Supporting Information

Catalyst-free Microwave-Assisted Azo-Povarov Reaction of *N*-Carbonyl Aryldiazenes with *trans*-Cyclooctene to access Ring-fused Cinnoline Derivatives

Xabier Jiménez-Aberásturi, Gurutze Padrones, Javier Vicario, Jesús M. de los Santos*

Department of Organic Chemistry I, Faculty of Pharmacy and Lascaray Research Center, University of the Basque Country (UPV/EHU), Paseo de la Universidad 7, 01006 Vitoria-Gasteiz, Spain.

**Corresponding author E-mail: jesus.delossantos@ehu.eus*

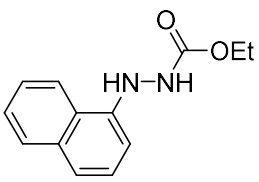
Table of contents

EXPERIMENTAL SECTION

General information. Solvents for extraction and chromatography were of reagent grade. All solvents used in reactions were freshly distilled and dried over 3Å molecular sieves before use. Unless otherwise mentioned, all other solvents and reagents were purchased from commercial vendors and either recrystallized, distilled as necessary, or used without further purification. All reactions were carried out under a dry nitrogen atmosphere. Photo-isomerization reactions were performed using a multilamp Photoreactor Model MLU18 equipped with Model 3020 lamps (254 nm) (Photochemical Reactors Limited, Reading RG4 PA, UK). Reaction progress was monitored by analytical thin-layer chromatography (TLC) on precoated Merck silica gel 60 F_{254} TLC aluminum plates, with spot visualized using VL-6C UV lamps (λ = 254 nm) or potassium permanganate stain. Melting points are uncorrected. ^{1}H (400 MHz), ^{13}C (100 or 75 MHz), and ^{19}F (376 MHz) NMR spectra were recorded on a Bruker Avance 400 (400 MHz) or Varian Unity Plus (300 MHz) spectrometers, respectively, using $CDCl_3$ as the solvent, as specified below. Chemical shifts (δ_H) are reported in parts per million (ppm), using the internal chloroform signal at 7.24 ppm as standard for ^{1}H NMR. Chemical shifts (δ_C and δ_F) are also reported in parts per million (ppm), with the internal chloroform signal at 77.0 ppm for ^{13}C NMR and the external fluorotrichloromethane ($CCFl_3$) signal at 0.0 ppm as standard for ^{19}F NMR. All coupling constants (J) values are given in Hz. ^{19}F and ^{13}C NMR spectra were recorded in a broadband hydrogen-decoupled mode. Distortionless Enhanced Polarization Transfer (DEPT) was used to support peak assignments for ^{13}C NMR. Multiplicity abbreviations are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, dq = double quartet, ddt = double double triplet, bs = broad singlet, bm = broad multiplet. Infrared

spectra were recorded on a Nicolet iS10 FTIR Termo Scientific spectrophotometer using the Smart iTR accessory. Absorbance frequencies are given at maximum of intensity in cm^{-1}. FTIR spectra were taken as pure solids or oils. High-resolution mass spectra (HRMS) were recorded by positive-ion electrospray ionization (ESI) using a time of flight (Q-TOF) system. Data are reported as *m/z* values. Chromatographic purification was performed using flash chromatography with commercially available silica gel (particle size finer than 230 mesh) under pressure. Functionalized hydrazines **1k** and **1p** are commercially available. However, functionalized hydrazines **1a**–**1g**,[1] **1h**,[2] **1i**,[1] **1l**–**1o**[1] and **1q**,[1] and *N*-carbonyl aryldiazenes **2a–2g**,[1] **2i**,[1] **2k**–**2q**,[1] were prepared according to literature procedures.

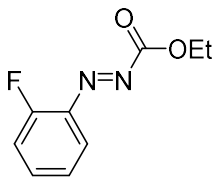
General procedure and spectral data for functionalized hydrazines 1. To a 0 ºC stirred solution of the corresponding hydrazine hydrochloride (15 mmol) in CH_3CN (30 mL) and pyridine (2.5 mL, 31.5 mmol), ethyl chloroformate (1.6 mL, 16.5 mmol) was added dropwise. The reaction mixture was stirred for 15 min at 0 ºC, then for 3 h at room temperature. Water (30 mL) was added, and the resulting mixture was acidified to pH 4–6 with 6M aqueous HCl. The crude product was extracted with CH_2Cl_2 (5 × 15 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to dryness under vacuum. Functionalized hydrazines **1** were used in the next step without further purification.



