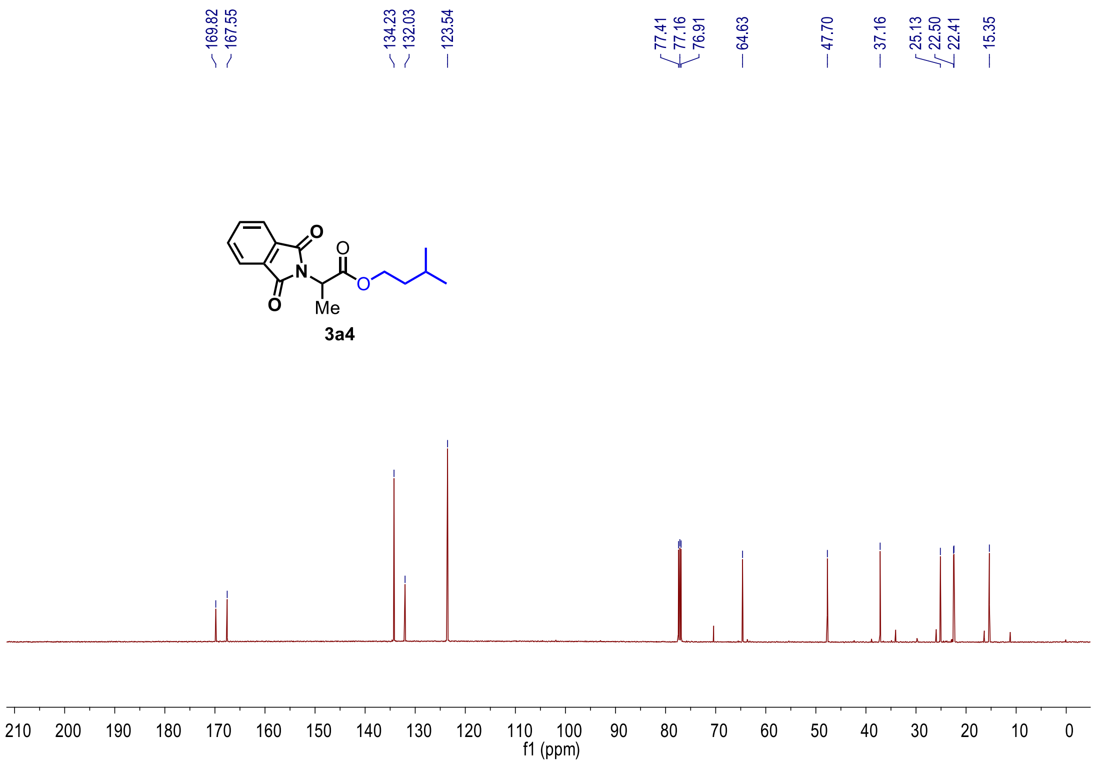
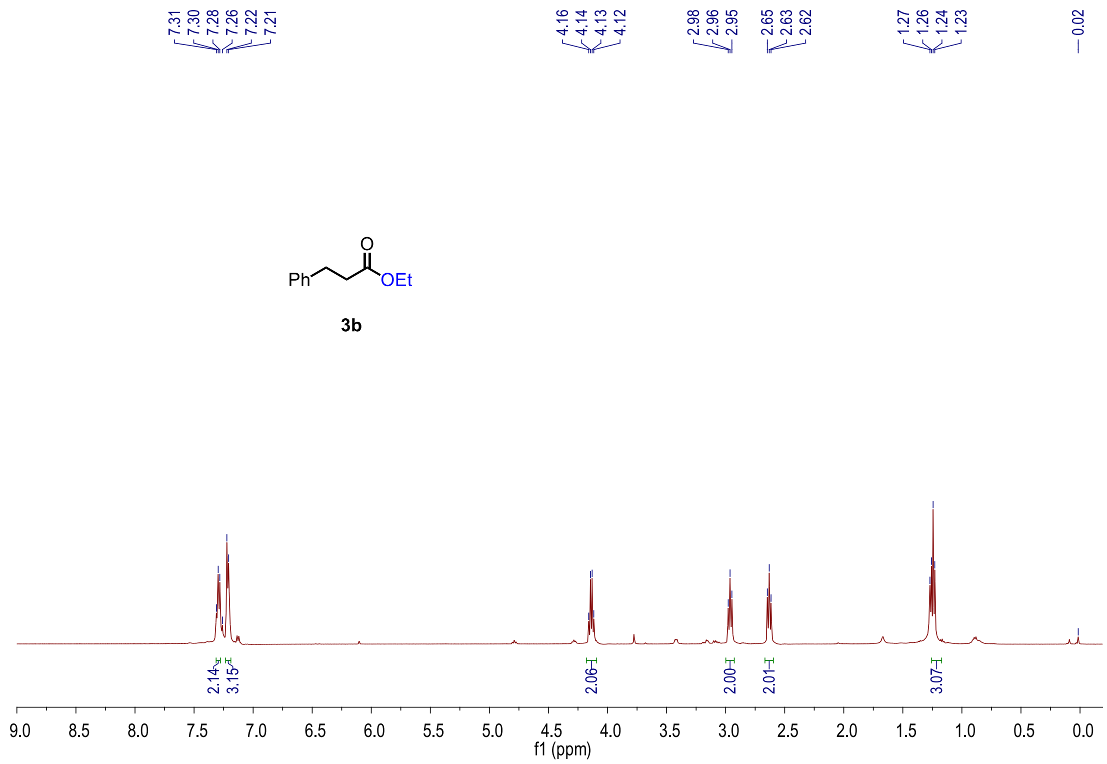
Oi-Bu
Me
3a3
f1 (ppm)



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7.26
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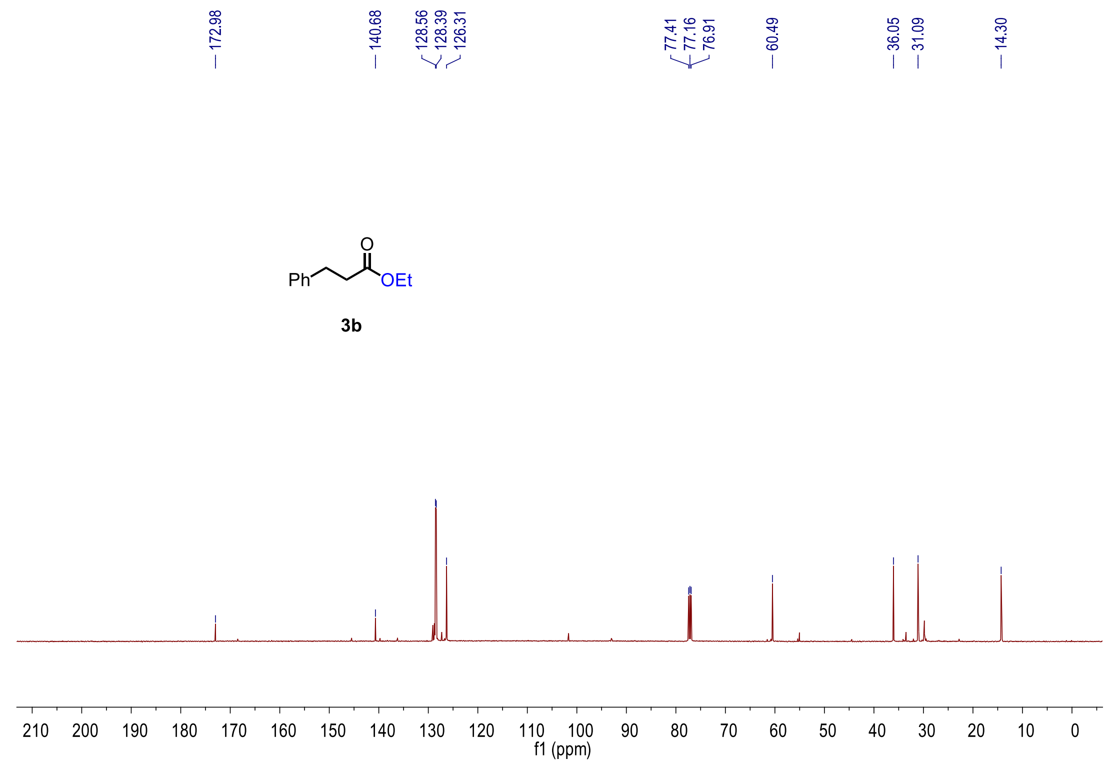
4.16
4.14
4.13
4.12
2.98
2.96
2.95
2.65
2.63
2.62
1.27
1.26
1.24
1.23
0.02
Ph
O
OEt
3b
2.14
3.15
2.06
2.00
2.01
3.07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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126.31
77.41
77.16
76.91
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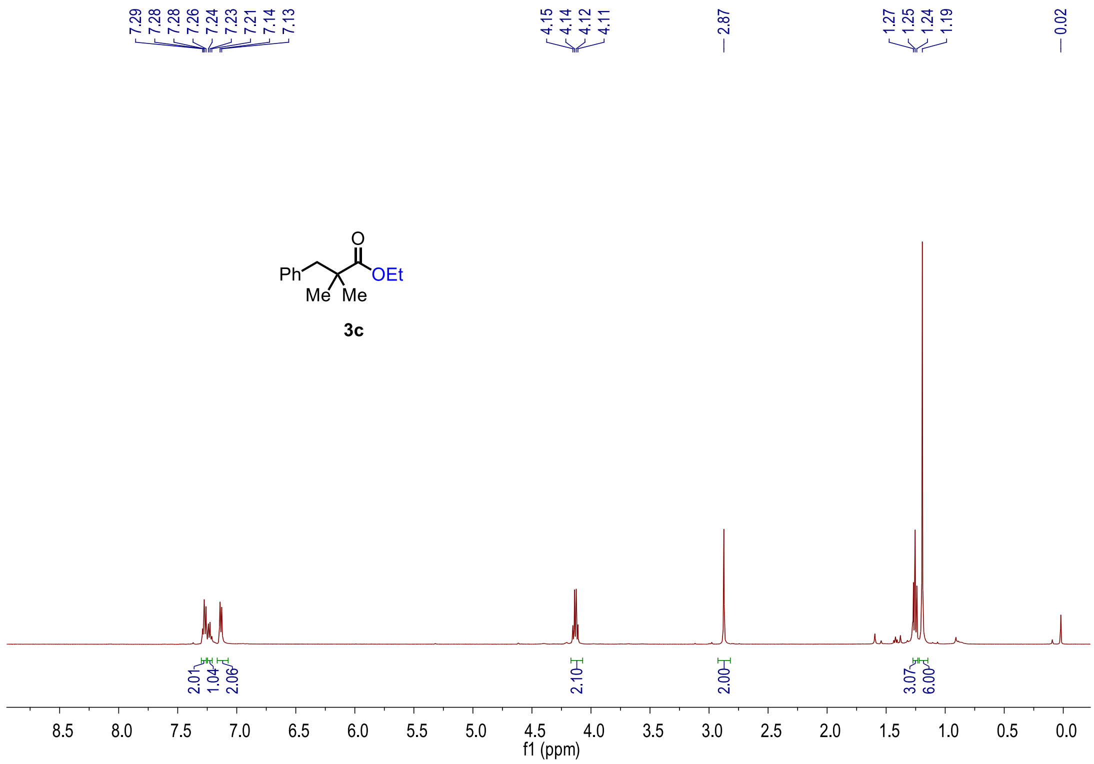
31.09
14.30
Ph
O
OEt
3b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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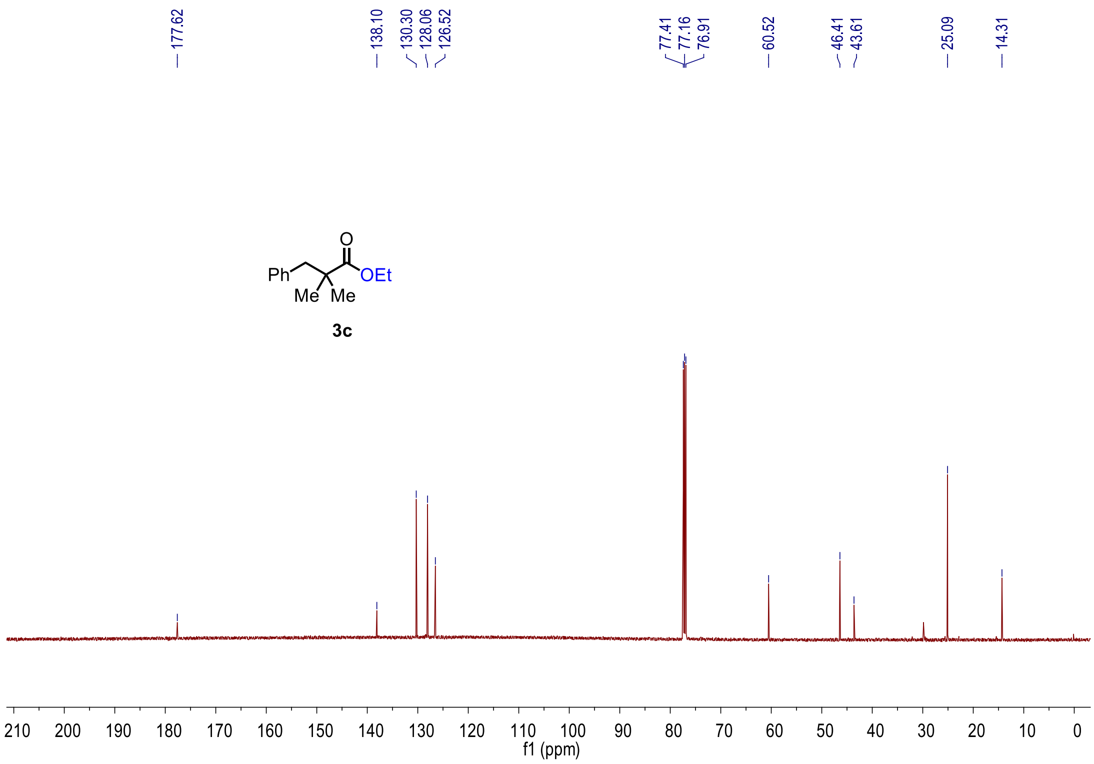
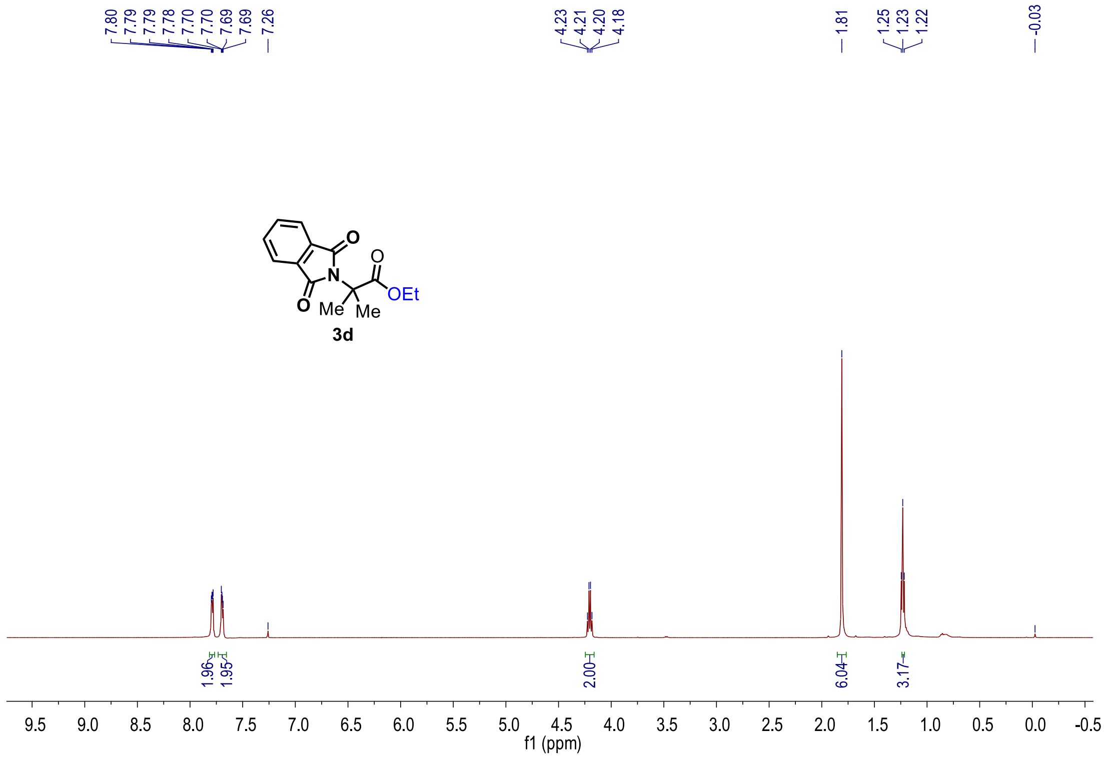
4.15 4.14 4.12 4.11
2.87
1.27 1.25 1.24 1.19
0.02
Ph
O
OEt
Me Me
3c
2.01 1.04 2.06
2.10
2.00
3.07 6.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


