Supporting Information

Metal-free semiconductor for the visible-light-induced carbocarboxylation of styrenes with aliphatic redox-active esters and CO_2

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1. General information

If not special indicated, reagents and solvents were used as commercially available without further purification. Column chromatographic purification of products was accomplished using 300-400 mesh silica gel. NMR spectrum were measured on a Bruker Avance spectrometer in the solvents indicated; Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Gas chromatography mass spectra (GC-MS) were taken at Thermo Trace 1300 gas chromatograph mass spectrometer and a TR-5MS column (0.25 mm × 30 m, Film: 0.25 μm). High resolution mass spectroscopy (HRMS) analysis was performed at an Exactive Plus (Thermo Scientific) or Agilent 8890-7250. X-ray diffraction (XRD) measurements were performed on a Bruker D8 Advance diffractometer with Cu Kα1 radiation (λ = 1.5406 Å). The fourier transform infrared (FT-IR) spectra were obtained on a Nicolet 670 FT-IR spectrometer with KBr as the diluents. The UV-vis diffuse reflectance spectra (UV-vis DRS) were performed on a Varian Cary 500 Scan UV visible system. The BET surface area was calculated using the Brunauer-Emmett-Teller (BET) method. X-Ray photoelectron spectroscopy (XPS) data were collected on a Thermo Scientific ESCALAB250 instrument with a monochromatized Al Kα line source (200 W). Transmission electron microscopy (TEM) was operated by Tecnai20 FEG microscope. The scanning emission microscope (SEM) measurements were carried out by using Hitachi S4800 Field Emission Scanning Electron Microscope.

2. Preparation of BCN

Ceramic BCN was synthesized according to Ref. [1-3] with slight modification. Typically, 1 g of boric acid, 2 g of urea and a certain amount of glucose were grinded fully in an agate mortar. Later, the mixed precursor was transferred to a horizontal tube furnace. A flow of ammonia (0.25 L min^{-1}) was pumped into the tube for 10 min to expel air before heating up. Then the mixture was heated to 373 K for 30 min and went on heating to 1523 K for 5 h at a heating rate of 5 K·min^{-1}. Next, the mixture was cooled to 773 K for 150 min at a cooling rate of 5 K·min^{-1}. Finally, the mixture is naturally cooled to room temperature. The obtained sample was washed with water and EtOH three times and dried, denoted as BCN$_x$, where x (600, 800, 1000) is the percentage weight content of glucose to boric acid.

3. Characterization of BCN

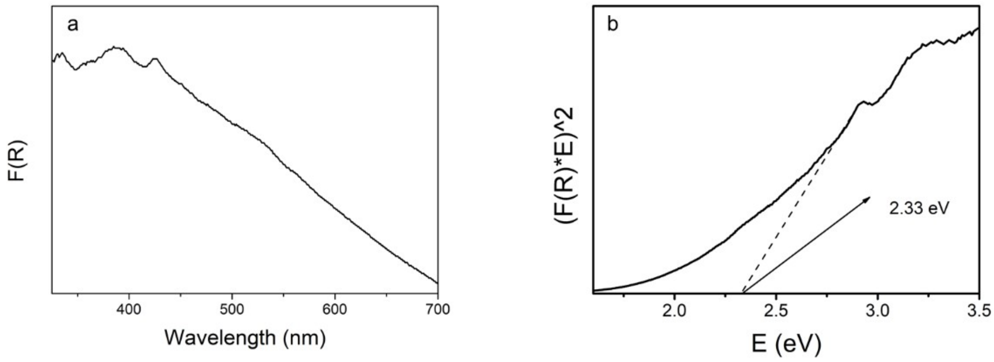


Figure S1. (a) UV-vis DRS of BCN; (b) the $(F(R)*E)^2$ versus E plot of BCN.

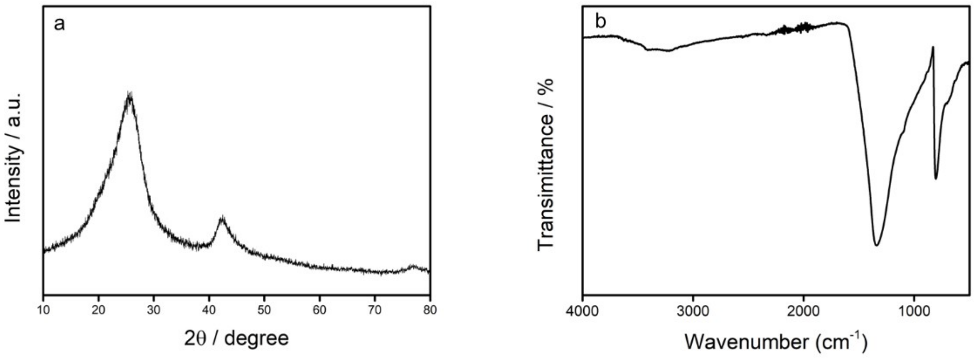


Figure S2. (a) Powder X-ray diffraction (XRD) pattern of BCN; (b) FT-IR of BCN.

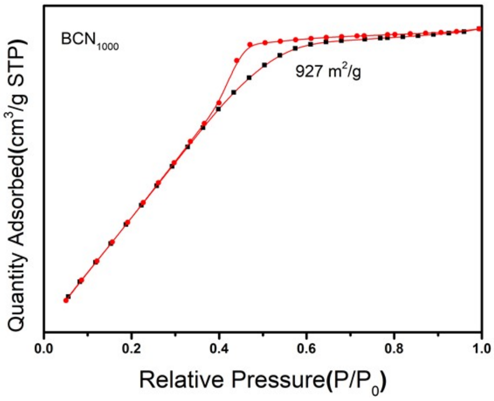


Figure S3. N_2 adsorption and desorption isotherms of BCN.

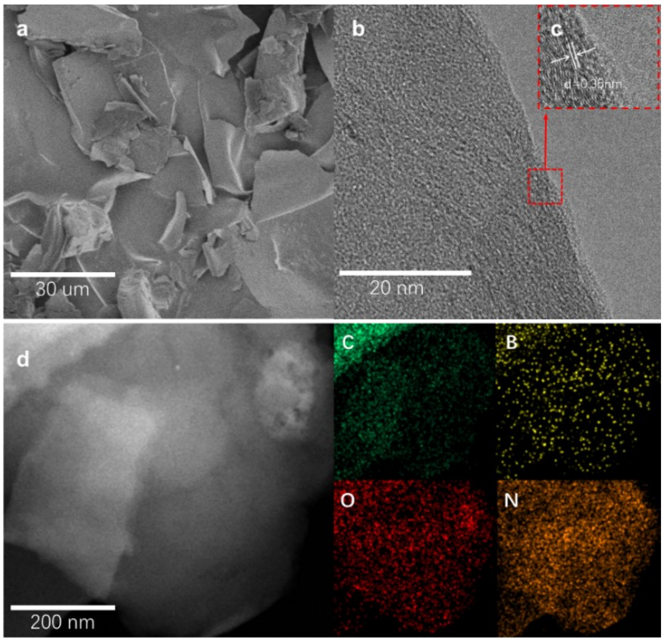


Figure S4. (a) SEM image of BCN; (b) TEM image of BCN; (c) HR-TEM image highlighted by the red dashed box in (b); (d) High-Angle Annular Dark Field (HAADF) image of BCN and elemental mapping images of B, C, N, O.

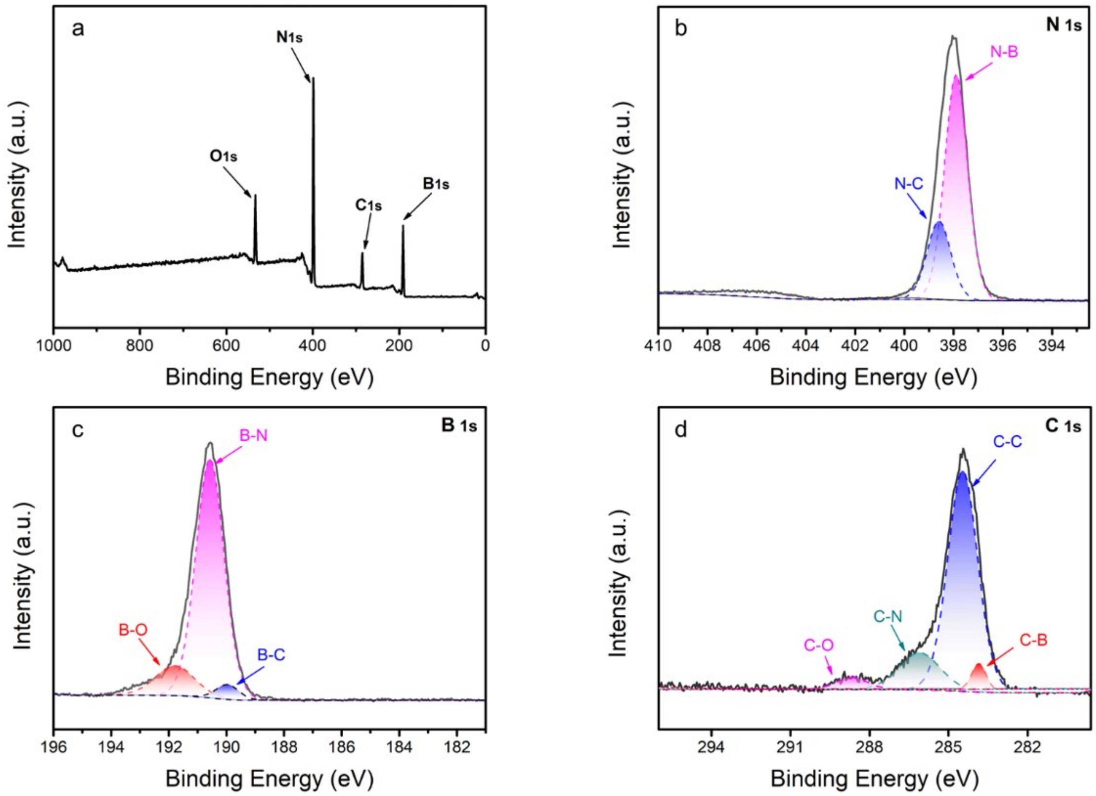
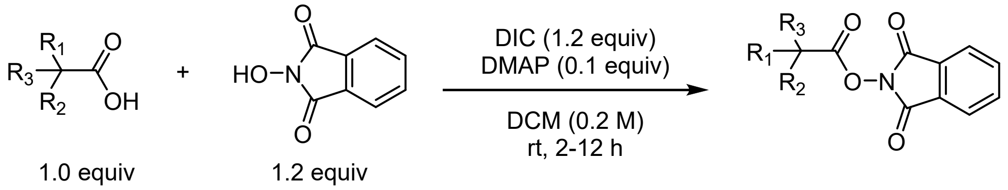


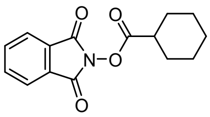
Figure S5. XPS spectra of BCN: (a) survey spectrum and the high-resolution spectra of (b) N 1s, (c) B 1s, (d) C 1s.

4. Synthesis of RAEs

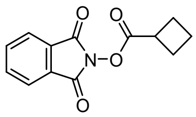


A round-bottom flask or culture tube was charged with (if solid) carboxylic acid (1.0 equiv), nucleophile (N-hydroxyphthalimide 1.2 equiv) and DMAP (0.1 equiv). Dichloromethane was added (0.2 M), and the mixture was stirred vigorously. Carboxylic acid (1.0 equiv) was added via syringe (if liquid). DIC (1.2 equiv) was then added dropwise via syringe, and the mixture was allowed to stir until the acid was consumed (determined by TLC). Typical reaction times were between 2 h and 12 h. The mixture was filtered (over Celite, SiO_2, or through a fritted funnel) and rinsed with additional CH_2Cl_2. The solvent was removed under reduced pressure, and purification by column chromatography afforded corresponding activated esters, which were used without further purification unless otherwise noted. [4-6]

RAEs (2a-q)



2a



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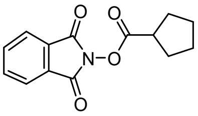

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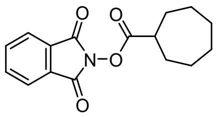

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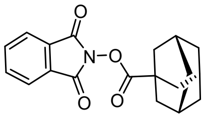
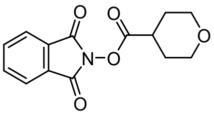


2e



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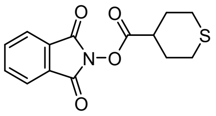

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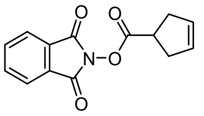

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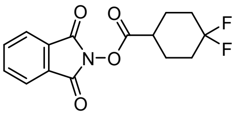

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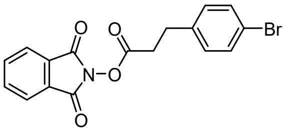

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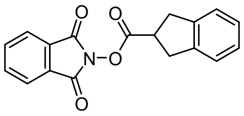

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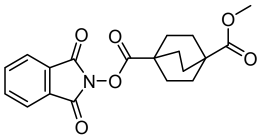

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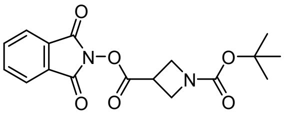
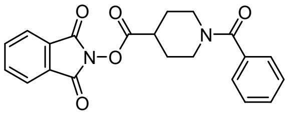
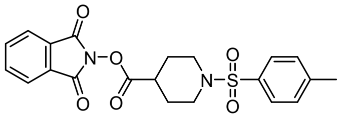


2l



2k



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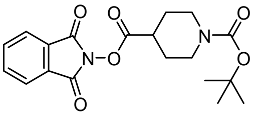

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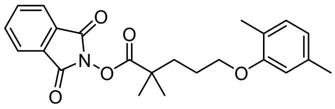

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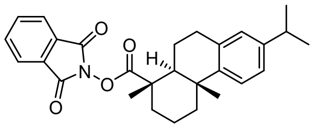
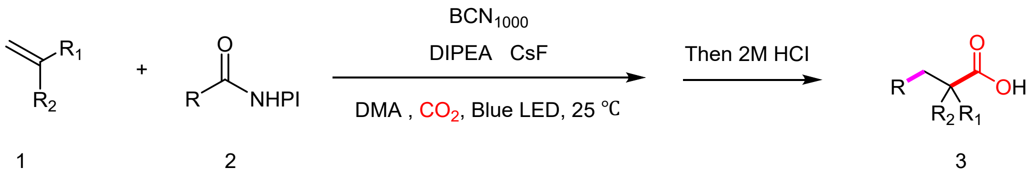


2r

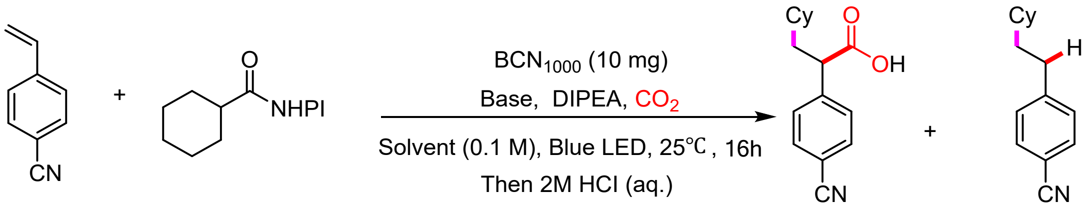
5. Experimental procedures

General procedure A



To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN_{1000} (10 mg), RAEs (0.15 mmol, 1.5 equiv) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with CO_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) and styrenes (0.1 mmol, 1.0 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a “freeze-pump-haw” procedure (3 times). Then the Schlenk tube was back-filled with CO_2 and sealed at atmospheric pressure of CO_2 (1 atm). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. After reaction, the resulting mixture was diluted with 3 mL EtOAc and quenched by 1 mL 2 M HCl, then stirred for 5 min. The reaction mixture was extracted by EtOAc three times and the combined organic phases were concentrated in vacuo. The residue was purified by silica gel flash column chromatography using petroleum ether/EtOAc/AcOH (0.5%) as eluent to give the pure desired product.

Table S1. Conditional screening for carboxylation of olefins. [a]



1a **2a** **3aa** **3aa'**

Entry[a]	PC	R_3N	Base	Solvent	Yield[b] 3aa（%）	Yield[b]3aa'（%）
1	BCN-1000	DIPEA	Cs_2CO_3	DMA	46	12
2	BCN-800	DIPEA	Cs_2CO_3	DMA	34	16
3	BCN-600	DIPEA	Cs_2CO_3	DMA	8	24
4	BCN-1000	DIPEA	K_2CO_3	DMA	38	8
5	BCN-1000	DIPEA	t-BuoK	DMA	trace	14
6	BCN-1000	DIPEA	DBU	DMA	14	trace
7	BCN-1000	DIPEA	CsF	DMA	68	12
8	BCN-1000	DIPEA	CsF	DMF	54	14
9	BCN-1000	DIPEA	CsF	NMP	32	12
10	BCN-1000	DIPEA	CsF	MeCN	nd	11
11[c]	BCN-1000	DIPEA	CsF	DMA	78	14
12	BCN-1000	Et_3N	CsF	DMA	32	19
13	BCN-1000	DABCO	CsF	DMA	14	10
14	*fac*-$Ir(ppy)_3$	DIPEA	CsF	DMA	28	16
15	$Ru(ppy)_3\ CI_3\ 6H_2O$	DIPEA	CsF	DMA	14	20

[a] Reaction conditions:**1a** (0.1 mmol), **2a** (0.15 mmol), BCN_{1000}(10 mg), base (0.15mmol), DIPEA (0.3 mmol), DMA (1mL),1 atm CO_2, blue LED, 25 °C, 16 h, quenched with HCl (2 M) solution, after extraction with ethyl acetate. [b] Yields determined by NMR using dibromomethane as an internal standard; [c] CsF (0.2 mmol).

6. Mechanistic studies

(a) Stern-Volmer quenching

For fluorescence quenching experiments, a suspension of the BCN photocatalyst (5 mg) in anhydrous DMA (2.5 mL,) was prepared under nitrogen atmosphere in a gas-tight 10 mm quartz cuvette. The BCN was excited with 375 nm and the change of the fluorescence emission upon addition of different potential quenchers was recorded.

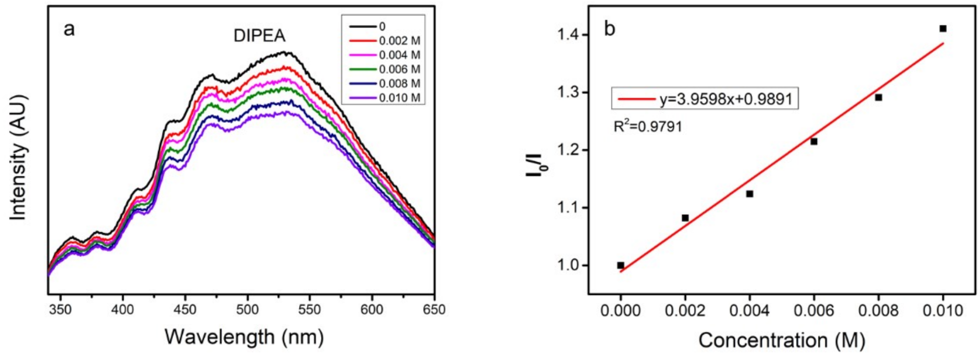


Figure S6. Stern –Volmer fluorescence quenching experiments with DIPEA.

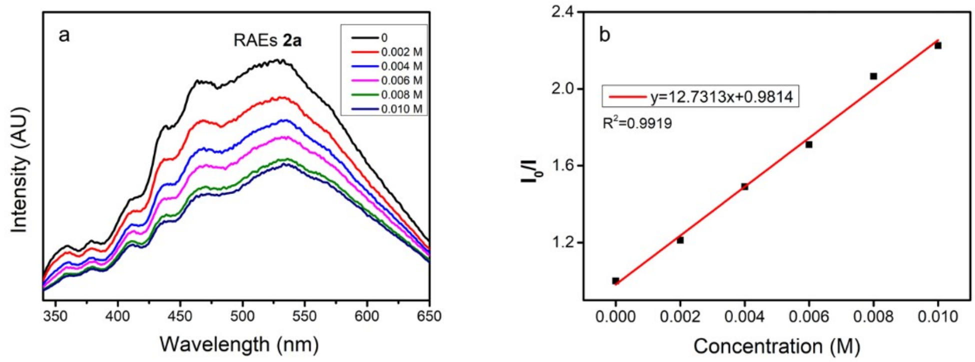


Figure S7. Stern –Volmer fluorescence quenching experiments with RAEs **2a**.

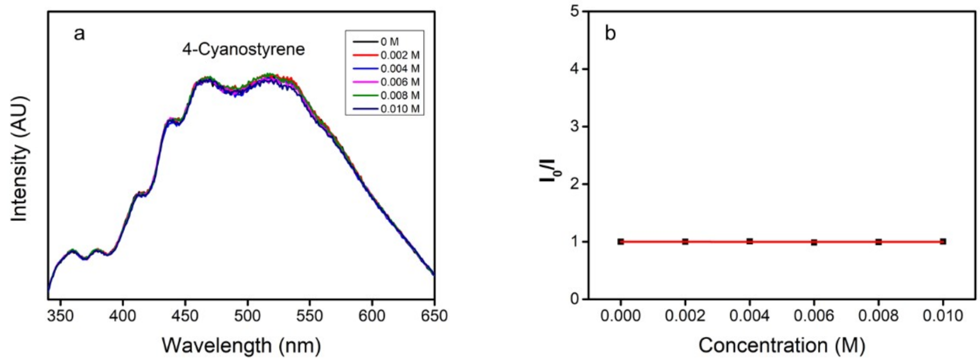


Figure S8: Stern –Volmer fluorescence quenching experiments with 4-cyanostyrene **1a**.

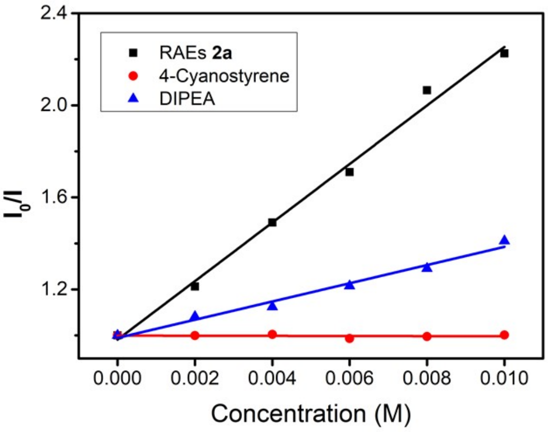
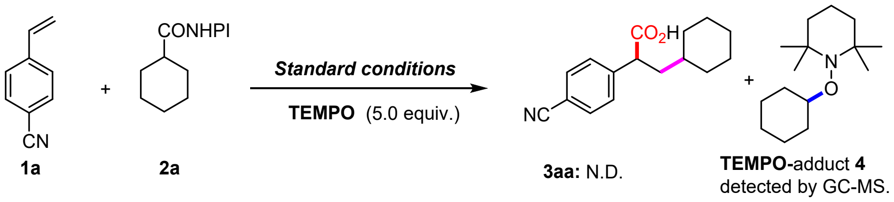


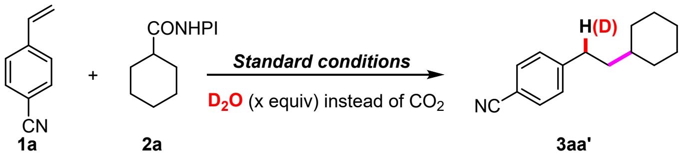
Figure S9: Comparison of quenching efficiency of 4-cyanostyrene **1a**, RAEs **2a**, and DIPEA.

(b) Radical trapping with TEMPO



To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN_{1000} (10 mg). **2a** (0.15 mmol, 1.5 equiv), anhydrous CsF (0.2 mmol, 2.0 equiv.) and TEMPO (0.5 mmol, 5.0 equiv). The tube was sealed and evacuated and back-filled with CO_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) and 4-cyanostyrene **1a** (0.1 mmol, 1.0 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a "freeze-pump-haw" procedure (3 times). Then the Schlenk tube was back-filled with CO_2 and sealed at atmospheric pressure of CO_2 (1 atm). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. Then we detected TEMPO-adduct **4** by **GC-MS**. This result might support the existence of radical species.

(c) Intercepting the carbanion intermediate with D_2O



0 equiv. of D_2O	80% yield (0% -**D**)
5 equiv. of D_2O	61% yield (64% -**D**)
10 equiv. of D_2O	52% yield (75% -**D**)

Following the general procedure, BCN_{1000} (10 mg), **2a** (0.15 mmol, 1.5 equiv) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with N_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) and D_2O (x equiv.) was added followed by DIPEA (0.3 mmol, 3 equiv.) and 4-cyanostyrene **1a** (0.1 mmol, 1.0 equiv.) under N_2 atmosphere. The product **3aa'** was isolated by flash column chromatography (petroleum ether/EtOAc 200/1) as a colorless oil in 61% yield with 64% deuterium incorporation or 52% yield with 75% deuterium incorporation. This result indirectly confirmed the existence of benzylic carbanion.

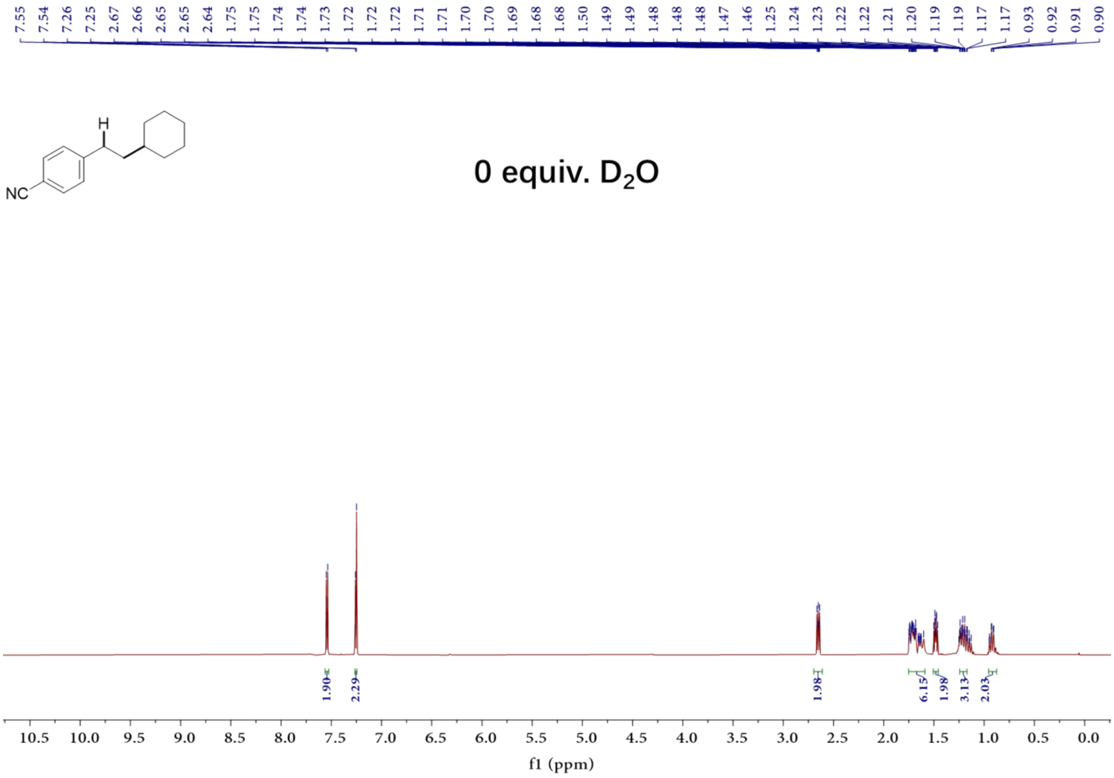


Figure S10. **1H NMR** Spectra of compound **3aa’**

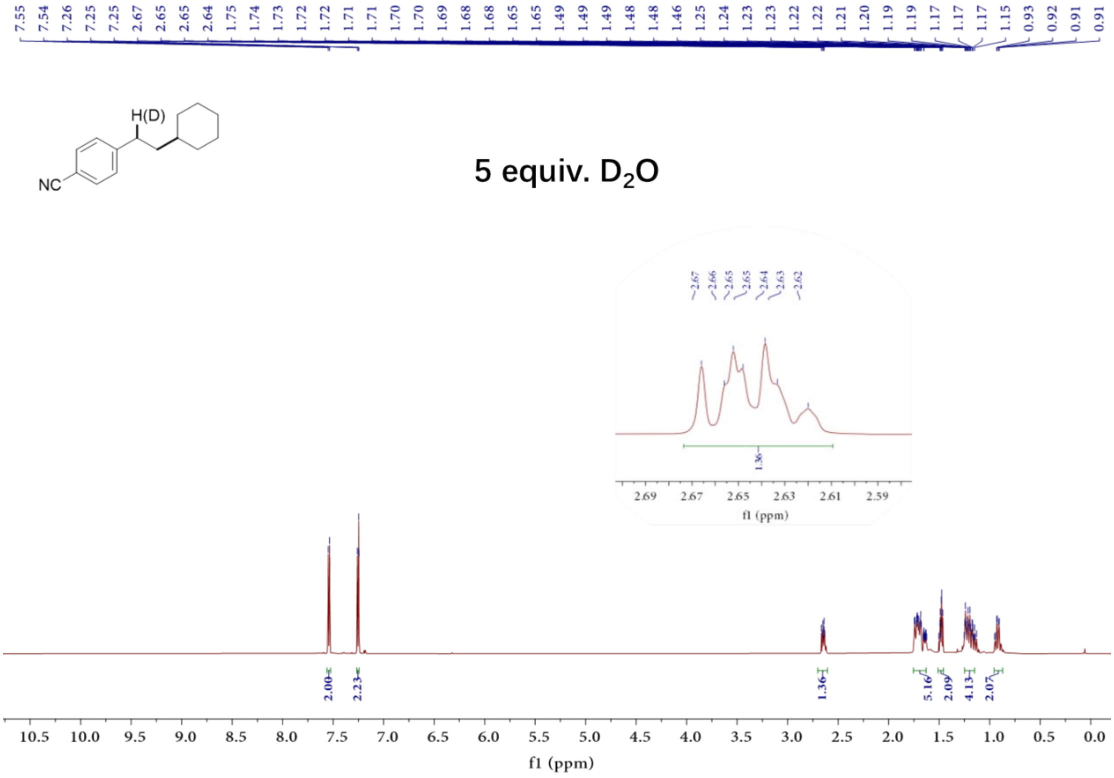


Figure S11. **1H NMR** Spectra of compound **3aa’**-H/D

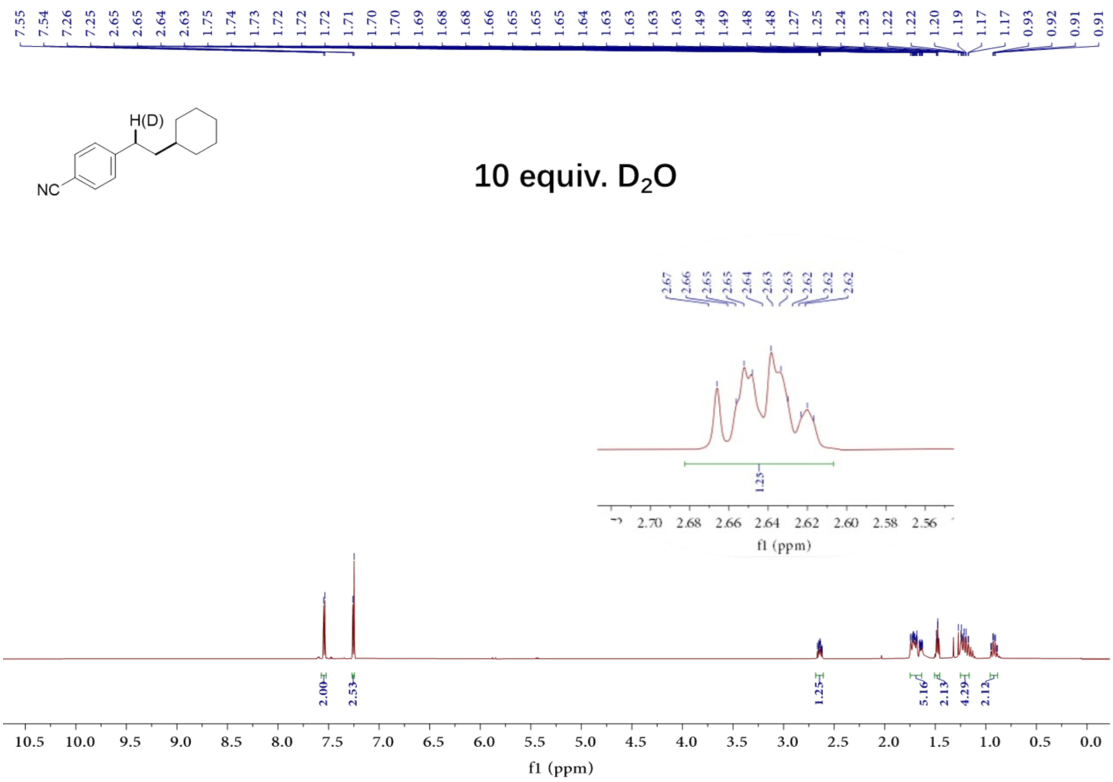
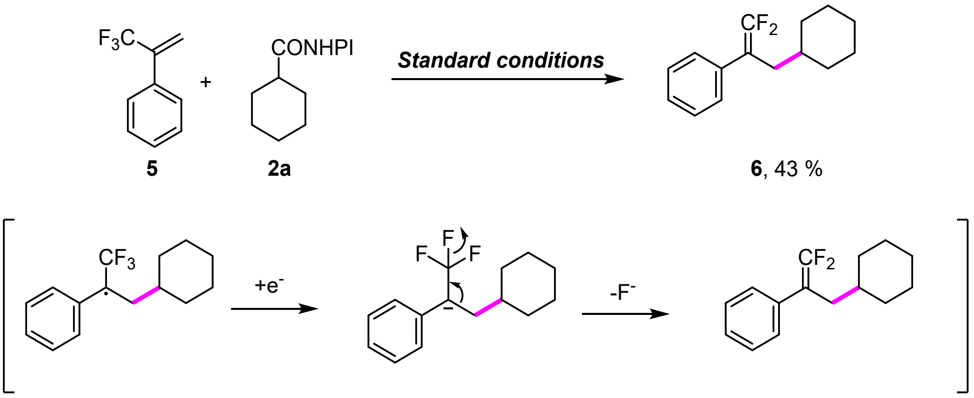


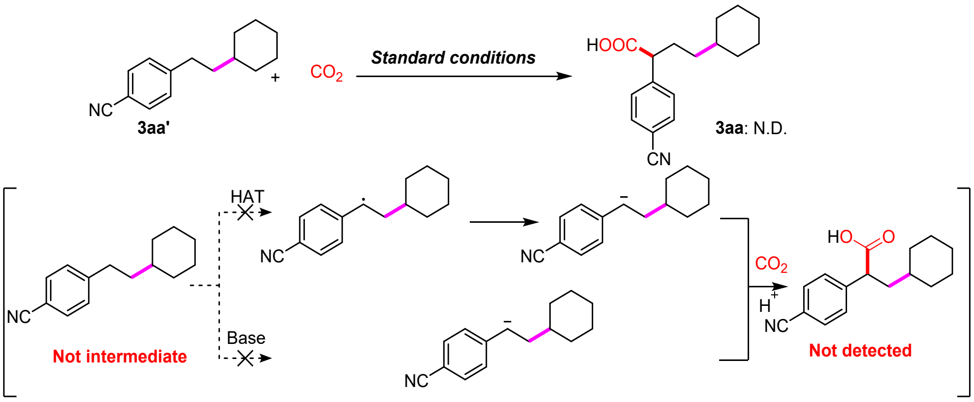
Figure S12. **1H NMR** Spectra of compound **3aa'**-H/D

(d) Defluorinative alkylation of trifluoromethylakenes



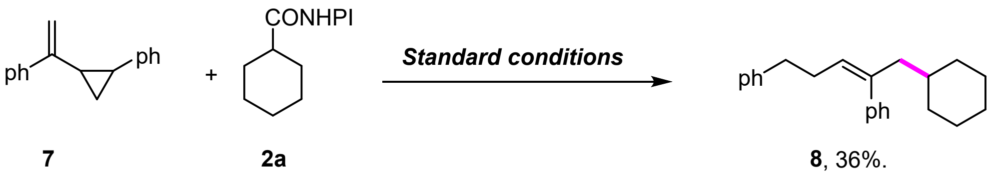
To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN$_{1000}$ (10 mg) **2a** (0.15 mmol, 1.5 equiv) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with N_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) and **5** (0.1 mmol, 1.0 equiv.) under N_2 atmosphere. Once added, the resulting mixture was degassed by using a "freeze-pump-haw" procedure (3 times). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. After reaction, the reaction mixture was extracted by EtOAc three times and the combined organic phases were concentrated in vacuo. The residue was purified by silica gel flash column chromatography using petroleum (petroleum ether/EtOAc 100/1) as eluent to give the pure desired product **6**. This result indirectly confirmed the existence of benzylic carbanion.

