Nickel(II)-catalyzed enantioselective α-alkylation of β-ketoamides with phenyliodonium ylide via a radical process

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1. General remarks

Reactions were carried out using commercially available reagents in over-dried apparatus. Nickel(II) trifluoromethanesulfonate and scandium(III) trifluoromethanesulfonate were purchased from Adamas Co. Ltd. and Alfa aesar chemical Co. Ltd. CH_2Cl_2 was dried over powdered CaH_2 and distilled under nitrogen just before use. Et_2O, THF and toluene were directly distilled before use. EtOAc from Tansoole Co. Ltd. was directly used. ^1H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm using solvent resonance as an internal standard [$CDCl_3$, δ = 7.26 ppm]. Data reported as: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets), coupling constants (Hz), integration and assignment. $^{13}C\{^1H\}$ NMR spectra were recorded on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm using solvent as an internal standard [$CDCl_3$, δ = 77.00 ppm]. $^{19}F\{^1H\}$ NMR was measured at 376 MHz, and $PhCF_3$ (-63.2 ppm) was used as an external standard. Enantiomeric excesses (ee) were determined b by high-performance liquid chromatography (HPLC) or supercritical fluid chromatography (SFC) analysis using the corresponding commercial chiral column as stated in the experimental procedures. Optical rotations were reported as follows: $[\alpha]_D^T$ = (*c* = g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (FTMS+c ESI). Chiral *N*,*N*′-dioxide ligands[1], phenyliodonium ylide malonate[2] and β-keto amide/ester[3] were prepared according to previously reported method.

2. General procedure for catalytic asymmetric α-alkylation reaction

General procedure for catalytic asymmetric α-alkylation reaction: A dry reaction tube was charged with **L-PiEt$_2$**/$Ni(OTf)_2$ (1:1, 10 mol%), and β-keto amide/ester **1** (0.1 mmol). Then, ethyl acetate (1.0 mL) was added and the mixture was stirred at 35 °C for 0.5 h. Finally, water (5 μL) and phenyliodonium ylide malonate **2** (0.12 mmol) were added under stirring. The reaction mixture was stirred at 35 °C for 12 h. The residue was purified by flash chromatography (petroleum ether/ethyl acetate 8:1 to 4:1) on silica gel to afford the product **3**. The enantiomeric excesses (ee) was determined by high-performance liquid chromatography (HPLC) with Chiralcel IA, IC and ADH.

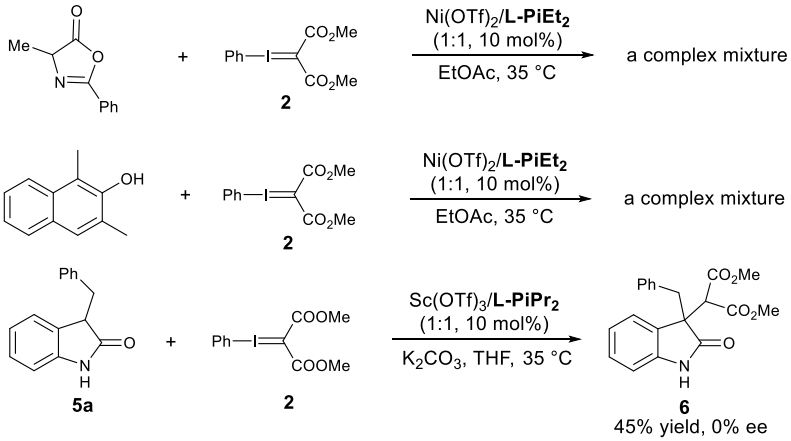
Typical procedure for the scale-up reaction: A flask (100 mL) was charged with **L-PiEt$_2$** (0.15 mmol, 90.0 mg), $Ni(OTf)_2$ (0.15 mmol, 54.0 mg), and **1a** (3.0 mmol, 0.93 g). Then, EtOAc (30 mL) was added and the mixture was stirred at 35 °C for 0.5 h. Finally, water (100 μL) and phenyliodonium ylide malonate **2** (3.3 mmol, 1.10 g) were added under stirring. The reaction mixture was stirred at 35 °C for 12 h. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 8/1) on silica gel to afford the product **3aa** as a white solid (1.16 g, 88% yield, 93% ee) and up to 99% ee can be achieved after recrystallization (1.00 g, 76% yield, 99% ee).

3. Experimental procedures for the reduction of 3aa

To a solution of the adduct **3aa** (43.9 mg, 0.1 mmol) in CH_3OH (1.0 mL) was added KBH_4 (14.6 mg) at 0 °C. The mixture was allowed to stir for 1 h. Then saturated NH_4Cl aqueous solution (2.0 mL) was added to the mixture. The mixture was extracted with CH_2Cl_2, drying over Na_2SO_4.

After evaporation of the solvent, the product **4** was purified on silica gel chromatography (petroleum ether/ethyl acetate = 2/1). The results were >99% yield, 2:1 dr, and 99% ee / 99% ee.

4. Extra optimization



Scheme S1. α-Alkylation of several substrates with phenyliodonium ylide malonate.

5. Mechanism study

(a) Electroparamagnetic resonance (EPR) analysis

EPR measurements: EPR spectra were recorded at room temperature on a Bruker ESP-300E: Receiver Gain = 1.78 e+004; Phase = 0 deg; Harmoni = 1; Mod. Frequency = 100.000 KHz; Mod. Amplitude = 6.00 G; Center Field = 3360.00 G; Sweep width 90.000 G; Resolution = 2048 points; Conversion Time =40.00ms; Time const. = 20.48 ms; Sweep time = 81.92s; Power = 60.39 mw.

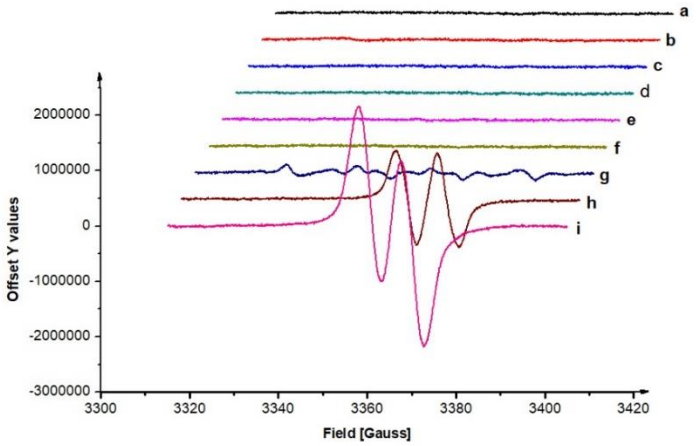


Figure S1. The electroparamagnetic resonance (EPR) spectra of α-alkylation. The electroparamagnetic resonance (EPR) spectra (X band, 9.43 GHz, RT; in EtOAc at room temperature) of a) **2** (0.05 mmol); b) **1a** (0.05 mmol); c) **L-PiEt$_2$** (0.05 mmol); d) Ni(OTf)$_2$ (0.05 mmol); e) the complex of Ni(OTf)$_2$/**L-PiEt$_2$** (0.01 mmol); f) Ni(OTf)$_2$ (0.01 mmol) and **2** (0.05 mmol); g) **L-PiEt$_2$** (0.01 mmol) and **2** (0.05 mmol); h) the complex of Ni(OTf)$_2$/**L-PiEt$_2$** (0.01

mmol), **1a** (0.05 mmol) and **2** (0.05 mmol); i) the complex of $Ni(OTf)_2$/**L-PiEt$_2$** (0.01 mmol), **1a** (0.05 mmol), **2** (0.05 mmol) and H_2O (3 μL).

Table S1. EPR experiments of β-ketoamide **1a** with **2**.

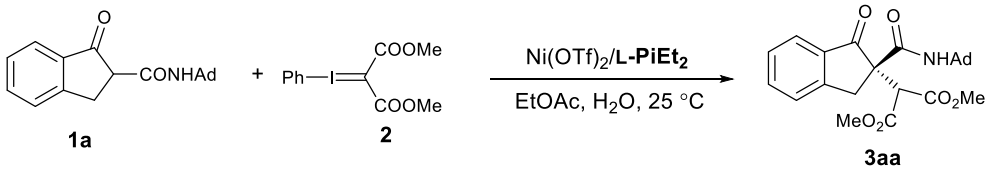


Figure S1	**2**	**1a**	**L-PiEt$_2$**	$Ni(OTf)_2$	H_2O	Signal
3a	√	-	-	-	-	No signal
3b	-	√	-	-	-	No signal
3c	-	-	√	-	-	No signal
3d	-	-	-	√	-	No signal
3e	-	-	√	√	-	No signal
3f	√	-	-	√	-	No signal
3g	√	-	√	-	-	weak signal
3h	√	√	√	√	-	strong signal
3i	√	√	√	√	√	strong signal

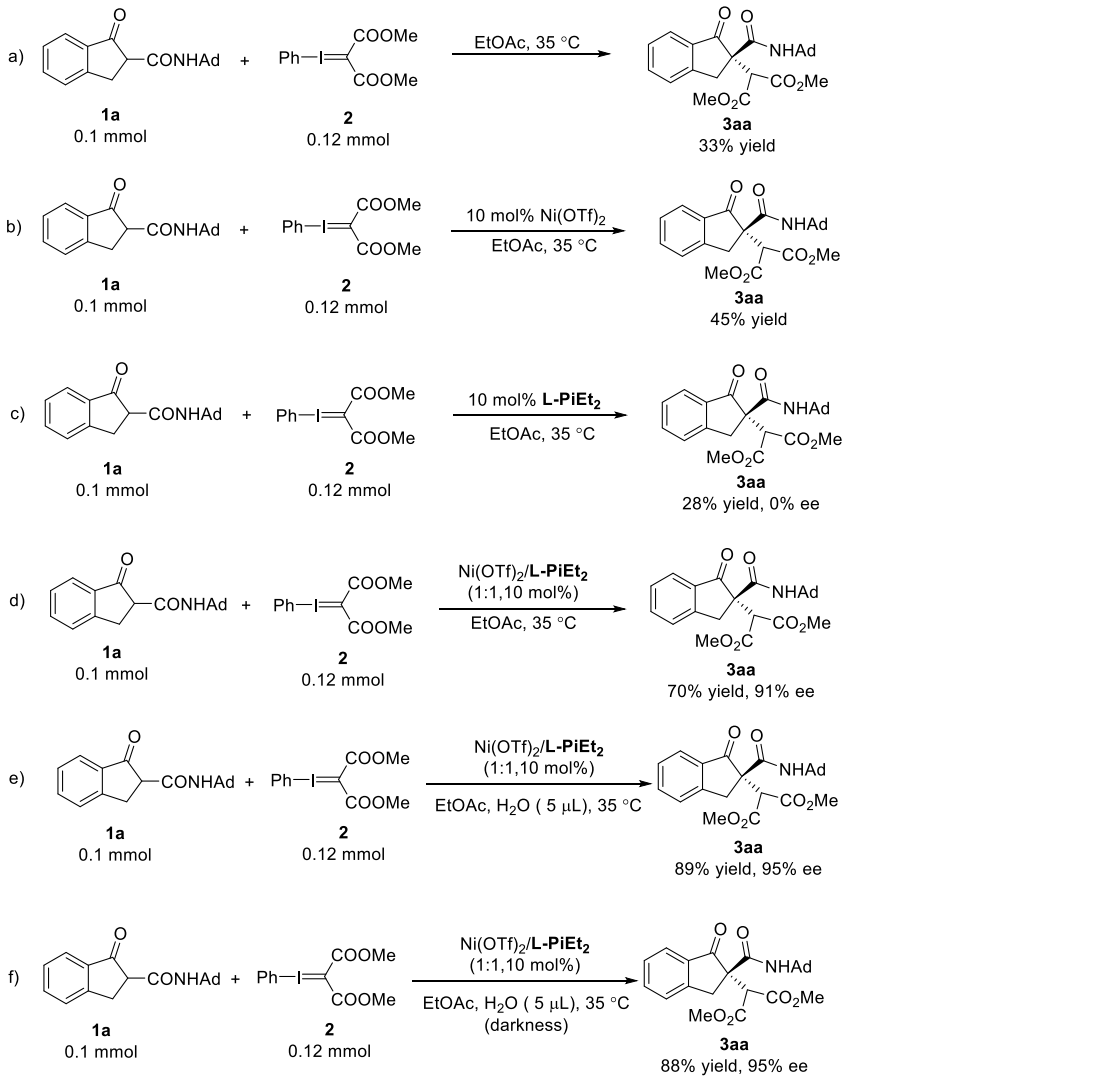
(1) No signal of the reagents and catalysts appeared from 3315.00 G to 3405.00 G (Figure S1a-e).

(2) No signal appeared when $Ni(OTf)_2$ and phenyliodonium ylide **2** was stirred in EtOAc (0.06 mL) at room temperature (Figure S1f).

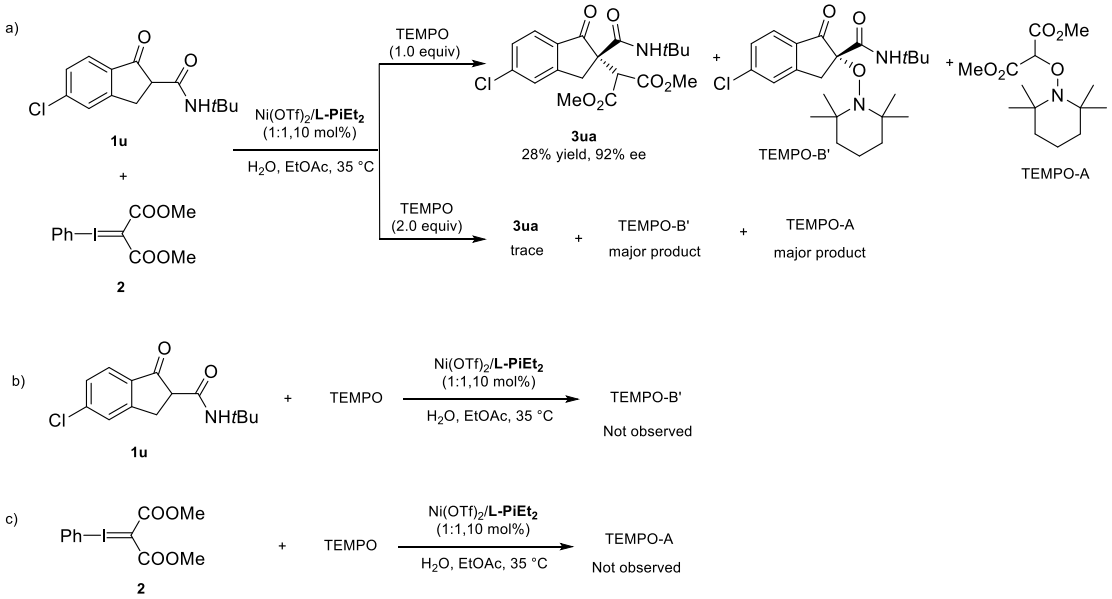
(3) Interestingly, the EPR spectrum of the mixture of **L-PiEt$_2$** and phenyliodonium ylide **2** in EtOAc (0.06 mL) exhibits weak signal (Figure S1g). This could be explained by the coordination of **L-PiEt$_2$** to the iodine(III) center, which activated phenyliodonium ylide **2**.

(4) The mixture of $Ni(OTf)_2$/ **L-PiEt$_2$** (0.01 mmol), **1a** (0.05 mmol) and **2** (0.05 mmol) exhibits double peaks and g-Factors are 2.006 and 2.001 (Figure S1h). The intensity of the signals is stronger when water is added (Figure S1i).

(b) Control experiments



Scheme S2. Control experiments.



Scheme S3. Control experiments.

(c) HRMS analysis

Preliminary studies of the mechanism were carried out by HRMS experiments (Figure S2). The coordination of *N*,*N*'-dioxide **L-PiEt$_2$** with Ni(OTf)$_2$ was confirmed by the ion peak at *m*/*z* ($C_{35}H_{52}N_4NiO_4^{2+}$) 325.1664, corresponding to the intermediate [Ni^{2+} + **L-PiEt$_2$**]$^{2+}$ (calculated. *m*/*z* 325.1666). The interaction of *β*-ketoamide **1a** with the catalyst was confirmed by the HRMS analysis of the mixture of β-ketoamide and the catalyst prepared in situ from Ni(OTf)$_2$, **L-PiEt$_2$** and **1a** (1:1:2) in EtOAc. A peak at *m*/*z* ($C_{55}H_{75}N_5NiO_6^{2+}$) 479.7533 was detected responding to the intermediate **TS-1** [Ni^{2+} + **L-PiEt$_2$** + **1a**]$^{2+}$ (calculated. *m*/*z* 479.7530). It implies the *β*-ketoamide **1a** could be activated by the coordination with the Ni(II) in a bidentate fashion through its two carbonyl groups.

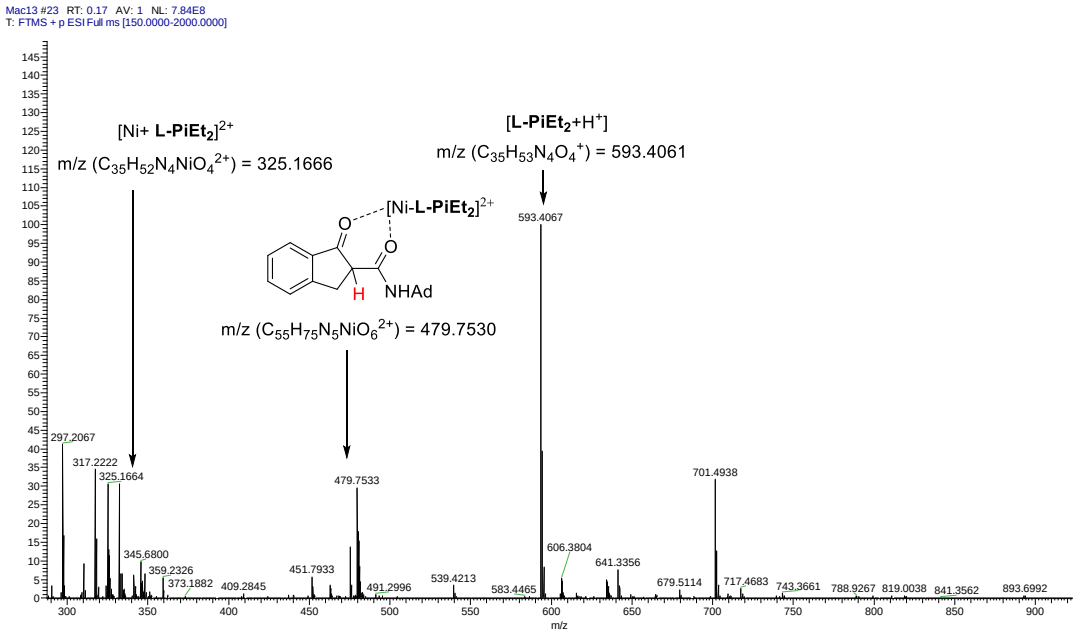


Figure S2. HRMS experiment: The mixture of **L-PiEt$_2$**, Ni(OTf)$_2$ and β-ketoamide **1a** (1:1:2)

Then, a peak at *m*/*z* 927.3762 was detected responding to the intermediate [**L-PiEt$_2$** + **2** + H^+]$^+$ (calculated. *m*/*z* 927.3763) by the HRMS analysis of the mixture of **L-PiEt$_2$** and **2** (1:1) in EtOAc (Figure S3). We suspected that the **2** could be activated by *N*,*N*'-dioxide **L-PiEt$_2$**. HRMS (*m*/*z*): [**L-PiEt$_2$** + H^+]$^+$ calculated. for $C_{35}H_{53}N_4O_4^+$, 593.4061, found 593.4061. HRMS (*m*/*z*): [**L-PiEt$_2$** + Na^+]$^+$ calculated. for $C_{35}H_{52}N_4O_4Na^+$, 615.3881, found 615.3877. HRMS (*m*/*z*): [**L-PiEt$_2$** + K^+]$^+$ calculated. for $C_{35}H_{52}N_4O_4K^+$, 631.3620, found 631.3616.

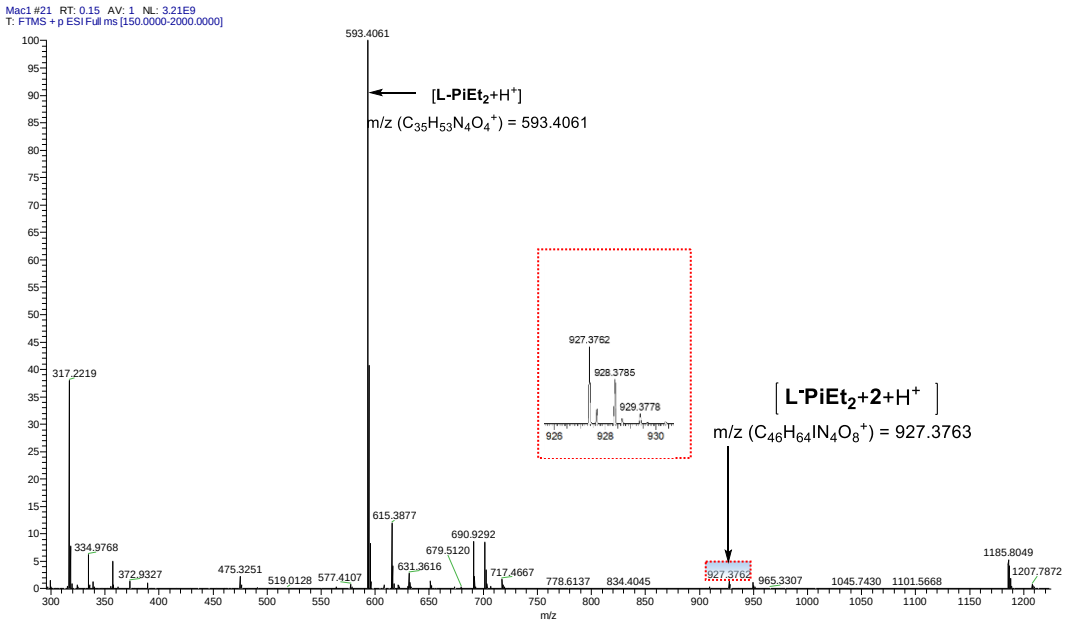
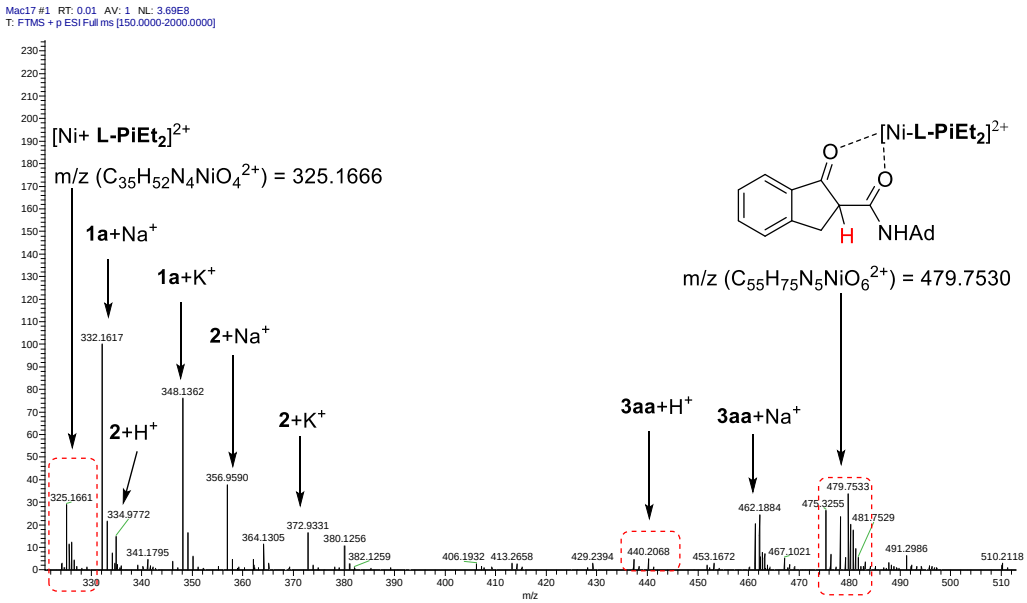


Figure S3. HRMS experiment: The mixture of **L-PiEt$_2$** and **2** (1:1)

When the mixture of β-ketoamide **1a**, the catalyst and **2** prepared in situ from **L-PiEt$_2$**, Ni(OTf)$_2$, **1a** and **2** (1:1:2:2) in EtOAc was carried out by HRMS experiment, intermediate [Ni^{2+} + **L-PiEt$_2$**]$^{2+}$ and intermediate **TS-1** [Ni^{2+} + **L-PiEt$_2$** + **1a**]$^{2+}$ were detected (Figure S4). In the mixture, we also observed the formation of carbene dimer A and homocoupling by-product B, as well as α-hydroxylated by-product C. HRMS (*m*/*z*): [by-product **A** + H$^+$]$^+$ calculated. for $C_{10}H_{13}O_8^+$, 261.0605, found 261.0605. HRMS (*m*/*z*): [by-product **B** + H$^+$]$^+$ calculated. for $C_{10}H_{15}O_8^+$, 263.0761, found 263.0768. HRMS (*m*/*z*): [by-product **C** + H$^+$]$^+$ calculated. for $C_{20}H_{24}NO_3^+$, 326.1751, found 326.1750.



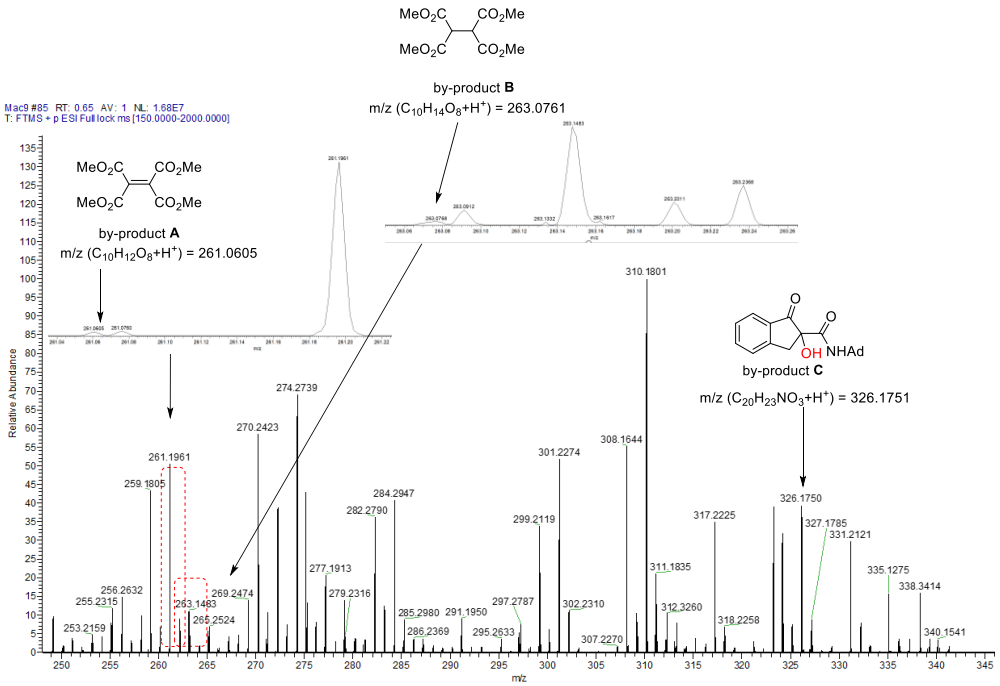


Figure S4. HRMS experiment: The mixture of **L-PiEt$_2$**, Ni(OTf)$_2$, **1a** and **2** (1:1:2:2)

The •CH(CO$_2$Me)$_2$ was captured by TEMPO, the ion signal at *m/z* 288.1805 appears to correspond to the [TEMPO-**A** +H$^+$] (calculated. *m/z* 288.1805) (Figure S5). At the same time, the ion signal at *m/z* 465.3111 appears to correspond to the [TEMPO-**B** +H$^+$] (calculated. *m/z* 465.3112), which was provided by TEMPO trapping the radical intermediate **TS-B**. We suspect that the free carbene promotes homolytic cleavage of the C-H of β-ketoamide **1a** to form the radical intermediate **TS-B** or the free carbene intermediate may also trigger weaker C-H bond cleavage *via* a proton-coupled electron transfer (PCET) process to access the radical intermediate **TS-B**.

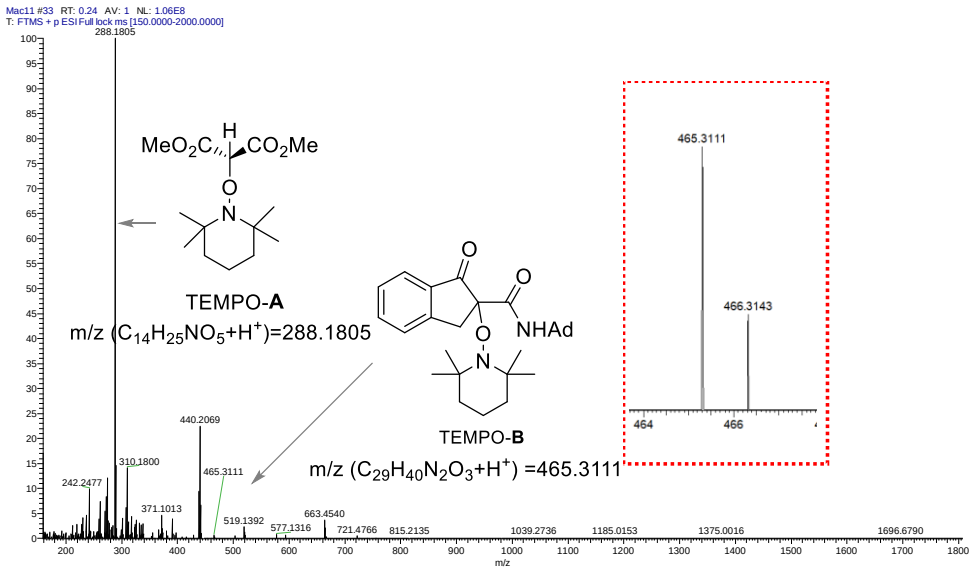


Figure S5. HRMS experiment: The mixture of **L-PiEt$_2$**, Ni(OTf)$_2$, **1a**, **2** and TEMPO (1:1:2:2:2)

6. The X-ray data for 3xa, TEMPO-B' and L-PiEt$_2$-Ni(ClO$_4$)$_2$

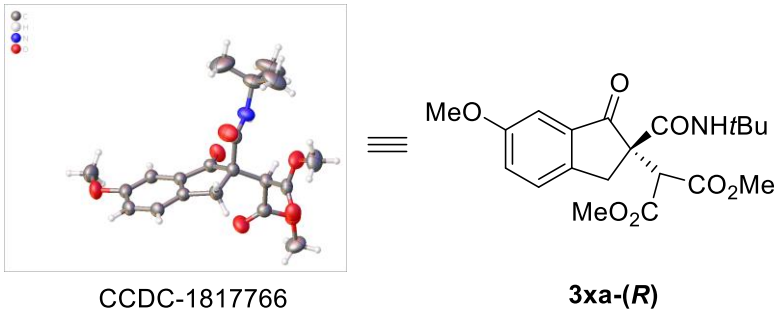


Figure S6. X-ray crystal structure of **3xa**, CCDC 1817766.

Crystals of product **3xa** (CCDC-1817766) suitable for the X-ray crystal structure analysis were obtained from a solution of obtained white solid in DCM, EtOAc and petroleum ether (1/1/4).

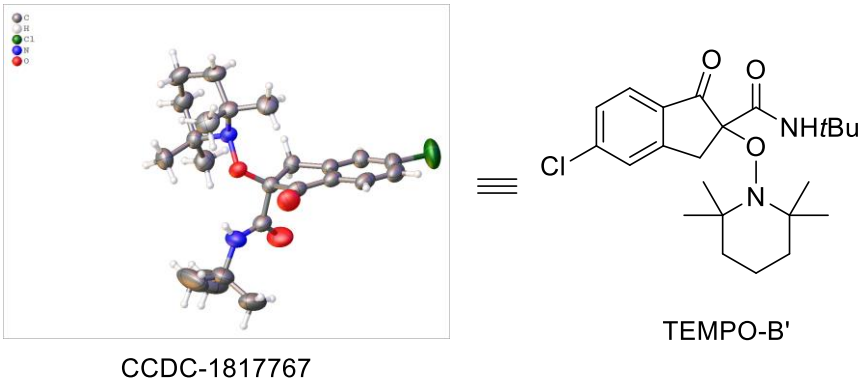


Figure S7. X-ray crystal structure of TEMPO-B', CCDC 1817767.

Crystals of product TEMPO-B' (CCDC-1817767) suitable for the X-ray crystal structure analysis were obtained from a solution of obtained white solid in DCM, MeOH and petroleum ether (1/1/4) in tube. Note, this single srystal was cultured from the mixture of TEMPO-A and TEMPO-B' because TEMPO-A and TEMPO-B' were hard to separate and purify in reaction system.

