Electronic Supplementary Material (ESI) for Photochemical & Photobiological Sciences.

Supporting Information

Photochromic Meta-diamides for Optical Modulation of Ligand Activity and Neuron Function

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1. Materials and General Methods

The main instruments and reagents for the experiment.^{1}H NMR spectra, ^{13}C NMR spectra, ^{19}F NMR spectra were recorded on a Bruker AM-400 spectrometer, using DMSO-d_6 or $CDCl_3$ as a solvent. TMS as an internal standard, and the chemical shift was reported as a δ (ppm) value. High-resolution mass spectrometry (HRMS) data was recorded on a MicroMass GCTCA 055 instrument under electron bombardment (70 eV). Melting points were recorded on a Büchi melting point apparatus B-540 and were uncorrected. The *cis-trans* isomer ratio was recorded using an ACQUITY UPLC H-Class. UV-Vis spectra, fatigue resistance and half-life were recorded using Lambda 650 UV-Vis spectrophotometer (PerkinElmer). The changes in membrane potential of sacral neurons were recorded by laser confocal microscopy. The drugs used in the experimental preparation and separation process are commercially available drugs, and the reagents are of analytical grade.

Optical Properties: UV-Vis spectra, *cis/trans* ratio, half-life time.

Test of UV-Vis spectra: The target compound solution was prepared in a concentration of 2×10^{-5} M with acetonitrile and stored at room temperature for 24 h in the dark. An appropriate volume of the solution was placed in a quartz cuvette (1 cm×1 cm), irradiated with ultraviolet (365 nm). The absorbance of the compound at 600-200 nm was recorded with an UV-Vis spectrophotometer until it no longer changed.

Test of isomer ratio: The target compound solution was prepared in a concentration of 25 ppm with acetonitrile and stored at room temperature for 24 h in the dark. The ratio of *cis/trans* isomer of the compound before illumination was measured by ultra performance liquid chromatography. Then the compound solution was irradiated with ultraviolet (365 nm), and the ratio of the *cis/trans* isomer was measured again.

Test of fatigue resistance: The target compound solution was prepared in a concentration of 2×10^{-5} M with acetonitrile and stored at room temperature for 24 h in the dark. An appropriate volume of the solution was placed in a quartz cuvette (1 cm×1 cm) and determined the absorbance of the initial solution at the maximum absorption wavelength. Then the solution was irradiated with a ultraviolet (365 nm), and the absorption value (A1) was recorded. The solution was irradiated with blue light, and the absorption value (A2) was recorded again. The above operation was repeated 6 times or more, and the original 8.5 was used for the drawing.

Test of half-life: The target compound solution was prepared in a concentration of 50 ppm with acetonitrile and stored at room temperature for 24 h in the dark. The absorption at the maximum absorption wavelength was measured by an UV-Vis spectrophotometer. Then the solution was irradiated with ultraviolet (365 nm) to maximize conversion into the *cis* configuration, and the absorption value was again measured. The solution is sealed and stored in the dark, and then the absorption value at the maximum absorption wavelength is measured at intervals. The half-life of the target compound from the *cis* configuration to the *trans* configuration is calculated.

Insecticidal Activity against Armyworm and *Aedes albopictus* larvae (*Mythimna separate*)

The armyworm larvae were provided by the worm house of the Institute of Pharmaceutical and Chemical Engineering, East China University of Science and Technology. The fourth-instar larvae of *Aedes albopictus* were provided by Shanghai Southern Pesticide Creation Center.

Test method for armyworm activity: leaf-dipping method: Two groups of solutions with the same concentration gradient were prepared, one of which was irradiated with ultraviolet (365 nm) for 30 min, and the other group was stored in the dark. The corn leaves were well immersed in two sets of solutions, dried naturally in the dark, then placed in a clean culture dishes, and placed into 10 3rd instar armyworms that were starved for 2 h. Each concentration of the drug solution is set in three parallels. The culture dishes were placed in the dark for 72 h, and the mortality of the armyworms was counted before and after illumination.

Test method for Aedes albopictus larvae activity: Two groups of solutions with the same concentration gradient were prepared, one of which was irradiated with ultraviolet (365 nm) for 30 min, and the other group was stored in the dark. Ten larvae of *Aedes albopictus* with the same size were selected and placed in a centrifuge tube. The solution was added to the centrifuge tube before and after illumination, and each concentration of the solution was set in three parallels. Then the centrifuge tube was placed in the dark for 24 h, and the mortality of *Aedes albopictus* larvae was counted before and after illumination.

Preparation of physiological solutions required for DUM neuron anatomy:

Physiological solution A (mmol/L): 185 mM NaCl, 3.0 mM KCl, 4 mM $MgCl_2$, 10 mM D-glucose, 10 mM HEPES, adjusted to pH 7.2 with NaOH, stored at 4 ℃.

Physiological solution B: A was added with type IA collagenase 1.5 mg/ml.

Physiological solution C: A was added with 5 mM $CaCl_2$, fetal calf serum (10% by volume), double antibody [1% penicillin (50 IU/mL) / streptomycin (50 mg/mL)].

$DiBAC_4(3)$ was dissolved in DMSO to make a 1 g/L stock solution, which was formulated to the required concentration and stored at 4 ℃ in the dark.

Primary culture of DUM neurons in American cockroach

a. Anatomy: A male adult of the American cockroach was selected, and the body surface was disinfected with 75% alcohol. The back was turned up under a dissecting microscope, and the body wall was cut along the midline and fixed in a wax plate. Carefully remove impurities such as trachea, digestive tract, fat body and dissection the ganglion into physiological solution A. The whole process is operated in a clean bench.

b. Enzymatic hydrolysis: The obtained ganglion was transferred to physiological solution B and hydrolyzed in a water bath at 37 ℃ for 20 min. After the enzymatic hydrolysis is completed, the ganglion is transferred to the physiological solution C, and the digestion is terminated by rinsing three times with the physiological solution C. Repeatedly gently blowing the ganglion in the physiological solution C, so that the cells in the ganglion are completely dispersed.

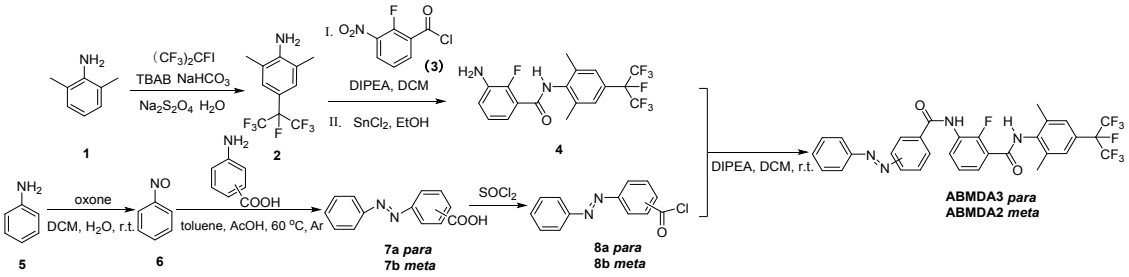
c. Static culture: The prepared cell suspension was filtered through a 200-mesh filter into a petri dish containing physiological solution C, and the morphology of the neuronal cells was observed using an inverted phase contrast microscope (200×). Then the culture ware allowed to stand at 28 ℃.

Determination of membrane potential of DUM neurons of *Periplaneta americana*:

ABMDA7 was dissolved in DMSO to form a certain concentration of mother liquor. The prepared solutions were divided into two groups, one of which was irradiated with ultraviolet (365 nm) for 30 min, and the other group was stored in the dark. 10 ul of each solution was added to 1 ml of DUM neuron cell culture medium. After 6 hours of incubation, 5 μmol/L

fluorescent dye $DiBAC_4(3)$ was added for further incubation for 30 min, then the dye was washed away. A 24-well plate containing DUM neuron cells was immobilized on a laser confocal microscope stage to detect changes in fluorescence intensity of DUM neurons before and after illumination. The excitation wavelength was 488 nm, and the emission wavelength was 525 nm, and each experiment was repeated three times.

2. Synthesis of intermediates and final compounds



Synthesis of 2,6-dimethyl-4-(perfluoropropan-2-yl) aniline ***2.*** Compound **1** (1.21 g, 10.00 mmol), TBAB (0.32 g, 1.00 mmol), $NaHCO_3$ (1.01 g, 12.00 mmol) and $(CF_3)_2CFI$ (3.60 g, 12.00 mmol) were dissolved in 20 ml of ethyl ether and 20 ml of water and Stirred under the ice bath, then Sodium dithionite (2.09 g, 12.00 mmol) was weighed and added to the reaction system in portions. The mixture was further stirred for 15 minutes in an ice bath, then stirred at room temperature overnight. The reaction was followed by TLC and completed 24 hours. Purification by column chromatography, PE/EA = 20:1 (v/v). The solvent was evaporated to give a brown oily liquid. (2.10 g, yield 72.7%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (s, 2H), 4.14 (s, 2H), 2.23 (s, 6H).

Synthesis of N-(2,6-dimethyl-4-(perfluoropropan-2-yl) phenyl)-2-fluoro-3-nitrobenzamide ***3.*** Compound **2** (3.49 g, 12.00 mmol) and DIPEA (2.33 g, 18.00 mmol) were dissolved in 15 ml of dichloromethane and stirred under ice bath. 3-Nitro-2fluoro-benzoyl chloride was dissolved in 5 ml of dichloromethane and slowly added to the reaction system with a dropper. The mixture was further stirred for 10 minutes in an ice bath, then stirred at room temperature overnight. Purification by column chromatography, PE/DCM = 1:2 (v/v). The solvent was evaporated to give a white solid. (3.58 g, yield 65.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46-8.38 (m, 1H), 8.29-8.21 (m, 1H), 7.88 (d, *J* = 11.2 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.38 (s, 2H), 2.36 (s, 6H).

Synthesis of 3-amino-N-(2,6-dimethyl-4-(perfluoropropan-2-yl) phenyl)-2-fluorobenzamide ***4.*** Compound **3** (2.28 g, 5.00 mmol) and anhydrous stannous chloride (3.79 g, 20.00 mmol) were dissolved in 40 ml of ethanol. The reaction system was replaced three times with nitrogen and stirred at 60 ℃. The reaction was followed by TLC and completed after 4 h. The mixture was adjusted to pH = 8 with a 1 M sodium hydroxide solution and was filtered to give a filter cake, which was washed and dried to give a white solid. (1.7 g, yield 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 13.0 Hz, 1H), 7.48-7.42 (m, 1H), 7.36 (s, 2H), 7.09 (t, *J* = 7.9 Hz, 1H), 7.03-6.95 (m, 1H), 3.91 (s, 2H), 2.36 (s, 6H).