(e) Direct carboxylation of the hydroalkylation product



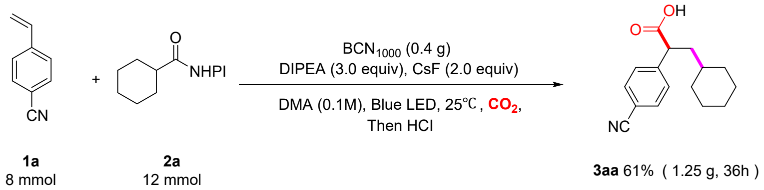
To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN_{1000} (10 mg) **3aa'** (0.1 mmol) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with CO_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a “freeze-pump-haw” procedure (3 times). Then the Schlenk tube was back-filled with CO_2 and sealed at atmospheric pressure of CO_2 (1 atm). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. The product **3aa** was not observed. This result suggested **3aa'** might not be the intermediate to produce the desired product **3aa**.

(f) Radical clock experiment:



To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN_{1000} (10 mg) **2a** (0.15 mmol, 1.5 equiv) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with CO_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) and **7** (0.1 mmol, 1.0 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a “freeze-pump-haw” procedure (3 times). Then the Schlenk tube was back-filled with CO_2 and sealed at atmospheric pressure of CO_2 (1 atm). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. After reaction, the resulting mixture was diluted with 3 mL EtOAc and quenched by 1.0 mL 2 M HCl, then stirred for 5 min. The reaction mixture was extracted by EtOAc three times and the combined organic phases were concentrated in vacuo. The residue was purified by silica gel flash column chromatography using petroleum (petroleum ether/EtOAc 200/1) as eluent to give the pure desired product **8**. This result might support the existence of radical species.

7. The gram-scale reaction



The reaction was scaled to 8 mmol using a reaction vessel, with a water-cooling system. The reaction vessel was equipped with BCN_{1000} (0.4 g), RAEs **2a** (12 mmol, 1.5 equiv) and anhydrous CsF (16 mmol, 2.0 equiv.). Subsequently, the vessel was opened, anhydrous DMA (80 mL) was added followed by DIPEA (24 mmol, 3 equiv.) and 4-cyanostyrene (8 mmol, 1.0 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a "freeze-pump-haw" procedure (3 times). Then the vessel was sealed and degassed with a vacuum pump and backfilled with CO_2 (1 atm). The reaction was stirred and irradiated with two 50 W 450 nm LEDs lamps (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 36 hours. After reaction, the resulting mixture was diluted with 50 mL EtOAc and quenched by 25 mL 2 M HCl, then stirred for 20 min. The reaction mixture was extracted by EtOAc three times and the combined organic phases were concentrated in vacuo. The residue was purified by silica gel flash column chromatography using petroleum ether/EtOAc/AcOH (0.5%) as eluent to give the pure desired product. Yield of **3aa**: 1.25g, 61%.

8. Recycling test

To an oven-dried Schlenk tube (10 mL) equipped with a magnetic stir bar was added BCN_{1000} (10 mg), **2a** (0.15 mmol, 1.5 equiv) and anhydrous CsF (0.2 mmol, 2.0 equiv.). The tube was sealed and evacuated and back-filled with CO_2 for 3 times. Subsequently, the tube was opened, anhydrous DMA (1 mL) was added followed by DIPEA (0.3 mmol, 3 equiv.) and 4-cyanostyrene (0.1 mmol, 1.0 equiv.) under CO_2 atmosphere. Once added, the resulting mixture was degassed by using a "freeze-pump-haw" procedure (3 times). Then the Schlenk tube was back-filled with CO_2 and sealed at atmospheric pressure of CO_2 (1 atm). The reaction was stirred and irradiated with a 50 W 450 nm LEDs lamp (1 cm away, with cooling fan to keep the reaction temperature at 25 °C and keeping the reaction region located in the center of LEDs lamp) for 16 hours. After completion, the reaction mixture was centrifuged to separate BCN_{1000} and the liquid mixture. The photocatalyst BCN_{1000} was washed thoroughly with EtOH and H_2O many times and reused in the subsequent recycling reaction.

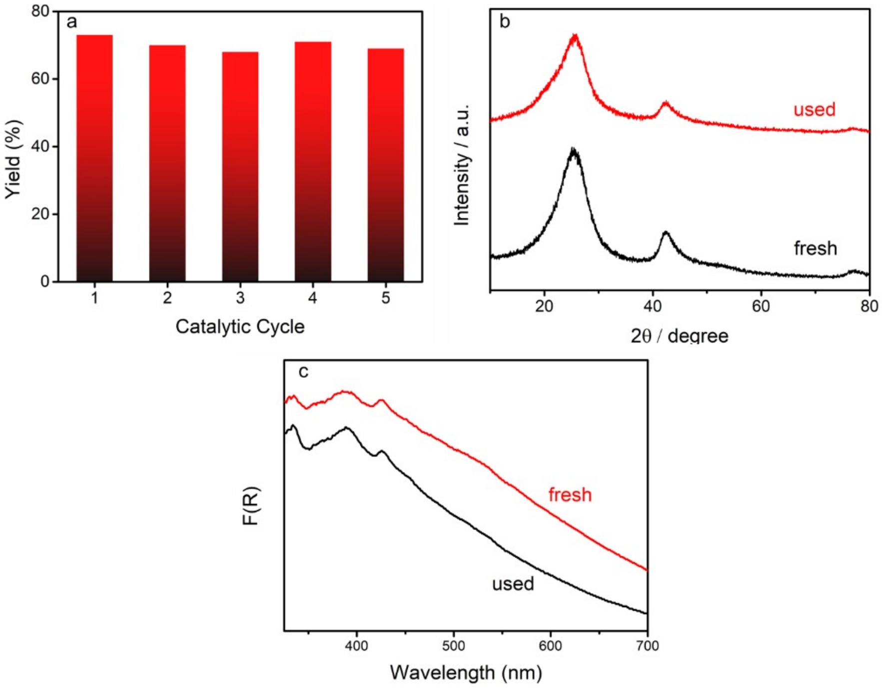


Figure S13. (a) Activity test with recycled BCN. (b) XRD pattern of fresh and used BCN. (c) UV-DRS pattern of fresh and used BCN.

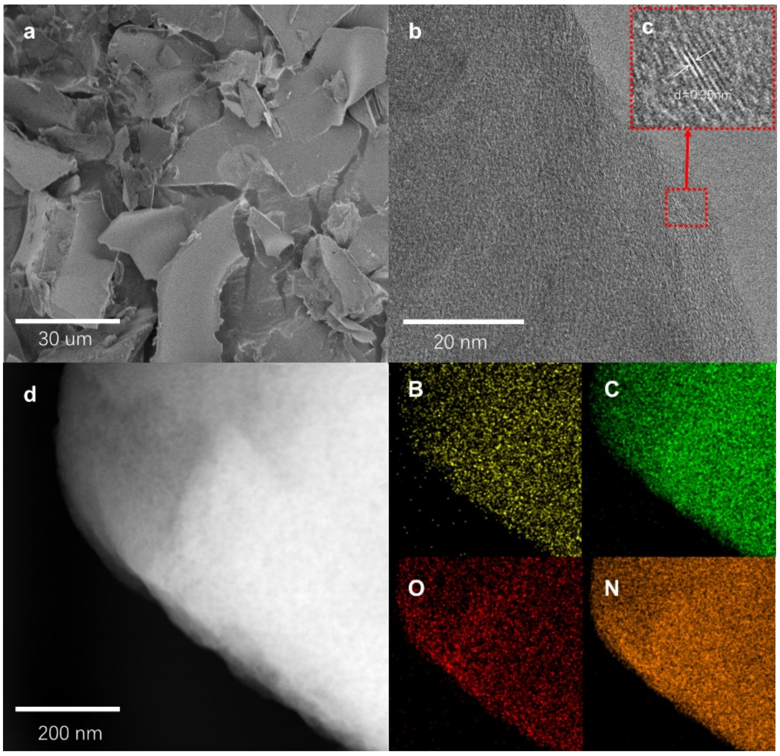
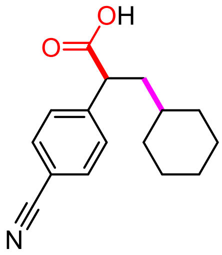


Figure S14. (a) SEM (scale bar: 30 um); (b) TEM (scale bar: 20 nm); (c) HR-TEM image highlighted by the red dashed box in (b); (d) High-Angle Annular Dark Field (HAADF) image of BCN and elemental mapping images of B, C, N, and O for recycled BCN.

9. Characterization Data for Products



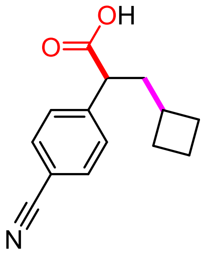
2-(4-cyanophenyl)-3-cyclohexylpropanoic acid (3aa)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p.: 101 – 103 °C), (18.7 mg, 73% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 3.75 (t, *J* = 7.7 Hz, 1H), 2.01 – 1.93 (m, 1H), 1.71 – 1.57 (m, 6H), 1.20 – 1.06 (m, 4H), 0.94 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.2, 144.2, 132.6, 129.1, 118.7, 111.5, 49.0, 40.7, 35.3, 33.4, 32.9, 26.4, 26.1, 26.1, 26.4.

HRMS (ESI-) $[M-H]^-$calculated m/z for $[C_{16}H_{18}NO_2]^-$: 256.1343, found: 256.1341.



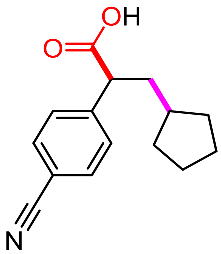
2-(4-cyanophenyl)-3-cyclobutylpropanoic acid (3ba)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (14.2 mg, 62% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 3.54 (t, *J* = 7.5 Hz, 1H), 2.24 – 2.09 (m, 2H), 2.05 – 1.97 (m, 1H), 1.97 – 1.84 (m, 2H), 1.85 – 1.73 (m, 2H), 1.68 – 1.60 (m, 1H), 1.60 – 1.49 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.3, 143.9, 132.6, 129.1, 118.7, 111.6, 49.7, 40.3, 33.9, 28.1, 18.5.

HRMS (ESI-) $[M-H]^-$calculated m/z for $[C_{14}H_{14}NO_2]^-$: 228.1030, found: 228.1023.



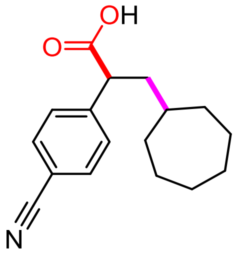
2-(4-cyanophenyl)-3-cyclopentylpropanoic acid (3ca)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (17.9 mg, 74% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 3.66 (t, *J* = 7.7 Hz, 1H), 2.13 – 2.03 (m, 1H), 1.86 – 1.78 (m, 1H), 1.78 – 1.67 (m, 2H), 1.67 – 1.55 (m, 3H), 1.54 – 1.42 (m, 2H), 1.18 – 1.02 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.1, 144.0, 132.6, 129.2, 118.7, 111.6, 51.0, 39.5, 37.8, 32.8, 32.3, 25.2, 25.1.

HRMS (ESI-) $[M-H]^-$calculated m/z for $[C_{15}H_{16}NO_2]^-$: 242.1187, found: 242.1182.



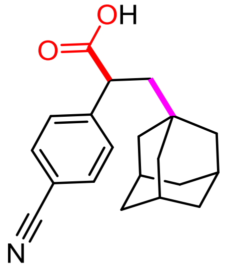
2-(4-cyanophenyl)-3-cycloheptylpropanoic acid (3da)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 105 – 107 °C), (14.6 mg, 54% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 3.72 (t, *J* = 7.7 Hz, 1H), 2.05 – 1.97 (m, 1H), 1.74 – 1.64 (m, 3H), 1.63 – 1.54 (m, 2H), 1.54 – 1.48 (m, 2H), 1.48 – 1.41 (m, 2H), 1.38 – 1.29 (m, 3H), 1.25 – 1.15 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.2, 144.1, 132.6, 129.2, 118.7, 111.5, 49.5, 41.1, 36.6, 34.6, 34.0, 28.6, 28.5, 26.1, 26.0.

HRMS (ESI-) $[M-H]^-$calculated m/z for $[C_{17}H_{20}NO_2]^-$: 270.1500, found: 270.1502.



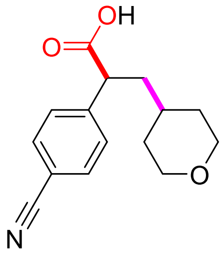
3-((3r,5r,7r)-adamantan-1-yl)-2-(4-cyanophenyl)propanoic acid (3ea)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (20.7 mg, 67% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 3.76 (dd, *J* = 8.2, 4.5 Hz, 1H), 2.15 – 2.08 (m, 1H), 1.93 – 1.90 (m, 3H), 1.70 – 1.65 (m, 3H), 1.60 – 1.55 (m, 3H), 1.50 – 1.43 (m, 4H), 1.43 – 1.38 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.5, 145.9, 132.6, 129.0, 118.7, 111.3, 47.6, 46.4, 42.4, 36.9, 33.2, 28.6.

HRMS (ESI-) $[M-H]^-$calculated m/z for $[C_{20}H_{22}NO_2]^-$:308.1656, found: 308.1652.



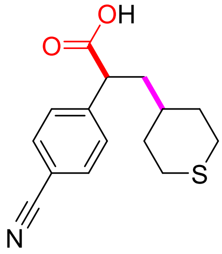
2-(4-cyanophenyl)-3-(tetrahydro-2H-pyran-4-yl)propanoic acid (3fa)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 157 – 159 ^{o}C), (17.8 mg, 68% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 3.95 – 3.91 (m, 2H), 3.74 (t, *J* = 7.8 Hz, 1H), 3.33 – 3.25 (m, 2H), 2.11 – 2.01 (m, 1H), 1.76 – 1.68 (m, 1H), 1.61 – 1.55 (m, 2H), 1.45 – 1.29 (m, 1H), 1.31 – 1.23 (m, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.5, 143.8, 132.7, 129.1, 118.6, 111.7, 67.8, 67.7, 48.4, 40.0, 32.9, 32.7, 32.6.

HRMS (ESI-) [M-H]$^{-}$calculated m/z for [$C_{15}H_{16}NO_3$]$^{-}$: 258.1136, found: 258.1139.



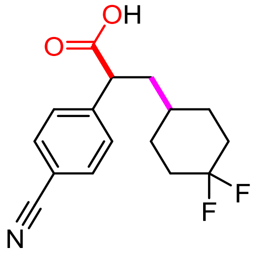
2-(4-cyanophenyl)-3-(tetrahydro-2H-thiopyran-4-yl)propanoic acid (3ga)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 125 – 127 ^{o}C), (13.7 mg, 50% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 3.74 (t, *J* = 7.8 Hz, 1H), 2.56 – 2.51 (m, 4H), 2.05 – 1.94 (m, 3H), 1.72 – 1.65 (m, 1H), 1.40 – 1.28 (m, 2H), 1.20 – 1.15 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.5, 143.6, 132.7, 129.1, 118.6, 111.8, 48.4, 40.3, 34.9, 34.2, 33.8, 28.5, 28.4.

HRMS (ESI-) [M-H]$^{-}$calculated m/z for [$C_{15}H_{16}NSO_2$]$^{-}$: 274.0907, found: 274.0904.



2-(4-cyanophenyl)-3-(4,4-difluorocyclohexyl)propanoic acid (3ha)

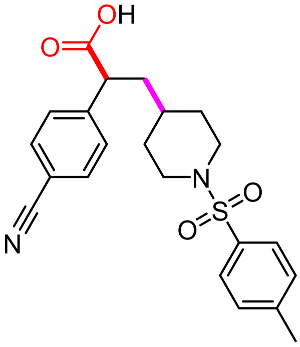
According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (22.3 mg, 73% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 3.72 (t, *J* = 7.8 Hz, 1H), 2.13 – 2.00 (m,3H), 1.79 – 1.70 (m, 3H), 1.68 – 1.54 (m, 2H), 1.33 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 178.6, 143.5, 132.7, 129.0, 118.5, 111.8, 49.2, 38.9, 29.0 (d, *J* = 9.6 Hz), 28.6 (d, *J* = 9.3 Hz).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -91.9 (d, *J* = 235.4 Hz), -102.1 (d, *J* = 235.0 Hz).

HRMS (ESI-) [M-H]$^-$calculated m/z for[$C_{16}H_{16}F_2NO_2$]$^-$: 292.1155, found: 292.1151.



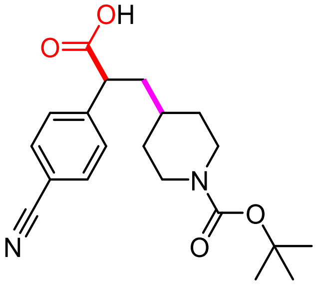
2-(4-cyanophenyl)-3-(1-tosylpiperidin-4-yl)propanoic acid (3ia)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (4/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 104 – 106 °C), (28.8 mg, 70% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62 – 7.57 (m, 4H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 3.80 – 3.71 (m,2H), 3.67 (t, *J* = 7.8 Hz, 1H), 2.42 (s, 3H), 2.16 – 2.07 (m, 2H), 2.04 – 1.96 (m, 1H), 1.73 – 1.71 (m, 3H), 1.37 – 1.25 (m, 2H), 1.09 – 0.99 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 177.3, 143.7, 143.4, 133.2, 132.7, 129.8, 129.0, 127.8, 118.5, 111.9, 48.5, 46.3, 46.2, 39.2, 32.9, 31.6, 31.2, 21.7.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{22}H_{23}N_2O_4S$]$^-$: 411.1384, found: 411.1386.



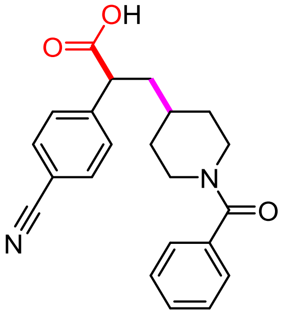
3-(1-(tert-butoxycarbonyl)piperidin-4-yl)-2-(4-cyanophenyl)propanoic acid (3ja)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (4/1/0.5%, v/v/v) as an eluent to provide as colorless oil (24.3 mg, 68% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 4.02 (s, 2H), 3.72 (t, *J* = 7.7 Hz, 1H), 2.58 (s, 2H), 2.08 – 1.97 (m, 1H), 1.72 – 1.58 (m, 3H), 1.41 (s, 9H), 1.33 – 1.25 (m, 1H), 1.14 – 1.03 (m, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 177.2, 155.1, 144.0, 132.7, 129.0, 118.6, 111.6, 79.9, 48.7, 39.7, 33.8, 28.5.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{20}H_{25}N_2O_4]^-$: 357.1820, found: 357.1817.



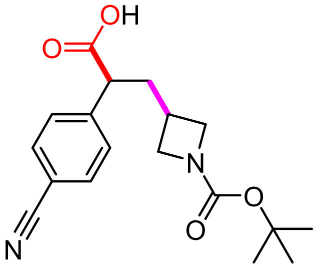
3-(1-benzoylpiperidin-4-yl)-2-(4-cyanophenyl)propanoic acid (3ka)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (4/1/0.5%, v/v/v) as an eluent to provide as colorless oil (21.7 mg, 60% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.41 – 7.30 (m, 7H), 4.73 – 4.57 (m, 1H), 3.68 (t, 2H), 2.95 – 2.60 (m, 2H), 2.09 – 2.01 (m, 1H), 1.86 – 1.72 (m, 1H), 1.71 – 1.55 (m, 2H), 1.48 – 1.41 (m, 1H), 1.27 – 1.04 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.9, 170.9, 144.2, 135.6, 132.6, 129.9, 129.0, 128.6, 126.9, 118.6, 111.5, 48.8, 47.9, 42.6, 39.6, 34.0, 31.6.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{22}H_{21}N_2O_3]^-$: 361.1558, found: 361.1557.



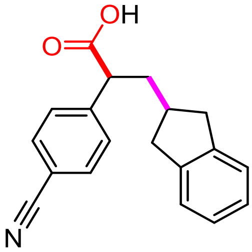
3-(1-(tert-butoxycarbonyl)azetidin-3-yl)-2-(4-cyanophenyl)propanoic acid (3la)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (4/1/0.5%, v/v/v) as an eluent to provide as colorless oil (13.8 mg, 42% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 3.97 (t, *J* = 8.2 Hz, 1H), 3.90 (t, *J* = 8.3 Hz, 1H), 3.67 – 3.57 (m, 1H), 3.54 (t, *J* = 7.5 Hz, 1H), 3.49 – 3.44 (m, 1H), 2.51 – 2.36 (m, 2H), 2.11 – 2.00 (m, 1H), 1.40 (s, 9H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 176.0, 156.6, 143.3, 132.8, 129.0, 118.5, 111.9, 80.1, 49.7, 37.8, 28.5, 27.2.

HRMS (ESI-) [M-H]$^-$calculated m/z for $[C_{18}H_{21}N_2O_4]^-$: 329.1507, found: 329.1507.



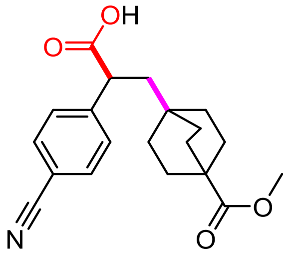
2-(4-cyanophenyl)-3-(2,3-dihydro-1H-inden-2-yl)propanoic acid (3ma)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 118 – 120 °C). (12.8 mg, 44% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.18 – 7.14 (m, 2H), 7.14 – 7.10 (m, 2H), 3.78 (t, *J* = 7.4 Hz, 1H), 3.07 – 2.94 (m, 2H), 2.68 – 2.55 (m, 2H), 2.39 – 2.28 (m, 2H), 2.08 – 2.00 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.8, 143.6, 142.7, 142.5, 132.6, 129.1, 126.5, 124.5, 118.6, 111.7, 50.7, 39.1, 38.9, 38.1.

HRMS (ESI-) [M-H]$^-$calculated m/z for [$C_{19}H_{16}NO_2$]$^-$: 290.1187, found: 290.1182.



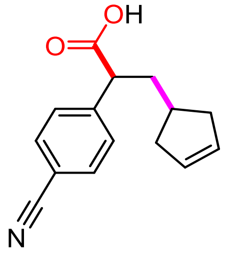
2-(4-cyanophenyl)-3-(4-(methoxycarbonyl)bicyclo[2.2.2]octan-1-yl)propanoic acid (3na)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (12/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 134 – 136 °C), (26.6 mg, 78% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 3.71 – 3.65 (m, 1H), 3.62 (s, 3H), 2.20 – 2.13 (m, 1H), 1.73 (t, *J* = 8.0 Hz, 6H), 1.55 – 1.45 (m, 1H), 1.43 – 1.21 (m, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.6, 178.4, 145.4, 129.0, 118.6, 111.5, 51.9, 47.3, 44.4, 38.8, 31.4, 28.4.

HRMS (ESI-) [M-H]$^-$calculated m/z for [$C_{20}H_{22}NO_2$]$^-$: 340.1554, found: 340.1548.



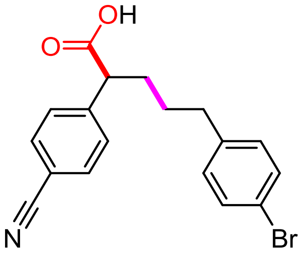
2-(4-cyanophenyl)-3-(cyclopent-3-en-1-yl)propanoic acid (3oa)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 95 – 97 °C), (13.0 mg, 54% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 5.63 (s, 2H), 3.68 (t, *J* = 7.7 Hz, 1H), 2.49 – 2.40 (m, 2H), 2.24 – 2.17 (m, 1H), 2.14 – 2.05 (m, 1H), 2.05 – 1.87 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.7, 143.8, 132.6, 129.9, 129.7, 129.2, 118.7, 111.7, 50.7, 39.7, 38.9, 38.6, 35.6.

HRMS (ESI-) [M-H]$^-$calculated m/z for [$C_{15}H_{14}NO_2$]$^-$: 240.1030, found: 240.1025.



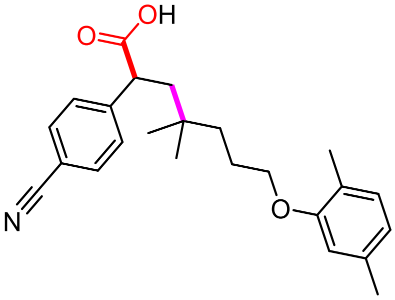
5-(4-bromophenyl)-2-(4-cyanophenyl)pentanoic acid (3pa)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (6/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 124 – 126 °C), (15.0 mg, 42% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.33 (m, 4H), 6.97 (d, *J* = 8.4 Hz, 2H), 3.59 (t, *J* = 7.6 Hz, 1H), 2.65 – 2.50 (m, 2H), 2.13 – 2.04 (m, 1H), 1.82 – 1.73 (m, 1H), 1.65 – 1.54 (m, 1H), 1.54 – 1.43 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.3, 143.5, 140.4, 132.7, 131.6, 130.2, 129.1, 119.9, 118.6, 111.8, 51.5, 34.9, 32.5, 29.0.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{18}H_{15}NBrO_2$]$^-$: 356.0292, found: 356.0287.



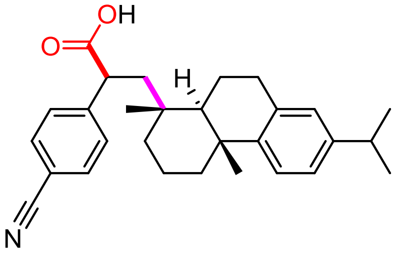
2-(4-cyanophenyl)-7-(2,5-dimethylphenoxy)-4,4-dimethylheptanoic acid (3qa)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 38 – 40 °C). (19.7 mg, 52% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.60 (s, 1H), 3.88 (t, *J* = 6.2 Hz, 2H), 3.74 – 3.69 (m, 1H), 2.36 – 2.26 (m, 4H), 2.17 (s, 3H), 1.77 – 1.66 (m, 2H), 1.66 – 1.60 (m, 1H), 1.45 – 1.35 (m, 2H), 0.89 (d, *J* = 3.8 Hz,6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.1, 157.0, 145.7, 136.6, 132.6, 130.5, 129.0, 123.7, 120.9, 118.7, 112.1, 111.4, 68.3, 47.9, 45.0, 38.5, 33.6, 27.1, 27.1, 24.3, 21.5, 15.9.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{24}H_{28}NO_3$]$^-$: 378.2075, found: 378.2072.



2-(4-cyanophenyl)-3-((1R,4aR,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-

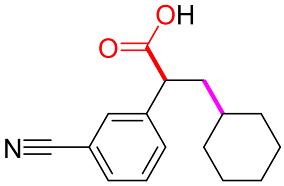
octahydrophenanthren-1-yl)propanoic acid (3ra)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 84 – 86 °C), (20.1mg, 47% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 1H), 7.02 – 6.98 (m, 1H), 6.85 (s, 1H), 3.76 – 3.71 (m, 1H), 2.92 – 2.77 (m, 3H), 2.33 – 2.26 (m, 2H), 1.85 – 1.78 (m, 2H), 1.76 – 1.64 (m, 2H), 1.64 – 1.51 (m, 1H), 1.50 – 1.44 (m, 1H), 1.44 – 1.34 (m, 2H), 1.25 – 1.21 (m, 6H), 1.20 (s, 4H), 0.90 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.7, 147.3, 146.0, 145.8, 134.6, 132.7, 129.1, 127.0, 124.3, 124.0, 118.7, 111.5, 48.8, 47.5, 47.2, 38.5, 37.8, 37.2, 37.0, 33.6, 30.2, 25.4, 24.1, 24.1, 20.3, 19.0, 18.9.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{29}H_{34}NO_2$]$^-$: 428.2595, found: 428.2596.



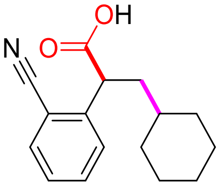
2-(3-cyanophenyl)-3-cyclohexylpropanoic acid (3ab)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (12.3 mg, 48% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.63 (t, *J* = 1.7 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 3.73 (t, *J* = 7.8 Hz, 1H), 2.02 – 1.94 (m, 1H), 1.74 – 1.60 (m, 6H), 1.20 – 1.08 (m, 4H), 1.00 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.8, 140.4, 132.9, 131.9, 131.3, 129.6, 118.8, 112.9, 48.4, 40.8, 35.2, 33.4, 32.9, 26.5, 26.1, 26.1.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{16}H_{18}NO_2$]$^-$: 256.1343, found: 256.1341.



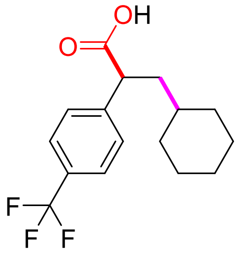
2-(2-cyanophenyl)-3-cyclohexylpropanoic acid (3ac)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (16.4mg, 64% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.66 – 7.61 (m, 1H), 7.61 – 7.54 (m, 1H), 7.52 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.39 – 7.33 (m, 1H), 4.21 (t, *J* = 7.6 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.78 – 1.58 (m, 6H), 1.19 – 1.09 (m, 4H), 0.97 – 0.88 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.6, 142.6, 133.3, 133.2, 128.2, 127.9, 117.7, 113.2, 46.6, 40.9, 35.4, 33.3, 33.0, 26.5, 26.1, 26.1.

HRMS (ESI-) [M-H]-calculated m/z for [$C_{16}H_{18}NO_2$]$^-$: 256.1343, found: 256.1341.



3-cyclohexyl-2-(4-(trifluoromethyl)phenyl)propanoic acid (3ad)

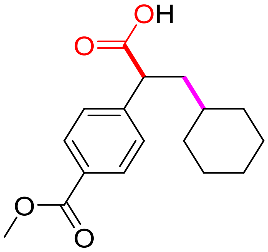
According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 95 – 97 °C), (19.5 mg, 65% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 3.77 (t, *J* = 7.8 Hz, 1H), 2.03 – 1.95 (m, 1H), 1.77 – 1.60 (m, 6H), 1.21 – 1.07 (m, 4H), 0.96 – 0.87 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 180.0, 142.8, 130.0, 129.8, 128.7, 125.8 (d, *J* = 3.9 Hz), 125.1, 123.3, 48.7, 40.7, 35.2, 33.4, 32.9, 26.5, 26.1 (d, *J* = 7.0 Hz).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -62.5.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{16}H_{18}F_3O_2]^-$: 299.1264, found: 299.1260.