177.62
138.10 130.30 128.06 126.52
77.41 77.16 76.91
60.52
46.41 43.61
25.09
14.31
Ph
O
OEt
Me Me
3c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.69
7.69
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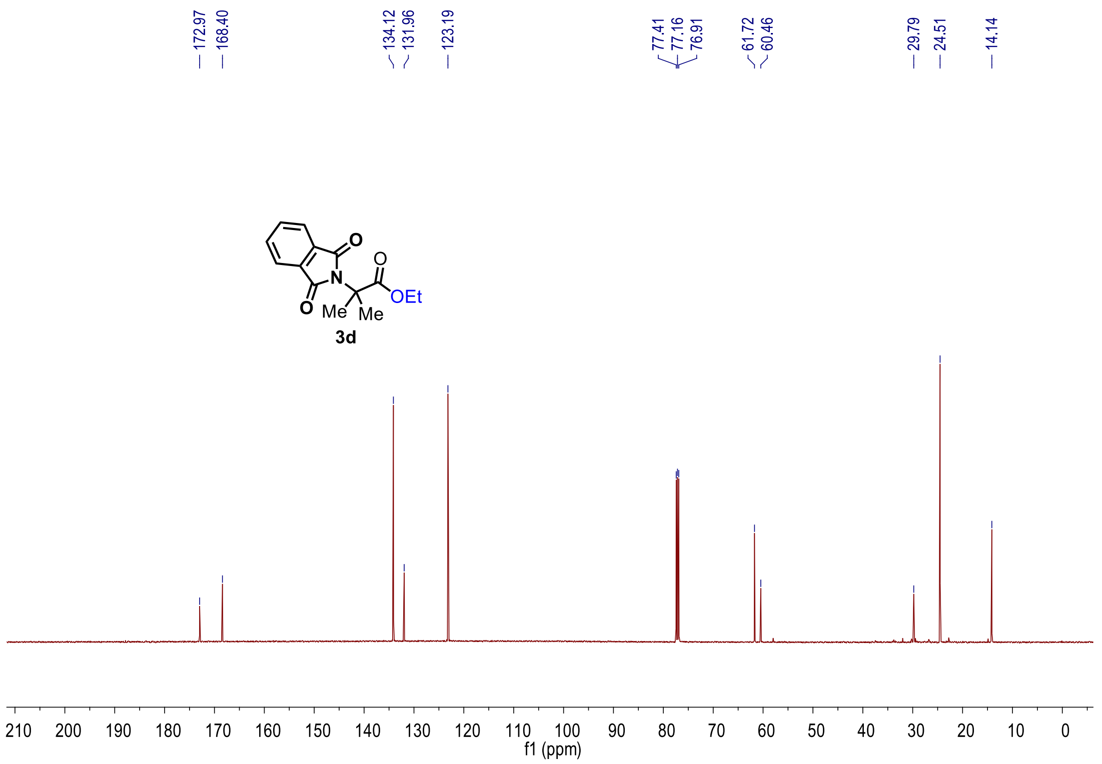
4.23
4.21
4.20
4.18
1.81
1.25
1.23
1.22
-0.03
O
N
O
O
OEt
Me
Me
3d
1.96
1.95
2.00
6.04
3.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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77.16
76.91
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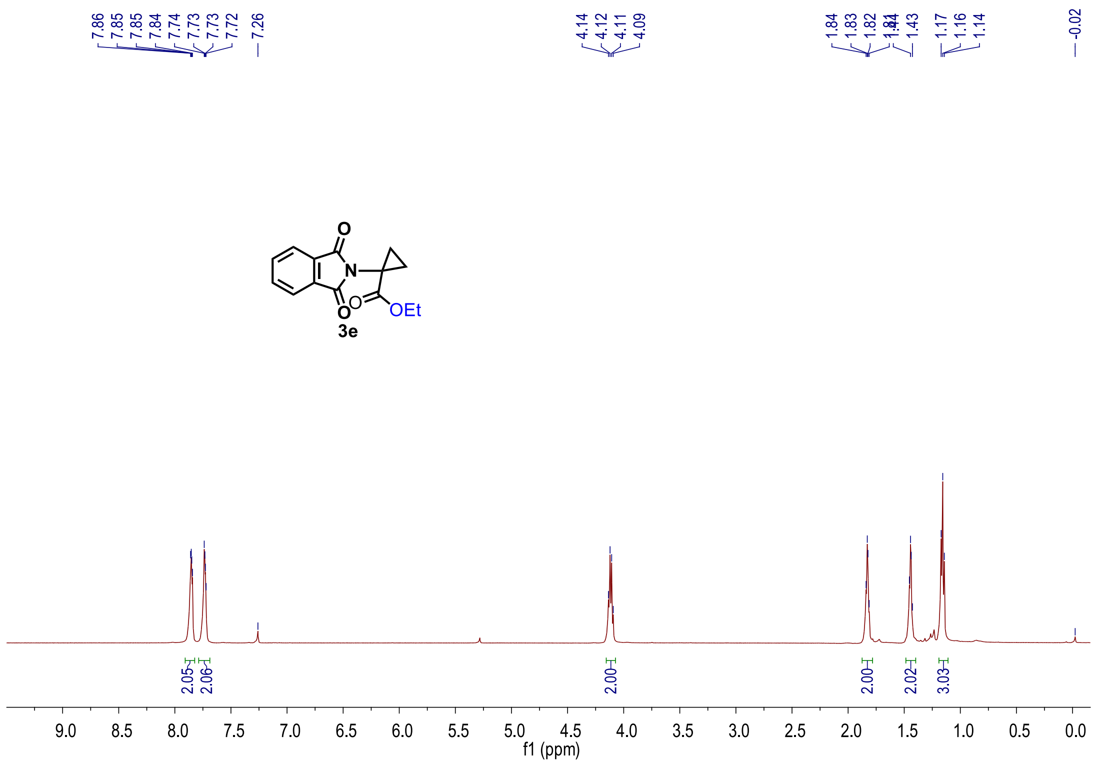
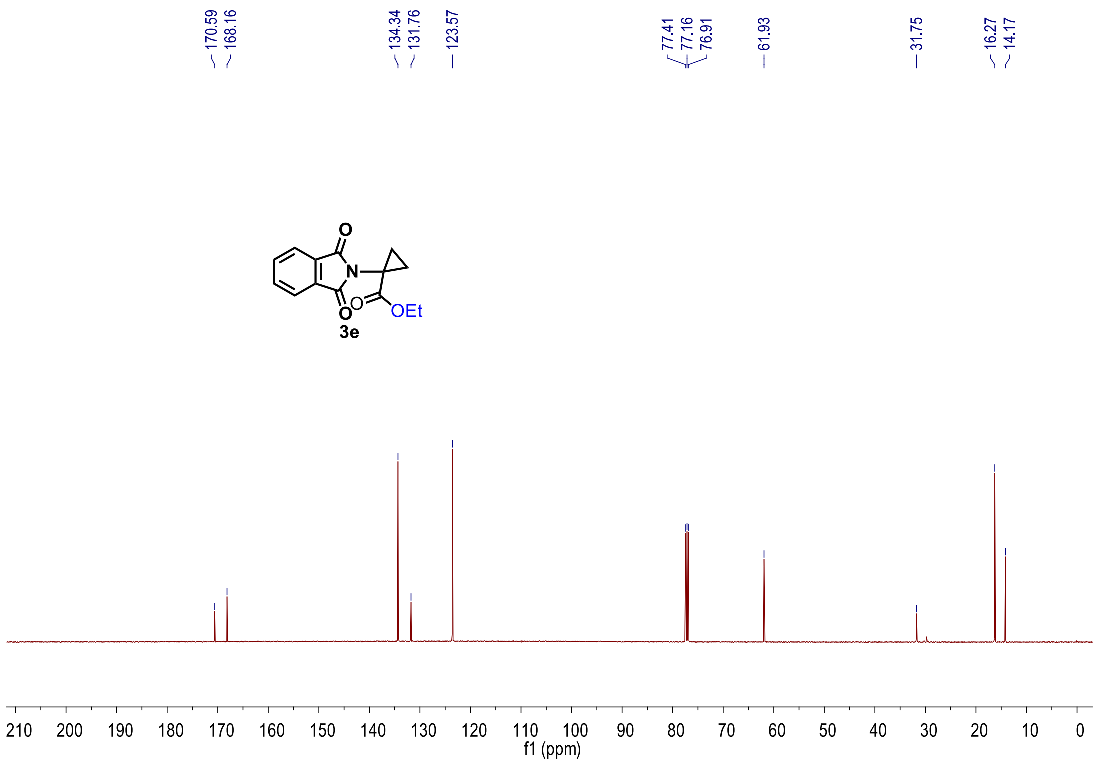
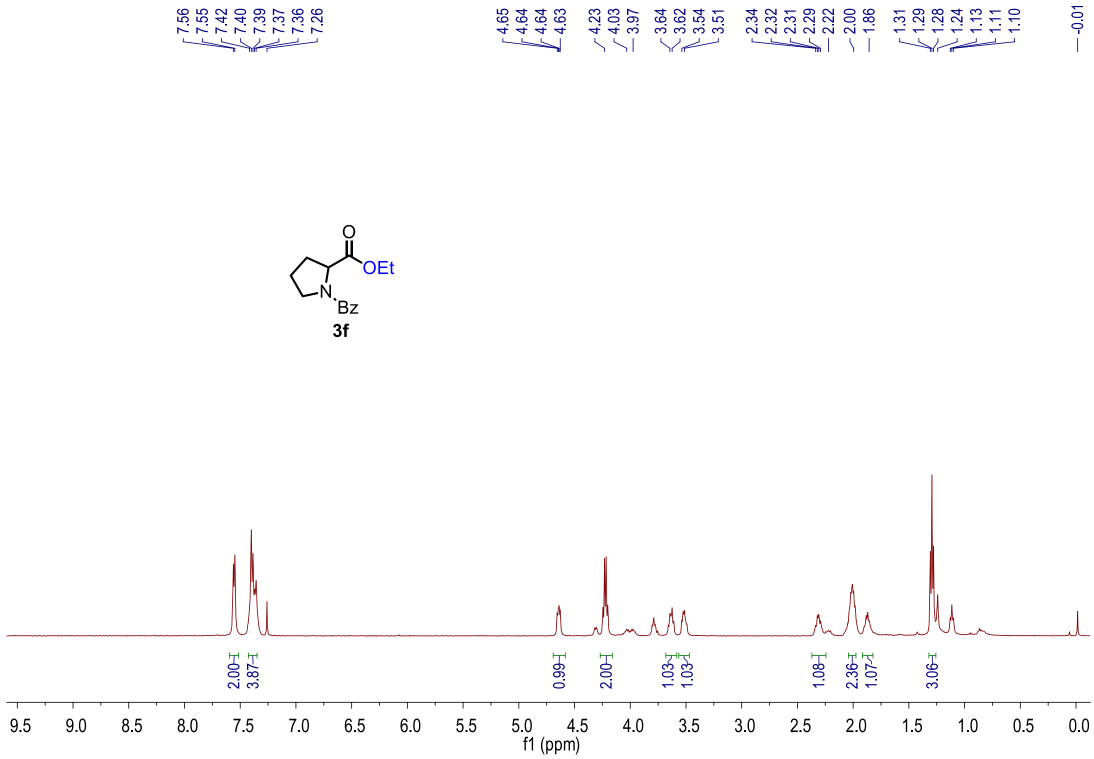
60.46
29.79
24.51
14.14
O
N
O
O
OEt
Me
Me
3d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)







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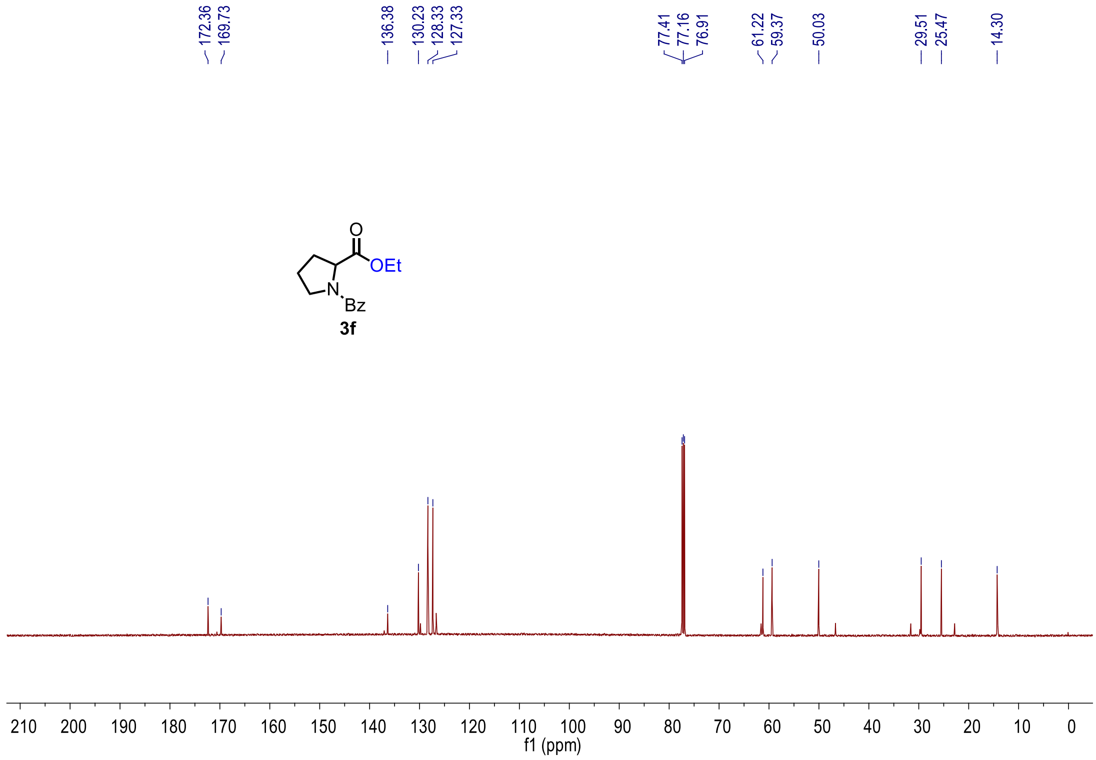
4.65 4.64 4.64 4.63
4.23 4.03 3.97
3.64 3.62 3.54 3.51
2.34 2.32 2.31 2.29 2.22 2.00 1.86
1.31 1.29 1.28 1.24 1.13 1.11 1.10
-0.01
O
OEt
N
Bz
3f
2.00 3.87 0.99 2.00 1.03 1.03 1.08 2.36 1.07 3.06
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

172.36 169.73
136.38 130.23 128.33 127.33
77.41 77.16 76.91
61.22 59.37
50.03
29.51 25.47
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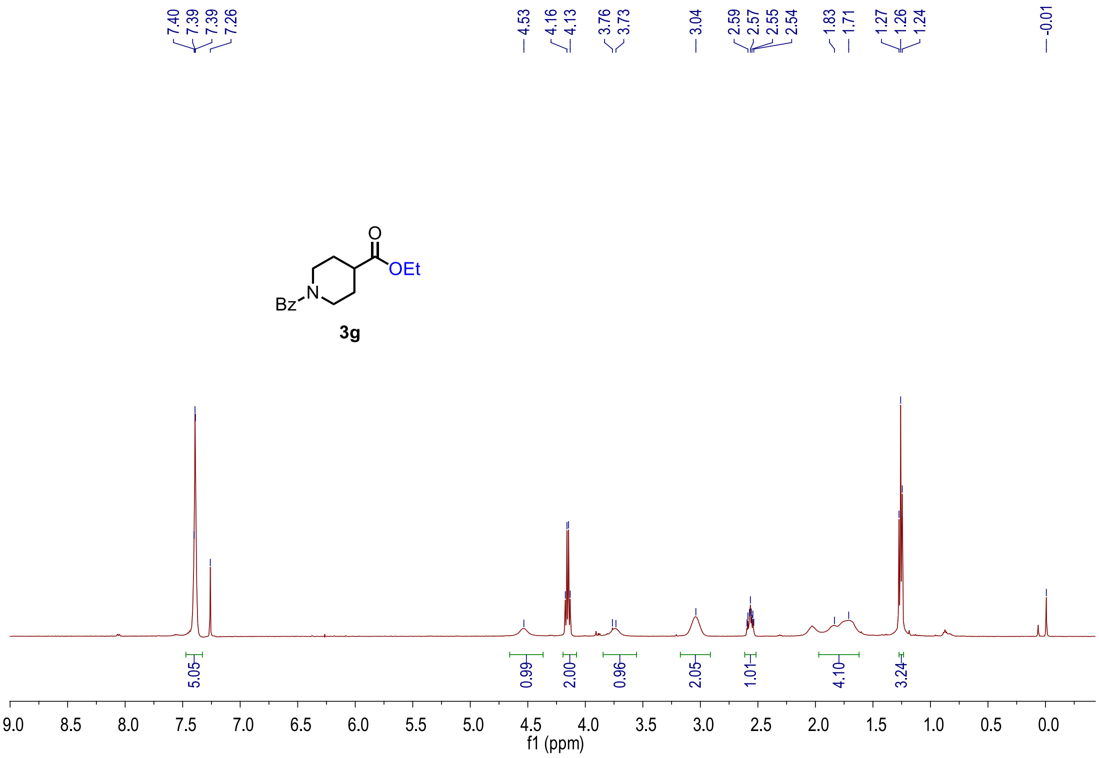
O
OEt
N
Bz
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.39
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4.16
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3.76
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3.04
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2.54
1.83
1.71
1.27
1.26
1.24
-0.01
OEt
Bz
N
O
3g
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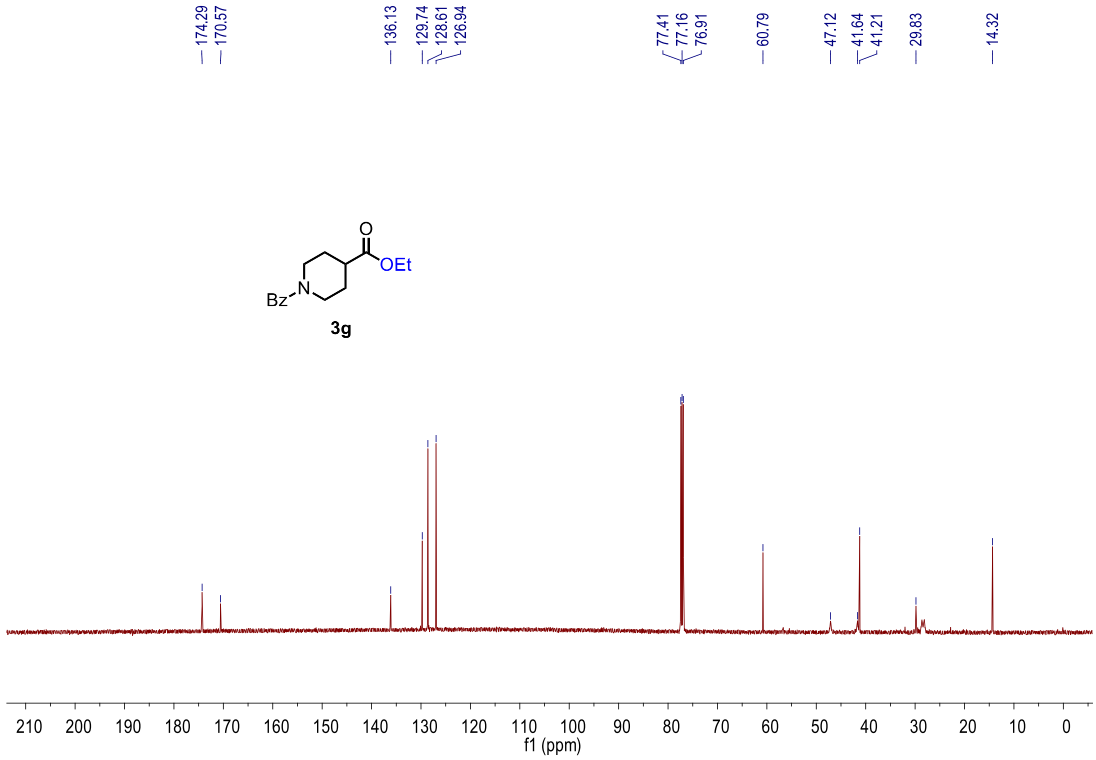
0.99
2.00
0.96
2.05
1.01
4.10
3.24
f1 (ppm)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126.94
77.41
77.16
76.91
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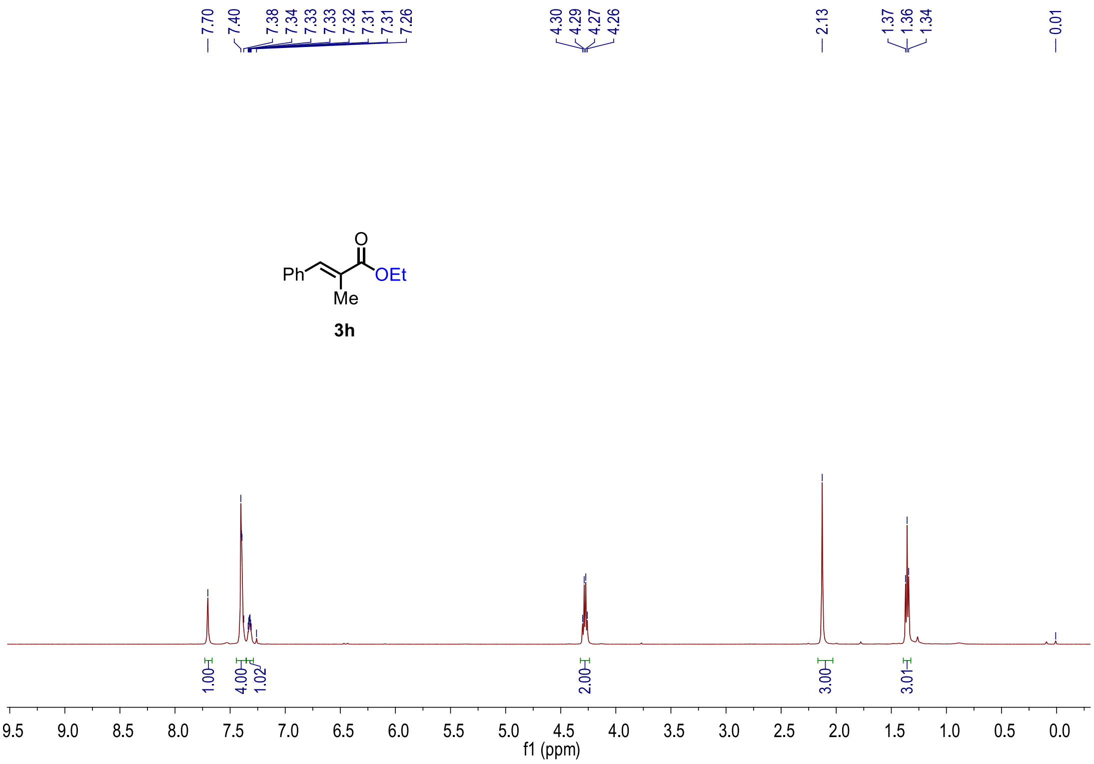
47.12
41.64
41.21
29.83
14.32
OEt
Bz
N
O
3g
f1 (ppm)