Synthesis of nitrosobenzene ***6***. The aniline **5** (1.86 g, 20.00 mmol) was dissolved in 20 ml of dichloromethane and stirred at room temperature. potassium peroxy-disulfate complex salt (Oxone, 24.58 g, 40.00 mmol) was dissolved in 100 ml of water and slowly added to the reaction

system. The reaction was completed after 0.5 h. The solution was extracted with dichloromethane and dried with $MgSO_4$, and the dichloromethane was evaporated to dryness to give a dark green oily liquid which was used directly for next step.

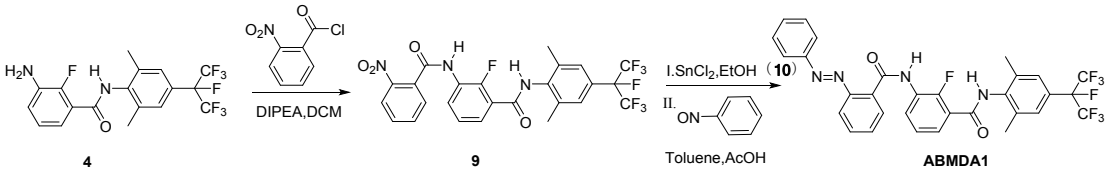
Synthesis of (E)-4-(phenyldiazenyl) benzoic acid ***7a***. The nitrosobenzene (0.64 g, 6.00 mmol) and p-aminobenzoic acid (0.69 g, 5.00 mmol) were dissolved in toluene (10 ml), then glacial acetic acid (1.20 g, 20.00 mmol) was added. The reaction system was replaced three times with nitrogen and stirred at 60 ℃. The reaction was followed by TLC and completed after 48 h. 40 ml of water was added to the reaction mixture, and the mixture was extracted with dichloromethane (3×30 mL). The organic phases were combined and dried over anhydrous $MgSO_4$. Purification by column chromatography, DCM/MeOH=40:1 (v/v). The solvent was evaporated to give an orange-yellow solid (0.37 g, yield 55%).

Synthesis of (E)-4-(phenyldiazenyl) benzoyl chloride ***8a***. 3-Carboxyazobenzene (0.32 g, 1.00 mmol) was dissolved in 10 ml of thionyl chloride, and the mixture was warmed to reflux. The reaction was followed by TLC. The excess thionyl chloride was evaporated to dryness to give an orange-brown solid which was used directly for next step.

The synthesis method of compound **7b** and **8b** is similar with the method of **7a** and **8a**

Synthesis of **ABMDA3**. Compound **4** (0.43 g, 1.00 mmol) and DIPEA (0.23 g, 1.80 mmol) were dissolved in 15 ml of dichloromethane and stirred in ice bath. **8a** was dissolved in 5 ml of dichloromethane and then slowly added to the reaction system. The reaction solution was stirred at room temperature overnight. Purification by column chromatography, PE/DCM=1:2 (v/v). The solvent was evaporated to give an orange-red solid. (0.33 g, yield 52.3%). mp = 235.4-236.5 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 10.10 (s, 1H), 8.24 (d, *J* = 8.4 Hz, 2H), 8.05 (d, *J* = 8.4 Hz, 2H), 8.01-7.93 (m, 2H), 7.85 (t, *J* = 7.2 Hz, 1H), 7.69-7.57 (m, 4H), 7.45 (s, 2H), 7.40 (t, *J* = 7.8 Hz, 1H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.88, 162.51, 153.90, 153.69, 151.92, 151.40, 138.15, 137.19, 135.83, 132.11, 129.55, 129.22, 129.08, 126.27, 125.20, 124.57, 124.21, 123.26, 122.78, 122.47, 18.19. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.96 (d, *J* = 8.1 Hz), -123.39--123.66 (m), -181.37 (dt, *J* = 15.3, 7.6 Hz). HRMS (ESI-TOF): calcd for $C_{31}H_{22}F_8N_4O_2Na$ [M + Na] $^+$, 657.1515, found 657.1512.

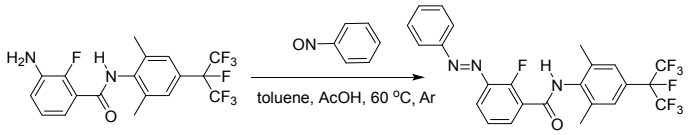
The synthesis method of compound **ABMDA2** is similar with the method of **ABMDA3**. *Data for* **ABMDA2**. Orange solid; yield 46.7%. mp = 188.1-189.4 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (s, 1H), 10.11 (s, 1H), 8.53 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.97 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.89-7.77 (m, 2H), 7.67-7.58 (m, 4H), 7.45 (s, 2H), 7.40 (t, *J* = 7.8 Hz, 1H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.93, 162.52, 153.93, 151.84, 151.42, 138.15, 137.21, 135.09, 131.91, 130.59, 129.80, 129.54, 129.11, 126.26, 125.84, 125.20, 124.58, 124.24, 123.27, 122.67, 121.71, 18.19. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.97 (d, *J* = 8.0 Hz), -123.40--123.60 (m), -181.36 (dt, *J* = 23.3, 7.6 Hz). HRMS (ESI-TOF): calcd for $C_{31}H_{23}F_8N_4O_2$ [M + H] $^+$,635.1695, found 635.1695.



The synthesis method of compound **9** is similar with the method of **3.** *Data for N-(2,6-dimethyl-4-(perfluoropropan-2-yl) phenyl)-2-fluoro-3-(2-nitrobenzamido) benzamide **9***. white solid; yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (t, *J* = 7.4 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.89-7.75 (m, 4H), 7.69 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 10.0 Hz, 3H), 2.35 (s, 6H).

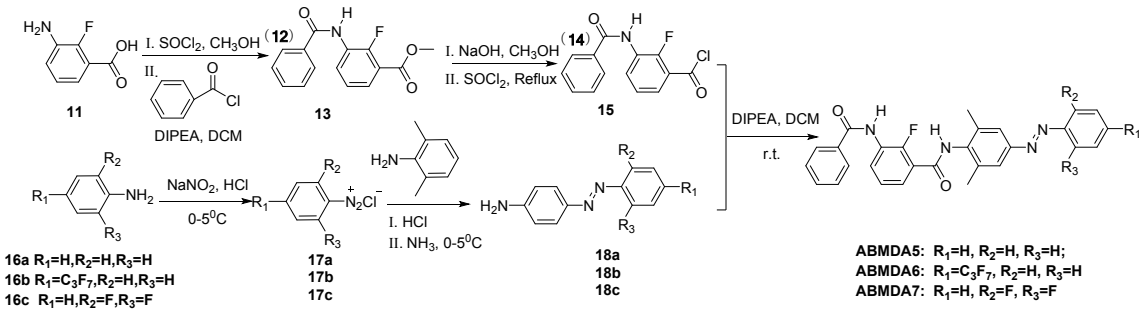
The synthesis method of compound **10** is similar with the method of **4.** *Data for 3-(2-aminobenzamido)-N-(2,6-dimethyl-4-(perfluoropropan-2-yl) phenyl)-2-fluorobenzamide **10***. white solid; yield 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (td, *J* = 8.0, 1.7 Hz, 1H), 8.06 (d, *J* = 2.3 Hz, 1H), 7.83 (ddd, *J* = 11.4, 8.7, 4.8 Hz, 2H), 7.53 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.39-7.28 (m, 4H), 6.75 (ddd, *J* = 5.7, 3.5, 1.2 Hz, 2H), 5.59 (s, 2H), 2.37 (s, 6H).

Synthesis of **ABMDA1**. The nitrosobenzene (0.43 g, 4.00 mmol) and the compound **10** (0.55 g, 1.00 mmol) were dissolved in 15 ml of toluene, then glacial acetic acid (0.60 g, 10 mmol) was added. The reaction system was replaced three times with nitrogen, then stirred at 60 ℃. The reaction was followed by TLC and completed after 24 hours. 40 ml of water was added to the reaction mixture, and the mixture was extracted with dichloromethane (3×30 mL). The organic phases were combined and dried over anhydrous $MgSO_4$. Purification by column chromatography, DCM/EA=60:1 (v/v). The solvent was evaporated to give an orange-yellow solid (0.32 g, yield 50.5%). mp = 218.6-219.7 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.60 (s, 1H), 10.09 (s, 1H), 8.16 (t, *J* = 7.2 Hz, 1H), 7.92 (dd, *J* = 6.2, 3.0 Hz, 3H), 7.82 (dd, *J* = 6.0, 3.2 Hz, 1H), 7.71 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.59 (dd, *J* = 6.4, 3.6 Hz, 3H), 7.51 (t, *J* = 6.2 Hz, 1H), 7.45 (s, 2H), 7.39 (t, *J* = 7.8 Hz, 1H), 2.34 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.93, 162.54, 152.32, 151.96, 149.83, 148.81, 138.11, 137.17, 134.84, 131.98, 131.35, 131.13, 129.43, 129.30, 126.73, 126.55, 125.03, 124.47, 124.34, 123.27, 122.86, 121.54, 118.71, 116.58, 18.18. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.96 (d, *J* = 8.1 Hz), -125.72--125.92 (m), -181.36 (dt, *J* = 15.5, 7.5 Hz). HRMS (ESI-TOF): calcd for $C_{31}H_{22}F_8N_4O_2Na$ [M + Na] $^+$, 657.1515, found 657.1514.



4 **ABMDA4**

The synthesis method of compound **ABMDA4** is similar with the method of **ABMDA1**. *Data for **ABMDA4***. Orange solid; yield 41.4%. mp = 176.3-177.8 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.00-7.87 (m, 4H), 7.70-7.61 (m, 3H), 7.50 (dd, *J* = 15.6, 7.2 Hz, 3H), 2.39 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.98, 157.41, 154.82, 152.07, 140.07, 138.04, 137.17, 132.62, 132.35, 129.62, 126.33, 125.04, 124.62, 123.53, 122.89, 121.84, 119.48, 118.71, 18.22. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.96 (d, *J* = 8.1 Hz), -125.58--125.97 (m), -181.36 (dt, *J* = 15.5, 7.5 Hz). HRMS (ESI-TOF): calcd for $C_{24}H_{18}F_8N_3O$ [M + H] $^+$, 516.1324, found 516.1323.



*Synthesis of methyl 3-amino-2-fluorobenzoate **12***. Compound **11** (2.30 g, 15.00 mmol) was dissolved in methanol and cooled to 0 ℃. Thionyl chloride (22.20 mL, 301.00 mmol) was slowly added to the solution. After the addition, the mixture was transferred to room temperature and stirred overnight. The reaction was followed by TLC and completed after 12 h. The solvent was removed in vacuo and the residue was taken in dichloromethane. A saturated $NaHCO_3$ solution was added to the reaction solution to adjust to pH = 7. The solution was separation and the combined organic layers dried with anhydrous $MgSO_4$. Used directly in the next step. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.00-6.94 (m, 3H), 5.35 (s, 2H), 3.82 (s, 3H).

