Supplementary Information

Multicomponent Synthesis of Unsymmetrical 1,2-Diamines via Photo-Induced Carbonyl Alkylative Amination

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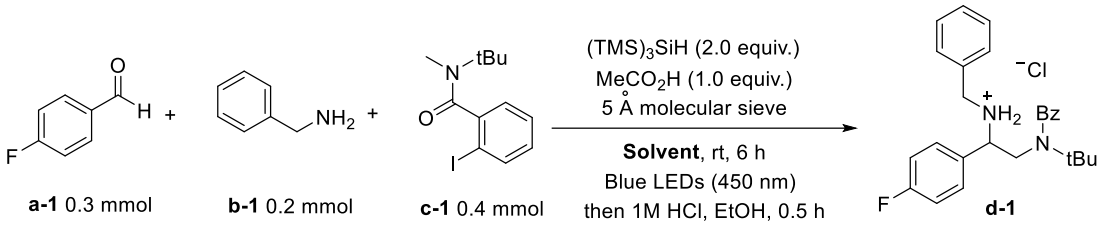
1. Experimental Section

a) General information

All reactions were carried out under an atmosphere of dry and deoxygenated argon in a glovebox (H_2O and O_2 < 0.1 ppm). ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), ^{19}F NMR (376 MHz) and ^{31}P NMR (162 MHz) spectra were recorded on a 400 MHz Quantum-I Plus 400 in $CDCl_3$ as a solvent and recorded in parts per million relative to the internal standard tetramethylsilane. The NMR spectra were referenced to tetramethylsilane (TMS, 0.0 ppm), $CDCl_3$ (7.26 ppm or 77.0 ppm for ^{1}H and ^{13}C respectively). The ^{1}H NMR spectra are reported as follows: δ, chemical shift; coupling constants (J are given in hertz, Hz); integration. Coupling constants are reported as follows: s = singlet, br. s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, etc. High-resolution mass spectroscopy (HRMS) data of the products were collected on a Waters Xevo G2QTOF/UPLC mass spectrometer using electrospray ionization. Analytical thin-layer chromatography (TLC) was performed on silicycle 250 mm silica gel F-254 plates. Products were purified by flash chromatography on 200-300 meshsilica gels, SiO_2. The photoreaction instrument (WPP-TEC-1020SL) was purchased from WATTCAS, China. Starting materials were purchased from J&K and 2-iodobenzamides were synthesized according to the reported literature.[1-4]

b) Optimization of the reaction conditions

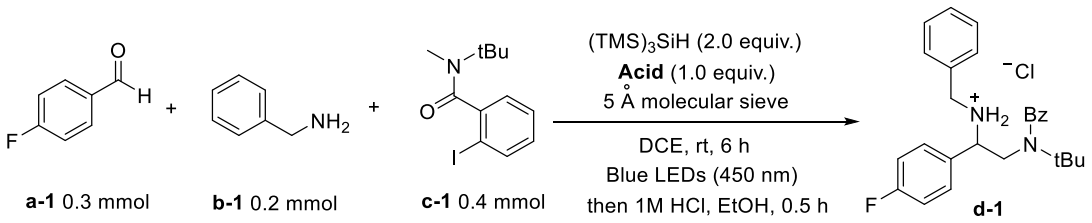
Table S1. Screening of Solvent



Entry	Solvent	Wavelength (10 W LEDs)	Yield of **d-1** (%)[a]
1	DCM	450 nm	68
2	DMF	450 nm	N.D.
3	DMSO	450 nm	trace
4	MeCN	450 nm	70
5	DCE	450 nm	75
6	EtOAc	450 nm	trace

[a] Yields of isolated products.

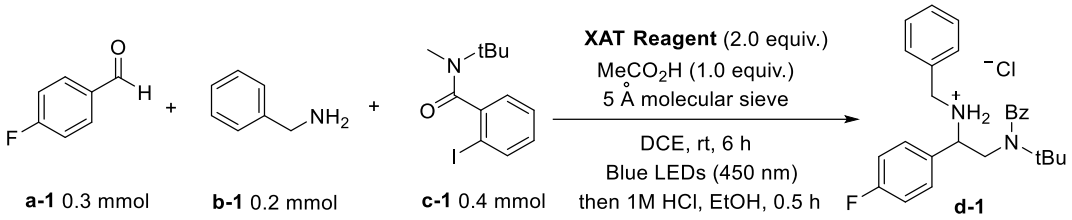
Table S2. Screening of Acid and light



Entry	Acid	Wavelength (10 W LEDs)	Yield of **d-1** (%)[a]
1	CH_3CH_2COOH	450 nm	72
2	HCl	450 nm	trace
3	HBr	450 nm	trace
5	-	450 nm	25
6	CH_3COOH	390 nm	52

[a] Yields of isolated products.

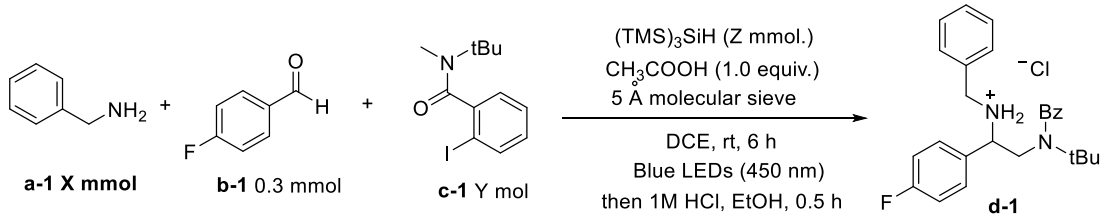
Table S3. Screening of XAT reagent



Entry	[SiH]	Wavelength (10 W LEDs)	Yield of **d-1** (%)[a]
1	Et_3SiH	450 nm	trace
2	Ph_3SiH	450 nm	trace

[a] Yields of isolated products.

Table S4. Screening of substrate ratio

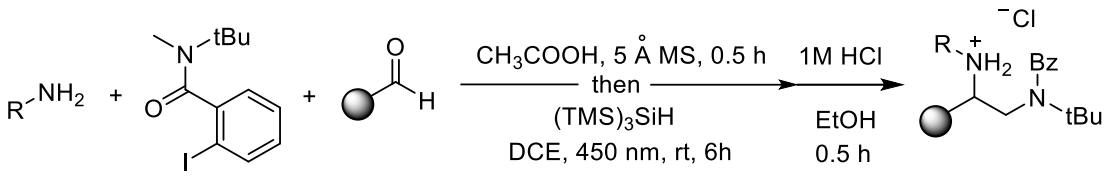


Entry	b1/c1/$(TMS)_3SiH$	Wavelength (10 W LEDs)	Yield of **d-1** (%)[a]
1	0.2:0.6:0.6	450 nm	66
2	0.2:0.6:0.4	450 nm	73

[a] Yields of isolated products.

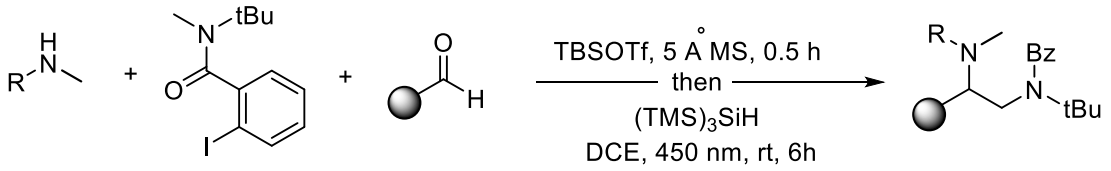
c) General procedure

General procedure A for 1,2-diamine hydrochloride salt:



The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a teflon-coated magnetic stir bar was added amine (0.2 mmol), aldehyde (0.3 mmol), CH_3COOH (0.2 mmol), DCE (4 mL) and 5Å molecular sieves (300 mg). The mixture was stirred 0.5 h at room temperature before the sequential addition of 2-iodobenzamide (0.4 mmol) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC). After irradiation, the resulting homogenous solution was transferred to a 25 mL round bottom flask with aid of DCM (2 x 3 mL). NEt_3 (approx. 0.5 mL) and SiO_2 were added to this solution and the volatiles were removed under reduced pressure, affording a powder which was loaded on column. Purification by flash column chromatography on SiO_2, pre-basified with NEt_3 using pentane: EtOAc mixtures afforded the corresponding products. The target product was dissolved in 10 ml ethanol, then protected by very slow dropwise addition (caution!) of 1M HCl (1 mL) and stirred 0.5 h to obtain the hydrochloride salt of the product.

General procedure B for 1,2-diamine:



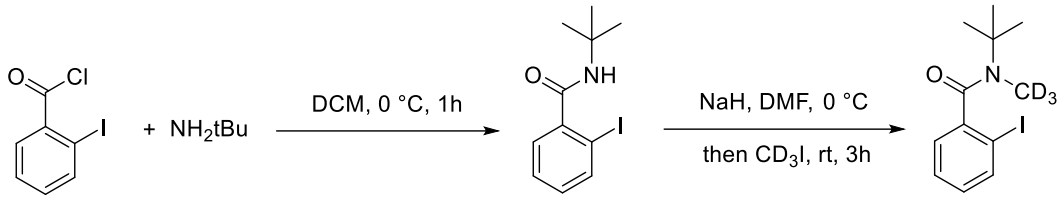
The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a teflon-coated magnetic stir bar was added amine (0.2 mmol), aldehyde (0.4 mmol), TBSOTf (0.2 mmol), DCE (4 mL) and 5Å molecular sieves (300 mg). The mixture was stirred 0.5 h at room temperature before the sequential addition

of 2-iodobenzamide (0.4 mmol) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 ° C until the reaction was complete (monitored by TLC). After irradiation, the resulting homogenous solution was transferred to a 25 mL round bottom flask with aid of DCM (2 x 3 mL). NEt_3 (approx. 0.5 mL) and SiO_2 were added to this solution and the volatiles were removed under reduced pressure, affording a powder which was loaded on column. Purification by flash column chromatography on SiO_2, pre-basified with NEt_3 using pentane: EtOAc mixtures afforded the corresponding products.

d) Mechanistic experiments

(1) Deuterium labeling and cross-over experiments

Synthesis of [D]-c-1



[D]-c-1

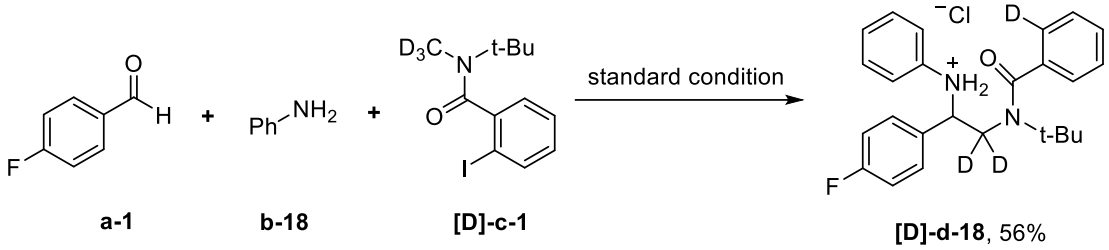
An oven dried 5 mL wheaton V-vial containing a stirring bar was charged with amine (10 mmol), trimethylamine (20 mmol) in dichloromethane (30 mL) and capped under N_2 atmosphere (glovebox) with an open-top cap with septum. Then, iodobenzoyl chloride (12 mmol, dissolved in 20 ml of DCM) was added and the reaction was stirred at room temperature for 1 h. After reaction, the solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent.

Charge a 100 mL round bottomed flask with *N*-(*tert*-butyl)-2-iodobenzamide in dry DMF (20 ml) under an argon atmosphere at 0°C.NaH (20 mmol) was added to the mixture, the reaction mixture was stirred for 15 minutes at 0°C. Iodomethane-d3 (15 mmol) was added to the mixture. Warm the reaction mixture to room temperature.The reaction mixture was stirred for 3 hours. After 3 hours, dilute the reaction mixture with ice water. Extract the reaction mixture with DCM (3 × 30 mL). The solvent was removed by rotary evaporation and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent.

Characterization of **[D]-c-1**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.21 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.04 (td, *J* = 7.7, 1.7 Hz, 1H), 1.58 (s, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.27, 144.94, 139.22, 129.53, 128.50, 126.80, 92.21, 57.20, 28.00.**HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}D_3INO$ 321.0538, Found 321.0536

Deuterium-labeling experiments

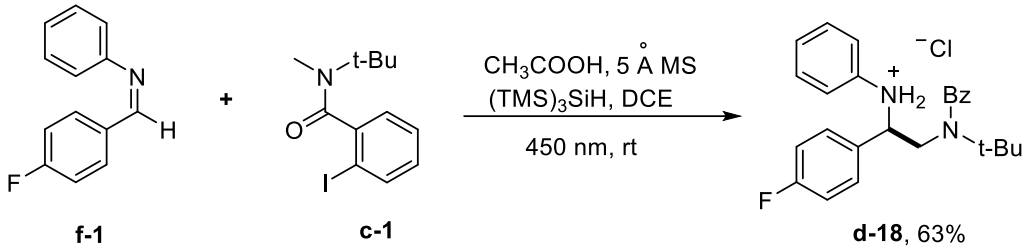


The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added aniline (0.2 mmol), *p*-fluoro benzaldehyde (0.3 mmol), CH_3COOH (0.2 mmol), DCE (4 mL) and MS 5Å (40 mg). The mixture was stirred 1h at room temperature before the sequential addition of **d'-c-1** (0.4 mmol) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 ° C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation. $NaHCO_3$ (sat. aq.) (10 mL) was added and the mixture stirred vigorously for 15 minutes. The organic layer was separated and dried over Na_2SO_4, filtered and evaporated to afford the crude product. The crude product was purified by short column chromatography on silica gel to give **[D]-d-18** as colorless oil (44 mg, 56 %).

Characterization of **[D]-d-1**8

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.87 – 9.41 (m, 2H), 7.40 – 7.33 (m, 1H), 7.27 – 7.17 (m, 3H), 7.16 – 7.02 (m, 7H), 7.01 – 6.94 (m, 2H), 6.28 – 6.03 (m, 1H), 1.66 – 1.50 (m, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.14, 164.10, 161.63, 139.64, 135.19, 131.92, 130.86, 130.78, 130.56, 130.11, 129.08, 128.63, 128.07, 127.83, 127.71, 116.04, 115.82, 60.92, 58.30, 26.23. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -111.80.**HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{25}D_3FN_2O^+$ 394.2368, Found 394.2366

(2) Determination of reaction intermediates

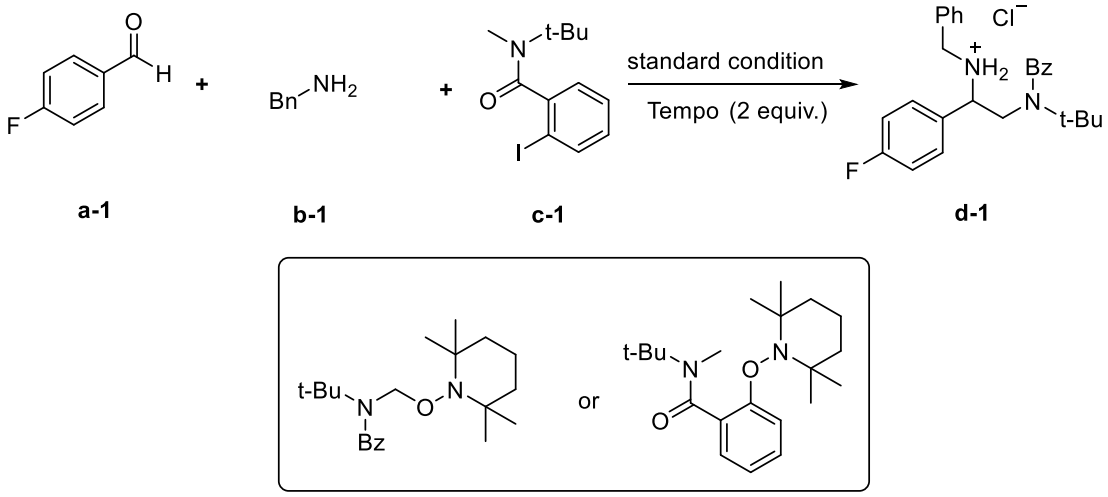


f-1 **c-1** **d-18**, 63%

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added 1-(4-fluorophenyl)-N-phenylmethanimine (0.2 mmol), CH_3COOH (0.2 mmol), DCE (4 mL), MS 5Å (300 mg), **1c** (0.4 mmol) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 ° C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation. $NaHCO_3$ (sat. aq.) (10 mL) was added and the mixture stirred vigorously for 15 minutes. The organic layer was separated and dried over Na_2SO_4, filtered and evaporated to afford the crude product. The crude product was purified by short column chromatography on silica gel to give **d-18** as colorless oil (49 mg, 63 %).

(3) Using TEMPO as a radical scavenger

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added aniline (0.2 mmol), p-Fluoro benzaldehyde (0.3 mmol), CH_3COOH (0.2 mmol), DCE (4 mL) and MS 5Å (300 mg). The mixture was stirred 1h at room temperature before the sequential addition of **1c-d** (0.4 mmol)、tris(trimethylsilyl)silane (0.4 mmol) and (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) (0.4 mmol, 2.0 equiv.). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and control the temperature at about 20 ° C until the reaction was complete (monitored by TLC). After reaction, the solvent was removed by rotary evaporation. $NaHCO_3$ (sat. aq.) (10 mL) was added and the mixture stirred vigorously for 15 minutes. No product **1** was observed.



HRMS calcd for $C_{21}H_{35}N_2O_2^+$
$[M+H]^+$: 347.2693
found:347.2695

HRMS (ESI) calcd for $C_{21}H_{35}N_2O_2^+$, [M+H]+: 347.2693, found: 347.2695.

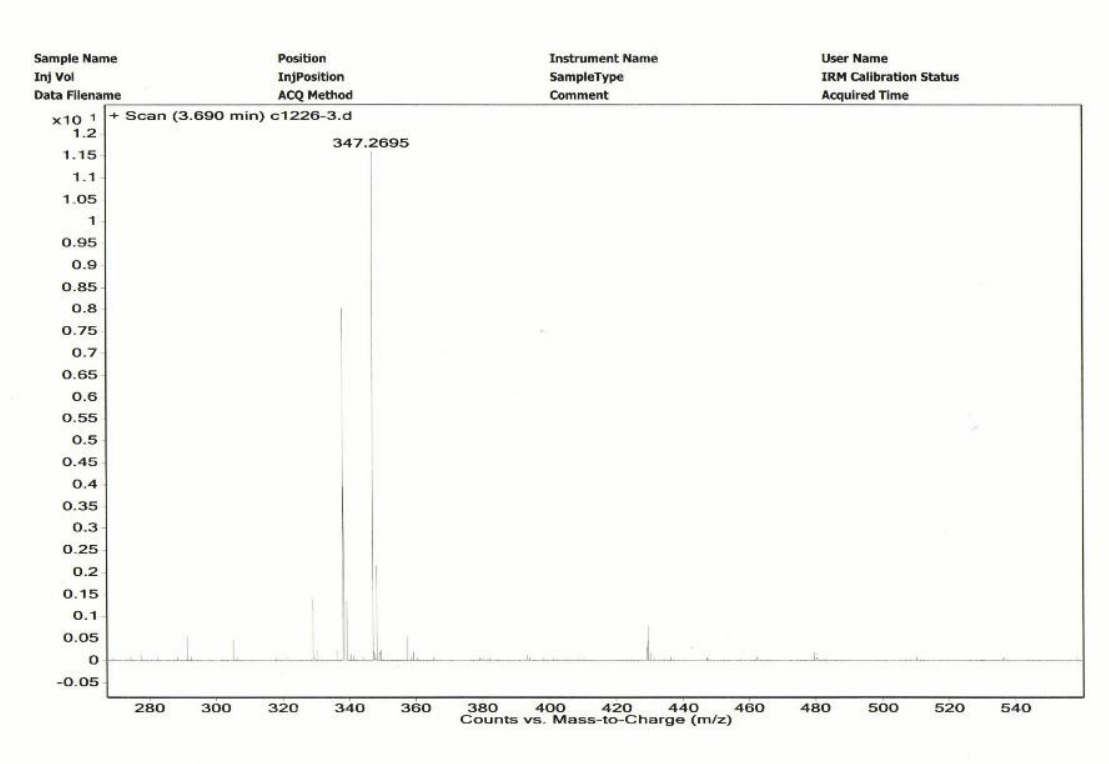
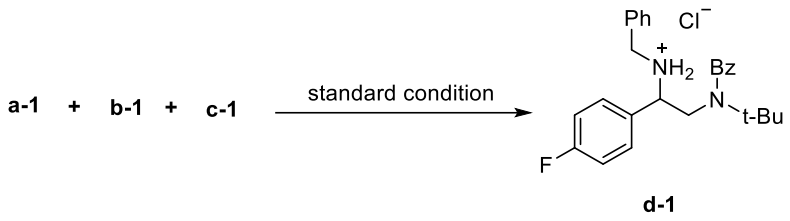


Figure S1 HRMS of TEMPO trapped adducts

(4) Light/dark cycle experiments for the model reaction

To study the necessity of continuous irradiation with visible light for the progress of the reaction, we started a reaction with successive irradiation and black periods. We determined the GC yields directly from the crude mixture using n-dodecane as internal standard. These results demonstrated that light is necessary and the reaction involves a radical chain process.



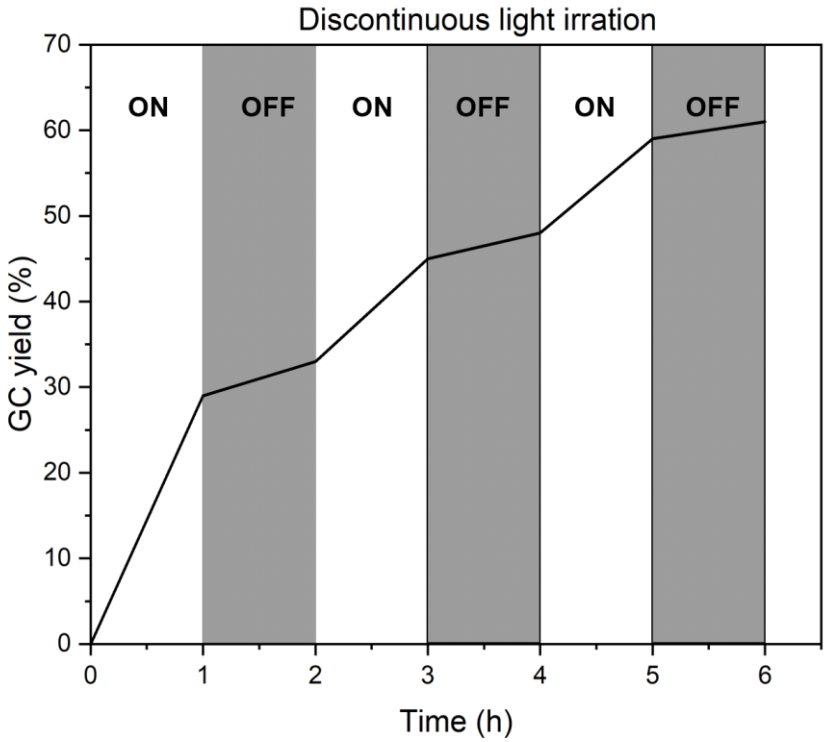


Figure S2. Each point of the graphic represents the GC yield, calculated from the relative amounts of an internal standard (n-dodecane). The grey boxes represent the periods in which the reaction vessels were covered (dark period). The reaction was carried out under standard condition.

(5) Spectroscopic studies

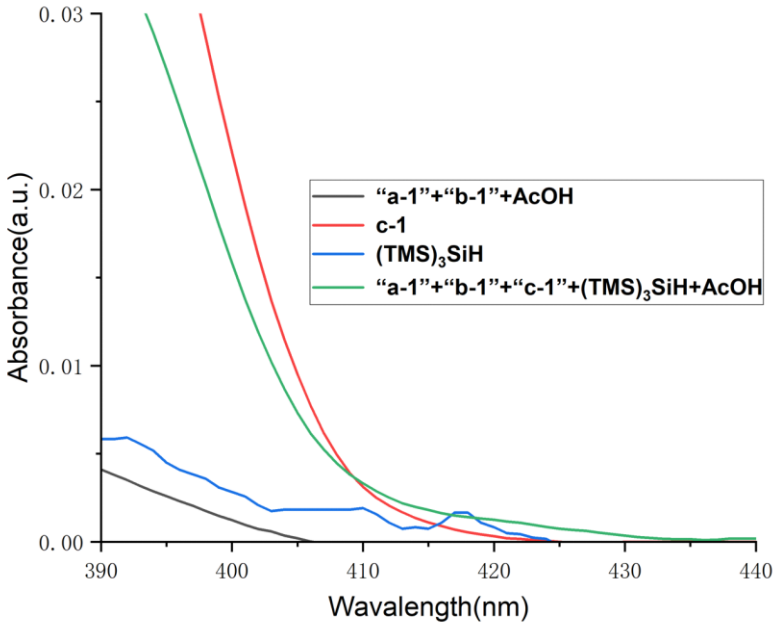
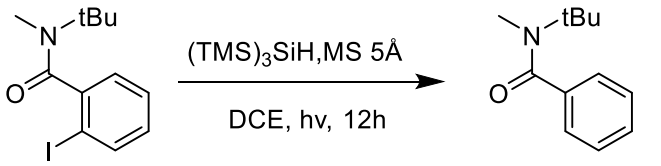


Figure S3. UV-Vis absorption spectra

Figure S3 indicates that iodoaromatic hydrocarbons have absorption in the visible light range. Due to the absence of a significant redshift, it indicates that the reaction did not go through the EDA process.

(6) Controlled Experiment



c-1 **g-1**, trace

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added **c-1** (0.4 mmol), MS 5Å (300 mg), DCE (4 mL) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and irradiated using a 10 W 450 nm LED lamp for 6 hours and purified by preparative thin layer chromatography (petroleum ether/ethyl acetate (10:1~10:3)) afforded 1.2 mg of the title compound.

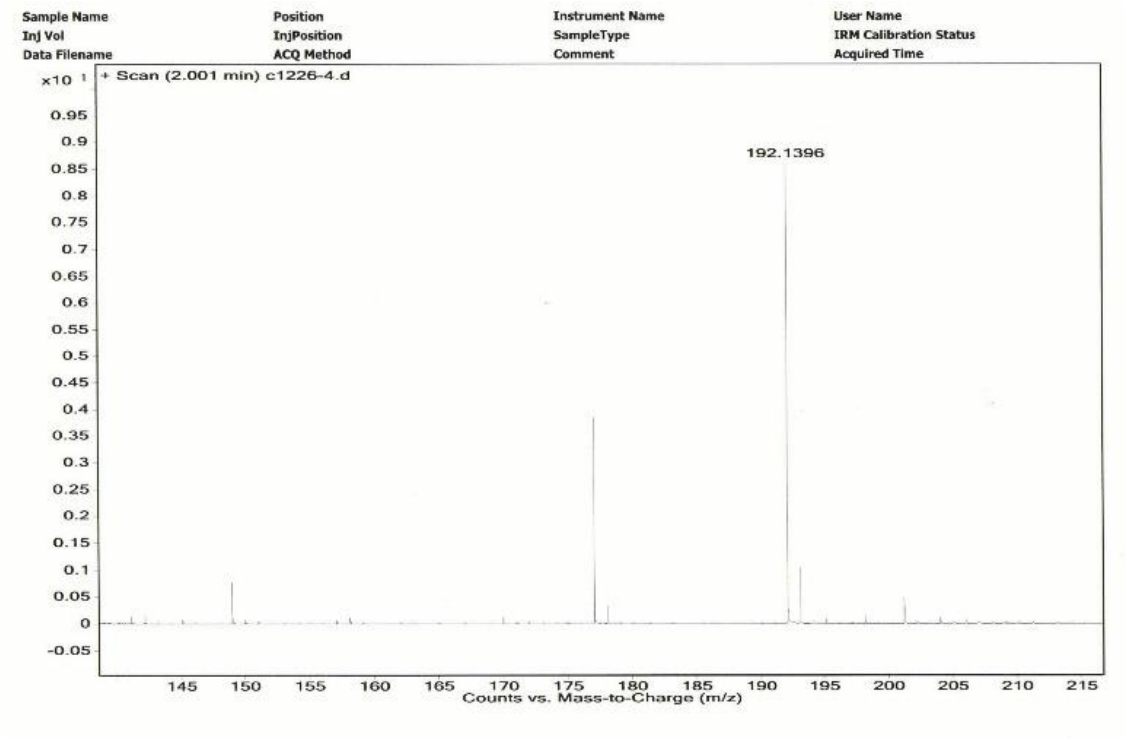
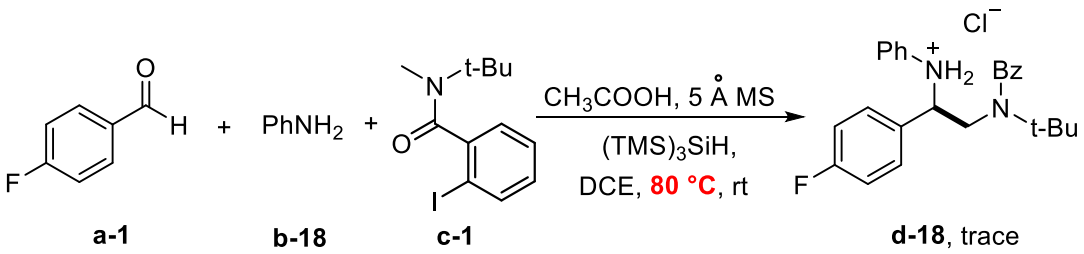
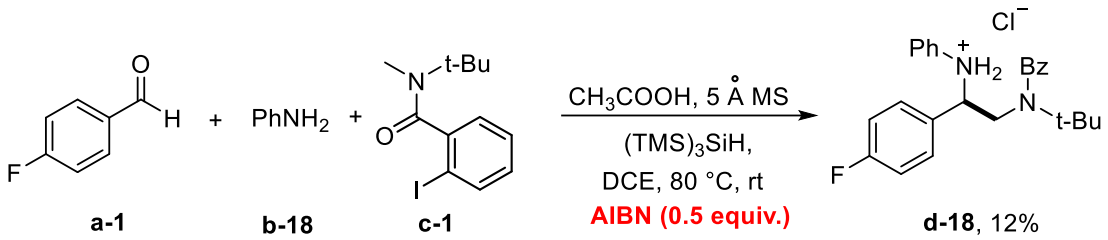


Figure S4 HRMS of Product monitoring



The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added aniline (0.2 mmol), p-fluoro benzaldehyde (0.3 mmol), CH_3COOH (0.2 mmol), DCE (4 mL) and MS 5Å (300 mg). The mixture was stirred 1h at room temperature before the sequential addition of **1c-d** (0.4 mmol) and tris(trimethylsilyl)silane (0.4 mmol). The reaction mixture was stirred and heated to 80 °C for 6 hours and find that trace amount of product **1** was observed.



a-1 **b-18** **c-1** **d-18**, 12%

The reaction was operated in a nitrogen-filled glove box. The oven-dried Schlenk tube (10 mL) equipped with a Teflon-coated magnetic stir bar was added aniline (0.2 mmol), p-fluoro benzaldehyde (0.3 mmol), CH_3COOH (0.2 mmol), DCE (4 mL) and MS 5Å (300 mg). The mixture was stirred 1h at room temperature before the sequential addition of **1c-d** (0.4 mmol), tris(trimethylsilyl)silane (0.4 mmol) and AIBN (0.1 mmol). The reaction mixture was stirred and heated to 80 °C for 6 hours and find that the product was obtained in 12% yield.

(7) Quantum yield measurement

Determination of the light intensity at 450 nm:

The photon flux was determined by ferrioxalate actinometry similar to a procedure by Yoon,[5] the photon flux of the LED (λmax= 450 nm) was first determined by standard ferrioxalate actinometry. For this, a 10 mL 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (0.737 g) in H_2SO_4 (10 mL of a 0.05 M solution). A 20 mL buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (20 mg) and sodium acetate (4.5 g) in H_2SO_4 (20 mL of a 0.5 M solution). Both solutions were stored in the dark. To determine the photon flux of the spectrophotometer, 4.00 mL of the ferrioxalate solution was placed in a cuvette and irradiated for 90 seconds at 450 nm with excitation and emission slit width of 10 nm on the benchtop under air. After irradiation, 1.00 mL of this irradiated ferrioxalate solution, 0.20 mL of phenanthroline buffer solution and 2.00 mL of water were added to an 8 mL scintillation vial with a stir bar. stirred for 1 h to allow the ferrous ions to completely coordinate with the phenanthroline. The absorption of the solution was measured at 510 nm. A non-irradiated sample was also prepared identically and the absorption at 510

nm was also measured. Each sample preparation and measurements were repeated two more times. The average of the absorption of the irradiated and non-irradiated samples were determined and used for the calculation of photon flux.

Conversion was calculated using equation 1.

$$\text{mol } Fe^{2+} = \frac{V \times \Delta A(510\ nm)}{l \times \varepsilon}$$

Where V is the total volume (0.0032 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.0 cm), and ε is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11100 L mol-1cm-1).10 The average value of the experiment was 5.375×10^{-7} mol of Fe^{2+}. The photon flux can be calculated using equation 2.

$$\text{Photonflux} = \frac{mol\ Fe^{2+}}{\Phi \times t \times f}$$

Where Φ is the quantum yield for the ferrioxalate actinometer (0.996 at 450 nm)[6, 7], t is the irradiation time, and f is the fraction of light absorbed at 450 nm($f = 1-10^{-cA}$, $A = 2.41$ at 450 nm, $f = 0.996$).

The average photon flux was calculated to be 6.247×10^{-9} einsteins s^{-1}

Determination of the amino(hetero)arylation reaction quantum yield

The oven-dried Schlenk tube (10 mL) containing a stirring bar was charged with amine (0.2 mmol, 1.0 equiv.) and 5Å molecular sieves was added followed by anhydrous dichloroethane (1 mL) 、 acetic acid (0.2 mmol, 1 equiv) and aldehyde (0.3 mmol, 1.5 equiv.) under nitrogen. This mixture was stirred for 1 hours at room temperature before the sequential addition of s Aryl iodide (0.4 mmol, 2 equiv.) and tris(trimethylsilyl)silane (0.4 mmol, 2 equiv.). The tube was put into the photoreactor, degassed and backfilled with nitrogen gas with a vacuum pump and a N_2 balloon. The tube was irradiated for 35 min. Then, the NMR yield was determined (14.3%) using 4-chlorobenzotrifluoride as internal standard. The reaction quantum yield was determined using equation 4, where photon flux was determined as above described, t is the reaction time, f is the fraction of incident light absorbed by the reaction mixture.

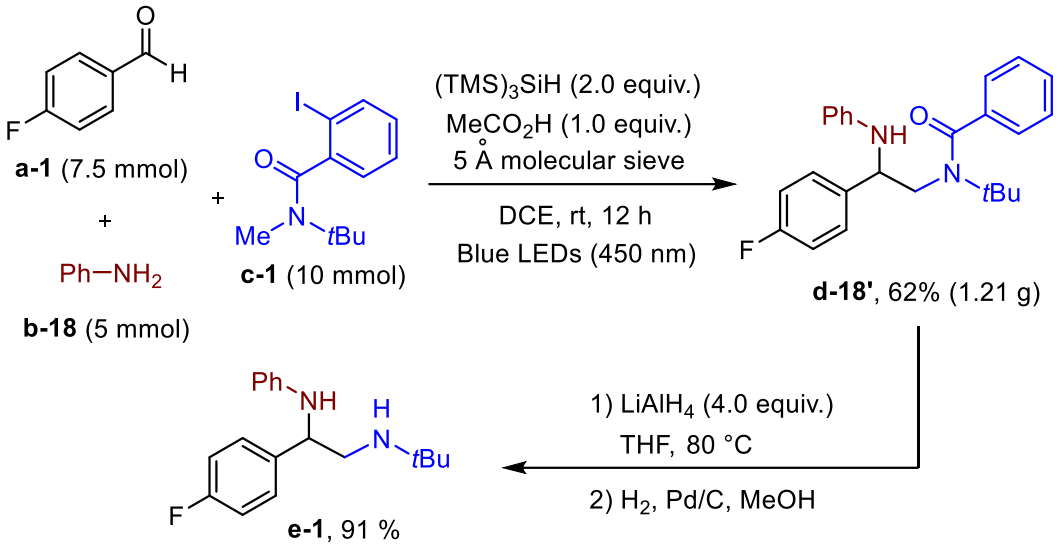
$$\Phi = \frac{mol\ of\ product\ formed}{photon\ flux \times t \times f}$$

According to the definition of quantum yield, the yield was calculated to be 2.202. f is the fraction of the absorbed light by the mixture and f is calculated to be 1 at half of reaction concentration under light irradiation for 30 min.

$$\Phi = \frac{0.0002 * 14.3\ \%}{6.247 \times 10^{-9} \times 2100 \times 0.99} = 2.202$$

The aminosulfonylation reaction quantum yield Φ was determined to be 2.202, which is above unity, indicating that a radical chain propagation might be operative in this reaction.

e) Gram-scale reaction and one-pot synthesis of secondary diamine

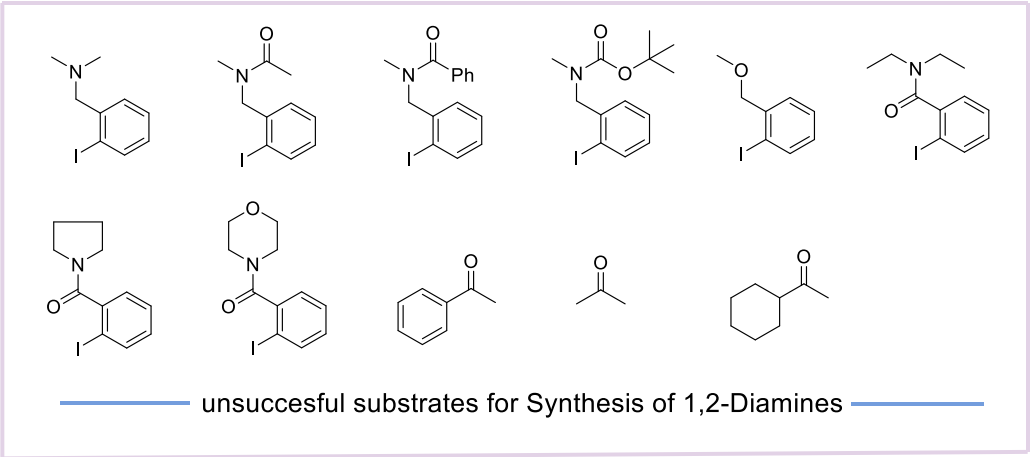


The reaction was operated in a nitrogen-filled glove box. The oven-dried round-bottom flask (250 mL) equipped with a Teflon-coated magnetic stir bar was added amine (5 mmol), aldehyde (7.5 mmol), CH_3COOH (5 mmol), DCE (100 mL) and MS 5Å (10 g). The mixture was stirred 1h at room temperature before the sequential addition of 2-iodobenzamides (10 mmol) and tris(trimethylsilyl)silane (10 mmol). The reaction mixture was stirred and irradiated using a 5×10 W 450 nm LED lamp for 12 hours and control the temperature at about 20 °C until the reaction was complete (monitored by TLC). After irradiation, the resulting homogenous solution was transferred to a 25 mL round bottom flask with aid of DCM (2 x 30 mL). NEt_3 (approx. 10 mL) and SiO_2 were added to this solution and the volatiles were removed under reduced pressure, affording a powder which was loaded on column. Purification by flash column chromatography on SiO_2, pre-basified with NEt_3 using pentane: EtOAc mixtures afforded **d-18'** (1.21 g, 62 %).

Dissolve the product with THF (100 mL) and place it at 0 ° C, lithium aluminum hydride (1M in THF, 12 ml) was added dropwise to the reaction solution and then continue stirring for 30 minutes. The reaction mixture was allowed to heated to 80 °C, stirred for 12 h and then treated successively with H_2O (10 mL), 15% aq NaOH (30 mL) and H_2O (40 mL). The reaction mixture was extracted with ethyl acetate (3 × 50 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated in

vacuo. The crude product was used for the next step without purification. The product was dissolved in solvent MeOH. 0.12 g palladium-10% on carbon was added to the solution. The reaction mixture was stirred under 1 atm of hydrogen overnight, then filtered and washed with dichloromethane. Purification by flash column chromatography on SiO_2, pre-basified with NEt_3 using DCM: MeOH mixtures afforded the **e-1** as light yellow solid (0.76 g, 91%).

f) Examples of unsuccessful substrates



Reference

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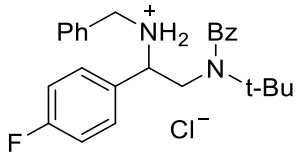
2. Spectral Data of Products

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethan-1-aminium chloride (d-1)

Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-1** as a colorless oil (66.0 mg, 75% yield).



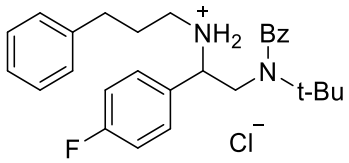
^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.85 (d, *J* = 10.3 Hz, 1H), 8.88 (s, 1H), 7.63 (dd, *J* = 6.6, 2.7 Hz, 2H), 7.39 (dd, *J* = 5.2, 1.7 Hz, 3H), 7.31 (dd, *J* = 7.5, 4.7 Hz, 2H), 7.15 – 7.07 (m, 3H), 6.90 (t, *J* = 8.3 Hz, 4H), 5.54 (m, 1H), 4.89 – 4.53 (m, 2H), 4.10 (m, 1H), 3.45 (m, 1H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.12, 163.73（d, J = 249.47）, 136.11, 135.96, 132.64, 130.77, 130.69, 130.26, 128.74, 128.57, 127.99, 127.77, 127.21, 115.74, 115.53, 60.04, 58.17, 54.82, 44.98, 26.08.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.85.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{26}H_{30}FN_2O^+$ 405.2337, Found 405.2330

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-3-phenylpropan-1-aminium chloride (d-2)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-2** as a colorless oil (52.4 mg, 56% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.87 (s, 1H), 8.98 (s, 1H), 7.45 (ddt, *J* = 33.7, 14.2, 7.2 Hz, 7H), 7.10 (dt, *J* = 21.3, 7.5 Hz, 5H), 6.80 (d, *J* = 6.7 Hz, 2H), 5.79 – 5.41

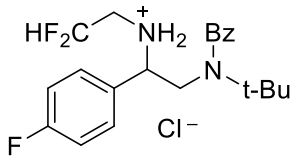
(m, 1H), 4.13 (q, *J* = 12.7, 9.3 Hz, 1H), 3.72 (q, *J* = 7.0 Hz, 1H), 3.42 (p, *J* = 7.1 Hz, 2H), 3.19 (dt, *J* = 15.4, 7.3 Hz, 1H), 2.20 (q, *J* = 6.1 Hz, 2H), 1.62 (t, *J* = 7.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.53, 162.8 (d, *J* = 249.47), 140.35, 135.98, 133.10, 130.07 (d, *J* = 8.1), 128.70, 128.39, 128.18, 126.59, 125.95, 116.33 (d, *J* = 22.2), 59.41, 58.06, 49.98, 45.48, 32.75, 30.57, 29.75, 26.15.

^{19}F NMR (376 MHz, CDCl3) δ -116.09.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{28}H_{34}FN_2O^+$ 433.2650, Found 433.2655

2-(N-(tert-butyl)benzamido)-N-(2,2-difluoroethyl)-1-(4-fluorophenyl)ethan-1-aminium chloride (d-3)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-3** as a colorless oil (51.3 mg, 62% yield).

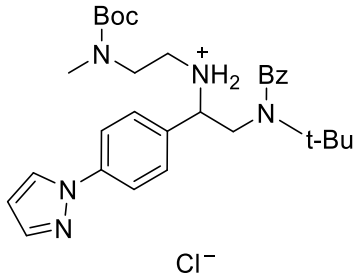
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (m, 1H), 8.84 (m, 1H), 7.64 (m, 2H), 7.57 (m, 2H), 7.49 – 7.45 (m, 3H), 7.09 (m, 2H), 5.95 (m, 0.8 H), 5.71 (m, 1.2 H), 4.31 (m, 1H), 3.84 (m, 2H), 3.54 (m, 1H), 1.54 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.61, 162.25 (d, *J* = 249.47), 135.41 (d, *J* = 15.1) 130.77 (d, *J* = 9.1), 130.10, 128.98, 127.06, 116.38, 116.17, 116.01, 113.59, 111.17, 60.20, 58.37, 44.76, 26.21.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.08, -120.96.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{21}H_{26}F_3N_2O^+$ 379.1992, Found 379.1983

1-(4-(1H-pyrazol-1-yl)phenyl)-N-(2-((tert-butoxycarbonyl)(methyl)amino)ethyl)-2-(N-(tert-butyl)benzamido)ethan-1-aminium chloride (d-4)



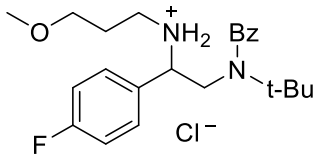
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 2:1, v/v) as eluent and protected by 1M HCl to afforded **d-4** as a yellow oil (98.8 mg, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.07 (s, 1H), 8.30 (s, 1H), 7.95 (d, *J* = 2.5 Hz, 1H), 7.73 (t, *J* = 2.8 Hz, 5H), 7.38 (dd, *J* = 5.1, 1.8 Hz, 3H), 7.28 – 7.20 (m, 2H), 6.47 (t, *J* = 2.1 Hz, 1H), 5.53 (d, *J* = 10.6 Hz, 1H), 4.98 (q, *J* = 11.0 Hz, 1H), 4.38 (t, *J* = 13.1 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 1H), 4.01 – 3.83 (m, 1H), 3.46 – 2.98 (m, 3H), 2.91 – 2.62 (m, 2H), 1.56 (d, *J* = 5.8 Hz, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.96, 156.88, 141.35, 140.26, 136.26, 136.26, 129.68, 128.99, 128.50, 126.86, 126.67, 119.61, 107.92, 81.08, 62.93, 60.42, 57.51, 49.73, 45.16, 33.93, 28.66, 26.13.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{30}H_{42}N_5O_3^+$ 520.3282, Found 520.3281

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-3-methoxypropan-1-aminium chloride (d-5)



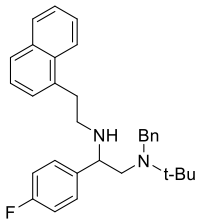
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-5** as a colorless oil (63.3 mg, 75% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.87 (s, 1H), 7.66 – 7.51 (m, 3H), 7.46 – 7.37 (m, 5H), 7.19 – 6.99 (m, 2H), 5.35 (d, *J* = 10.3 Hz, 1H), 4.55 (d, *J* = 10.2 Hz, 1H), 3.71 (dt, *J* = 14.9, 7.1 Hz, 1H), 3.45 – 3.34 (m, 2H), 3.26 (d, *J* = 2.1 Hz, 4H), 3.05 (t, *J* = 9.5 Hz, 1H), 2.36 (s, 1H), 1.53 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.24, 164.16, 161.70 (d, *J* = 248.46) ,136.72, 133.45, 130.08 (d, *J* = 24.2), 129.88, 128.78, 126.82, 116.27 (d, *J* = 116.27), 72.42, 60.39, 59.03, 57.75, 50.54, 45.74, 28.58, 26.39.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{23}H_{32}FN_2O_2^+$ 387.2442, Found 387.2445

N^2-benzyl-N^2-(tert-butyl)-1-(4-fluorophenyl)-N^1-(2-(naphthalen-1-yl)ethyl)ethane-1,2-diamine (d-6)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-6** as a colorless oil (61.8 mg, 68% yield).

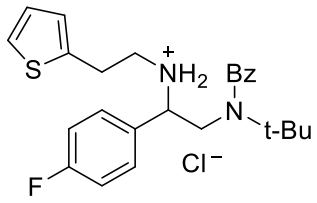
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.58 – 7.27 (m, 11H), 7.11 (t, *J* = 8.5 Hz, 2H), 4.17 (dd, *J* = 8.8, 5.7 Hz, 1H), 4.05 (d, *J* = 13.9 Hz, 1H), 3.44 (d, *J* = 13.8 Hz, 1H), 3.38 – 3.14 (m, 3H), 2.99 (ddd, *J* = 13.3, 10.6, 6.0 Hz, 1H), 2.84 (dd, *J* = 11.1, 5.7 Hz, 1H), 2.70 (ddd, *J* = 13.2, 10.1, 5.0 Hz, 1H), 1.16 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2 (d, *J* = 249.12), 140.06, 136.43, 134.24, 133.91, 132.00, 130.38 (d, *J* = 7.1), 130.34, 128.77, 128.72, 128.53, 127.14, 126.91, 126.84, 125.83, 125.59, 125.50, 123.76, 115.22 (d, *J* = 21.2), 63.83, 54.71, 51.28, 50.58, 43.69, 32.53, 28.91.

^{19}F NMR (376 MHz, $CDCl_3$) δ -114.85.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{31}H_{36}FN_2^+$ 455.2857, Found 455.2855

2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)-N-(2-(thiophen-2-yl)ethyl)ethan-1-aminium chloride (d-7)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-7** as a colorless oil (62.6 mg, 68% yield).

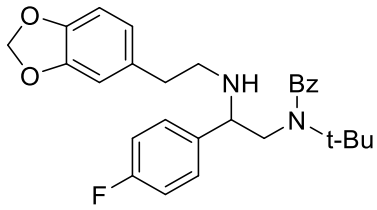
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (m, 1H), 9.07 (m, 1H), 7.62 (m, 2H), 7.56 – 7.51 (m, 2H), 7.44 (m, 3H), 7.14 (m, 2H), 7.00 (m, 1H), 6.77 (m, 1H), 6.40 (m 1H), 5.94 – 5.55 (m, 1H), 4.23 (m, 1H), 3.72 (m, 1H), 3.56 – 3.35 (m, 2H), 2.84 (m, 1H), 2.63 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.38, 162.93（d, J = 249.47）, 139.55, 136.04, 130.22 (d, J = 8.8), 128.74, 126.98, 126.70, 125.66, 123.98, 116.43 (d, J = 22.2), 59.46, 58.15, 52.27, 45.33, 29.66, 26.17.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.06.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{25}H_{30}FN_2OS^+$ 425.2057, Found 425.2058

N-(2-(benzo[d][1,3]dioxol-5-yl)ethyl)-2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethan-1-aminium chloride (d-8)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-8** as a colorless oil (75.7 mg, 76% yield).

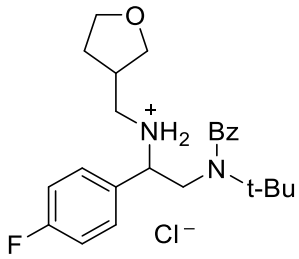
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.69 (s, 1H), 9.22 (s, 1H), 7.53 (dt, J = 47.7, 7.5 Hz, 7H), 7.13 (t, J = 8.1 Hz, 2H), 6.52 (d, J = 7.8 Hz, 1H), 6.16 – 5.94 (m, 2H), 5.84 (s, 2H), 5.77 (d, J = 9.1 Hz, 1H), 4.10 (d, J = 67.5 Hz, 1H), 3.70 – 3.27 (m, 3H), 2.47 (td, J = 13.9, 12.8, 5.8 Hz, 1H), 2.33 – 2.15 (m, 1H), 1.51 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.36, 164.15, 161.68, 162.91 (d, *J* = 249.47), 147.48, 146.11, 136.15, 133.15, 131.21, 130.23 (d, *J* = 9.1), 128.69, 126.75, 121.60, 116.36 (d, *J* = 21.2), 108.92, 108.20, 100.82, 59.12, 58.10, 52.13, 45.24, 35.42, 29.75, 26.15.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.85.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{28}H_{32}FN_2O_3^+$ 463.2391, Found 463.2390

2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)-N-((tetrahydrofuran-3-yl)methyl)ethan-1-aminium chloride (d-9)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-9** as a colorless oil (59.1 mg, 68% yield).

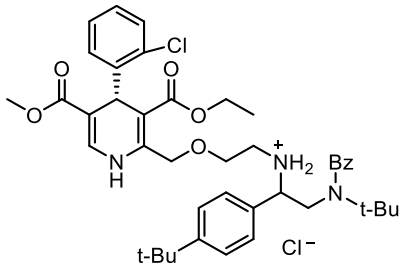
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (d, *J* = 58.6 Hz, 1H), 8.38 (d, *J* = 49.9 Hz, 1H), 7.75 – 7.53 (m, 4H), 7.47 (d, *J* = 4.7 Hz, 3H), 7.15 (t, *J* = 7.8 Hz, 2H), 5.43 (d, *J* = 7.2 Hz, 1H), 4.77 – 4.10 (m, 2H), 3.79 – 3.30 (m, 6H), 3.21 – 2.97 (m, 1H), 2.43 (d, *J* = 42.6 Hz, 1H), 2.29 (s, 1H), 1.62 (d, *J* = 17.6 Hz, 10H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.26, 162.81 (d, *J* = 249.47 Hz), 136.00, 133.95, 130.23 (q, *J* = 6.1 Hz), 129.97, 128.96, 128.93, 127.25, 116.45 (q, *J* = 9.1 Hz), 70.90, 70.73, 67.45, 67.27, 60.99, 60.78, 58.24, 58.17, 54.75, 54.60, 45.80, 45.75, 38.66, 38.28, 30.05, 29.78, 26.22.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.98, -112.07.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{24}H_{32}FN_2O_2^+$ 399.2442, Found399.2441

2-(N-(tert-butyl)benzamido)-1-(4-(tert-butyl)phenyl)-N-(2-(((S)-4-(2-chlorophenyl)-3-(ethoxycarbonyl)-5-(methoxycarbonyl)-1,4-dihydropyridin-2-yl)methoxy)ethyl)ethan-1-aminium chloride (d-10)



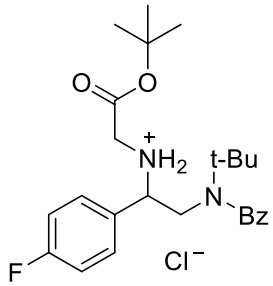
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 1:1, v/v) as eluent and protected by 1M HCl to afforded **d-10** as a white solid (111.6 mg, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.74 – 8.21 (m, 2H), 7.56 – 7.33 (m, 10H), 7.26 – 7.19 (m, 1H), 7.15 – 7.01 (m, 1H), 7.07 – 6.69 (m, 1H), 5.72 – 5.52 (m, 1H), 5.50 – 5.37 (m, 1H), 4.75 – 4.31 (m, 3H), 4.19 – 3.87 (m, 2H), 3.83 – 3.25 (m, 8H), 2.60 – 2.39 (m, 3H), 1.68 – 1.48 (m, 9H), 1.38 – 1.29 (m, 9H), 1.21 – 1.08 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.53, 176.09, 168.24, 168.20, 167.18, 167.06, 152.37, 152.32, 146.29, 146.21, 146.13, 144.17, 143.97, 135.79, 135.57, 133.16, 132.77, 132.13, 132.10, 131.45, 131.32, 130.38, 130.33, 129.20, 128.85, 127.93, 127.72, 127.39, 127.35, 127.09, 127.03, 126.94, 126.88, 126.37, 104.97, 104.38, 102.72, 102.48, 68.23, 67.16, 66.99, 60.46, 60.23, 59.91, 59.86, 57.96, 57.89, 50.79, 45.61, 45.38, 37.15, 37.12, 34.75, 34.72, 31.28, 31.24, 26.22, 26.16, 19.34, 19.25, 14.29.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{42}H_{53}ClN_3O_6^+$ 730.3617, Found 730.3625

2-(tert-butoxy)-N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-2-oxoethan-1-aminium chloride (d-11)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-11** as a colorless oil (64.1 mg, 69% yield).

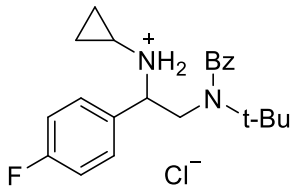
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.92 (t, *J* = 10.3 Hz, 1H), 8.00 – 7.87 (m, 1H), 7.74 (d, *J* = 1.7 Hz, 1H), 7.65 – 7.54 (m, 4H), 7.51 – 7.36 (m, 5H), 6.63 – 6.44 (m, 3H), 6.37 (s, 1H), 5.77 (dd, *J* = 17.2, 1.4 Hz, 2H), 5.64 – 5.47 (m, 1H), 4.72 – 4.47 (m, 2H), 4.21 (s, 1H), 4.13 – 3.88 (m, 1H), 3.59 (ddt, *J* = 13.7, 9.4, 4.2 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.68, 147.74, 147.22, 141.02, 139.53, 136.04, 135.21, 131.72, 130.23, 129.82, 128.79, 127.34, 127.18, 121.89, 119.28, 108.40, 108.25, 108.02, 101.09, 77.39, 59.81, 58.26, 54.67, 44.68, 26.01, 18.40.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.86

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{25}H_{34}FN_2O_3^+$ 429.2548, Found 429.2554

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)cyclopropanaminium chloride (d-12)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-12** as a colorless oil (57.7 mg, 74% yield).

