

Supporting information

Enantioselective Addition of Thiols to Trifluoromethyl ketimines: synthesis of *N,S*-ketals

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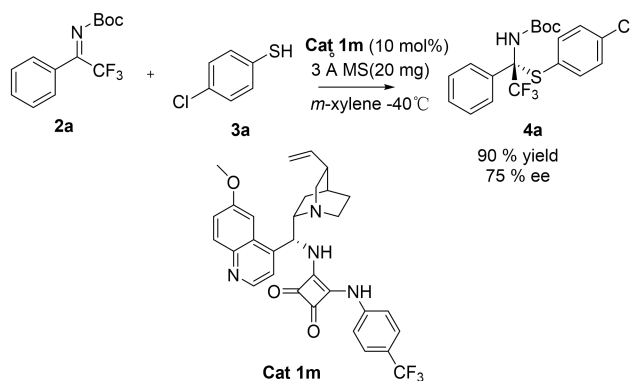
1. General information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All solvents were obtained from commercial sources and were purified according to standard procedures. TLC was carried out on silica gel plates (HSGF 254), which were visualized with UV light and/or staining with phosphomolybdic acids solution. Purification of reaction products was carried out by column chromatography using silica gel (200-300 mesh). ^1H , ^{13}C NMR, and ^{19}F NMR spectra were recorded on a Varian Mercury-300BB (300 MHz), a Bruker NMR Spectrometer (400 MHz). All chemical shifts (δ) were given in ppm. Chemical shifts are relative to the resonance of the deuterated solvent as the internal standard (CDCl_3 , δ 7.26 ppm for proton NMR, δ 77.16 ppm for carbon NMR; DMSO-d_6 , δ 2.50 ppm for proton NMR, δ 39.52 ppm for carbon NMR). Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = double, t = triplet, q = quartet, m = multiplet), and coupling constant in hertz. Mass spectra were recorded on a Bruker Agilent 1290 MicroTOF-Q II instrument. Melting points were measured on a melting points apparatus and were uncorrected. The enantioselectivity value determination was carried out using chiral HPLC (Waters) instrumentation with a Chiracel AD-H column and IA-3 column. Optical rotations were measured on a Shanghai ShenGuang SGW-2 polarimeter at $\lambda = 589$ nm. Optical rotations are reported as follows: $[\alpha]_D^{25}$ (c = g/100mL, solvent).

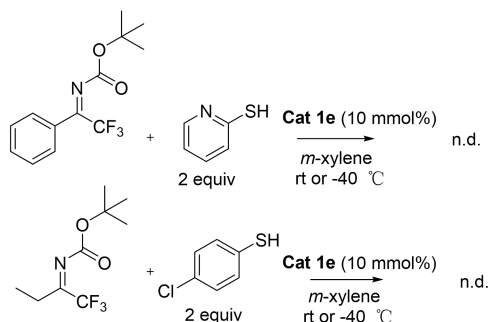
2. Starting Materials.

2,2,2-trifluoroacetophenone were prepared according to literature procedures.¹ All trifluoromethyl ketimines **2** were prepared using reported procedures from corresponding 2,2,2-trifluoroacetophenone.² All thiols **3** were purchased from commercial suppliers and used directly. The chiral catalysts **1a-1m** were prepared according to the procedure had been reported.³

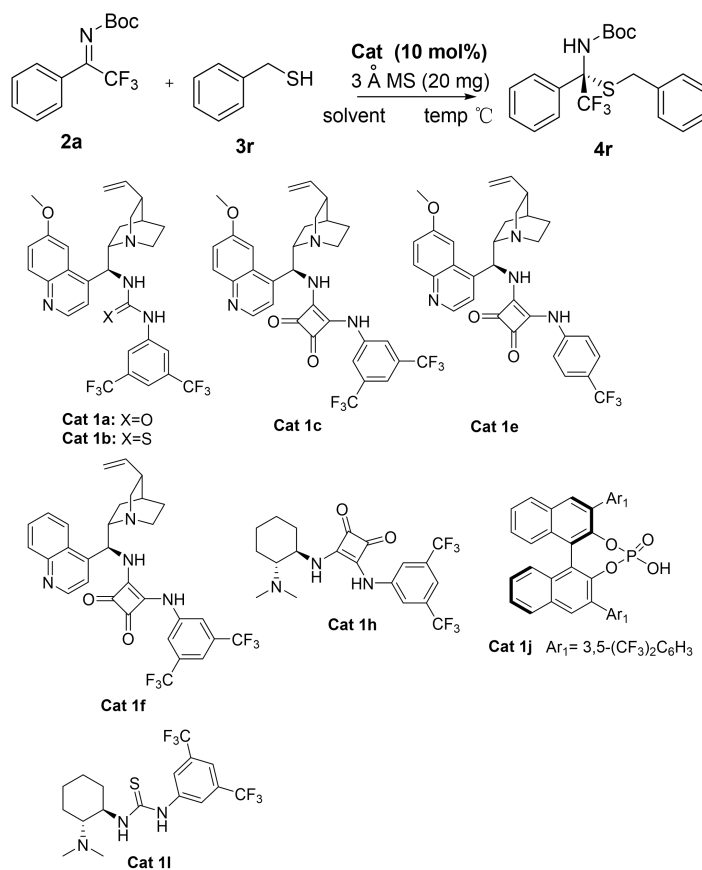
3. Carried out with the corresponding quinidine-based catalyst



4. Reaction of heteroaromatic thiol or aliphatic ketimines



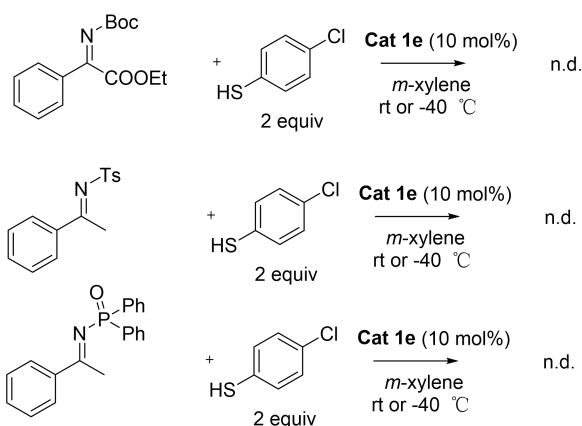
5. Optimization of the reaction conditions of benzyl thiol^[a]



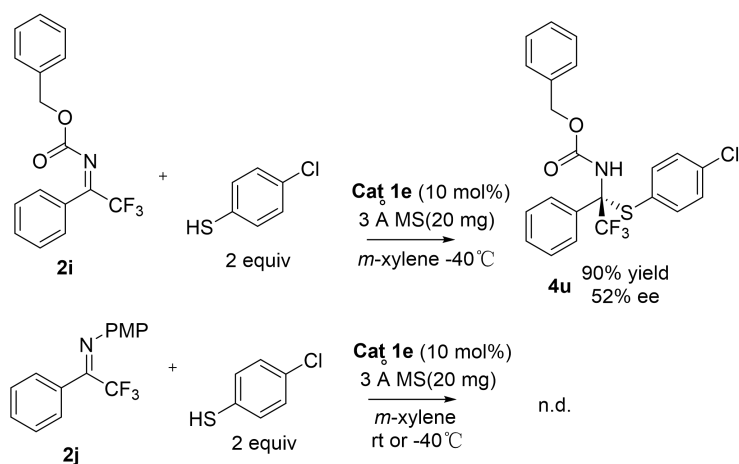
entry	Cat	solvent	temp	Yield (%)	Ee (%)
1	1a	<i>m</i> -xylene	-40	84	38
2	1b	<i>m</i> -xylene	-40	88	43
3	1c	<i>m</i> -xylene	-40	86	12
4	1e	<i>m</i> -xylene	-40	88	20
5	1f	<i>m</i> -xylene	-40	79	-
6	1j	<i>m</i> -xylene	-40	80	-
7	1h	<i>m</i> -xylene	-40	83	48
8	1l	<i>m</i> -xylene	-40	85	56
9	1l	CH ₂ Cl ₂	-40	84	21
10	1l	CHCl ₃	-40	83	9
10	1l	MTBE	-40	87	48
11	1l	toluene	-40	87	57

^[a]Unless otherwise noted, reactions were carried out with 0.1 mmol of **2a**, 10 mol% of catalyst and 0.2 mmol of **3r** in 1 ml of solvent. ^[b]Yield of isolated product. ^[c]Determined by HPLC using a chiral stationary phase.

6. The addition of thiols to other ketimines



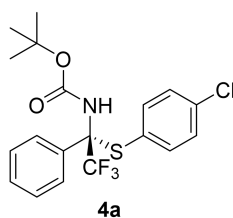
7. Reaction with Cbz and PMP protecting group ketimines



8. General Procedure for the Addition of Thiols to Trifluoromethyl ketimines and Characterization of Products 4a-4u.

Ketimines **2** (0.1 mmol) and catalyst **1e** (0.010 mmol, 10 mol %) were dissolved in *m*-xylene (1 ml), and 3 Å MS (20 mg) was added. Until the mixture was cooled to $-40\text{ }^\circ\text{C}$, the thiols **3** were added freshly in one portion. The mixture was stirred sharply at $-40\text{ }^\circ\text{C}$ until the reaction was judged to be completed by TLC. Then the solvent was removed in vacuo via evaporation. The crude product was purified by chromatography (PE/EA).

tert-butyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-phenylethyl)carbamate (**4a**)

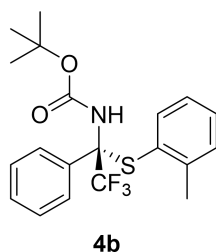


Purified by silica gel column chromatography (PE/EA=20:1), white solid, 40.1 mg, 96% yield, mp = $125\text{--}127\text{ }^\circ\text{C}$, $[\alpha]_{\text{D}}^{25} = -12.8$ ($c = 0.1$, CHCl_3). The ee value was 94% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.80$ min, $t_{\text{minor}} = 5.57$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.64 – 7.57 (m, 2H), 7.54 (d, $J = 8.4$ Hz, 2H), 7.43 – 7.32 (m, 5H), 5.20 (s, 1H), 1.39 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 152.0, 139.7, 136.9, 134.0, 129.1, 129.1, 128.1,

127.5, 127.3, 124.5 (q, $J = 284.2$ Hz), 81.4, 73.5 (q, $J = 27.9$ Hz), 28.0. ^{19}F NMR (377 MHz, CDCl_3) δ -74.26. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{19}\text{H}_{19}\text{ClF}_3\text{NO}_2\text{S}$ 440.0664; found 440.0669.

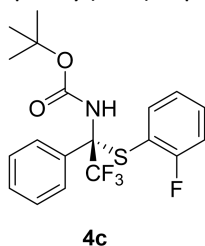
tert-butyl (S)-(2,2,2-trifluoro-1-phenyl-1-(*o*-tolylthio)ethyl)carbamate (**4b**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 37.3 mg, 94% yield, mp =163-164 °C, $[\alpha]_D^{25} = -20.4$ ($c=0.1$, CHCl_3). The ee value was 64% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.63$ min, $t_{\text{minor}} = 6.05$ min).

^1H NMR (400 MHz, CDCl_3) δ 7.72 – 7.65 (m, 2H), 7.49 (d, $J = 7.6$ Hz, 1H), 7.42 – 7.27 (m, 5H), 7.16 (d, $J = 8.7$ Hz, 1H), 5.22 (s, 1H), 2.57 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 152.2, 145.2, 139.2, 130.8, 130.3, 129.0, 128.7, 128.5, 127.9, 127.7, 126.1, 124.5 (q, $J = 284.4$ Hz), 81.2, 73.3 (q, $J = 28.0$ Hz), 28.0, 21.0. ^{19}F NMR (377 MHz, CDCl_3) δ -74.55. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{20}\text{H}_{22}\text{F}_3\text{NO}_2\text{S}$ 420.1203; found 420.1216.

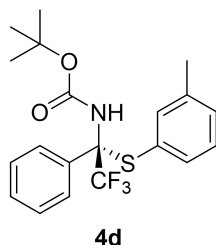
tert-butyl (S)-(2,2,2-trifluoro-1-((2-fluorophenyl)thio)-1-phenylethyl)carbamate (**4c**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 37.3 mg, 92% yield, mp = 124-125 °C, $[\alpha]_D^{25} = -14.8$ ($c=0.1$, CHCl_3). The ee value was 96% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 6.92$ min, $t_{\text{minor}} = 8.42$ min).

^1H NMR (400 MHz, CDCl_3) δ 7.71 – 7.64 (m, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.50 – 7.36 (m, 4H), 7.19 – 7.12 (m, 2H), 5.29 (s, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 164.5 (d, $J = 250.7$ Hz), 152.1, 140.7, 133.0 (d, $J = 8.3$ Hz), 131.3, 129.1, 128.1, 127.6, 124.4, 124.2 (q, $J = 284.4$ Hz), 116.3, 116.1, 81.3, 73.9 (q, $J = 29.1$ Hz), 28.0. ^{19}F NMR (377 MHz, CDCl_3) δ -74.57, -103.26. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{19}\text{H}_{19}\text{F}_4\text{NO}_2\text{S}$ 424.0960; found 424.0965.

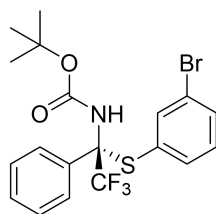
tert-butyl (S)-(2,2,2-trifluoro-1-phenyl-1-(*m*-tolylthio)ethyl)carbamate (**4d**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 36.1mg, 91% yield, mp =128-129 °C, $[\alpha]_D^{25} = -5.16$ ($c=0.1$, CHCl_3). The ee value was 99% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.91$ min, $t_{\text{minor}} = 6.80$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.61 (m, 2H), 7.48 – 7.37 (m, 5H), 7.27 (d, *J* = 1.1 Hz, 1H), 5.21 (s, 1H), 2.37 (s, 3H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 152.2, 139.0, 138.6, 135.5, 131.0, 128.9, 128.6, 128.4, 128.0, 127.6, 124.6 (q, *J* = 284.1 Hz), 120.3, 81.1, 73.2 (q, *J* = 28.3 Hz), 28.1, 21.2. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.04. **HRMS** (ESI) *m/z*: [M + Na]⁺ calculated for C₂₀H₂₂F₃NO₂S 420.1206; found 420.1216.

tert-butyl (S)-1-((3-bromophenyl)thio)-2,2,2-trifluoro-1-phenylethylcarbamate (**4e**)

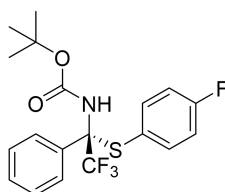


4e

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 42.1 mg, 91% yield, mp =150-151 °C, [α]_D²⁵ =-35.2 (c =0.1, CHCl₃). The ee value was 81% (Chiralpak IA-3, hexane/ethyl alcohol= 95:5, 254 nm, 1 mL/min, *t*_{major} =4.71 min, *t*_{minor} =4.45 min).

¹H NMR (400 MHz, CDCl₃) δ 7.78 (s, 1H), 7.63 (td, *J* = 8.8, 7.9, 2.9 Hz, 4H), 7.43 (dd, *J* = 5.1, 2.0 Hz, 3H), 7.29 (d, *J* = 6.9 Hz, 1H), 5.28 (s, 1H), 1.46 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 152.0, 140.7, 137.0, 133.3, 130.9, 130.1, 129.2, 128.6, 128.1, 127.4, 124.4 (q, *J* = 284.2 Hz), 122.3, 81.6, 73.7 (q, *J* = 28.7 Hz), 28.1. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.15. **HRMS** (ESI) *m/z*: [M + Na]⁺ calculated for C₁₉H₁₉BrF₃NO₂S 484.0175; found 484.0164.

tert-butyl (S)-2,2,2-trifluoro-1-((4-fluorophenyl)thio)-1-phenylethylcarbamate (**4f**)

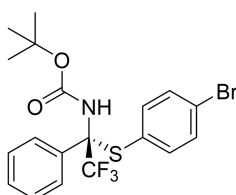


4f

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 36.5 mg, 91% yield, mp =157-158 °C, [α]_D²⁵ =-28 (c =0.1, CHCl₃). The ee value was 83% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, *t*_{major} =5.93 min, *t*_{minor} =5.53 min).

¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.49 (m, 4H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.08 (t, *J* = 8.7 Hz, 2H), 5.20 (s, 1H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 163.1 (d, *J* = 249.3 Hz), 152.1, 139.7, 137.1, 129.4 (d, *J* = 8.3 Hz), 129.2, 127.0, 124.3 (q, *J* = 284.1 Hz), 120.1, 115.2 (d, *J* = 21.8 Hz), 81.6, 73.0 (q, *J* = 28.2 Hz), 28.1. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.25, -109.82. **HRMS** (ESI) *m/z*: [M + Na]⁺ calculated for C₁₉H₁₉F₄NO₂S 424.0954; found 424.0965

tert-butyl (S)-1-((4-bromophenyl)thio)-2,2,2-trifluoro-1-phenylethylcarbamate (**4g**)



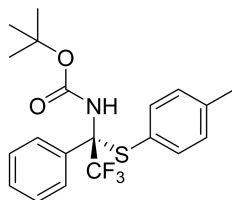
4g

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 43.0 mg, 93% yield, mp

=112-113 °C, $[\alpha]_D^{25} = -13.6$ ($c = 0.1$, CHCl_3). The ee value was 99% (Chiralpak IA-3, hexane/ethyl alcohol = 95:5, 214 nm, 1 mL/min, $t_{\text{major}} = 4.50$ min, $t_{\text{minor}} = 5.12$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.63 – 7.58 (m, 2H), 7.52 – 7.36 (m, 8H), 5.19 (s, 1H), 1.39 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 152.0, 139.9, 138.5, 134.0, 132.1, 129.1, 128.1, 127.9, 127.4, 125.3, 124.5 (q, $J = 283.9$ Hz), 81.4, 73.5 (q, $J = 29.2$ Hz), 28.0. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.27. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{19}\text{H}_{19}\text{BrF}_3\text{NO}_2\text{S}$ 484.0166; found 484.0164.

tert-butyl (S)-(2,2,2-trifluoro-1-phenyl-1-(p-tolylthio)ethyl)carbamate (**4h**)

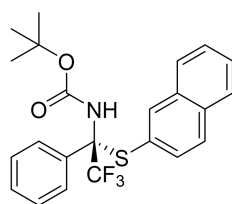


4h

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 38.1 mg, 96% yield, mp = 104-105 °C, $[\alpha]_D^{25} = -12$ ($c = 0.1$, CHCl_3). The ee value was 62% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.68$ min, $t_{\text{minor}} = 6.46$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.0$ Hz, 2H), 7.49 (d, $J = 7.9$ Hz, 2H), 7.38 (dd, $J = 5.2, 2.1$ Hz, 3H), 7.17 (d, $J = 7.9$ Hz, 2H), 5.15 (s, 1H), 2.39 (s, 3H), 1.39 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 153.3, 140.6, 138.4, 135.4, 129.7, 128.9, 128.0, 127.5, 125.2, 124.6 (q, $J = 284.3$ Hz), 81.1, 73.1 (q, $J = 27.6$ Hz), 28.0, 21.4. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.18. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{20}\text{H}_{22}\text{F}_3\text{NO}_2\text{S}$ 420.1209; found 420.1216.

tert-butyl (S)-(2,2,2-trifluoro-1-(naphthalen-2-ylthio)-1-phenylethyl)carbamate (**4i**)

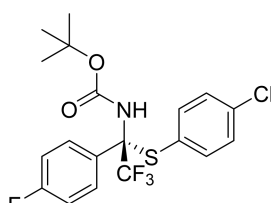


4i

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 40.2 mg, 93% yield, mp = 165-166 °C, $[\alpha]_D^{25} = -14.2$ ($c = 0.1$, CHCl_3). The ee value was 93% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 10.63$ min, $t_{\text{minor}} = 8.49$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.15 (s, 1H), 7.85 (dd, $J = 20.4, 8.1$ Hz, 3H), 7.66 (t, $J = 7.3$ Hz, 3H), 7.55 (dd, $J = 6.8, 1.3$ Hz, 2H), 7.44 – 7.37 (m, 3H), 5.20 (s, 1H), 1.38 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 152.2, 139.2, 136.0, 134.2, 133.8, 133.3, 129.0, 128.8, 128.3, 128.2, 128.1, 127.7, 127.6, 126.6, 126.0, 121.8 (q, $J = 283.5$ Hz), 81.2, 73.5 (q, $J = 27.9$ Hz), 28.1. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{NO}_2\text{S}$ 456.1225; found 456.1216.

tert-butyl (S)-(1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-(4-fluorophenyl)ethyl)carbamate (**4j**)



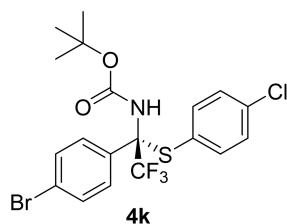
4j

Purified by silica gel column chromatography (PE/EA=20:1), white solid, 40.8 mg, 94% yield, mp

=136-137 °C, $[\alpha]_D^{25} = -13.4$ ($c = 0.1$, CHCl_3). The ee value was 72% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.35$ min, $t_{\text{minor}} = 4.64$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.67 – 7.49 (m, 4H), 7.34 (d, $J = 8.5$ Hz, 2H), 7.08 (t, $J = 8.7$ Hz, 2H), 5.20 (s, 1H), 1.40 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 164.2 (d, $J = 251.5$ Hz), 140.6 (d, $J = 8.8$ Hz), 133.8, 130.7, 129.1, 128.1, 127.5, 124.6 (q, $J = 284.3$ Hz), 124.2, 116.0 (d, $J = 21.8$ Hz), 81.3, 73.3 (q, $J = 25.5$ Hz), 28.0. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.28, -109.82. **HRMS (ESI)** m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{19}\text{H}_{18}\text{ClF}_4\text{NO}_2\text{S}$ 458.0578; found 458.0575.

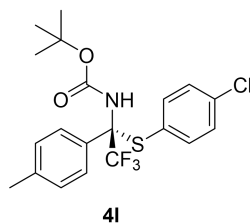
tert-butyl (S)-1-(4-bromophenyl)-1-((4-chlorophenyl)thio)-2,2,2-trifluoroethylcarbamate (**4k**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 45.6 mg, 92% yield, mp =170-171 °C, $[\alpha]_D^{25} = -10.6$ ($c = 0.1$, CHCl_3). The ee value was 86% (Chiralpak IA-3, hexane/ethyl alcohol = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 4.50$ min, $t_{\text{minor}} = 4.28$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.56 – 7.45 (m, 6H), 7.34 (d, $J = 8.5$ Hz, 2H), 5.17 (s, 1H), 1.40 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 152.0, 142.3, 139.7, 137.2, 133.1, 131.3, 129.2, 126.8, 124.2 (q, $J = 284.1$ Hz), 123.7, 81.7, 73.1 (q, $J = 28.8$ Hz), 28.1. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.42. **HRMS (ESI)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{18}\text{BrClF}_3\text{NO}_2\text{S}$ 517.9780; found 517.9774.

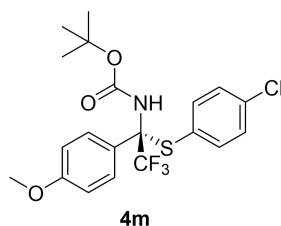
tert-butyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-(p-tolyl)ethylcarbamate (**4l**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 41.3 mg, 96% yield, mp =175-176 °C, $[\alpha]_D^{25} = -8.4$ ($c = 0.1$, CHCl_3). The ee value was 66% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 5.26$ min, $t_{\text{minor}} = 4.53$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.52 (dd, $J = 8.5, 4.6$ Hz, 4H), 7.33 (d, $J = 8.5$ Hz, 2H), 6.90 (d, $J = 9.0$ Hz, 2H), 5.15 (s, 1H), 3.82 (s, 3H), 1.40 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 152.0, 139.7, 139.1, 136.8, 131.0, 129.0, 128.9, 127.4, 127.3, 124.5 (q, $J = 284.0$ Hz), 81.3, 73.4 (q, $J = 28.5$ Hz), 28.1, 21.1. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.49. **HRMS (ESI)** m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{20}\text{H}_{21}\text{ClF}_3\text{NO}_2\text{S}$ 454.0820; found 454.0826.

tert-butyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-(4-methoxyphenyl)ethylcarbamate (**4m**)

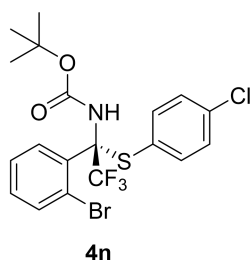


Purified by silica gel column chromatography (PE/EA=20:1), white solid, 42.5 mg, 95% yield, mp

=146-147 °C, $[\alpha]_D^{25} = -10.8$ ($c = 0.1$, CHCl_3). The ee value was 99% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254nm, 1 mL/min, $t_{\text{major}} = 6.80$ min, $t_{\text{minor}} = 6.19$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.52 (dd, $J = 19.8, 8.3$ Hz, 4H), 7.34 (d, $J = 8.5$ Hz, 2H), 7.20 (d, $J = 8.3$ Hz, 2H), 5.19 (s, 1H), 2.37 (s, 3H), 1.41 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 160.1, 139.6, 136.8, 132.6, 129.1, 128.7, 127.4, 124.49 (q, $J = 284.0$ Hz), 118.2, 113.5, 81.3, 73.6 (q, $J = 24.3$ Hz), 55.3, 28.1. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.43. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{20}\text{H}_{21}\text{ClF}_3\text{NO}_3\text{S}$ 470.0782; found 470.0775.

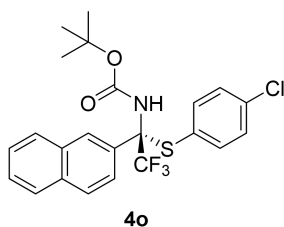
tert-butyl (S)-1-(2-bromophenyl)-1-((4-chlorophenyl)thio)-2,2,2-trifluoroethylcarbamate (**4n**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 47.6 mg, 96% yield, mp =121-123 °C, $[\alpha]_D^{25} = -8.6$ ($c = 0.1$, CHCl_3). The ee value was 99% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254nm, 1mL/min, $t_{\text{major}} = 11.04$ min, $t_{\text{minor}} = 7.28$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.59 (s, 1H), 7.51 (t, $J = 8.4$ Hz, 3H), 7.39 – 7.30 (m, 4H), 5.20 (s, 1H), 1.40 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 151.8, 142.7, 139.7, 137.3, 136.1, 133.0, 132.1, 130.5, 130.1, 129.1, 127.2, 125.0 (q, $J = 285.7$ Hz), 81.2, 73.6 (q, $J = 23.8$ Hz), 28.1. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -71.69. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{19}\text{H}_{18}\text{BrClF}_3\text{NO}_2\text{S}$ 517.9761; found 517.9774.

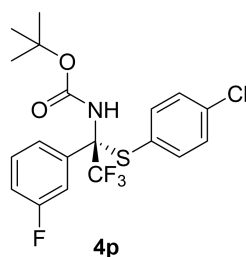
tert-butyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-(naphthalen-2-yl)ethylcarbamate (**4o**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 43.0 mg, 92% yield, mp =160-161 °C, $[\alpha]_D^{25} = -15.4$ ($c = 0.1$, CHCl_3). The ee value was 84% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254nm, 1mL/min, $t_{\text{major}} = 7.83$ min, $t_{\text{minor}} = 6.06$ min).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.13 (s, 1H), 7.92 – 7.81 (m, 3H), 7.68 (d, $J = 8.7$ Hz, 1H), 7.61 – 7.48 (m, 4H), 7.39 – 7.32 (m, 2H), 5.29 (s, 1H), 1.39 (s, 9H). **$^{13}\text{C NMR}$** (101 MHz, CDCl_3) δ 152.2, 139.2, 136.0, 134.2, 133.8, 133.3, 129.0, 128.8, 128.3, 128.2, 128.1, 127.7, 127.6, 126.6, 126.0, 124.6 (q, $J = 285.0$ Hz), 81.2, 73.5 (q, $J = 27.9$ Hz), 28.1. **$^{19}\text{F NMR}$** (377 MHz, CDCl_3) δ -74.06. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{23}\text{H}_{21}\text{ClF}_3\text{NO}_2\text{S}$ 490.0841; found 490.0826.

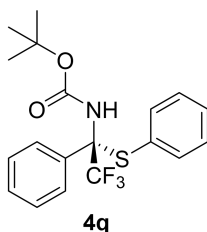
tert-butyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-(3-fluorophenyl)ethylcarbamate (**4p**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 40.1 mg, 94% yield, mp = 123-124 °C, $[\alpha]_D^{25} = -5.6$ ($c = 0.1$, CHCl₃). The ee value was 67% (ChiralpakAD-H, hexane/*i*-PrOH= 98:2, 254nm, 0.8 mL/min, $t_{\text{major}} = 12.71$ min, $t_{\text{minor}} = 11.56$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, $J = 8.3$ Hz, 2H), 7.44 – 7.30 (m, 5H), 7.09 (dd, $J = 8.1, 2.3, 1.1$ Hz, 1H), 5.22 (s, 1H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 162.4 (d, $J = 245.9$ Hz), 152.0, 139.7, 137.2, 136.5, 135.4, 129.6 (d, $J = 8.1$ Hz), 129.2, 125.0 (d, $J = 362.7$ Hz), 124.3 (q, $J = 284.2$ Hz), 116.2 (d, $J = 21.1$ Hz), 115.1 (d, $J = 24.6$ Hz), 81.7, 73.0 (q, $J = 27.1$ Hz), 28.0. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.19, -112.68. **HRMS** (ESI) m/z : $[M + Na]^+$ calculated for C₁₉H₁₈ClF₄NO₂S 458.0580; found 458.0575.

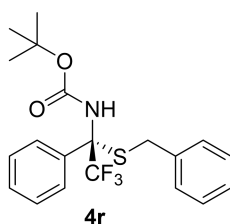
tert-butyl (S)-2-(2,2,2-trifluoro-1-(phenylthio)ethyl)carbamate (**4q**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 36.4 mg, 95% yield, mp = 132-133 °C, $[\alpha]_D^{25} = -8.2$ ($c = 0.1$, CHCl₃). The ee value was 80% (ChiralpakAD-H, hexane/*i*-PrOH= 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 6.42$ min, $t_{\text{minor}} = 7.28$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.64 (t, $J = 6.5$ Hz, 4H), 7.49 – 7.34 (m, 6H), 5.19 (s, 1H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 152.2, 138.5, 130.2, 129.0, 128.9, 128.8, 128.0, 127.5, 124.6 (q, $J = 284.2$ Hz), 120.3, 81.2, 73.3 (q, $J = 28.3$ Hz), 28.1. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.21. **HRMS** (ESI) m/z : $[M + Na]^+$ calculated for C₁₉H₂₀F₃NO₂S 406.1055; found 406.1059.

tert-butyl (S)-2-(1-(benzylthio)-2,2,2-trifluoro-1-phenylethyl)carbamate (**4r**)

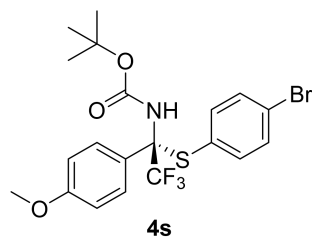


Purified by silica gel column chromatography (PE/EA=20:1), white solid, 35 mg, 88% yield, mp = 134-135 °C, $[\alpha]_D^{25} = -9.2$ ($c = 0.1$, CHCl₃). The ee value was 20% (ChiralpakAD-H, hexane/ethyl alcohol= 95:5, 254 nm, 1 mL/min, $t_{\text{major}} = 6.19$ min, $t_{\text{minor}} = 7.11$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.52 (m, 2H), 7.40 – 7.21 (m, 8H), 5.61 (s, 1H), 3.97 (d, $J = 11.3$ Hz, 1H), 3.86 (d, $J = 11.3$ Hz, 1H), 1.38 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 152.3, 135.7, 129.4, 129.0, 128.7, 128.1, 127.5, 127.3, 125.2 (q, $J = 284.2$ Hz), 120.9, 81.4, 71.6 (q, $J = 29.0$ Hz), 35.3, 28.0. **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.43. **HRMS** (ESI) m/z : $[M + Na]^+$ calculated for C₂₀H₂₂F₃NO₂S

420.1229; found 420.1216.

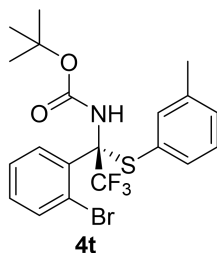
tert-butyl (S)-1-((4-bromophenyl)thio)-2,2,2-trifluoro-1-(4-methoxyphenyl)ethyl)carbamate (**4s**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 46.2 mg, 94% yield, mp = 116-117 °C, $[\alpha]_D^{25} = -6.2$ ($c = 0.1$, CHCl₃). The ee value was 92% (ChiralpakAD-H, hexane/ethyl alcohol = 95:5, 254nm, 1mL/min, $t_{major} = 7.23$ min, $t_{minor} = 5.77$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.48 (p, $J = 9.1, 8.6$ Hz, 6H), 6.94 – 6.86 (m, 2H), 5.17 (s, 1H), 3.82 (s, 3H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 160.1, 152.0, 146.0, 139.8, 132.0, 128.8, 128.1, 125.2, 124.5 (q, $J = 284.1$ Hz), 113.5, 81.3, 73.3 (q, $J = 28.8$ Hz), 55.3, 28.1 **¹⁹F NMR** (377 MHz, CDCl₃) δ -74.44. **HRMS** (ESI) m/z : $[M + Na]^+$ calculated for C₂₀H₂₁BrF₃NO₃S 514.0283; found 514.0270.

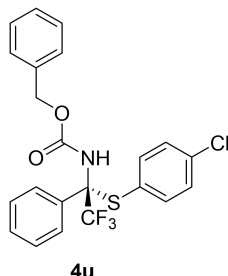
tert-butyl (S)-1-(2-bromophenyl)-2,2,2-trifluoro-1-(m-tolylthio)ethyl)carbamate (**4t**)



Purified by silica gel column chromatography (PE/EA=20:1), white solid, 45.7 mg, 96% yield, mp = 89-92 °C, $[\alpha]_D^{25} = -10.6$ ($c = 0.1$, CHCl₃). The ee value was 99% (ChiralpakAD-H, hexane/*i*-PrOH = 95:5, 254nm, 1mL/min, $t_{major} = 7.57$ min, $t_{minor} = 6.45$ min).

¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, $J = 7.8$ Hz, 2H), 7.49 – 7.27 (m, 3H), 7.25 – 7.11 (m, 3H), 5.15 (s, 1H), 2.34 (s, 3H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 151.9, 139.0, 136.0, 135.6, 131.4, 130.4, 129.9, 129.3, 128.7, 128.1, 127.1, 125.1 (q, $J = 285.6$ Hz), 122.4, 120.8, 80.9, 72.4 (q, $J = 20.1$ Hz), 28.1, 21.2. **¹⁹F NMR** (377 MHz, CDCl₃) δ -71.15. **HRMS** (ESI) m/z : $[M + Na]^+$ calculated for C₂₀H₂₁BrF₃NO₂S 498.0343; found 498.0321.

benzyl (S)-1-((4-chlorophenyl)thio)-2,2,2-trifluoro-1-phenylethyl)carbamate (**4u**)

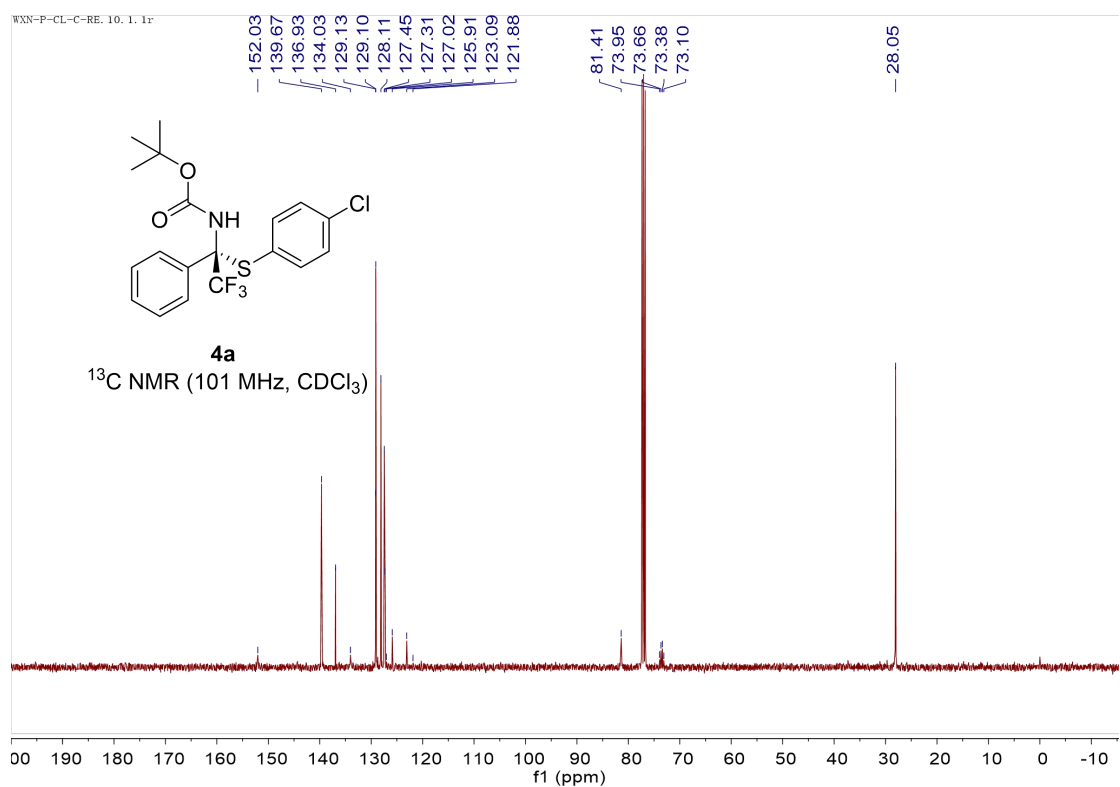
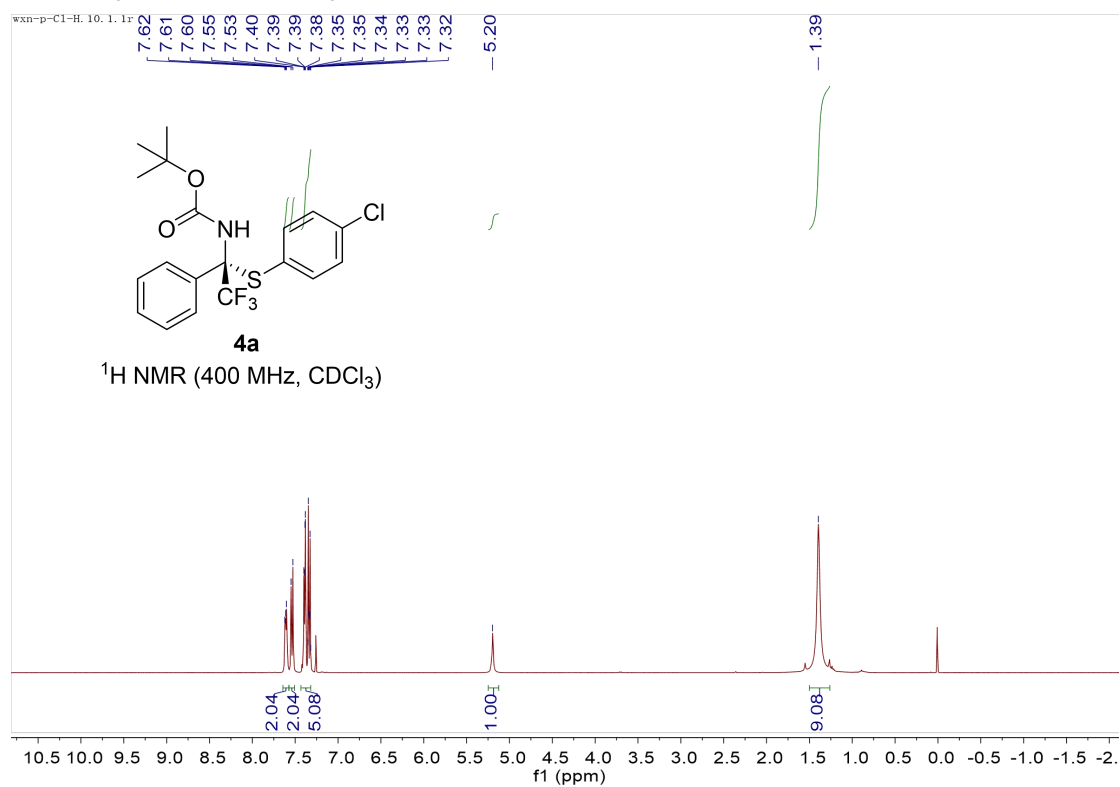


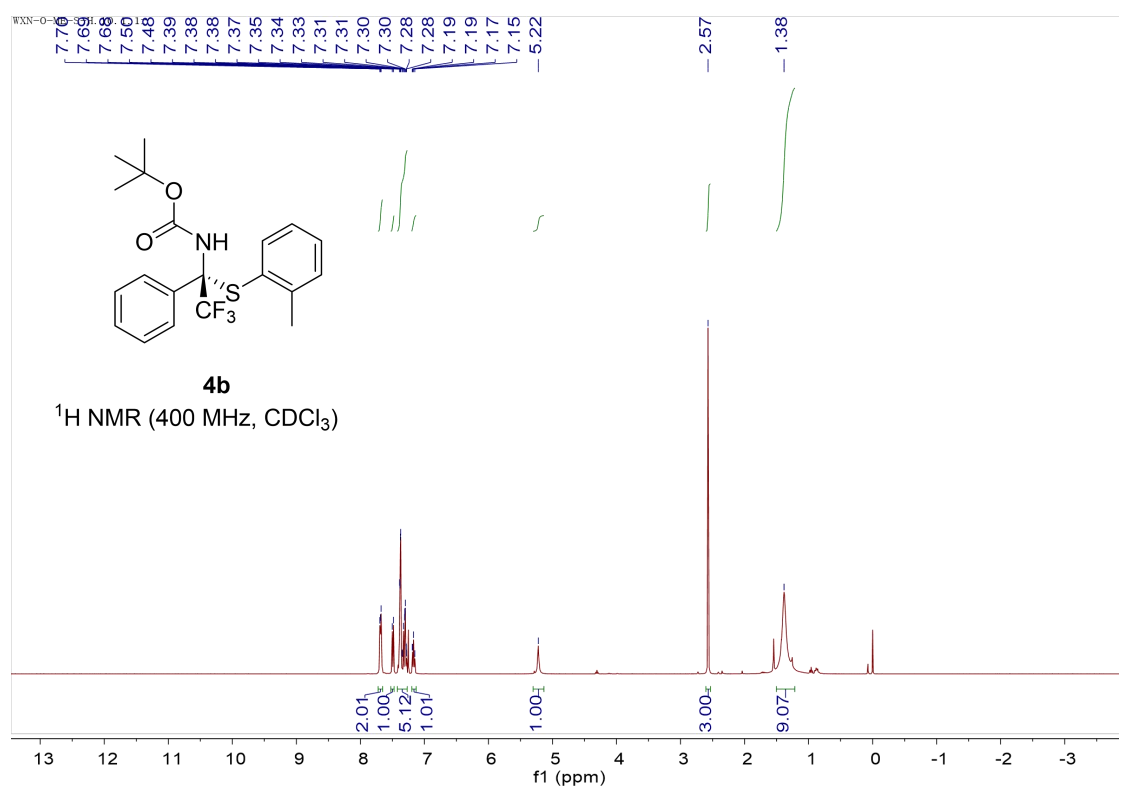
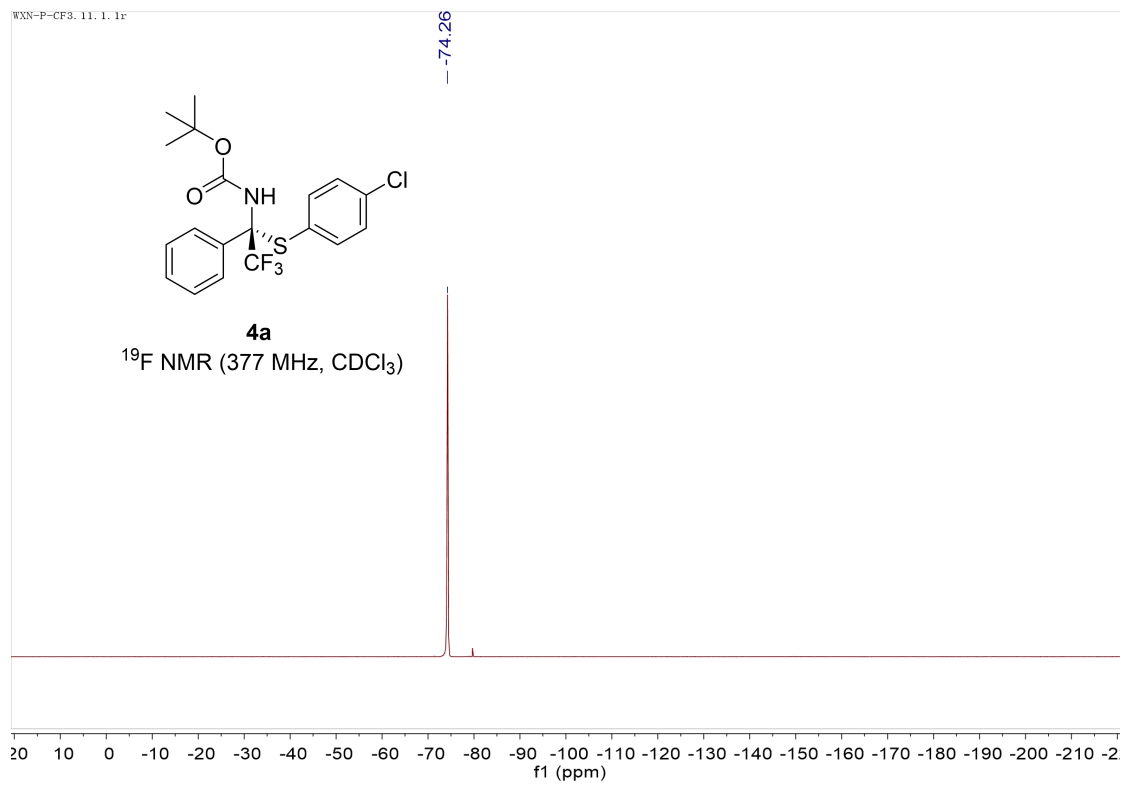
Purified by silica gel column chromatography (PE/EA=20:1), white solid, 40.7 mg, 90% yield, mp = 70-72 °C, $[\alpha]_D^{25} = -12.8$ ($c = 0.1$, CHCl₃). The ee value was 52% (Chiralpak AD-H, hexane/*i*-PrOH = 95:5, 254 nm, 1 mL/min, $t_{major} = 12.29$ min, $t_{minor} = 8.77$ min).

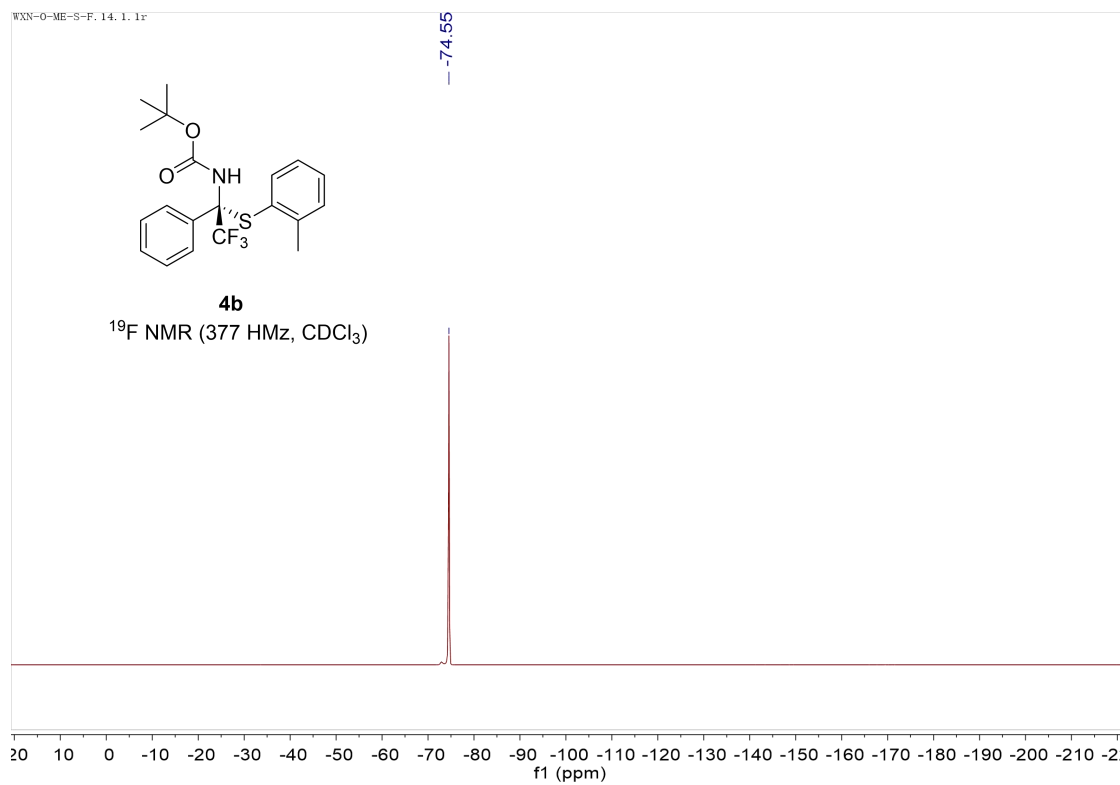
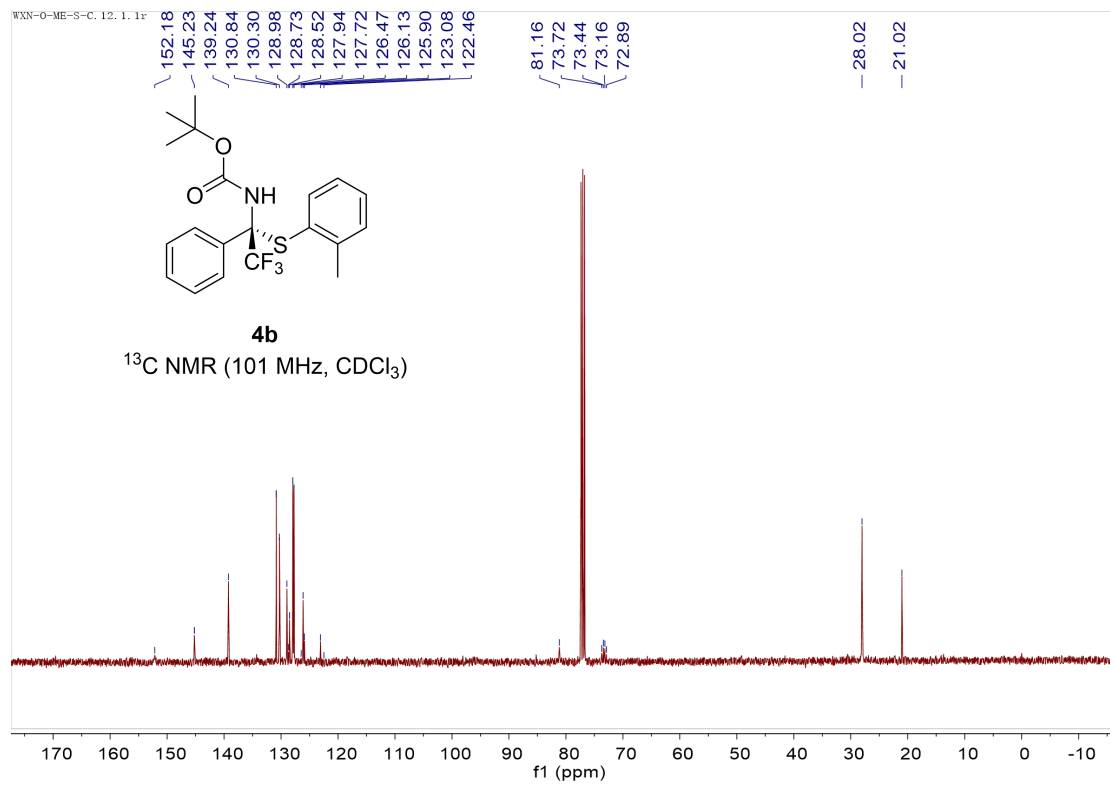
¹H NMR (400 MHz, CDCl₃) δ 7.62 (dd, $J = 6.4, 2.5$ Hz, 2H), 7.48 – 7.29 (m, 10H), 7.09 (d, $J = 7.8$ Hz,

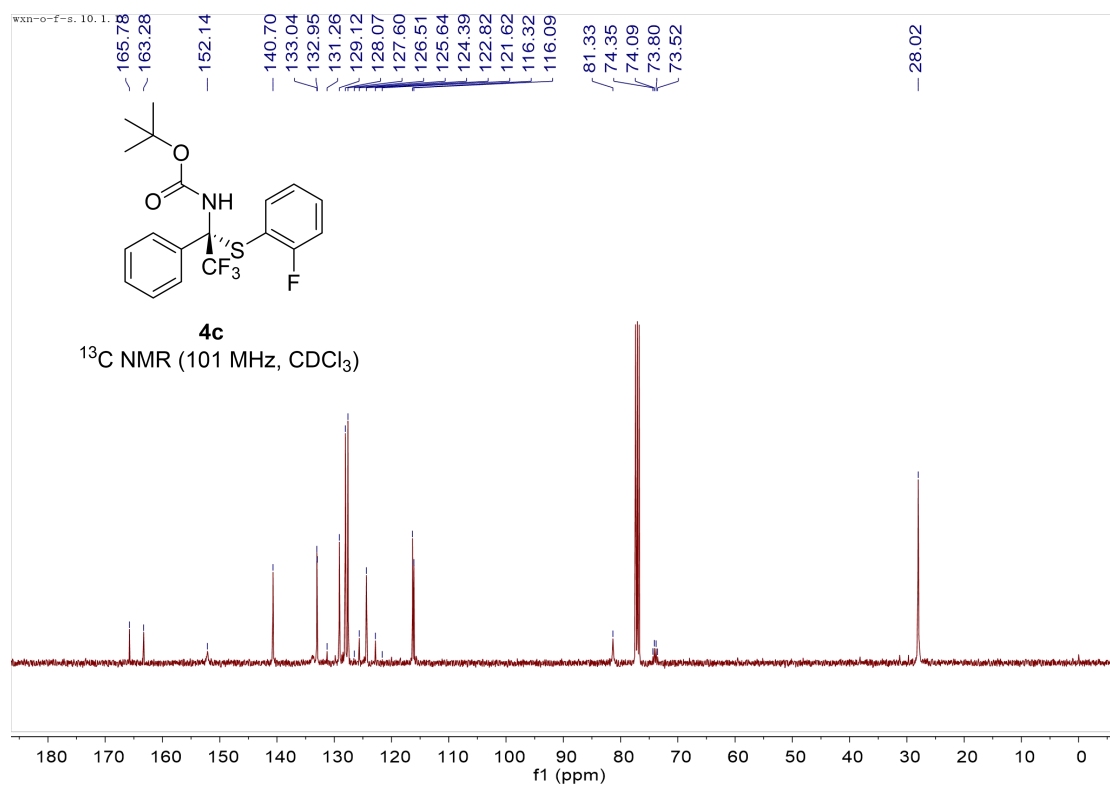
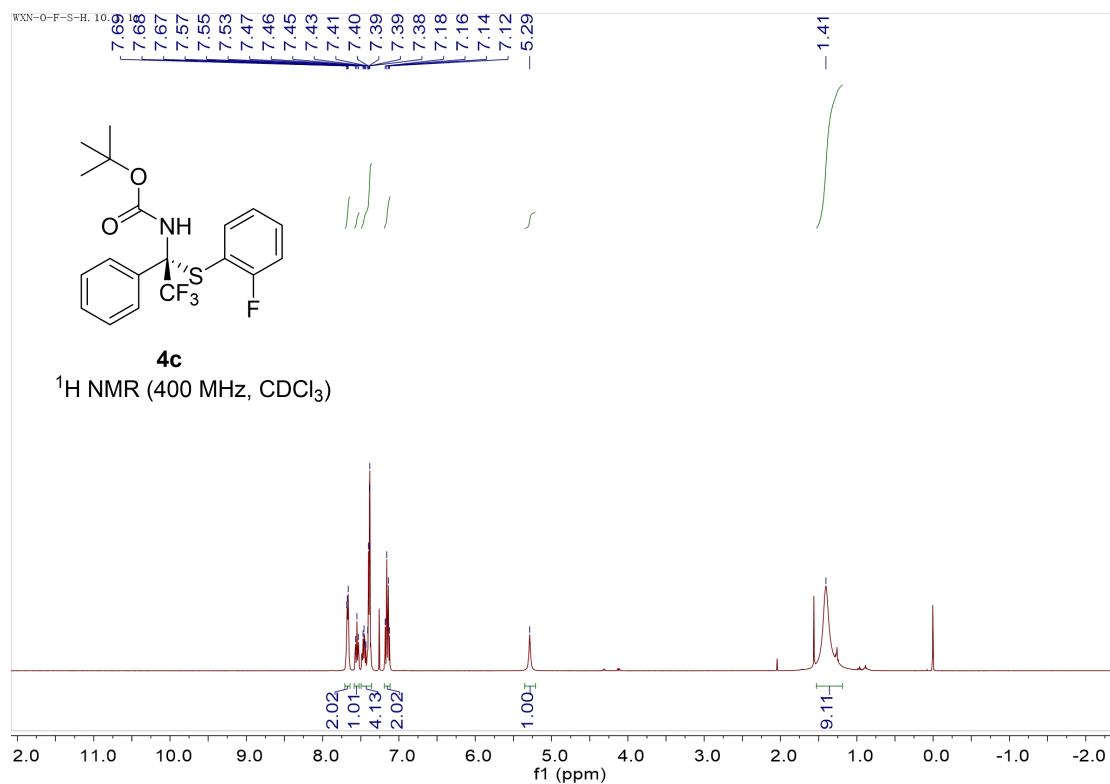
2H), 5.40 (s, 1H), 5.23 (d, $J = 11.8$ Hz, 1H), 4.95 (d, $J = 12.0$ Hz, 1H). **^{13}C NMR** (101 MHz, CDCl_3) δ 152.9, 139.6, 137.0, 135.5, 133.4, 129.4, 129.1, 128.7, 128.3, 127.5, 126.8, 124.3 (q, $J = 284.1$ Hz), 73.5 (q, $J = 28.5$ Hz), 67.6. **^{19}F NMR** (377 MHz, CDCl_3) δ -74.22. **HRMS** (ESI) m/z : $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{22}\text{H}_{17}\text{ClF}_3\text{NO}_2\text{S}$ 474.1480; found 474.1452.

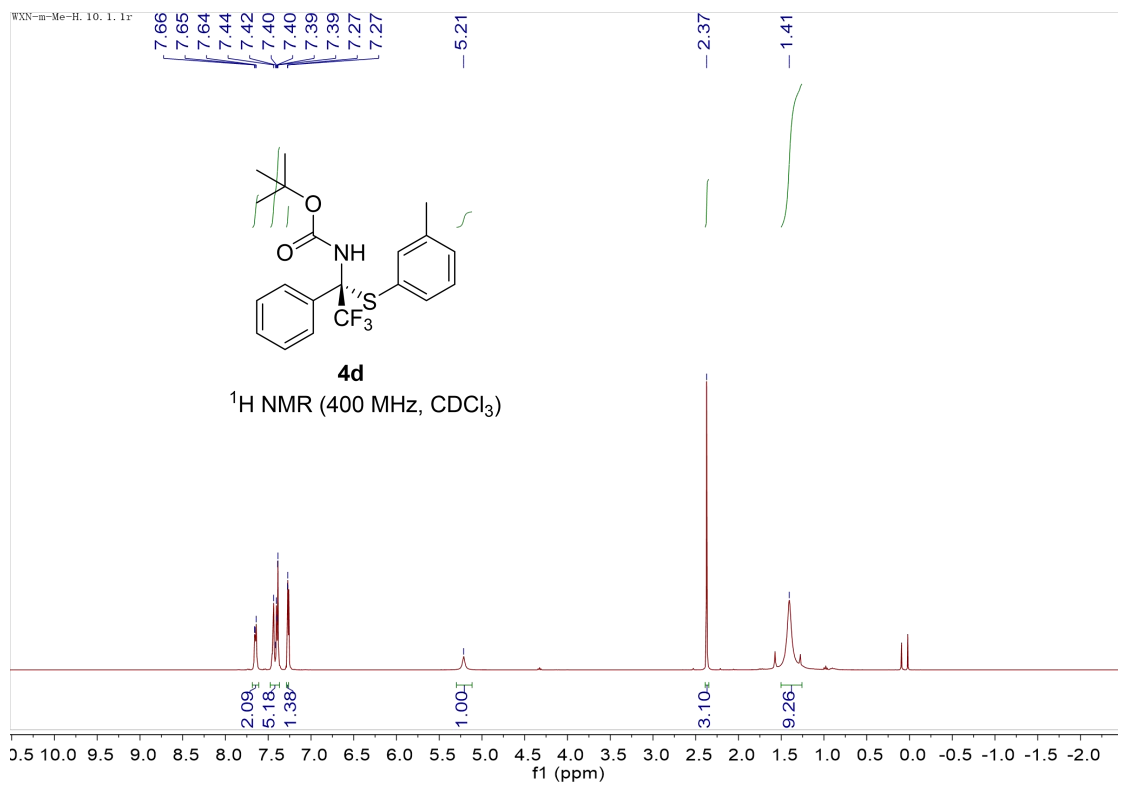
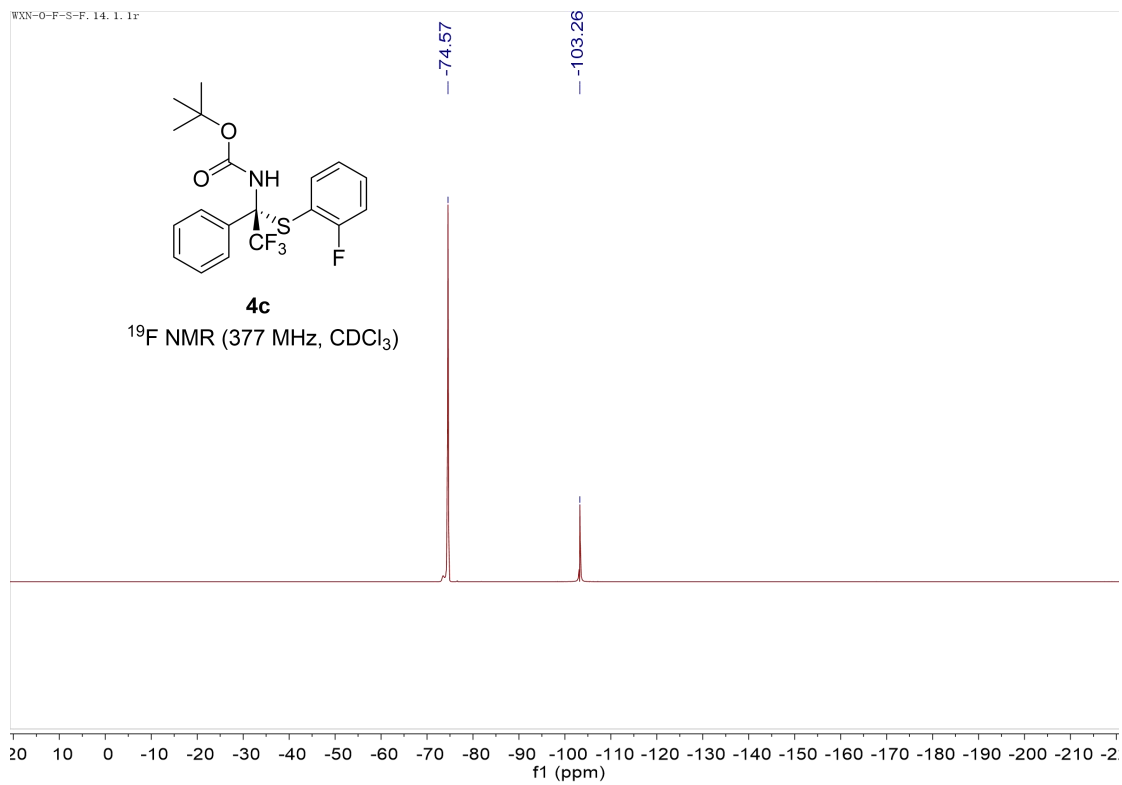
9. NMR spectra of addition products 4a-4u.

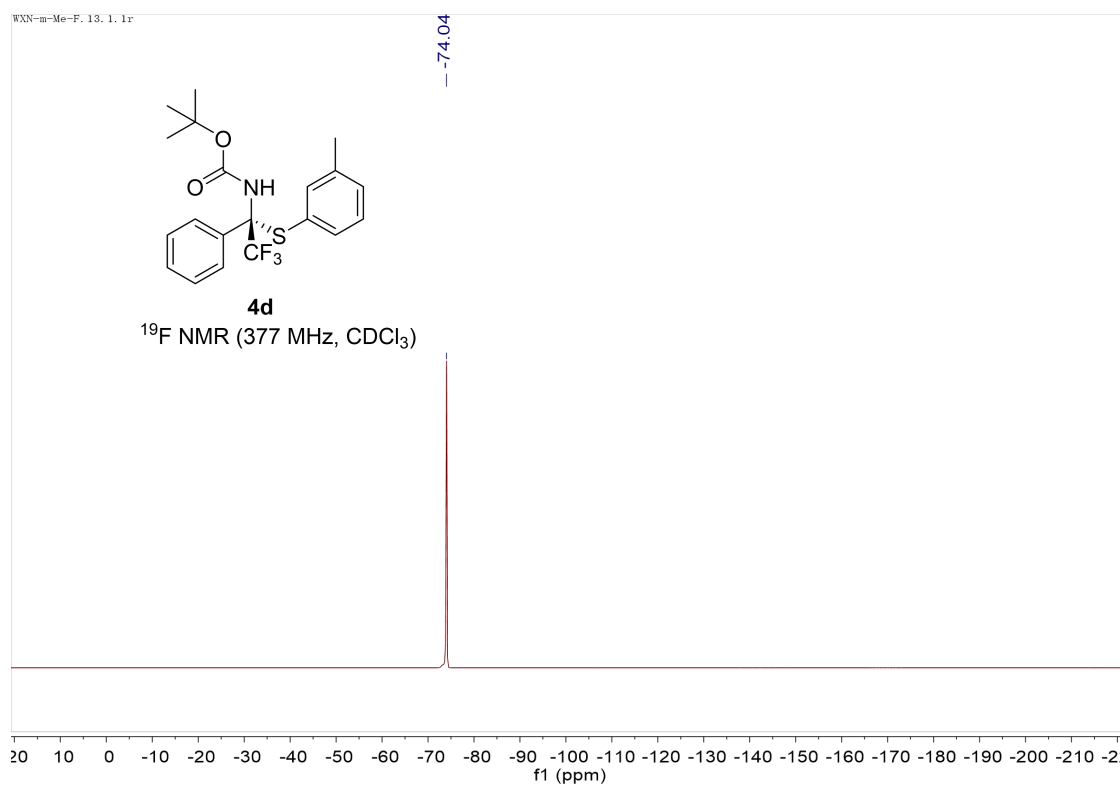
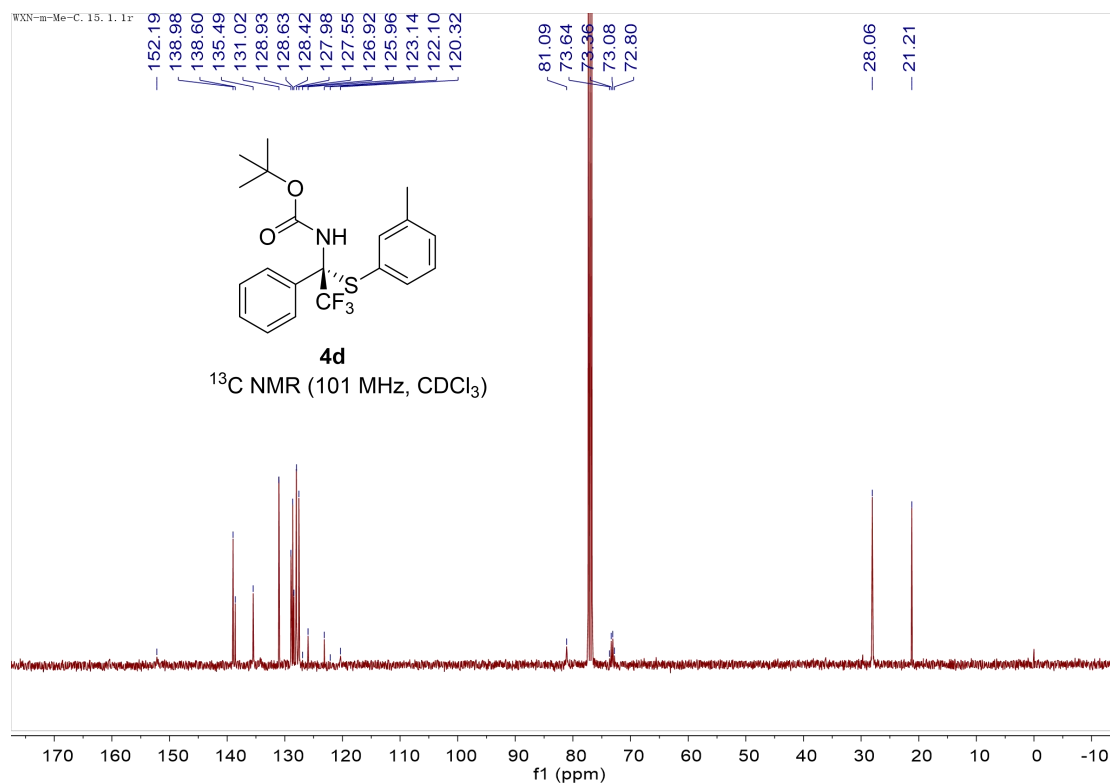