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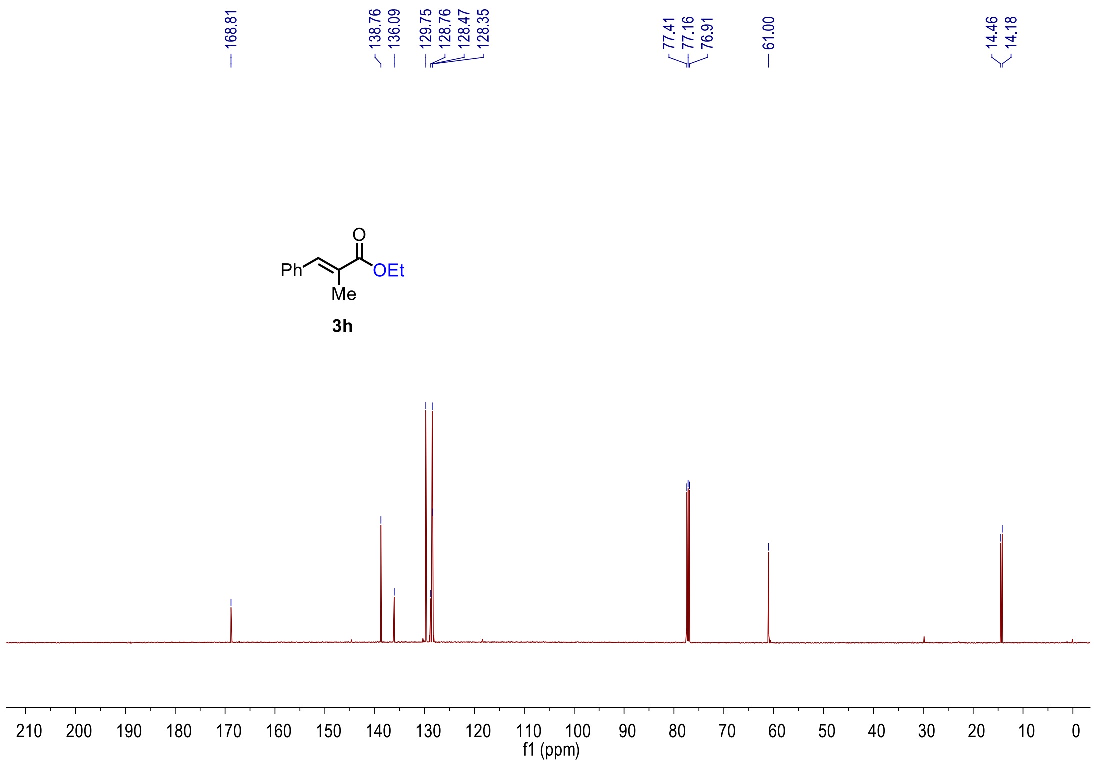
7.33
7.32
7.31
7.31
7.26
4.30
4.29
4.27
4.26
2.13
1.37
1.36
1.34
0.01
Ph
O
OEt
Me
3h
1.00
4.00
1.02
2.00
3.00
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

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138.76
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77.41
77.16
76.91
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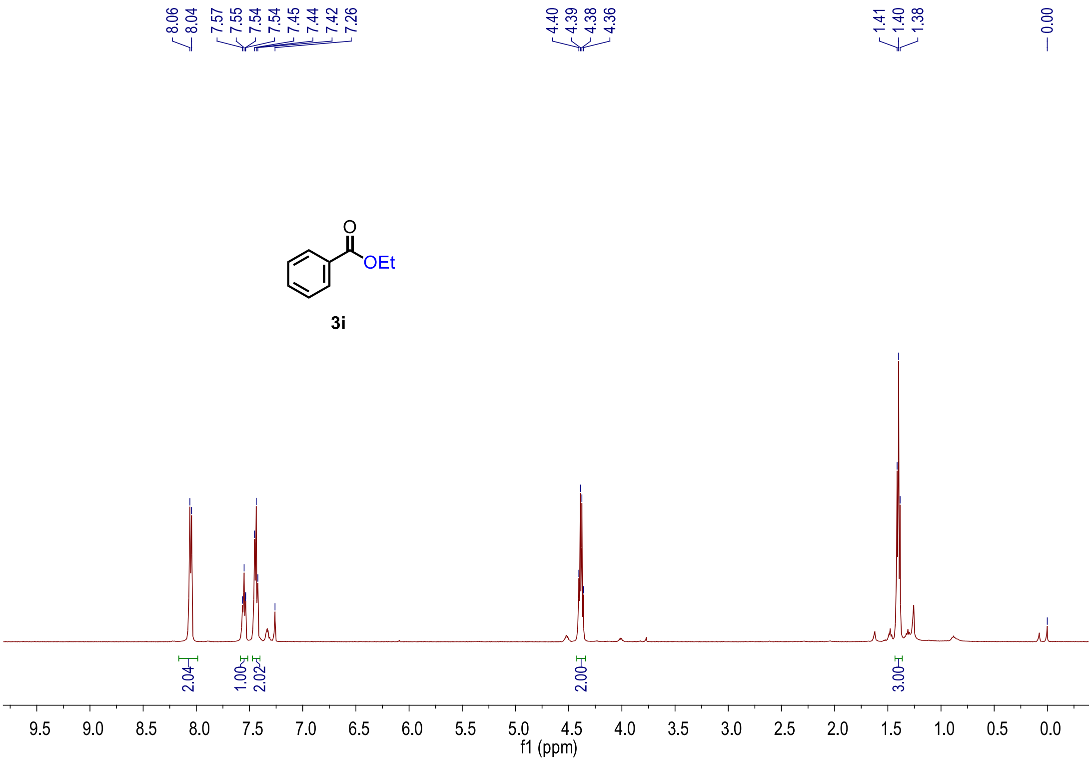
14.46
14.18
Ph
O
OEt
Me
3h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.26
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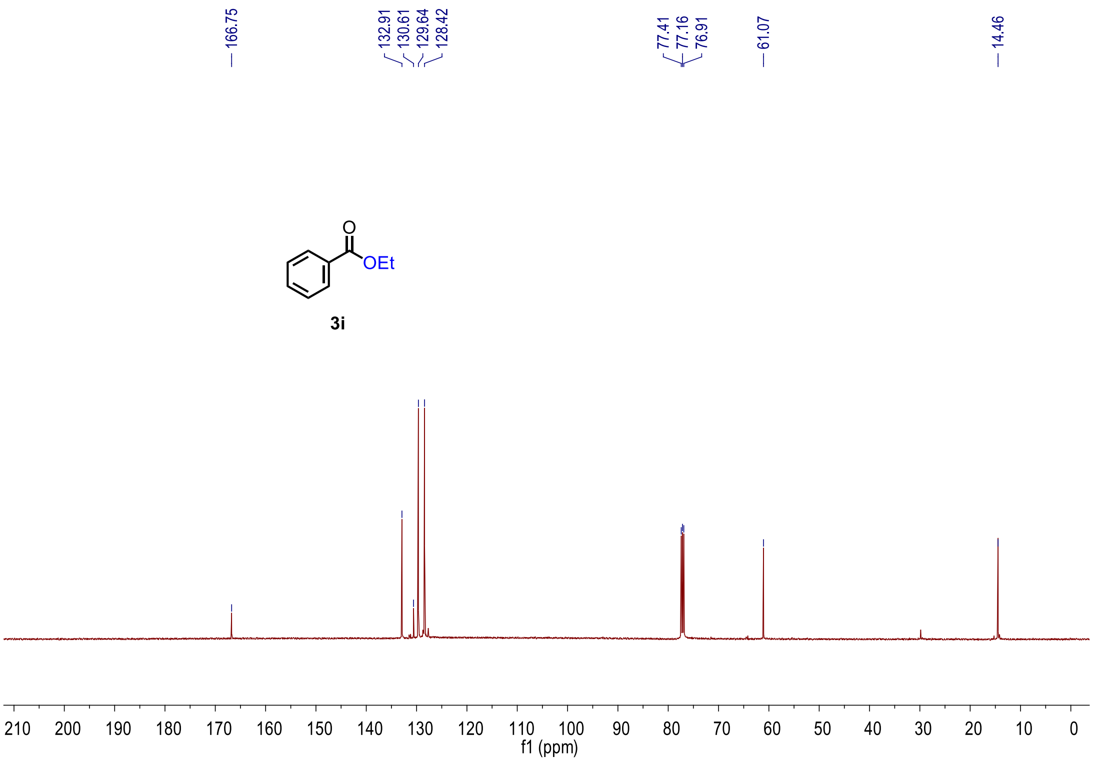
4.38
4.36
1.41
1.40
1.38
0.00
OEt
O
3i
2.04
1.00
2.02
2.00
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.42
77.41
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76.91
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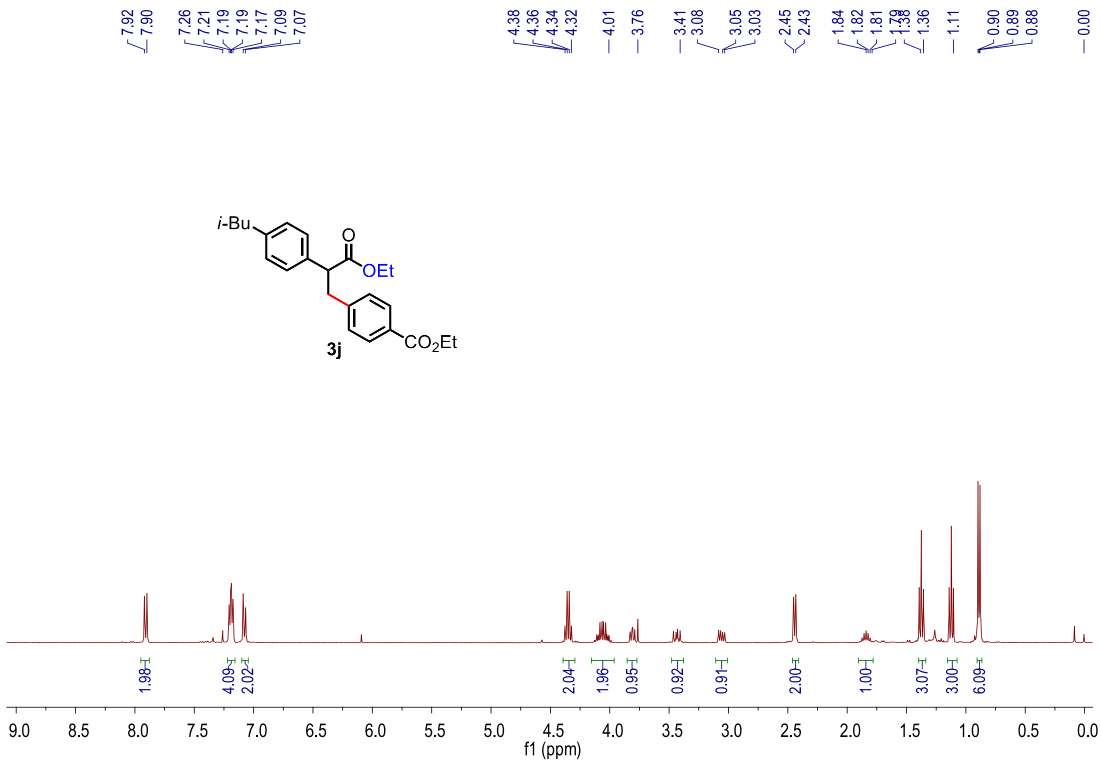
14.46
OEt
O
3i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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4.38
4.36
4.34
4.32
4.01
3.76
3.41
3.08
3.05
3.03
2.45
2.43
1.84
1.82
1.81
1.36
1.11
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0.89
0.88
0.00
i-Bu
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3j
CO2Et
1.98
4.09
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1.96
0.95
0.92
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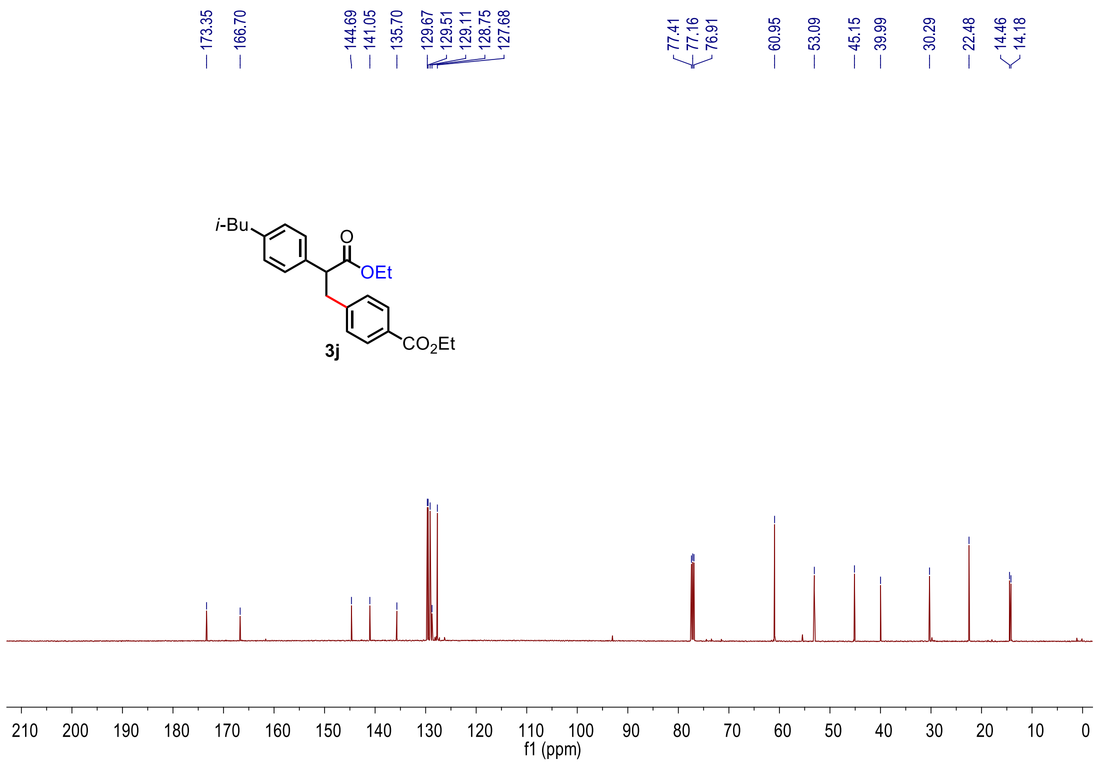
2.00
1.00
3.07
3.00
6.09
f1 (ppm)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76.91
60.95
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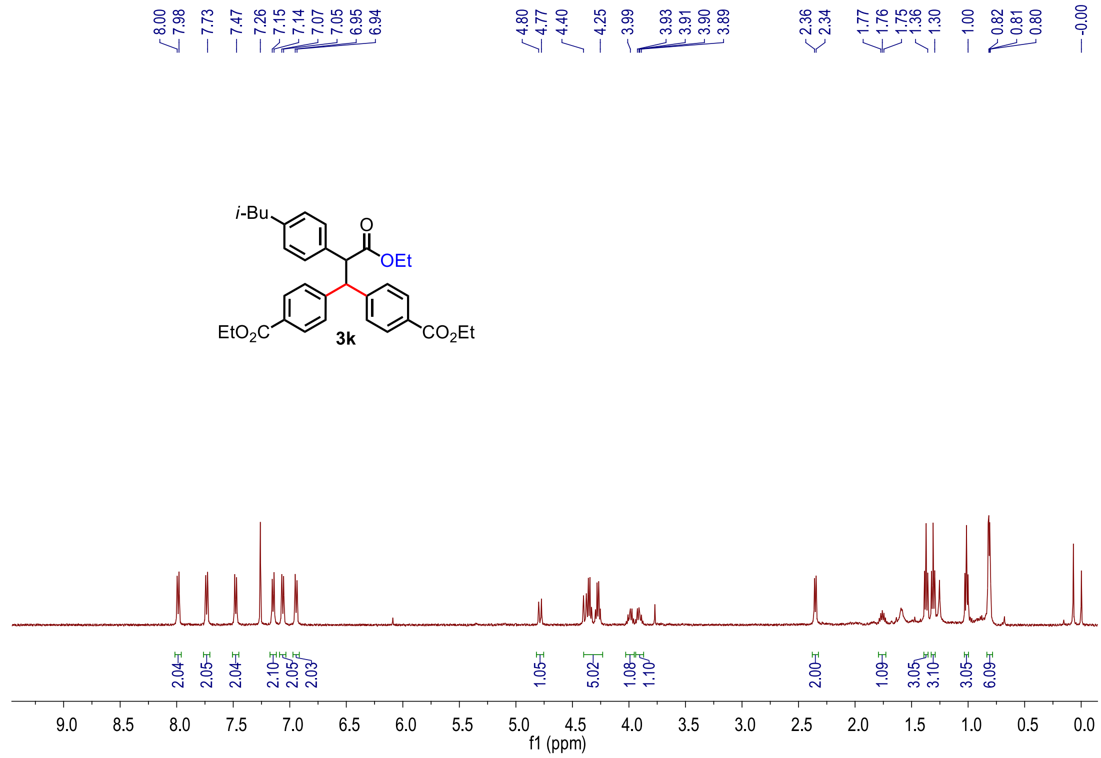
OEt
3j
CO2Et
f1 (ppm)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7.15
7.14
7.07
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6.95
6.94
4.80
4.77
4.40
4.25
3.99
3.93
3.91
3.90
3.89
2.36
2.34
1.77
1.76
1.75
1.36
1.30
1.00
0.82
0.81
0.80
-0.00
i-Bu
O
OEt
EtO2C
CO2Et
3k
2.04
2.05
2.04
2.10
2.05
2.03
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1.10
2.00
1.09
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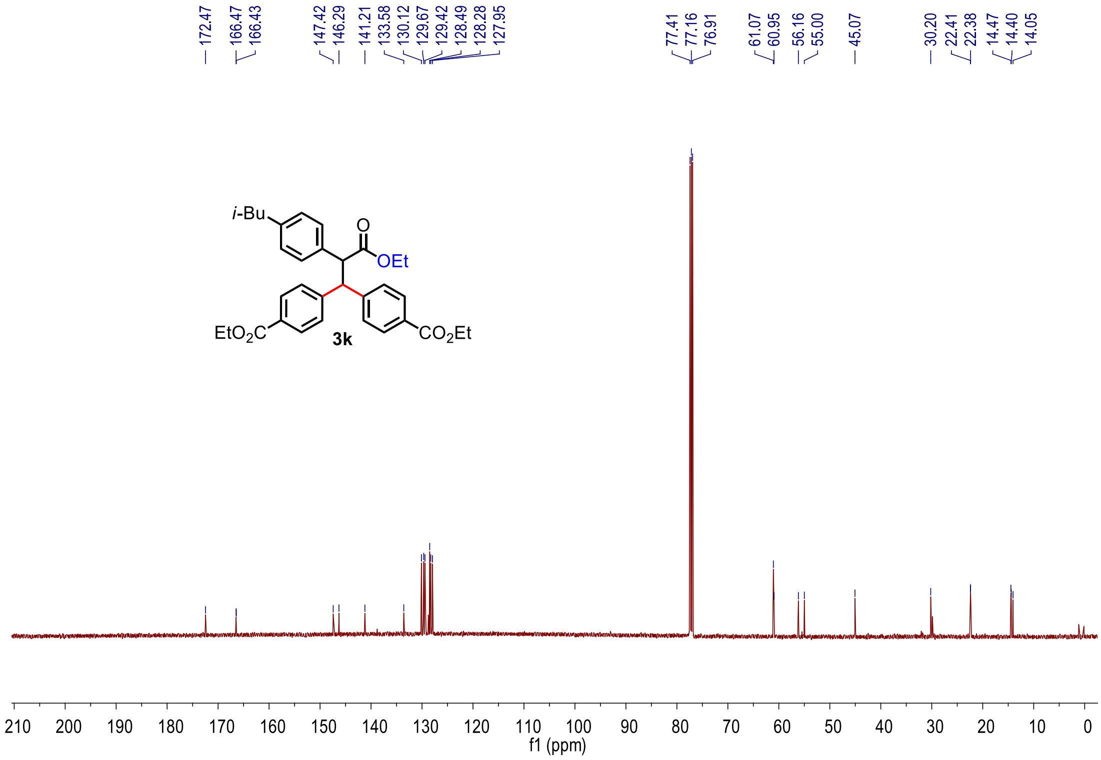
3.05
6.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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127.95
77.41
77.16
76.91
61.07
60.95
56.16
55.00
45.07
30.20
22.41
22.38
14.47
14.40
14.05
i-Bu
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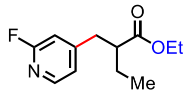
OEt
EtO2C
CO2Et
3k
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