Ethyl-2-(naphthalen-1-yl)diazene-1-carboxylate (1j). The procedure was followed using naphthalen-1-ylhydrazine hydrochloride (2.92 g, 15 mmol), affording 3.42 g (99%) of **1j** as a brown solid. Mp: 105–107 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3289, 3049, 2981, 1714; ^{1}H NMR

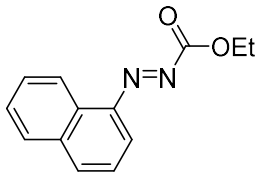
(400 MHz, $CDCl_3$) δ (ppm): 7.80 (d, J = 8.2 Hz, 1H, CH_{ar}), 7.75 (d, J = 8.2 Hz, 1H, CH_{ar}), 7.46–7.30 (m, 4H, 4×CH_{ar}), 6.91 (bs, 1H, NH), 6.77 (bs, 1H, CH_{ar}), 6.51 (bs, 1H, NH), 4.23–4.18 (q, $^3J_{HH}$ = 6.9 Hz, 2H, CH_2O), 1.33–1.18 (t, $^3J_{HH}$ = 6.9 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 157.2 (C=O), 142.6 ($C_{quat}N$), 134.0 (C_{quat}), 128.4 (CH_{ar}), 125.9 (CH_{ar}), 125.8 (CH_{ar}), 125.1 (CH_{ar}), 122.8 (C_{quat}), 120.9 (CH_{ar}), 119.9 (CH_{ar}), 106.6 (CH_{ar}), 61.9 (CH_2O), 14.5 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{13}H_{14}N_2O_2$ $[M+H]^{+\cdot}$ 231.1134, found 231.1119.

General procedure and spectral data for *N*-carbonyl aryldiazenes 2. Following a modified literature procedure,[1] pyridine (0.68 mL, 8.4 mmol) was added to a stirred solution of the corresponding functionalized hydrazine **1** (3 mmol) in CH_2Cl_2 (21 mL). Then, NBS (599 mg, 3.30 mmol) was added portion-wise. The reaction mixture was stirred for 30 min and then washed sequentially with 5% aqueous HCl (30 mL), 1.5% aqueous sodium thiosulfate (15 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated to dryness under vacuum. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 98:2) to afford pure aryl and alkyldiazene carboxylates **2**.



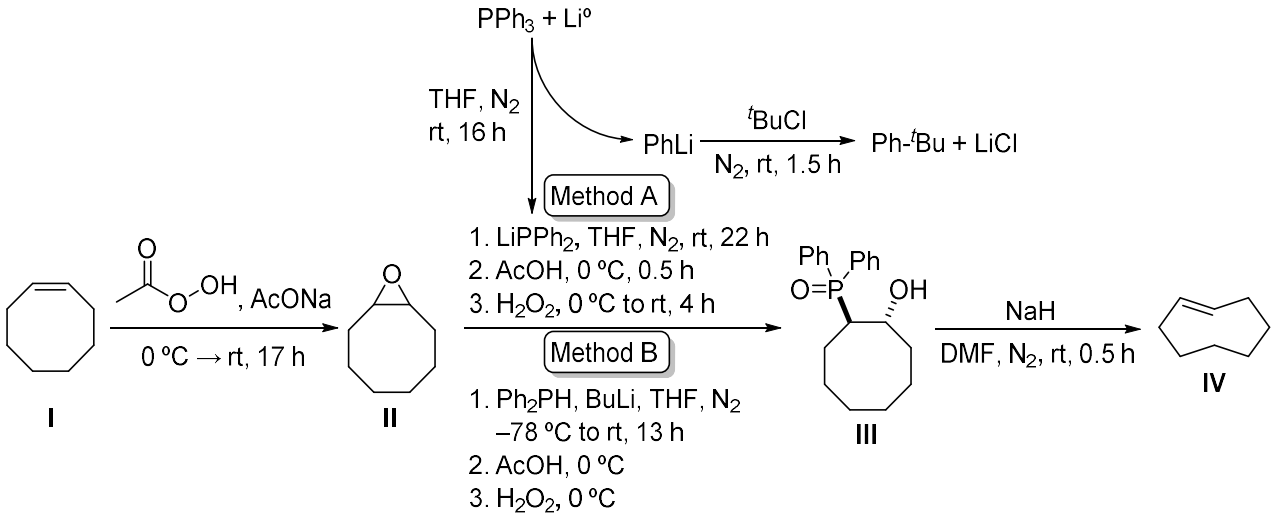
Ethyl 2-(2-fluorophenyl)diazene-1-carboxylate (2h). The procedure was followed using *m*-fluorophenylhydrazine (**1h**), affording 582 mg, (99%) of **2h** as a red oil. FTIR (neat) ν_{max} (cm^{-1}) 2983, 1757, 1604; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.67 (m, 1H, CH_{ar}), 7.57 (m, 1H, CH_{ar}), 7.28 (m, 1H, CH_{ar}), 7.21 (m, 1H, CH_{ar}), 4.50 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 1.45 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ (ppm): 161.9 (C=O), 160.8 (d, $^1J_{CF}$ = 262.6 Hz, $C_{quat}F$), 139.4 (d, $^2J_{CF}$ = 6.7 Hz, $C_{quat}N$), 135.6 (d, $^3J_{CF}$ = 8.8 Hz, CH_{ar}), 124.3 (d, $^3J_{CF}$ = 3.8 Hz, CH_{ar}), 117.4 (d, $^2J_{CF}$ = 19.6 Hz, CH_{ar}), 117.3 (CH_{ar}), 64.4 (CH_2O), 13.9 (CH_3);

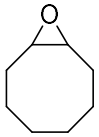
^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –121.0; HRMS (ESI-TOF) *m/z* calcd. for $C_9H_9FN_2O_2$ $[M+H]^{+\cdot}$ 197.0726, found 197.0729.