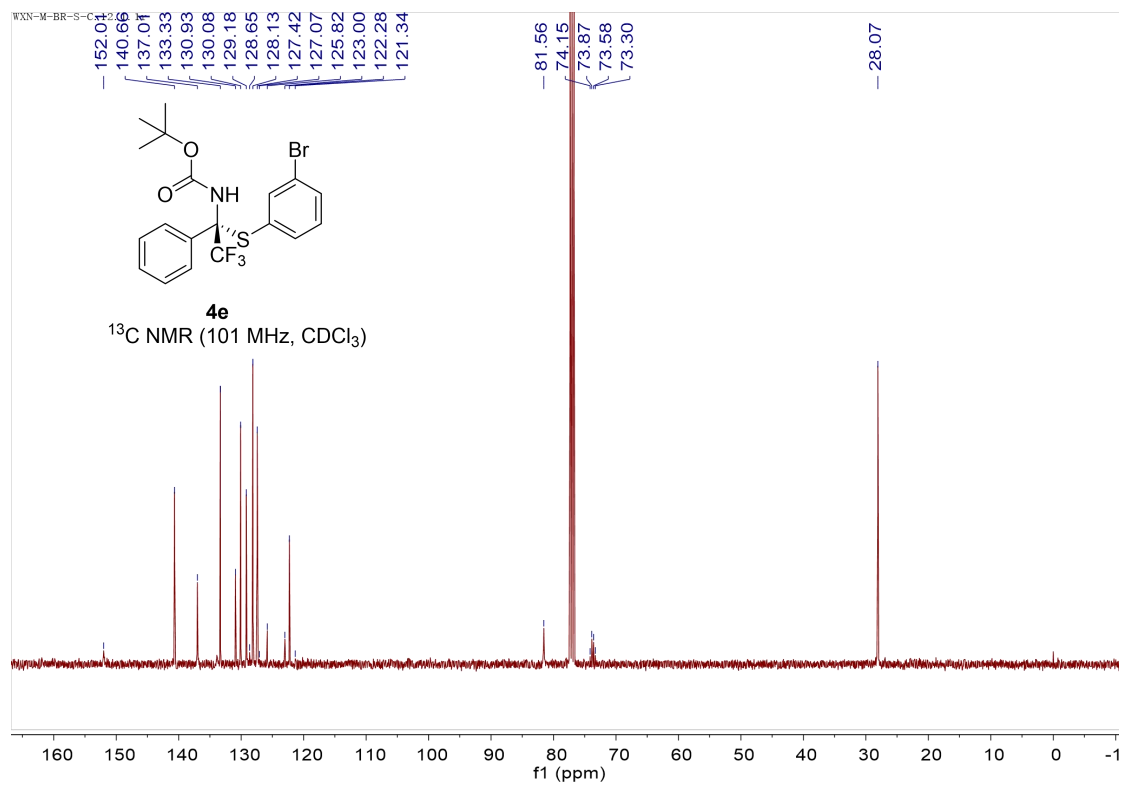
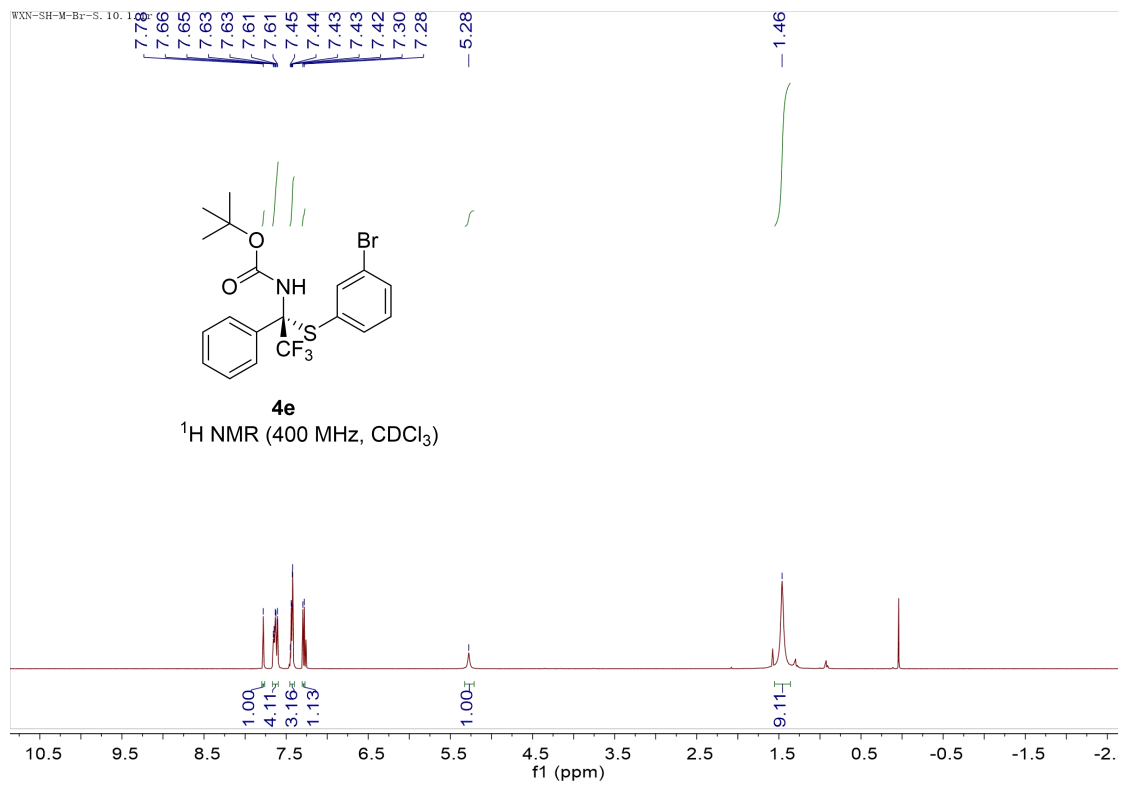


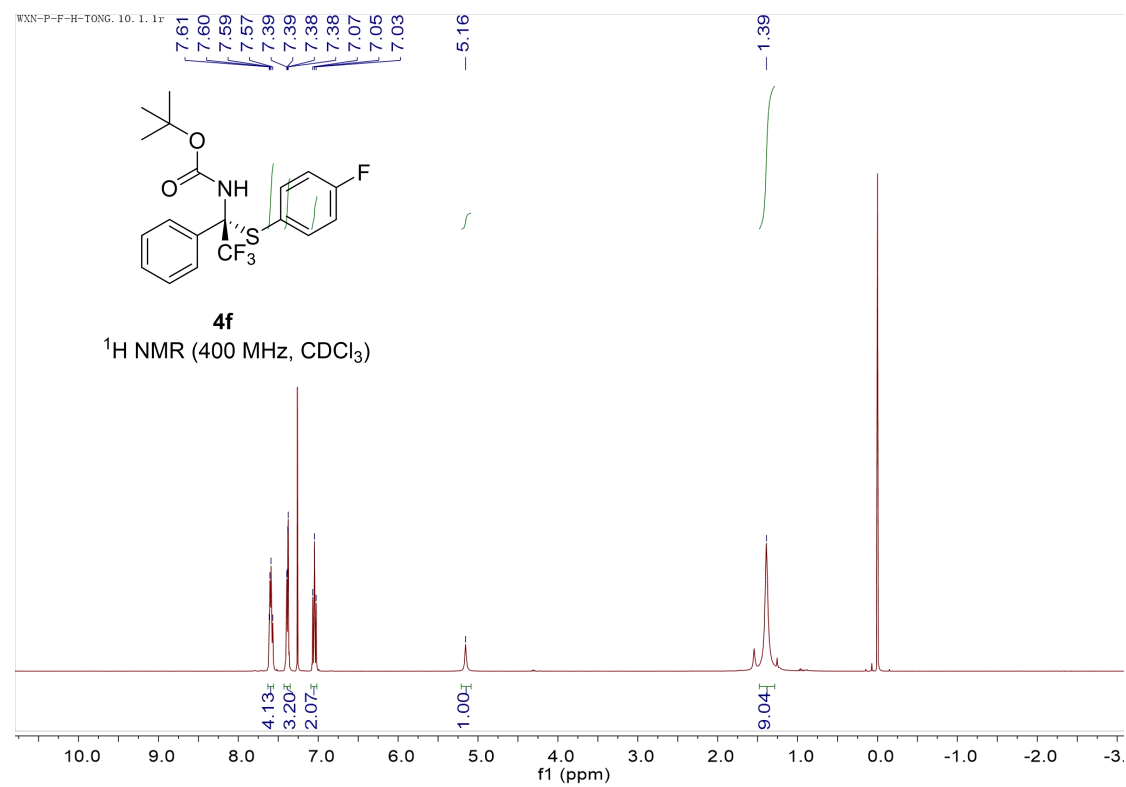
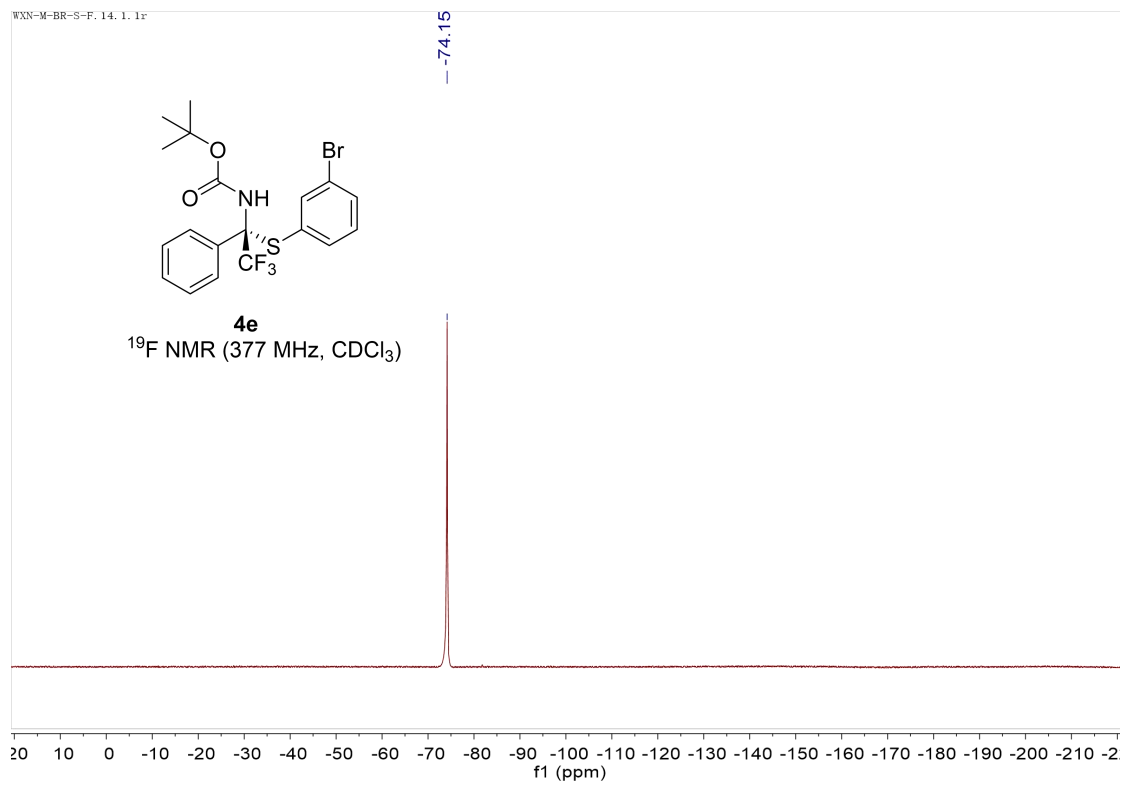


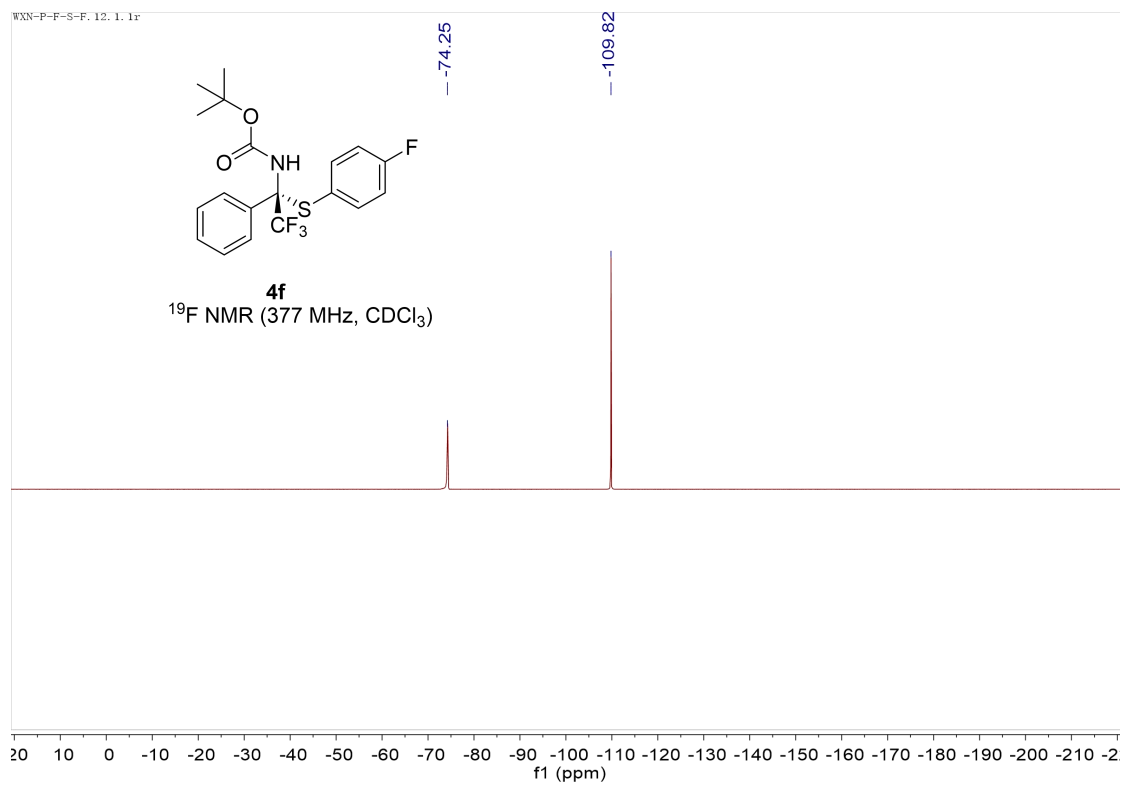
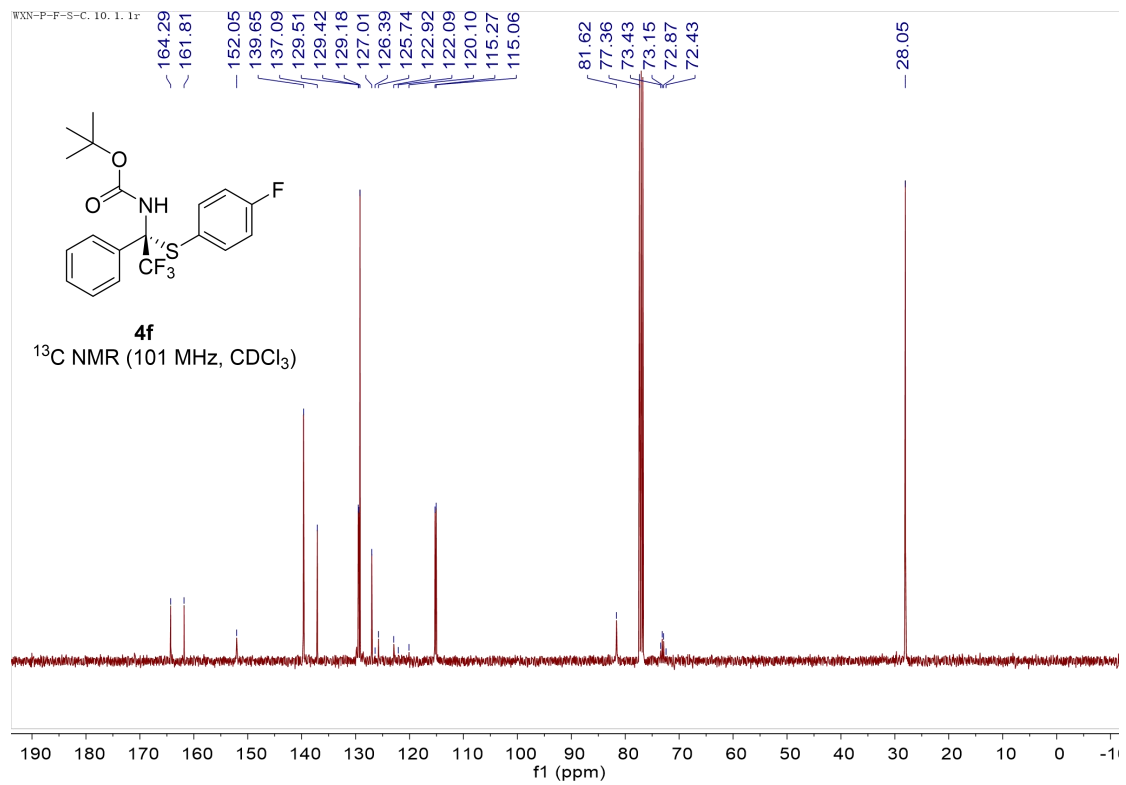


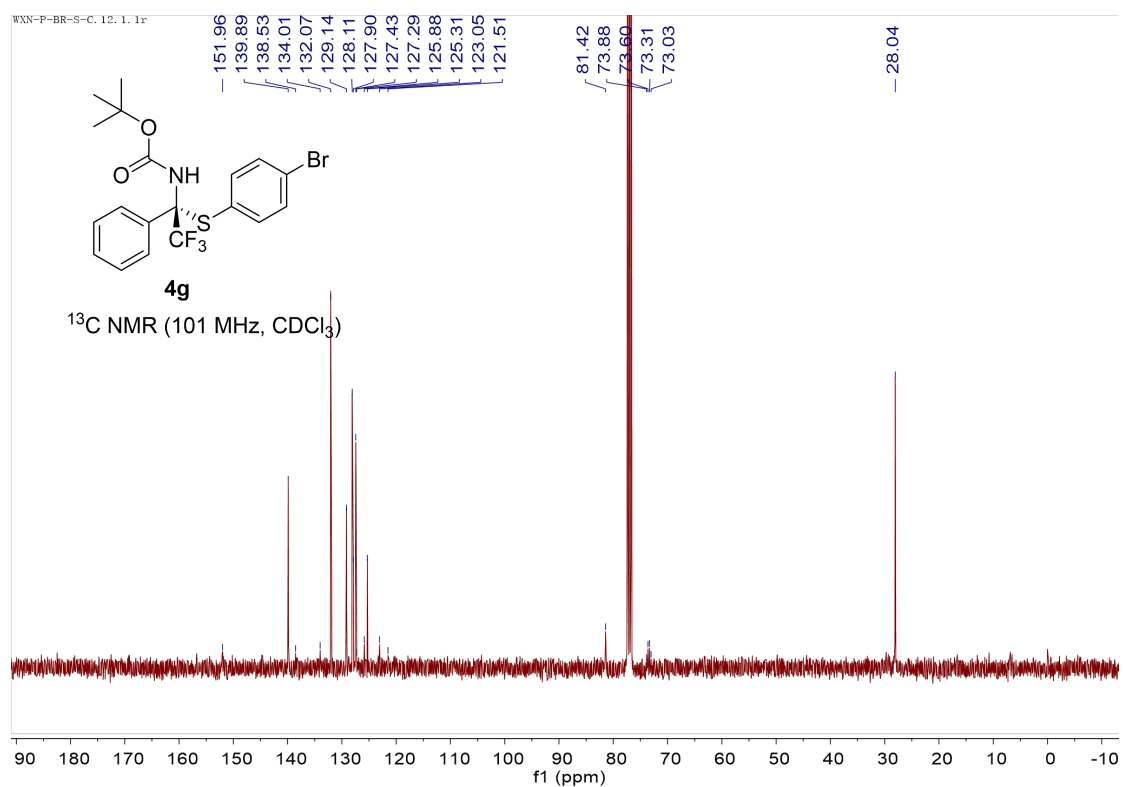
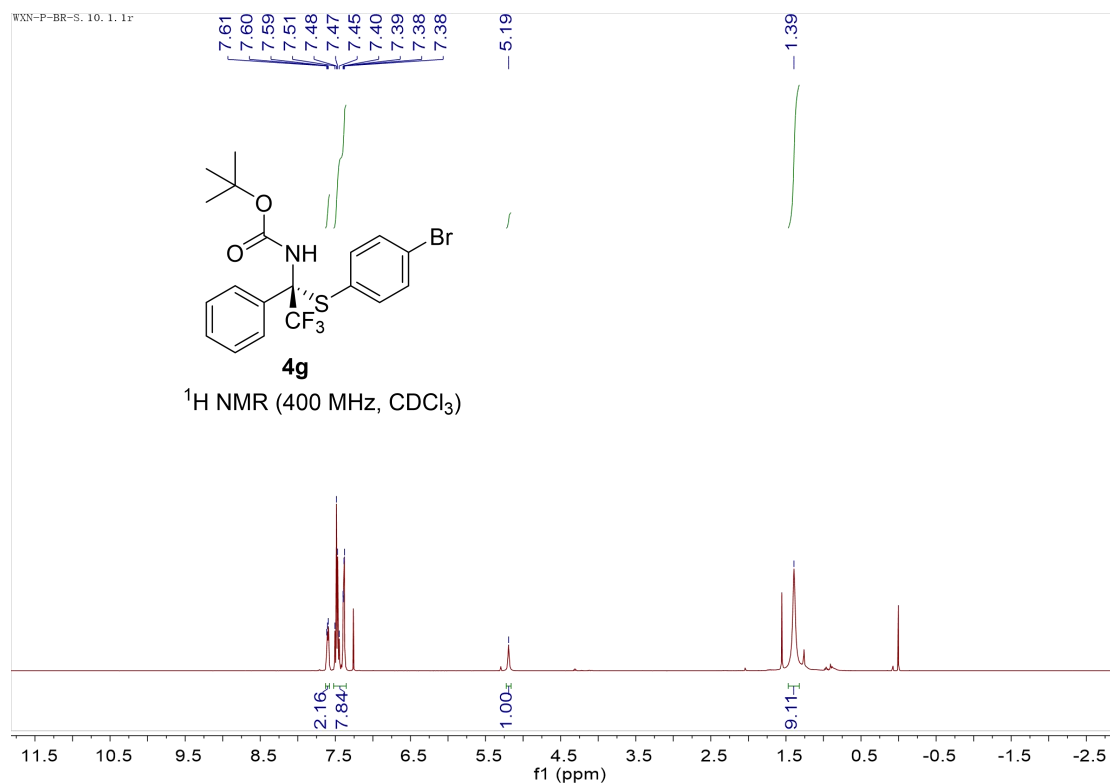


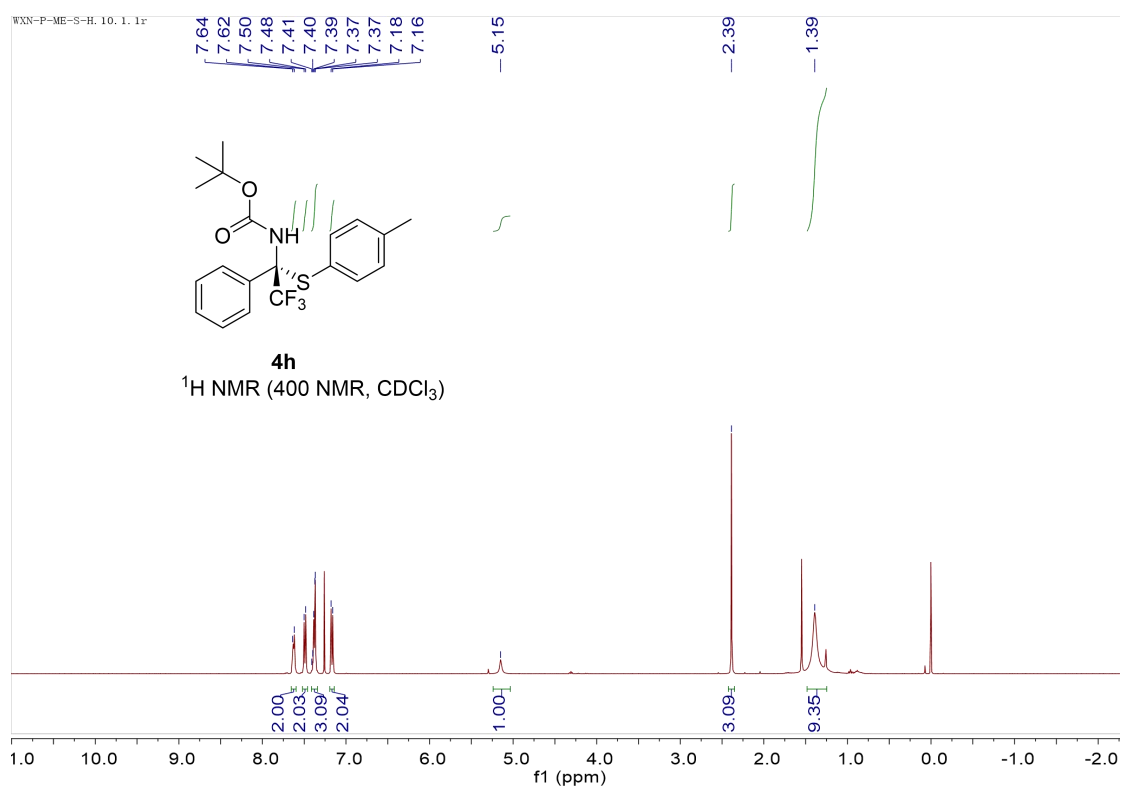
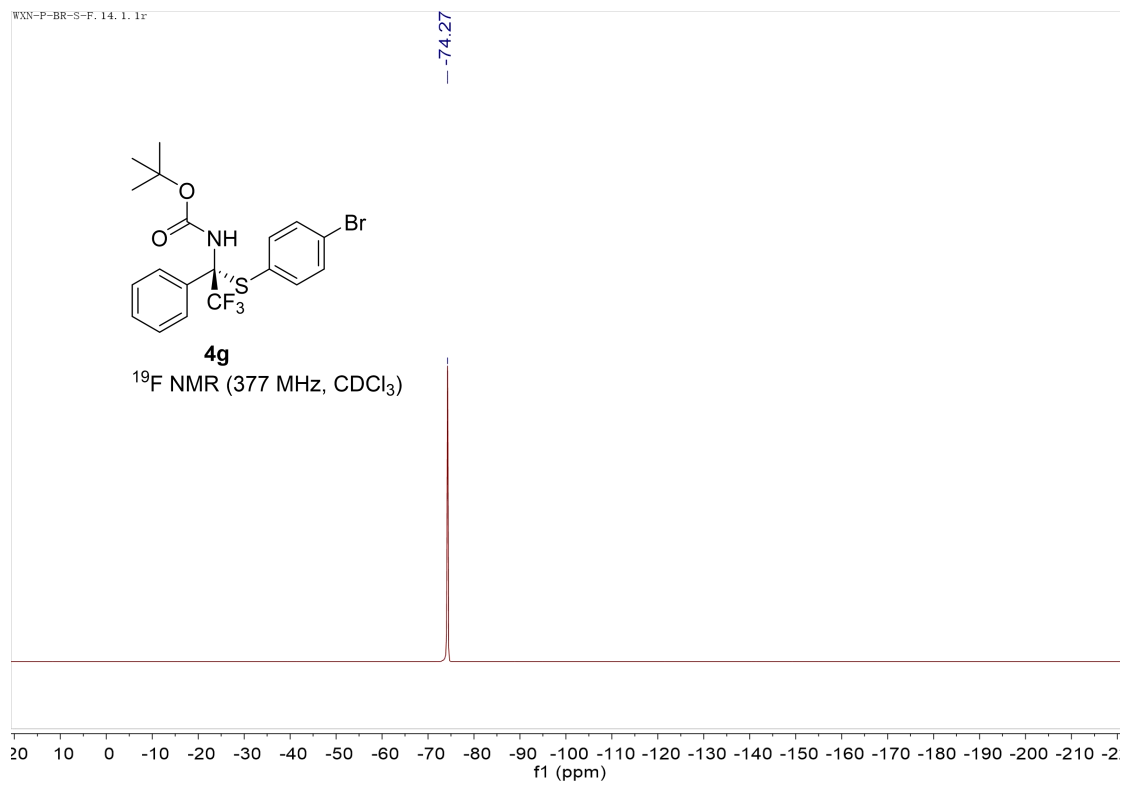


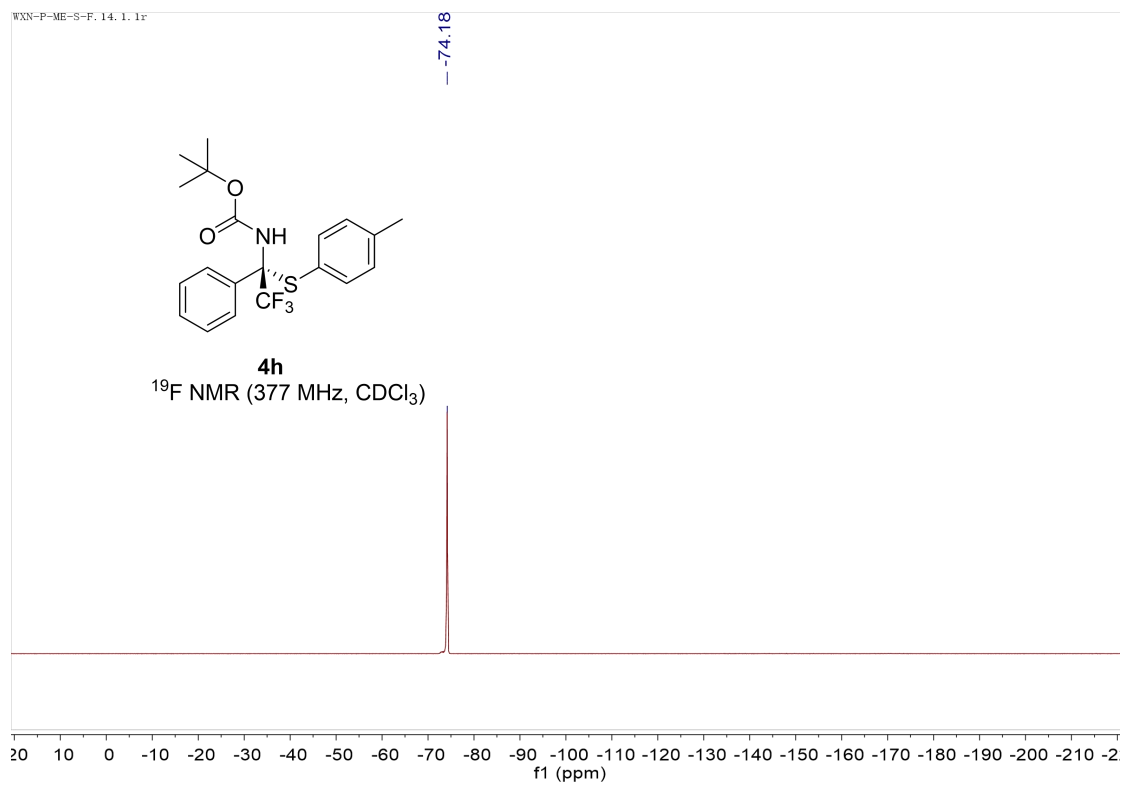
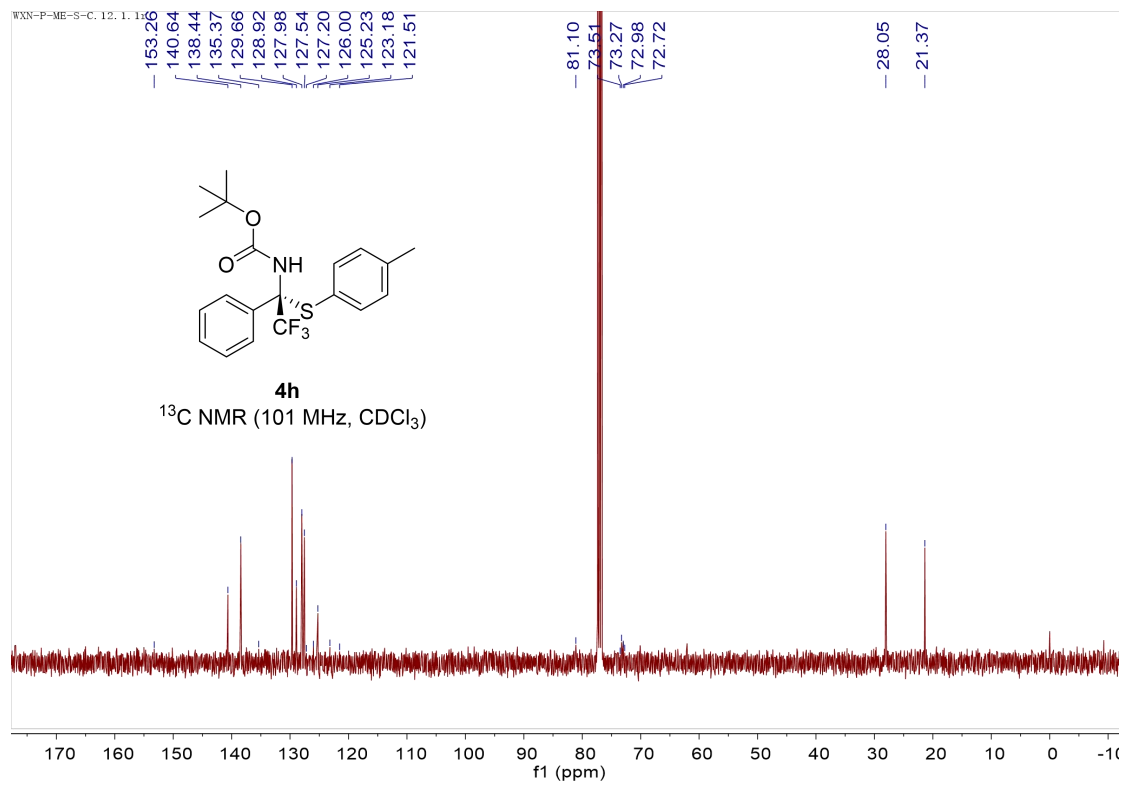


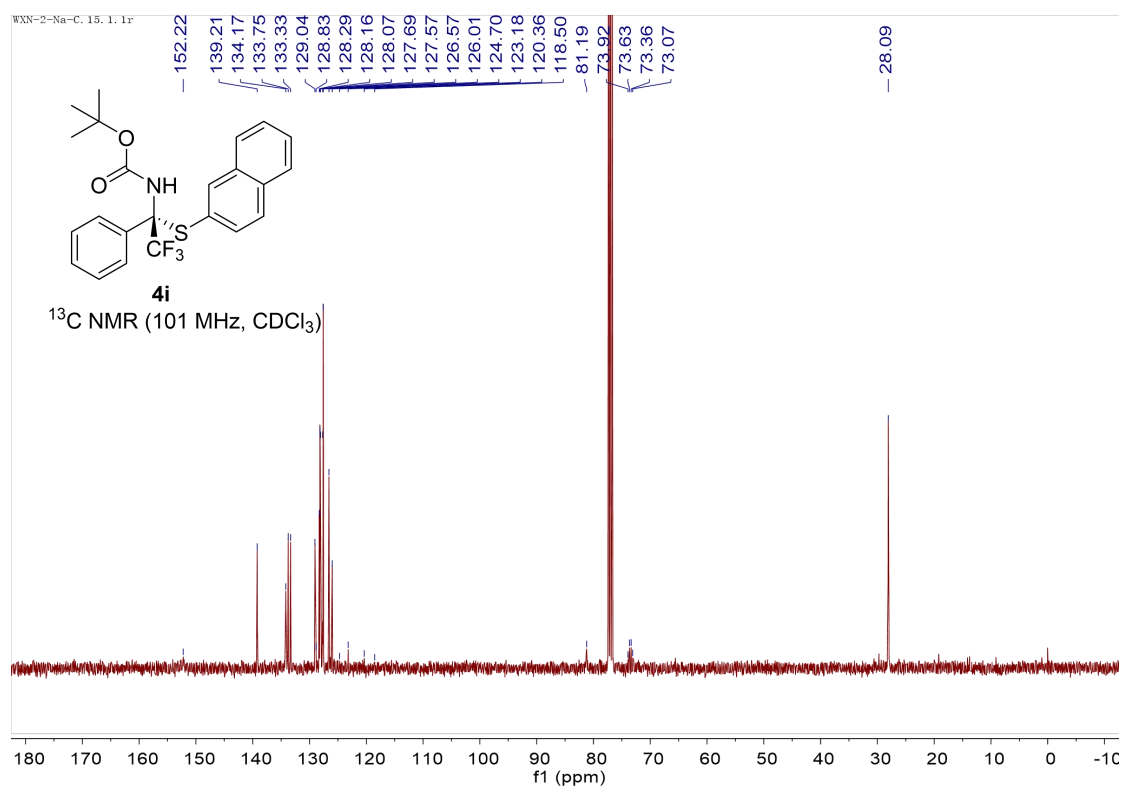
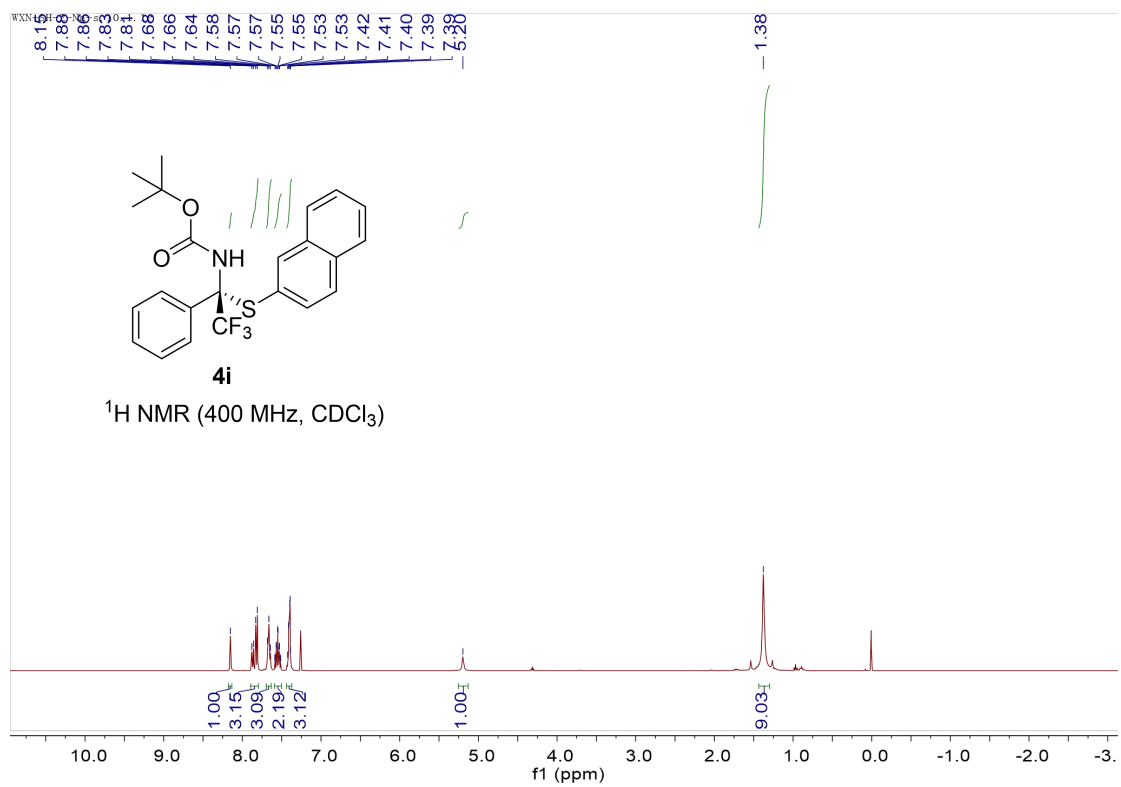