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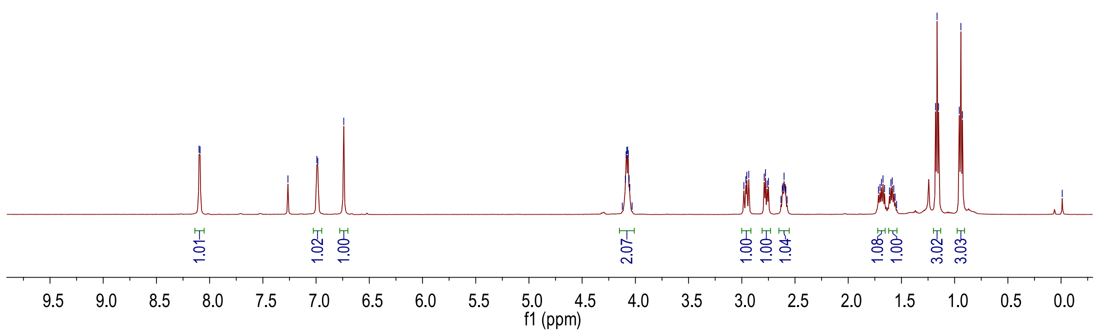

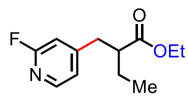

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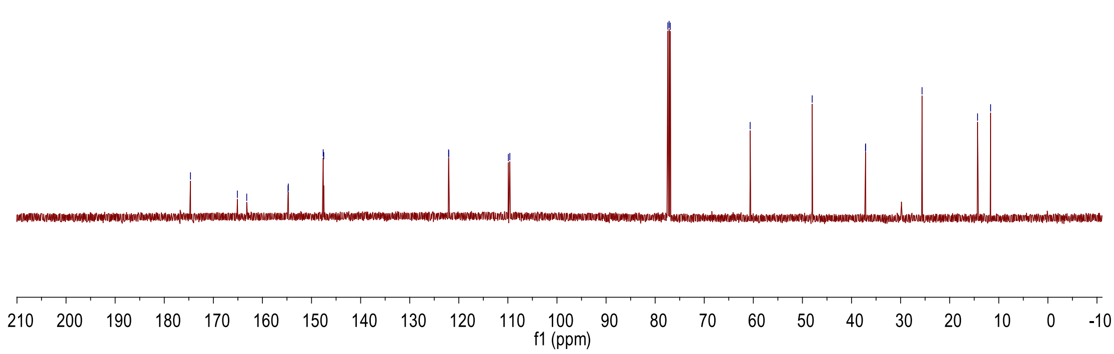
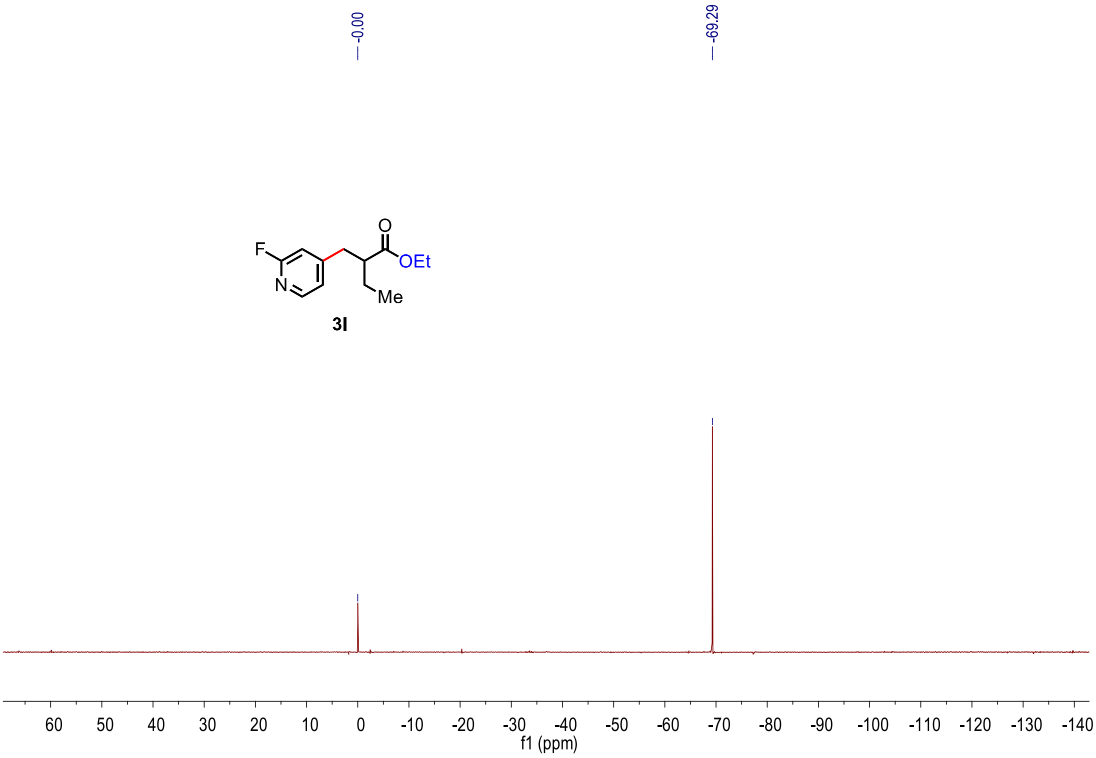
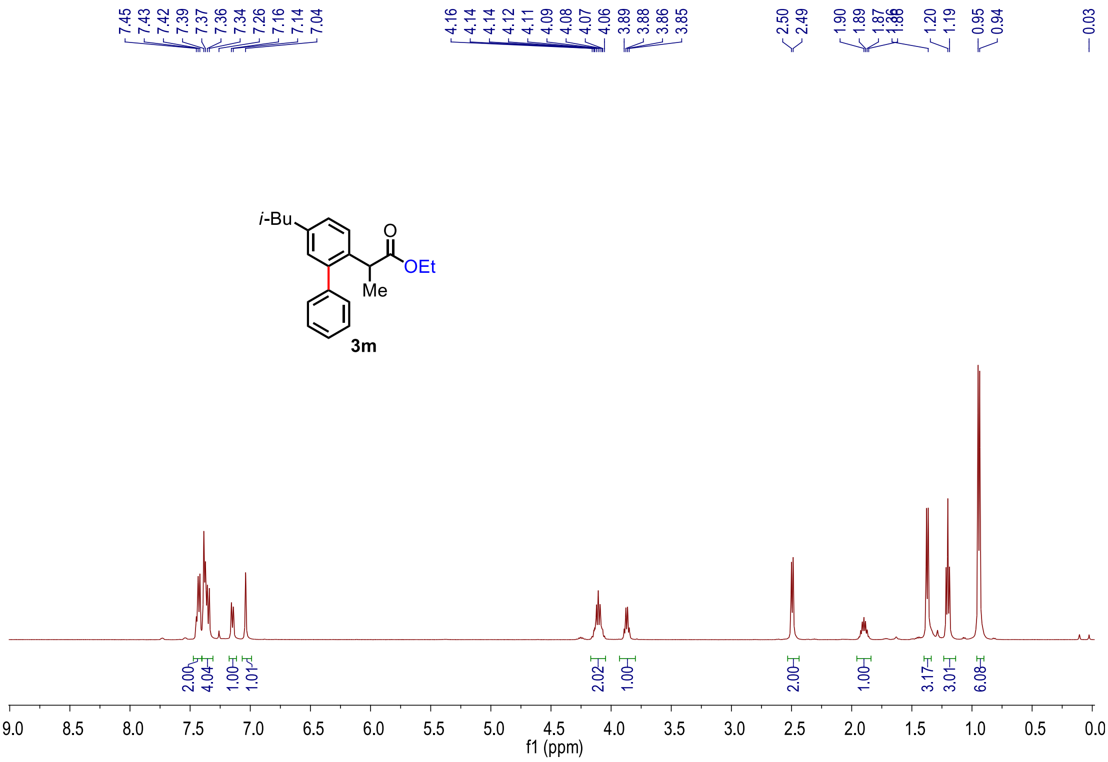
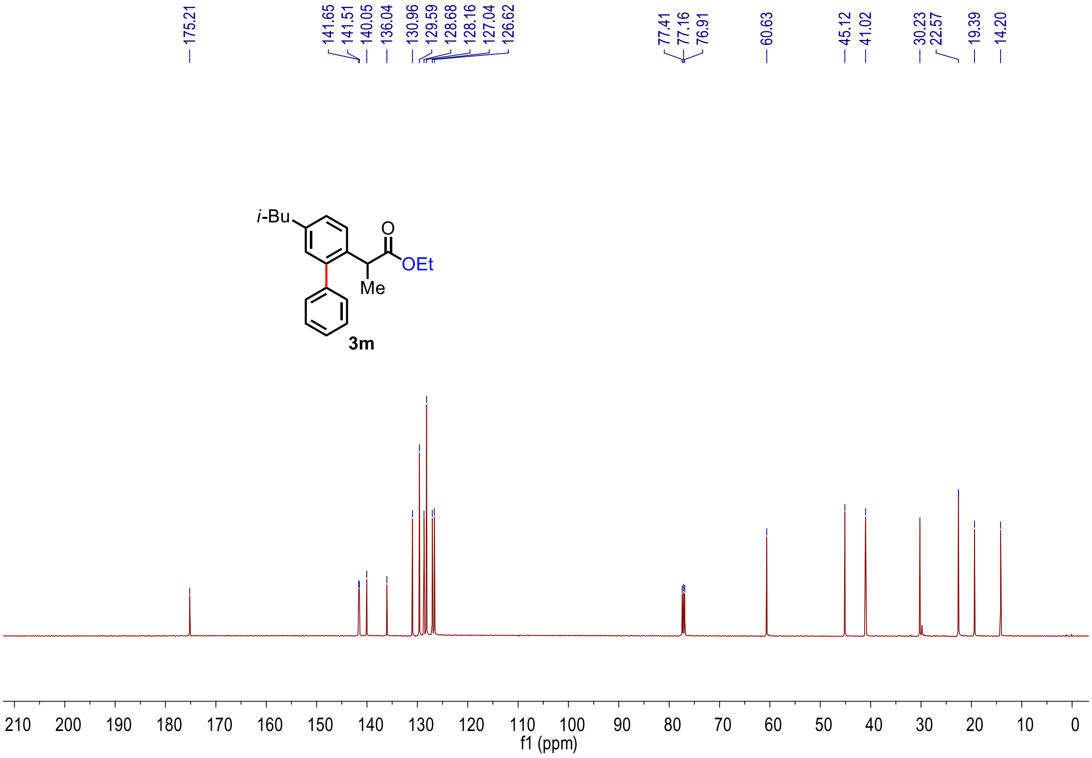
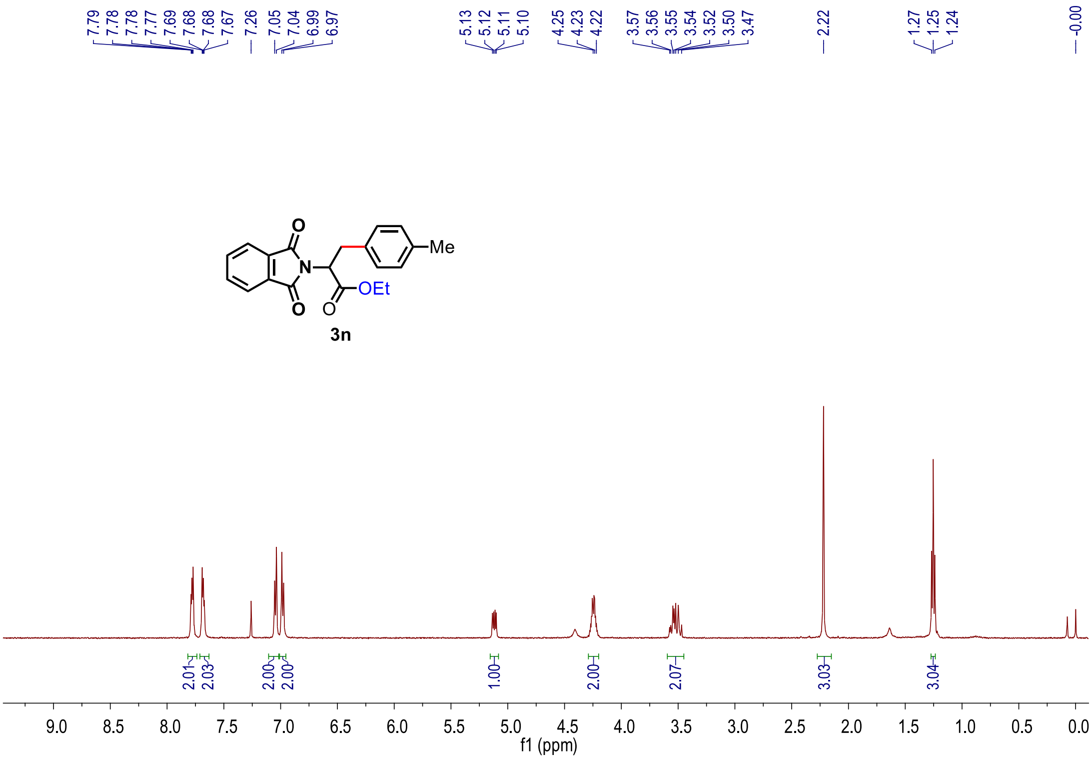



