Rational Design of Chiral Single-Benzene-Based Fluorophores via Enantioselective Twofold C−H Activation: Solid-State and Circular Polarization Luminescence, and Cellular Imaging Application

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1. General

Experimental: Unless otherwise noted, all the reactions were set up under N_2 atmosphere utilizing glassware that was flame-dried and cooled under vacuum. All non-aqueous manipulations were using standard Schlenk techniques. Reactions were monitored using thin-layer chromatography (TLC) on Silica Gel plates. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain. Silica-gel flash column chromatography was performed using 200–300 mesh silica gel.

Materials: Unless otherwise indicated, starting catalysts and materials were obtained from Energy Chemicals, Bidepharm and J&K Scientific. Moreover, commercially available reagents were used without additional purification.

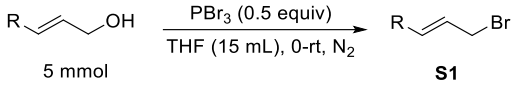
Instrumentation: ^{1}H NMR spectra were recorded at 400 MHz NMR spectrometers using TMS as an internal standard, ^{13}C NMR spectra were recorded at 101 MHz spectrometers using TMS as an internal standard, and were fully decoupled by broad band proton decoupling. ^{1}H NMR chemical shifts are reported in parts per million (ppm) and are referenced to residual protium in the NMR solvent (δ 0.00 for TMS). ^{13}C NMR chemical shifts are reported in parts per million (ppm) and are referenced to the carbon resonances of the solvent residual peak (δ 77.16 for $CDCl_3$). Data for ^{1}H NMR and ^{13}C NMR are reported as follows: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz) and integration. High-resolution mass spectra (HRMS) were obtained using ESI-TOF in positive or negative mode. Analytical HPLC was performed on Thermo Series or Angilent 1260 instrument using Daicel Chiralcel® columns as noted. Optical rotation values were measured on a Schmidt Haensch polarimeter.

Photophysical studies: UV-visible absorption and fluorescence emission spectra were recorded on a commercial spectrophotometer (Shimadzu UV-2450 and Edinburgh FS5 spectrometers, 190-900 nm scan range). Absolute fluorescence quantum yields were determined using a Hamamatsu Quantaurus spectrofluorometer equipped with an integrating sphere. The corresponding sample was measured at various dilutions to approach a value without self-quenching contributions. Each measurement was repeated three times and the average was calculated. Fluorescence lifetime (τ) were determined by Time-Correlated Single Photon Counting (TCSPC) technique with the FLS 1000 spectrometer by exciting the sample with pulsed laser diodes at 380 nm under magic angle conditions and using a fast PMT detector (R928P) for fluorescence detection. The fitting process was performed with the programs Fluoracle and FAST and completed when ca. χ^2<1.2 was reached. Radiative rate (k_r) constant according to Φ_F/τ_F. Non-radiative rate constant (k_{nr}) according to $(1-\Phi_F)/\tau_F$.

2. Preparation of Substrates

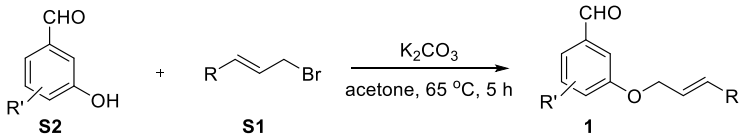
General procedure A[1a-b]

The synthesis of allyl bromides (**S1**).



To a 50 mL Schlenk flask equipped with a stirring bar was added allyl alcohol (5 mmol). The mixture was then evacuated and backfilled with nitrogen for three times. After that, THF (15 mL) and PBr_3 (0.5 equiv.) were added by syringe at 0 °C. The mixture was then stirred at room temperature for another 1.5 h. the reaction was quenched by adding H_2O (20 mL) and saturated $NaHCO_3$, extracted with ethyl acetate (25 mL × 2). After removing all of the solvent, the product was used for the next step directly without further purification.

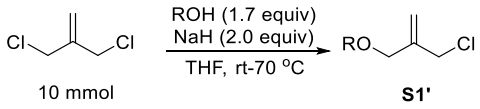
The synthesis of substrates **1**.



To a 50 mL one-neck round flask equipped with a stirring bar was added **S2** (3 mmol) and K_2CO_3 (6 mmol) in acetone (20 mL), followed by allyl *br*omide (5 mmol). The mixture was stirred at 65 °C for 5 h. The solvent was removed and reaction mixture was extracted with H_2O (20 mL) and ethyl acetate (40 mL). Dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 20 : 1) to get substrate **1**.

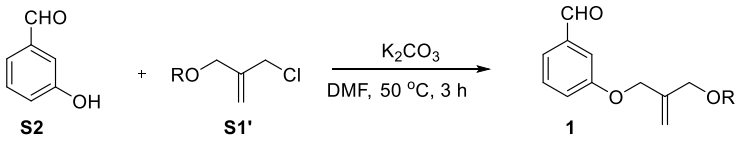
General procedure B[1c]

The synthesis of allyl chlorides (**S1'**).



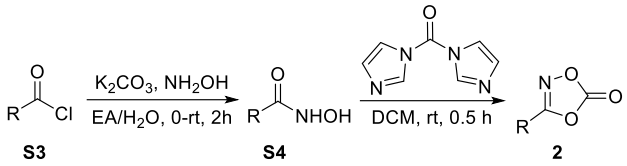
To a 50 mL one-neck round flask equipped with a stirring bar were added alcohol (17 mmol) and THF (20 mL). The mixture was added NaH (20 mmol) and stirred at room temperature for 0.5 h. After that, the solution of allyl chloride (10 mmol) in THF (5 mL) was added slowly at 0 °C. The mixture was then stirred at 70 °C for another 12 h. The reaction was quenched by adding H_2O (20 mL) and saturated $NaHCO_3$, extracted with CH_2Cl_2 (25 mL × 2). After removing all of the solvent, the product **S1'** was used for the next step directly without further purification.

The synthesis of substrates **1**.



To a 50 mL one-neck round flask equipped with a stirring bar was added **S2** (4 mmol) and K_2CO_3 (8 mmol) in DMF (15 mL), followed by **S1'** (4 mmol). The mixture was stirred at 50 ºC for 3 h. The solvent was removed and reaction mixture was extracted with H_2O (20 mL) and CH_2Cl_2 (40 mL). Dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 20 : 1) to get substrate **1**.

The synthesis of substrates **2.**[2]

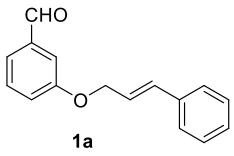


To a stirred biphasic mixture of $NH_2OH{\cdot}HCl$ (10 mmol, 2.0 equiv.) in ethyl acetate (40 mL) and H_2O (20 mL) was added K_2CO_3 (10 mmol, 2.0 equiv.). The solution was cooled to 0 °C followed by dropwise addition of acid chloride (5 mmol), and then warmed to room temperature and stirred for additional 1.5 h. The reaction mixture was extracted with ethyl acetate (25 mL × 2) and dried over anhydrous Na_2SO_4, filtered and removed all of organic solvent. The crude product (**S4**) was directly used for the next step without purification.

To a stirred mixture of hydroxamic acid (**S4**) in CH_2Cl_2 (50 mL) was added 1,1'-carbonyldiimidazole (5.5 mmol, 1.1 equiv.). The residue was stirred for 0.5 h. The reaction was quenched with 1 M HCl (15 mL) and extracted with CH_2Cl_2 (25 mL × 2). The combined organic phase was washed with H_2O (50 mL), dried over anhydrous Na_2SO_4 and removed all of organic solvent to afford crude 3-substituted 1,4,2-dioxazol-5-ones. The crude product was purified through a short silica gel chromatography quickly (petroleum ether/ethyl acetate = 20 : 1) to get pure product of **2**.

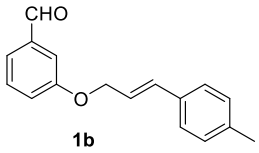
3. Characterization of Substrates

(*E*)-3-(Cinnamyloxy)benzaldehyde



By following the general procedure **A**, the product **1a** was afforded (0.56 g, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.50–7.40 (m, 5H), 7.36–7.31 (m, 2H), 7.29–7.22 (m, 2H), 6.76 (d, J = 16.0 Hz, 1H), 6.42 (dt, J = 16.0, 5.8 Hz, 1H), 4.77 (dd, J = 5.8, 1.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 138.0, 136.4, 133.7, 130.3, 128.8 (2C), 128.2, 126.7 (2C), 123.81, 123.78, 122.3, 113.2, 69.0; **HRMS** (ESI) Calcd for $C_{16}H_{15}O_2$ $[M+H]^+$ 239.1067; found 239.1068.

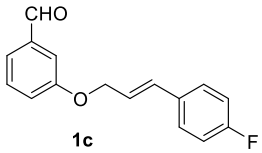
(*E*)-3-((3-(4-Tolyl)allyl)oxy)benzaldehyde



1b

By following the general procedure **A**, the product **1b** was afforded (0.58 g, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.50–7.43 (m, 3H), 7.32 (d, J = 8.2 Hz, 2H), 7.27–7.21 (m, 1H), 7.14 (d, J = 7.8 Hz, 2H), 6.72 (d, J = 16.0 Hz, 1H), 6.36 (dt, J = 15.9, 5.9 Hz, 1H), 4.74 (d, J = 5.7 Hz, 2H), 2.34 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 138.1, 137.9, 133.7, 133.5, 130.2, 129.4 (2C), 126.7 (2C), 123.7, 122.7, 122.3, 113.3, 69.1, 21.4; **HRMS** (ESI) Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$ 253.1223; found 253.1223.

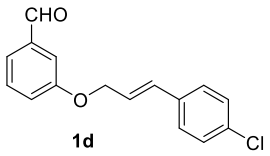
(*E*)-3-((3-(4-Fluorophenyl)allyl)oxy)benzaldehyde



1c

By following the general procedure **A**, the product **1c** was afforded (0.49 g, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.51–7.42 (m, 3H), 7.42–7.35 (m, 2H), 7.23 (dt, J = 6.5, 2.7 Hz, 1H), 7.06–6.99 (m, 2H), 6.72 (d, J = 16.0 Hz, 1H), 6.33 (dt, J = 15.9, 5.8 Hz, 1H), 4.75 (dd, J = 5.9, 1.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 162.7 (d, J = 247.5 Hz), 159.3, 138.0, 132.6, 132.5, 130.3, 128.3 (d, J = 8.1 Hz, 2C), 123.9, 123.5 (d, J = 2.3 Hz), 122.3, 115.7 (d, J = 21.7 Hz, 2C), 113.1, 68.9; **HRMS** (ESI) Calcd for $C_{16}H_{14}FO_2$ $[M+H]^+$ 257.0972; found 257.0972.

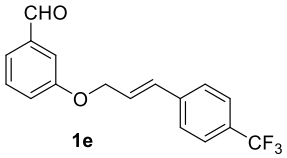
(*E*)-3-((3-(4-Chlorophenyl)allyl)oxy)benzaldehyde



1d

By following the general procedure **A**, the product **1d** was afforded (0.56 g, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.50–7.41 (m, 3H), 7.36–7.27 (m, 4H), 7.23 (dt, J = 6.7, 2.6 Hz, 1H), 6.70 (d, J = 16.0 Hz, 1H), 6.38 (dt, J = 16.0, 5.7 Hz, 1H), 4.74 (dd, J = 5.7, 1.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.1, 137.8, 134.8, 133.7, 132.1, 130.2, 128.8 (2C), 127.9 (2C), 124.4, 123.9, 122.1, 113.0, 68.6; **HRMS** (ESI) Calcd for $C_{16}H_{14}ClO_2$ $[M+H]^+$ 273.0677; found 273.0677.

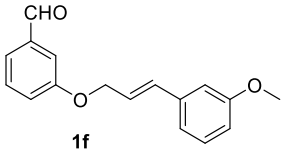
(*E*)-3-((3-(4-(Trifluoromethyl)phenyl)allyl)oxy)benzaldehyde



1e

By following the general procedure **A**, the product **1e** was afforded (0.54 g, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.54–7.43 (m, 5H), 7.27–7.23 (m, 1H), 6.80 (d, J = 16.1 Hz, 1H), 6.51 (dt, J = 16.0, 5.5 Hz, 1H), 4.79 (dd, J = 5.5, 1.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.1, 139.9, 138.0, 131.8, 130.3, 129.9 (q, J = 32.4 Hz), 126.9 (2C), 126.6, 125.7 (q, J = 3.8 Hz, 2C), 124.2 (q, J = 273.1 Hz), 124.1, 122.3, 113.0, 68.5; **HRMS** (ESI) Calcd for $C_{17}H_{14}F_3O_2$ $[M+H]^+$ 307.0940; found 307.0945.

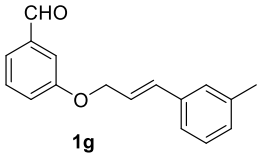
(*E*)-3-((3-(3-Methoxyphenyl)allyl)oxy)benzaldehyde



1f

By following the general procedure **A**, the product **1f** was afforded (0.69 g, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.51–7.42 (m, 3H), 7.28–7.21 (m, 2H), 7.01 (d, J = 7.6 Hz, 1H), 6.95 (s, 1H), 6.83 (dd, J = 7.9, 2.0 Hz, 1H), 6.73 (d, J = 16.0 Hz, 1H), 6.41 (dt, J = 15.9, 5.7 Hz, 1H), 4.76 (dd, J = 5.8, 1.5 Hz, 2H), 3.82 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.9, 159.3, 138.0, 137.8, 133.5, 130.3, 129.8, 124.1, 123.8, 122.3, 119.4, 113.8, 113.2, 112.0, 68.9, 55.4; **HRMS** (ESI) Calcd for $C_{17}H_{17}O_3$ $[M+H]^+$ 269.1172; found 269.1174.

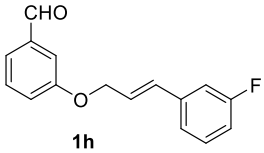
(*E*)-3-((3-(3-Tolyl)allyl)oxy)benzaldehyde



1g

By following the general procedure **A**, the product **1g** was afforded (0.60 g, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.48–7.41 (m, 3H), 7.25–7.19 (m, 4H), 7.11–7.04 (m, 1H), 6.71 (d, J = 16.0 Hz, 1H), 6.39 (dt, J = 15.9, 5.8 Hz, 1H), 4.73 (dd, J = 5.9, 1.5 Hz, 2H), 2.34 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 138.3, 137.9, 136.2, 133.7, 130.2, 128.9, 128.6, 127.4, 123.8, 123.7, 123.5, 122.2, 113.2, 68.9, 21.5; **HRMS** (ESI) Calcd for $C_{17}H_{17}O_2$ $[M+H]^+$ 253.1223; found 253.1224.

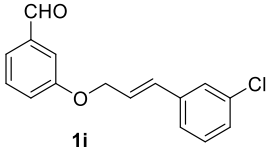
(*E*)-3-((3-(3-Fluorophenyl)allyl)oxy)benzaldehyde



1h

By following the general procedure **A**, the product **1h** was afforded (0.49 g, 63% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.51–7.43 (m, 3H), 7.33–7.22 (m, 2H), 7.17 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 10.1 Hz, 1H), 6.96 (td, *J* = 8.4, 2.6 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.42 (dt, *J* = 15.9, 5.6 Hz, 1H), 4.76 (dd, *J* = 5.7, 1.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0, 163.1 (d, *J* = 245.5 Hz), 159.1, 138.6 (d, *J* = 7.7 Hz), 137.9, 132.0 (2.6 Hz), 130.2, 130.1 (d, *J* = 9.5 Hz), 125.2, 123.8, 122.6 (d, *J* = 2.8 Hz), 122.1, 114.8 (d, *J* = 21.1 Hz), 113.04, 113.03 (d, *J* = 21.9 Hz), 68.4; **HRMS** (ESI) Calcd for $C_{16}H_{14}FO_2$ $[M+H]^+$ 257.0972; found 257.0974.

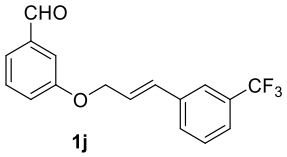
(*E*)-3-((3-(3-Chlorophenyl)allyl)oxy)benzaldehyde



1i

By following the general procedure **A**, the product **1i** was afforded (0.52 g, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.51–7.41 (m, 3H), 7.39 (s, 1H), 7.30–7.19 (m, 4H), 6.69 (d, *J* = 16.0 Hz, 1H), 6.41 (dt, *J* = 15.8, 5.6 Hz, 1H), 4.78–4.70 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.1, 138.2, 137.9, 134.7, 131.9, 130.3, 130.0, 128.0, 126.6, 125.4, 124.9, 123.9, 122.2, 113.1, 68.5; **HRMS** (ESI) Calcd for $C_{16}H_{14}ClO_2$ $[M+H]^+$ 273.0677; found 273.0678.

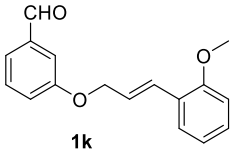
(*E*)-3-((3-(3-(Trifluoromethyl)phenyl)allyl)oxy)benzaldehyde



1j

By following the general procedure **A**, the product **1j** was afforded (0.70 g, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.66 (s, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.54–7.41 (m, 5H), 7.26–7.21 (m, 1H), 6.79 (d, *J* = 16.0 Hz, 1H), 6.49 (dt, *J* = 16.0, 5.5 Hz, 1H), 4.79 (d, *J* = 5.7 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1, 159.1, 137.9, 137.1, 131.6, 131.0 (q, *J* = 32.1 Hz), 130.3, 129.8, 129.2, 125.9, 124.6 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 273.4 Hz), 123.9, 123.3 (q, *J* = 3.8 Hz), 122.1, 113.0, 68.4; **HRMS** (ESI) Calcd for $C_{17}H_{14}F_3O_2$ $[M+H]^+$ 307.0940; found 307.0943.

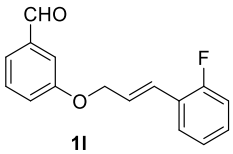
(*E*)-3-((3-(2-Methoxyphenyl)allyl)oxy)benzaldehyde



1k

By following the general procedure **A**, the product **1k** was afforded (0.44 g, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.50–7.42 (m, 4H), 7.28–7.22 (m, 2H), 7.08 (d, *J* = 16.0 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.44 (dt, *J* = 16.1, 6.0 Hz, 1H), 4.77 (dd, *J* = 6.0, 1.5 Hz, 2H), 3.86 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 159.4, 157.0, 137.9, 130.2, 129.3, 129.0, 127.4, 125.4, 124.4, 123.6, 122.3, 120.8, 113.5, 111.0, 69.6, 55.6; **HRMS** (ESI) Calcd for $C_{17}H_{17}O_3$ $[M+H]^+$ 269.1172; found 269.1174.

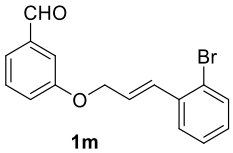
(*E*)-3-((3-(2-Fluorophenyl)allyl)oxy)benzaldehyde



1l

By following the general procedure **A**, the product **1l** was afforded (0.38 g, 49% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.53–7.42 (m, 4H), 7.28–7.20 (m, 2H), 7.11 (td, *J* = 7.6, 1.3 Hz, 1H), 7.05 (ddd, *J* = 10.9, 8.2, 1.2 Hz, 1H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.51 (dt, *J* = 16.1, 5.7 Hz, 1H), 4.78 (dd, *J* = 5.7, 1.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 160.5 (d, *J* = 249.7 Hz), 159.2, 138.0, 130.3, 129.5 (d, *J* = 8.4 Hz), 127.8 (d, *J* = 3.6 Hz), 126.5 (d, *J* = 5.1 Hz), 126.0 (d, *J* = 3.5 Hz), 124.3 (d, *J* = 3.5 Hz), 124.2 (d, *J* = 12.0 Hz), 123.8, 122.2, 115.9 (d, *J* = 22.0 Hz), 113.3, 69.0; **HRMS** (ESI) Calcd for $C_{16}H_{14}FO_2$ $[M+H]^+$ 257.0972; found 257.0973.

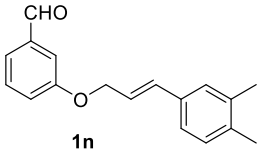
(*E*)-3-((3-(2-Bromophenyl)allyl)oxy)benzaldehyde



1m

By following the general procedure **A**, the product **1m** was afforded (0.41 g, 43% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.58–7.53 (m, 2H), 7.51–7.44 (m, 3H), 7.32–7.23 (m, 2H), 7.16–7.08 (m, 2H), 6.35 (dt, *J* = 15.9, 5.7 Hz, 1H), 4.80 (dd, *J* = 5.7, 1.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.2, 138.0, 136.4, 133.1, 132.4, 130.3, 129.4, 127.7, 127.4, 126.9, 123.9, 123.8, 122.3, 113.4, 68.7; **HRMS** (ESI) Calcd for $C_{16}H_{14}BrO_2$ $[M+H]^+$ 317.0172; found 317.0171.

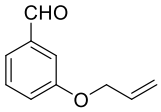
(*E*)-3-((3-(3,4-Dimethylphenyl)allyl)oxy)benzaldehyde



1n

By following the general procedure **A**, the product **1n** was afforded (0.62 g, 77% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.46–7.38 (m, 3H), 7.24–7.16 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 15.9 Hz, 1H), 6.33 (dt, *J* = 16.0, 5.9 Hz, 1H), 4.69 (d, *J* = 5.8 Hz, 2H), 2.23 (s, 3H), 2.22 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 159.4, 137.9, 136.9, 136.8, 134.0, 133.8, 130.2, 130.0, 128.0, 124.2, 123.7, 122.5, 122.3, 113.4, 69.2, 19.9, 19.7; **HRMS** (ESI) Calcd for $C_{18}H_{18}NaO_2$ $[M+Na]^+$ 289.1199; found 289.1199.

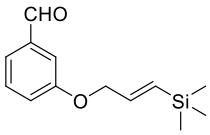
3-(Allyloxy)benzaldehyde



1o

By following the general procedure **A**, the product **1o** was afforded (0.35 g, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.50–7.36 (m, 3H), 7.23–7.15 (m, *J* = 7.0, 2.3 Hz, 1H), 6.12–5.99 (m, 1H), 5.43 (dd, *J* = 17.3, 1.8 Hz, 1H), 5.31 (dd, *J* = 10.6, 1.7 Hz, 1H), 4.62–4.56 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1, 159.2, 137.8, 132.7, 130.1, 123.6, 122.1, 118.1, 113.2, 69.0; **HRMS** (ESI) Calcd for $C_{10}H_{11}O_2$ $[M+H]^+$ 163.0754; found 163.0737.

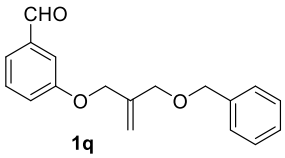
(*E*)-3-((3-(Trimethylsilyl)allyl)oxy)benzaldehyde



1p

By following the general procedure **A**, the product **1p** was afforded (0.48 g, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.47–7.40 (m, 2H), 7.38 (d, *J* = 2.2 Hz, 1H), 7.19 (dt, *J* = 6.7, 2.5 Hz, 1H), 6.21 (dt, *J* = 18.8, 4.4 Hz, 1H), 6.08 (d, *J* = 18.8 Hz, 1H), 4.60 (d, *J* = 4.5 Hz, 2H), 0.09 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 159.4, 139.8, 137.9, 133.7, 130.2, 123.6, 122.2, 113.4, 70.9, -1.33 (3C); **HRMS** (ESI) Calcd for $C_{13}H_{17}O_2Si$ $[M-H]^-$ 233.1003; found 233.1033.

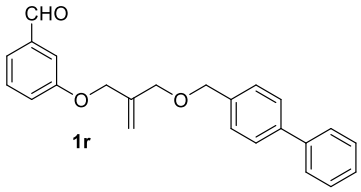
3-((2-((Benzyloxy)methyl)allyl)oxy)benzaldehyde



1q

By following the general procedure **B**, the product **1q** was afforded (0.86 g, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.48–7.40 (m, 3H), 7.36–7.26 (m, 5H), 7.19 (ddd, J = 7.6, 2.7, 1.7 Hz, 1H), 5.38–5.35 (m, 1H), 5.34–5.32 (m, 1H), 4.64 (s, 2H), 4.54 (s, 2H), 4.13 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 141.0, 138.1, 137.9, 130.2, 128.5 (2C), 127.8 (3C), 123.6, 122.1, 115.6, 113.5, 72.4, 70.8, 68.8; **HRMS** (ESI) Calcd for $C_{18}H_{19}O_3$ $[M+H]^+$ 283.1329; found 283.1328.

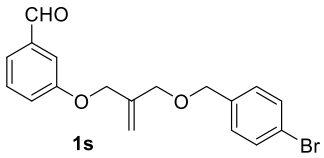
3-((2-(([1,1'-Biphenyl]-4-ylmethoxy)methyl)allyl)oxy)benzaldehyde



1r

By following the general procedure **B**, the product **1r** was afforded (1.01 g, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.61–7.55 (m, 4H), 7.48–7.39 (m, 7H), 7.37–7.32 (m, 1H), 7.23–7.18 (m, 1H), 5.38 (s, 1H), 5.36 (s, 1H), 4.66 (s, 2H), 4.59 (s, 2H), 4.16 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 141.1, 141.0, 140.8, 137.9, 137.2, 130.2, 128.9 (2C), 128.3 (2C), 127.4, 127.3 (2C), 127.2 (2C), 123.7, 122.1, 115.7, 113.5, 72.1, 70.9, 68.9; **HRMS** (ESI) Calcd for $C_{24}H_{23}O_3$ $[M+H]^+$ 359.1642; found 359.1648.

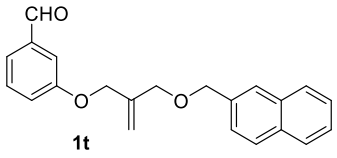
3-((2-(((4-Bromobenzyl)oxy)methyl)allyl)oxy)benzaldehyde



1s

By following the general procedure **B**, the product **1s** was afforded (0.99 g, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.49–7.40 (m, 5H), 7.23–7.17 (m, 3H), 5.37 (d, J = 1.6 Hz, 1H), 5.33 (d, J = 1.2 Hz, 1H), 4.63 (s, 2H), 4.48 (s, 2H), 4.12 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.2, 140.8, 137.9, 137.1, 131.6 (2C), 130.2, 129.4 (2C), 123.8, 122.1, 121.7, 115.9, 113.3, 71.6, 70.9, 68.8; **HRMS** (ESI) Calcd for $C_{18}H_{18}BrO_3$ $[M+H]^+$ 361.0434; found 361.0433.

3-((2-((Naphthalen-2-ylmethoxy)methyl)allyl)oxy)benzaldehyde

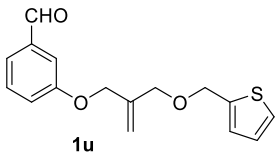


1t

By following the general procedure **B**, the product **1t** was afforded (0.84 g, 63% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.84–7.75 (m, 4H), 7.50–7.37 (m, 6H), 7.17 (ddd, J = 7.8, 2.8, 1.4 Hz, 1H), 5.37 (d, J = 1.6 Hz, 1H), 5.35 (s, 1H), 4.69 (s, 2H),

4.64 (s, 2H), 4.16 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 141.0, 137.9, 135.6, 133.3, 133.1, 130.2, 128.3, 128.0, 127.8, 126.6, 126.3, 126.0, 125.8, 123.6, 122.0, 115.7, 113.6, 72.5, 70.8, 68.8; **HRMS** (ESI) Calcd for $C_{22}H_{21}O_3$ $[M+H]^+$ 333.1485; found 333.1487.

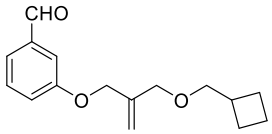
3-((2-((Thiophen-2-ylmethoxy)methyl)allyl)oxy)benzaldehyde



1u

By following the general procedure **B**, the product **1u** was afforded (0.61 g, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.49–7.39 (m, 3H), 7.28 (dd, J = 5.0, 1.3 Hz, 1H), 7.19 (ddd, J = 7.4, 2.7, 1.7 Hz, 1H), 7.02–6.95 (m, 2H), 5.37 (d, J = 1.6 Hz, 1H), 5.32 (d, J = 1.2 Hz, 1H), 4.70 (s, 2H), 4.62 (s, 2H), 4.13 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 140.8 (2C), 137.9, 130.2, 126.8, 126.7, 126.1, 123.6, 122.1, 115.8, 113.6, 70.4, 68.8, 66.7; **HRMS** (ESI) Calcd for $C_{16}H_{17}O_3S$ $[M+H]^+$ 289.0893; found 289.0891.

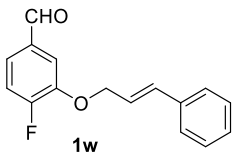
3-((2-((Cyclobutylmethoxy)methyl)allyl)oxy)benzaldehyde



1v

By following the general procedure **B**, the product **1v** was afforded (0.49 g, 47% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.49–7.39 (m, 3H), 7.24–7.18 (m, 1H), 5.35–5.31 (m, 1H), 5.30–5.26 (m, 1H), 4.61 (s, 2H), 4.07 (s, 2H), 3.42 (d, J = 6.8 Hz, 2H), 2.65–2.52 (m, 1H), 2.10–2.00 (m, 2H), 1.97–1.81 (m, 2H), 1.80–1.68 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 159.3, 141.3, 137.8, 130.1, 123.6, 122.1, 115.1, 113.5, 75.1, 71.7, 68.8, 35.2, 25.2 (2C), 18.7; **HRMS** (ESI) Calcd for $C_{16}H_{21}O_3$ $[M+H]^+$ 261.1485; found 261.1488.

(*E*)-3-(Cinnamyloxy)-4-fluorobenzaldehyde

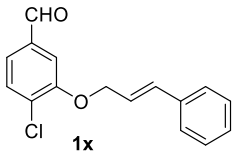


1w

By following the general procedure **A**, the product **1w** was afforded (0.53 g, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.57 (dd, J = 8.0, 2.0 Hz, 1H), 7.46 (ddd, J = 8.2, 4.5, 2.0 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.3 Hz, 2H), 7.30–7.22 (m, 2H), 6.78 (d, J = 15.9 Hz, 1H), 6.42 (dt, J = 15.9, 6.0 Hz, 1H), 4.84 (d, J = 5.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.8, 156.9 (d, J = 257.5 Hz), 147.7 (d, J = 11.3

Hz), 136.2, 134.4, 133.3 (d, *J* = 3.2 Hz), 128.8 (2C), 128.3, 126.8 (2C), 125.6 (d, *J* = 8.4 Hz), 123.1, 116.9 (d, *J* = 19.7 Hz), 113.7 (d, *J* = 3.6 Hz), 70.1; **HRMS** (ESI) Calcd for $C_{16}H_{14}FO_2$ $[M+H]^+$ 257.0972; found 257.0970.

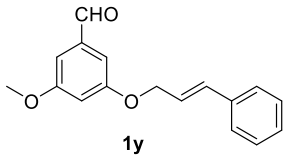
(*E*)-4-Chloro-3-(cinnamyloxy)benzaldehyde



1x

By following the general procedure **A**, the product **1x** was afforded (0.42 g, 51% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 1.7 Hz, 1H), 7.45–7.39 (m, 3H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.30–7.24 (m, 1H), 6.81 (d, *J* = 16.0 Hz, 1H), 6.43 (dt, *J* = 16.0, 5.7 Hz, 1H), 4.86 (dd, *J* = 5.8, 1.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.1, 154.9, 136.3, 136.1, 134.0, 131.1, 130.4, 128.8 (2C), 128.3, 126.8 (2C), 124.6, 123.1, 111.9, 69.9; **HRMS** (ESI) Calcd for $C_{16}H_{14}ClO_2$ $[M+H]^+$ 273.0677; found 273.0669.

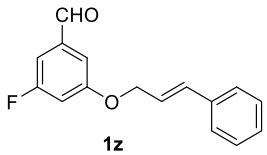
(*E*)-3-(Cinnamyloxy)-5-methoxybenzaldehyde



1y

By following the general procedure **A**, the product **1y** was afforded (0.55 g, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.41 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.30–7.23 (m, 1H), 7.09–7.05 (m, 1H), 7.04–7.01 (m, 1H), 6.79–6.71 (m, 2H), 6.40 (dt, *J* = 15.9, 5.8 Hz, 1H), 4.73 (dd, *J* = 5.9, 1.5 Hz, 2H), 3.84 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1, 161.4, 160.3, 138.5, 136.3, 133.7, 128.8 (2C), 128.2, 126.7 (2C), 123.7, 108.1, 108.0, 107.4, 69.1, 55.8; **HRMS** (ESI) Calcd for $C_{17}H_{17}O_3$ $[M+H]^+$ 269.1172; found 269.1164.

(*E*)-3-(Cinnamyloxy)-5-fluorobenzaldehyde

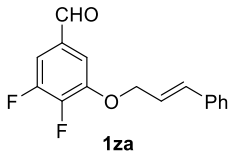


1z

By following the general procedure **A**, the product **1z** was afforded (0.42 g, 54% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.90 (d, *J* = 1.6 Hz, 1H), 7.43–7.38 (m, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.29–7.23 (m, 2H), 7.16 (ddd, *J* = 7.9, 2.4, 1.3 Hz, 1H), 6.92 (dt, *J* = 10.0, 2.4 Hz, 1H), 6.74 (d, *J* = 15.9 Hz, 1H), 6.37 (dt, *J* = 16.0, 5.8 Hz, 1H), 4.72 (dd, *J* = 5.9, 1.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.8 (d, *J* = 2.8 Hz), 163.8 (d, *J*

= 248.8 Hz), 160.5 (d, *J* = 10.6 Hz), 138.8 (d, *J* = 8.0 Hz), 136.1, 134.0, 128.8 (2C), 128.3, 126.7 (2C), 123.1, 111.0 (d, *J* = 2.7 Hz), 109.1 (d, *J* = 22.5 Hz), 108.9 (d, *J* = 25.2 Hz), 69.4; **HRMS** (ESI) Calcd for $C_{16}H_{12}FO_2$ [M-H]$^-$ 255.0827; found 255.0834.

(*E*)-3-(Cinnamyloxy)-4,5-difluorobenzaldehyde



1za

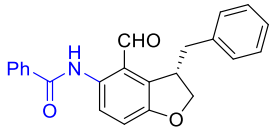
By following the general procedure **A**, the product **1za** was afforded (0.34 g, 41% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.42 (d, *J* = 6.9 Hz, 2H), 7.40–7.27 (m, 5H), 6.78 (d, *J* = 15.9 Hz, 1H), 6.41 (dt, *J* = 15.9, 6.0 Hz, 1H), 4.86 (d, *J* = 5.9 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7 (d, *J* = 2.5 Hz), 151.3 (dd, *J* = 251.0, 11.6 Hz), 149.13 (d, *J* = 5.5 Hz), 145.7 (dd, *J* = 257.1, 11.9 Hz), 136.0, 134.8, 131.8 (dd, *J* = 6.1, 3.9 Hz), 128.8 (2C), 128.5, 126.9 (2C), 122.6, 112.0 (d, *J* = 18.3 Hz), 110.0 (d, *J* = 2.5 Hz), 70.7; **HRMS** (ESI) Calcd for $C_{16}H_{11}F_2O_2$ [M-H]$^-$ 273.0733; found 273.0736.

4. General Procedure for the Construction via Rh-Catalyzed Enantioselective Twofold C−H Activation

To a 25 mL of Schlenk tube equipped with a magnetic stirring bar were added substrates **1** (0.15 mmol), **2** (0.375 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (0.225 mmol) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, chiral amine (50 mol%), HFIP (0.9 mL) and DCE (0.9 mL) were added subsequently. After stirring at 60 ºC for 36 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10 : 1) as the eluent to give the corresponding products **3**.

5. Characterization of Products

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide

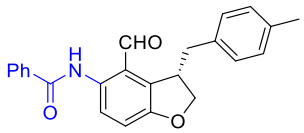


3aa

By following the general procedure, the reaction of **1a** (36.0 mg, 0.15 mmol) with **2a** (61.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.6 mg, 0.225 mmol), $AgSbF_6$ (11.5 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3aa** (46.6 mg, 87% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 9.57 (s, 1H), 8.82 (d, *J* = 9.0 Hz, 1H), 8.02 (d, *J* = 7.0 Hz, 2H), 7.60–7.47 (m, 3H), 7.36–

7.27 (m, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.10–7.03 (m, 2H), 4.58–4.47 (m, 2H), 4.00–3.91 (m, 1H), 2.99 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.90 (dd, *J* = 13.6, 7.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 165.8, 155.7, 137.9, 134.94, 134.85, 134.7, 132.0, 129.4 (2C), 129.0 (2C), 128.9 (2C), 127.5 (2C), 127.3, 120.9, 118.9, 117.7, 76.9, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{23}H_{20}NO_3$ $[M+H]^+$ 358.1438; found 358.1436; $[\alpha]^{18}_D$ = -24.7 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 91%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 13.3 min, t_{major} = 18.4 min.

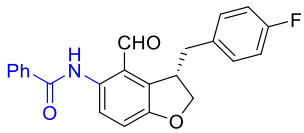
(S)-*N*-(4-Formyl-3-(4-methylbenzyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ba

By following the general procedure, the reaction of **1b** (38.0 mg, 0.15 mmol) with **2a** (60.6 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (11.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ba** (41.4 mg, 74% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 9.70 (s, 1H), 8.82 (d, *J* = 8.9 Hz, 1H), 8.07–8.03 (m, 2H), 7.59–7.49 (m, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 7.9 Hz, 2H), 4.54 (dd, *J* = 9.0, 2.1 Hz, 1H), 4.49 (dd, *J* = 9.0, 7.1 Hz, 1H), 3.96 (qd, *J* = 7.4, 2.0 Hz, 1H), 2.97–2.85 (m, 2H), 2.34 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 165.8, 155.7, 136.9, 135.2, 134.9, 134.8 (2C), 132.0, 129.7 (2C), 129.3 (2C), 128.9 (2C), 127.5 (2C), 120.9, 118.9, 117.7, 76.8, 43.0, 42.3, 21.2; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_3$ $[M+H]^+$ 372.1594; found 372.1623; $[\alpha]^{18}_D$ = -52.0 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 16.1 min, t_{major} = 20.0 min.

(S)-*N*-(3-(4-Fluorobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide

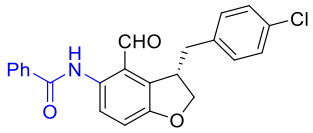


3ca

By following the general procedure, the reaction of **1c** (38.6 mg, 0.15 mmol) with **2a** (60.6 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.5 mg, 0.225 mmol), $AgSbF_6$ (11.0 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ca** (40.7 mg, 72% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.86 (s, 1H), 9.70 (s, 1H), 8.82 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 2H), 7.60–7.49 (m, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.07–6.96 (m, 4H), 4.56–4.46 (m, 2H), 4.01–3.91 (m, 1H), 3.00–2.86 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 165.9, 162.1 (d, *J* = 246.1 Hz), 155.7, 135.0, 134.71, 134.70, 133.6 (d, *J* = 3.3 Hz), 132.1, 130.9 (d, *J* = 8.0 Hz, 2C), 129.0

(2C), 127.5 (2C), 121.1, 118.8, 117.8, 115.9 (d, J = 21.4 Hz, 2C), 76.7, 42.9, 41.7; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1335; $[\alpha]^{18}_D$ = -44.2 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 91%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 17.0 min, t_{major} = 21.5 min.

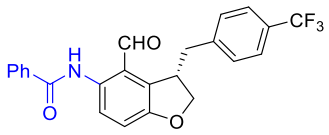
(S)-*N*-(3-(4-Chlorobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3da

By following the general procedure, the reaction of **1d** (41.0 mg, 0.15 mmol) with **2a** (60.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (10.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3da** (45.4 mg, 77% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 9.80 (s, 1H), 8.81 (d, J = 9.0 Hz, 1H), 8.08–8.01 (m, 2H), 7.60–7.49 (m, 3H), 7.30–7.25 (m, 2H), 7.14 (d, J = 9.0 Hz, 1H), 7.01 (d, J = 8.1 Hz, 2H), 4.52–4.45 (m, 2H), 4.01–3.92 (m, 1H), 2.91 (d, J = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 165.8, 155.7, 136.3, 135.0, 134.7, 134.6, 133.2, 132.1, 130.7 (2C), 129.1 (2C), 129.0 (2C), 127.5 (2C), 121.2, 118.7, 117.9, 76.5, 42.6, 41.8; **HRMS** (ESI) Calcd for $C_{23}H_{19}ClNO_3$ $[M+H]^+$ 392.1048; found 392.1037; $[\alpha]^{18}_D$ = -49.4 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 17.2 min, t_{major} = 21.3 min.

(S)-*N*-(4-Formyl-3-(4-(trifluoromethyl)benzyl)-2,3-dihydrobenzofuran-5-yl)benzamide

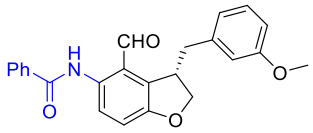


3ea

By following the general procedure, the reaction of **1e** (46.6 mg, 0.15 mmol) with **2a** (60.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.6 mg, 0.225 mmol), $AgSbF_6$ (11.3 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.1 mg, 0.045 mmol) afforded **3ea** (42.2 mg, 66% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 9.88 (s, 1H), 8.82 (dd, J = 9.0, 1.5 Hz, 1H), 8.06–8.00 (m, 2H), 7.61–7.49 (m, 5H), 7.22 (d, J = 7.9 Hz, 2H), 7.15 (dd, J = 9.0, 1.6 Hz, 1H), 4.52–4.44 (m, 2H), 4.08–3.99 (m, 1H), 3.07–2.94 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0, 165.9, 155.7, 142.0, 135.1, 134.6, 134.4, 132.1, 129.7 (2C), 129.6 (q, J = 32.6 Hz), 129.0 (2C), 127.5 (2C), 125.9 (q, J = 3.8 Hz, 2C), 124.2 (q, J = 272.1 Hz), 121.3, 118.6, 118.0, 76.2, 42.4, 42.2; **HRMS** (ESI) Calcd for $C_{24}H_{19}F_3NO_3$ $[M+H]^+$ 426.1312; found 426.1330; $[\alpha]^{18}_D$ = -

68.9 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 92%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 12.1 min, t_{major} = 14.4 min.

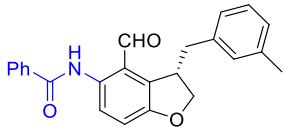
(S)-*N*-(4-Formyl-3-(3-methoxybenzyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3fa

By following the general procedure, the reaction of **1f** (40.7 mg, 0.15 mmol) with **2a** (60.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (11.1 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.3 mg, 0.045 mmol) afforded **3fa** (43.6 mg, 75% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 9.62 (s, 1H), 8.83 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 6.6 Hz, 2H), 7.60–7.48 (m, 3H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.16 (d, *J* = 9.0 Hz, 1H), 6.83 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 6.59 (s, 1H), 4.58–4.48 (m, 2H), 3.96 (qd, *J* = 7.5, 2.3 Hz, 1H), 3.76 (s, 3H), 3.00–2.84 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 165.8, 160.1, 155.7, 139.5, 135.0, 134.9, 134.8, 132.1, 130.1, 128.9 (2C), 127.5 (2C), 121.7, 121.0, 119.0, 117.7, 115.3, 112.5, 76.9, 55.3, 42.9, 42.7; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543; found 388.1542; $[\alpha]^{18}_D$ = -52.0 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 14.9 min, t_{major} = 21.2 min.

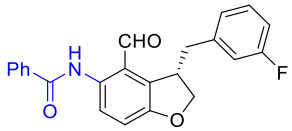
(S)-*N*-(4-Formyl-3-(3-methylbenzyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ga

By following the general procedure, the reaction of **1g** (38.7 mg, 0.15 mmol) with **2a** (61.7 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), KH_2PO_4 (30.5 mg, 0.225 mmol), $AgSbF_6$ (11.0 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ga** (40.4 mg, 73% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 9.58 (s, 1H), 8.82 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 6.2 Hz, 2H), 7.59–7.47 (m, 3H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.90–6.84 (m, 2H), 4.57–4.46 (m, 2H), 3.99–3.89 (m, 1H), 2.98–2.82 (m, 2H), 2.31 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 165.8, 155.7, 138.7, 137.9, 135.1, 134.9, 134.8, 132.0, 130.2, 128.9 (3C), 128.0, 127.5 (2C), 126.4, 120.9, 119.0, 117.7, 76.9, 43.1, 42.6, 21.5; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_3$ $[M+H]^+$ 372.1594; found 372.1607; $[\alpha]^{18}_D$ = -48.1 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 88%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 14.8 min, t_{major} = 20.2 min.

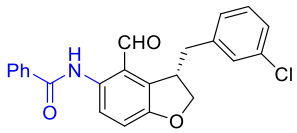
(S)-*N*-(3-(3-Fluorobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3ha

By following the general procedure, the reaction of **1h** (39.3 mg, 0.15 mmol) with **2a** (62.0 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (11.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.6 mg, 0.045 mmol) afforded **3ha** (39.6 mg, 70% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 9.70 (s, 1H), 8.82 (d, J = 9.0 Hz, 1H), 8.03 (d, J = 6.8 Hz, 2H), 7.59–7.48 (m, 3H), 7.31–7.23 (m, 1H), 7.15 (d, J = 9.0 Hz, 1H), 7.01–6.94 (m, 1H), 6.87–6.78 (m, 2H), 4.54–4.46 (m, 2H), 4.02–3.93 (m, 1H), 3.00–2.87 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 165.8, 163.1 (d, J = 247.2 Hz), 155.7, 140.4 (d, J = 7.1 Hz), 135.0, 134.7, 134.5, 132.1, 130.6 (d, J = 8.3 Hz), 128.9 (2C), 127.5 (2C), 125.1 (d, J = 3.0 Hz), 121.2, 118.8, 117.9, 116.2 (d, J = 21.1 Hz), 114.2 (d, J = 21.0 Hz), 76.6, 42.6, 42.2 (d, J = 1.8 Hz); **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1329; $[\alpha]^{18}_D$ = -65.0 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 92%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 17.5 min, t_{major} = 22.1 min.

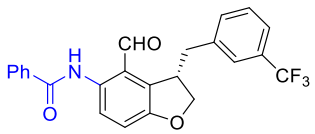
(S)-*N*-(3-(3-Chlorobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3ia

By following the general procedure, the reaction of **1i** (41.0 mg, 0.15 mmol) with **2a** (60.9 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.4 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (13.5 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ia** (50.2 mg, 85% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.87 (s, 1H), 9.73 (s, 1H), 8.84 (d, J = 9.0 Hz, 1H), 8.07–8.01 (m, 2H), 7.60–7.49 (m, 3H), 7.30–7.22 (m, 2H), 7.17 (d, J = 9.0 Hz, 1H), 7.12–7.09 (m, 1H), 6.95 (dt, J = 6.9, 1.7 Hz, 1H), 4.54–4.48 (m, 2H), 4.02–3.94 (m, 1H), 2.99–2.87 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.2, 165.9, 155.7, 139.9, 135.1, 134.9, 134.7, 134.5, 132.1, 130.3, 129.5, 129.0 (2C), 127.6, 127.5 (3C), 121.3, 118.8, 118.0, 76.6, 42.7, 42.1; **HRMS** (ESI) Calcd for $C_{23}H_{19}ClNO_3$ $[M+H]^+$ 392.1048; found 392.1036; $[\alpha]^{18}_D$ = -7.8 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 93%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 17.0 min, t_{major} = 22.0 min.

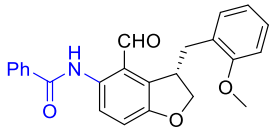
(S)-*N*-(4-Formyl-3-(3-(trifluoromethyl)benzyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ja

By following the general procedure, the reaction of **1j** (46.0 mg, 0.15 mmol) with **2a** (61.9 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (31.5 mg, 0.225 mmol), $AgSbF_6$ (10.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.4 mg, 0.045 mmol) afforded **3ja** (39.0 mg, 61% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.82 (s, 1H), 9.69 (s, 1H), 8.84 (d, *J* = 9.0 Hz, 1H), 8.05–8.00 (m, 2H), 7.60–7.49 (m, 4H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.31–7.26 (m, 2H), 7.18 (d, *J* = 9.0 Hz, 1H), 4.56–4.49 (m, 2H), 4.05–3.97 (m, 1H), 3.09–2.96 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.9, 165.9, 155.6, 138.8, 135.1, 134.7, 134.2, 132.8, 132.1, 131.4 (q, *J* = 32.3 Hz), 129.5, 129.0 (2C), 127.5 (2C), 126.2 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 273.8 Hz), 121.4, 118.8, 118.0, 76.5, 42.6, 42.1; **HRMS** (ESI) Calcd for $C_{24}H_{19}F_3NO_3$ $[M+H]^+$ 426.1312; found 426.1324; $[\alpha]^{18}_D$ = -15.6 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 9.9 min, t_{major} = 11.1 min.

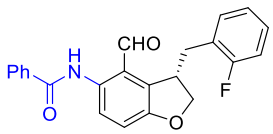
(S)-*N*-(4-Formyl-3-(2-methoxybenzyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ka

By following the general procedure, the reaction of **1k** (41.1 mg, 0.15 mmol) with **2a** (61.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (11.0 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.4 mg, 0.045 mmol) afforded **3ka** (29.8 mg, 51% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.95 (s, 1H), 9.90 (s, 1H), 8.81 (d, *J* = 8.9 Hz, 1H), 8.05 (d, *J* = 6.5 Hz, 2H), 7.57–7.49 (m, 3H), 7.33–7.27 (m, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 6.98 (dd, *J* = 7.3, 1.8 Hz, 1H), 6.89 (t, *J* = 7.7 Hz, 2H), 4.56 (dd, *J* = 9.0, 1.7 Hz, 1H), 4.49–4.43 (m, 1H), 4.12–4.05 (m, 1H), 3.86 (s, 3H), 2.95 (dd, *J* = 13.2, 6.1 Hz, 1H), 2.88 (dd, *J* = 13.3, 8.8 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.6, 165.8, 157.8, 155.7, 136.1, 134.9, 134.8, 132.0, 131.2, 128.9 (2C), 128.8, 127.5 (2C), 126.6, 120.8, 120.7, 119.0, 117.5, 110.5, 77.0, 55.5, 40.8, 38.2; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543; found 388.1547; $[\alpha]^{18}_D$ = +50.7 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 73%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 11.7 min, t_{major} = 15.7 min.

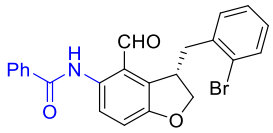
(S)-*N*-(3-(2-Fluorobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3la

By following the general procedure, the reaction of **1l** (38.6 mg, 0.15 mmol) with **2a** (60.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (11.3 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3la** (35.8 mg, 64% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.91 (s, 1H), 9.85 (s, 1H), 8.84 (d, *J* = 9.0 Hz, 1H), 8.06–8.01 (m, 2H), 7.59–7.49 (m, 3H), 7.32–7.25 (m, 1H), 7.17 (d, *J* = 9.0 Hz, 1H), 7.12–7.04 (m, 2H), 7.01 (td, *J* = 7.4, 1.8 Hz, 1H), 4.55 (dd, *J* = 9.1, 1.9 Hz, 1H), 4.49 (dd, *J* = 9.1, 7.1 Hz, 1H), 4.10–4.02 (m, 1H), 2.97 (d, *J* = 7.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6, 165.8, 161.6 (d, *J* = 245.3 Hz), 155.6, 135.1, 135.0, 134.8, 132.1, 131.7 (d, *J* = 4.6 Hz), 129.3 (d, *J* = 8.2 Hz), 129.0 (2C), 127.5 (2C), 125.1 (d, *J* = 15.5 Hz), 124.6 (d, *J* = 3.6 Hz), 121.1, 118.8, 117.8, 115.8 (d, *J* = 21.6 Hz), 76.7, 41.3 (d, *J* = 1.8 Hz), 36.4; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1320; $[\alpha]^{18}_D$ = -15.6 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 85%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 16.8 min, t_{major} = 18.8 min.

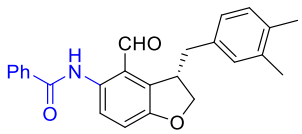
(S)-*N*-(3-(2-Bromobenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3ma

By following the general procedure, the reaction of **1m** (48.1 mg, 0.15 mmol) with **2a** (60.7 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (5.0 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (10.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ma** (28.9 mg, 44% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 9.72 (d, *J* = 0.7 Hz, 1H), 8.84 (d, *J* = 9.0 Hz, 1H), 8.05–8.00 (m, 2H), 7.60 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.58–7.48 (m, 3H), 7.25–7.14 (m, 3H), 6.97 (dd, *J* = 7.4, 1.9 Hz, 1H), 4.56 (dd, *J* = 9.1, 1.6 Hz, 1H), 4.49 (dd, *J* = 9.0, 7.1 Hz, 1H), 4.22–4.14 (m, 1H), 3.09 (dd, *J* = 13.5, 8.3 Hz, 1H), 3.01 (dd, *J* = 13.5, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.8, 165.8, 155.7, 137.2, 135.0, 134.9, 134.8, 133.4, 132.3, 132.1, 129.2, 128.9 (2C), 127.9, 127.5 (2C), 125.0, 121.1, 119.1, 117.7, 76.5, 42.5, 40.4; **HRMS** (ESI) Calcd for $C_{23}H_{19}BrNO_3$ $[M+H]^+$ 436.0543; found 436.0570; $[\alpha]^{18}_D$ = +55.5 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 83%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 16.5 min, t_{major} = 22.4 min.

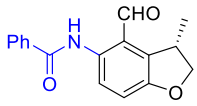
(S)-*N*-(3-(3,4-Dimethylbenzyl)-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3na

By following the general procedure, the reaction of **1n** (40.1 mg, 0.15 mmol) with **2a** (62.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (11.3 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.3 mg, 0.045 mmol) afforded **3na** (33.6 mg, 58% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.91 (s, 1H), 9.72 (s, 1H), 8.82 (d, J = 9.0 Hz, 1H), 8.07–8.00 (m, 2H), 7.60–7.48 (m, 3H), 7.15 (d, J = 9.0 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.87–6.80 (m, 2H), 4.54 (dd, J = 9.0, 2.0 Hz, 1H), 4.48 (dd, J = 9.0, 7.2 Hz, 1H), 3.99–3.90 (m, 1H), 2.87 (d, J = 7.7 Hz, 2H), 2.25 (s, 3H), 2.22 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.7, 165.8, 155.7, 137.3, 135.5, 135.34, 135.32, 134.9, 134.8, 132.0, 130.7, 130.2, 128.9 (2C), 127.5 (2C), 126.7, 120.9, 118.9, 117.7, 76.8, 43.1, 42.3, 19.9, 19.6; **HRMS** (ESI) Calcd for $C_{25}H_{24}NO_3$ $[M+H]^+$ 386.1751; found 386.1775; $[\alpha]^{18}_D$ = +26.0 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 15.1 min, t_{major} = 20.1 min.

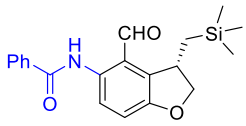
(S)-*N*-(4-Formyl-3-methyl-2,3-dihydrobenzofuran-5-yl)benzamide



3oa

By following a modified procedure at 70 °C for 24 h, the reaction of **1o** (25.6 mg, 0.15 mmol) with **2a** (61.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (31.1 mg, 0.225 mmol), $AgSbF_6$ (13.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.3 mg, 0.045 mmol) afforded **3oa** (12.7 mg, 30% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.91 (s, 1H), 10.26 (s, 1H), 8.79 (d, J = 9.0 Hz, 1H), 8.08–8.03 (m, 2H), 7.60–7.50 (m, 3H), 7.13 (d, J = 8.9 Hz, 1H), 4.66 (t, J = 8.4 Hz, 1H), 4.36 (dd, J = 8.8, 2.7 Hz, 1H), 3.99–3.89 (m, 1H), 1.43 (d, J = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.1, 165.9, 155.5, 137.3, 135.1, 134.8, 132.1, 129.0 (2C), 127.5 (2C), 120.9, 118.4, 117.8, 79.1, 35.7, 23.2; **HRMS** (ESI) Calcd for $C_{17}H_{16}NO_3$ $[M+H]^+$ 282.1125; found 282.1123; $[\alpha]^{18}_D$ = +5.3 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 49%; CHIRALPAK®IG (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 21.1 min, t_{major} = 22.2 min.

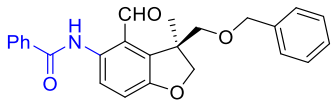
(S)-*N*-(4-Formyl-3-((trimethylsilyl)methyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3pa

By following a modified procedure at 70 °C for 24 h, the reaction of **1p** (36.8 mg, 0.15 mmol) with **2a** (62.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.9 mg, 0.0075 mmol), KH_2PO_4 (31.1 mg, 0.225 mmol), $AgSbF_6$ (12.6 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3pa** (21.2 mg, 40% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.91 (s, 1H), 10.22 (s, 1H), 8.77 (d, J = 9.0 Hz, 1H), 8.05 (dd, J = 8.1, 1.7 Hz, 2H), 7.60–7.50 (m, 3H), 7.11 (d, J = 9.0 Hz, 1H), 4.59 (t, J = 8.2 Hz, 1H), 4.35 (dd, J = 8.7, 2.5 Hz, 1H), 4.01–3.93 (m, 1H), 1.26–1.19 (m, 1H), 0.93–0.87 (m, 1H), 0.07 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.0, 165.8, 155.2, 138.9, 135.2, 134.9, 132.1, 129.0 (2C), 127.5 (2C), 120.6, 117.9, 117.7, 78.3, 37.3, 27.0, -0.9 (3C); **HRMS** (ESI) Calcd for $C_{20}H_{24}NO_3Si$ $[M+H]^+$ 354.1520; found 354.1522; $[\alpha]^{18}_D$ = +8.4 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 70%; CHIRALPAK®AD-H (90% hexanes: 10% isopropanol, 1 mL/min) t_{minor} = 8.4 min, t_{major} = 9.9 min.

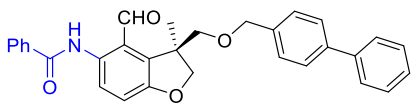
(S)-*N*-(3-((Benzyloxy)methyl)-4-formyl-3-methyl-2,3-dihydrobenzofuran-5-yl)benzamide



3qa

By following a modified procedure at 50 °C for 36 h, the reaction of **1q** (43.5 mg, 0.15 mmol) with **2a** (61.7 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (5.2 mg, 0.0075 mmol), $AgSbF_6$ (11.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.6 mg, 0.075 mmol) afforded **3qa** (38.7 mg, 64% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.14 (s, 1H), 10.42 (s, 1H), 8.82 (d, J = 9.1 Hz, 1H), 8.06 (dd, J = 8.0, 1.7 Hz, 2H), 7.58–7.52 (m, 3H), 7.35–7.27 (m, 3H), 7.25–7.20 (m, 2H), 7.12 (d, J = 9.0 Hz, 1H), 4.55 (d, J = 12.2 Hz, 1H), 4.51–4.46 (m, 2H), 4.19 (d, J = 8.8 Hz, 1H), 3.60 (s, 2H), 1.61 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.5, 166.0, 156.4, 137.5, 135.8, 135.4, 135.0, 132.0, 129.0 (2C), 128.6 (2C), 128.1, 127.8 (2C), 127.6 (2C), 121.7, 120.5, 117.9, 81.2, 76.0, 73.7, 48.9, 24.3; **HRMS** (ESI) Calcd for $C_{25}H_{23}NO_4$ $[M+H]^+$ 402.1700; found 402.1701; $[\alpha]^{18}_D$ = +21.4 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 86%; CHIRALPAK®IG (80% hexanes: 20% isopropanol, 1 mL/min) t_{major} = 14.7 min, t_{minor} = 15.4 min.

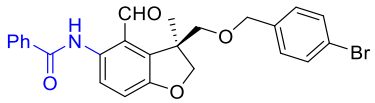
(S)-*N*-(3-(([1,1'-Biphenyl]-4-ylmethoxy)methyl)-4-formyl-3-methyl-2,3-dihydrobenzofuran-5-yl)benzamide



3ra

By following a modified procedure at 50 °C for 36 h, the reaction of **1r** (54.2 mg, 0.15 mmol) with **2a** (61.2 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (5.0 mg, 0.0075 mmol), $AgSbF_6$ (10.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.4 mg, 0.075 mmol) afforded **3ra** (30.9 mg, 43% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.14 (s, 1H), 10.44 (s, 1H), 8.84 (d, J = 9.0 Hz, 1H), 8.07–8.02 (m, 2H), 7.59–7.49 (m, 7H), 7.45–7.39 (m, 2H), 7.36–7.31 (m, 1H), 7.28 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 9.1 Hz, 1H), 4.59 (d, J = 12.2 Hz, 1H), 4.52 (dd, J = 10.7, 1.8 Hz, 2H), 4.20 (d, J = 8.8 Hz, 1H), 3.64 (s, 2H), 1.62 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.4, 165.9, 156.4, 140.9, 140.8, 136.5, 135.7, 135.4, 134.9, 132.0, 128.92 (2C), 128.88 (2C), 128.3 (2C), 127.51 (2C), 127.47, 127.3 (2C), 127.2 (2C), 121.7, 120.5, 117.9, 81.1, 76.0, 73.4, 48.9, 24.3; **HRMS** (ESI) Calcd for $C_{31}H_{28}NO_4$ $[M+H]^+$ 478.2013; found 478.2016; $[\alpha]^{18}_D$ = +37.5 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IG (70% hexanes: 30% isopropanol, 1 mL/min) t_{major} = 14.3 min, t_{minor} = 16.4 min.

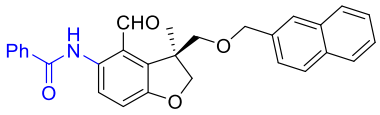
(S)-*N*-(3-(((4-Bromobenzyl)oxy)methyl)-4-formyl-3-methyl-2,3-dihydrobenzofuran-5-yl)benzamide



3sa

By following a modified procedure at 50 °C for 36 h, the reaction of **1s** (53.6 mg, 0.15 mmol) with **2a** (61.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (5.1 mg, 0.0075 mmol), $AgSbF_6$ (11.1 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.6 mg, 0.075 mmol) afforded **3sa** (36.5 mg, 51% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.13 (s, 1H), 10.41 (s, 1H), 8.83 (d, J = 9.0 Hz, 1H), 8.08–8.03 (m, 2H), 7.58–7.50 (m, 3H), 7.45 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 9.1 Hz, 1H), 7.11–7.07 (m, 2H), 4.49–4.40 (m, 3H), 4.19 (d, J = 8.9 Hz, 1H), 3.59 (s, 2H), 1.61 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.3, 165.9, 156.4, 136.5, 135.5, 135.4, 134.9, 132.0, 131.7 (2C), 129.4 (2C), 128.9 (2C), 127.5 (2C), 121.9, 121.7, 120.5, 117.9, 81.0, 76.2, 72.9, 48.8, 24.2; **HRMS** (ESI) Calcd for $C_{25}H_{23}BrNO_4$ $[M+H]^+$ 480.0805; found 480.0809; $[\alpha]^{18}_D$ = +20.8 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 87%; CHIRALPAK®IG (80% hexanes: 20% isopropanol, 1 mL/min) t_{major} = 13.1 min, t_{minor} = 13.8 min.

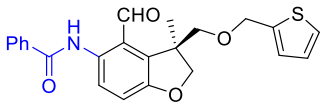
(S)-*N*-(4-Formyl-3-methyl-3-((naphthalen-2-ylmethoxy)methyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ta

By following a modified procedure at 50 °C for 36 h, the reaction of **1t** (49.2 mg, 0.15 mmol) with **2a** (61.3 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (5.3 mg, 0.0075 mmol), $AgSbF_6$ (11.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.6 mg, 0.075 mmol) afforded **3ta** (31.4 mg, 46% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.12 (s, 1H), 10.42 (s, 1H), 8.83 (d, J = 9.0 Hz, 1H), 8.07–8.01 (m, 2H), 7.82–7.74 (m, 3H), 7.63 (s, 1H), 7.60–7.50 (m, 3H), 7.48–7.42 (m, 2H), 7.32 (dd, J = 8.4, 1.7 Hz, 1H), 7.12 (d, J = 9.0 Hz, 1H), 4.70 (d, J = 12.3 Hz, 1H), 4.63 (d, J = 12.3 Hz, 1H), 4.50 (d, J = 8.8 Hz, 1H), 4.19 (d, J = 8.8 Hz, 1H), 3.63 (s, 2H), 1.61 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.4, 165.9, 156.4, 135.7, 135.4, 134.9 (2C), 133.2, 133.1, 132.0, 128.9 (2C), 128.5, 127.9, 127.8, 127.5 (2C), 126.8, 126.4, 126.2, 125.6, 121.7, 120.5, 117.8, 81.1, 76.0, 73.7, 48.9, 24.3; **HRMS** (ESI) Calcd for $C_{29}H_{26}NO_4$ $[M+H]^+$ 452.1856; found 452.1859; $[\alpha]^{18}_D$ = +19.8 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 88%; CHIRALPAK®IG (70% hexanes: 30% isopropanol, 1 mL/min) t_{major} = 13.9 min, t_{minor} = 15.2 min.

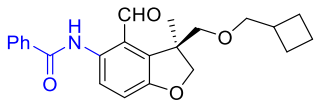
(S)-*N*-(4-Formyl-3-methyl-3-((thiophen-2-ylmethoxy)methyl)-2,3-dihydrobenzofuran-5-yl)benzamide



3ua

By following a modified procedure at 50 °C for 36 h, the reaction of **1u** (43.2 mg, 0.15 mmol) with **2a** (61.3 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), $AgSbF_6$ (10.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.1 mg, 0.075 mmol) afforded **3ua** (34.0 mg, 56% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.16 (s, 1H), 10.42 (s, 1H), 8.82 (d, J = 9.0 Hz, 1H), 8.08–8.02 (m, 2H), 7.59–7.50 (m, 3H), 7.28 (dd, J = 4.9, 1.4 Hz, 1H), 7.11 (d, J = 9.0 Hz, 1H), 6.97–6.91 (m, 2H), 4.70 (d, J = 12.8 Hz, 1H), 4.65 (d, J = 12.8 Hz, 1H), 4.47 (d, J = 8.9 Hz, 1H), 4.17 (d, J = 8.9 Hz, 1H), 3.61 (s, 2H), 1.59 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.5, 165.9, 156.4, 140.3, 135.7, 135.5, 135.0, 132.0, 128.9 (2C), 127.6 (2C), 126.8 (2C), 126.4, 121.7, 120.5, 117.9, 81.1, 75.5, 68.0, 48.8, 24.2; **HRMS** (ESI) Calcd for $C_{23}H_{22}NO_4S$ $[M+H]^+$ 408.1264; found 408.1266; $[\alpha]^{18}_D$ = +16.2 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 87%; CHIRALPAK®IG (70% hexanes: 30% isopropanol, 1 mL/min) t_{major} = 12.6 min, t_{minor} = 13.5 min.

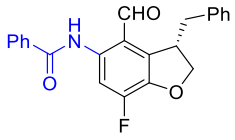
(S)-*N*-(3-((Cyclobutylmethoxy)methyl)-4-formyl-3-methyl-2,3-dihydrobenzofuran-5-yl)benzamide



3va

By following a modified procedure at 50 °C for 36 h, the reaction of **1v** (39.2 mg, 0.15 mmol) with **2a** (61.3 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), $AgSbF_6$ (11.3 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and $MesCO_2H$ (12.5 mg, 0.075 mmol) afforded **3va** (31.2 mg, 55% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.21 (s, 1H), 10.47 (s, 1H), 8.82 (d, *J* = 9.0 Hz, 1H), 8.06 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.59–7.48 (m, 3H), 7.11 (d, *J* = 9.0 Hz, 1H), 4.42 (d, *J* = 8.9 Hz, 1H), 4.18 (d, *J* = 8.9 Hz, 1H), 3.60–3.49 (m, 2H), 3.44–3.32 (m, 2H), 2.59–2.46 (m, 1H), 2.05–1.93 (m, 2H), 1.93–1.76 (m, 2H), 1.73–1.63 (m, 2H), 1.61 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.3, 165.9, 156.3, 136.1, 135.4, 135.0, 131.9, 128.9 (2C), 127.5 (2C), 121.5, 120.7, 117.6, 81.1, 76.8, 76.2, 49.0, 35.0, 25.1, 25.0, 24.1, 18.7; **HRMS** (ESI) Calcd for $C_{23}H_{26}NO_4$ $[M+H]^+$ 380.1856; found 380.1857; $[\alpha]^{18}_D$ = +17.7 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 83%; CHIRALPAK®IG (70% hexanes: 30% isopropanol, 1 mL/min) t_{major} = 9.8 min, t_{minor} = 10.7 min.

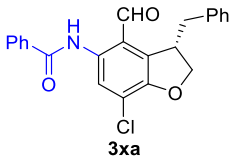
(S)-*N*-(3-Benzyl-7-fluoro-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3wa

By following the general procedure, the reaction of **1w** (37.6 mg, 0.15 mmol) with **2a** (62.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.9 mg, 0.0075 mmol), KH_2PO_4 (30.9 mg, 0.225 mmol), $AgSbF_6$ (11.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.7 mg, 0.045 mmol) afforded **3wa** (39.8 mg, 71% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.09 (s, 1H), 9.51 (s, 1H), 8.77 (d, *J* = 13.3 Hz, 1H), 8.02 (d, *J* = 6.8 Hz, 2H), 7.60–7.49 (m, 3H), 7.36–7.28 (m, 3H), 7.10–7.05 (m, 2H), 4.65 (dd, *J* = 9.0, 1.9 Hz, 1H), 4.60 (dd, *J* = 9.1, 7.1 Hz, 1H), 4.00 (q, *J* = 7.6 Hz, 1H), 3.02 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.94 (dd, *J* = 13.7, 7.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.1, 165.9, 151.9 (d, *J* = 257.2 Hz), 142.5 (d, *J* = 12.0 Hz), 138.8 (d, *J* = 6.4 Hz), 137.5, 136.8 (d, *J* = 10.4 Hz), 134.3, 132.3, 129.4 (2C), 129.1 (2C), 129.0 (2C), 127.54 (2C), 127.45, 115.2 (d, *J* = 3.0 Hz), 108.7 (d, *J* = 24.2 Hz), 78.1, 43.7 (d, *J* = 1.9 Hz), 42.4; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1344; $[\alpha]^{18}_D$ = -22.1 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 91%; CHIRALPAK®IG (50% hexanes: 50% isopropanol, 1 mL/min) t_{minor} = 13.5 min, t_{major} = 17.6 min.

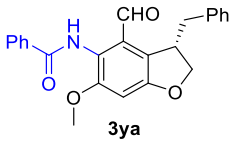
(S)-*N*-(3-Benzyl-7-chloro-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3xa

By following the general procedure, the reaction of **1x** (41.1 mg, 0.15 mmol) with **2a** (61.4 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), KH_2PO_4 (31.0 mg, 0.225 mmol), $AgSbF_6$ (13.5 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3xa** (35.6 mg, 61% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.93 (s, 1H), 9.50 (s, 1H), 8.99 (s, 1H), 8.04–7.98 (m, 2H), 7.60–7.49 (m, 3H), 7.36–7.29 (m, 3H), 7.10–7.05 (m, 2H), 4.66 (dd, *J* = 9.1, 2.1 Hz, 1H), 4.61 (dd, *J* = 9.0, 7.0 Hz, 1H), 4.07–3.99 (m, 1H), 3.03 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.94 (dd, *J* = 13.7, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.5, 165.9, 151.7, 137.5, 136.0, 135.5, 134.4, 132.3, 129.5 (2C), 129.2 (2C), 129.0 (2C), 127.54 (2C), 127.50, 124.1, 121.0, 117.5, 77.6, 44.0, 42.5; **HRMS** (ESI) Calcd for $C_{23}H_{19}ClNO_3$ $[M+H]^+$ 392.1048; found 392.1050; $[\alpha]^{18}_D$ = -20.8 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 85%; CHIRALPAK®IG (90% hexanes: 10% isopropanol, 1 mL/min) t_{major} = 26.4 min, t_{minor} = 33.1 min.

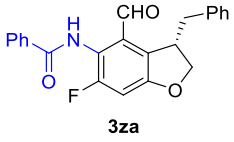
(S)-*N*-(3-Benzyl-4-formyl-6-methoxy-2,3-dihydrobenzofuran-5-yl)benzamide



3ya

By following the general procedure, the reaction of **1y** (40.5 mg, 0.15 mmol) with **2a** (61.4 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.9 mg, 0.0075 mmol), KH_2PO_4 (31.2 mg, 0.225 mmol), $AgSbF_6$ (13.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.0 mg, 0.045 mmol) afforded **3ya** (25.0 mg, 43% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.08 (s, 1H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.66–7.47 (m, 3H), 7.36–7.19 (m, 5H), 6.70 (s, 1H), 4.50 (d, *J* = 8.9 Hz, 1H), 4.35 (t, *J* = 8.5 Hz, 1H), 4.16–4.06 (m, 1H), 3.87 (s, 3H), 3.15 (dd, *J* = 13.2, 3.5 Hz, 1H), 2.63–2.51 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.1, 167.7, 159.4, 153.4, 139.8, 133.9, 132.4, 129.5 (2C), 129.0 (2C), 128.6 (2C), 127.6 (2C), 127.0, 126.4, 123.0, 121.0, 98.9, 76.8, 56.5, 43.9, 40.1; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543; found 388.1542; $[\alpha]^{18}_D$ = -18.2 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 82%; CHIRALPAK®IG (50% hexanes: 50% isopropanol, 1 mL/min) t_{major} = 9.6 min, t_{minor} = 13.0 min.

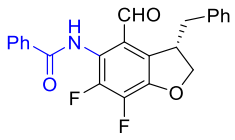
(S)-*N*-(3-Benzyl-6-fluoro-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3za

By following the general procedure, the reaction of **1z** (39.3 mg, 0.15 mmol) with **2a** (61.5 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.9 mg, 0.0075 mmol), KH_2PO_4 (30.5 mg, 0.225 mmol), $AgSbF_6$ (13.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (12.9 mg, 0.045 mmol) afforded **3za** (37.1 mg, 66% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.62 (s, 1H), 7.96 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.28–7.24 (m, 1H), 7.21 (d, *J* = 7.3 Hz, 2H), 6.88 (d, *J* = 9.8 Hz, 1H), 4.55 (dd, *J* = 9.0, 2.0 Hz, 1H), 4.44 (t, *J* = 8.3 Hz, 1H), 4.11–4.01 (m, 1H), 3.02 (dd, *J* = 13.5, 5.0 Hz, 1H), 2.71 (dd, *J* = 13.5, 9.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7 (d, *J* = 3.2 Hz), 166.9, 159.3 (d, *J* = 12.4 Hz), 156.9 (d, *J* = 249.1 Hz), 138.7, 133.4, 132.6, 129.4 (2C), 128.98 (2C), 128.95 (d, *J* = 2.5 Hz), 128.9 (2C), 127.7 (2C), 126.9, 126.8 (d, *J* = 2.2 Hz), 119.2 (d, *J* = 14.5 Hz), 104.0 (d, *J* = 25.6 Hz), 77.4, 43.2, 40.9; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1342; $[\alpha]^{18}_D$ = -20.2 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 81%; CHIRALPAK®IG (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 19.5 min, t_{major} = 21.1 min.

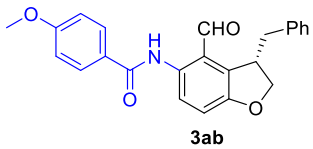
(S)-*N*-(3-Benzyl-6,7-difluoro-4-formyl-2,3-dihydrobenzofuran-5-yl)benzamide



3zaa

By following the general procedure, the reaction of **1za** (41.9 mg, 0.15 mmol) with **2a** (61.8 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.8 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (13.7 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3zaa** (29.7 mg, 50% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.93 (s, 1H), 7.97 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.30–7.25 (m, 1H), 7.19 (d, *J* = 6.8 Hz, 2H), 4.66 (dd, *J* = 9.1, 2.0 Hz, 1H), 4.55 (dd, *J* = 9.1, 7.5 Hz, 1H), 4.15–4.06 (m, 1H), 3.02 (dd, *J* = 13.5, 5.4 Hz, 1H), 2.77 (dd, *J* = 13.5, 9.3 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 188.9 (d, *J* = 2.8 Hz), 166.6, 146.4 (d, *J* = 8.1 Hz), 145.8 (dd, *J* = 252.5, 11.3 Hz), 140.7 (dd, *J* = 260.5, 15.6 Hz), 138.2, 133.1, 132.8, 131.4 (d, *J* = 3.1 Hz), 129.4 (2C), 129.1 (2C), 129.0 (2C), 127.8 (2C), 127.2, 121.42 (d, *J* = 7.0 Hz), 121.35, 78.7, 43.8, 40.9; **HRMS** (ESI) Calcd for $C_{23}H_{18}F_2NO_3$ $[M+H]^+$ 394.1249; found 394.1250; $[\alpha]^{18}_D$ = -38.4 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 88%; CHIRALPAK®IG (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 8.2 min, t_{major} = 9.0 min.

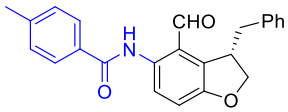
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-4-methoxybenzamide



3ab

By following the general procedure, the reaction of **1a** (35.3 mg, 0.15 mmol) with **2b** (72.6 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.8 mg, 0.0075 mmol), KH_2PO_4 (31.0 mg, 0.225 mmol), $AgSbF_6$ (11.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.4 mg, 0.045 mmol) afforded **3ab** (43.3 mg, 74% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.82 (s, 1H), 9.59 (s, 1H), 8.81 (d, *J* = 9.0 Hz, 1H), 8.03–7.97 (m, 2H), 7.35–7.28 (m, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.07 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.03–6.98 (m, 2H), 4.58–4.48 (m, 2H), 4.00–3.93 (m, 1H), 3.88 (s, 3H), 2.99 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.92 (dd, *J* = 13.6, 7.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.4, 165.4, 162.7, 155.5, 138.0, 135.3, 134.9, 129.5 (2C), 129.4 (2C), 129.0 (2C), 127.3, 127.1, 120.9, 118.8, 117.8, 114.1 (2C), 76.9, 55.6, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543; found 388.1548; $[\alpha]^{18}_D$ = -10.4 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 89%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 21.0 min, t_{major} = 27.3 min.

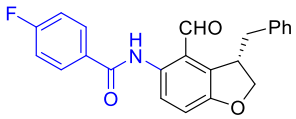
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-4-methylbenzamide



3ac

By following the general procedure, the reaction of **1a** (36.0 mg, 0.15 mmol) with **2c** (67.5 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (12.1 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ac** (43.2 mg, 78% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 9.58 (s, 1H), 8.81 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.34–7.26 (m, 5H), 7.14 (d, *J* = 9.0 Hz, 1H), 7.09–7.03 (m, 2H), 4.56–4.46 (m, 2H), 4.00–3.91 (m, 1H), 2.98 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.90 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.42 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 165.8, 155.5, 142.5, 137.9, 135.0, 134.9, 131.9, 129.6 (2C), 129.4 (2C), 129.0 (2C), 127.5 (2C), 127.2, 120.9, 118.8, 117.7, 76.9, 43.0, 42.6, 21.6; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_3$ $[M+H]^+$ 372.1594; found 372.1575; $[\alpha]^{18}_D$ = +17.3 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 94%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 17.3 min, t_{major} = 22.5 min.

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-4-fluorobenzamide

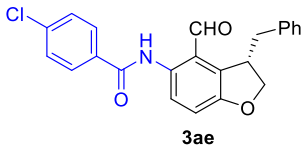


3ad

By following the general procedure, the reaction of **1a** (36.0 mg, 0.15 mmol) with **2d** (68.9 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (31.5 mg, 0.225 mmol), $AgSbF_6$ (11.7 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.3 mg, 0.045 mmol) afforded **3ad**

(40.1 mg, 71% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 9.56 (s, 1H), 8.78 (d, *J* = 9.0 Hz, 1H), 8.03 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.35–7.27 (m, 3H), 7.22–7.13 (m, 3H), 7.09–7.04 (m, 2H), 4.58–4.48 (m, 2H), 4.01–3.92 (m, 1H), 3.00 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.91 (dd, *J* = 13.7, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 165.1 (d, *J* = 253.7 Hz), 164.7, 155.8, 137.9, 135.0, 134.8, 131.0 (d, *J* = 3.1 Hz), 129.9 (d, *J* = 9.0 Hz, 2C), 129.5 (2C), 129.1 (2C), 127.3, 120.9, 118.9, 117.8, 116.0 (d, *J* = 22.0 Hz, 2C), 77.0, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1355; $[\alpha]^{18}_D$ = -27.8 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 10.9 min, t_{major} = 12.6 min.

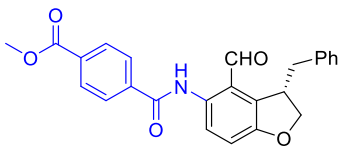
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-4-chlorobenzamide



3ae

By following the general procedure, the reaction of **1a** (36.1 mg, 0.15 mmol) with **2e** (75.0 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.8 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (12.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ae** (49.6 mg, 84% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 9.55 (s, 1H), 8.79 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.35–7.28 (m, 3H), 7.16 (d, *J* = 9.0 Hz, 1H), 7.10–7.04 (m, 2H), 4.59–4.49 (m, 2H), 4.01–3.92 (m, 1H), 3.01 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 164.7, 155.9, 138.4, 137.8, 135.1, 134.7, 133.2, 129.5 (2C), 129.2 (2C), 129.1 (2C), 129.0 (2C), 127.3, 121.0, 119.0, 117.8, 77.0, 43.0, 42.7; **HRMS** (ESI) Calcd for $C_{23}H_{19}ClNO_3$ $[M+H]^+$ 392.1048; found 392.1045; $[\alpha]^{18}_D$ = -40.3 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 12.9 min, t_{major} = 15.1 min.

(S)-Methyl-4-((3-benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)carbamoyl)benzoate

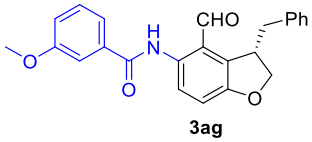


3af

By following the general procedure, the reaction of **1a** (35.7 mg, 0.15 mmol) with **2f** (83.4 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.9 mg, 0.225 mmol), $AgSbF_6$ (12.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.9 mg, 0.045 mmol) afforded **3af** (26.7 mg, 43% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.96 (s, 1H), 9.56

(s, 1H), 8.81 (d, *J* = 9.0 Hz, 1H), 8.19–8.15 (m, 2H), 8.10–8.06 (m, 2H), 7.35–7.28 (m, 3H), 7.17 (d, *J* = 9.0 Hz, 1H), 7.07 (dd, *J* = 7.4, 2.0 Hz, 2H), 4.59–4.50 (m, 2H), 4.01–3.93 (m, 4H), 3.01 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 166.4, 164.8, 156.0, 138.6, 137.8, 135.1, 134.5, 133.1, 130.2 (2C), 129.5 (2C), 129.1 (2C), 127.5 (2C), 127.3, 121.0, 119.0, 117.7, 77.0, 52.6, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{25}H_{22}NO_5$ $[M+H]^+$ 416.1492; found 416.1496; $[\alpha]^{18}_D$ = +44.2 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 93%; CHIRALPAK®IC (50% hexanes: 50% isopropanol, 1 mL/min) t_{minor} = 17.2 min, t_{major} = 22.0 min.

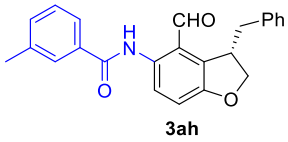
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-3-methoxybenzamide



3ag

By following the general procedure, the reaction of **1a** (36.3 mg, 0.15 mmol) with **2g** (73.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.8 mg, 0.0075 mmol), KH_2PO_4 (30.8 mg, 0.225 mmol), $AgSbF_6$ (12.1 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.4 mg, 0.045 mmol) afforded **3ag** (48.7 mg, 87% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.87 (s, 1H), 9.59 (s, 1H), 8.80 (d, *J* = 9.0 Hz, 1H), 7.60–7.56 (m, 2H), 7.41 (t, *J* = 8.1 Hz, 1H), 7.34–7.26 (m, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.11–7.04 (m, 3H), 4.57–4.48 (m, 2H), 4.00–3.92 (m, 1H), 3.89 (s, 3H), 2.98 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 165.7, 160.1, 155.7, 137.9, 136.3, 135.0, 134.8, 129.9, 129.4 (2C), 129.0 (2C), 127.3, 120.9, 119.3, 118.9, 118.6, 117.7, 112.5, 76.9, 55.5, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_4$ $[M+H]^+$ 388.1543; found 388.1569; $[\alpha]^{18}_D$ = -37.7 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 89%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 19.3 min, t_{major} = 26.2 min.

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-3-methylbenzamide

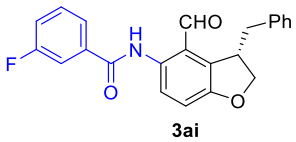


3ah

By following the general procedure, the reaction of **1a** (35.7 mg, 0.15 mmol) with **2h** (68.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.9 mg, 0.225 mmol), $AgSbF_6$ (11.7 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ah** (39.7 mg, 71% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.83 (s, 1H), 9.61 (s, 1H), 8.81 (d, *J* = 9.0 Hz, 1H), 7.84 (s, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.43–7.27 (m, 5H), 7.15 (d, *J* = 9.1 Hz, 1H), 7.10–7.04 (m, 2H), 4.58–4.47 (m, 2H), 4.01–3.92 (m, 1H), 3.04–2.87 (m, 2H), 2.45 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 166.1, 155.7, 138.8, 137.9, 135.0, 134.9, 134.8, 132.8, 129.4 (2C), 129.0 (2C), 128.8, 128.4,

127.3, 124.4, 121.0, 118.9, 117.7, 76.9, 43.0, 42.6, 21.6; **HRMS** (ESI) Calcd for $C_{24}H_{22}NO_3$ $[M+H]^+$ 372.1594; found 372.1618; $[\alpha]^{18}_D$ = -20.8 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 91%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 19.1 min, t_{major} = 23.6 min.

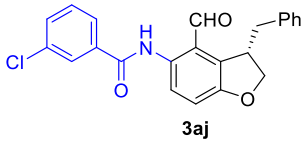
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-3-fluorobenzamide



3ai

By following the general procedure, the reaction of **1a** (35.8 mg, 0.15 mmol) with **2i** (68.4 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.5 mg, 0.225 mmol), $AgSbF_6$ (11.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ai** (41.5 mg, 74% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 9.56 (s, 1H), 8.79 (d, *J* = 9.0 Hz, 1H), 7.81–7.76 (m, 1H), 7.73 (dt, *J* = 9.5, 2.1 Hz, 1H), 7.49 (td, *J* = 8.0, 5.6 Hz, 1H), 7.35–7.21 (m, 4H), 7.16 (d, *J* = 8.9 Hz, 1H), 7.09–7.04 (m, 2H), 4.59–4.49 (m, 2H), 4.01–3.93 (m, 1H), 3.00 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.4, 164.4 (d, *J* = 2.7 Hz), 163.1 (d, *J* = 247.8 Hz), 155.9, 137.8, 137.1 (d, *J* = 6.8 Hz), 135.1, 134.6, 130.6 (d, *J* = 7.8 Hz), 129.5 (2C), 129.1 (2C), 127.4, 122.8 (d, *J* = 3.0 Hz), 121.0, 119.1 (d, *J* = 21.4 Hz), 119.0, 117.7, 115.0 (d, *J* = 23.1 Hz), 77.0, 43.0, 42.7; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1355; $[\alpha]^{18}_D$ = -13.0 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (80% hexanes: 20% isopropanol, 1 mL/min) t_{minor} = 12.8 min, t_{major} = 16.6 min.

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-3-chlorobenzamide

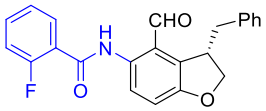


3aj

By following the general procedure, the reaction of **1a** (35.7 mg, 0.15 mmol) with **2j** (75.3 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.9 mg, 0.225 mmol), $AgSbF_6$ (11.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3aj** (39.8 mg, 68% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.87 (s, 1H), 9.55 (s, 1H), 8.77 (d, *J* = 8.9 Hz, 1H), 8.01 (t, *J* = 1.9 Hz, 1H), 7.87 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.55–7.49 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.35–7.28 (m, 3H), 7.16 (d, *J* = 9.0 Hz, 1H), 7.09–7.04 (m, 2H), 4.59–4.49 (m, 2H), 4.01–3.92 (m, 1H), 3.00 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.4, 164.4, 155.9, 137.8, 136.6, 135.2, 135.1, 134.5, 132.0, 130.2, 129.4 (2C), 129.1 (2C), 128.1, 127.3, 125.2, 121.0, 119.0, 117.7, 77.0, 43.0, 42.6; **HRMS** (ESI) Calcd for

$C_{23}H_{19}ClNO_3$ $[M+H]^+$ 392.1048; found 392.1053; $[\alpha]^{18}_D$ = -29.5 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 91%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 11.3 min, t_{major} = 13.2 min.

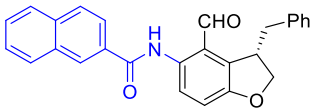
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-2-fluorobenzamide



3ak

By following the general procedure, the reaction of **1a** (36.1 mg, 0.15 mmol) with **2k** (69.4 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.5 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (13.4 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.3 mg, 0.045 mmol) afforded **3ak** (49.5 mg, 88% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.64 (d, *J* = 7.8 Hz, 1H), 9.65 (s, 1H), 8.74 (d, *J* = 9.0 Hz, 1H), 8.03 (td, *J* = 7.7, 1.9 Hz, 1H), 7.53–7.46 (m, 1H), 7.33–7.23 (m, 4H), 7.21–7.15 (m, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.09–7.05 (m, 2H), 4.56–4.45 (m, 2H), 3.97 (qd, *J* = 7.4, 2.0 Hz, 1H), 2.99–2.87 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.5, 162.6 (d, *J* = 2.7 Hz), 160.3 (d, *J* = 250.8 Hz), 156.1, 137.9, 134.9, 133.8, 133.6 (d, *J* = 8.9 Hz), 131.7 (d, *J* = 2.1 Hz), 129.4 (2C), 129.0 (2C), 127.2, 124.8 (d, *J* = 3.5 Hz), 122.7 (d, *J* = 12.1 Hz), 122.0, 119.6, 117.1, 116.6 (d, *J* = 23.6 Hz), 76.8, 42.9, 42.5; **HRMS** (ESI) Calcd for $C_{23}H_{19}FNO_3$ $[M+H]^+$ 376.1343; found 376.1342; $[\alpha]^{18}_D$ = +22.1 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 13.8 min, t_{major} = 18.2 min.

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-2-naphthamide

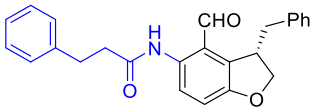


3al

By following the general procedure, the reaction of **1a** (35.8 mg, 0.15 mmol) with **2l** (81.2 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.9 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (11.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3al** (51.1 mg, 84% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.04 (s, 1H), 9.62 (s, 1H), 8.87 (d, *J* = 9.0 Hz, 1H), 8.55 (s, 1H), 8.08 (dd, *J* = 8.6, 1.9 Hz, 1H), 8.01 (dd, *J* = 7.1, 2.2 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H), 7.92–7.87 (m, 1H), 7.62–7.52 (m, 2H), 7.35–7.26 (m, 3H), 7.17 (d, *J* = 9.0 Hz, 1H), 7.10–7.05 (m, 2H), 4.58–4.48 (m, 2H), 4.01–3.92 (m, 1H), 2.99 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.92 (dd, *J* = 13.6, 7.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.4, 165.9, 155.7, 137.9, 135.1, 135.0 (2C), 132.8, 132.0, 129.47, 129.45 (2C), 129.1 (2C), 128.8, 128.5, 128.0, 127.9, 127.3, 126.9, 123.7, 121.0, 119.0, 117.8, 76.9, 43.0, 42.6; **HRMS** (ESI) Calcd for $C_{27}H_{22}NO_3$ $[M+H]^+$ 408.1594;

found 408.1599; $[\alpha]^{18}_D$ = -33.8 (c = 0.4, $CHCl_3$); HPLC analysis: ee = 90%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 18.0 min, t_{major} = 19.8 min.

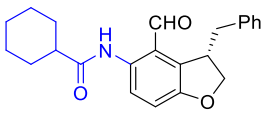
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)-3-phenylpropanamide



3am

By following the general procedure, the reaction of **1a** (35.9 mg, 0.15 mmol) with **2m** (66.1 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.7 mg, 0.0075 mmol), KH_2PO_4 (30.7 mg, 0.225 mmol), $AgSbF_6$ (12.8 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3am** (27.8 mg, 48% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.88 (s, 1H), 9.54 (s, 1H), 8.57 (d, *J* = 9.0 Hz, 1H), 7.33–7.23 (m, 7H), 7.22–7.17 (m, 1H), 7.09 (d, *J* = 9.0 Hz, 1H), 7.07–7.02 (m, 2H), 4.52 (dd, *J* = 9.0, 2.0 Hz, 1H), 4.47 (dd, *J* = 9.0, 7.1 Hz, 1H), 3.96–3.88 (m, 1H), 3.10–3.02 (m, 2H), 2.94 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.87 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.76–2.69 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0, 171.2, 155.6, 140.7, 137.9, 134.7, 134.5, 129.4 (2C), 129.0 (2C), 128.6 (2C), 128.5 (2C), 127.2, 126.4, 121.0, 118.6, 117.5, 76.8, 42.9, 42.6, 40.1, 31.5; **HRMS** (ESI) Calcd for $C_{25}H_{24}NO_3$ $[M+H]^+$ 386.1751; found 386.1784; $[\alpha]^{18}_D$ = +114.4 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 87%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 10.9 min, t_{major} = 15.9 min.

(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)cyclohexanecarboxamide

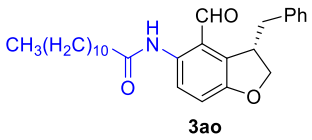


3an

By following the general procedure, the reaction of **1a** (36.3 mg, 0.15 mmol) with **2n** (63.9 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol), KH_2PO_4 (31.0 mg, 0.225 mmol), $AgSbF_6$ (13.2 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.5 mg, 0.045 mmol) afforded **3an** (28.4 mg, 52% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.93 (s, 1H), 9.59 (s, 1H), 8.62 (d, *J* = 9.0 Hz, 1H), 7.35–7.27 (m, 3H), 7.11–7.04 (m, 3H), 4.53 (dd, *J* = 9.0, 2.0 Hz, 1H), 4.48 (dd, *J* = 9.0, 7.1 Hz, 1H), 3.98–3.89 (m, 1H), 2.96 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.89 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.34–2.24 (m, 1H), 2.04–1.95 (m, 2H), 1.88–1.79 (m, 2H), 1.74–1.67 (m, 1H), 1.60–1.47 (m, 2H), 1.40–1.22 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1, 175.5, 155.4, 138.0, 134.9, 134.7, 129.4 (2C), 129.0 (2C), 127.3, 121.0, 118.7, 117.6, 76.8, 47.2, 43.0, 42.6, 29.8, 29.7, 25.87 (2C), 25.85; **HRMS** (ESI) Calcd for $C_{23}H_{26}NO_3$ $[M+H]^+$ 364.1907; found 364.1928; $[\alpha]^{18}_D$ = +36.4

(c = 0.2, $CHCl_3$); HPLC analysis: ee = 88%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 8.0 min, t_{major} = 12.5 min.

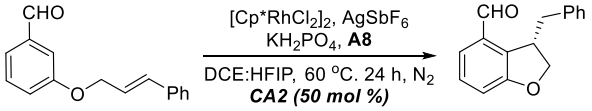
(S)-*N*-(3-Benzyl-4-formyl-2,3-dihydrobenzofuran-5-yl)dodecanamide



3ao

By following the general procedure, the reaction of **1a** (35.9 mg, 0.15 mmol) with **2o** (85.2 mg, 0.375 mmol), $[Cp^*RhCl_2]_2$ (4.8 mg, 0.0075 mmol), KH_2PO_4 (31.1 mg, 0.225 mmol), $AgSbF_6$ (12.9 mg, 0.03 mmol), (R)-(+)-1-(1-naphthyl)ethylamine (12.0 µL, 0.075 mmol), and *N*-Phthaloyl-L-Phenylalanine (13.2 mg, 0.045 mmol) afforded **3ao** (39.4 mg, 60% yield). Yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.89 (s, 1H), 9.58 (s, 1H), 8.59 (d, *J* = 9.0 Hz, 1H), 7.34–7.27 (m, 3H), 7.09 (d, *J* = 9.0 Hz, 1H), 7.08–7.04 (m, 2H), 4.55–4.44 (m, 2H), 3.97–3.89 (m, 1H), 2.99–2.85 (m, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 1.76–1.70 (m, 2H), 1.37–1.20 (m, 16H), 0.91–0.84 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0, 172.5, 155.4, 138.0, 134.72, 134.66, 129.4 (2C), 129.0 (2C), 127.2, 120.9, 118.5, 117.6, 76.8, 43.0, 42.6, 38.7, 32.0, 29.7 (2C), 29.6, 29.5 (2C), 29.3, 25.7, 22.8, 14.3; **HRMS** (ESI) Calcd for $C_{28}H_{38}NO_3$ $[M+H]^+$ 436.2846; found 436.2856; $[\alpha]^{18}_D$ = +41.6 (c = 0.2, $CHCl_3$); HPLC analysis: ee = 86%; CHIRALPAK®IC (70% hexanes: 30% isopropanol, 1 mL/min) t_{minor} = 7.1 min, t_{major} = 8.4 min.

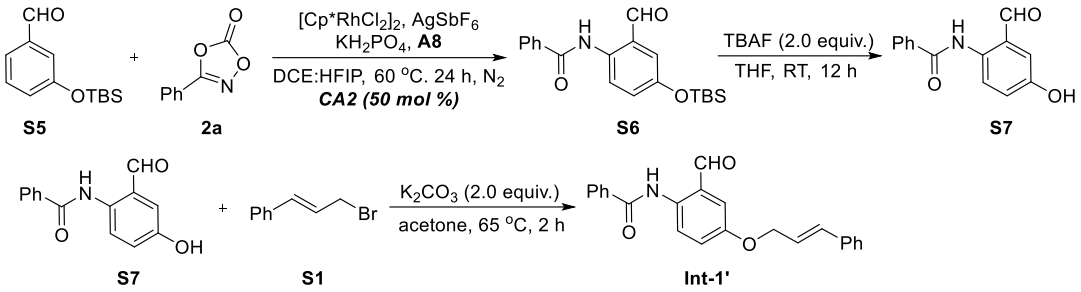
6. Procedure for the Synthesis of Int-1



1a **Int-1**

To a 25 mL Schlenk tube equipped with a magnetic stirring bar were added substrate **1a** (0.15 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (0.375 mmol) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, amine (50 mol%), HFIP (0.9 mL) and DCE (0.9 mL) were added subsequently. After stirring at 60 °C for 24 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (50 : 1) as the eluent to give **Int-1**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.45–7.16 (m, 7H), 7.05 (d, *J* = 7.1 Hz, 1H), 4.51 (d, *J* = 9.1 Hz, 1H), 4.36 (t, *J* = 8.5 Hz, 1H), 4.18–4.04 (m, 1H), 3.10 (dd, *J* = 13.4, 4.1 Hz, 1H), 2.59 (dd, *J* = 13.5, 10.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.3, 161.0, 139.4, 133.0, 131.7, 129.4 (2C), 129.2, 128.7 (2C), 126.6, 125.2, 115.6, 76.3, 43.6, 40.1; **HRMS** (ESI) Calcd for $C_{16}H_{14}O_2$ $[M+H]^+$ 239.1067; found 239.1067.

7. Procedure for the Synthesis of Int-1'

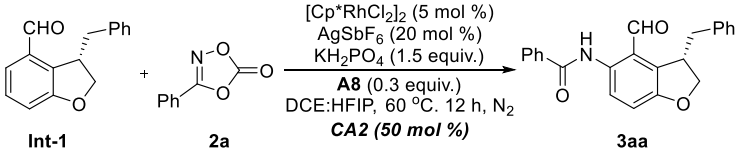


To a 25 mL Schlenk flask equipped with a magnetic stirring bar were added substrate **S5** (0.75 mmol), **2a** (2.5 equiv.), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (1.5 equiv.) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, amine (50 mol%), HFIP (6 mL) and DCE (6 mL) were added subsequently. After stirring at 60 °C for 24 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10 : 1) as the eluent to give **S6**.

To a 20 mL vial were added **S6** (0.5 mmol), TBAF (1.0 mmol) and THF (8 mL). The mixture was stirred at room temperature for 12 h. The solvent was removed and the reaction mixture was extracted with H_2O (8 mL) and ethyl acetate (8 mL). The organic phase was dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The crude **S7** was directly used for the next step without any purification.