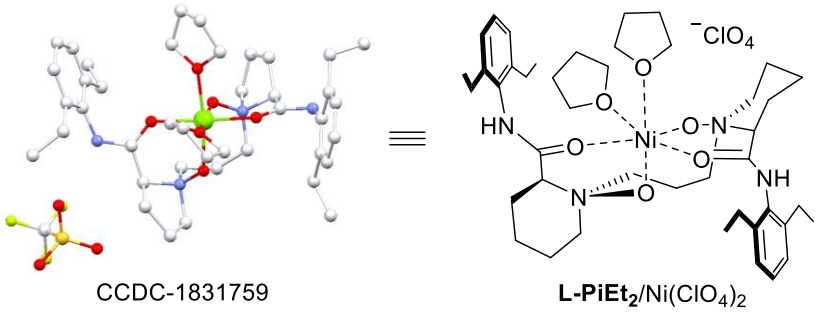


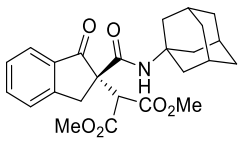
Figure S8. X-ray crystal structure of the **L-PiEt$_2$**/Ni(ClO$_4$)$_2$, CCDC 1831759.

Crystals of **L-PiEt$_2$**/Ni(ClO$_4$)$_2$ complex (CCDC-1831759) suitable for the X-ray crystal structure analysis were obtained from a solution of green solid in THF and n-hexane (1/2) in NMR tube.

CCDC-1817766 (**3xa**), CCDC-1817767 (TEMPO-B') and CCDC-1831759 [**L-PiEt$_2$**/Ni(ClO$_4$)$_2$] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk./data_request/cif.

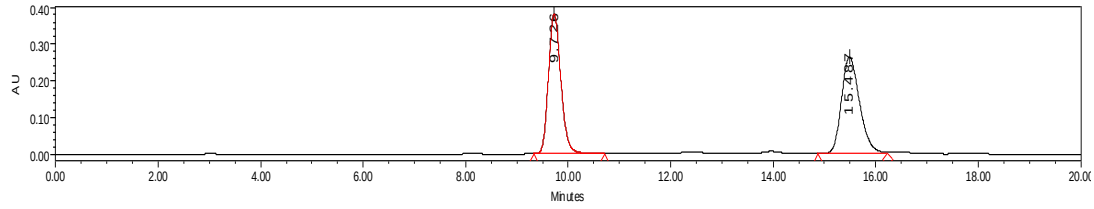
7. Spectral characterization data for the products

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-1-oxo-2,3-dihydro-1*H*-inden-2-yl] malonate (3aa):



3aa

Prepared according to the general procedure (12 h). The compound **3aa** was obtained as a white solid in 89% yield, 95% ee. Mp: 119-121 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.91 min, t_r (minor) = 15.95 min. $[\alpha]^{25.3}_D$ = −23.9 (*c* = 0.94, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 6.24 (s, 1H), 4.38 (s, 1H), 4.02 (d, *J* = 17.8 Hz, 1H), 3.77 (s, 3H), 3.58 (s, 3H), 3.44 (d, *J* = 17.8 Hz, 1H), 2.02 (s, 3H), 1.89 (s, 6H), 1.62 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.28, 167.51, 167.36, 164.27, 154.45, 135.62, 134.89, 127.42, 126.42, 124.40, 61.48, 57.23, 57.22, 52.76, 52.75, 52.72, 52.70, 52.30, 40.91, 36.15, 33.46, 29.29. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{29}NO_6H^+$ ([M]+H$^+$) = 440.2068, found 440.2070.



	Retention Time	Area	% Area
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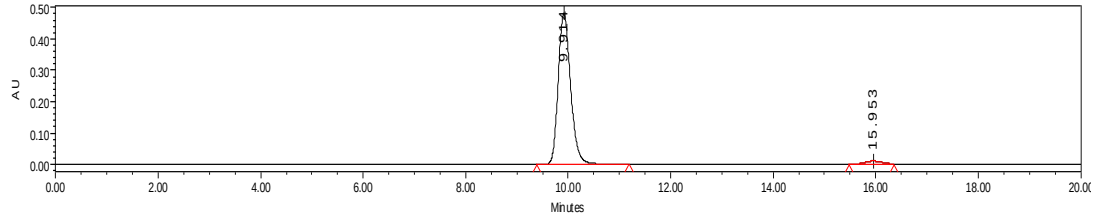
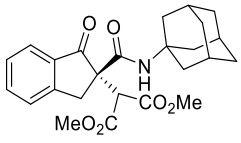
2	15.487	6519831	50.31



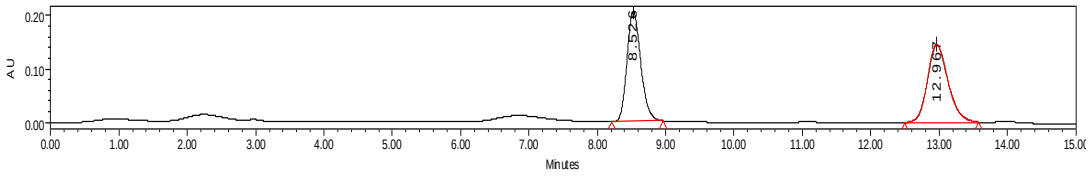
	Retention Time	Area	% Area
1	9.914	8045245	97.32
2	15.953	221408	2.68

Gram-scale synthesis of 3aa:



3aa

Prepared according to the general procedure (36 h). The compound **3aa** was obtained as a white amorphous solid in 1.159 g, 88% yield, 93% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.52 min, t_r (minor) = 13.00 min. After recrystallization 1.001 g, 76% yield, 99.5:0.5 er. **^{1}H NMR** (400 MHz, CDCl3) δ 7.75 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 6.24 (s, 1H), 4.38 (s, 1H), 4.02 (d, J = 17.8 Hz, 1H), 3.77 (s, 3H), 3.58 (s, 3H), 3.44 (d, J = 17.8 Hz, 1H), 2.02 (s, 3H), 1.89 (s, 6H), 1.62 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.28, 167.51, 167.36, 164.27, 154.45, 135.62, 134.89, 127.42, 126.42, 124.40, 61.48, 57.23, 57.22, 52.76, 52.75, 52.72, 52.70, 52.30, 40.91, 36.15, 33.46, 29.29. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{29}NO_6H^+$ ([M]+H$^+$) = 440.2068, found 440.2070.



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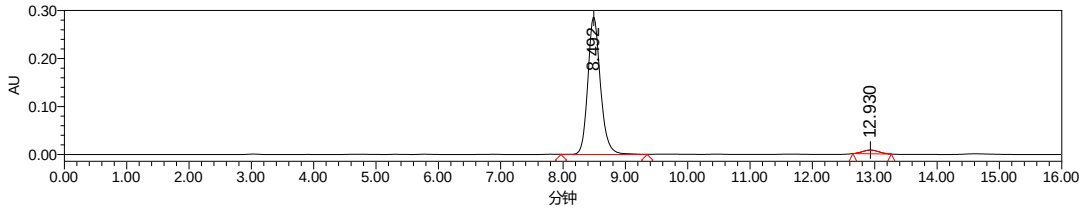

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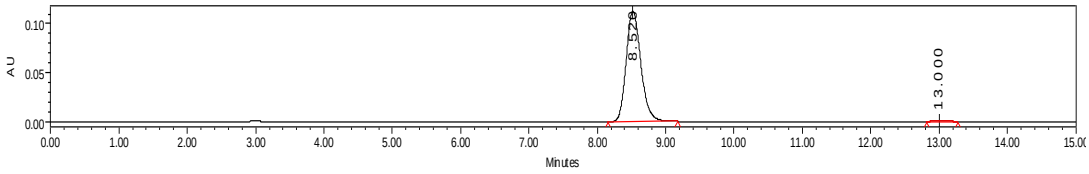
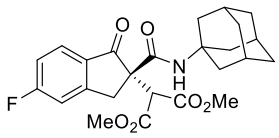
2	12.930	143137	3.44



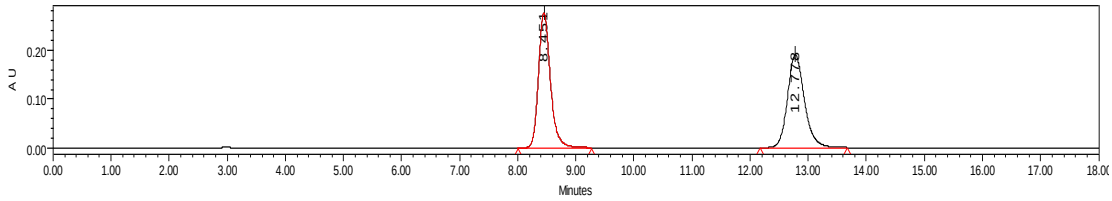
	Retention Time	Area	% Area
1	8.520	1672841	99.68
2	13.000	5406	0.32

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-5-fluoro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ba):

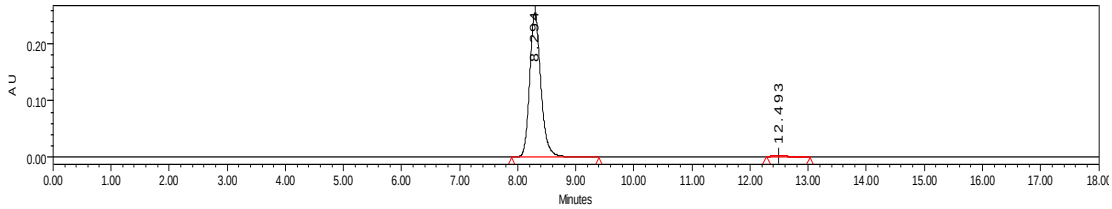


3ba

Prepared according to the general procedure (12 h). The compound **3ba** was obtained as a white amorphous solid in 77% yield, 97% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.29 min, t_r (minor) = 12.49 min. $[\alpha]^{26.3}_D$ = −20.1 (*c* = 0.54, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.4, 5.2 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.07 (td, *J* = 8.8, 1.6 Hz, 1H), 6.28 (s, 1H), 4.35 (s, 1H), 4.03 (d, *J* = 18.0 Hz, 1H), 3.43 (d, *J* = 18.0 Hz, 1H), 2.04 (s, 3H), 1.90 (d, *J* = 2.0 Hz, 6H), 1.64 (s, 7H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 202.6, 167.8 (*J* = 257 Hz, 1C), 167.4, 164.0, 157.6 (*J* = 11 Hz, 1C), 131.3 (*J* = 2 Hz, 1C), 126.8 (*J* = 10 Hz, 1C), 115.9 (*J* = 23 Hz, 1C), 113.3 (*J* = 22 Hz, 1C), 61.8, 57.27, 57.26, 52.89, 52.87, 52.83, 52.81, 52.4, 41.0, 36.2, 33.3, 29.3. **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −100.77. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}FNO_6H^+$ ([M]+H^+) = 458.1973, found 458.1973.

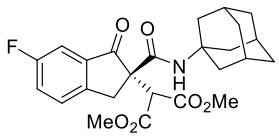


	Retention Time	Area	% Area
1	8.451	3914220	50.42
2	12.778	3848760	49.58



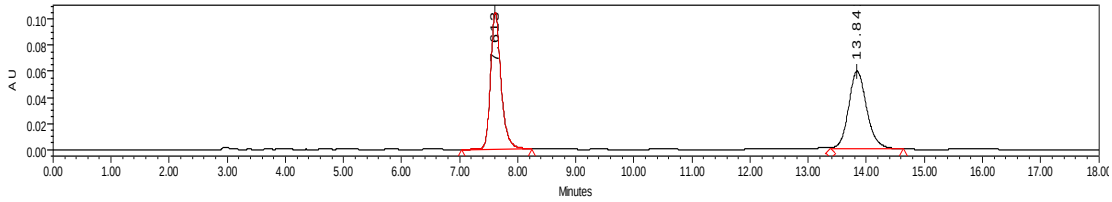
	Retention Time	Area	% Area
1	8.294	3443139	98.51
2	12.493	52212	1.49

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-6-fluoro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ca):

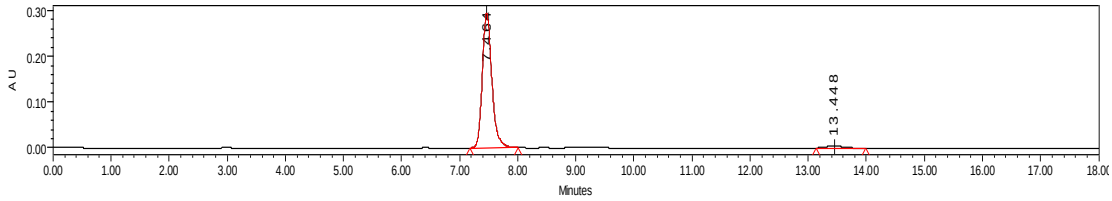


3ca

Prepared according to the general procedure (12 h). The title compound **3ca** was obtained as a white amorphous solid in 78% yield, 94% ee. Mp: 105-108 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.46 min, t_r (minor) = 13.45 min. $[\alpha]^{26.3}_D$ = −19.6 (*c* = 0.65, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.39 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.33 (td, *J* = 8.4, 2.4 Hz, 1H), 6.20 (s, 1H), 4.37 (s, 1H), 3.99 (d, *J* = 17.6 Hz, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 3.39 (d, *J* = 17.6 Hz, 1H), 2.04 (s, 3H), 1.90 (d, *J* = 2.4 Hz, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.6, 167.4, 167.3, 163.8, 162.2 (*J* = 246 Hz, 1C), 150.0 (*J* = 2 Hz, 1C), 136.5 (*J* = 7 Hz, 1C), 127.9 (*J* = 8 Hz, 1C), 123.3 (*J* = 24 Hz, 1C), 110.2 (*J* = 22 Hz, 1C), 62.5, 57.36, 57.36, 52.91, 52.90, 52.82, 52.80, 52.5, 40.9, 36.2, 33.0, 29.3. **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −114.30. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}FNO_6H^+$ ([M]+H^+) = 458.1973, found 458.1973.

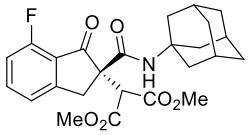


	Retention Time	Area	% Area
1	7.613	1306153	50.10
2	13.841	1301010	49.90



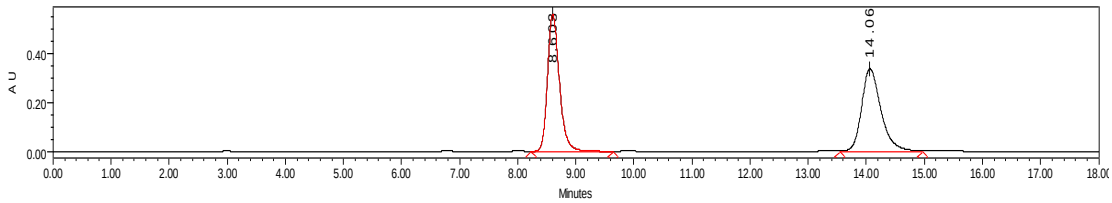
	Retention Time	Area	% Area
1	7.464	3374415	97.19
2	13.448	97417	2.81

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-7-fluoro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3da):

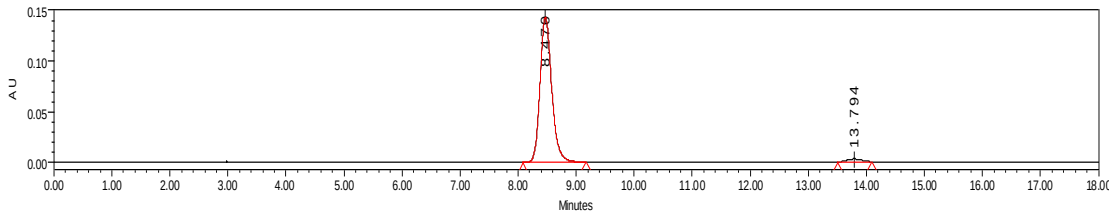


3da

Prepared according to the general procedure (12 h). The title compound **3da** was obtained as a white amorphous solid in 77% yield, 95% ee. Mp: 135-138 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.47 min, t_r (minor) = 13.79 min. $[\alpha]^{26.4}_D$ = −11.5 (*c* = 0.56, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (td, *J* = 8.0, 5.2 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 6.98 (t, *J* = 8.8 Hz, 1H), 6.30 (s, 1H), 4.35 (s, 1H), 4.05 (d, *J* = 18.0 Hz, 1H), 3.77 (s, 3H), 3.62 (s, 3H), 3.45 (d, *J* = 18.0 Hz, 1H), 2.04 (s, 3H), 1.92 (s, 6H), 1.64 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 200.8 (*J* = 2 Hz, 1C), 167.3, 167.3, 163.7, 159.2 (*J* = 263 Hz, 1C), 156.5 (*J* = 1 Hz, 1C), 137.6 (*J* = 9 Hz, 1C), 122.9 (*J* = 13 Hz, 1C), 122.3 (*J* = 4 Hz, 1C), 114.2 (*J* = 19 Hz, 1C), 61.9, 57.32, 57.31, 52.92, 52.90, 52.82, 52.80, 52.5, 40.9, 36.2, 33.2, 29.3. **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −113.50. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}FNO_6H^+$ ([M]+H^+) = 458.1973, found 458.1974.

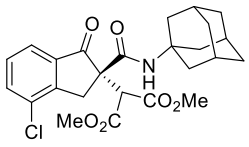


	Retention Time	Area	% Area
1	8.603	7915120	50.38
2	14.061	7795335	49.62



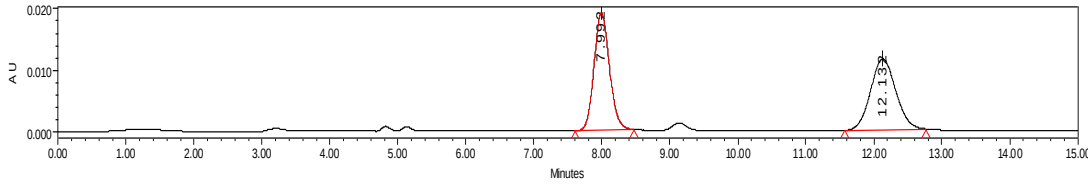
	Retention Time	Area	% Area
1	8.470	2002427	97.50
2	13.794	51404	2.50

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-4-chloro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ea):

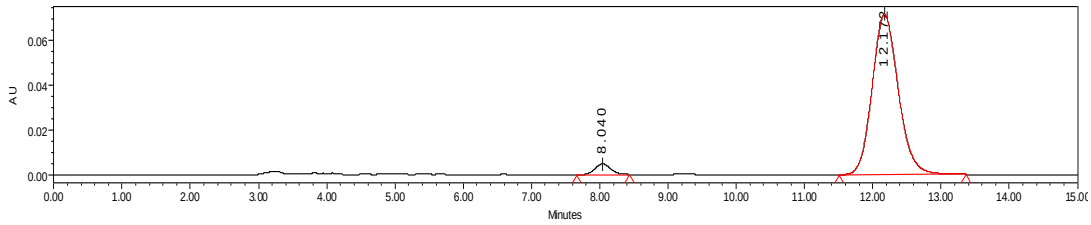


3ea

Prepared according to the general procedure (12 h). The title compound **3ea** was obtained as yellow oil in 91% yield, 92% ee. HPLC (Chiralcel **IC**, *n*-hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 12.17 min, t_r (minor) = 8.04 min. $[\alpha]^{26.1}_D = -46.5$ (*c* = 0.34, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.22 (s, 1H), 4.39 (s, 1H), 4.08 (d, *J* = 18.4 Hz, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.36 (d, *J* = 18.4 Hz, 1H), 2.04 (s, 3H), 1.91 (d, *J* = 2.0 Hz, 6H), 1.64 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.7, 167.4, 167.2, 163.7, 152.0, 136.8, 135.4, 132.7, 129.0, 122.6, 61.6, 57.54, 57.53, 52.97, 52.96, 52.90, 52.88, 52.5, 41.0, 36.2, 32.7, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}ClNO_6H^+$ ([M]+H$^+$) = 474.1678, 476.1648, found 474.1678, 476.1652.

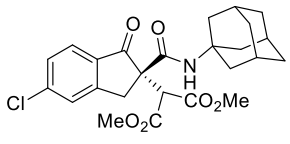


	Retention Time	Area	% Area
1	7.992	300946	50.30
2	12.132	297308	49.70



	Retention Time	Area	% Area
1	8.040	75923	3.82
2	12.172	1912678	96.18

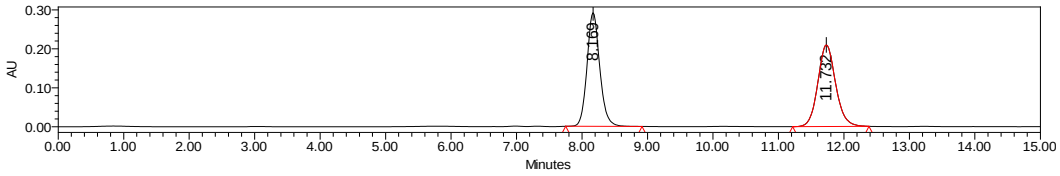
Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-5-chloro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3fa):



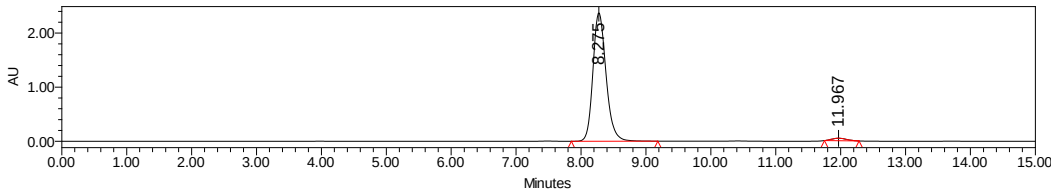
3fa

Prepared according to the general procedure (12 h). The title compound **3fa** was obtained as a white solid in 76% yield, 96% ee. Mp: 164-168 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.27 min, t_r (minor) = 11.96 min. $[\alpha]^{19.6}_D = -53.6$ (*c* = 0.50, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 1H), 7.48 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 6.24 (s, 1H), 4.35 (s, 1H), 4.01 (d, *J* = 18.0 Hz, 1H), 3.77 (s, 3H), 3.60 (s, 3H), 3.41 (d, *J* = 18.0 Hz, 1H), 2.03 (s, 3H), 1.90 (s, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.0, 167.3, 167.3, 163.8, 155.9, 142.4, 133.4, 128.3, 126.7, 125.5, 61.7, 57.30,

57.29, 52.91, 52.89, 52.82, 52.81, 52.4, 40.9, 36.2, 33.1, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}ClNO_6H^+$ ([M]+H$^+$) = 474.1678, 476.1648, found 474.1680, 476.1653.

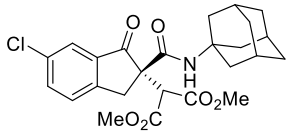


	Retention Time	Area	% Area
1	8.169	3945045	50.03
2	11.732	3939563	49.97



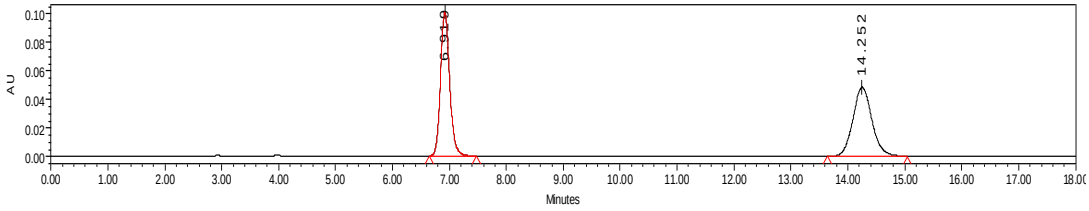
	Retention Time	Area	% Area
1	8.275	33205603	97.84
2	11.967	733882	2.16

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-6-chloro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ga):

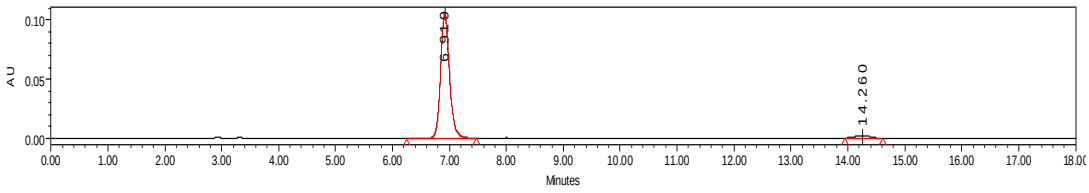


3ga

Prepared according to the general procedure (12 h). The title compound **3ga** was obtained as yellow oil in 72% yield, 93% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.91 min, t_r (minor) = 14.26 min. $[\alpha]^{25.5}_D = -10.0$ (*c* = 0.49, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 6.21 (s, 1H), 4.36 (s, 1H), 3.99 (d, *J* = 18.0 Hz, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 3.39 (d, *J* = 18.0 Hz, 1H), 2.04 (s, 3H), 1.90 (d, *J* = 2.0 Hz, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.3, 167.4, 167.3, 163.7, 152.6, 136.4, 135.6, 133.8, 127.7, 124.2, 62.1, 57.4, 52.93, 52.92, 52.83, 52.81, 52.5, 40.9, 36.2, 33.1, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}ClNO_6H^+$ ([M]+H$^+$) = 474.1678, 476.1648, found 474.1672, 476.1646.

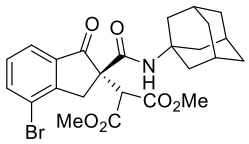


	Retention Time	Area	% Area
1	6.919	1128738	49.87
2	14.252	1134715	50.13



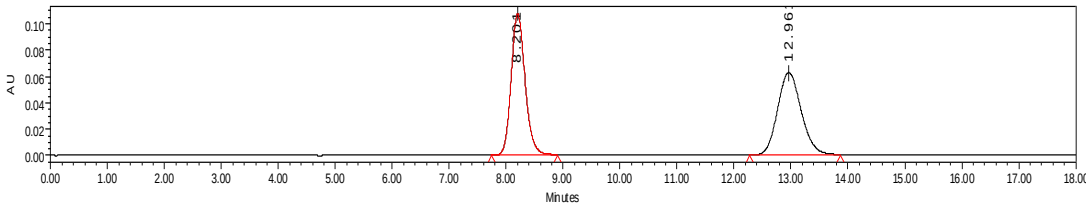
	Retention Time	Area	% Area
1	6.919	1162880	96.59
2	14.260	41067	3.41

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-4-bromo-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ha):

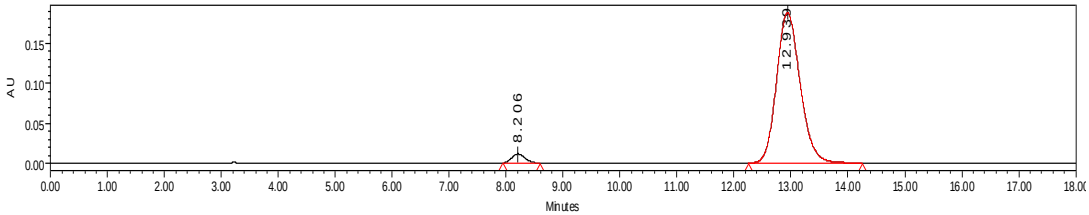


3ha

Prepared according to the general procedure (12 h). The title compound **3ha** was obtained as yellow oil in 82% yield, 94% ee. HPLC (Chiralcel **IC**, *n*-hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 12.94 min, t_r (minor) = 8.20 min. $[\alpha]^{26.1}_D$ = −55.6 (*c* = 0.75, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.24 (m, 2H), 6.21 (s, 1H), 4.39 (s, 1H), 4.02 (d, *J* = 18.4 Hz, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.32 (d, *J* = 18.4 Hz, 1H), 2.04 (s, 3H), 1.90 (d, *J* = 2.0 Hz, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.8, 167.3, 167.2, 163.6, 154.1, 138.4, 136.8, 129.1, 123.2, 121.9, 61.6, 57.52, 57.51, 52.96, 52.94, 52.88, 52.86, 52.5, 40.9, 36.2, 34.7, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}BrNO_6Na^+$ ([M]+Na^+) = 540.0992, 542.0972, found 540.0998, 542.0980.

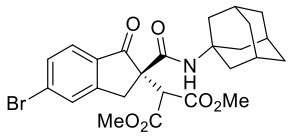


	Retention Time	Area	% Area
1	8.201	1825689	50.20
2	12.961	1810958	49.80



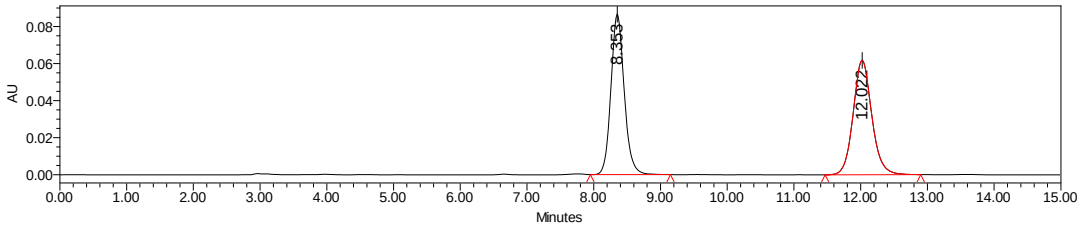
	Retention Time	Area	% Area
1	8.206	183596	3.27
2	12.939	5423366	96.73

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-5-bromo-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ia):

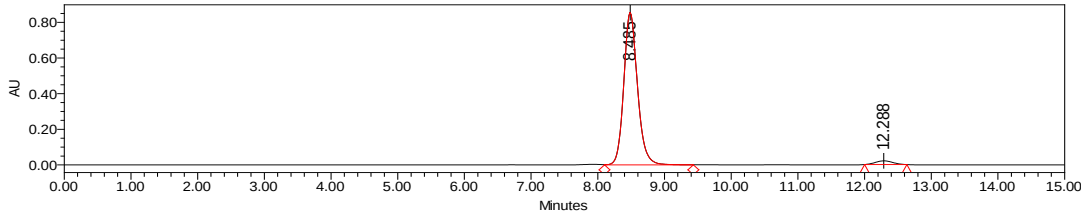


3ia

Prepared according to the general procedure (12 h). The title compound **3ia** was obtained as a white solid in 81% yield, 94% ee. Mp: 167-171 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.48 min, t_r (minor) = 12.28 min. $[\alpha]^{19.6}_D = -55.5$ (*c* = 0.51, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.7 (s, 1H), 7.7 (d, *J* = 8.4 Hz, 1H), 7.4 (d, *J* = 8.0 Hz, 1H), 6.2 (s, 1H), 4.4 (d, *J* = 2.0 Hz, 1H), 4.0 (d, *J* = 18.0 Hz, 1H), 3.8 (d, *J* = 2.0 Hz, 3H), 3.6 (d, *J* = 2.0 Hz, 3H), 3.4 (d, *J* = 18.0 Hz, 1H), 2.0 (s, 3H), 1.9 (s, 6H), 1.6 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.3, 167.4, 167.3, 163.8, 156.0, 133.8, 131.4, 131.14, 129.8, 125.5, 61.6, 57.30, 57.29, 52.93, 52.92, 52.84, 52.82, 52.5, 40.9, 36.2, 33.1, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}BrNO_6Na^+$ ([M]+Na^+) = 540.0992, 542.0972, found 540.0995, 542.0976.

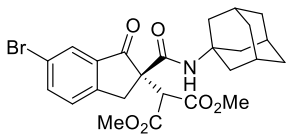


	Retention Time	Area	% Area
1	8.353	1197069	50.02
2	12.022	1196199	49.98



	Retention Time	Area	% Area
1	8.485	12213265	97.02
2	12.288	374582	2.98

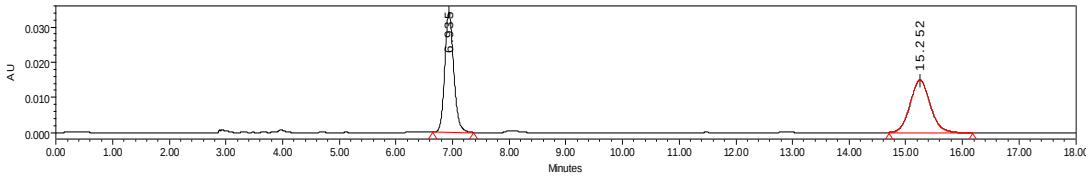
Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl)}6-bromo-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ja):



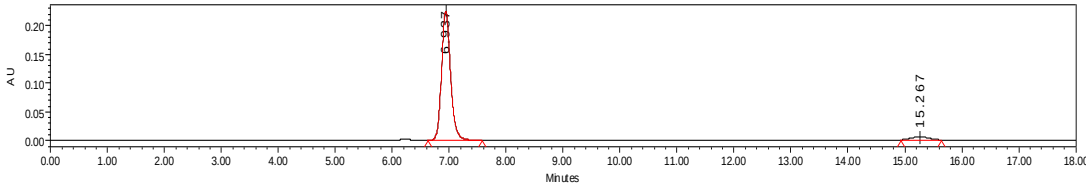
3ja

Prepared according to the general procedure (12 h). The title compound **3ja** was obtained as yellow oil in 77% yield, 92% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.93 min, t_r (minor) = 15.26 min. $[\alpha]^{24.8}_D = -7.3$ (*c* = 0.53, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 6.22 (s, 1H), 4.36 (d, *J* = 2.0 Hz, 1H), 3.98 (d, *J* = 18.0 Hz, 1H), 3.77 (d, *J* = 2.0 Hz, 3H), 3.61 (d, *J* = 2.0 Hz, 3H), 3.37 (d, *J* = 18.0 Hz, 1H), 2.04 (s, 3H), 1.90 (s, 6H), 1.64 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.2, 167.4, 167.3, 163.7, 153.1, 138.3, 136.73, 128.0, 127.3, 121.6,

62.0, 57.4, 52.94, 52.94, 52.84, 52.82, 52.5, 40.9, 36.2, 33.2, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}BrNO_6H^+$ ([M]+H^+) = 518.1173, 520.1153, found 518.1169, 520.1149.