Ethyl-2-(naphthalen-1-yl)diazene-1-carboxylate (2j). The procedure was followed using naphthalen-1-ylhydrazine **1j** (230 mg, 1 mmol), affording 226 mg (99%) of **2j** as a red oil. FTIR (neat) ν_{max} (cm^{-1}) 2985, 1755; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.82 (d, $^3J_{HH}$ = 8.1 Hz, 1H, CH_{ar}), 8.03 (d, $^3J_{HH}$ = 8.2 Hz, 1H, CH_{ar}), 7.87 (dd, $^3J_{HH}$ = 8.2, $^4J_{HH}$ = 1 Hz, 1H, CH_{ar}), 7.81 (dd, $^3J_{HH}$ = 8.6, $^4J_{HH}$ = 1 Hz, 1H, CH_{ar}), 7.63 (m, 1H, CH_{ar}), 7.55 (m, 1H, CH_{ar}), 7.49 (dd, seen as a t, $^3J_{HH}$ = 7.9 Hz, 1H, CH_{ar}), 4.55 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 1.48 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 162.3 (C=O), 146.6 ($C_{quat}N$), 134.3 (CH_{ar}), 134.1 (C_{quat}), 131.4 (C_{quat}), 127.9 (CH_{ar}), 127.7 (CH_{ar}), 126.8 (CH_{ar}), 125.1 (CH_{ar}), 123.0 (CH_{ar}), 112.6 (CH_{ar}), 64.3 (CH_2O), 14.1 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{13}H_{12}N_2O_2$ $[M+H]^{+\cdot}$ 229.0977, found 229.0973.

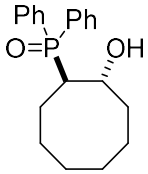
Synthesis of *trans*-cyclooctene IV





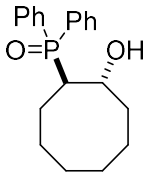
Procedure for the synthesis of 9-oxabicyclo[6.1.0]nonane (II). A solution of peracetic acid (15%, 50 mL, 110 mmol) and sodium acetate (8.3 g, 100 mmol) was added dropwise to *cis*-cyclooctene **I** (14 mL, 100 mmol) at 0 ºC. The reaction mixture was then stirred at room temperature for 17 h. After completion, the reaction mixture was cooled to 0 ºC and quenched with 40% aqueous NaOH until pH ~ 7 was reached. The crude product was extracted with Et_2O (5×100 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum at 0 ºC, to obtain 12.36 g (98%) of **II** as a white solid, which was used in the next reaction step without further purification. The spectral data are consistent with those reported in the literature.[3]

Procedure for the preparation of a $LiPPh_2$ solution in THF. Following a modified literature procedure,[4] Li(0) was cut into fine strips, washed with THF, and added to degassed THF (44 mL) in a flame dried Schlenk flask under a nitrogen atmosphere. A solution of PPh_3 (14.58 g, 55 mmol) in degassed THF (66 mL) was then added dropwise, and the reaction mixture was stirred at room temperature for 16 h. The reaction gradually turned dark red, after which ^{t}BuCl (6 mL, 55 mmol) was added dropwise, and stirring was continued for an additional 1.5 h. A white precipitate was formed, and stirring was then stopped to allow the precipitate to settle at the bottom of the flask. The red solution was transferred *via* a nitrogen-purged syringe to a second flame dried Schlenk flask, also purged with nitrogen, ready to be used in the next reaction step.

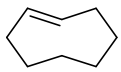


Method A for the synthesis of (2-hydroxycyclooctyl)diphenylphosphine oxide (III). Following a modified literature procedure,[5] a solution of **II** (6.31 g, 50 mmol) in degassed THF (100 mL) was added dropwise to a freshly prepared solution of $LiPPh_2$ in THF (~0.5 M, 110 mL). The reaction mixture was stirred at room temperature for 22 h. AcOH (3.7 mL, 65 mmol) was then added dropwise

at 0 ºC, and the reaction was stirred for 30 min at 0 ºC. Next, H_2O_2 (3%, 80 mL) was added dropwise at 0 ºC, and the reaction was stirred at room temperature for an additional 4 h. The resulting mixture was extracted with CH_2Cl_2 (250 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum. The product was precipitated from toluene, yielding 12.45 g (76%) of **III** as a white solid. The spectral data are consistent with those reported in the literature.[6]