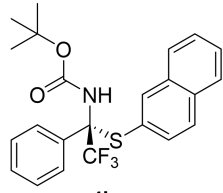






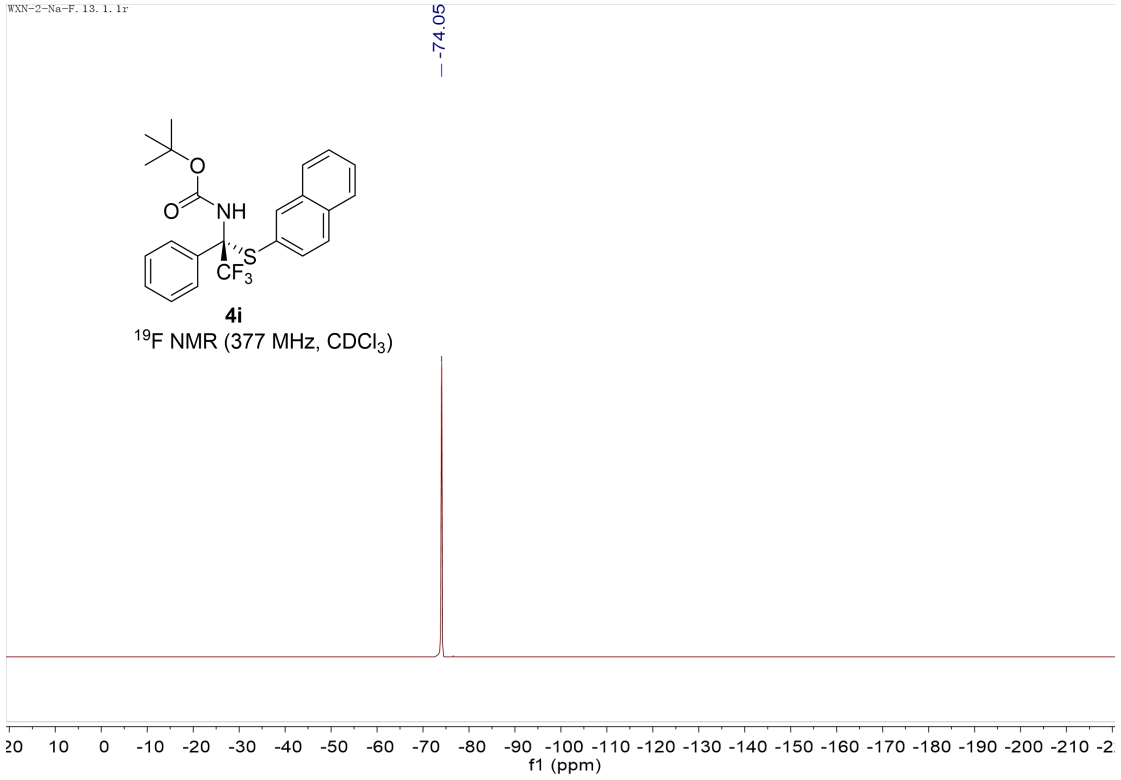


WXN-2-Na-F. 13. 1. 1r

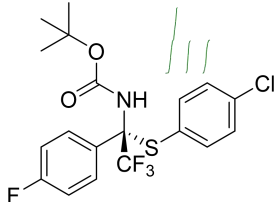


4i

¹⁹F NMR (377 MHz, CDCl₃)

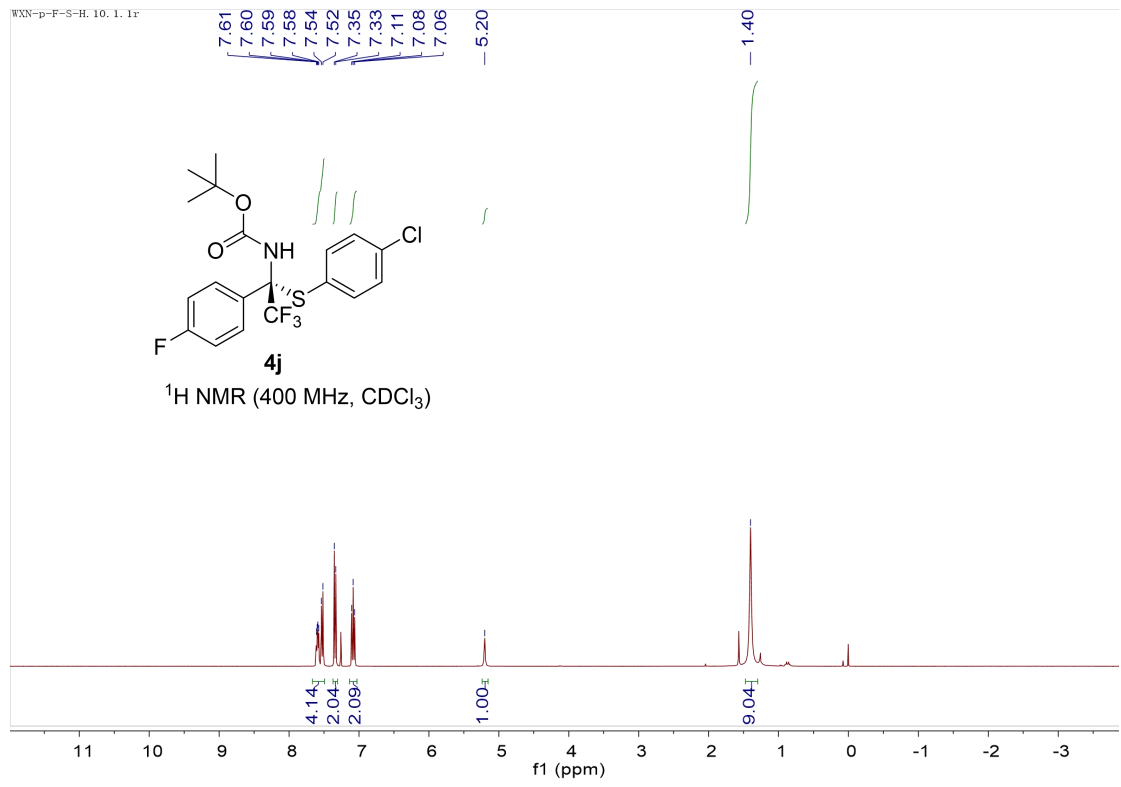


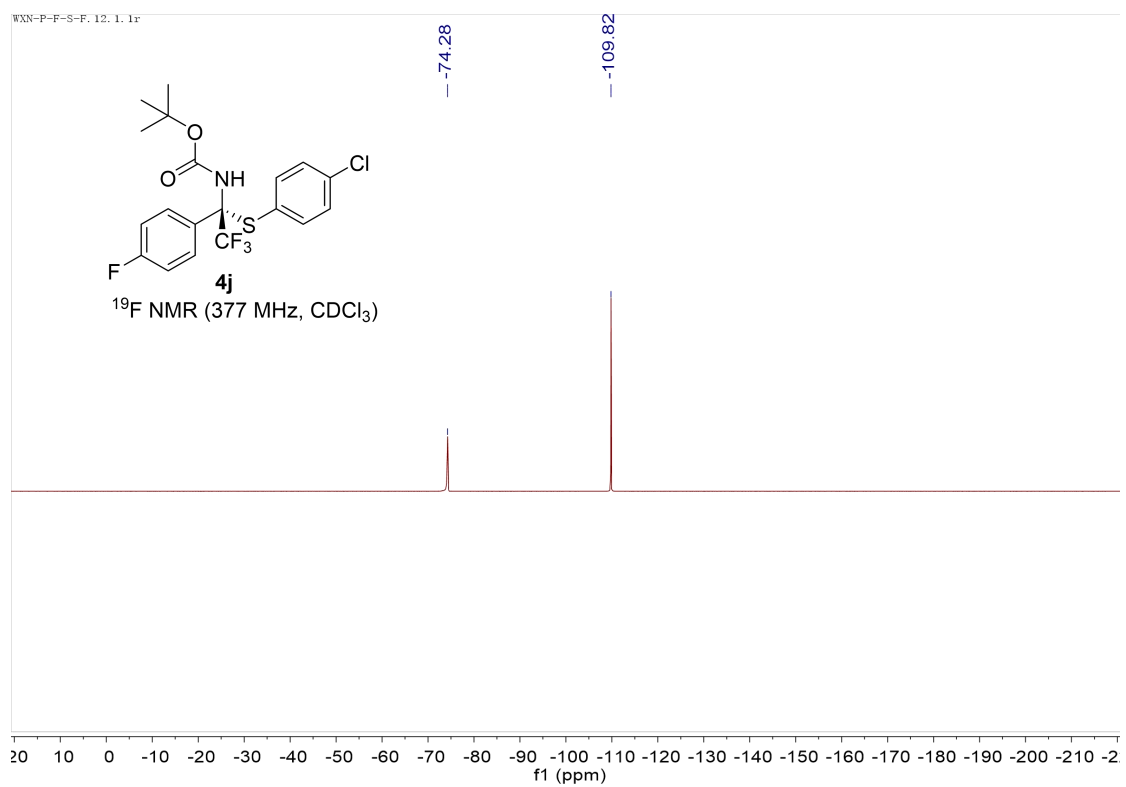
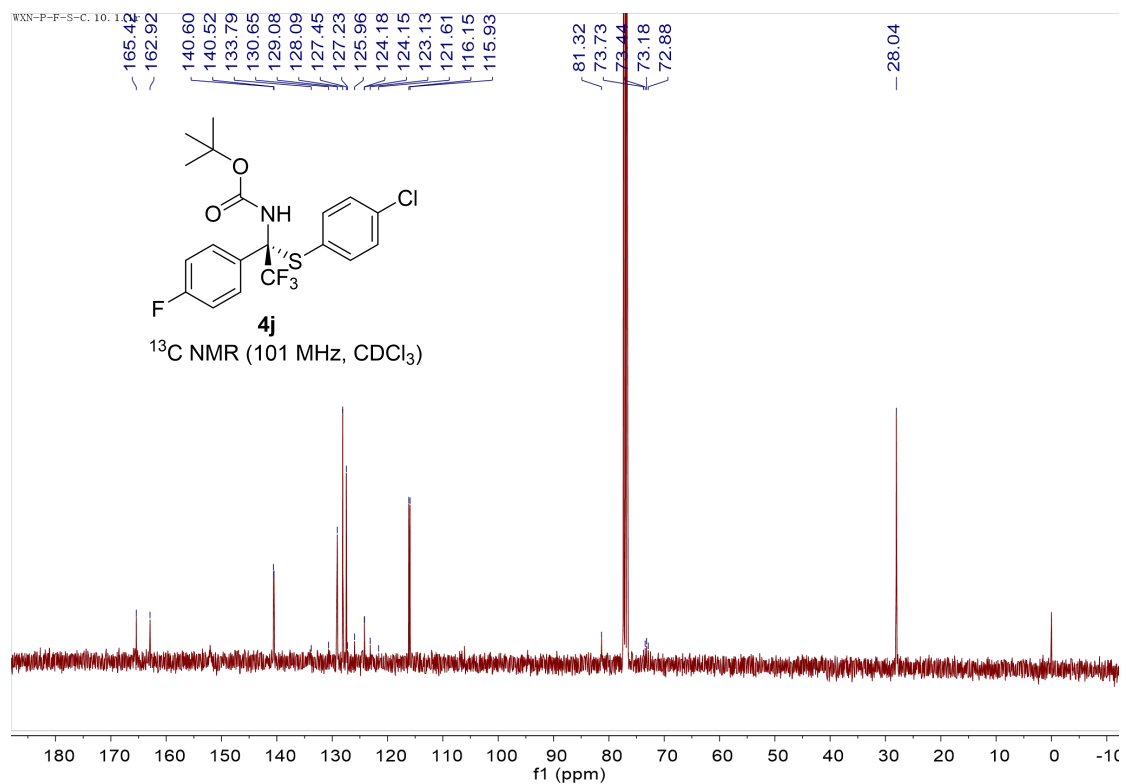
WXN-p-F-S-H. 10. 1. 1r

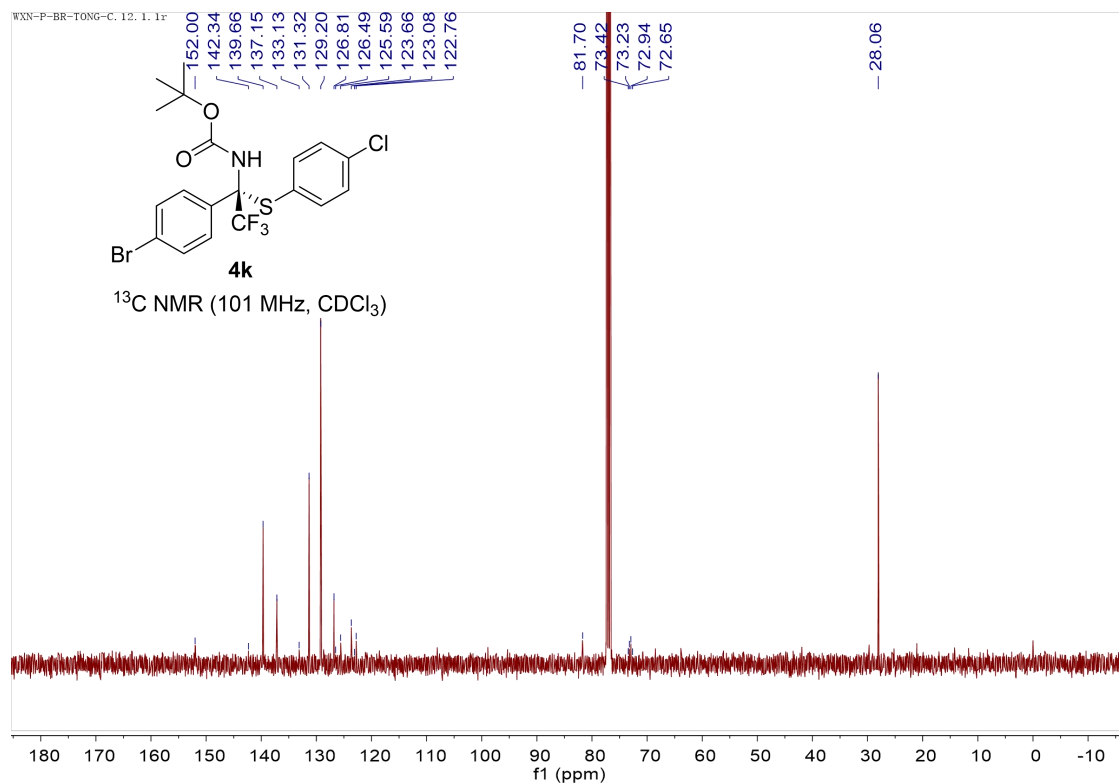
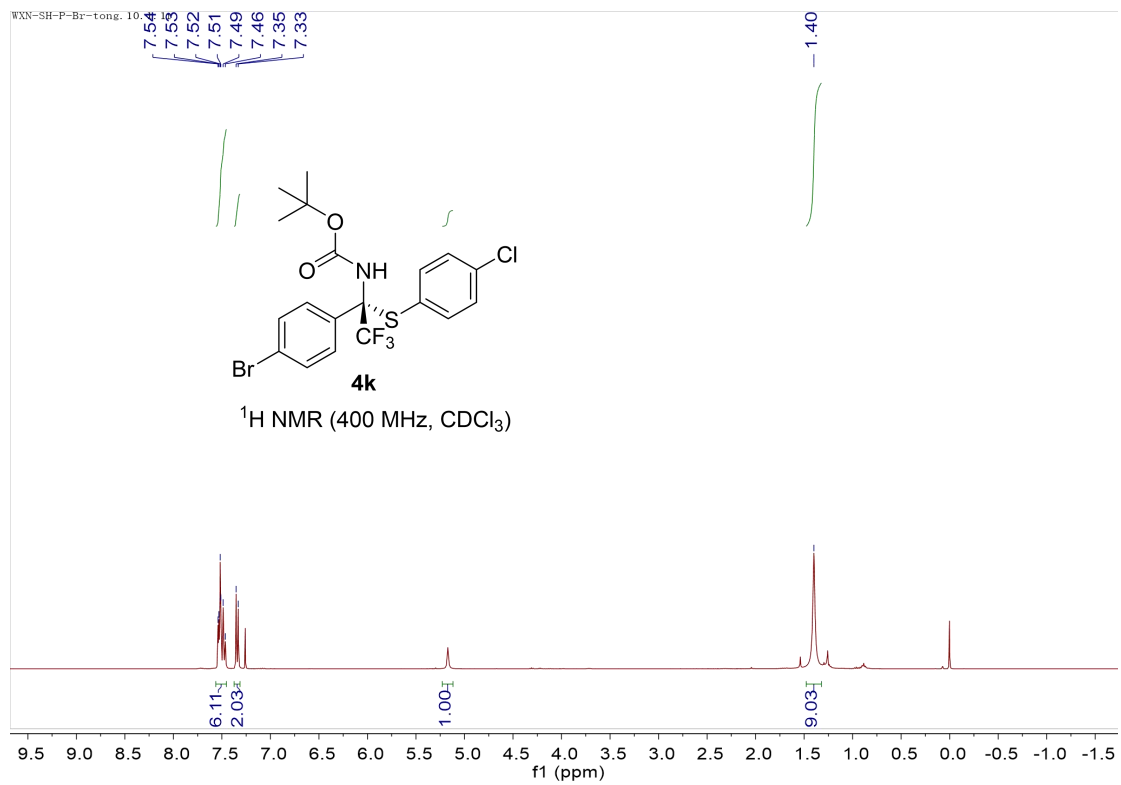


4j

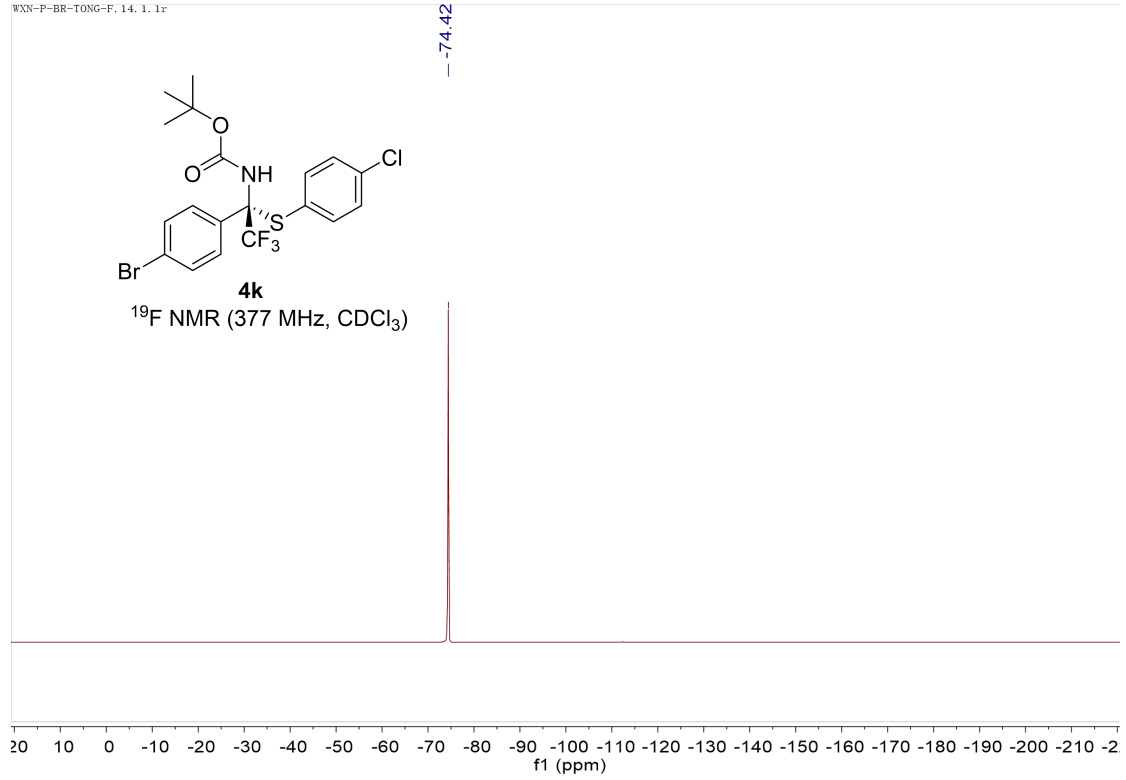
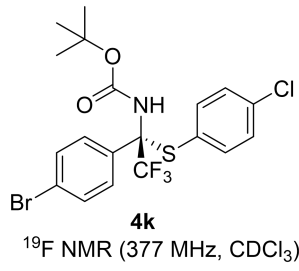
¹H NMR (400 MHz, CDCl₃)



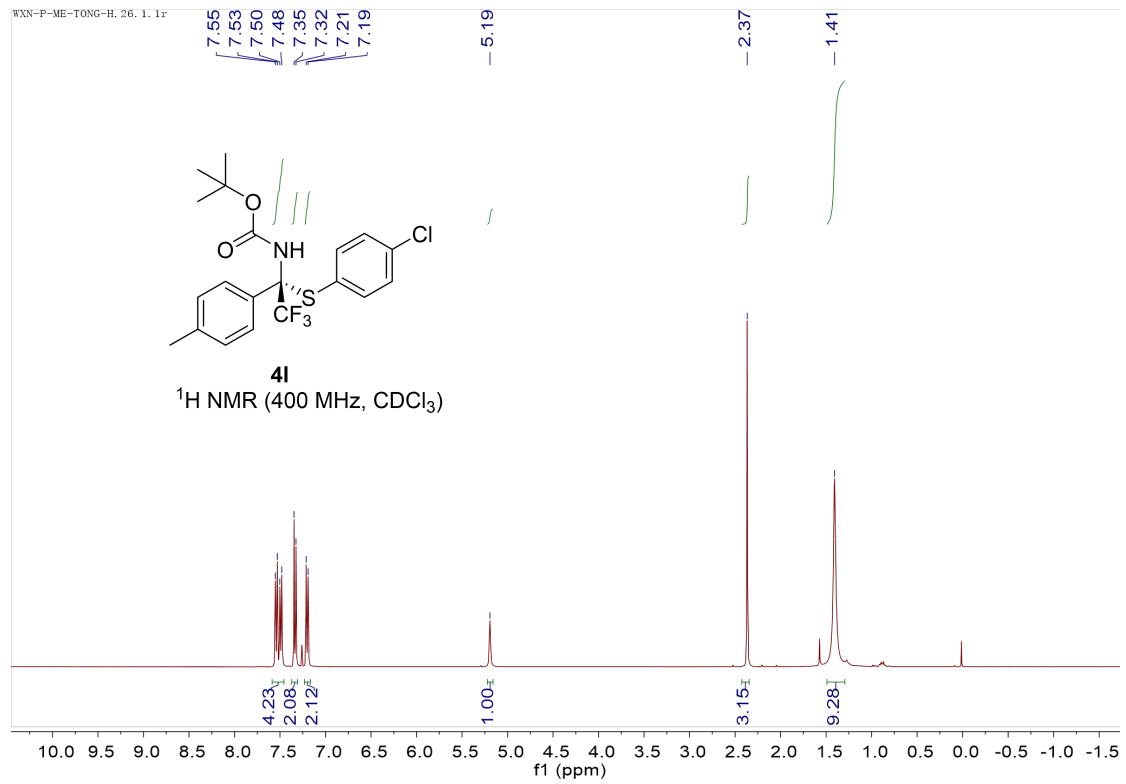
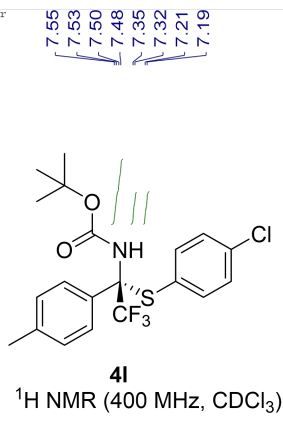


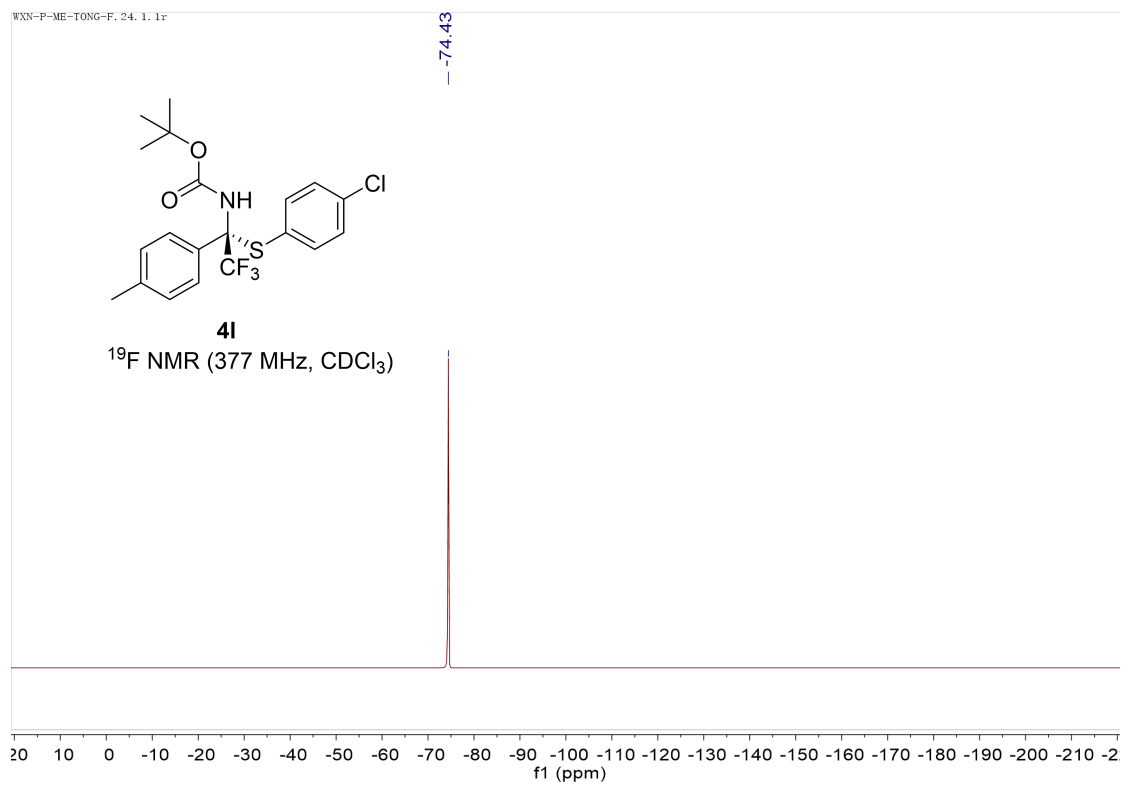
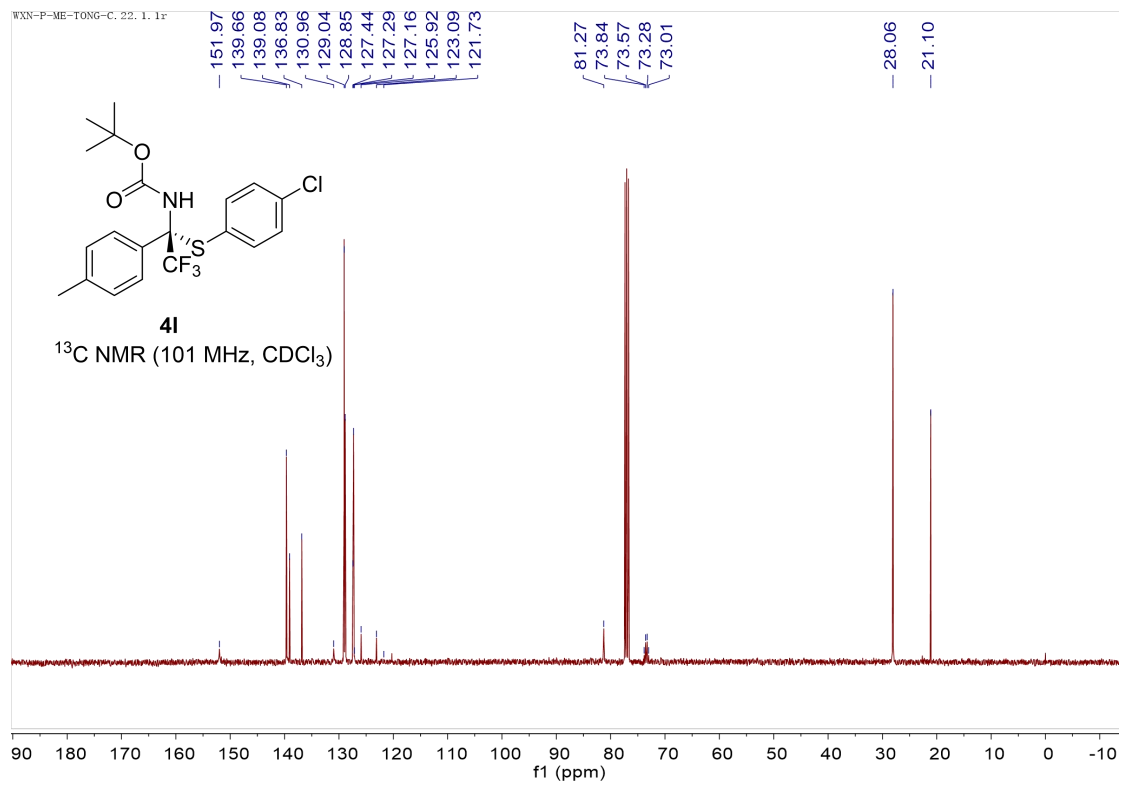


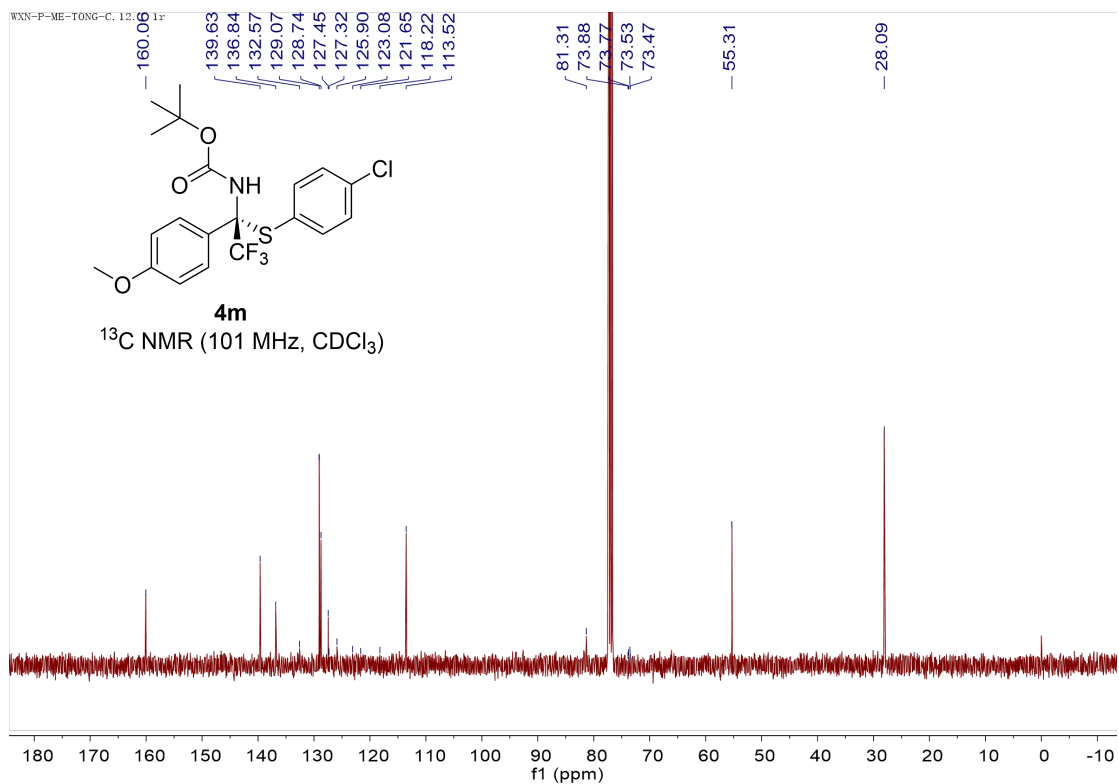
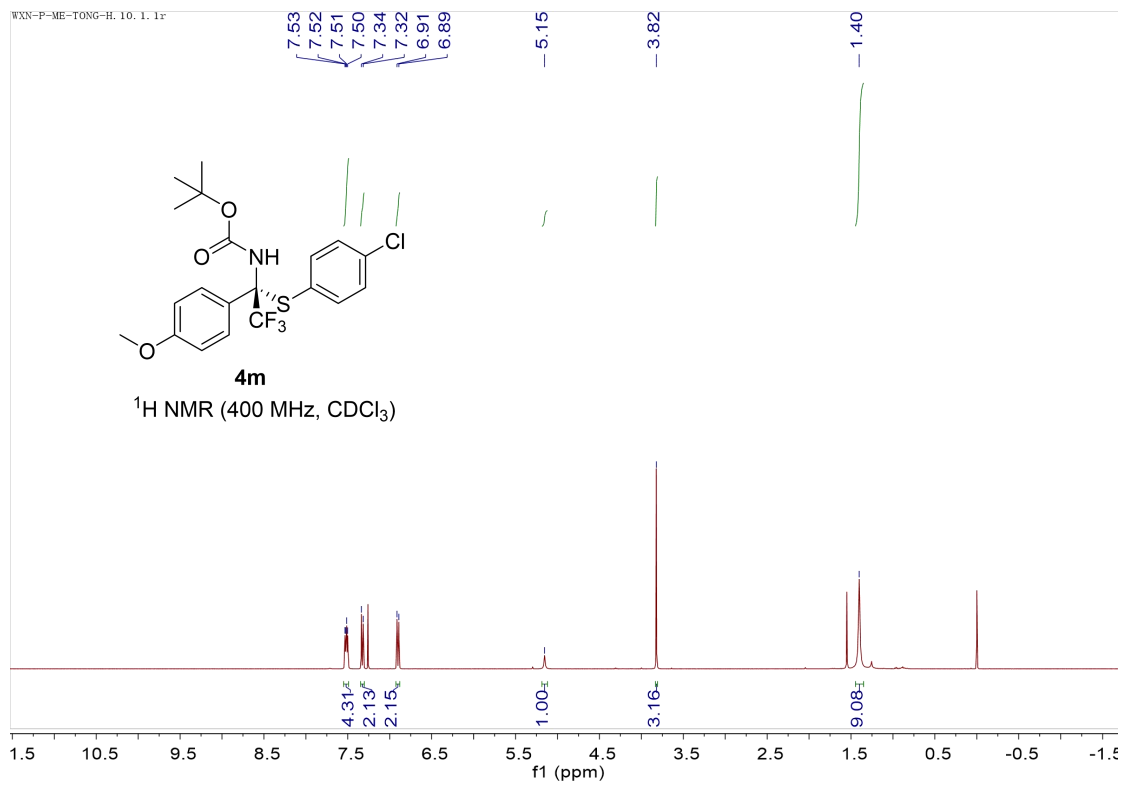
WXN-P-BR-TONG-F. 14. 1. 1f



