

Supplementary Information

Direct construction of d_3 -methylated all-carbon quaternary stereocenters through carbene-catalyzed desymmetrization

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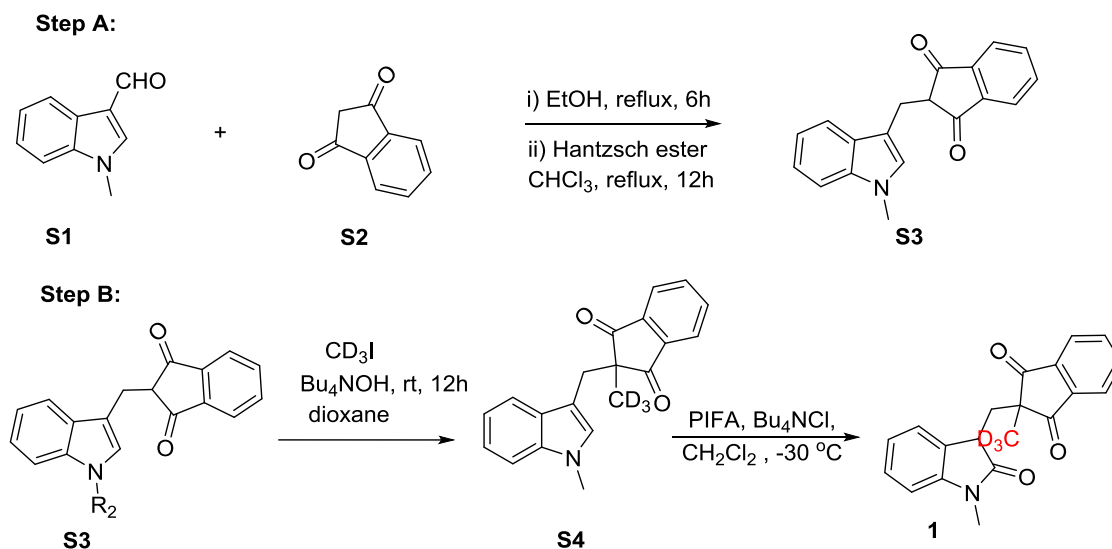
I	General information
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I: General Information

Chemicals were purchased as reagent grade and used without further purification. Solvents (THF, toluene) were distilled from appropriate drying agents prior to use. In addition, more solvents were purchased from commercial suppliers and dried over molecular sieves. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker (400 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker (400 MHz) (100 MHz) spectrometer. Fourier transform infrared spectroscopy (FT-IR, a Bruker model VECTOR-22 Fourier transform spectrometer). High resolution mass spectral analysis (HRMS) was performed on a Waters Q-TOF Premier Spectrometer. X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffractionmeter. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 precoated silica gel plate (0.2 mm thickness).

II. General procedure

a) General procedure for the synthesis of indole derivatives **1** (**1a** as an example).



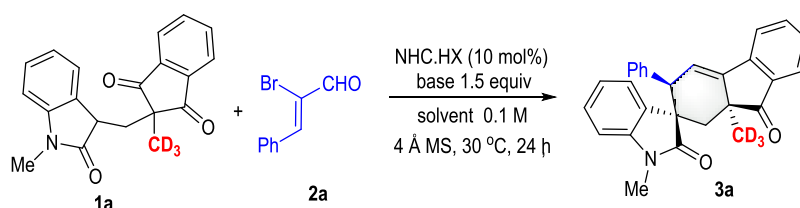
Step A: Aldehyde **S1**^[1, 2] (1.05 equiv.) and 1,3-indandione **S2** (10 mmol, 1.0 equiv.) were dissolved in 100 mL ethanol. The reaction mixture was stirred at reflux temperature for about 6 hours, at which time the condensation product precipitates from the reaction mixture. Removing the solvent through decompression filtration, the yellow solid product was obtained in almost equivalent yield which was used directly in the next step. Condensation product (5 mmol, 1.0 equiv.) and Hantzsch ester (1.0 equiv.) were dissolved in 50 mL CHCl₃ and the mixture was stirred at reflux temperature for about 12 hours, after the complete conversion of starting material, the reaction mixture was concentrated *in vacuo* to afford a yellow solid. Crystallization of solids from EtOAc/PE to remove reduction of the product, given substrate **S3** as pale yellow solids in excellent yield (two steps, >80% yield).

Step B: To a solution of substrate **S3** (5.0 mmol, 1.0 equiv.) in 1,4-dioxane was added Bu₄NOH (40% in H₂O, 1.2 equiv.). After the mixture was stirred at room temperature for 30 min, CD₃I (1.05 equiv.) was slowly added and the solution was stirred for further 12 h at room temperature. When the reaction is complete, the mixture was poured into aqueous NH₄Cl solution, and diluted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel to afford the desired fluorination product **S4** as a yellow solid.

A solution of PIFA (3.6 mmol, 1.2 equiv.) in CH₂Cl₂ (5 mL) was added dropwise to the reaction mixture of **S4** (3.0 mmol, 1.0 equiv.) and Bu₄NCl (3.6 mmol, 1.2 equiv.) in 20 mL CH₂Cl₂ at -30 °C. The reaction was completed in ten minutes, upon which time the mixture was poured into water, and extracted with CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel using DCM/PE (4:1-1:0) as eluent to

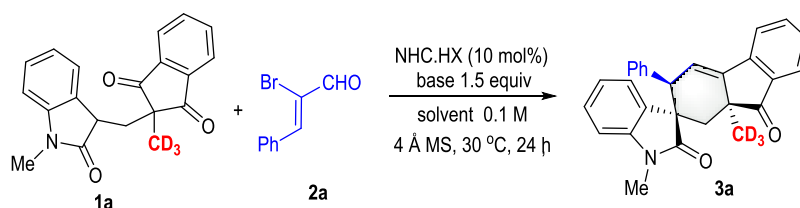
afford the desired product as a white solid.

b) General procedure for the synthesis of product 3. (3a as an example).



To an oven-dried screw-capped test tube equipped with a magnetic stirring bar the triazolium salt NHC **C** (4.2 mg, 10 mol %), NaOAc (12.0 mg, 0.15 mmol), anhydrous 4Å MS (100 mg), **2a** (0.12 mmol, 1.2 equiv) and **1a** (0.10 mmol, 1.0 equiv) were added. To this mixture was added anhydrous mesitylene (1.0 mL, 0.1M). The resultant reaction mixture was kept stirring at room temperature for 24 h. Then the reaction was added to 100 mg silica gel and was kept stirring at 70 °C for 10 h. When the reaction is complete, the crude residue was purified by flash column chromatography on silica gel using PE/EtOAc (3:1) as eluent to afford the desired product **3**.

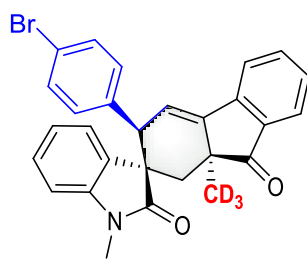
c) Experimental procedure for the scale-up reaction.



A dry 25 mL Schlenk tube equipped with a magnetic stirring bar was successively charged with **1a** (1.0 g, 3.1 mmol), NHC **C** (127.1 mg, 0.31 mmol), NaOAc (372 mg, 4.7 mmol), anhydrous 4Å MS (500 mg) and **2a** (3.72 mmol). To this mixture was added anhydrous mesitylene (8 mL). The resultant reaction mixture was kept stirring at room temperature for 24 h. Then the reaction was added to 3000 mg silica gel and was kept stirring at 70 °C for 10 h. When the reaction is complete, the crude residue was purified by flash column chromatography on silica gel using PE/EtOAc (3:1) to afford the **3a** as white solid (1230 mg, 97% yield, >20:1 dr and >99% ee).

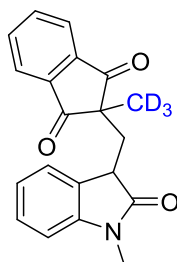
d) Stereochemistry determination **3h** via X-ray crystallographic analysis

Product **3h** was crystallized as a colorless crystal *via* vaporization of a hexane/ethyl acetate solution, and its absolute configuration was determined by *x*-ray structure analysis. CCDC 2027679 contains the supplementary crystallographic data that can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



III. Characterizations of products, reference

a) Characterizations of products

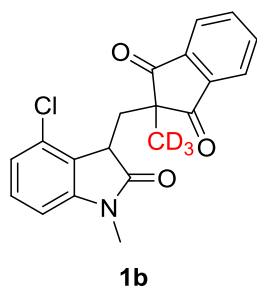


1a

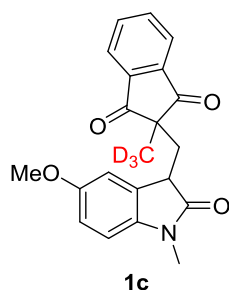
2-(Methyl-*d*₃)-2-((1-methyl-2-oxoindolin-3-yl)methyl)-1*H*-indene-1,3(2*H*)-dione

(1a): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.82 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.43-7.47 (m, 2H), 7.03-7.20 (m, 5H), 6.83 (d = 7.2, 1H), 6.43 (d, *J* = 3.6 Hz, 1H), 6.418 (d, *J* = 8 Hz, 1H), 4.04 (d, *J* = 3.2 Hz, 1H), 2.62 (s, 1H), 2.33 (dd, *J* = 14.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.4, 202.5, 176.6, 144.2, 131.5, 130.0, 140.4, 135.7, 135.1, 128.3, 128.0, 127.9, 124.7, 123.4, 123.1, 122.3, 107.8, 100.0, 77.4, 77.1, 76.8, 52.4, 42.0, 34.1, 26.1; ²H NMR

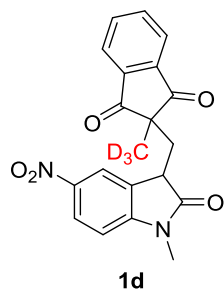
(61.4 MHz, CHCl₃) δ = 0.75 (s, 3D); HRMS (ESI) Calcd for C₂₀H₁₅D₃NO₃⁺ [M+H]⁺ 323.1470; Found: 323.1471.



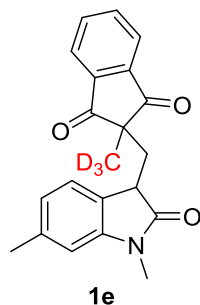
2-((4-Chloro-1-methyl-2-oxoindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1b): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.85-7.88 (m, 1H), 7.80-7.84 (m, 1H), 7.75-7.78 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 3.38-3.41 (m, 1H), 2.96 (s, 1H), 2.44-2.56 (m, 1H), 2.24 (t, *J* = 16.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 202.9, 201.6, 175.7, 145.7, 141.3, 140.5, 135.6, 135.0, 131.5, 129.7, 125.4, 123.3, 122.1, 123.0, 106.2, 77.4, 77.1, 76.8, 52.2, 42.5, 34.8, 26.2; ²H NMR (61.4 MHz, CHCl₃) δ = 1.18 (s, 3D); HRMS (ESI) Calcd for C₂₀H₁₄D₃ClNO₃⁺ [M+H]⁺ 357.1080; Found: 357.1082.



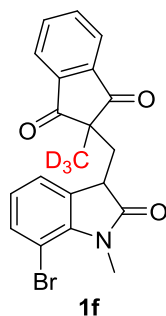
2-((5-methoxy-1-methyl-2-oxoindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1c): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.88-7.74 (m, 4H), 7.76-7.41 (m, 3H), 3.75 (s, 3H), 3.41 (dd, *J* = 16.8, 8.0 Hz, 1H), 2.95 (s, 3H), 2.48 (dd, *J* = 9.2, 12.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.3, 202.5, 176.3, 155.8, 141.6, 140.4, 135.1, 130.5, 123.1, 113.6, 111.4, 108.7, 77.5, 77.1, 76.8, 56.4, 43.1, 34.7, 27.0; ²H NMR (61.4 MHz, CHCl₃) δ = 1.14 (s, 3D); HRMS (ESI) Calcd for C₂₁H₁₇D₃NO₄⁺ [M+H]⁺ 353.1575; Found: 352.1571.



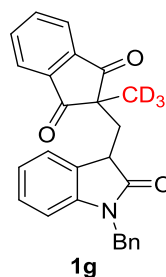
2-((Methyl-*d*₃)-2-((1-methyl-5-nitro-2-oxindolin-3-yl)methyl)-1*H*-indene-1,3(2*H*)-dione (1d): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 8.15 (d, *J* = 10.2 Hz, 1H), 8.07-8.02(m, 1H), 7.99 -7.90 (m, 2H), 7.89 - 7.78 (m, 2H), 6.72 (d, *J* = 8.0 Hz, 1H), 3.60 (dd, *J* =16.8, 8.0 Hz, 1H), 3.10 (s, 3H), 2.57- 2.43 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ= 202.9, 202.1, 176.8, 149.8, 141.4, 140.3, 136.1, 135.5, 128.9, 125.7, 123.7, 123.5, 121.8, 120.4, 117.9, 106.9, 77.5, 77.2, 76.3, 52.3, 41.6, 33.5, 26.7.; ²H NMR (61.4 MHz, CHCl₃) δ =1.42 (s, 3D); HRMS (ESI) Calcd for C₂₀H₁₃D₃N₂O₅⁺ [M+H]⁺ 368.1320; Found: 368.1320.



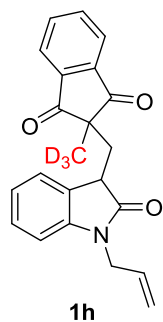
2-((1,6-Dimethyl-2-oxindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1e) : white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.85-7.88 (m, 1H), 7.80-7.84 (m, 1H), 7.75-7.78 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 3.39-3.41 (m, 1H), 2.96 (s, 1H), 2.21-2.55 (m, 1H), 2.24 (t, *J* = 16.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ= 203.3, 202.6 , 177.0, 144.3, 141.5, 140.4, 138.4, 135.2, 135.0, 124.7, 124.5, 123.4, 123.0, 122.8, 108.7, 77.4, 77.1, 76.8, 52.5, 42.0, 34.5, 26.0, 21.7; ²H NMR (61.4 MHz, CHCl₃) δ =1.14 (s, 3D); HRMS (ESI) Calcd for C₂₁H₁₇N₃DO₃⁺ [M+H]⁺ 337.1626; Found: 337.1630.



2-((7-Bromo-1-methyl-2-oxoindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1f): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.93-7.91 (m, 1H), 7.84-7.75 (m, 3H), 7.19 (d, *J* = 8 Hz, 1H), 7.07 (d, *J* = 8 Hz, 1H), 6.78 (t, *J* = 8 Hz, 1H), 3.46-3.42 (m, 1H), 3.34 (s, 3H), 2.55-2.43 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.0, 202.5, 176.8, 141.4, 141.3, 140.3, 137.7, 135.3, 134.0, 130.6, 124.1, 123.4, 123.4, 123.0, 102.1, 100.0, 77.4, 77.1, 76.8, 52.3, 42.0, 34.3, 29.7; ²H NMR (61.4 MHz, CHCl₃) δ = 1.19 (s, 3D); HRMS (ESI) Calcd for C₂₀H₁₄D₃NBrO₃⁺ [M+H]⁺ 401.0575; Found: 401.0570.

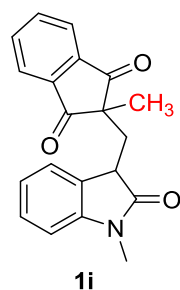


2-((1-Benzyl-2-oxoindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1g): white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.90-7.94 (m, 1H), 7.76-7.81 (m, 2H), 7.28 (d, *J* = 8 Hz, 2H), 7.18-7.23 (m, 4H), 7.02 (t, *J* = 4 Hz, 1H), 6.93 (t, *J* = 8 Hz, 1H), 6.48 (d, *J* = 8 Hz, 1H), 4.62-4.78 (m, 2H), 3.56-3.59 (m, 1H), 2.44-2.57 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.5, 202.2, 176.8, 143.2, 141.6, 140.4, 135.7, 135.1, 128.8, 128.3, 128.2, 127.6, 127.4, 124.5, 123.6, 123.4, 123.3, 122.4, 109.0, 77.4, 77.1, 76.8, 52.5, 43.7, 41.8, 34.4; ²H NMR (61.4 MHz, CHCl₃) δ = 1.47 (s, 3D); HRMS (ESI) Calcd for C₂₆H₁₉D₃O₃N⁺ [M+H]⁺ 399.1783; Found: 399.1781.



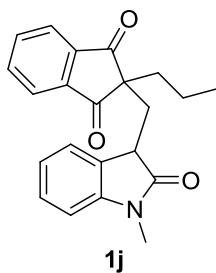
2-((1-Allyl-2-oxoindolin-3-yl)methyl)-2-(methyl-*d*₃)-1*H*-indene-1,3(2*H*)-dione (1h):

white solid. ¹H NMR (400 MHz, CDCl₃) δ = 7.92-7.82 (m, 2H), 7.80 -7.72 (m, 2H), 7.16 -7.07 (m, 2H), 6.93 (t, *J* = 8.0 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 3.42 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.98 (s, 3H), 2.56-2.36 (m, 2H), 1.87 (q, *J* = 8.0Hz, 2H). δ = 7.85-7.88 (m, 1H), 7.80-7.84 (m, 1H), 7.75-7.78 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 3.38-3.41 (m, 1H), 2.96 (s, 1H), 2.44-2.56 (m, 1H), 2.24 (t, *J* = 16.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃)δ = 203.6, 202.7, 144.2, 141.7, 135.6, 135.0, 128.3, 128.0, 124.8, 123.0, 122.6, 122.3, 106.6, 77.5, 77.2, 76.8, 56.9, 42.0, 33.6, 31.6, 26.1, 9.1. ²H NMR (61.4 MHz, CHCl₃) δ =1.51 (s, 3D); HRMS (ESI) Calcd for C₂₂H₁₇NO₃D₃⁺ [M+H]⁺ 349.1626; Found: 349.1629.



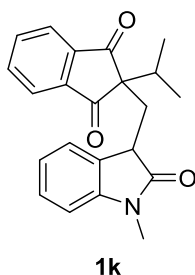
2-Methyl-2-((1-methyl-2-oxoindolin-3-yl)methyl)-1*H*-indene-1,3(2*H*)-dione (1i):

white solid. ¹H NMR (400 MHz, CDCl₃) δ = 8.19 (s, 1H), 7.75-7.83 (m, 3H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.44-7.53 (m, 3H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 4.15 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ= 203.3, 202.4, 176.6, 144.2, 141.6, 140.4, 135.7, 135.1, 128.3, 128.0, 124.7, 123.5, 123.1, 122.3, 77.4, 77.1, 76.8, 52.6, 42.0, 34.2, 26.1, 23.8; HRMS (ESI) Calcd for C₂₀H₁₈NO₃⁺ [M+H]⁺ 320.1281; Found: 320.1285.



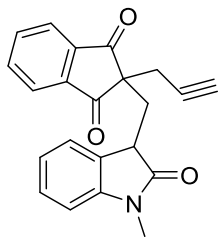
2-((1-Methyl-2-oxoindolin-3-yl)methyl)-2-propyl-1H-indene-1,3(2H)-dione (1j):

white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.85-7.89 (m, 2H), 7.75-7.77 (m, 2H), 7.08-7.15 (m, 2H), 6.91-6.95 (m, 1H), 6.53 (d, J = 8 Hz, 1H), 3.40-3.43 (m, 1H), 2.98 (s, 3H), 2.41-2.52 (m, 2H), 1.77-1.81 (m, 2H), 0.97-1.07 (m, 2H), 0.76 (d, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 203.5, 202.8, 176.6, 144.2, 142.8, 141.6, 135.0, 128.3, 128.0, 124.7, 123.0, 123.2, 122.6, 122.3, 107.8, 77.4, 77.1, 76.8, 56.8, 42.0, 40.6, 34.0, 26.1, 18.1, 14.4; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{22}\text{NO}_3^+$ $[\text{M}+\text{H}]^+$ 348.1594; Found: 348.1595.



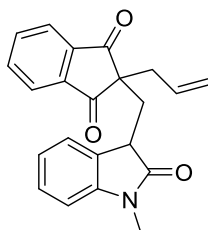
2-Isopropyl-2-((1-methyl-2-oxoindolin-3-yl)methyl)-1H-indene-1,3(2H)-dione

(1k): white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.83-7.88 (m, 2H), 7.71-7.77 (m, 2H), 7.08-7.15 (m, 2H), 6.91 (t, J = 8 Hz, 1H), 6.54 (d, J = 8 Hz, 1H), 3.38-3.41 (m, 1H), 2.99 (s, 3H), 2.47-2.58 (m, 2H), 2.13-2.02 (m, 1H), 1.68 (d, J = 4Hz, 1H), 0.97 (d, J = 8 Hz, 3H), 0.82 (d, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 203.4, 202.5, 176.4, 142.8, 141.6, 140.4, 135.8, 136.5, 135.0, 128.0, 124.9, 123.5, 123.2, 121.7, 111.6, 77.5, 77.1, 76.7, 52.5, 44.7, 42.0, 35.8, 19.8; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{22}\text{NO}_3^+$ $[\text{M}+\text{H}]^+$ 348.1594; Found: 348.1598.



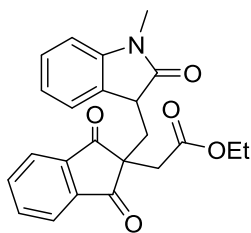
1l

2-((1-Methyl-2-oxoindolin-3-yl)methyl)-2-(prop-2-yn-1-yl)-1H-indene-1,3(2H)-dione (1l): white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.66-7.69 (m, 1H), 7.61-7.64 (m, 1H), 7.55-7.58 (m, 2H), 7.07-7.16 (m, 2H), 6.88-6.98 (m, 6H), 6.51 (d, J = 8 Hz, 1H), 3.45-3.48 (m, 1H), 3.11-3.19 (m, 1H), 2.99 (s, 3H), 2.54-2.66 (m, 2H), 2.13-2.02 (m, 1H), 1.68 (d, J = 4Hz, 1H), 0.97 (d, J = 8 Hz, 3H), 0.82 (d, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 201.2, 200.7, 176.3, 144.2, 142.7, 141.5, 135.8, 135.2, 128.5, 127.5, 124.8, 123.2, 122.8, 122.4, 107.8, 100.0, 77.9, 77.4, 77.1, 76.8, 72.2, 55.0, 41.9, 33.2, 26.6, 26.1; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{18}\text{NO}_3^+$ $[\text{M}+\text{H}]^+$ 344.1281; Found: 344.1287.



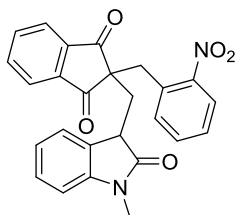
1m

2-Allyl-2-((1-methyl-2-oxoindolin-3-yl)methyl)-1H-indene-1,3(2H)-dione (1m): white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.88-7.84 (m, 2H), 7.78-7.74 (m, 2H), 7.09-7.15(m, 1H) ,6.93 (d, J =4 Hz, 1H) ,6.52 (d, J = 4 Hz, 1H) , 5.45 (d, J = 4 Hz, 1H), 5.01 (d, J = 4Hz, 1H), 4.91 (d, J = 4Hz, 1H), 5.14 (d, J = 8 Hz, 2H), 3.44-3.41 (m, 1H), 2.98 (s, 1H), 2.56 (d, J = 8 Hz, 1H), 2.51-2.54 (m, 2H), 2.39-2.45 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ = 203.4, 202.3, 176.4, 143.4, 141.6, 140.4, 135.7, 135.1,131.6, 128.2, 124.6, 123.5, 122.3, 117.6, 108.8, 77.1, 76.8, 77.2, 52.5, 42.3, 41.8, 34.3; HRMS (ESI) Calcd for $\text{C}_{22}\text{H}_{20}\text{NO}_3^+$ $[\text{M}+\text{H}]^+$ 346.1438; Found: 346.1437.



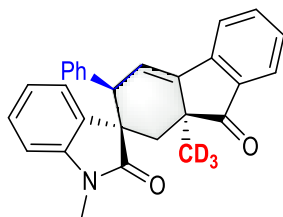
1n

Ethyl 2-(2-((1-methyl-2-oxoindolin-3-yl)methyl)-1,3-dioxo-2,3-dihydro-1H-inden-2-yl)acetate (1n): white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.92 (d, J = 4 Hz, 1H), 7.68-7.75 (m, 2H), 7.08-7.15 (m, 2H), 7.00 (t, J = 4Hz, 1H), 6.47 (d, J = 4 Hz, 1H), 3.85-3.91 (m, 2H), 3.50 (t, J = 4Hz, 1H), 3.15 (s, 2H), 2.98 (s, 3H), 2.34-2.46 (m, 2H), 1.01 (t, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 201.8, 201.3, 176.1, 170.2, 144.0, 142.2, 141.6, 135.5, 135.1, 128.5, 127.2, 124.8, 123.0, 122.8, 122.5, 107.8, 100.0, 77.9, 77.4, 77.1, 76.8, 61.2, 53.7, 41.9, 39.7, 34.2, 26.2, 13.8; HRMS (ESI) Calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_5^+$ $[\text{M}+\text{H}]^+$ 392.1492; Found: 392.1497.



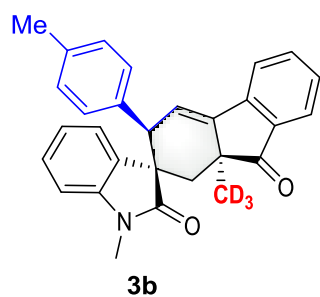
1o

2-((1-Methyl-2-oxoindolin-3-yl)methyl)-2-(2-nitrobenzyl)-1H-indene-1,3(2H)-dione (1o): white solid. ^1H NMR (400 MHz, CDCl_3) δ = 7.50-7.53 (m, 1H), 7.41-7.45 (m, 2H), 7.35-7.37 (m, 1H), 7.18-7.30 (m, 4H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 201.7, 201.0, 176.4, 149.7, 144.2, 142.1, 141.1, 135.7, 135.1, 133.8, 132.6, 128.5, 125.4, 124.8, 123.2, 122.8, 122.4, 107.8, 77.4, 77.1, 76.8, 56.8, 41.8, 39.2, 33.5, 26.1; HRMS (ESI) Calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_5^+$ $[\text{M}+\text{H}]^+$ 441.1445; Found: 441.14457.

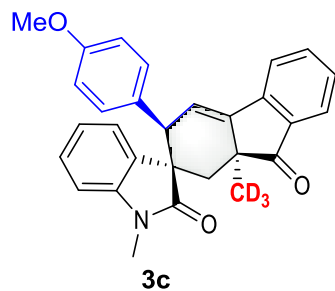


3a

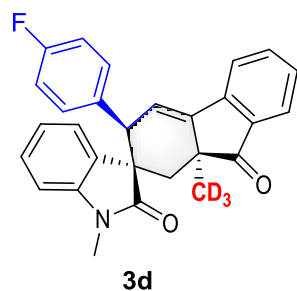
(2*R*,3*R*,9*aS*)-1'-Methyl-9*a*-(methyl-*d*₃)-3-phenyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(*IH*)-dione (3a): white solid, 38.8 mg, 95% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0, CHCl₃) = + 56.0. ¹H NMR (400 MHz, CDCl₃) δ = 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.64-7.68 (m, 1H), 7.42-7.47 (m, 2H), 7.03-7.20 (m, 5H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 4.04 (d, *J* = 4.0 Hz, 1H), 2.62 (s, 1H), 2.34 (dd, *J* = 12.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.4, 202.5, 176.7, 28.0, 124.7, 123.5, 123.1, 122.4, 111.2, 107.9, 77.5, 77.2, 76.8, 52.5, 42.1, 34.2, 26.1; ²H NMR (61.4 MHz, CHCl₃) δ = 1.14 (s, 3D); HRMS (ESI) Calcd for C₂₈H₂₁NO₂D₃⁺ [M+H]⁺ 409.1990; Found: 409.1904; >99% ee as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 23.5 min, *t*_r (minor) = 17.2 min.



(2*R*,3*R*,9*aS*)-1'-Methyl-9*a*-(methyl-*d*₃)-3-(*p*-tolyl)-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(*IH*)-dione (3b): white solid, 31 mg, 90% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0, CHCl₃) = + 73.1. ¹H NMR (400 MHz, CDCl₃) δ = 7.81 (d, *J* = 4 Hz, 1H), 7.73 (d, *J* = 8 Hz, 1H), 7.63-7.68 (m, 1H), 7.42-7.46 (m, 2H), 7.11-7.20 (m, 2H), 6.85 (d, *J* = 8 Hz, 2H), 6.72 (d, *J* = 8 Hz, 2H), 6.61 (d, *J* = 4 Hz, 1H), 6.44 (d, *J* = 8 Hz, 2H), 4.01 (d, *J* = 4 Hz, 1H), 2.65 (s, 3H), 2.32 (dd, *J* = 12.0 Hz, 2H), 2.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.2, 178.5, 147.0, 143.8, 143.4, 136.6, 135.5, 134.0, 135.2, 134.1, 134.0, 129.1, 128.8, 128.2, 128.0, 124.5, 123.0, 122.6, 122.4, 121.8, 107.6, 77.4, 77.1, 76.8, 56.7, 49.4, 48.8, 37.4, 25.6, 21.1; ²H NMR (61.4 MHz, CHCl₃) δ = 1.79 (s, 3D); HRMS (ESI) Calcd for C₂₉H₂₃N₂OD₃⁺ [M+H]⁺ 423.2146; Found: 423.2149; >99% ee as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 36.5 min, *t*_r (minor) = 18.3 min.

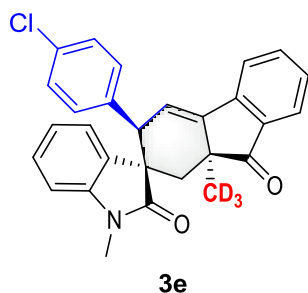


(2R,3R,9aS)-3-(4-Methoxyphenyl)-1'-methyl-9a-(methyl-*d*₃)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3c): white solid, 37 mg, 94% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 87.5. ¹H NMR (400 MHz, CDCl₃) δ = 7.81 (d, *J* = 4 Hz, 1H), 7.73 (d, *J* = 8 Hz, 1H), 7.64-7.66 (m, 1H), 7.42-7.45 (m, 2H), 7.13-7.18 (m, 2H), 6.74 (d, *J* = 8 Hz, 2H), 6.59 (d, *J* = 4 Hz, 3H), 6.44 (d, *J* = 8 Hz, 1H), 4.01 (d, *J* = 4 Hz, 1H), 3.70 (s, 3H), 2.66 (s, 3H), 2.31 (dd, *J* = 12.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.3, 178.6, 158.6, 147.0, 143.8, 143.4, 135.2, 134.2, 134.0, 130.6, 129.9, 129.1, 128.1, 124.5, 123.0, 122.6, 122.5, 123.0, 121.8, 112.8, 107.7, 100, 77.4, 77.1, 76.8, 56.7, 55.2, 49.0, 48.7, 37.4, 25.6; ²H NMR (61.4 MHz, CHCl₃) δ = 1.78 (s, 3D); HRMS (ESI) Calcd for C₂₉H₂₃NO₃D₃⁺ [M+H]⁺ 439.2096; Found: 439.2098; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 37.7 min, *t*_r (minor) = 22.8 min.

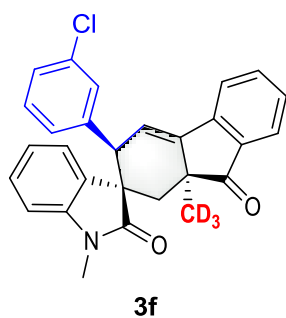


(2R,3R,9aS)-3-(4-Fluorophenyl)-1'-methyl-9a-(methyl-*d*₃)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3d): white solid, 38.3 mg, 90% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = -32.5. ¹H NMR (400 MHz, CDCl₃) δ = 7.85-7.88 (m, 1H), 7.80-7.84 (m, 1H), 7.75-7.78 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 3.38-3.41 (m, 1H), 2.96 (s, 1H), 2.44-2.56 (m, 1H), 2.24 (t, *J* = 16.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.0, 178.4, 163.2, 160.8, 146.9,

144.2, 143.3, 135.3, 134.4, 134.0, 130.5, 129.3, 128.3, 124.6, 123.1, 122.8, 121.9, 114.4, 114.2, 107.8, 77.3, 77.2, 76.8, 56.6, 49.1, 48.8, 37.3, 25.6. ^2H NMR (61.4 MHz, CHCl_3) δ = 1.18 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{NO}_2\text{FD}_3^+$ $[\text{M}+\text{H}]^+$ 427.1896; Found: 427.1899; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 30.8 min, t_r (minor) = 17.7 min.

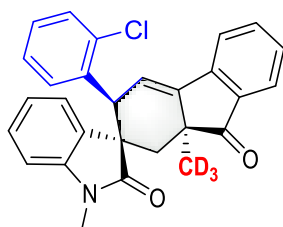


(2R,3R,9aS)-3-(4-Chlorophenyl)-1'-methyl-9a-(methyl- d_3)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3e): white solid, 38 mg, 91% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl_3) = + 103.1. ^1H NMR (400 MHz, CDCl_3) δ = 7.86-7.64 (m, 4H), 7.45(t, J = 7.6 Hz, 2H), 6.97-7.22 (m, 5H), 6.61-6.78 (m, 3H), 6.54 (d, J = 3.6 Hz, 1H), 6.47 (dd, J = 2.8, 8.0 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ = 206.9, 178.2, 146.8, 144.3, 143.3, 137.2, 135.3, 134.0, 133.7, 133.0, 130.3, 130.1, 129.3, 128.4, 127.7, 124.6, 123.0, 122.8, 121.9, 121.3, 107.9, 77.1, 56.5, 49.2, 48.8, 37.4, 25.6, 14.2; ^2H NMR (61.4 MHz, CHCl_3) δ = 1.18 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{NO}_2\text{ClD}_3^+$ $[\text{M}+\text{H}]^+$ 443.1600; Found: 443.1605; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 38.3 min, t_r (minor) = 19.1 min.



(2R,3R,9aS)-3-(3-Chlorophenyl)-1'-methyl-9a-(methyl- d_3)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3f): white solid, 39 mg, 90%

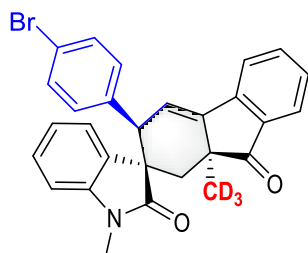
yield. $[\alpha]_D^{25}$ (c 1.0, CHCl_3) = + 93.4. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.81-7.83 (m, 1H), 7.74-7.77 (m, 1H), 7.64-7.69 (m, 1H), 7.43-7.47 (m, 2H), 7.14-7.21 (m, 2H), 6.72-6.82 (m, 4H), 6.45-6.48 (m, 1H), 6.57 (d, J = 4.0 Hz, 1H), 6.47 (d, J = 4.0 Hz, 1H), 4.04 (d, J = 4.0 Hz, 1H), 2.67 (d, J = 8.0 Hz, 2H), 2.33 (dd, J = 12.0 Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 178.1, 146.8, 144.4, 143.3, 140.7, 140.4, 135.3, 134.0, 133.3, 129.3, 129.0, 128.6, 128.4, 127.2, 124.6, 123.0, 122.8, 121.9, 120.9, 107.8, 77.5, 77.1, 76.8, 56.4, 49.6, 48.8, 37.2, 25.5; $^2\text{H NMR}$ (61.4 MHz, CHCl_3) δ = 1.47 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{NO}_2\text{ClD}_3^+$ $[\text{M}+\text{H}]^+$ 443.1600; Found: 443.1603; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 24.6 min, t_r (minor) = 17.4 min.



3g

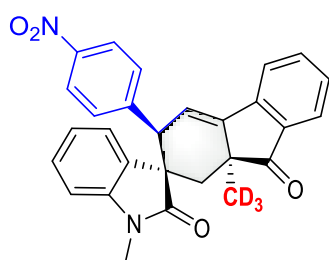
(2*R*,3*S*,9*aS*)-3-(2-Chlorophenyl)-1'-methyl-9*a*-(methyl-*d*₃)-3,9*a*-

dihydrospiro[fluorene-2,3'-indoline]-2,9(*IH*)-dione (3g): white solid, 39 mg, 92% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl_3) = + 63.3. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.81 (d, J = 4 Hz, 1H), 7.52-7.70 (m, 2H), 7.48 (d, J = 8 Hz, 2H), 7.33 (d, J = 4 Hz, 1H), 7.05-7.15 (m, 5H), 6.44 (d, J = 4 Hz, 1H), 6.42 (d, J = 8 Hz, 1H), 4.89 (d, J = 4 Hz, 1H), 2.81 (s, 3H), 2.46 (dd, J = 12 Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ = 207.2, 178.5, 147.0, 144.2, 142.7, 137.6, 135.2, 134.2, 133.9, 131.9, 129.9, 129.0, 128.9, 128.4, 128.2, 126.5, 124.6, 122.3, 121.8, 121.8, 107.2, 77.4, 77.1, 76.8, 56.0, 48.4, 44.2, 38.2, 25.7; $^2\text{H NMR}$ (61.4 MHz, CHCl_3) δ = 1.79 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{NO}_2\text{D}_3\text{S}^+$ $[\text{M}+\text{H}]^+$ 443.1600; Found: 443.1601; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 24.3 min, t_r (minor) = 28.4 min.



3h

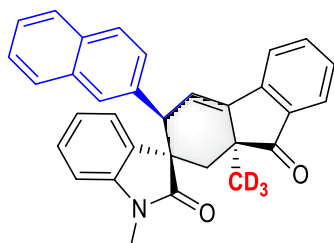
(2*R*,3*R*,9*aS*)-3-(4-Bromophenyl)-1'-methyl-9*a*-(methyl-*d*₃)-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(*1H*)-dione (3h): white solid, 34 mg, 90% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = - 63.9. ¹H NMR (400 MHz, CDCl₃) δ = 7.89-7.93 (m, 2H), 7.65-7.84 (m, 3H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.15-7.24 (m, 2H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.46-6.53 (m, 2H), 6.38-6.49 (m, 3H), 4.17 (d, *J* = 4.0 Hz, 1H), 2.66 (d, *J* = 4.0 Hz, 3H), 2.31 (dd, *J* = 12.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 206.9, 178.2, 146.8, 144.3, 143.3, 137.7, 135.3, 134.0, 133.6, 131.1, 130.7, 130.6, 129.3, 128.4, 124.6, 123.0, 122.9, 121.9, 121.2, 107.9, 77.4, 77.1, 76.8, 56.4, 49.2, 48.8, 37.4, 25.7; ²H NMR (61.4 MHz, CHCl₃) δ = 1.18 (s, 3D); HRMS (ESI) Calcd for C₂₈H₂₀NO₂D₃Br⁺ [M+H]⁺ 487.1095; Found: 487.1090; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 42.1 min, *t*_r (minor) = 21.2 min.



3i

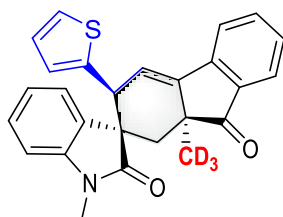
(2*R*,3*R*,9*aS*)-1'-Methyl-9*a*-(methyl-*d*₃)-3-(4-nitrophenyl)-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(*1H*)-dione (3i): white solid, 35 mg, 91% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 56.1. ¹H NMR (400 MHz, CDCl₃) δ = 7.89-7.93 (m, 2H), 7.65-7.84 (m, 3H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.15-7.24 (m, 2H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.46-6.53 (m, 2H), 6.38-6.49 (m, 3H), 4.17 (d, *J* = 4.0 Hz, 1H), 2.66 (d, *J* = 4.0 Hz, 3H), 2.29-3.41 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 206.5, 177.8, 147.0, 146.5, 143.3, 135.4, 134.0, 133.6, 133.0, 130.0, 129.5, 128.7, 124.6, 123.0, 122.6,

121.9, 119.7, 108.0, 100.0, 77.4, 77.1, 76.8, 56.3, 49.5, 48.8, 37.5, 25.7; ^2H NMR (61.4 MHz, CHCl_3) δ = 1.16 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{ClF}_6\text{N}_2\text{O}_4\text{D}_3^+$ $[\text{M}+\text{H}]^+$ 454.1841; Found: 454.1841; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 68.8 min, t_r (minor) = 41.0 min.



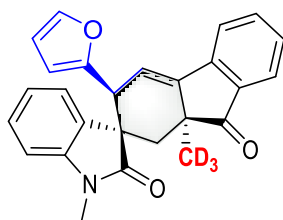
3j

(2*R*,3*R*,9*aS*)-1'-Methyl-9*a*-(methyl-*d*₃)-3-(naphthalen-2-yl)-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (3j): white solid, 43 mg, 97% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0, CHCl_3) = - 56.9. ^1H NMR (400 MHz, CDCl_3) δ = 7.77-7.85 (m, 2H), 7.66-7.72 (m, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.52(d, J = 8.0 Hz, 2H), 7.39 (d, J = 4.0 Hz, 1H), 7.30 (s, 1H), 7.13-7.18 (m, 2H), 6.98 (d, J = 8.0 Hz, 1H), 6.72 (d, J = 4.0 Hz, 1H), 6.29 (d, J = 8.0 Hz, 1H), 4.22 (d, J = 4.0 Hz, 1H), 2.51 (s, 3H), 2.38 (dd, J = 12.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ = 207.2, 178.5,144.7, 144.1, 143.3, 136.2, 135.3, 134.0, 133.9, 132.9, 132.4, 129.2, 128.2, 127.9, 127.4, 127.2, 126.9, 125.9, 125.8, 124.6, 123.1, 122.5, 122.0, 107.7, 77.1, 56.6, 50.0, 48.9, 37.5, 29.8, 25.5; ^2H NMR (61.4 MHz, CHCl_3) δ = 1.17(s, 3D); HRMS (ESI) Calcd for $\text{C}_{32}\text{H}_{23}\text{NO}_2\text{D}_3^+$ $[\text{M}+\text{H}]^+$ 459.2146; Found: 459.2145; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 28.1 min, t_r (minor) = 21.0 min.



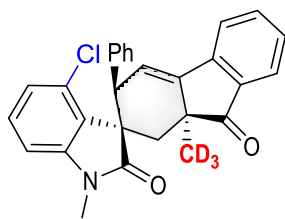
3k

(2*R*,3*S*,9*aS*)-1'-Methyl-9a-(methyl-*d*₃)-3-(thiophen-2-yl)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(*1H*)-dione (3k): white solid, 37 mg, 92% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 37.8. ¹H NMR (400 MHz, CDCl₃) δ = 7.82 (d, *J* = 4 Hz, 1H), 7.79-7.71(m, 1H), 7.63-7.68 (m, 1H), 7.41-7.44 (m, 2H), 6.85 (d, *J* = 4 Hz, 1H), 6.80 (d, *J* = 4 Hz, 1H), 6.75 (d, *J* = 4 Hz, 1H), 6.72 (d, *J* = 4 Hz, 1H), 6.63 (d, *J* = 4 Hz, 1H), 6.54 (d, *J* = 8 Hz, 2H), 4.38 (d, *J* = 4 Hz, 1H), 2.76 (s, 3H), 2.32 (dd, *J* = 12.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ =178.4, 146.7, 144.1, 143.9, 141.3, 135.3, 134.0, 129.3, 128.4, 126.2, 125.9, 124.5, 124.2, 123.0, 122.8, 122.3, 122.0, 107.7, 100.0, 77.4, 77.1, 76.8, 56.6, 48.6, 44.9, 37.7, 25.8; ²H NMR (61.4 MHz, CHCl₃) δ = 1.79 (s, 3D); HRMS (ESI) Calcd for C₂₆H₁₉NO₂D₃S⁺ [M+H]⁺ 415.1554; Found: 415.1550; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) =28.0 min, *t*_r (minor) = 19.6 min.



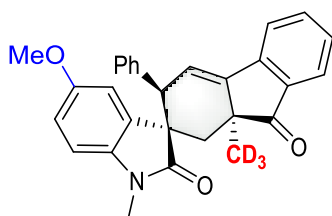
3l

(2*R*,3*S*,9*aS*)-3-(Furan-2-yl)-1'-methyl-9a-(methyl-*d*₃)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(*1H*)-dione (3l): white solid, 38 mg, 90% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 79.2. ¹H NMR (400 MHz, CDCl₃) δ = 7.81-7.74 (m, 2H), 6.64 (d, *J* = 4 Hz, 1H), 7.46-7.38 (m, 2H), 7.24 (d, *J* = 4 Hz, 1H), 7.10 (d, *J* = 4 Hz, 2H), 6.60 (m, 2H), 6.1 (d, *J* = 8 Hz, 1H), 5.72 (d, *J* = 8 Hz, 1H), 4.24 (m, 1H), 2.85 (s, 3H), 2.30 (dd, *J* = 12.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ =178.5, 152.8, 146.7, 144.1, 143.6, 141.7, 135.3, 129.3, 134.0, 129.3, 128.3, 124.5, 122.9, 122.8, 122.0, 119.5, 110.2, 107.6, 107.1, 77.5, 77.1, 76.8, 55.2, 48.7, 43.8, 37.7, 25.9; ²H NMR (61.4 MHz, CHCl₃) δ = 1.75 (s, 3D); HRMS (ESI) Calcd for C₂₆H₁₉NO₃D₃⁺ [M+H]⁺ 399.1783; Found: 399.1780; >99% *ee* as determined by HPLC (Chiralcel IC, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 42.4 min, *t*_r (minor) = 26.6 min.



3m

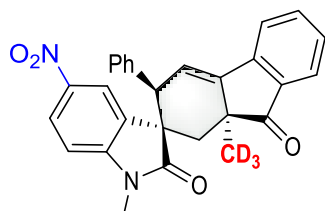
(2R,3R,9aS)-4'-Chloro-1'-methyl-9a-(methyl-*d*₃)-3-phenyl-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3m): white solid, 40 mg, 95% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 63.4. ¹H NMR (400 MHz, CDCl₃) δ = 7.80 (d, *J* = 4 Hz, 1H), 7.77 (d, *J* = 4 Hz, 1H), 7.66 (t, *J* = 4 Hz, 1H), 7.43 (t, *J* = 4 Hz, 1H), 6.97-7.07 (m, 7H), 6.50 (d, *J* = 4 Hz, 1H), 6.26 (d, *J* = 4 Hz, 1H), 4.74 (d, *J* = 4 Hz, 1H), 2.89 (d, *J* = 4 Hz, 1H), 2.74 (s, 3H), 2.37 (d, *J* = 4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.3, 177.7, 147.2, 144.9, 143.9, 139.4, 135.0, 133.6, 130.1, 129.5, 128.9, 128.4, 127.6, 127.2, 124.5, 123.6, 121.8, 120.6, 106.1, 77.4, 77.1, 76.8, 56.7, 48.9, 44.4, 33.0, 29.8, 25.1; ²H NMR (61.4 MHz, CHCl₃) δ = 1.96 (s, 3D); HRMS (ESI) Calcd for C₂₈H₂₀NO₂D₃Cl⁺ [M+H]⁺ 443.1600; Found: 443.1600; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 14.6 min, *t*_r (minor) = 22.7 min.



3n

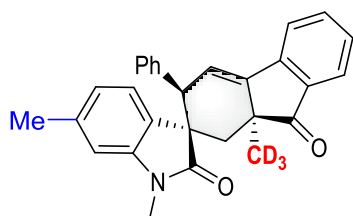
(2R,3R,9aS)-5'-Methoxy-1'-methyl-9a-(methyl-*d*₃)-3-phenyl-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3n): white solid, 40 mg, 95% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 78.0. ¹H NMR (400 MHz, CDCl₃) δ = 7.62-7.82 (m, 3H), 7.40-7.46 (m, 2H), 7.23-7.27 (m, 1H), 7.01-7.09 (m, 3H), 6.79-6.83 (m, 1H), 6.38-6.49 (m, 3H), 4.88 (d, *J* = 8.0 Hz, 1H), 3.38 (d, *J* = 4.0 Hz, 3H), 2.74 (d, *J* = 4.0 Hz, 3H), 2.27-2.44 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 178.9, 156.5, 147.3, 143.7, 143.0, 135.1, 133.8, 133.2, 129.3, 128.8, 128.1, 127.6, 124.5, 122.9, 121.7,

121.6, 120.1, 109.4, 106.9, 77.4, 77.1, 76.8, 56.2, 54.8, 49.1, 40.4, 37.9, 27.3; ^2H NMR (61.4 MHz, CHCl_3) δ = 1.14 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_3\text{D}_3^+$ $[\text{M}+\text{H}]^+$ 439.2096; Found: 439.2098; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 64.3 min, t_r (minor) = 21.2 min.



3o

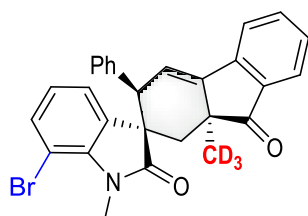
(2*R*,3*R*,9*aS*)-1'-Methyl-9*a*-(methyl-*d*₃)-5'-nitro-3-phenyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (3o): white solid, 39 mg, 94% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0, CHCl_3) = + 106.1. ^1H NMR (400 MHz, CDCl_3) δ = 8.34 (s, 1H), 8.29 (d, J = 4 Hz, 1H), 7.83 (d, J = 4 Hz, 1H), 7.74 (d, J = 4 Hz, 1H), 7.68 (t, J = 4 Hz, 1H), 7.48 (t, J = 4 Hz, 1H), 7.05-7.14 (m, 3H), 6.82 (d, J = 8 Hz, 2H), 6.51 (dd, J = 8 Hz, 2H), 4.74 (d, J = 4 Hz, 1H), 4.08 (d, J = 4 Hz, 1H), 2.72 (s, 3H), 2.34 (dd, J = 12 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ = 207.3, 177.7, 147.2, 144.9, 143.9, 139.4, 135.0, 133.6, 130.1, 129.5, 128.9, 128.4, 127.6, 127.2, 126.5, 124.5, 123.6, 121.8, 120.6, 106.1, 77.4, 77.1, 76.8, 56.7, 48.9, 44.4, 33.0, 25.7; ^2H NMR (61.4 MHz, CHCl_3) δ = 1.96 (s, 3D); HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_4\text{D}_3^+$ $[\text{M}+\text{H}]^+$ 454.1841; Found: 454.1840; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 72.9 min, t_r (minor) = 38.2 min.



3p

(2*R*,3*R*,9*aS*)-1',6'-Dimethyl-9*a*-(methyl-*d*₃)-3-phenyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (3p): white solid, 43 mg, 96% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0,

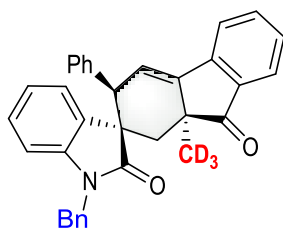
CHCl₃) = +119.1. ¹H NMR (400 MHz, CDCl₃) δ=8.34 (s, 1H), 8.29 (d, *J* = 4 Hz, 1H), 7.83 (d, *J* = 4 Hz, 1H), 7.74 (d, *J* = 4 Hz, 1H), 7.68 (t, *J* = 4 Hz, 1H), 7.48 (t, *J* = 4 Hz, 1H), 7.05-7.14 (m, 3H), 1.54 (s, 3H), 6.49 (d, *J* = 4 Hz, 1H), 4.08 (d, *J* = 4 Hz, 1H), 2.72 (s, 3H), 2.36 (dd, *J* = 12 Hz, 2H), 1.59 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ= 207.1, 178.4, 148.2, 143.2, 142.9, 139.4, 135.0, 133.6, 130.1, 129.5, 128.9, 128.4, 127.6, 127.2, 126.5, 124.5, 123.6, 121.8, 120.6, 106.1, 77.4, 77.1, 76.8, 56.3, 53.5, 49.8, 36.5, 31.9, 25.5, 9.9; ²H NMR (61.4 MHz, CHCl₃) δ= 1.79 (s, 3D); HRMS (ESI) Calcd for C₂₉H₂₃NO₂D₃⁺ [M+H]⁺ 423.2146; Found: 423.2150; >99% *ee* as determined by HPLC (Chiralcel ADH, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 25.5 min, *t*_r (minor) = 17.6 min.



3q

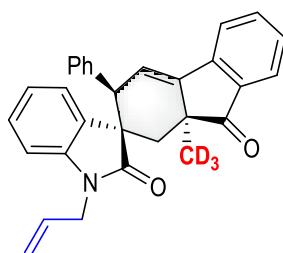
(2*R*,3*R*,9*aS*)-7'-Bromo-1'-methyl-9*a*-(methyl-*d*₃)-3-phenyl-3,9*a*-

dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (3q): white solid, 41 mg, 97% yield. [α]_D²⁵ (c 1.0, CHCl₃) = + 99.3. ¹H NMR (400 MHz, CDCl₃) δ = 7.82 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.30 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 2H), 6.98 (t, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.59 (d, *J* = 4.0 Hz, 1H), 3.98 (d, *J* = 4.0 Hz, 1H), 2.98 (s, 3H), 2.32 (dd, *J* = 4.0 Hz, 12 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃)δ = 135.5, 135.4, 134.8, 134.1, 129.4, 129.1, 128.3, 127.8, 127.1, 124.6, 123.5, 122.5, 122.2, 122.0, 109.6, 101.5, 77.5, 77.2, 76.8, 62.2, 56.2, 54.5, 50.1, 49.4, 38.2, 29.9, 19.1, 18.4. ²H NMR (61.4 MHz, CHCl₃) δ= 1.85(s, 3D); HRMS (ESI) Calcd for C₂₈H₂₀NBrO₂D₃⁺ [M+H]⁺ 487.1095; Found: 487.1099; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 23.5min, *t*_r (minor) = 16.5 min.