—0.00
—-69.29
F
N
O
OEt
Me
3l
60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140
f1 (ppm)


7.45 7.43 7.42 7.39 7.37 7.36 7.34 7.26 7.16 7.14 7.04
4.16 4.14 4.14 4.12 4.11 4.09 4.08 4.07 4.06 3.89 3.88 3.86 3.85
2.50 2.49
1.90 1.89 1.87 1.20 1.19 0.95 0.94
—0.03
i-Bu
O
OEt
Me
3m
2.00 4.04 1.00 1.01 2.02 1.00 2.00 1.00 3.17 3.01 6.08
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
f1 (ppm)


175.21
141.65
141.51
140.05
136.04
130.96
129.59
128.68
128.16
127.04
126.62
77.41
77.16
76.91
60.63
45.12
41.02
30.23
22.57
19.39
14.20
i-Bu
O
OEt
Me
3m
f1 (ppm)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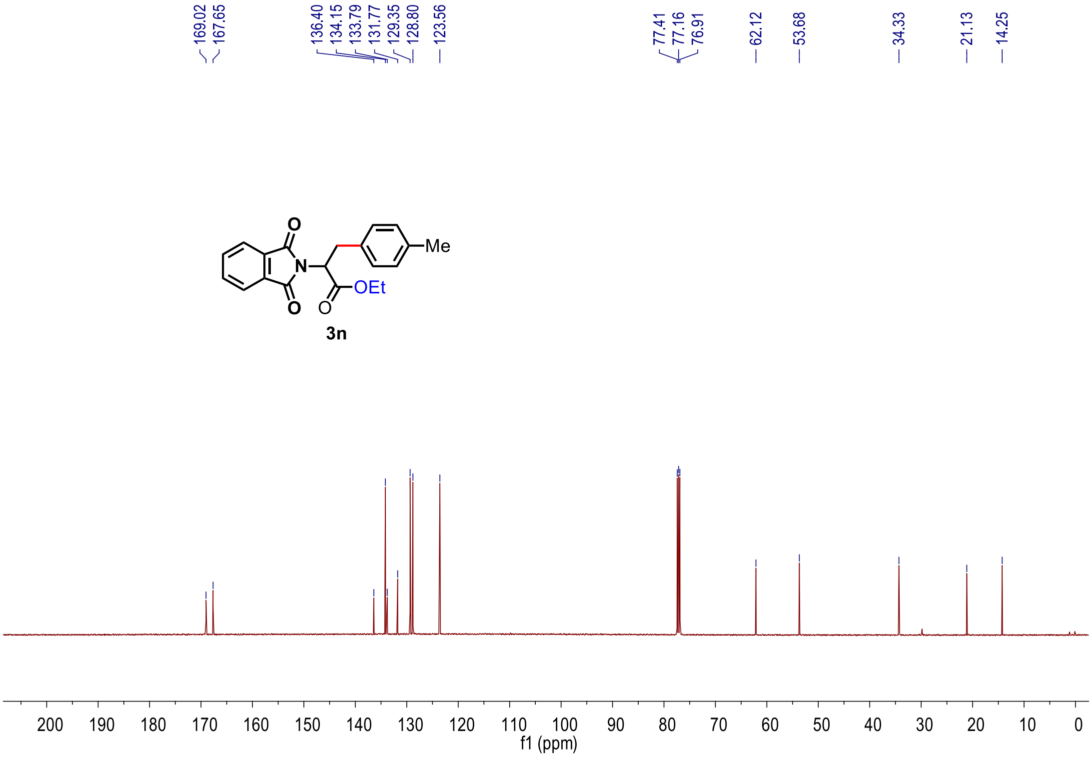
7.78
7.78
7.77
7.69
7.68
7.68
7.67
7.26
7.05
7.04
6.99
6.97
5.13
5.12
5.11
5.10
4.25
4.23
4.22
3.57
3.56
3.55
3.54
3.52
3.50
3.47
2.22
1.27
1.25
1.24
-0.00
O
N
O
Me
OEt
3n
2.01
2.03
2.00
2.00
1.00
2.00
2.07
3.03
3.04
f1 (ppm)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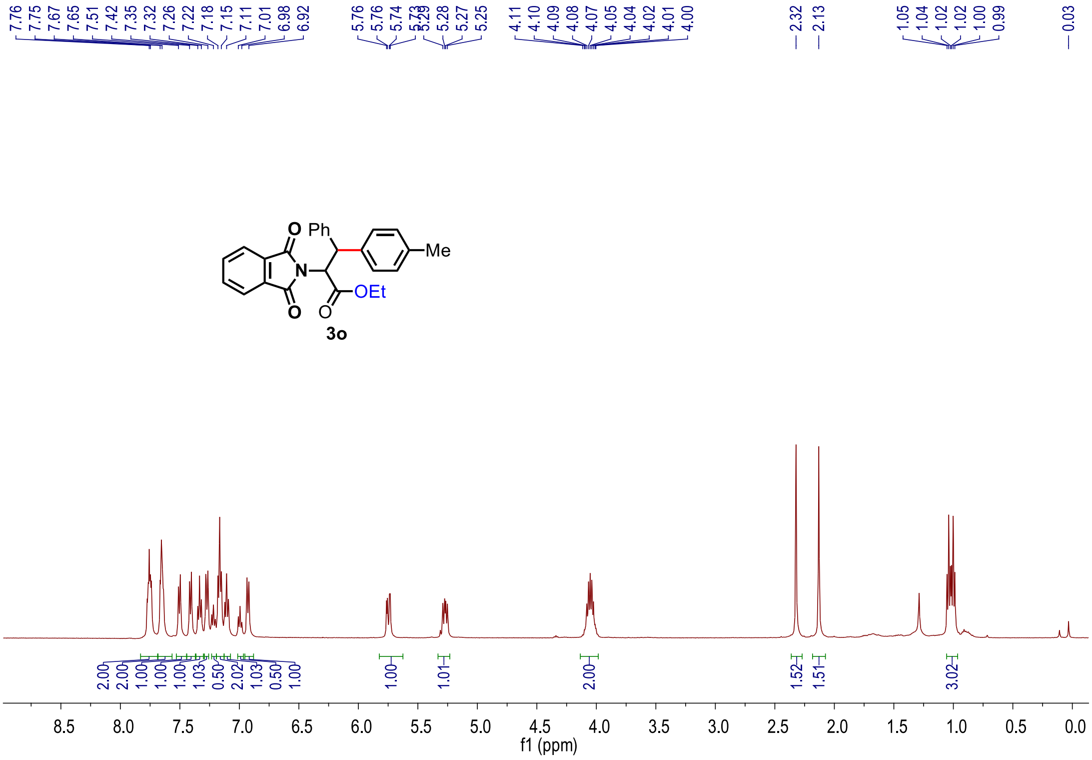
167.65
136.40
134.15
133.79
131.77
129.35
128.80
123.56
77.41
77.16
76.91
62.12
53.68
34.33
21.13
14.25
Me
OEt
3n
f1 (ppm)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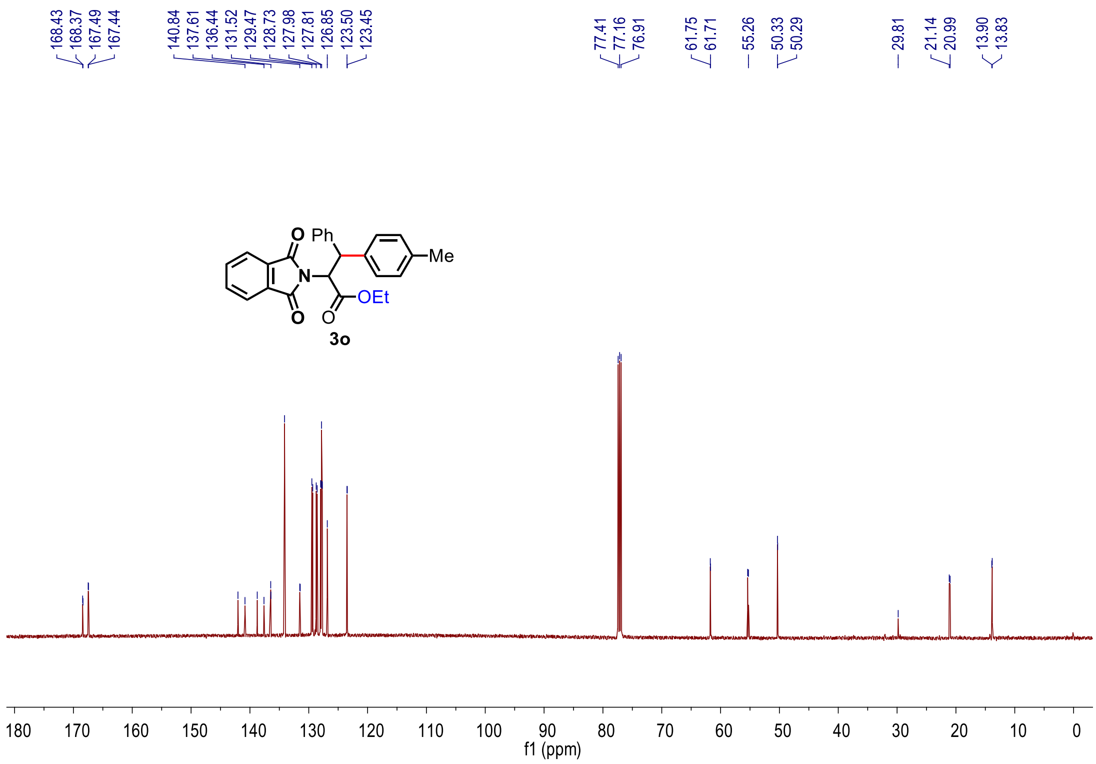
7.75
7.67
7.65
7.51
7.42
7.35
7.32
7.26
7.22
7.18
7.15
7.11
7.01
6.98
6.92
5.76
5.76
5.74
5.73
5.29
5.28
5.27
5.25
4.11
4.10
4.09
4.08
4.07
4.05
4.04
4.02
4.01
4.00
2.32
2.13
1.05
1.04
1.02
1.02
1.00
0.99
0.03
Ph
Me
OEt
3o
2.00
2.00
1.00
1.00
1.00
1.03
0.50
2.02
1.03
0.50
1.00
1.00
1.01
2.00
1.52
1.51
3.02
f1 (ppm)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168.37
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140.84
137.61
136.44
131.52
129.47
128.73
127.98
127.81
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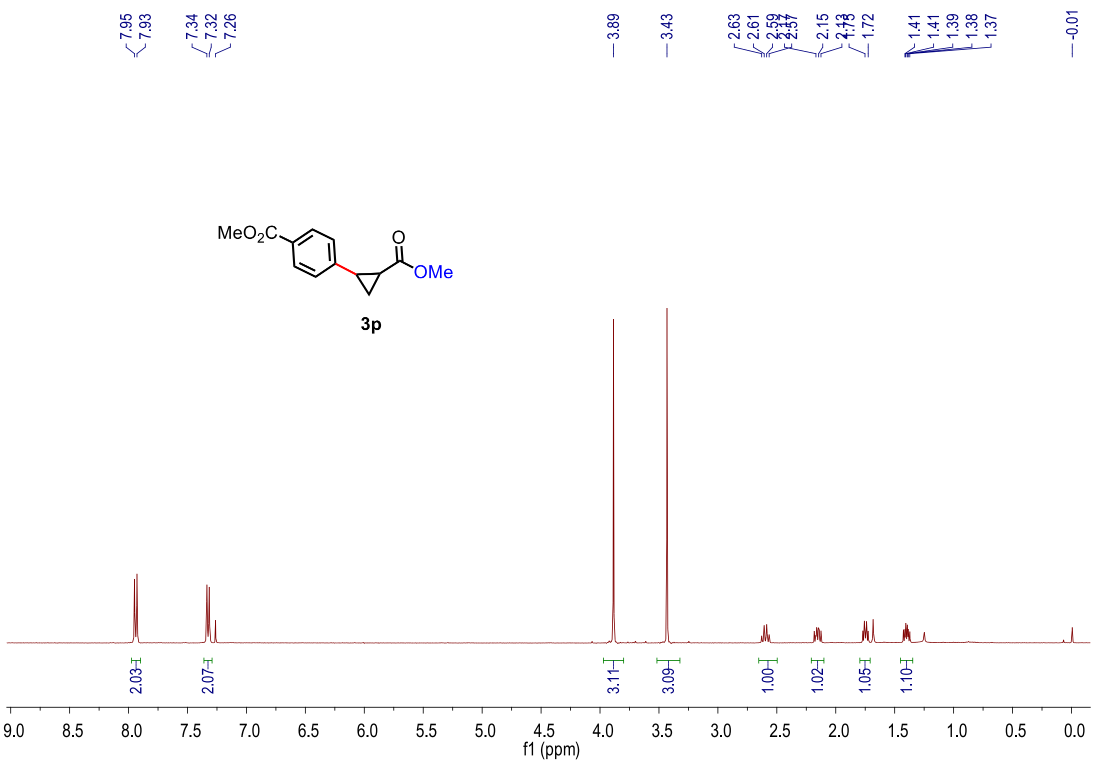
123.50
123.45
77.41
77.16
76.91
61.75
61.71
55.26
50.33
50.29
29.81
21.14
20.99
13.90
13.83
Ph
Me
OEt
3o
f1 (ppm)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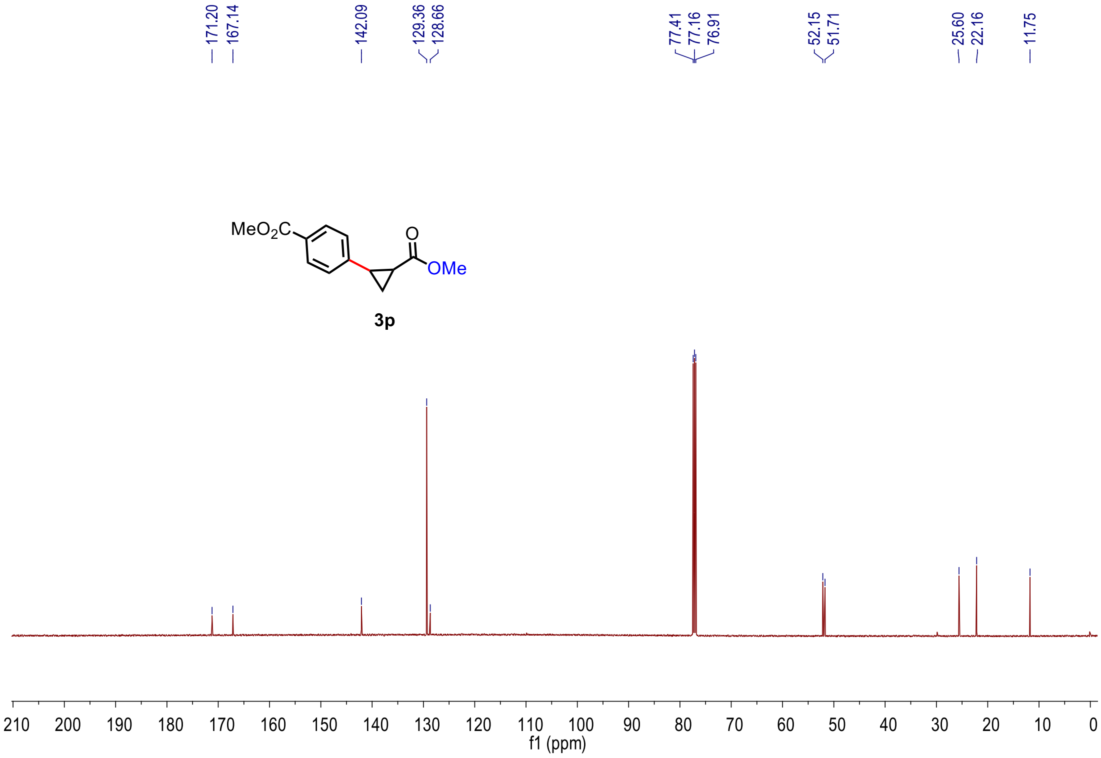
7.93
7.34
7.32
7.26
3.89
3.43
2.63
2.61
2.15
1.72
1.41
1.41
1.39
1.38
1.37
-0.01
OMe
3p
2.03
2.07
3.11
3.09
1.00
1.02
1.05
1.10
f1 (ppm)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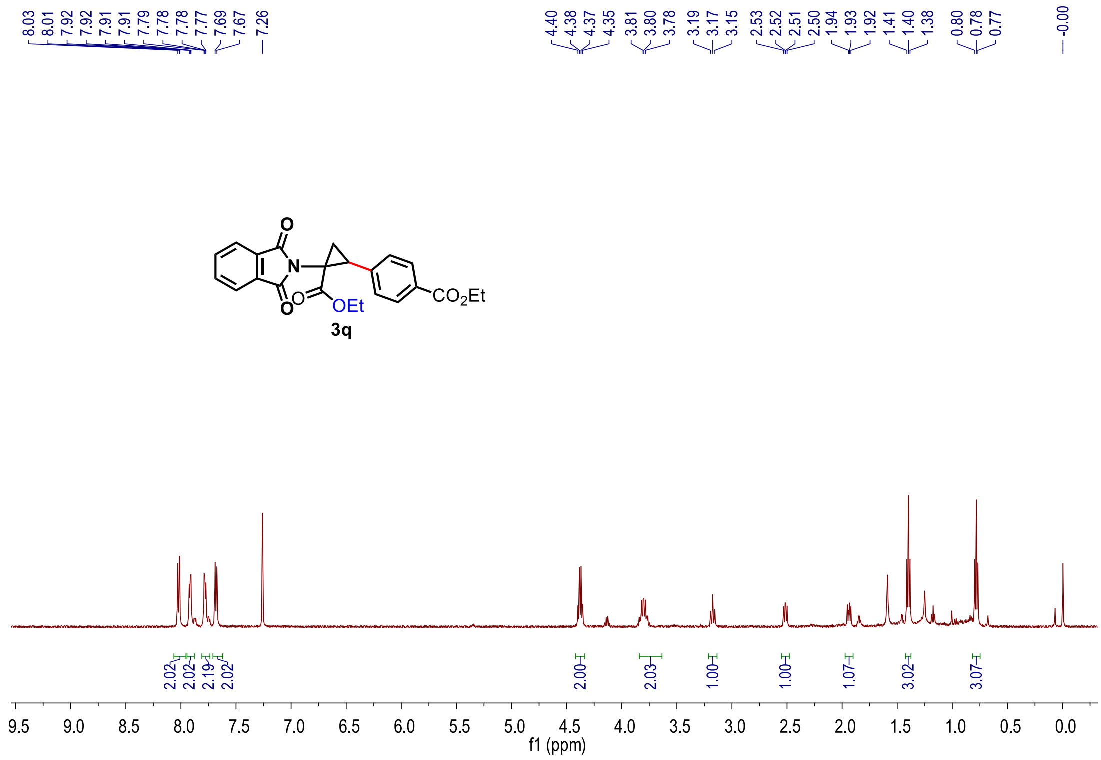
167.14
142.09
129.36
128.66
77.41
77.16
76.91
52.15
51.71
25.60
22.16
11.75
MeO2C
O
OMe
3p
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.01
7.92
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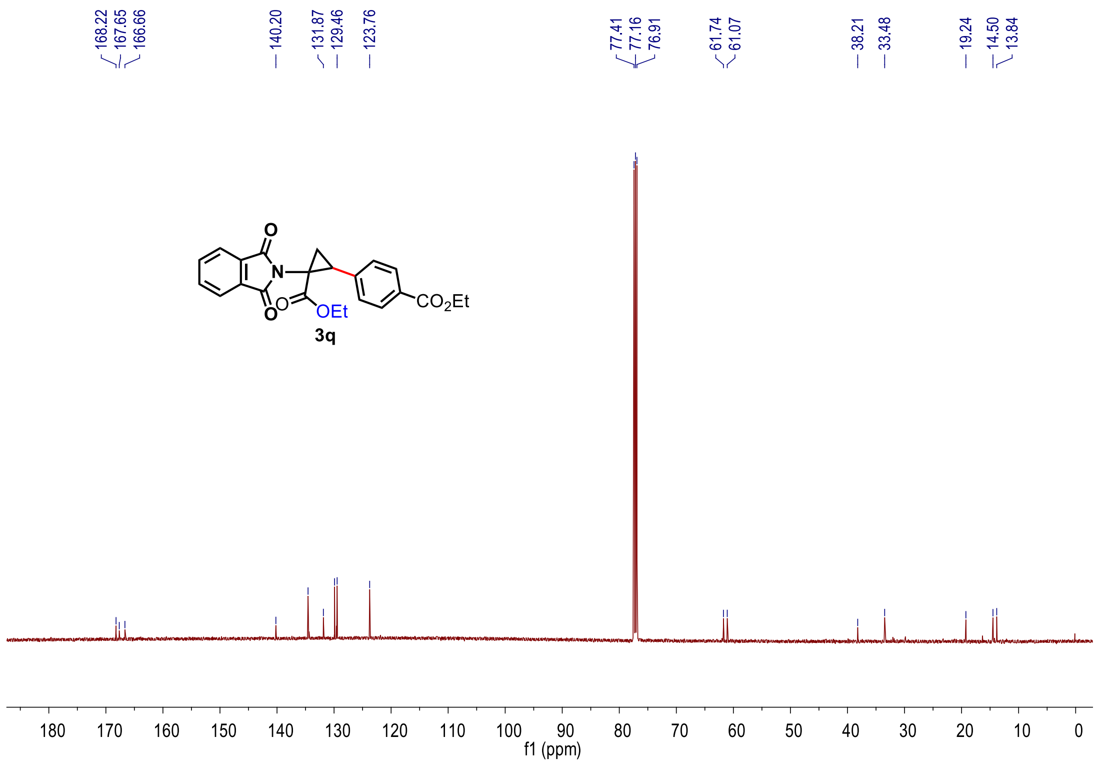
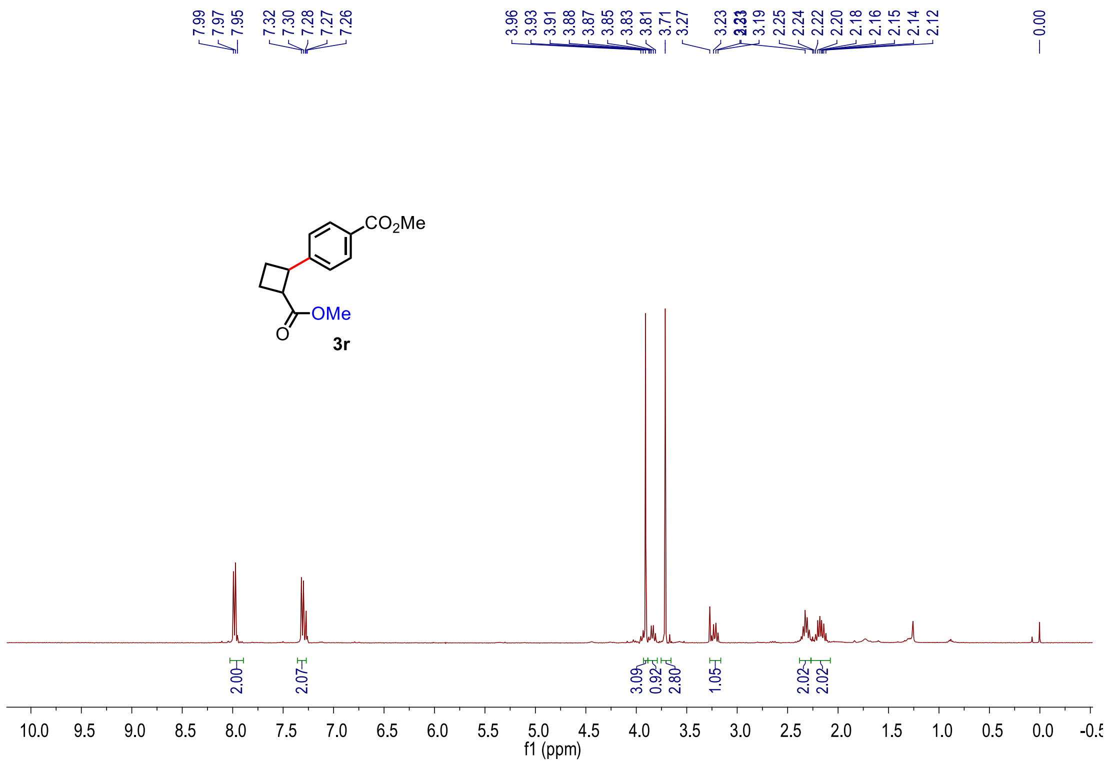
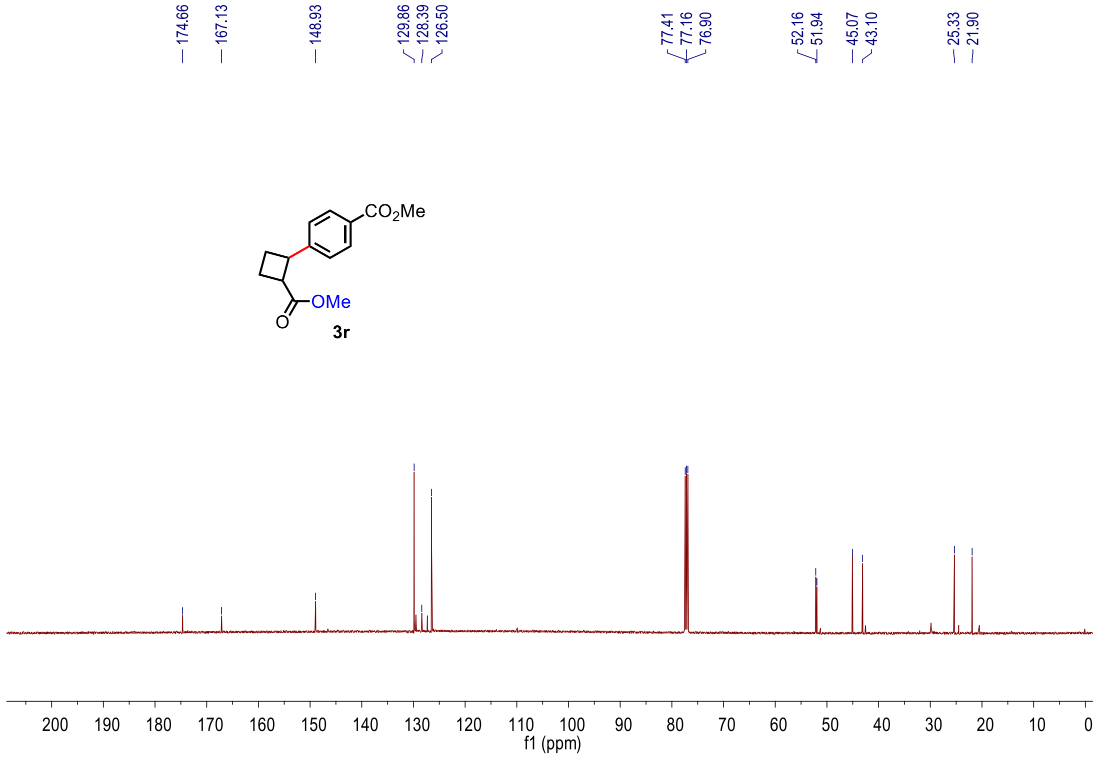
7.91
7.91
7.79
7.78
7.78
7.77
7.69
7.67
7.26
4.40
4.38
4.37
4.35
3.81
3.80
3.78
3.19
3.17
3.15
2.53
2.52
2.51
2.50
1.94
1.93
1.92
1.41
1.40
1.38
0.80
0.78
0.77
-0.00
O
N
O
O
OEt
CO2Et
3q
2.02
2.02
2.19
2.02
2.00
2.03
1.00
1.00
1.07
3.02
3.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