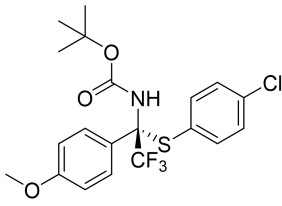
WXN-P-ME-TONG-H. 26. 1. 1f







WXN-P-ME-TONG-F. 14. 1. 1f



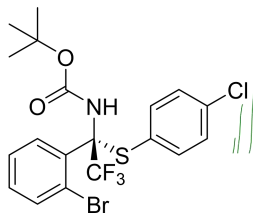
^{19}F NMR (377 MHz, CDCl_3)

-74.49

20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2

f1 (ppm)

WXN-3-Cl-tong-H. 10. 1. 1f



^1H NMR (400 MHz, CDCl_3)

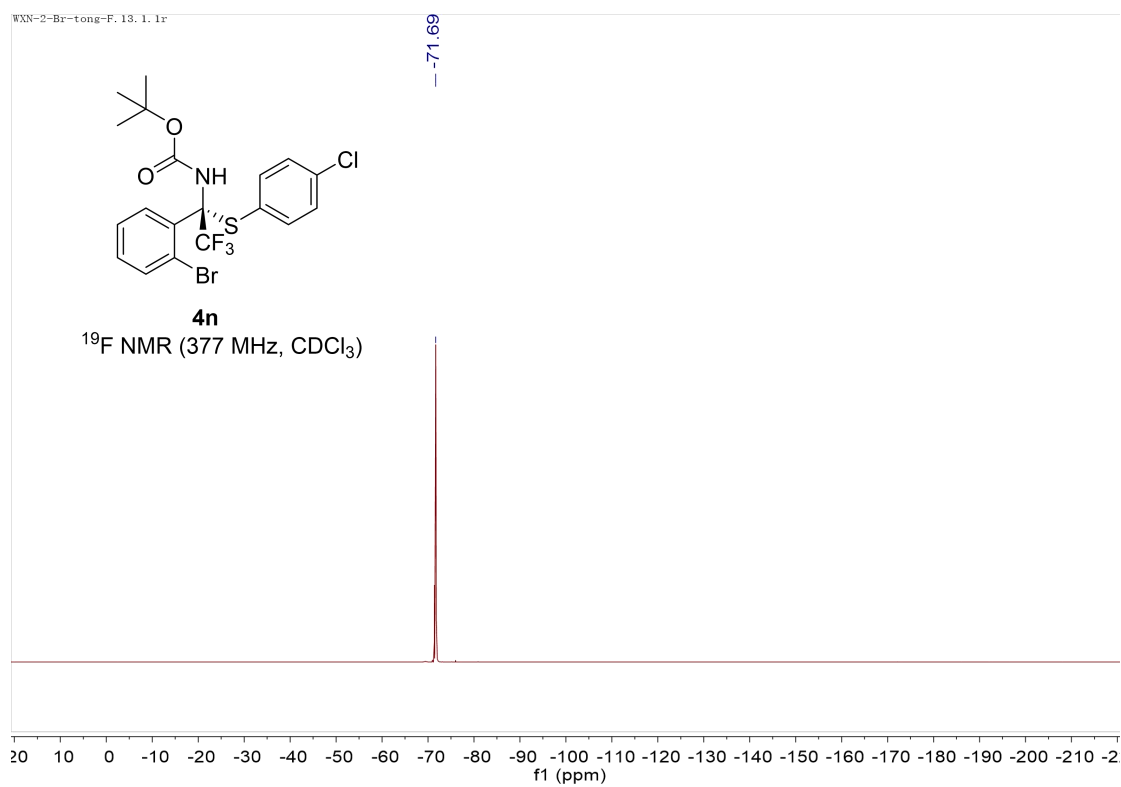
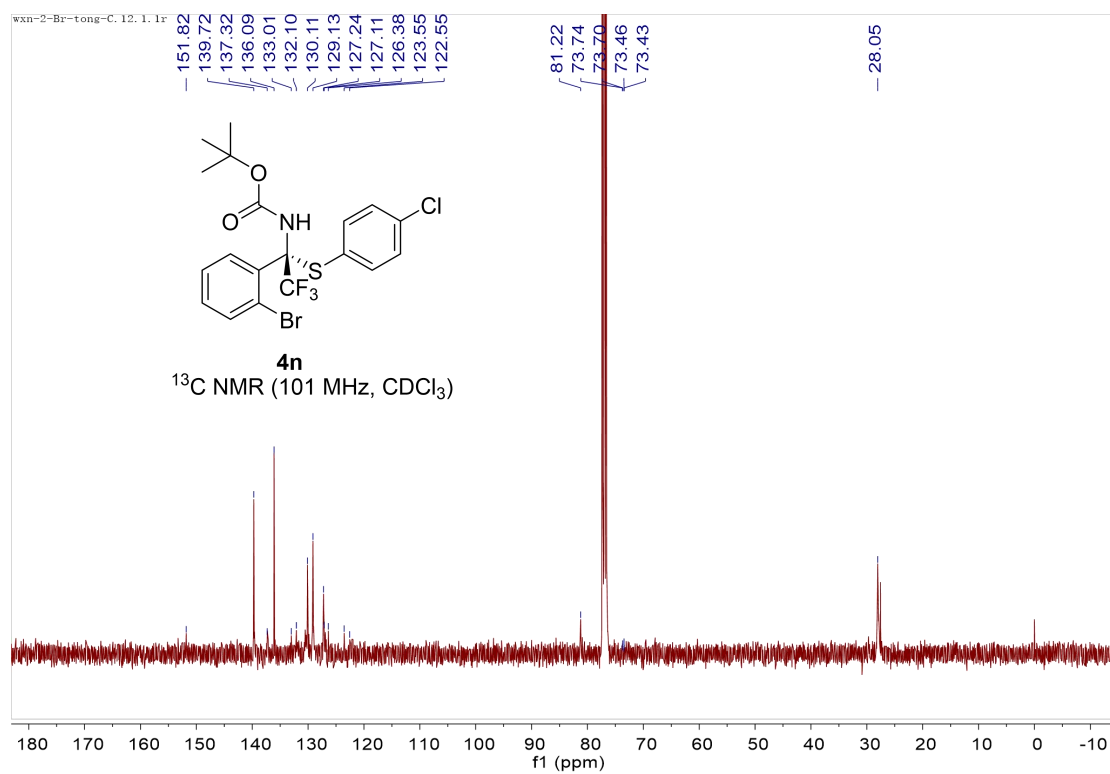
7.59
7.54
7.51
7.49
7.38
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.33
7.31
5.20

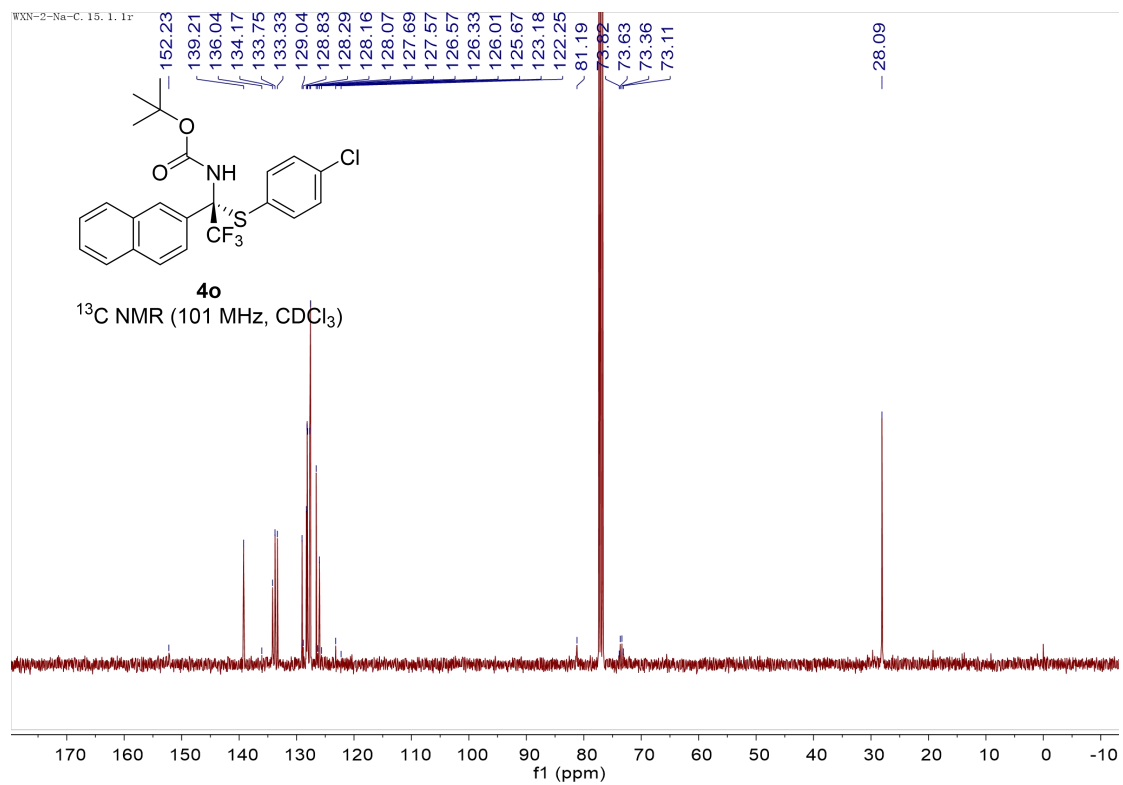
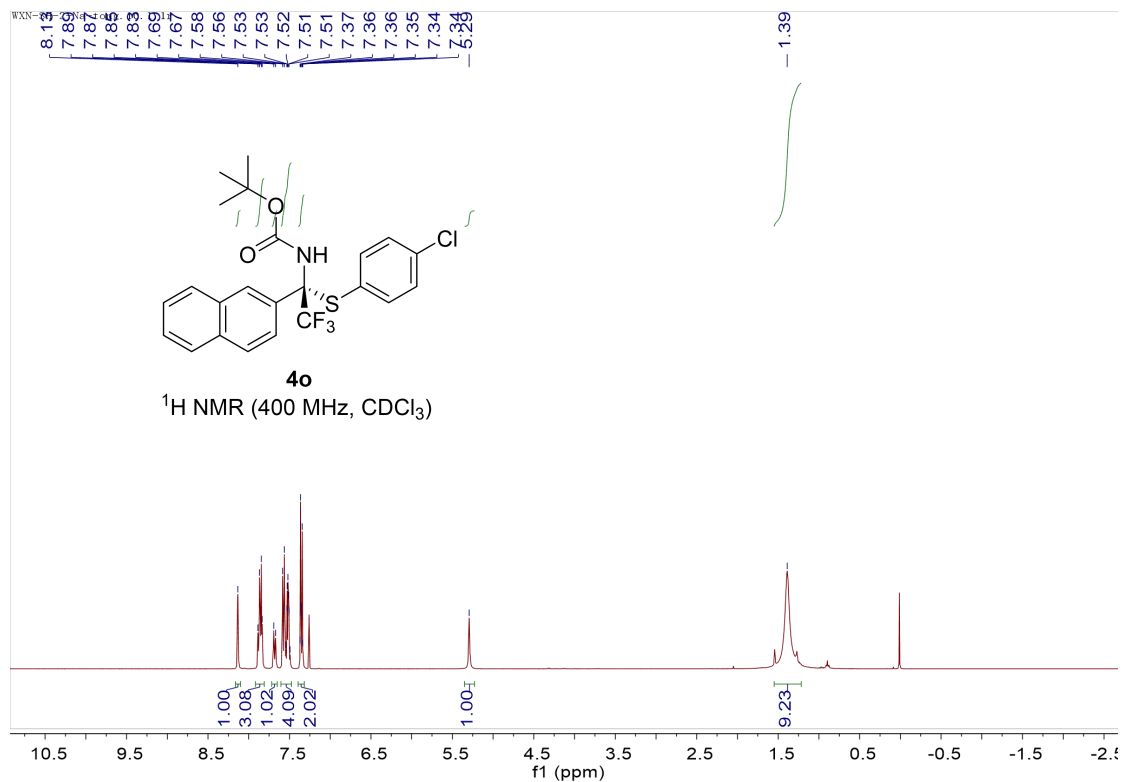
1.40

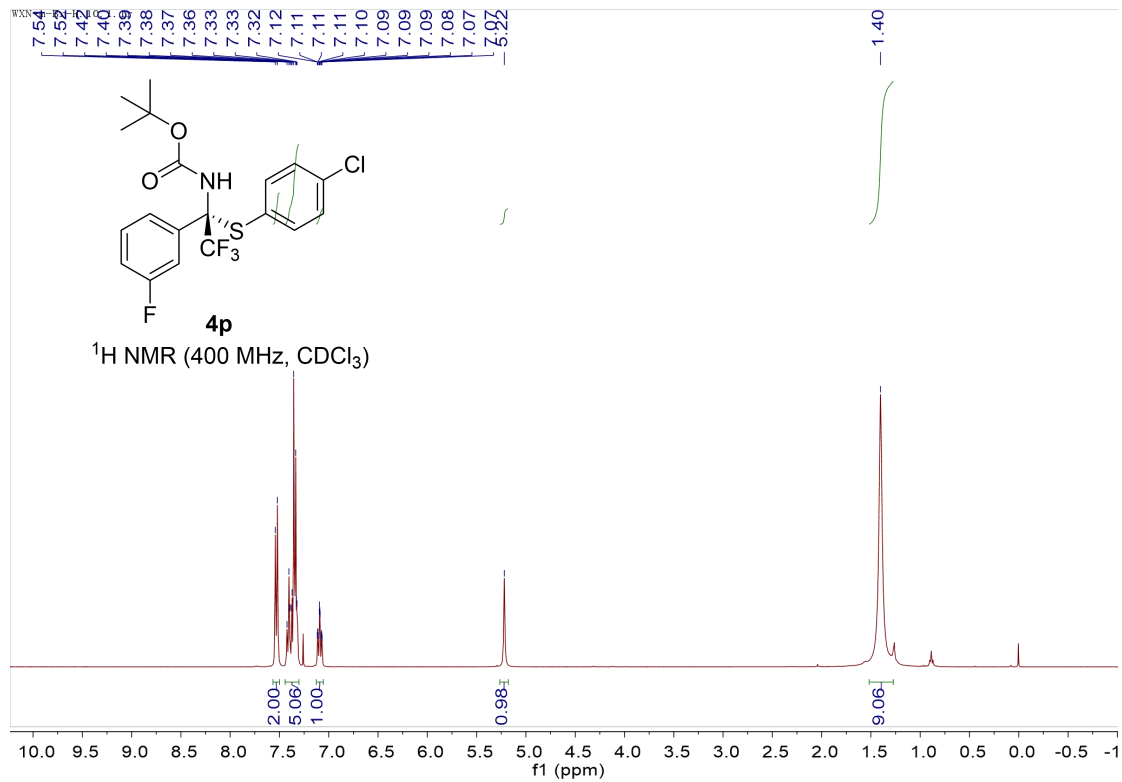
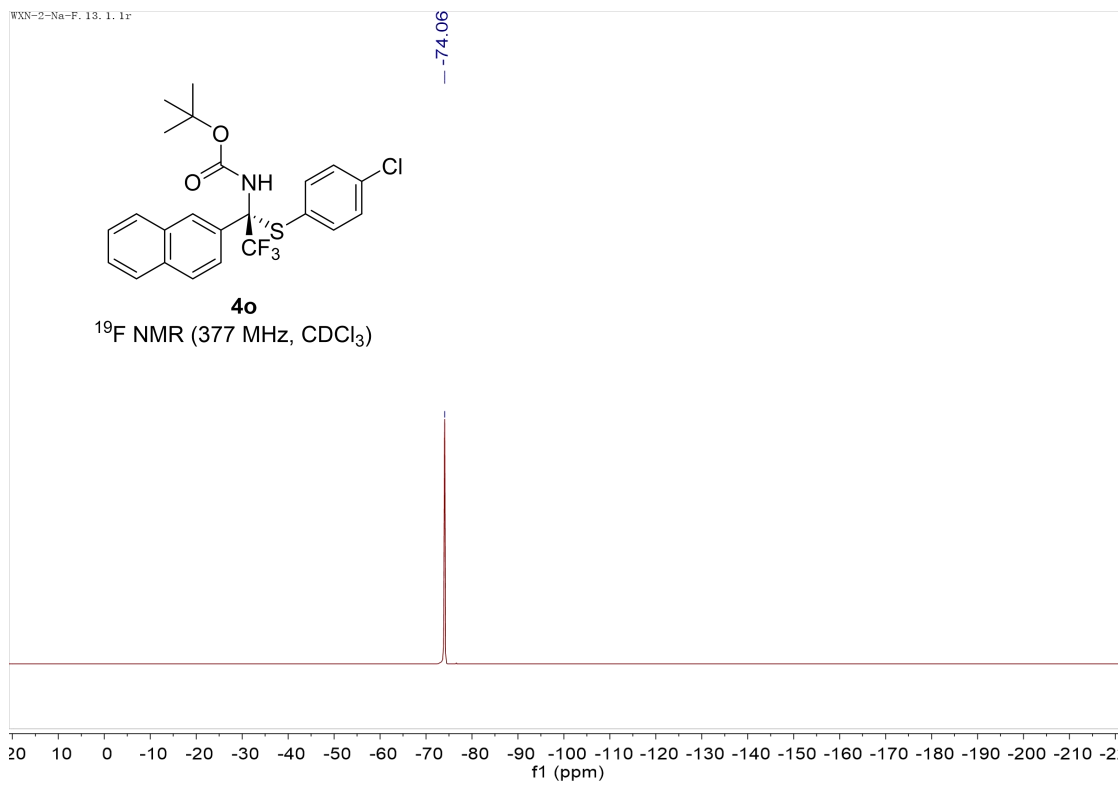
1.00
3.16
4.29
1.00
9.24

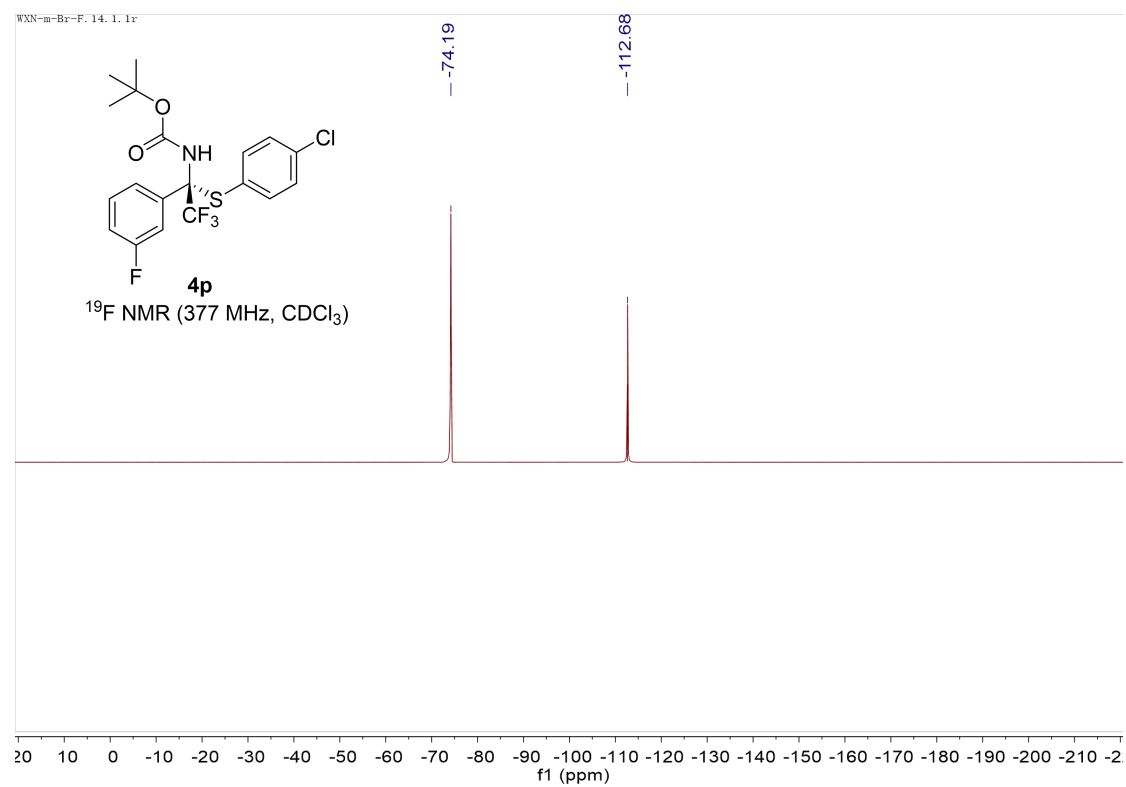
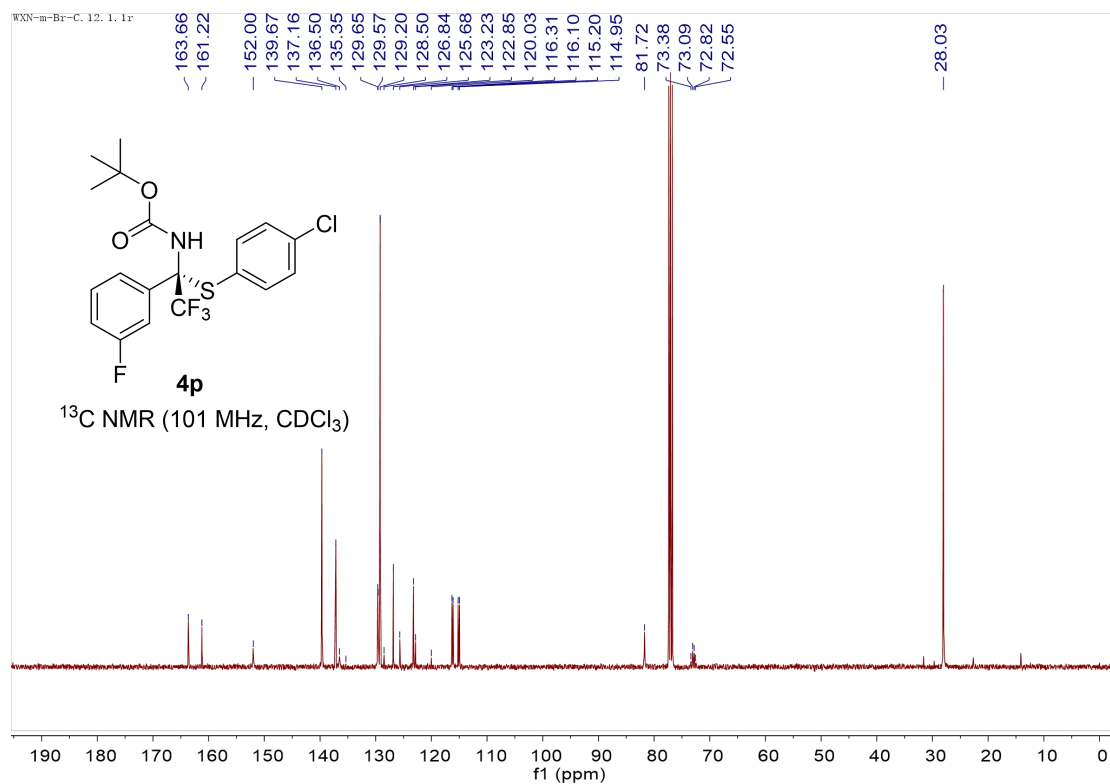
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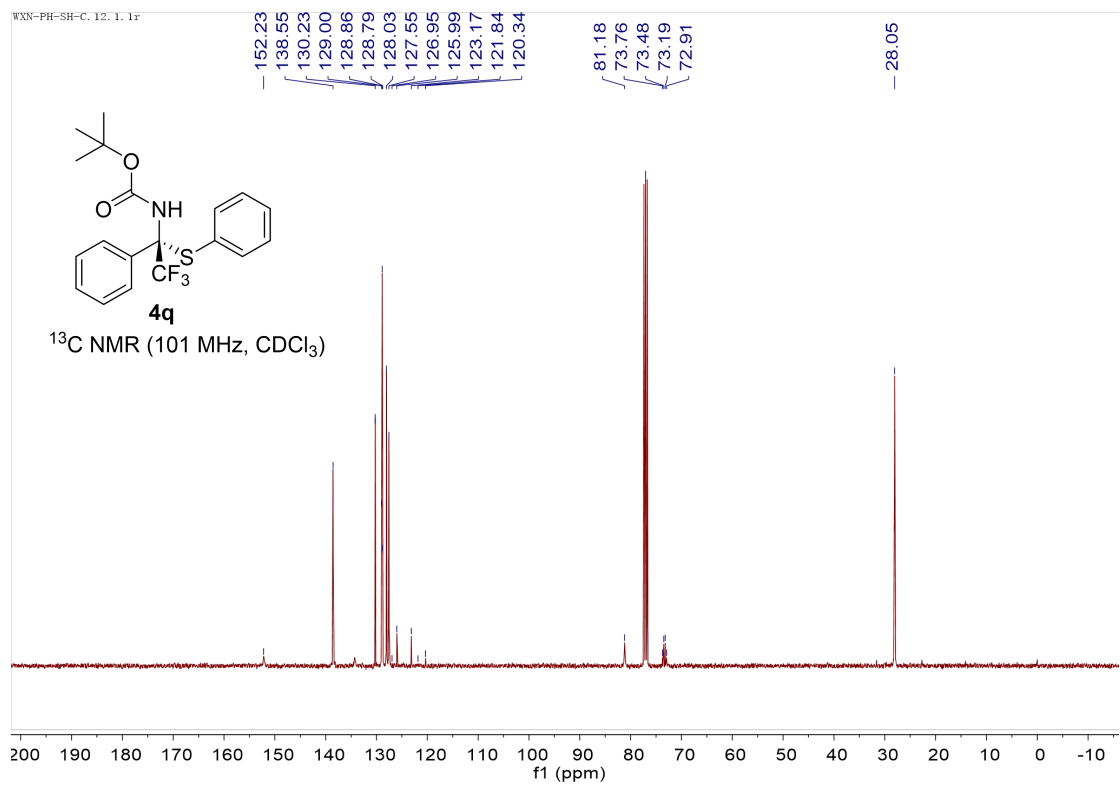
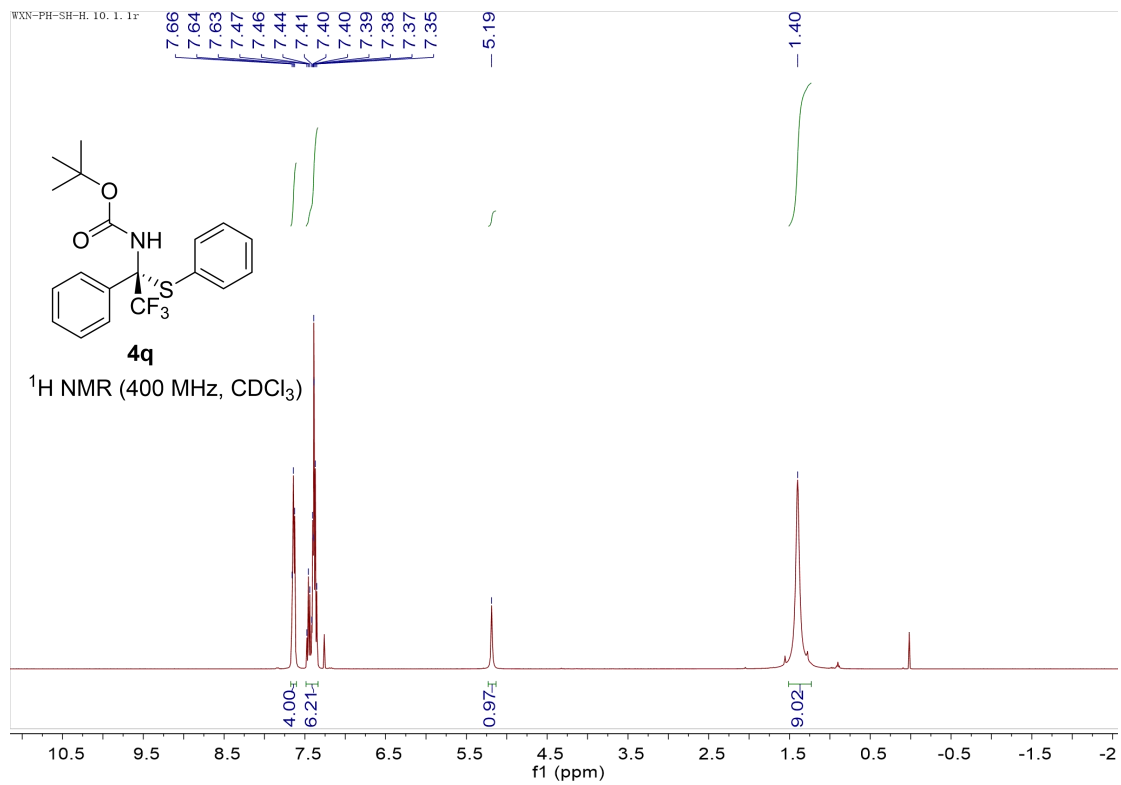
f1 (ppm)

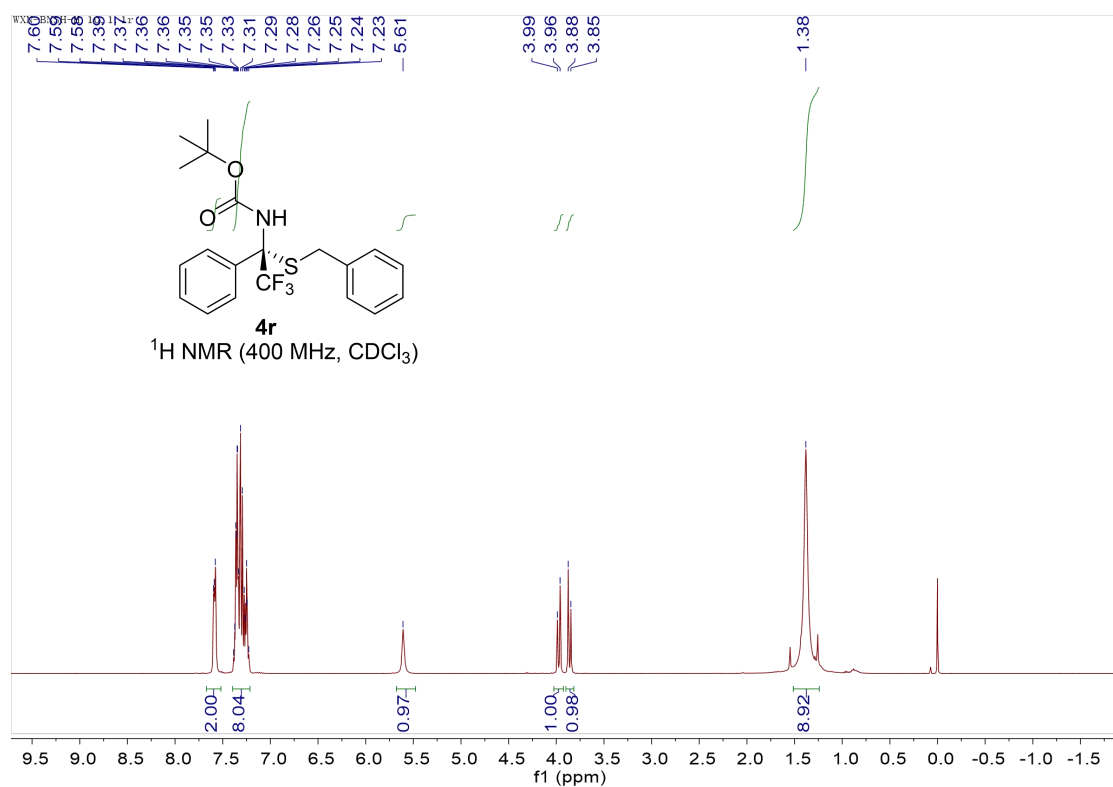
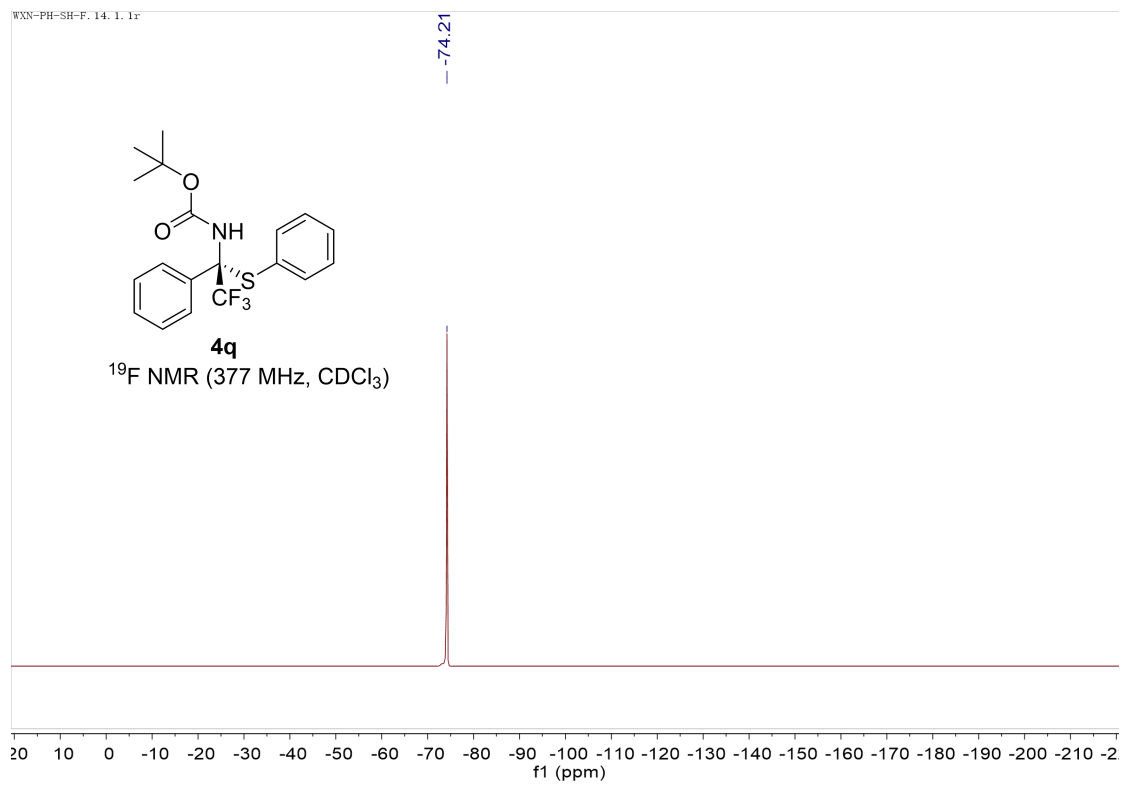