3r

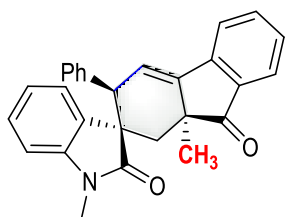
(2R,3R,9aS)-1'-benzyl-9a-(methyl-*d*₃)-3-phenyl-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3r): white solid, 38 mg, 94% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 123.1. ¹H NMR (400 MHz, CDCl₃) δ = 7.82(dd, *J* = 8Hz, 2H), 7.70 (d, *J* = 4Hz, 1H), 7.65(d, *J* = 4Hz, 1H), 7.52(d, *J* = 4Hz, 1H), 7.26-7.48 (m, 8H), 7.12 (d, *J* = 8 Hz, 2H), 6.73 (d, *J* = 4 Hz, 1H), 6.54 (d, *J* = 8Hz, 2H), 6.31 (d, *J* = 4 Hz, 1H), 4.36 (dd, *J* = 8 Hz, 2H), 4.20 (s, 1H), 2.40 (dd, *J* = 8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.1, 178.8, 143.8, 142.6, 138.9, 135.4, 135.3, 134.2, 134.0, 129.5, 129.2, 128.2, 128.1, 128.0, 127.2, 126.0, 124.6, 123.3, 122.8, 125.5, 121.9, 109.1, 77.4, 77.4, 77.1, 76.8, 56.7, 48.8, 48.7, 43.6, 39.0; ²H NMR (61.4 MHz, CHCl₃) δ = 1.46 (s, 3D); HRMS (ESI) Calcd for C₃₄H₂₅NO₂D₃⁺ [M+H]⁺ 485.2303; Found: 485.2300; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 25.7min, *t*_r (minor) = 30.1 min.



3s

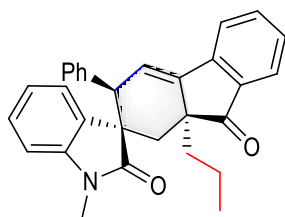
(2R,3R,9aS)-1'-Allyl-9a-(methyl-*d*₃)-3-phenyl-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1H)-dione (3s): white solid, 31 mg, 87% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 56.2. ¹H NMR (400 MHz, CDCl₃) δ = 7.81(d, *J* = 4Hz, 1H), 7.75(d, *J* = 4Hz, 1H), 7.64 (t, *J* = 4Hz, 1H), 7.43-7.51 (m, 2H), 7.05-7.16 (m, 5H), 6.89(d, *J* = 8Hz, 2H), 6.67(d, *J* = 4Hz, 1H), 6.47(d, *J* = 4Hz, 1H), 5.00-5.14 (m, 1H), 4.90 (d, *J* = 4 Hz, 1H), 4.88 (d, *J* = 4 Hz, 1H), 4.61(d, *J* = 4Hz, 1H), 4.11 (d, *J* = 4 Hz, 1H), 3.99 (d, *J* = 4 Hz,

1H), 3.67-3.72 (m, 1H), 2.33 (dd, $J = 12$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) $\delta = 207.2, 178.2, 147.0, 143.9, 142.7, 138.7, 135.3, 134.1, 134.0, 131.3, 129.3, 129.2, 128.0, 127.8, 127.1, 124.6, 123.3, 122.7, 122.3, 121.9, 117.2, 108.8, 77.5, 77.1, 76.8, 56.6, 49.2, 48.7, 42.1, 38.2$; ^2H NMR (61.4 MHz, CHCl_3) $\delta = 1.50$ (s, 3D); HRMS (ESI) Calcd for $\text{C}_{30}\text{H}_{23}\text{NO}_2\text{D}_3^+$ $[\text{M}+\text{H}]^+$ 435.2146; Found: 435.2150; 96% *ee* as determined by HPLC (Chiralcel IA, 97:3 hexanes/*i*-PrOH, 0.7 mL/min), t_r (major) = 62.5 min, t_r (minor) = 74.5 min.



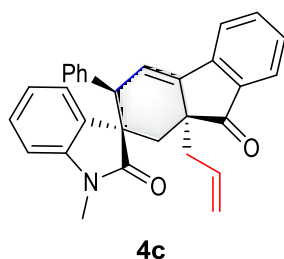
4a

(2*R*,3*R*,9*aS*)-1',9*a*-Dimethyl-3-phenyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (4a): white solid, 39 mg, 96% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl_3) = + 43.4. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.82$ (d, $J = 8.6$ Hz, 1H), 7.75 (d, $J = 6.9$ Hz, 1H), 7.70 - 7.63 (m, 1H), 7.51 - 7.42 (m, 2H), 7.21 - 7.02 (m, 5H), 6.83 (d, $J = 7.1$ Hz, 2H), 6.63 (d, $J = 3.6$ Hz, 1H), 6.42 (d, $J = 7.7$ Hz, 1H), 4.05 (d, $J = 3.6$ Hz, 1H), 2.62 (s, 3H), 2.34 (dd, $J = 14.4$ Hz, 2H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) $\delta = 207.2, 178.4, 147.0, 145.2, 144.0, 143.4, 138.5, 135.3, 134.0, 131.6, 129.2, 129.0, 128.2, 127.5, 127.1, 126.6, 124.6, 123.1, 122.6, 122.1, 121.9, 107.6, 77.5, 77.1, 76.8, 56.7, 49.9, 49.0, 37.4, 25.5, 24.8$; HRMS (ESI) Calcd for $\text{C}_{28}\text{H}_{24}\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 406.1802; Found: 406.1800; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 21.0 min, t_r (minor) = 11.3 min.

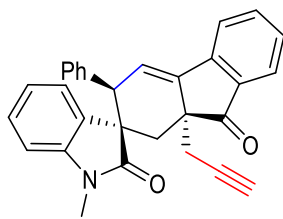


4b

(2*R*,3*R*,9*aS*)-1'-Methyl-3-phenyl-9*a*-propyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (4b): white solid, 34 mg, 87% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = -63.5. ¹H NMR (400 MHz, CDCl₃) δ = 7.73-7.80 (d, *J* = 8 Hz, 2H) 7.66 (d, *J* = 4 Hz, 1H), 7.38-7.45 (m, 2H), 7.03-7.19 (m, 5H), 6.82-6.86 (m, 2H), 6.62 (s, 1H), 6.40 (d, *J* = 4 Hz, 1H), 4.07 (d, *J* = 4 Hz, 1H), 2.63 (s, 3H), 2.36 (s, 3H), 1.99-2.13 (m, 2H), 1.20-1.35 (m, 2H), 0.91 (d, *J* = 4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 207.2, 178.4, 148.0, 143.1, 138.7, 135.2, 135.1, 133.7, 128.9, 128.1, 127.1, 123.9, 123.0, 122.5, 122.3, 121.4, 107.6, 77.5, 77.2, 76.8, 56.4, 53.2, 49.8, 41.4, 36.7, 25.5, 18.9, 14.7; HRMS (ESI) Calcd for C₃₀H₂₈NO₂⁺ [M+H]⁺ 434.2115; Found: 434.2110; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 1.0 mL/min), *t*_r (major) = 31.4 min, *t*_r (minor) = 40.9 min.

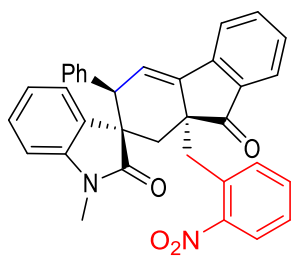


(2*R*,3*R*,9*aS*)-9*a*-Allyl-1'-methyl-3-phenyl-3,9*a*-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (4c): white solid, 35 mg, 96% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 66.4. ¹H NMR (400 MHz, CDCl₃) δ = 7.76 (dd, *J*₁ = 22.4 Hz, *J*₂ = 7.6 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.40-7.45 (m, 2H), 7.01-7.16 (m, 5H), 6.83 (d, *J* = 6.8 Hz, 2H), 6.40 (d, *J* = 3.2 Hz, 1H), 6.39 (d, *J* = 8.4 Hz, 1H), 5.71-5.81 (m, 1H), 5.19 (d, *J* = 15.2 Hz, 1H), 4.02 (d, *J* = 3.2 Hz, 1H), 2.66 (s, 5H), 2.41 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 206.0, 178.3, 147.7, 143.3, 142.4, 138.9, 135.1, 134.5, 133.4, 129.0, 128.9, 127.7, 127.5, 127.0, 124.2, 122.9, 122.7, 122.4, 121.5, 119.3, 107.5, 77.4, 77.1, 76.8, 55.8, 53.2, 50.1, 43.6, 35.3, 25.5; HRMS (ESI) Calcd for C₃₀H₂₆NO₂⁺ [M+H]⁺ 432.1958; Found: 432.1959; >99% *ee* as determined by HPLC (Chiralcel IC, 97:3 hexanes/*i*-PrOH, 0.8 mL/min), *t*_r (major) = 42.3 min, *t*_r (minor) = 35.8 min.



4d

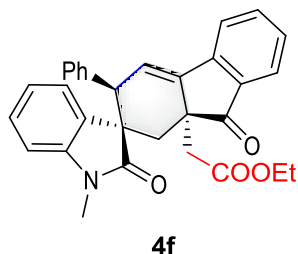
(2*R*,3*R*,9*aS*)-1'-Methyl-3-phenyl-9a-(prop-2-yn-1-yl)-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (4d): white solid, 35 mg, 97% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 82.4. ¹H NMR (400 MHz, CDCl₃) δ = 7.78 (dd, *J* = 24.0, 8.0 Hz, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.45 (q, *J* = 8.0 Hz, 2H), 7.18 -6.97 (m, 5H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 4.0 Hz, 1H), 6.40 (d, *J* = 4.0 Hz, 1H), 4.19 (d, *J* = 4.0 Hz, 1H), 2.80 (s, 2H), 2.67 (s, 3H), 2.61 (s, 1H), 2.50 (d, *J* = 12.0 Hz, 1H), 2.07 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ = 204.4, 178.2, 147.7, 143.2, 141.6, 138.8, 135.4, 133.7, 132.9, 128.8, 128.2, 127.5, 127.1, 124.5, 123.9, 123.0, 122.5, 121.7, 107.6, 80.3, 77.5, 77.2, 76.8, 71.4, 55.4, 52.2, 50.0, 34.8, 29.2, 25.5. HRMS (ESI) Calcd for C₃₀H₂₄NO₂⁺ [M+H]⁺ 430.1802; Found: 430.1800; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 1.0 mL/min), *t_r* (major) = 23.3 min, *t_r* (minor) = 27.2 min.



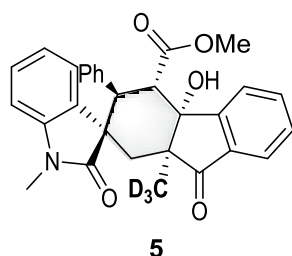
4e

(2*R*,3*R*,9*aS*)-1'-methyl-9a-(2-nitrobenzyl)-3-phenyl-3,9a-dihydrospiro[fluorene-2,3'-indoline]-2',9(1*H*)-dione (4e): white solid, 40 mg, 96% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 103.8. ¹H NMR (400 MHz, CDCl₃) δ = 7.44-7.57 (m, 5H), 7.32-7.44 (m, 3H), 7.23-7.28 (m, 2H), 7.07-7.17 (m, 3H), 6.89 (d, *J* = 8Hz, 2H), 6.54 (d, *J* = 4Hz, 1H), 6.40 (d, *J* = 4 Hz, 1H), 4.30 (d, *J* = 4Hz, 1H), 3.78 (d, *J* = 4 Hz, 1H), 3.53 (d, *J* = 4 Hz, 1H), 2.65 (s, 3H), 2.43 (d, *J* = 4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ = 206.2, 178.3, 150.4, 148.1, 143.3, 140.4, 138.5, 135.2, 134.4, 133.8, 133.3, 131.9, 131.2,

128.9, 128.8, 128.2, 127.9, 127.5, 127.0, 125.9, 124.8, 123.5, 123.0, 122.6, 121.2, 107.6, 100.0, 56.2, 54.6, 50.0, 40.4, 36.8, 25.6; HRMS (ESI) Calcd for $C_{34}H_{27}N_2O_4^+$ $[M+H]^+$ 527.1965; Found: 527.1960; >99% *ee* as determined by HPLC (Chiralcel IA, 90:10 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 41.3 min, t_r (minor) = 57.7 min.

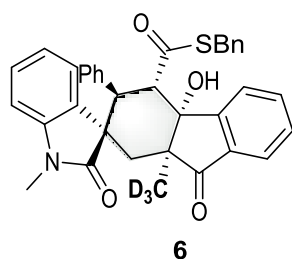


Ethyl 2-((2*R*,3*R*,9*aR*)-1'-methyl-2',9-dioxo-3-phenyl-3,9-dihydrospiro[fluorene-2,3'-indolin]-9*a*(1*H*)-yl)acetate (4f): white solid, 33 mg, 90% yield. $[\alpha]_D^{25}$ (c 1.0, $CHCl_3$) = + 39.9. 1H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, J = 4 Hz, 1H), 7.69-7.79 (m, 3H), 7.00-7.16 (m, 2H), 6.98 (d, J = 4 Hz, 1H), 6.48 (d, J = 8 Hz, 2H), 3.86-3.91 (m, 2H), δ = 3.51 (t, J = 8 Hz, 1H) 3.15 (s, 2H), 2.98 (s, 3H), 2.34-2.46 (m, 2H), δ = 1.01 (t, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 201.8, 176.2, 170.2 144.0, 142.2, 141.6, 135.5, 135.1, 128.5, 127.2, 124.8, 123.0, 122.8, 122.5, 107.8, 77.4, 77.1, 76.8, 61.2, 53.8, 41.9, 39.7, 34.8, 26.2, 13.8; HRMS (ESI) Calcd for $C_{31}H_{28}NO_4^+$ $[M+H]^+$ 478.2013; Found: 478.2010; >99% *ee* as determined by HPLC (Chiralcel ODH, 80:20 hexanes/*i*-PrOH, 0.8 mL/min), t_r (major) = 18.1 min, t_r (minor) = 25.6 min.

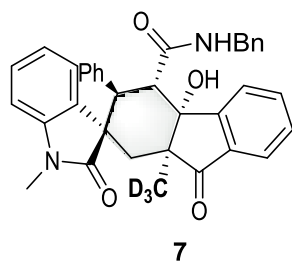


Methyl (2*R*,3*R*,4*S*,4*aR*,9*aS*)-4*a*-hydroxy-1'-methyl-9*a*-(methyl-*d*3)-2',9-dioxo-3-phenyl-1,3,4,4*a*,9,9*a*-hexahydrospiro[fluorene-2,3'-indoline]-4-carboxylate (5): white solid, 41 mg, 74% yield. $[\alpha]_D^{25}$ (c 1.0, $CHCl_3$) = + 45.7. 1H NMR (400 MHz, $CDCl_3$) δ = 7.94 (d, J = 8 Hz, 1H), 6.62 (t, J = 4 Hz, 1H), 6.58 (t, J = 4 Hz, 1H), δ =

7.33-7.38 (m, 2H), 7.04-7.09 (m, 2H), 6.90-7.03 (m, 4H), 6.43(d, $J = 4$ Hz, 1H), 4.40 (d, $J = 4$ Hz, 1H), 3.70 (d, $J = 4$ Hz, 1H), 3.19 (s, 3H), 2.93 (s, 3H), 2.63 (d, $J = 4$ Hz, 1H), 2.20 (d, $J = 4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) $\delta = 203.0, 177.5, 176.0, 155.4, 142.8, 135.8, 134.4, 133.2, 131.9, 129.1, 128.1, 127.3, 127.2, 125.0, 122.6, 122.4, 107.8, 78.0, 77.5, 77.2, 76.8, 54.1, 51.6, 50.9, 50.3, 48.6, 36.0, 25.9$; ^2H NMR (61.4 MHz, CHCl_3) $\delta = 1.25$ (s, 3D); HRMS (ESI) Calcd for $\text{C}_{31}\text{H}_{26}\text{D}_3\text{O}_5^+$ $[\text{M}+\text{H}]^+$ 484.2198; Found: 484.2199; >99% *ee* as determined by HPLC (Chiralcel ID, 90:10 hexanes/*i*-PrOH, 1.0 mL/min), t_r (major) = 4.1 min, t_r (minor) = 15.8min.



S-Benzyl (2*R*,3*R*,4*S*,4*aR*,9*aS*)-4*a*-hydroxy-1'-methyl-9*a*-(methyl-*d*₃)-2',9-dioxo-3-phenyl-1,3,4,4*a*,9,9*a*-hexahydrospiro[fluorene-2,3'-indoline]-4-carbothioate (6): white solid, 43 mg, 70% yield. $[\alpha]_{\text{D}}^{25}$ (c 1.0, CHCl_3) = + 67.4. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.90$ (d, $J = 4$ Hz, 1H), $\delta = 7.48$ -7.51 (m, 2H), 7.48 (d, $J = 4$ Hz, 1H), 7.47 (s, 1H), $\delta = 7.33$ -7.36 (m, 3H), 7.11-7.17 (m, 2H), 6.83-7.09 (m, 5H), 6.62 (d, $J = 8$ Hz, 2H), 6.47 (d, $J = 4$ Hz, 1H), 5.30 (t, $J = 4$ Hz, 1H), 4.10 (t, $J = 4$ Hz, 1H), 3.95 (d, $J = 4$ Hz, 1H), 3.83 (d, $J = 4$ Hz, 1H), 2.98 (s, 3H), 2.59 (d, $J = 4$ Hz, 1H), 2.23 (d, $J = 4$ Hz, 1H), 1.63 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) $\delta = 203.5, 178.3, 173.5, 156.0, 143.9, 143.5, 143.2, 142.5, 138, 136.6, 134.2, 133.3, 132.3, 128.9, 128.6, 128.1, 127.7, 127.5, 127.3, 124.7, 123.6, 122.7, 107.8, 78.4, 77.5, 77.2, 76.8, 54.2, 51.4, 50.4, 48.3, 43.4, 36.4, 26.0$; ^2H NMR (61.4 MHz, CHCl_3) $\delta = 1.23$ (s, 3D); HRMS (ESI) Calcd for $\text{C}_{36}\text{H}_{30}\text{D}_3\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}]^+$ 560.2623; Found: 560.2625; >99% *ee* as determined by HPLC (Chiralcel IA, 75:25 hexanes/*i*-PrOH, 1.0 mL/min), t_r (major) = 49.6 min, t_r (minor) = 31.7 min.

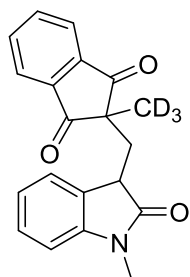


(2R,3R,4S,4aR,9aS)-N-Benzyl-4a-hydroxy-1'-methyl-9a-(methyl-*d*3)-2',9-dioxo-3-phenyl-1,3,4,4a,9,9a-hexahydrospiro[fluorene-2,3'-indoline]-4-carboxamide (7): white solid, 40 mg, 63% yield. $[\alpha]_D^{25}$ (c 1.0, CHCl₃) = + 65.9. ¹H NMR (400 MHz, CDCl₃) δ = 7.91 (d, *J* = 4 Hz, 1H), 7.45 (t, *J* = 4 Hz, 1H), δ = 7.46-7.30 (m, 2H), 7.17 (d, *J* = 4 Hz, 3H), 7.06-7.16 (m, 4H), 6.98-7.03 (m, 3H), 6.80-6.82 (m, 2H), 6.65 (s, 1H), 6.44 (d, *J* = 4 Hz, 1H), 5.23 (t, *J* = 4 Hz, 1H), 4.61 (d, *J* = 4 Hz, 1H), 3.84 (t, *J* = 8 Hz, 2H), 2.97 (s, 3H), 2.60 (d, *J* = 4 Hz, 1H), 2.18 (d, *J* = 4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 203.5, 178.3, 173.5, 155.9, 154.8, 143.4, 143.1, 143.0, 142.5, 138.0, 136.9, 136.5, 134.2, 133.3, 132.3, 128.8, 128.6, 128.1, 127.7, 127.5, 127.3, 125.1, 124.7, 123.6, 122.7, 112.6, 107.8, 78.4, 77.4, 77.1, 76.8, 54.2, 51.4, 50.4, 48.3, 43.4, 38.5, 36.3, 26.0; ²H NMR (61.4 MHz, CHCl₃) δ = 1.22 (s, 3D); HRMS (ESI) Calcd for C₃₆H₂₉D₃NSO₄⁺ [M+H]⁺ 577.2235; Found: 577.2238; >99% *ee* as determined by HPLC (Chiralcel ID, 95:5 hexanes/*i*-PrOH, 0.8 mL/min), *t_r* (major) = 32.4 min, *t_r* (minor) = 29.7 min.

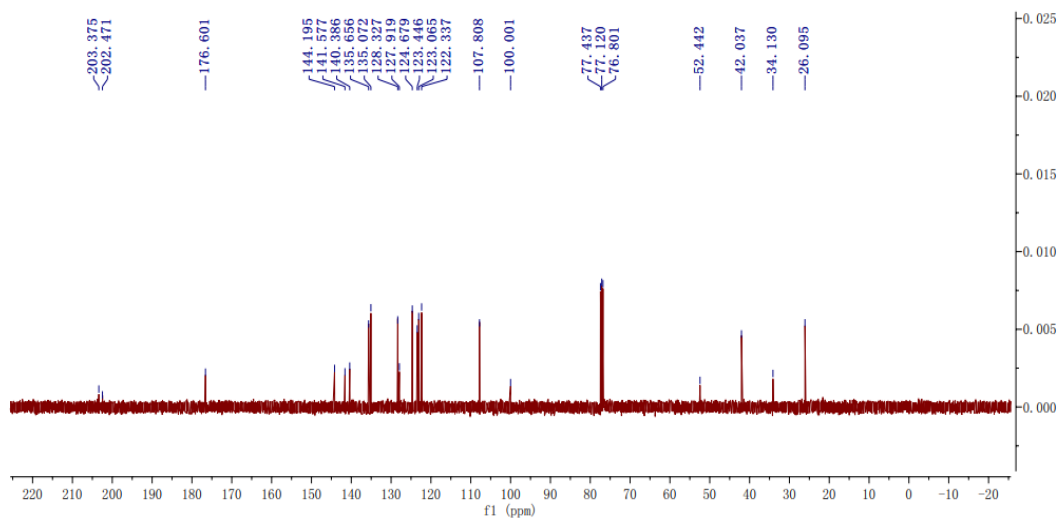
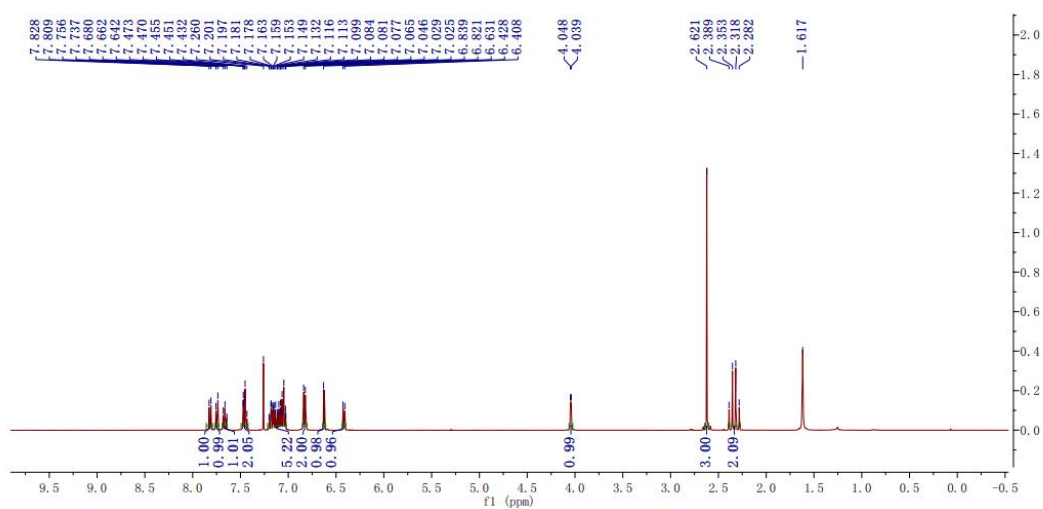
b) Reference

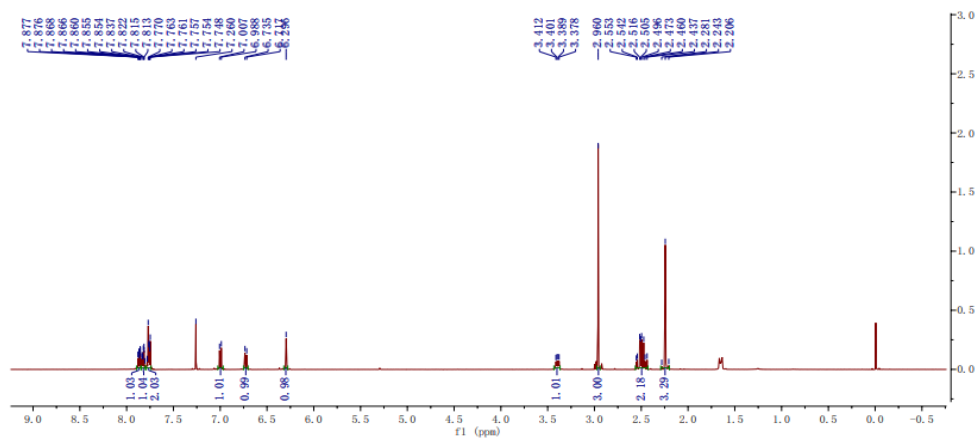
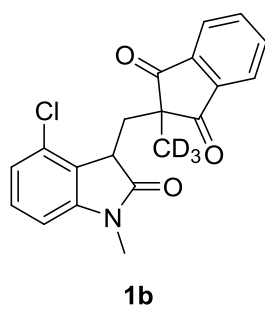
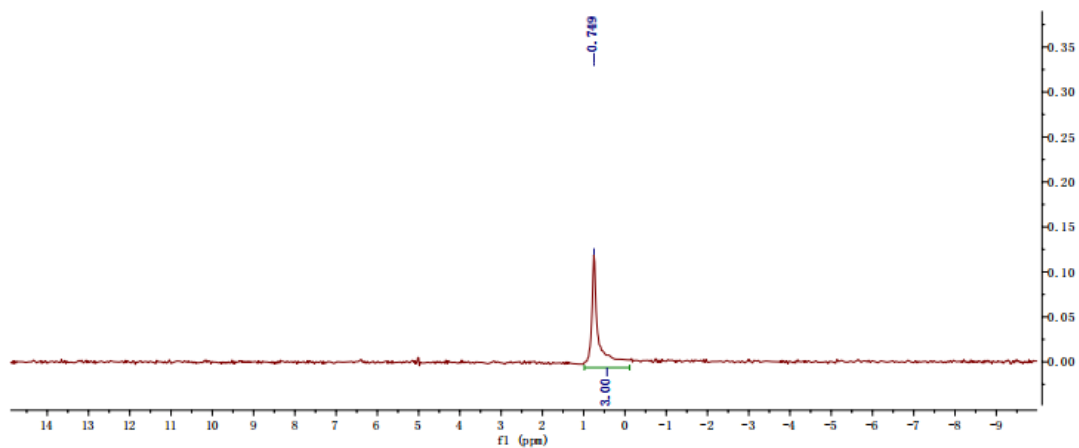
- 1 Netz, Natalie; et al , A Modular Formal Total Synthesis of (±)Cycloclavine. *Journal of Organic Chemistry* (2016), 81(4), 1723-1730
- 2 Wang, Qingmin; et al. The gem-difluoro lactam spiro benzo five-membered heterocyclic compound has structure in formula **I**, and shows good anti-TMV activity and insecticidal activity. *China, CN111264542 A* 2020-06-12

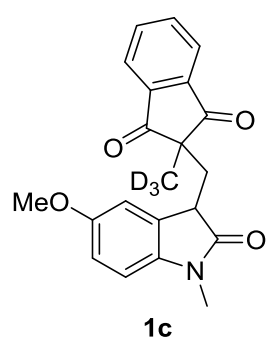
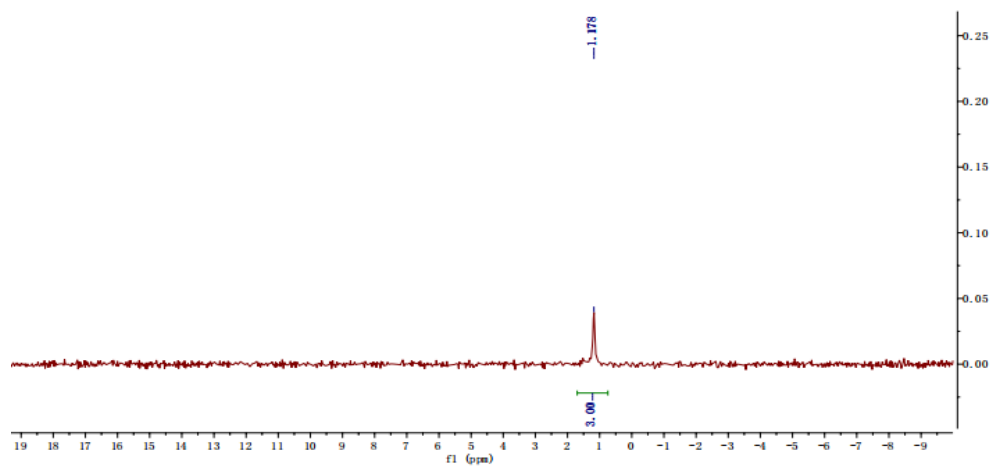
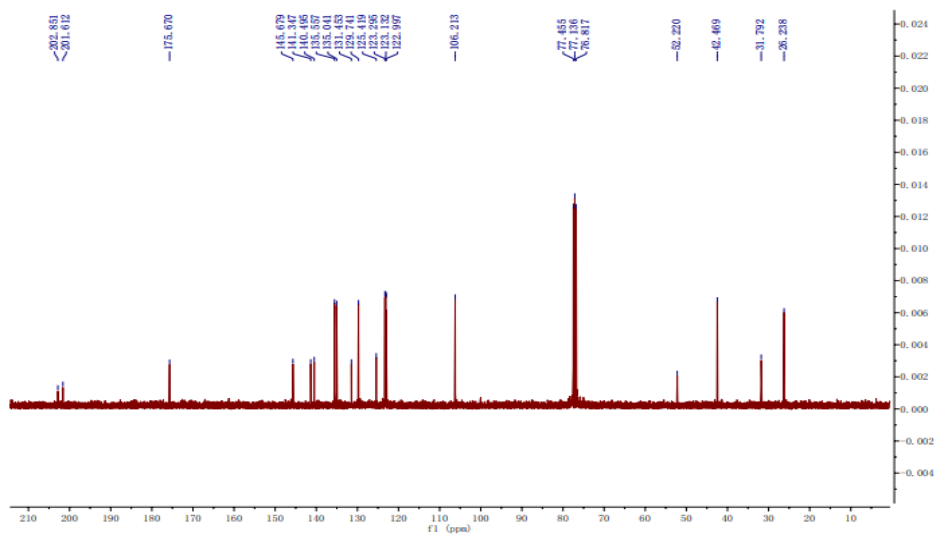
IV: ¹H, ¹³C NMR spectra and HPLC data of products

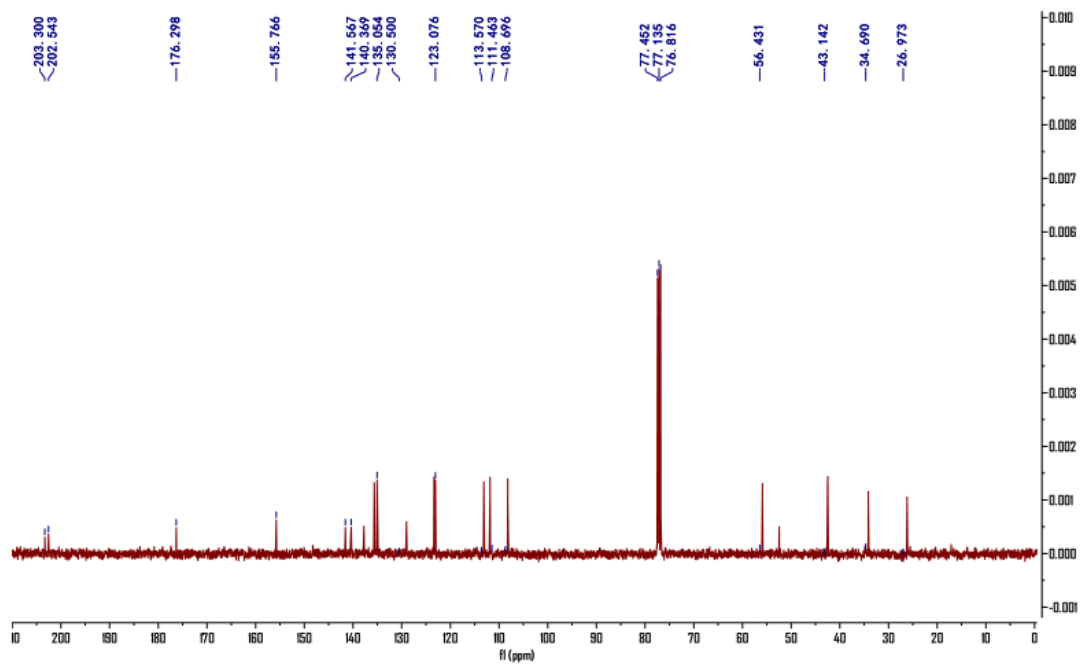
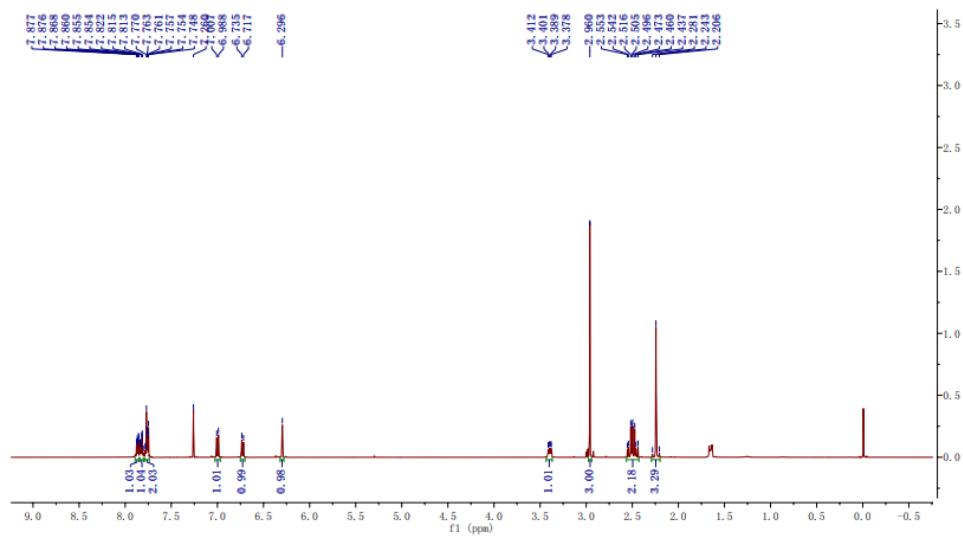


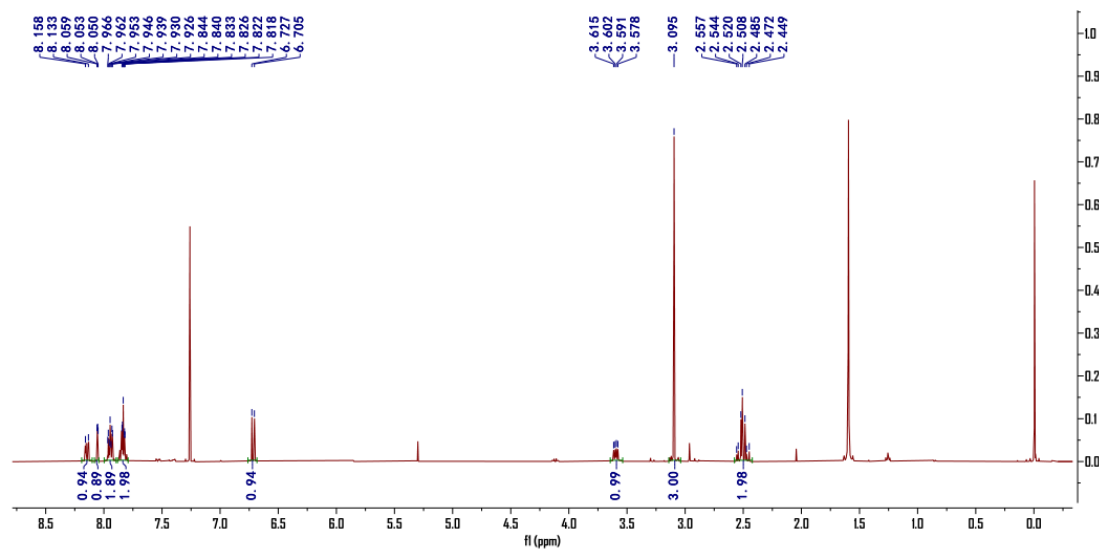
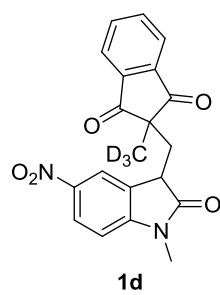
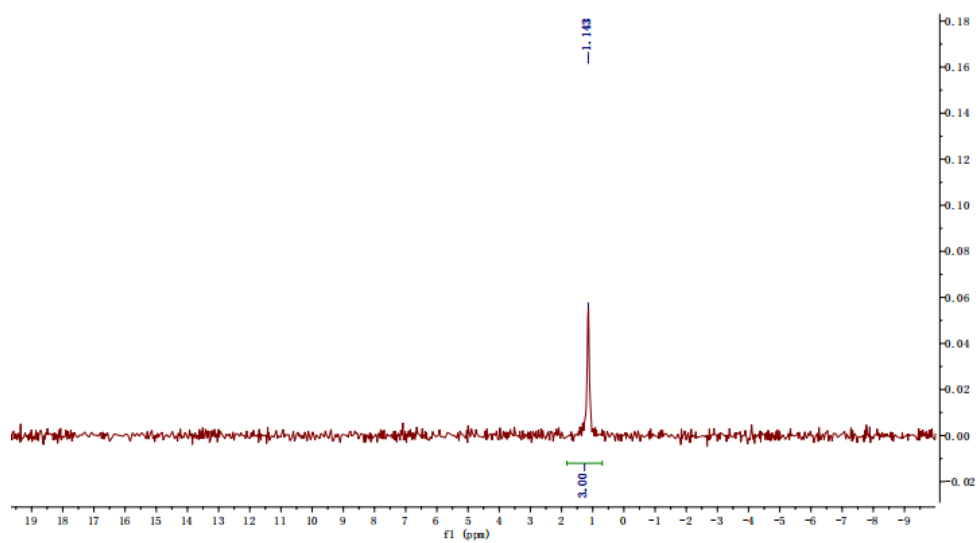
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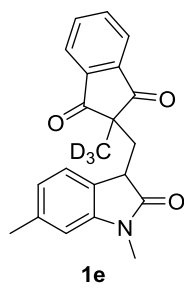
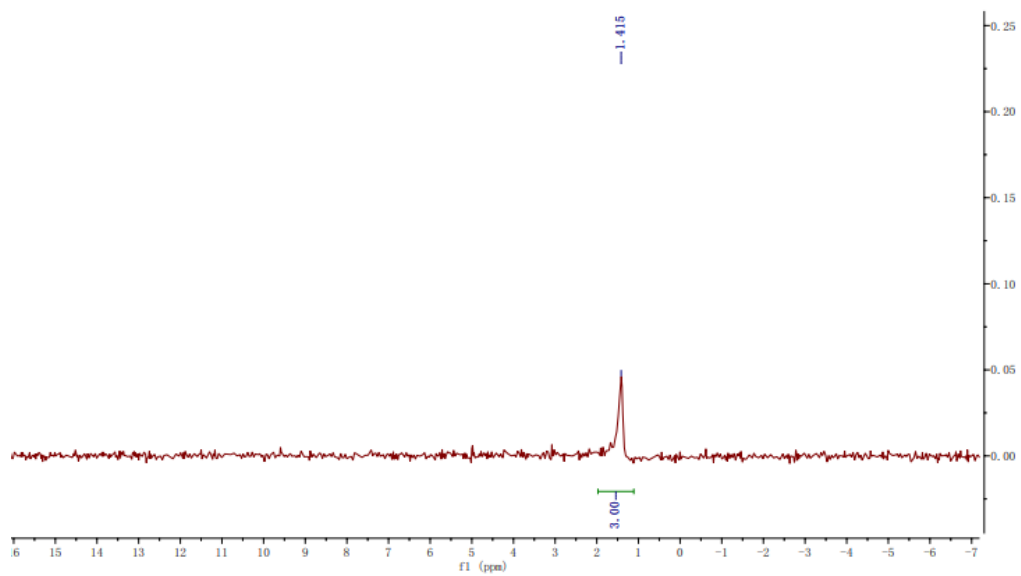
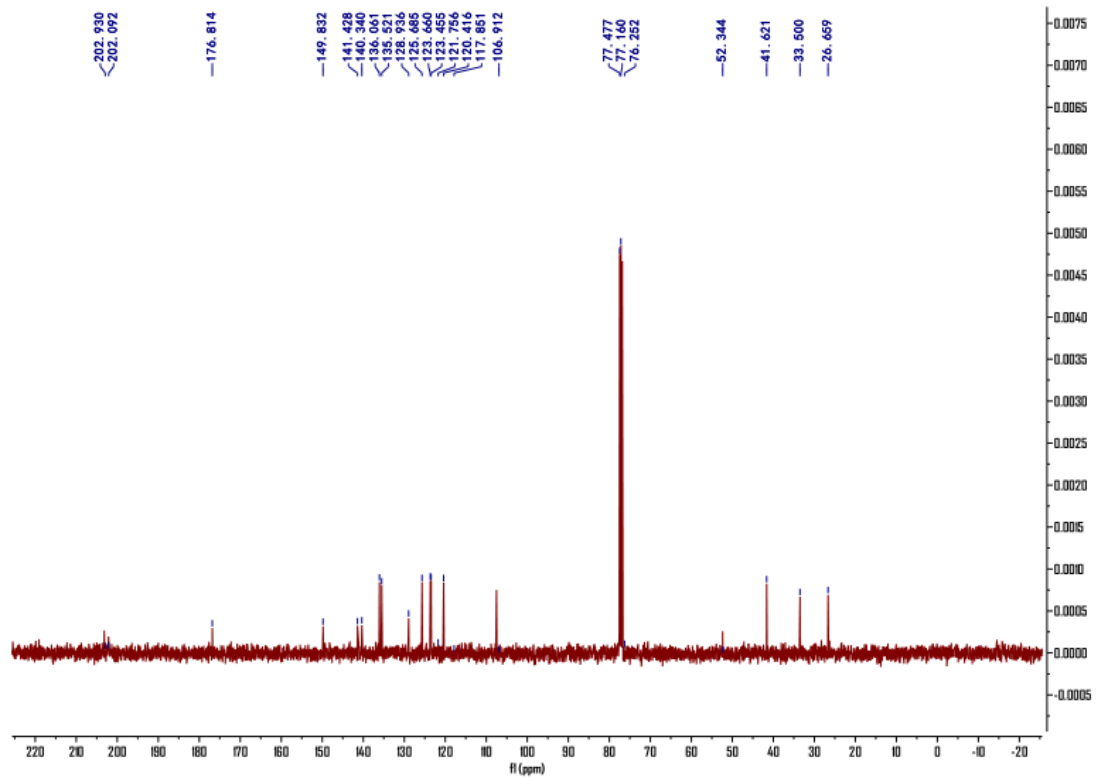


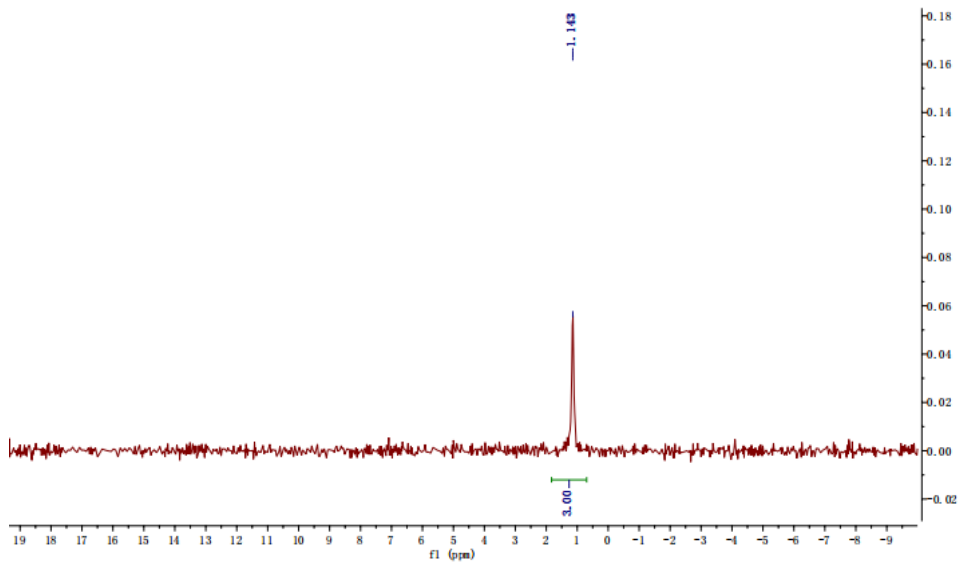
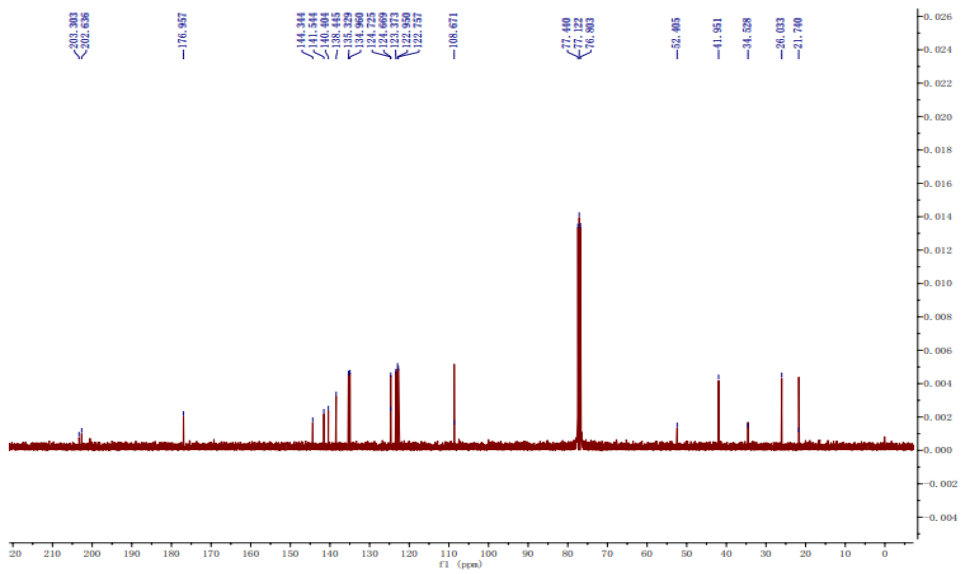
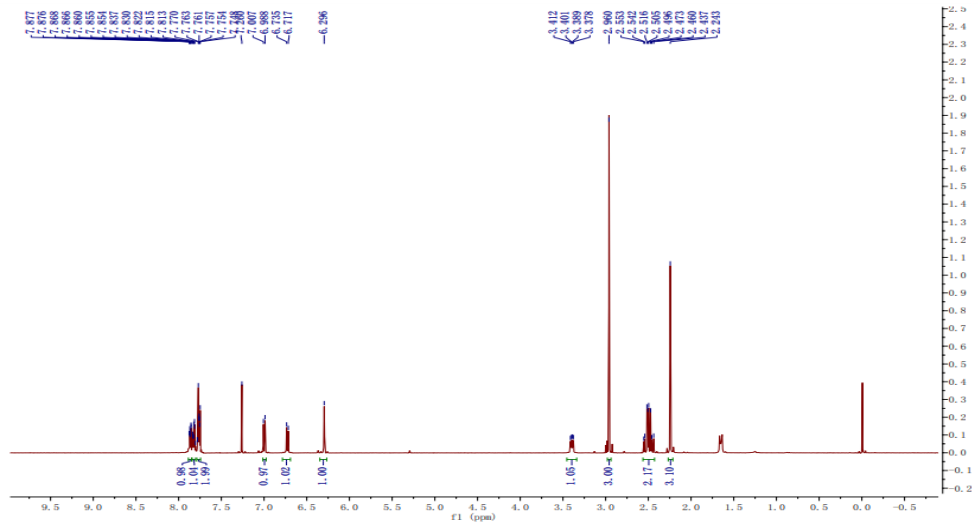


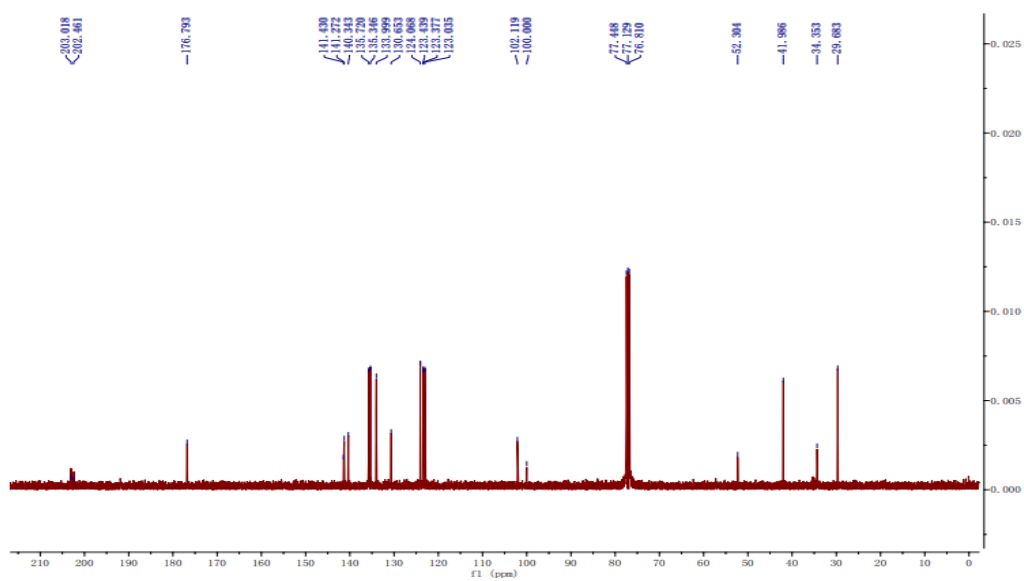
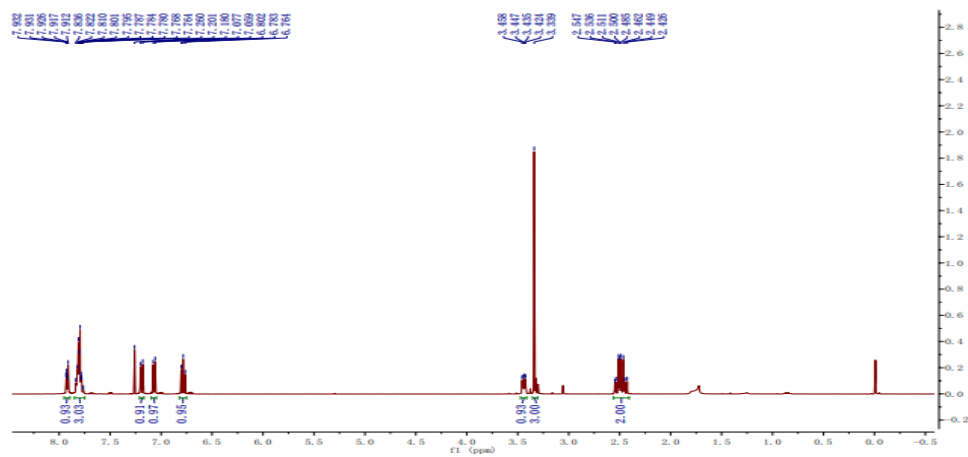
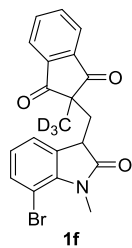


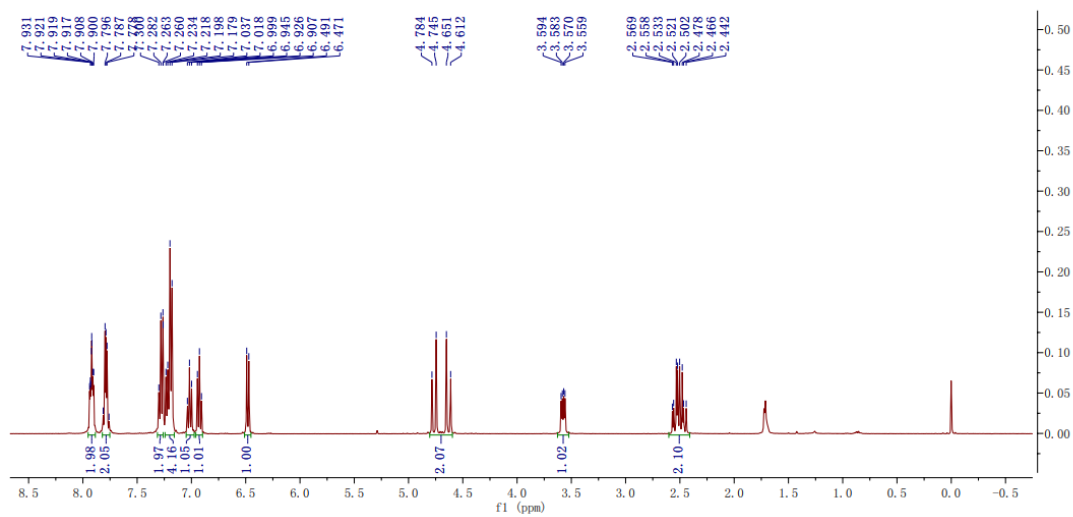
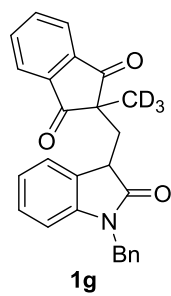
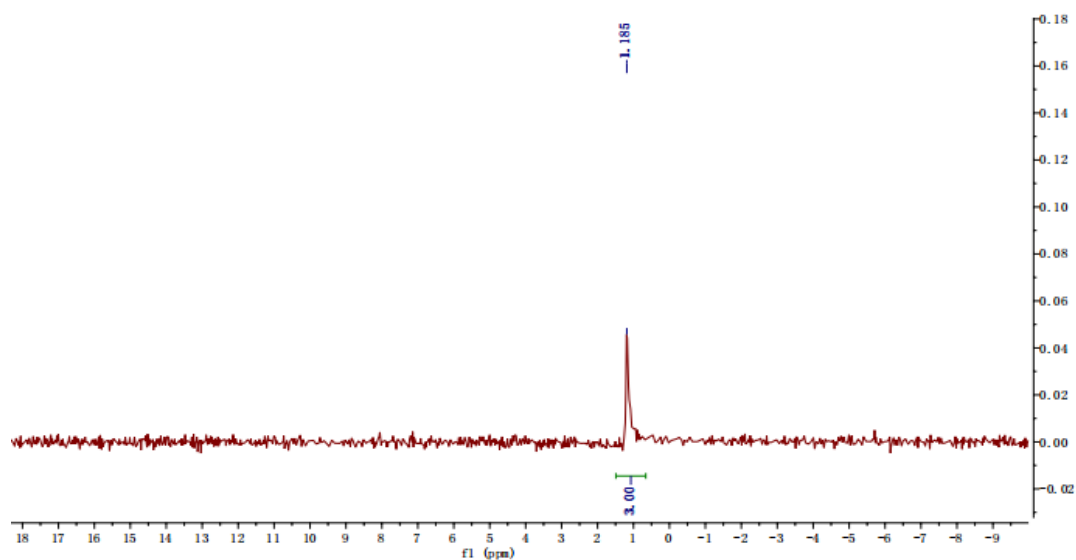