168.22
167.65
166.66
140.20
131.87
129.46
123.76
77.41
77.16
76.91
61.74
61.07
38.21
33.48
19.24
14.50
13.84
OEt
CO2Et
3q
f1 (ppm)

CO2Me
OMe
3r
f1 (ppm)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167.13
148.93
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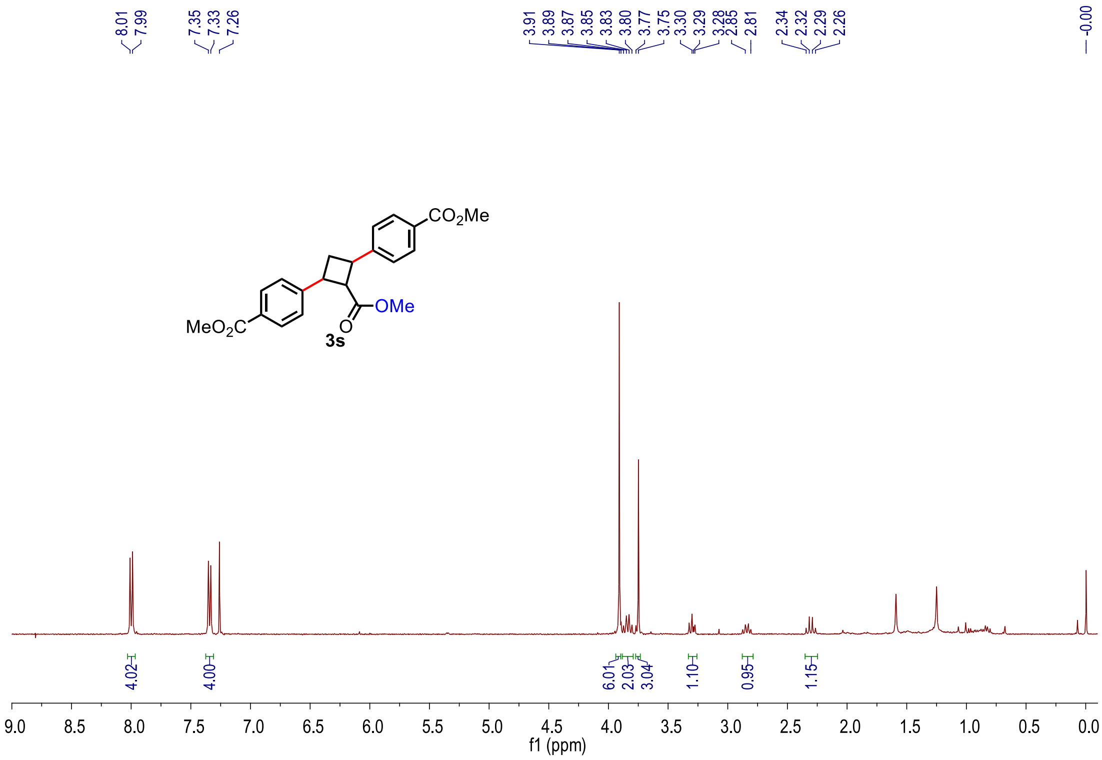
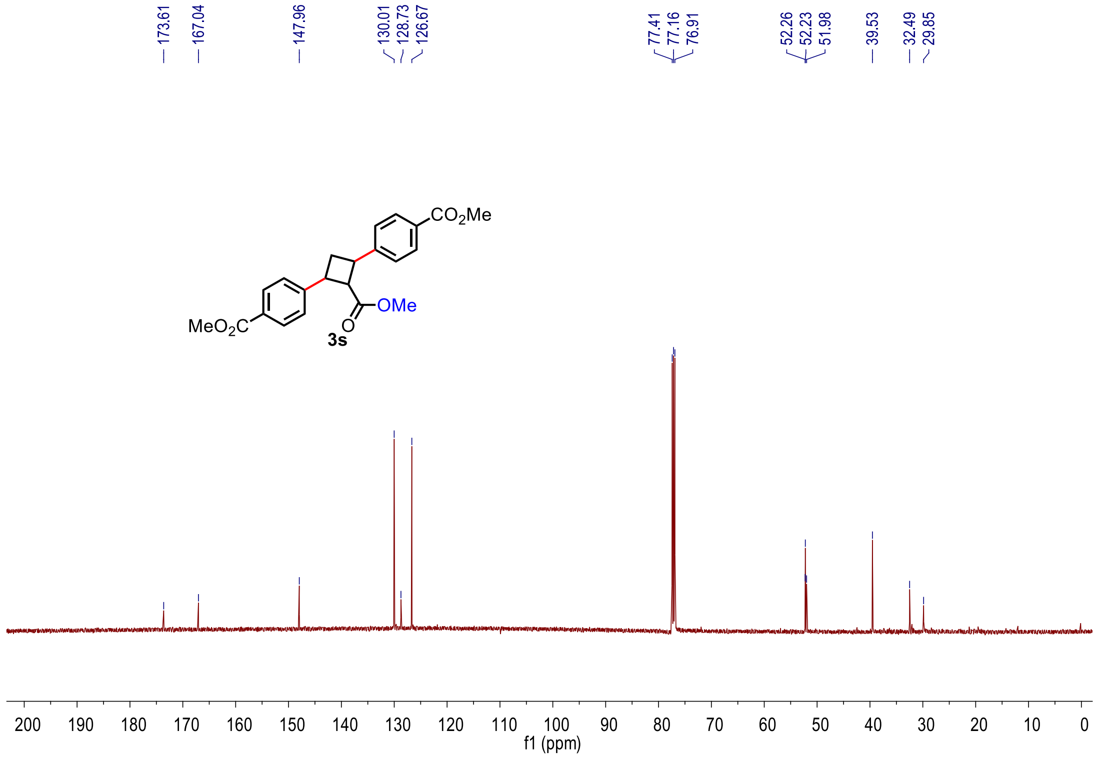
128.39
126.50
77.41
77.16
76.90
52.16
51.94
45.07
43.10
25.33
21.90
CO2Me
OMe
O
3r
f1 (ppm)


