Supplementary Information

Facile preparation of dihydro-1,4-benzothiazine derivatives via oxidative ring-expansion of 2-aminobenzothiazoles with olefins

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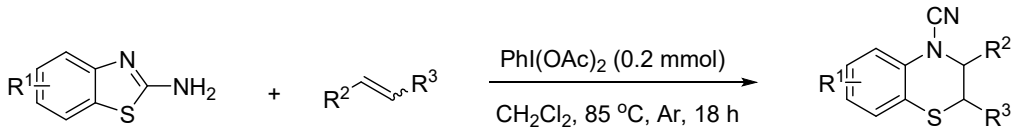
1. General Information

The commercially available reagents were used without further purification unless otherwise noted. Dry solvents were distilled over CaH_2 and stored under argon in Schlenk tubes. All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in preheated glassware under an argon atmosphere using standard Schlenk techniques. Flash column chromatography was performed with silica gel (300–400 mesh). NMR spectra were recorded on Varian Inova–600 MHz, Inova–400 MHz, Bruker DRX–400 spectrometer. Data were reported as chemical shifts in ppm relative to TMS (0.00 ppm) for ^{1}H and $CDCl_3$ (77.0 ppm) for ^{13}C, respectively. The abbreviations used for explaining the multiplicities were as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ^{19}F-NMR spectra were recorded on a BRUKER AVANCE III HD (376 MHz) spectrometer. Mass spectra were measured with an Agilent Technologies 6120 Quadrupole LC/MS. High resolution mass spectrometry (HRMS) were measured with a GCT Premier™ and BRUKER micrOTF-Q III. X-ray crystal structure analyses were measured on a Bruker D8 Venture instrument. Melting points were measured using INESA WRR and values are uncorrected.

2. Experimental Section

2.1 General procedure for preparation of dihydro-1,4-benzothiazine derivatives via oxidative ring-expansion of 2-aminobenzothiazoles with olefins



1 **2** **3**

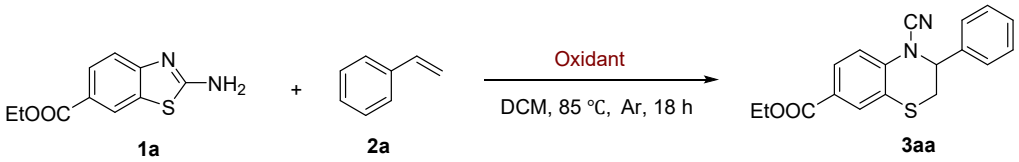
A 10 mL pressure-resistant tube equipped with a magnetic stir bar was charged with the $PhI(OAc)_2$ (64.4 mg, 0.2 mmol), 2-benzoaminothiazole **1** (0.1 mmol, 1.0 equiv), Then the tube was evacuated and backfilled with argon for three times. Then under Ar atmosphere, dichloromethane (1 mL) and Olefins **2** (0.3 mmol, 3.0 equiv) were added to the system. The mixture was stirred at 85 °C for 18 hours. After completion of the reaction (monitored by TLC), then cooled to room temperature. Solvent and volatile reagents were removed by rotary evaporation and the residue was purified by flash column chromatography on silica gel to give the target product.

2.2 General procedure for the scaled-up reaction

A 25 mL round bottom flask equipped with a magnetic stir bar was charged with the $PhI(OAc)_2$ (644 mg, 2 mmol), Ethyl 2-amino-1,3-benzothiazole-6-carboxylate **1a** (222.3 mg, 1 mmol), Then the tube was evacuated and backfilled with argon for three times. Then under Ar atmosphere, chlorobenzene (10 mL) and Styrene **2** (350 μl, 3 mmol) were added to the system. The mixture was stirred at 85 °C for 18 hours. After completion of the reaction (monitored by TLC), then cooled to room temperature. Solvent and volatile reagents were removed by rotary evaporation and the residue was purified by flash column chromatography on silica gel to give the target product.

3. Optimization of Reaction Conditions

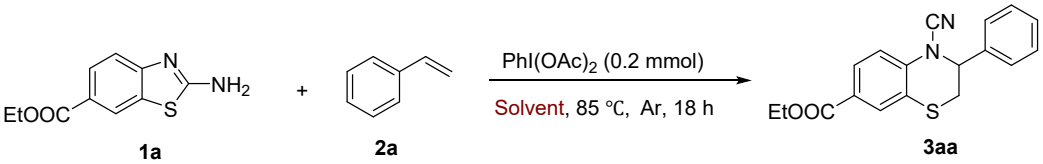
3.1 Table S1. Screening of oxidants



Entry[a]	Oxidant	Yield of **3aa** (%)[b]
1	---	0
2	$PhI(OAc)_2$	97
3[c]	$PhI(OAc)_2$	75
4[d]	$PhI(OAc)_2$	83
5[e]	$PhI(OAc)_2$	96
4	$PhI(OPiv)_2$	96
5	PhIO	68
6	PIFA[f]	0
7	IBX[g]	Trace
8	DMP[h]	0
9	KIO_4	0
10	$Mn(OAc)_3$	0
11	$K_2S_2O_8$	0

[a]Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1 equiv), **2a** (0.3 mmol, 3 equiv), Oxidant (0.2 mmol, 2 equiv), dichloromethane (1 mL) under Ar atmosphere at 85 °C for 18 h. [b]Isolated yields after chromatography are shown. [c]0.1 mmol $PhI(OAc)_2$ was added. [d]DCM solvent without anhydrous treatment and performed under air atmosphere. [e]Using anhydrous DCM solvent and performed under air atmosphere. [f]PIFA: [Bis(trifluoroacetoxy)iodo] benzene. [g]IBX: 2-Iodoxybenzoic acid. [h]DMP: Dess-Martin Periodinane.

3.2 Table S2. Screening of solvents

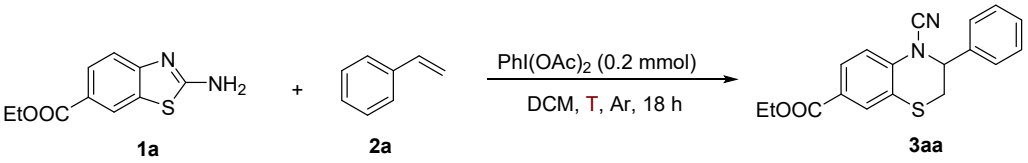


Entry[a]	Solvent	Yield of **3aa** (%)[b]
1	DCM	97
2	DCE	87
3	MeCN	66
4	THF	82
5	CH_3OH	Trace
6	EA	78

7	PhCl	85
8	$CHCl_3$	28
9	DMSO	Trace

[a]Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1 equiv), **2a** (0.3 mmol, 3 equiv), $PhI(OAc)_2$ (0.2 mmol, 2 equiv), solvent (1 mL) under Ar atmosphere at 85 °C for 18 h. [b]Isolated yields after chromatography are shown.

3.3 Table S3. Screening of temperature

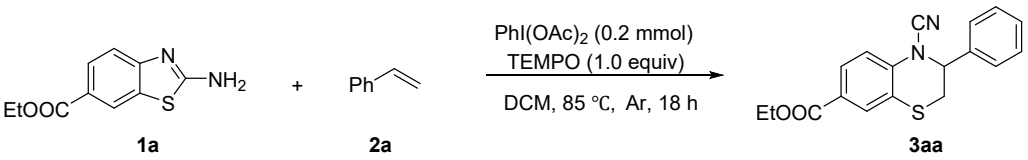


Entry[a]	Temperature (°C)	Yield of **3aa** (%)[b]
1	65	76
2	85	97
3	105	97

[a]Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1 equiv), **2a** (0.3 mmol, 3 equiv), $PhI(OAc)_2$ (0.2 mmol, 2 equiv), dichloromethane (1 mL) under Ar atmosphere at 85 °C for 18 h. [b]Isolated yields after chromatography are shown.

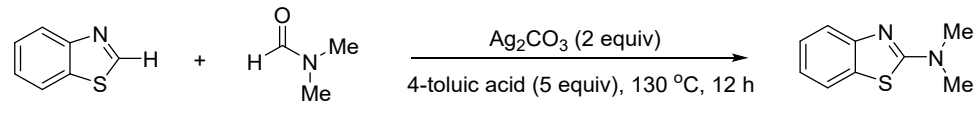
4. Mechanistic Experiments

Radical trapping experiment



A 10 mL pressure-resistant tube equipped with a magnetic stir bar was charged with the $PhI(OAc)_2$ (64.4 mg, 0.2 mmol), **1a** (0.1 mmol, 1.0 equiv) and TEMPO (0.1 mmol, 1 equiv). Then the tube was evacuated and backfilled with argon for three times. Then under Ar atmosphere, dichloromethane (1 mL) and **2a** (0.3 mmol, 3.0 equiv) were added to the system. The mixture was stirred at 85 °C for 18 hours. After completion of the reaction (monitored by TLC), then cooled to room temperature. Solvent and volatile reagents were removed by rotary evaporation and the residue was purified by flash column chromatography on silica gel to afford 20.5 mg of **3aa** (63%).

General procedure for the synthesis of N,N-dimethylbenzo[d]thiazol-2-amine (1p)



1p was synthesized according to relevant literature[1]. To a test tube equipped with a magnetic stir bar was charged with Ag_2CO_3 (275 mg, 1.0 mmol, 2 equiv), 4-toluic acid (340 mg, 2.5 mmol, 5 equiv), DMF (40 equiv) and Benzothiazole (0.5 mmol, 1 equiv) under air. The test tube was sealed with a rubber seuptum, and stirred for 12 h at 130 °C under air. The crude mixture was filtered through a plug of celite and then washed with EtOAc (20 mL). The filtrate was washed with a saturated solution of $NaHCO_3$ (3 x 20 mL) and the aqueous layer was extracted again with EtOAc (3 x 20 mL). Organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was purified by flash column chromatography to afford light yellow solid.

Reaction procedure of 1p with 2a

A 10 mL pressure-resistant tube equipped with a magnetic stir bar was charged with **1p** (0.1 mmol) and $PhI(OAc)_2$ (0.2 mmol, 2 equiv) in 1 mL DCM was added **2a** (0.3 mmol, 3 equiv) , under an argon atmosphere, at 85 °C. The reaction mixture was then stirred for 18 hours.

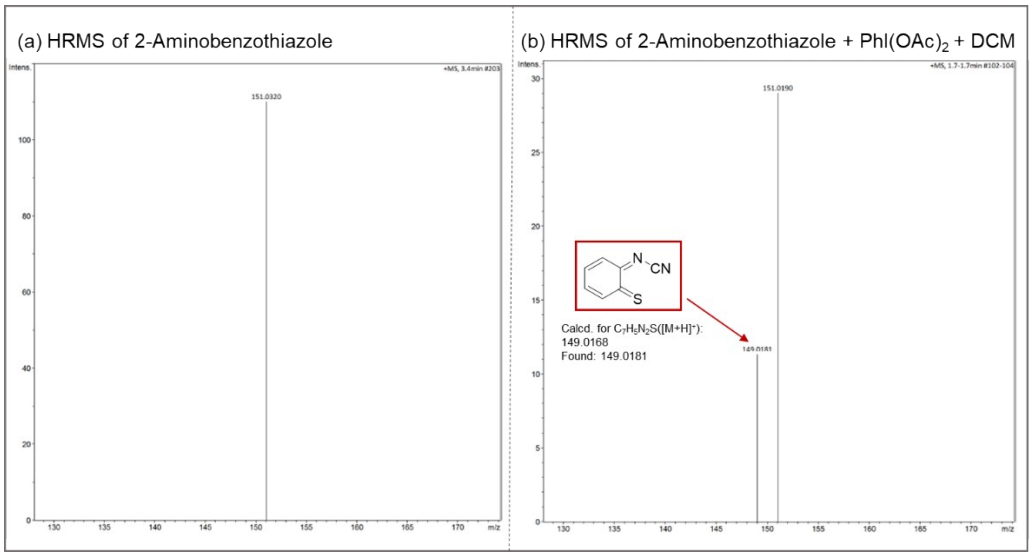


Figure S1. HRMS analysis for 2-aminobenzothiazole and its conversion in the presence of $PhI(OAc)_2$ (0.2 mmol) in DCM (1 mL).

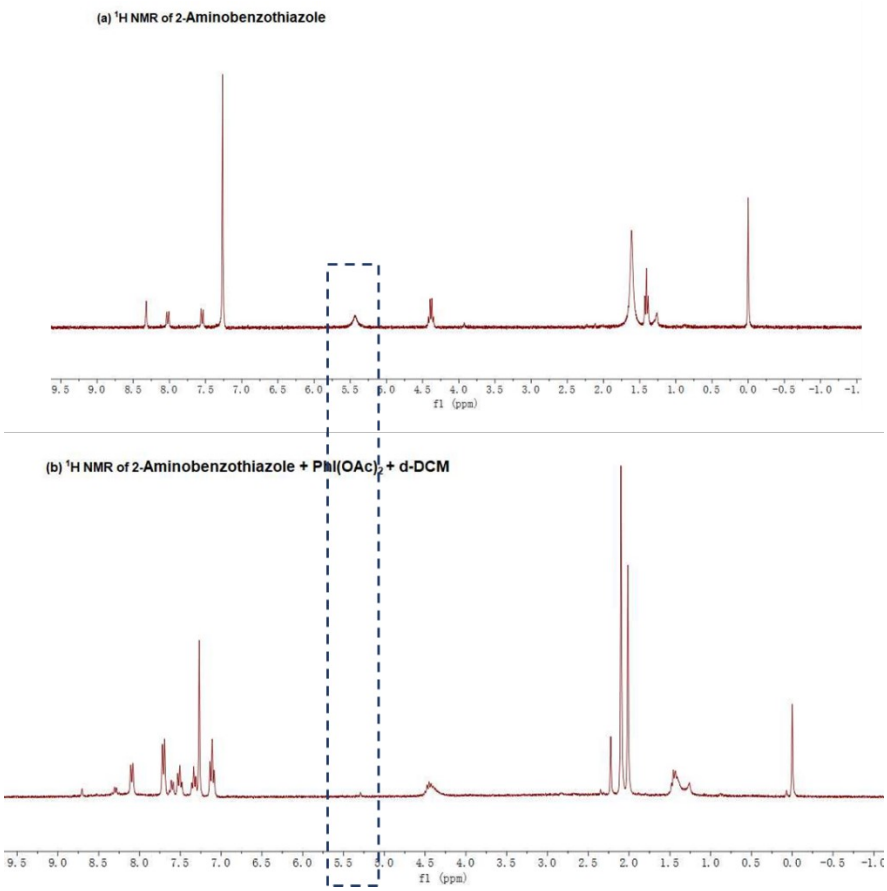
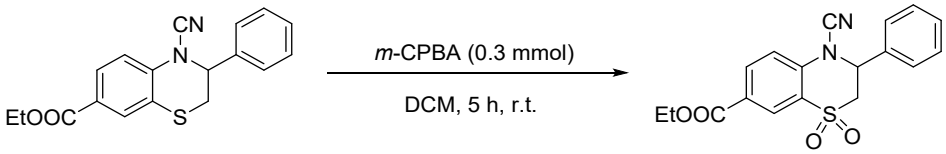


Figure S2. Comparison of ^{1}H NMR of 2-aminobenzothiazole and its conversion in the presence of $PhI(OAc)_2$ (0.2 mmol) in d-DCM (1 mL).

5. Transformations of the synthesized product 3aa

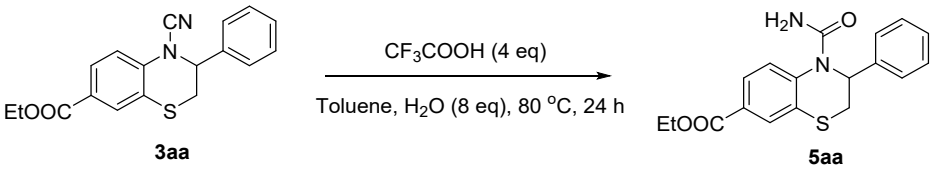
Oxidation Experiments



3aa **4aa**

At room temperature, **3aa** (32.4 mg, 0.1 mmol), 85% *m*-CPBA (60.7 mg, 0.3 mmol) and 1mL CH_2Cl_2 was added to a reaction tube. The mixture was then stirred for 5 h until substrate consumed as indicated by TLC. The resulting mixture was concentrated and extracted with dichloromethane (3 x 15 mL). The combined organic layer was washed with brine (20 mL), dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography with petroleum ether (PE)/ethyl acetate (EA) (5:1) as the eluent to give **4aa** as a white solid (33.5 mg, 94% yield).

Hydrolysis of cyanamide



5aa was synthesized according to literature[2]. **3aa** (0.2 mmol, 1 equiv), trifluoroacetic acid (0.8 mmol, 4 equiv) and H_2O (1.6 mmol, 8 equiv) were added to a round flask (10 mL), heated to 80 °C and kept it stirring for 24 h. The mixture was cooled to room temperature, extracted with EtOAc; the organic layers were combined, washed by brine, dried by $MgSO_4$ and concentrated under reduced pressure to give a residue which was purified by silica gel column chromatography with petroleum ether (PE)/ethyl acetate (EA) (1:1) as the eluent to give product.

6. Computational Studies

6.1 Computational methods

The B3LYP density functional method with Grimme-D3 correction[3] was employed to carry out the computational studies. For geometry optimizations, the LANL2DZ basis set in conjunction with the LANL2DZ pseudopotential[4] was used for I atom. The 6-31G(d,p) basis set was used for other atoms. Vibrational frequency analyses at the same level of theory were performed on all the optimized geometries to characterize stationary points as local minima (no imaginary frequency) or transition states (one imaginary frequency). In addition, intrinsic reaction coordinate (IRC) calculations[5] were used to verify that the transition state connects with appropriate reactant and product. The gas-phase Gibbs energies for all species were obtained at 298.15 K and 1 atm at their respective optimized structures. To consider the effect of solvation, B3LYP-D3 functional with the SMD[6] continuum solvation model (in acetonitrile solvent) was used in single-point energy calculations. A larger basis set, SDD[7] for I atom and 6-311++G(d,p) for the remaining atoms, was utilized for such single-point energy calculation. The solvation Gibbs energy was used for discussion and its value was obtained from the addition of solvation single-point energy and gas-phase thermal correction to Gibbs energy. All calculations were carried out with the Gaussian 09 suite of programs[8]. The 3D structures of optimized intermediates or transition states were demonstrated using the software of CYLView[9].

6.2 More computational results

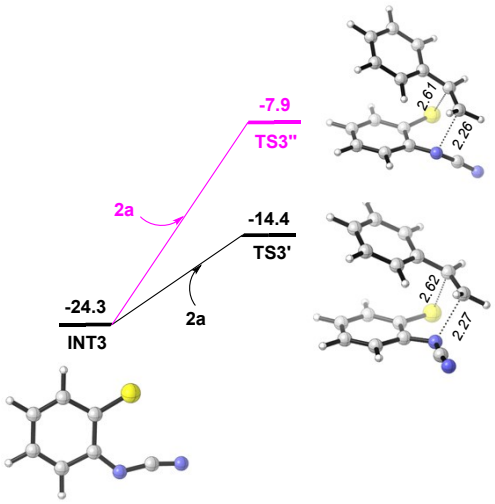


Figure S3. Comparison of the orientation of the cyanamide group in **TS3′** and **TS3″**.

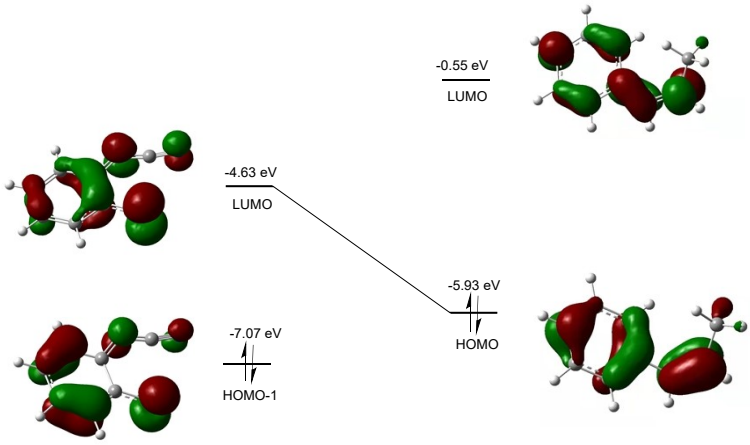


Figure S4. Frontier molecular orbital analysis for **INT3** and **2s** in the [4+2] cycloaddition.

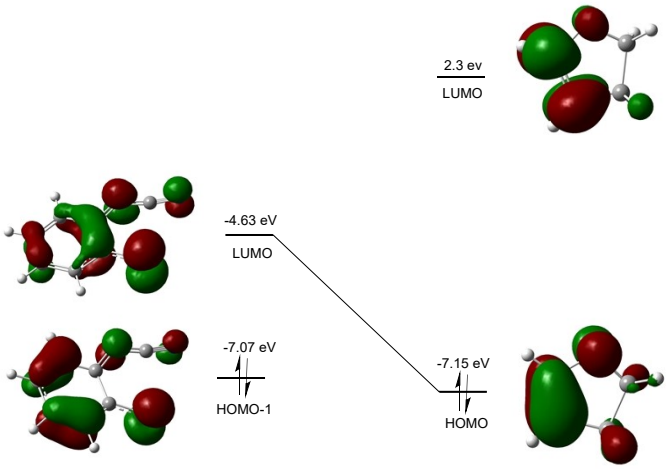


Figure S5. Frontier molecular orbital analysis for **INT3** and **2u** in the [4+2] cycloaddition.

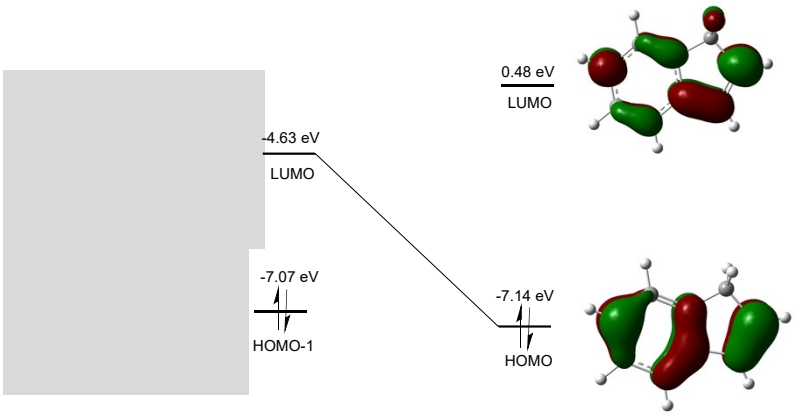
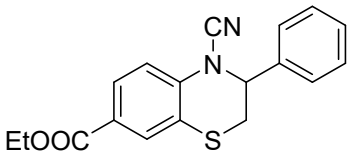


Figure S6. Frontier molecular orbital analysis for **INT3** and **2v** in the [4+2] cycloaddition.

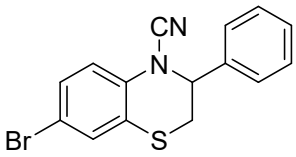
7. Characterization of Compounds

ethyl 4-cyano-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3aa)



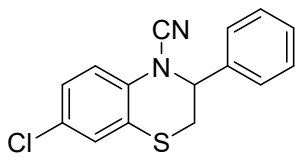
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3aa** after flash column chromatography (10 vol % EtOAc in petroleum ether) as a colorless solid (31.5 mg, 97 %), m.p. 110.6-112.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 2H), 7.46 – 7.39 (m, 4H), 7.33 – 7.28 (m, 2H), 5.23 (dd, *J* = 7.0, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.30 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.18 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 138.3, 137.1, 130.3, 129.5, 129.2, 128.1, 126.8, 125.9, 120.6, 117.2, 111.4, 62.9, 61.2, 31.9, 14.4. HRMS (ESI-TOF): calcd. for $C_{18}H_{16}N_2NaO_2S$([M+Na]$^+$): 347.0825, found: 347.0820.

7-bromo-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ba)



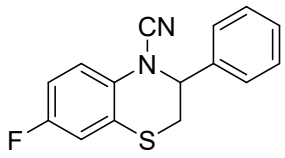
With general procedure 2.1, reaction of **1b** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ba** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow solid (24.7 mg, 75 %). m.p. 125.8-126.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 3H), 7.34 – 7.24 (m, 5H), 5.18 (dd, *J* = 7.1, 3.4 Hz, 1H), 3.27 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.16 (dd, *J* = 13.6, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 133.8, 130.9, 129.7, 129.5, 129.2, 126.8, 122.9, 119.0, 116.2, 111.7, 62.6, 32.0. HRMS (ESI-TOF): calcd. for $C_{15}H_{11}BrN_2NaS$([M+Na]$^+$): 352.9719, found: 352.9728.

7-chloro-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ca)



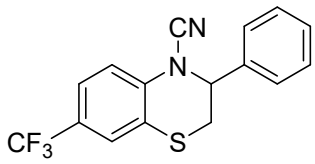
With general procedure 2.1, reaction of **1c** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ca** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (20.6 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 3H), 7.34 – 7.27 (m, 3H), 7.19 – 7.13 (m, 2H), 5.17 (dd, *J* = 7.1, 3.4 Hz, 1H), 3.27 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.16 (dd, *J* = 13.6, 7.1 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 133.2, 129.4, 129.2, 128.8, 128.1, 126.8, 122.5, 118.7, 111.8, 62.6, 32.1. HRMS (ESI-TOF): calcd. for $C_{15}H_{11}ClN_2NaS([M+Na]^+)$: 309.0224, found: 309.0226.

7-fluoro-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3da)



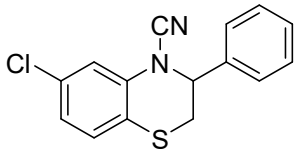
With general procedure 2.1, reaction of **1d** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3da** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (14.3 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 6H), 6.95 – 6.86 (m, 2H), 5.16 (dd, *J* = 7.2, 3.5 Hz, 1H), 3.27 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.18 (dd, *J* = 13.6, 7.2 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4 (d, d, $J_{C\text{-}F}$ = 244 Hz), 137.2, 130.8 (d, $J_{C\text{-}F}$ = 2.9 Hz), 129.4, 129.2, 126.8, 122.7 (d, $J_{C\text{-}F}$ = 8.5 Hz), 119.0 ($J_{C\text{-}F}$ = 8.6 Hz), 115.2 (d, $J_{C\text{-}F}$ = 25.1 Hz), 113.9 (d, $J_{C\text{-}F}$ = 23.1 Hz), 112.3, 62.5, 32.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.9 (s, 1F). HRMS (ESI-TOF): calcd. for $C_{15}H_{11}FN_2NaS([M+Na]^+)$: 293.0519, found: 293.0523.

3-phenyl-7-(trifluoromethyl)-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ea)



With general procedure 2.1, reaction of **1e** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ea** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (28.1 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.38 (m, 6H), 7.32 – 7.26 (m, 2H), 5.23 (dd, *J* = 6.9, 3.4 Hz, 1H), 3.29 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.18 (dd, *J* = 13.7, 6.9 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 137.0, 129.6, 129.3, 126.8, 126.3, (d, $J_{C\text{-}F}$ = 33.4 Hz), 126.0 (q, $J_{C\text{-}F}$ = 3.8 Hz), 126.0 (d, $J_{C\text{-}F}$ = 33.4 Hz), 125.0, 123.8 (q, $J_{C\text{-}F}$= 3.7 Hz), 122.3, 121.6, 62.8, 31.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.2 (s, 3F). HRMS (ESI-TOF): calcd. for $C_{16}H_{11}F_3N_2NaS([M+Na]^+)$: 343.0487, found: 343.0477.

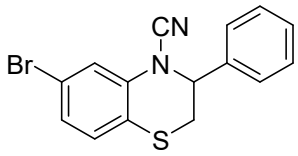
6-chloro-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3fa)



With general procedure 2.1, reaction of **1f** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3fa** after flash column

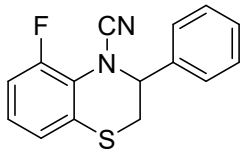
chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (19.2 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.35 (m, 4H), 7.29 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.1 Hz, 1H), 5.18 (dd, *J* = 7.1, 3.4 Hz, 1H), 3.26 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.15 (dd, *J* = 13.6, 7.2 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 135.6, 132.3, 129.7, 129.5, 129.2, 126.8, 123.9, 119.2, 117.6, 111.6, 62.7, 32.1. HRMS (ESI-TOF): calcd. for $C_{15}H_{11}ClN_2NaS$([M+Na]$^+$): 309.0224, found: 309.0223.

6-bromo-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ga)



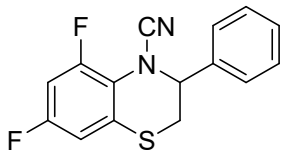
With general procedure 2.1, reaction of **1g** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ga** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (21.2 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 1.9 Hz, 1H), 7.41 (qd, *J* = 5.3, 1.8 Hz, 3H), 7.29 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.12 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 5.17 (dd, *J* = 7.1, 3.5 Hz, 1H), 3.26 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.14 (dd, *J* = 13.6, 7.1 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 135.7, 129.9, 129.5, 129.2, 126.8, 126.8, 120.4, 119.9, 119.7, 111.6, 62.7, 32.1. HRMS (ESI-TOF): calcd. for $C_{15}H_{11}BrN_2NaS$([M+Na]$^+$): 352.9719, found: 352.9710.

5-fluoro-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ha)



With general procedure 2.1, reaction of **1h** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ha** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (17.5 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 5H), 7.03 – 6.94 (m, 3H), 5.15 (dd, *J* = 8.6, 4.1 Hz, 1H), 3.37 (dd, *J* = 13.6, 4.1 Hz, 1H), 3.21 (dd, *J* = 13.6, 8.6 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4 (d, $J_{C\text{-}F}$ = 250.8 Hz), 136.4, 129.3, 129.2, 127.8, 126.7, 125.3 (d, $J_{C\text{-}F}$ = 8.4 Hz), 124.1 (d, $J_{C\text{-}F}$ = 8.4 Hz), 124.0 (d, $J_{C\text{-}F}$ = 10.8 Hz), 114.1 (d, $J_{C\text{-}F}$ = 19.7 Hz), 112.7, 64.8, 33.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.0 (s, 1F). HRMS (ESI-TOF): calcd. for $C_{15}H_{11}FN_2NaS$([M+Na]$^+$): 293.0519, found: 293.0531.

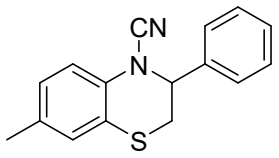
5,7-difluoro-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ia)



With general procedure 2.1, reaction of **1i** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ia** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (14.3 mg, 50%). m.p. 105.1-106.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.35 (m, 5H), 6.81 – 6.71 (m, 2H), 5.10 (dd, *J* = 8.4, 4.0

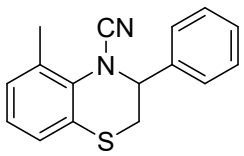
Hz, 1H), 3.43 (dd, J = 13.6, 4.0 Hz, 1H), 3.31 (dd, J = 13.5, 8.4 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0 (dd, $J_{C\text{-}F}$ = 247.9, 12.0 Hz), 154.6 (dd, $J_{C\text{-}F}$ = 253.4, 12.8 Hz), 135.8, 129.4, 129.3, 126.8, 120.2 (dd, $J_{C\text{-}F}$ = 11.4, 3.9 Hz), 112.5, 110.6 (dd, $J_{C\text{-}F}$ = 24.5, 3.8 Hz), 102.6 (dd, $J_{C\text{-}F}$ = 26.6, 23.4 Hz), 63.7, 32.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.1 (d, J = 6.0 Hz, 1F), -117.0 (d, J = 6.1 Hz, 1F). HRMS (ESI-TOF): calcd. for $C_{15}H_{10}F_2N_2NaS([M+Na]^+)$: 311.0425, found: 311.0443.

7-methyl-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ja)



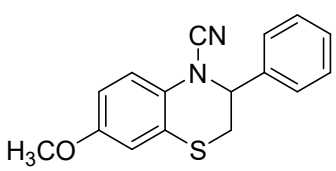
With general procedure 2.1, reaction of **1j** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ja** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (12.1 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 3H), 7.34 – 7.28 (m, 3H), 7.03 – 6.97 (m, 2H), 5.17 (dd, J = 7.2, 3.5 Hz, 1H), 3.27 (dd, J = 13.5, 3.5 Hz, 1H), 3.15 (dd, J = 13.5, 7.2 Hz, 1H), 2.28 (s, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 133.5, 132.1, 129.2, 129.1, 129.0, 127.7, 126.8, 120.4, 117.6, 112.6, 62.6, 32.4, 20.5. HRMS (ESI-TOF): calcd. for $C_{16}H_{14}N_2NaS([M+Na]^+)$: 289.0770, found: 289.0811.

5-methyl-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ka)



With general procedure 2.1, reaction of **1k** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ka** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (20.9 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (ddt, J = 8.5, 6.1, 3.2 Hz, 5H), 7.11 (q, J = 4.0, 3.5 Hz, 1H), 7.04 (d, J = 5.0 Hz, 2H), 5.00 (dd, J = 9.6, 4.7 Hz, 1H), 3.39 (dd, J = 13.3, 4.7 Hz, 1H), 3.33 (dd, J = 13.3, 9.6 Hz, 1H), 2.43 (s, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 134.1, 132.8, 129.2, 129.2, 129.2, 128.3, 127.0, 126.3, 126.2, 113.4, 65.4, 33.3, 18.4. HRMS (ESI-TOF): calcd. for $C_{16}H_{14}N_2NaS([M+Na]^+)$: 289.0770, found: 289.0773.

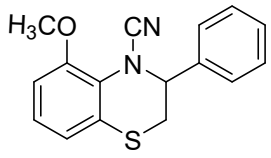
7-methoxy-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3la)



With general procedure 2.1, reaction of **1l** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3la** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (15.0 mg, 53%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 3H), 7.34 – 7.29 (m, 3H), 6.78 – 6.71 (m, 2H), 5.13 (dd, J = 7.3, 3.5 Hz, 1H), 3.76 (s, 3H), 3.26 (dd, J = 13.5, 3.6 Hz, 1H), 3.16 (dd, J = 13.5, 7.3 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 137.6, 129.2, 129.1,

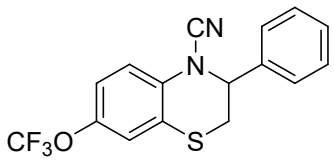
127.9, 126.9, 122.0, 118.9, 113.2, 113.2, 112.9, 62.5, 55.7, 32.5. HRMS (ESI-TOF): calcd. for $C_{16}H_{14}N_2NaOS([M+Na]^+)$: 305.0719, found: 305.0728.

5-methoxy-3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3ma)



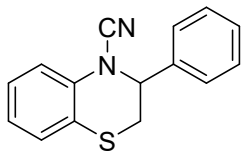
With general procedure 2.1, reaction of **1m** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3ma** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (18.1 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 5H), 7.04 (t, *J* = 8.1 Hz, 1H), 6.79 (ddd, *J* = 17.8, 8.1, 1.3 Hz, 2H), 5.12 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.95 (s, 3H), 3.39 (dd, *J* = 13.4, 4.3 Hz, 1H), 3.20 (dd, *J* = 13.4, 8.9 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 137.0, 129.0, 128.9, 127.5, 126.7, 125.5, 124.5, 120.5, 113.8, 109.6, 65.0, 56.2, 33.5. HRMS (ESI-TOF): calcd. for $C_{16}H_{14}N_2NaOS([M+Na]^+)$: 305.0719, found: 305.0730.

3-phenyl-7-(trifluoromethoxy)-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3na)



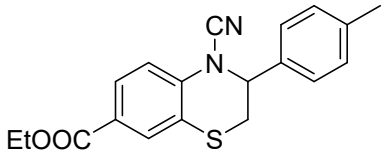
With general procedure 2.1, reaction of **1n** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3na** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (24.1 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 4H), 7.33 – 7.28 (m, 2H), 7.09 – 7.04 (m, 2H), 5.19 (dd, *J* = 7.1, 3.5 Hz, 1H), 3.28 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.19 (dd, *J* = 13.6, 7.1 Hz, 1H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6 (d, $J_{C\text{-}F}$= 2.2 Hz), 137.1, 133.3, 129.5, 129.3, 126.8, 122.5, 121.2, 120.4 (d, $J_{C\text{-}F}$ = 257.9 Hz), 119.6, 118.6, 111.8, 62.6, 32.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.1 (s, 3F). HRMS (ESI-TOF): calcd. for $C_{16}H_{11}F_3N_2NaOS([M+Na]^+)$: 359.0436, found: 359.0432.

3-phenyl-2,3-dihydro-4H-benzo[b][1,4]thiazine-4-carbonitrile (3oa)



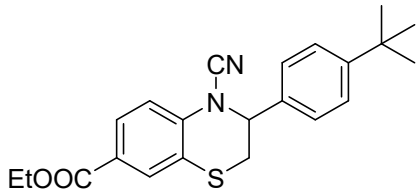
With general procedure 2.1, reaction of **1o** (0.1 mmol) and **2a** (0.3 mmol) provided the product **3oa** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (14.1 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dtd, *J* = 6.7, 5.1, 1.4 Hz, 4H), 7.31 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.22 – 7.17 (m, 2H), 7.03 – 6.98 (m, 1H), 5.19 (dd, *J* = 7.1, 3.5 Hz, 1H), 3.27 (dd, *J* = 13.5, 3.5 Hz, 1H), 3.16 (dd, *J* = 13.5, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 134.6, 129.3, 129.1, 128.8, 126.9, 126.9, 123.7, 120.8, 117.7, 112.3, 62.8, 32.3. HRMS (ESI-TOF): calcd. for $C_{15}H_{12}N_2NaS([M+Na]^+)$: 275.0613, found: 275.0620.

ethyl 4-cyano-3-(p-tolyl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ab)



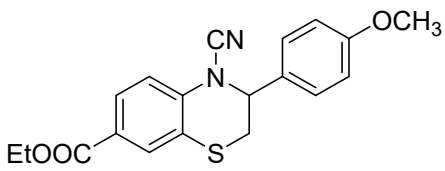
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2b** (0.3 mmol) provided the product **3ab** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (25.4 mg, 75%). m.p. 163.7-164.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.80 (m, 2H), 7.43 (d, *J* = 8.7 Hz, 1H), 7.25 – 7.16 (m, 4H), 5.17 (dd, *J* = 7.2, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.26 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.18 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.36 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 139.5, 138.4, 134.1, 130.2, 129.9, 128.0, 126.8, 125.8, 120.6, 117.2, 111.4, 62.8, 61.2, 31.9, 21.3, 14.4. HRMS (ESI-TOF): calcd. for $C_{19}H_{18}N_2NaO_2S$([M+Na]$^+$): 361.0981, found: 361.0988.

ethyl 3-(4-(tert-butyl)phenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ac)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2c** (0.3 mmol) provided the product **3ac** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (31.9 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H), 7.44 (dd, *J* = 8.5, 6.0 Hz, 3H), 7.26 – 7.21 (m, 2H), 5.21 (dd, *J* = 7.1, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.29 (dd, *J* = 13.6, 3.5 Hz, 1H), 3.18 (dd, *J* = 13.6, 7.1 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.32 (s, 9H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 152.5, 138.4, 134.1, 130.3, 128.1, 126.6, 126.1, 125.8, 120.7, 117.2, 111.5, 62.7, 61.2, 34.7, 32.0, 31.3, 14.4. HRMS (ESI-TOF): calcd. for $C_{22}H_{24}N_2NaO_2S$([M+Na]$^+$): 403.1451, found: 403.1447.