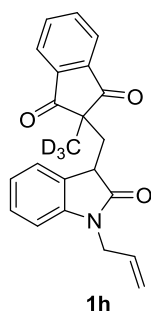
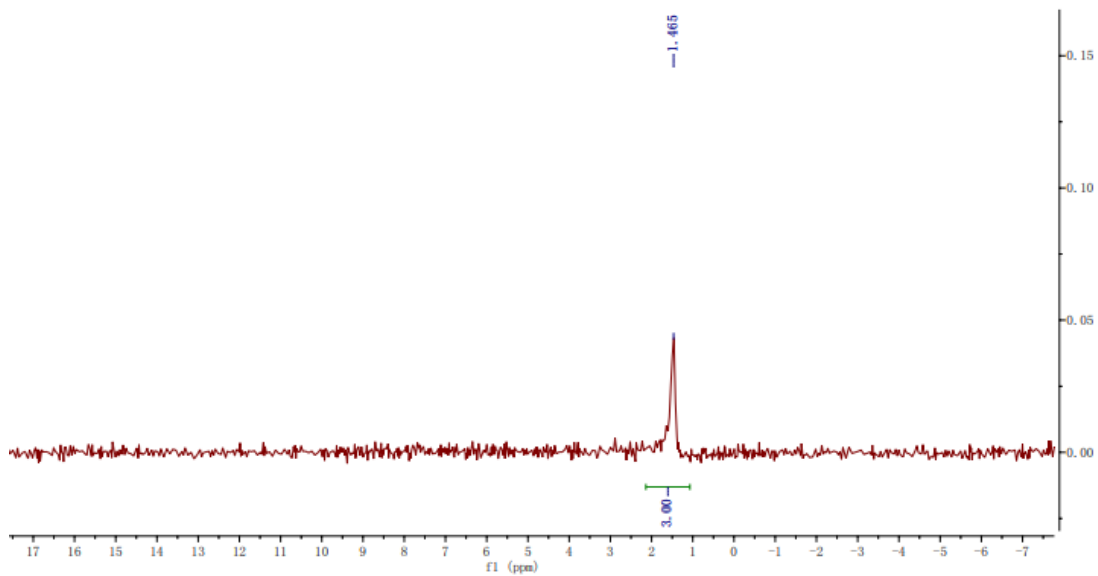
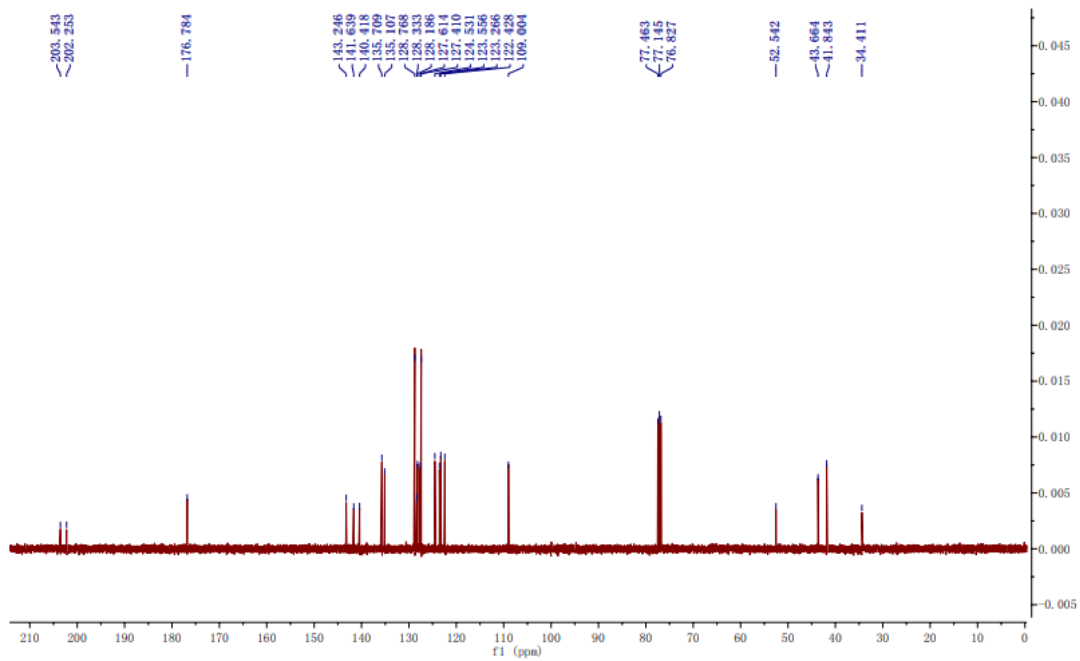


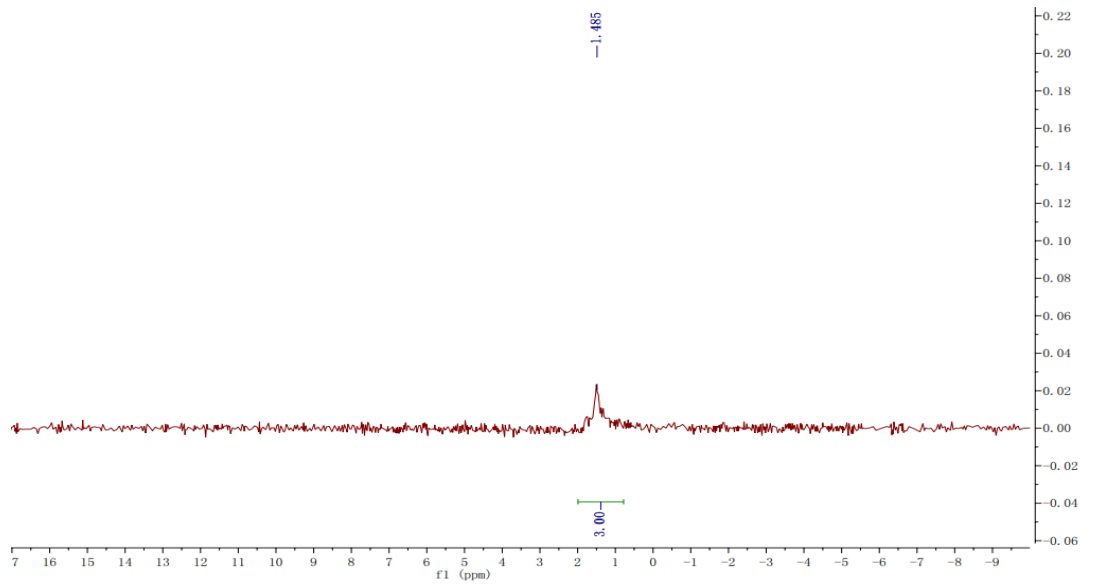
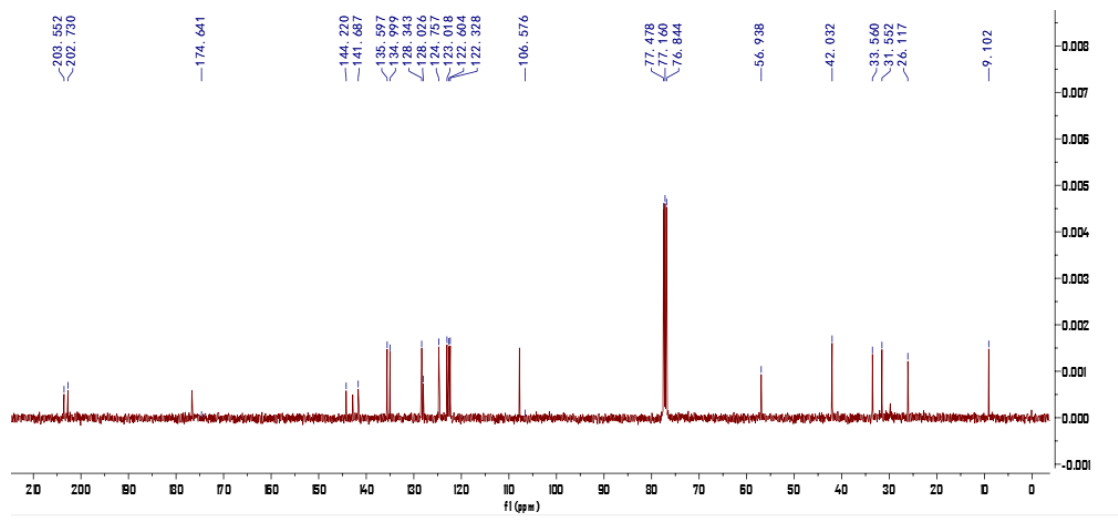
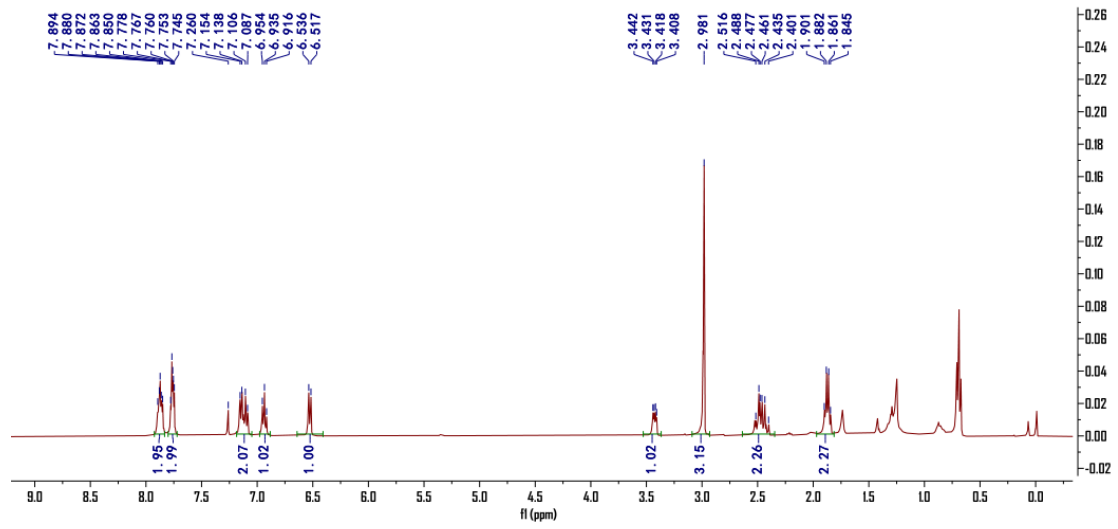


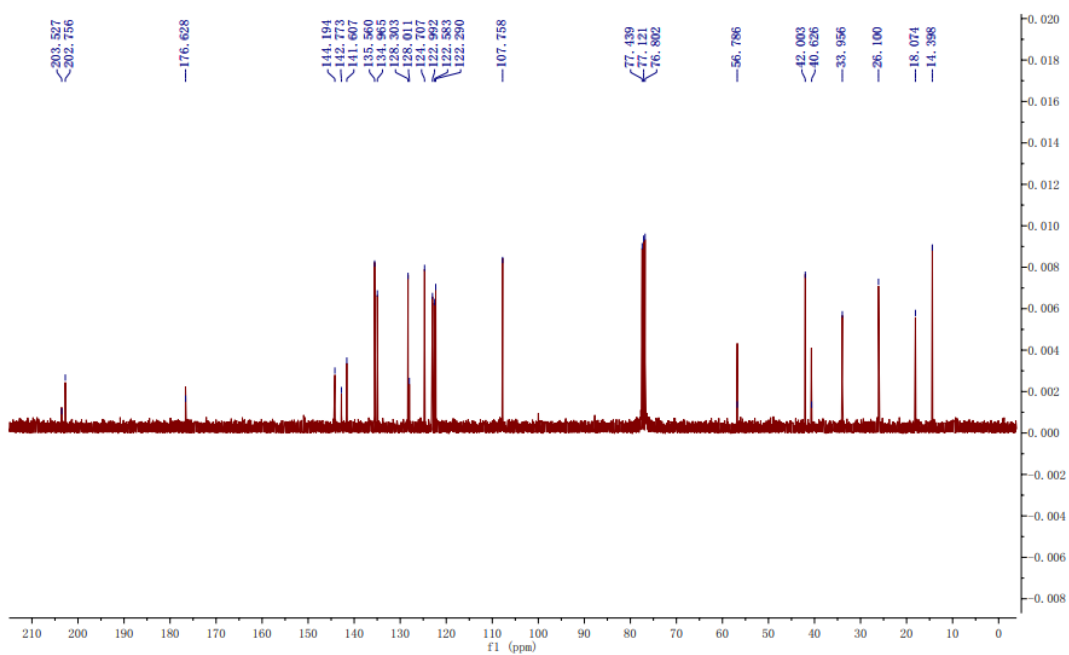
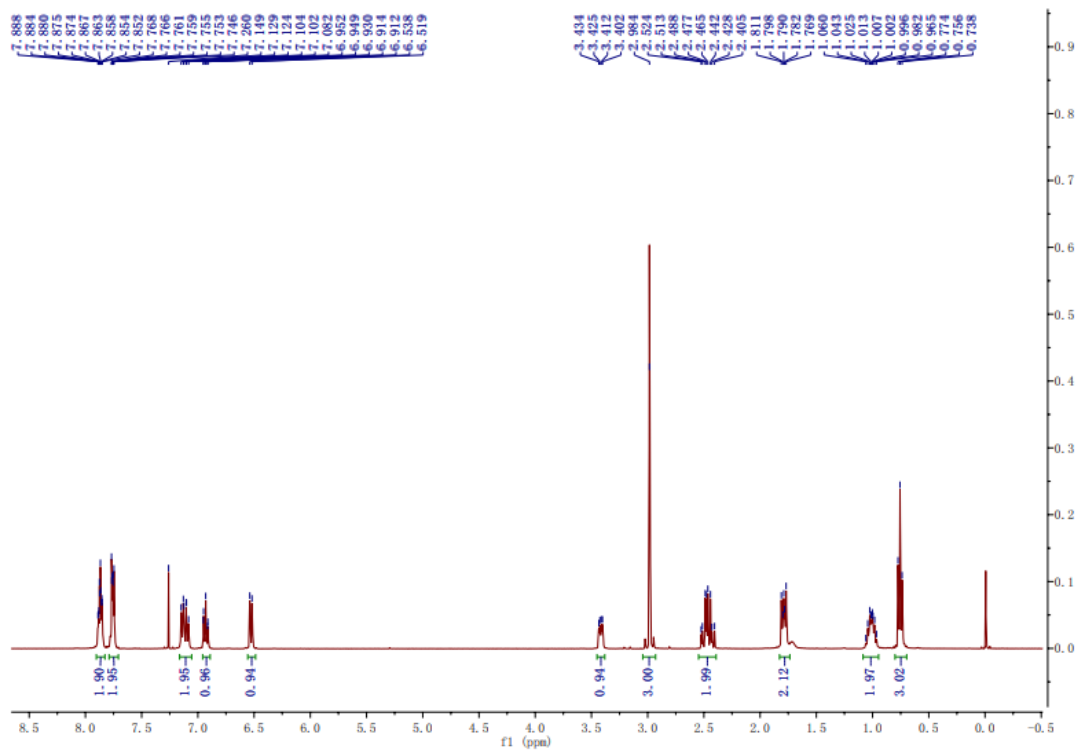
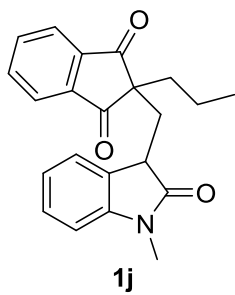


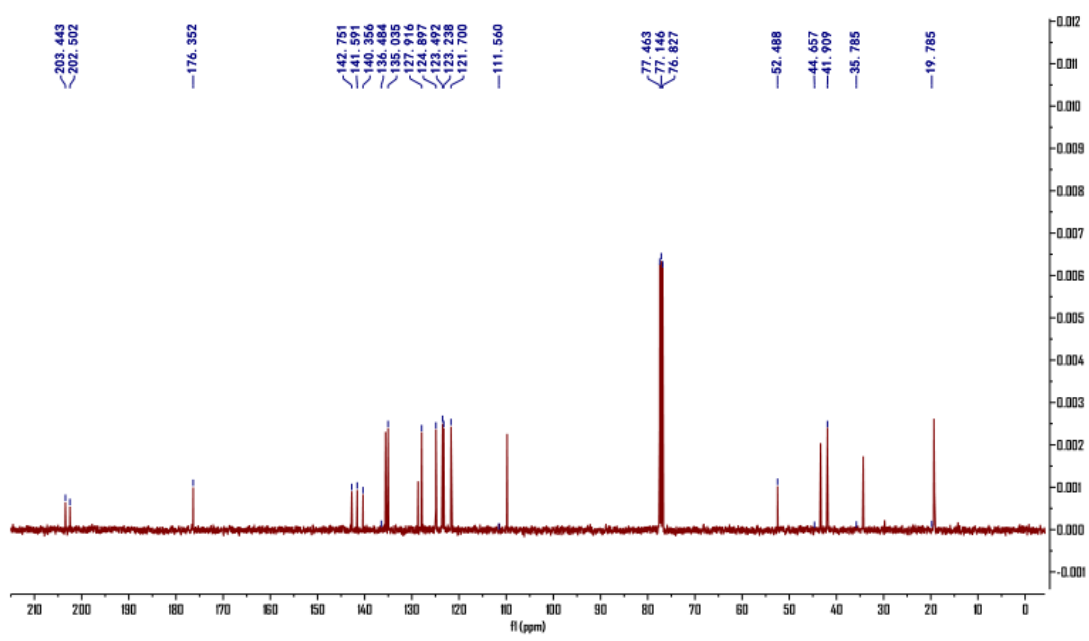
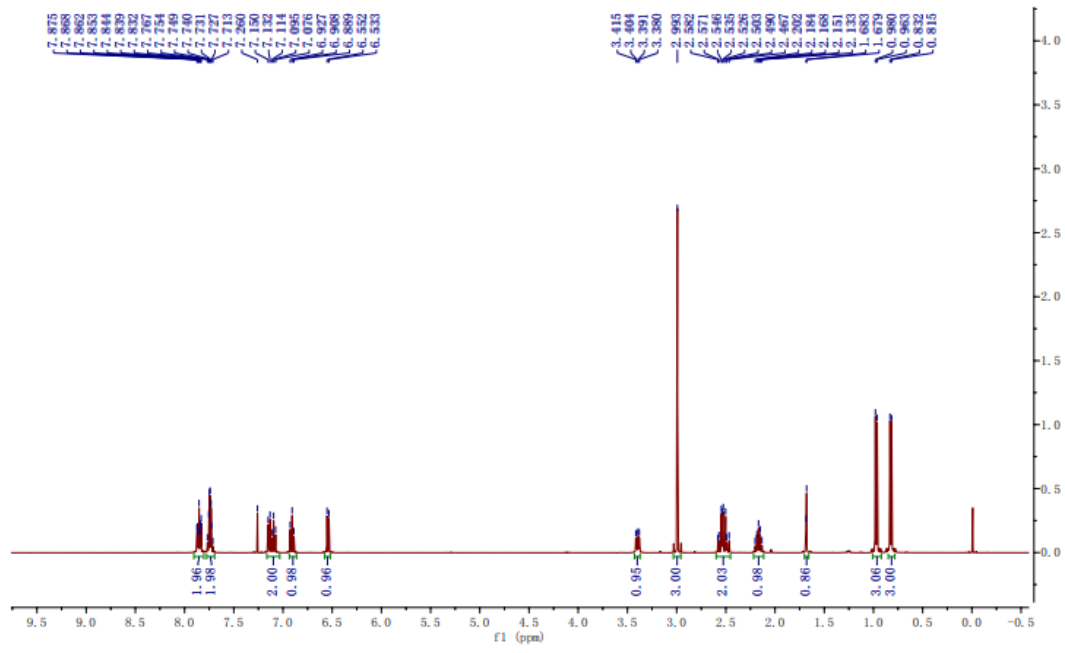
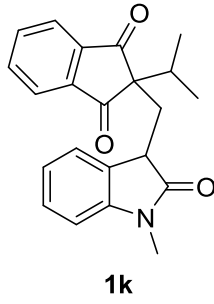


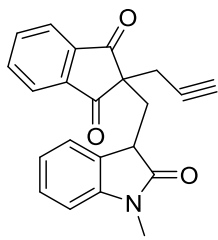




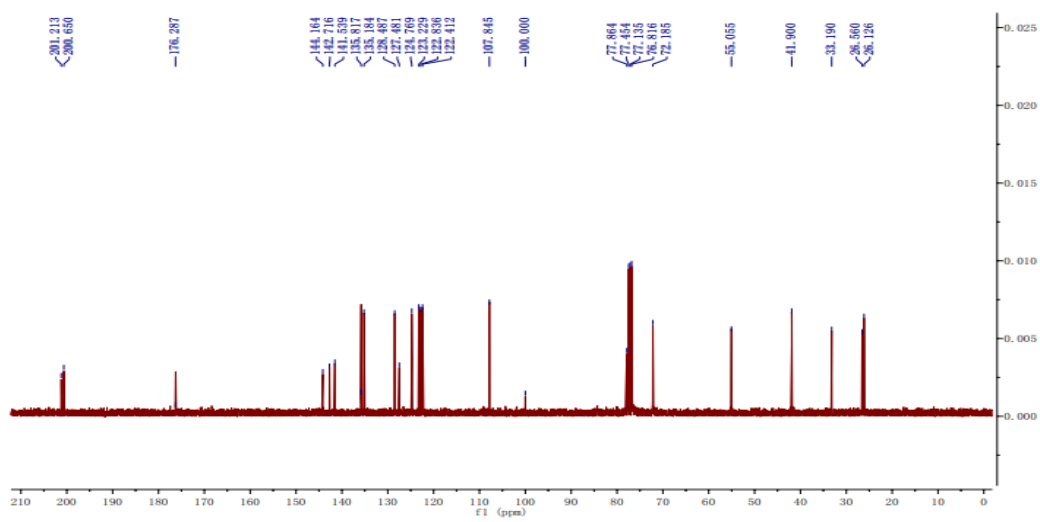
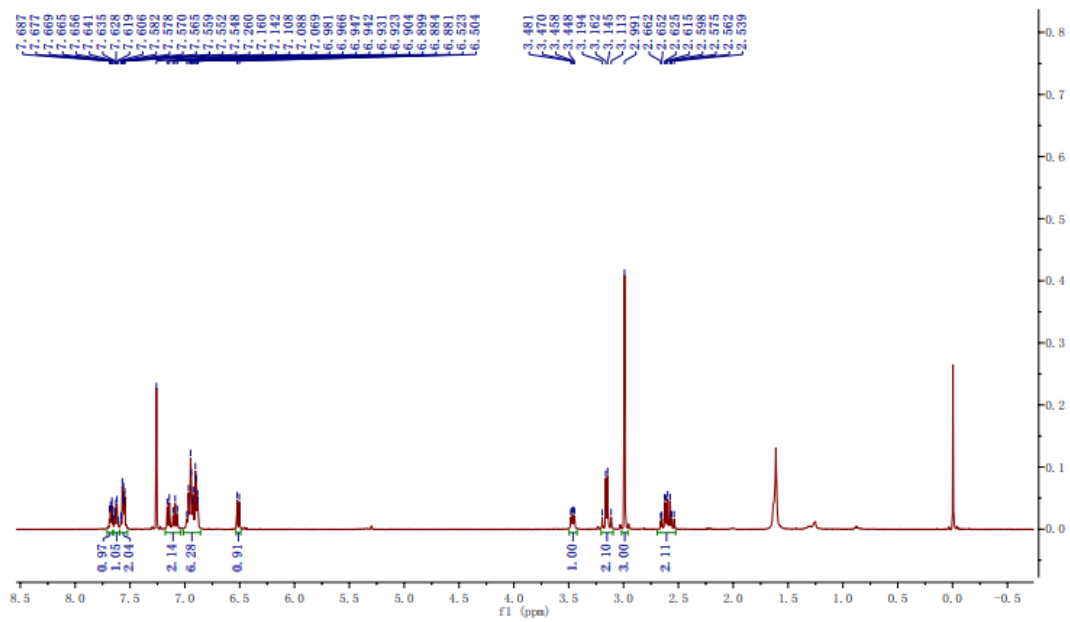


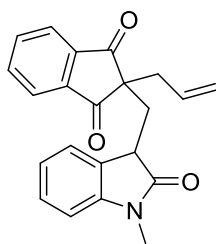




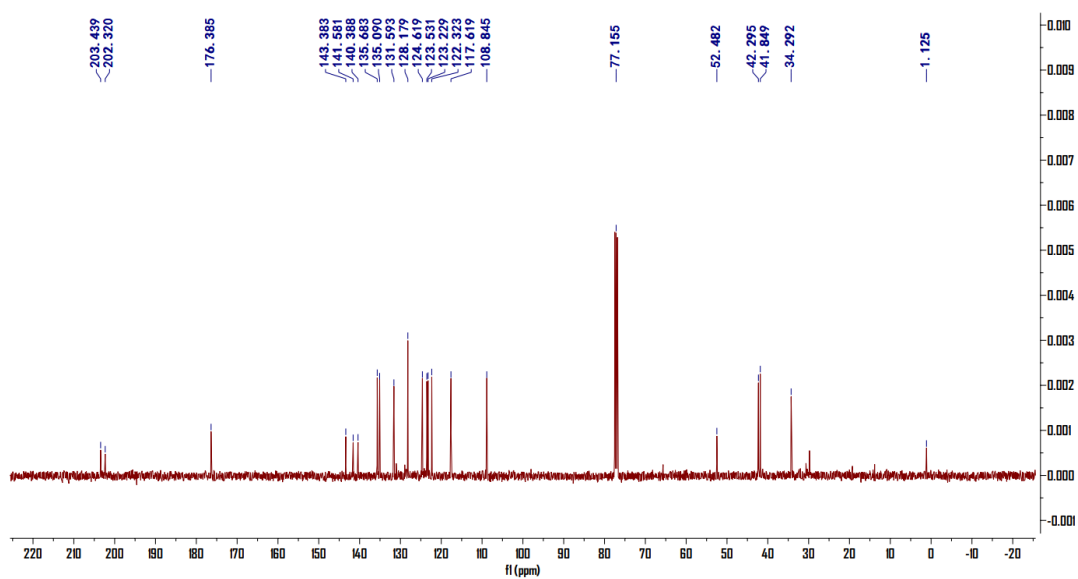
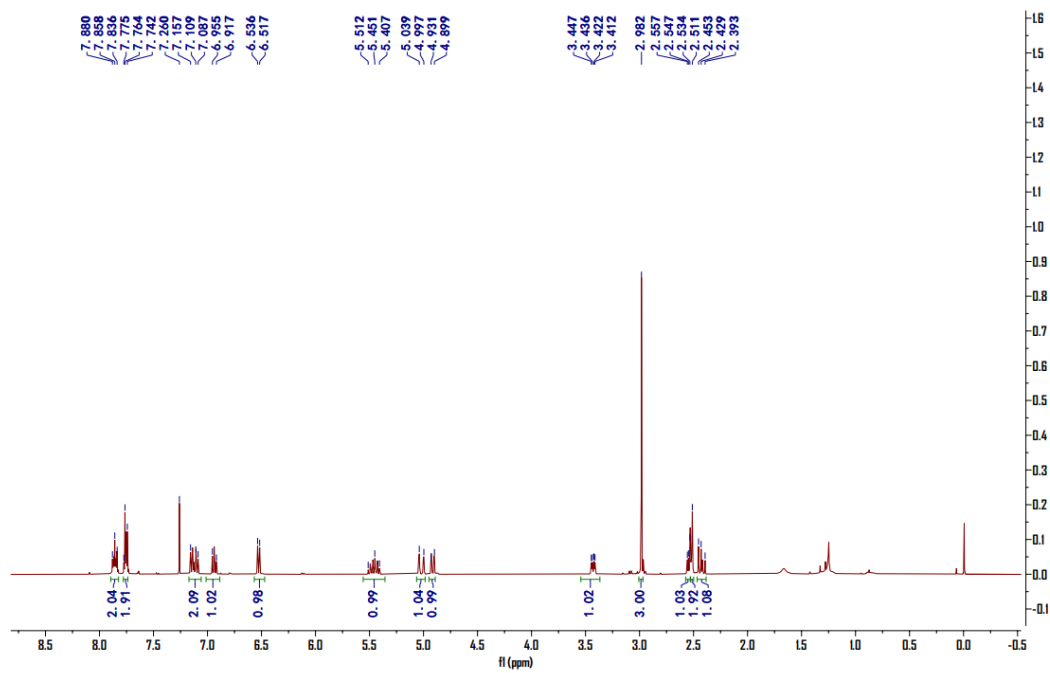


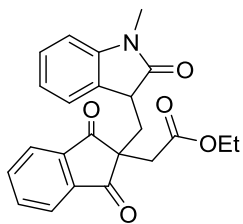
11



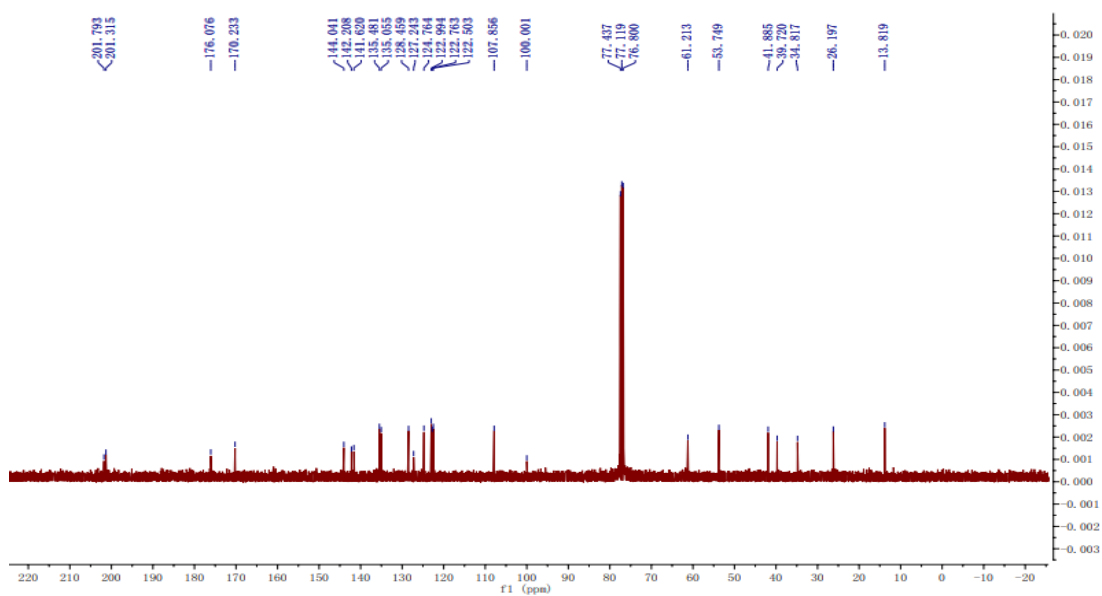
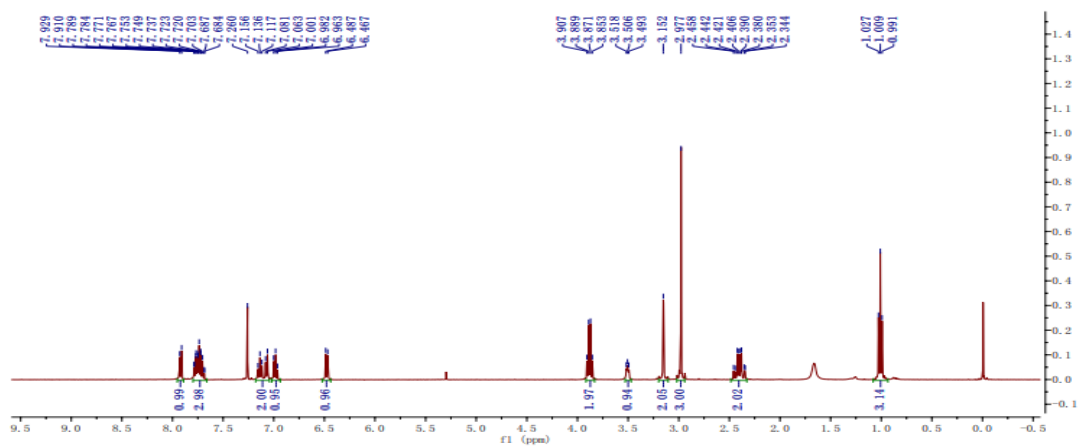


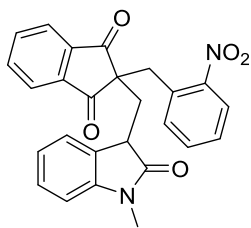
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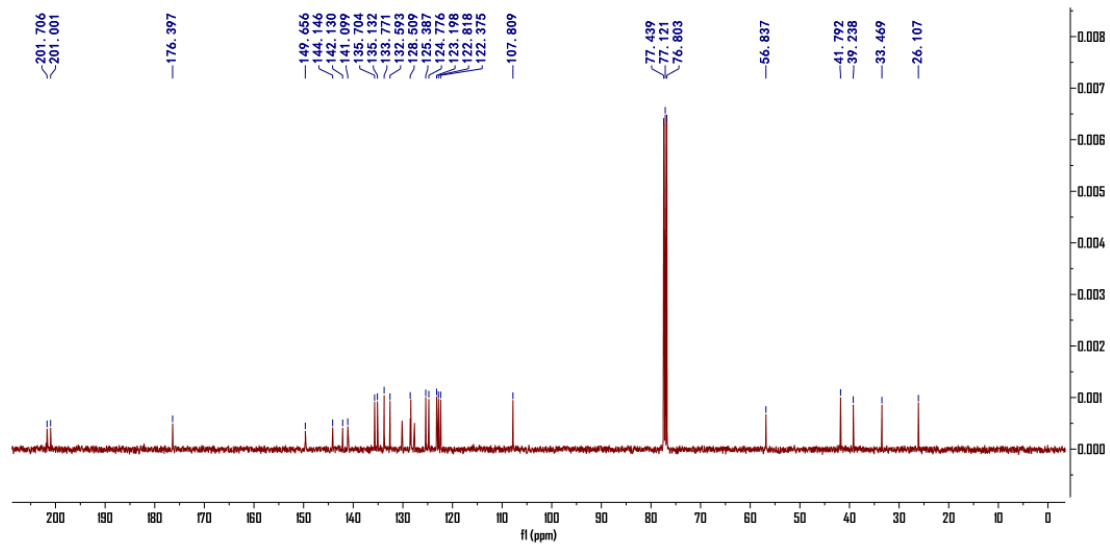
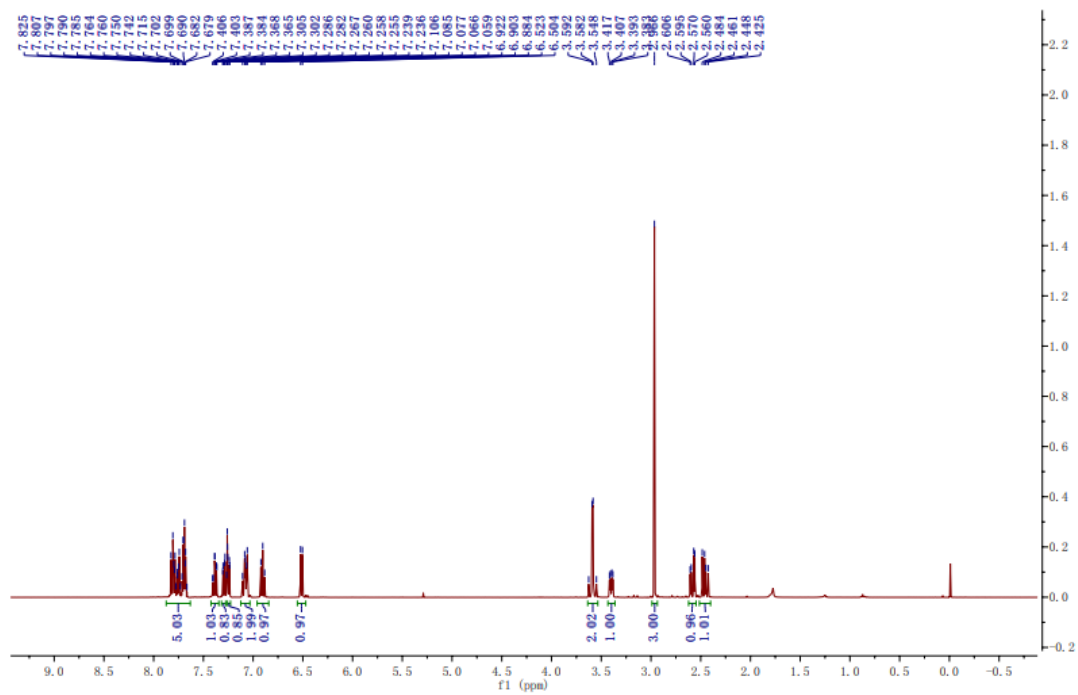


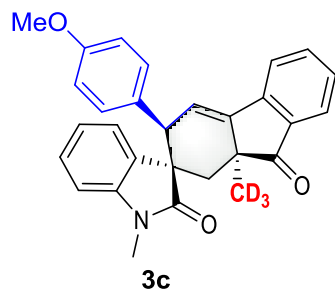
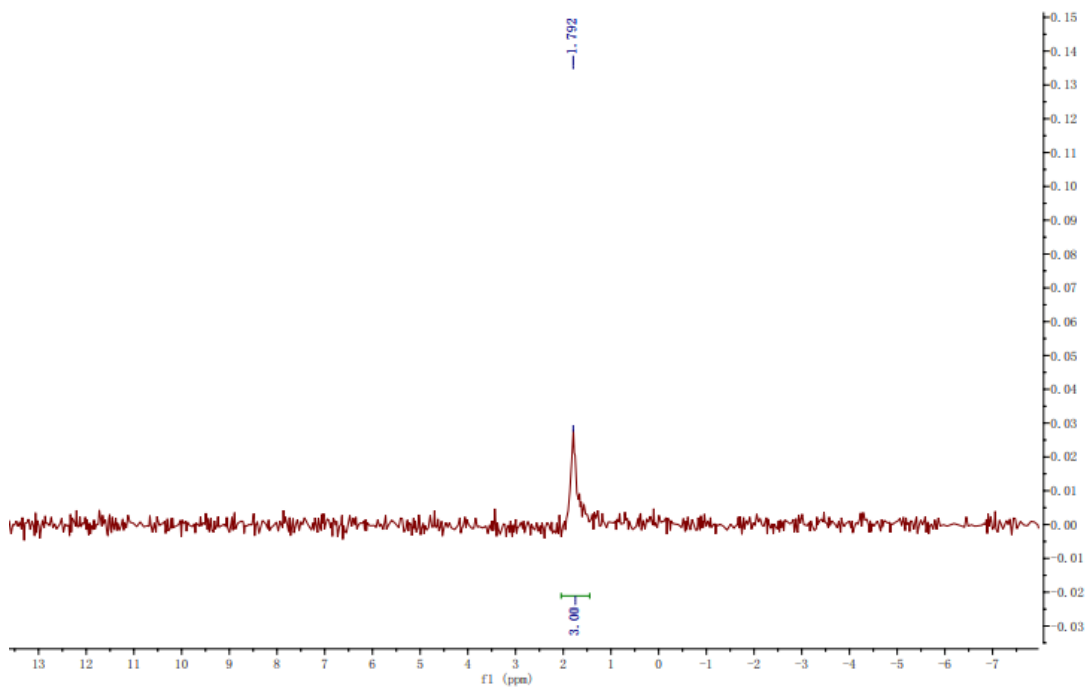
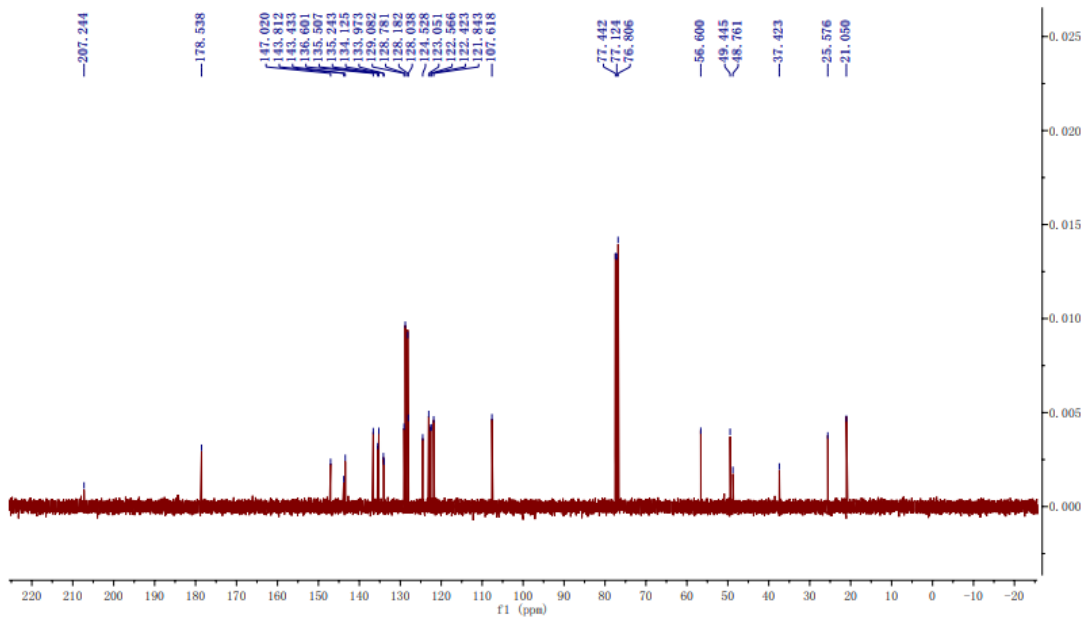
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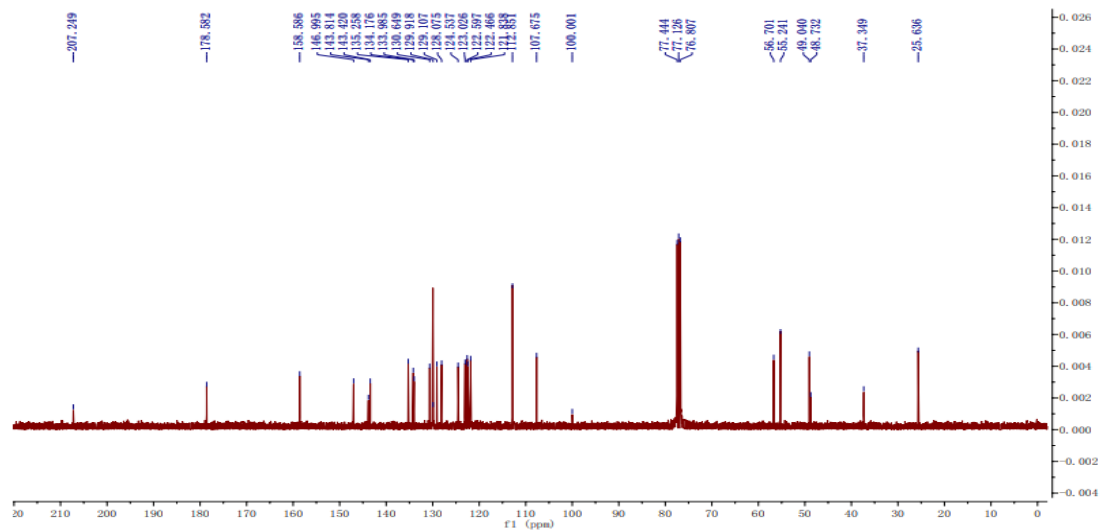
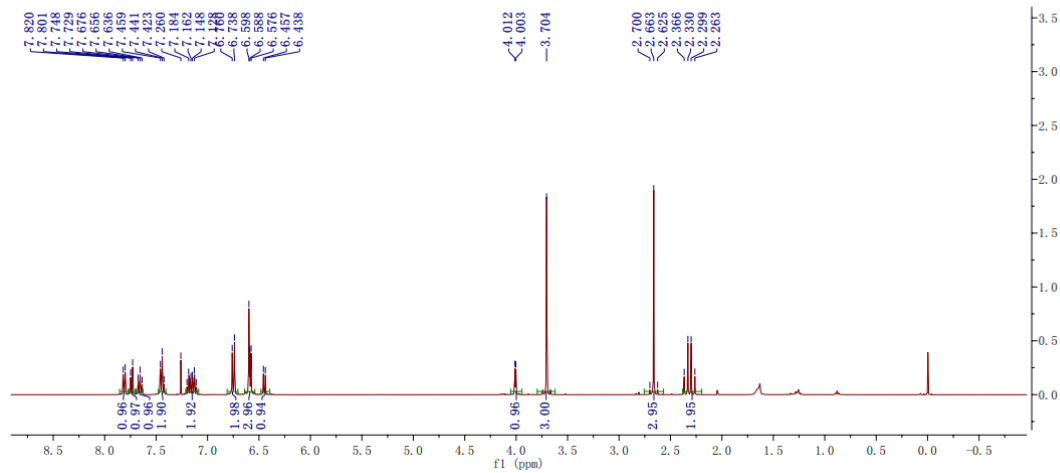


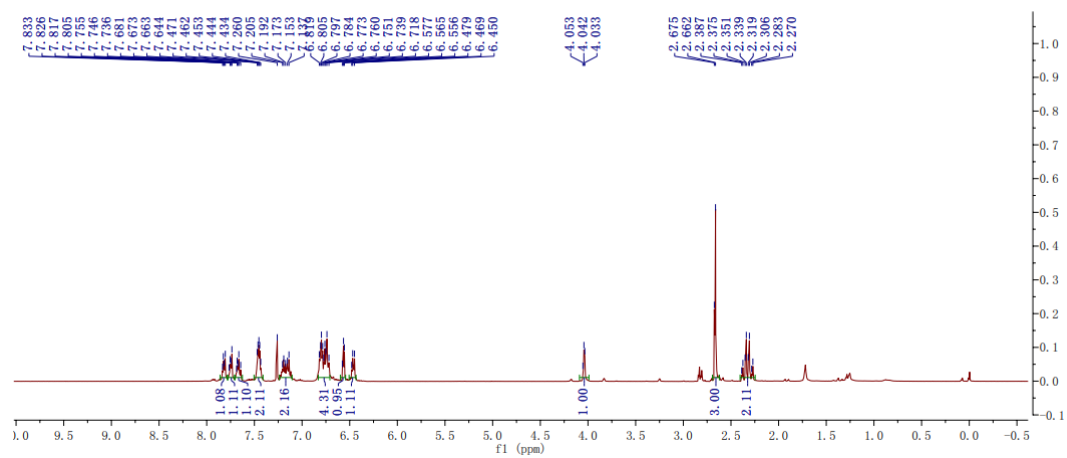
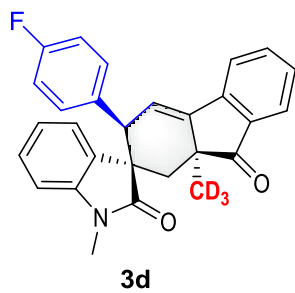
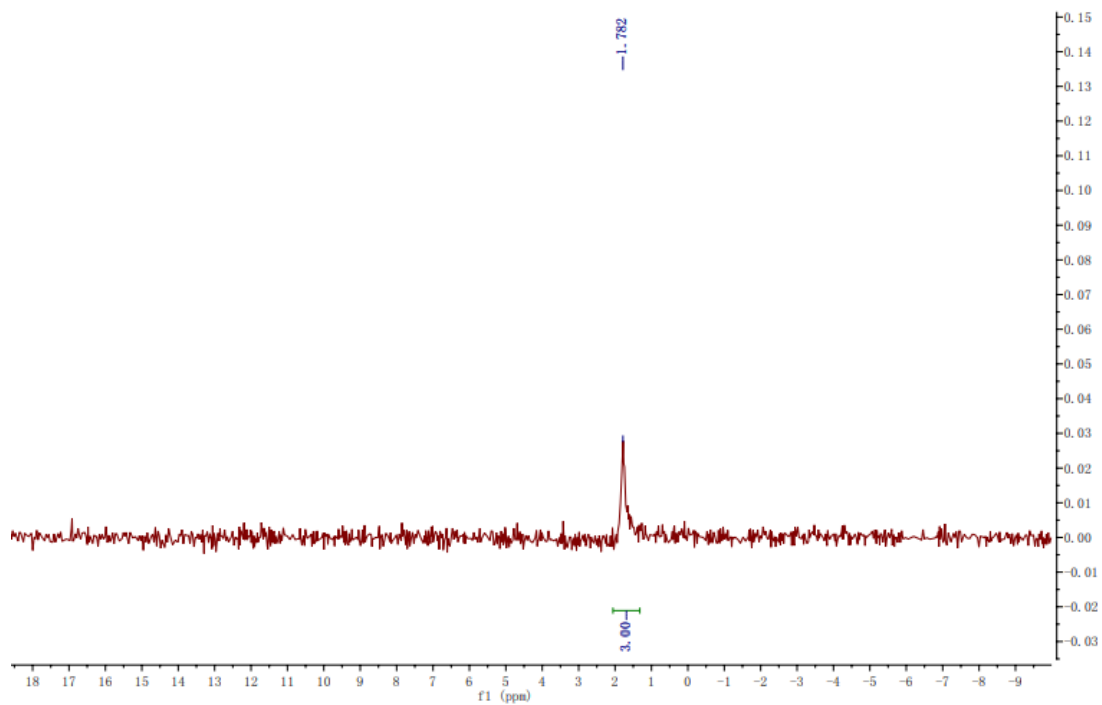


