Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

Silver-catalyzed stereoselective C-4 arylthiodifluoromethylation of coumarin-3-carboxylic acids *via* a double decarboxylative strategy

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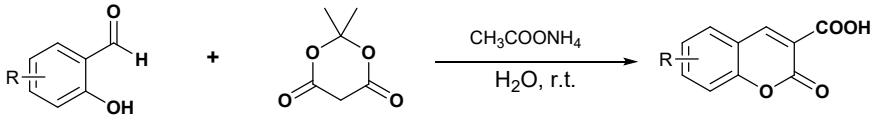
1. General information

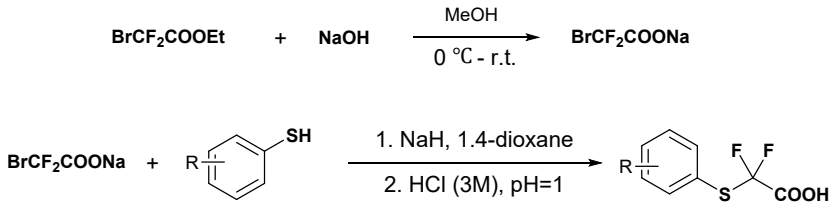
All reagents were obtained from commercial sources and used without further purification unless otherwise indicated. The starting materials and **2n** were purchased from Aladdin (https://www.aladdin-e.com/). Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. Reactions were stirred using Teflon-coated magnetic stir bars. Thin-layer chromatography (TLC) was used to monitor the reaction.Melting points were determined using a Büchi B-540 capillary melting point apparatus. ^{1}H NMR (400/600 MHz), ^{13}C NMR (100/150 MHz) and ^{19}F NMR (376/565 MHz) spectra were recorded with $CDCl_3$. Chemical shifts are reported downfield from TMS (=0) for ^{1}H NMR. For $^{13}C\{^{1}H\}$ NMR, chemical shifts are reported in the scale relative to $CDCl_3$ (= 77.0). High resolution mass spectrometry (HRMS) analysis was performed on an Agilent 1290–6540 UHPLC Q-Tof HR-MS System (ESI) spectrometer.

2.1 General procedure for the synthesis of products 1[1]



Add salicylaldehyde (2.0 g, 16.3 mmol), meldrum acid (3.5 g, 24.5 mmol) and ammonium acetate (125 mg, 1.6 mmol) to a 50.0 mL bottle, and add 25.0 mL of water. Stir at room temperature for 6 h. The reaction mixture was adjusted to pH 4 with 3M HCl (aq.), and then extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (n-hexane/ethyl acetate = 10/1 to 1/1, v/v) to obtain coumarin-3-carboxylic acids **1**.

2.2 General procedure for the synthesis of products 2[2]



To a 250 mL oven-dried round-bottom flask equipped with a stir bar were added sodium hydroxide (4.0 g, 100.0 mmol) and MeOH (100 mL). Then, $BrCF_2CO_2Et$ (20.3 g, 100.0 mmol) was added to the resulting solution at 0 ºC. Upon addition, the mixture was warmed to room temperature and stirred for 24 h. The solvent was evaporated under vacuum and the residue was further dried under reduced pressure to give $BrCF_2CO_2Na$ as a white solid (19.0 g, 97%)。

To a 100 mL oven-dried Schlenk tube equipped with a stir bar was added thiophenol (2.2 g, 20.0 mmol, 1.0 equiv.) under N_2 atmosphere. 1,4-Dioxane (30.0 mL) was added to dissolve the phenol or thiophenol. Then, NaH (60% purity) (880 mg, 22.0 mmol, 1.1 equiv.) and 1,4-dioxane (5.0 mL) were added under N_2 atmosphere. The solution was stirred at room temperature for 30 min. Then $BrCF_2COONa$ (4.3 g, 22.0 mmol, 1.1 equiv.) and 1,4-dioxane (5.0 mL) were added. After the mixture was heated at 60-70 ℃ in an oil bath for hours (monitor by TLC), then the mixture was cooled down to room temperature and acidified with 3M HCl (aq.) to pH 1. The mixture was extracted with ethyl acetate for three times. The combined organic phase was washed by saturated brines and dried over Na_2SO_4. After the solution was filtered and the solvent was evaporated under vacuum, the crude product was purified by flash column chromatography (n-hexane/ethyl acetate = 5:1, v/v) to give the product **2**.

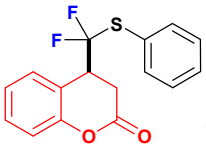
3. References

1 a) B. Sepulveda, C. Quispe, M. Simirgiotis, A. Torres-Benítez, J. Reyes-Ortíz, C. Areche and O. García-Beltrán, Gastroprotective activity of synthetic coumarins: Role of endogenous prostaglandins, nitric oxide, non-protein sulfhydryls and vanilloid receptors, *Bioorg. Med. Chem. Lett.,* 2016, **26**, 5732-5735. b) B. Dong, W. Song, Y. Lu, X. Kong, A. H. Mehmood and W. Lin, An ultrasensitive ratiometric fluorescent probe based on the ICT-PET-FRET mechanism for the quantitative measurement of pH values in the endoplasmic reticulum (ER), *Chem. Commun.,* 2019, **55**, 10776-10779.

2 a) X.-L. Zhu, Y. Huang, X.-H. Xu and F.-L. Qing, Silver-Catalyzed C–H Aryloxydifluoromethylation and Arylthiodifluoromethylation of Heteroarenes, *Org. Lett.,* 2020, **22**, 5451-5455. b) M. Zhou, C. Ni, Z. He and J. Hu, O-Trifluoromethylation of Phenols: Access to Aryl Trifluoromethyl Ethers by O-Carboxydifluoromethylation and Decarboxylative Fluorination, *Org. Lett.,* 2016, **18**, 3754-3757.

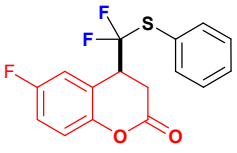
4. Analytical data of the synthesized derivatives

4-(difluoro(phenylthio)methyl)chroman-2-one (3aa)



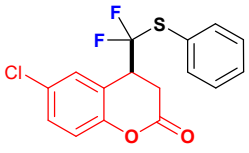
White solid; m.p.= 101.6-105.6 ℃; 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 3H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 3.77 – 3.53 (m, 1H), 3.33 (d, *J* = 17.0 Hz, 1H), 2.90 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 152.2, 136.3, 130.6, 130.4, 130.1, 129.2 (t, J_{C-F}= 283.8 Hz), 129.1, 125.1, 124.4, 117.5, 116.6, 43.9 (t, J_{C-F}= 25.2 Hz), 29.8 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.9, -76.4, -78.2, -78.7. HRMS-ESI (m/z): calcd for $C_{16}H_{13}F_2O_2S^+$ $[M+H]^+$ 307.0599, found 307. 0603.

4-(difluoro(phenylthio)methyl)-6-fluorochroman-2-one (3ba)



White solid; m.p.= 91.6-93.8 ℃; 70% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.0 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.10 – 7.06 (m, 2H), 7.05 (d, *J* = 9.8 Hz, 1H), 3.70 – 3.56 (m, 1H), 3.32 (dd, *J* = 17.0, 1.8 Hz, 1H), 2.89 (dd, *J* = 17.0, 7.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 159.5, 157.8, 148.4 (d, *J* = 2.8 Hz), 136.3, 130.3, 129.2, 129.0 (t, J_{C-F}= 283.8 Hz), 125.0, 118.8 (d, *J* = 8.6 Hz), 117.3 (d, *J* = 23.4 Hz), 117.0 (d, *J* = 24.4 Hz), 44.0 (t, J_{C-F}= 25.6 Hz), 29.5 (t, J_{C-F}= 4.6 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.6, -76.0, -78.4, -78.8, -117.7. HRMS-ESI (m/z): calcd for $C_{16}H_{12}F_3O_2S^+$ $[M+H]^+$ 325.0505, found 325.0508.

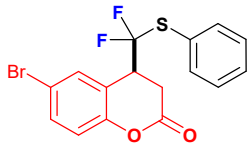
6-chloro-4-(difluoro(phenylthio)methyl)chroman-2-one (3ca)



Yellow solid; m.p.= 109.5-112.8 ℃; 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.37 – 7.29 (m, 2H), 7.05 (d, *J* = 8.6 Hz, 1H), 3.85 – 3.51 (m, 1H), 3.34 (d, *J* = 17.0 Hz, 1H),

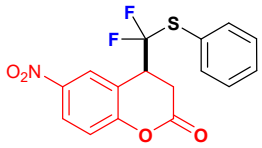
2.89 (dd, J = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 150.8, 136.3, 130.5, 130.3, 130.3, 129.5, 129.3, 128.9 (t, $J_{C\text{-}F}$= 283.8 Hz), 124.9, 118.8, 118.2, 43.8 (t, $J_{C\text{-}F}$= 25.2 Hz), 29.6 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.5, -76.0, -78.7, -79.2. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0214.

6-bromo-4-(difluoro(phenylthio)methyl)chroman-2-one (3da)



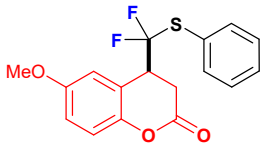
White solid; m.p.= 122.8-126.7 °C; 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.2 Hz, 2H), 7.49 (dd, J = 8.6, 2.4 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.38 (t, J = 7.4 Hz, 2H), 6.99 (d, J = 8.6 Hz, 1H), 3.76 – 3.46 (m, 1H), 3.34 (d, J = 17.0 Hz, 1H), 2.89 (dd, J = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 151.4, 136.3, 133.4, 133.2, 130.3, 129.3, 129.0 (t, $J_{C\text{-}F}$= 283.8 Hz), 124.9, 119.2, 118.6, 116.9, 43.7 (t, $J_{C\text{-}F}$= 25.2 Hz), 29.6 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.4, -76.0, -78.7, -79.3. HRMS-ESI (m/z): calcd for $C_{16}H_{12}BrF_2O_2S^+$ $[M+H]^+$ 384.9704, found 384.9706.

4-(difluoro(phenylthio)methyl)-6-nitrochroman-2-one (3ea)



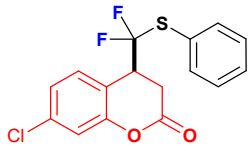
Brown solid; m.p.= 134.3-139.2 °C; 55% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H), 7.48 (dd, J = 8.6, 2.4 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.37 (t, J = 7.6 Hz, 2H), 6.99 (d, J = 8.6 Hz, 1H), 3.73 – 3.55 (m, 1H), 3.33 (d, J = 17.0 Hz, 1H), 2.88 (dd, J = 17.0, 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 151.4, 136.3, 133.4, 133.2, 130.3, 129.3, 129.0 (t, $J_{C\text{-}F}$= 283.8 Hz), 125.0, 119.2, 118.7, 116.9, 43.8 (t, $J_{C\text{-}F}$= 24.2 Hz), 29.6 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.7, -76.2, -79.3, -79.9. HRMS-ESI (m/z): calcd for $C_{16}H_{12}F_2NO_4S^+$ $[M+H]^+$ 352.0450, found 352.0448.

4-(difluoro(phenylthio)methyl)-6-methoxychroman-2-one (3fa)



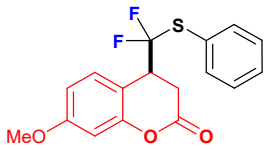
Yellow liquid; 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.0 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.84 (s, 1H), 3.80 (s, 3H), 3.71 – 3.54 (m, 1H), 3.29 (d, *J* = 17.0 Hz, 1H), 2.88 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 155.9, 146.1, 136.3, 130.1, 129.1 (t, J_{C-F}= 288.8 Hz), 125.1, 118.2, 118.1, 117.3, 115.7, 115.3, 55.7, 44.3 (t, J_{C-F}= 28.2 Hz), 29.8 (t, J_{C-F}= 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7, -76.3, -77.7, -78.3. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_3S^+$ $[M+H]^+$ 337.0704, found 337.0709.

7-chloro-4-(difluoro(phenylthio)methyl)chroman-2-one (3ga)



Yellow solid; m.p.= 103.2-104.3 °C; 53% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 3.8 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.12 (s, 1H), 3.70 – 3.59 (m, 1H), 3.33 (d, *J* = 17.0 Hz, 1H), 2.89 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 152.7, 136.3, 135.9, 131.4, 130.2, 129.2, 129.0 (t, J_{C-F}= 283.8 Hz), 125.0, 124.7, 117.9, 115.2, 43.7 (t, J_{C-F}= 24.2 Hz), 29.6 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -76.0, -76.4, -78.4, -78.8. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0212.

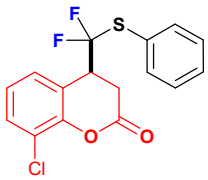
4-(difluoro(phenylthio)methyl)-7-methoxychroman-2-one (3ha)



White solid; m.p.= 95.9-98.7 °C; 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.0 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.64 (d, *J* = 2.6 Hz, 1H), 3.80 (s, 3H), 3.69 – 3.53 (m, 1H), 3.30 (d, *J* = 17.0 Hz, 1H), 2.88 (dd, *J* = 17.0, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 161.2, 153.2, 136.3, 131.1, 130.0, 129.4 (t, J_{C-F}= 284.8 Hz),

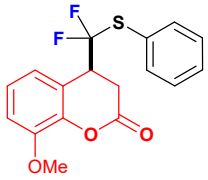
129.1, 125.3, 110.8, 108.3, 102.6, 55.5, 43.4 (t, J_{C-F}= 24.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.5, -77.0, -78.0, -78.5. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_3S^+$ $[M+H]^+$ 337.0704, found 337.0707.

8-chloro-4-(difluoro(phenylthio)methyl)chroman-2-one (3ia)



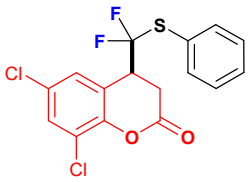
White solid; m.p.= 118.0-123.1℃; 67% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.2 Hz, 1H), 7.15 (dd, J = 8.2, 2.2 Hz, 1H), 7.12 (d, J = 2.2 Hz, 1H), 3.73 – 3.54 (m, 1H), 3.33 (d, J = 17.0 Hz, 1H), 2.89 (dd, J = 17.0, 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.8, 152.8, 136.3, 135.9, 131.4, 130.2, 129.2, 129.0 (t, J_{C-F}= 283.8 Hz), 125.0, 124.7, 117.9, 115.2, 43.7 (t, J_{C-F}= 24.2 Hz), 29.7 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -76.0, -76.4, -78.4, -78.8. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0215.

4-(difluoro(phenylthio)methyl)-8-methoxychroman-2-one (3ja)



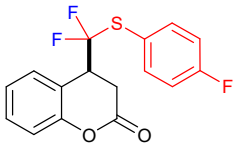
Yellow solid; m.p.= 121.4-126.2 ℃; 72% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, J = 7.0 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.12 (t, J = 8.0 Hz, 1H), 6.99 (dd, J = 8.4, 1.4 Hz, 1H), 6.93 (d, J = 7.7 Hz, 1H), 3.92 (s, 1H), 3.73 – 3.64 (m, 1H), 3.33 (d, J = 17.0 Hz, 1H), 2.92 (dd, J = 16.8, 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9, 155.9, 146.2, 136.3, 130.1, 129.2 (t, J_{C-F}= 283.8 Hz), 129.2, 125.2, 118.3, 117.4, 115.8, 115.3, 55.7, 44.3 (t, J_{C-F}= 25.6 Hz), 29.8 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.8, -76.2, -77.7, -78.1. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_3S^+$ $[M+H]^+$ 337.0704, found 337.0708.

6,8-dichloro-4-(difluoro(phenylthio)methyl)chroman-2-one (3ka)



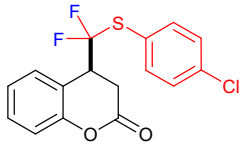
Brown solid; m.p.= 108.0-112.4 ℃; 61% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.0 Hz, 2H), 7.45 – 7.42 (m, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.21 (d, *J* = 2.4 Hz, 1H), 3.69 – 3.57 (m, 1H), 3.36 (d, *J* = 17.0 Hz, 1H), 2.90 (dd, *J* = 17.0, 7.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 147.2, 137.1, 136.6, 136.3, 130.9, 130.7 (t, $J_{C\text{-}F}$= 286.8 Hz), 130.4, 129.3, 128.7, 123.4, 119.6, 44.2 (t, $J_{C\text{-}F}$= 25.6 Hz), 29.4 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.3, -75.7, -78.6, -79.0. HRMS-ESI (m/z): calcd for $C_{16}H_{11}Cl_2F_2O_2S^+$ $[M+H]^+$ 374.9819, found 374.9815.

4-(difluoro((4-fluorophenyl)thio)methyl)chroman-2-one (3ab)



White solid; m.p.= 104.1-105.7 ℃; 55% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.05 (t, *J* = 8.6 Hz, 2H), 3.80 – 3.60 (m, 1H), 3.31 (d, 17.0 Hz, 1H), 2.92 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 152.3, 138.7, 138.6, 130.5, 130.5, 129.0 (t, $J_{C\text{-}F}$= 284.8 Hz), 124.5, 120.3, 117.6, 116.5, 116.3, 44.1 (t, $J_{C\text{-}F}$= 24.2 Hz), 29.8 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.5, -77.0, -77.9, -78.5, -109.8. HRMS-ESI (m/z): calcd for $C_{16}H_{12}F_3O_2S^+$ $[M+H]^+$ 325.0505, found 325.0498.

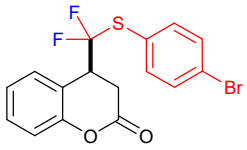
4-(((4-chlorophenyl)thio)difluoromethyl)chroman-2-one (3ac)



White solid; m.p.= 132.3-135.1 ℃; 46% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.37 – 7.29 (m, 3H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 3.79 – 3.58 (m, 1H), 3.30 (d, *J* = 17.0 Hz, 1H), 2.92 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 152.3, 137.6, 136.8, 130.6, 130.5, 129.4, 129.0 (t, $J_{C\text{-}F}$= 285.8 Hz), 124.5, 123.5, 117.6, 116.4, 44.2 (t,

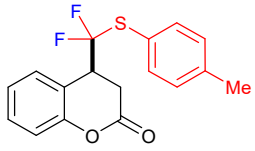
$J_{C\text{-}F}$= 25.2 Hz), 29.8 (t, $J_{C\text{-}F}$= 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.1, -76.7, -77.4, -77.9. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0206.

4-(((4-bromophenyl)thio)difluoromethyl)chroman-2-one (3ad)



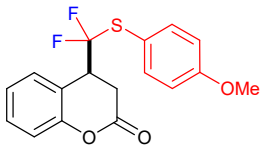
White solid; m.p.= 149.5-151.7 ℃; 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.39 (dd, J = 8.8, 7.0 Hz, 3H), 7.33 (d, J = 7.6 Hz, 1H), 7.17 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 3.83 – 3.55 (m, 1H), 3.29 (d, J = 17.0 Hz, 1H), 2.92 (dd, J = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 152.2, 137.7, 132.4, 130.6, 130.5, 129.0 (t, $J_{C\text{-}F}$= 285.8 Hz), 125.1, 124.5, 124.1, 117.6, 116.4, 44.1 (t, $J_{C\text{-}F}$= 25.2 Hz), 29.8 (t, $J_{C\text{-}F}$= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.0, -76.6, -77.3, -77.8. HRMS-ESI (m/z): calcd for $C_{16}H_{12}BrF_2O_2S^+$ $[M+H]^+$ 384.9704, found 384.9700.

4-(difluoro(p-tolylthio)methyl)chroman-2-one (3ae)



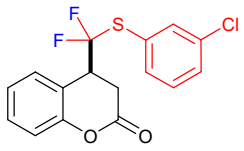
White solid; m.p.= 105.0-106.8 ℃; 65% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.16 (d, J = 7.6 Hz, 3H), 7.10 (d, J = 8.0 Hz, 1H), 3.74 – 3.65 (m, 1H), 3.32 (d, J = 17.0 Hz, 1H), 2.89 (dd, J = 17.0, 7.4 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 152.3, 140.6, 136.4, 130.6, 130.4, 130.0, 129.2 (t, $J_{C\text{-}F}$= 283.8 Hz), 124.4, 121.7, 117.5, 116.8, 43.9 (t, $J_{C\text{-}F}$= 24.2 Hz), 29.9 (t, $J_{C\text{-}F}$= 3.0 Hz), 21.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -76.2, -76.6, -78.8, -79.1. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_2S^+$ $[M+H]^+$ 321.0755, found 321.0758.

4-(difluoro((4-methoxyphenyl)thio)methyl)chroman-2-one (3af)



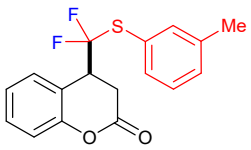
Yellow solid; m.p.= 109.3-113.6 ℃; 68% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.8 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 3.85 – 3.78 (m, 3H), 3.71 – 3.57 (m, 1H), 3.33 (d, *J* = 17.0 Hz, 1H), 2.90 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 161.3, 152.3, 138.2, 130.6, 130.4, 129.1 (t, J_{C-F}= 283.8 Hz), 124.4, 117.5, 116.8, 115.5, 114.7, 55.4, 43.8 (t, J_{C-F}= 25.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -76.7, -77.2, -79.3, -79.9. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_3S^+$ $[M+H]^+$ 337.0704, found 337.0709.

4-(((3-chlorophenyl)thio)difluoromethyl)chroman-2-one (3ag)



White solid; m.p.= 104.3-106.0 ℃; 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.0 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.32 (m, 3H), 7.30 – 7.21 (m, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 3.78 – 3.65 (m, 1H), 3.39 (d, *J* = 17.0 Hz, 1H), 2.94 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 152.3, 140.0, 138.7, 131.6, 130.6, 130.5, 130.4, 129.2(t, J_{C-F}= 285.8 Hz), 127.3, 124.8, 124.4, 117.5, 116.4, 44.3 (t, J_{C-F}= 24.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.1, -75.7, -78.0, -78.6. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0212.

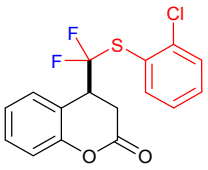
4-(difluoro(m-tolylthio)methyl)chroman-2-one (3ah)



Yellow solid; m.p.= 81.3-83.2 ℃; 68% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 4H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 3.6 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 3.71 – 3.62 (m, 1H), 3.32 (d, *J* = 17.0 Hz, 1H), 2.90 (dd, *J* = 17.0, 7.4 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 152.3, 139.1, 136.8, 133.3, 130.9, 130.6, 130.4, 129.3 (t, J_{C-F}= 283.8 Hz), 128.9, 124.4, 117.5,

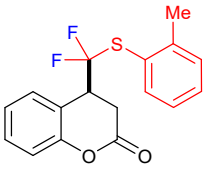
117.3, 116.7, 44.1 (t, J_{C-F}= 24.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz), 21.1. ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.9, -76.2, -78.2, -78.6. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_2S^+$ $[M+H]^+$ 321.0755, found 321.0759.

4-(((2-chlorophenyl)thio)difluoromethyl)chroman-2-one (3ai)



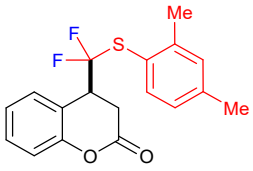
White solid; m.p.= 92.8-95.1 °C; 43% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 18.2, 7.2 Hz, 3H), 7.26 (t, *J* = 3.6 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 3.76 – 3.67 (m, 1H), 3.39 (d, *J* = 17.0 Hz, 1H), 2.94 (dd, *J* = 17.0, 7.4 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6, 152.3, 140.0, 138.7, 131.6, 130.6, 130.5, 130.4, 129.3 (t, J_{C-F}= 285.4 Hz), 127.3, 124.9, 124.4, 117.5, 116.4, 44.3 (t, J_{C-F}= 24.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz). ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.2, -75.5, -78.0, -78.3. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0215.

4-(difluoro(o-tolylthio)methyl)chroman-2-one (3aj)



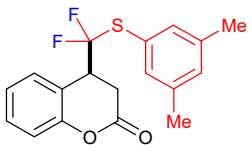
White solid; m.p.= 83.1-84.2 °C; 46% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.17 (q, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 1H), 3.81 – 3.62 (m, 1H), 3.34 (dd, *J* = 17.0, 1H), 2.93 (dd, *J* = 17.0, 7.4 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 152.3, 144.0, 138.2, 130.8, 130.6, 130.4, 129.6 (t, J_{C-F}= 283.8 Hz), 126.5, 126.2, 124.4, 124.4, 117.5, 116.7, 44.3 (t, J_{C-F}= 24.2 Hz), 30.0 (t, J_{C-F}= 3.0 Hz), 21.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.9, -76.2, -77.2, -77.6. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_2S^+$ $[M+H]^+$ 321.0755, found 321.0758.

4-(((2,4-dimethylphenyl)thio)difluoromethyl)chroman-2-one (3ak)



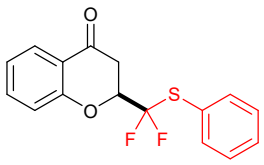
White solid; m.p.= 79.5-81.0 ℃; 65% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.0 Hz, 1H), 7.37 (m, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.13 – 7.07 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 3.76 – 3.59 (m, 1H), 3.33 (d, *J* = 17.0 Hz, 1H), 2.91 (dd, *J* = 17.0, 7.4 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 152.3, 143.8, 141.0, 138.2, 131.7, 130.6, 130.3, 129.6 (t, J_{C-F}= 283.8 Hz), 127.3, 124.4, 120.9, 117.5, 116.8, 44.3 (t, J_{C-F}= 24.2 Hz), 30.0 (t, J_{C-F}= 3.0 Hz), 21.2, 21.1. ^{19}F NMR (565 MHz, $CDCl_3$) δ -76.2, -76.5, -77.7, -78.0. HRMS-ESI (m/z): calcd for $C_{18}H_{17}F_2O_2S^+$ $[M+H]^+$ 335.0912, found 335.0915.

4-(((3,5-dimethylphenyl)thio)difluoromethyl)chroman-2-one (3al)



Yellow solid; m.p.= 93.4-95.8 ℃; 70% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.20 – 7.12 (m, 3H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.03 (s, 1H), 3.72 – 3.59 (m, 1H), 3.33 (d, *J* = 17.0 Hz, 1H), 2.90 (dd, *J* = 17.0, 7.4 Hz, 1H), 2.30 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 152.3, 138.8, 133.8, 131.9, 130.6, 130.4, 129.3 (t, J_{C-F}= 283.8 Hz), 124.6, 124.4, 117.5, 116.8, 44.1 (t, J_{C-F}= 24.2 Hz), 29.9 (t, J_{C-F}= 3.0 Hz), 21.0. ^{19}F NMR (565 MHz, $CDCl_3$) δ -75.9, -76.2, -78.3, -78.7. HRMS-ESI (m/z): calcd for $C_{18}H_{17}F_2O_2S^+$ $[M+H]^+$ 335.0912, found 335.0914.

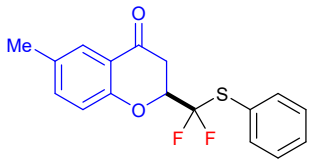
2-(difluoro(phenylthio)methyl)chroman-4-one (5aa)



Colorless liquid; 55% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.0 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.12 – 7.05 (m, 2H), 4.85 – 4.55 (m, 1H), 3.06 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.94 (dd, *J* = 17.0, 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.5,

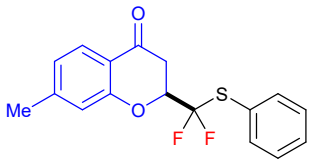
159.7, 136.7, 136.5, 136.4, 130.3, 129.2 (t, $J_{C\text{-}F}$= 12.0 Hz), 126.9, 125.0, 122.4, 120.8, 118.0, 77.9 (dd, $J_{C\text{-}F}$ = 32.0, 27.8 Hz), 36.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -82.3, -82.7, -86.3, -86.7. HRMS-ESI (m/z): calcd for $C_{16}H_{13}F_2O_2S^+$ $[M+H]^+$ 307.0599, found 307.0595.

2-(difluoro(phenylthio)methyl)-6-methylchroman-4-one (5ba)



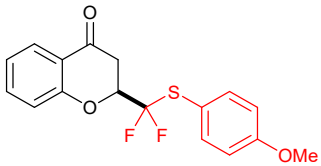
Colorless liquid; 50% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.8 (d, *J* = 8.0 Hz, 1H), 7.7 (d, *J* = 7.0 Hz, 2H), 7.5 – 7.4 (m, 1H), 7.4 (t, *J* = 7.4 Hz, 2H), 6.9 – 6.9 (m, 2H), 4.8 – 4.6 (m, 1H), 3.0 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.9 (dd, *J* = 17.0, 3.4 Hz, 1H), 2.4 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.2, 159.8, 148.2, 136.7, 130.2, 129.2, 127.2 (t, $J_{C\text{-}F}$= 282.4 Hz), 126.8, 125.0, 123.7, 118.5, 118.0, 77.9 (dd, $J_{C\text{-}F}$ = 31.8, 27.8 Hz), 36.8, 21.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -82.3, -82.7, -86.3, -86.7. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_2S^+$ $[M+H]^+$ 321.0755, found 321.0759.

2-(difluoro(phenylthio)methyl)-7-methylchroman-4-one (5ca)

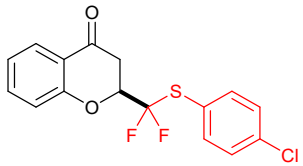


White solid; m.p.= 83.2-84.5 ℃; 52% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.8 (d, *J* = 8.0 Hz, 1H), 7.7 (d, *J* = 7.4 Hz, 2H), 7.4 (t, *J* = 7.4 Hz, 1H), 7.4 (t, *J* = 7.6 Hz, 2H), 6.9 – 6.9 (m, 2H), 4.8 – 4.5 (m, 1H), 3.0 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.9 (dd, *J* = 17.0, 3.6 Hz, 1H), 2.4 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.1, 159.7, 148.1, 136.7, 130.2, 129.2, 127.1 (t, $J_{C\text{-}F}$= 282.4 Hz), 126.8, 125.0, 123.7, 118.5, 118.0, 77.9 (dd, $J_{C\text{-}F}$ = 31.8, 27.8 Hz), 36.8, 21.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -82.3, -82.6, -86.3, -86.7. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_2S^+$ $[M+H]^+$ 321.0755, found 321.0760.

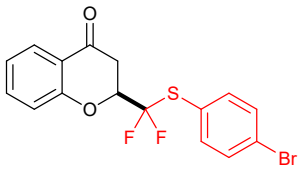
2-(difluoro((4-methoxyphenyl)thio)methyl)chroman-4-one (5ab)

 White solid; m.p.= 83.4-84.6 ℃; 64% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.56 – 7.50 (m, 1H), 7.17 – 6.99 (m, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.76 – 4.56 (m, 1H), 3.81 (s, 3H), 3.05 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.93 (dd, *J* = 17.0, 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.6, 161.4, 159.8, 138.5, 136.4, 127.0 (t, J_{C-F}= 280.8 Hz), 126.9, 122.4, 120.8, 118.0, 115.3, 114.8, 77.6 (dd, J_{C-F} = 32.0, 27.8 Hz), 55.3, 36.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -83.3, -83.7, -87.5, -87.8. HRMS-ESI (m/z): calcd for $C_{17}H_{15}F_2O_3S^+$ $[M+H]^+$ 337.0704, found 337.0700.

2-(((4-chlorophenyl)thio)difluoromethyl)chroman-4-one (5ac)

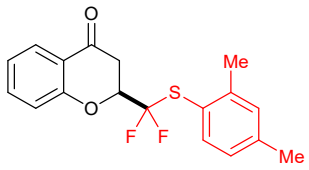
 Yellow solid; m.p.= 107.8-110.0 ℃; 61% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.57 – 7.49 (m, 1H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.13 – 7.05 (m, 2H), 4.78 – 4.69 (m, 1H), 3.05 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.94 (dd, *J* = 17.0, 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.2, 159.6, 137.9, 137.7, 137.0, 136.5, 129.5 (t, J_{C-F}= 12.0 Hz), 127.0, 123.3, 122.5, 120.8, 117.9, 77.9 (dd, J_{C-F} = 31.8, 28.0 Hz), 36.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -81.9, -82.2, -86.1, -86.4. HRMS-ESI (m/z): calcd for $C_{16}H_{12}ClF_2O_2S^+$ $[M+H]^+$ 341.0209, found 341.0204.

2-(((4-bromophenyl)thio)difluoromethyl)chroman-4-one (5ad)

 Yellow solid; m.p.= 93.3-95.1 ℃; 60% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.53 (dd, *J* = 8.8, 3.0 Hz, 5H), 7.09 (t, *J* = 7.4 Hz, 2H), 4.81 – 4.61 (m, 1H), 3.05 (dd, *J* = 17.0, 12.6 Hz, 1H), 2.94 (dd, *J* = 17.0, 3.6

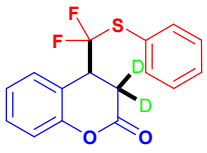
Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.2, 159.6, 138.1, 137.8, 136.5, 132.5 (t, J_{C-F}= 12.0 Hz), 127.0, 125.3, 124.0, 122.5, 120.7, 117.9, 77.9 (dd, J_{C-F} = 31.8, 28.0 Hz), 36.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ -81.8, -82.2, -86.0, -86.4. HRMS-ESI (m/z): calcd for $C_{16}H_{12}BrF_2O_2S^+$ $[M+H]^+$ 384.9704, found 384.9700.