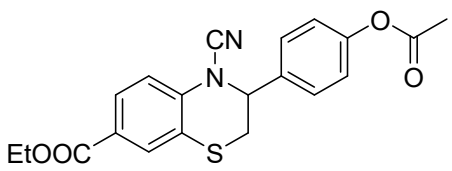
ethyl 4-cyano-3-(4-methoxyphenyl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ad)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2d** (0.3 mmol) provided the product **3ad** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (28.4 mg, 80%). m.p. 146.7-167.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 2.0 Hz, 1H), 7.83 (dd, *J* = 9.2, 1.9 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.25 (dd, *J* = 9.0, 2.4 Hz, 2H), 6.95 – 6.92 (m, 2H), 5.14 (dd, *J* = 7.2, 3.6 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.24 – 3.16 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 160.5, 138.5, 130.2, 129.0, 128.3, 128.0, 125.8, 120.6, 117.3, 114.6, 111.3,

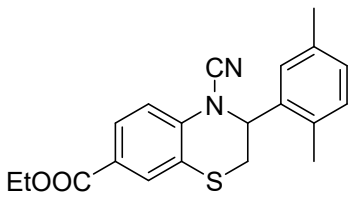
62.6, 61.2, 55.4, 32.0, 14.3. HRMS (ESI-TOF): calcd. for $C_{19}H_{18}N_2NaO_3S([M+Na]^+)$: 377.0930, found: 377.0939.

ethyl 3-(4-acetoxyphenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ae)



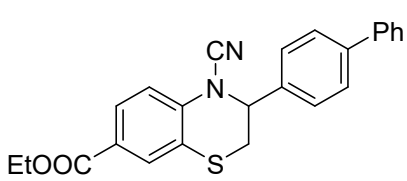
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2e** (0.3 mmol) provided the product **3ae** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (29.1 mg, 76%). m.p. 168.9-171.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.44 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 2H), 5.26 (dd, *J* = 6.8, 3.4 Hz, 1H), 4.37 (qd, *J* = 7.1, 0.9 Hz, 2H), 3.31 (ddd, *J* = 12.9, 3.9, 1.8 Hz, 1H), 3.15 (dd, *J* = 14.4, 6.1 Hz, 1H), 2.30 (d, *J* = 1.2 Hz, 3H), 1.39 (td, *J* = 7.1, 0.9 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 165.3, 151.4, 138.1, 134.6, 130.3, 128.2, 128.0, 126.0, 122.4, 120.6, 117.2, 111.3, 62.4, 61.2, 31.9, 21.1, 14.3. HRMS (ESI-TOF): calcd. for $C_{20}H_{18}N_2NaO_4S([M+Na]^+)$: 405.0879, found: 405.0873.

ethyl 4-cyano-3-(2,5-dimethylphenyl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3af)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2f** (0.3 mmol) provided the product **3af** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (27.2 mg, 77%). m.p. 132.4-133.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.9 Hz, 1H), 7.86 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.14 – 7.08 (m, 2H), 7.02 (s, 1H), 5.38 (dd, *J* = 6.6, 4.8 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.20 – 3.16 (m, 2H), 2.37 (s, 3H), 2.30 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 139.0, 136.5, 134.7, 132.2, 131.3, 130.4, 130.2, 128.2, 127.3, 125.8, 120.8, 117.3, 111.3, 61.2, 60.3, 30.8, 21.2, 18.8, 14.4. HRMS (ESI-TOF): calcd. for $C_{20}H_{20}N_2NaO_2S([M+Na]^+)$: 375.1138, found: 375.1135.

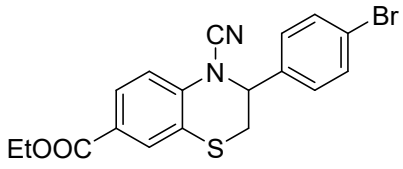
ethyl 3-([1,1'-biphenyl]-4-yl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ag)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2g** (0.3 mmol) provided the product **3ag** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (25.9 mg,

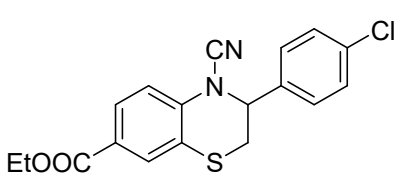
65%). m.p. 169.3-170.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.84 (m, 2H), 7.66 – 7.60 (m, 2H), 7.60 – 7.54 (m, 2H), 7.49 – 7.42 (m, 3H), 7.39 – 7.33 (m, 3H), 5.29 (dd, *J* = 6.9, 3.4 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.33 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.21 (dd, *J* = 13.7, 7.0 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 142.4, 140.1, 138.3, 136.0, 130.4, 128.9, 128.2, 127.9, 127.8, 127.3, 127.2, 125.9, 120.6, 117.2, 111.5, 62.7, 61.3, 32.0, 14.4. HRMS (ESI-TOF): calcd. for $C_{24}H_{20}N_2NaO_2S([M+Na]^+)$: 423.1138, found: 423.1144.

ethyl 3-(4-bromophenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ah)



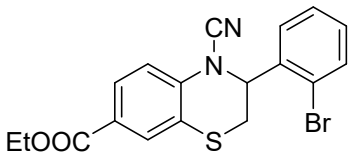
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2h** (0.3 mmol) provided the product **3ah** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (29.4 mg, 73%). m.p. 144.2-145.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.81 (m, 2H), 7.59 – 7.51 (m, 2H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.21 – 7.15 (m, 2H), 5.24 (dd, *J* = 6.6, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.31 (dd, *J* = 13.7, 3.4 Hz, 1H), 3.13 (dd, *J* = 13.7, 6.6 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.9, 136.2, 132.4, 130.4, 128.5, 128.3, 126.1, 123.6, 120.4, 117.2, 111.2, 62.3, 61.3, 31.8, 14.3. HRMS (ESI-TOF): calcd. for $C_{18}H_{15}BrN_2NaO_2S([M+Na]^+)$: 424.9930, found: 424.9935.

ethyl 3-(4-chlorophenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ai)



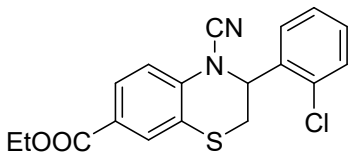
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2i** (0.3 mmol) provided the product **3ai** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (18.3 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H), 7.47 – 7.36 (m, 3H), 7.28 – 7.21 (m, 2H), 5.25 (dd, *J* = 6.7, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.31 (dd, *J* = 13.7, 3.4 Hz, 1H), 3.14 (dd, *J* = 13.7, 6.7 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.9, 135.7, 135.5, 130.4, 129.5, 128.3, 128.2, 126.1, 120.4, 117.2, 111.2, 62.3, 61.3, 31.8, 14.3. HRMS (ESI-TOF): calcd. for $C_{18}H_{15}ClN_2NaO_2S([M+Na]^+)$: 381.0435, found: 381.0436.

ethyl 3-(2-bromophenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3aj)



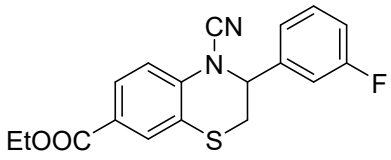
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2j** (0.3 mmol) provided the product **3aj** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (20.2 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.86 (m, 2H), 7.63 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.34 (td, *J* = 7.5, 1.3 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.19 (dd, *J* = 7.7, 1.7 Hz, 1H), 5.77 – 5.72 (m, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.35 (dd, *J* = 13.8, 3.7 Hz, 1H), 3.26 (dd, *J* = 13.8, 5.1 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 138.1, 136.2, 133.6, 130.7, 130.6, 128.5, 128.5, 128.0, 126.0, 121.9, 120.5, 116.9, 111.3, 62.4, 61.3, 29.9, 14.4. HRMS (ESI-TOF): calcd. for $C_{18}H_{15}BrN_2NaO_2S$([M+Na]$^+$): 424.9930, found: 424.9905.

ethyl 3-(2-chlorophenyl)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ak)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2k** (0.3 mmol) provided the product **3ak** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (23.3mg, 65%). m.p. 131.8-132.7 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.83 (m, 2H), 7.46 (dd, *J* = 16.7, 8.2 Hz, 2H), 7.35 – 7.27 (m, 2H), 7.20 (dd, *J* = 7.6, 1.9 Hz, 1H), 5.78 (t, *J* = 4.4 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.35 (dd, *J* = 13.8, 4.4 Hz ,1H), 3.25 (dd, *J* = 13.8, 5.2 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 138.0, 134.7, 131.9, 130.6, 130.4, 130.3, 128.4, 128.4, 127.4, 126.0, 120.5, 116.9, 111.3, 61.3, 60.2, 29.7, 14.4. HRMS (ESI-TOF): calcd. for $C_{18}H_{15}ClN_2NaO_2S$([M+Na]$^+$): 381.0435, found: 381.0431.

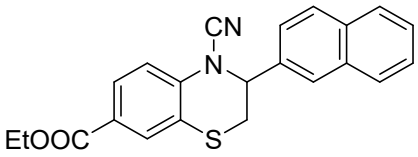
ethyl 4-cyano-3-(3-fluorophenyl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3al)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2l** (0.3 mmol) provided the product **3al** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (13.1 mg, 38%). m.p. 167.6-168.4 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.84 (m, 2H), 7.48 – 7.36 (m, 2H), 7.10 (dq, *J* = 8.2, 5.0, 3.7 Hz, 2H), 7.01 (dt, *J* = 9.3, 2.2 Hz, 1H), 5.28 (dd, *J* = 6.5, 3.5 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.34 (dd, *J* = 13.7, 3.5 Hz, 1H), 3.16 (dd, *J* = 13.7, 6.4 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 163.0 (d, $J_{C\text{-}F}$ = 248.1 Hz), 139.6 (d, $J_{C\text{-}F}$ = 6.6 Hz), 137.8, 131.0 (d, $J_{C\text{-}F}$ = 8.1 Hz), 130.4, 128.3, 126.1, 122.4 (d, $J_{C\text{-}F}$ = 2.9 Hz), 120.5, 117.2, 116.5 (d, $J_{C\text{-}F}$ = 21.1 Hz), 113.9 (d, $J_{C\text{-}F}$ =

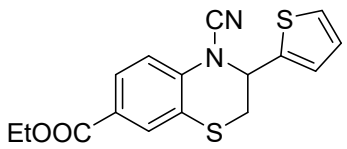
23.1 Hz), 111.3, 62.3 (d, $J_{C\text{-}F}$ = 2.0 Hz), 61.3, 31.7, 14.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.9 (s, 1F). HRMS (ESI-TOF): calcd. for $C_{18}H_{15}FN_2NaO_2S$([M+Na]$^+$): 365.0730, found: 365.0758.

ethyl 4-cyano-3-(naphthalen-2-yl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3am)



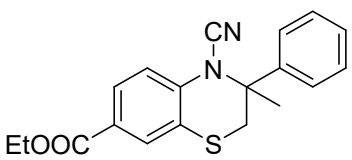
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2m** (0.3 mmol) provided the product **3am** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (27.3 mg, 73%). m.p. 146.9-147.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.78 (m, 5H), 7.74 (s, 1H), 7.53 – 7.45 (m, 3H), 7.36 (dd, *J* = 8.5, 1.9 Hz, 1H), 5.37 (dd, *J* = 6.9, 3.7 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.34 – 3.22 (m, 2H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 138.4, 134.4, 133.6, 133.1, 130.4, 129.4, 128.3, 128.2, 127.9, 127.0, 126.9, 126.8, 125.9, 123.5, 120.7, 117.3, 111.5, 63.2, 61.3, 32.0, 14.3. HRMS (ESI-TOF): calcd. for $C_{22}H_{18}N_2NaO_2S$([M+Na]$^+$): 397.0981, found: 397.1006.

ethyl 4-cyano-3-(thiophen-2-yl)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3an)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2n** (0.3 mmol) provided the product **3an** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow solid (23.2 mg, 70%). m.p. 91.2-92.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 1.9 Hz, 1H), 7.82 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.20 – 7.14 (m, 1H), 7.03 (dd, *J* = 5.1, 3.6 Hz, 1H), 5.52 (dd, *J* = 6.4, 3.4 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.43 (dd, *J* = 13.6, 3.4 Hz, 1H), 3.26 (dd, *J* = 13.6, 6.4 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 139.0, 137.3, 130.0, 128.1, 128.0, 127.4, 127.0, 126.0, 120.3, 117.4, 111.1, 61.3, 58.2, 31.8, 14.4. HRMS (ESI-TOF): calcd. for $C_{16}H_{14}N_2NaO_2S_2$([M+Na]$^+$): 353.0389, found: 353.0411.

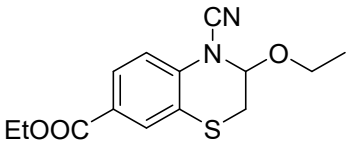
ethyl 4-cyano-3-methyl-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ao)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2o** (0.3 mmol) provided the product **3ao** after flash column chromatography (1 vol % EtOAc in petroleum

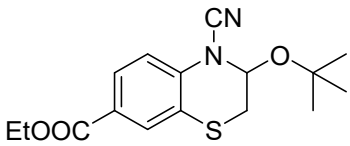
ether) as a colorless solid (31.3 mg, 92%). m.p. 131.3-132.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.76 (m, 2H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.39 – 7.28 (m, 5H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.30 (d, *J* = 13.8 Hz, 1H), 3.18 (d, *J* = 13.6 Hz, 1H), 2.05 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 141.2, 138.4, 130.0, 129.1, 128.5, 127.8, 125.8, 125.3, 120.9, 117.7, 110.6, 63.3, 61.2, 38.1, 27.9, 14.4. HRMS (ESI-TOF): calcd. for $C_{19}H_{18}N_2NaO_2S$([M+Na]$^+$): 361.0981, found: 361.1000.

ethyl 4-cyano-3-ethoxy-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ap)



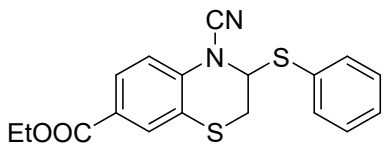
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2p** (0.3 mmol) provided the product **3ap** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless oil (16.1 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.9 Hz, 1H), 7.81 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 5.38 (dd, *J* = 3.9, 2.3 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.97 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.86 – 3.79 (m, 1H), 3.27 (dd, *J* = 13.3, 2.3 Hz, 1H), 3.11 (dd, *J* = 13.3, 3.9 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 135.5, 129.5, 127.5, 126.4, 120.6, 117.5, 111.8, 84.3, 65.4, 61.2, 29.9, 14.9, 14.3. HRMS (ESI-TOF): calcd. For $C_{14}H_{16}N_2NaO_3S$([M+Na]$^+$): 315.0774, found: 315.0778.

ethyl 3-(tert-butoxy)-4-cyano-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3aq)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2q** (0.3 mmol) provided the product **3aq** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (9.9 mg, 31%). m.p. 87.3-88.2 °C. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.84 (d, *J* = 2.0 Hz, 1H), 7.77 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 1H), 5.47 (dd, *J* = 5.3, 2.4 Hz, 1H), 4.31 (t, *J* = 7.1 Hz, 2H), 3.23 (dd, *J* = 13.0, 2.4 Hz, 1H), 2.96 (dd, *J* = 13.1, 5.2 Hz, 1H), 1.36 (d, *J* = 2.4 Hz, 12H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 165.2, 136.8, 129.1, 127.2, 126.1, 120.8, 117.8, 111.0, 79.0, 76.8, 61.1, 32.1, 28.1, 14.1. HRMS (ESI-TOF): calcd. For $C_{16}H_{20}N_2NaO_3S$([M+Na]$^+$): 343.1087, found: 343.1086.

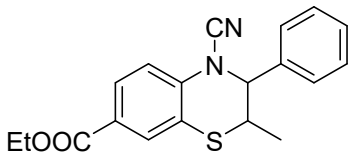
ethyl 4-cyano-3-(phenylthio)-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3ar)



With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2r** (0.3 mmol) provided the product **3ar** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (24.2 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.78 (m, 2H), 7.62 – 7.56 (m, 2H), 7.43 – 7.35 (m, 3H), 7.29 (d,

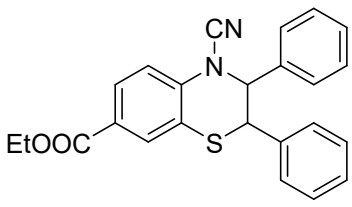
J = 8.5 Hz, 1H), 5.42 (dd, *J* = 5.2, 3.2 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.56 (dd, *J* = 13.4, 3.2 Hz, 1H), 3.20 (dd, *J* = 13.5, 5.2 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 136.0, 135.4, 130.0, 130.0, 129.8, 129.7, 127.9, 126.6, 120.8, 118.1, 110.7, 67.7, 61.3, 31.4, 14.3. HRMS (ESI-TOF): calcd. For $C_{18}H_{16}N_2NaO_2S_2$([M+Na]$^+$): 379.0545, found: 379.0540.

ethyl 4-cyano-2-methyl-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3as)



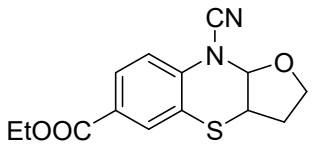
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2s** (0.3 mmol) provided the product **3as** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (31.2 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2.0H, single isomer), 7.51 – 7.33 (m, 4.3H, three isomers), 7.26 (dq, *J* = 5.0, 2.3 Hz, 2.1H, two isomers), 5.14 (d, *J* = 3.6 Hz, 0.5H, single isomer), 4.83 (d, *J* = 6.8 Hz, 1.0H, single isomer), 4.36 (q, *J* = 7.1 Hz, 2.1H, two isomers), 3.67 (p, *J* = 3.6 Hz, 0.5H, single isomer), 3.36 (p, *J* = 6.8 Hz, 1.0H, single isomer), 1.38 (m, *J* = 7.1 Hz, 3.2H, two isomers), 1.33 (d, *J* = 6.8 Hz, 3.0H, single isomer), 1.18 (d, *J* = 7.0 Hz, 0.2H, single isomer). ^{13}C NMR (100 MHz, $CDCl_3$), major product: δ 165.4, 138.0, 136.9, 130.3, 129.5, 129.2, 128.0, 127.1, 126.1, 120.4, 116.9, 111.7, 69.1, 61.2, 39.1, 19.3, 14.4. HRMS (ESI-TOF): calcd. For $C_{19}H_{18}N_2NaO_2S$([M+Na]$^+$): 361.0981, found: 361.0992.

ethyl 4-cyano-2,3-diphenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (3at)



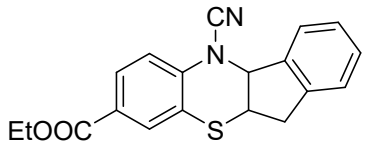
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2t** (0.3 mmol) provided the product **3at** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a yellow oil (20.0 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.9 Hz, 1H), 7.89 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.28 (dd, *J* = 5.0, 1.8 Hz, 3H), 7.23 (dd, *J* = 5.0, 1.8 Hz, 3H), 7.14 (dd, *J* = 6.7, 2.7 Hz, 4H), 5.20 (d, *J* = 8.4 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.32 (d, *J* = 8.4 Hz, 1H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 138.9, 136.3, 135.8, 130.0, 129.5, 129.0, 128.6, 128.3, 128.2, 127.5, 126.1, 122.4, 117.4, 111.3, 77.4, 77.1, 76.8, 69.5, 61.3, 49.4, 14.4. HRMS (ESI-TOF): calcd. For $C_{24}H_{21}N_2O_2S$([M+H]$^+$): 401.1318, found: 401.1332.

ethyl 9-cyano-3,3a,9,9a-tetrahydro-2H-benzo[b]furo[2,3-e][1,4]thiazine-6-carboxylate (3au)



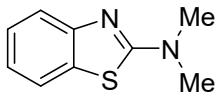
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2u** (0.3 mmol) provided the product **3au** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (14.3 mg, 49%). m.p. 87.8-88.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.90 (m, 2H), 7.39 (d, *J* = 8.5 Hz, 1H), 5.73 (d, *J* = 6.3 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 4.11 – 3.98 (m, 2H), 3.82 (td, *J* = 8.9, 6.2 Hz, 1H), 2.40 (dtd, *J* = 13.3, 7.7, 5.1 Hz, 1H), 1.90 – 1.84 (m, 1H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 139.8, 131.3, 129.3, 127.0, 120.2, 117.8, 111.0, 91.0, 68.4, 61.3, 41.7, 30.3, 14.3. HRMS (ESI-TOF): calcd. For $C_{14}H_{14}N_2NaO_3S([M+Na]^+)$: 313.0617, found: 313.0618.

ethyl 10-cyano-4b,10,10a,11-tetrahydrobenzo[b]indeno[2,1-e][1,4]thiazine-7-carboxylate (3av)



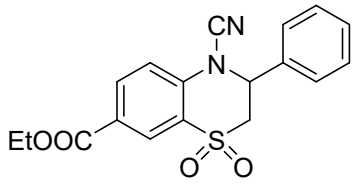
With general procedure 2.1, reaction of **1a** (0.1 mmol) and **2v** (0.3 mmol) provided the product **3av** after flash column chromatography (1 vol % EtOAc in petroleum ether) as a colorless solid (28.6mg, 85%). m.p. 112.6-113.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.0 Hz, 1H), 7.79 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.66 – 7.57 (m, 1H), 7.36 – 7.17 (m, 4H), 5.37 (d, *J* = 6.3 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.16 (q, *J* = 6.4 Hz, 1H), 3.30 (dd, *J* = 16.4, 6.9 Hz, 1H), 2.98 (dd, *J* = 16.4, 6.1 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 140.7, 139.6, 138.7, 130.7, 130.1, 128.3, 127.7, 126.5, 125.4, 125.2, 122.0, 117.8, 112.3, 67.2, 61.2, 43.3, 38.2, 14.3. HRMS (ESI-TOF): calcd. For $C_{19}H_{16}N_2NaO_2S([M+Na]^+)$: 359.0825, found: 359.0848.

N,N-dimethylbenzo[d]thiazol-2-amine (1p)



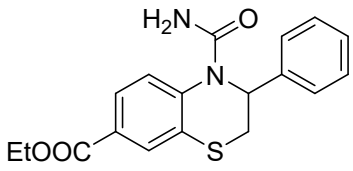
With general procedure 4.2, reaction of Benzothiazole (0.5 mmol) and DMF (40 equiv) provided the product **1p** after flash column chromatography (10 vol % EtOAc in petroleum ether) as a yellow solid (40 mg, 45%). m.p. 84.3-85.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (td, *J* = 7.3, 6.7, 1.2 Hz, 2H), 7.23 – 7.16 (m, 1H), 6.96 (td, *J* = 7.6, 1.2 Hz, 1H), 3.10 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 153.3, 131.2, 125.9, 120.9, 120.6, 118.8, 40.2. HRMS (ESI-TOF): calcd. For $C_9H_{11}N_2S([M+H]^+)$: 179.0637, found: 179.0635.

ethyl 4-cyano-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate 1,1-dioxide (4aa)



With general procedure 5, reaction of **3aa** (0.1 mmol) and *m*-CPBA (0.3 mmol) provided the product **4aa** after flash column chromatography (20 vol % EtOAc in petroleum ether) as a white solid (33.5 mg, 94%). m.p. 142.1-143.5 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.0 Hz, 1H), 8.25 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.55 – 7.46 (m, 6H), 5.53 (dd, *J* = 12.7, 2.6 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.83 (dd, *J* = 14.4, 12.7 Hz, 1H), 3.58 (dd, *J* = 14.3, 2.6 Hz, 1H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 164.1, 139.7, 135.8, 133.4, 131.2, 129.9, 128.0, 126.7, 126.6, 126.4, 117.8, 108.5, 62.0, 61.9, 53.4, 14.3. HRMS (ESI-TOF): calcd. For $C_{18}H_{16}N_2NaO_4S([M+Na]^+)$: 379.0723, found: 379.0754.

ethyl 4-carbamoyl-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carboxylate (5aa)



With general procedure 6, reaction of **3aa** (0.2 mmol), trifluoroacetic acid (0.8 mmol) and H_2O (1.6 mmol) provided the product **5aa** after flash column chromatography (50 vol % EtOAc in petroleum ether) as a colorless oil (32.4 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 2.0 Hz, 1H), 7.77 (dd, J = 8.4, 2.0 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.27 – 7.23 (m, 2H), 7.21 – 7.16 (m, 1H), 6.13 (t, J = 5.9 Hz, 1H), 5.10 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.60 (dd, J = 13.1, 5.9 Hz, 1H), 3.31 (dd, J = 13.1, 5.9 Hz, 1H), 1.36 (t, J = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 156.5, 140.5, 138.9, 131.1, 129.9, 128.6, 127.7, 127.5, 127.0, 126.6, 126.5, 61.3, 55.0, 33.7, 14.3. HRMS (ESI-TOF): calcd. For $C_{18}H_{18}N_2NaO_3S([M+Na]^+)$: 365.0930, found: 365.0899.

8. X-ray Crystal Structures

X-ray Crystal Structures for **3ba**

Identification code	**3ba**
Empirical formula	$C_{15}H_{11}BrN_2S$
Formula weight	331.23
Temperature/K	290.45
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.9320(3)

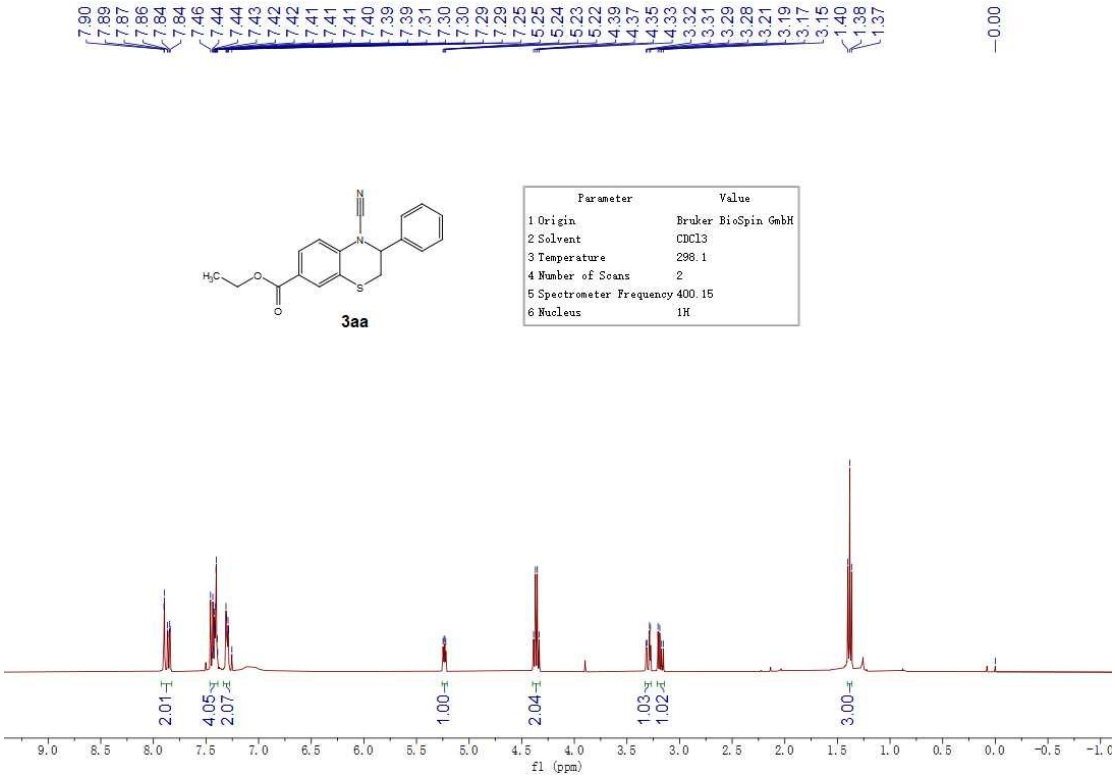
b/Å	9.4729(4)
c/Å	17.8231(7)
α/°	90
β/°	97.434(4)
γ/°	90
Volume/Å^3	1327.95(9)
Z	25
ρ_{calc}g/cm^3	10.355
μ/mm^{-1}	34.775
F(000)	4150.0
Crystal size/mm^3	0.4500 × 0.4000 × 0.3000
Radiation	CuK$^{\alpha}$ (λ = 1.54184)
2Θ range for data collection/°	10.01 to 155.15
Index ranges	-9 ≤ h ≤ 10, -10 ≤ k ≤ 12, -22 ≤ l ≤ 22
Reflections collected	8540
Independent reflections	2809 [R_{int} = 0.0532, R_{sigma} = 0.0398]
Data/restraints/parameters	2809/0/216
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0553, wR_2 = 0.1393
Final R indexes [all data]	R_1 = 0.0607, wR_2 = 0.1476
Largest diff. peak/hole / e Å^{-3}	0.46/-0.74

9. References

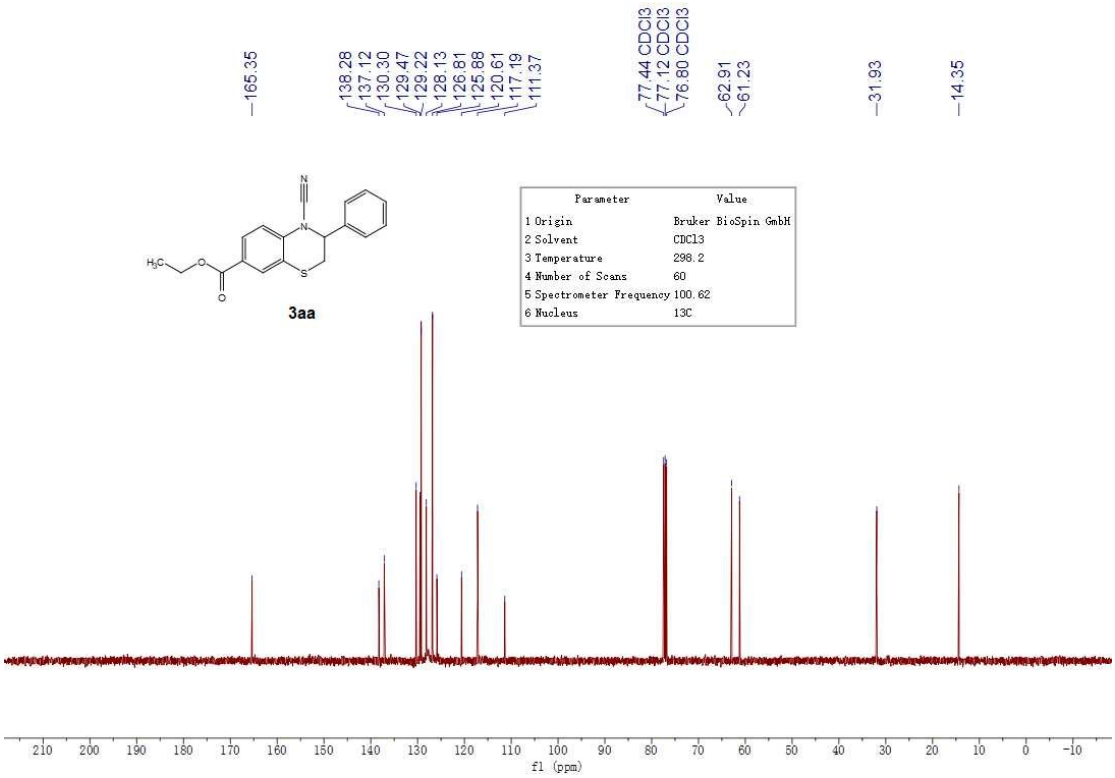
1. S. H. Cho, J. Y. Kim, S. Y. Lee and S. Chang, *Angew. Chem. Int. Ed.,* 2009, **48**, 9127-9130.
2. J. Li, X. Zheng, W. Li, W. Zhou, W. Zhu and Y. Zhang, *New J. Chem.*, 2016, **40**, 77-80.
3. (a) A. D. Becke, Density-Functional Thermochemistry. III. *J. Chem. Phys.*, 1993, **98**, 5648–5652; (b) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B.*, 1988, **37**, 785–789; (c) S. Grimme, J. Antony, S. Ehrlich and H. Krieg, *J. Chem. Phys*., 2010, **132**, 154104–154118.
4. P. J. Hay and W. R. Wadt, *J. Chem. Phys*., 1985, **82**, 299–310.
5. K. Fukui, *Acc. Chem. Res.,* 1981, **14**, 363–368.

6. A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. B,* 2009, **113**, 6378–6396.
7. (a) M. Dolg, U. Wedig, H. Stoll and H. Preuss, *J. Chem. Phys.,* 1987, **86**, 866–872; (b) D. Andrae, U. Häußermann, M. Dolg, H. Stoll and H. Preuss, *Theor. Chim. Acta.,* 1990, **77**, 123–141.
8. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. M. Tomasi, N. Cossi, N. J. Rega, M. Millam, J. E. Klene, J. B. Knox, V. Cross, C. Bakken, Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision C.01*, Gaussian, Inc., Wallingford CT, 2010.
9. C. Y. Legault, CYLview, 1.0b; Université de Sherbrooke: Sherbrooke, Quebec, Canada, 2009.

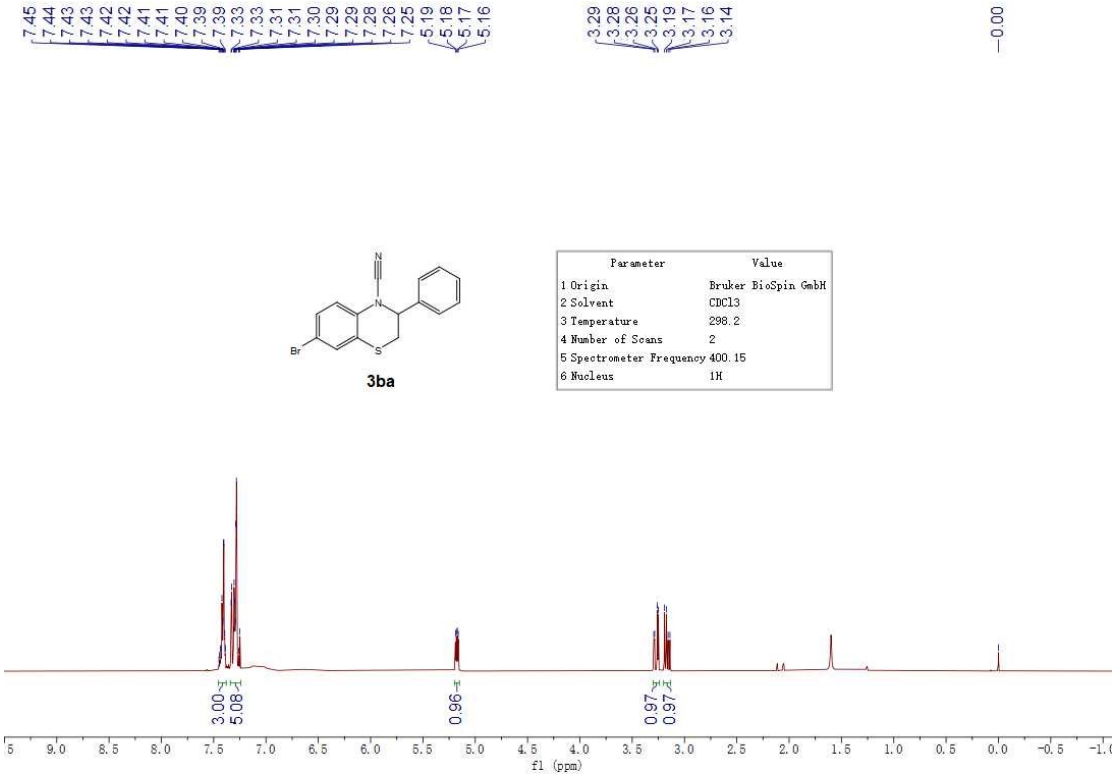
10. NMR spectra



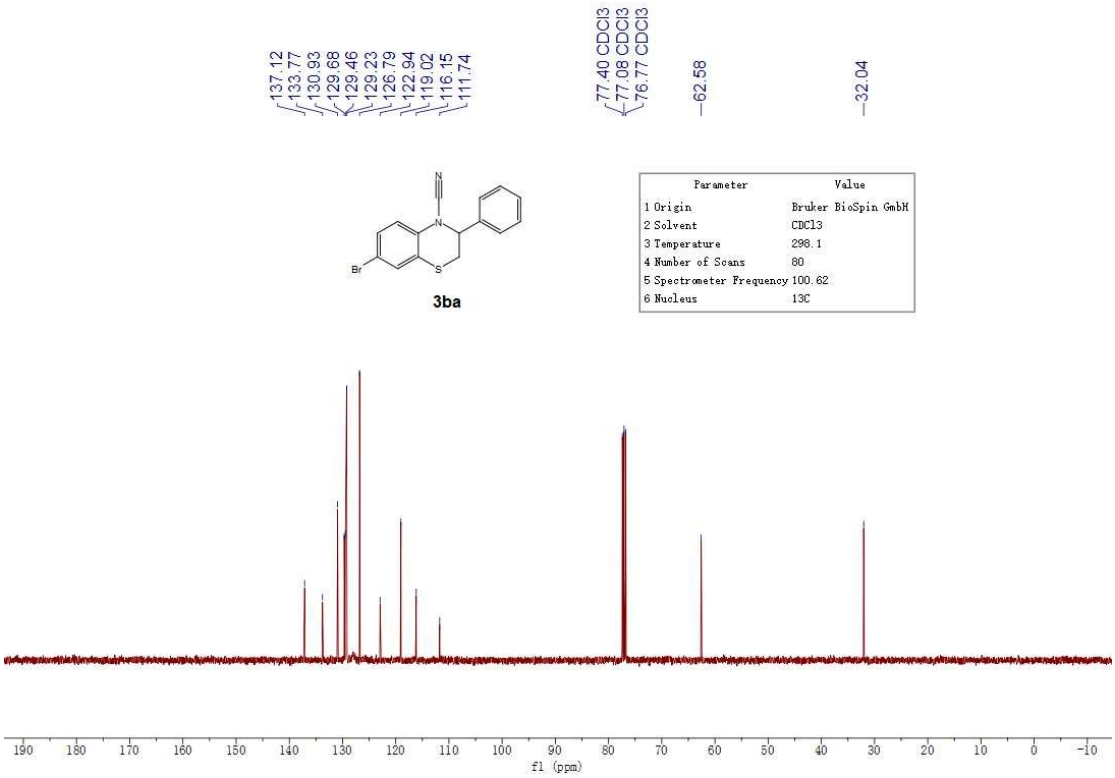
^{1}H NMR spectrum of **3aa** (400 MHz, $CDCl_3$)



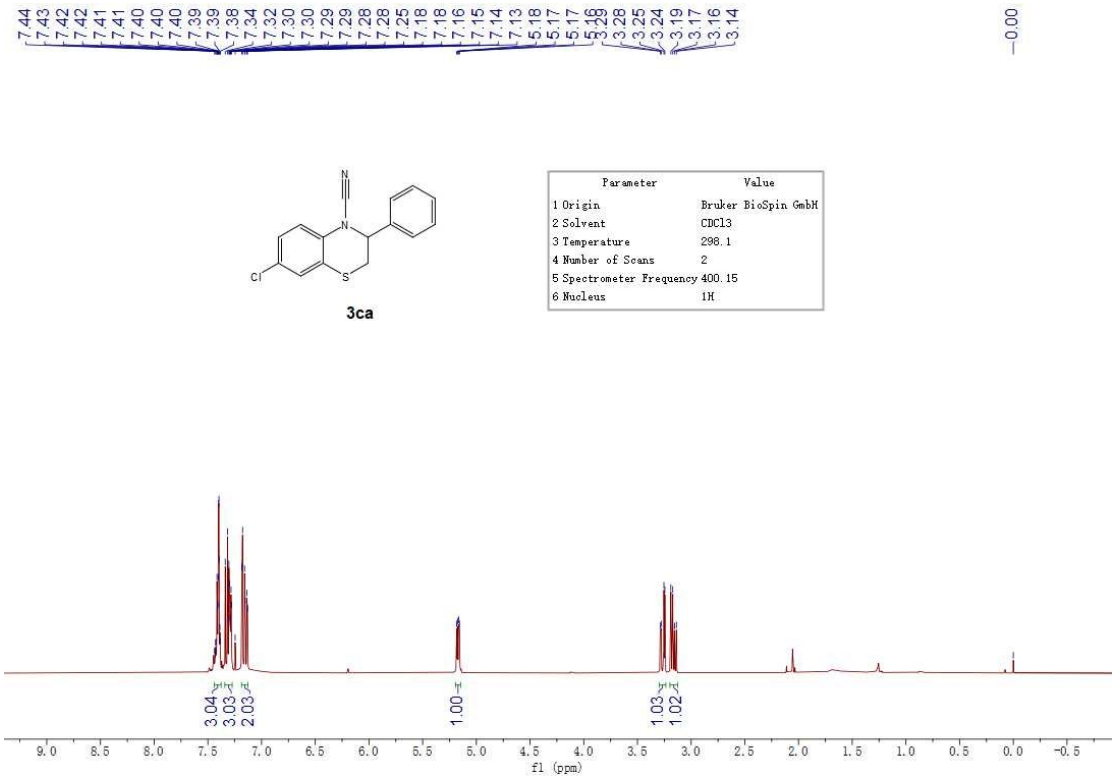
^{13}C NMR spectrum of **3aa** (100 MHz, $CDCl_3$)