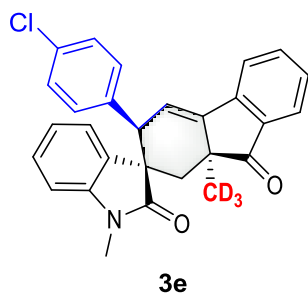
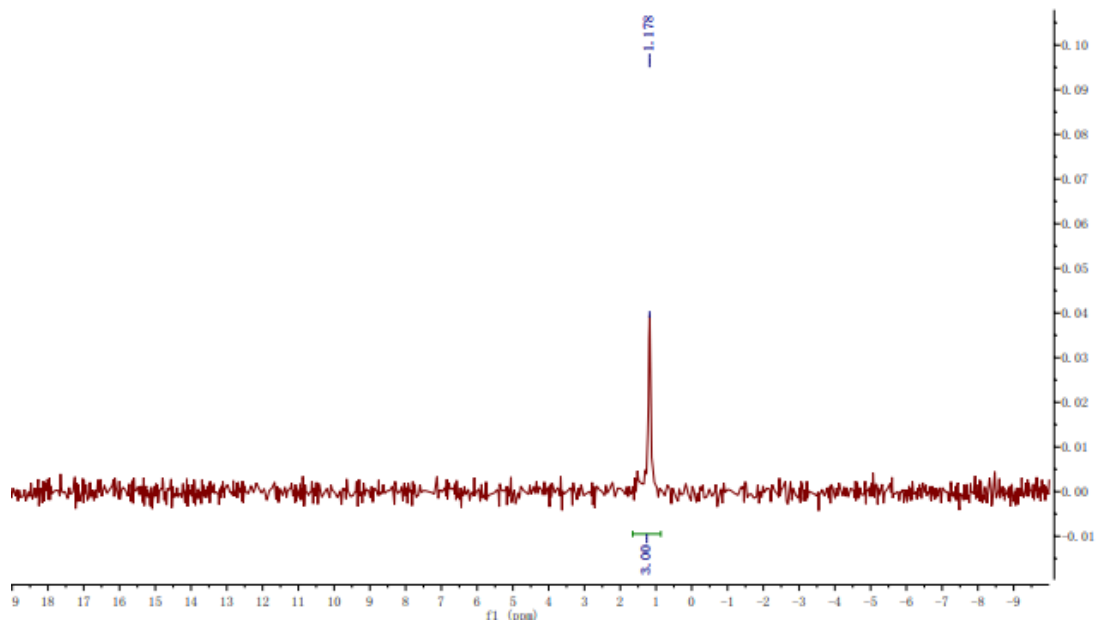
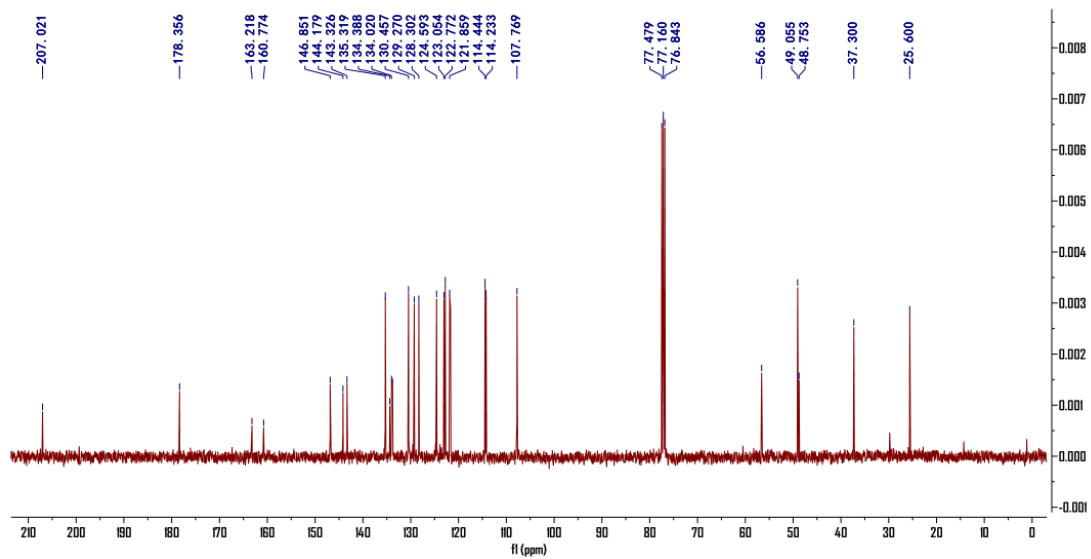
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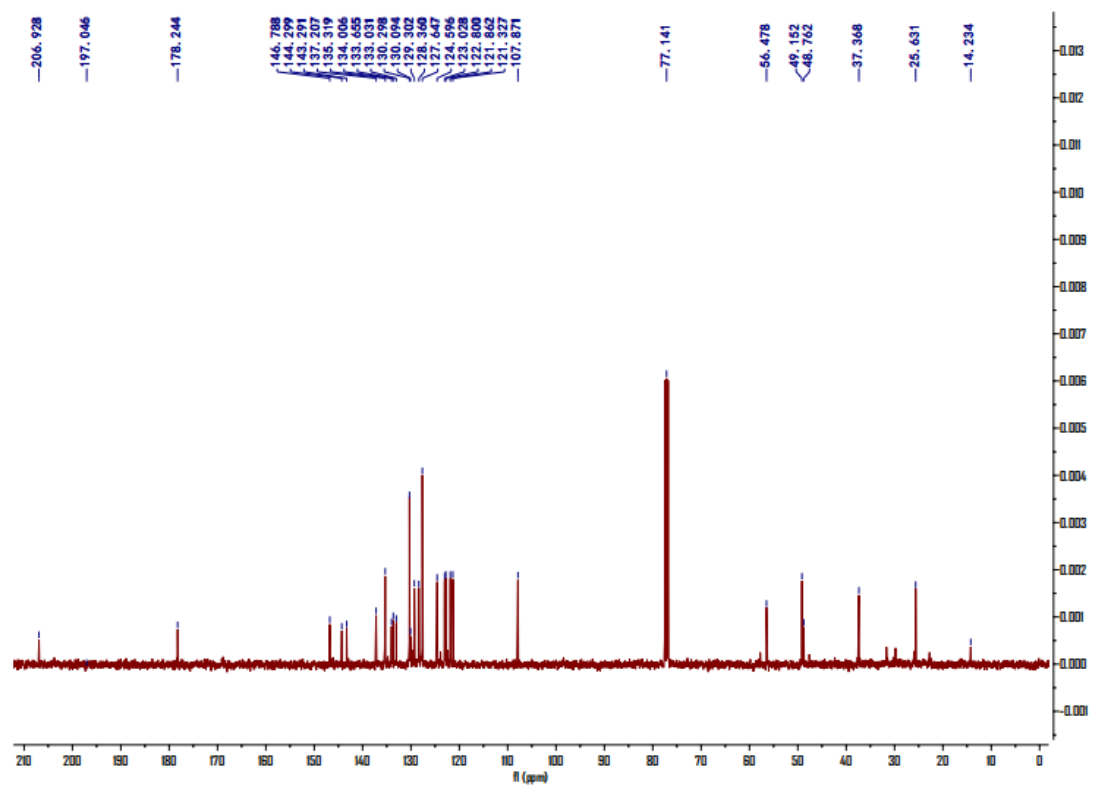
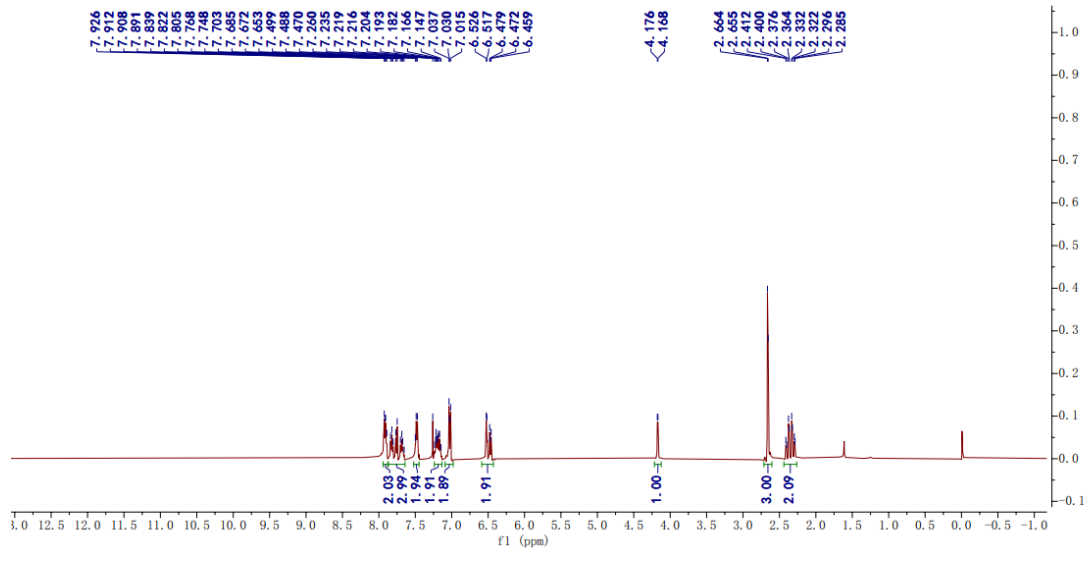


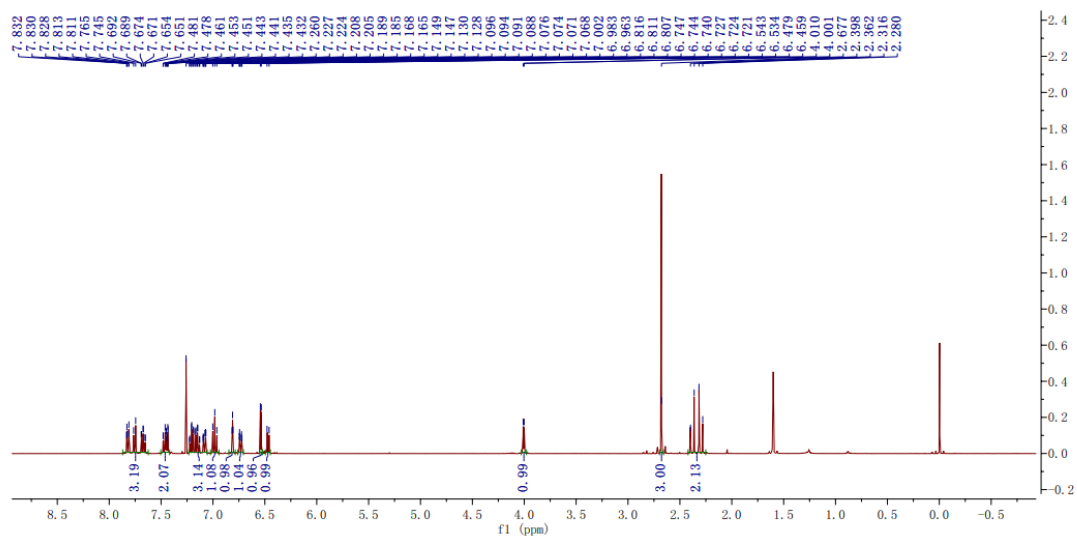
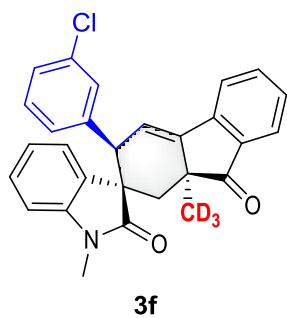
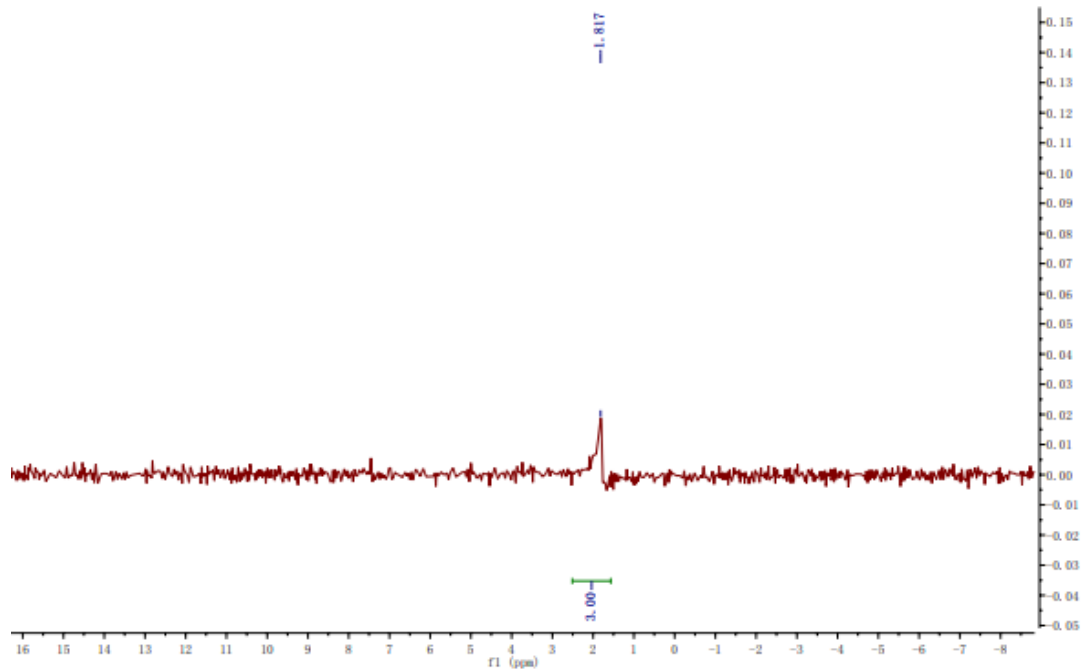


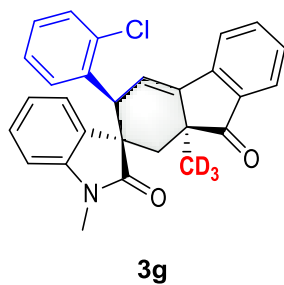
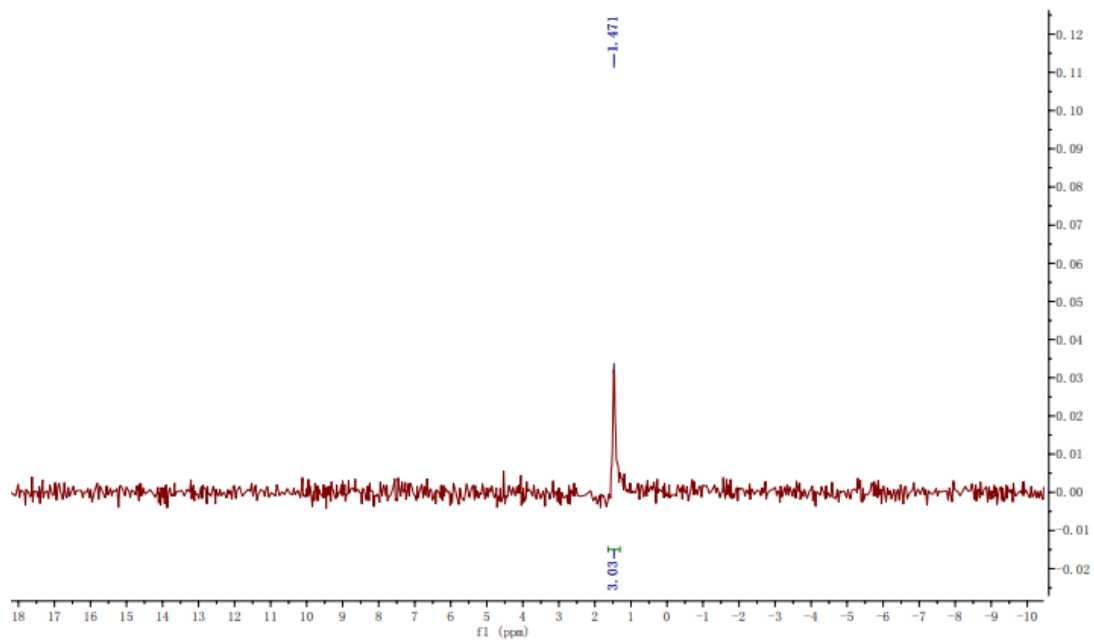
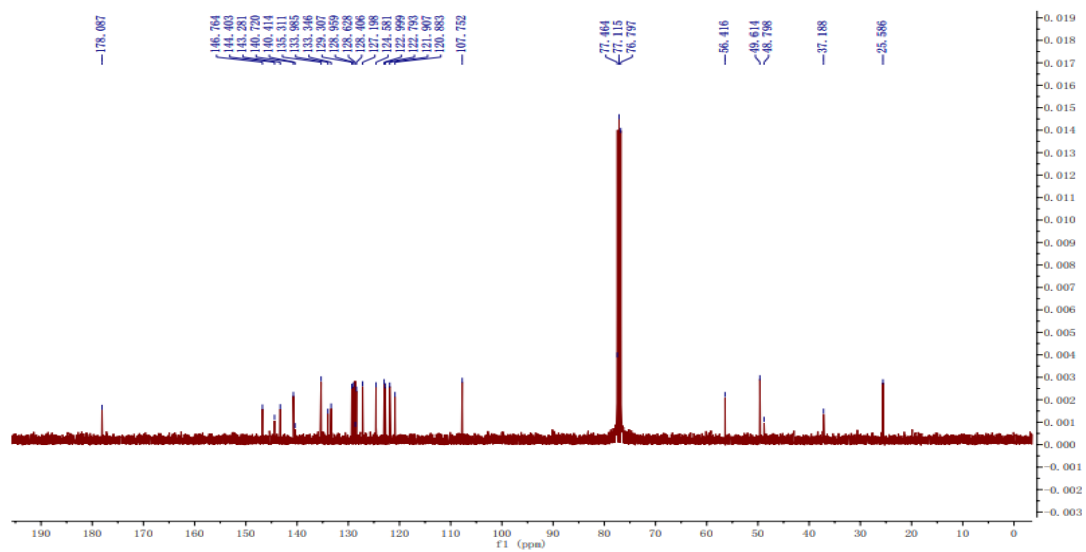


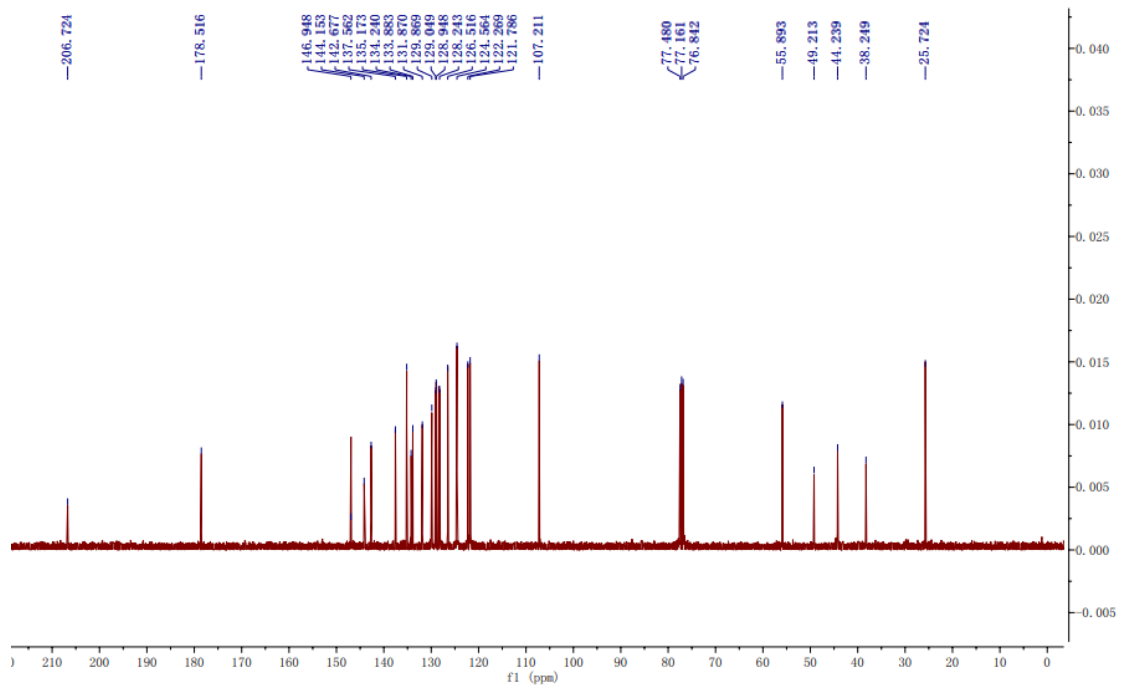
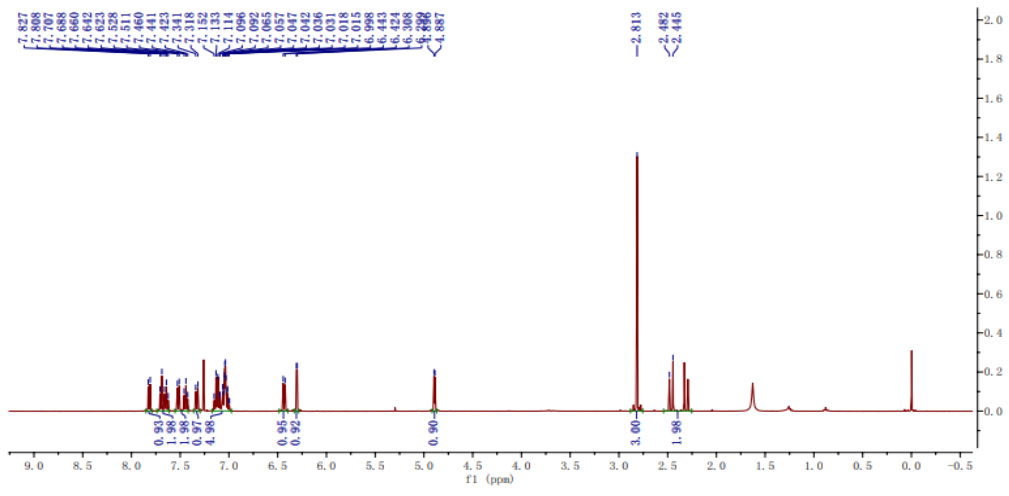


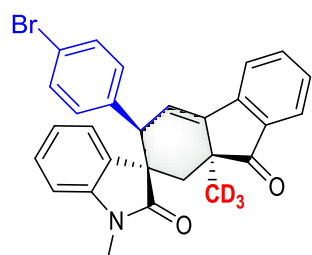
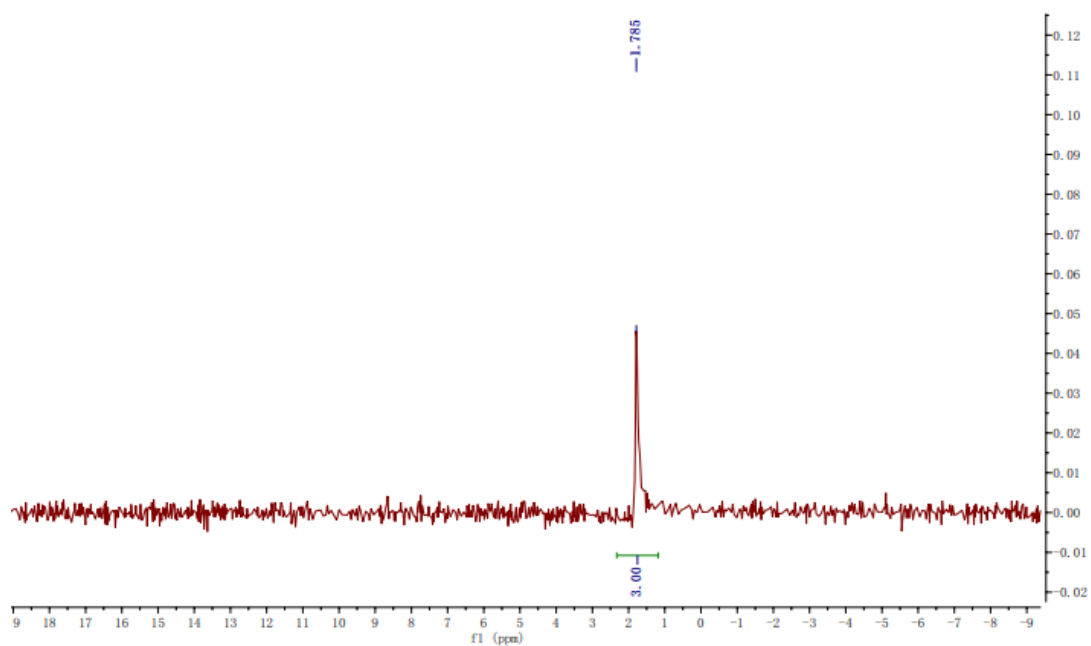




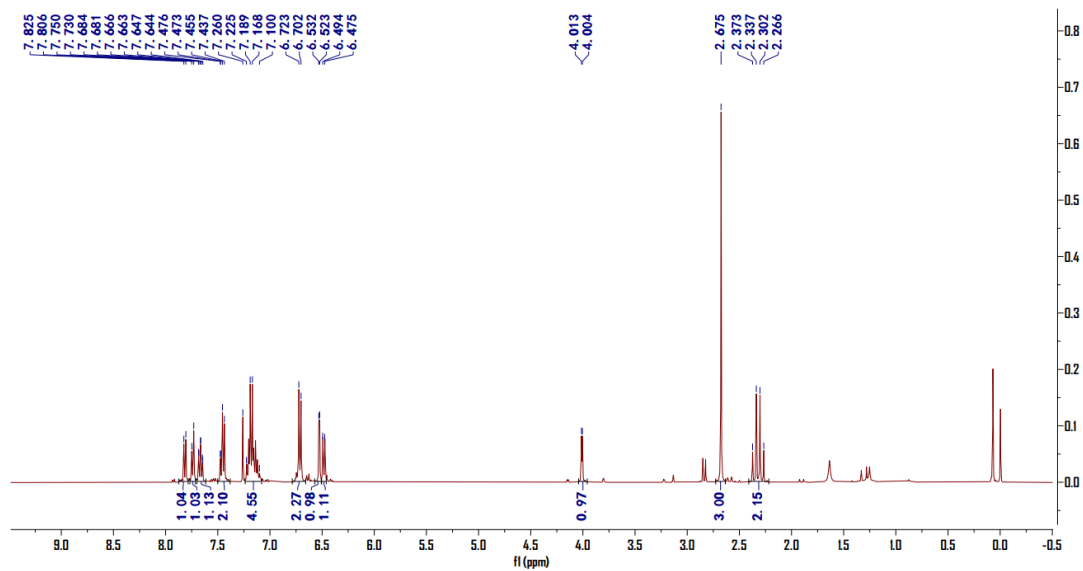


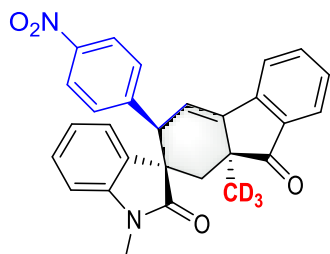
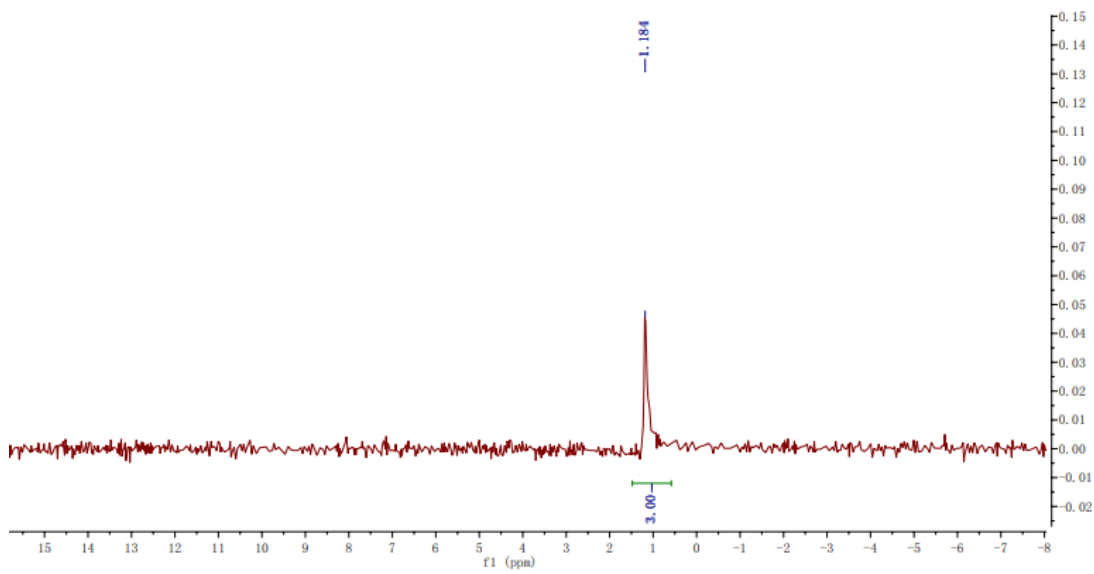
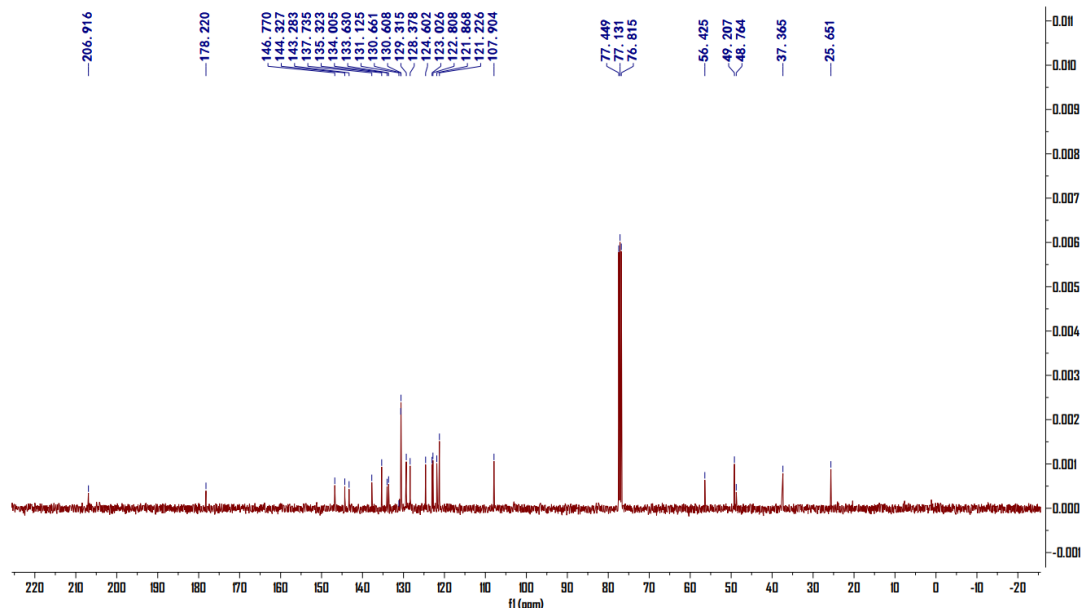




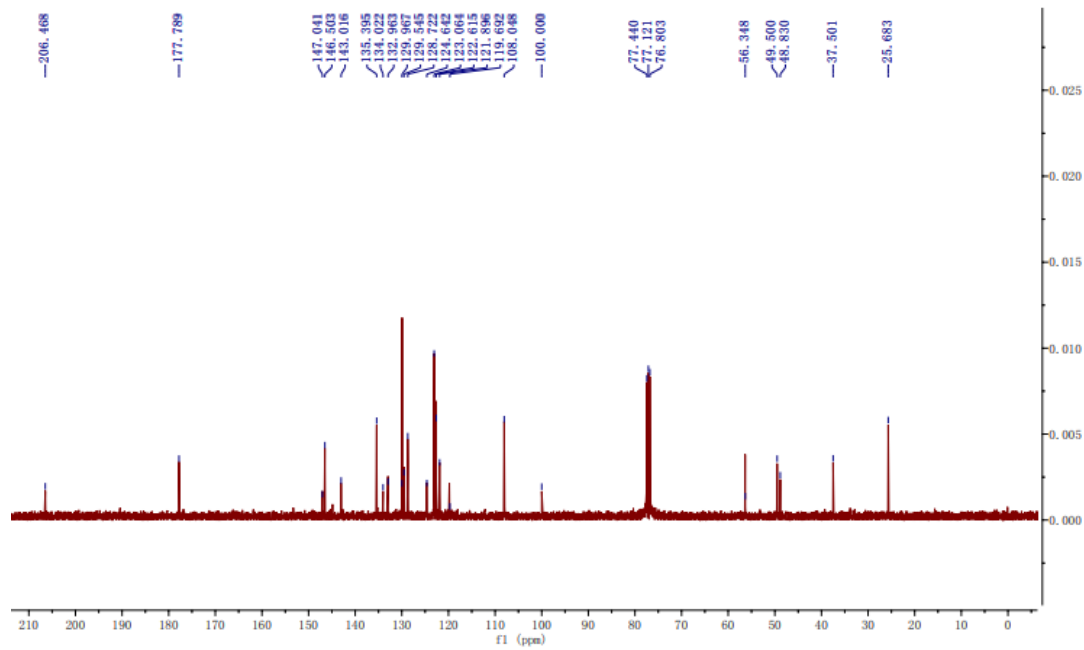
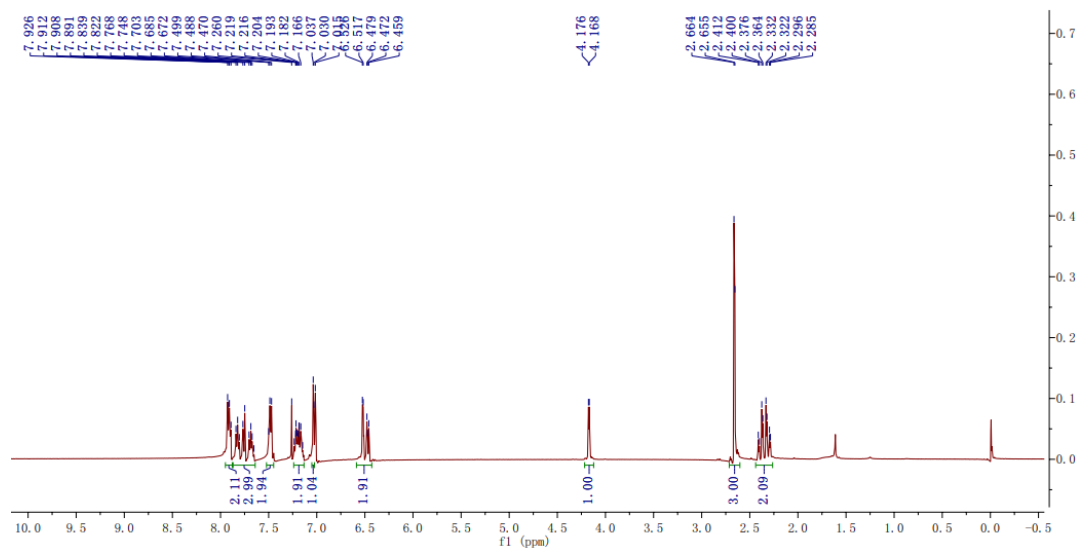


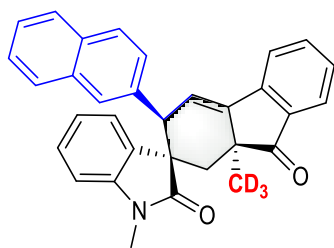
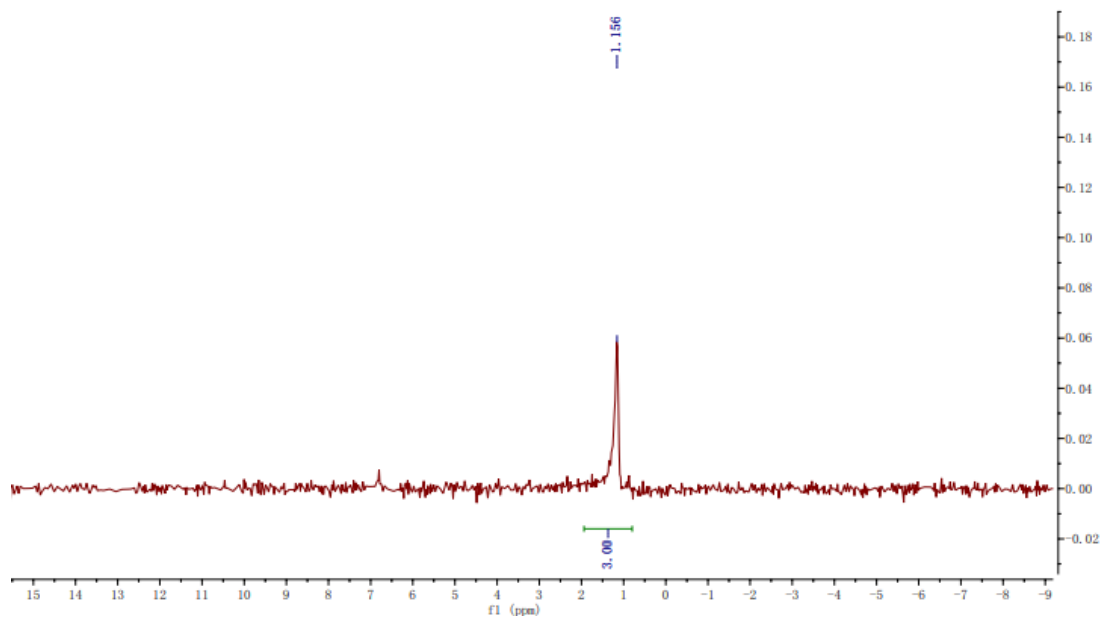
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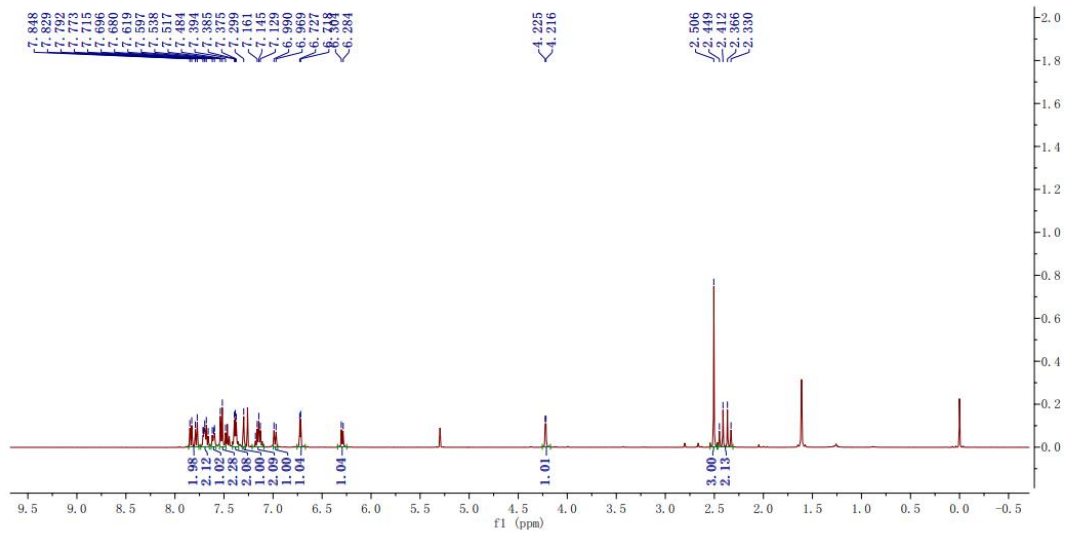


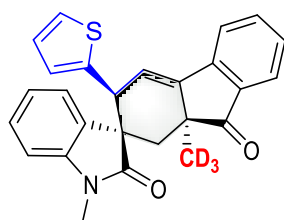
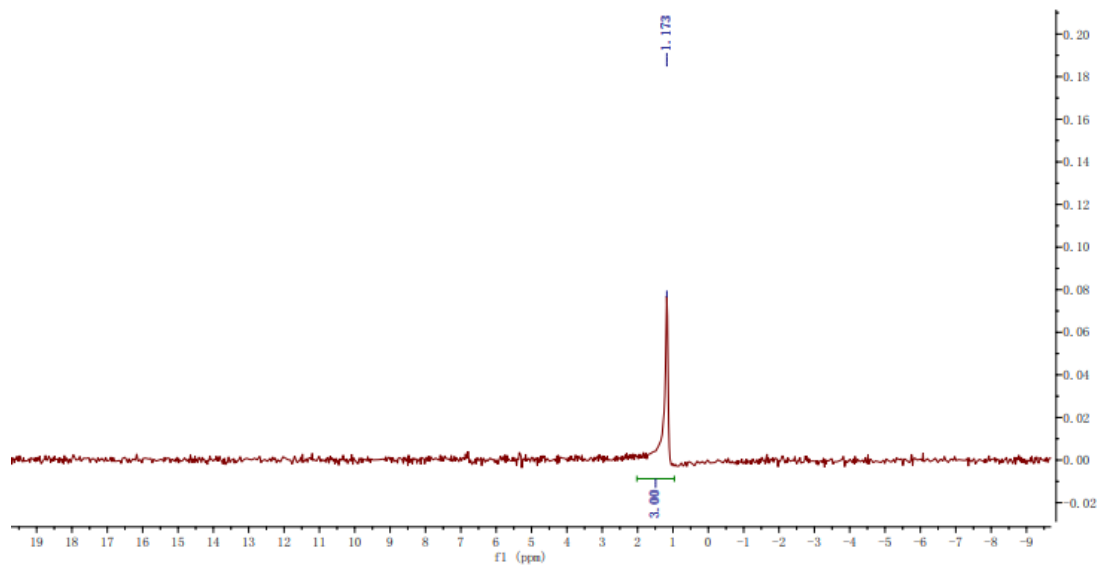
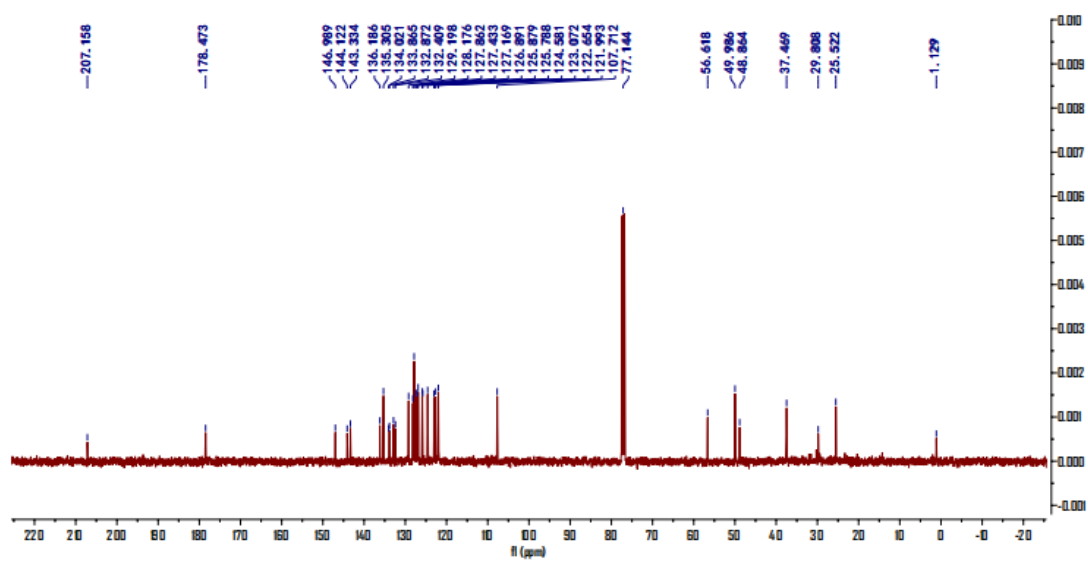
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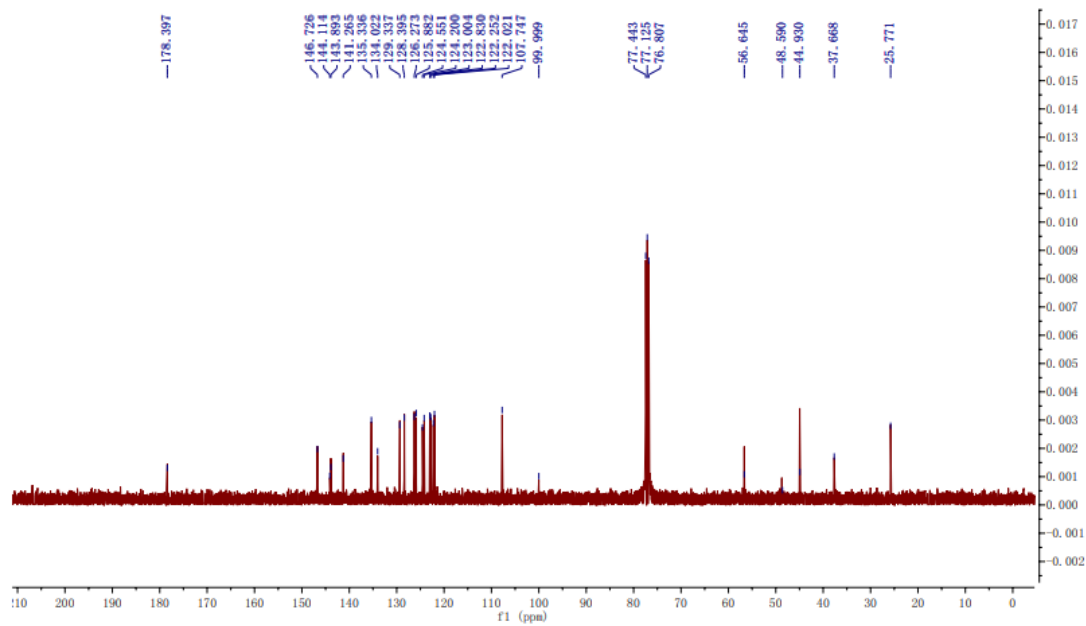
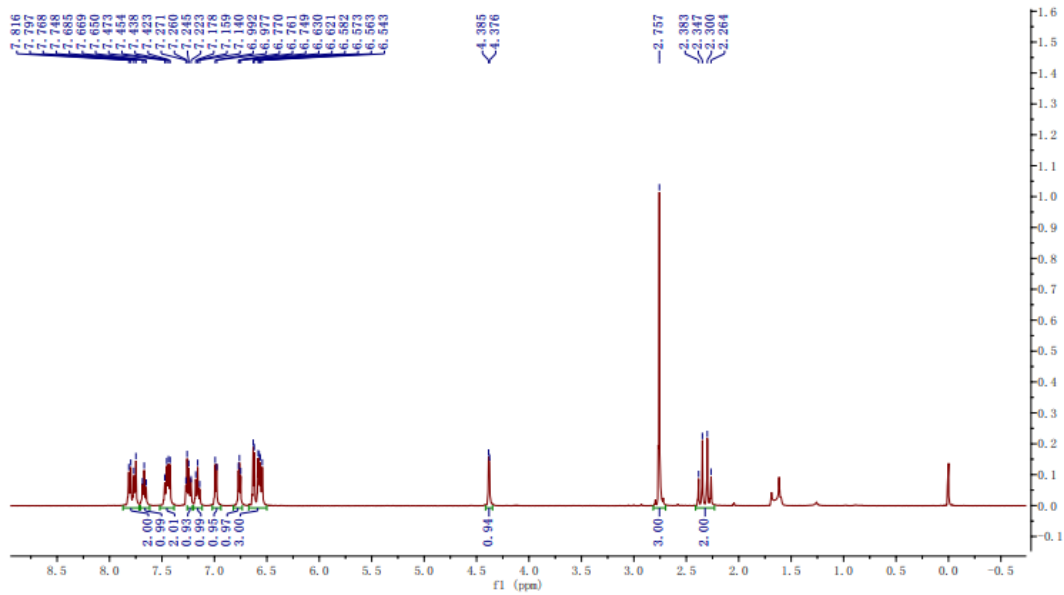


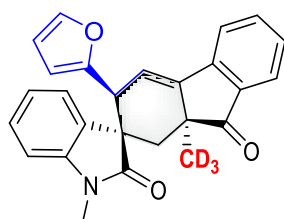
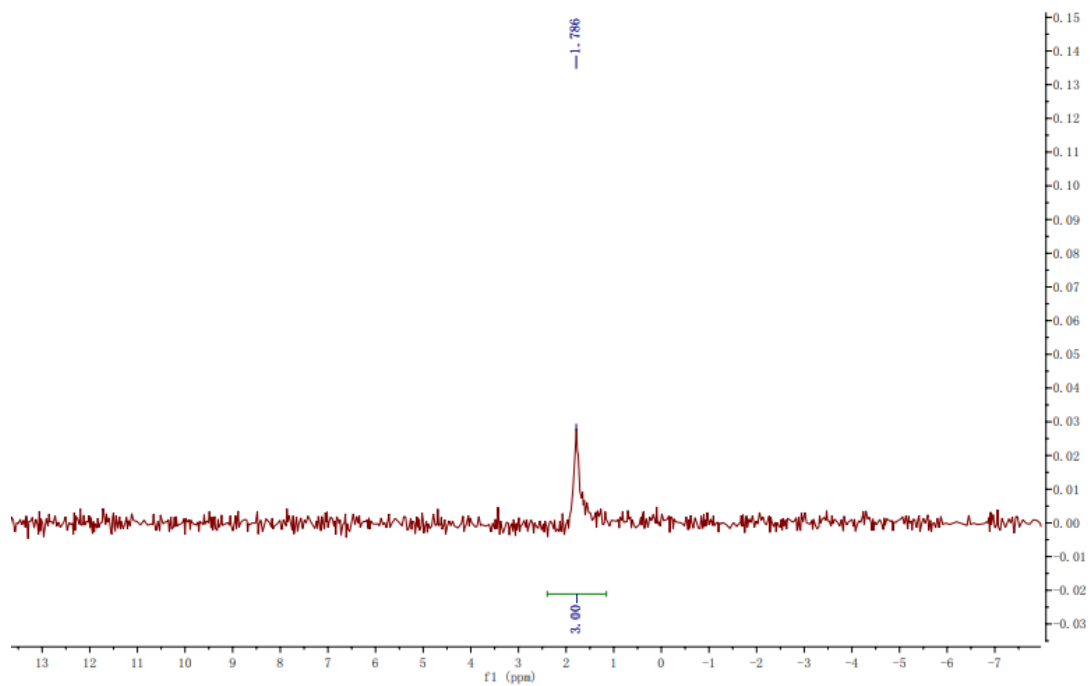
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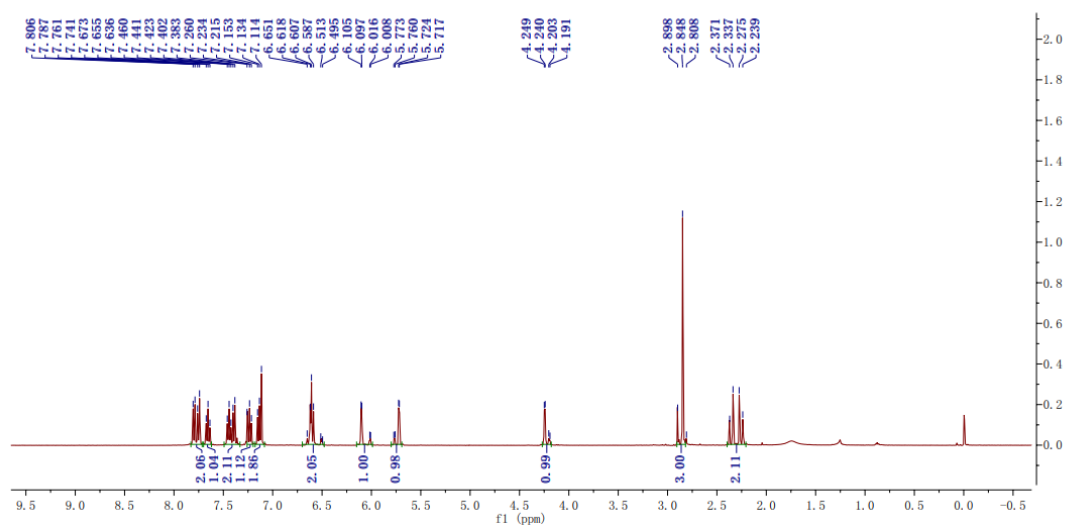