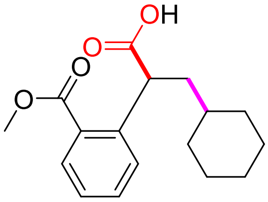
3-cyclohexyl-2-(4-(methoxycarbonyl)phenyl)propanoic acid (3ae)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 84 – 86 °C), (15.7 mg, 54% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 3.90 (s, 3H), 3.76 (t, *J* = 7.8 Hz, 1H), 2.02 – 1.94 (m, 1H), 1.75 – 1.63 (m, 6H), 1.15 – 1.08 (m, 4H), 0.95 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.1, 167.0, 144.0, 130.1, 129.5, 128.3, 52.3, 48.8, 40.7, 35.3, 33.4, 32.9, 26.5, 26.2, 26.1.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{17}H_{21}O_4]^-$: 289.1445, found: 289.1444.



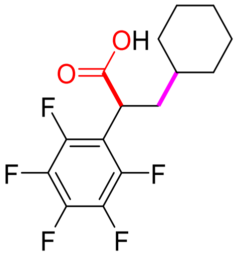
3-cyclohexyl-2-(2-(methoxycarbonyl)phenyl)propanoic acid (3af)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as colorless oil (15.6mg, 54% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.88 – 7.84 (m, 1H), 7.54 – 7.46 (m, 2H), 7.35 – 7.29 (m, 1H), 4.65 – 4.60 (m, 1H), 3.93 (s, 3H), 2.13 – 2.04 (m, 1H), 1.73 – 1.58 (m, 6H), 1.22 – 1.08 (m, 4H), 0.95 – 0.86 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.1, 169.2, 140.3, 132.7, 129.8, 128.9, 127.2, 52.8, 44.3, 40.2, 35.6, 33.4, 33.2, 26.6, 26.2, 26.2.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{17}H_{21}O_4]^-$: 289.1445, found: 289.1444.



3-cyclohexyl-2-(perfluorophenyl)propanoic acid (3ag)

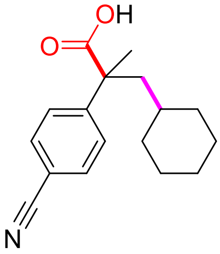
According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (25/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 88 – 90 °C). (22.5 mg, 70% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.17 – 4.12 (m, 1H), 2.12 – 2.05 (m, 1H), 1.83 – 1.75 (m, 2H), 1.73 – 1.59 (m, 4H), 1.21 – 1.09 (m, 3H), 1.09 – 1.00 (m, 1H), 1.00 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 178.1, 146.8 – 145.7 (m), 145.2 – 144.0 (m), 142.2 – 140.9 (m), 140.2 – 139.5 (m), 139.0 – 138.1 (m), 137.3 – 136.5 (m), 113.1 – 112.8 (m), 38.1, 37.6, 35.5, 32.2, 26.5, 26.2, 26.1.

^{19}F NMR (565 MHz, Chloroform-d) δ -140.7 – -142.5 (m), -155.0 (d, J = 20.8 Hz), -161.0 – -163.0 (m).

HRMS (ESI-) [M-H]-calculated m/z for $[C_{15}H_{14}F_5O_2]^-$: 321.0919, found: 321.0917.



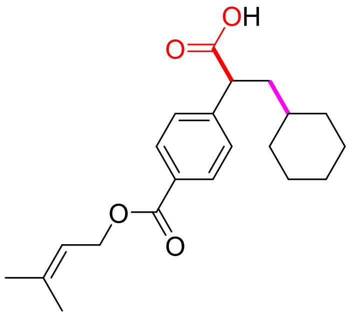
2-(4-cyanophenyl)-3-cyclohexyl-2-methylpropanoic acid (3ah)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (11.1mg, 41% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 2.01 (dd, *J* = 14.1, 5.9 Hz, 1H), 1.81 (dd, *J* = 14.1, 5.3 Hz, 1H), 1.65 – 1.55 (m, 7H), 1.41 – 1.35 (m, 1H), 1.27 – 1.23 (m, 1H), 1.18 – 1.06 (m, 3H), 1.02 – 0.95 (m, 1H), 0.90 – 0.83 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 149.0, 132.3, 127.4, 118.8, 111.1, 50.3, 46.2, 35.2, 34.7, 34.5, 26.5, 26.4, 26.2, 22.4.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{17}H_{20}NO_2]^-$: 270.1500, found: 270.1499.



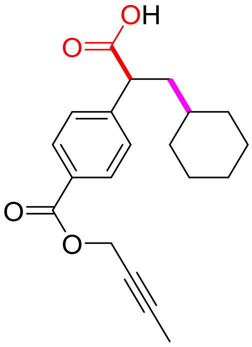
3-cyclohexyl-2-(4-(((3-methylbut-2-en-1-yl)oxy)carbonyl)phenyl)propanoic acid (3ai)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (13/1/0.5%, v/v/v) as an eluent to provide as colorless oil (22.0mg, 64% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 5.47 – 5.41 (m, 1H), 4.79 (d, *J* = 7.2 Hz, 2H), 3.74 (t, *J* = 7.8 Hz, 1H), 1.99 – 1.92 (m, 1H), 1.79 – 1.74 (m, 6H), 1.72 – 1.57 (m,6H), 1.17 – 1.08 (m, 4H), 0.93 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.8, 166.6, 143.9, 139.3, 130.1, 129.8, 128.3, 118.8, 62.0, 48.9, 40.6, 35.2, 33.4, 32.9, 26.5, 26.1, 26.1, 25.9, 18.2.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{21}H_{27}O_{4}]^{-}$: 343.1915, found: 343.1921.



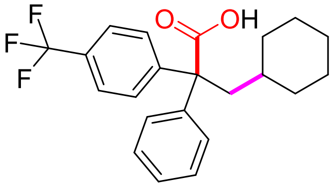
2-(4-((but-2-yn-1-yloxy)carbonyl)phenyl)-3-cyclohexylpropanoic acid (3aj)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as colorless oil (16.4 mg, 50% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 4.88 – 4.84 (m, 2H), 3.74 (t, *J* = 7.8 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.85 (t, *J* = 2.4 Hz, 3H), 1.72 – 1.58 (m, 6H), 1.15 – 1.07 (m, 4H), 0.93 – 0.86 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.5, 165.9, 144.4, 130.3, 129.0, 128.4, 83.4, 73.4, 53.4, 48.9, 40.6, 35.2, 33.4, 32.9, 26.5, 26.2, 26.1, 3.8.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{20}H_{23}O_{4}]^{-}$: 327.1602, found: 327.1600.



3-cyclohexyl-2-phenyl-2-(4-(trifluoromethyl)phenyl)propanoic acid (3ak)

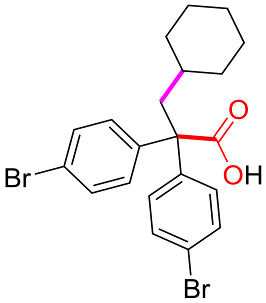
According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (20/1/0.5%, v/v/v) as an eluent to provide as white solid (m.p. = 54 - 56 °C), (16.5 mg, 44% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.24 (m, 5H), 2.39 – 2.31 (m, 1H), 2.29 – 2.23 (m, 1H), 1.52 – 1.47 (m, 3H), 1.25 – 1.21 (m, 1H), 1.20 – 1.15 (m, 1H), 1.08 – 0.94 (m, 4H), 0.93 – 0.81 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.9, 147.3, 142.7, 129.7, 129.0, 128.3, 127.5, 124.9 (d, *J* = 3.8 Hz), 59.9, 45.2, 34.7 (d, *J* = 10.2 Hz), 34.4, 26.4, 26.3.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -62.4.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{22}H_{22}F_3O_2]^-$: 375.1577, found: 375.1572.



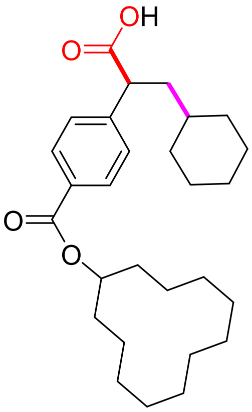
2,2-bis(4-bromophenyl)-3-cyclohexylpropanoic acid (3al)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (18.6 mg, 40% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 8.3 Hz, 4H), 7.20 (d, *J* = 8.3 Hz, 4H), 2.24 (d, *J* = 5.3 Hz, 2H), 1.52 (d, *J* = 8.6 Hz, 3H), 1.28 – 1.25 (m, 1H), 1.24 – 1.21 (m, 1H), 1.08 – 0.98 (m, 4H), 0.91 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.8, 142.0, 131.2, 130.9, 121.4, 59.2, 45.1, 34.7, 34.5, 26.4, 26.2.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{21}H_{21}Br_2O_2]^-$: 462.9914, found: 462.9912.



2-(4-((cyclododecyloxy)carbonyl)phenyl)-3-cyclohexylpropanoic acid (3am)

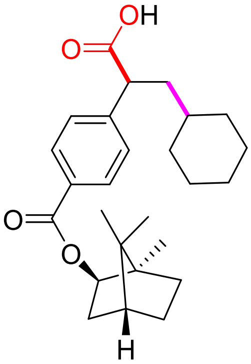
According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (15/1/0.5%, v/v/v) as an eluent to provide as colorless oil (21.2mg, 48% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 5.26 – 5.19

(m, 1H), 3.74 (t, *J* = 7.8 Hz, 1H), 1.98 – 1.93 (m, 1H), 1.83 – 1.76 (m, 2H), 1.73 – 1.58 (m, 8H), 1.47 – 1.32 (m, 18H), 1.16 – 1.08 (m, 4H), 0.93 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.4, 166.2, 143.7, 130.3, 130.0, 128.3, 73.1, 48.8, 40.6, 35.2, 33.5, 32.9, 29.3, 26.5, 26.2, 26.1, 24.3, 24.1, 23.5, 23.3, 21.0.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{28}H_{41}O_4]^-$: 441.3010, found: 441.3009.



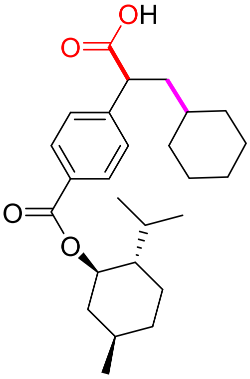
3-cyclohexyl-2-(4-((((1R,2R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)carbonyl)phenyl)propanoic acid (3an)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as colorless oil (25.1 mg, 61% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 4.91 – 4.86 (m, 1H), 3.74 (t, *J* = 7.8 Hz, 1H), 1.99 – 1.85 (m, 3H), 1.80 – 1.76 (m, 1H), 1.73 – 1.56 (m, 8H), 1.23 – 1.19 (m, 1H), 1.15 – 1.09 (m, 8H), 0.96 – 0.83 (m, 8H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.7, 165.9, 143.8, 130.1, 130.0, 128.3, 81.9, 49.1, 48.8, 47.2, 45.2, 40.6, 39.0, 35.2, 33.9, 33.4, 32.9, 27.2, 26.5, 26.2, 26.1, 20.3, 20.2, 11.7.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{26}H_{35}O_4]^-$: 411.2541, found: 411.2545.



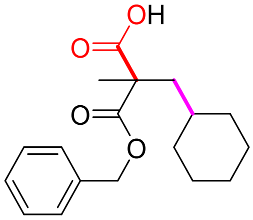
3-cyclohexyl-2-(4-((((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)carbonyl)phenyl)propanoic acid (3ao)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (10/1/0.5%, v/v/v) as an eluent to provide as colorless oil (23.2 mg, 56% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 4.94 – 4.87 (m, 1H), 3.75 (t, *J* = 7.8 Hz, 1H), 2.11 – 2.06 (m, 1H), 2.00 – 1.90 (m, 2H), 1.77 – 1.63 (m, 7H), 1.61 – 1.49 (m, 3H), 1.18 – 1.05 (m, 6H), 0.90 (t, *J* = 7.1 Hz, 9H), 0.78 – 0.75 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 179.6, 166.0, 143.8, 130.1, 130.1, 128.3, 75.0, 48.8, 47.4, 41.1, 40.6, 35.2, 34.4, 34.3, 33.4, 32.9, 31.6, 26.6, 26.5, 26.2, 26.1, 23.7, 22.2, 20.9, 16.6.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{26}H_{37}O_4]^-$: 413.2697, found: 413.2692.



3-(benzyloxy)-2-(cyclohexylmethyl)-2-methyl-3-oxopropanoic acid (3ap)

According to general **Procedure A,** crude product was purified by flash column chromatography on silica gel using petroleum ether/EtOAc/AcOH (8/1/0.5%, v/v/v) as an eluent to provide as colorless oil (13.4 mg, 44% yield).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 5H), 5.23 – 5.15 (m, 2H), 1.95 – 1.88 (m, 1H), 1.85 – 1.79 (m,1H), 1.61 – 1.53 (m, 5H), 1.49 (s, 3H), 1.30 – 1.27 (m, 1H), 1.16 – 1.06 (m, 3H), 0.92 – 0.87 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 176.5, 174.1, 135.3, 128.7, 128.7, 128.4, 67.6, 52.9, 43.5, 34.4, 34.3, 34.1, 26.4, 26.3, 26.2, 21.6.

HRMS (ESI-) [M-H]-calculated m/z for $[C_{18}H_{23}O_4]^-$: 303.1602, found: 303.1606.

10. Reference

[1] J. Shi, T. Yuan, M. Zheng and X. Wang, *ACS Catalysis*, 2021, **11**, 3040-3047.

[2] C. Huang, C. Chen, M. Zhang, L. Lin, X. Ye, S. Lin, M. Antonietti and X. Wang, *Nat. Commun.,* 2015, **6**, 7698.

[3] Y. Wang, J. Zhang, X. Wang, M. Antonietti and H. Li, *Angew. Chem., Int Ed.*, 2010, **49**, 3356-3359.

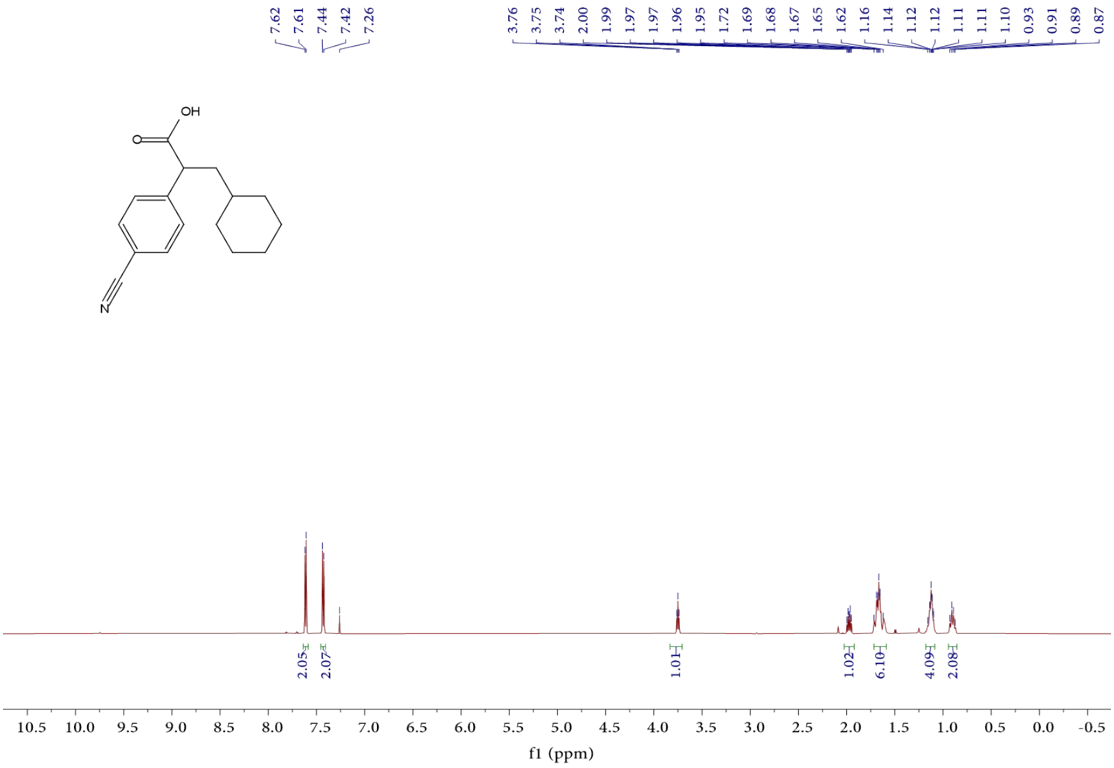
[4] D.-H. Bao, F.-L. Wei, T. Zhou, M. D. Eastgate and P. S. Baran, *Nature*, 2017, **545**, 213-218.

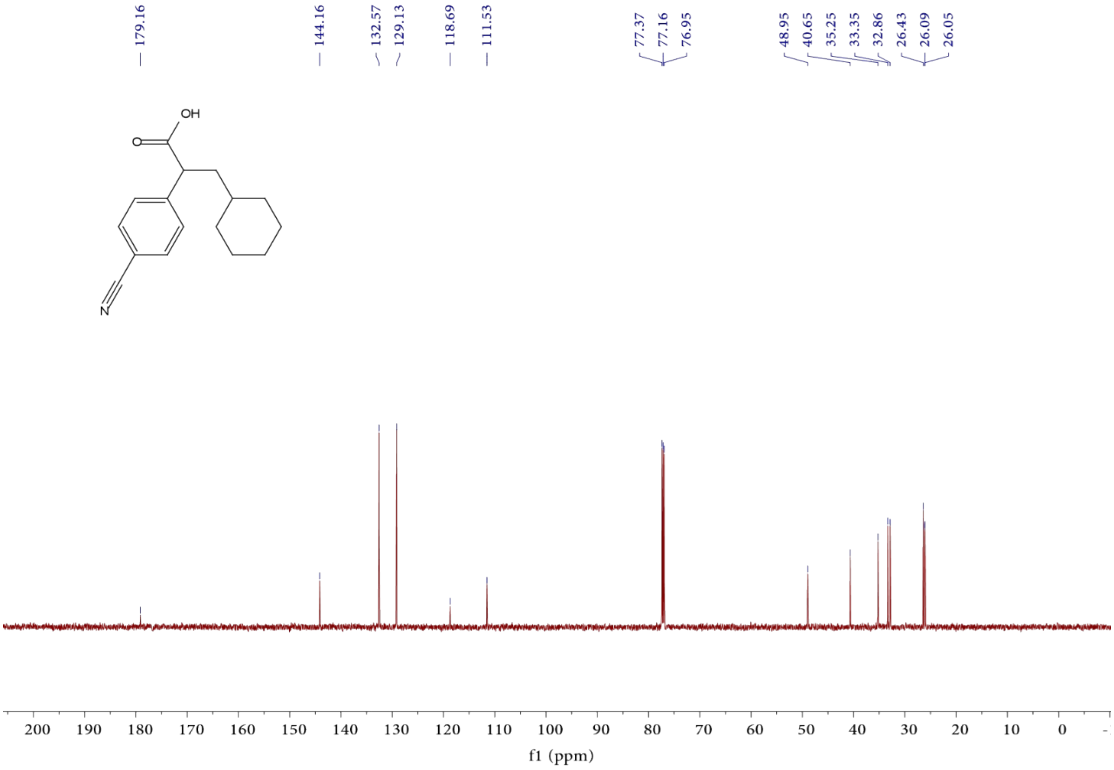
[5] F. Toriyama, J. Cornella, L. Wimmer, T.-G. Chen, D. D. Dixon, G. Creech and P. S. Baran, *J. Am. Chem. Soc,* 2016, **138**, 11132-11135.

[6] J. T. Edwards, R. R. Merchant, K. S. McClymont, K. W. Knouse, T. Qin, L. R. Malins, B. Vokits, S. A. Shaw, D.-H. Bao, F.-L. Wei, T. Zhou, M. D. Eastgate and P. S. Baran, *Nature*, 2017, **545**, 213-218.

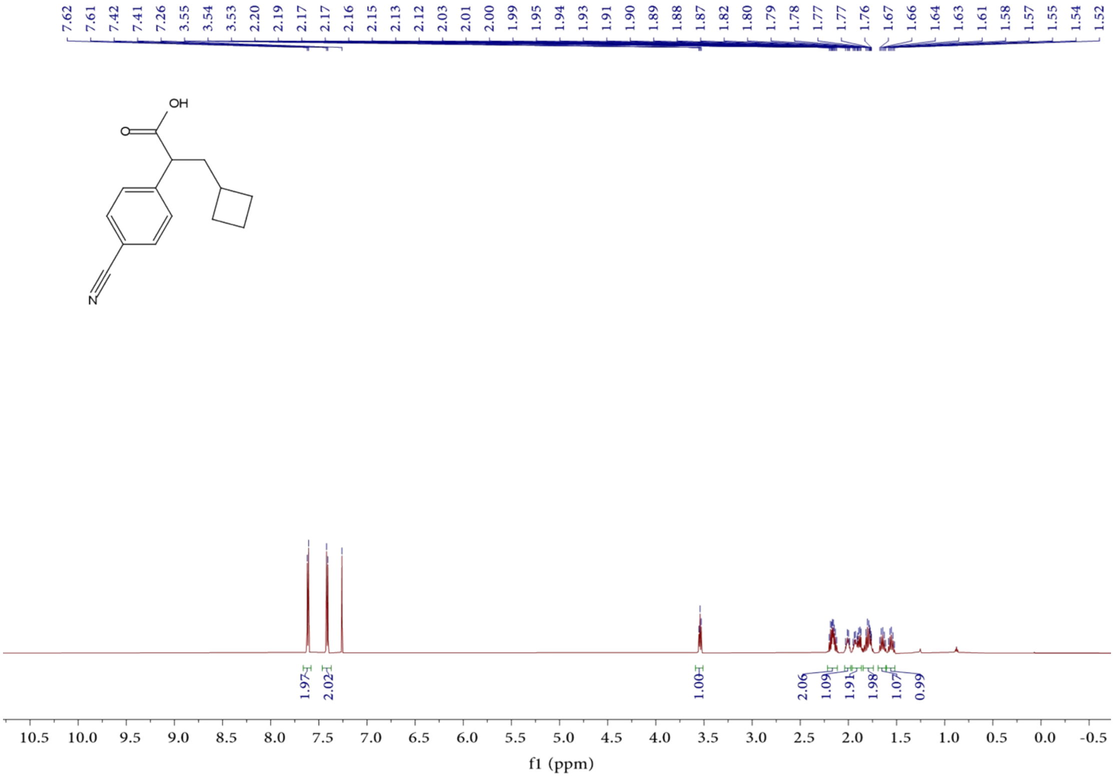
11. NMR spectra

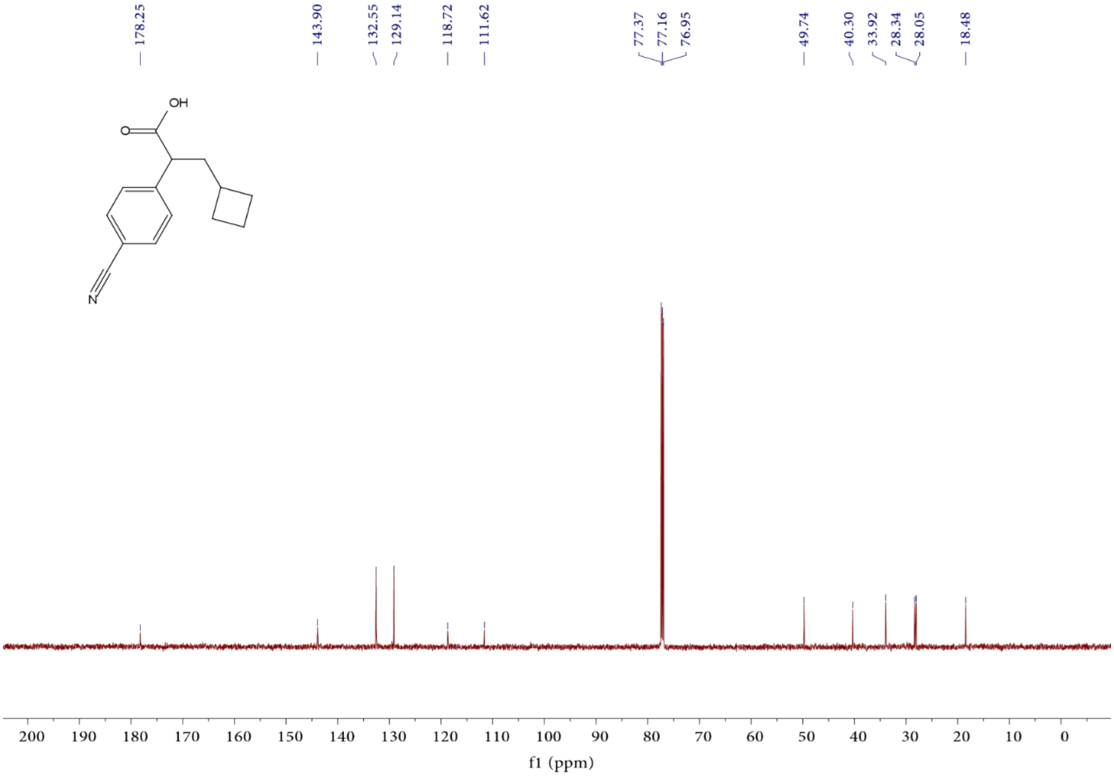
2-(4-cyanophenyl)-3-cyclohexylpropanoic acid (3aa)



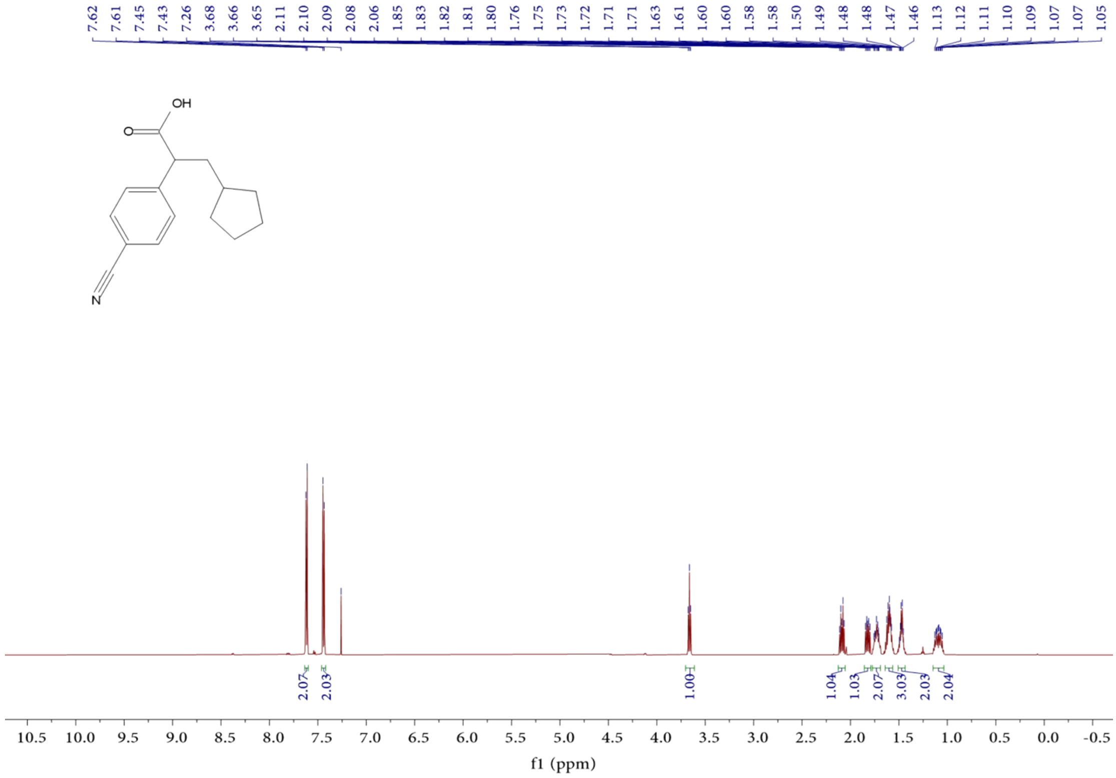


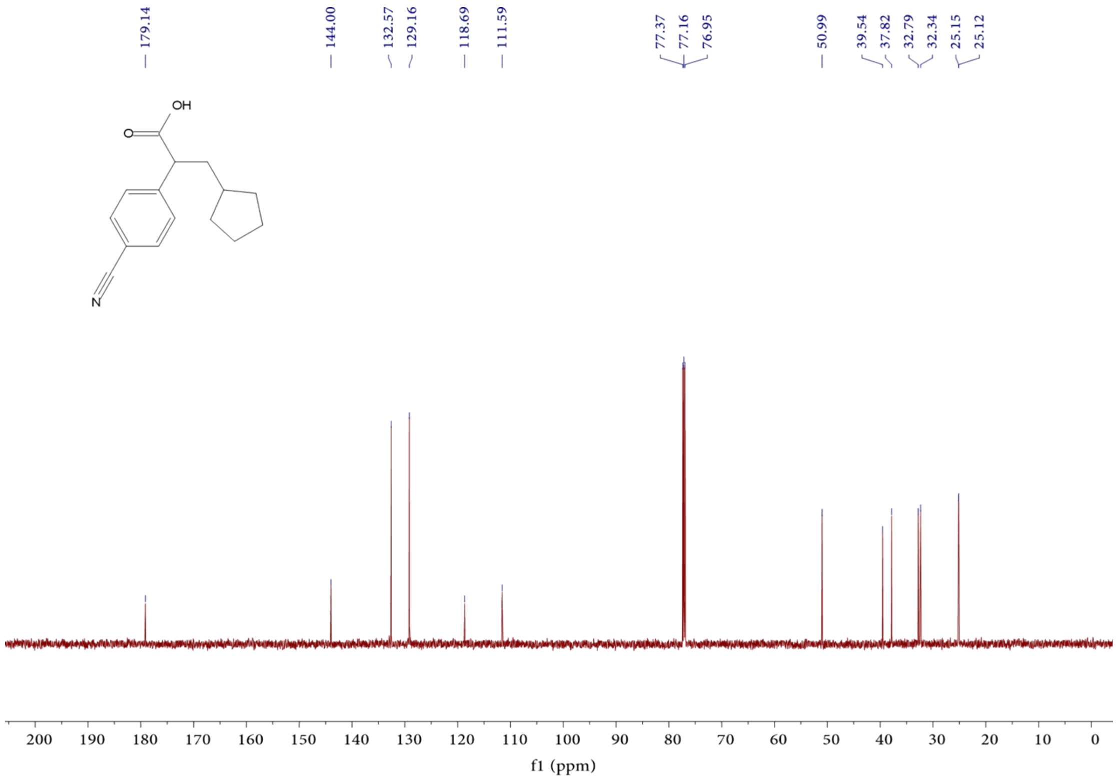
2-(4-cyanophenyl)-3-cyclobutylpropanoic acid (3ba)



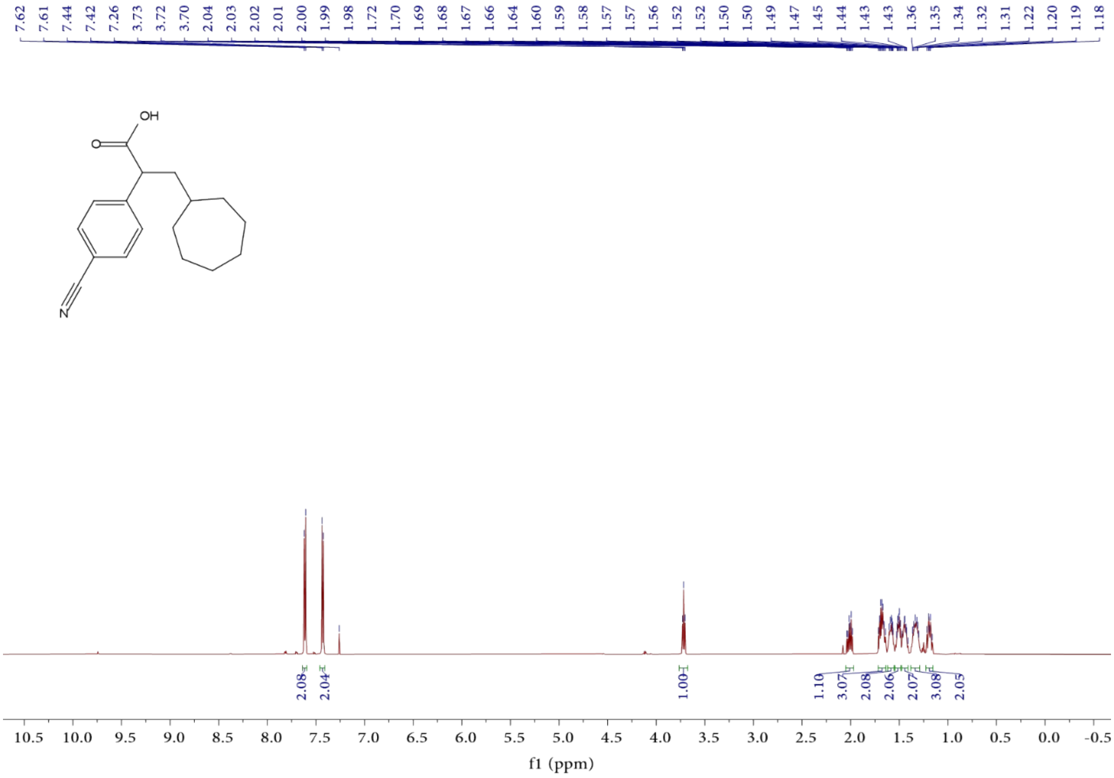


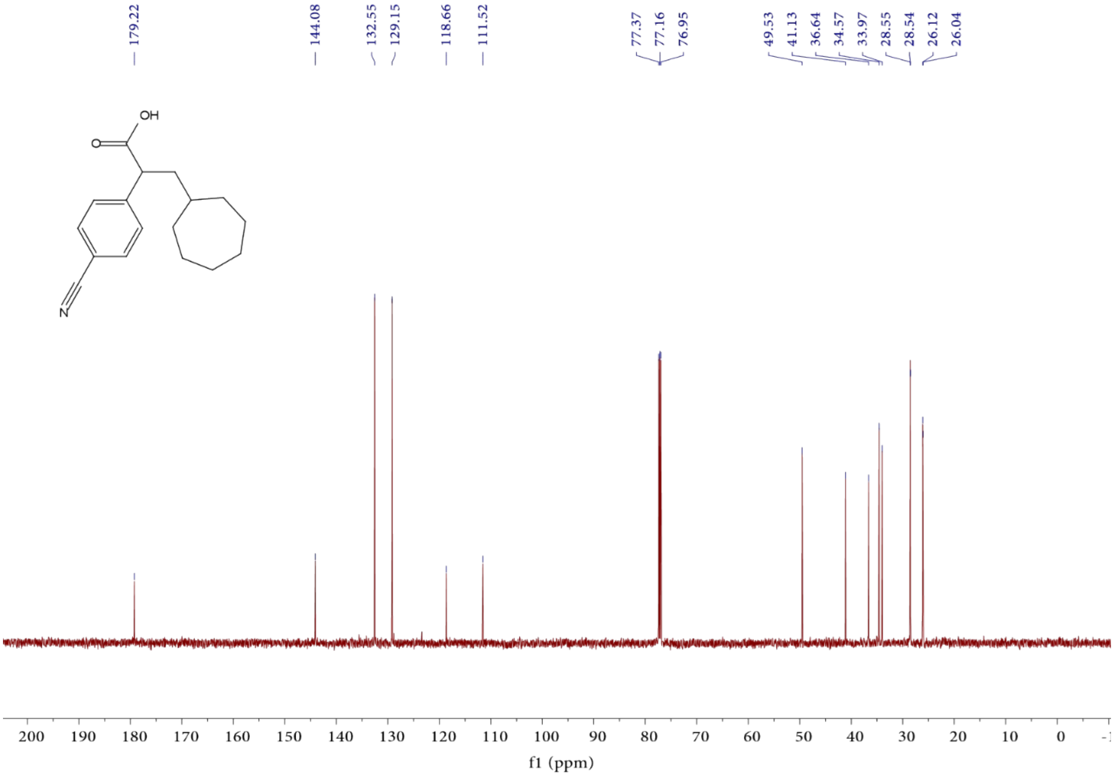
2-(4-cyanophenyl)-3-cyclopentylpropanoic acid (3ca)