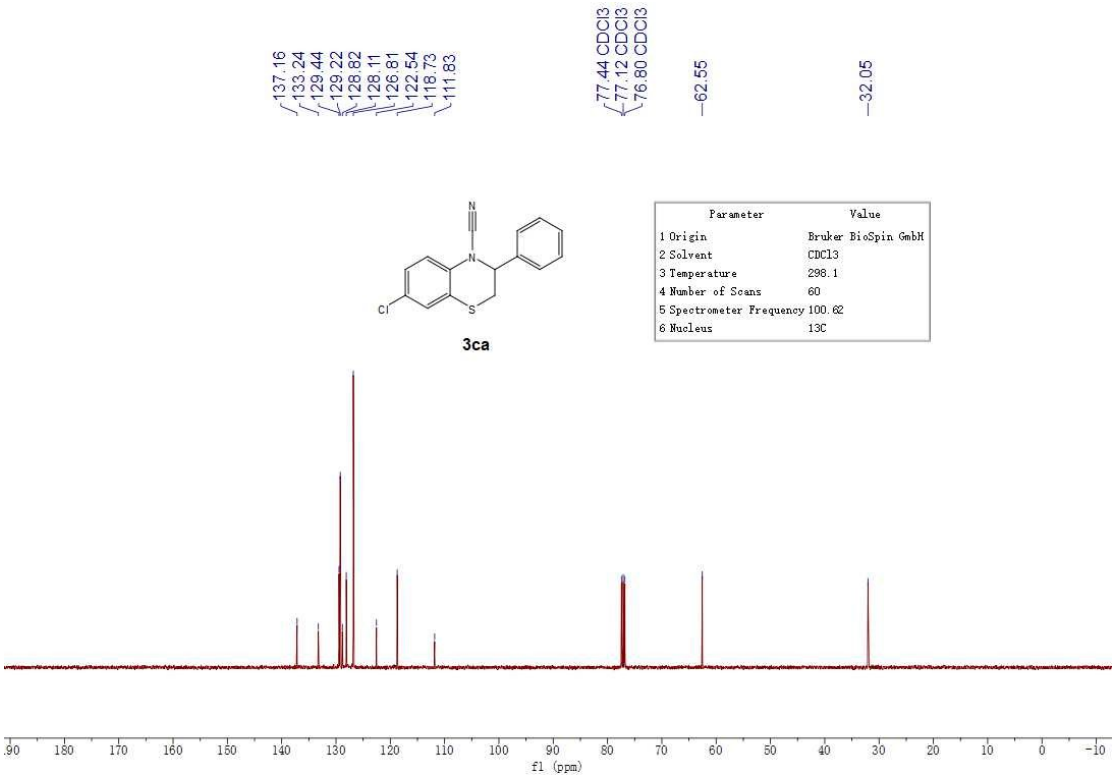
^{1}H NMR spectrum of **3ba** (400 MHz, $CDCl_3$)



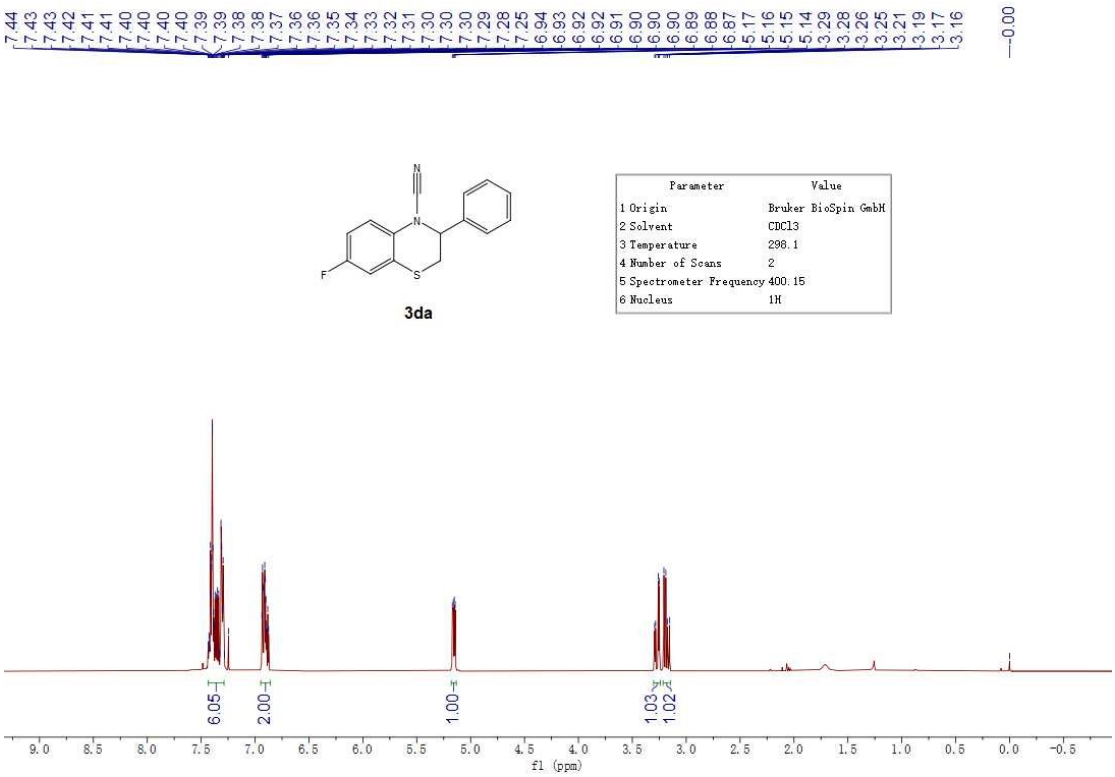
^{13}C NMR spectrum of **3ba** (100 MHz, $CDCl_3$)



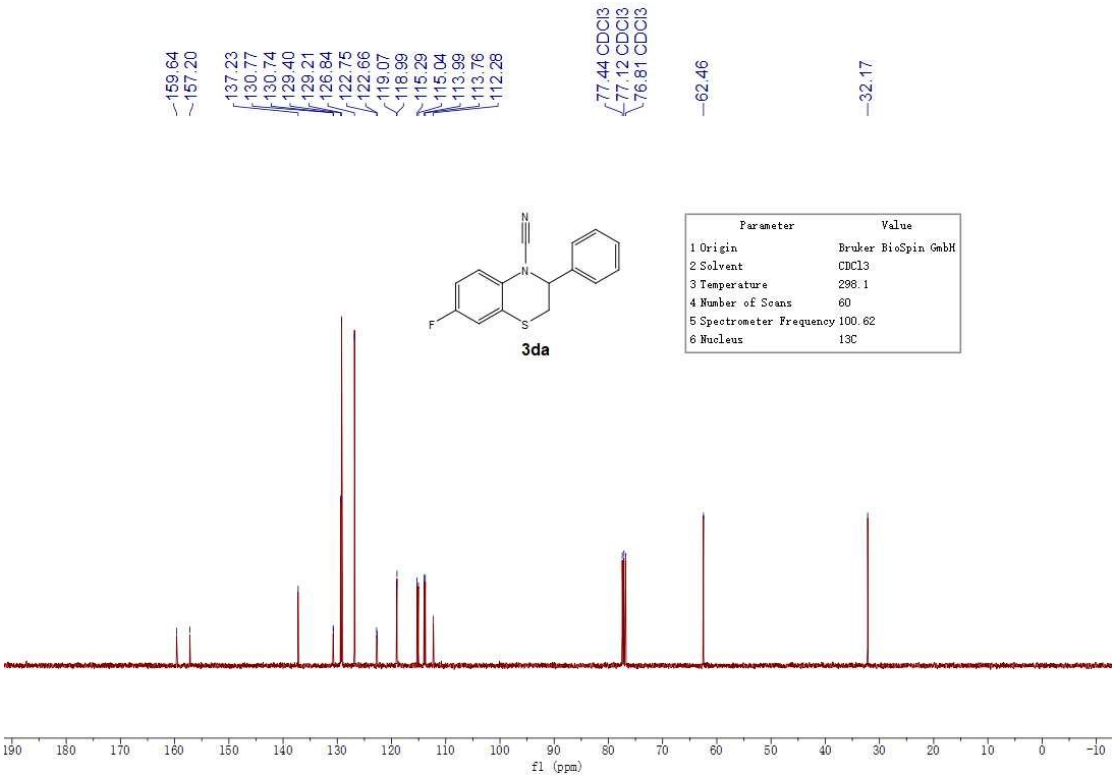
^{1}H NMR spectrum of **3ca** (400 MHz, $CDCl_3$)



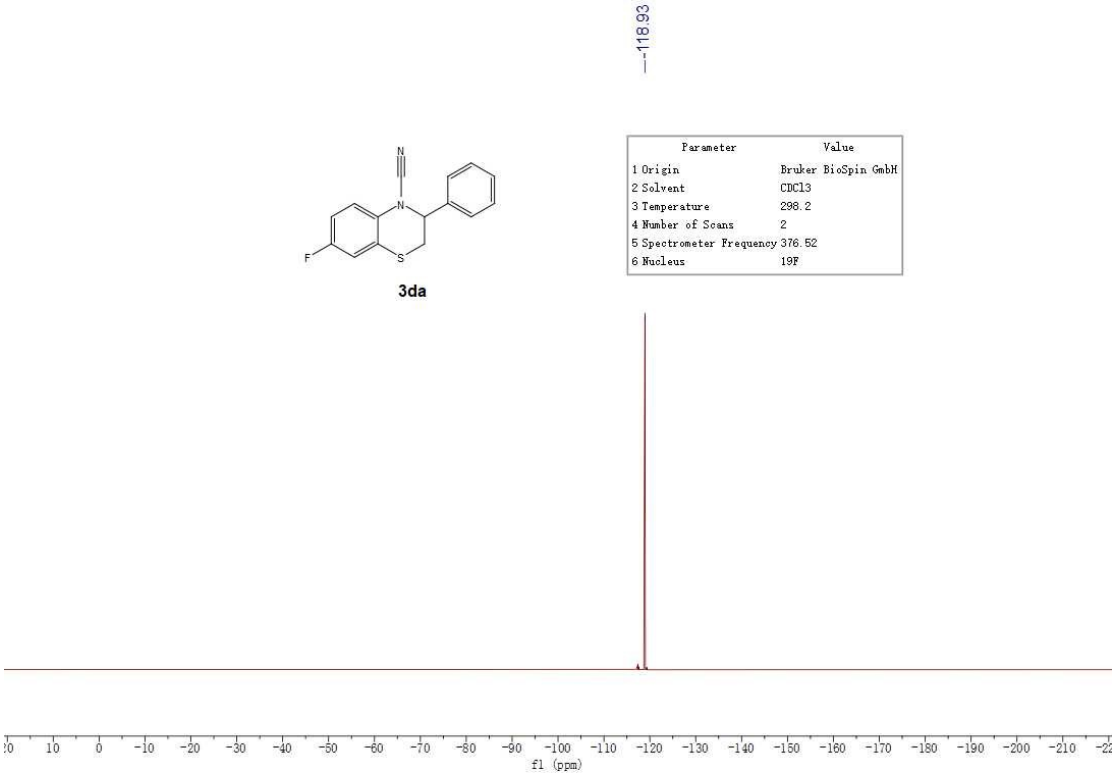
^{13}C NMR spectrum of **3ca** (100 MHz, $CDCl_3$)



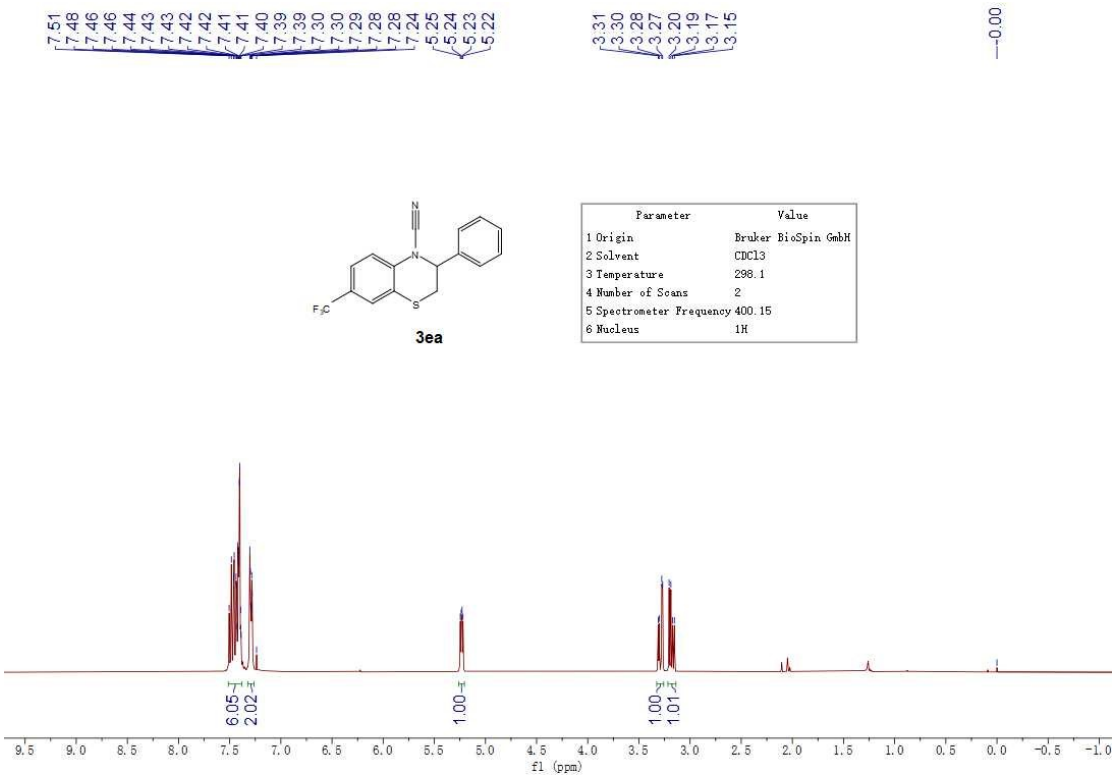
^{1}H NMR spectrum of **3da** (400 MHz, $CDCl_3$)



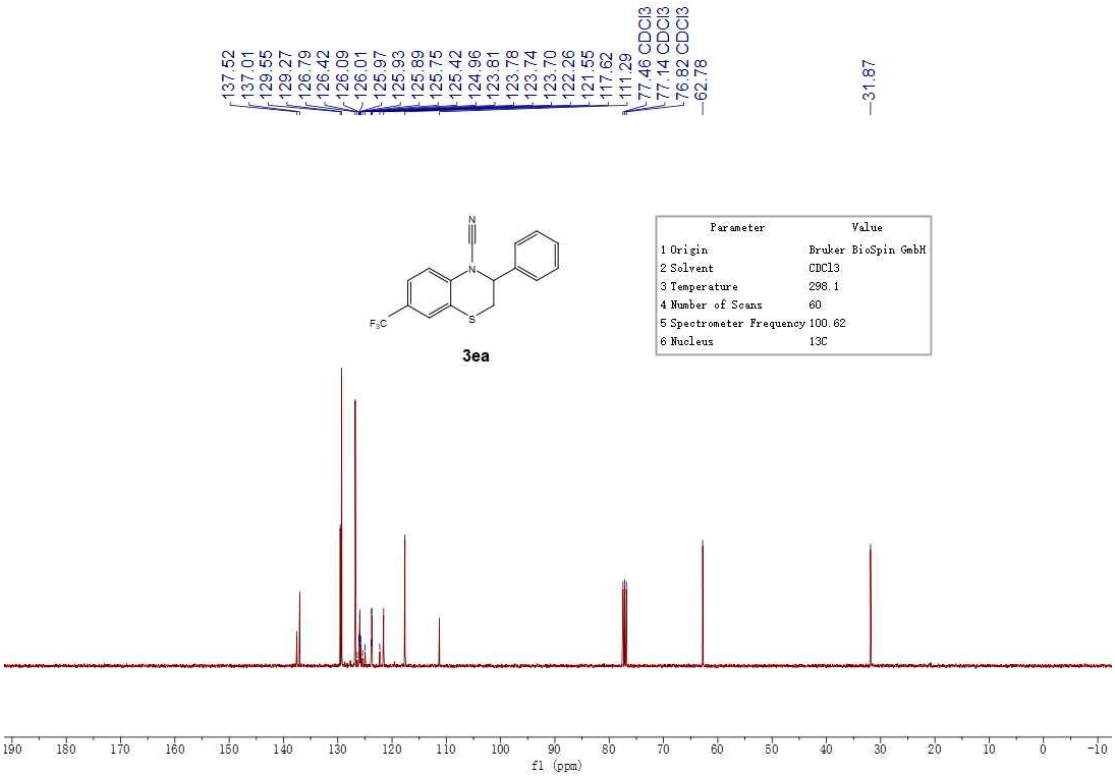
^{13}C NMR spectrum of **3da** (100 MHz, $CDCl_3$)



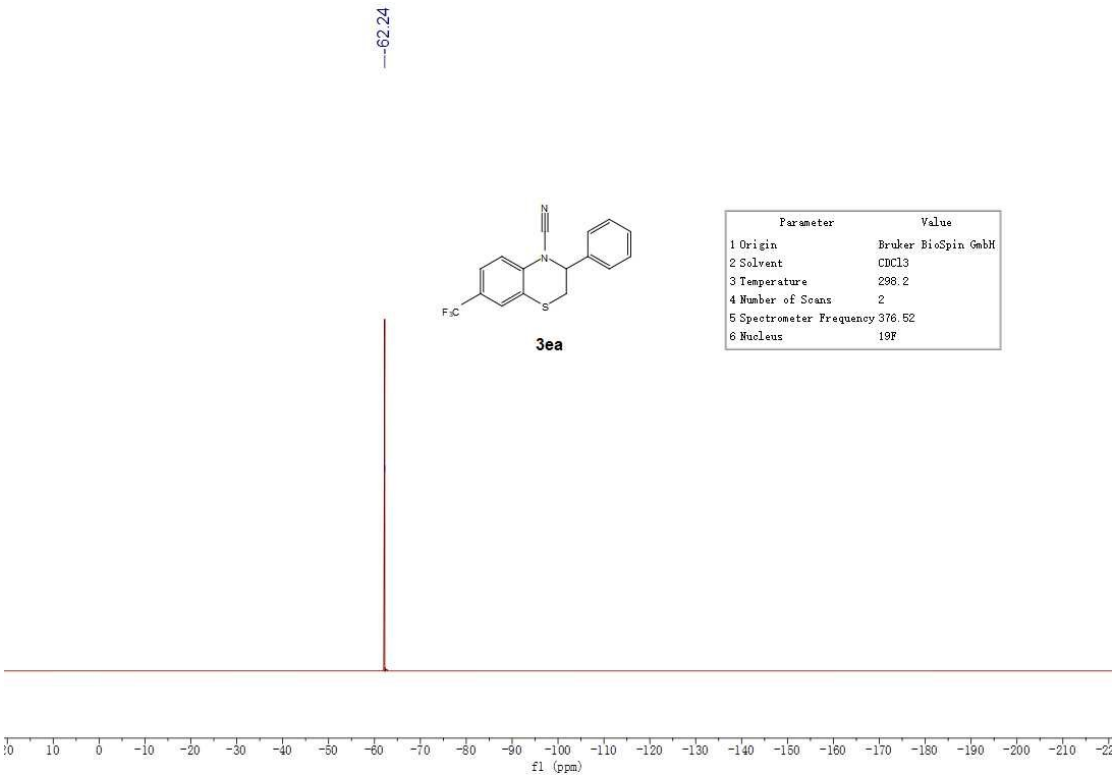
^{19}F NMR spectrum of **3da** (376 MHz, $CDCl_3$)



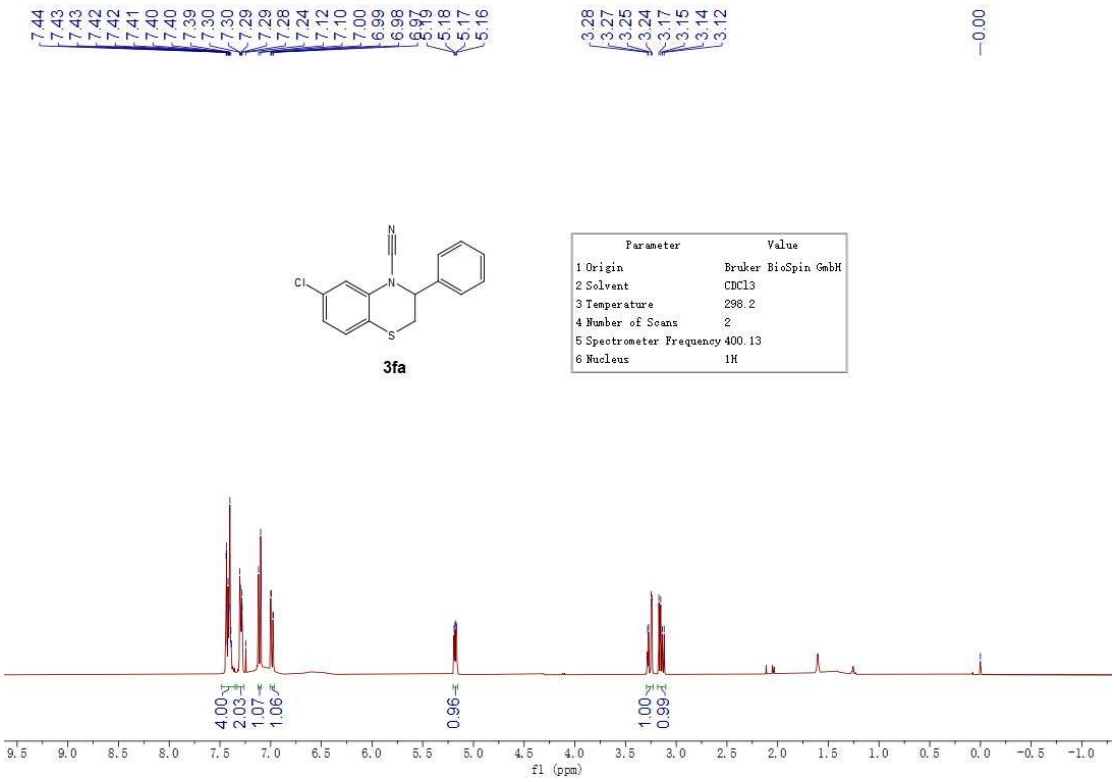
^{1}H NMR spectrum of **3ea** (400 MHz, $CDCl_3$)



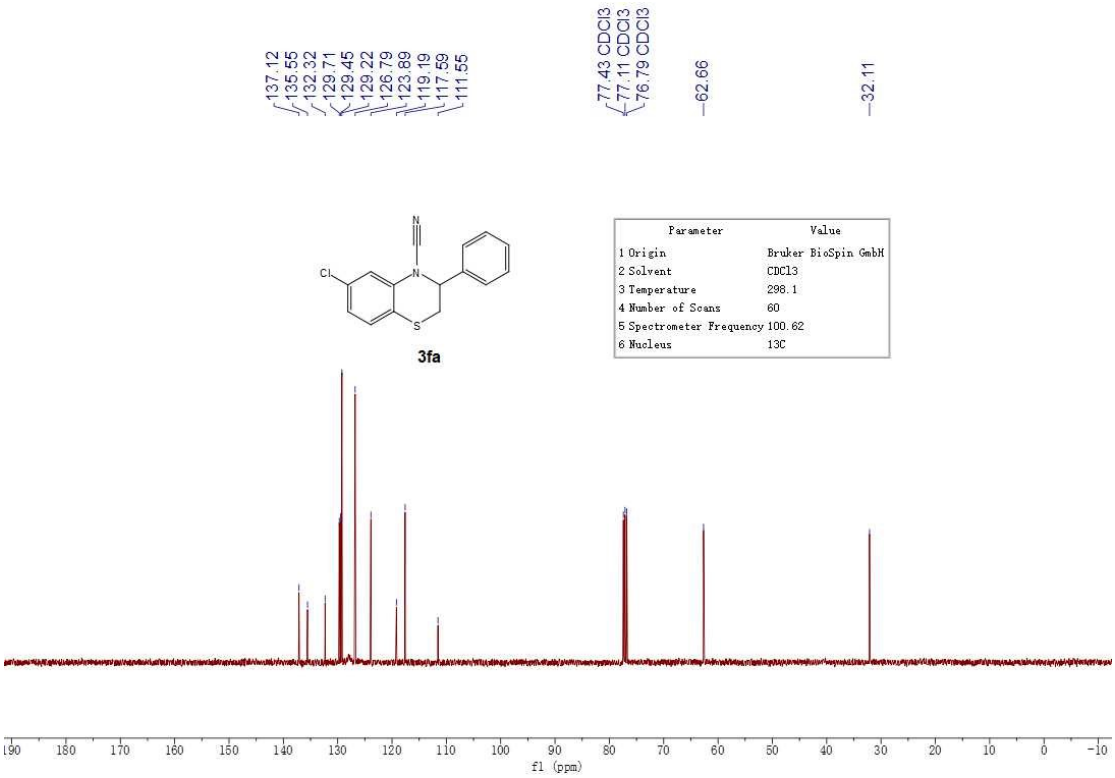
^{13}C NMR spectrum of **3ea** (100 MHz, $CDCl_3$)



^{19}F NMR spectrum of **3ea** (376 MHz, $CDCl_3$)



^{1}H NMR spectrum of **3fa** (400 MHz, $CDCl_3$)



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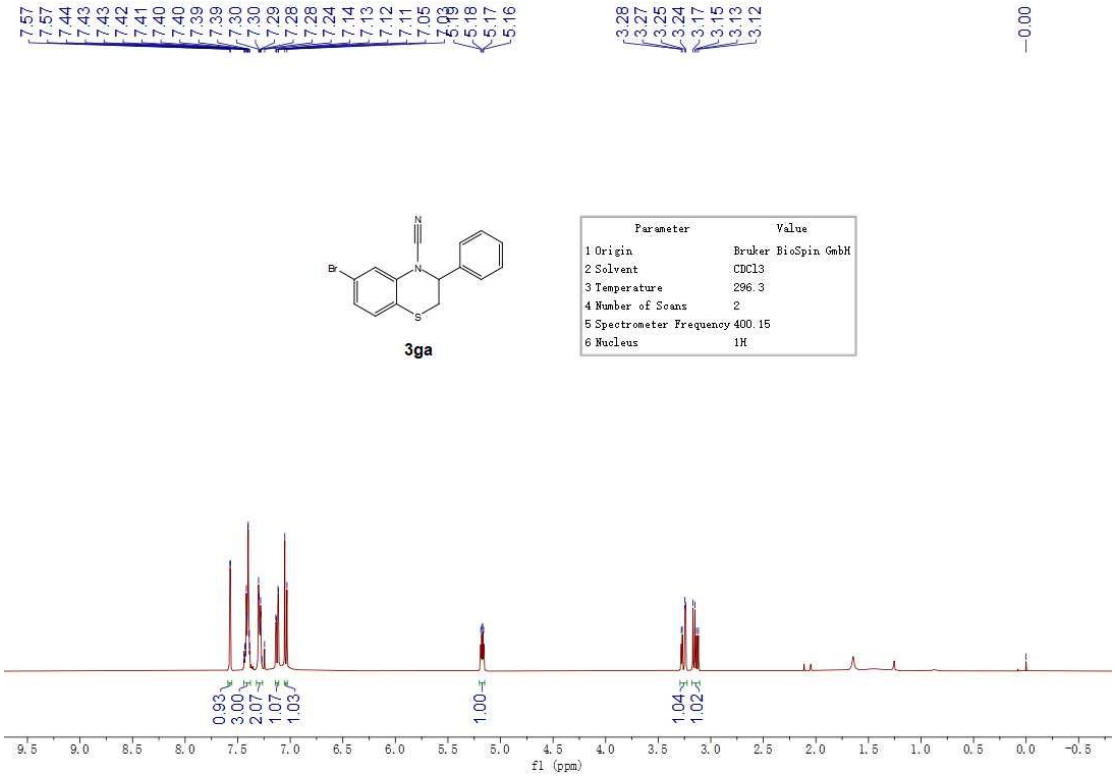
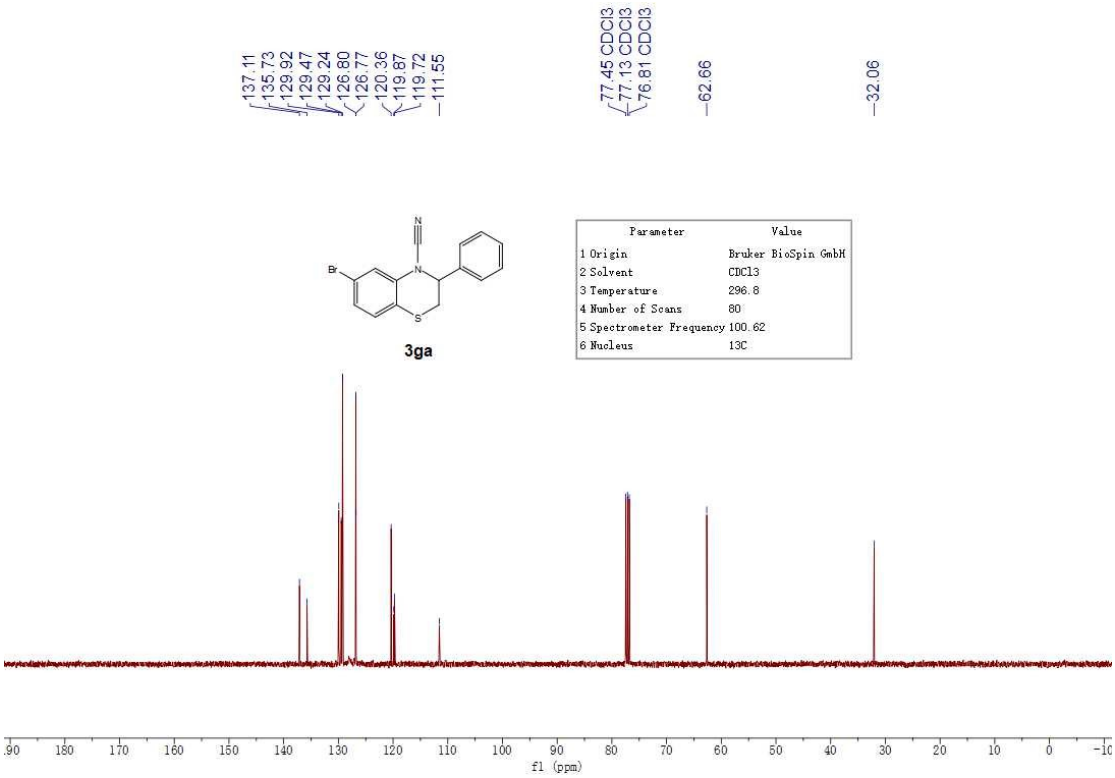
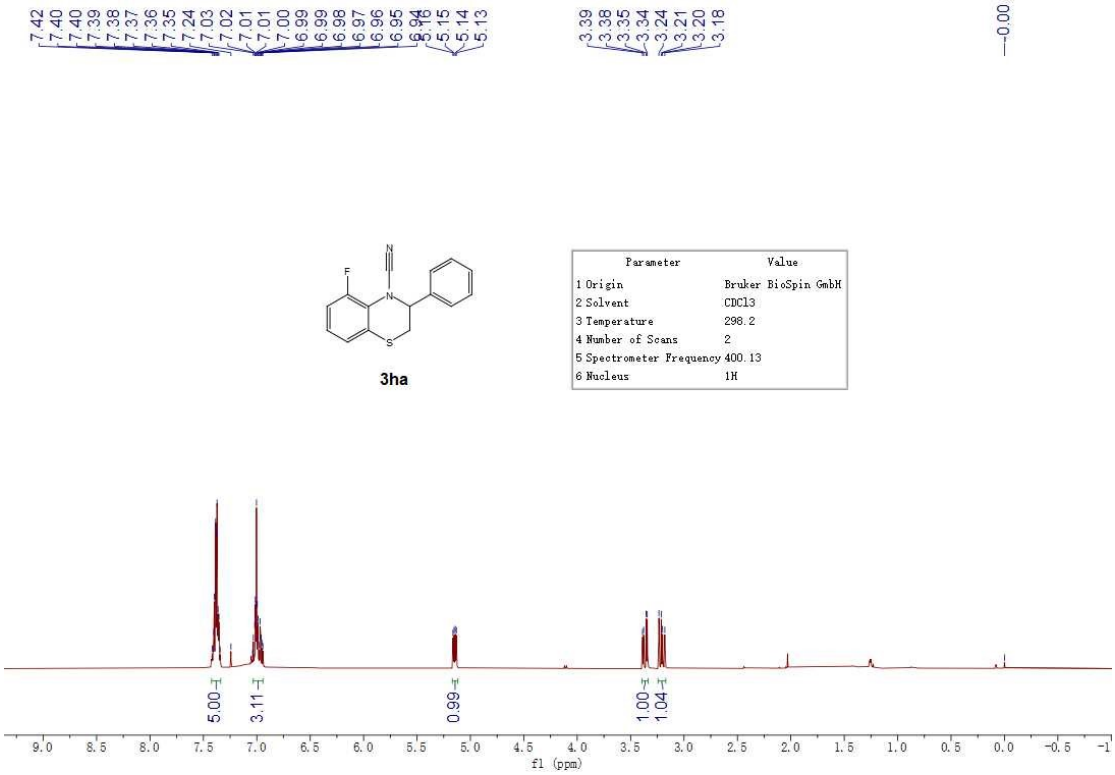


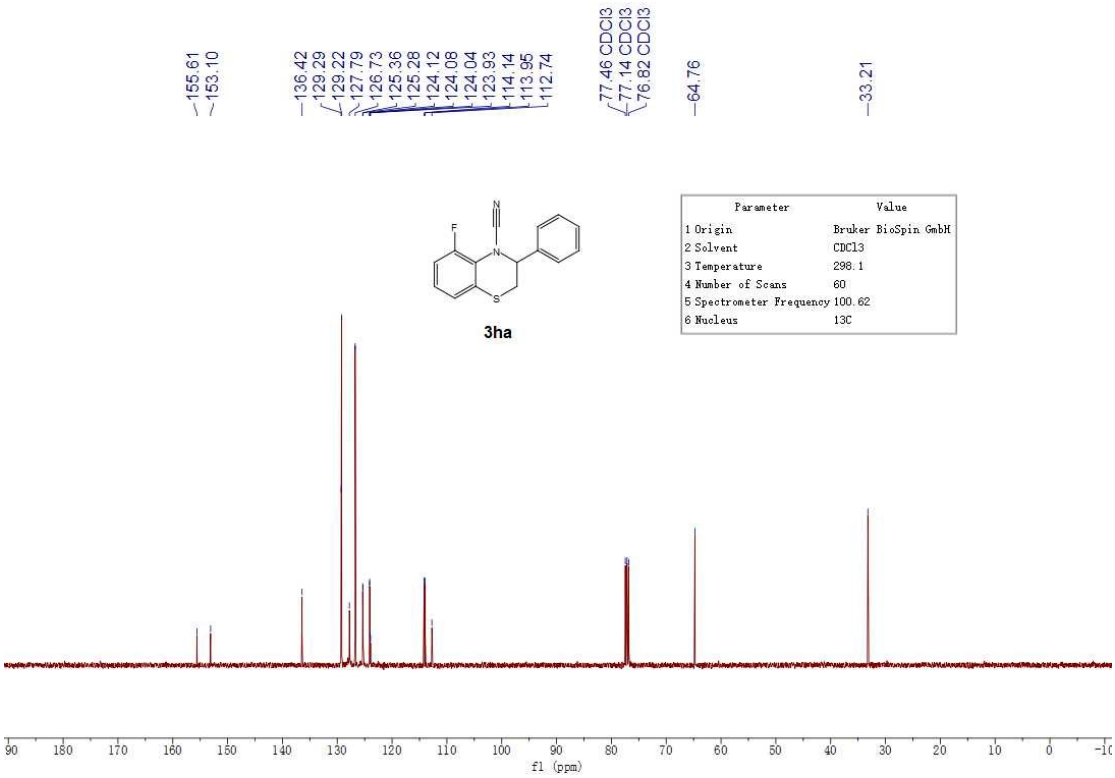
^{1}H NMR spectrum of **3ga** (400 MHz, $CDCl_3$)



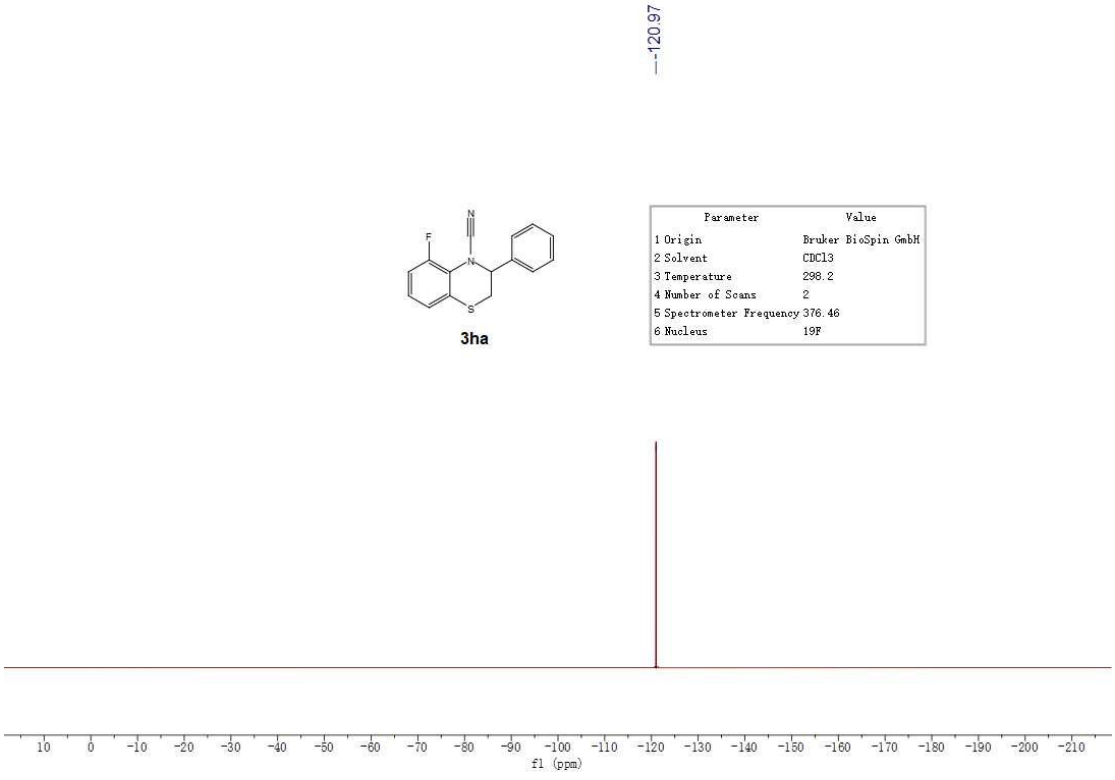
^{13}C NMR spectrum of **3ga** (100 MHz, $CDCl_3$)



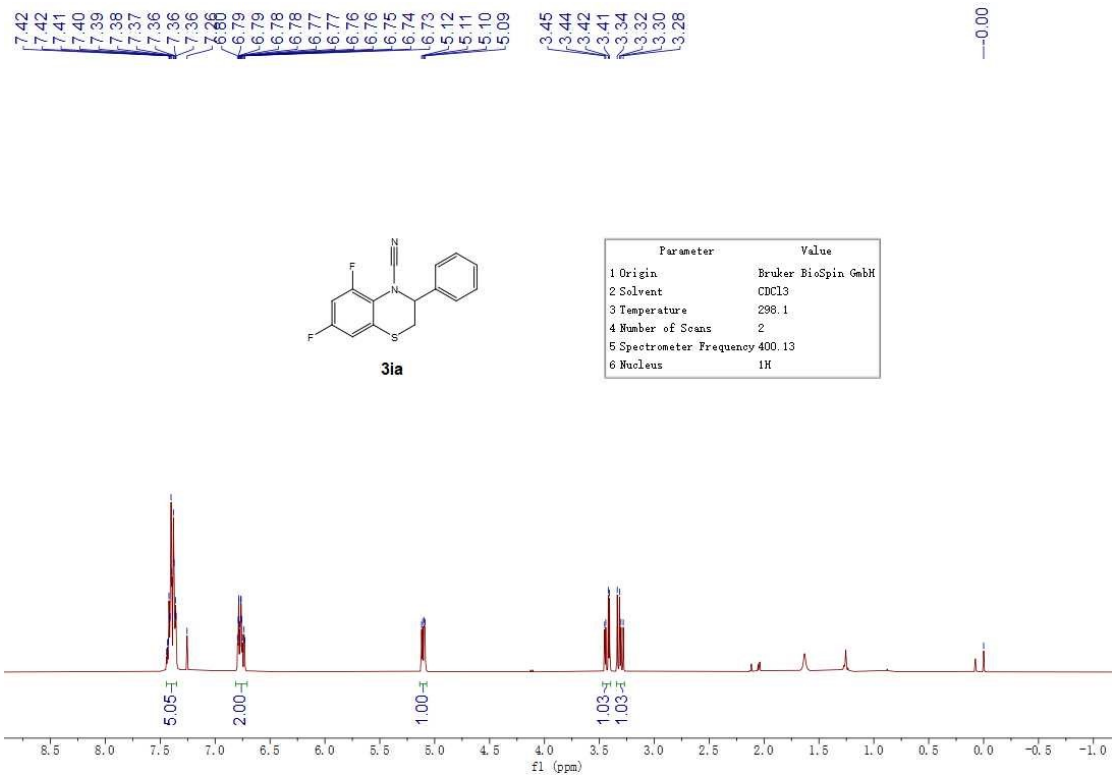
^{1}H NMR spectrum of **3ha** (400 MHz, $CDCl_3$)