To a 10 mL round flask equipped with a stirring bar was added the crude **S7** (0.5 mmol) and K_2CO_3 (1.0 mmol) in acetone (5 mL), followed by allyl *br*omide (1.0 mmol). The mixture was stirred at 65 °C for 2 h. The solvent was removed and the reaction mixture was extracted with H_2O (6 mL) and ethyl acetate (6 mL). The organic phase was dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The residue was purified by flash chromatography with petroleum ether/ethyl acetate (10 : 1) as the eluent to give **Int-1'**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 9.96 (s, 1H), 8.93 (d, J = 9.0 Hz, 1H), 8.08–8.03 (m, 2H), 7.60–7.50 (m, 3H), 7.45–7.40 (m, 2H), 7.38–7.27 (m, 5H), 6.77 (d, J = 16.0 Hz, 1H), 6.42 (dt, J = 16.0, 5.8 Hz, 1H), 4.78 (dd, J = 5.8, 1.5 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.7, 166.0, 154.3, 136.3, 135.3, 134.6, 133.8, 132.2, 129.0 (2C), 128.8 (2C), 128.3, 127.6 (2C), 126.8 (2C), 123.8, 123.3, 123.0, 121.9, 121.1, 69.4. **HRMS** (ESI) Calcd for $C_{23}H_{20}NO_3$ $[M+H]^+$ 358.1438; found 358.1438.

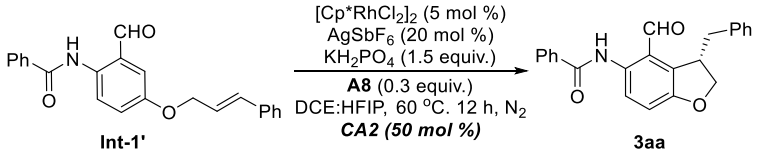
8. Procedure for Rh-Catalyzed C-H Activation with Int-1



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added substrate

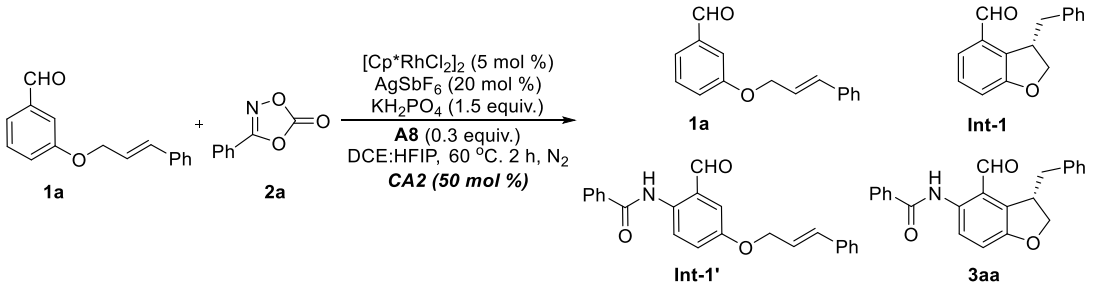
Int-1 (0.05 mmol), **2a** (0.125 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (0.075 mmol) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, chiral amine (50 mol%), HFIP (0.3 mL) and DCE (0.3 mL) were added subsequently. After stirring at 60 °C for 12 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10 : 1) as the eluent to give the corresponding product **3aa** (72%).

9. Procedure for Rh-Catalyzed C-H Activation with Int-1'



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added substrate **Int-1'** (0.05 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (0.075 mmol) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, chiral amine (50 mol%), HFIP (0.3 mL) and DCE (0.3 mL) were added subsequently. After stirring at 60 °C for 12 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (10 : 1) as the eluent to give the corresponding product **3aa** (57%).

10. Crude ^{1}H NMR with 1,3,5-Trimethoxybenzene as Internal Standard



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added substrate **1a** (0.05 mmol), **2a** (0.125 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $AgSbF_6$ (20 mol%), KH_2PO_4 (0.075 mmol) and acid (0.3 equiv.) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, chiral amine (50 mol%), HFIP (0.3 mL) and DCE (0.3 mL) were added subsequently. After stirring at 60 °C for 2 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was filtered on silica gel with ethyl acetate as the eluent. The crude residue was added internal standard (1,3,5-trimethoxybenzene, 0.05 mmol) and checked ^{1}H NMR. The specific signals of these compounds (peak a for **1a**, peak b for **3aa**, peak c for **Int-1**, peak d for **Int-1'**) and the crude ^{1}H NMR were labeled below.

Figure S1. Comparison of different components for 2 h.

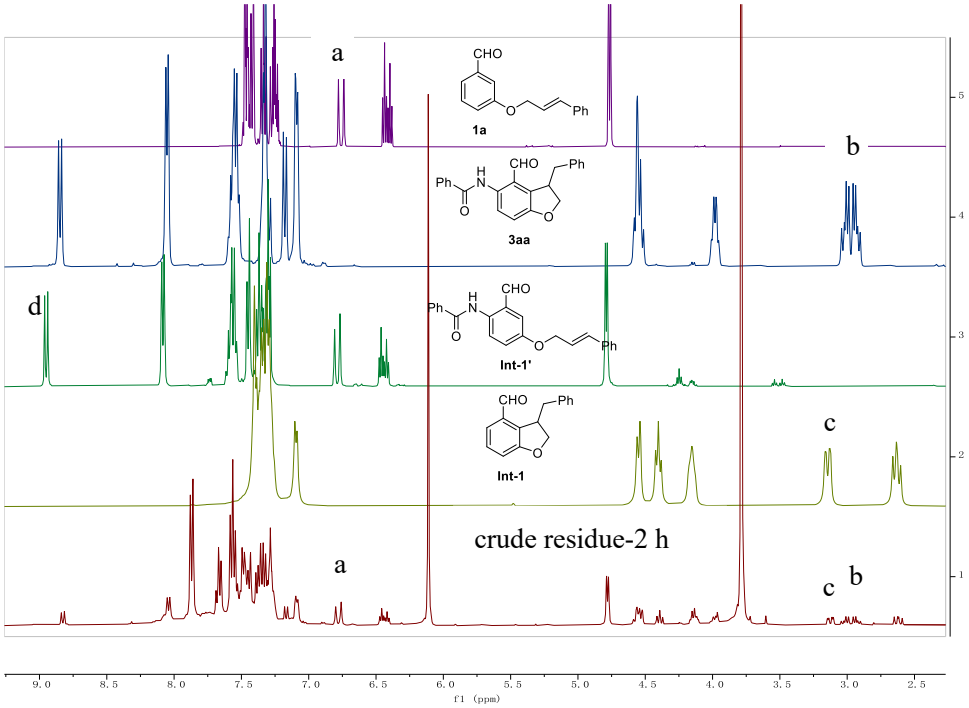
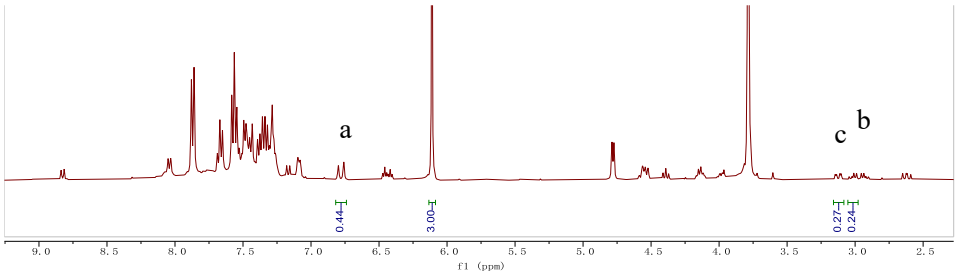
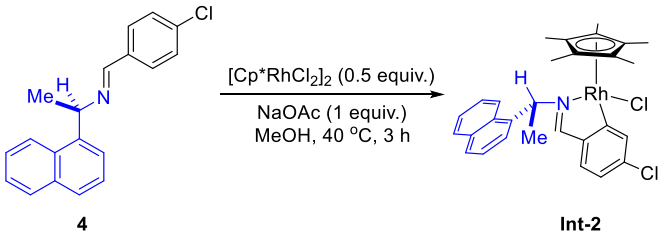


Figure S2. NMR yields for 2 h.



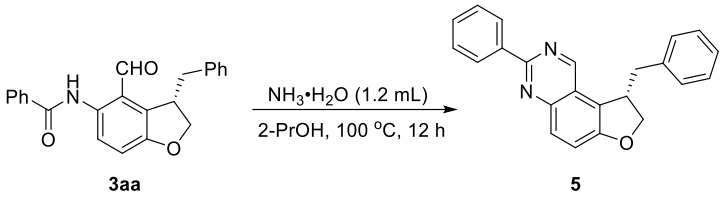
11. Procedure for the Synthesis of Int-2.



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added imine **4** (29.4 mg, 0.1 mmol), $[Cp^*RhCl_2]_2$ (31.0 mg, 0.05 mmol), NaOAc (8.3 mg, 0.1 mmol), 4-Clbenzaldehyde (7.2 mg, 0.05 mmol) and MeOH (1 mL). The mixture was stirred at 40 °C for 3 h. After removing all of the solvent, the crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3 : 1) to get the pure compound **Int-2** (36.1 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.3 Hz, 1H), 7.90 (d, J = 7.9 Hz, 2H), 7.70 (d, J = 1.9 Hz, 1H), 7.61 (d, J = 3.2 Hz, 1H), 7.58–7.45 (m, 4H), 7.06 (d, J = 8.0 Hz, 1H), 6.89 (dd, J = 8.0, 1.9 Hz, 1H), 6.02 (q, J =

7.0 Hz, 1H), 2.09 (d, *J* = 7.0 Hz, 3H), 1.71 (s, 15H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.4 (d, *J* = 33.8 Hz), 170.7 (d, *J* = 1.5 Hz), 144.2, 136.3 (d, *J* = 1.9 Hz), 135.5, 135.4, 134.1, 131.3, 129.4, 129.30, 129.27, 126.8, 126.0, 125.8, 125.6, 123.4, 122.8, 96.5 (d, *J* = 6.2 Hz, 5C), 63.6, 21.8, 9.6 (5C); **HRMS** (ESI) Calcd for $C_{29}H_{30}Cl_2NaNRh$ $[M+Na]^+$ 588.0703; found 588.0704.

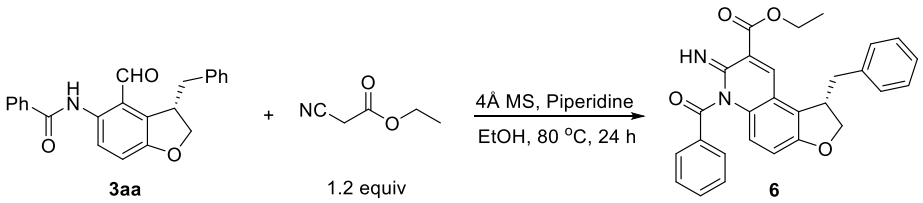
12. Procedure for the Synthesis of 5.



3aa **5**

To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added **3aa** (35.7 mg, 0.1 mmol), 25% $NH_3 \cdot H_2O$ (1.2 mL) and 2-propanol (0.8 mL). The reaction mixture was stirred at 100 °C for 12 h. After removing all of the solvent, the crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to get the pure compound **5** (24.4 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.58–8.52 (m, 2H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.56–7.44 (m, 4H), 7.33–7.23 (m, 3H), 7.16–7.10 (m, 2H), 4.70–4.61 (m, 2H), 4.20–4.10 (m, 1H), 3.24 (dd, *J* = 13.8, 5.6 Hz, 1H), 2.94 (dd, *J* = 13.8, 9.1 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.6, 158.4, 155.7, 147.2, 138.6, 138.3, 130.34, 130.26, 129.2 (2C), 129.0 (2C), 128.7 (2C), 128.2 (2C), 127.0, 122.2, 121.0, 120.3, 77.6, 43.1, 41.5; **HRMS** (ESI) Calcd for $C_{23}H_{19}N_2O$ $[M+H]^+$ 339.1492; found 339.1488.

13. Procedure for the Synthesis of 6.

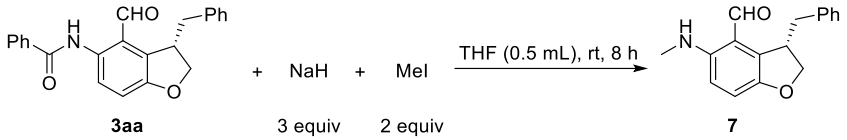


3aa 1.2 equiv **6**

To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added **3aa** (35.8 mg, 0.1 mmol), 4Å molecular sieves (30.8 mg), ethylcyanoacetate (13 μL, 0.12 mmol, 1.2 equiv.), piperidine (0.2 μL, 2%, 2 μmol) and ethanol (1 mL). The reaction mixture was stirred under nitrogen at 80 °C for 24 h. After removing all of the solvent, the crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5 : 1) to get the pure compound **6** (31.8 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 8.32 (s, 1H), 8.09 (d, *J* = 6.8 Hz, 2H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.60–7.49 (m, 3H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.28–7.17 (m, 3H), 7.06 (d, *J* = 5.8 Hz, 2H), 4.67 (t, *J* = 8.5 Hz, 1H), 4.61 (dd, *J* = 9.1, 2.8 Hz, 1H), 4.54–4.35 (m, 2H), 4.10–4.01 (m, 1H), 3.11 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.97 (dd, *J* = 13.7, 7.9 Hz, 1H), 1.46 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.2, 164.7, 157.6, 147.0, 145.0, 138.9,

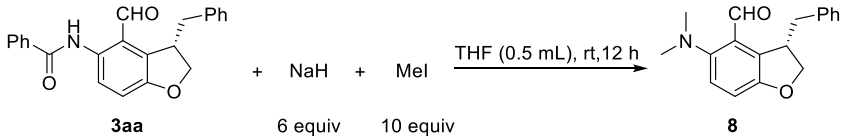
137.2, 135.1, 132.1, 130.1, 129.3 (2C), 128.9 (2C), 128.8 (2C), 127.7 (2C), 126.7, 123.5, 121.9, 118.5, 113.0, 77.8, 62.3, 43.6, 41.6, 14.4; **HRMS** (ESI) Calcd for $C_{28}H_{25}N_2O_4$ $[M+H]^+$ 453.1809; found 453.1814.

14. Procedure for the Synthesis of 7.



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added **3aa** (36.4 mg, 0.1 mmol), NaH (12.1 mg, 0.3 mmol) and THF (0.5 mL), and followed by the addition of MeI (12.5 μL, 0.2 mmol). The reaction mixture was stirred at room temperature for 8 h. After quenching the reaction by water, the mixed solution was extracted with DCM (5 mL). The organic phase was dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5 : 1) to get the pure compound **7** (25.3 mg, 93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.09 (br, 1H), 7.34–7.28 (m, 2H), 7.28–7.22 (m, 1H), 7.16–7.11 (m, 2H), 7.02 (d, J = 9.0 Hz, 1H), 6.52 (d, J = 8.9 Hz, 1H), 4.43 (dd, J = 8.9, 1.9 Hz, 1H), 4.35 (dd, J = 8.9, 7.4 Hz, 1H), 3.93–3.86 (m, 1H), 3.00 (dd, J = 13.8, 5.5 Hz, 1H), 2.91 (d, J = 4.7 Hz, 3H), 2.84 (dd, J = 13.8, 9.5 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.3, 149.7, 147.8, 138.9, 133.7, 129.3 (2C), 128.8 (2C), 126.9, 119.4, 113.8, 110.9, 75.8, 43.5, 42.1, 29.9; **HRMS** (ESI) Calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.1332; found 268.1333.

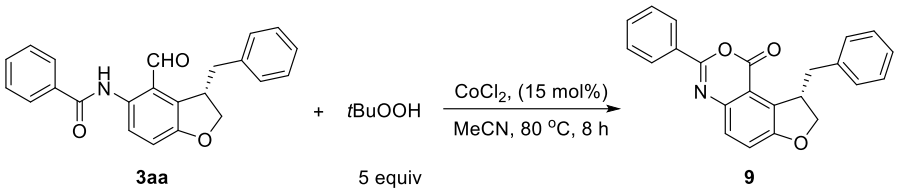
15. Procedure for the Synthesis of 8.



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added **3aa** (35.6 mg, 0.1 mmol), NaH (24.3 mg, 0.6 mmol) and THF (0.5 mL), and followed by the addition of MeI (62 μL, 1.0 mmol). The reaction mixture was stirred at room temperature for 8 h. After quenching the reaction by water, the mixed solution was extracted with DCM (5 mL). The organic phase was dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to get the pure compound **8** (22.6 mg, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 7.36–7.29 (m, 4H), 7.25–7.20 (m, 1H), 7.01 (d, J = 8.6 Hz, 1H), 6.97 (d, J = 8.6 Hz, 1H), 4.44 (dd, J = 8.9, 2.0 Hz, 1H), 4.27 (t, J = 8.3 Hz, 1H), 4.10–4.03 (m, 1H), 3.11 (dd, J = 13.4, 3.2 Hz, 1H), 2.83 (s, 6H), 2.51 (dd, J = 13.4, 10.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.1, 156.0, 151.9, 140.1, 132.8, 129.4 (2C), 128.6 (2C), 126.4, 125.8, 119.4,

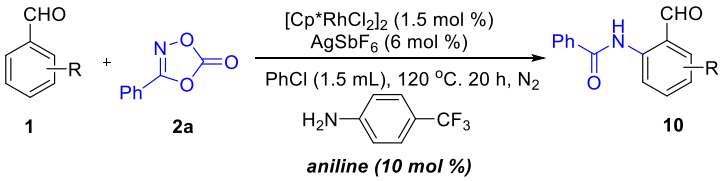
115.6, 76.0, 47.1 (2C), 44.6, 39.8. **HRMS** (ESI) Calcd for $C_{18}H_{20}NO_2$ $[M+H]^+$ 282.1489; found 282.1490.

16. Procedure for the Synthesis of 9.



To a 10 mL of Schlenk tube equipped with a magnetic stirring bar were added **3aa** (36.0 mg, 0.1 mmol), $CoCl_2$ (2.0 mg, 15 mol%), TBHP (70% in H_2O, 70.5 μL, 5.0 equiv.) and MeCN (0.4 mL). The reaction mixture was stirred at 80 °C for 8 h. The mixed solution was extracted with H_2O (5 mL) and ethyl acetate (10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtration and removed all of organic solvent. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10 : 1) to get the pure compound **9** (26.2 mg, 58%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32–8.26 (m, 2H), 7.59–7.48 (m, 4H), 7.36–7.31 (m, 4H), 7.29–7.23 (m, 2H), 4.62 (dd, J = 9.1, 2.3 Hz, 1H), 4.47 (t, J = 8.5 Hz, 1H), 4.30–4.21 (m, 1H), 3.34 (dd, J = 13.4, 3.2 Hz, 1H), 2.64 (dd, J = 13.4, 10.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 158.9, 154.8, 141.7, 139.4, 132.2, 131.9, 130.6, 129.4 (2C), 128.9 (2C), 128.7 (2C), 128.3, 128.0 (2C), 126.7, 118.7, 114.0, 76.9, 44.8, 40.0; **HRMS** (ESI) Calcd for $C_{23}H_{18}NO_3$ $[M+H]^+$ 356.1281; found 356.1287.

17. General Procedure for the Synthesis of 10.



To a 25 mL of Schlenk tube equipped with a magnetic stirring bar were added **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (1.5 mol%) and $AgSbF_6$ (6 mol%) under air. The mixture was then evacuated and backfilled with nitrogen for three times. After that, aldehyde (0.3 mmol), 4-trifluoromethyl aniline (10 mol%) and PhCl (1.5 mL) were added subsequently. After stirring at 120 °C for 20 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (5 : 1) as the eluent to give the corresponding products **10**. **10a–10c** are known compounds.[3]

Compound **10d** (74%): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.27 (s, 1H), 10.56 (s, 1H), 8.79 (d, J = 9.3 Hz, 1H), 8.08–8.03 (m, 2H), 7.59–7.49 (m, 3H), 7.18 (d, J = 9.3 Hz, 1H), 3.87 (s, 3H), 2.57 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.4, 166.1, 153.2,

135.2, 135.0, 132.0, 131.8, 128.9 (2C), 127.6 (2C), 120.9, 118.8 (2C), 56.4, 10.4; **HRMS** (ESI) Calcd for $C_{16}H_{16}NO_3$ $[M+H]^+$ 270.1225; found 270.1227.

Compound **10e** (71%): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.88 (s, 1H), 10.18 (s, 1H), 8.77 (d, J = 8.9 Hz, 1H), 8.05 (d, J = 7.9 Hz, 2H), 7.58–7.49 (m, 3H), 7.11 (d, J = 9.0 Hz, 1H), 4.70 (t, J = 8.8 Hz, 2H), 3.59 (t, J = 8.7 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.4, 165.8, 156.3, 134.9, 134.8, 132.1, 132.0, 129.0 (2C), 127.5 (2C), 120.6, 118.8, 117.5, 71.6, 28.4; **HRMS** (ESI) Calcd for $C_{16}H_{14}NO_3$ $[M+H]^+$ 268.0968; found 268.0970.

18. Cellular studies of 3al and 3ao.

18.1 Cell culture: Human cervical cancer cells (HeLa) were cultured in 25 cm^3 culture flasks containing RMPI-1640 medium supplemented with heat-inactivated 10% fetal bovine serum, 100 units mL^{-1} penicillin, and 100 μg/mL streptomycin at 37 °C in a humidified incubator containing 5% CO_2.

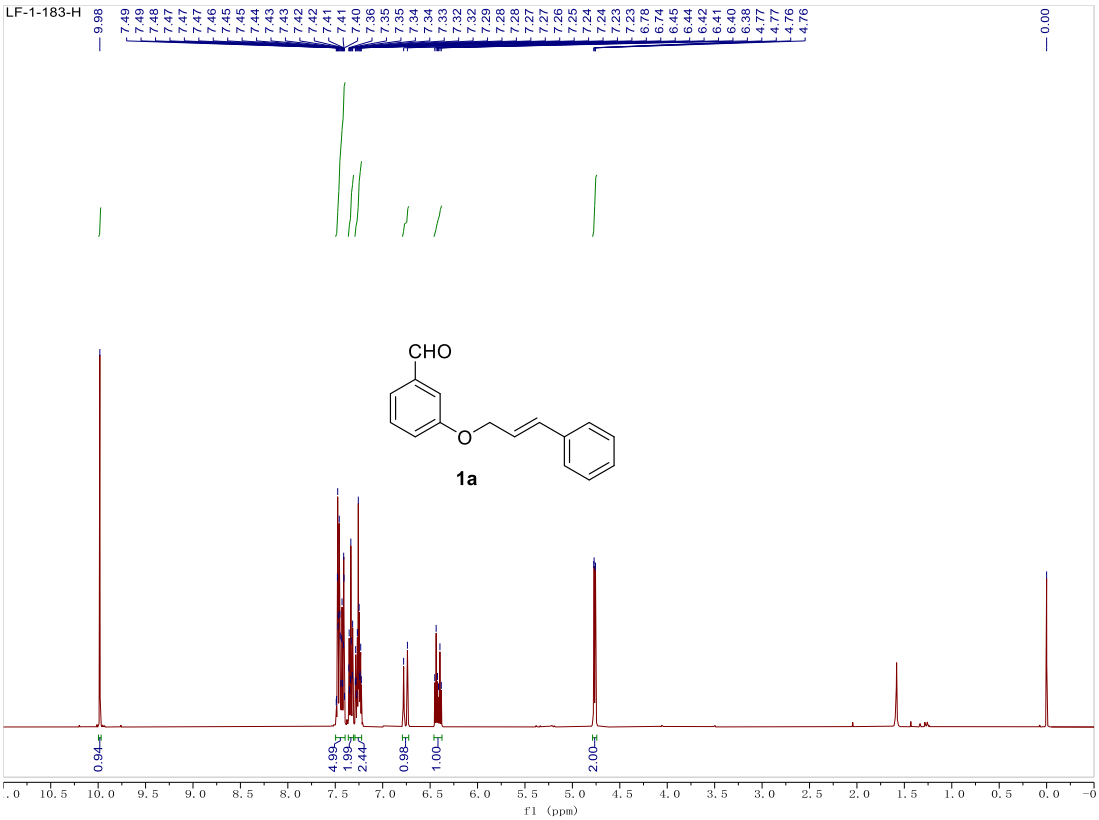
18.2 Cytotoxicity: The cytotoxicity of the **3al**/**3ao** was evaluated on HeLa cells. These cells were seeded into 96-well plates with a density of 5000 cells per well and cultured overnight. Then, **3al**/**3ao** solutions with a serious of concentrations were added and incubated with cells for 24 h. Each experiment was performed for six times. The working solutions were then removed, and the cells were washed with PBS buffer. A total of 10 μL of CCK-8 (Cell Counting Kit-8, BIOMIKY) was added into each well (total 100 μL), and the cells were further incubated at 37 °C for 2 h. Then the plate was shaken for 25 min (protection from light), and the absorbance at 450 nm was measured with a microplate reader (Multiskan Sky).

18.3 Colocalization imaging: HeLa cells were seeded onto a confocal dish (Nest Scientific) at a density of 3×10^4 cells 24 h before the microscopy measurement. For LDs colocalization study, after removed of the culture medium, the HeLa cells were co-incubated with **3al**/**3ao** (3 μM) and Nile Red (1 μM) in 1.0 mL of fresh culture medium for 1 h. Then, the morphologies of the cells were observed using a confocal fluorescence microscope (λ_{ex}: 405 nm, λ_{em}: 440-530 nm for **3al**/**3ao**; λ_{ex}: 552 nm, λ_{em}: 650-800 nm for Nile Red). No washing steps were performed.

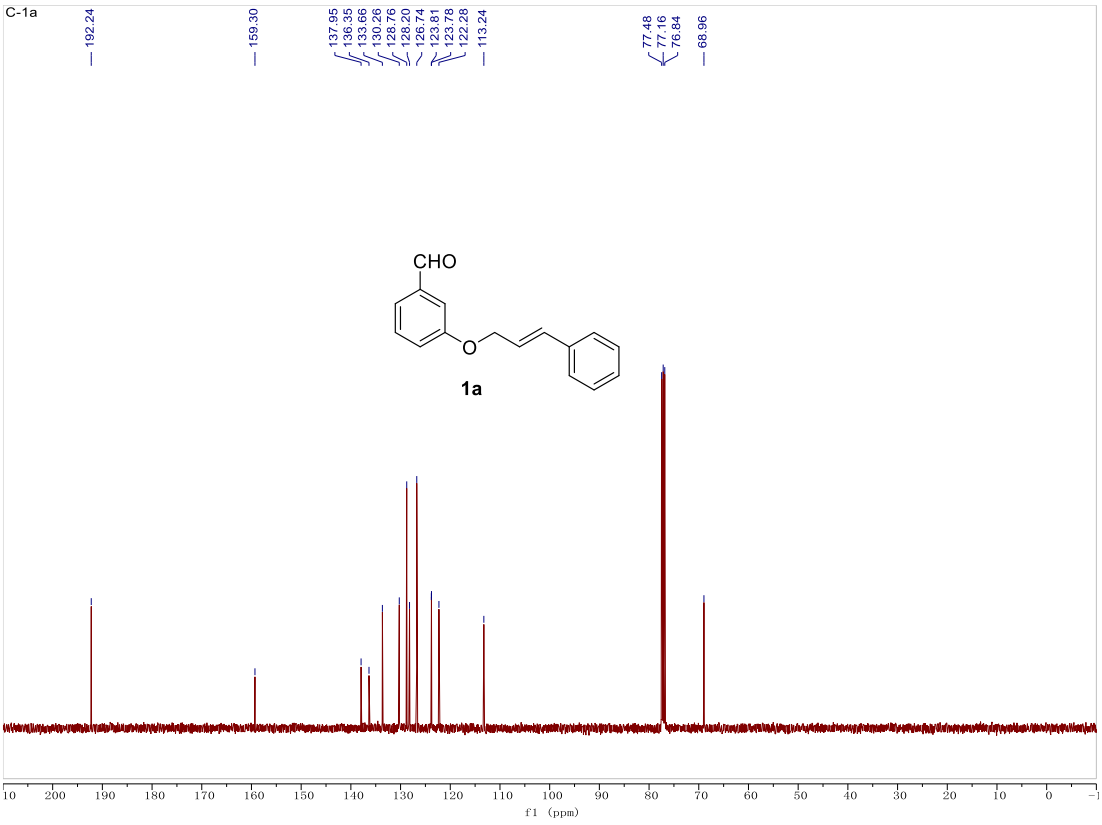
18.4 Multicolor imaging: HeLa cells were seeded onto a confocal dish (Nest Scientific) at a density of 3×10^4 cells 24 h before the microscopy measurement. After removed of the culture medium, the HeLa cells were co-incubated with **3al**/**3ao** (3 μM) and DIR (1 μM) in 1.0 mL of fresh culture medium for 1 h. Then, the morphologies of the cells were observed using a confocal fluorescence microscope (λ_{ex}: 405 nm, λ_{em}: 440-530 nm for **3al**/**3ao**; λ_{ex}: 638 nm, λ_{em}: 650-800 nm for DIR). No washing steps were performed.

19. NMR and HPLC Spectra of 1a-1za, 3aa-3zaa, 3ab-3ao, Int-1-10e

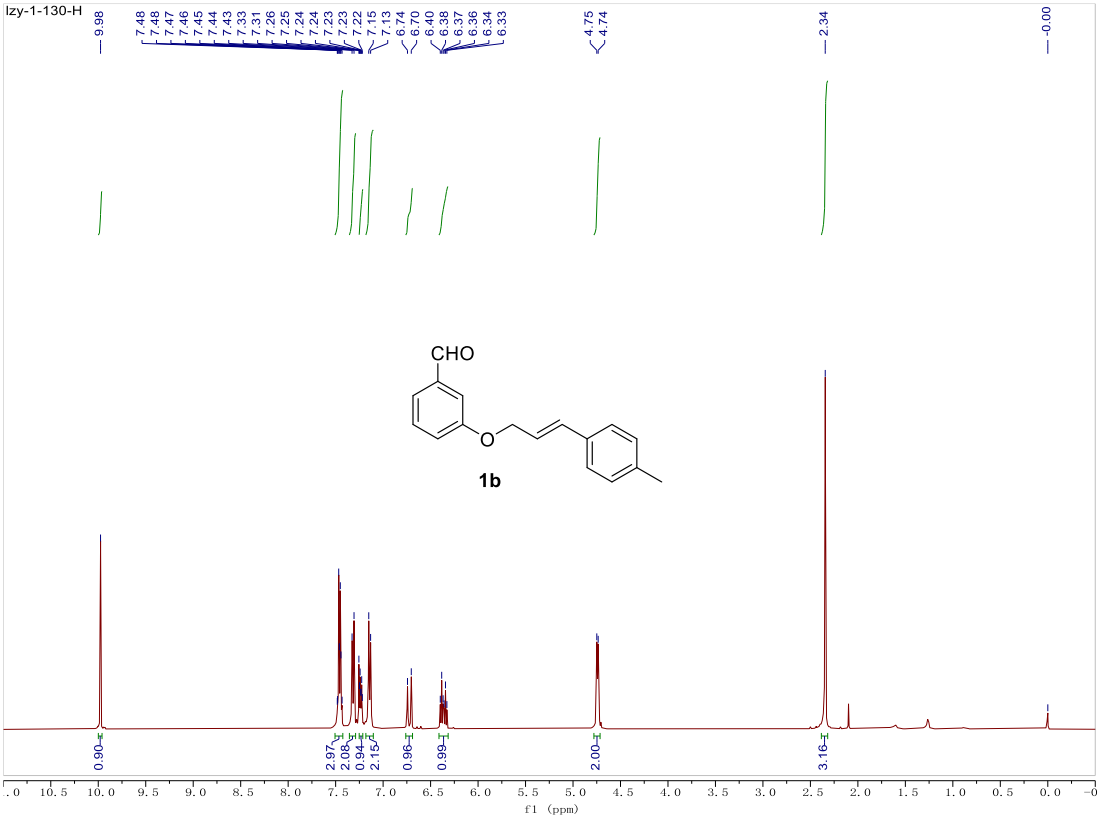
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1a**



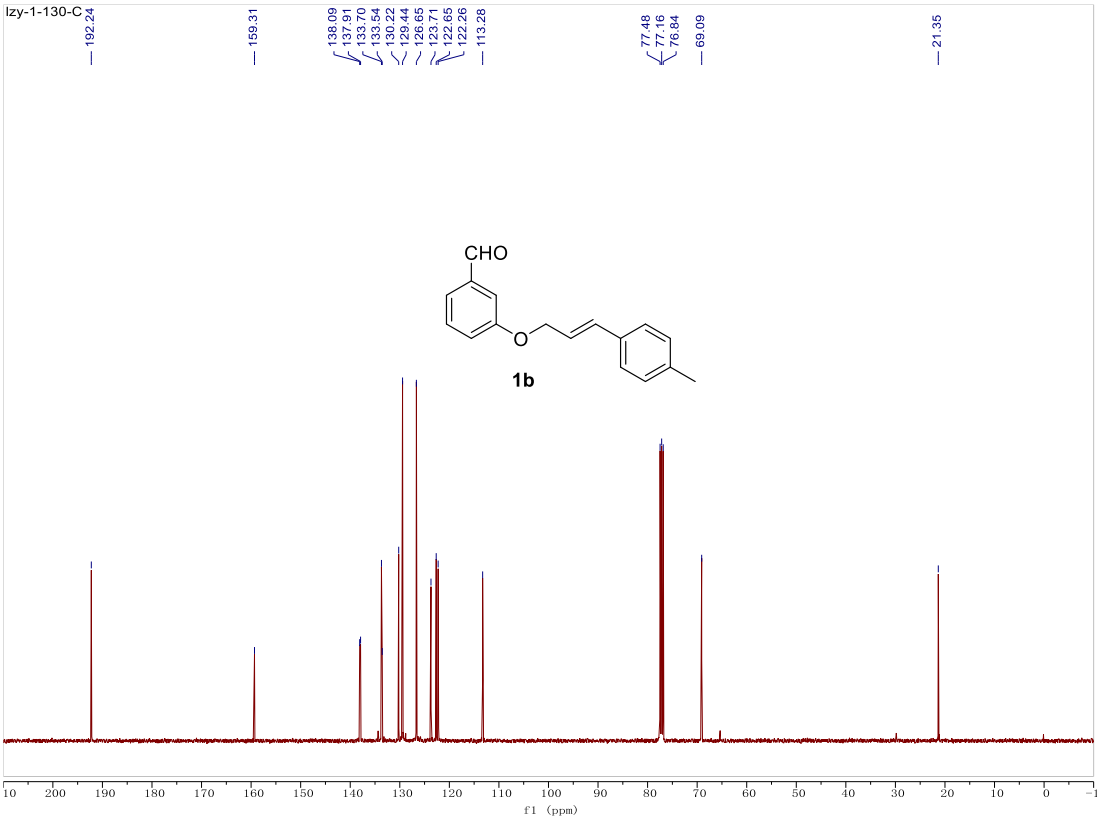
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1a**



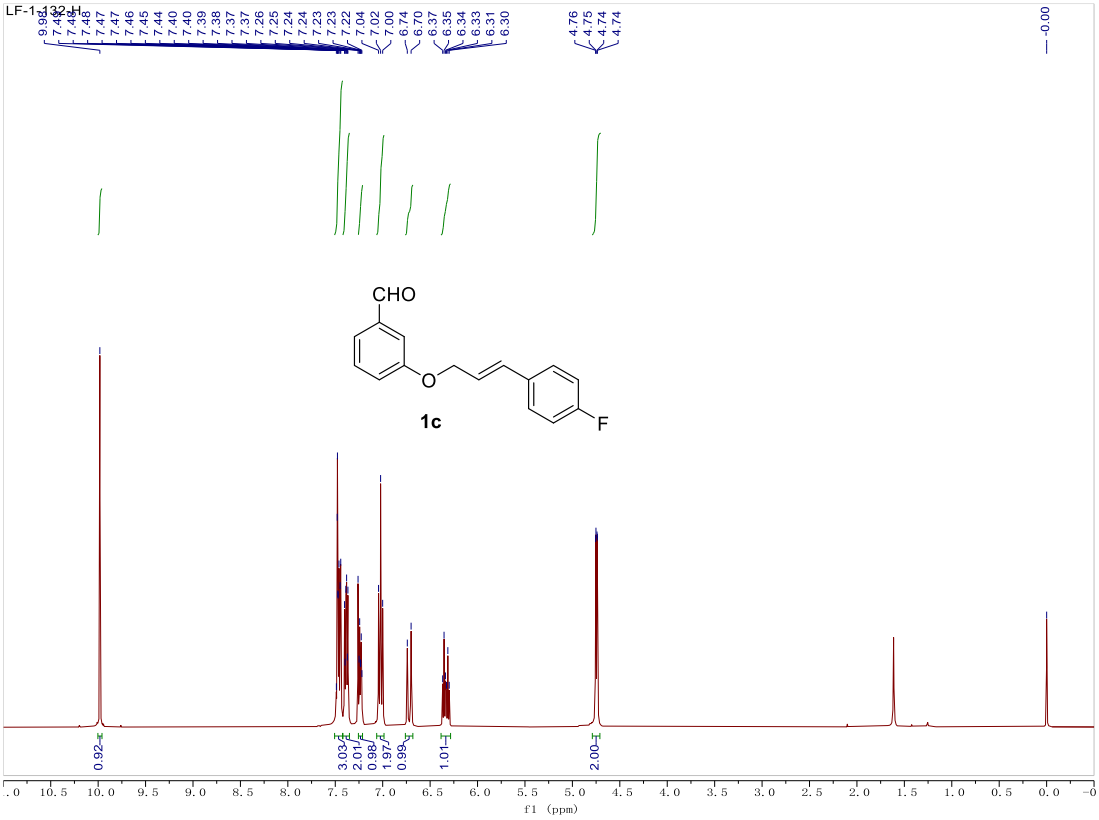
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1b**



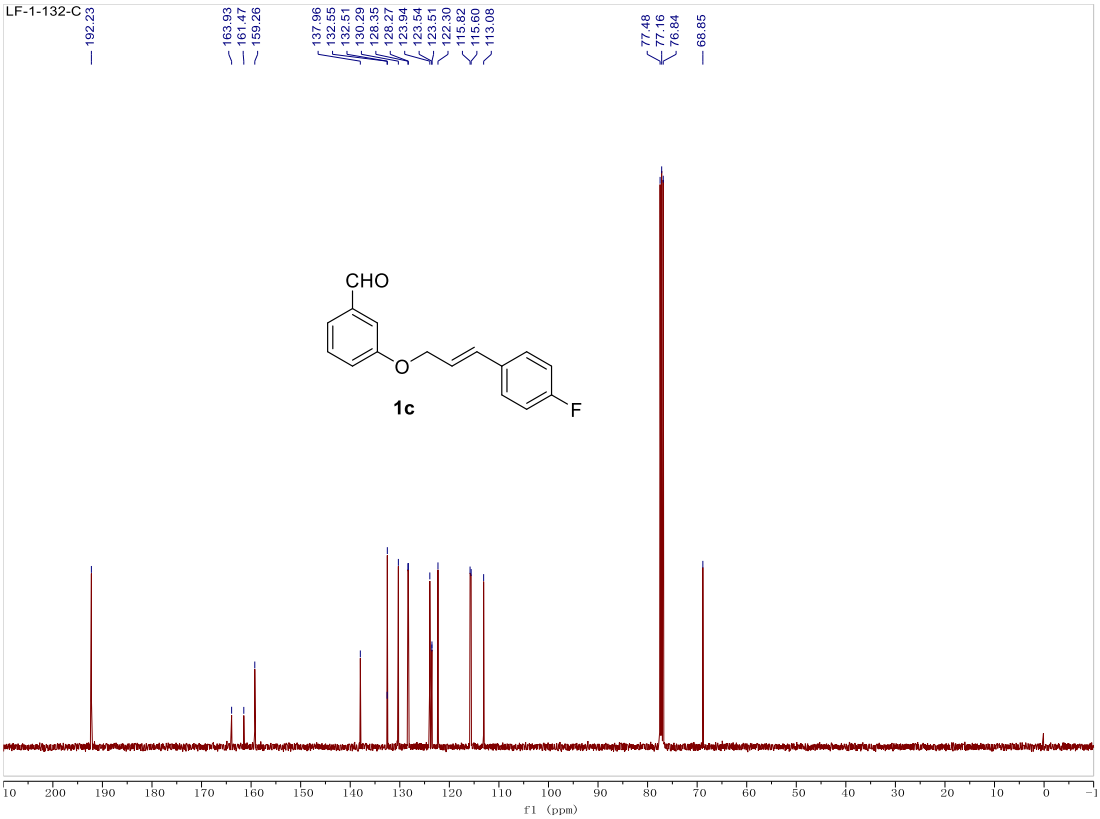
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1b**



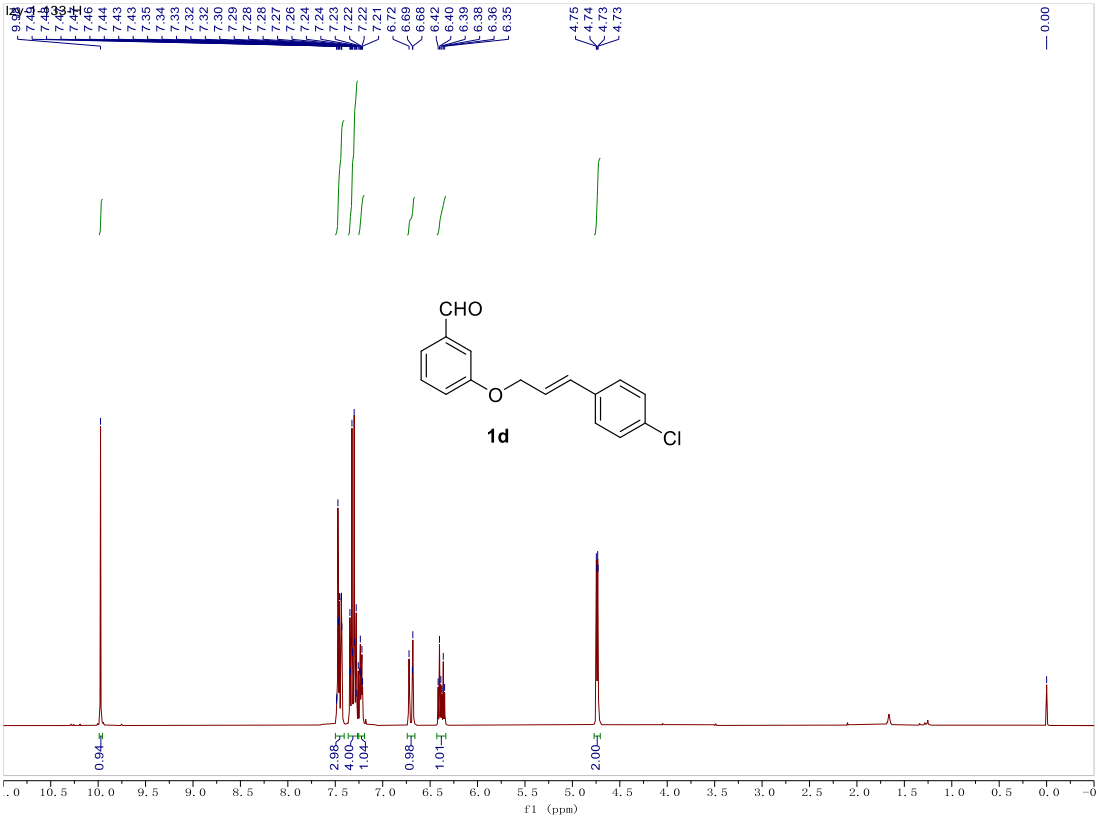
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1c**



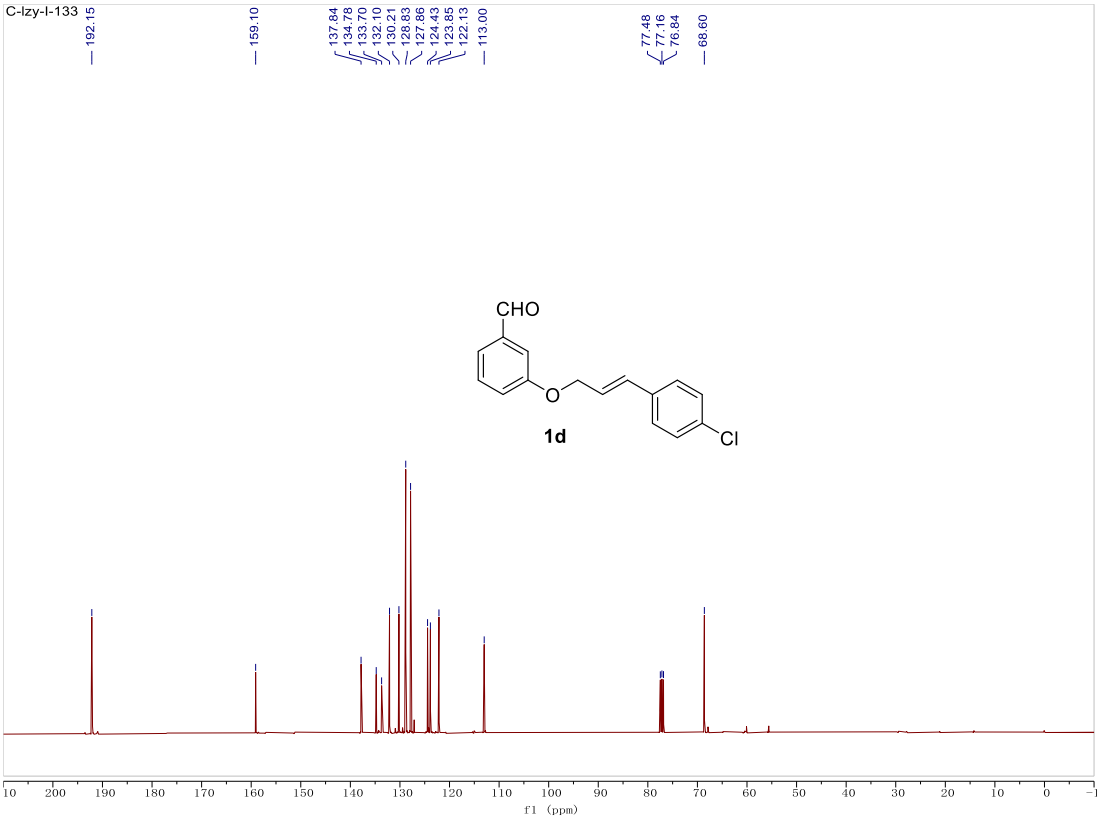
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1c**



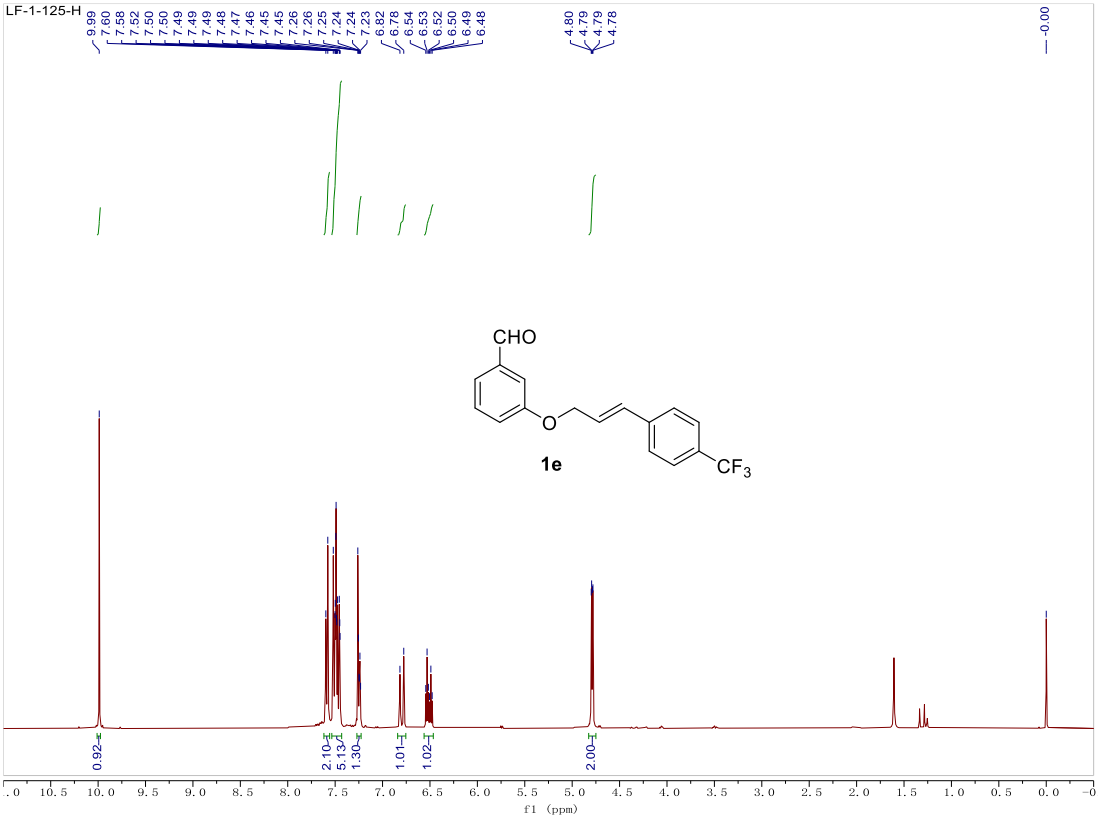
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1d**



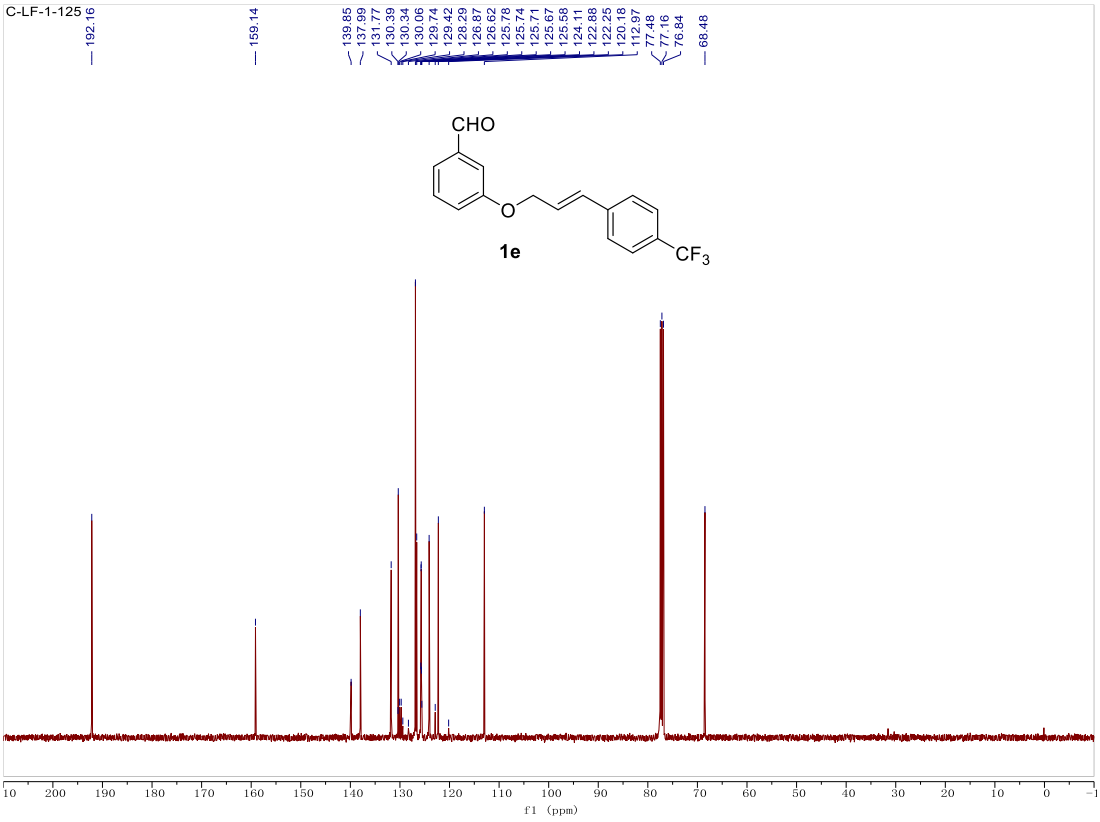
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1d**



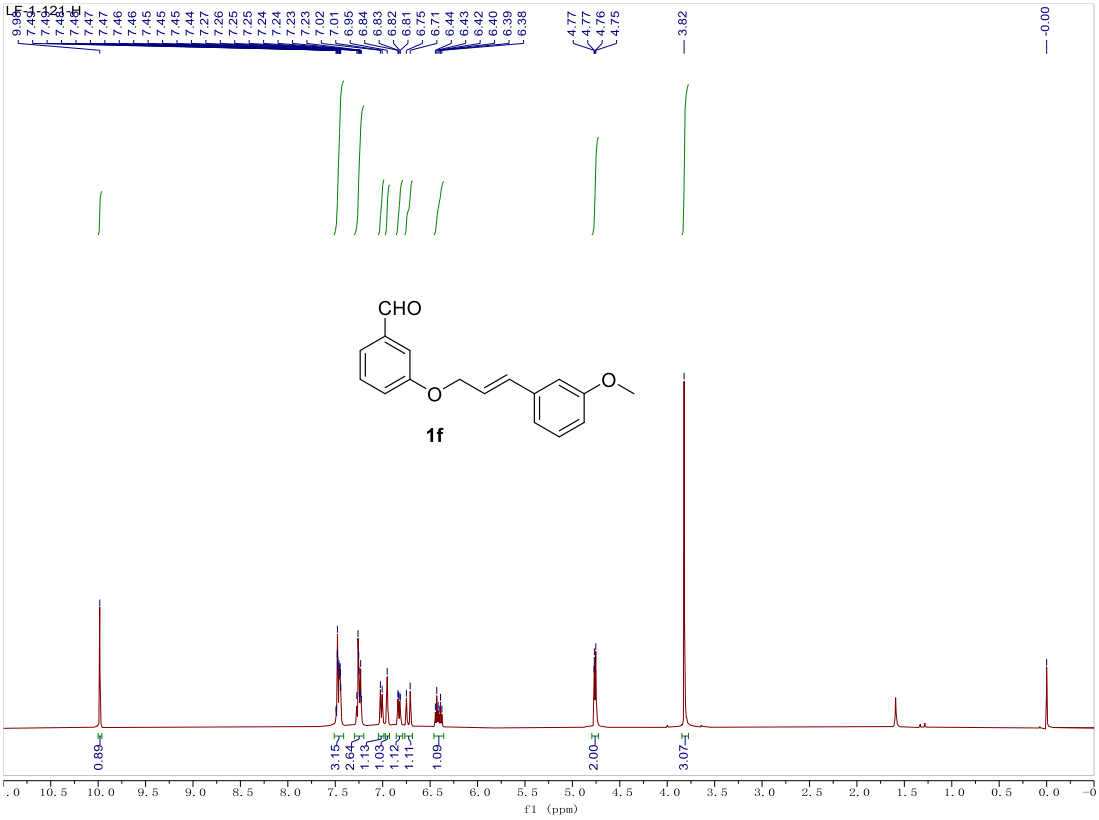
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1e**



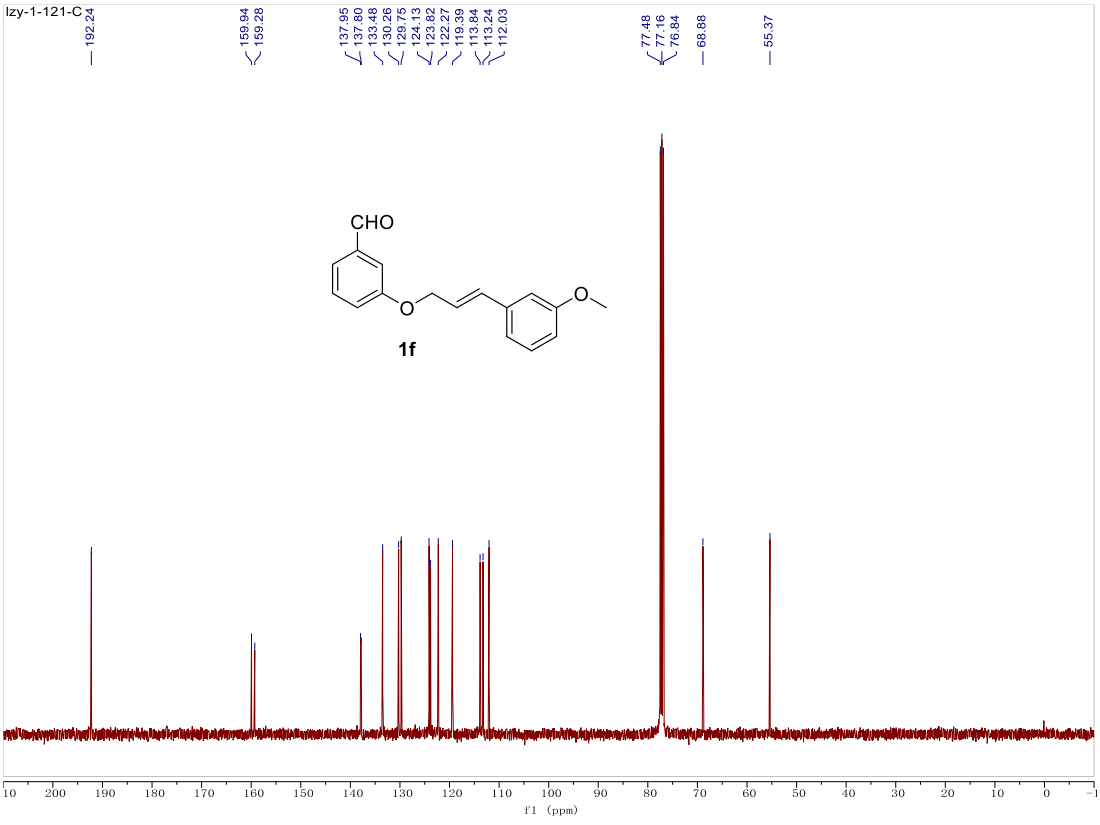
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1e**



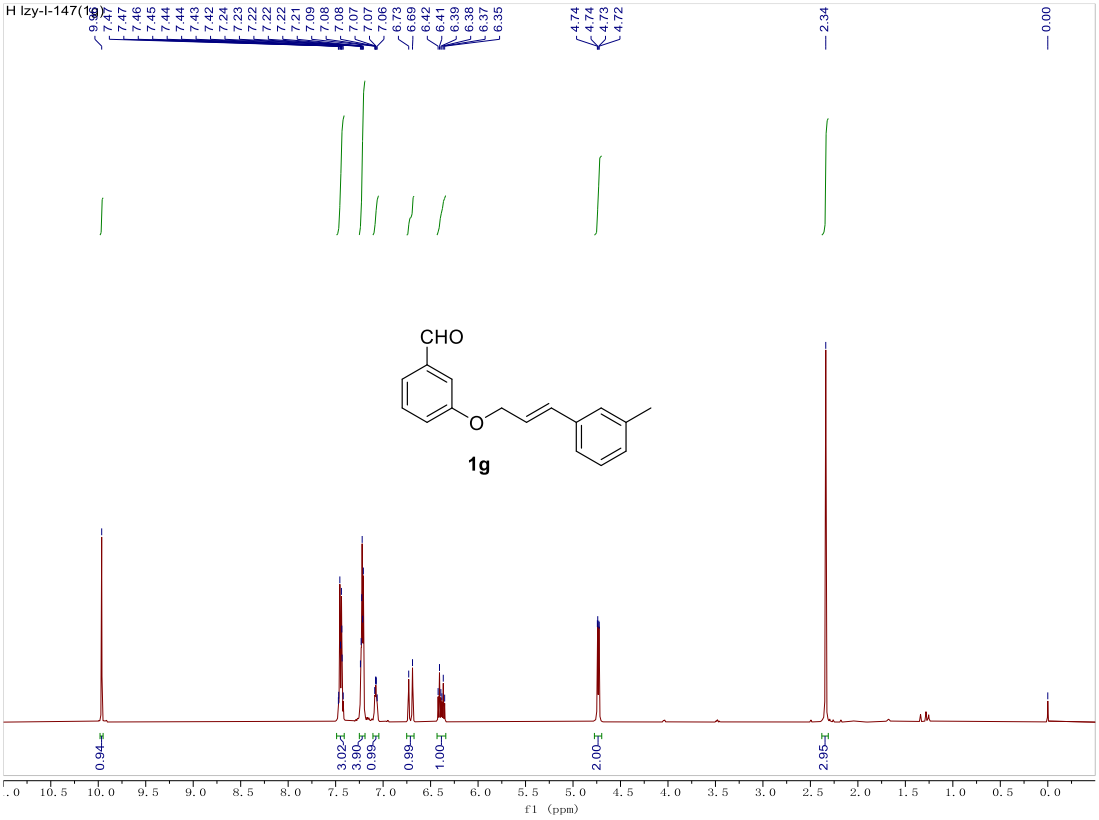
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1f**



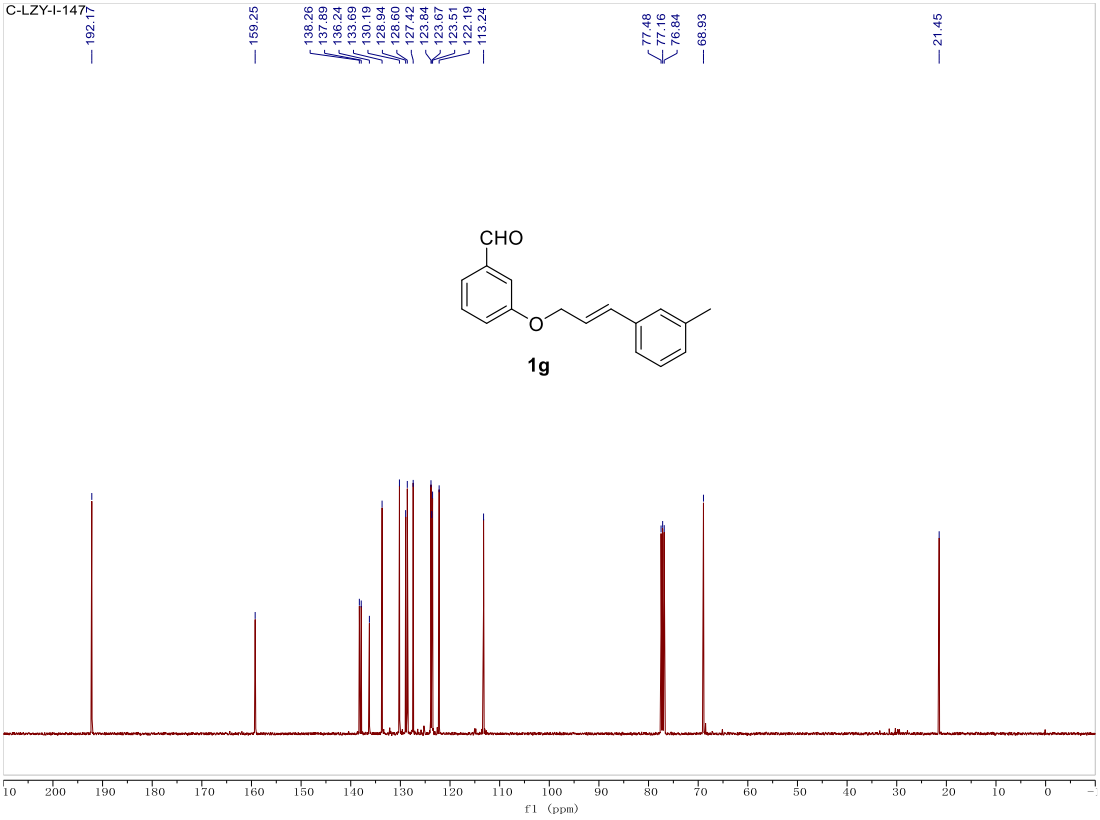
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1f**



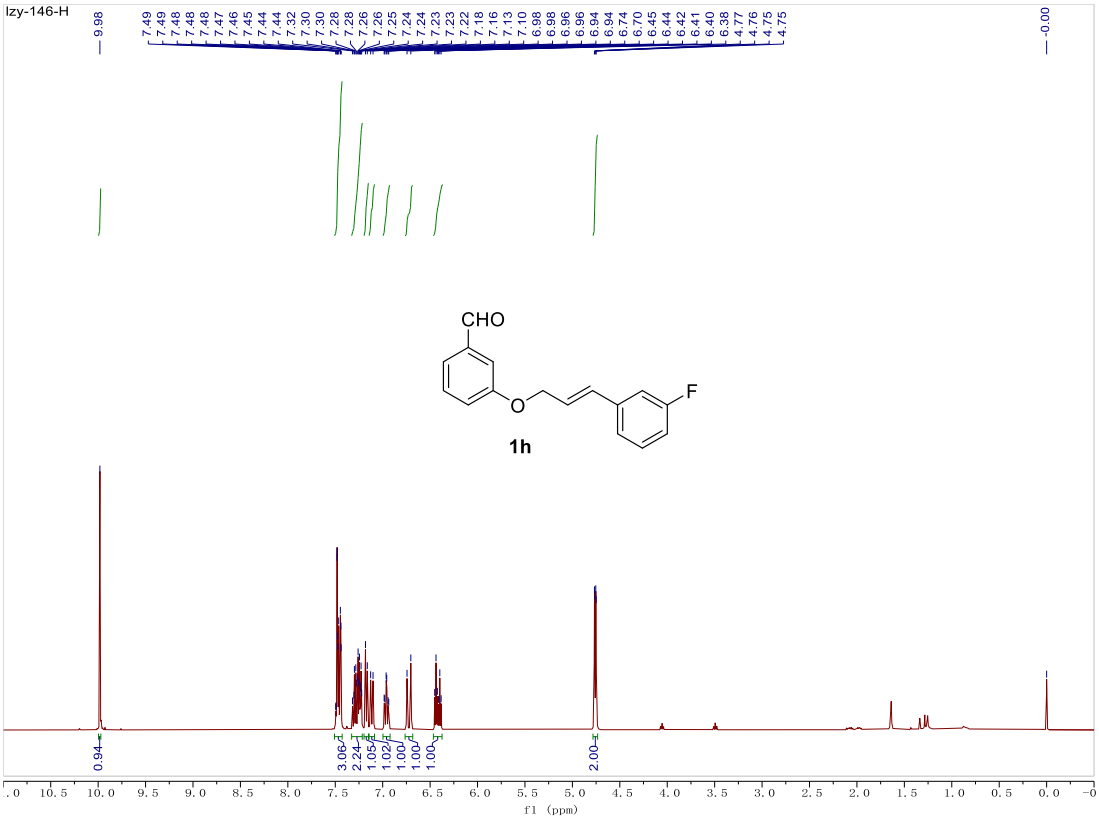
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1g**



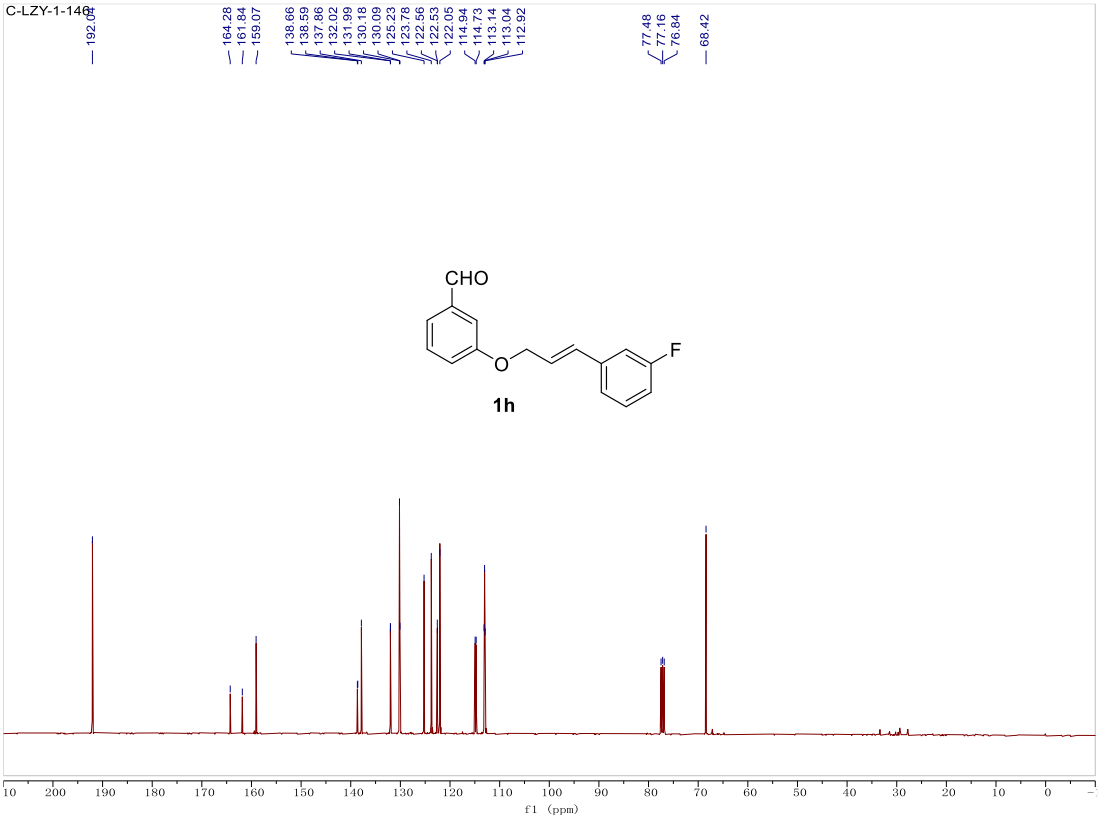
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1g**



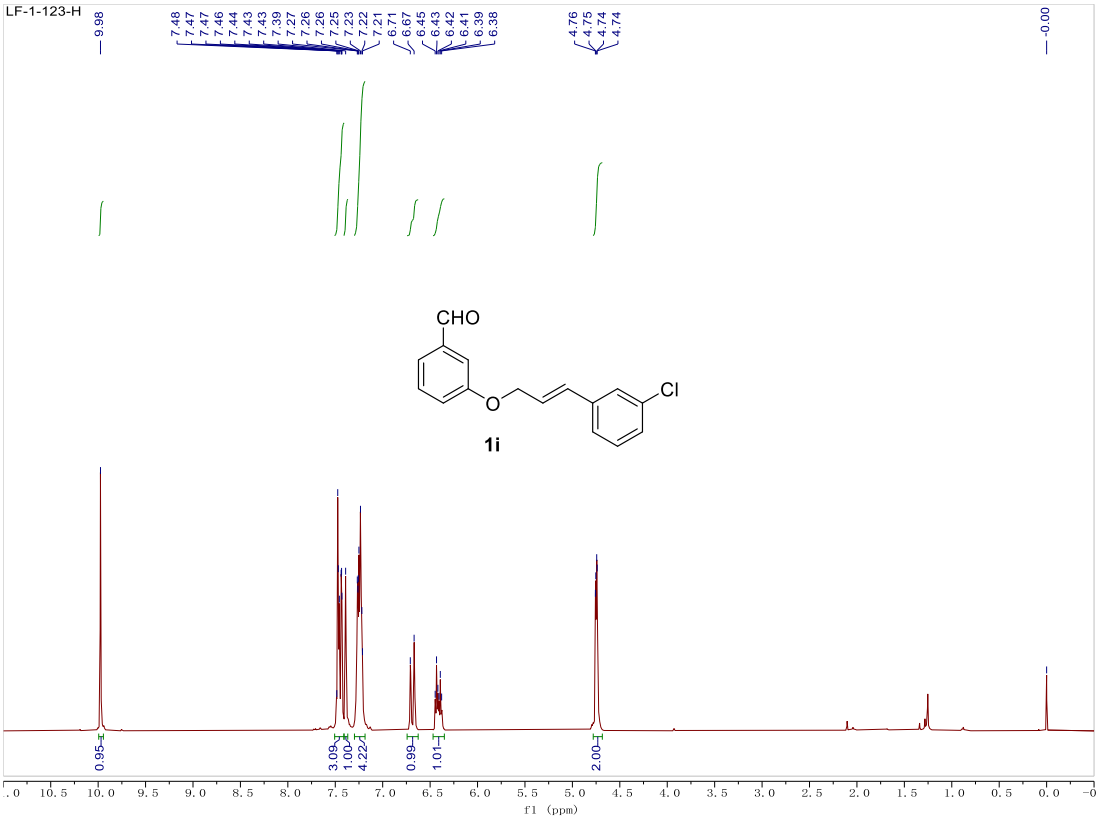
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1h**



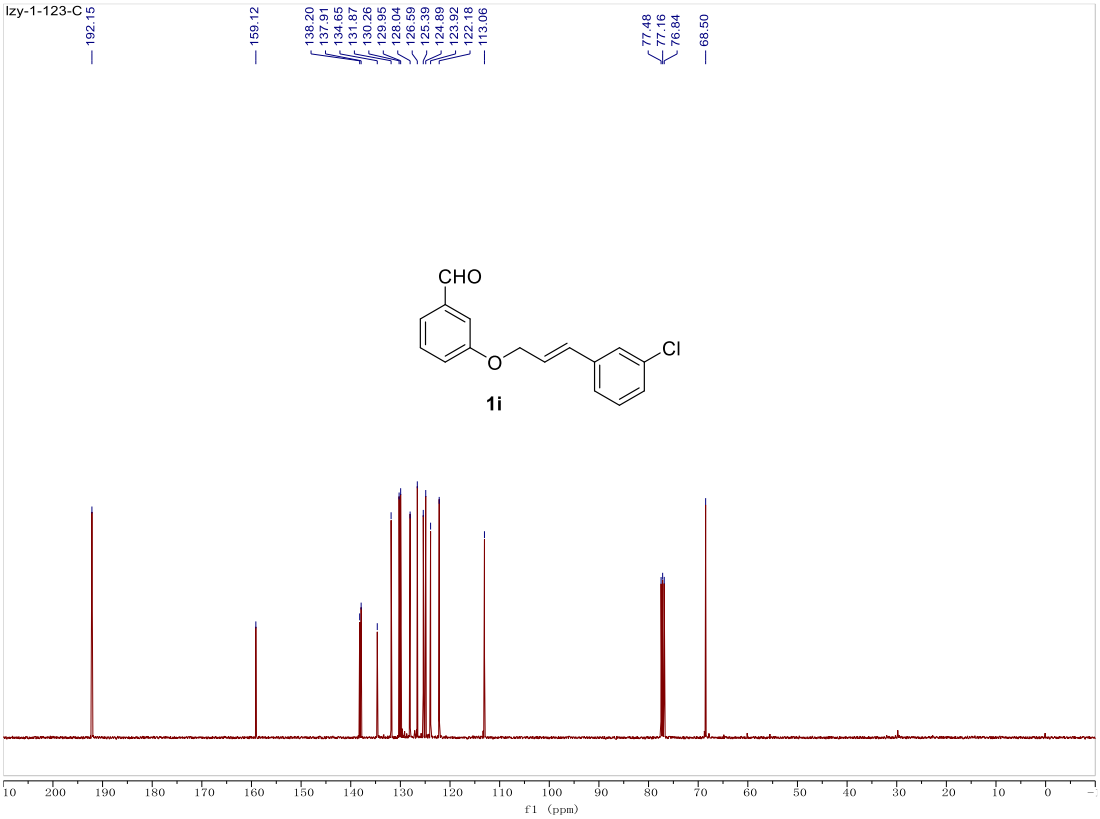
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1h**



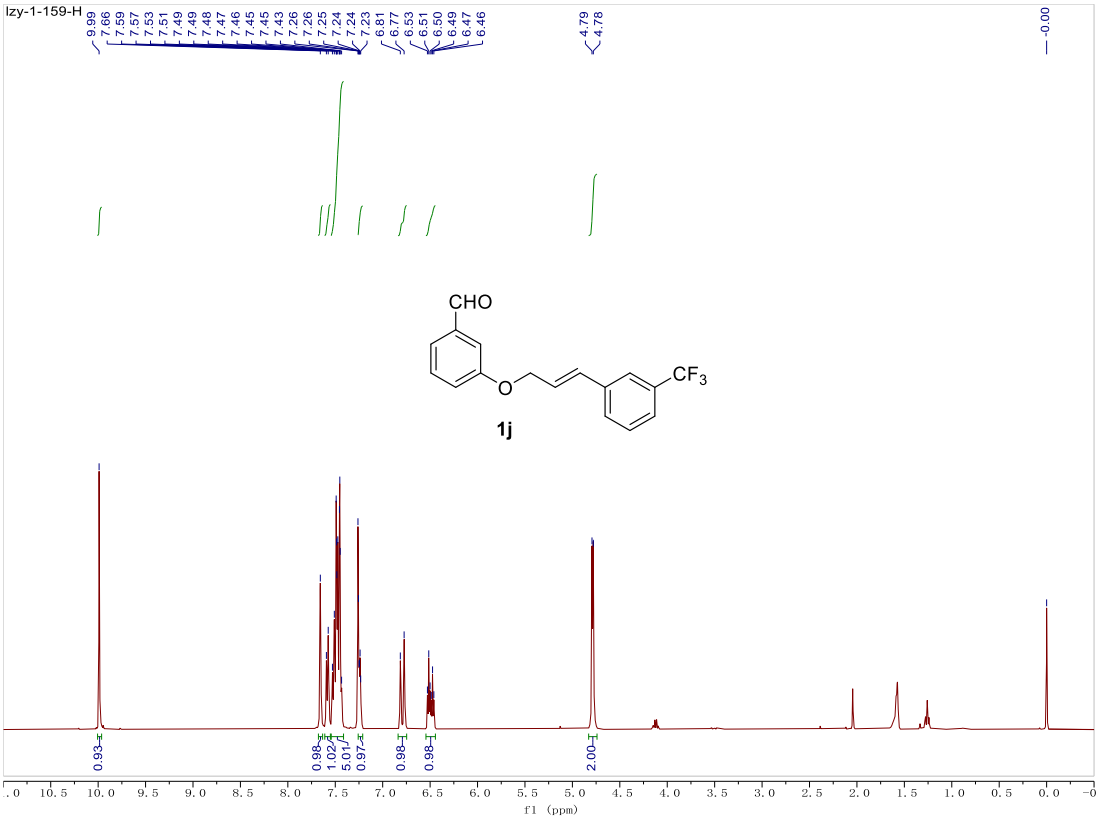
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1i**



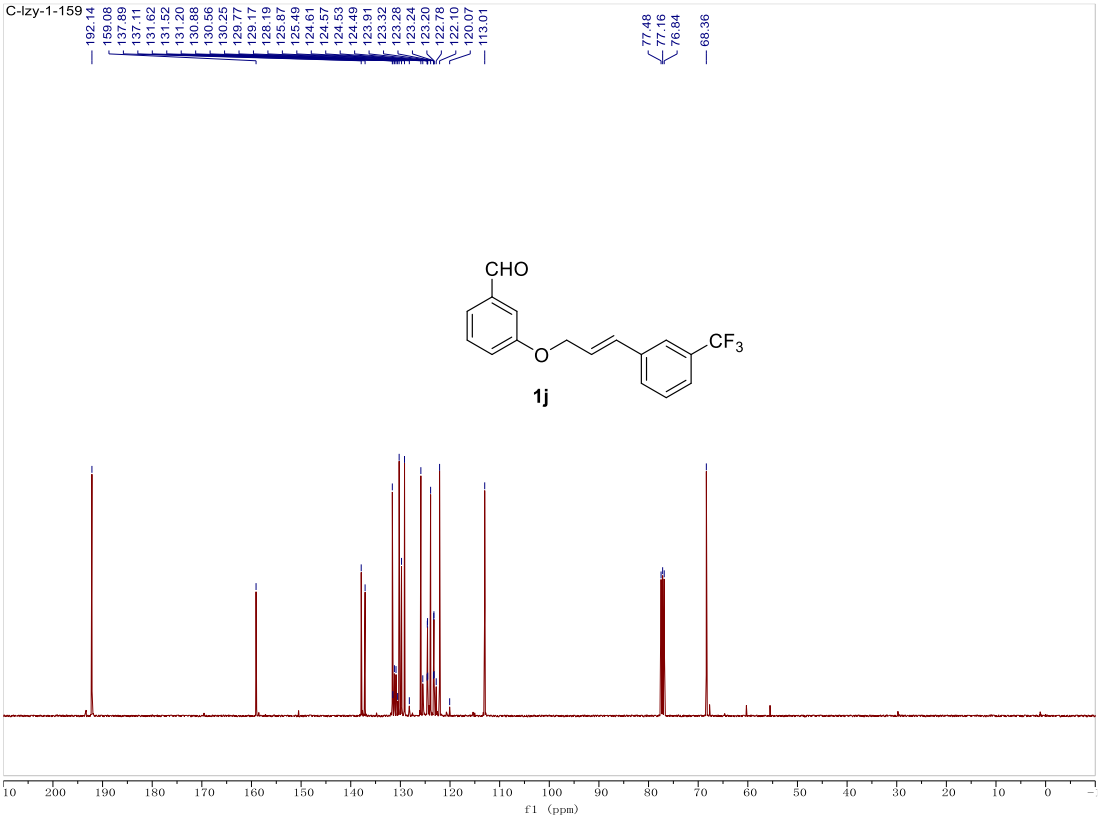
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1i**



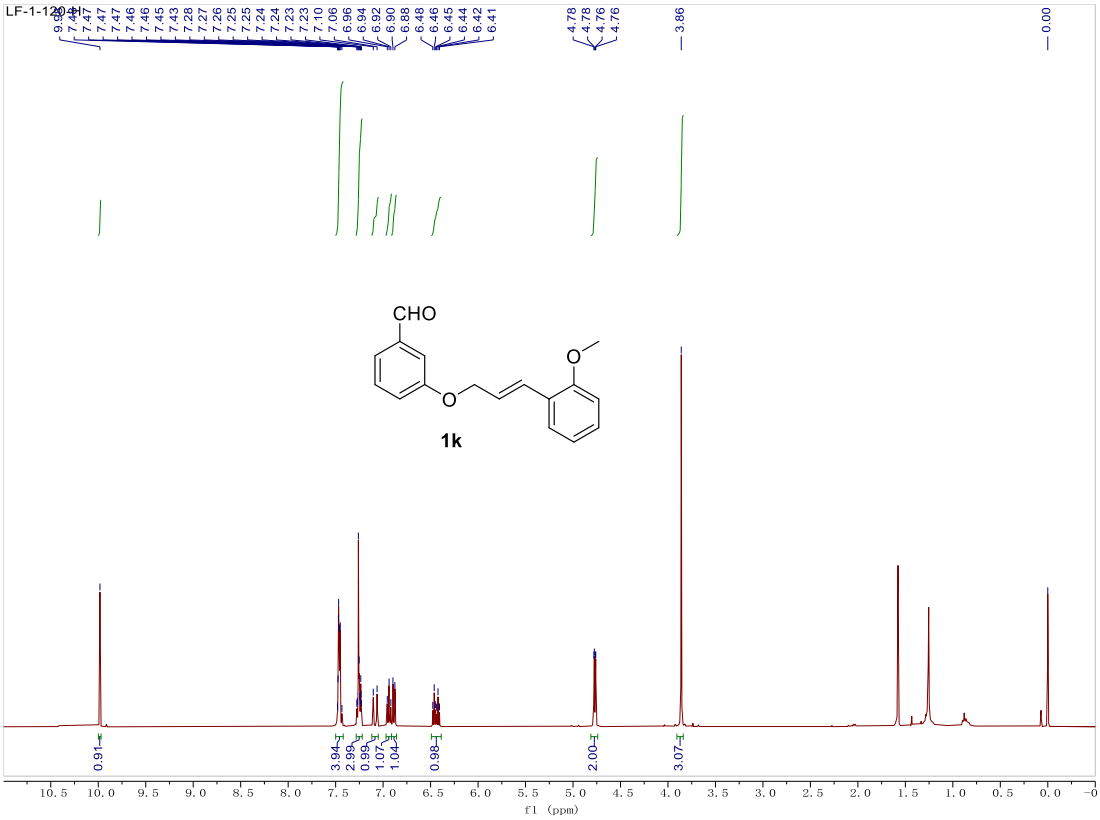
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1j**



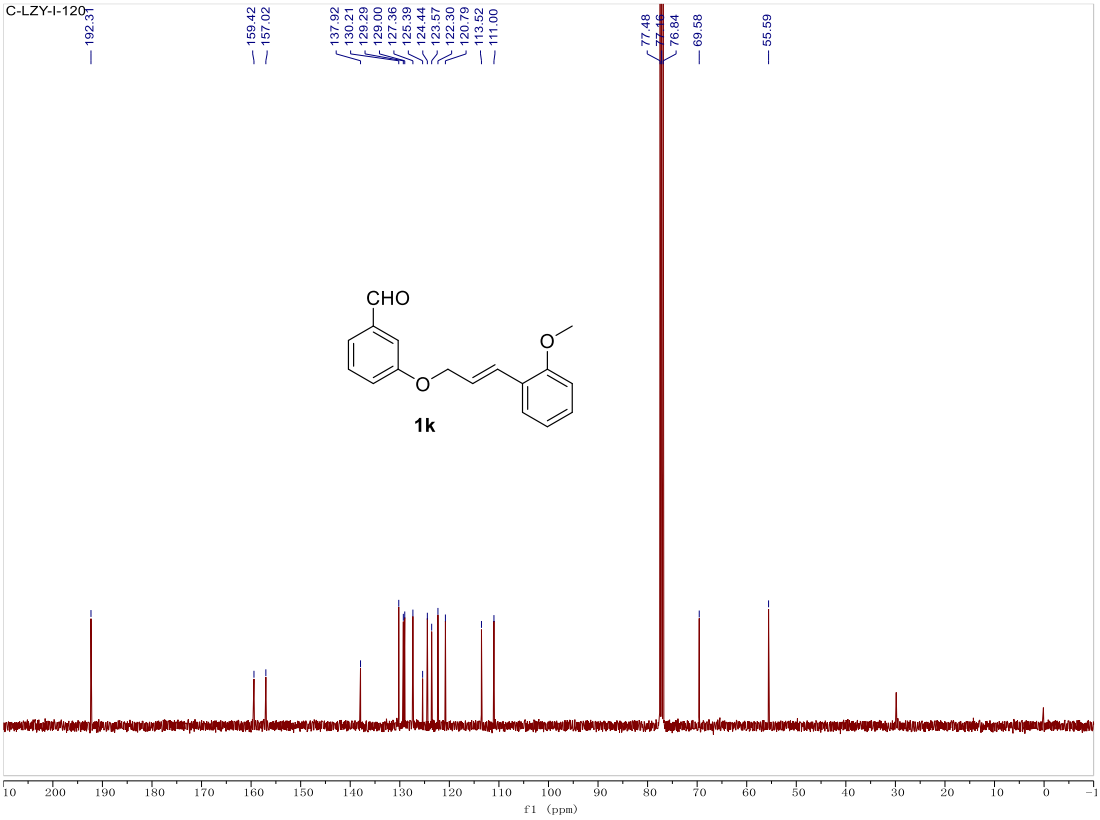
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1j**



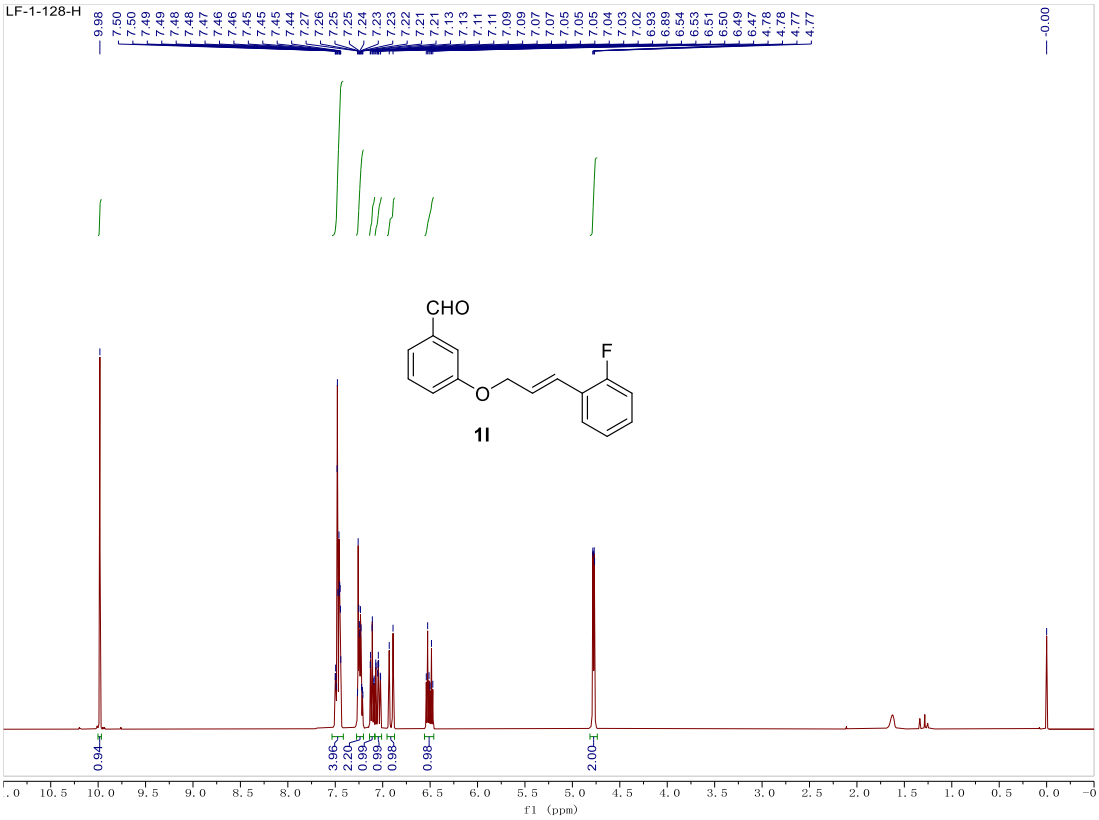
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1k**



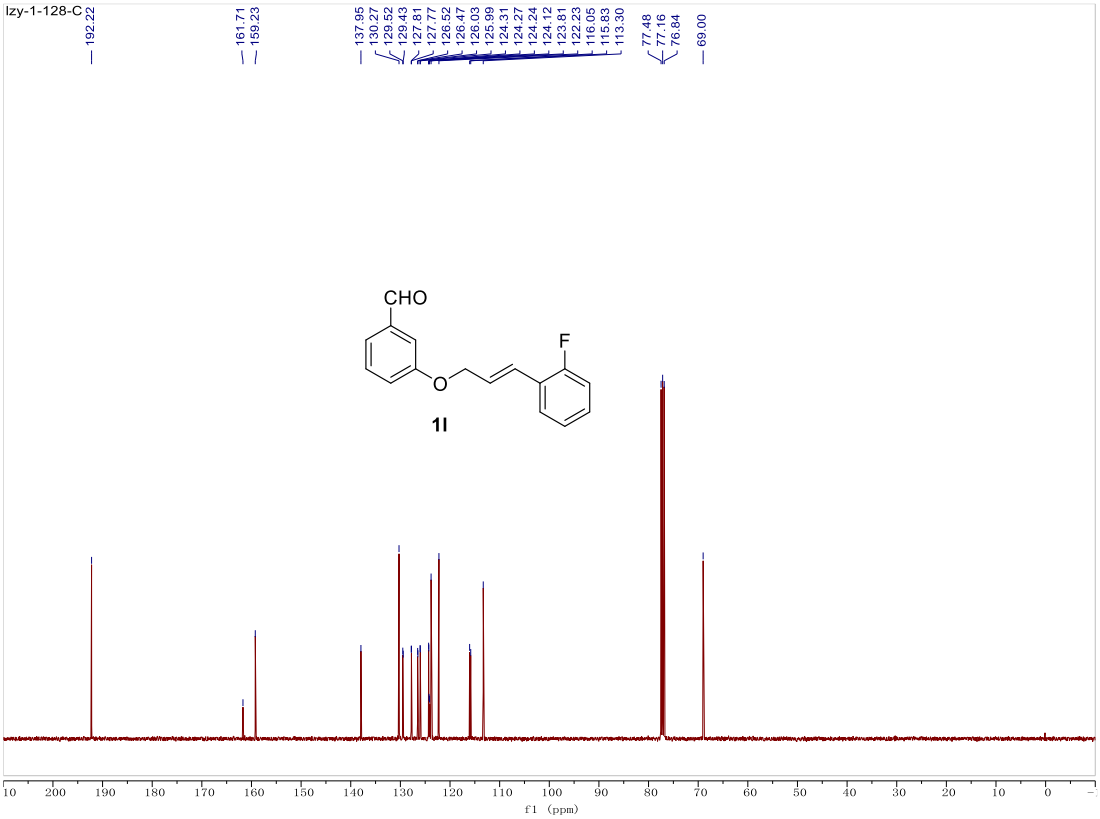
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1k**



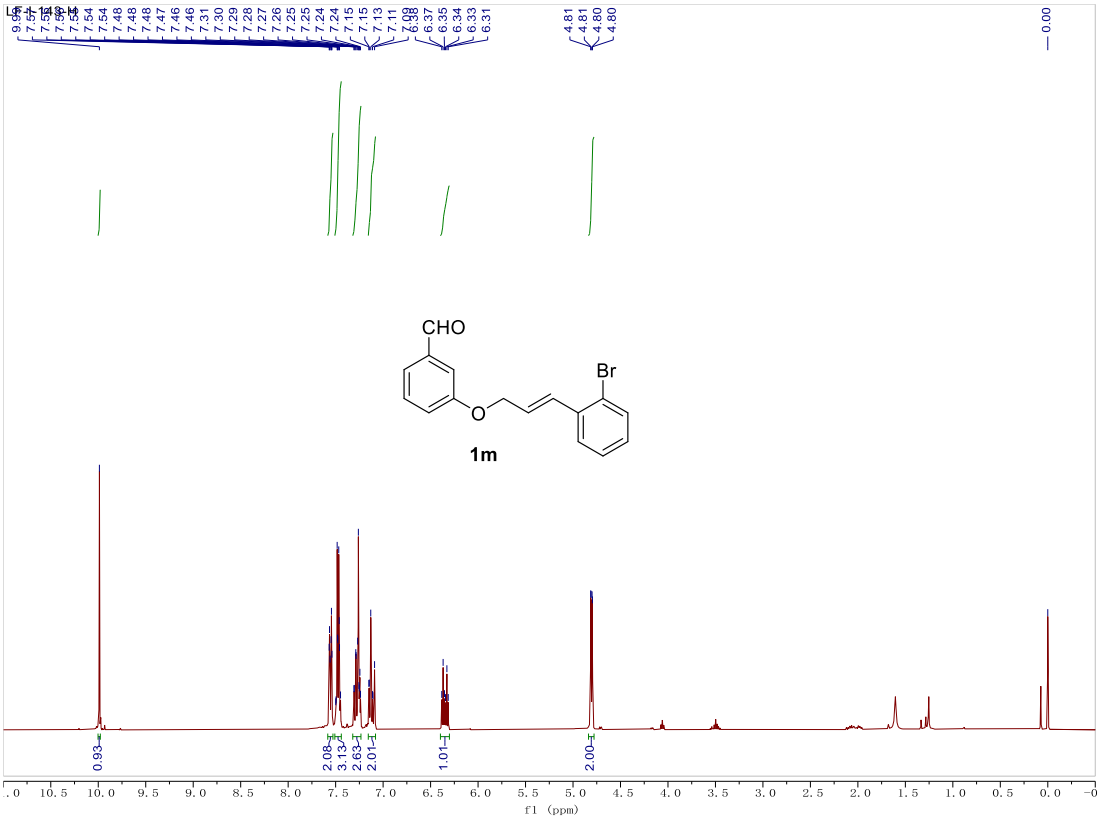
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1l**



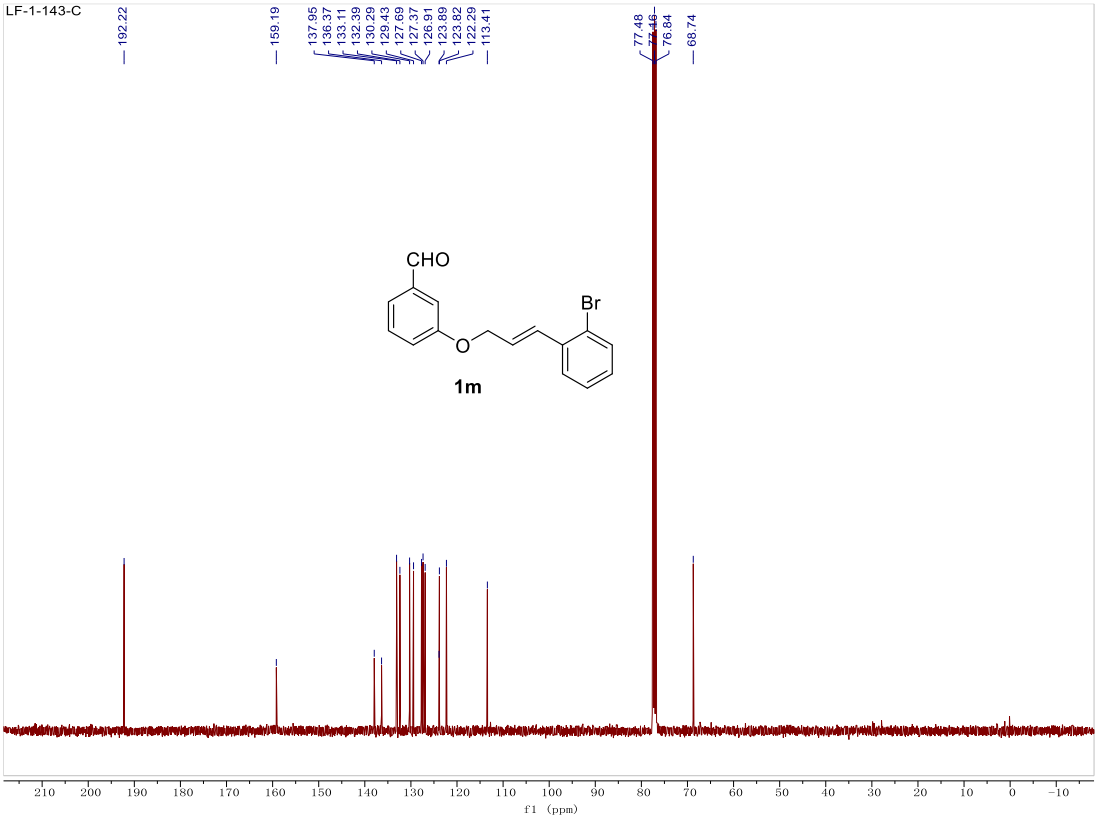
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1l**



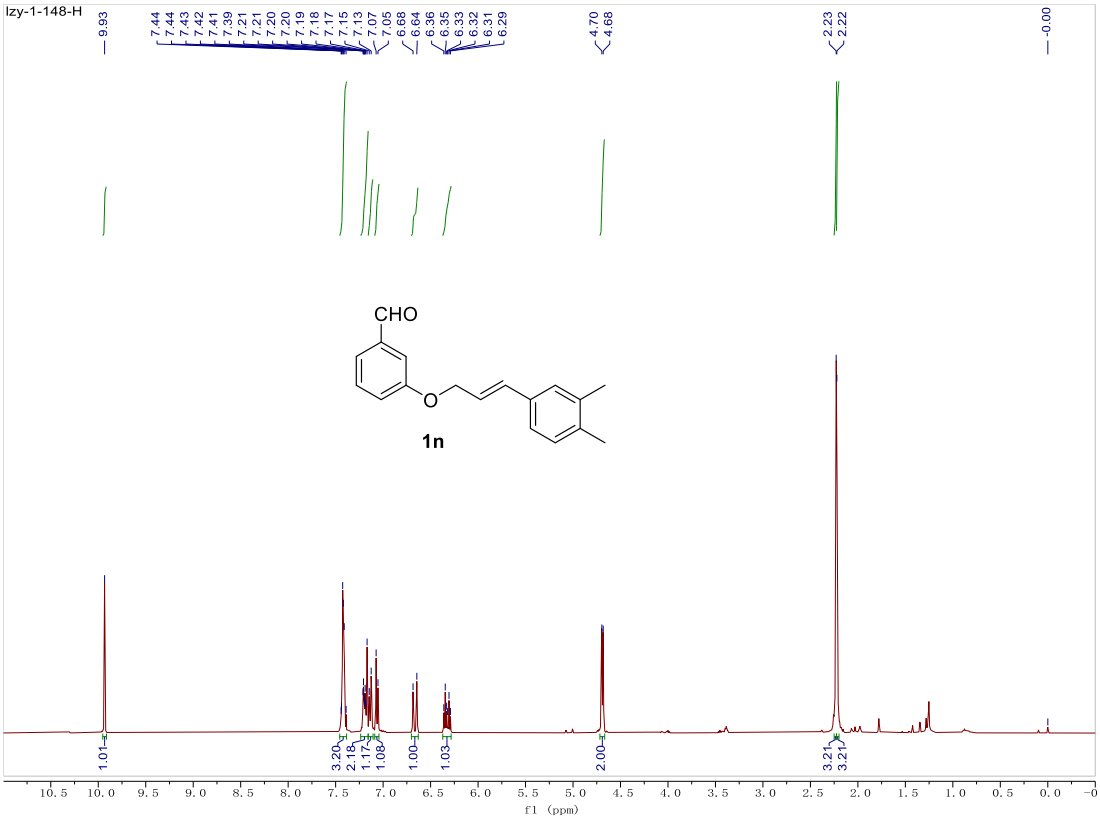
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1m**