2-(((2,4-dimethylphenyl)thio)difluoromethyl)chroman-4-one (5ae)



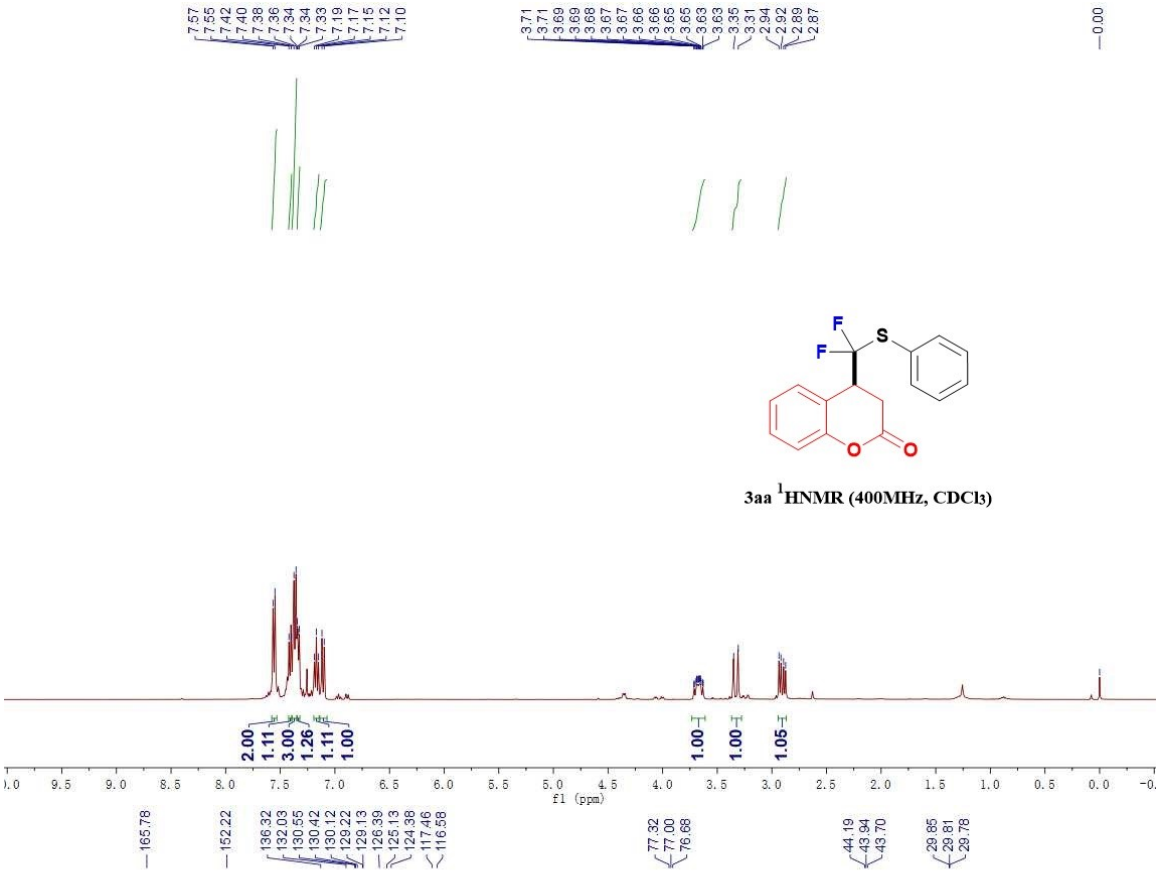
Yellow solid; m.p.= 79.0-80.2 ℃; 76% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.9 (dd, J = 7.8, 1.8 Hz, 1H), 7.6 – 7.5 (m, 2H), 7.2 – 7.1 (m, 3H), 7.0 (d, J = 7.8 Hz, 1H), 4.8 – 4.6 (m, 1H), 3.1 (dd, J = 17.0, 12.6 Hz, 1H), 2.9 (dd, J = 17.0, 3.4 Hz, 1H), 2.5 (s, 3H), 2.3 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.6, 159.8, 144.0, 141.2, 138.5, 136.4, 131.8, 127.5, 127.5 (t, J_{C-F}= 282.4 Hz), 126.9, 122.4, 120.8, 120.8, 118.0, 77.9(dd, J_{C-F} = 32.4, 27.8 Hz), 37.0, 21.3, 21.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -81.9, -82.2, -86.7, -87.1. HRMS-ESI (m/z): calcd for $C_{18}H_{17}F_2O_2S^+$ $[M+H]^+$ 335.0912, found 335.0916.

4-(difluoro(phenylthio)methyl)chroman-2-one-3,3-*d*$_2$ (3aa')

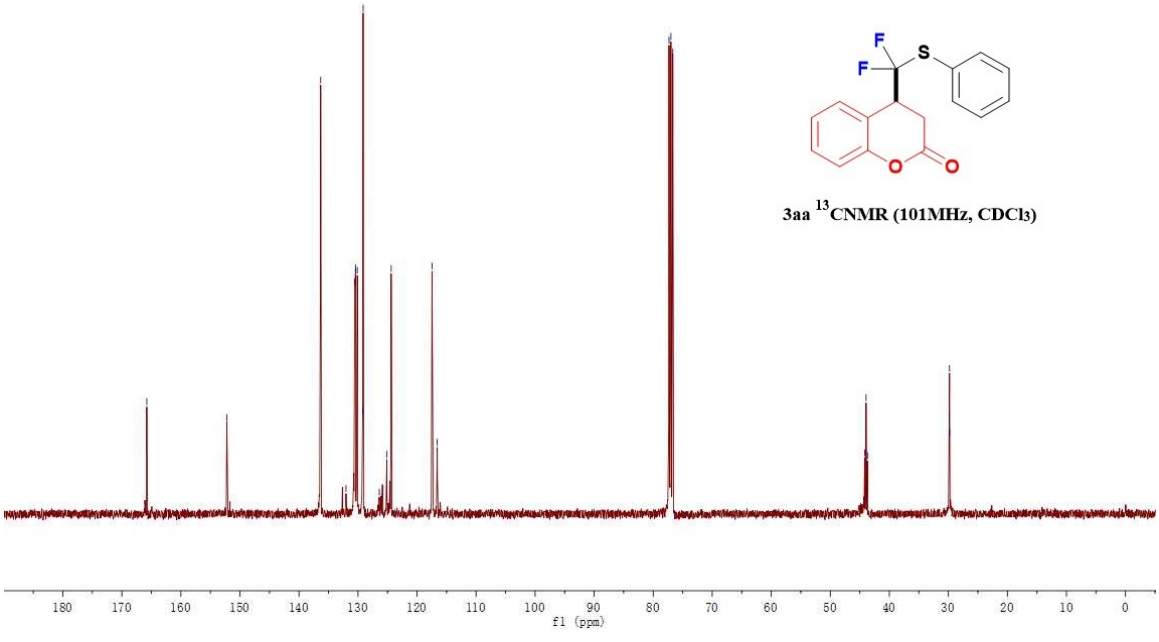


White solid; m.p.= 101.2-104.8 ℃; 83% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.4 Hz, 1H), 7.36 (d, J = 6.0 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.16 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 8.2 Hz, 1H), 3.65 (dd, J = 14.4, 10.8 Hz, 1H). HRMS-ESI (m/z): calcd for $C_{16}H_{11}D_2F_2O_2S^+$ $[M+H]^+$ 309.0724, found 309.0722.

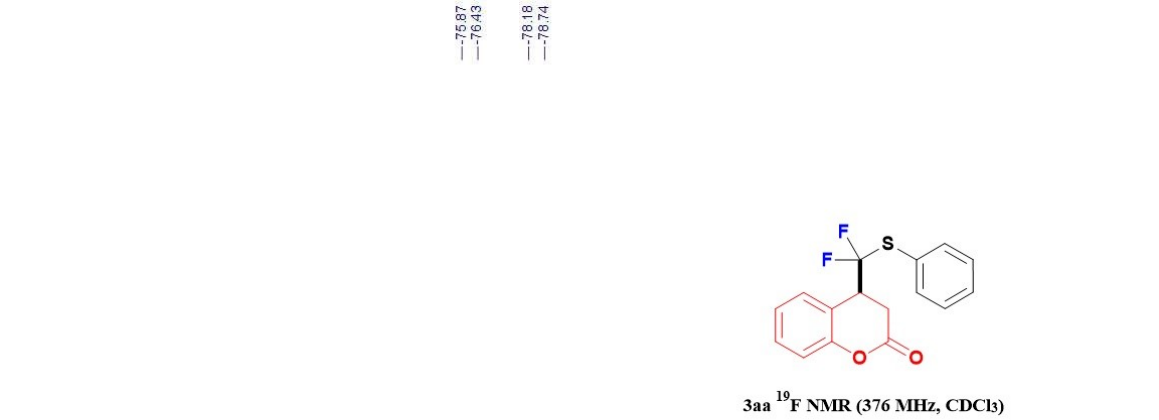
5. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR of compounds



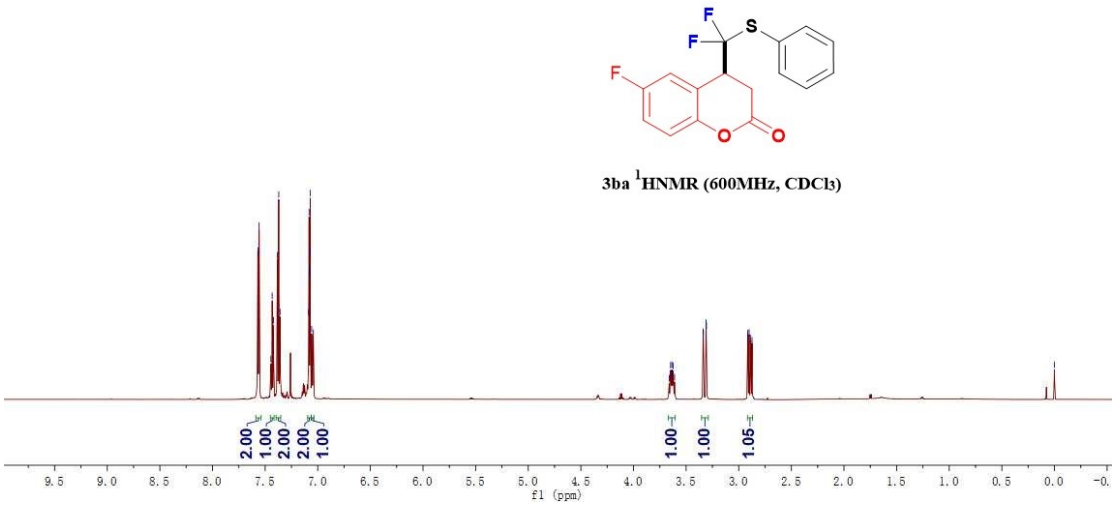
3aa ^{1}HNMR (400MHz, CDCl3)



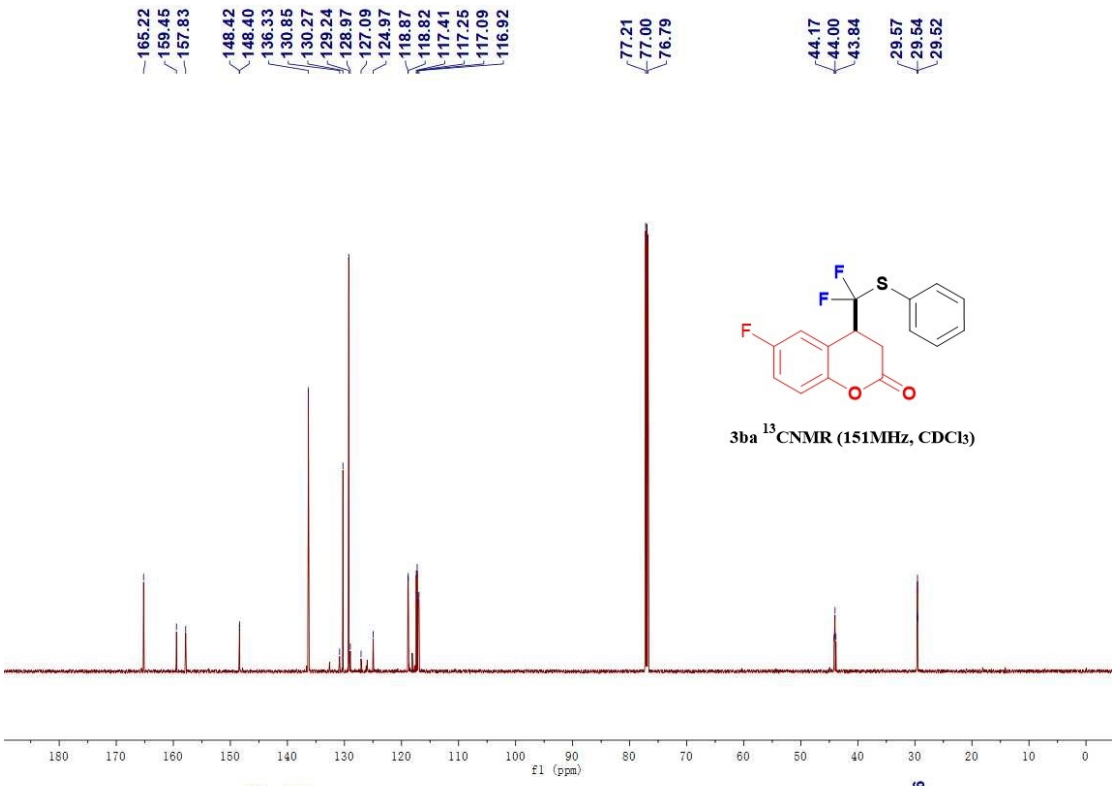
3aa ^{13}CNMR (101MHz, CDCl3)



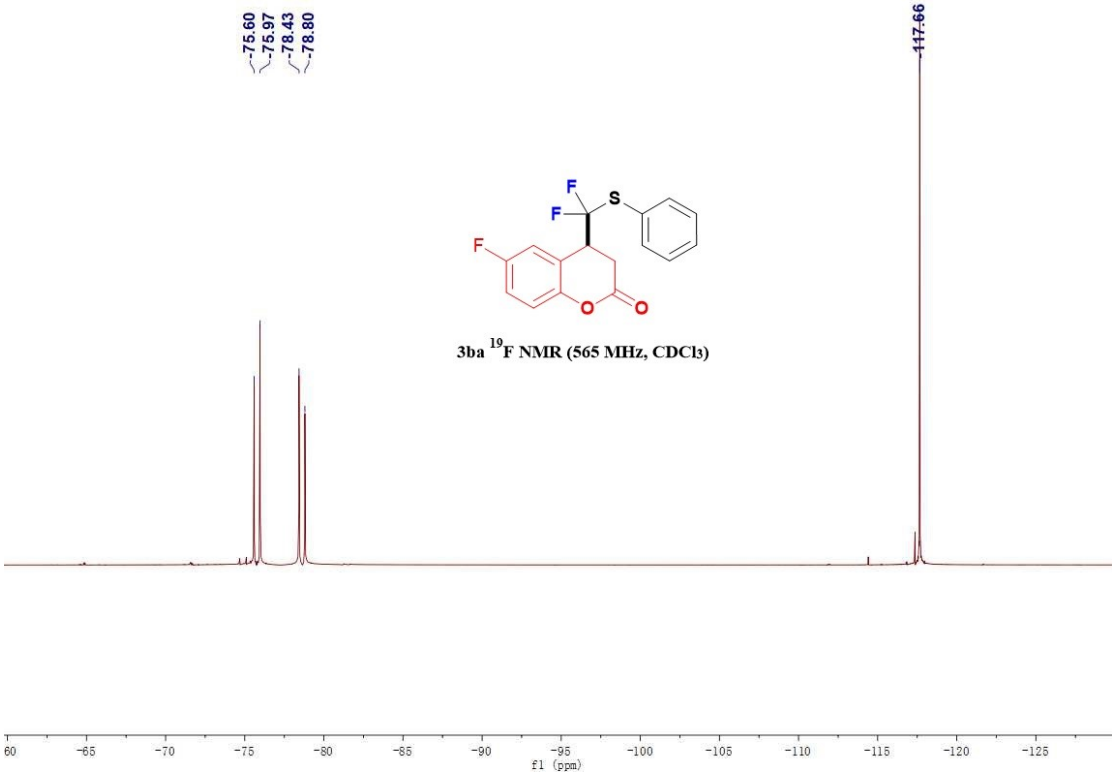
3aa ^{19}F NMR (376 MHz, CDCl3)



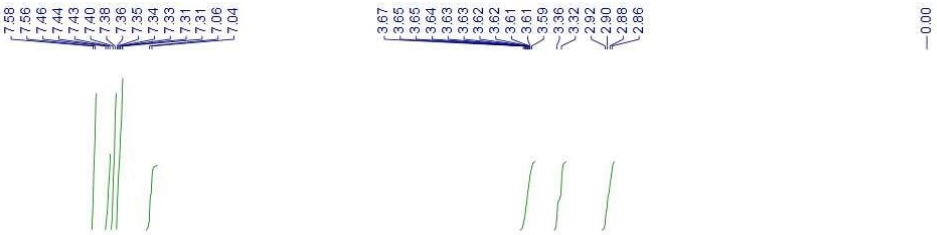
3ba ^{1}HNMR (600MHz, CDCl3)

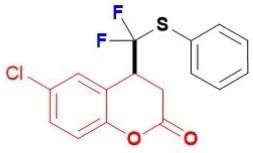


3ba ^{13}CNMR (151MHz, CDCl3)

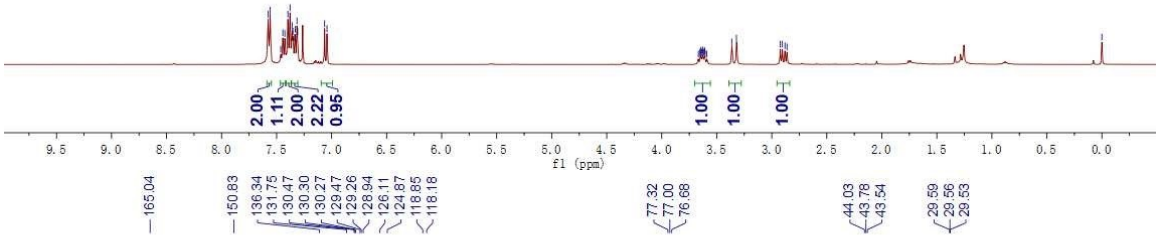


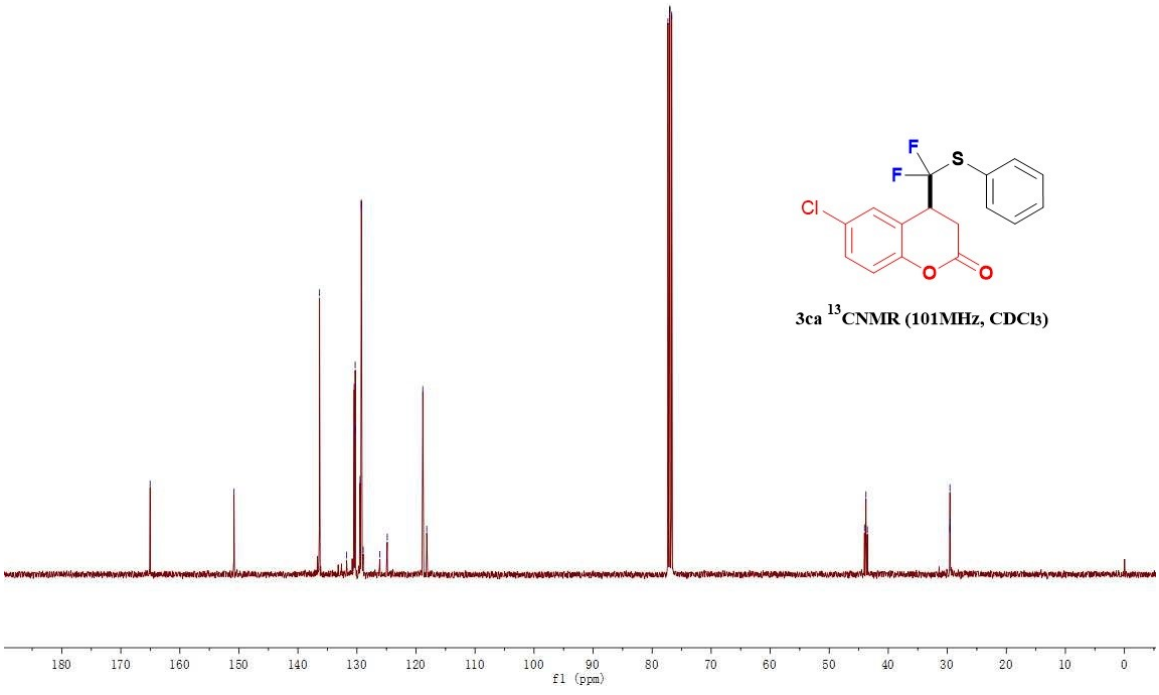
3ba ^{19}F NMR (565 MHz, CDCl3)



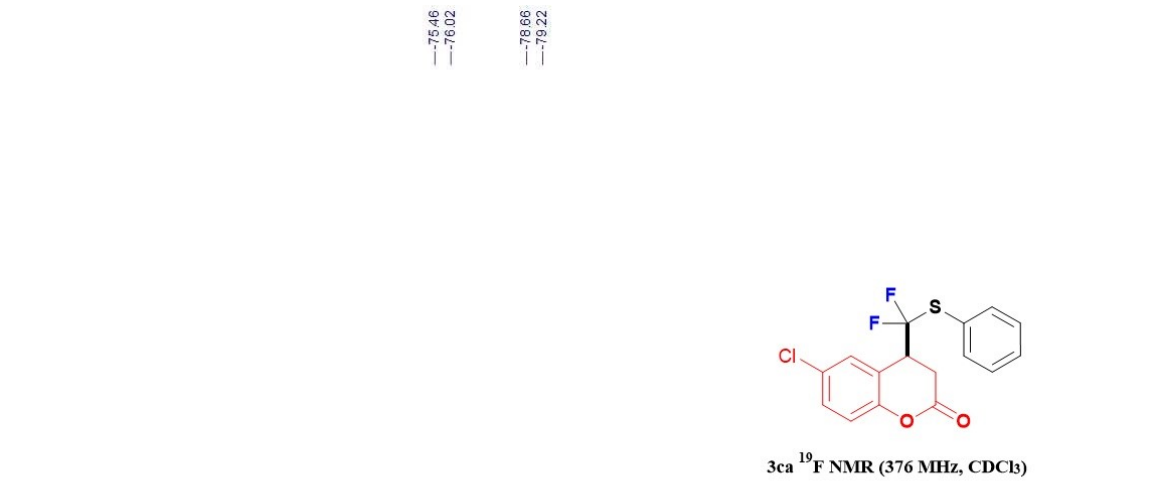


3ca ^{1}HNMR (400MHz, CDCl3)

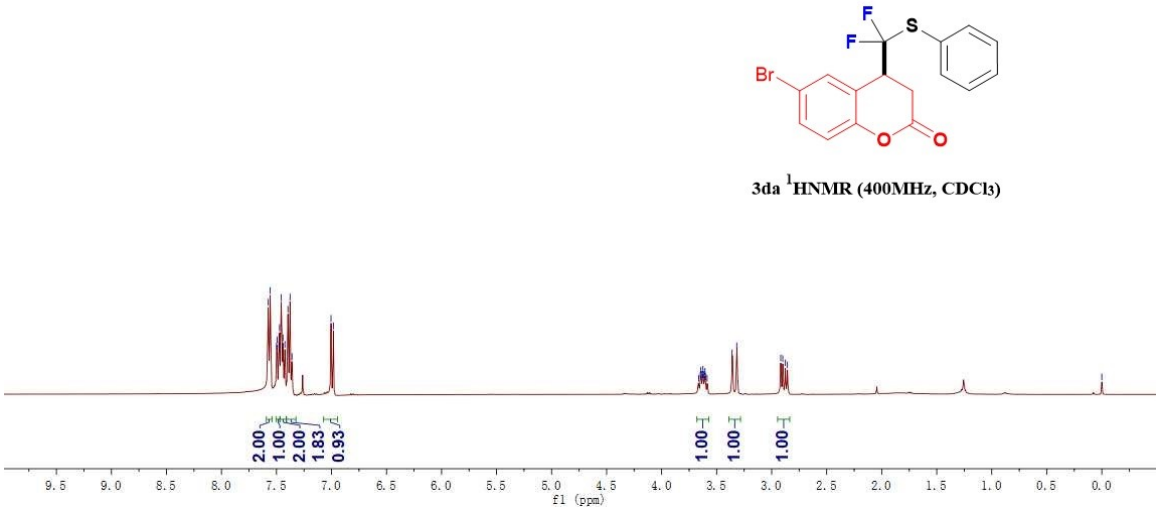




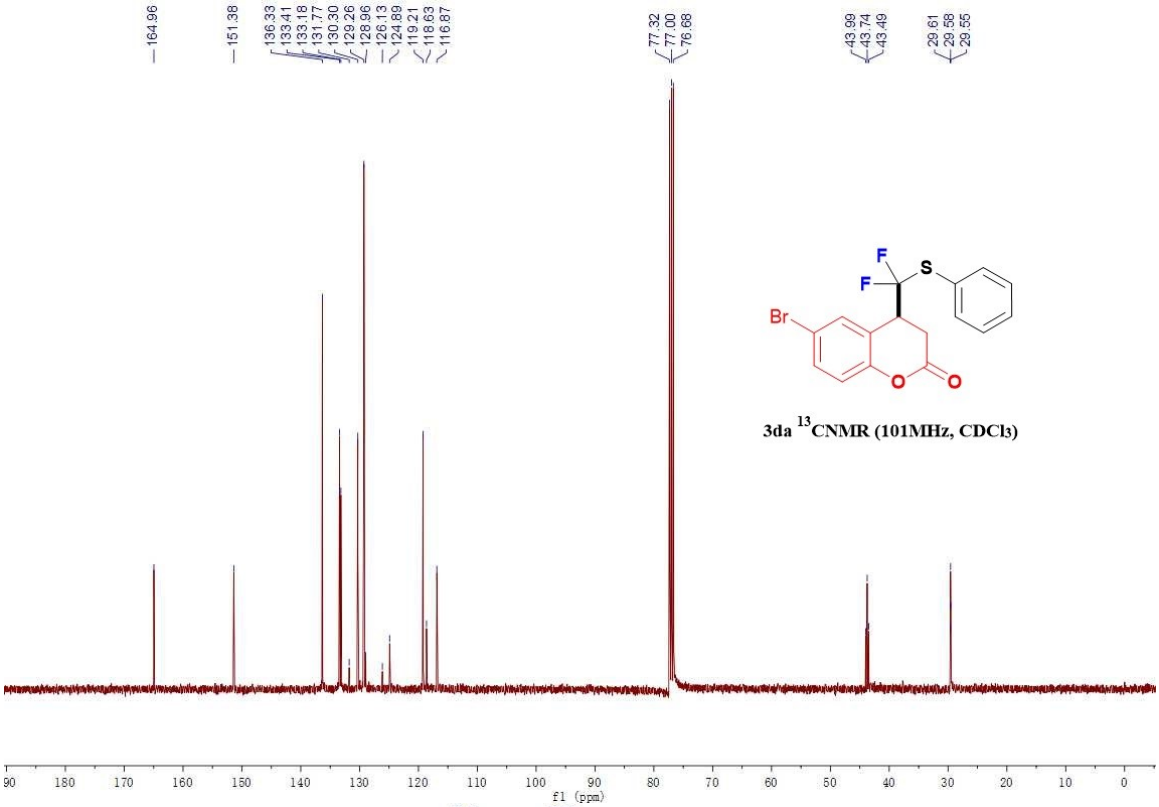
3ca ^{13}CNMR (101MHz, CDCl3)



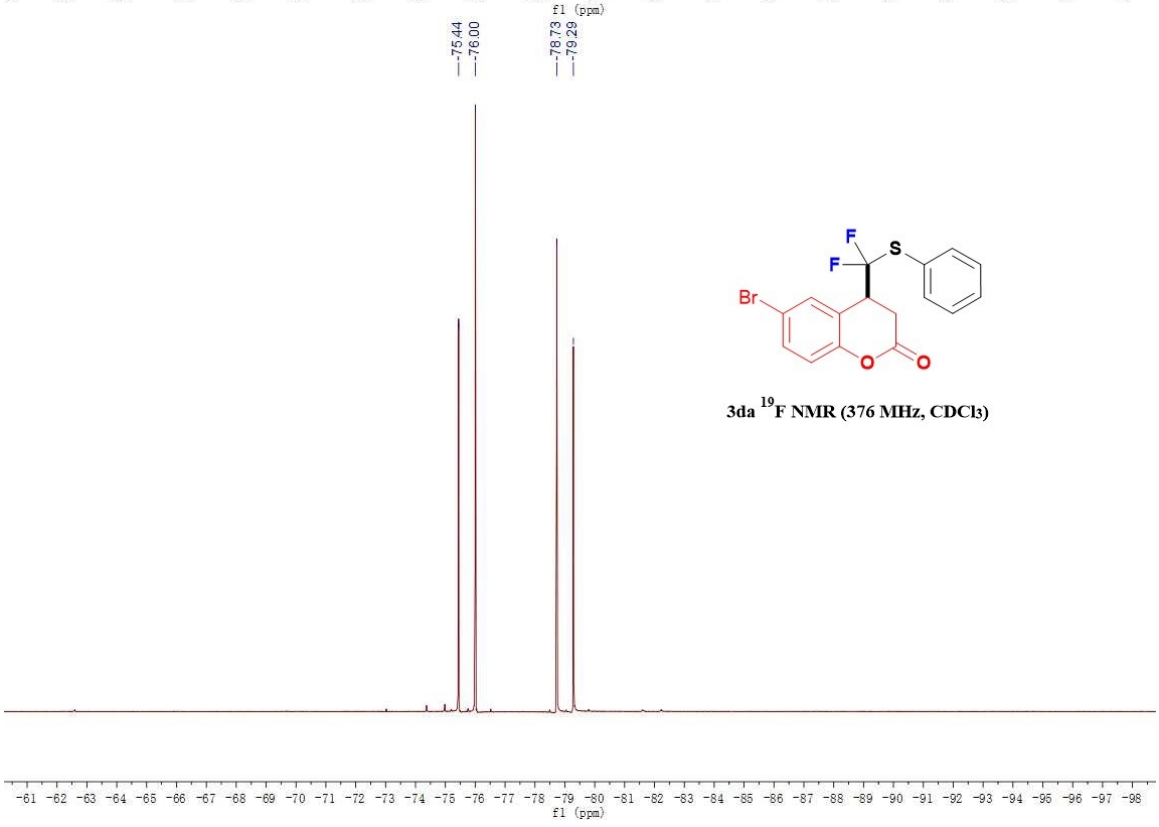
3ca ^{19}F NMR (376 MHz, CDCl3)



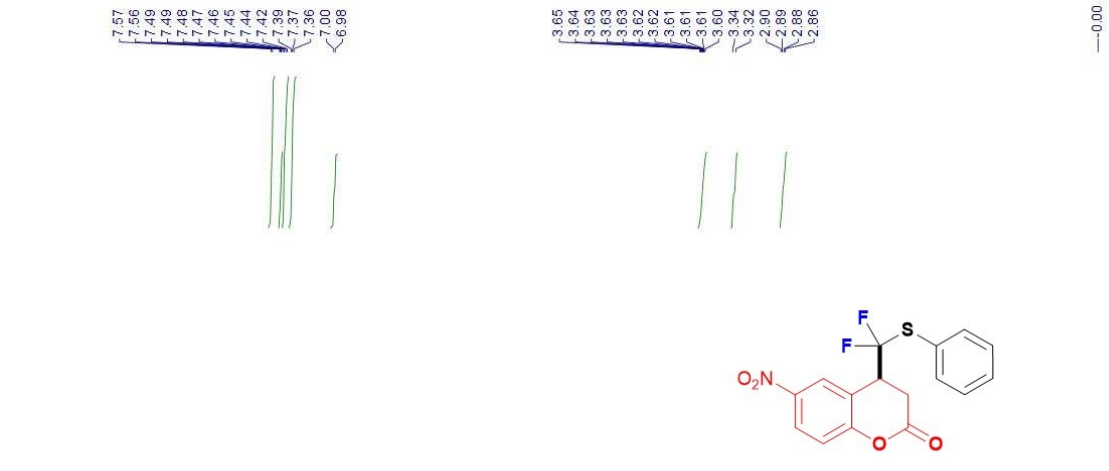
3da ^{1}HNMR (400MHz, CDCl3)



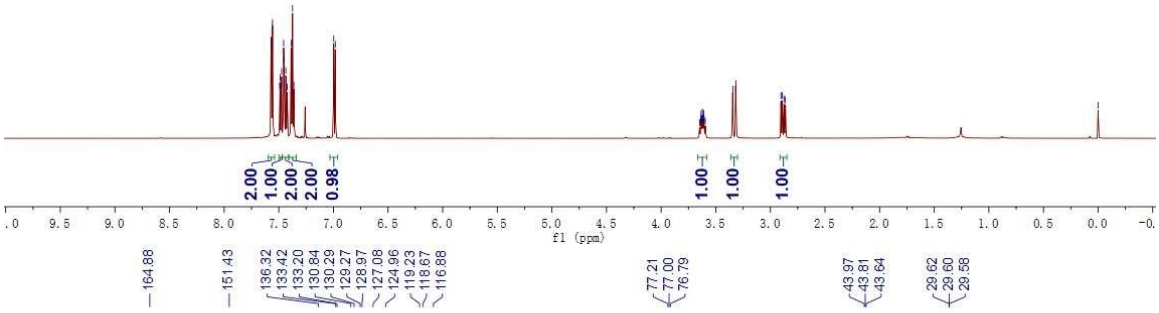
3da ^{13}CNMR (101MHz, CDCl3)

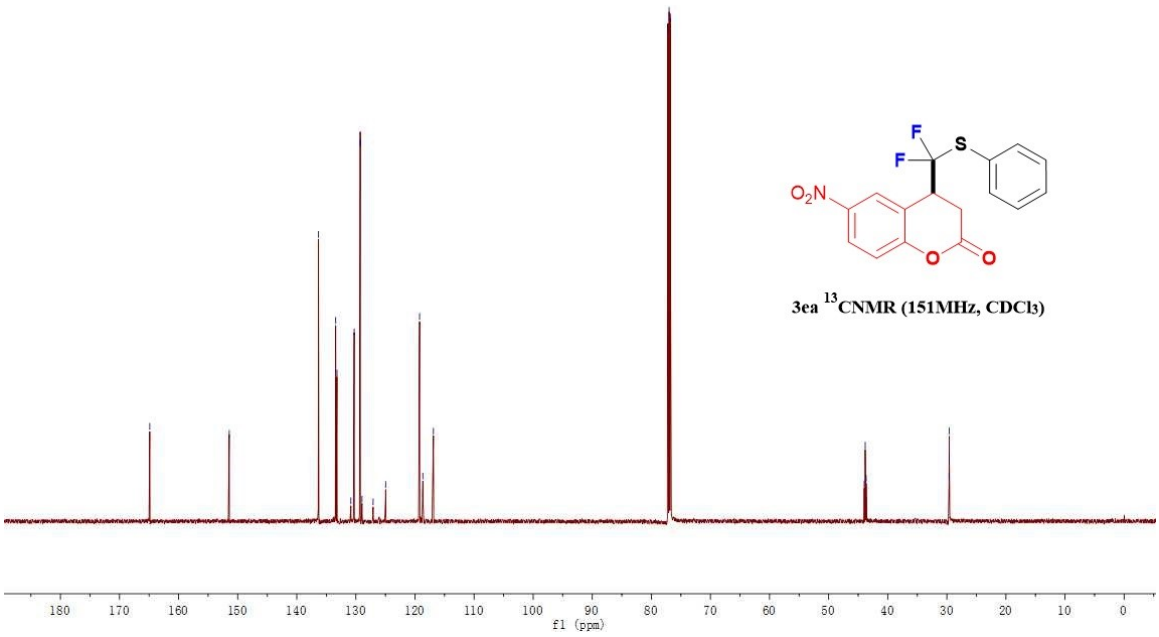


3da ^{19}F NMR (376 MHz, CDCl3)