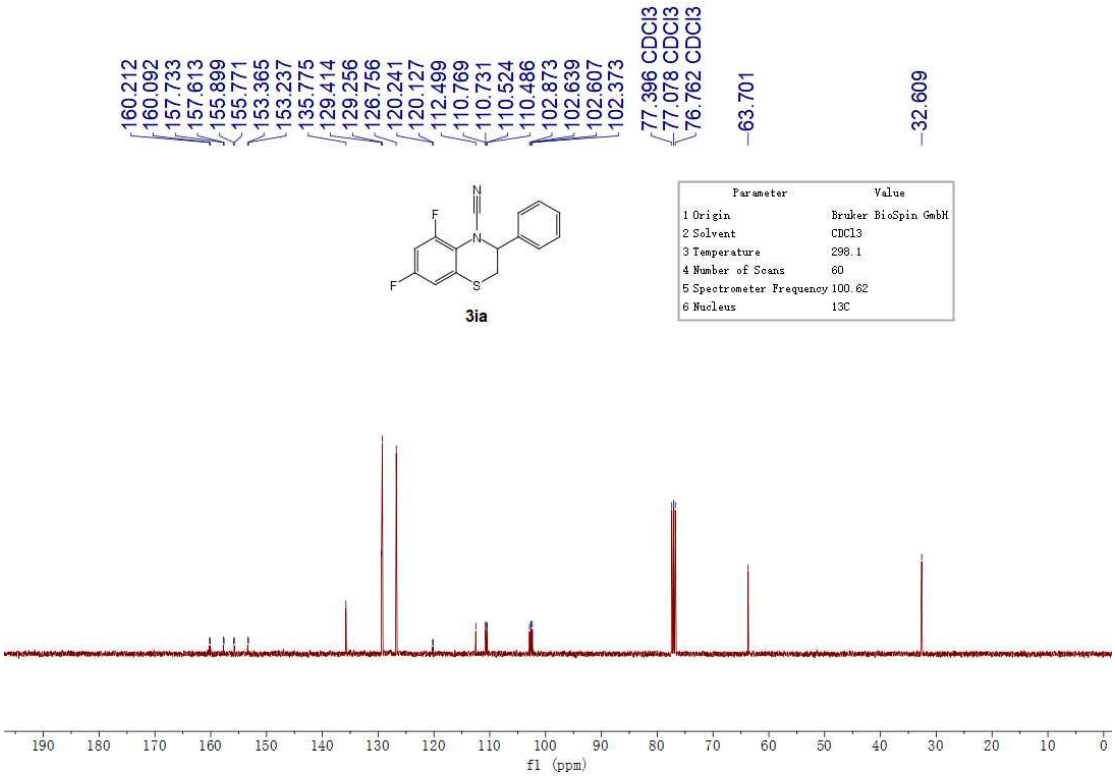
^{13}C NMR spectrum of **3ha** (100 MHz, $CDCl_3$)



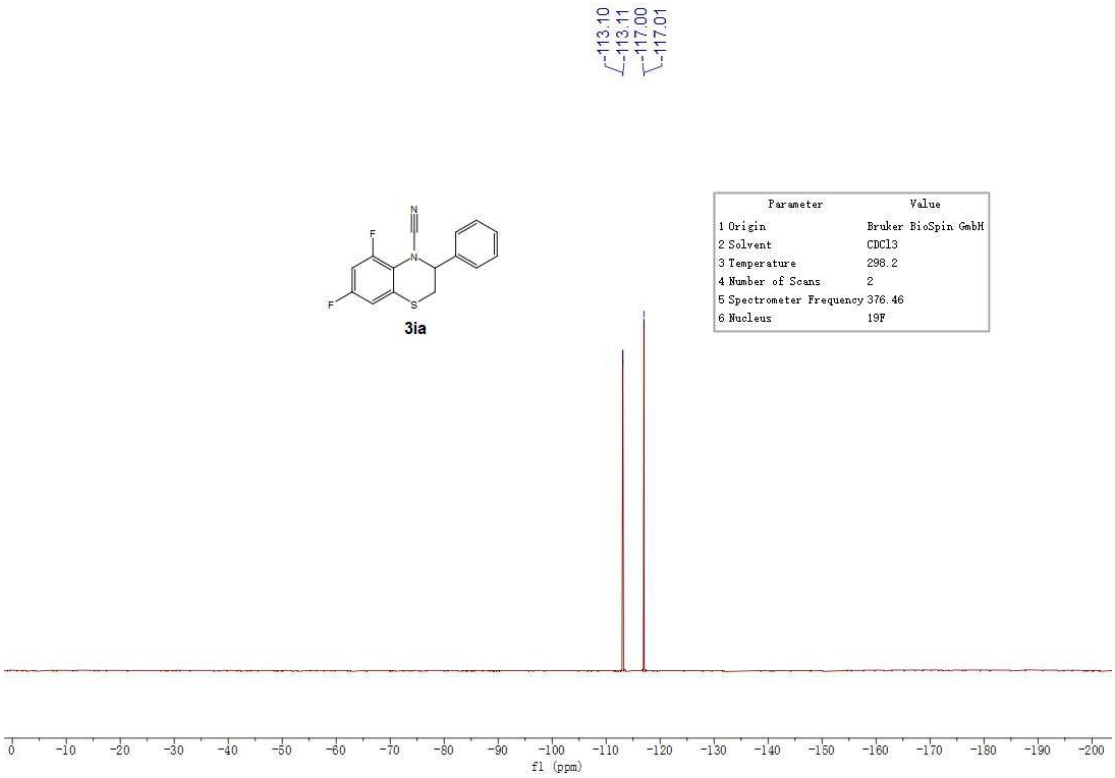
^{19}F NMR spectrum of **3ha** (376 MHz, $CDCl_3$)



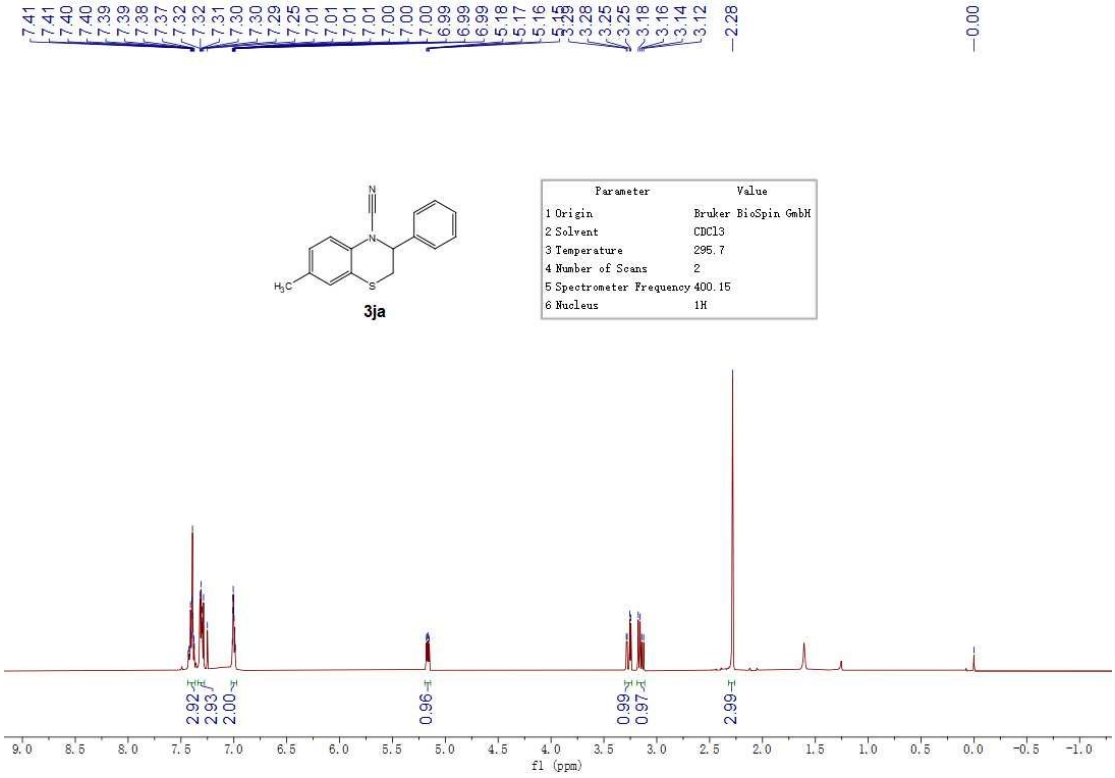
^{1}H NMR spectrum of **3ia** (400 MHz, $CDCl_3$)



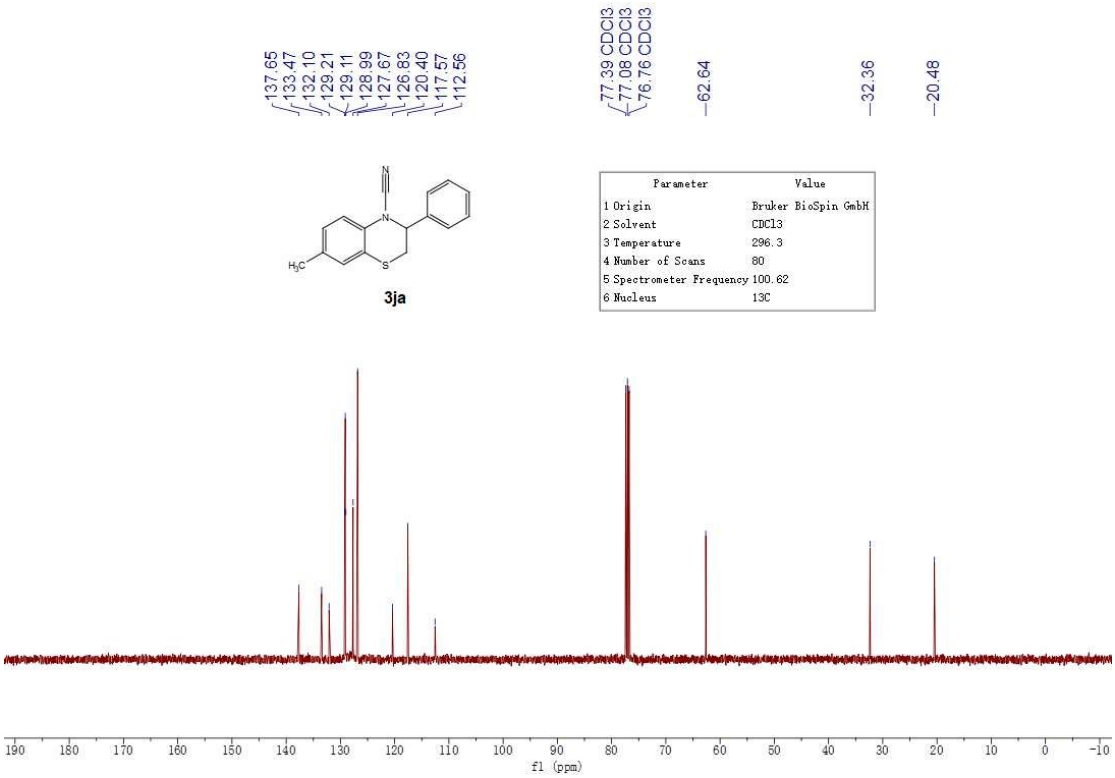
^{13}C NMR spectrum of **3ia** (100 MHz, $CDCl_3$)



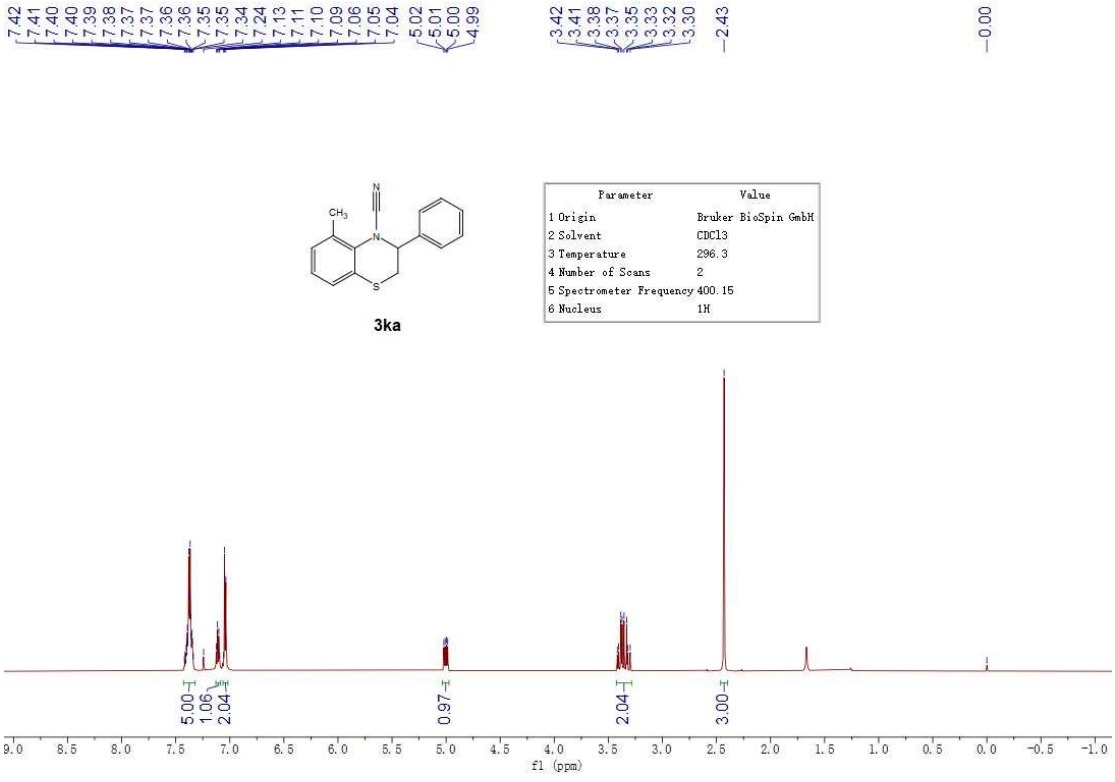
^{19}F NMR spectrum of **3ia** (376 MHz, $CDCl_3$)



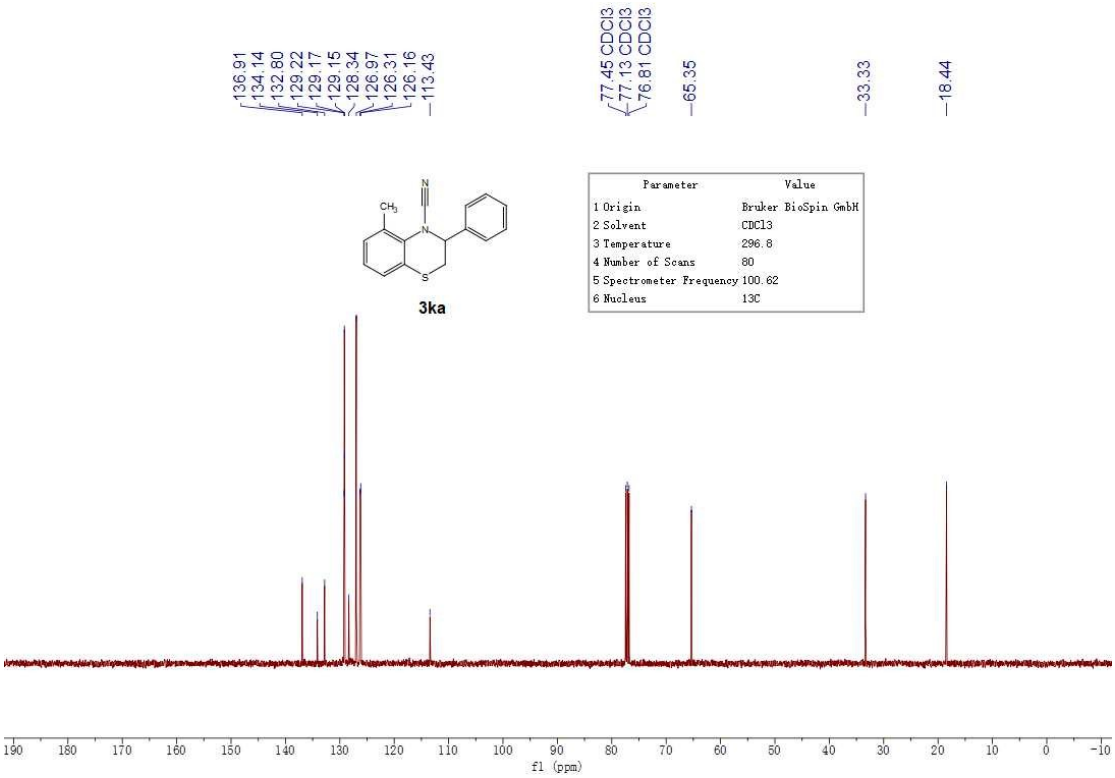
^{1}H NMR spectrum of **3ja** (400 MHz, $CDCl_3$)



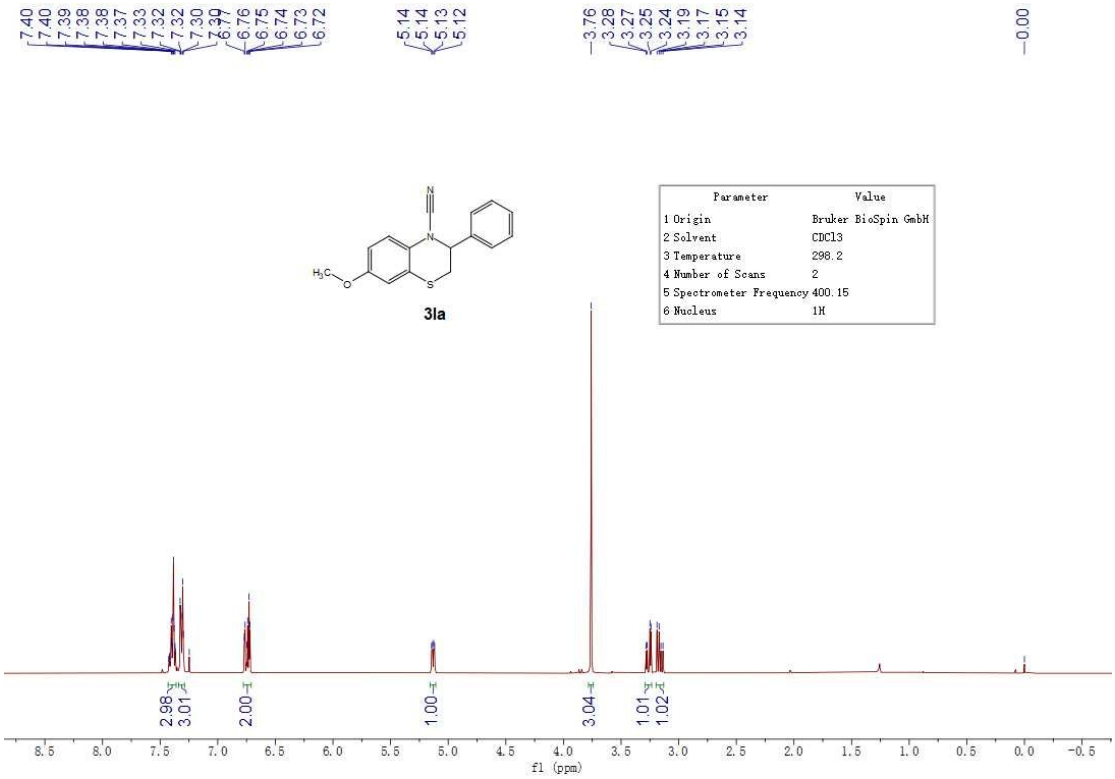
^{13}C NMR spectrum of **3ja** (100 MHz, $CDCl_3$)



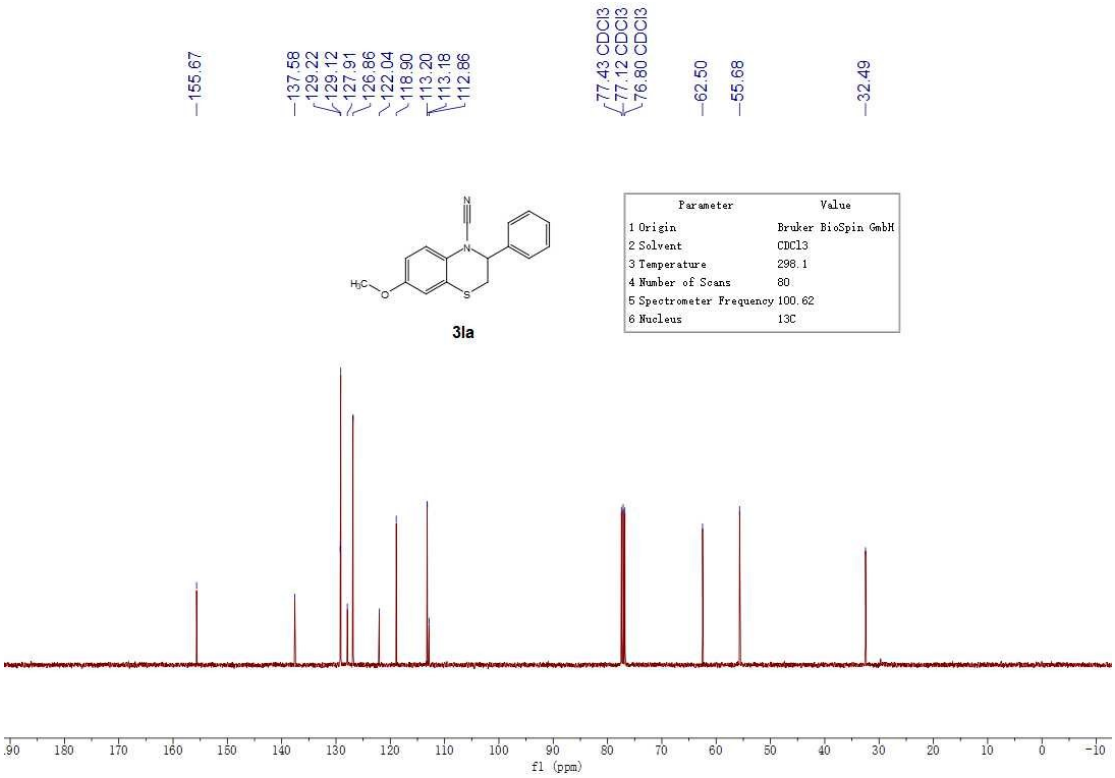
^{1}H NMR spectrum of **3ka** (400 MHz, $CDCl_3$)



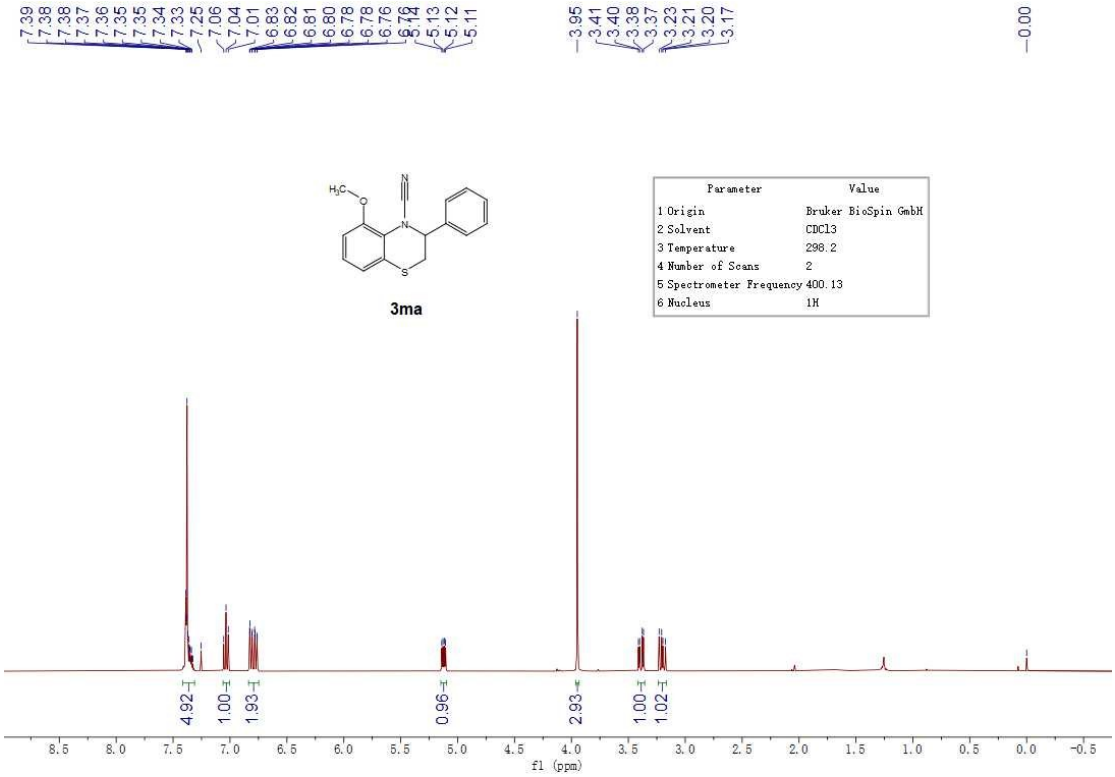
^{13}C NMR spectrum of **3ka** (100 MHz, $CDCl_3$)



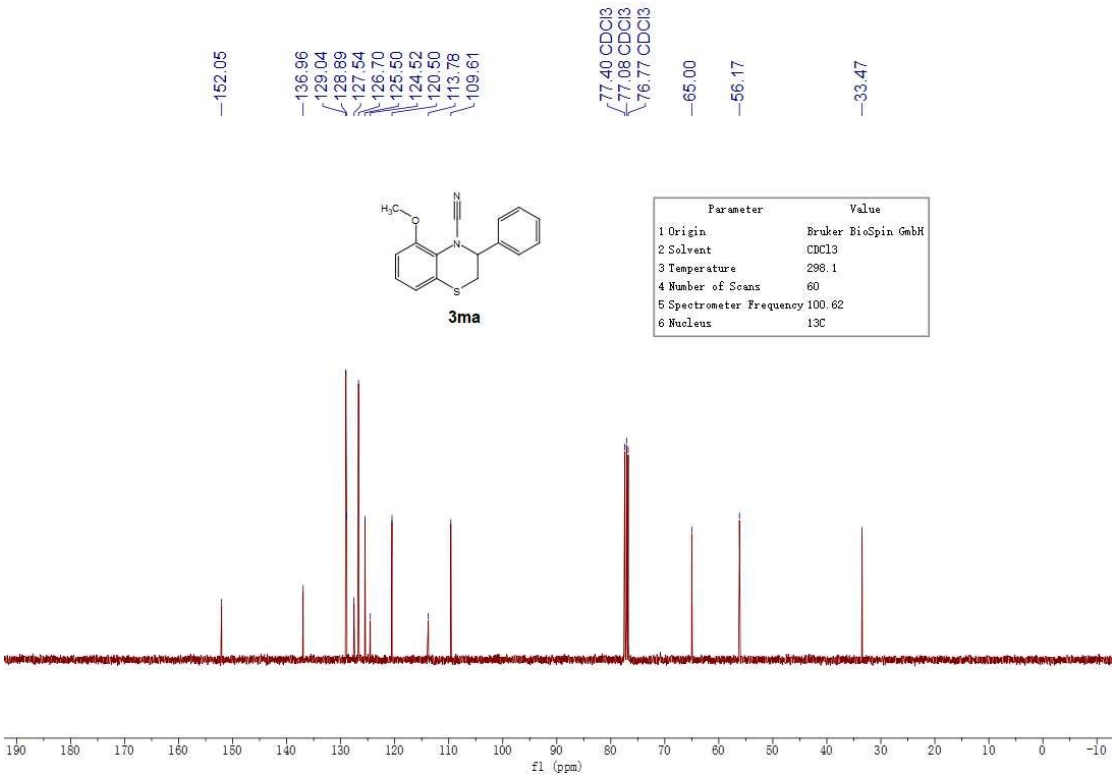
^{1}H NMR spectrum of **3la** (400 MHz, $CDCl_3$)



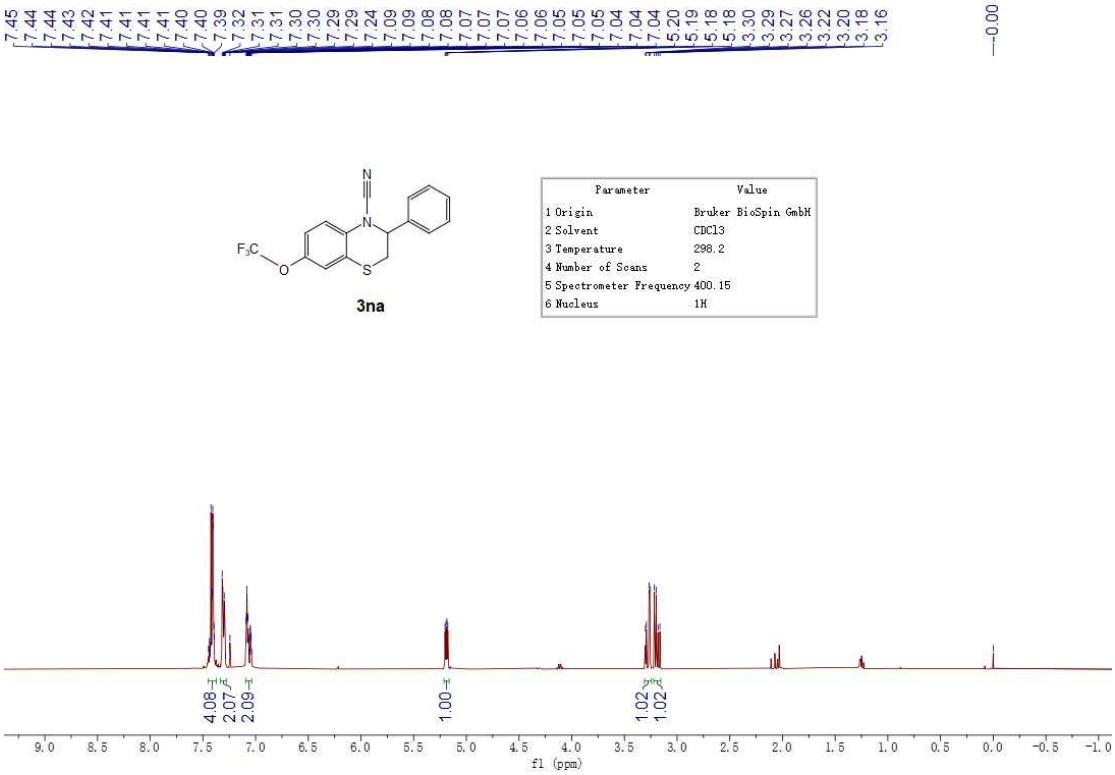
^{13}C NMR spectrum of **3la** (100 MHz, $CDCl_3$)



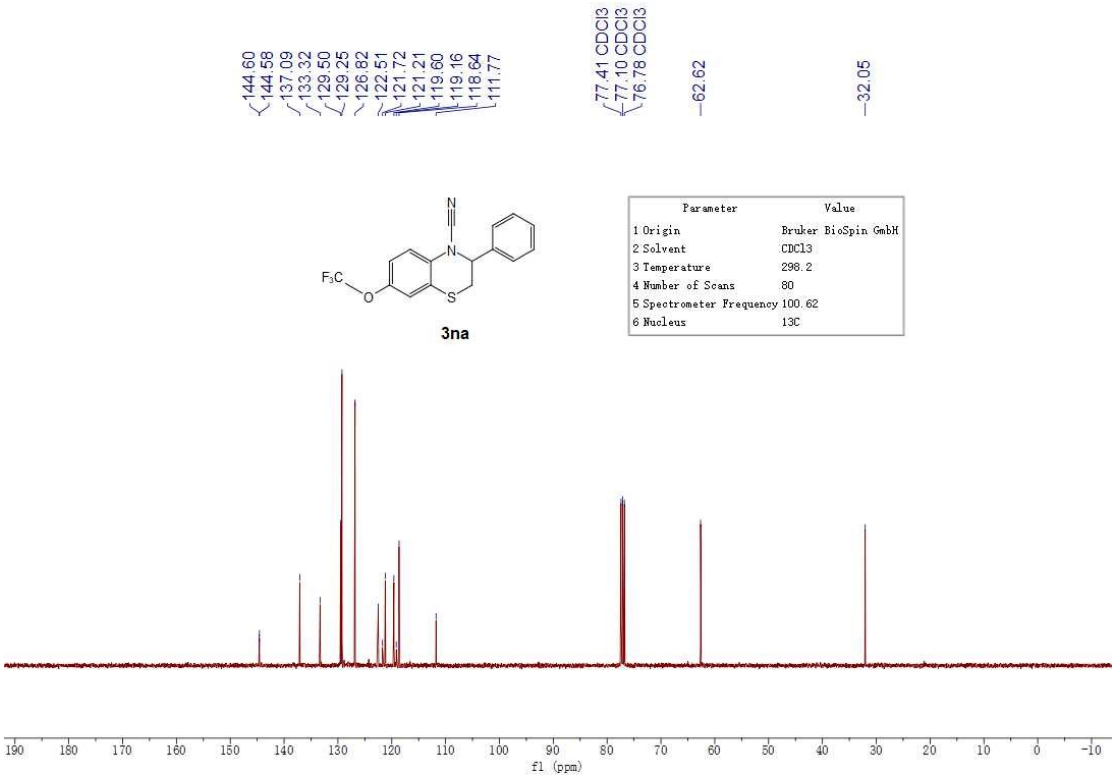
^{1}H NMR spectrum of **3ma** (400 MHz, $CDCl_3$)



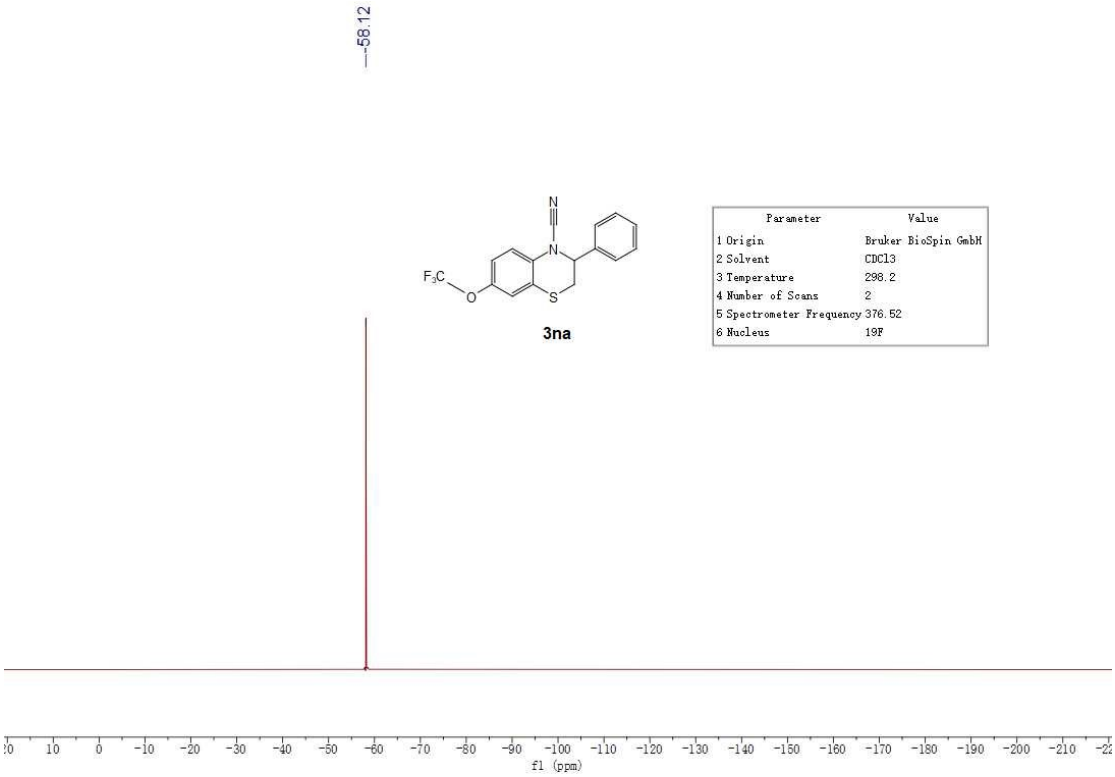
^{13}C NMR spectrum of **3ma** (100 MHz, $CDCl_3$)



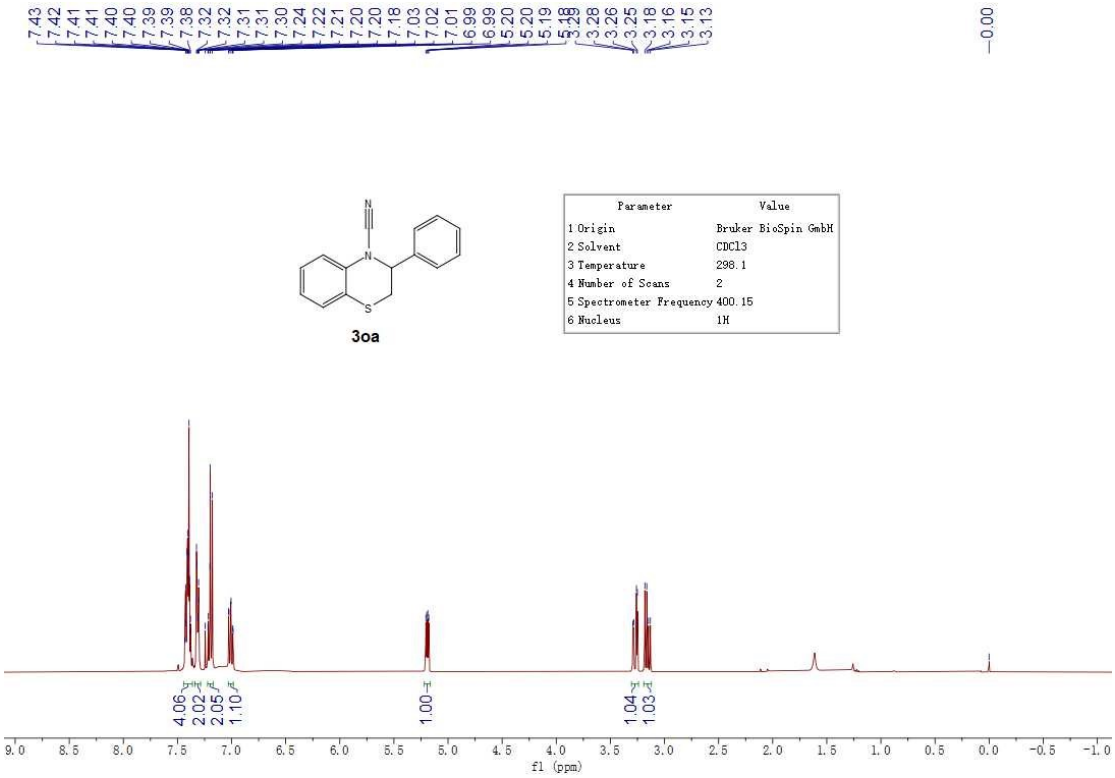
^{1}H NMR spectrum of **3na** (400 MHz, $CDCl_3$)



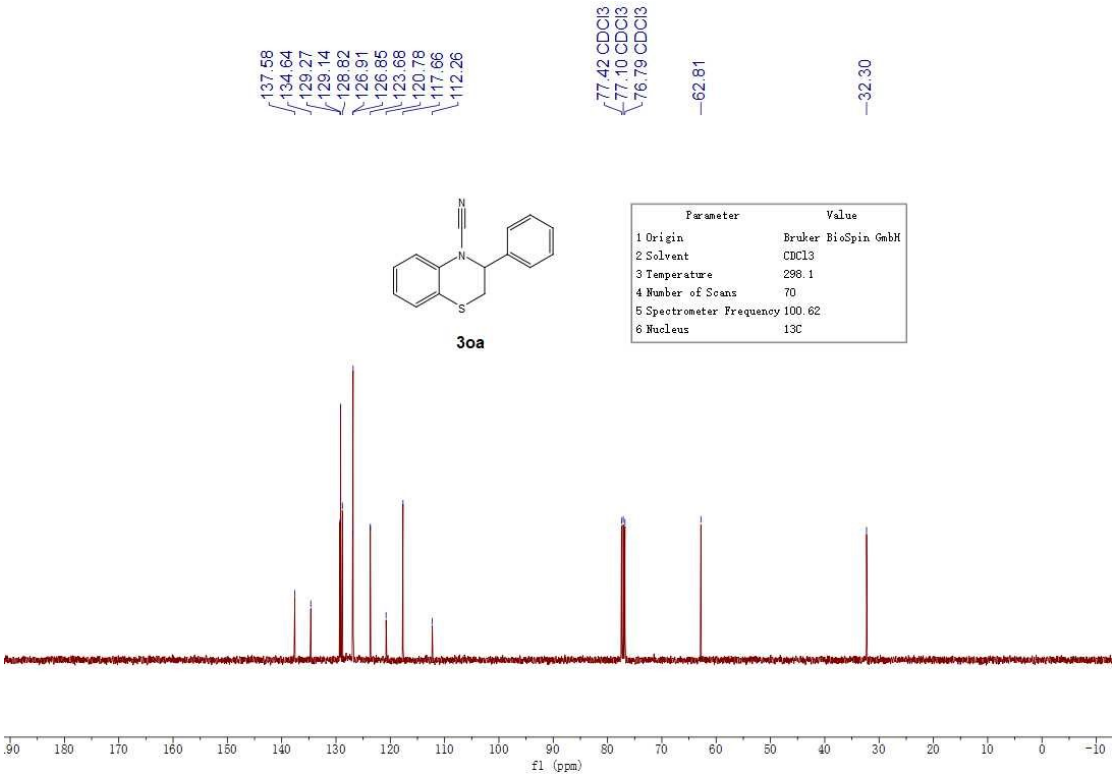
^{13}C NMR spectrum of **3na** (100 MHz, $CDCl_3$)