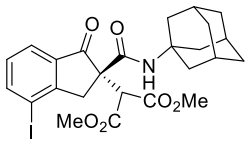


	Retention Time	Area	% Area
1	6.935	375887	50.47
2	15.252	368931	49.53



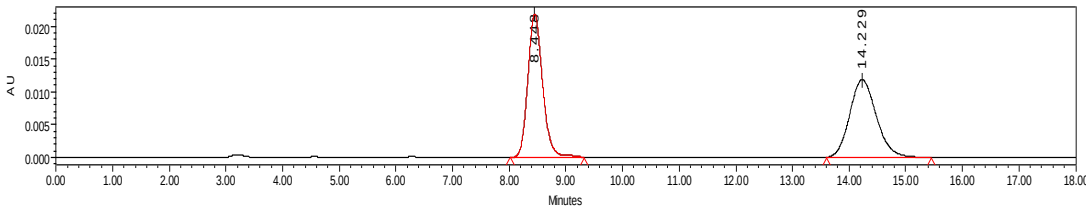
	Retention Time	Area	% Area
1	6.937	2477683	95.80
2	15.267	108637	4.20

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-4-iodo-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ka):

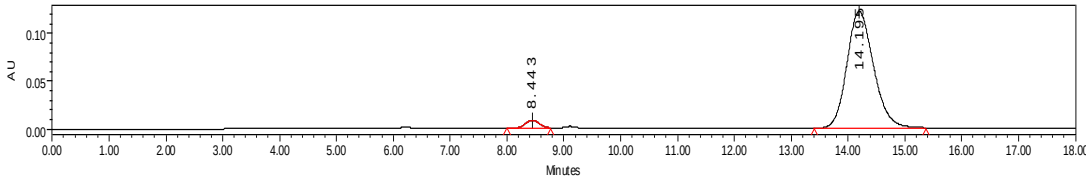


3ka

Prepared according to the general procedure (12 h). The title compound **3ka** was obtained as a white solid in 82% yield, 93% ee. Mp: 135-138 °C. HPLC (Chiralcel **IC**, *n*-hexane/*i*-PrOH = 70/30, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 14.20 min, t_r (minor) = 8.44 min. $[\alpha]^{26.1}_D$ = −67.6 (*c* = 0.75, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.21 (s, 1H), 4.39 (s, 1H), 3.90 (d, *J* = 18.0 Hz, 1H), 3.79 (s, 3H), 3.61 (s, 3H), 3.24 (d, *J* = 18.0 Hz, 1H), 2.03 (s, 3H), 1.90 (s, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.2, 167.3, 167.2, 163.6, 158.1, 144.7, 136.3, 129.2, 124.0, 95.9, 61.9, 57.5, 52.96, 52.94, 52.88, 52.86, 52.5, 41.0, 38.4, 36.2, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}INO_6Na^+$ ([M]+Na^+) = 588.0854, 590.0921, found 588.0853, 590.0912.

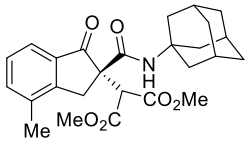


	Retention Time	Area	% Area
1	8.448	395782	50.50
2	14.229	387938	49.50



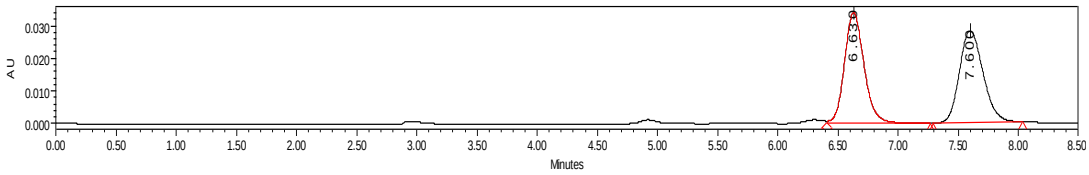
	Retention Time	Area	% Area
1	8.443	141046	3.42
2	14.195	3983793	96.58

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-4-methyl-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3la):

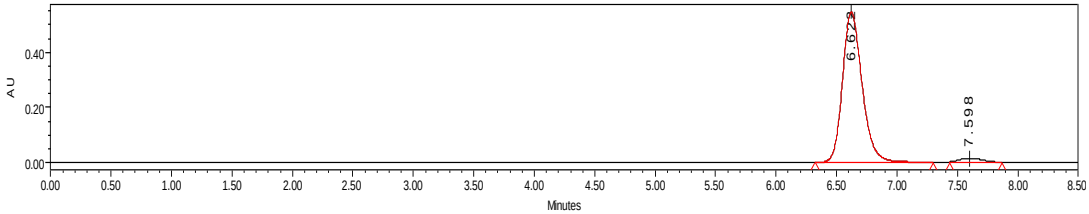


3la

Prepared according to the general procedure (12 h). The title compound **3la** was obtained as a white solid in 71% yield, 94% ee. Mp: 120-124 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.62 min, t_r (minor) = 7.60 min. $[\alpha]^{26.2}_D$ = −37.2 (*c* = 0.48, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.31 (s, 1H), 4.39 (s, 1H), 3.95 (d, *J* = 17.8 Hz, 1H), 3.78 (s, 3H), 3.59 (s, 3H), 3.28 (d, *J* = 17.8 Hz, 1H), 2.37 (s, 3H), 2.03 (s, 3H), 1.90 (d, *J* = 1.6 Hz, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.7, 167.6, 167.4, 164.4, 153.5, 136.2, 135.8, 134.7, 127.6, 121.8, 61.5, 57.31, 57.30, 52.80, 52.79, 52.76, 52.74, 52.3, 41.0, 36.2, 32.3, 29.3, 17.9. **HRMS** (ESI-FTMS) calculated for $C_{26}H_{31}NO_6H^+$ ([M]+H^+) = 454.2224, found 454.2224.

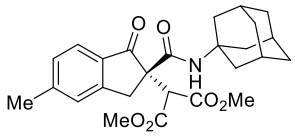


	Retention Time	Area	% Area
1	6.630	386456	50.21
2	7.600	383269	49.79



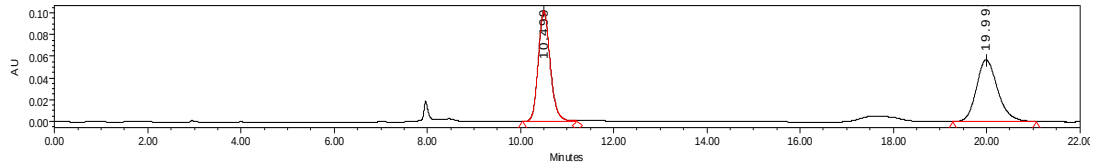
	Retention Time	Area	% Area
1	6.622	6138200	97.24
2	7.598	174490	2.76

Dimethyl 2-((*R*)-2-(((3*S*,5*S*,7*S*)-adamantan-1-yl)carbamoyl)-5-methyl-1-oxo-2,3-dihydro-1*H*-inden-2-yl)malonate (3ma):

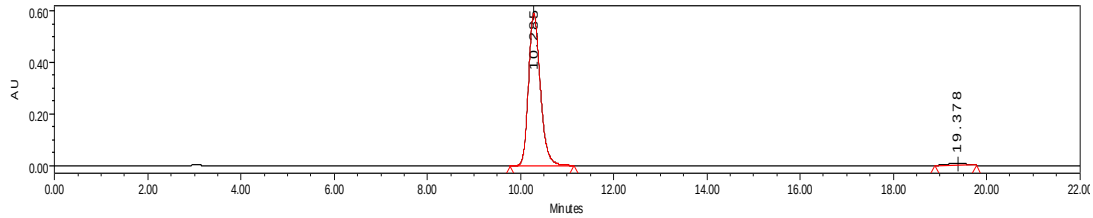


3ma

Prepared according to the general procedure (12 h). The title compound **3ma** was obtained as a white solid in 66% yield, 96% ee. Mp: 146-149 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 10.28 min, t_r (minor) = 19.38 min. $[\alpha]^{25.4}_D$ = −45.4 (*c* = 0.46, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.6 Hz, 1H), 7.29 (s, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.26 (s, 1H), 4.37 (d, *J* = 1.6 Hz, 1H), 3.96 (d, *J* = 18.0 Hz, 1H), 3.77 (d, *J* = 2.0 Hz, 3H), 3.59 (d, *J* = 2.0 Hz, 3H), 3.40 (d, *J* = 18.0 Hz, 1H), 2.43 (s, 3H), 2.03 (s, 3H), 1.90 (s, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.6, 167.6, 167.4, 164.6, 154.9, 147.2, 132.6, 128.78, 126.83, 124.3, 61.6, 57.1, 52.77, 52.75, 52.73, 52.70, 52.3, 40.9, 36.2, 33.3, 29.3, 22.2. **HRMS** (ESI-FTMS) calculated for $C_{26}H_{31}NO_6H^+$ ([M]+H^+) = 454.2224, found 454.2219.

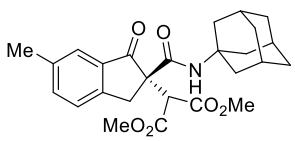


	Retention Time	Area	% Area
1	10.499	1827953	50.33
2	19.993	1804180	49.67



	Retention Time	Area	% Area
1	10.285	10357085	97.78
2	19.378	235580	2.22

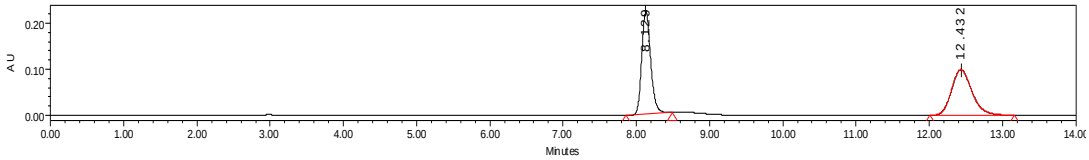
Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-6-methyl-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3na):



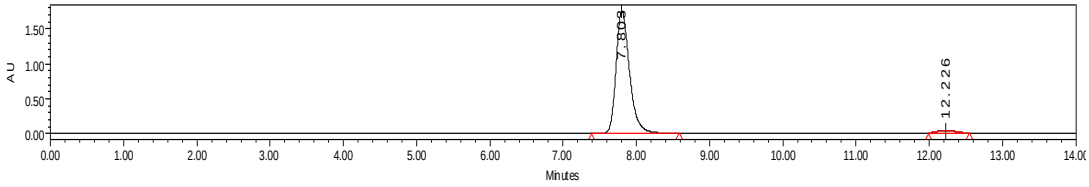
3na

Prepared according to the general procedure (12 h). The title compound **3na** was obtained as a white amorphous solid in 67% yield, 94% ee. Mp: 104-109 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.80 min, t_r (minor) = 12.22 min. $[\alpha]^{25.3}_D$ = −23.3 (*c* = 0.40, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.41 (dd, *J* = 23.6, 7.6 Hz, 2H), 6.22 (s, 1H), 4.38 (s, 1H), 3.95 (d, *J* = 18.0 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 3.38 (d, *J* = 17.6 Hz, 1H), 2.39 (s, 3H), 2.03 (s, 3H), 1.89 (s, 6H), 1.63 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.3, 167.6, 167.4, 164.5, 151.9, 137.4, 137.0, 135.1, 126.1,

124.4, 61.8, 57.2, 52.79, 52.78, 52.73, 52.71, 52.3, 41.0, 36.2, 33.2, 29.3, 21.1. **HRMS** (ESI-FTMS) calculated for $C_{26}H_{31}NO_6H^+$ ([M]+H^+) = 454.2224, found 454.2220.

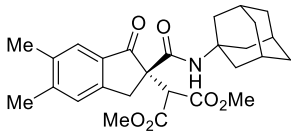


	Retention Time	Area	% Area
1	8.129	1896405	49.58
2	12.432	1928394	50.42



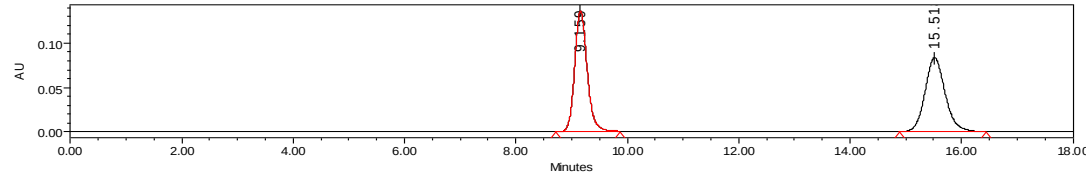
	Retention Time	Area	% Area
1	7.803	22467010	96.88
2	12.226	723159	3.12

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-5,6-dimethyl-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3oa):

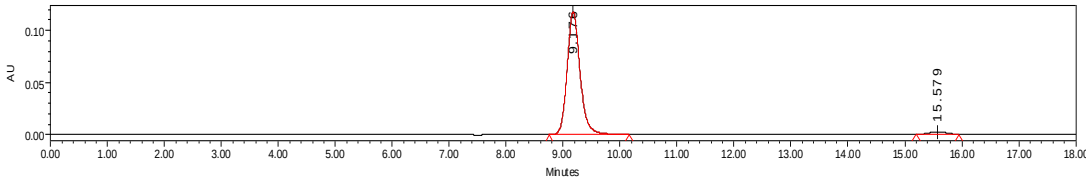


3oa

Prepared according to the general procedure (12 h). The title compound **3oa** was obtained as a white amorphous solid in 65% yield, 94% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.17 min, t_r (minor) = 15.57 min. $[\alpha]^{19.8}_D$ = −34.2 (*c* = 0.42, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.26 (s, 1H), 6.25 (s, 1H), 4.37 (s, 1H), 3.92 (d, *J* = 17.6 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 3.36 (d, *J* = 17.6 Hz, 1H), 2.33 (s, 3H), 2.29 (s, 3H), 2.02 (s, 3H), 1.89 (s, 6H), 1.62 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.8, 167.7, 167.5, 164.7, 152.7 146.3, 136.5, 133.1, 127.2, 124.8, 61.7, 57.1, 52.76, 52.74, 52.70, 52.69, 52.2, 41.0, 36.2, 33.1, 29.3, 20.8, 19.7. **HRMS** (ESI-FTMS) calculated for $C_{27}H_{33}NO_6H^+$ ([M]+H^+) = 468.2383, found 468.2383.

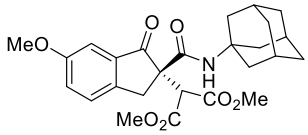


	Retention Time	Area	% Area
1	9.159	2105255	50.19
2	15.518	2089570	49.81



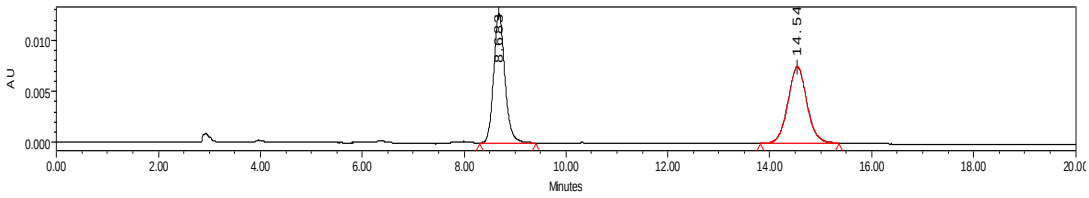
	Retention Time	Area	% Area
1	9.176	1863585	96.99
2	15.579	57830	3.01

Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-6-methoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3pa):

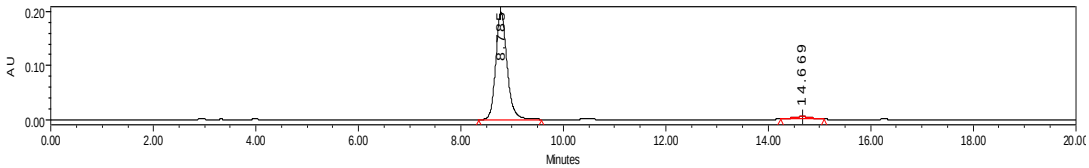


3pa

Prepared according to the general procedure (12 h). The title compound **3pa** was obtained as a white solid in 61% yield, 93% ee. Mp: 114-119 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 8.78 min, t_r (minor) = 14.66 min. $[\alpha]^{25.4}_D$ = −21.2 (*c* = 0.32, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.20 (s, 1H), 6.19 (s, 1H), 4.40 (s, 1H), 3.93 (d, *J* = 17.6 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.61 (s, 3H), 3.36 (d, *J* = 17.6 Hz, 1H), 2.04 (s, 3H), 1.90 (s, 6H), 1.64 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.1, 167.6, 167.5, 164.4, 159.5, 147.5, 136.0, 127.2, 125.1, 105.6, 62.3, 57.2, 55.54, 55.53, 52.83, 52.83, 52.82, 52.76, 52.7, 52.3, 41.0, 36.2, 33.0, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{26}H_{31}NO_7H^+$ ([M]+H^+) = 470.2173, found 470.2170.



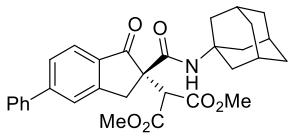
	Retention Time	Area	% Area
1	8.683	194384	49.68
2	14.540	196857	50.32



	Retention Time	Area	% Area
1	8.785	3029585	96.65
2	14.669	104932	3.35

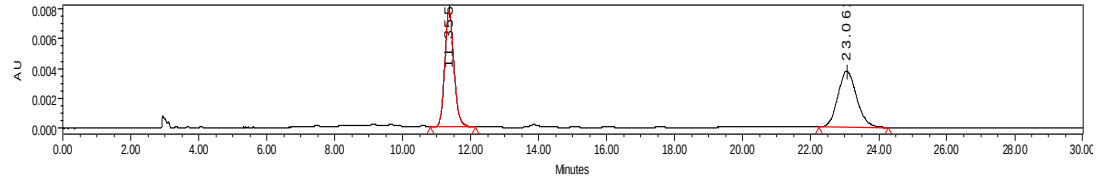
Dimethyl 2-[(*R*)-2-{[(3*S*,5*S*,7*S*)-adamantan-1-yl]carbamoyl}-1-oxo-5-phenyl-2,3-dihydro-

1*H*-inden-2-yl]malonate (3qa):

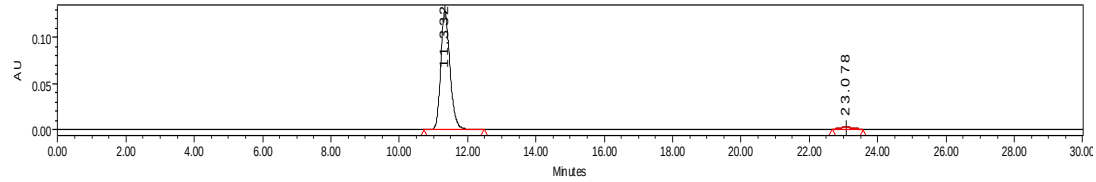


3qa

Prepared according to the general procedure (12 h). The title compound **3qa** was obtained as a white solid in 75% yield, 95% ee. Mp: 177-181 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 11.35 min, t_r (minor) = 23.07 min. $[\alpha]^{20.5}_D = -82.4$ (*c* = 0.50, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.68 (s, 1H), 7.61 (t, *J* = 7.6 Hz, 3H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 6.31 (s, 1H), 4.41 (s, 1H), 4.09 (d, *J* = 17.6 Hz, 1H), 3.79 (s, 3H), 3.62 (s, 3H), 3.50 (d, *J* = 18.0 Hz, 1H), 2.04 (s, 3H), 1.92 (s, 6H), 1.64 (d, *J* = 2.0 Hz, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.9, 167.6, 167.5, 164.4, 155.1, 148.8, 140.1, 133.8, 128.9, 128.4, 127.5, 127.0, 124.9, 124.8, 61.8, 57.32, 57.31, 52.86, 52.85, 52.79, 52.77, 52.4, 41.0, 36.2, 33.5, 29.3. **HRMS** (ESI-FTMS) calculated for $C_{31}H_{33}NO_6H^+$ ([M]+H^+) = 516.2381, found 516.2383.

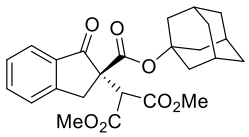


	Retention Time	Area	% Area
1	11.355	145148	50.12
2	23.061	144425	49.88



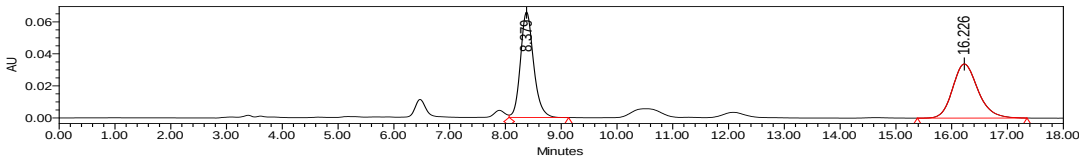
	Retention Time	Area	% Area
1	11.332	2435921	97.58
2	23.078	60365	2.42

Dimethyl 2-[(*R*)-2-({[(3*S*,5*S*,7*S*)-adamantan-1-yl]oxy}carbonyl)-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ra):

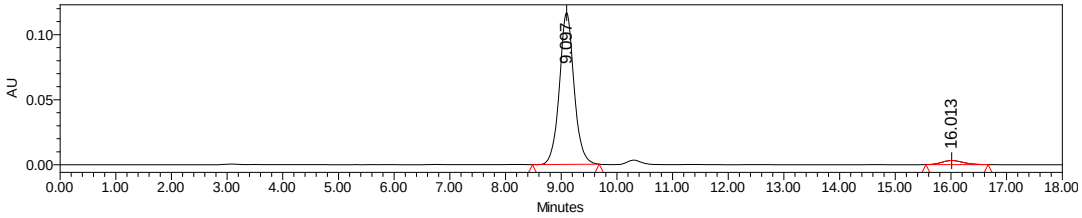


3ra

Prepared according to the general procedure (12 h). The title compound **3ra** was obtained as colorless oil in 50% yield, 92% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 9.09 min, t_r (minor) = 16.01 min. $[\alpha]^{20.3}_D = -79.6$ (*c* = 0.27, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 4.71 (s, 1H), 3.82 (d, *J* = 17.6 Hz, 1H), 3.82 (s, 3H), 3.51 (s, 3H), 3.41 (d, *J* = 17.6 Hz, 1H), 2.10 (s, 3H), 1.95 (d, *J* = 2.4 Hz, 6H), 1.58 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 199.7, 168.7, 167.8, 167.1, 154.2, 135.1, 134.9, 127.5, 126.1, 124.7, 83.1, 62.1, 54.8, 52.70, 52.68, 52.66, 40.7, 35.9, 30.8. **HRMS** (ESI-FTMS) calculated for $C_{25}H_{28}O_7H^+$ ([M]+H^+) = 441.1908, found 441.1905.

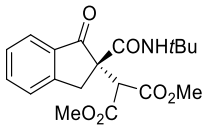


	Retention Time	Area	% Area
1	8.379	1077608	50.26
2	16.226	1066628	49.74



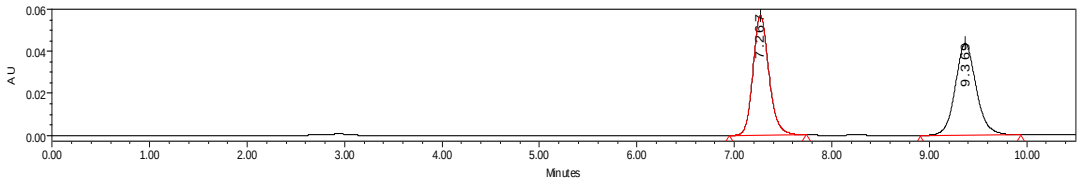
	Retention Time	Area	% Area
1	9.097	2130267	96.16
2	16.013	85157	3.84

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3sa):

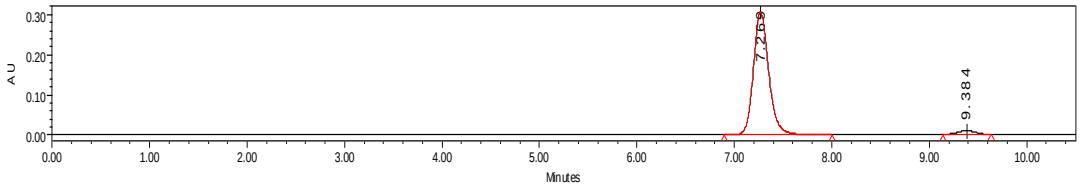


3sa

Prepared according to the general procedure (12 h). The title compound **3sa** was obtained as yellow oil in 70% yield, 93% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.26 min, t_r (minor) = 9.38 min. $[\alpha]^{26.1}_D = -48.6$ (*c* = 0.36, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 6.41 (s, 1H), 4.38 (s, 1H), 4.04 (d, *J* = 17.6 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 3.46 (d, *J* = 17.6 Hz, 1H), 1.27 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.5, 167.5, 167.4, 164.7, 154.5, 135.7, 134.9, 127.5, 126.5, 124.4, 61.4, 57.29, 57.28, 52.82, 52.81, 52.73, 52.71, 51.7, 33.4, 28.3. **HRMS** (ESI-FTMS) calculated for $C_{19}H_{23}NO_6H^+$ ([M]+H^+) = 362.1598, found 362.1595.

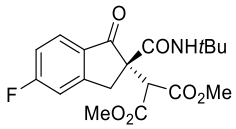


	Retention Time	Area	% Area
1	7.267	645841	49.73
2	9.369	652775	50.27



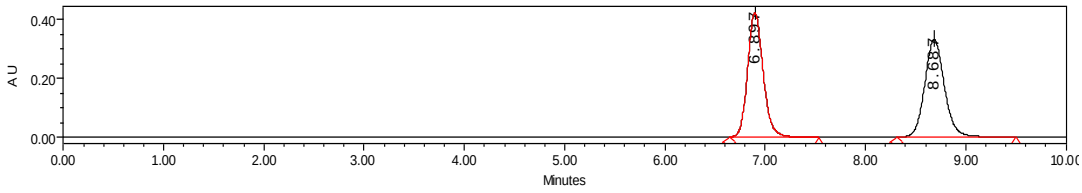
	Retention Time	Area	% Area
1	7.269	3331233	96.41
2	9.384	123996	3.59

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-5-fluoro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ta):

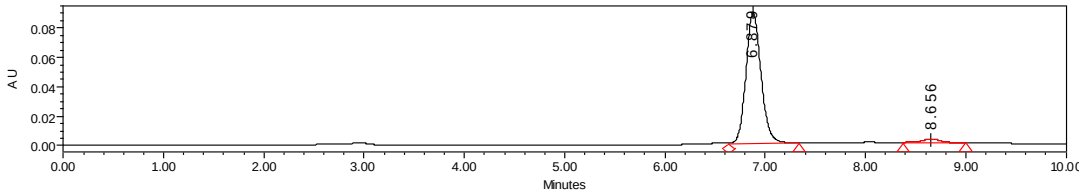


3ta

Prepared according to the general procedure (12 h). The title compound **3ta** was obtained as a white amorphous solid in 70% yield, 94% ee. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.87 min, t_r (minor) = 8.65 min. $[\alpha]^{19.4}_D$ = −17.6 (*c* = 0.32, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.4, 5.2 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 8.8 Hz, 1H), 6.44 (s, 1H), 4.34 (s, 1H), 4.04 (d, *J* = 18.0 Hz, 1H), 3.76 (s, 3H), 3.61 (s, 3H), 3.45 (d, *J* = 18.0 Hz, 1H), 1.27 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 202.7, 167.8 (*J* = 257 Hz, 1C), 167.3, 167.3, 166.5, 164.3, 157.6 (*J* = 10 Hz, 1C), 131.3 (*J* = 1 Hz, 1C), 126.8 (*J* = 11 Hz, 1C), 115.9 (*J* = 24 Hz, 1C),, 113.3 (*J* = 22 Hz, 1C), 61.6, 57.27, 57.25, 52.90, 52.88, 52.79, 52.77, 51.8, 33.2, 28.2. **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −100.68. **HRMS** (ESI-FTMS) calculated for $C_{19}H_{22}FNO_6H^+$ ([M]+H^+) = 380.1504, found 380.1504.

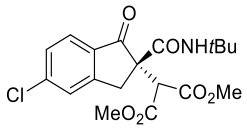


	Retention Time	Area	% Area
1	6.897	4559111	49.75
2	8.687	4604255	50.25



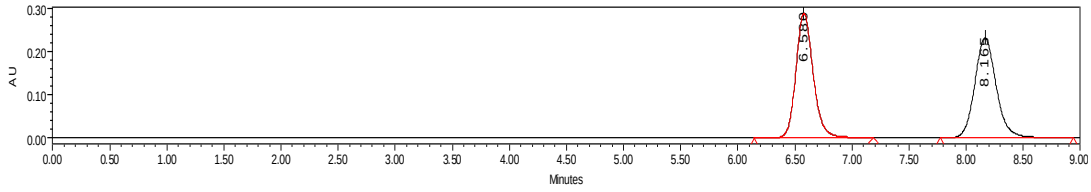
	Retention Time	Area	% Area
1	6.879	937521	96.98
2	8.656	29158	3.02

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-5-chloro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3ua):

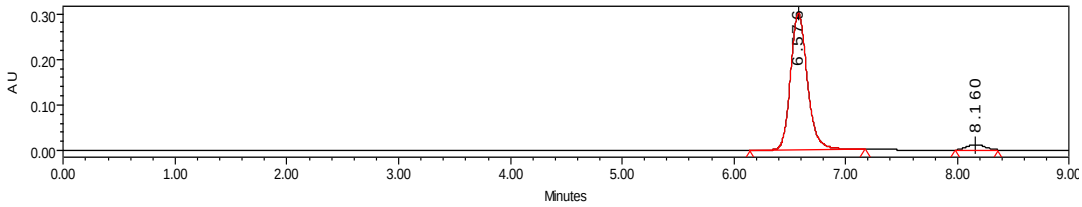


3ua

Prepared according to the general procedure (12 h). The title compound **3ua** was obtained as a white solid in 80% yield, 92% ee. Mp: 125-129 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.57 min, t_r (minor) = 8.16 min. $[\alpha]^{20.7}_D$ = −46.9 (*c* = 0.19, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 1H), 7.48 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 6.41 (s, 1H), 4.35 (s, 1H), 4.03 (d, *J* = 18.0 Hz, 1H), 3.76 (s, 3H), 3.61 (s, 3H), 3.43 (d, *J* = 18.0 Hz, 1H), 1.27 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.2, 167.32, 167.30, 164.2, 156.0, 142.4, 133.3, 128.3, 126.7, 125.5, 61.6, 57.3, 57.3, 52.92, 52.91, 52.79, 52.78, 51.8, 33.1, 28.2. **HRMS** (ESI-FTMS) calculated for $C_{19}H_{22}ClNO_6Na^+$ ([M]+Na^+) = 418.1028, 420.0998, found 418.1028, 420.0997.

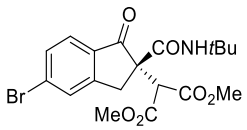


	Retention Time	Area	% Area
1	6.580	3041577	50.09
2	8.165	3030677	49.91



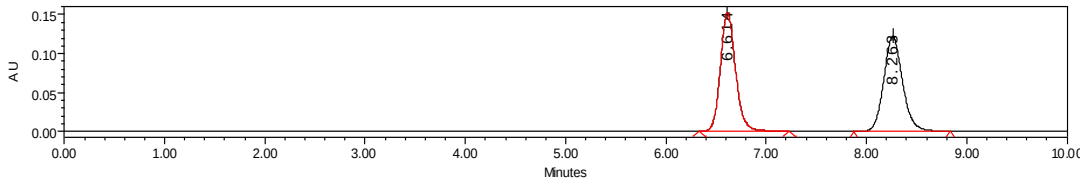
	Retention Time	Area	% Area
1	6.576	3148155	95.92
2	8.160	133856	4.08

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-5-bromo-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3va):

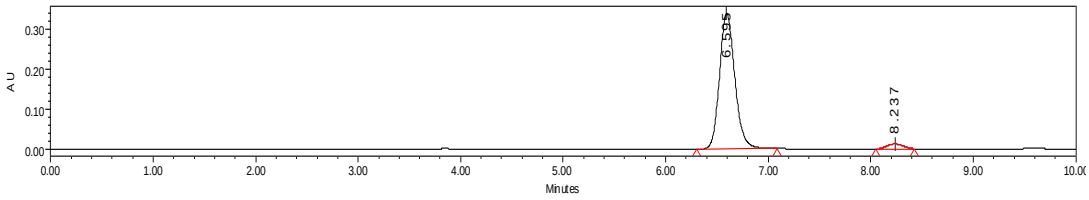


3va

Prepared according to the general procedure (12 h). The title compound **3va** was obtained as a white solid in 85% yield, 92% ee. Mp: 106-109 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 6.59 min, t_r (minor) = 8.23 min. $[\alpha]^{19.5}_D$ = −43.4 (*c* = 0.38, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 6.40 (s, 1H), 4.35 (d, *J* = 2.0 Hz, 1H), 4.03 (d, *J* = 18.0 Hz, 1H), 3.76 (d, *J* = 2.0 Hz, 3H), 3.61 (d, *J* = 2.0 Hz, 3H), 3.44 (d, *J* = 18.0 Hz, 1H), 1.27 (d, *J* = 2.0 Hz, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.4, 167.32, 167.29, 164.1, 156.1, 133.7, 131.4, 131.2, 129.8, 125.5, 61.5, 57.3, 52.93, 52.80, 52.78, 51.8, 33.0, 28.2. **HRMS** (ESI-FTMS) calculated for $C_{19}H_{22}BrNO_6Na^+$ ([M]+Na^+) = 462.0523, 464.0502, found 462.0526, 464.0509.