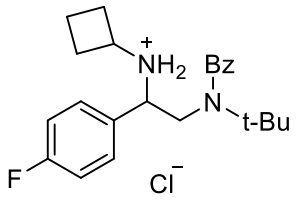
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.64 – 10.26 (m, 1H), 9.10 – 8.67 (m, 1H), 7.69 – 7.58 (m, 2H), 7.57 – 7,37 (m, 5H), 7.21 – 7.08 (m, 2H), 5.71 – 5.47 (m, 1H), 4.34 – 4.02 (m, 1H), 3.39 – 3.20 (m, 1H), 2.75 – 2.54 (m, 1H), 1.63 – 1.45 (m, 9H), 0.96 – 0.68 (m, 2H), 0.56 – 0.24 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.07, 162.77 (d, *J* = 250.48 Hz), 136.41, 133.52, 130.83, 129.62 (d, *J* = 9.1 Hz), 128.32, 127.85, 116.33 (d, *J* = 21.2 Hz), 62.61, 57.84, 45.57, 33.90, 26.19, 10.68, 10.17.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.34.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{22}H_{28}FN_2O^+$ 355.2180, Found 355.2186

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)cyclobutanaminium chloride (d-13)



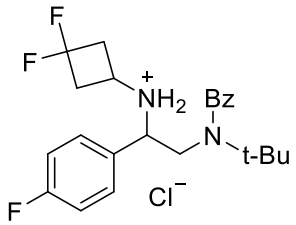
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-13** as a colorless oil (55.7 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78-10.12 (s, 1H), 8.67-8.12 (s, 1H), 7.72 – 7.37 (m, 7H), 7.25-6.92 (d, *J* = 8.2 Hz, 2H), 5.62-5.26 (s, 1H), 4.23-3.88 (dt, *J* = 13.3, 6.7 Hz, 2H), 3.64-3.29 (m, 1H), 2.39 – 2.08 (m, 2H), 1.67-1.57 (m, 2H), 1.56-1.38 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.15, 162.62 (d, *J* = 249.47 Hz), 136.76, 133.90, 133.87, 130.75, 129.31 (d, *J* = 9.1 Hz), 128.66, 127.12, 116.24 (d, *J* = 21.2 Hz), 58.05, 57.75, 55.30, 45.98, 30.27, 30.05, 26.20, 14.46.

HRMS (ESI) m/z: $[M-Cl]^+$ Calcd for $C_{23}H_{29}FN_2O^+$ 369.2337, Found 369.2330

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-3,3-difluorocyclobutan-1-aminium chloride (d-14)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-14** as a colorless oil (57.2 mg, 65% yield).

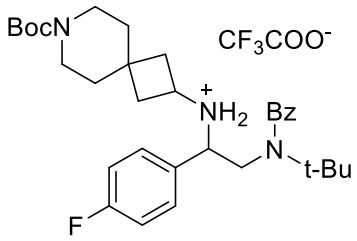
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78-10.61 (m, 1H), 8.27-8.09 (m, 1H), 7.63 – 7.38 (m, 7H), 7.23-7.11 (m, 2H), 5.46-5.36 (m, 1H), 4.38 – 4.02 (m, 2H), 3.52-3.31 (m, 1H), 3.04 – 2.74 (m, 2H), 2.45-2.12 (m, 2H), 1.62-1.43 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.70, 162.86 (d, *J* = 250.48 Hz), 136.38, 133.93, 133.90, 131.24, 129.1 (d, 8.1 Hz), 128.98, 127.07, 119.39, 116.70 (d, *J* =22.2 Hz), 113.93, 59.25, 58.24, 46.05 (d, *J* = 7.1 Hz), 45.79, 42.30 (t, *J* = 23.2 Hz), 26.23.

^{19}F NMR (376 MHz, $CDCl_3$) δ -84.58, -85.11, -102.41, -102.94, -111.91.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{23}H_{28}F_3N_2O^+$ 405.2148, Found 405.2148

7-(tert-butoxycarbonyl)-N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-7-azaspiro[3.5]nonan-2-aminium 2,2,2-trifluoroacetate (d-15)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-15** as a yellow oil (65.1 mg, 50% yield).

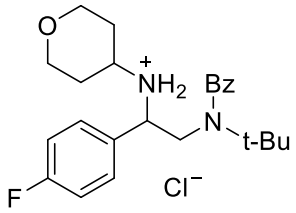
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.04-9.80 (m, 1H), 9.61-9.34 (m, 1H), 7.87-7.66 (s, 1H), 7.59-7.44 (m, 6H), 7.20-7.12 (m, 2H), 5.22-5.12 (m, 1H), 4.29 – 3.98 (m, 2H), 3.59-3.47 (m, 1H), 3.22-3.10 (m, 4H), 1.87 – 1.70 (m, 3H), 1.61 – 1.55 (m, 1H), 1.51-1.44 (m, 9H), 1.44-1.35 (m, 9H), 1.35 – 1.28 (m, 2H), 1.28-1.12 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.01, 162.91 (d, *J* = 239.37 Hz), 161.34, 160.96, 155.00, 136.32, 133.11, 131.05, 129.08 (d, *J* = 8.1 Hz), 128.83, 126.75, 116.62 (d, *J* = 21.2 Hz), 79.79, 58.15, 58.00, 51.17, 46.26, 38.76, 38.63, 38.11, 34.86, 31.26, 28.41, 26.09.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.80, -112.08.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{32}H_{45}FN_3O_3^+$ 538.3439, Found 538.3442

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)tetrahydro-2H-pyran-4-aminium chloride (d-16)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-16** as a colorless oil (45.1 mg, 52% yield).

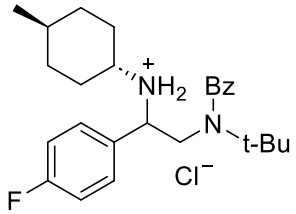
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15-8.79 (m, 2H), 7.86-7.68 (m, 2H), 7.58-7.40 (m, 5H), 7.21-7.03 (m, 2H), 5.43-5.17 (m, 1H), 4.22 – 3.95 (m, 2H), 3.93 – 3.75 (m, 3H), 3.23-3.06 (m, 1H), 3.06-2.92 (m, 1H), 2.55-2.35 (m, 2H), 2.05-1.90 (m, 1H), 1.84 – 1.68 (m, 1H), 1.60-1.43 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.68, 162.68 (d, J = 250.48 Hz), 136.56, 133.55, 130.44, 130.36, 130.29 (d, J =7.1 Hz), 129.02, 125.94, 116.38, 116.16 (d, J = 22.2 Hz), 67.34, 67.15, 59.03, 58.49, 56.09, 46.41, 32.43, 31.79, 26.17.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.66.

HRMS (ESI) m/z: $[M-Cl]^+$ Calcd for $C_{24}H_{32}FN_2O_2^+$ 399.2442, Found 399.2443

(1r,4r)-N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-4-methylcyclohexan-1-aminium chloride (d-17)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-17** as a colorless oil (54.4 mg, 61% yield).

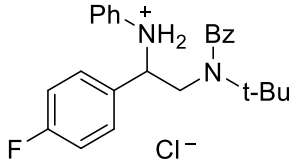
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75-9.46 (m, 0.5H), 8.71-8.34 (m, 1.5H), 8.11-7.33 (m, 7H), 7.25-7.03 (m, 2H), 5.66 – 2.64 (m, 4H), 2.48-2.11 (dd, J = 47.0, 12.3 Hz, 1H), 2.01 – 1.56 (m, 6H), 1.56 – 1.26 (m, 9H), 0.89 – 0.68 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.46, 167.96, 162.59 (d, *J* = 249.47 Hz), 136.34, 132.88, 131.95, 131.76, 131.73, 130.75 (d, *J* = 8.1 Hz), 130.48 (d, *J* = 8.1 Hz), 130.32, 128.96, 128.52, 127.80, 125.83, 116.55 (d, *J* = 22.2 Hz), 116.18 (d, *J* = 8.1 Hz), 116.08, 61.87, 60.37, 59.15, 56.23, 55.26, 46.42, 43.31, 34.13, 34.10, 33.03, 31.90, 31.27, 31.14, 31.04, 27.72, 26.32, 21.85, 21.75.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.02, -112.91.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{26}H_{36}FN_2O^+$ 411.2806, Found 411.2807

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)benzenaminium chloride (d-18)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-18** as a colorless oil (55.3 mg, 65% yield).

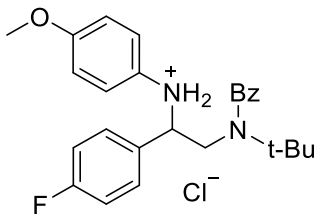
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87-9.44 (m, 2H), 7.42 – 7.32 (m, 2H), 7.27 – 7.15 (m, 3H), 7.15-7.04 (m, 7H), 7.00-6.92 (m, 2H), 6.27-6.14 (m, 1H), 4.23-4.03 (m, 1H), 3.68 – 3.33 (m, 1H), 1.67-1.48 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.20, 162.86 (d, *J* = 249.47 Hz), 139.56, 135.26, 131.91, 131.88, 130.78 (d, *J* = 8.1 Hz), 130.56, 130.09, 129.05, 128.61, 128.07, 127.81, 116.02, 115.91 (d, *J* = 22.2 Hz), 60.99, 58.32, 45.24, 26.16.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.80.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{25}H_{28}FN_2O^+$ 391.2180, Found 391.2189

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-4-methoxybenzenaminium chloride (d-19)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-19** as a colorless oil (54.7 mg, 60% yield).

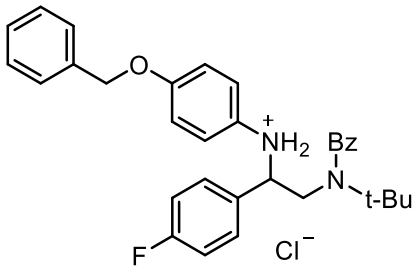
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (d, *J* = 242.4 Hz, 2H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 7.1 Hz, 4H), 6.99 (t, *J* = 8.2 Hz, 3H), 6.59 (d, *J* = 7.9 Hz, 2H), 6.15 (d, *J* = 9.4 Hz, 1H), 4.25 – 3.60 (m, 5H), 3.44 (d, *J* = 6.9 Hz, 1H), 1.59 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.84, 162.89 (d, *J* = 249.47 Hz), 158.93, 135.19, 131.89, 131.78, 131.75, 131.50, 130.87 (d, *J* = 8.1 Hz), 130.07, 128.56, 127.87, 115.96 (d, *J* = 22.2 Hz), 114.09, 60.76, 58.27, 55.31, 45.22, 26.14.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.85.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{26}H_{30}FN_2O_2^+$ 421.2286, Found 421.2289

4-(benzyloxy)-N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)benzenaminium chloride (d-20)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-20** as a colorless oil (73.4 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 – 9.77 (m, 1H), 9.70 – 9.22 (m, 1H), 7.43 – 7.31 (m, 7H), 7.24 – 7.10 (m, 5H), 7.04 – 6.90 (m, 3H), 6.76 – 6.48 (m, 2H), 6.36 – 6.02 (m,

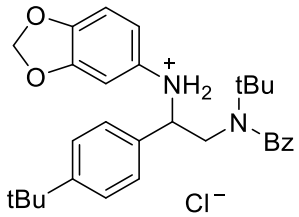
1H), 5.05 – 4.65 (m, 2H), 4.31 – 3.94 (m, 1H), 3.61 – 3.26 (m, 1H), 2.53 – 2.17 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.57, 162.87 (d, *J* = 250.48 Hz), 158.07, 136.32, 135.30, 131.90, 130.89 (d, *J* = 8.1 Hz), 130.85, 130.01, 128.59, 128.13, 127.86, 127.56, 124.42, 123.52, 119.14, 115.94 (d, *J* = 21.2 Hz), 115.11, 70.06, 60.66, 58.29, 45.26, 26.19.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.66.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{32}H_{34}FN_2O_2^+$ 497.2599, Found 497.2601

N-(2-(N-(tert-butyl)benzamido)-1-(4-(tert-butyl)phenyl)ethyl)benzo[d][1,3]dioxol-5-aminium chloride (d-21)



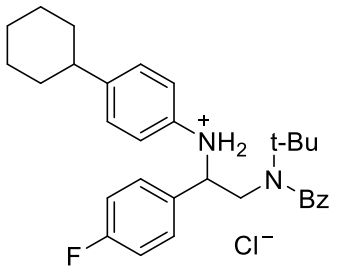
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-21** as a colorless oil (72.1 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.75-9.75 (m, 1H), 9.68-8.90 (m, 1H), 7.57 – 7.27 (m, 5H), 7.26-6.90 (m, 6H), 6.52-6.44 (m, 1H), 6.12-6.04 (m, 1H), 5.86-5.77 (m, 2H), 4.32-4.02 (m, 1H), 3.62 – 2.08 (m, 2H), 1.61-1.51 (m, 9H), 1.32-1.28 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.82, 152.50, 147.47, 147.09, 135.37, 132.60, 129.99, 128.59, 128.41, 127.87, 125.83, 125.10, 111.31, 107.82, 101.57, 61.26, 58.15, 45.11, 34.71, 31.25, 26.10.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{30}H_{37}N_2O_3^+$ 473.2799, Found 473.2791

N-(2-(N-(tert-butyl)benzamido)-1-(4-fluorophenyl)ethyl)-4-cyclohexylbenzenaminium chloride (d-22)



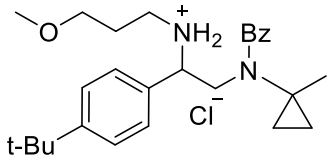
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-22** as a colorless oil (70.9 mg, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 – 9.28 (m, 2H), 7.40-7.30 (m, 2H), 7.24 – 7.20 (m, 2H), 7.13-7.06 (m, 1H), 7.00-6.92 (m, 2H), 6.91-6.86 (m, 3H), 6.21-6.12 (m, 2H), 6.17 (dd, *J* = 9.7, 3.4 Hz, 1H), 4.18-3.95 (s, 1H), 3.51 (t, *J* = 10.1 Hz, 1H), 2.32 (tt, *J* = 11.6, 3.3 Hz, 1H), 1.77 (dt, *J* = 12.1, 3.0 Hz, 2H), 1.69 (d, *J* = 12.3 Hz, 3H), 1.30 – 1.22 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.97, 162.79 (d, *J* = 250.48 Hz), 148.09, 136.90, 135.35, 132.07, 132.04, 130.80 (d, *J* = 8.1 Hz), 130.21, 129.97, 128.69, 127.68, 127.31, 115.74 (d, *J* = 22.2 Hz), 60.57, 58.28, 45.08, 43.88, 34.20, 26.69, 26.12, 26.00.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{31}H_{38}FN_2O^+$ 473.2963, Found 473.2971

N-(1-(4-(tert-butyl)phenyl)-2-(N-(1-methylcyclopropyl)benzamido)ethyl)-3-methoxypropan-1-aminium chloride (d-23)



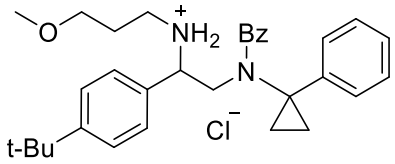
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-23** as a colorless oil (57.7 mg, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 – 9.66 (m, 2H), 7.59 – 7.49 (m, 2H), 7.48 – 7.43 (m, 2H), 7.42 – 7.30 (m, 5H), 4.82 – 4.57 (m, 1H), 4.47 – 4.24 (m, 1H), 4.17 – 3.96 (m, 1H), 3.55 – 3.39 (m, 2H), 3.32 – 3.26 (m, 3H), 3.03 – 2.85 (m, 2H), 2.25 – 2.00 (m, 2H), 1.34 – 1.29 (m, 9H), 1.04 – 0.89 (m, 3H), 0.86 – 0.15 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.80, 152.99, 137.33, 129.99, 129.83, 128.43, 128.09, 126.80, 126.31, 70.55, 61.34, 58.84, 53.49, 45.95, 44.87, 39.54, 34.78, 31.27, 25.63, 23.94, 8.75.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{27}H_{39}N_2O_2^+$ 423.3006, Found 423.3011

N-(1-(4-(tert-butyl)phenyl)-2-(N-(1-phenylcyclopropyl)benzamido)ethyl)-3-methoxypropan-1-aminium chloride (d-24)



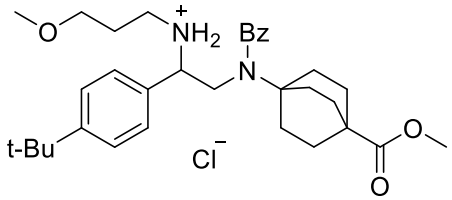
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-24** as a colorless oil (60.3 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.66 – 10.13 (m, 1H), 10.13 – 9.53 (m, 1H), 7.66 – 7.01 (m, 12H), 6.96 – 6.64 (m, 2H), 5.33 – 4.04 (m, 2H), 3.61 – 3.25 (m, 5H), 3.08 – 2.75 (m, 2H), 2.68 – 2.43 (m, 1H), 2.30 – 1.95 (m, 2H), 1.38 – 1.20 (m, 11H), 1.09 – 0.74 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.93, 153.06, 142.89, 136.16, 130.01, 128.94, 128.20, 127.86, 127.38, 126.50, 126.08, 123.55, 70.58, 62.71, 58.92, 55.54, 45.54, 44.98, 34.78, 31.24, 25.70, 24.42, 21.08.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{32}H_{41}N_2O_2^+$ 485.3163, Found 485.3166

N-(1-(4-(tert-butyl)phenyl)-2-(N-(4-(methoxycarbonyl)bicyclo[2.2.2]octan-1-yl)benzamido)ethyl)-3-methoxypropan-1-aminium chloride (d-25)



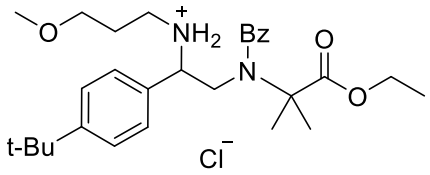
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-25** as a colorless oil (60.5 mg, 53% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.12 – 10.64 (m, 1H), 8.06 – 7.80 (m, 1H), 7.51 – 7.37 (m, 9H), 5.43 – 5.22 (m, 1H), 4.49 – 4.27 (m, 1H), 3.71 – 3.56 (m, 4H), 3.45 – 3.29 (m, 2H), 3.27 – 3.14 (m, 4H), 3.11 – 2.99 (m, 1H), 2.30 – 2.17 (m, 1H), 2.16 – 2.03 (m, 6H), 2.02 – 1.91 (m, 7H), 1.35 – 1.32 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.45, 175.52, 152.07, 136.53, 133.96, 130.12, 128.64, 127.45, 126.81, 126.20, 71.83, 60.38, 58.74, 57.61, 52.08, 49.72, 45.58, 38.23, 34.71, 31.30, 28.49, 28.08, 27.52.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{33}H_{47}N_2O_4^+$ 535.3530, Found 535.3533

N-(1-(4-(tert-butyl)phenyl)-2-(N-(1-ethoxy-2-methyl-1-oxopropan-2-yl)benzamido)ethyl)-3-methoxypropan-1-aminium chloride (d-26)



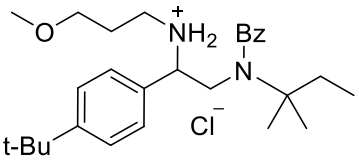
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-26** as a colorless oil (81.9 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 – 9.71 (m, 2H), 7.42 – 7.35 (m, 1H), 7.31 – 7.24 (m, 4H), 7.23 – 7.16 (m, 2H), 7.07 – 6.93 (m, 2H), 4.57 – 4.34 (m, 2H), 4.26 – 4.18 (m, 2H), 4.15 – 4.04 (m, 1H), 3.51 – 3.35 (m, 2H), 3.36 – 3.22 (m, 3H), 2.89 – 2.66 (m, 2H), 2.15 – 1.97 (m, 2H), 1.94 – 1.79 (m, 3H), 1.70 – 1.49 （m, 3H）1.33 – 1.30 (m, 9H), 1.29 – 1.25 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.57, 172.38, 152.64, 135.75, 130.03, 128.60, 128.37, 128.29, 126.95, 126.52, 69.69, 63.06, 62.62, 61.74, 58.76, 49.08, 44.29, 34.72, 31.25, 26.07, 25.70, 24.69, 14.15.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{29}H_{43}N_2O_4^+$ 483.3217, Found 483.3216

N-(1-(4-(tert-butyl)phenyl)-2-(N-(tert-pentyl)benzamido)ethyl)-3-methoxypropan-1-aminium chloride (d-27)



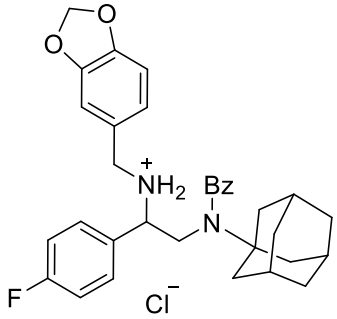
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-27** as a colorless oil (67.4 mg, 71% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.31 – 9.67 (m, 1H), 8.40 – 7.77 (m, 1H), 7.61 – 7.36 (m, 9H), 5.65 – 5.39 (m, 1H), 4.57 – 4.21 (m, 1H), 3.68 – 3.55 (m, 1H), 3.49 – 3.38 (m, 1H), 3.32 – 3.13 (m, 5H), 3.11 – 2.97 (m, 1H), 2.36 – 2.01 (m, 2H), 2.00 – 1.80 (m, 2H), 1.54 – 1.47 (m, 6H), 1.37 – 1.33 (m, 9H), 1.10 – 1.00 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.74, 152.21, 136.39, 133.58, 130.08, 128.66, 127.72, 126.73, 126.26, 71.68, 61.22, 59.97, 58.69, 49.26, 45.60, 34.73, 31.77, 31.31, 28.78, 23.06, 23.04, 8.17.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{28}H_{43}N_2O_2^+$ 439.3319, Found 439.3322

2-(N-((3s,5s,7s)-adamantan-1-yl)benzamido)-N-(benzo[d][1,3]dioxol-5-ylmethyl)-1-(4-fluorophenyl)ethan-1-aminium chloride (d-28)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-28** as a colorless oil (92.2 mg, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 – 9.77 (m, 1H), 8.65 – 8.19 (m, 1H), 7.72 – 7.52 (m, 2H), 7.47 – 7.38 (m, 3H), 7.38 – 7.31 (m, 2H), 6.99 – 6.87 (m, 2H), 6.57 – 6.50 (m, 1H), 6.47 – 6.37 (m, 1H), 6.32 – 6.19 (m, 1H), 5.89 – 5.76 (m, 2H), 5.54 – 5.41 (m, 1H), 4.77 – 4.54 (m, 2H), 4.19 – 4.08 (m, 1H), 3.53 – 3.37 (m, 1H), 2.20 – 2.14 (m, 3H), 2.13 – 2.07 (m, 3H), 2.06 – 2.04 (m, 2H), 2.03 – 2.00 (m, 1H), 1.75 – 1.60 (m,

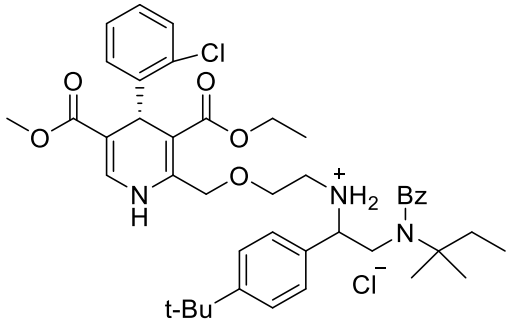
6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.05, 162.42 (d, *J* = 249.47 Hz), 147.65, 147.12, 136.10, 130.56, 130.52 (d, *J* = 8.1 Hz), 128.81, 127.21, 121.89, 115.56 (d, *J* = 21.2 Hz), 108.36, 108.12, 101.08, 60.21, 58.55, 54.97, 43.13, 38.71, 35.49, 29.07.

^{19}F NMR (376 MHz, $CDCl_3$) δ -118.28.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{33}H_{36}FN_2O_3^+$ 527.2704, Found 527.2708

1-(4-(tert-butyl)phenyl)-N-(2-(((S)-4-(2-chlorophenyl)-3-(ethoxycarbonyl)-5-(methoxycarbonyl)-1,4-dihydropyridin-2-yl)methoxy)ethyl)-2-(N-(tert-pentyl)benzamido)ethan-1-aminium chloride (d-29)



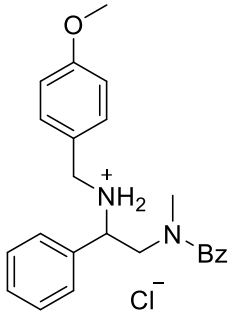
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 1:1, v/v) as eluent and protected by 1M HCl to afforded **d-29** as a colorless oil (101.3 mg, 65% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.38 – 9.83 (m, 1H), 8.98 – 8.35 (m, 1H), 7.55 – 7.34 (m, 10H), 7.27 – 7.19 (m, 1H), 7.14 – 6.98 (m, 2H), 5.78 – 5.51 (m, 1H), 5.51 – 5.33 (m, 1H), 4.78 – 4.13 (m, 3H), 4.09 – 3.96 (m, 2H), 3.80 – 3.31 (m, 8H), 2.57 – 2.43 (m, 3H), 1.99 – 1.85 (m, 2H), 1.55 – 1.43 (m, 6H), 1.36 – 1.31 (m, 9H), 1.20 – 1.13 (m, 3H), 1.11 – 1.02 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.48, 176.11, 168.20, 167.23, 167.10, 152.41, 146.23, 146.10, 144.01, 143.93, 135.86, 135.67, 133.14, 132.13, 131.46, 131.31, 130.29, 129.21, 128.90, 128.87, 128.01, 127.78, 127.38, 127.33, 127.07, 127.00, 126.79, 126.75, 126.39, 105.07, 104.46, 102.67, 102.49, 68.36, 67.17, 67.02, 60.95, 60.89, 60.62, 60.35, 59.91, 59.88, 50.77, 49.54, 49.02, 45.40, 45.17, 37.24, 37.15, 34.74, 31.83, 31.28, 31.24, 29.74, 23.17, 23.01, 19.35, 19.25, 14.28, 8.05.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{43}H_{55}ClN_3O_6^+$ 744.3774, Found 744.3779

N-(4-methoxybenzyl)-2-(N-methylbenzamido)-1-phenylethan-1-aminium chloride (d-30)



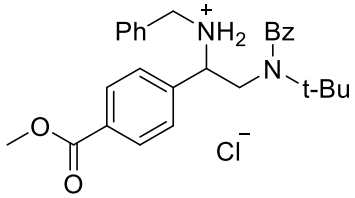
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-30** as a colorless oil (75.4 mg, 92% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 10.66 – 9.98 (m, 2H), 7.85 – 7.38 (m, 6H), 7.37 – 6.70 (m, 8H), 4.74 – 3.74 (m, 4.5H), 3.72 – 3.58 (m, 3H), 3.06 – 2.82 (m, 0.5H), 2.78 – 2.37 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.28, 160.19, 135.54, 132.70, 132.23, 129.83, 129.76, 129.42, 129.10, 128.35, 127.05, 121.93, 114.18, 58.74, 55.19, 51.74, 48.58, 40.05.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{24}H_{27}N_2O_2^+$ 375.2067, Found 375.2073

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-(methoxycarbonyl)phenyl)ethan-1-aminium chloride (d-31)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-31** as a colorless oil (69.1 mg, 72% yield).

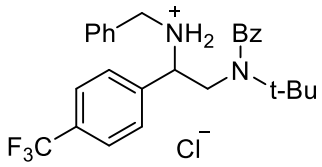
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 – 10.14 (m, 1H), 8.83 – 8.55 (m, 1H), 7.94 – 7.85 (m, 2H), 7.70 – 7.58 (m, 2H), 7.46 – 7.38 (m, 5H), 7.16 – 7.07 (m, 3H), 6.98 – 6.87 (m,

2H), 5.75 – 5.49 (m, 1H), 4.87 – 4.55 (m, 2H), 4.19 – 3.96 (m, 1H), 3.94 – 3.86 (m, 3H), 3.59 – 3.31 (m, 1H), 1.50 – 1.42 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.19, 166.51, 141.86, 135.92, 135.86, 130.36, 130.07, 129.97, 128.83, 128.68, 128.64, 128.20, 127.96, 127.23, 60.46, 58.15, 55.18, 52.31, 44.77, 26.13.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{28}H_{33}N_2O_3^+$ 445.2486, Found 445.2486

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-(trifluoromethyl)phenyl)ethan-1-aminium chloride (d-32)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-32** as a yellow oil (57.8 mg, 59% yield).

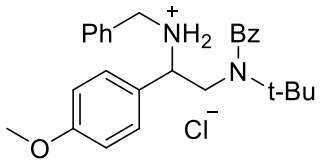
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 – 10.12 (m, 1H), 8.78 – 8.43 (m, 1H), 7.73 – 7.64 (m, 2H), 7.51 – 7.39 (m, 7H), 7.15 – 7.01 (m, 3H), 7.00 – 6.85 (m, 2H), 5.72 – 5.42 (m, 1H), 4.93 – 4.62 (m, 2H), 4.36 – 4.01 (m, 1H), 3.63 – 3.25 (m, 1H), 1.52 – 1.45 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) 175.10, 141.07, 135.88, 130.36 (q, J = 32.3 Hz), 128.56（q, J = 273.7 Hz）, 129.05, 128.85, 128.58, 128.18, 127.93, 127.80, 127.27, 125.56, 125.52, 60.52, 58.20, 55.48, 44.69, 26.13.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.79.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{27}H_{30}F_3N_2O^+$ 455.2305, Found 455.2304

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-methoxyphenyl)ethan-1-aminium chloride (d-33)



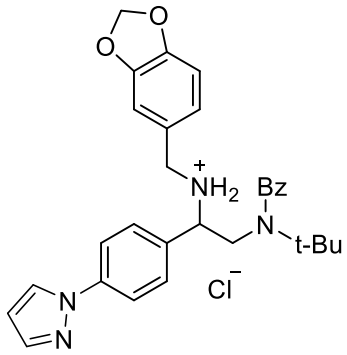
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-33** as a colorless oil (64.2 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 – 9.79 (m, 1H), 8.86 – 8.53 (m, 1H), 7.75 – 7.57 (m, 2H), 7.48 – 7.34 (m, 3H), 7.28 – 7.13 (m, 4H), 6.92 – 6.75 (m, 2H), 6.71 – 6.56 (m, 2H), 5.59 – 5.38 (m, 1H), 4.76 – 4.45 (m, 2H), 4.18 – 3.95 (m, 1H), 3.77 – 3.63 (m, 3H), 3.54 – 3.35 (m, 1H), 1.48 – 1.40 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.95, 159.26, 135.95, 135.44, 134.24, 130.29, 130.10, 129.57, 128.81, 128.77, 127.85, 127.24, 114.03, 59.91, 58.22, 55.36, 54.47, 44.73, 26.06.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{27}H_{33}N_2O_2^+$ 417.2537, Found 417.2538

1-(4-(1H-pyrazol-1-yl)phenyl)-N-benzyl-2-(N-(tert-butyl)benzamido)ethan-1-aminium chloride (d-34)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 2:1, v/v) as eluent and protected by 1M HCl to afforded **d-34** as a colorless oil (86.1 mg, 81% yield).

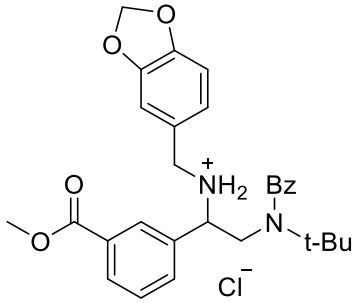
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 – 9.71 (m, 1H), 9.01 – 8.82 (m, 1H), 8.00 – 7.87 (m, 1H), 7.77 – 7.69 (m, 1H), 7.65 – 7.54 (m, 4H), 7.51 – 7.36 (m, 5H), 6.63 – 6.44 (m, 3H), 6.42 – 6.29 (m, 1H), 5.85 – 5.71 (m, 2H), 5.64 – 5.47 (m, 1H), 4.72 – 4.47 (m, 2H), 4.31 – 4.14 (m, 1H), 4.13 – 3.88 (m, 1H), 3.64 – 3.51 (m, 1H), 1.56 – 1.39 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.68, 147.74, 147.22, 141.02, 139.53, 136.04, 135.21, 130.23, 130.10, 128.79, 127.34, 127.18, 121.89, 119.28, 108.41, 108.25, 108.09, 108.02,

101.09, 59.82, 58.26, 54.62, 44.68, 26.01.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{30}H_{33}N_4O_3^+$ 497.2547, Found 497.2546

N-(benzo[d][1,3]dioxol-5-ylmethyl)-2-(N-(tert-butyl)benzamido)-1-(3-(methoxycarbonyl)phenyl)ethan-1-aminium chloride (d-35)



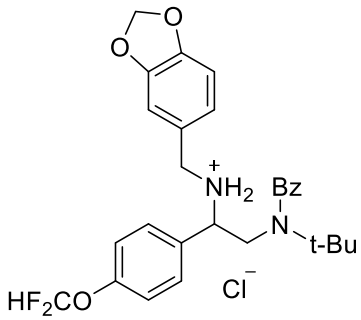
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-35** as a colorless oil (57.7 mg, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 – 9.48 (m, 1H), 8.94 – 8.41 (m, 1H), 7.92 – 7.85 (m, 1H), 7.81 – 7.75 (m, 1H), 7.71 – 7.58 (m, 3H), 7.46 – 7.39 (m, 3H), 7.39 – 7.32 (m, 1H), 6.59 – 6.37 (m, 2H), 6.35 – 6.14 (m, 1H), 5.86 – 5.71 (m, 2H), 5.66 – 5.47 (m, 1H), 4.80 – 4.46 (m, 2H), 4.17 – 4.05 (m, 1H), 3.93 – 3.86 (m, 3H), 3.61 – 3.44 (m, 1H), 1.57 – 1.41 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.12, 166.47, 147.73, 147.24, 137.22, 135.82, 133.40, 130.35, 130.25, 129.57, 129.47, 129.06, 128.84, 127.28, 122.05, 108.38, 108.21, 101.14, 59.86, 58.43, 54.70, 52.36, 44.91, 26.20.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{29}H_{33}N_2O_5^+$ 489.2384, Found 489.2389

N-(benzo[d][1,3]dioxol-5-ylmethyl)-2-(N-(tert-butyl)benzamido)-1-(4-(difluoromethoxy)phenyl)ethan-1-aminium chloride (d-36)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-36** as a yellow oil (64.9 mg, 61% yield).

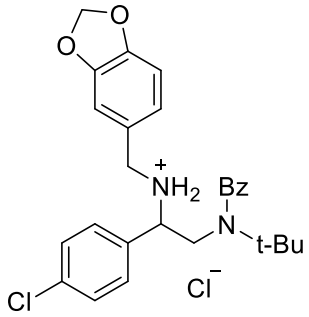
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 – 9.66 (m, 1H), 8.95 – 8.47 (m, 1H), 7.71 – 7.62 (m, 2H), 7.46 – 7.32 (m, 5H), 7.08 – 6.86 (m, 2H), 6.58 – 6.52 (m, 1H), 6.51 – 6.17 (m, 3H), 5.87 – 5.74 (m, 2H), 5.61 – 5.38 (m, 1H), 4.86 – 4.57 (m, 2H), 4.27 – 4.05 (m, 1H), 3.74 – 3.61 (m, 0.5H), 3.55 – 3.38 (m, 1H), 3.34 – 3.08 (m, 0.5H), 1.61 – 1.38 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.96, 150.90, 147.65, 147.13, 136.01, 134.43, 130.31, 129.77, 128.83, 127.25, 121.90, 119.58, 118.38, 115.79 (t, J = 261.59), 113.20, 108.36, 108.14, 101.11, 60.00, 58.16, 54.96, 44.91, 26.15.

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.96, -80.99, -81.16, -81.18.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{28}H_{31}F_2N_2O_4^+$ 497.2246, Found 497.2245

N-(benzo[d][1,3]dioxol-5-ylmethyl)-2-(N-(tert-butyl)benzamido)-1-(4-chlorophenyl)ethan-1-aminium chloride (d-37)



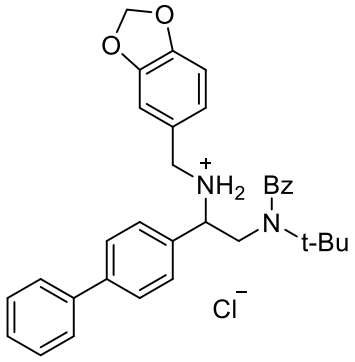
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-37** as a colorless oil (79 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 – 9.79 (m, 1H), 8.74 – 8.42 (m, 1H), 7.70 – 7.57 (m, 2H), 7.46 – 7.37 (m, 3H), 7.33 – 7.26 (m, 2H), 7.24 – 7.17 (m, 2H), 6.62 – 6.51 (m, 1H), 6.51 – 6.35 (m, 1H), 6.35 – 6.19 (m, 1H), 5.91 – 5.75 (m, 2H), 5.56 – 5.36 (m, 1H), 4.75 – 4.50 (m, 2H), 4.25 – 4.03 (m, 1H), 3.57 – 3.37 (m, 1H), 1.55 – 1.38 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.96, 147.71, 147.23, 135.93, 135.67, 134.23, 130.36, 130.10, 129.64, 128.84, 128.79, 127.26, 121.92, 108.40, 108.21, 101.16, 60.01, 58.34, 54.98, 44.85, 26.16.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{27}H_{30}ClN_2O_3^+$ 465.1939, Found 465.1933

1-([1,1'-biphenyl]-4-yl)-N-benzyl-2-(N-(tert-butyl)benzamido)ethan-1-aminium chloride (d-38)



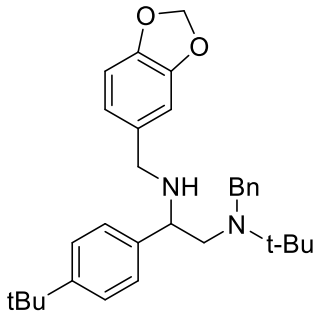
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-38** as a colorless oil (63.9 mg, 59% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.10 – 9.71 (m, 1H), 9.01 – 8.67 (m, 1H), 7.69 – 7.50 (m, 5H), 7.49 – 7.43 (m, 3H), 7.43 – 7.31 (m, 6H), 6.65 – 6.38 (m, 2H), 6.38 – 6.15 (m, 1H), 5.96 – 5.69 (m, 1.8H), 5.69 – 5.23 (m, 1H), 4.72 – 4.52 (m, 1.79H), 4.22 – 3.92 (m, 1.21H), 3.70 – 3.50 (m, 1H), 1.63 – 1.31 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.34, 147.64, 147.09, 141.40, 140.24, 135.97, 135.69, 130.31, 129.77, 129.11, 128.91, 128.81, 127.69, 127.42, 127.28, 127.07, 121.81, 108.38, 108.18, 101.06, 60.04, 58.22, 54.36, 45.09, 26.18.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{33}H_{35}N_2O_3^+$ 507.2642, Found 507.2646

N-(benzo[d][1,3]dioxol-5-ylmethyl)-2-(N-(tert-butyl)benzamido)-1-(4-(tert-butyl)phenyl)ethan-1-aminium chloride (d-39)



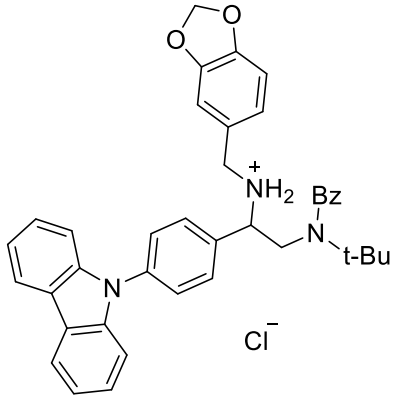
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-39** as a colorless oil (81.4 mg, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.32 (m, 6H), 7.32 – 7.20 (m, 3H), 6.97 (d, *J* = 1.4 Hz, 1H), 6.90 – 6.67 (m, 2H), 5.98 (s, 2H), 3.97 – 3.89 (m, 1.8H), 3.84 – 3.72 (m, 1.2H), 3.31 (dd, *J* = 11.3, 9.6 Hz, 1H), 3.16 (dd, *J* = 17.7, 13.6 Hz, 2H), 2.79 (dd, *J* = 11.3, 5.3 Hz, 1H), 1.41 (s, 10H), 1.13 (s, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.25, 147.83, 146.57, 140.21, 134.15, 134.04, 128.89, 128.87, 128.46, 126.98, 125.04, 121.98, 109.19, 108.01, 100.88, 62.07, 53.66, 53.63, 50.19, 43.29, 34.61, 31.48, 29.07.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{31}H_{41}N_2O_2^+$ 473.3163, Found 473.3166

1-(4-(9H-carbazol-9-yl)phenyl)-N-(benzo[d][1,3]dioxol-5-ylmethyl)-2-(N-(tert-butyl)benzamido)ethan-1-aminium chloride (d-40)



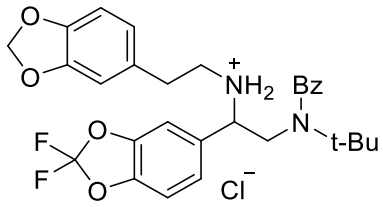
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-40** as a yellow oil (51.8 mg, 41% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 8.59 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 2H), 7.87 – 7.75 (m, 2H), 7.62 (d, *J* = 7.9 Hz, 2H), 7.54 – 7.36 (m, 9H), 7.35 – 7.27 (m, 2H), 6.56 (s, 2H), 6.40 (s, 1H), 5.78 – 5.73 (m, 1H), 5.70 (dd, *J* = 13.7, 5.4 Hz, 2H), 5.03 – 4.71 (m, 2H), 4.52 (d, *J* = 18.4 Hz, 1H), 3.57 (s, 1H), 1.60 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.25, 147.65, 147.15, 140.62, 137.58, 136.71, 136.16, 130.37, 130.15, 129.93, 128.90, 127.40, 126.99, 126.03, 123.47, 122.09, 120.40, 120.20, 109.71, 108.52, 108.08, 101.04, 60.80, 58.34, 55.57, 45.03, 26.28.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{39}H_{38}N_3O_3^+$ 596.2908, Found 596.2911

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)ethan-1-aminium chloride (d-41)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-41** as a colorless oil (85.4 mg, 85% yield).

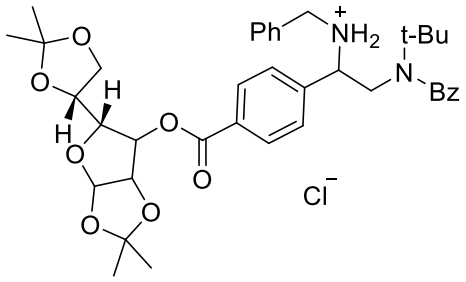
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 – 9.77 (m, 1H), 8.90 – 8.43 (m, 1H), 7.60 – 7.52 (m, 2H), 7.52 – 7.42 (m, 4H), 7.42 – 7.33 (m, 1H), 7.18 – 7.08 (m, 1H), 6.61 – 6.48 (m, 1H), 6.24 – 6.14 (m, 1H), 6.14 – 6.04 (m, 1H), 5.89 – 5.82 (m, 2H), 5.74 – 5.60 (m, 1H), 4.29 – 4.13 (m, 1H), 3.77 – 3.58 (m, 1H), 3.56 – 3.35 (m, 2H), 2.66 – 2.53 (m, 1H), 2.53 – 2.40 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.28, 147.56, 146.20, 144.39, 144.02, 136.04, 133.92, 131.71 (t, *J* = 258.56 Hz), 131.07, 130.37, 128.74, 126.76, 123.96, 121.64, 110.01, 109.62, 108.93, 108.24, 100.87, 60.29, 58.25, 52.99, 45.48, 35.29, 26.18.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.73, -49.74.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{27}H_{29}F_2N_2O_3^+$ 467.2141, Found 467.2146

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-((((5R)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-6-yl)oxy)carbonyl)phenyl)ethan-1-aminium chloride (d-42)



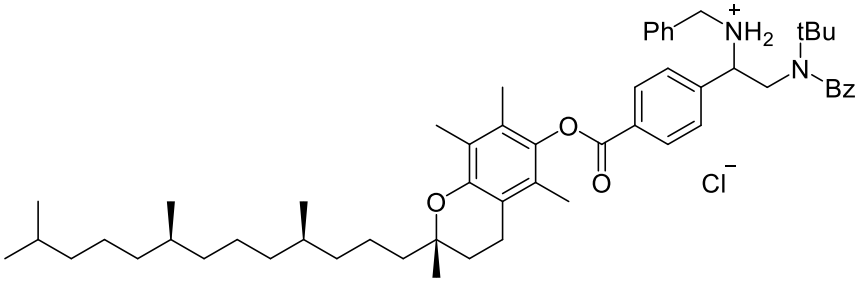
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-42** as a white solid (93.5 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 – 8.52 (m, 2H), 8.06 – 7.81 (m, 2H), 7.73 – 7.59 (m, 2H), 7.48 – 7.34 (m, 5H), 7.17 – 6.83 (m, 5H), 5.68 – 5.43 (m, 2H), 4.84 – 4.61 (m, 3H), 4.55 – 4.48 (m, 1H), 4.48 – 4.39 (m, 1H), 4.39 – 4.30 (m, 2H), 4.22 – 3.94 (m, 2H), 3.57 – 3.35 (m, 1H), 1.55 – 1.52 (m, 3H), 1.50 – 1.41 (m, 12H), 1.38 – 1.34 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.16, 165.82, 141.98, 135.95, 135.85, 130.33, 130.09, 129.99, 128.81, 128.67, 128.64, 128.23, 127.94, 127.26, 109.75, 108.86, 96.35, 71.17, 70.77, 70.55, 66.16, 64.11, 60.57, 58.17, 44.88, 26.18, 26.13, 26.03, 25.05, 24.55.

HRMS (ESI) m/z: $[M\text{-}Cl]^+$ Calcd for $C_{39}H_{49}N_2O_8^+$ 673.3483, Found 673.3488

N-benzyl-2-(N-(tert-butyl)benzamido)-1-(4-((((S)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)carbonyl)phenyl)ethan-1-aminium chloride (d-43)



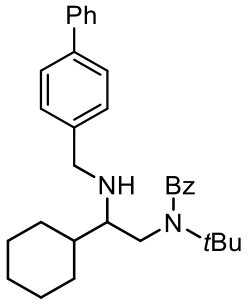
Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-43** as a grey solid (107.2 mg, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 – 10.09 (m, 1H), 8.92 – 8.59 (m, 1H), 8.14 – 8.08 (m, 2H), 7.73 – 7.67 (m, 2H), 7.55 – 7.48 (m, 2H), 7.47 – 7.42 (m, 3H), 7.17 – 7.09 (m, 3H), 7.03 – 6.94 (m, 2H), 5.86 – 5.55 (m, 1H), 4.94 – 4.69 (m, 2H), 4.28 – 4.03 (m, 1H), 3.66 – 3.42 (m, 1H), 2.69 – 2.61 (m, 2H), 2.17 – 2.14 (m, 3H), 2.08 – 2.06 (m, 3H), 2.04 – 2.02 (m, 3H), 1.90 – 1.75 (m, 2H), 1.61 – 1.43 (m, 16H), 1.33 – 1.27 (m, 11H), 1.21 – 1.09 (m, 6H), 0.92 – 0.88 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.34, 164.61, 149.60, 142.40, 140.57, 135.91, 130.52, 130.42, 129.59, 128.90, 128.86, 128.65, 128.23, 127.93, 127.28, 126.81, 125.06, 123.24, 117.58, 77.45, 77.13, 76.81, 75.18, 60.52, 58.17, 44.84, 39.43, 37.47, 37.34, 32.84, 32.78, 31.71, 31.49, 28.04, 26.17, 24.87, 24.51, 24.26, 23.74, 22.79, 22.70, 21.11, 20.70, 19.83, 19.76, 13.08, 12.24, 11.92.

HRMS (ESI) m/z: $[M-Cl]^+$ Calcd for $C_{56}H_{79}N_2O_4^+$ 843.6034, Found 843.6033

N-(2-(([1,1'-biphenyl]-4-ylmethyl)amino)-2-cyclohexylethyl)-N-(tert-butyl)benzamide (d-44)



Following General Procedure A, Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-44** as a brown oil (70.35 mg, 75% yield).

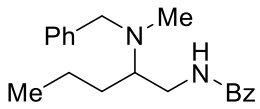
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 – 7.63 (m, 2H), 7.63 – 7.51 (m, 6H), 7.50-7.27 (m, 6H), 5.50 – 4.83 (m, 1H), 4.17 – 4.07 (m, 1H), 3.83 – 2.24 (m, 4H), 2.06 – 1.43 (m, 6H), 1.41 – 0.93 (m, 8H), 0.85-0.65 (m, 6H).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{32}H_{41}N_2O^+$ 469.3213, Found 469.3211

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.57, 174.50, 141.96, 141.02, 140.34, 139.88, 138.51, 137.29, 135.69, 134.58, 130.51, 129.34, 129.10, 129.04, 128.84, 128.72, 128.47, 128.17, 128.00, 127.94, 127.43, 127.30, 127.13, 126.99, 77.00, 66.18, 64.52, 49.77, 43.82, 42.21, 42.03, 39.30, 32.29, 30.73, 30.14, 28.68, 26.51, 26.21, 26.12, 26.02, 25.96, 25.67, 18.49.

HRMS (ESI) m/z: [M+H]+ Calcd for $C_{32}H_{41}N_2O^+$ 469.3213, Found 469.3213

N-(2-(benzyl(methyl)amino)pentyl)benzamide (d-45)



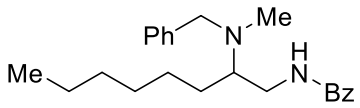
Following General Procedure B Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-45** as a colorless oil (52.7 mg, 85% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (t, *J* = 5.6 Hz, 1H), 8.21 (s, 1H), 7.92 – 7.82 (m, 2H), 7.61 – 7.47 (m, 3H), 7.34 – 7.17 (m, 5H), 3.67 (s, 2H), 3.56 – 3.45 (m, 1H), 3.26 (dt, *J* = 12.9, 6.0 Hz, 1H), 2.86 (p, *J* = 6.7 Hz, 1H), 2.18 (s, 3H), 1.58 – 1.33 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, DMSO) δ 166.52, 140.85, 135.29, 131.51, 128.78, 128.76, 128.54, 127.61, 127.10, 61.61, 58.04, 36.50, 31.16, 20.26, 14.64.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{27}N_2O^+$ 311.2118, Found 311.2112

N-(2-(benzyl(methyl)amino)octyl)benzamide (d-46)



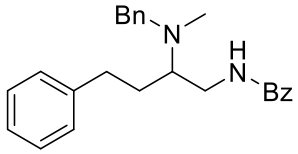
Following General Procedure B Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-46** as a yellow oil (37.4 mg, 53% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.3 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.48 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.32 (dd, *J* = 13.3, 4.0 Hz, 6H), 3.91 – 3.70 (m, 2H), 3.60 (d, *J* = 13.2 Hz, 1H), 3.16 – 3.02 (m, 1H), 2.80 (s, 1H), 2.29 (s, 3H), 1.52 – 1.26 (m, 10H), 0.95 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.19, 134.84, 131.30, 128.88, 128.53, 128.52, 127.33, 127.30, 127.00, 61.01, 58.27, 40.30, 35.87, 31.80, 29.66, 27.08, 25.65, 22.68, 14.16, 1.09.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{33}N_2O^+$ 353.2587, Found 353.2588

N-(2-(benzyl(methyl)amino)-4-phenylbutyl)benzamide (d-47)



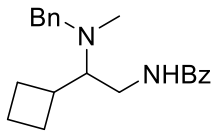
Following General Procedure B Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-47** as a yellow oil (38.7 mg, 52% yield).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.37 (t, *J* = 5.6 Hz, 1H), 7.92 – 7.82 (m, 2H), 7.61 – 7.47 (m, 3H), 7.34 – 7.17 (m, 5H), 3.67 (s, 2H), 3.56 – 3.45 (m, 1H), 3.26 (dt, *J* = 12.9, 6.0 Hz, 1H), 2.86 (p, *J* = 6.7 Hz, 1H), 2.18 (s, 3H), 1.58 – 1.33 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, DMSO) δ 166.52, 140.85, 135.29, 131.51, 128.78, 128.76, 128.54, 127.61, 127.10, 61.61, 58.04, 36.50, 31.16, 20.26, 14.64.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{29}N_2O^+$ 373.2274, Found373.2277

N-(2-(benzyl(methyl)amino)-2-cyclobutylethyl)benzamide (d-48)



Following General Procedure B Purification by column chromatography using pre-basified silica with pentane/EtOAc (10:1 to 3:1, v/v) as eluent and protected by 1M HCl to afforded **d-48** as a yellow oil (28.9 mg, 45% yield).

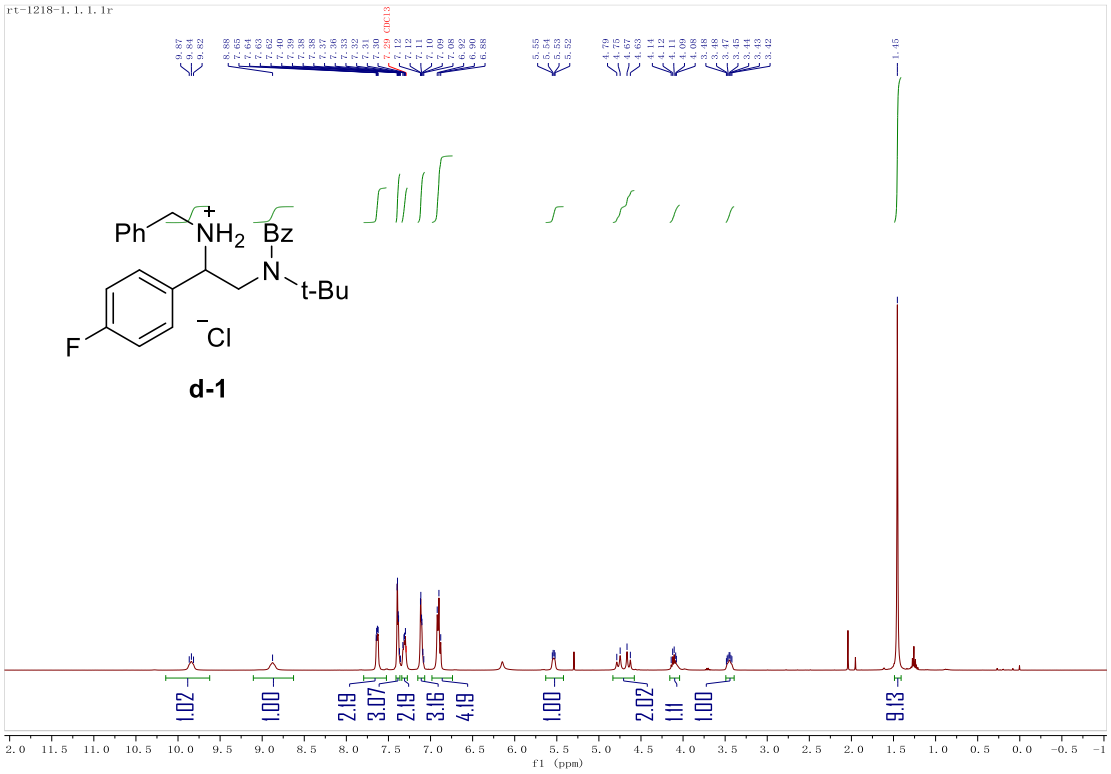
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.39 (m, 5H), 7.30 (dq, *J* = 9.2, 3.4 Hz, 5H), 7.07 (s, 1H), 3.85 – 3.58 (m, 3H), 3.10 – 2.90 (m, 1H), 2.90 – 2.63 (m, 2H), 2.35 – 2.14 (m, 4H), 2.14 – 1.74 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.20, 139.96, 134.90, 131.30, 128.73, 128.55, 128.51, 127.20, 126.97, 66.54, 59.45, 38.31, 36.42, 35.32, 29.33, 27.32, 19.72, 1.11.