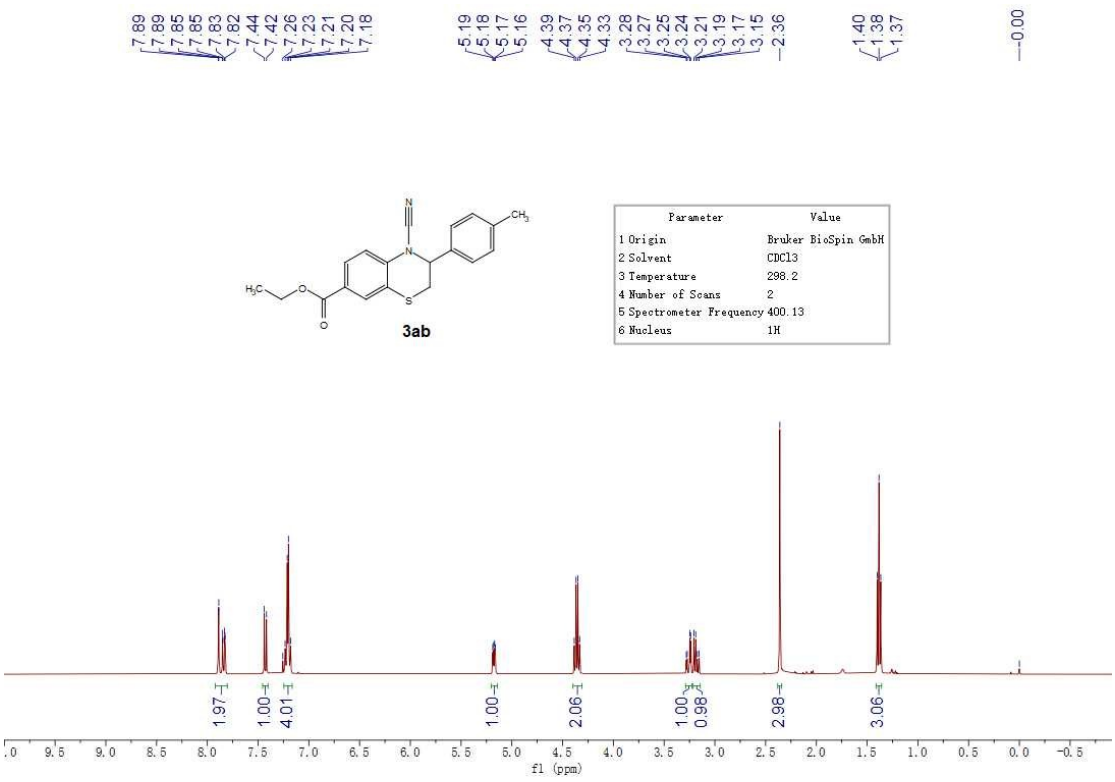
^{19}F NMR spectrum of **3na** (376 MHz, $CDCl_3$)



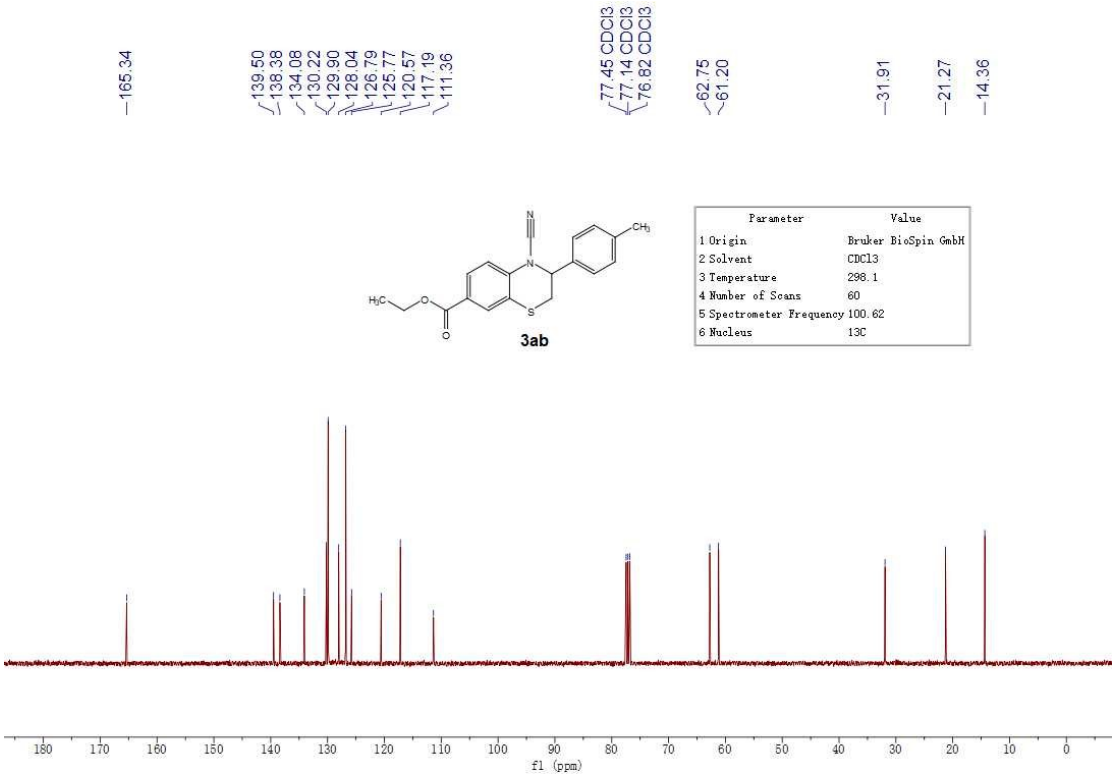
^{1}H NMR spectrum of **3oa** (400 MHz, $CDCl_3$)



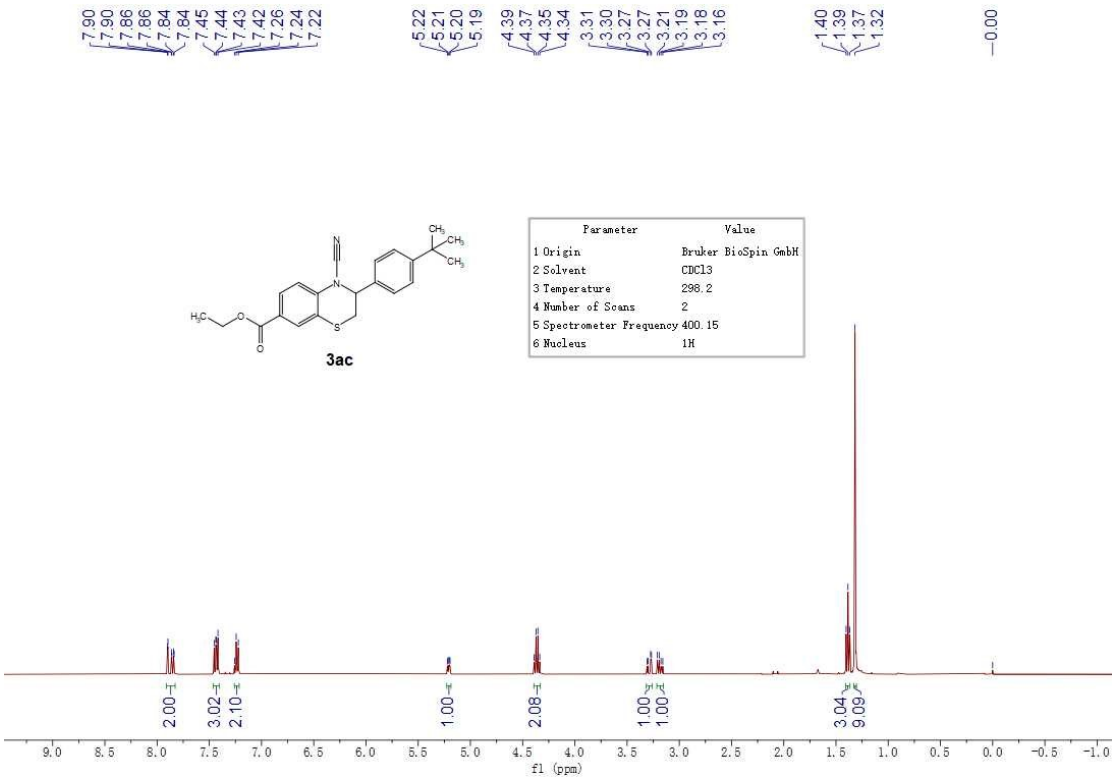
^{13}C NMR spectrum of **3oa** (100 MHz, $CDCl_3$)



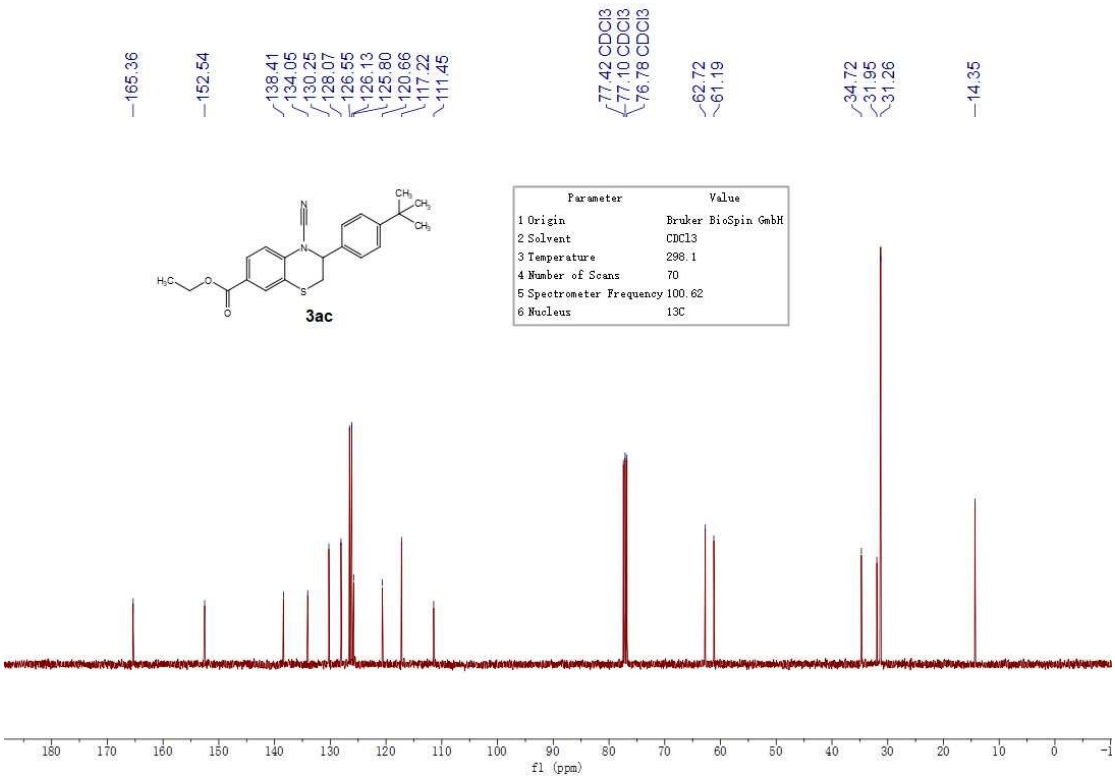
^{1}H NMR spectrum of **3ab** (400 MHz, $CDCl_3$)



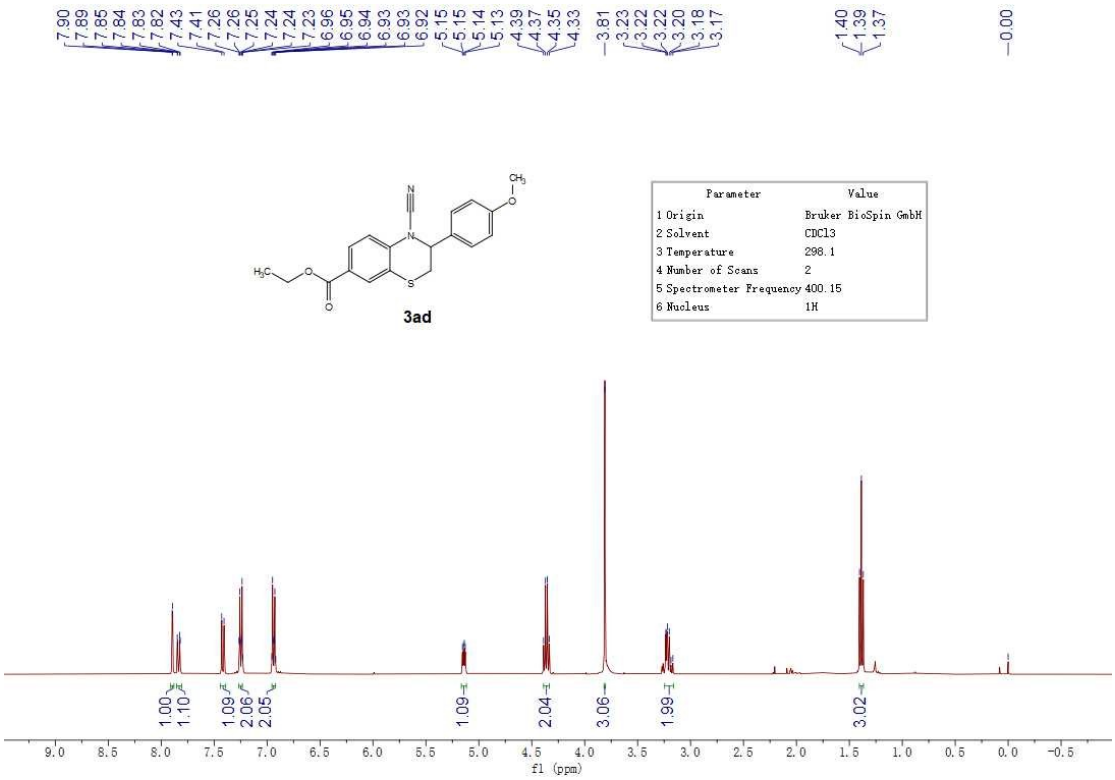
^{13}C NMR spectrum of **3ab** (100 MHz, $CDCl_3$)



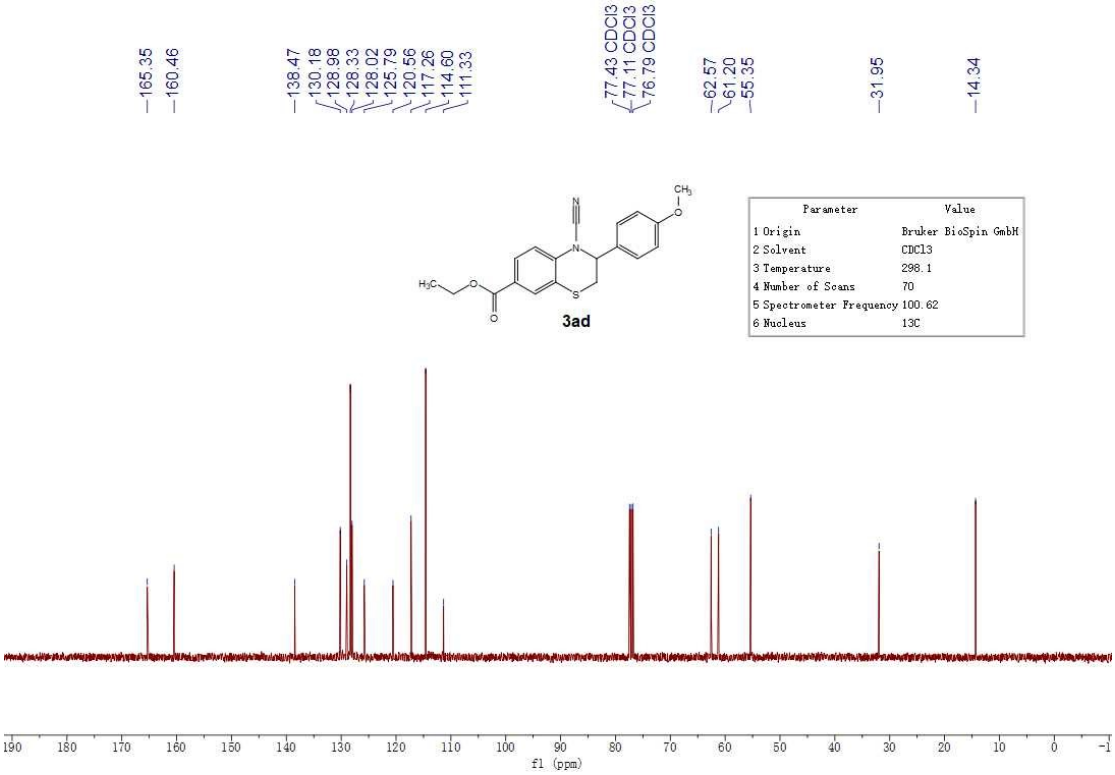
^{1}H NMR spectrum of **3ac** (400 MHz, $CDCl_3$)



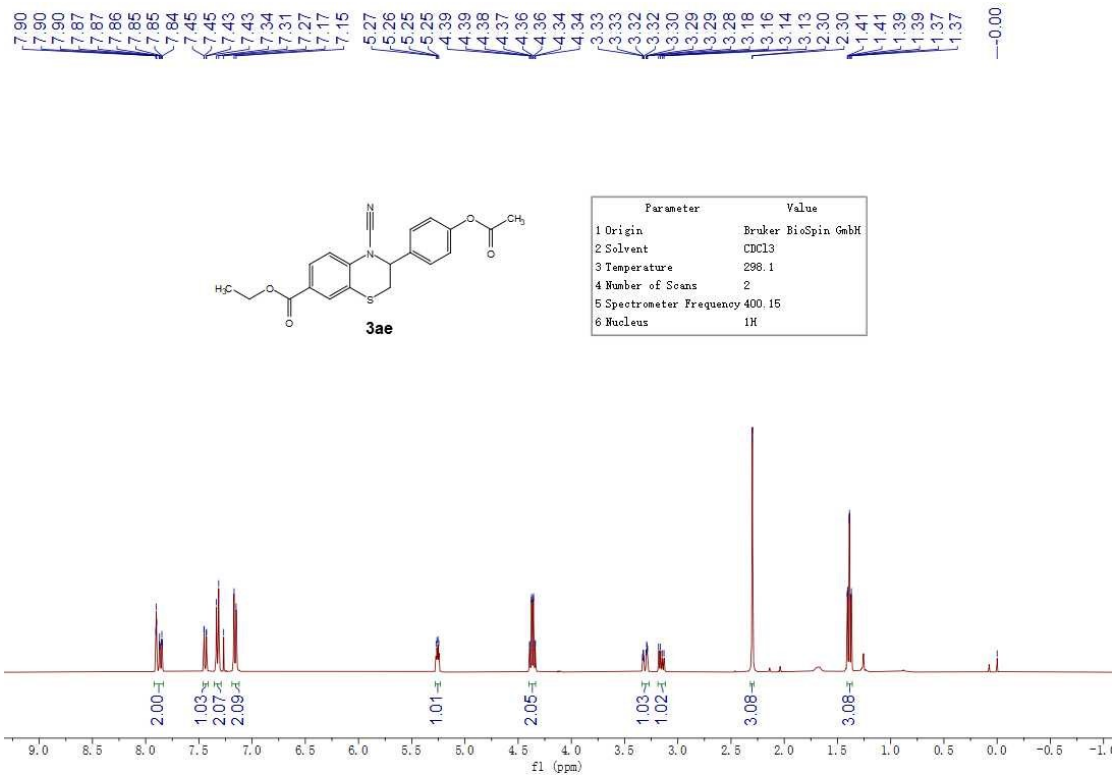
^{13}C NMR spectrum of **3ac** (100 MHz, $CDCl_3$)



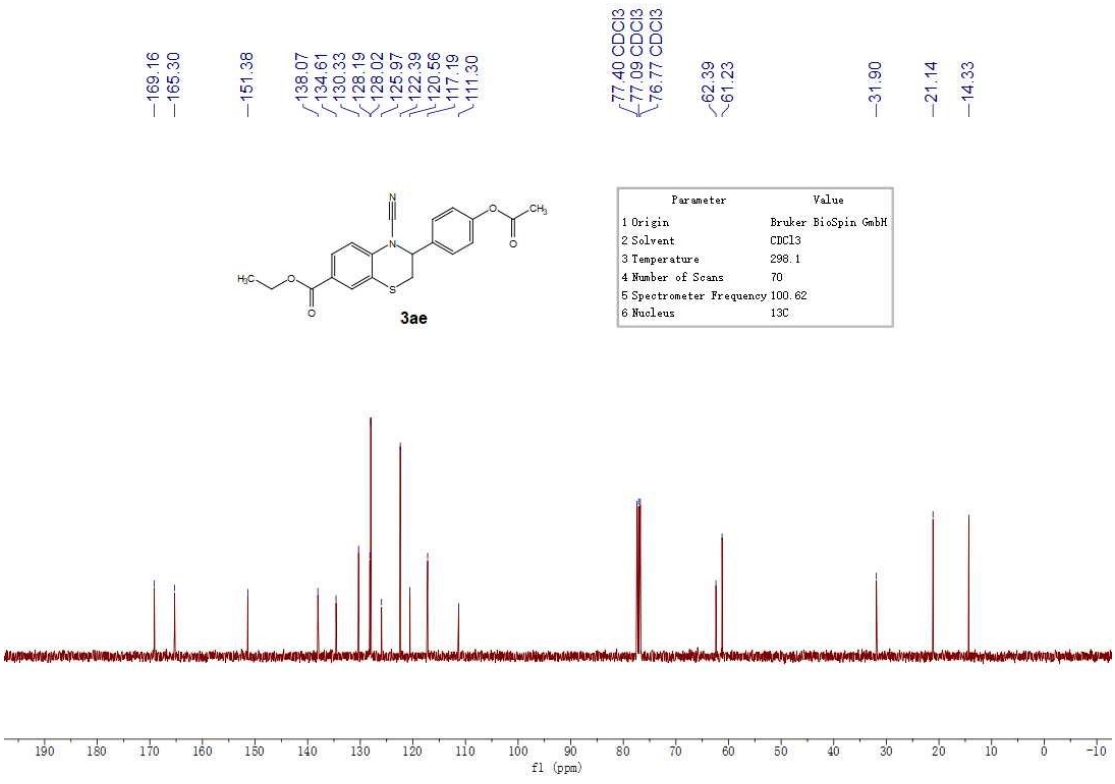
^{1}H NMR spectrum of **3ad** (400 MHz, $CDCl_3$)



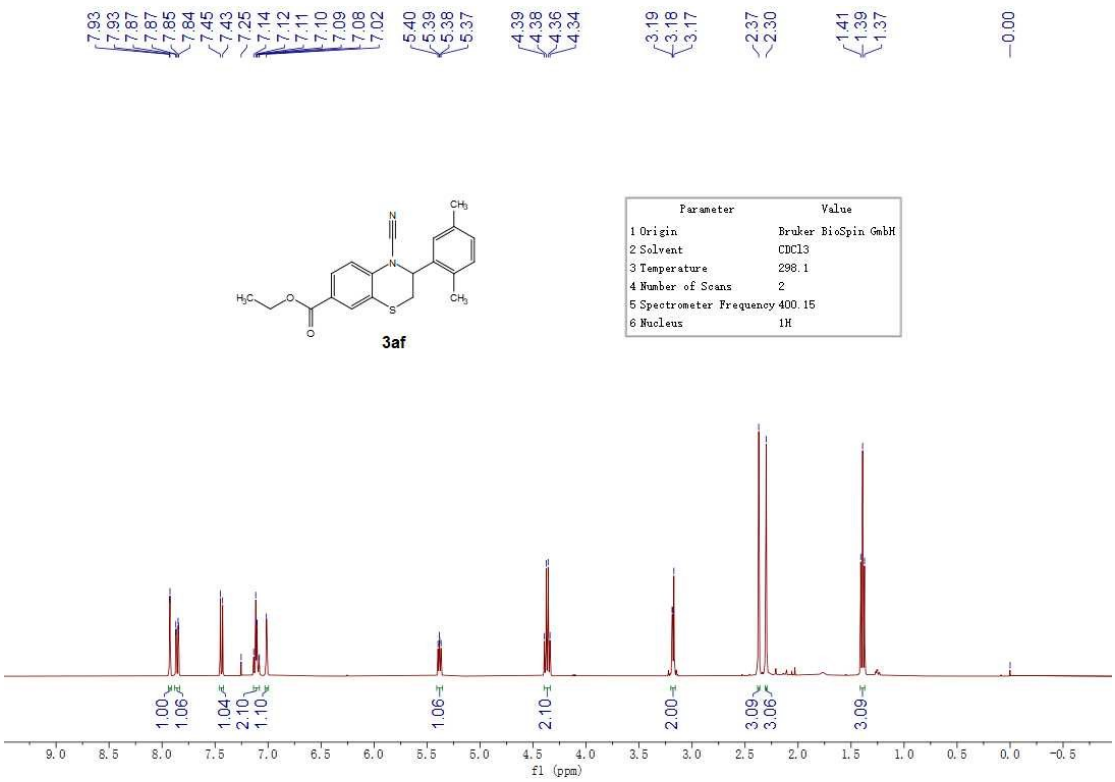
^{13}C NMR spectrum of **3ad** (100 MHz, $CDCl_3$)



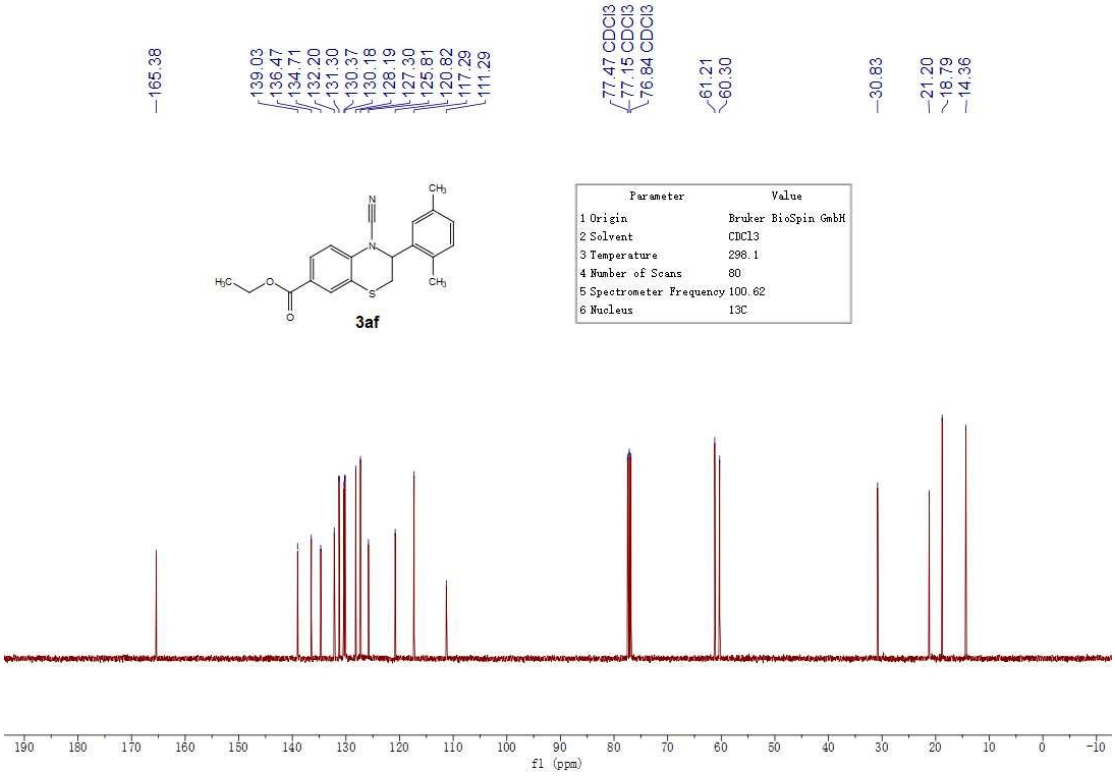
^{1}H NMR spectrum of **3ae** (400 MHz, $CDCl_3$)



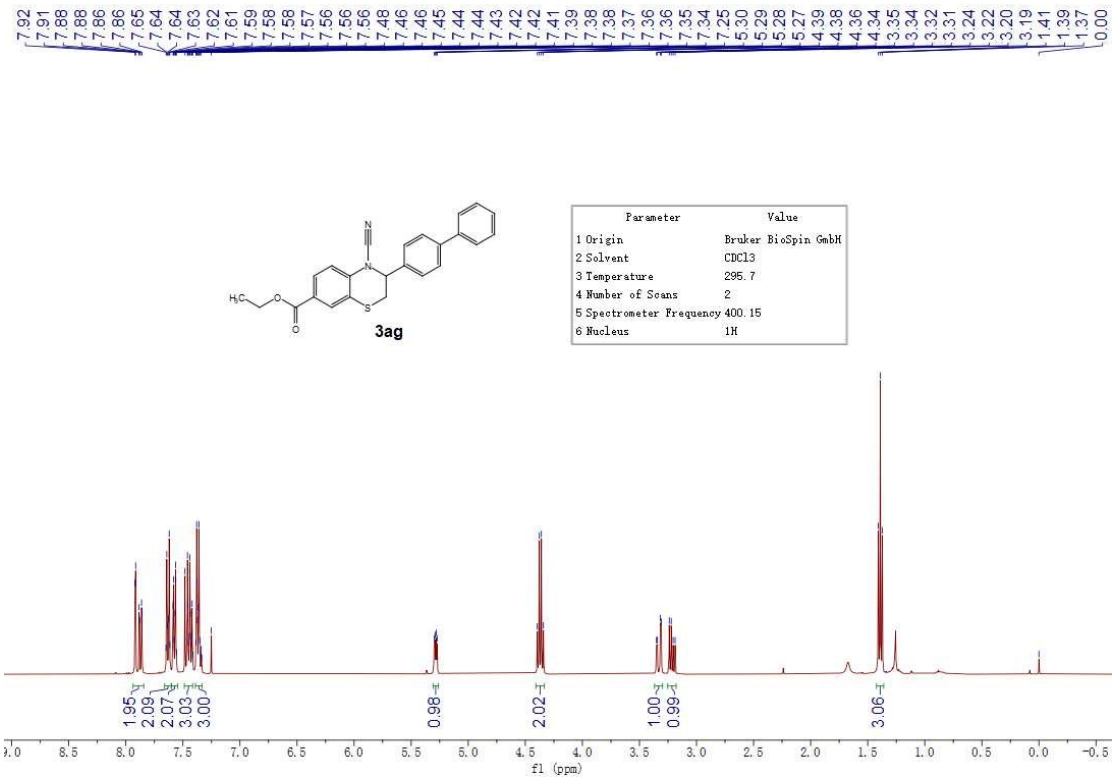
^{13}C NMR spectrum of **3ae** (100 MHz, $CDCl_3$)



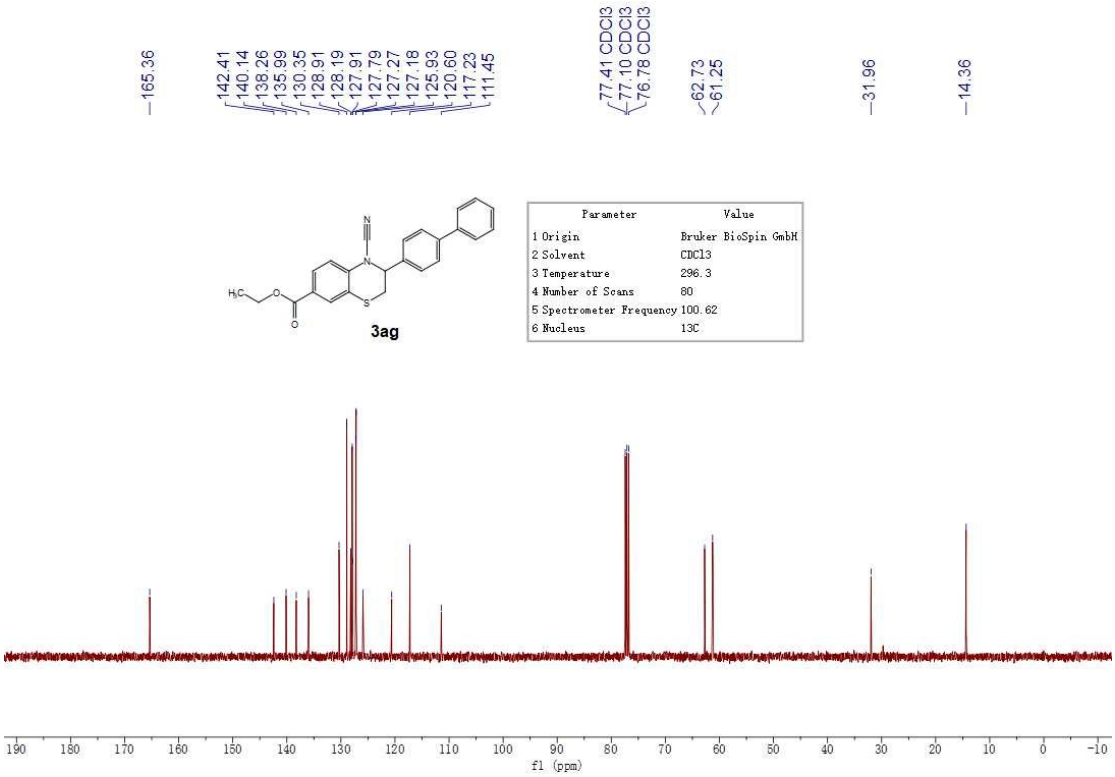
^{1}H NMR spectrum of **3af** (400 MHz, $CDCl_3$)



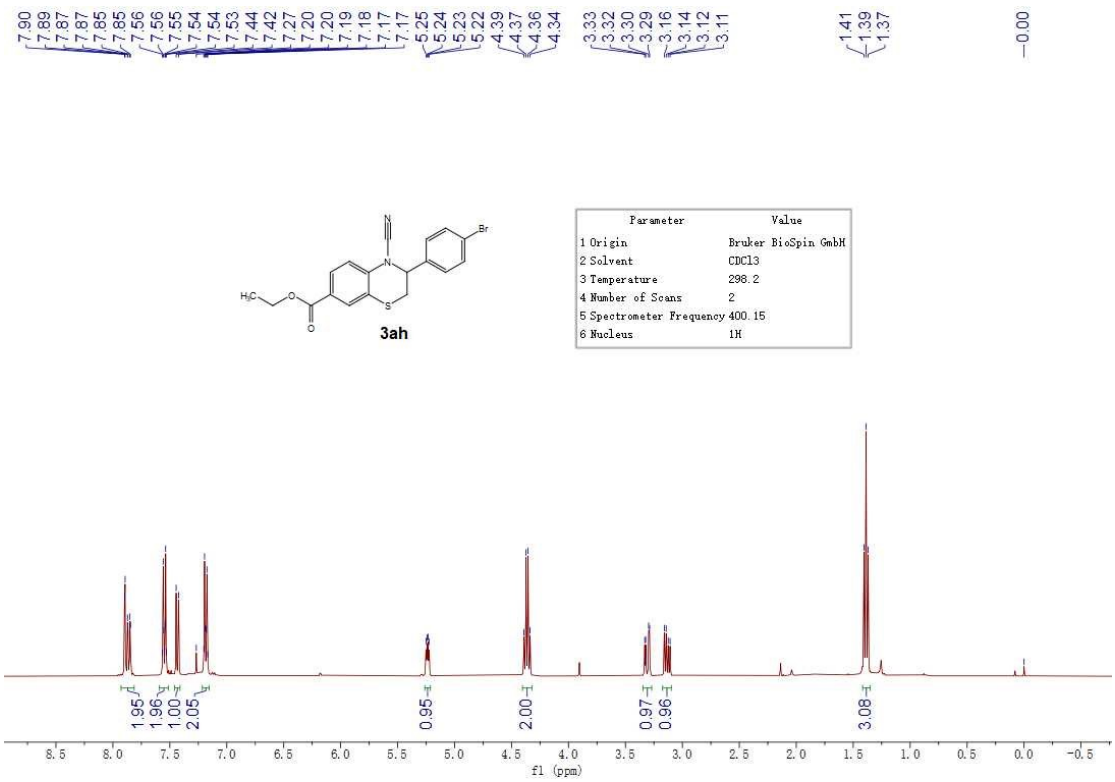
^{13}C NMR spectrum of **3af** (100 MHz, $CDCl_3$)



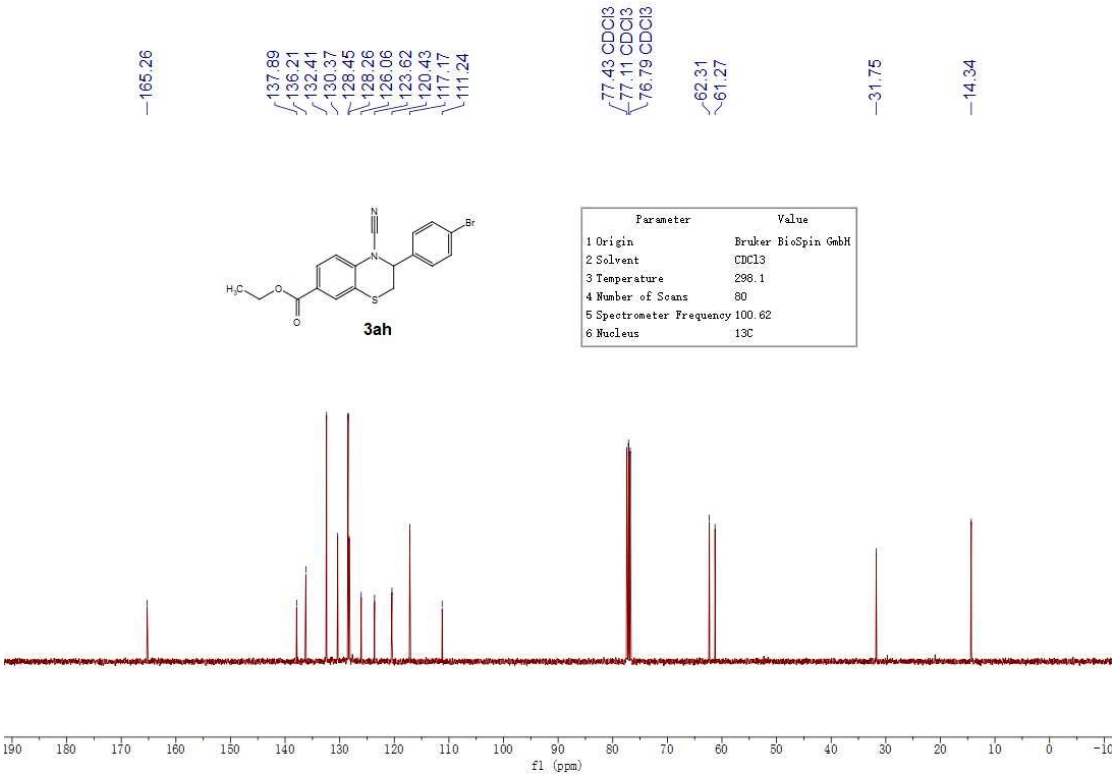
^{1}H NMR spectrum of **3ag** (400 MHz, $CDCl_3$)