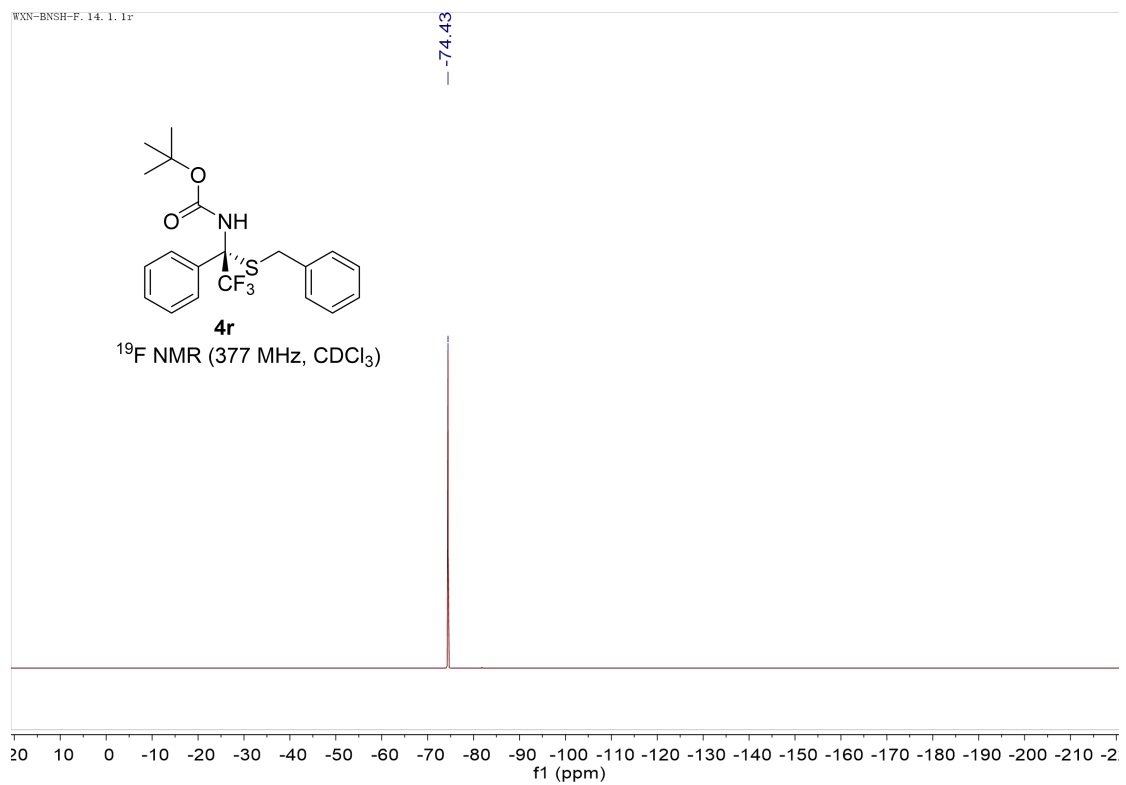
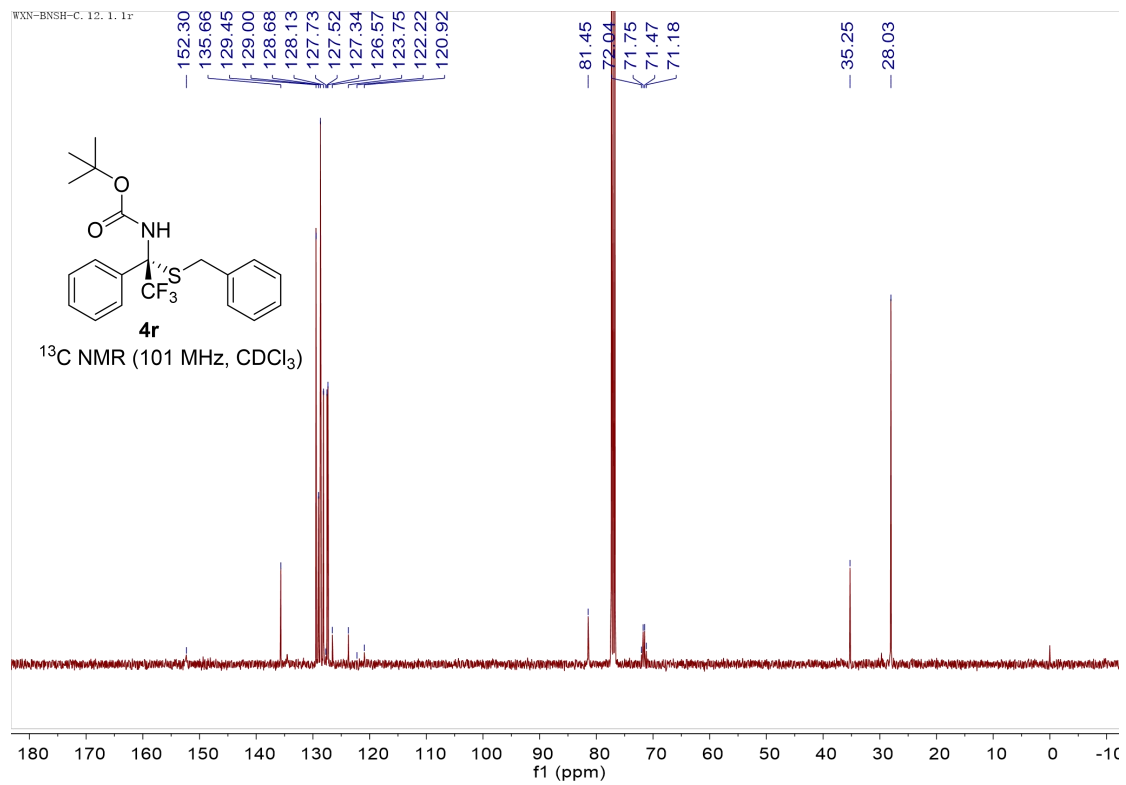


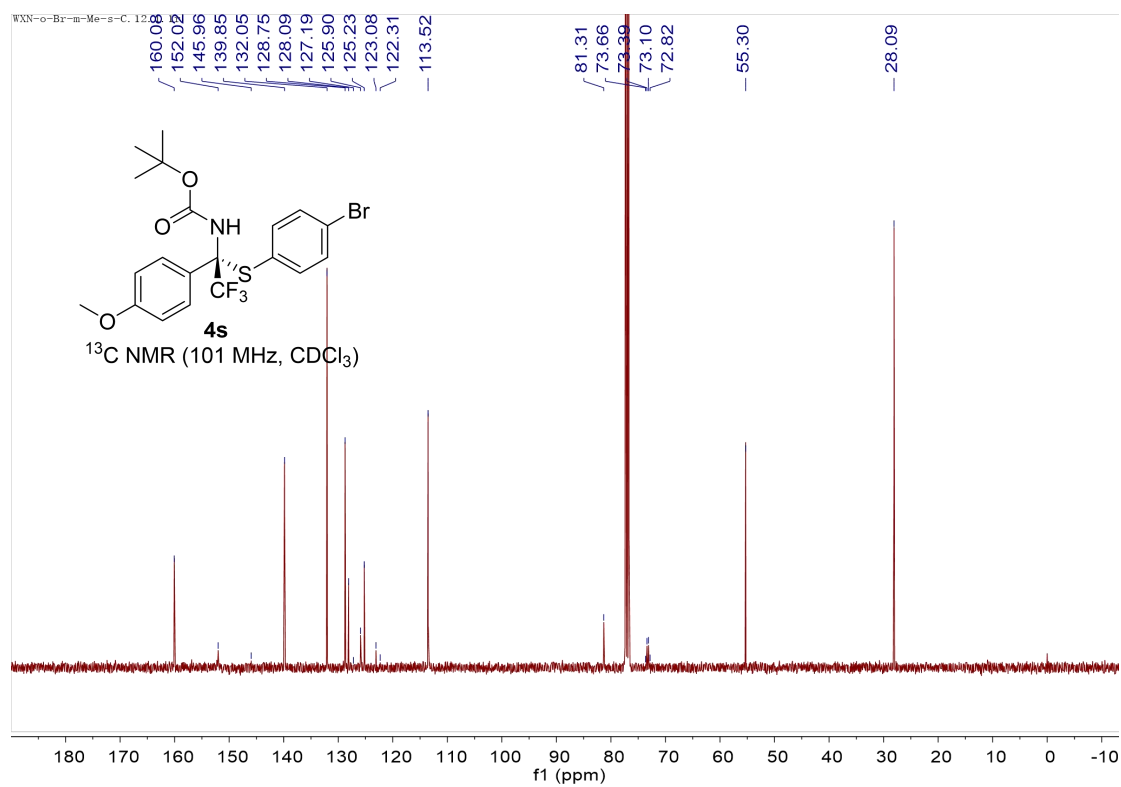
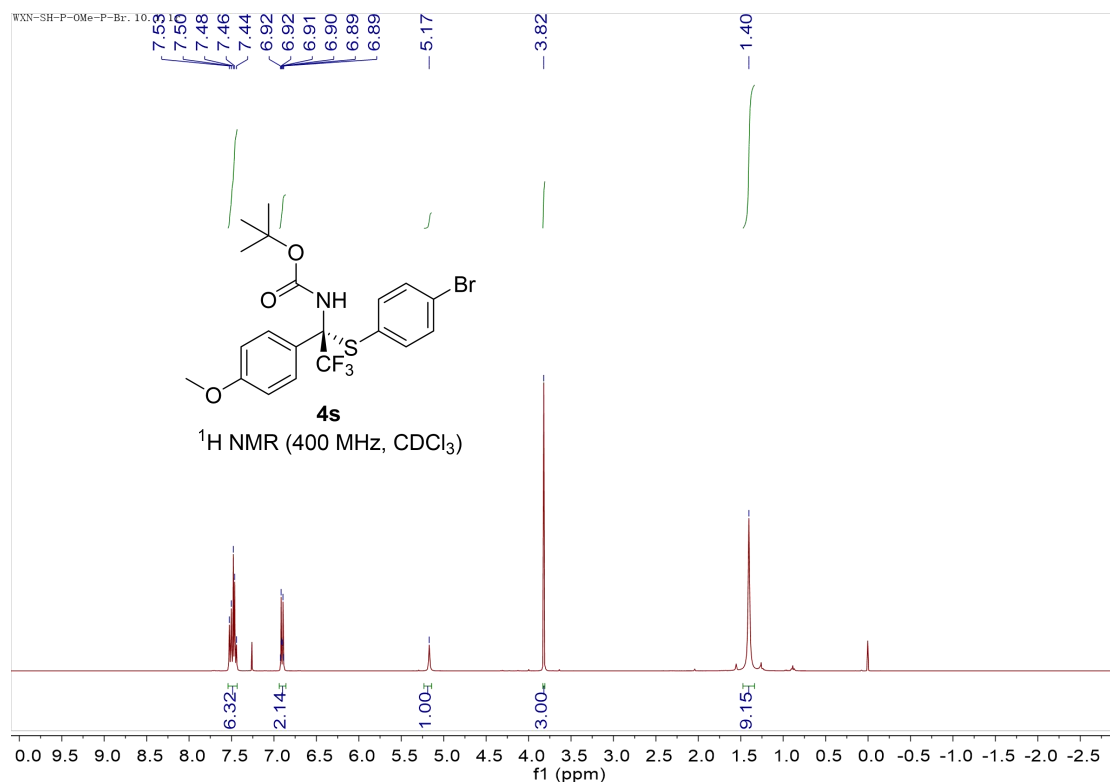


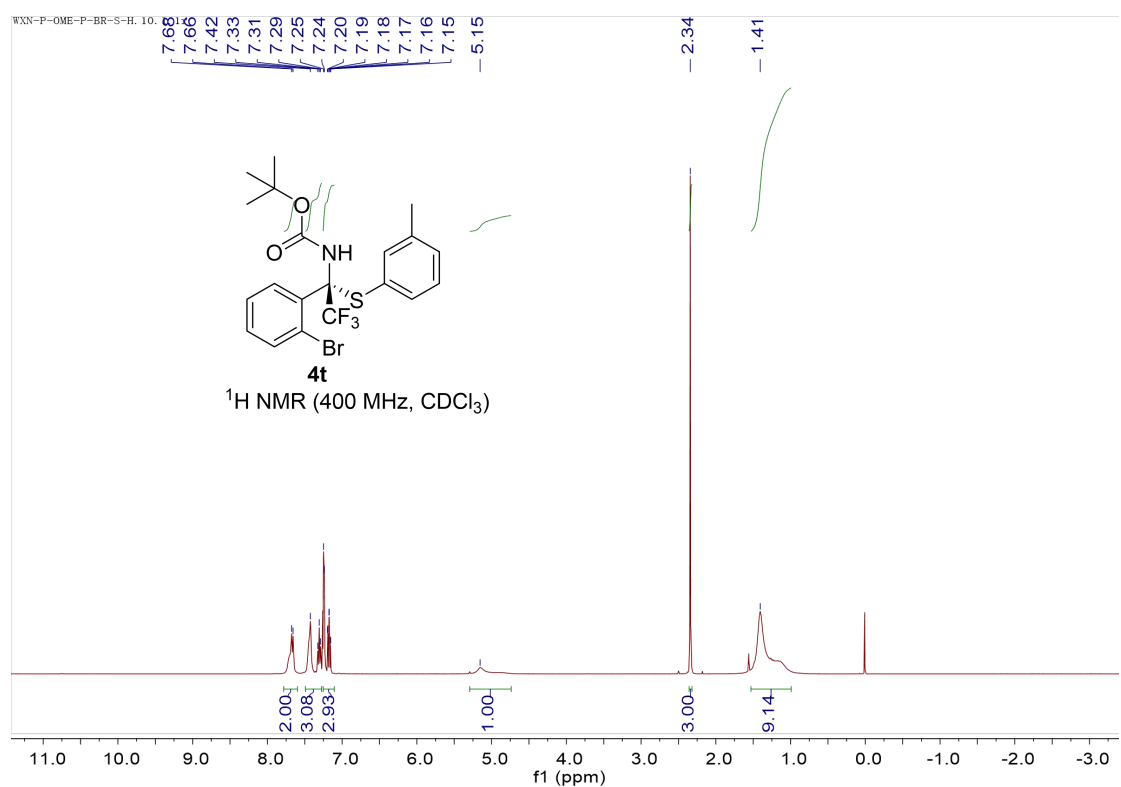
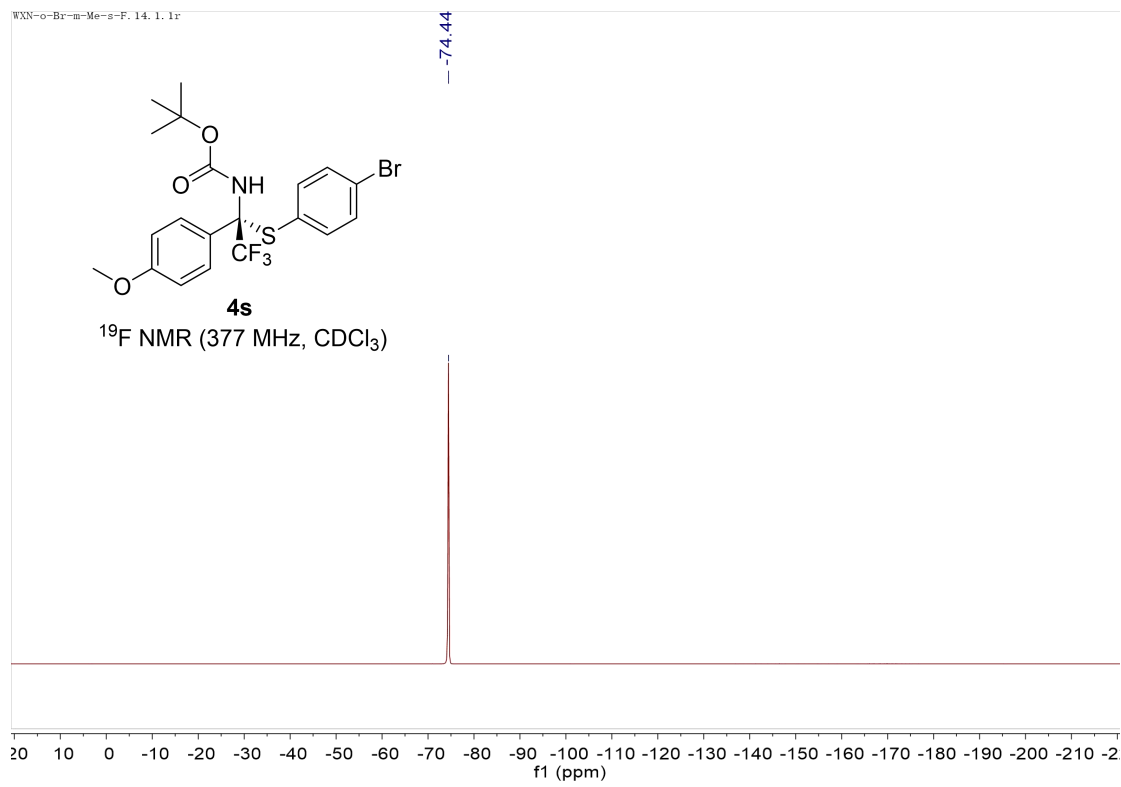


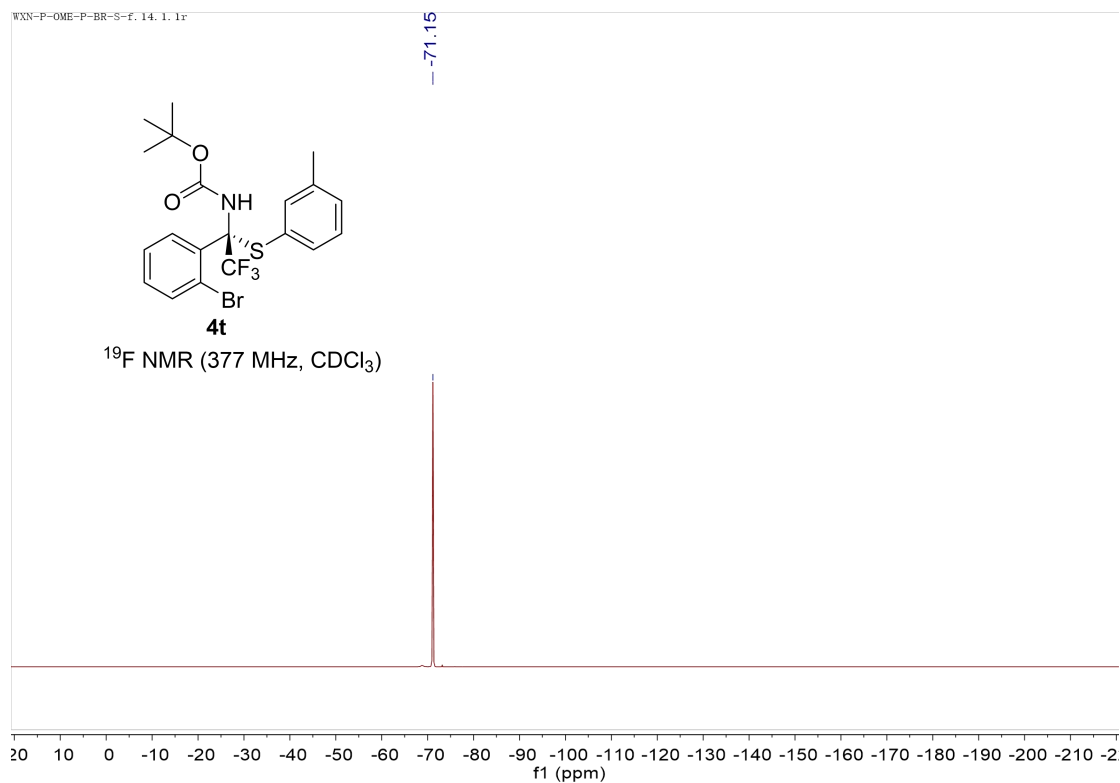
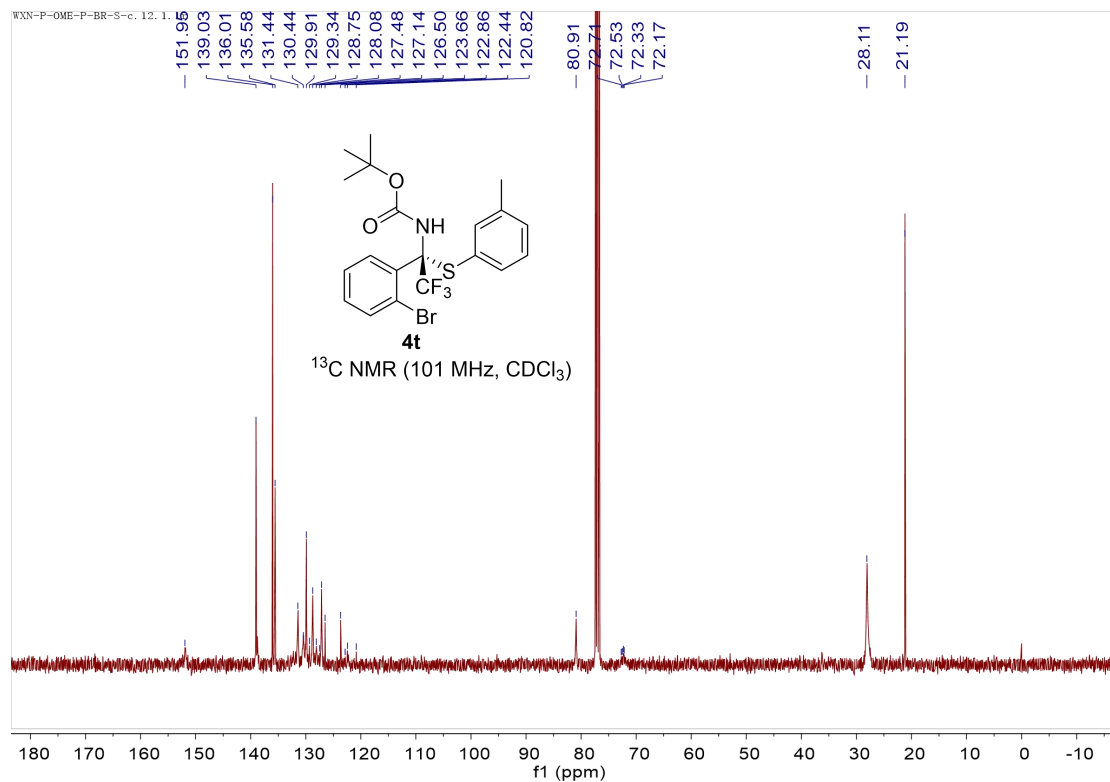


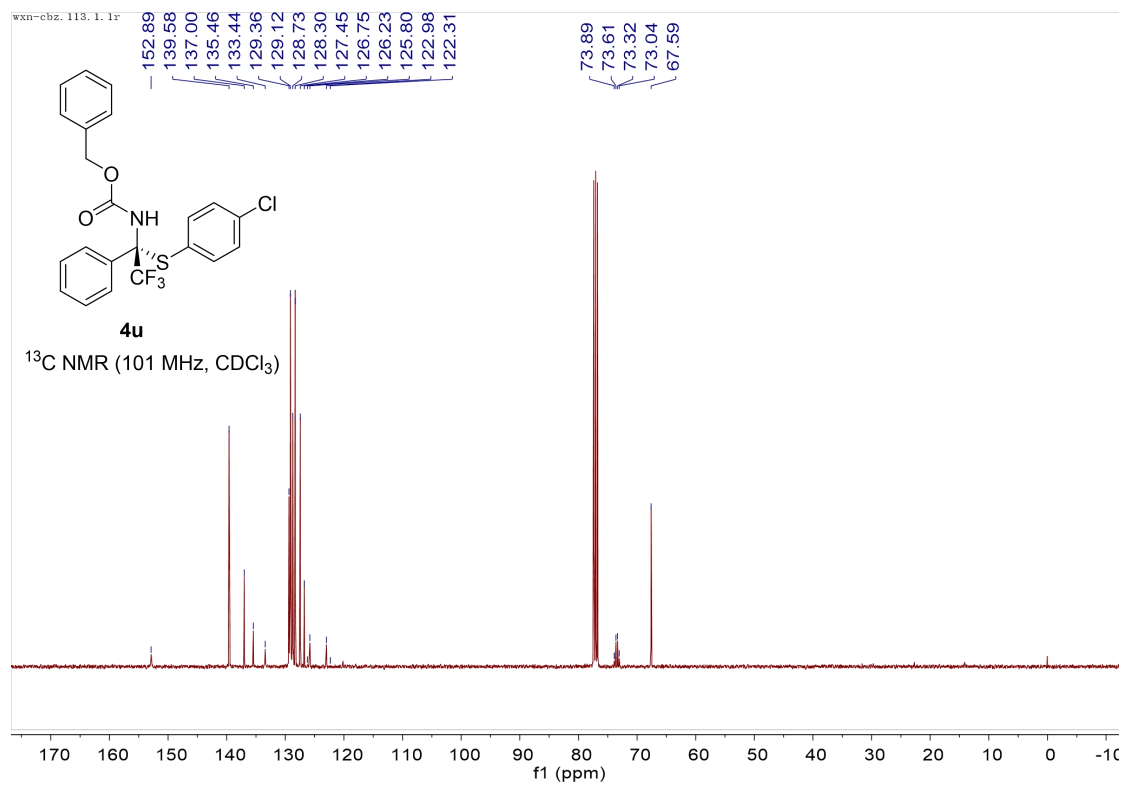
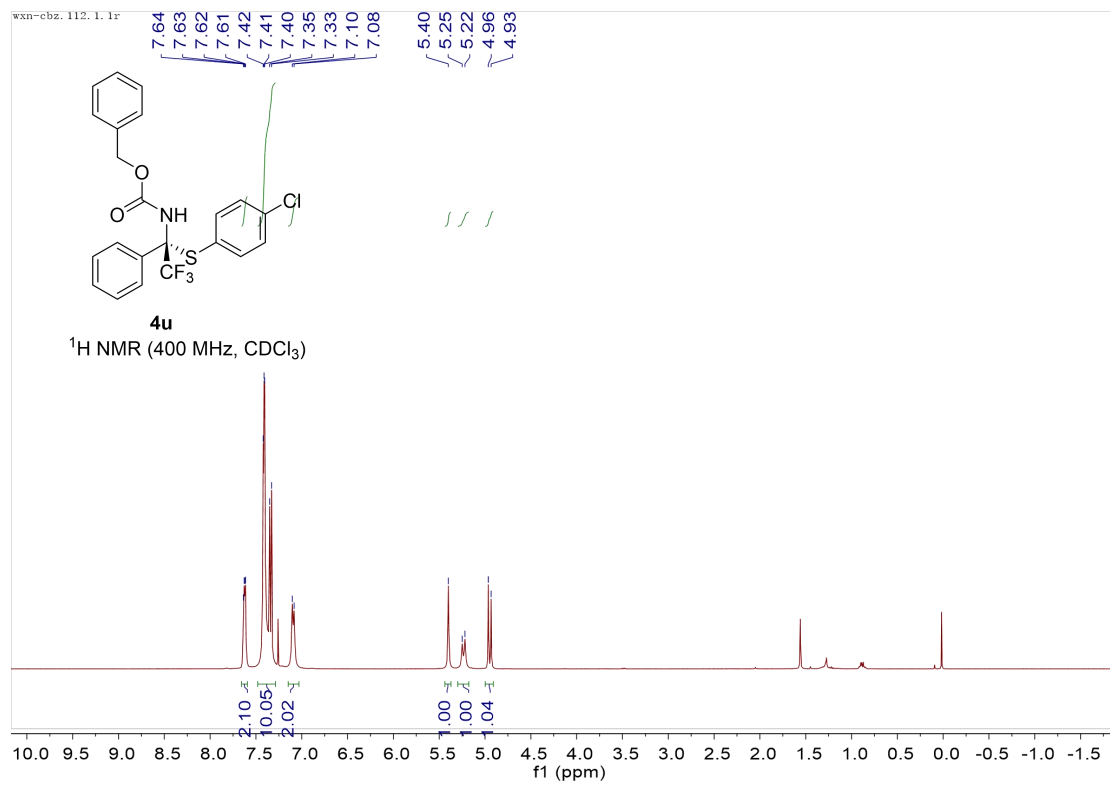




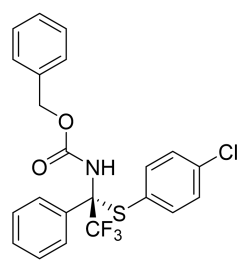






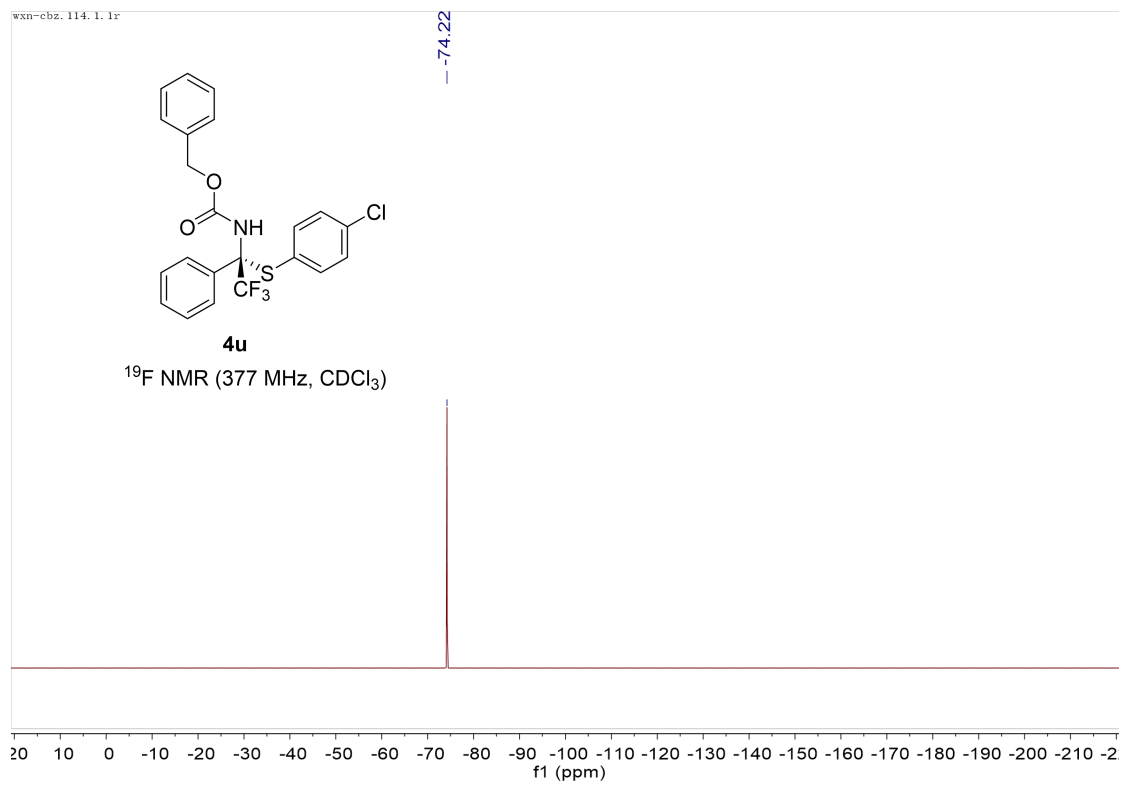


wxn-cbz. 114. 1. 1r

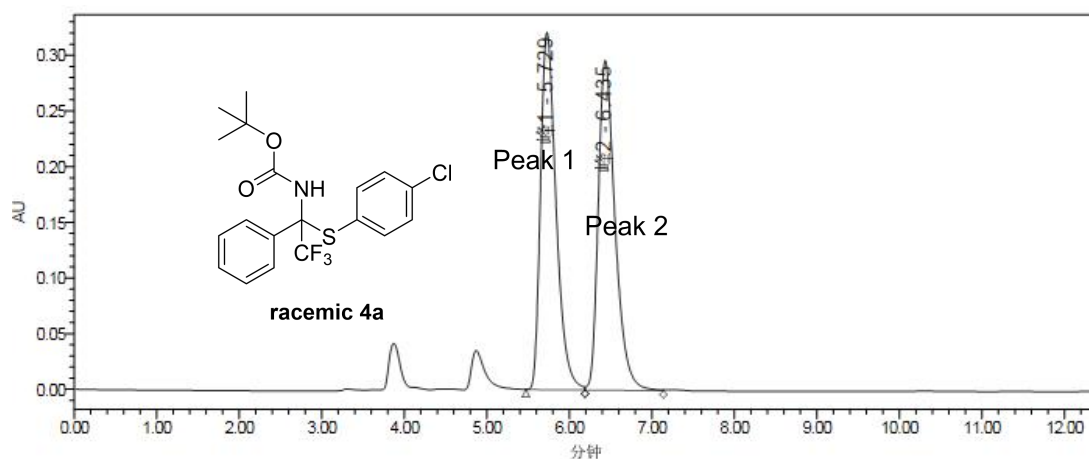


4u

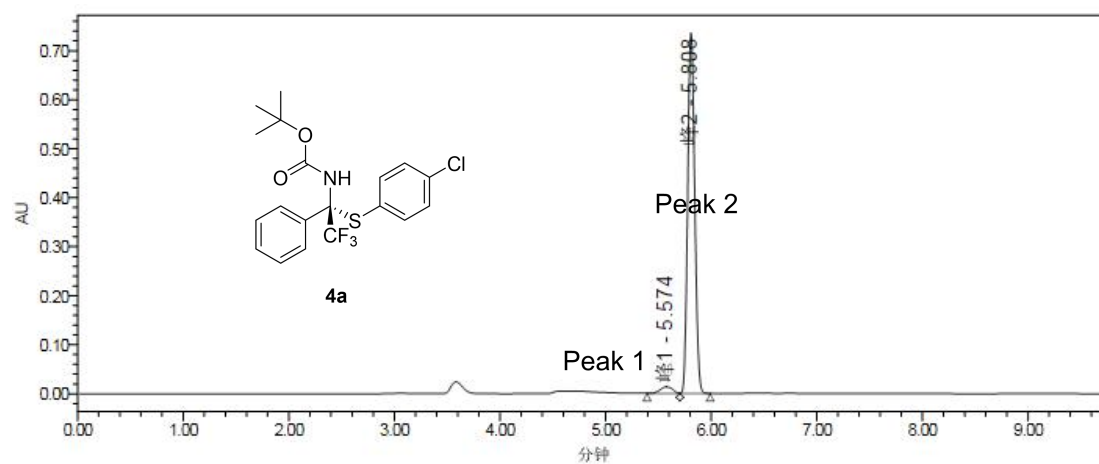
¹⁹F NMR (377 MHz, CDCl₃)



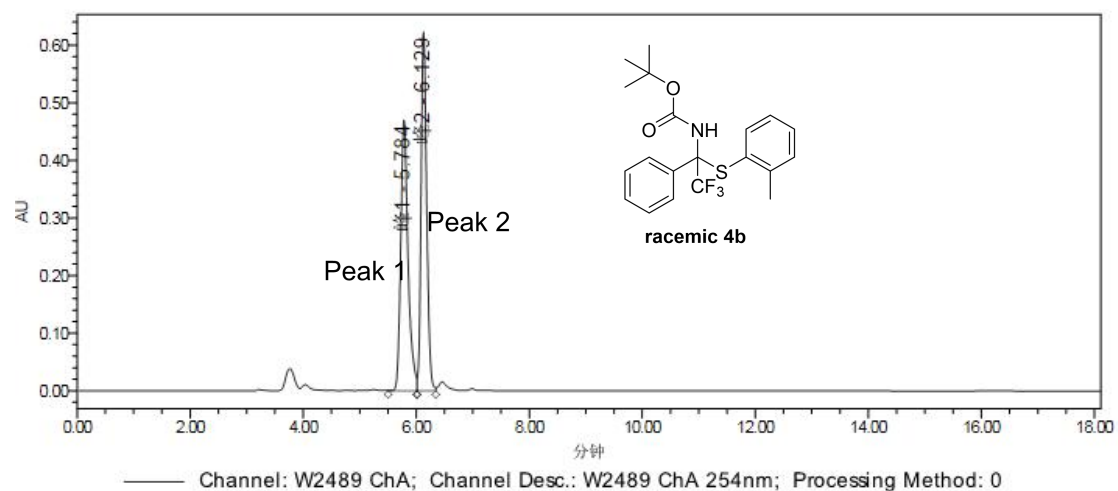
10. HPLC traces of compounds 4a-4u.