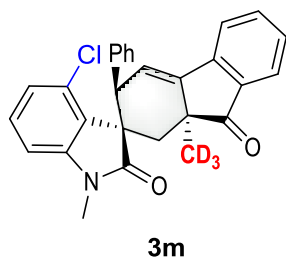
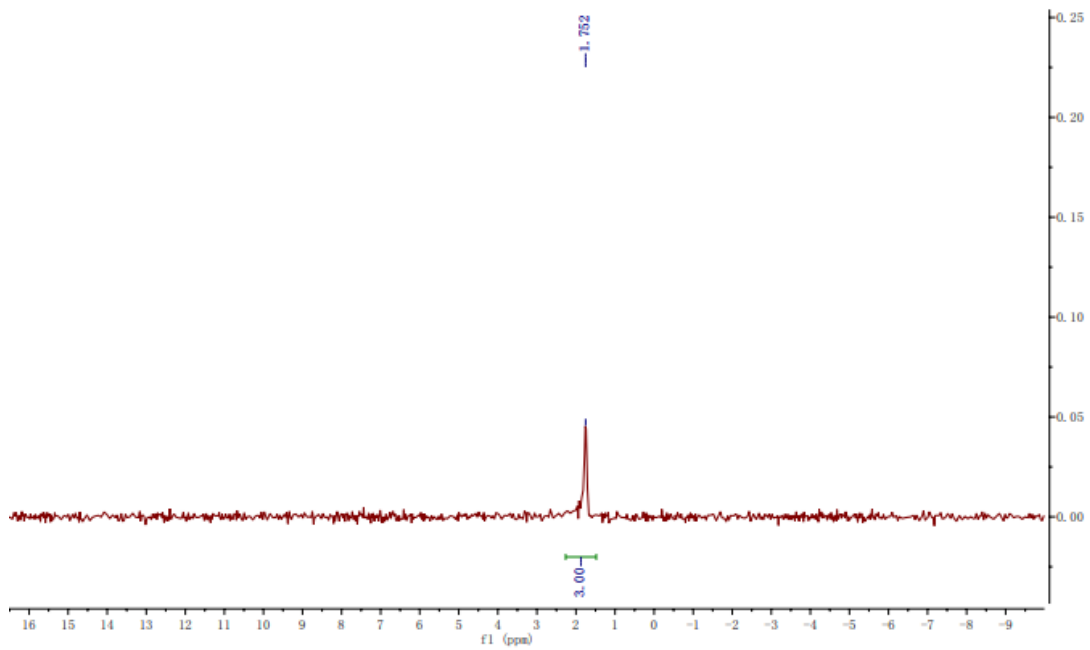
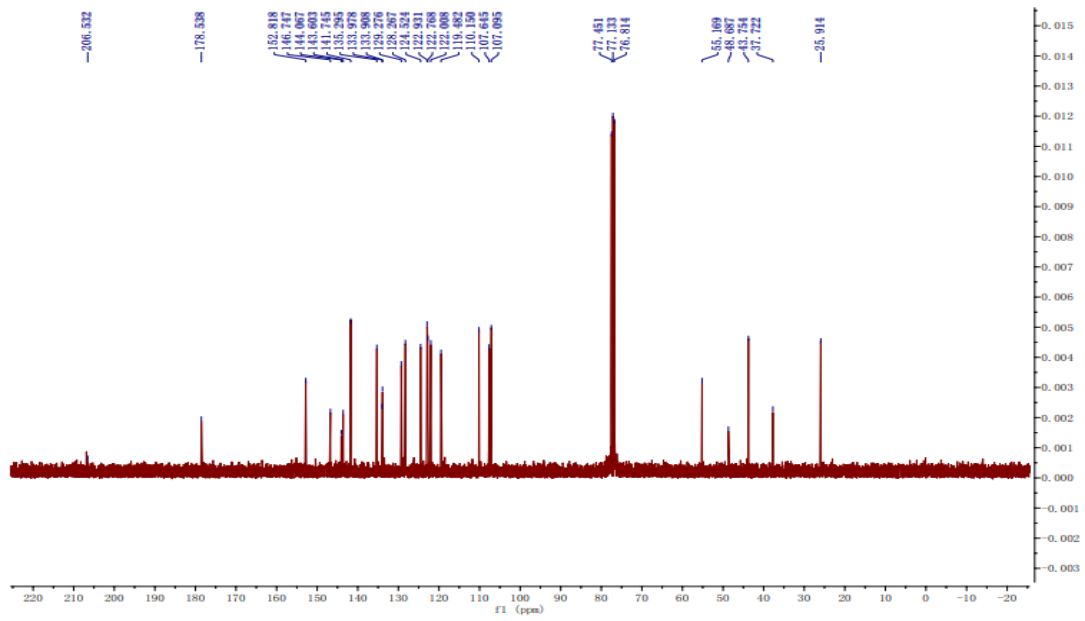
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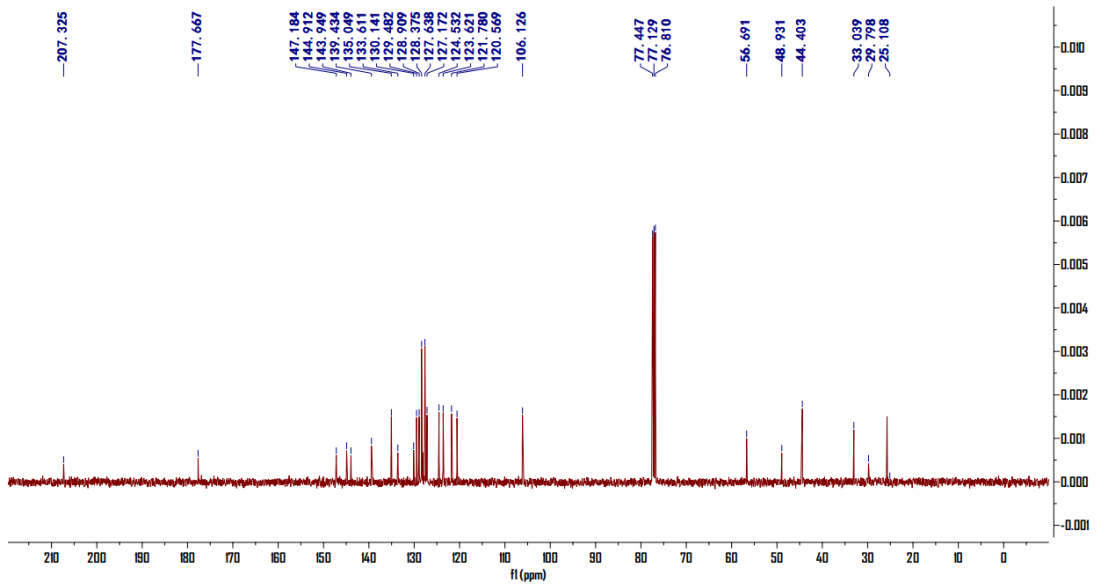
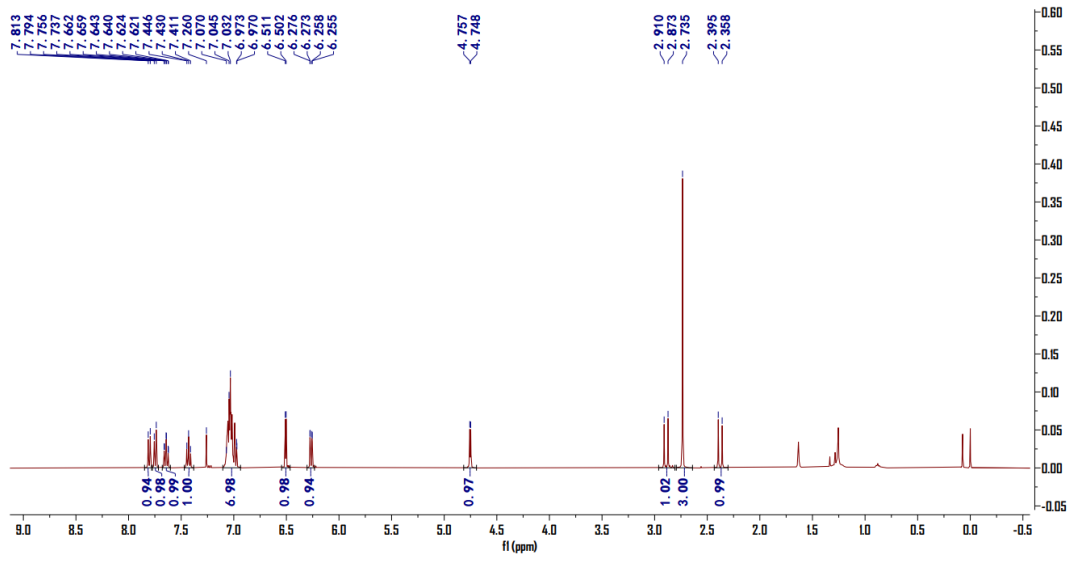


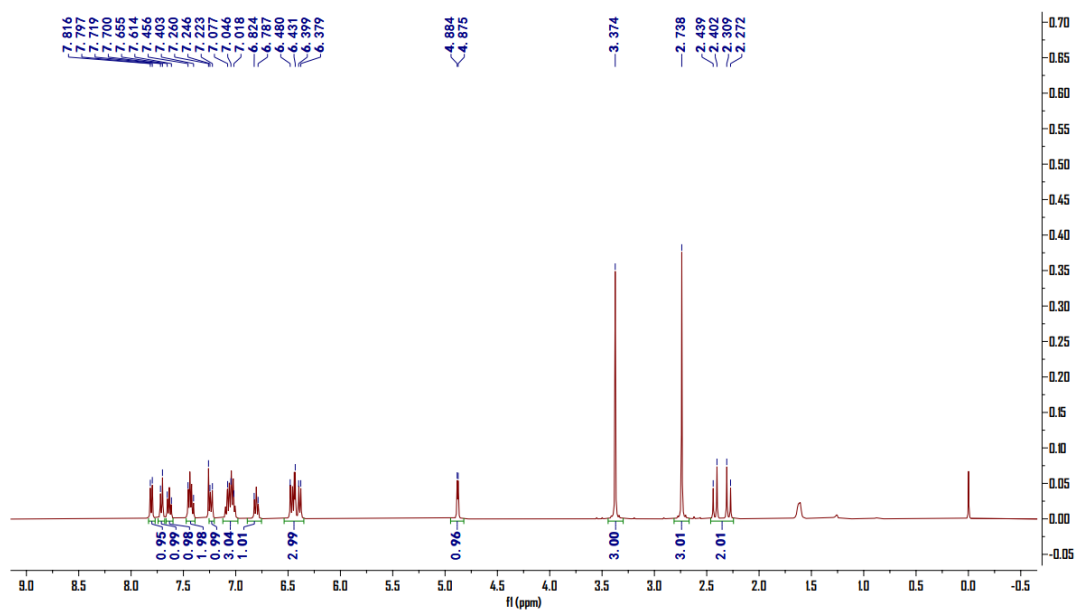
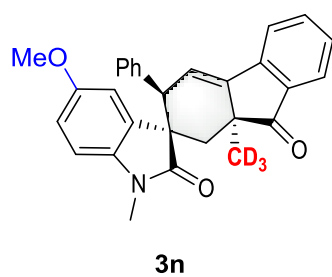
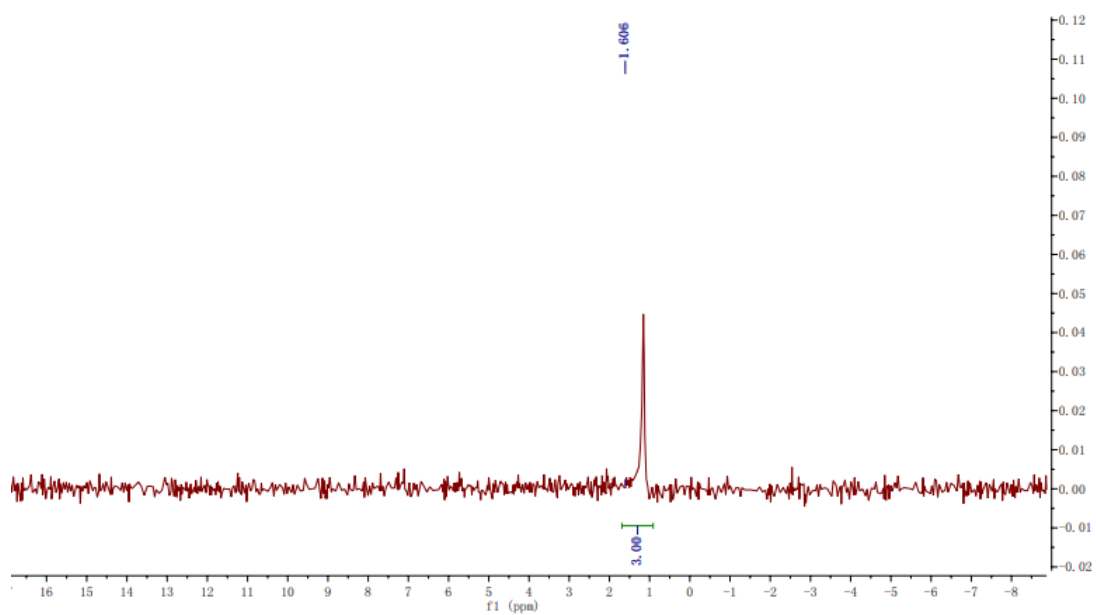


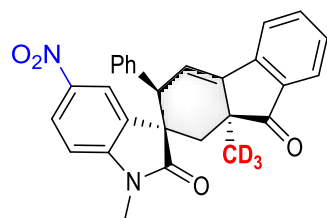
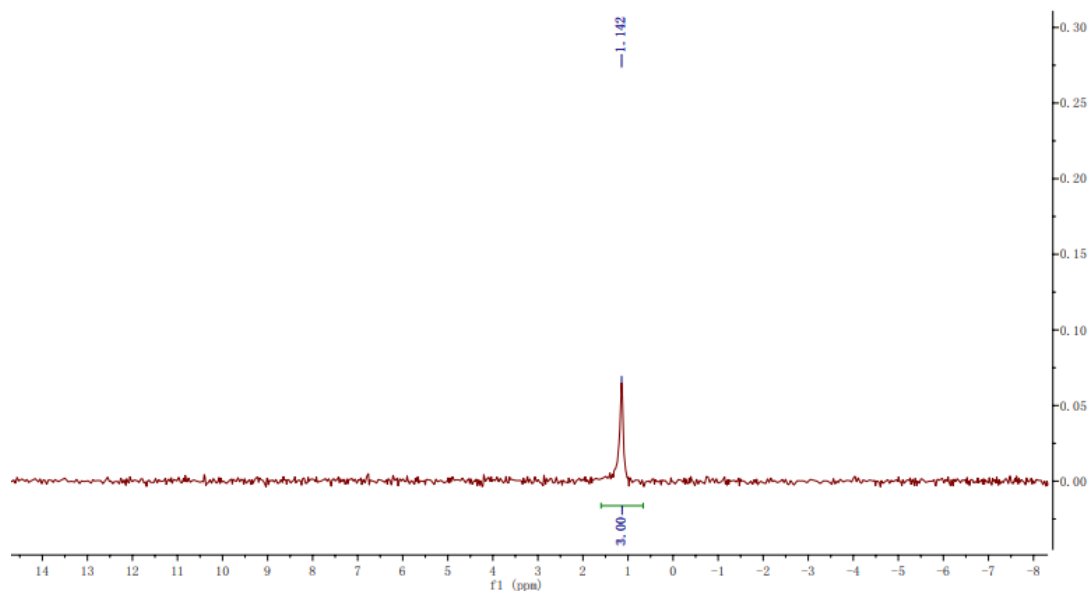
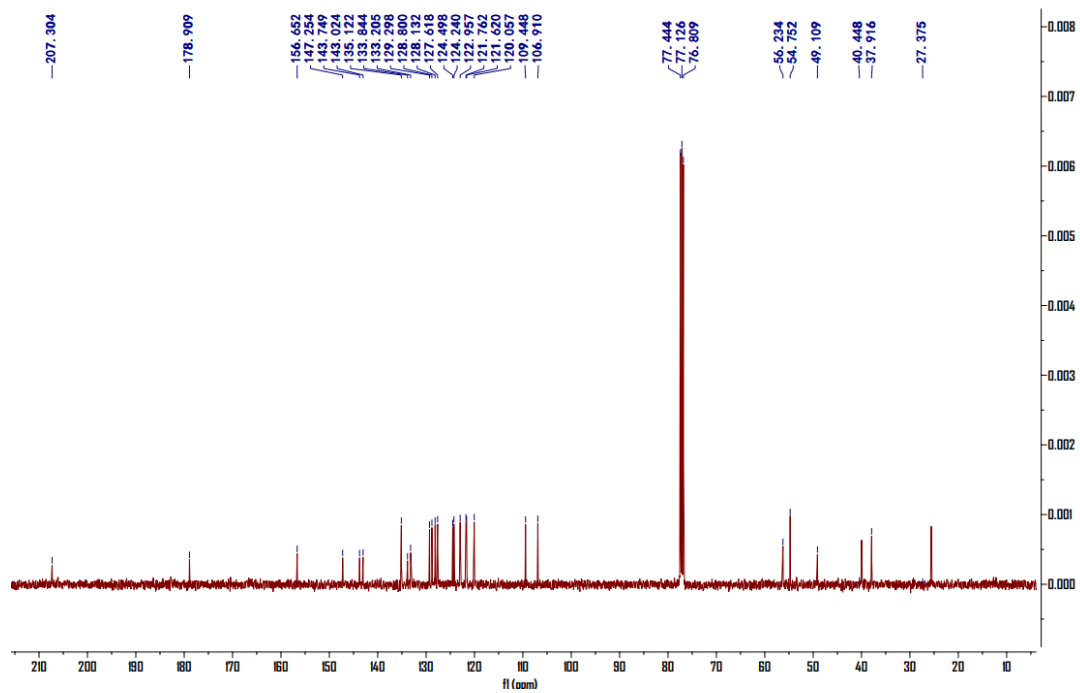
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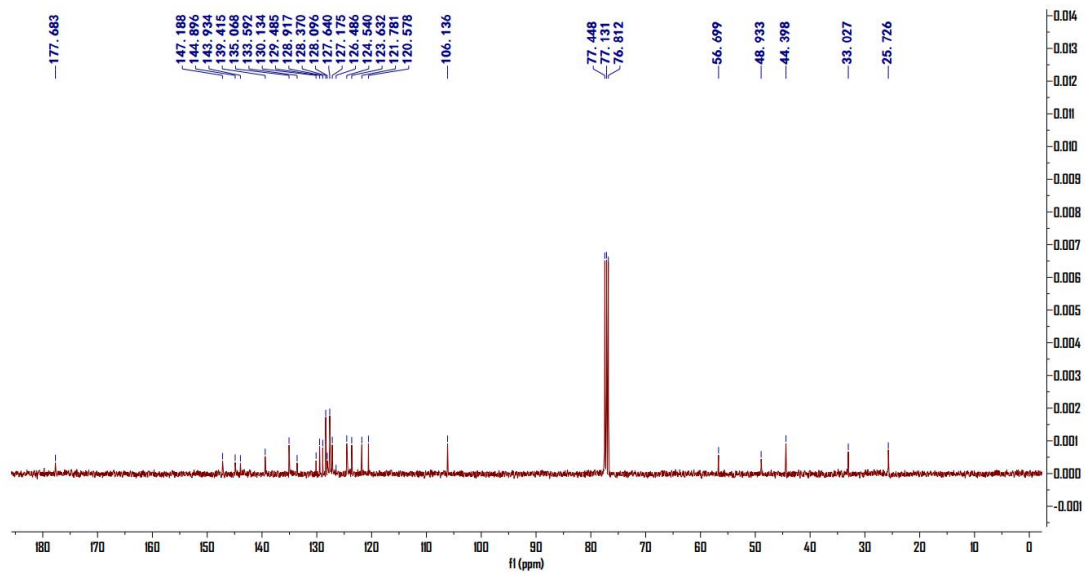
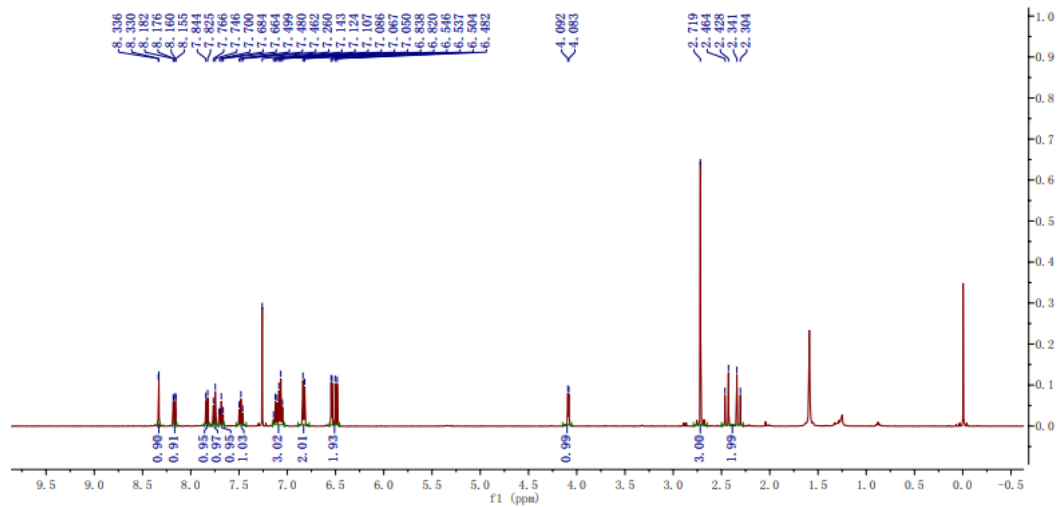


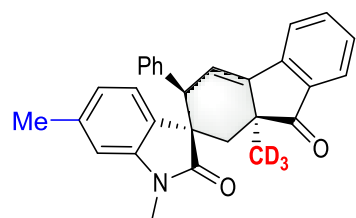
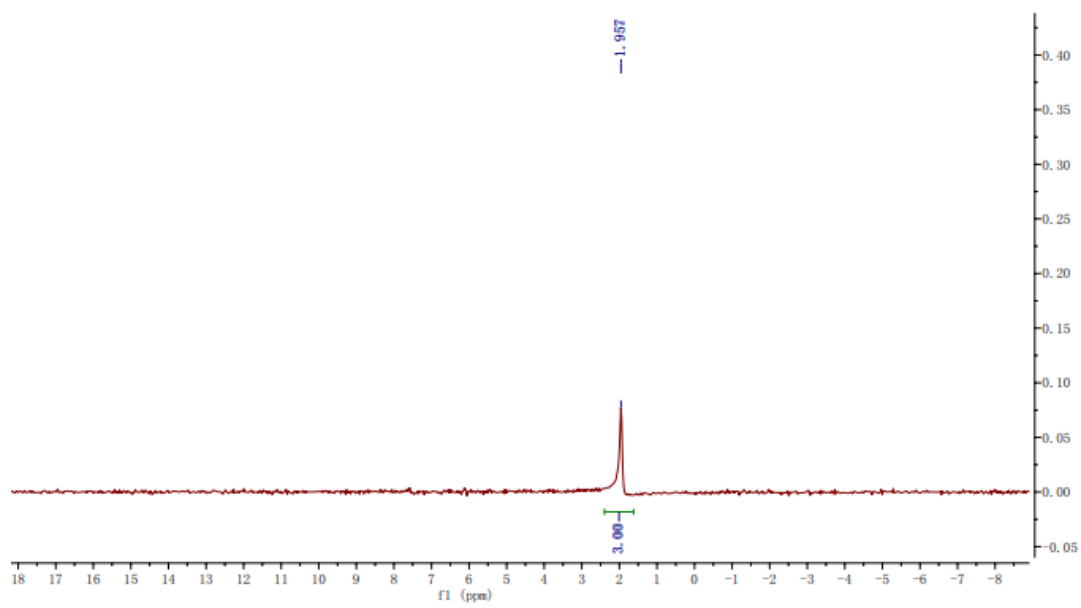




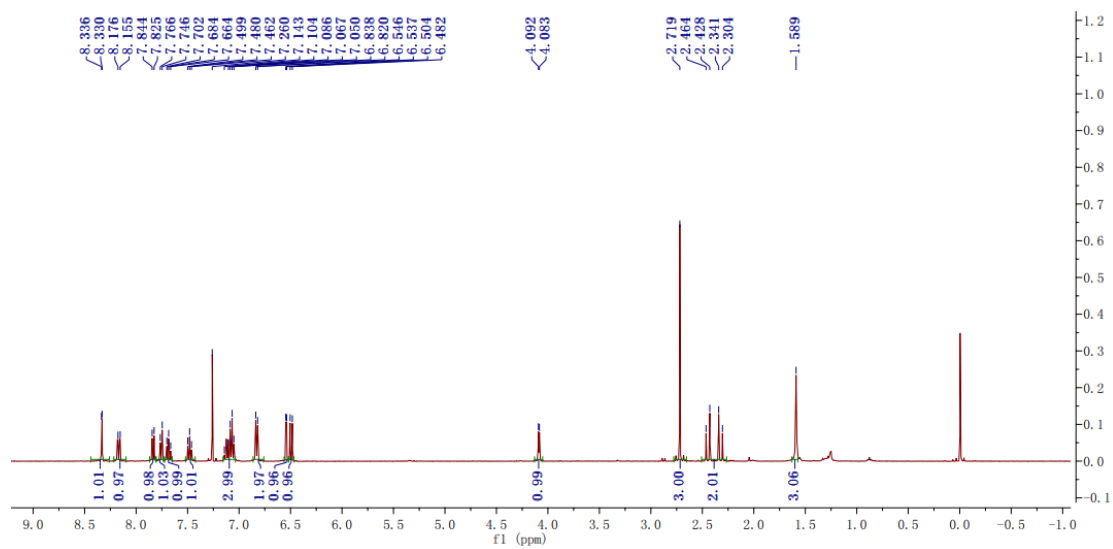


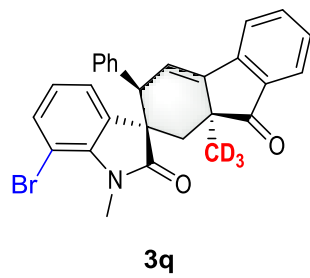
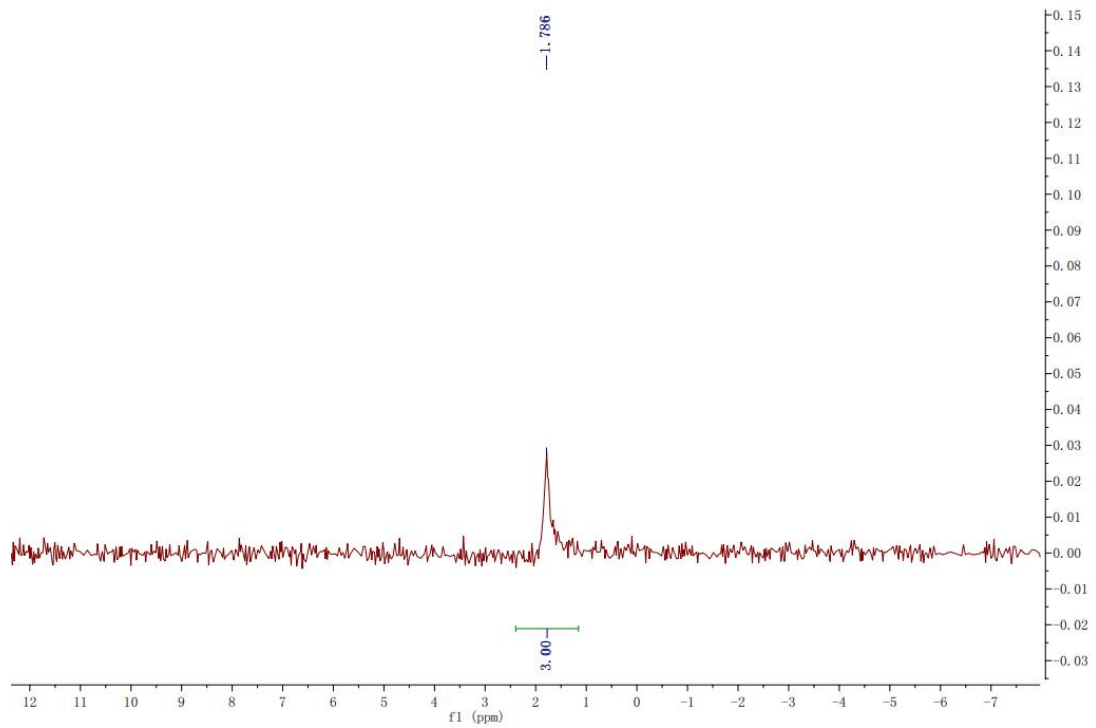
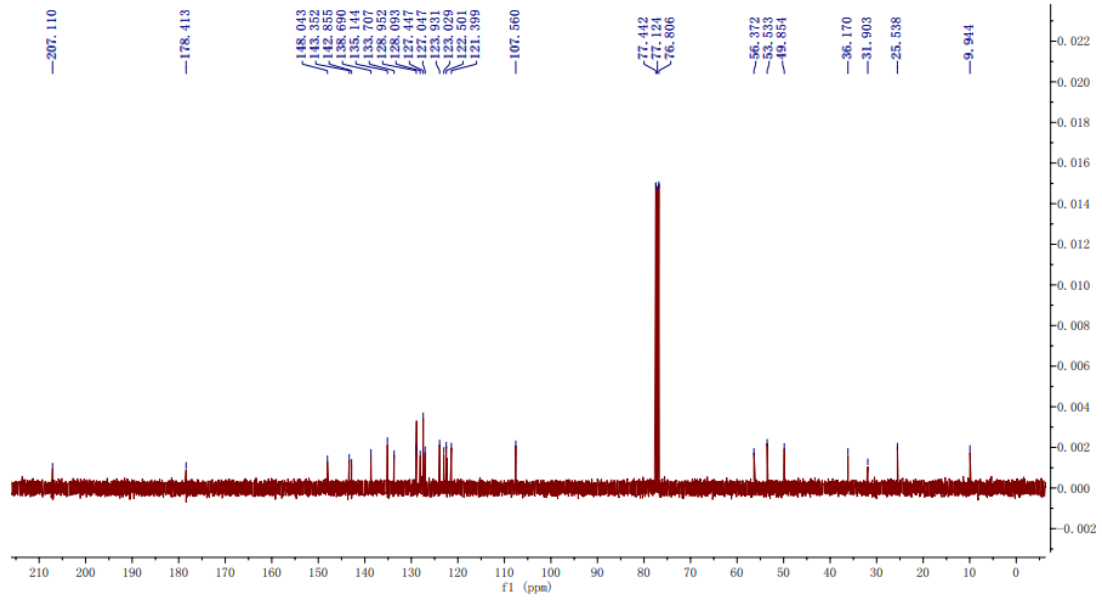
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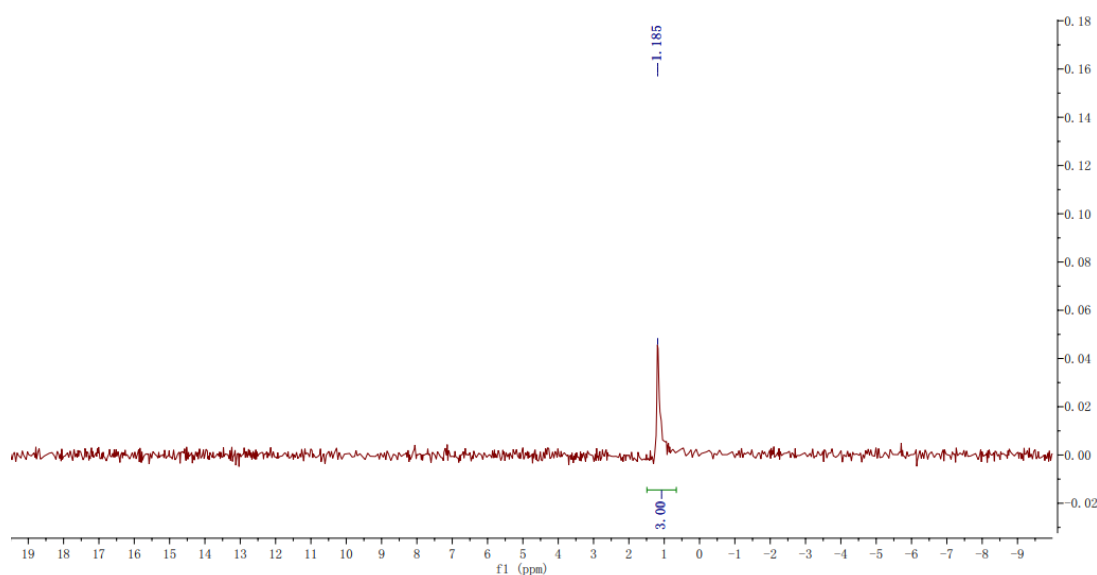
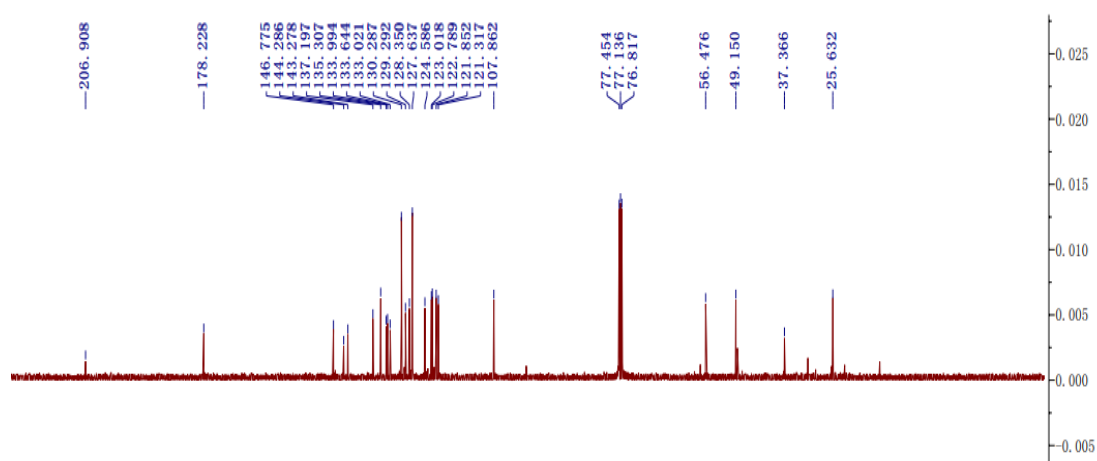
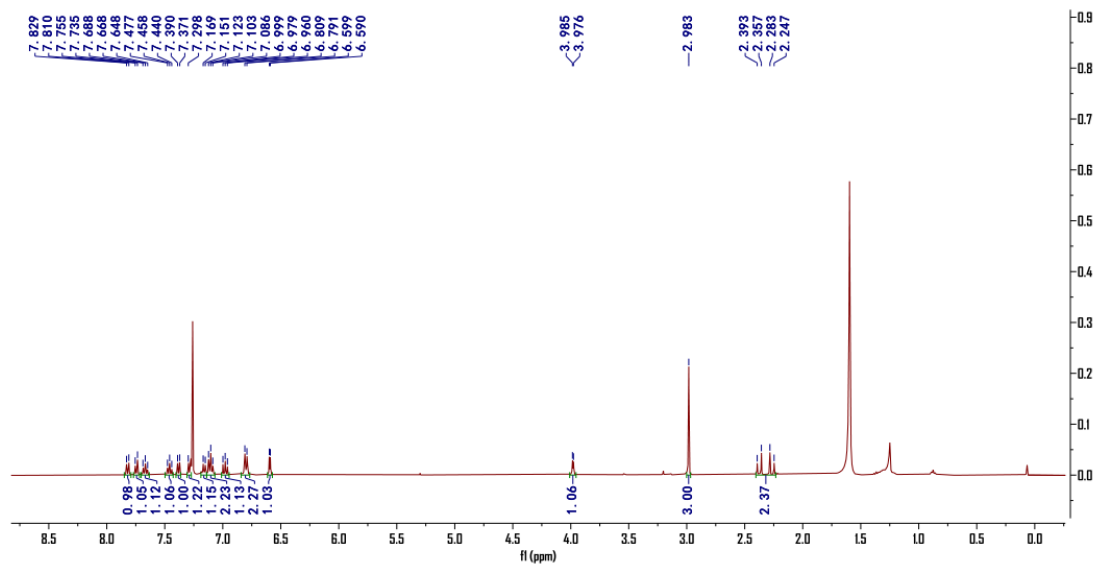


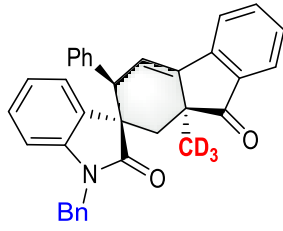


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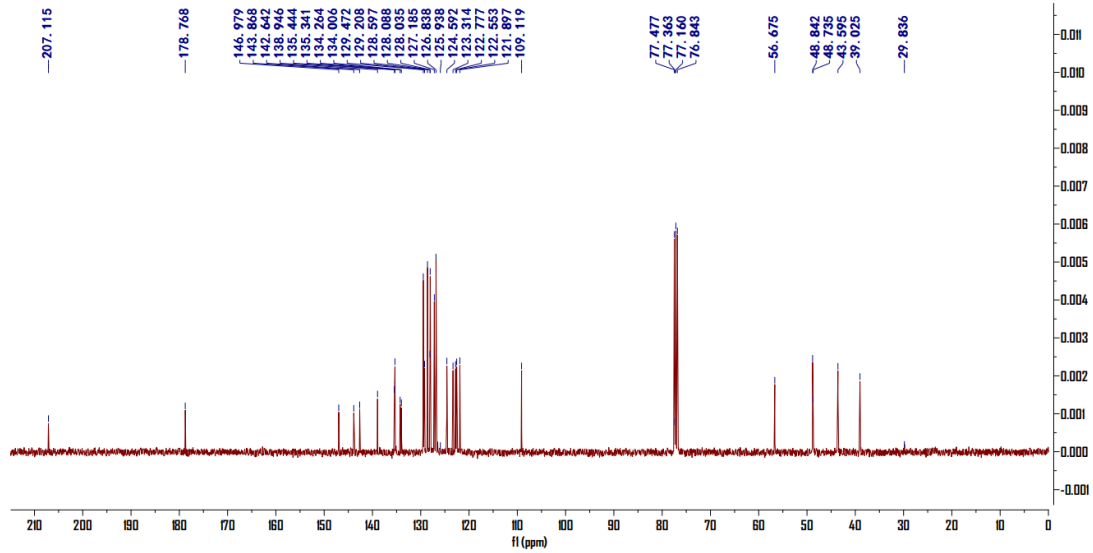
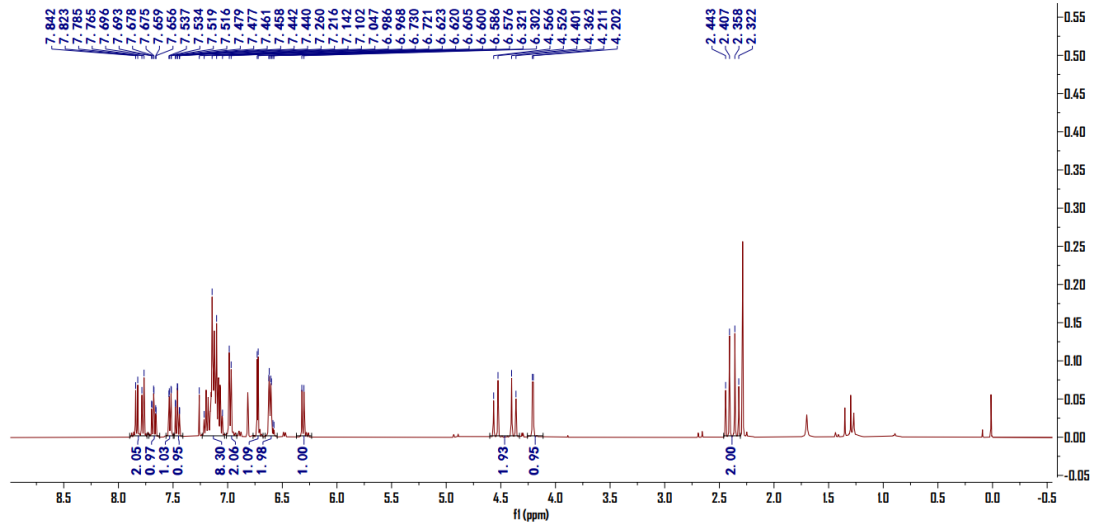


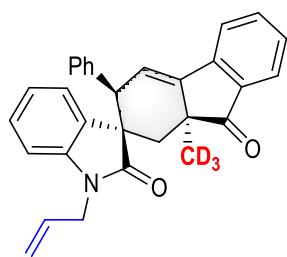
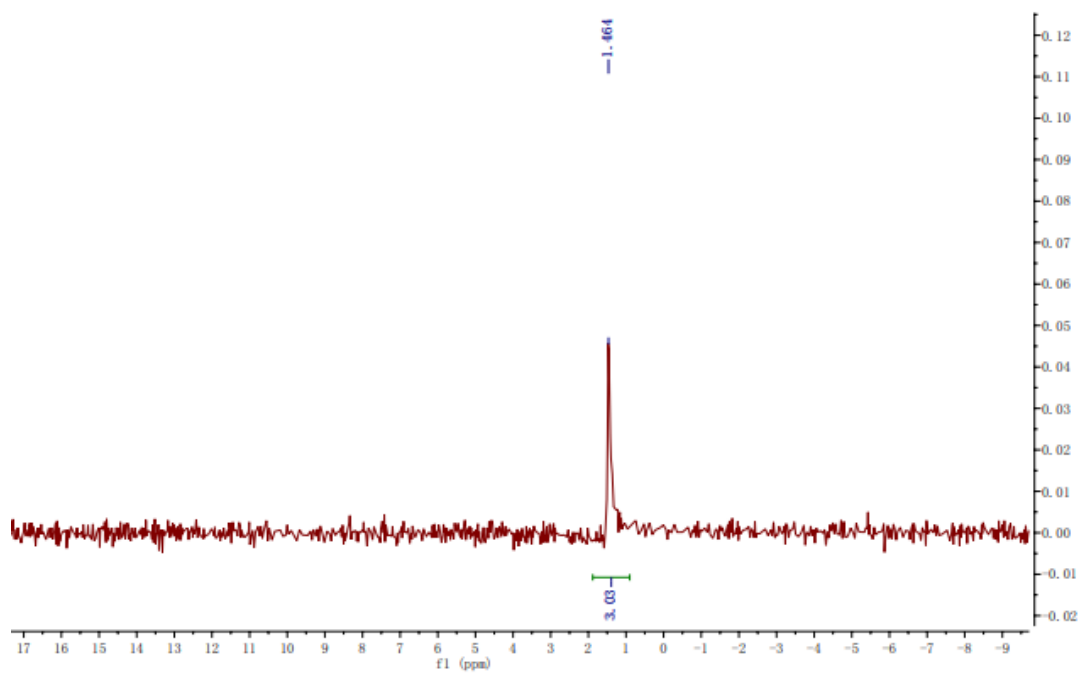




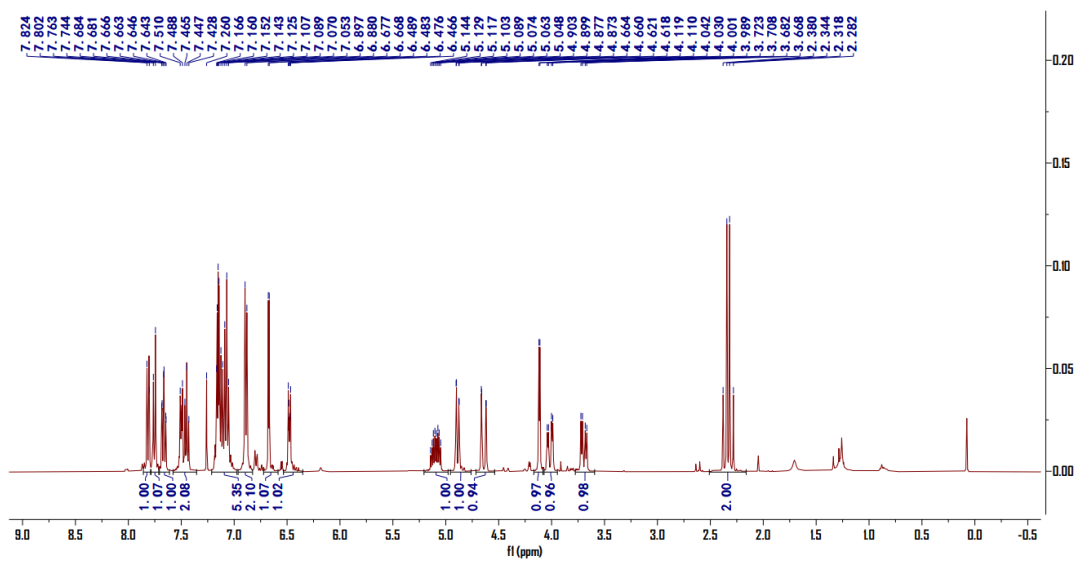


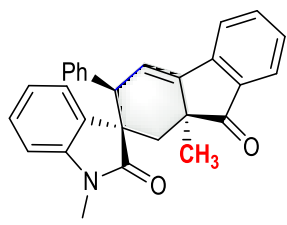
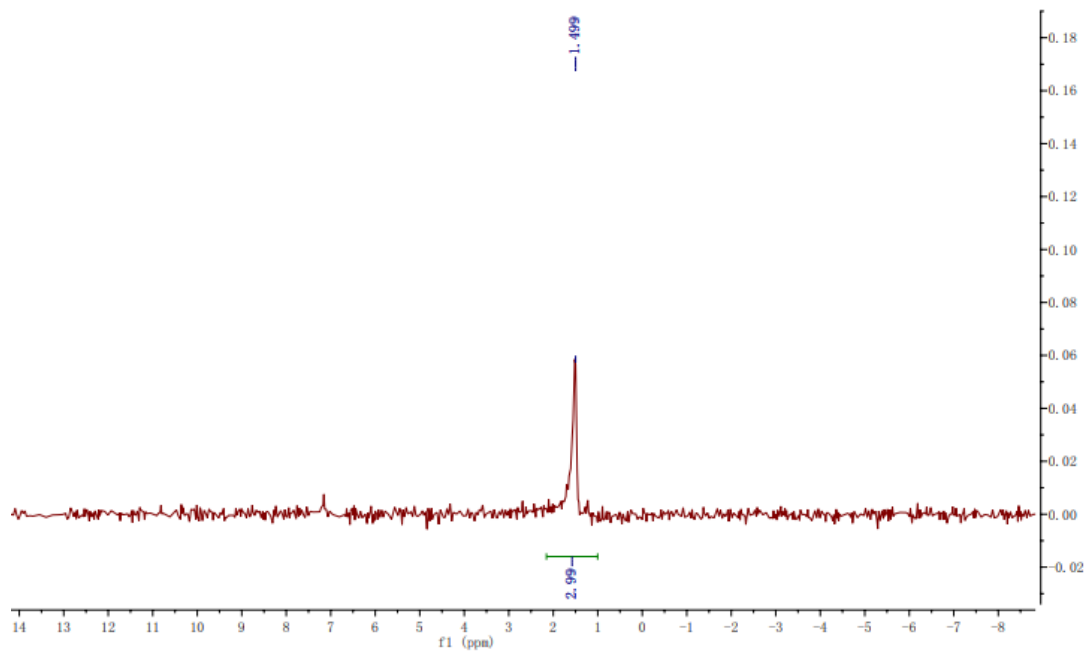
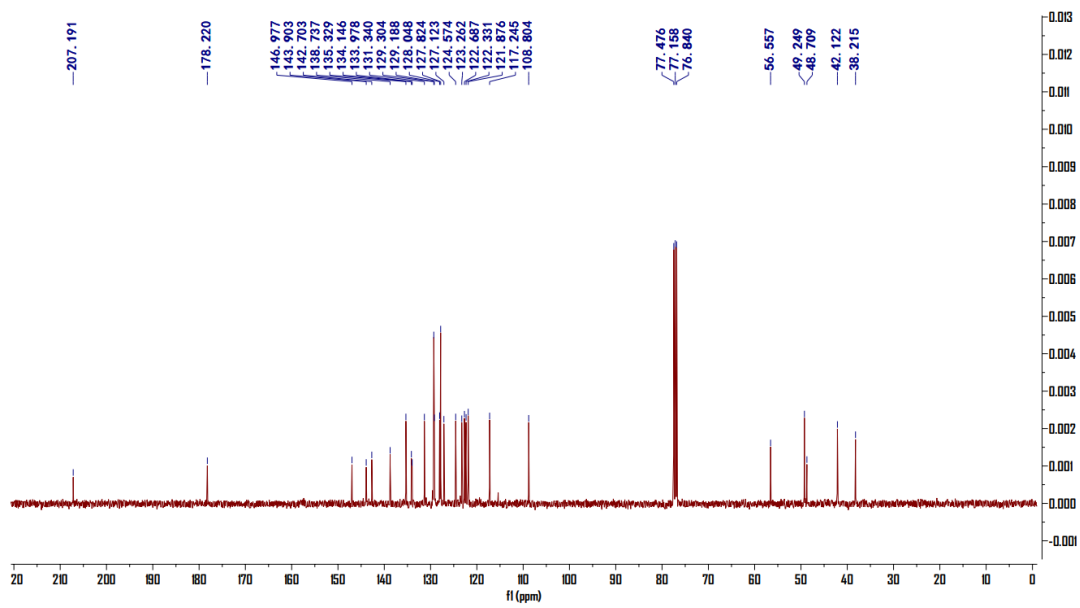
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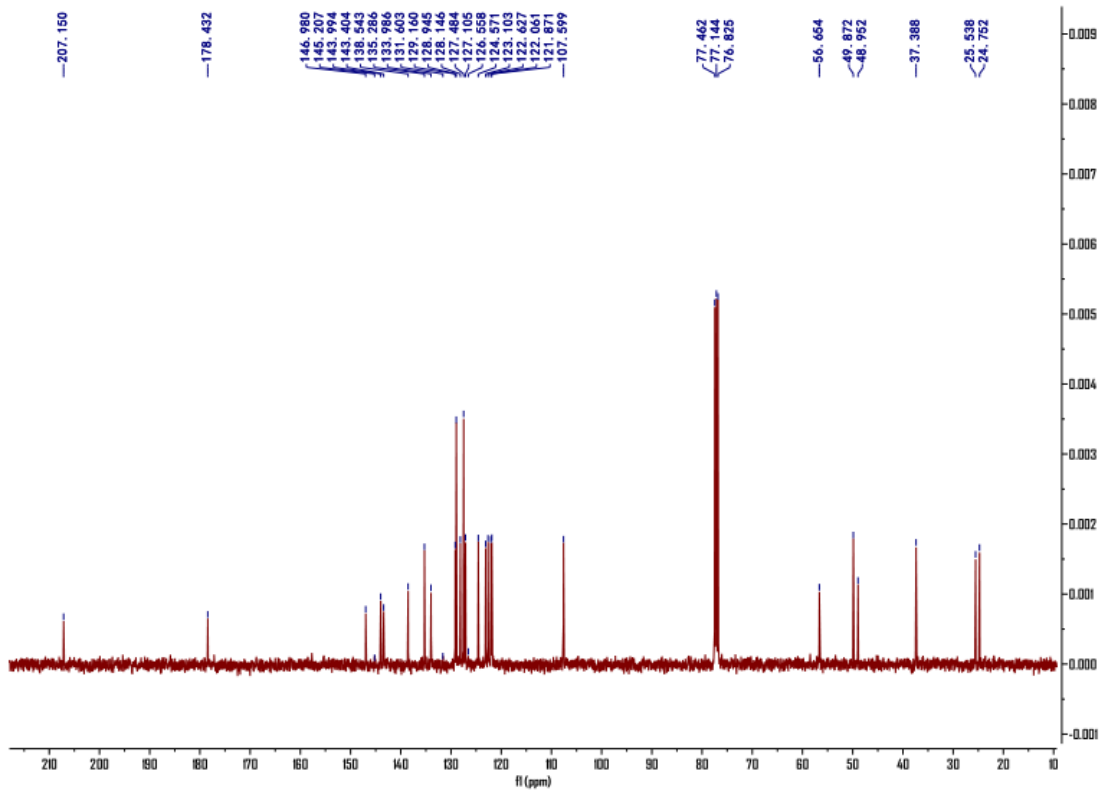
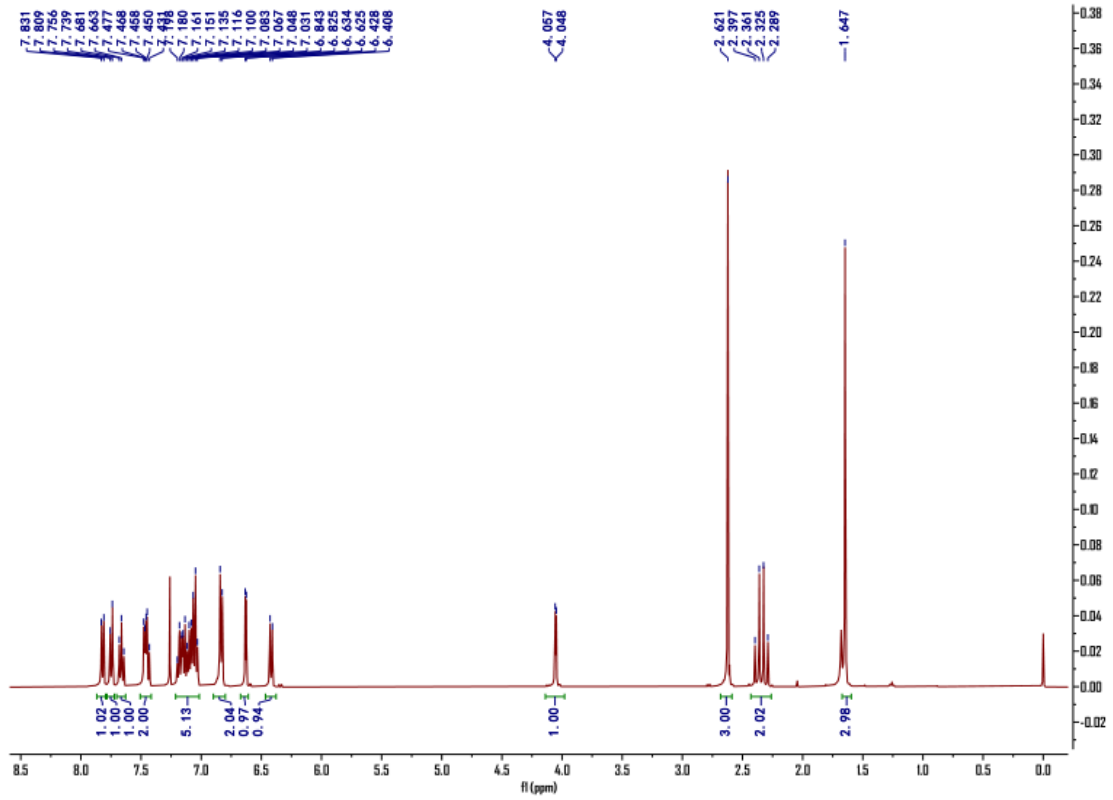


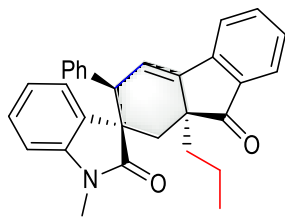
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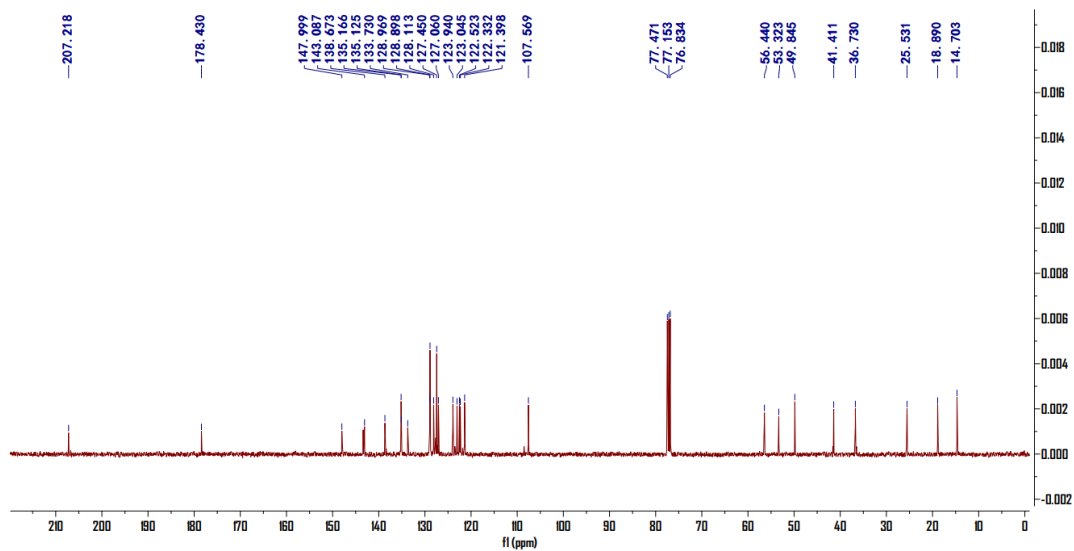
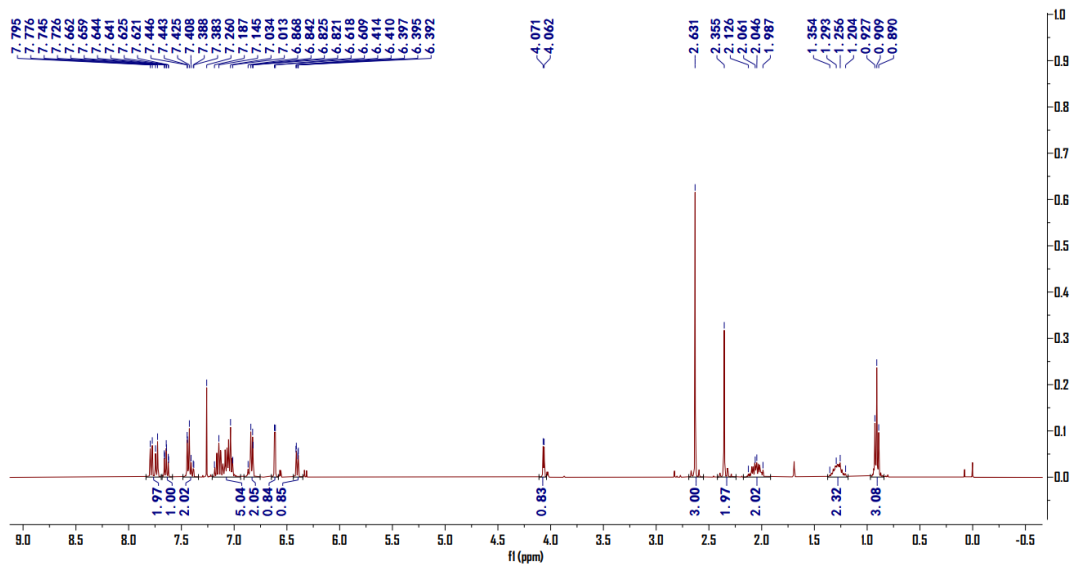