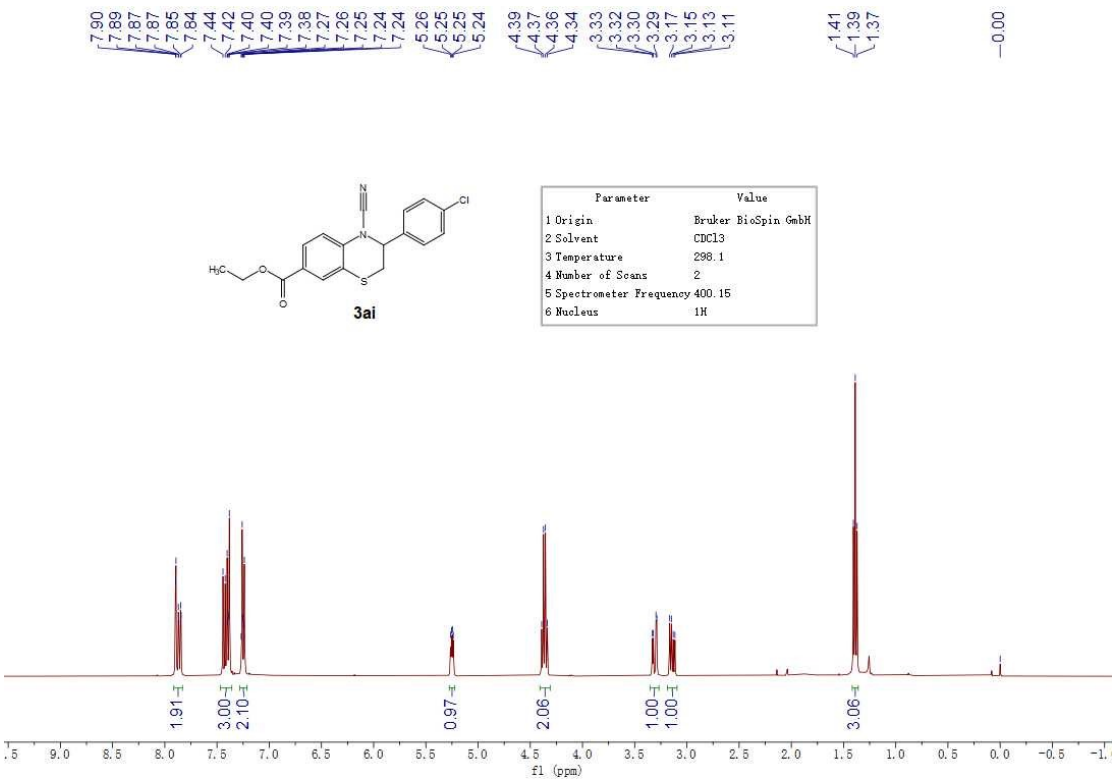
^{13}C NMR spectrum of **3ag** (100 MHz, $CDCl_3$)



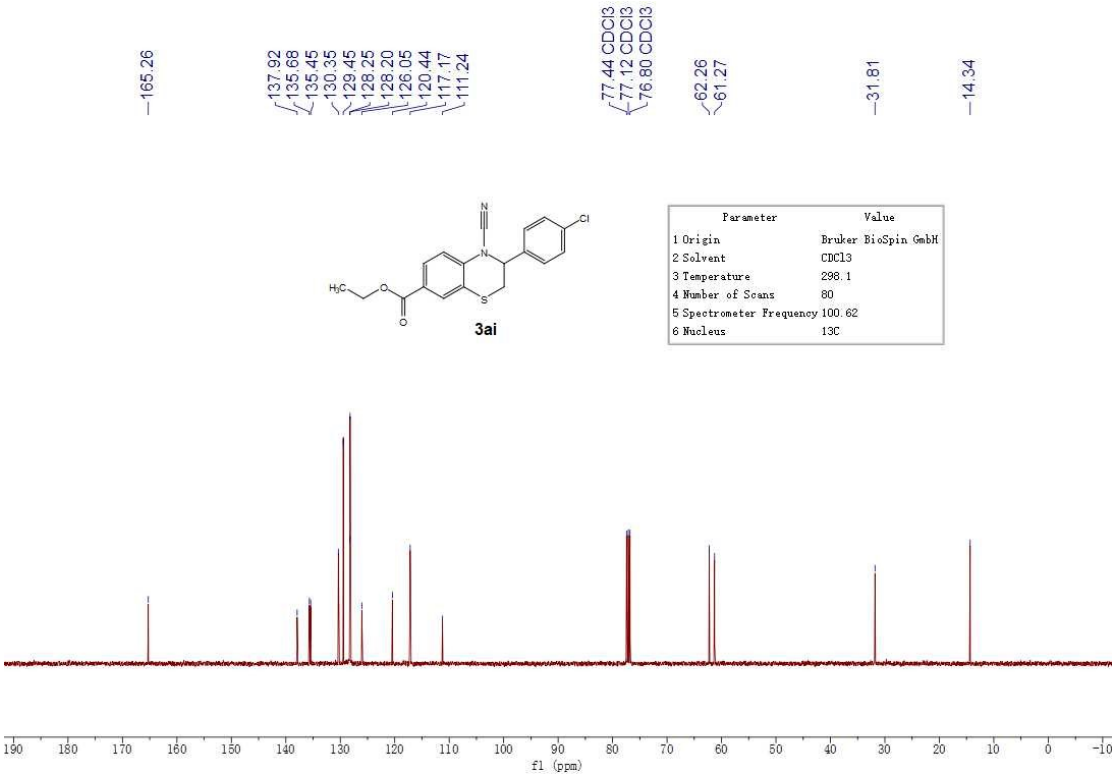
^{1}H NMR spectrum of **3ah** (400 MHz, $CDCl_3$)



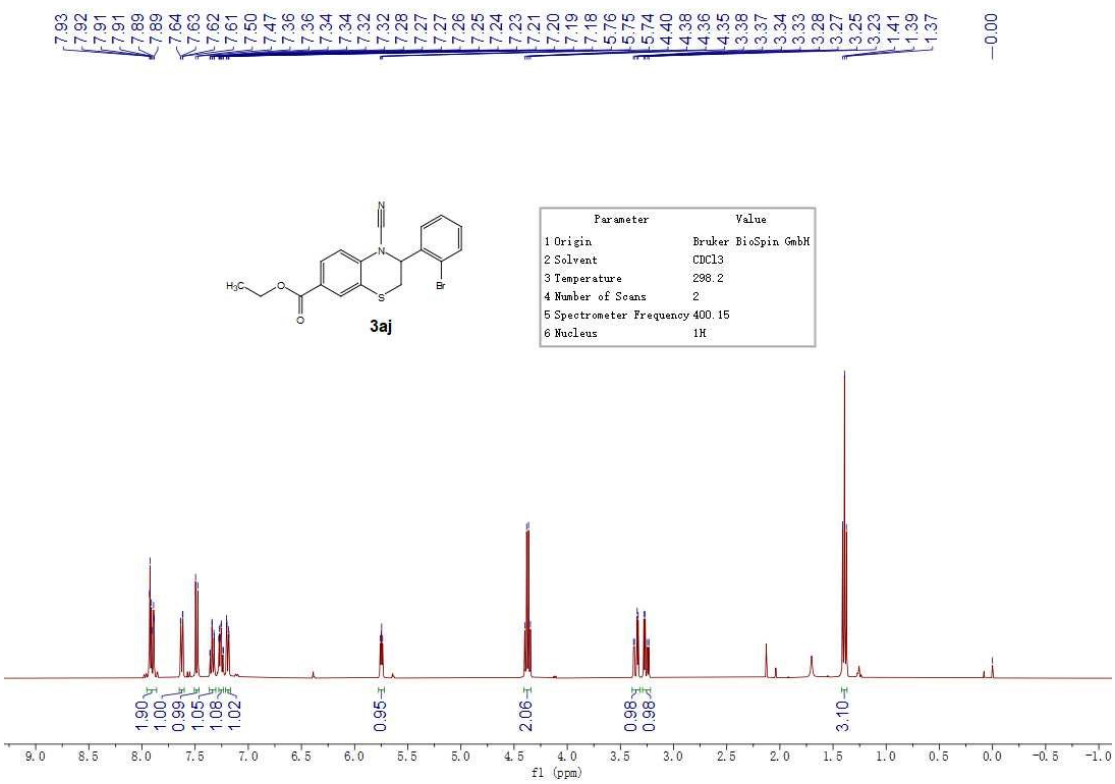
^{13}C NMR spectrum of **3ah** (100 MHz, $CDCl_3$)



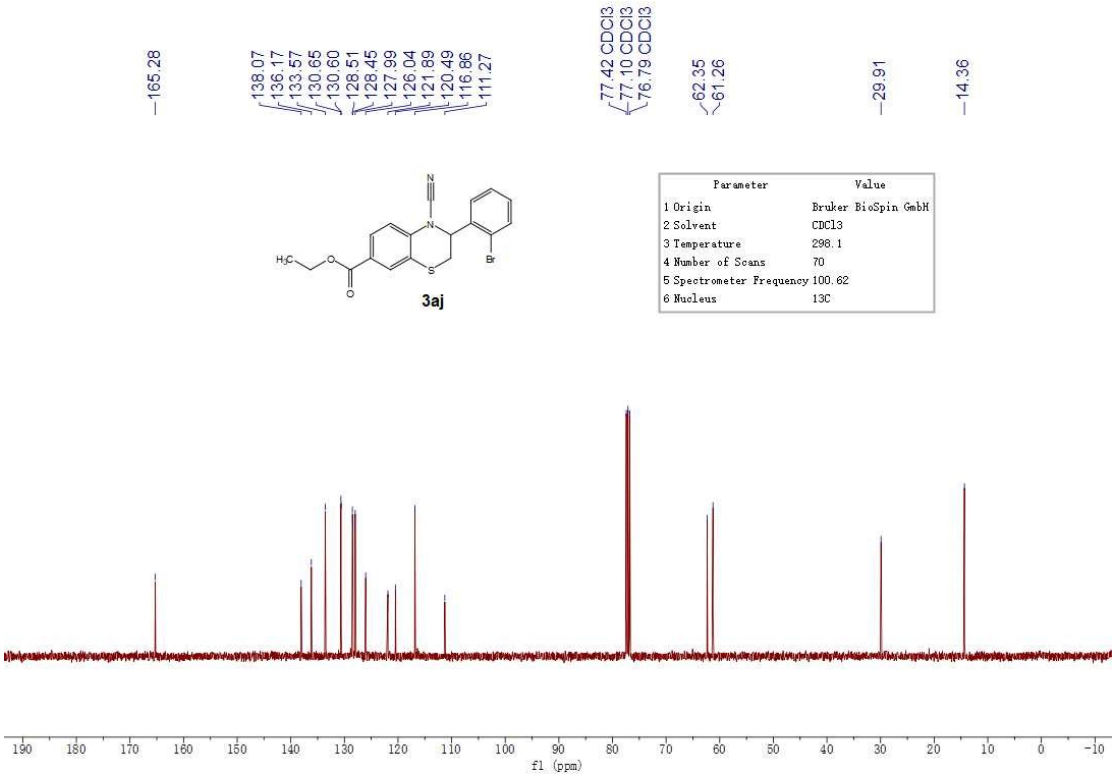
^{1}H NMR spectrum of **3ai** (400 MHz, $CDCl_3$)



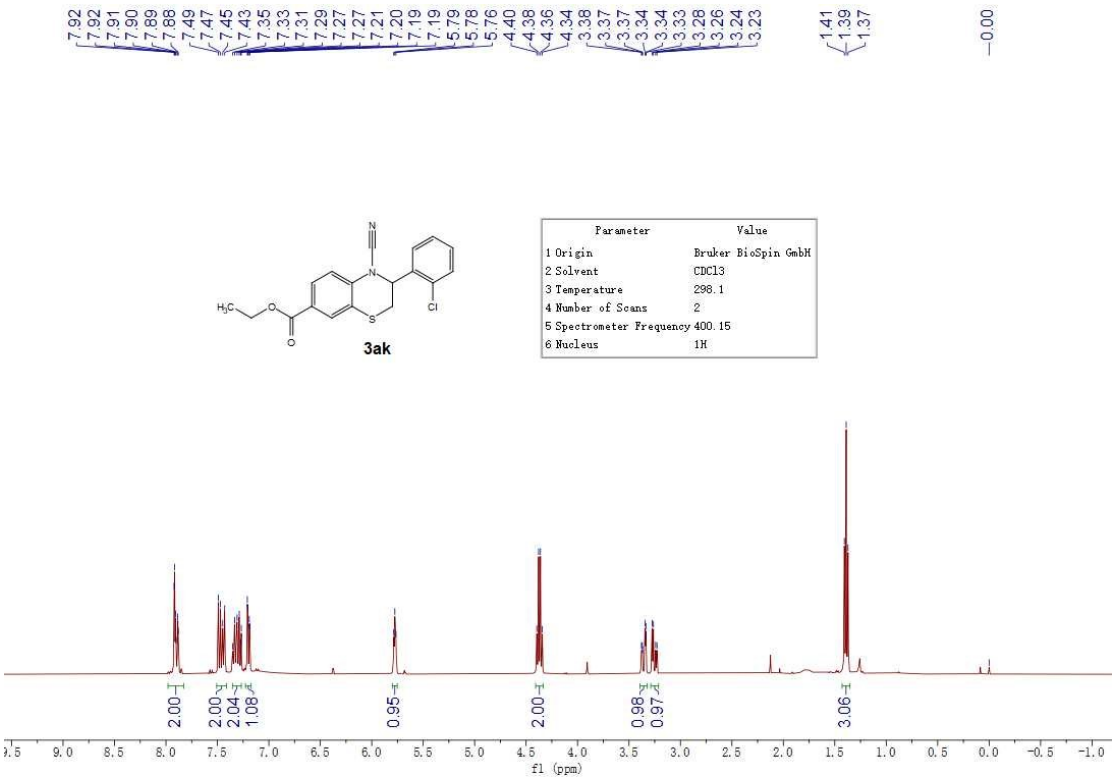
^{13}C NMR spectrum of **3ai** (100 MHz, $CDCl_3$)



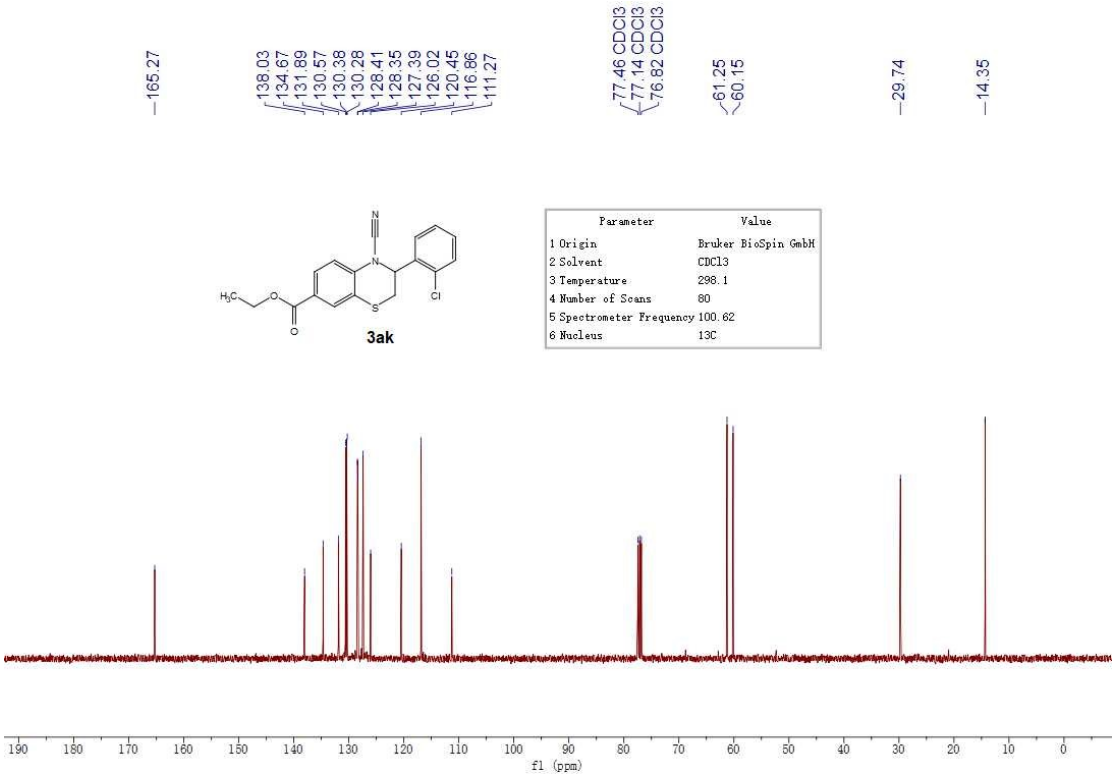
^{1}H NMR spectrum of **3aj** (400 MHz, $CDCl_3$)



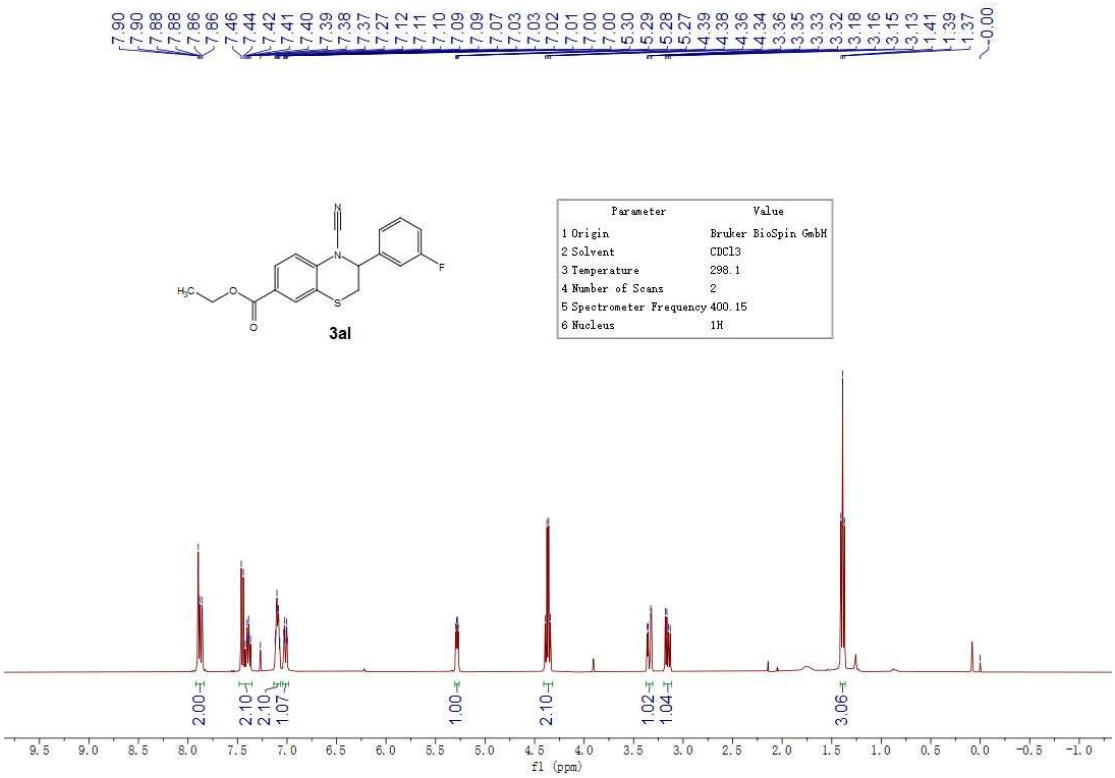
^{13}C NMR spectrum of **3aj** (100 MHz, $CDCl_3$)



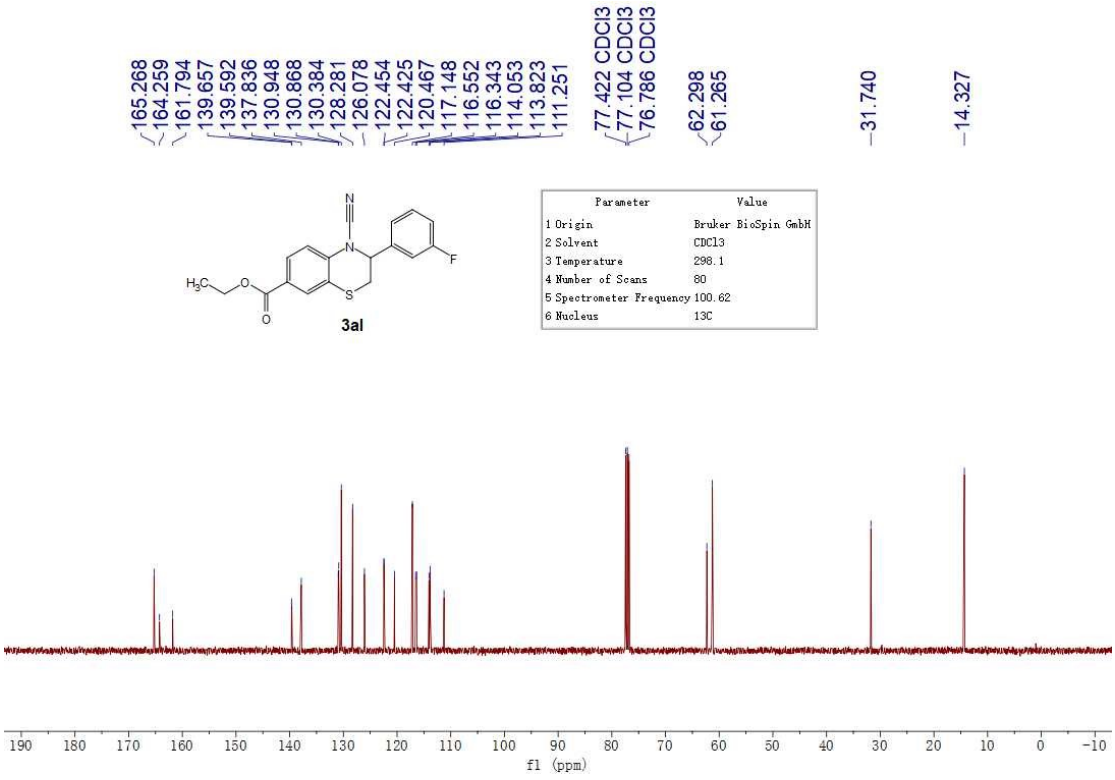
^{1}H NMR spectrum of **3ak** (400 MHz, $CDCl_3$)



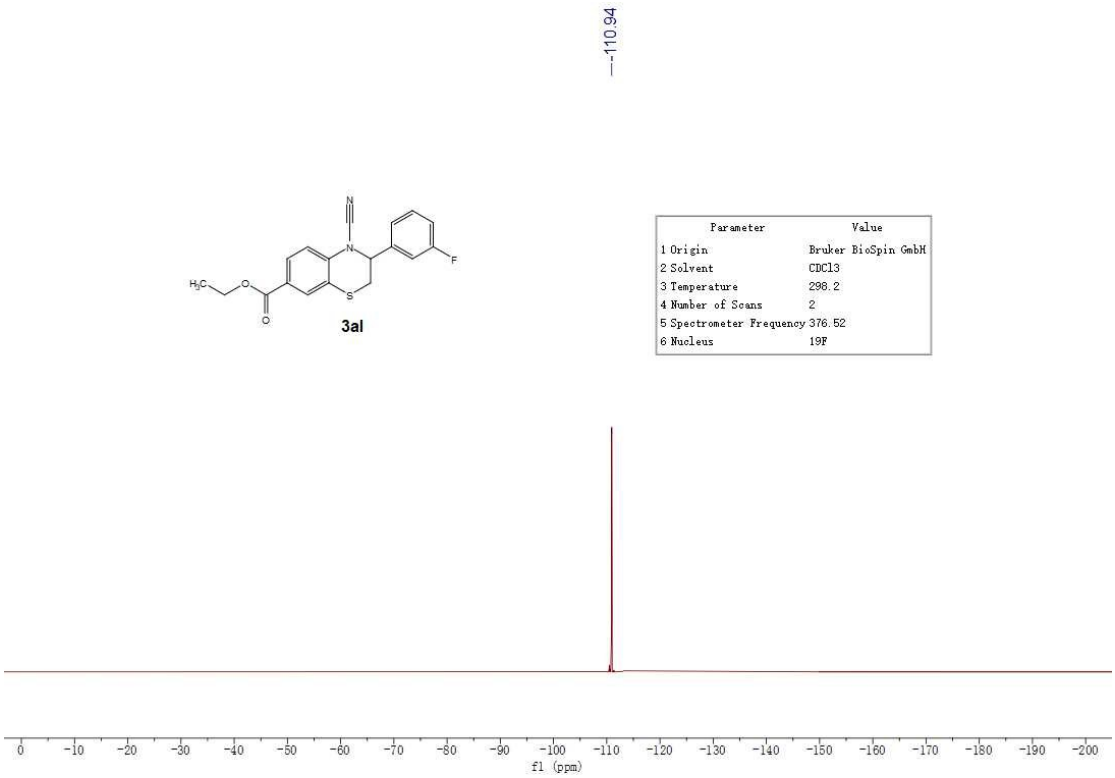
^{13}C NMR spectrum of **3ak** (100 MHz, $CDCl_3$)



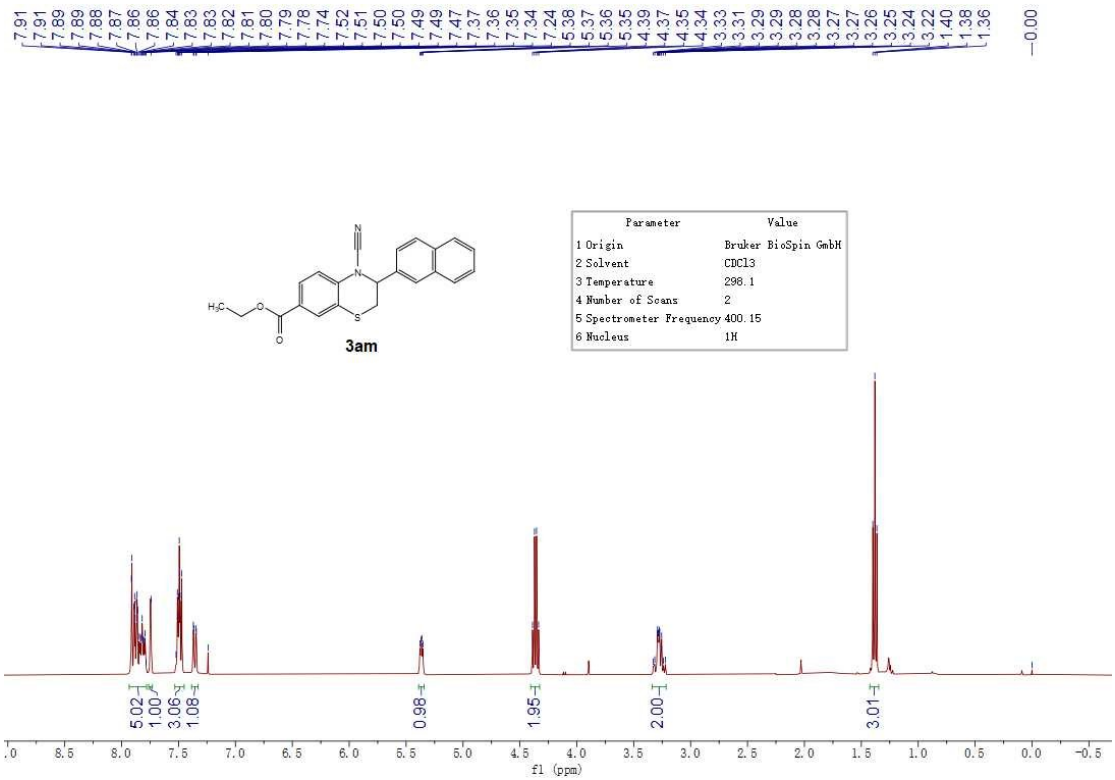
^{1}H NMR spectrum of **3al** (400 MHz, $CDCl_3$)



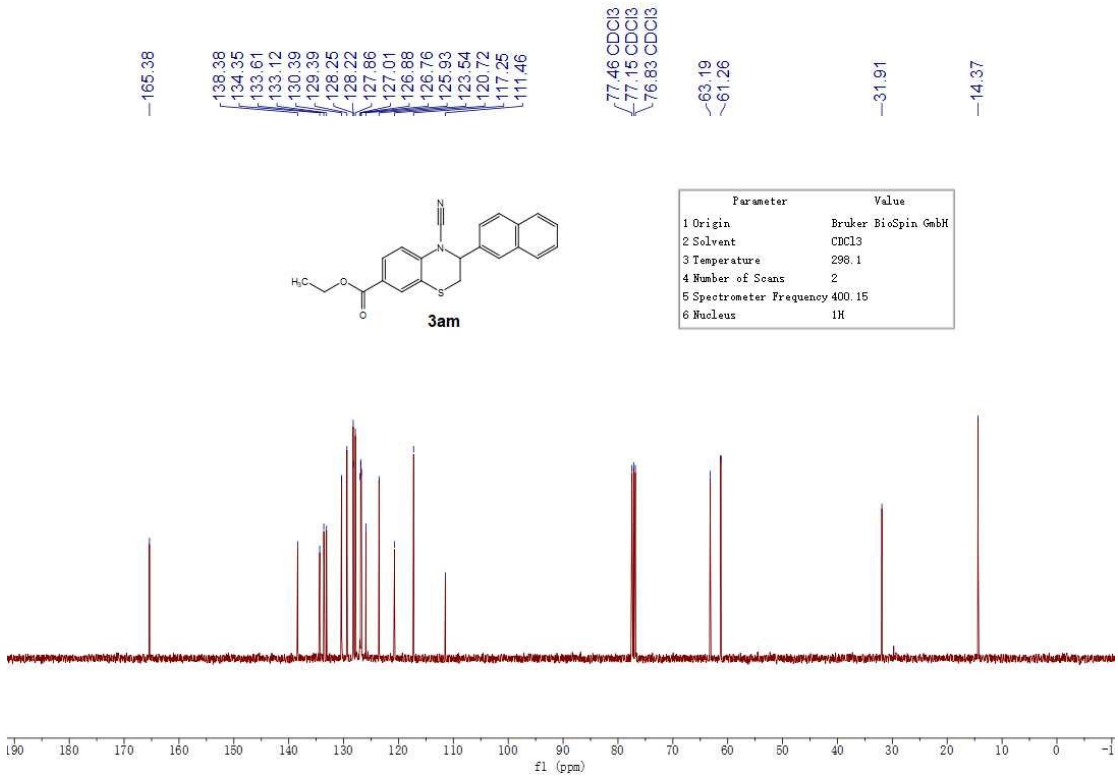
^{13}C NMR spectrum of **3al** (100 MHz, $CDCl_3$)



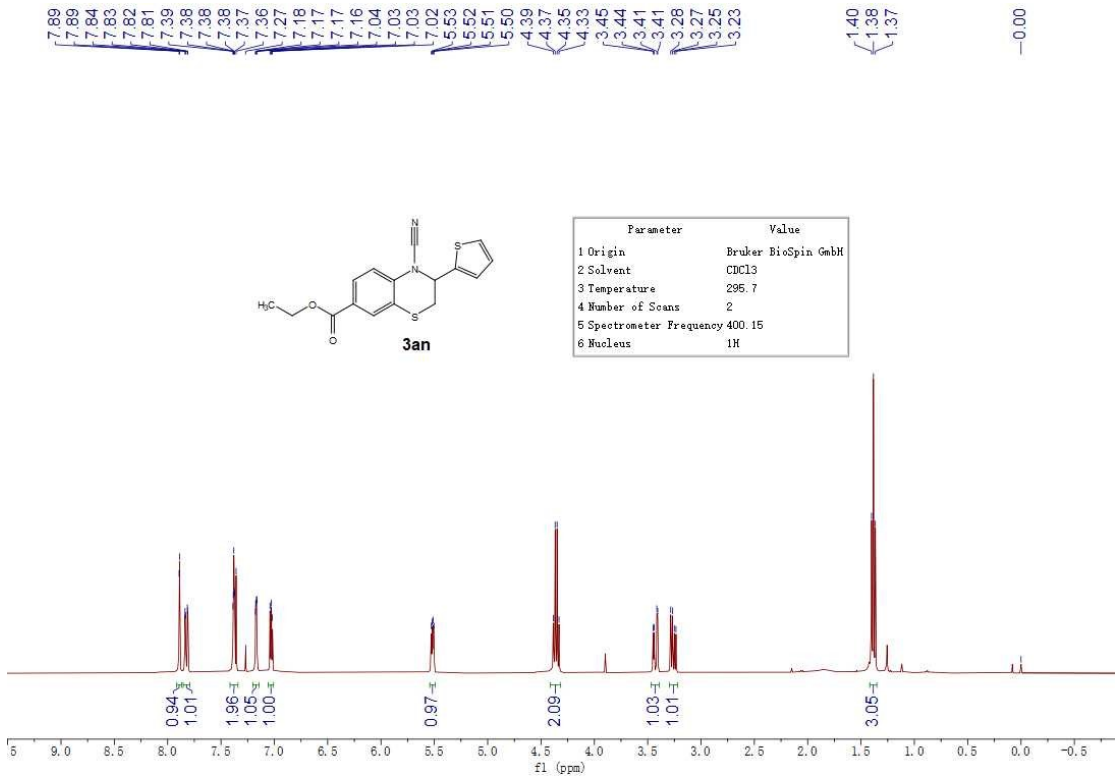
^{19}F NMR spectrum of **3al** (376 MHz, $CDCl_3$)



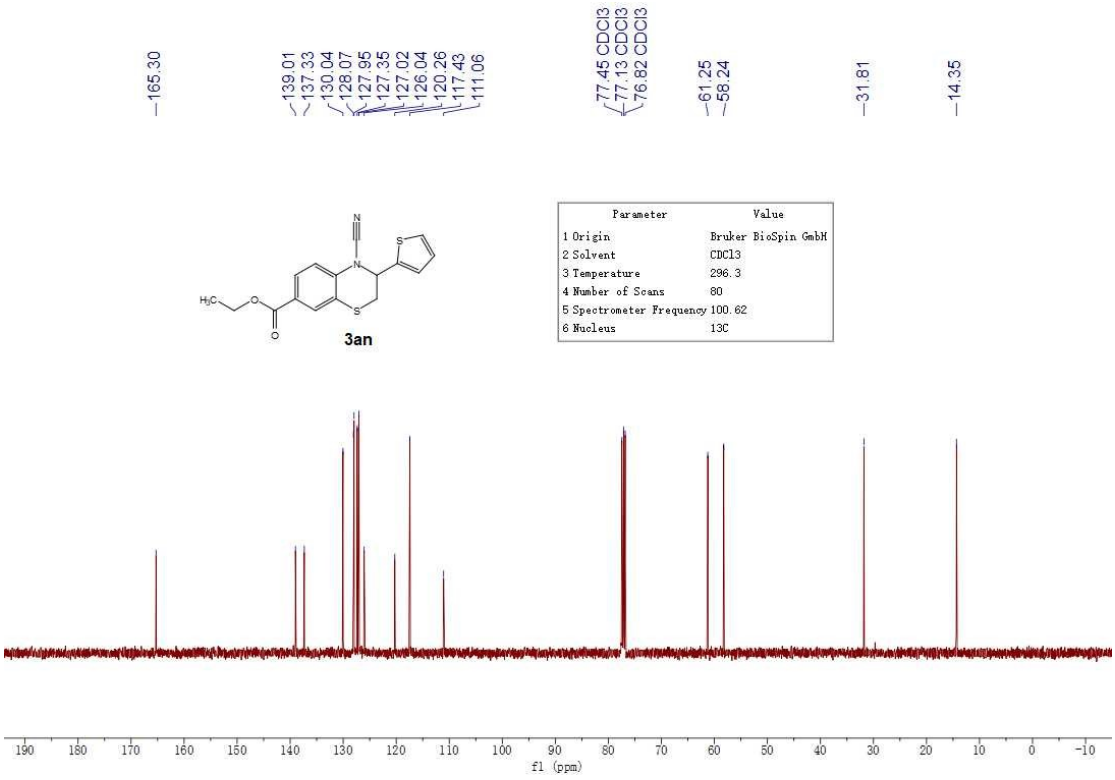
^{1}H NMR spectrum of **3am** (400 MHz, $CDCl_3$)



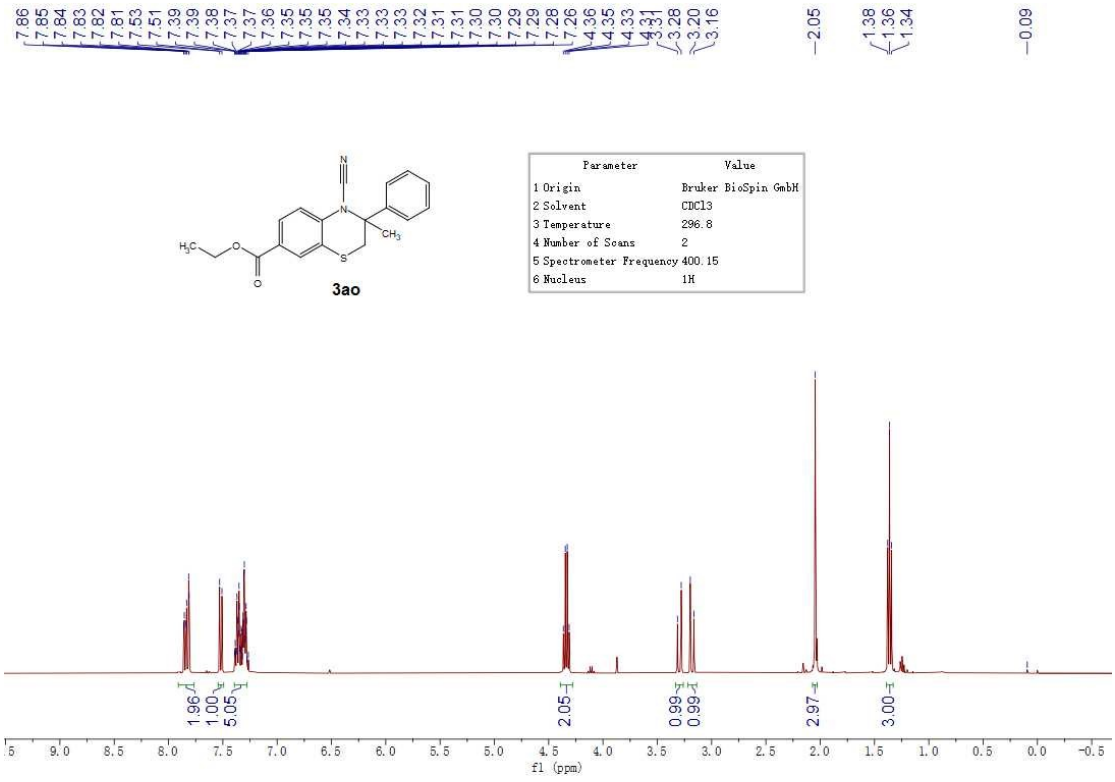
^{13}C NMR spectrum of **3am** (100 MHz, $CDCl_3$)



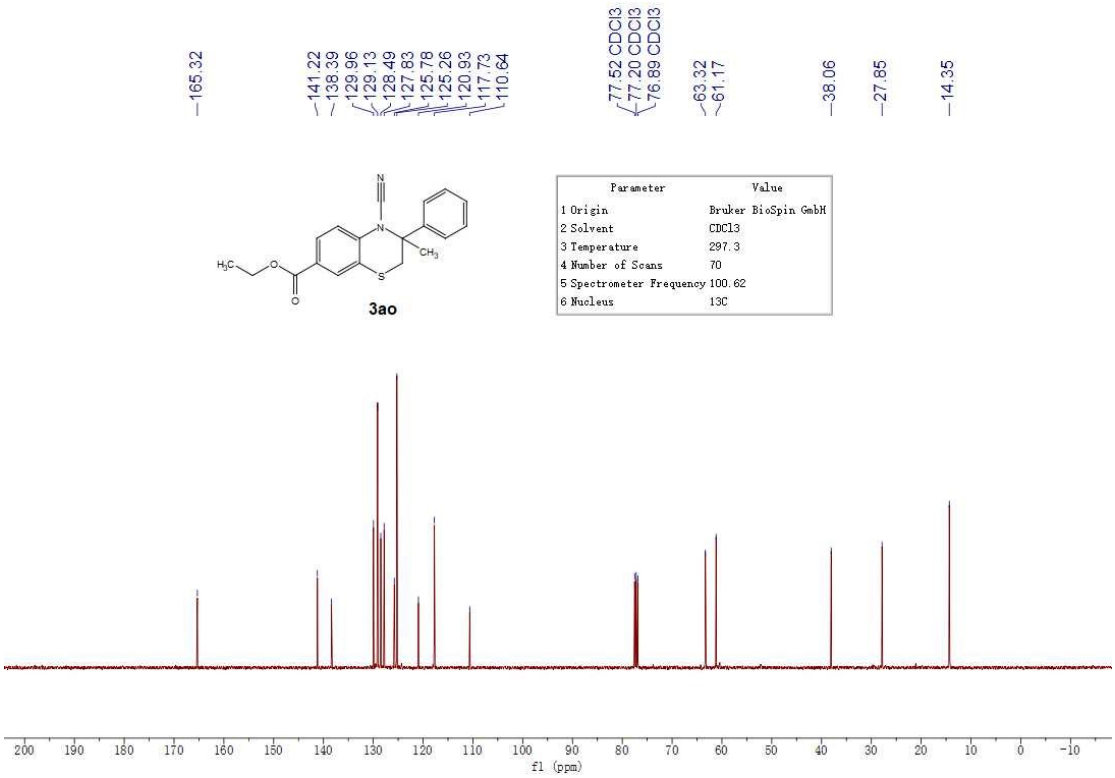
^{1}H NMR spectrum of **3an** (400 MHz, $CDCl_3$)