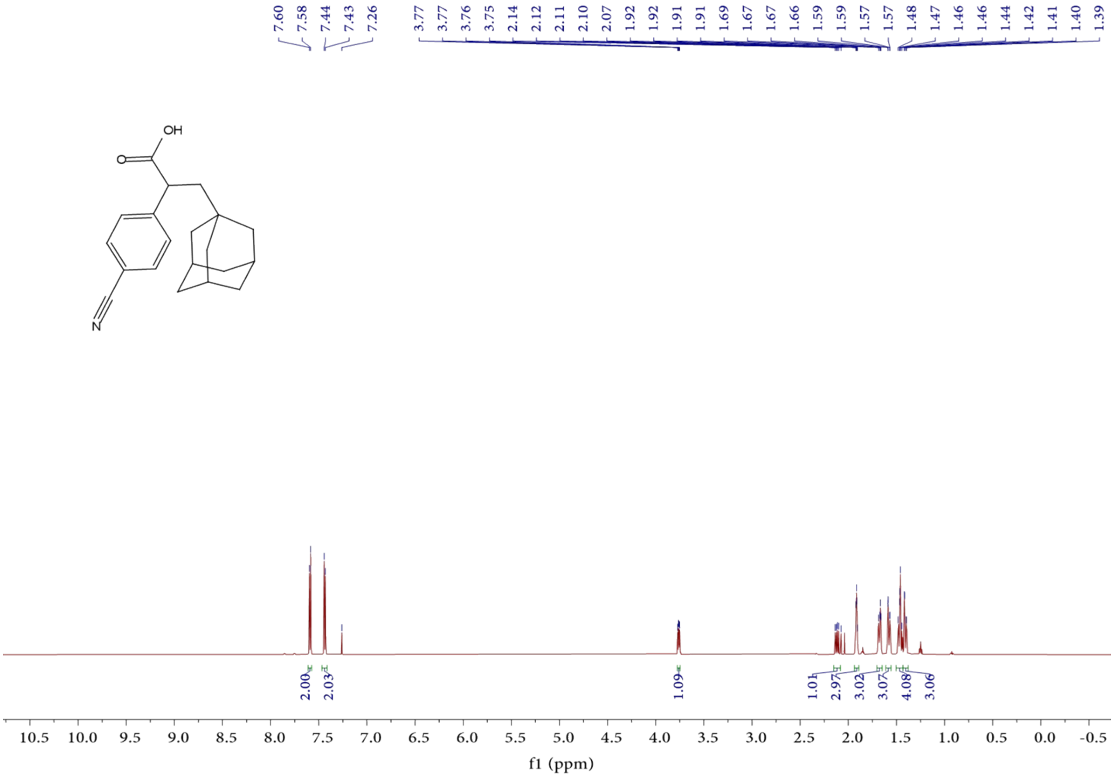


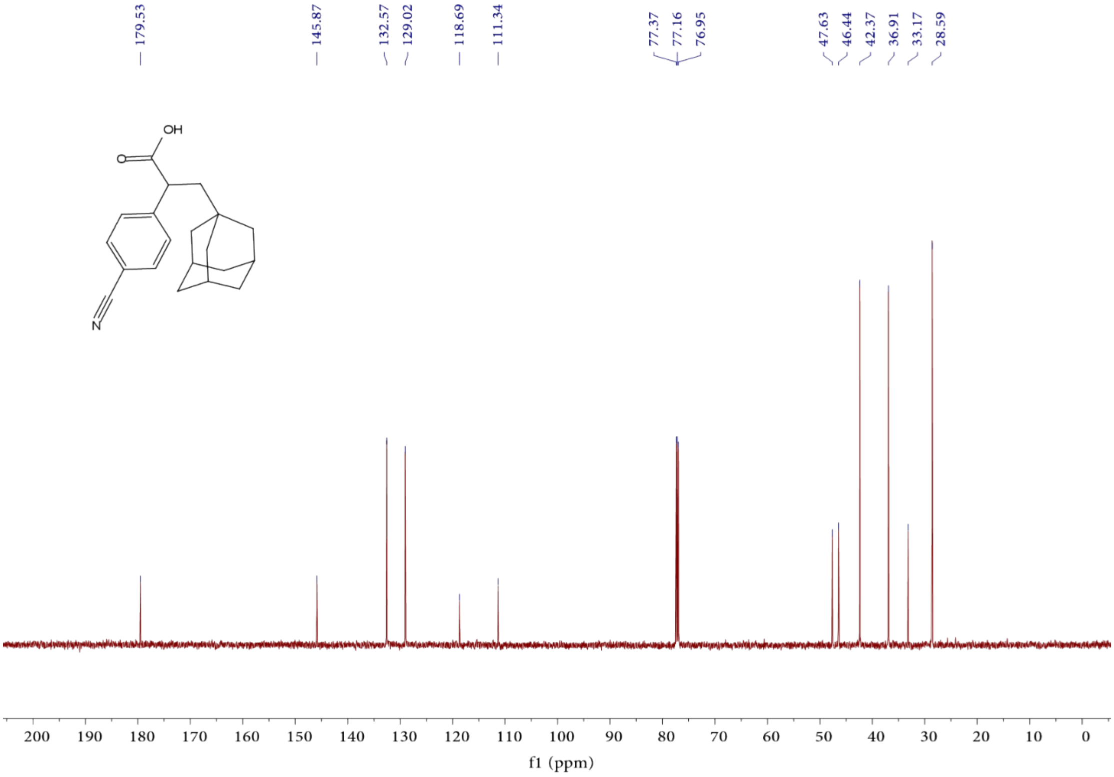
2-(4-cyanophenyl)-3-cycloheptylpropanoic acid (3da)



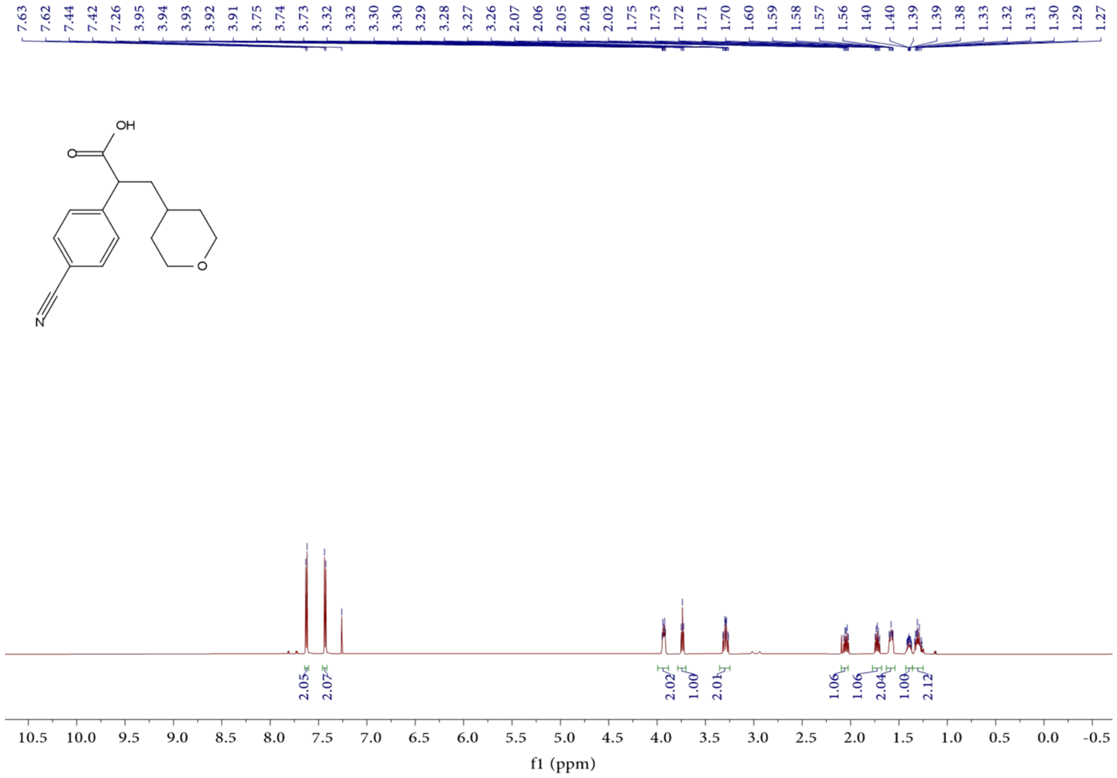


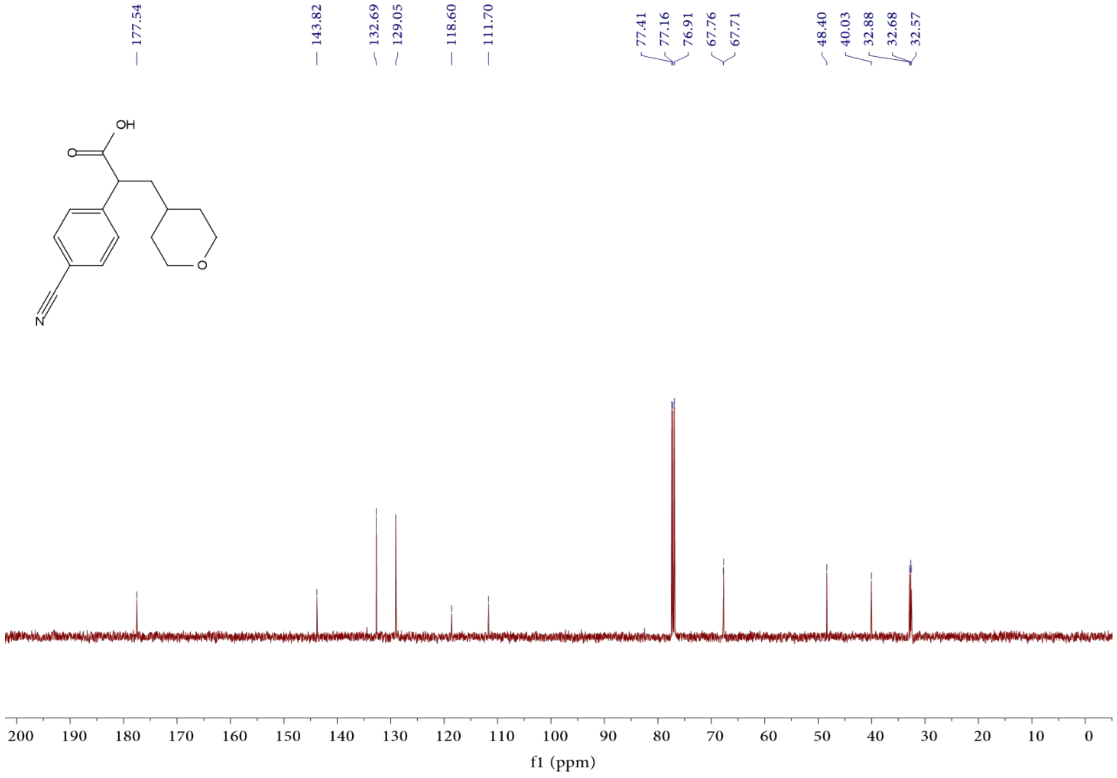
3-((3r,5r,7r)-adamantan-1-yl)-2-(4-cyanophenyl)propanoic acid (3ea)



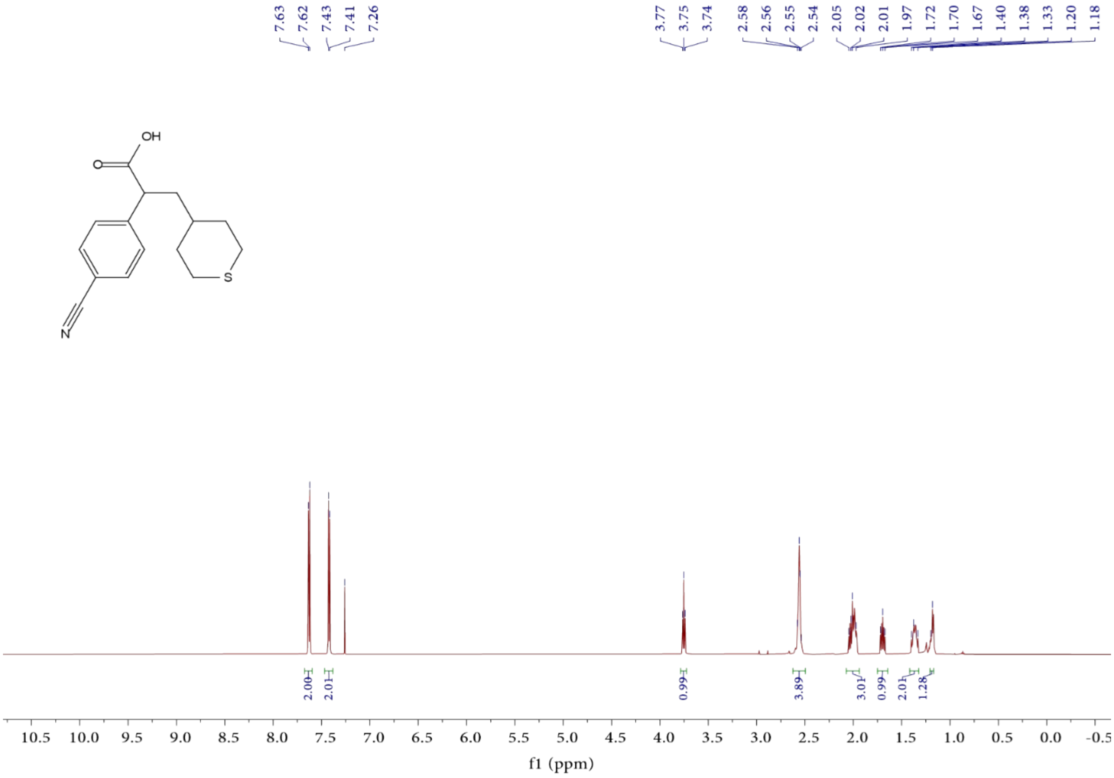


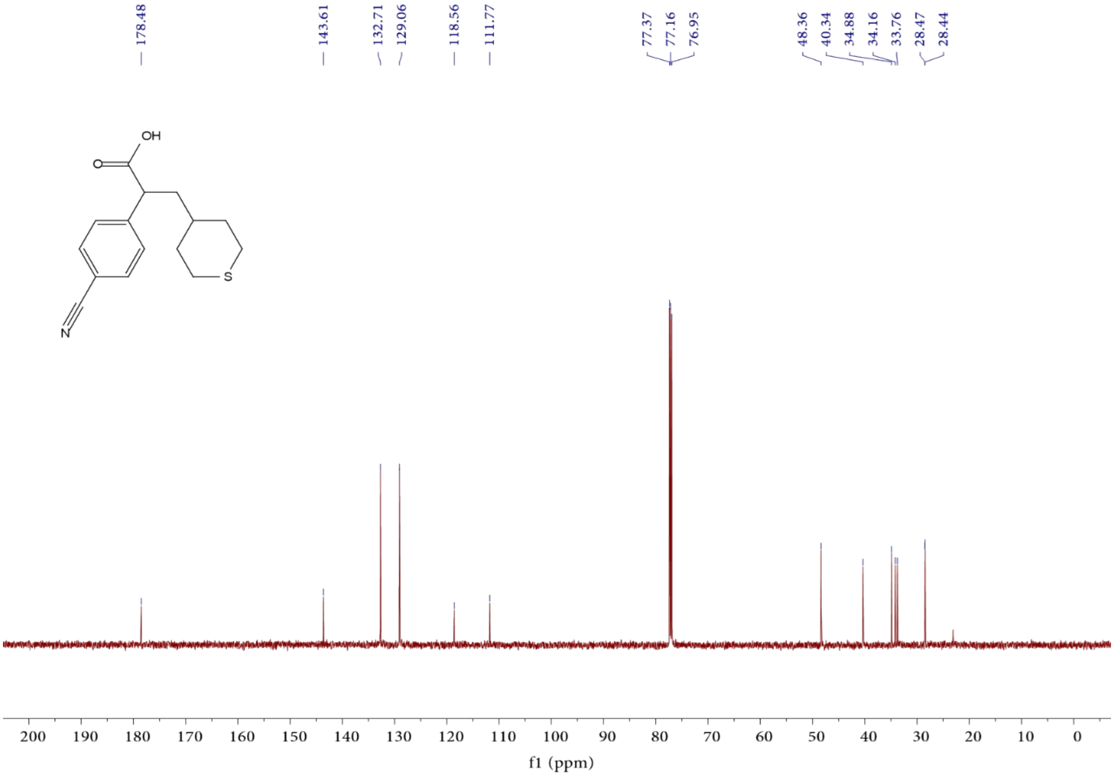
2-(4-cyanophenyl)-3-(tetrahydro-2H-pyran-4-yl)propanoic acid (3fa)



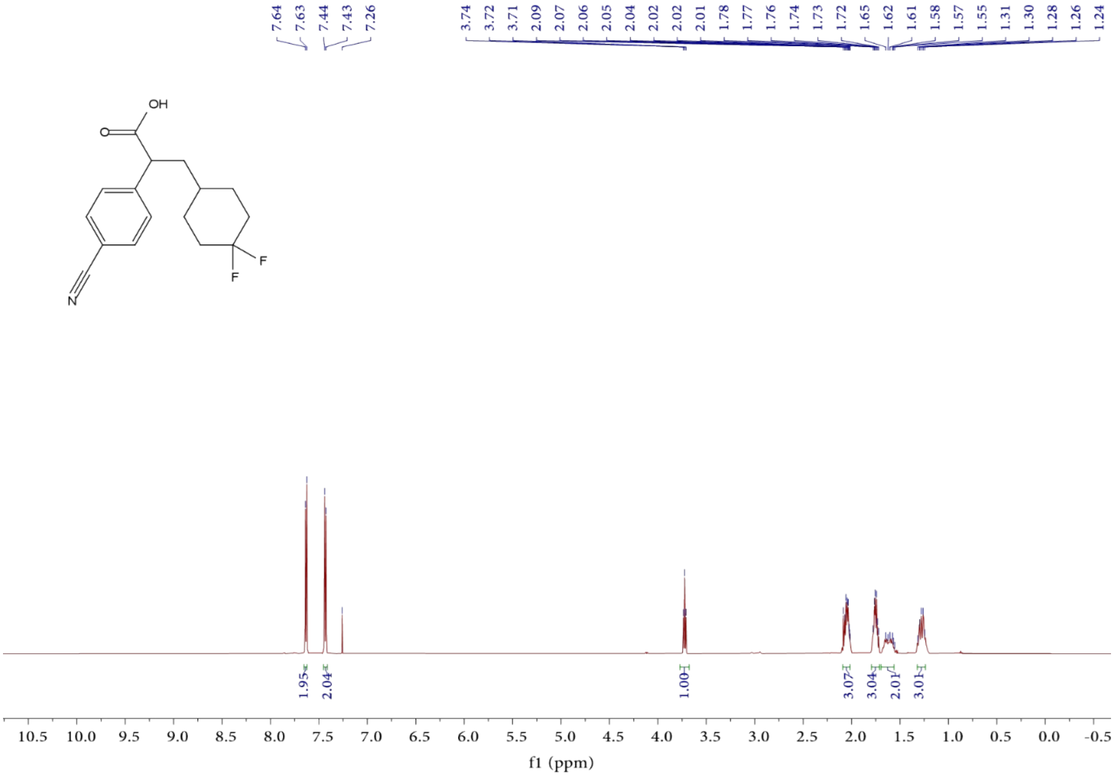


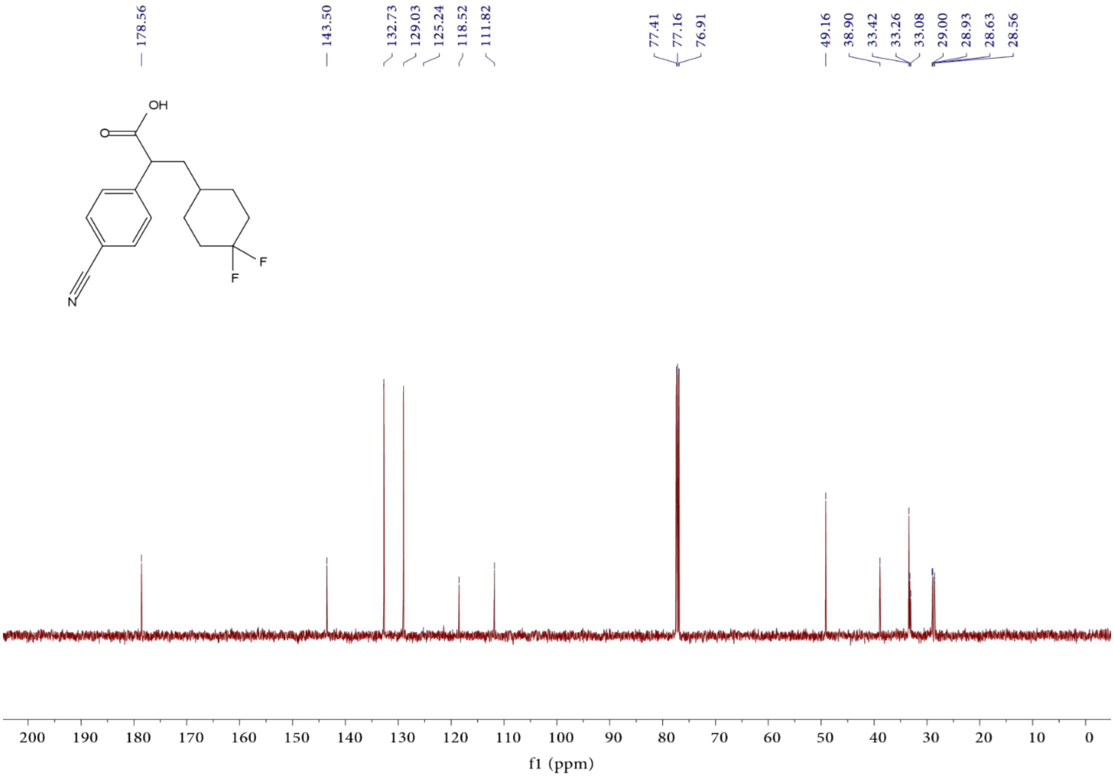
2-(4-cyanophenyl)-3-(tetrahydro-2H-thiopyran-4-yl)propanoic acid (3ga)

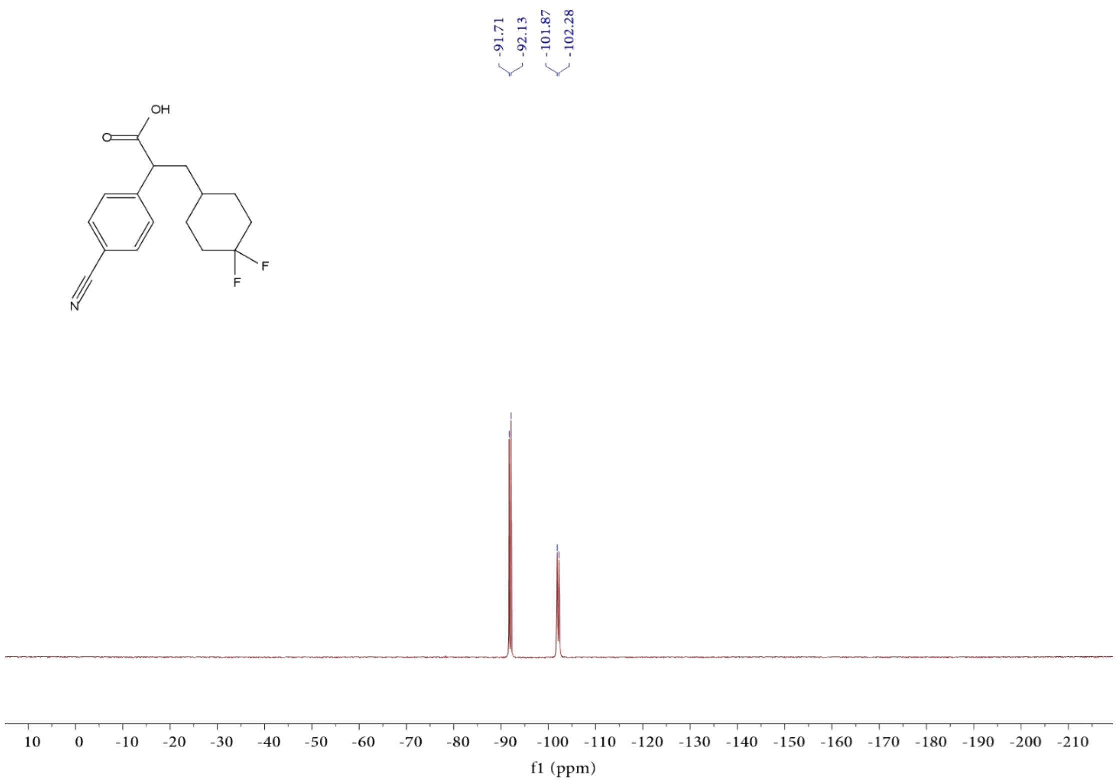




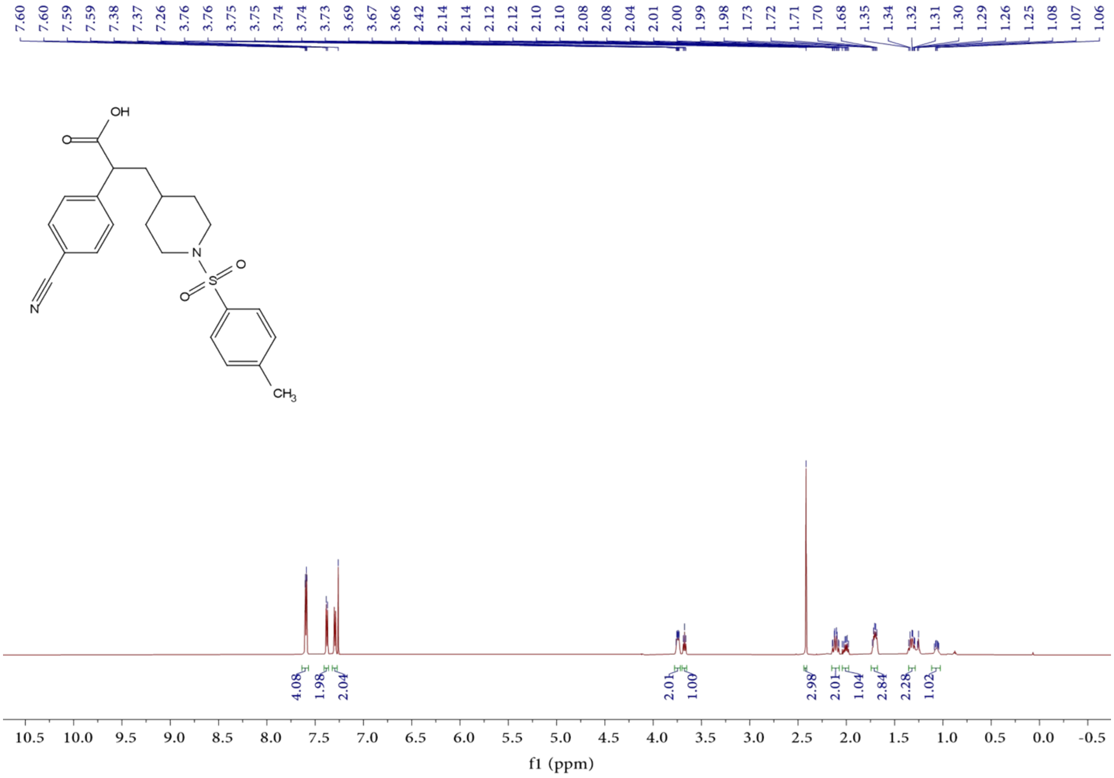
2-(4-cyanophenyl)-3-(4,4-difluorocyclohexyl)propanoic acid (3ha)

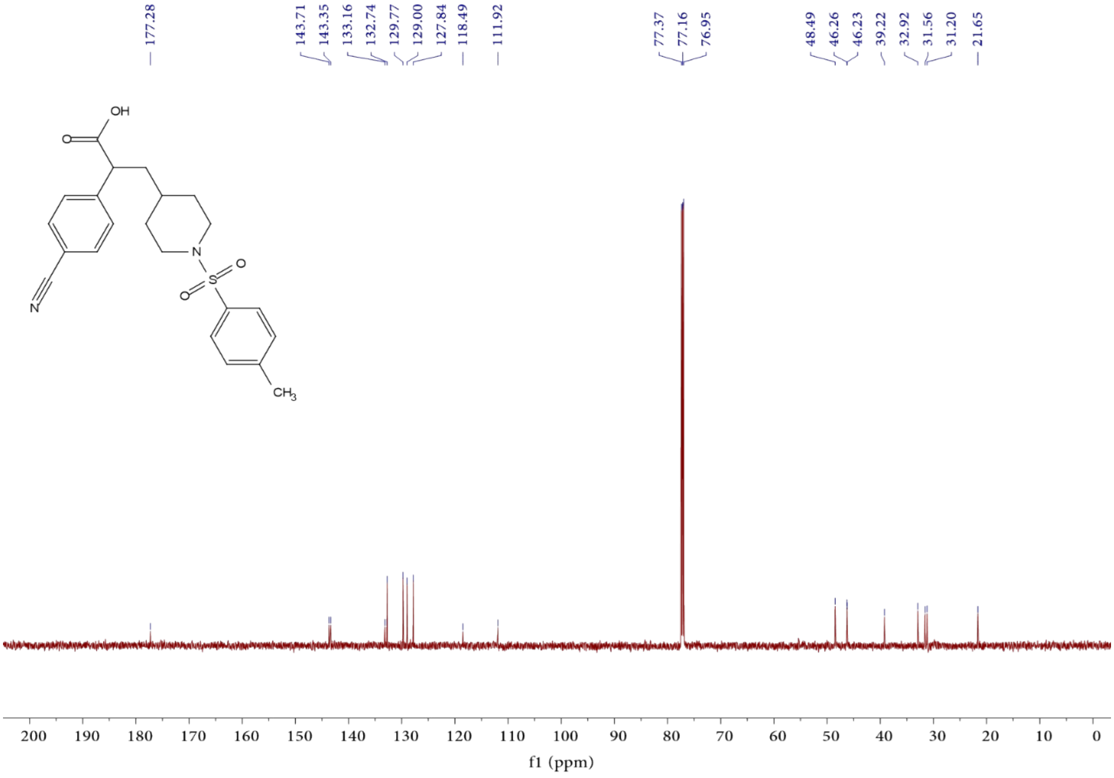




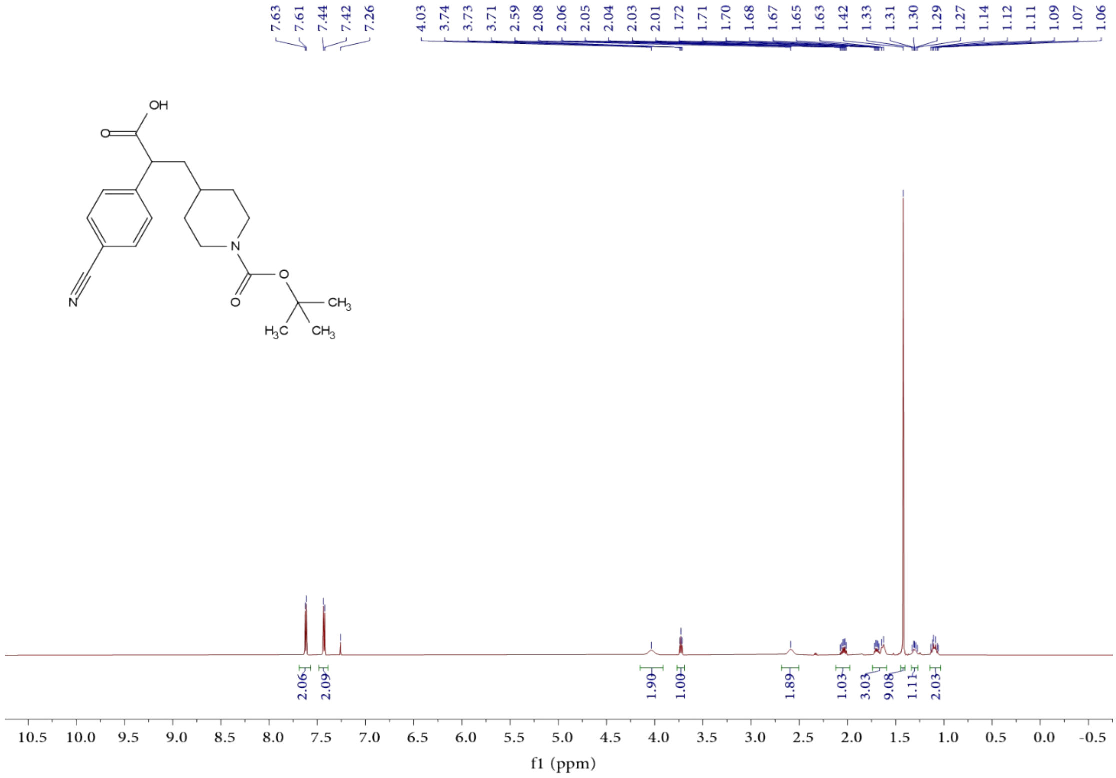

-91.71
-92.13
-101.87
-102.28
OH
O
N
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