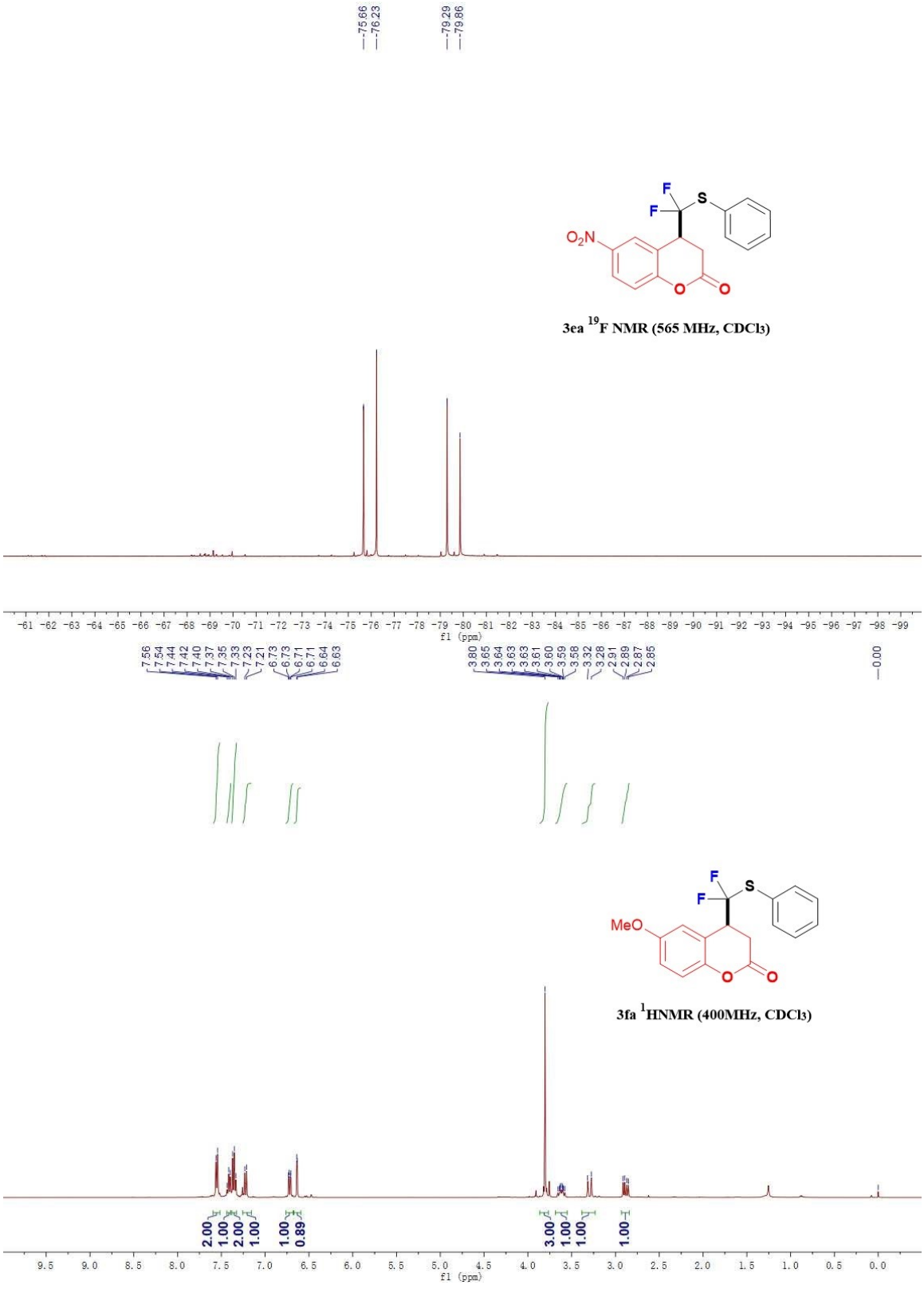


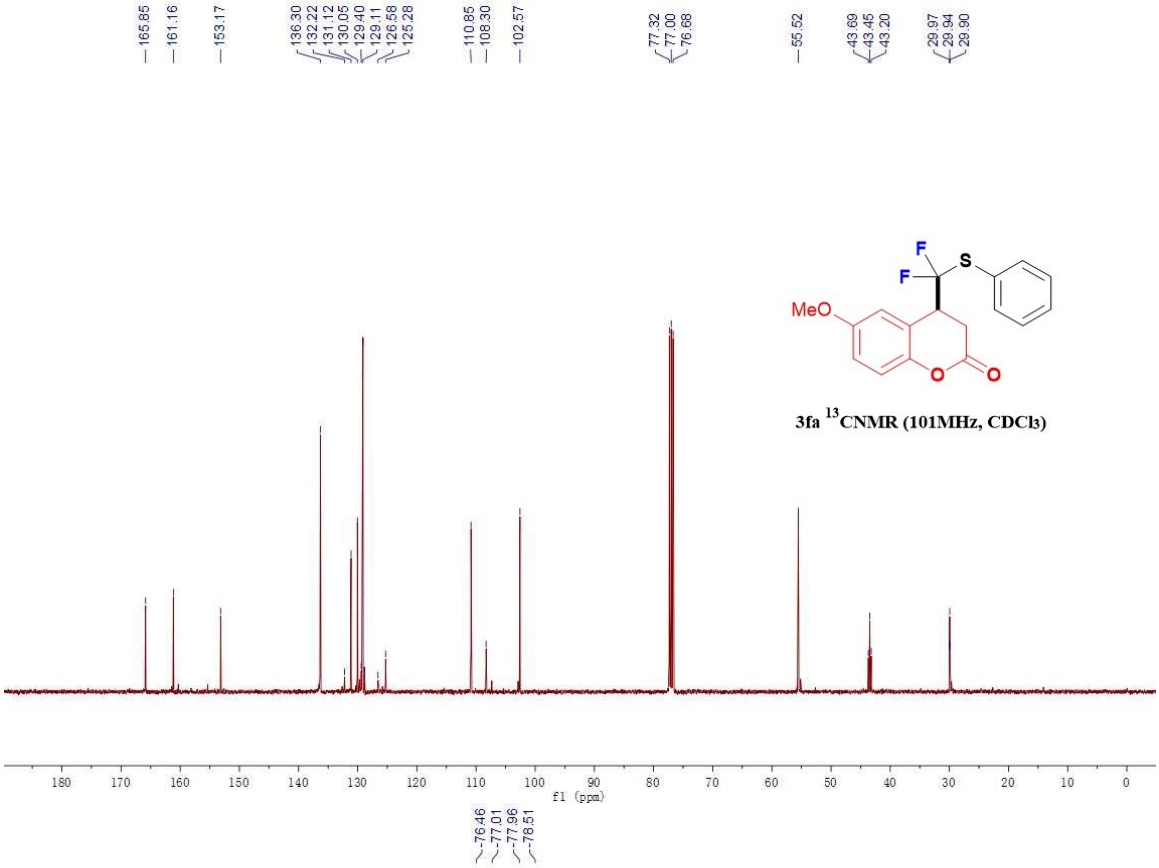
3ea ^{1}HNMR (600MHz, CDCl3)



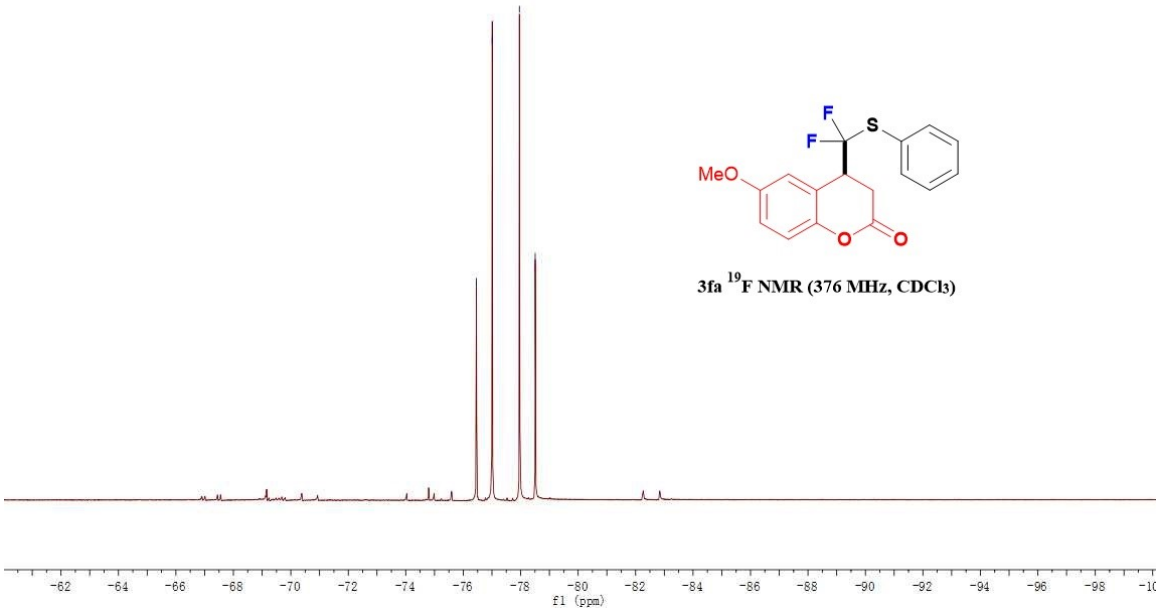


3ea ^{13}CNMR (151MHz, CDCl3)

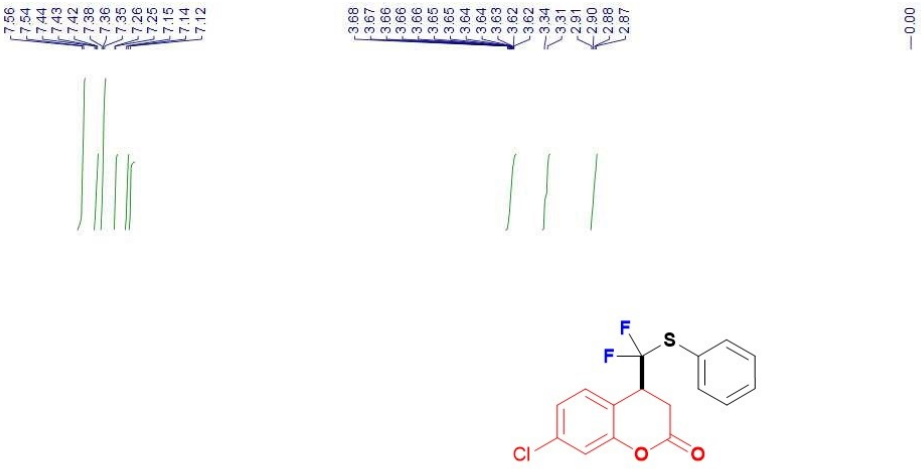

-75.66
-76.23
-79.29
-79.86
F
F
S
O2N
O
O
3ea 19F NMR (565 MHz, CDCl3)
f1 (ppm)
7.56
7.54
7.44
7.42
7.40
7.37
7.35
7.33
7.23
7.21
6.73
6.73
6.71
6.71
6.64
6.63
3.80
3.65
3.64
3.63
3.63
3.61
3.60
3.59
3.58
3.32
3.28
2.91
2.89
2.87
2.85
0.00
F
F
S
MeO
O
O
3fa 1HNMR (400MHz, CDCl3)
2.00
1.00
2.00
1.00
1.00
0.89
3.00
1.00
1.00
1.00
f1 (ppm)



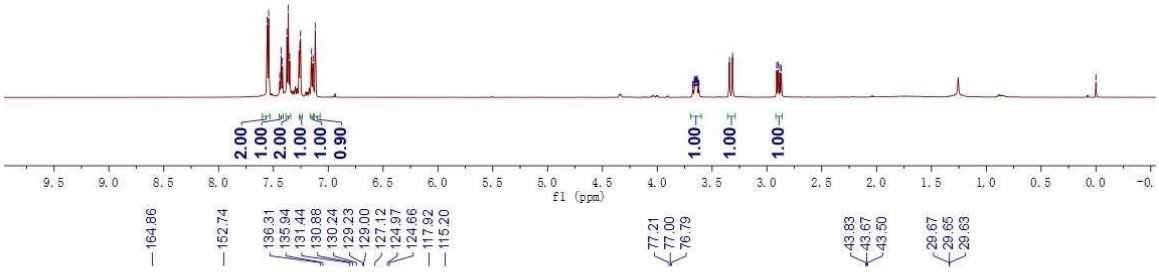
3fa ^{13}CNMR (101MHz, CDCl3)

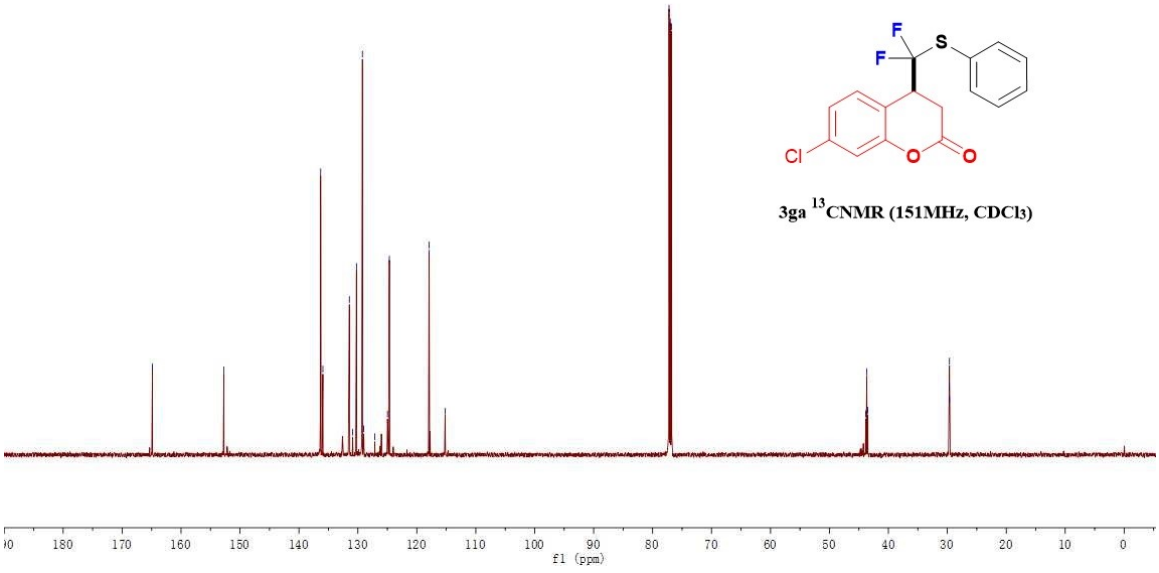


3fa ^{19}F NMR (376 MHz, CDCl3)

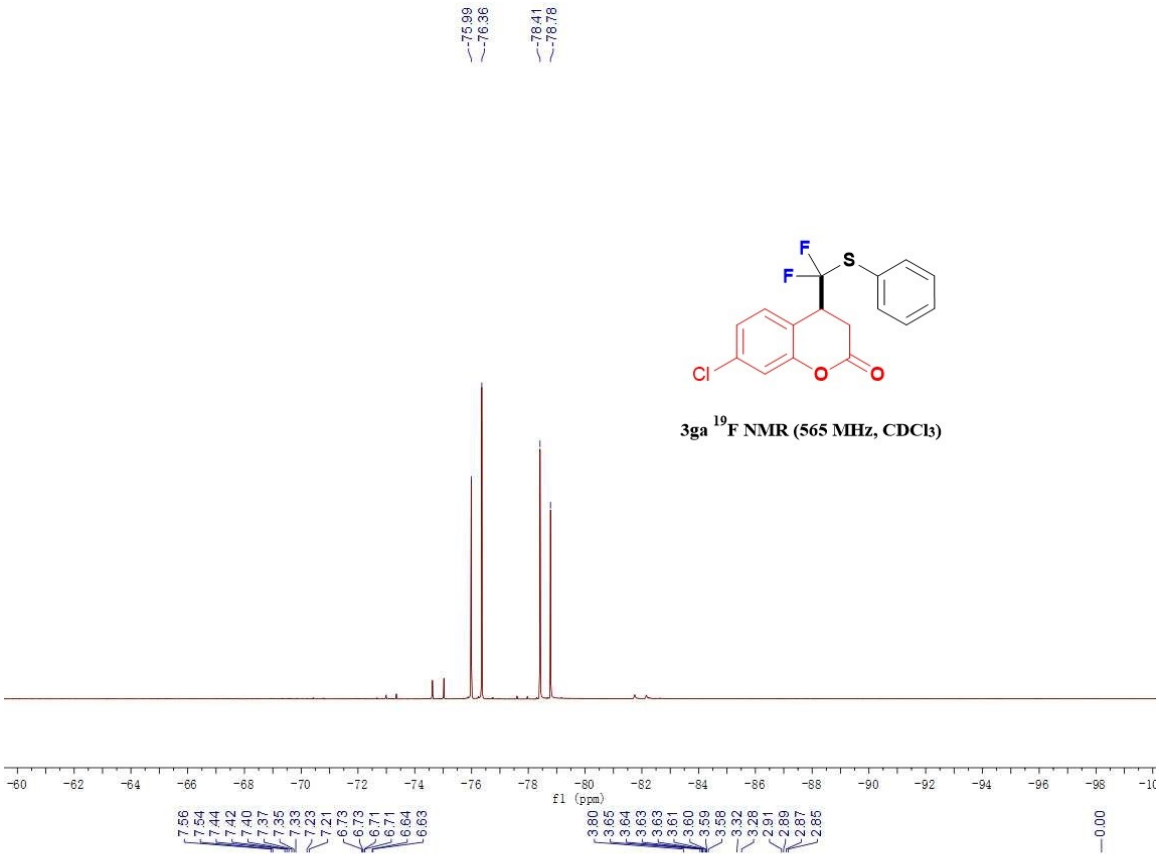


3ga ^{1}HNMR (600MHz, CDCl$_3$)

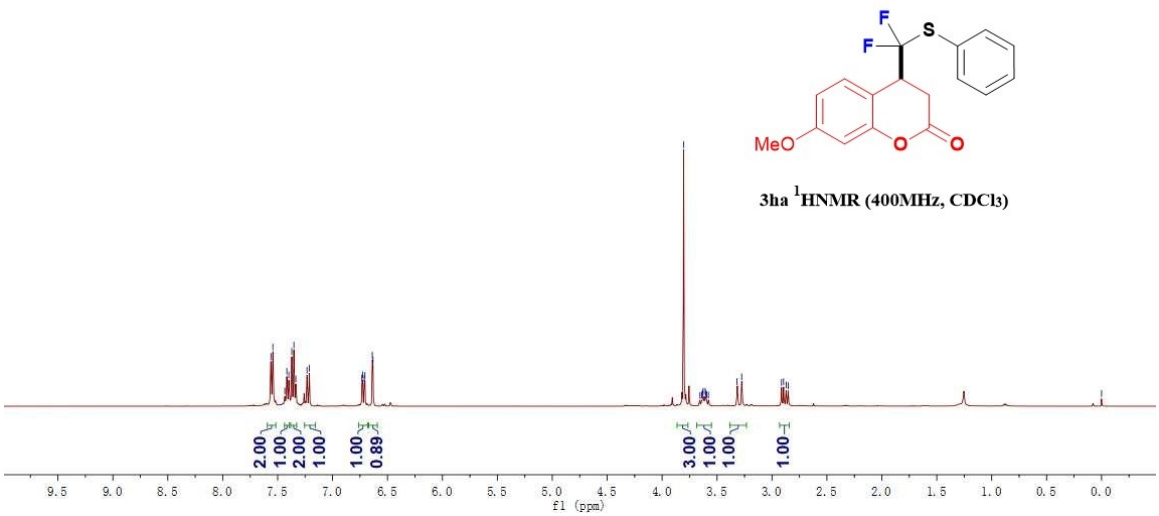




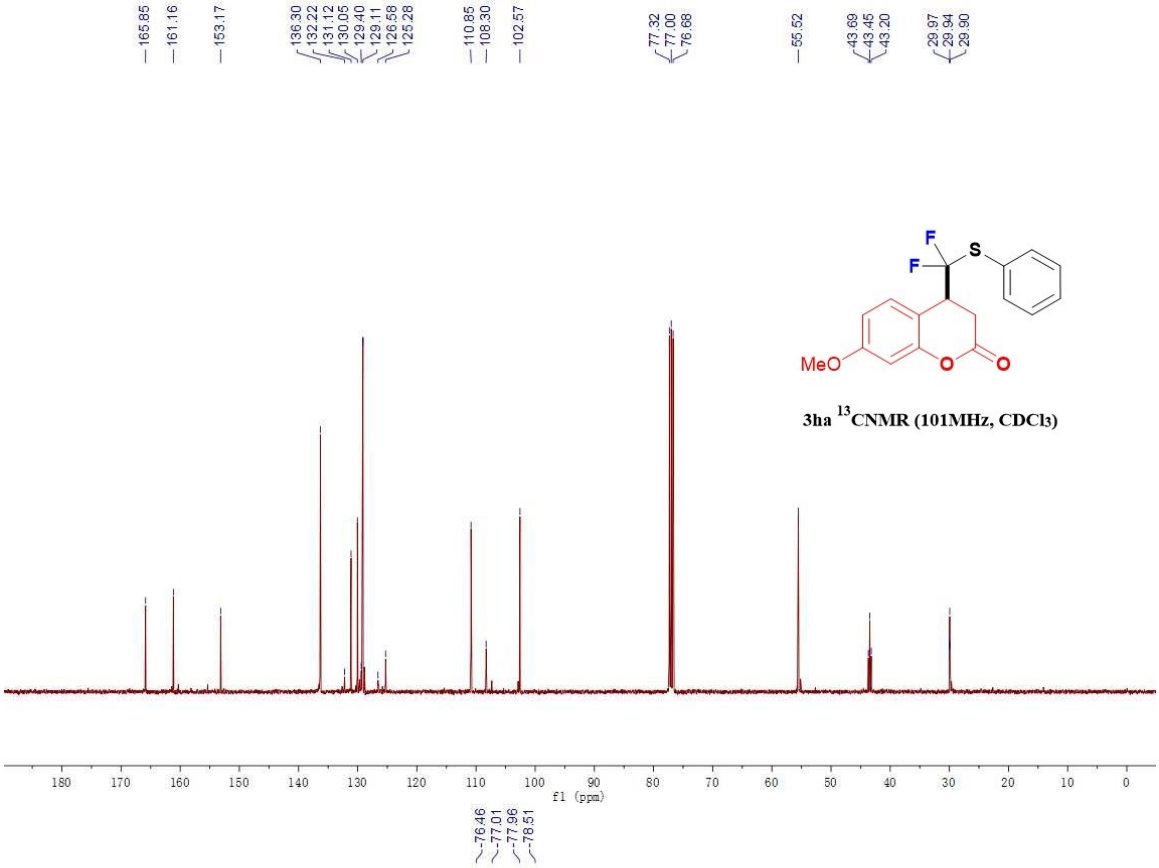
3ga ^{13}CNMR (151MHz, CDCl$_3$)



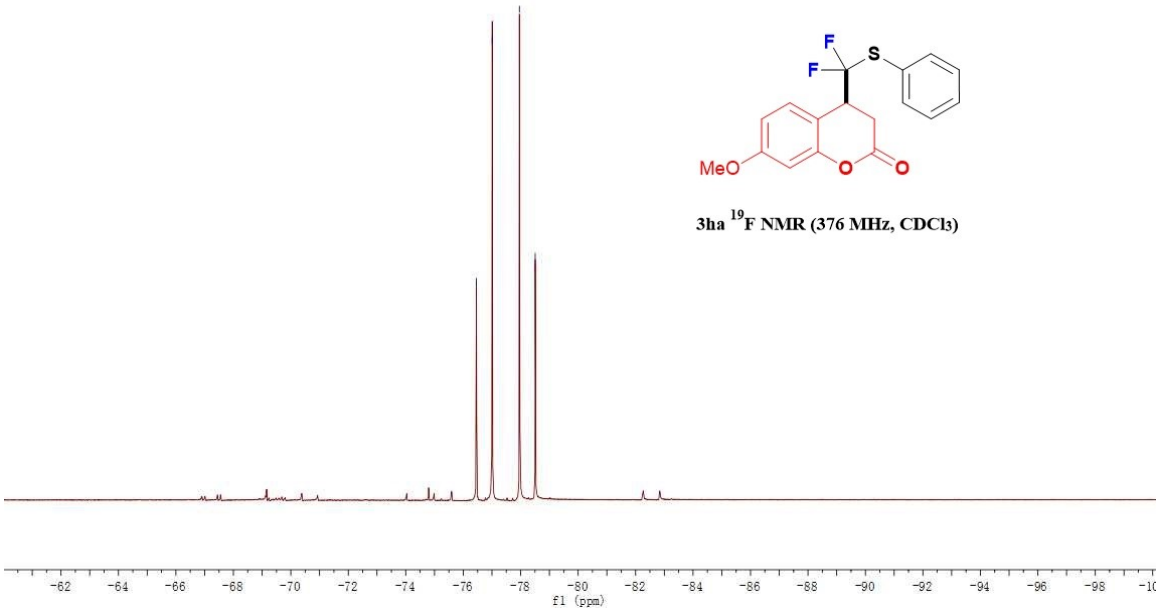
3ga ^{19}F NMR (565 MHz, CDCl3)



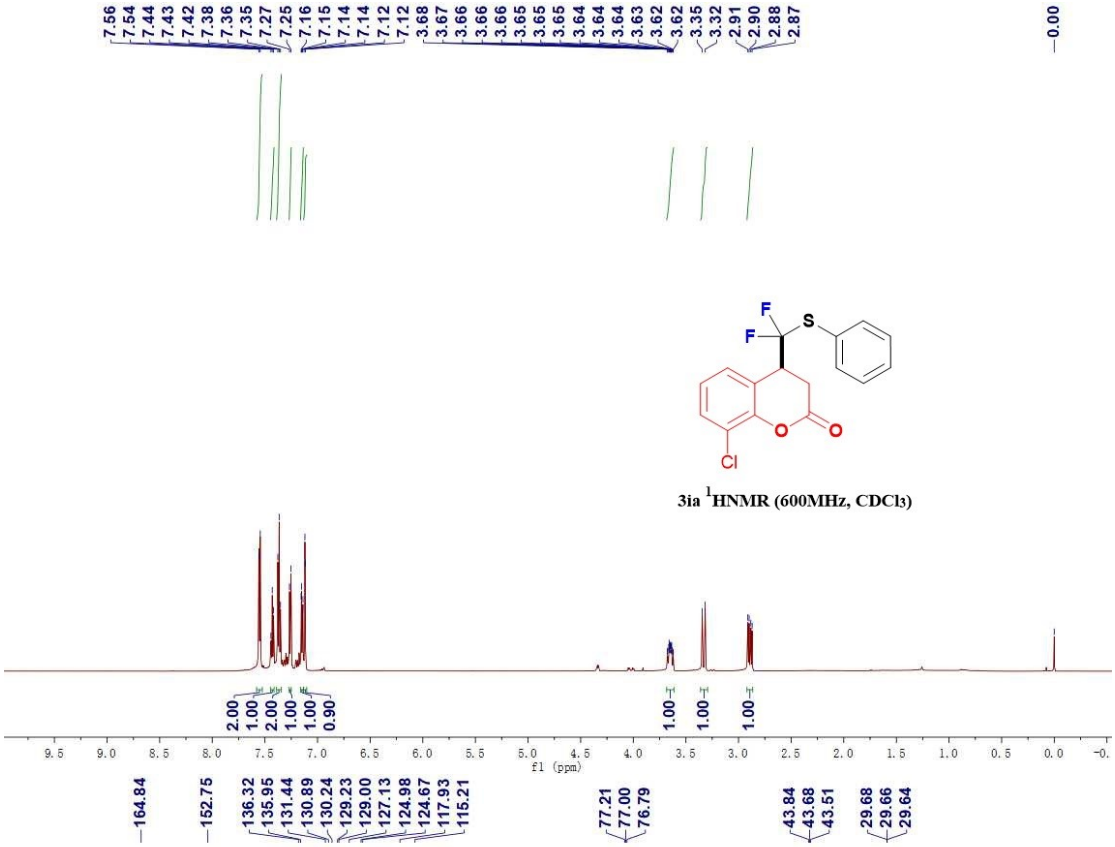
3ha ^{1}HNMR (400MHz, CDCl3)



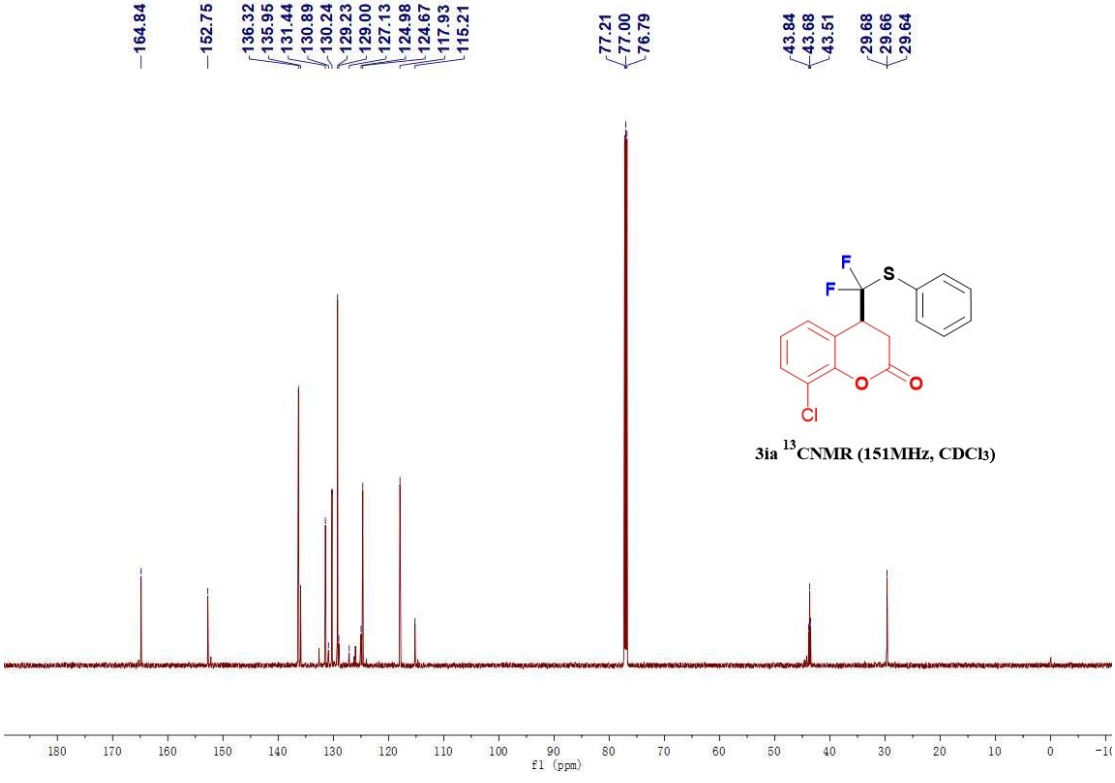
3ha ^{13}CNMR (101MHz, CDCl3)



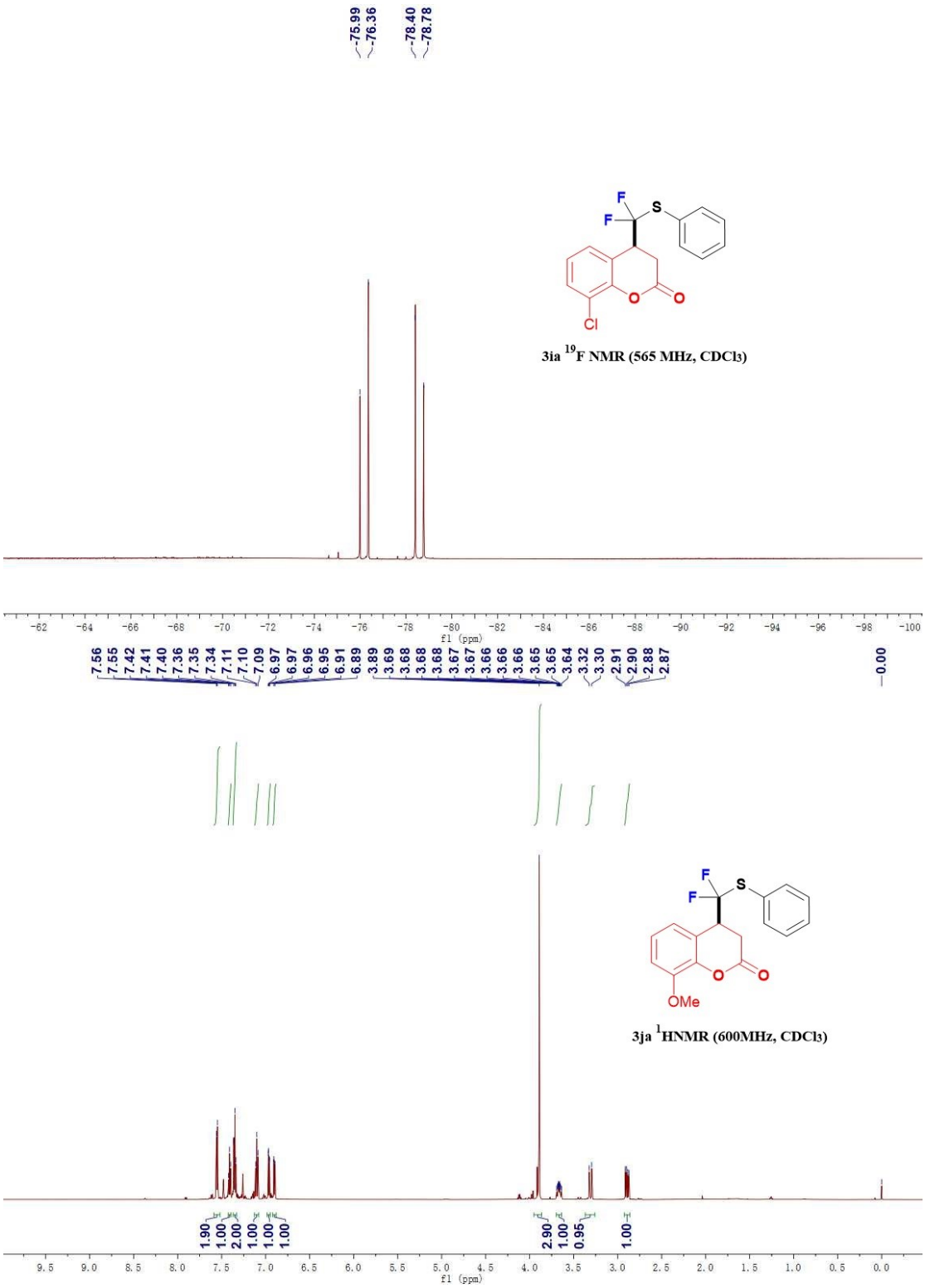
3ha ^{19}F NMR (376 MHz, CDCl3)