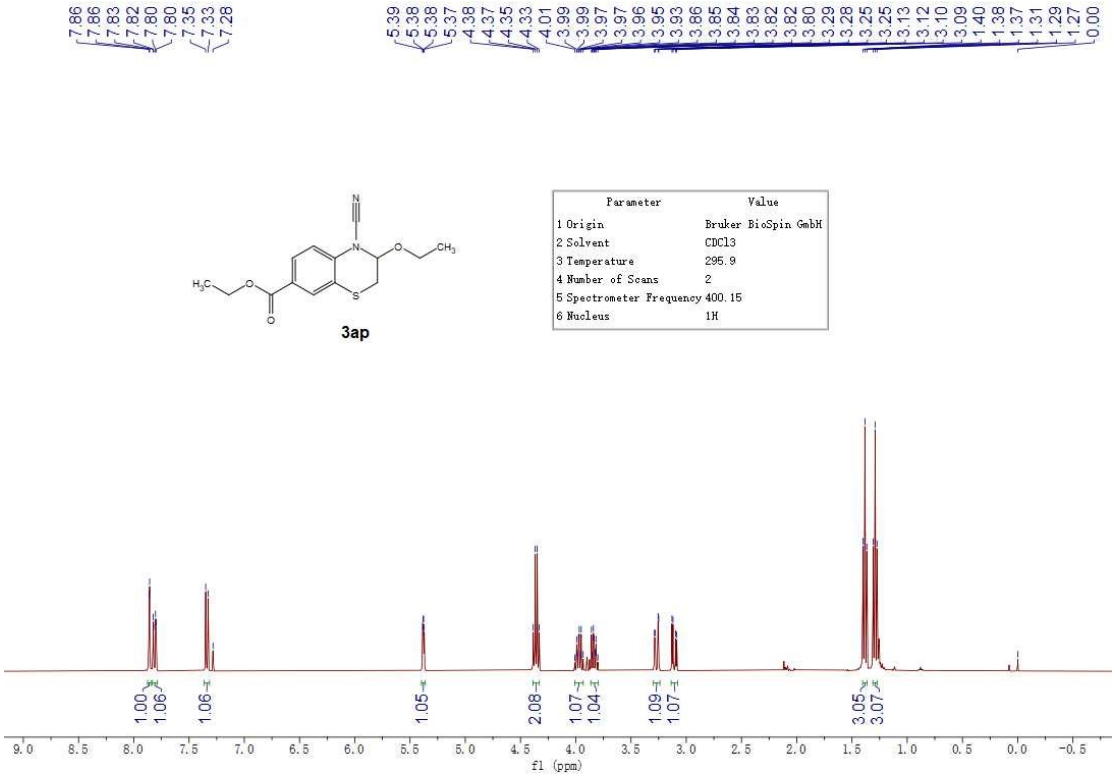
^{13}C NMR spectrum of **3an** (100 MHz, $CDCl_3$)



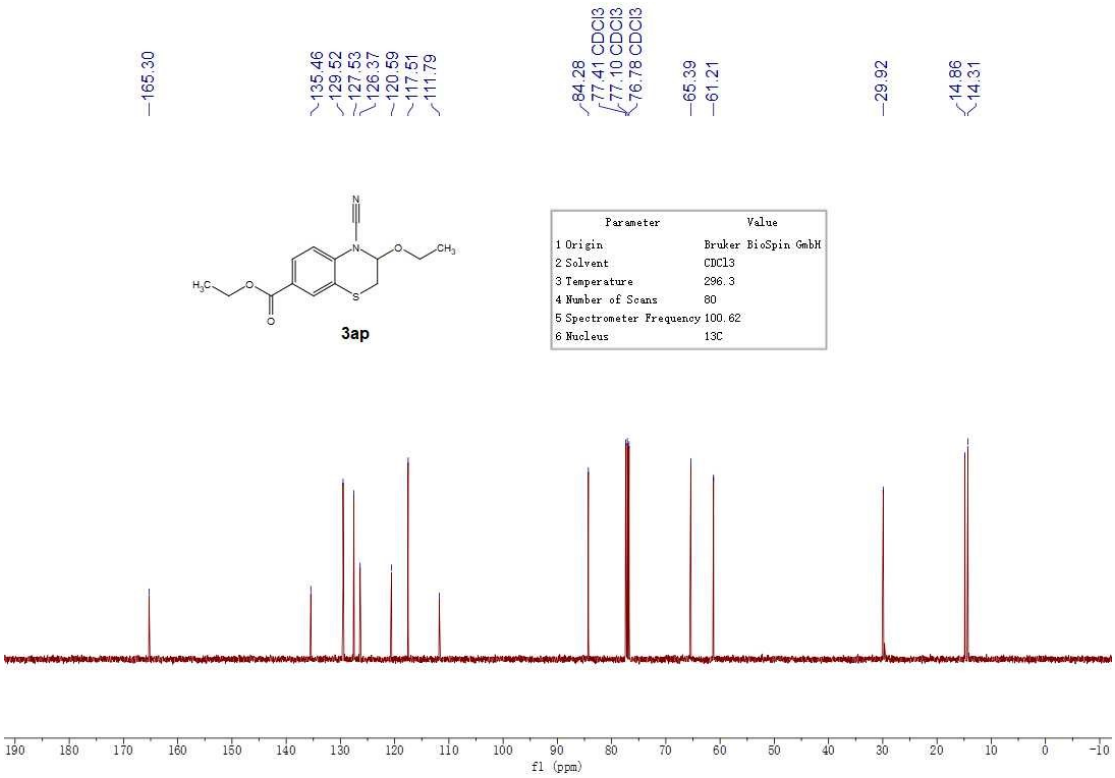
^{1}H NMR spectrum of **3ao** (400 MHz, $CDCl_3$)



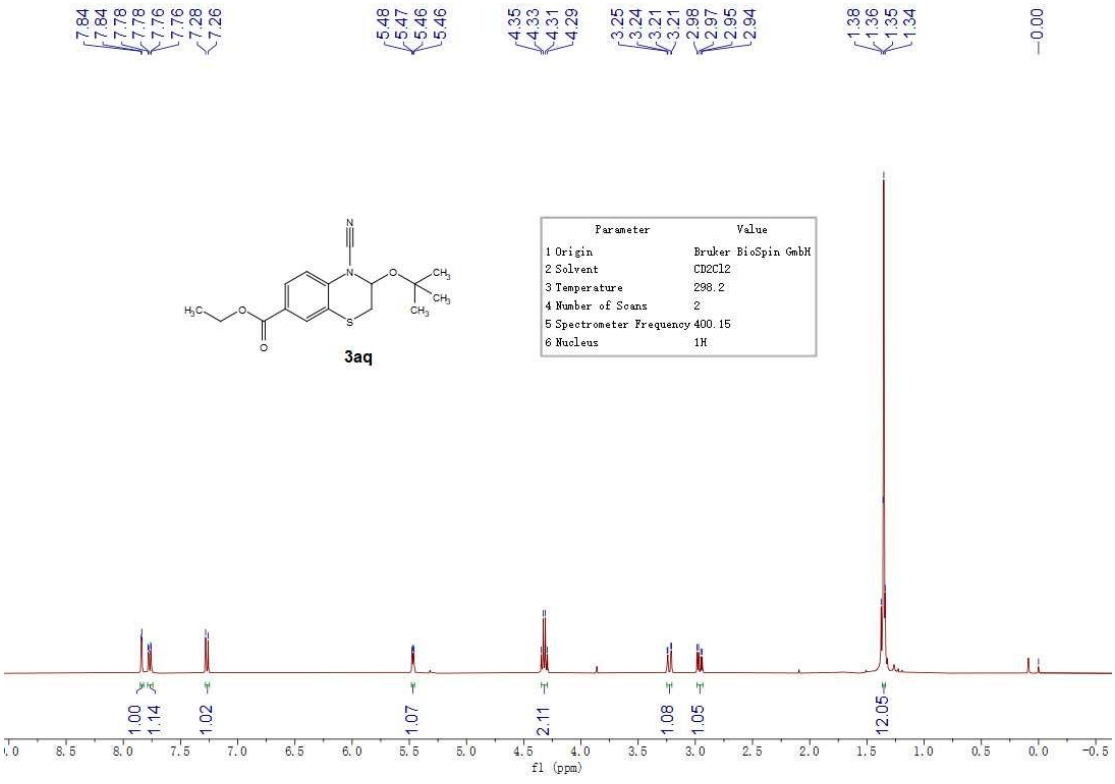
^{13}C NMR spectrum of **3ao** (100 MHz, $CDCl_3$)



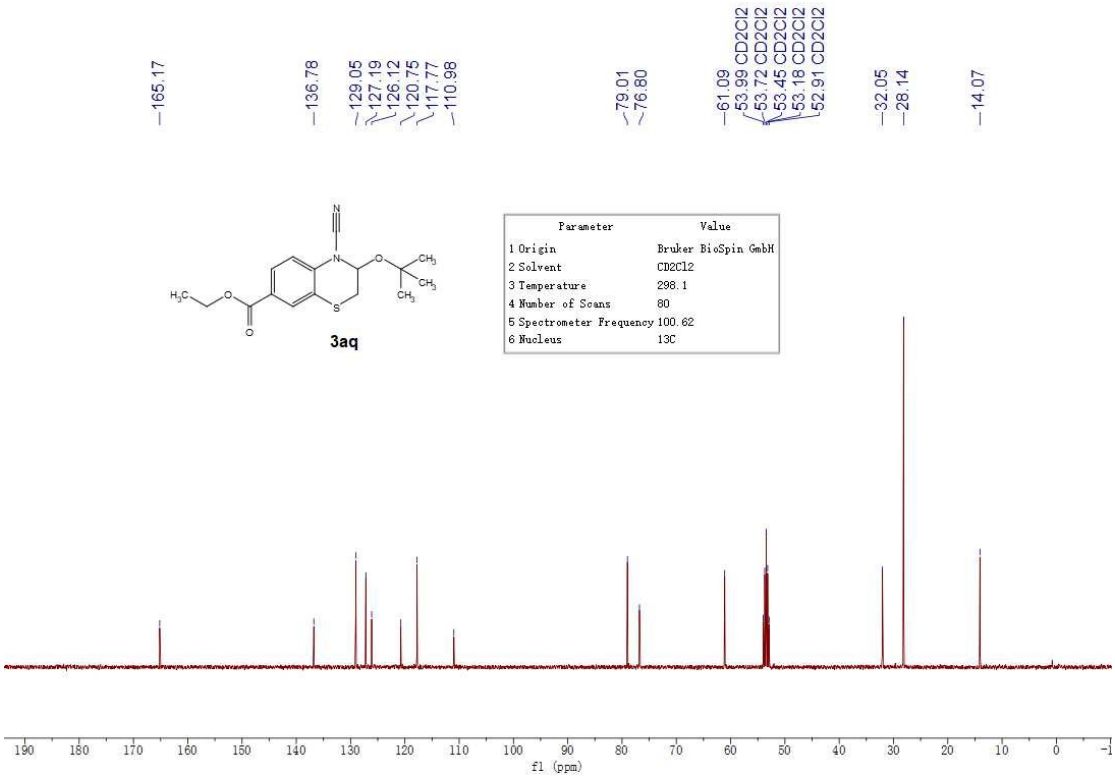
^{1}H NMR spectrum of **3ap** (400 MHz, $CDCl_3$)



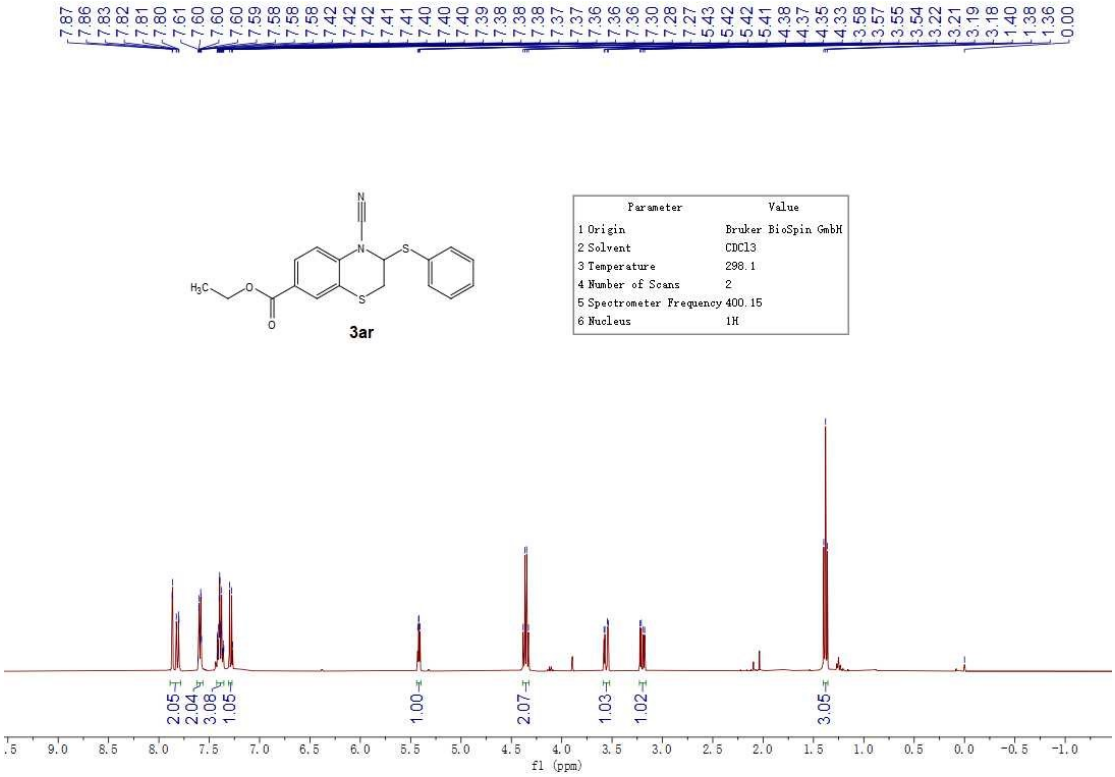
^{13}C NMR spectrum of **3ap** (100 MHz, $CDCl_3$)



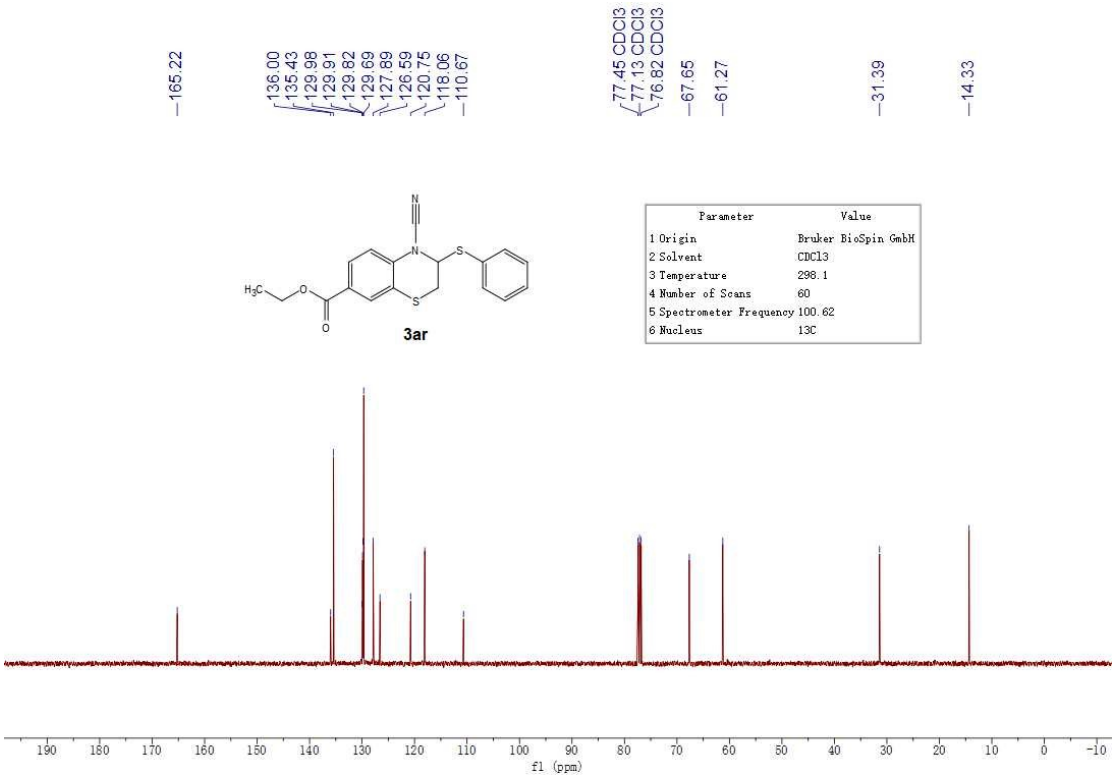
^{1}H NMR spectrum of **3aq** (400 MHz, CD_2Cl_2)



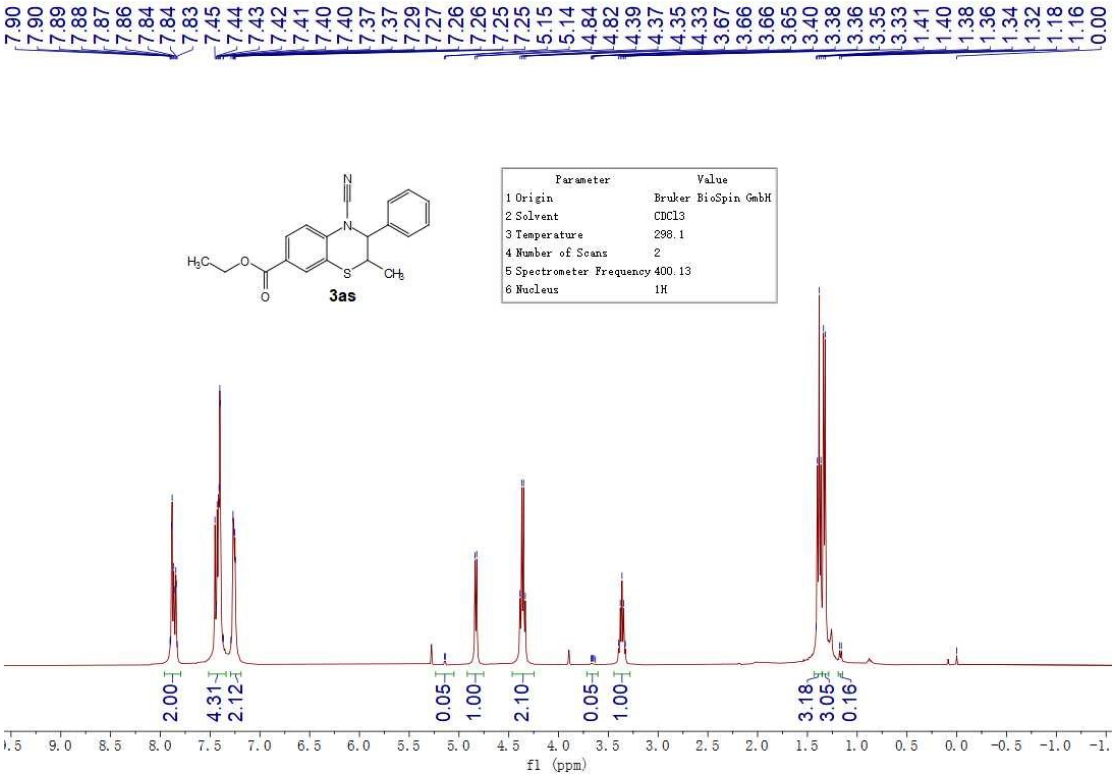
^{13}C NMR spectrum of **3aq** (100 MHz, CD_2Cl_2)



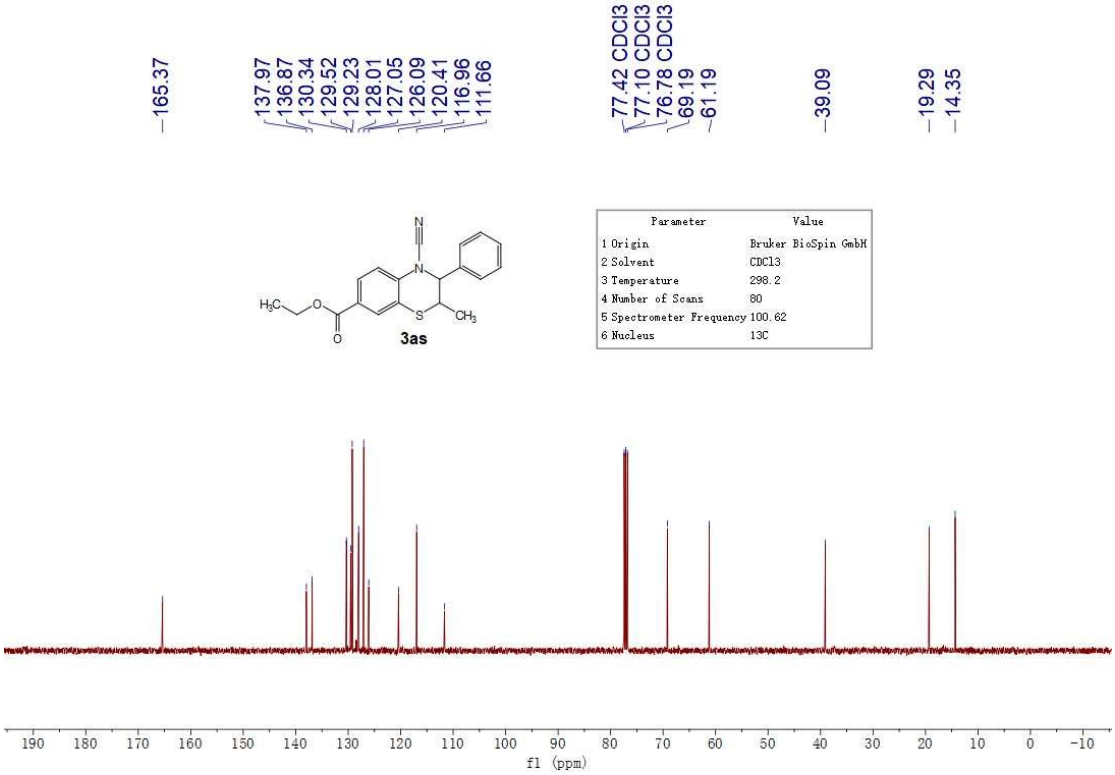
^{1}H NMR spectrum of **3ar** (400 MHz, $CDCl_3$)



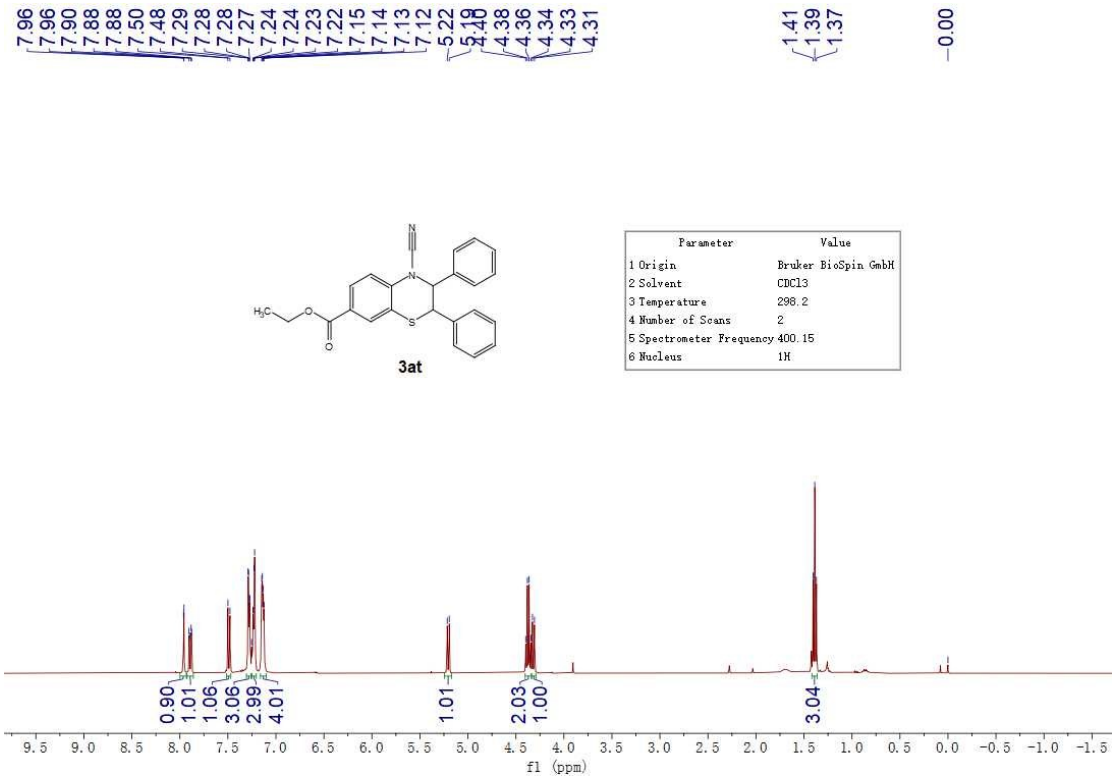
^{13}C NMR spectrum of **3ar** (100 MHz, $CDCl_3$)



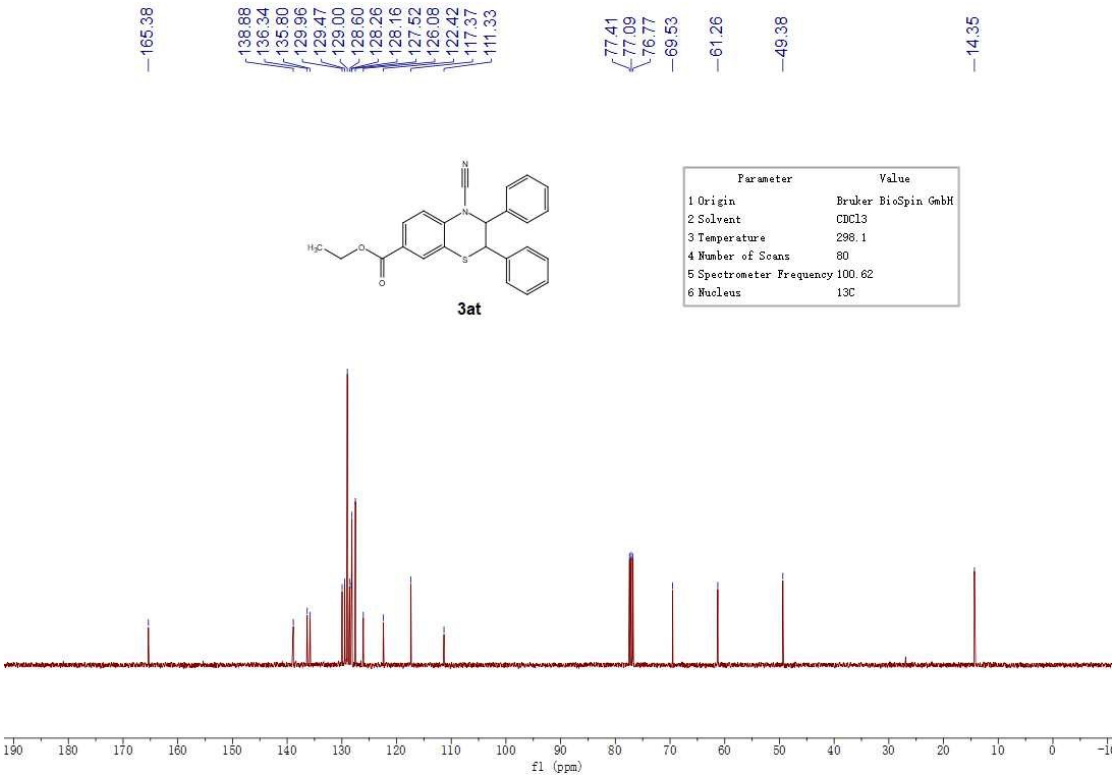
^{1}H NMR spectrum of **3as** (400 MHz, $CDCl_3$)



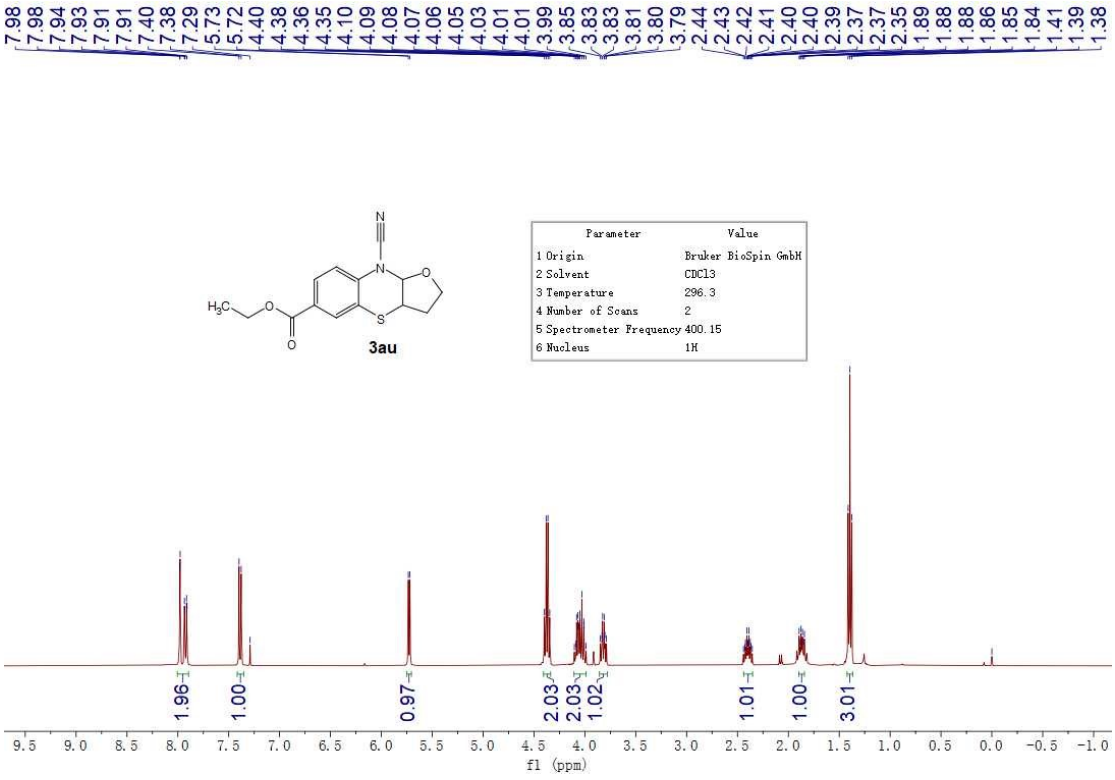
^{13}C NMR spectrum of **3as** (100 MHz, $CDCl_3$)



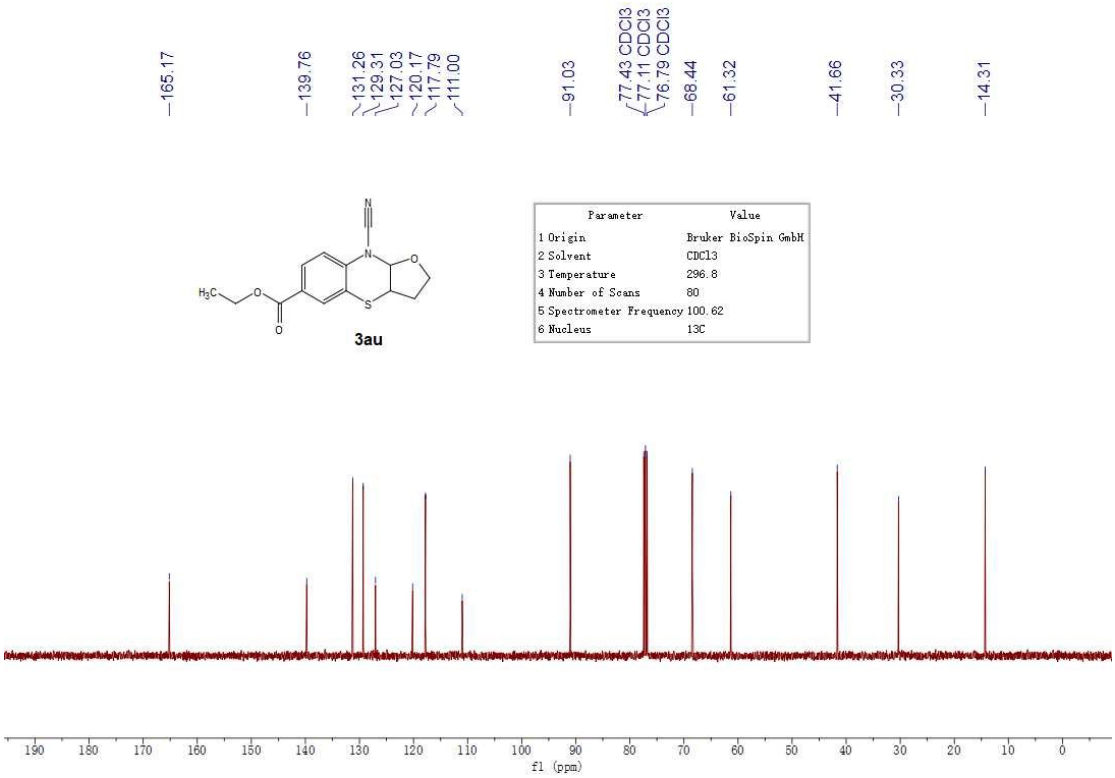
^{1}H NMR spectrum of **3at** (400 MHz, $CDCl_3$)



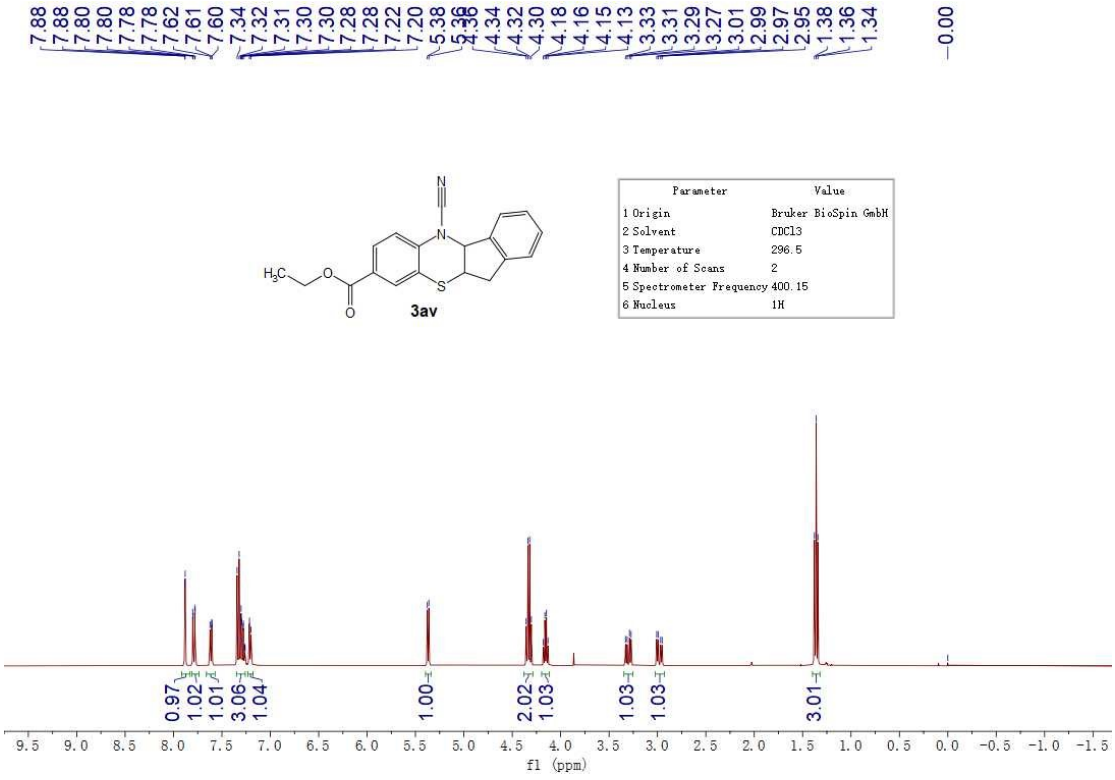
^{13}C NMR spectrum of **3at** (100 MHz, $CDCl_3$)



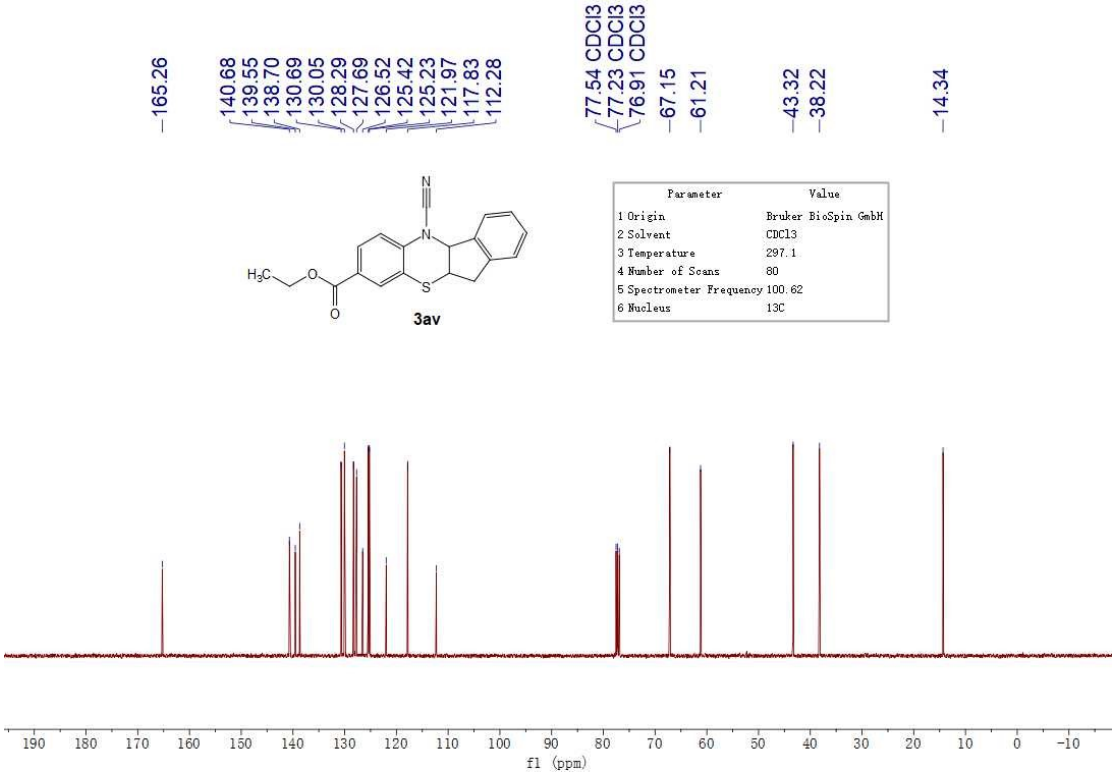
^{1}H NMR spectrum of **3au** (400 MHz, $CDCl_3$)



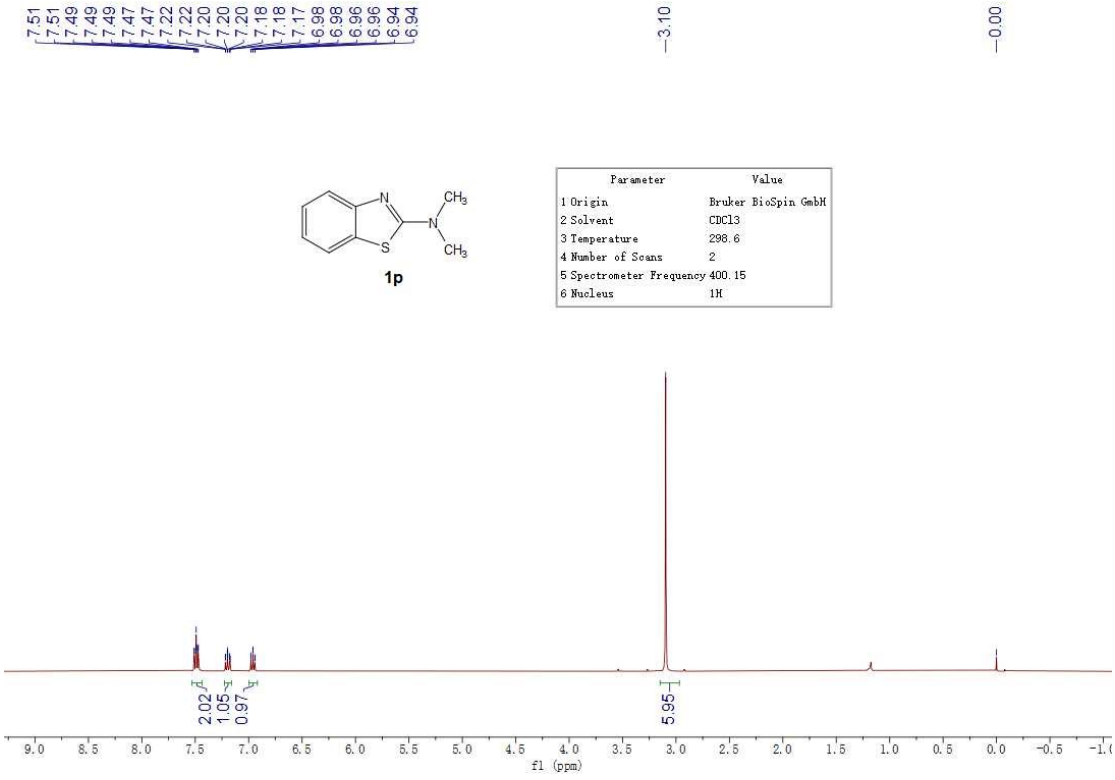
^{13}C NMR spectrum of **3au** (100 MHz, $CDCl_3$)