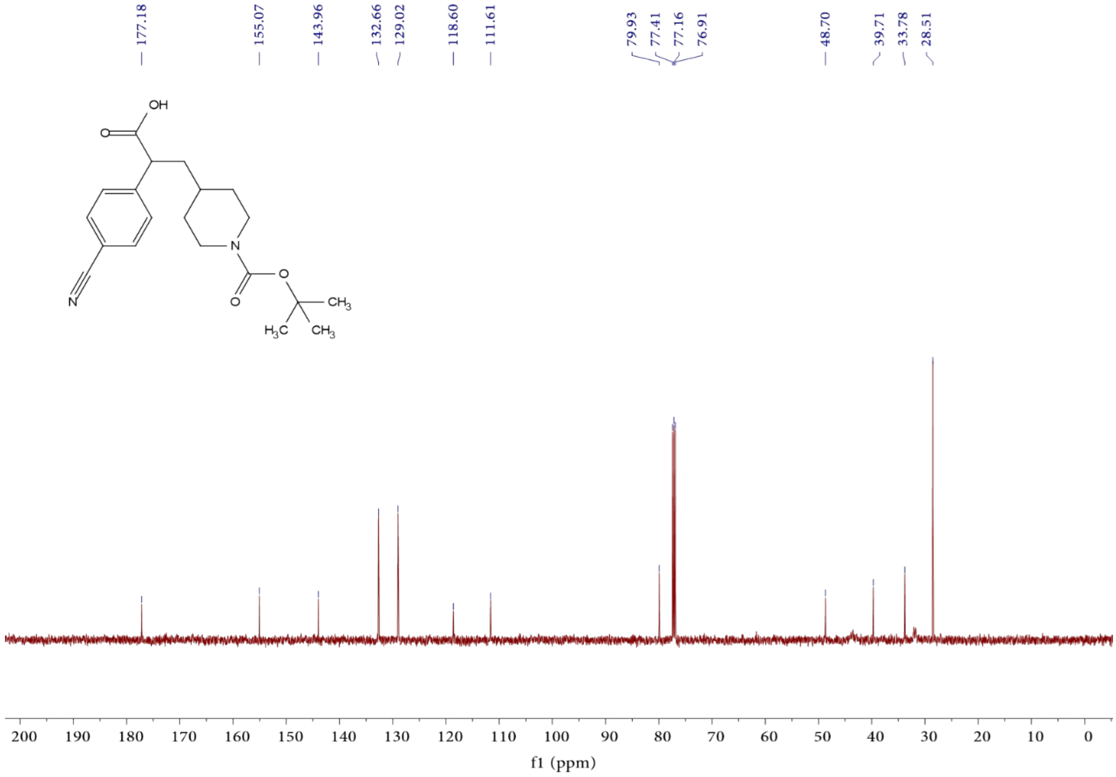
2-(4-cyanophenyl)-3-(1-tosylpiperidin-4-yl)propanoic acid (3ia)



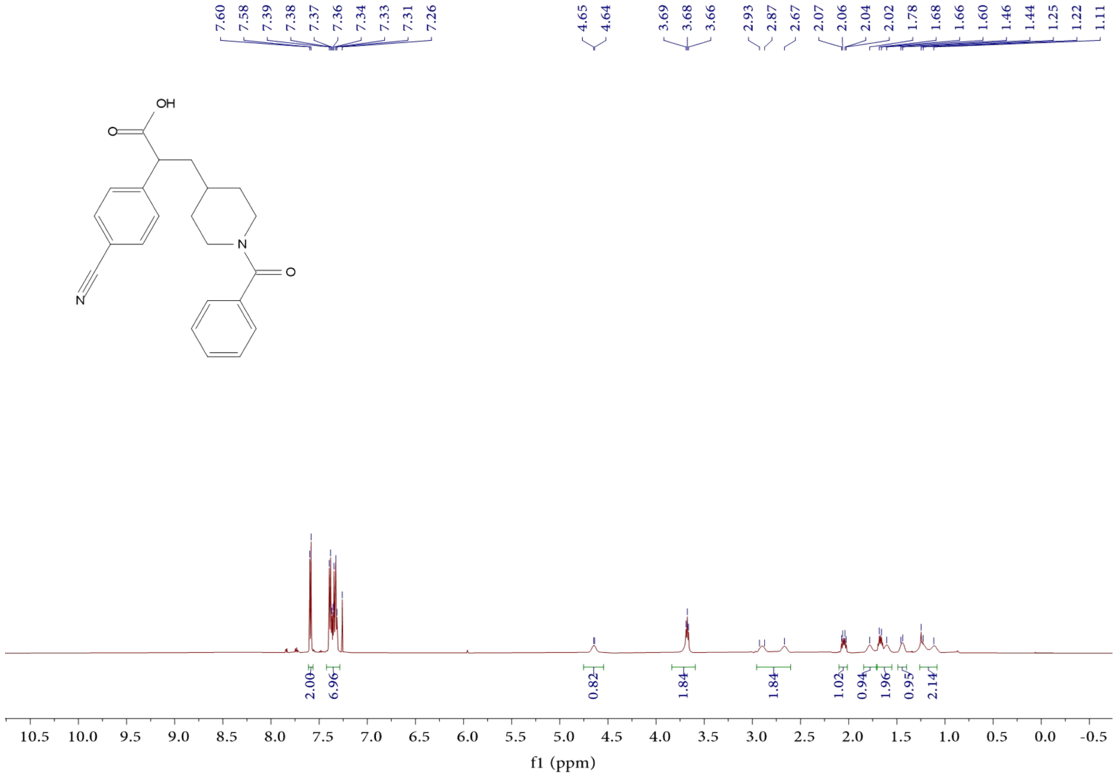


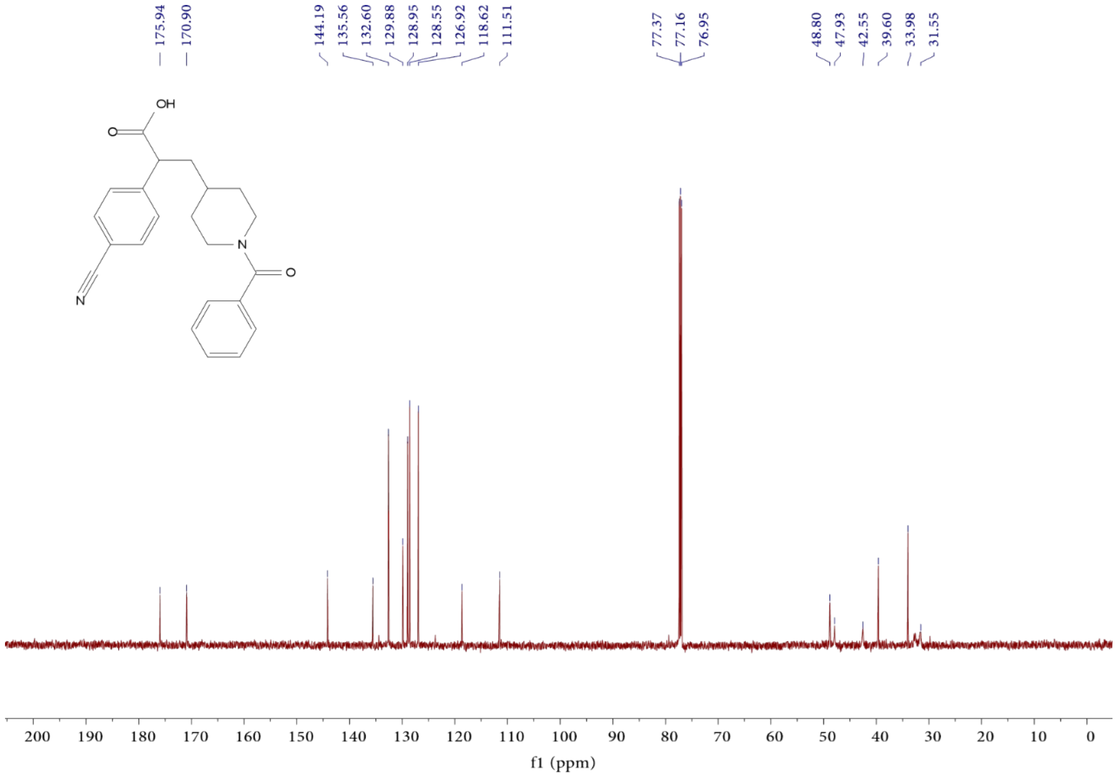
3-(1-(tert-butoxycarbonyl)piperidin-4-yl)-2-(4-cyanophenyl)propanoic acid (3ja)



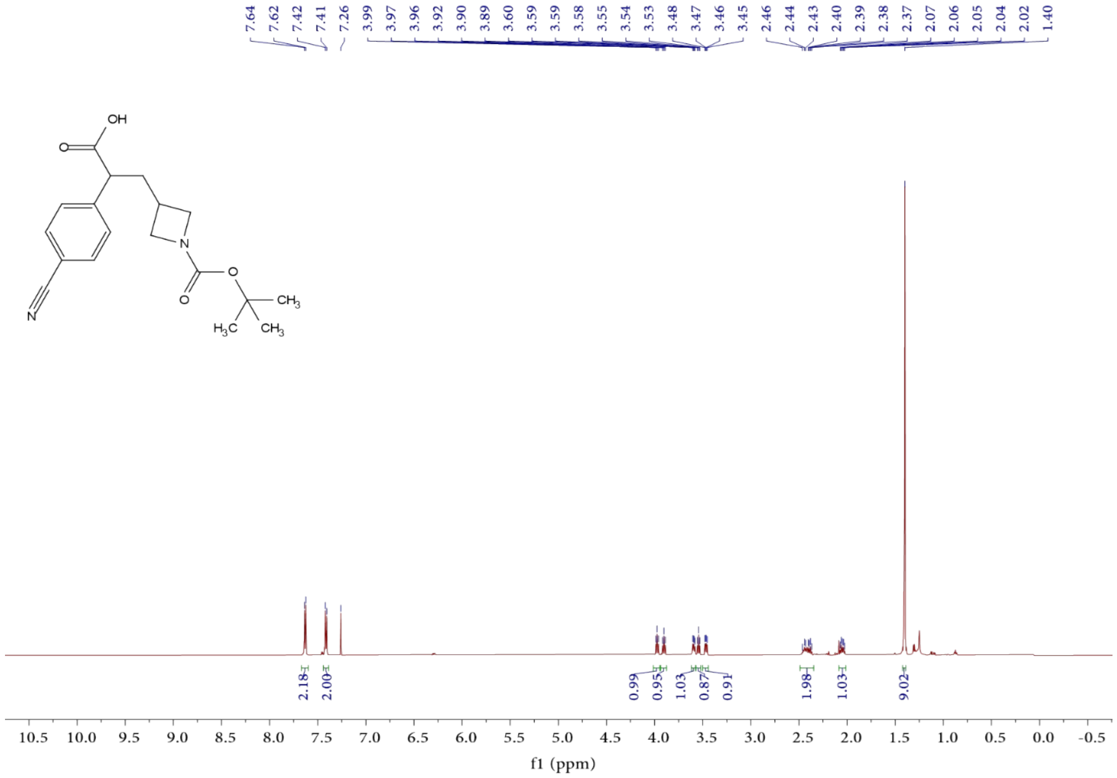


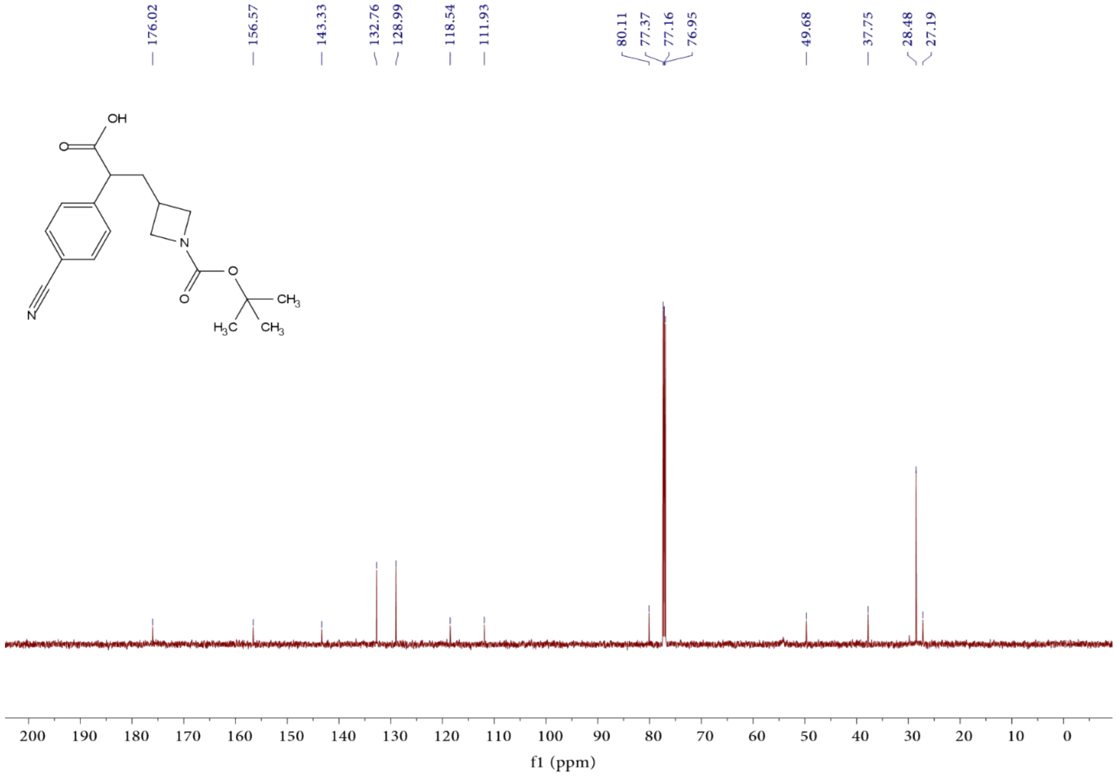
3-(1-benzoylpiperidin-4-yl)-2-(4-cyanophenyl)propanoic acid (3ka)



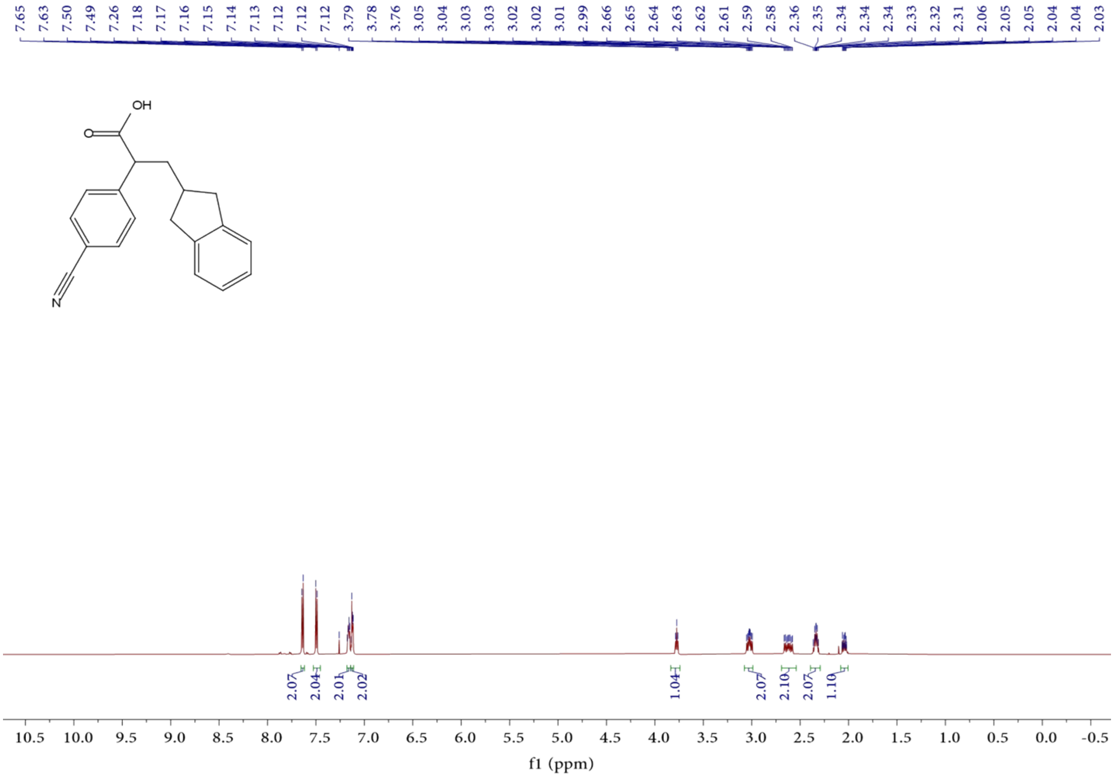


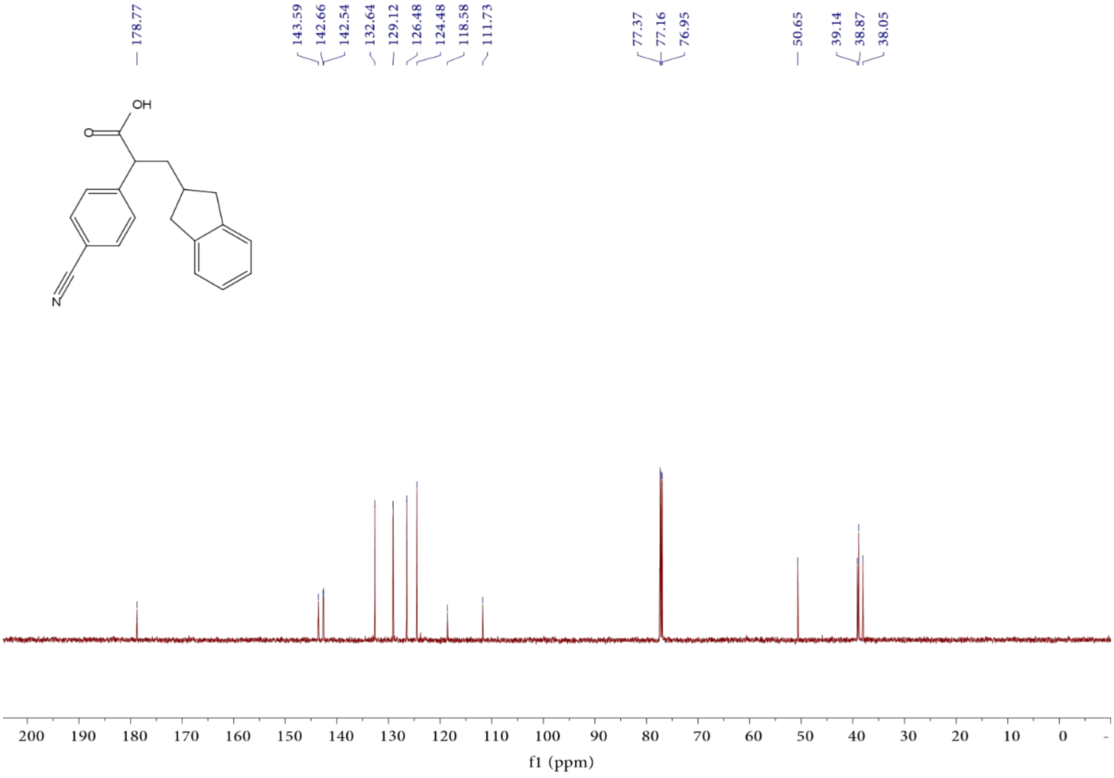
3-(1-(tert-butoxycarbonyl)azetidin-3-yl)-2-(4-cyanophenyl)propanoic acid (3la)



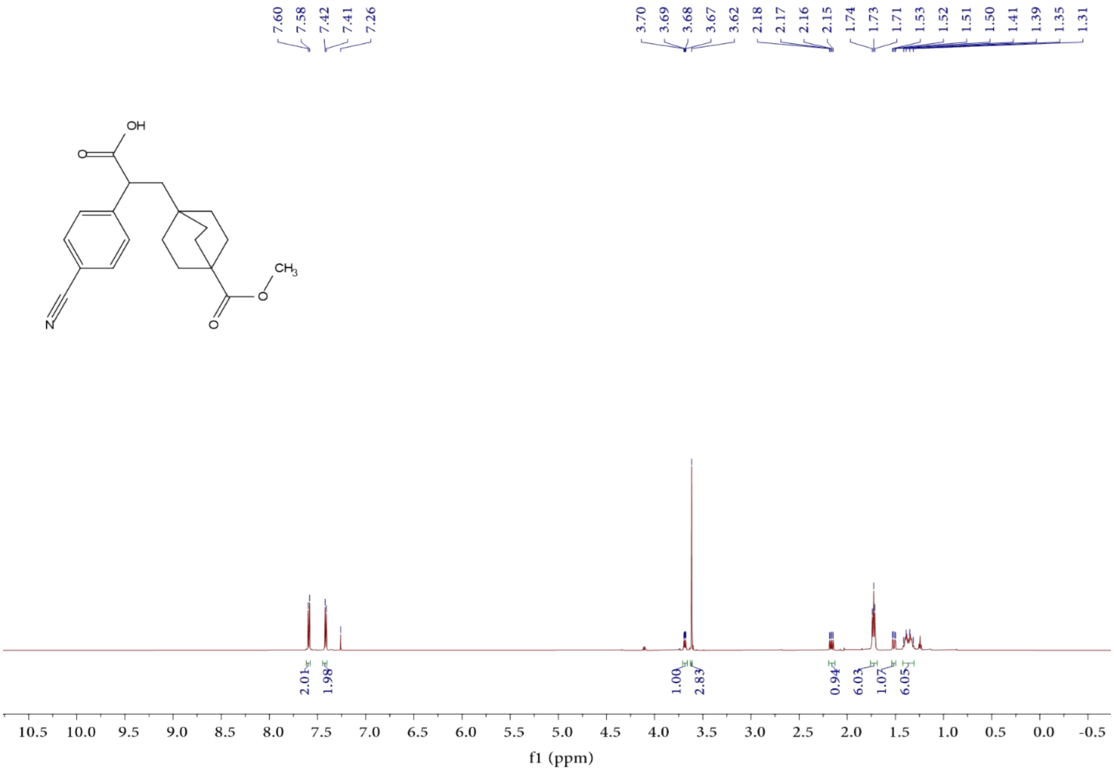


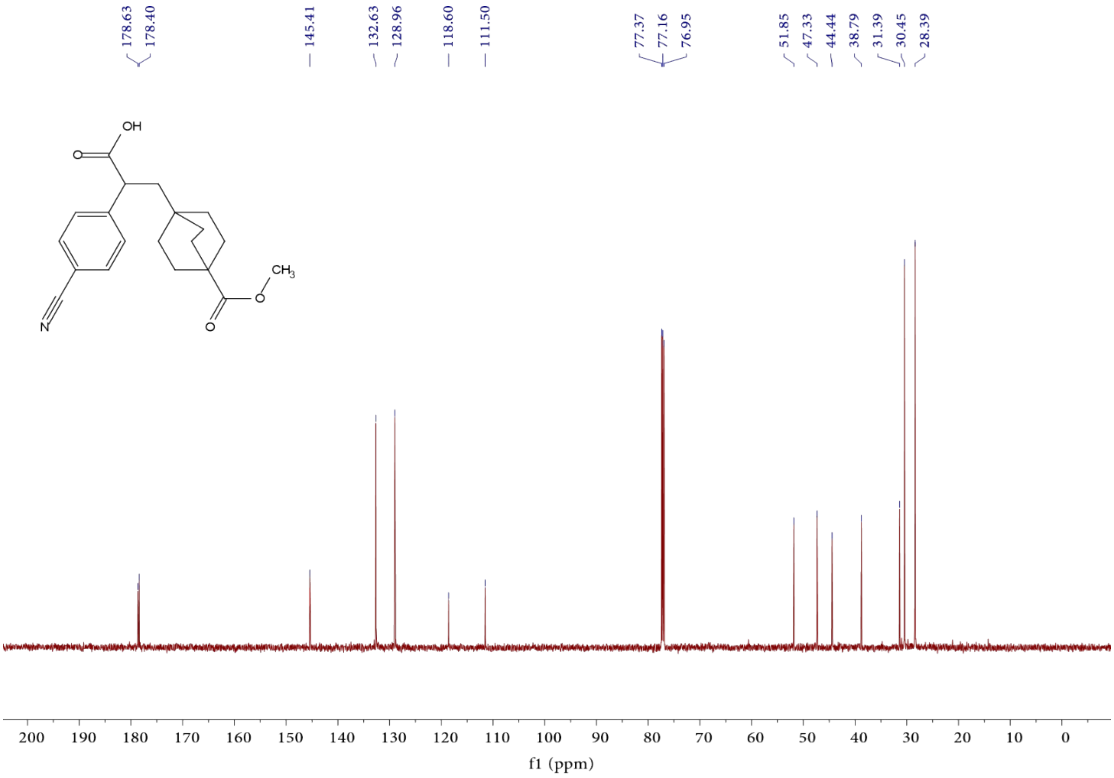
2-(4-cyanophenyl)-3-(2,3-dihydro-1H-inden-2-yl)propanoic acid (3ma)



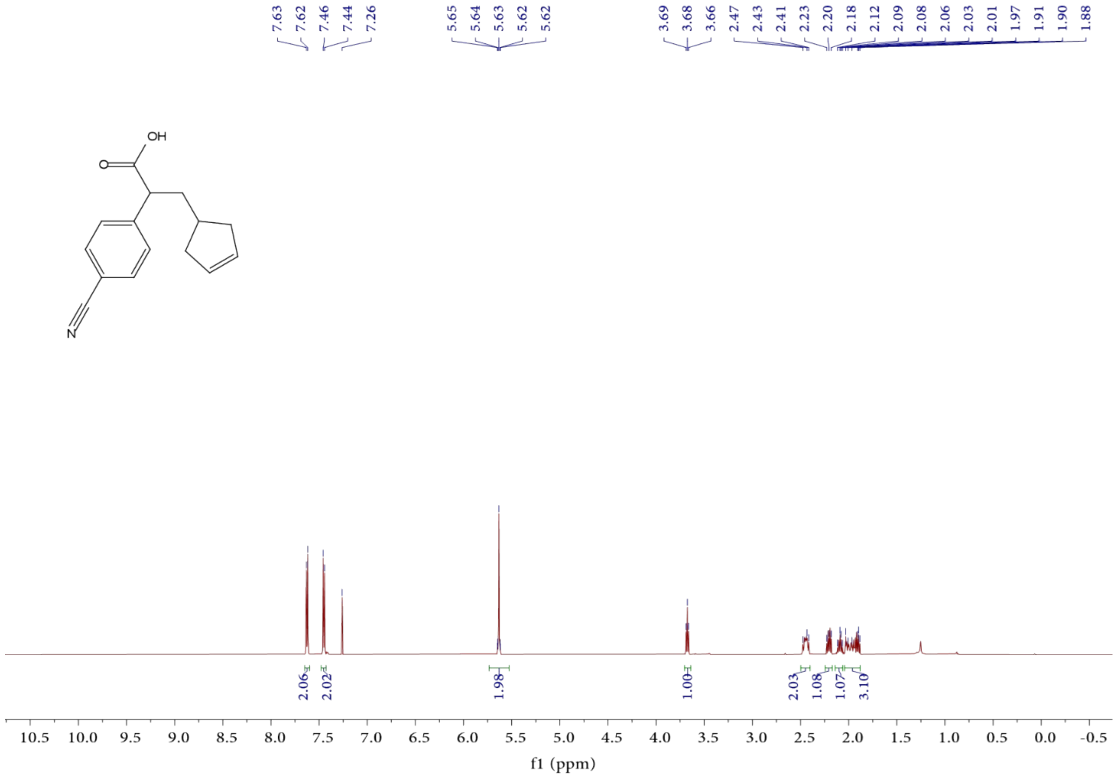


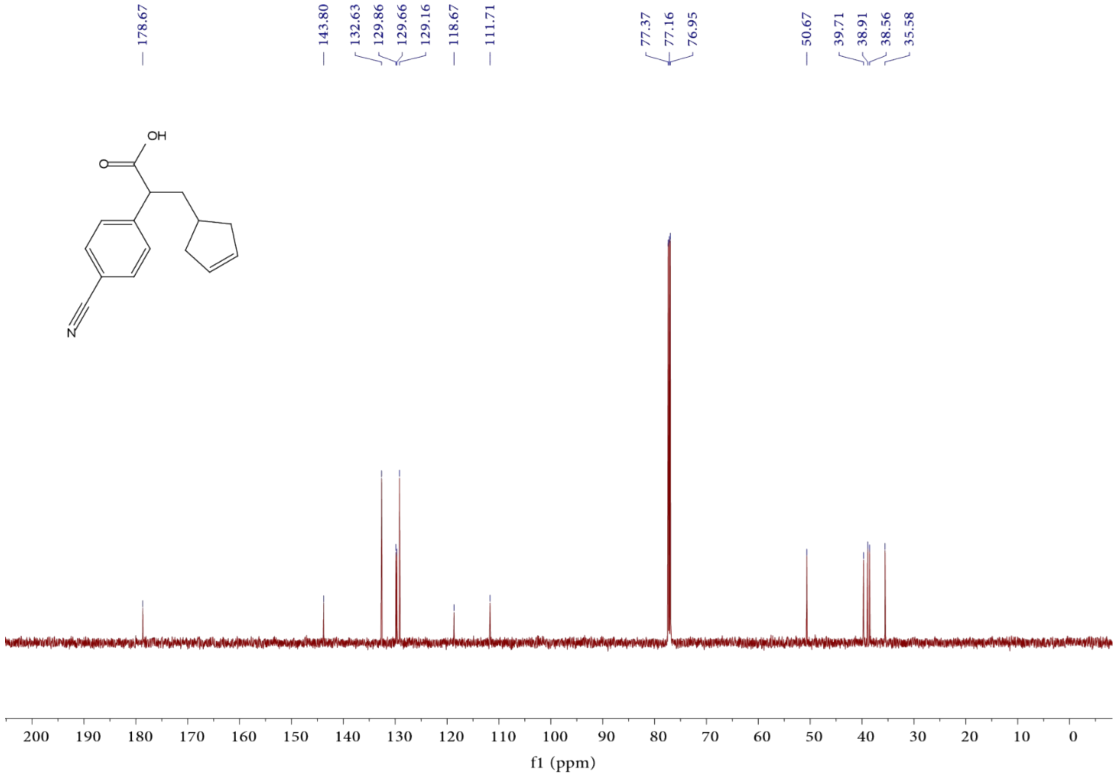
2-(4-cyanophenyl)-3-(4-(methoxycarbonyl)bicyclo[2.2.2]octan-1-yl)propanoic acid (3na)