3ia ^{1}HNMR (600MHz, CDCl3)

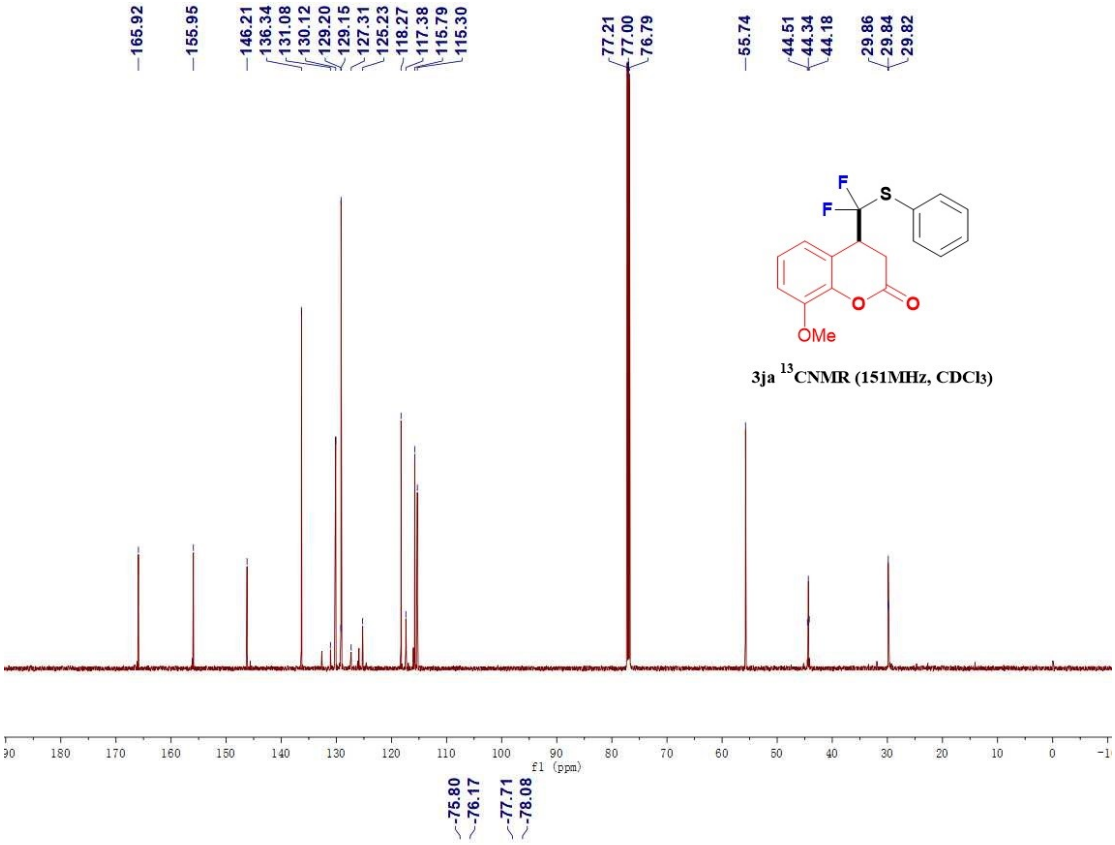


3ia ^{13}CNMR (151MHz, CDCl3)

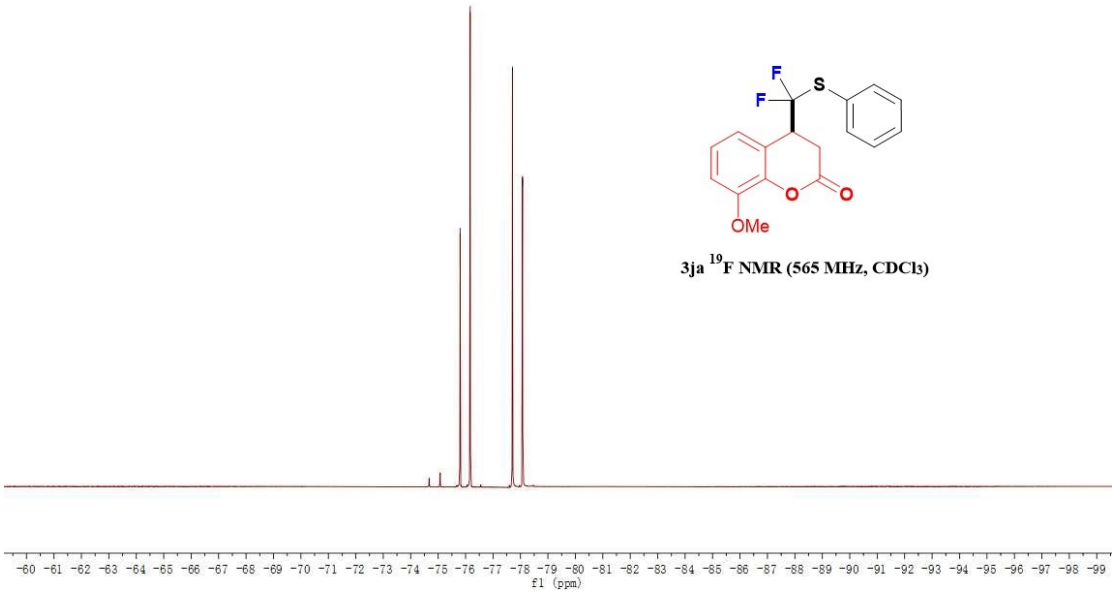


3ia ^{19}F NMR (565 MHz, CDCl3)

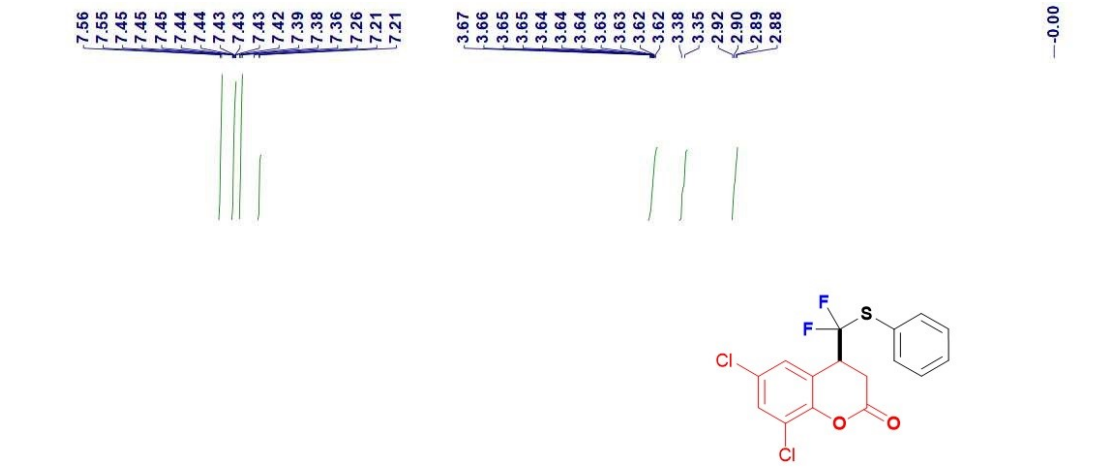
3ja ^{1}HNMR (600MHz, CDCl3)



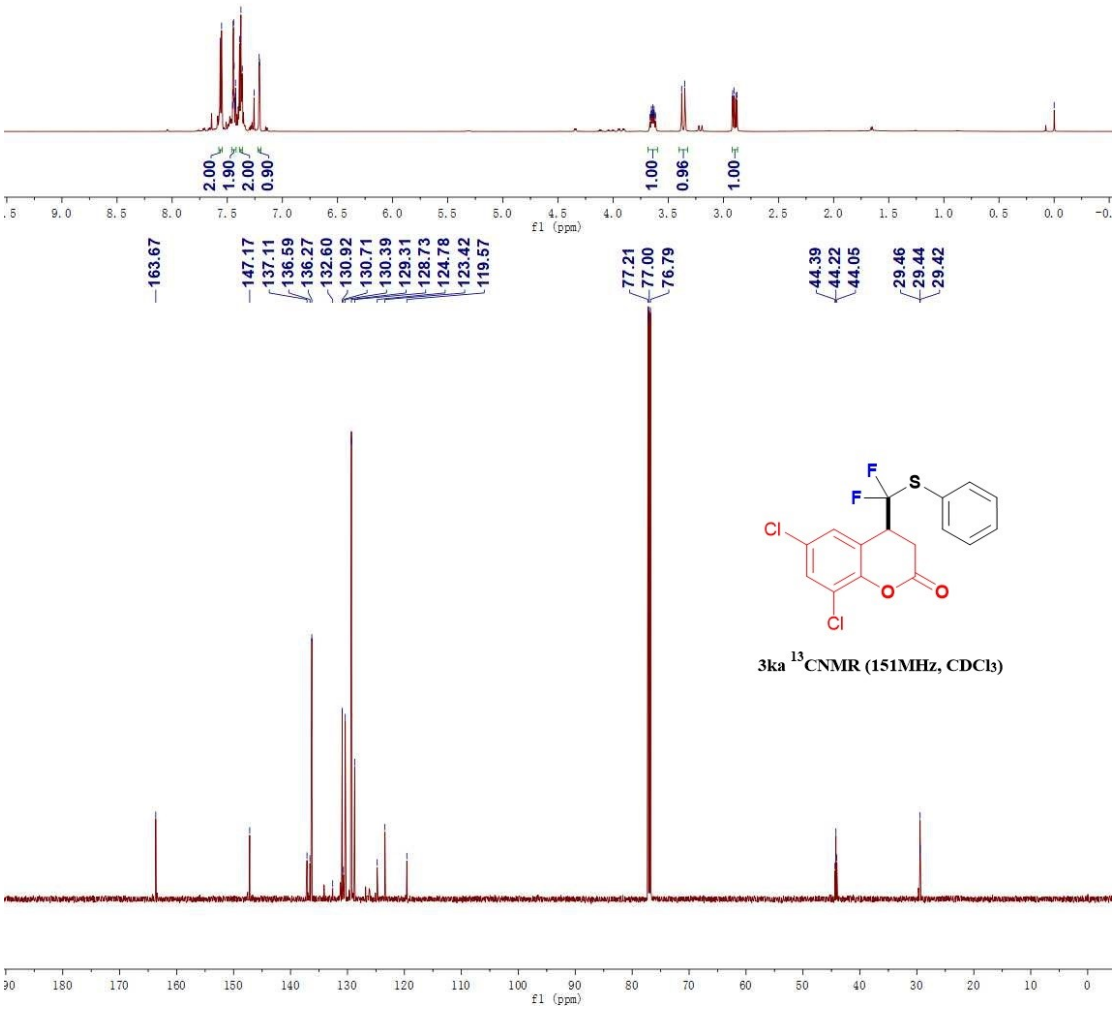
3ja ^{13}CNMR (151MHz, CDCl3)



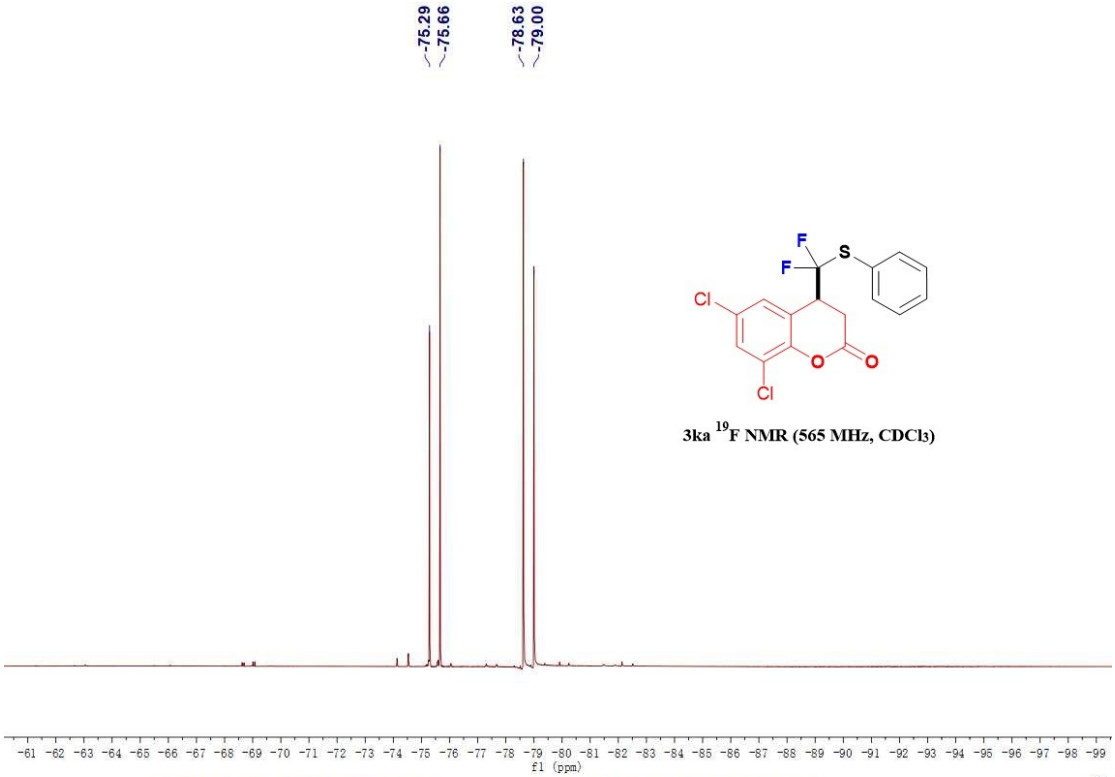
3ja ^{19}F NMR (565 MHz, CDCl3)



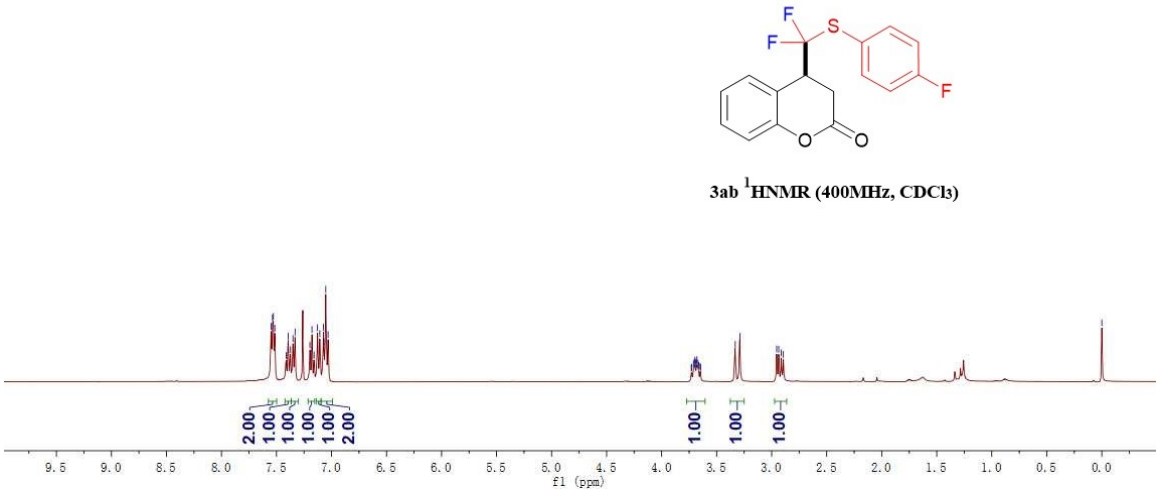
3ka ^{1}HNMR (600MHz, CDCl3)



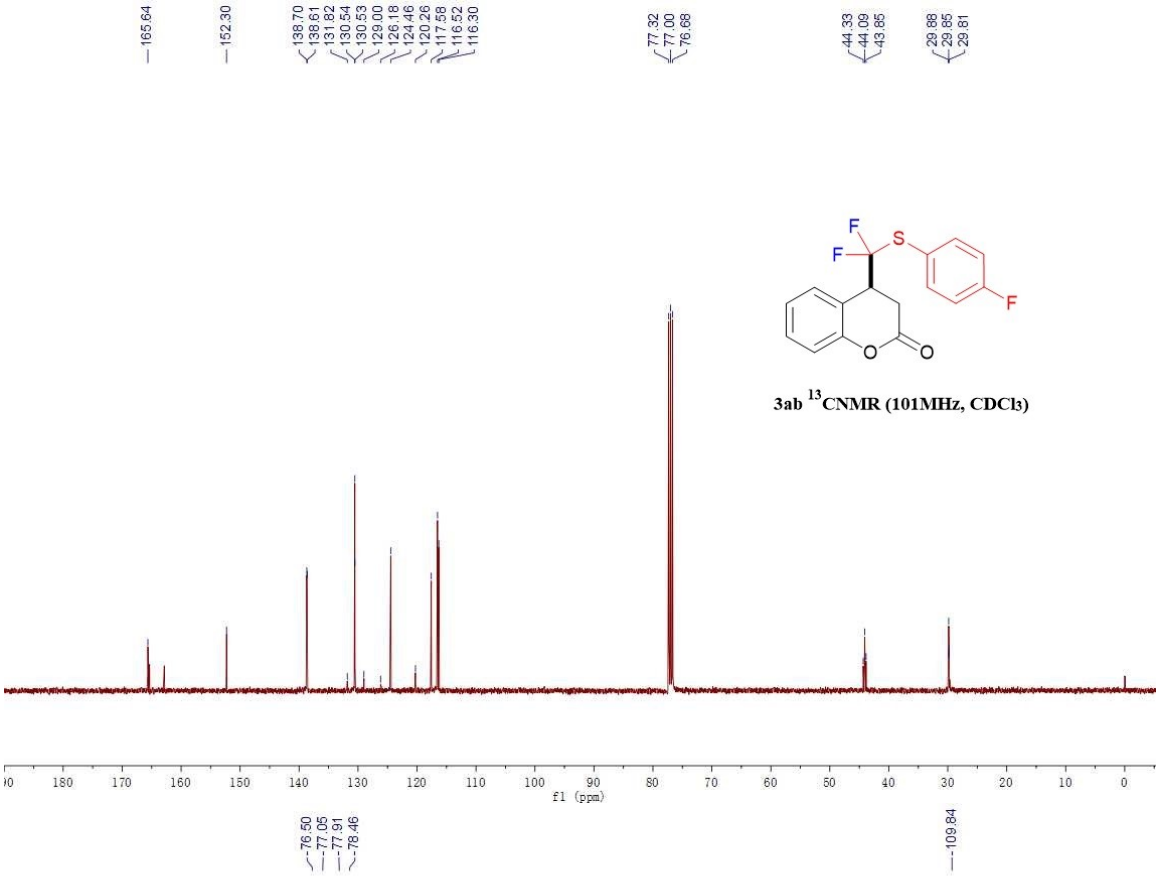
3ka ^{13}CNMR (151MHz, CDCl3)



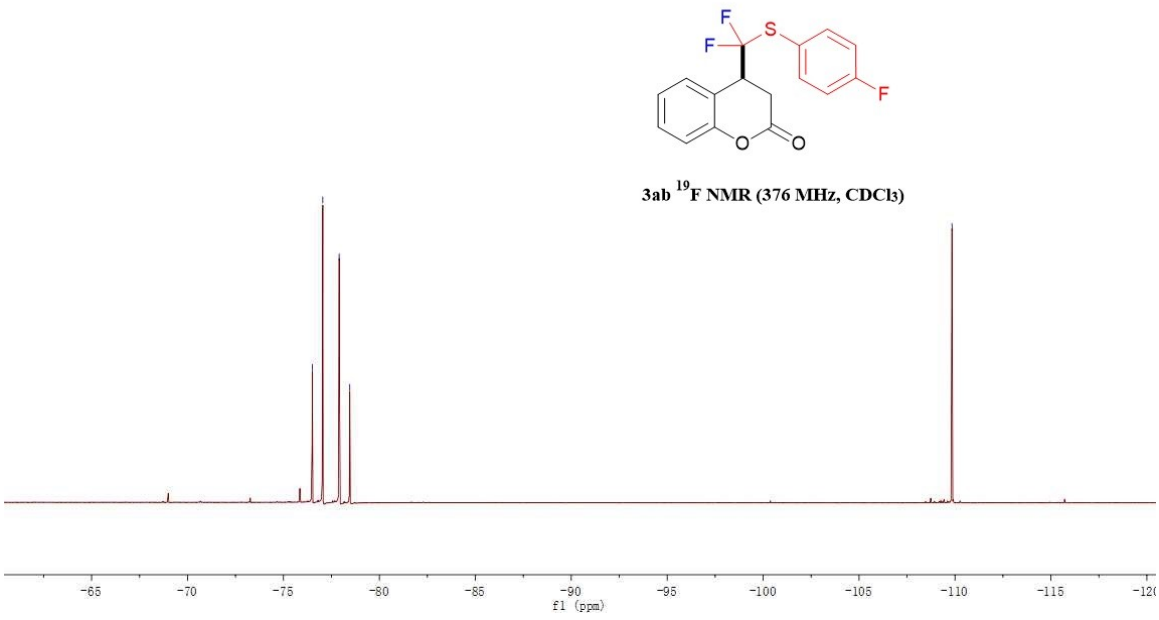
3ka ^{19}F NMR (565 MHz, CDCl3)



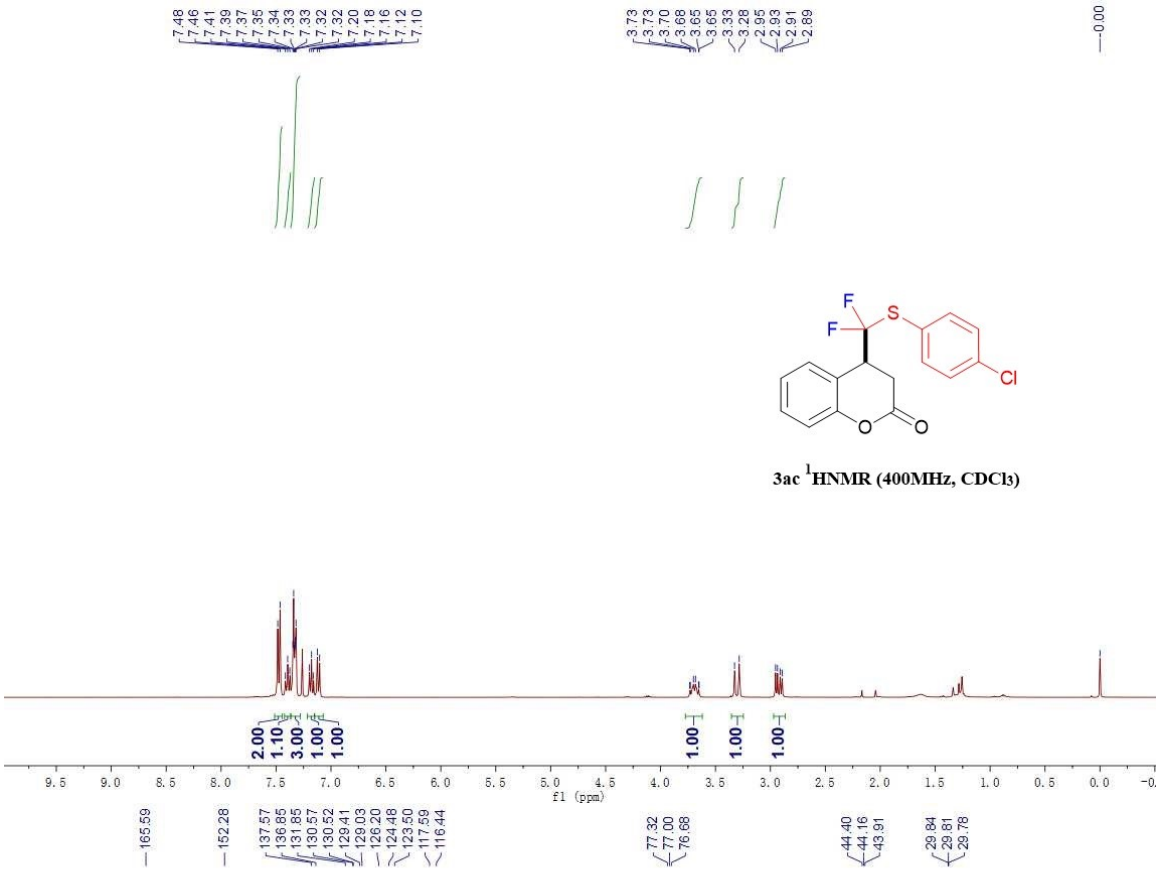
3ab ^{1}HNMR (400MHz, CDCl3)



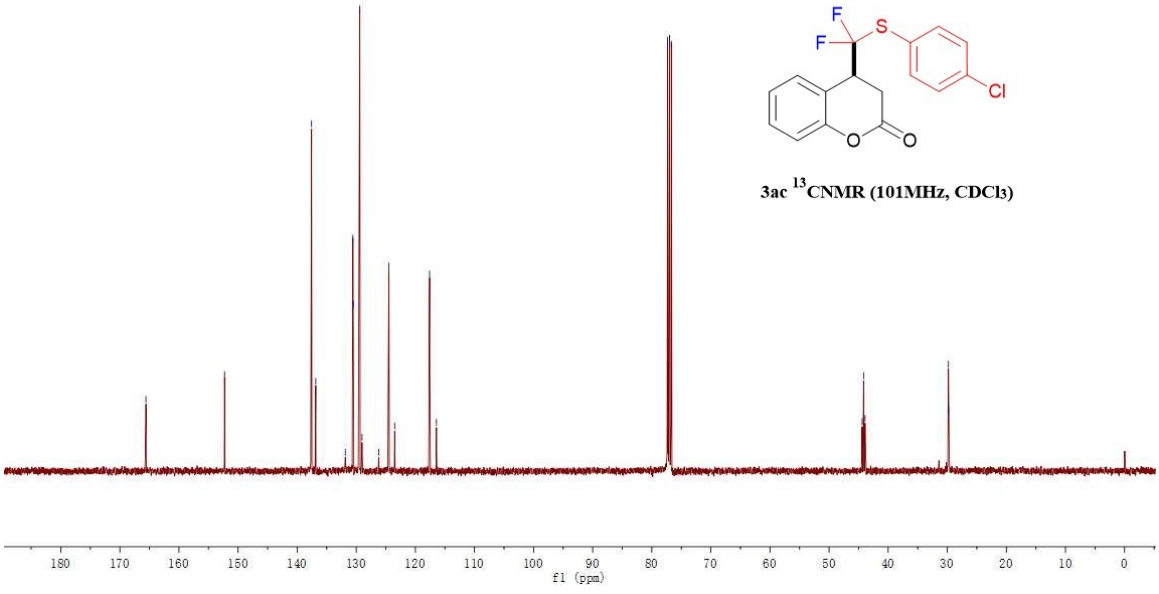
3ab ^{13}CNMR (101MHz, CDCl$_3$)



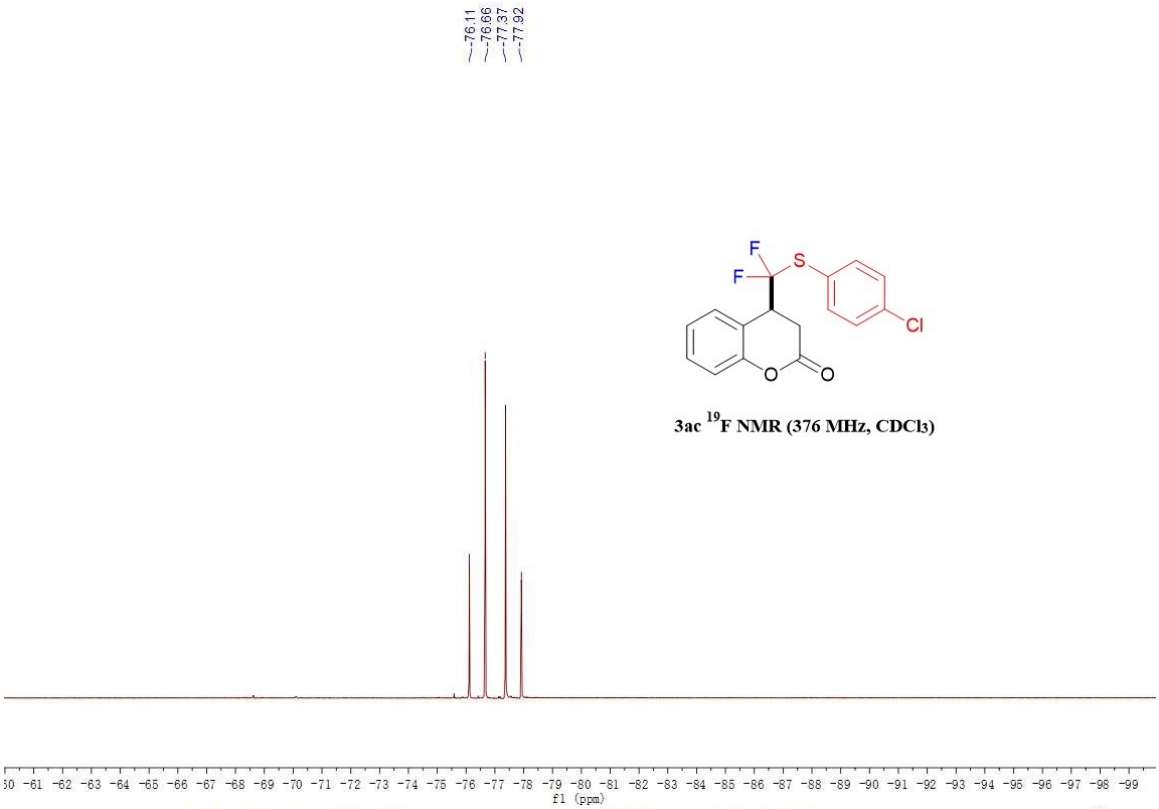
3ab ^{19}F NMR (376 MHz, CDCl$_3$)



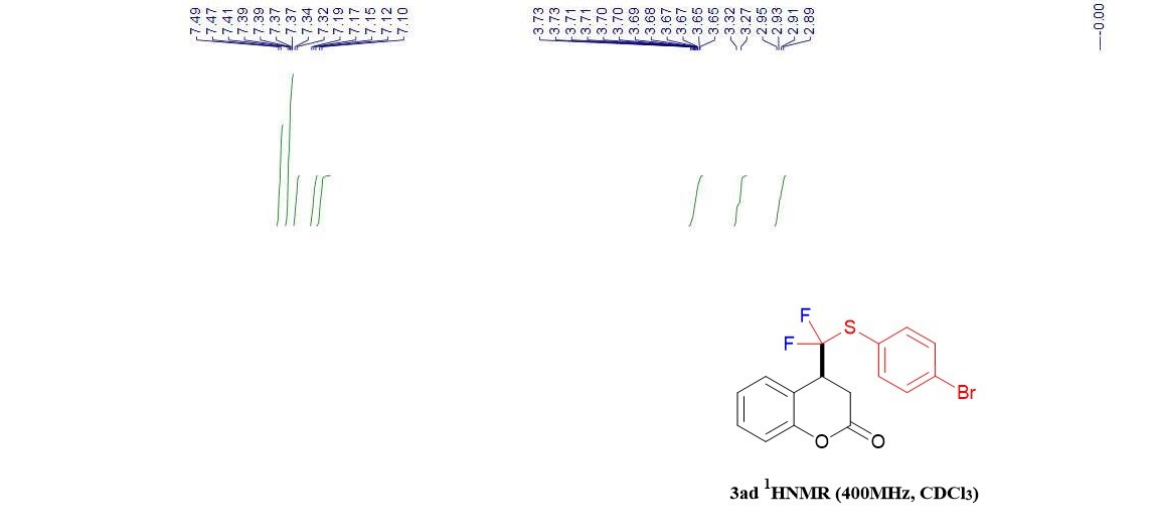
3ac ^{1}HNMR (400MHz, CDCl3)



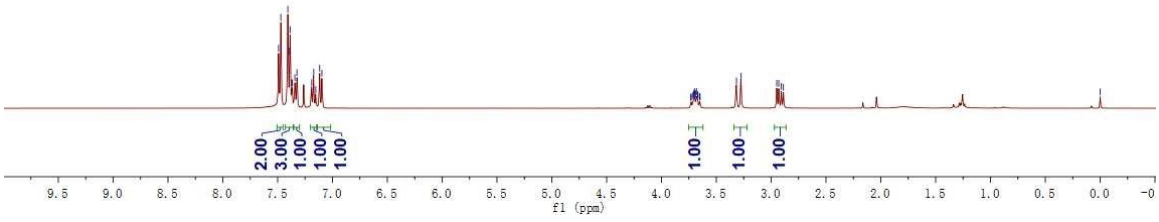
3ac ^{13}CNMR (101MHz, CDCl3)