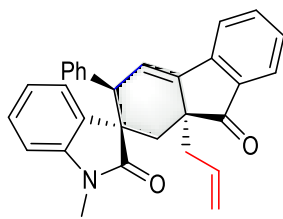
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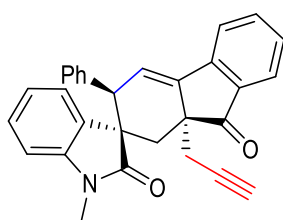
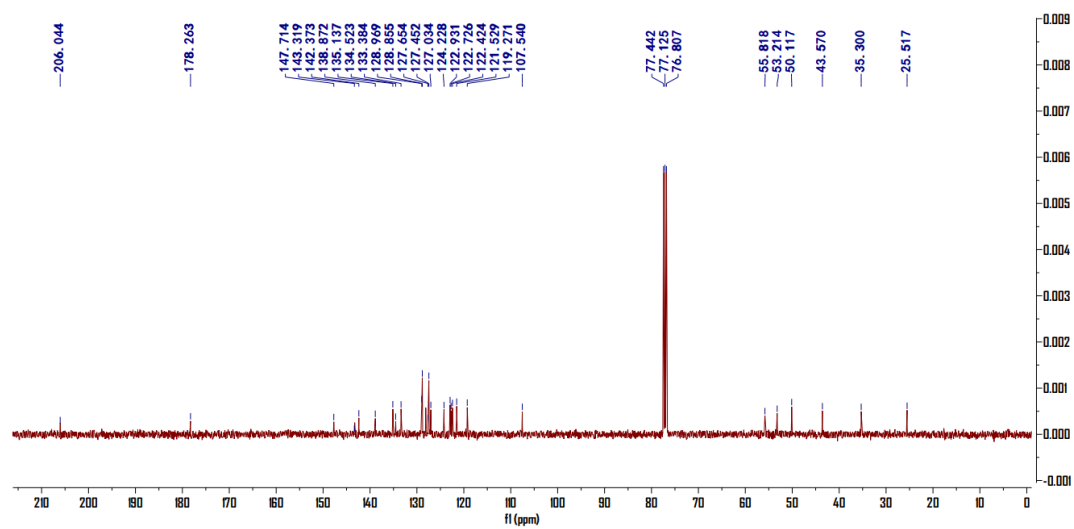
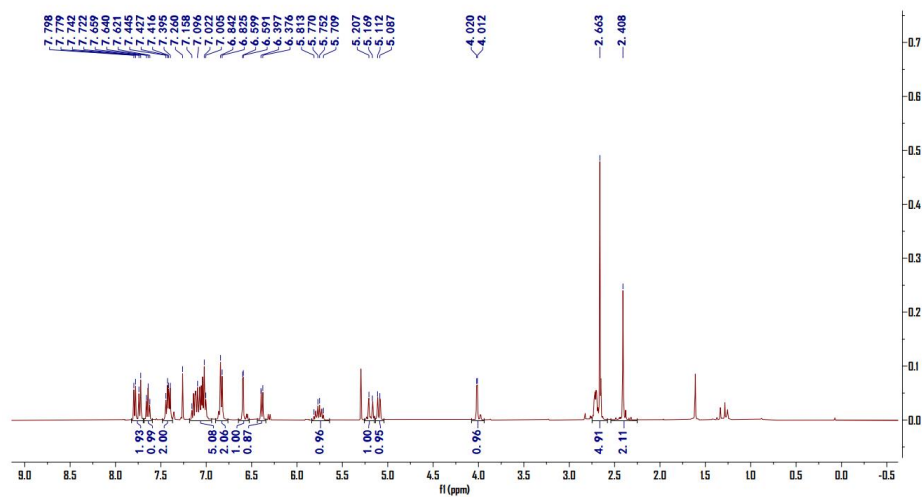


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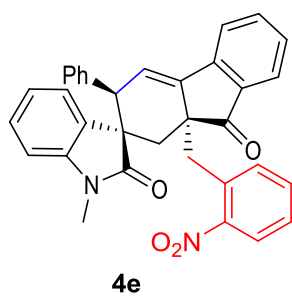
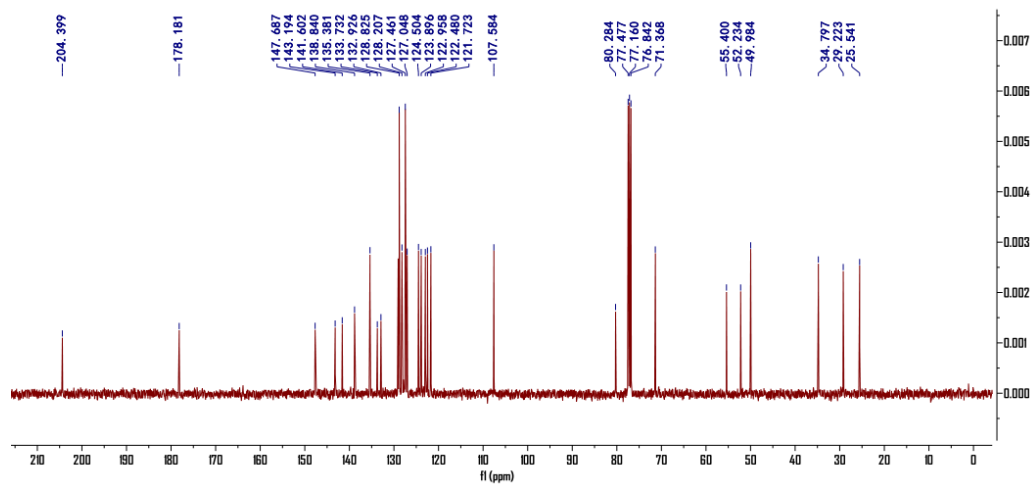
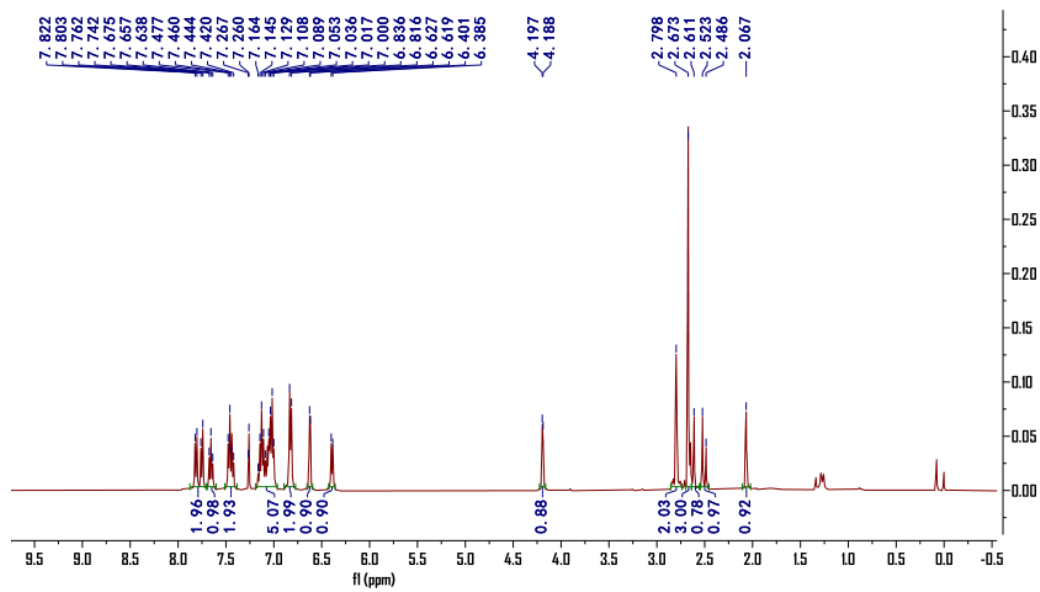


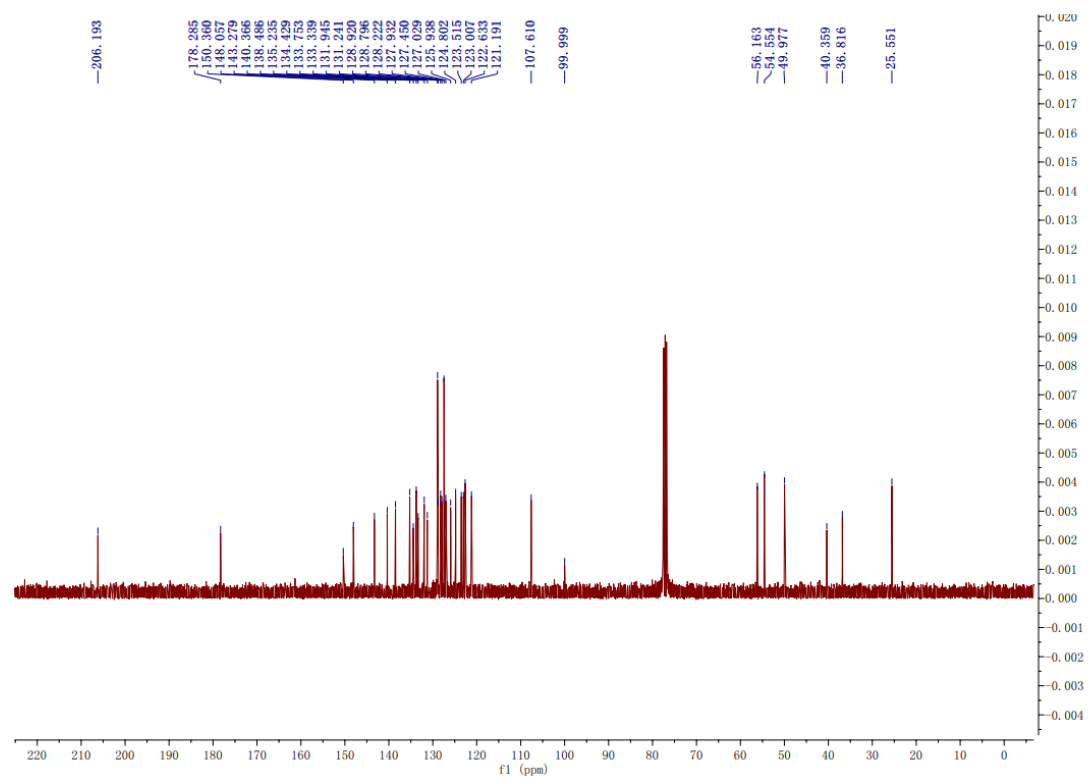
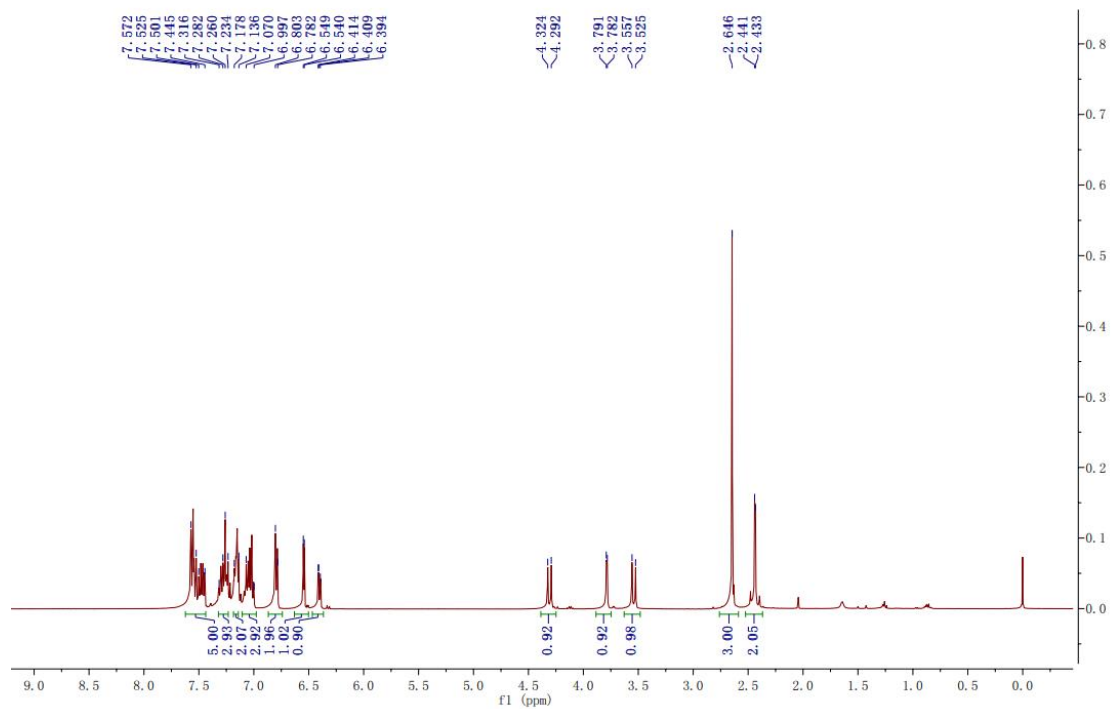


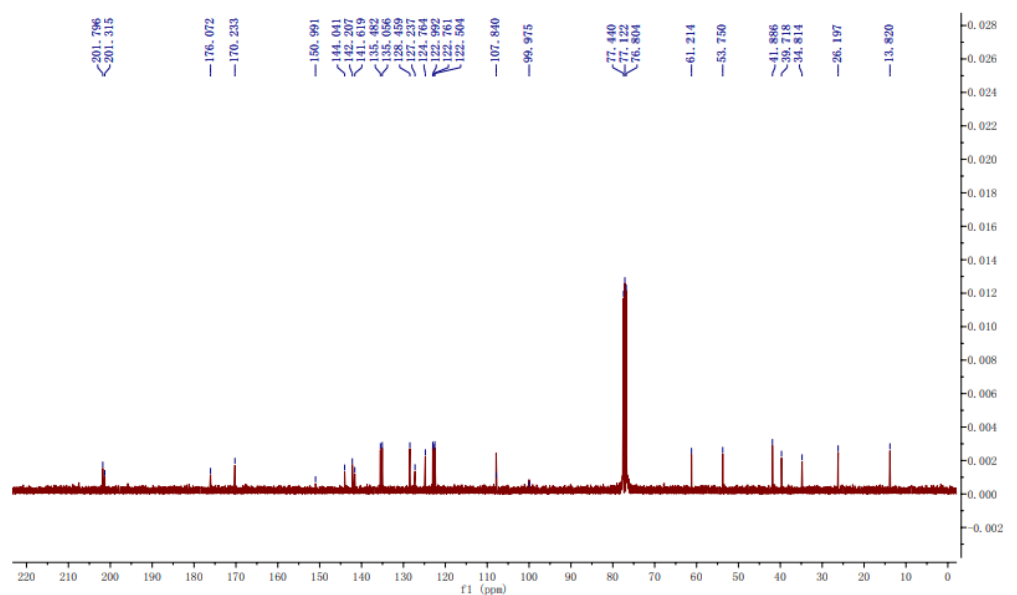
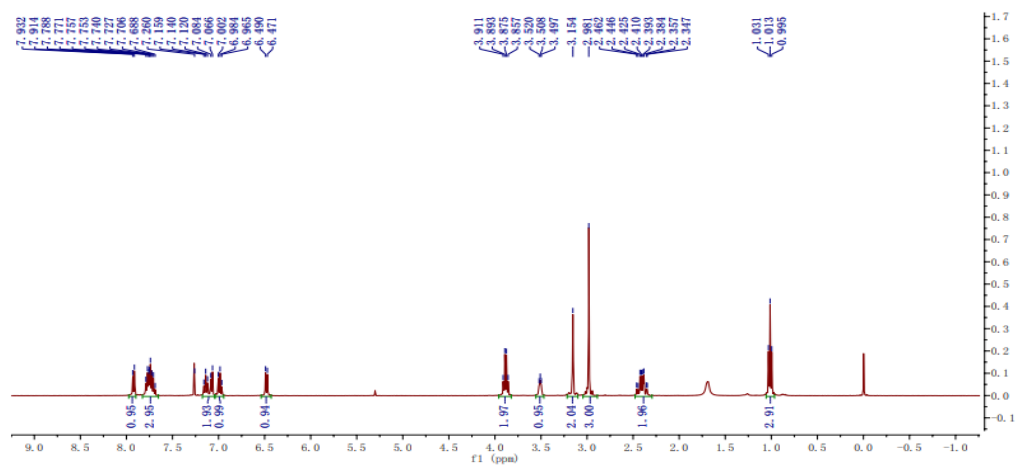
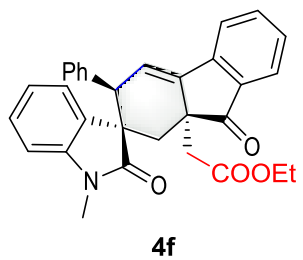
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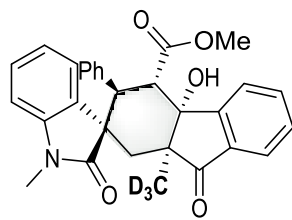


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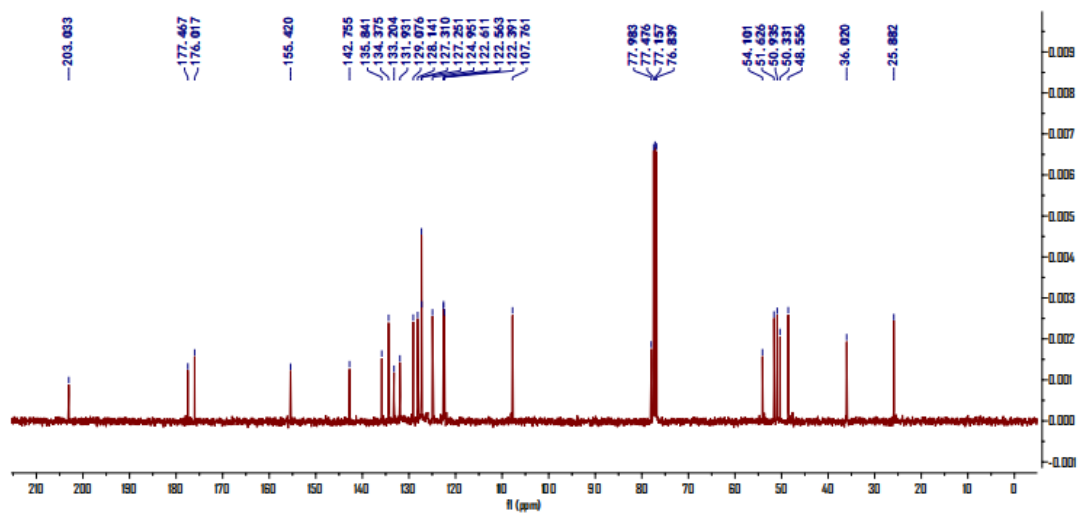
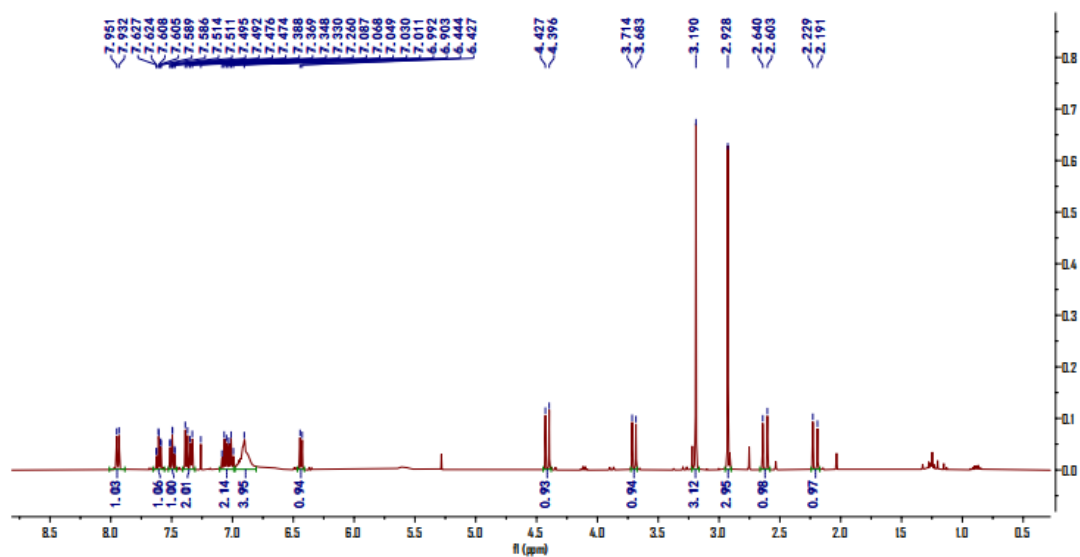


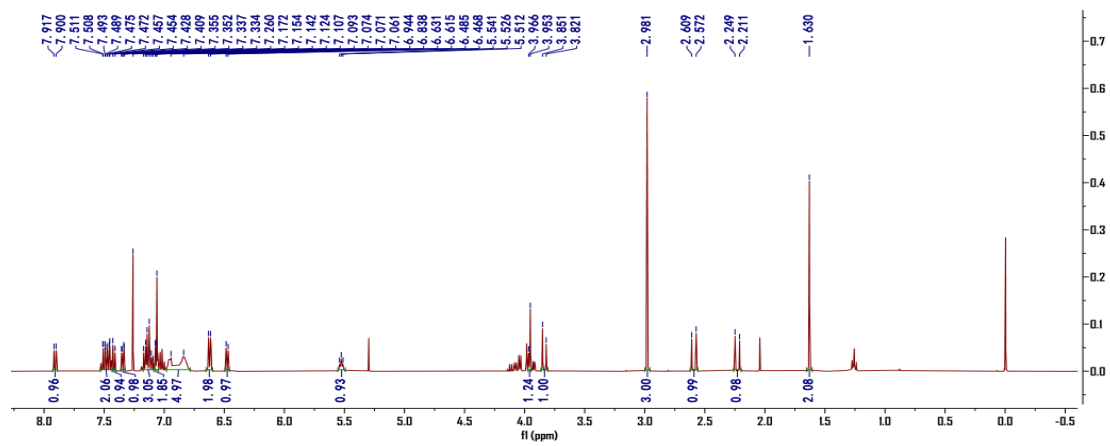
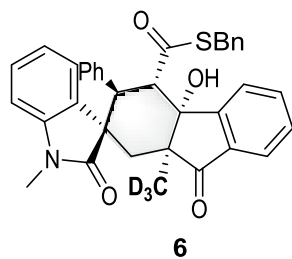
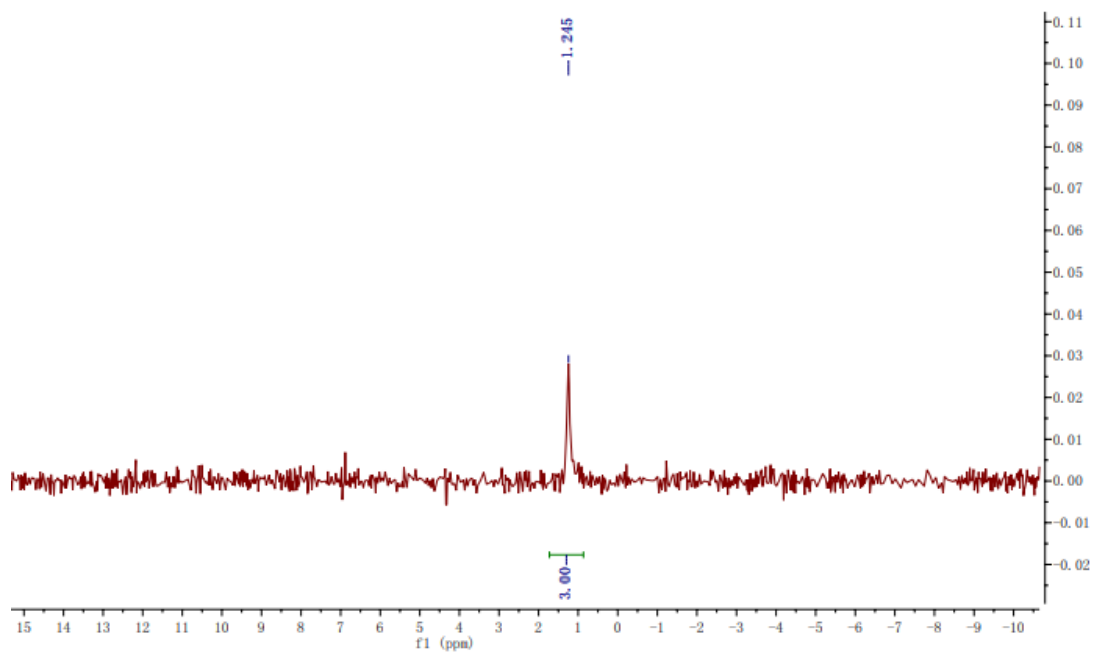


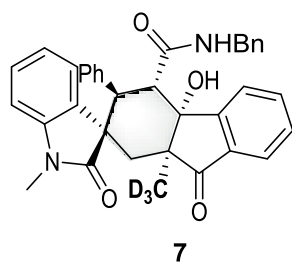
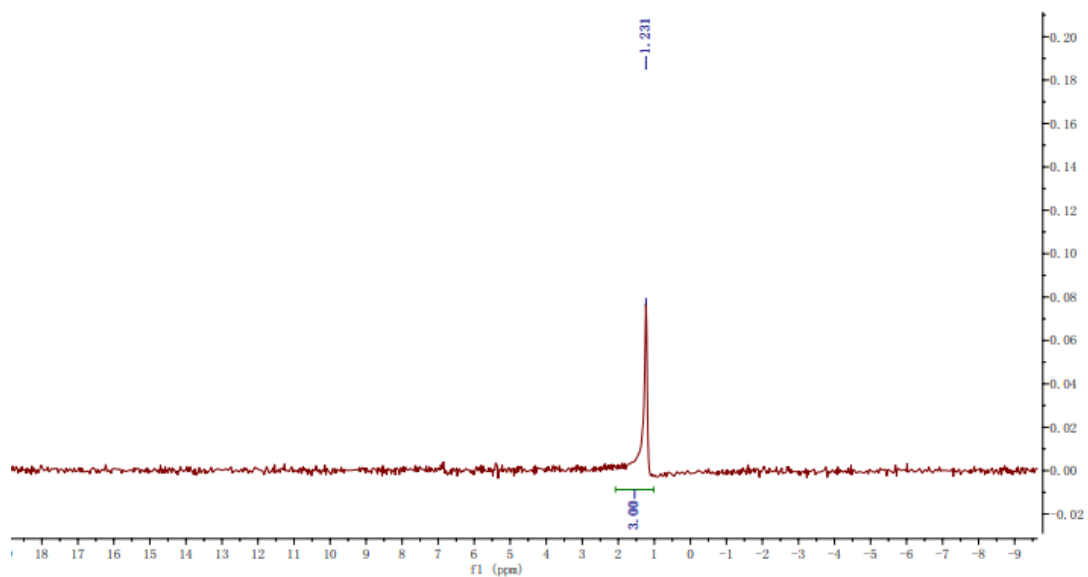
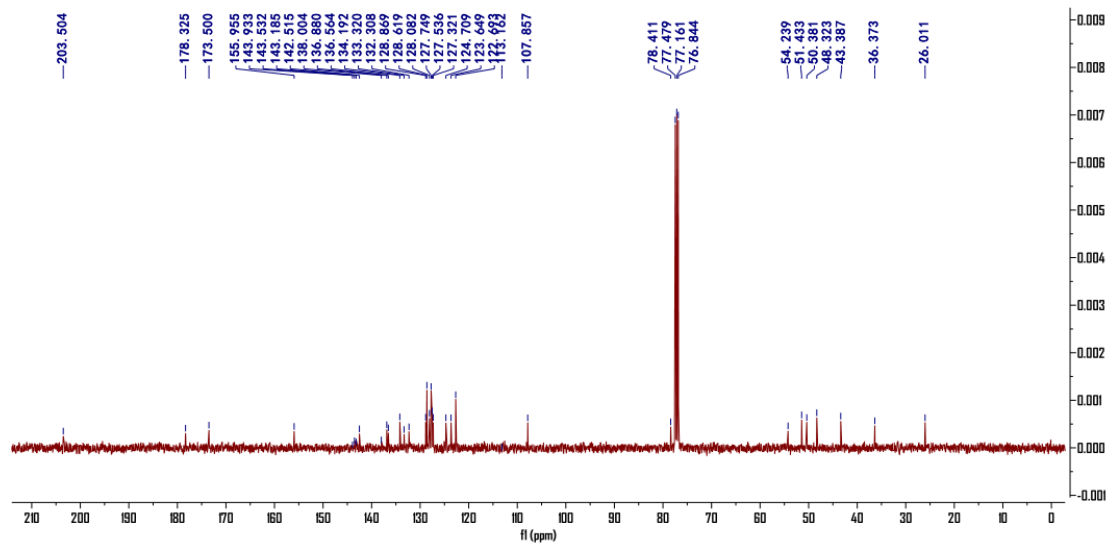




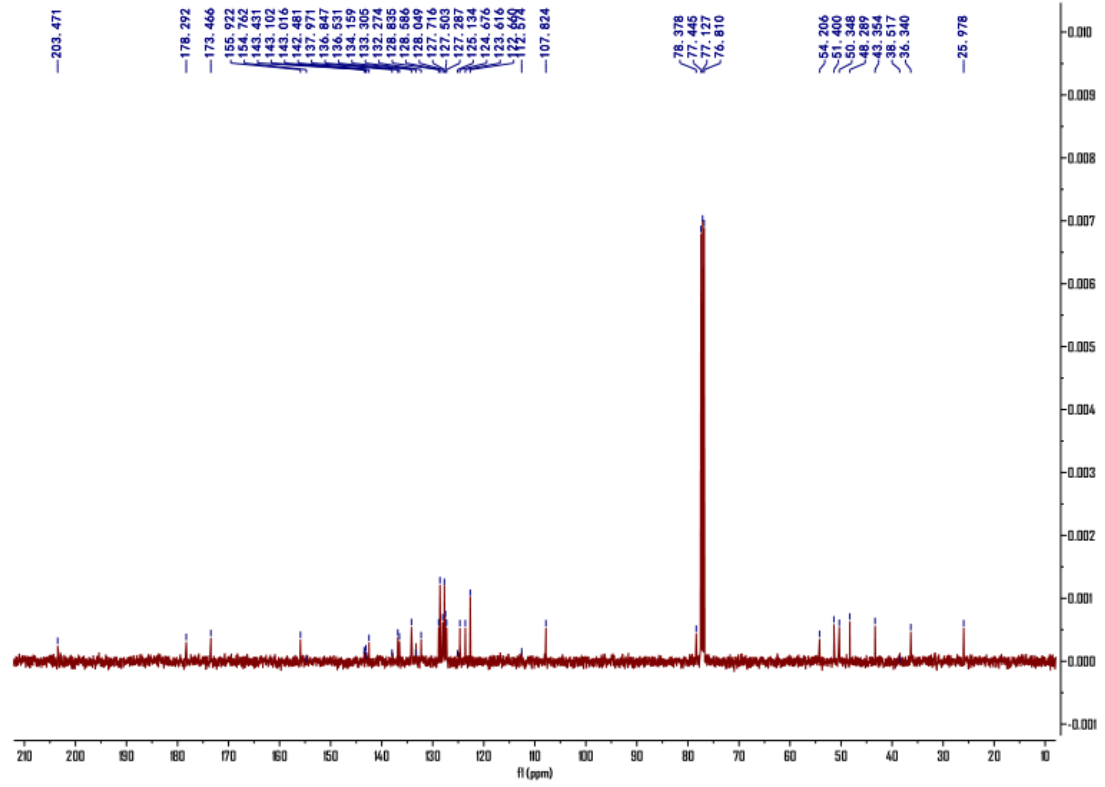
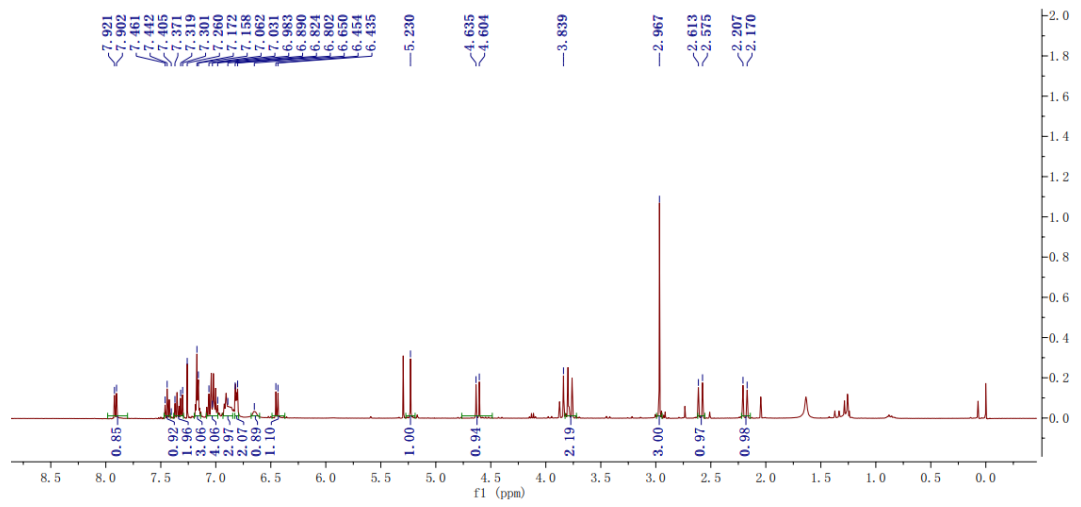
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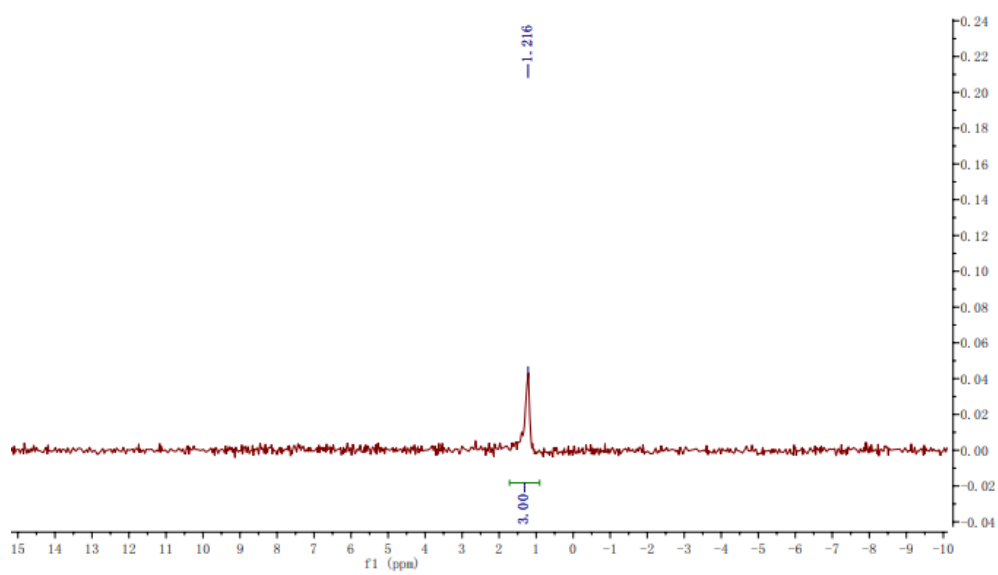




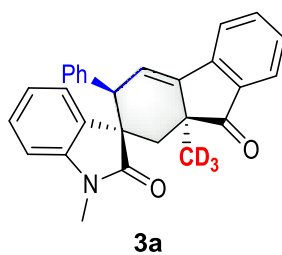


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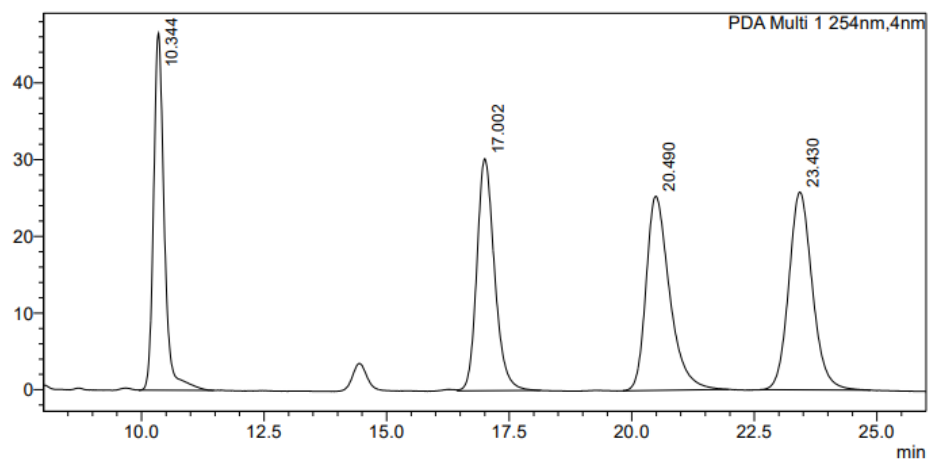


HPLC spectra of the products.



<Chromatogram>

mAU



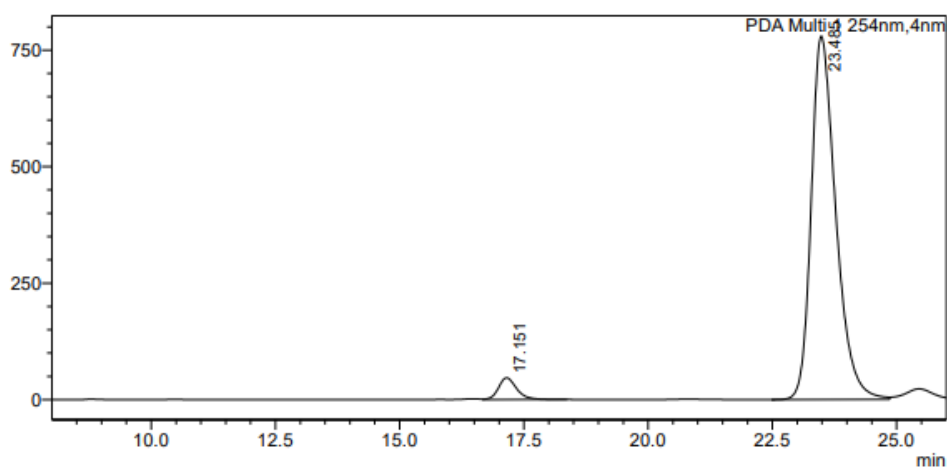
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	10.344	705297	22.242	46551
2	17.002	759995	23.967	30255
3	20.490	845344	26.658	25325
4	23.430	860429	27.134	25792
Total		3171064	100.000	127922

<Chromatogram>

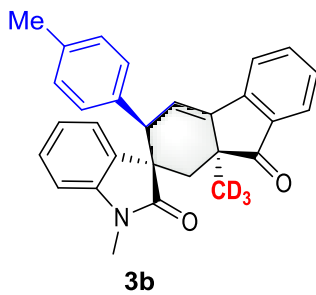
mAU



<Peak Table>

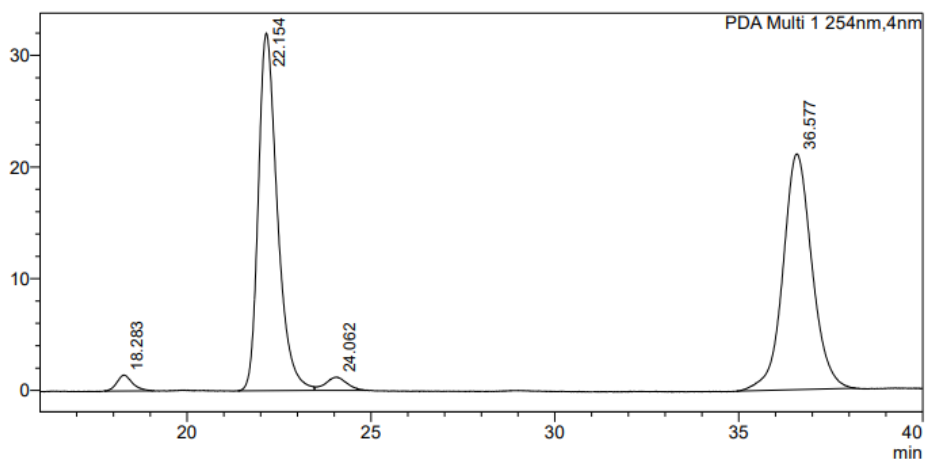
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	17.151	1184709	4.222	46664
2	23.485	26878788	95.778	779770
Total		28063498	100.000	826434



<Chromatogram>

mAU



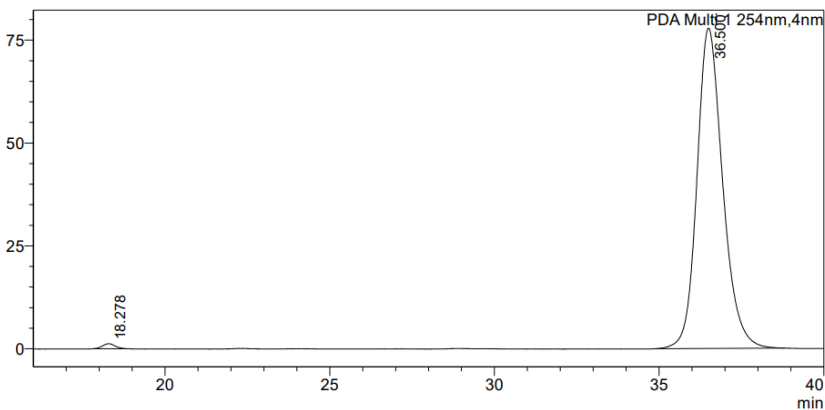
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.283	41910	1421	1.745
2	22.154	1155794	32017	48.112
3	24.062	47976	1191	1.997
4	36.577	1156599	21115	48.146
Total		2402278	55744	100.000

<Chromatogram>

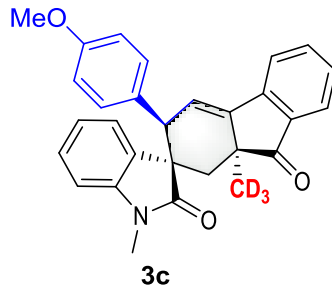
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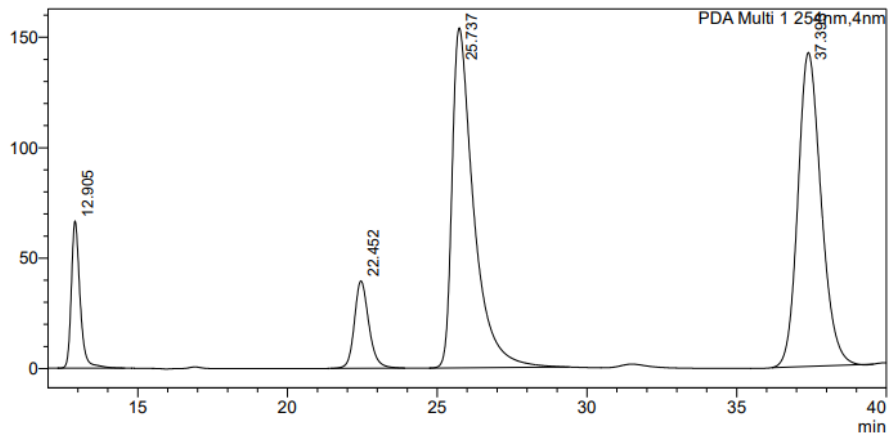
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.278	33955	1260	0.795
2	36.500	4238192	77879	99.205
Total		4272146	79139	100.000



<Chromatogram>

mAU



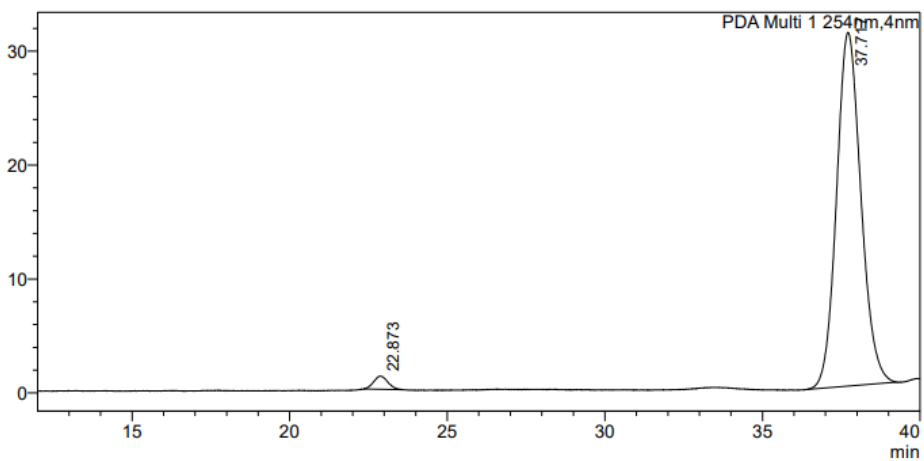
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	12.905	1351425	66567	7.479
2	22.452	1323515	39537	7.325
3	25.737	7729181	153875	42.777
4	37.393	7664309	142065	42.418
Total		18068431	402044	100.000

<Chromatogram>

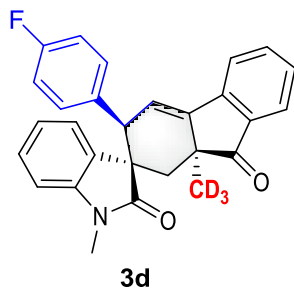
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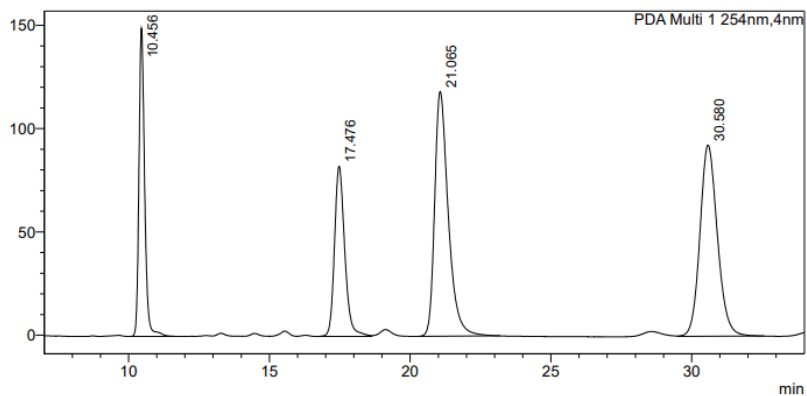
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	22.873	36116	1145	2.113
2	37.717	1672691	31056	97.887
Total		1708806	32202	100.000



<Chromatogram>

mAU

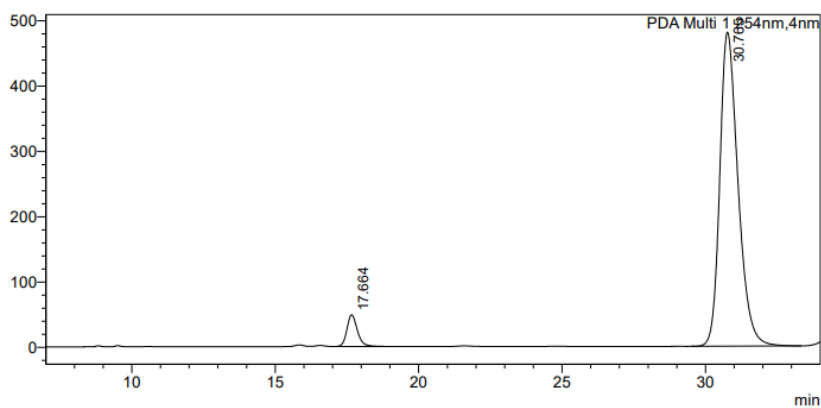


<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	10.456	2092849	17.196	149105
2	17.476	2089040	17.165	82333
3	21.065	3994764	32.823	118470
4	30.580	3993811	32.816	92551
Total		12170464	100.000	442458

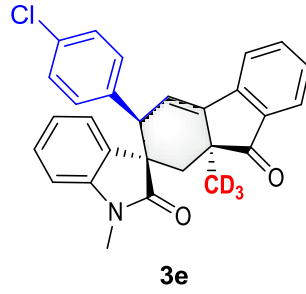
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mAU

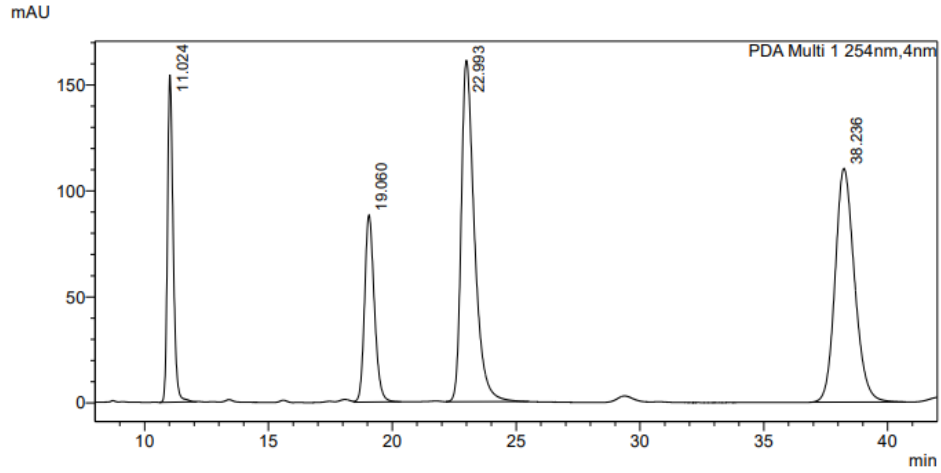


<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	17.664	1232656	5.474	48561
2	30.765	21284424	94.526	480746
Total		22517080	100.000	529307



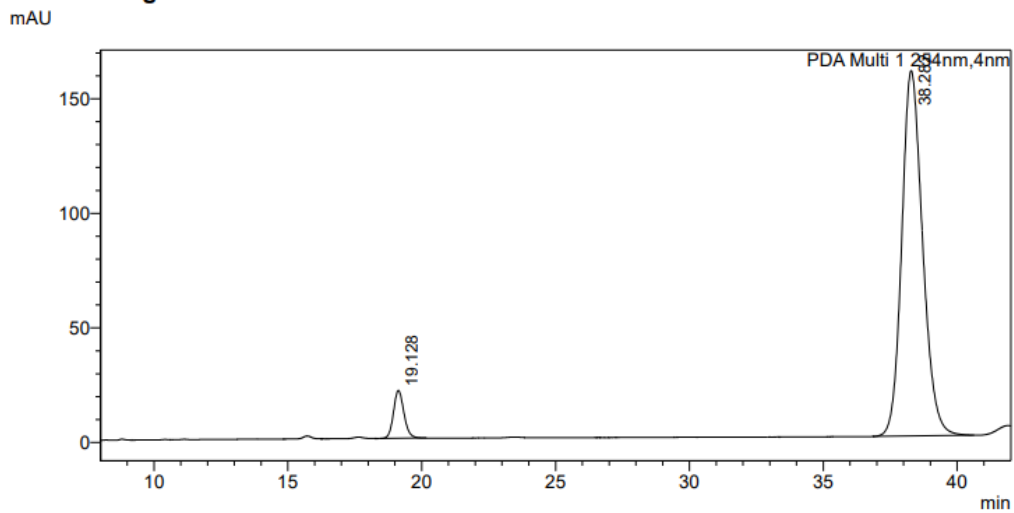
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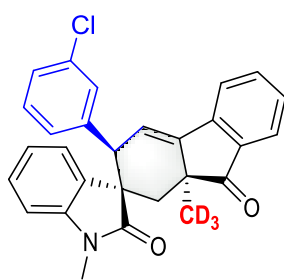
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	11.024	2453540	14.562	154331
2	19.060	2418093	14.352	88283
3	22.993	5973187	35.452	161062
4	38.236	6003621	35.633	110309
Total		16848441	100.000	513985

<Chromatogram>



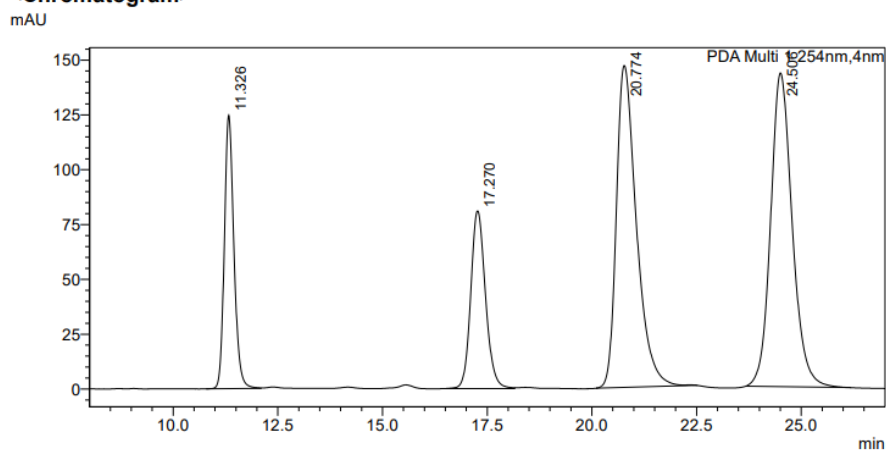
<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	19.128	567596	6.162	20905
2	38.282	8644279	93.838	159415
Total		9211874	100.000	180320