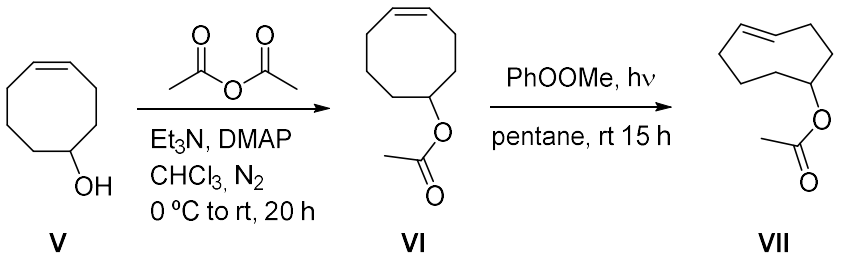
Method B for the synthesis of (2-hydroxycyclooctyl)diphenylphosphine oxide (III). Following a modified literature procedure,[6] ^{n}BuLi (1.6 M, 18.8 mL, 30 mmol) was added dropwise to a solution of **II** (3.16 g, 25 mmol) and Ph_2PH (5.12 g, 27.5 mmol) in degassed THF (100 mL) at –78 ºC. The reaction mixture was stirred for 1 h at the same temperature. The reaction was then allowed to warm to room temperature and stirred for an additional 13 h. AcOH (2.1 mL, 37.5 mmol) was added dropwise at 0 ºC, and the mixture was stirred for 30 min. H_2O_2 (30%, 3.8 mL, 37.5 mmol) was then added at 0 ºC, and the resulting mixture was warmed to room temperature and stirred for 4 h. The solution was extracted with CH_2Cl_2 (4 × 150 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum. The product was precipitated from toluene to afford 2.92 g (36%) of **III** as a white solid. The spectral data are consistent with those reported in the literature.[6]

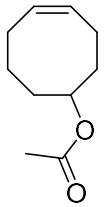


Procedure for the synthesis of *trans*-cyclooctene (IV). Following a modified literature procedure,[5] NaH (60%, 1.60 g, 40 mmol) was washed with toluene (40 mL) and pentane (4×40 mL), then poured into degassed DMF (75 mL). A solution of **III** (6.57 g, 20 mmol) in degassed DMF (75 mL) was added dropwise, and the resulting mixture was stirred vigorously for 30 min at room temperature. The reaction was quenched with ice, and the product was extracted with pentane (200 mL), dried over

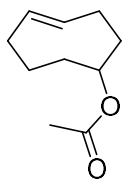
anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum at 0 ºC to afford 1.67 g (76%) of **IV** as a colorless liquid.[5] The spectral data are consistent with those reported in the literature.

Synthesis of (*E*)-cyclooct-4-en-1-yl acetate VII





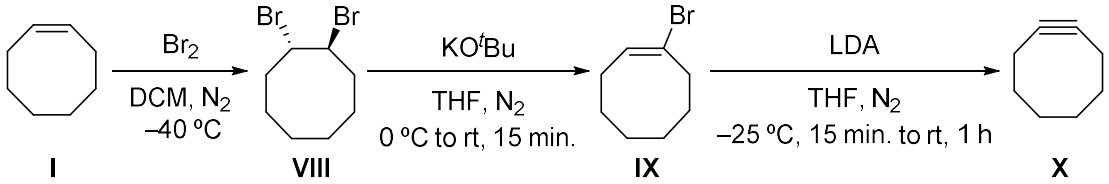
Procedure for the synthesis of (*Z*)-cyclooct-4-en-1-yl acetate (VI). Following a modified literature procedure,[7] acetic anhydride (10.6 mL, 112.5 mmol) was added dropwise to a solution of (*Z*)-cyclooct-4-en-1-ol **V** (1.89 g, 15 mmol), triethylamine (10.4 mL, 75 mmol), and 4-dimethylaminopyridine (92 mg, 0.75 mmol) in $CHCl_3$ (30 mL) at 0 ºC. The reaction mixture was stirred at 0 ºC for 15 minutes, then at room temperature for 20 h. The reaction mixture was cooled to 0 ºC and quenched with water. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 95:5) to yield 2.22 g (88%) of **VI** as a colourless oil. The spectral data are consistent with those reported in the literature.[7]

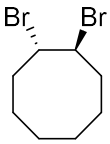


Procedure for the synthesis of (*E*)-cyclooct-4-en-1-yl acetate (VII). A solution of (*Z*)-cyclooct-4-en-1-yl acetate **VI** (2.22 g, 13.3 mmol) and methyl benzoate (3.3 mL, 26.4 mmol) in pentane (26 mL), was irradiated at 254 nm for 15 h. The crude product was extracted with an aqueous solution of $AgNO_3$ (15%, 50 mL), and the aqueous phase was washed with pentane (50 mL). NH_4OH (30%, 40 mL)

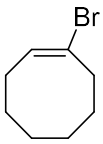
was added to the aqueous phase, the product was extracted with pentane (2 × 30 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum to afford 322 mg (15%) of **VII** as a colourless oil. The spectral data are consistent with those reported in the literature.[7]

Synthesis of cyclooctyne X



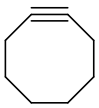


Procedure for the synthesis of (1*S*,2*S*)-1,2-dibromocyclooctane (VIII). Following a modified literature procedure,[8] a solution of Br_2 (12.9 mL, 250 mmol) in CH_2Cl_2 (12 mL) was added dropwise over a solution of *cis*-cyclooctene **I** (34.3 mL, 250 mmol) in CH_2Cl_2 (100 mL) at –40 °C. The reaction mixture was allowed to warm to 0 °C and was then quenched with an aqueous solution of Na_2SO_3 (10%, 50 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under vacuum to yield 59.07 g (88%) of **VIII**, which was used in the next step without further purification. The spectral data are consistent with those reported in the literature.[8]