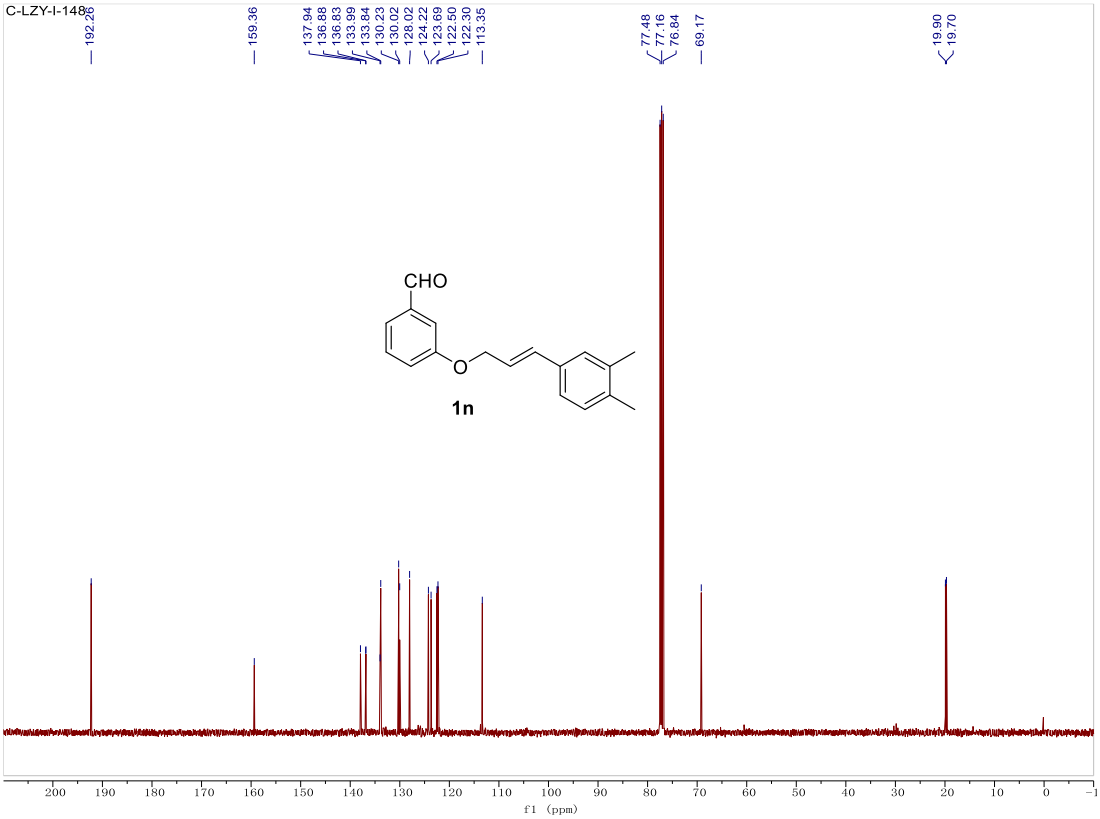
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1m**



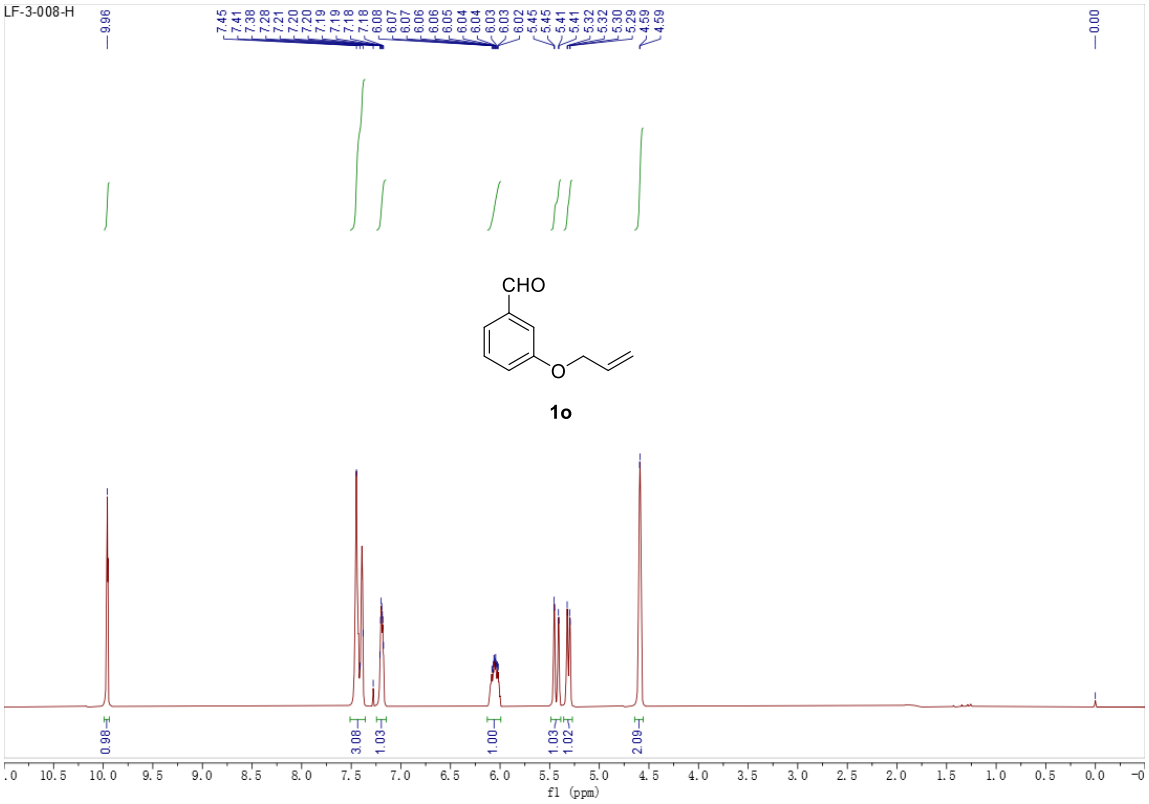
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1n**



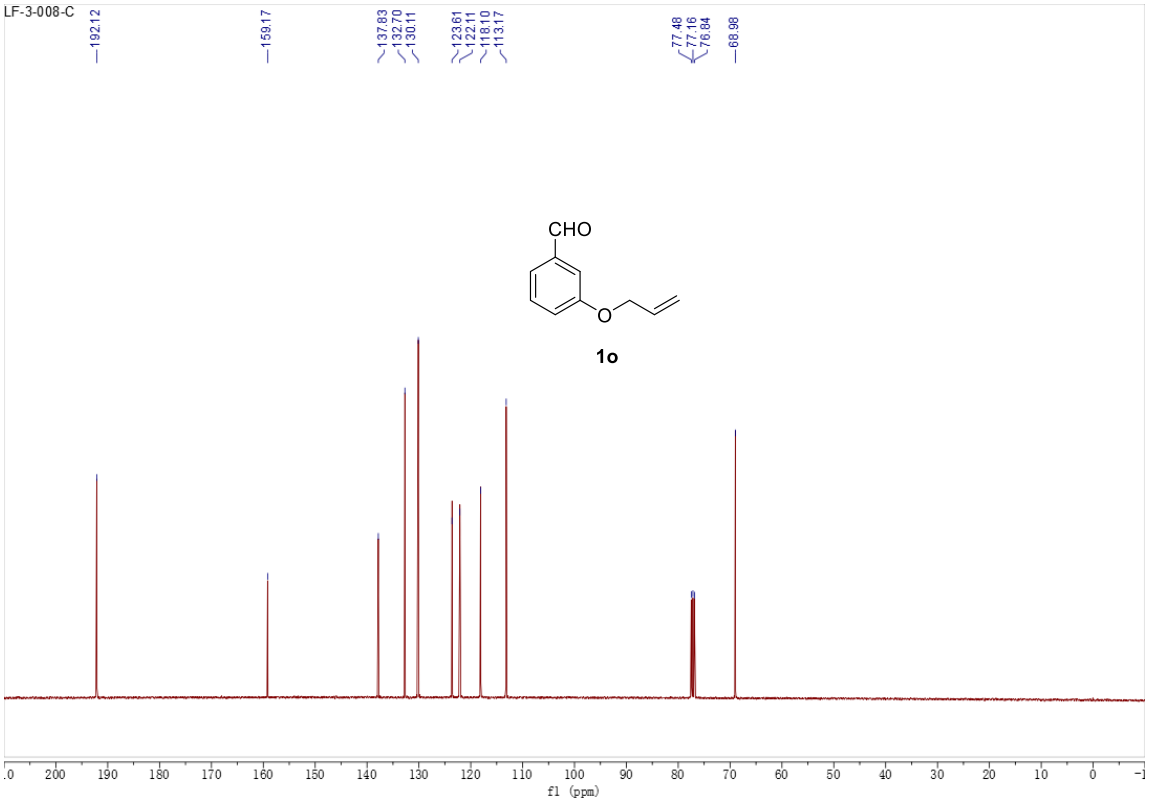
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1n**



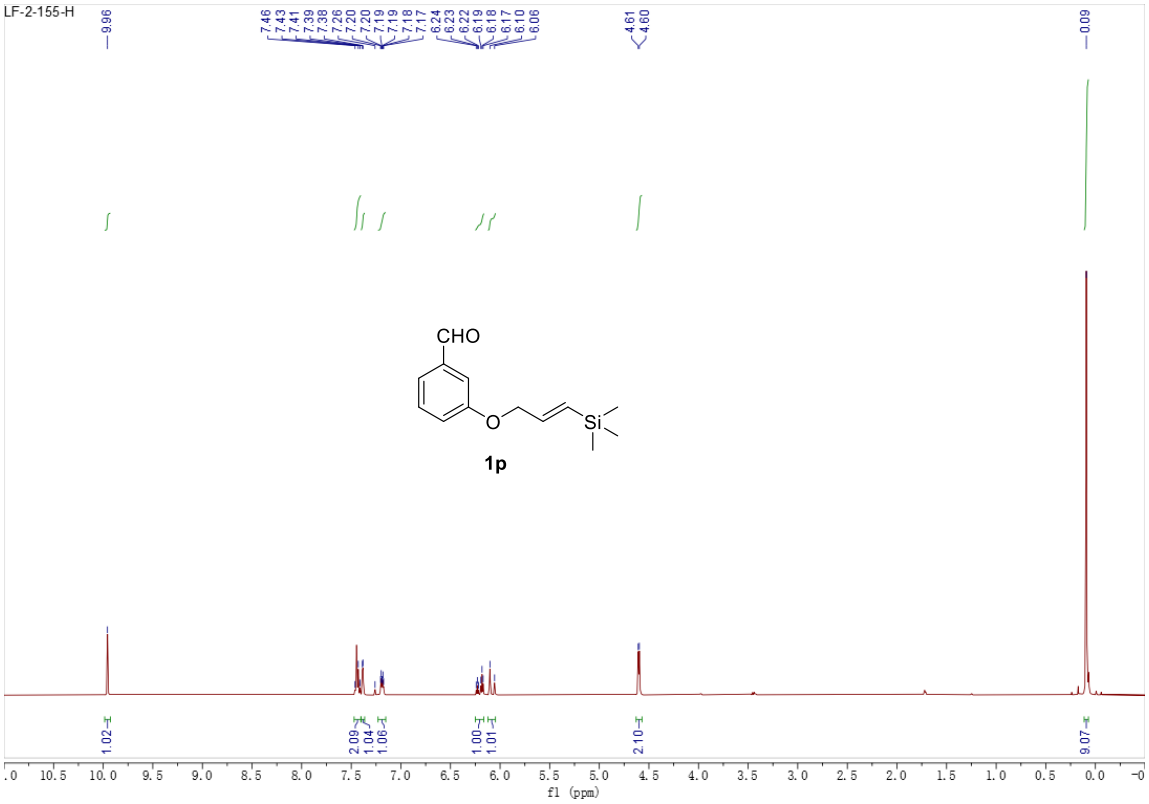
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1o**



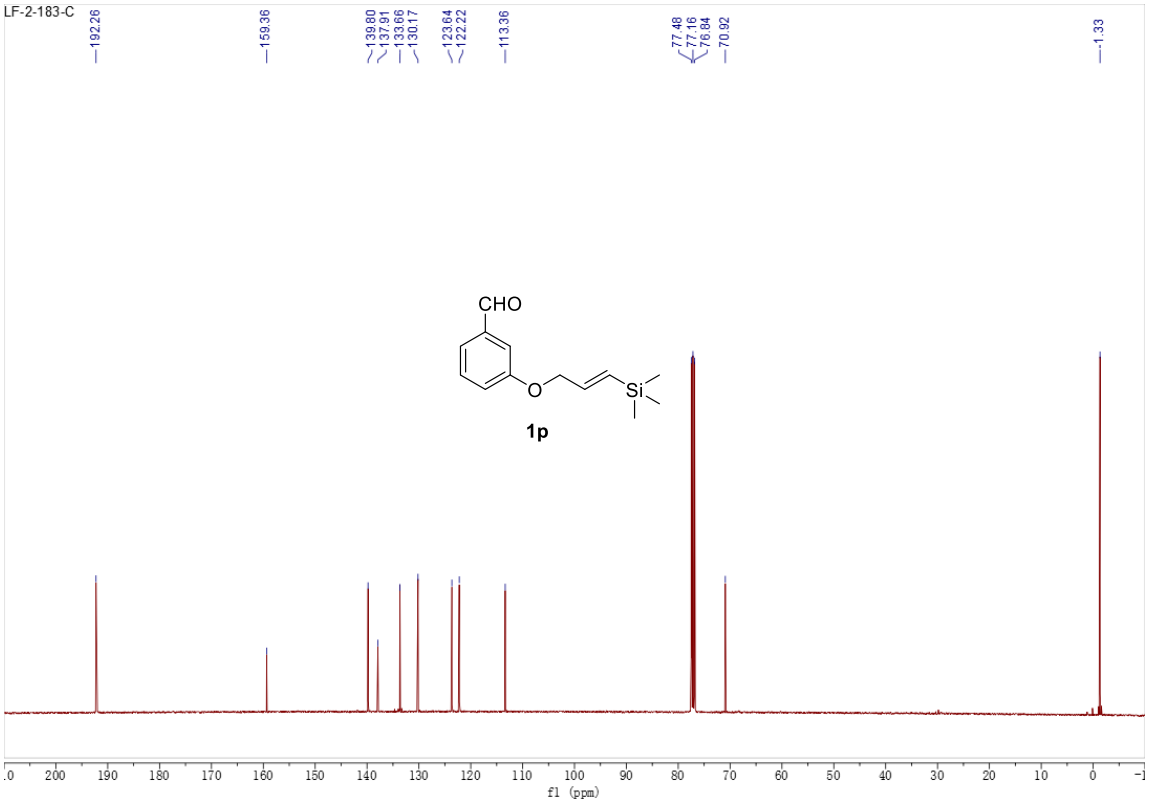
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1o**



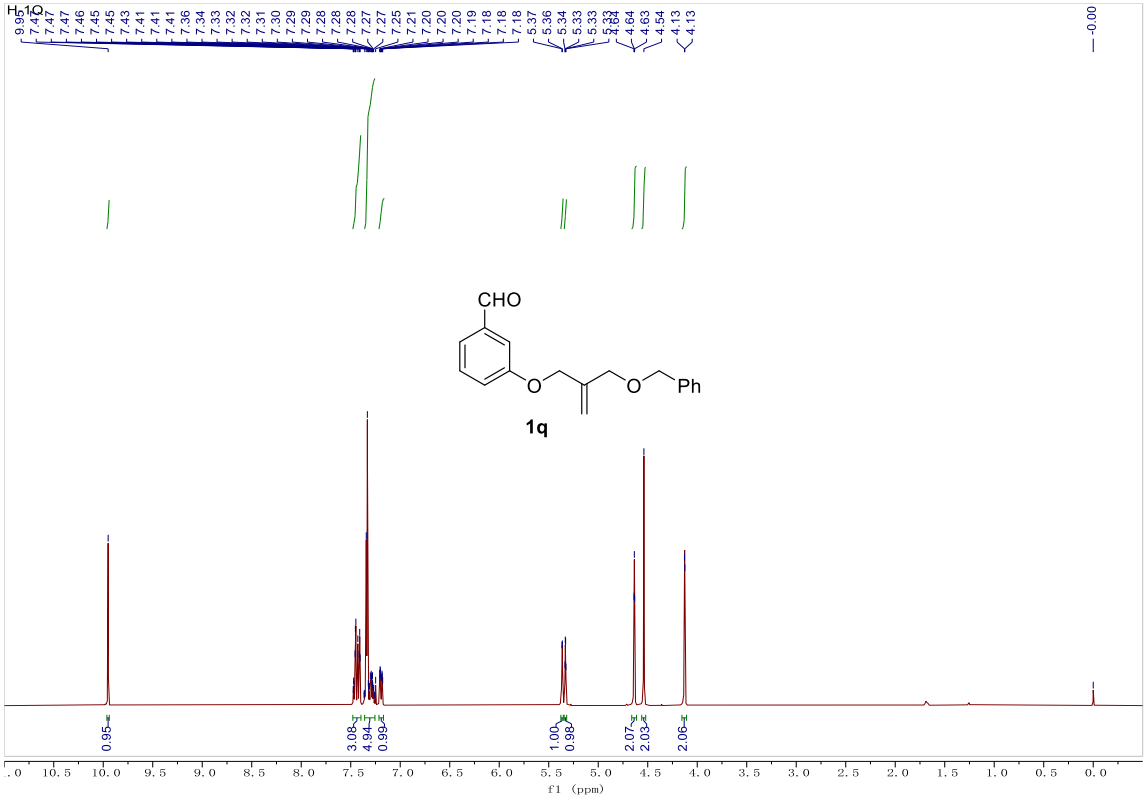
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1p**



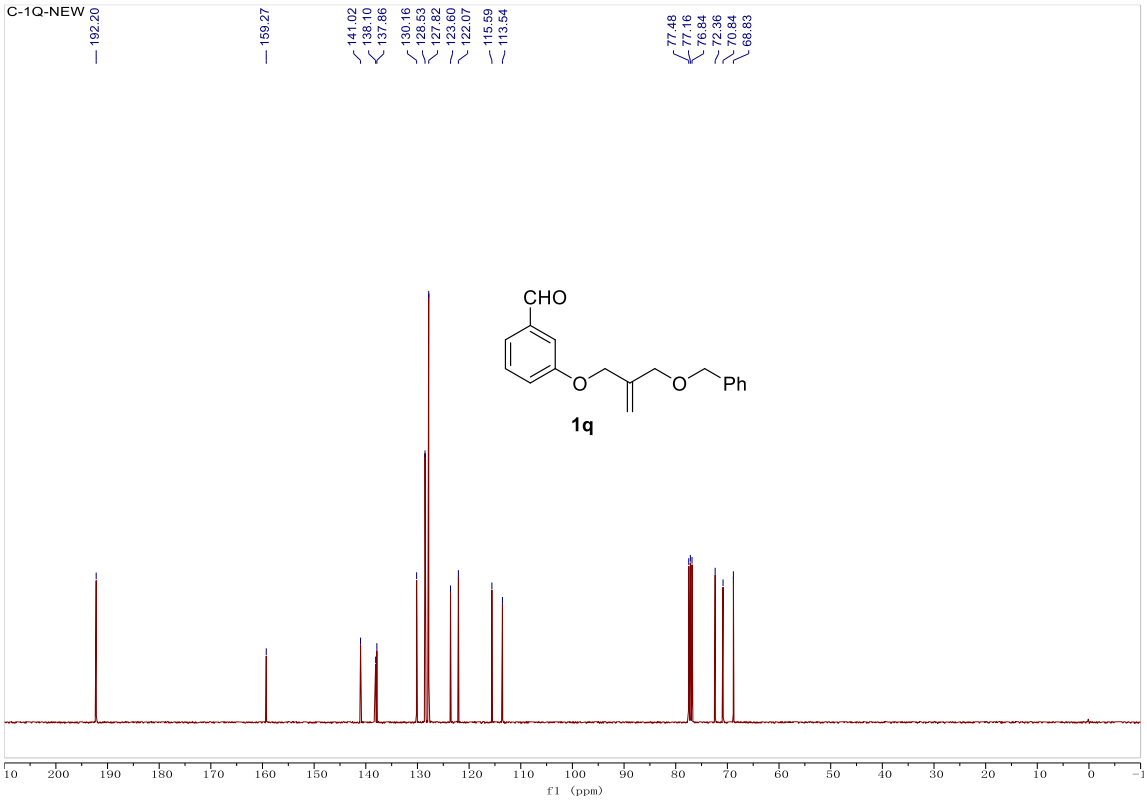
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1p**



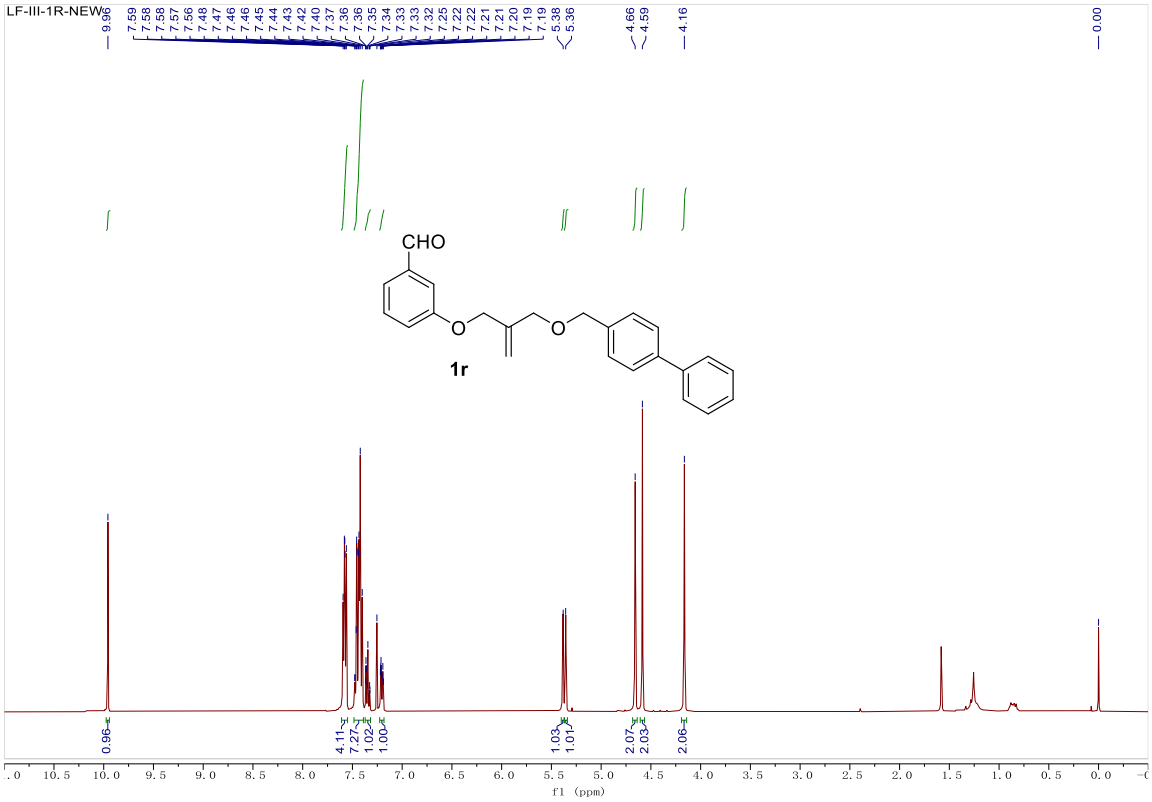
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1q**



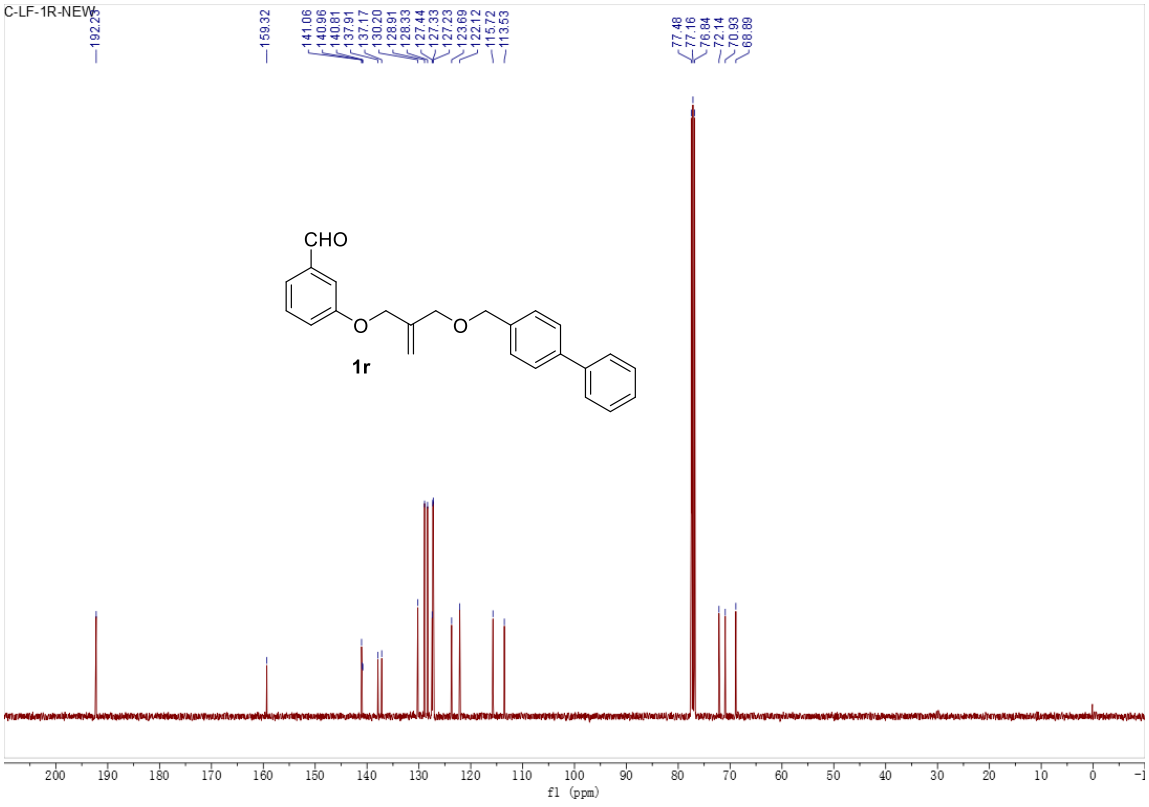
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1q**



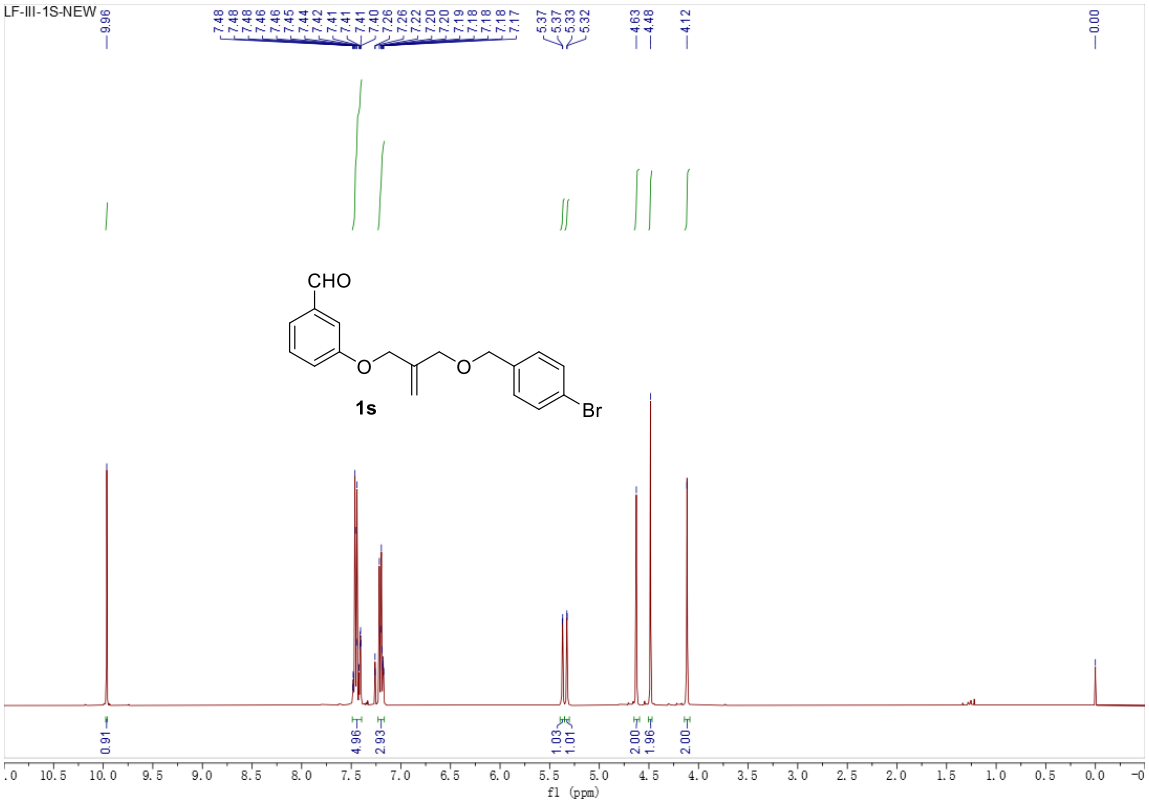
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1r**



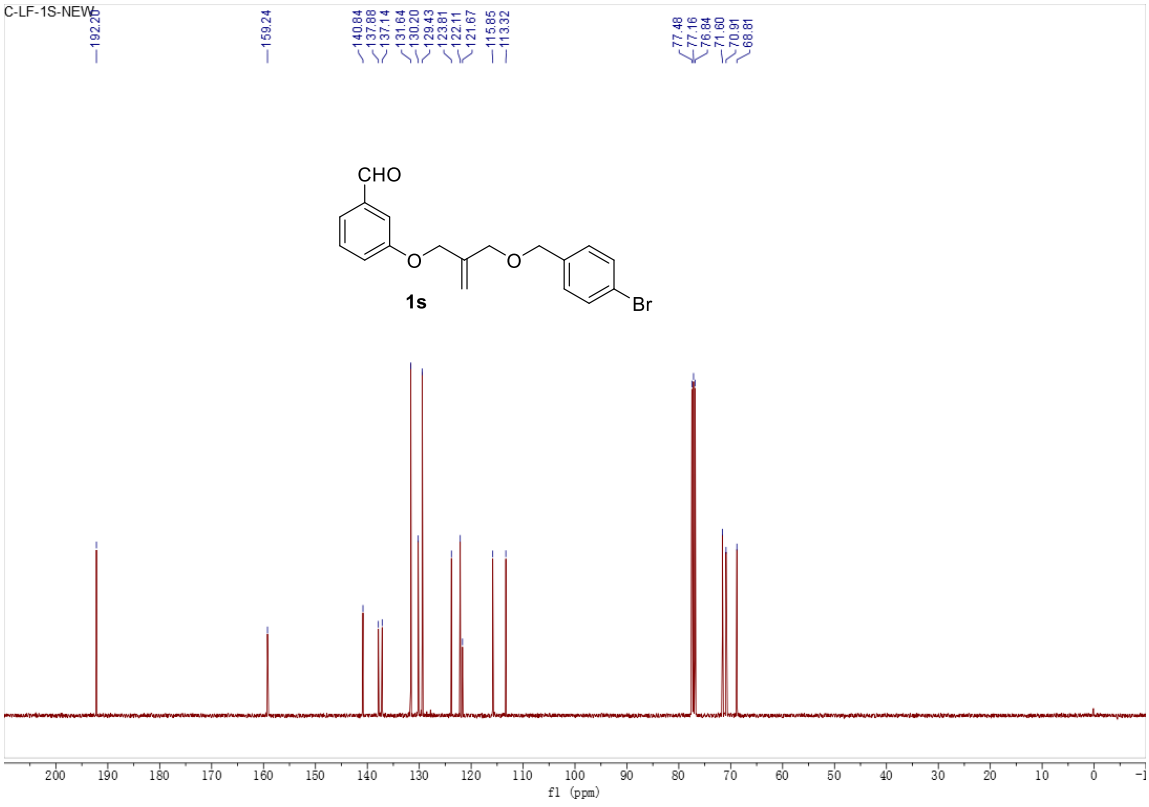
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1r**



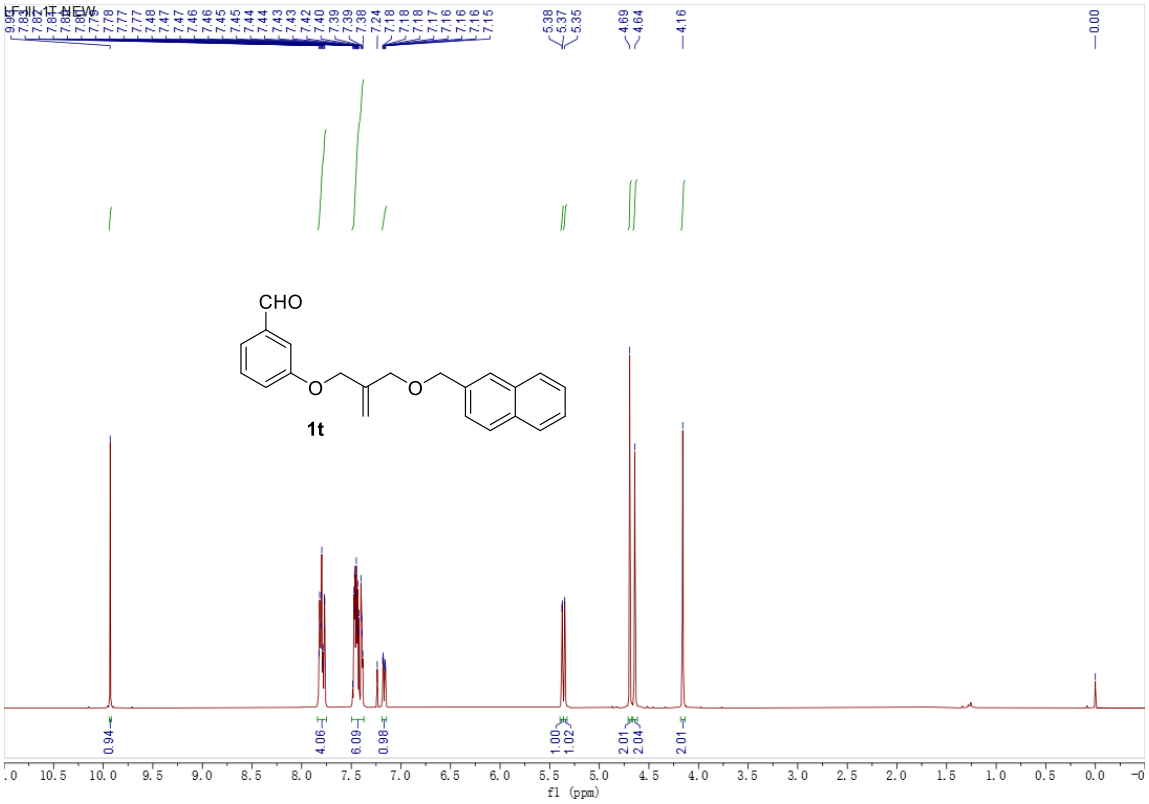
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1s**



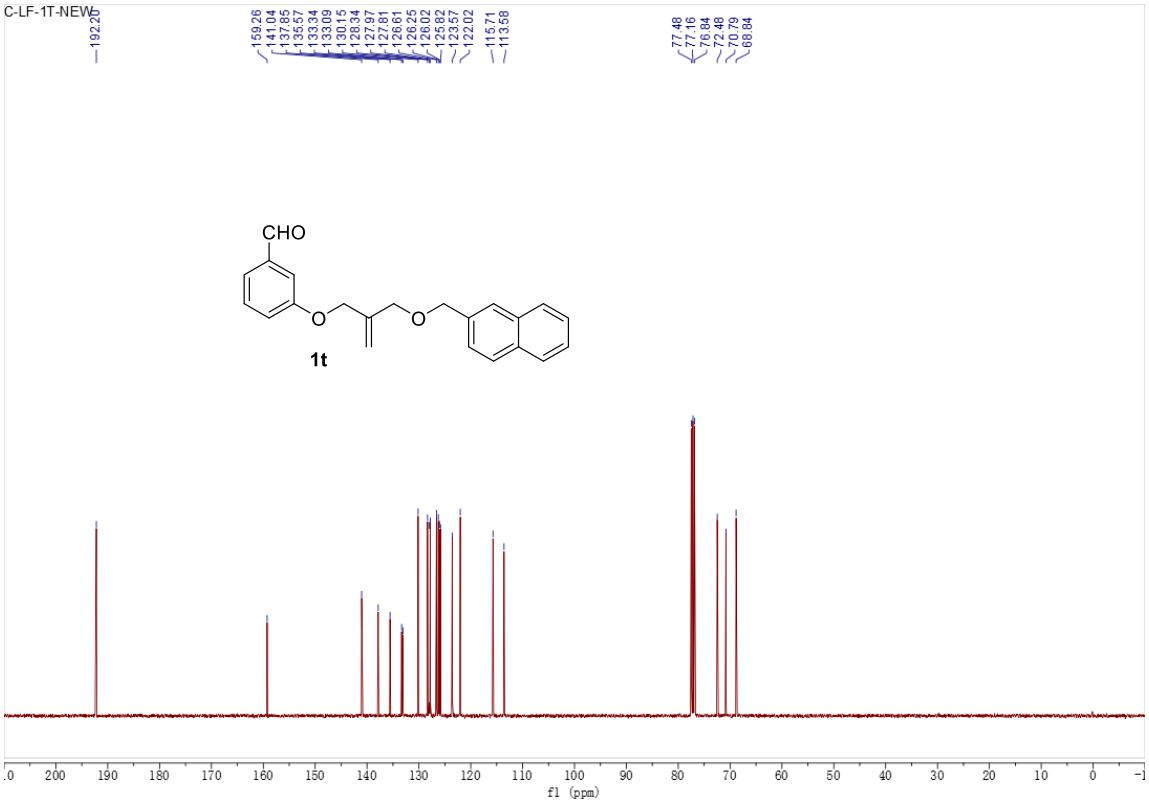
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1s**



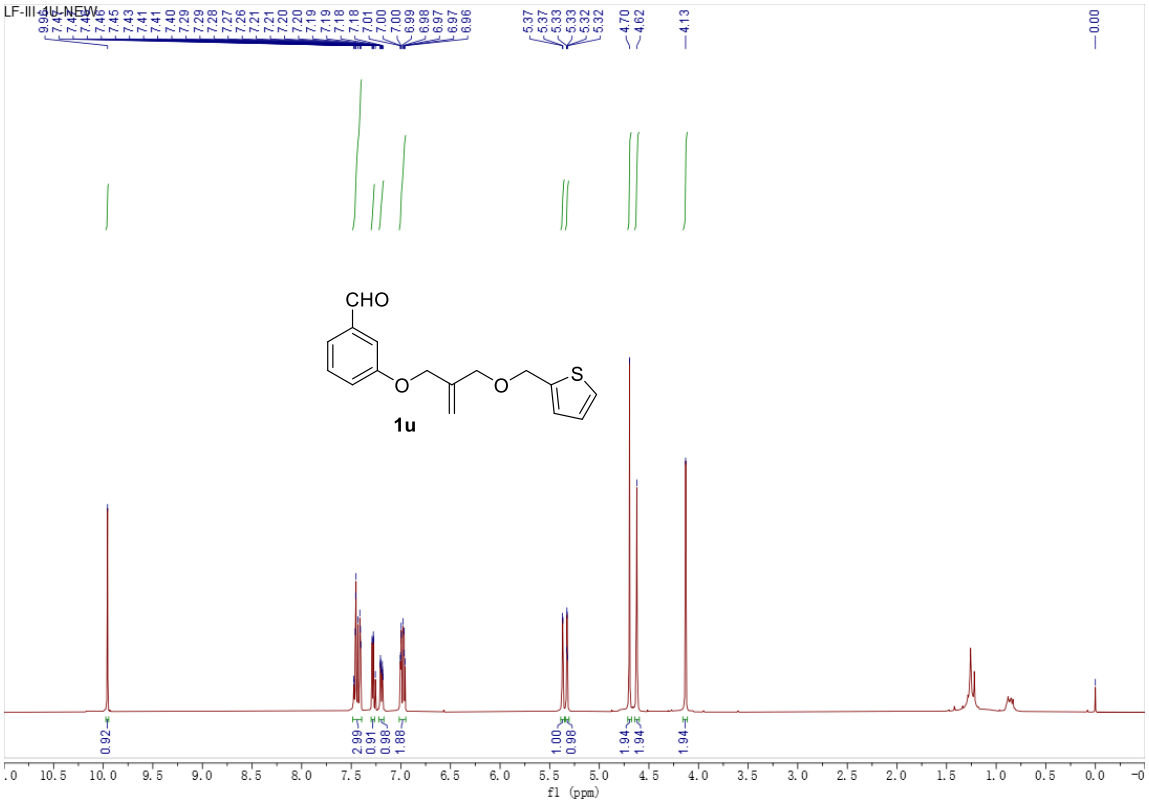
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1t**



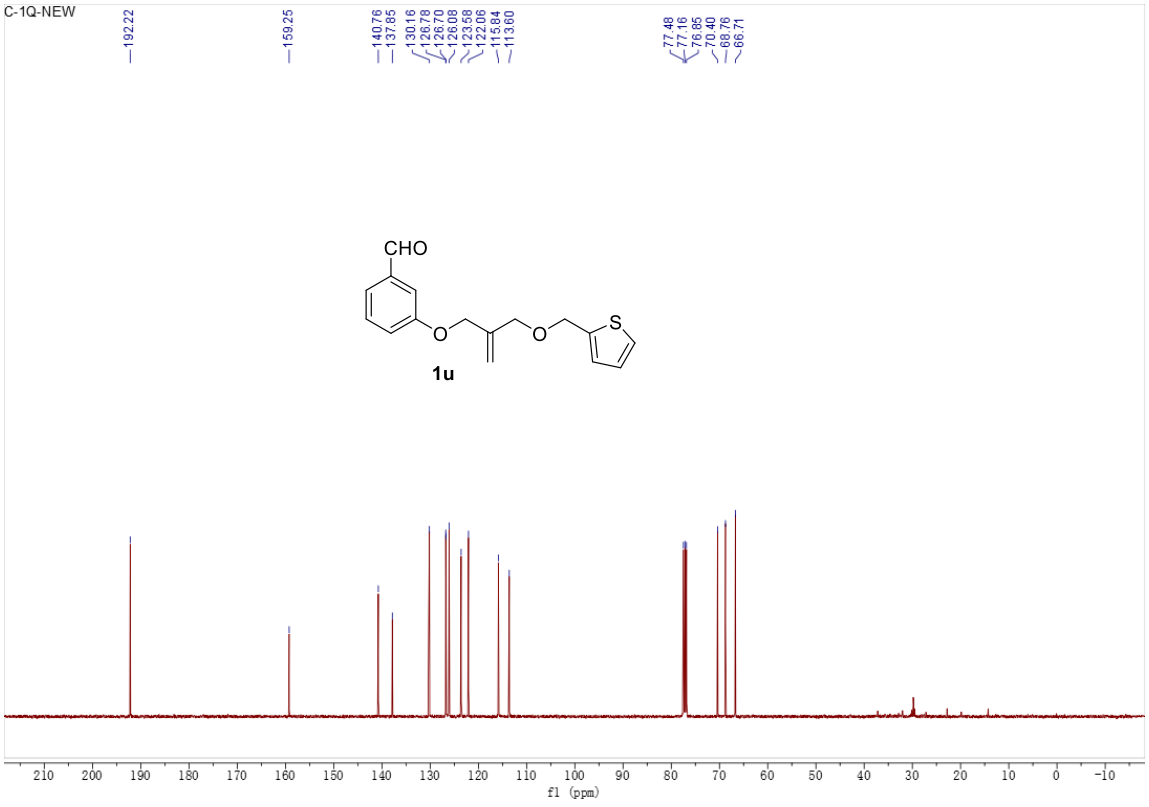
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1t**



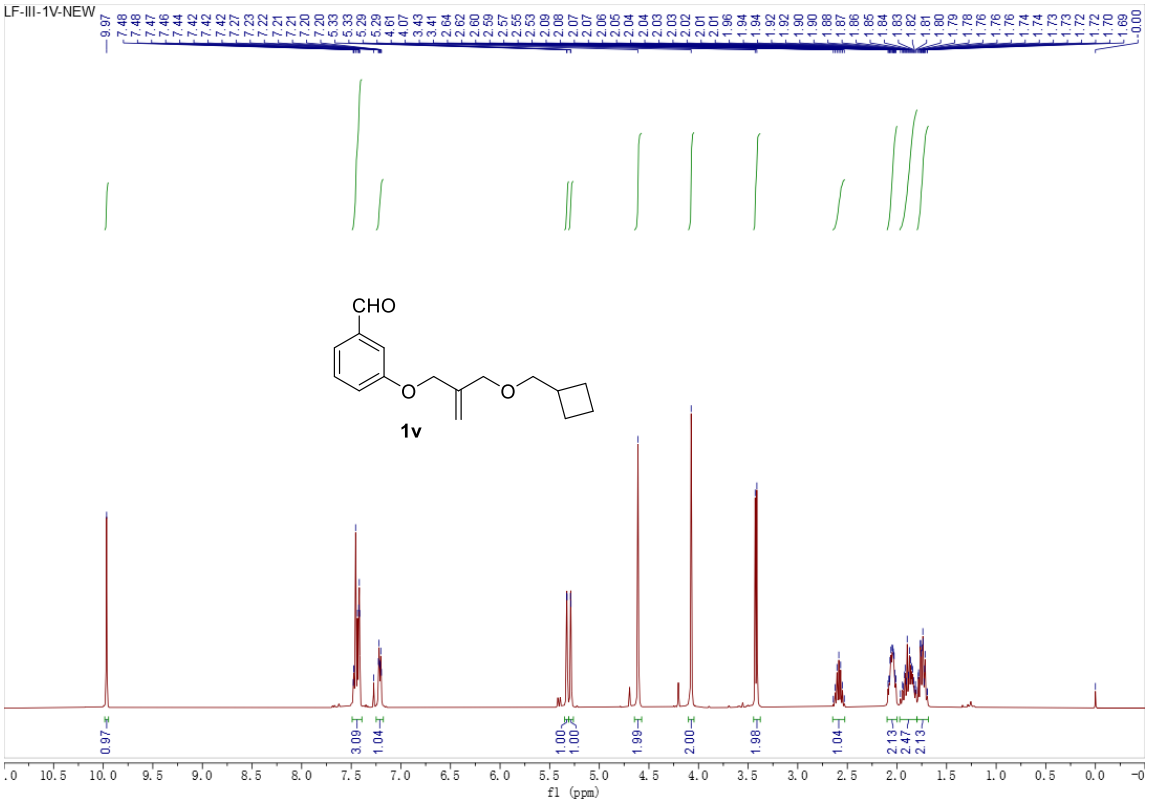
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1u**



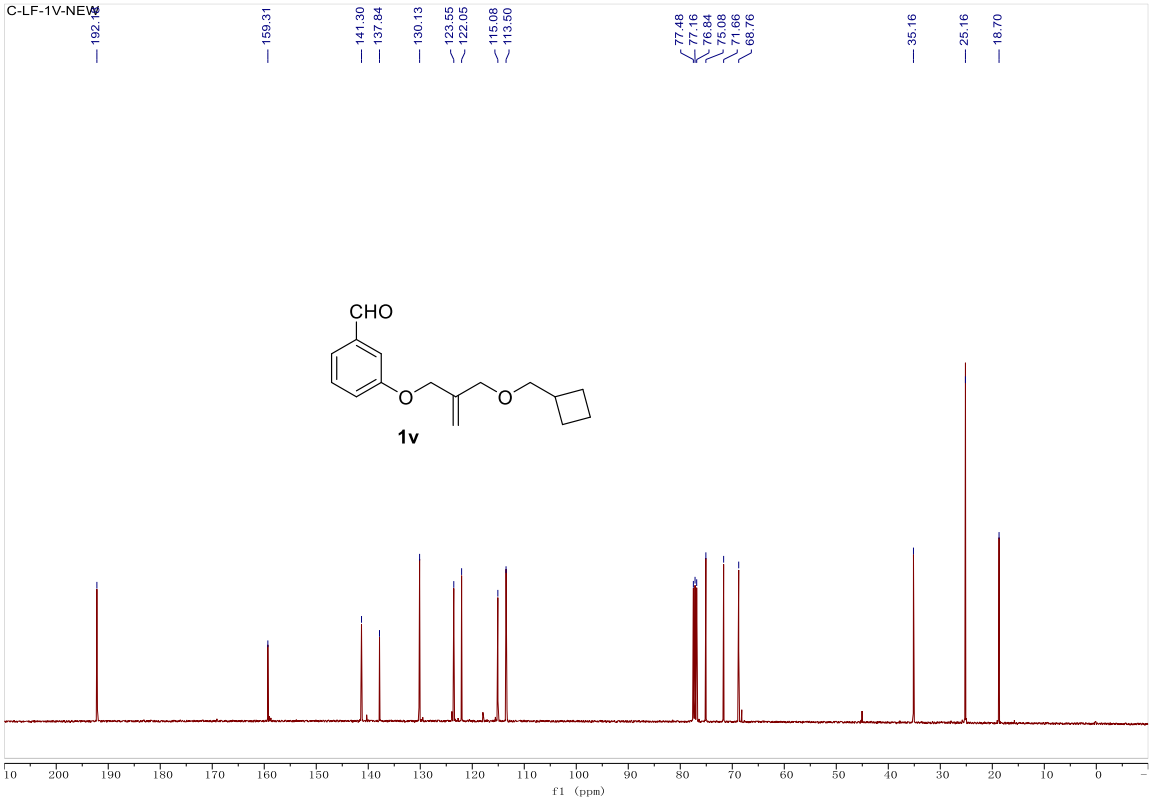
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1u**



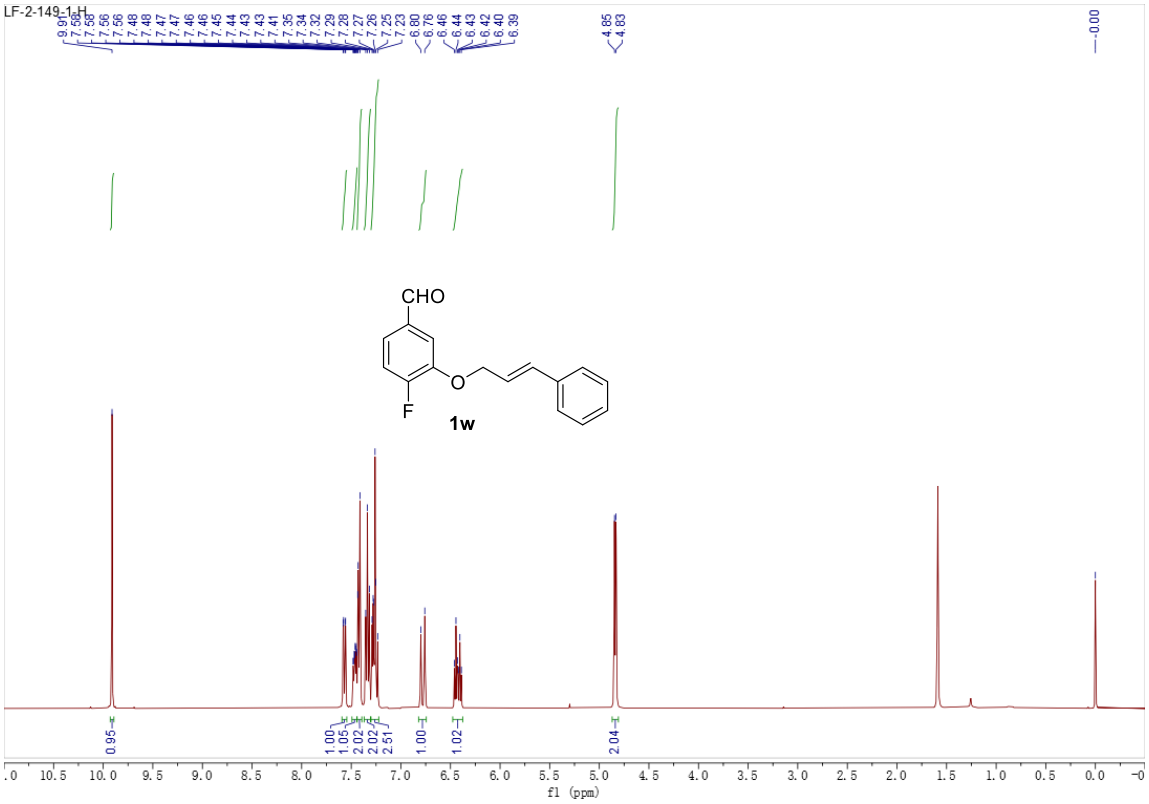
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1v**



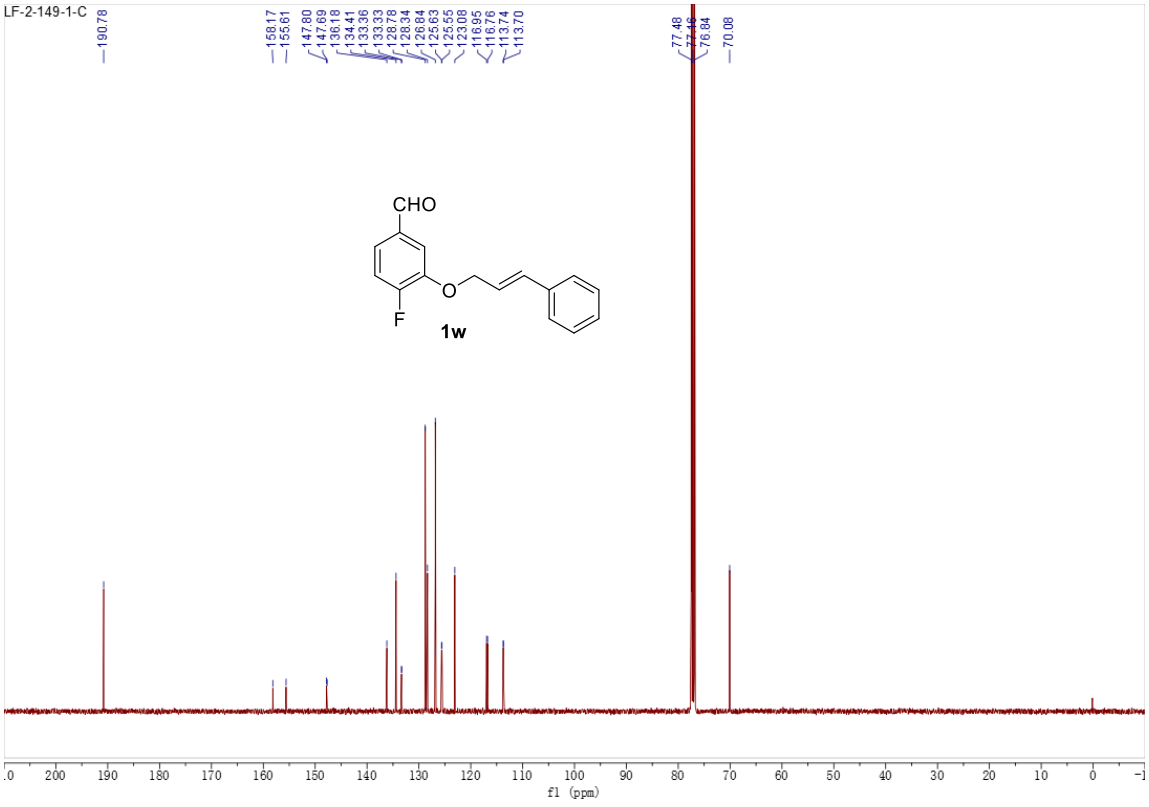
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1v**



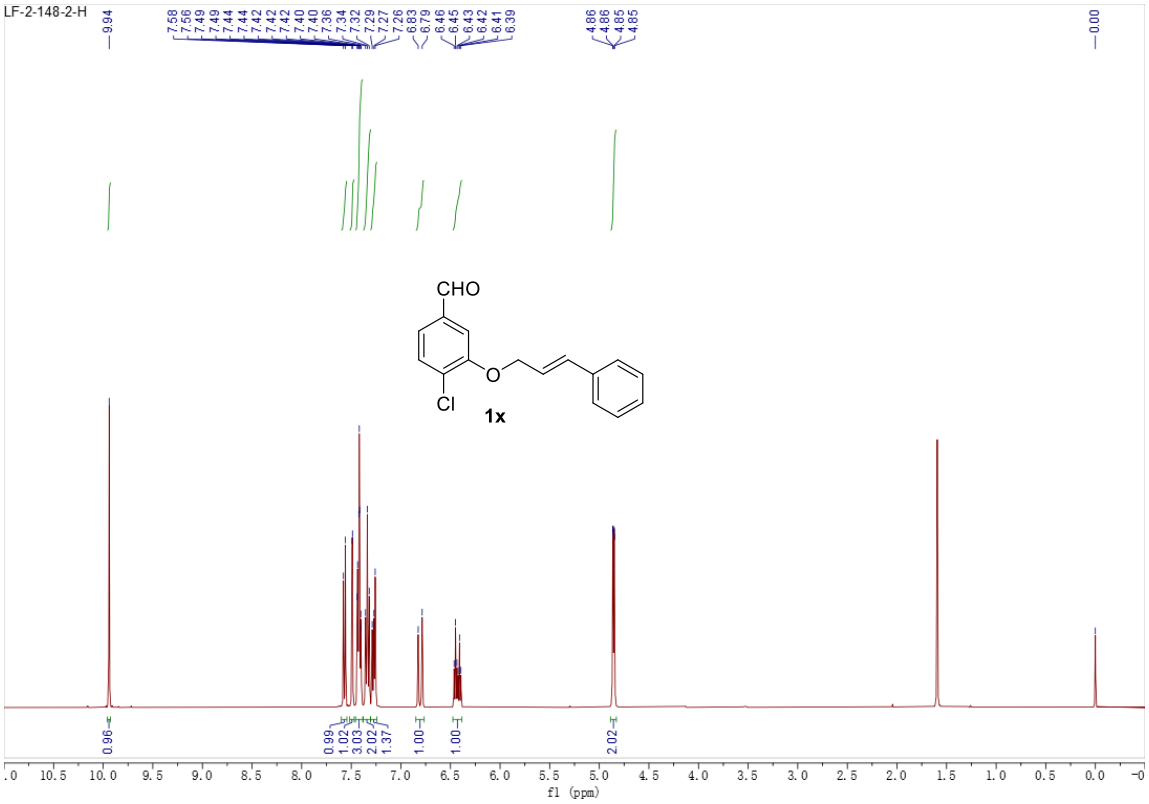
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1w**



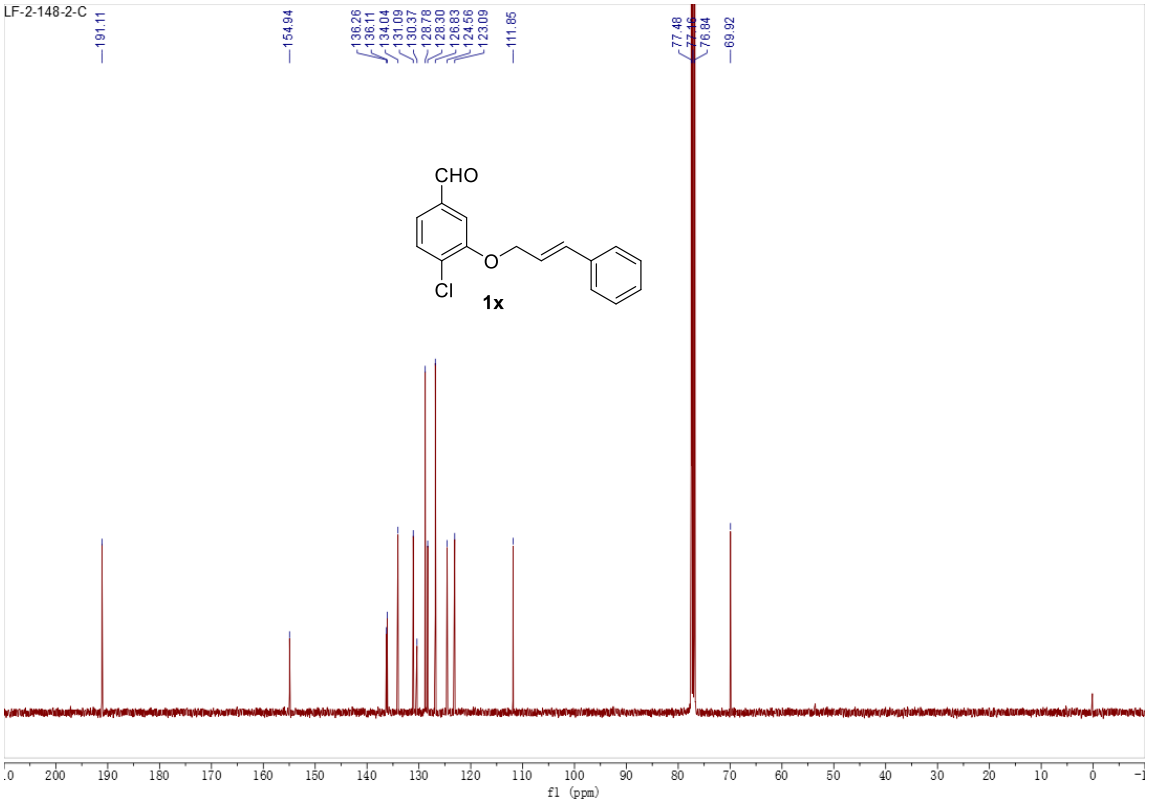
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1w**



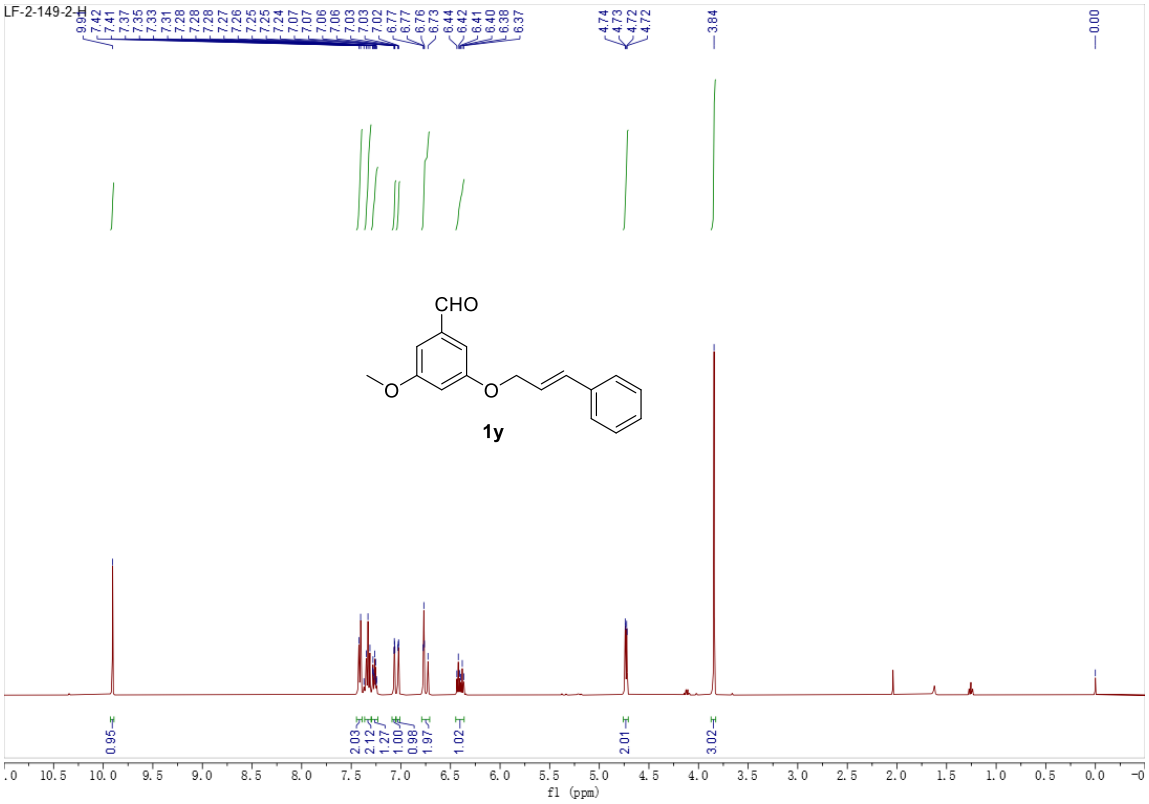
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1x**



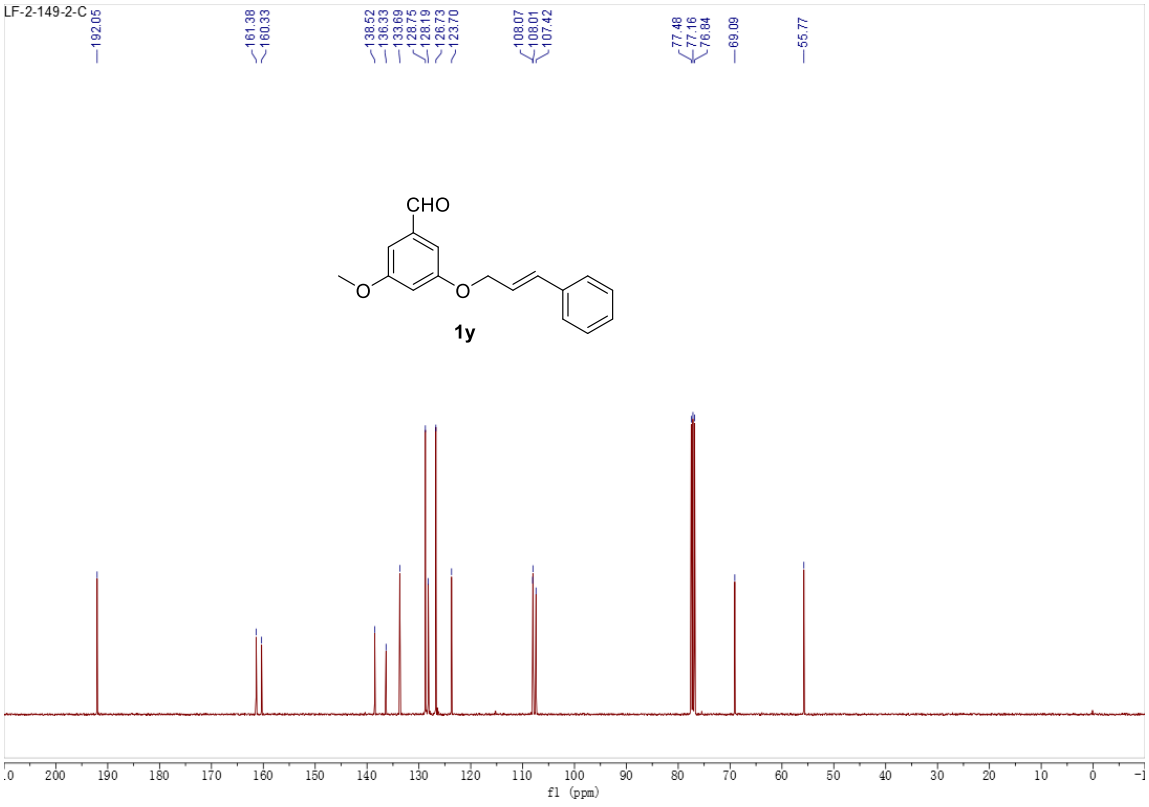
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1x**



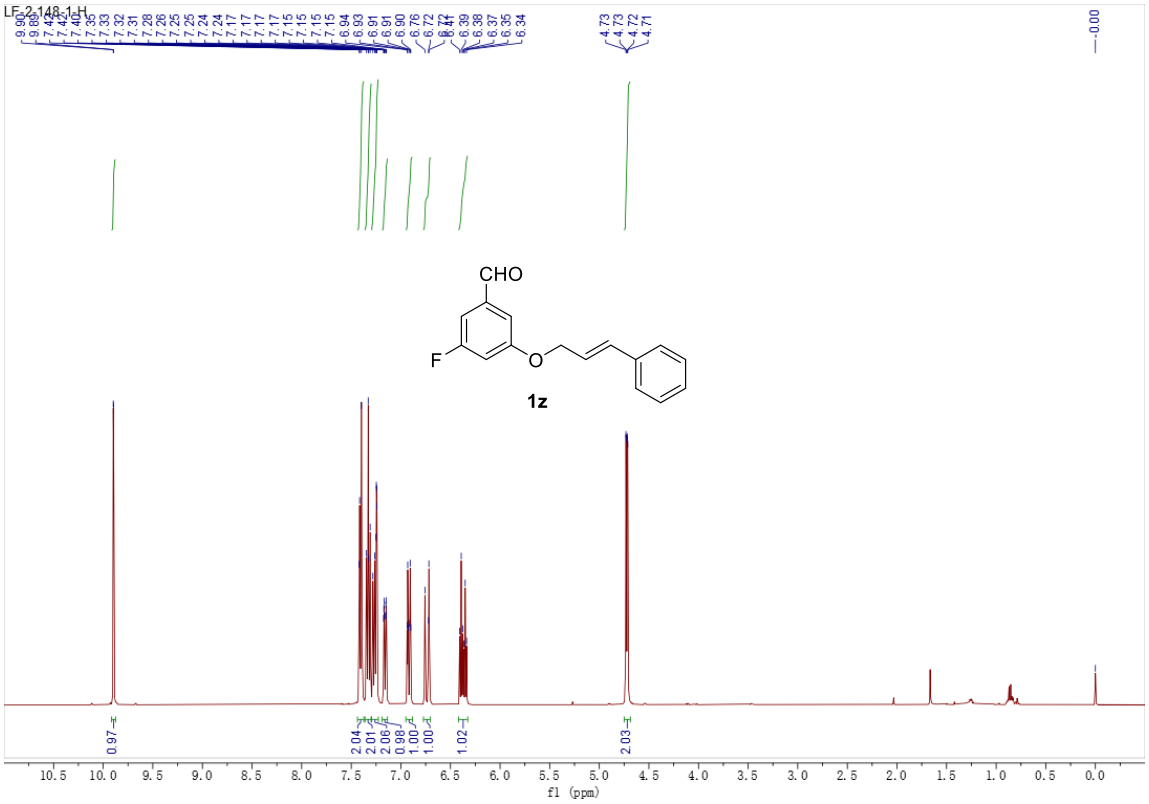
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1y**



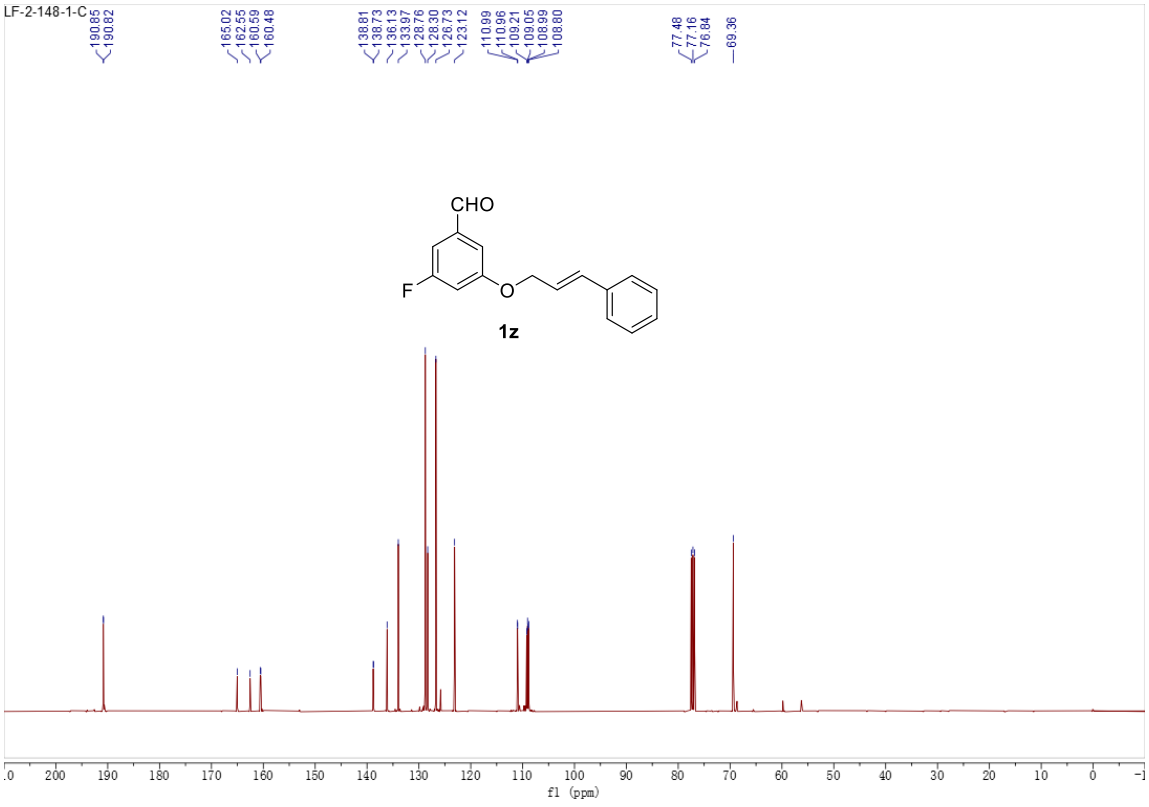
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1y**



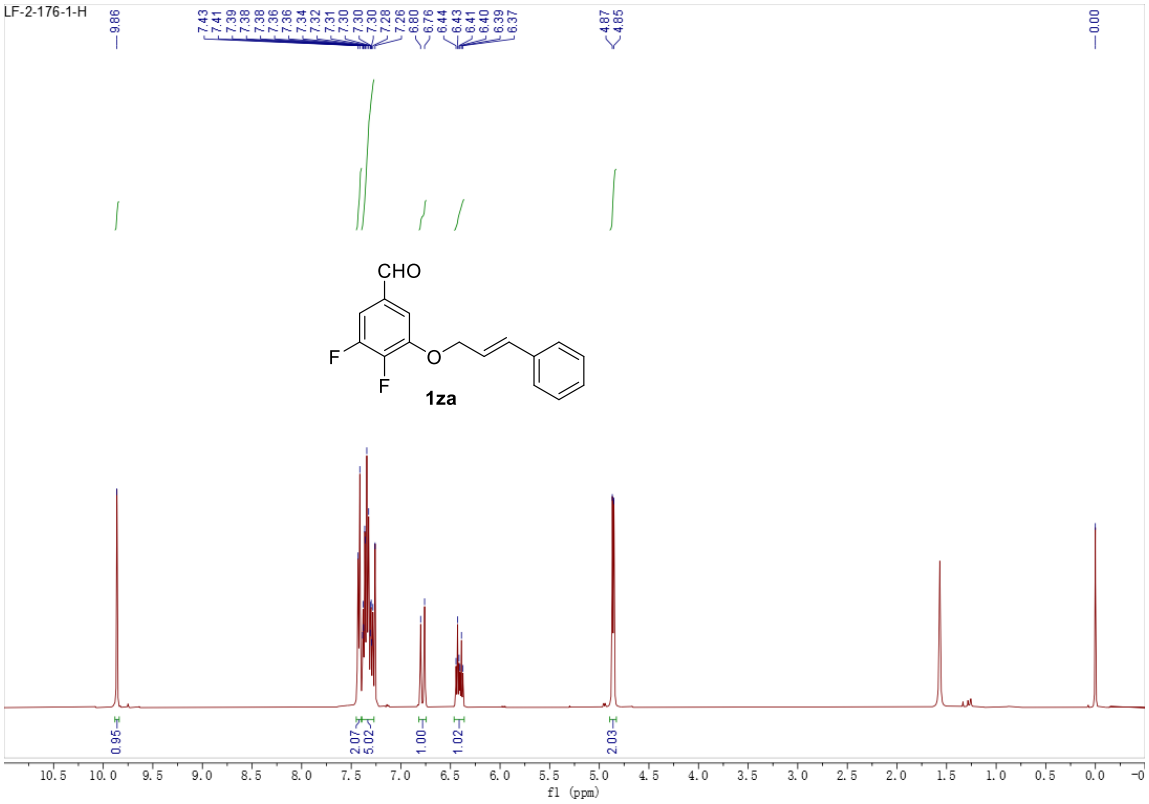
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1z**



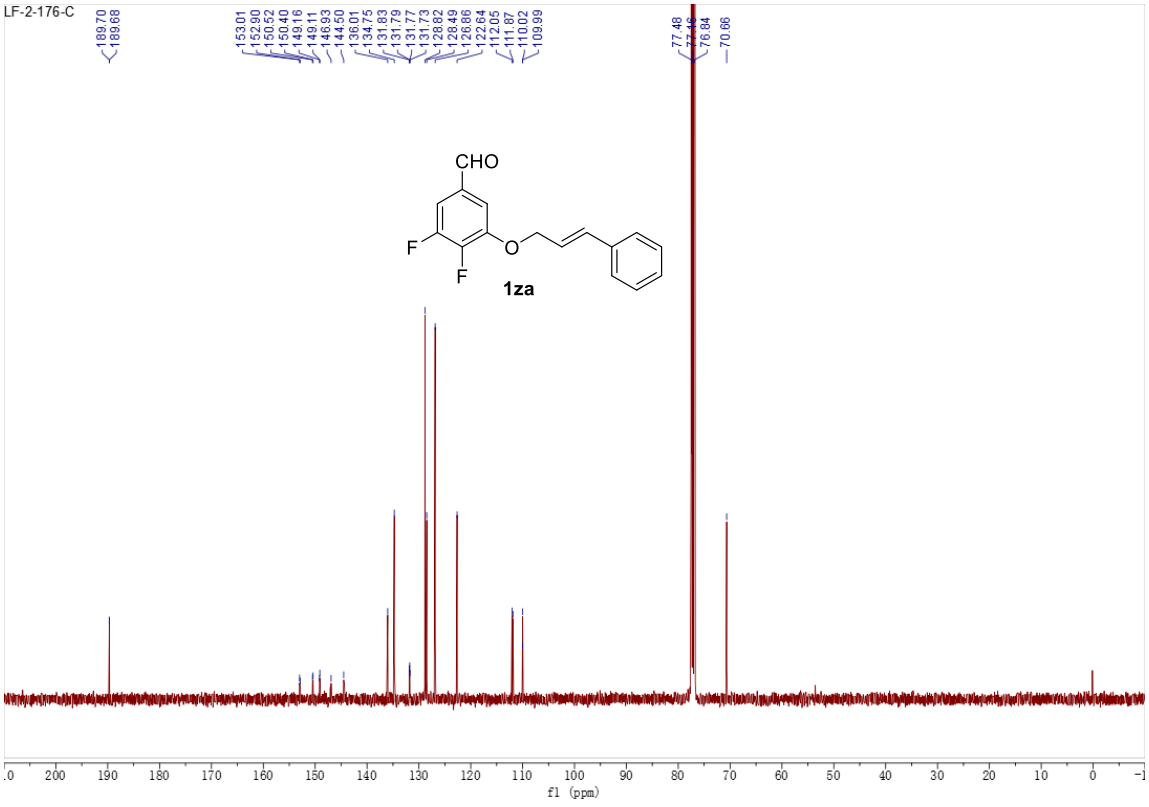
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1z**



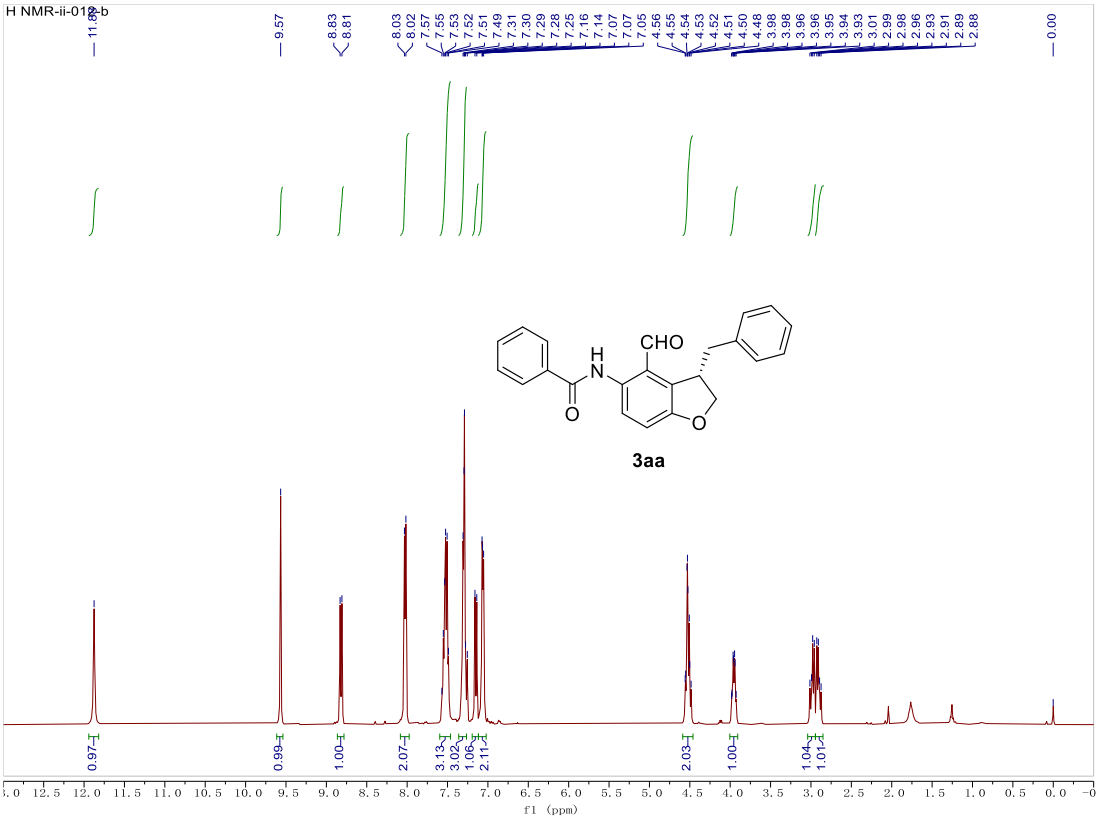
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1za**



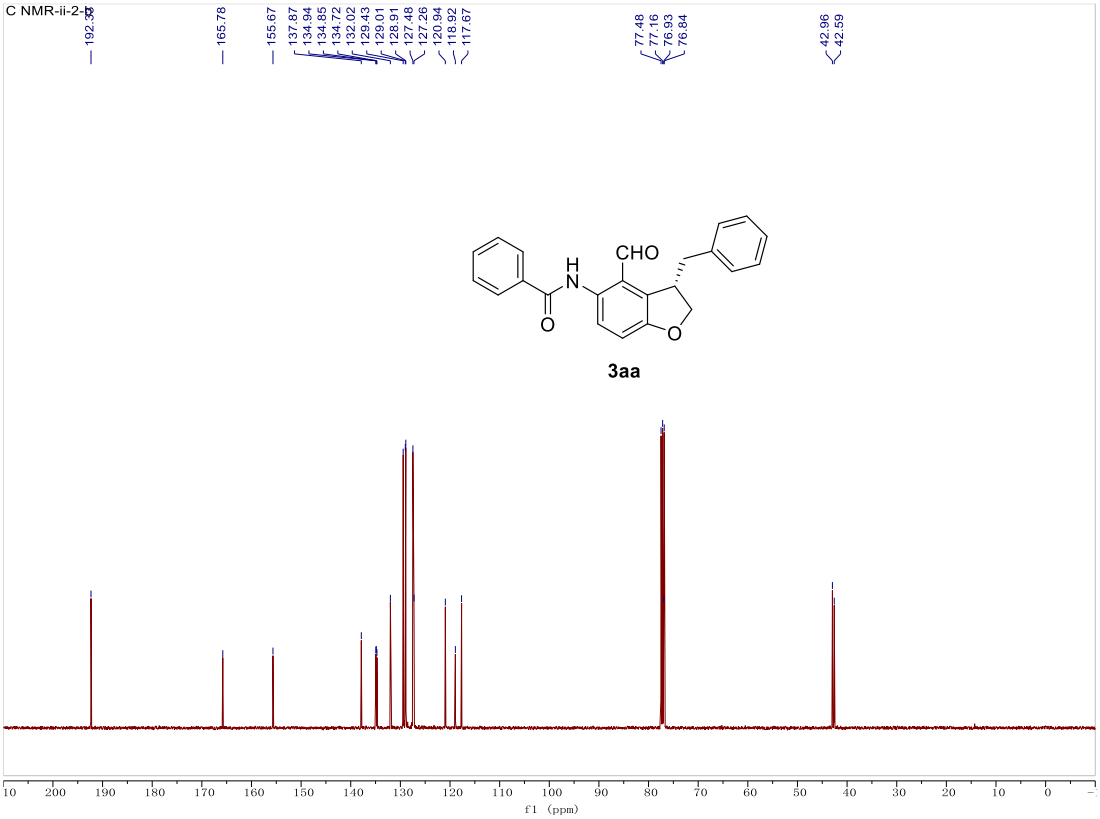
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1za**



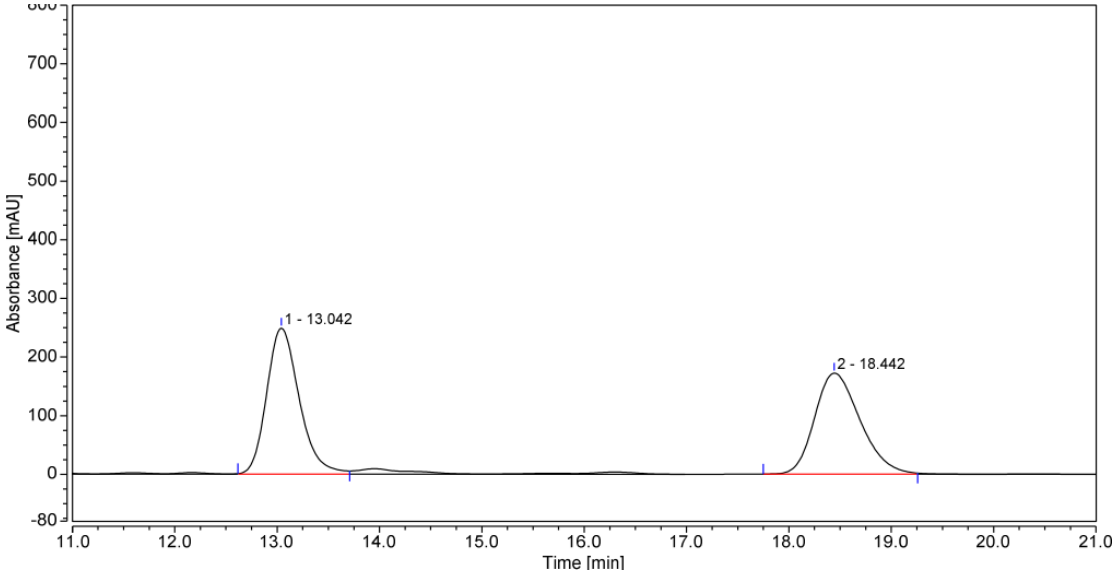
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3aa**



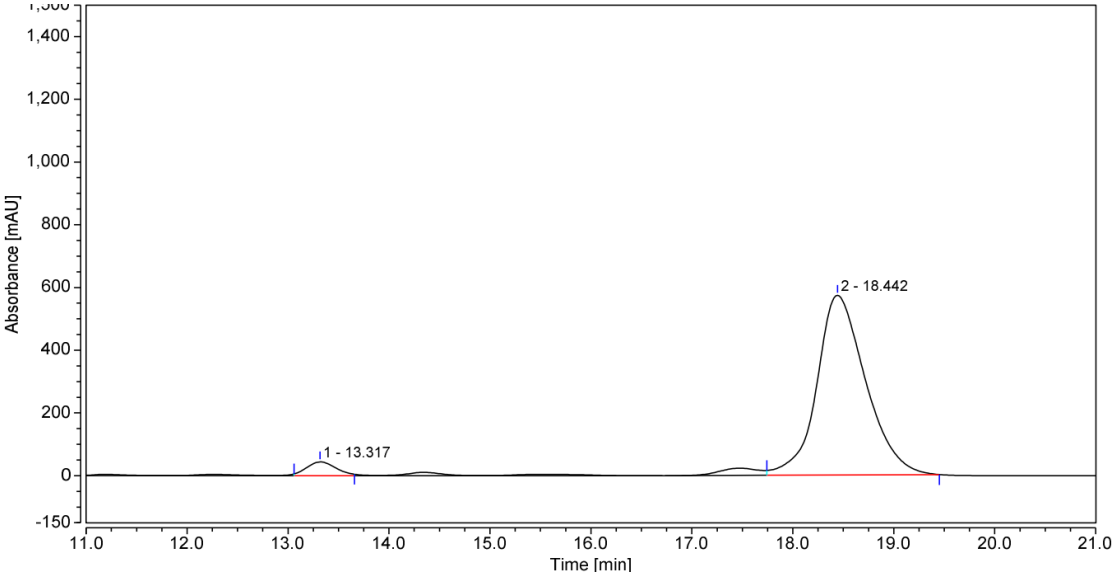
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3aa**



HPLC spectra and data of compound **3aa**

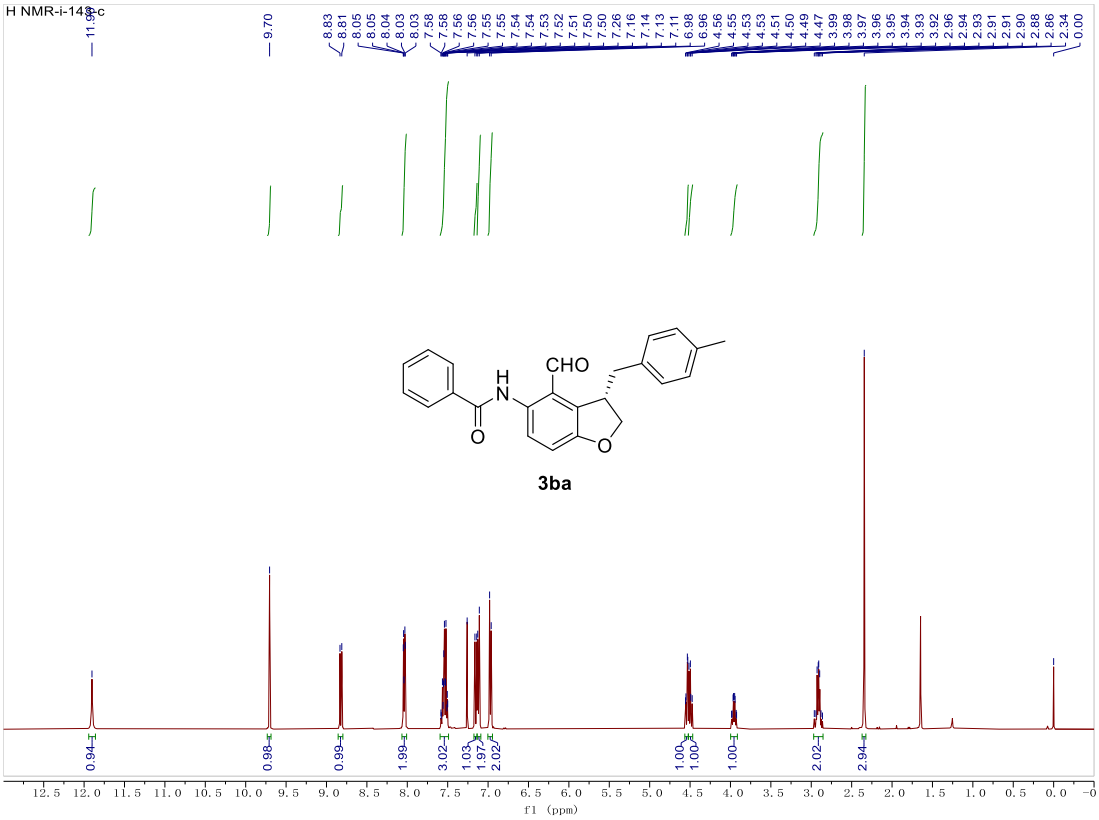


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.042	91.917	249.015	50.95	59.11	n.a.
2		18.442	88.487	172.269	49.05	40.89	n.a.
Total:			**180.404**	**421.285**	**100.00**	**100.00**	

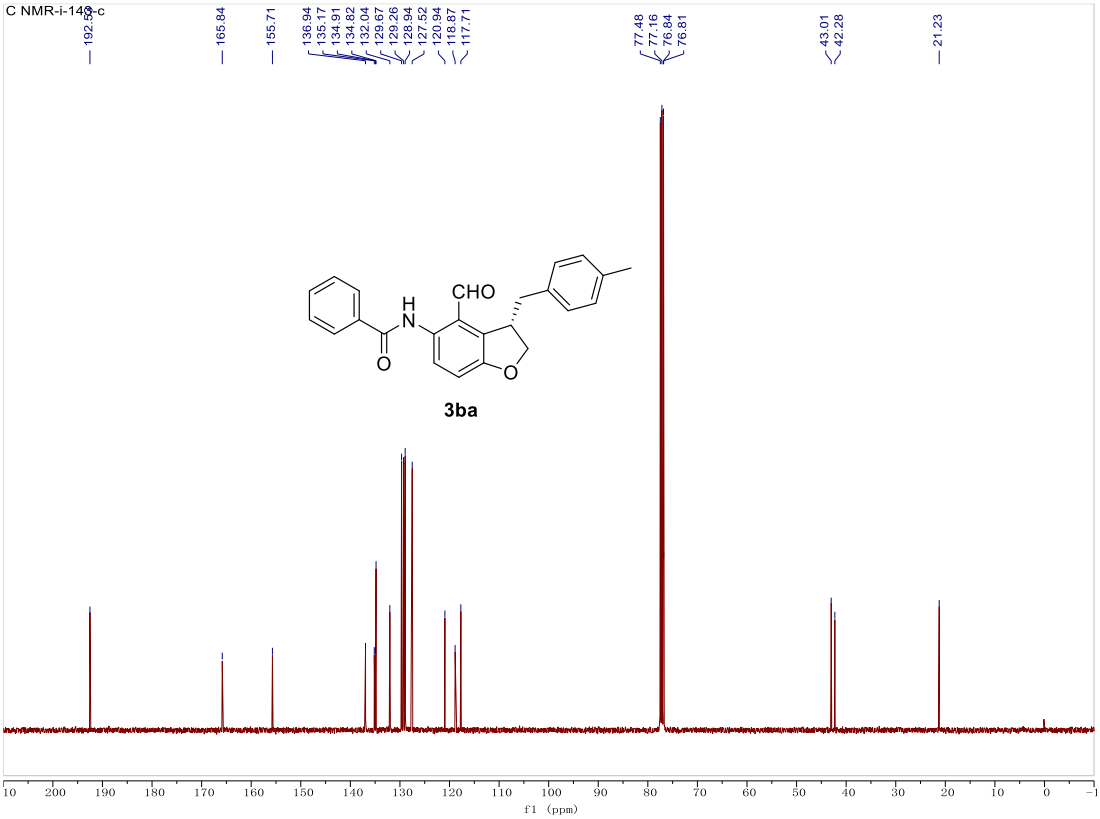


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.317	14.646	43.730	4.37	7.10	n.a.
2		18.442	320.692	572.615	95.63	92.90	n.a.
Total:			**335.337**	**616.346**	**100.00**	**100.00**	

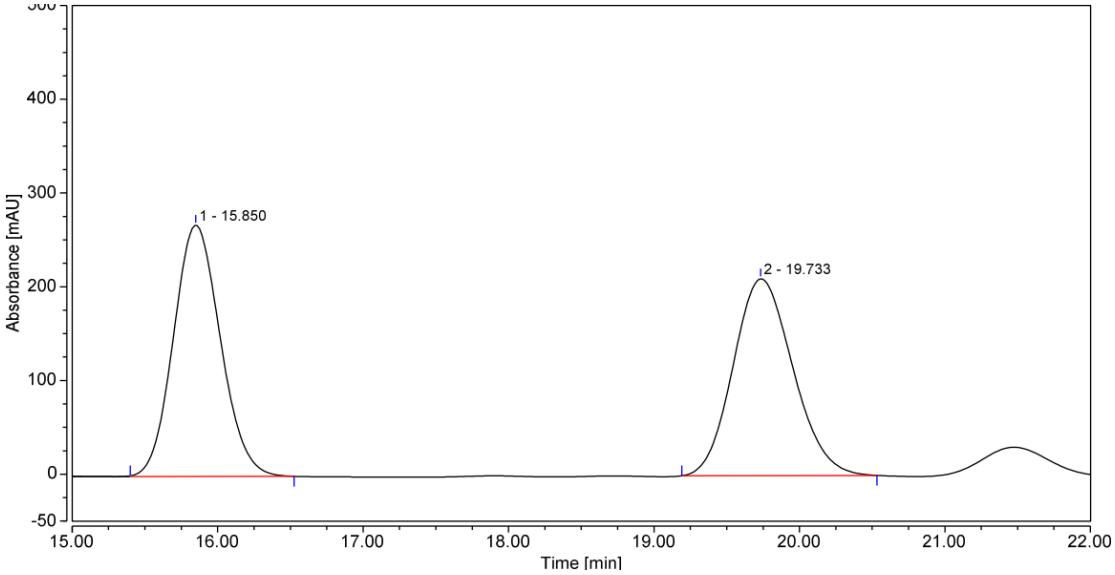
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ba**



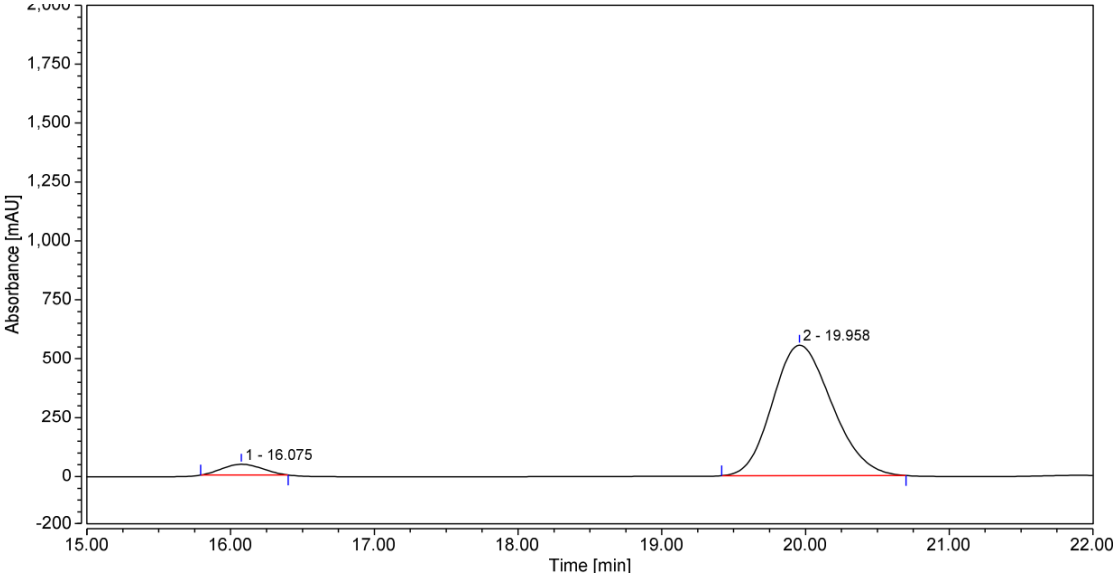
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ba**