The synthesis method of compound **13** is similar with the method of **3**. *Data for methyl 3-benzamido-2-fluorobenzoate **13***. white solid; yield 61.9%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 7.99 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.91-7.84 (m, 1H), 7.75 (ddd, *J* = 8.1, 6.6, 1.7 Hz, 1H), 7.65-7.60 (m, 1H), 7.58-7.52 (m, 2H), 7.35 (t, *J* = 7.9 Hz, 1H), 3.88 (s, 3H).

*Synthesis of 3-benzamido-2-fluorobenzoic acid **14.*** Compound **13** (3.90 g) was dissolved in 25 ml of methanol, then 20 ml of 1 M NaOH solution was added, and the solution was stirred at 50 ℃. The reaction was followed by TLC and completed after 2 h. The methanol in the solution was evaporated and filtered to give a white solid. Used directly in the next step.^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (s, 1H), 10.23 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 2H), 7.87-7.80 (m, 1H), 7.77-7.69 (m, 1H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 1H).

The synthesis method of compound **15** is similar with the method of **8a.** Used directly in the next step.

*Synthesis of (E)-2,6-dimethyl-4-(phenyldiazenyl) aniline **18a***. The aniline **16a** (1.84 g, 20.00 mmol) was added dropwise to 37% concentrated HCl and stirred under ice-cooling. A sodium nitrite aqueous solution (1.40 g, 20.00 mmol) was added to the reaction mixture and stirred for 1 hour to obtain a yellow transparent diazo Salt solution. 2,6-Dimethylaniline (2.42 g, 20.00 mmol) was added to a solution of hydrochloric acid (1N, 22 ml) and stirred vigorously at 0 °C-5 ℃. The diazonium salt solution was added to the coupling solution, then stirred at 5 ℃ for 3 h, and the reaction was completed. The reaction solution was slowly added to aqueous ammonia (1 N, 30 mL) to give an orange-yellow precipitate. The precipitate was filtered and washed several times with water containing a small amount of sodium hydrogencarbonate (Ph=8). Purification by column chromatography, PE/DCM=1:2 (v/v). The solvent was evaporated to give a dark red solid (2.2 g, yield 48.9%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.5 Hz, 2H), 7.63 (s, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 3.99 (s, 2H), 2.26 (s, 6H).

The synthesis method of compound **18b** is similar with the method of **18a**. *Data (E)-2,6-dimethyl-4-((4-(perfluoropropan-2-yl) phenyl) diazenyl) aniline**18b***. Orange solid; yield 59.7%. ^{1}H

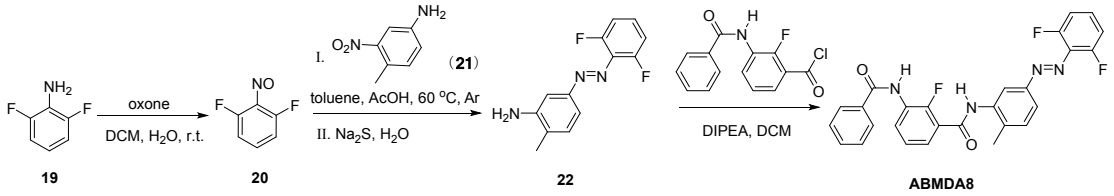
NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.67 (s, 2H), 4.32 (s, 2H), 2.27 (s, 6H).

The synthesis method of compound**18c** is similar with the method of**18a**. *Data for (E)-4-((2,6-difluorophenyl) diazenyl)-2,6-dimethylaniline **18c***. Orange solid; yield 68.6%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 2H), 7.21 (td, *J* = 8.3, 4.2 Hz, 1H), 7.00 (p, *J* = 3.1 Hz, 2H), 4.35 (s, 2H), 2.27 (s, 6H).

Synthesis of **ABMDA5**. Compound **18a** (0.23 g, 1.00 mmol) and DIPEA (0.16 g, 1.20 mmol) were dissolved in 15 ml of dichloromethane and stirred under ice bath. Compound **15** (0.33 g, 1.20 mmol) was dissolved in 5 ml of dichloromethane, and then slowly added to the reaction system. The mixture was stirred for 10 minutes in an ice bath, then transferred to room temperature and stirred overnight. Purification by column chromatography, DCM/EA = 40:1 (v/v). The solvent was evaporated to give a yellow solid. (0.28 g, yield 61.3%). mp = 198.1-198.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 10.08 (s, 1H), 8.05-8.02 (m, 2H), 7.91 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.82 (td, *J* = 8.0, 1.4 Hz, 1H), 7.71 (s, 2H), 7.65-7.54 (m, 7H), 7.38 (t, *J* = 7.8 Hz, 1H), 2.38 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.60, 162.55, 153.93, 151.97, 151.43, 150.21, 137.82, 136.79, 133.77, 131.94, 129.45, 129.00, 128.47, 127.81, 126.45, 126.13, 125.24, 124.15, 122.47, 121.88, 18.24. ^{19}F NMR (376 MHz, DMSO-d_6) δ -123.59 (t, *J* = 6.6 Hz). HRMS (ESI-TOF): calcd for $C_{28}H_{24}FN_4O_2$ [M + H] $^+$, 467.1885, found 467.1884.

The synthesis method of compound **ABMDA6** is similar with the method of **ABMDA5**. *Data for* **ABMDA6**. Orange solid; yield 50.3%. mp = 157.8-158.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.21 (s, 1H), 10.05 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 2H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.75 (s, 2H), 7.66-7.52 (m, 4H), 7.37 (t, *J* = 7.8 Hz, 1H), 2.39 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.60, 162.54, 153.94, 153.58, 151.44, 150.09, 138.65, 136.95, 133.76, 131.92, 129.03, 128.45, 127.80, 127.10, 126.89, 126.46, 126.13, 125.32, 124.14, 123.24, 122.26, 18.20. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.96 (d, *J* = 8.1 Hz), -125.58--125.97 (m), -181.36 (dt, *J* = 15.5, 7.5 Hz). HRMS (ESI-TOF): calcd for $C_{31}H_{23}F_8N_4O_2$[M + H] $^+$, 635.1695, found 635.1694.

The synthesis method of compound **ABMDA7** is similar with the method of **ABMDA5**. *Data for* **ABMDA7**. Orange solid; yield 59.7%. mp = 206.2-207.4 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 10.12 (s, 1H), 8.05-8.01 (m, 2H), 7.85-7.79 (m, 1H), 7.69 (s, 2H), 7.66-7.53 (m, 5H), 7.36 (dt, *J* = 15.5, 8.3 Hz, 3H), 2.38 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.60, 162.52, 156.07, 153.93, 153.47, 151.43, 150.80, 138.84, 137.01, 133.76, 131.93, 131.57, 130.48, 129.04, 128.46, 127.80, 126.45, 126.12, 125.30, 124.15, 121.90, 113.00, 18.18. ^{19}F NMR (376 MHz, DMSO-d_6) δ -122.47 (dd, *J* = 9.2, 6.1 Hz), -123.56 (t, *J* = 6.7 Hz). HRMS (ESI-TOF): calcd for $C_{28}H_{21}F_3N_4O_2Na$ [M + Na] $^+$, 525.1517, found 525.1513.



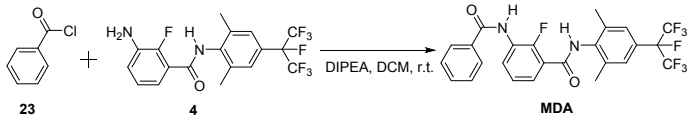
The synthesis method of compound **20** is similar with the method of compound **6**. Used directly in the next step.

The synthesis method of compound **21** is similar with the method of compound **7a**. *Data for (E)-1-(2,6-difluorophenyl)-2-(4-methyl-3-nitrophenyl) diazene **21***. Orange solid; yield 63.2%. ^{1}H NMR

(400 MHz, DMSO-d_6) δ 8.36 (d, *J* = 2.0 Hz, 1H), 8.12 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.63 (tt, *J* = 8.4, 6.1 Hz, 1H), 7.41-7.33 (m, 2H), 2.63 (s, 3H).

*Synthesis of (E)-5-((2,6-difluorophenyl) diazenyl)-2-methylaniline**22***. Compound **21** (1.39 g, 5.00 mmol) was dissolved in a solution of 90 ml of THF/H_2O (v/v=3:1), then Na_2S (1.17 g, 15.00 mmol) was added. The red-black suspension was stirred under reflux, then the reaction was followed by TLC and completed after 48 h. The THF was removed under reduced pressure and the residue was extracted with dichloromethane. The organic phases were combined and washed with 1M NaOH. (0.3 g, yield 24.4%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (tt, *J* = 8.2, 6.2 Hz, 1H), 7.34-7.27 (m, 2H), 7.17 (d, *J* = 7.9 Hz, 1H), 7.12 (d, *J* = 1.9 Hz, 1H), 7.08 (dd, *J* = 7.8, 1.9 Hz, 1H), 5.27 (s, 2H), 2.16 (s, 3H).

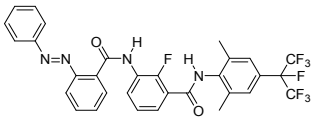
The synthesis method of compound **ABMDA8** is similar with the method of **ABMDA1.** *Data for* **ABMDA8.** Orange solid; yield 53.8%. mp = 206.1-206.8 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (s, 1H), 10.17 (s, 1H), 8.13-7.98 (m, 3H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.60 (dt, *J* = 16.4, 7.1 Hz, 6H), 7.42-7.30 (m, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.59, 162.81, 156.12, 154.04, 153.57, 151.54, 151.03, 137.72, 136.96, 133.76, 131.93, 131.62, 131.44, 130.35, 129.24, 128.46, 127.81, 126.44, 125.06, 124.09, 120.86, 118.49, 113.03, 18.07. HRMS (ESI-TOF): calcd for $C_{27}H_{19}F_3N_4O_2Na$ [M + Na] $^+$, 511.1360, found 511.1357.