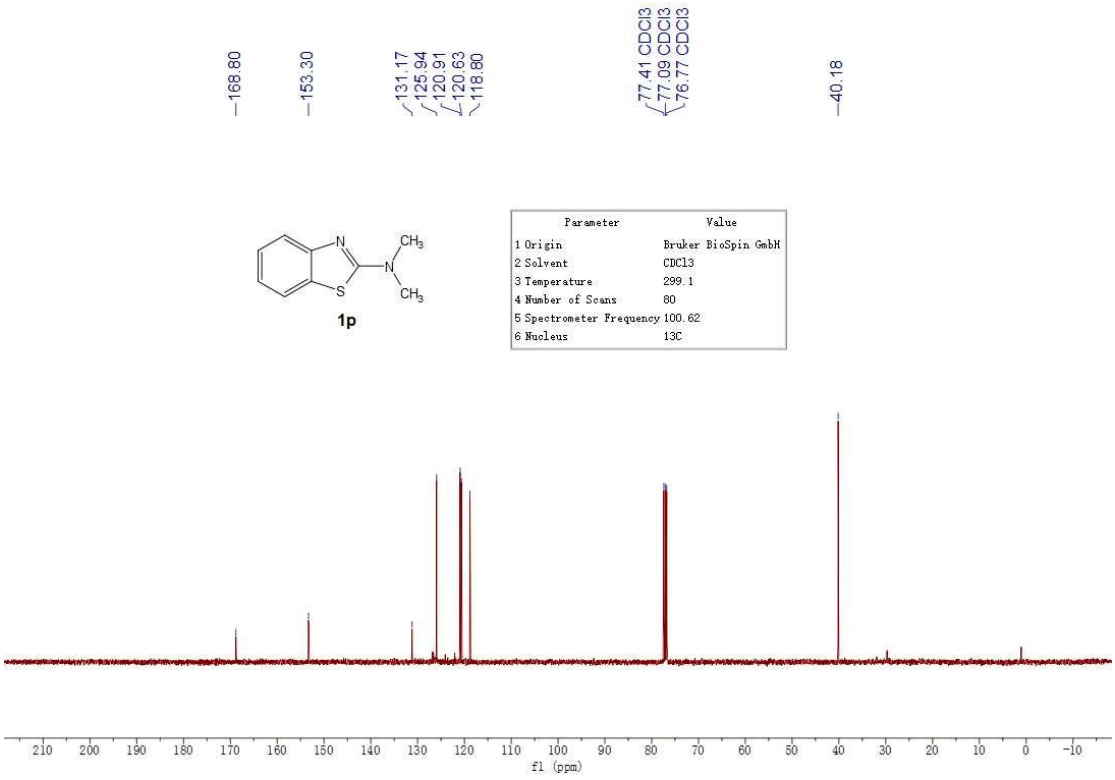
^{1}H NMR spectrum of **3av** (400 MHz, $CDCl_3$)



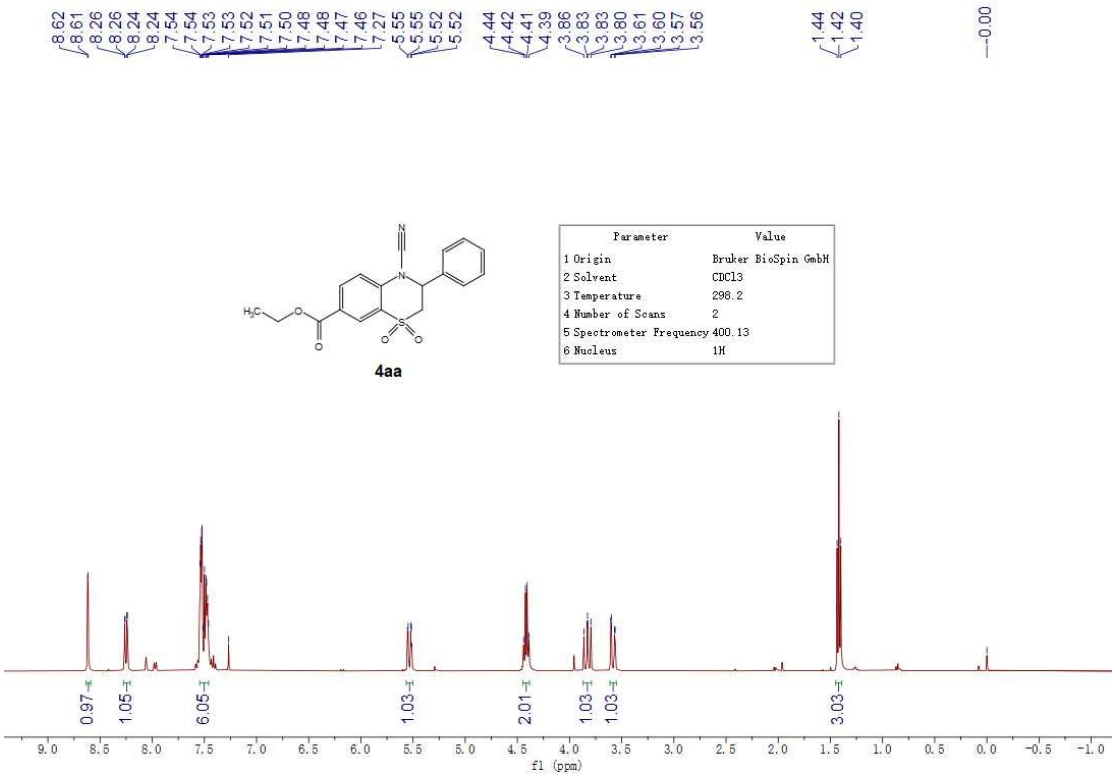
^{13}C NMR spectrum of **3av** (100 MHz, $CDCl_3$)



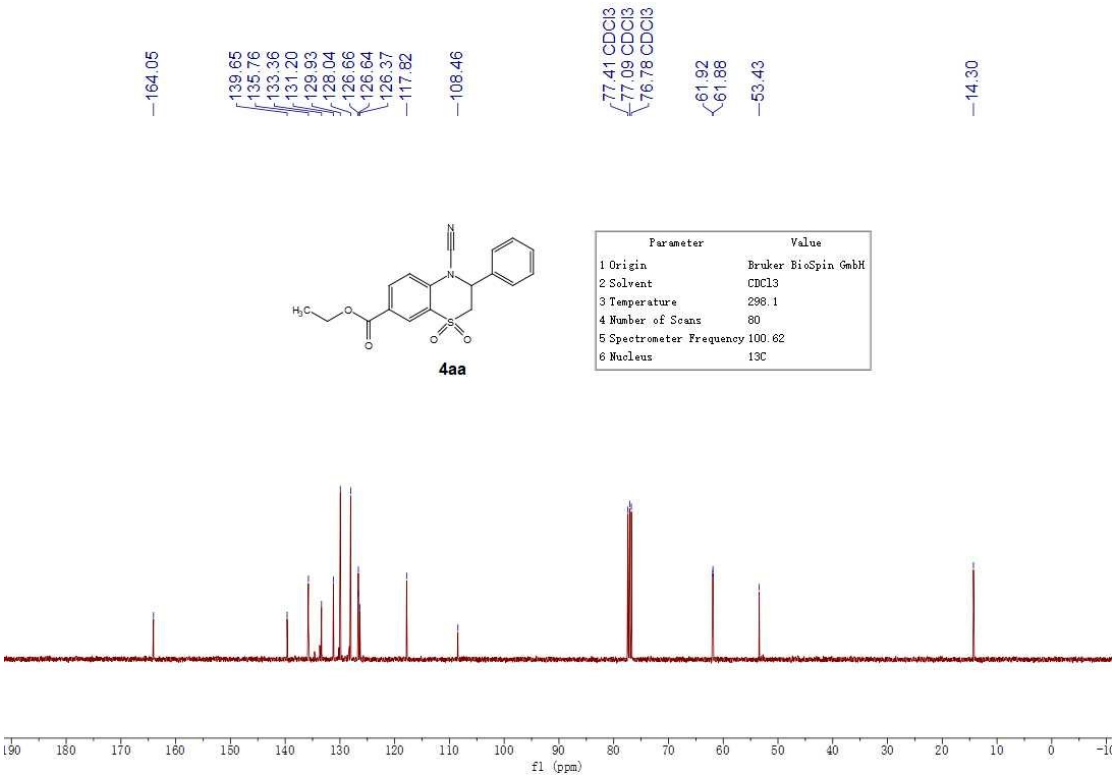
^{1}H NMR spectrum of **1p** (400 MHz, $CDCl_3$)



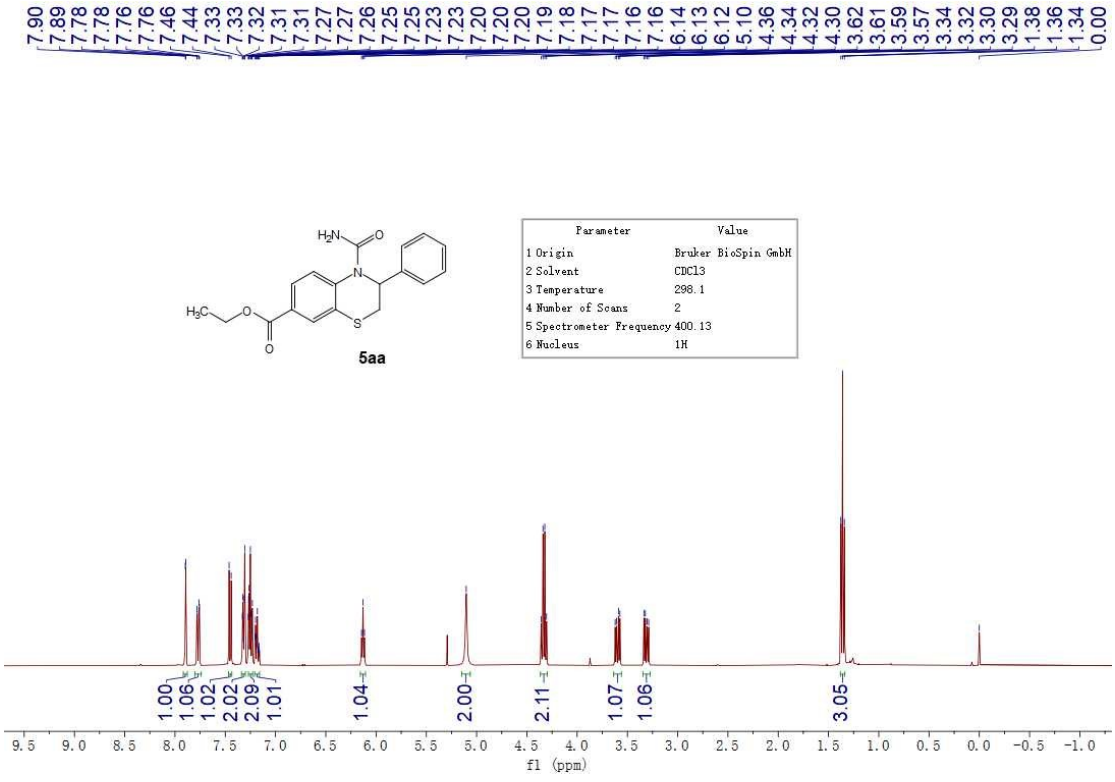
^{13}C NMR spectrum of **1p** (100 MHz, $CDCl_3$)



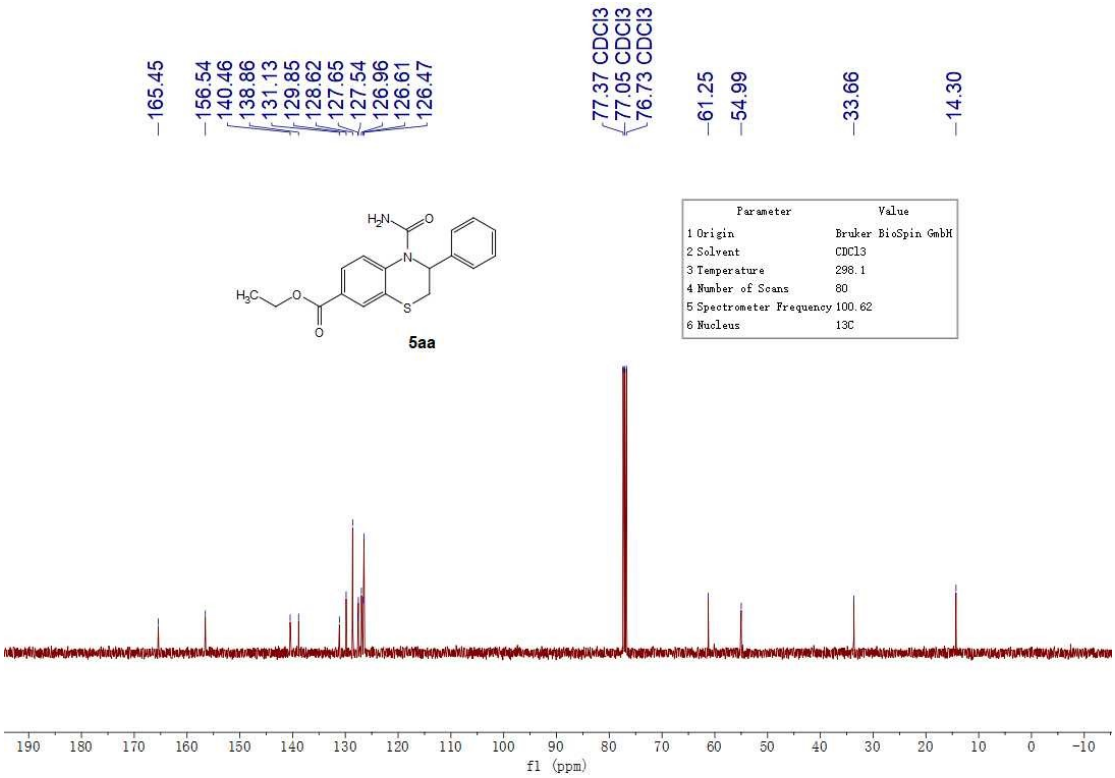
^{1}H NMR spectrum of **4aa** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **4aa** (100 MHz, $CDCl_3$)



^{1}H NMR spectrum of **5aa** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **5aa** (100 MHz, $CDCl_3$)

11. Cartesian Coordinates and Energies

1a

C	-0.40024300	-0.64833200	-0.00062600
C	-0.33449400	0.76728600	-0.00472900
C	-1.52546500	1.50129100	-0.00352900
C	-2.74192400	0.82418600	0.00263700
C	-2.78916200	-0.57637400	0.00858000
C	-1.61414000	-1.32855500	0.00788200
C	1.84006700	0.37802100	0.00032700
H	-1.47814900	2.58473200	-0.00738800
H	-3.66812500	1.39027300	0.00287800
H	-3.74785400	-1.08492000	0.01324300
H	-1.64888900	-2.41284600	0.01188500
S	1.23597600	-1.30671800	-0.01102200
N	0.94254900	1.31177600	0.00260600
N	3.18881900	0.60841400	-0.05937800
H	3.44245300	1.56731600	0.13775600
H	3.79753900	-0.08352800	0.35213700

Zero-point correction= 0.119633 (Hartree/Particle)
Thermal correction to Energy= 0.127450
Thermal correction to Enthalpy= 0.128394
Thermal correction to Gibbs Free Energy= 0.087123
Sum of electronic and zero-point Energies= -777.989534
Sum of electronic and thermal Energies= -777.981716
Sum of electronic and thermal Enthalpies= -777.980772
Sum of electronic and thermal Free Energies= -778.022043
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -778.246807

2a

C	-1.78011800	-1.04429000	0.00002100
C	-0.40696700	-1.28201500	0.00000100
C	0.51441500	-0.22262400	-0.00002000
C	0.01271000	1.09082600	-0.00002800
C	-1.35708300	1.33005500	-0.00000900
C	-2.26137200	0.26411900	0.00001700
H	-2.47266900	-1.88054400	0.00003800
H	-0.03618100	-2.30352000	0.00000400
H	0.69958000	1.93079700	-0.00005700
H	-1.72377100	2.35218700	-0.00001700

H	-3.33009900	0.45469500	0.00003100
C	1.95193800	-0.53209500	-0.00003300
C	2.96953500	0.33614200	0.00004300
H	2.18388900	-1.59635800	-0.00010700
H	3.99744900	-0.00987700	0.00002400
H	2.82345200	1.41190700	0.00013100

Zero-point correction= 0.133588 (Hartree/Particle)
Thermal correction to Energy= 0.140370
Thermal correction to Enthalpy= 0.141314
Thermal correction to Gibbs Free Energy= 0.101989
Sum of electronic and zero-point Energies= -309.554914
Sum of electronic and thermal Energies= -309.548132
Sum of electronic and thermal Enthalpies= -309.547187
Sum of electronic and thermal Free Energies= -309.586513
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -309.770148

PhI(OAc)$_2$

C	0.98215300	2.19279800	0.72240700
C	0.97458200	3.58914000	0.71430000
C	-0.00005600	4.28616000	0.00000000
C	-0.97467500	3.58910900	-0.71429400
C	-0.98220900	2.19276700	-0.72239200
C	-0.00001900	1.52495600	0.00000900
H	1.74690400	1.64367600	1.25521200
H	1.73478300	4.12705800	1.27201700
H	-0.00007000	5.37161200	-0.00000400
H	-1.73489100	4.12700300	-1.27201400
H	-1.74694600	1.64362200	-1.25519200
I	0.00000800	-0.62899800	0.00001500
O	2.18209800	-0.29242900	-0.10860100
O	-2.18209000	-0.29248100	0.10852100
C	2.76495300	-1.47422900	-0.12153800
C	4.27730300	-1.39750800	-0.18395500
H	4.69472900	-2.40385700	-0.20395300
H	4.58227600	-0.84530000	-1.07701100
H	4.65588200	-0.85182300	0.68487800
C	-2.76491300	-1.47429800	0.12158000
C	-4.27726900	-1.39761100	0.18383200
H	-4.65577400	-0.85197300	-0.68506200
H	-4.69467400	-2.40396900	0.20383100
H	-4.58234400	-0.84537200	1.07683400
O	2.14051600	-2.53011300	-0.08753900
O	-2.14044700	-2.53016600	0.08761600

Zero-point correction= 0.193141 (Hartree/Particle)
Thermal correction to Energy= 0.210168
Thermal correction to Enthalpy= 0.211112
Thermal correction to Gibbs Free Energy= 0.144696
Sum of electronic and zero-point Energies= -699.764581
Sum of electronic and thermal Energies= -699.747554
Sum of electronic and thermal Enthalpies= -699.746610
Sum of electronic and thermal Free Energies= -699.813026
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -700.216862

PhI

C	-2.65765200	-1.20693400	0.00000100
C	-1.26122400	-1.21539400	0.00000100
C	-0.57901400	-0.00000500	0.00000000
C	-1.26122200	1.21539300	0.00000000
C	-2.65764300	1.20693900	0.00000100
C	-3.35754700	0.00000200	0.00000100
H	-3.19470600	-2.15067600	0.00000100
H	-0.71799100	-2.15324400	0.00000000
H	-0.71797500	2.15323500	0.00000000
H	-3.19470100	2.15067800	0.00000200
H	-4.44298300	0.00001000	0.00000100
I	1.56441800	0.00000000	-0.00000100

Zero-point correction= 0.090250 (Hartree/Particle)
Thermal correction to Energy= 0.096130
Thermal correction to Enthalpy= 0.097074
Thermal correction to Gibbs Free Energy= 0.058500
Sum of electronic and zero-point Energies= -242.963958
Sum of electronic and thermal Energies= -242.958078
Sum of electronic and thermal Enthalpies= -242.957134
Sum of electronic and thermal Free Energies= -242.995708
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -243.152906

AcOH

C	-0.09155000	0.12523100	0.00044500
O	-0.64329300	1.20243400	-0.00014300
O	-0.77929300	-1.04564700	-0.00014100

C	1.39578100	-0.11091000	0.00003300
H	1.68012800	-0.69307700	0.88122200
H	1.67968300	-0.69331700	-0.88114500
H	1.91521100	0.84603100	-0.00023400
H	-1.71972300	-0.79986000	-0.00044000

Zero-point correction= 0.062022 (Hartree/Particle)
Thermal correction to Energy= 0.066566
Thermal correction to Enthalpy= 0.067511
Thermal correction to Gibbs Free Energy= 0.034924
Sum of electronic and zero-point Energies= -229.036463
Sum of electronic and thermal Energies= -229.031918
Sum of electronic and thermal Enthalpies= -229.030974
Sum of electronic and thermal Free Energies= -229.063560
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -229.180854

INT1

C	3.66545700	0.48339000	1.02539300
C	3.93797000	-0.10174900	-0.23615600
C	4.98212200	-1.02696800	-0.34408000
C	5.72610200	-1.34921100	0.78862700
C	5.44521500	-0.75981900	2.02864800
C	4.40907300	0.16657300	2.15805900
C	2.23193400	1.15830500	-0.85938100
H	5.19572700	-1.47476300	-1.30889400
H	6.53651600	-2.06726400	0.70884200
H	6.03663800	-1.02421000	2.89950200
H	4.18962400	0.62309900	3.11764100
S	2.30813600	1.59688100	0.87122900
N	3.11273000	0.30061800	-1.27711600
N	1.22939500	1.66365400	-1.62911000
H	1.31554800	1.50343700	-2.62223700
H	0.66825400	2.45205000	-1.32001100
C	-2.99872800	-2.18427100	-0.23765300
C	-4.00307600	-3.02111100	0.25501600
C	-4.71361200	-2.67418300	1.40450400
C	-4.42814900	-1.48343800	2.07489800
C	-3.42289900	-0.63593700	1.60698600
C	-2.73198900	-1.01194700	0.46026300
H	-2.44284600	-2.43275500	-1.13489300
H	-4.23041400	-3.94268600	-0.27151700
H	-5.49376100	-3.33035200	1.77748000
H	-4.98258500	-1.21036800	2.96723600
H	-3.20244800	0.29873000	2.10714700
I	-1.17922100	0.26886500	-0.26601800
O	0.21556300	-1.36145000	-0.27441500
O	-2.72133700	1.86160700	0.04417200
C	0.31095100	-2.05572100	-1.40920800
C	1.61386000	-2.82071800	-1.48233200
H	1.52806300	-3.62778900	-2.21045100
H	2.38472200	-2.11142000	-1.80140400
H	1.90164900	-3.20310800	-0.50168300
C	-2.18246900	3.02956100	-0.18990000
C	-3.12692100	4.19175500	0.04678200
H	-4.00182900	4.09084800	-0.60138100
H	-3.48284500	4.17322200	1.08054100
H	-2.61614000	5.13261000	-0.15695700
O	-0.52838800	-2.05077700	-2.29655900
O	-1.01824700	3.19734700	-0.56931200

Zero-point correction= 0.314032 (Hartree/Particle)
Thermal correction to Energy= 0.340640
Thermal correction to Enthalpy= 0.341584
Thermal correction to Gibbs Free Energy= 0.251393
Sum of electronic and zero-point Energies= -1477.765734
Sum of electronic and thermal Energies= -1477.739125
Sum of electronic and thermal Enthalpies= -1477.738181
Sum of electronic and thermal Free Energies= -1477.828372
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1478.475749

TS1

C	3.75698300	0.06852200	0.95005900
C	3.73815700	-0.60173700	-0.30192500
C	4.71035300	-1.57597600	-0.56643800
C	5.66673900	-1.86568800	0.40273500
C	5.67167300	-1.19491100	1.63412400
C	4.71557900	-0.21814700	1.91766400
C	1.97001000	0.69734300	-0.64187500
H	4.70522200	-2.08179600	-1.52650300
H	6.42151300	-2.61971800	0.20124600
H	6.42657400	-1.43430700	2.37647600
H	4.72081000	0.30221500	2.86991800

S	2.43965100	1.23216700	1.00460200
N	2.72298100	-0.23472000	-1.16587700
N	0.85941000	1.24211100	-1.19821700
H	0.77457800	0.91972800	-2.16185500
H	0.45445100	2.51306300	-0.90672500
C	-3.64058100	-1.67817700	-0.44259700
C	-4.70151400	-2.48211800	-0.02621200
C	-5.06962200	-2.51544400	1.32108700
C	-4.37544500	-1.75161900	2.26056700
C	-3.30419400	-0.95176400	1.85774500
C	-2.95077600	-0.92656300	0.50992700
H	-3.34268100	-1.64869000	-1.48563600
H	-5.24201000	-3.07901200	-0.75437700
H	-5.89996400	-3.13833700	1.63891400
H	-4.66119200	-1.78131100	3.30747000
H	-2.75570400	-0.36277400	2.58551400
I	-1.32375600	0.33069100	-0.15652000
O	-0.22154600	-1.43861400	-0.25322000
O	-1.93386200	2.87874200	-0.02329400
C	-0.08706200	-1.95599700	-1.49091800
C	0.90633700	-3.09393000	-1.47644400
H	0.71336700	-3.74642200	-2.32829400
H	1.89766300	-2.64144400	-1.57349700
H	0.86675400	-3.64789800	-0.53801800
C	-1.07573800	3.76265400	-0.23259100
C	-1.43569200	5.21430000	0.00876300
H	-1.34787200	5.76882200	-0.93016700
H	-2.44996500	5.29786000	0.39777500
H	-0.72242000	5.65289000	0.71229900
O	-0.66246600	-1.53688700	-2.47372900
O	0.13256500	3.57796100	-0.65175200

Zero-point correction= 0.309599 (Hartree/Particle)
Thermal correction to Energy= 0.335381
Thermal correction to Enthalpy= 0.336325
Thermal correction to Gibbs Free Energy= 0.247540
Sum of electronic and zero-point Energies= -1477.740588
Sum of electronic and thermal Energies= -1477.714806
Sum of electronic and thermal Enthalpies= -1477.713862
Sum of electronic and thermal Free Energies= -1477.802648
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1478.446944

INT2

C	-3.00529800	-0.92128900	0.07537000
C	-3.06958300	0.50426300	0.12374100
C	-4.28304200	1.15641500	-0.16882000
C	-5.38874600	0.39514700	-0.50699600
C	-5.31010200	-1.01191700	-0.55733300
C	-4.12527500	-1.68127000	-0.27110300
C	-0.93619400	0.28042200	0.68024800
H	-4.31972200	2.23926900	-0.12744600
H	-6.32979500	0.88366400	-0.73804400
H	-6.19275200	-1.58526900	-0.82314900
H	-4.07532800	-2.76411500	-0.31046400
S	-1.40262500	-1.45063000	0.50331200
N	-1.89966600	1.13983900	0.43528300
N	0.30848400	0.58407200	1.12280900
H	0.40231300	1.65162000	1.30469900
C	1.78066800	-2.51887500	-1.17914900
C	1.77415200	-3.89179700	-0.92176700
C	1.87835500	-4.35758500	0.38877700
C	1.99500200	-3.45242300	1.44643700
C	2.01237300	-2.07985100	1.19845000
C	1.90662700	-1.62613900	-0.11620100
H	1.67502300	-2.15549200	-2.19653700
H	1.67374800	-4.59241700	-1.74506900
H	1.86388200	-5.42468800	0.58768100
H	2.07111900	-3.81393600	2.46735300
H	2.07616700	-1.37093300	2.01578900
I	1.89582900	0.48733500	-0.52604800
O	1.44951600	2.91808800	-0.72294300
C	1.06633300	3.61135900	0.28005300
C	1.04194600	5.11887200	0.05618400
H	0.16831400	5.36887200	-0.55485300
H	0.96786500	5.64005400	1.01153400
H	1.93147200	5.43860100	-0.49118300
O	0.69619900	3.16275300	1.39210200

Zero-point correction= 0.248967 (Hartree/Particle)
Thermal correction to Energy= 0.269428
Thermal correction to Enthalpy= 0.270372
Thermal correction to Gibbs Free Energy= 0.194698

Sum of electronic and zero-point Energies= -1248.695344
Sum of electronic and thermal Energies= -1248.674883
Sum of electronic and thermal Enthalpies= -1248.673939
Sum of electronic and thermal Free Energies= -1248.749613
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1249.269409

TS2

C	-2.98109000	-0.97930000	0.07863700
C	-3.08191400	0.44598100	0.08120200
C	-4.31384800	1.05777300	-0.22578700
C	-5.40131500	0.25988000	-0.53506000
C	-5.28659400	-1.14607300	-0.54234000
C	-4.08440600	-1.77593300	-0.24123600
C	-0.93020200	0.30828700	0.63327900
H	-4.37723400	2.14021100	-0.21794100
H	-6.35540000	0.71698700	-0.77682400
H	-6.15556100	-1.74948500	-0.78616100
H	-4.00748400	-2.85790900	-0.24750600
S	-1.36820400	-1.45467800	0.51661600
N	-1.93003800	1.12306200	0.35859300
N	0.28396500	0.67789800	1.08154000
H	0.37099100	1.91910200	1.21713100
C	1.90013200	-2.52775200	-1.16106200
C	1.90753800	-3.89414800	-0.87148900
C	1.95207000	-4.32913500	0.45307200
C	1.99347500	-3.39932100	1.49448900
C	1.99573200	-2.03216600	1.21752900
C	1.95098700	-1.61299100	-0.11149500
H	1.84304000	-2.18793000	-2.18998100
H	1.86560100	-4.61430400	-1.68282300
H	1.94910900	-5.39175200	0.67487000
H	2.02092000	-3.73640100	2.52609500
H	1.99573300	-1.30231500	2.01877400
I	1.90167000	0.48628200	-0.54040100
O	1.46780700	3.05827000	-0.71358200
C	0.97772500	3.68315500	0.25797700
C	0.91874300	5.19926800	0.19343100
H	-0.12406000	5.50573300	0.06248100
H	1.26775200	5.62303300	1.13845900
H	1.51428500	5.57534700	-0.63864100
O	0.49661500	3.15544000	1.32228900

Zero-point correction= 0.244930 (Hartree/Particle)
Thermal correction to Energy= 0.265153
Thermal correction to Enthalpy= 0.266097
Thermal correction to Gibbs Free Energy= 0.190930
Sum of electronic and zero-point Energies= -1248.697856
Sum of electronic and thermal Energies= -1248.677633
Sum of electronic and thermal Enthalpies= -1248.676688
Sum of electronic and thermal Free Energies= -1248.751856
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1249.265191

INT3

C	0.27103800	0.72650400	-0.00010400
C	0.09619000	-0.76372400	0.00001800
C	1.28346200	-1.59786200	0.00027400
C	2.52373100	-1.05386600	0.00022700
C	2.69821900	0.37771100	-0.00016200
C	1.62969100	1.21787800	-0.00045600
C	-2.25825500	-0.91395500	-0.00038000
H	1.11920500	-2.66902100	0.00041600
H	3.40103900	-1.69227600	0.00039500
H	3.70506800	0.78332000	-0.00022700
H	1.76013700	2.29378800	-0.00081500
S	-1.01592000	1.76924600	0.00030500
N	-1.03724200	-1.41195600	-0.00011700
N	-3.41921300	-0.72802300	-0.00004700

Zero-point correction= 0.093881 (Hartree/Particle)
Thermal correction to Energy= 0.102119
Thermal correction to Enthalpy= 0.103063
Thermal correction to Gibbs Free Energy= 0.059665
Sum of electronic and zero-point Energies= -776.711046
Sum of electronic and thermal Energies= -776.702808
Sum of electronic and thermal Enthalpies= -776.701864
Sum of electronic and thermal Free Energies= -776.745262
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -776.943953

TS3

C	1.05333300	2.76491600	0.02084400
C	-0.00820000	2.35238600	-0.74350100
C	-0.88631100	1.32079400	-0.29842500

C	-0.63667500	0.70961400	1.00416000
C	0.54677700	1.10317300	1.71058900
C	1.34668200	2.11212000	1.24937000
H	1.69207200	3.57097500	-0.32572200
H	-0.21084200	2.80465600	-1.70816500
H	0.74611900	0.59728000	2.64765600
H	2.21468100	2.41923300	1.82401700
C	-0.60726000	-1.91159800	-0.46345200
C	-1.50725400	-1.54734700	-1.46088100
H	-2.51776700	-1.93230800	-1.40340800
N	-1.34476300	-0.27775200	1.55140300
C	-2.59707800	-0.60925700	1.29777800
N	-3.68599300	-1.04959200	1.25959300
C	0.77351600	-1.51544600	-0.41656200
C	1.58779700	-1.96420200	0.65000700
C	1.33261200	-0.61695900	-1.35099500
C	2.90490300	-1.54935700	0.76368600
H	1.15706000	-2.63101400	1.39053000
C	2.65053300	-0.19470900	-1.22652000
H	0.72785900	-0.24208200	-2.16744100
C	3.44045400	-0.65733500	-0.17347400
H	3.51596500	-1.90471500	1.58713300
H	3.06045000	0.50564000	-1.94662600
H	4.46868100	-0.32285900	-0.07775200
H	-1.13884800	-1.32341800	-2.45666900
H	-0.96561200	-2.53300000	0.34976500
S	-2.11859300	0.71889100	-1.29787700

Zero-point correction= 0.229618 (Hartree/Particle)
Thermal correction to Energy= 0.244658
Thermal correction to Enthalpy= 0.245602
Thermal correction to Gibbs Free Energy= 0.187430
Sum of electronic and zero-point Energies= -1086.281944
Sum of electronic and thermal Energies= -1086.266904
Sum of electronic and thermal Enthalpies= -1086.265959
Sum of electronic and thermal Free Energies= -1086.324131
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1086.728456

TS3′

C	-0.45545100	2.59875100	1.05509900
C	-0.48116100	1.38688100	1.69566500
C	0.49017000	0.38064500	1.41129000
C	1.43179600	0.62790900	0.33211600
C	1.41120900	1.89595100	-0.32995100
C	0.51333900	2.85894700	0.04650000
H	-1.17934300	3.36549300	1.31122000
H	-1.22061900	1.17014300	2.45767700
H	2.13435200	2.07834500	-1.11825600
H	0.52514600	3.82695000	-0.44487700
C	1.05240700	-2.22648200	-0.66647300
C	-0.20535000	-2.17096700	-0.09618700
N	2.23395000	-0.39541900	-0.02485600
C	3.08167400	-0.22371900	-1.03712100
N	3.85220500	-0.18923700	-1.91883600
H	1.23449100	-1.82452600	-1.65441700
S	0.48331500	-1.11340600	2.19687700
H	1.79075300	-2.91889300	-0.28498900
H	-0.49140400	-2.94033300	0.61414100
C	-1.24864700	-1.25613500	-0.54029400
C	-2.53349100	-1.33304400	0.03219100
C	-0.98986500	-0.22628300	-1.46374400
C	-3.52196200	-0.42160600	-0.31099200
H	-2.73625300	-2.10583800	0.76766300
C	-1.98081400	0.69099600	-1.80238800
H	-0.01175400	-0.13612300	-1.91956000
C	-3.24720800	0.59924900	-1.22829300
H	-4.50599400	-0.49579200	0.14103800
H	-1.75749700	1.48330300	-2.50935800
H	-4.01787700	1.31780500	-1.48896300

Zero-point correction= 0.229951 (Hartree/Particle)
Thermal correction to Energy= 0.244967
Thermal correction to Enthalpy= 0.245911
Thermal correction to Gibbs Free Energy= 0.187173
Sum of electronic and zero-point Energies= -1086.278978
Sum of electronic and thermal Energies= -1086.263962
Sum of electronic and thermal Enthalpies= -1086.263017
Sum of electronic and thermal Free Energies= -1086.321755
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1086.723899

INT4

C	-3.83983400	0.72933900	1.08567300

C	-2.86855200	1.51754400	0.48162600
C	-1.73113800	0.94961600	-0.10766500
C	-1.57924800	-0.45005600	-0.09570300
C	-2.57416700	-1.24056200	0.49852500
C	-3.68953800	-0.65822500	1.08714500
H	-4.70922200	1.19246100	1.53983400
H	-2.97960600	2.59715200	0.45403300
H	-2.45862700	-2.31871600	0.50163000
H	-4.44065600	-1.29364000	1.54430600
C	0.72375500	-0.38842000	-1.24159800
C	0.26295600	0.89142300	-1.94782200
H	-0.42667100	0.64569400	-2.75948500
N	-0.44855100	-1.09180000	-0.67880100
C	-0.32351500	-2.41951600	-0.58099700
N	-0.19881400	-3.57864300	-0.52378900
C	1.82455700	-0.14912800	-0.22603000
C	1.55959400	-0.01647600	1.13879400
C	3.14046200	-0.02477600	-0.68310600
C	2.59827500	0.24407600	2.03215400
H	0.54511900	-0.12038700	1.50615700
C	4.17806000	0.24001600	0.20816700
H	3.35539000	-0.14311400	-1.74264100
C	3.90753900	0.37564200	1.57053500
H	2.38188700	0.34348000	3.09115800
H	5.19593900	0.32943600	-0.15832600
H	4.71434800	0.57581600	2.26855700
H	1.13165000	1.40577300	-2.36168200
H	1.11399500	-1.05244100	-2.02085100
S	-0.52670200	2.05803700	-0.79767100

Zero-point correction= 0.234620 (Hartree/Particle)
Thermal correction to Energy= 0.249109
Thermal correction to Enthalpy= 0.250053
Thermal correction to Gibbs Free Energy= 0.191173
Sum of electronic and zero-point Energies= -1086.348683
Sum of electronic and thermal Energies= -1086.334194
Sum of electronic and thermal Enthalpies= -1086.333250
Sum of electronic and thermal Free Energies= -1086.392130
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1086.795447

TS3″

C	-0.44087600	2.75075900	0.87953000
C	-0.13532200	1.57980100	1.52928400
C	0.80685200	0.65686800	0.98747400
C	1.40029800	0.97054900	-0.29801100
C	0.98885600	2.15126800	-0.98056300
C	0.12588300	3.03993600	-0.38857400
H	-1.14103400	3.45092700	1.32558900
H	-0.59919900	1.32957400	2.47700900
H	1.43263900	2.34566700	-1.95130600
H	-0.13169400	3.96576400	-0.89438300
C	0.98244000	-1.69463100	-1.45411500
C	0.03845600	-1.93246300	-0.46205000
N	2.22492100	0.13405200	-0.97625600
C	3.19049100	-0.56584600	-0.38434300
N	4.14699800	-1.16385600	-0.06499600
H	0.72274200	-1.14687000	-2.35018500
S	1.07903100	-0.86302500	1.68533200
H	1.86332500	-2.32086200	-1.51433600
H	0.16503800	-2.81543200	0.15675000
C	-1.27138200	-1.28536800	-0.42552100
C	-2.26570000	-1.77614100	0.44166100
C	-1.55965200	-0.14729200	-1.19765400
C	-3.50563300	-1.15720900	0.52590200
H	-2.04519700	-2.64047900	1.06210800
C	-2.79863700	0.48136200	-1.10266200
H	-0.81108700	0.26095400	-1.86593200
C	-3.77636600	-0.02103200	-0.24526300
H	-4.26172800	-1.55134200	1.19854100
H	-2.99670600	1.36747500	-1.69835400
H	-4.74327800	0.46829300	-0.17263100

Zero-point correction= 0.230049 (Hartree/Particle)
Thermal correction to Energy= 0.245091
Thermal correction to Enthalpy= 0.246035
Thermal correction to Gibbs Free Energy= 0.186787
Sum of electronic and zero-point Energies= -1086.247980
Sum of electronic and thermal Energies= -1086.232939
Sum of electronic and thermal Enthalpies= -1086.231994
Sum of electronic and thermal Free Energies= -1086.291243
B3LYP-D3/6-311++G(d,p)-SDD/SMD//B3LYP-D3/6-31+G(d,p)-LANL2DZ energy = -1086.713186