HPLC spectra and data of compound **3ba**

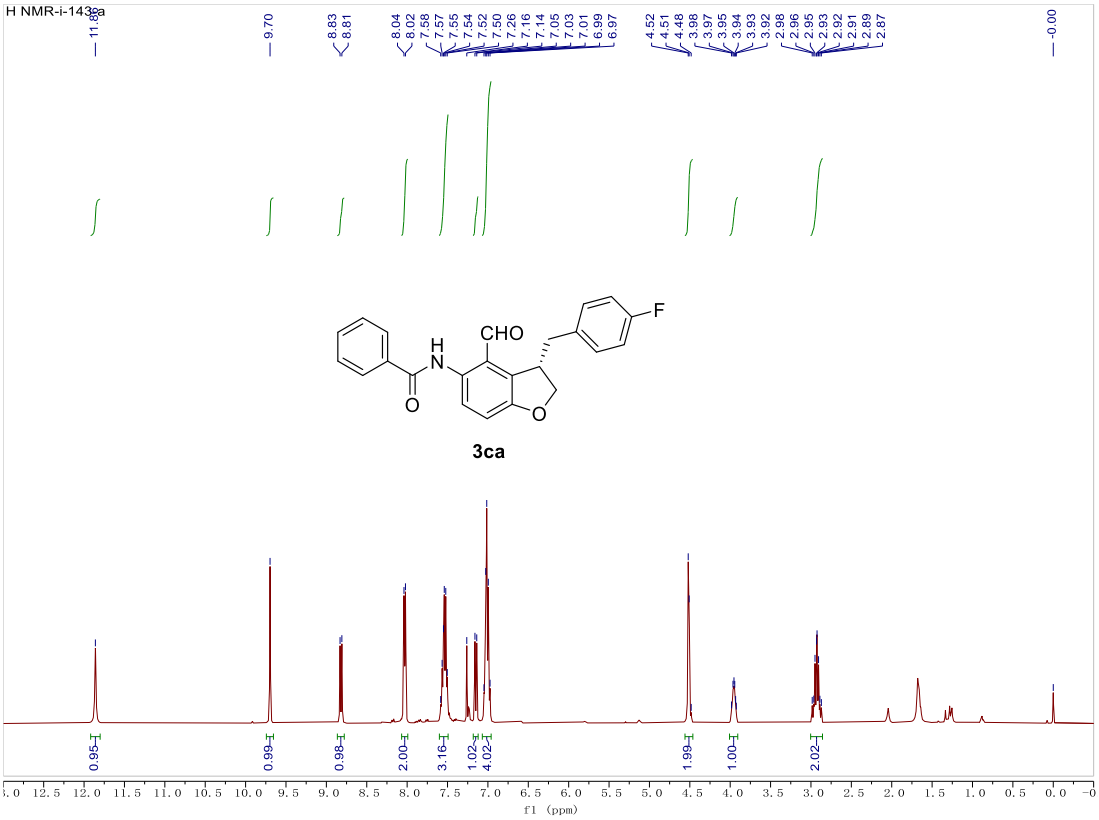


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.850	100.250	268.104	50.09	56.10	n.a.
2		19.733	99.887	209.824	49.91	43.90	n.a.
Total:			**200.137**	**477.927**	**100.00**	**100.00**	

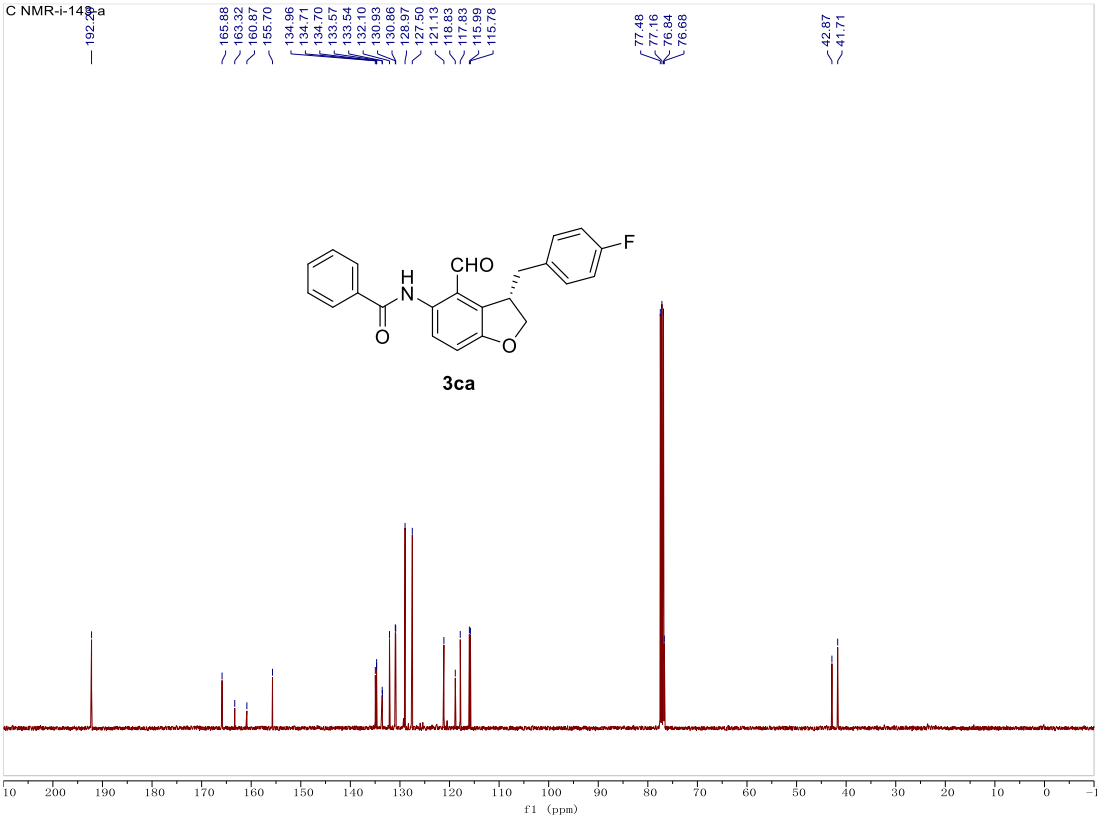


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.075	14.722	45.821	5.25	7.64	n.a.
2		19.958	265.460	553.658	94.75	92.36	n.a.
Total:			**280.182**	**599.479**	**100.00**	**100.00**	

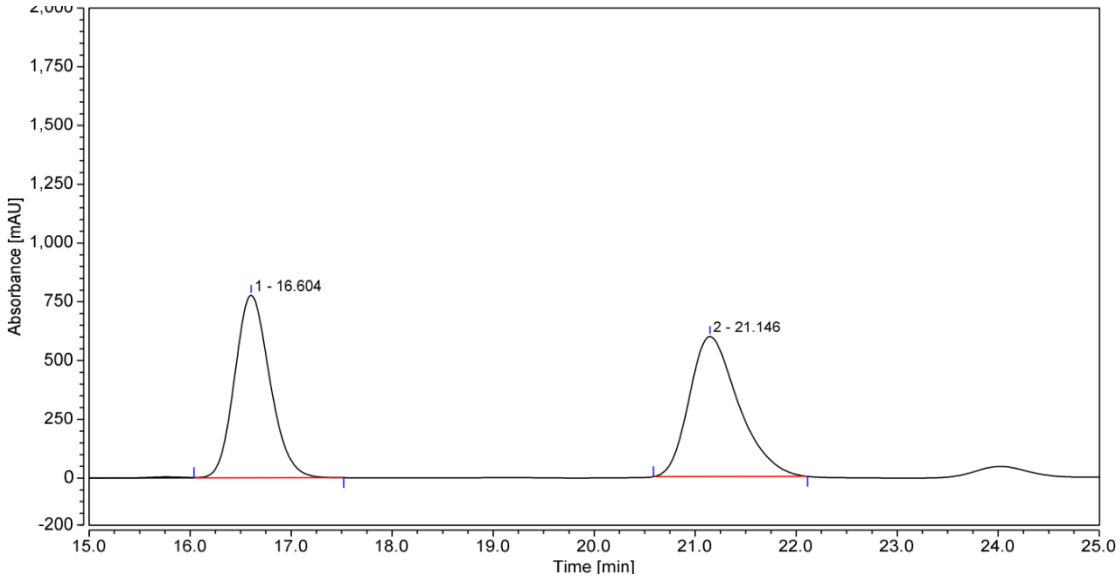
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ca**



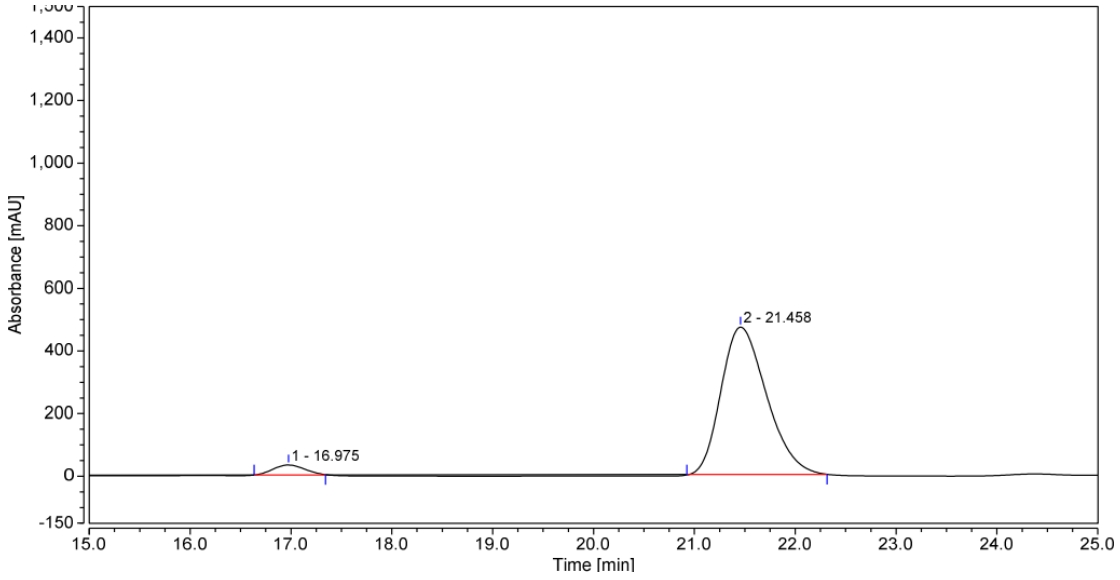
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ca**



HPLC spectra and data of compound **3ca**

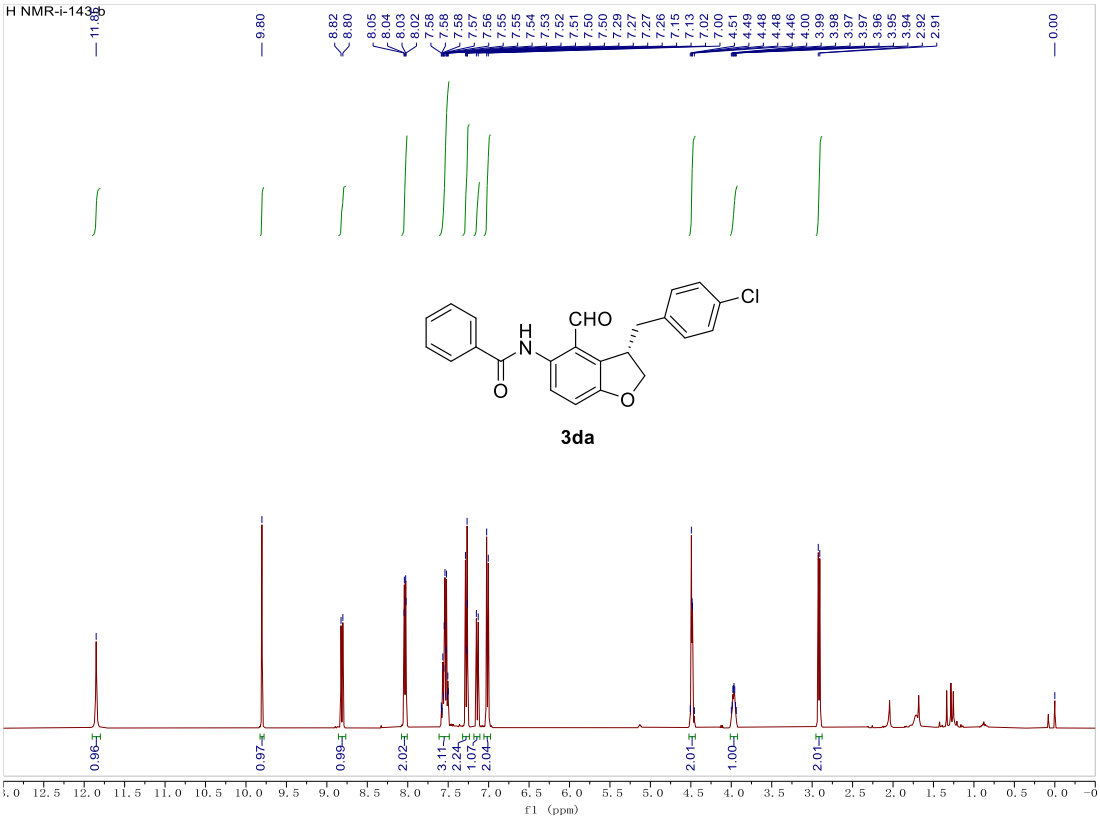


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.604	313.746	776.700	48.28	56.58	n.a.
2		21.146	336.137	596.048	51.72	43.42	n.a.
Total:			**649.883**	**1372.748**	**100.00**	**100.00**	

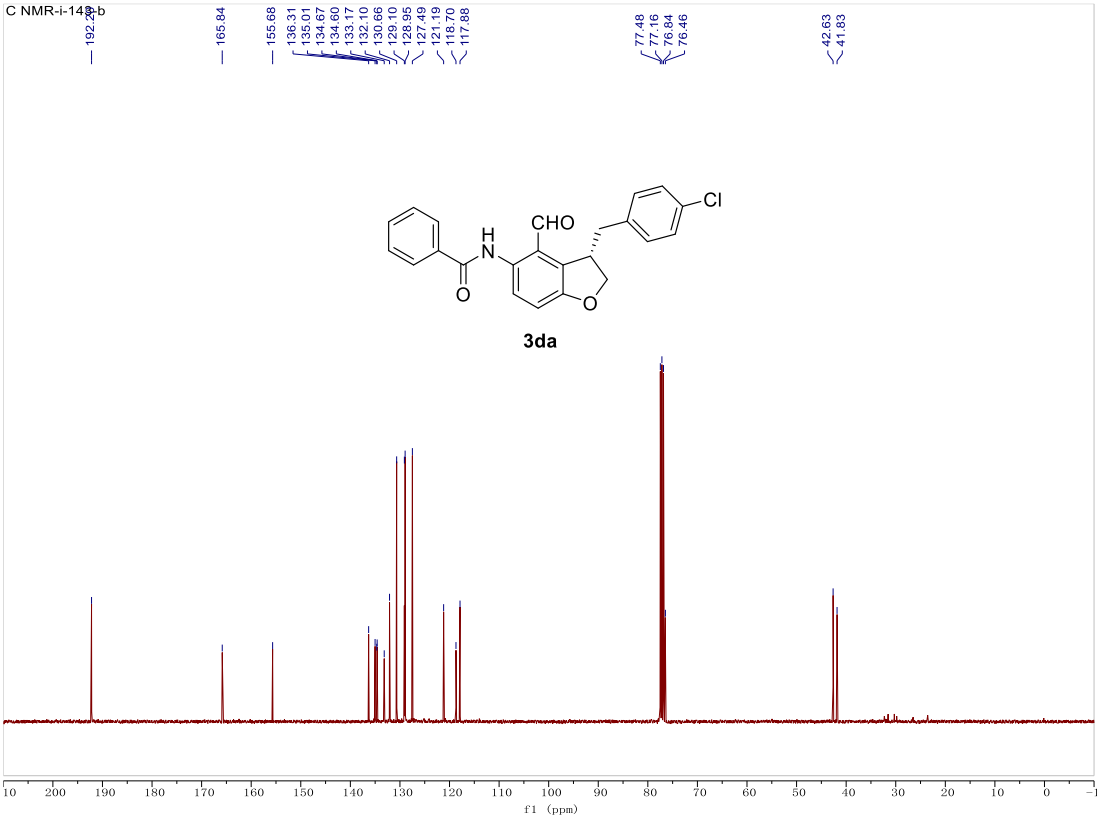


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.975	11.460	31.651	4.46	6.31	n.a.
2		21.458	245.779	470.330	95.54	93.69	n.a.
Total:			**257.240**	**501.980**	**100.00**	**100.00**	

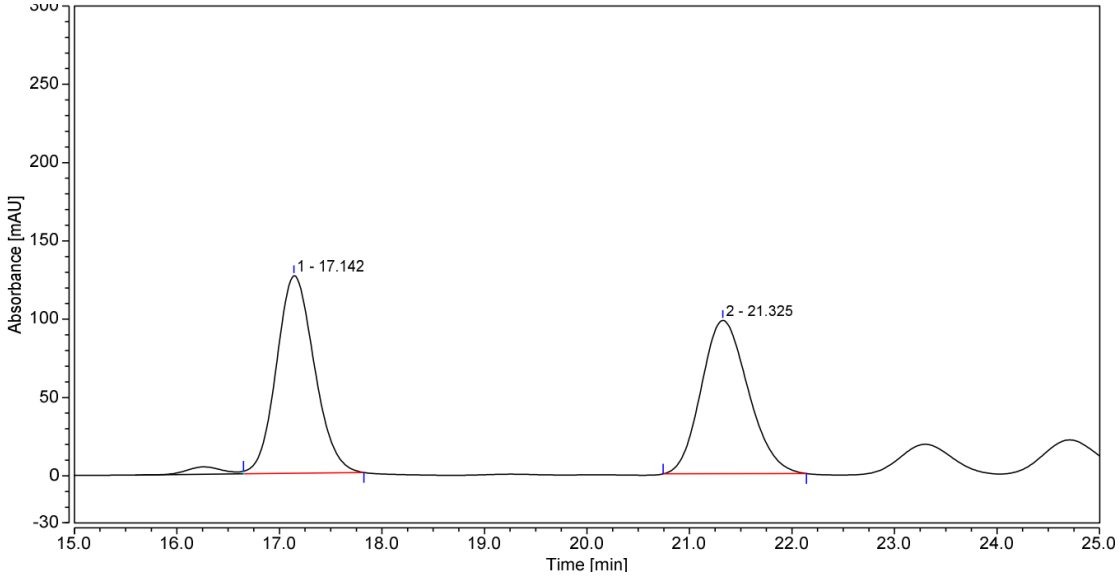
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3da**



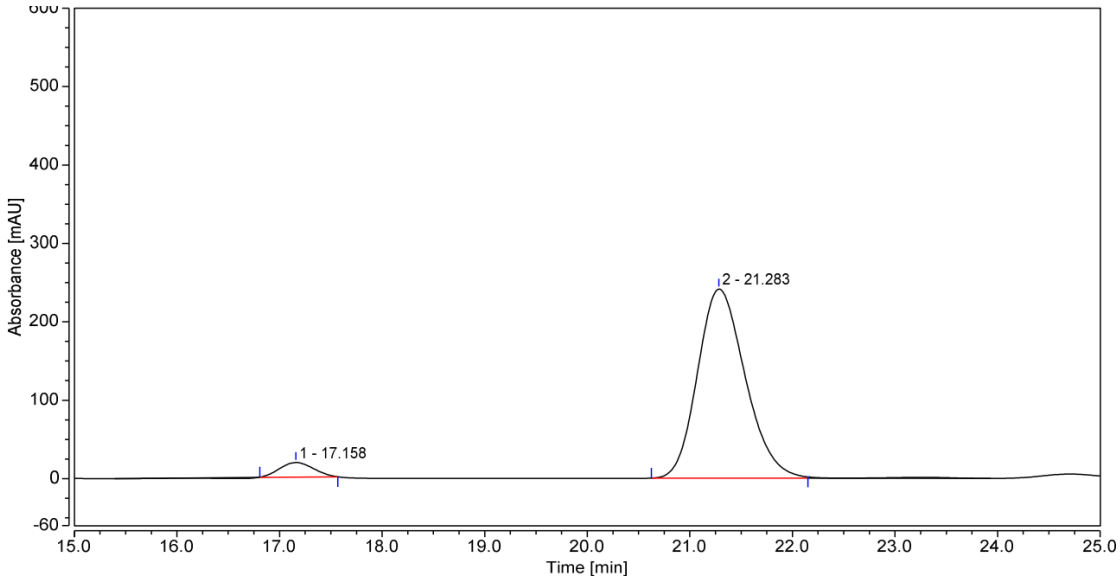
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3da**



HPLC spectra and data of compound **3da**

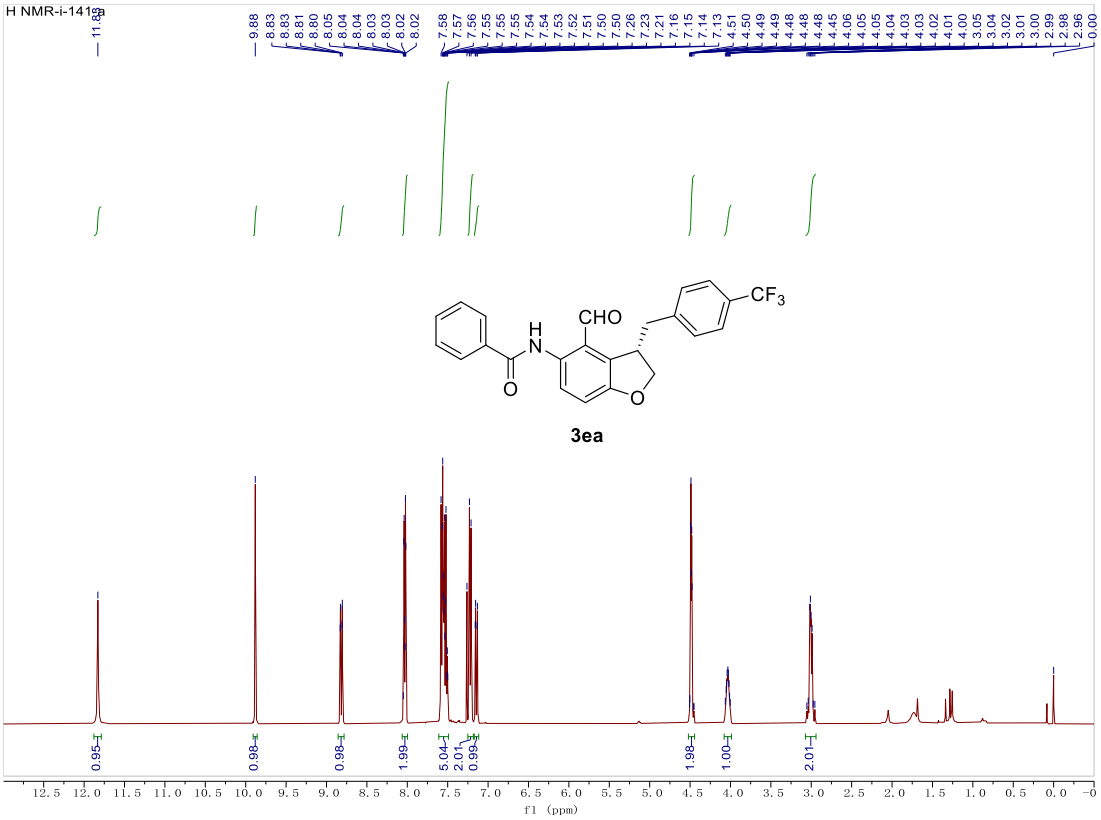


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.142	54.056	126.183	50.95	56.30	n.a.
2		21.325	52.037	97.948	49.05	43.70	n.a.
Total:			**106.093**	**224.131**	**100.00**	**100.00**	

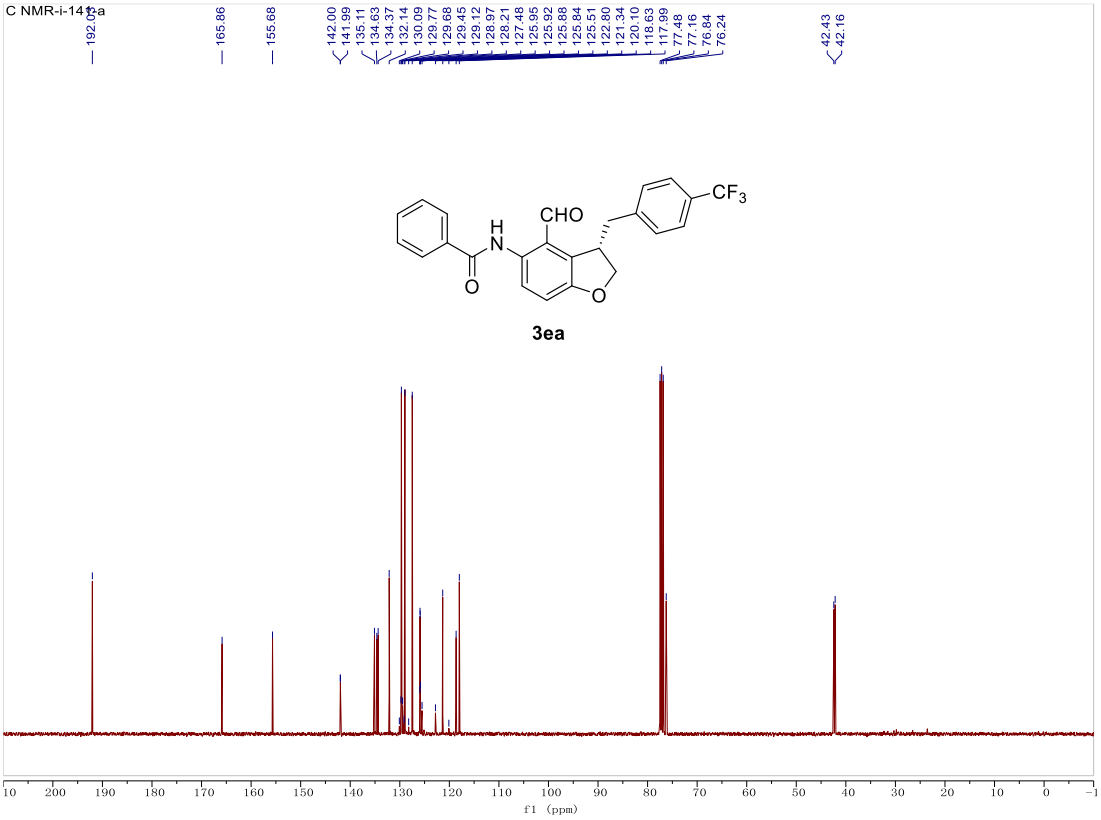


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.158	7.099	18.616	5.18	7.16	n.a.
2		21.283	129.909	241.339	94.82	92.84	n.a.
Total:			**137.007**	**259.956**	**100.00**	**100.00**	

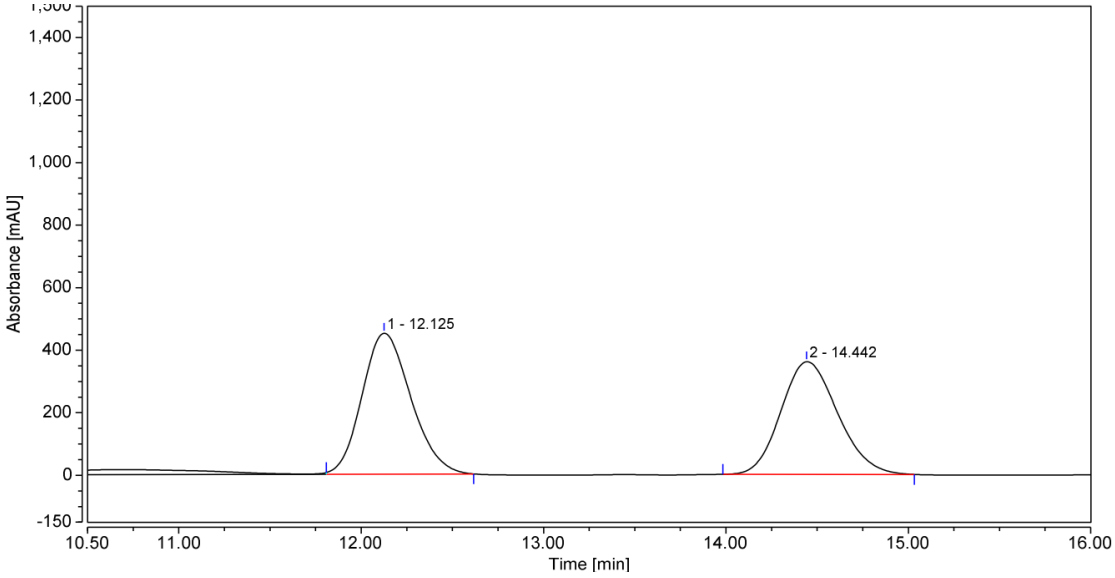
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ea**



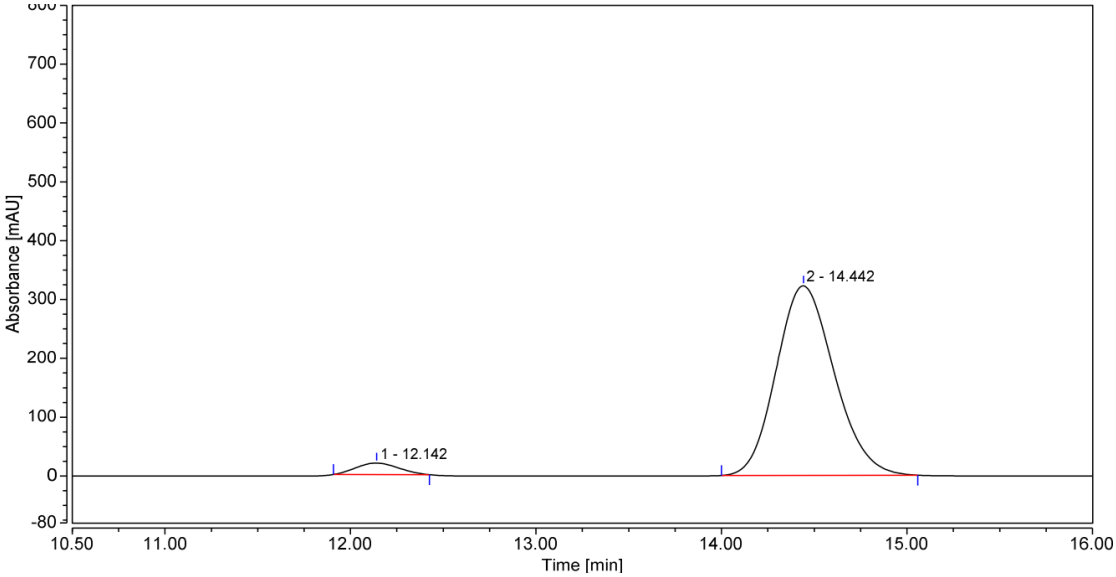
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ea**



HPLC spectra and data of compound **3ea**

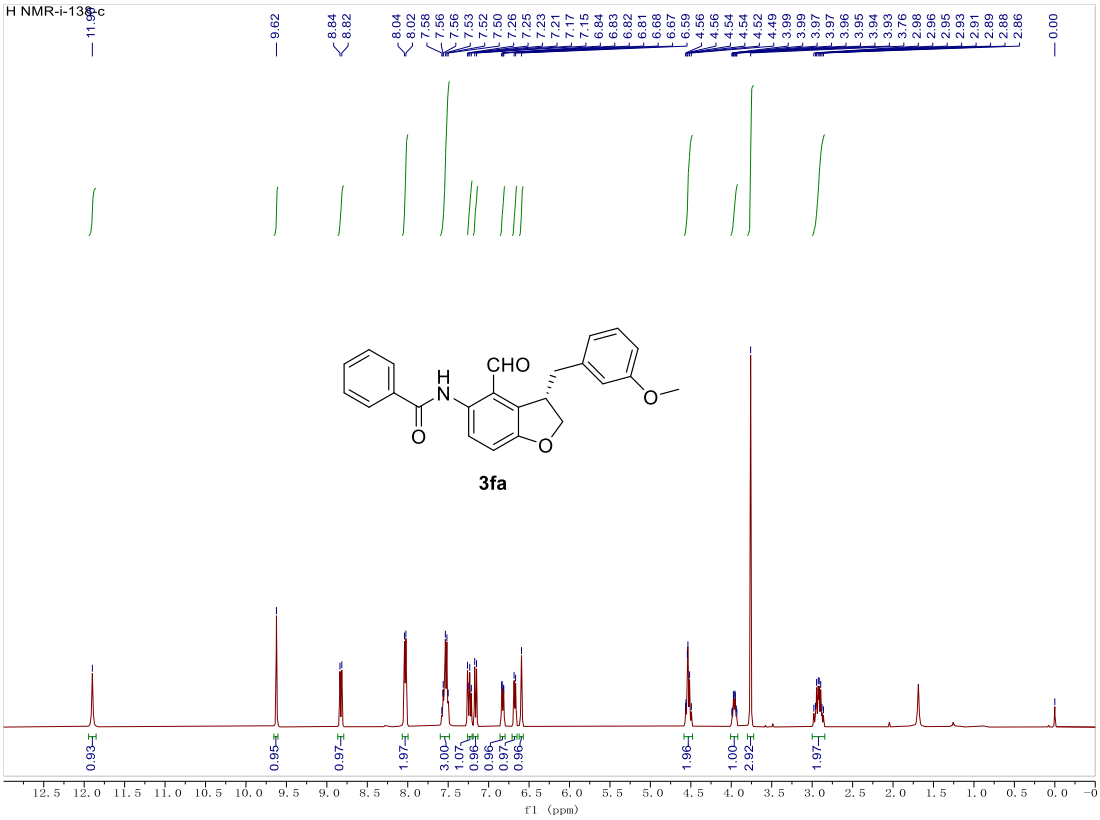


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.125	139.705	450.592	51.78	55.58	n.a.
2		14.442	130.096	360.160	48.22	44.42	n.a.
Total:			**269.801**	**810.752**	**100.00**	**100.00**	

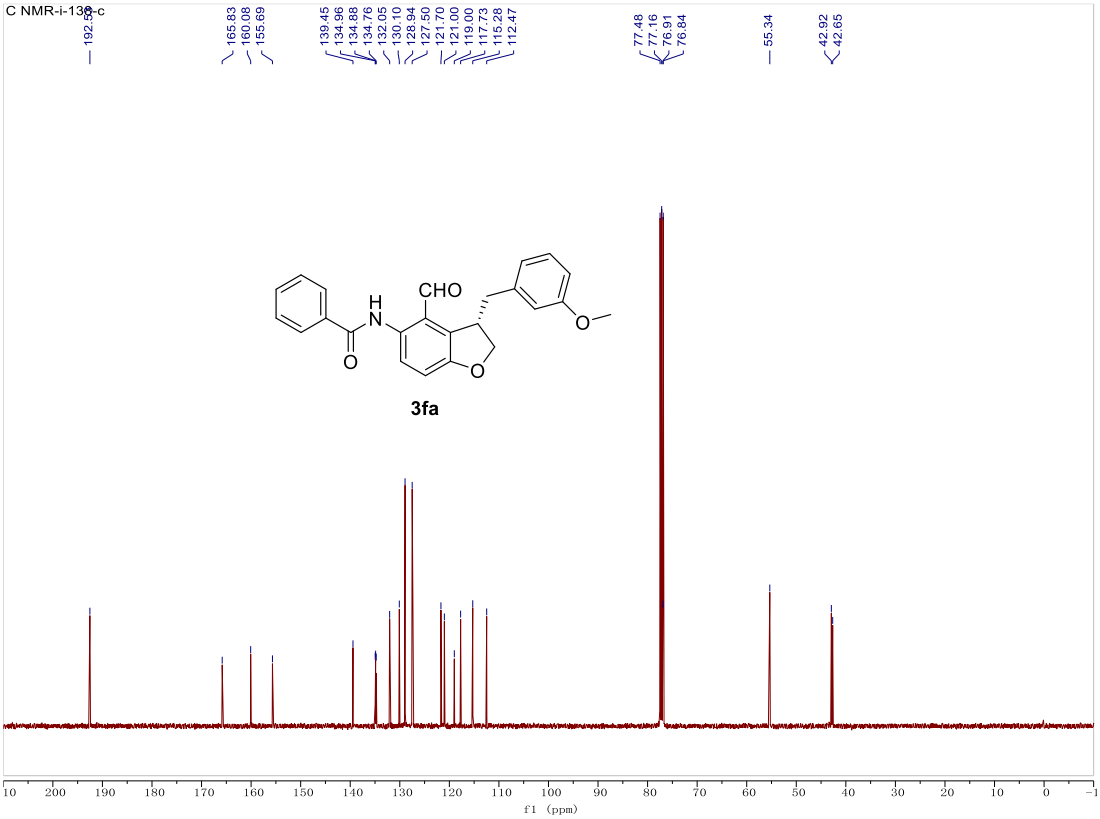


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.142	5.175	19.557	4.25	5.73	n.a.
2		14.442	116.563	321.998	95.75	94.27	n.a.
Total:			**121.738**	**341.556**	**100.00**	**100.00**	

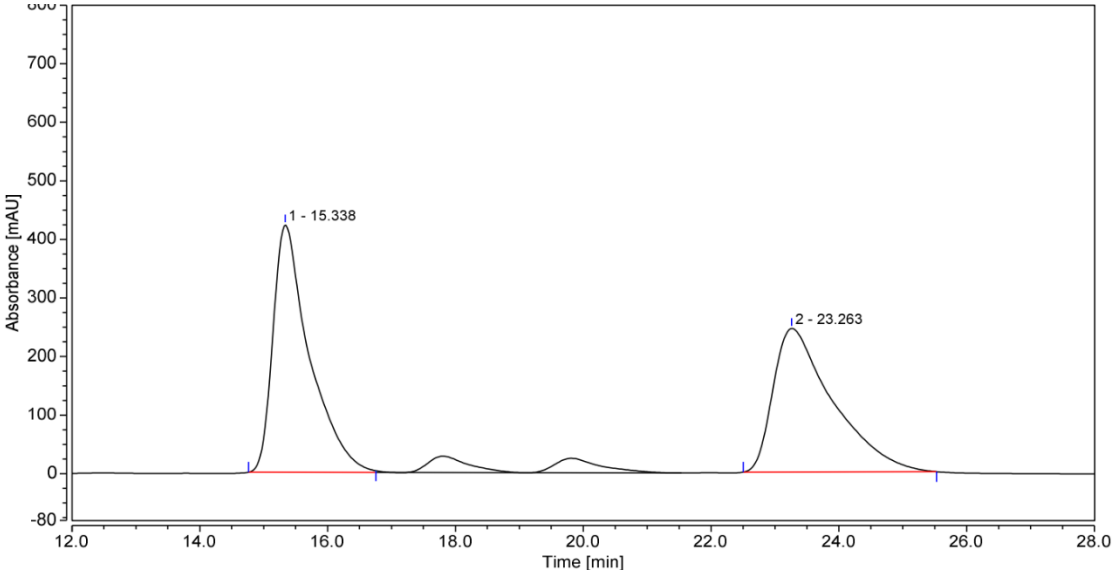
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3fa**



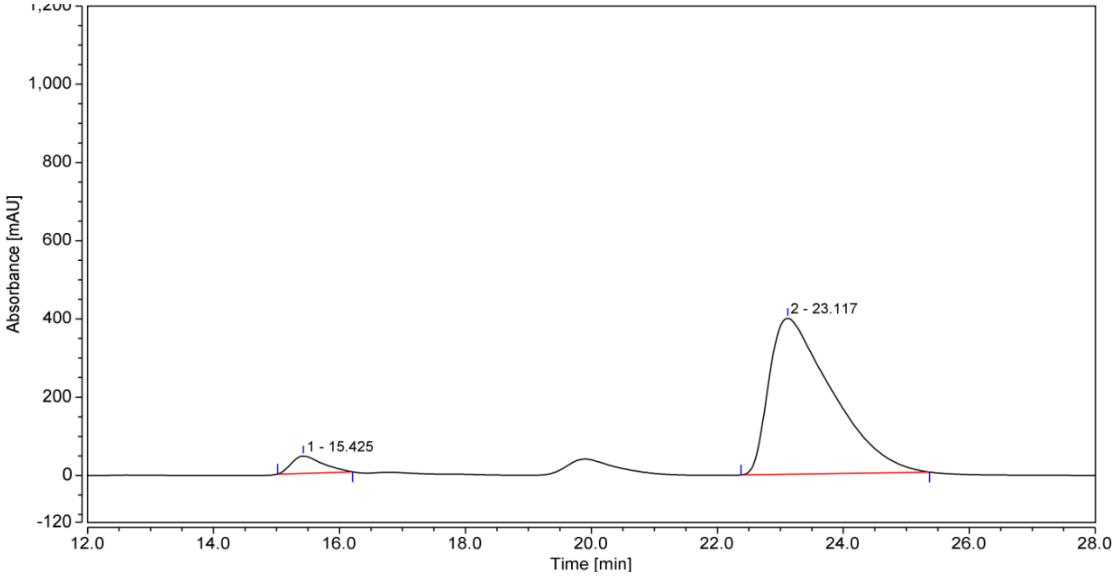
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3fa**



HPLC spectra and data of compound **3fa**

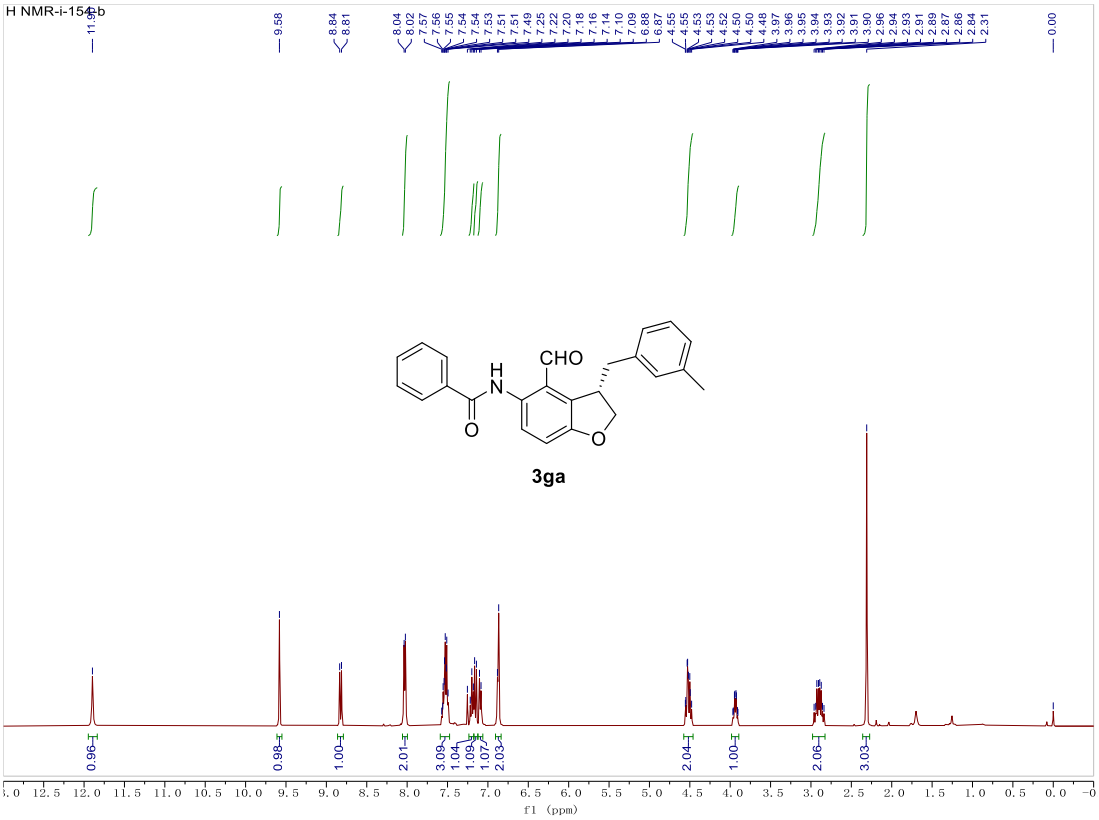


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.338	277.842	422.398	51.27	63.28	n.a.
2		23.263	264.086	245.098	48.73	36.72	n.a.
Total:			**541.928**	**667.495**	**100.00**	**100.00**	

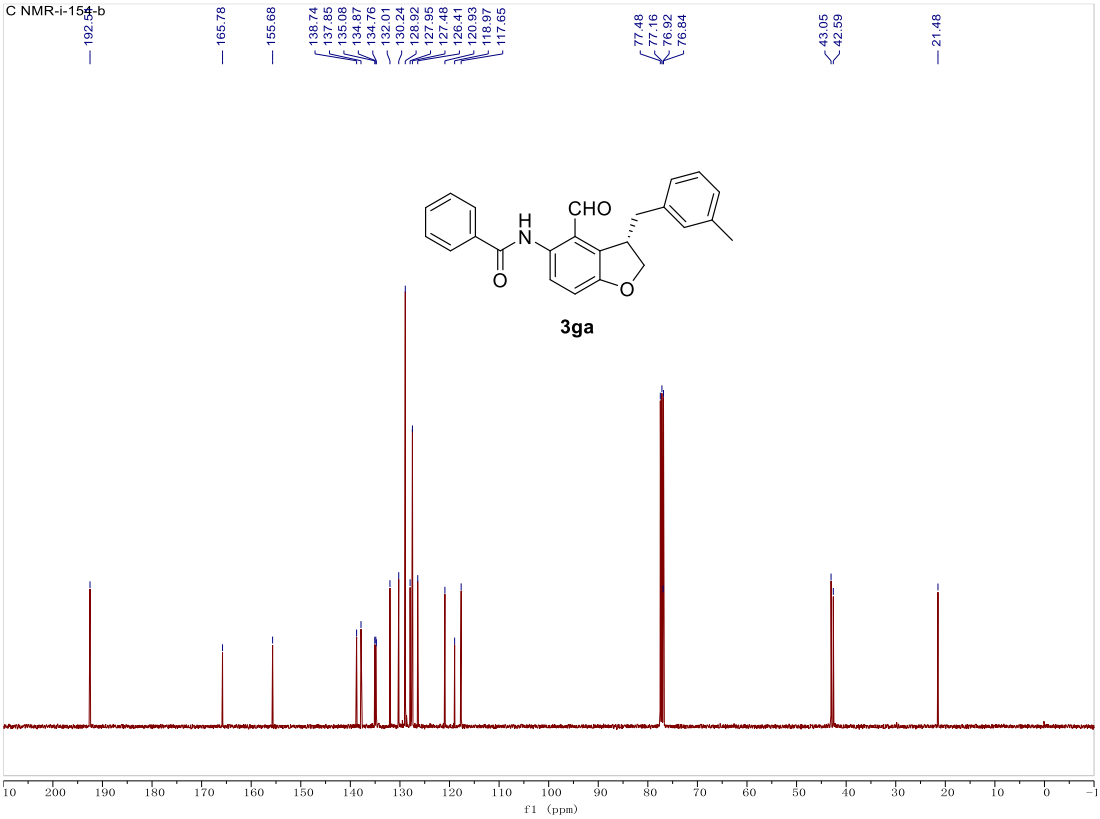


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.425	25.213	44.203	5.17	9.98	n.a.
2		23.117	462.478	398.785	94.83	90.02	n.a.
Total:			**487.691**	**442.988**	**100.00**	**100.00**	

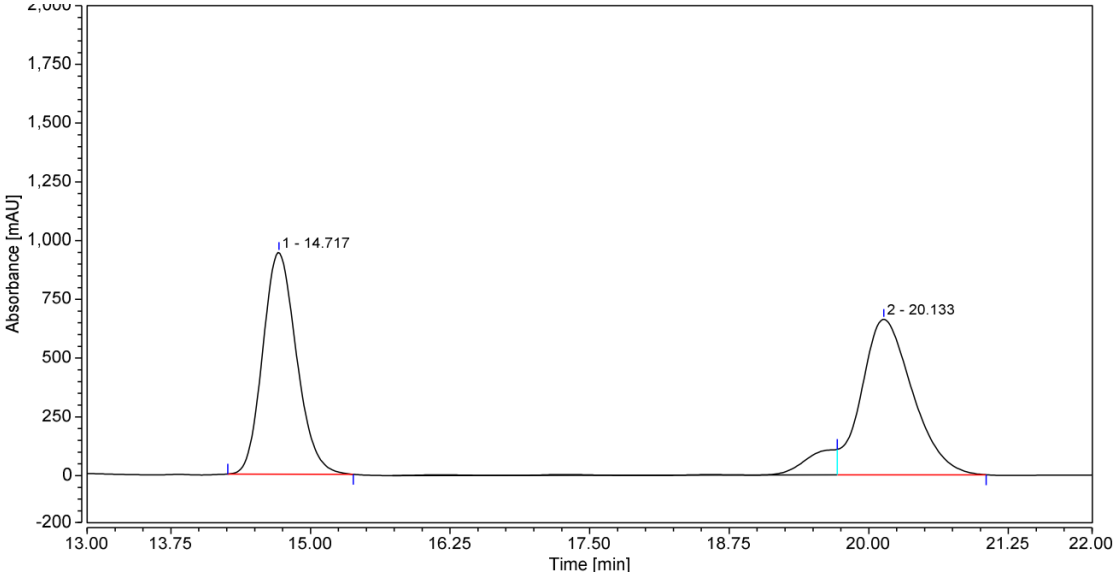
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ga**



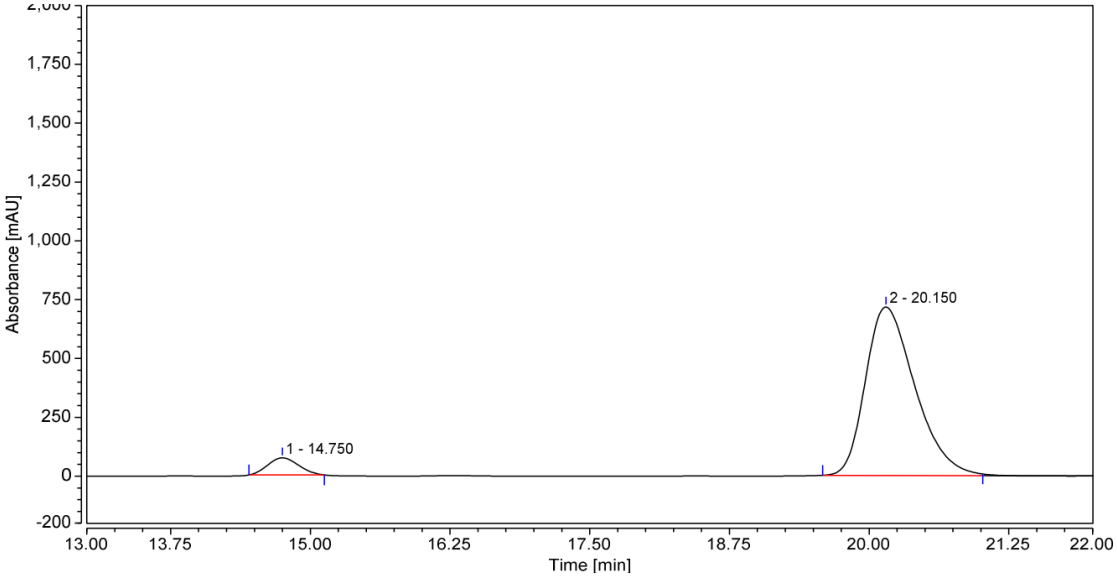
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ga**



HPLC spectra and data of compound **3ga**

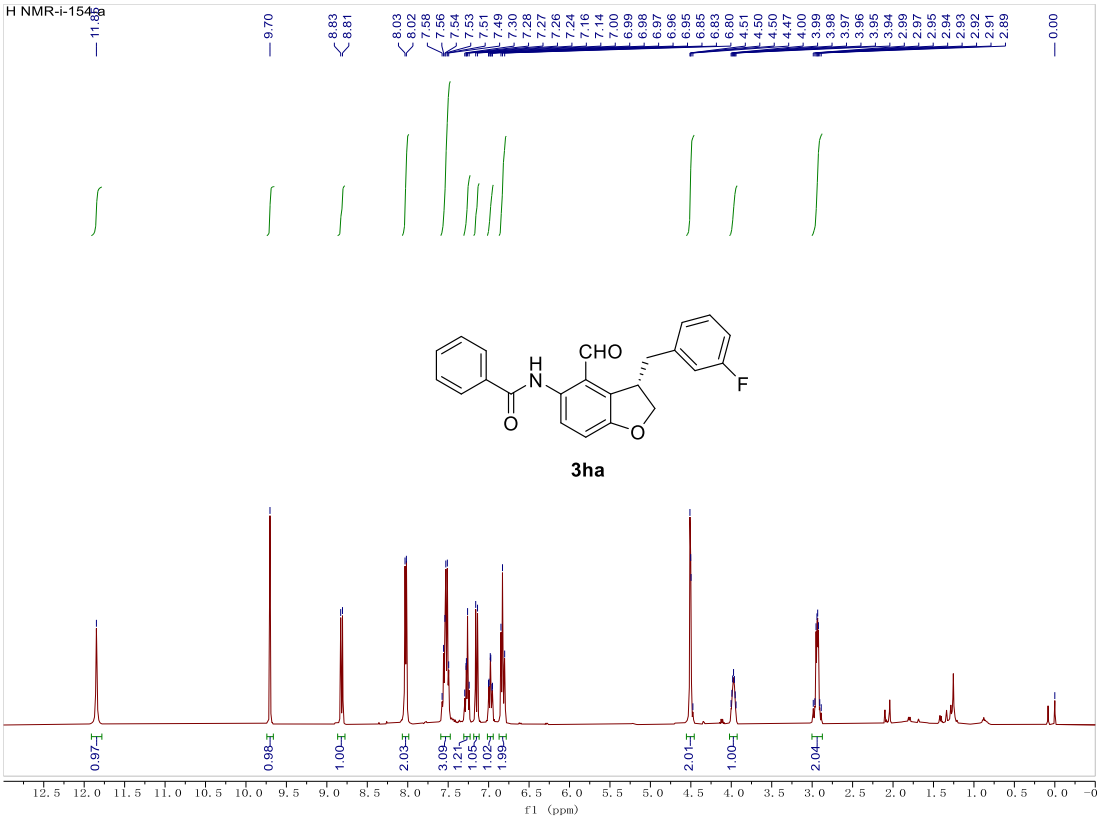


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		14.717	330.875	943.252	48.56	58.75	n.a.
2		20.133	350.475	662.188	51.44	41.25	n.a.
Total:			**681.350**	**1605.441**	**100.00**	**100.00**	

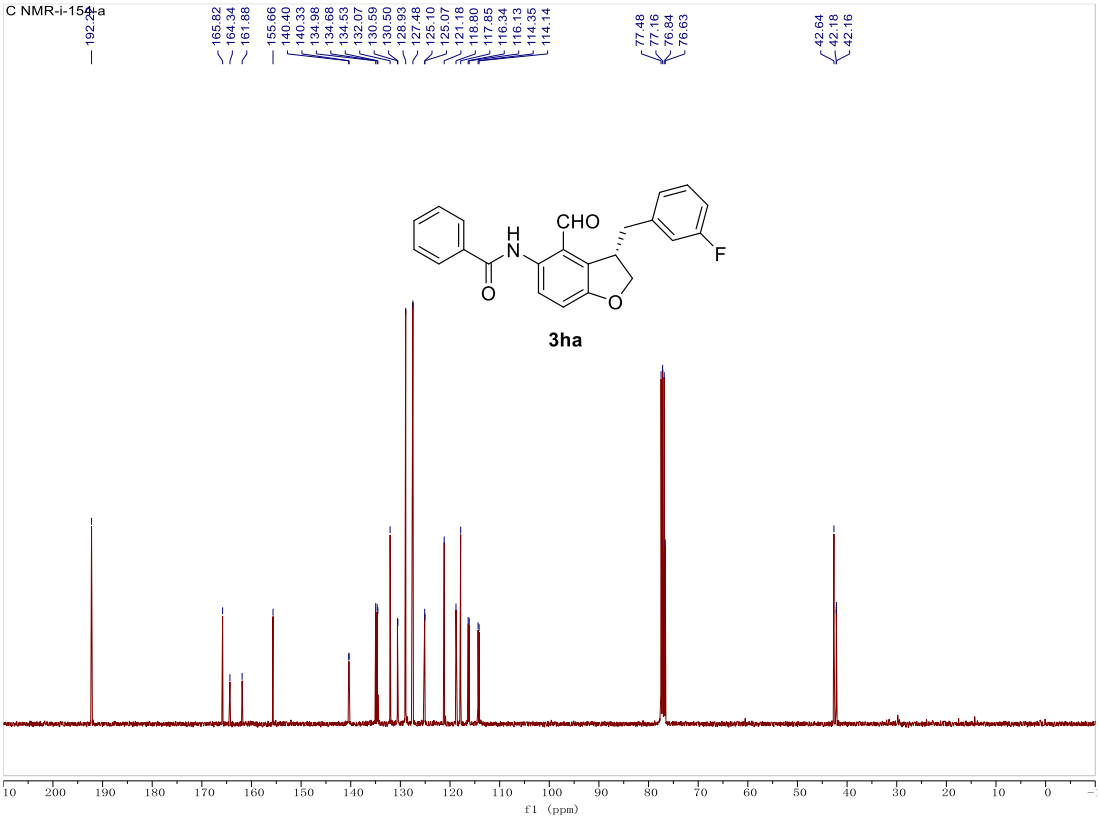


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		14.750	23.125	72.336	5.93	9.18	n.a.
2		20.150	366.630	715.564	94.07	90.82	n.a.
Total:			**389.756**	**787.900**	**100.00**	**100.00**	

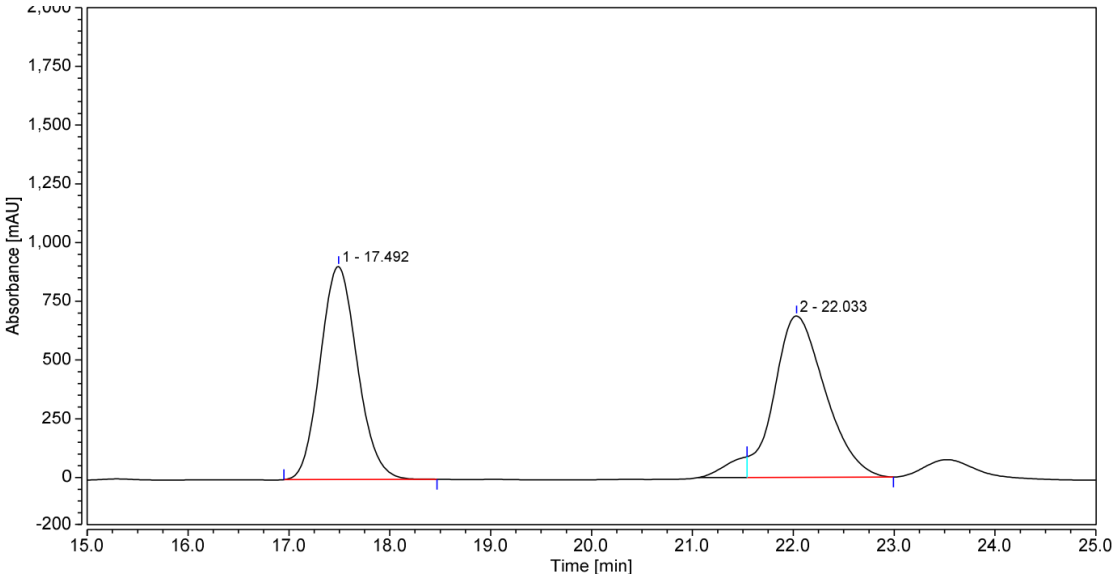
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ha**



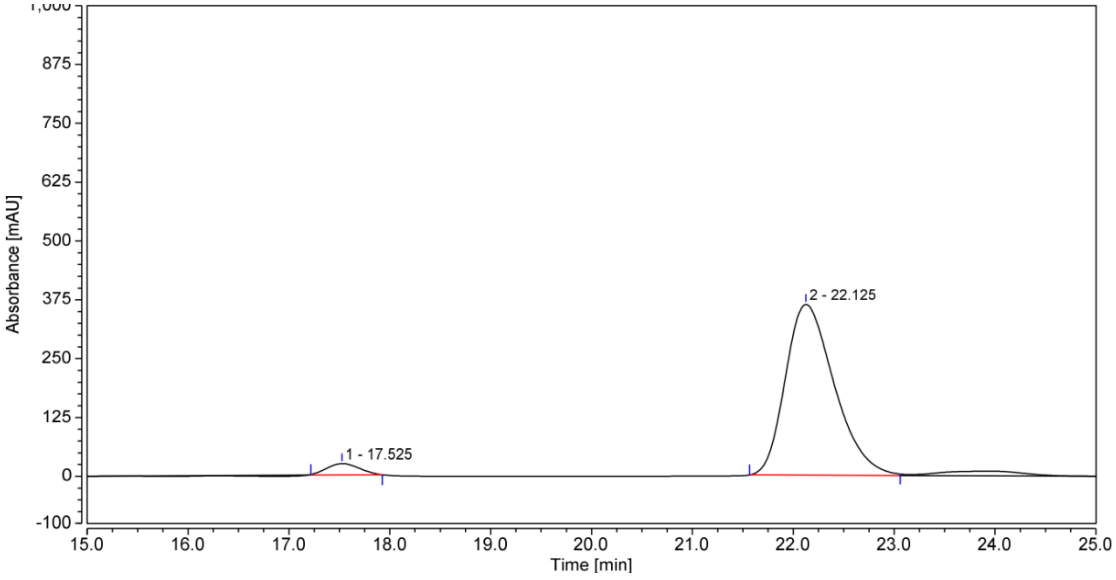
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ha**



HPLC spectra and data of compound **3ha**

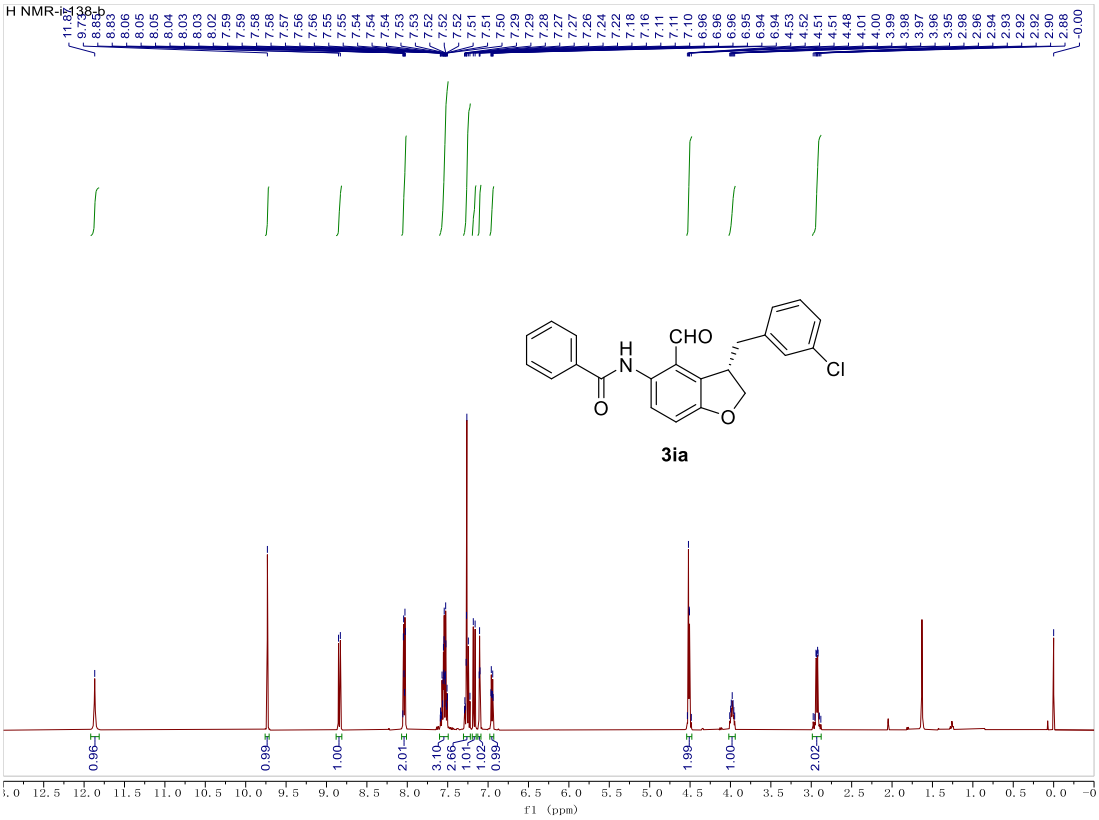


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.492	387.043	906.498	49.18	56.88	n.a.
2		22.033	400.011	687.087	50.82	43.12	n.a.
Total:			**787.053**	**1593.585**	**100.00**	**100.00**	

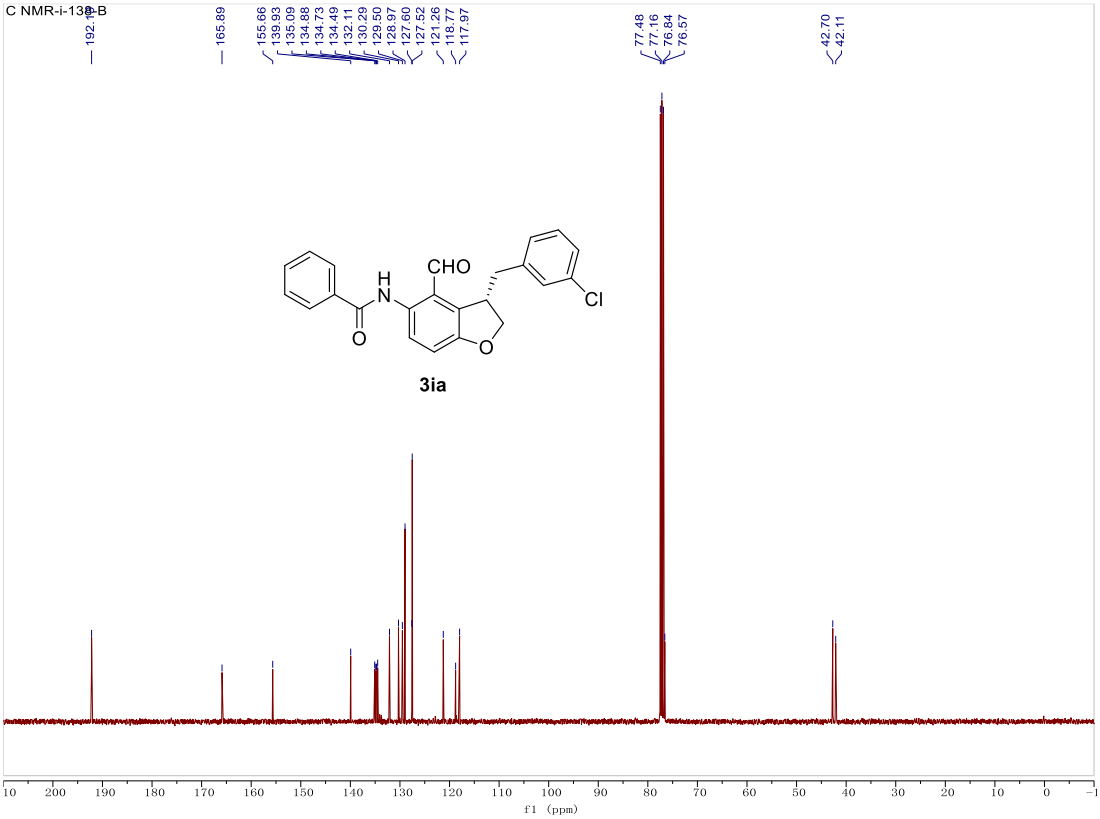


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.525	9.001	24.057	4.23	6.22	n.a.
2		22.125	203.593	362.767	95.77	93.78	n.a.
Total:			**212.594**	**386.824**	**100.00**	**100.00**	

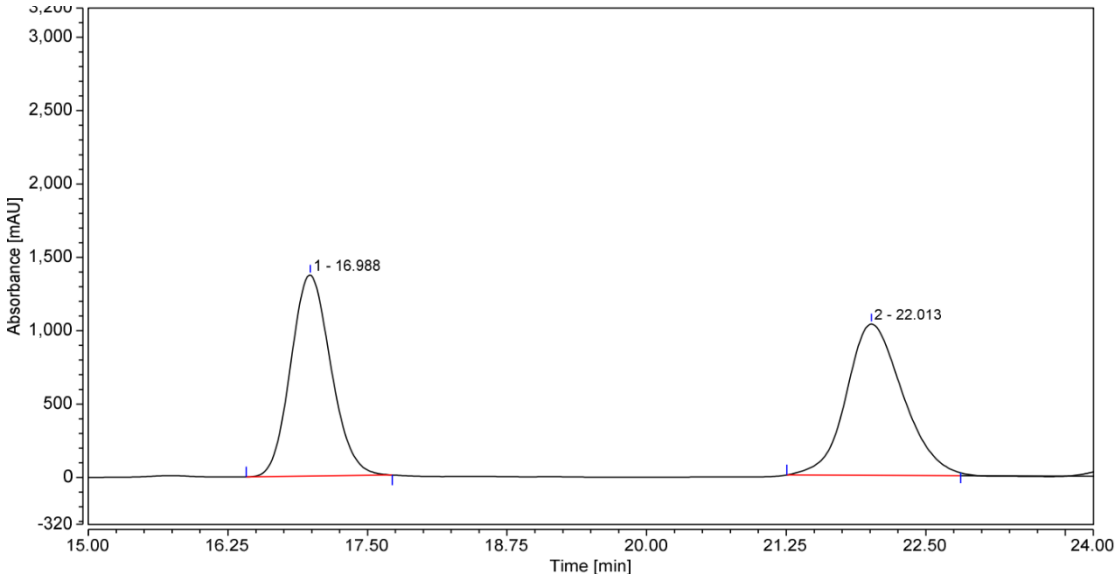
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ia**



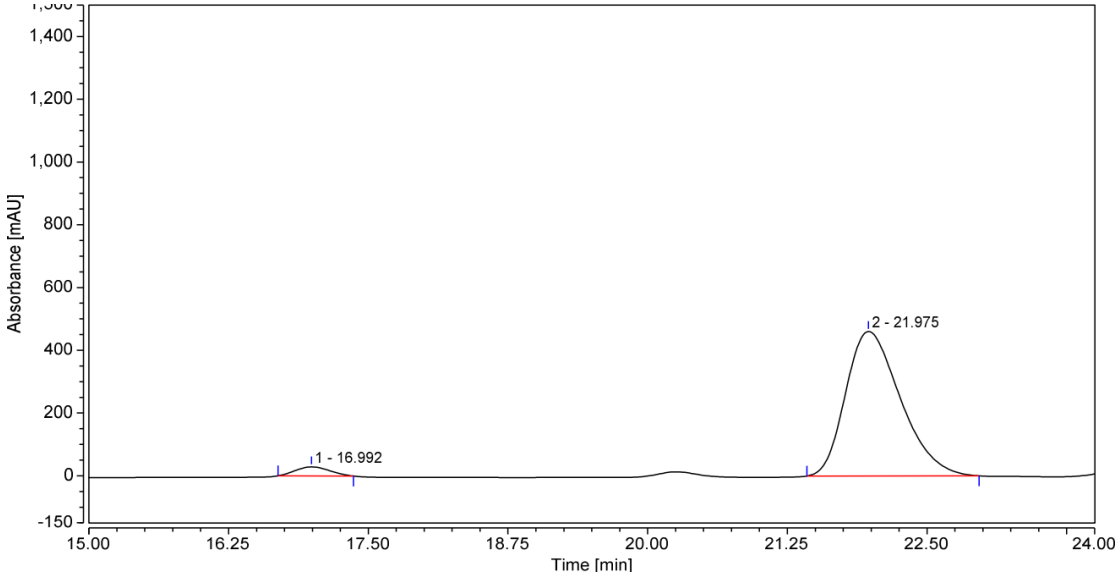
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ia**



HPLC spectra and data of compound **3ia**

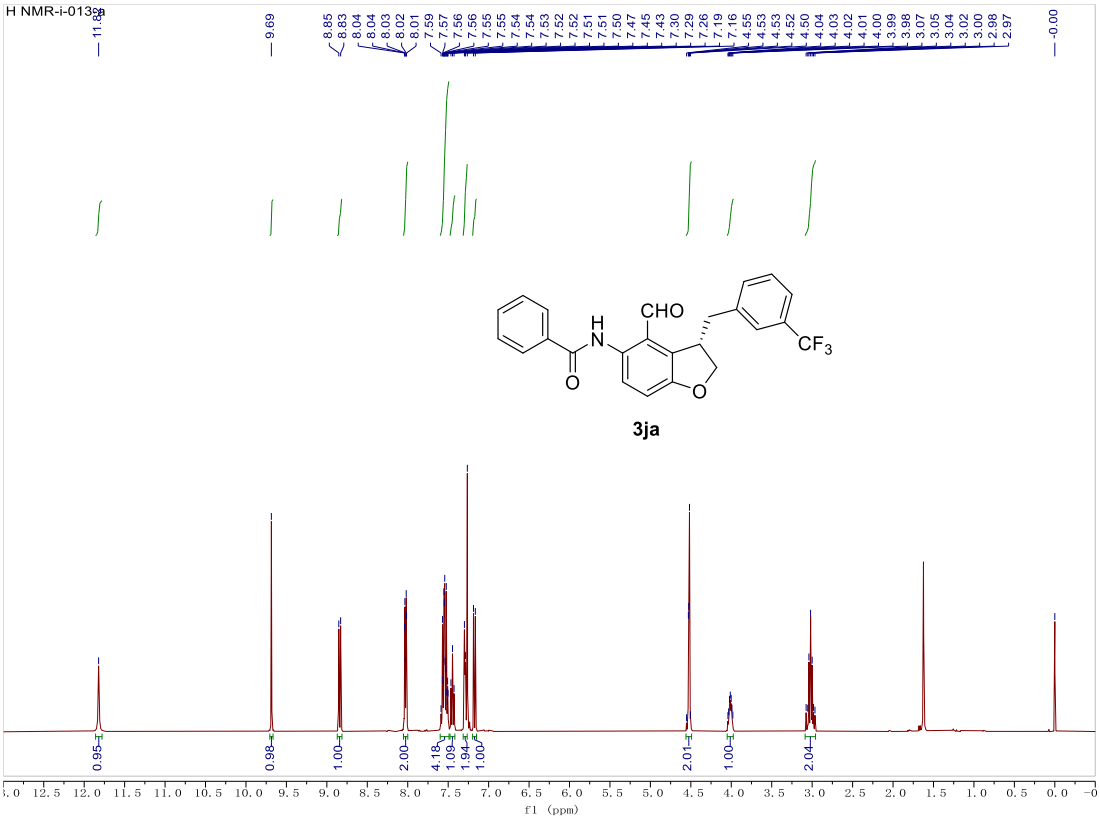


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.988	571.887	1370.680	48.63	57.07	n.a.
2		22.013	604.078	1031.095	51.37	42.93	n.a.
Total:			**1175.965**	**2401.775**	**100.00**	**100.00**	

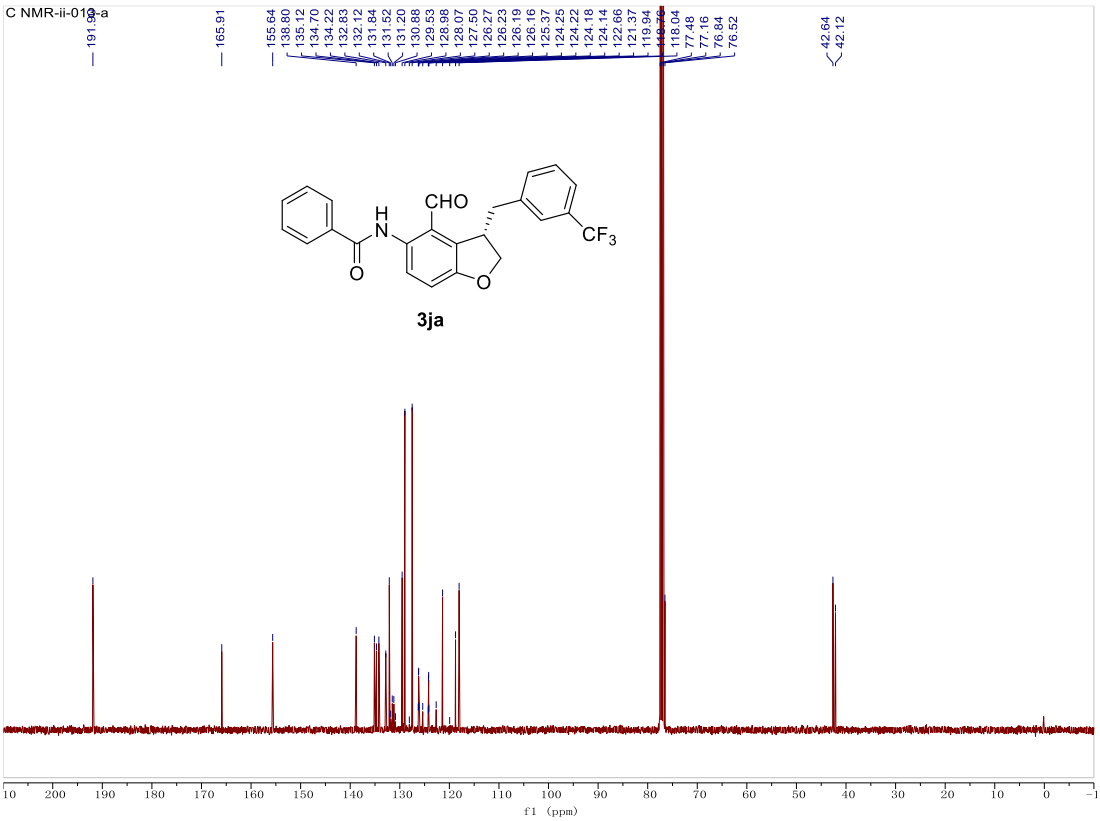


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.992	10.167	28.675	3.74	5.86	n.a.
2		21.975	261.822	460.653	96.26	94.14	n.a.
Total:			**271.989**	**489.328**	**100.00**	**100.00**	

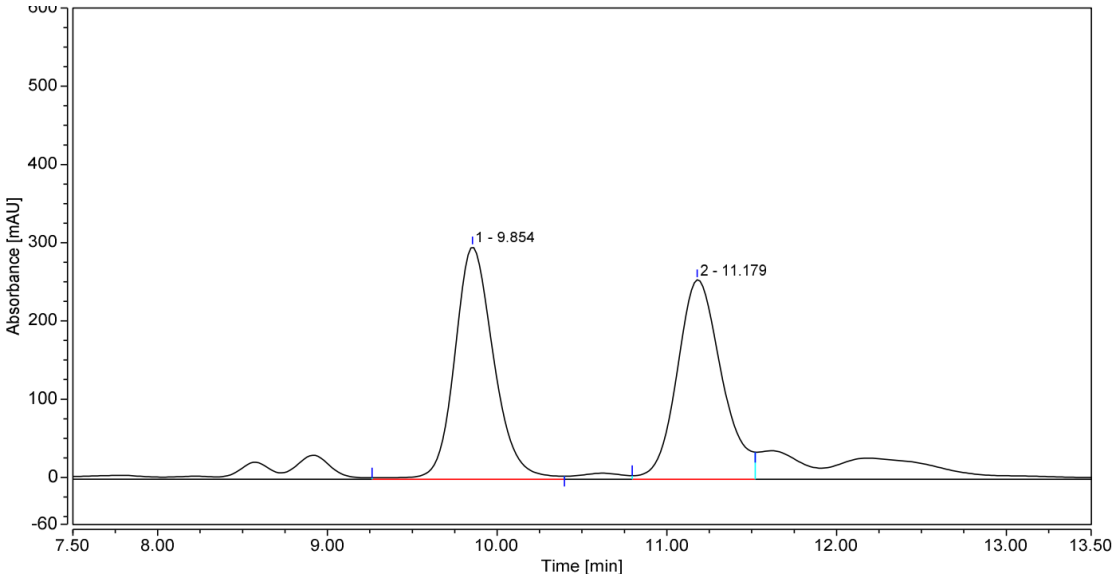
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ja**



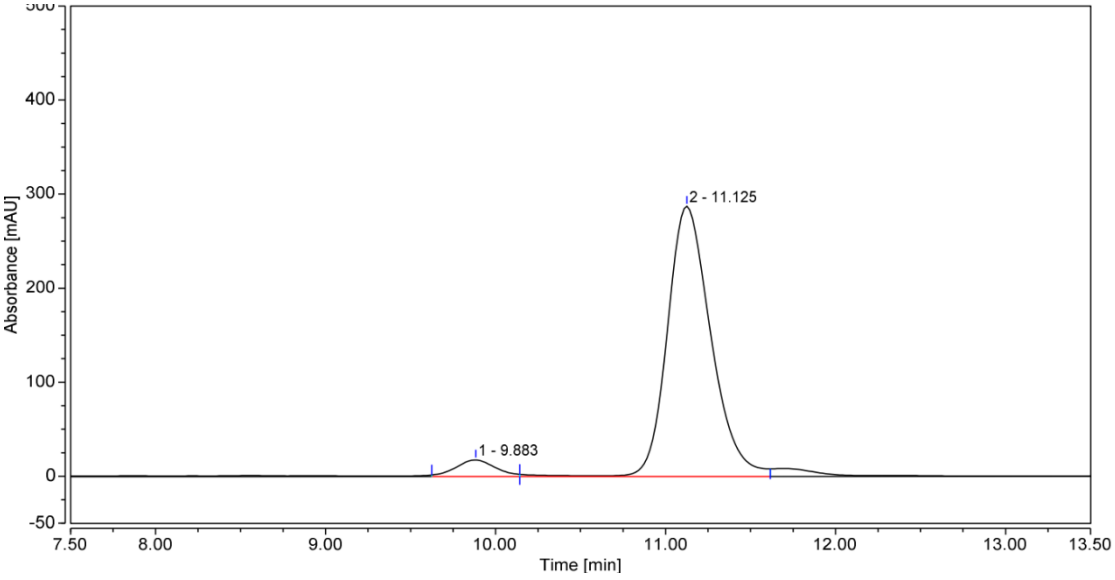
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ja**



HPLC spectra and data of compound **3ja**

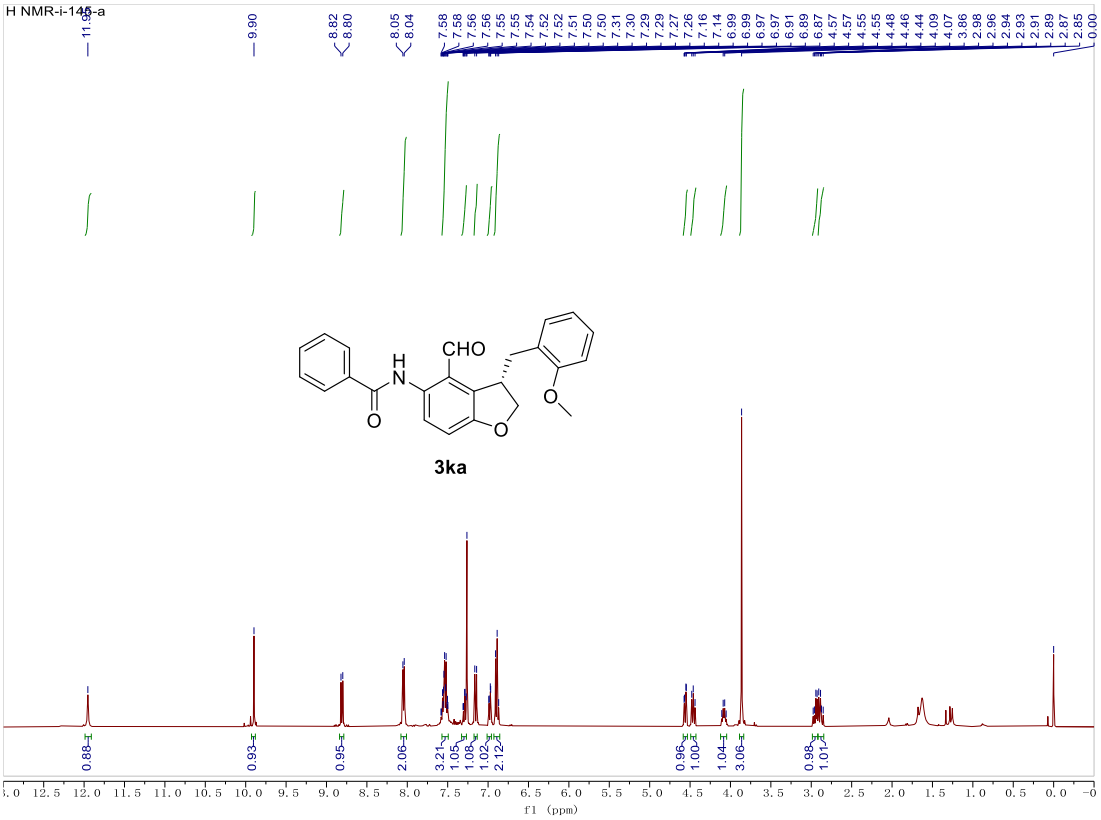


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.854	79.259	296.887	50.60	53.81	n.a.
2		11.179	77.374	254.850	49.40	46.19	n.a.
Total:			**156.633**	**551.737**	**100.00**	**100.00**	

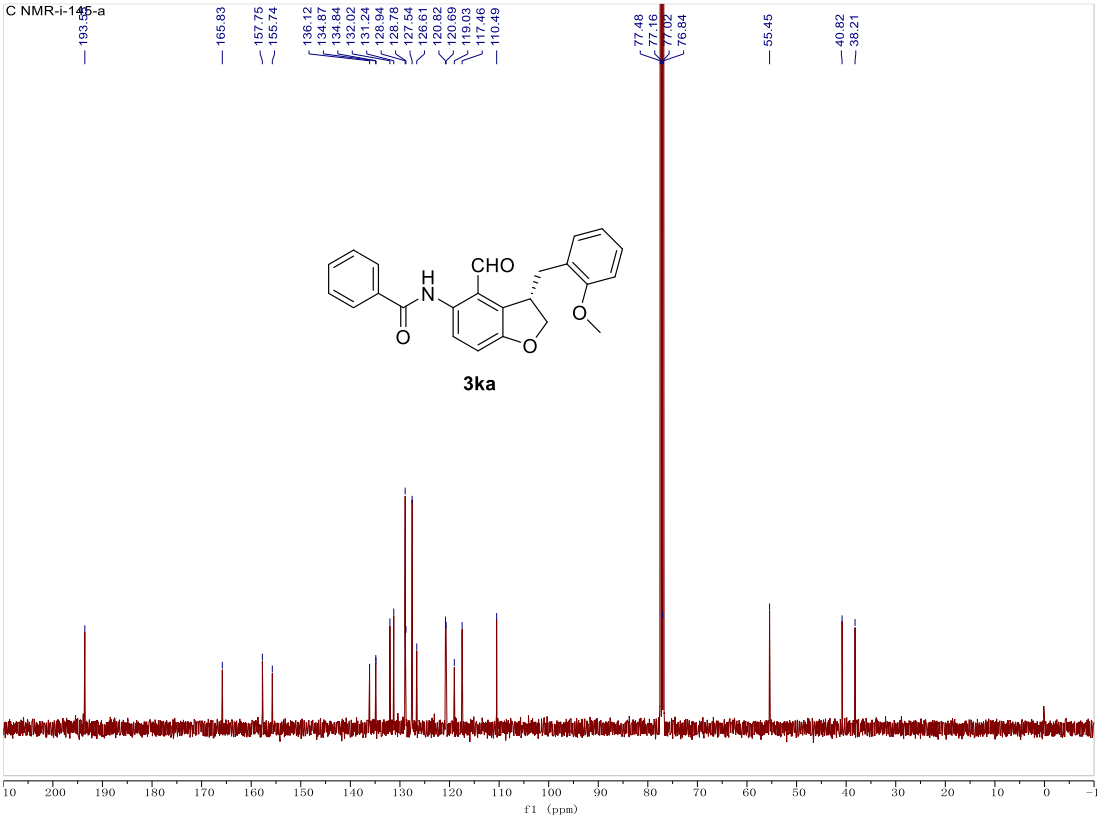


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.883	4.761	17.649	5.30	5.79	n.a.
2		11.125	85.062	287.325	94.70	94.21	n.a.
Total:			**89.823**	**304.974**	**100.00**	**100.00**	

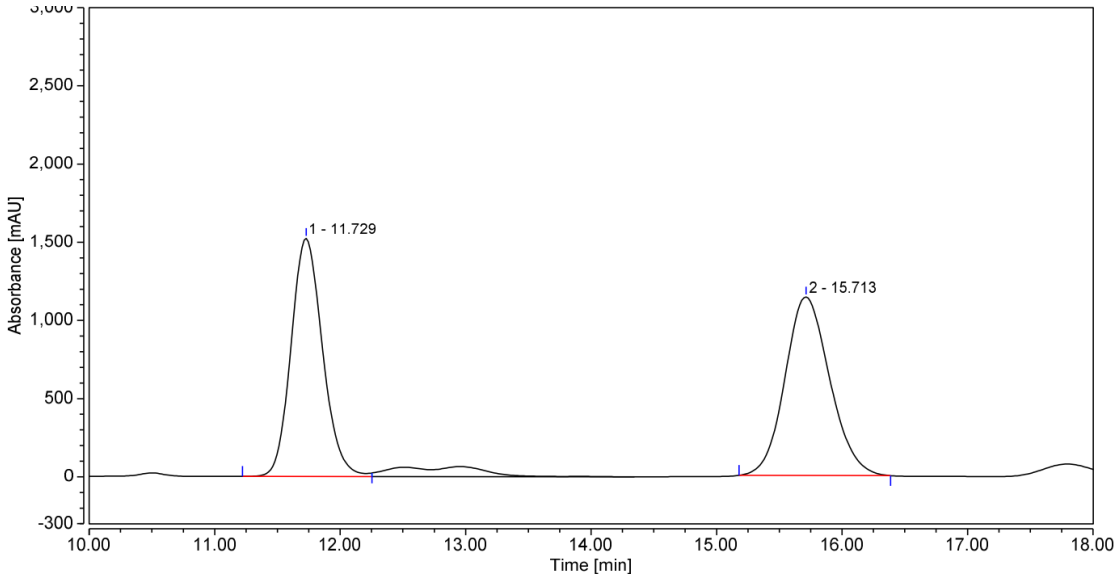
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ka**



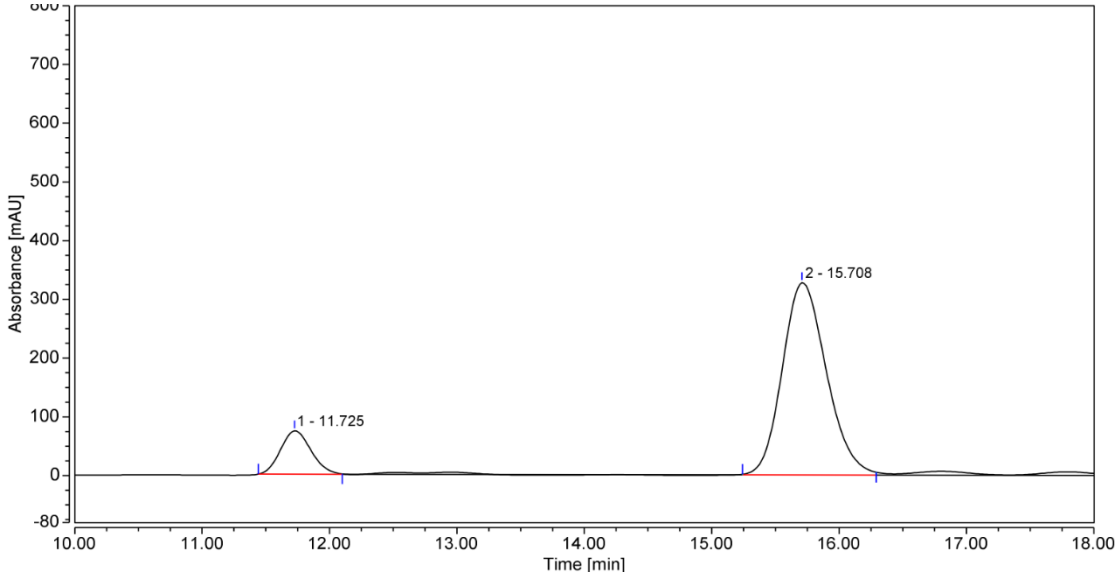
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ka**



HPLC spectra and data of compound **3ka**

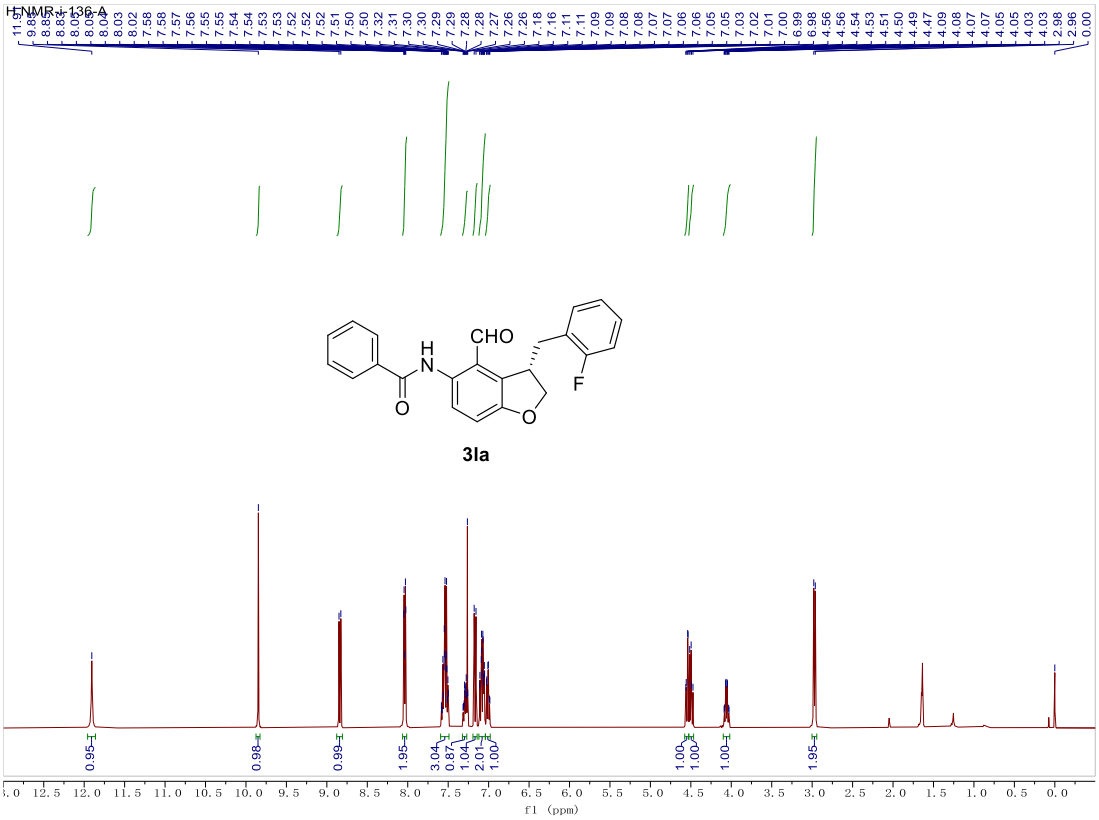


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.729	443.361	1522.172	48.45	57.14	n.a.
2		15.713	471.786	1141.837	51.55	42.86	n.a.
Total:			**915.147**	**2664.009**	**100.00**	**100.00**	

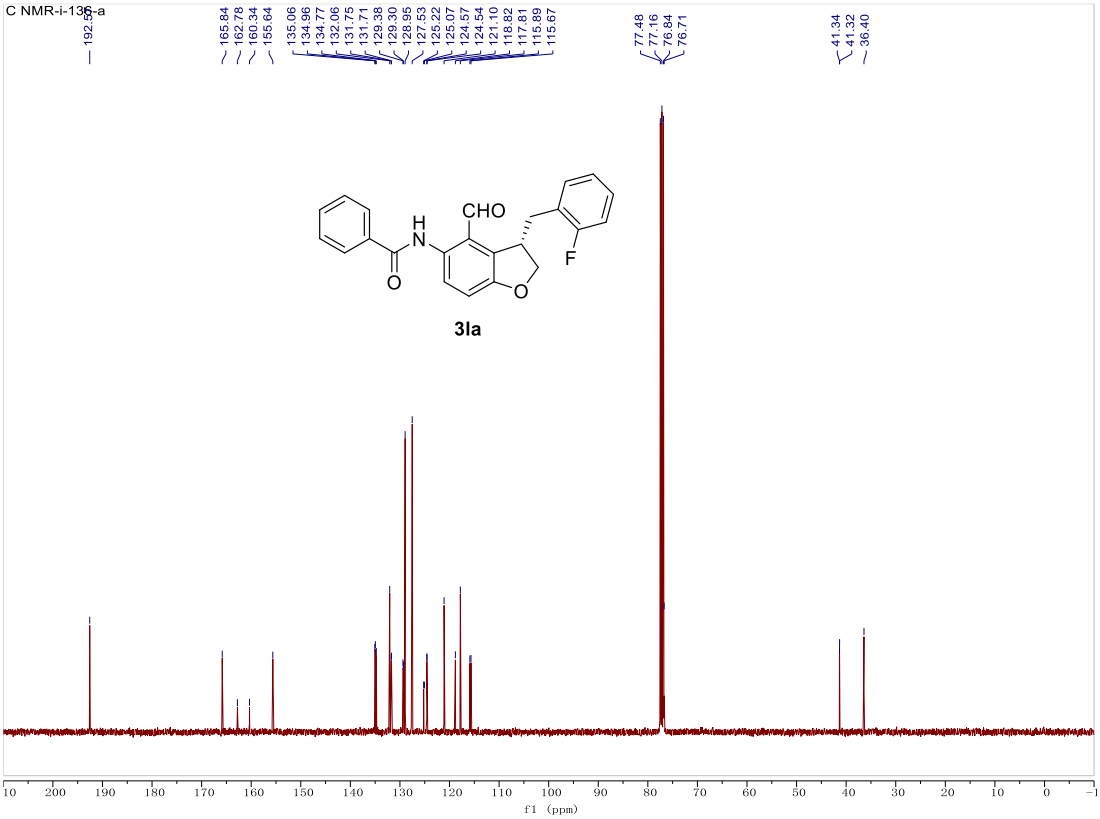


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.725	20.393	73.738	13.48	18.39	n.a.
2		15.708	130.873	327.285	86.52	81.61	n.a.
Total:			**151.266**	**401.024**	**100.00**	**100.00**	

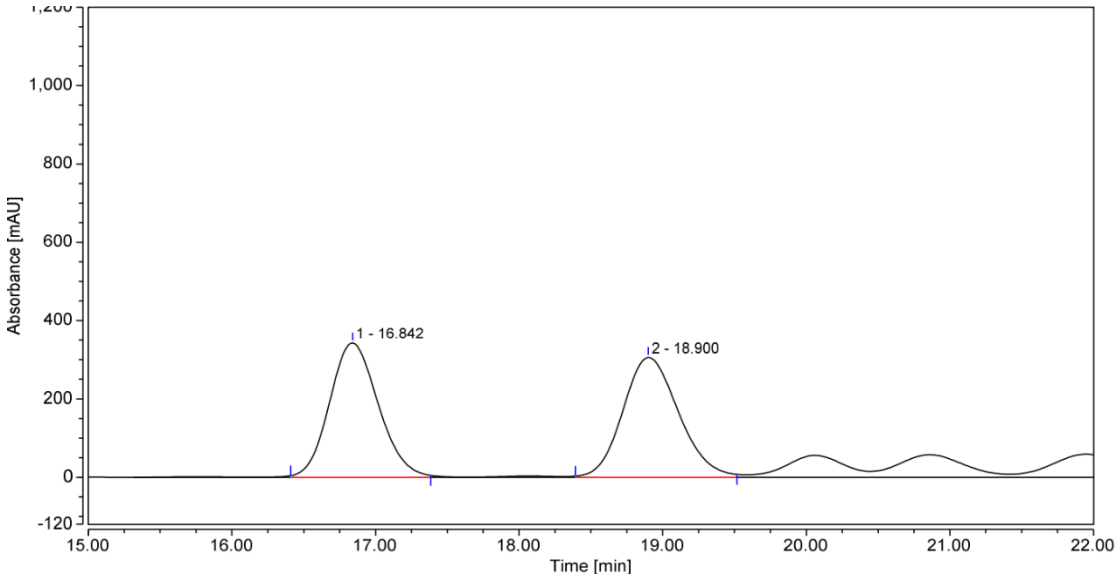
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3la**