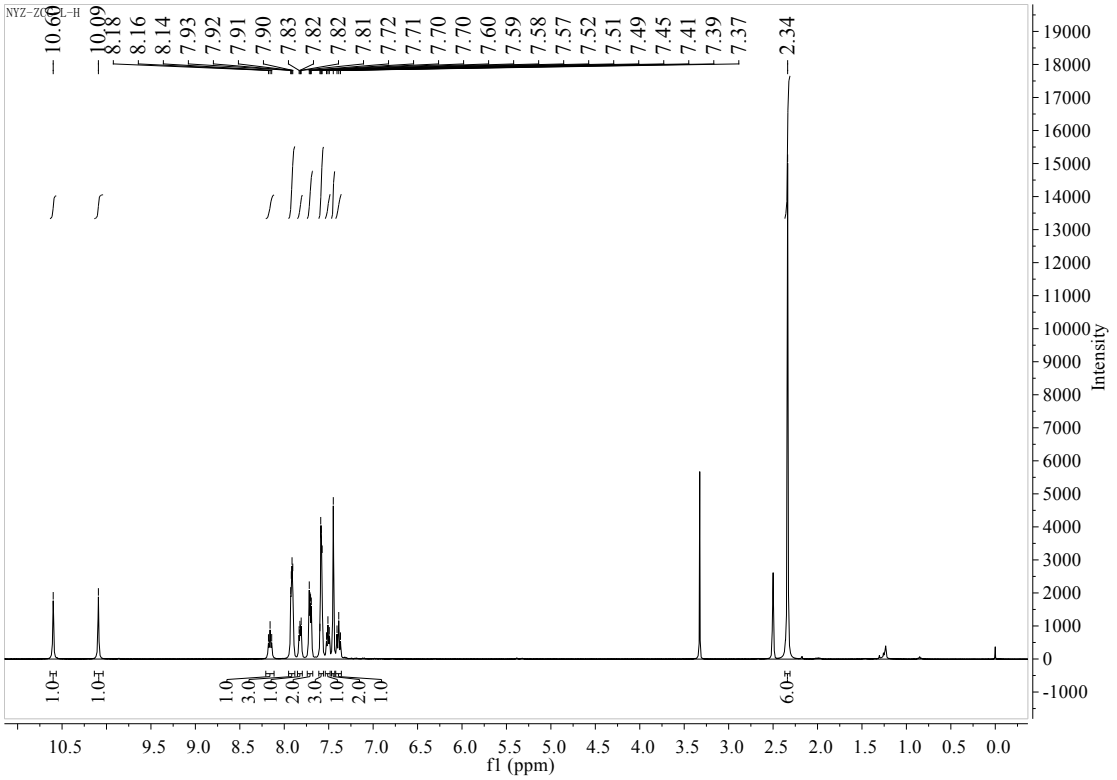


23 **4** **MDA**

The synthesis method of compound **MDA** is similar with the method of **3.** *Data for* **MDA.** White solid; yield 54.6%. mp = 197.6-198.8 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 10.09 (s, 1H), 8.02 (d, *J* = 7.2 Hz, 2H), 7.80 (t, *J* = 7.0 Hz, 1H), 7.59 (dt, *J* = 28.7, 6.8 Hz, 4H), 7.45 (s, 2H), 7.37 (t, *J* = 7.6 Hz, 1H), 2.35 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.83, 167.78, 159.15, 156.65, 143.40, 142.45, 138.96, 137.20, 134.37, 133.71, 133.04, 131.70, 131.36, 130.38, 129.83, 129.72, 129.44, 128.49, 23.43. ^{19}F NMR (376 MHz, DMSO-d_6) δ -74.96 (d, *J* = 8.1 Hz), -125.58--125.97 (m), -181.36 (dt, *J* = 15.5, 7.5 Hz). HRMS (ESI-TOF): calcd for $C_{25}H_{18}F_8N_2O_2Na$ [M + Na] $^+$, 553.1141, found 553.1137.

3. Copies of NMR Spectra of Compounds

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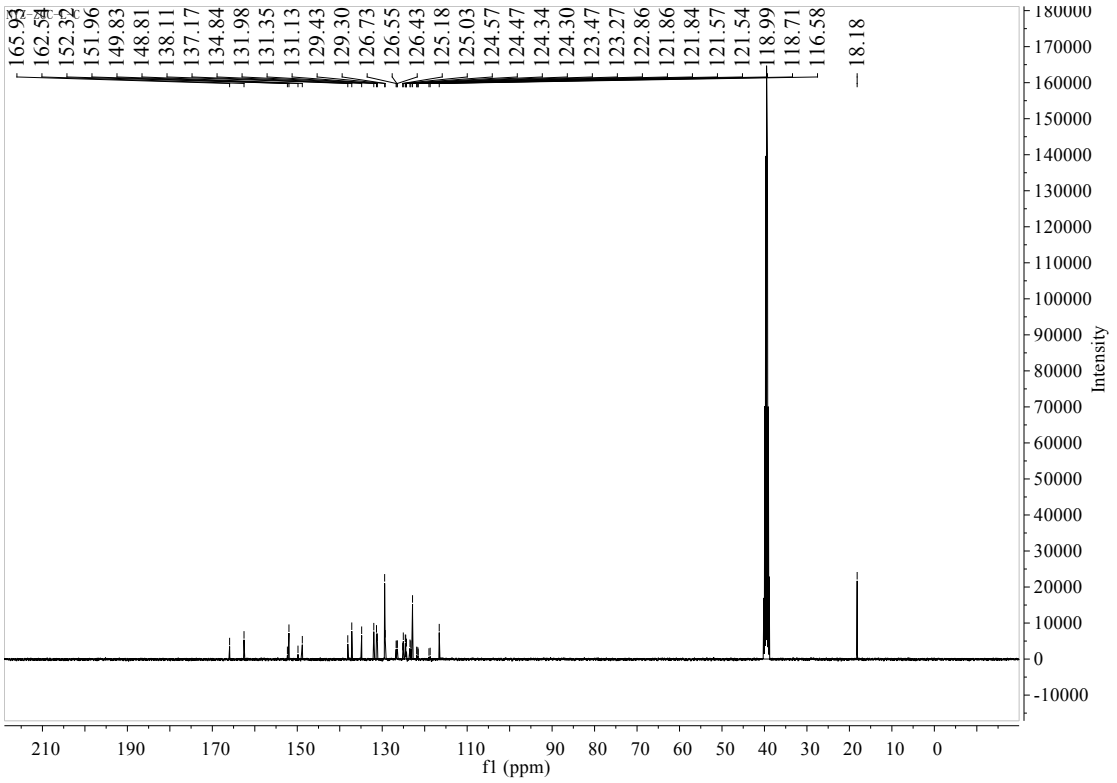
fl (ppm)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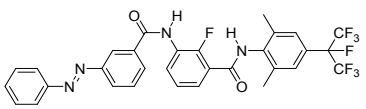
fl (ppm)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N
F
H
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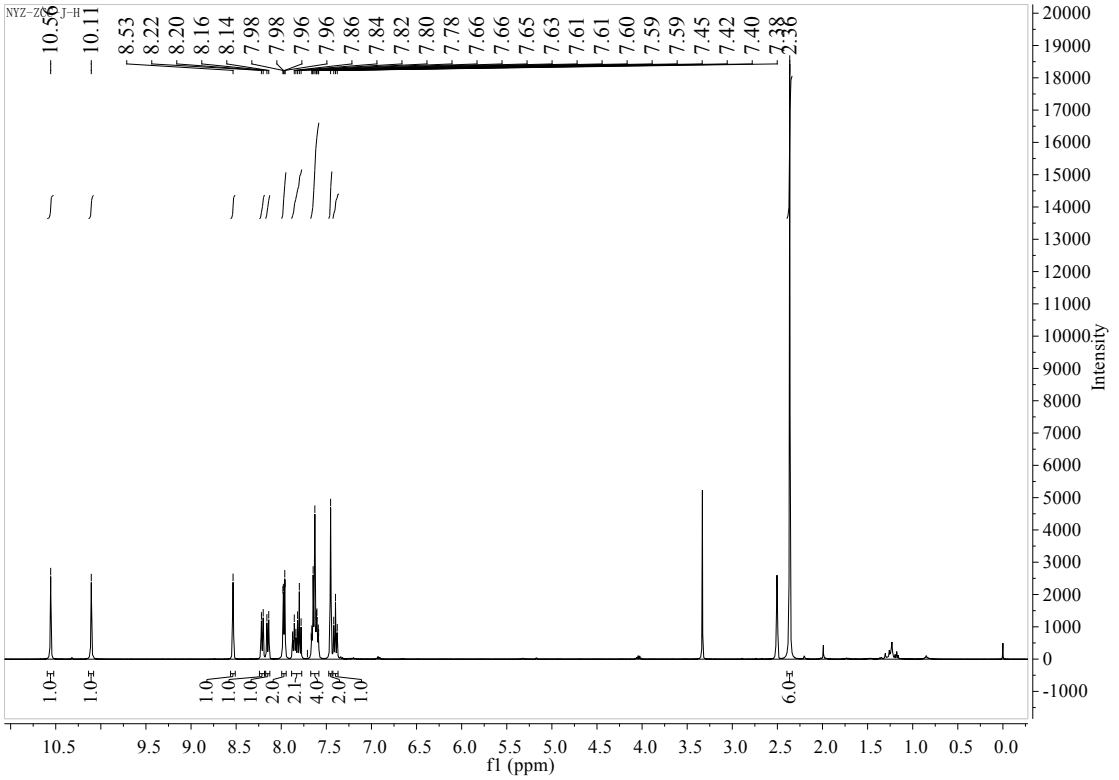
CF3
F
CF3
O
N
N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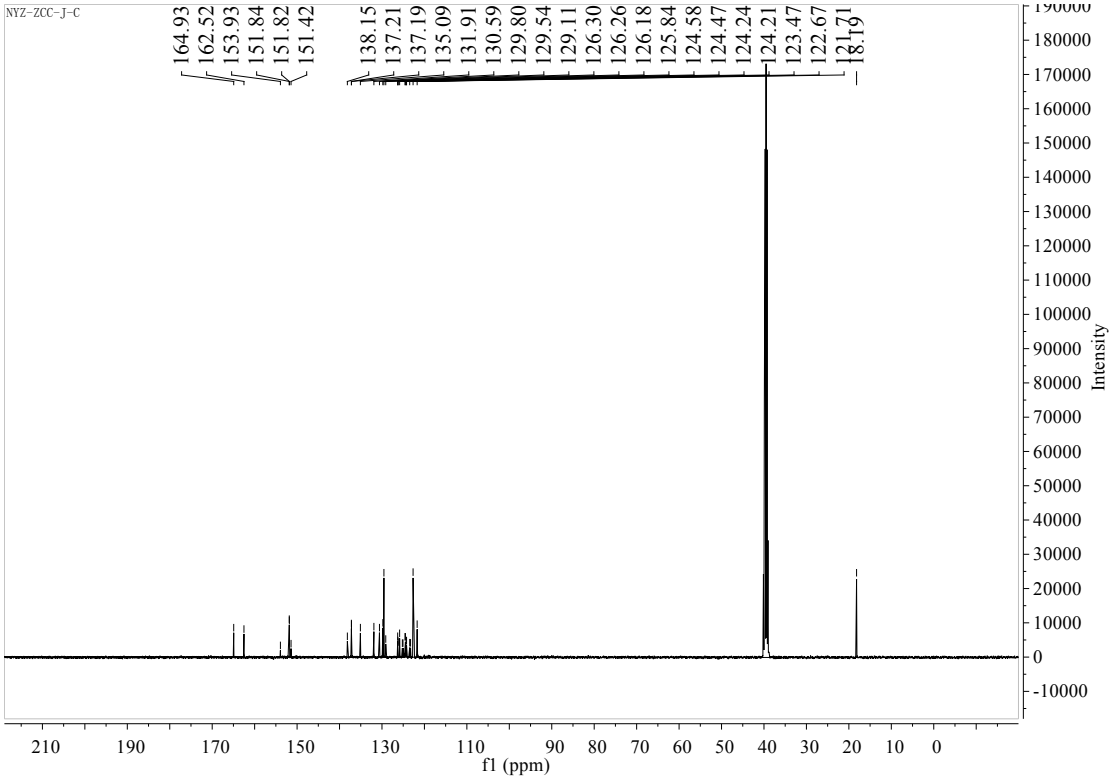
Intensity
fl (ppm)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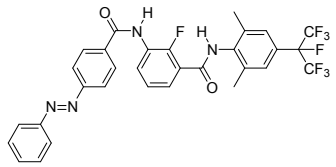
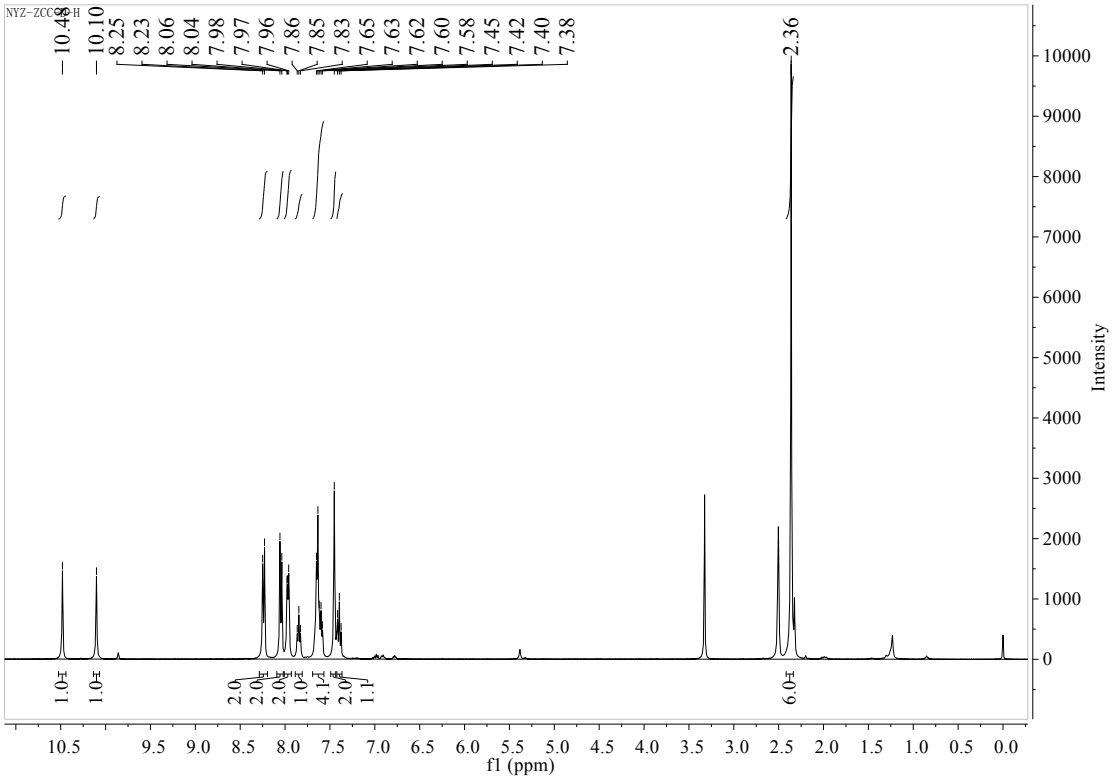
18.19
Intensity
fl (ppm)