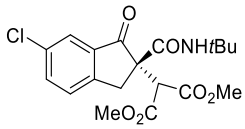


	Retention Time	Area	% Area
1	6.614	1618176	6.614
2	8.263	1595478	8.263



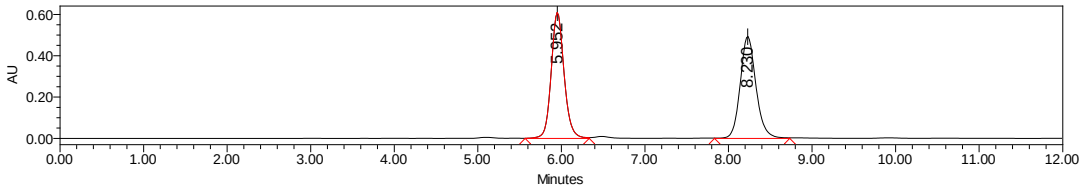
	Retention Time	Area	% Area
1	6.595	3489245	96.12
2	8.237	140702	3.88

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-6-chloro-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3wa):

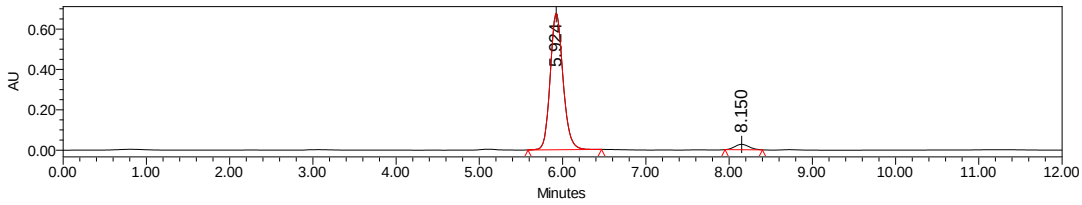


3wa

Prepared according to the general procedure (12 h). The title compound **3wa** was obtained as a white solid in 81% yield, 92% ee. Mp:105-110 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 5.92 min, t_r (minor) = 8.15 min. $[\alpha]^{19.9}_D$ = −10.1 (*c* = 0.41, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 1.6 Hz, 1H), 7.57 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 6.38 (s, 1H), 4.35 (s, 1H), 4.01 (d, *J* = 18.0 Hz, 1H), 3.76 (s, 3H), 3.61 (s, 3H), 3.41 (d, *J* = 18.0 Hz, 1H), 1.27 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 203.4, 167.3, 167.3, 164.1, 152.7, 136.4, 135.6, 133.8, 127.7, 124.1, 62.0, 57.4, 57.4, 52.95, 52.94, 52.80, 52.78, 51.9, 33.0, 28.2. **HRMS** (ESI-FTMS) calculated for $C_{19}H_{22}ClNO_6Na^+$ ([M]+Na^+) = 418.1028, 420.0998, found 418.1028, 420.0999.

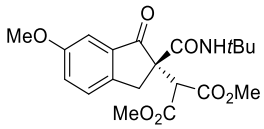


	Retention Time	Area	% Area
1	5.952	6508772	50.17
2	8.230	6463471	49.83



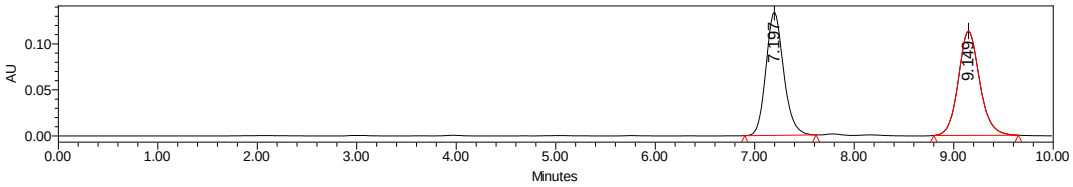
	Retention Time	Area	% Area
1	5.924	7192064	95.76
2	8.150	318376	4.24

Dimethyl (*R*)-2-[2-(*tert*-butylcarbamoyl)-6-methoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl]malonate (3xa):

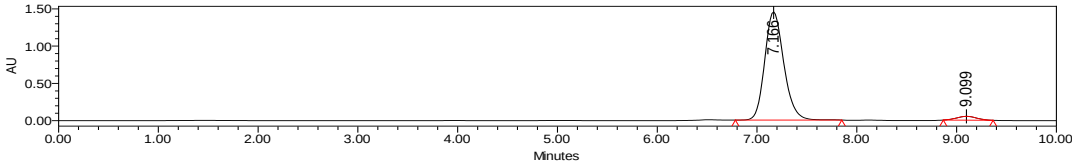


3xa

Prepared according to the general procedure (12 h). The title compound **3xa** was obtained as a white solid in 60% yield, 93% ee. Mp: 154-158 °C. HPLC (Chiralcel **IA**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 7.16 min, t_r (minor) = 9.10 min. $[\alpha]^{19.8}_D$ = −24.5 (*c* = 0.50, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.16 (m, 2H), 6.36 (s, 1H), 4.38 (s, 1H), 3.93 (d, *J* = 17.6 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.60 (s, 3H), 3.36 (d, *J* = 17.6 Hz, 1H), 1.26 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 204.2, 167.6, 167.4, 164.8, 159.4, 147.5, 136.0, 127.2, 125.2, 105.5, 62.2, 57.2, 55.53, 55.51, 52.84, 52.82, 52.71, 52.69, 51.7, 32.9, 28.3. **HRMS** (ESI-FTMS) calculated for $C_{20}H_{25}NO_7H^+$ ([M]+H$^+$) = 392.1704, found 392.1706.

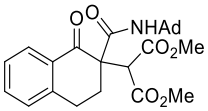


	Retention Time	Area	% Area
1	7.197	1652407	49.53
2	9.149	1684088	50.47



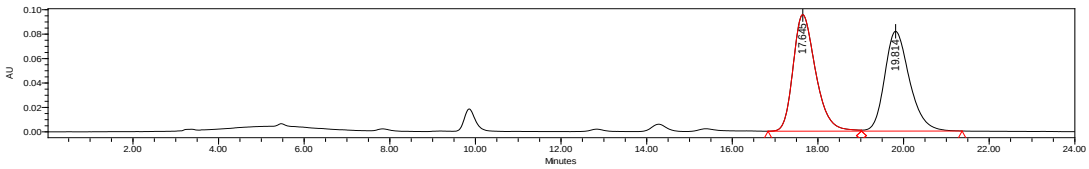
	Retention Time	Area	% Area
1	7.166	19229507	96.41
2	9.099	716628	3.59

Dimethyl 2-(2-(((3r)-adamantan-1-yl)carbamoyl)-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl) malonate (3ya):

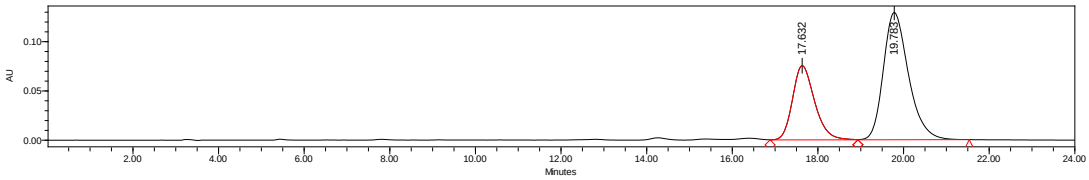


3ya

Prepared according to the general procedure (12 h). The title compound **3ya** was obtained as colorless oil in 28% yield, 32% ee. HPLC (Chiralcel **IC**, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) t_r (major) = 19.78 min, t_r (minor) = 17.63 min. $[\alpha]^{26.0}_D$ = 20.1 (*c* = 0.25, in CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 1H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 5.98 (s, 1H), 4.45 (s, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.16 – 3,07 (m, 1H), 2.88 – 2.79 (m, 1H), 2.75 – 2.70 (m, 1H), 2.53 (td, *J* = 13.2, 4.4 Hz, 1H), 2.03 (s, 3H), 1.94 – 1.84 (m, 6H), 1.62 (s, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 198.5, 167.9, 167.8, 164.3, 144.2, 134.4, 131.5, 128.7, 128.1, 126.7, 59.5, 57.6, 52.7, 52.5, 40.9, 36.2, 29.3, 27.6, 26.1. **HRMS** (ESI-FTMS) calculated for $C_{26}H_{31}NO_6H^+$ ([M]+H^+) = 454.2224, found 454.2224.

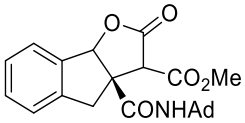


	Retention Time	Area	% Area
1	17.645	3474737	51.44
2	19.814	3279885	48.56



	Retention Time	Area	% Area
1	17.632	2698297	33.89
2	19.783	5263314	66.11

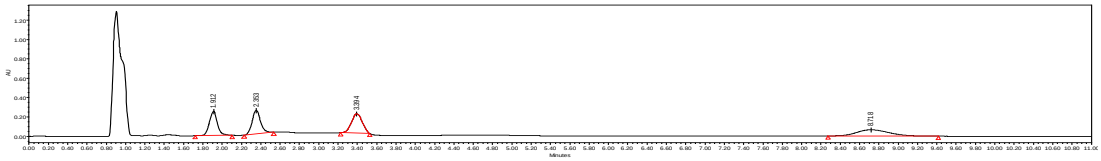
methyl (3a*R*)-3a-{[(3*R*)-adamantan-1-yl]carbamoyl}-2-oxo-3,3a,4,8b-tetrahydro-2H-indeno [1,2-b]furan-3-carboxylate (4):



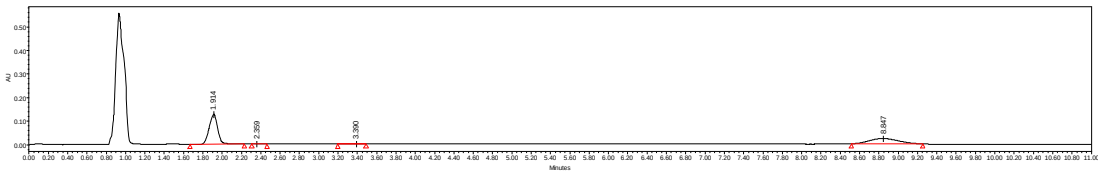
4

The title compound **4** was obtained as a white solid in 80 % yield, 2:1 dr, 99%/99% ee. SFC (Chiralcel **AS**, CO_2/MeOH = 80/20, flow rate 2.0 mL/min, λ = 210 nm) $t_{r\text{-major isomer}}$ (major) = 1.91 min, $t_{r\text{-major isomer}}$ (minor) = 2.36 min, $t_{r\text{-minor isomer}}$ (major) = 8.85 min, $t_{r\text{-minor isomer}}$ (minor) = 3.39 min. **^{1}H NMR** mixture of diastereoisomers (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.2 Hz, 1H), 7.42 – 7.27 (m, 3H), 6.08 – 5.84 (1H, major isomer: δ 5.84, 0.7H, minor isomer: δ 6.08, 0.3H), 5.84 – 4.99 (1H, major isomer: δ 5.84, 0.7H, minor isomer: δ 4.99, 0.3H), 4.41 – 3.69 (1H, major isomer: δ 4.41, 0.7H, minor isomer: δ 3.69, 0.3H), 3.84 (d, *J* = 0.8 Hz, 2H), 3.81 (d, *J* = 0.8 Hz, 1H), 3.48 (dd, *J* = 17.1, 10.2 Hz, 1H), 3.34 (dd, *J* = 17.6, 16.8 Hz, 1H), 2.02 (s, 3H), 1.86 (s, 6H), 1.62 (s, 5H). Major isomer: **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) 169.89, 169.04, 167.72, 142.47, 137.06, 130.76, 128.14, 126.75, 124.81, 87.64, 59.18, 53.19, 53.17, 52.70, 52.69, 52.31, 41.17, 39.18, 36.09, 29.23. Minor isomer: **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) 169.57, 169.26, 166.80, 141.11, 137.14, 130.80, 128.31,

126.55, 125.42, 87.77, 60.94, 55.57, 55.56, 53.02, 53.00, 52.49, 41.82, 41.13, 36.09, 29.23. **HRMS** (ESI-FTMS) calculated for $C_{24}H_{27}NO_5H^+$ ([M]+H^+) = 410.1962, found 410.1965.

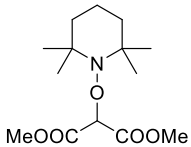


	Retention Time	Area	% Area
1	1.912	1434979	24.18
2	2.353	1473687	24.84
3	3.394	1531447	25.81
4	8.718	1493359	25.17



	Retention Time	Area	% Area
1	1.914	770373	64.79
2	2.359	2138	0.18
3	3.390	6696	0.56
4	8.847	409775	34.46

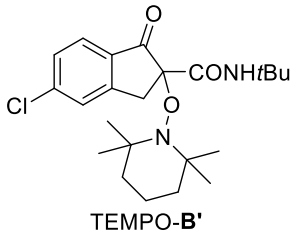
Dimethyl 2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]malonate (TEMPO-A):



TEMPO-A

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96 (d, *J* = 1.2 Hz, 1H), 3.78 (d, *J* = 1.2 Hz, 6H), 1.47 – 1.40 (m, 4H), 1.33 – 1.24 (m, 2H), 1.19 (s, 6H), 1.05 (s, 5H). **HRMS** (ESI-FTMS) calculated for $C_{14}H_{25}NO_5H^+$ ([M]+H^+) = 288.1805, found 288.1805.

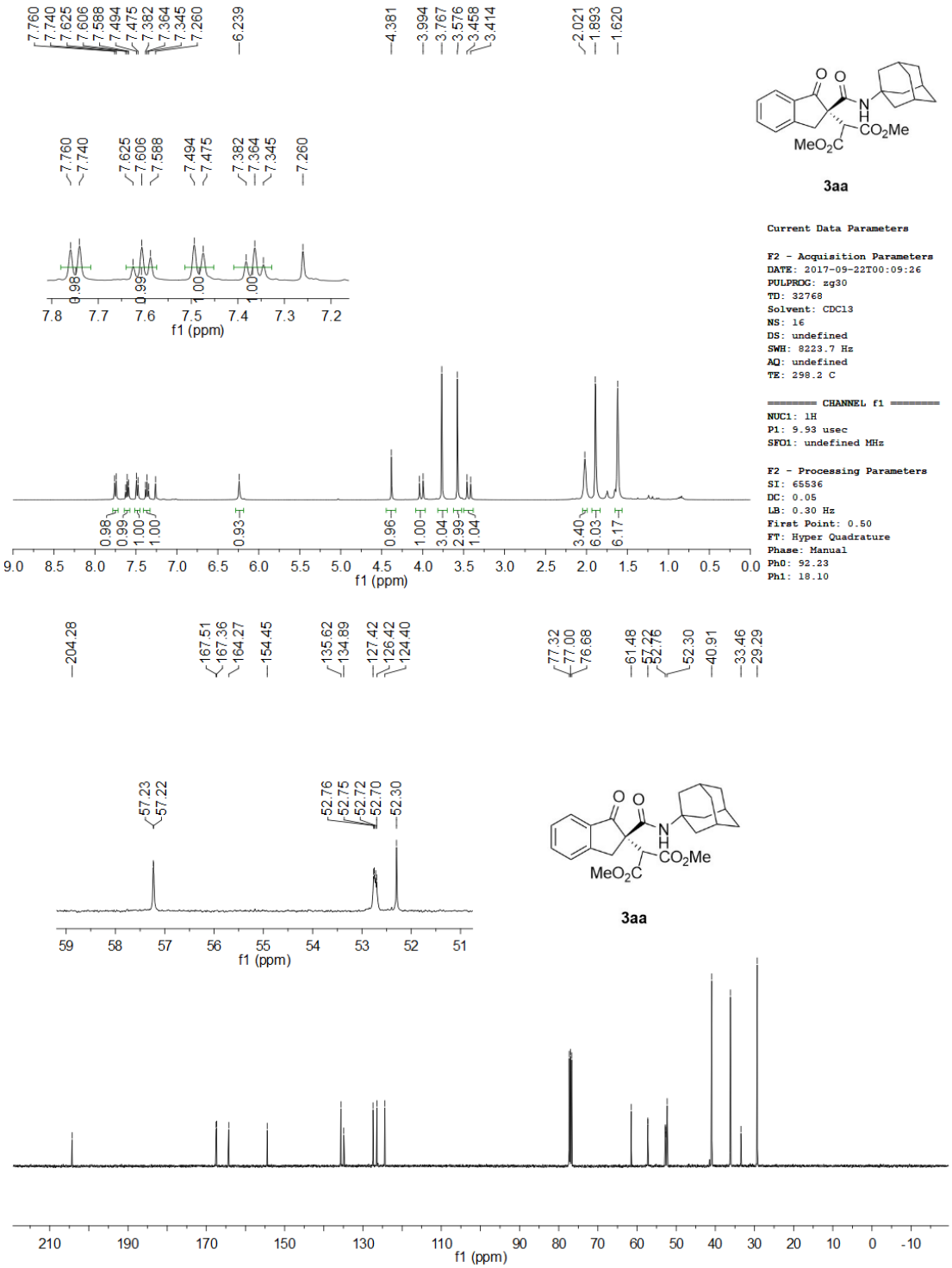
***N*-(tert-butyl)-5-chloro-1-oxo-2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]-2,3-dihydro-1H-indene-2-carboxamide (TEMPO-B'):**

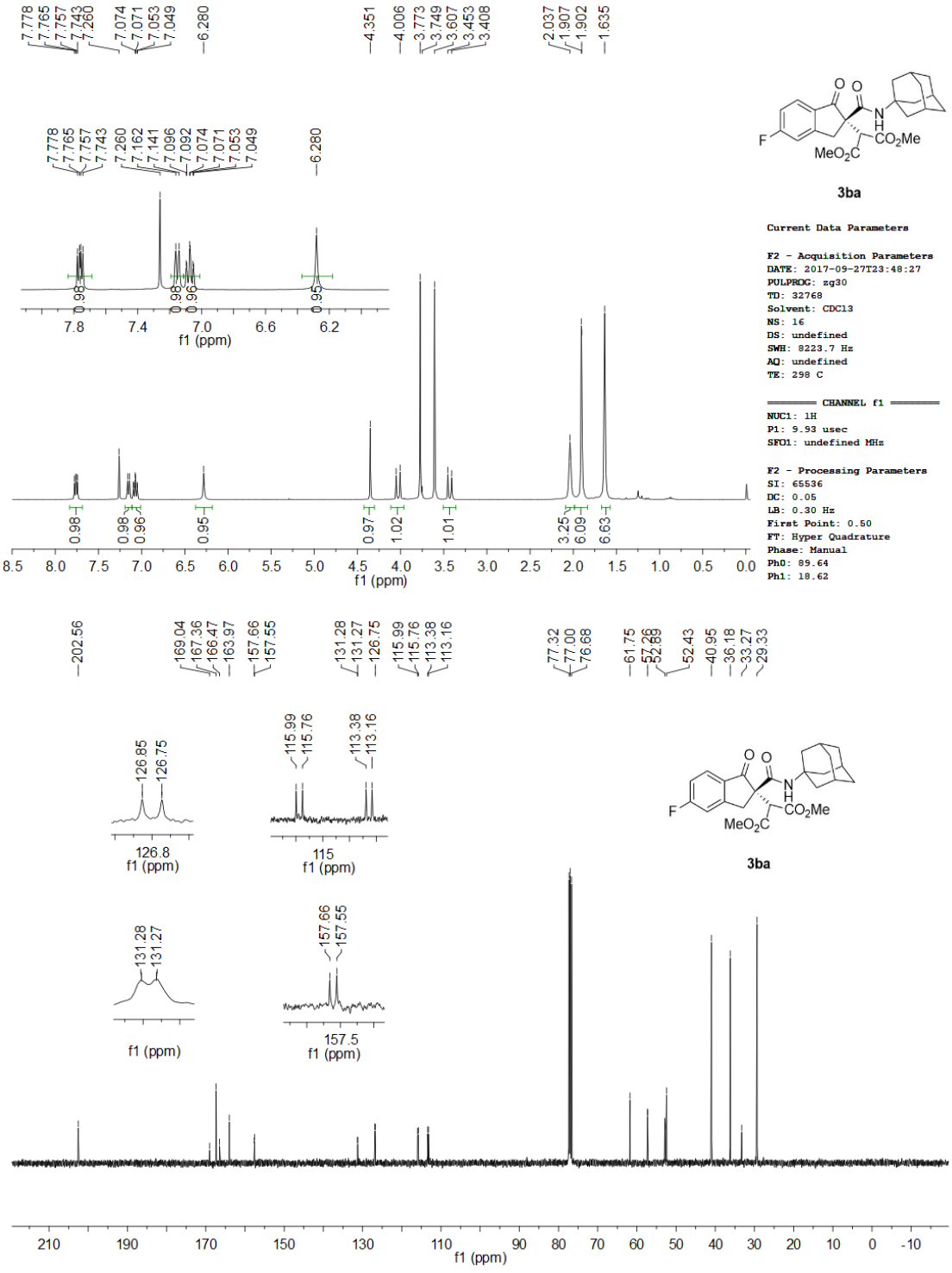


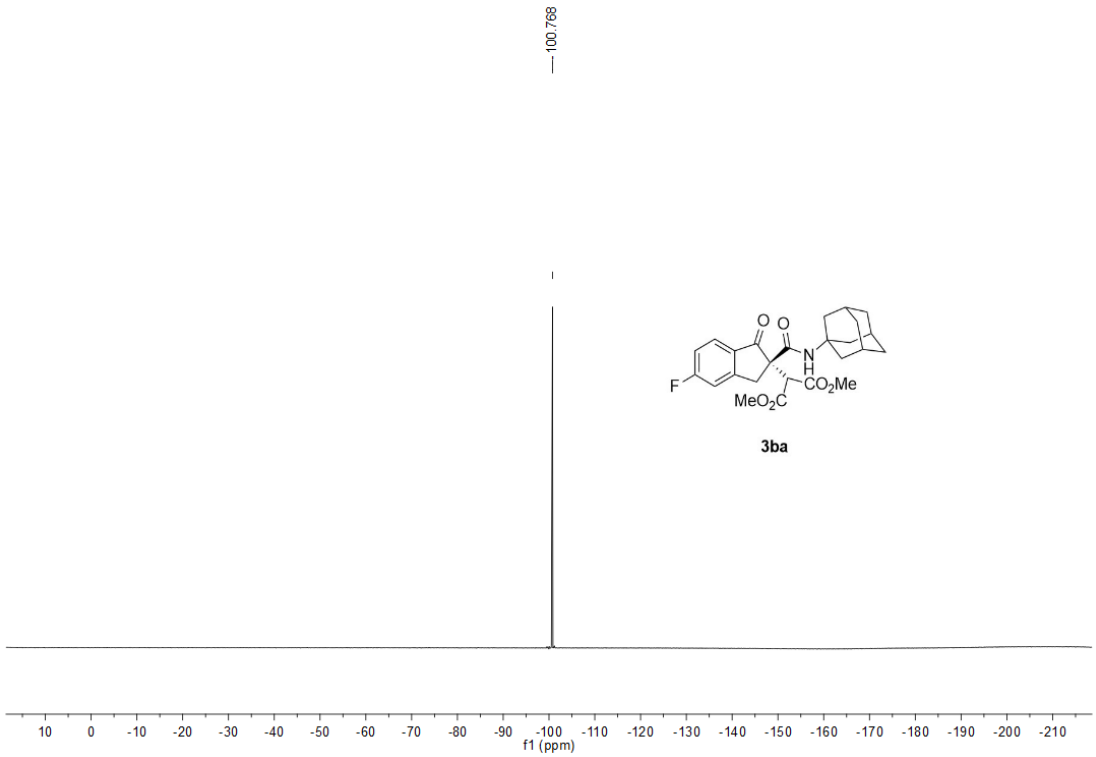
TEMPO-**B'**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.4 Hz, 1H), 7.46 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 4.31 (d, *J* = 17.6 Hz, 1H), 3.53 (d, *J* = 17.6 Hz, 1H), 1.60 – 1.39 (m, 5H), 1.37 (s, 9H), 1.34 – 1.30 (m, 1H), 1.22 (s, 3H), 1.18 (s, 3H), 1.07 (s, 3H), 0.61 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ = 201.4, 167.7, 155.5, 142.1, 132.4, 128.0, 126.2, 125.5, 91.3, 60.0, 59.5, 51.2, 40.3, 40.0, 32.2, 32.0, 28.5, 20.7, 20.6, 16.7. **HRMS** (ESI-FTMS) calculated for $C_{23}H_{33}ClN_2O_3H^+$ ([M]+H^+) = 421.2252, 423.2223, found 421.2246, 423.2216.

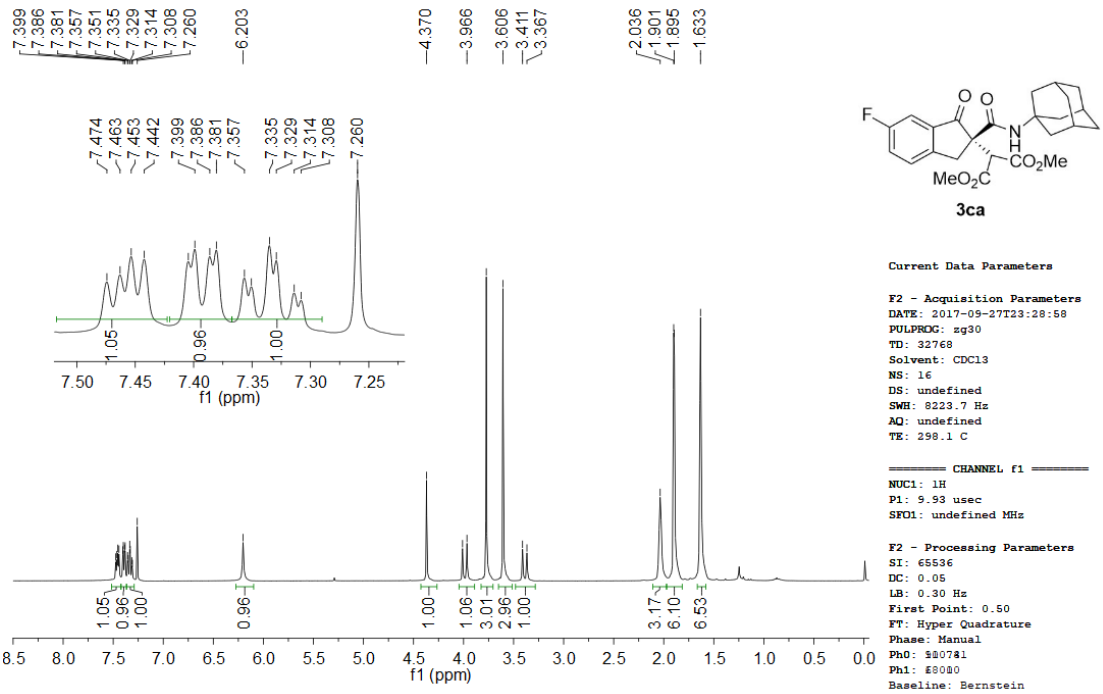
8. Copy of NMR spectra




7.778
7.765
7.757
7.743
7.260
7.074
7.071
7.053
7.049
6.280
4.351
4.006
3.773
3.749
3.607
3.453
3.408
2.037
1.907
1.902
1.635
3ba
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-09-27T23:48:27
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 89.64
Ph1: 18.62
f1 (ppm)
202.56
169.04
167.36
166.47
163.97
157.66
157.55
131.28
131.27
126.75
115.99
115.76
113.38
113.16
77.32
77.00
76.68
61.75
52.89
52.43
40.95
36.18
33.27
29.33
126.85
126.75
126.8
115
157.5



3ba



3ca

Current Data Parameters

F2 - Acquisition Parameters
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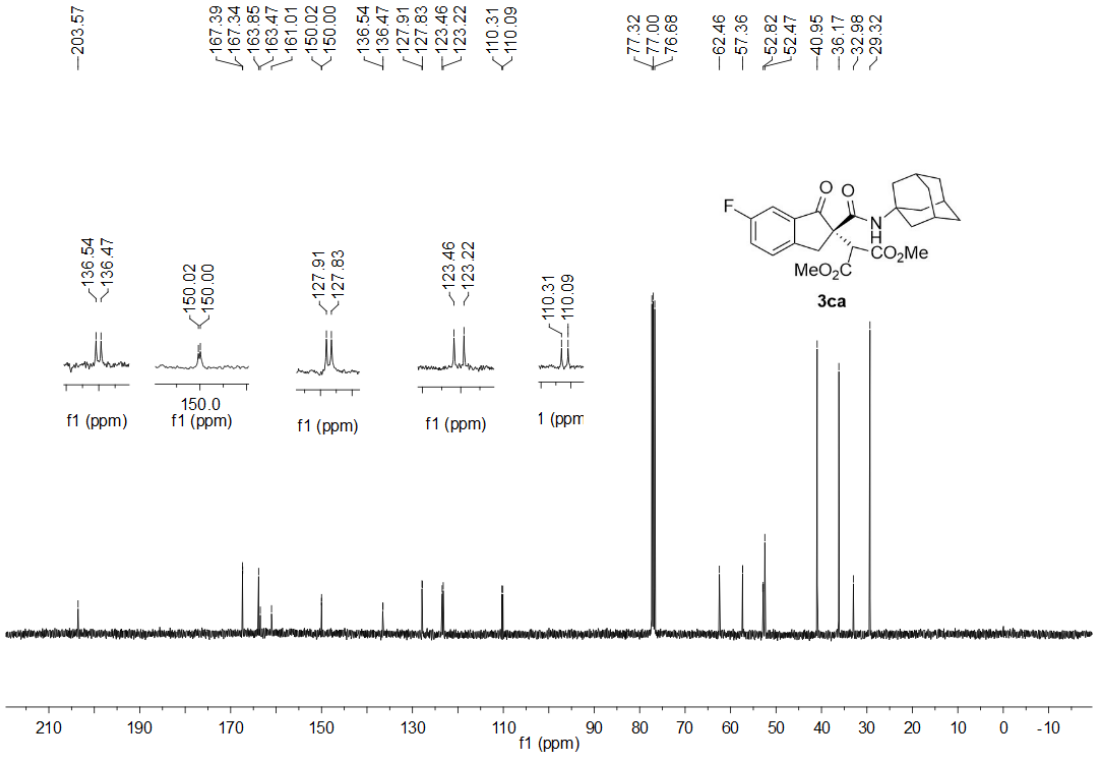
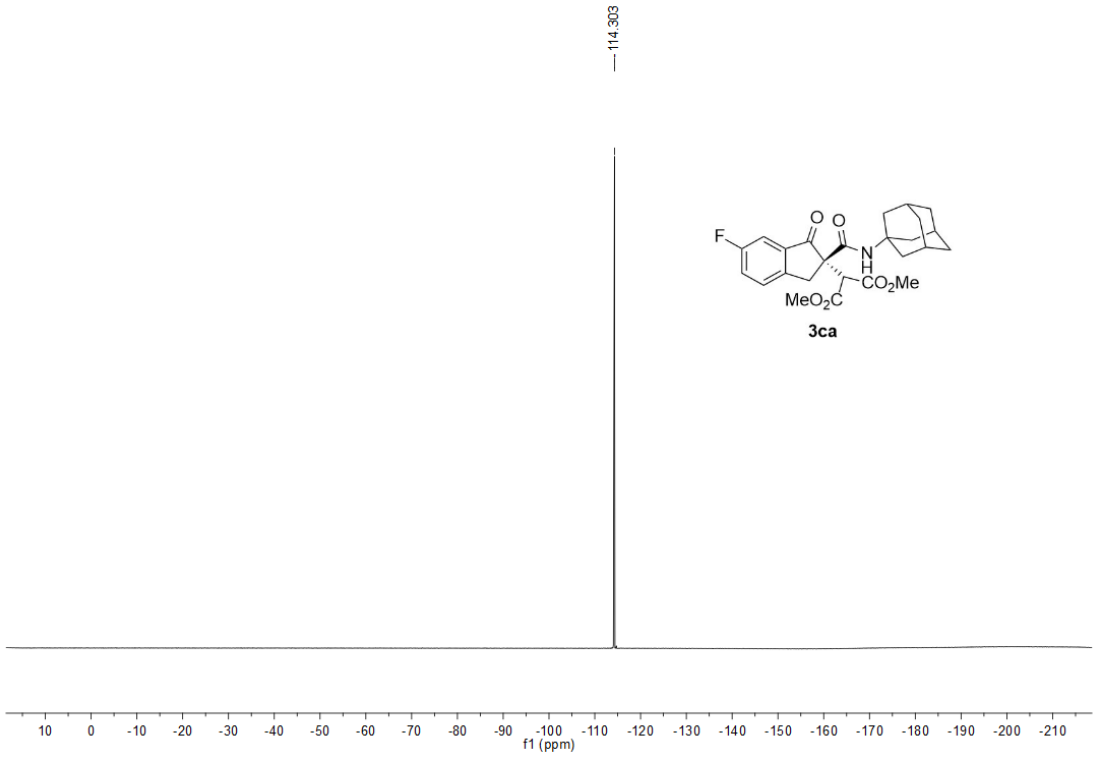
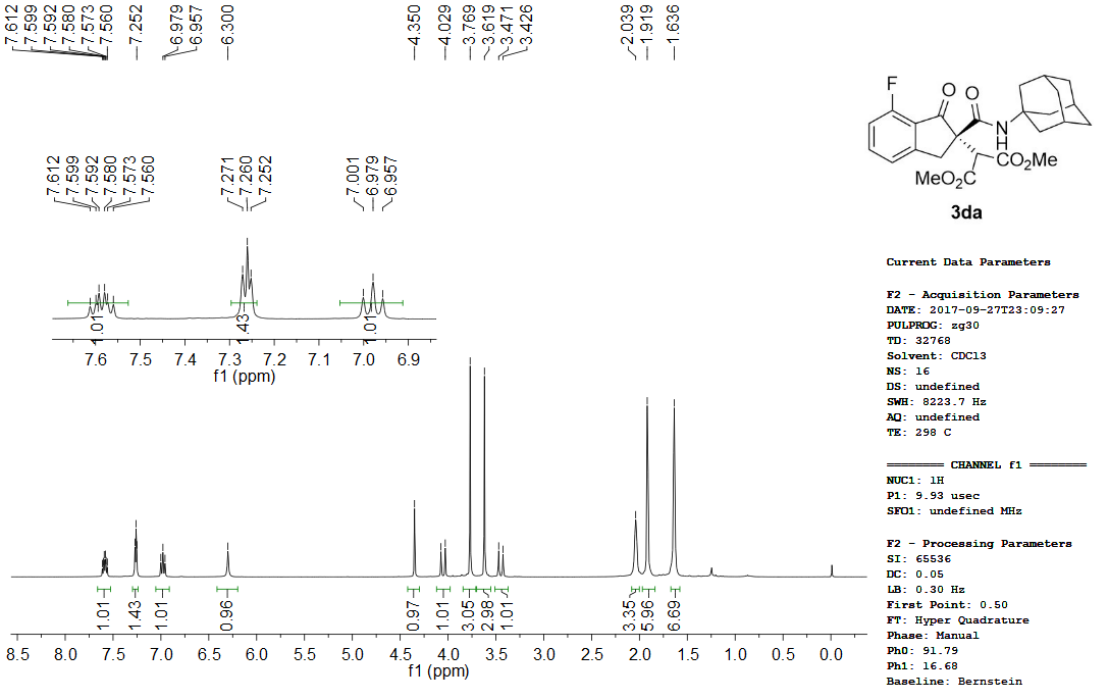
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.1 C