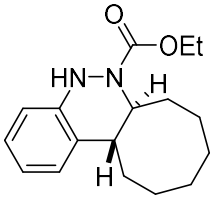
Procedure for the synthesis of (*E*)-1-bromocyclooct-1-ene (IX). Following a modified literature procedure,[8] a solution of **VIII** (62.84 g, 219 mmol) in THF (88 mL) was added dropwise to a suspension of KO^{t}Bu (33.37 g, 333 mmol) in THF (75 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature, stirred for 15 minutes, and then quenched with a saturated aqueous solution of NH_4Cl (100 mL). THF was removed under vacuum, and the crude product was extracted with CH_2Cl_2 (2 × 100 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent

was removed under vacuum. The crude product was distilled under vacuum (b.p. = 60–67 °C / 10 mbar) to yield 38.66 g (93%) of **IX** as a colourless liquid. The spectral data are consistent with those reported in the literature.[8]

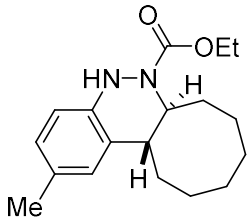


Procedure for the synthesis of cyclooctyne (X). Following a modified literature procedure,[8] a solution of ^{n}BuLi in hexanes (1.6 M, 29.9 mL, 43 mmol) was added dropwise to a solution of $^{i}Pr_2NH$ (6.7 mL, 47 mmol) in THF (75 mL) at 0 ºC. The reaction mixture was stirred for 10 minutes at 0 ºC and then cooled to –25 ºC. **IX** (8.13 g, 43 mmol) was added all at once, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was quenched with an aqueous solution of HCl (3 M, 50 mL), and the crude product was extracted with pentane (50 mL). The organic phase was washed with H_2O (8 × 50 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent was remover under vacuum at 0 ºC. The crude product was distilled under vacuum (b.p. = 36–43 °C / 10 mbar) to yield 3.74 g (80%) of **X** as a colourless liquid. The spectral data are consistent with those reported in the literature.[9]

General procedure and spectral data for the synthesis of functionalized cinnoline derivatives 3–6. To a stirred solution of *N*-carbonyl aryldiazene **2** (0.5 mmol, 1 equiv.) in $CHCl_3$ (1 mL), the corresponding dienophile (0.75 mmol, 1.5 equiv.) was added under a nitrogen atmosphere. The reaction mixture was stirred in a microwave reactor and heated to 111 ºC at 44 psi using a microwave power of 200 W. The crude residue was then purified by flash-column chromatography, as described below for each specific case, to afford the corresponding cinnoline derivatives **3**.

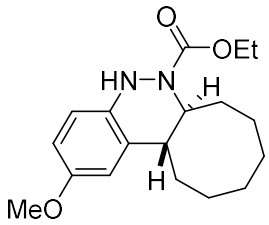


Ethyl (6a*S*,12a*R***)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3a)**. The general procedure was followed using aryldiazene carboxylate **2a** (89 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 121 mg (84%) of **3a** as a yellow solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 97:3). Mp: 113–114 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3322, 2922, 2853, 1690; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 7.05 (dd seen as t, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 6.92 (dd seen as t, $^3J_{HH}$ = 7.6, 1H, CH_{ar}), 6.82 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 6.31 (bs, 1H, NH), 4.52 (m, 1H, CHN), 4.12 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.84 (m, 1H, CH), 2.25 (m, 1H, CH_2), 2.11 (m, 1H, CH_2), 1.85–1.61 (m, 8H, 4×CH_2), 1.55–1.43 (m, 2H, CH_2), 1.22 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.6 (C=O), 146.2 ($C_{quat}N$), 129.4 (C_{quat}), 126.7 (CH_{ar}), 125.7 (CH_{ar}), 121.7 (CH_{ar}), 114.4 (CH_{ar}), 61.9 (CH_2O), 55.8 (CHN), 34.9 (CH), 32.5 (CH_2), 31.9 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.6 (CH_2), 24.6 (CH_2), 14.5 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{24}N_2O_2$ $[M+H]^{+\cdot}$ 289.1916, found 289.1909.

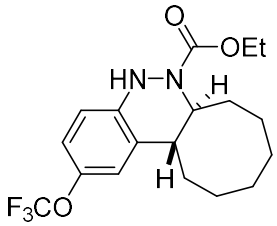


Ethyl (6a*S*,12a*R***)-2-methyl-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3b)**. The general procedure was followed using aryldiazene carboxylate **2b** (96 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 101 mg (67%) of **3b** as a yellow oil after 9 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). FTIR (neat) ν_{max} (cm^{-1}) 3332, 2930, 2856, 1690; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.09 (s, 1H, CH_{ar}), 6.87 (d, $^3J_{HH}$ = 7.9, 1H, CH_{ar}), 6.73 (d, $^3J_{HH}$ = 7.9, 1H, CH_{ar}), 6.22 (bs, 1H, NH), 4.50 (m, 1H, CHN), 4.15–4.09 (m, 2H, CH_2O), 2.82 (m, 1H, CH), 2.30 (m, 1H, CH_2), 2.27 (s, 3H,