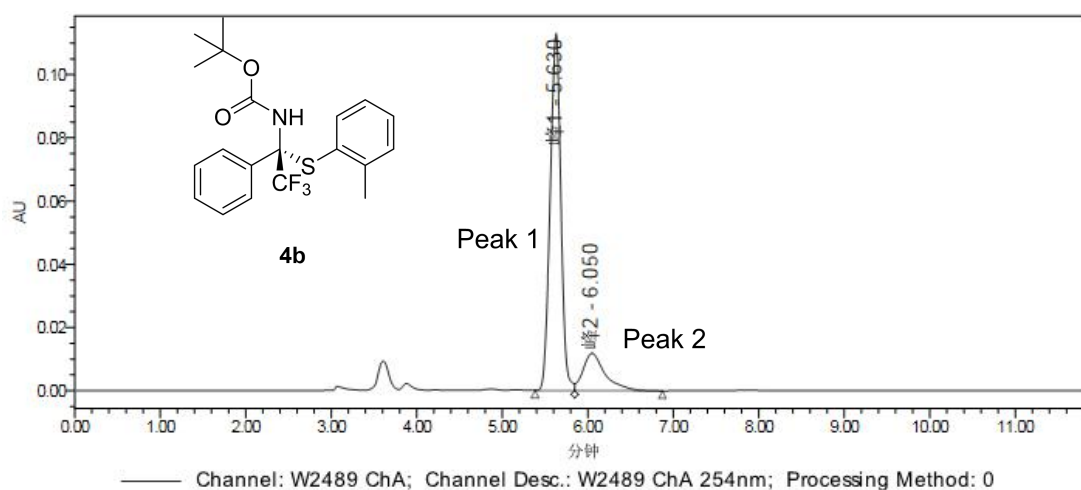
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	5.729	4197789	49.95	320667
2	W2489 ChA 254nm	峰2 Peak 2	6.435	4205570	50.05	295891



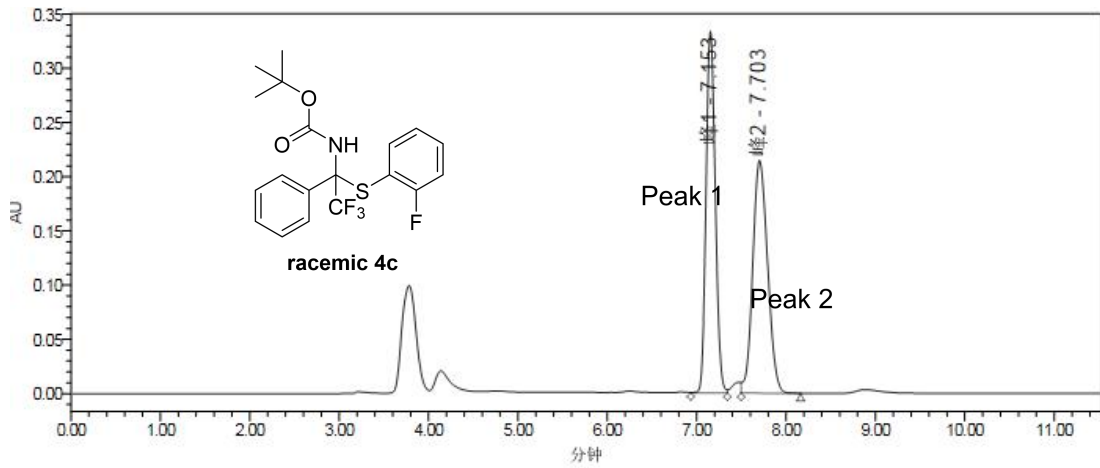
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	5.574	107627	3.07	13281
2	W2489 ChA 254nm	峰2 Peak 2	5.808	3402806	96.93	735666



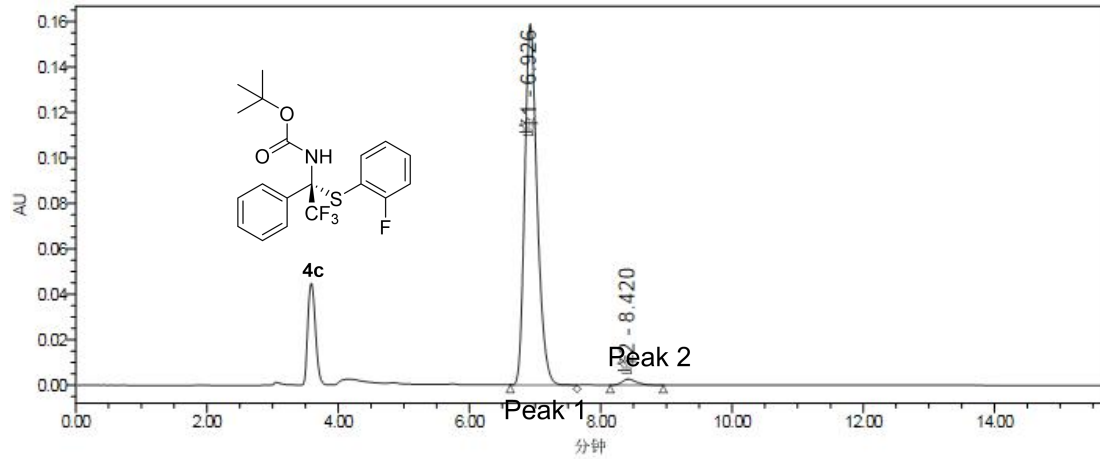
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	5.784	4217705	49.60	469375
2	W2489 ChA 254nm	峰2 Peak 2	6.129	4285422	50.40	622072



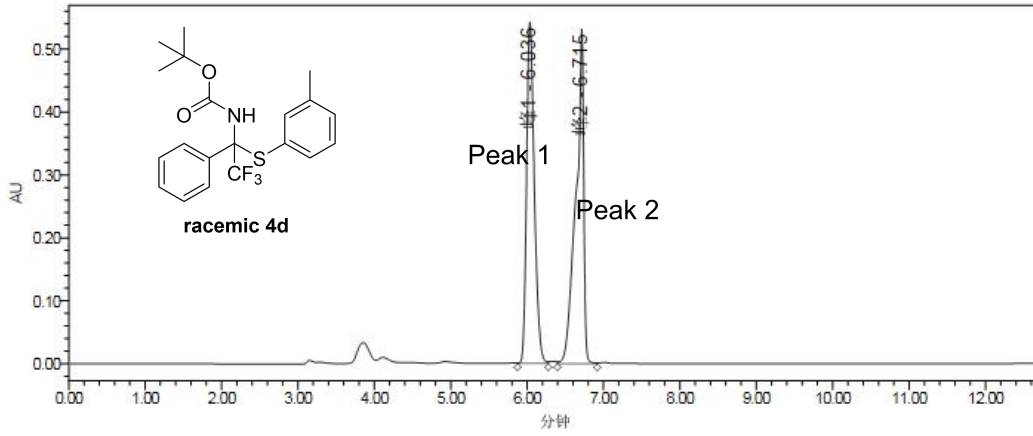
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	5.630	977015	82.25	112855
2	W2489 ChA 254nm	峰2 Peak 2	6.050	210803	17.75	11786



Peak Name	Channel Description	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
峰1 Peak 1	W2489 ChA 254nm	7.153	2379754	48.96	332959
峰2 Peak 2	W2489 ChA 254nm	7.703	2480669	51.04	214222

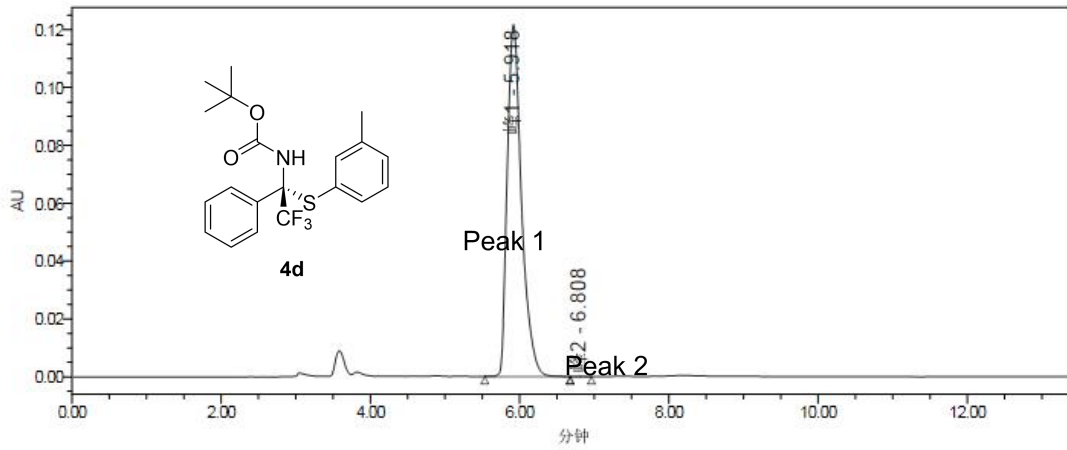


Peak Name	Channel Description	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
峰1 Peak 1	W2489 ChA 254nm	6.926	2084711	98.09	158646
峰2 Peak 2	W2489 ChA 254nm	8.420	40675	1.91	2661



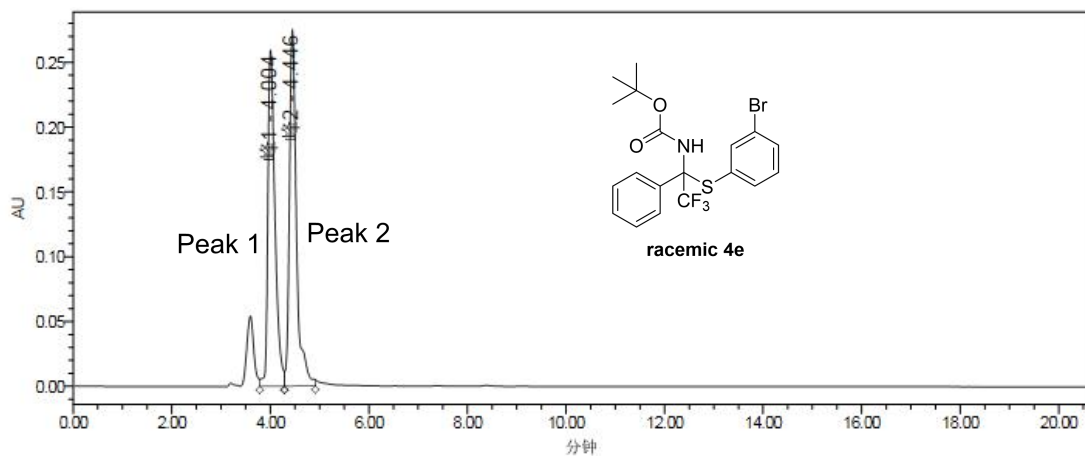
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	6.036	3814919	50.10	542049
2	W2489 ChA 254nm	峰2	6.715	3799479	49.90	531784



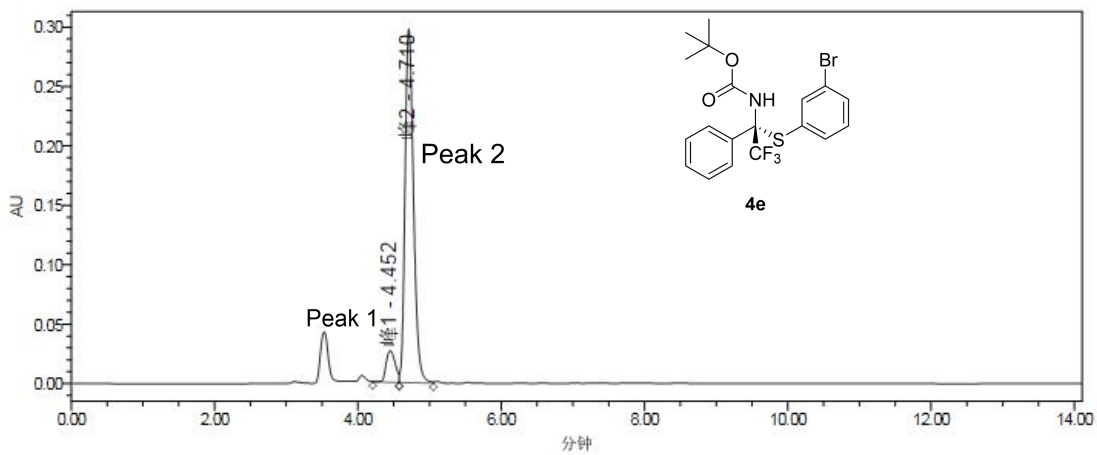
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	5.918	1617939	99.98	121483
2	W2489 ChA 254nm	峰2	6.808	280	0.02	33



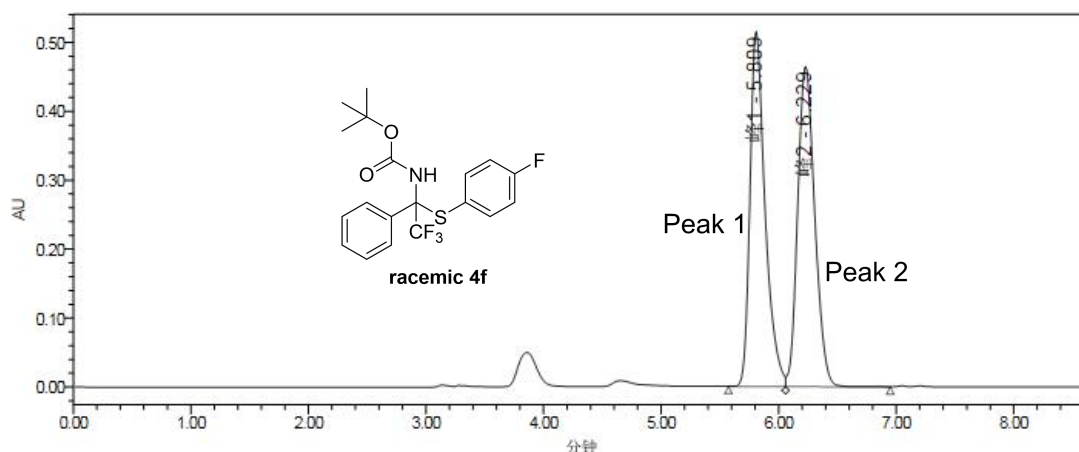
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1 Peak 1	4.004	2589352	48.74	259267
2	W2489 ChA 254nm	峰2 Peak 2	4.446	2722840	51.26	274741

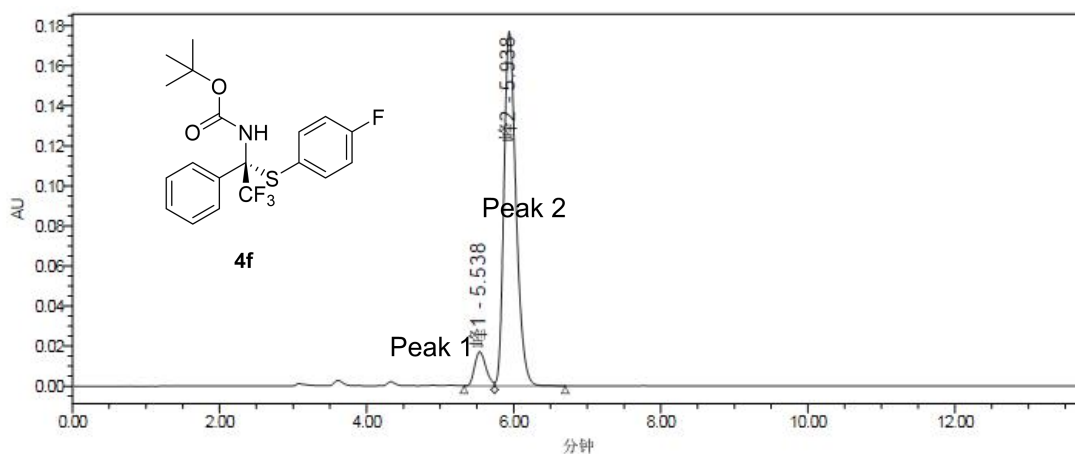


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

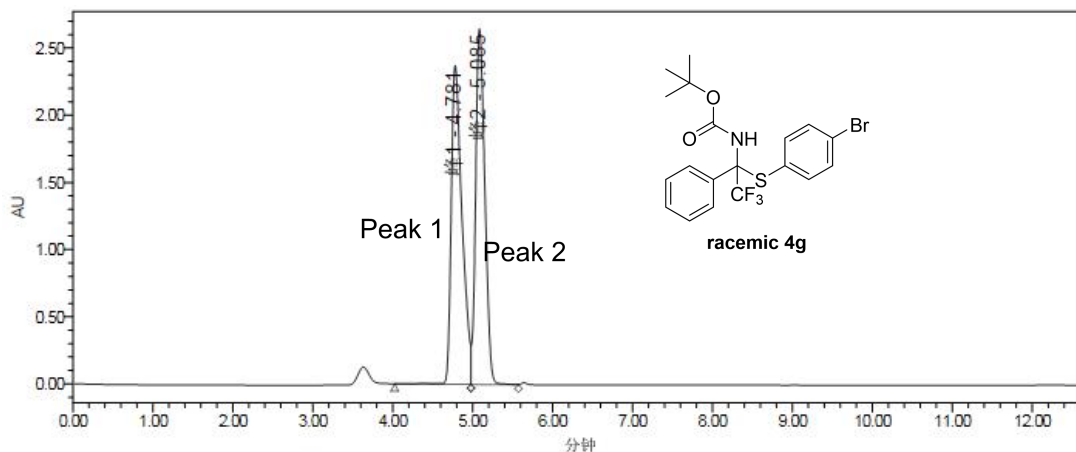
	Channel Description	Peak Name	RT (min)	Area (峰*sec)	% Area	Height (峰)
1	W2489 ChA 254nm	峰1 Peak 1	4.452	233907	8.75	26254
2	W2489 ChA 254nm	峰2 Peak 2	4.710	2439108	91.25	297386



	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	5.809	4596247	49.54	514255
2	W2489 ChA 254nm	峰2	6.229	4682057	50.46	464198

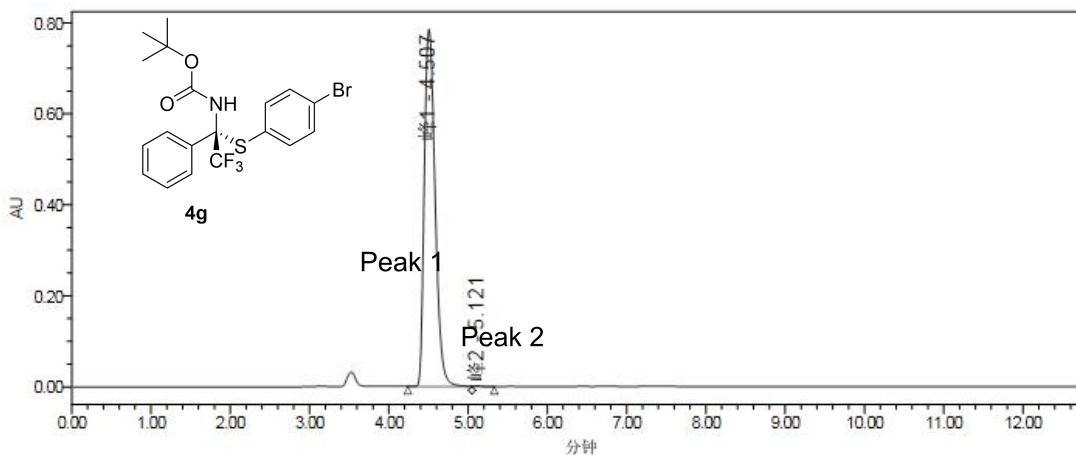


	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	5.538	181489	8.26	16976
2	W2489 ChA 254nm	峰2	5.938	2015624	91.74	176867



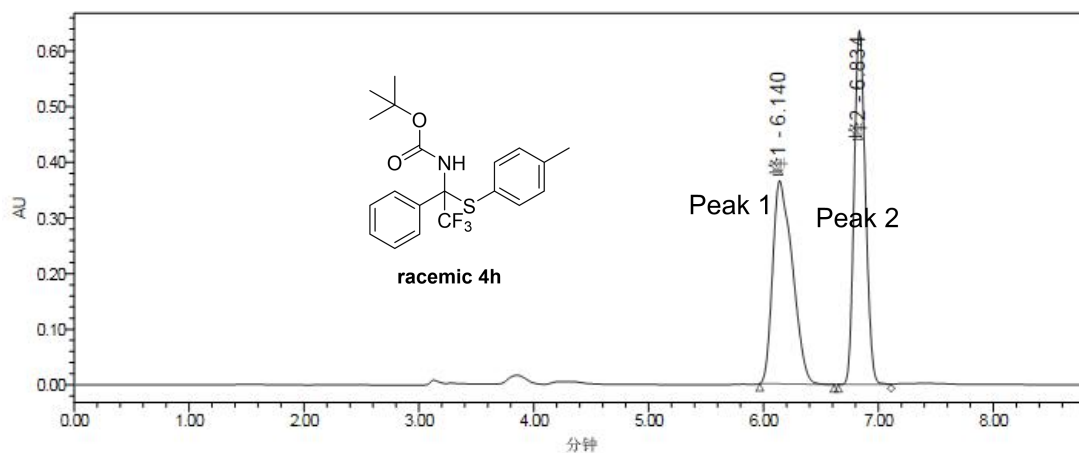
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	4.781	22139983	51.25	2371254
2	W2489 ChA 254nm	峰2	5.085	21059606	48.75	2644359



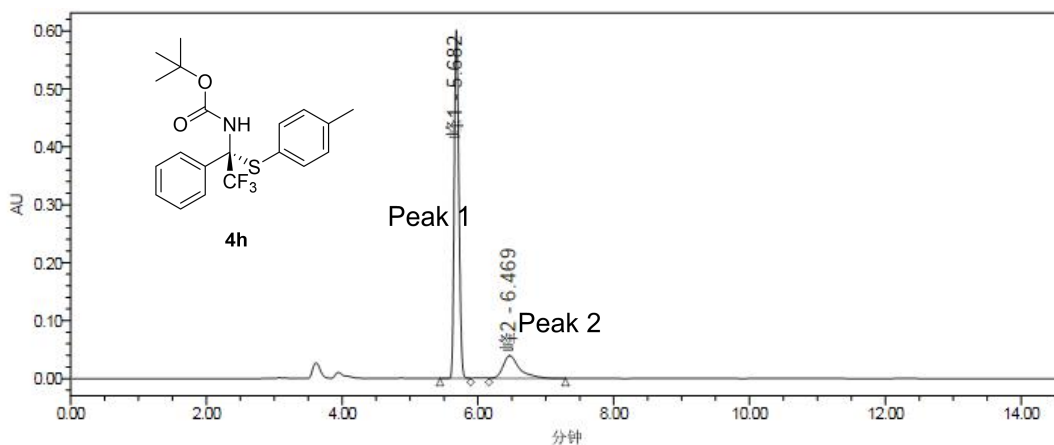
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	4.507	7411260	99.86	784443
2	W2489 ChA 254nm	峰2	5.121	10608	0.14	1675



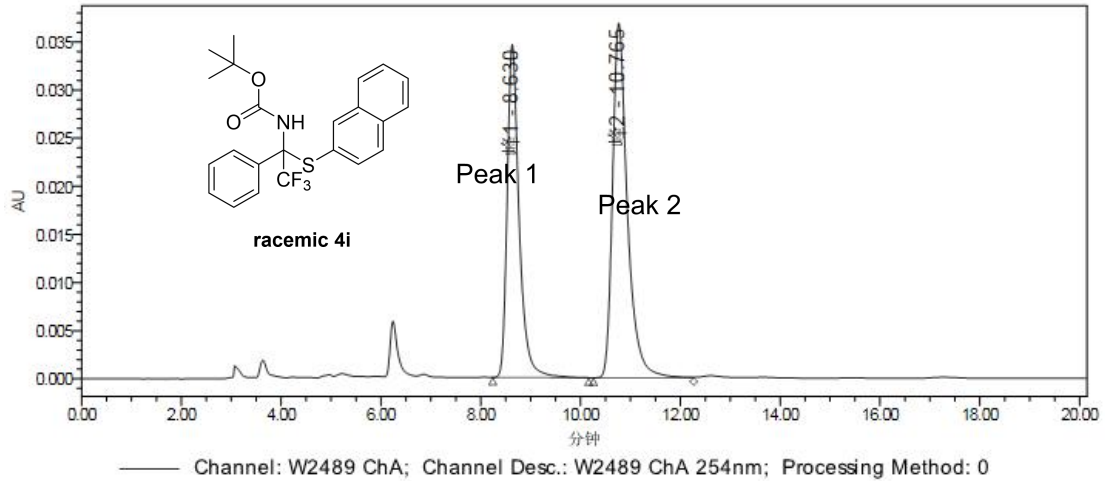
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (μAU*sec)	% Area	Height (μAU)
1	W2489 ChA 254nm	峰1	6.140	4372475	50.14	365040
2	W2489 ChA 254nm	峰2	6.834	4347900	49.86	635595

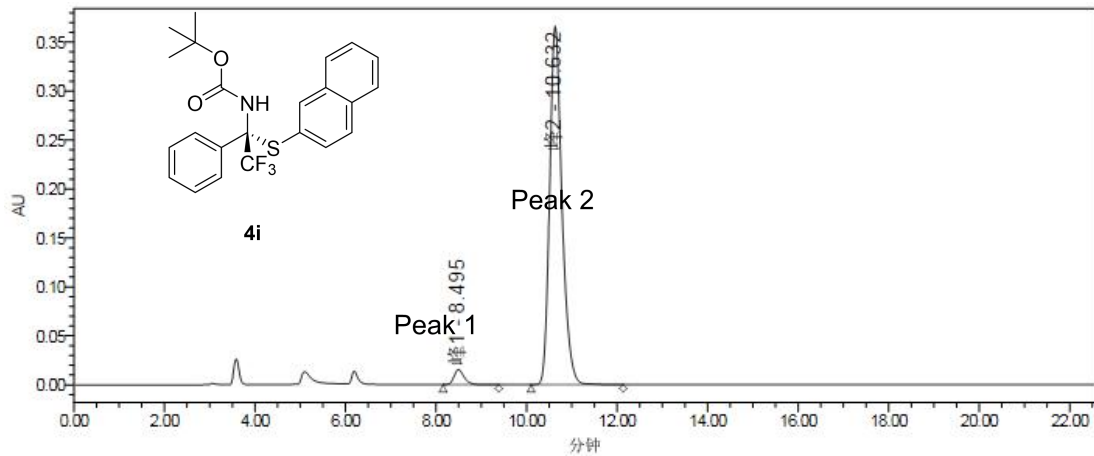


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

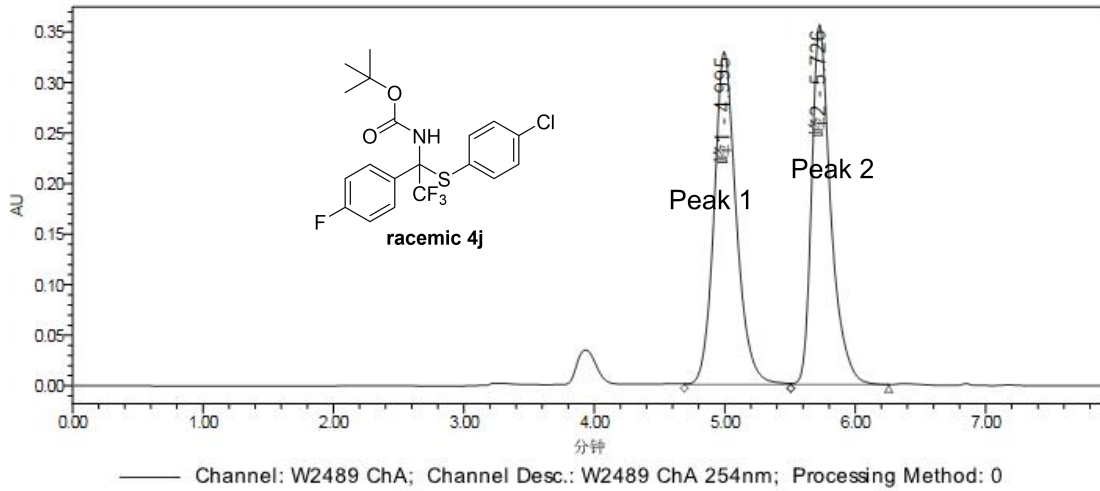
	Channel Description	Peak Name	RT (min)	Area (μAU*sec)	% Area	Height (μAU)
1	W2489 ChA 254nm	峰1	5.682	2648642	80.98	601392
2	W2489 ChA 254nm	峰2	6.469	669094	19.02	39397



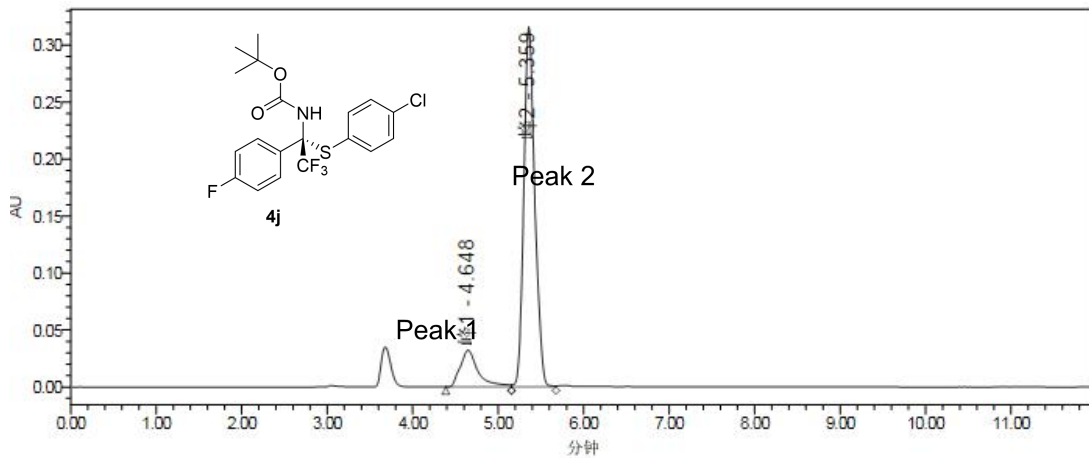
Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1 W2489 ChA 254nm	峰1	8.630	576901	43.14	34571
2 W2489 ChA 254nm	峰2	10.765	760334	56.86	36811



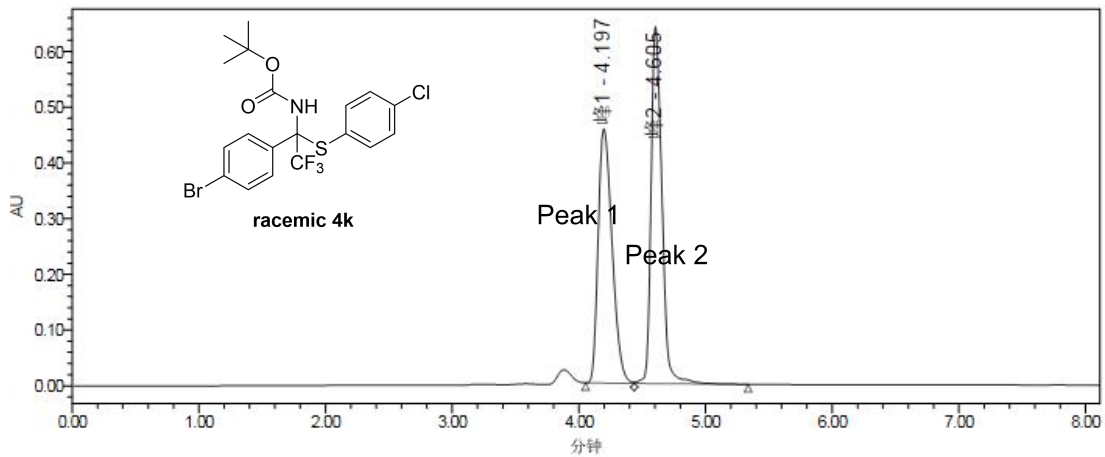
Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1 W2489 ChA 254nm	峰1	8.495	239187	3.35	15420
2 W2489 ChA 254nm	峰2	10.632	6905248	96.65	365796



	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	Peak 1	4.995	3904418	51.76	328950
2	W2489 ChA 254nm	Peak 2	5.726	3638880	48.24	355774

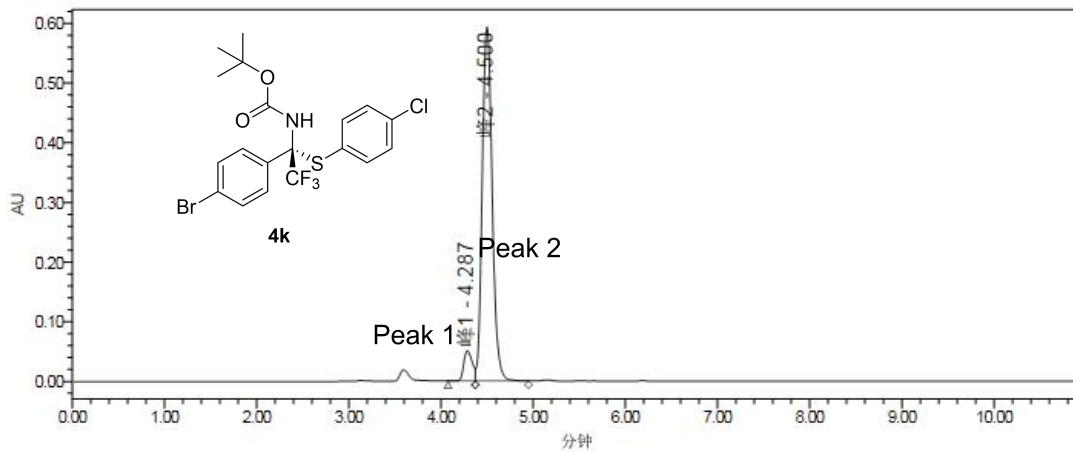


	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	4.648	465695	14.22	32053
2	W2489 ChA 254nm	峰2	5.359	2809119	85.78	315489



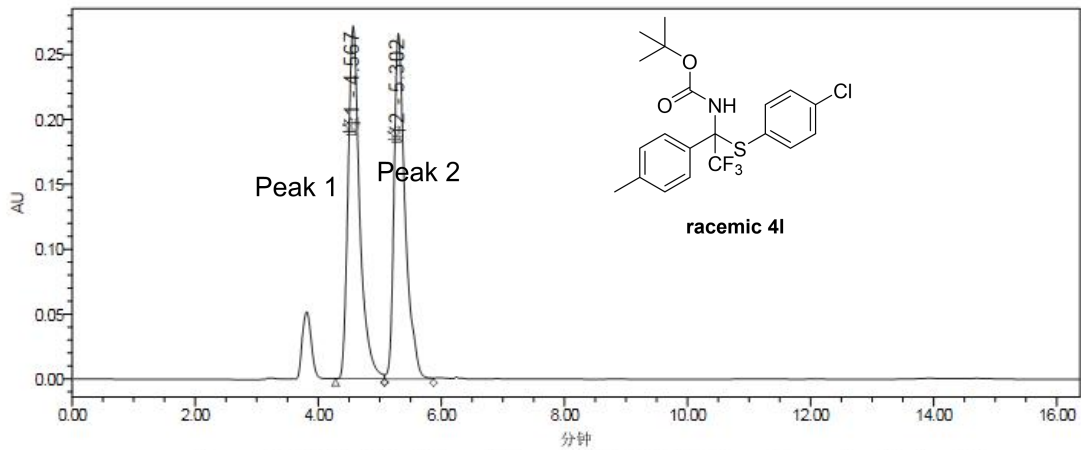
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	4.197	3485760	47.93	455844
2	W2489 ChA 254nm	峰2	4.605	3786682	52.07	639957



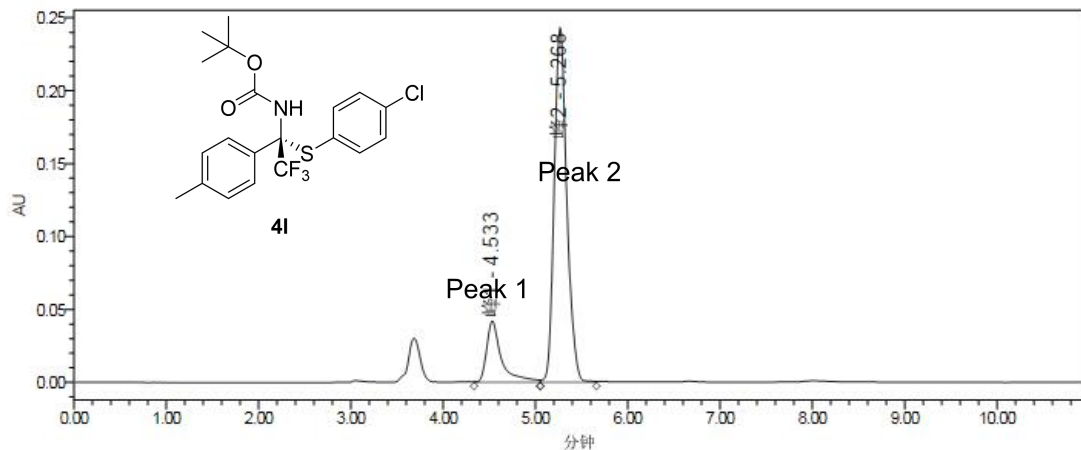
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	4.287	322638	6.75	50474
2	W2489 ChA 254nm	峰2	4.500	4454457	93.25	592710