^{13}C NMR (101 MHz, $CDCl_3$) of compound **3la**

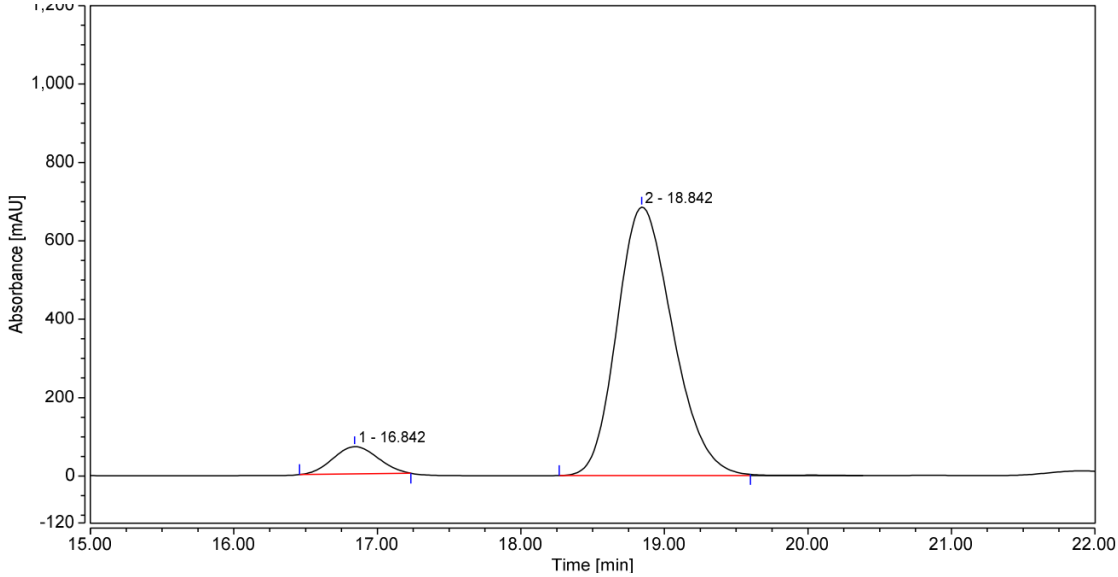


HPLC spectra and data of compound **3la**



Integration Results

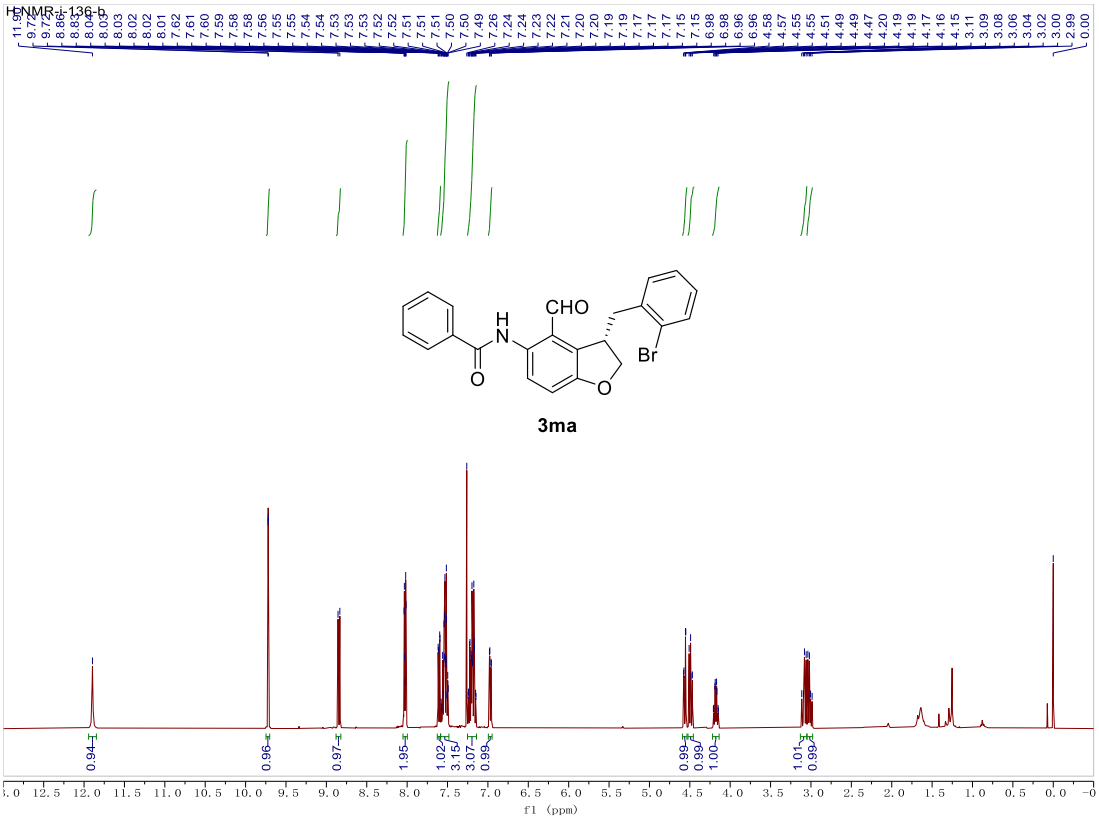
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.842	134.577	342.855	49.48	52.86	n.a.
2		18.900	137.390	305.804	50.52	47.14	n.a.
Total:			**271.967**	**648.660**	**100.00**	**100.00**	



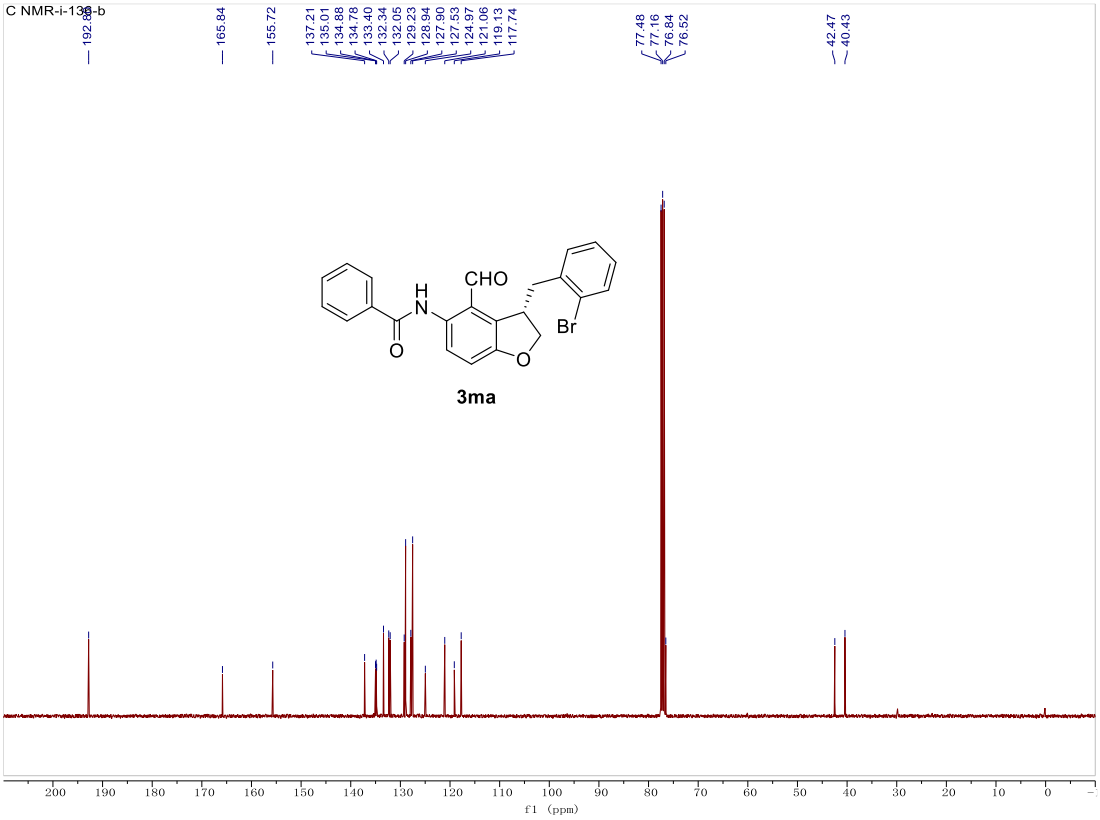
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.842	25.302	69.733	7.57	9.24	n.a.
2		18.842	308.894	684.707	92.43	90.76	n.a.
Total:			**334.197**	**754.440**	**100.00**	**100.00**	

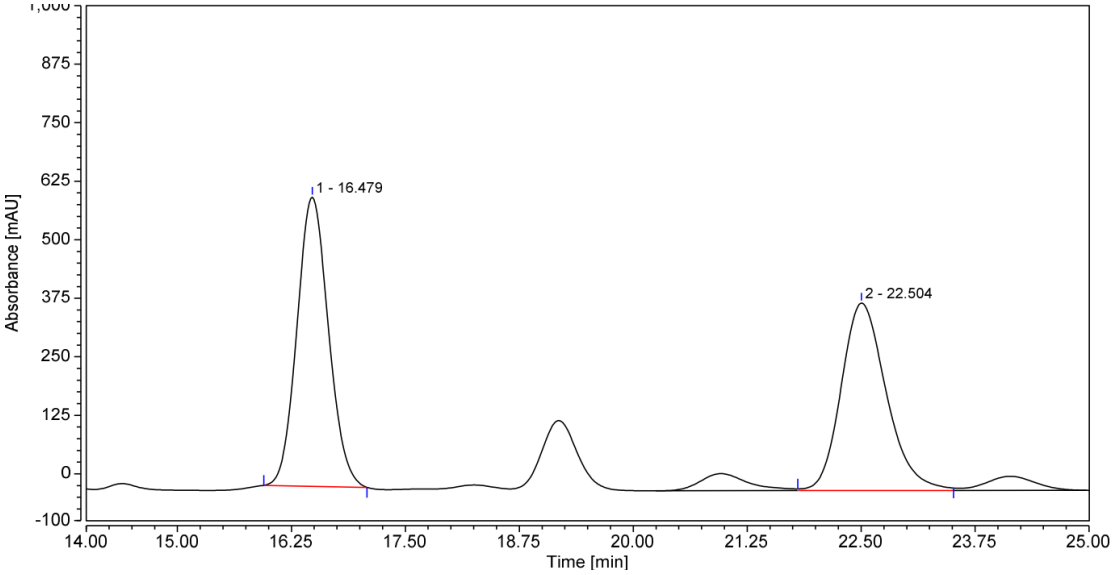
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ma**



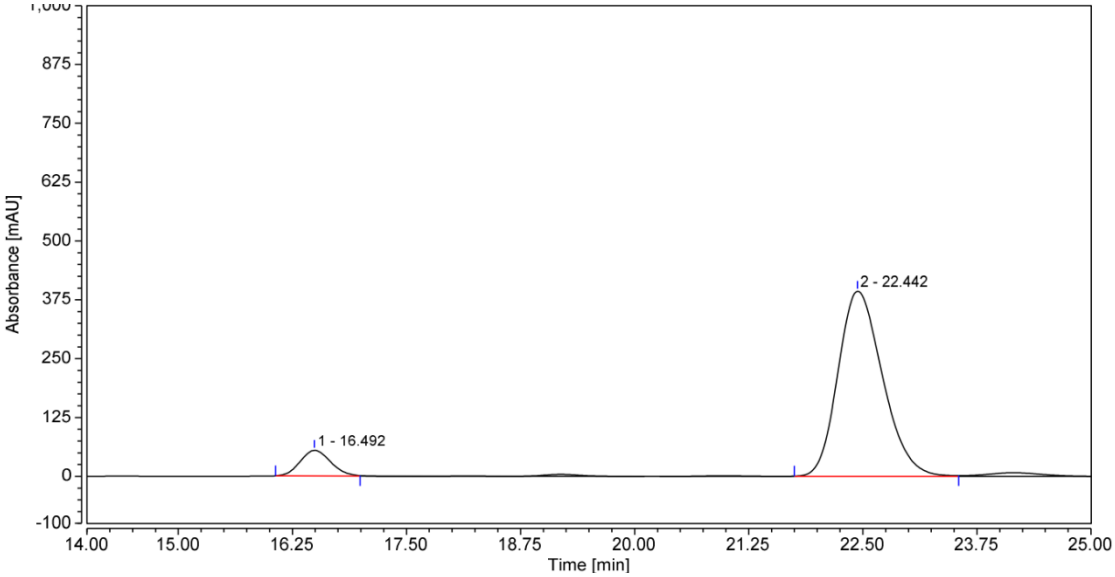
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ma**



HPLC spectra and data of compound **3ma**

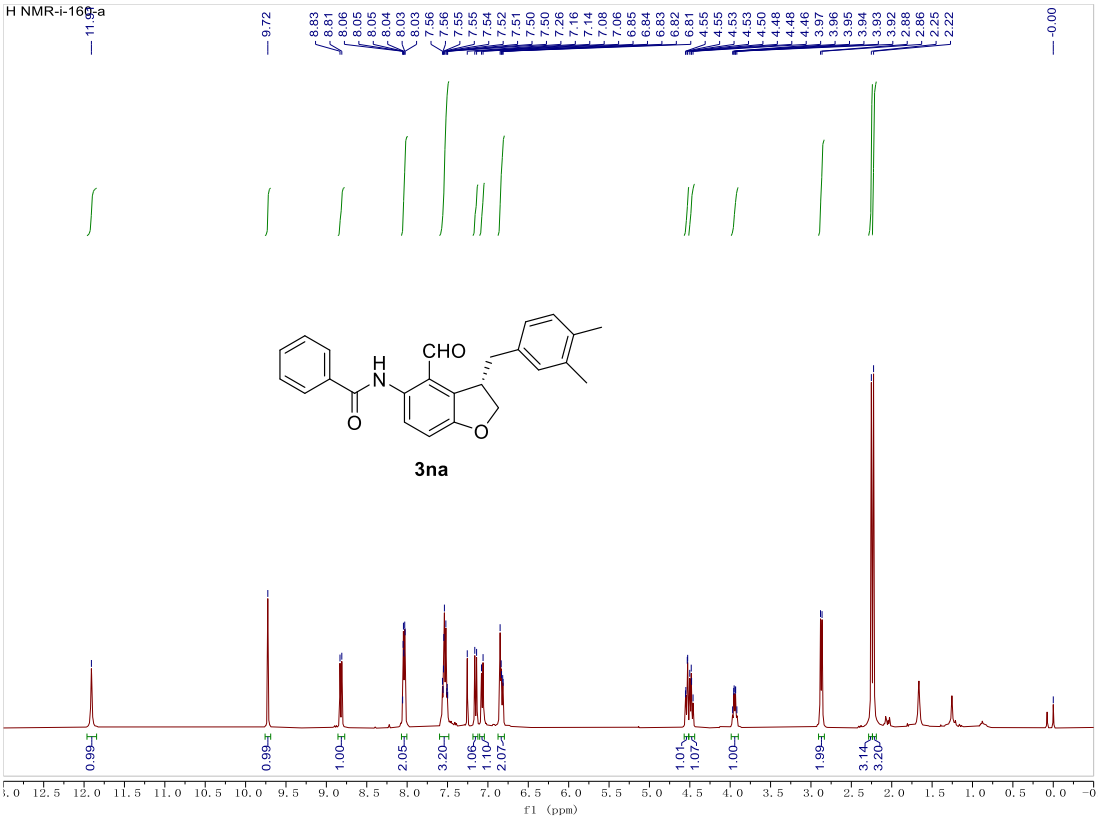


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.479	247.072	617.258	51.81	60.65	n.a.
2		22.504	229.805	400.424	48.19	39.35	n.a.
Total:			**476.878**	**1017.681**	**100.00**	**100.00**	

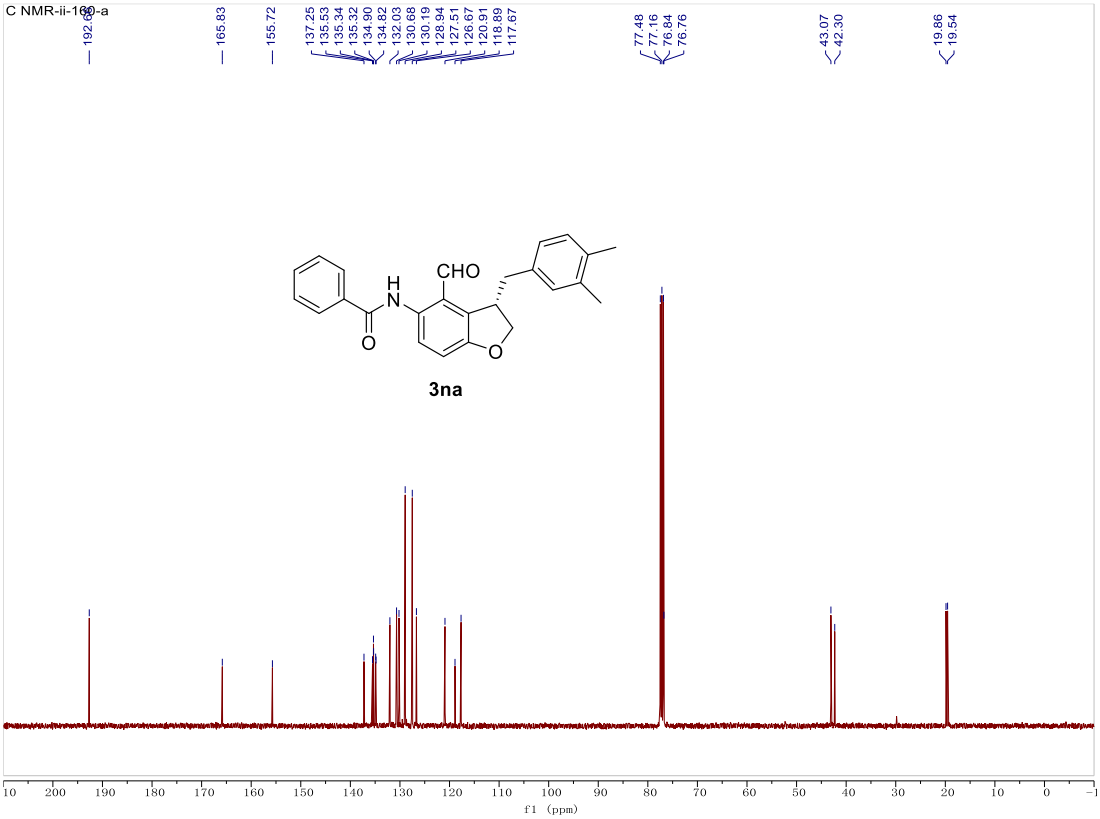


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.492	20.998	54.470	8.61	12.16	n.a.
2		22.442	222.866	393.292	91.39	87.84	n.a.
Total:			**243.864**	**447.762**	**100.00**	**100.00**	

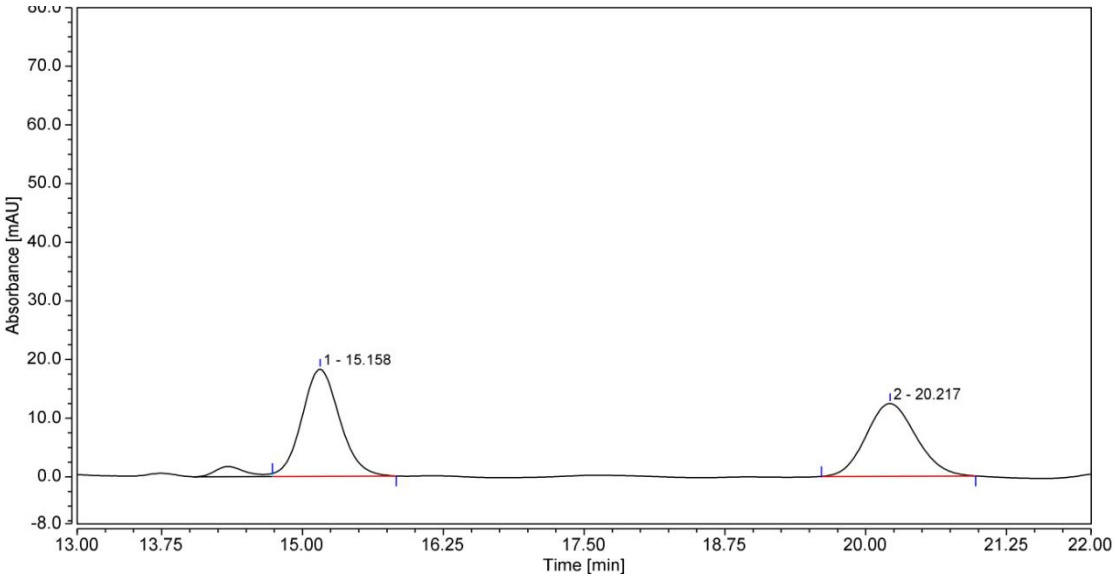
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3na**



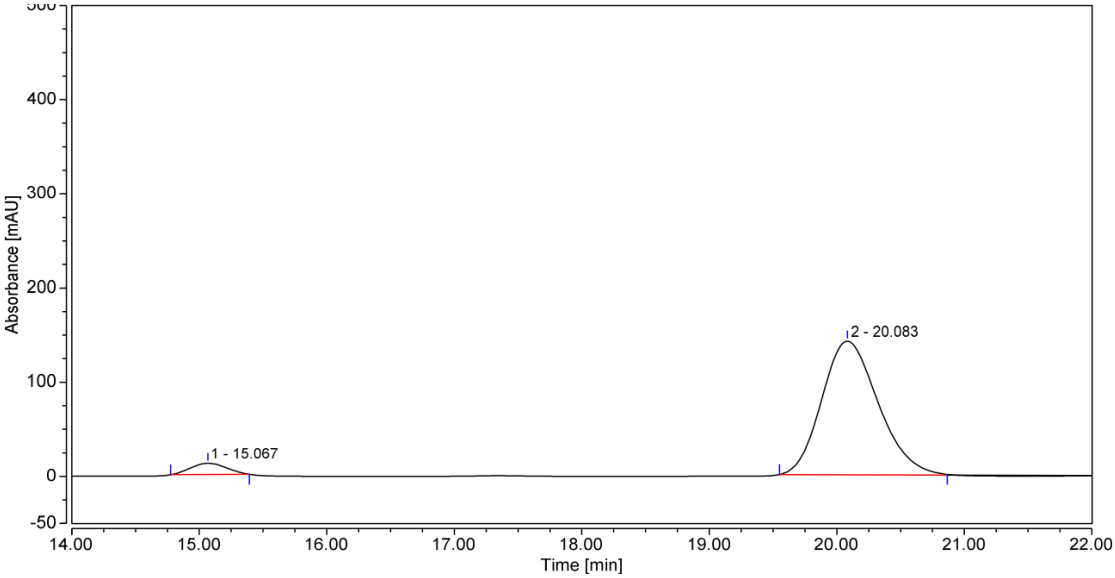
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3na**



HPLC spectra and data of compound **3na**

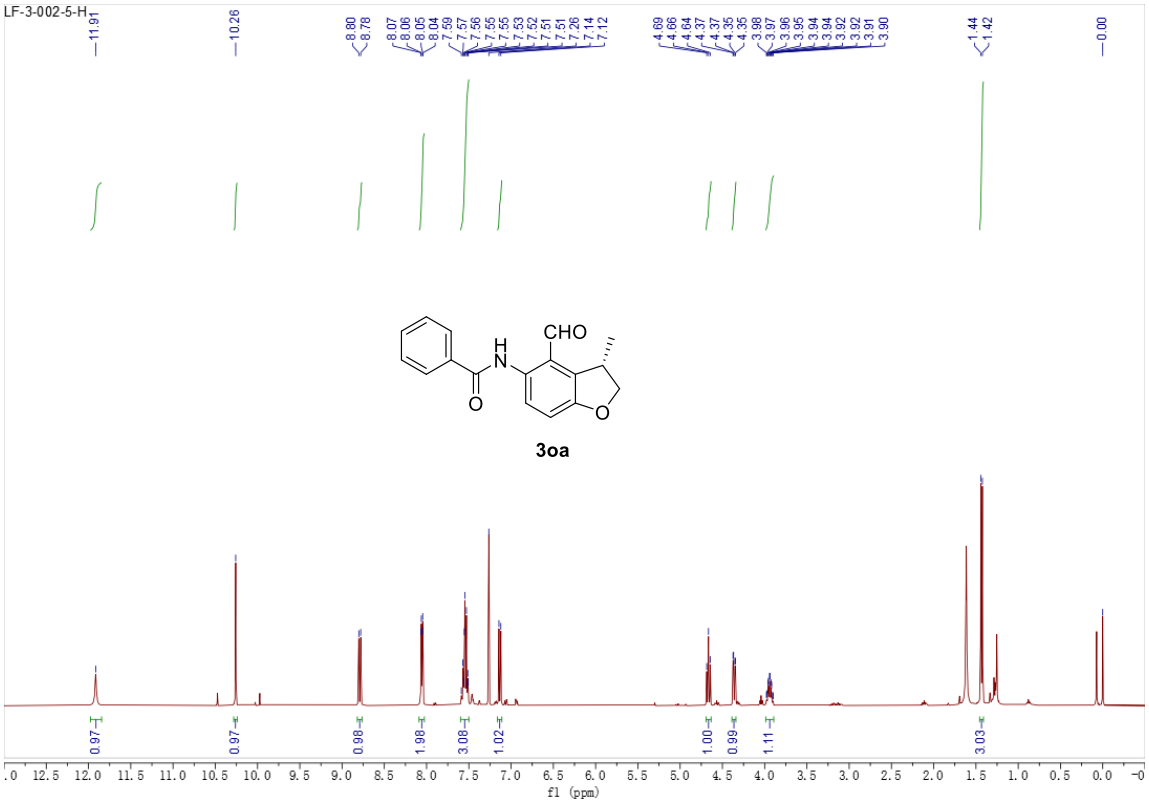


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.158	7.114	18.246	52.70	59.52	n.a.
2		20.217	6.386	12.409	47.30	40.48	n.a.
Total:			**13.500**	**30.655**	**100.00**	**100.00**	

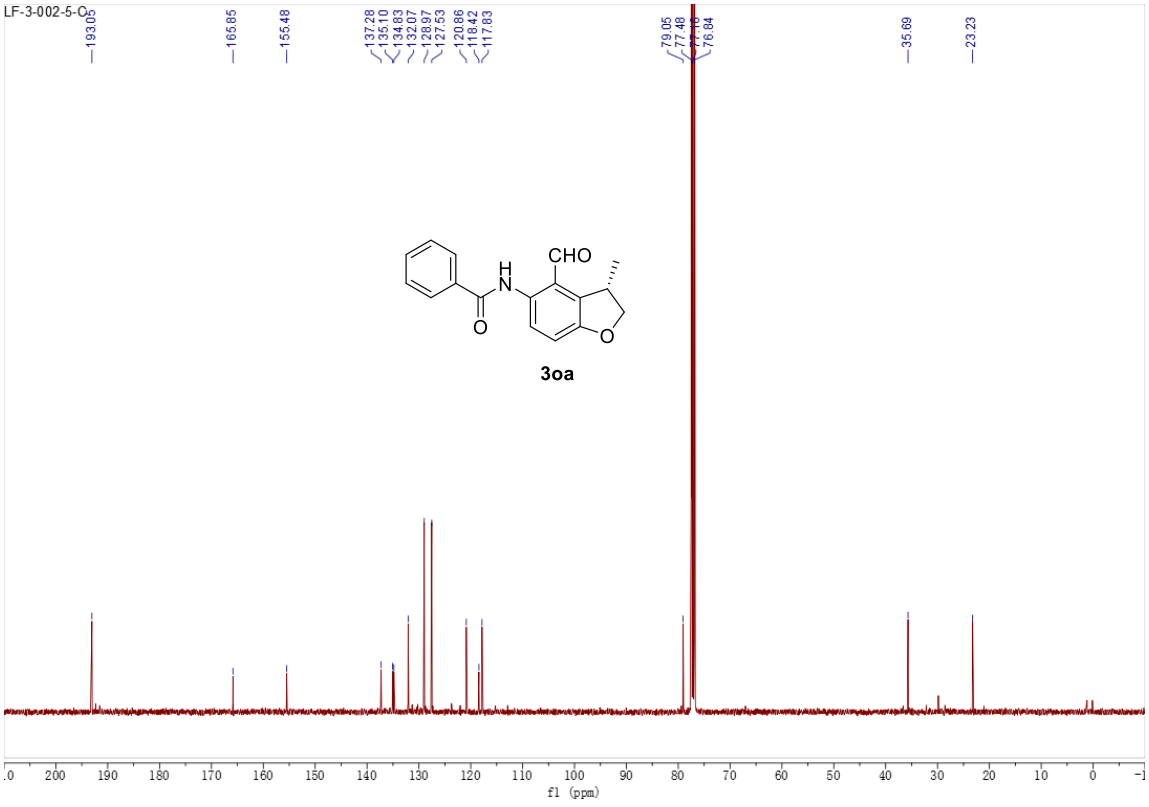


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.067	3.865	11.947	5.05	7.77	n.a.
2		20.083	72.670	141.898	94.95	92.23	n.a.
Total:			**76.534**	**153.845**	**100.00**	**100.00**	

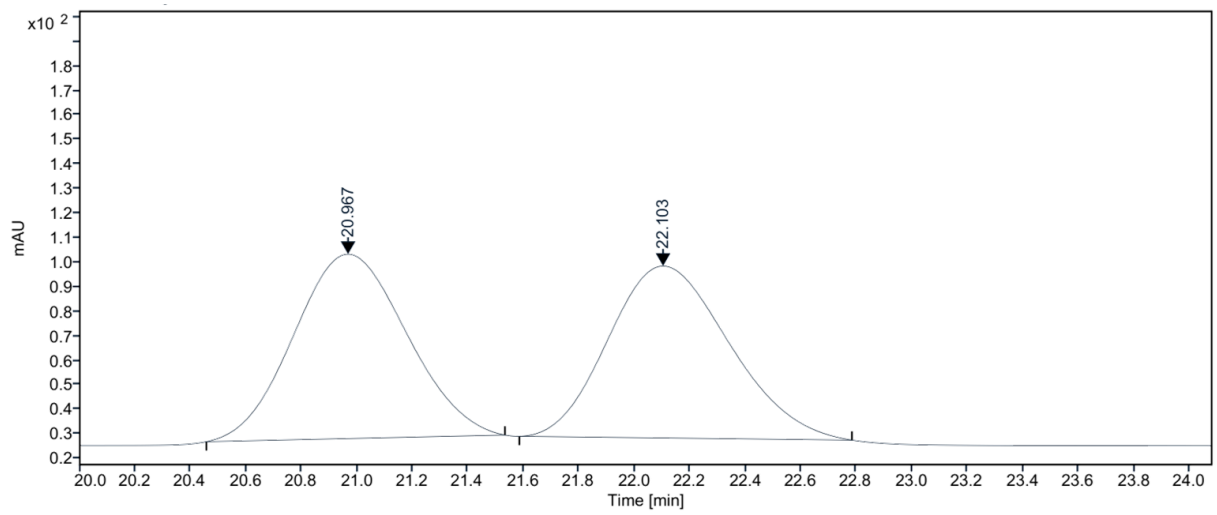
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3oa**



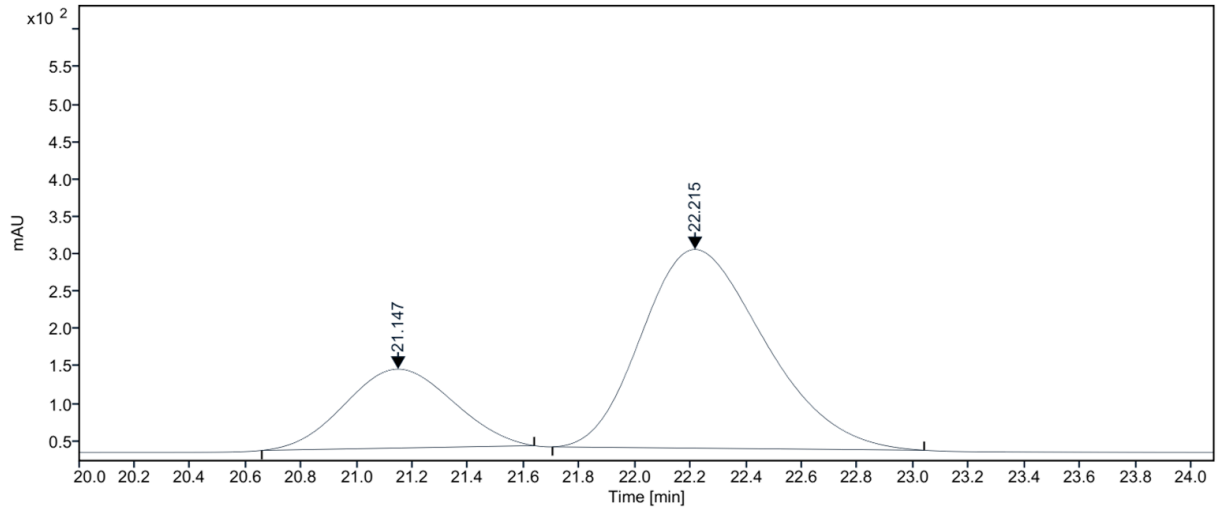
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3oa**



HPLC spectra and data of compound **3oa**

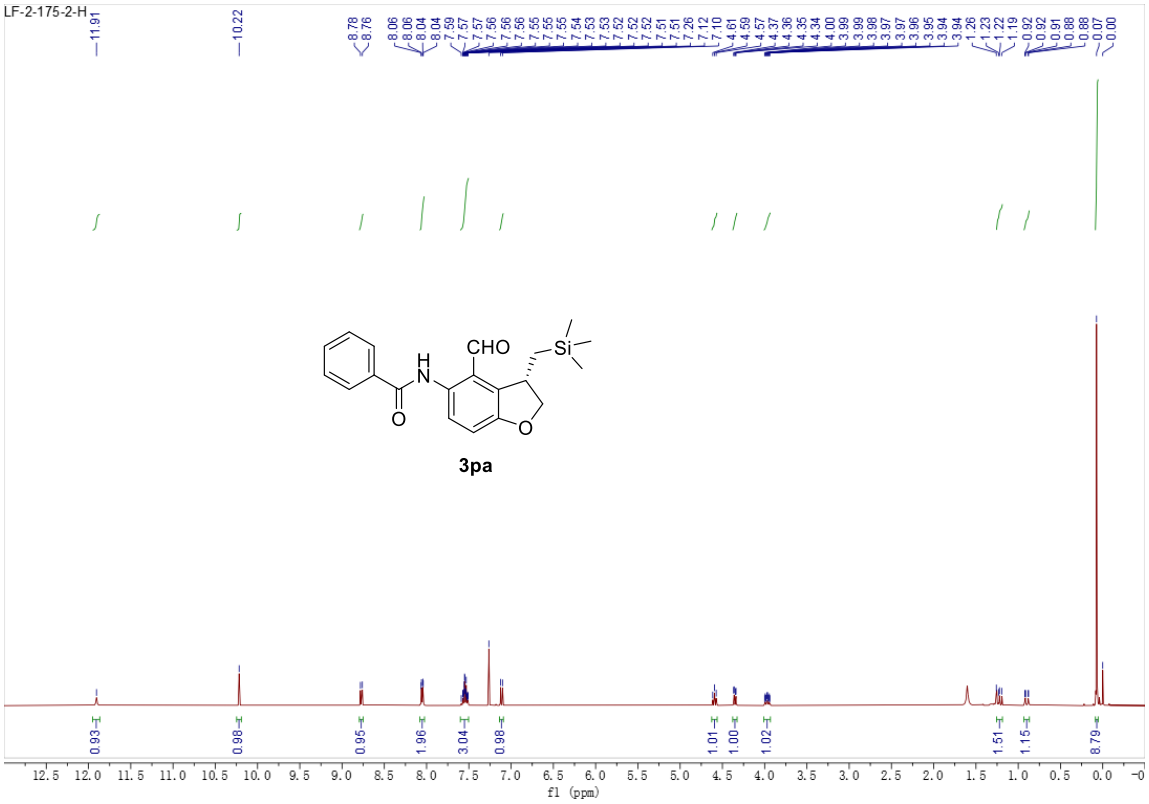


RT [min]	Height	Height%	Area	Area%
20.967	75.194	51.74	2124.55021	50.01
22.103	70.123	48.26	2123.67054	49.99

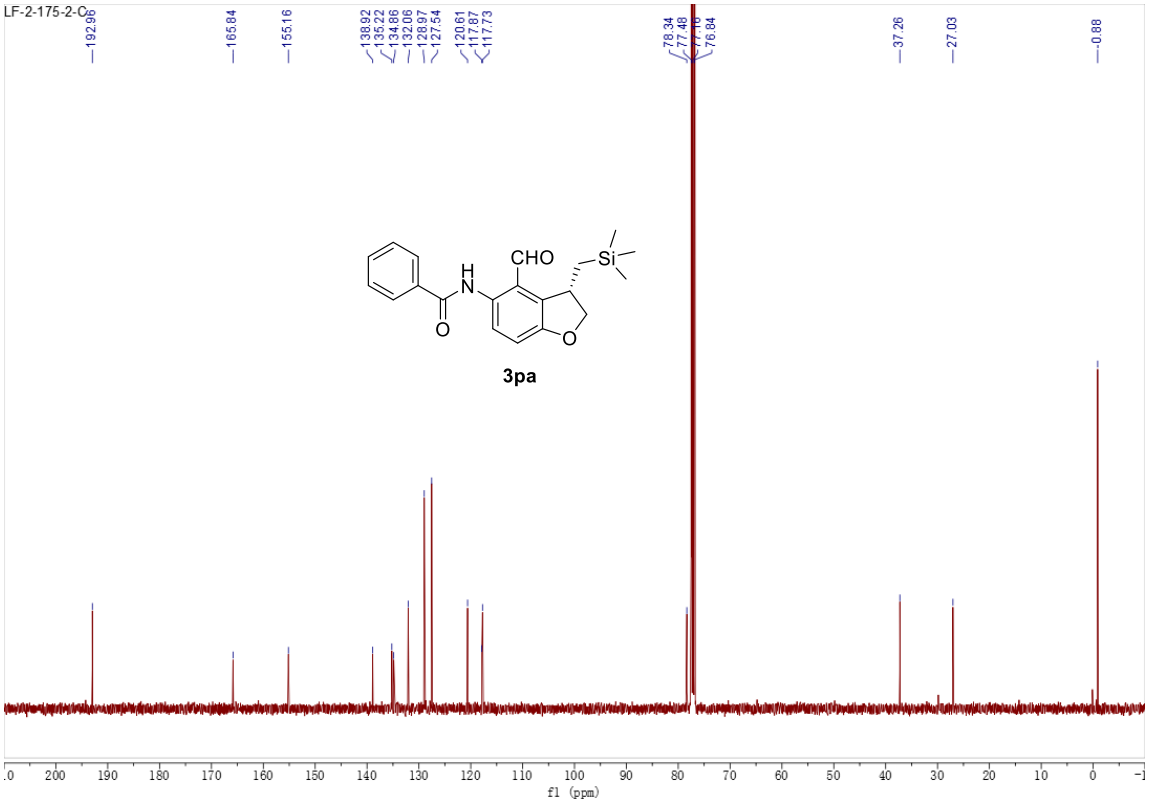


RT [min]	Height	Height%	Area	Area%
21.147	99.553	28.29	2662.33526	25.63
22.215	252.332	71.71	7723.34120	74.37

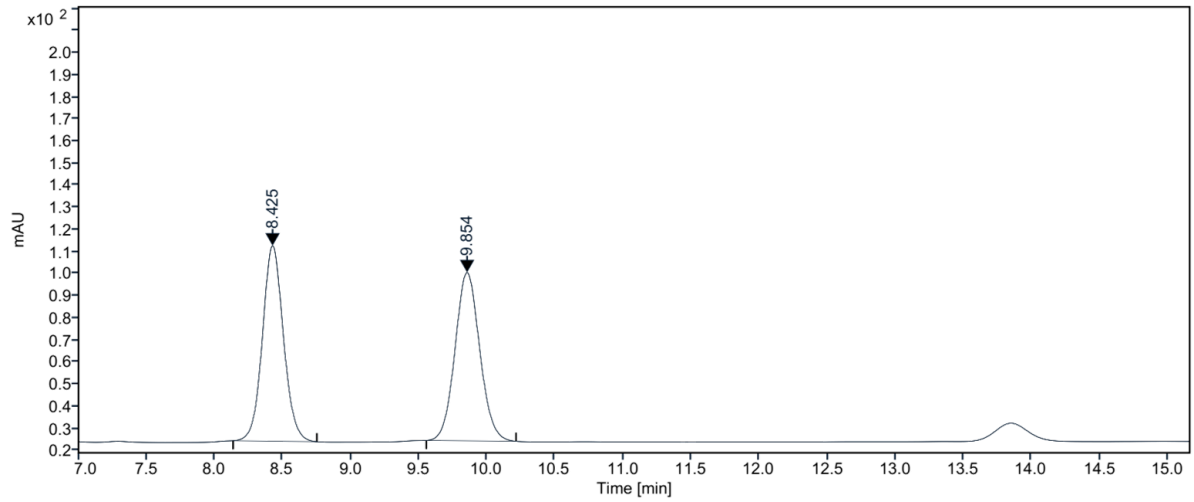
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3pa**



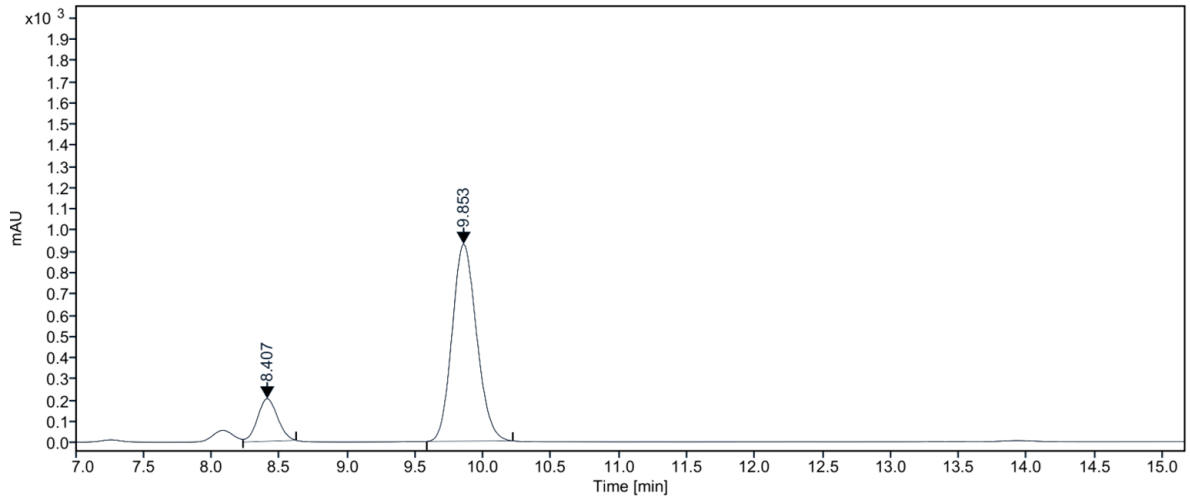
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3pa**



HPLC spectra and data of compound **3pa**

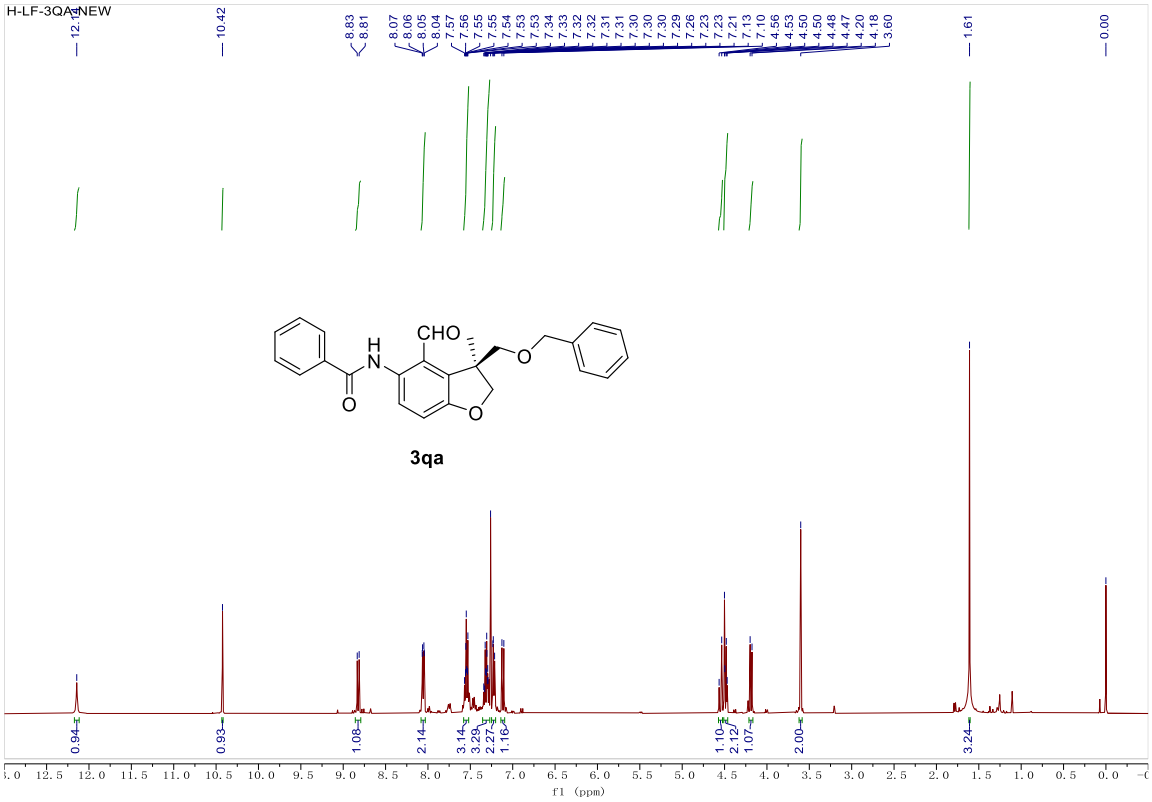


RT [min]	Height	Height%	Area	Area%
8.425	88.466	53.73	949.70314	49.71
9.854	76.197	46.27	960.96245	50.29

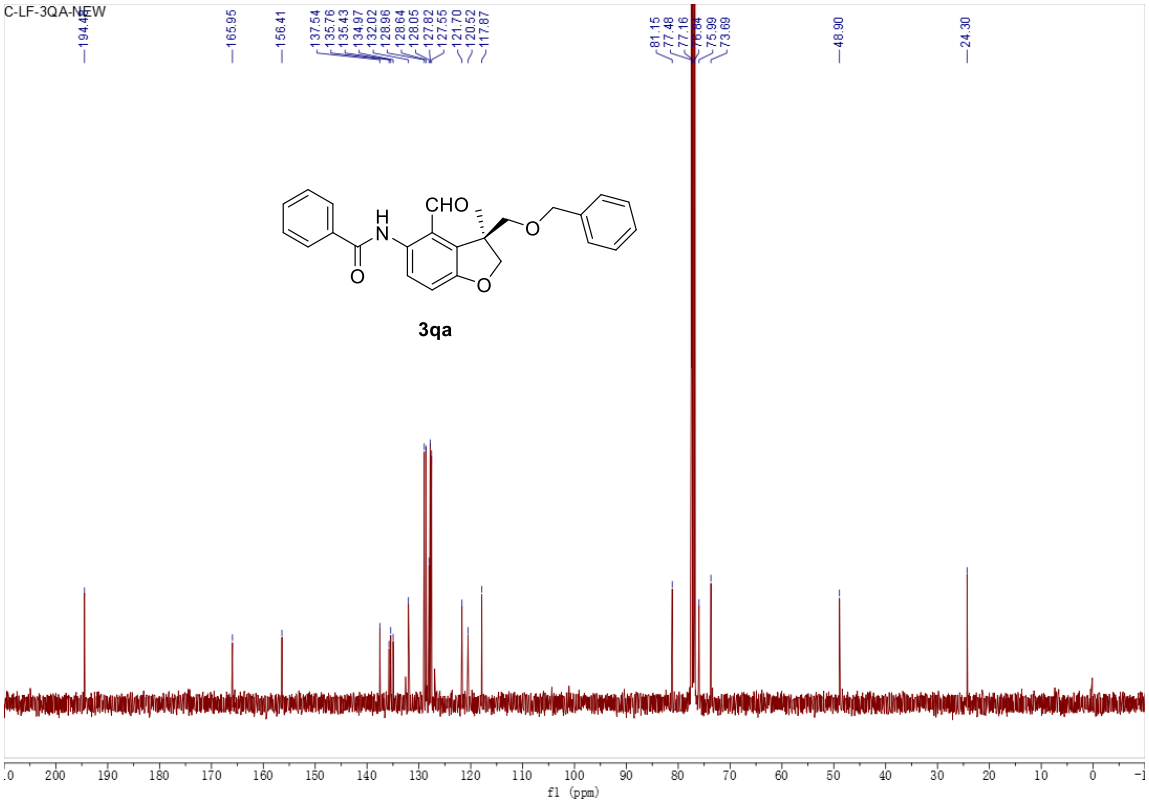


RT [min]	Height	Height%	Area	Area%
8.407	200.224	17.75	2063.29536	15.03
9.853	927.748	82.25	11664.83442	84.97

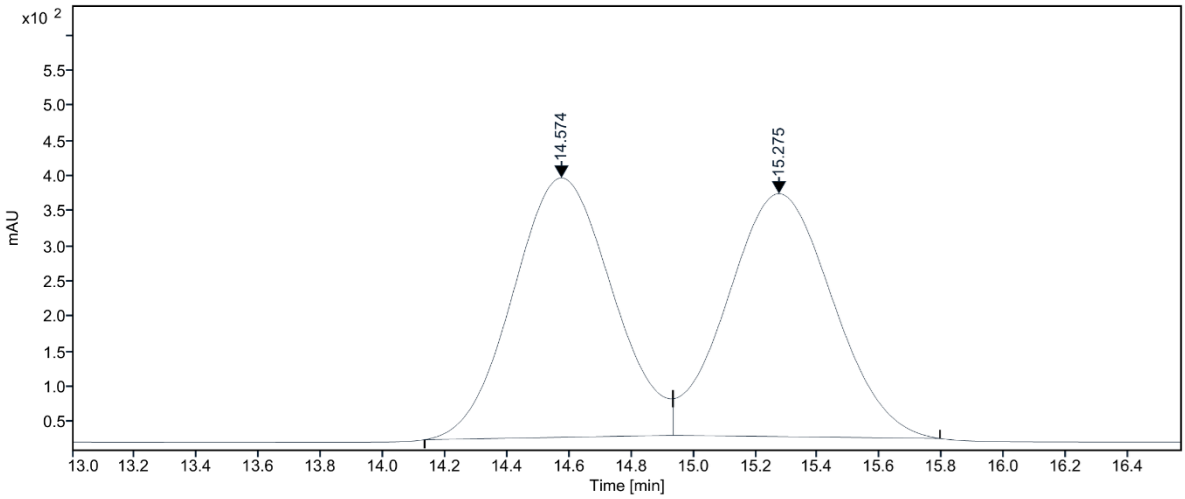
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3qa**



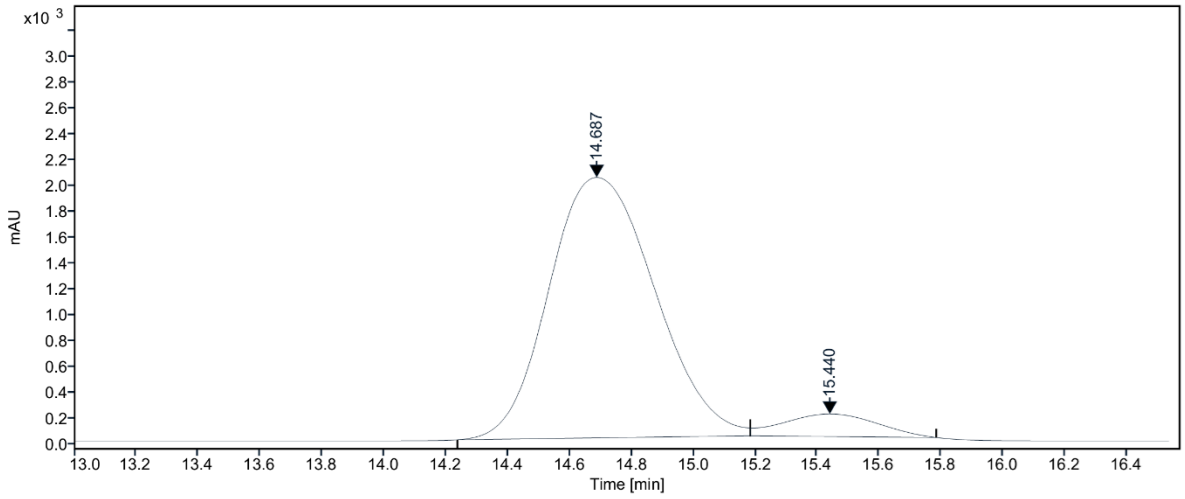
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3qa**



HPLC spectra and data of compound **3qa**

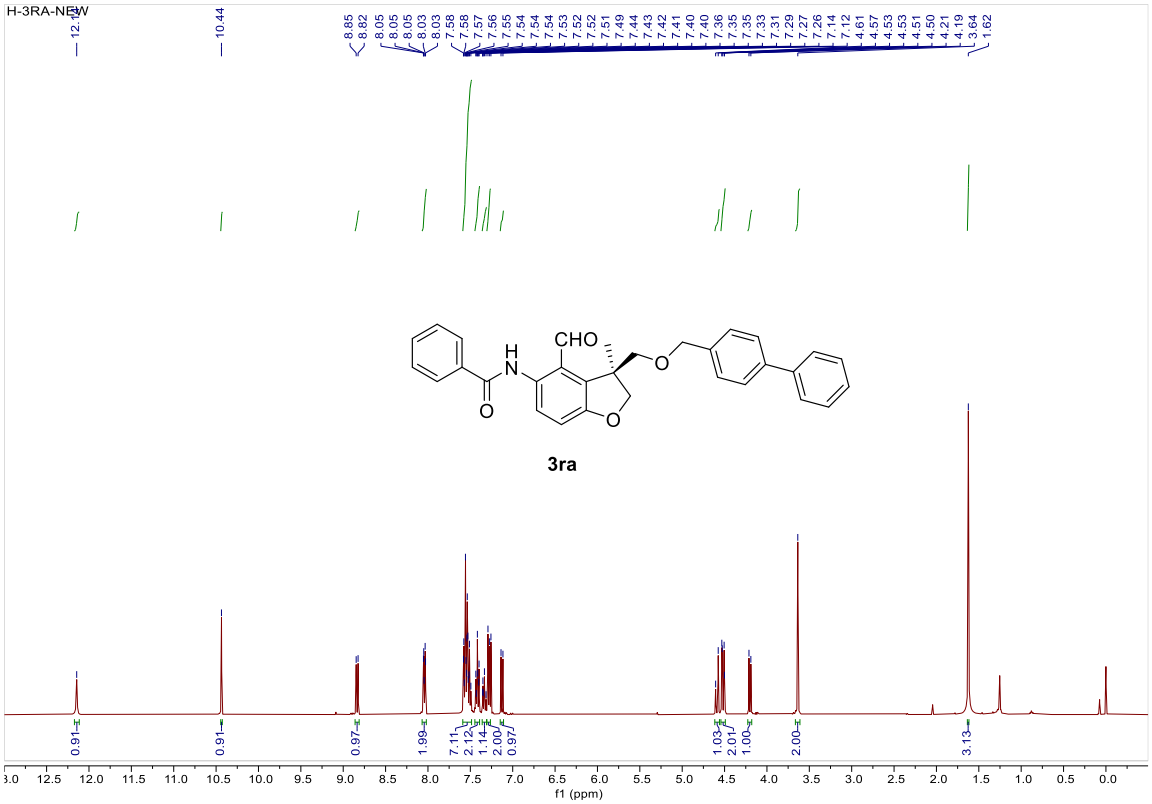


RT [min]	Height	Height%	Area	Area%
14.574	368.844	51.64	8214.09034	50.09
15.275	345.387	48.36	8185.59269	49.91

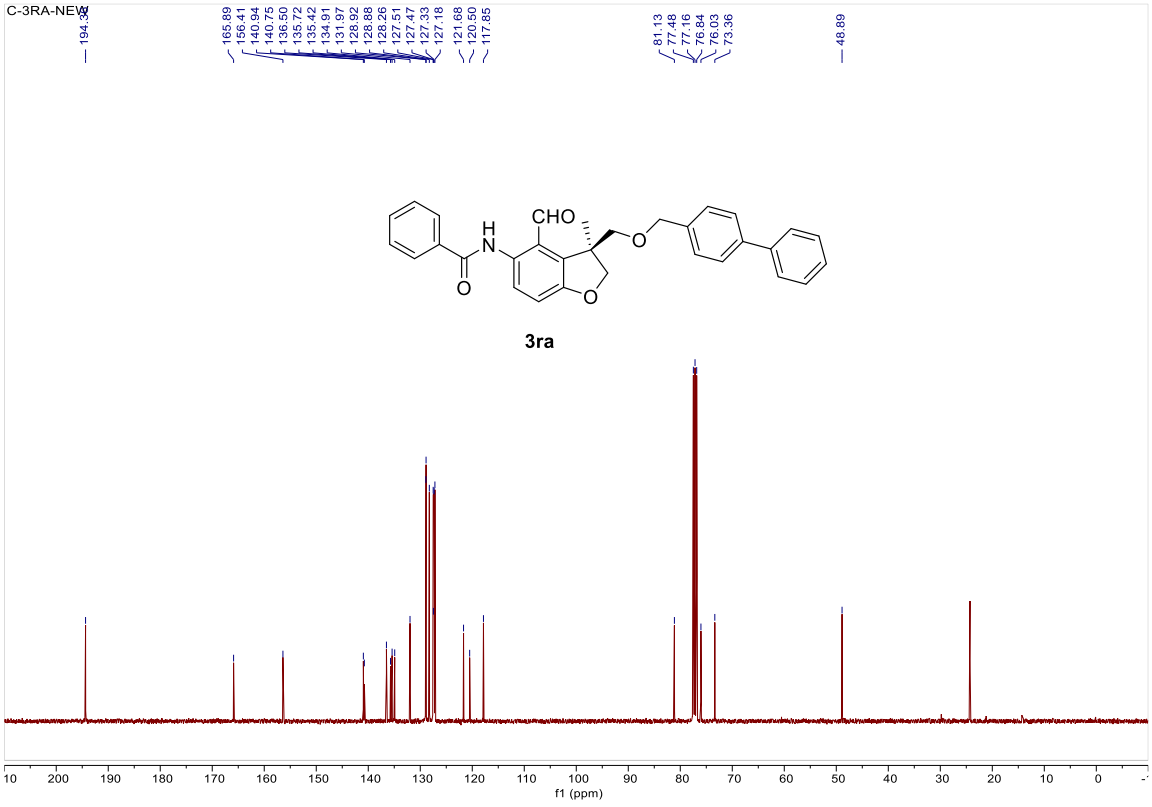


RT [min]	Height	Height%	Area	Area%
14.687	2023.190	92.03	48075.82572	92.85
15.440	175.164	7.97	3700.88422	7.15

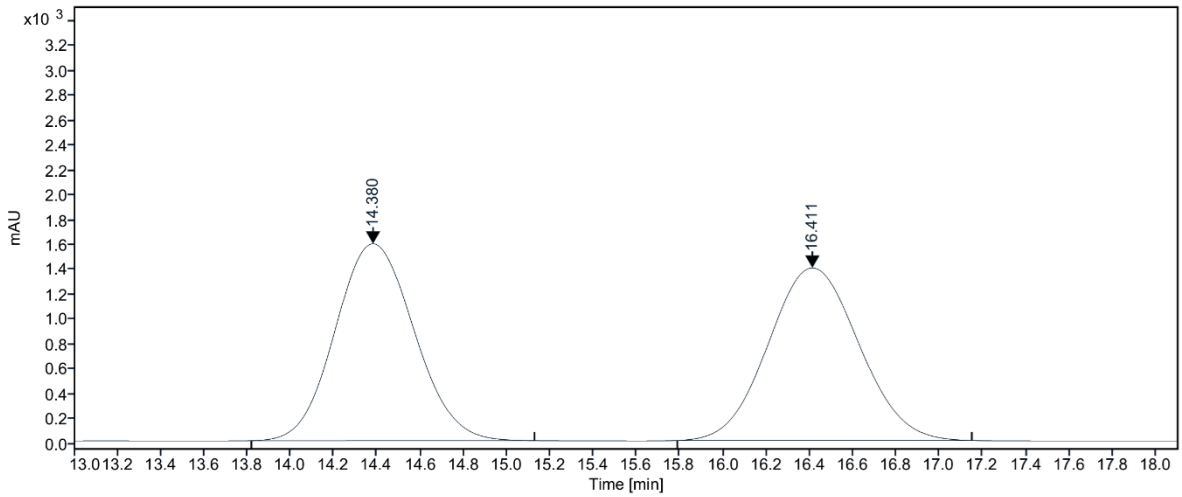
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ra**



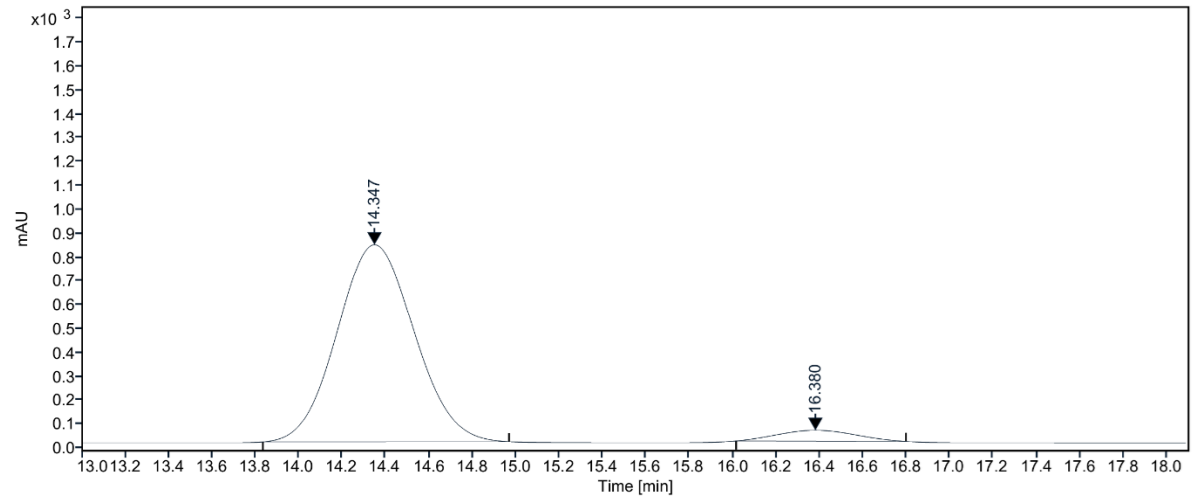
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ra**



HPLC spectra and data of compound **3ra**

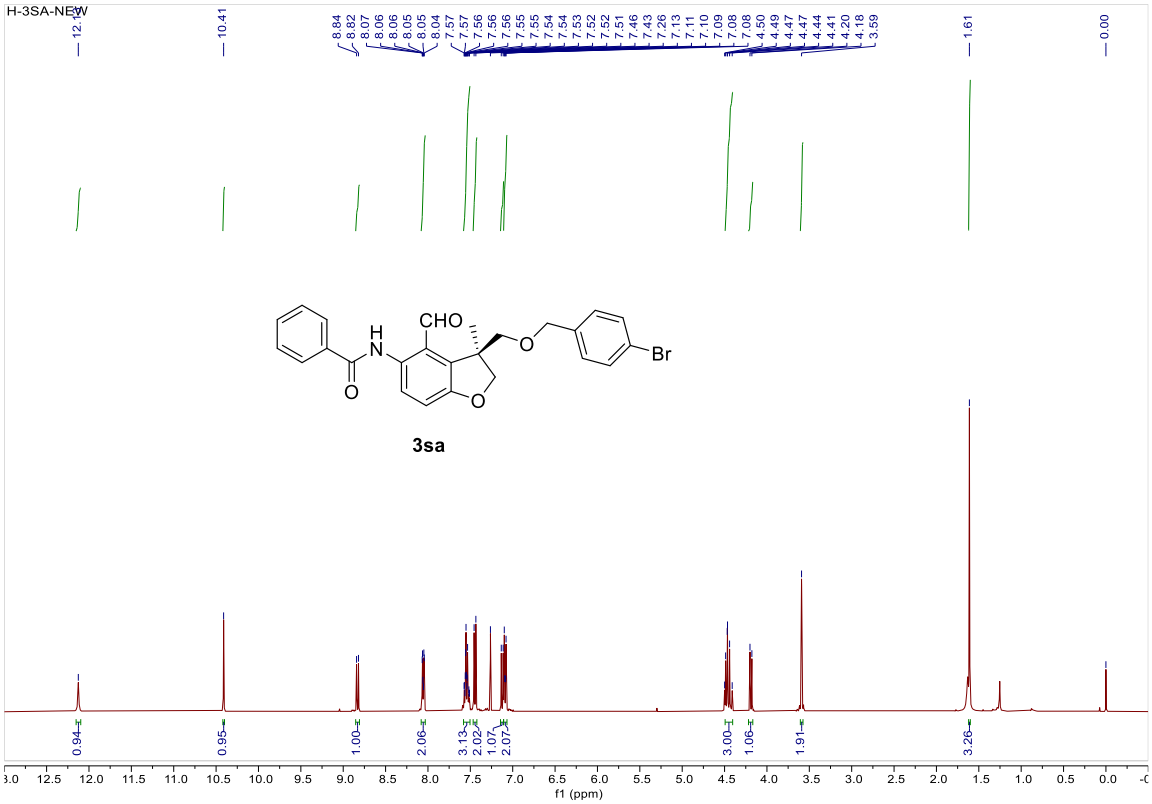


RT [min]	Height	Height%	Area	Area%
14.380	1584.672	53.29	40282.68269	49.86
16.411	1388.728	46.71	40515.44733	50.14

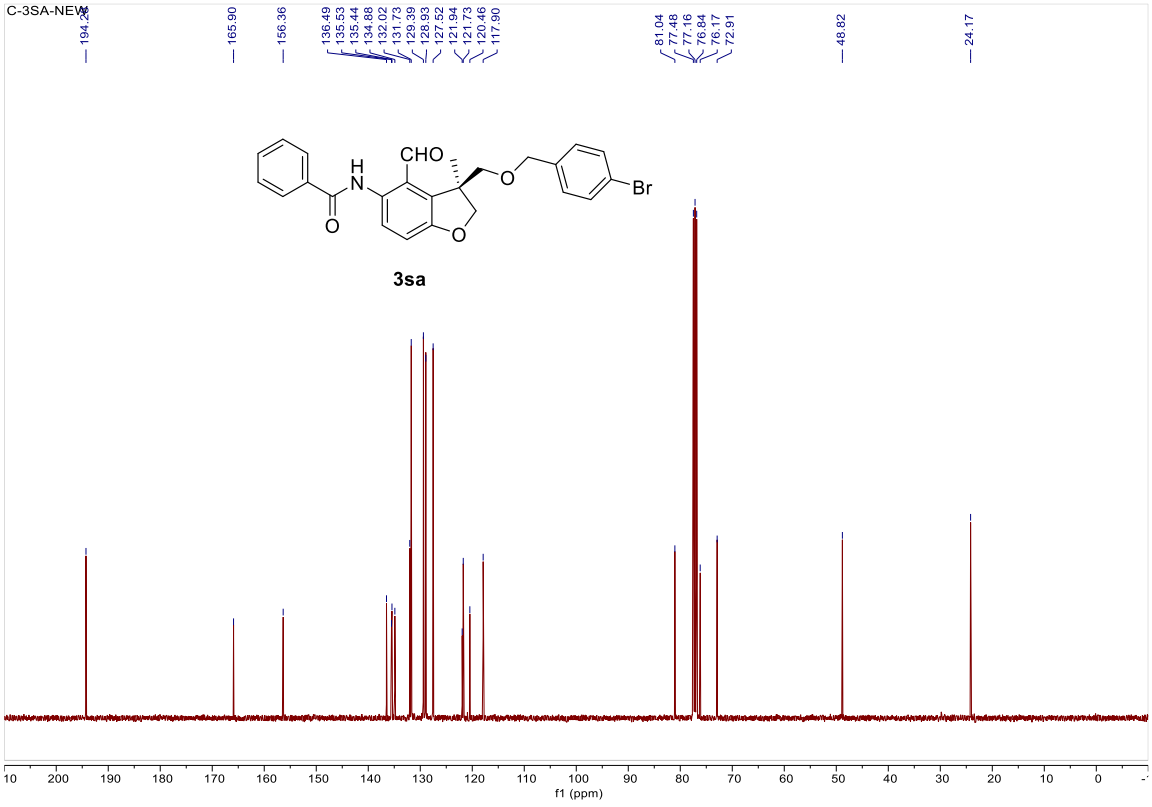


RT [min]	Height	Height%	Area	Area%
14.347	825.554	94.76	20424.59700	94.75
16.380	45.684	5.24	1130.61033	5.25

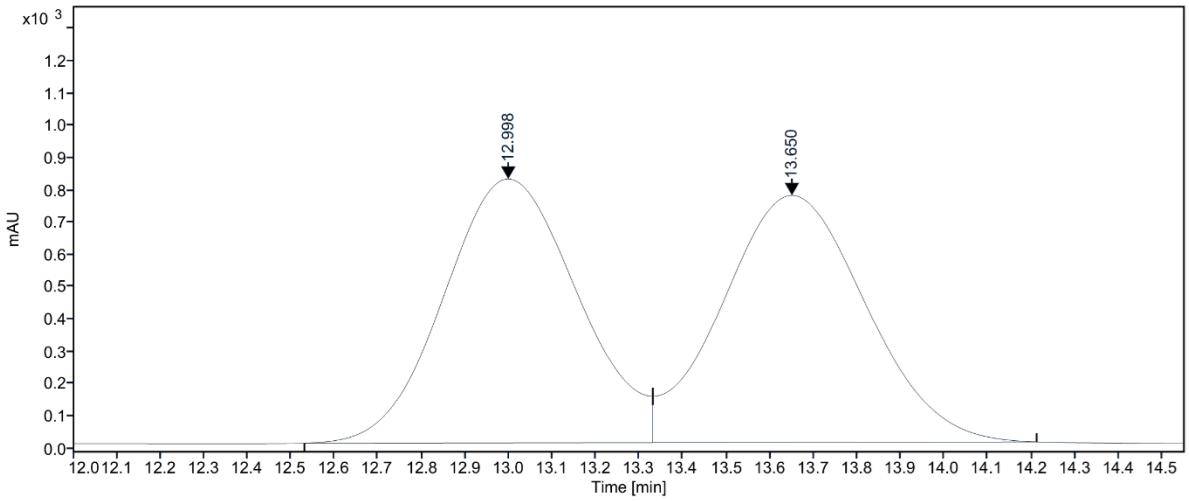
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3sa**



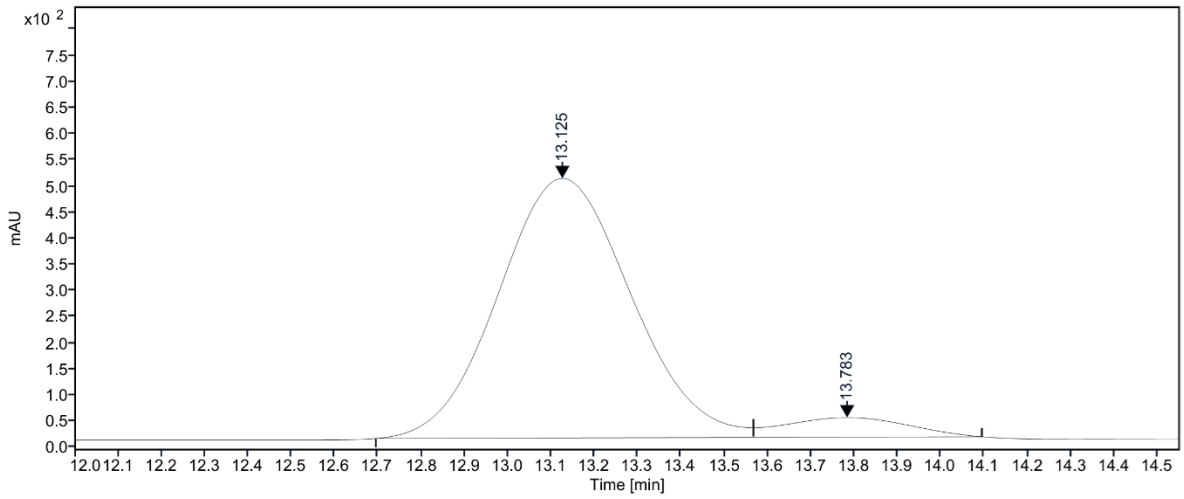
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3sa**



HPLC spectra and data of compound **3sa**

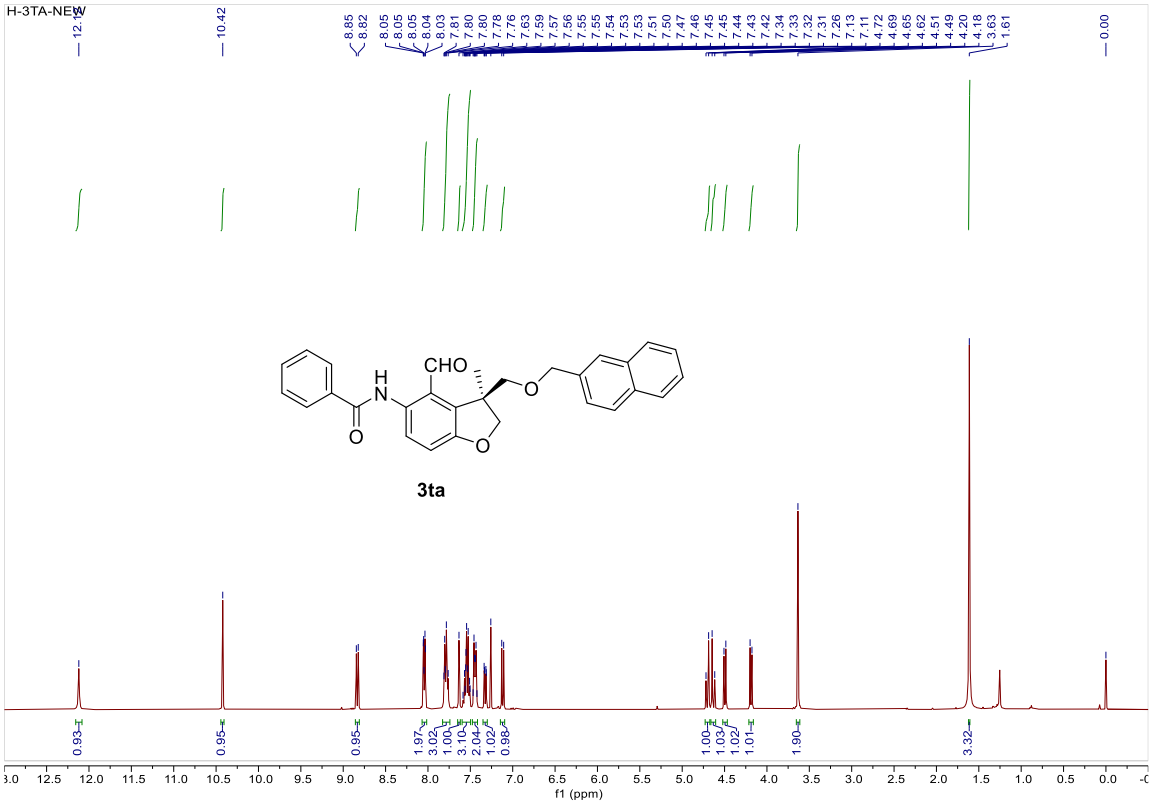


RT [min]	Height	Height%	Area	Area%
12.998	818.475	51.65	17484.81784	49.81
13.650	766.044	48.35	17617.69826	50.19

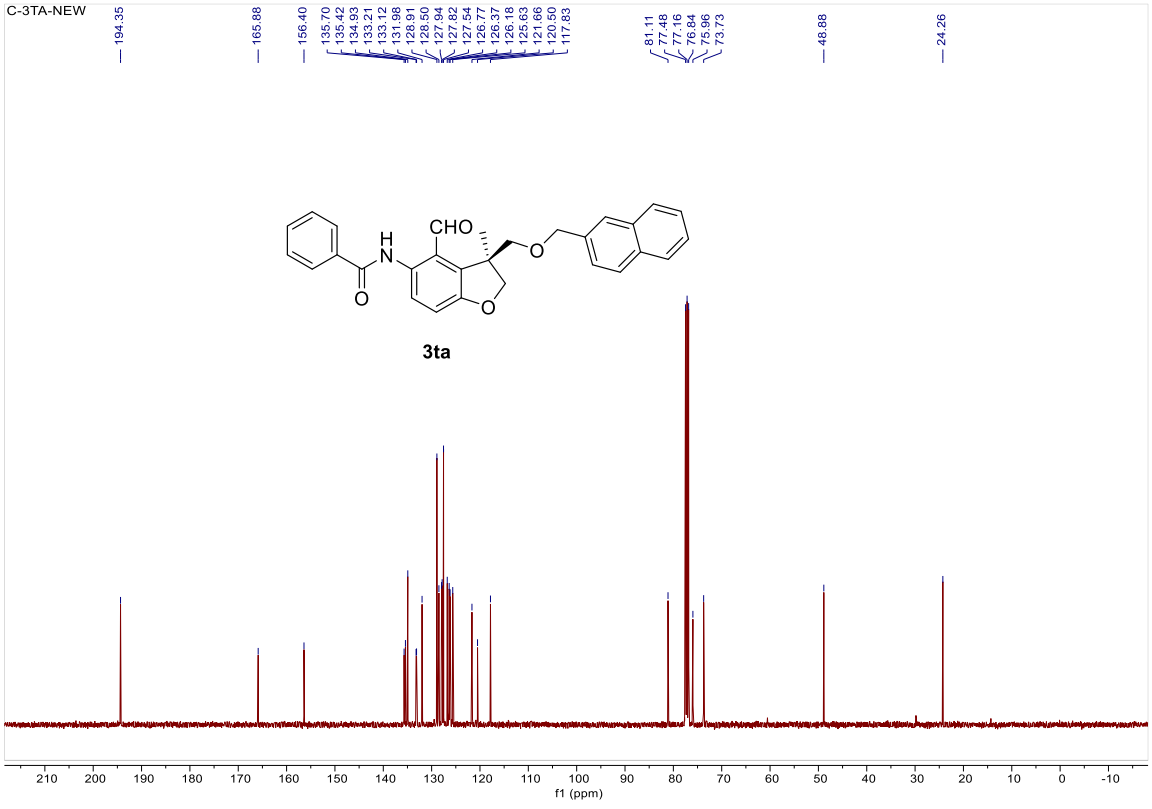


RT [min]	Height	Height%	Area	Area%
13.125	496.670	92.99	10560.05529	93.46
13.783	37.455	7.01	738.54995	6.54

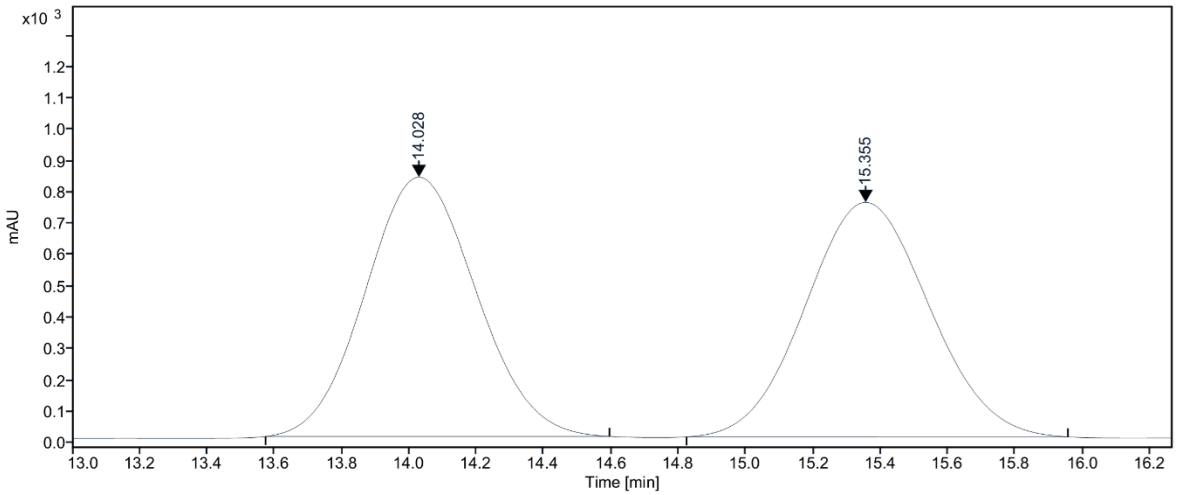
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ta**



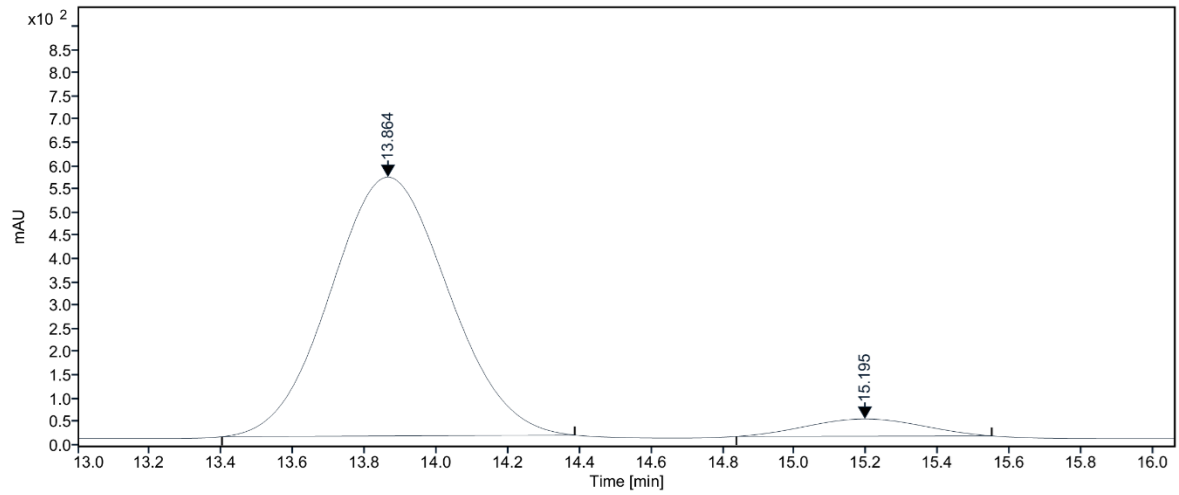
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ta**



HPLC spectra and data of compound **3ta**

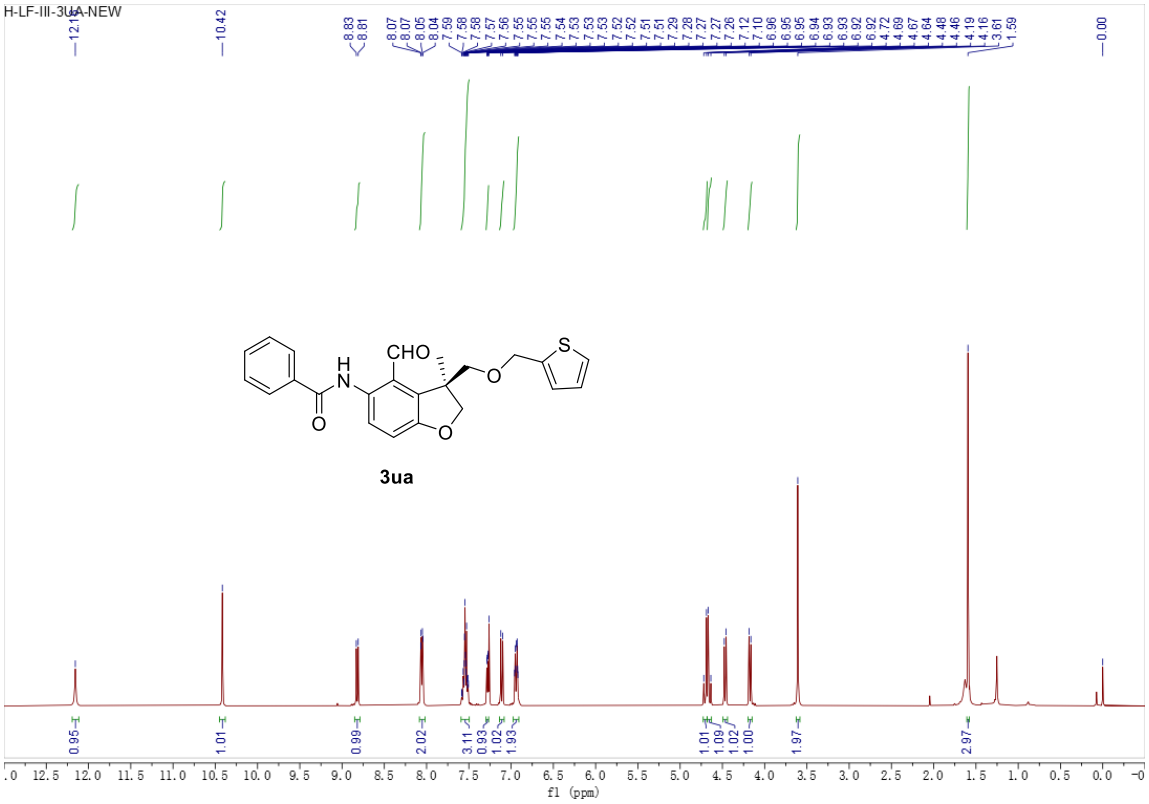


RT [min]	Height	Height%	Area	Area%
14.028	827.989	52.50	18987.04679	49.79
15.355	749.137	47.50	19148.00343	50.21

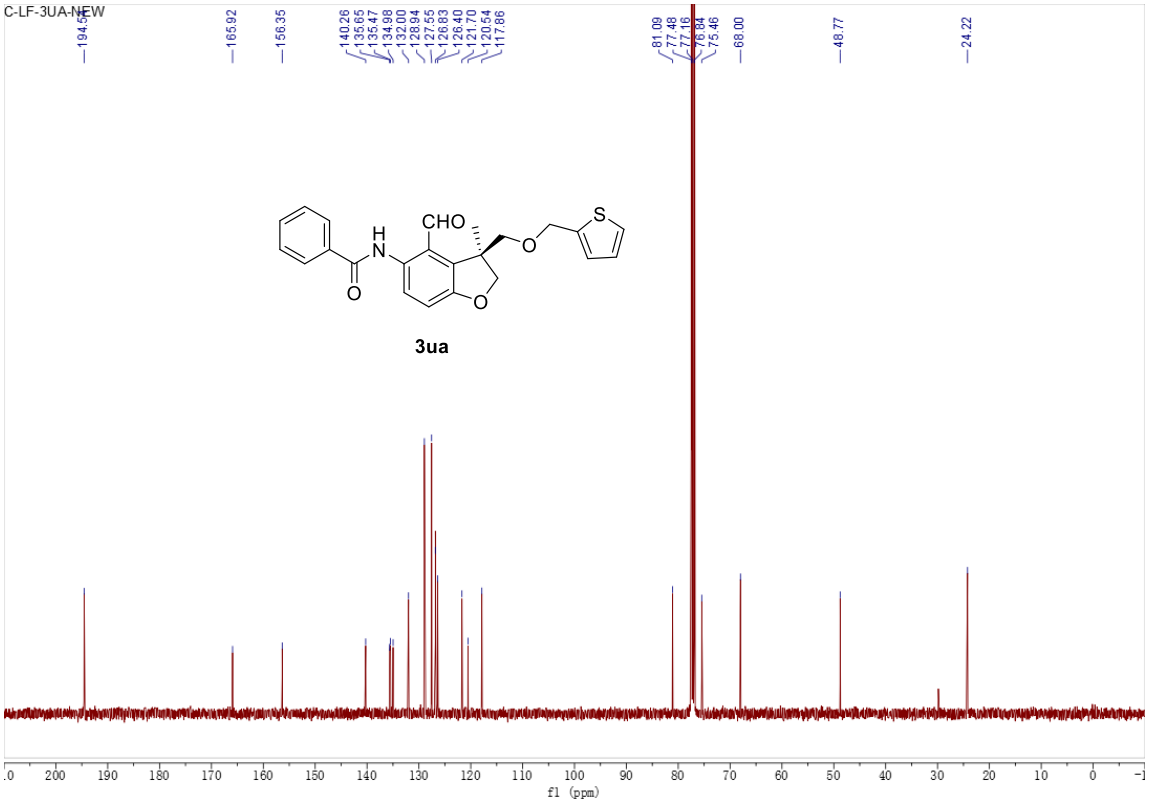


RT [min]	Height	Height%	Area	Area%
13.864	556.469	93.75	12737.52164	93.89
15.195	37.073	6.25	828.28386	6.11

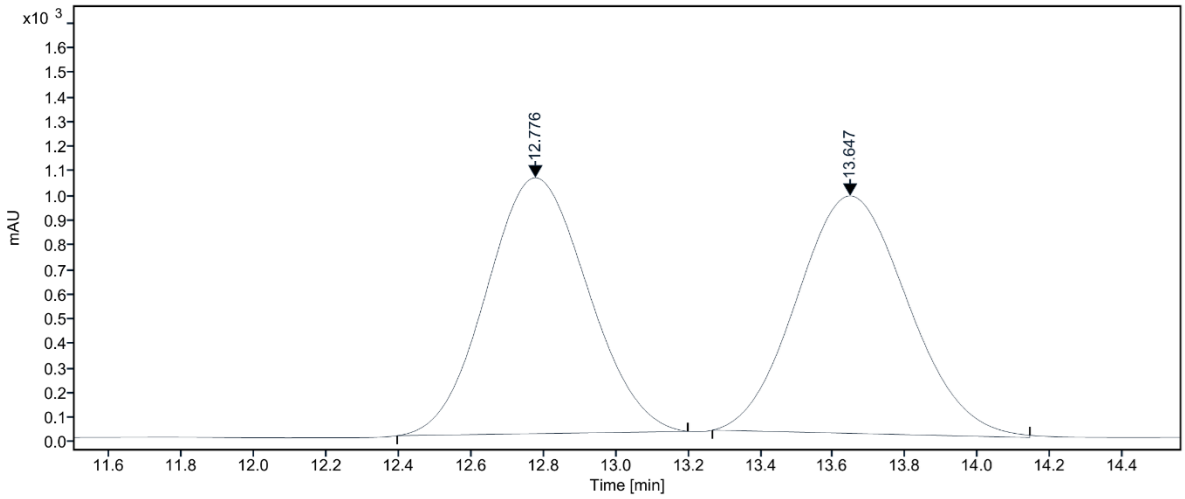
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ua**



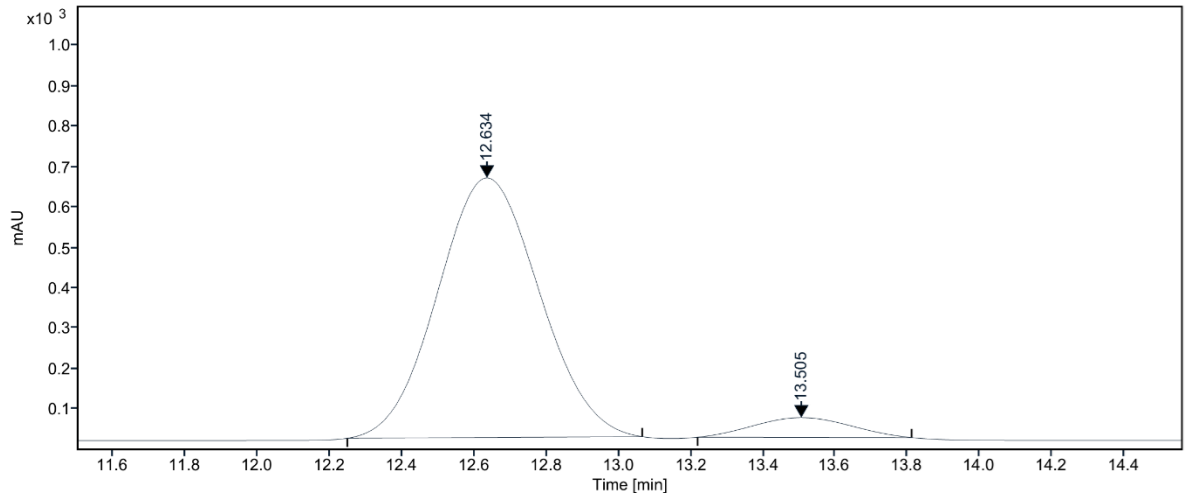
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ua**



HPLC spectra and data of compound **3ua**

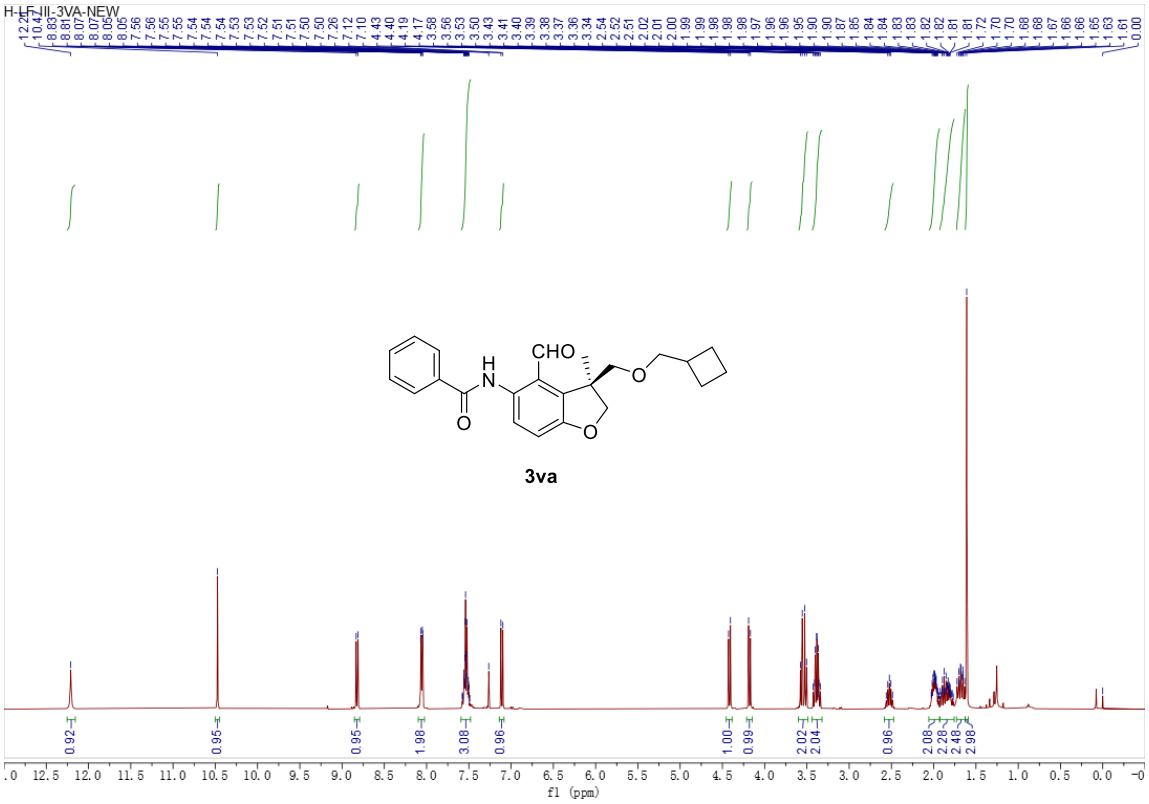


RT [min]	Height	Height%	Area	Area%
12.776	1038.551	51.87	20201.76839	49.53
13.647	963.668	48.13	20581.33836	50.47

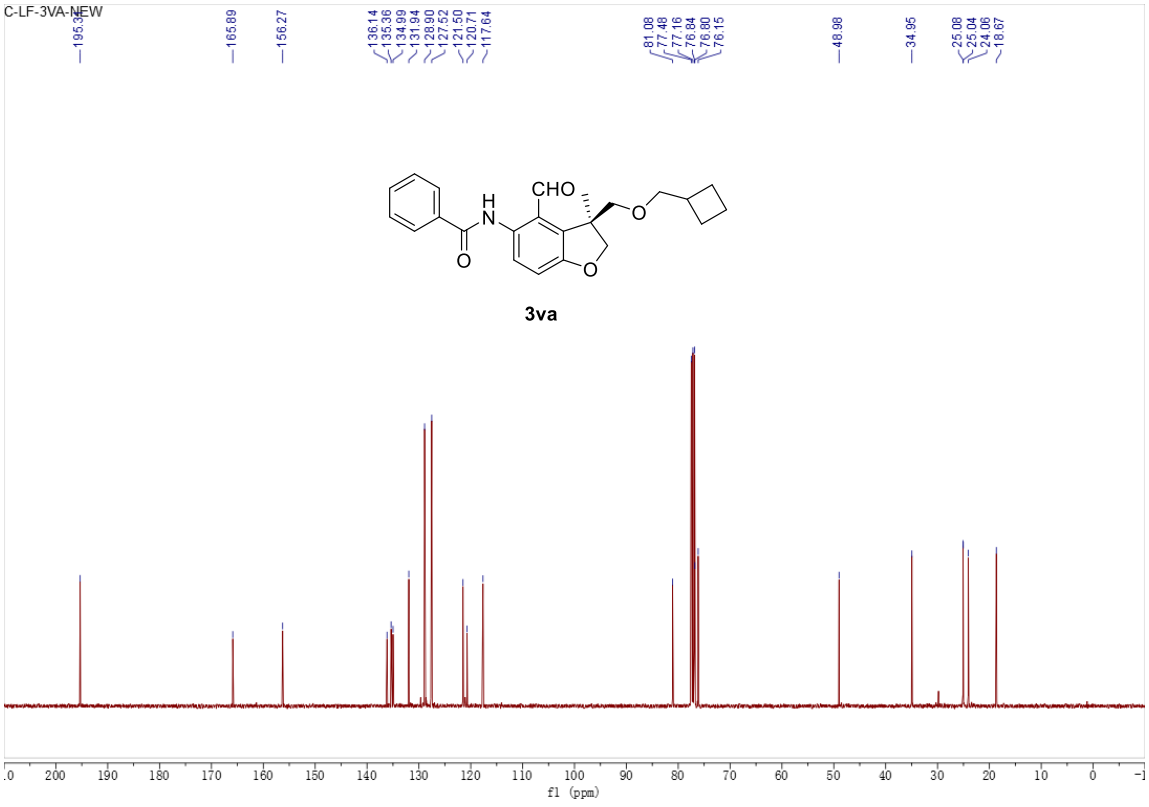


RT [min]	Height	Height%	Area	Area%
12.634	642.114	92.94	12570.84940	93.26
13.505	48.798	7.06	908.76650	6.74

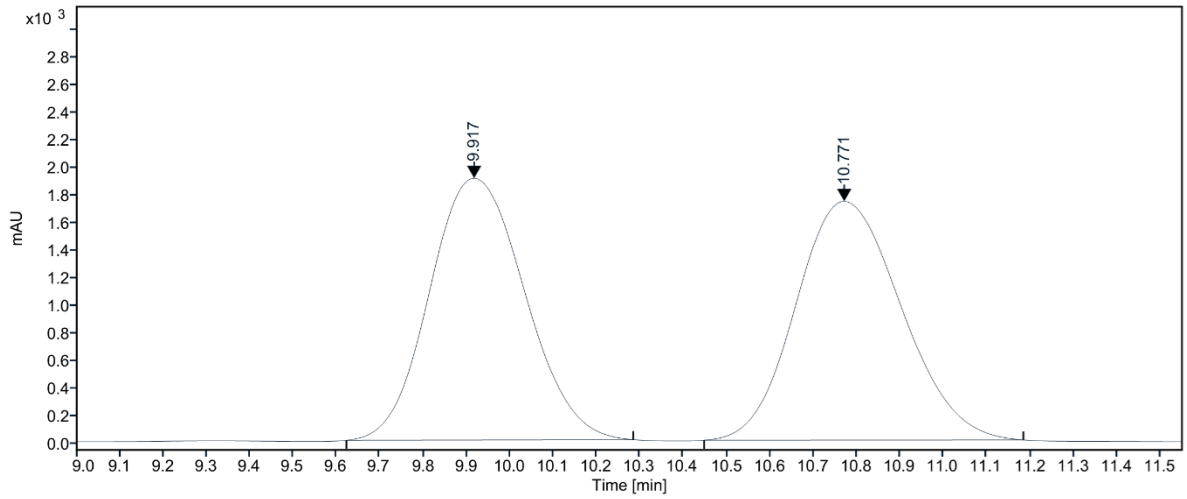
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3va**