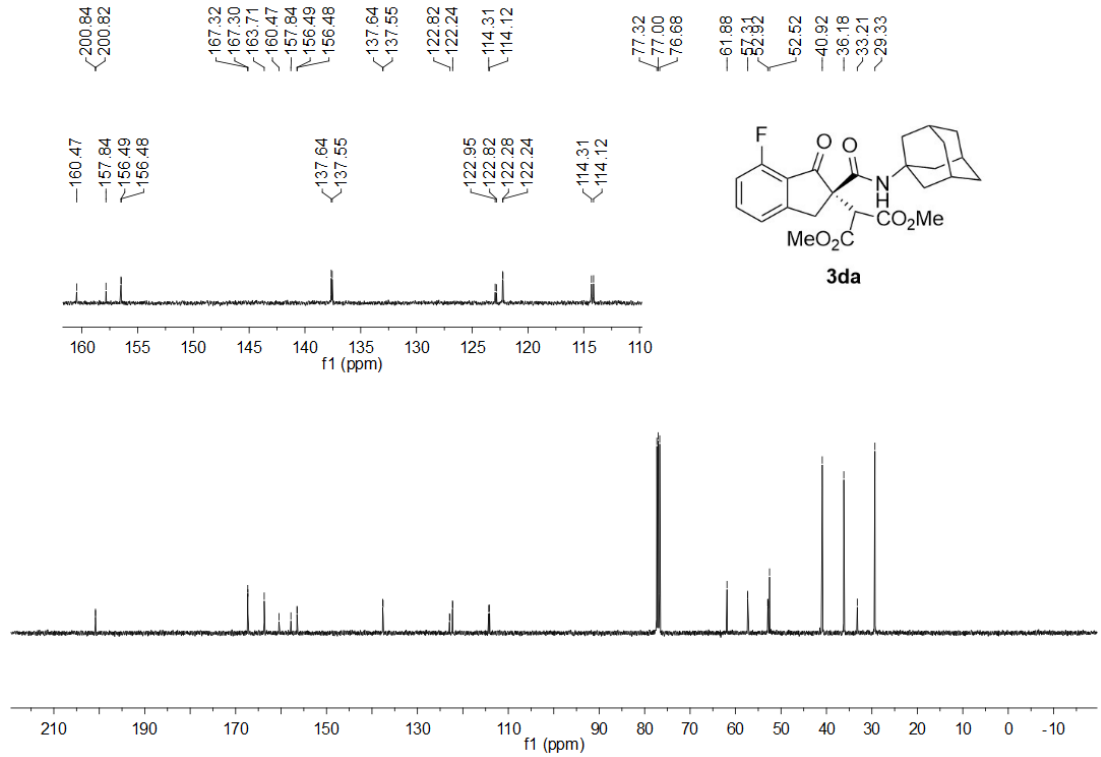
======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

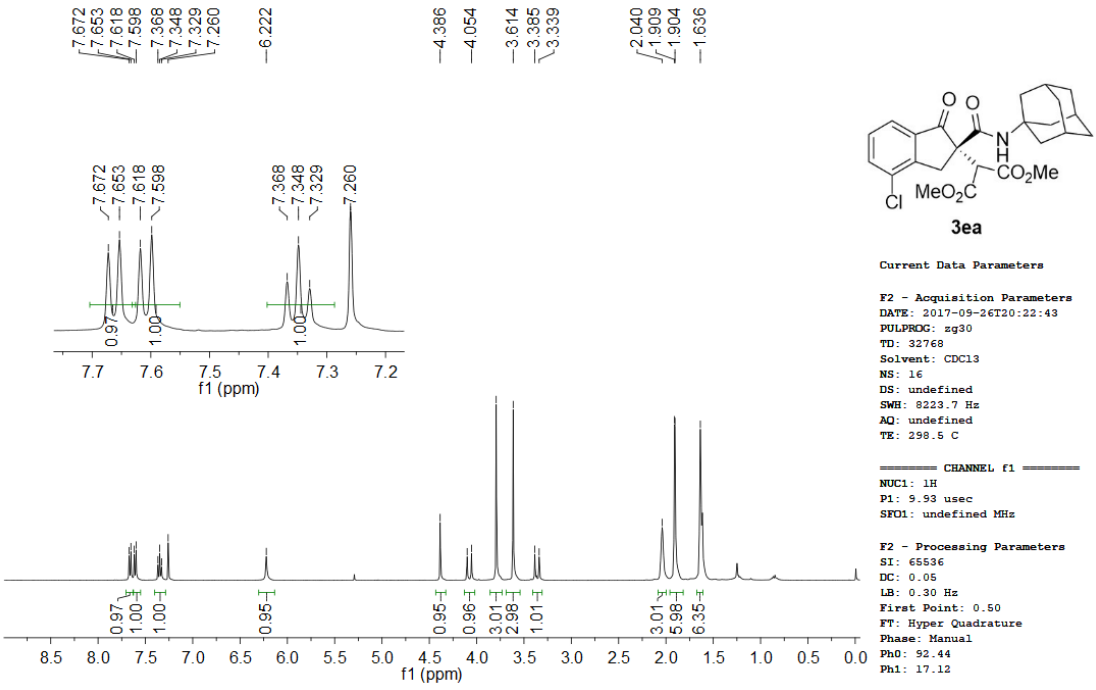
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: [illegible]
Ph1: [illegible]
Baseline: Bernstein


203.57
167.39
167.34
163.85
163.47
161.01
150.02
150.00
136.54
136.47
127.91
127.83
123.46
123.22
110.31
110.09
77.32
77.00
76.68
62.46
57.36
52.82
52.47
40.95
36.17
32.98
29.32
F
O
O
N
H
CO2Me
MeO2C
3ca
f1 (ppm)


114.303
F
O
O
N
H
CO2Me
MeO2C
3ca
f1 (ppm)


7.612
7.599
7.592
7.580
7.573
7.560
7.252
6.979
6.957
6.300
4.350
4.029
3.769
3.619
3.471
3.426
2.039
1.919
1.636
F
O
O
N
H
CO2Me
MeO2C
3da
7.271
7.260
7.252
7.001
6.979
6.957
1.01
1.43
1.01
f1 (ppm)
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-09-27T23:09:27
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.79
Ph1: 16.68
Baseline: Bernstein
1.01
1.43
1.01
0.96
0.97
1.01
3.05
2.98
1.01
3.35
5.96
6.69
f1 (ppm)


200.84
200.82
167.32
167.30
163.71
160.47
157.84
156.49
156.48
137.64
137.55
122.82
122.24
114.31
114.12
77.32
77.00
76.68
61.88
57.31
52.92
52.52
40.92
36.18
33.21
29.33
160.47
157.84
156.49
156.48
137.64
137.55
122.95
122.82
122.28
122.24
114.31
114.12
F
O
O
N
H
CO2Me
MeO2C
3da
f1 (ppm)
f1 (ppm)



Current Data Parameters

F2 - Acquisition Parameters
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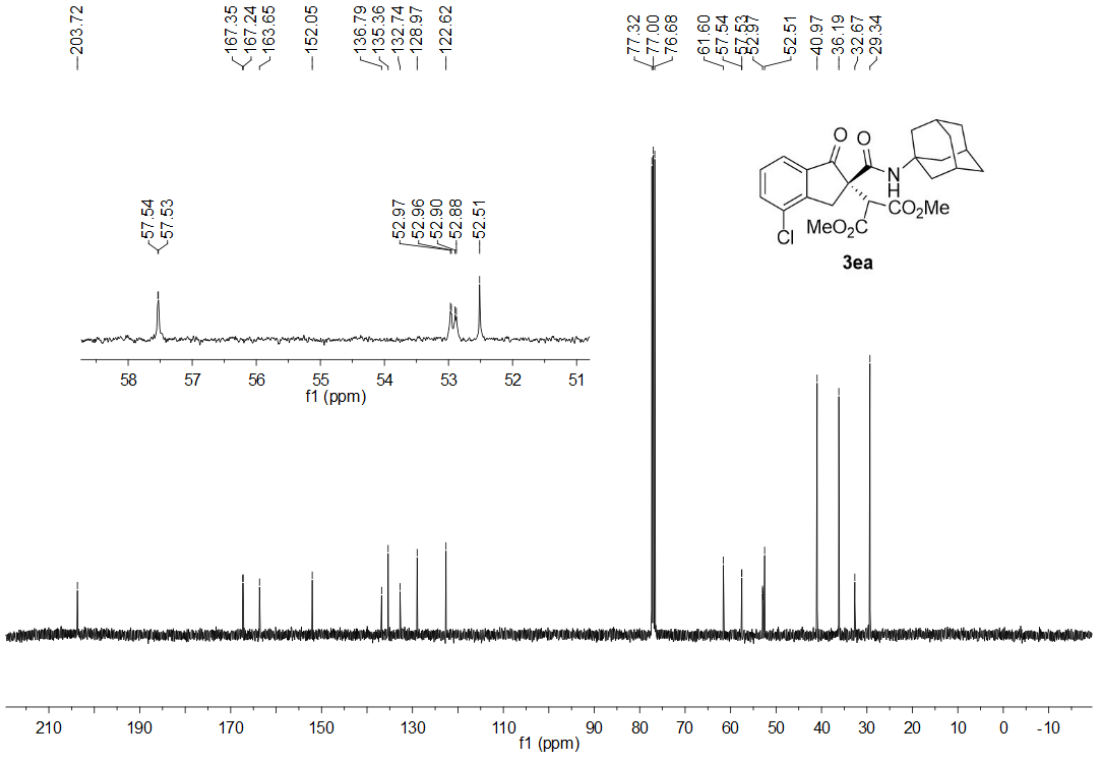
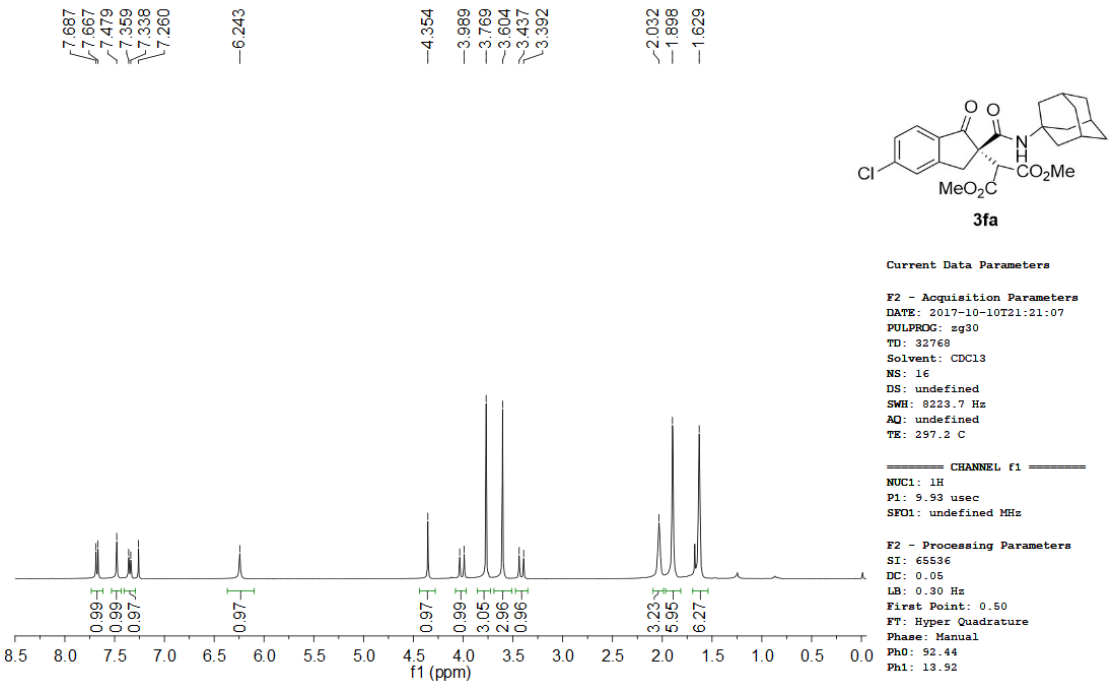
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.5 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.44
Ph1: 17.12






```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-10-10T21:21:07
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TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.2 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.44
Ph1: 13.92
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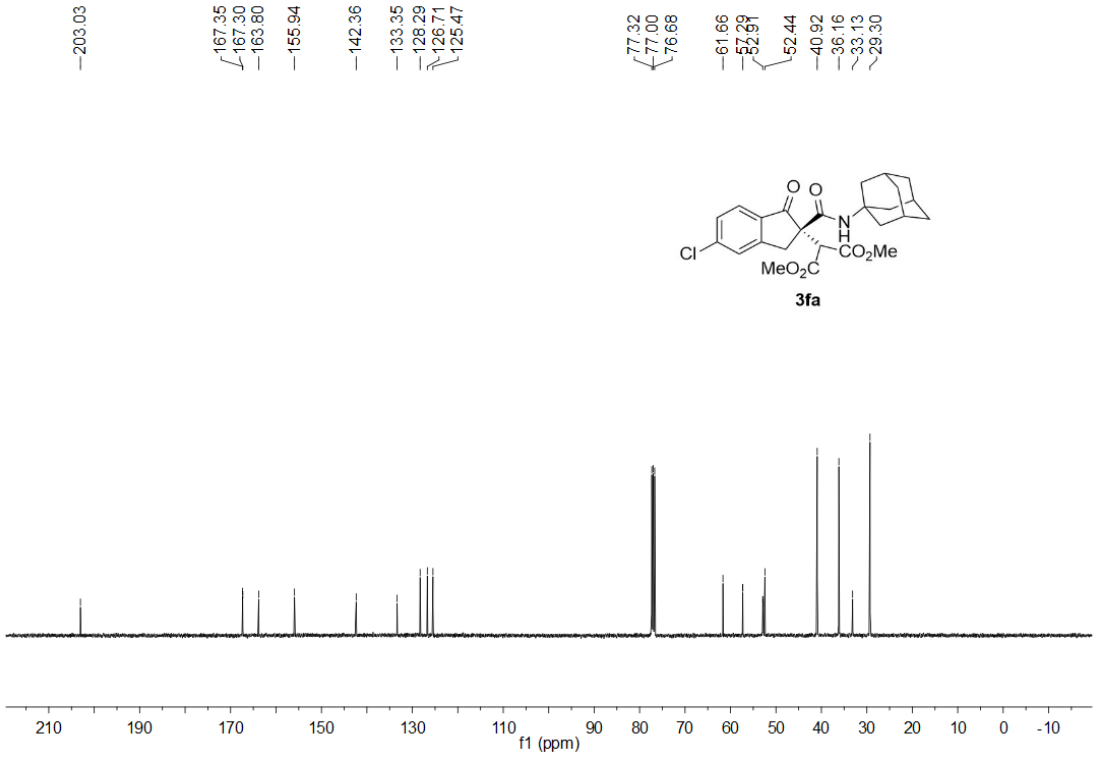

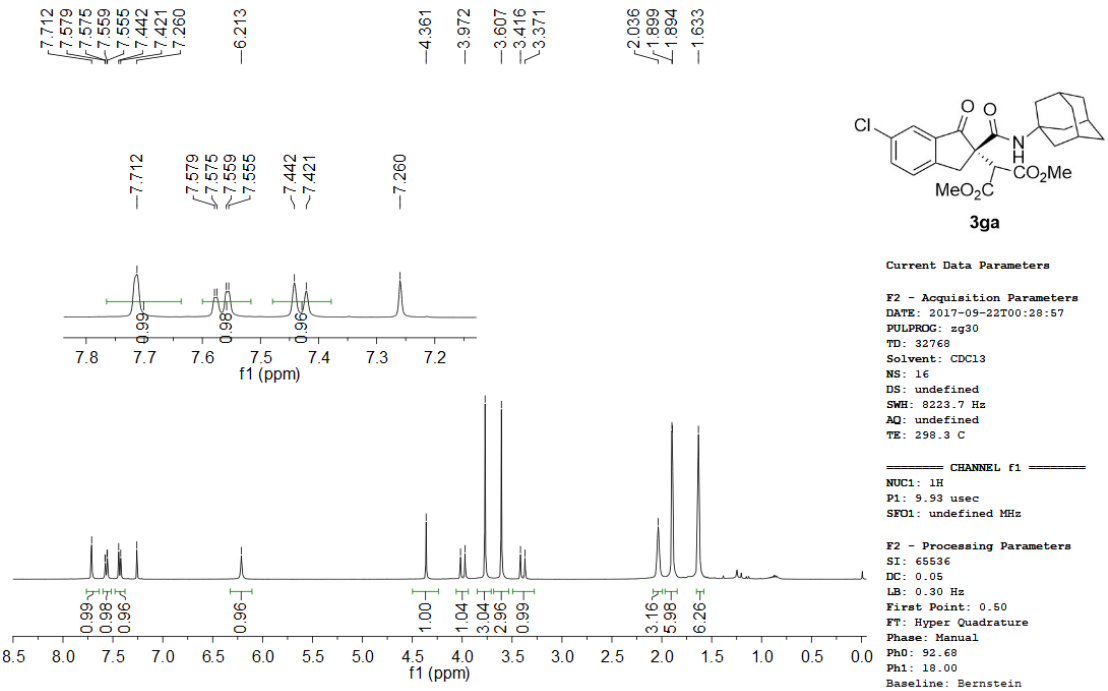


```
Current Data Parameters

F2 - Acquisition Parameters
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PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.3 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.68
Ph1: 18.00
Baseline: Bernstein
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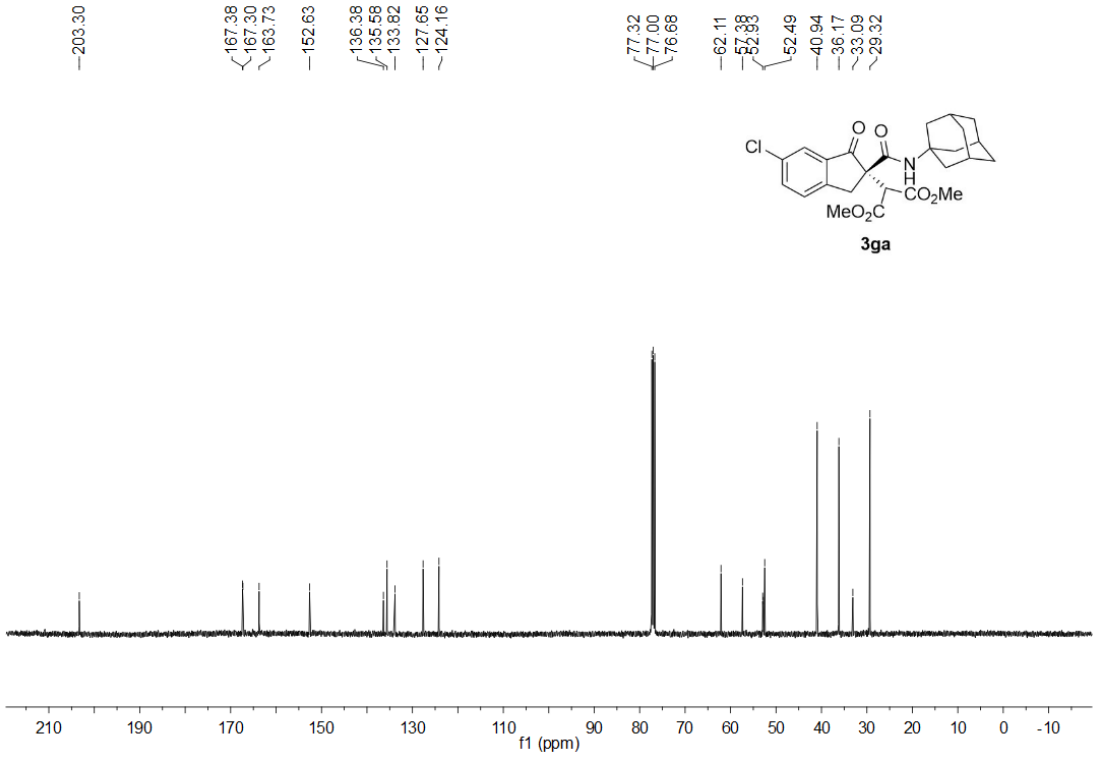

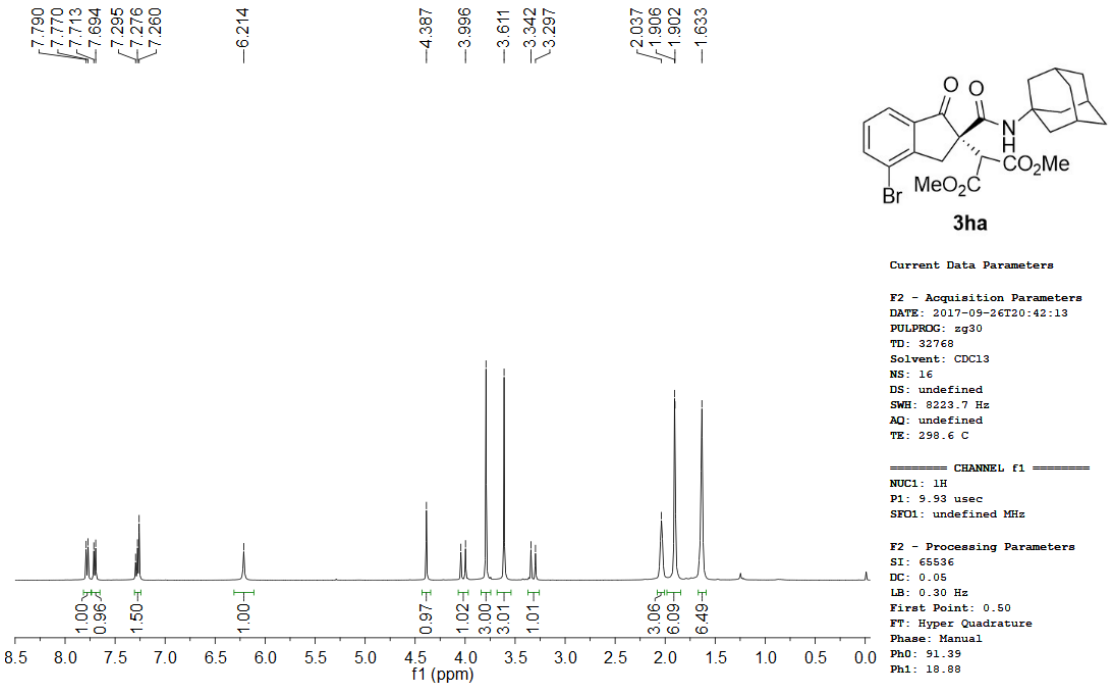


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Current Data Parameters

F2 - Acquisition Parameters
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PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.6 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.39
Ph1: 18.88
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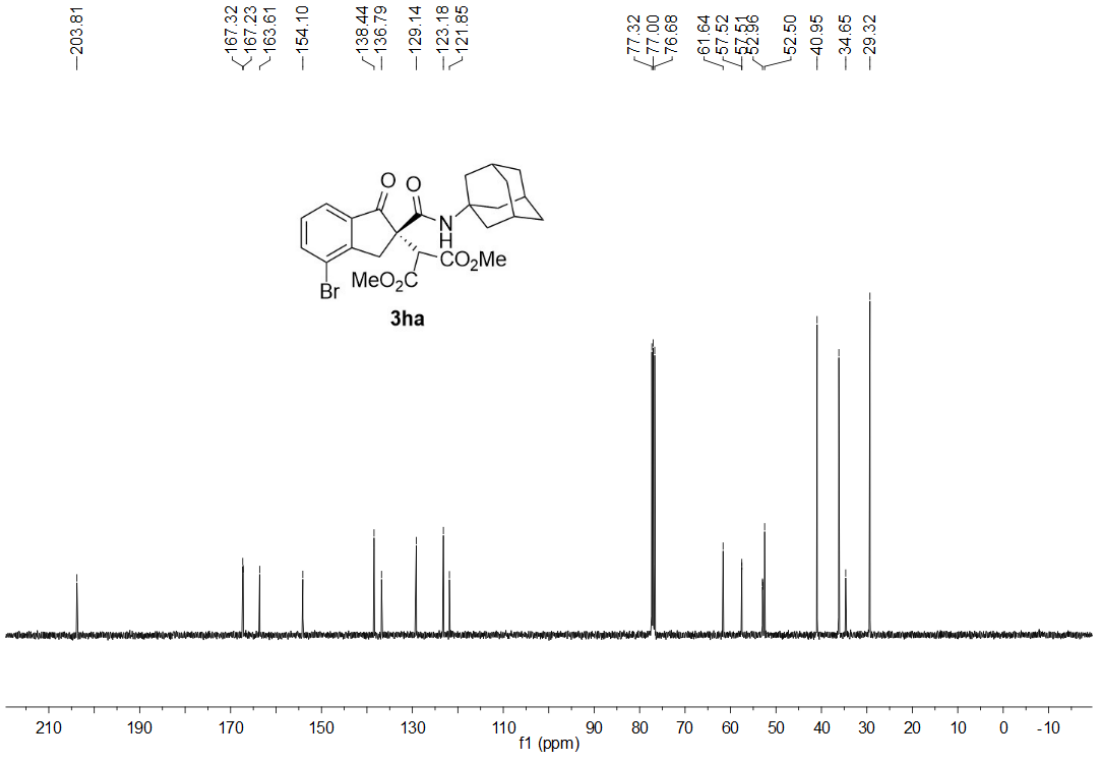
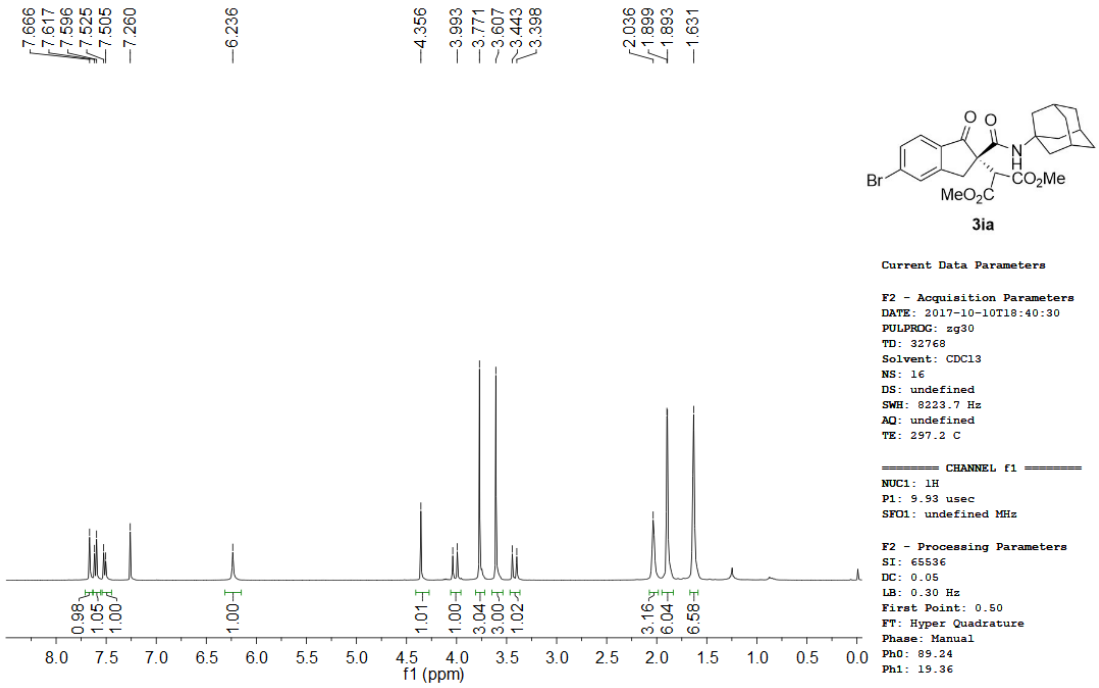




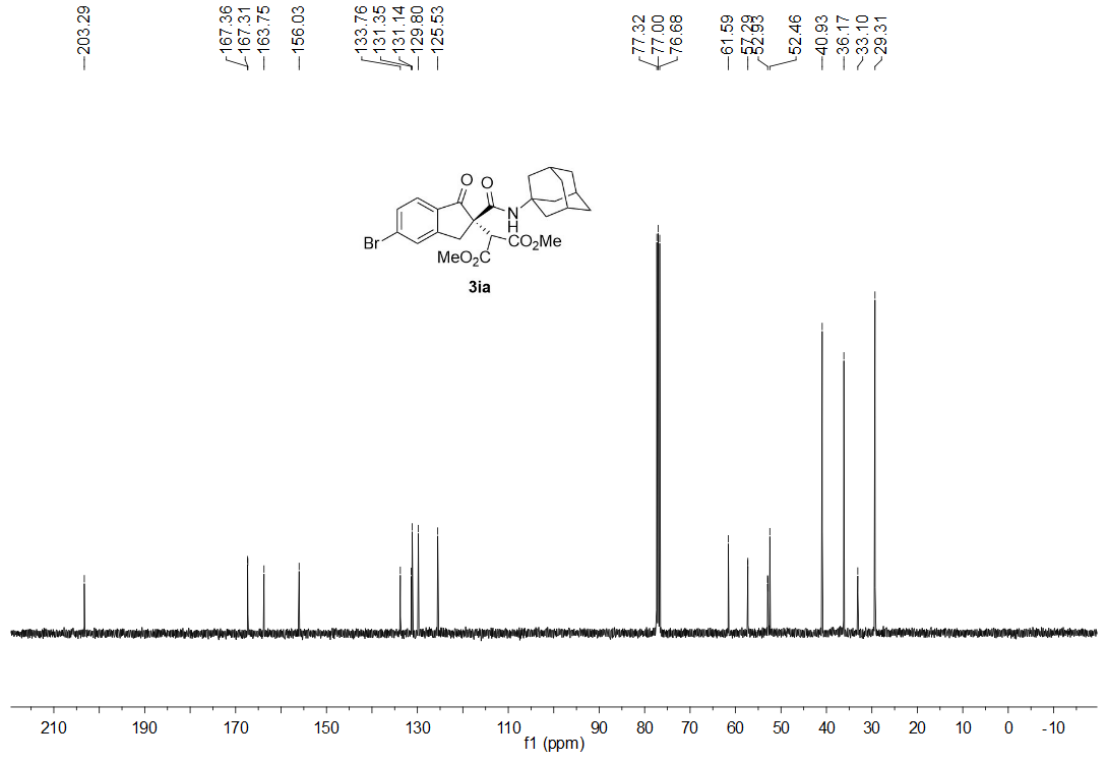
3ia

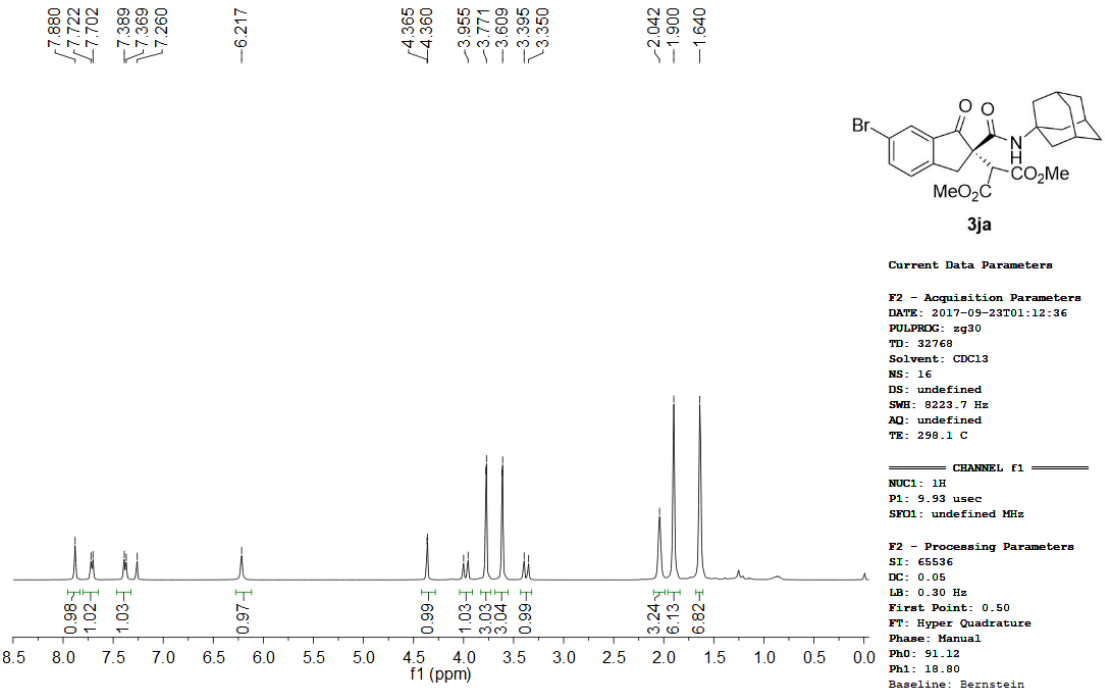
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-10-10T18:40:30
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.2 C

CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 89.24
Ph1: 19.36



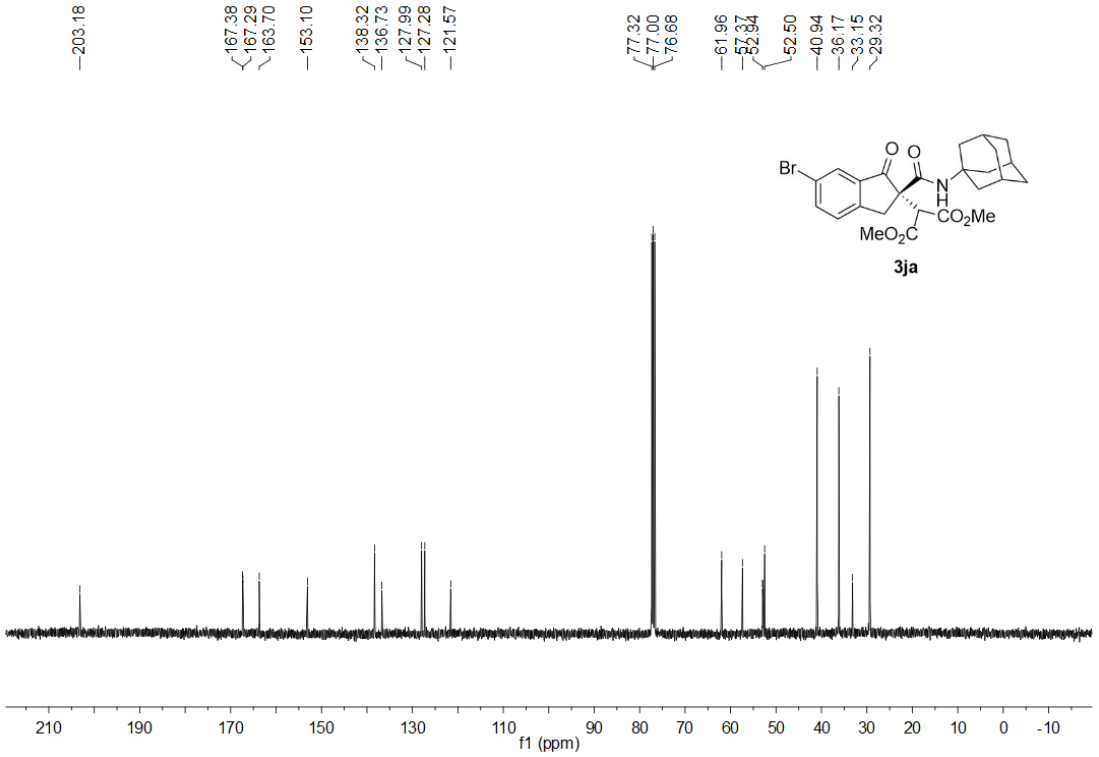


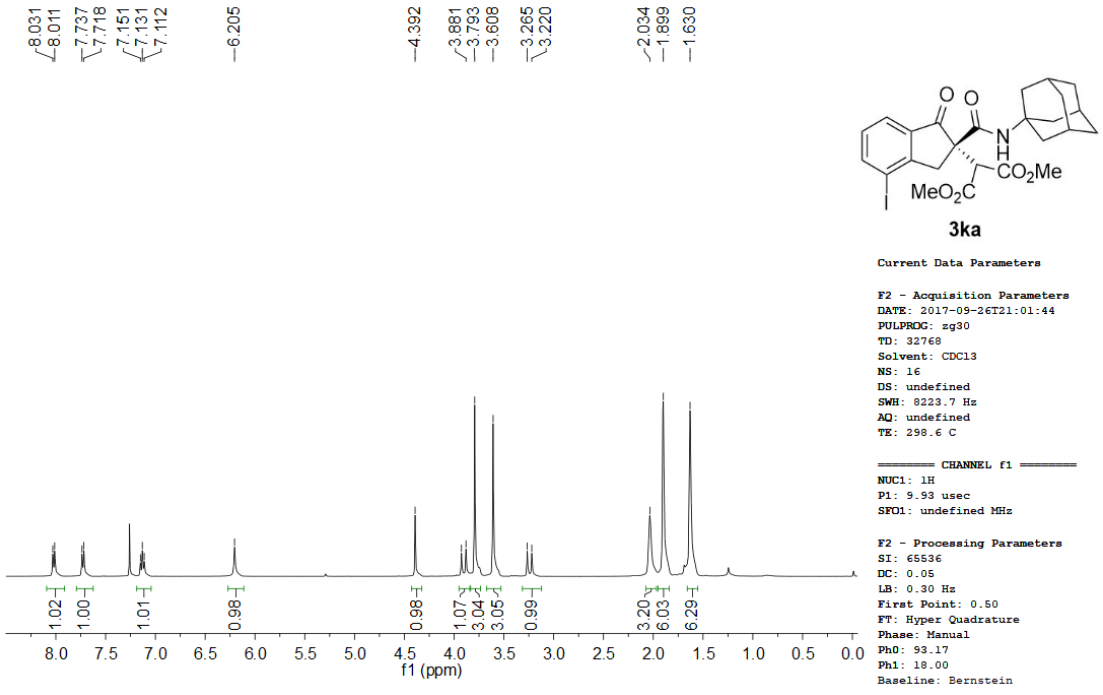
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-23T01:12:36
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.1 C

CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.12
Ph1: 18.80
Baseline: Bernstein



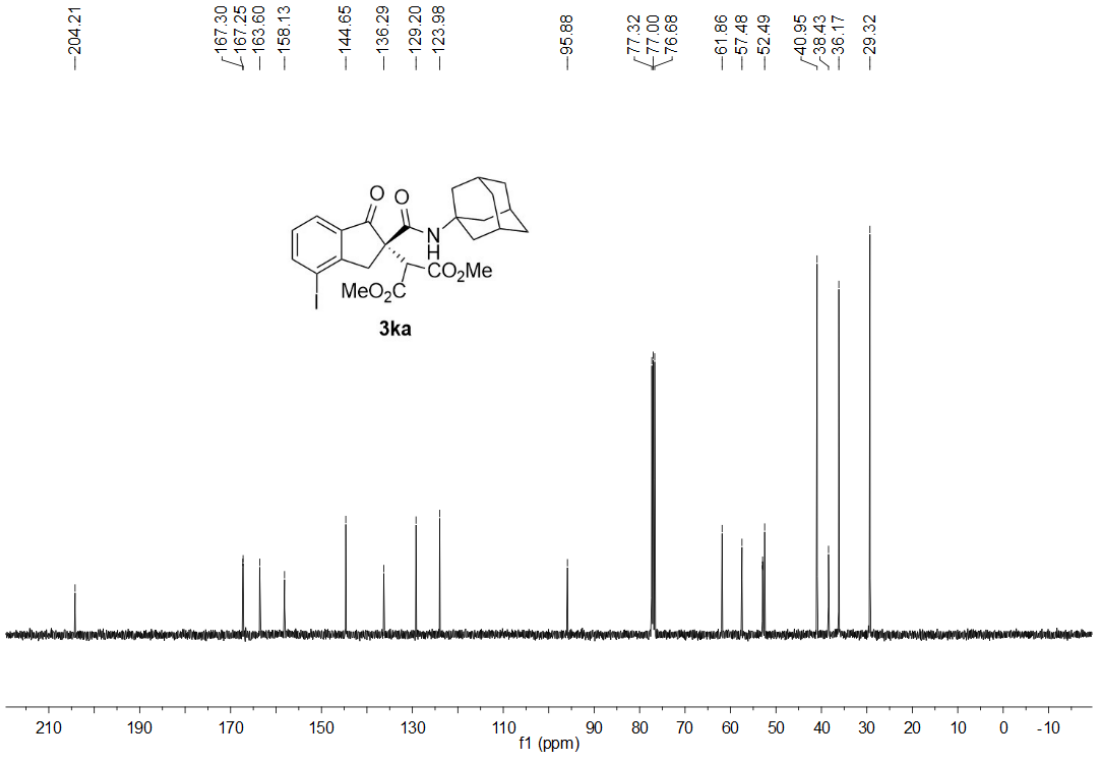


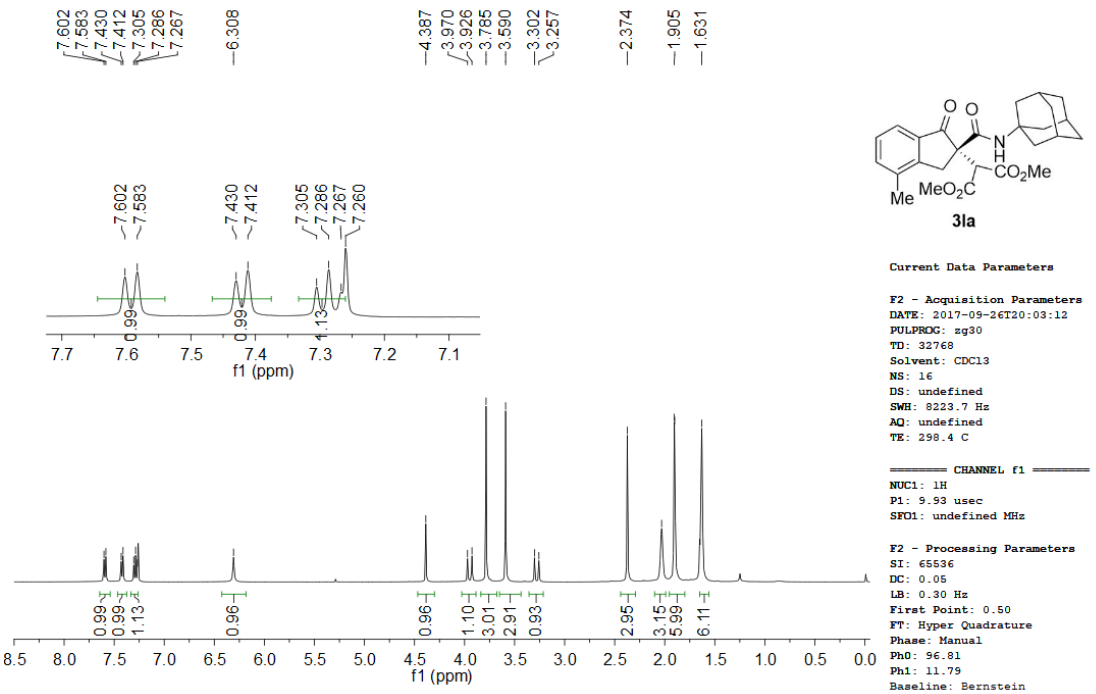
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-26T21:01:44
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.6 C

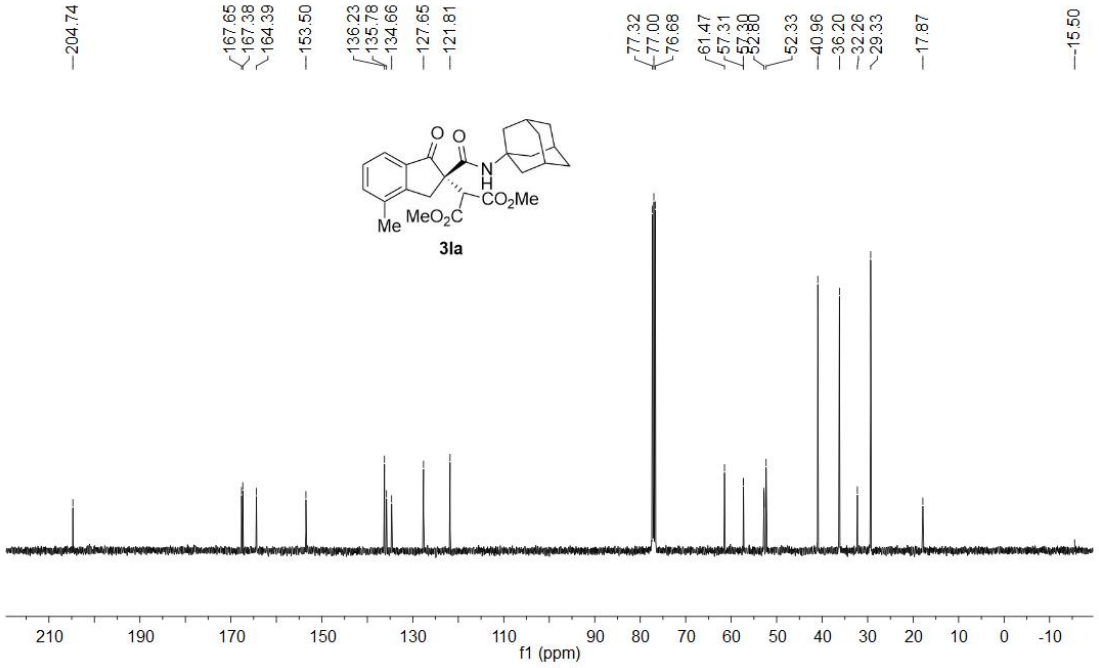
======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

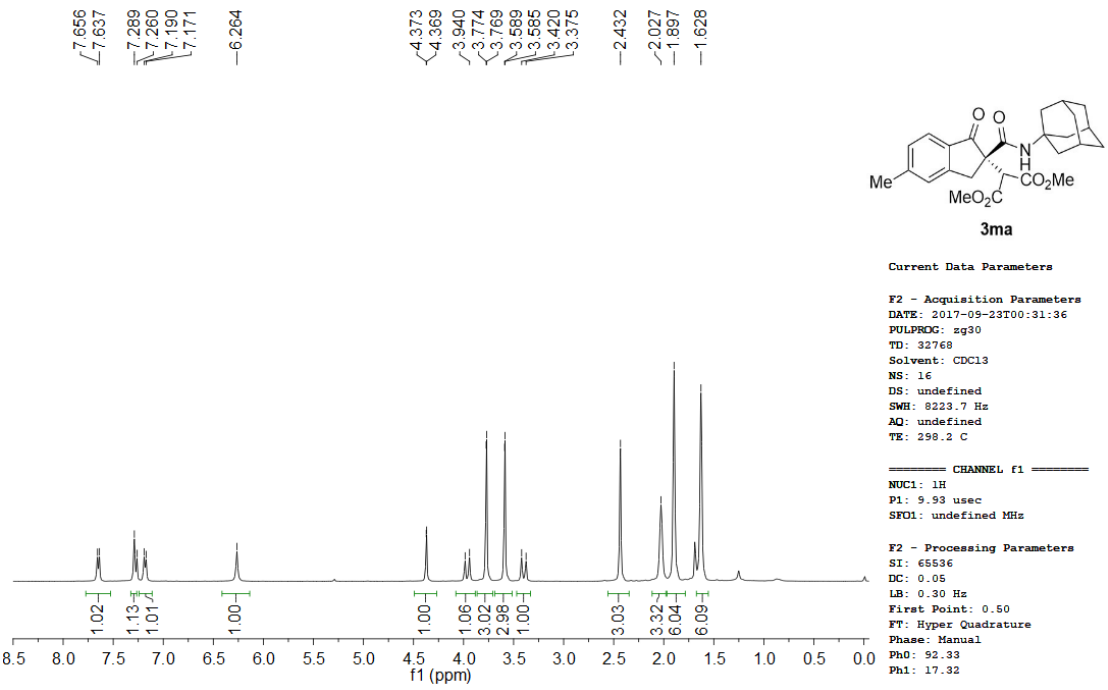
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 93.17
Ph1: 18.00
Baseline: Bernstein






```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-26T20:03:12
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.4 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 96.81
Ph1: 11.79
Baseline: Bernstein
```



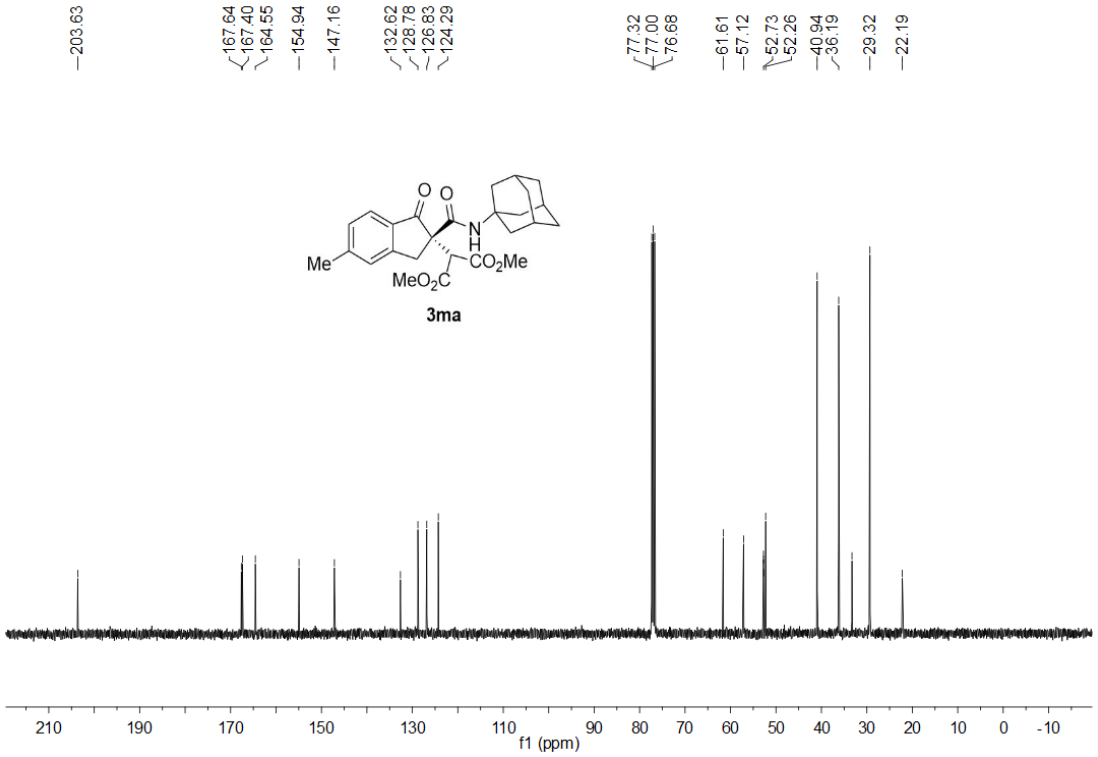


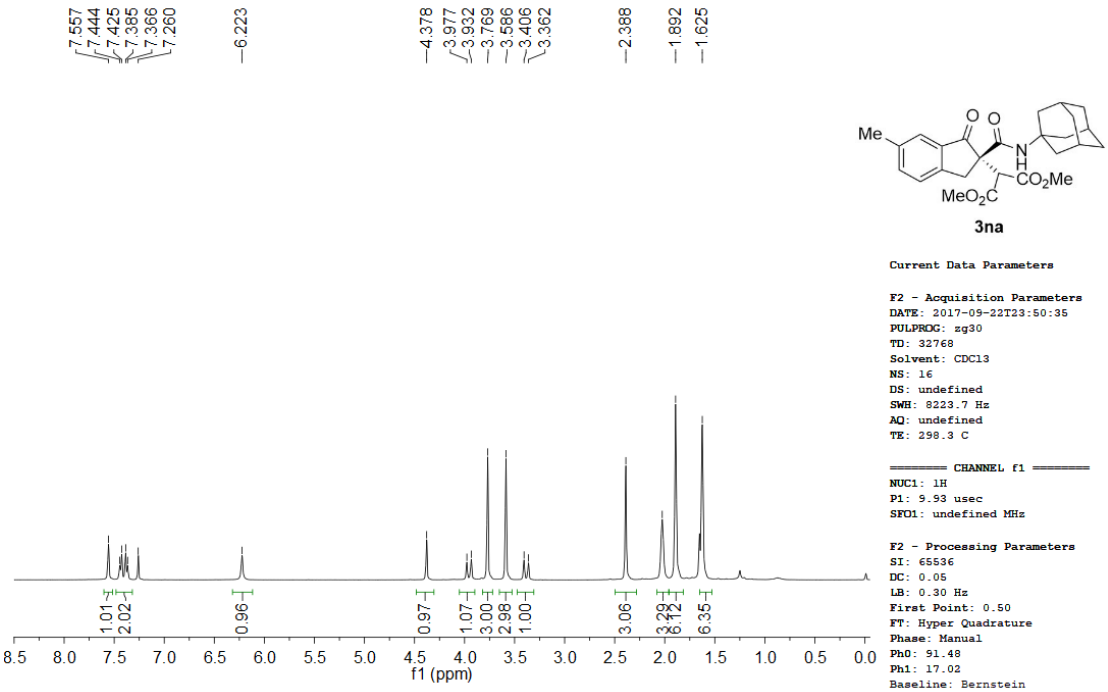
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-23T00:31:36
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.2 C

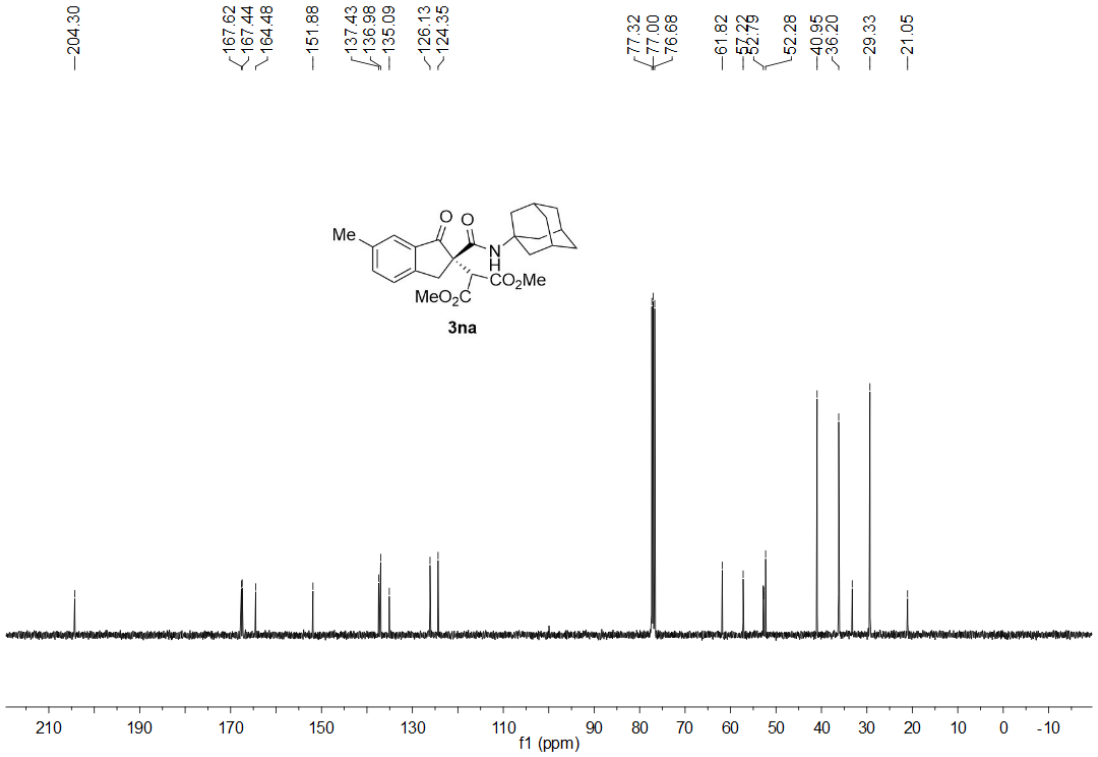
======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

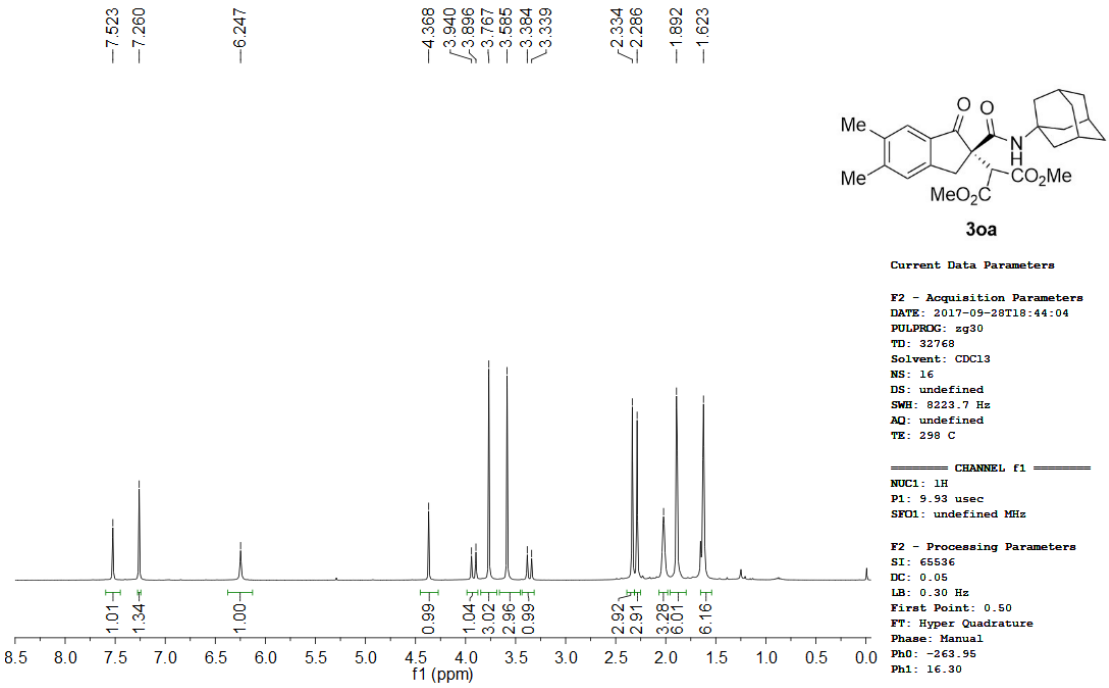
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.33
Ph1: 17.32

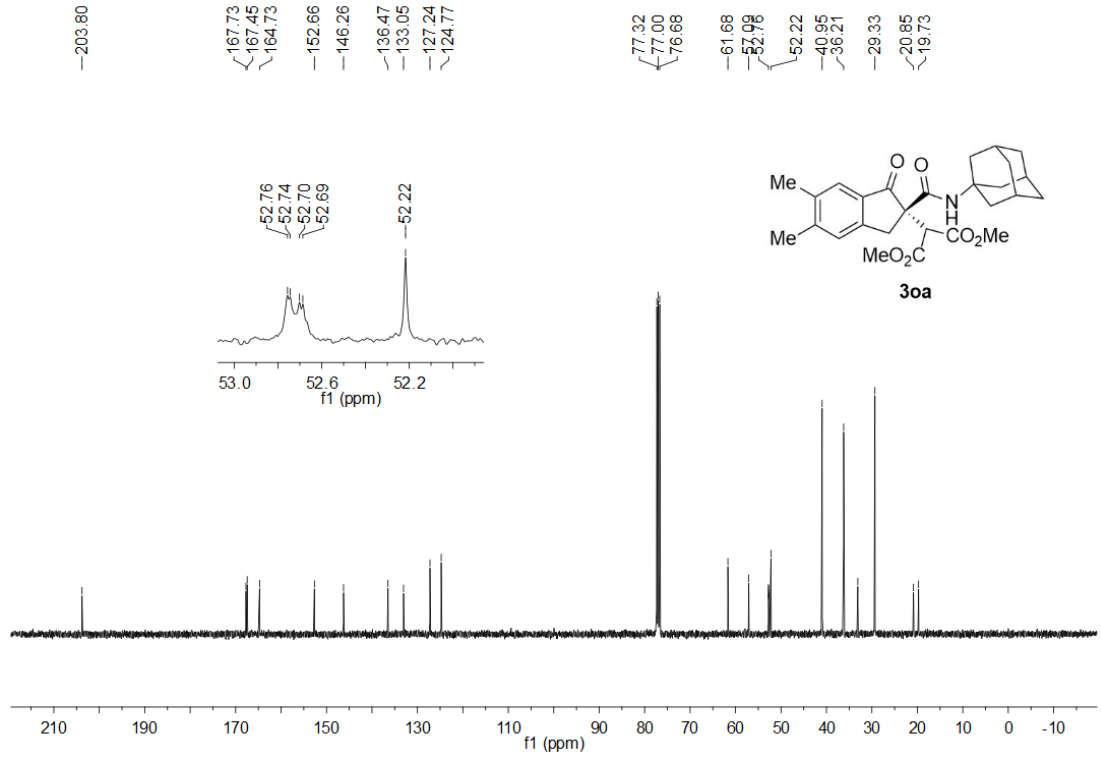


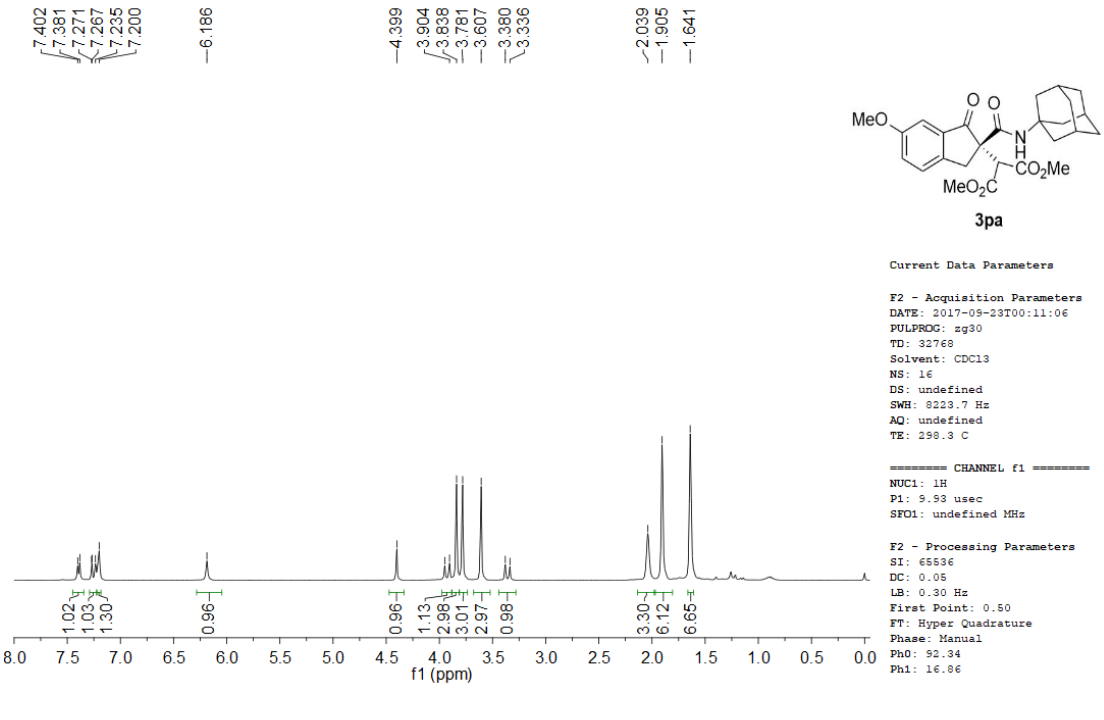



```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-22T23:50:35
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.3 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.48
Ph1: 17.02
Baseline: Bernstein
```