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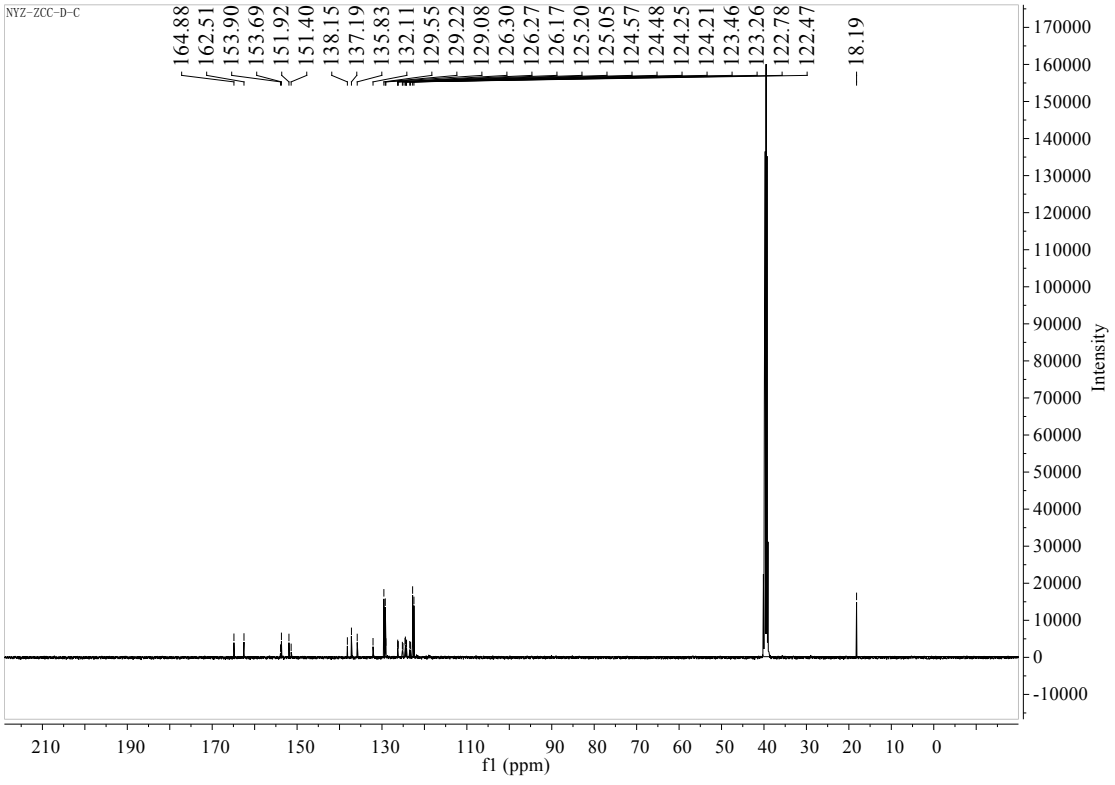
Intensity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125.20
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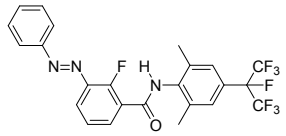
Intensity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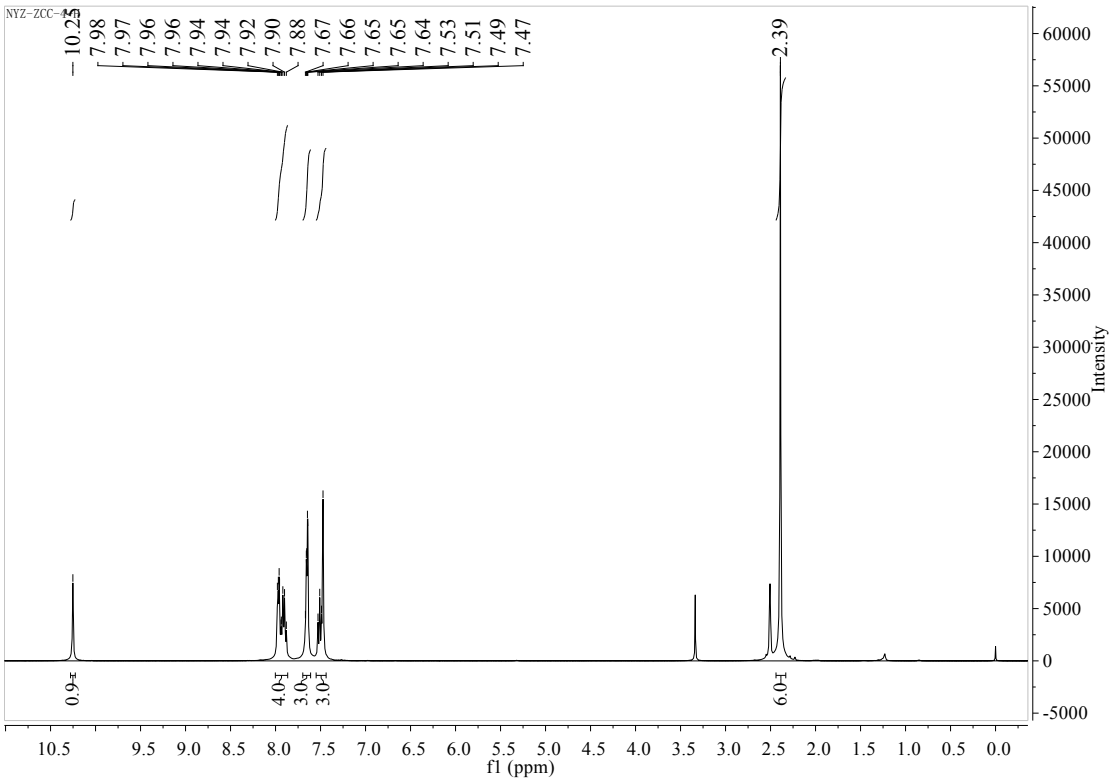
F
CF3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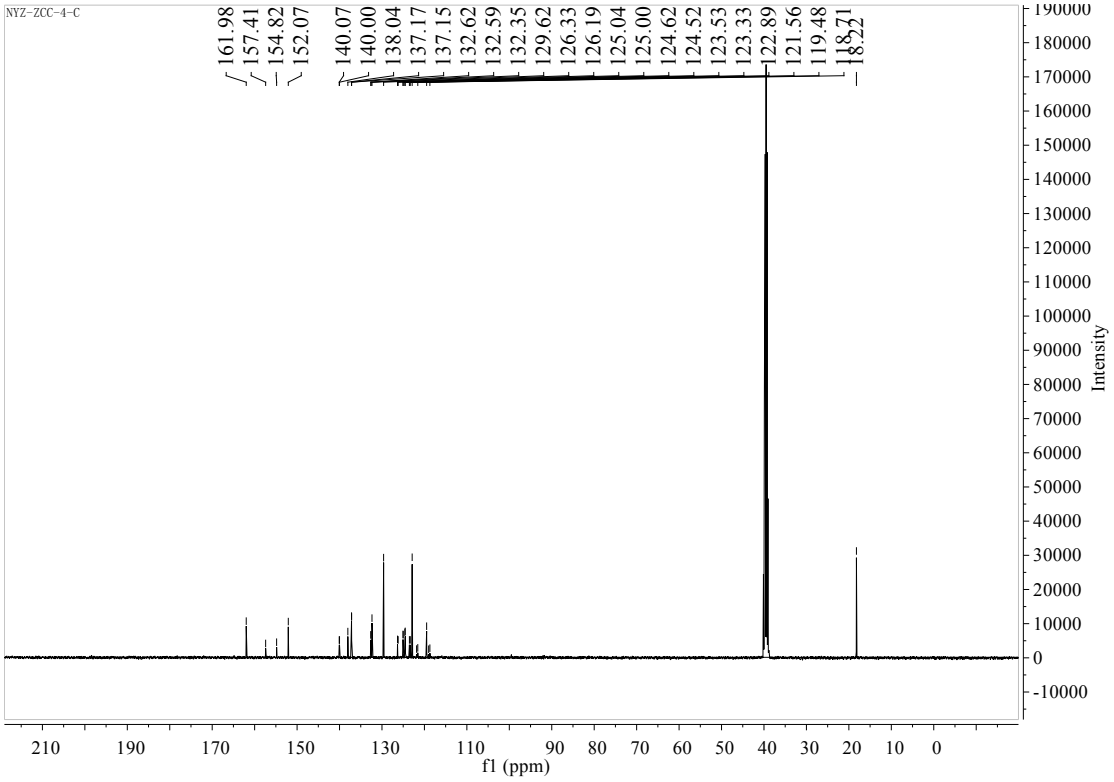
Intensity
f1 (ppm)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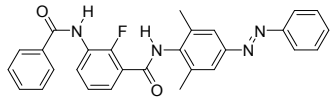
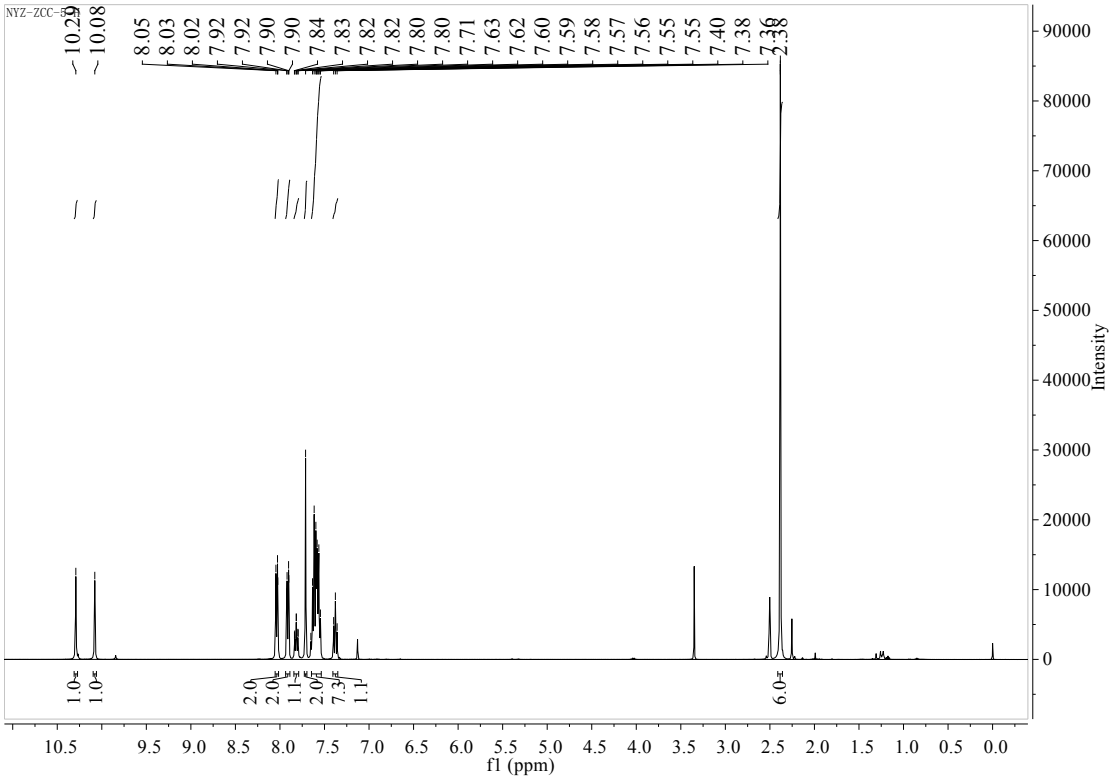
Intensity
f1 (ppm)