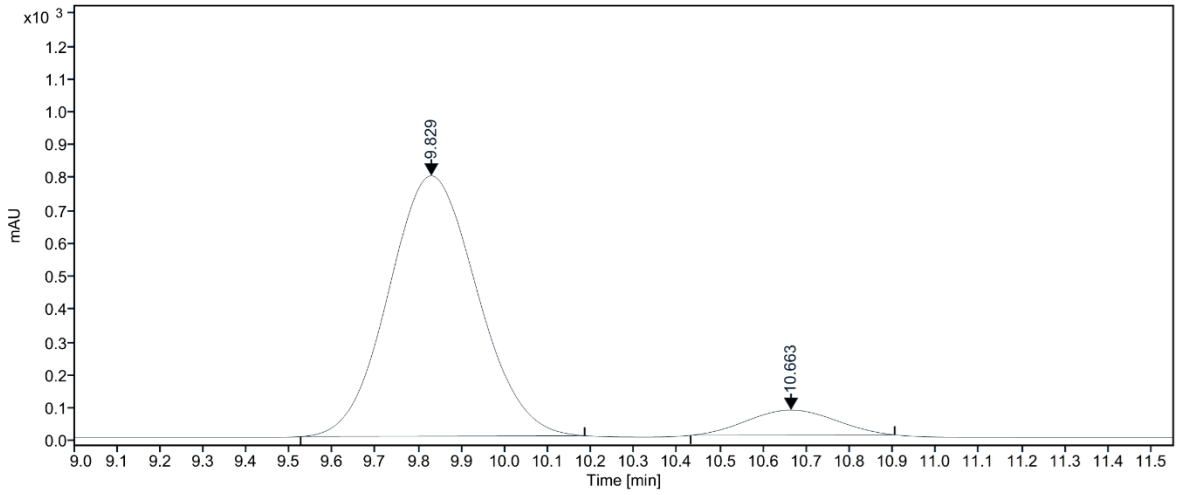
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3va**



HPLC spectra and data of compound **3va**

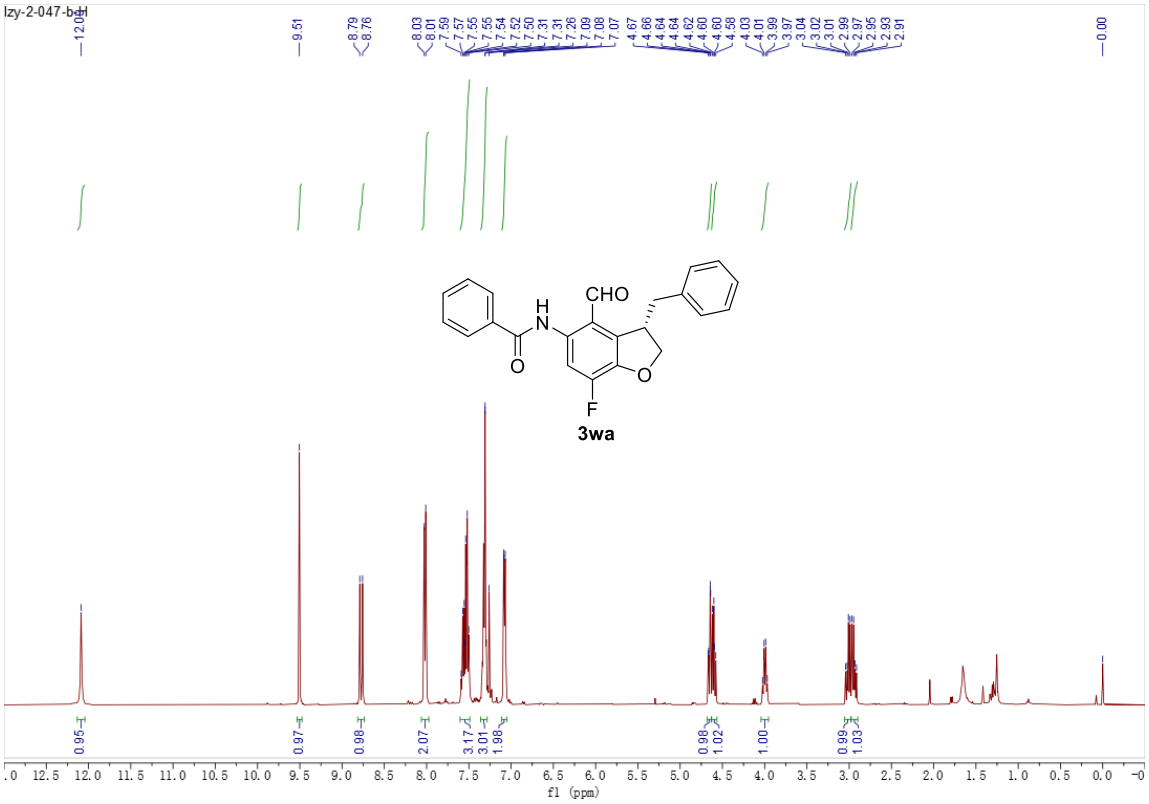


RT [min]	Height	Height%	Area	Area%
9.917	1901.956	52.30	29003.41422	49.78
10.771	1734.871	47.70	29259.35333	50.22

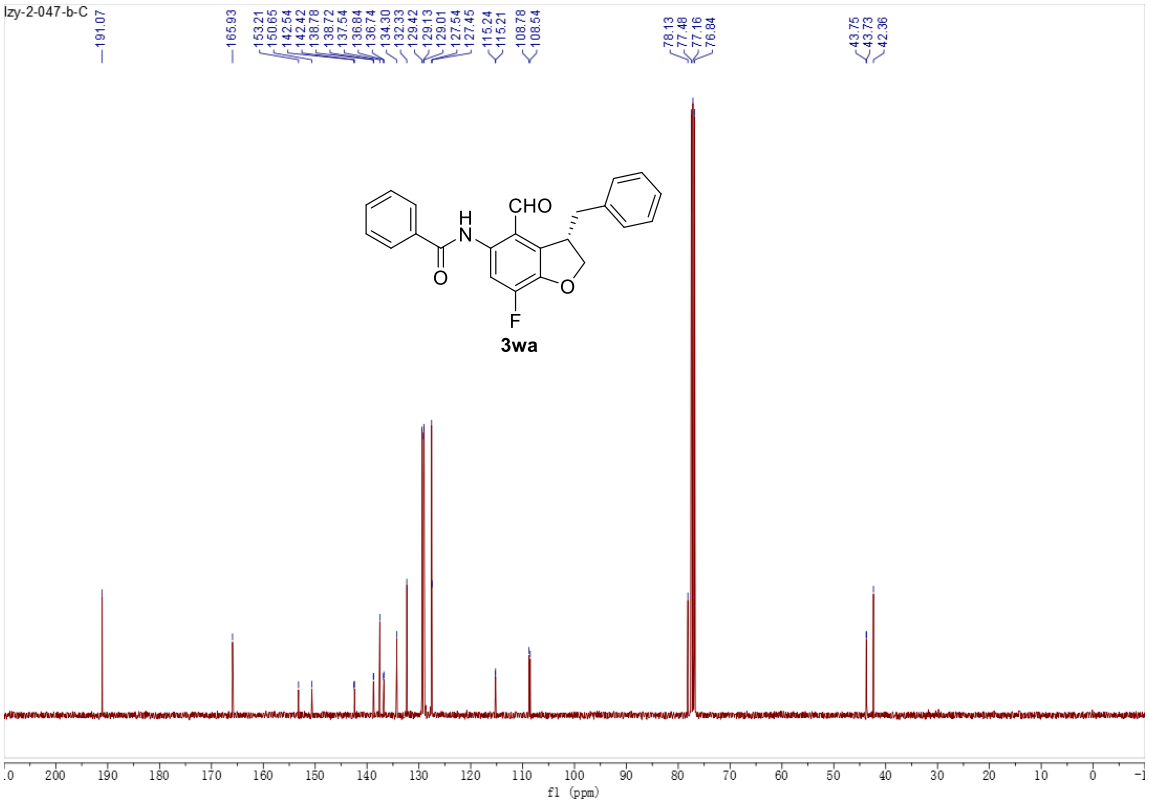


RT [min]	Height	Height%	Area	Area%
9.829	792.165	91.23	11316.13086	91.26
10.663	76.147	8.77	1084.28134	8.74

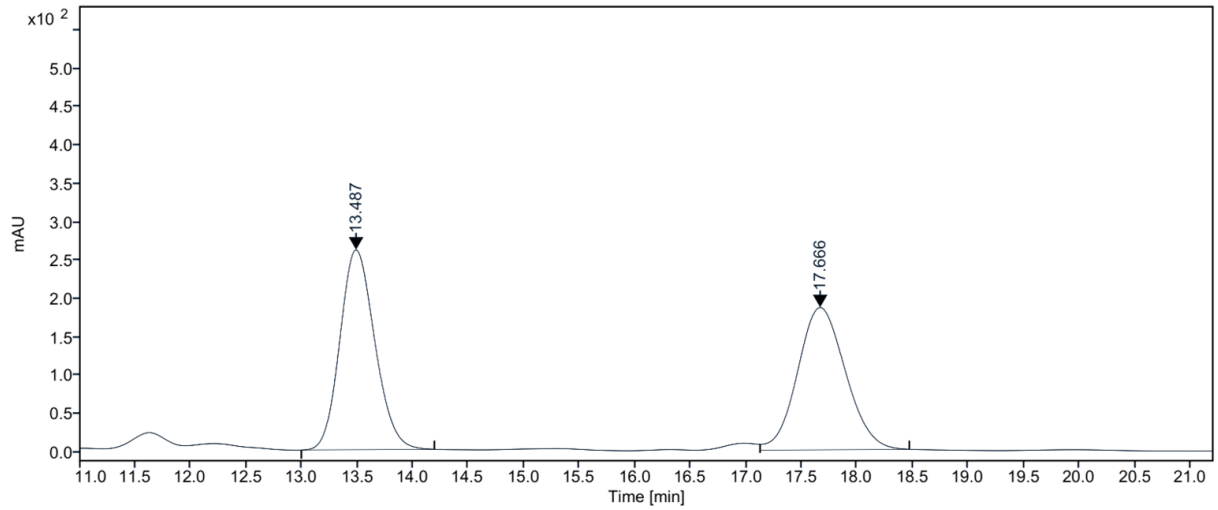
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3wa**



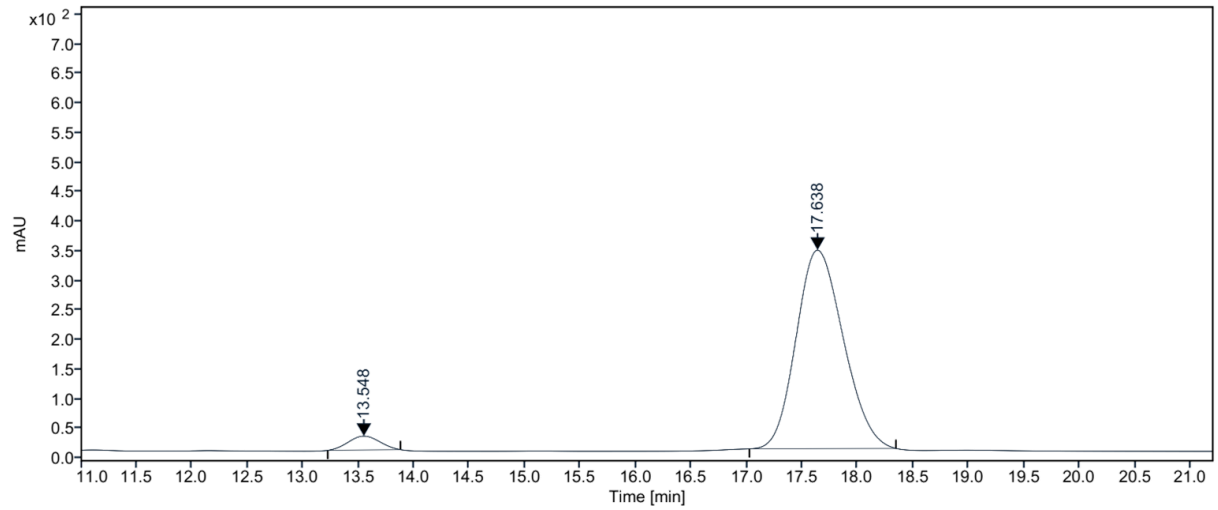
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3wa**



HPLC spectra and data of compound **3wa**

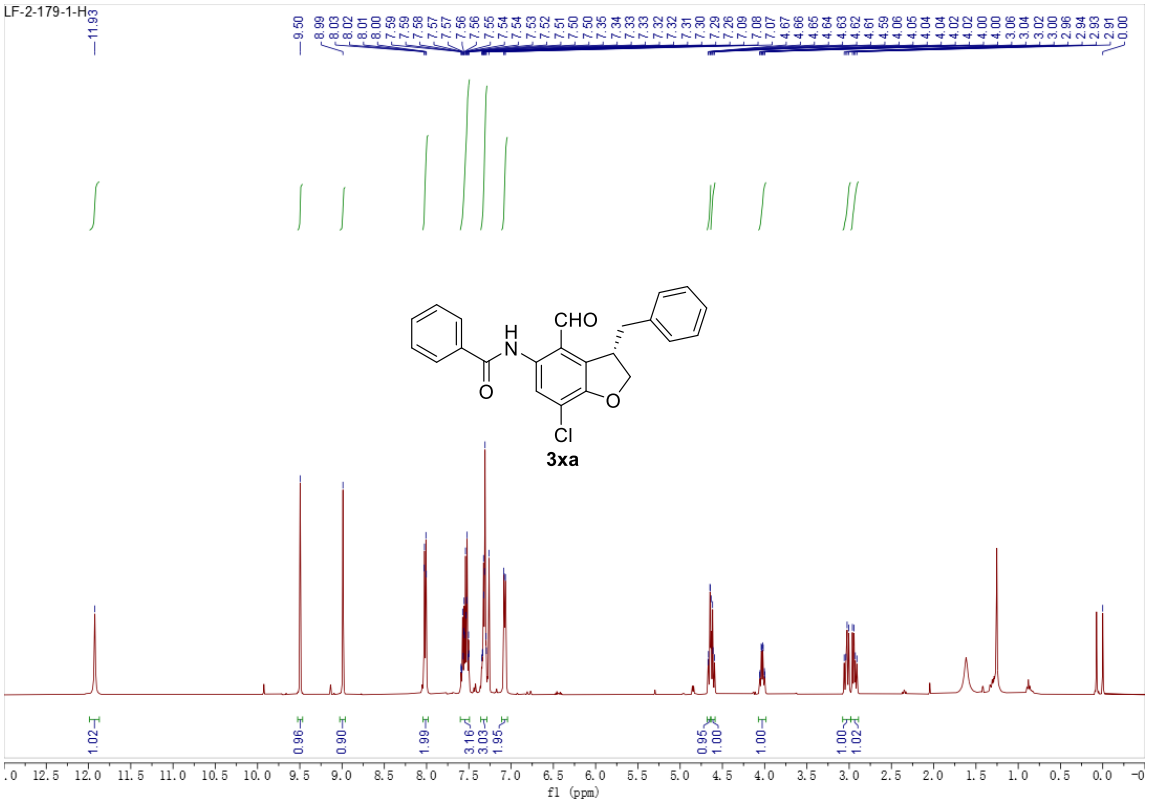


RT [min]	Height	Height%	Area	Area%
13.487	260.464	58.39	5688.90916	50.56
17.666	185.625	41.61	5563.85477	49.44

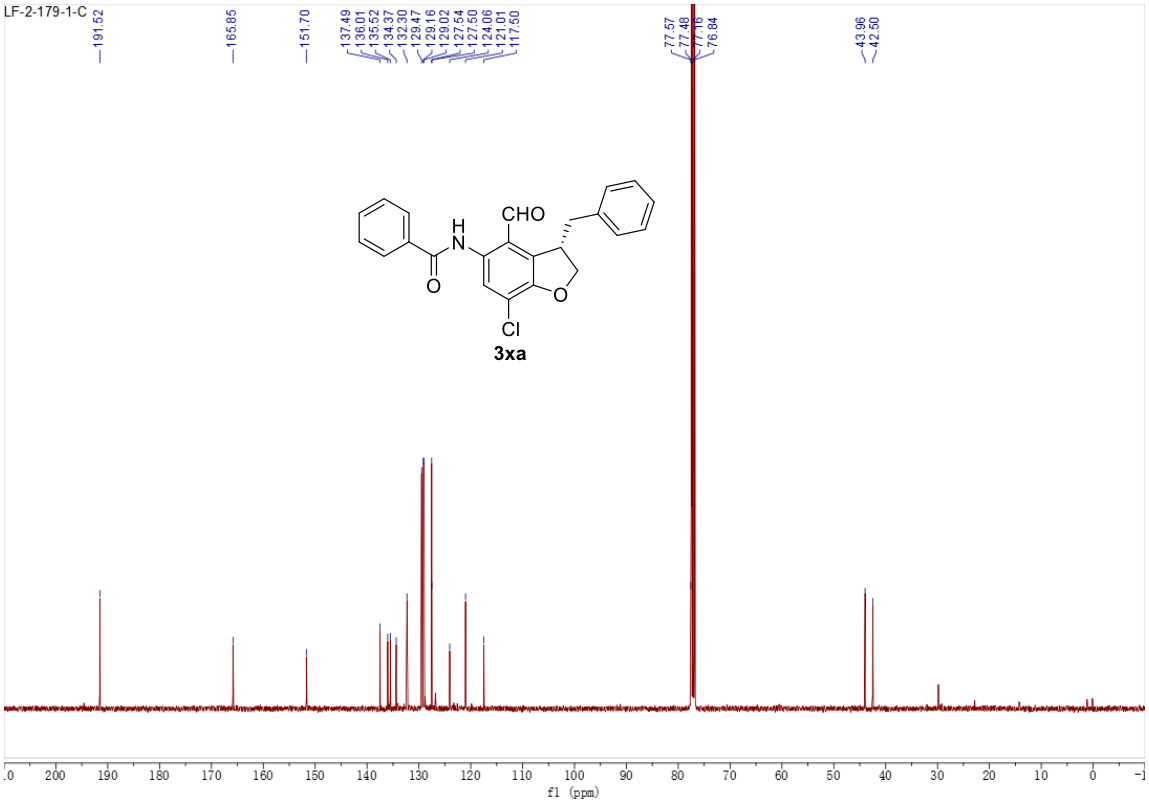


RT [min]	Height	Height%	Area	Area%
13.548	23.461	6.54	460.32897	4.43
17.638	335.505	93.46	9939.02292	95.57

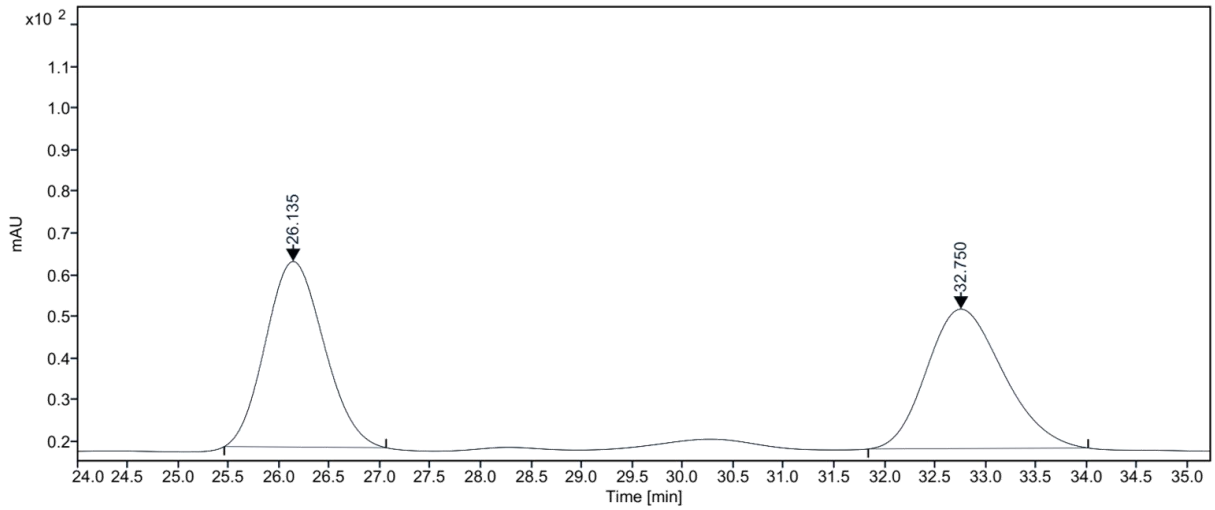
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3xa**



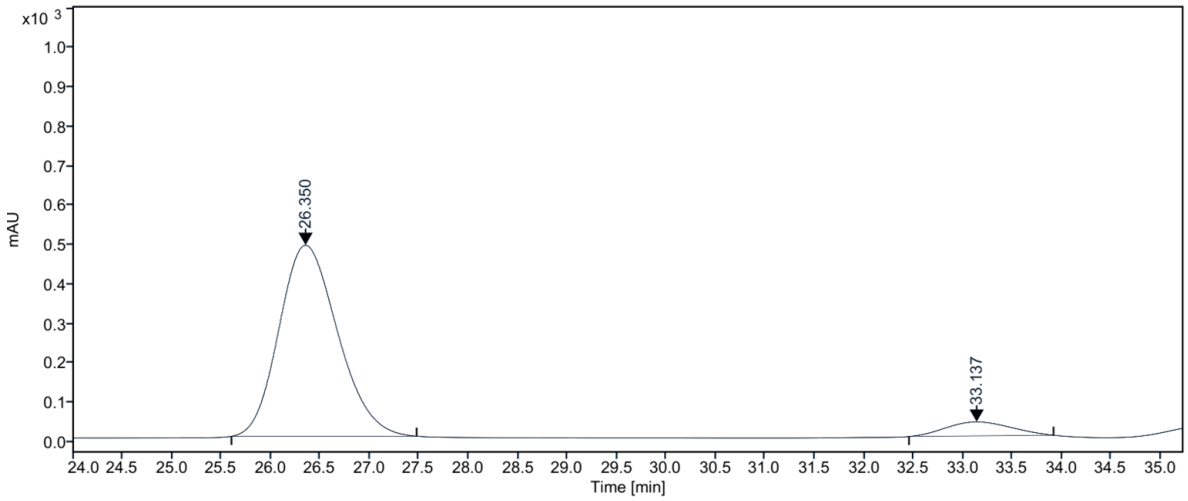
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3xa**



HPLC spectra and data of compound **3xa**

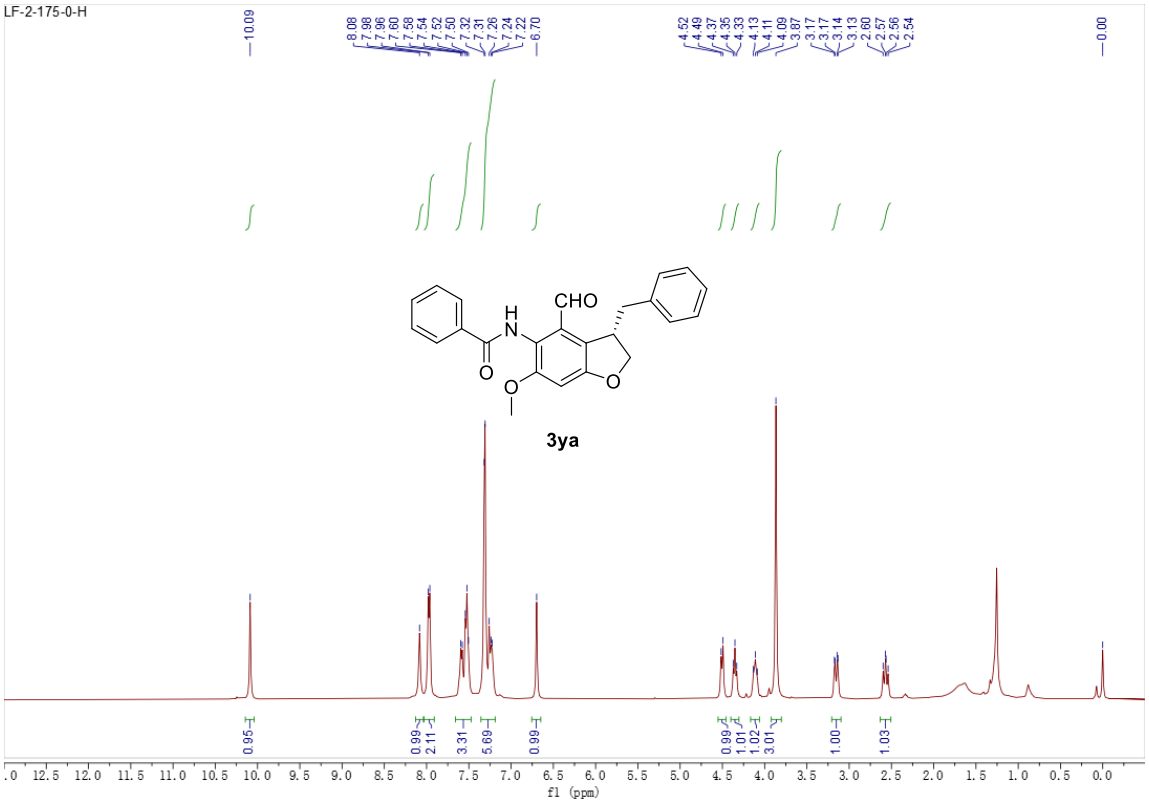


RT [min]	Height	Height%	Area	Area%
26.135	44.498	57.09	1790.07065	50.40
32.750	33.446	42.91	1761.55989	49.60

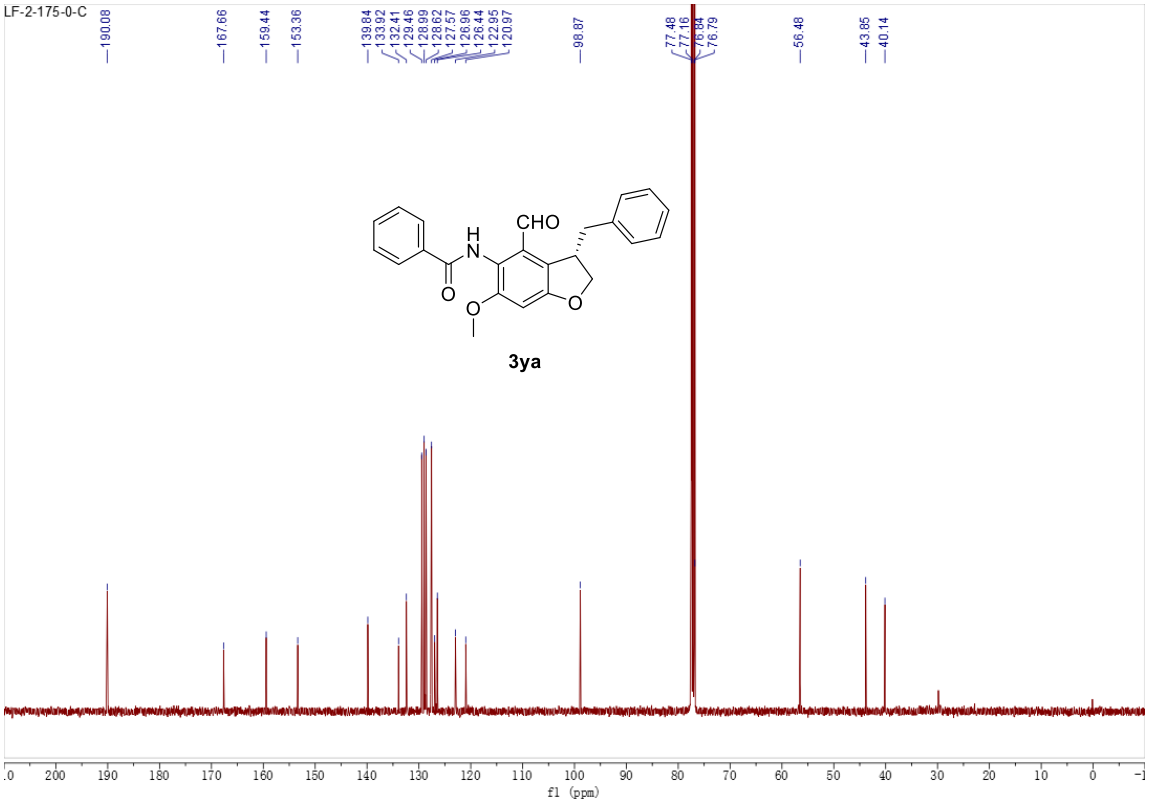


RT [min]	Height	Height%	Area	Area%
26.350	484.660	93.19	19989.82508	92.52
33.137	35.429	6.81	1616.67913	7.48

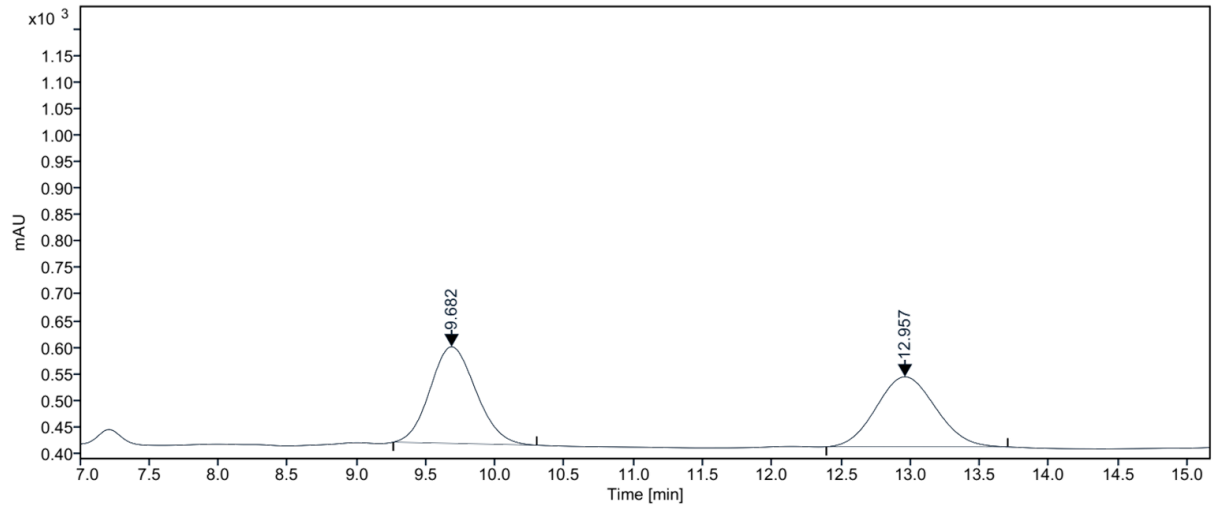
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ya**



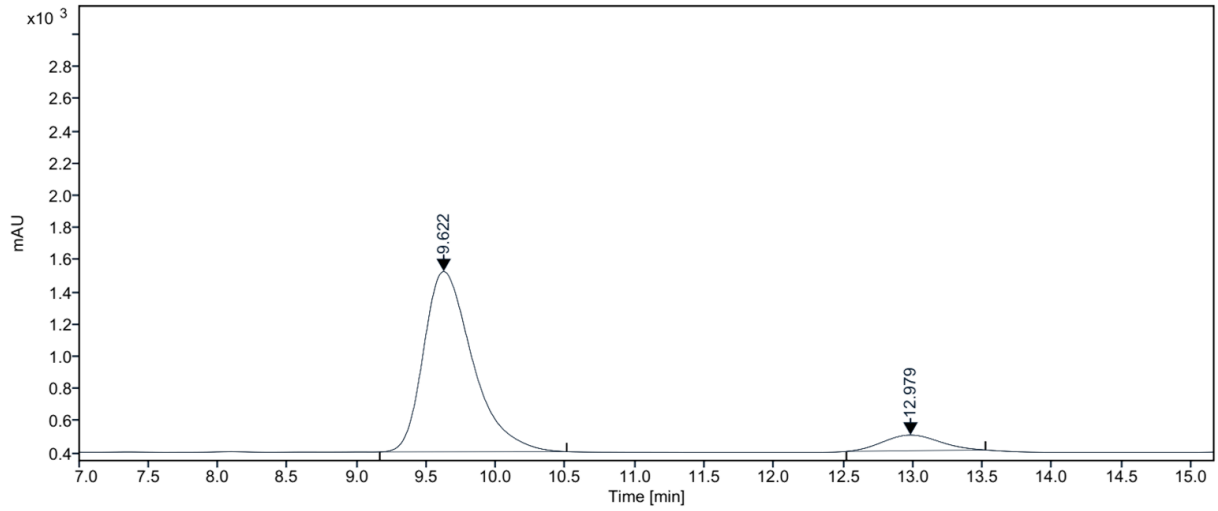
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ya**



HPLC spectra and data of compound **3ya**

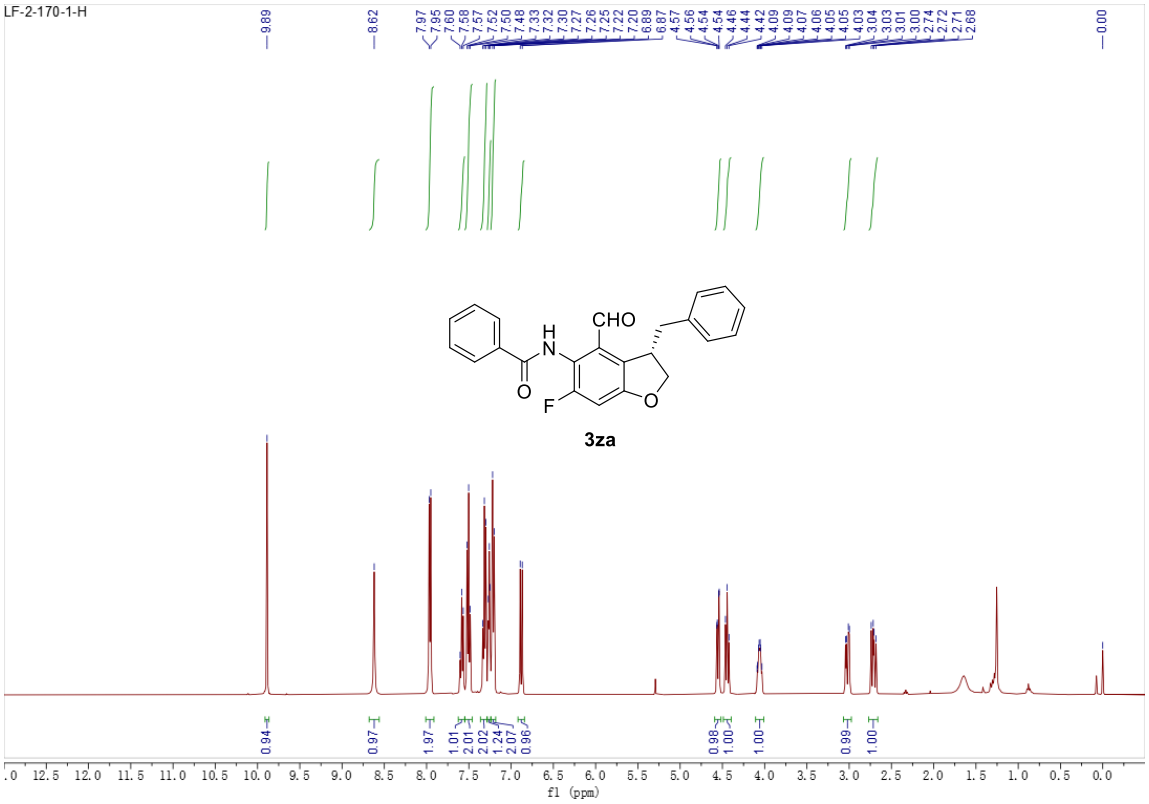


RT [min]	Height	Height%	Area	Area%
9.682	182.063	57.98	4192.78467	51.53
12.957	131.961	42.02	3943.31139	48.47

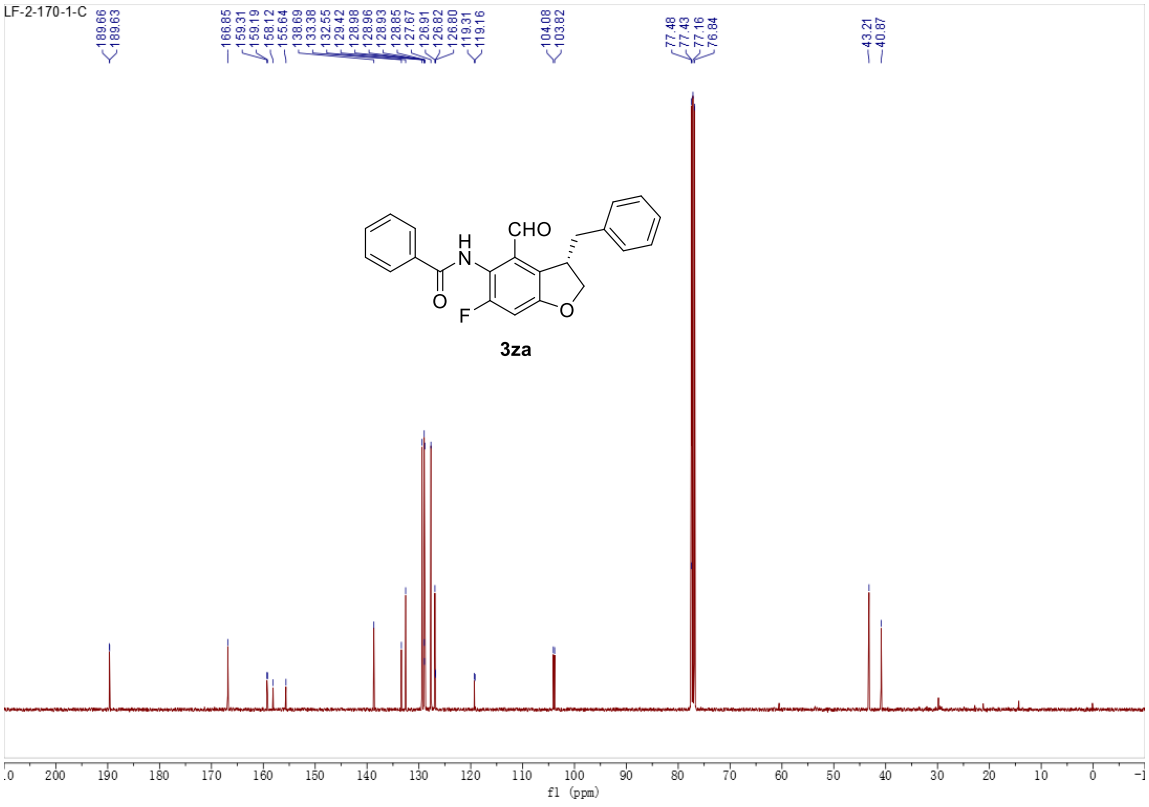


RT [min]	Height	Height%	Area	Area%
9.622	1120.270	92.00	27448.25459	90.86
12.979	97.430	8.00	2761.96801	9.14

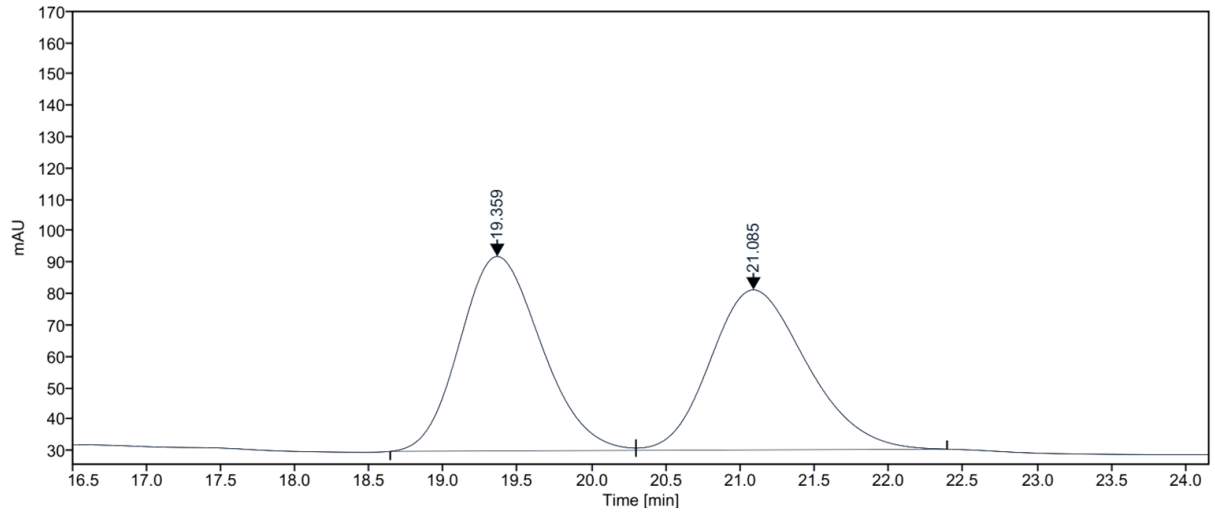
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3za**



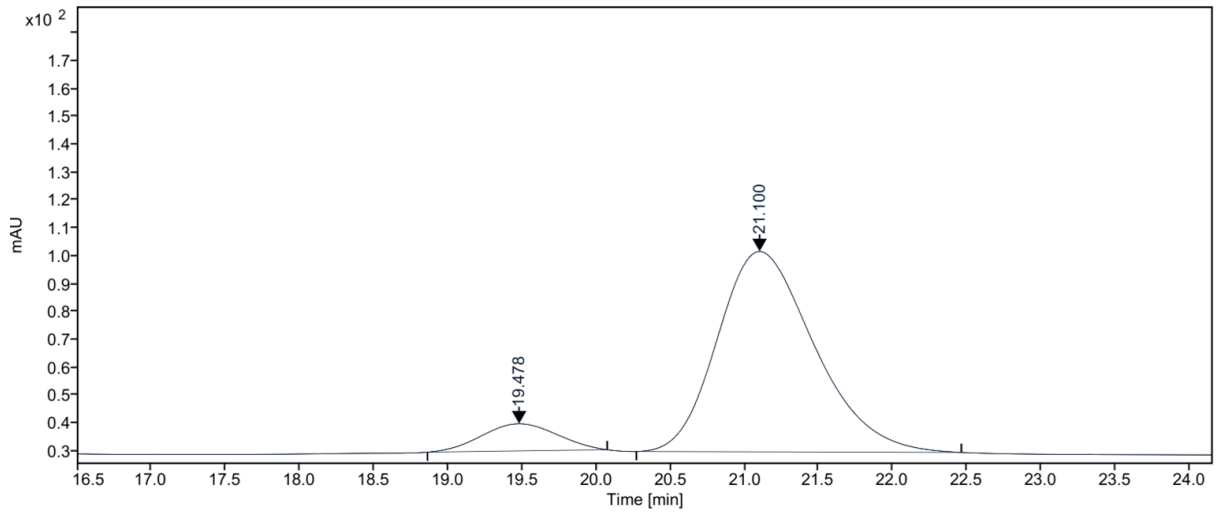
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3za**



HPLC spectra and data of compound **3za**

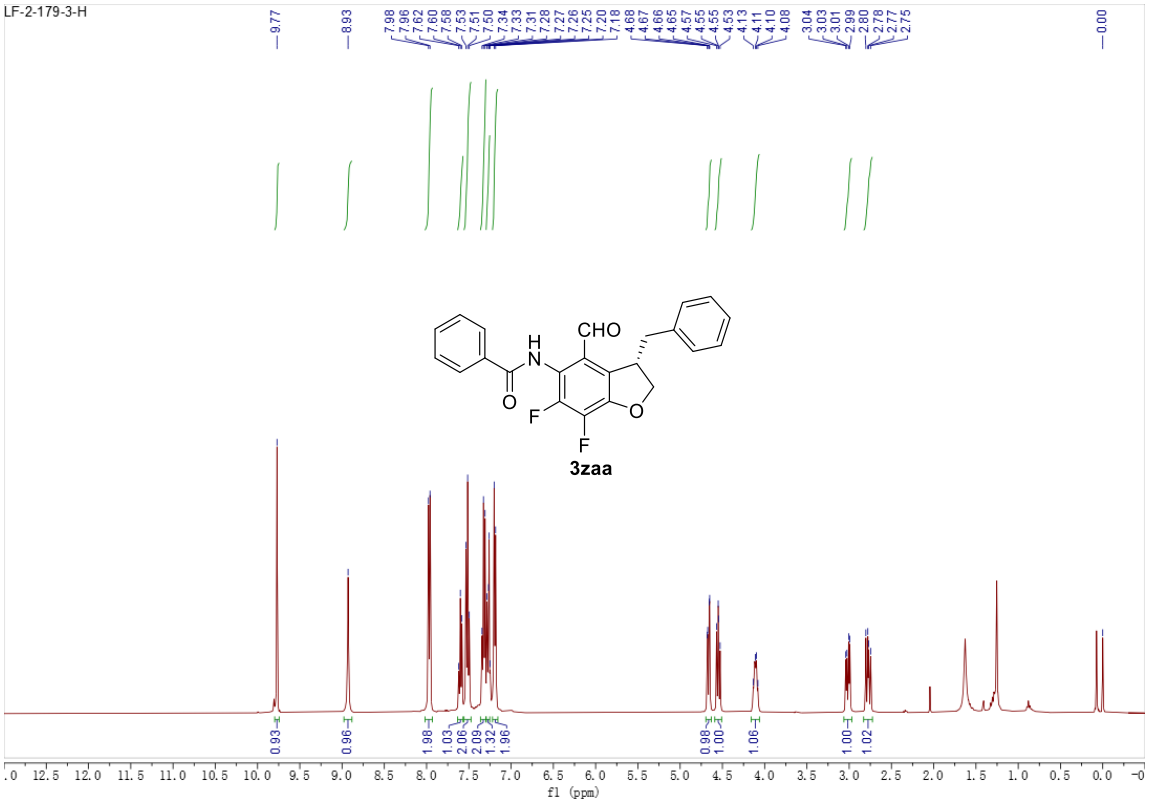


RT [min]	Height	Height%	Area	Area%
19.359	62.015	54.86	2364.68054	50.64
21.085	51.020	45.14	2304.98397	49.36

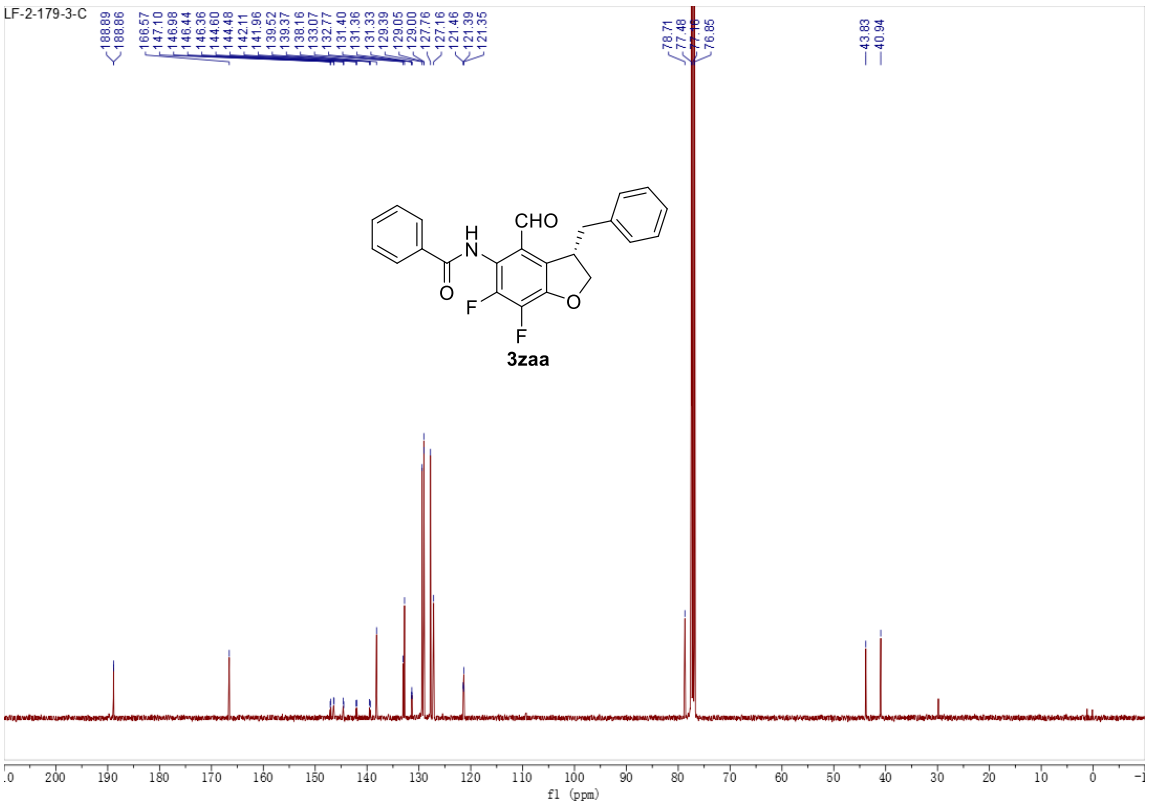


RT [min]	Height	Height%	Area	Area%
19.478	9.733	11.93	344.04322	9.54
21.100	71.859	88.07	3263.70923	90.46

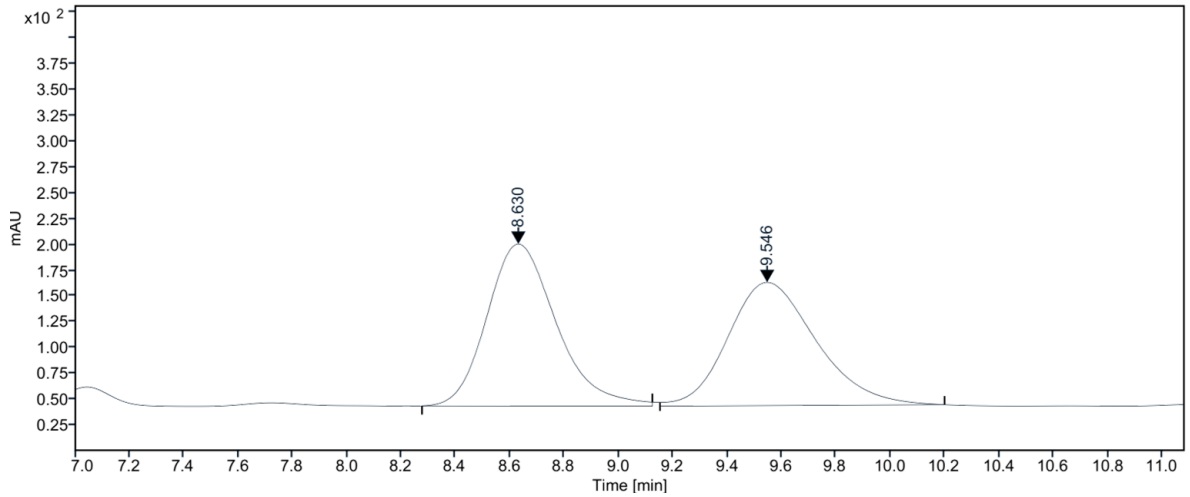
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3zaa**



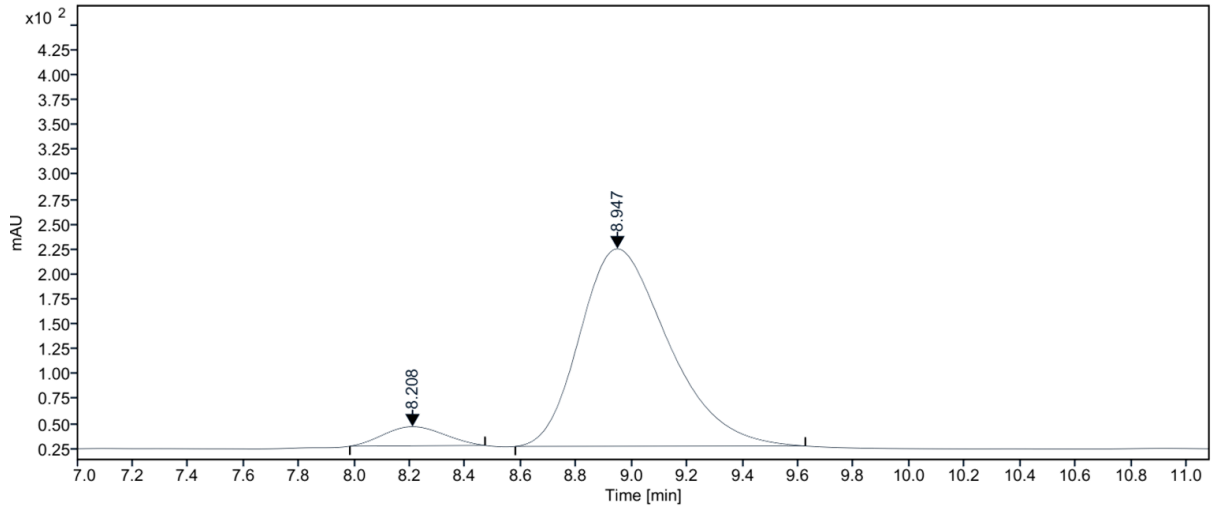
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3zaa**



HPLC spectra and data of compound **3zaa**

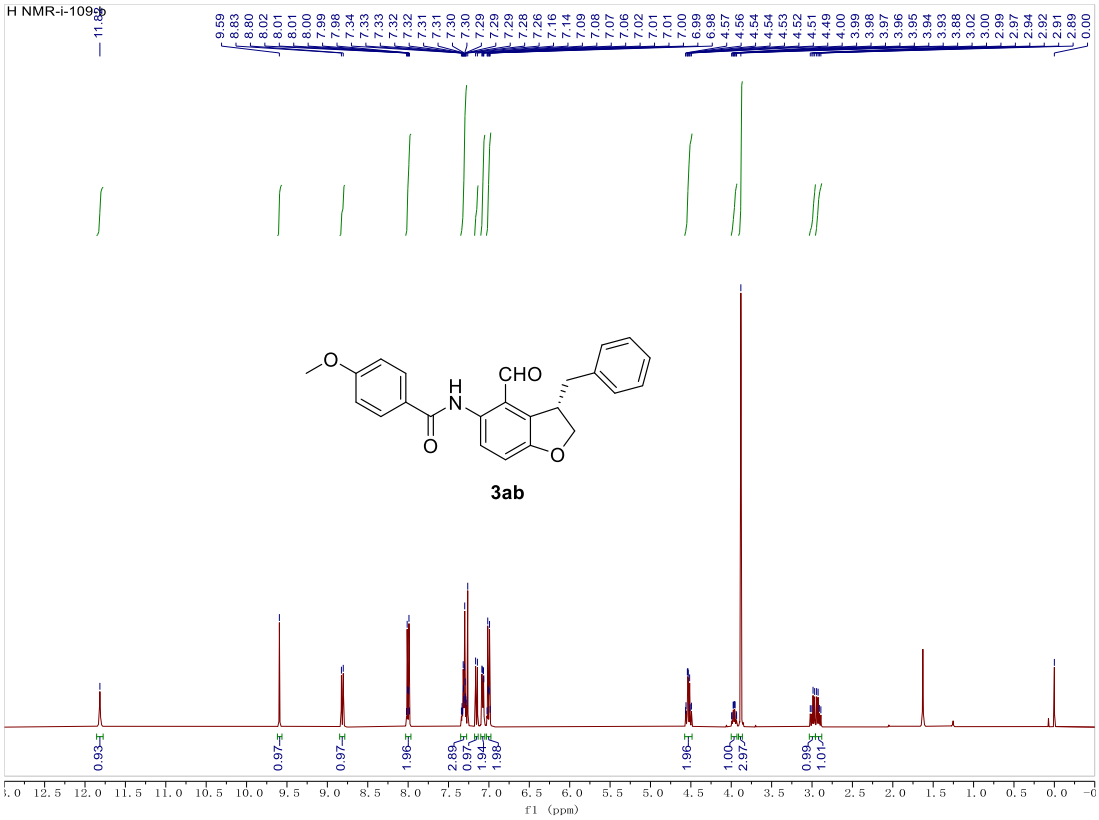


RT [min]	Height	Height%	Area	Area%
8.630	156.681	56.79	2776.59394	50.78
9.546	119.207	43.21	2690.79094	49.22

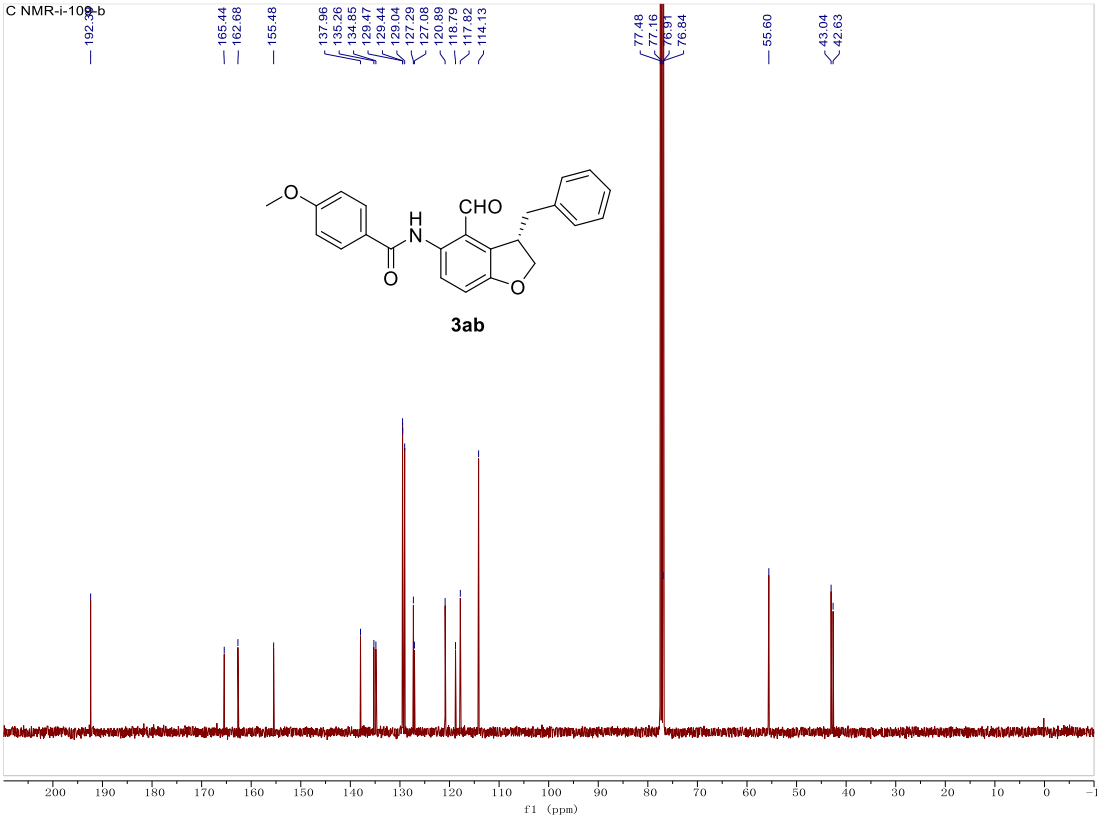


RT [min]	Height	Height%	Area	Area%
8.208	19.178	8.83	290.41814	6.20
8.947	198.090	91.17	4396.15056	93.80

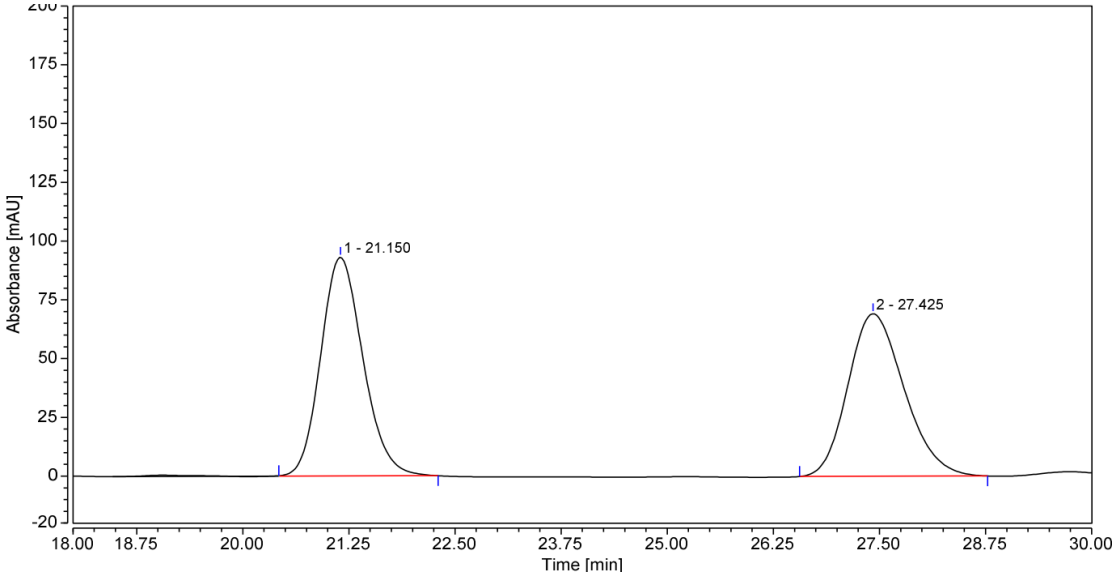
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ab**



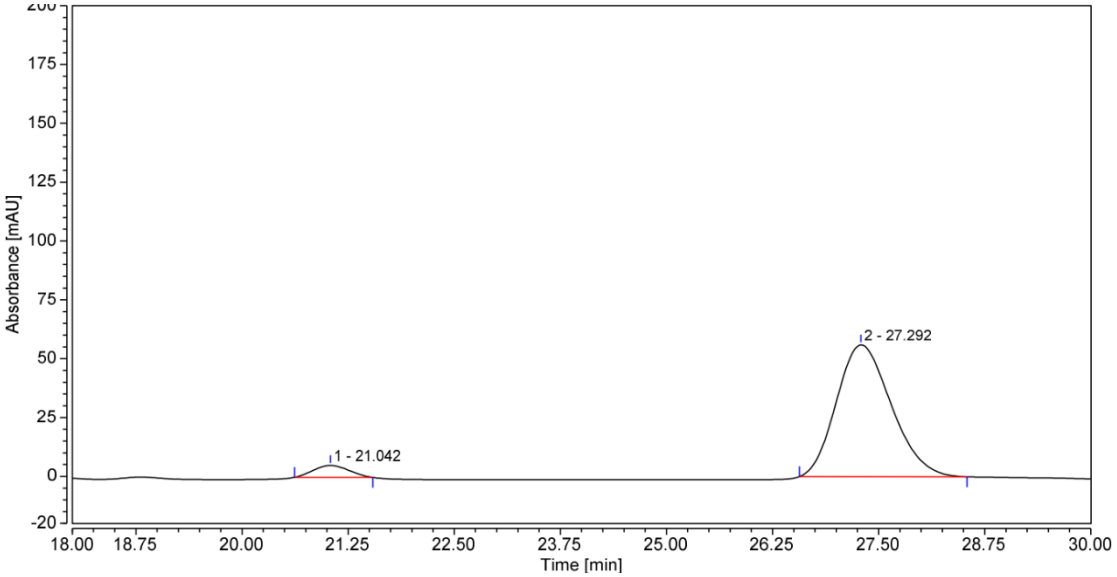
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ab**



HPLC spectra and data of compound **3ab**

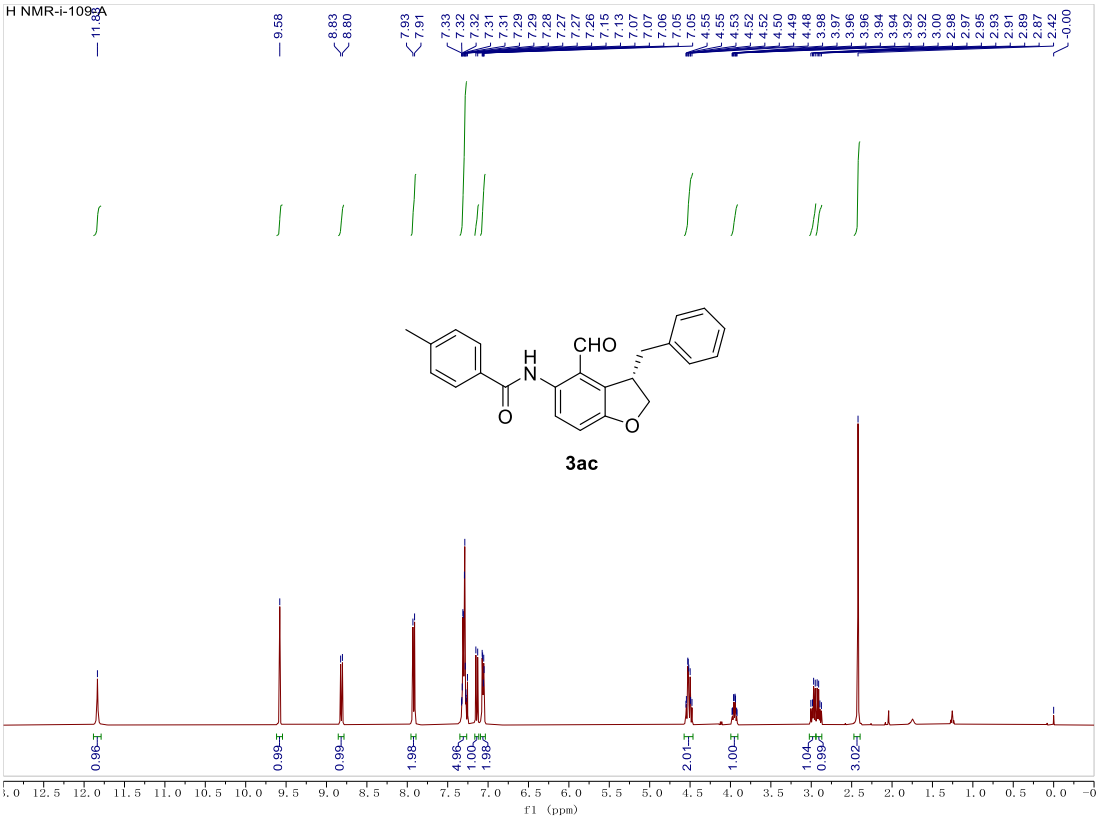


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.150	53.775	93.035	50.32	57.36	n.a.
2		27.425	53.084	69.159	49.68	42.64	n.a.
Total:			**106.859**	**162.194**	**100.00**	**100.00**	

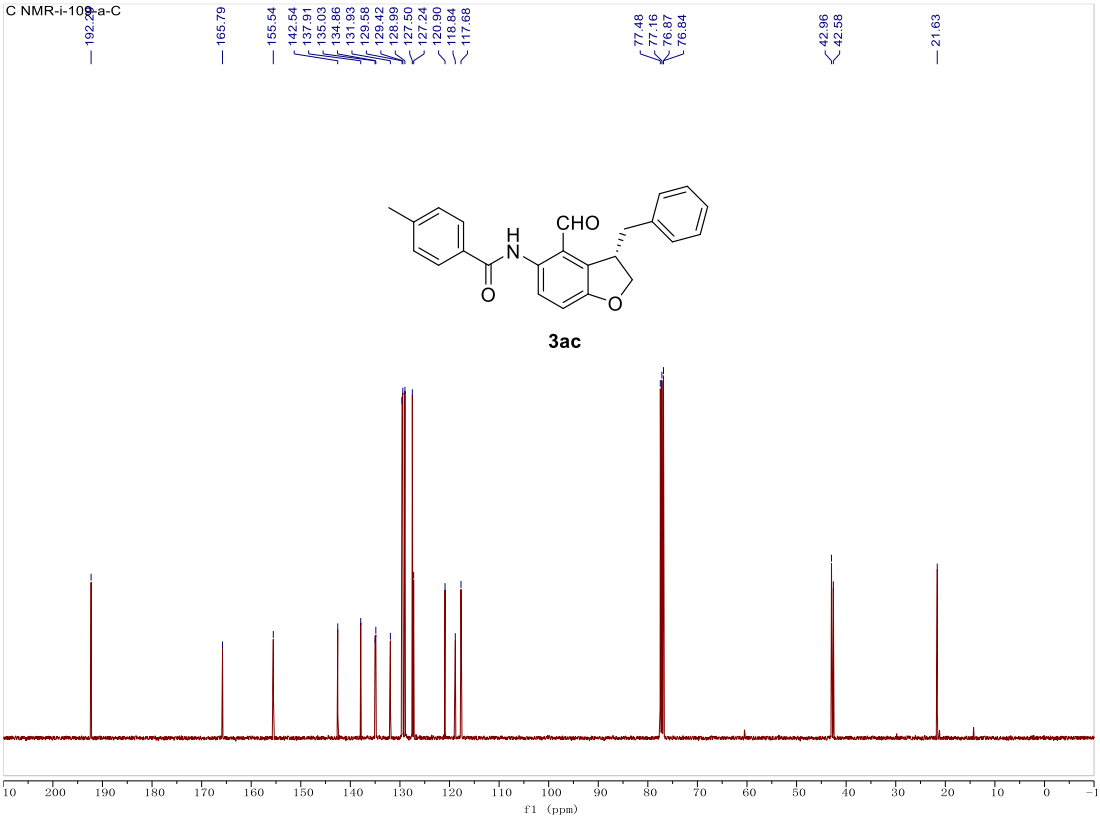


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.042	2.457	5.038	5.53	8.25	n.a.
2		27.292	41.947	56.004	94.47	91.75	n.a.
Total:			**44.404**	**61.042**	**100.00**	**100.00**	

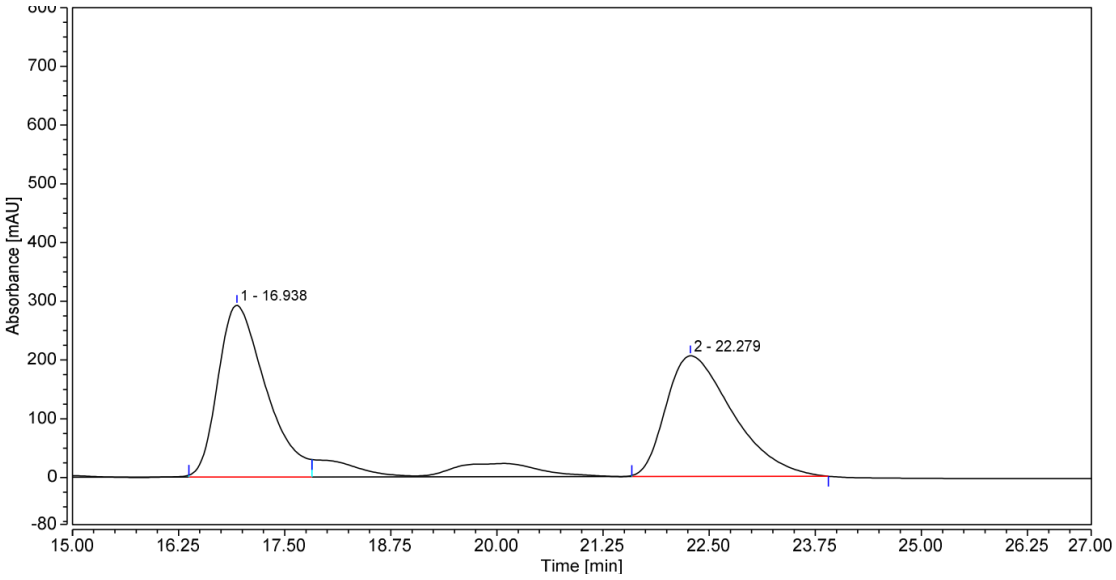
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ac**



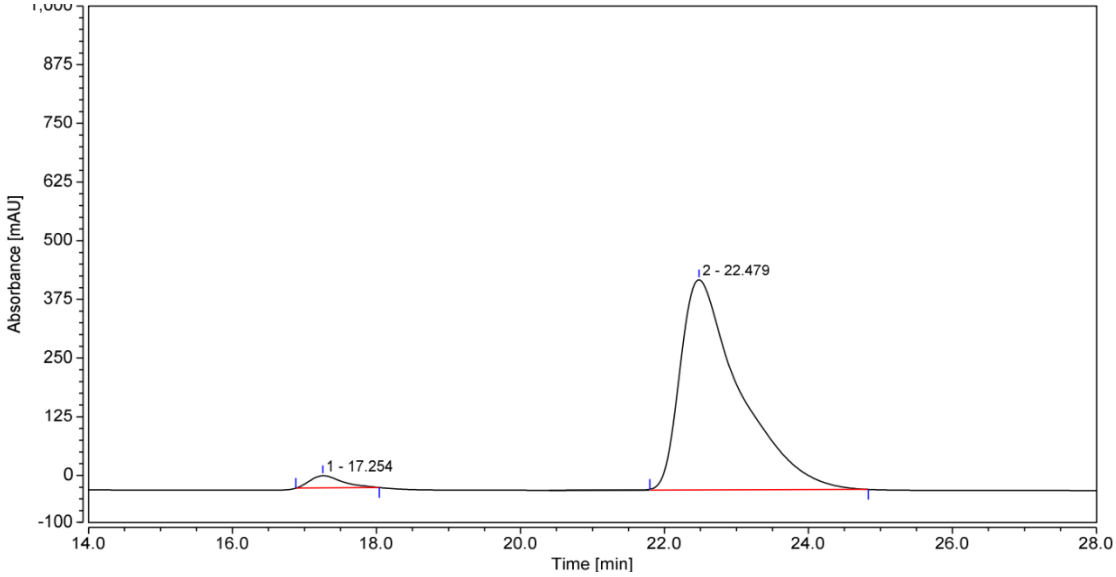
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ac**



HPLC spectra and data of compound **3ac**

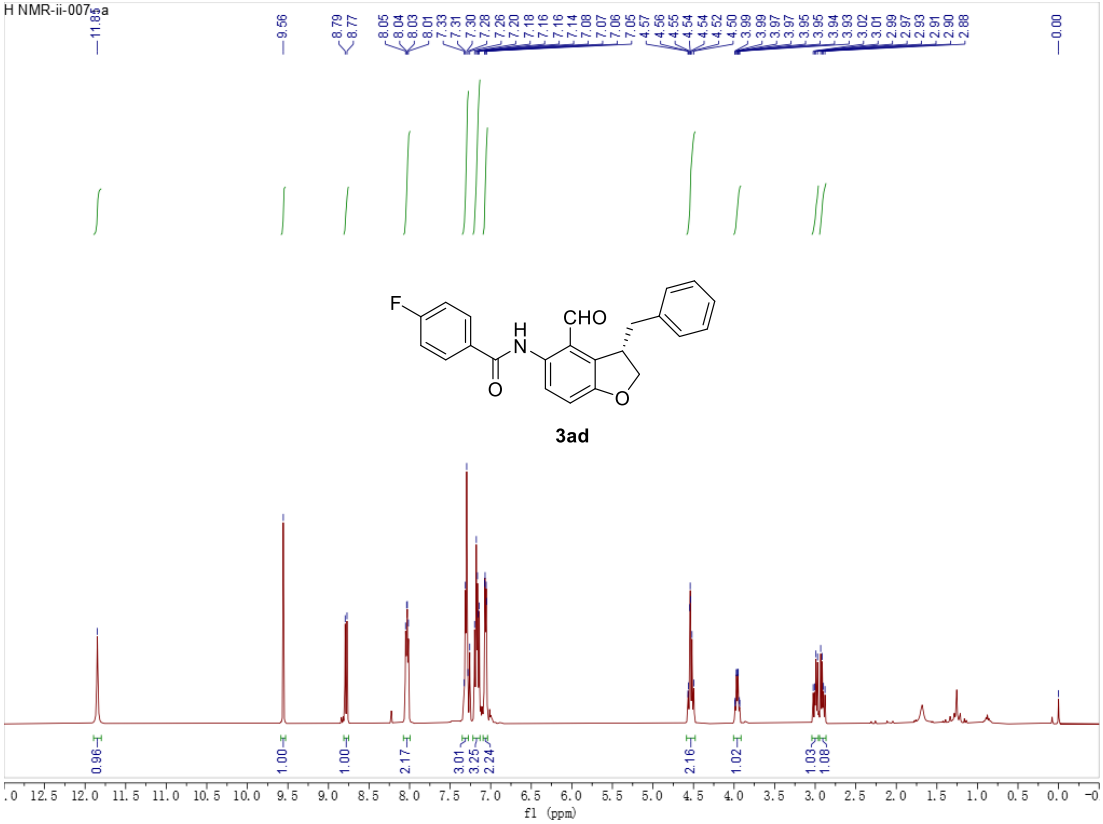


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.938	191.293	292.406	50.56	58.74	n.a.
2		22.279	187.083	205.366	49.44	41.26	n.a.
Total:			**378.376**	**497.772**	**100.00**	**100.00**	

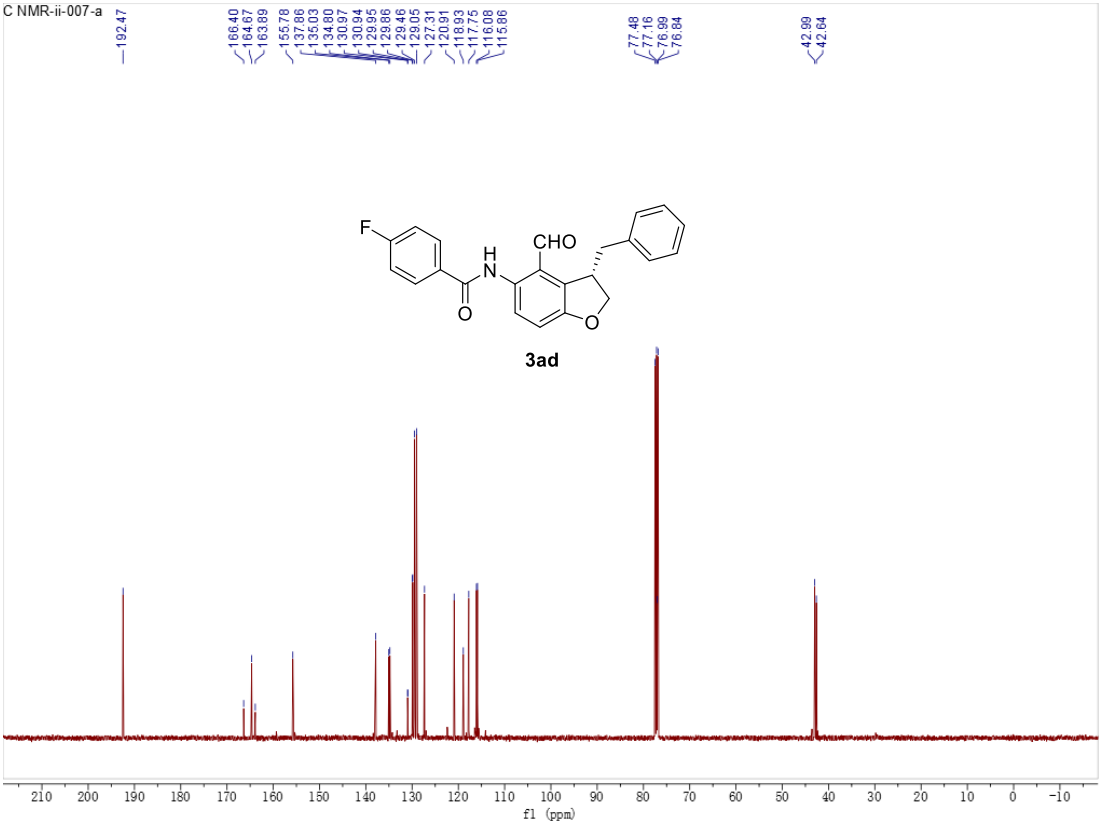


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.254	13.687	26.002	3.09	5.49	n.a.
2		22.479	429.470	447.652	96.91	94.51	n.a.
Total:			**443.157**	**473.654**	**100.00**	**100.00**	

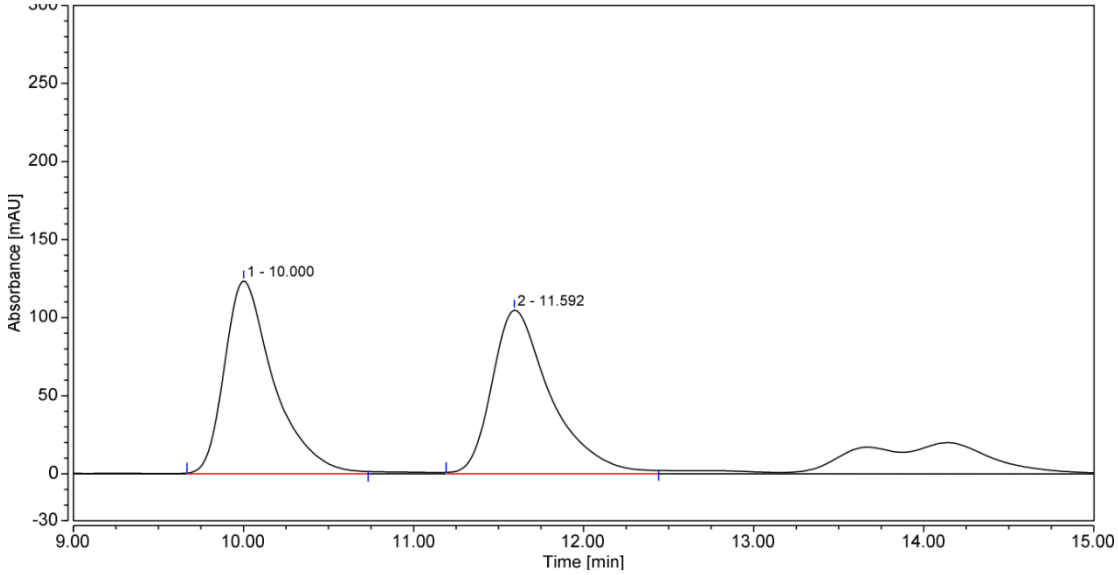
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ad**



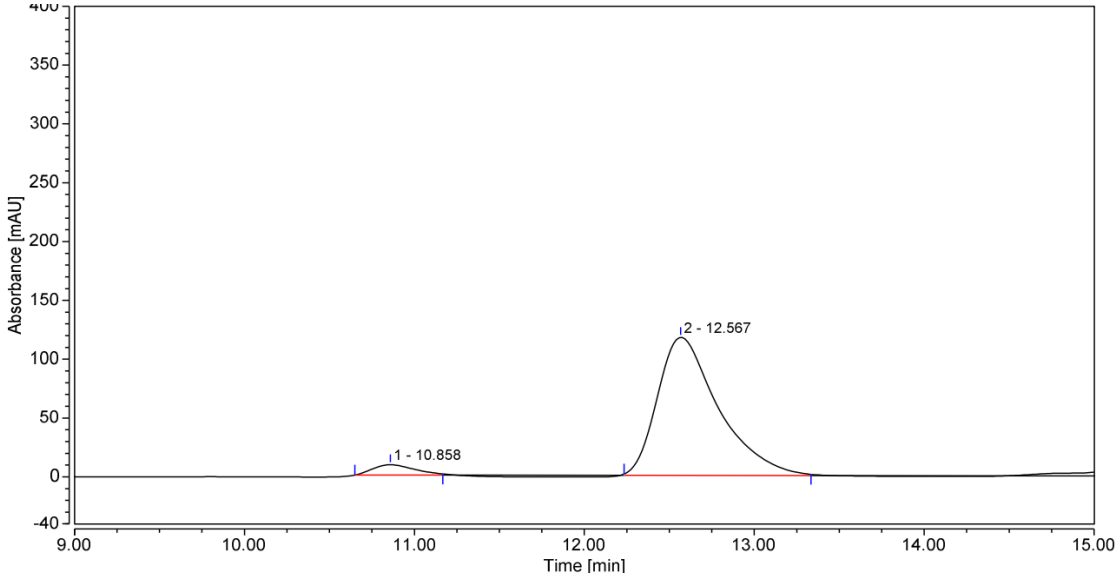
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ad**



HPLC spectra and data of compound **3ad**

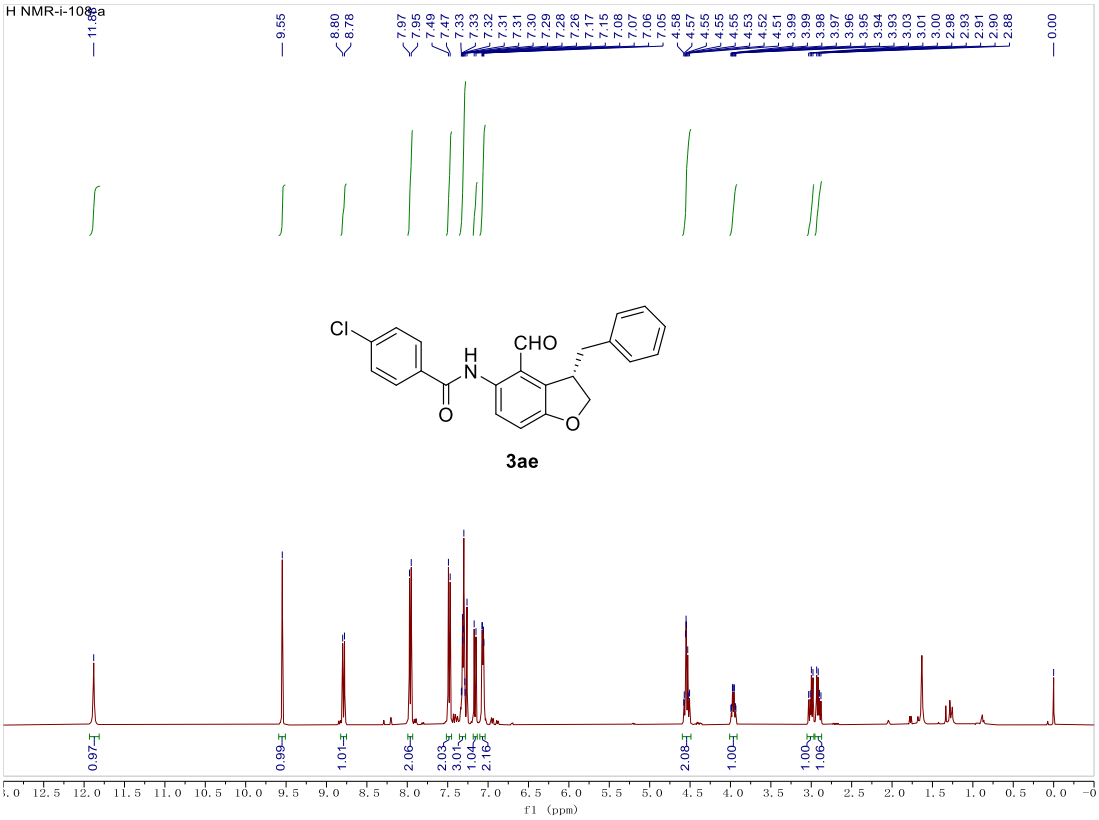


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.000	41.655	123.588	49.72	54.09	n.a.
2		11.592	42.118	104.908	50.28	45.91	n.a.
Total:			**83.774**	**228.496**	**100.00**	**100.00**	

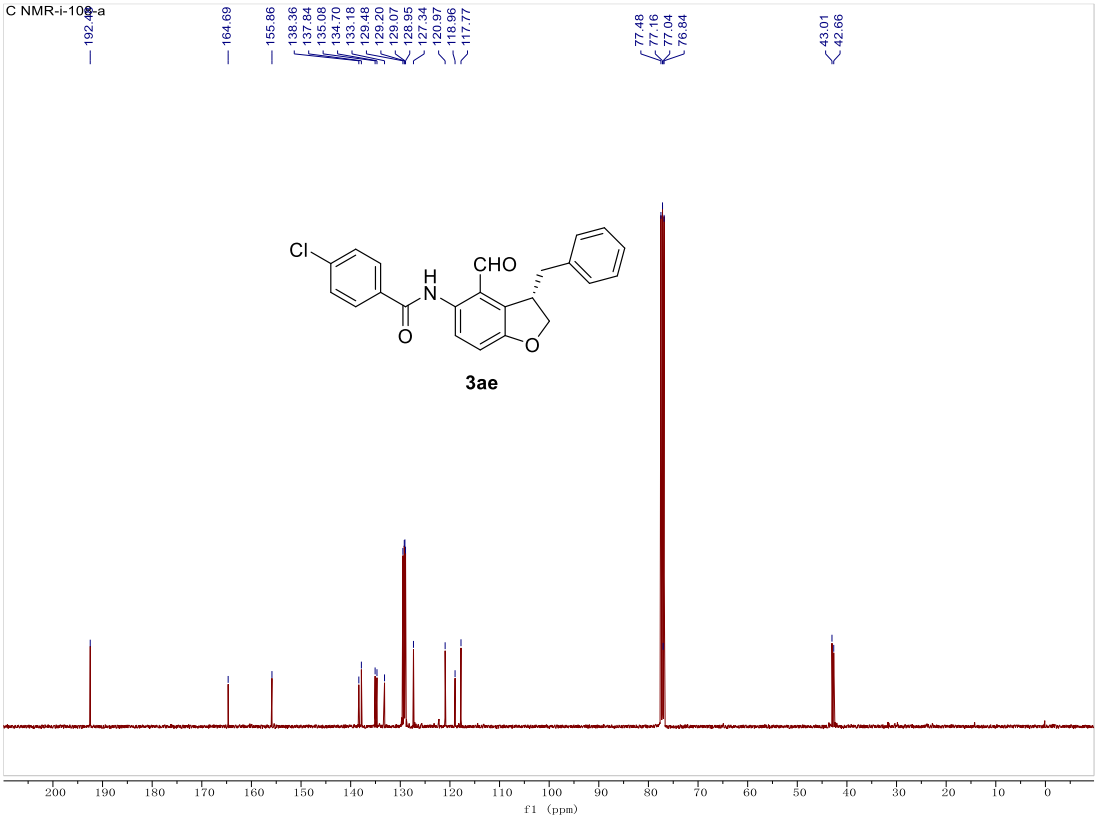


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.858	2.520	8.804	4.93	6.98	n.a.
2		12.567	48.577	117.382	95.07	93.02	n.a.
Total:			**51.097**	**126.186**	**100.00**	**100.00**	

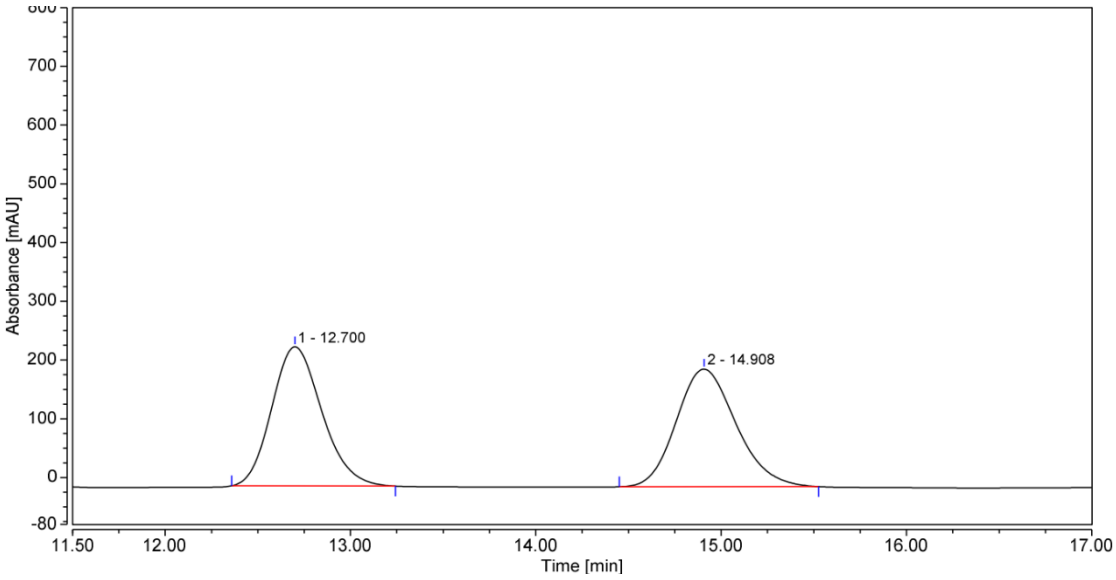
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ae**



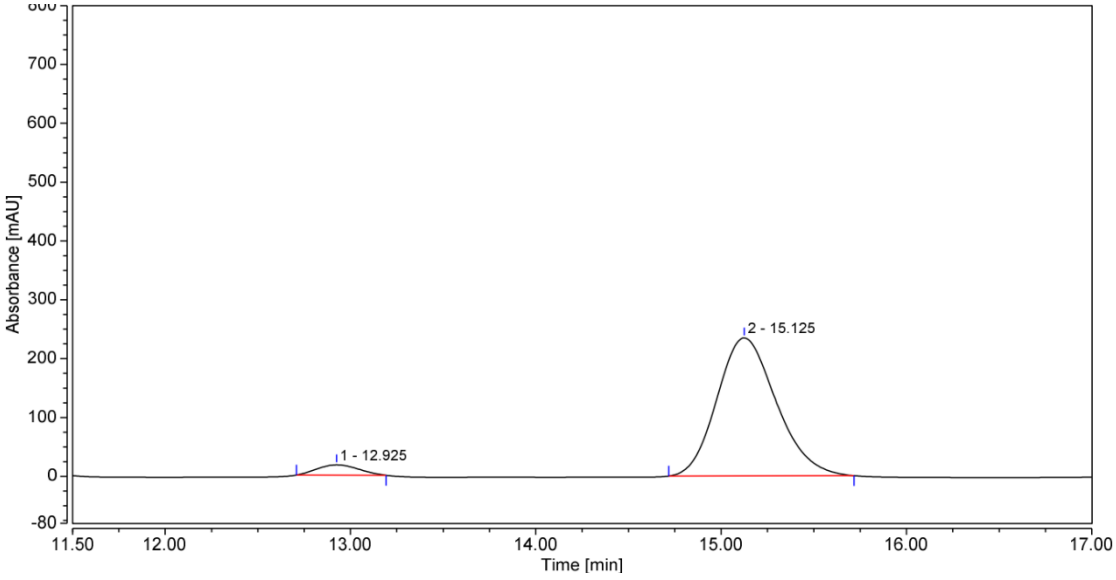
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ae**



HPLC spectra and data of compound **3ae**

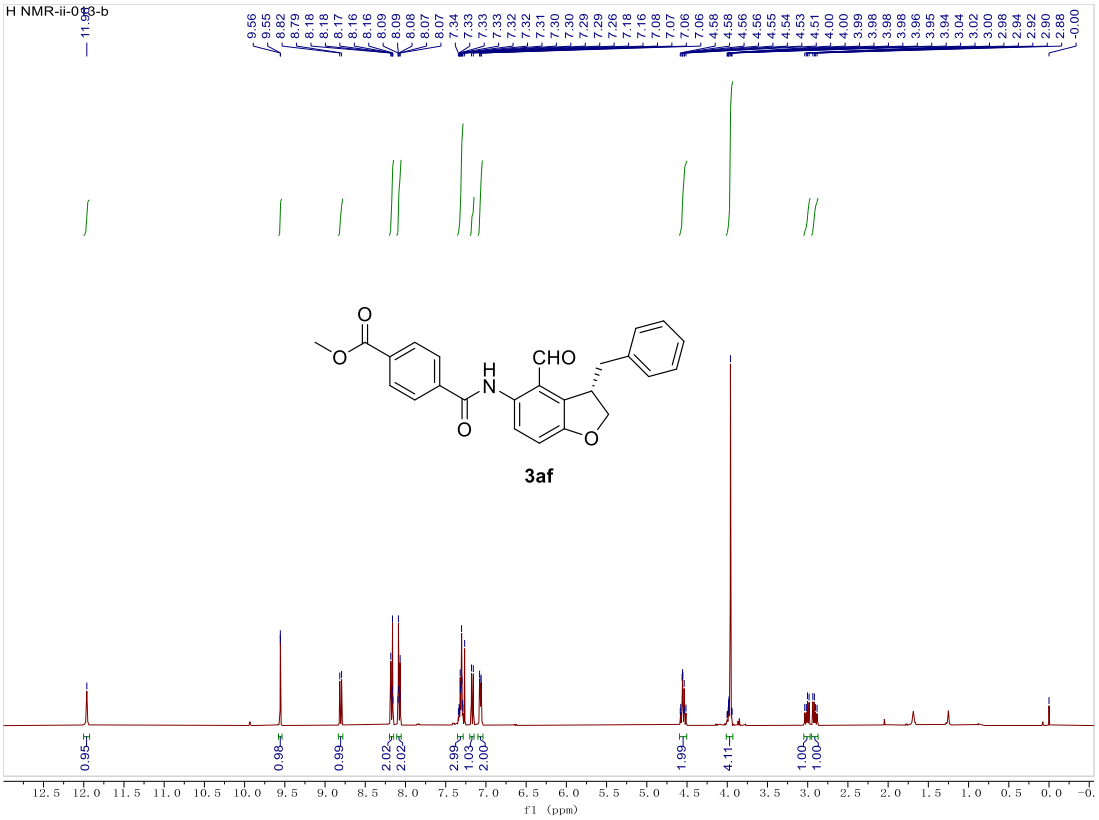


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.700	74.411	236.826	49.85	54.18	n.a.
2		14.908	74.857	200.251	50.15	45.82	n.a.
Total:			**149.268**	**437.078**	**100.00**	**100.00**	

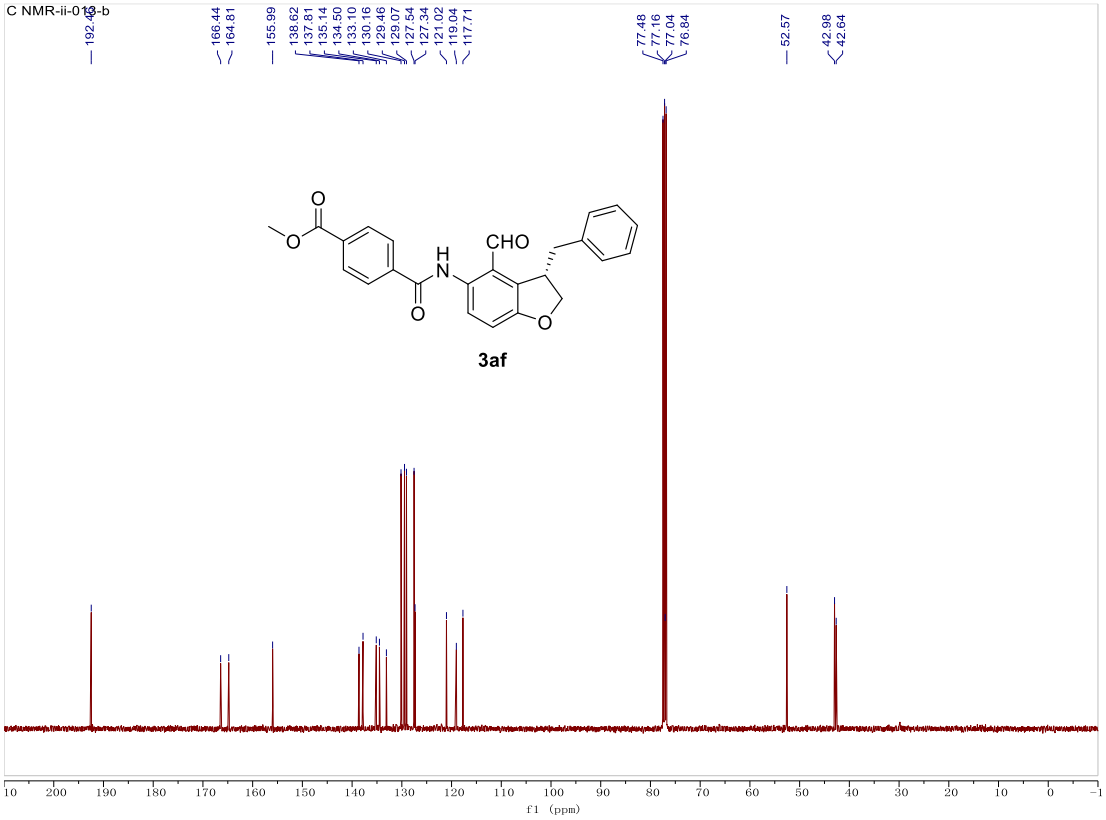


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.925	4.510	17.475	4.93	6.93	n.a.
2		15.125	86.898	234.639	95.07	93.07	n.a.
Total:			**91.408**	**252.113**	**100.00**	**100.00**	