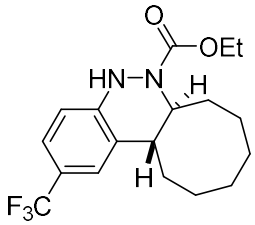
CH_3), 2.11 (m, 1H, CH_2), 1.86–1.72 (m, 6H, 3×CH_2), 1.71–1.60 (m, 2H, CH_2), 1.55–1.43 (m, 2H, CH_2), 1.23 (dd seen as t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.6 (C=O), 143.7 ($C_{quat}N$), 131.0 (C_{quat}), 129.4 (C_{quat}), 127.3 (CH_{ar}), 126.2 (CH_{ar}), 114.5 (CH_{ar}), 61.9 (CH_2O), 55.7 (CHN), 34.9 (CH), 32.6 (CH_2), 31.9 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.7 (CH_2), 24.6 (CH_2), 20.9 (CH_3), 14.5 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{26}N_2O_2$ $[M+H]^{+\cdot}$ 303.2073 found, 303.2068.



Ethyl (6a*S,12a*R**)-2-methoxy-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3c)**. The general procedure was followed using aryldiazene carboxylate **2c** (104 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 111 mg (70%) of **3c** as a brown oil after 4 h reaction. The crude product was purified by flash-column chromatography (Al_2O_3, hexanes/AcOEt 95:5). FTIR (neat) ν_{max} (cm^{-1}) 3317, 2929, 2854, 1703; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.84 (d, $^4J_{HH}$ = 2.7 Hz, 1H, CH_{ar}), 6.76 (d, $^3J_{HH}$ = 8.5 Hz, 1H, CH_{ar}), 6.61 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.7 Hz, 1H, CH_{ar}), 6.08 (bs, 1H, NH), 4.43 (m, 1H, CHN), 4.10 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 3.73 (s, 3H, CH_3), 2.80 (m, 1H, CH), 2.21 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 1.83–1.70 (m, 6H, 3×CH_2), 1.69–1.61 (m, 2H, CH_2), 1.54–1.40 (m, 2H, CH_2), 1.20 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 155.1 ($C_{quat}O$), 139.9 ($C_{quat}N$), 131.4 (C_{quat}), 115.6 (CH_{ar}), 113.16 (CH_{ar}), 110.76 (CH_{ar}), 61.9 (CH_2O), 55.7 (CHN), 55.6 (CH_3O), 35.5 (CH), 32.8 (CH_2), 31.8 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.4 (CH_2), 24.5 (CH_2), 14.6 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{26}N_2O_3$ $[M+H]^{+\cdot}$ 319.2022, found 319.2009.

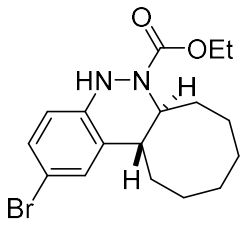


Ethyl (6a*S,12a*R**)-2-(trifluoromethoxy)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3d)**. The general procedure was followed using aryldiazene carboxylate **2d** (118 mg, 0.45 mmol) and *trans*-cyclooctene (88 µL, 0.675 mmol), affording 99 mg (59%) of **3d** as a red solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 98:2). Mp: 55–57 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3326, 2932, 2860, 1690; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.11 (s, 1H, CH_{ar}), 6.91 (d, $^3J_{HH}$ = 8.5 Hz, 1H, CH_{ar}), 6.79 (d, $^3J_{HH}$ = 8.5 Hz, 1H, CH_{ar}), 6.34 (bs, 1H, NH), 4.48 (m, 1H, CHN), 4.12 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.81 (m, 1H, CH), 2.18 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 1.84–1.58 (m, 8H, 4×CH_2), 1.53–1.41 (m, 2H, CH_2), 1.21 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 145.1 ($C_{quat}N$), 143.9 (q, $^3J_{CF}$ = 2.0 Hz, $C_{quat}O$), 131.2 (C_{quat}), 120.5 (q, $^1J_{CF}$ = 256.0 Hz, CF_3), 120.2 (q, $^4J_{CF}$ = 0.7 Hz, CH_{ar}), 118.7 (q, $^4J_{CF}$ = 0.7 Hz, CH_{ar}), 115.1 (CH_{ar}) 62.2 (CH_2O), 55.6 (CHN), 35.3 (CH), 32.6 (CH_2), 31.9 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.5 (CH_2), 24.5 (CH_2), 14.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –58.2; HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{23}F_3N_2O_3$ $[M+H]^{+\cdot}$ 373.1739, found 373.1733.