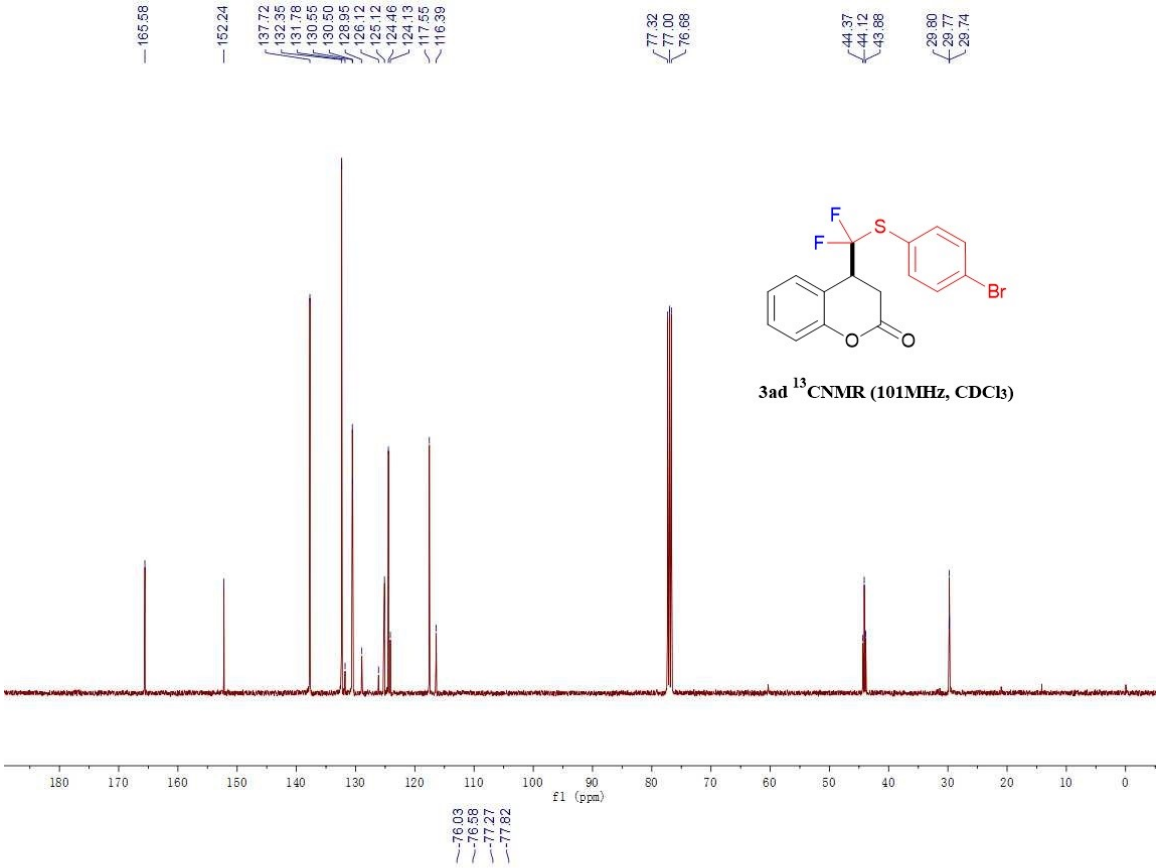


3ac ^{19}F NMR (376 MHz, CDCl3)

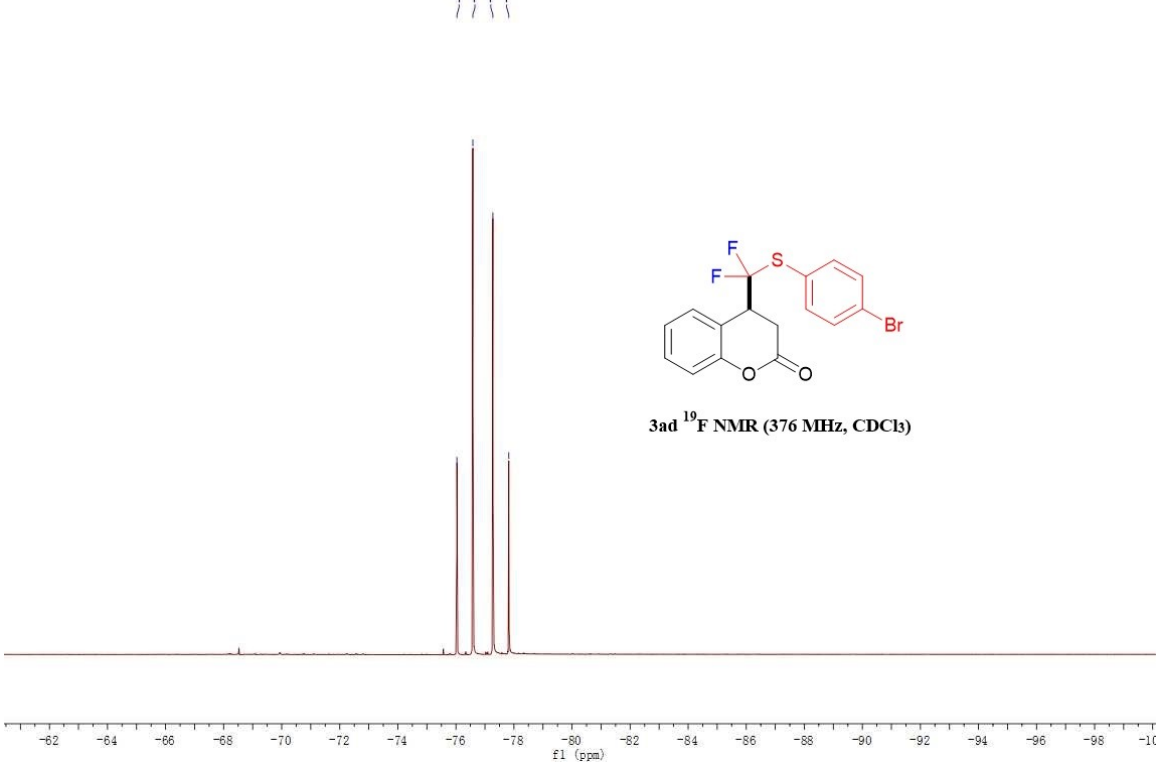


3ad ^{1}HNMR (400MHz, CDCl3)

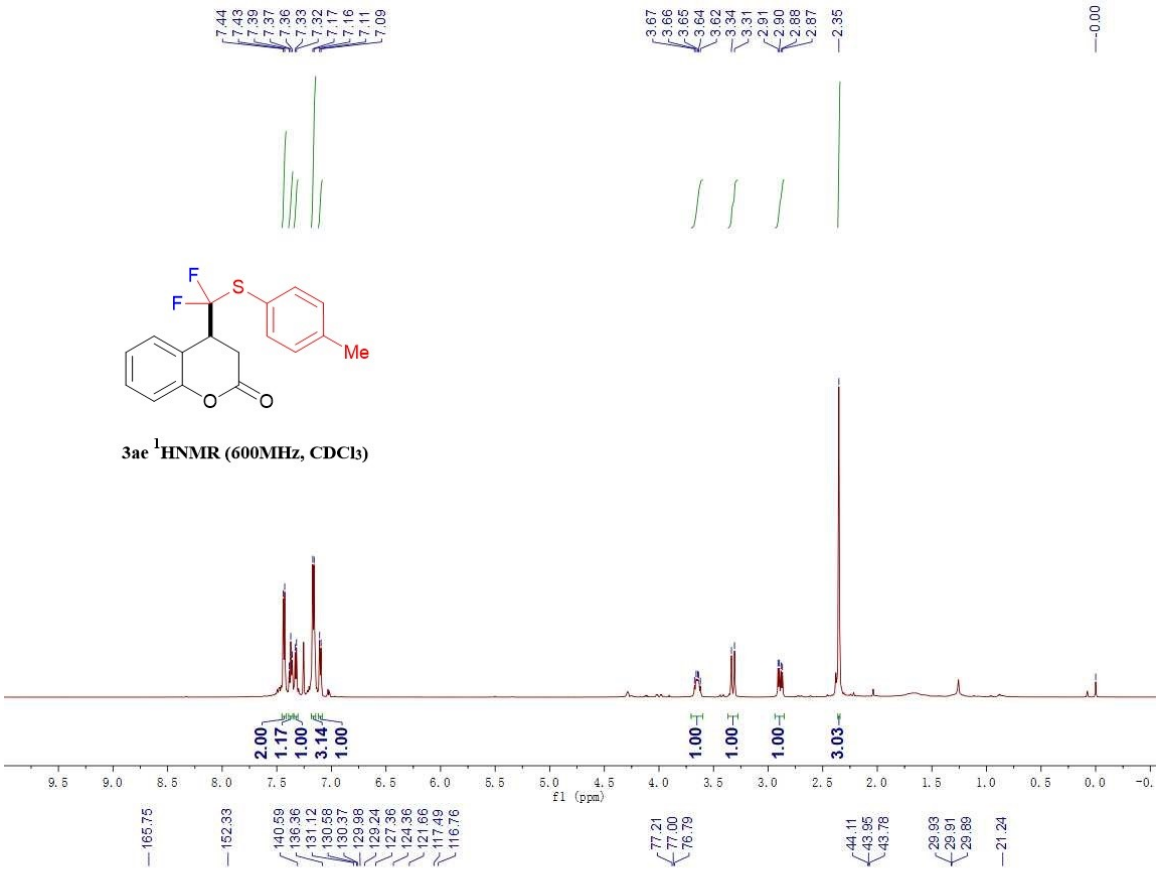




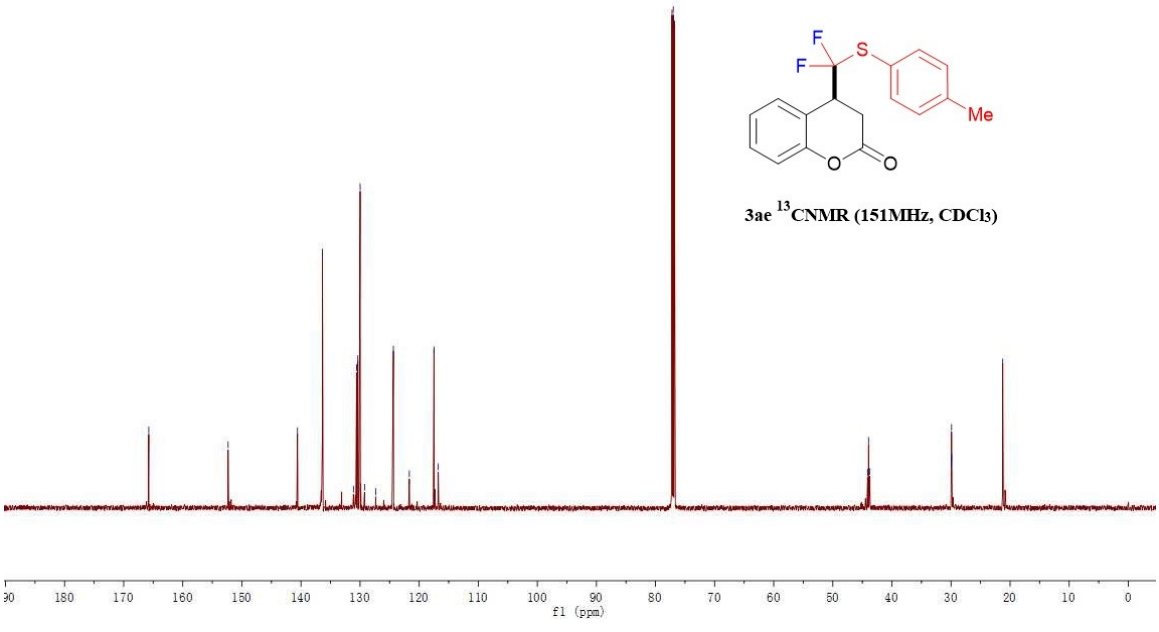
3ad ^{13}CNMR (101MHz, CDCl3)



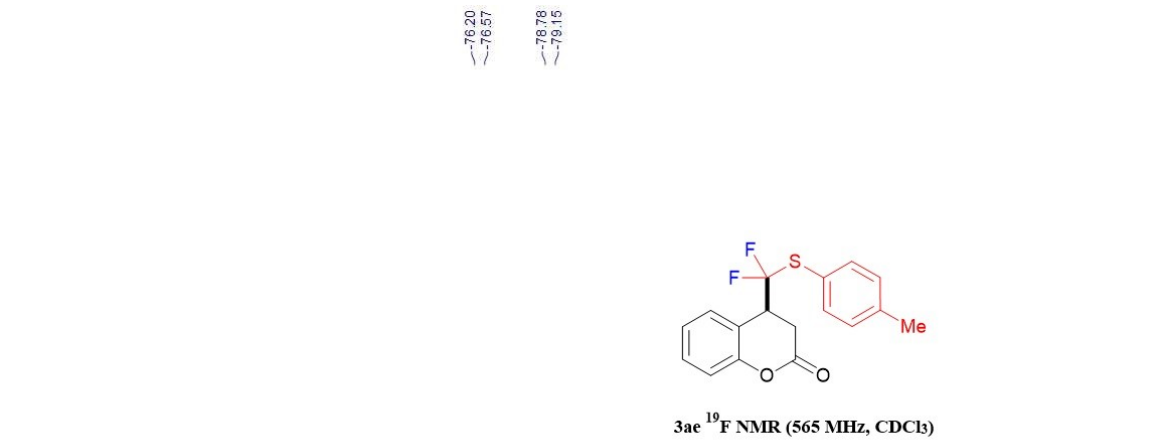
3ad ^{19}F NMR (376 MHz, CDCl3)



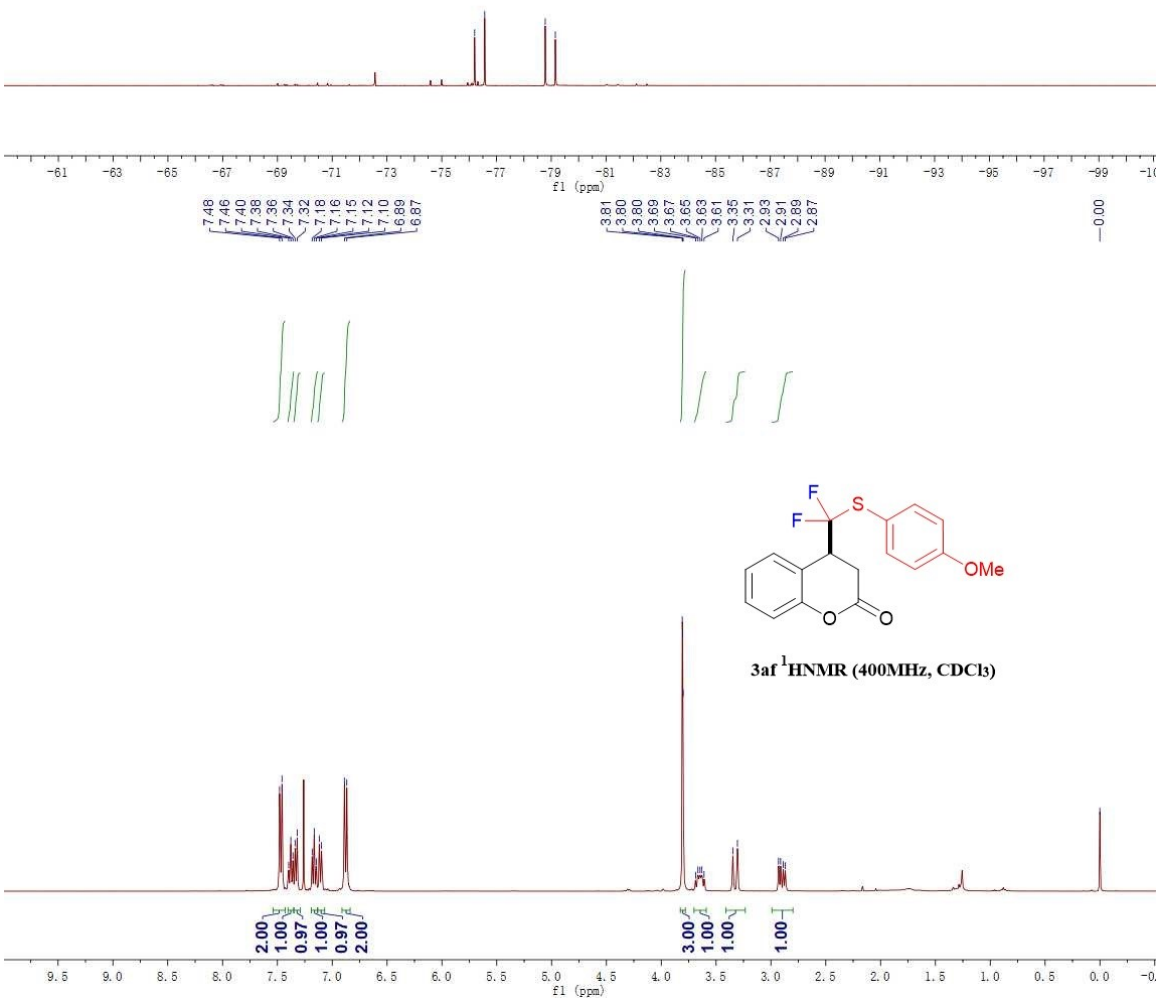
3ae ^{1}HNMR (600MHz, CDCl3)



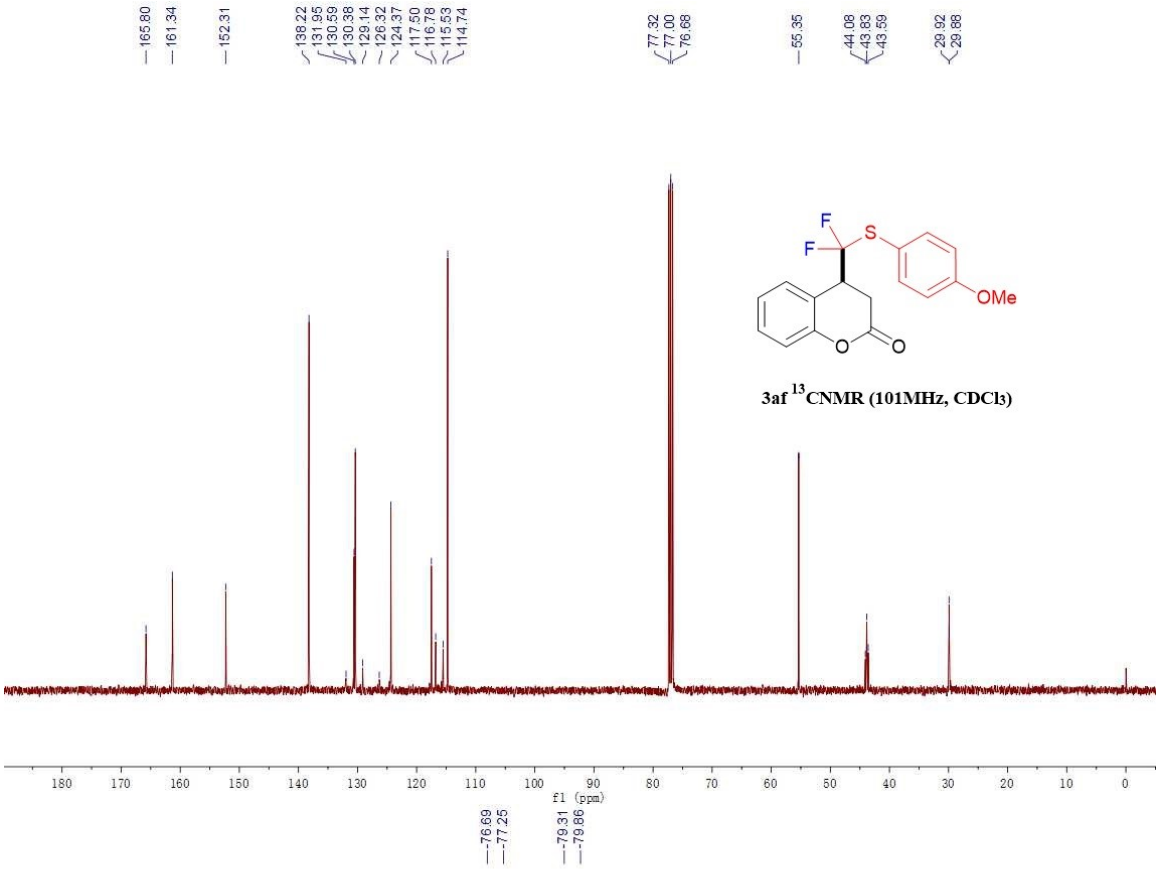
3ae ^{13}CNMR (151MHz, CDCl3)



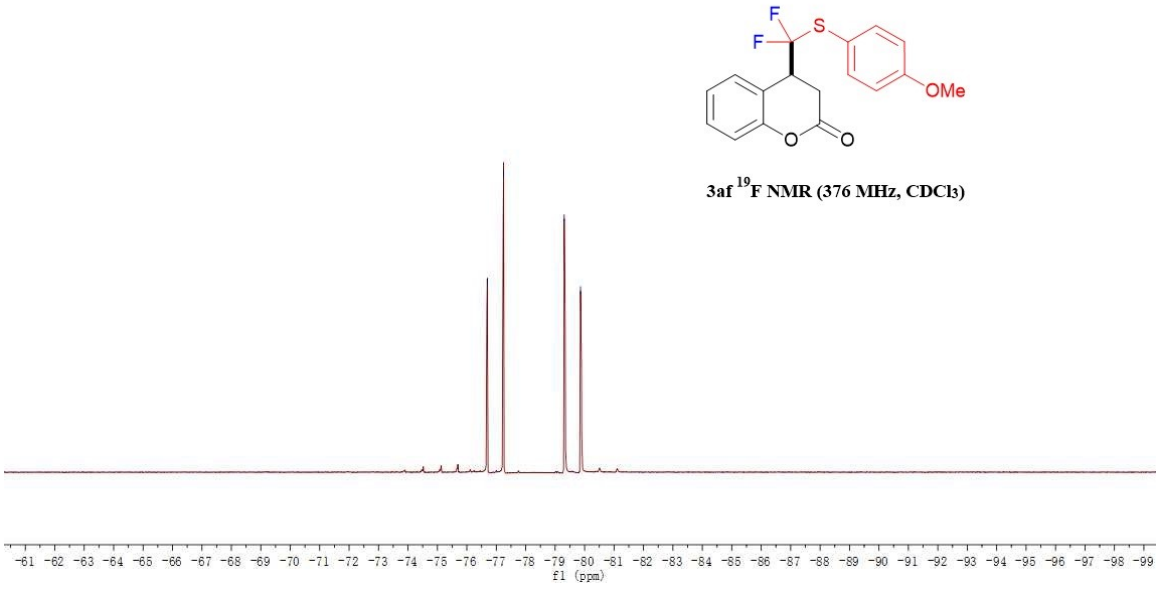
3ae ^{19}F NMR (565 MHz, CDCl3)



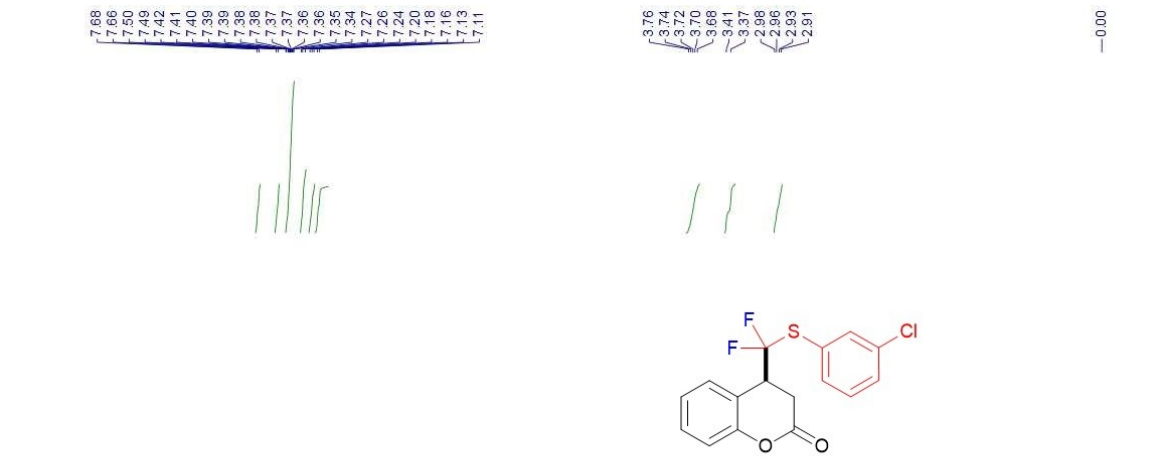
3af ^{1}HNMR (400MHz, CDCl3)



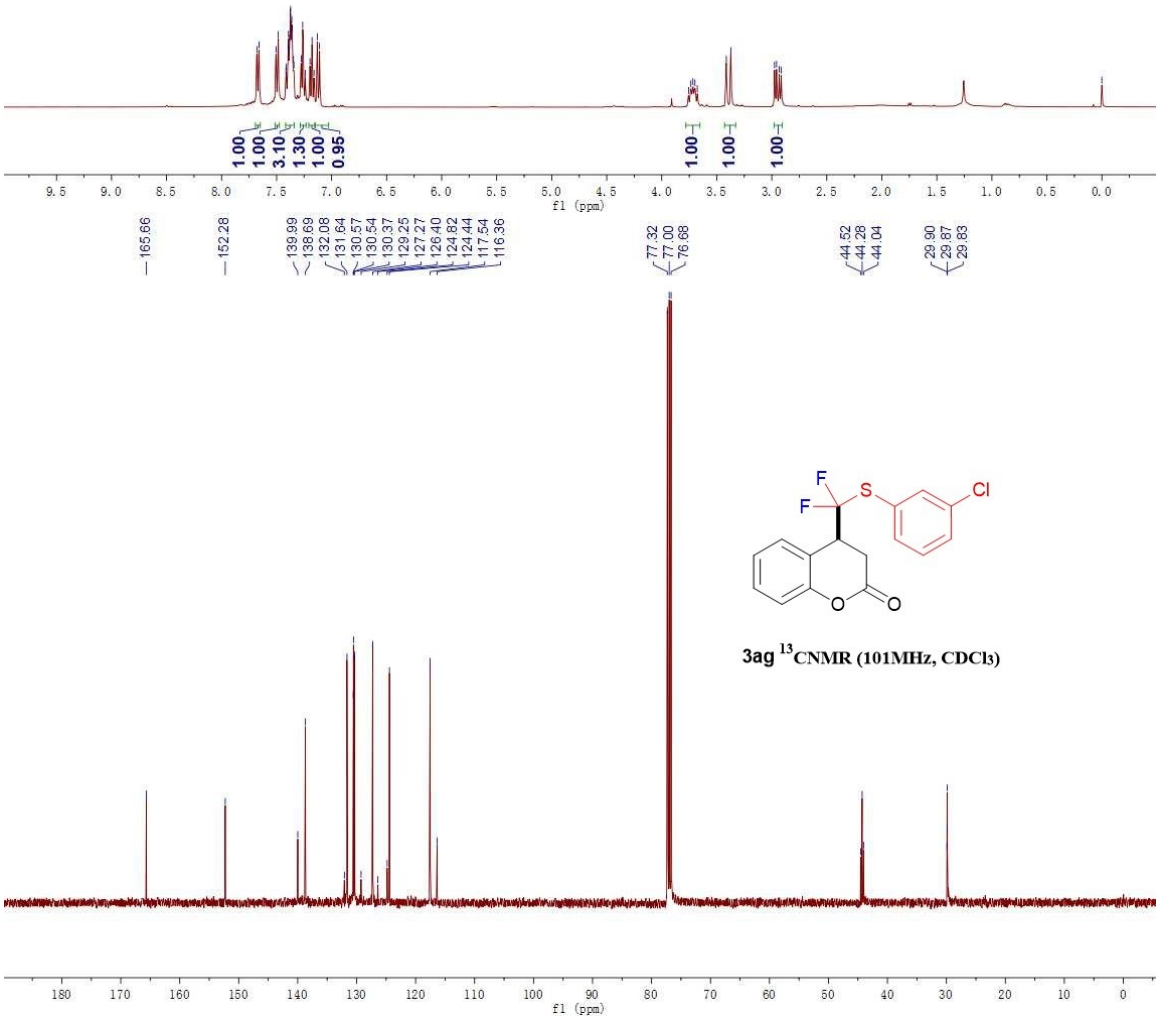
3af ^{13}CNMR (101MHz, CDCl3)



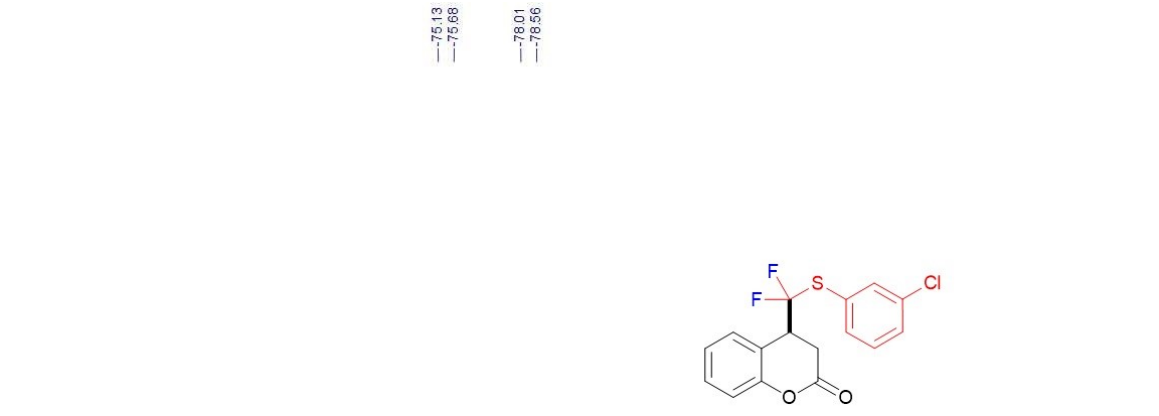
3af ^{19}F NMR (376 MHz, CDCl3)



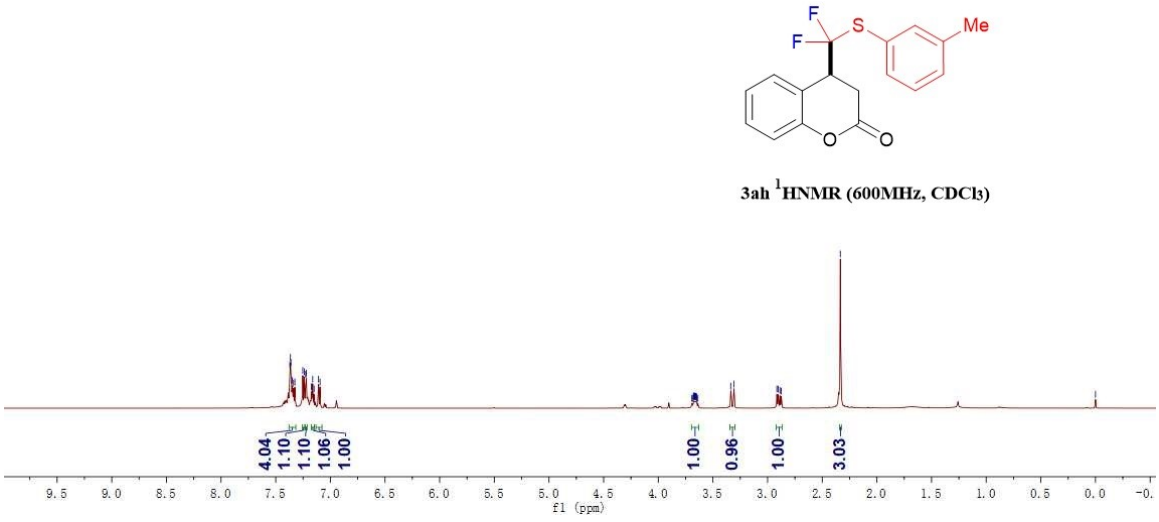
3ag ^{1}HNMR (400MHz, CDCl3)



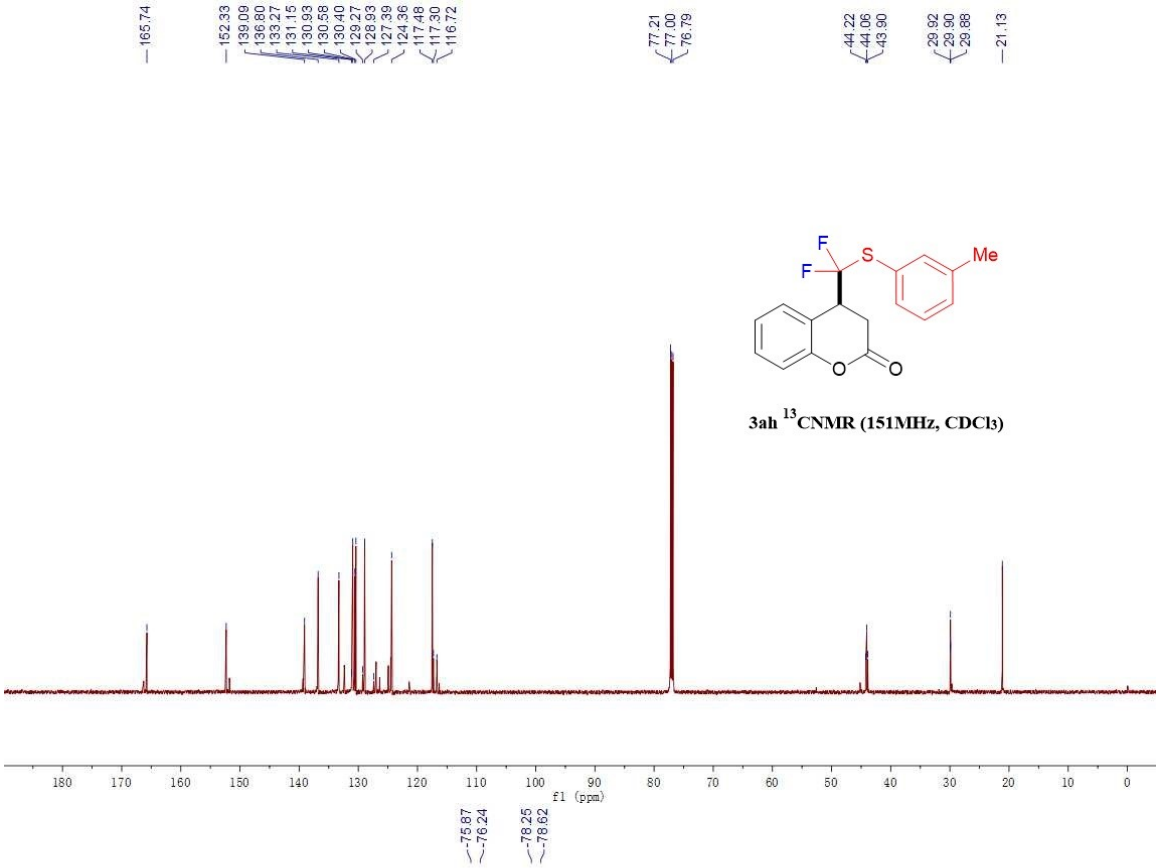
3ag ^{13}CNMR (101MHz, CDCl3)