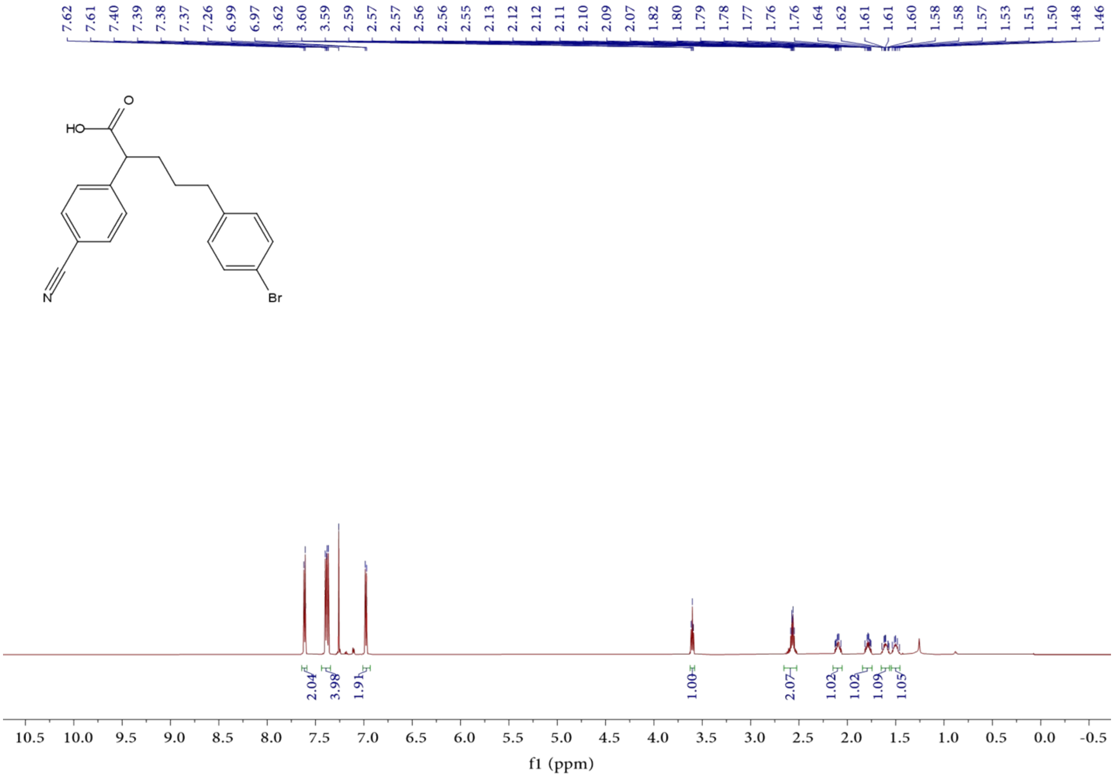


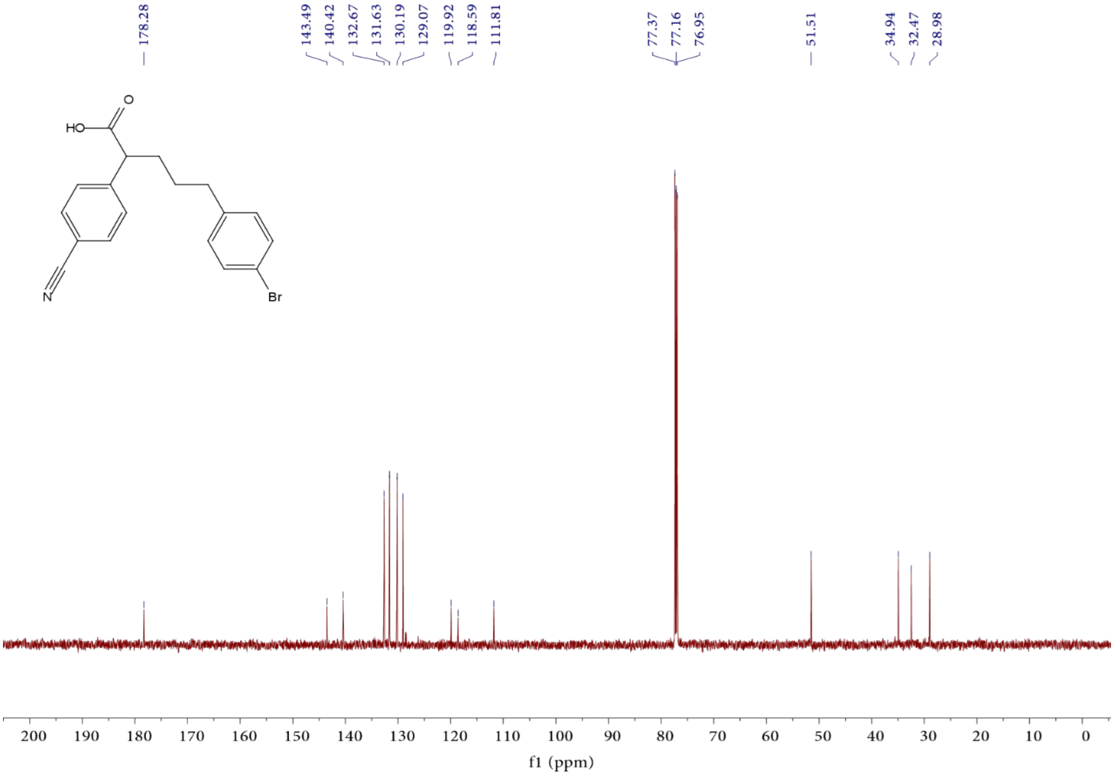
2-(4-cyanophenyl)-3-(cyclopent-3-en-1-yl)propanoic acid (3oa)



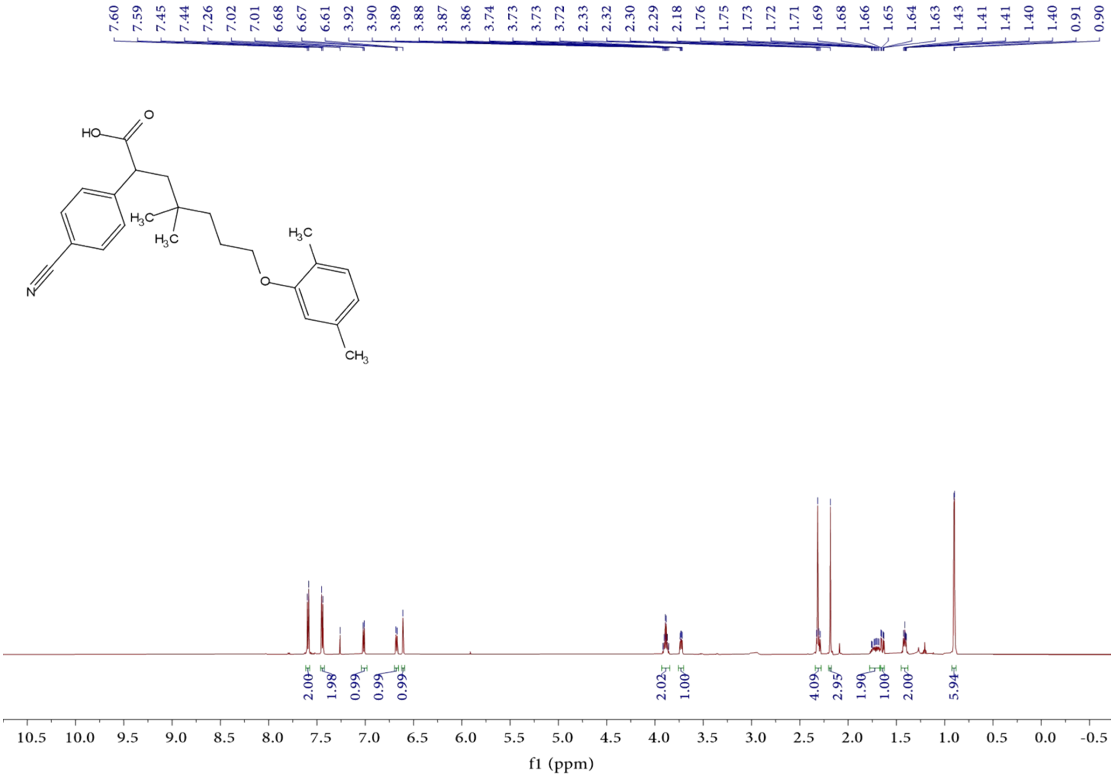


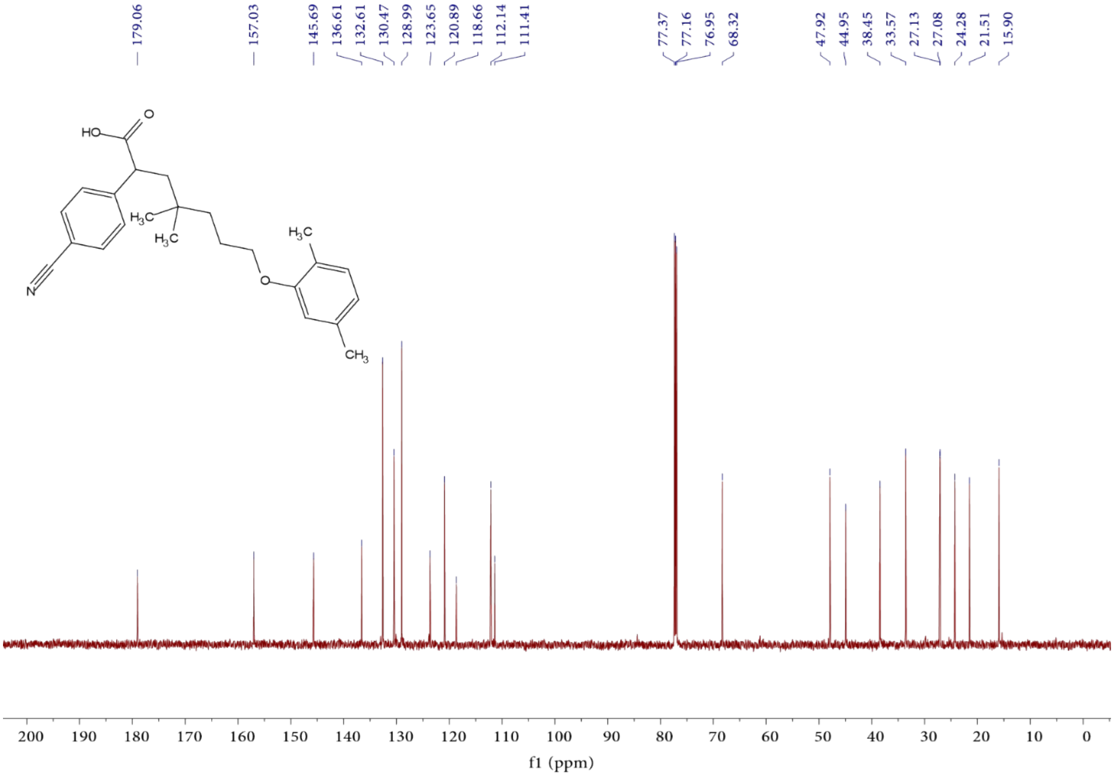
5-(4-bromophenyl)-2-(4-cyanophenyl)pentanoic acid (3pa)



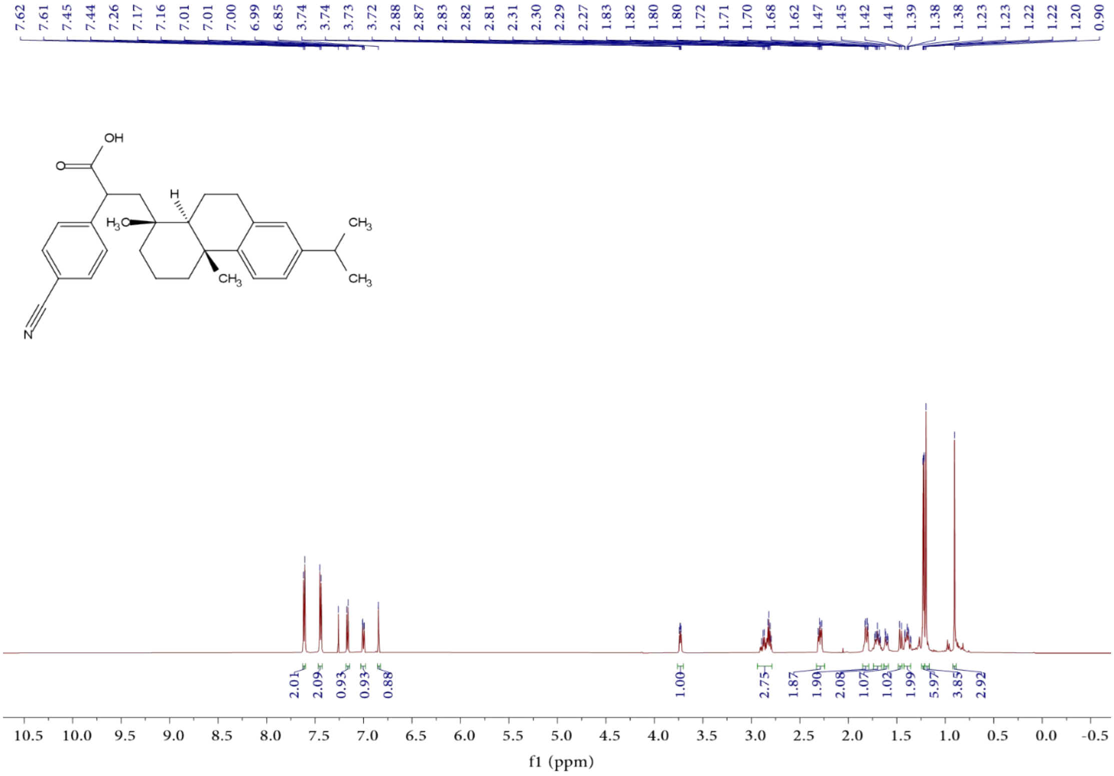


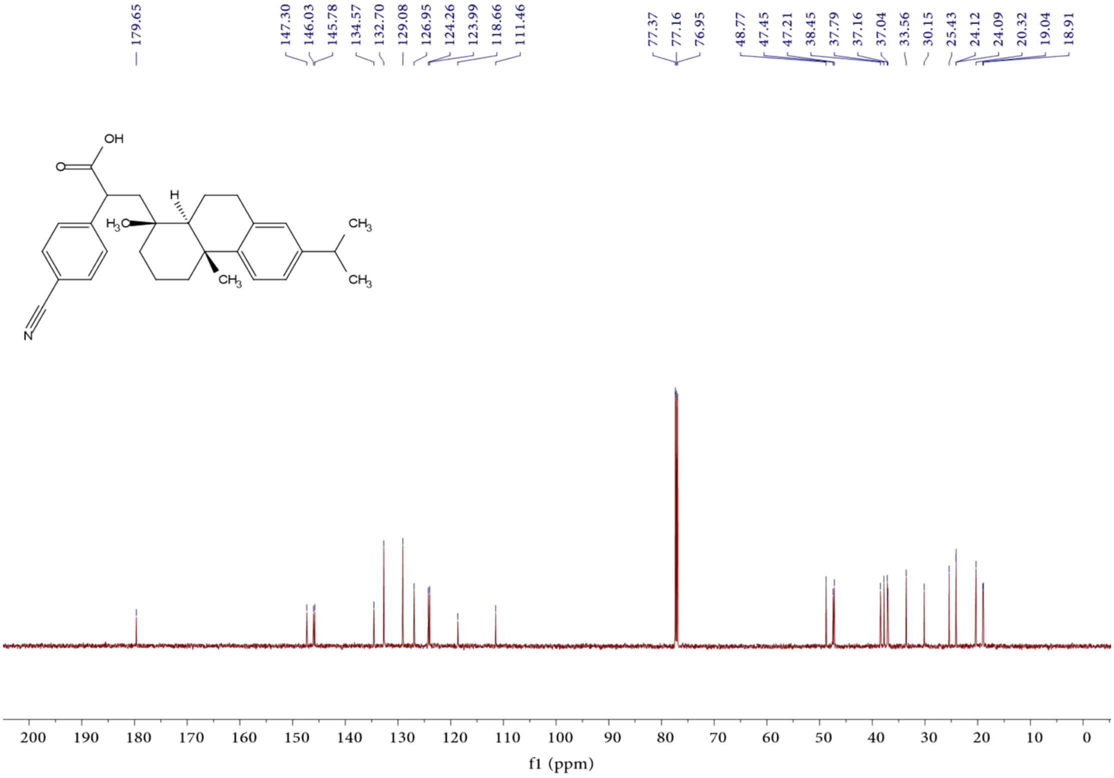
2-(4-cyanophenyl)-7-(2,5-dimethylphenoxy)-4,4-dimethylheptanoic acid (3qa)



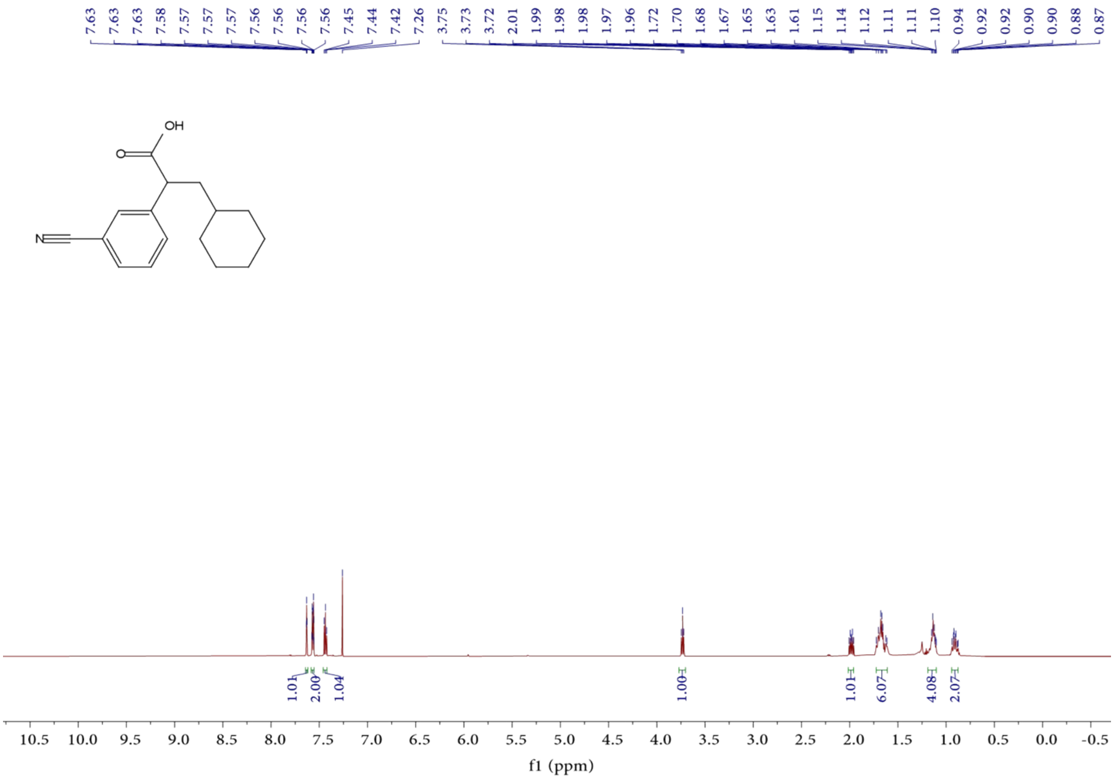


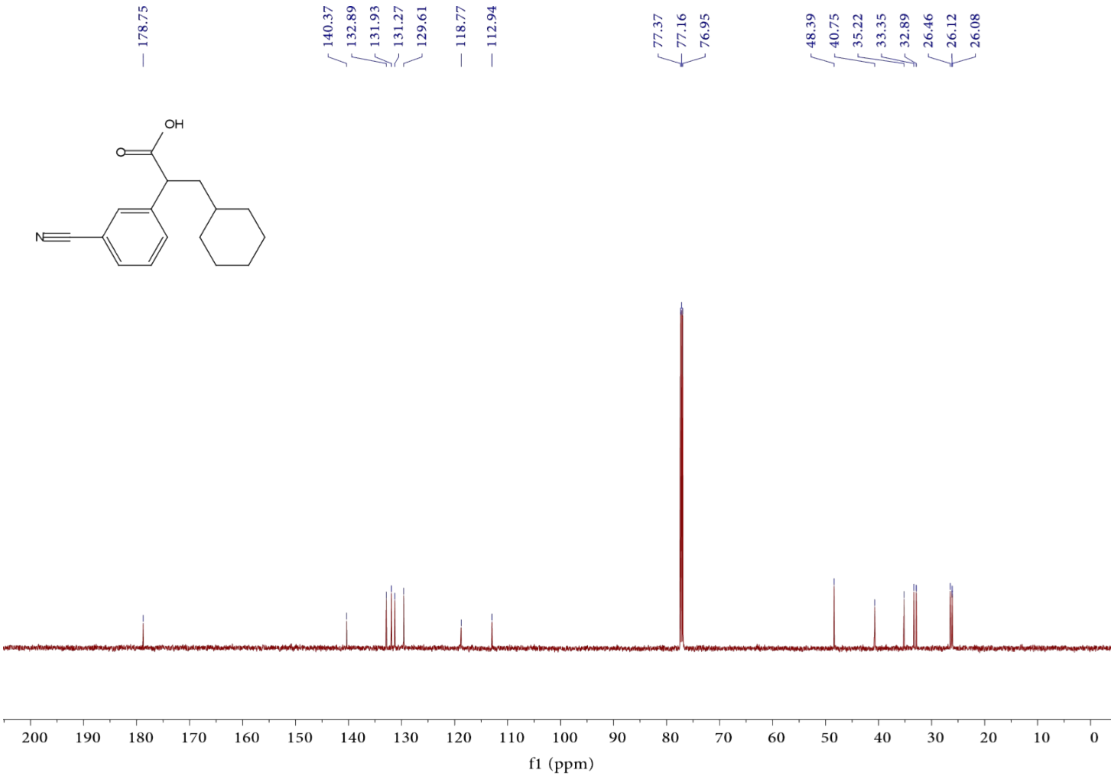
2-(4-cyanophenyl)-3-((1R,4aR,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)propanoic acid (3ra)



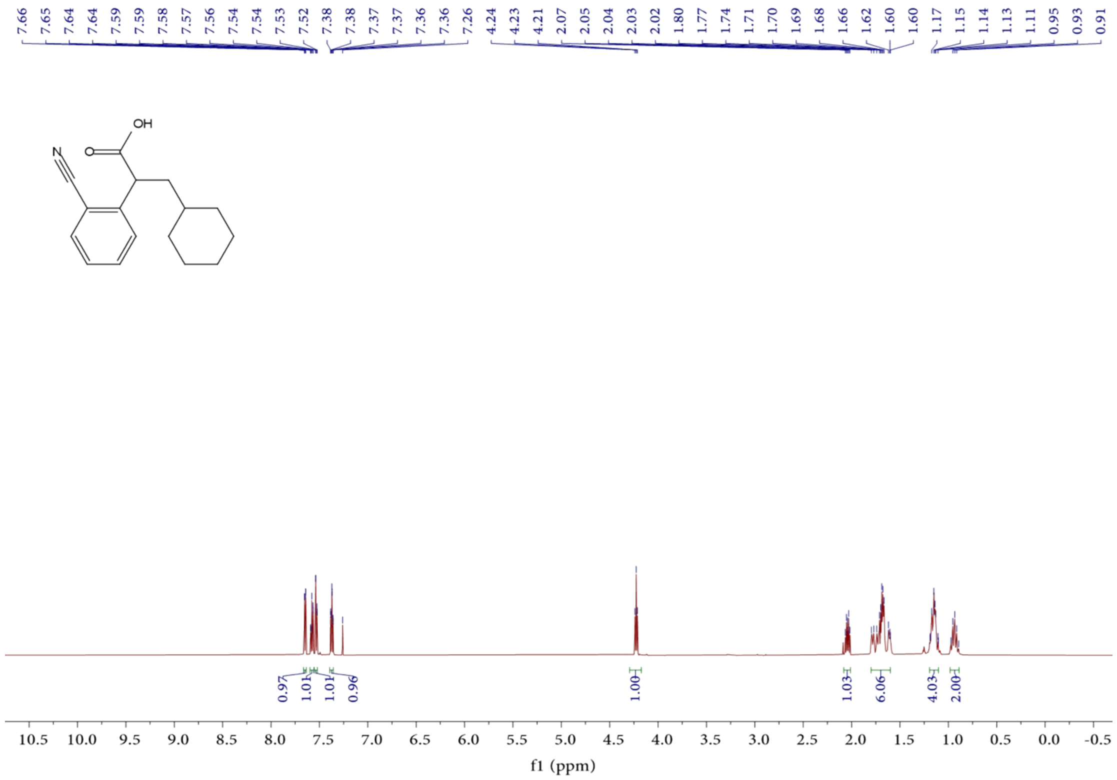


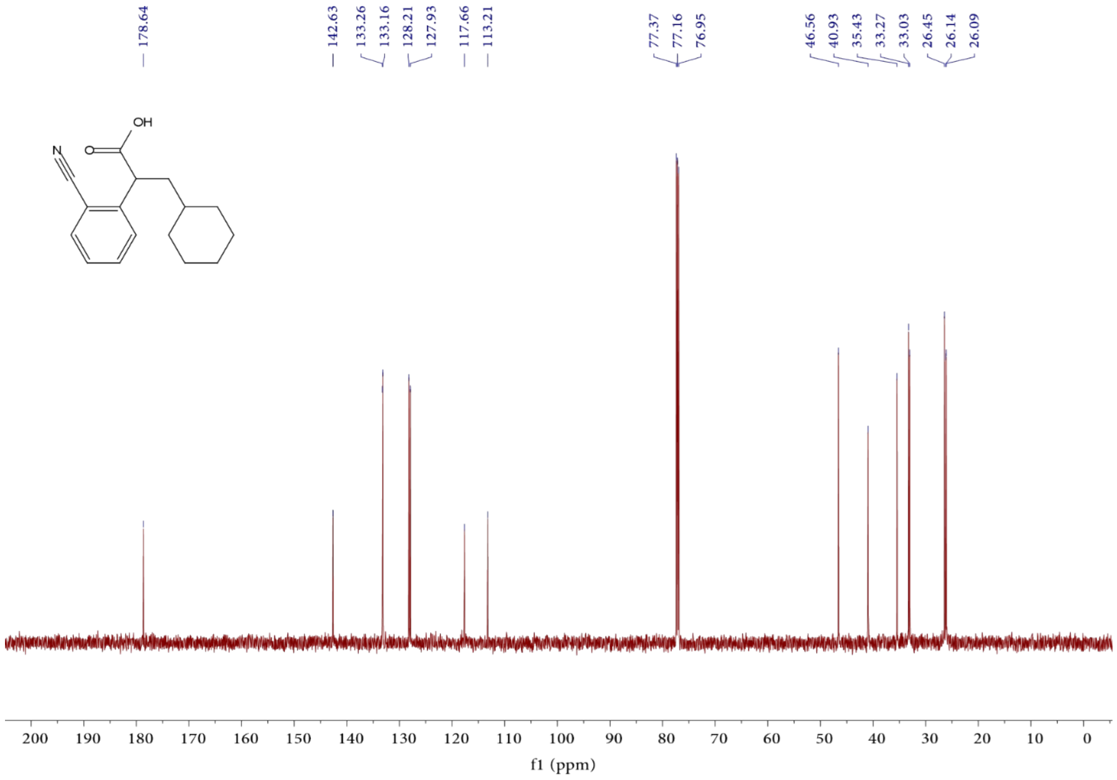
2-(3-cyanophenyl)-3-cyclohexylpropanoic acid (3ab)



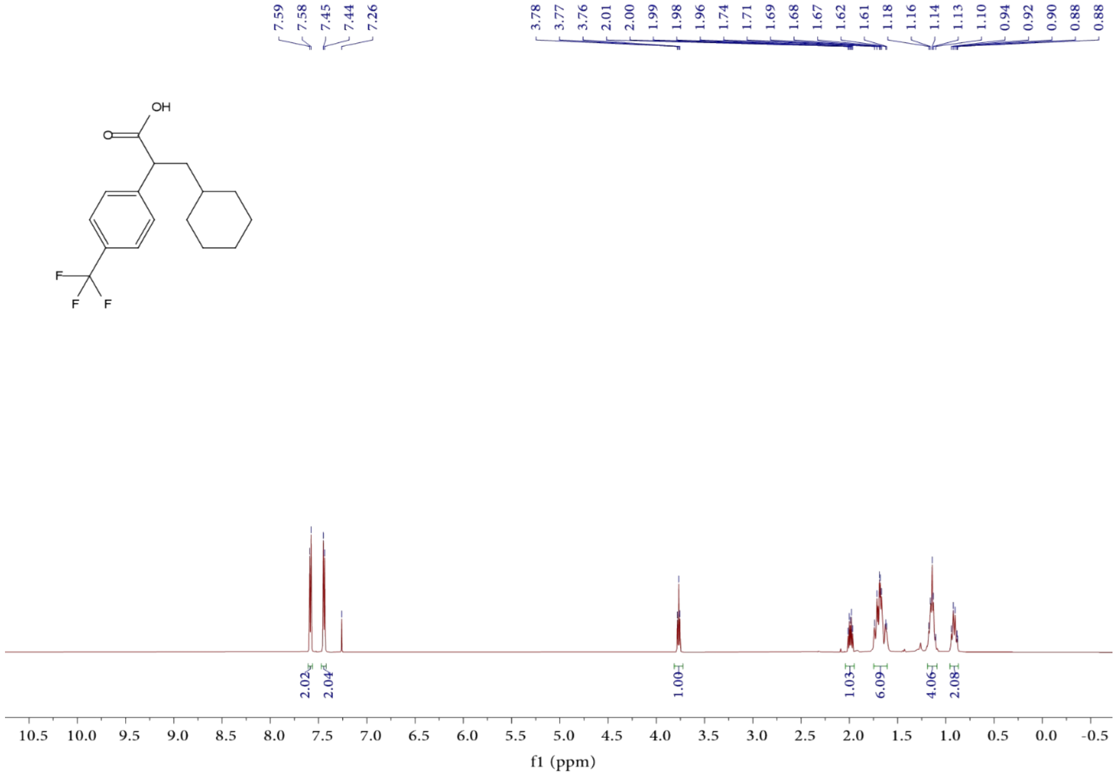


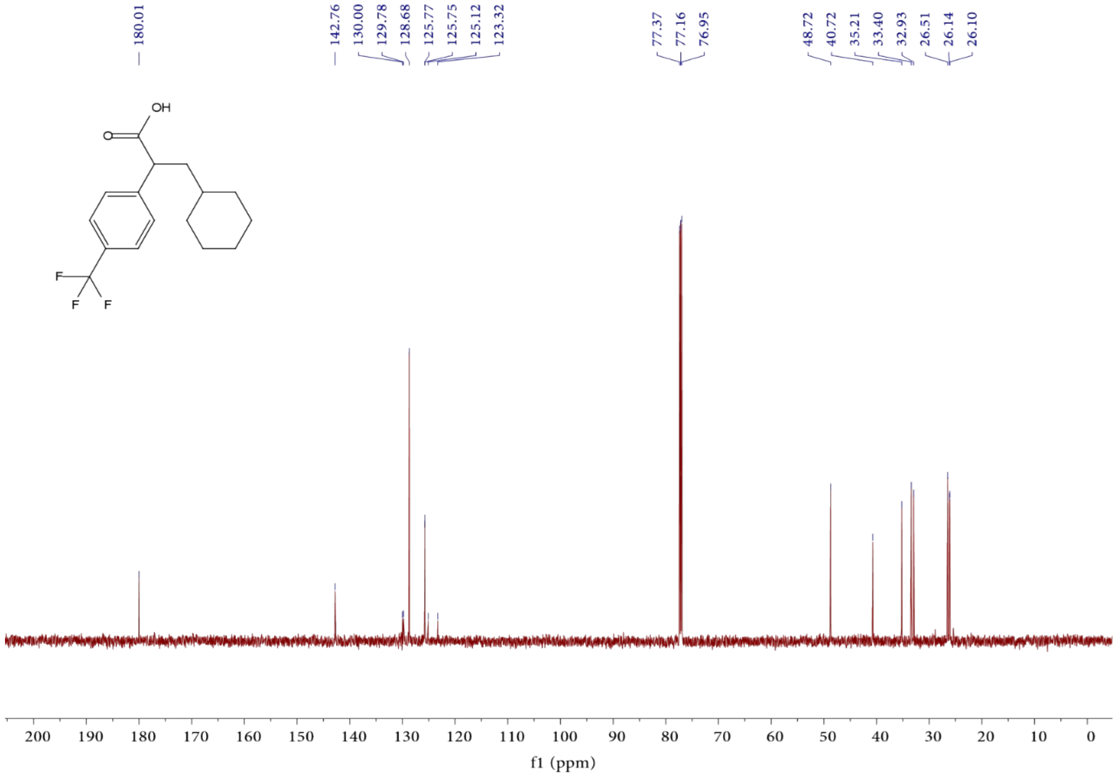
2-(2-cyanophenyl)-3-cyclohexylpropanoic acid (3ac)

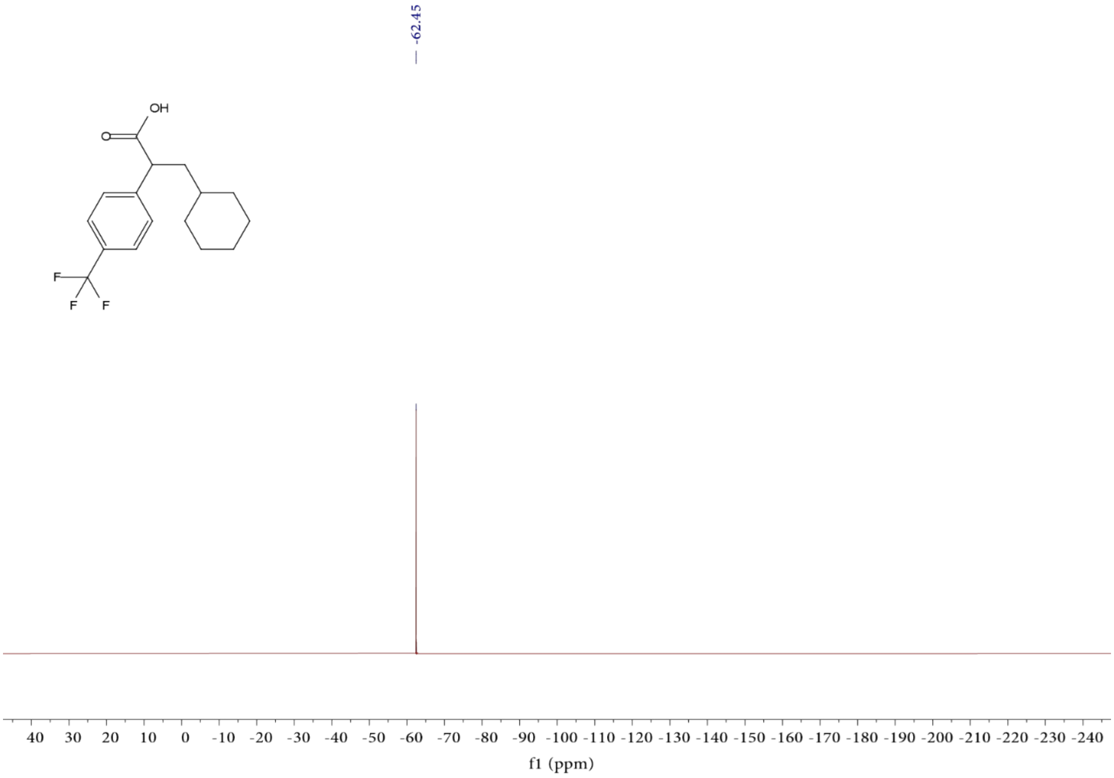




3-cyclohexyl-2-(4-(trifluoromethyl)phenyl)propanoic acid (3ad)