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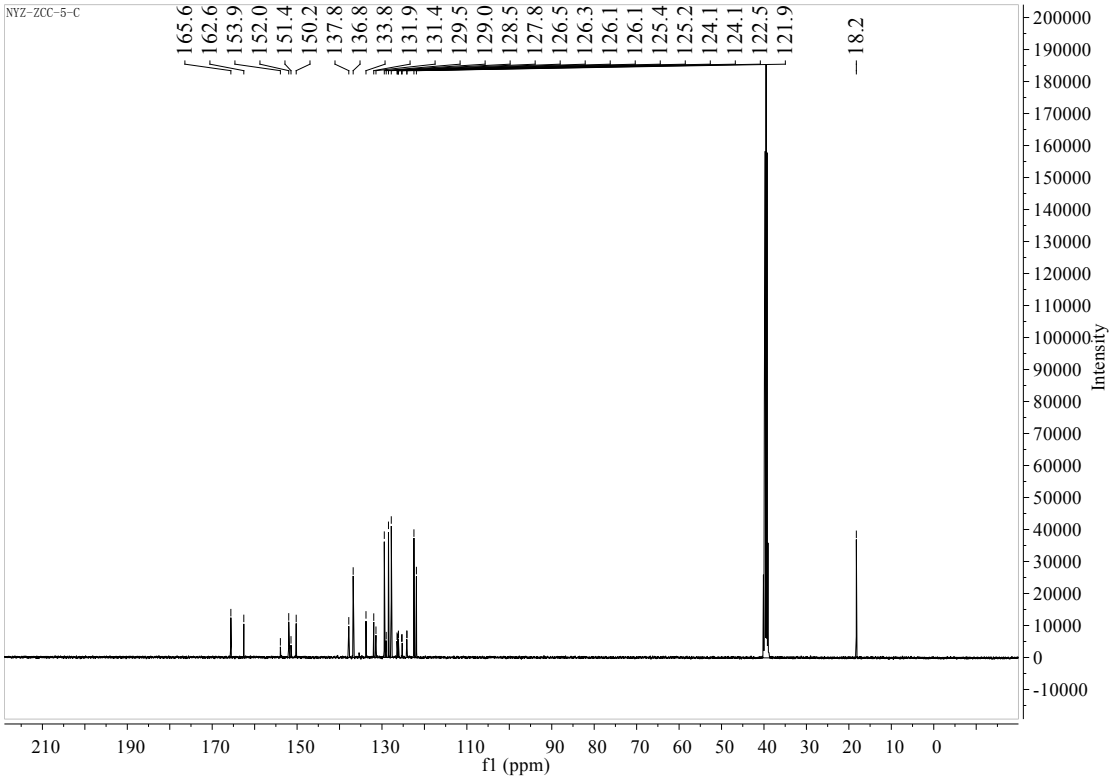
f1 (ppm)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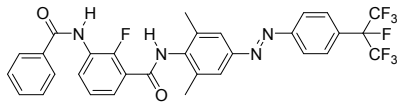
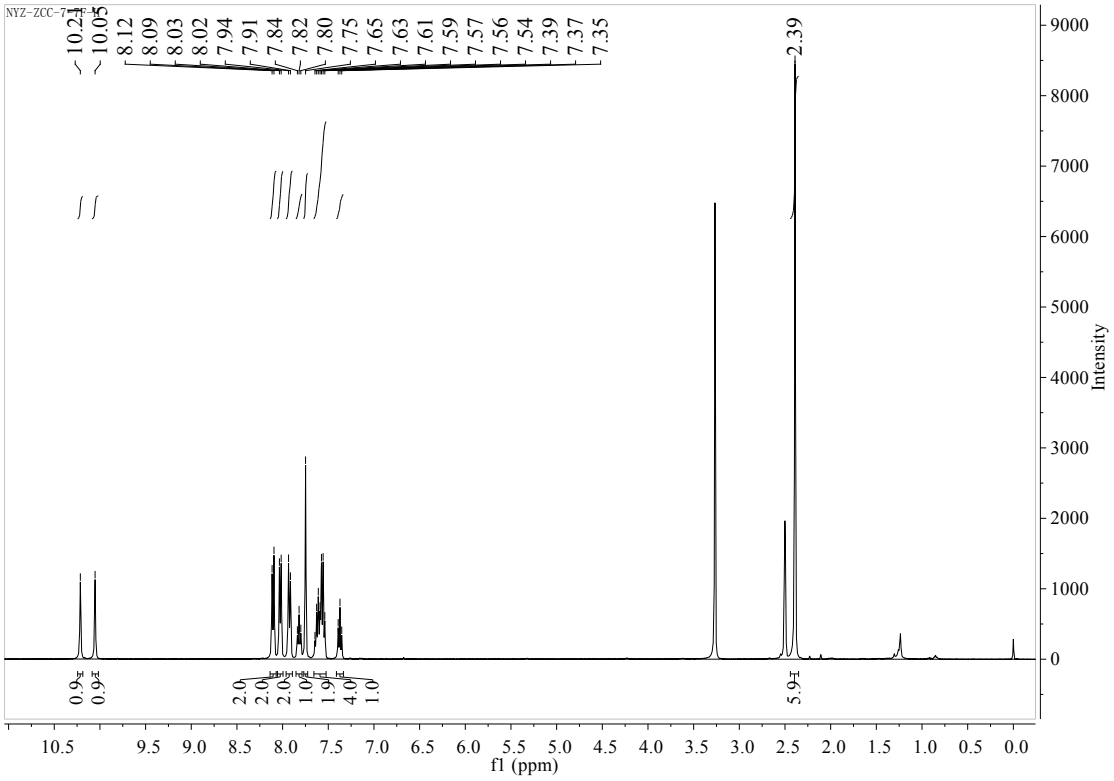
f1 (ppm)