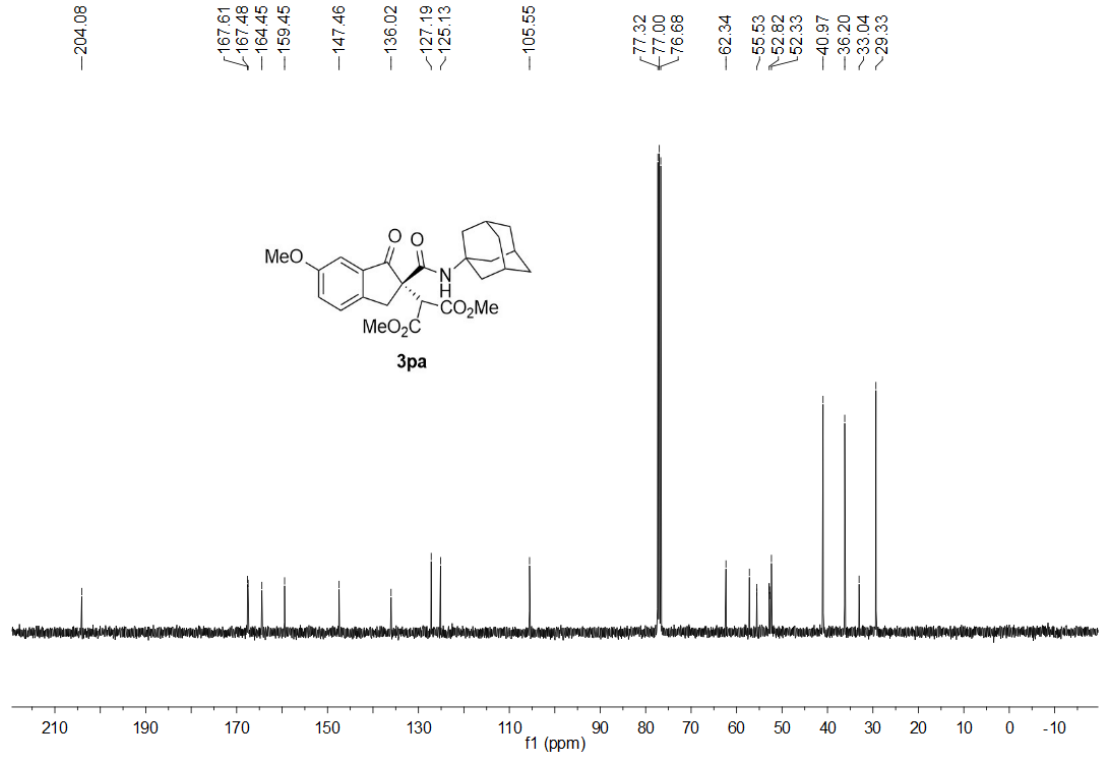

204.30
167.62
167.44
164.48
151.88
137.43
136.98
135.09
126.13
124.35
77.32
77.00
76.68
61.82
52.79
52.28
40.95
36.20
29.33
21.05
Me
O
O
N
H
CO2Me
MeO2C
3na
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

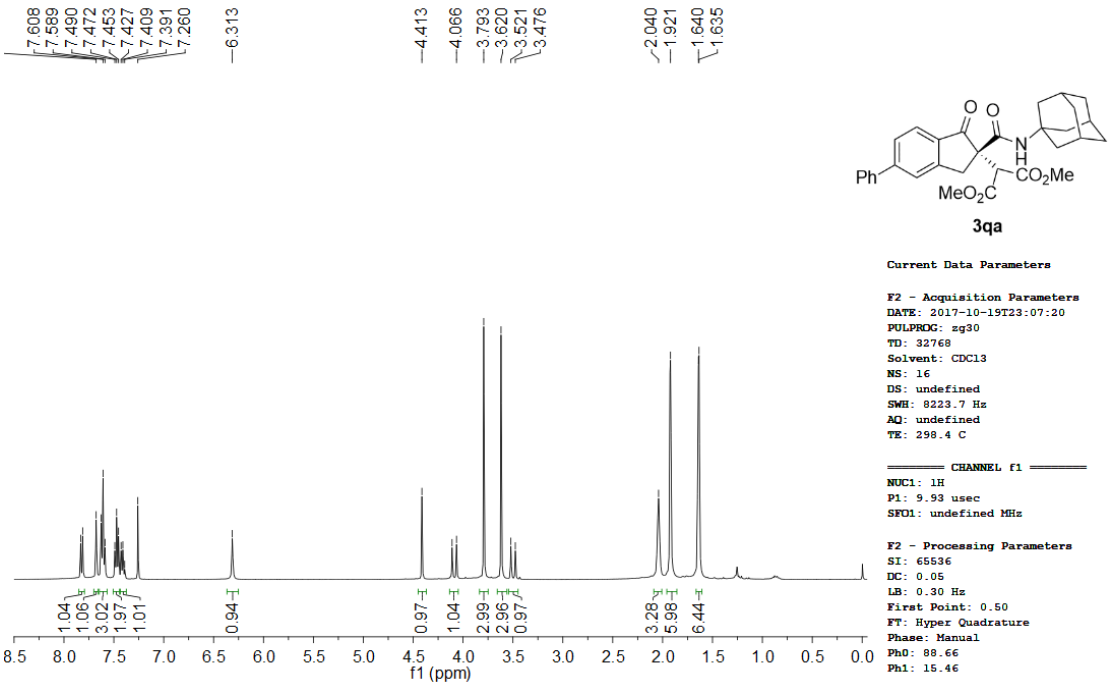

7.523
7.260
6.247
4.368
3.940
3.896
3.767
3.585
3.384
3.339
2.334
2.286
1.892
1.623
Me
Me
O
O
N
H
CO2Me
MeO2C
3oa
1.01
1.34
1.00
0.99
1.04
3.02
2.96
0.99
2.92
2.91
3.28
6.01
6.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-09-28T18:44:04
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -263.95
Ph1: 16.30



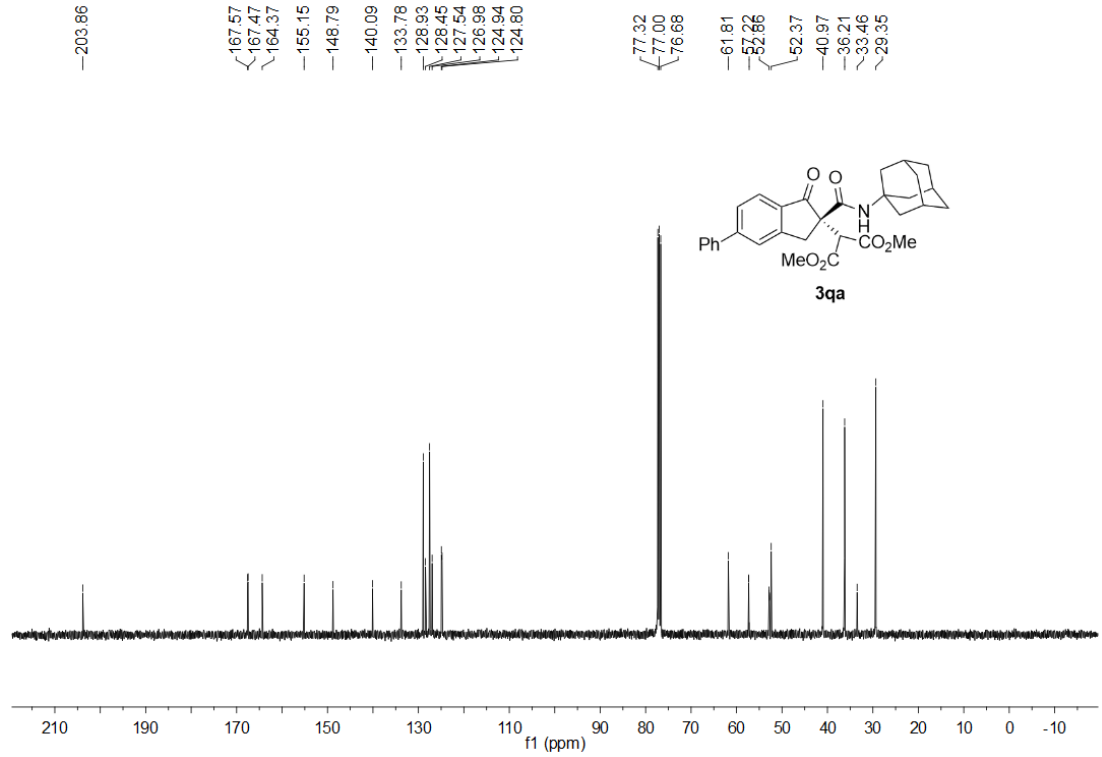


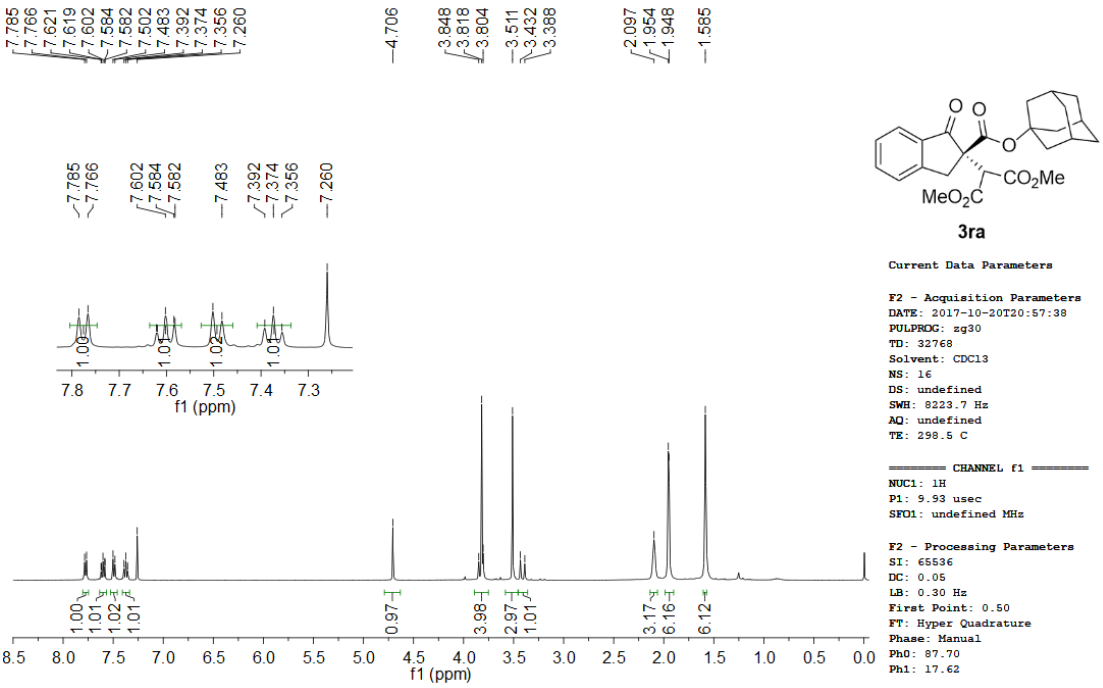

```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-23T00:11:06
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.3 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.34
Ph1: 16.86
```






```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-10-19T23:07:20
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.4 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 88.66
Ph1: 15.46
```



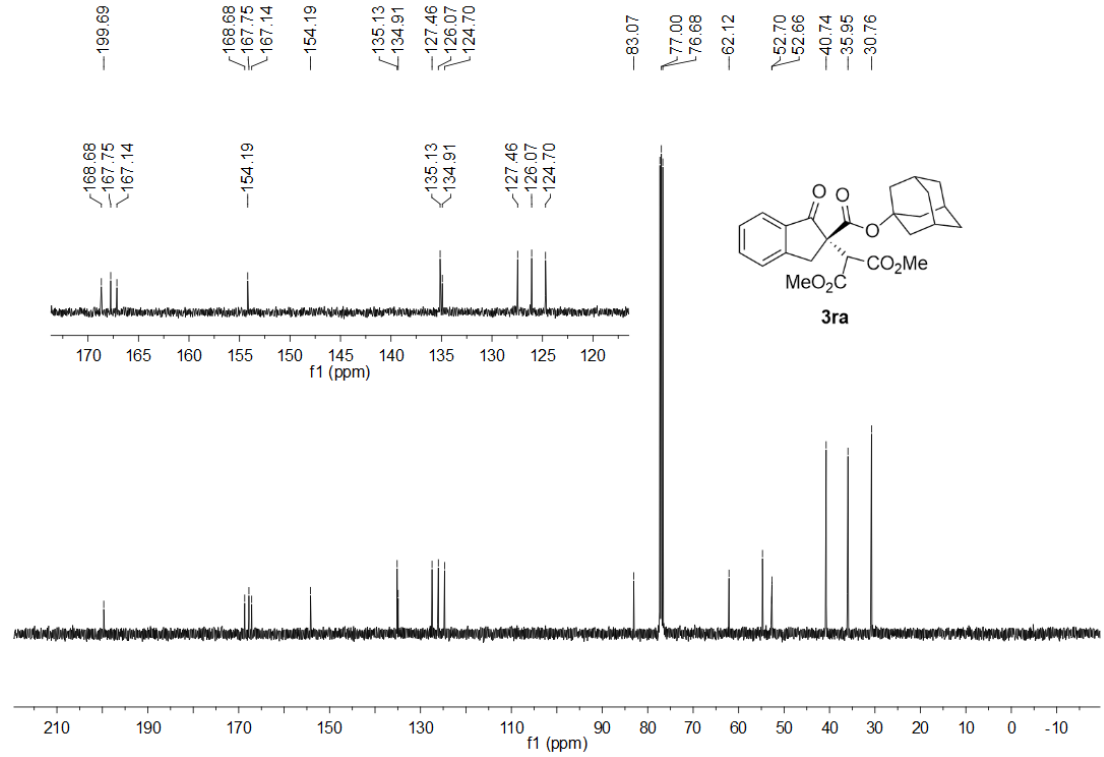


Current Data Parameters

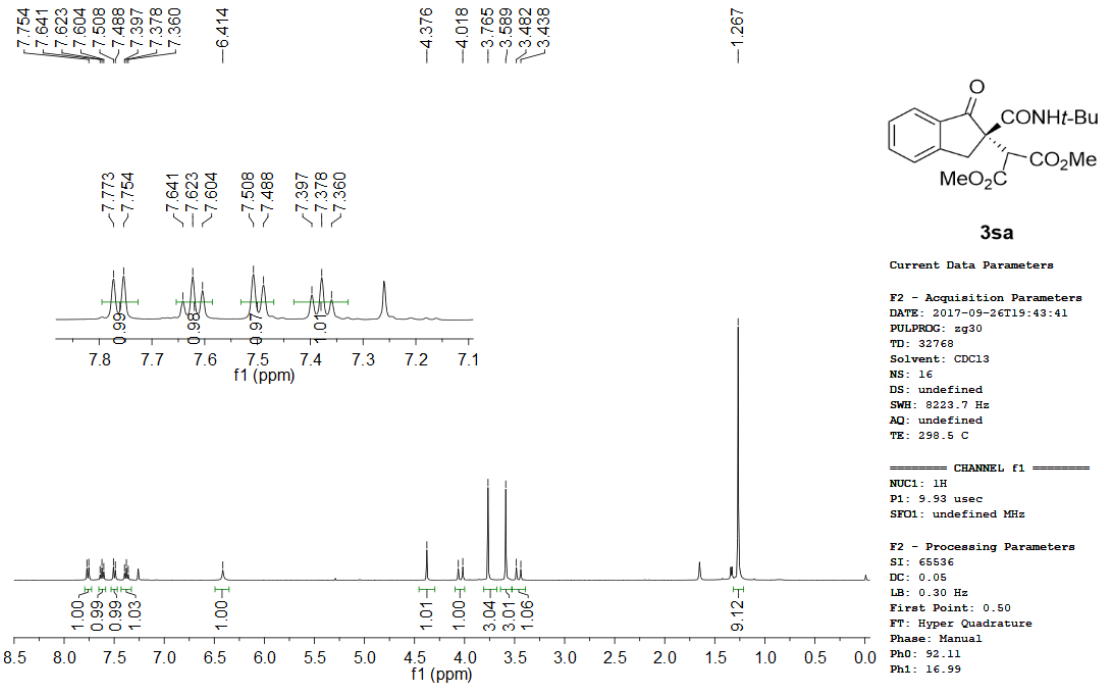
F2 - Acquisition Parameters
DATE: 2017-10-20T20:57:38
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.5 C

CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 87.70
Ph1: 17.62



3ra



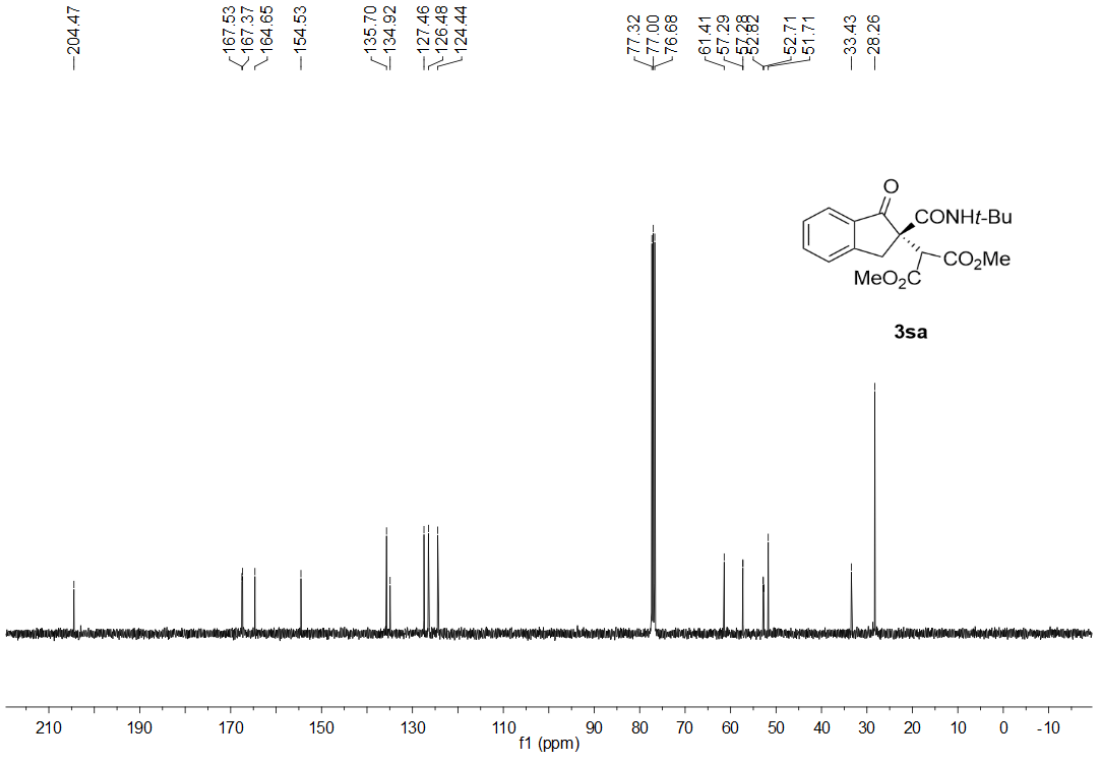
3sa

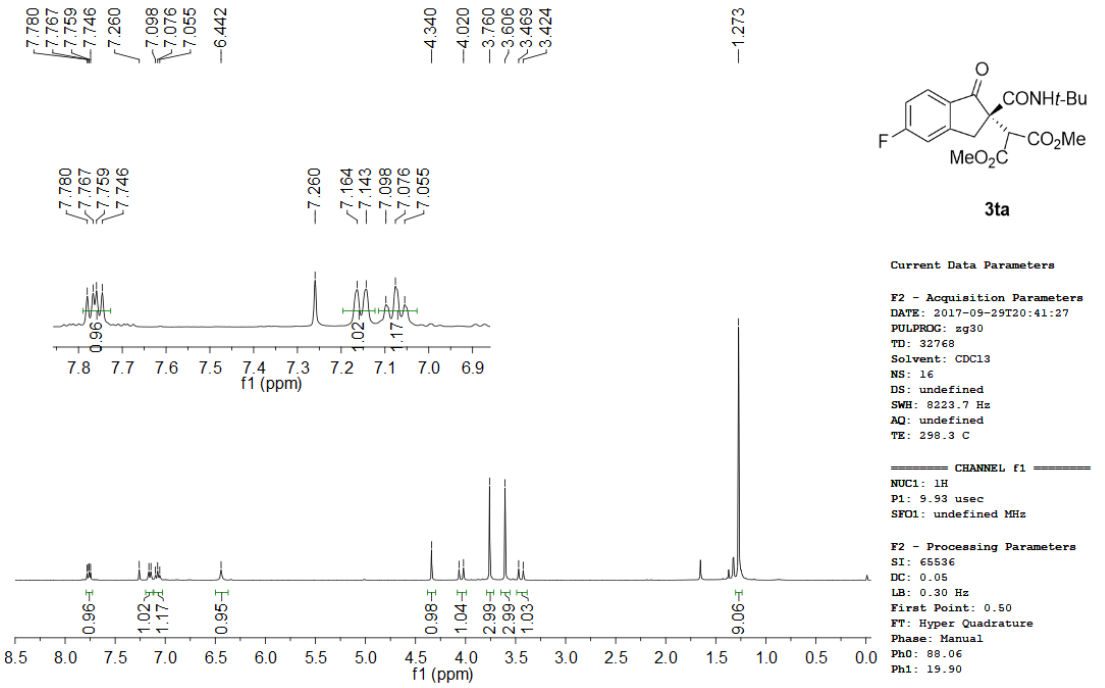
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-26T19:43:41
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.5 C

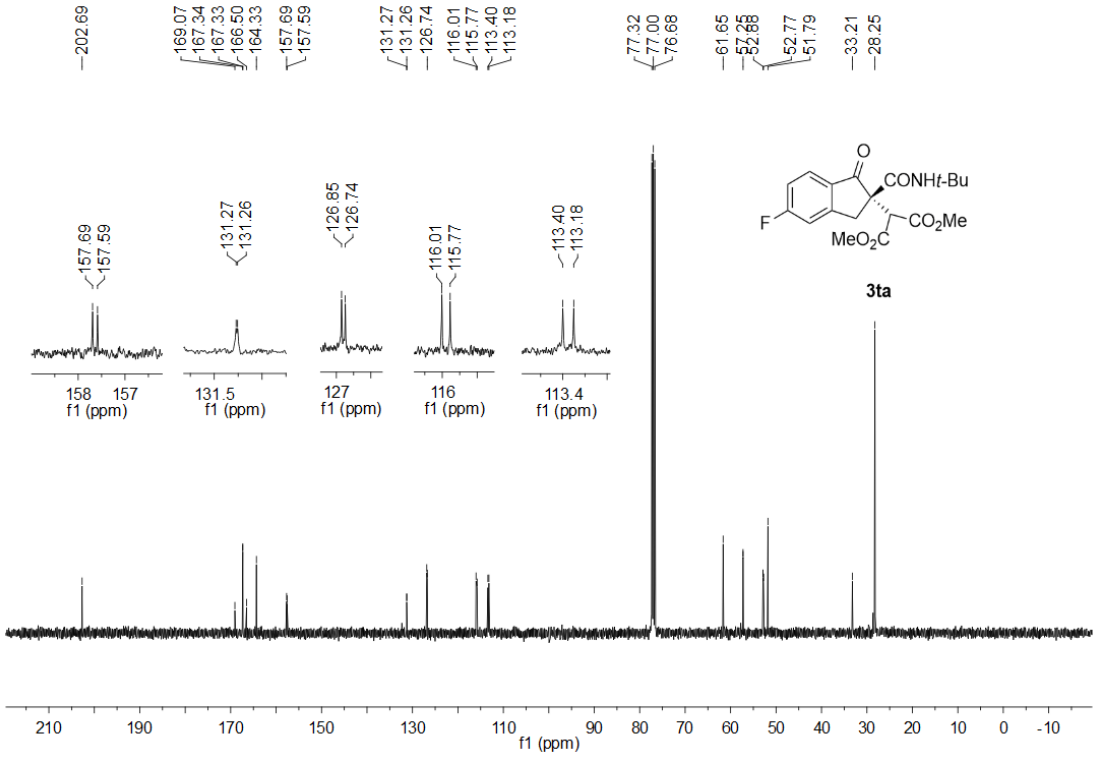
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

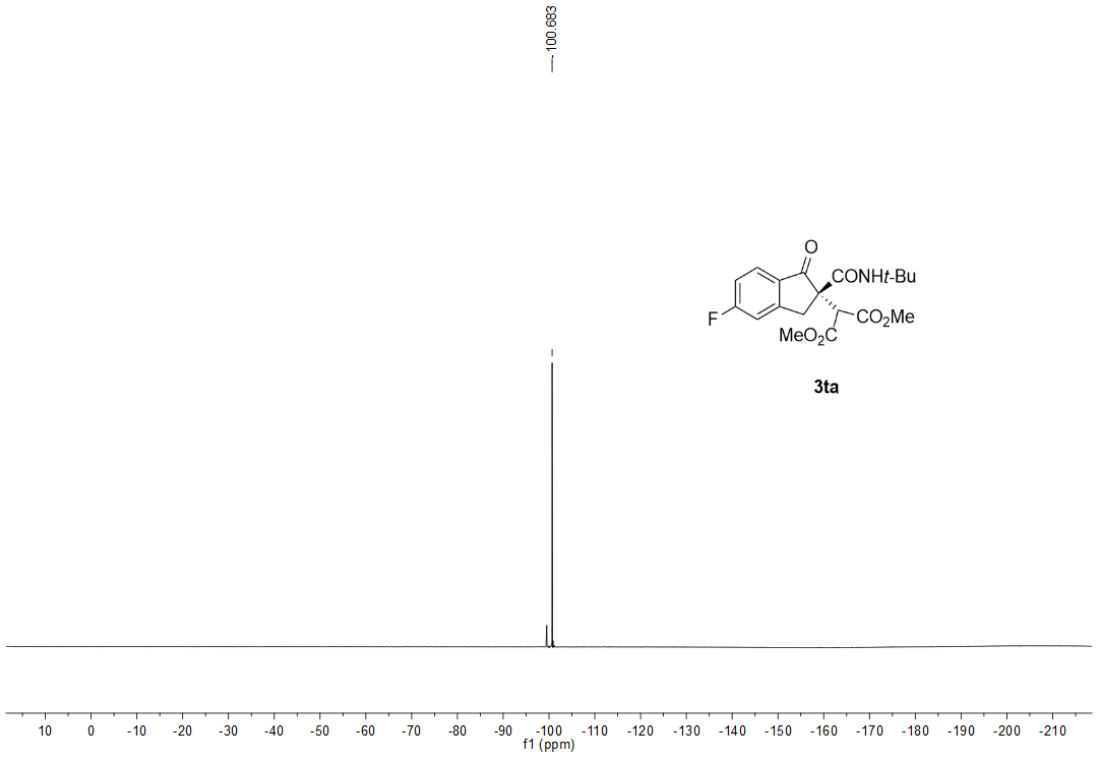
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 92.11
Ph1: 16.99

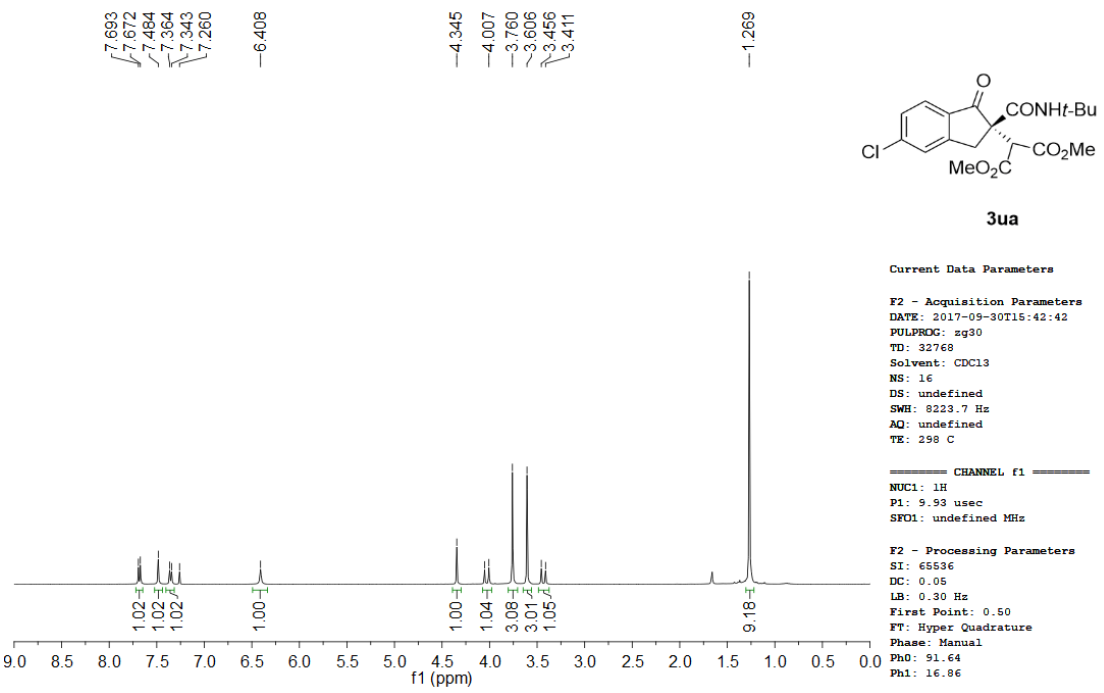


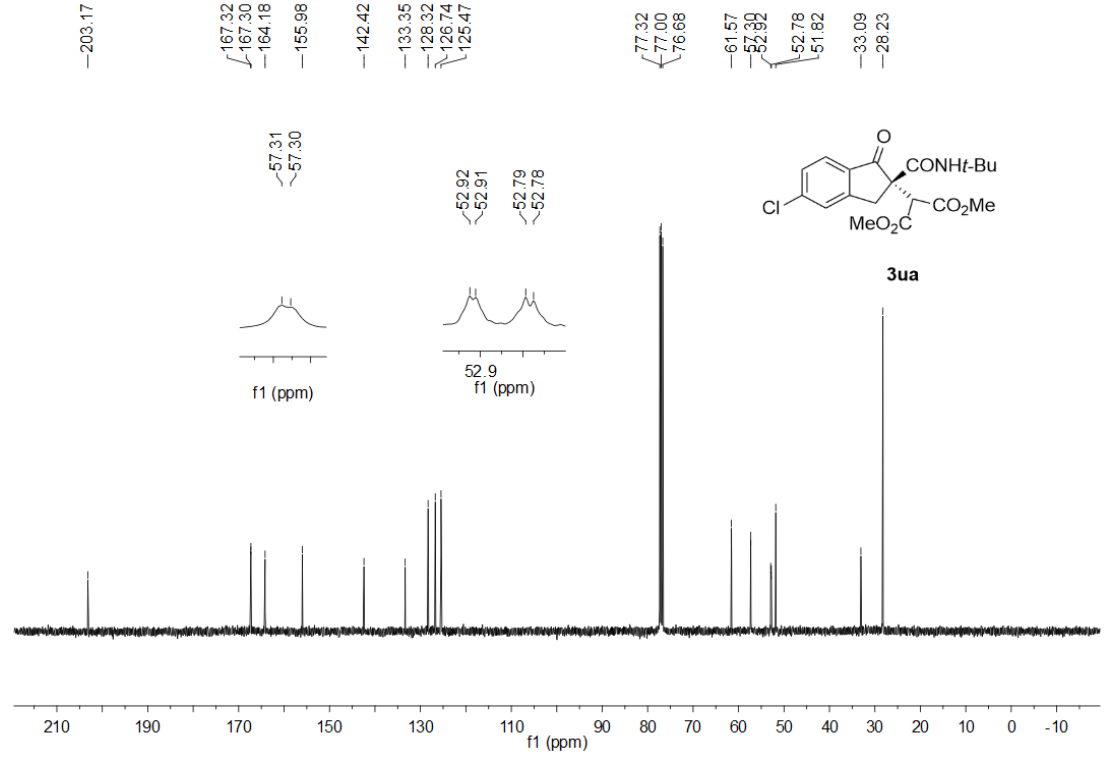


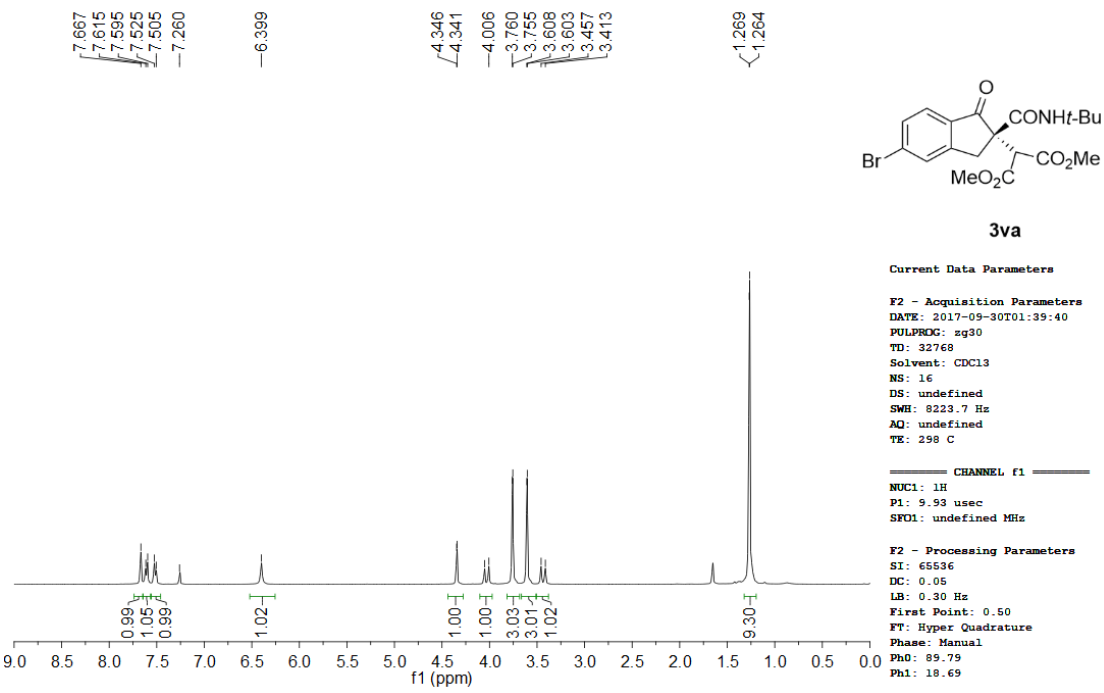

```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-09-29T20:41:27
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.3 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 88.06
Ph1: 19.90
```