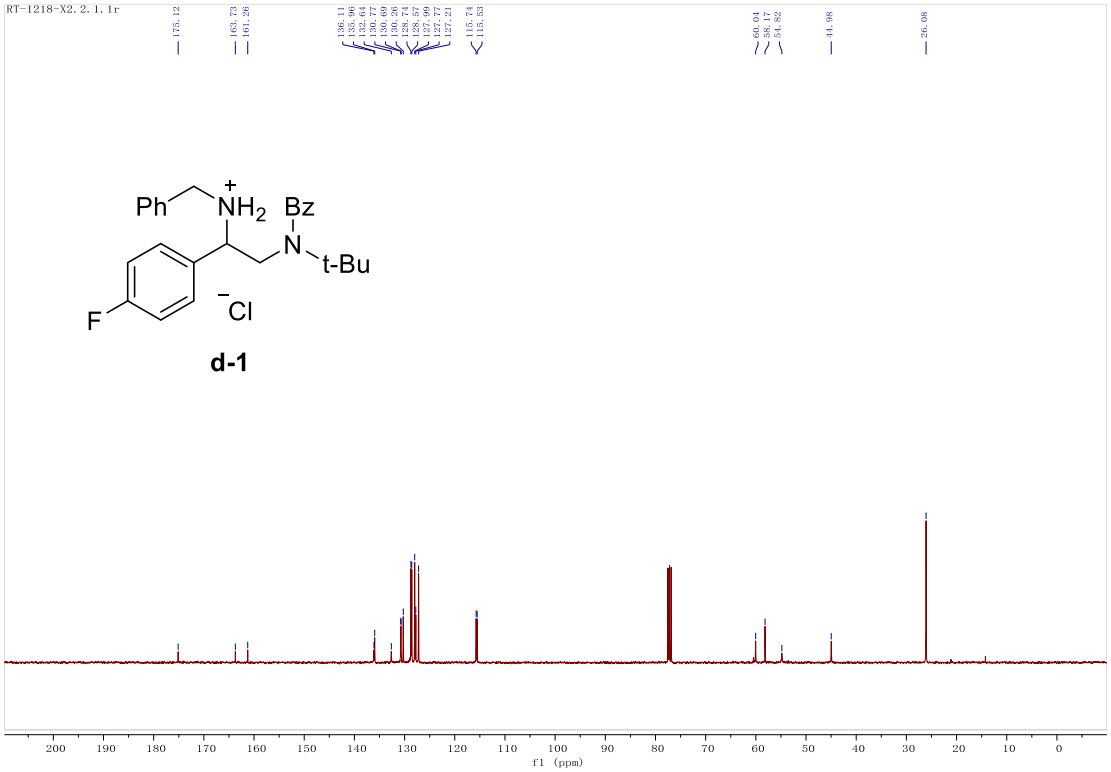
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{27}N_2O^+$ 323.2118, Found 323.2125

3. NMR Spectra for the Products

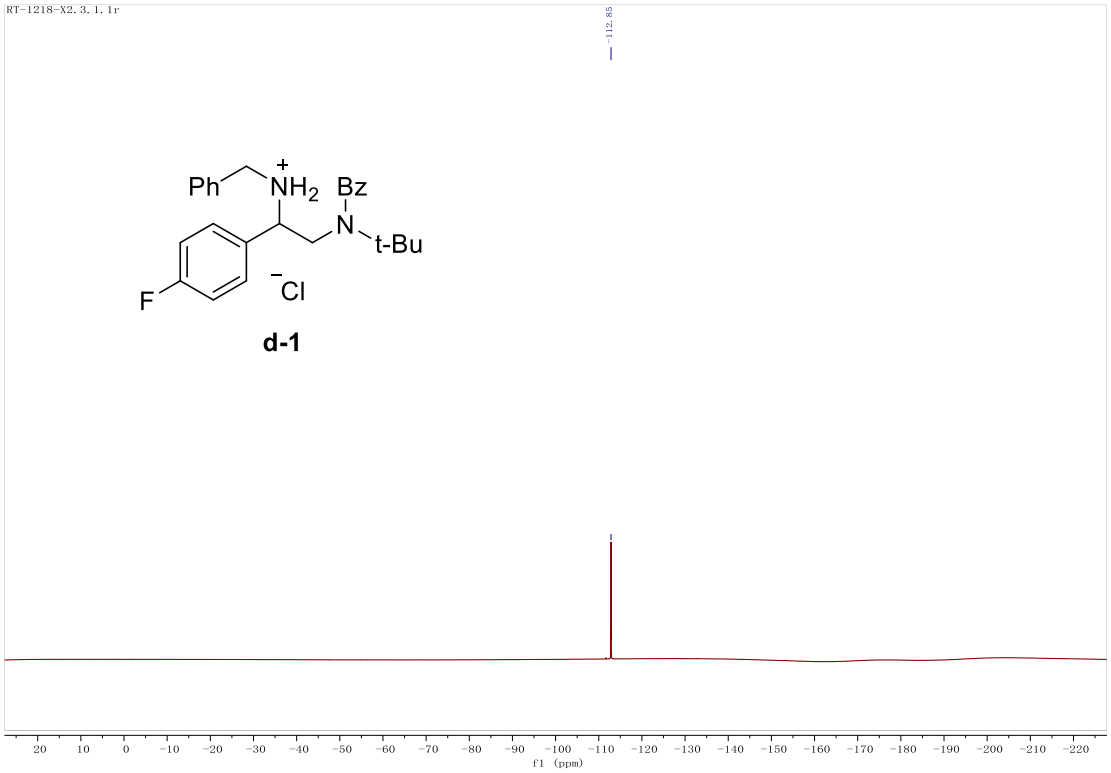
d-1 ^{1}H NMR (400 MHz)



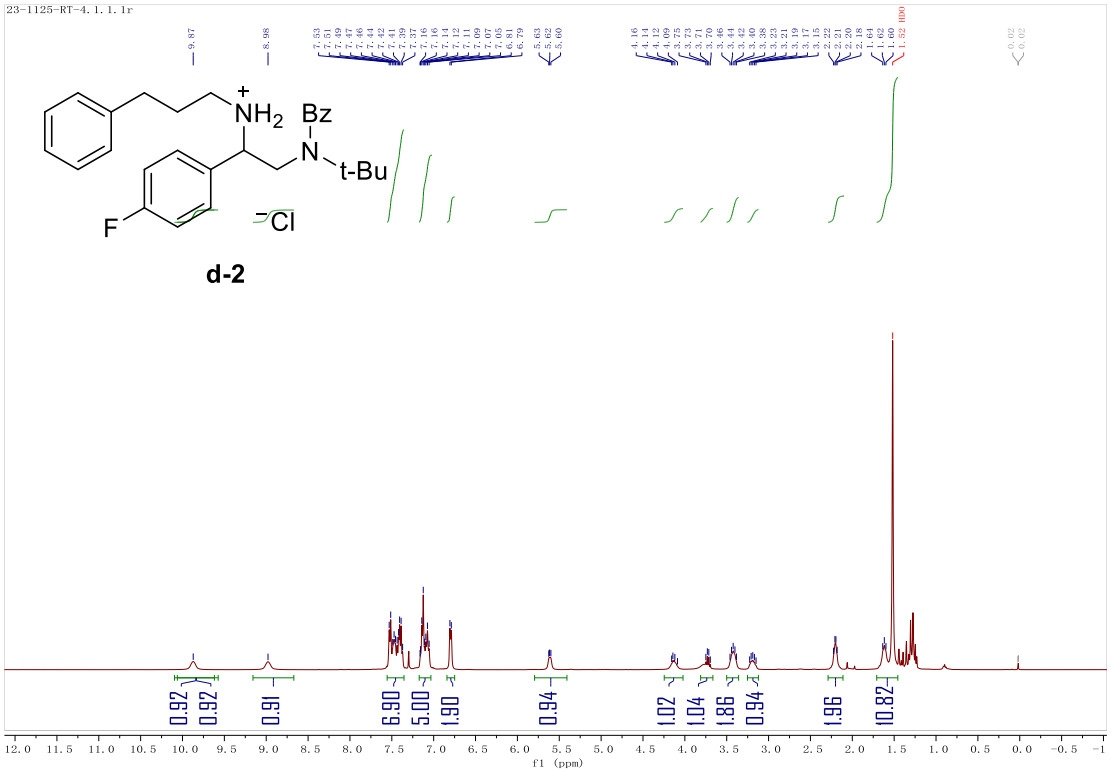
^{13}C NMR (101 MHz)



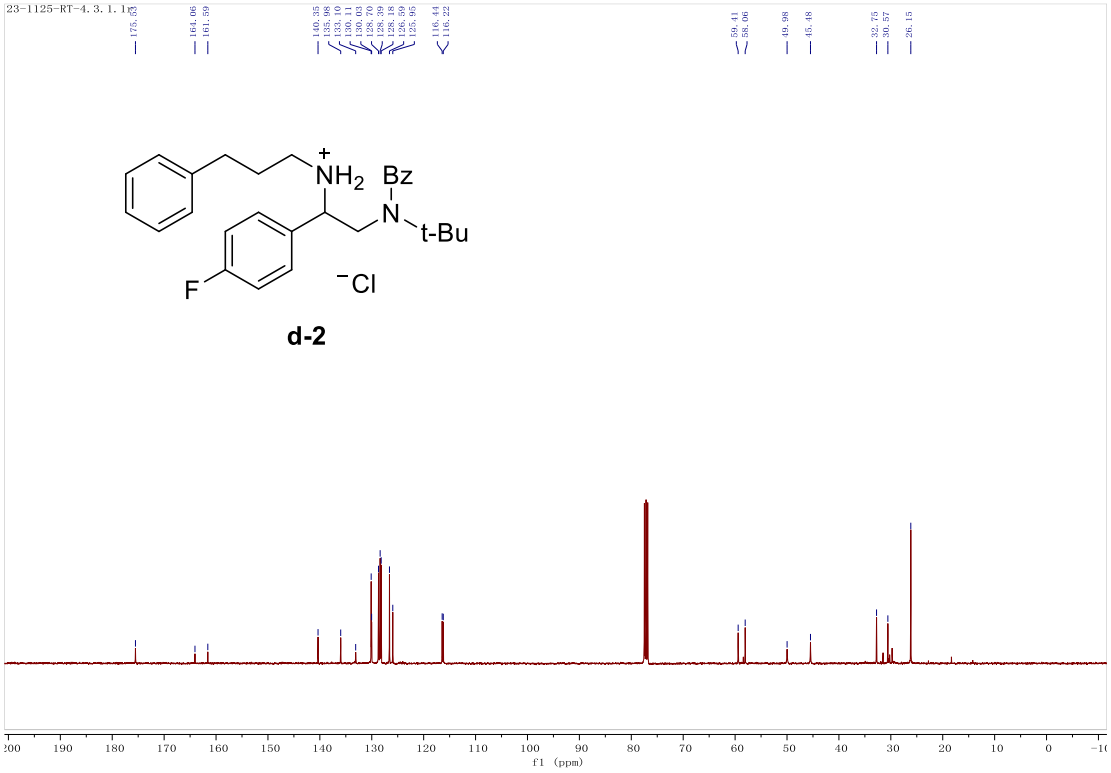
^{19}F NMR (376 MHz)



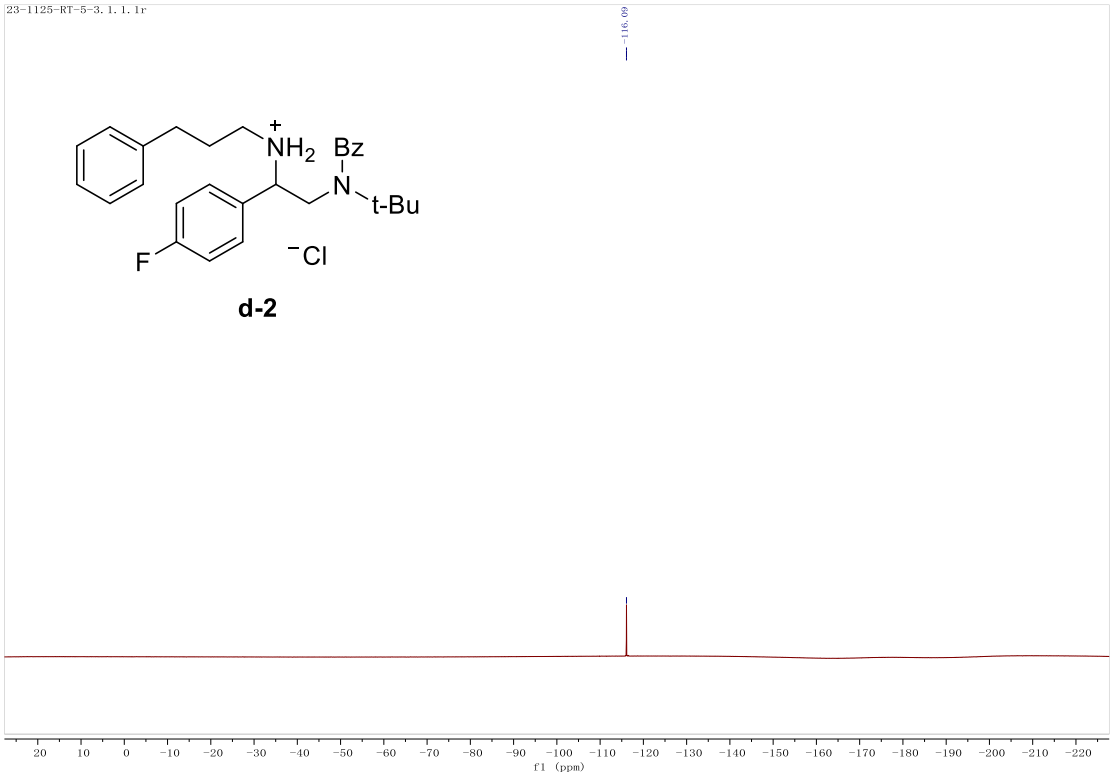
d-2 ^{1}H NMR (400 MHz)



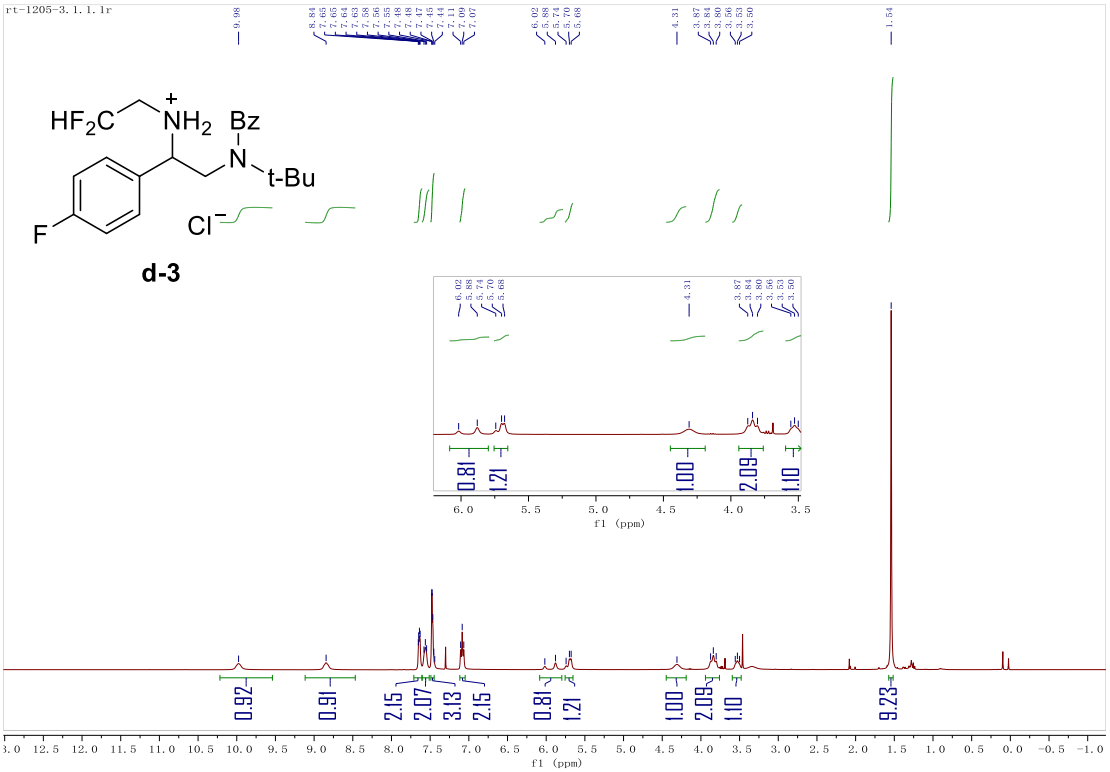
^{13}C NMR (101 MHz)



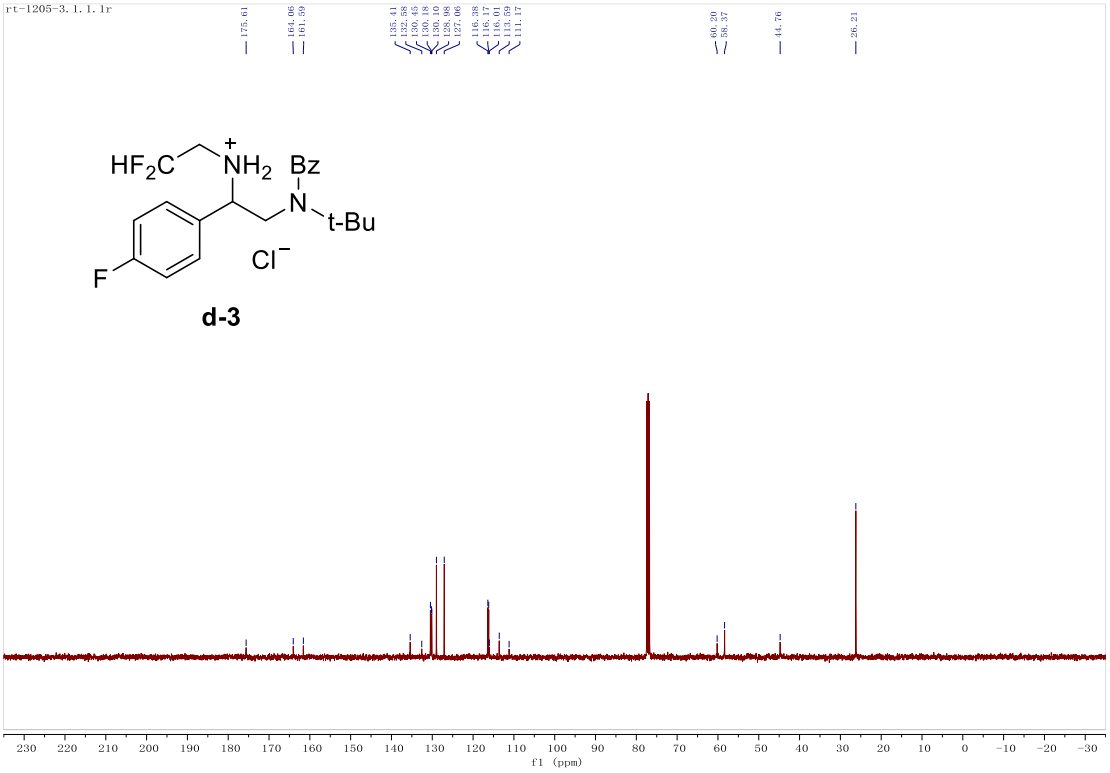
^{19}F NMR (376 MHz)



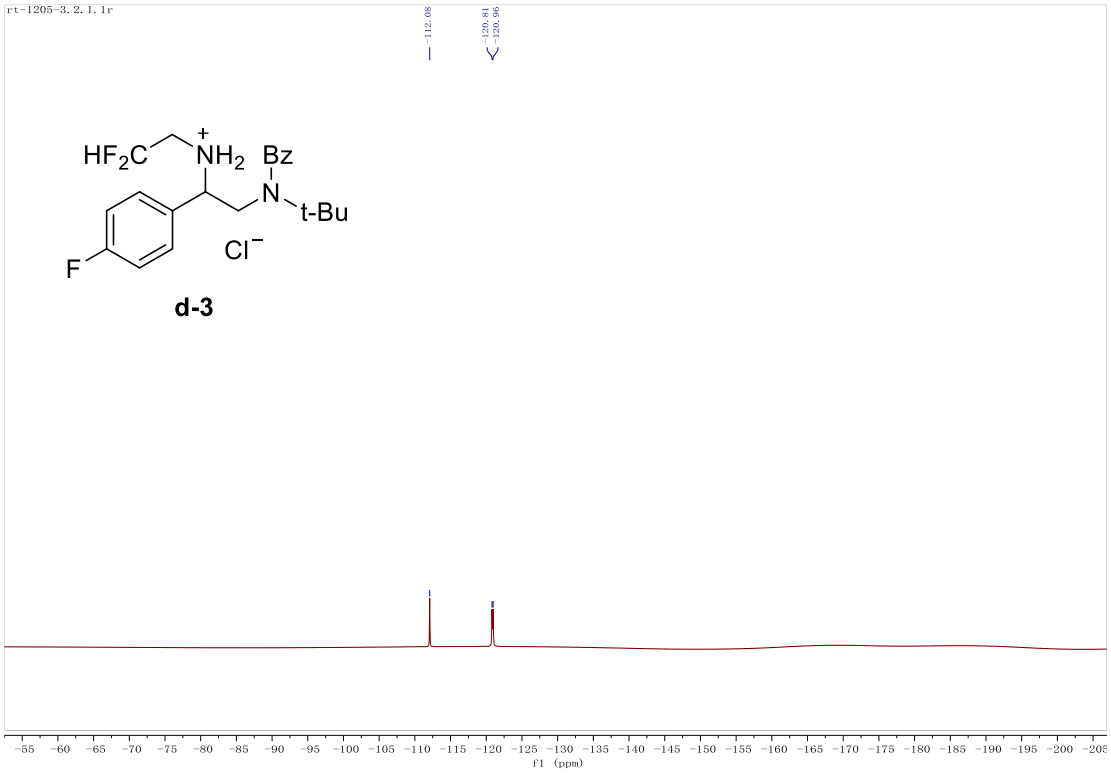
d-3 ^{1}H NMR (400 MHz)



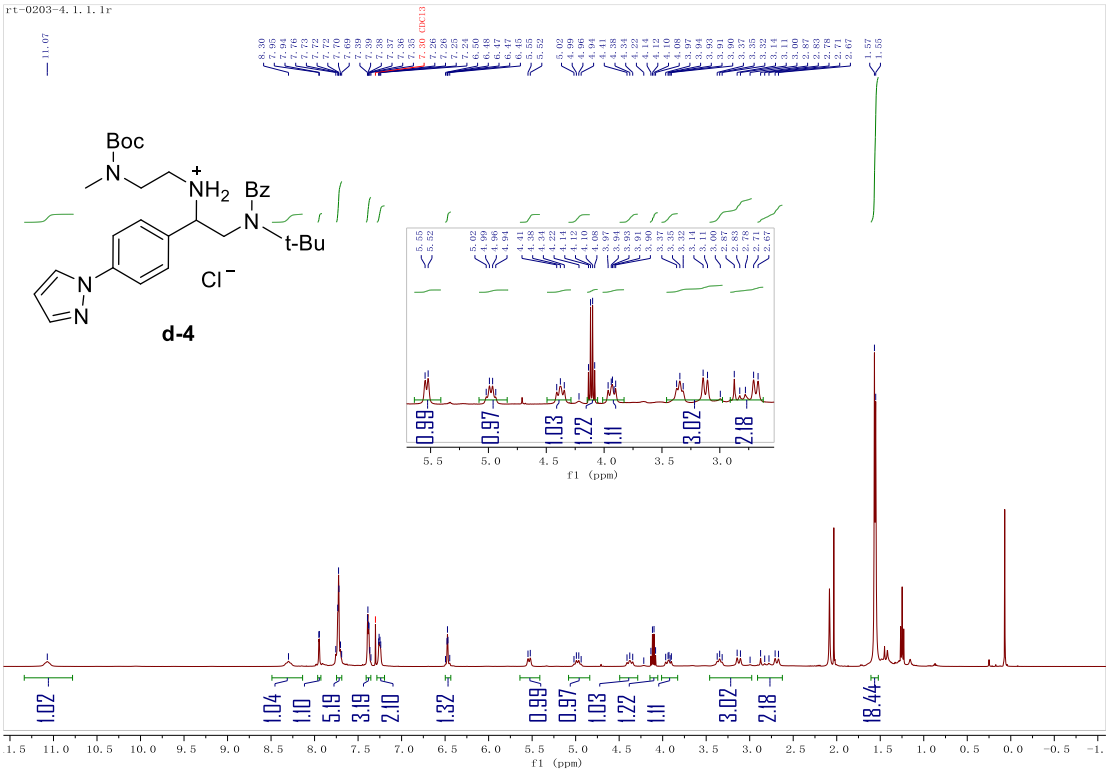
^{13}C NMR (101 MHz)



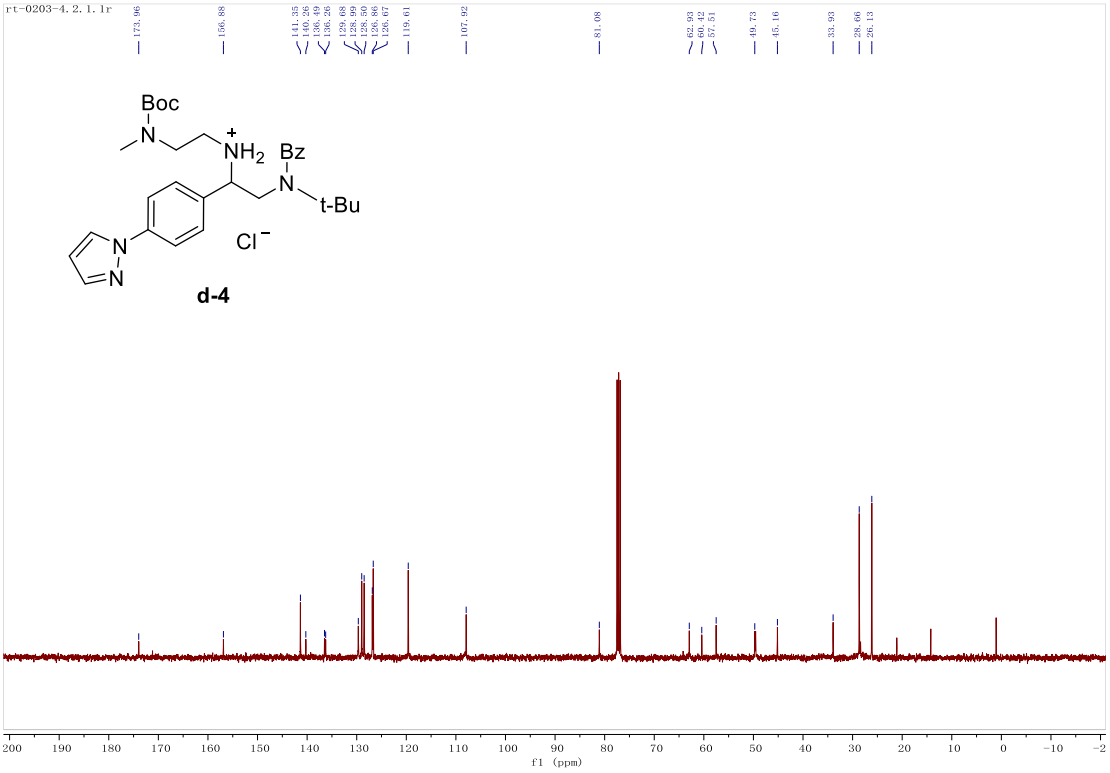
^{19}F NMR (376 MHz)



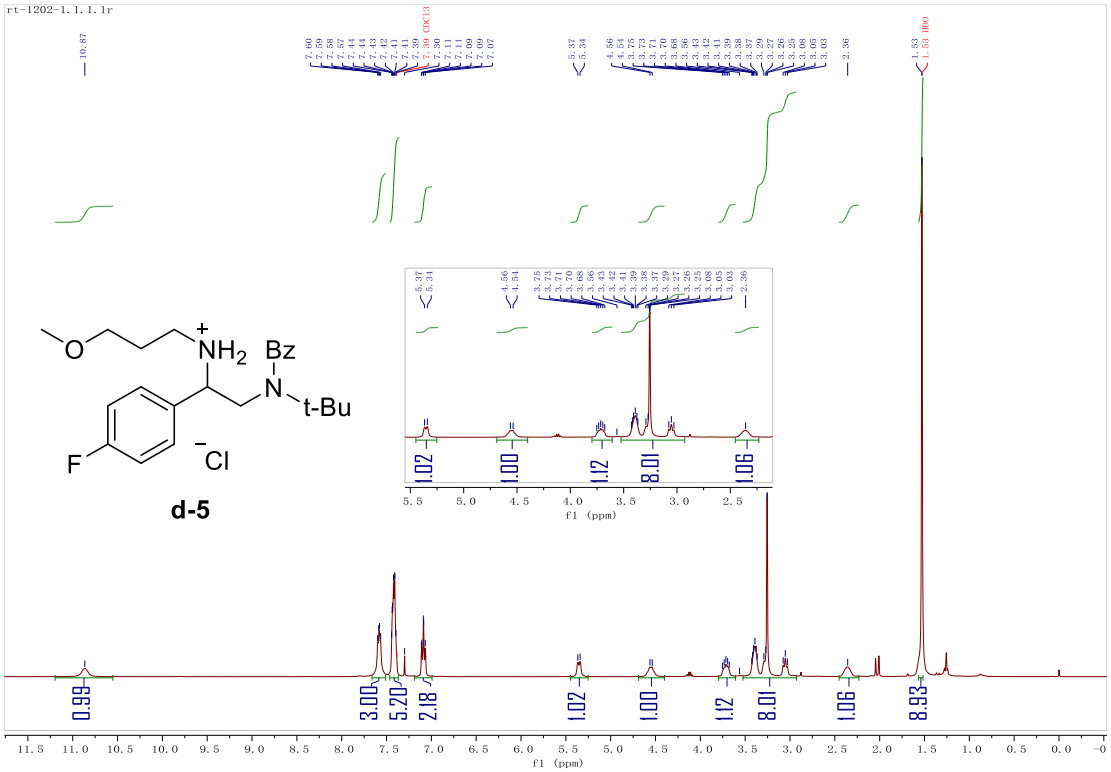
d-4 ^{1}H NMR (400 MHz)



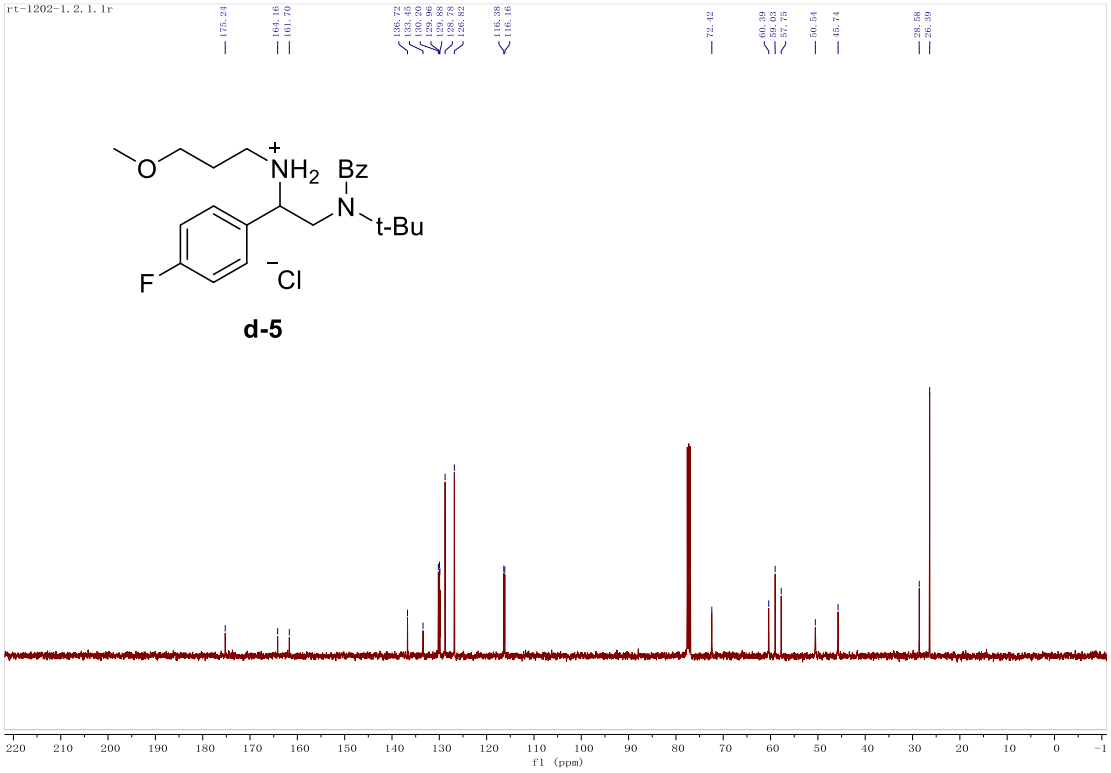
^{13}C NMR (101 MHz)



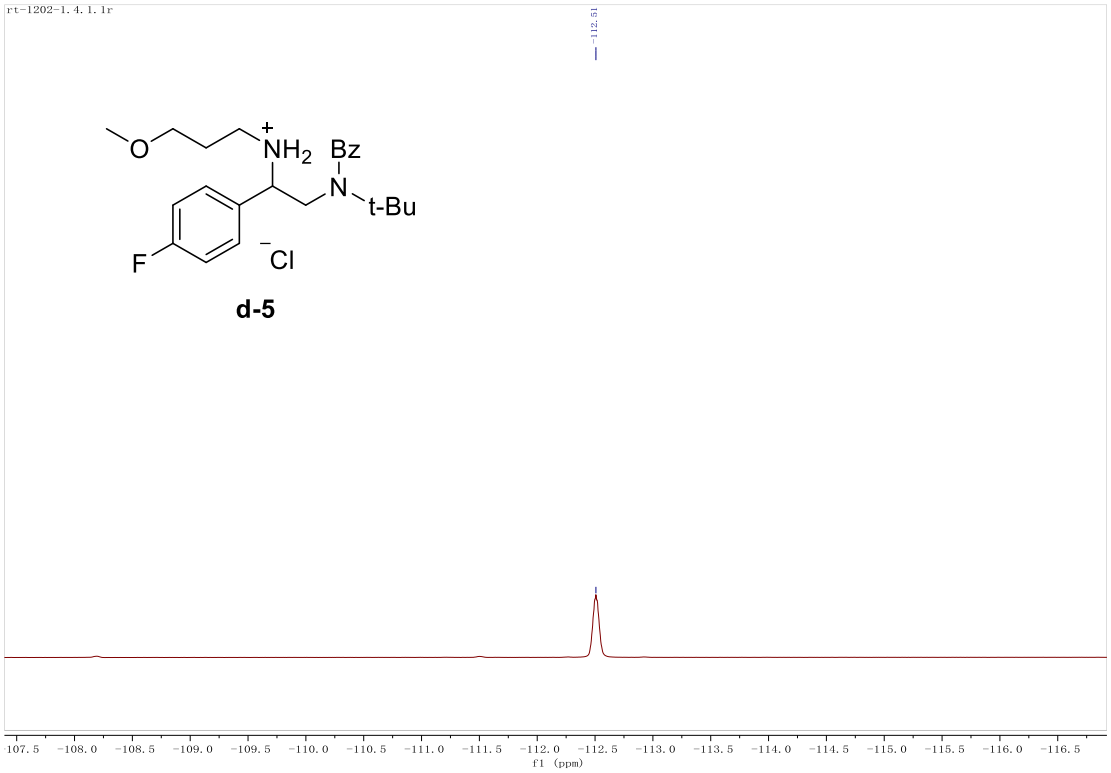
d-5 ^{1}H NMR (400 MHz)



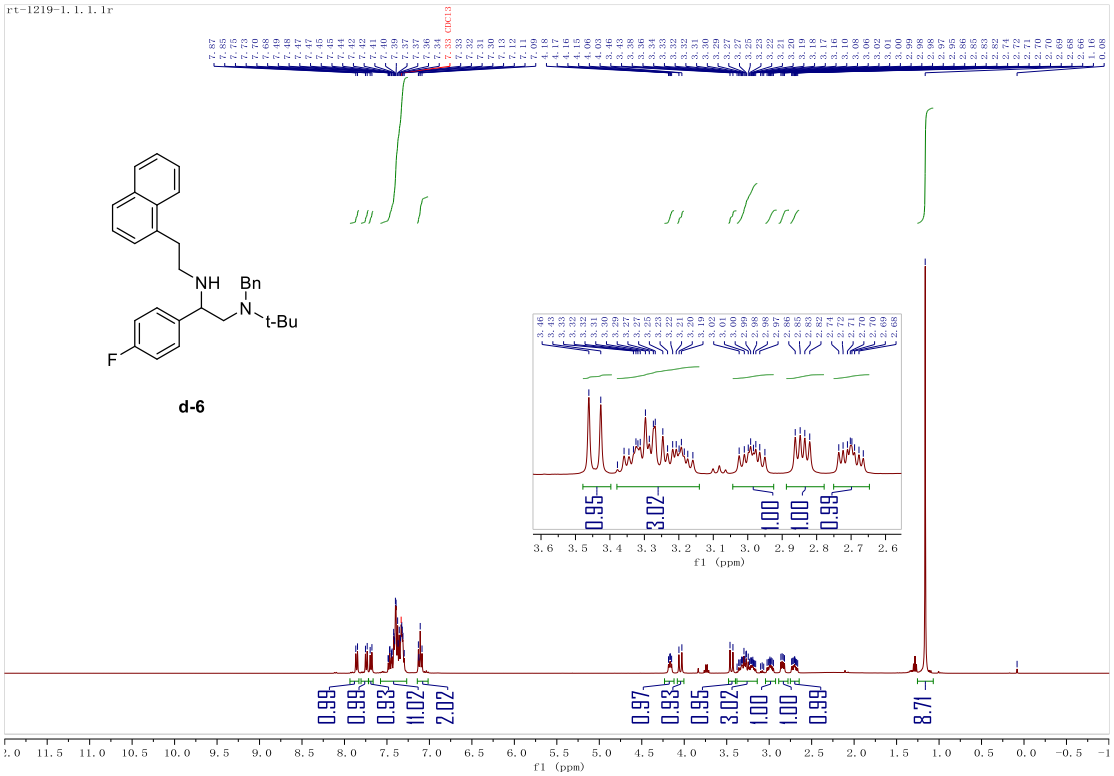
^{13}C NMR (101 MHz)



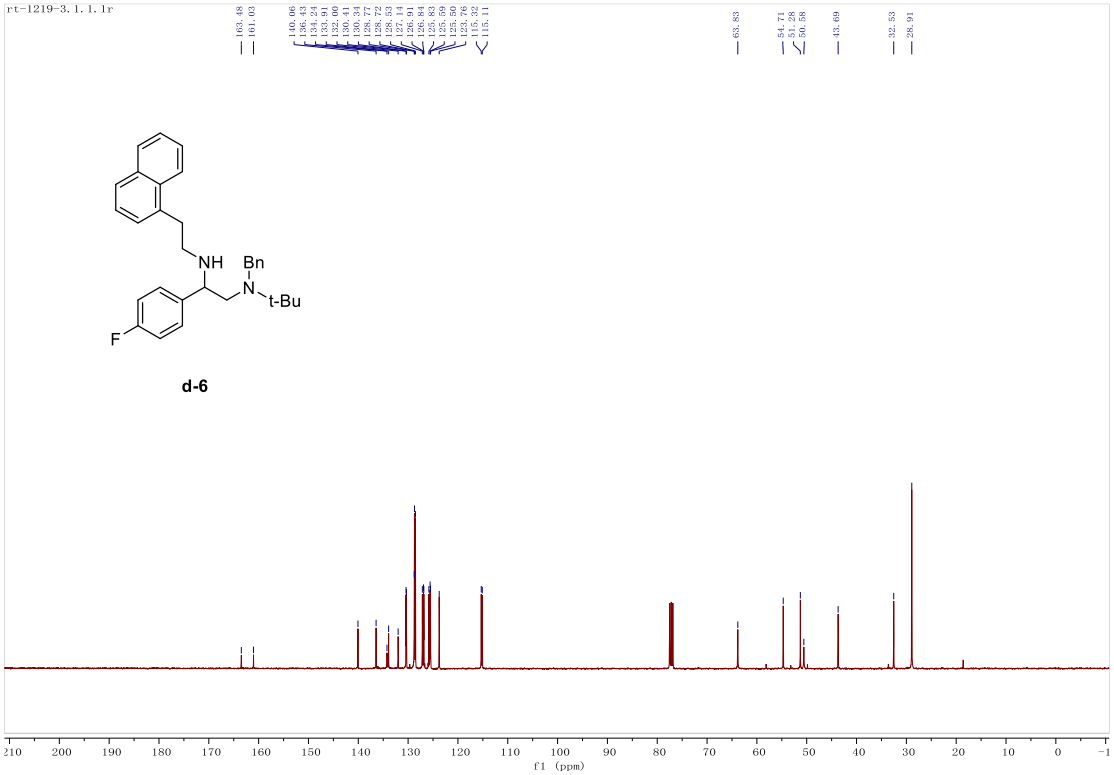
^{19}F NMR (376 MHz)



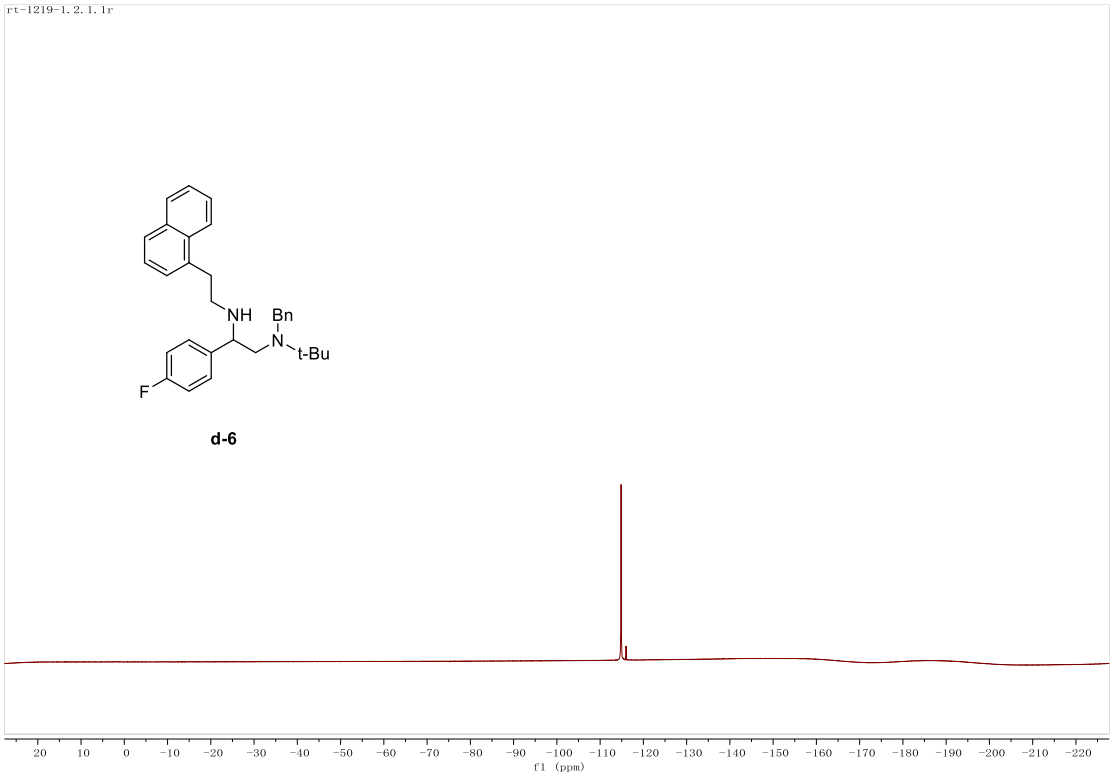
d-6 ^{1}H NMR (400 MHz)



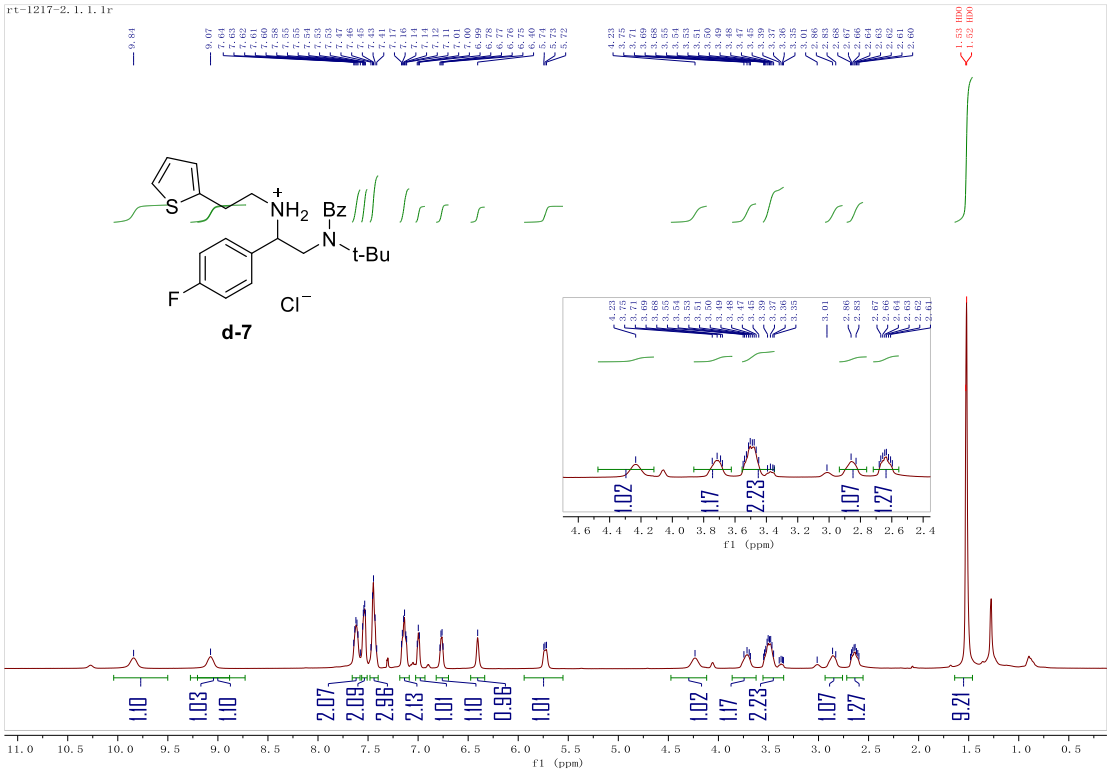
^{13}C NMR (101 MHz)



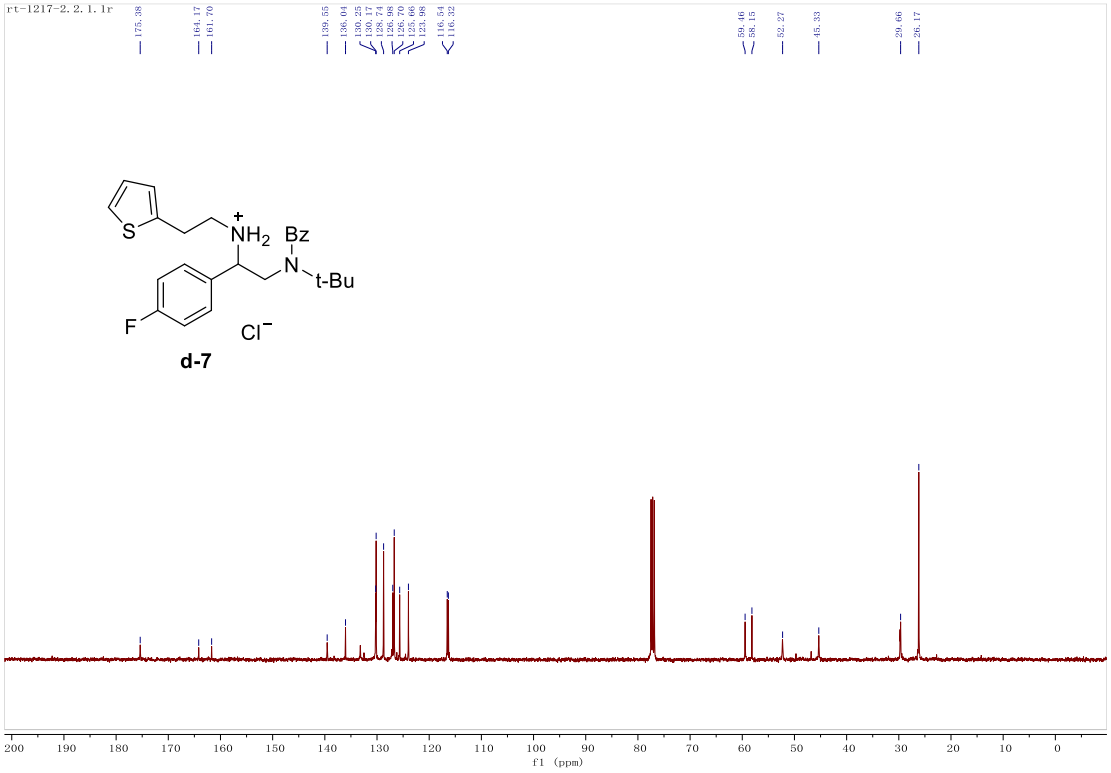
^{19}F NMR (376 MHz)



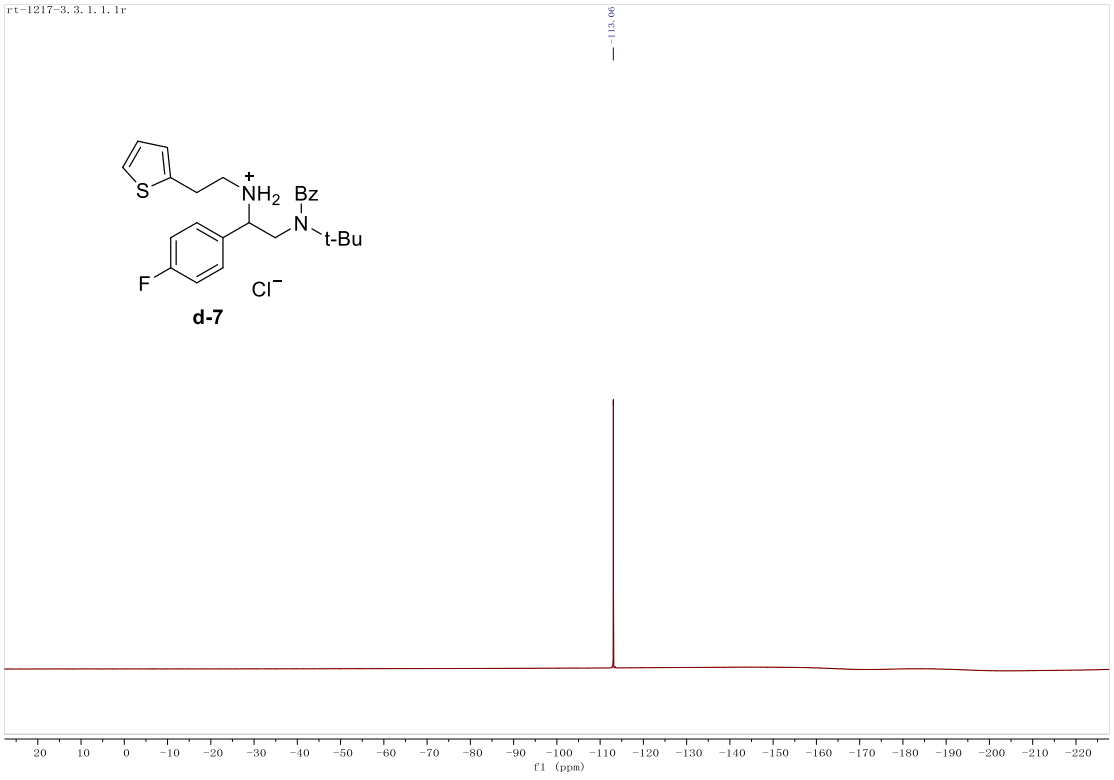
d-7 ^{1}H NMR (400 MHz)



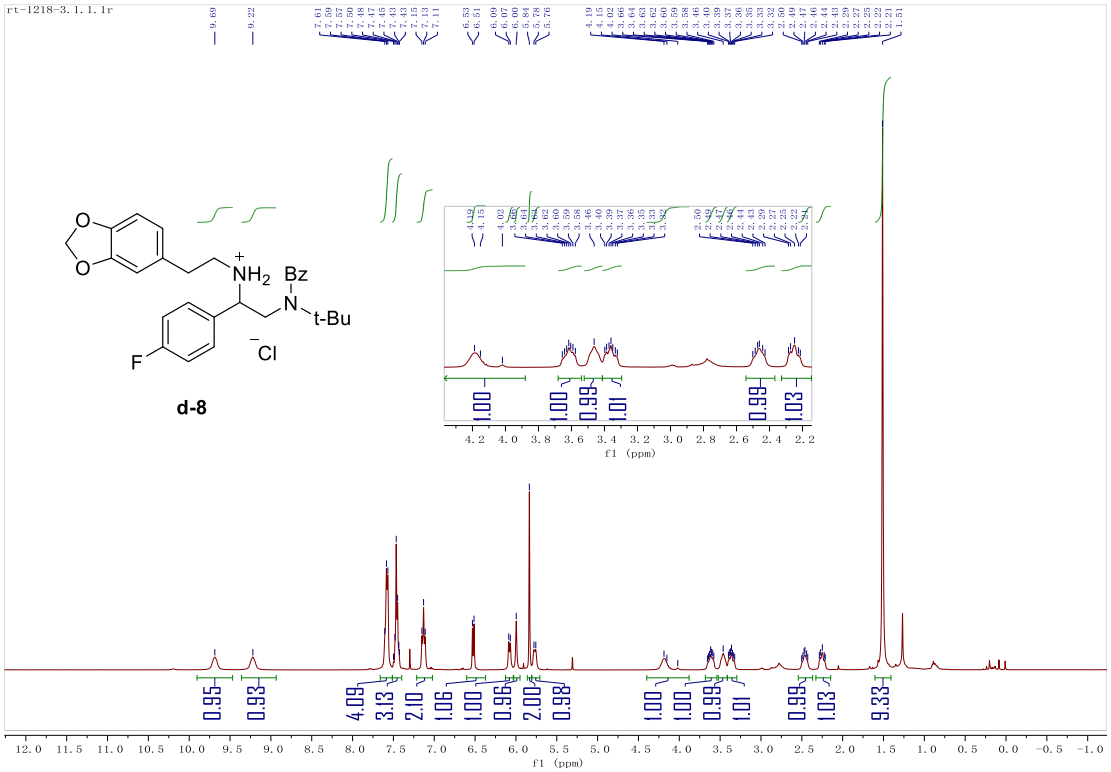
^{13}C NMR (101 MHz)



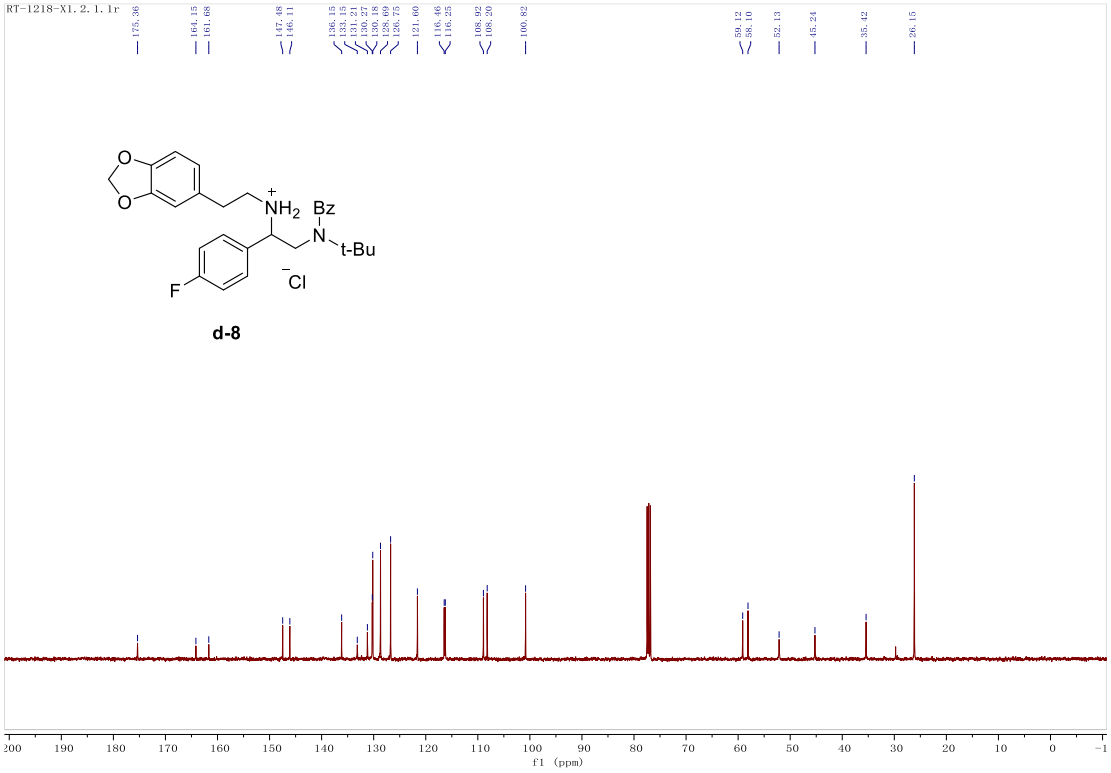
^{19}F NMR (376 MHz)