3f

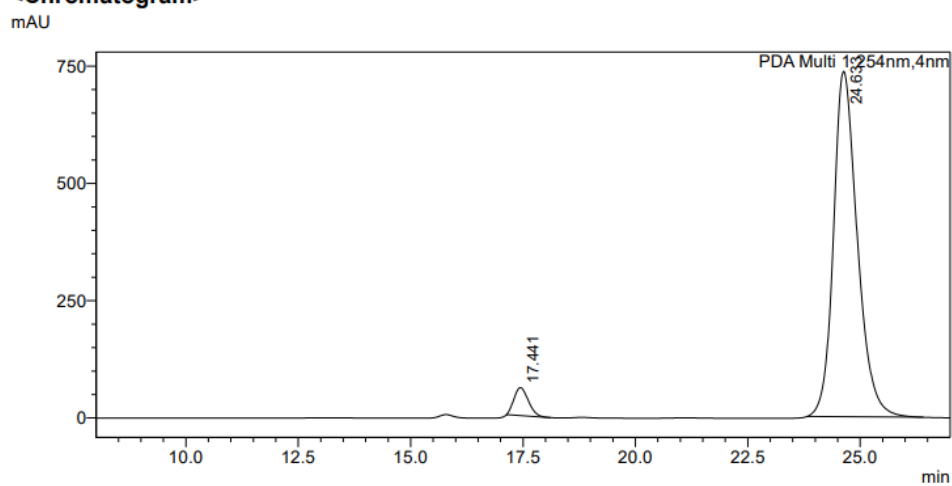
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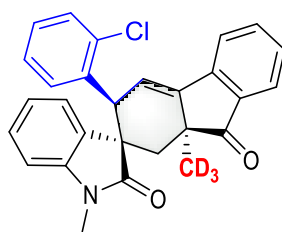
Peak#	Ret. Time	Area	Area%	Height
1	11.326	1983102	14.179	124647
2	17.270	1983652	14.182	81022
3	20.774	4890929	34.969	146695
4	24.506	5128941	36.670	143019
Total		13986624	100.000	495384

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<Peak Table>

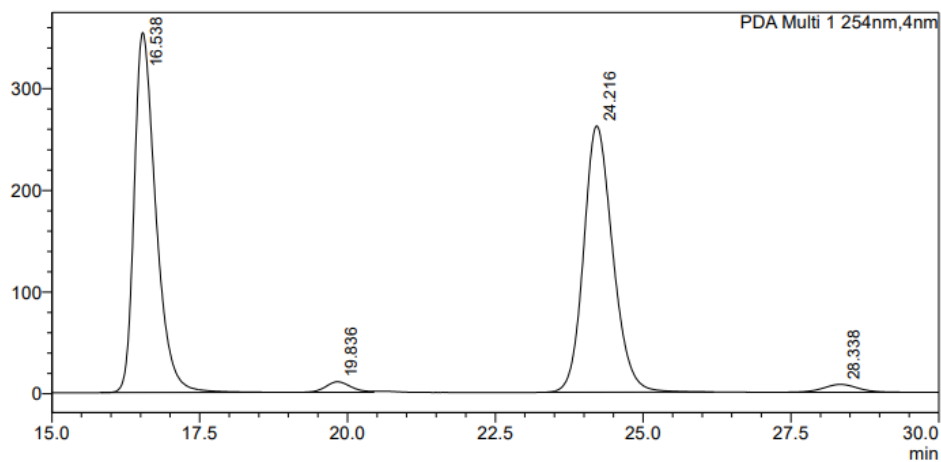
Peak#	Ret. Time	Area	Area%	Height
1	17.441	1327930	4.654	59786
2	24.633	27204308	95.346	736288
Total		28532238	100.000	796074



3g

<Chromatogram>

mAU



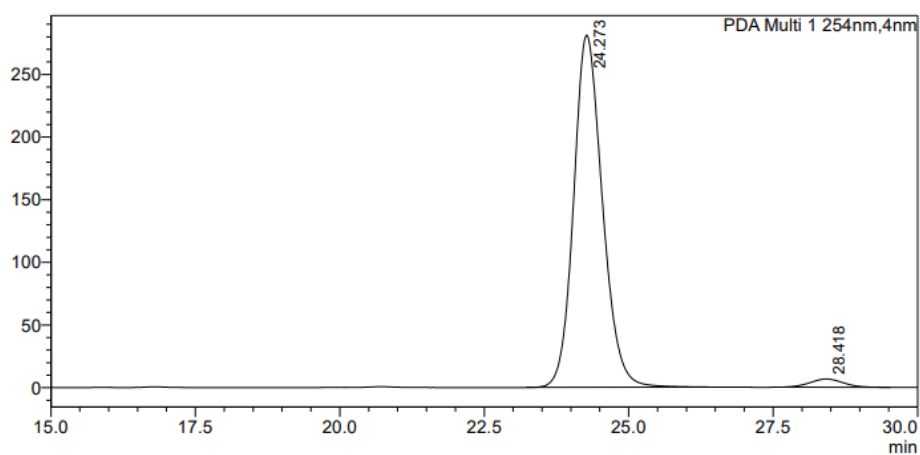
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	16.538	8999796	48.391	353990
2	19.836	311687	1.676	10368
3	24.216	8982132	48.296	261937
4	28.338	304522	1.637	7644
Total		18598136	100.000	633940

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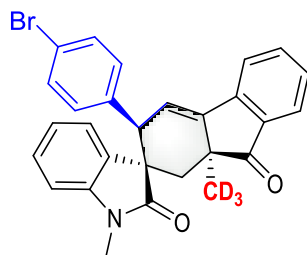
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<Peak Table>

PDA Ch1 254nm

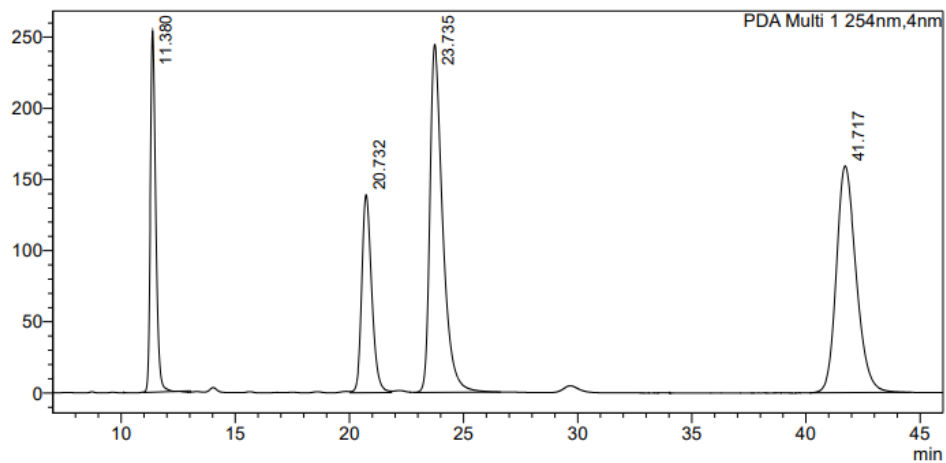
Peak#	Ret. Time	Area	Area%	Height
1	24.273	9740646	97.337	280985
2	28.418	266481	2.663	6599
Total		10007127	100.000	287585



3h

<Chromatogram>

mAU



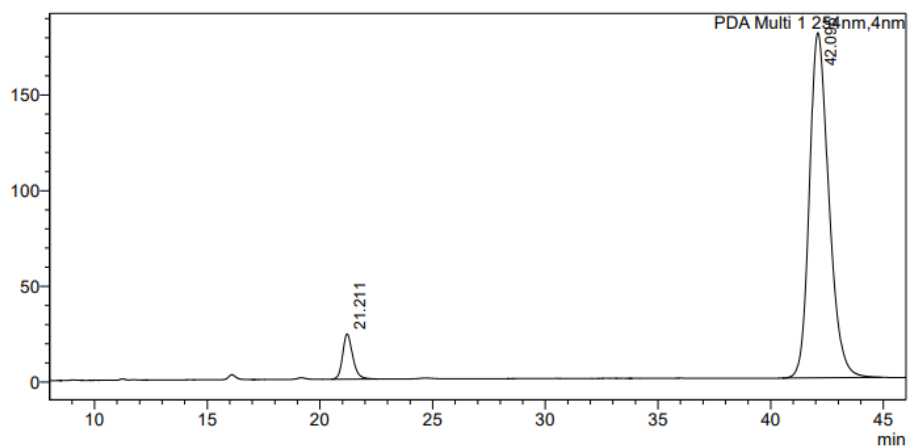
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	11.380	4169534	15.164	253668
2	20.732	4199268	15.272	139106
3	23.735	9535452	34.680	244386
4	41.717	9591406	34.883	159278
Total		27495661	100.000	796437

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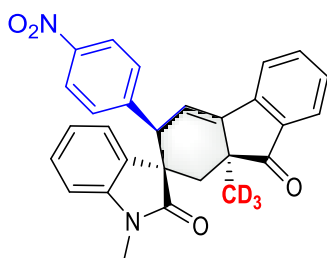
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<Peak Table>

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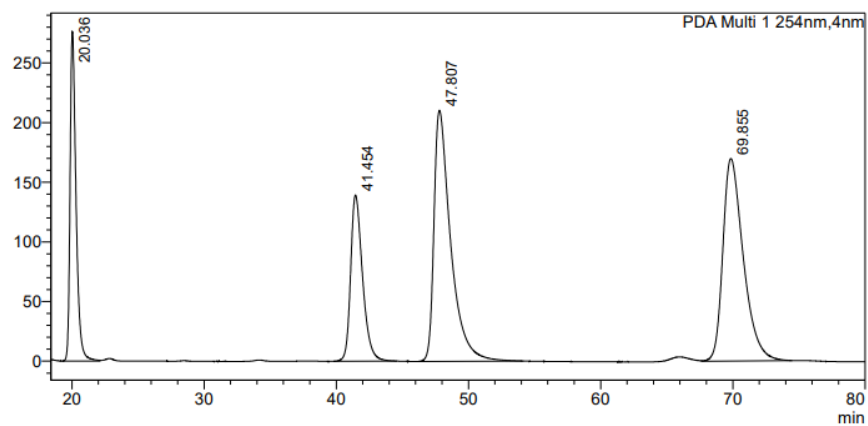
Peak#	Ret. Time	Area	Area%	Height
1	21.211	731869	6.332	23566
2	42.095	10826732	93.668	180320
Total		11558601	100.000	203886



3i

<Chromatogram>

mAU



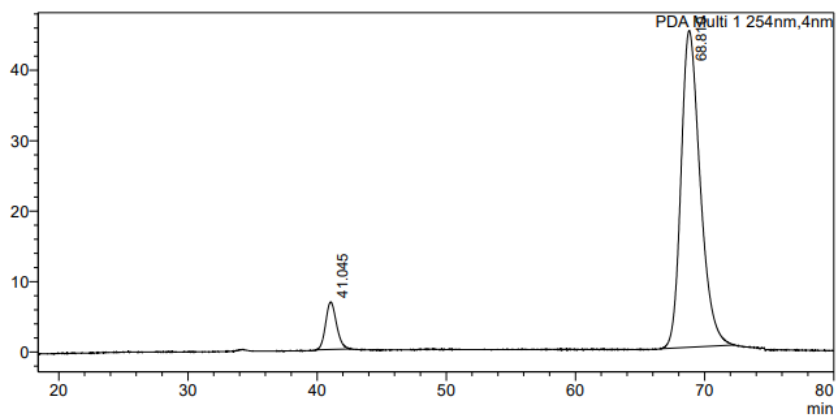
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	20.036	8667134	16.014	276358
2	41.454	8724699	16.120	139314
3	47.807	18454557	34.098	210417
4	69.855	18276418	33.768	169818
Total		54122808	100.000	795908

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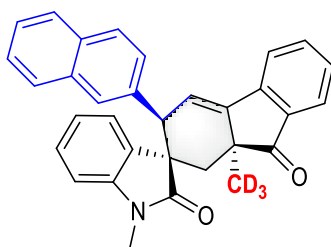
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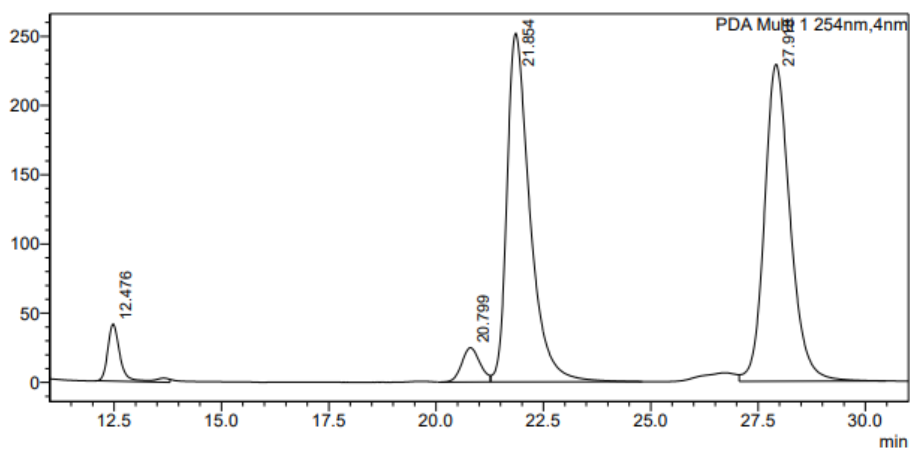
Peak#	Ret. Time	Area	Height	Area%
1	41.045	396102	6755	7.866
2	68.810	4639323	44946	92.134
Total		5035425	51700	100.000



3j

<Chromatogram>

mAU



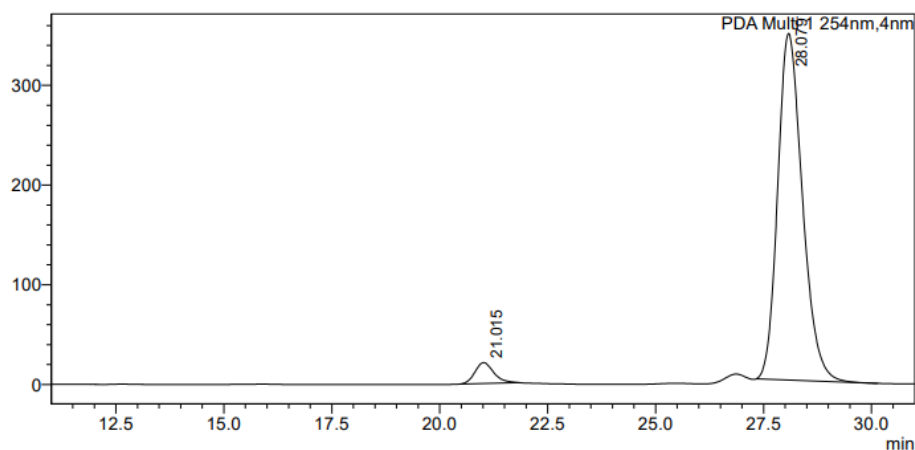
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PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	12.476	861872	4.204	41183
2	20.799	733198	3.577	24741
3	21.854	9358901	45.653	251742
4	27.918	9546144	46.566	228877
Total		20500114	100.000	546544

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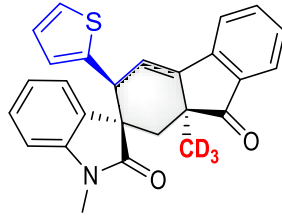
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<Peak Table>

PDA Ch1 254nm

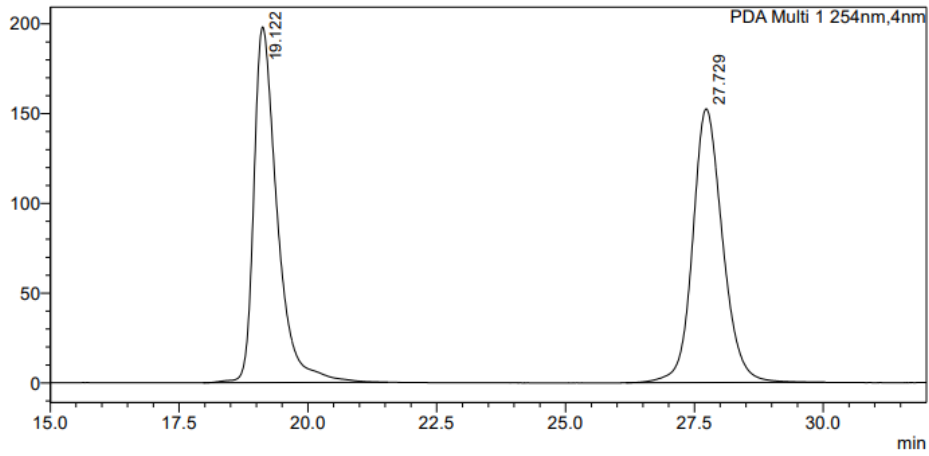
Peak#	Ret. Time	Area	Area%	Height
1	21.015	631244	4.364	20860
2	28.079	13832656	95.636	347587
Total		14463900	100.000	368447



3k

<Chromatogram>

mAU



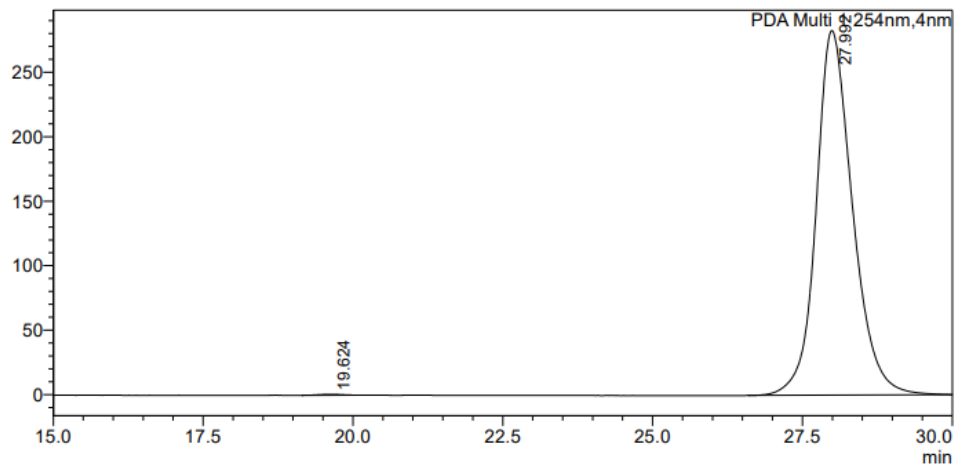
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	19.122	6244765	50.279	198087
2	27.729	6175533	49.721	152492
Total		12420297	100.000	350578

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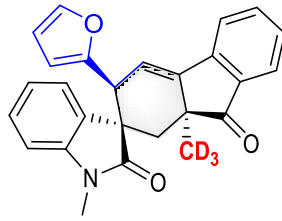
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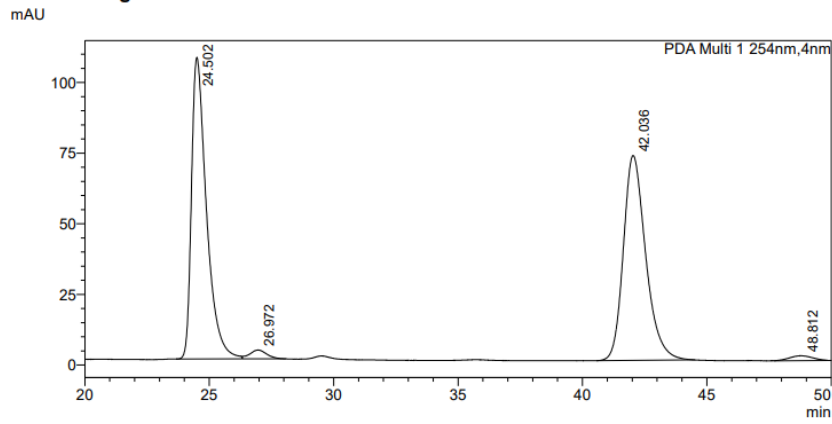
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	19.624	18720	0.156	693
2	27.992	11946981	99.844	282581
Total		11965701	100.000	283274



31

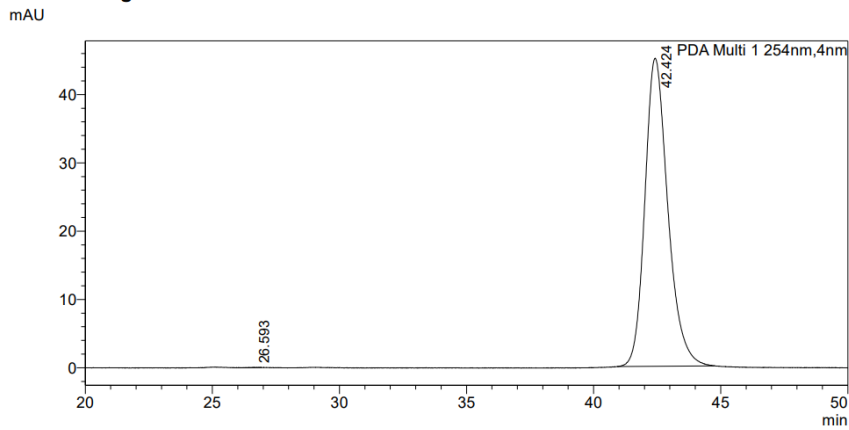
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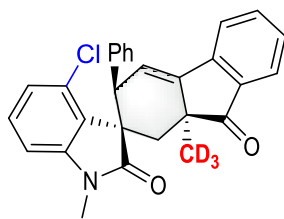
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	24.502	4475339	106716	48.260
2	26.972	149157	3132	1.608
3	42.036	4535175	72550	48.906
4	48.812	113653	1740	1.226
Total		9273324	184138	100.000

<Chromatogram>



<Peak Table>

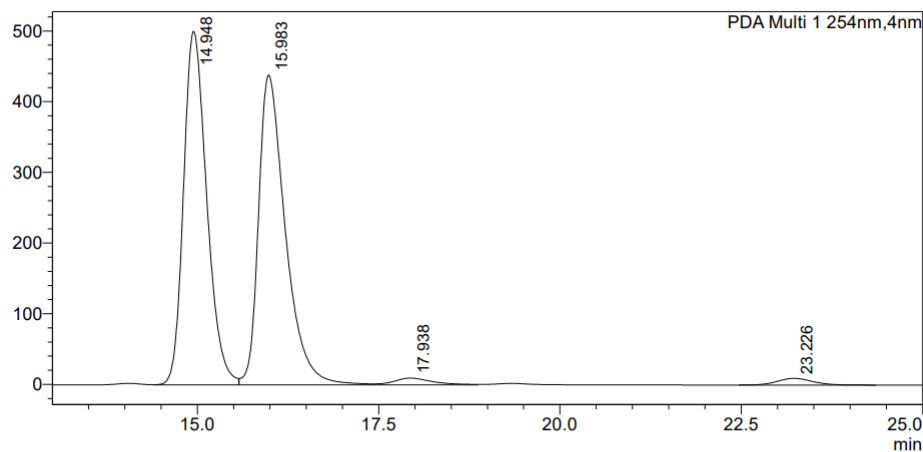
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	26.593	281	33	0.010
2	42.424	2835374	45111	99.990
Total		2835655	45144	100.000



3m

<Chromatogram>

mAU



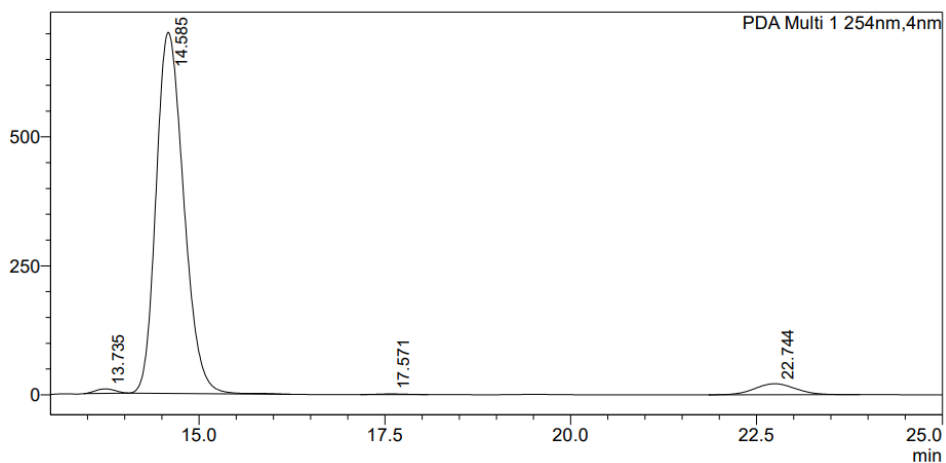
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.948	11148100	500144	48.273
2	15.983	11276200	438102	48.828
3	17.938	352269	9508	1.525
4	23.226	317232	9397	1.374
Total		23093801	957151	100.000

<Chromatogram>

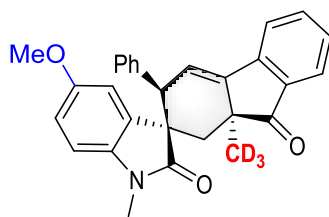
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PDA Ch1 254nm

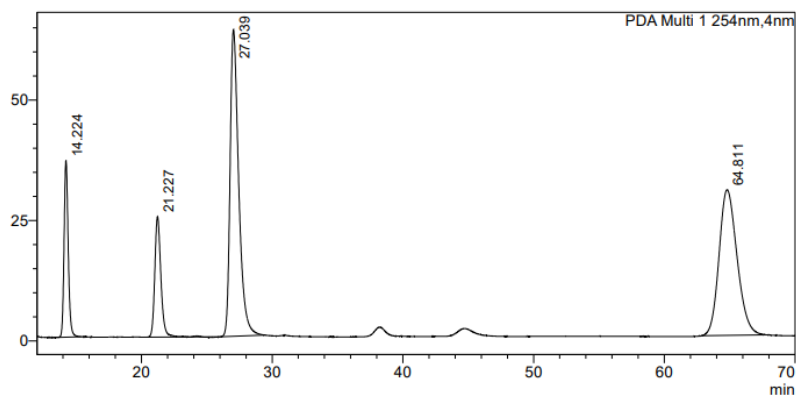
Peak#	Ret. Time	Area	Height	Area%
1	13.735	160673	8645	0.842
2	14.585	18069751	699836	94.687
3	17.571	34879	1265	0.183
4	22.744	818409	21304	4.289
Total		19083712	731049	100.000



3n

<Chromatogram>

mAU



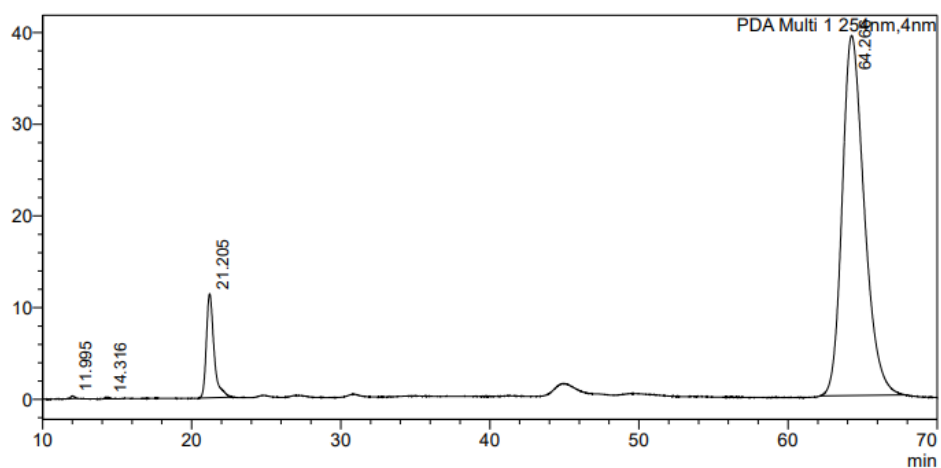
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.224	800799	36648	10.789
2	21.227	809165	25043	10.902
3	27.039	2916960	63701	39.300
4	64.811	2895432	30241	39.010
Total		7422357	155633	100.000

<Chromatogram>

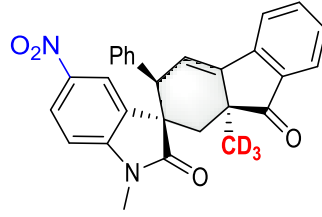
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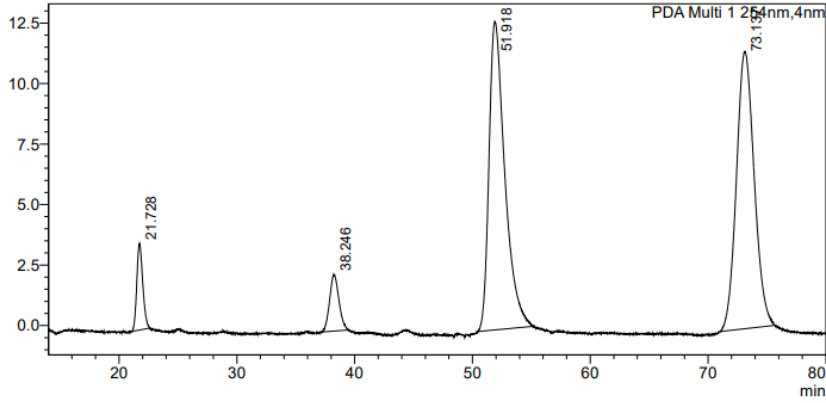
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.995	4717	288	0.106
2	14.316	4082	201	0.092
3	21.205	403029	11322	9.047
4	64.266	4042761	39241	90.755
Total		4454589	51052	100.000



3o

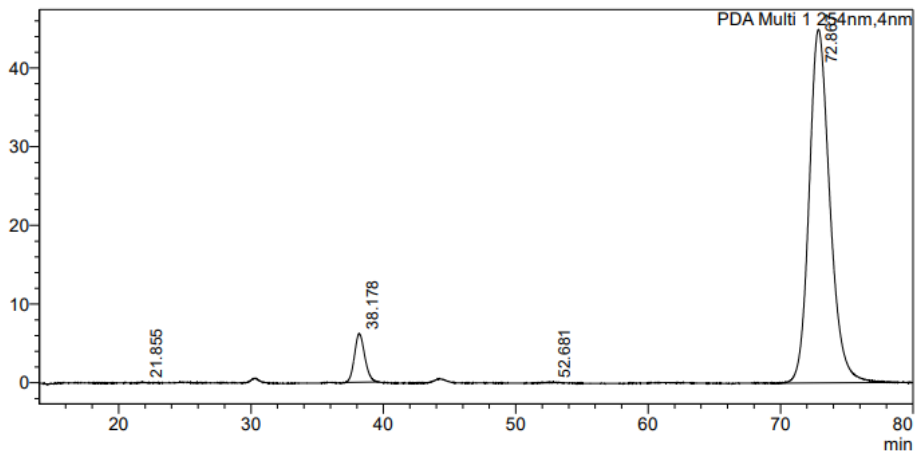
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<Peak Table>

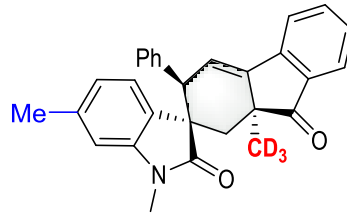
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	21.728	125649	4.749	3573
2	38.246	128003	4.838	2327
3	51.918	1189821	44.966	12747
4	73.137	1202572	45.448	11451
Total		2646045	100.000	30097

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mAU



<Peak Table>

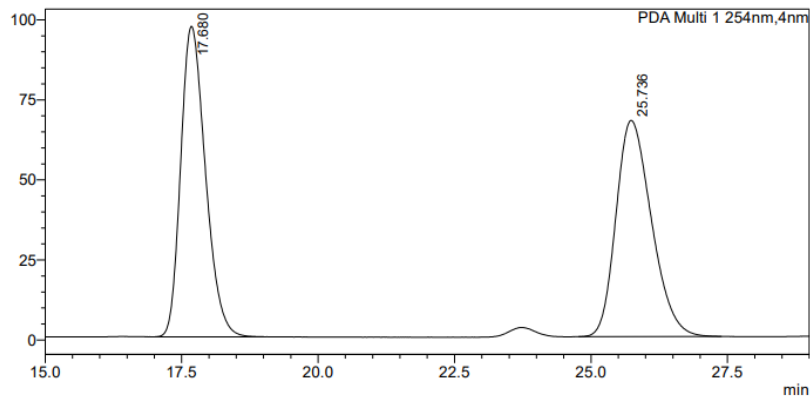
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	21.855	1940	0.037	79
2	38.178	335560	6.415	6162
3	52.681	3986	0.076	72
4	72.867	4889329	93.472	44914
Total		5230816	100.000	51227



3p

<Chromatogram>

mAU



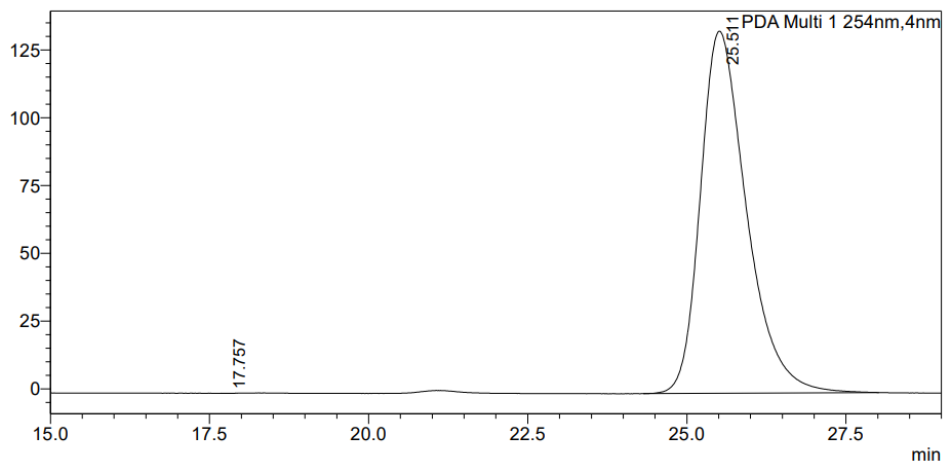
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	17.680	3055054	96926	50.017
2	25.736	3053017	67484	49.983
Total		6108070	164410	100.000

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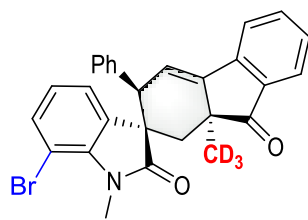
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PDA Ch1 254nm

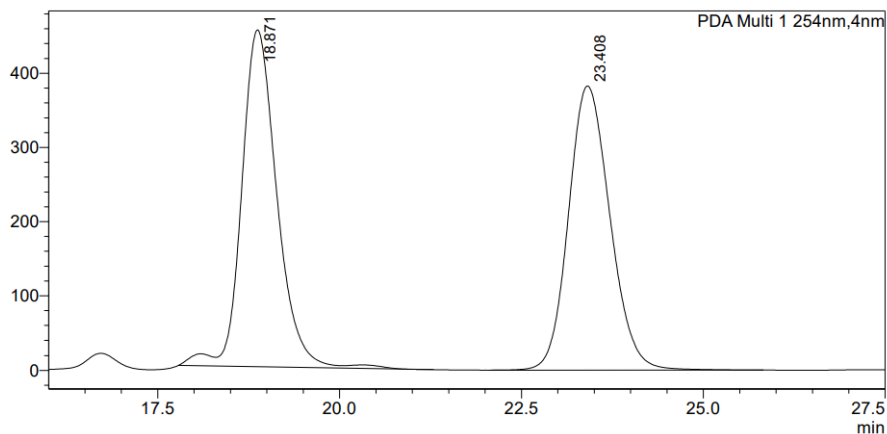
Peak#	Ret. Time	Area	Height	Area%
1	17.757	77	19	0.001
2	25.511	6734931	133551	99.999
Total		6735009	133570	100.000



3q

<Chromatogram>

mAU



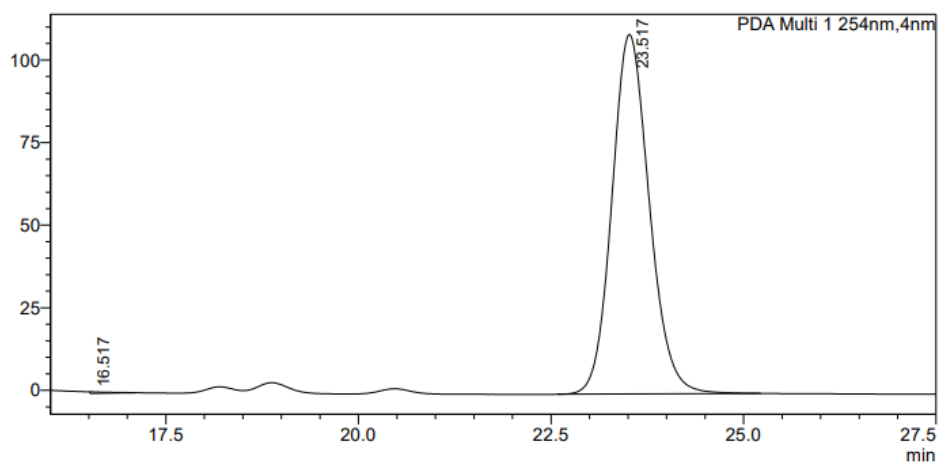
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.871	15392539	453443	50.389
2	23.408	15155016	382476	49.611
Total		30547554	835919	100.000

<Chromatogram>

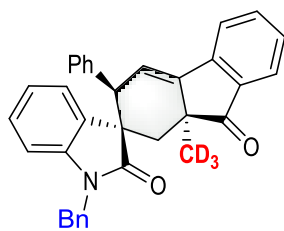
mAU



<Peak Table>

PDA Ch1 254nm

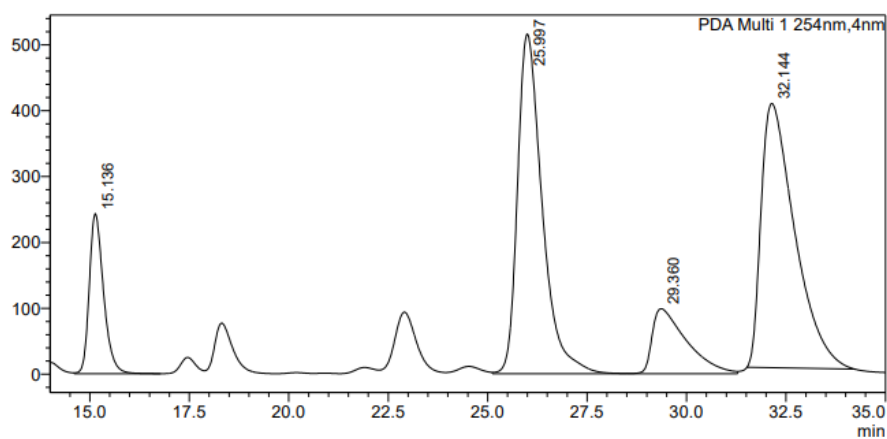
Peak#	Ret. Time	Area	Height	Area%
1	16.517	7406	460	0.201
2	23.517	3676672	108829	99.799
Total		3684078	109289	100.000



3r

<Chromatogram>

mAU



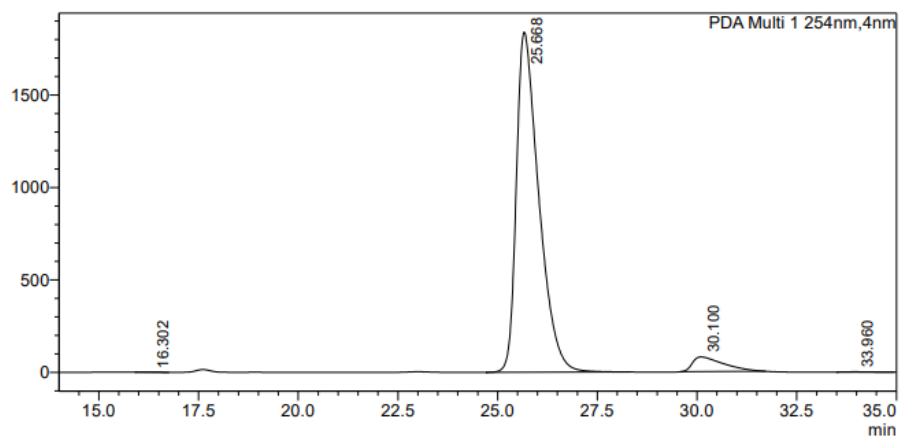
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.136	6068468	242793	10.475
2	25.997	22290074	515809	38.477
3	29.360	5932516	98701	10.241
4	32.144	23640259	401036	40.807
Total		57931318	1258339	100.000

<Chromatogram>

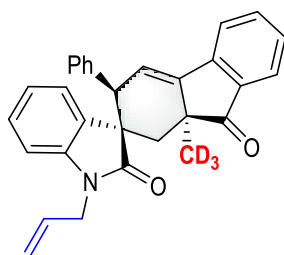
mAU



<Peak Table>

PDA Ch1 254nm

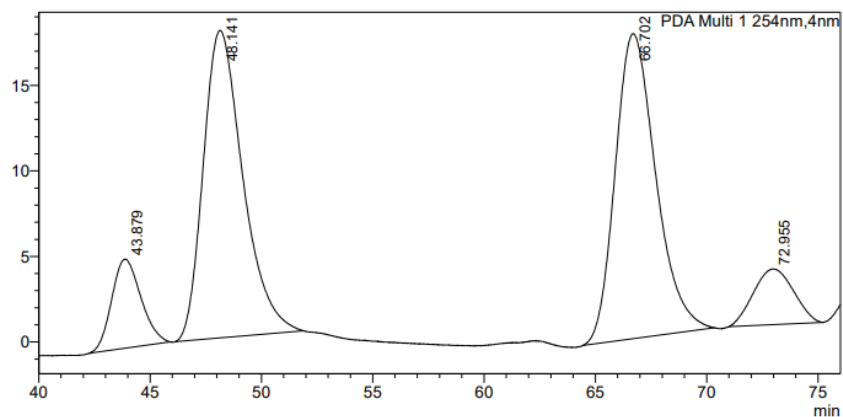
Peak#	Ret. Time	Area	Height	Area%
1	16.302	13905	624	0.018
2	25.668	72123866	1839469	94.266
3	30.100	4294852	79426	5.613
4	33.960	78154	1837	0.102
Total		76510777	1921356	100.000



3s

<Chromatogram>

mAU



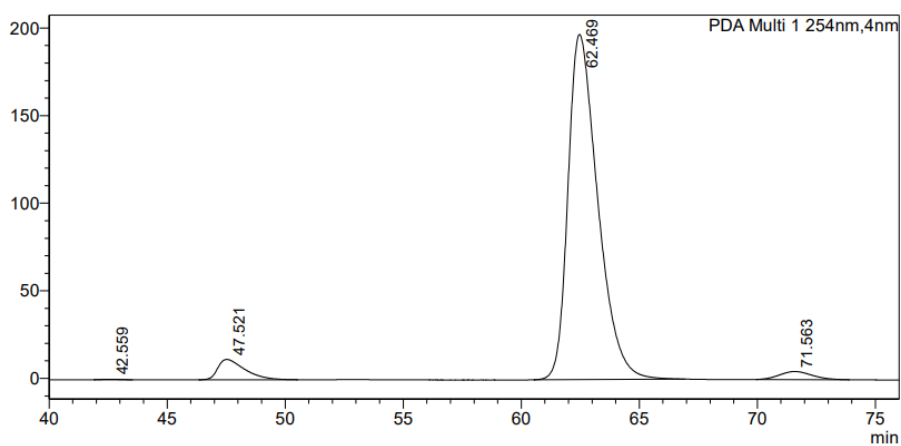
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	43.879	475209	5204	8.861
2	48.141	2222664	17974	41.445
3	66.702	2259458	17829	42.132
4	72.955	405532	3250	7.562
Total		5362864	44258	100.000

<Chromatogram>

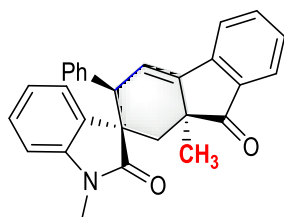
mAU



<Peak Table>

PDA Ch1 254nm

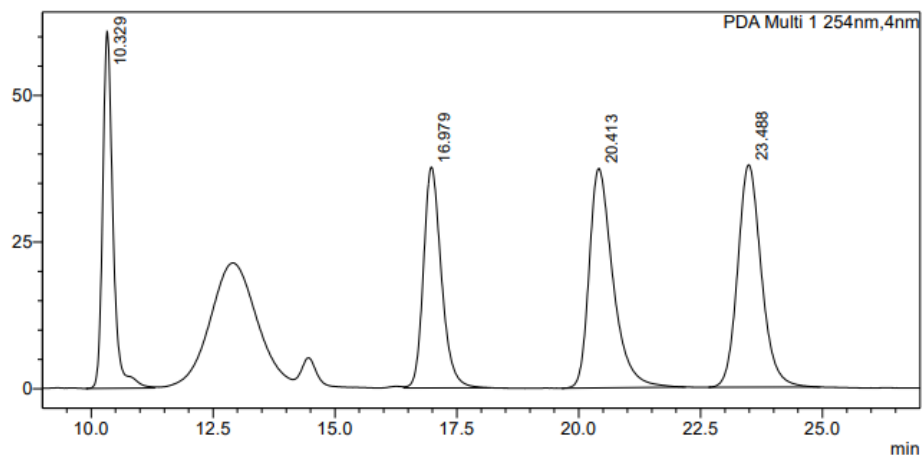
Peak#	Ret. Time	Area	Height	Area%
1	42.559	13291	264	0.071
2	47.521	919790	11613	4.932
3	62.469	17277847	197015	92.652
4	71.563	437195	4588	2.344
Total		18648124	213480	100.000



4a

<Chromatogram>

mAU



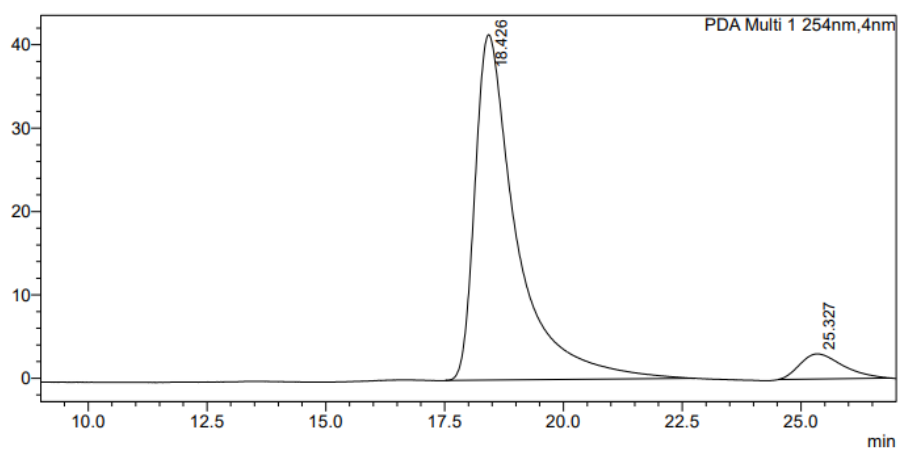
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.329	893548	60723	20.271
2	16.979	962538	37625	21.836
3	20.413	1271625	37386	28.848
4	23.488	1280282	37915	29.045
Total		4407993	173649	100.000

<Chromatogram>

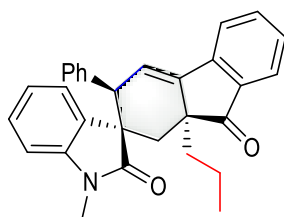
mAU



<Peak Table>

PDA Ch1 254nm

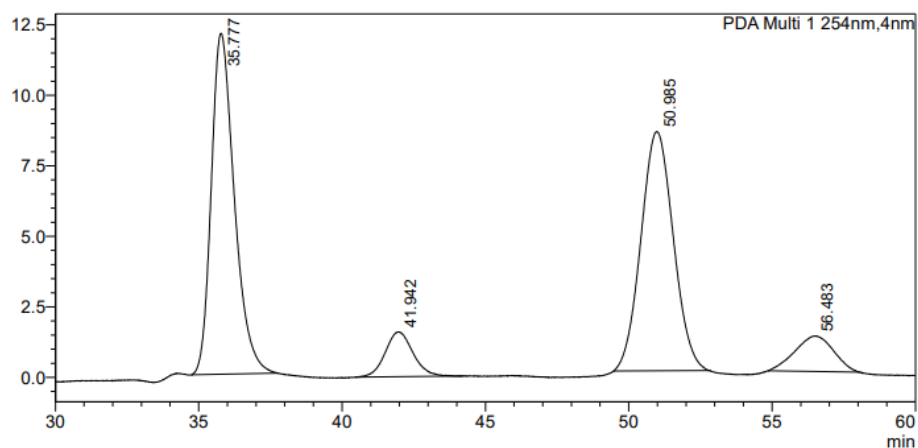
Peak#	Ret. Time	Area	Height	Area%
1	18.426	2525357	41420	92.999
2	25.327	190101	3021	7.001
Total		2715458	44441	100.000



4b

<Chromatogram>

mAU



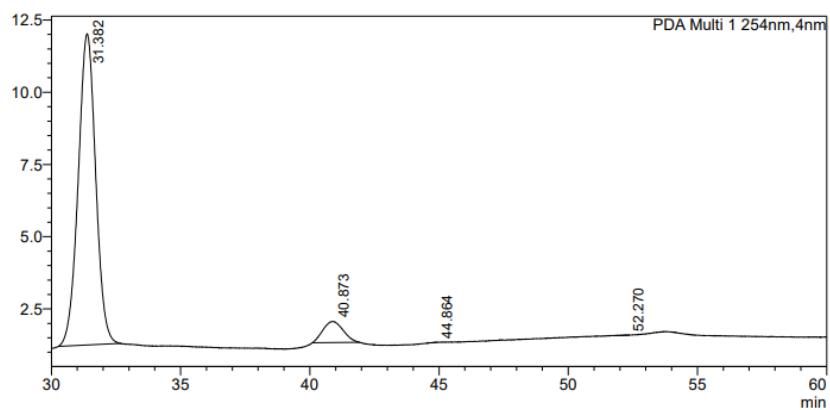
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	35.777	677249	43.136	12081
2	41.942	107067	6.819	1588
3	50.985	667942	42.543	8477
4	56.483	117790	7.502	1254
Total		1570048	100.000	23401

<Chromatogram>

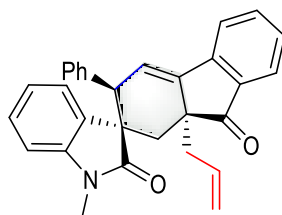
mAU



<Peak Table>

PDA Ch1 254nm

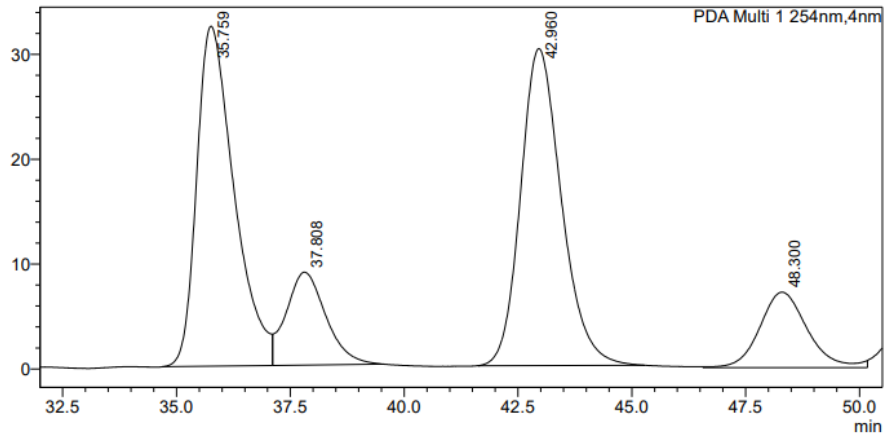
Peak#	Ret. Time	Area	Area%	Height
1	31.382	506801	92.688	10771
2	40.873	39920	7.301	731
3	44.864	44	0.008	3
4	52.270	16	0.003	9
Total		546781	100.000	11514



4c

<Chromatogram>

mAU

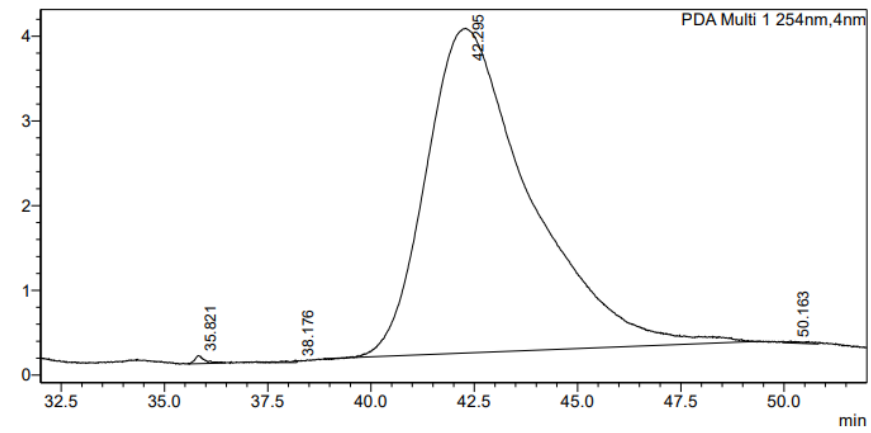


<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	35.759	1856043	32429	38.619
2	37.808	537790	8862	11.190
3	42.960	1888051	30224	39.285
4	48.300	524102	7195	10.905
Total		4805987	78710	100.000