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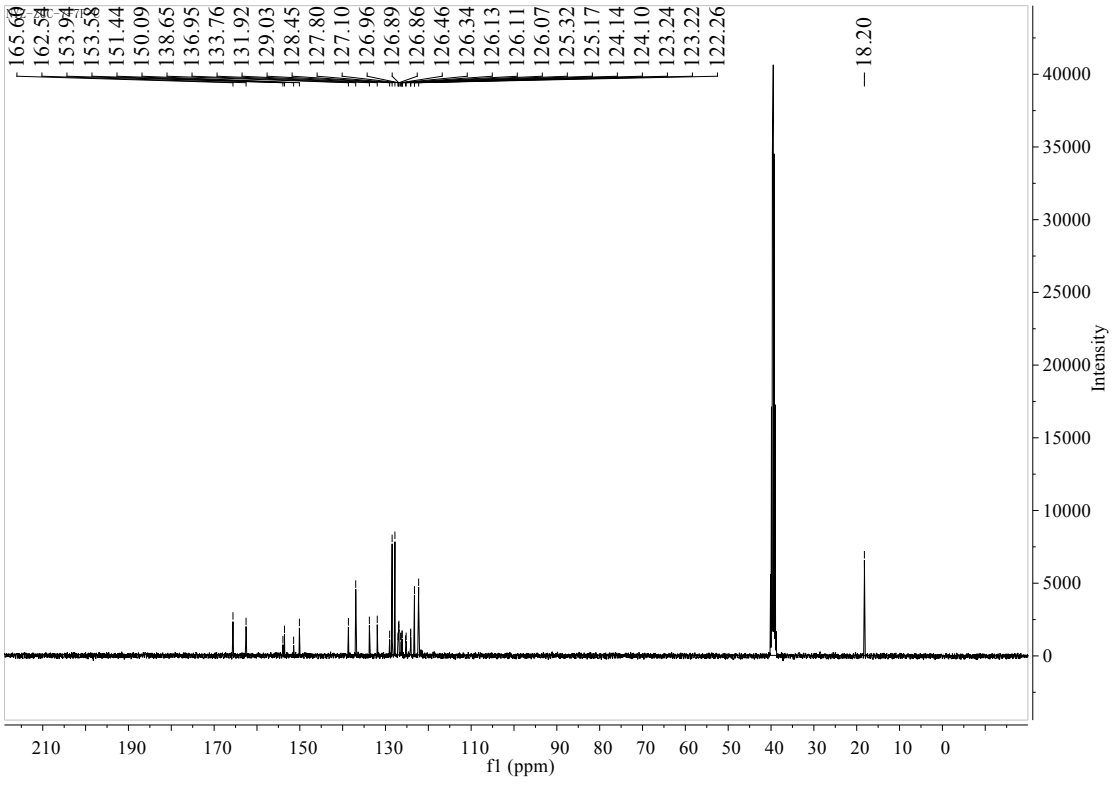
Intensity
f1 (ppm)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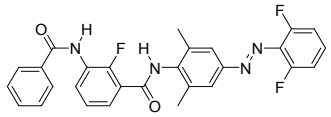
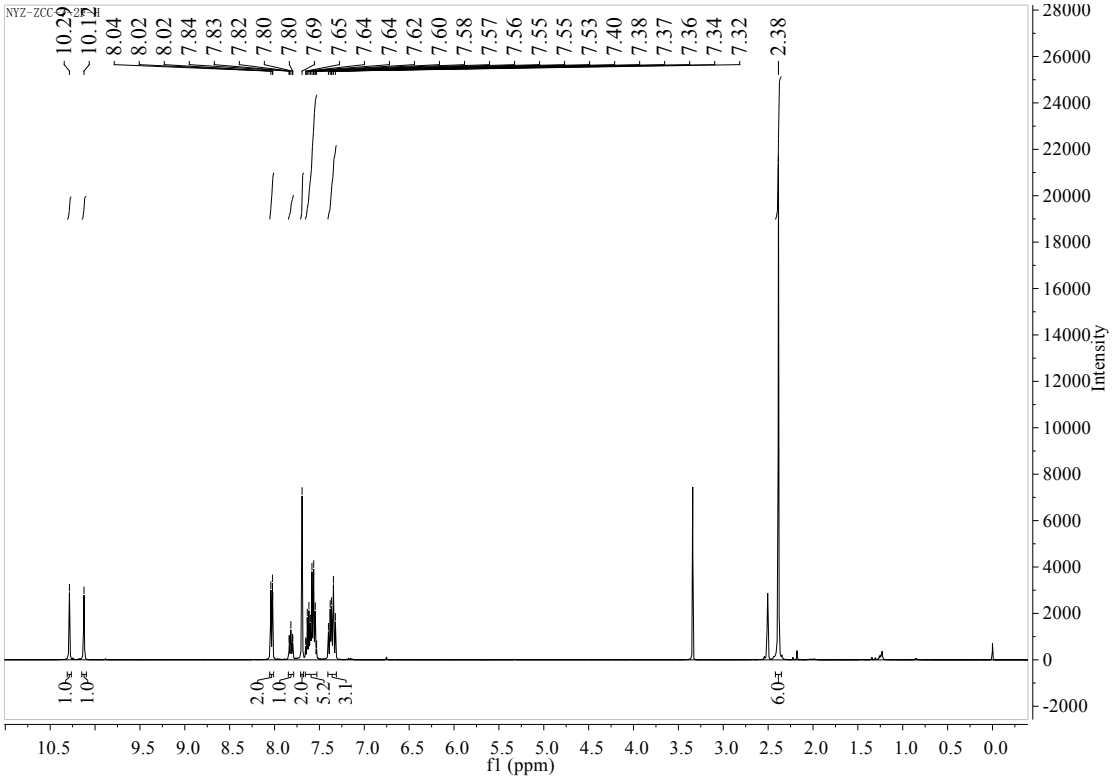
Intensity
f1 (ppm)