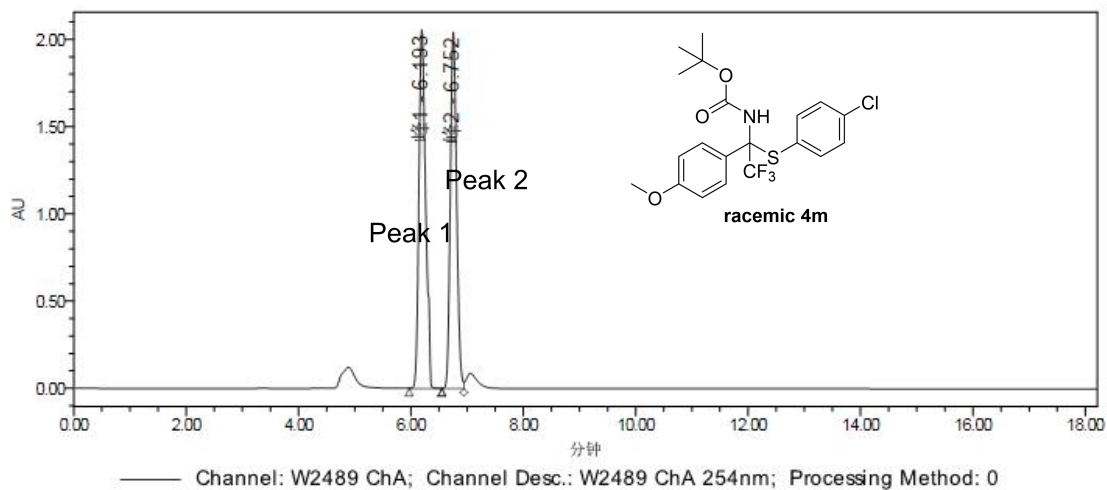
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	4.567	3591173	51.71	271558
2	W2489 ChA 254nm	峰2	5.302	3353624	48.29	265898

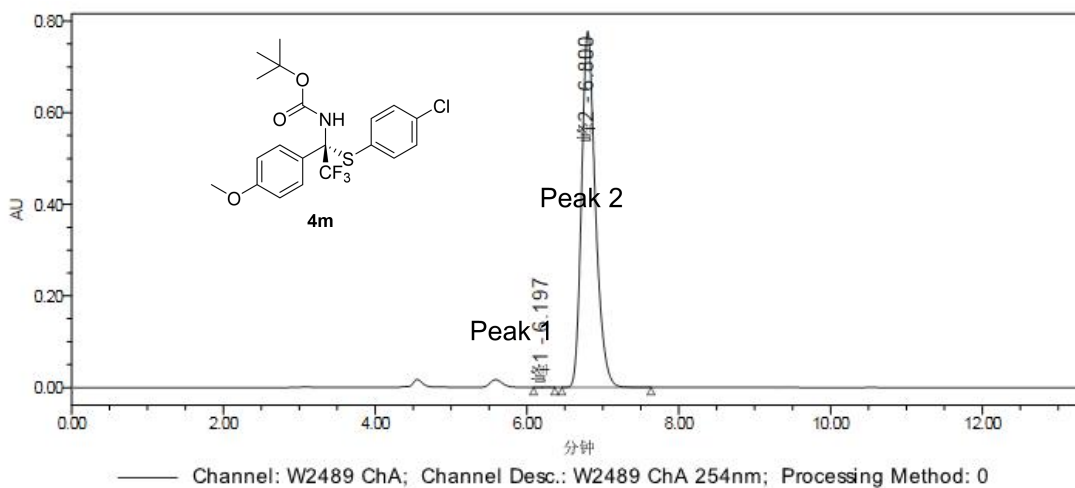


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

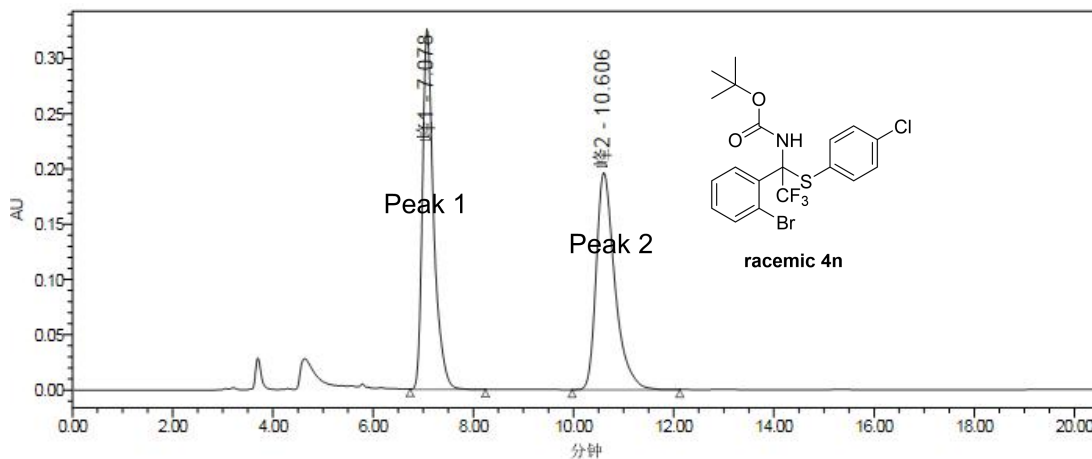
	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	4.533	470268	16.98	41851
2	W2489 ChA 254nm	峰2	5.268	2299870	83.02	242946



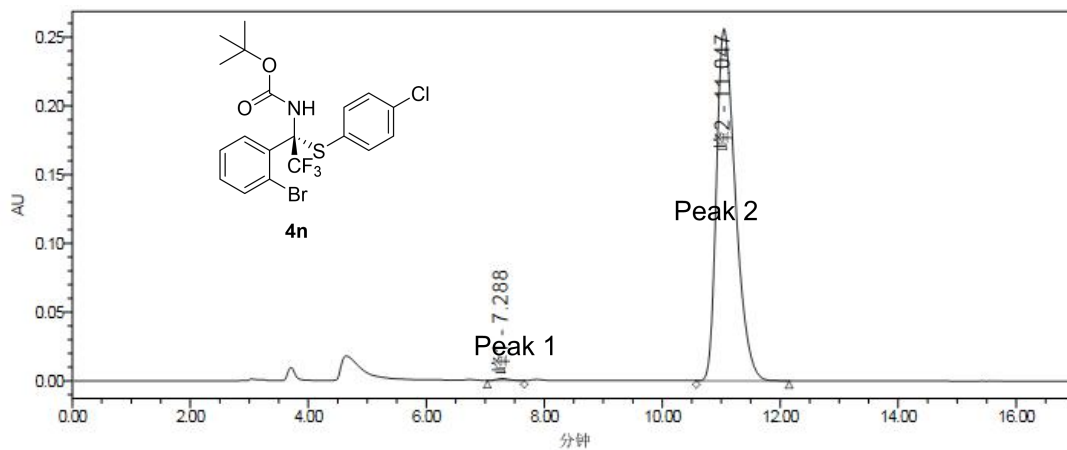
	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	6.193	17127554	51.88	2053448
2	W2489 ChA 254nm	峰2 Peak 2	6.752	15885436	48.12	2041806



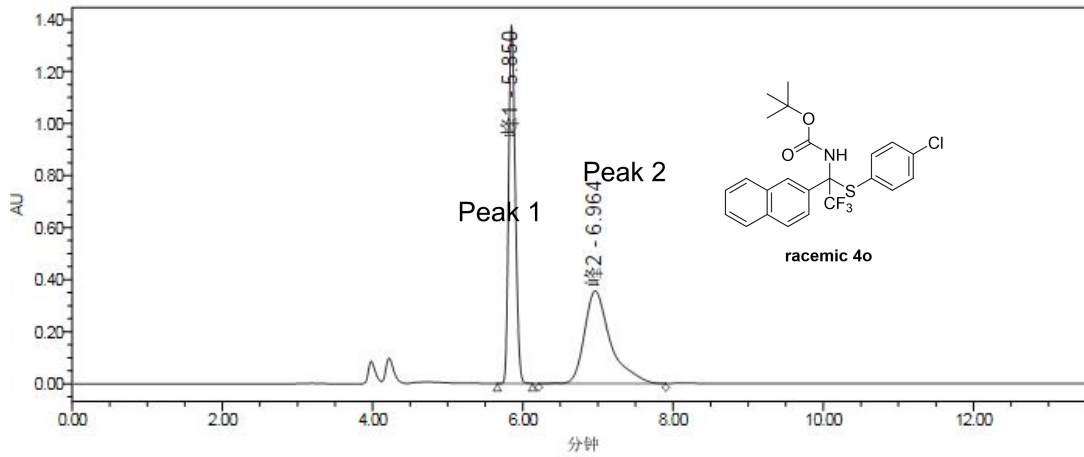
	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	6.197	420	0.00	52
2	W2489 ChA 254nm	峰2 Peak 2	6.800	9866533	100.00	777047



Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
W2489 ChA 254nm	峰1	7.078	5059177	49.85	325763
W2489 ChA 254nm	峰2	10.606	5089818	50.15	196247

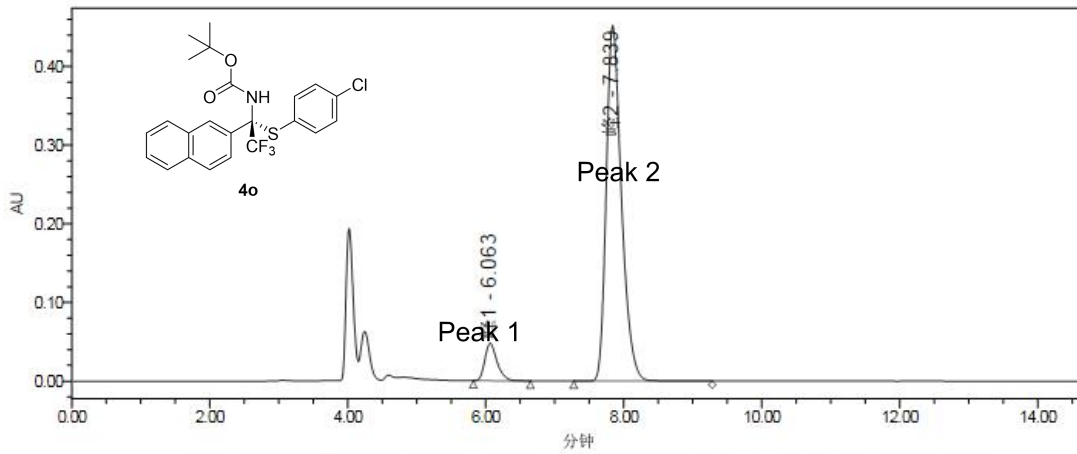


Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
W2489 ChA 254nm	峰1	7.288	20737	0.36	1494
W2489 ChA 254nm	峰2	11.047	5707054	99.64	255738



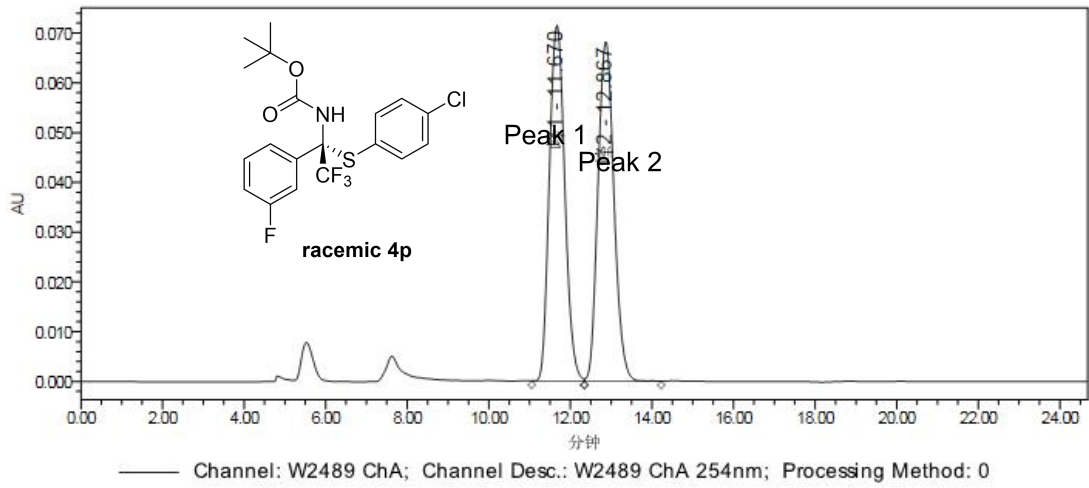
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	5.850	8458689	49.66	1375896
2	W2489 ChA 254nm	峰2 Peak 2	6.964	8574334	50.34	355909

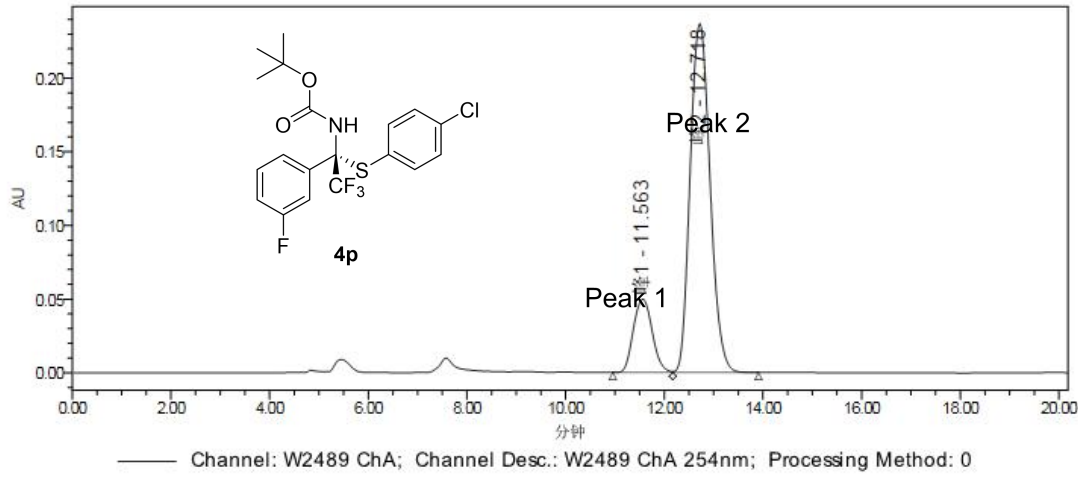


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

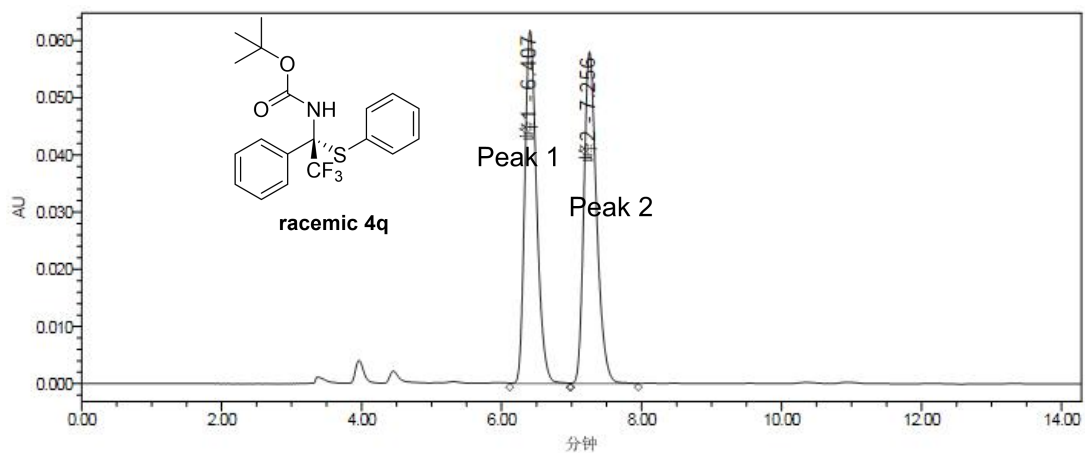
	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	6.063	586616	7.82	47454
2	W2489 ChA 254nm	峰2 Peak 2	7.839	6911303	92.18	451453



	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	11.670	1877466	50.15	71427
2	W2489 ChA 254nm	峰2	12.867	1866068	49.85	68160

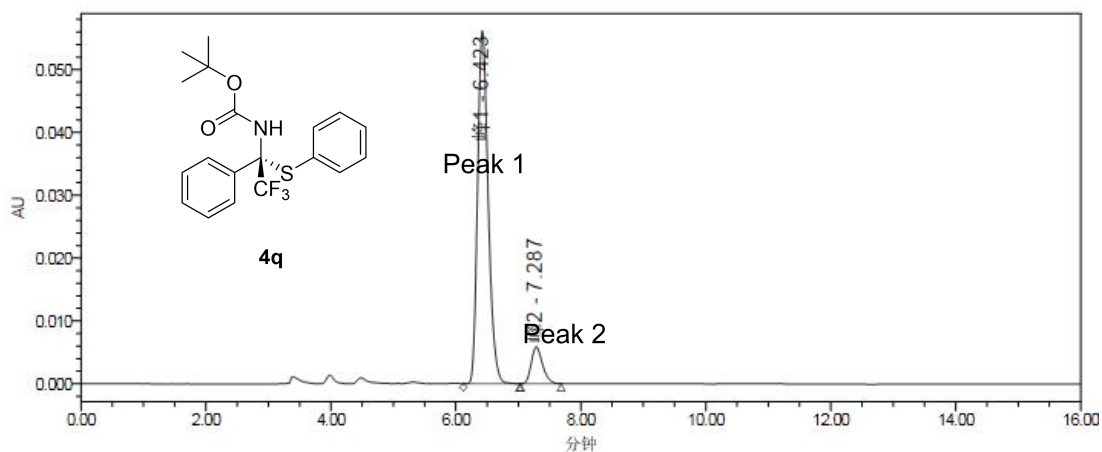


	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	11.563	1321132	16.64	49667
2	W2489 ChA 254nm	峰2	12.718	6616103	83.36	236548



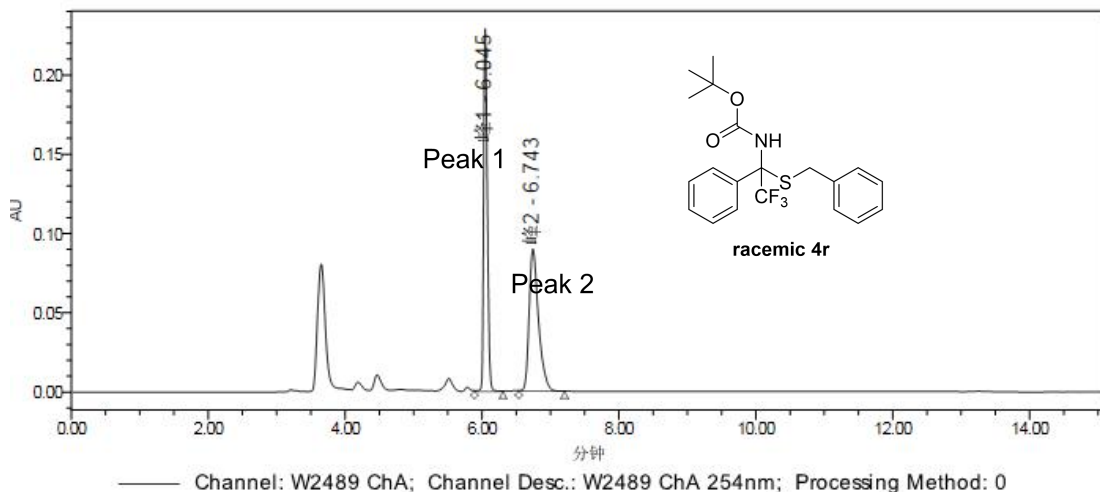
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	6.407	726615	49.91	61663
2	W2489 ChA 254nm	峰2	7.256	729265	50.09	57931

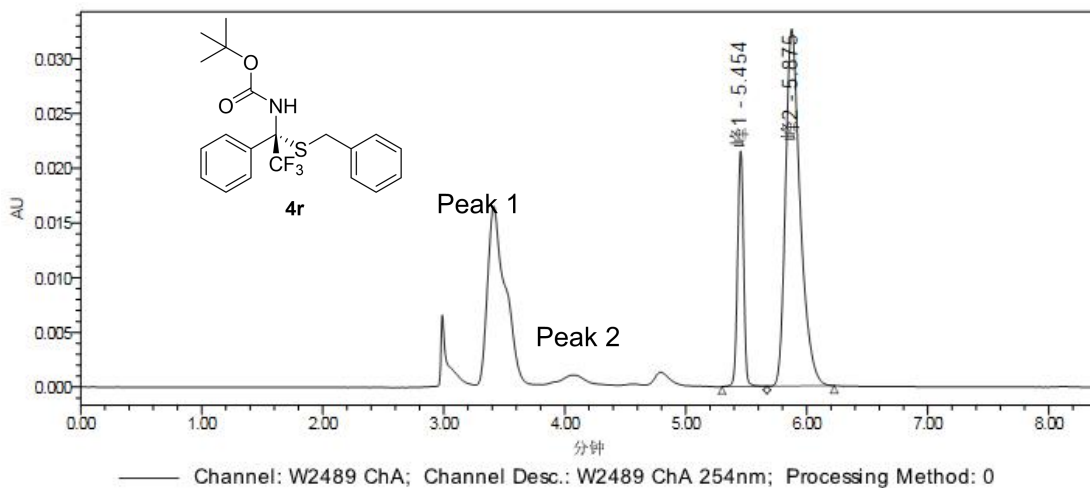


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

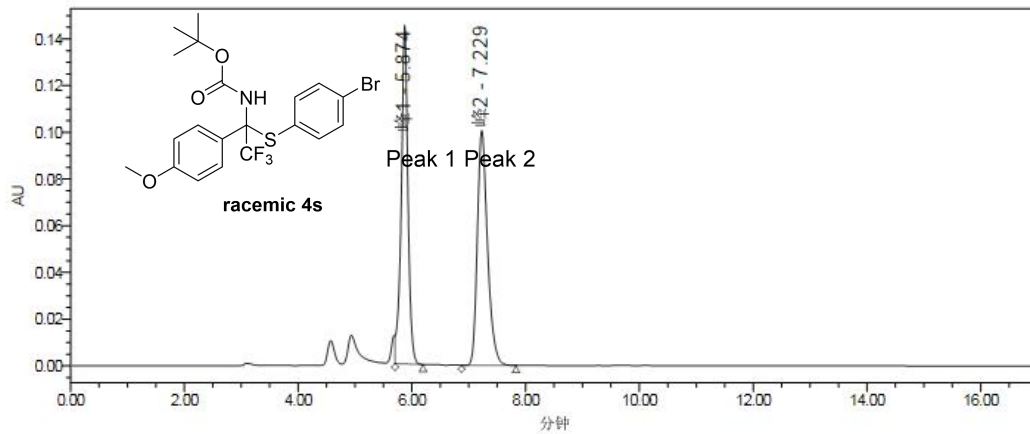
	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1	6.423	660947	90.02	56100
2	W2489 ChA 254nm	峰2	7.287	73237	9.98	5830



	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	6.045	867882	50.38	228688
2	W2489 ChA 254nm	峰2	6.743	854923	49.62	89492

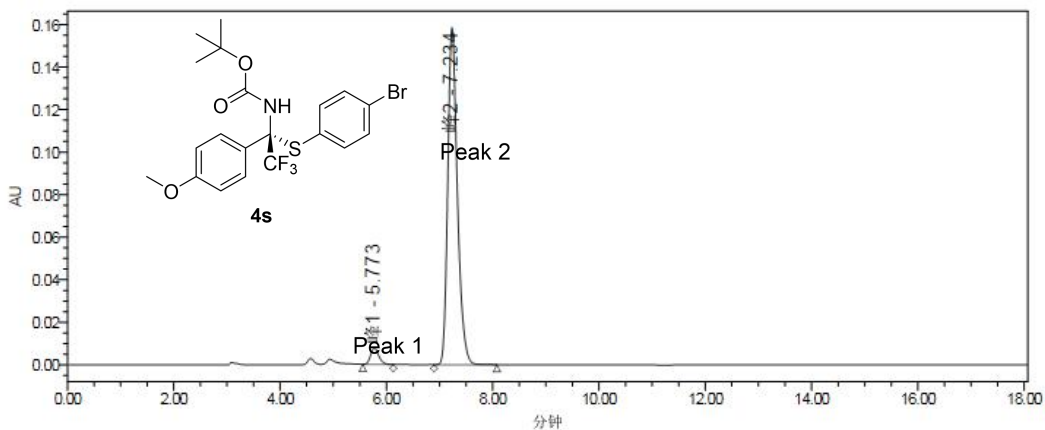


	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1	5.454	47199	21.38	21499
2	W2489 ChA 254nm	峰2	5.875	275530	78.62	32575



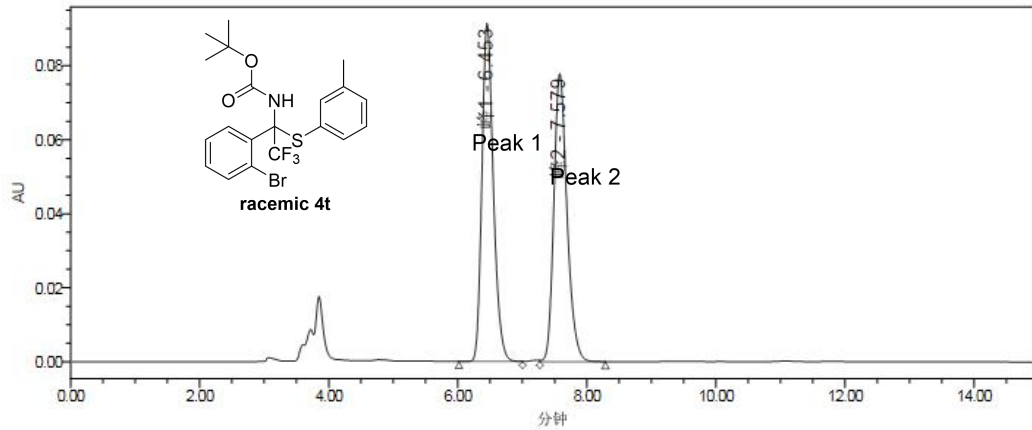
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	5.874	1184856	48.71	144816
2	W2489 ChA 254nm	峰2 Peak 2	7.229	1247607	51.29	100406



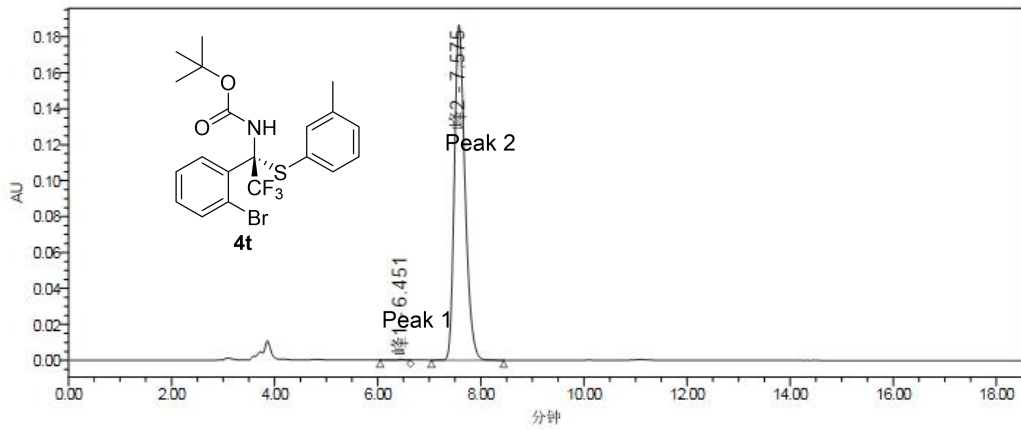
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (峰*sec) μAU*sec	% Area	Height (峰) μAU
1	W2489 ChA 254nm	峰1 Peak 1	5.773	82905	4.00	7754
2	W2489 ChA 254nm	峰2 Peak 2	7.234	1990182	96.00	158393



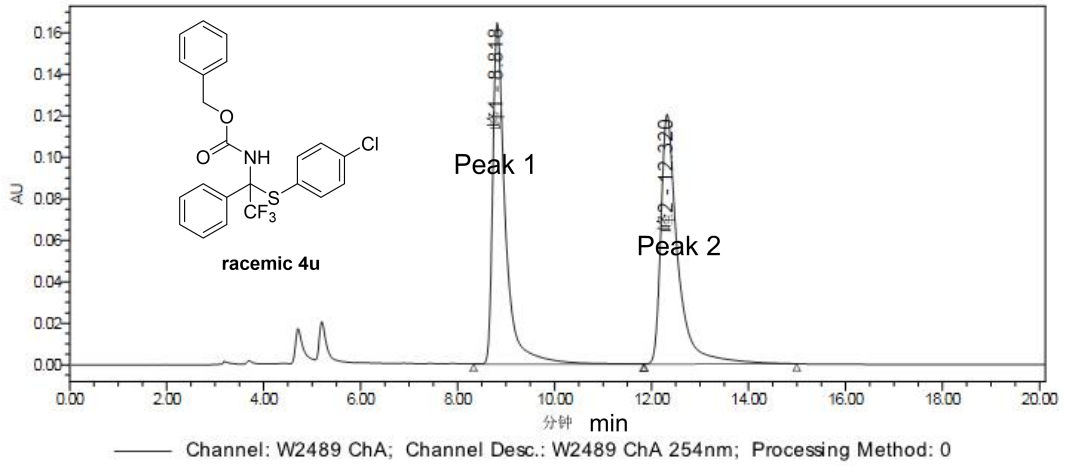
Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	6.453	1123792	50.55	91241
2	W2489 ChA 254nm	峰2 Peak 2	7.579	1099481	49.45	77773

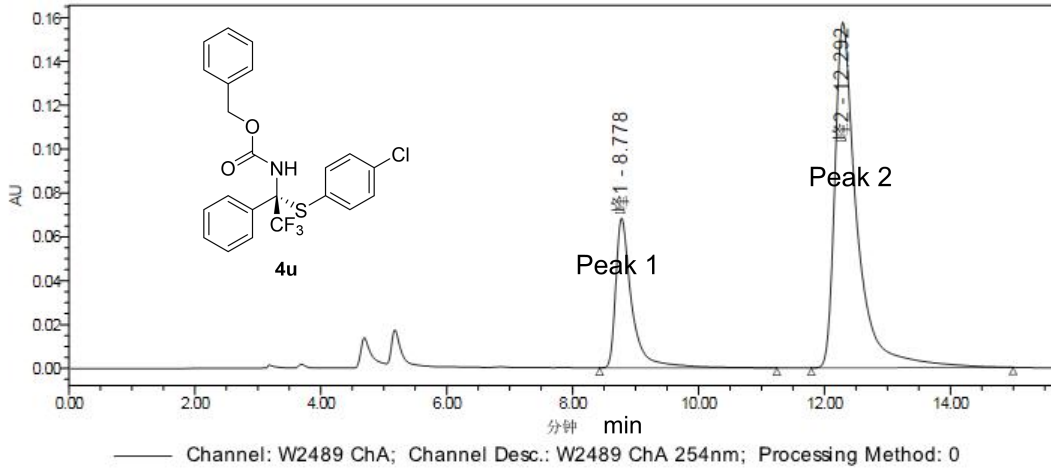


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: 0

	Channel Description	Peak Name	RT (min)	Area (AU*sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	6.451	4640	0.17	399
2	W2489 ChA 254nm	峰2 Peak 2	7.575	2675570	99.83	186494



	Channel Description	Peak Name	RT (min)	Area (AU·sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	8.818	2953489	50.25	164225
2	W2489 ChA 254nm	峰2 Peak 2	12.320	2924396	49.75	120260



	Channel Description	Peak Name	RT (min)	Area (AU·sec)	% Area	Height (AU)
1	W2489 ChA 254nm	峰1 Peak 1	8.778	1217642	24.03	68157
2	W2489 ChA 254nm	峰2 Peak 2	12.292	3849861	75.97	157401

Index ranges	-10 ≤ h ≤ 10, -13 ≤ k ≤ 13, -9 ≤ l ≤ 16
Reflections collected	5748
Independent reflections	4007 [R _{int} = 0.0147, R _{sigma} = 0.0301]
Data/restraints/parameters	4007/0/247
Goodness-of-fit on F ²	1.028
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0556, wR ₂ = 0.1462
Final R indexes [all data]	R ₁ = 0.0744, wR ₂ = 0.1635
Largest diff. peak/hole / e Å ⁻³	0.37/-0.23

12. References

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2. (a) I. V. Kutovaya, O. I. Shmatova, V. M. Tkachuk, N. V. Melnichenko, M. V. Vovk and V. G. Nenajdenko, Aza-Henry Reaction with CF₃-Ketimines: An Efficient Approach to Trifluoromethylated β-Nitroamines, 1,2-Diamines, α-Aminooximes, and Imidazolidinones, *Eur. J. Org. Chem.*, 2015, **2015**, 6749-6761. (b) M. Du, L. Yu, T. Du, Z. Li, Y. Luo, X. Meng, Z. Tian, C. Zheng, W. Cao and G. Zhao, N-Protecting group tuning of the enantioselectivity in Strecker reactions of trifluoromethyl ketimines to synthesize quaternary α-trifluoromethyl amino nitriles by ion pair catalysis, *Chem. Commun.*, 2020, **56**, 1581-1584.
3. (a) S. del Pozo, S. Vera, M. Oiarbide and C. Palomo, Catalytic Asymmetric Synthesis of Quaternary Barbituric Acids, *J. Am. Chem. Soc.*, 2017, **139**, 15308-15311. (b) M.-X. Zhao, H.-L. Bi, R.-H. Jiang, X.-W. Xu and M. Shi, Cinchona Alkaloid Squaramide/AgOAc Cooperatively Catalyzed Diastereo- and Enantioselective Mannich/Cyclization Cascade Reaction of Isocyanoacetates and Cyclic Trifluoromethyl Ketimines, *Org. Lett.*, 2014, **16**, 4566-4569. (c) W. Yang and D.-M. Du, Highly Enantioselective Michael Addition of Nitroalkanes to Chalcones Using Chiral Squaramides as Hydrogen Bonding Organocatalysts, *Org. Lett.*, 2010, **12**, 5450-5453. (d) V. Kumar and S. Mukherjee, Synergistic Lewis base and anion-binding catalysis for the enantioselective vinylogous addition of deconjugated butenolides to allenates, *Chem. Comm.*, 2013, **49**, 11203-11205. (e) Y. Qian, G. Ma, A. Lv, H.-L. Zhu, J. Zhao and V. H. Rawal, Squaramide-catalyzed enantioselective Friedel-Crafts reaction of indoles with imines, *Chem. Comm.*, 2010, **46**, 3004-3006. (f) P. S. Bhadury, Y. Zhang, S. Zhang, B. Song, S. Yang, D. Hu, Z. Chen, W. Xue and L. Jin, An effective route to fluorine containing asymmetric α-aminophosphonates using chiral Bronsted acid catalyst, *Chirality*, 2009, **21**, 547-557. (g) M. Hatano, T. Ikeno, T. Matsumura, S. Torii and K. Ishihara, Chiral lithium salts of phosphoric acids as lewis acid-base conjugate catalysts for the enantioselective cyanosilylation of ketones, *Adv. Synth. Catal.*, 2008, **350**, 1776-1780.