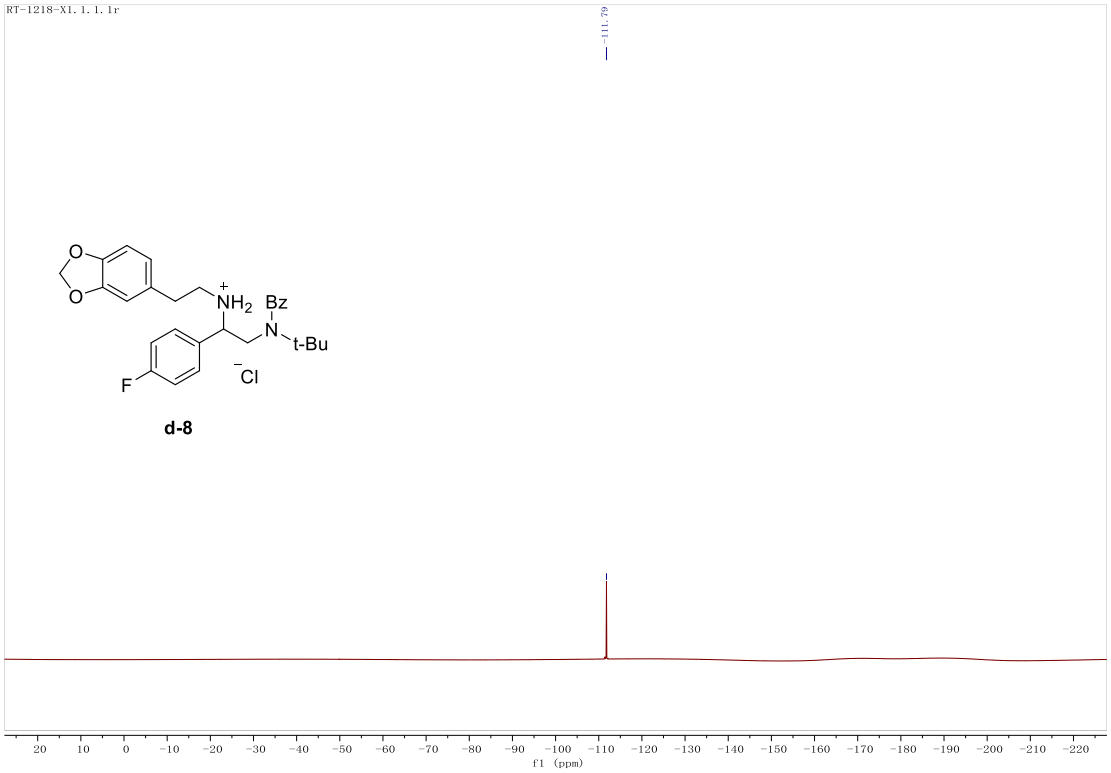
d-8 ^{1}H NMR (400 MHz)



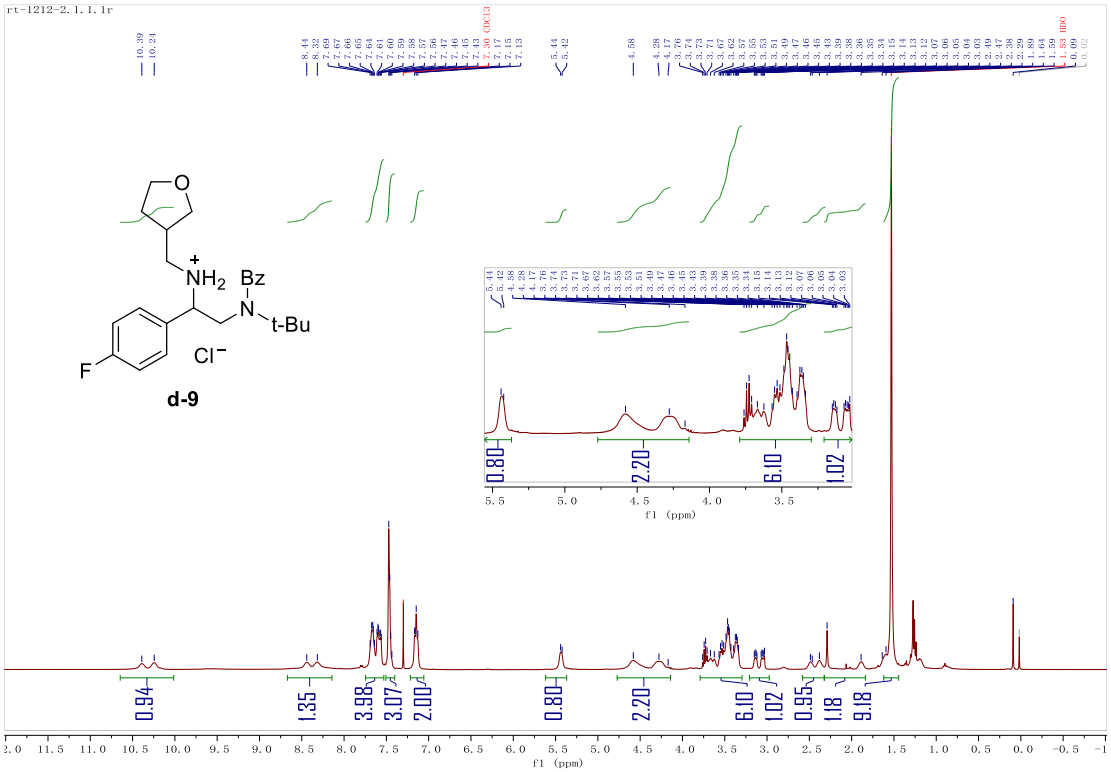
^{13}C NMR (101 MHz)



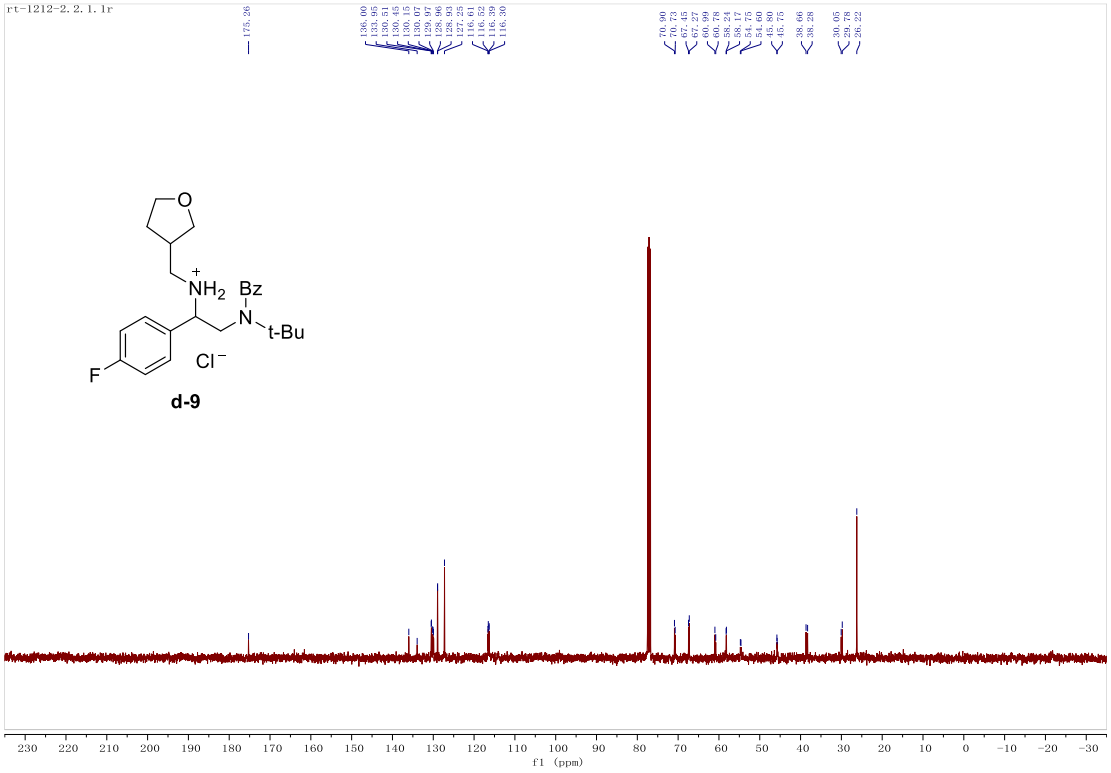
^{19}F NMR (376 MHz)



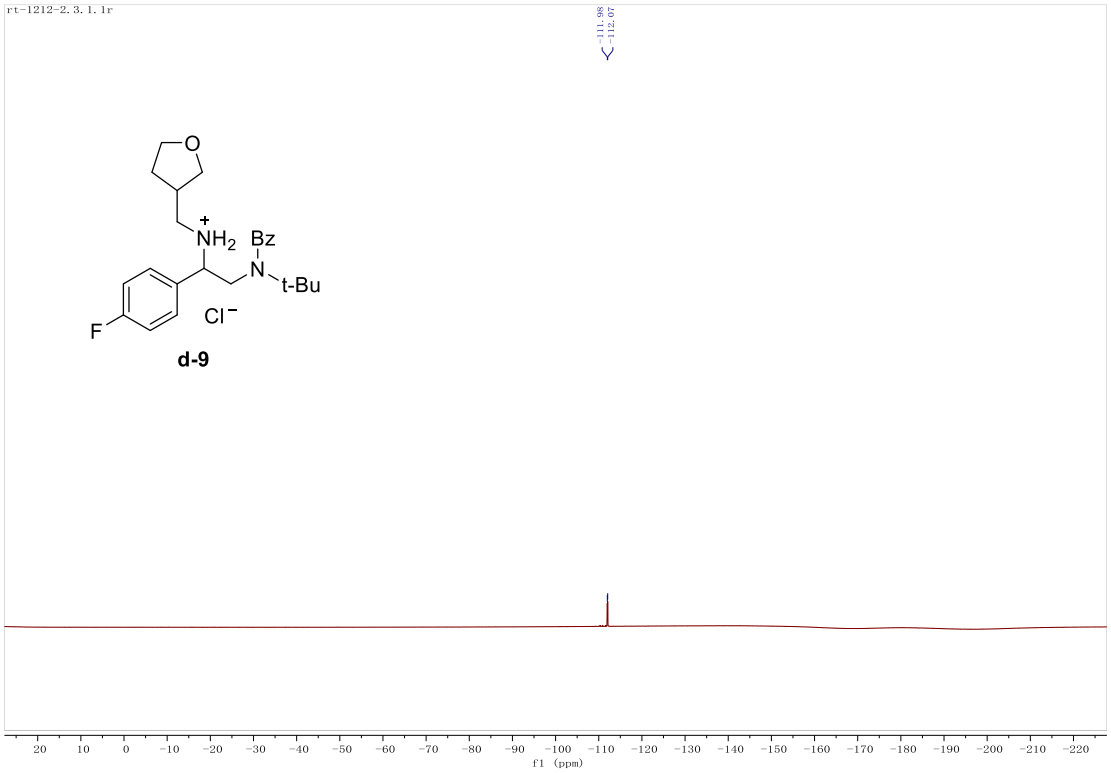
d-9 ^{1}H NMR (400 MHz)



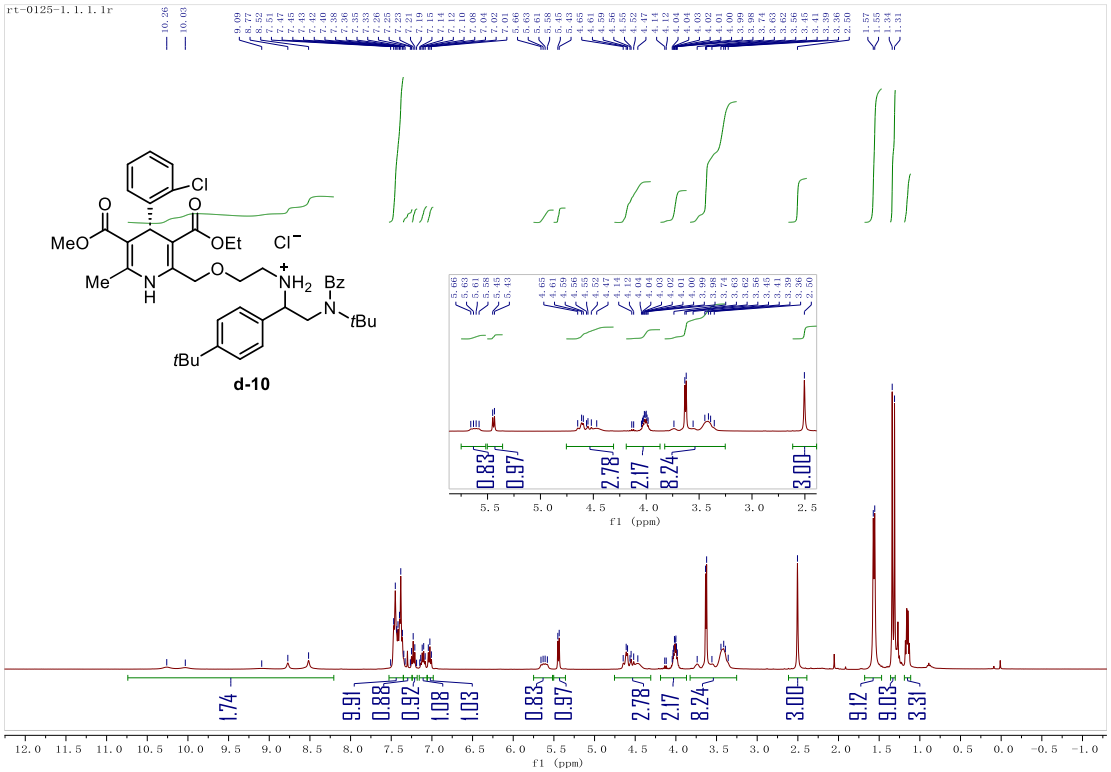
^{13}C NMR (101 MHz)



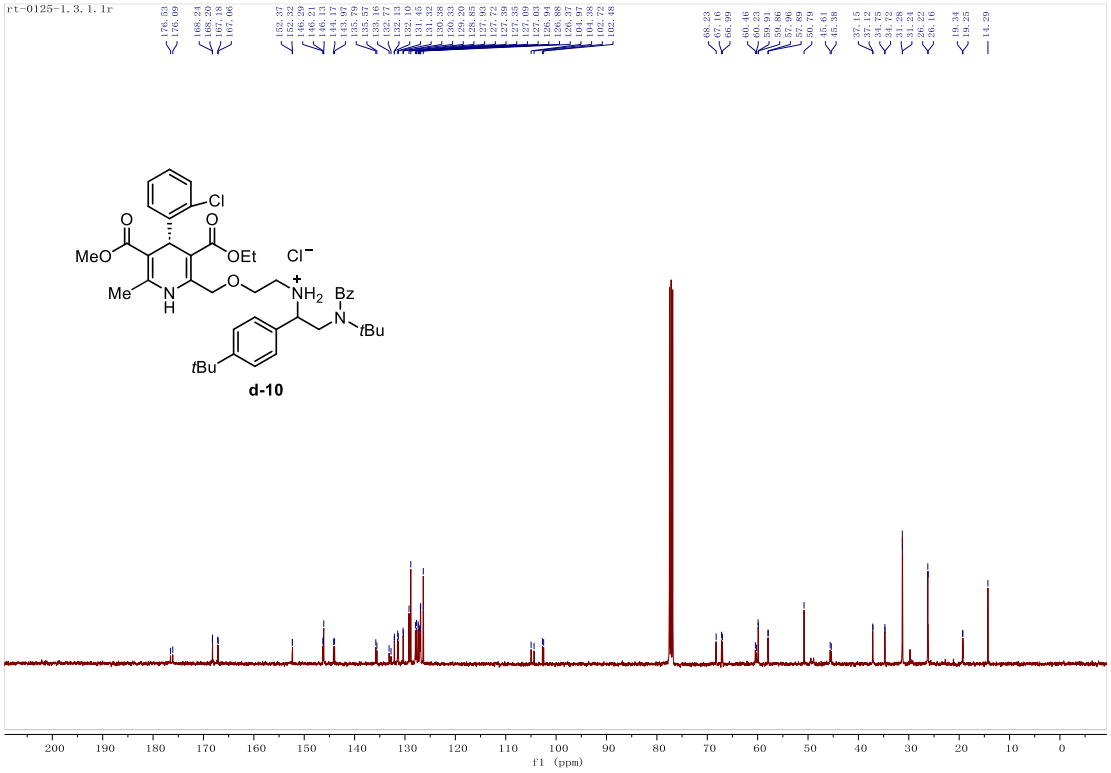
^{19}F NMR (376 MHz)



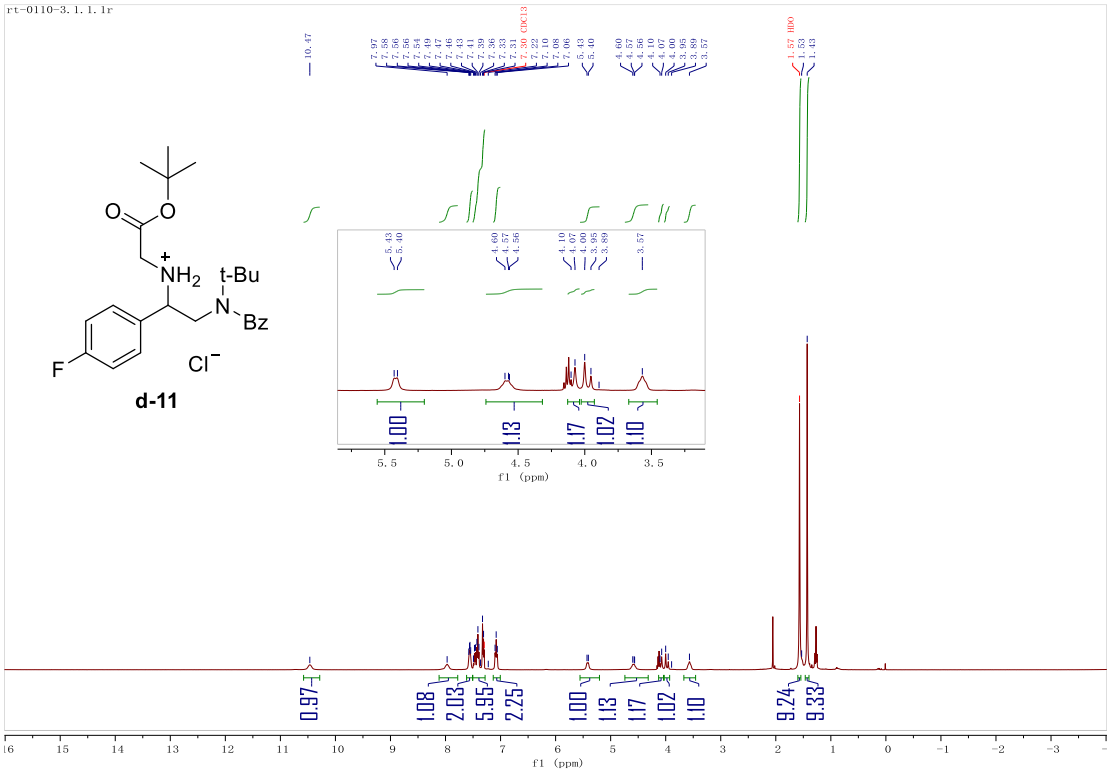
d-10 ^{1}H NMR (400 MHz)



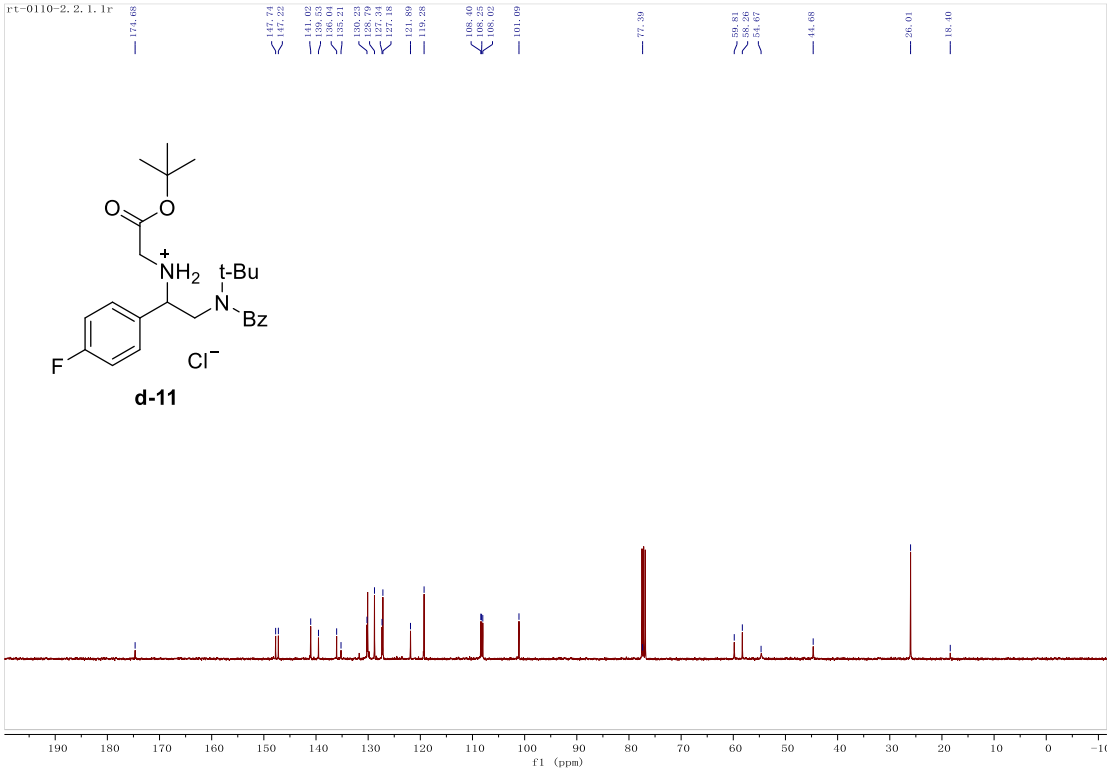
^{13}C NMR (101 MHz)



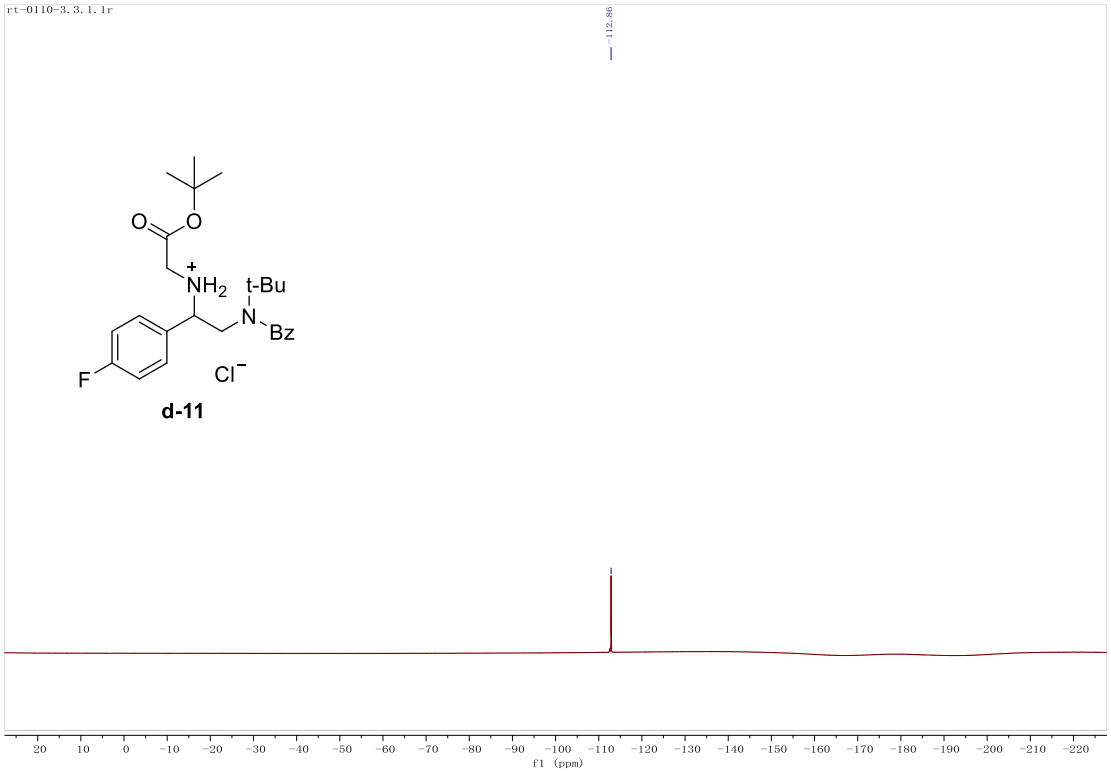
d-11 ^{1}H NMR (400 MHz)



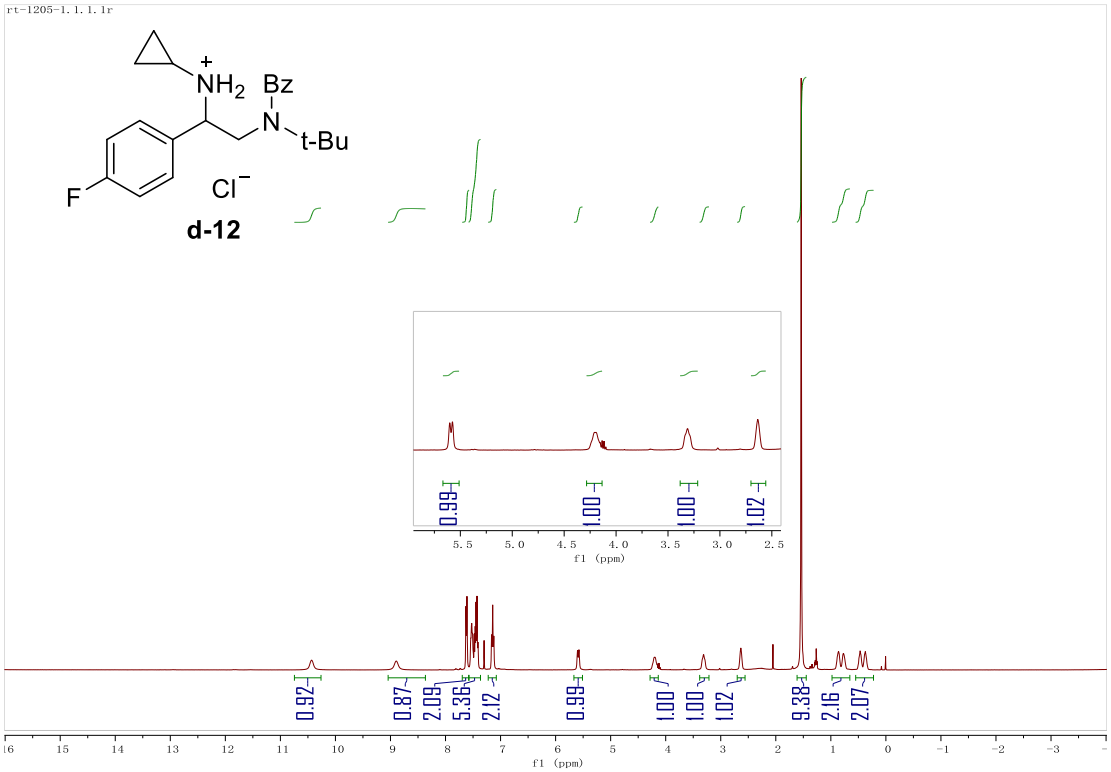
^{13}C NMR (101 MHz)



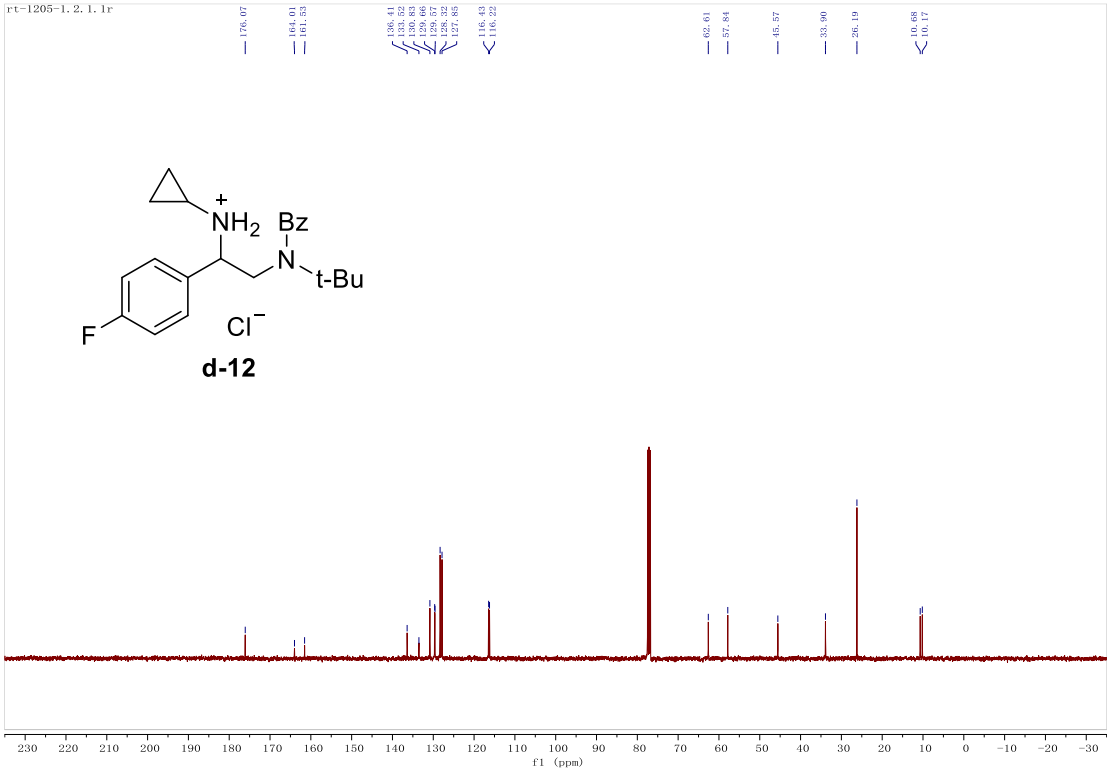
^{19}F NMR (376 MHz)



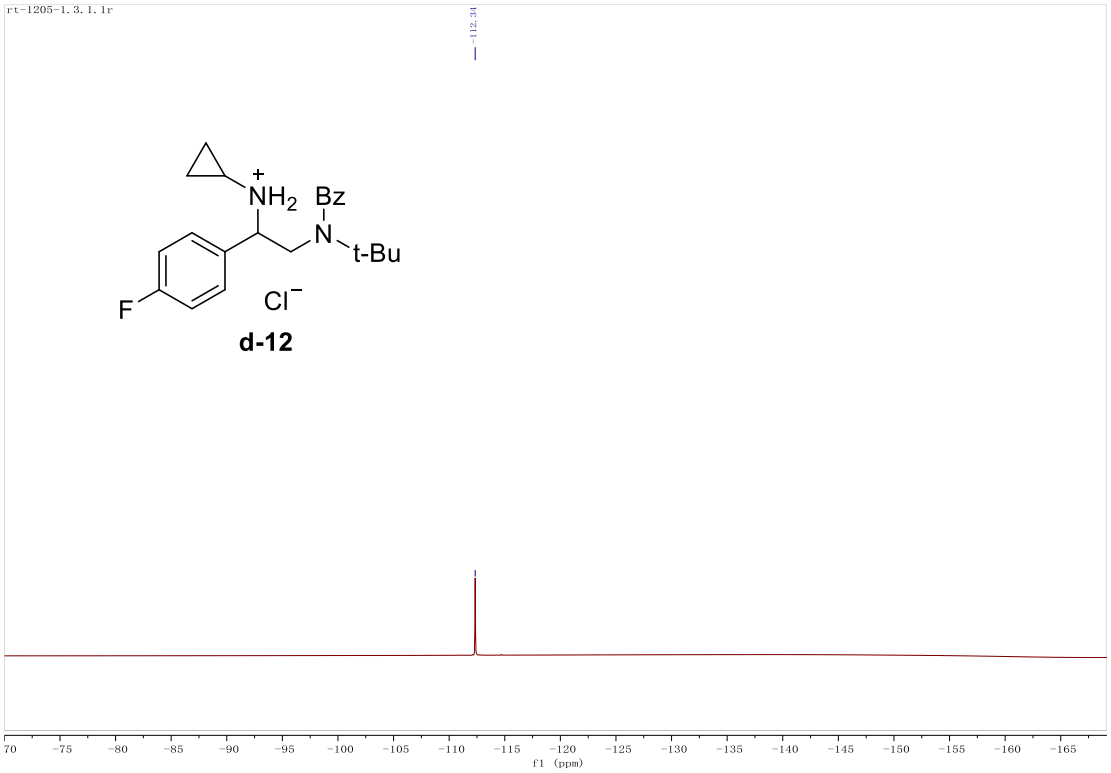
d-12 ^{1}H NMR (400 MHz)



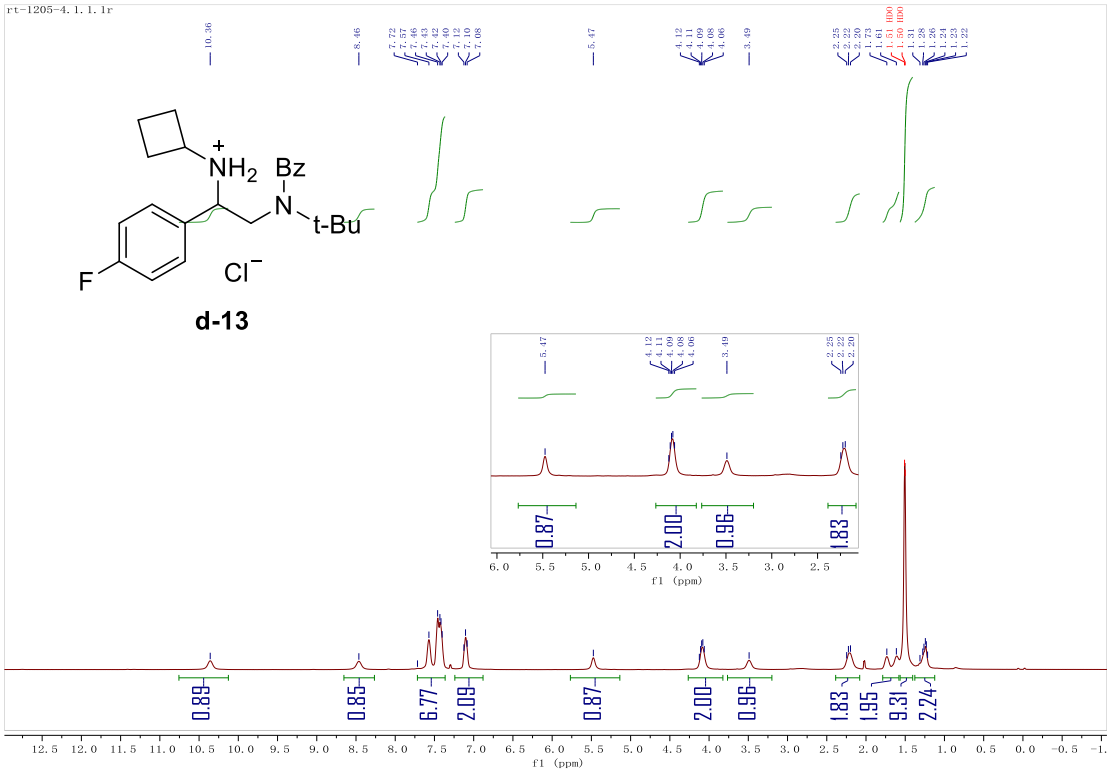
^{13}C NMR (101 MHz)



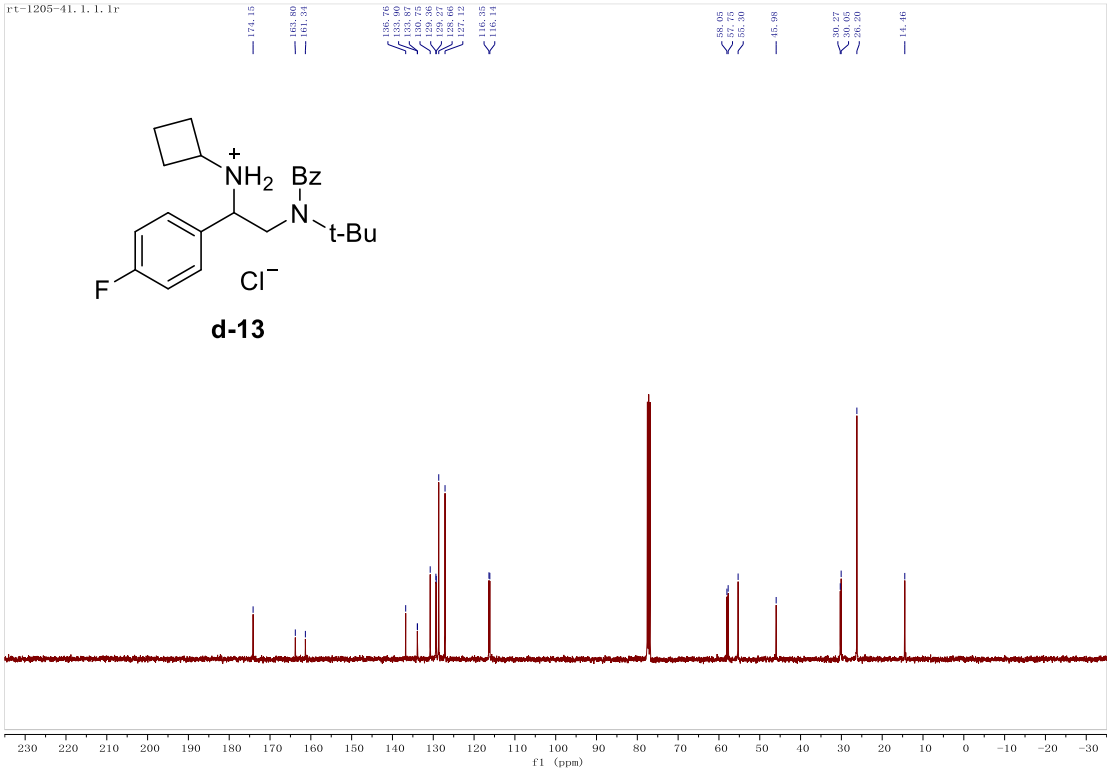
^{19}F NMR (376 MHz)



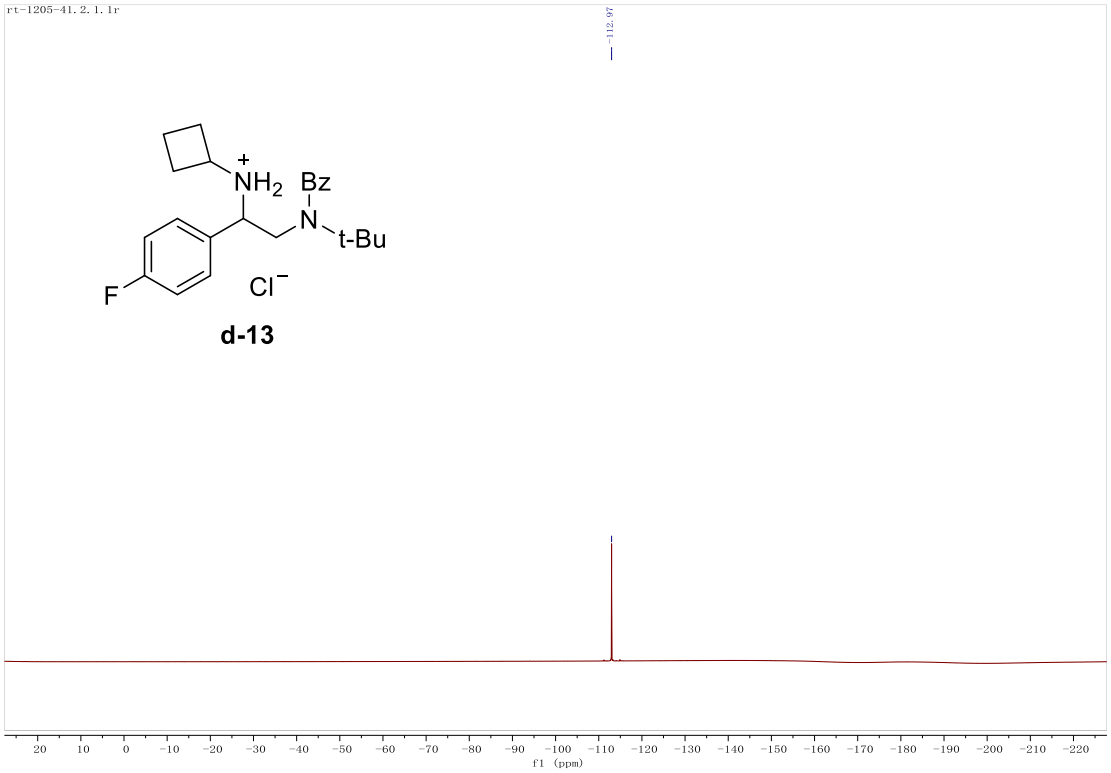
d-13 ^{1}H NMR (400 MHz)



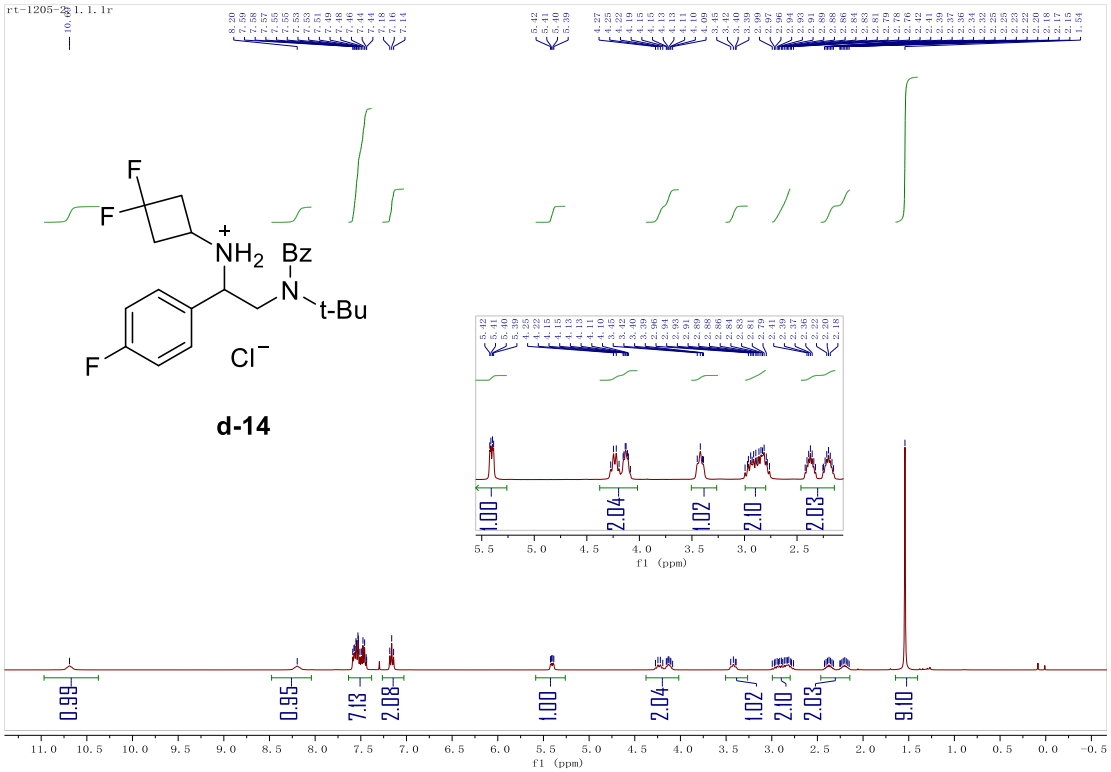
^{13}C NMR (101 MHz)



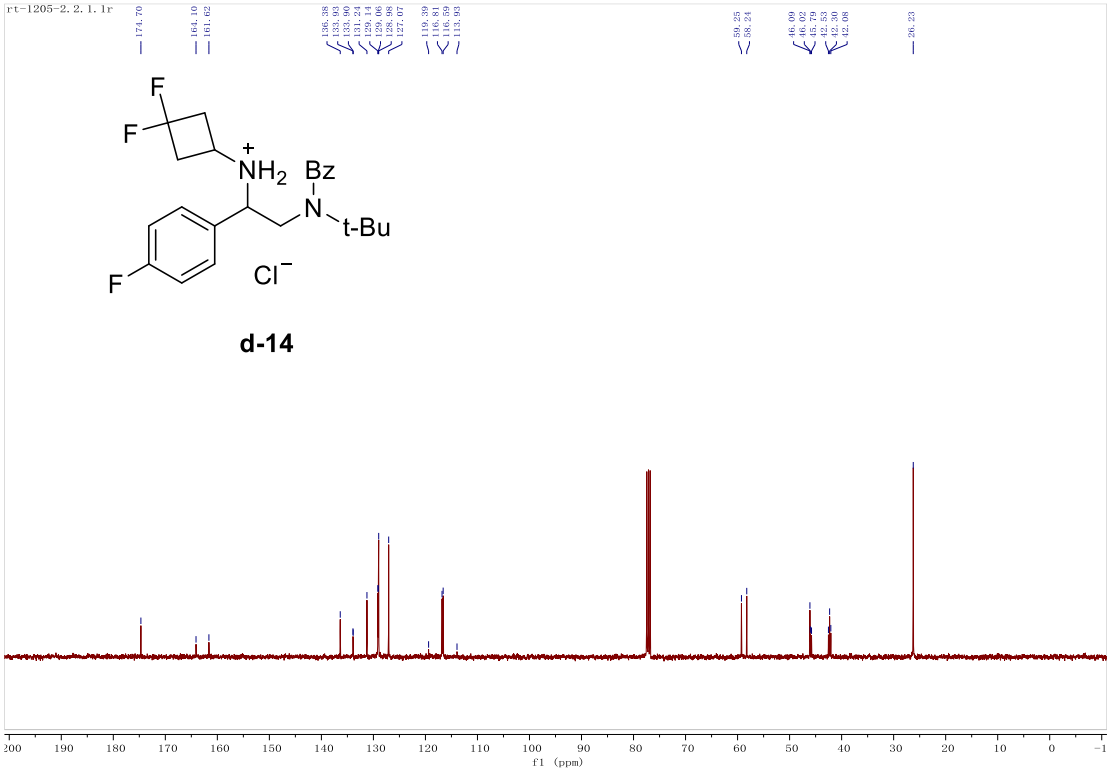
^{19}F NMR (376 MHz)



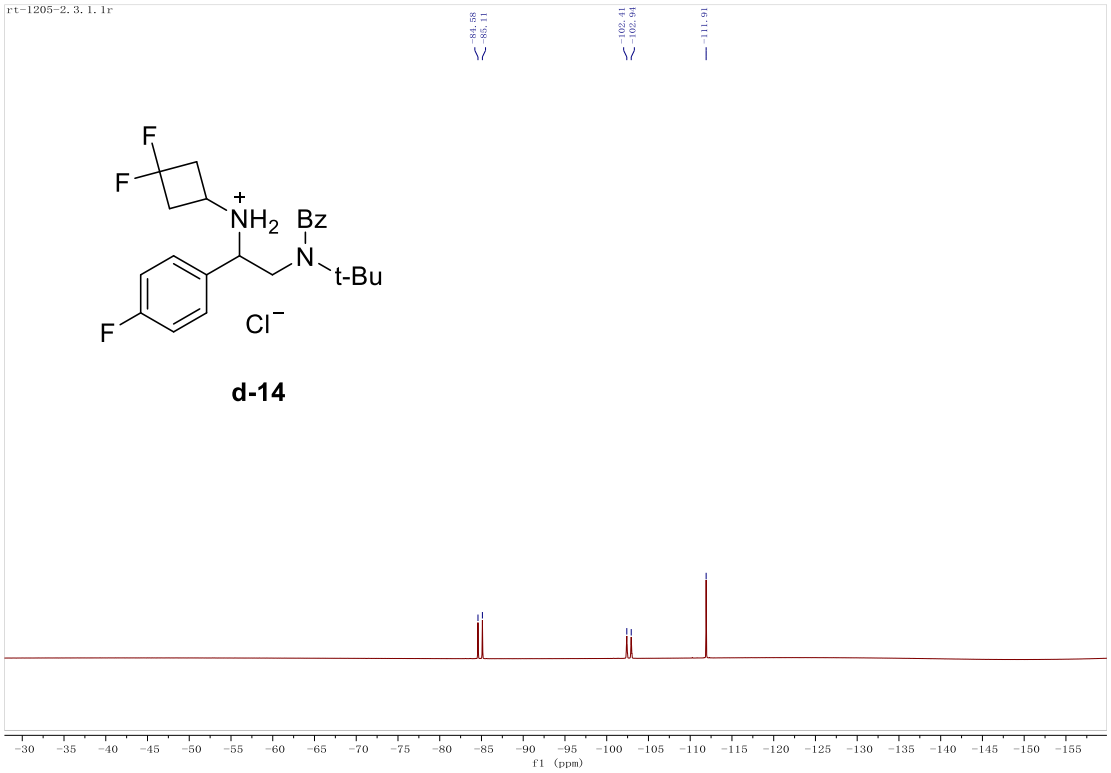
d-14 ^{1}H NMR (400 MHz)



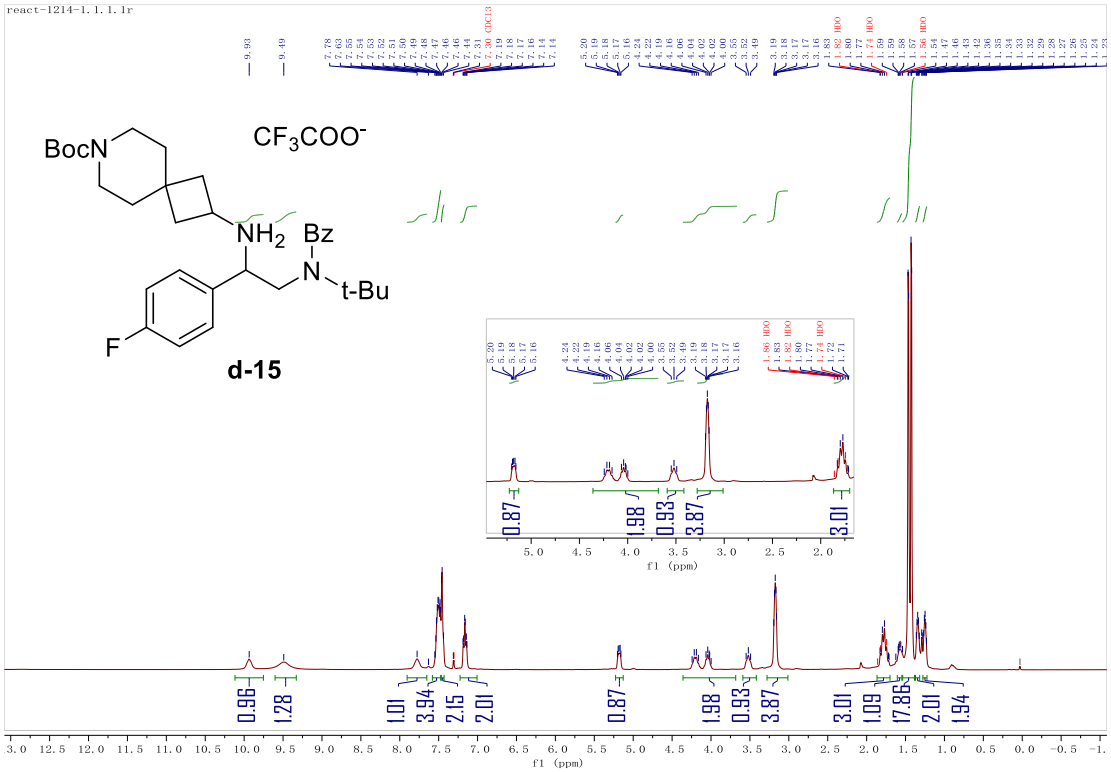
^{13}C NMR (101 MHz)



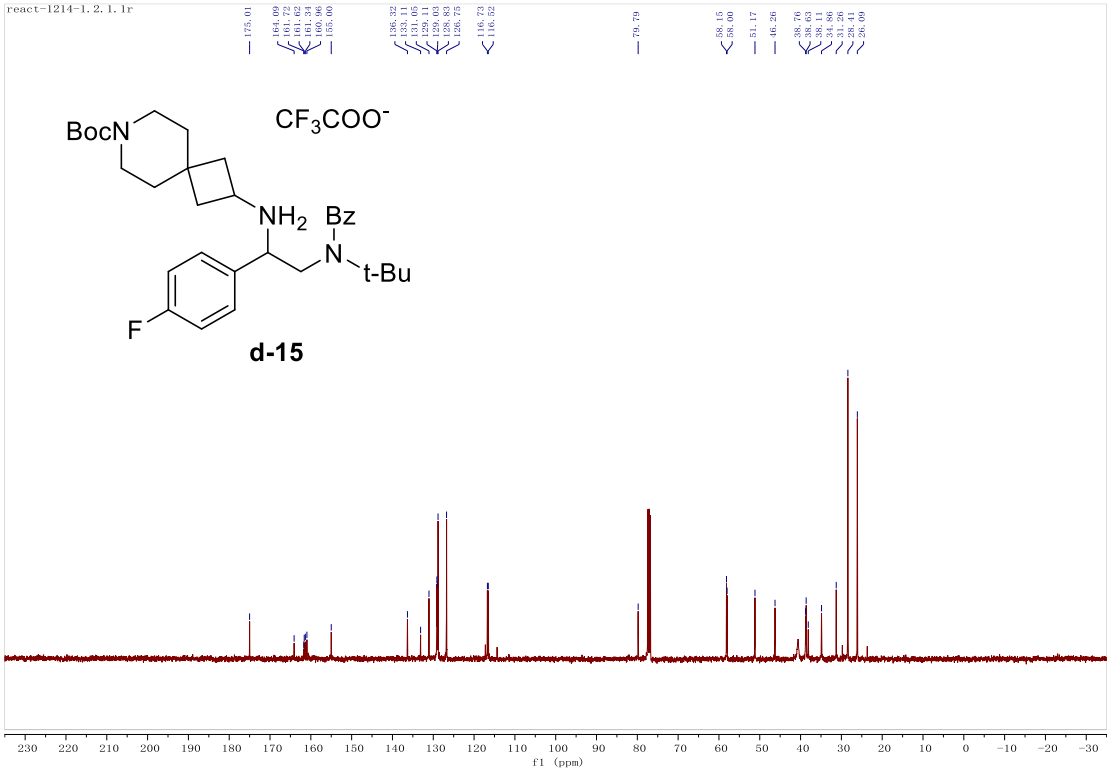
^{19}F NMR (376 MHz)



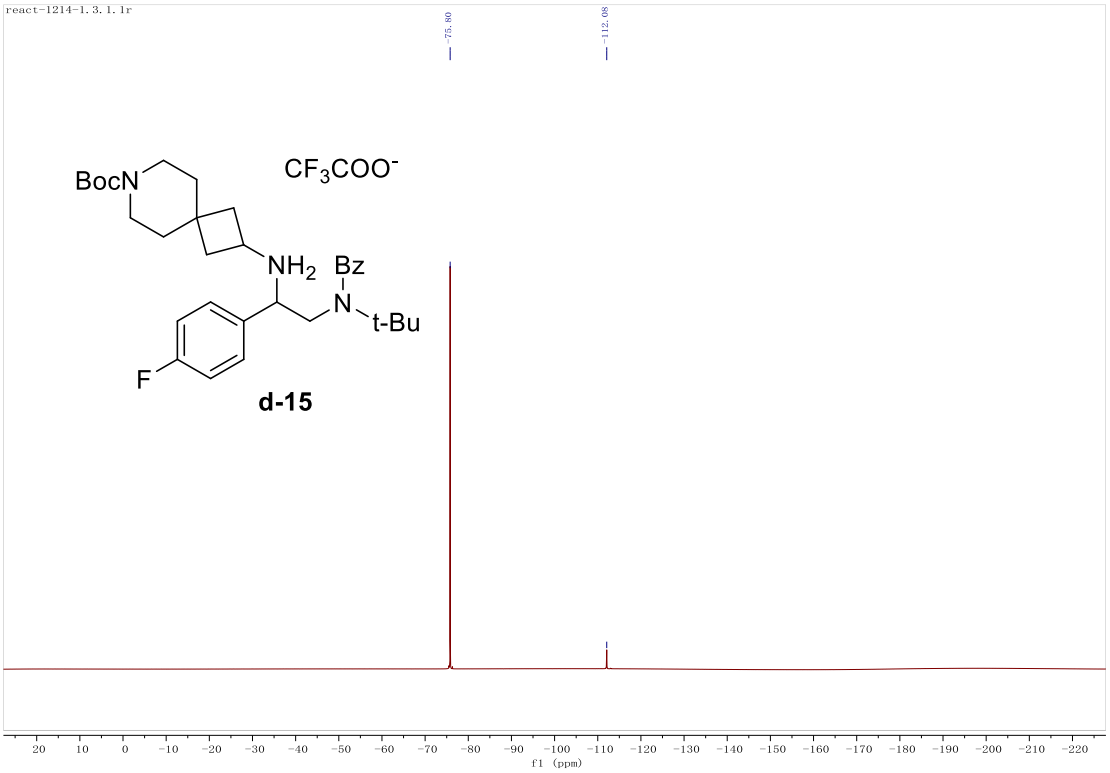
d-15 ^{1}H NMR (400 MHz)