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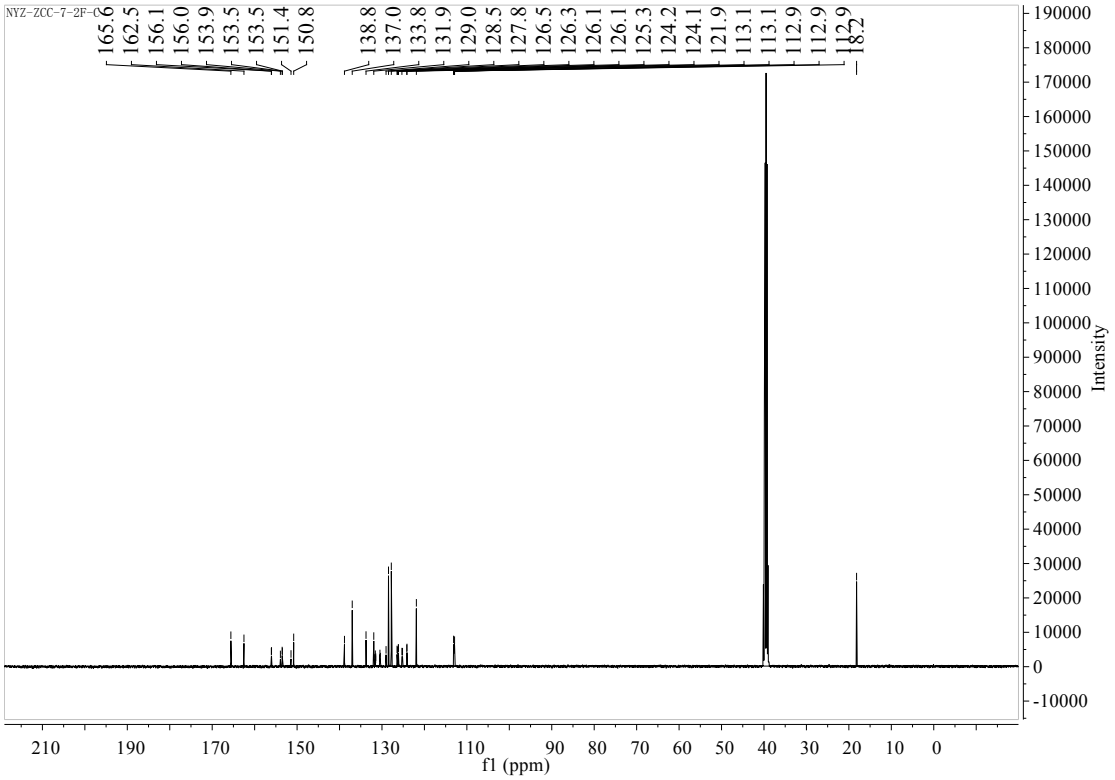
Intensity
f1 (ppm)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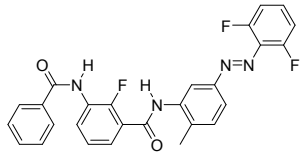
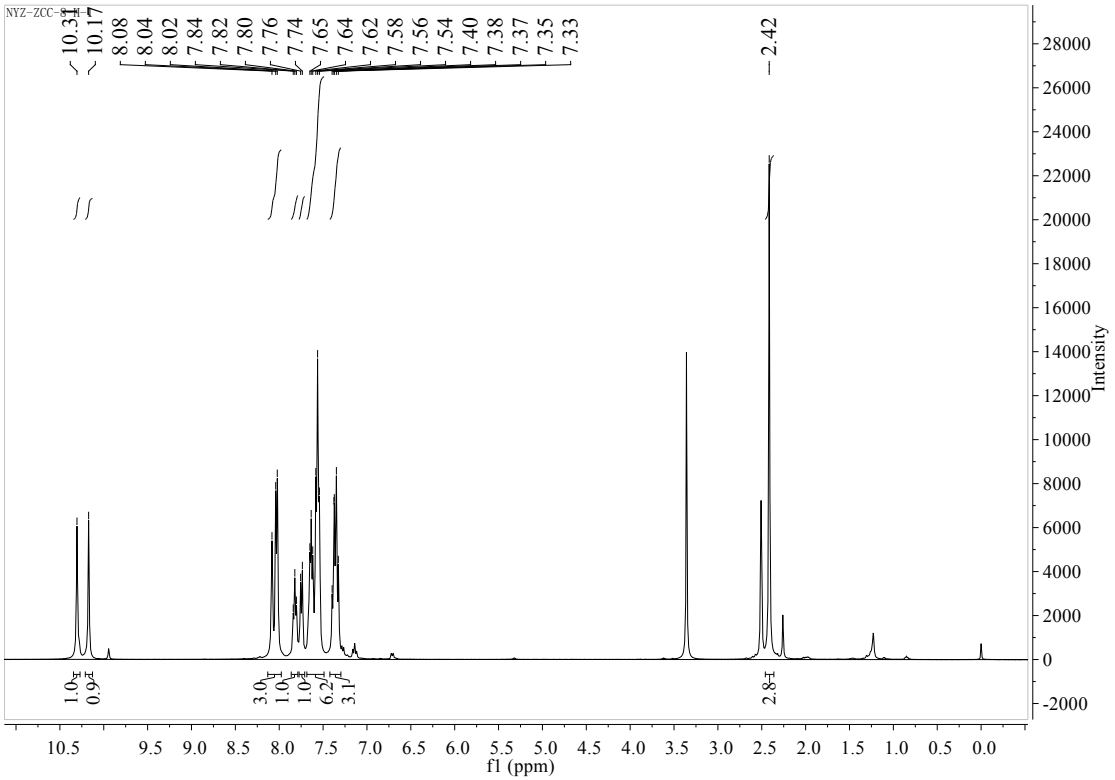
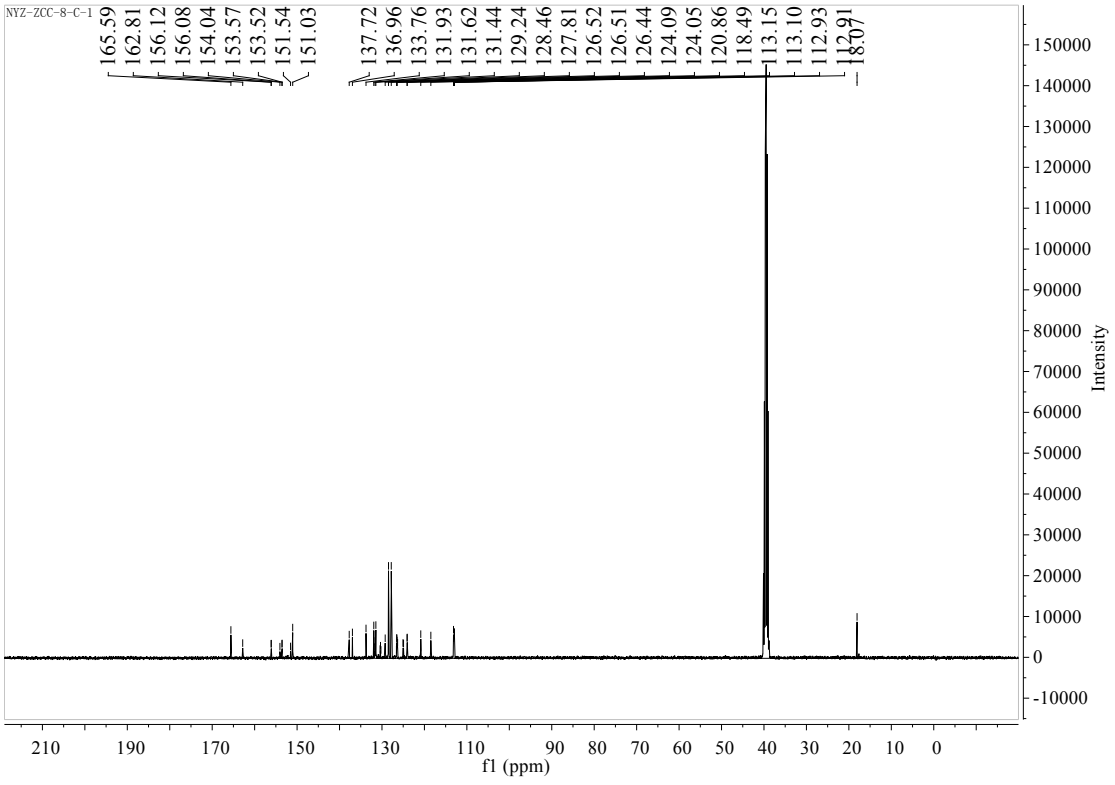
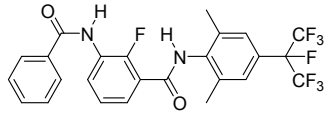
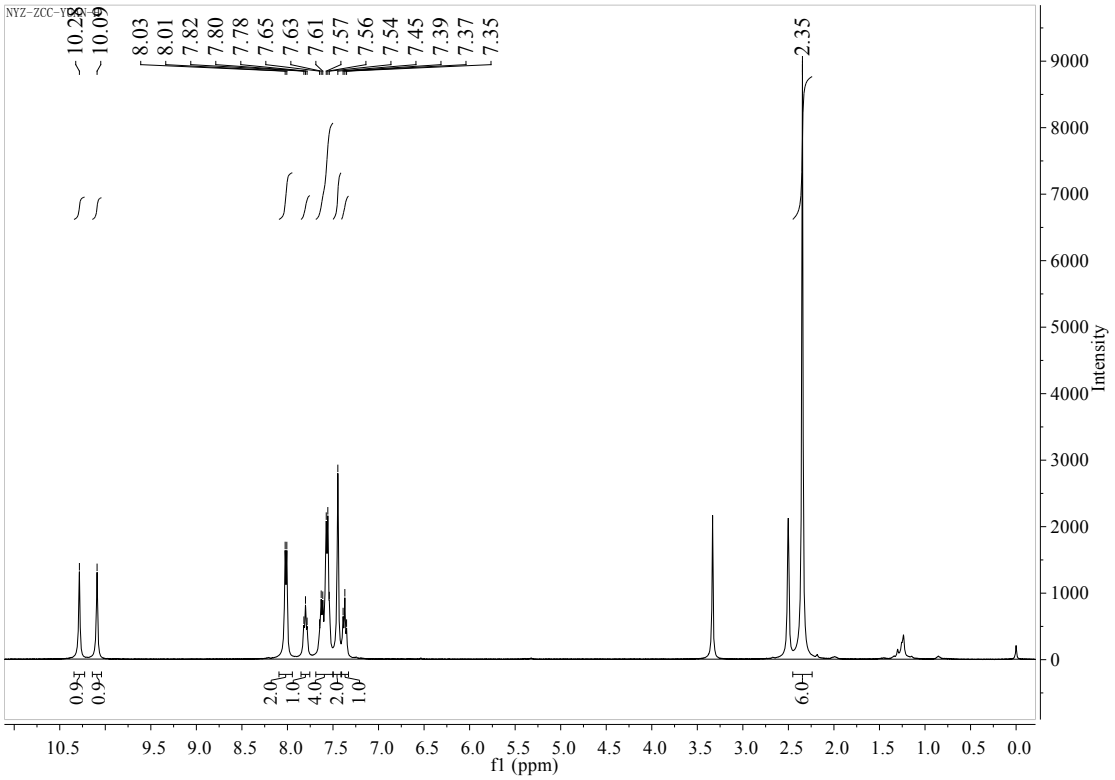
128.5
127.8
126.5
126.3
126.1
126.1
125.3
124.2
124.1
121.9
113.1
113.1
112.9
112.9
112.9
18.2
Intensity
f1 (ppm)

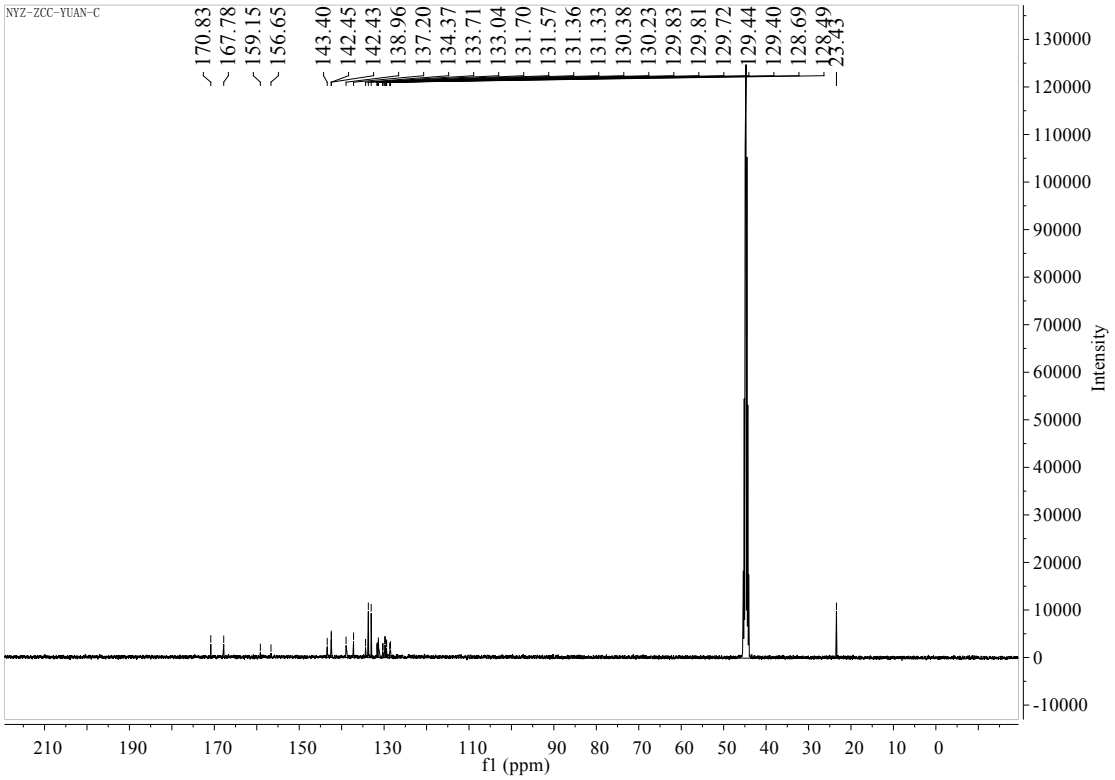

F
O
H
N
F
H
N
N=N
F
O


NYZ-ZCC-8
10.33
10.17
8.08
8.04
8.02
7.84
7.82
7.80
7.76
7.74
7.65
7.64
7.62
7.58
7.56
7.54
7.40
7.38
7.37
7.35
7.33
2.42
1.0
0.9
3.0
1.0
1.0
6.2
3.1
2.8
Intensity
f1 (ppm)


NYZ-ZCC-8-C-1
165.59
162.81
156.12
156.08
154.04
153.57
153.52
151.54
151.03
137.72
136.96
133.76
131.93
131.62
131.44
129.24
128.46
127.81
126.52
126.51
126.44
124.09
124.05
120.86
118.49
113.15
113.10
112.93
112.91
18.07
Intensity
f1 (ppm)




NYZ-ZCC-YUAN-H
10.23
10.09
8.03
8.01
7.82
7.80
7.78
7.65
7.63
7.61
7.57
7.56
7.54
7.45
7.39
7.37
7.35
2.35
0.9
0.9
2.0
1.0
4.0
2.0
1.0
6.0
Intensity
fl (ppm)


NYZ-ZCC-YUAN-C
170.83
167.78
159.15
156.65
143.40
142.45
142.43
138.96
137.20
134.37
133.71
133.04
131.70
131.57
131.36
131.33
130.38
130.23
129.83
129.81
129.72
129.44
129.40
128.69
128.49
23.43
Intensity
fl (ppm)