-62.45
OH
O
F
F
F
40
30
20
10
0
-10
-20
-30
-40
-50
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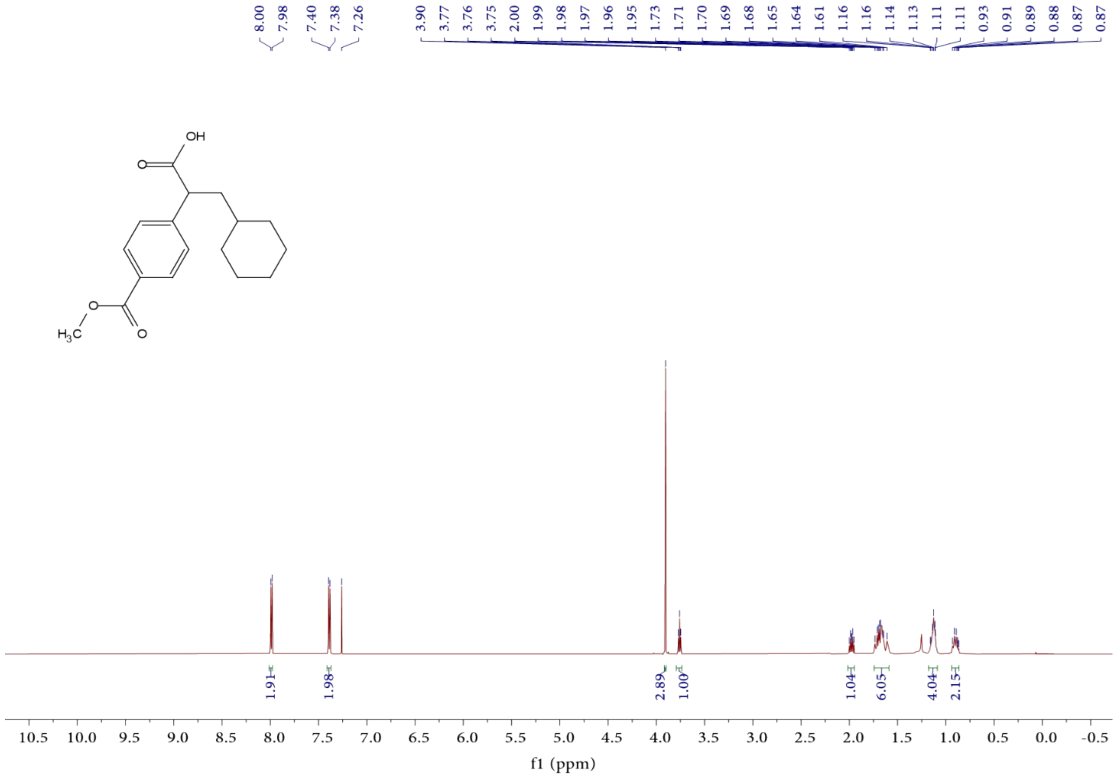
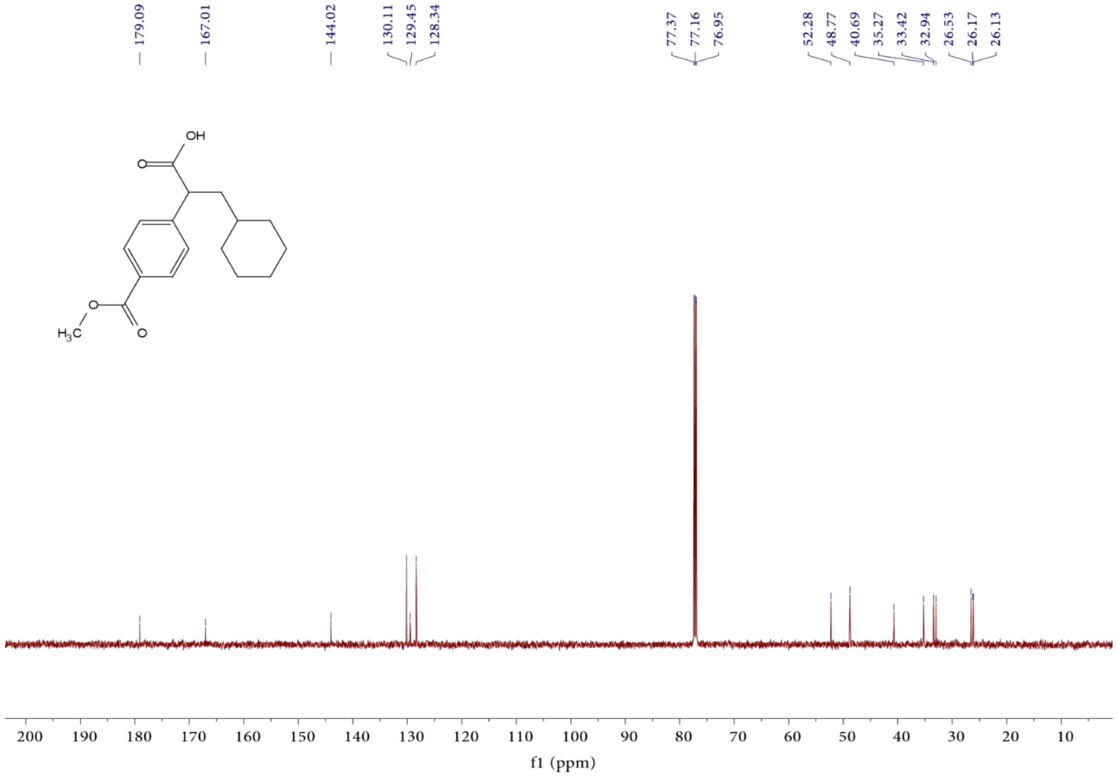
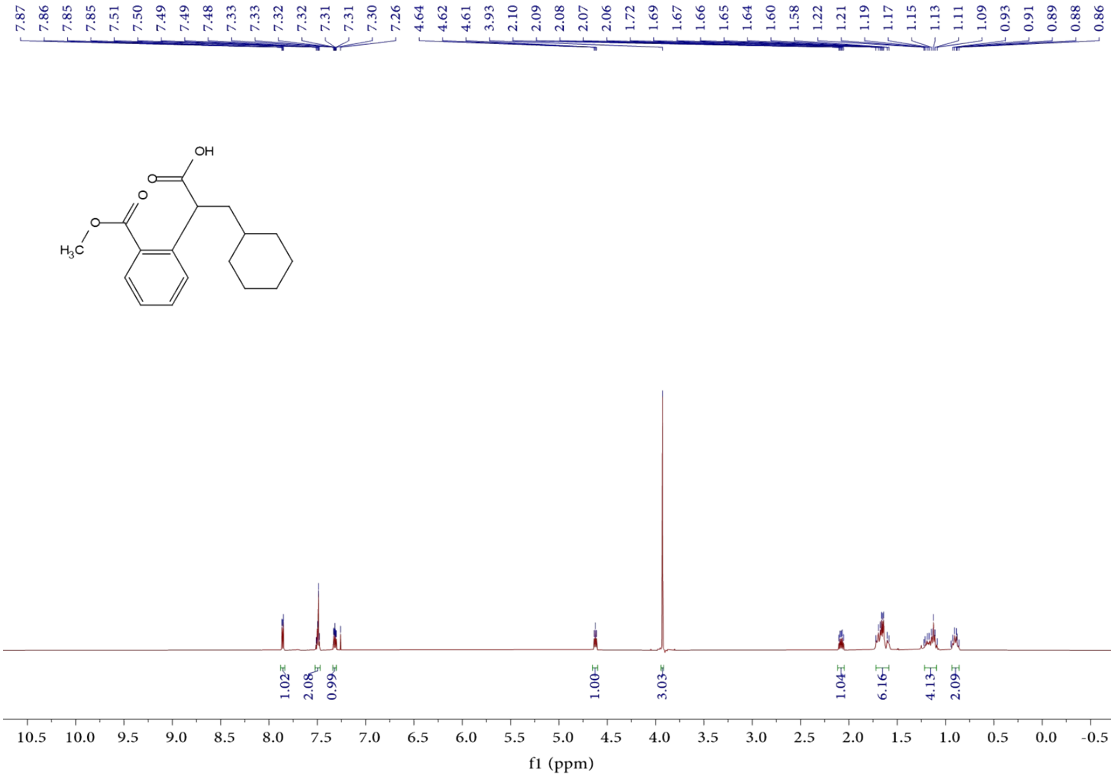
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

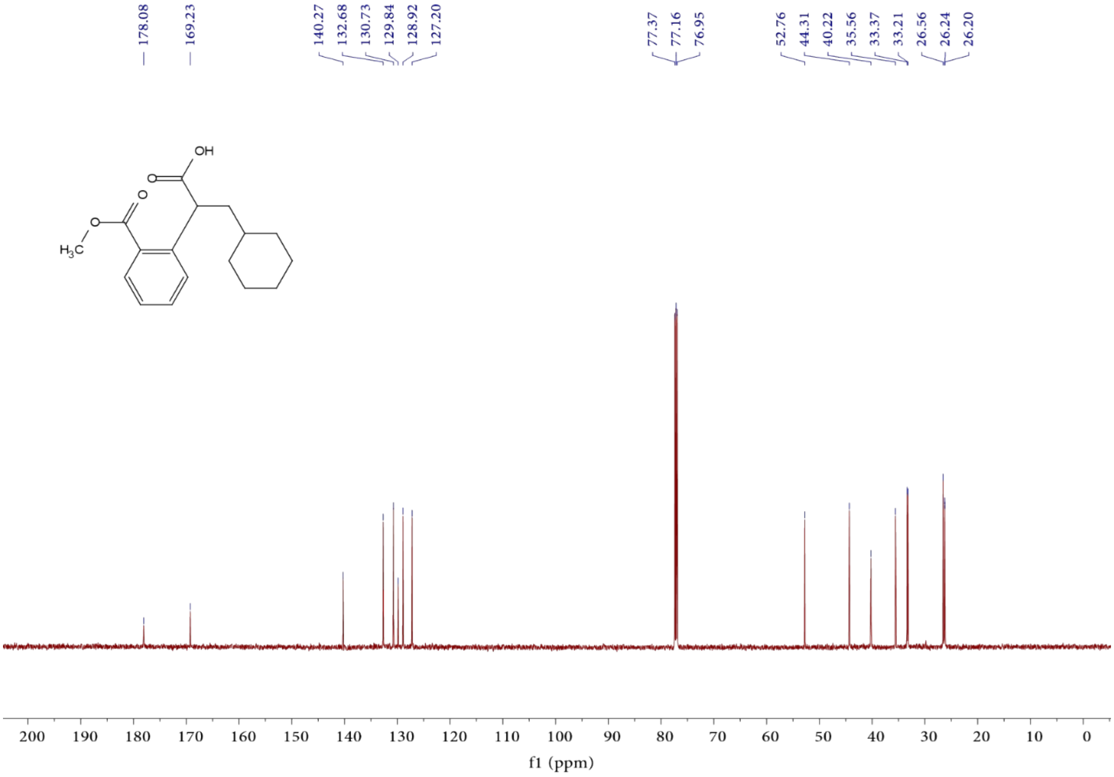
3-cyclohexyl-2-(4-(methoxycarbonyl)phenyl)propanoic acid (3ae)



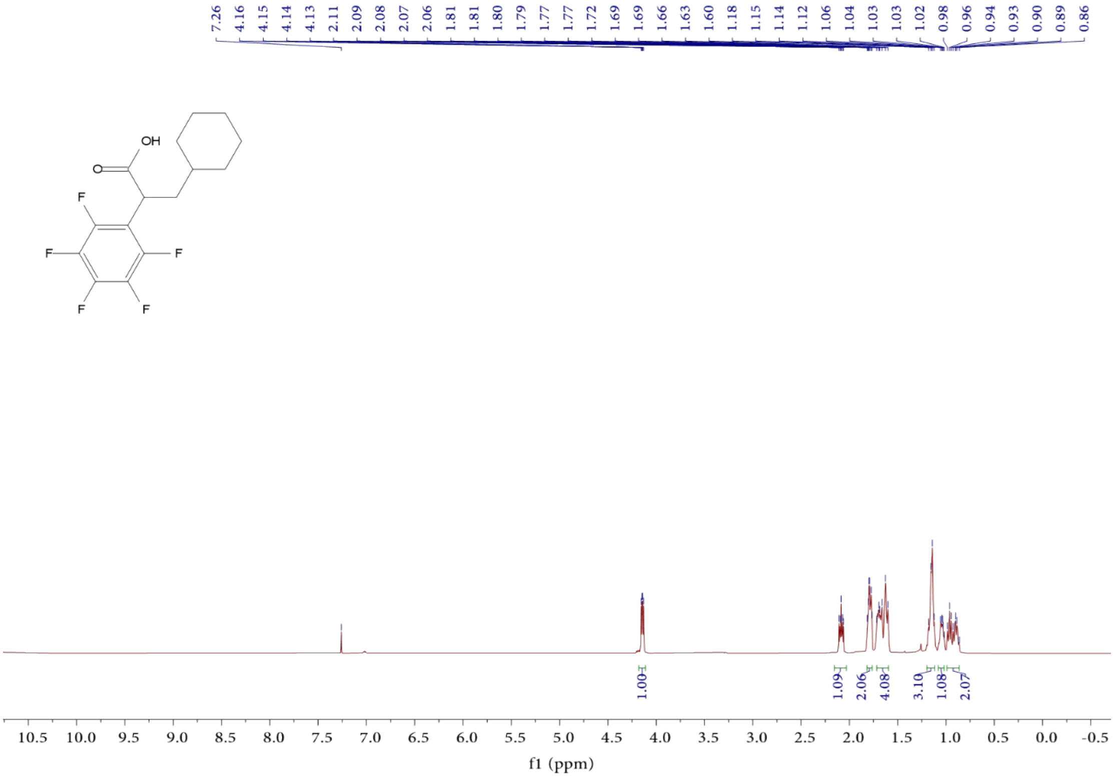


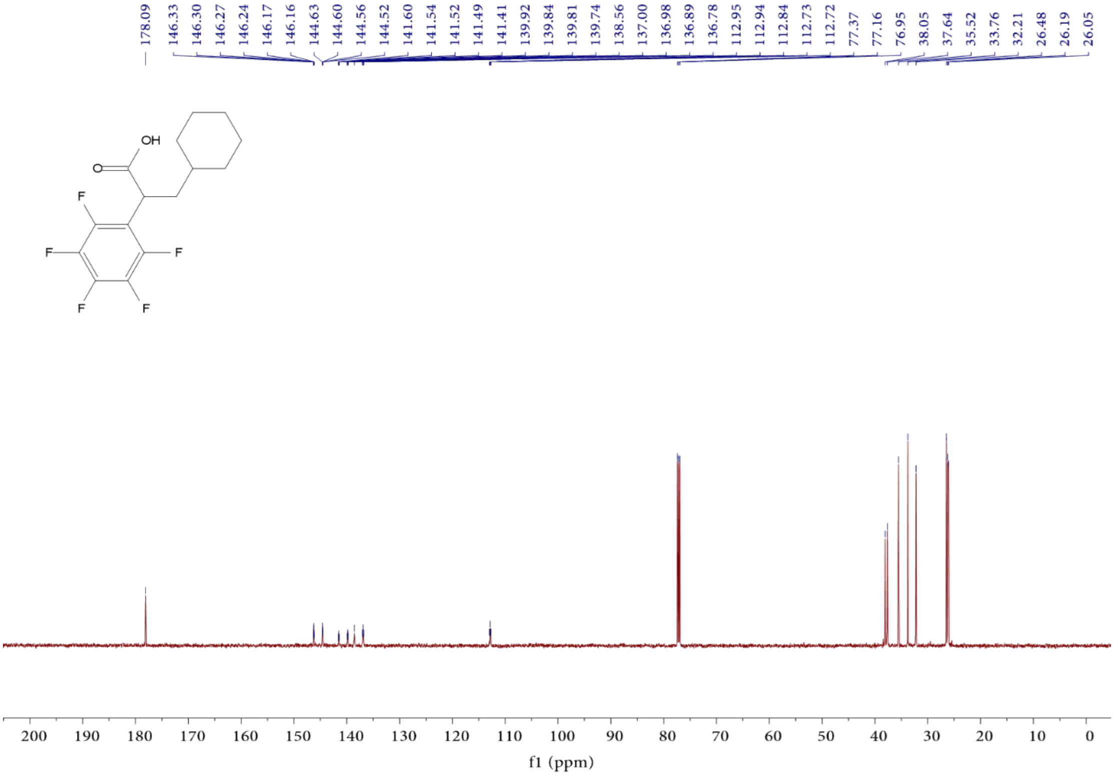
3-cyclohexyl-2-(2-(methoxycarbonyl)phenyl)propanoic acid (3af)

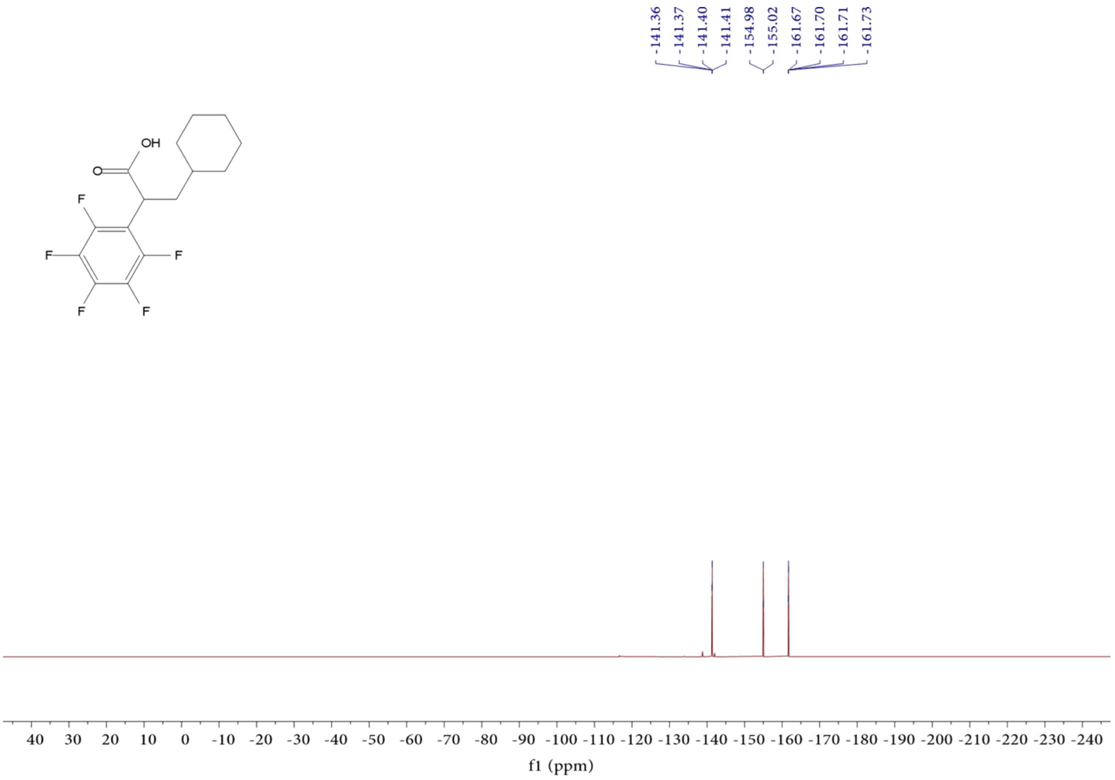




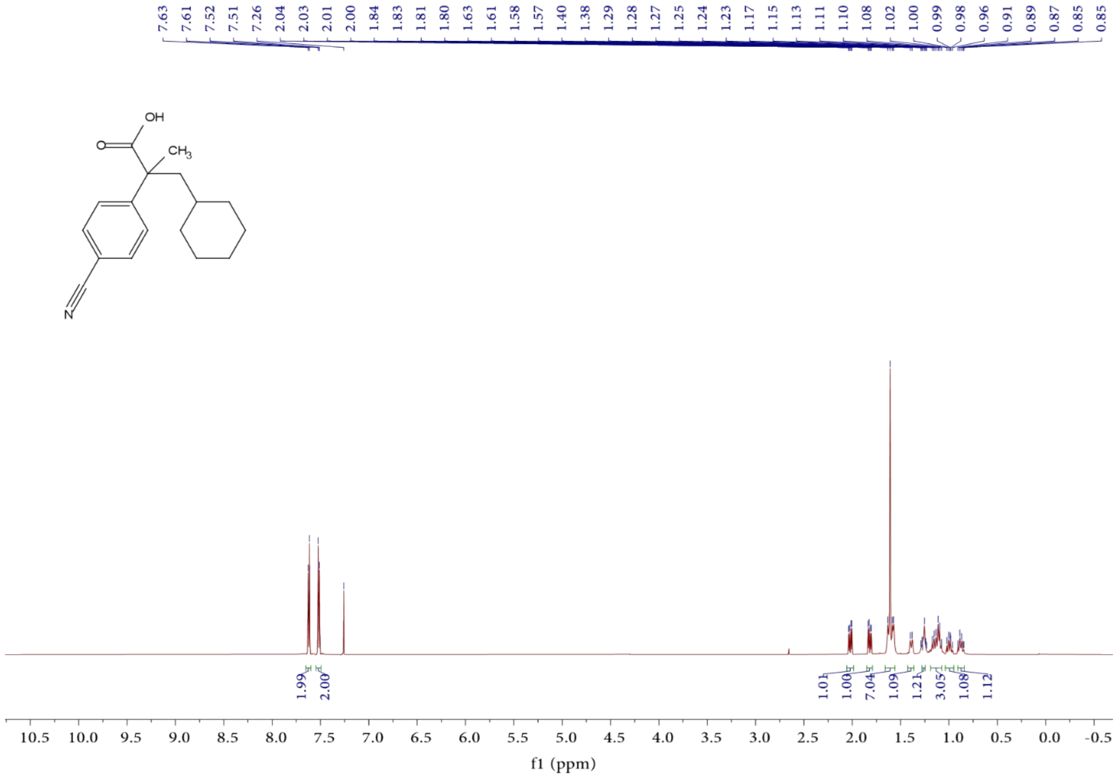
3-cyclohexyl-2-(perfluorophenyl)propanoic acid (3ag)

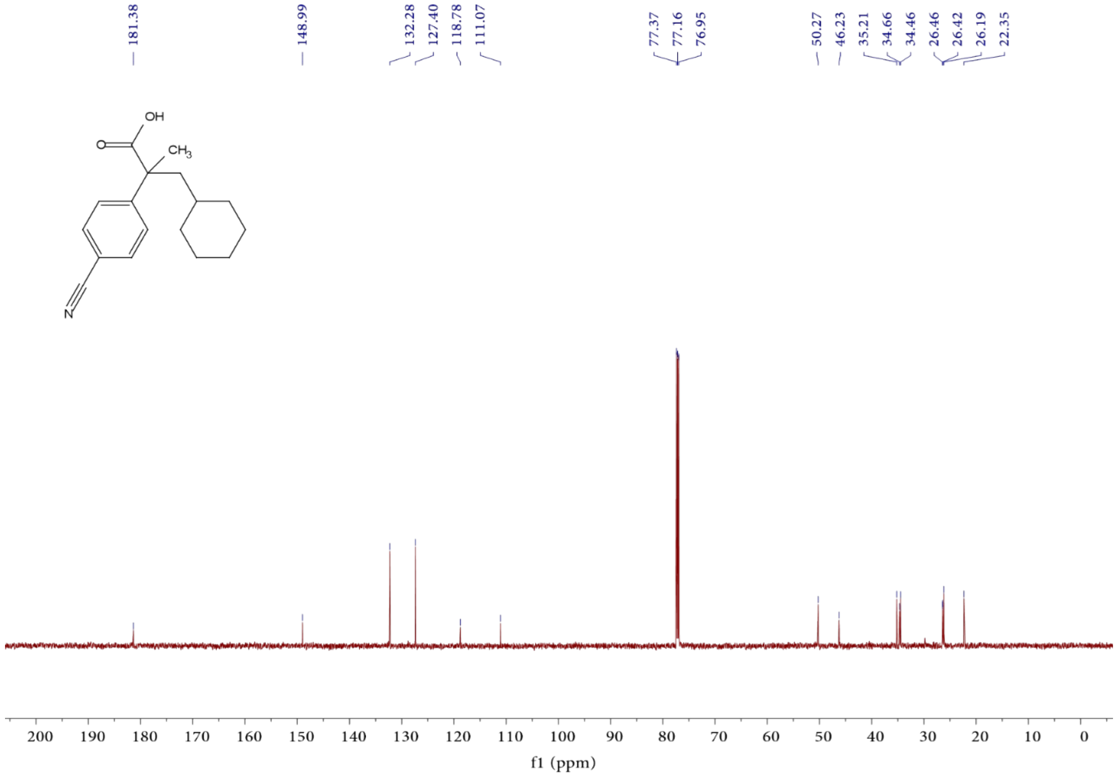




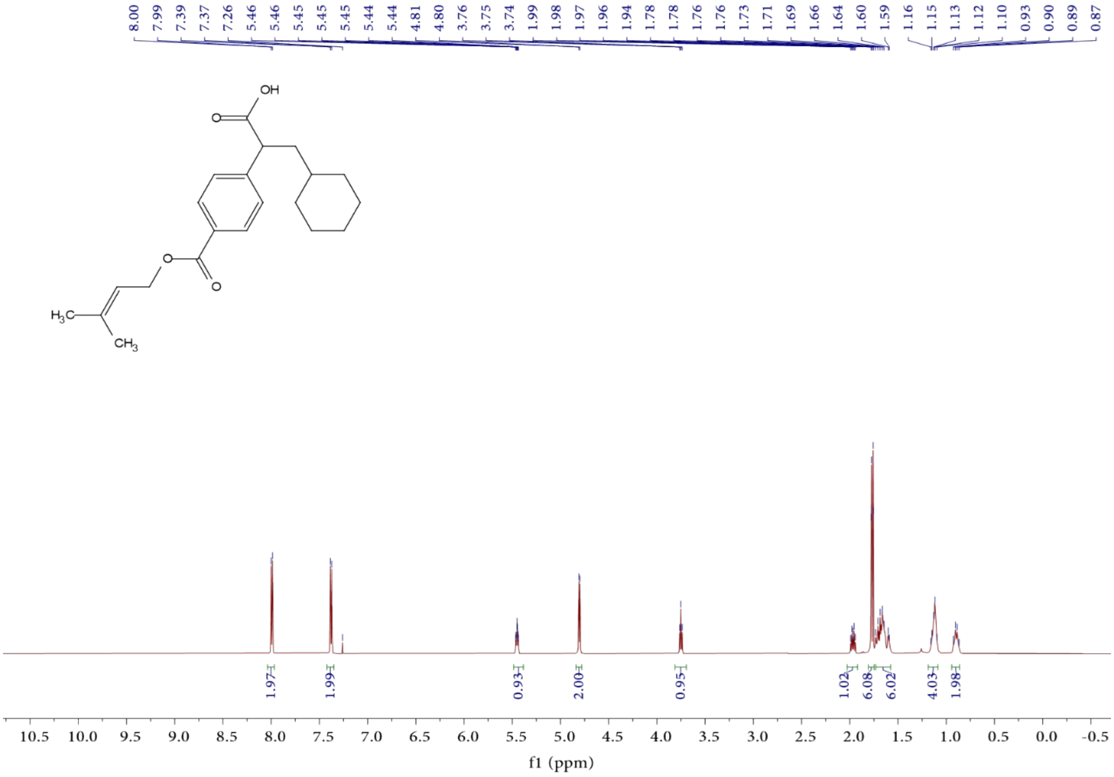

-141.36
-141.37
-141.40
-141.41
-154.98
-155.02
-161.67
-161.70
-161.71
-161.73
OH
O
F
F
F
F
F
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

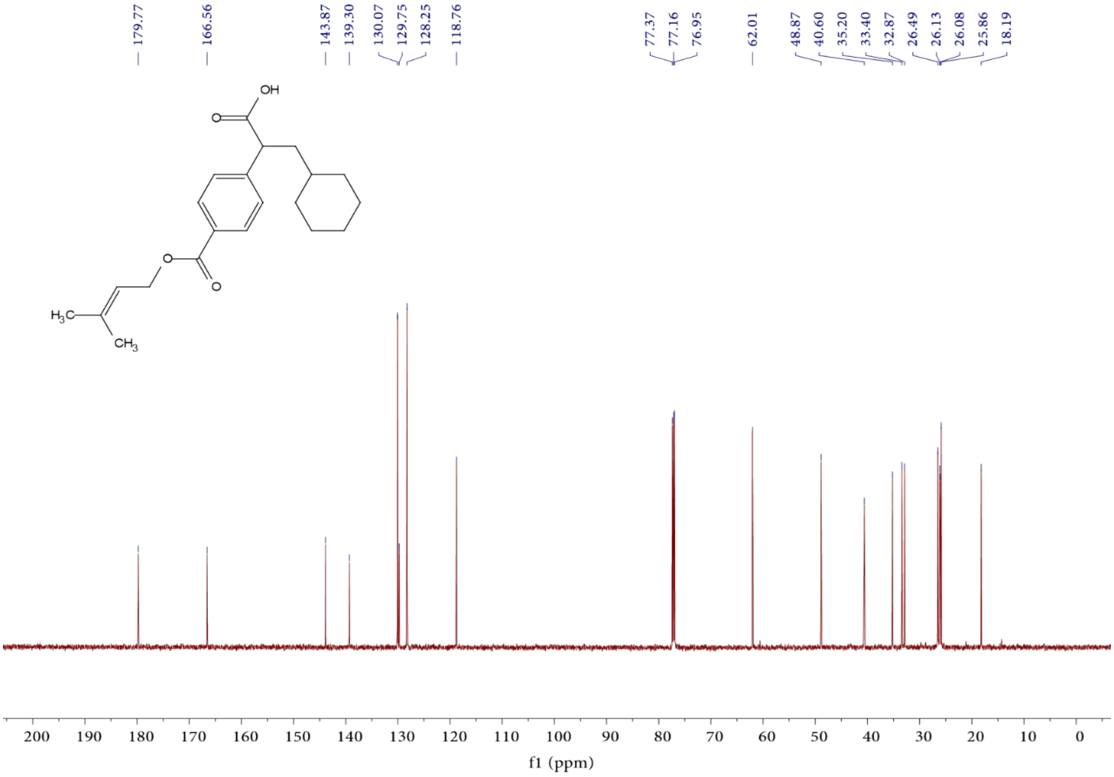
2-(4-cyanophenyl)-3-cyclohexyl-2-methylpropanoic acid (3ah)