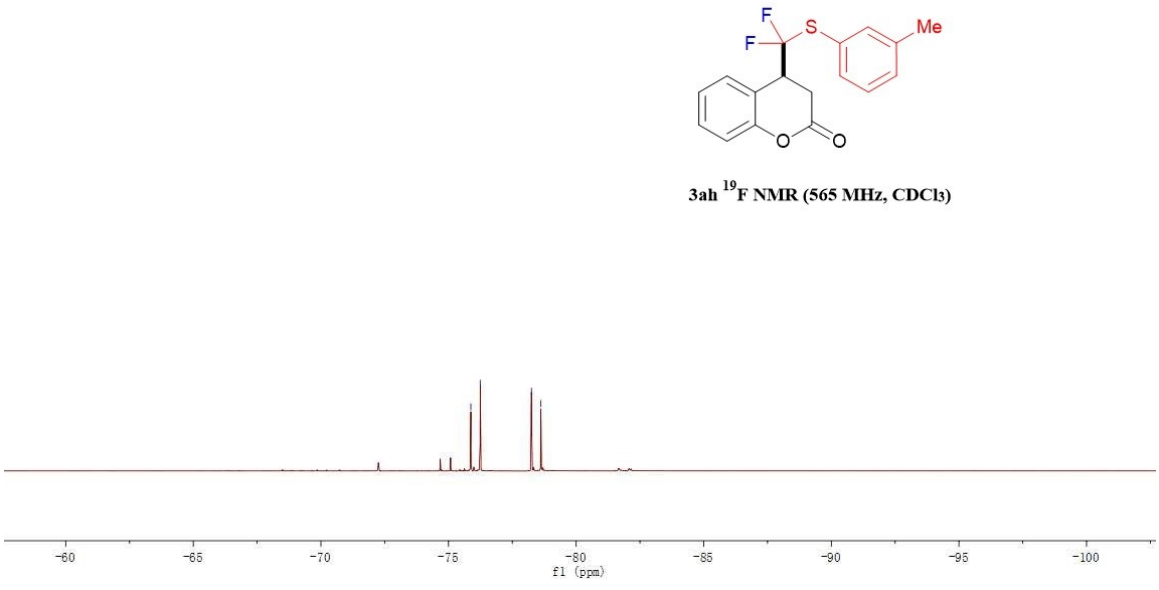
3ag ^{19}F NMR (376 MHz, CDCl3)



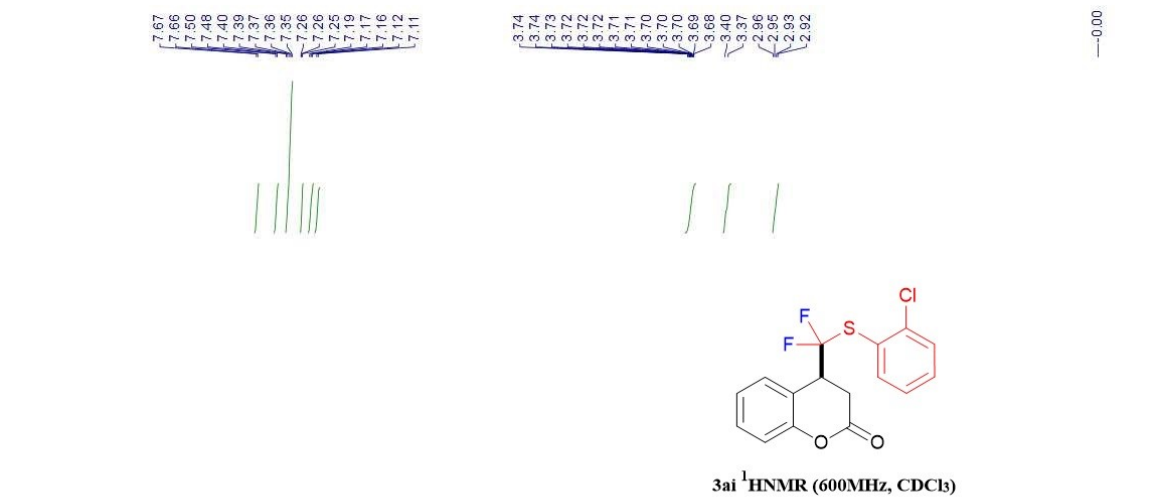
3ah ^{1}HNMR (600MHz, CDCl3)



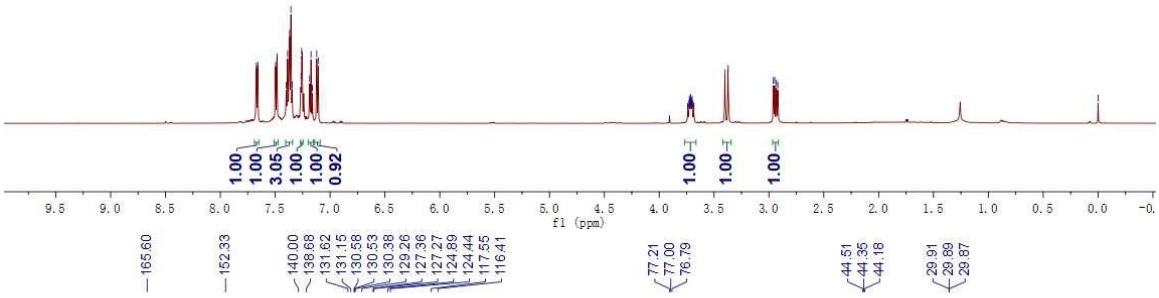
3ah ^{13}CNMR (151MHz, CDCl3)

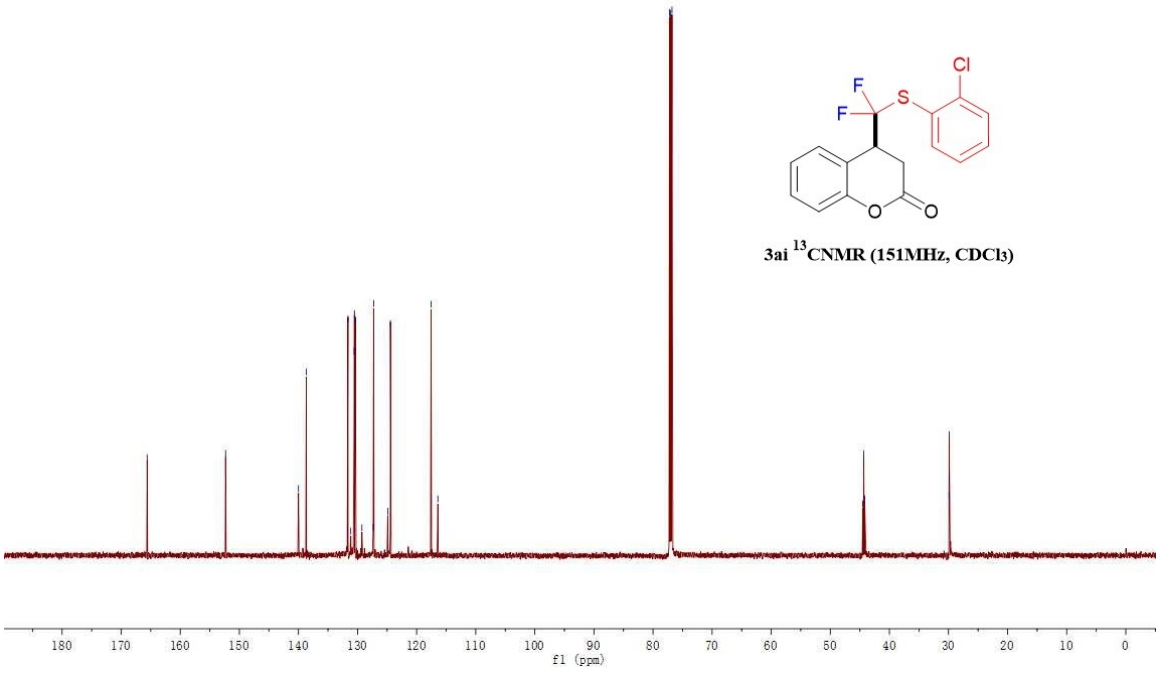


3ah ^{19}F NMR (565 MHz, CDCl3)

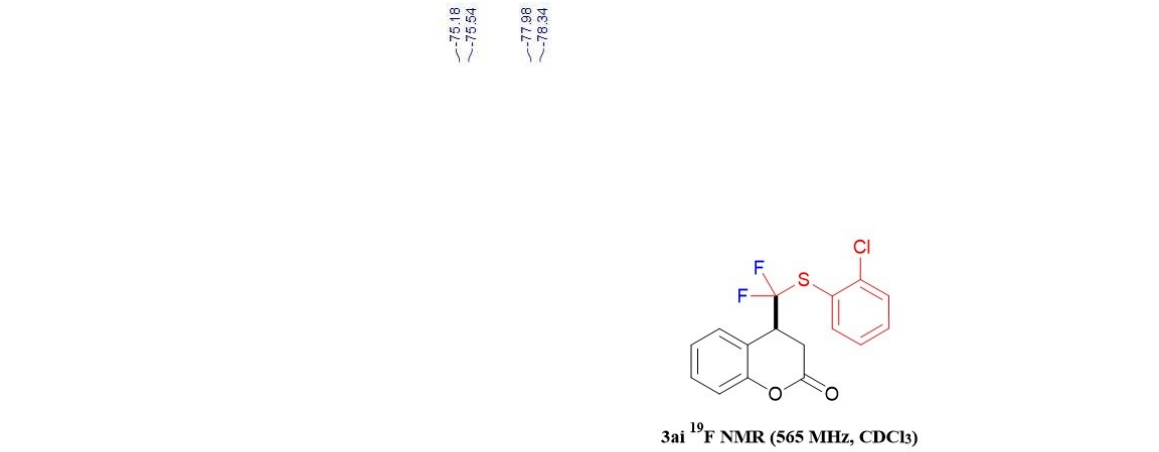


3ai ^{1}HNMR (600MHz, CDCl3)

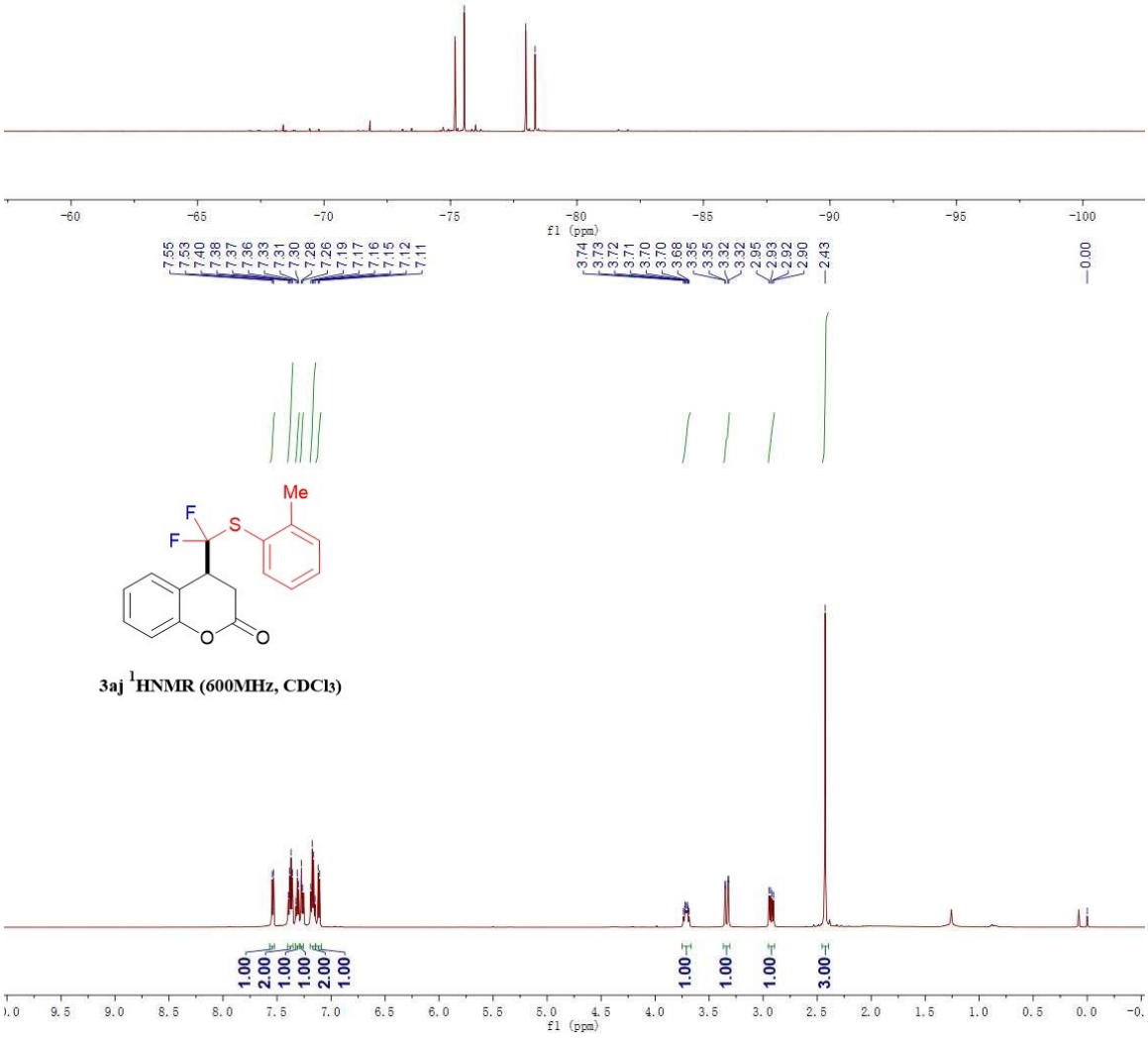




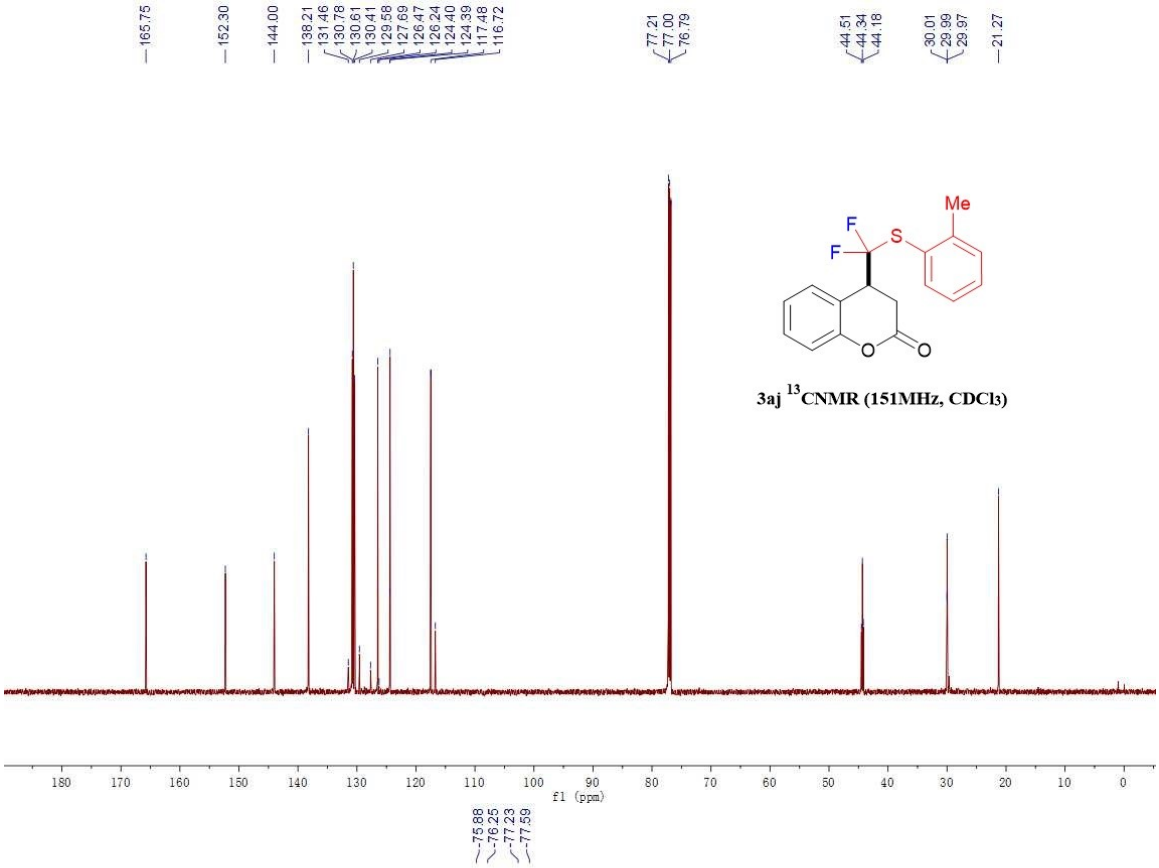
3ai ^{13}CNMR (151MHz, CDCl3)



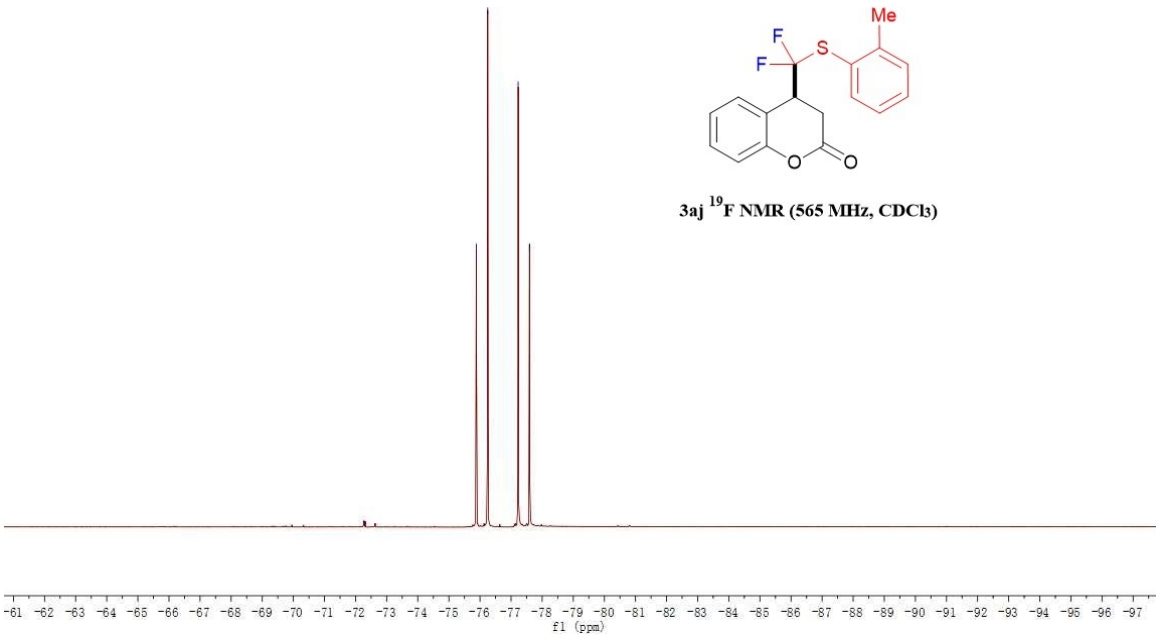
3ai ^{19}F NMR (565 MHz, CDCl3)



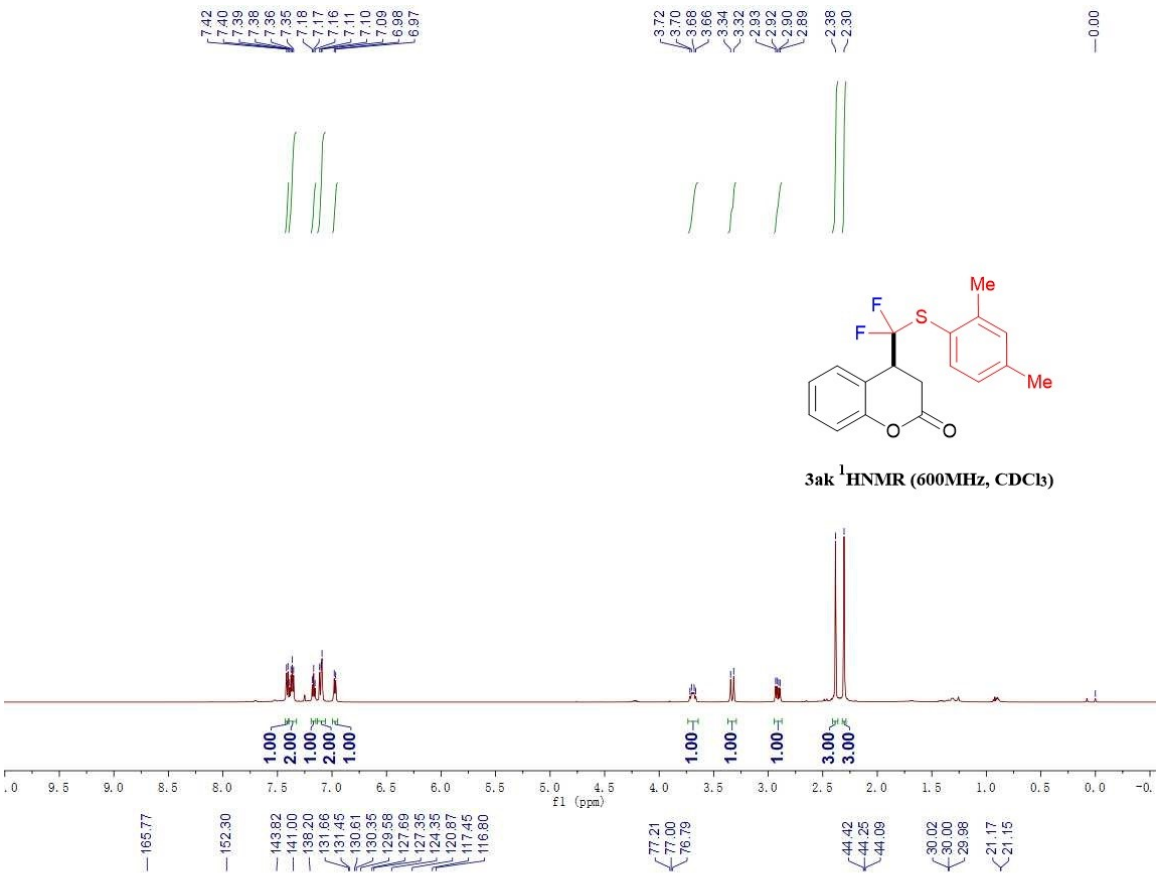
3aj ^{1}HNMR (600MHz, CDCl3)



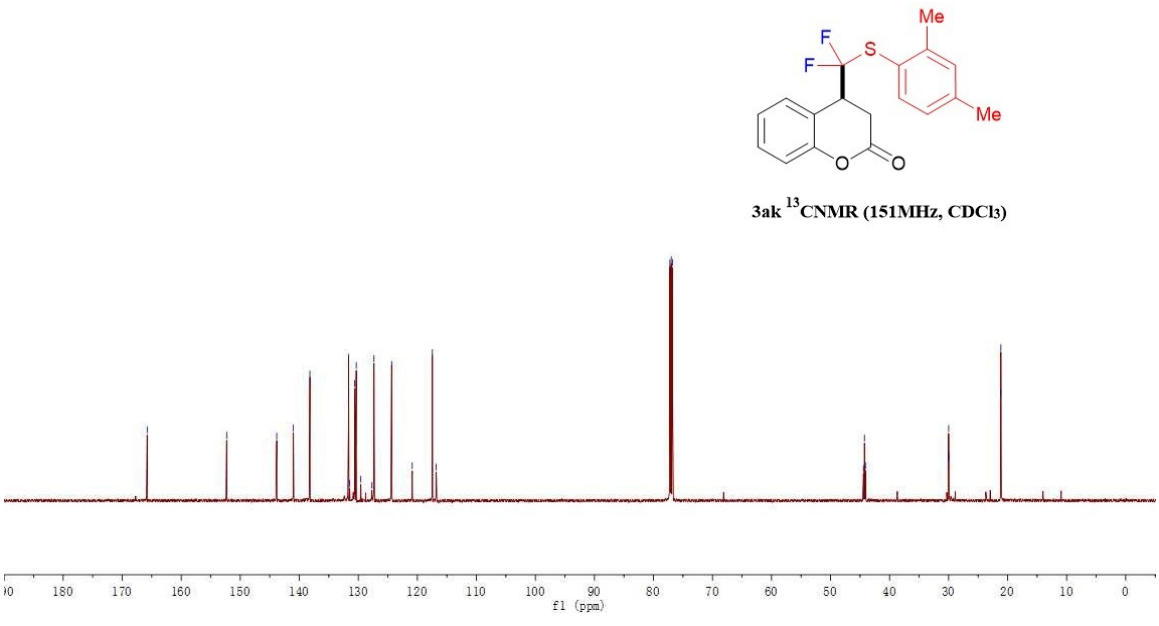
3aj ^{13}CNMR (151MHz, CDCl3)



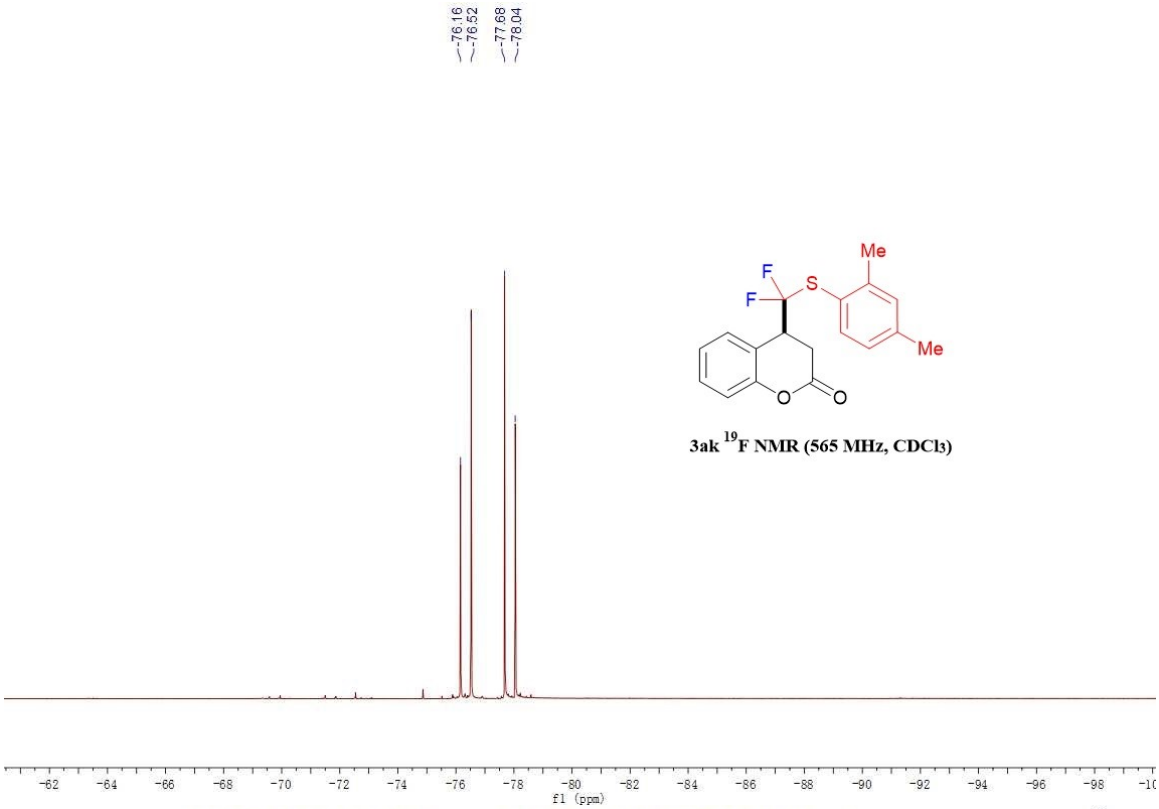
3aj ^{19}F NMR (565 MHz, CDCl3)



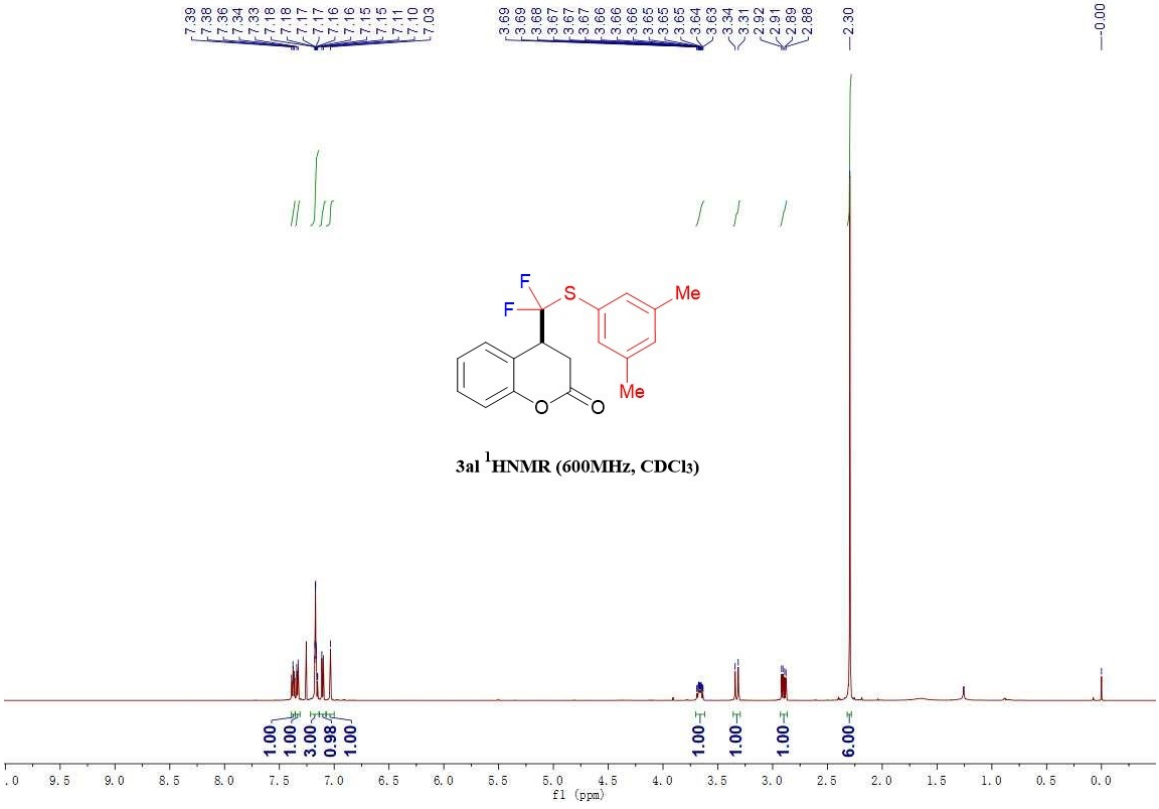
3ak ^{1}HNMR (600MHz, CDCl3)



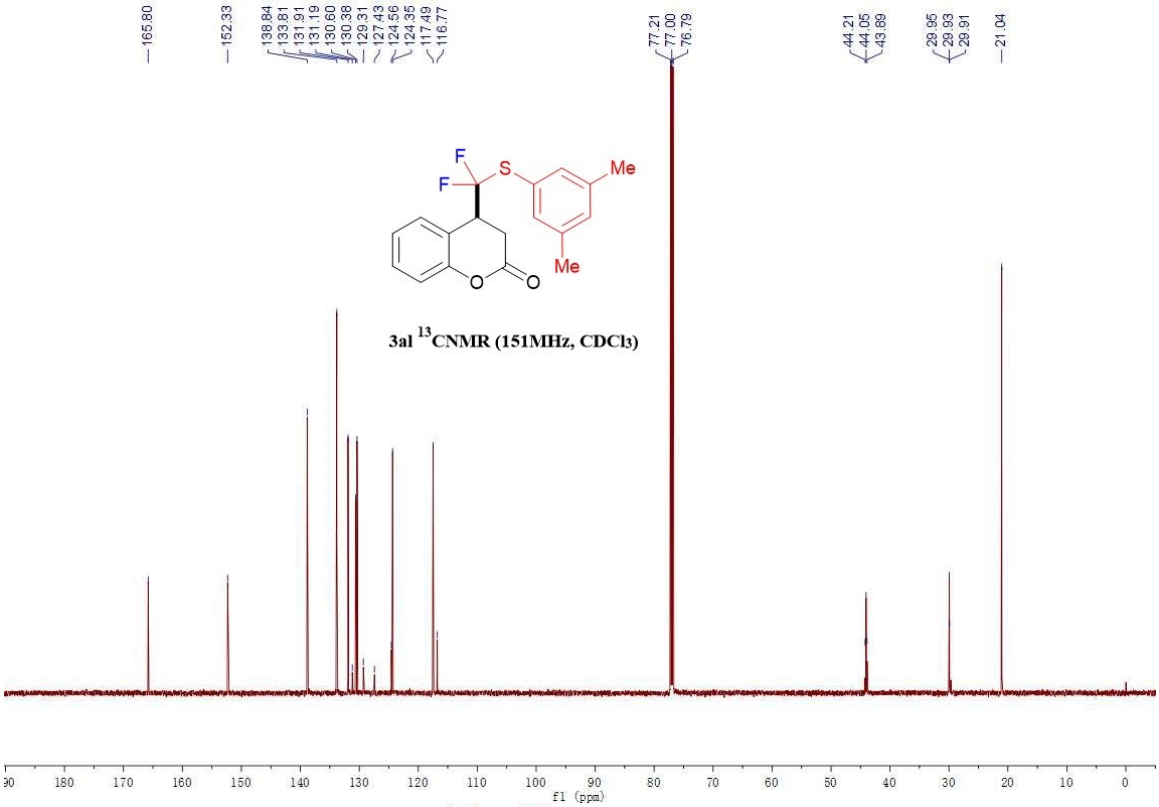
3ak ^{13}CNMR (151MHz, CDCl3)



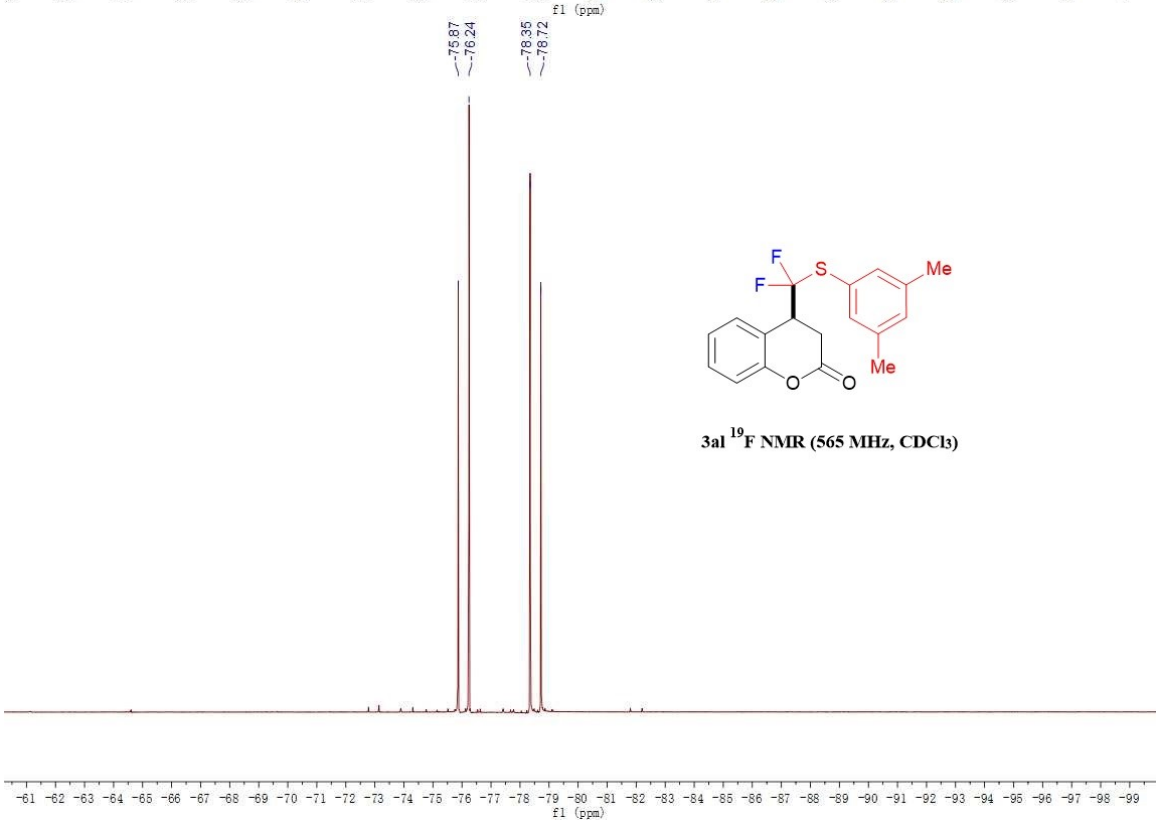
3ak ^{19}F NMR (565 MHz, CDCl3)