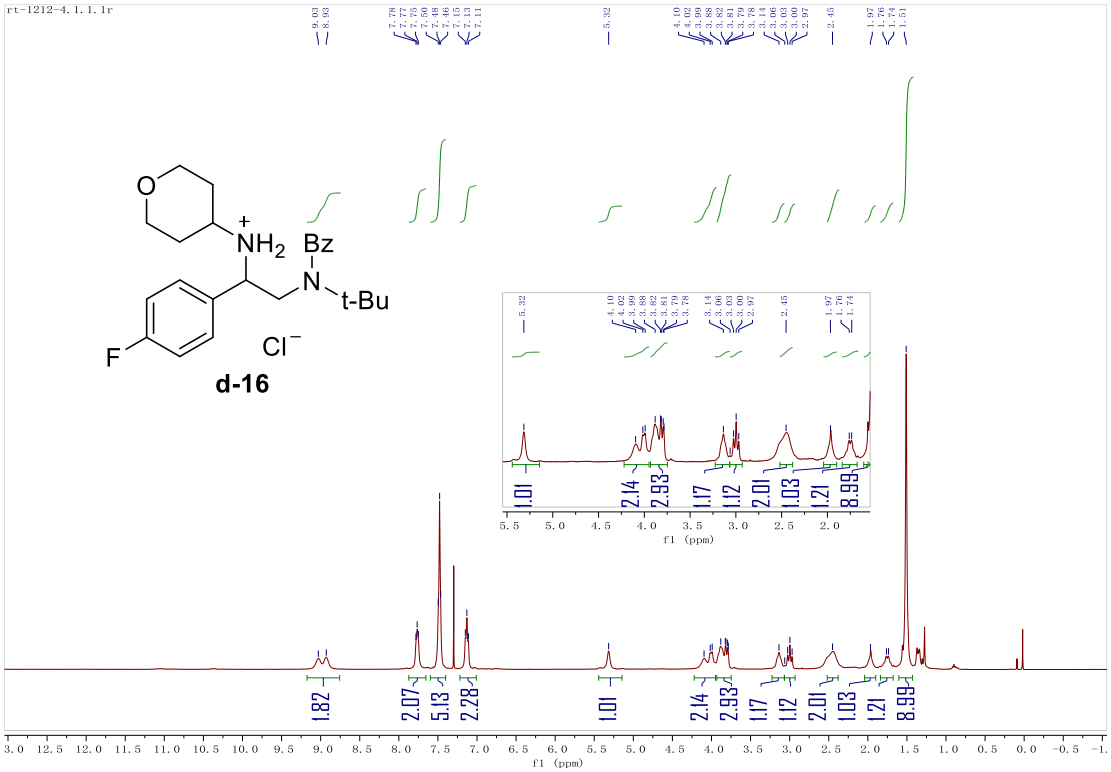
^{13}C NMR (101 MHz)



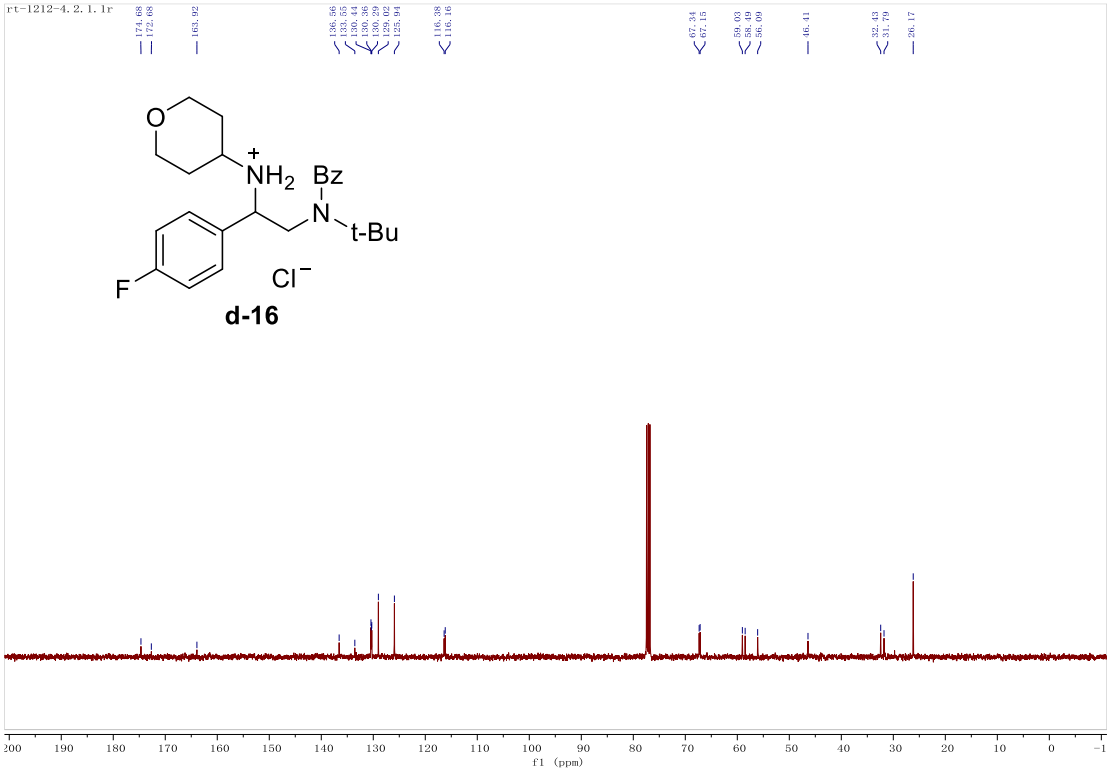
^{19}F NMR (376 MHz)



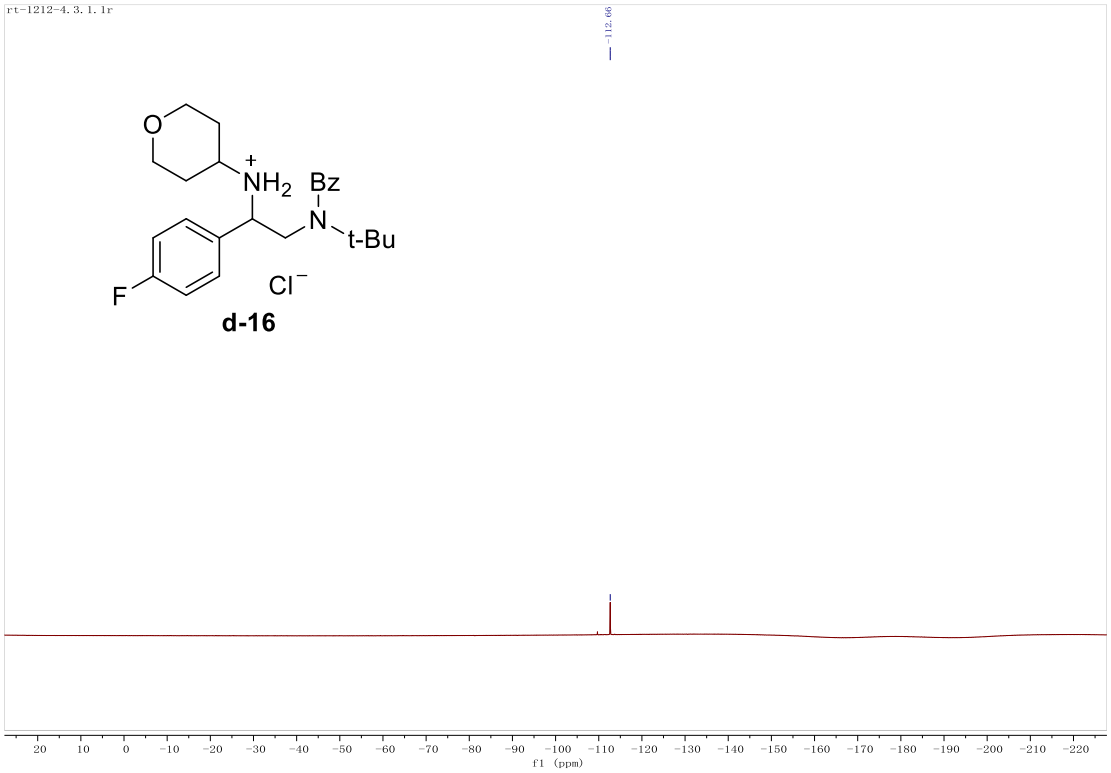
d-16 ^{1}H NMR (400 MHz)



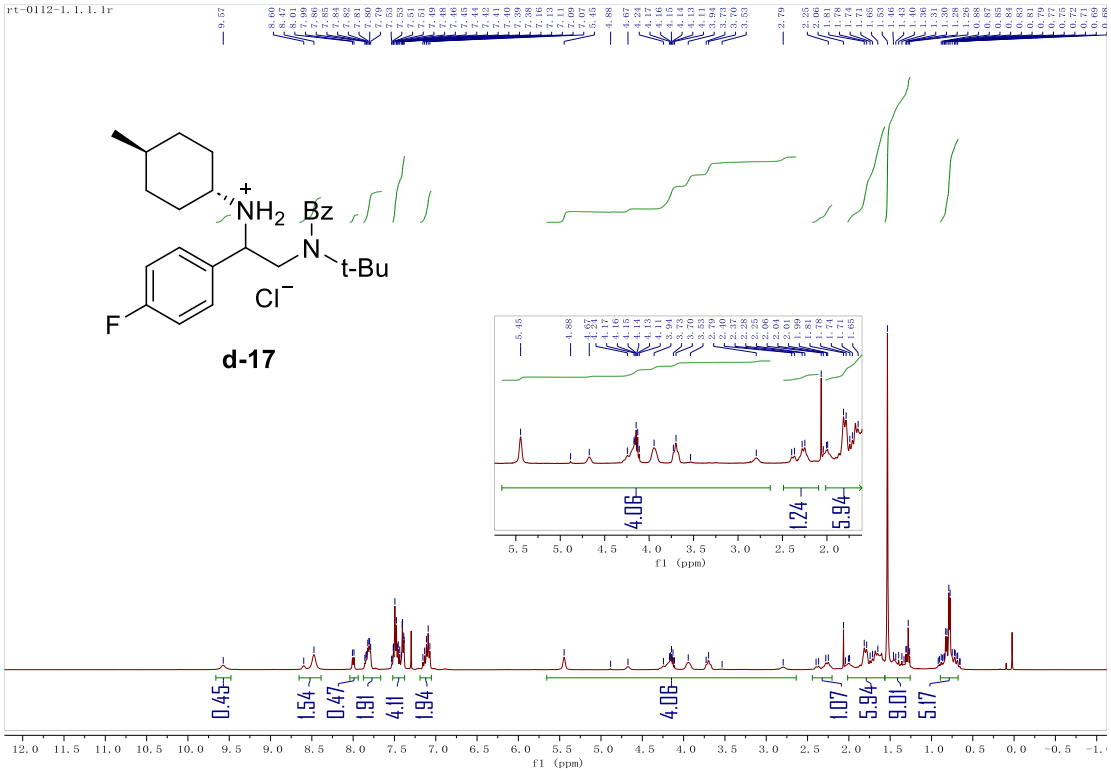
^{13}C NMR (101 MHz)



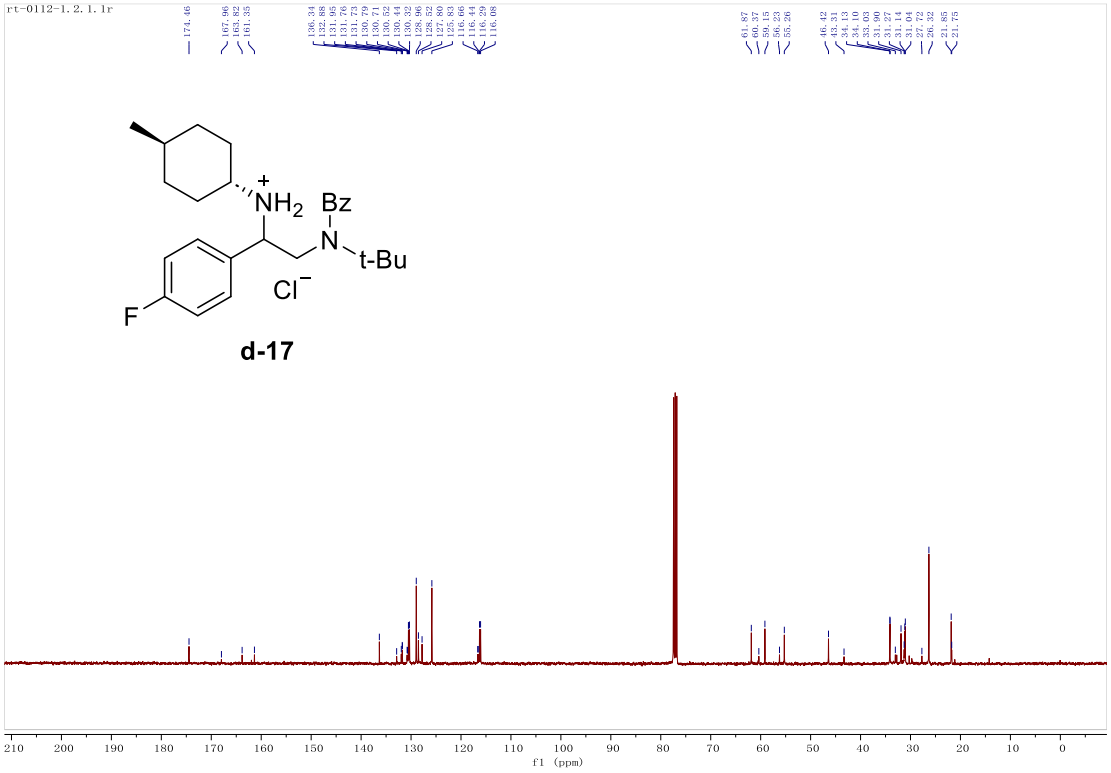
^{19}F NMR (376 MHz)



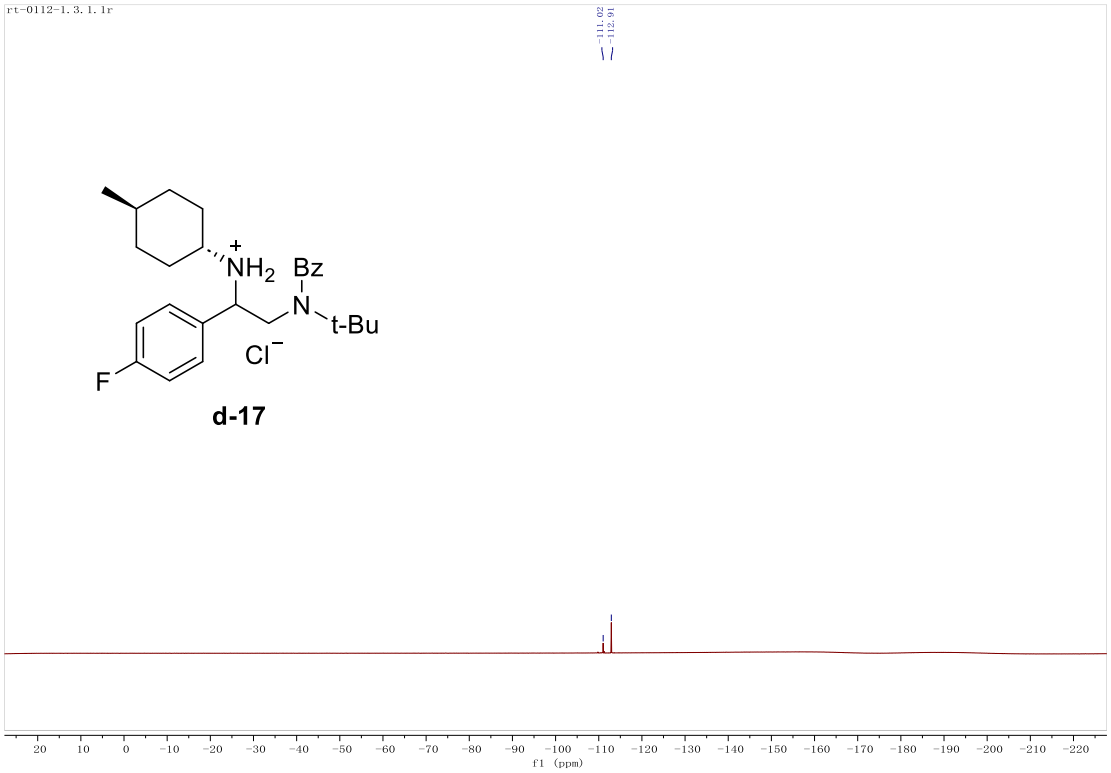
d-17 ^{1}H NMR (400 MHz)



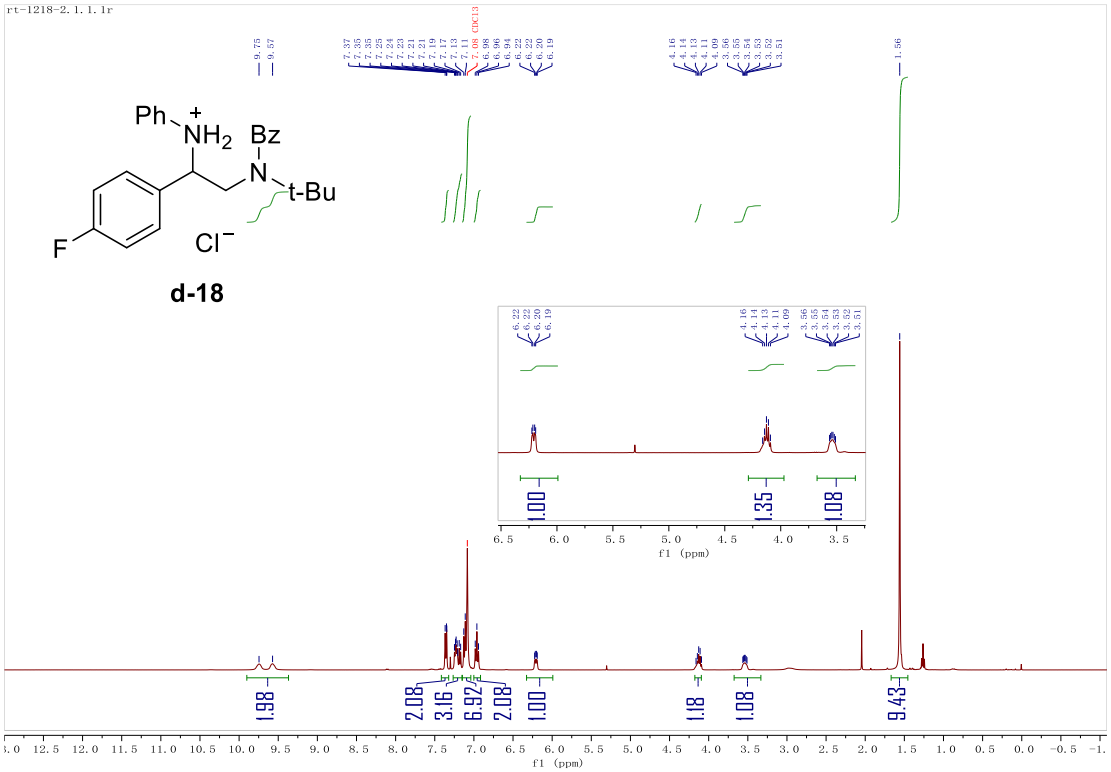
^{13}C NMR (101 MHz)



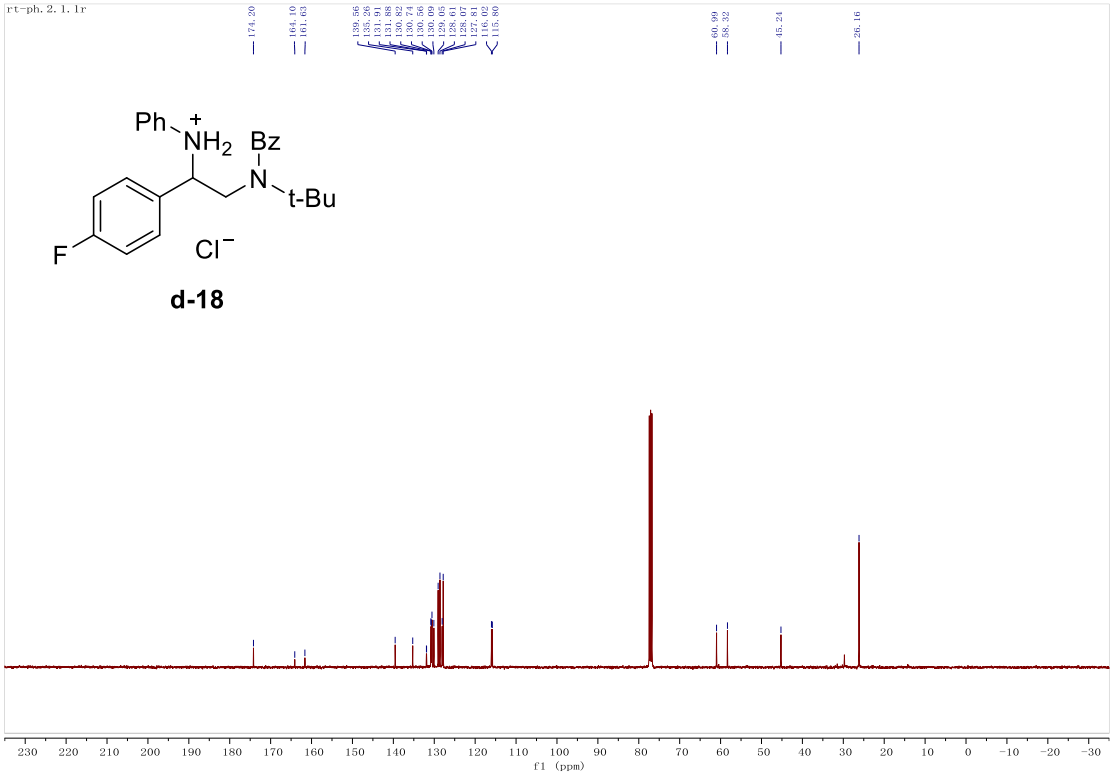
^{19}F NMR (376 MHz)



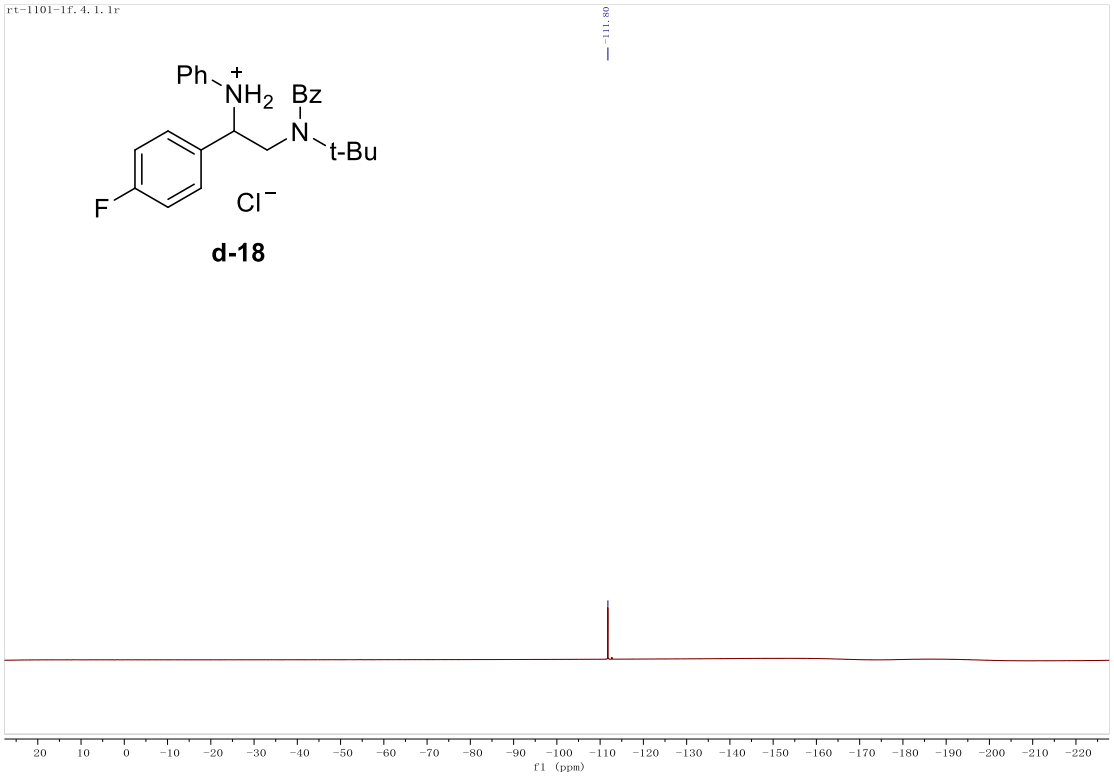
d-18 ^{1}H NMR (400 MHz)



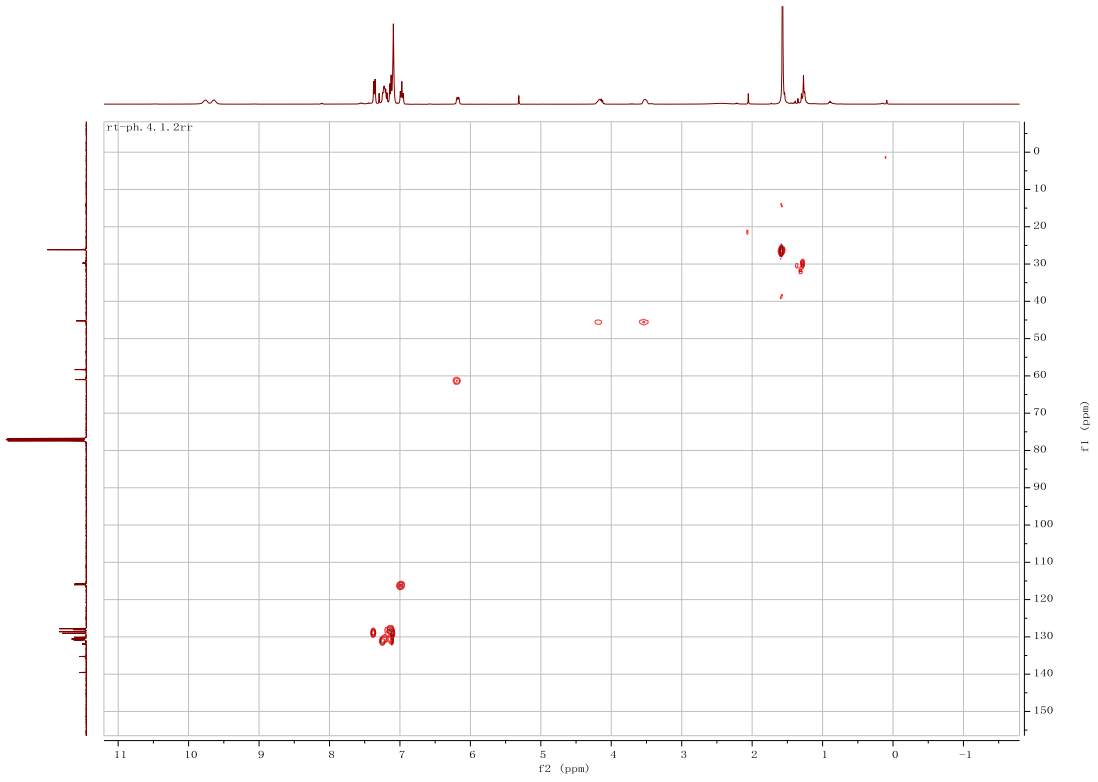
^{13}C NMR (101 MHz)



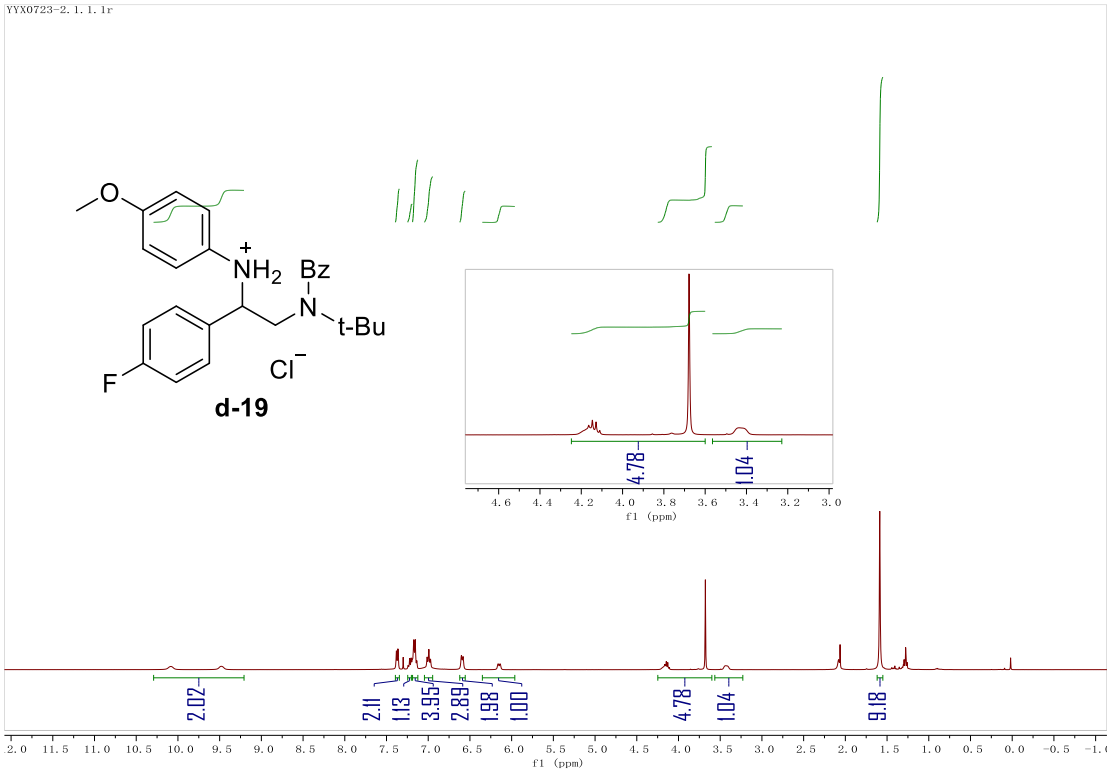
^{19}F NMR (376 MHz)



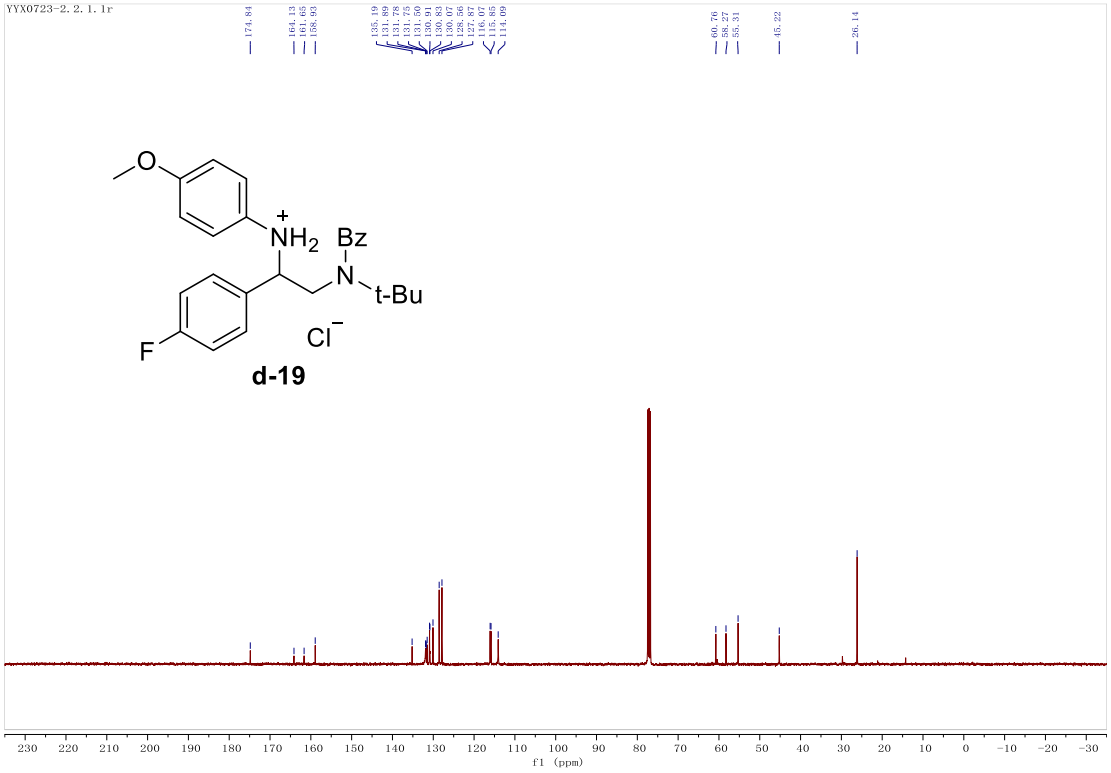
HSQC NMR



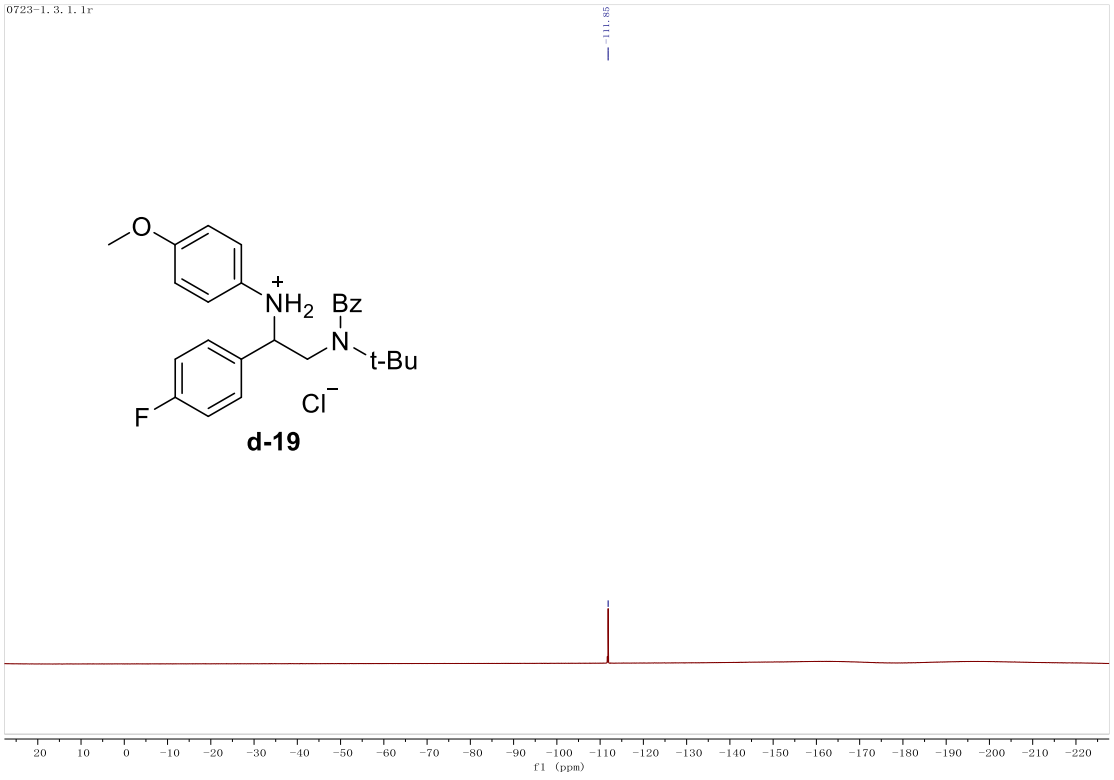
d-19 ^{1}H NMR (400 MHz)



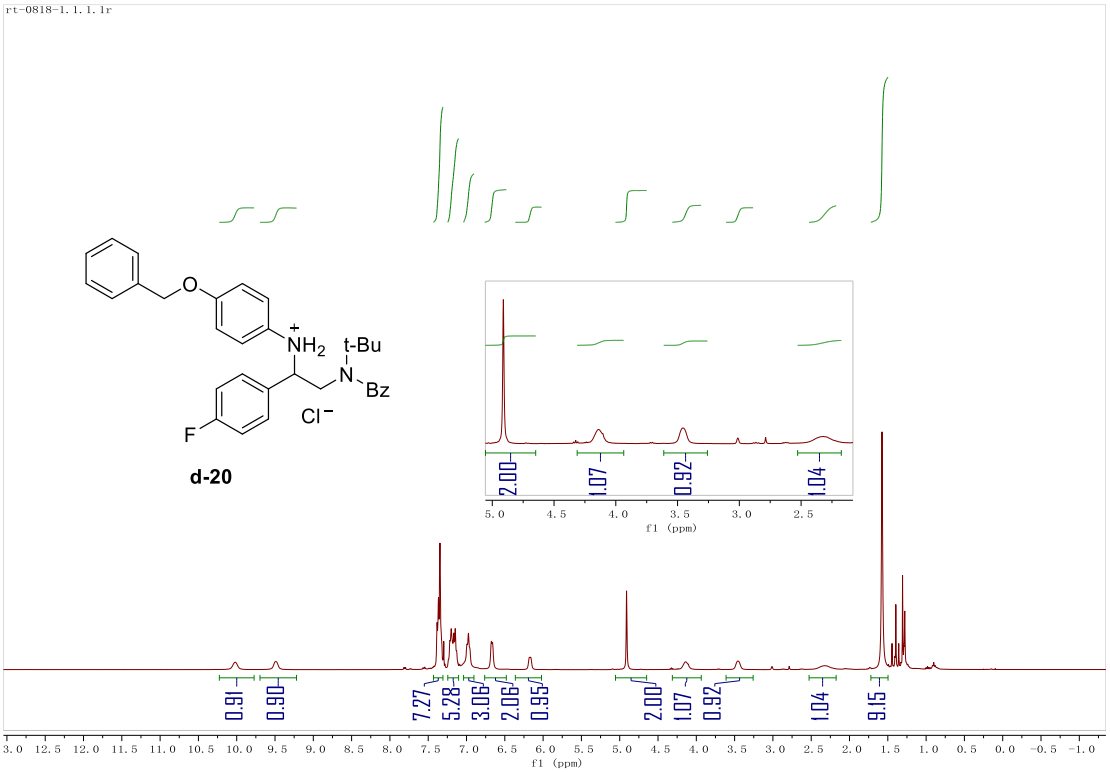
^{13}C NMR (101 MHz)



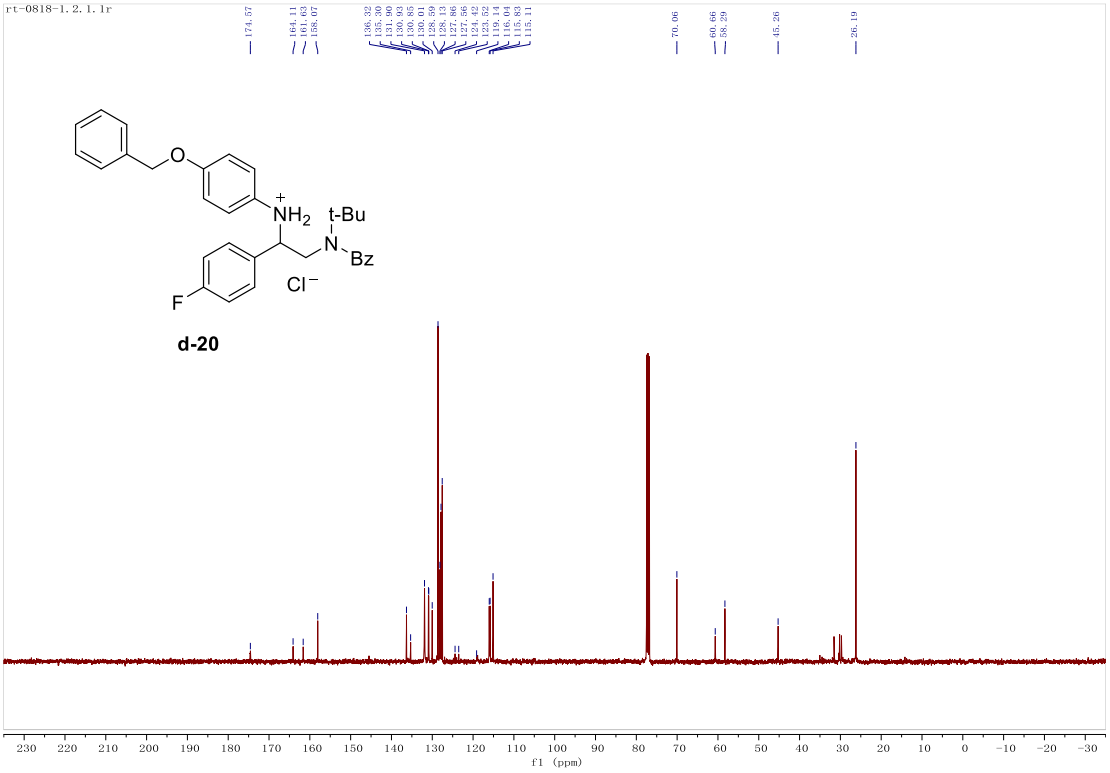
^{19}F NMR (376 MHz)



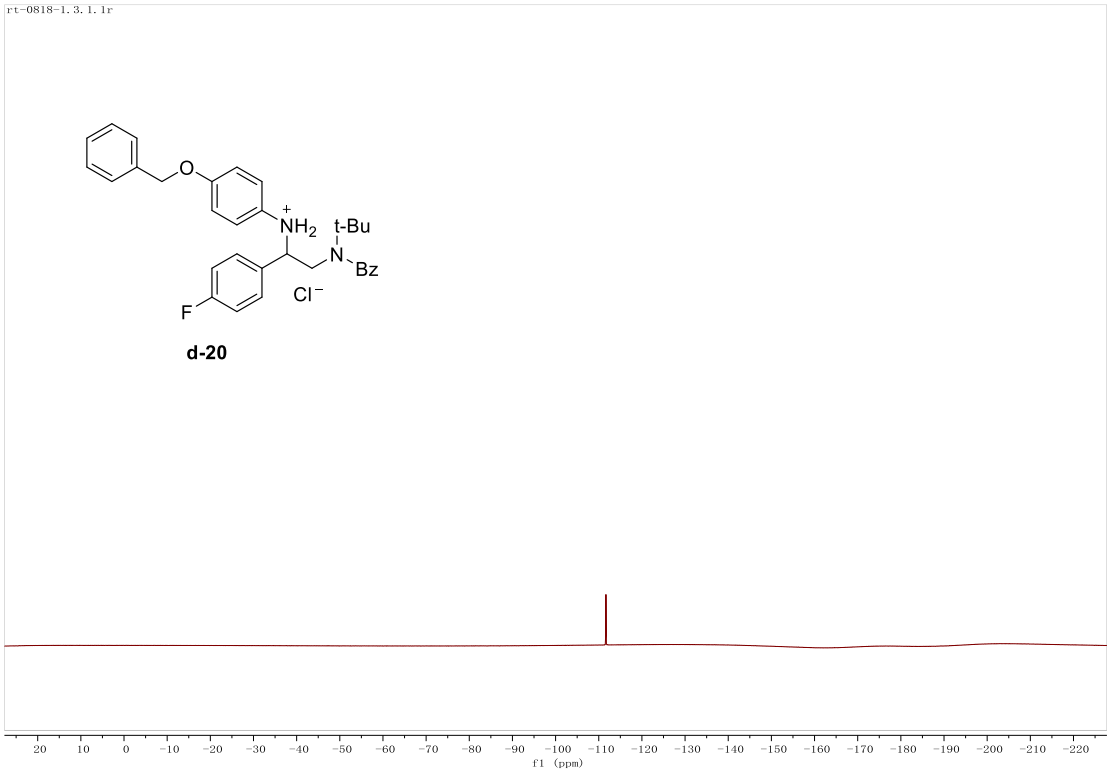
d-20 ^{1}H NMR (400 MHz)



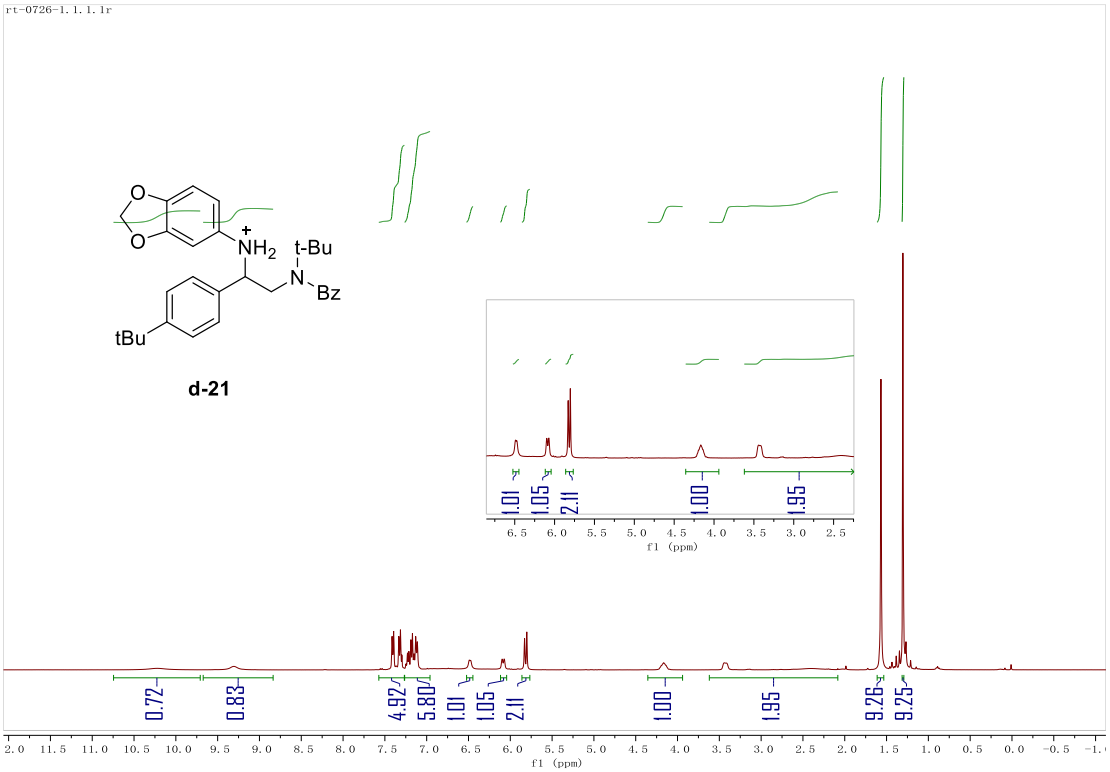
^{13}C NMR (101 MHz)



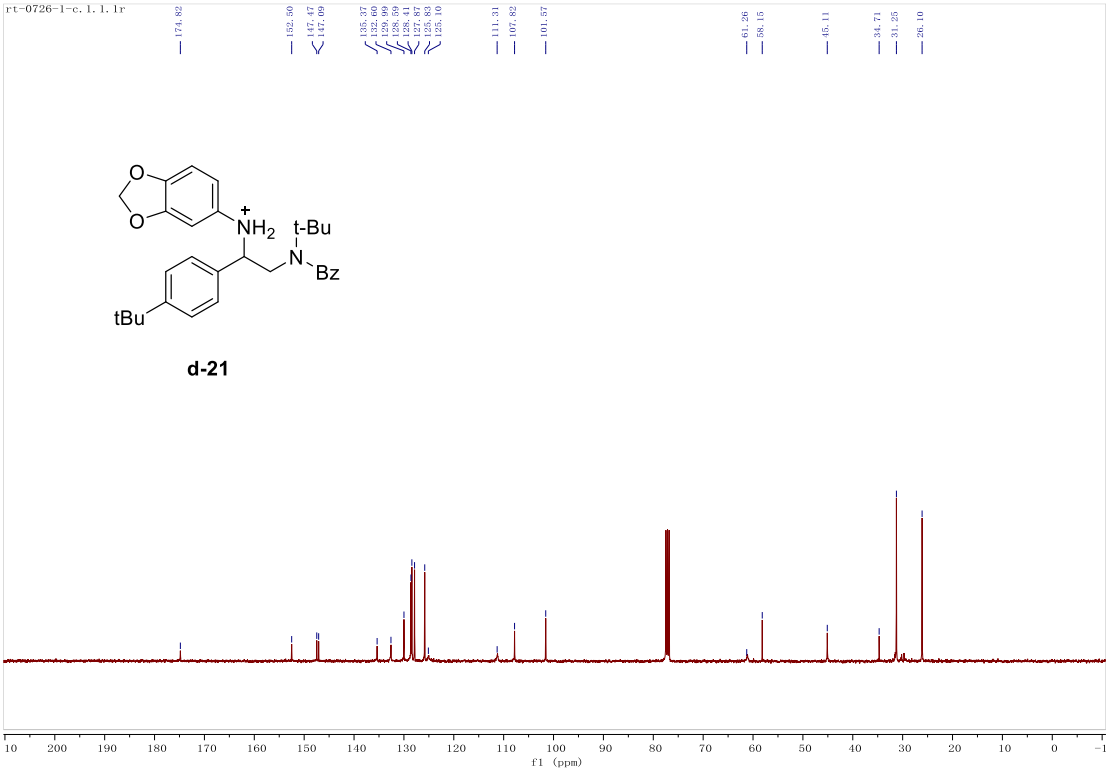
^{19}F NMR (376 MHz)



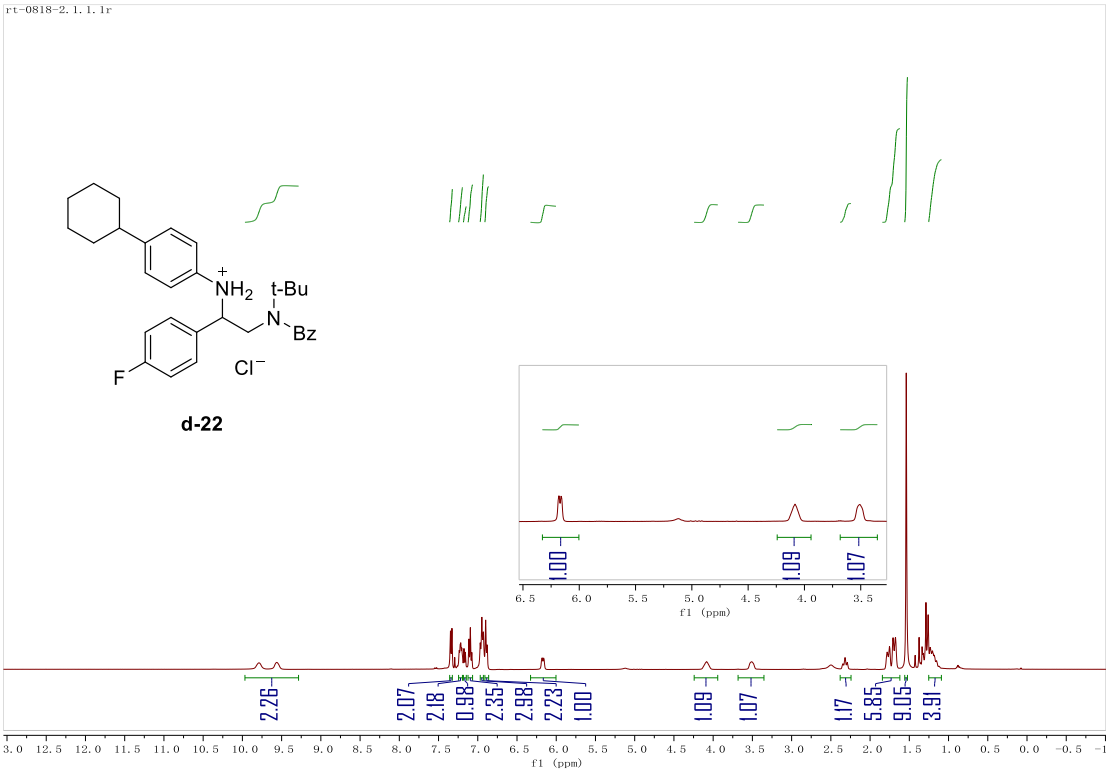
d-21 ^{1}H NMR (400 MHz)



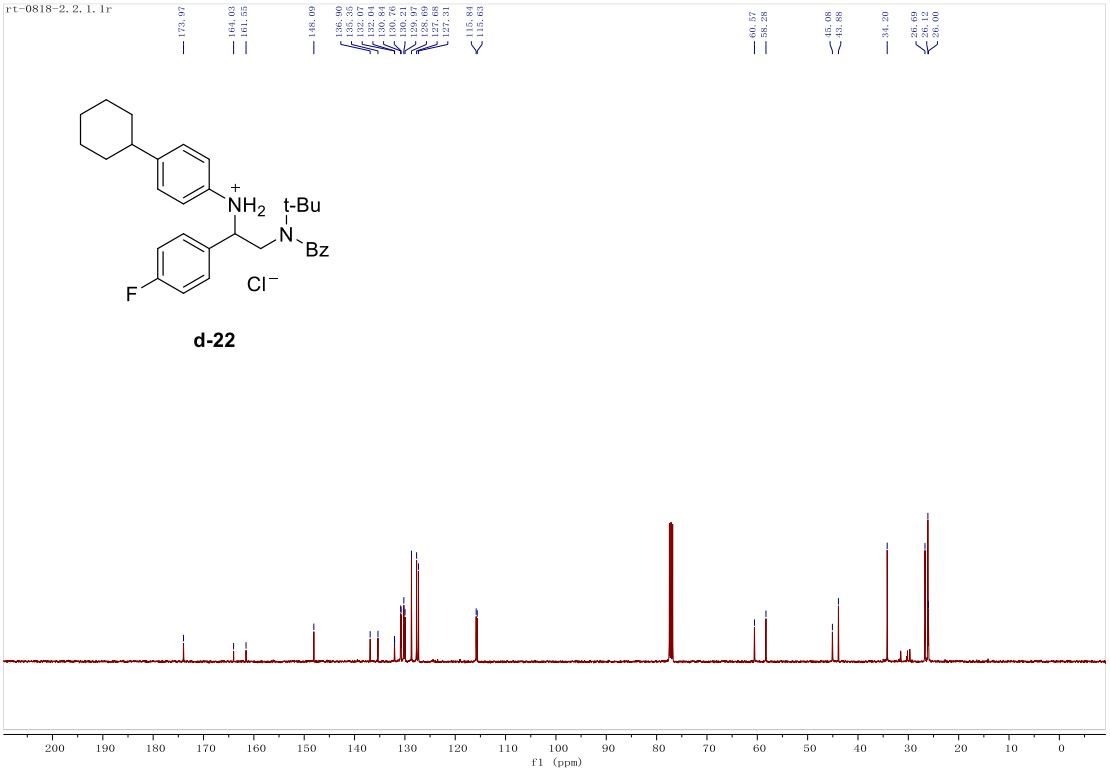
^{13}C NMR (101 MHz)



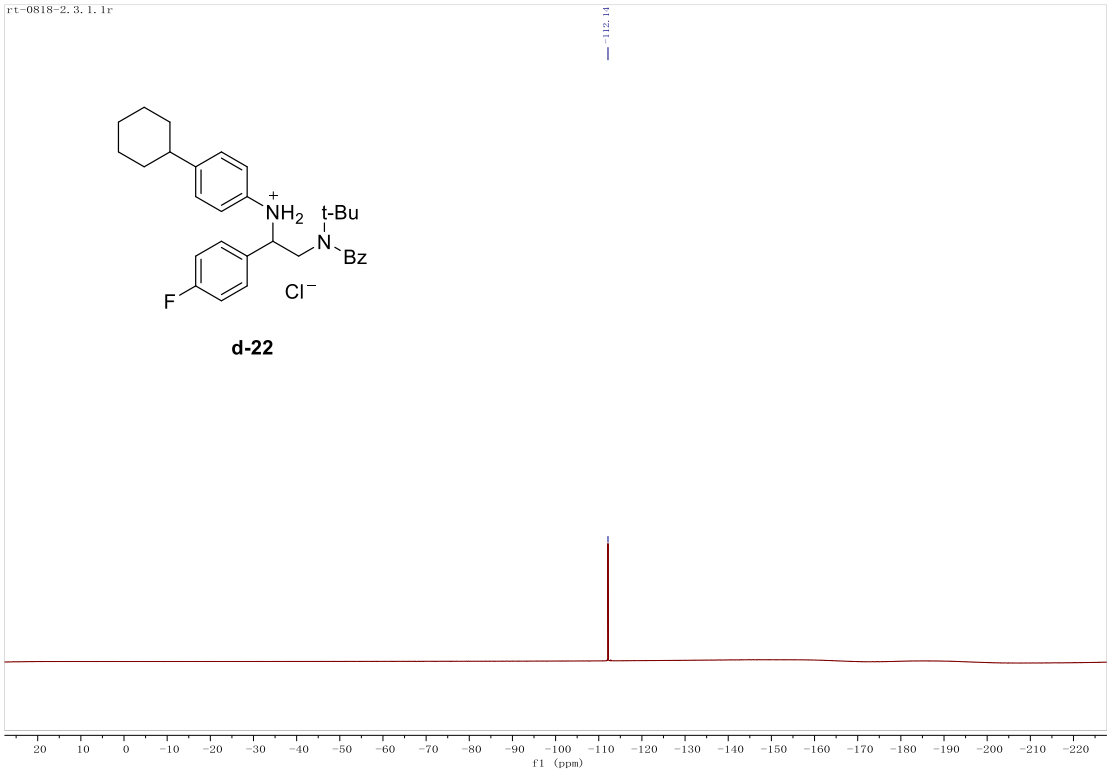
d-22 ^{1}H NMR (400 MHz)