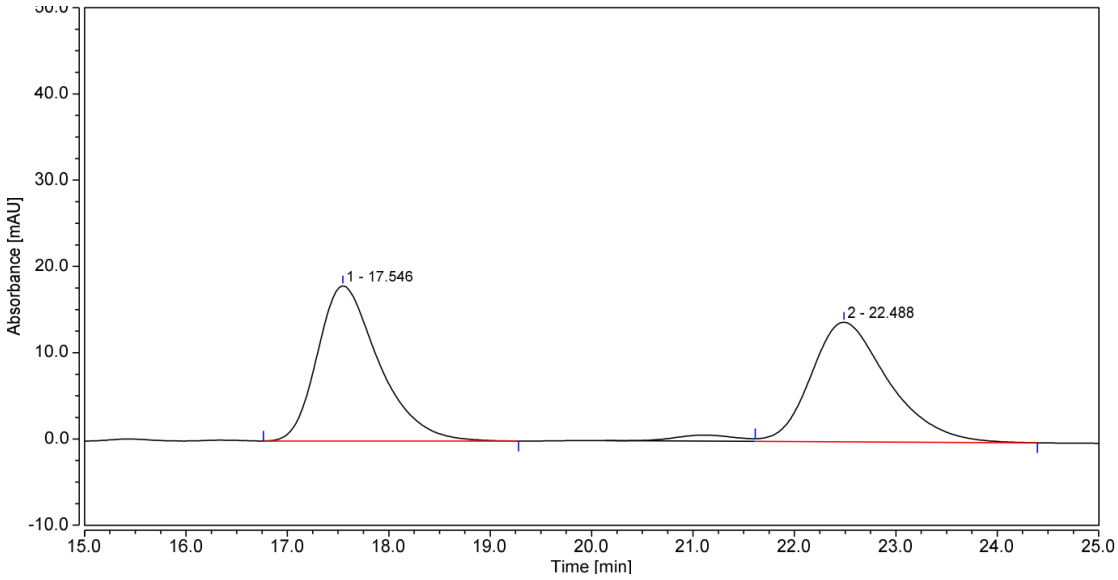
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3af**



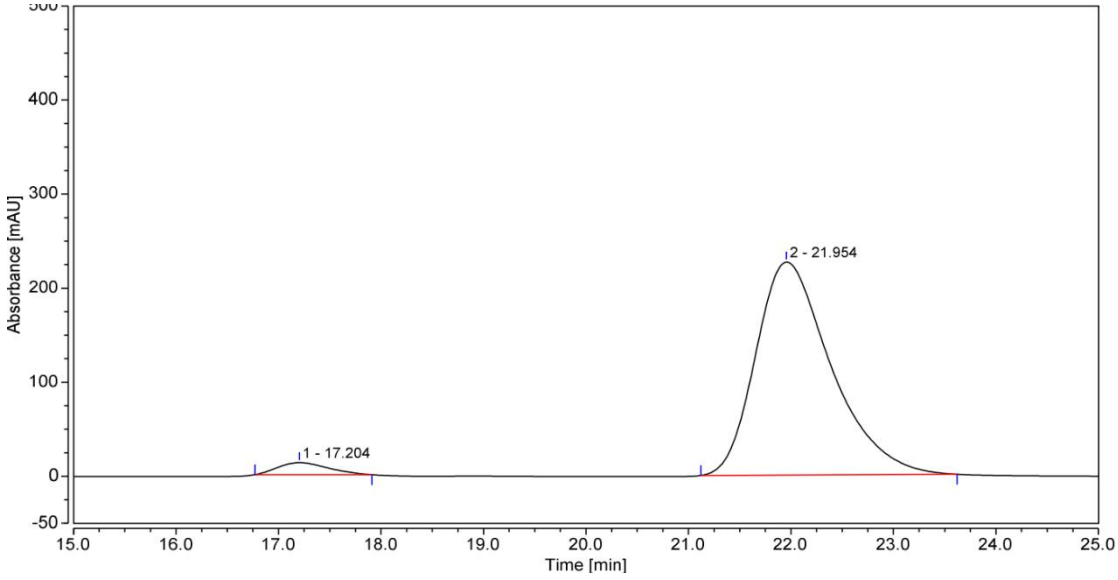
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3af**



HPLC spectra and data of compound **3af**

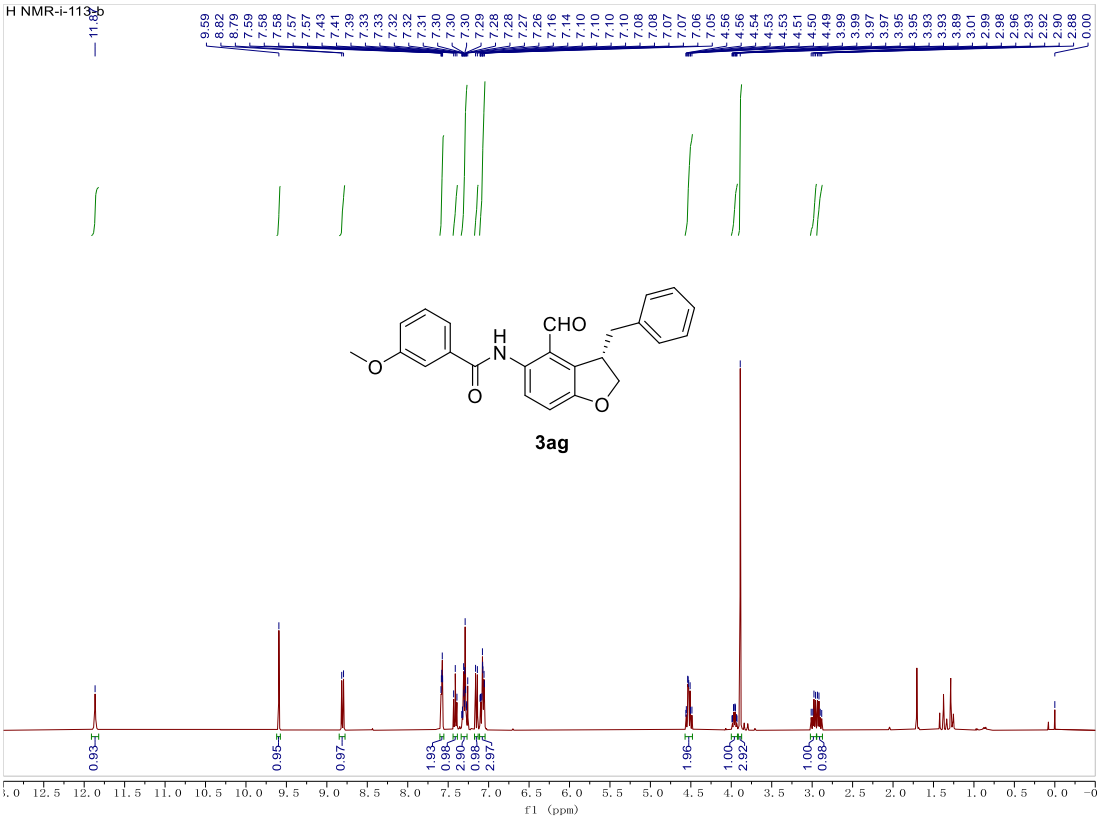


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.546	12.631	17.970	50.77	56.44	n.a.
2		22.488	12.250	13.866	49.23	43.56	n.a.
Total:			**24.881**	**31.836**	**100.00**	**100.00**	

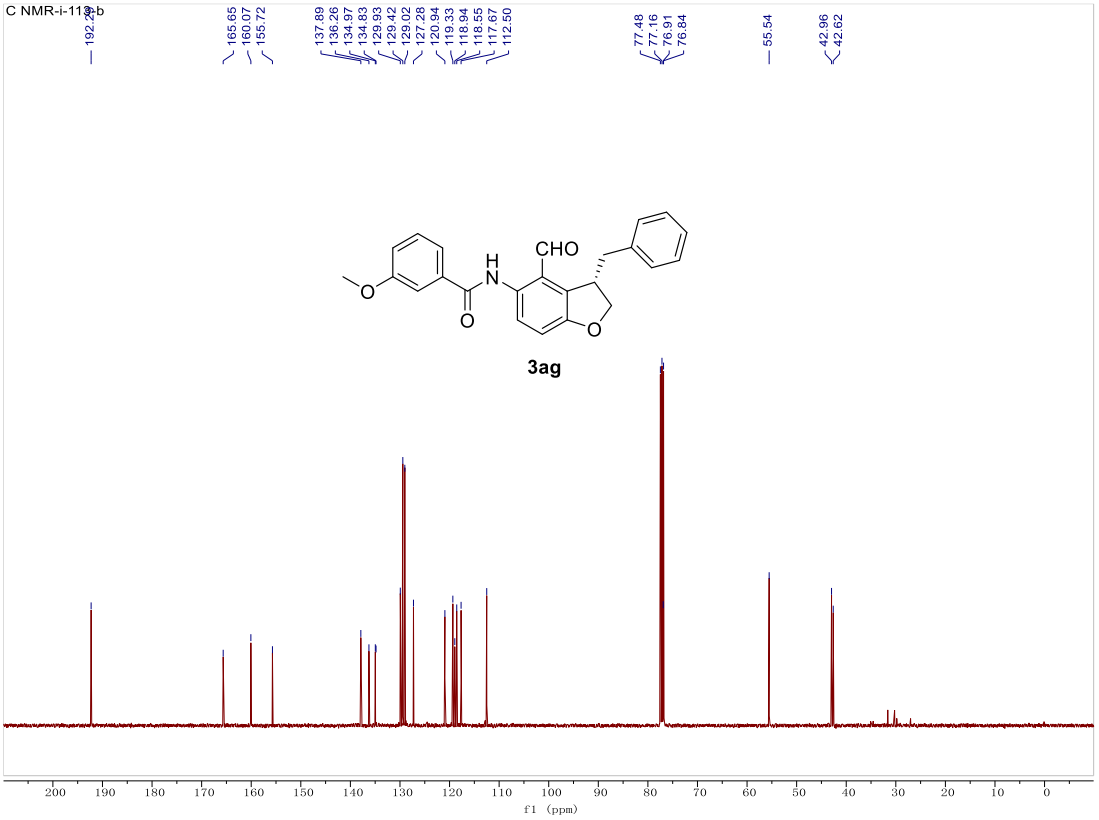


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.204	7.229	12.740	3.61	5.33	n.a.
2		21.954	192.889	226.473	96.39	94.67	n.a.
Total:			**200.118**	**239.213**	**100.00**	**100.00**	

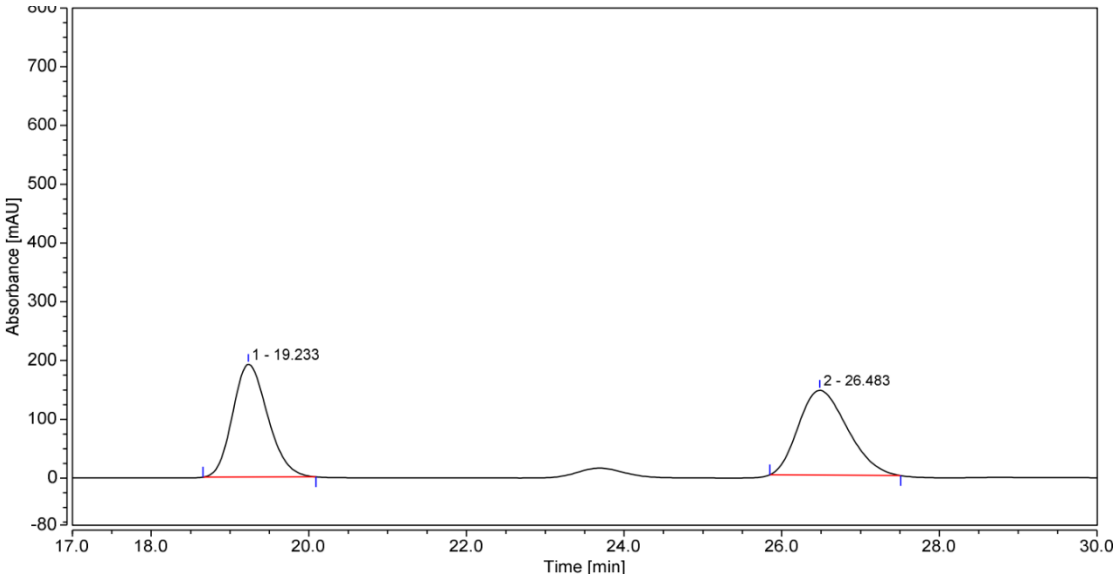
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ag**



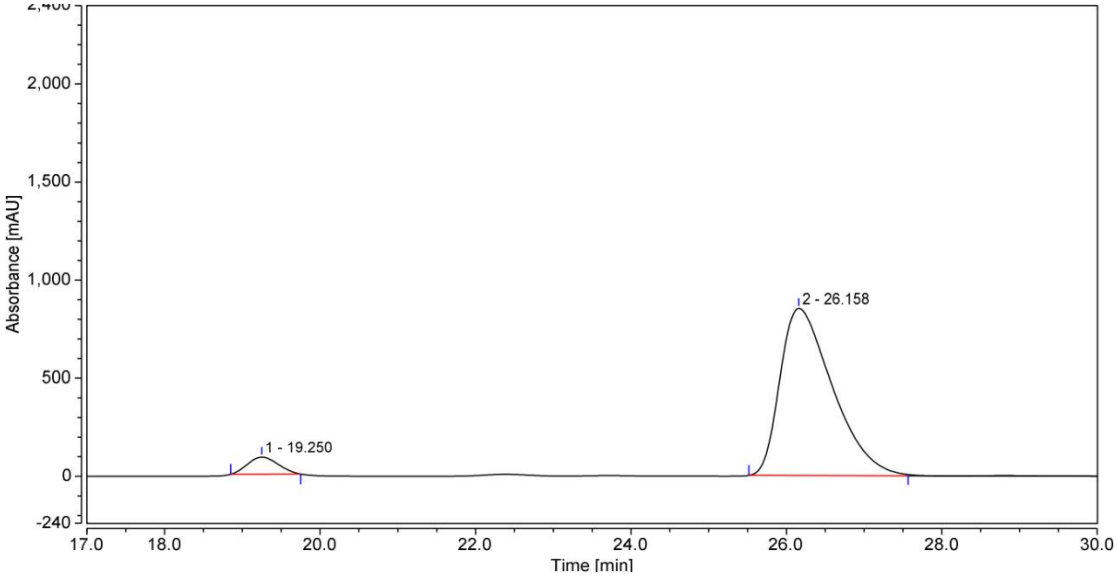
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ag**



HPLC spectra and data of compound **3ag**

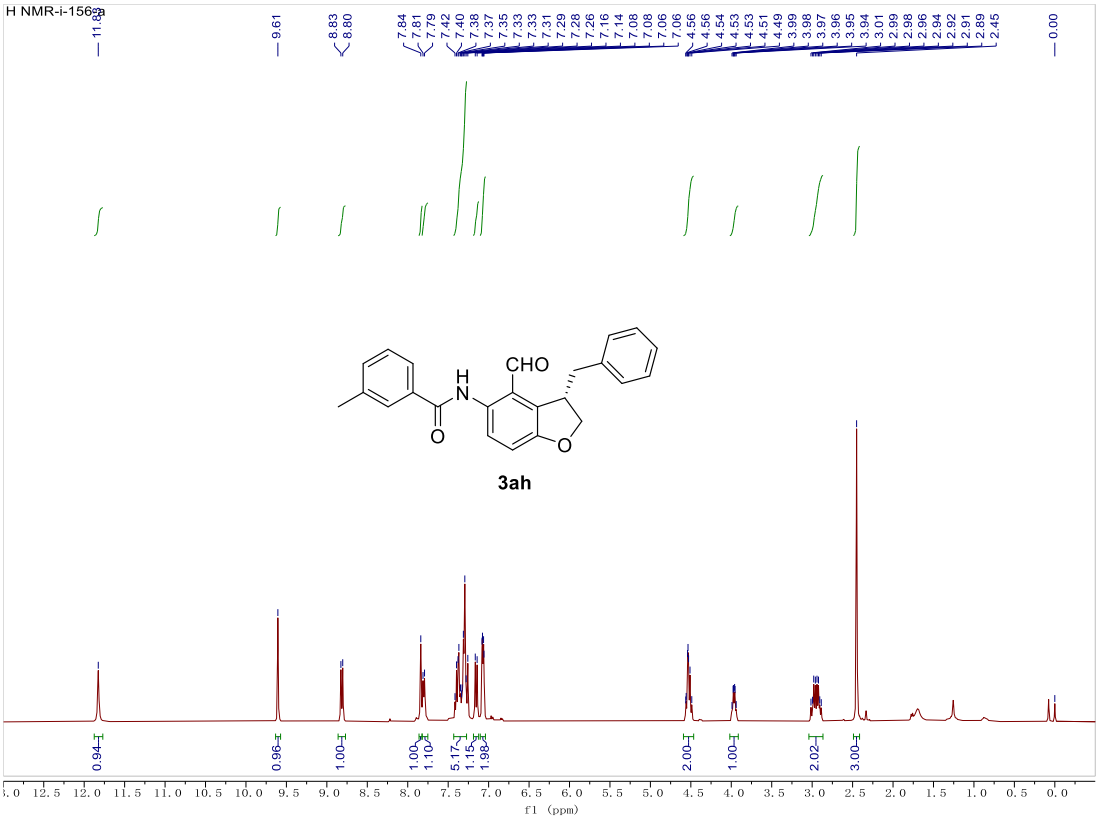


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.233	99.132	192.029	48.86	57.11	n.a.
2		26.483	103.775	144.221	51.14	42.89	n.a.
Total:			**202.906**	**336.250**	**100.00**	**100.00**	

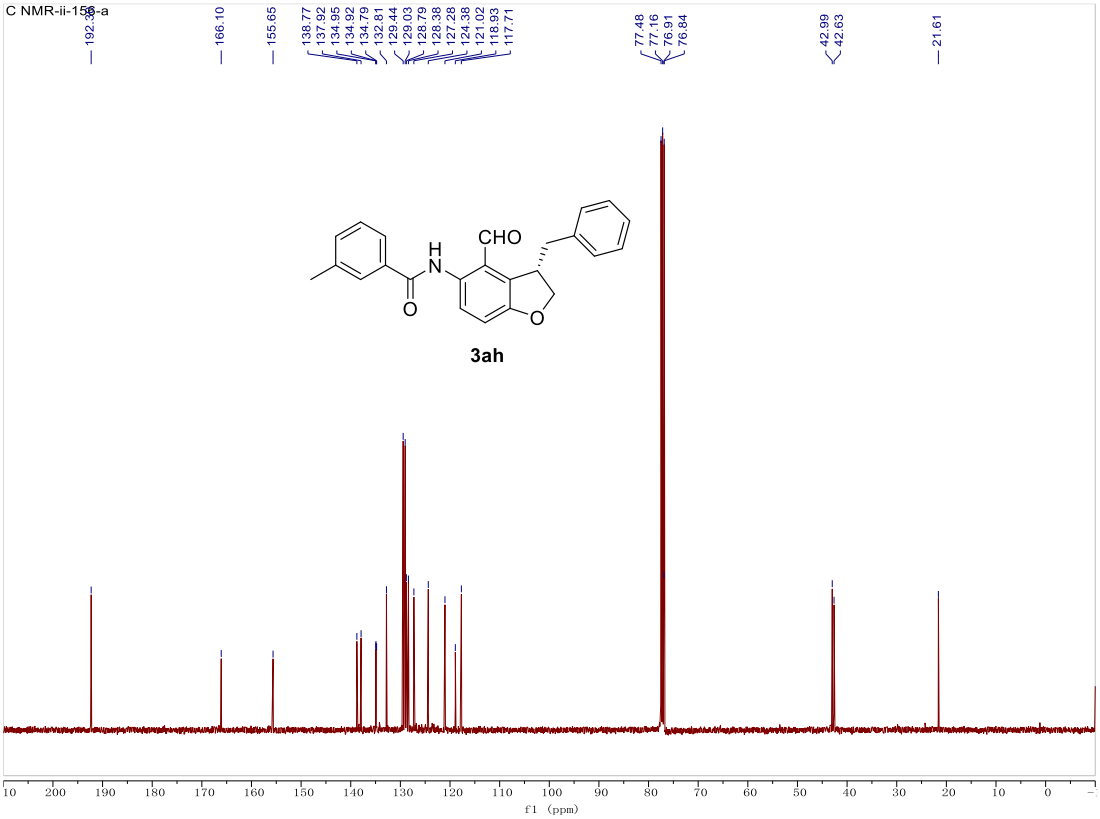


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.250	39.405	86.408	5.59	9.21	n.a.
2		26.158	665.562	852.076	94.41	90.79	n.a.
Total:			**704.967**	**938.484**	**100.00**	**100.00**	

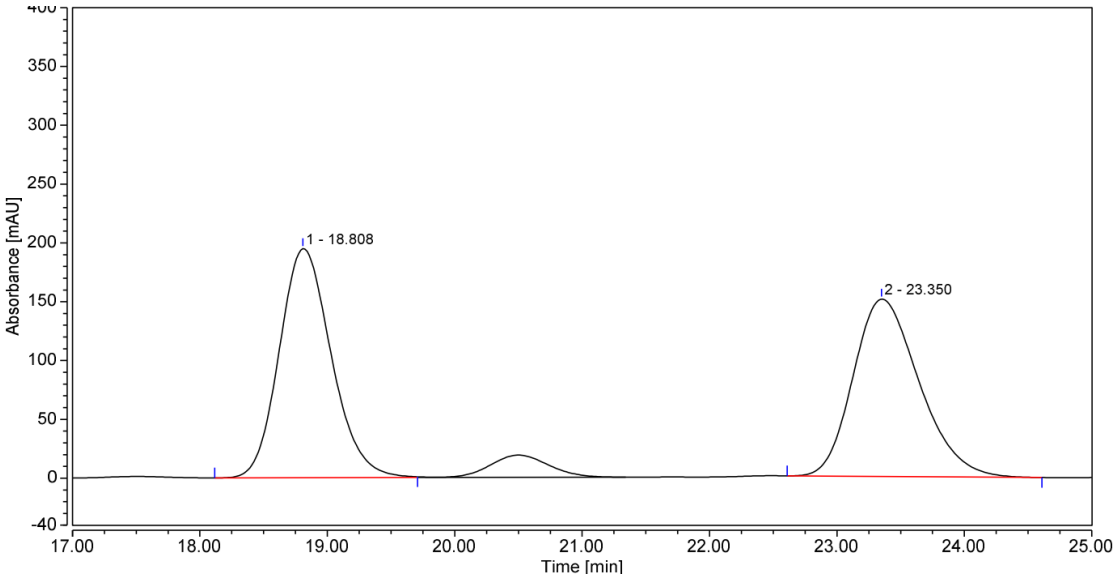
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ah**



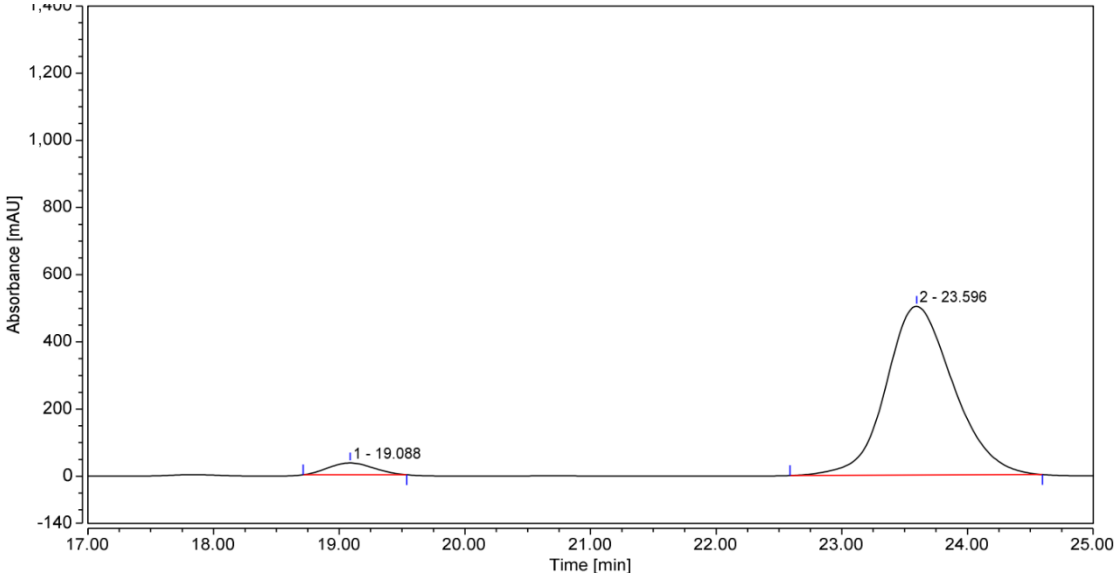
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ah**



HPLC spectra and data of compound **3ah**

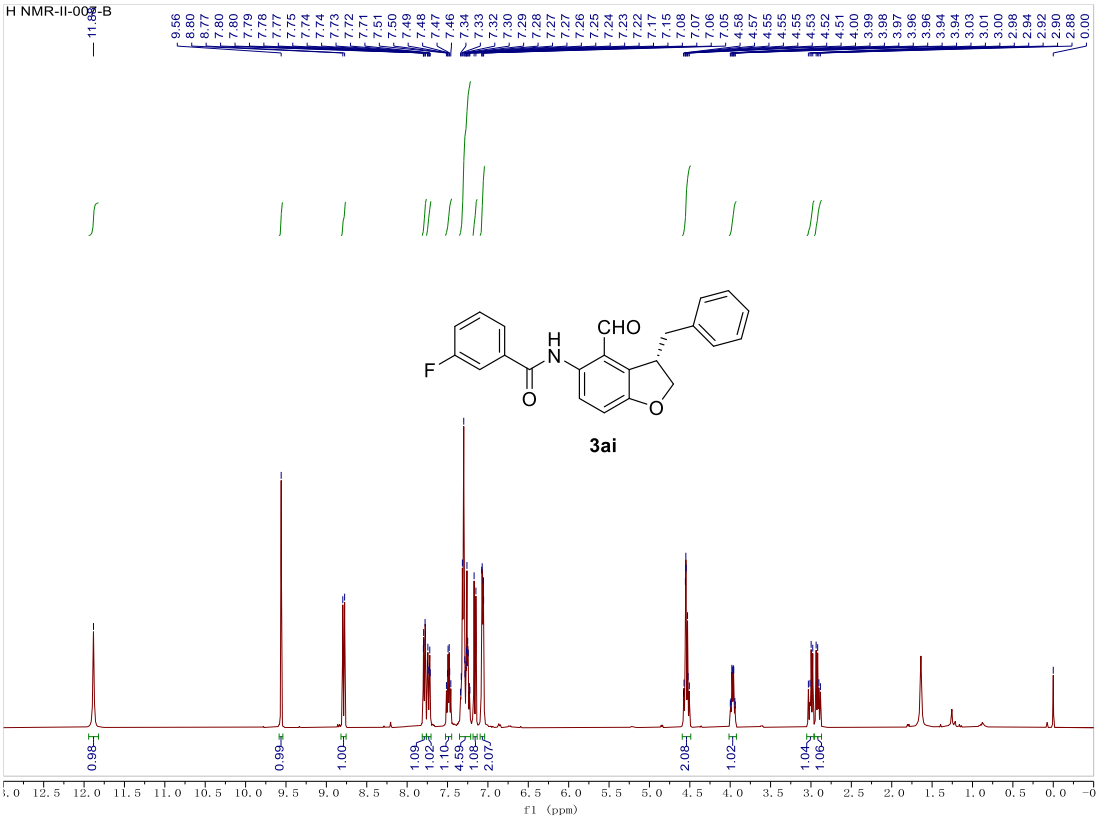


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		18.808	92.165	194.780	50.42	56.36	n.a.
2		23.350	90.623	150.792	49.58	43.64	n.a.
Total:			**182.788**	**345.572**	**100.00**	**100.00**	

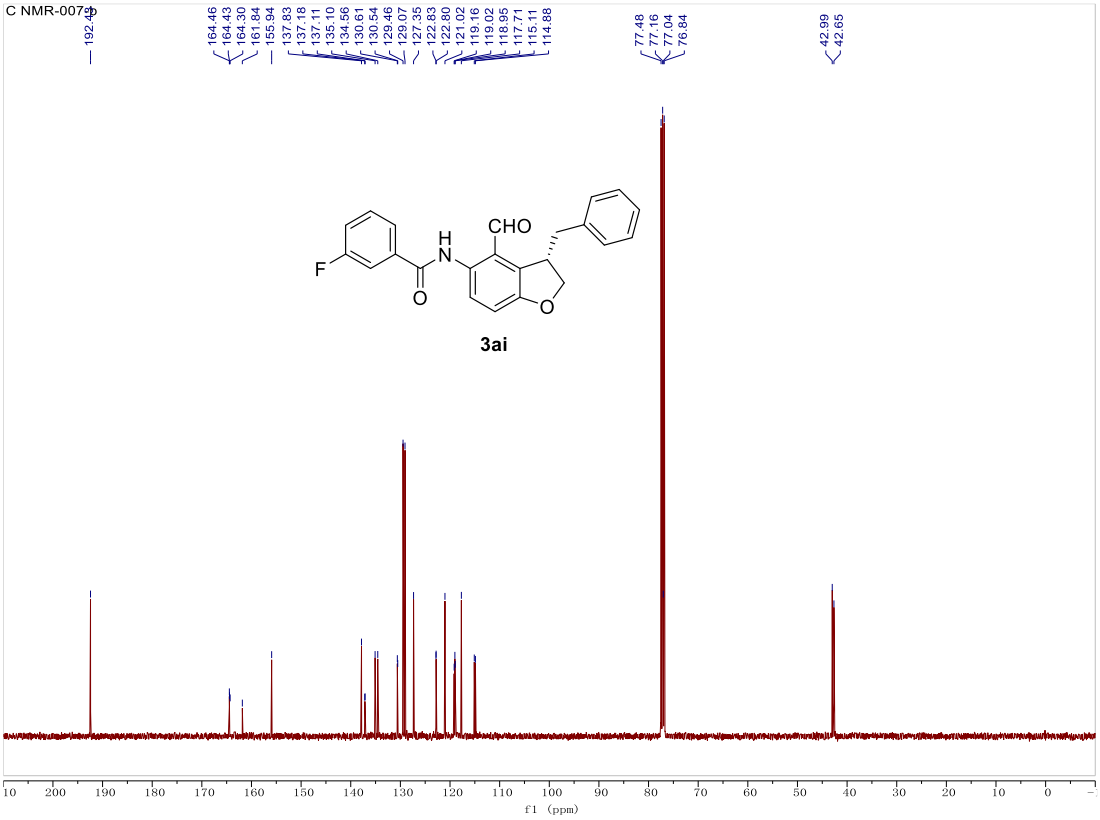


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		19.088	14.608	35.177	4.48	6.54	n.a.
2		23.596	311.522	502.748	95.52	93.46	n.a.
Total:			**326.130**	**537.925**	**100.00**	**100.00**	

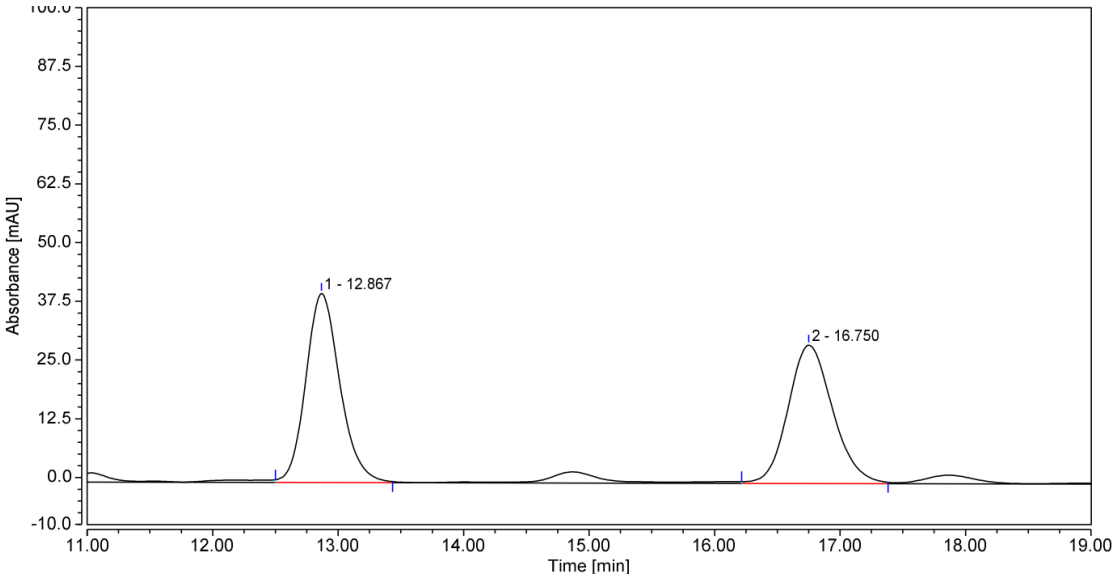
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ai**



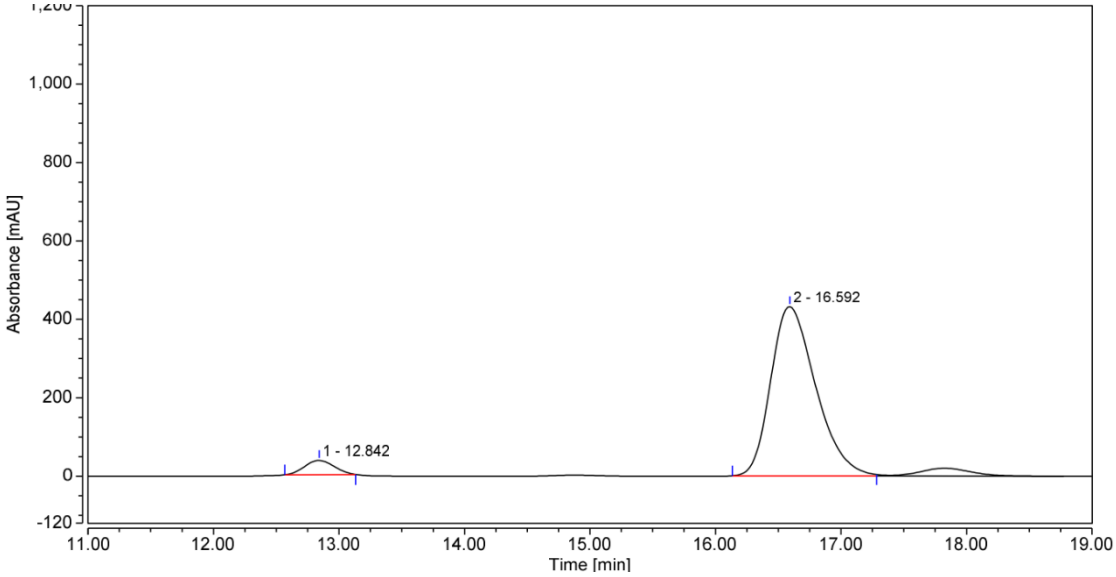
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ai**



HPLC spectra and data of compound **3ai**

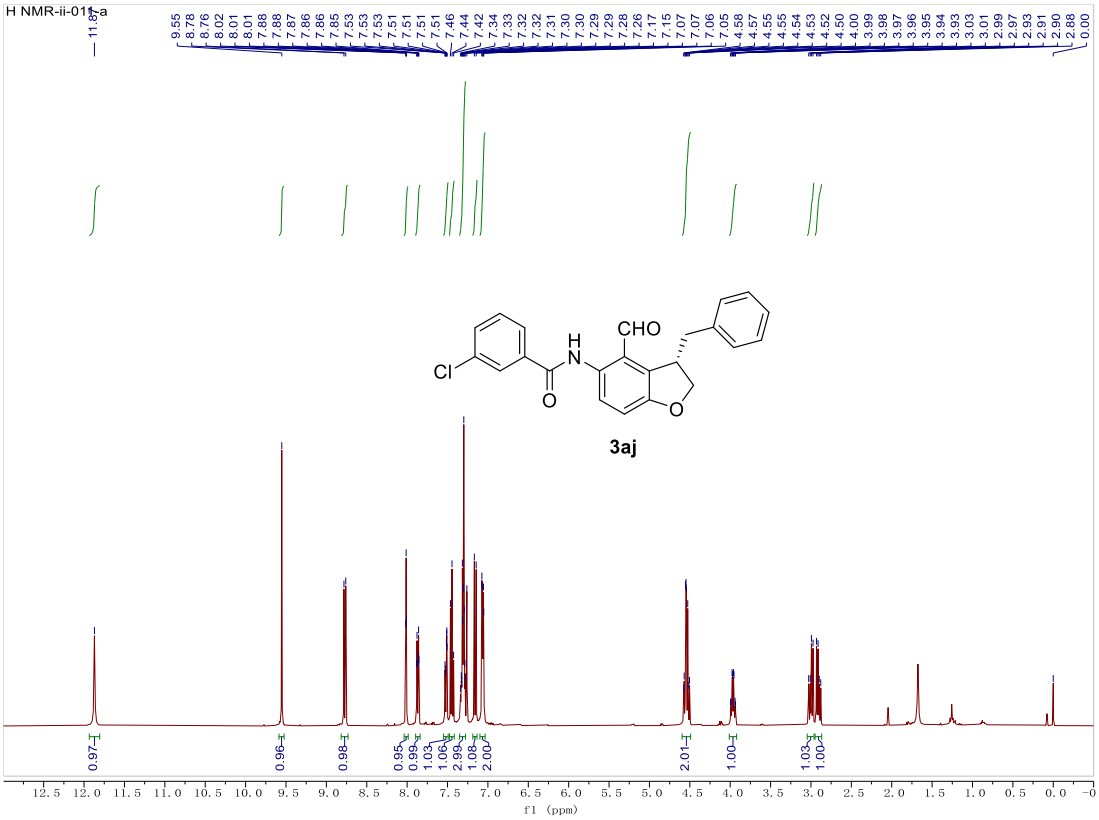


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.867	12.681	40.276	51.08	57.74	n.a.
2		16.750	12.145	29.484	48.92	42.26	n.a.
Total:			**24.826**	**69.760**	**100.00**	**100.00**	

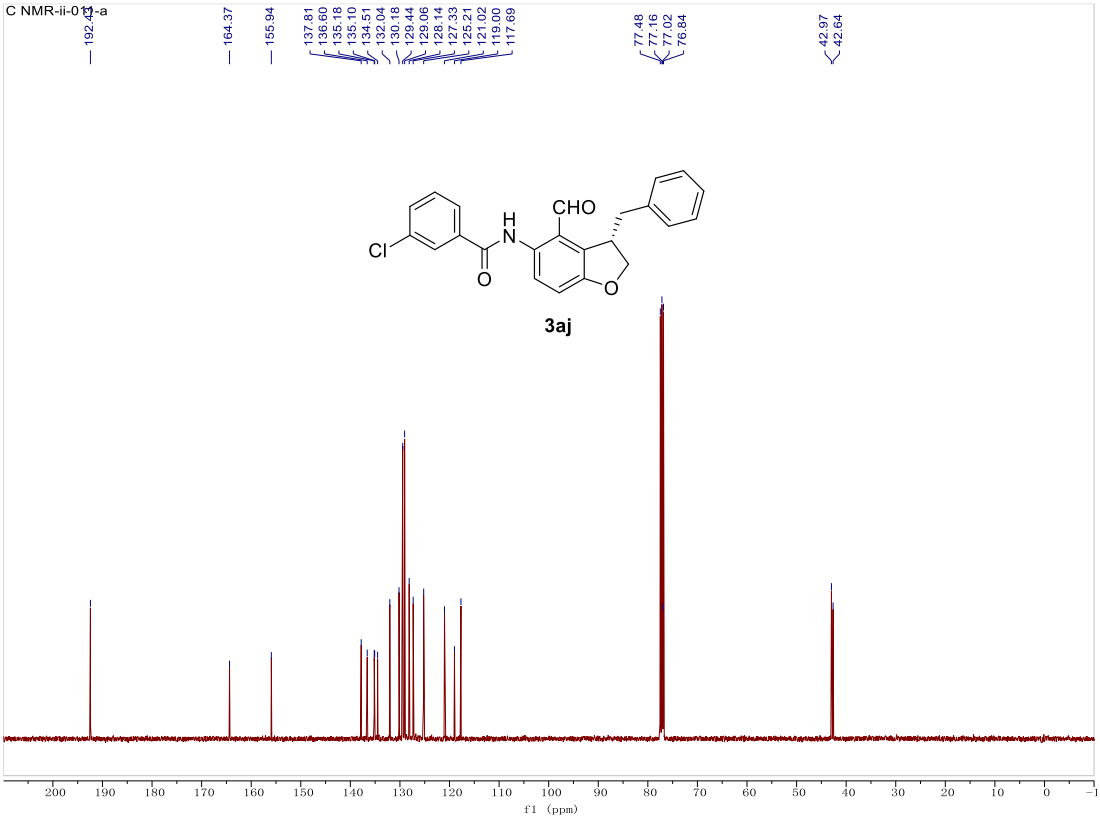


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.842	9.935	36.422	5.26	7.78	n.a.
2		16.592	178.865	431.953	94.74	92.22	n.a.
Total:			**188.800**	**468.375**	**100.00**	**100.00**	

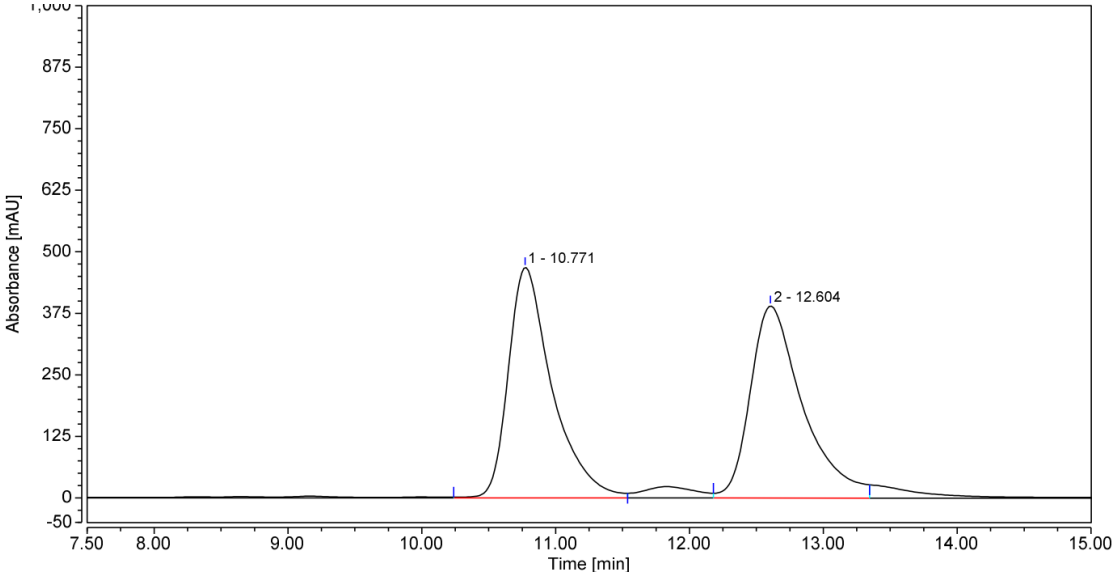
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3aj**



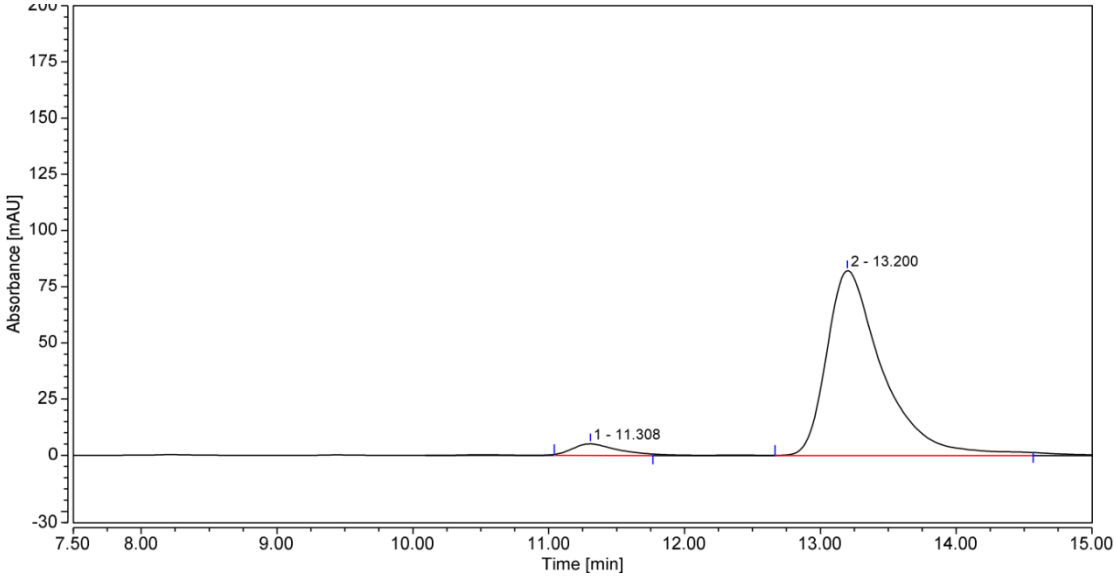
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3aj**



HPLC spectra and data of compound **3aj**

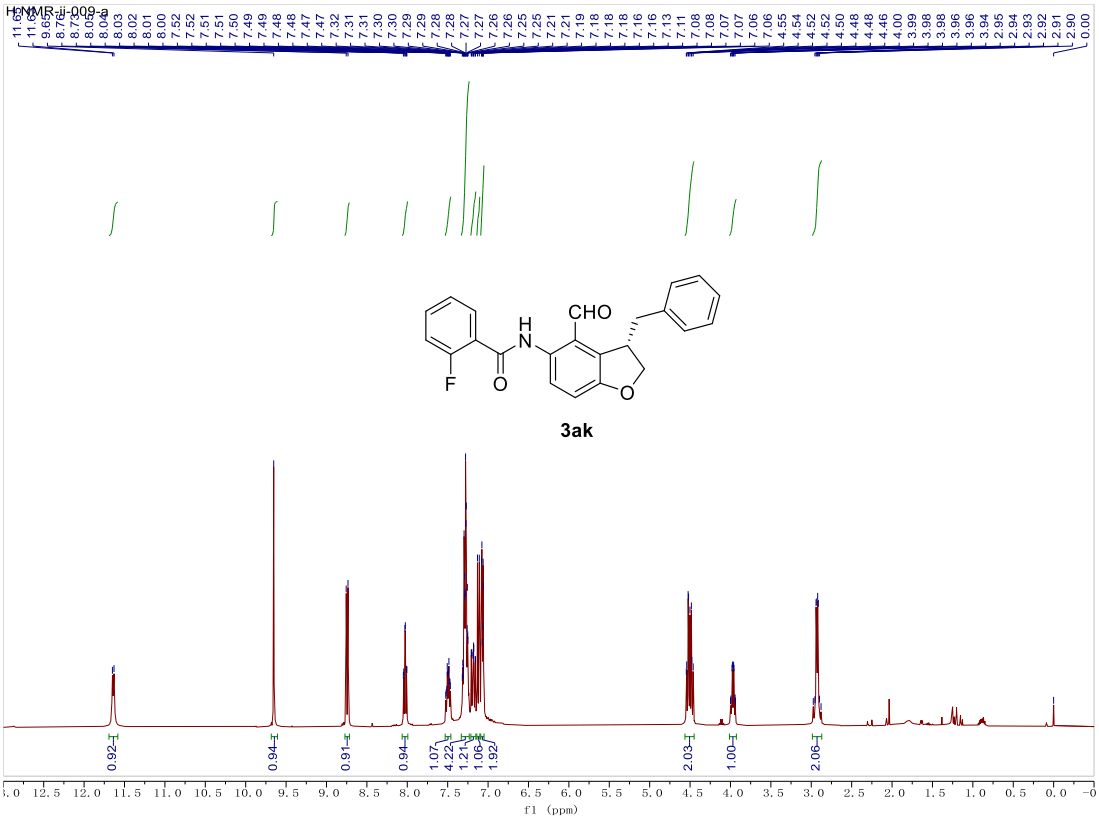


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.771	177.317	468.253	50.00	54.55	n.a.
2		12.604	177.300	390.089	50.00	45.45	n.a.
Total:			**354.618**	**858.342**	**100.00**	**100.00**	

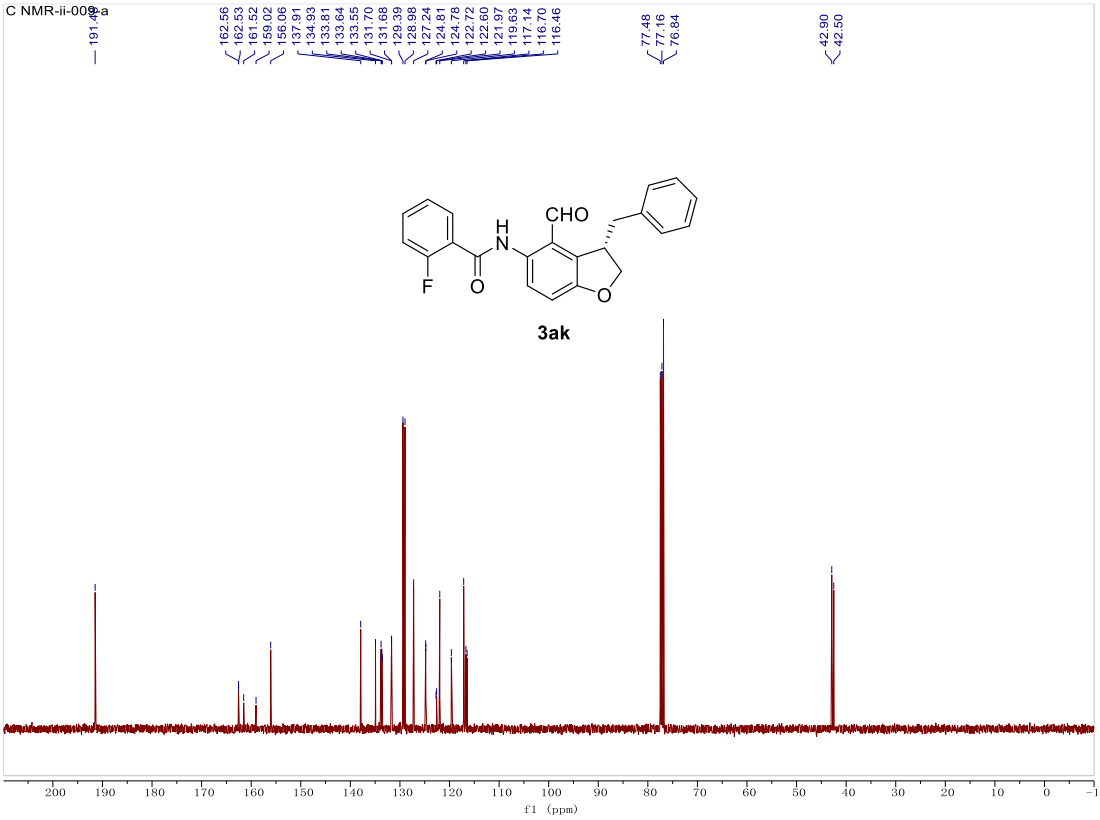


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.308	1.956	5.165	4.75	5.91	n.a.
2		13.200	39.180	82.243	95.25	94.09	n.a.
Total:			**41.136**	**87.409**	**100.00**	**100.00**	

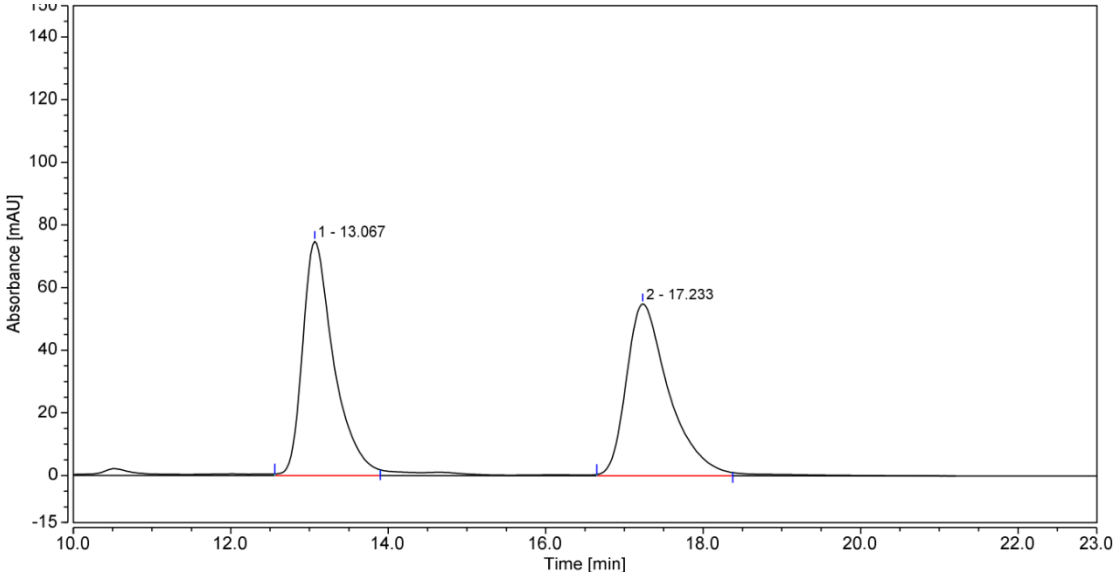
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ak**



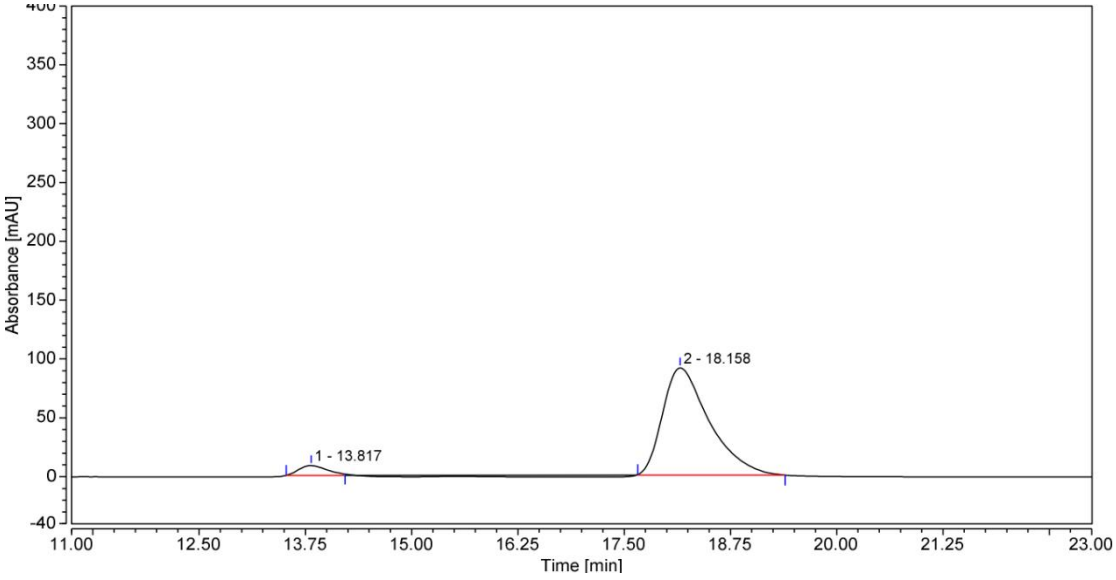
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ak**



HPLC spectra and data of compound **3ak**

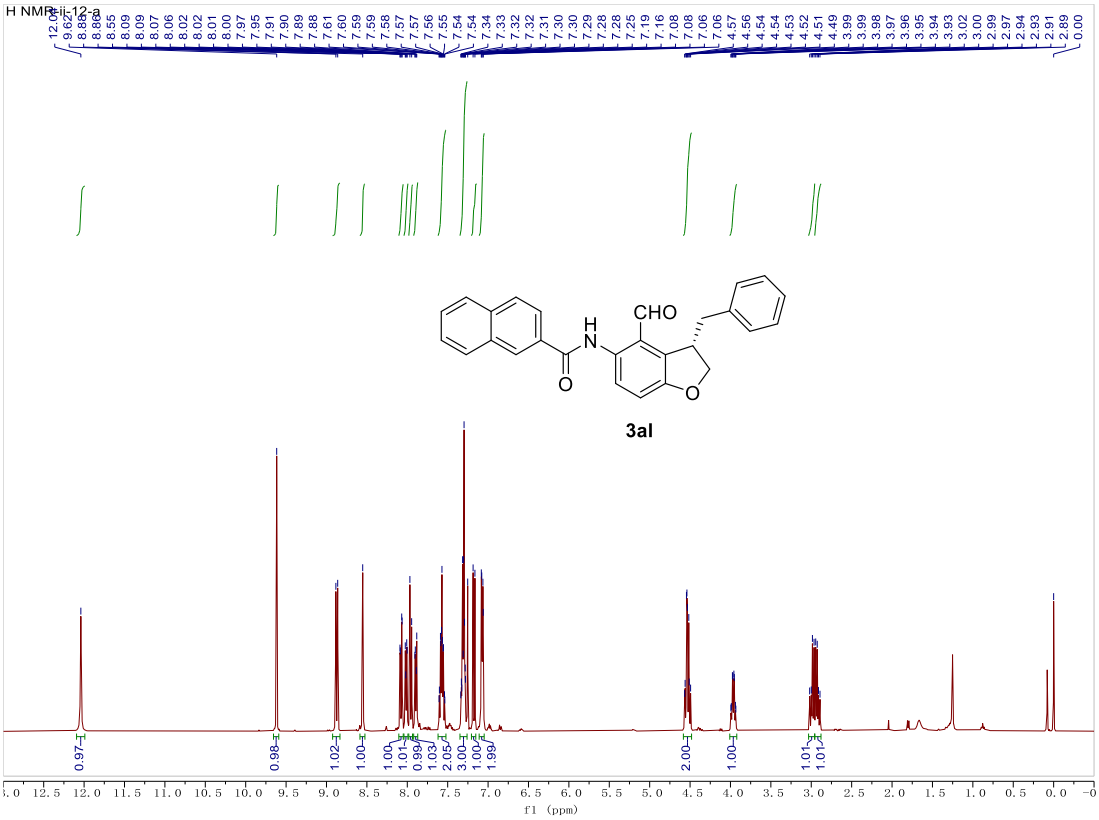


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.067	34.260	74.776	50.04	57.67	n.a.
2		17.233	34.201	54.878	49.96	42.33	n.a.
Total:			**68.461**	**129.653**	**100.00**	**100.00**	

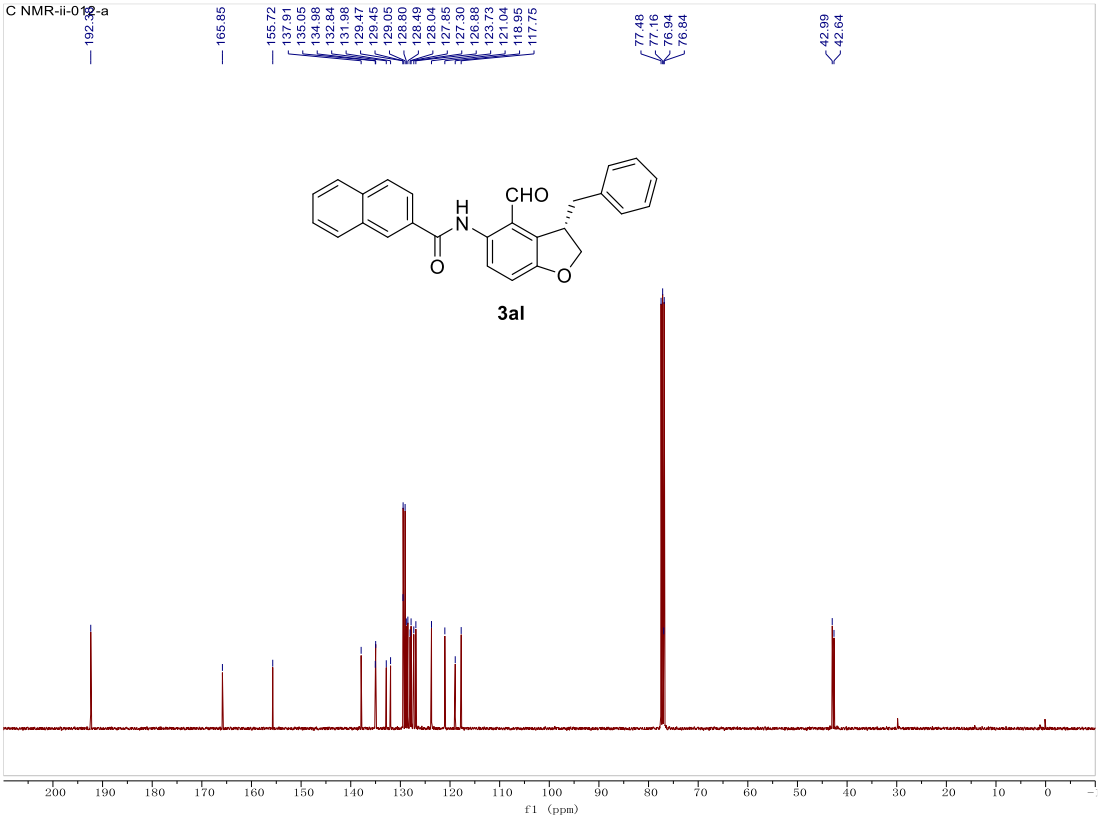


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.817	3.196	8.290	5.22	8.34	n.a.
2		18.158	58.016	91.162	94.78	91.66	n.a.
Total:			**61.213**	**99.452**	**100.00**	**100.00**	

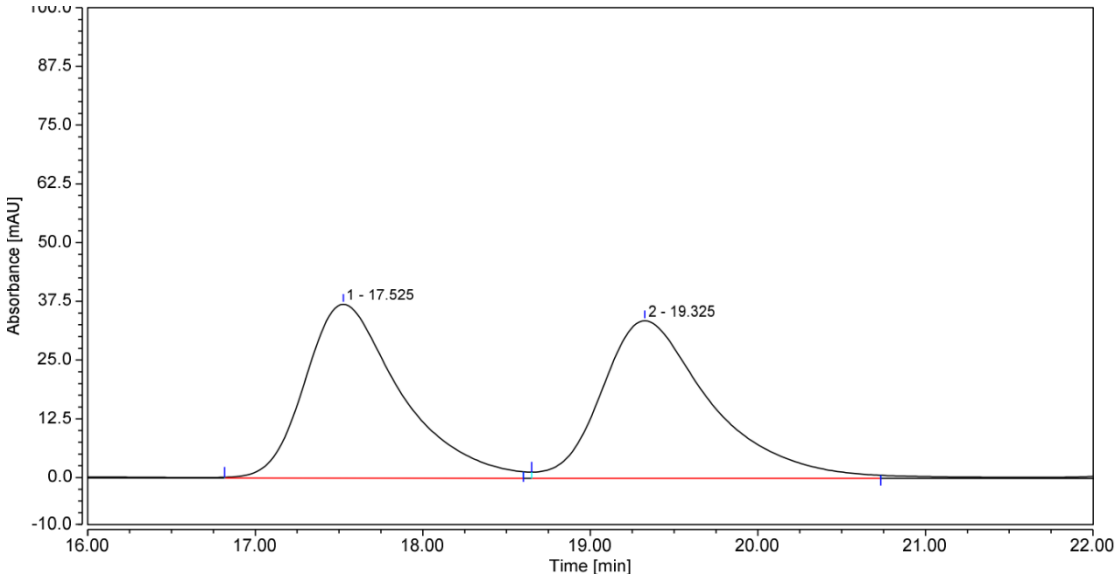
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3al**



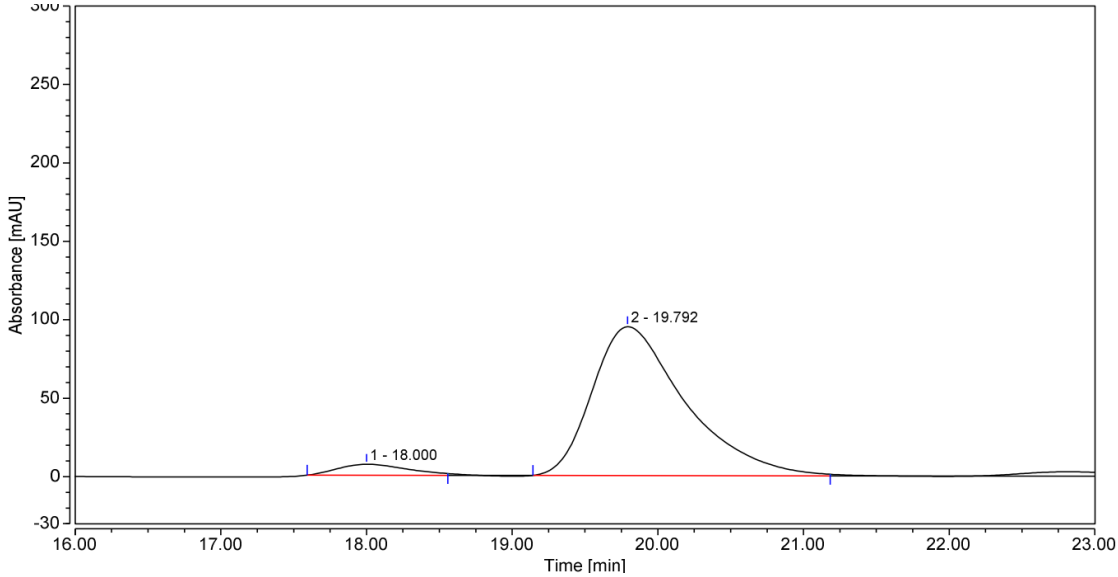
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3al**



HPLC spectra and data of compound **3al**

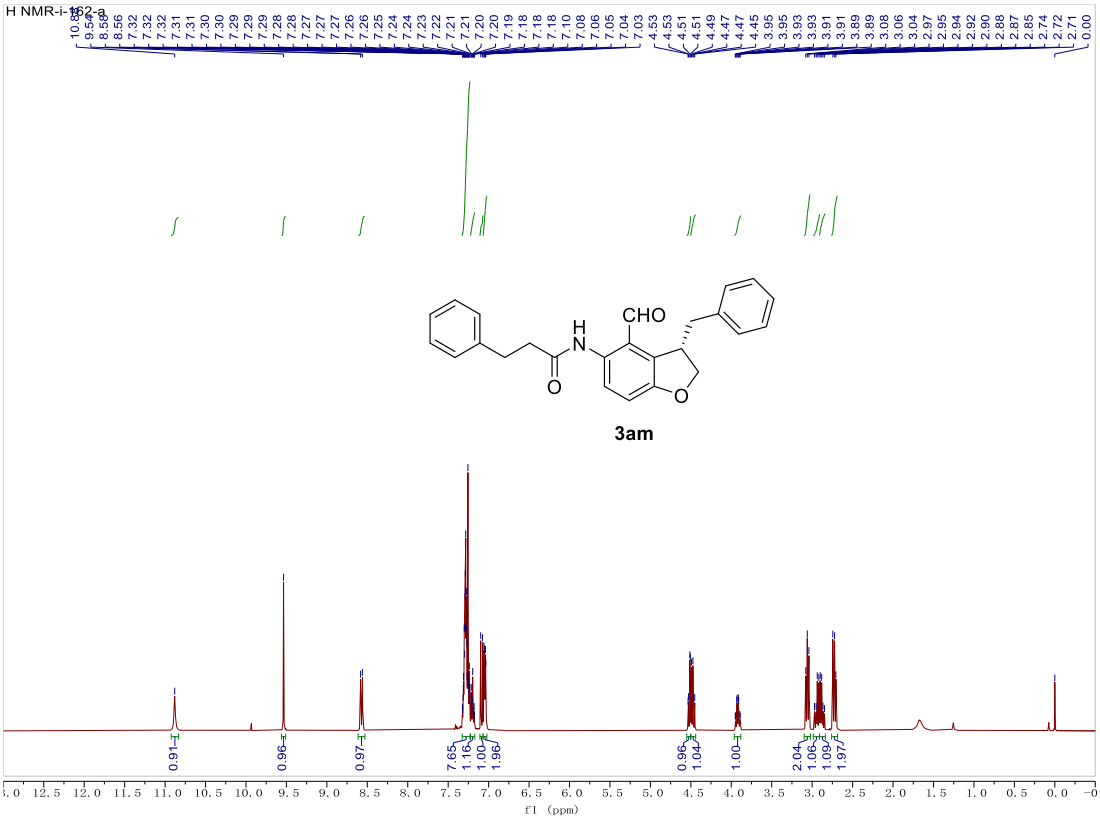


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.525	24.551	37.017	49.31	52.47	n.a.
2		19.325	25.243	33.534	50.69	47.53	n.a.
Total:			**49.794**	**70.551**	**100.00**	**100.00**	

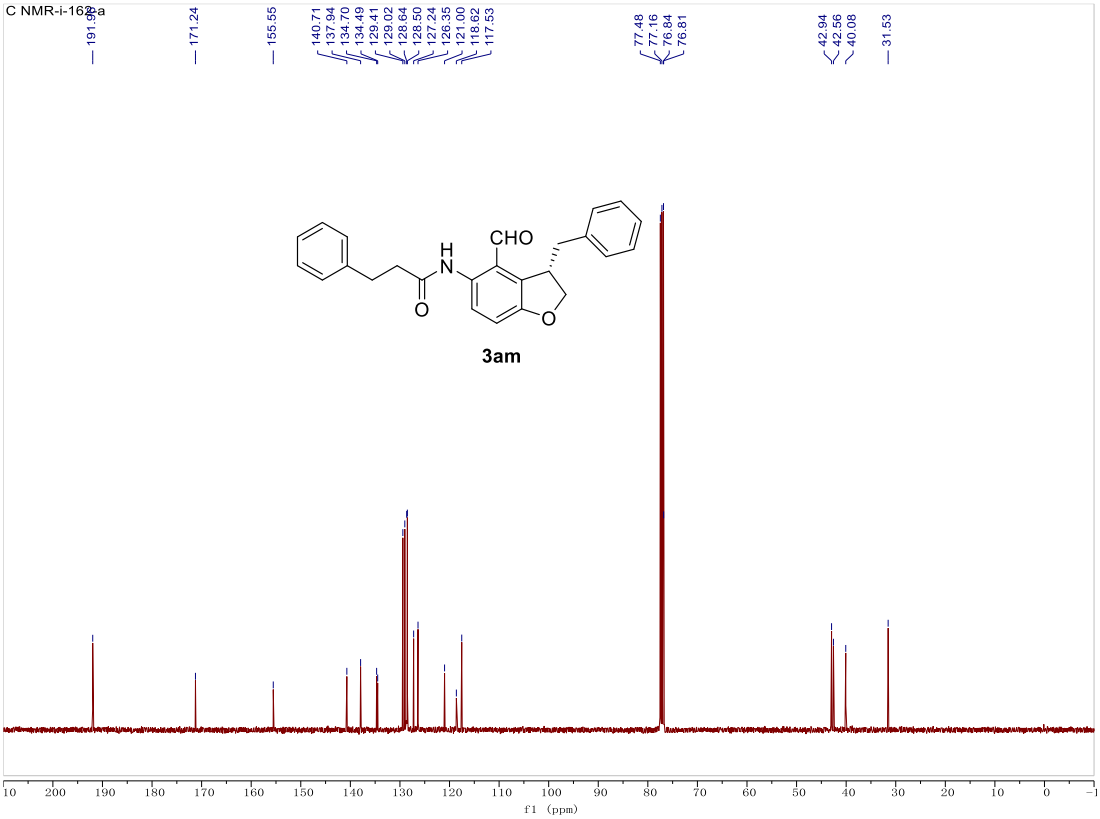


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		18.000	3.874	7.010	5.24	6.88	n.a.
2		19.792	70.103	94.877	94.76	93.12	n.a.
Total:			**73.978**	**101.887**	**100.00**	**100.00**	

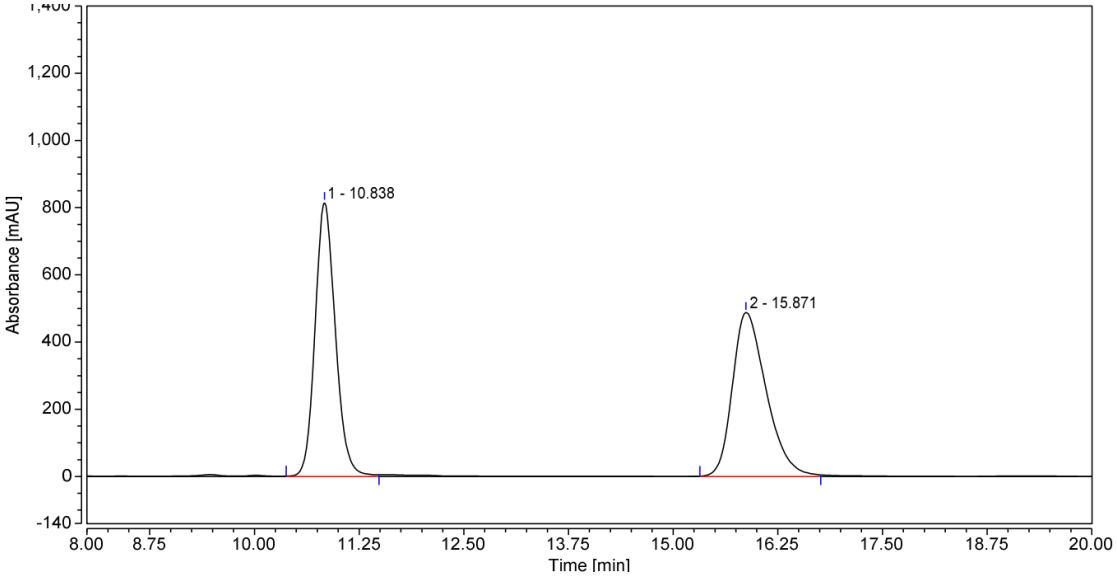
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3am**



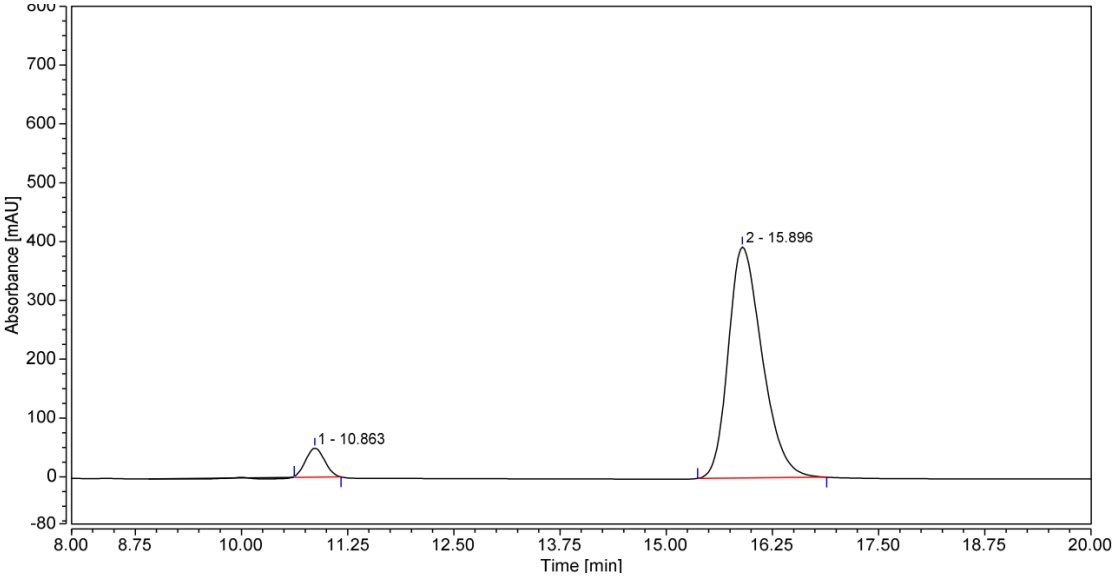
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3am**



HPLC spectra and data of compound **3am**

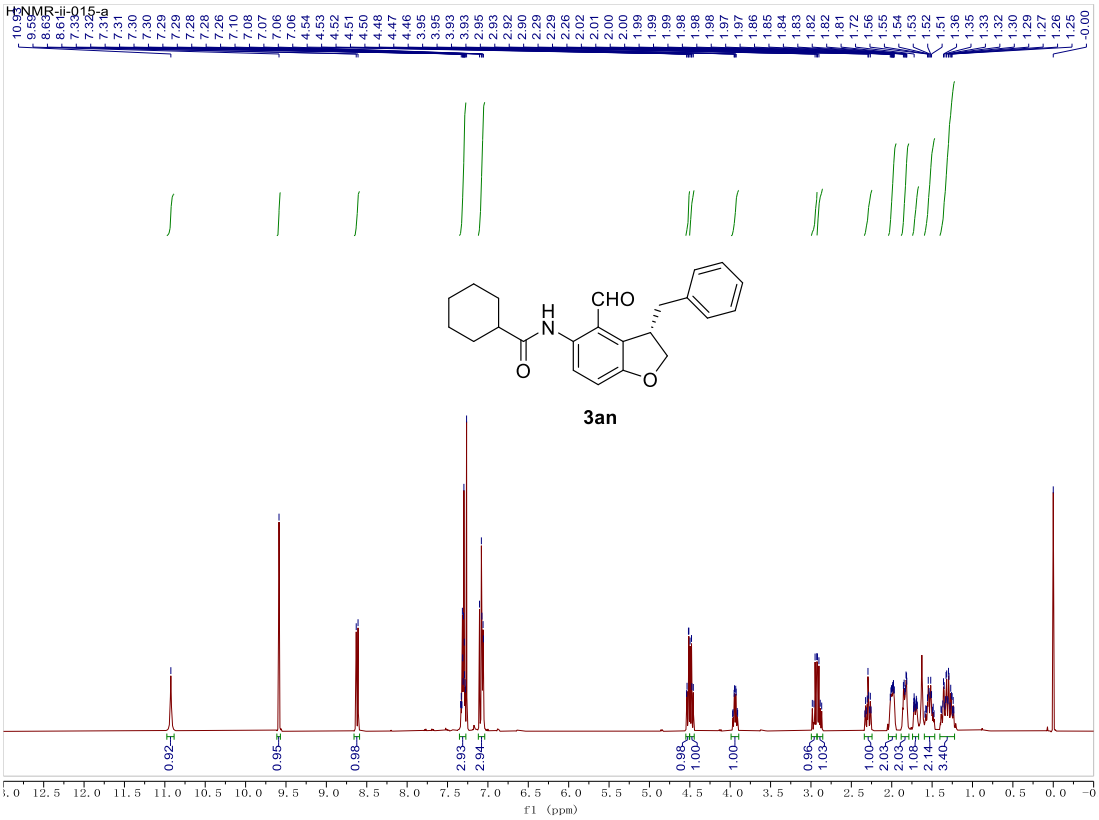


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.838	229.109	815.419	50.06	62.54	n.a.
2		15.871	228.597	488.469	49.94	37.46	n.a.
Total:			**457.705**	**1303.889**	**100.00**	**100.00**	

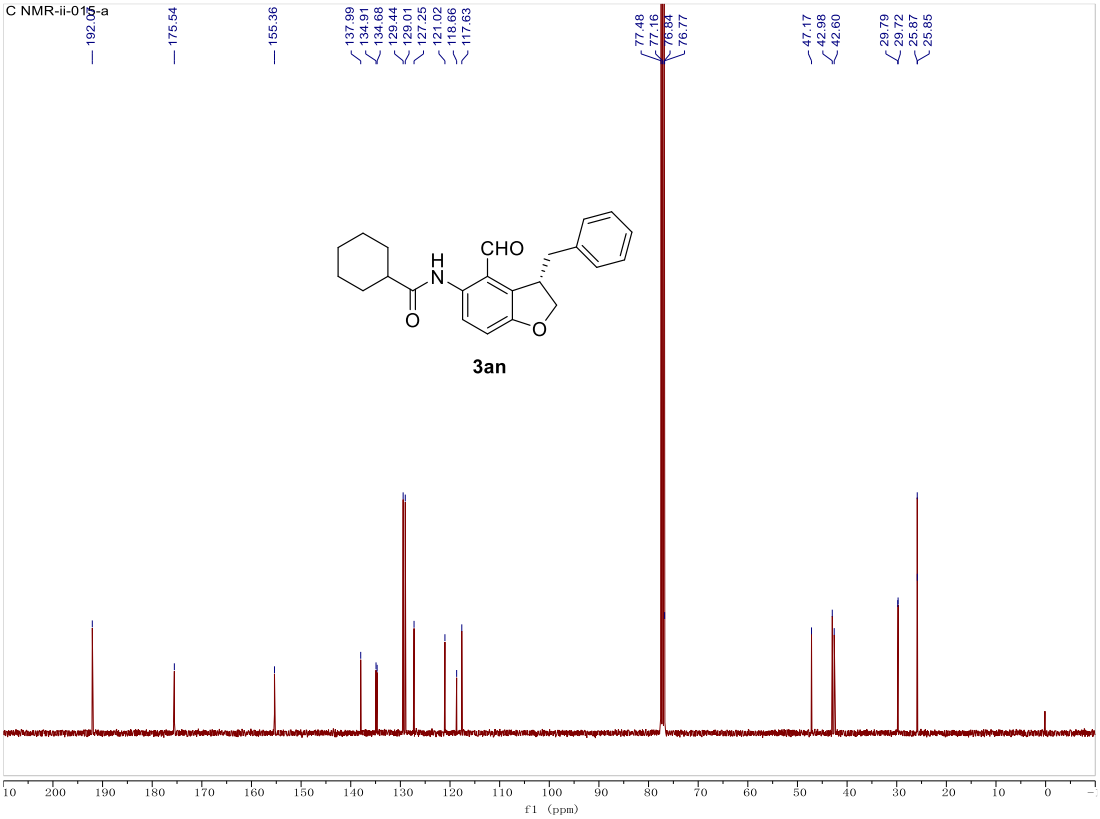


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.863	12.885	49.541	6.63	11.20	n.a.
2		15.896	181.570	392.846	93.37	88.80	n.a.
Total:			**194.455**	**442.386**	**100.00**	**100.00**	

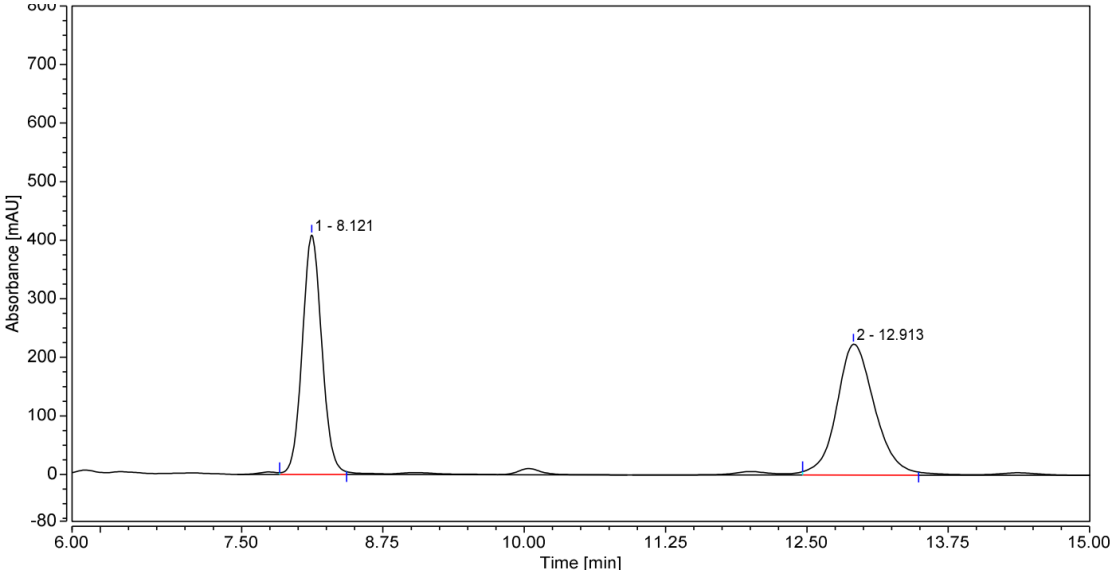
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3an**



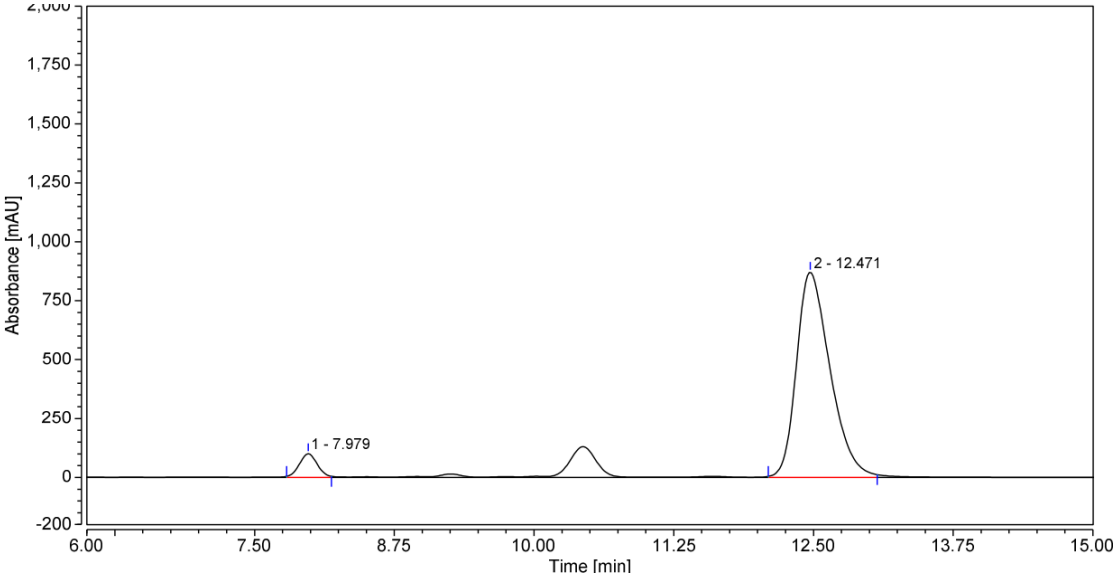
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3an**



HPLC spectra and data of compound **3an**

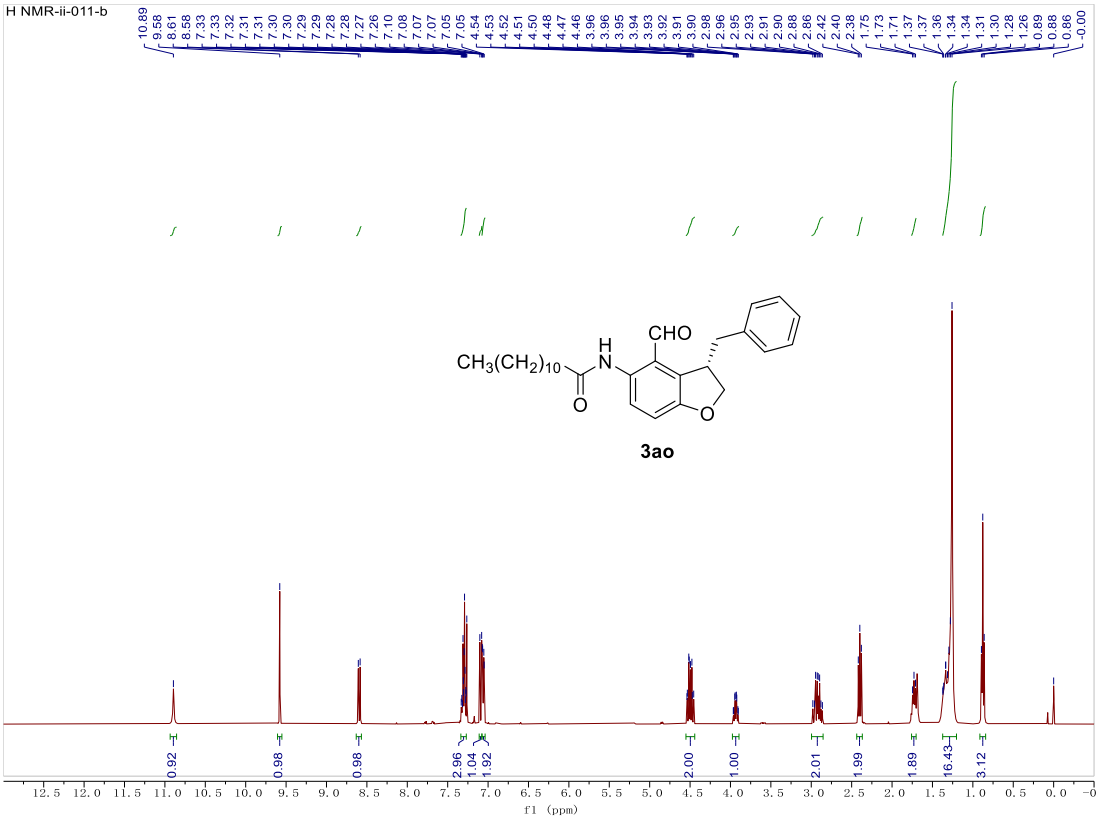


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		8.121	82.036	409.033	48.66	64.64	n.a.
2		12.913	86.558	223.792	51.34	35.36	n.a.
Total:			**168.594**	**632.825**	**100.00**	**100.00**	

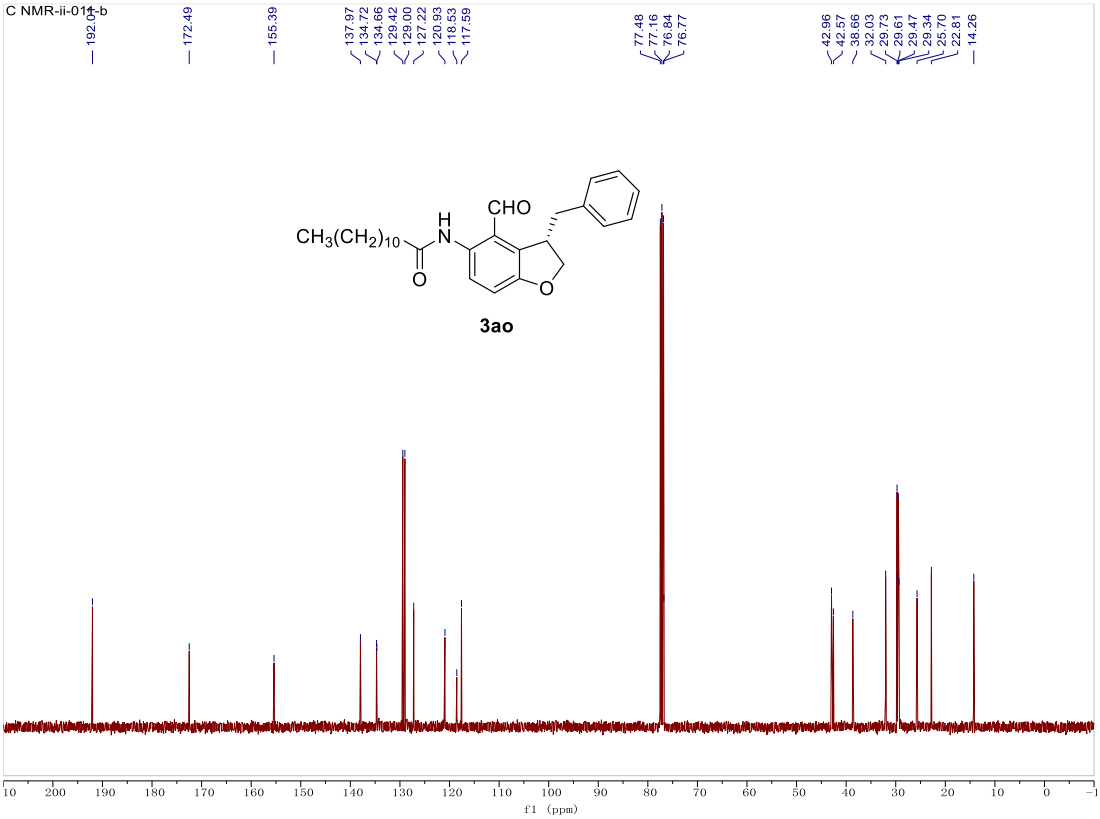


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.979	18.809	100.355	5.84	10.33	n.a.
2		12.471	303.221	870.753	94.16	89.67	n.a.
Total:			**322.030**	**971.108**	**100.00**	**100.00**	

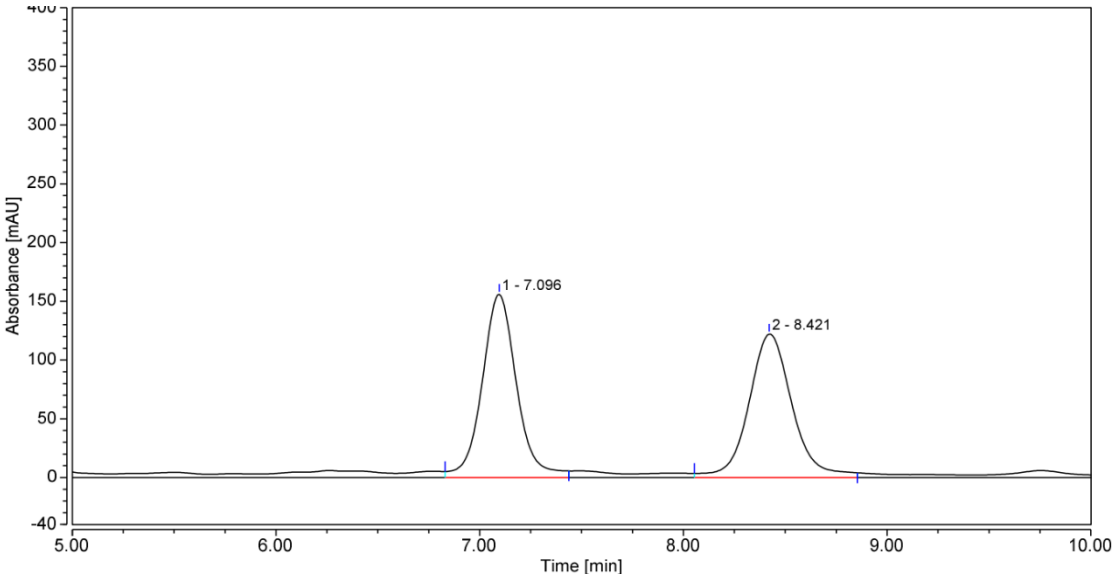
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3ao**



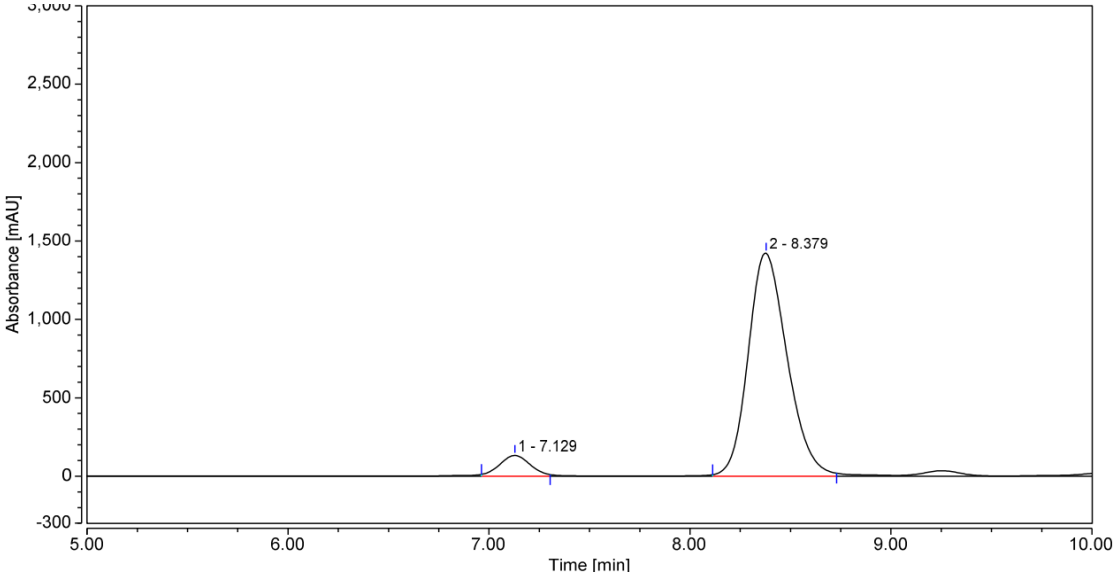
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3ao**



HPLC spectra and data of compound **3ao**

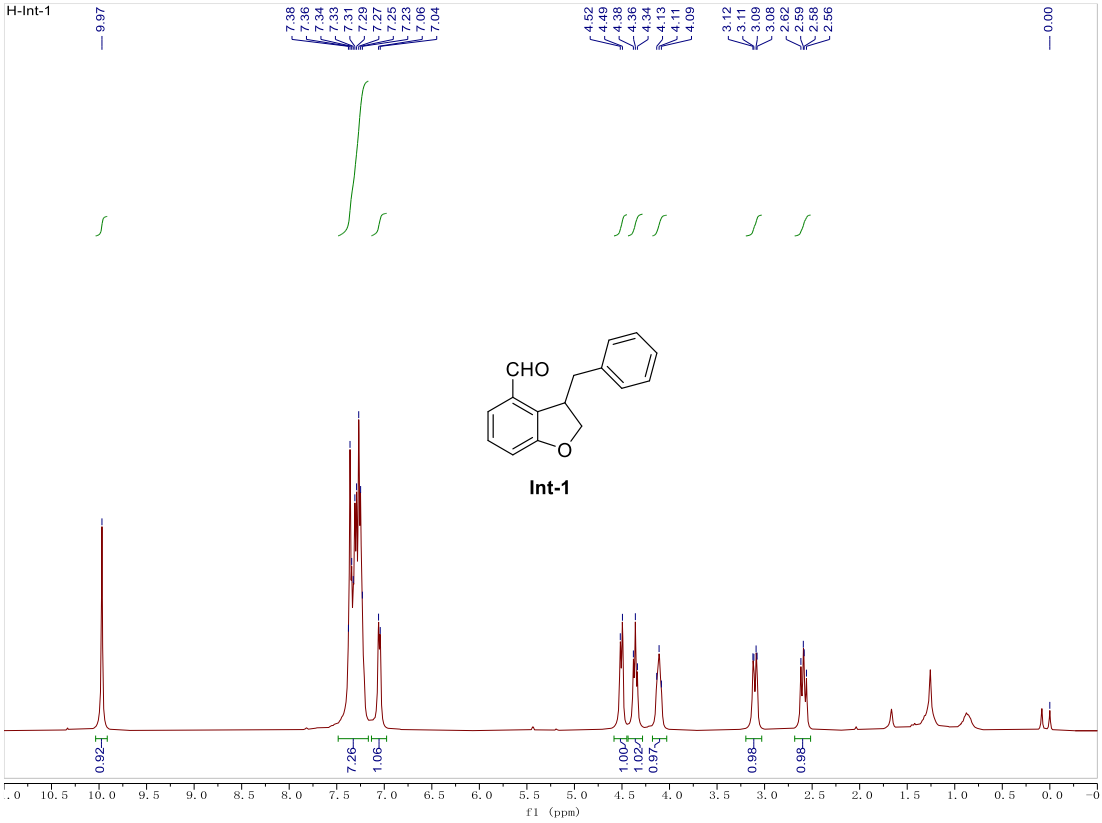


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.096	30.620	155.910	50.44	56.08	n.a.
2		8.421	30.086	122.113	49.56	43.92	n.a.
Total:			**60.706**	**278.023**	**100.00**	**100.00**	

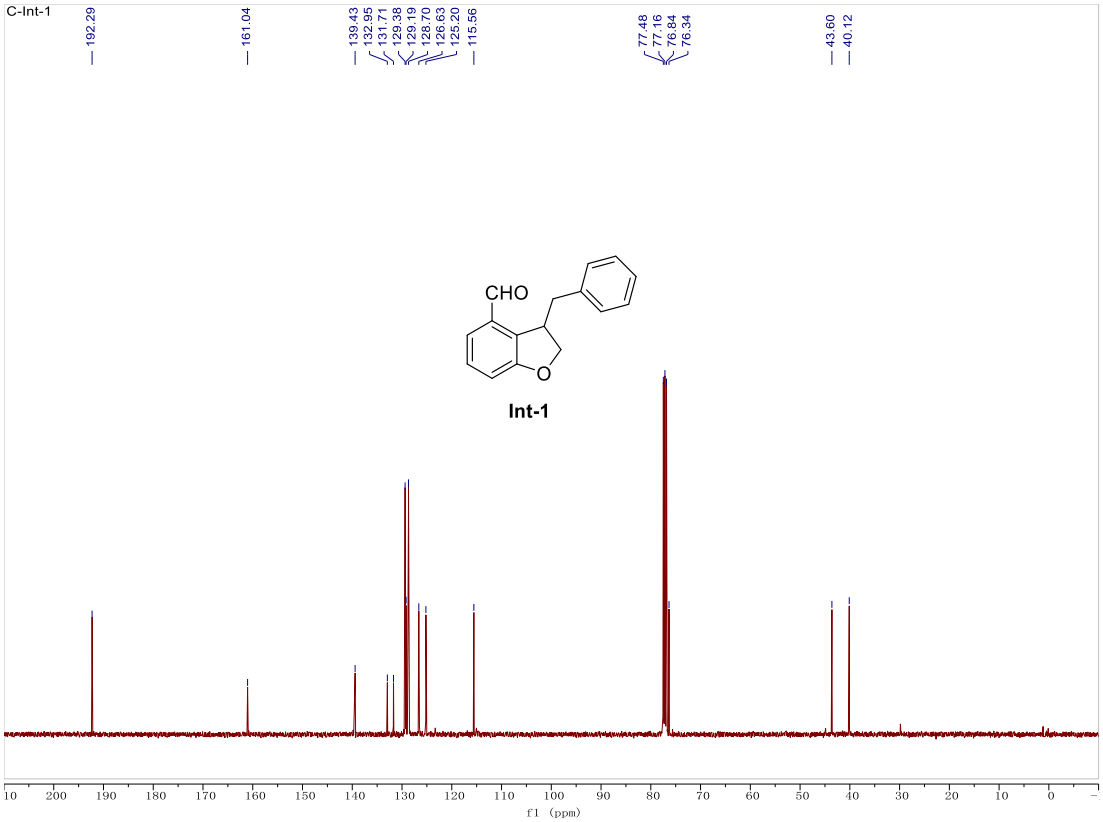


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.129	23.426	132.621	6.83	8.53	n.a.
2		8.379	319.519	1422.083	93.17	91.47	n.a.
Total:			**342.945**	**1554.704**	**100.00**	**100.00**	