8.01
7.99
7.35
7.33
7.26
3.91
3.89
3.87
3.85
3.83
3.80
3.77
3.75
3.30
3.29
3.28
2.85
2.81
2.34
2.32
2.29
2.26
-0.00
CO2Me
MeO2C
OMe
O
3s
4.02
4.00
6.01
2.03
3.04
1.10
0.95
1.15
f1 (ppm)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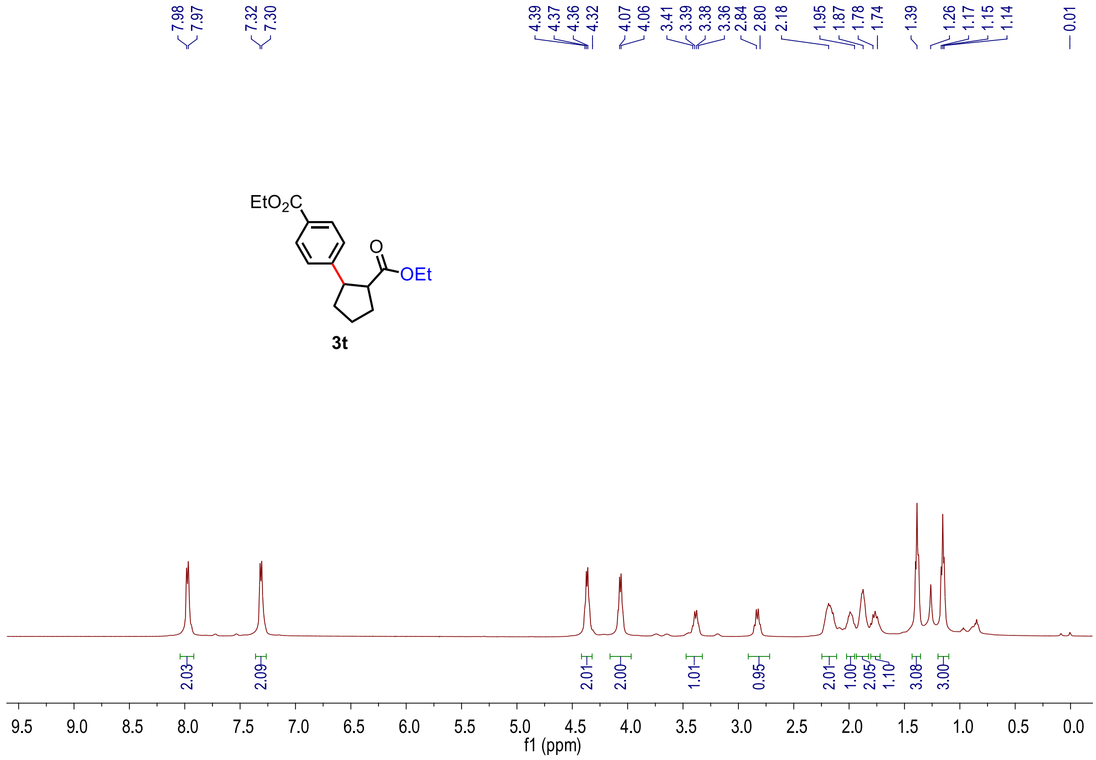
167.04
147.96
130.01
128.73
126.67
77.41
77.16
76.91
52.26
52.23
51.98
39.53
32.49
29.85
$CO_2Me$
$MeO_2C$
OMe
O
3s
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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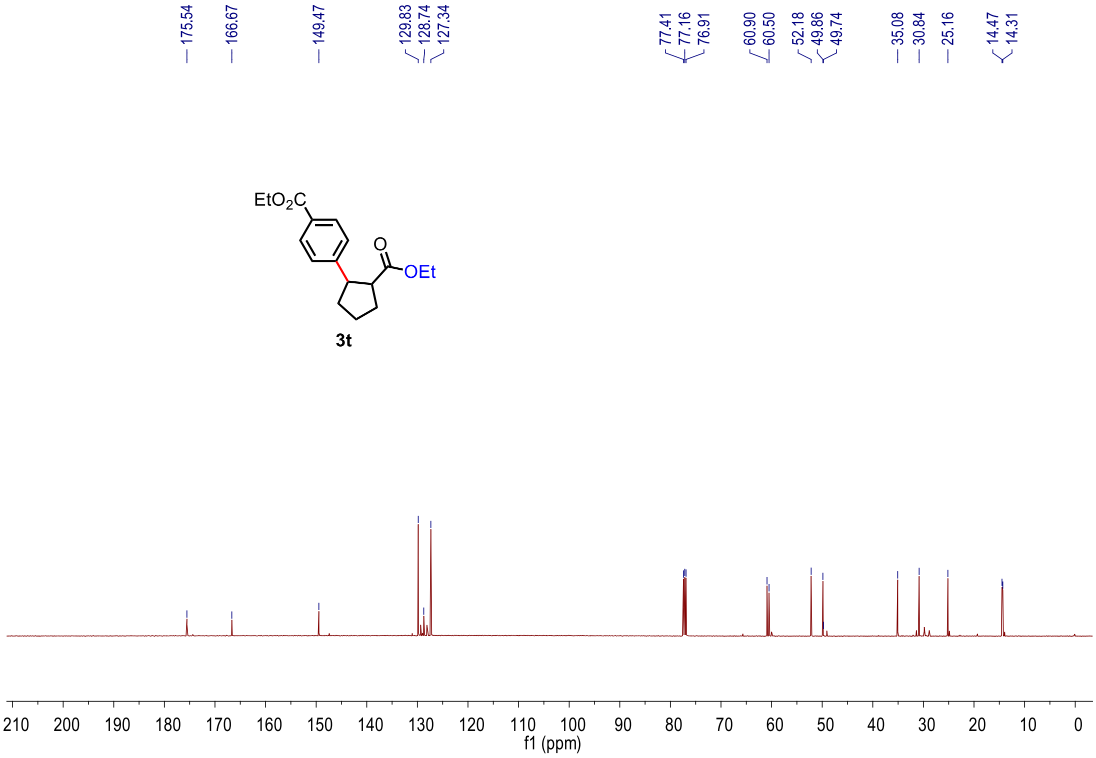
7.97
7.32
7.30
4.39
4.37
4.36
4.32
4.07
4.06
3.41
3.39
3.38
3.36
2.84
2.80
2.18
1.95
1.87
1.78
1.74
1.39
1.26
1.17
1.15
1.14
-0.01
$EtO_2C$
O
OEt
3t
2.03
2.09
2.01
2.00
1.01
0.95
2.01
1.00
2.05
1.10
3.08
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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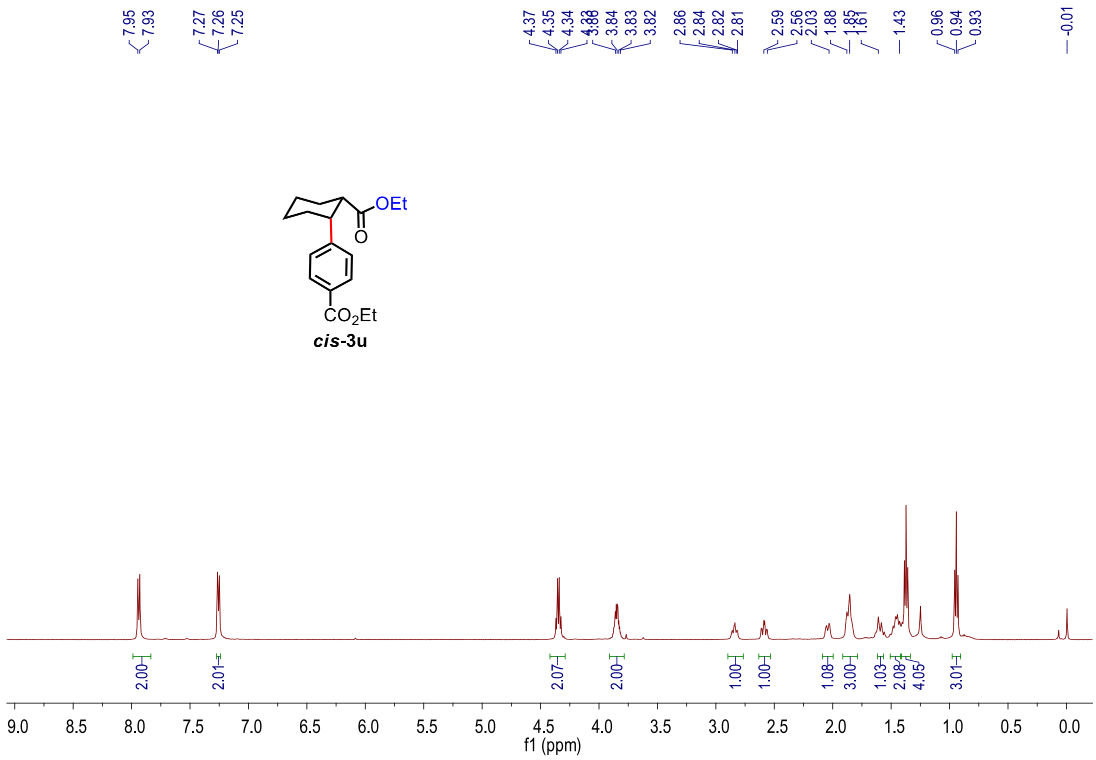
128.74
127.34
77.41
77.16
76.91
60.90
60.50
52.18
49.86
49.74
35.08
30.84
25.16
14.47
14.31
EtO2C
O
OEt
f1 (ppm)

**3t**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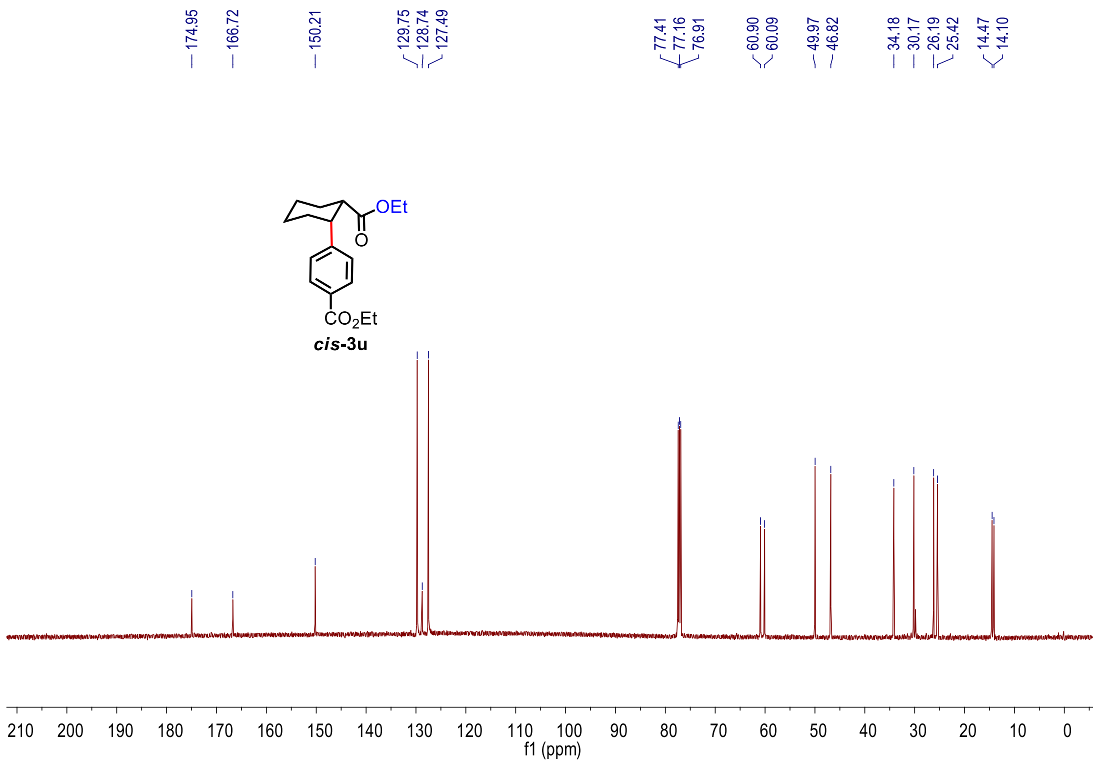
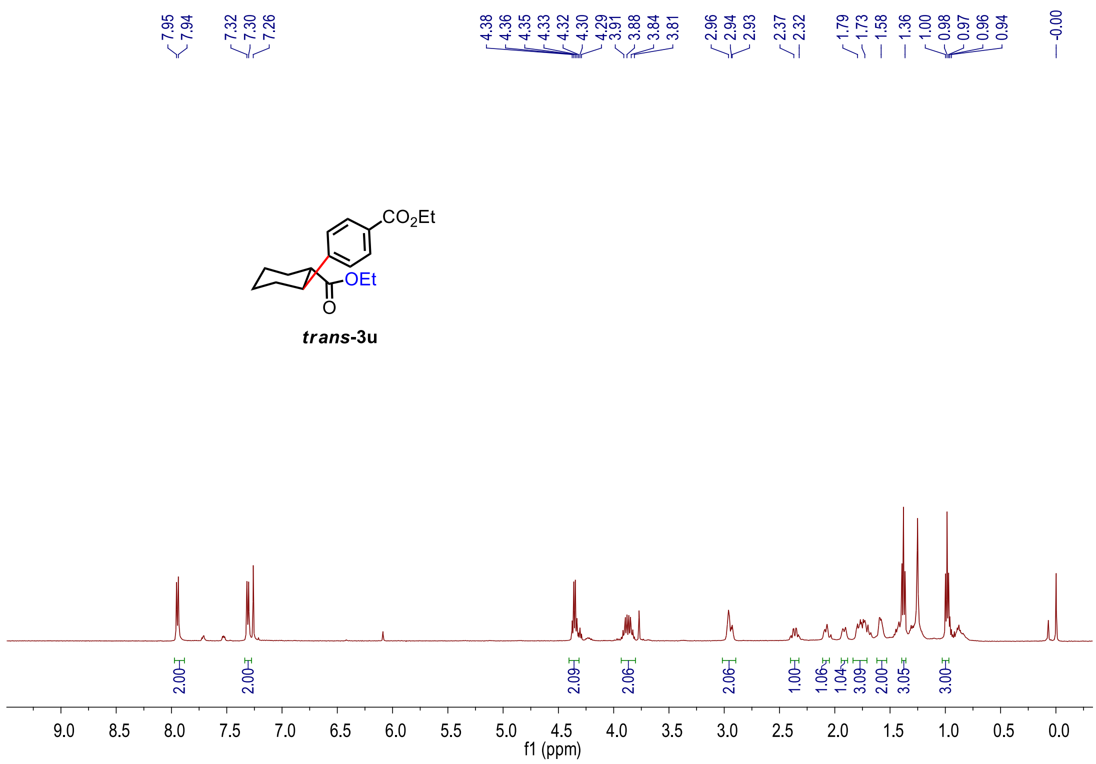
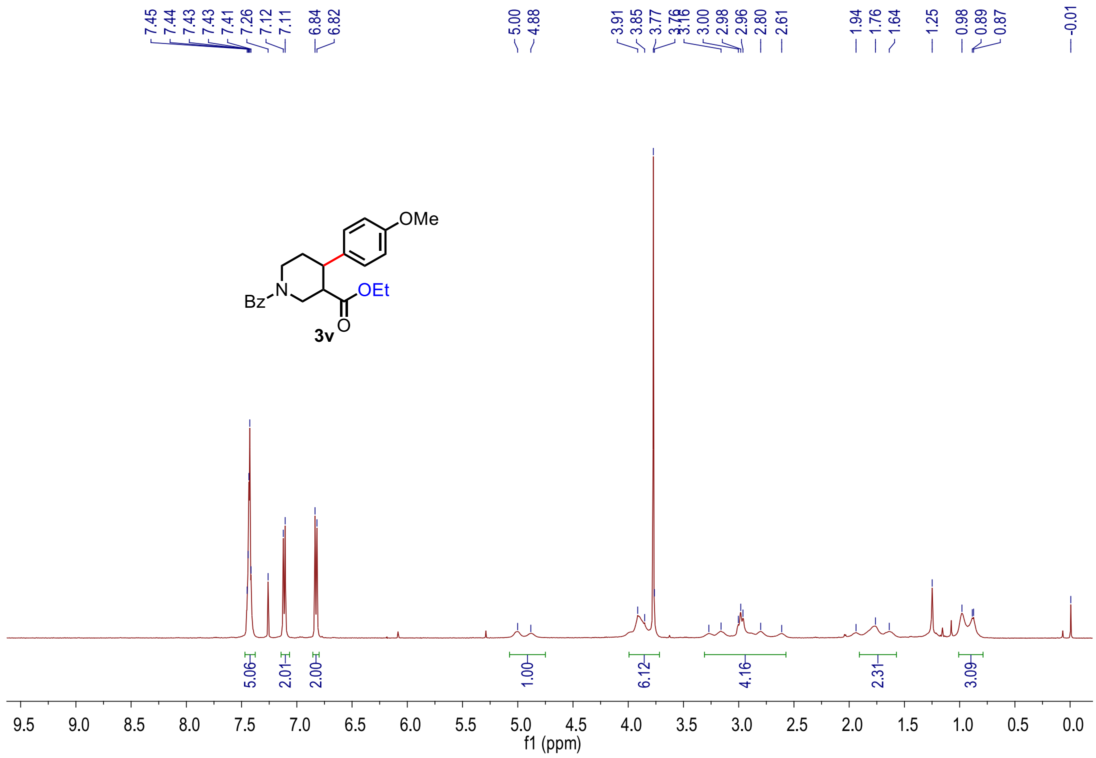
7.93
7.27
7.26
7.25
4.37
4.35
4.34
3.84
3.83
3.82
2.86
2.84
2.82
2.81
2.59
2.56
2.03
1.88
1.43
0.96
0.94
0.93
-0.01
OEt
O
CO2Et
2.00
2.01
2.07
2.00
1.00
1.00
1.08
3.00
1.03
2.08
4.05
3.01
f1 (ppm)

***cis*-3u**


OEt
O
$CO_2Et$
*cis*-3u
f1 (ppm)