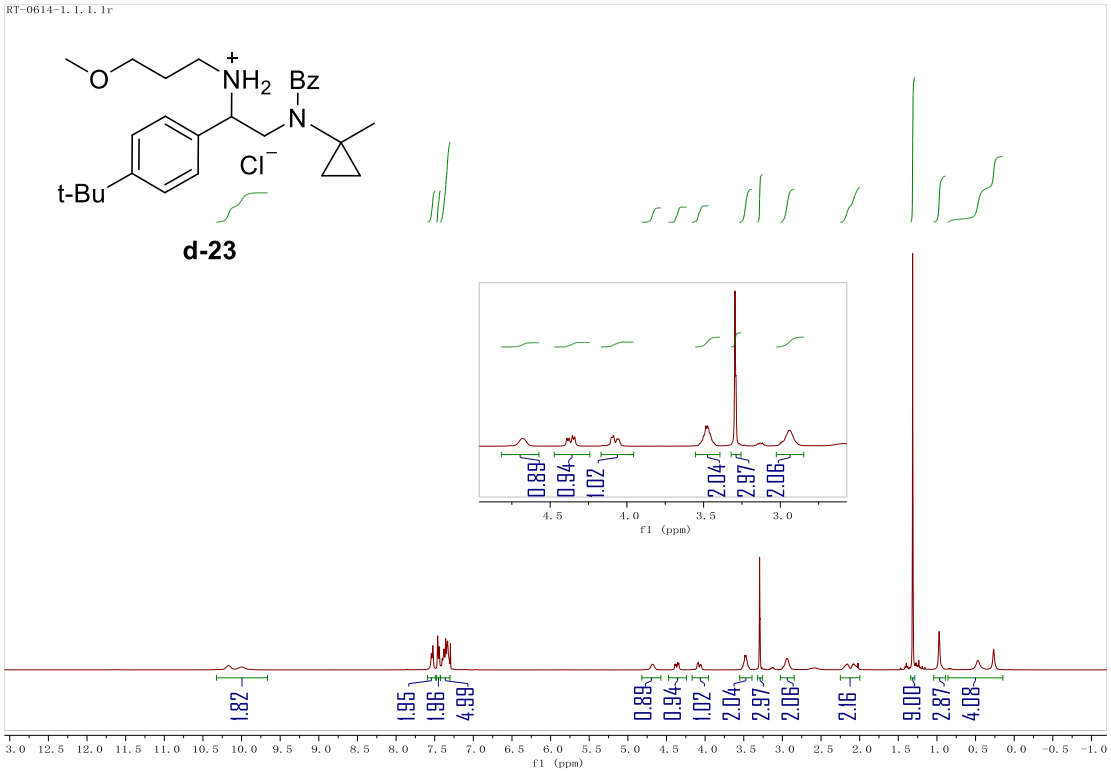
^{13}C NMR (101 MHz)



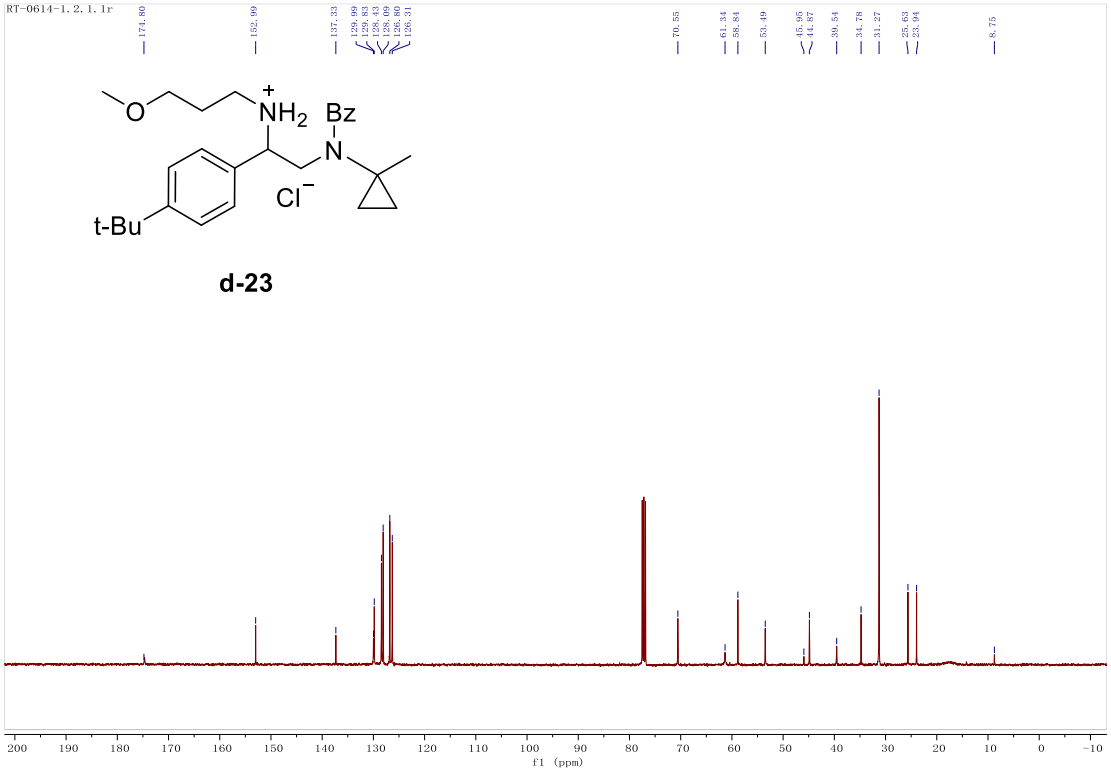
^{19}F NMR (376 MHz)



d-23 ^{1}H NMR (400 MHz)

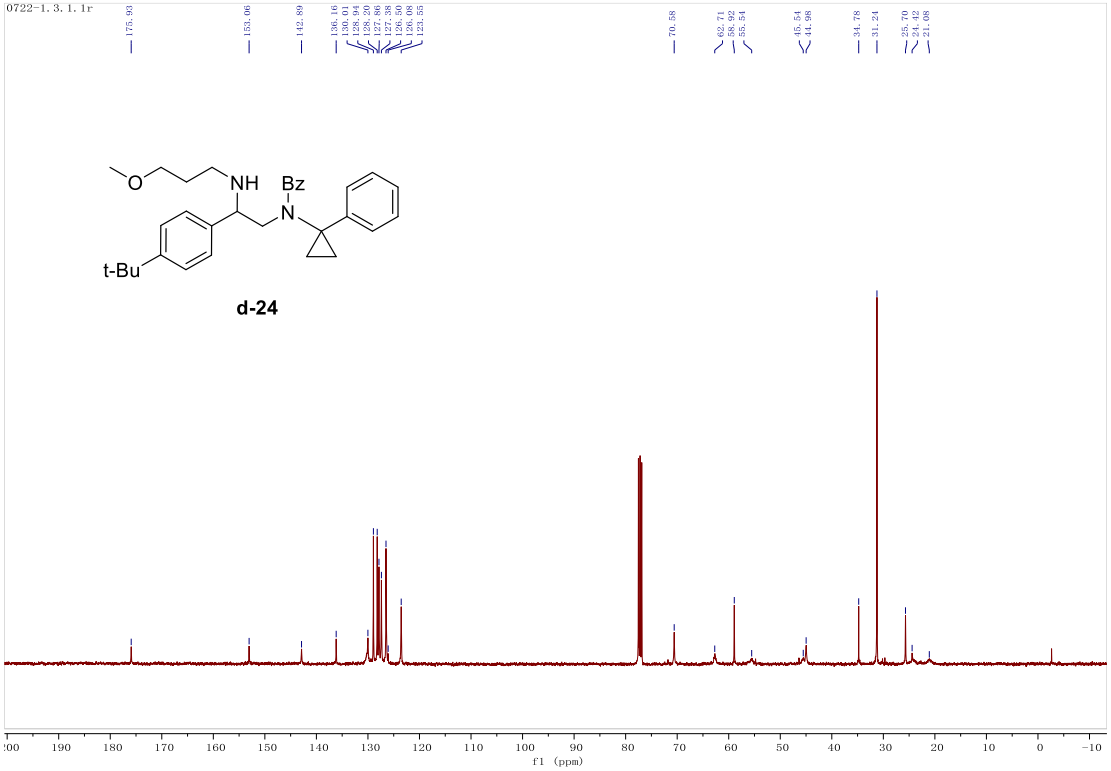


^{13}C NMR (101 MHz)

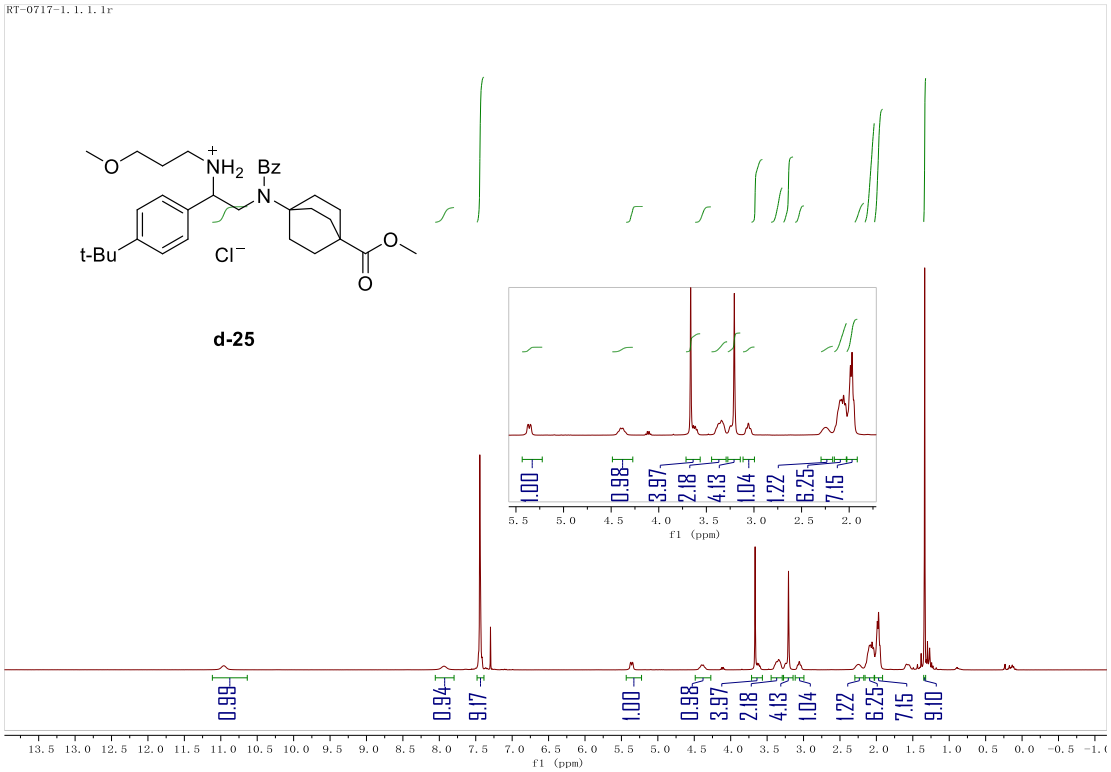


d-24 ^{1}H NMR (400 MHz)

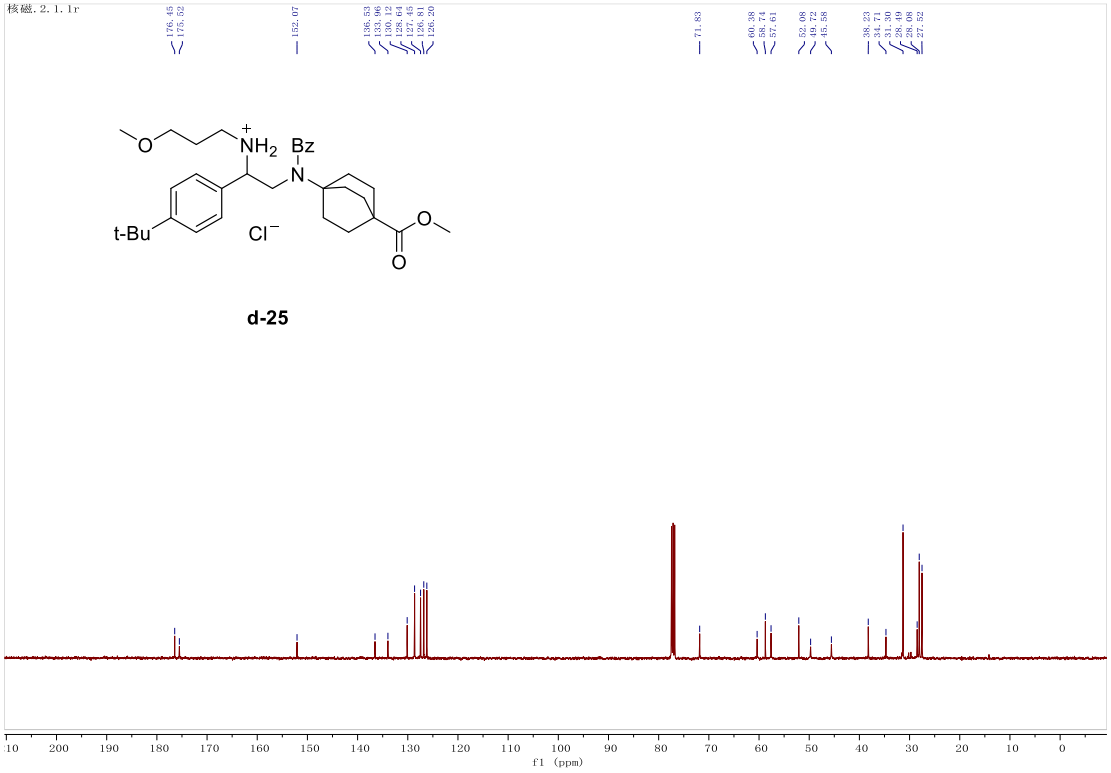
^{13}C NMR (101 MHz)



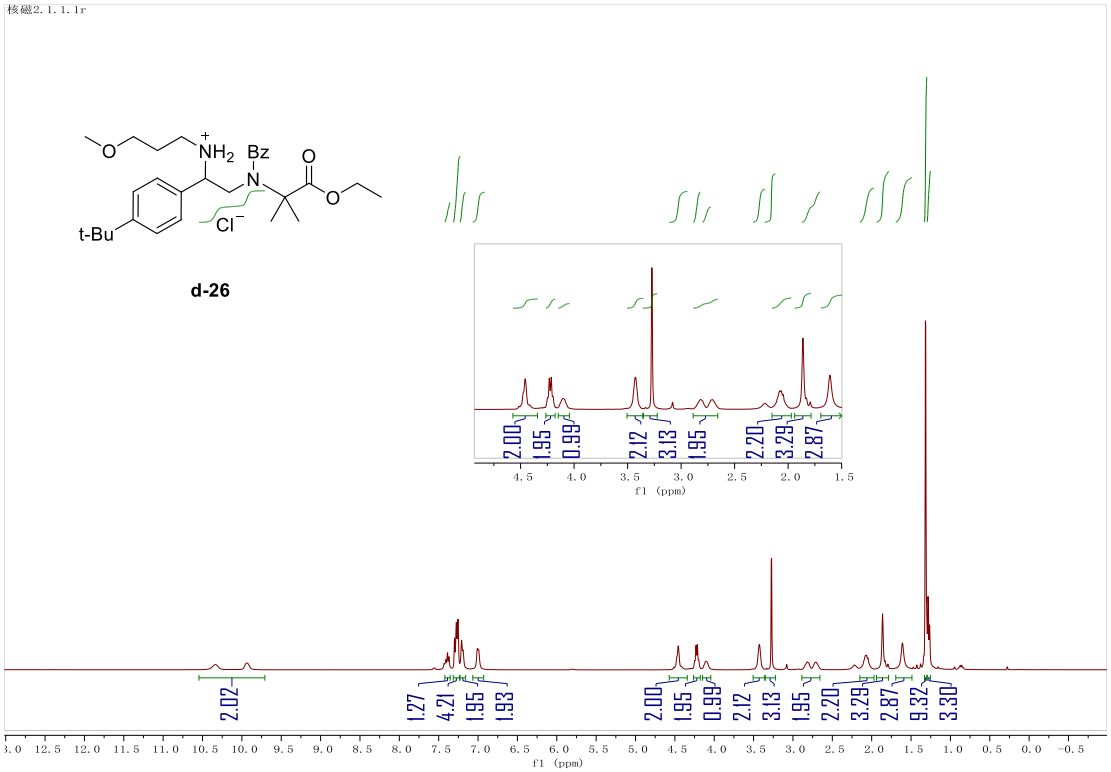
d-25 ^{1}H NMR (400 MHz)



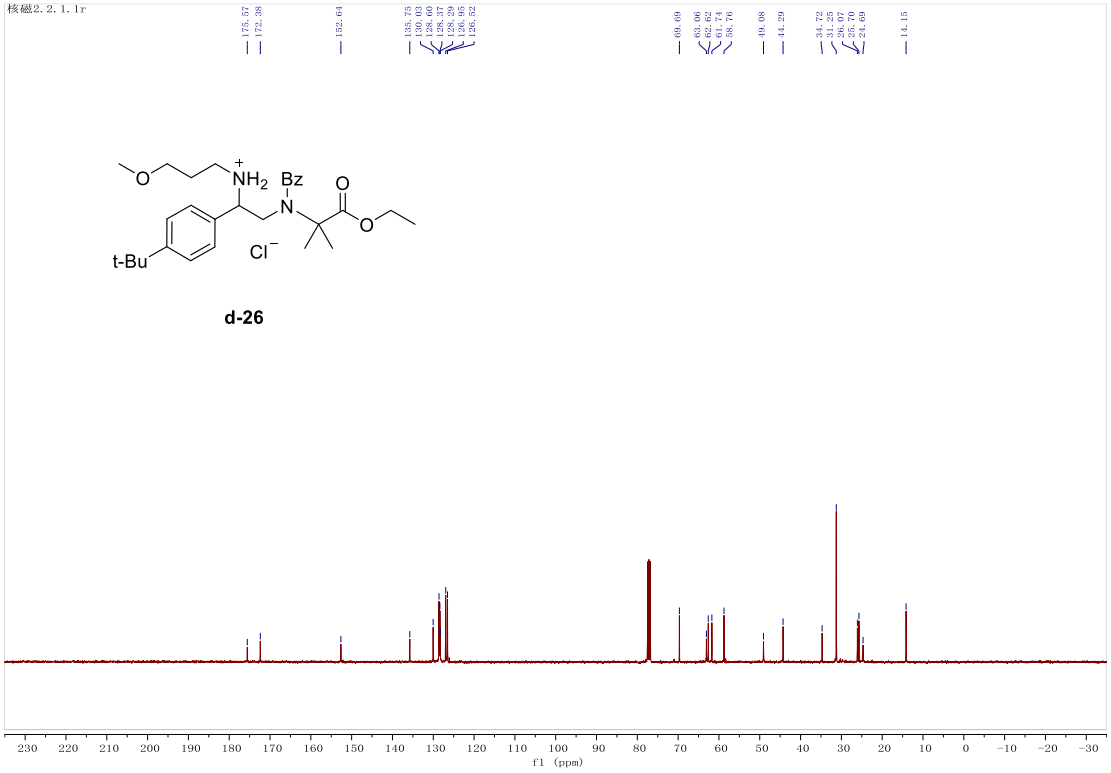
^{13}C NMR (101 MHz)



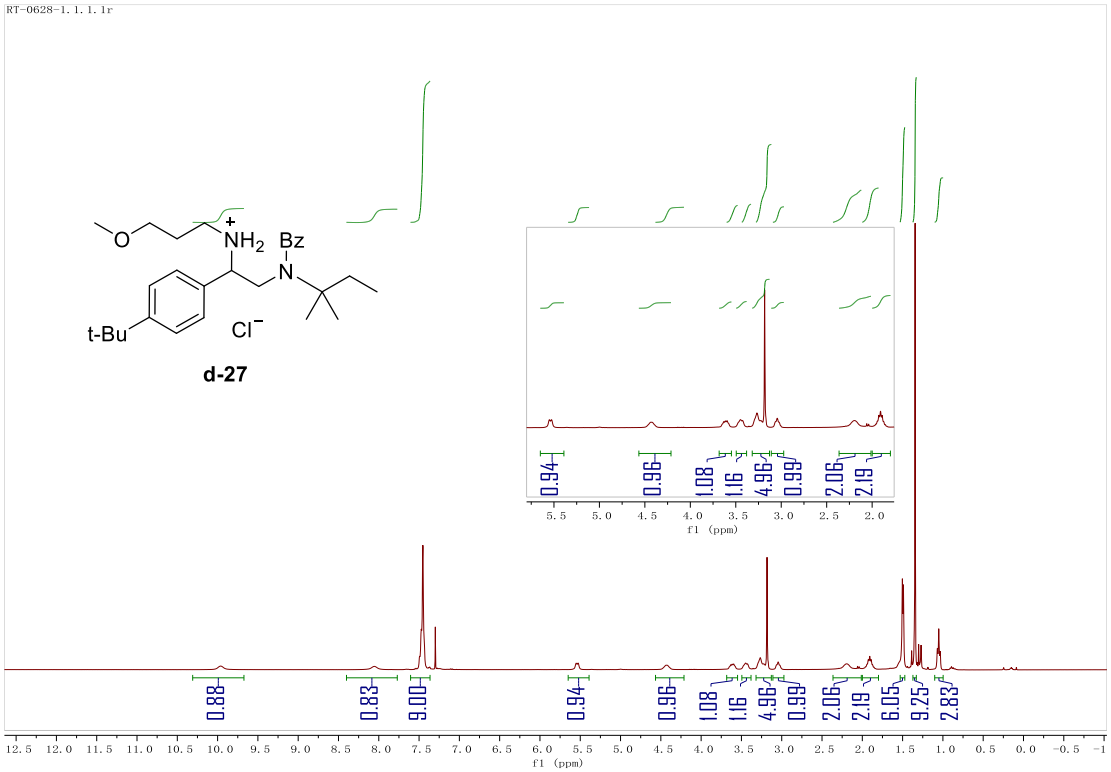
d-26 ^{1}H NMR (400 MHz)



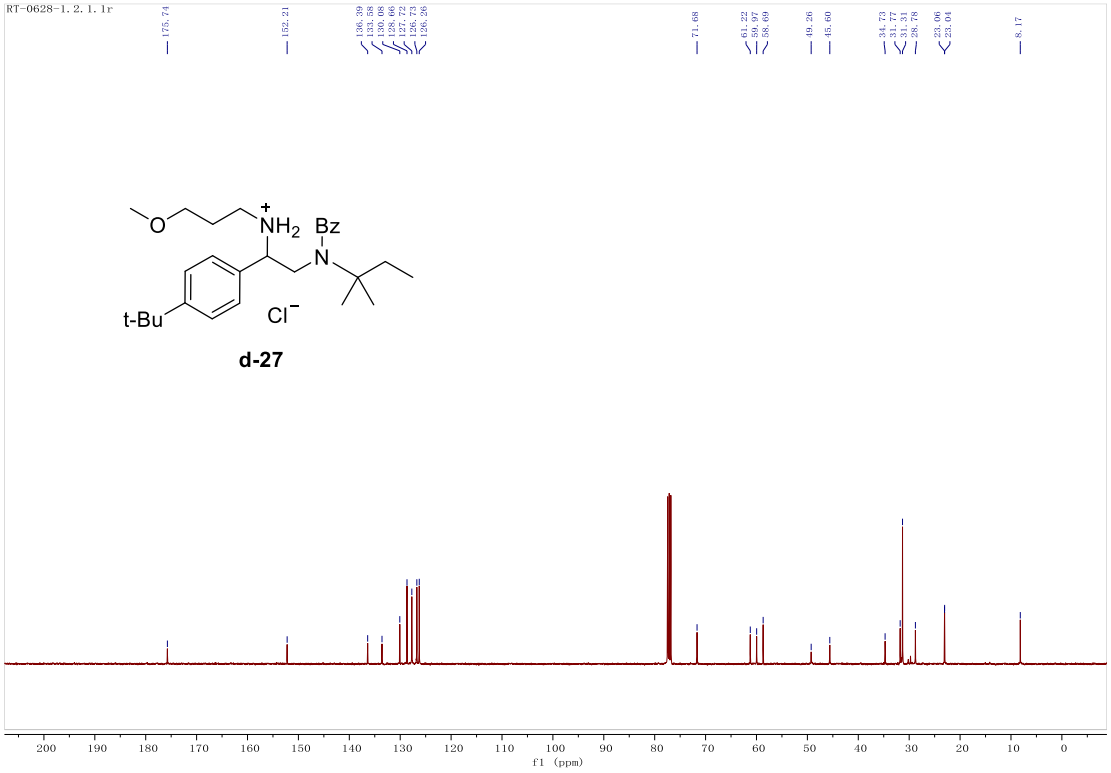
^{13}C NMR (101 MHz)



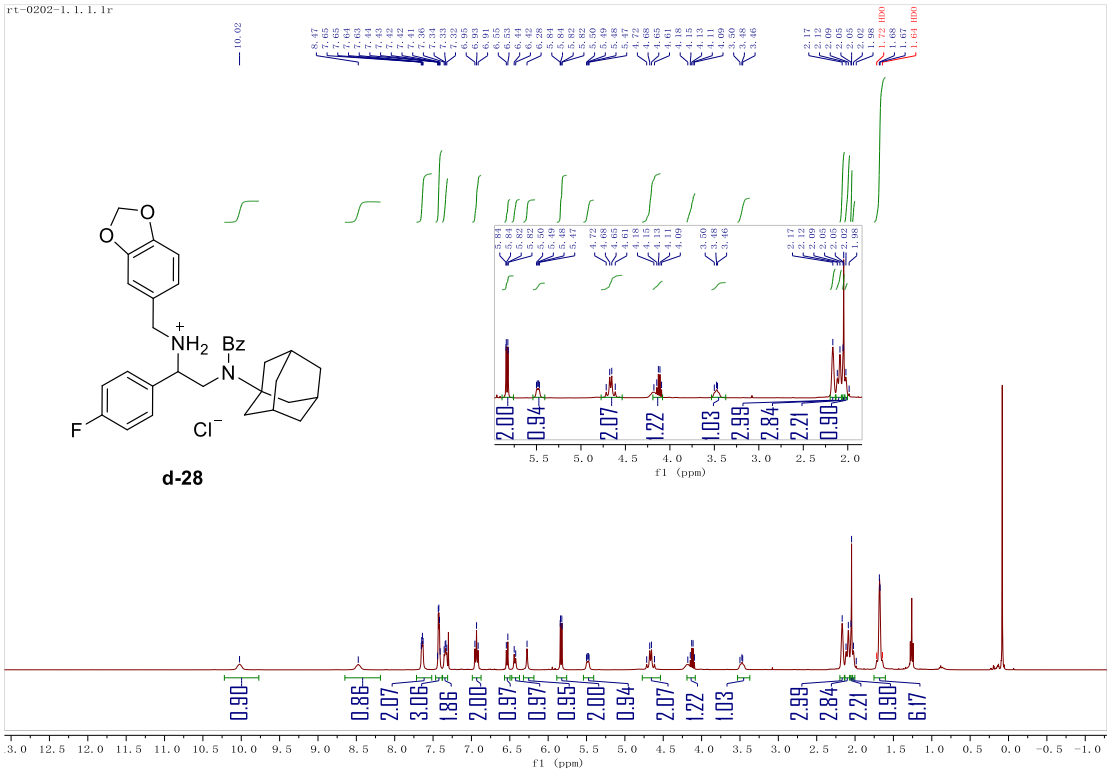
d-27 ^{1}H NMR (400 MHz)



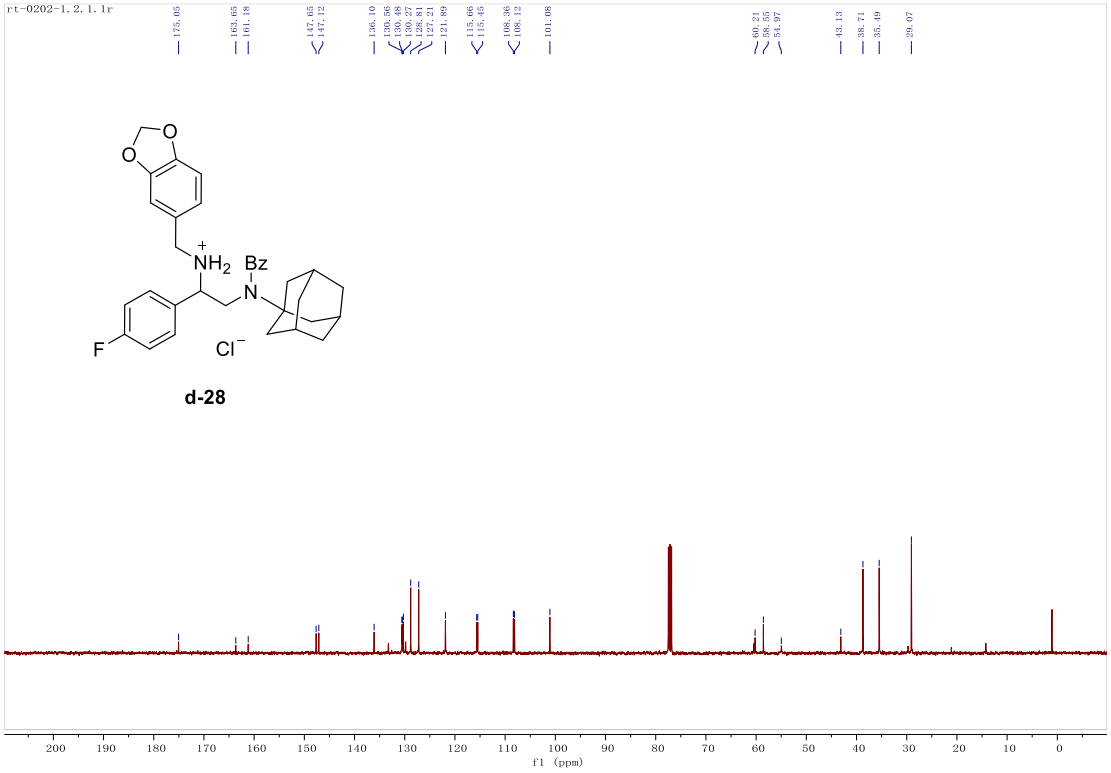
^{13}C NMR (101 MHz)



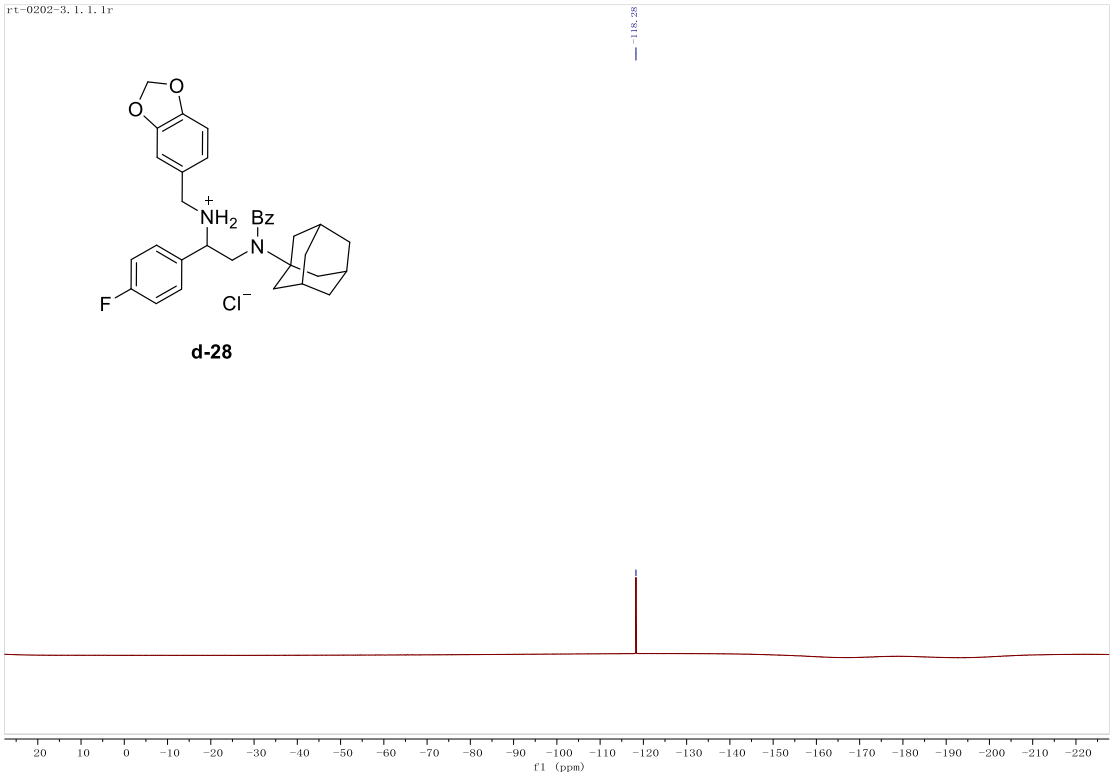
d-28 ^{1}H NMR (400 MHz)



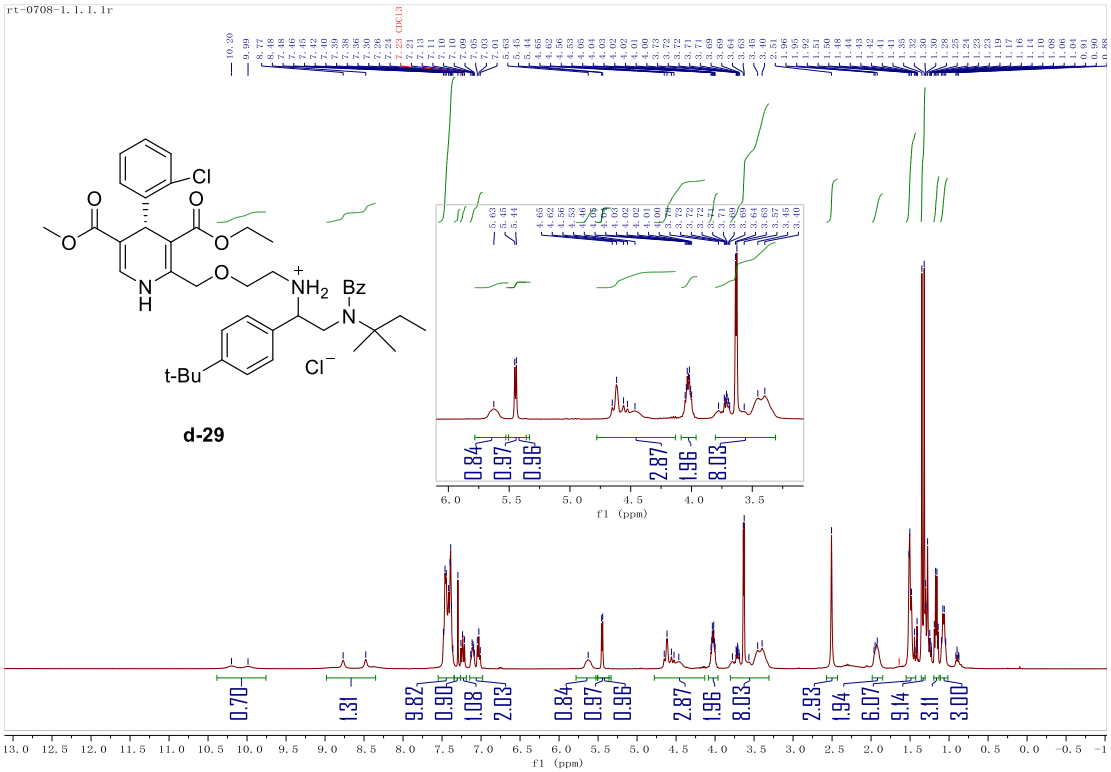
^{13}C NMR (101 MHz)



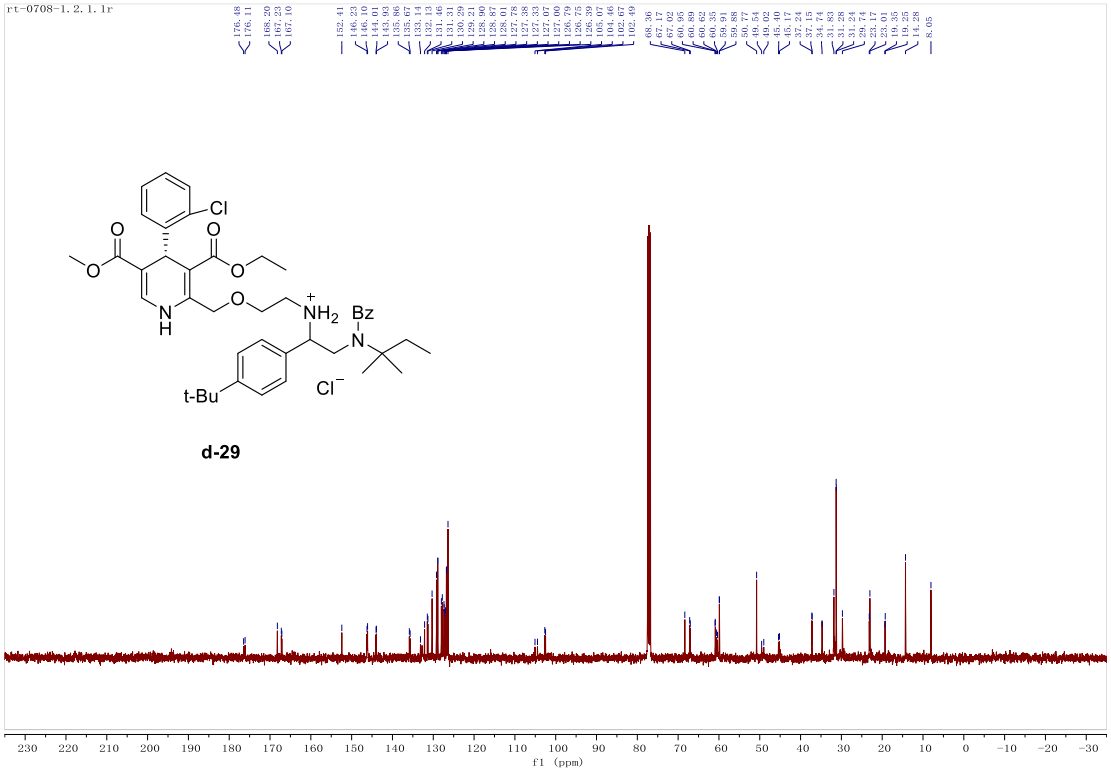
^{19}F NMR (376 MHz)



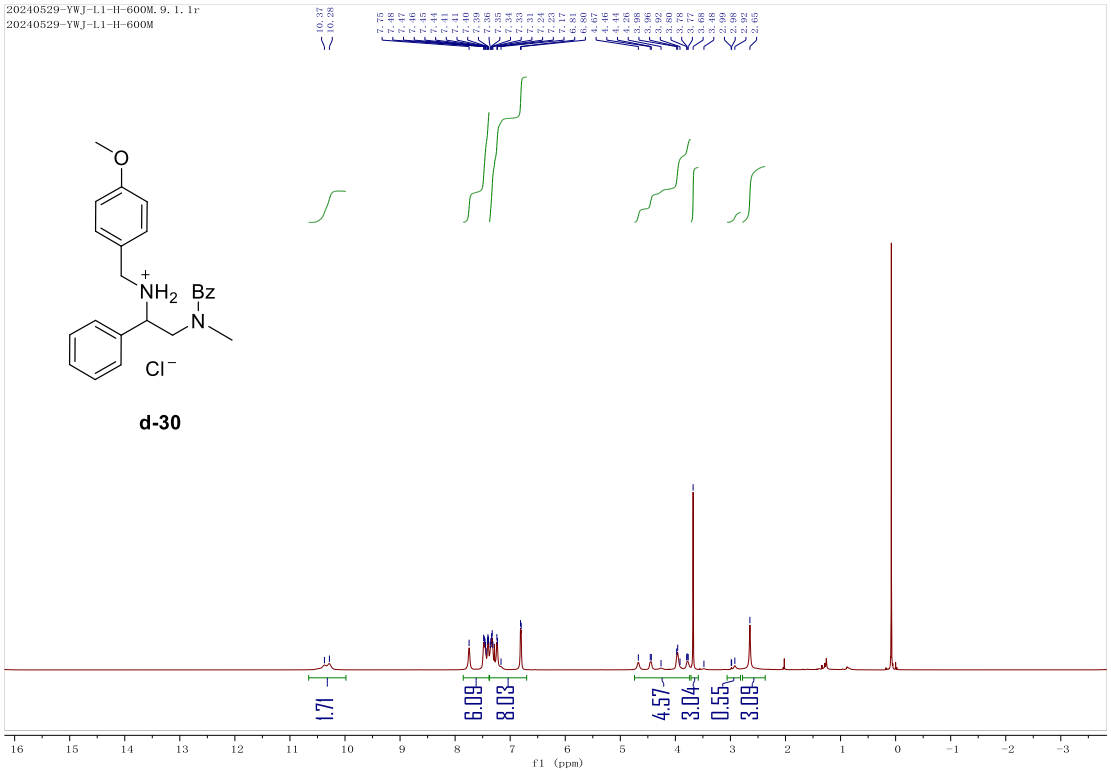
d-29 ^{1}H NMR (400 MHz)



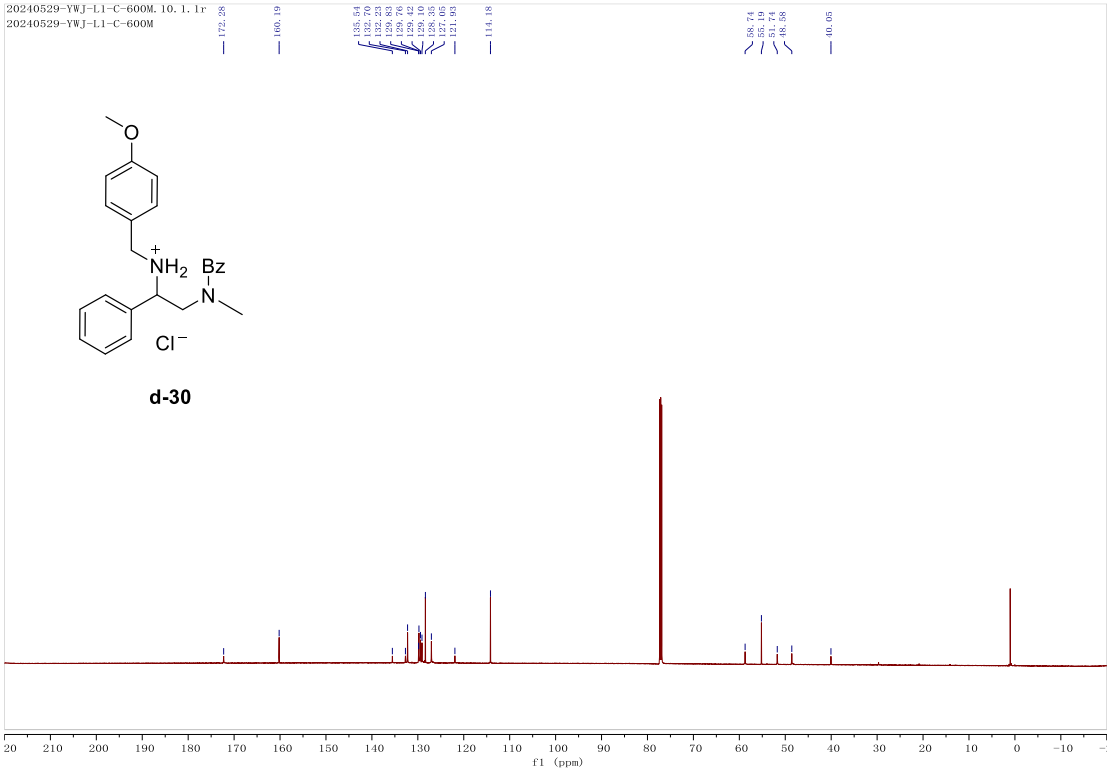
^{13}C NMR (101 MHz)



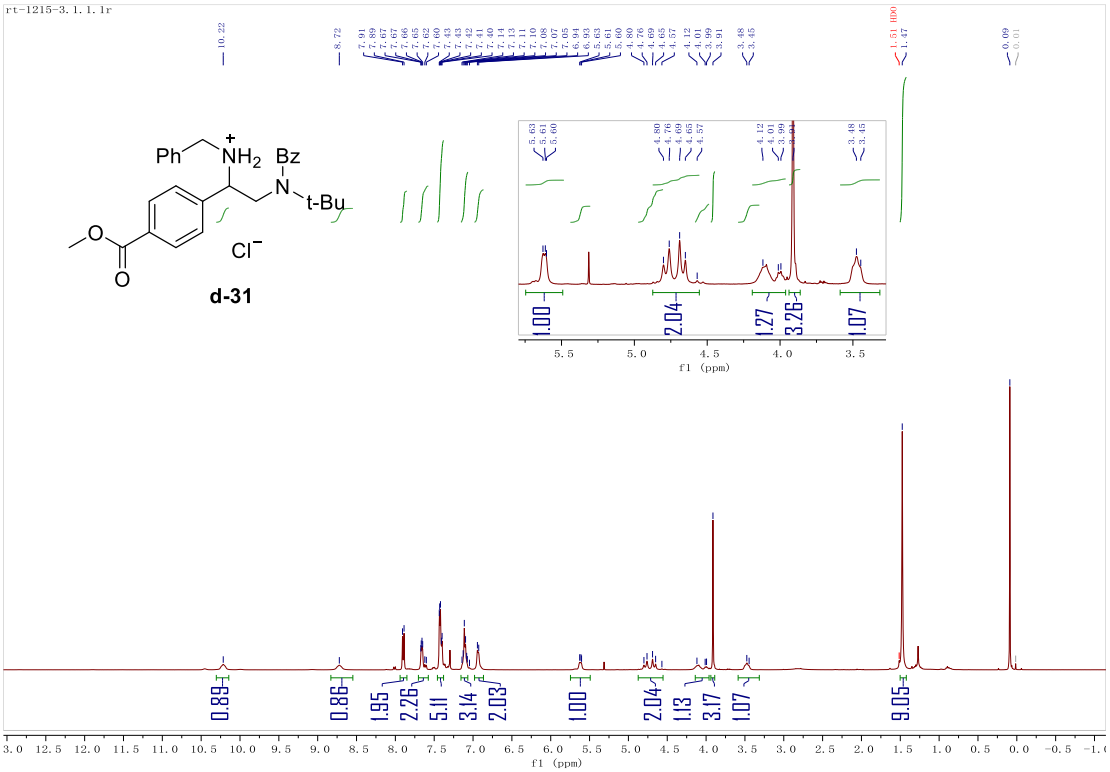
d-30 ^{1}H NMR (400 MHz)



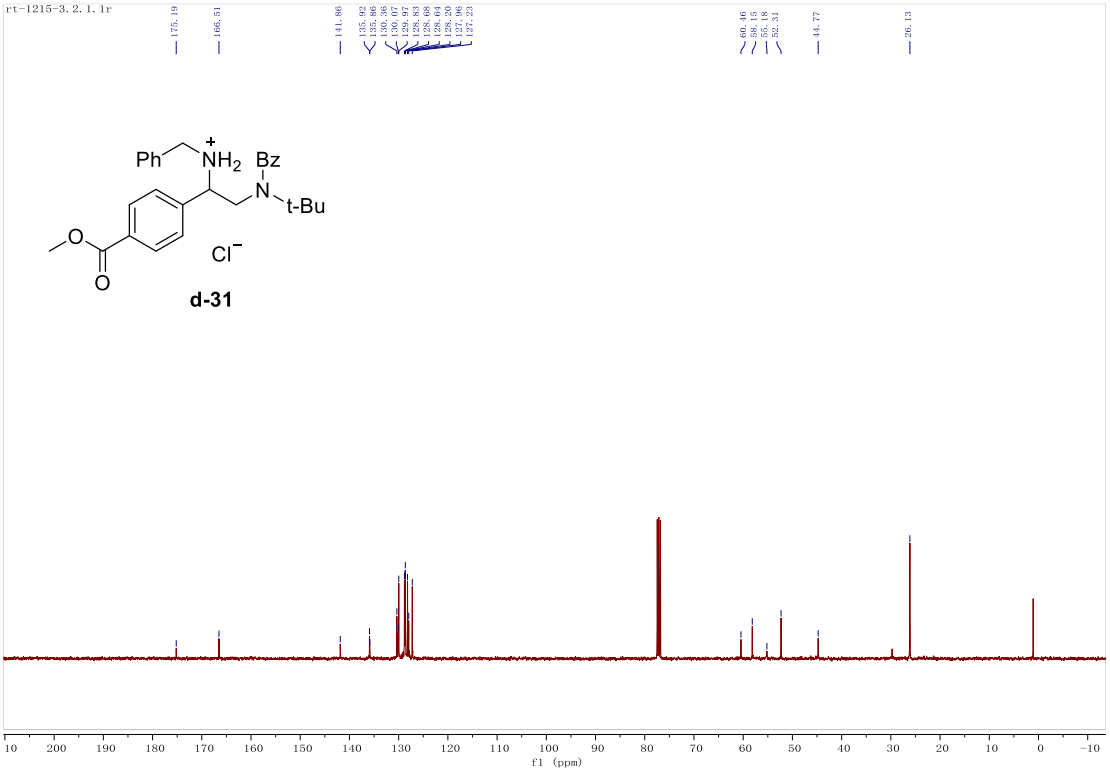
^{13}C NMR (101 MHz)



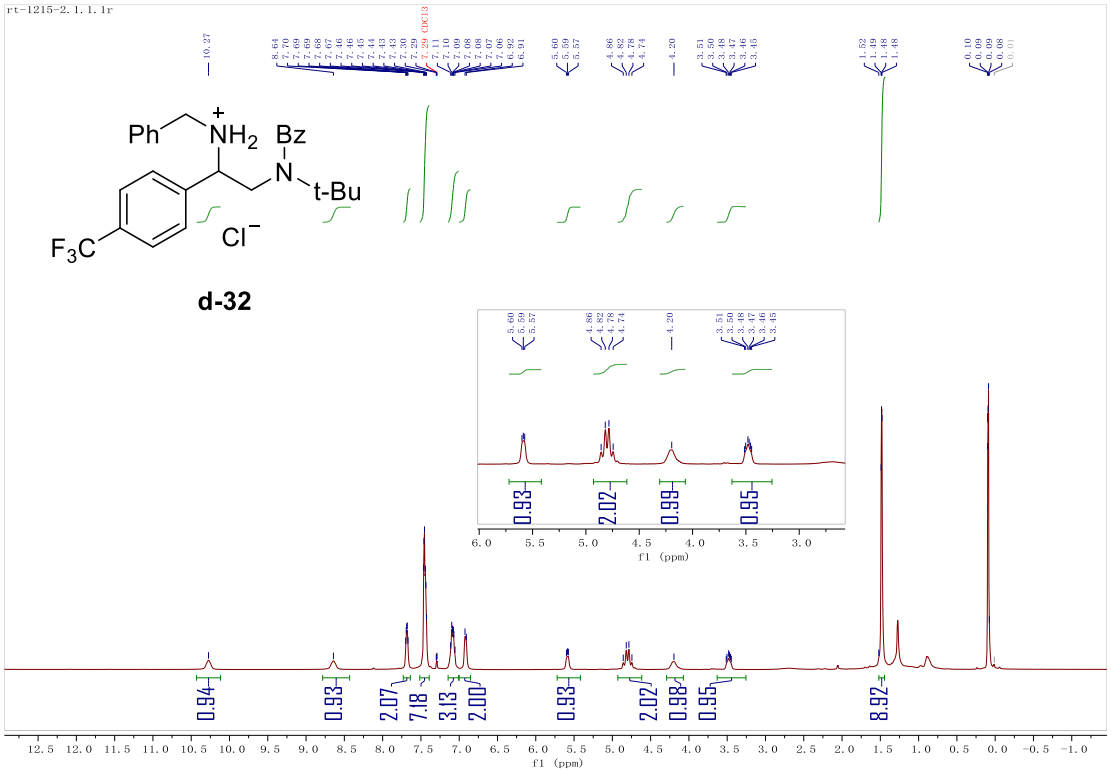
d-31 ^{1}H NMR (400 MHz)



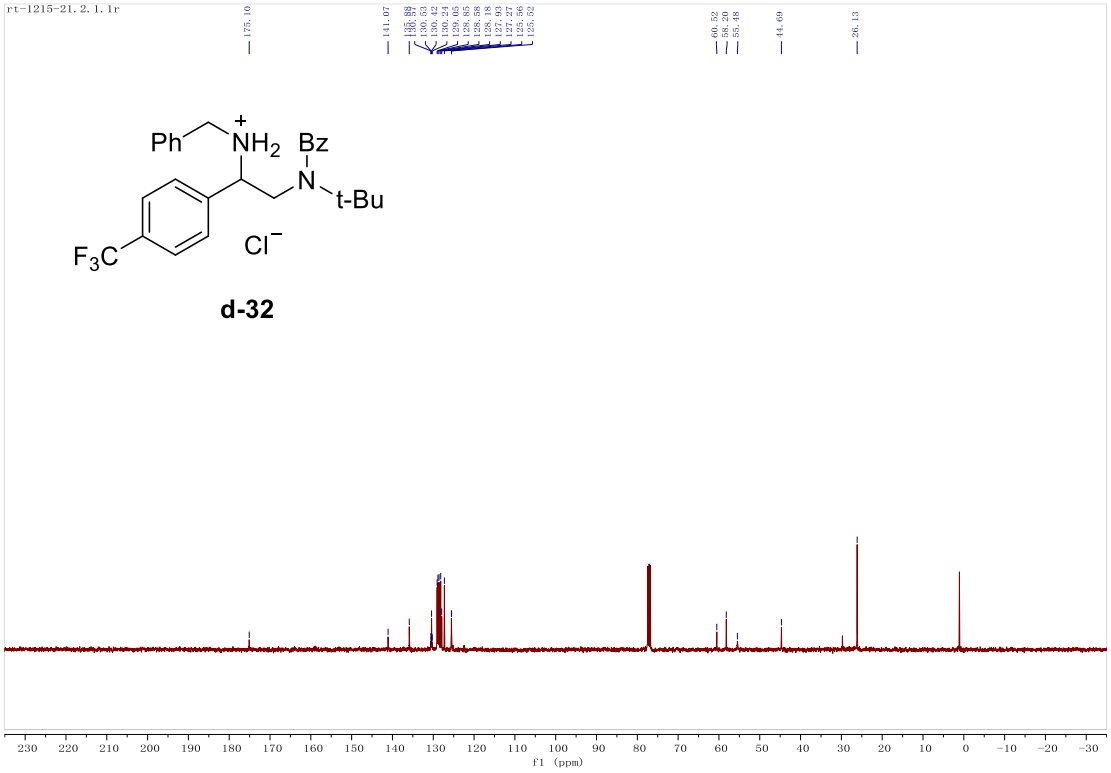
^{13}C NMR (101 MHz)



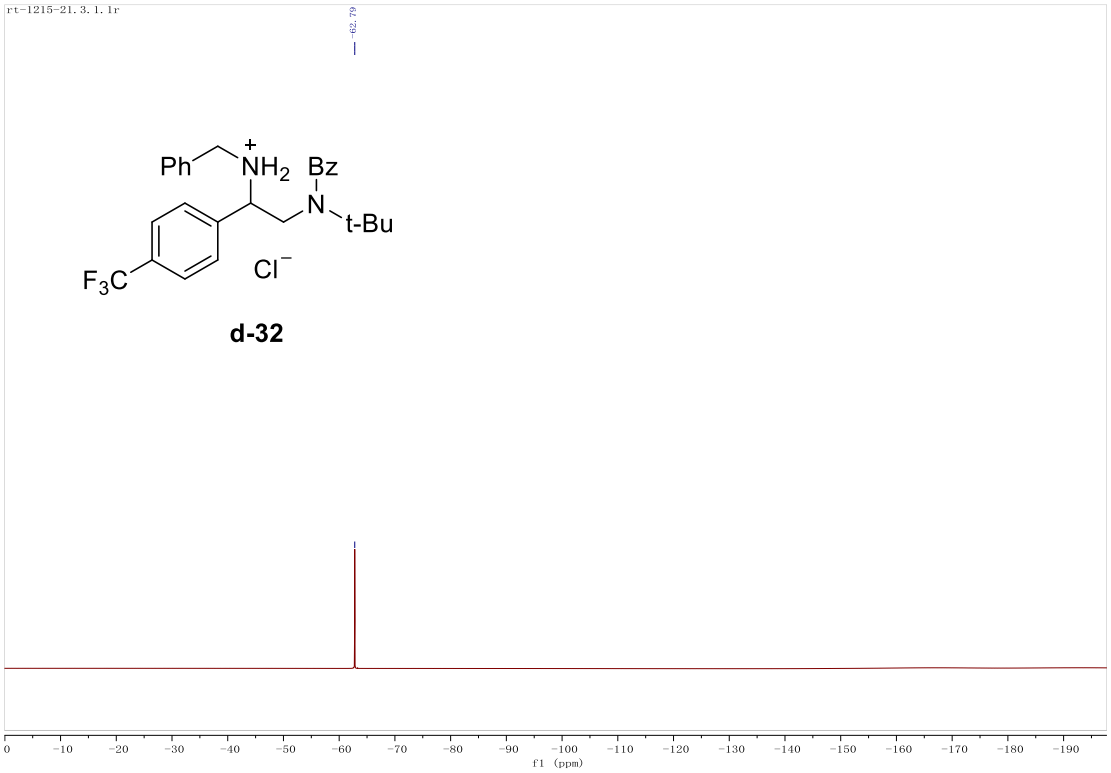
d-32 ^{1}H NMR (400 MHz)