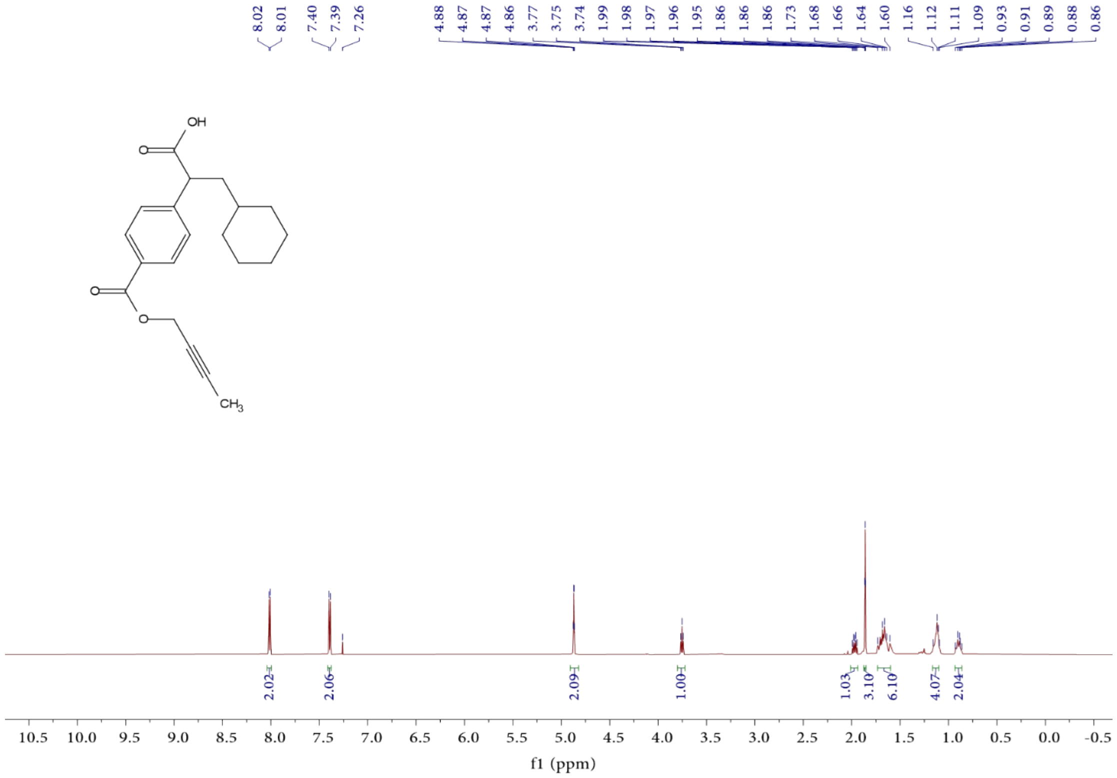


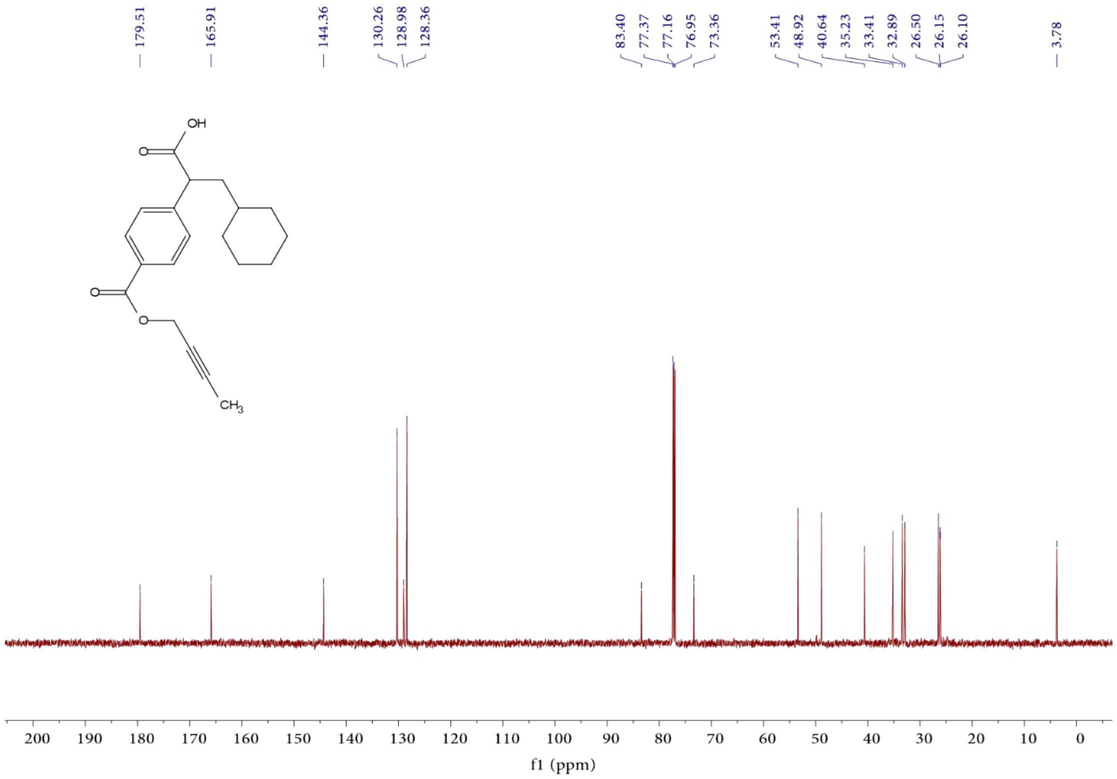
3-cyclohexyl-2-(4-(((3-methylbut-2-en-1-yl)oxy)carbonyl)phenyl)propanoic acid (3ai)



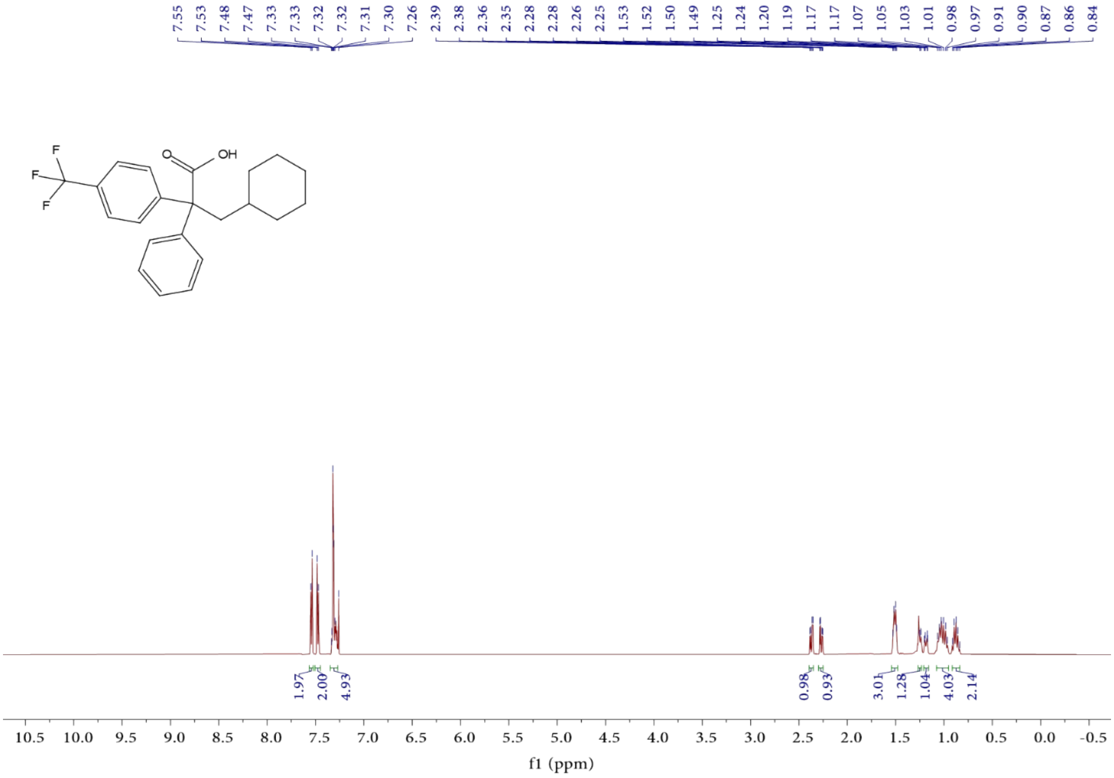


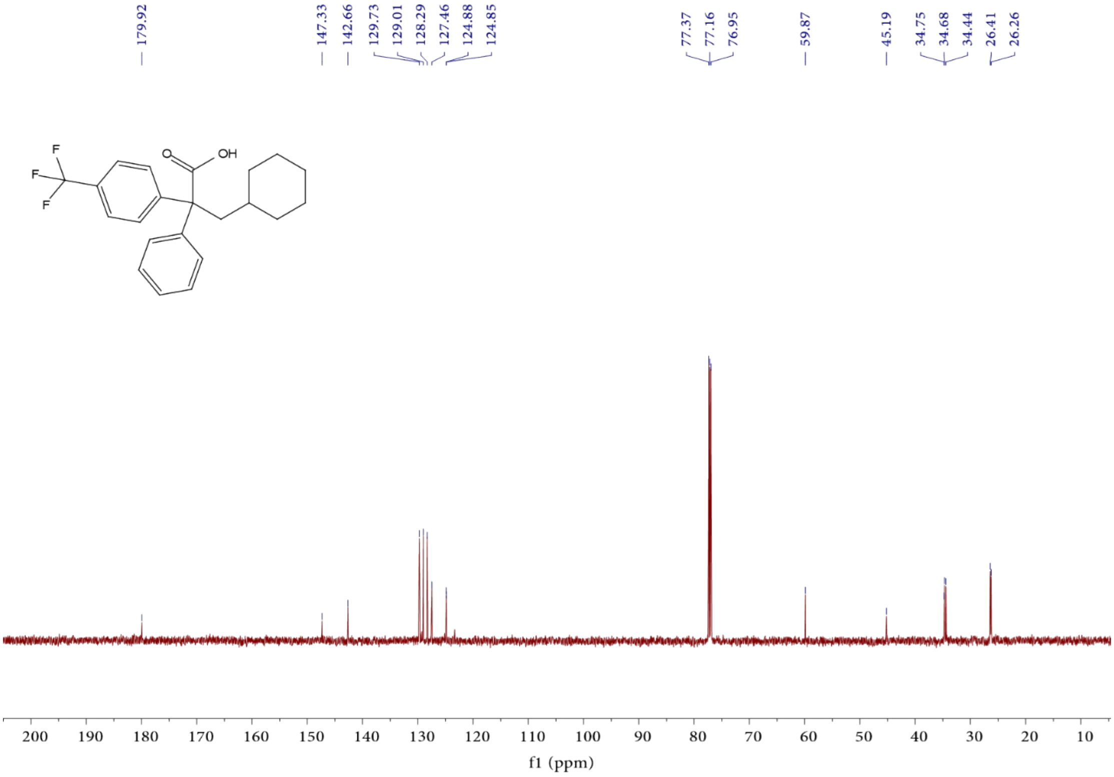
2-(4-((but-2-yn-1-yloxy)carbonyl)phenyl)-3-cyclohexylpropanoic acid (3aj)

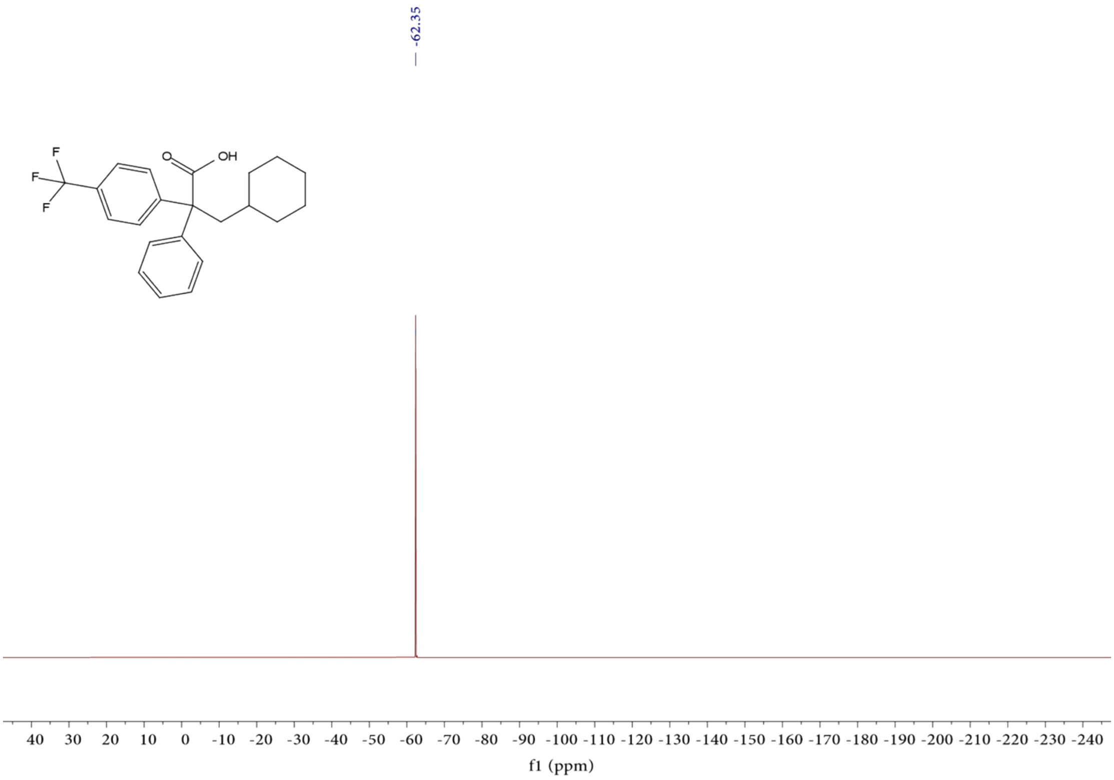




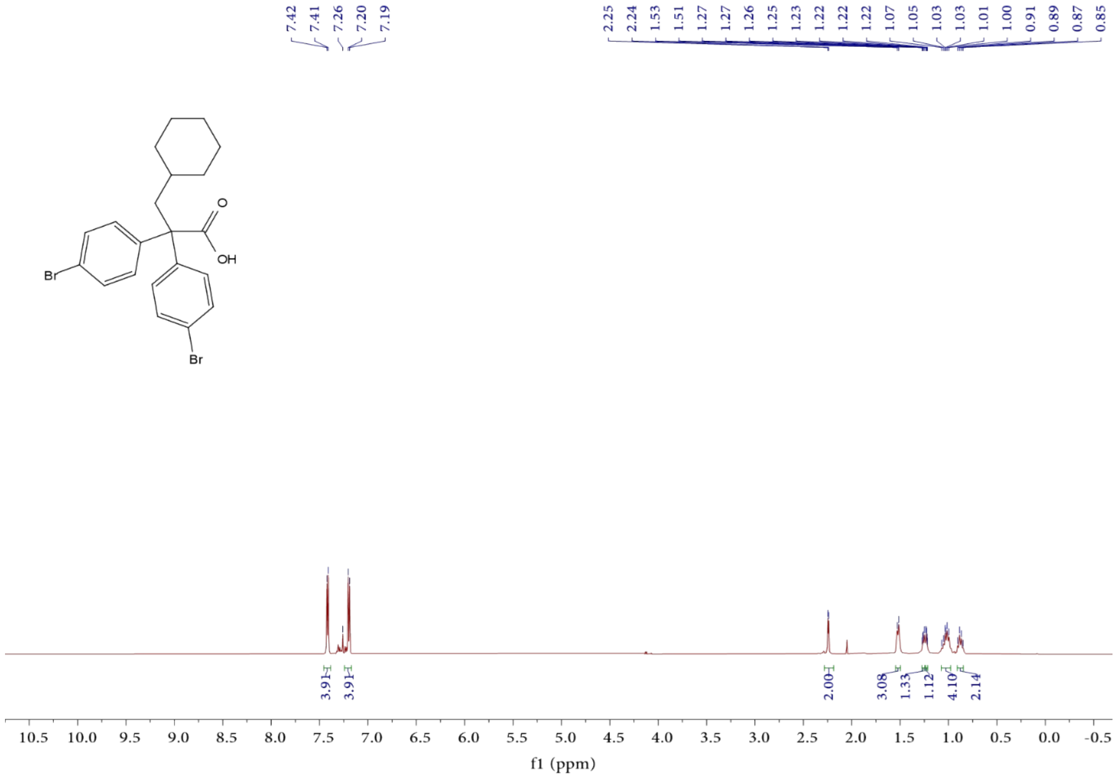
3-cyclohexyl-2-phenyl-2-(4-(trifluoromethyl)phenyl)propanoic acid (3ak)

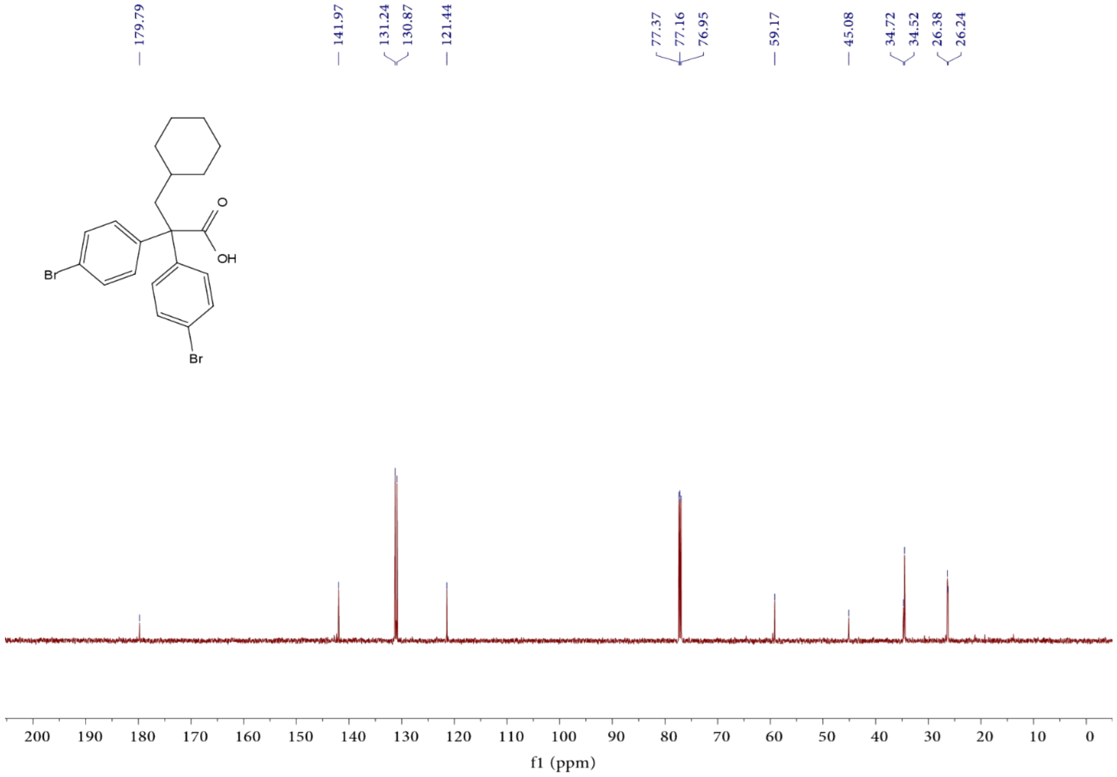




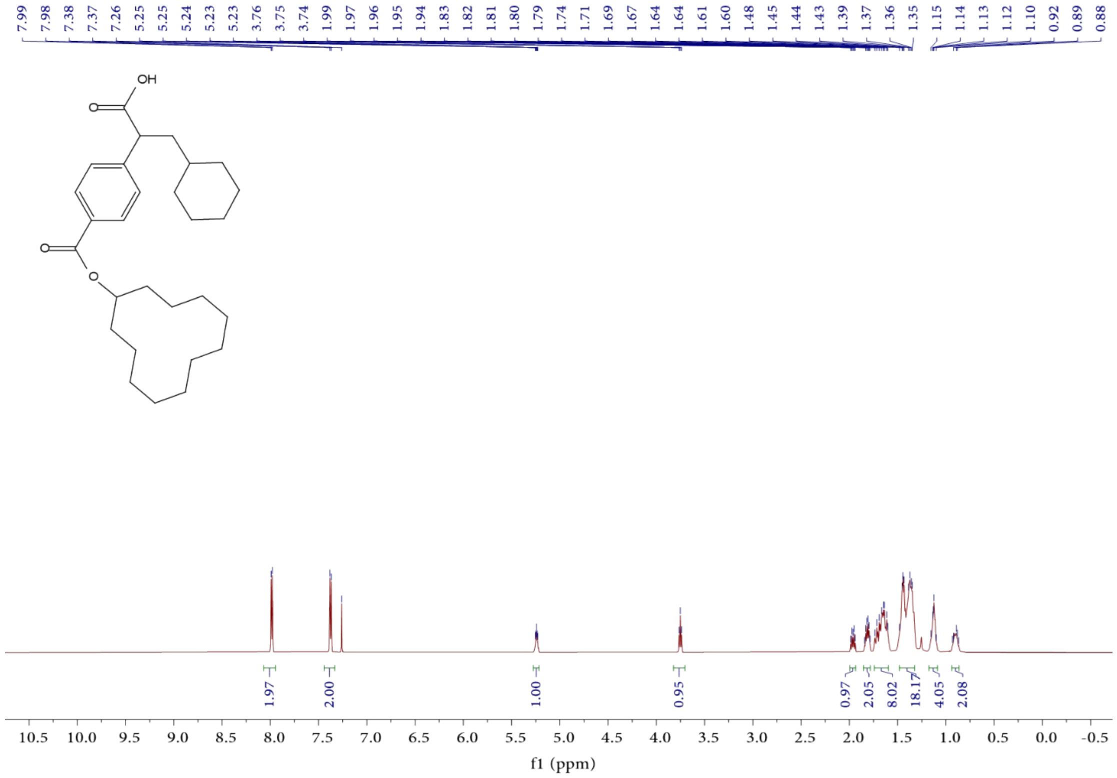

-62.35
F
F
F
O
OH
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

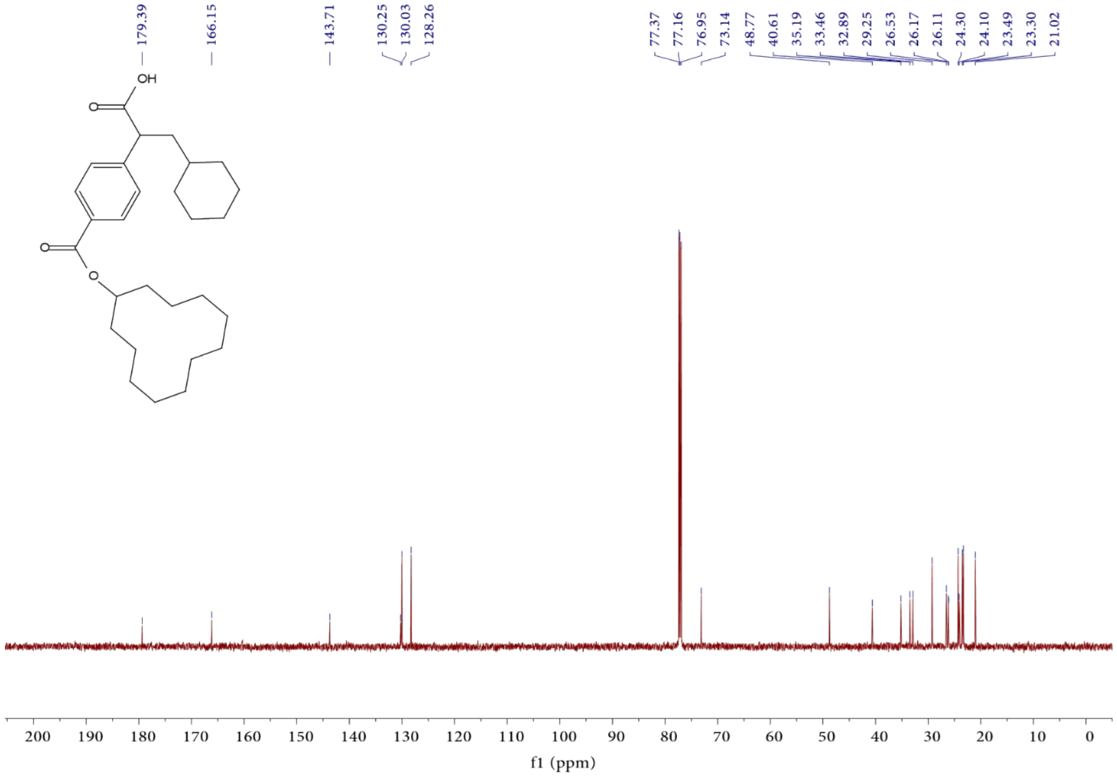
2,2-bis(4-bromophenyl)-3-cyclohexylpropanoic acid (3al)



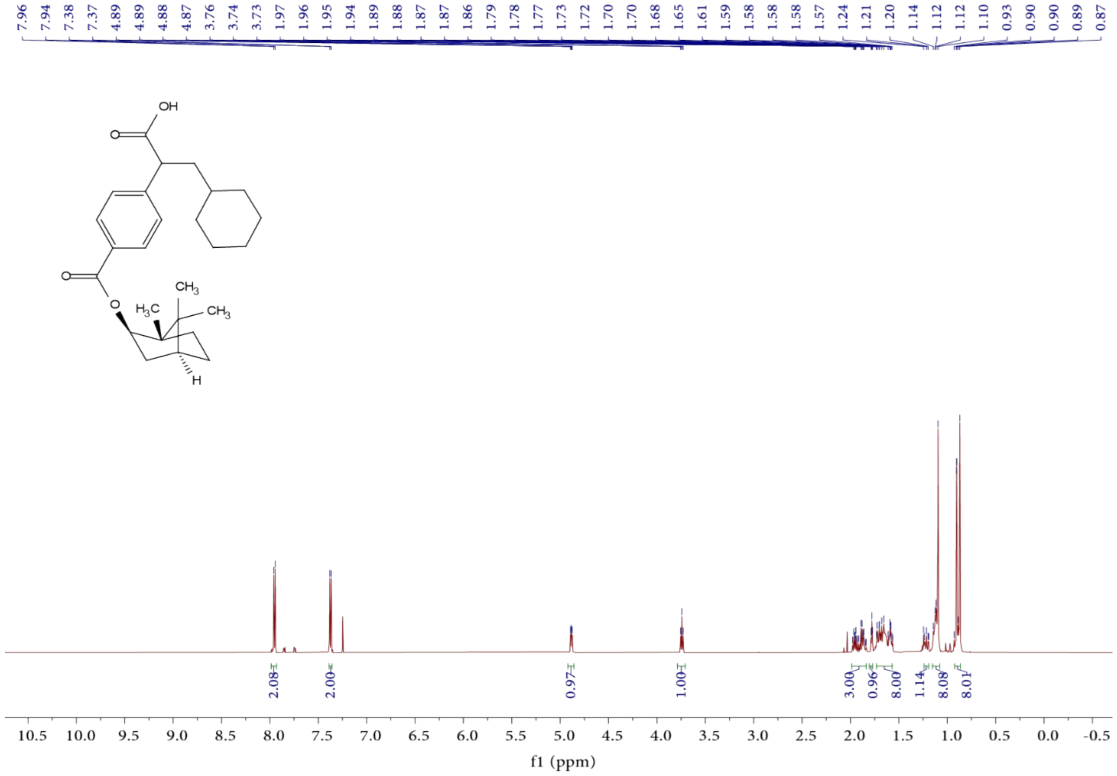


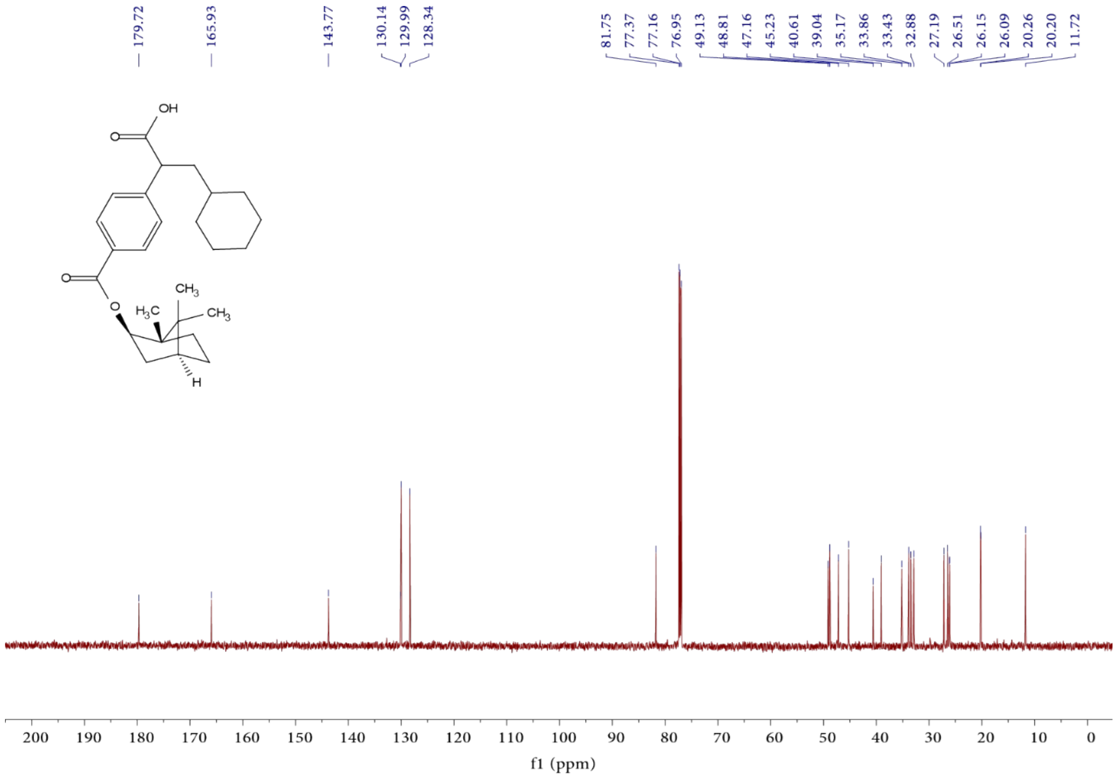
2-(4-((cyclododecyloxy)carbonyl)phenyl)-3-cyclohexylpropanoic acid (3am)



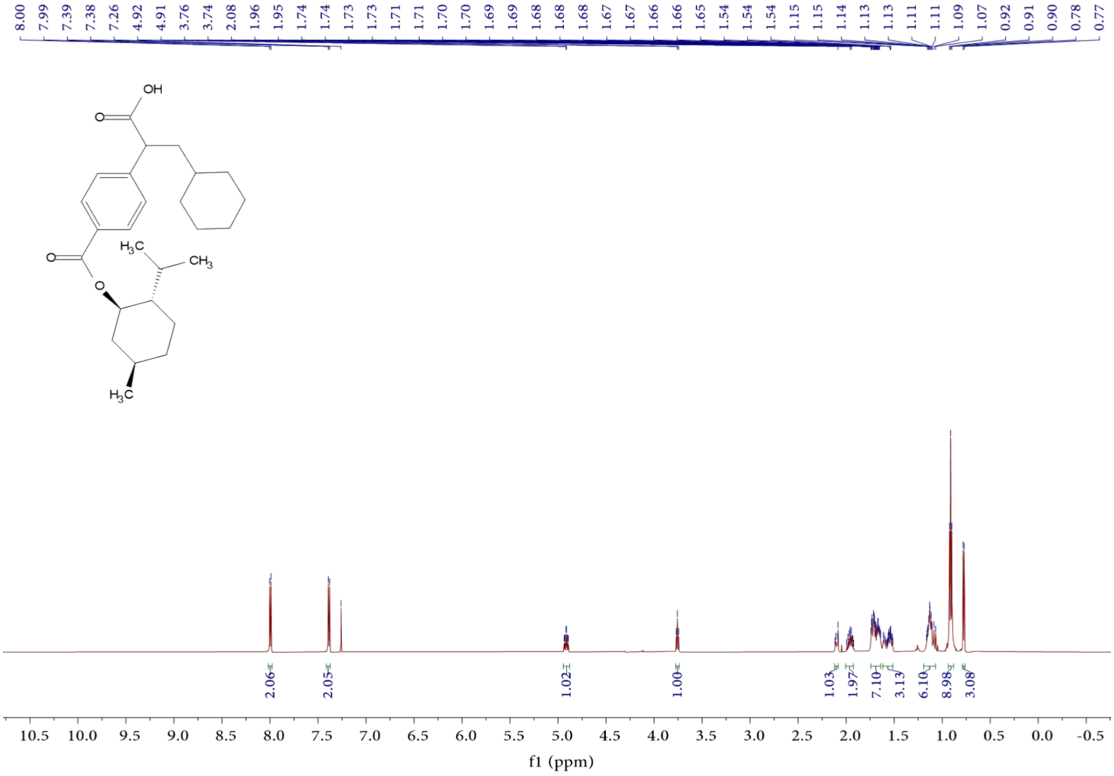


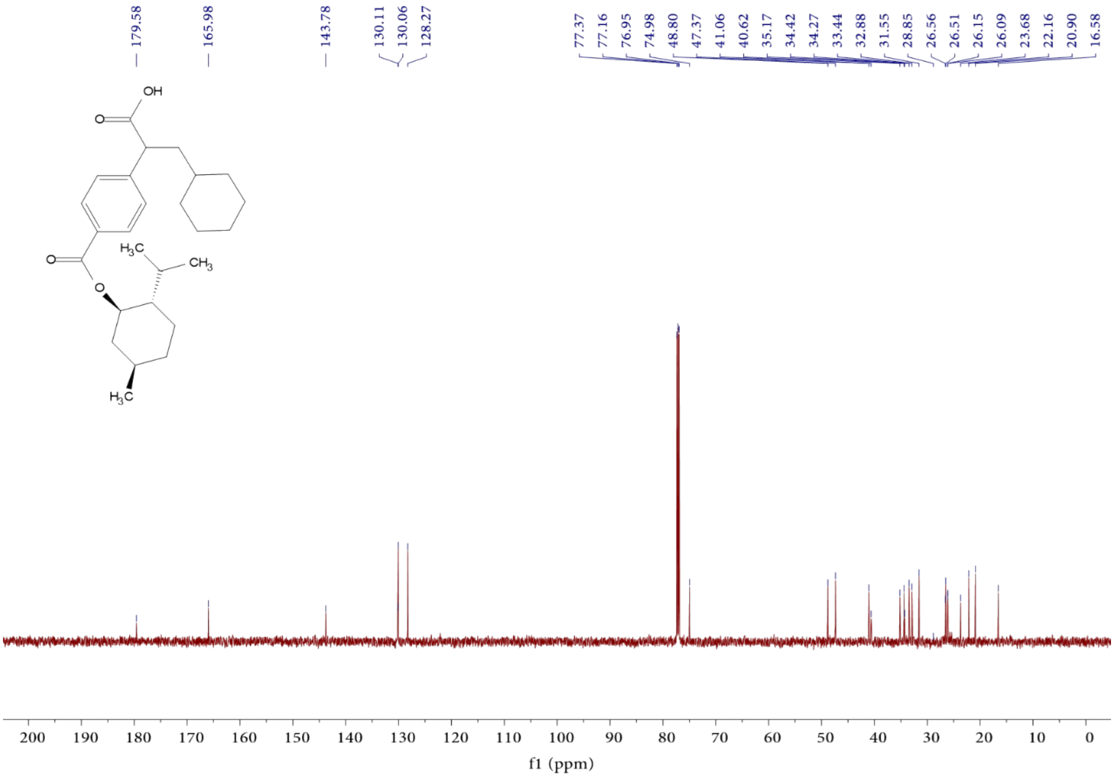
3-cyclohexyl-2-(4-((((1R,2R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)carbonyl)phenyl)propanoic acid (3an)





3-cyclohexyl-2-(4-((((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)carbonyl)phenyl)propanoic acid (3ao)





3-(benzyloxy)-2-(cyclohexylmethyl)-2-methyl-3-oxopropanoic acid (3ap)