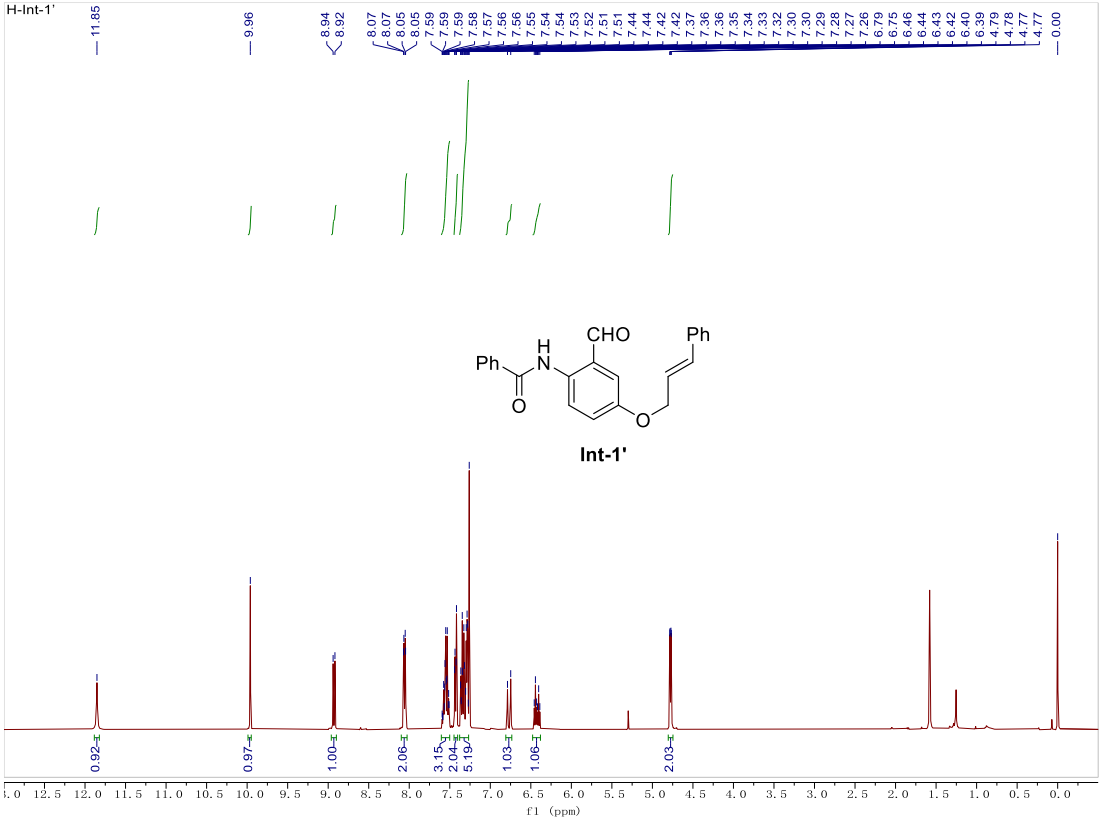
^{1}H NMR (400 MHz, $CDCl_3$) of compound **Int-1**



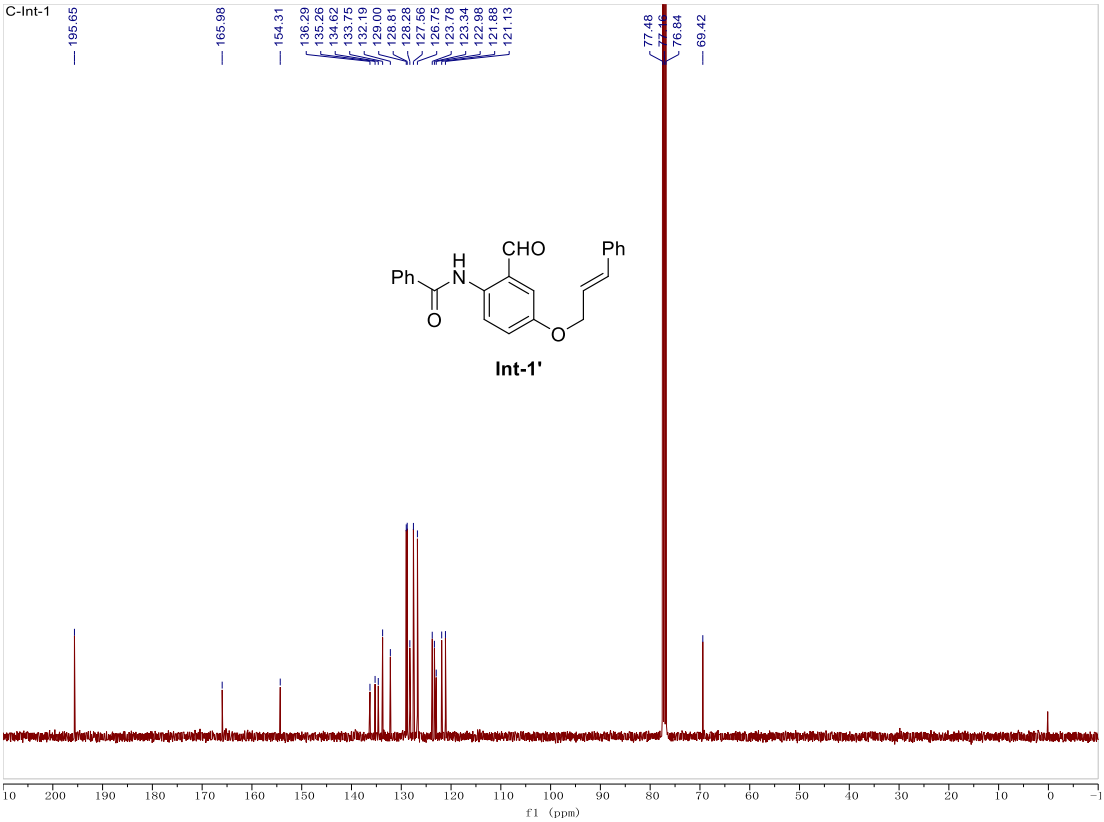
^{13}C NMR (101 MHz, $CDCl_3$) of compound **Int-1**



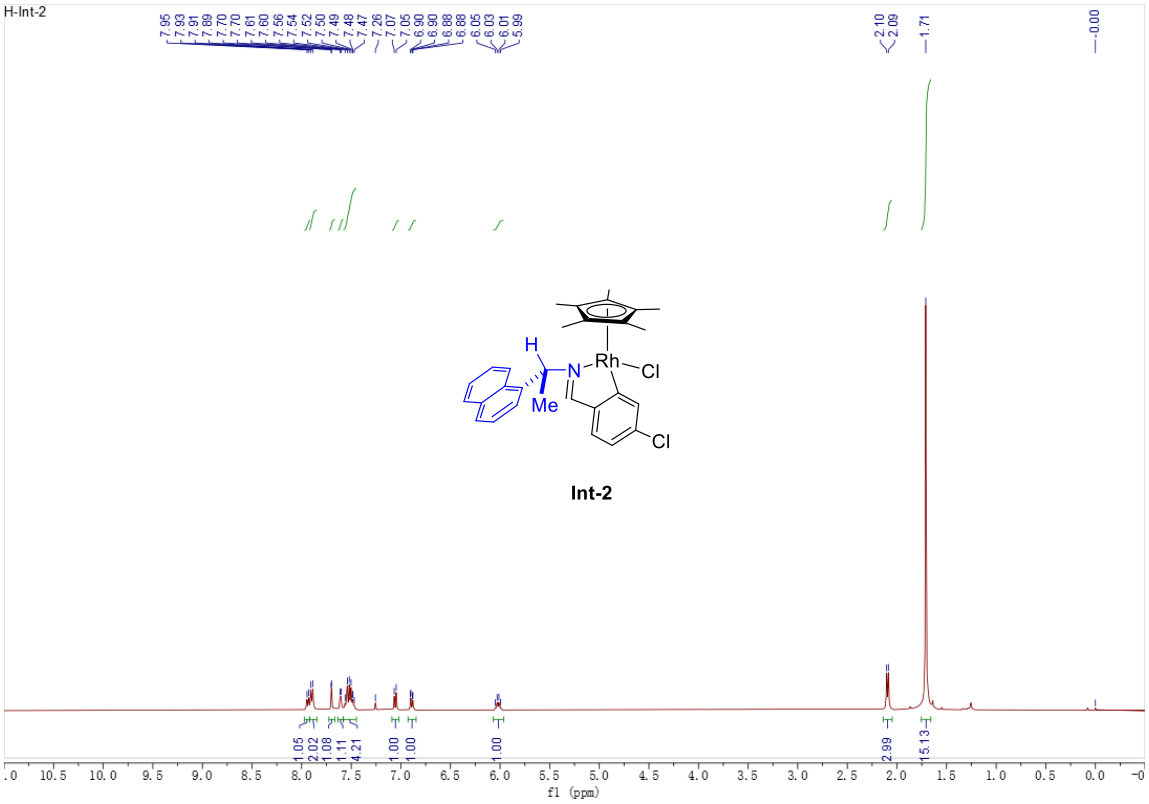
^{1}H NMR (400 MHz, $CDCl_3$) of compound **Int-1'**



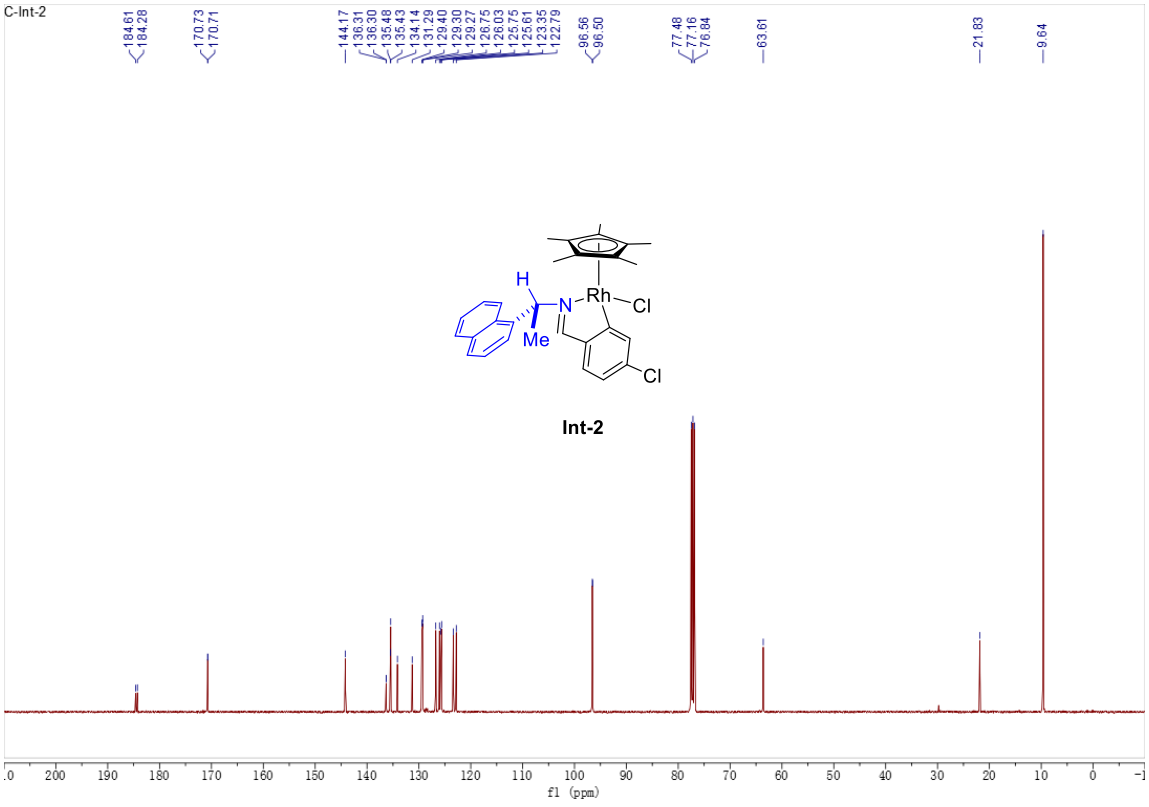
^{13}C NMR (101 MHz, $CDCl_3$) of compound **Int-1'**



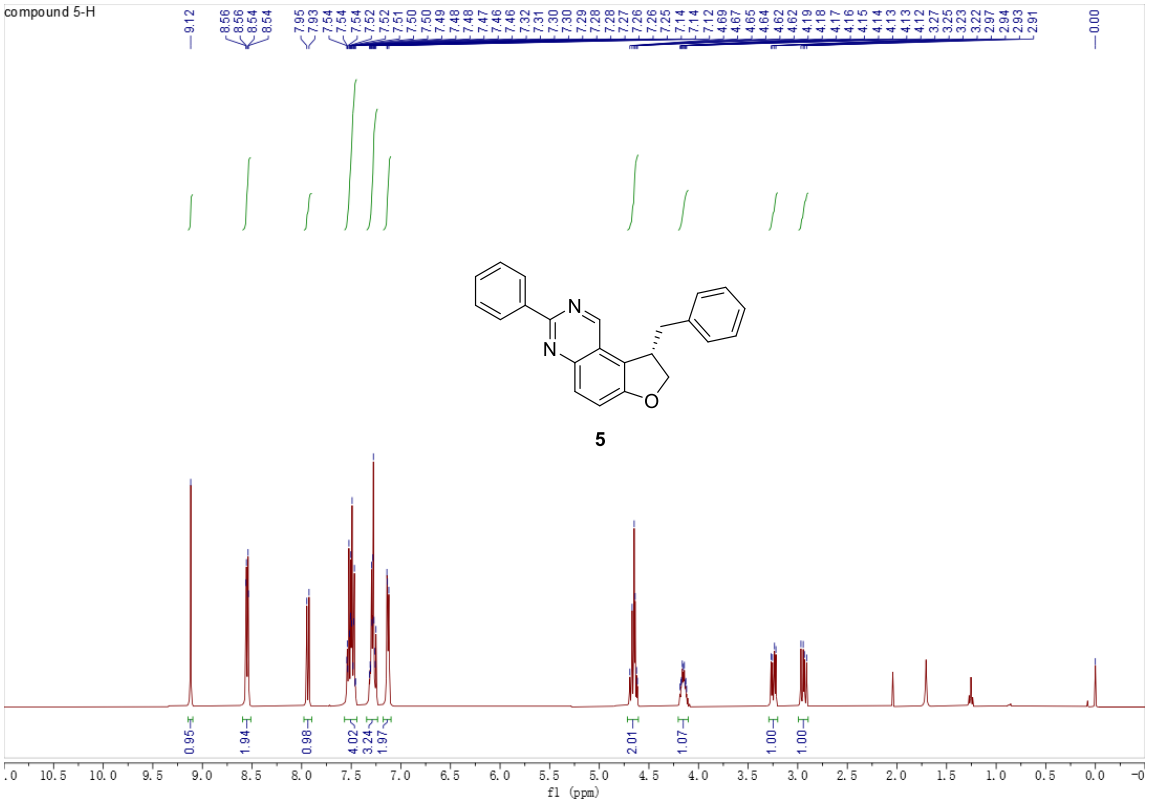
^{1}H NMR (400 MHz, $CDCl_3$) of compound **Int-2**



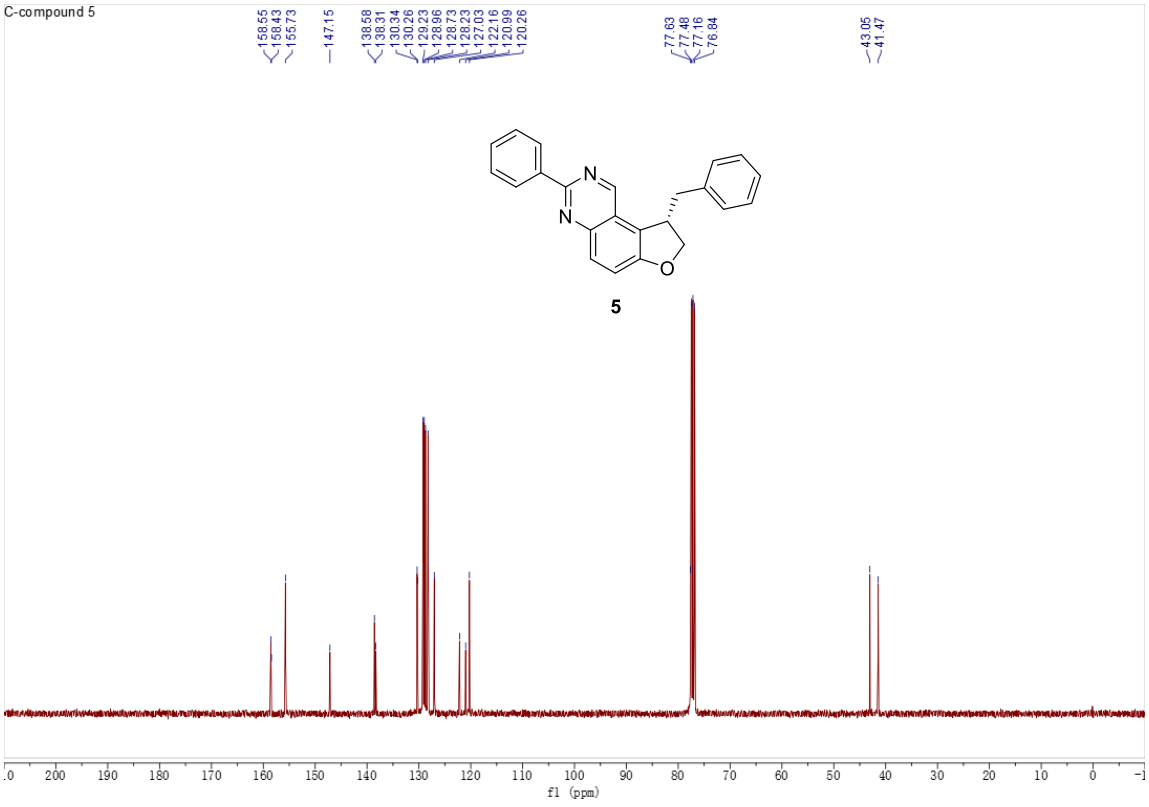
^{13}C NMR (101 MHz, $CDCl_3$) of compound **Int-2**



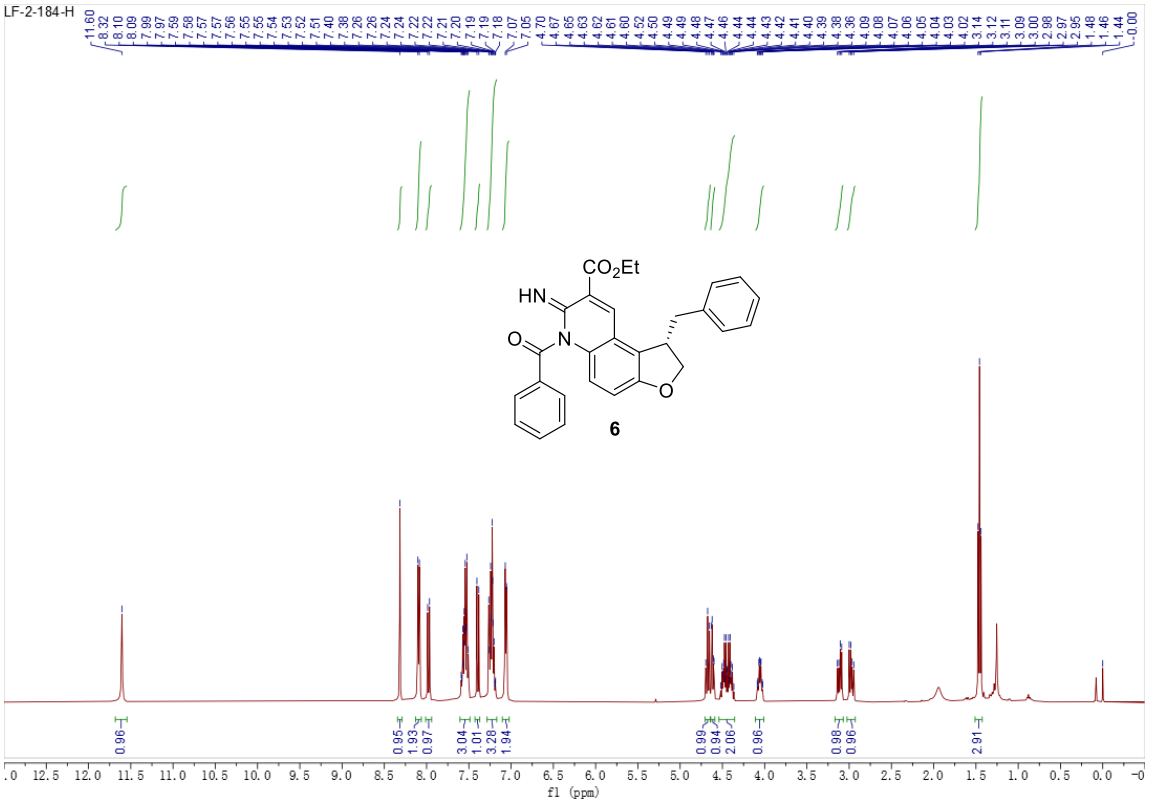
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5**



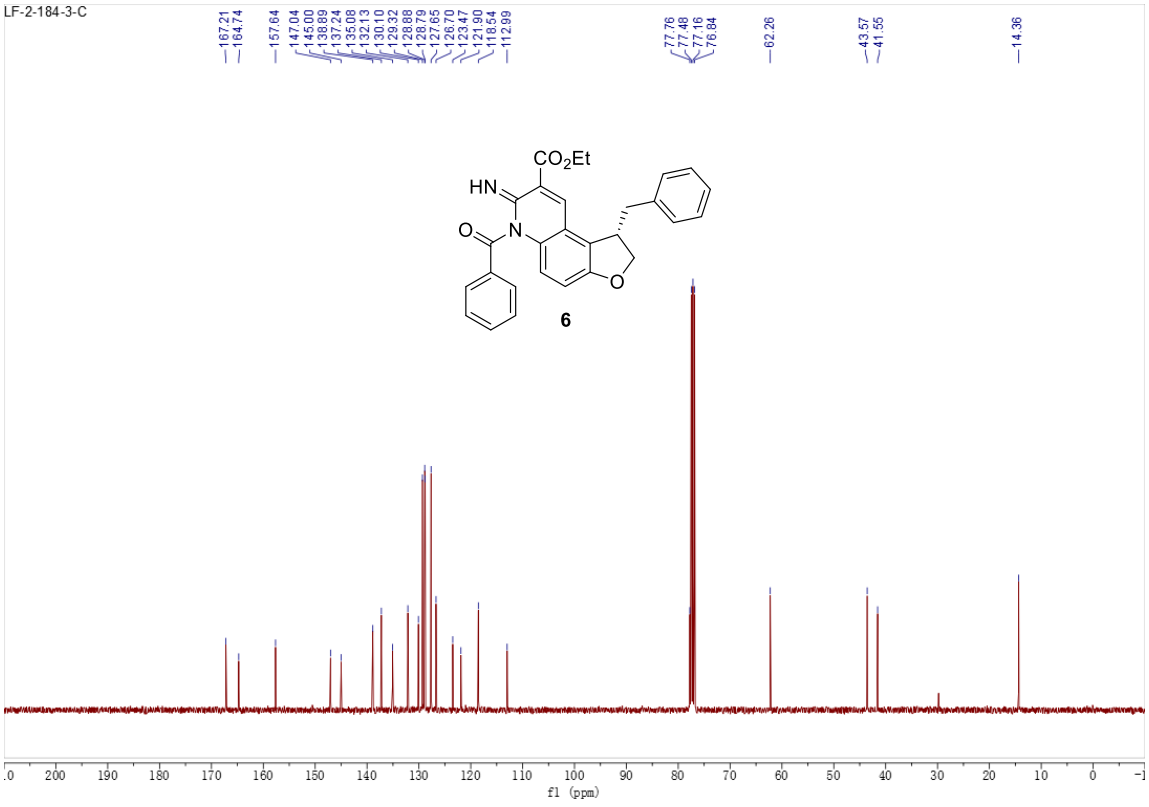
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5**



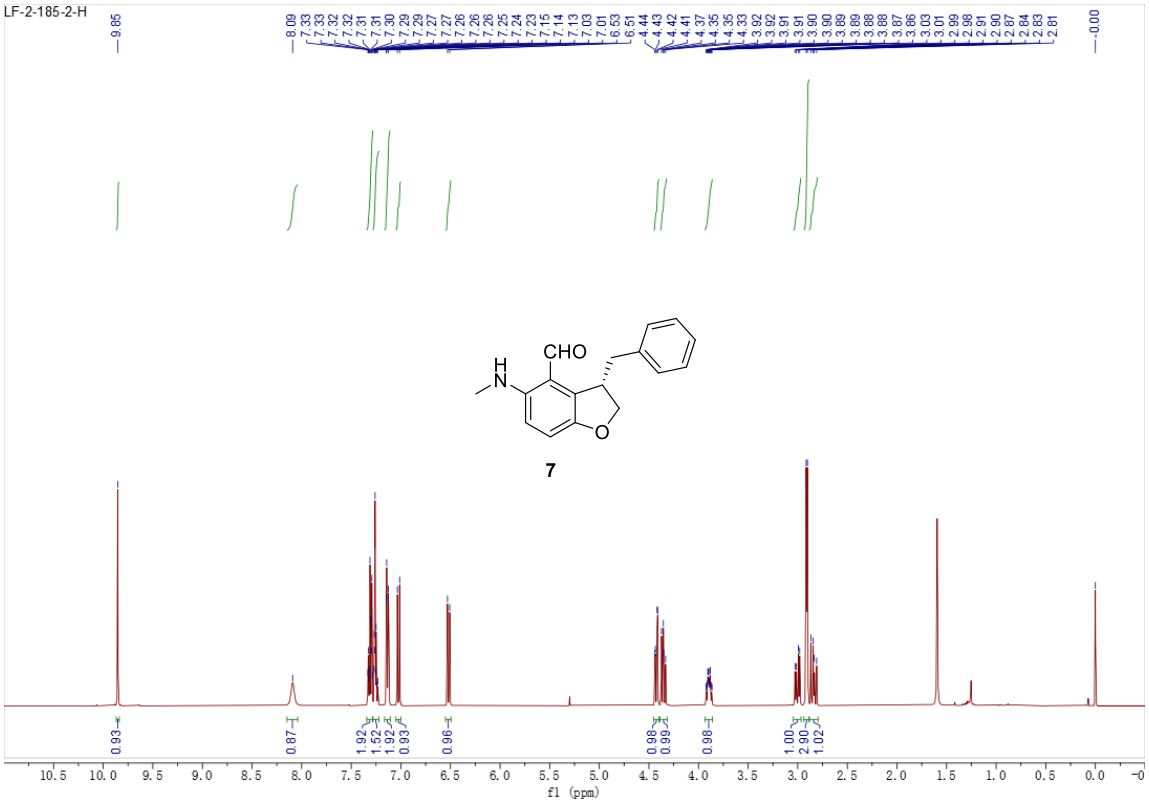
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6**



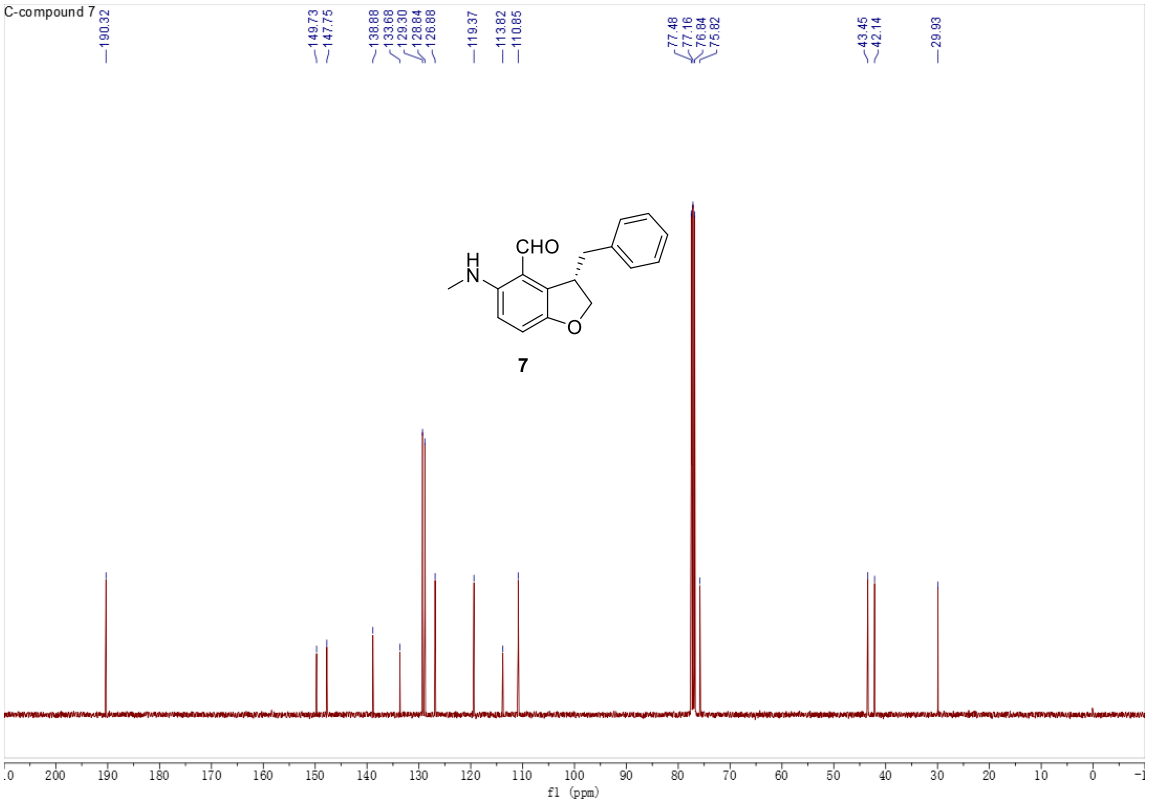
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6**



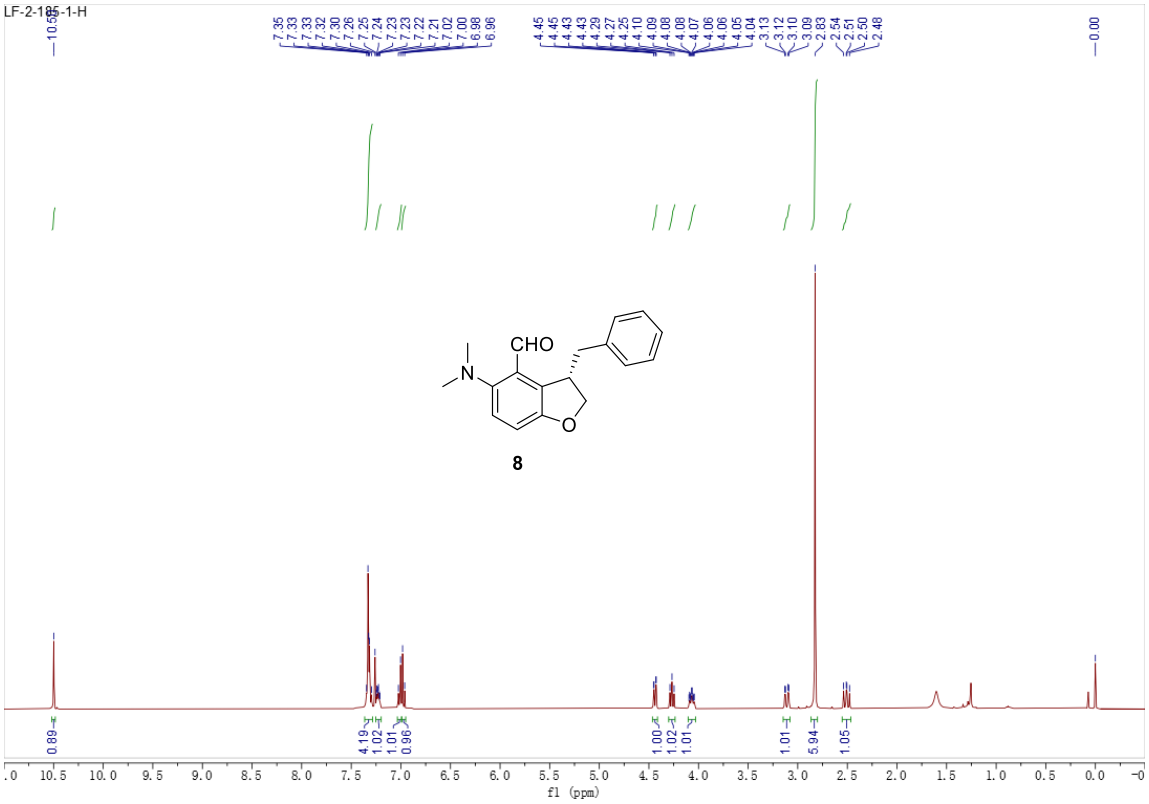
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7**



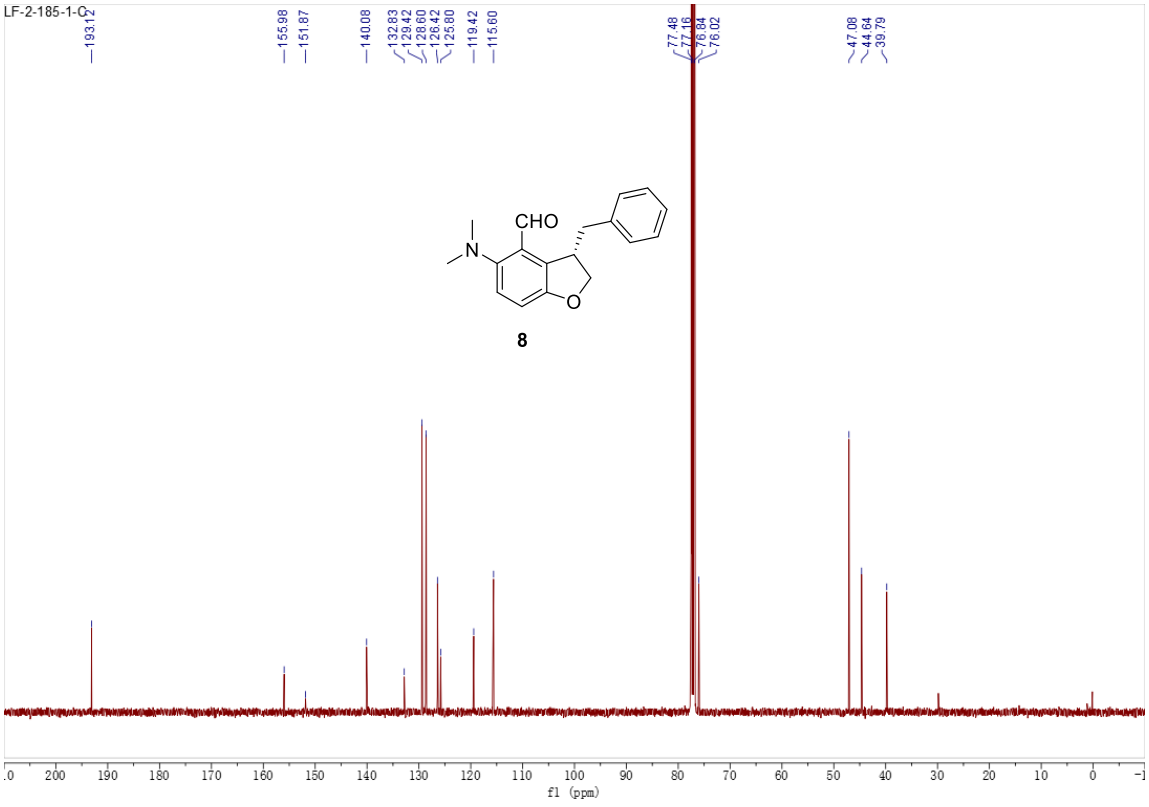
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7**



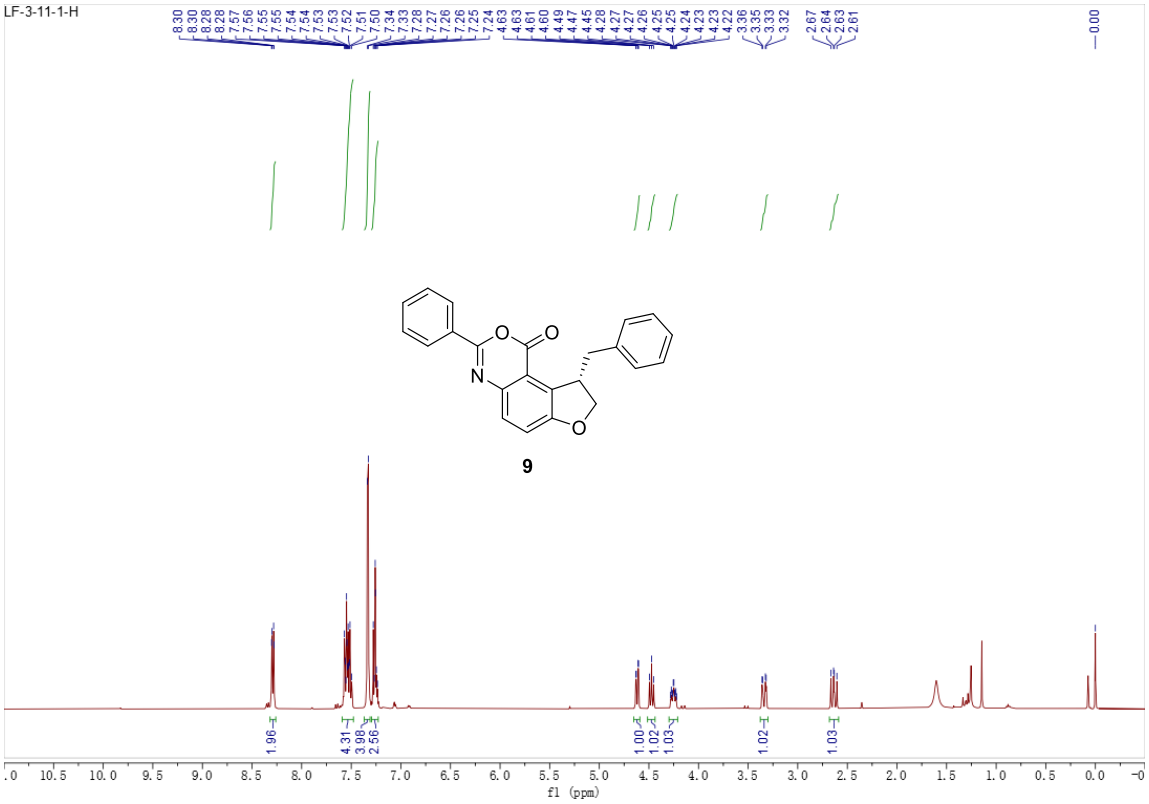
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8**



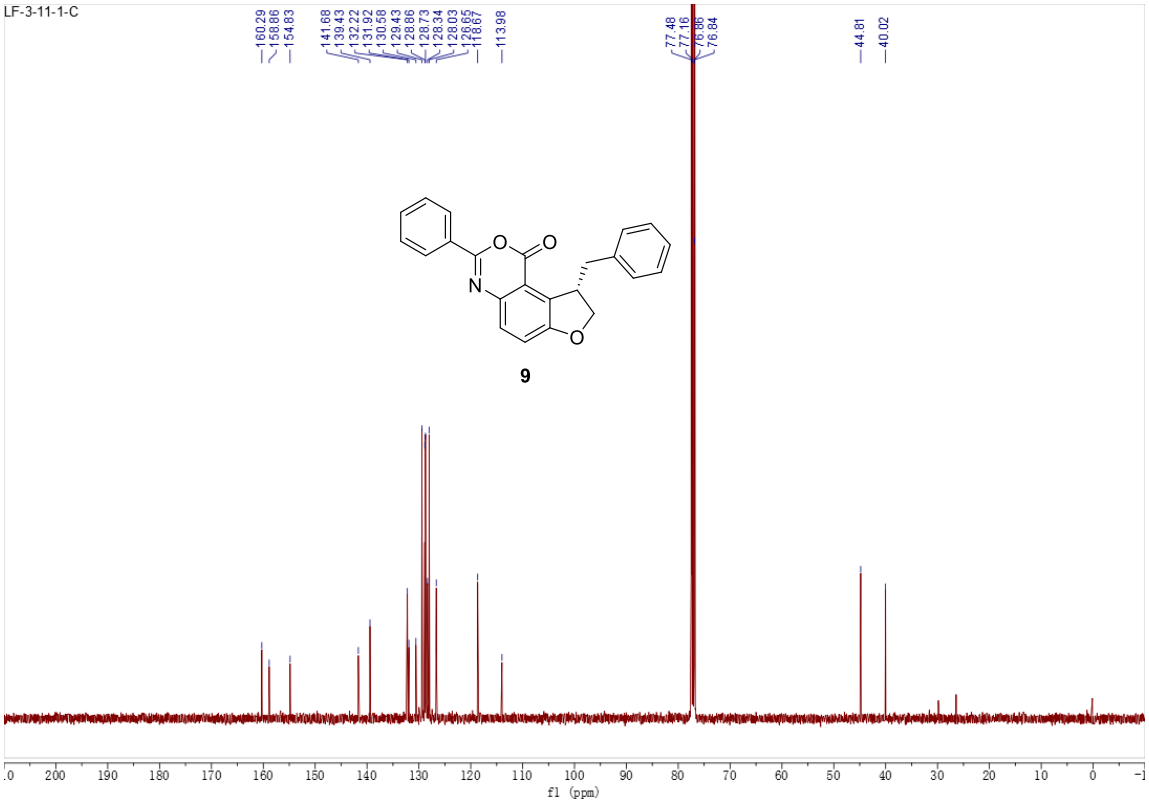
^{13}C NMR (101 MHz, $CDCl_3$) of compound **8**



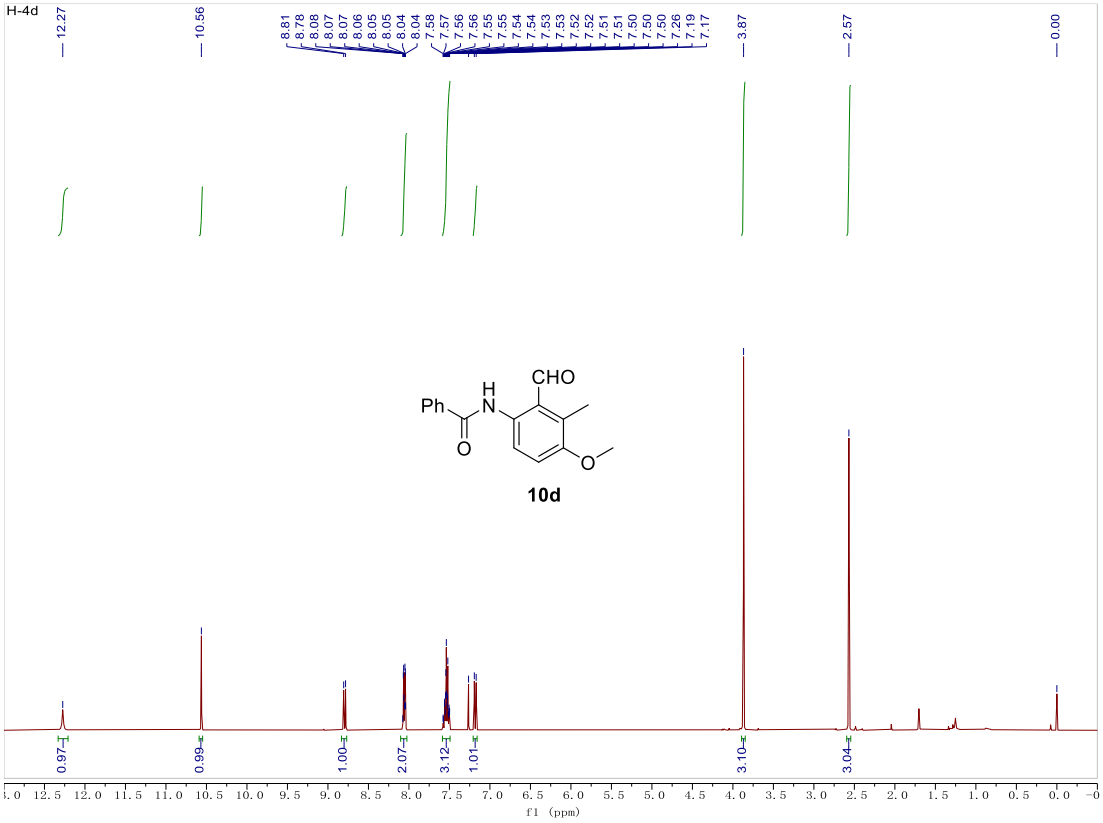
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9**



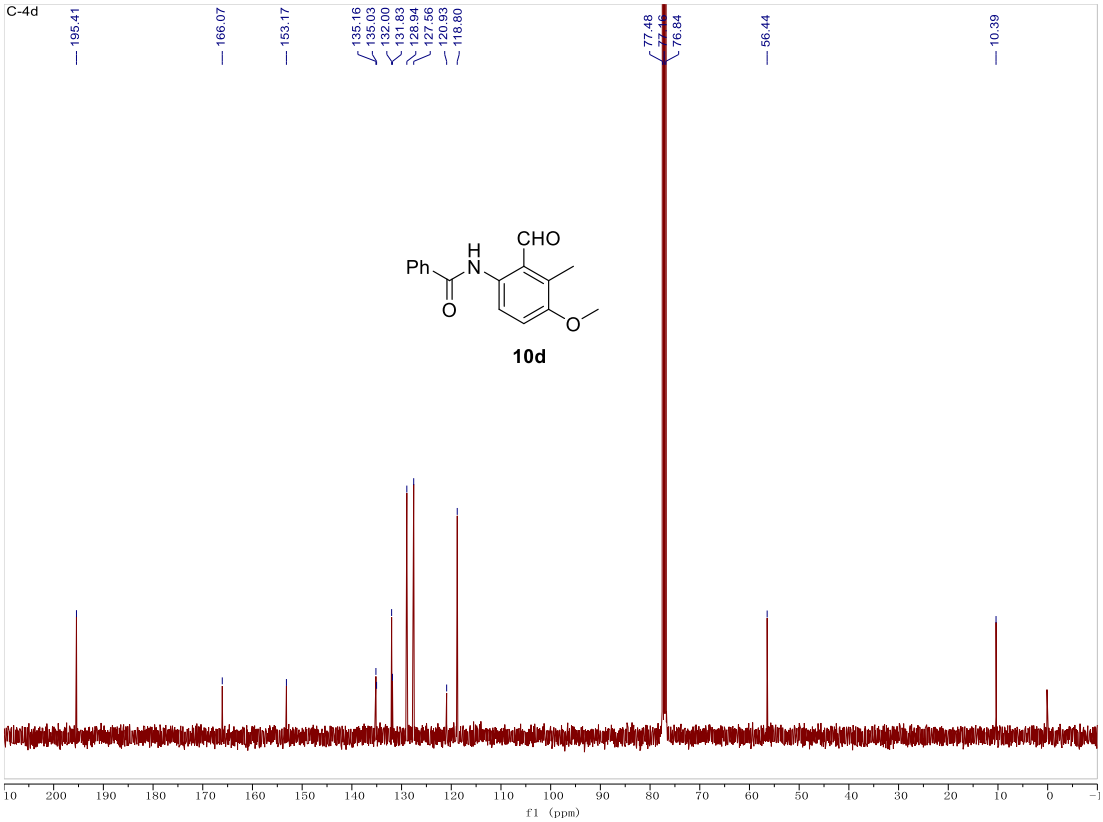
^{13}C NMR (101 MHz, $CDCl_3$) of compound **9**



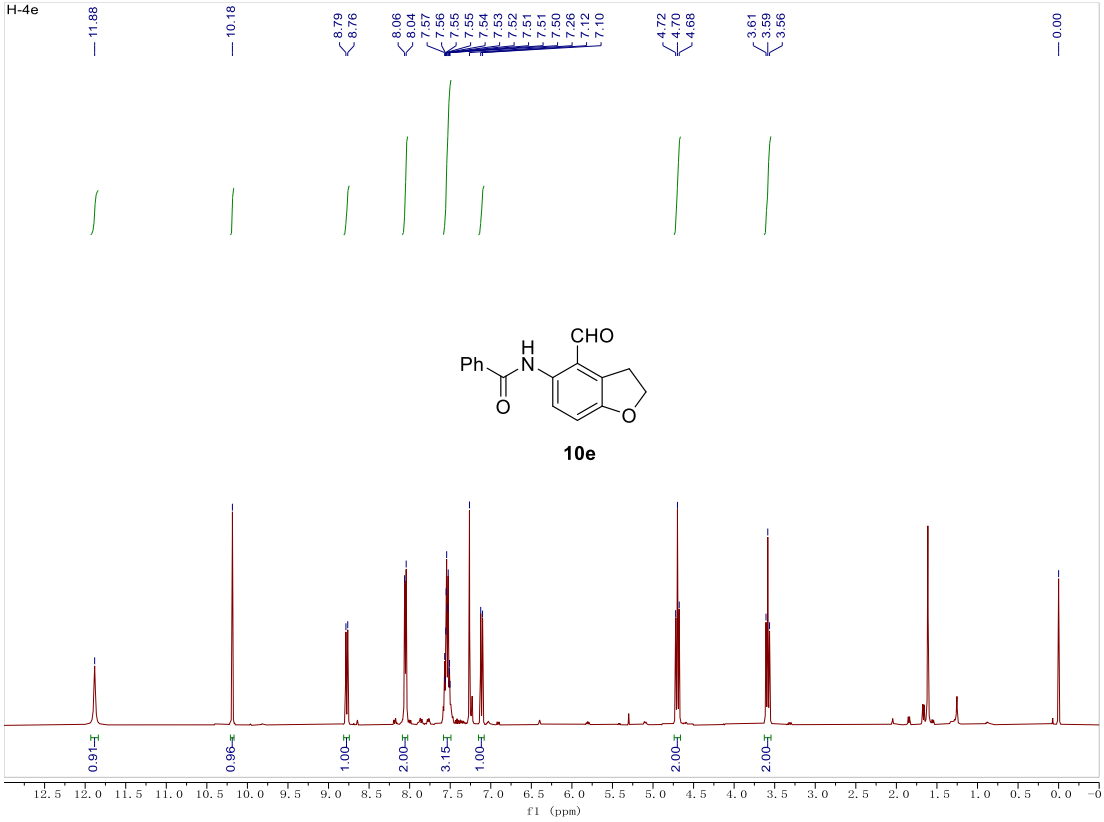
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10d**



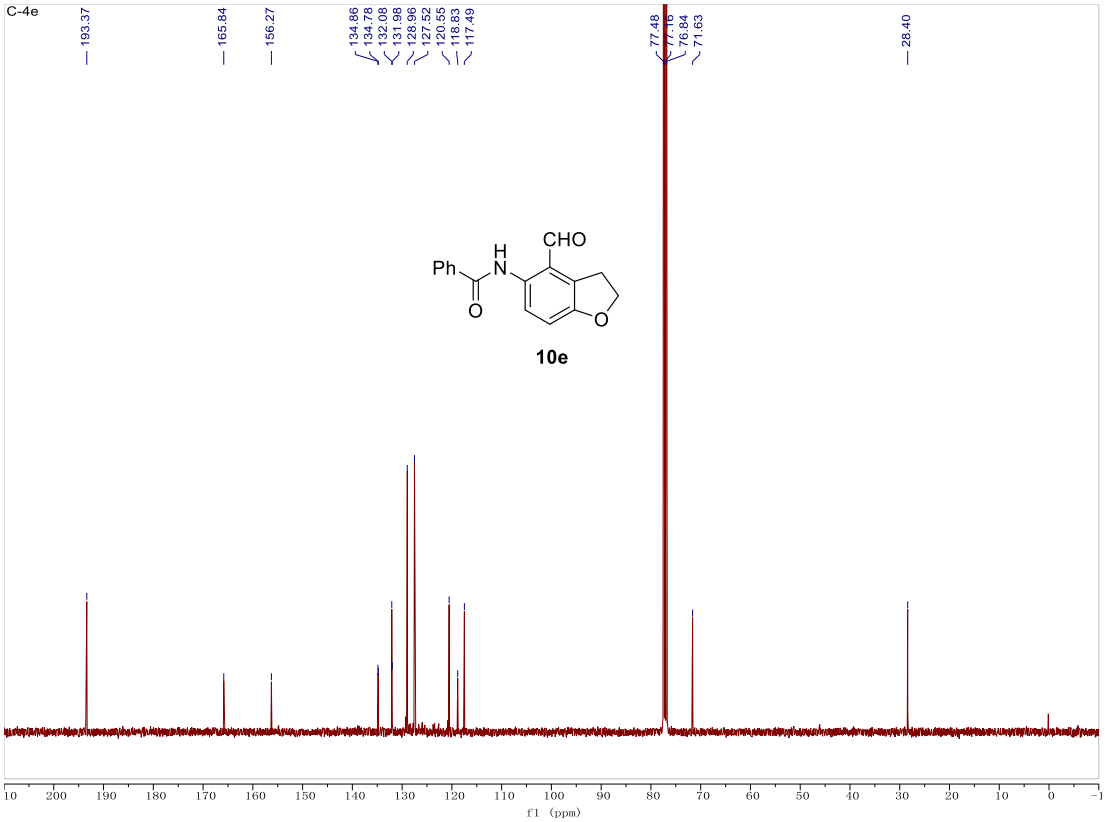
^{13}C NMR (101 MHz, $CDCl_3$) of compound **10d**



^{1}H NMR (400 MHz, $CDCl_3$) of compound **10e**

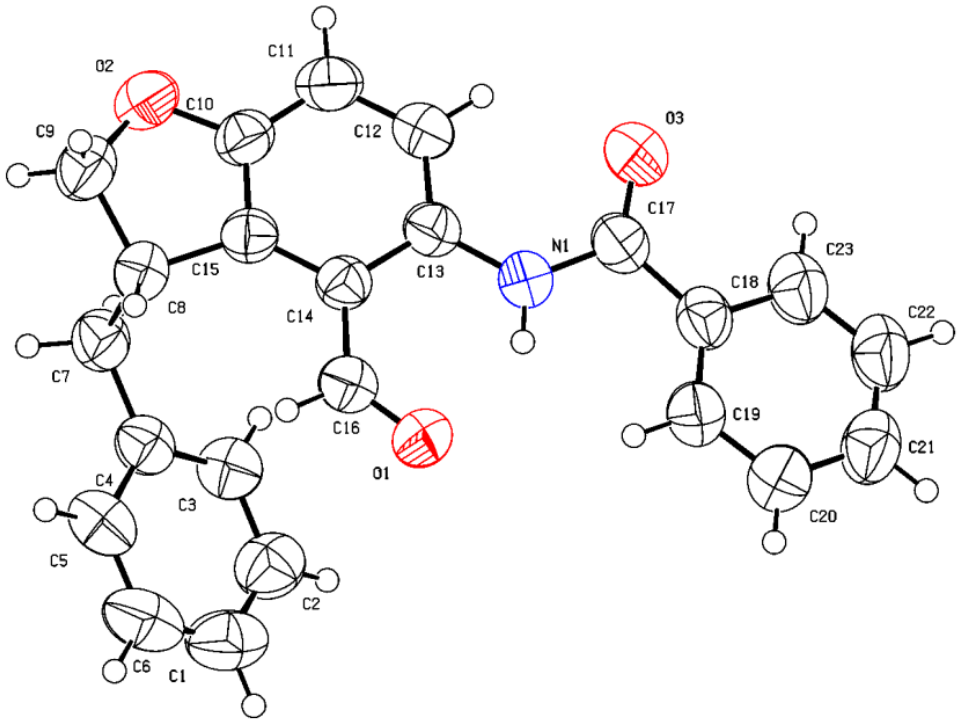


^{13}C NMR (101 MHz, $CDCl_3$) of compound **10e**



20. Crystallographic Data for 3aa

Crystals of **3aa** (CCDC 2240386) suitable for X-ray analysis were obtained by slow evaporation of a concentrated solution of the compound in a mixture of DCM/Hexanes. Diffraction was performed on a Bruker SMART APEXII CCD area detector diffractometer using graphite-monochromated Cu-Kα radiation (λ = 1.5418 Å) at 273 K, with φ and ω scan techniques. An empirical absorption correction was applied with the SADABS program. The structures were solved using Olex2[1] by direct methods using the ShelXT[2] structure solution program. Non-hydrogen atoms were anisotropically refined by full-matrix least-squares calculations based on F^2 using the ShelXL program.[3] Hydrogen atom coordinates were calculated with SHELXTL by using an appropriate riding model with varied thermal parameters. The residual electron densities were not chemical significant. The corresponding data could be obtained from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



ORTEP diagram drawn with 50% ellipsoid probability of compound **3aa**

Bond precision: C-C = 0.0057 A Wavelength = 1.54178

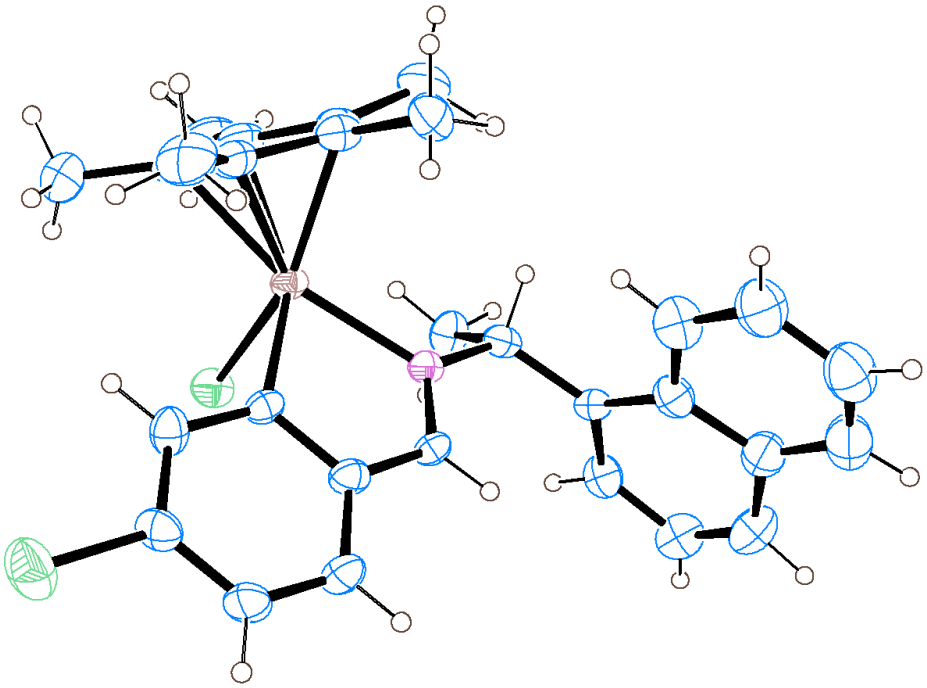
Cell: a = 5.0070 (1) b = 17.1218 (4) c = 21.1670 (4)
alpha = 90 beta = 90 gamma = 90
Temperature: 273 K

	Calculated	Reported
Volume	1814.62 (7)	1814.62 (7)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C23H19NO3	4 (C23H19NO3)
Sum formula	C23H19NO3	C92H76N4O12
Mr	357.39	1429.56
Dx,g cm-3	1.308	1.308
Z	4	1
Mu (mm-1)	0.698	0.698
F000	752.0	752.0
F000’	754.27	
h,k,lmax	5, 20, 25	5, 20, 25
Nref	3201 [1894]	3196
Tmin,Tmax		0.646, 0.753
Tmin’		

Correction method= # Reported T Limits: Tmin= 0.646 Tmax = 0.753
AbsCorr = NONE
Data completeness= 1.69/1.00 Theta (max) = 66.732
R (reflections)= 0.0584 (2311) wR2 (reflections) = 0.1415 (3196)
S = 1.011 Npar= 244

21. Crystallographic Data for Int-2

Crystals of **Int-2** (CCDC 2279645) suitable for X-ray analysis were obtained by slow evaporation of a concentrated solution of the compound in a mixture of DCM/Hexanes. Diffraction was performed on a Bruker SMART APEXII CCD area detector diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) at 297 K, with φ and ω scan techniques. An empirical absorption correction was applied with the SADABS program. The structures were solved using Olex2[1] by direct methods using the ShelXT[2] structure solution program. Non-hydrogen atoms were anisotropically refined by full-matrix least-squares calculations based on F^2 using the ShelXL program.[3] Hydrogen atom coordinates were calculated with SHELXTL by using an appropriate riding model with varied thermal parameters. The residual electron densities were not chemical significant. The corresponding data could be obtained from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



ORTEP diagram drawn with 30% ellipsoid probability of compound **Int-2**

Bond precision: C-C = 0.0177 A Wavelength= 0.71073

Cell: a = 7.7412 (5) b = 15.9286 (16) c = 26.521 (3)
alpha = 90 beta = 90 gamma = 90
Temperature: 297 K

	Calculated	Reported
Volume	3270.2 (5)	3270.2 (5)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C29H30Cl2NRh[+solvent]	C29H30Cl2NRh
Sum formula	C29H30Cl2NRh[+solvent]	C29H30Cl2NRh
Mr	566.35	566.35
Dx,g cm-3	1.150	1.150
Z	4	4
Mu (mm-1)	0.699	0.699
F000	1160.0	1160.0
F000’	1157.01	
h,k,lmax	9, 19, 32	8, 19, 32
Nref	6099 [3469]	5886
Tmin,Tmax	0.857, 0.870	0.618, 0.746
Tmin’	0.857	

Correction method= # Reported T Limits: Tmin = 0.618 Tmax = 0.746
AbsCorr = NONE
Data completeness= 1.70/0.97 Theta (max) = 25.498
R (reflections)= 0.0713 (4478) wR2 (reflections) = 0.2188 (5886)
S = 1.067 Npar = 284

22. Photophysical Spectra of 3aa-3zaa, 3ab–3ao, 7, 8 and 10a–10e

Table S1. Photophysical properties of selected compounds in DCM.

compounds	λ^{abs}_{max} (nm)	λ^{em}_{max} (nm)	$\varepsilon_{max}{}^{a}$	Φ^{b}	Stokes shift (cm^{-1})
3aa	394	500	7500	0.223	5400
3ba	392	502	5700	0.203	5600
3ca	396	501	6400	0.223	5300
3da	394	500	5300	0.228	5400
3ea	396	500	6100	0.245	5300
3fa	394	502	6900	0.188	5500
3ga	396	499	6400	0.230	5200
3ha	396	496	7000	0.204	5100
3ia	392	502	5800	0.222	5600
3ja	394	498	7300	0.220	5300
3ka	392	498	6400	0.171	5400
3la	396	501	6100	0.212	5300
3ma	396	497	6800	0.199	5100
3na	396	502	7300	0.203	5300
3oa	395	501	3100	0.185	5400
3pa	398	505	6400	0.191	5300
3qa	394	501	8400	0.160	5400
3ra	394	501	3900	0.153	5400
3sa	392	501	3900	0.152	5600
3ta	394	501	3300	0.151	5400
3ua	390	502	4700	0.149	5700
3va	388	502	5900	0.143	5900
3wa	375	477	7500	0.225	5700
3xa	385	487	3900	0.233	5400
3ya	363	496	200	0.010	7400
3za	351	472	400	0.026	7300
3zaa	336	525	700	0.041	10700
3ab	398	504	6600	0.212	5300
3ac	396	504	8500	0.245	5400
3ad	394	500	6000	0.161	5400
3ae	394	502	600	0.165	5500
3af	394	499	7600	0.163	5300
3ag	396	503	6600	0.214	5400
3ah	394	498	6200	0.224	5300
3ai	394	499	6600	0.136	5300
3aj	392	499	6200	0.141	5500
3ak	388	495	6700	0.092	5600
3al	394	502	7200	0.178	5500
3am	390	498	5500	0.196	5600
3an	388	498	5400	0.258	5700
3ao	386	498	6200	0.248	5800
7	442	538	5100	0.056	3400
8	404	519	5400	0.366	5500
10a	340	418, 544	5200	0.323	11000

10b	355	432, 556	5600	0.019	10200
10c	369	456	5500	0.287	5200
10d	386	500	7600	0.045	5900
10e	398	500	6800	0.232	5100

[a] Corresponding to the strongest absorption maximum, the unit for ε is M^{-1} cm^{-1}. [b] Absolute fluorescence quantum yield.

Table S2. Photophysical properties of compound 3aa in different solvents.

solvent	λ^{abs}_{max} (nm)	λ^{em}_{max} (nm)	ε_{max}[a]	Φ[b]	Stokes shift (cm^{-1})
hexanes	398	485	3900	0.204	4500
toluene	396	495	4600	0.217	5100
THF	394	498	4300	0.107	5300
DMSO	372	501	2000	0.063	6900

[a] Corresponding to the strongest absorption maximum, the unit for ε is M^{-1} cm^{-1}. [b] Absolute fluorescence quantum yield.

Figure S3. Absorption and emission spectra of 3aa in water/DMSO solution

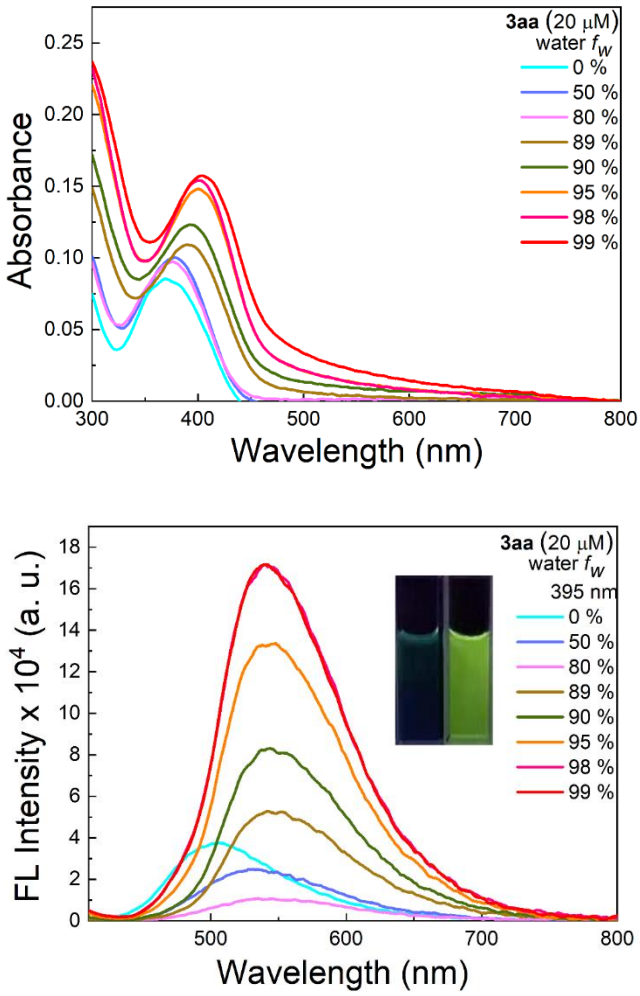


Figure S4. Emission spectra of 10a in different solvents

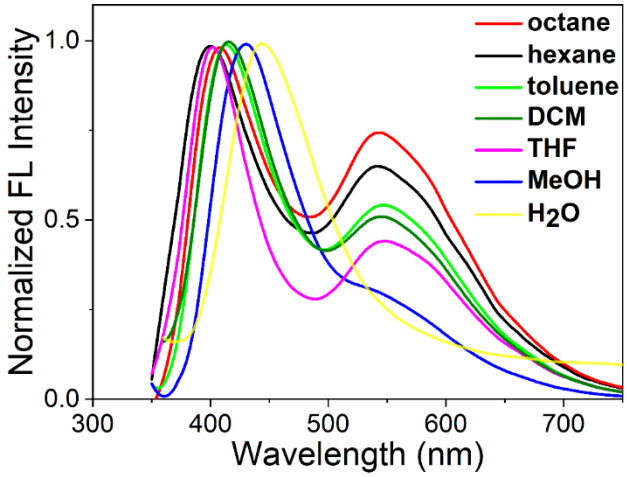
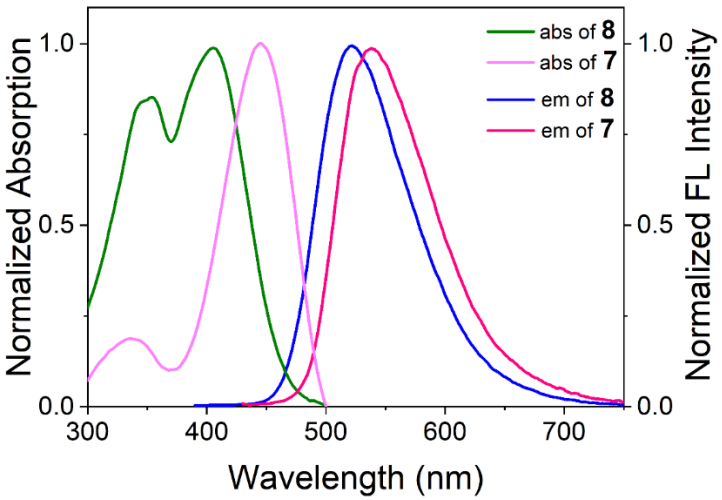
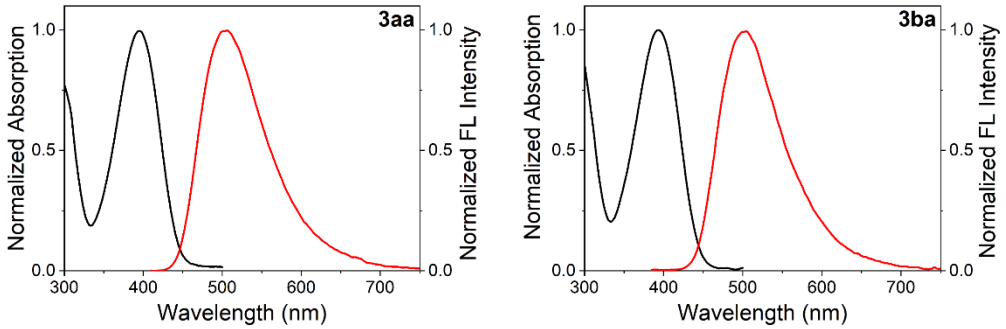
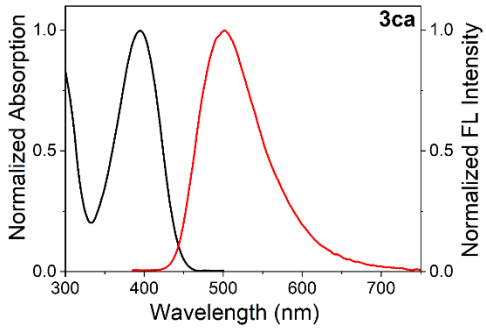


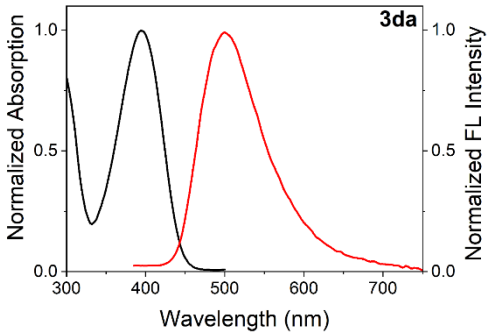
Figure S5. Absorption and emission spectra of 7 and 8 in DCM solution

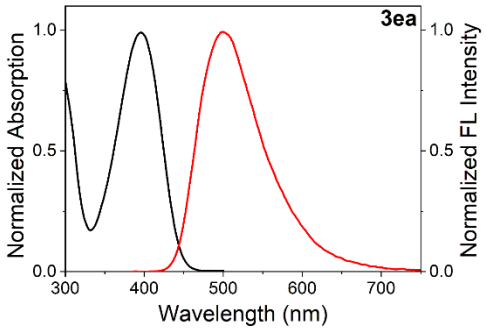


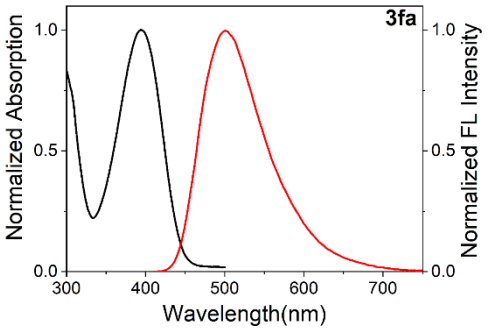
Absorption and emission spectra of substrates

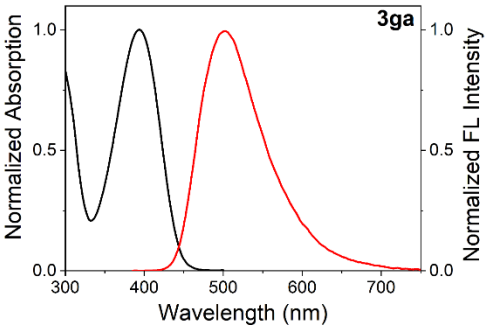


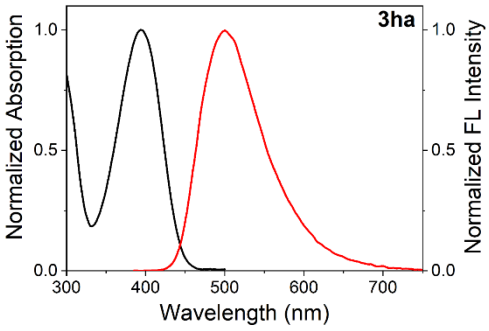

3ca
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

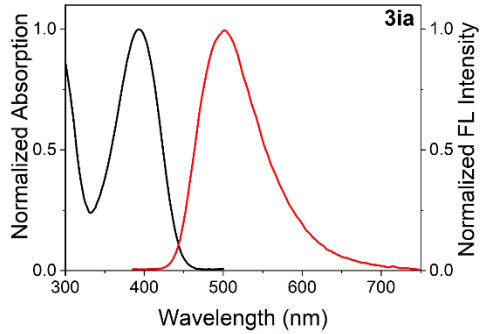

3da
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

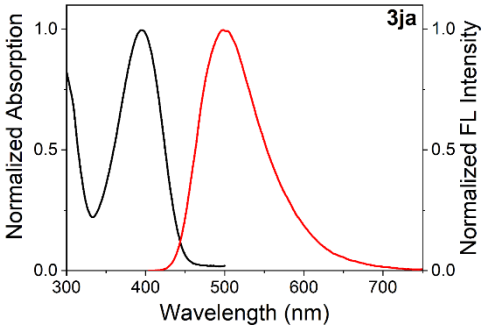

3ea
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

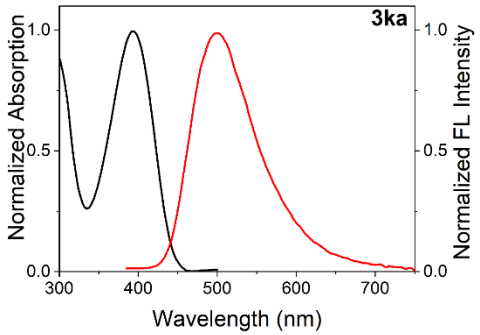

3fa
Normalized Absorption
Normalized FL Intensity
Wavelength(nm)

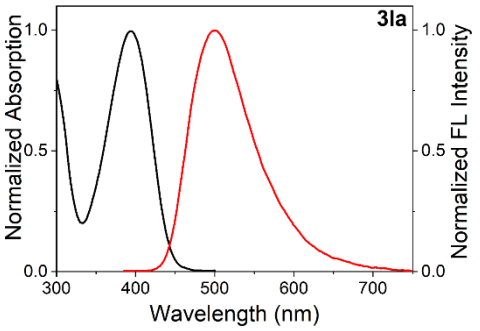

3ga
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

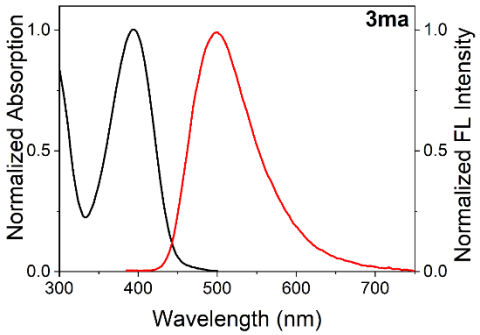

3ha
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

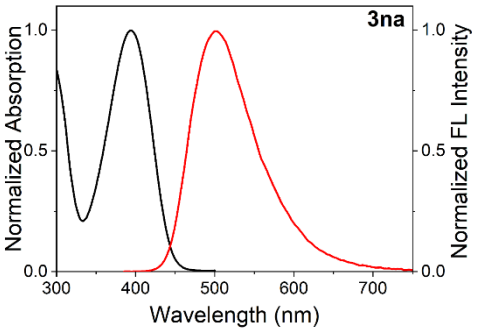

3ia
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

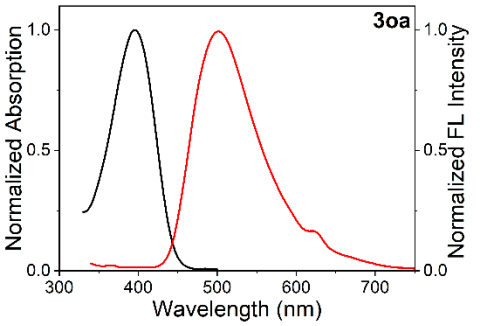

3ja
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

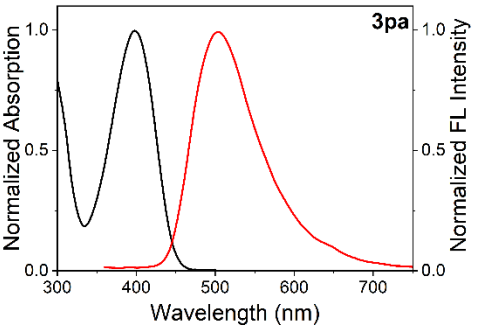

3ka
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

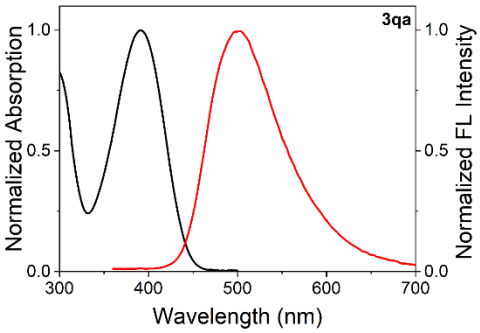

3la
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

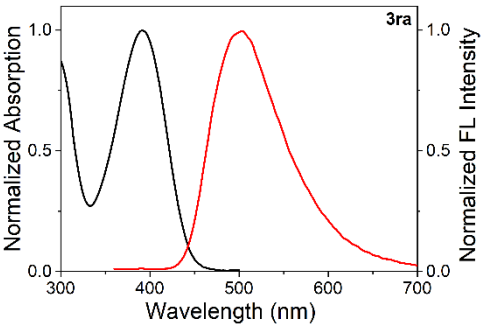

3ma
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

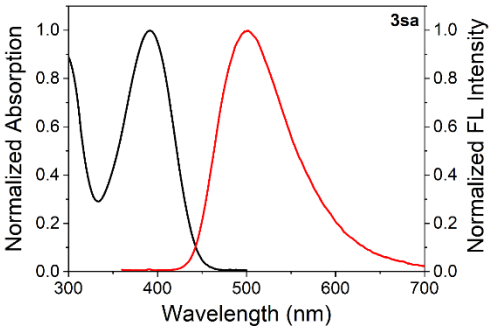

3na
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

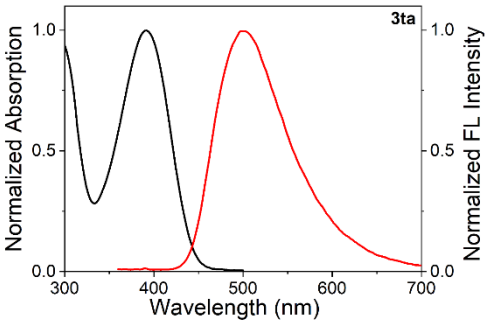

3oa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

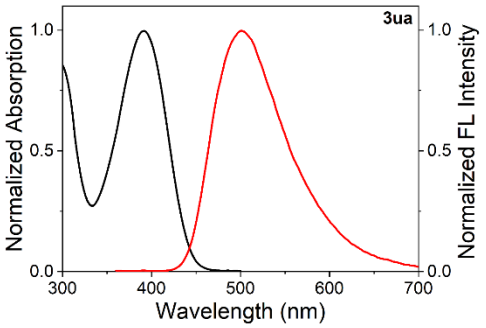

3pa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

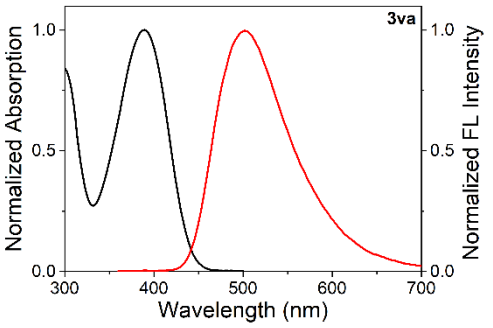

3qa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3ra
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3sa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3ta
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3ua
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3va
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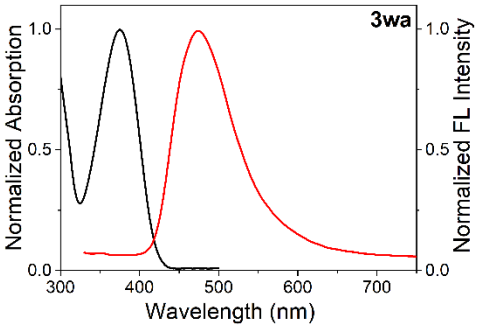
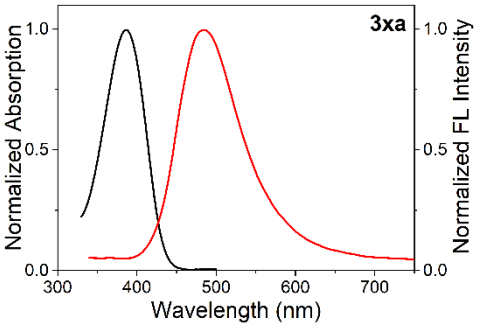
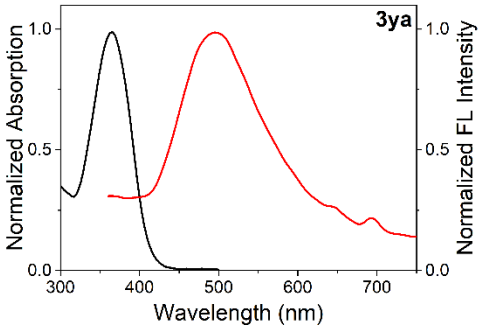
Normalized FL Intensity
Wavelength (nm)


3wa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3xa
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)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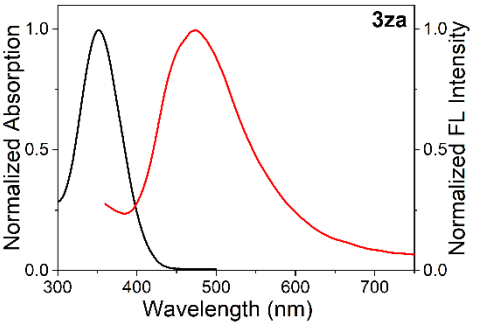
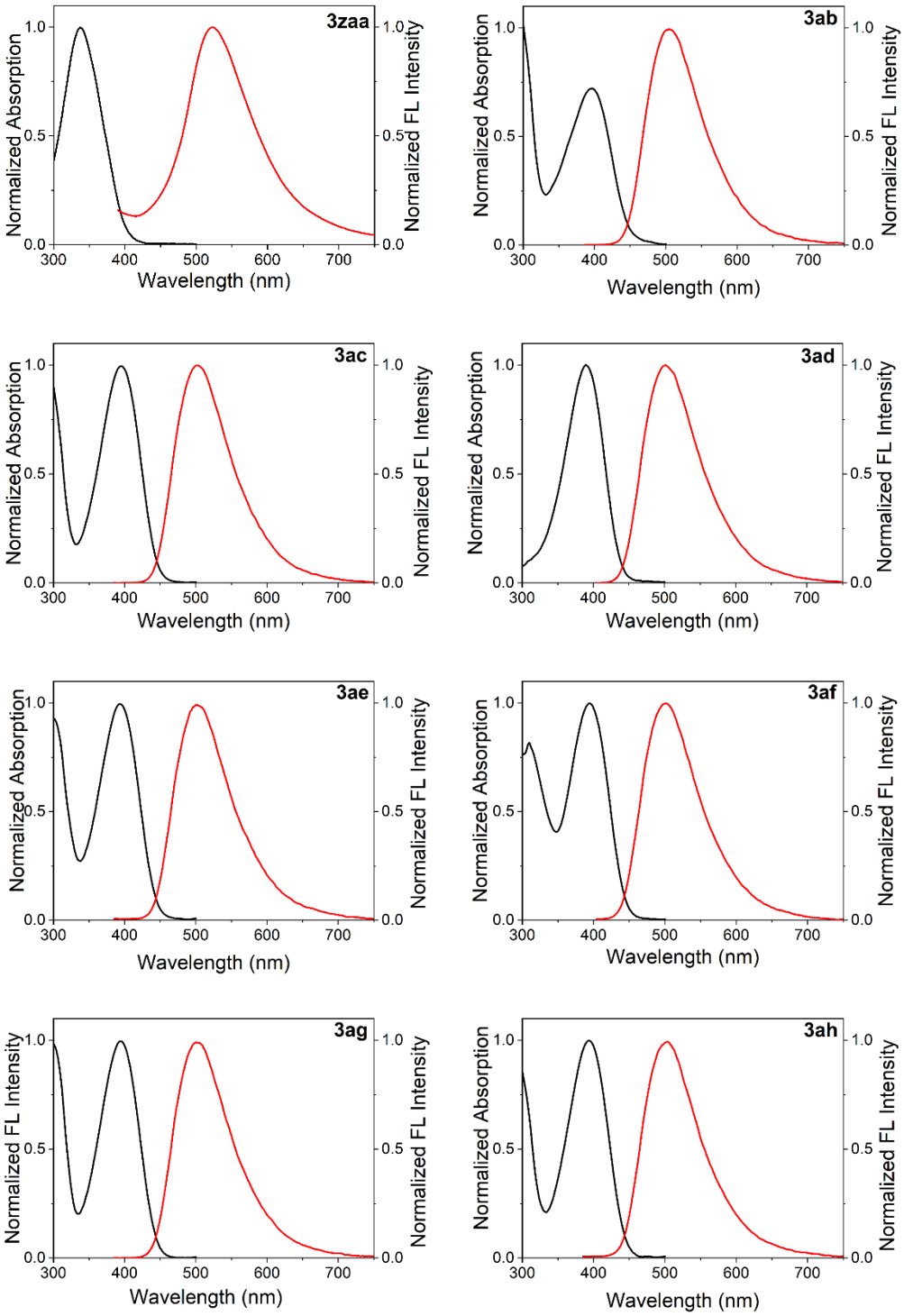
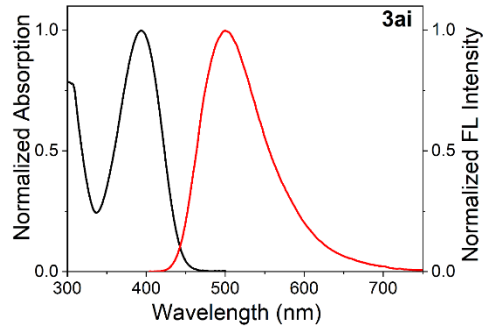
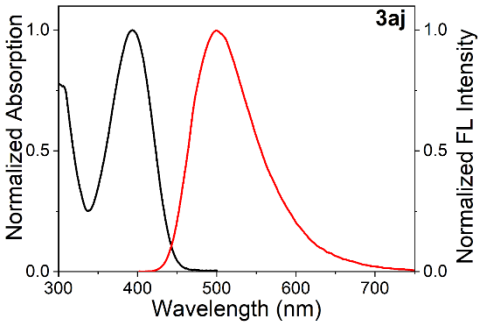
Normalized FL Intensity
Wavelength (nm)


3za
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


3zaa
3ab
3ac
3ad
3ae
3af
3ag
3ah
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)
0.0
0.5
1.0
300
400
500
600
700


3ai
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)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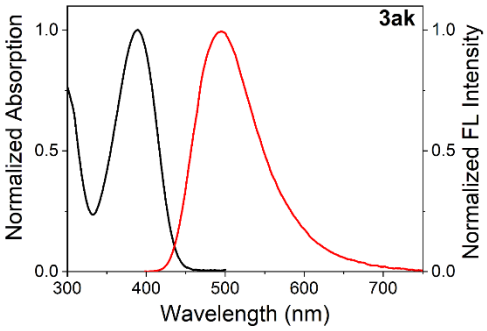
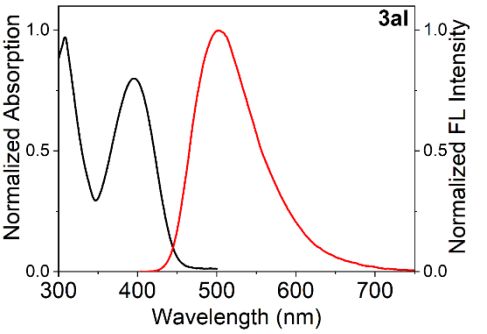
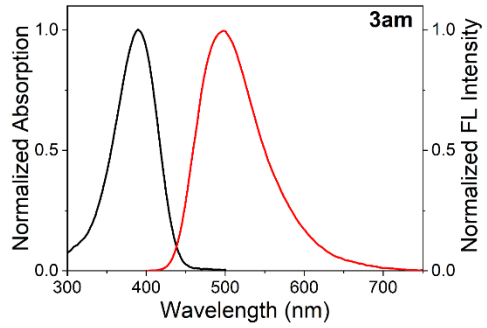
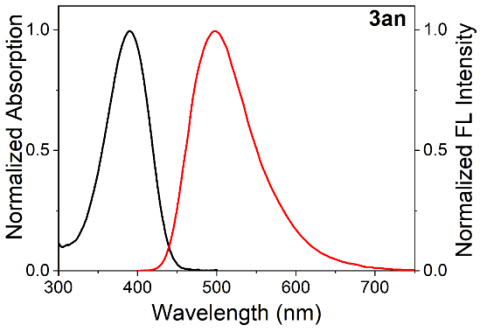
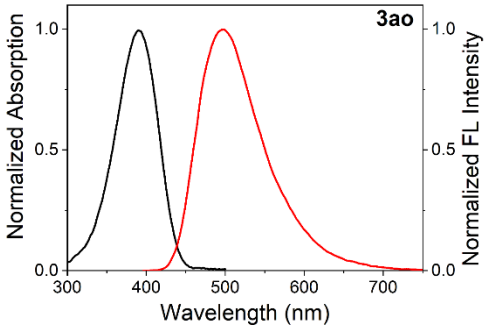
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

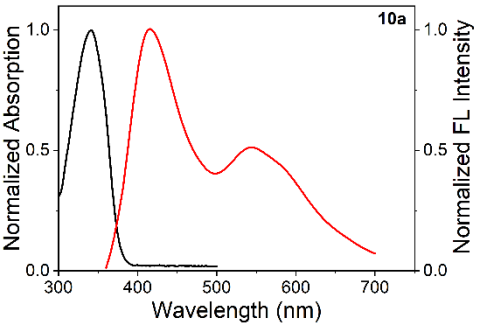

3ak
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

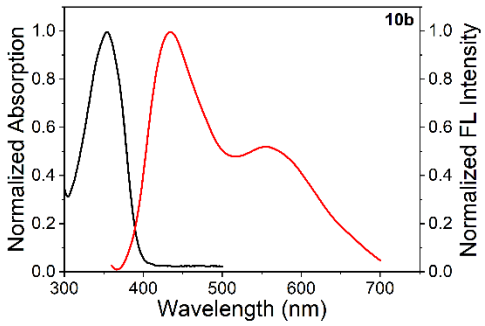

3al
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

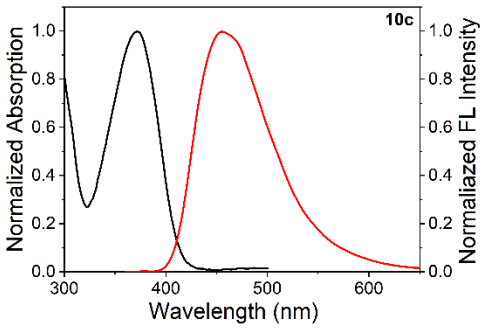

3am
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

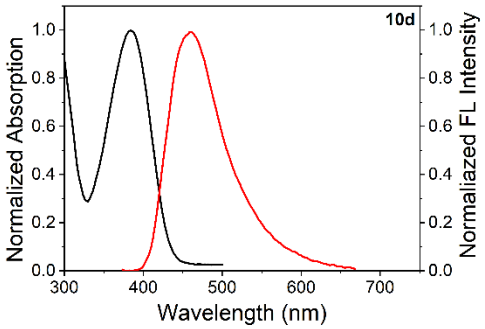

3an
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)

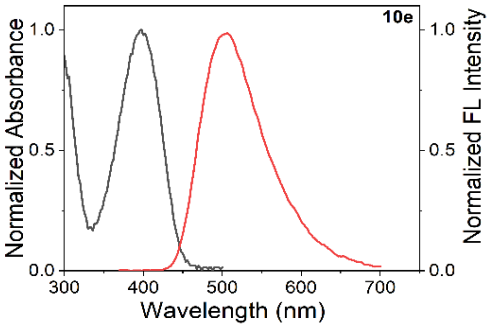

3ao
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


10a
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


10b
Normalized Absorption
Normalized FL Intensity
Wavelength (nm)


10c
Normalized Absorption
Normaliazed FL Intensity
Wavelength (nm)


10d
Normalized Absorption
Normaliazed FL Intensity
Wavelength (nm)


10e
Normalized Absorbance
Normalized FL Intensity
Wavelength (nm)

23. DFT Calculation of 10e.

The ground state geometry was optimized by using DFT method at B3LYP/6-31G(d,p) level. The same method was used for vibrational analysis to verify that the optimized structures correspond to local minima on the energy surface. TD-DFT computations were used the optimized ground state geometries under the B3LYP/6-31G(d,p) theoretical level. The calculated molecules in dichloromethane were done using the Self-Consistent Reaction Field (SCRF) method and Polarizable Continuum Model (PCM). The geometries of the lowest singlet (S1) excited states were also optimized at the TDB3LYP/6-31G(d,p) level of theory. All of the calculations were carried out by the methods implemented in Gaussian 09 package.[4]

Table S2. Main vertical singlet electronic energies, ΔE, oscillator strengths, f, and main transitions for molecule **10e** calculated by B3LYP/6-31G(d,p) level in dichloromethane solvent.

Dye	**Electronic transition[a]**	**TD//B3LYP/6-31G(d, p)**			
		ΔE (eV, nm)	***f*** **[b]**	**Composition [c]**	**CI [d]**
10e	$S_0 \rightarrow S_1$	3.0140 eV 411.37 nm	0.1903	HOMO → LUMO	0.7013
	$S_0 \rightarrow S_2$	3.7466 eV 330.93 nm	0.0003	HOMO -5 → LUMO	0.3972
				HOMO -3 → LUMO	0.4128
				HOMO -1 → LUMO	0.3769
	$S_0 \rightarrow S_3$	4.0118 eV 309.05 nm	0.2160	HOMO -4 → LUMO	0.1145
				HOMO → LUMO +1	0.6934
	$S_0 \rightarrow S_7$	4.7706 eV 259.89 nm	0.1617	HOMO -4 → LUMO	0.6256
				HOMO → LUMO +3	0.2224
	$S_0 \rightarrow S_{12}$	5.2698 eV 235.27 nm	0.3337	HOMO → LUMO +3	0.6000
				HOMO -4 → LUMO	0.2360
				HOMO -2 → LUMO +1	0.1314

[a] Only the selected low-lying excited states are presented. [b] Oscillator strength. [c] Only the main configurations are presented. [d] The CI coefficients are in absolute values.

Optimized Geometries of the Compounds.

10e, optimized S_0 state Geometry.

O	-0.03982100	2.48212500	0.25719200
O	-4.87468600	-0.94321300	-0.05231500
N	0.61728900	-0.12454600	0.05328900
H	0.81563900	0.86746700	0.17755600
O	1.55797600	-2.22257600	-0.06503800
C	-1.65645600	0.70766700	0.09397900
C	-0.75417400	-0.40354900	0.02877100
C	-3.03808800	0.45319800	0.05353500
C	-1.20958200	2.09562100	0.19806500
H	-2.02077300	2.84450000	0.22507300
C	1.67744000	-0.99663800	-0.02249800
C	-4.23627300	1.37486600	0.15352100
H	-4.20535500	2.21924300	-0.53999500
C	-3.51283400	-0.84937400	-0.03931200
C	3.03404300	-0.34979100	-0.03911100
C	-1.27019100	-1.70748400	-0.06228300
H	-0.57835500	-2.53487600	-0.10644400
C	-5.39637600	0.40913600	-0.18791000
H	-6.25399100	0.50205500	0.47987800
H	-5.73225700	0.53648000	-1.22251300
C	-2.64601400	-1.93697100	-0.09808800
H	-3.03291200	-2.94781200	-0.17016200
C	4.13042100	-1.15515200	0.30274100
H	3.94863900	-2.19042000	0.56926000
C	3.25517600	0.98719600	-0.40537400
H	2.43200100	1.62634100	-0.70869000
C	5.63317000	0.70262000	-0.05730600
H	6.63905200	1.11157700	-0.06333400
C	4.54934000	1.50758800	-0.41372300
H	4.71029500	2.54079400	-0.70548800
C	5.42080600	-0.63155600	0.30025000
H	6.26064300	-1.26228500	0.57543200
H	-4.33384400	1.78379800	1.16614900

SCF done: -899.20368434 Hartree
No imaginary Frequency.

10e, optimized S_1 state Geometry.

O	-0.09752400	2.43377000	-0.18170300
O	4.83271800	-0.91191700	0.08515300
N	-0.57185300	-0.13930000	-0.04606500
H	-0.72851700	0.89052000	-0.12879300
O	-1.52602900	-2.23668400	-0.02472300
C	1.63988600	0.75279100	-0.06059100
C	0.77725400	-0.41353300	-0.01747700

C	3.00514200	0.47804700	-0.02131700
C	1.14106000	2.11421600	-0.13655800
H	1.90083500	2.90664100	-0.16169800
C	-1.65350600	-1.00877500	-0.01946500
C	4.18466000	1.40640900	-0.04114900
H	4.17414900	2.09827000	0.81011300
C	3.49660400	-0.85470100	0.05646600
C	-2.99574300	-0.35610700	0.00999200
C	1.30304600	-1.73407900	0.06106000
H	0.59427000	-2.54896700	0.08671400
C	5.38466800	0.44199000	0.02150300
H	6.02170700	0.47693700	-0.86447500
H	6.00365100	0.56777900	0.91184600
C	2.67027200	-1.98261700	0.09914100
H	3.07655500	-2.98385200	0.15749700
C	-4.11171400	-1.18981900	-0.18270400
H	-3.94210900	-2.24745800	-0.35022700
C	-3.20142100	1.01693700	0.24270300
H	-2.36875800	1.69007900	0.41839500
C	-5.59650300	0.69994200	0.06661300
H	-6.60165400	1.11025300	0.08619000
C	-4.49542100	1.53486800	0.27041800
H	-4.64297800	2.59445700	0.45528300
C	-5.40003000	-0.66625600	-0.15937900
H	-6.25225200	-1.32053200	-0.31626800
H	4.20522900	2.02372800	-0.94745500

SCF done: -897.89939488 Hartree
No imaginary Frequency.

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