$CO_2Et$
OEt
O
*trans*-3u
f1 (ppm)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7.43
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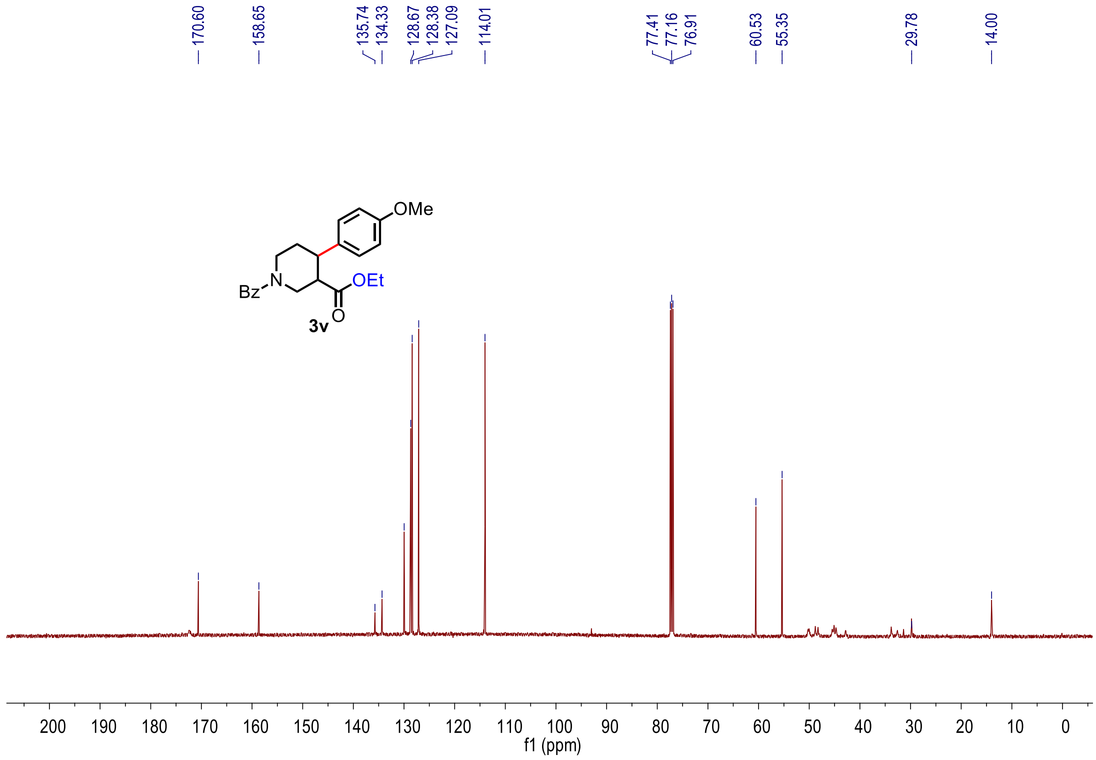
7.41
7.26
7.12
7.11
6.84
6.82
5.00
4.88
3.91
3.85
3.77
3.16
3.00
2.98
2.96
2.80
2.61
1.94
1.76
1.64
1.25
0.98
0.89
0.87
-0.01
OMe
OEt
Bz
N
O
3v
5.06
2.01
2.00
1.00
6.12
4.16
2.31
3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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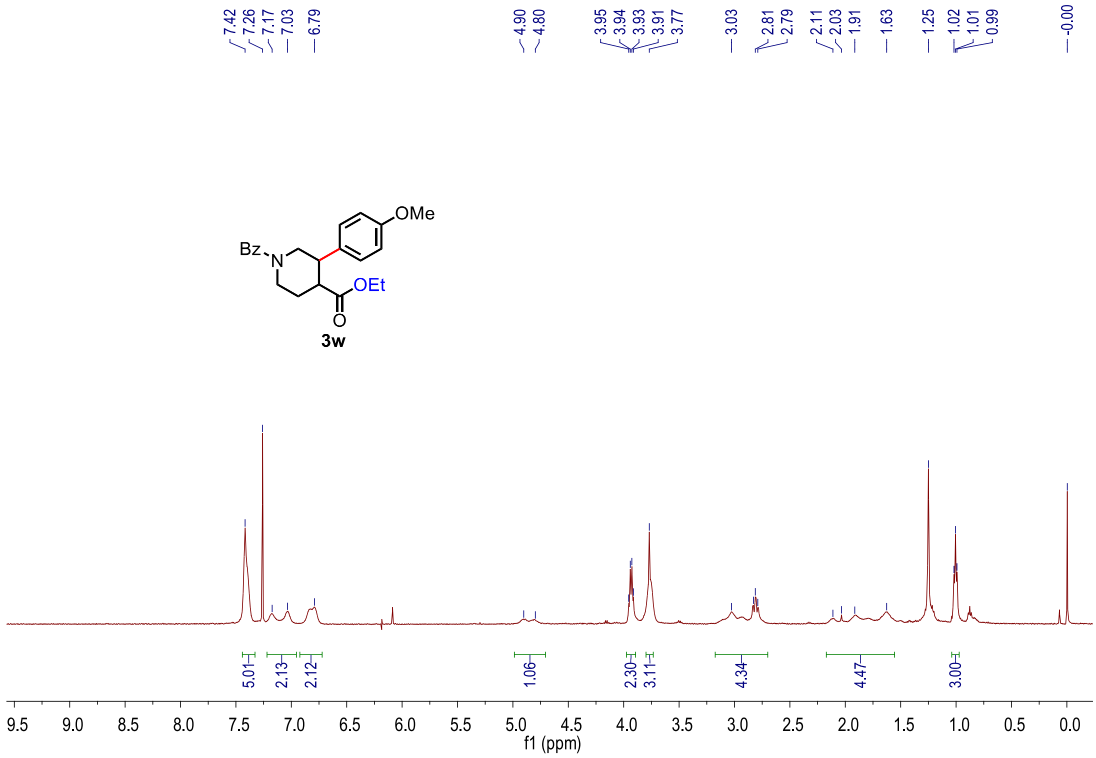
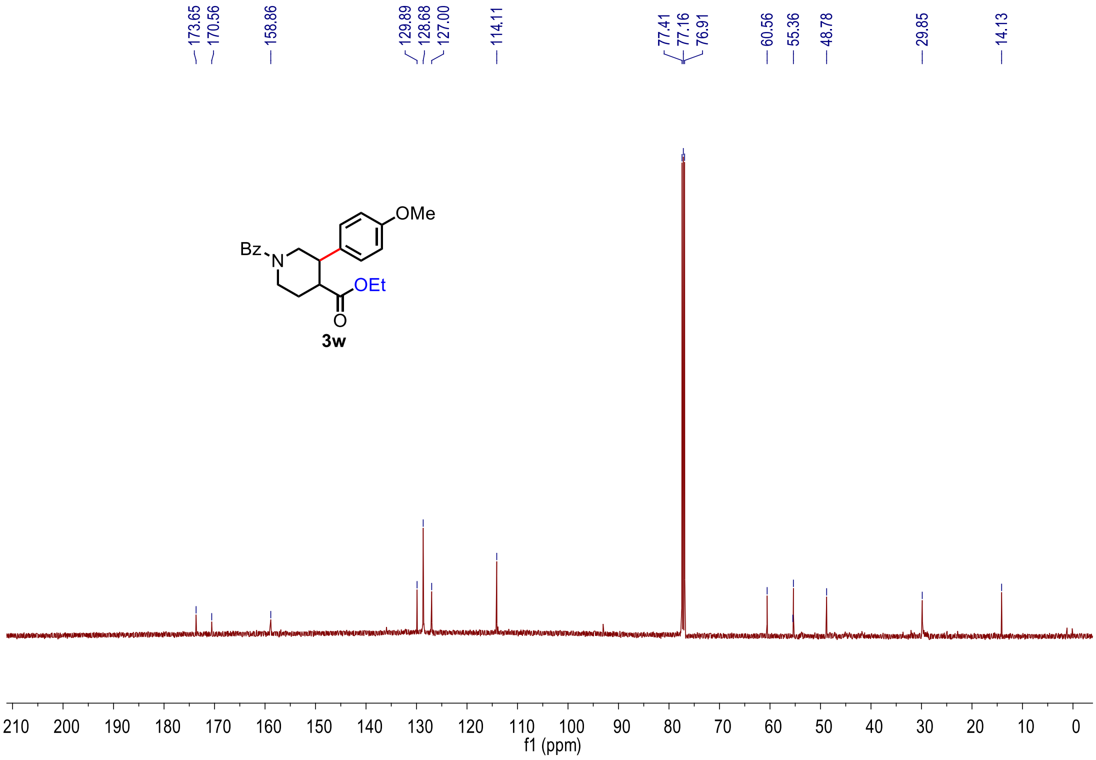
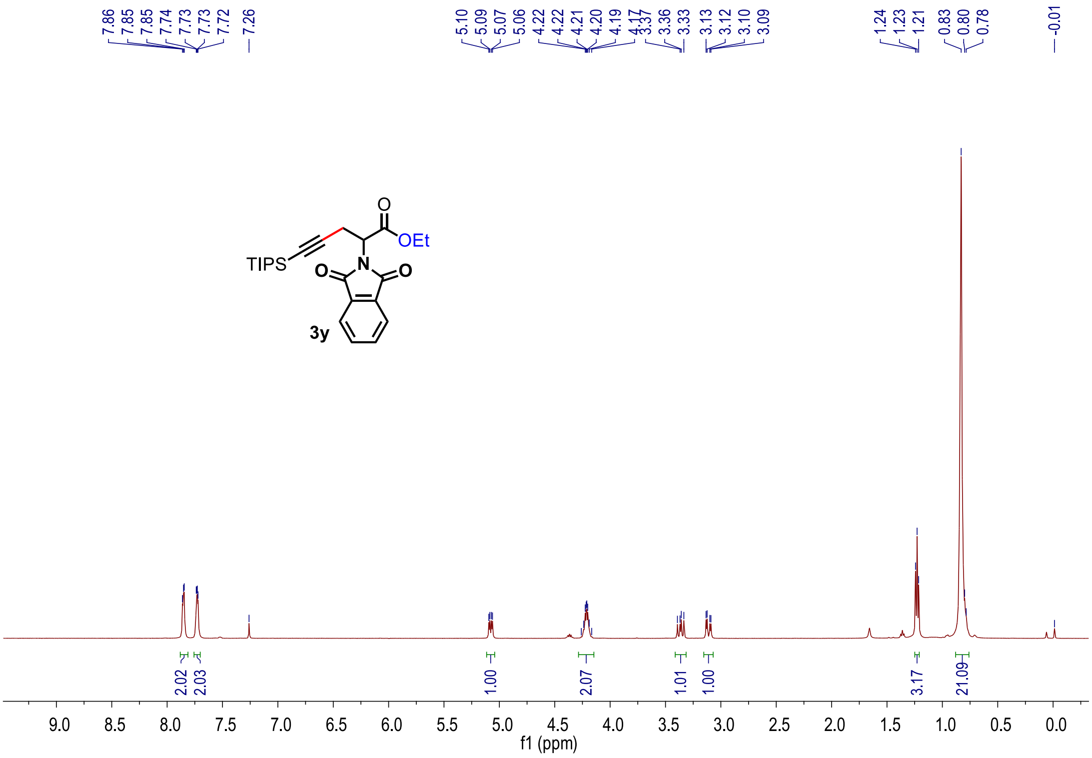
135.74
134.33
128.67
128.38
127.09
114.01
77.41
77.16
76.91
60.53
55.35
29.78
14.00
OMe
OEt
Bz
N
O
3v
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

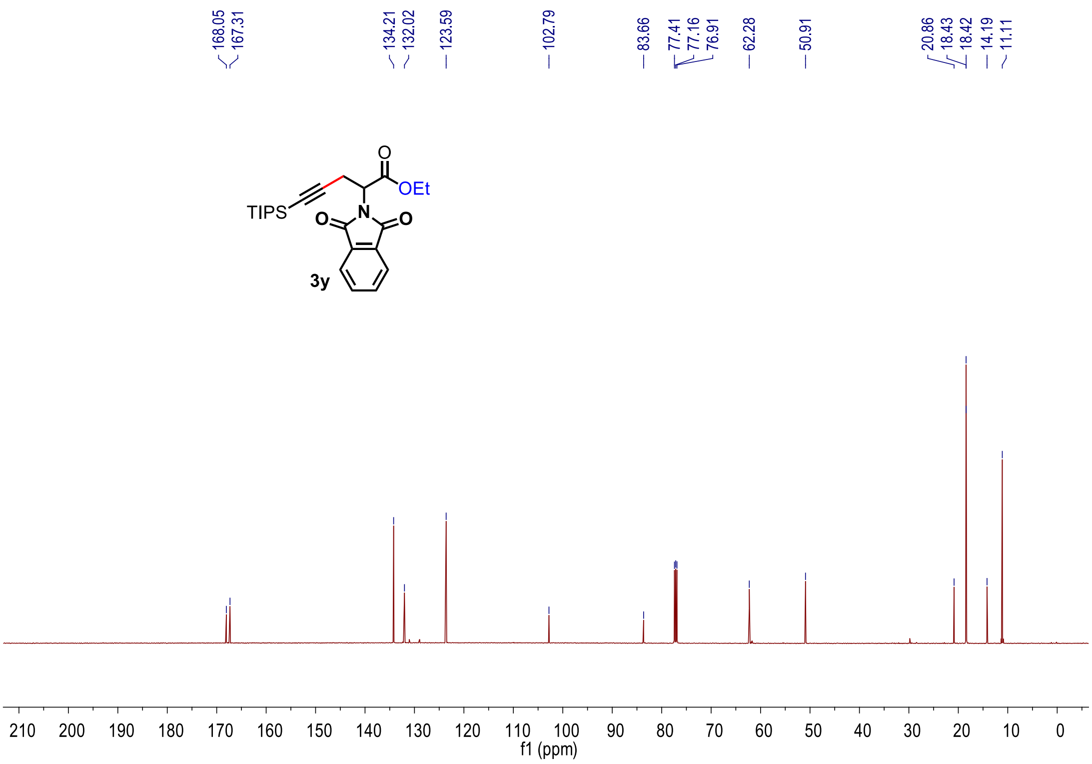


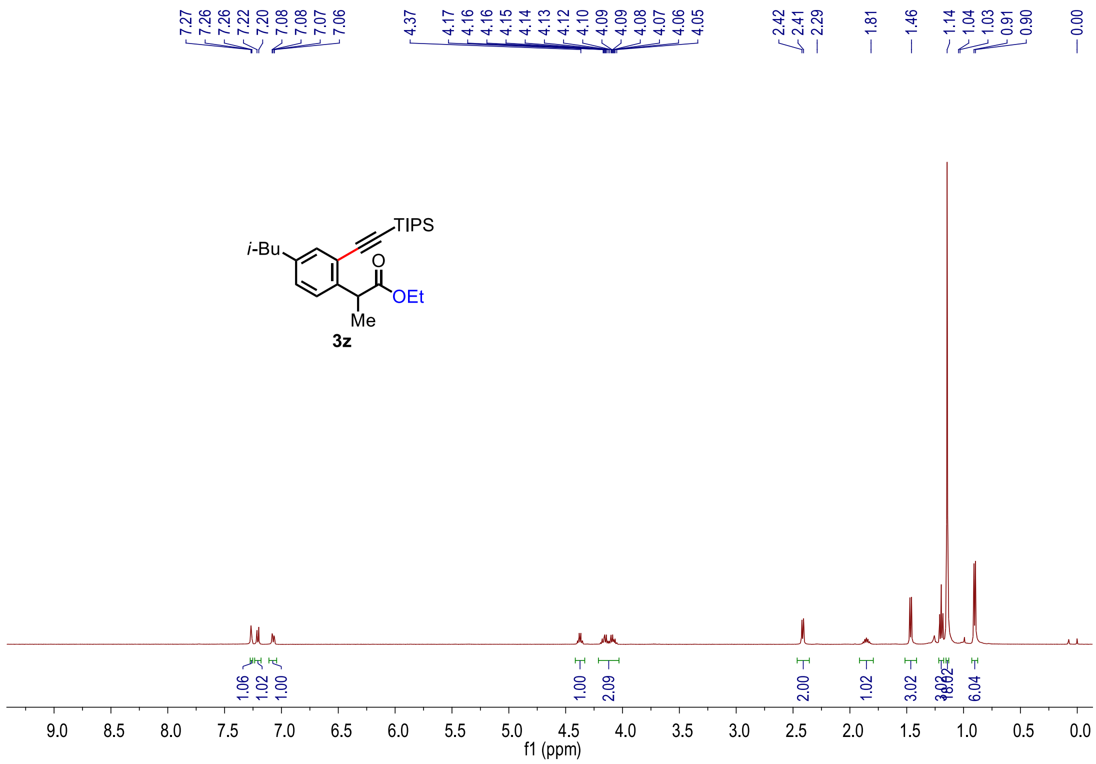
3w

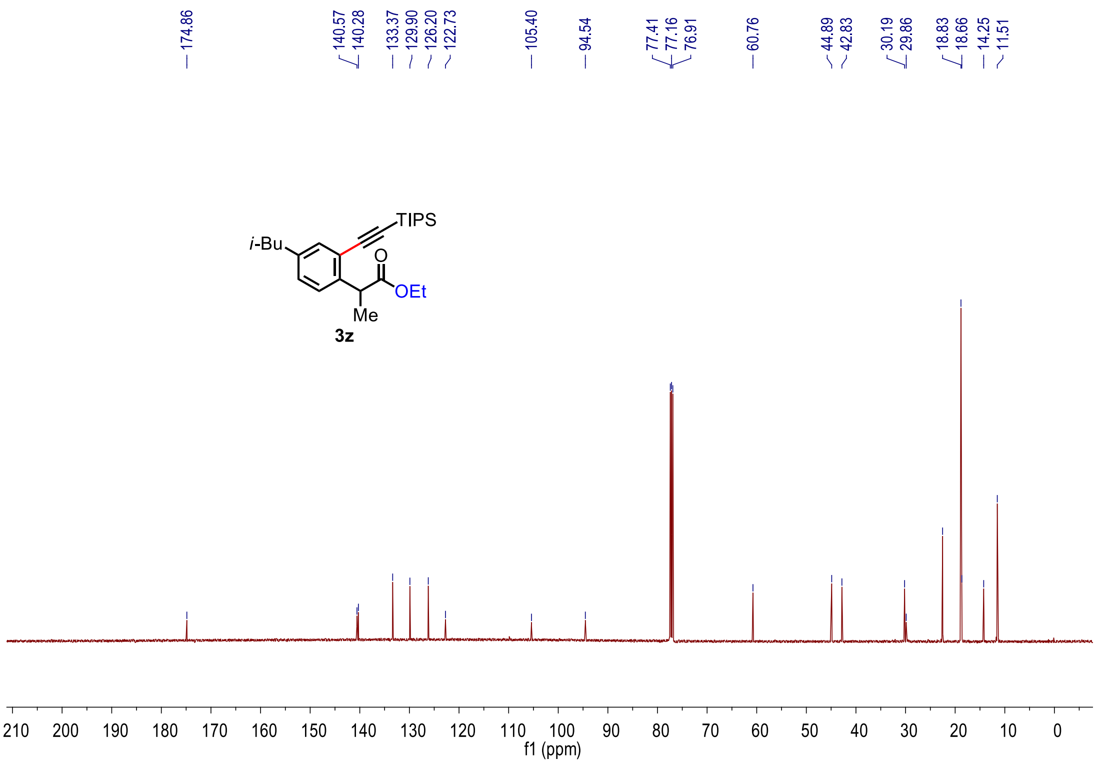


3w






TIPS
i-Bu
O
OEt
Me
3z
7.27 7.26 7.26 7.22 7.20 7.08 7.08 7.07 7.06
4.37 4.17 4.16 4.16 4.15 4.14 4.13 4.12 4.10 4.09 4.09 4.08 4.07 4.06 4.05
2.42 2.41 2.29 1.81 1.46 1.14 1.04 1.03 0.91 0.90 0.00
1.06 1.02 1.00 1.00 2.09 2.00 1.02 3.02 6.04
f1 (ppm)


TIPS
i-Bu
O
OEt
Me
3z
174.86 140.57 140.28 133.37 129.90 126.20 122.73 105.40 94.54 77.41 77.16 76.91 60.76 44.89 42.83 30.19 29.86 18.83 18.66 14.25 11.51
f1 (ppm)