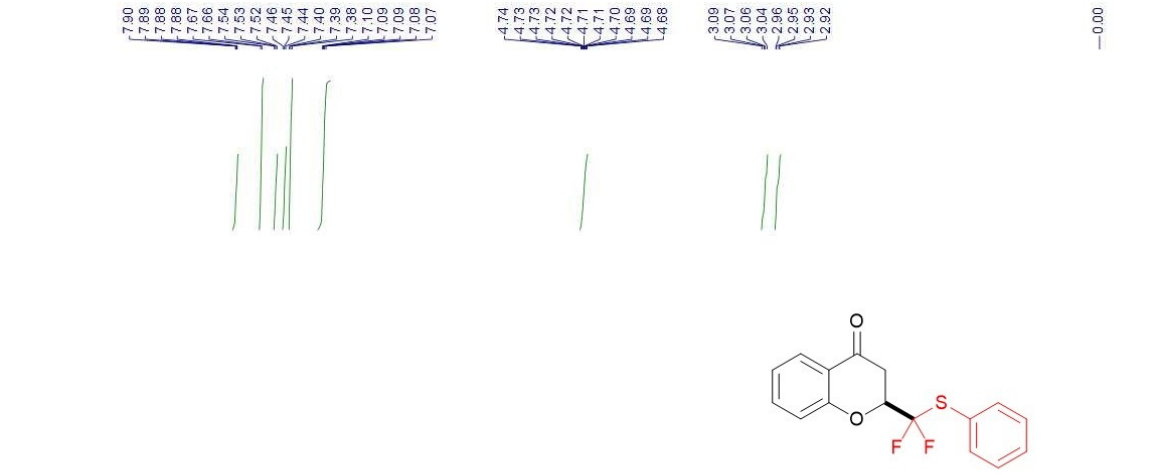
3al ^{1}HNMR (600MHz, CDCl3)



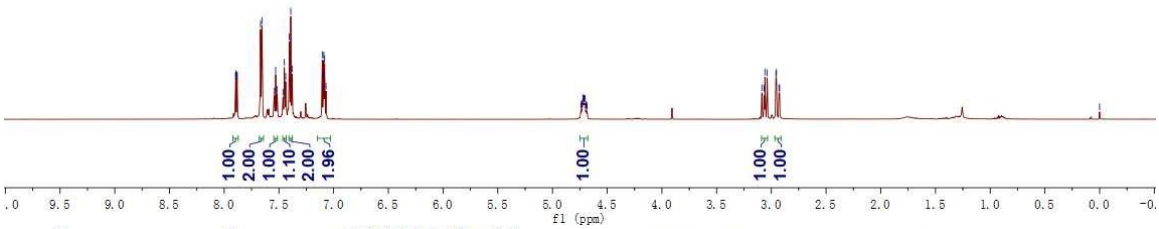
3al ^{13}CNMR (151MHz, CDCl3)

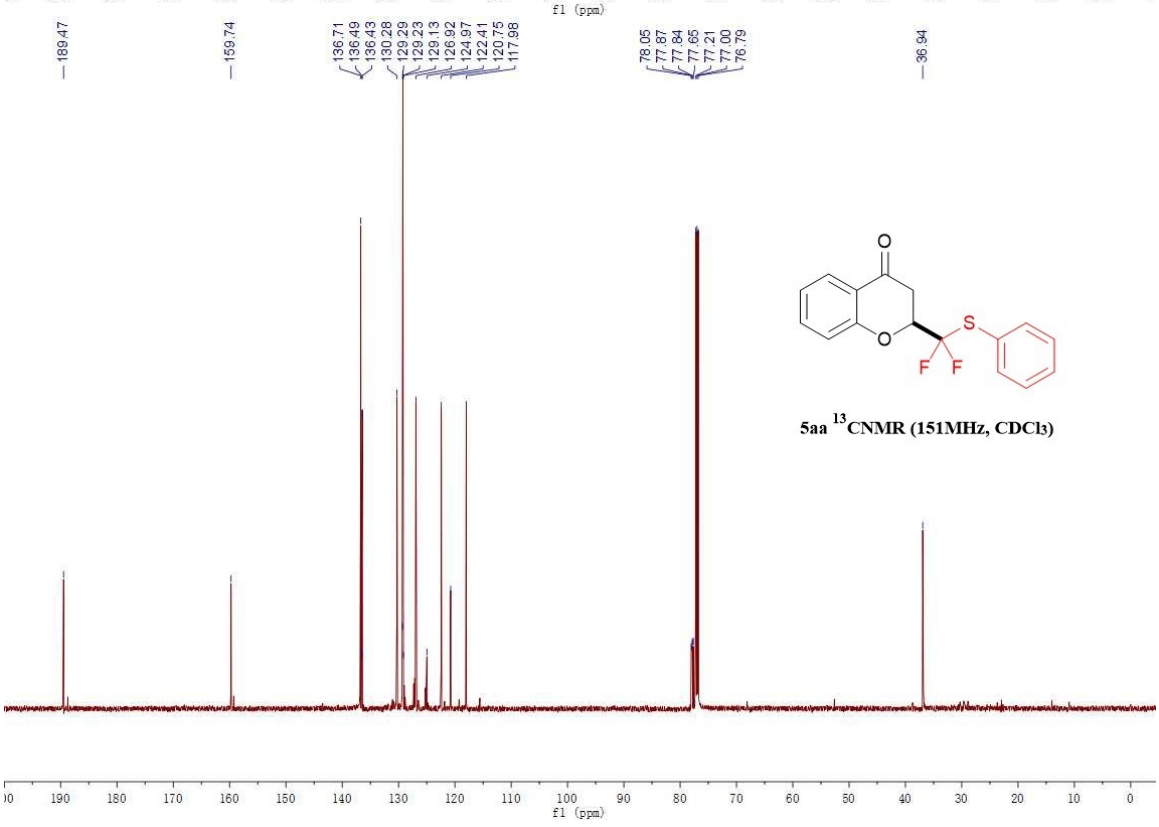


3al ^{19}F NMR (565 MHz, CDCl3)

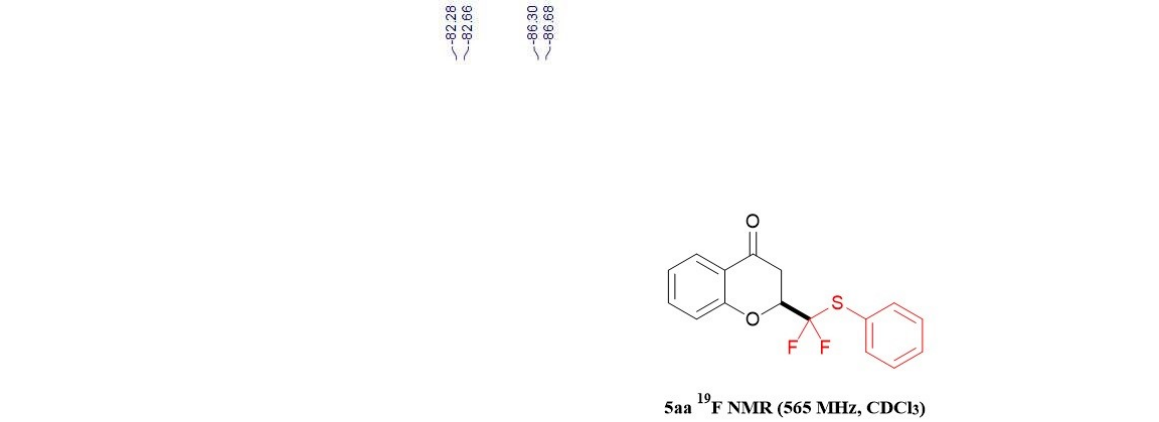


5aa ^{1}HNMR (600MHz, CDCl3)

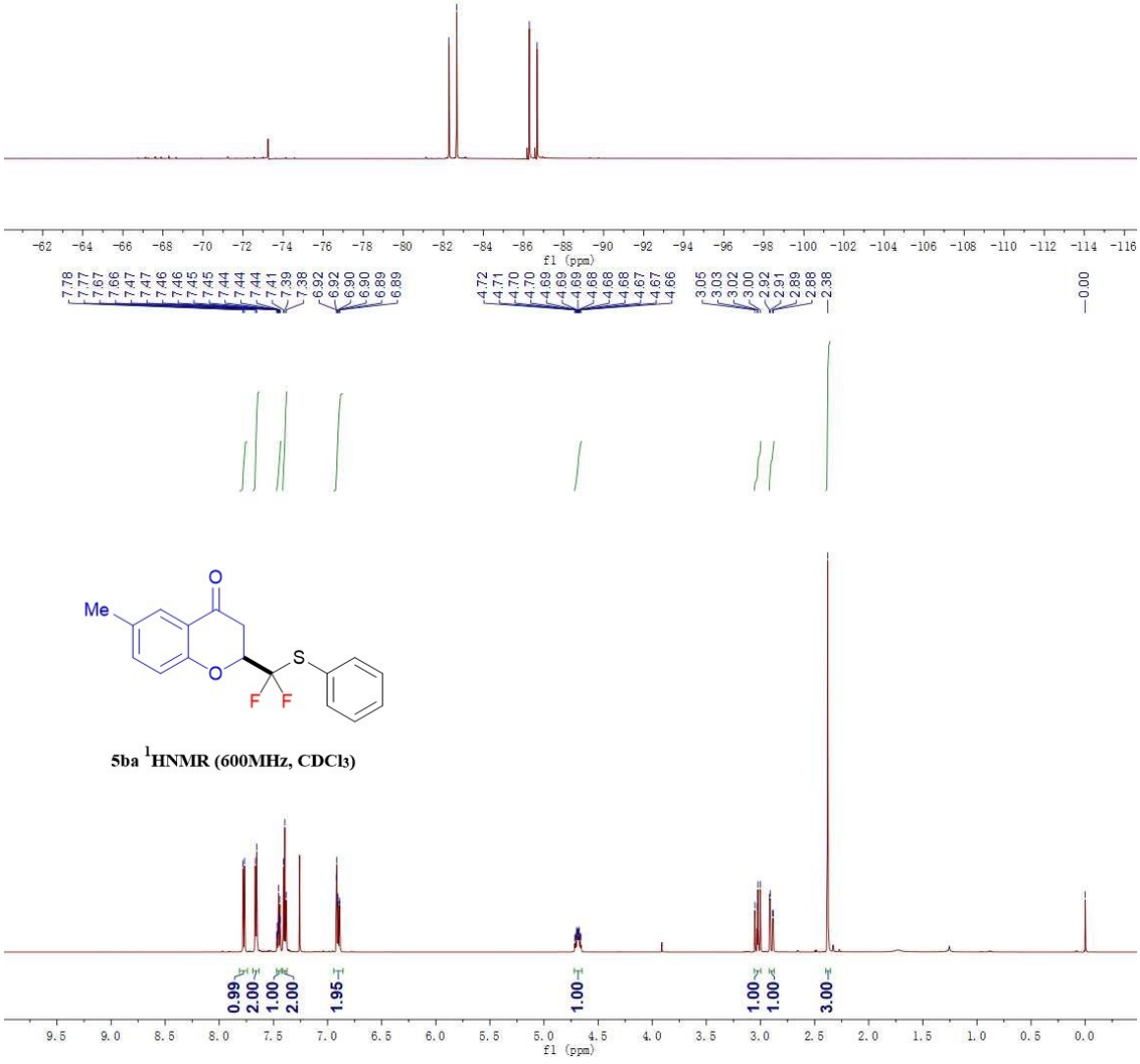




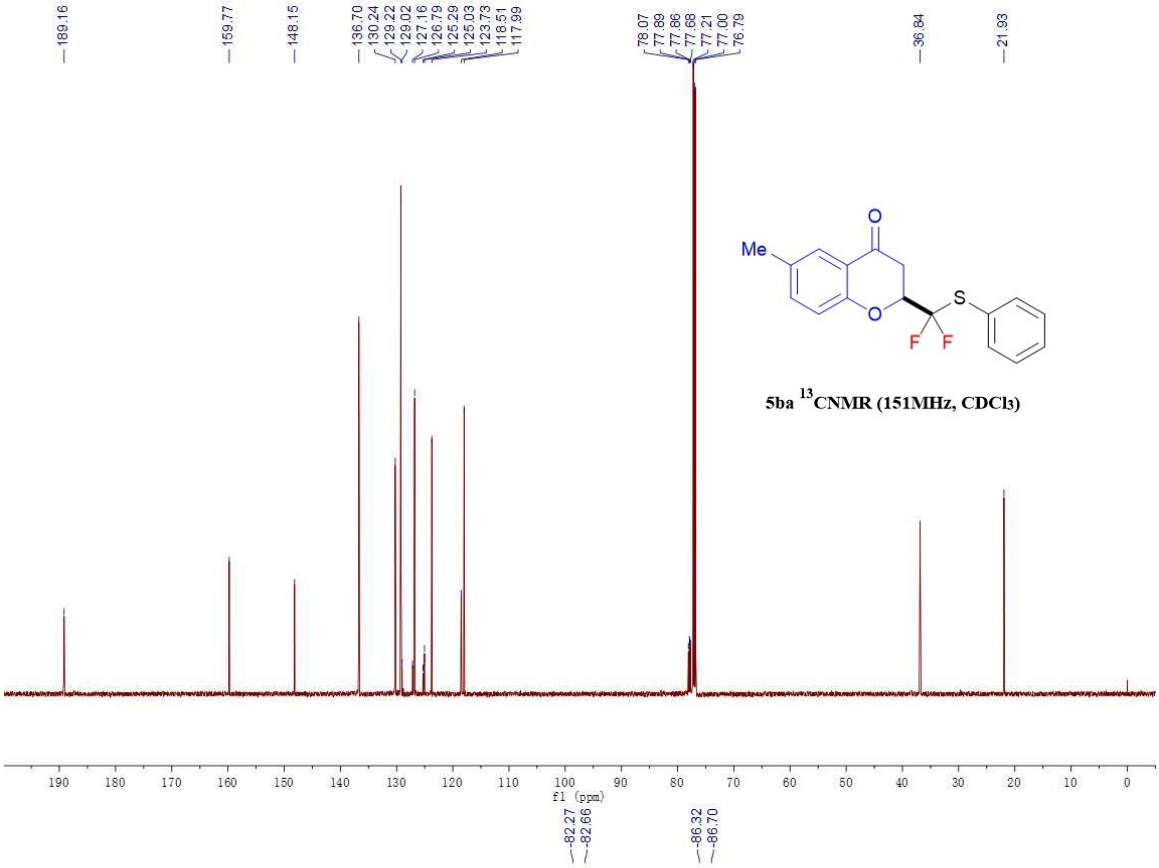
5aa ^{13}CNMR (151MHz, CDCl3)



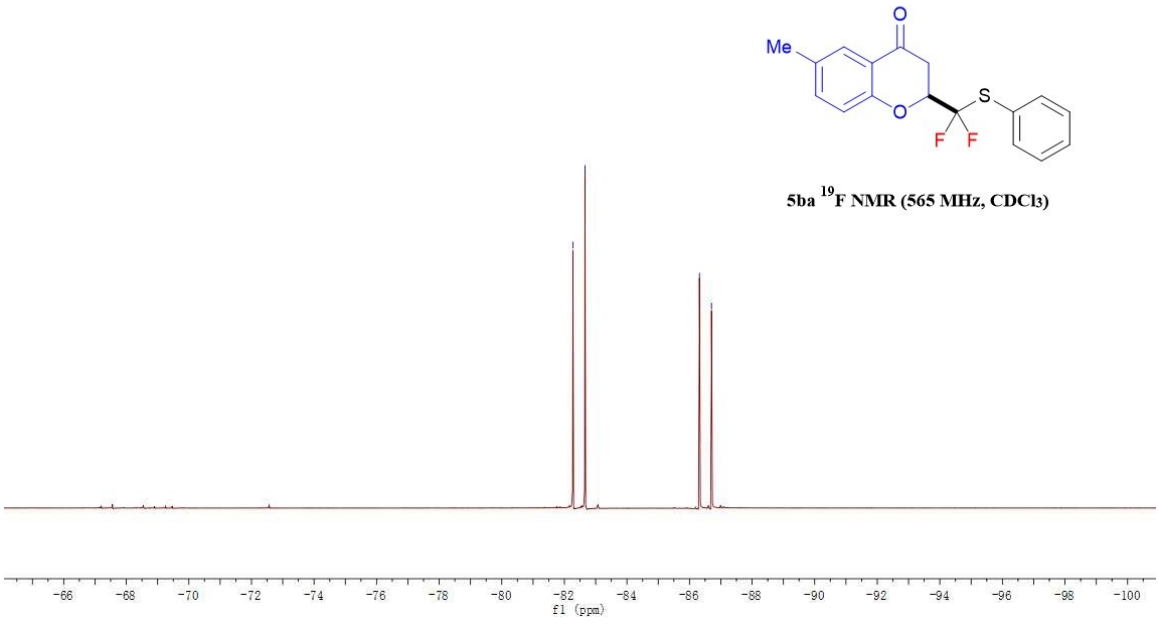
5aa ^{19}F NMR (565 MHz, CDCl3)



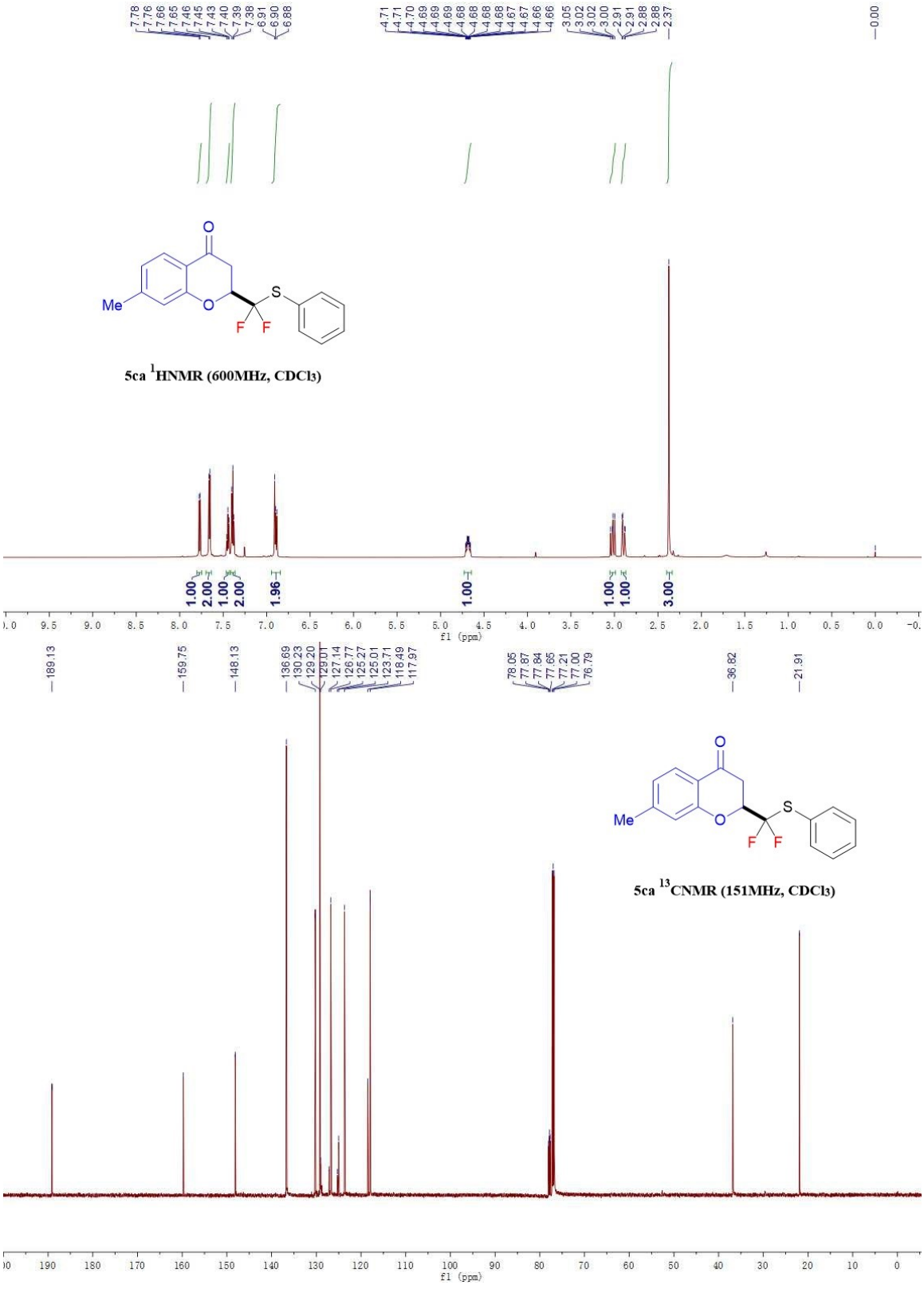
5ba ^{1}HNMR (600MHz, CDCl3)



5ba ^{13}CNMR (151MHz, CDCl3)

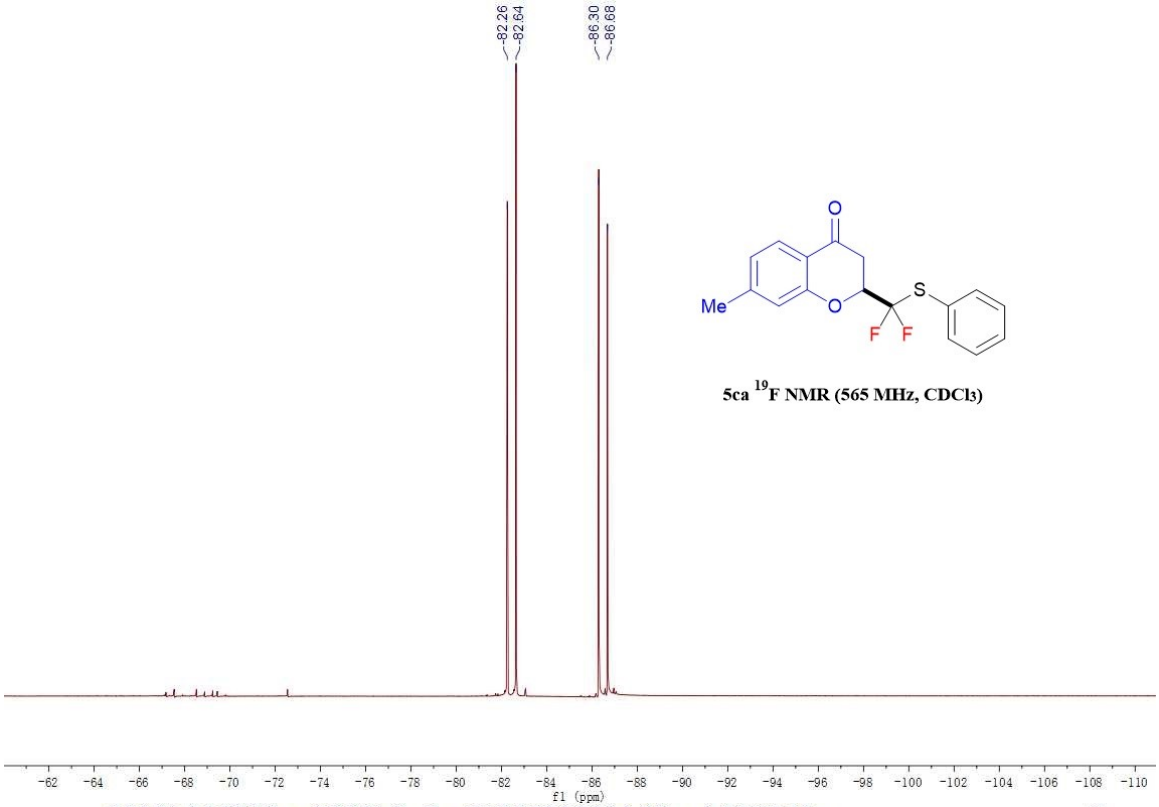


5ba ^{19}F NMR (565 MHz, CDCl3)

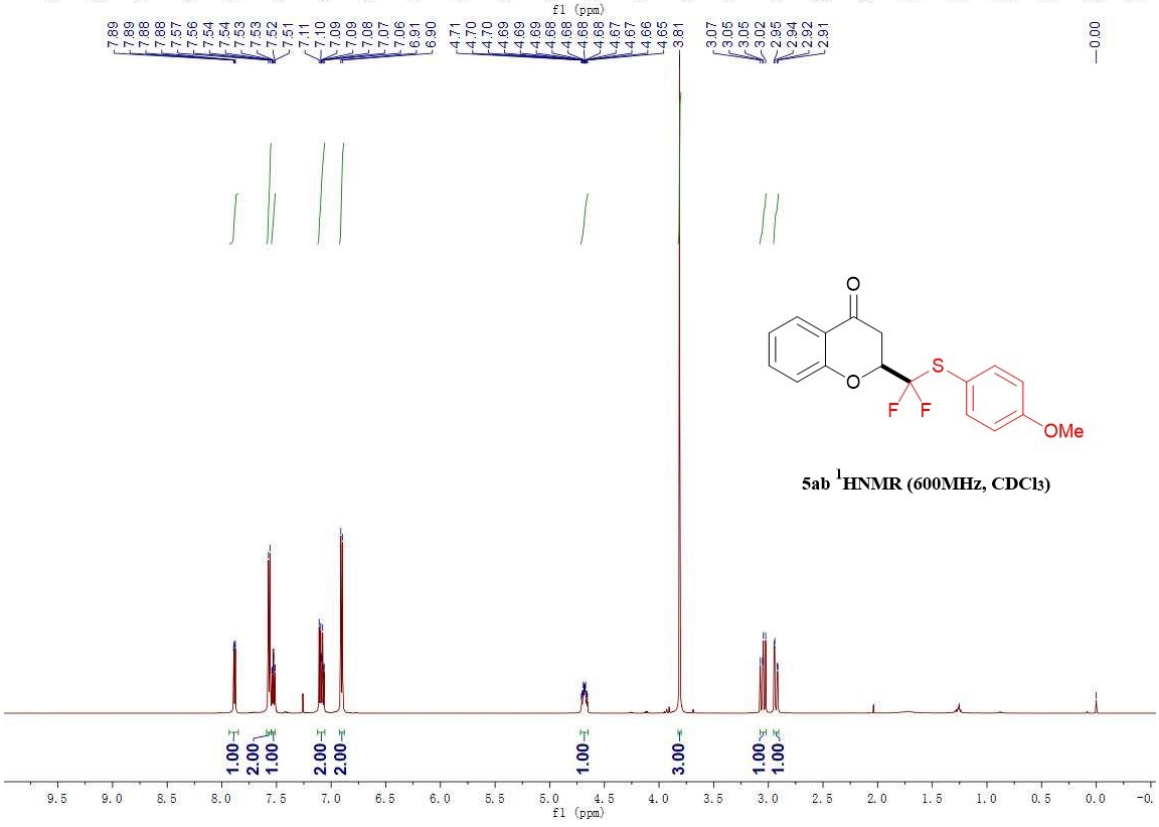


5ca ^{1}HNMR (600MHz, CDCl3)

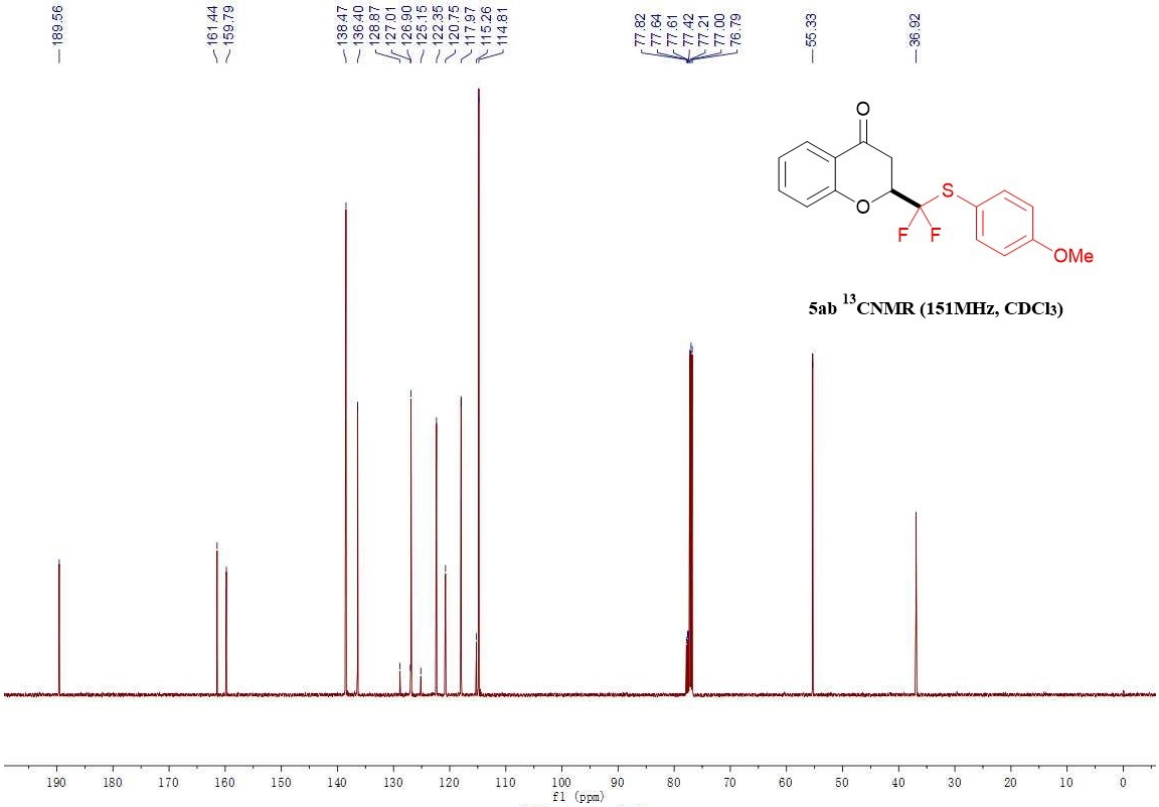
5ca ^{13}CNMR (151MHz, CDCl3)



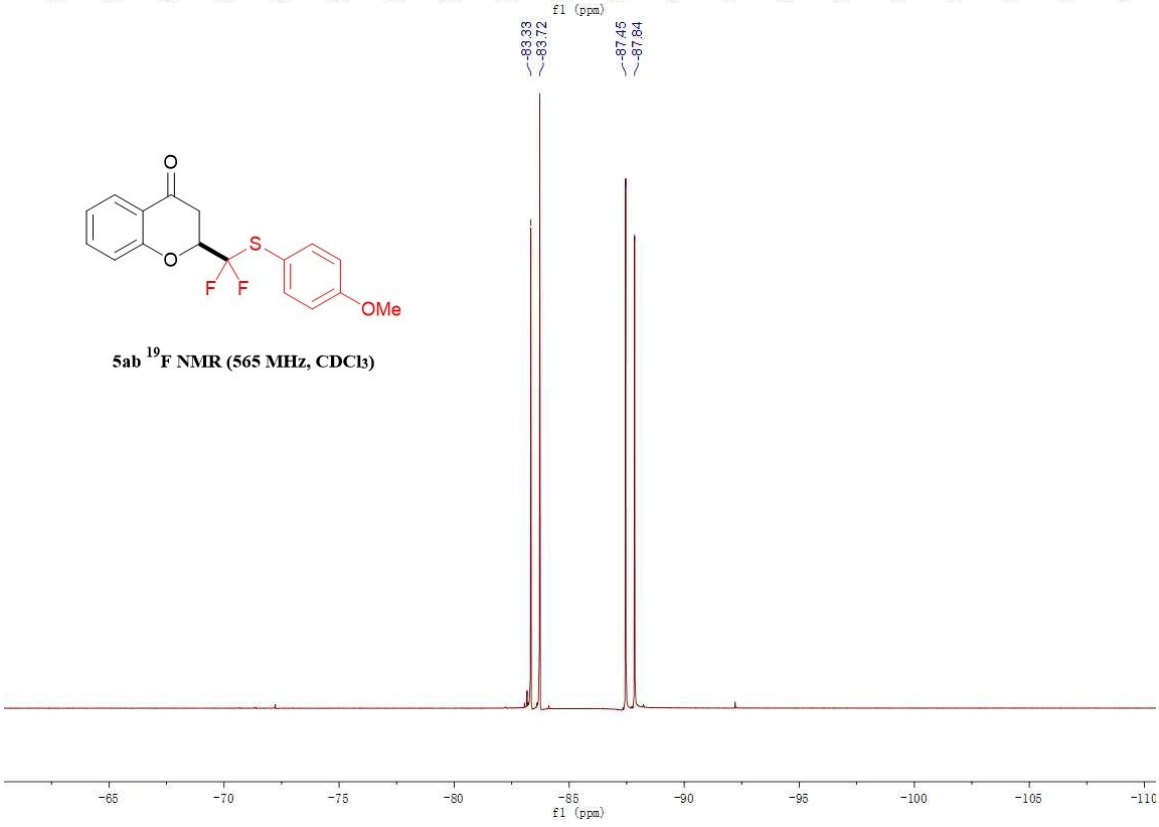
5ca ^{19}F NMR (565 MHz, CDCl3)