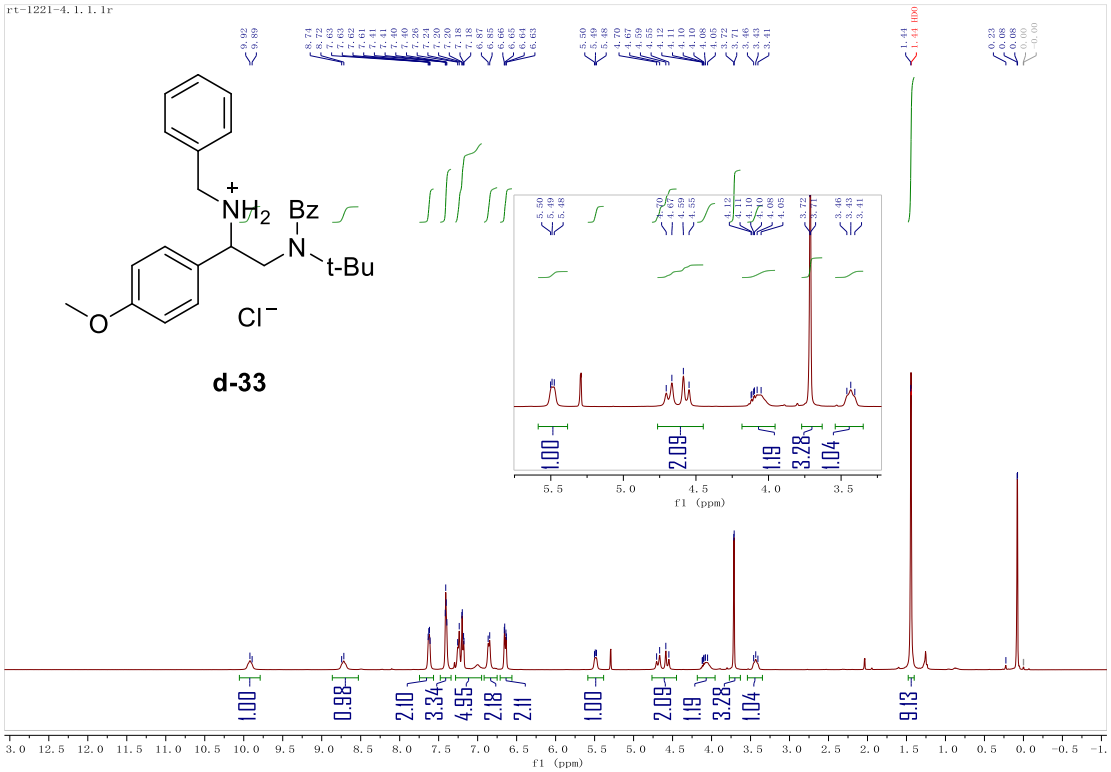
^{13}C NMR (101 MHz)



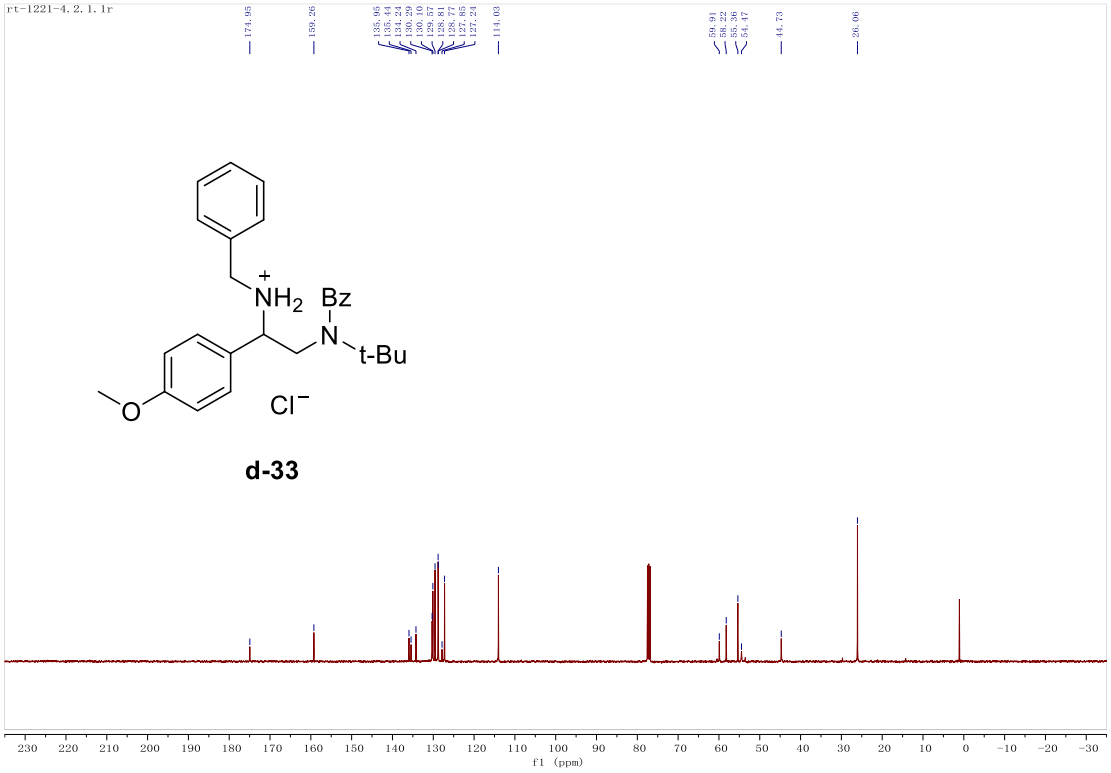
^{19}F NMR (376 MHz)



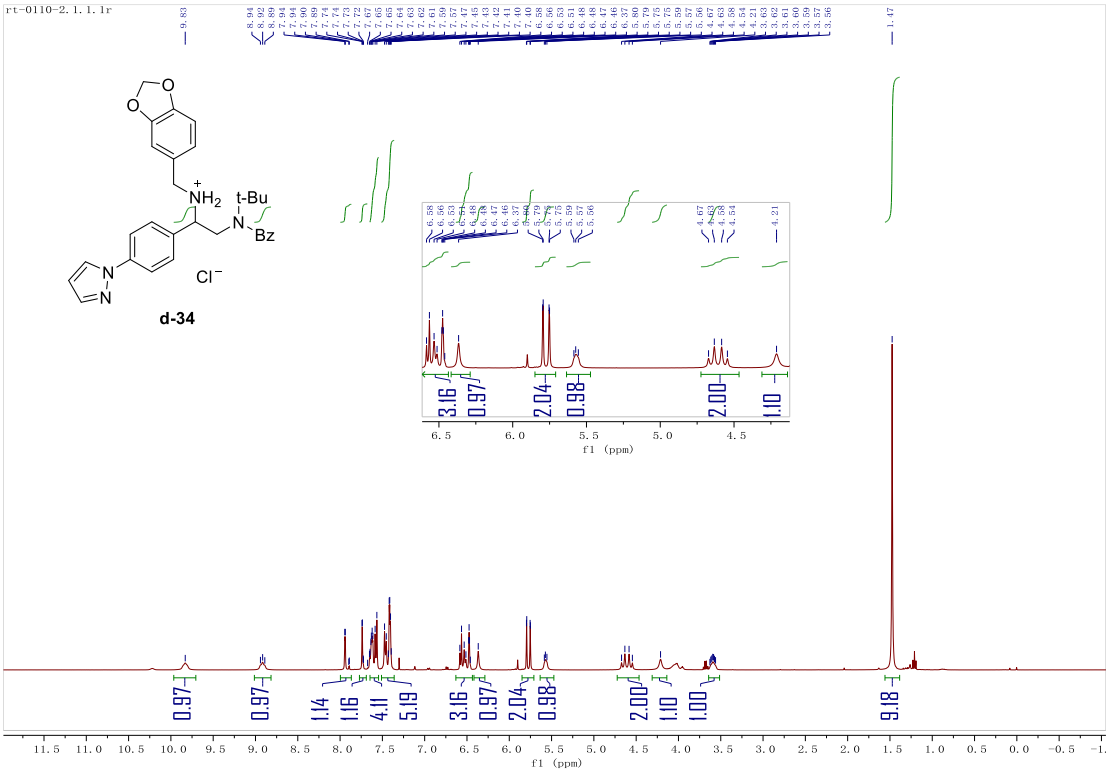
d-33 ^{1}H NMR (400 MHz)



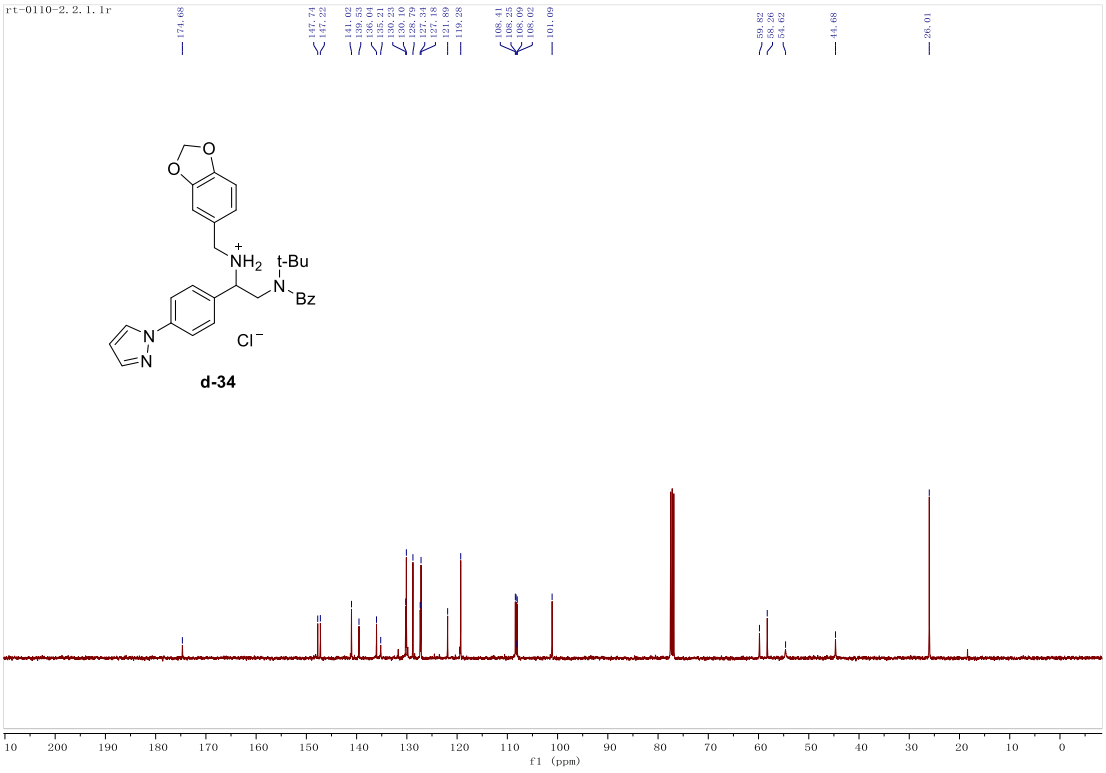
^{13}C NMR (101 MHz)



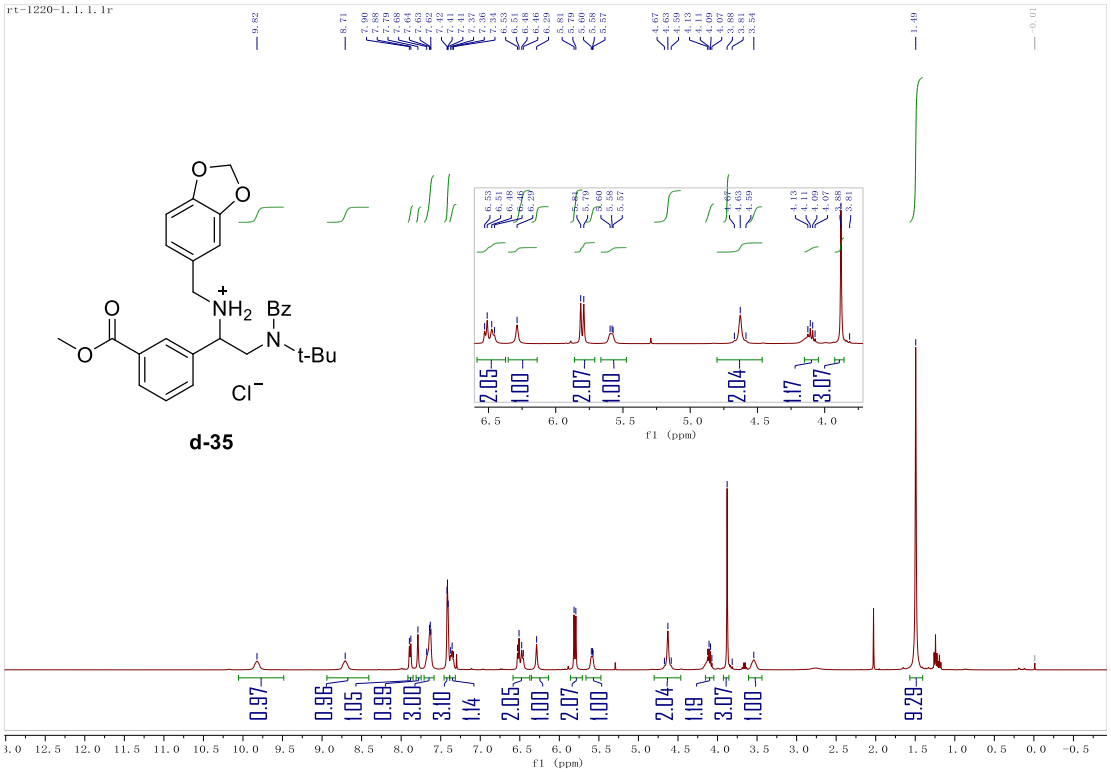
d-34 ^{1}H NMR (400 MHz)



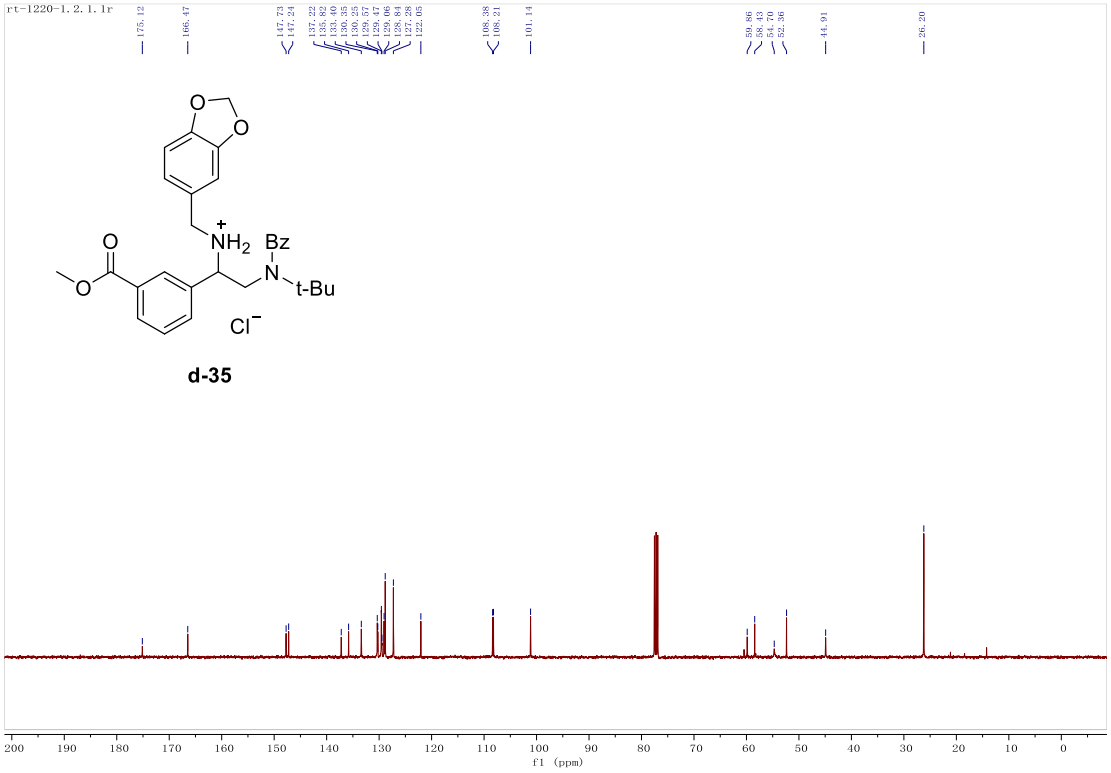
^{13}C NMR (101 MHz)



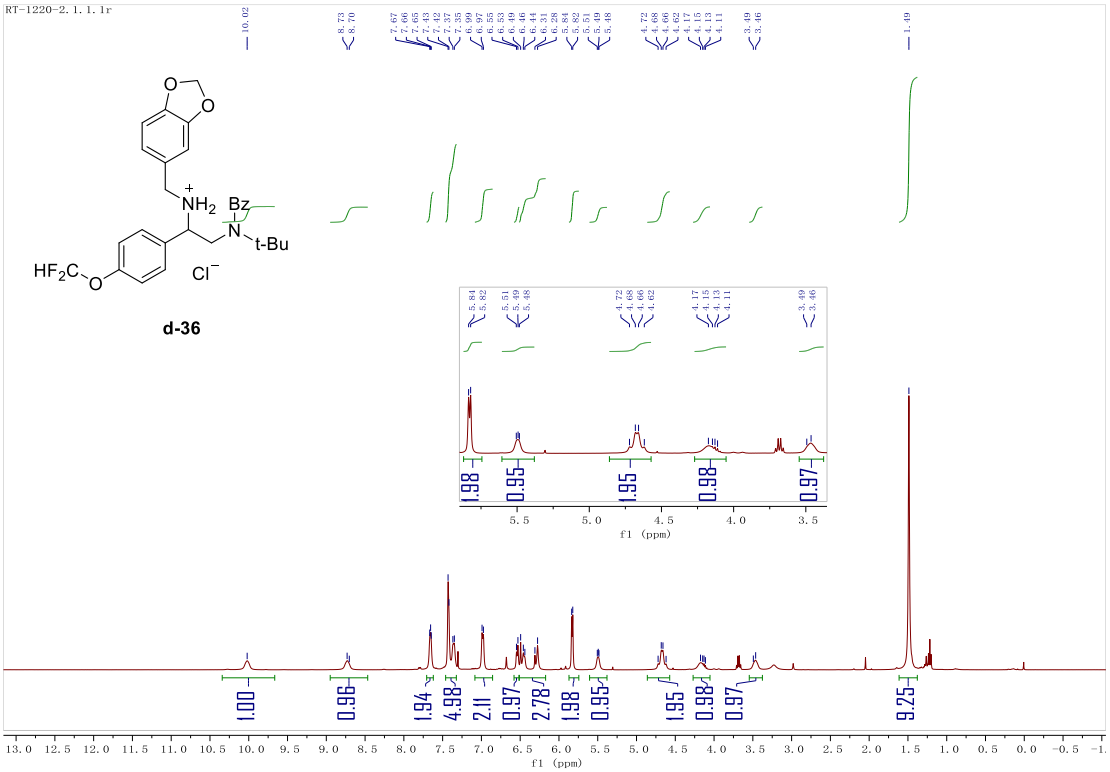
d-35 ^{1}H NMR (400 MHz)



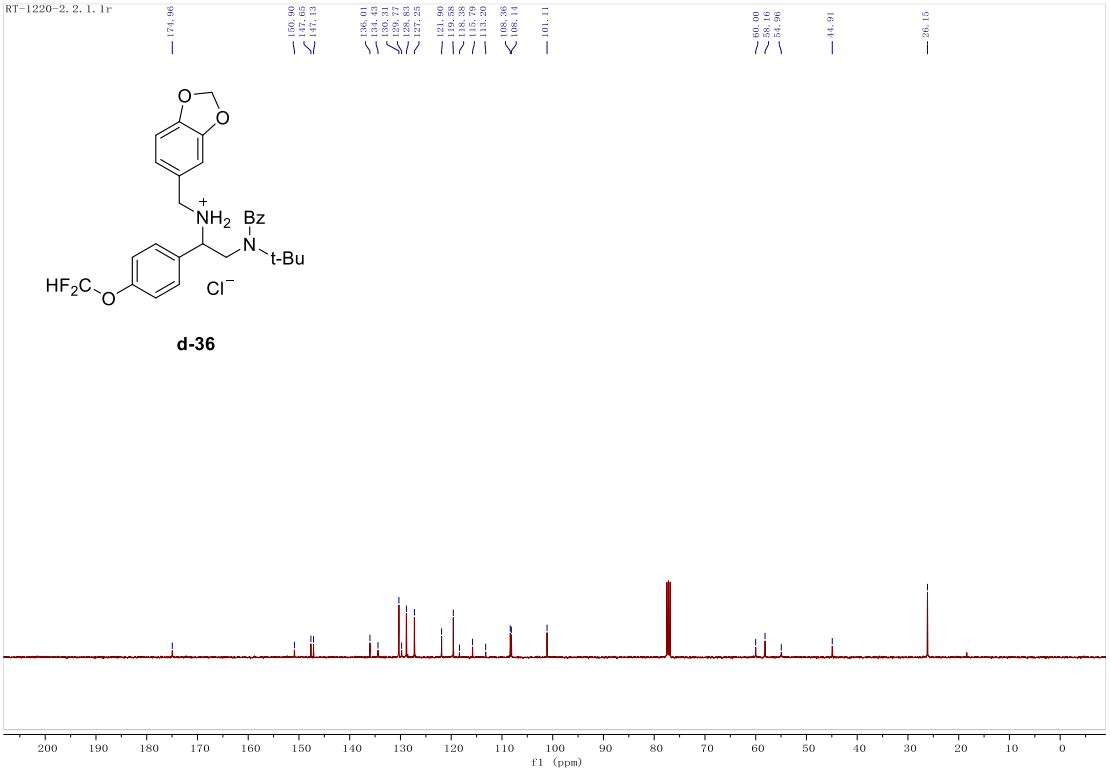
^{13}C NMR (101 MHz)



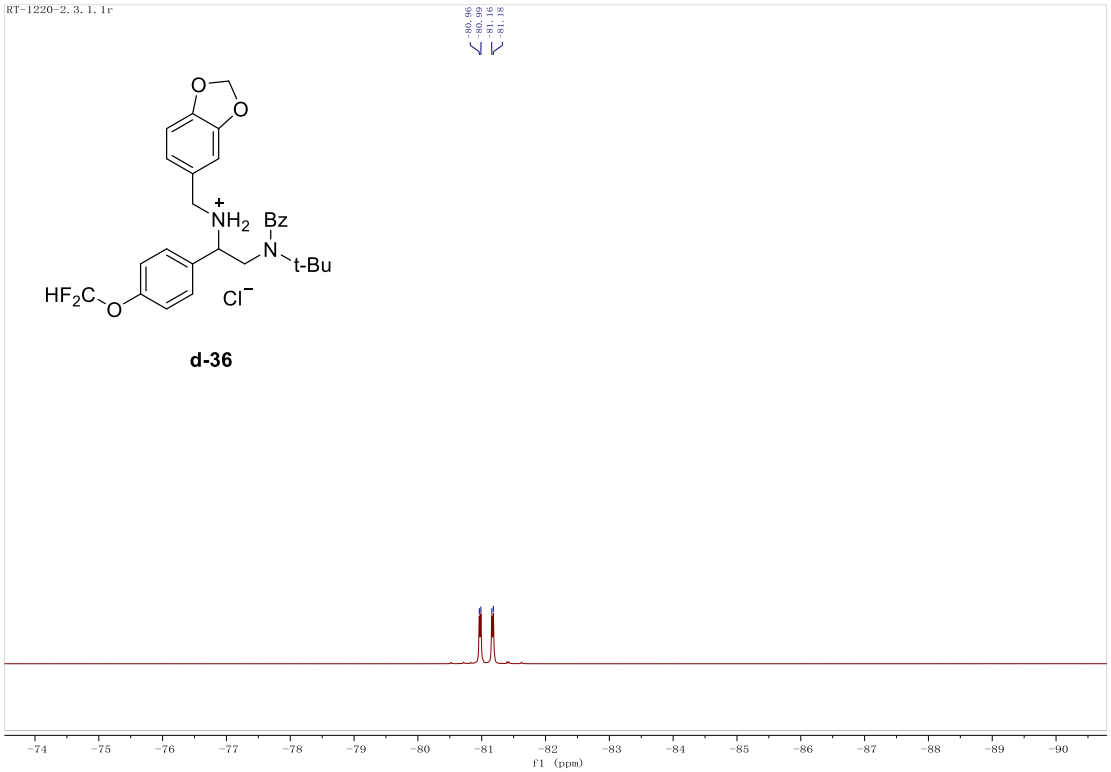
d-36 ^{1}H NMR (400 MHz)



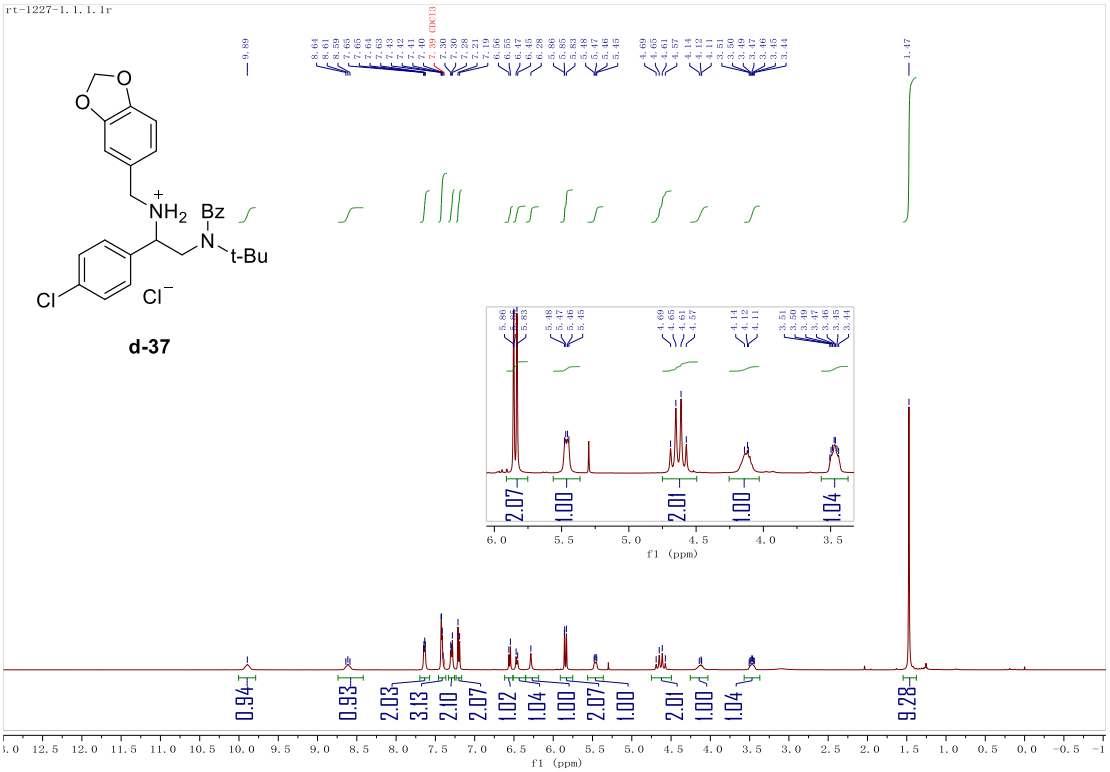
^{13}C NMR (101 MHz)



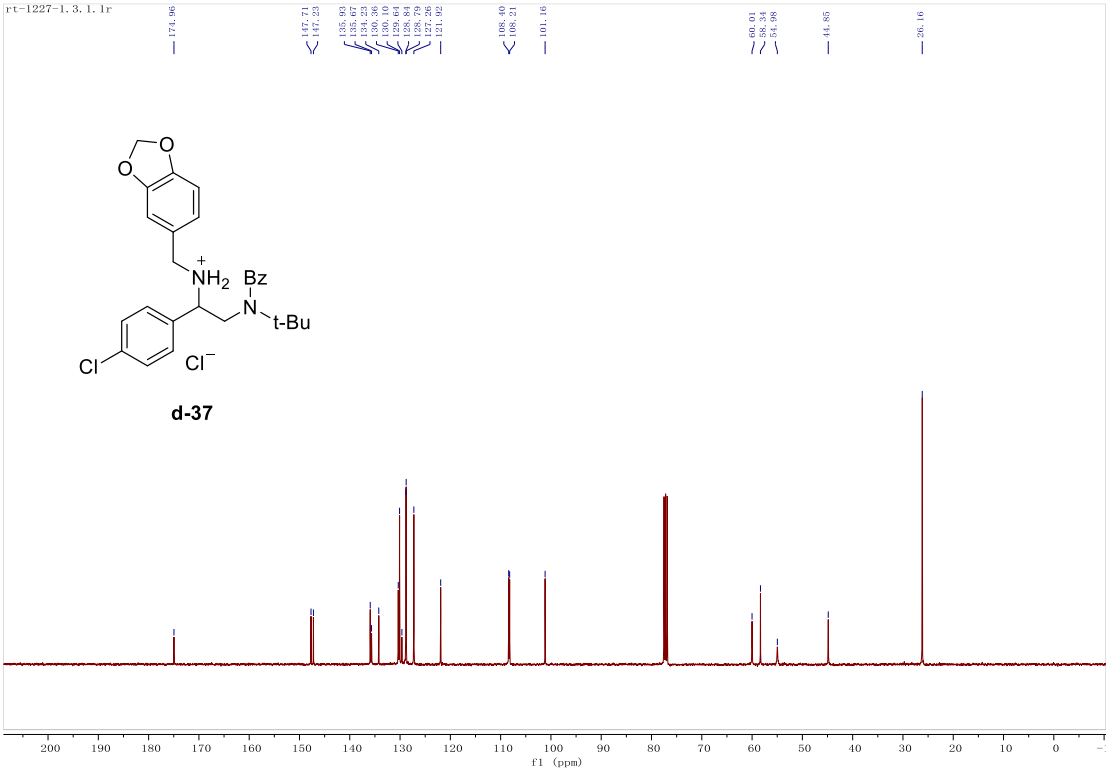
^{19}F NMR (376 MHz)



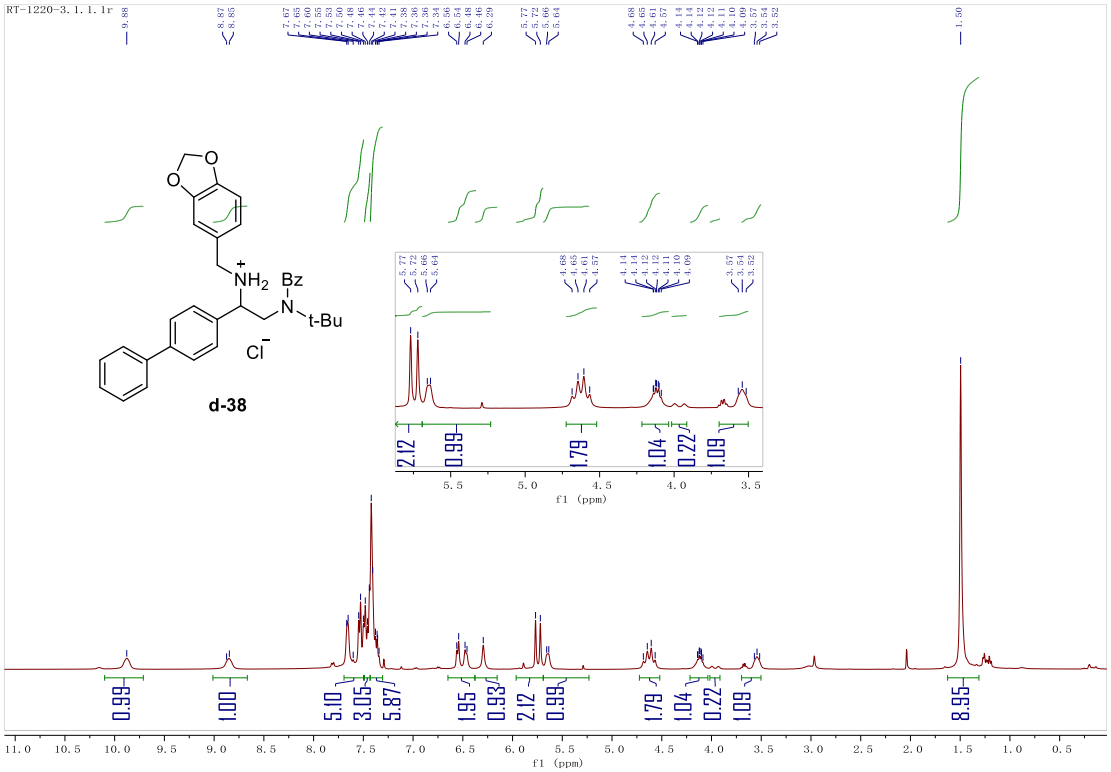
d-37 ^{1}H NMR (400 MHz)



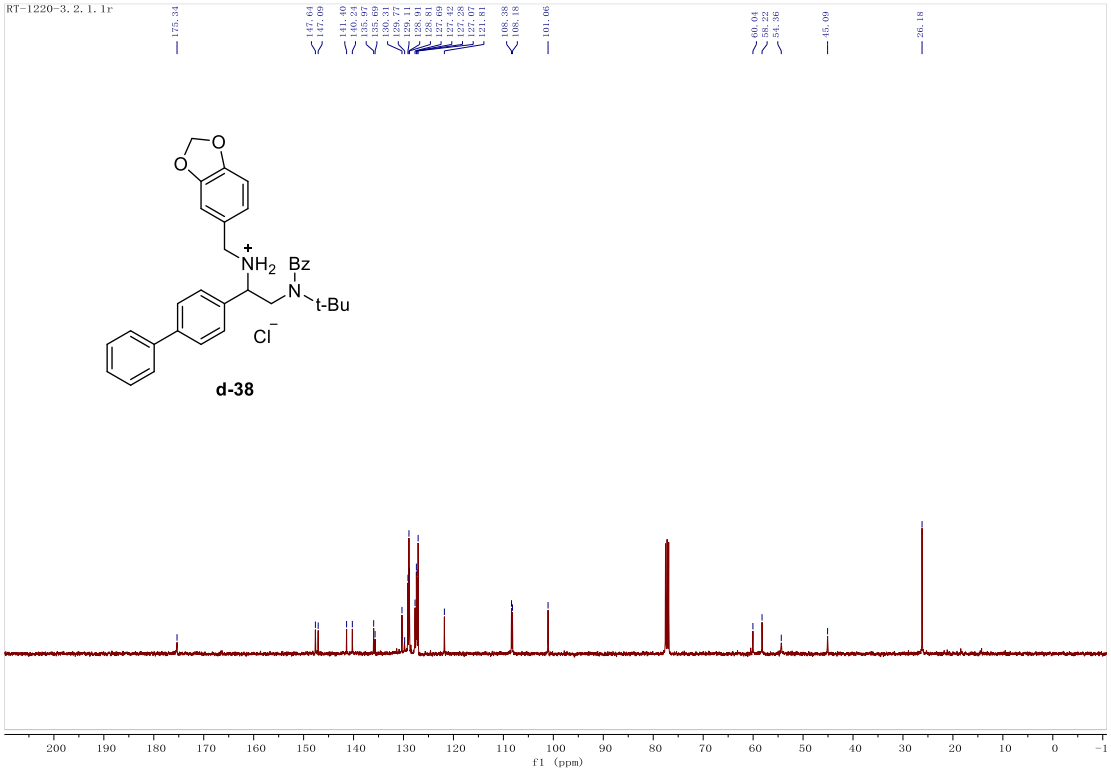
^{13}C NMR (101 MHz)



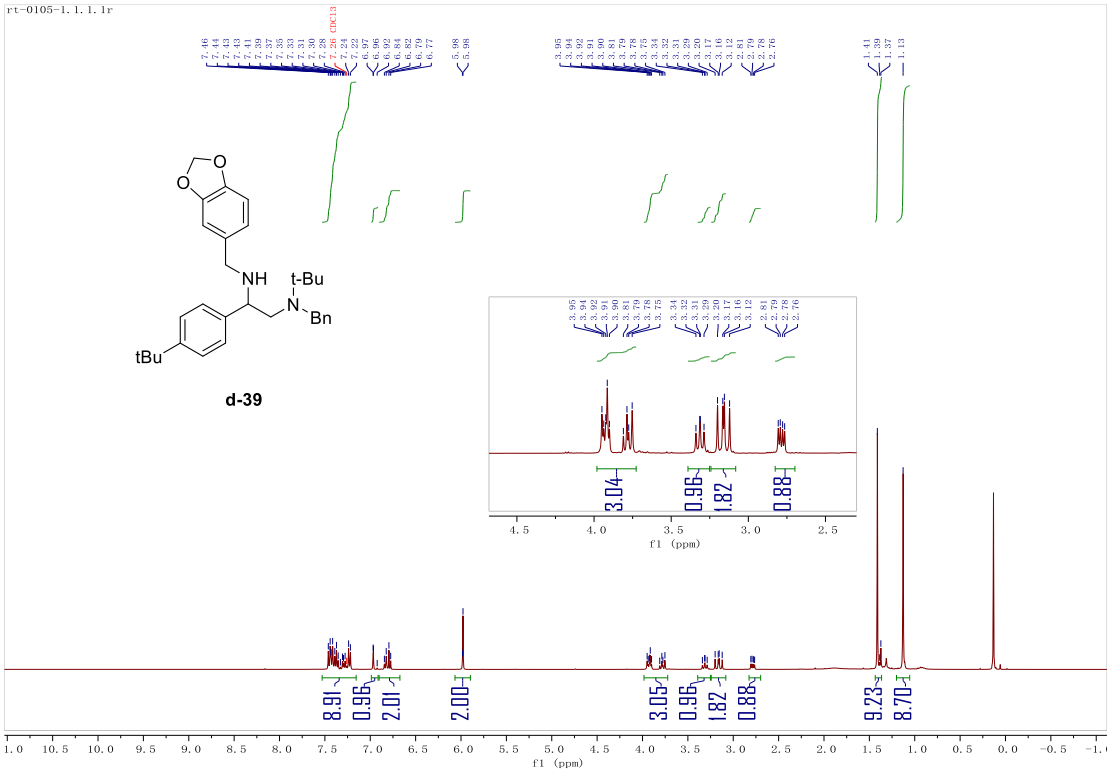
d-38 ^{1}H NMR (400 MHz)



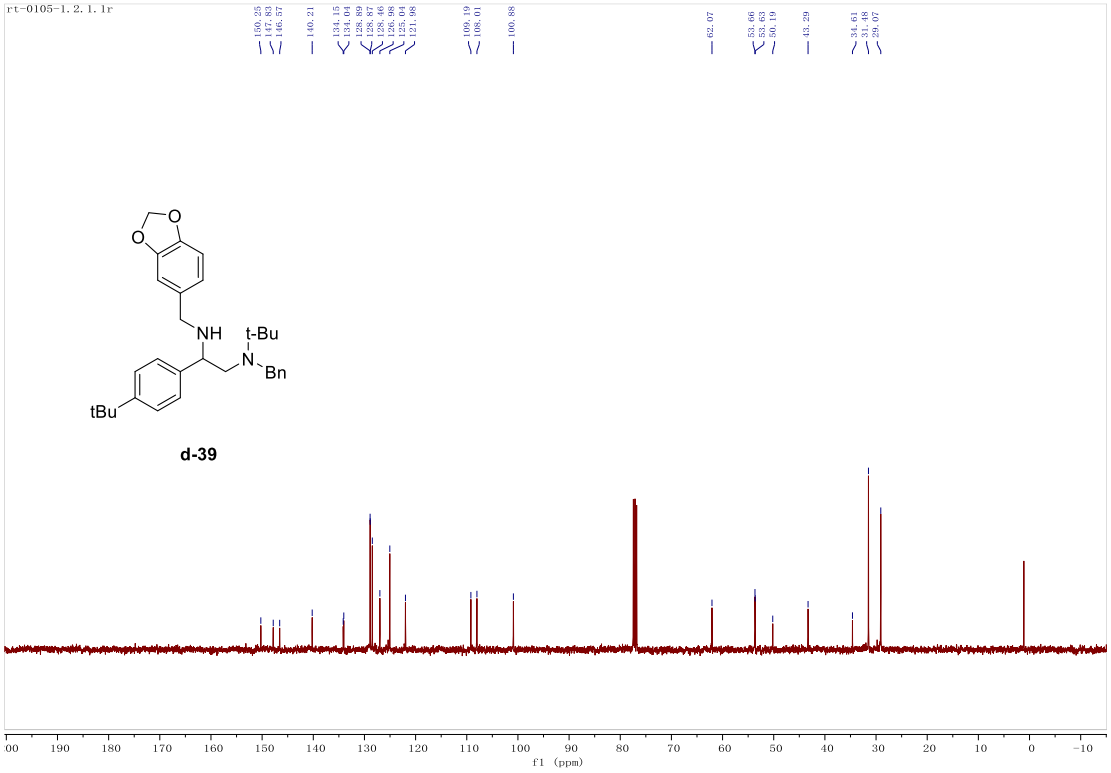
^{13}C NMR (101 MHz)



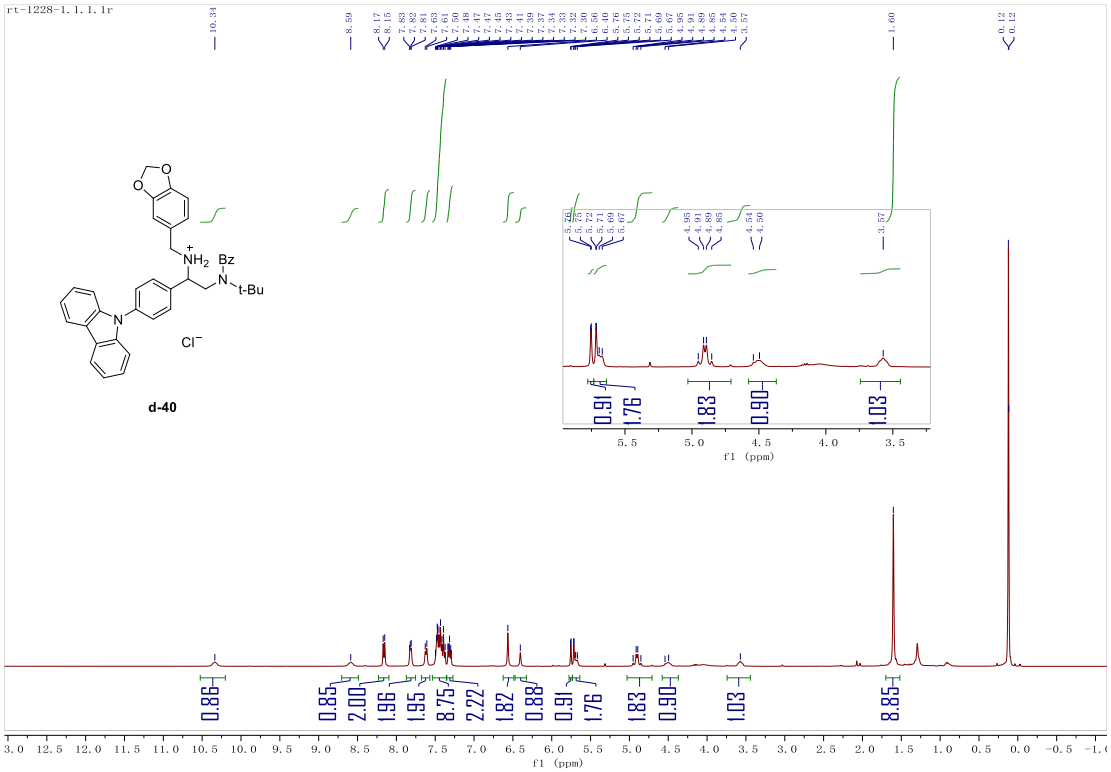
d-39 ^{1}H NMR (400 MHz)



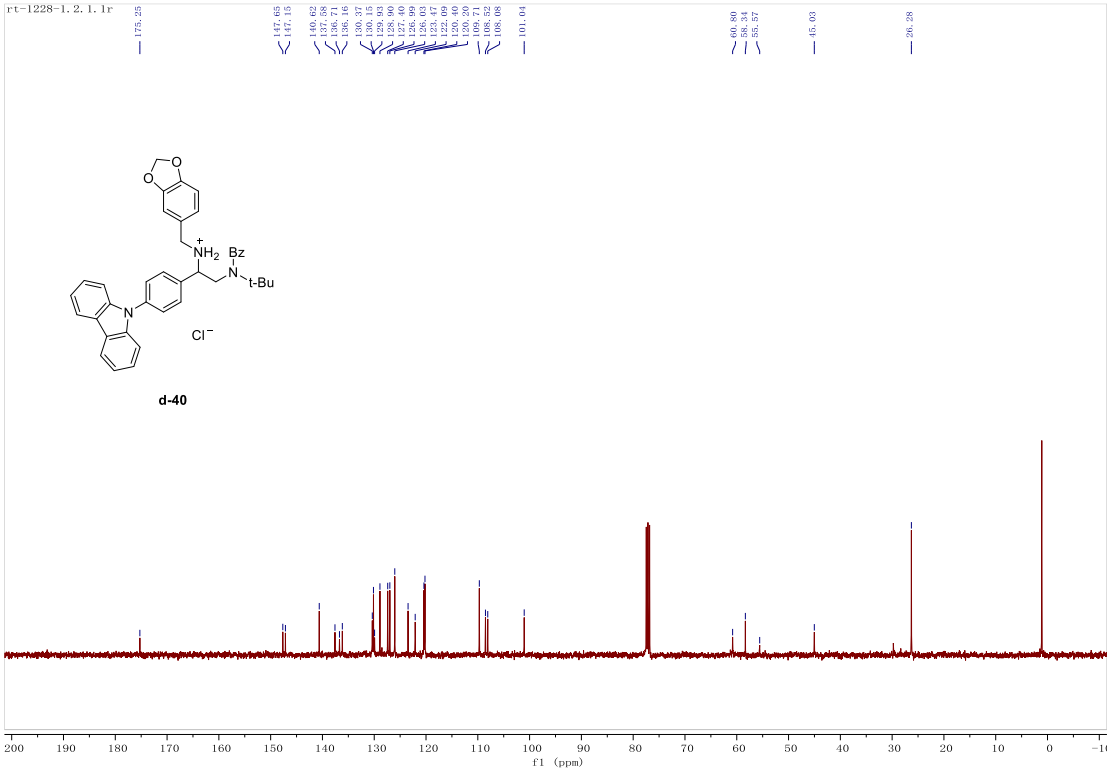
^{13}C NMR (101 MHz)



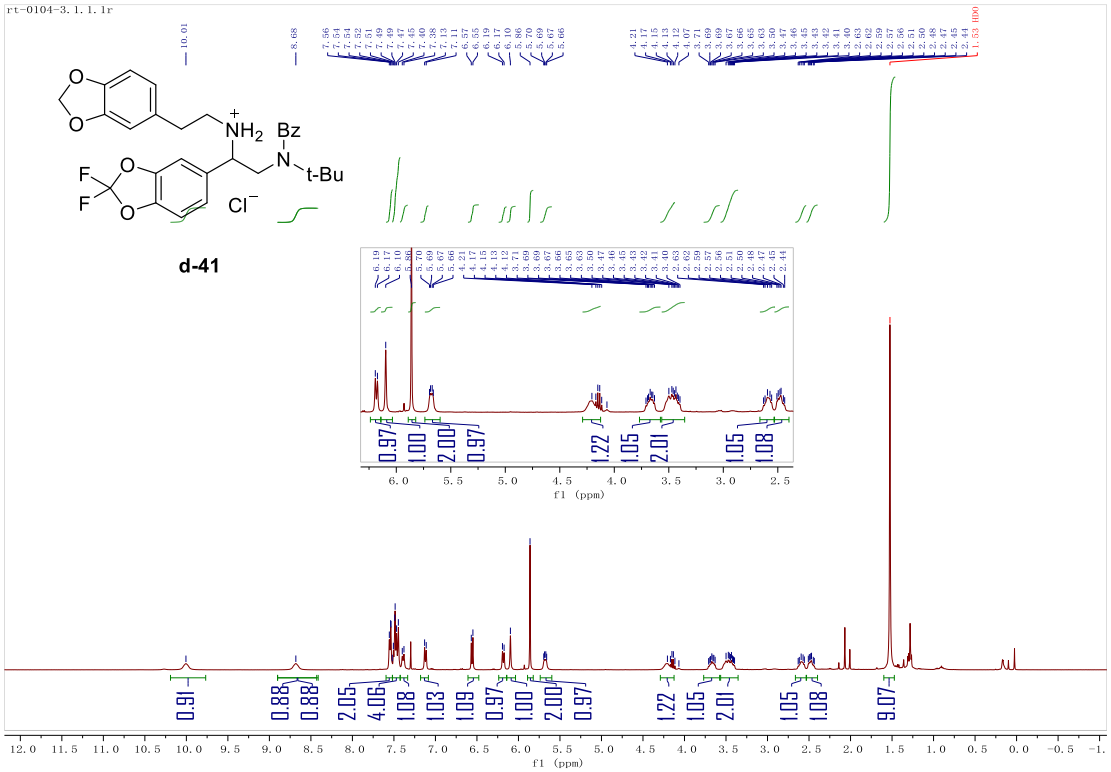
d-40 ^{1}H NMR (400 MHz)



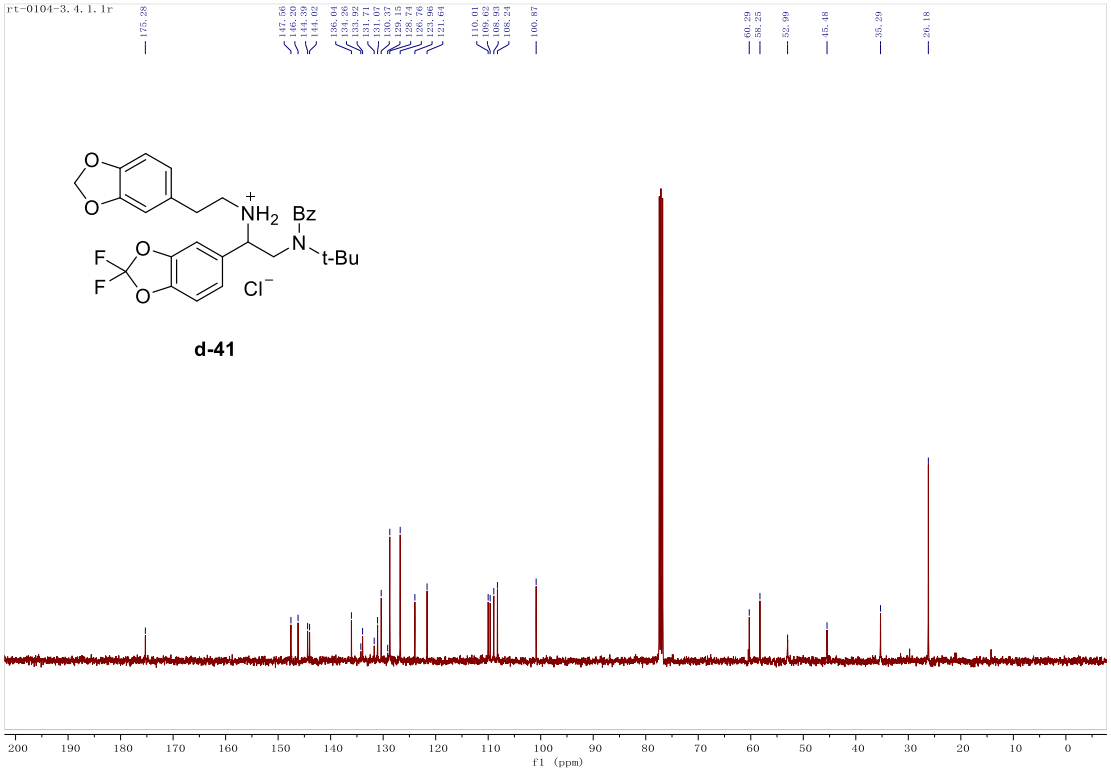
^{13}C NMR (101 MHz)



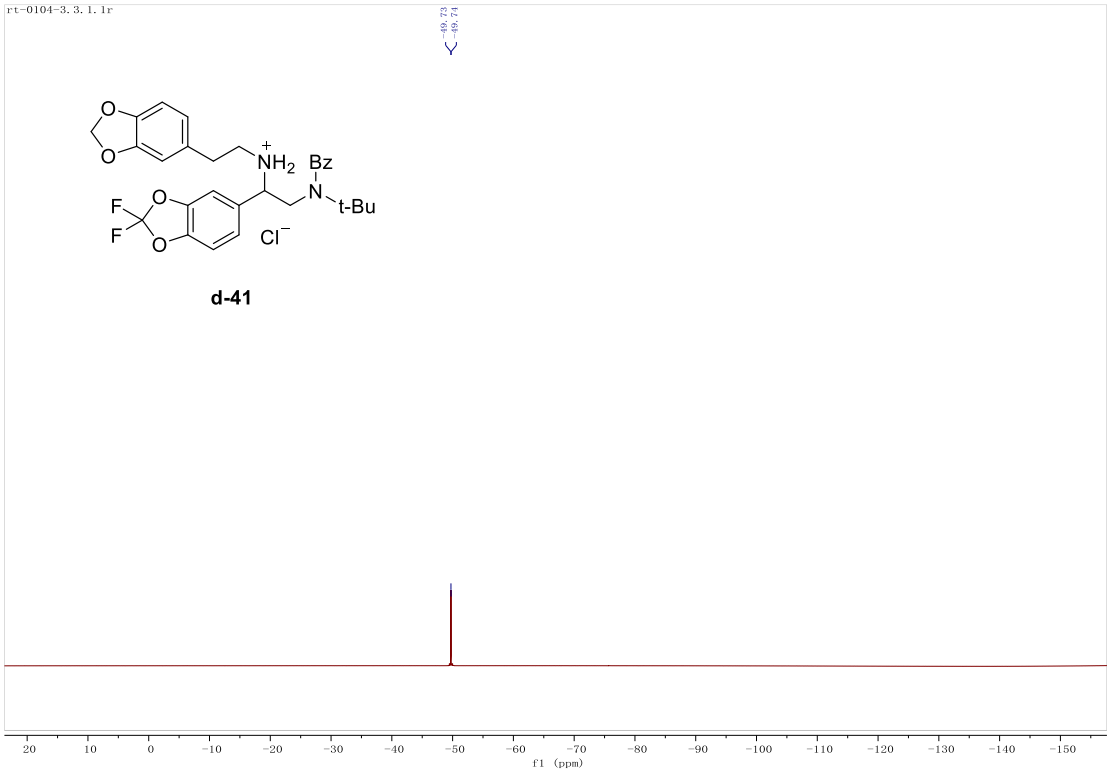
d-41 ^{1}H NMR (400 MHz)