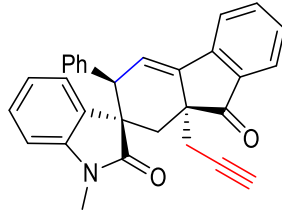
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mAU



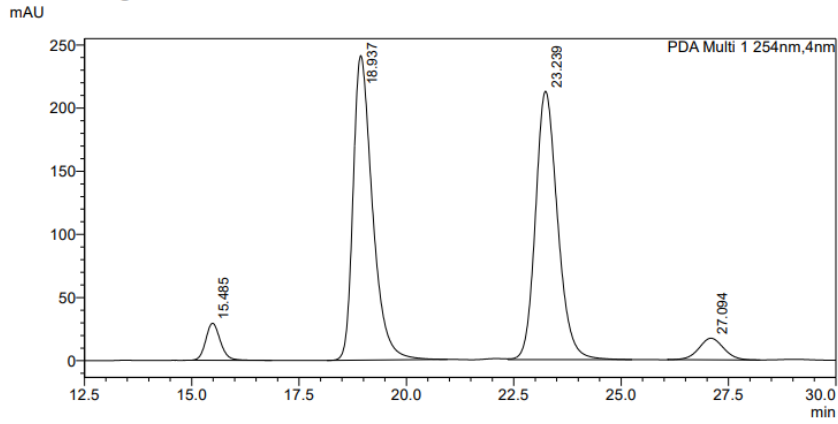
<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	35.821	1617	93	0.240
2	38.176	513	26	0.076
3	42.295	671290	3833	99.572
4	50.163	754	23	0.112
Total		674175	3975	100.000



4d

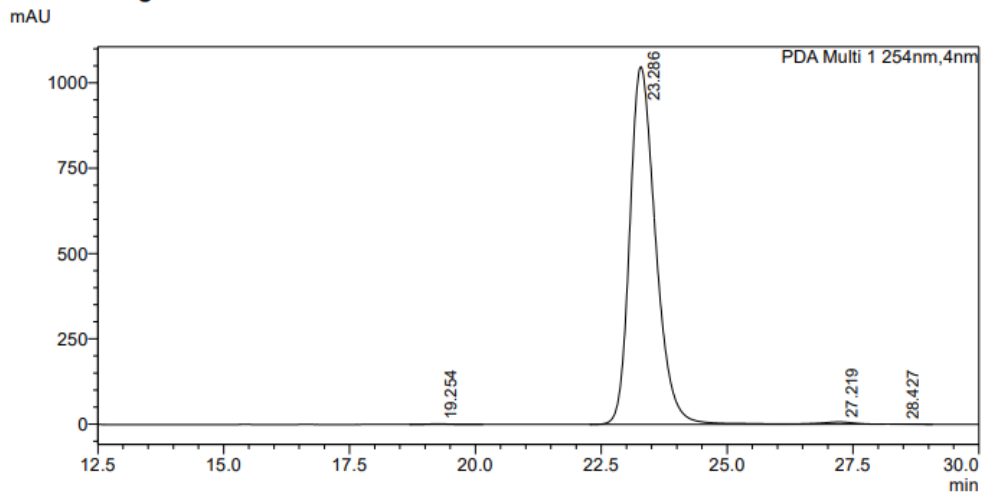
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<Peak Table>

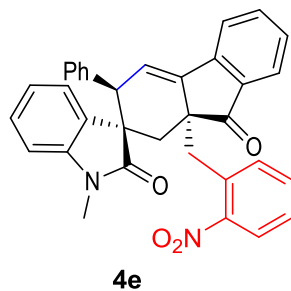
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	15.485	696169	4.204	29383
2	18.937	7564635	45.684	241056
3	23.239	7612563	45.974	212484
4	27.094	685077	4.137	17064
Total		16558444	100.000	499987

<Chromatogram>



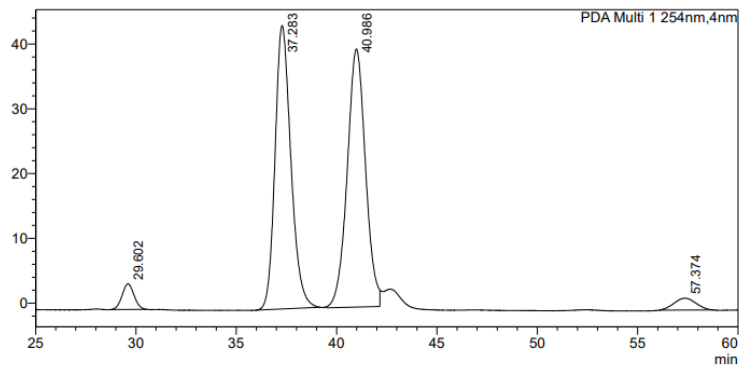
<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	19.254	55966	0.148	1796
2	23.286	37422989	98.997	1047878
3	27.219	317944	0.841	6519
4	28.427	5067	0.013	173
Total		37801964	100.000	1056365



<Chromatogram>

mAU



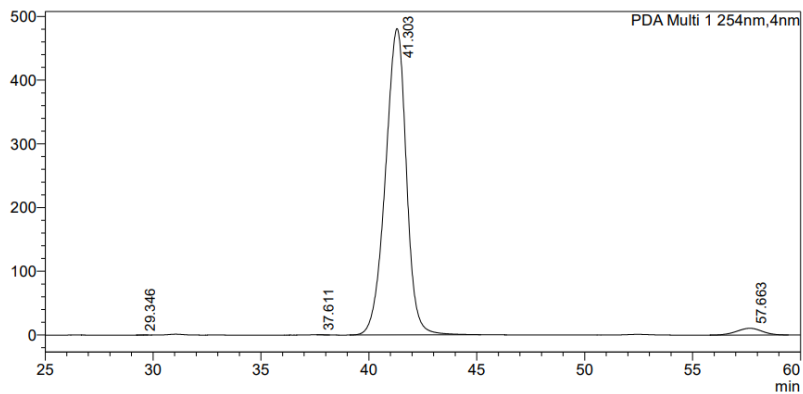
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%	Height
1	29.602	164176	3.134	3959
2	37.283	2405550	45.914	43728
3	40.986	2529599	48.282	39818
4	57.374	139930	2.671	1850
Total		5239254	100.000	89355

<Chromatogram>

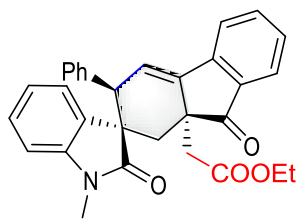
mAU



<Peak Table>

PDA Ch1 254nm

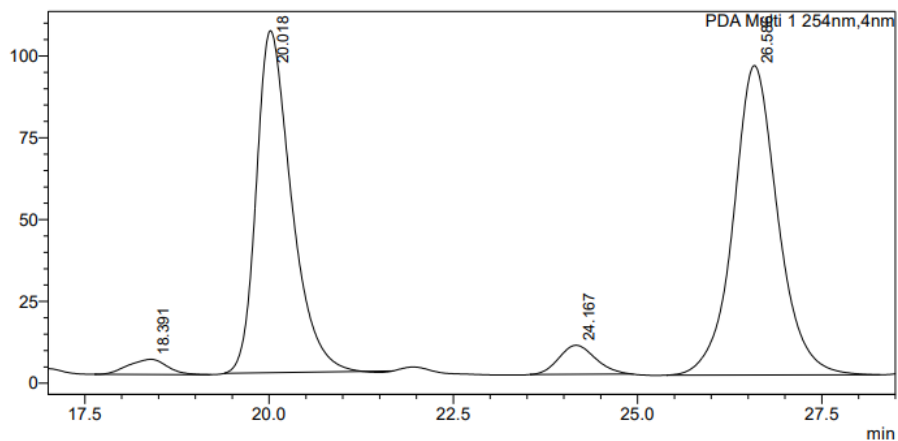
Peak#	Ret. Time	Area	Area%	Height
1	29.346	327	0.001	33
2	37.611	925	0.003	30
3	41.303	32402574	97.385	480733
4	57.663	868696	2.611	10582
Total		33272521	100.000	491379



4f

<Chromatogram>

mAU



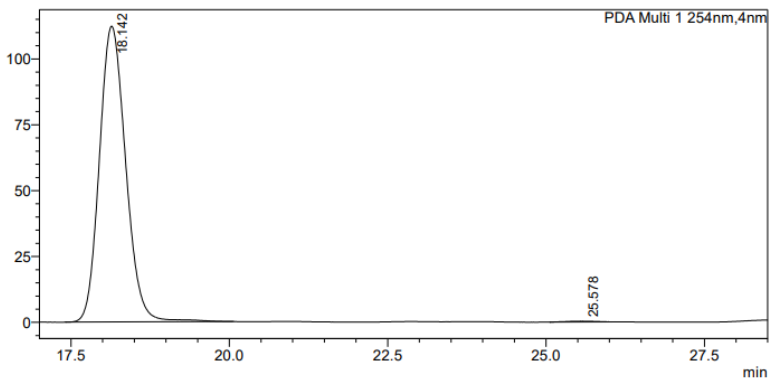
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.391	168863	4645	2.132
2	20.018	3464278	104494	43.747
3	24.167	307638	8875	3.885
4	26.586	3978070	94530	50.235
Total		7918850	212543	100.000

<Chromatogram>

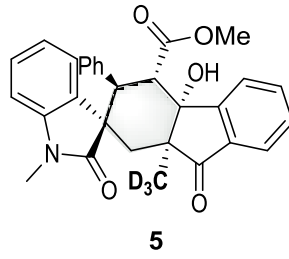
mAU



<Peak Table>

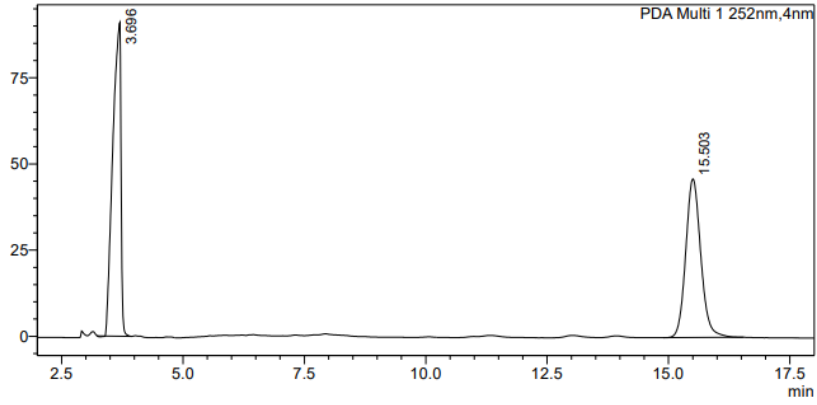
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.142	3247640	112279	99.686
2	25.578	10244	310	0.314
Total		3257884	112589	100.000



<Chromatogram>

mAU



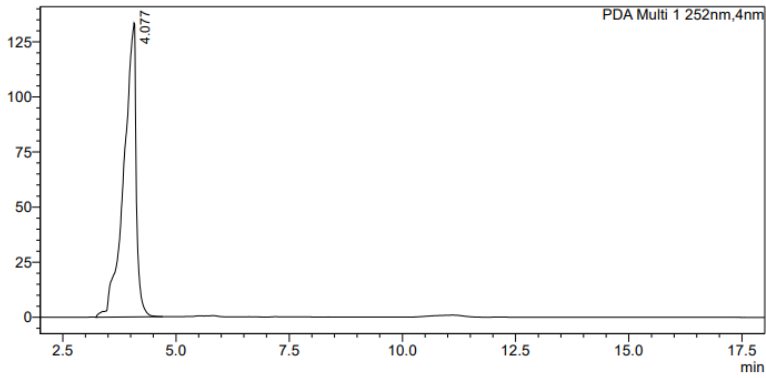
<Peak Table>

PDA Ch1 252nm

Peak#	Ret. Time	Area	Area%	Height
1	3.696	1066147	51.799	91029
2	15.503	992073	48.201	46016
Total		2058219	100.000	137045

<Chromatogram>

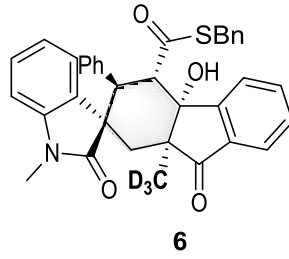
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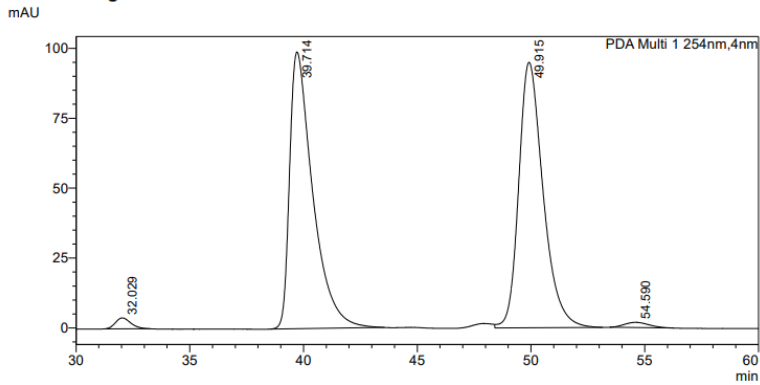
<Peak Table>

PDA Ch1 252nm

Peak#	Ret. Time	Area	Area%	Height
1	4.077	2551105	100.000	133398
Total		2551105	100.000	133398



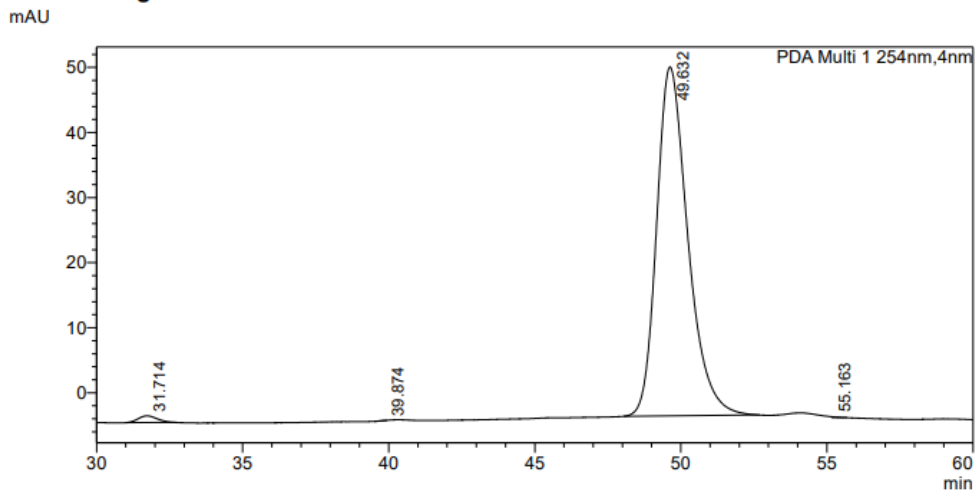
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<Peak Table>

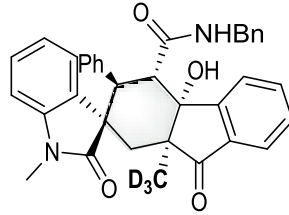
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	32.029	184880	3924	1.284
2	39.714	6994546	98942	48.568
3	49.915	7082293	94962	49.178
4	54.590	139748	1862	0.970
Total		14401468	199690	100.000

<Chromatogram>



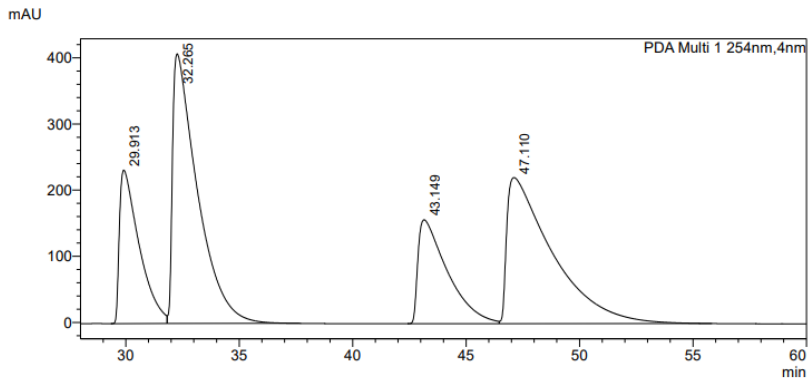
<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	Height
1	31.714	46931	1.164	1038
2	39.874	22	0.001	8
3	49.632	3983532	98.800	53621
4	55.163	1451	0.036	126
Total		4031935	100.000	54793



7

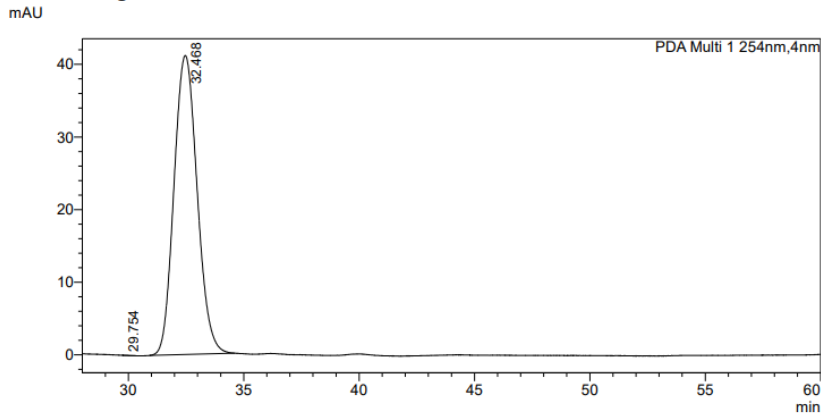
<Chromatogram>



<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	29.913	14072841	232001	15.587
2	32.265	31141332	407672	34.493
3	43.149	14191474	157017	15.719
4	47.110	30878609	220806	34.202
Total		90284257	1017496	100.000

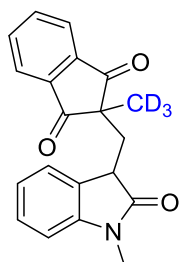
<Chromatogram>



<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	29.754	248	4	0.009
2	32.468	2872558	41181	99.991
Total		2872806	41185	100.000

V. Copies of MS spectra



1a

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

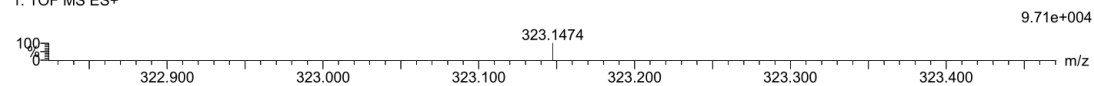
2 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 20-21 1H: 15-17 2H: 3-3 N: 1-1 O: 3-3

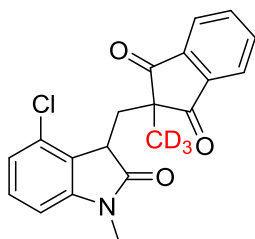
zyy-3ai 287 (2.067)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
323.1474	323.1475	-0.1	-0.3	12.5	35.1	n/a	n/a	C20 1H15 2H3 N O3



1b

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

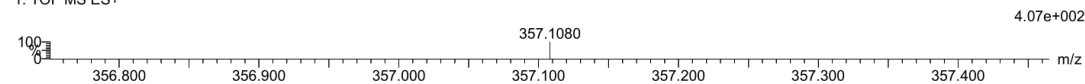
2 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 20-21 1H: 14-15 2H: 0-3 N: 1-1 O: 3-3 Cl: 0-1

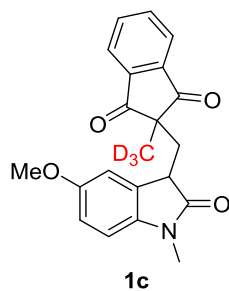
zyy-2n 219 (1.582)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
357.1080	357.1085	-0.5	-1.4	12.5	21.9	n/a	n/a	C20 1H14 2H3 N O3 Cl



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

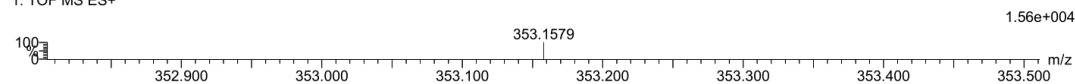
1 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 21-21 1H: 17-17 2H: 3-3 N: 1-1 O: 4-4

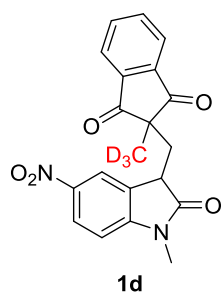
zyxx-5 421 (3.022)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
353.1579	353.1581	-0.2	-0.6	12.5	30.6	n/a	n/a	C21 1H17 2H3 N 04



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

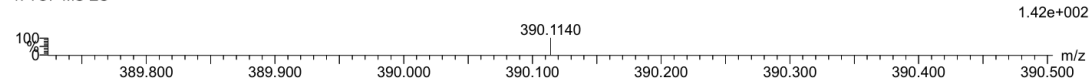
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 20-20 1H: 13-13 2H: 3-3 N: 2-2 O: 0-5 Na: 1-1

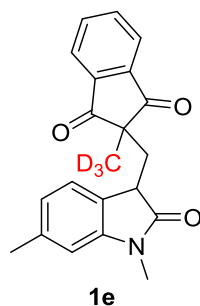
zyy-2h 483 (3.464)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
390.1140	390.1145	-0.5	-1.3	13.5	18.8	n/a	n/a	C20 1H13 2H3 N2 O5 Na



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

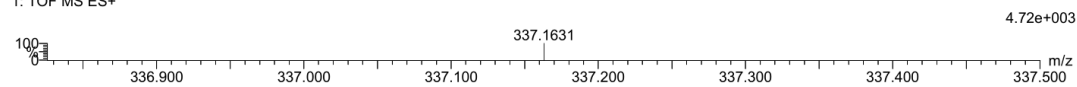
7 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 20-22 1H: 16-18 2H: 3-3 N: 0-1 O: 0-5

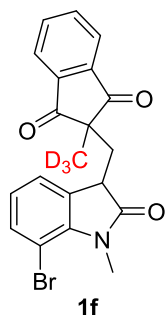
zyxx-3a 373 (2,680)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
337.1631	337.1631	0.0	0.0	12.5	27.6	n/a	n/a	C21 1H17 2H3 N O3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

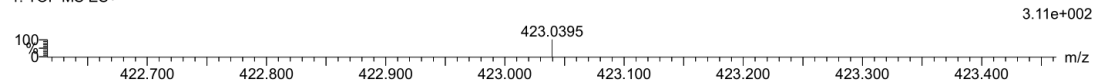
63 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 20-22 1H: 12-14 2H: 3-3 N: 0-1 O: 0-4 Na: 1-1 Br: 0-2

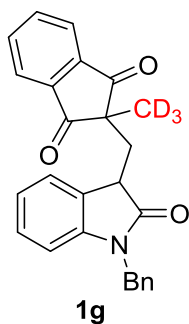
zyxx-2n 490 (3,514)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
423.0395	423.0400	-0.5	-1.2	12.5	22.0	n/a	n/a	C20 1H13 2H3 N O3 Na Br



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

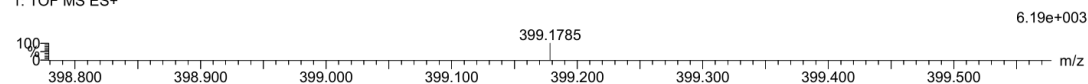
Monoisotopic Mass, Even Electron Ions

44 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

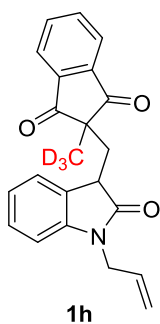
C: 20-27 1H: 18-20 2H: 3-3 N: 0-1 O: 0-4 Br: 0-2

zyxx-4 283 (2.038)
1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
399.1785	399.1788	-0.3	-0.8	16.5	28.6	n/a	n/a	C26 H19 2H3 N O3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

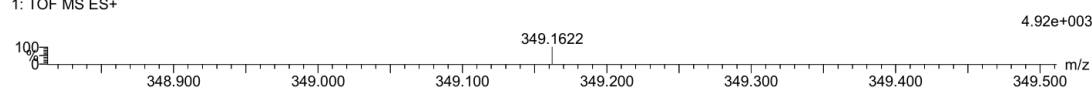
Monoisotopic Mass, Even Electron Ions

78 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

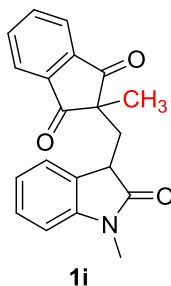
C: 20-23 1H: 15-18 2H: 3-3 N: 0-1 O: 0-4 Br: 0-2

zyxx-4 243 (1.752)
1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
349.1622	349.1631	-0.9	-2.6	13.5	27.9	n/a	n/a	C22 H17 2H3 N O3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

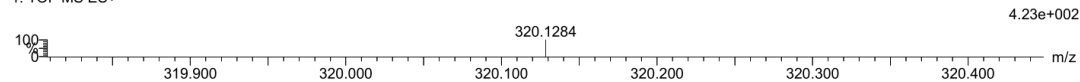
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-21 H: 10-19 N: 0-1 O: 0-4

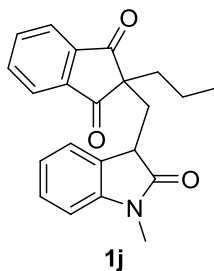
zyxx-4 472 (3,386)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
320.1284	320.1287	-0.3	-0.9	12.5	21.4	n/a	n/a	C20 H18 N O3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

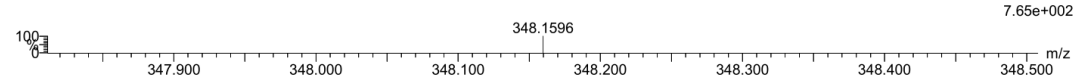
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-22 H: 10-22 N: 0-1 O: 0-3

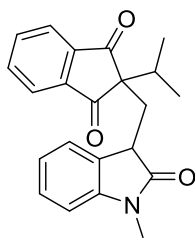
zyxx-5 334 (2,402)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
348.1596	348.1600	-0.4	-1.1	12.5	23.1	n/a	n/a	C22 H22 N O3



1k

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

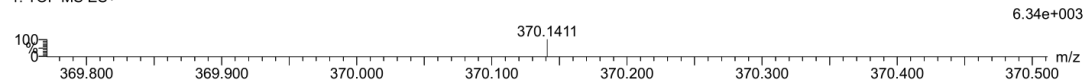
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-22 H: 10-22 N: 0-1 O: 0-3 Na: 1-1

zyxx-3b 347 (2.494)

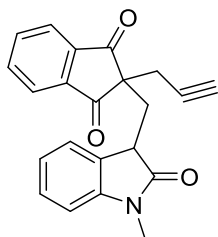
1: TOF MS ES+



6.34e+003

Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
370.1411	370.1419	-0.8	-2.2	12.5	28.6	n/a	n/a	C22 H21 N O3 Na



1l

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

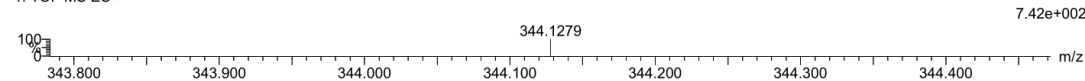
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-23 H: 10-19 N: 0-1 O: 0-3 Na: 1-1

zyxx-3d 345 (2.480)

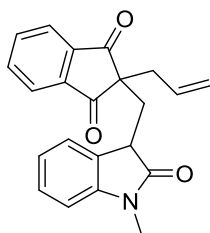
1: TOF MS ES+



7.42e+002

Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
344.1279	344.1263	1.6	4.6	11.5	23.3	n/a	n/a	C20 H19 N O3 Na



1m

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

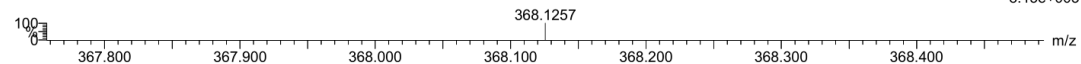
3 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-23 H: 10-21 N: 0-1 O: 0-3 Na: 1-1

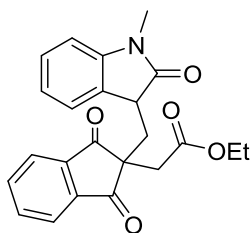
zyxx-3f 156 (1.132)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
368.1257	368.1263	-0.6	-1.6	13.5	29.1	n/a	n/a	C22 H19 N O3 Na



1n

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

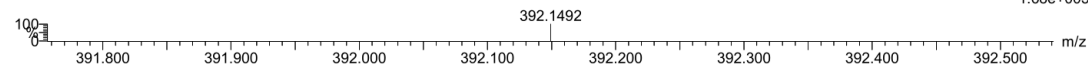
8 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-23 H: 10-24 N: 0-1 O: 0-5

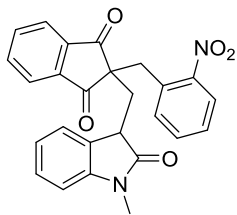
zyxx-3f 370 (2.658)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
392.1492	392.1498	-0.6	-1.5	13.5	25.3	n/a	n/a	C23 H22 N O5



1o

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

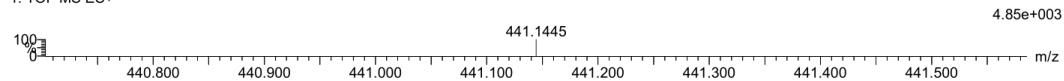
10 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-26 H: 10-24 N: 0-2 O: 0-5

zyxx-3g 261 (1.881)

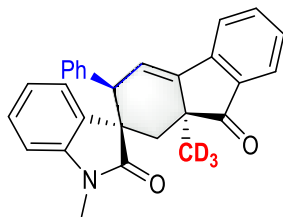
1: TOF MS ES+



4.85e+003

Minimum: -1.5
 Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
441.1445	441.1450	-0.5	-1.1	17.5	28.2	n/a	n/a	C26 H21 N2 O5



3a

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

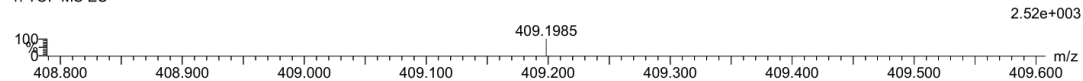
3 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-28 N: 0-2 O: 0-2 1H: 10-21 2H: 3-3

zyy-3ac 422 (3.029)

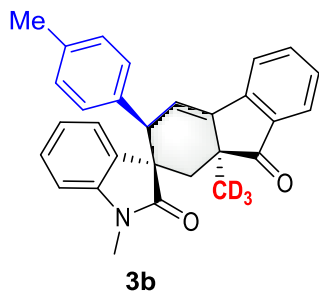
1: TOF MS ES+



2.52e+003

Minimum: -1.5
 Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
409.1985	409.1995	-1.0	-2.4	17.5	26.6	n/a	n/a	C28 N O2 1H21 2H3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

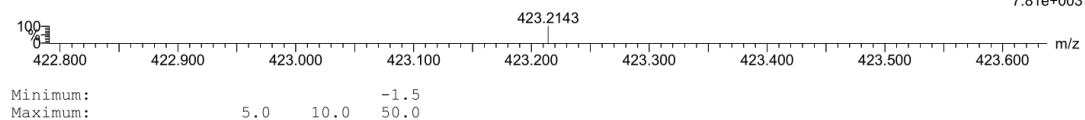
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

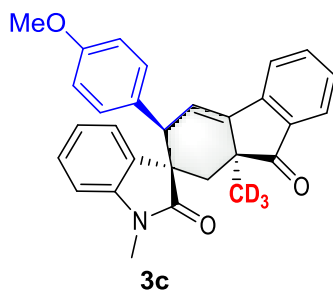
C: 19-29 1H: 10-23 2H: 3-3 N: 0-2 O: 0-2

zyy-3v 353 (2.537)

1: TOF MS ES+



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
423.2143	423.2152	-0.9	-2.1	17.5	29.4	n/a	n/a	C29 1H23 2H3 N O2



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

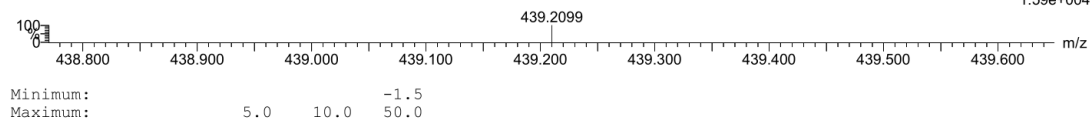
17 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

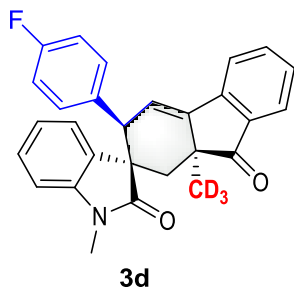
C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3

zyy-3q 316 (2.273)

1: TOF MS ES+



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
439.2099	439.2101	-0.2	-0.5	17.5	31.1	n/a	n/a	C29 1H23 2H3 N O3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

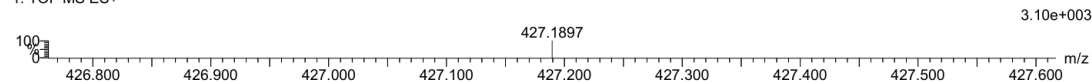
40 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3 F: 0-1

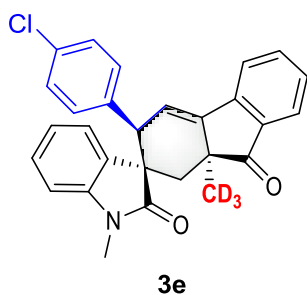
zyy-3aa 281 (2.024)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
427.1897	427.1901	-0.4	-0.9	17.5	27.0	n/a	n/a	C28 H20 2H3 N O2 F



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

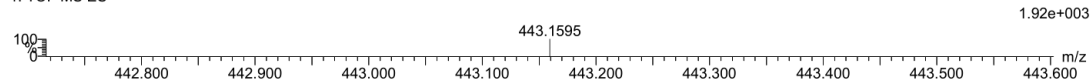
45 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3 Cl: 0-1

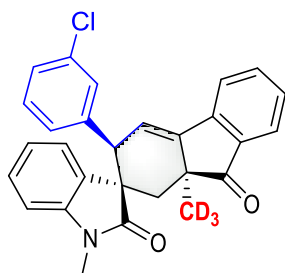
zyy-3y 381 (2.737)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
443.1595	443.1606	-1.1	-2.5	17.5	26.2	n/a	n/a	C28 H20 2H3 N O2 Cl



3f

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

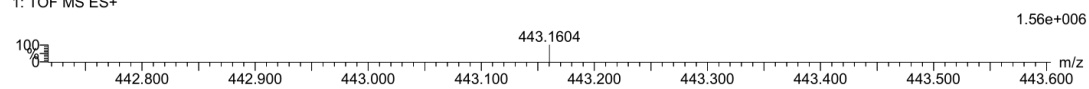
45 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3 Cl: 0-1

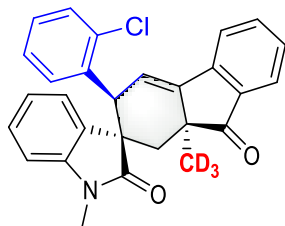
zyy-3i 351 (2.523)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
443.1604	443.1606	-0.2	-0.5	17.5	42.8	n/a	n/a	C28 1H20 2H3 N O2 Cl



3g

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

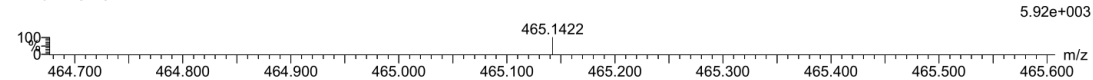
46 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3 Na: 1-1 Cl: 0-1

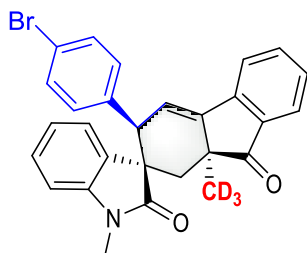
zyy-3o 457 (3.279)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
465.1422	465.1425	-0.3	-0.6	17.5	28.9	n/a	n/a	C28 1H19 2H3 N O2 Na Cl



3h

Elemental Composition Report

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Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

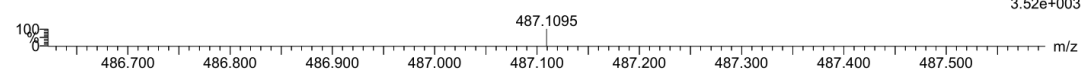
223 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-3 Br: 0-2

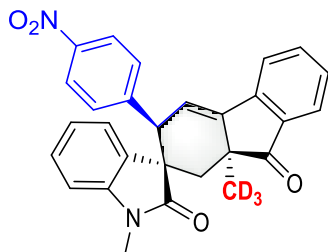
zyy-3t 357 (2,566)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
487.1095	487.1100	-0.5	-1.0	17.5	28.2	n/a	n/a	C28 1H20 2H3 N O2 Br



3i

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

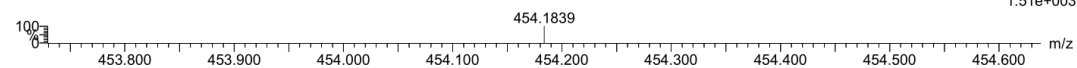
46 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-29 1H: 10-29 2H: 3-3 N: 0-2 O: 0-4

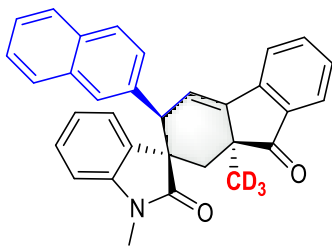
zyy-3ab 244 (1,760)

1: TOF MS ES+



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
454.1839	454.1846	-0.7	-1.5	18.5	25.3	n/a	n/a	C28 1H20 2H3 N2 O4



3j

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

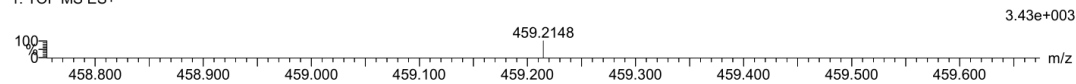
25 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-32 1H: 10-29 2H: 3-3 N: 0-2 O: 0-4

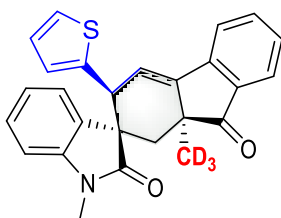
zyy-3p 463 (3.321)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
459.2148	459.2152	-0.4	-0.9	20.5	27.4	n/a	n/a	C32 1H23 2H3 N O2



3k

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

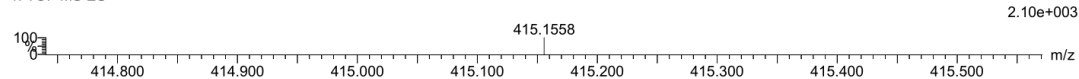
82 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-26 1H: 10-29 2H: 3-3 N: 0-2 O: 0-4 S: 0-1

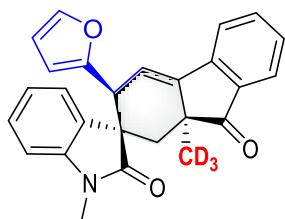
zyy-3z 480 (3.439)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
415.1558	415.1560	-0.2	-0.5	16.5	26.0	n/a	n/a	C26 1H19 2H3 N O2 S



3l

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

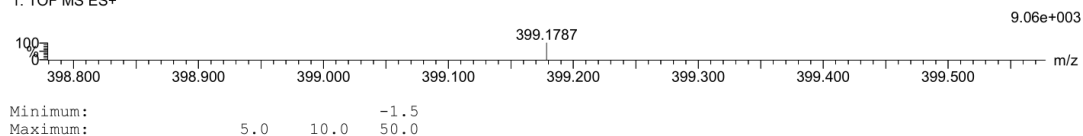
30 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-26 1H: 10-29 2H: 3-3 N: 0-2 O: 0-4

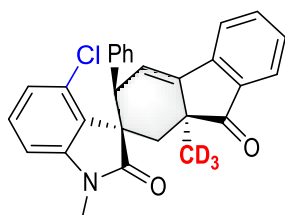
zyxx-2l 317 (2.280)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
399.1787	399.1788	-0.1	-0.3	16.5	29.6	n/a	n/a	C26 1H19 2H3 N O3



3m

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

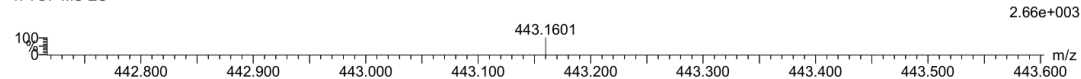
81 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-28 1H: 10-29 2H: 3-3 N: 0-2 O: 0-4 Cl: 0-1

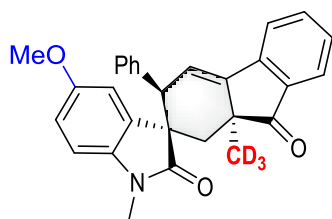
zyxx-2c 410 (2.944)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
443.1601	443.1606	-0.5	-1.1	17.5	26.9	n/a	n/a	C28 1H20 2H3 N O2 Cl



3n

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

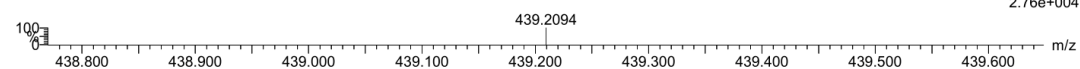
64 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-36 1H: 10-30 2H: 3-3 N: 0-2 O: 0-5

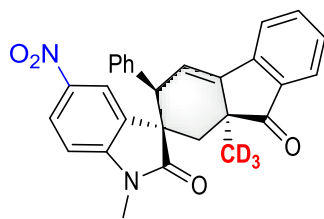
zyxx-3j 420 (3.015)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
439.2094	439.2101	-0.7	-1.6	17.5	32.6	n/a	n/a	C29 1H23 2H3 N 03



3o

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

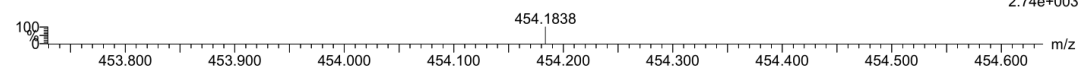
19 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 1H: 10-23 2H: 3-3 N: 0-2 O: 0-4

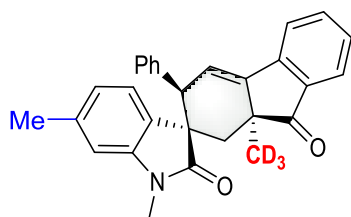
zyxx-3l 459 (3.293)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
454.1838	454.1846	-0.8	-1.8	18.5	26.9	n/a	n/a	C28 1H20 2H3 N2 O4



3p

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

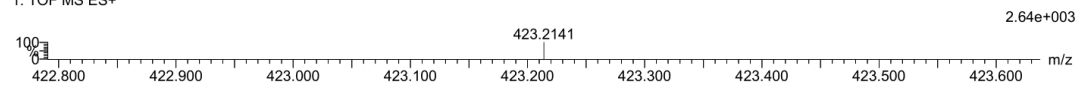
21 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 1H: 10-23 2H: 3-3 N: 0-2 O: 0-4

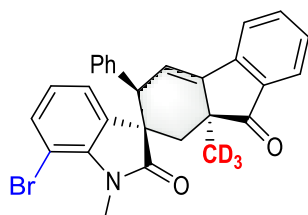
zyxx-3m 415 (2.979)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
423.2141	423.2152	-1.1	-2.6	17.5	26.8	n/a	n/a	C29 1H23 2H3 N O2



3q

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

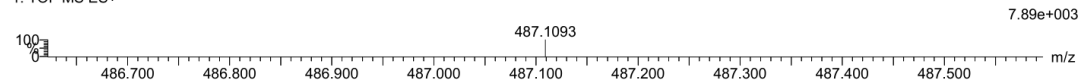
159 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 1H: 10-23 2H: 3-3 N: 0-2 O: 0-4 Br: 0-2

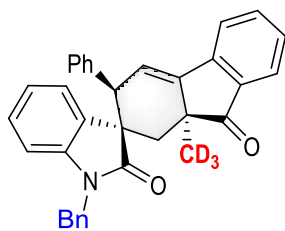
zyxx-3n 366 (2.630)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
487.1093	487.1100	-0.7	-1.4	17.5	30.2	n/a	n/a	C28 1H20 2H3 N O2 Br



3r

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

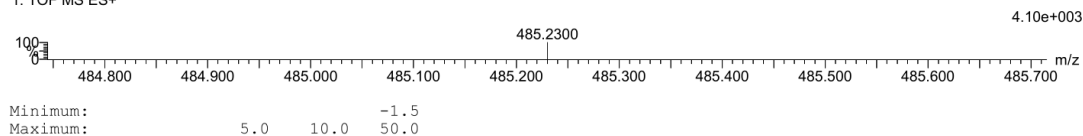
18 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-34 1H: 10-25 2H: 3-3 N: 0-2 O: 0-4

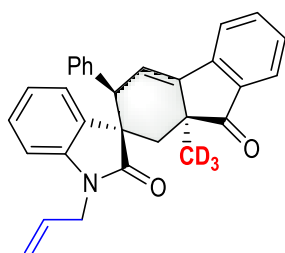
zyxx-3p 353 (2.537)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
485.2300	485.2308	-0.8	-1.6	21.5	28.1	n/a	n/a	C34 1H25 2H3 N O2



3s

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

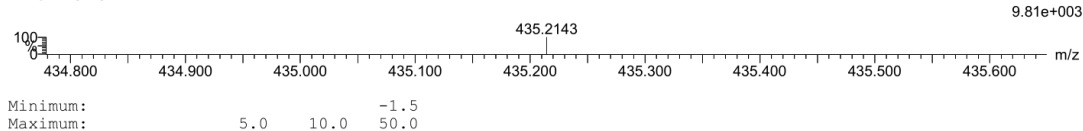
37 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-34 1H: 10-25 2H: 3-3 N: 0-2 O: 0-4

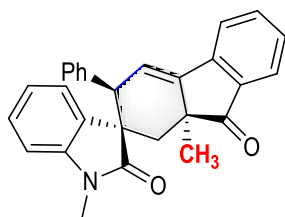
zyxx-3q 299 (2.152)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
435.2143	435.2152	-0.9	-2.1	18.5	30.1	n/a	n/a	C30 1H23 2H3 N O2



4a

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

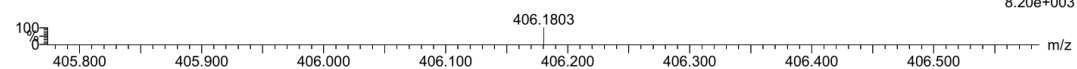
3 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-28 H: 10-24 N: 0-2 O: 0-2

zyxx-3s 359 (2.580)

1: TOF MS ES+



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
406.1803	406.1807	-0.4	-1.0	17.5	29.4	n/a	n/a	C28 H24 N O2

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

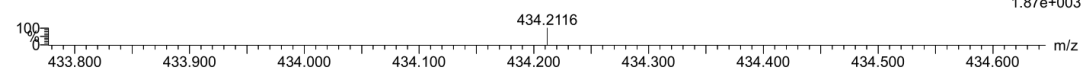
3 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

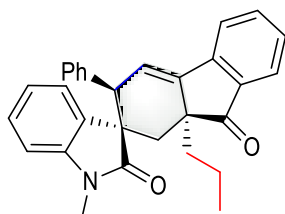
C: 19-30 H: 10-28 N: 0-2 O: 0-2

zyxx-3t 422 (3.029)

1: TOF MS ES+



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
434.2116	434.2120	-0.4	-0.9	17.5	25.8	n/a	n/a	C30 H28 N O2



4b

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

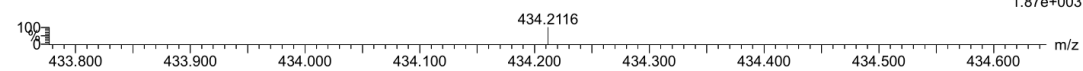
3 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 H: 10-28 N: 0-2 O: 0-2

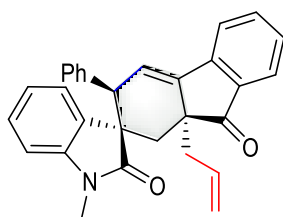
zyxx-3l 422 (3.029)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
434.2116	434.2120	-0.4	-0.9	17.5	25.8	n/a	n/a	C30 H28 N O2



4c

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

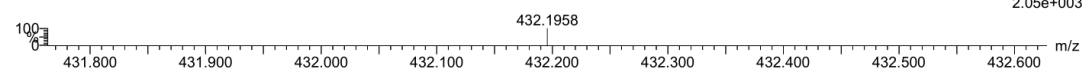
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 H: 10-28 N: 0-2 O: 0-2

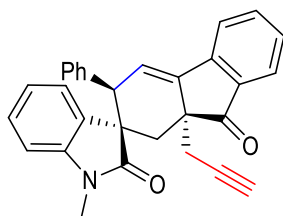
zyxx-3u 462 (3.314)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
432.1958	432.1964	-0.6	-1.4	18.5	26.1	n/a	n/a	C30 H26 N O2



4d

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

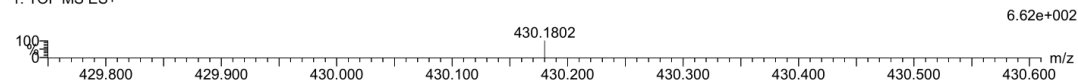
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-30 H: 10-28 N: 0-2 O: 0-2

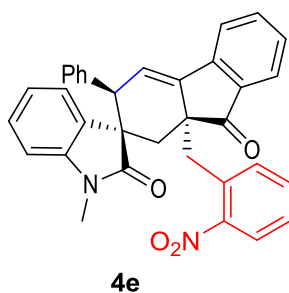
zyxx-3o 350 (2.516)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
430.1802	430.1807	-0.5	-1.2	19.5	23.2	n/a	n/a	C30 H24 N O2



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

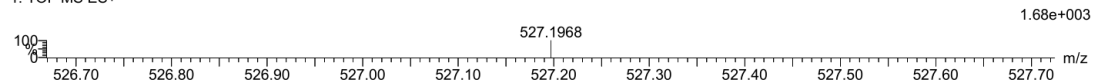
7 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-34 H: 10-28 N: 0-2 O: 0-4

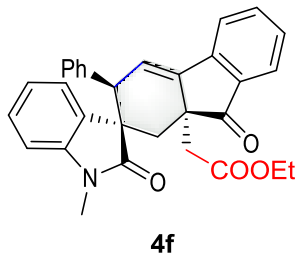
zyxx-3k 416 (2.986)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
527.1968	527.1971	-0.3	-0.6	22.5	25.8	n/a	n/a	C34 H27 N2 O4



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

12 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

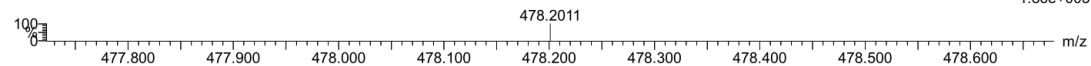
Elements Used:

C: 19-34 H: 10-28 N: 0-2 O: 0-4

zyxx-3r 370 (2.658)

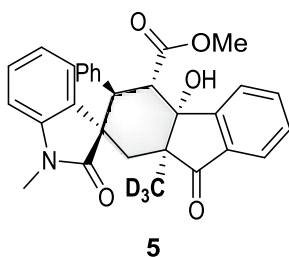
1: TOF MS ES+

1.86e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
478.2011	478.2018	-0.7	-1.5	18.5	26.0	n/a	n/a	C31 H28 N O4



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

7 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

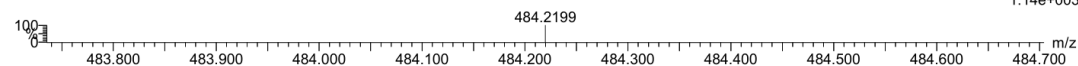
Elements Used:

C: 19-34 O: 0-5 1H: 10-26 2H: 3-3

zpy-4b 448 (3.214)

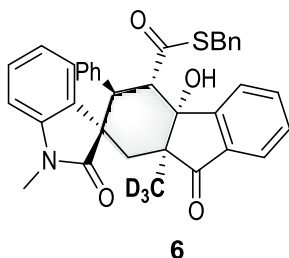
1: TOF MS ES+

1.14e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
484.2199	484.2203	-0.4	-0.8	17.5	24.7	n/a	n/a	C31 O5 1H26 2H3



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

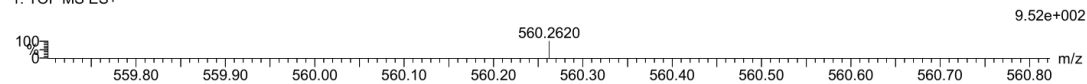
73 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-36 1H: 10-30 2H: 3-3 N: 0-2 O: 0-5

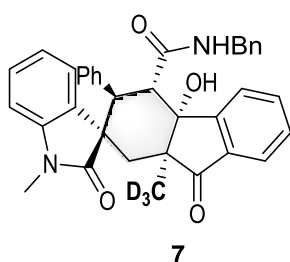
zyy-4c 232 (1.675)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
560.2620	560.2629	-0.9	-1.6	21.5	24.6	n/a	n/a	C36 1H30 2H3 N2 O4



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

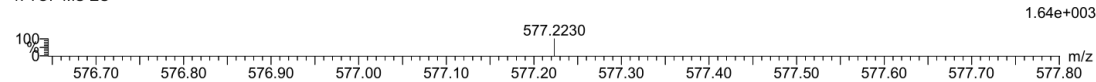
174 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 19-36 1H: 10-30 2H: 3-3 N: 0-2 O: 0-5 S: 0-1

zyxx-8 469 (3.364)

1: TOF MS ES+



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
577.2230	577.2240	-1.0	-1.7	21.5	26.1	n/a	n/a	C36 1H29 2H3 N O4 S