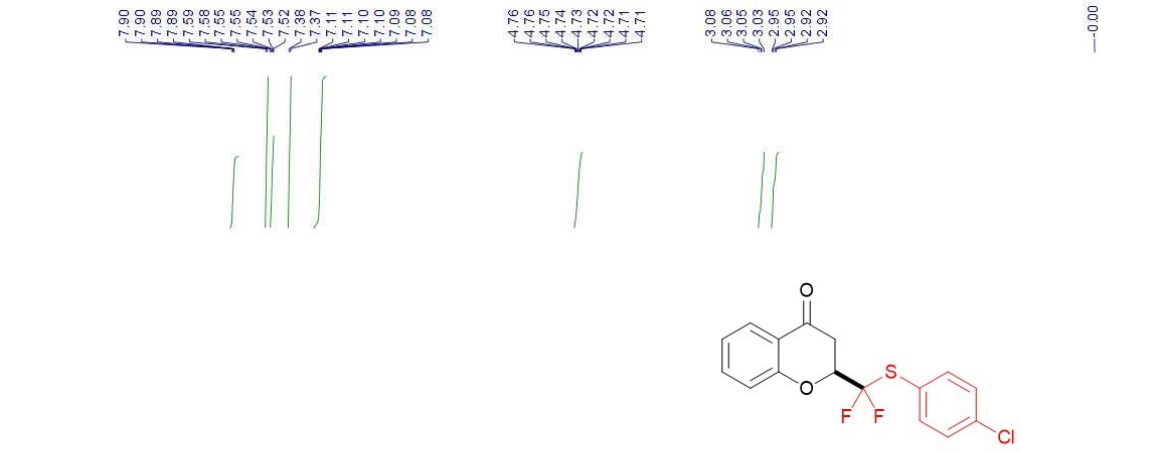
5ab ^{1}HNMR (600MHz, CDCl3)



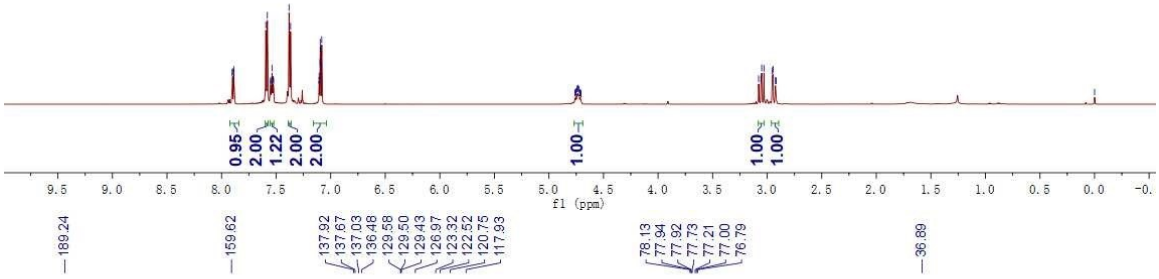
5ab ^{13}CNMR (151MHz, CDCl3)

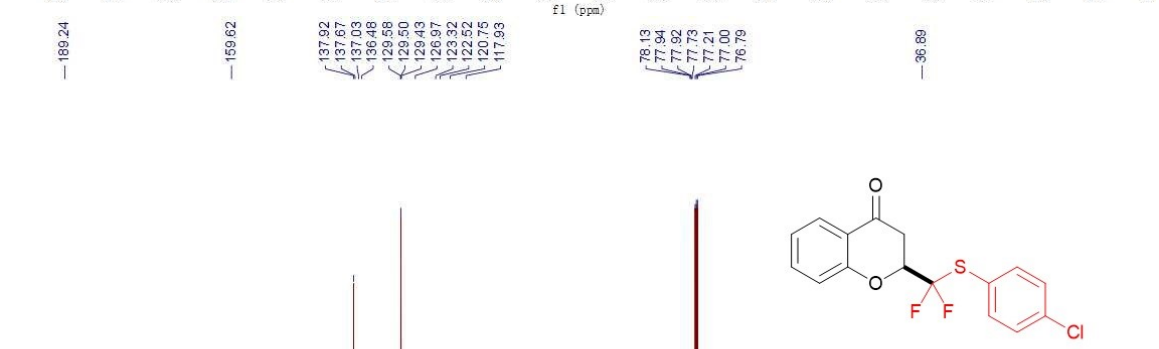


5ab ^{19}F NMR (565 MHz, CDCl3)

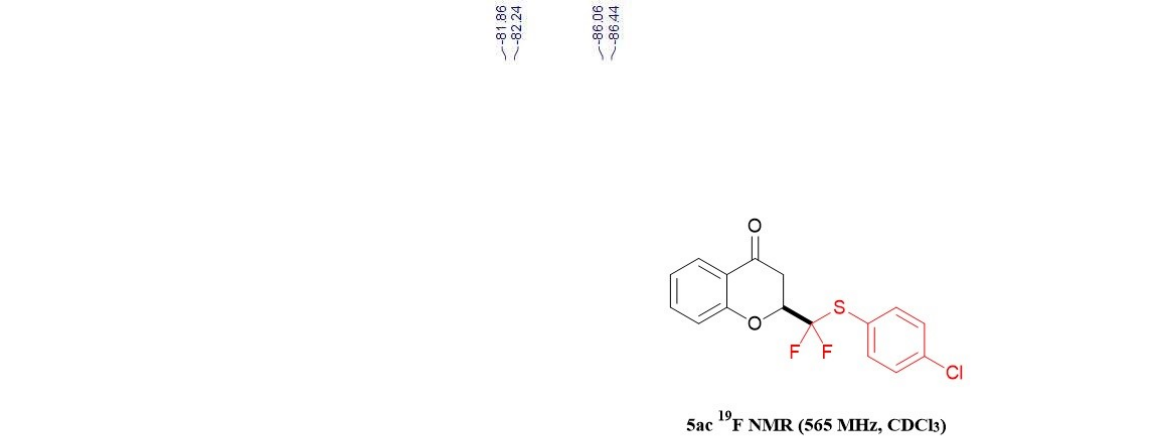


5ac ^{1}HNMR (600MHz, CDCl$_3$)

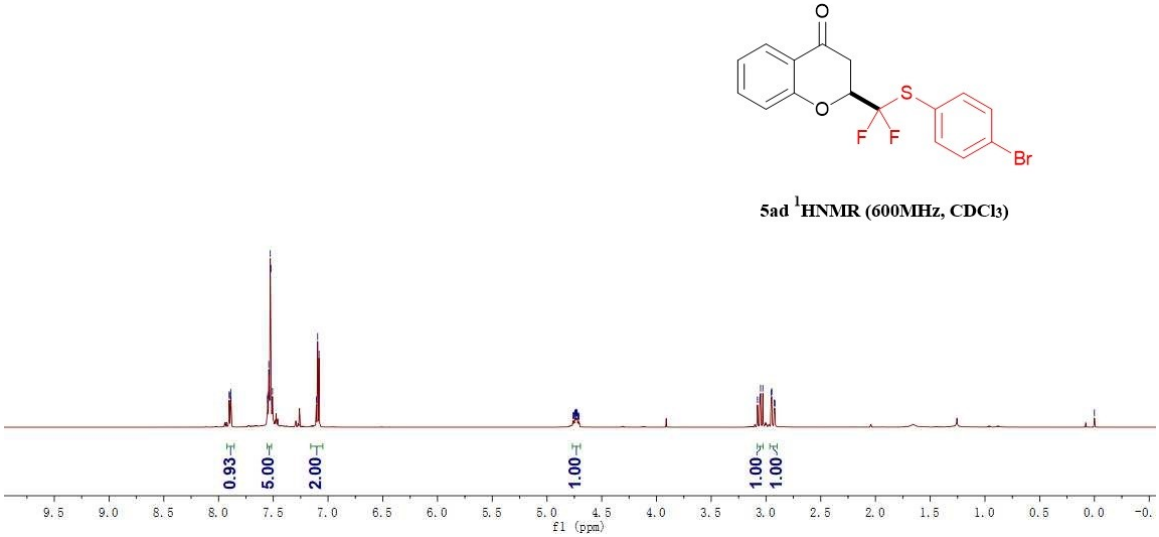




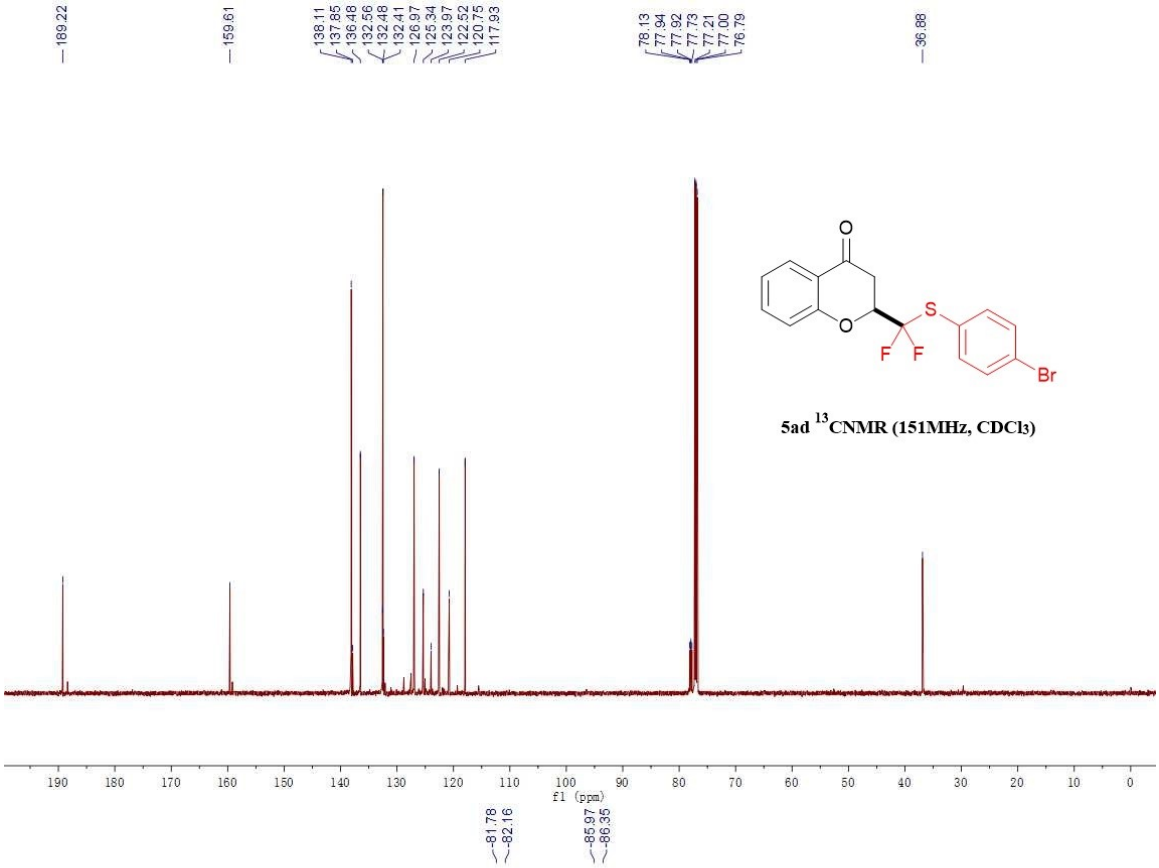
5ac ^{13}CNMR (151MHz, CDCl$_3$)



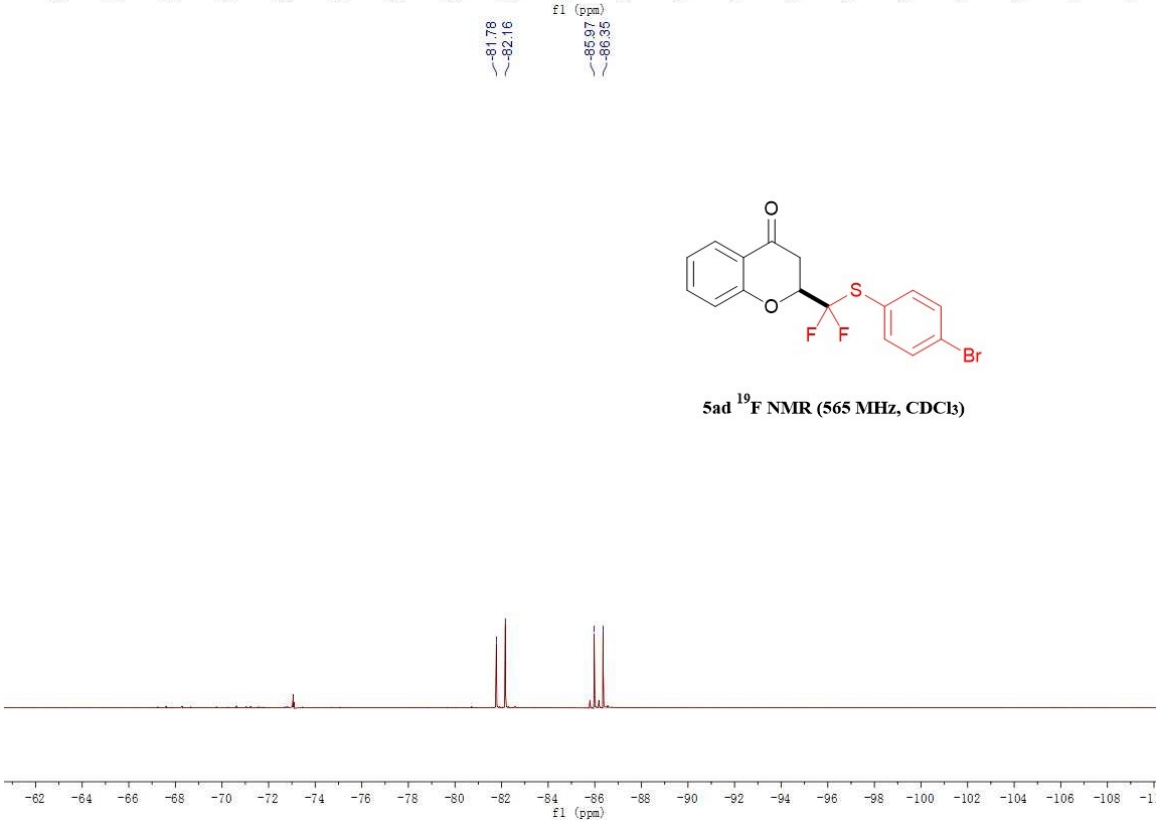
5ac ^{19}F NMR (565 MHz, CDCl3)



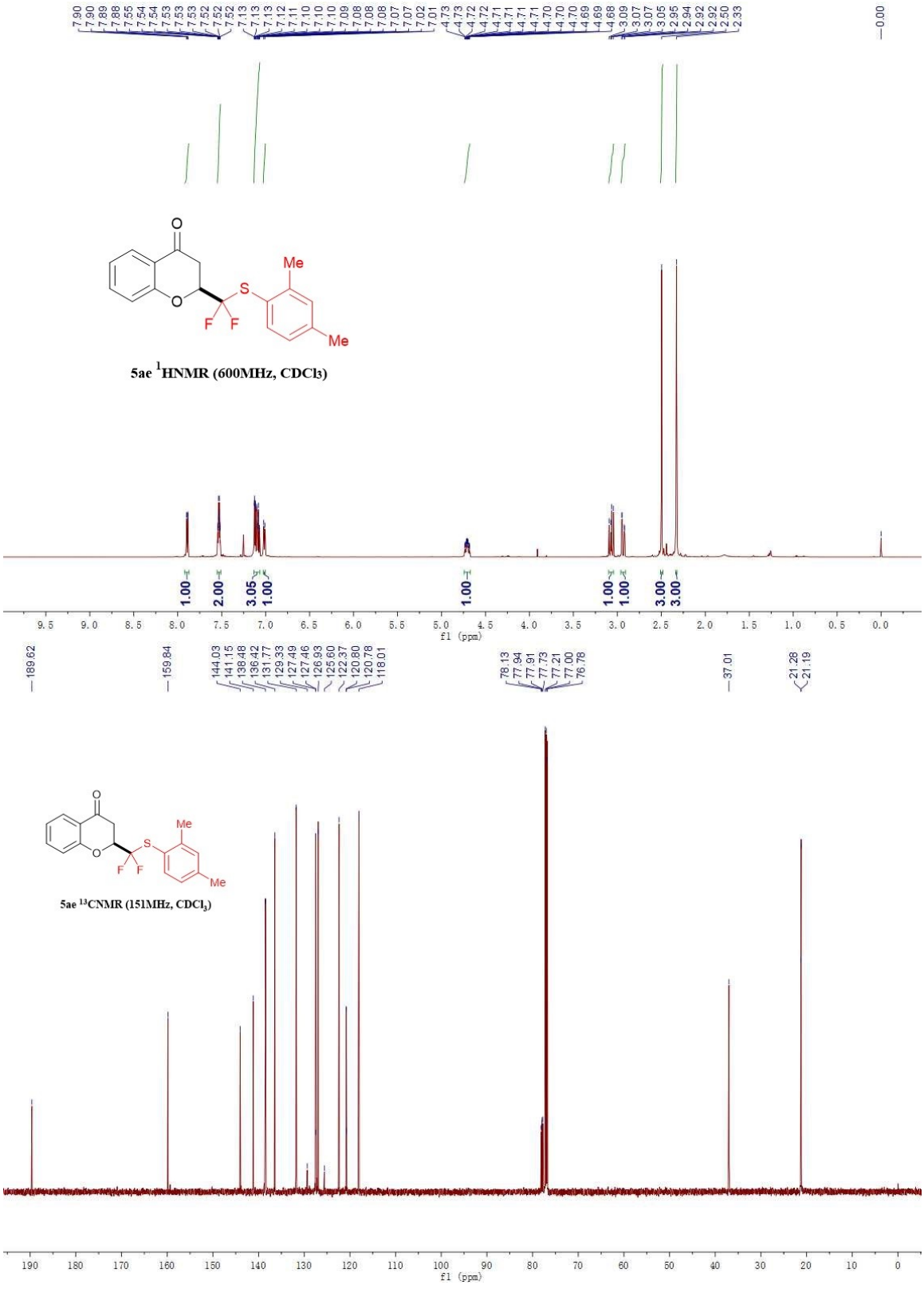
5ad ^{1}HNMR (600MHz, CDCl3)

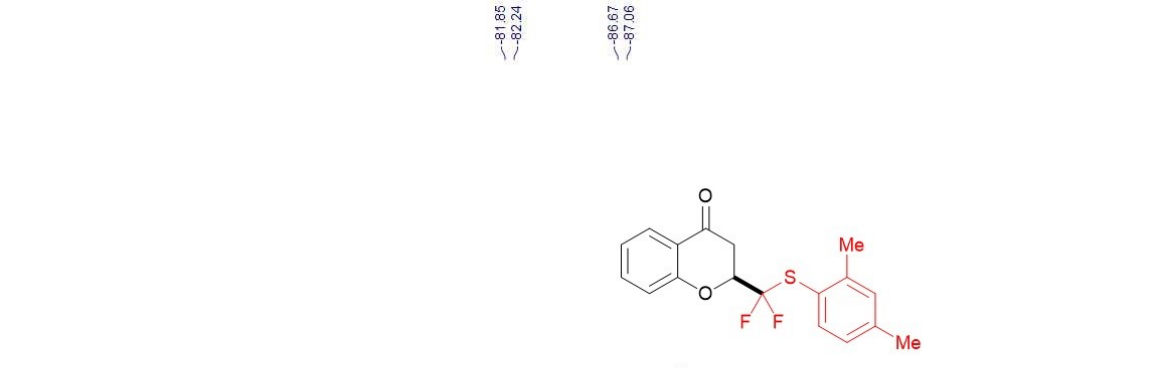


5ad ^{13}CNMR (151MHz, CDCl3)

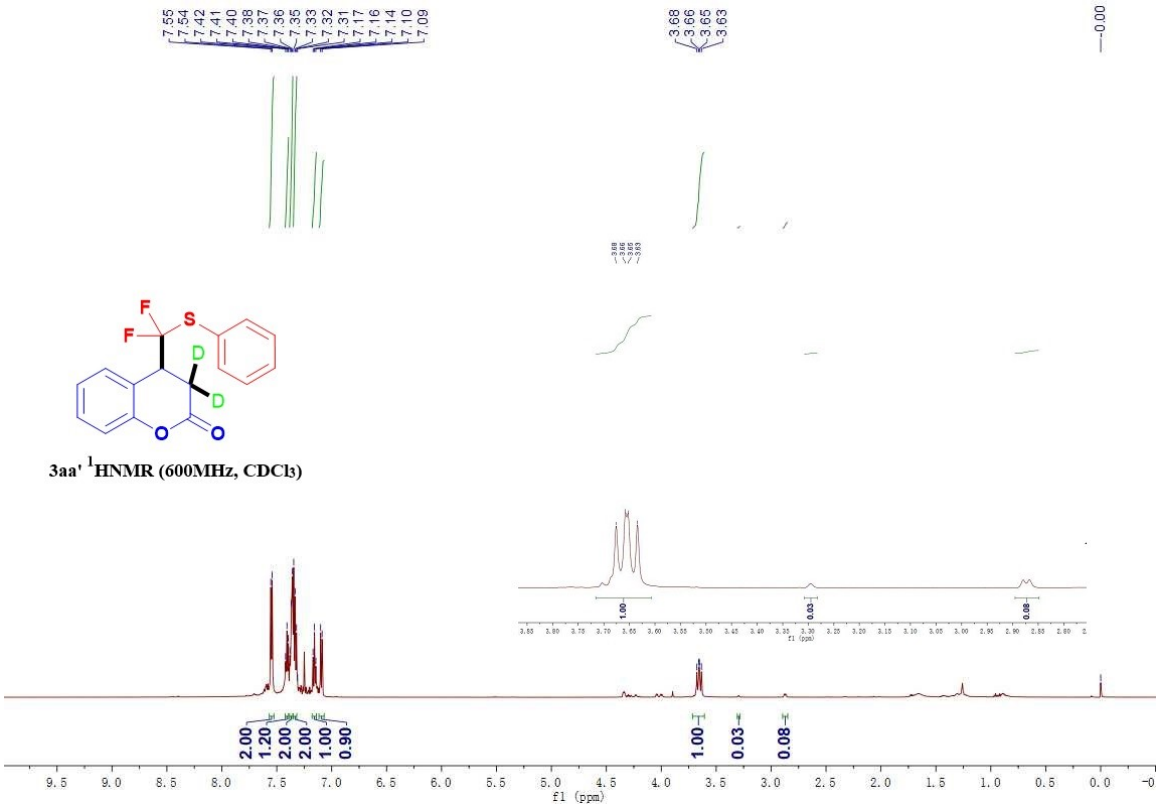


5ad ^{19}F NMR (565 MHz, CDCl3)


7.90 7.90 7.89 7.88 7.55 7.54 7.54 7.53 7.53 7.52 7.52 7.52 7.13 7.13 7.12 7.11 7.10 7.10 7.09 7.08 7.08 7.08 7.07 7.07 7.02 7.01 4.73 4.73 4.72 4.72 4.71 4.71 4.71 4.71 4.70 4.70 4.70 4.69 4.69 4.68 3.09 3.07 3.07 3.05 2.95 2.94 2.92 2.92 2.50 2.33 0.00
O
O
S
F F
Me
Me
5ae ^{1}HNMR (600MHz, CDCl3)
1.00 2.00 3.05 1.00 1.00 1.00 1.00 3.00 3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
189.62 159.84 144.03 141.15 138.48 136.42 131.77 129.33 127.49 127.46 126.93 125.60 122.37 120.80 120.78 118.01 78.13 77.94 77.91 77.73 77.21 77.00 76.78 37.01 21.28 21.19
O
O
S
F F
Me
Me
5ae ^{13}CNMR (151MHz, CDCl$_3$)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



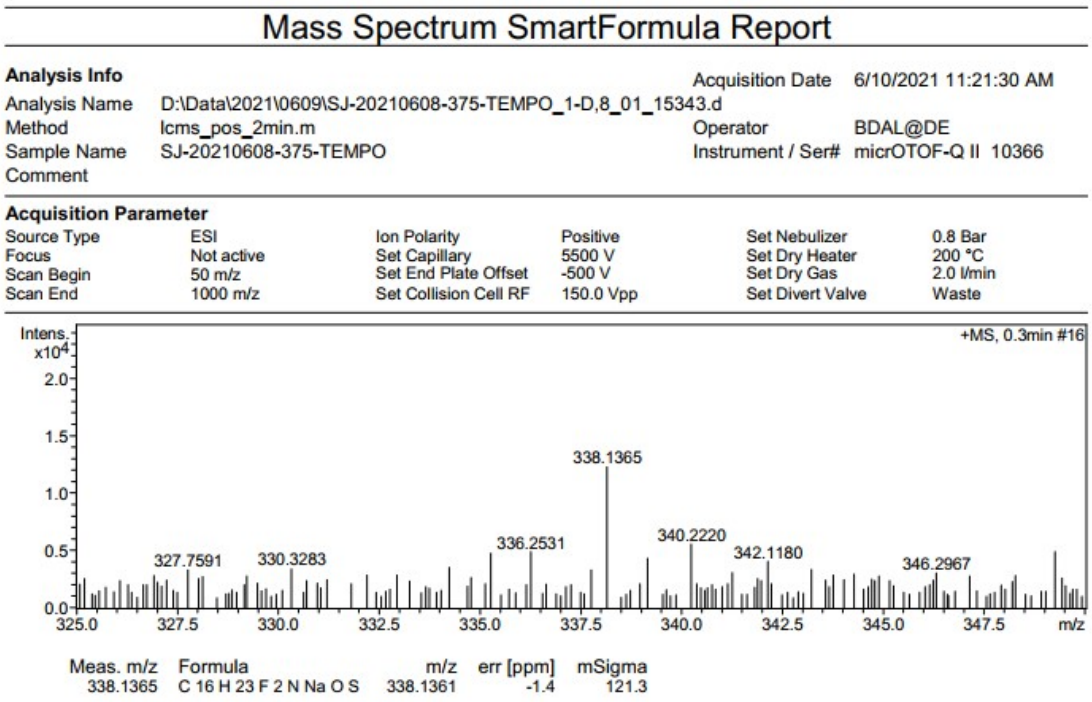
5ae ^{19}F NMR (565 MHz, CDCl3)



3aa' ^{1}HNMR (600MHz, CDCl3)

6.The HRMS spectra for Compound 7

HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{23}F_2NNaOS$ + 338.1361; found 338.1365.



Mass Spectrum SmartFormula Report

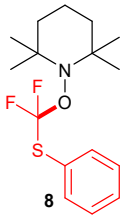
Analysis Info

Analysis Name	D:\Data\2021\0609\SJ-20210608-375-TEMPO_1-D,8_01_15343.d	Acquisition Date	6/10/2021 11:21:30 AM
Method	lcms_pos_2min.m	Operator	BDAL@DE
Sample Name	SJ-20210608-375-TEMPO	Instrument / Ser#	micrOTOF-Q II 10366
Comment			

Acquisition Parameter

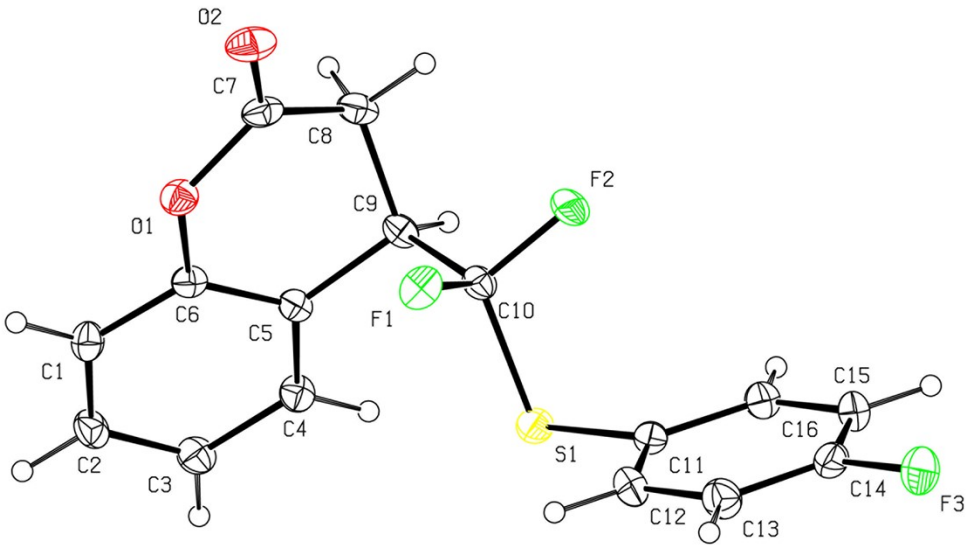
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.8 Bar
Focus	Not active	Set Capillary	5500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	2.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	150.0 Vpp	Set Divert Valve	Waste

Meas. m/z	Formula	m/z	err [ppm]	mSigma
338.1365	C 16 H 23 F 2 N Na O S	338.1361	-1.4	121.3



8

7.X-ray crystallography date of 3ab



Crystal structure determination of 3ab.

Crystal Data for $C_{16}H_{11}F_3O_2S$ (M =324.31 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 15.060(7) Å, b = 5.814(3) Å, c = 17.346(7) Å, β = 114.484(18)°, V = 1382.2(11) Å^3, Z = 4, T = 170.0 K, μ(MoKα) = 0.273 mm^{-1}, *Dcalc* = 1.558 g/cm^3, 22040 reflections measured (4.77° ≤ 2Θ ≤ 54.234°), 3064 unique (R_{int} = 0.0280, R_{sigma} = 0.0172) which were used in all calculations. The final R_1 was 0.0288 (I > 2σ(I)) and wR_2 was 0.0735 (all data).

Table 1 Crystal data and structure refinement for 3ab.

Identification code	mo_211008_sj_1_0m
Empirical formula	$C_{16}H_{11}F_3O_2S$
Formula weight	324.31
Temperature/K	170.0
Crystal system	monoclinic
Space group	$P2_1/c$

a/Å	15.060(7)
b/Å	5.814(3)
c/Å	17.346(7)
α/°	90
β/°	114.484(18)
γ/°	90
Volume/Å^3	1382.2(11)
Z	4
ρ_{calc}g/cm^3	1.558
μ/mm^{-1}	0.273
F(000)	664.0
Crystal size/mm^3	0.48 × 0.12 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.77 to 54.234
Index ranges	-19 ≤ h ≤ 19, -6 ≤ k ≤ 7, -22 ≤ l ≤ 22
Reflections collected	22040
Independent reflections	3064 [R_{int} = 0.0280, R_{sigma} = 0.0172]
Data/restraints/parameters	3064/0/199
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0288, wR_2 = 0.0699
Final R indexes [all data]	R_1 = 0.0338, wR_2 = 0.0735
Largest diff. peak/hole / e Å^{-3}	0.28/-0.22

Table 2 Bond lengths for 3ab.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	C10	1.8077(14)	C4	C5	1.3917(18)
S1	C11	1.7776(15)	C5	C6	1.3869(18)
F1	C10	1.3709(16)	C5	C9	1.5095(17)
F2	C10	1.3660(15)	C7	C8	1.496(2)
F3	C14	1.3540(16)	C8	C9	1.5323(19)
O1	C6	1.3982(15)	C9	C10	1.5210(19)
O1	C7	1.3679(17)	C11	C12	1.389(2)
O2	C7	1.2011(17)	C11	C16	1.3925(19)
C1	C2	1.3828(19)	C12	C13	1.384(2)
C1	C6	1.3840(18)	C13	C14	1.375(2)
C2	C3	1.388(2)	C14	C15	1.374(2)
C3	C4	1.3889(19)	C15	C16	1.385(2)

Table 3 Bond angles for 3ab.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°

C11	S1	C10	99.40(7)	C10	C9	C8	110.57(11)
C7	O1	C6	120.35(11)	F1	C10	S1	110.59(9)
C2	C1	C6	119.17(13)	F1	C10	C9	110.32(10)
C1	C2	C3	120.03(12)	F2	C10	S1	110.10(9)
C2	C3	C4	119.91(12)	F2	C10	F1	104.52(10)
C3	C4	C5	120.95(13)	F2	C10	C9	108.58(10)
C4	C5	C9	123.00(12)	C9	C10	S1	112.42(9)
C6	C5	C4	117.76(11)	C12	C11	S1	120.69(10)
C6	C5	C9	119.11(11)	C12	C11	C16	119.97(13)
C1	C6	O1	115.75(12)	C16	C11	S1	119.32(11)
C1	C6	C5	122.18(12)	C13	C12	C11	120.45(13)
C5	C6	O1	122.05(11)	C14	C13	C12	118.05(14)
O1	C7	C8	116.81(11)	F3	C14	C13	118.20(13)
O2	C7	O1	117.19(14)	F3	C14	C15	118.65(12)
O2	C7	C8	125.95(13)	C15	C14	C13	123.15(13)
C7	C8	C9	113.38(11)	C14	C15	C16	118.41(13)
C5	C9	C8	108.41(11)	C15	C16	C11	119.97(13)
C5	C9	C10	113.70(10)				

Table 4 Torsion angles for 3ab.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
S1	C11	C12	C13	178.28(11)	C6	C5	C9	C10	95.58(14)
S1	C11	C16	C15	−178.68(10)	C7	O1	C6	C1	−161.63(11)
F3	C14	C15	C16	−179.72(12)	C7	O1	C6	C5	19.71(17)
O1	C7	C8	C9	-39.74(16)	C7	C8	C9	C5	49.29(14)
O2	C7	C8	C9	142.73(13)	C7	C8	C9	C10	-75.97(14)
C1	C2	C3	C4	-0.3(2)	C8	C9	C10	S1	-178.89(9)
C2	C1	C6	O1	−177.75(11)	C8	C9	C10	F1	57.17(13)
C2	C1	C6	C5	0.90(19)	C8	C9	C10	F2	-56.82(14)
C2	C3	C4	C5	0.8(2)	C9	C5	C6	O1	-5.91(17)
C3	C4	C5	C6	-0.44(19)	C9	C5	C6	C1	175.52(11)
C3	C4	C5	C9	−176.22(12)	C10	S1	C11	C12	89.82(12)
C4	C5	C6	O1	178.13(11)	C10	S1	C11	C16	-91.92(12)
C4	C5	C6	C1	-0.43(18)	C11	S1	C10	F1	-72.33(9)
C4	C5	C9	C8	147.91(12)	C11	S1	C10	F2	42.67(10)
C4	C5	C9	C10	-88.69(15)	C11	S1	C10	C9	163.88(9)
C5	C9	C10	S1	58.89(13)	C11	C12	C13	C14	0.4(2)
C5	C9	C10	F1	-65.05(13)	C12	C11	C16	C15	-0.4(2)
C5	C9	C10	F2	−	C12	C13	C14	F3	179.36(12)

				179.04(10)			
C6	O1	C7	O2	−177.81(11)	C12	C13	C14	C15	−0.4(2)
C6	O1	C7	C8	4.44(16)	C13	C14	C15	C16	0.0(2)
C6	C1	C2	C3	−0.5(2)	C14	C15	C16	C11	0.4(2)
C6	C5	C9	C8	−27.82(15)	C16	C11	C12	C13	0.0(2)