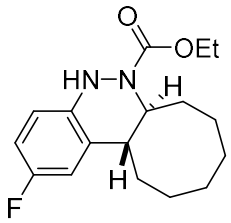
Ethyl (6a*S,12a*R**)-2-(trifluoromethyl)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3e)**. The general procedure was followed using aryldiazene carboxylate **2e** (123 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 162 mg (91%) of **3e** as a white solid after 9 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 74–75 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3319, 2931, 1690, 1617; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm):

7.49 (s, 1H, CH_{ar}), 7.30 (dq, $^{3}J_{HH}$ = 8.2 Hz, $^{4}J_{FH}$ = 0.9 Hz, 1H, CH_{ar}), 6.85 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, CH_{ar}), 6.44 (bs, 1H, NH), 4.54 (m, 1H, CHN), 4.15–4.10 (m, 2H, CH_2O), 2.84 (m, 1H, CH), 2.24 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 1.90–1.72 (m, 6H, 3×CH_2), 1.66 (m, 1H, CH_2), 1.58 (m, 1H, CH_2), 1.52–1.38 (m, 2H, CH_2), 1.22 (dd seen as t, $^{3}J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 149.1 ($C_{quat}N$), 129.3 (C_{quat}), 124.5 (q, $^{1}J_{CF}$ = 271.7 Hz, CF_3), 124.1 (q, $^{3}J_{CF}$ = 3.6 Hz, CH_{ar}), 123.4 (q, $^{2}J_{CF}$ = 32.2 Hz, C_{quat}), 122.9 (q, $^{3}J_{CF}$ = 3.7 Hz, CH_{ar}), 114.1 (CH_{ar}), 62.2 (CH_2O), 55.6 (CHN), 34.8 (CH), 32.4 (CH_2), 32.0 (CH_2), 27.4 (CH_2), 27.3 (CH_2), 24.7 (CH_2), 24.7 (CH_2), 14.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –61.6; HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{23}F_3N_2O_2$ $[M+H]^{+\cdot}$ 357.1790, found 357.1787.

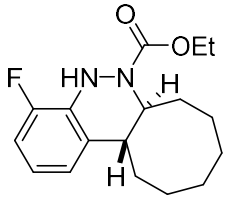


Ethyl (6a*S,12a*R**)-2-bromo-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3f)**. The general procedure was followed using aryldiazene carboxylate **2f** (129 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 145 mg (79%) of **3f** as a red oil after 5 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). FTIR (neat) ν_{max} (cm^{-1}) 3315, 2979, 2922, 2860; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.36 (s, 1H, CH_{ar}), 7.13 (d, $^{3}J_{HH}$ = 8.4 Hz, 1H, CH_{ar}), 6.68 (d, $^{3}J_{HH}$ = 8.4 Hz, 1H, CH_{ar}), 6.26 (bs, 1H, NH), 4.47 (m, 1H, CHN), 4.10 (q, $^{3}J_{HH}$ = 7.2 Hz, 2H, CH_2O), 2.79 (m, 1H, CH), 2.17 (m, 1H, CH_2), 2.05 (m, 1H, CH_2), 1.80–1.56 (m, 8H, 4×CH_2), 1.51–1.38 (m, 2H, CH_2), 1.20 (t, $^{3}J_{HH}$ = 7.2 Hz, 3H, CH_3); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.7 (C=O), 145.4 ($C_{quat}N$), 131.8 (C_{quat}), 129.8 (CH_{ar}), 128.5 (CH_{ar}), 116.0 (CH_{ar}), 114.3 ($C_{quat}Br$), 62.1 (CH_2O), 55.6 (CHN), 35.1 (CH), 32.6 (CH_2), 31.9 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.5

(CH_2), 24.5 (CH_2), 14.5 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{23}BrN_2O_2$ $[M+H]^{+\cdot}$ 367.1021, found 367.1015.

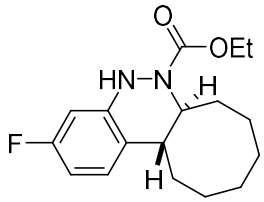


Ethyl (6a*S,12a*R**6a*R*,12a*S*)-2-fluoro-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3g)**. The general procedure was followed using aryldiazene carboxylate **2g** (98 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 52 mg (34%) of **3g** as a brown solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 98:2). Mp: 74–75 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3328, 2926, 2851, 1688; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.98 (d, $^3J_{HH}$ = 9.9 Hz, 1H, CH_{ar}), 6.75–6.73 (m, 2H, 2×CH_{ar}), 6.19 (bs, 1H, NH), 4.45 (m, 1H, CHN), 4.11 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.79 (m, 1H, CH), 2.17 (m, 1H, CH_2), 2.08 (m, 1H, CH_2), 1.83–1.58 (m, 8H, 4×CH_2), 1.54–1.42 (m, 2H, CH_2), 1.20 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 158.4 (d, $^1J_{CF}$ = 238.9 Hz, $C_{quat}F$), 155.8 (C=O), 142.5 (d, $^4J_{CF}$ = 2.1 Hz, $C_{quat}N$), 131.8 (d, $^3J_{CF}$ = 6.3 Hz, C_{quat}), 115.5 (d, $^3J_{CF}$ = 8.1 Hz, CH_{ar}), 113.6 (d, $^2J_{CF}$ = 23.4 Hz, CH_{ar}), 112.2 (d, $^2J_{CF}$ = 22.8 Hz, CH_{ar}), 62.1 (CH_2O), 55.7 (CHN), 35.5 (d, $^4J_{CF}$ = 1.1 Hz, CH), 32.8 (CH_2), 31.8 (CH_2), 27.5 (CH_2), 27.2 (CH_2), 24.4 (CH_2), 24.3 (CH_2), 14.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –121.4; HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{23}FN_2O_2$ $[M+H]^{+\cdot}$ 307.1822 found 307.1815.