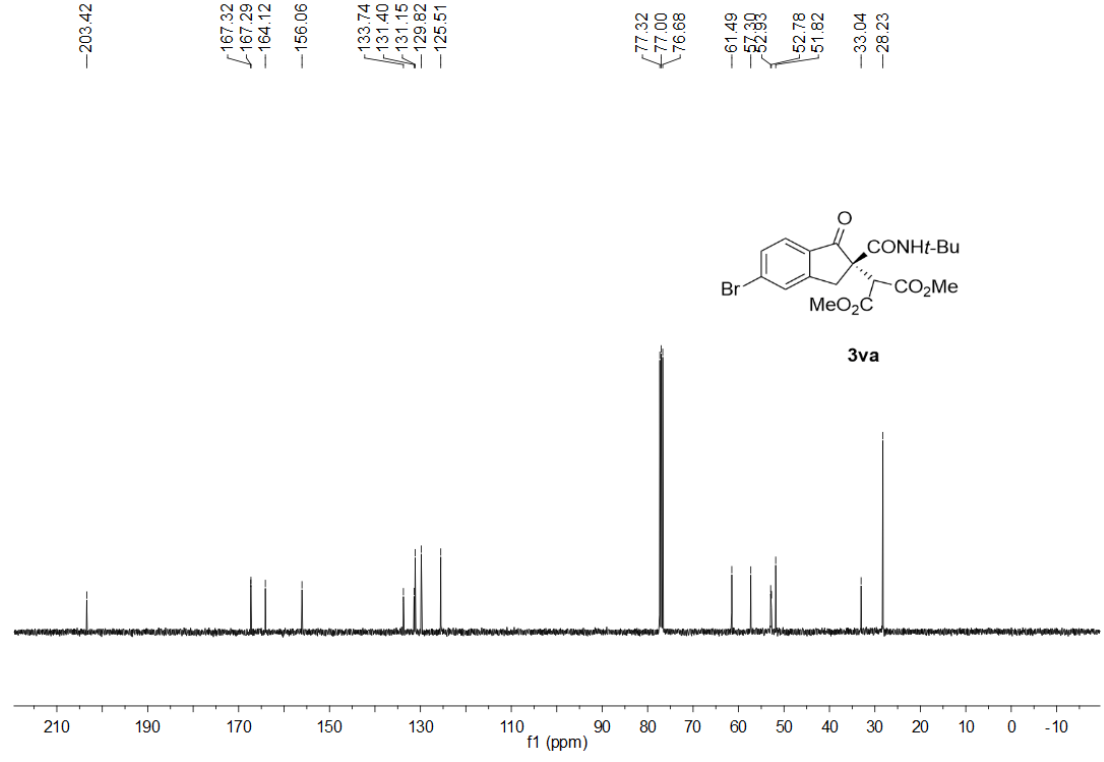

202.69
169.07
167.34
167.33
166.50
164.33
157.69
157.59
131.27
131.26
126.74
116.01
115.77
113.40
113.18
77.32
77.00
76.68
61.65
52.77
51.79
33.21
28.25
O
CONHt-Bu
F
CO2Me
MeO2C
3ta
158
157
131.5
127
116
113.4
f1 (ppm)

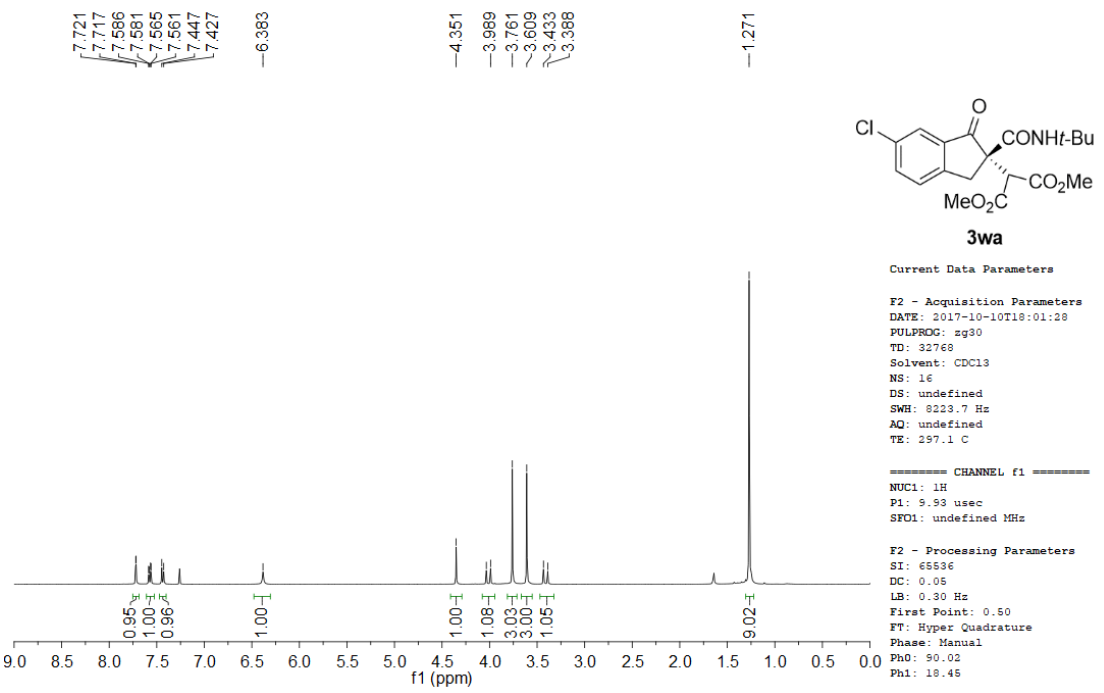

100.683
O
CONHt-Bu
F
CO2Me
MeO2C
3ta
f1 (ppm)

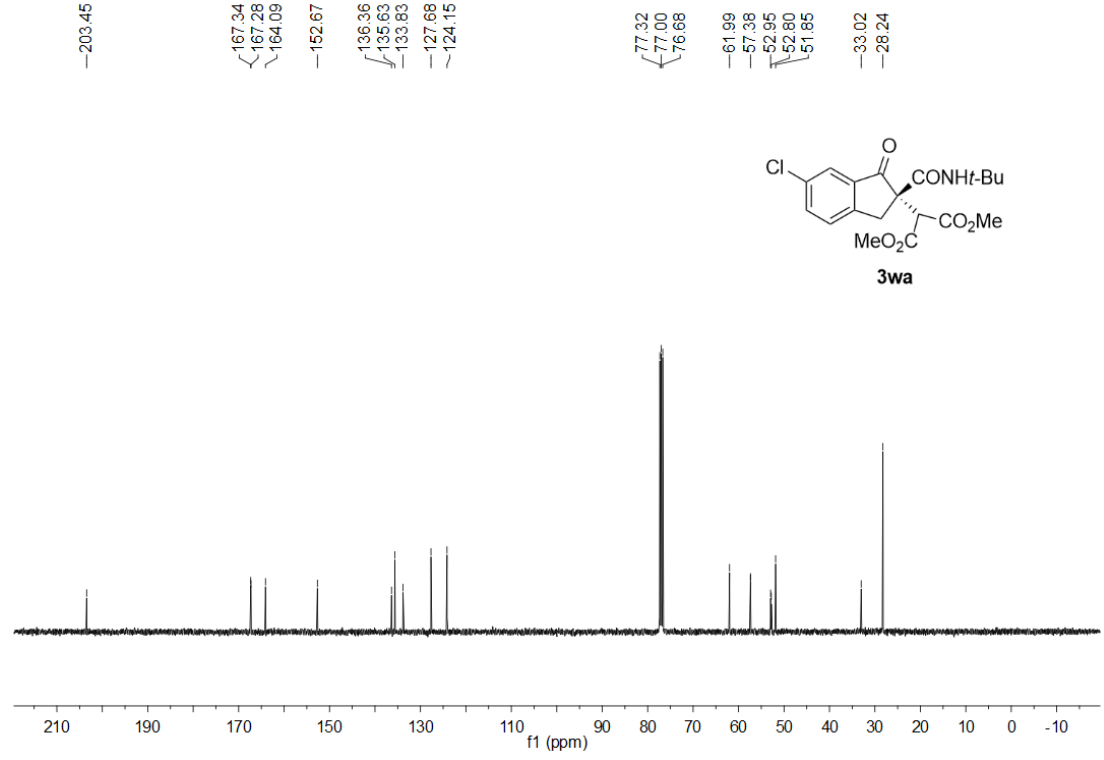

7.693
7.672
7.484
7.364
7.343
7.260
6.408
4.345
4.007
3.760
3.606
3.456
3.411
1.269
O
CONHt-Bu
Cl
CO2Me
MeO2C
3ua
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-09-30T15:42:42
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.64
Ph1: 16.86
1.02
1.02
1.02
1.00
1.00
1.04
3.08
3.01
1.05
9.18
f1 (ppm)

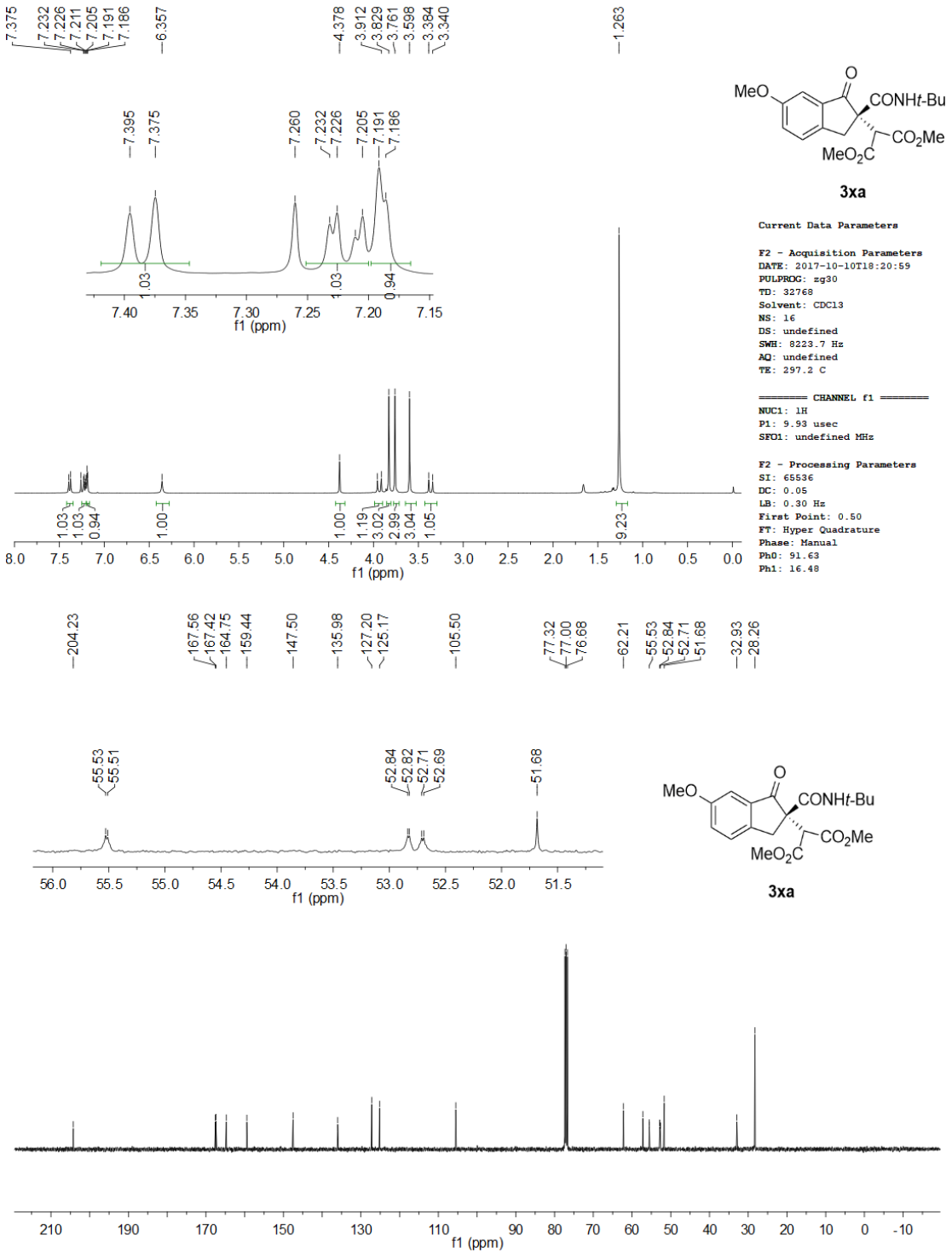

203.17
167.32
167.30
164.18
155.98
142.42
133.35
128.32
126.74
125.47
77.32
77.00
76.68
61.57
52.92
52.78
51.82
33.09
28.23
57.31
57.30
52.92
52.91
52.79
52.78
O
CONHt-Bu
Cl
CO2Me
MeO2C
3ua
f1 (ppm)
52.9
f1 (ppm)
f1 (ppm)

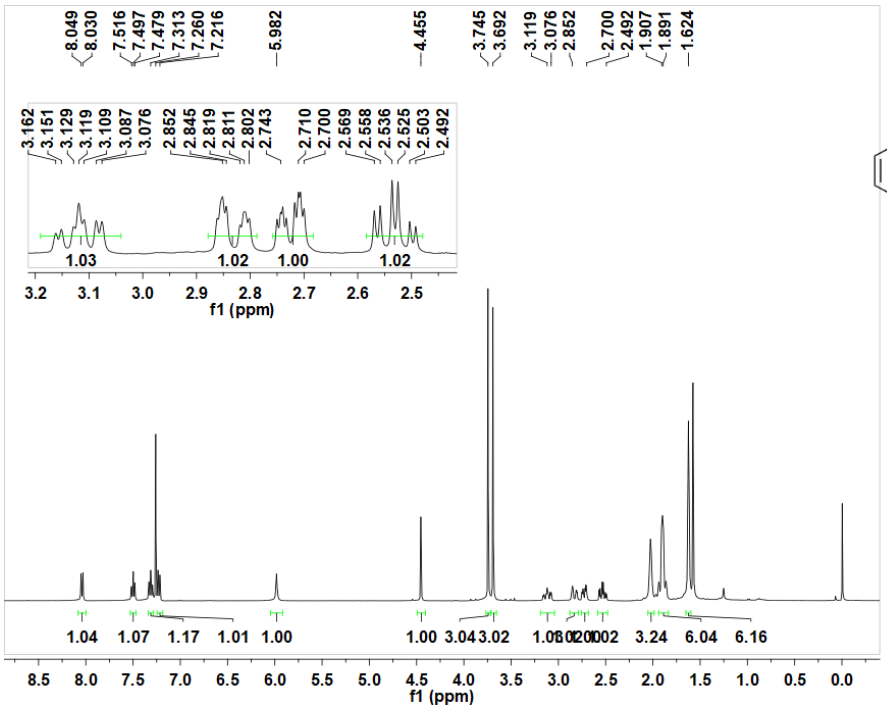

7.667
7.615
7.595
7.525
7.505
7.260
6.399
4.346
4.341
4.006
3.760
3.755
3.608
3.603
3.457
3.413
1.269
1.264
O
CONHt-Bu
Br
CO2Me
MeO2C
3va
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-09-30T01:39:40
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 89.79
Ph1: 18.69
0.99
1.05
0.99
1.02
1.00
1.00
3.03
3.01
1.02
9.30
f1 (ppm)

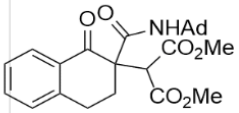

203.42
167.32
167.29
164.12
156.06
133.74
131.40
131.15
129.82
125.51
77.32
77.00
76.68
61.49
57.30
52.93
52.78
51.82
33.04
28.23
O
CONHt-Bu
Br
CO2Me
MeO2C
3va
f1 (ppm)


7.721
7.717
7.586
7.581
7.565
7.561
7.447
7.427
6.383
4.351
3.989
3.761
3.609
3.433
3.388
1.271
Cl
O
CONHt-Bu
CO2Me
MeO2C
3wa
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-10-10T18:01:28
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.1 C
======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 90.02
Ph1: 18.45
0.95
1.00
0.96
1.00
1.00
1.08
3.03
3.00
1.05
9.02
f1 (ppm)


203.45
167.34
167.28
164.09
152.67
136.36
135.63
133.83
127.68
124.15
77.32
77.00
76.68
61.99
57.38
52.95
52.80
51.85
33.02
28.24
Cl
O
CONHt-Bu
CO2Me
MeO2C
3wa
f1 (ppm)


7.375
7.232
7.226
7.211
7.205
7.191
7.186
6.357
4.378
3.912
3.829
3.761
3.598
3.384
3.340
1.263
MeO
O
CONHt-Bu
CO2Me
MeO2C
3xa
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-10-10T18:20:59
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.2 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 91.63
Ph1: 16.48
f1 (ppm)
204.23
167.56
167.42
164.75
159.44
147.50
135.98
127.20
125.17
105.50
77.32
77.00
76.68
62.21
55.53
52.84
52.71
51.68
32.93
28.26
55.53
55.51
52.84
52.82
52.71
52.69
51.68
f1 (ppm)
MeO
O
CONHt-Bu
CO2Me
MeO2C
3xa
f1 (ppm)





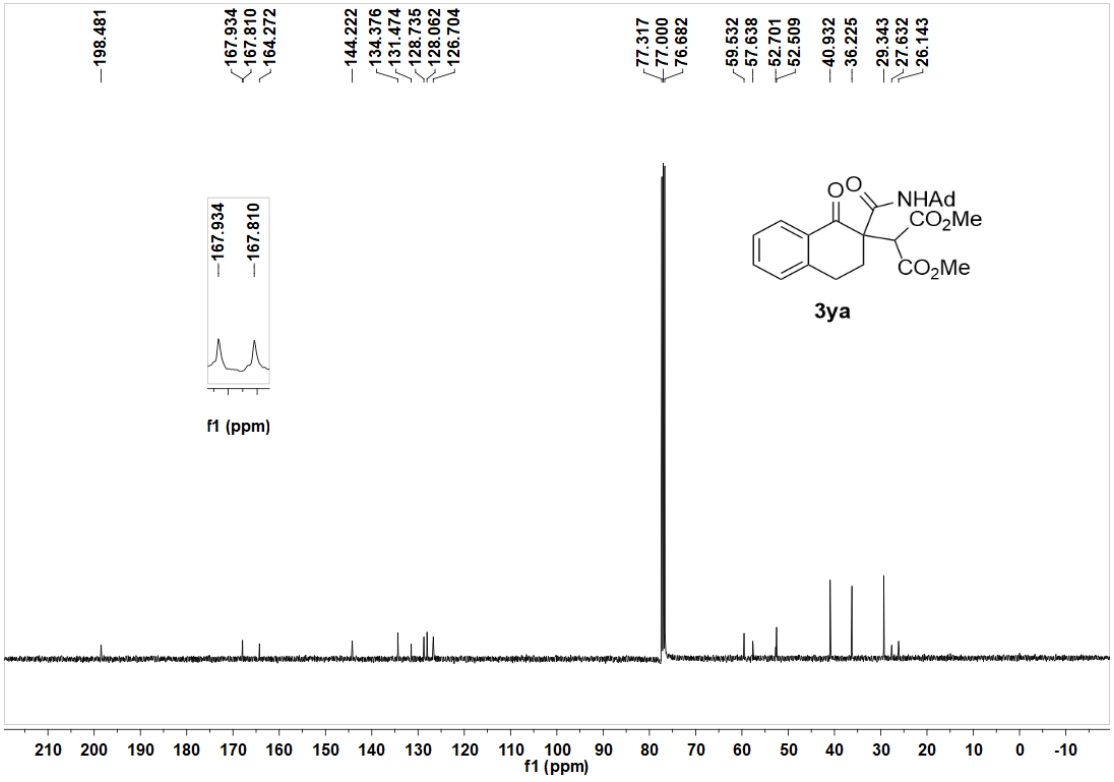
3ya

Current Data Parameters

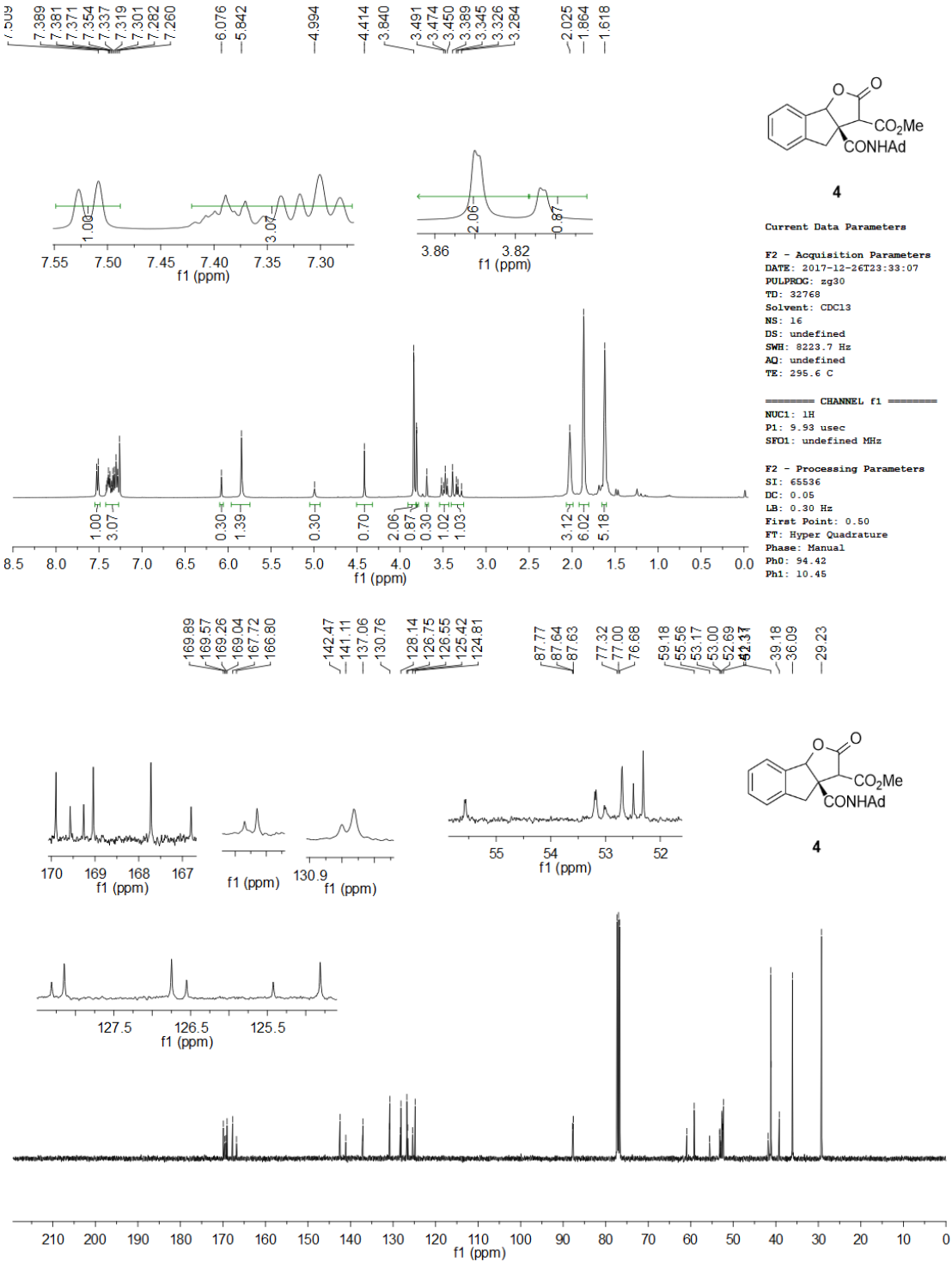
F2 - Acquisition Parameters
DATE: 2018-09-22T07:18:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 128
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.7 C

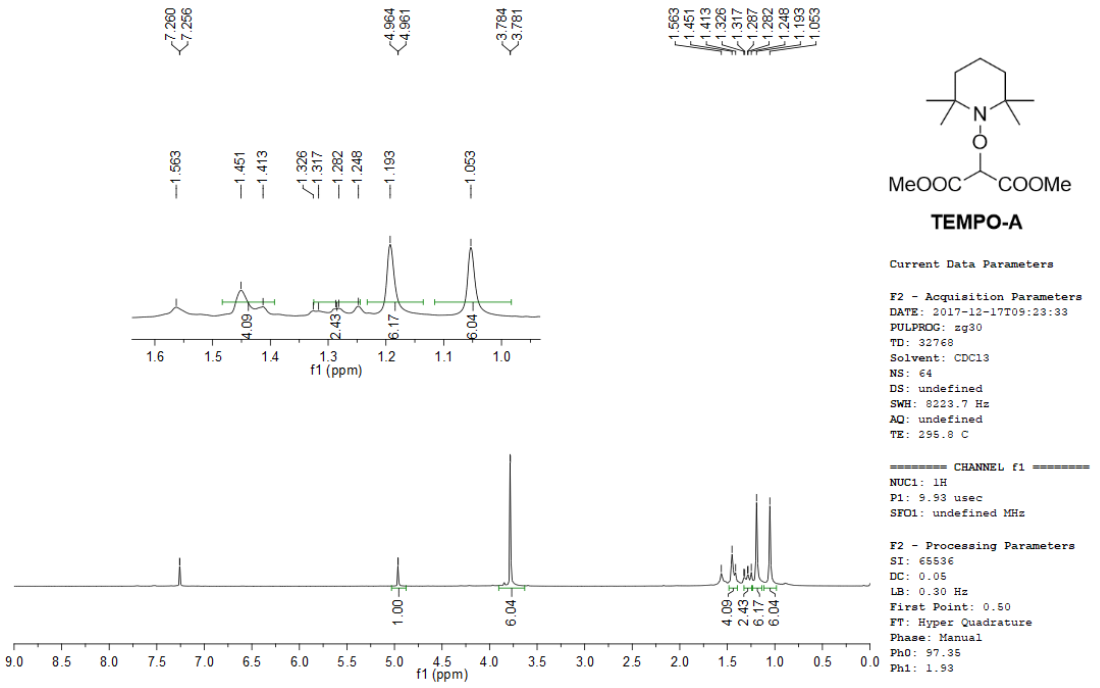
======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
FT: Hyper Quadrature
Phase: Global
Baseline: Bernstein



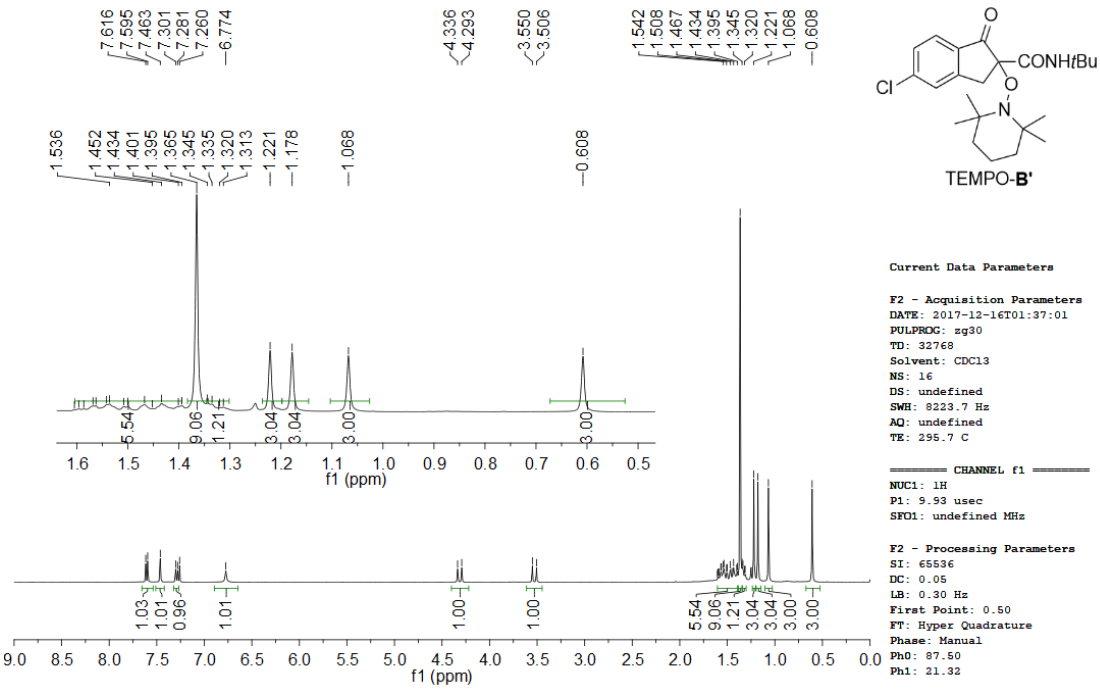
3ya


7.389
7.381
7.371
7.354
7.337
7.319
7.301
7.282
7.260
6.076
5.842
4.994
4.414
3.840
3.491
3.474
3.450
3.389
3.345
3.326
3.284
2.025
1.864
1.618
CO2Me
CONHAd
4
Current Data Parameters
F2 - Acquisition Parameters
DATE: 2017-12-26T23:33:07
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.6 C
CHANNEL f1
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz
F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 94.42
Ph1: 10.45
f1 (ppm)
169.89
169.57
169.26
169.04
167.72
166.80
142.47
141.11
137.06
130.76
128.14
126.75
126.55
125.42
124.81
87.77
87.64
87.63
77.32
77.00
76.68
59.18
55.56
53.17
53.00
52.69
39.18
36.09
29.23



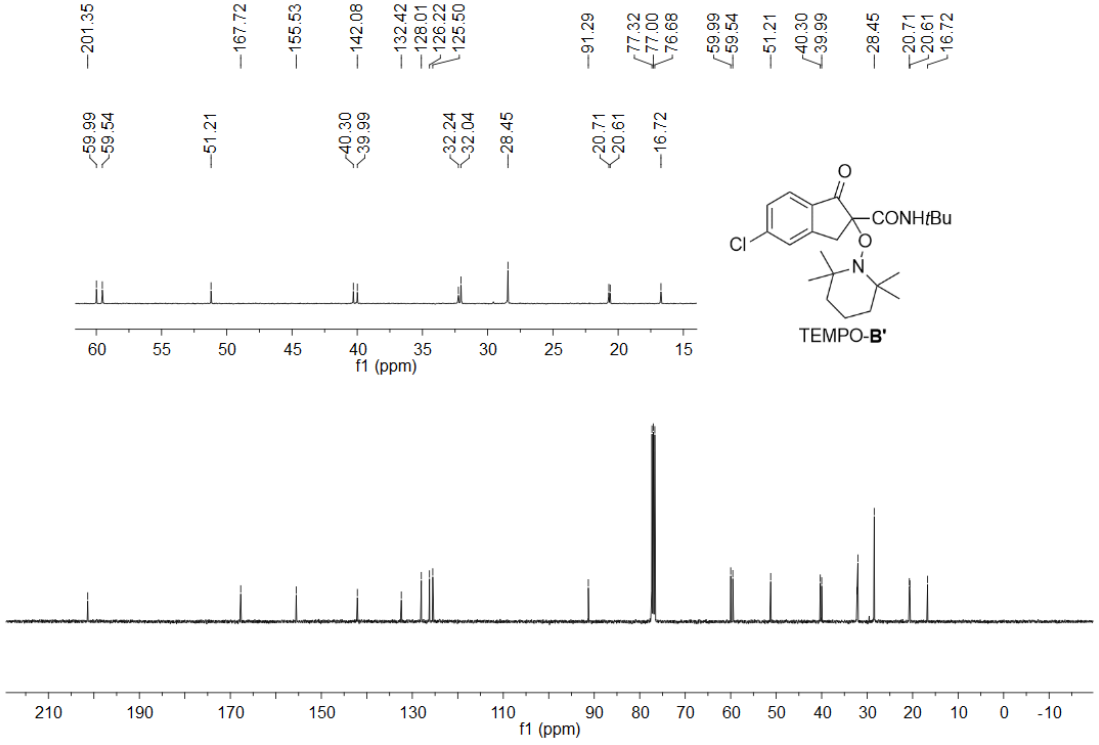
TEMPO-A

```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-12-17T09:23:33
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 64
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.8 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 97.35
Ph1: 1.93
```



TEMPO-**B'**

```
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2017-12-16T01:37:01
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.7 C

======== CHANNEL f1 ========
NUC1: 1H
P1: 9.93 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 87.50
Ph1: 21.32
```



9. References

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2 J. Guo, Y. B. Liu, X. Q. Li, X. H. Liu, L. L. Lin, X. M. Feng, *Chem. Sci.* 2016, **7**, 2717.

3 J. Guo, L. L. Lin, Y. B. Liu, X. Q. Li, X. H. Liu, X. M. Feng, *Org. Lett.* 2016, **18**, 5540.