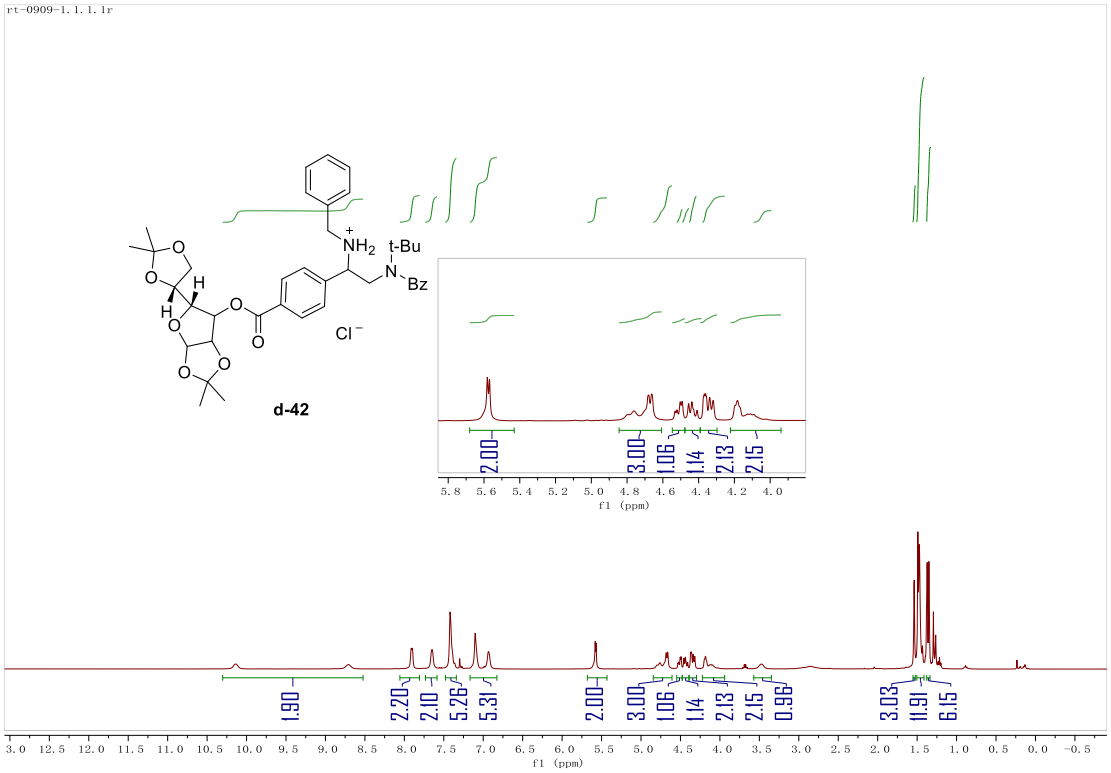
^{13}C NMR (101 MHz)



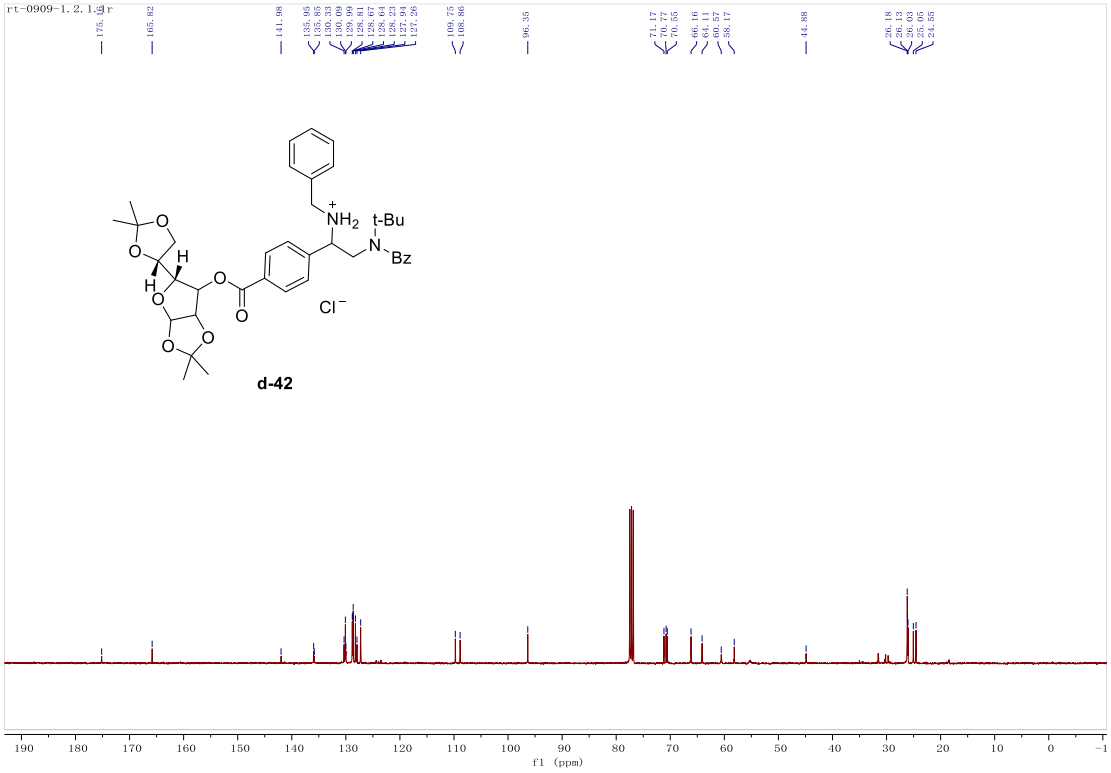
^{19}F NMR (376 MHz)



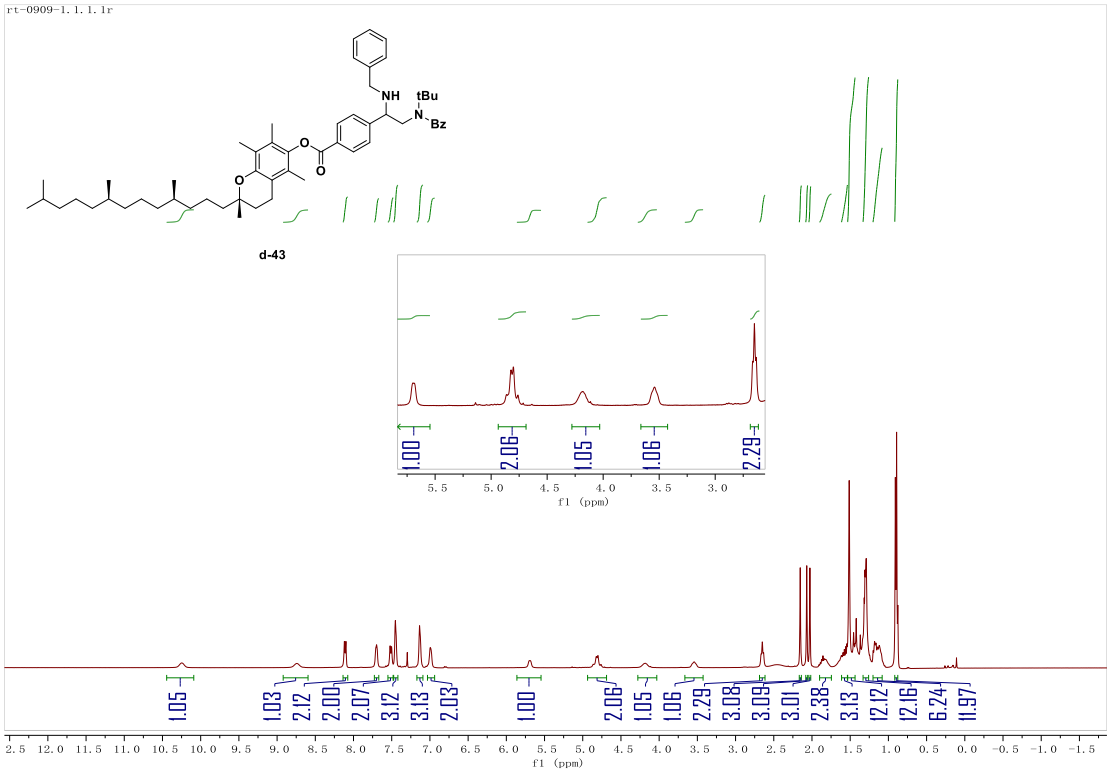
d-42 ^{1}H NMR (400 MHz)



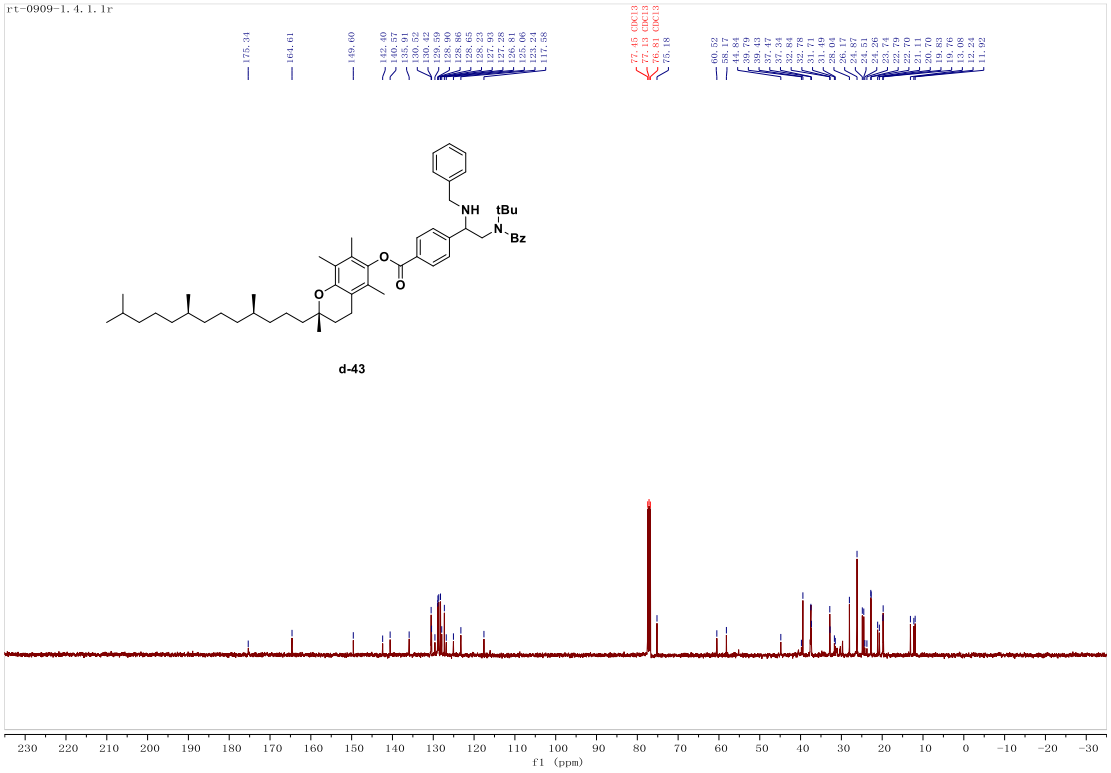
^{13}C NMR (101 MHz)



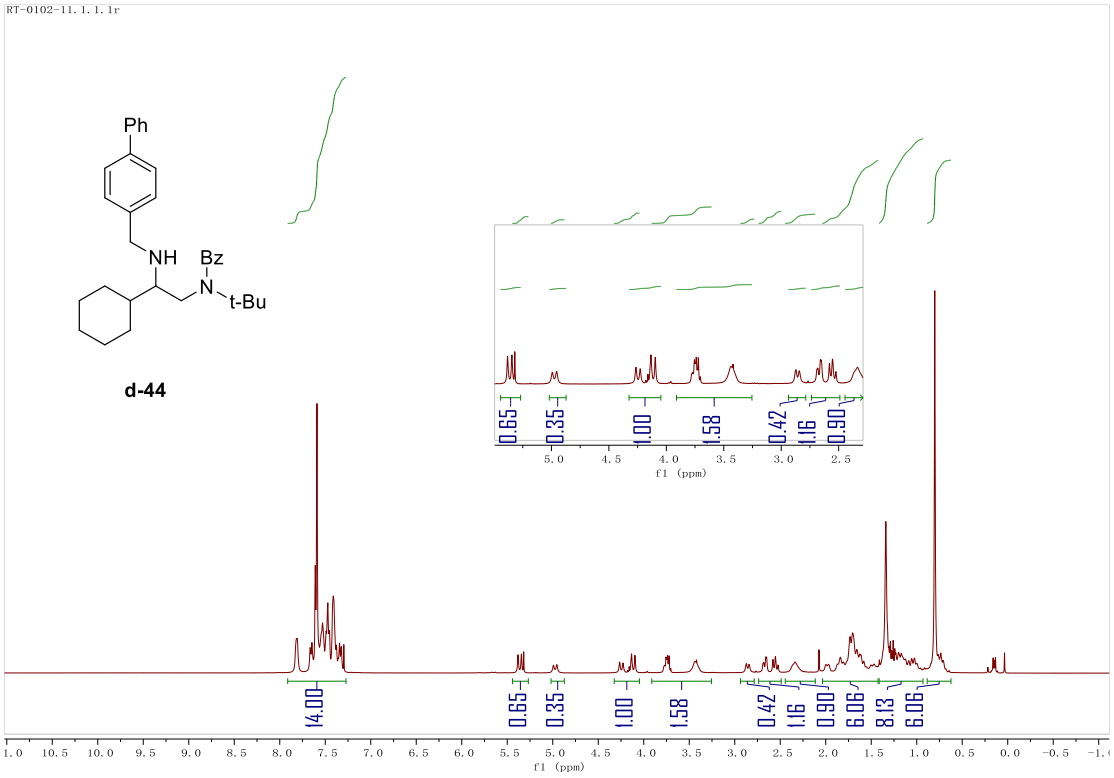
d-43 ^{1}H NMR (400 MHz)



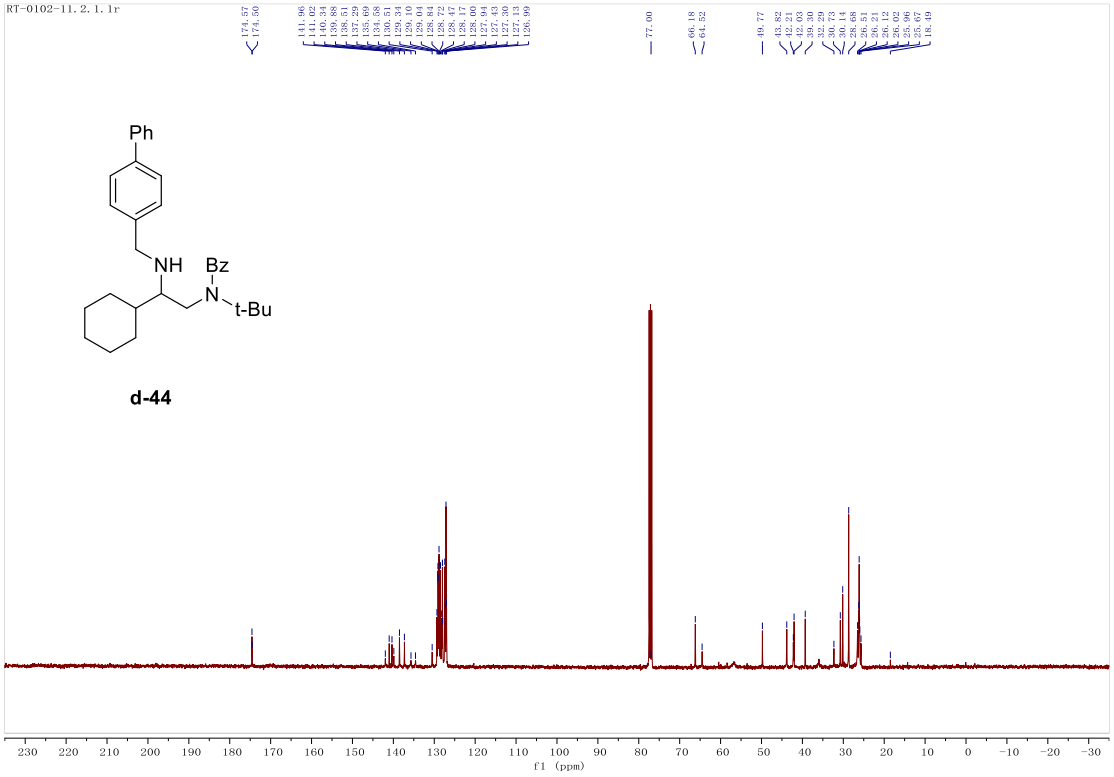
^{13}C NMR (101 MHz)



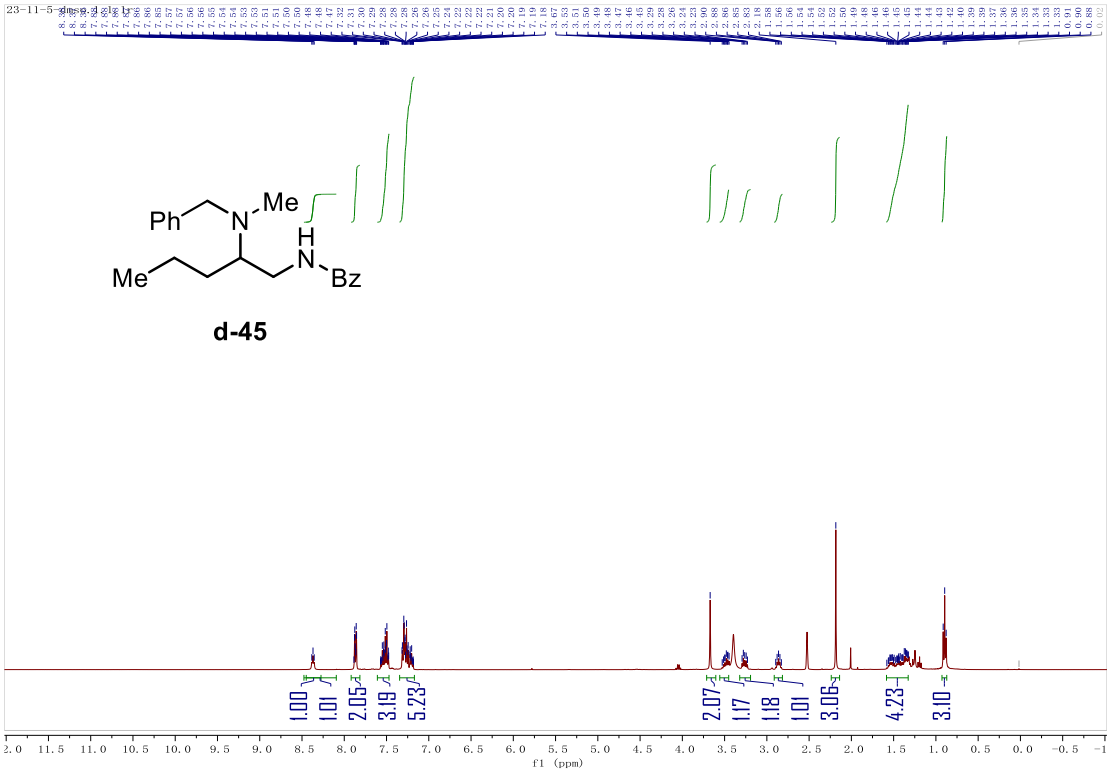
d-44 ^{1}H NMR (400 MHz)



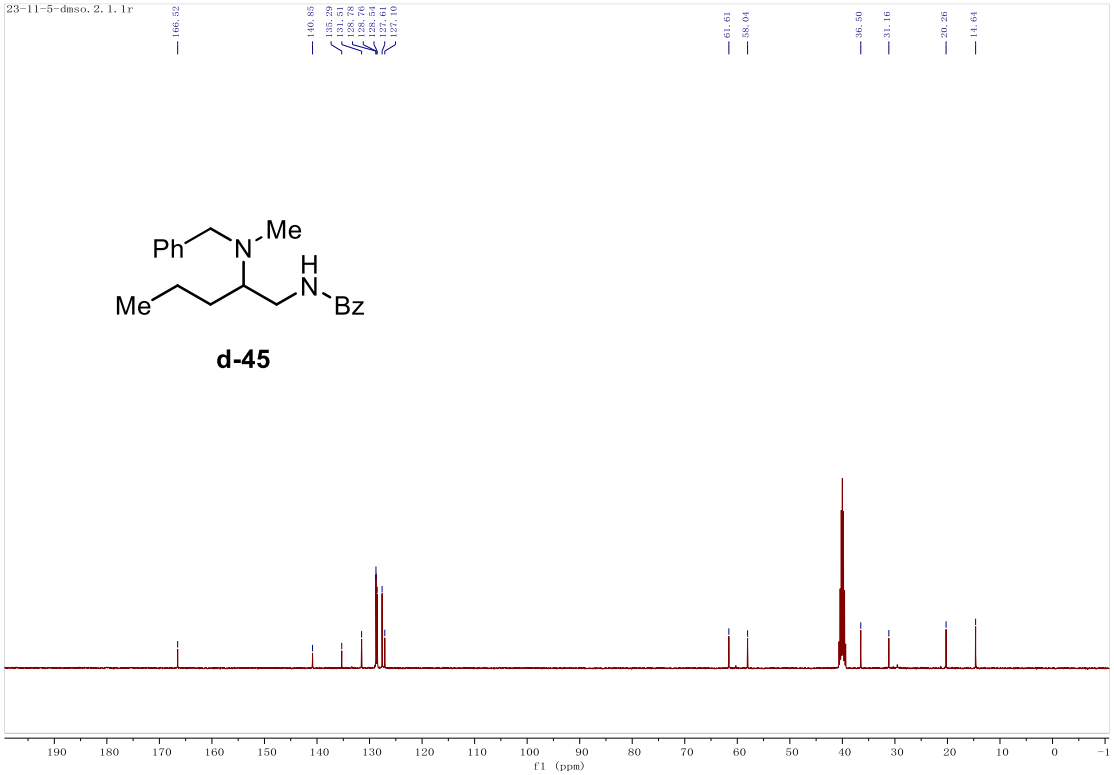
^{13}C NMR (101 MHz)



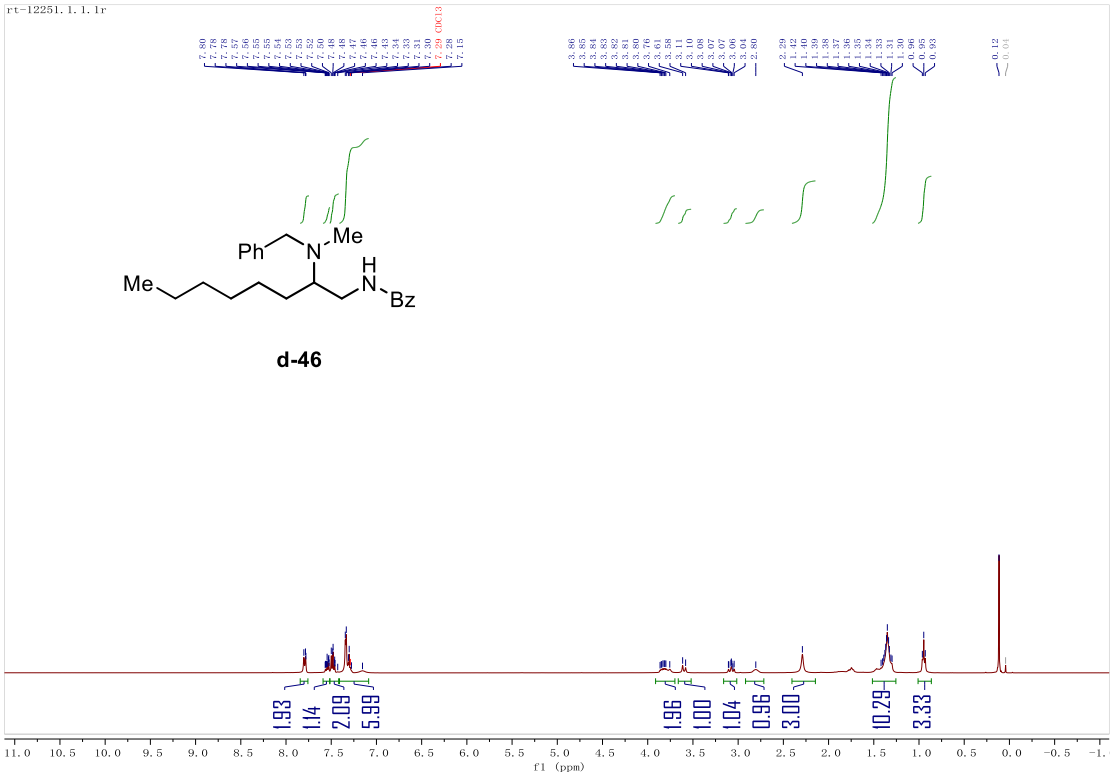
d-45 ^{1}H NMR (400 MHz)



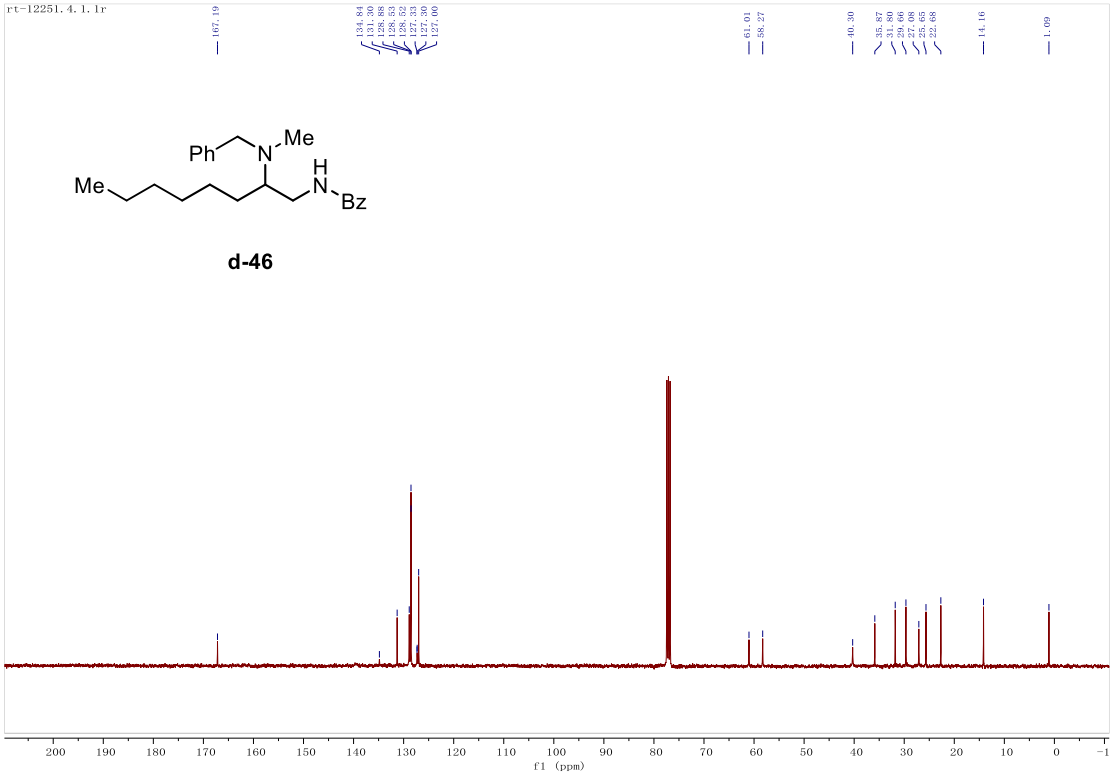
^{13}C NMR (101 MHz)



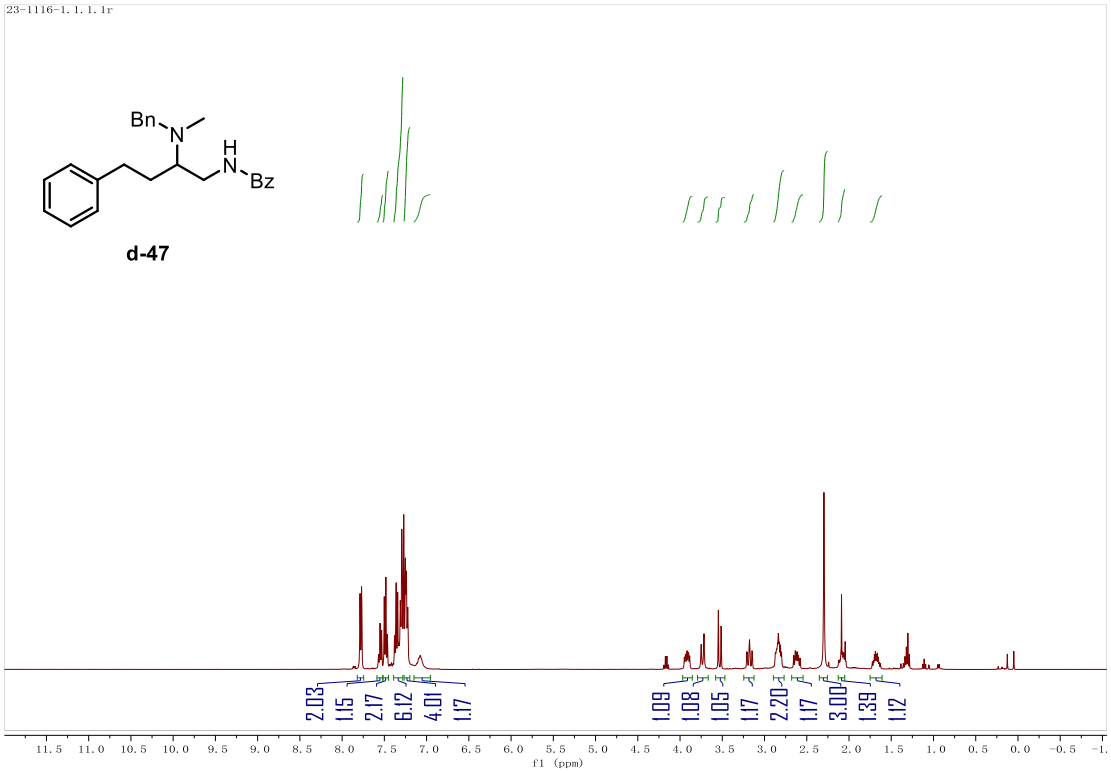
d-46 ^{1}H NMR (400 MHz)



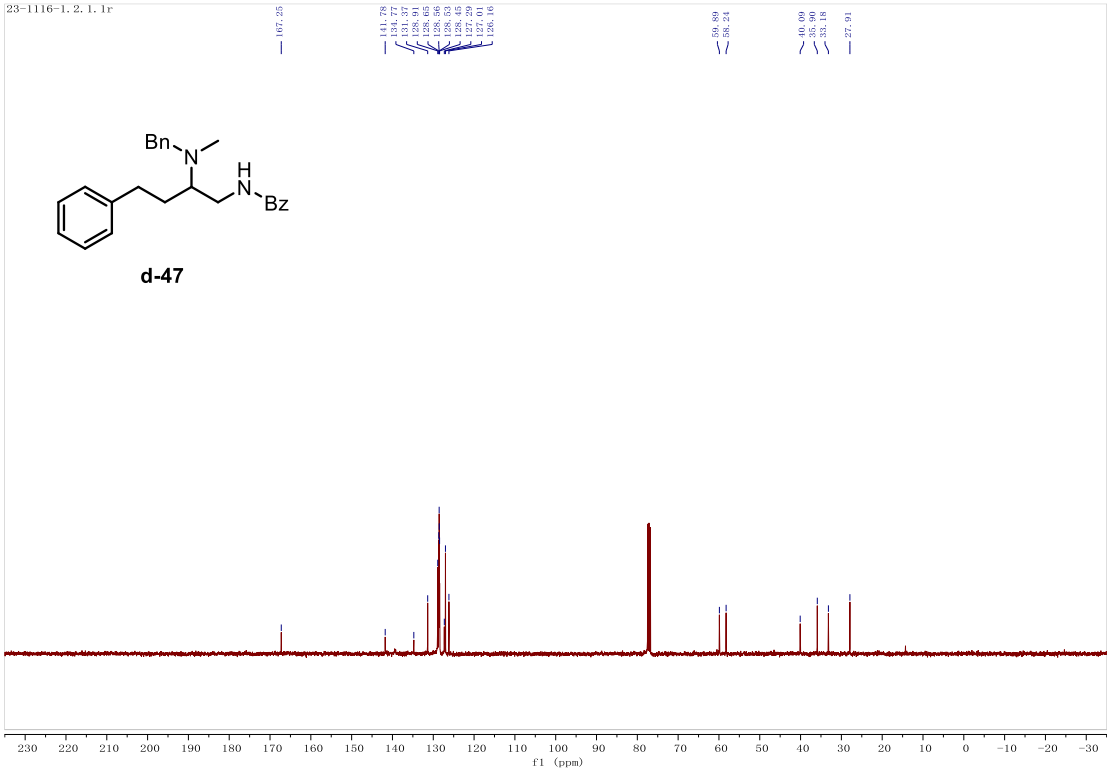
^{13}C NMR (101 MHz)



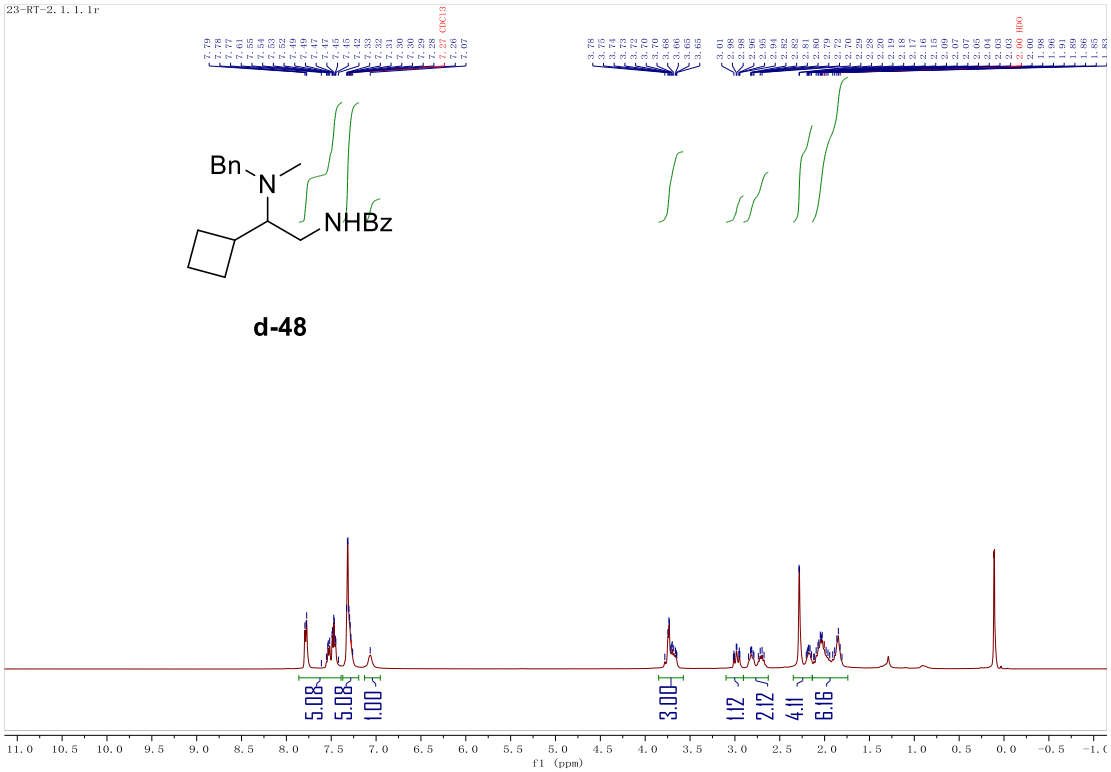
d-47 ^{1}H NMR (400 MHz)



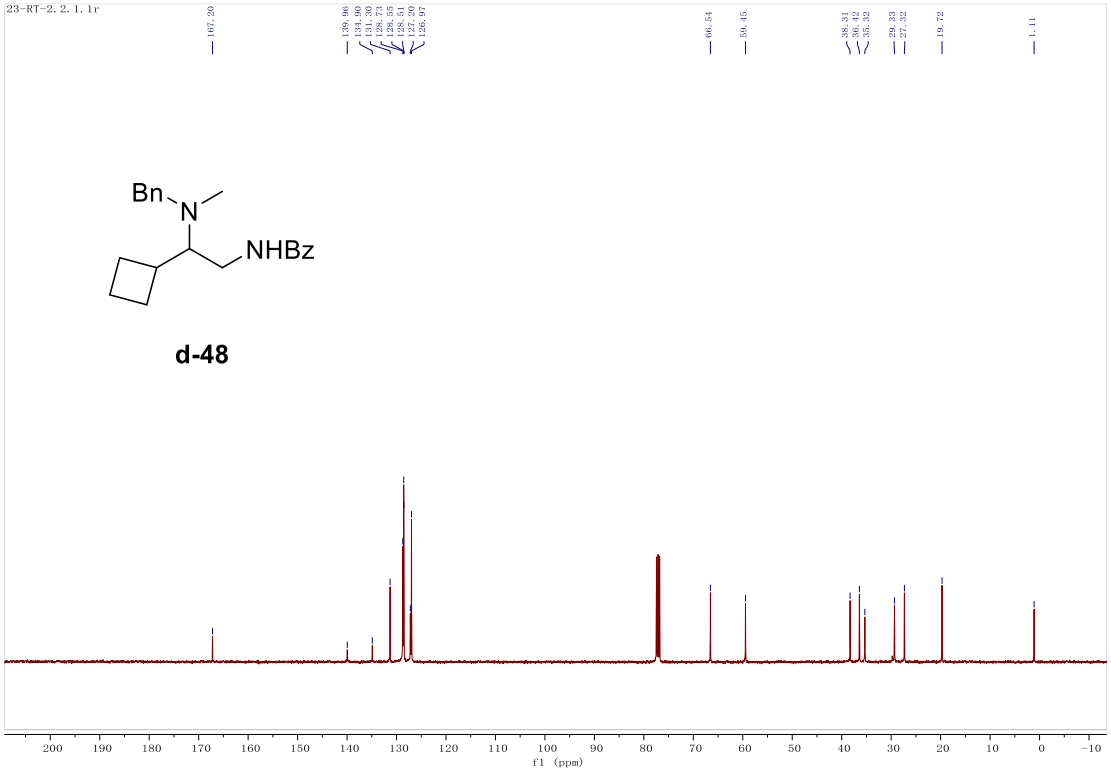
^{13}C NMR (101 MHz)



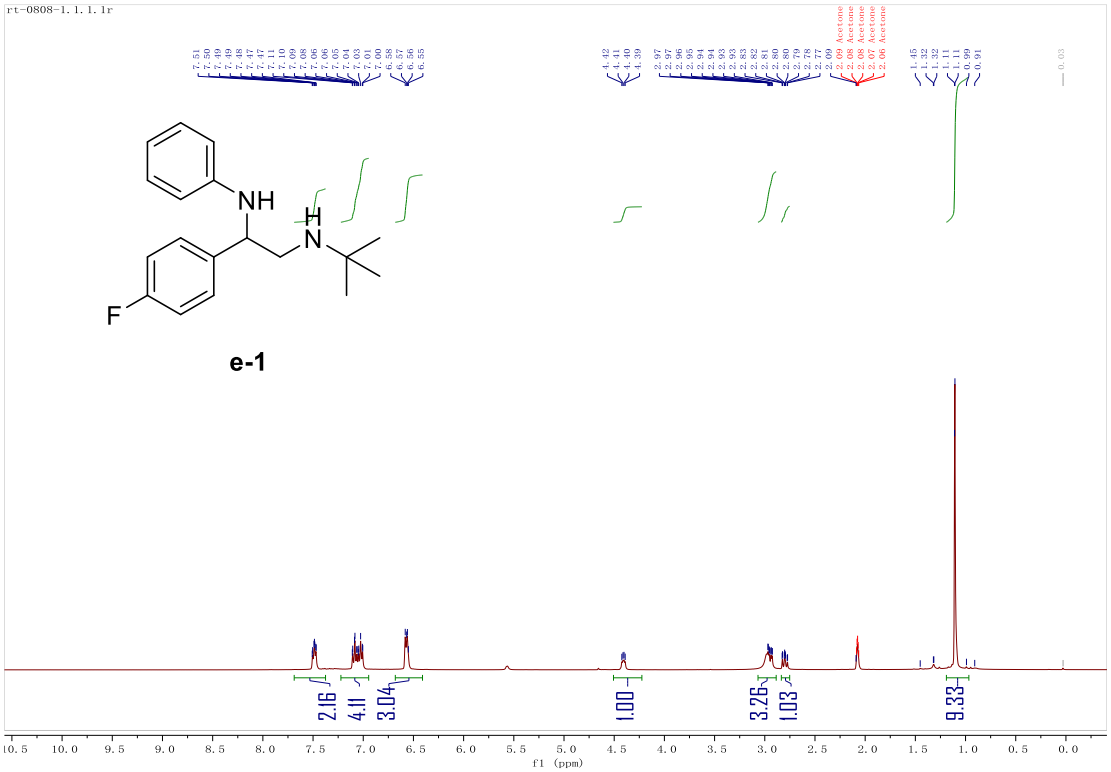
d-48 ^{1}H NMR (400 MHz)



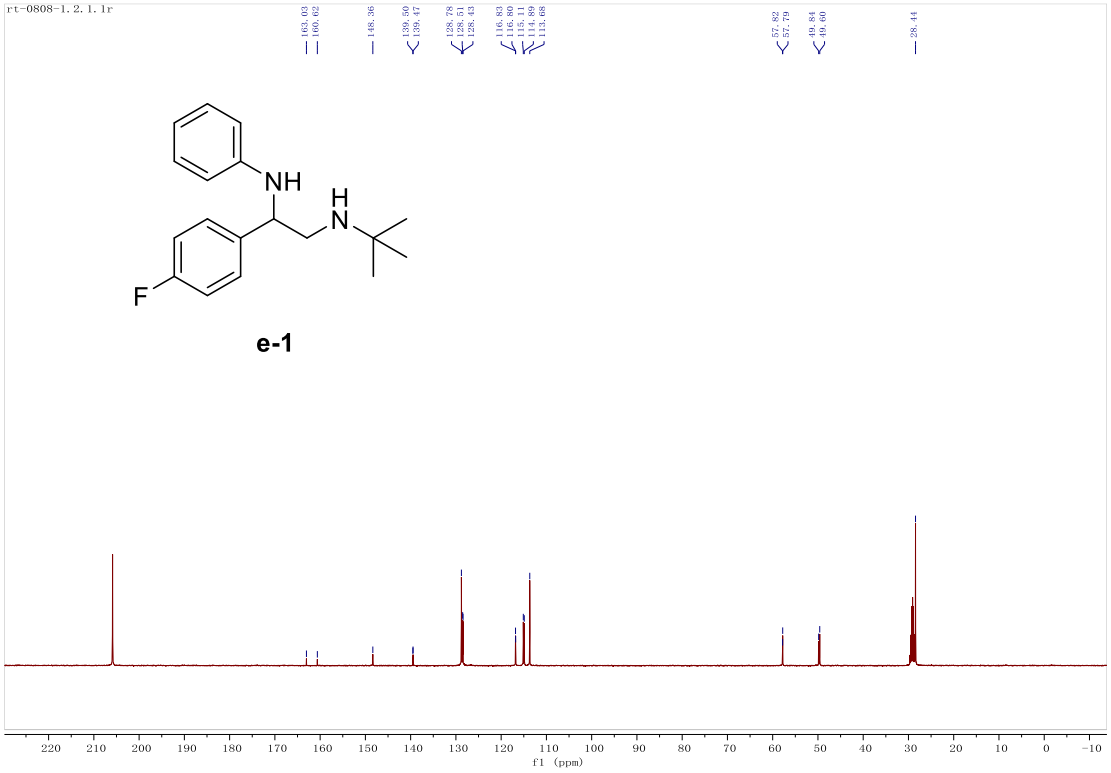
^{13}C NMR (101 MHz)



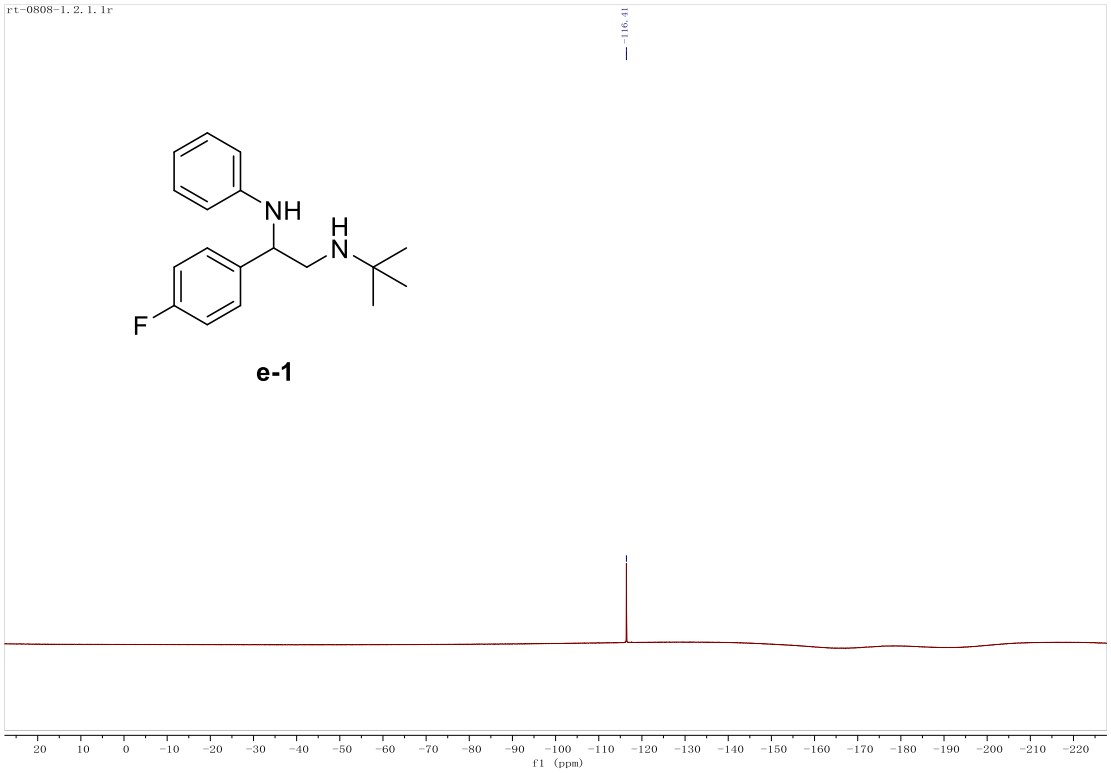
e-1 ^{1}H NMR (400 MHz)



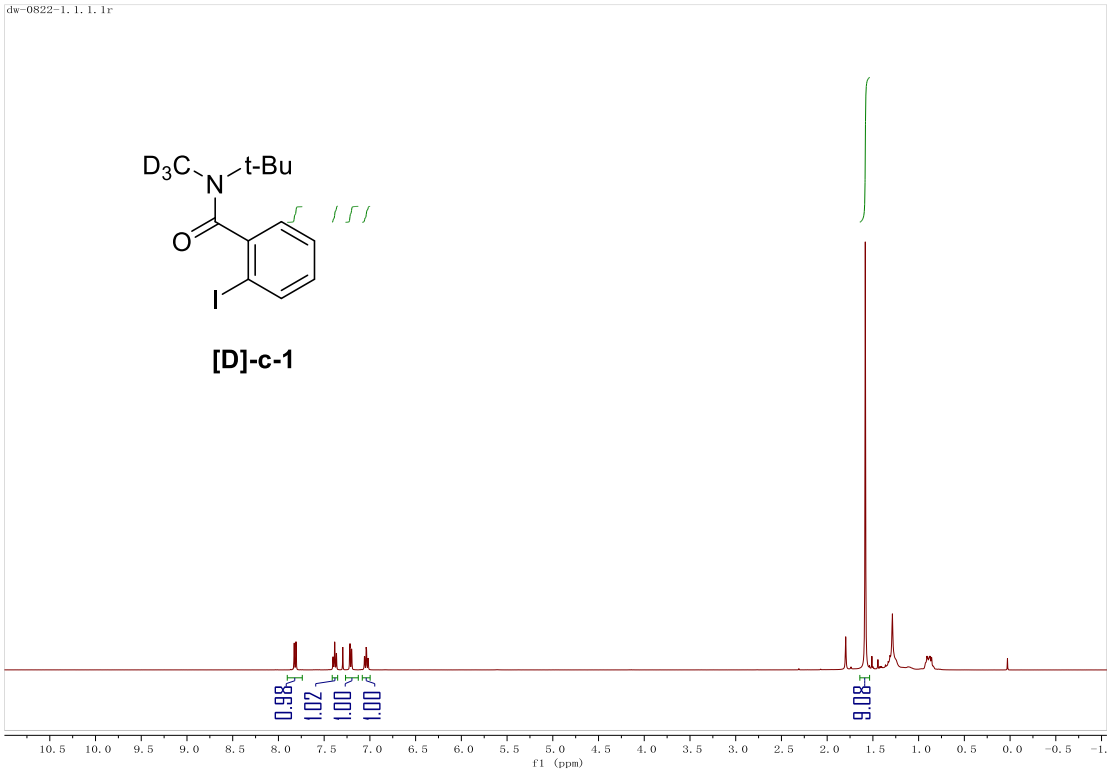
^{13}C NMR (101 MHz)



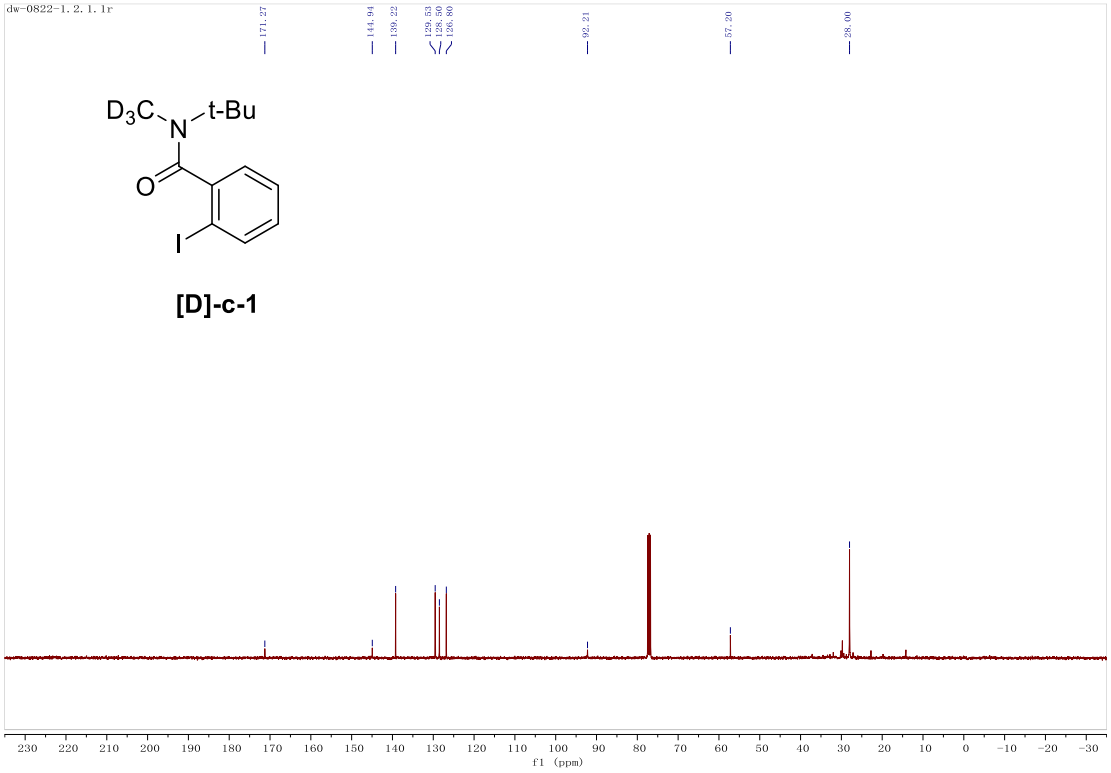
^{19}F NMR (376 MHz)



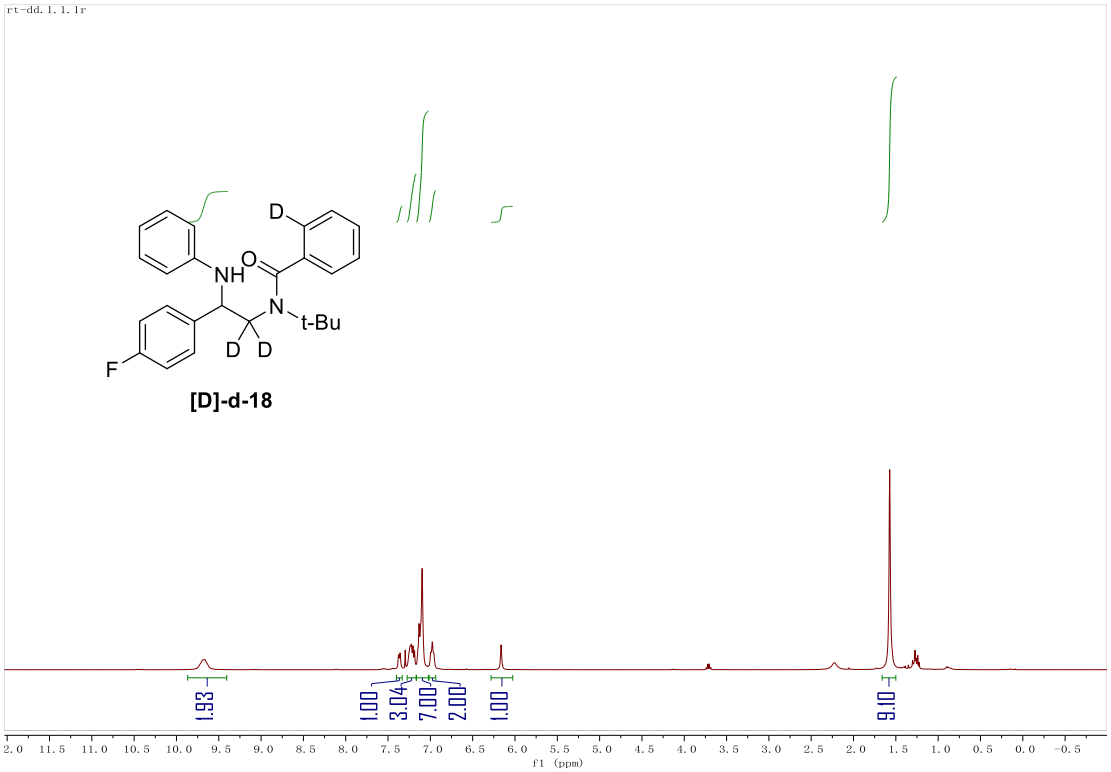
[D]-c-1 ^{1}H NMR (400 MHz)



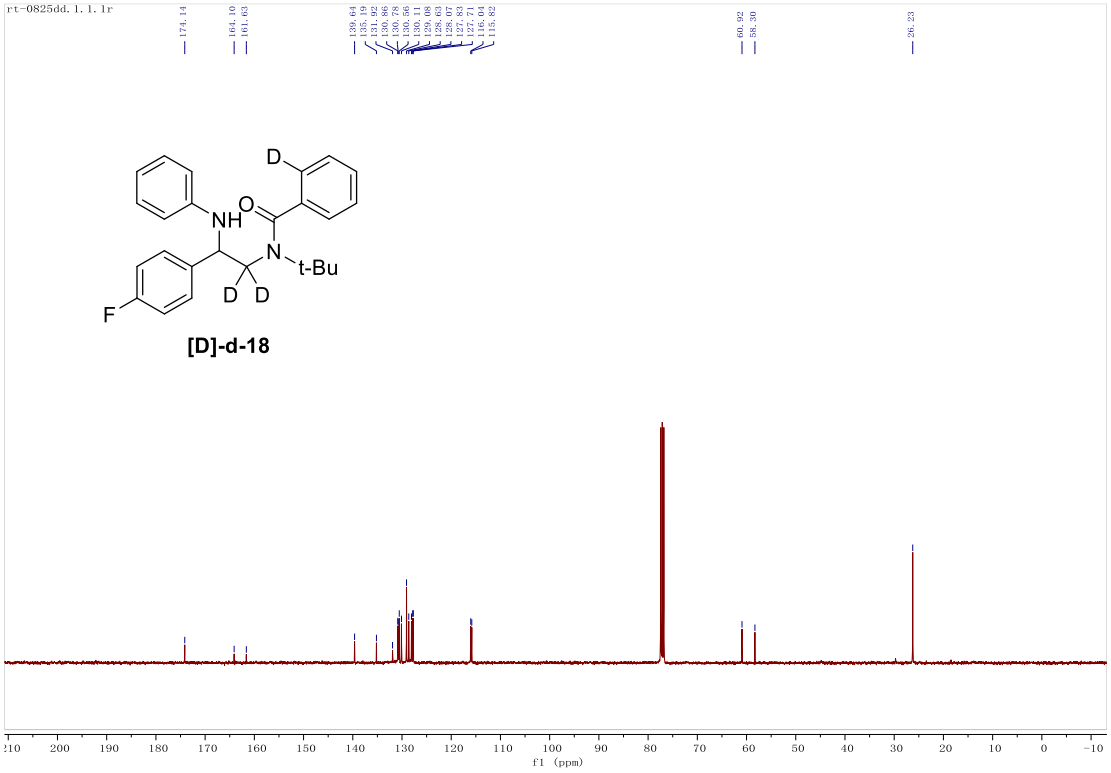
^{13}C NMR (101 MHz)



[D]-d-18 ^{1}H NMR (400 MHz)



^{13}C NMR (401 MHz)



^{19}F NMR (376 MHz)