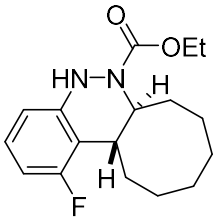
Ethyl (6a*S,12a*R**)-4-fluoro-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3h)**. The general procedure was followed using aryldiazene carboxylate **2h** (98 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 115 mg (75%) of **3h** as a green solid after 2.5 h reaction. The crude product was purified by flash-column

chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 80–82 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3335, 2926, 2860, 1703; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.02 (m, 1H, CH_{ar}), 6.86–6.78 (m, 2H, 2×CH_{ar}), 6.63 (bs, 1H, NH), 4.54 (m, 1H, CHN), 4.11 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.83 (m, 1H, CH), 2.21 (m, 1H, CH_2), 2.10 (m, 1H, CH_2), 1.85–1.57 (m, 8H, 4×CH_2), 1.52–1.38 (m, 2H, CH_2), 1.20 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 150.4 (d, $^1J_{CF}$ = 240.3 Hz, $C_{quat}F$), 134.4 (d, $^2J_{CF}$ = 14.2 Hz, $C_{quat}N$), 131.8 (C_{quat}), 122.0 (d, $^4J_{CF}$ = 3.1 Hz, CH_{ar}), 121.0 (d, $^3J_{CF}$ = 7.3 Hz, CH_{ar}), 111.9 (d, $^2J_{CF}$ = 18.2 Hz, CH_{ar}), 62.1 (CH_2O), 55.5 (CHN), 34.7 (d, $^4J_{CF}$ = 2.2 Hz, CH), 32.5 (CH_2), 32.2 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 24.7 (CH_2), 24.6 (CH_2), 14.4 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –136.8; ESI- HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{23}FN_2O_2$ $[M+H]^{+\cdot}$ 307.1822, found 307.1819.

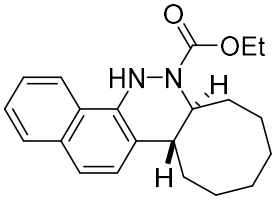


Ethyl (6a*S,12a*R**)-3-fluoro-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3i$_1$)**. The general procedure was followed using aryldiazene carboxylate **2i** (98 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 46 mg (30%) of **3i$_1$** a yellow solid after 8 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 63–65 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3323, 2930, 2852, 1690; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.17 (m, 1H, CH_{ar}), 6.62–6.52 (m, 2H, 2×CH_{ar}), 6.26 (bs, 1H, NH), 4.48 (bm, 1H, CHN), 4.12 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.77 (m, 1H, CH), 2.19 (m, 1H, CH_2), 2.05 (m, 1H, CH_2), 1.82–1.73 (m, 6H, 3×CH_2), 1.69–1.58 (m, 2H, CH_2), 1.50–1.41 (m, 2H, CH_2), 1.22 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 160.8 (d, $^1J_{CF}$ = 244.4 Hz, $C_{quat}F$), 155.9 (C=O), 147.5 (d, $^3J_{CF}$ = 8.9 Hz, $C_{quat}N$), 128.1 (d, $^3J_{CF}$ = 9.1 Hz, CH_{ar}), 124.9 (C_{quat}), 108.3 (d, $^2J_{CF}$ = 21.1 Hz, CH_{ar}), 101.8 (d, $^2J_{CF}$ = 24.3 Hz, CH_{ar}), 62.2 (CH_2O), 55.8 (CHN),

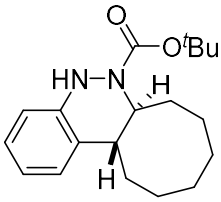
34.6 (CH), 32.5 (CH_2), 32.2 (CH_2), 27.6 (CH_2), 27.4 (CH_2), 24.7 (CH_2), 24.7 (CH_2), 14.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –116.8; HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{23}FN_2O_2$ $[M+H]^{+\cdot}$ 307.1822, found 307.1820.



Ethyl (6a*S,12a*R**)-1-fluoro-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3i2)**. The general procedure was followed using aryldiazene carboxylate **2i** (98 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 73 mg (48%) of **3i2** as a yellow solid after 8 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 69–71 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3320, 2925, 2866, 1695; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.98 (ddd seen as td, $^3J_{HH}$ = 8.1 Hz, $^4J_{FH}$ = 5.9 Hz, 1H, CH_{ar}), 6.57–6.51 (m, 2H, 2×CH_{ar}), 6.44 (bs, 1H, NH), 4.62 (m, 1H, CHN), 4.25–4.09 (m, 2H, CH_2O), 3.06 (m, 1H, CH), 2.27 (m, 1H, CH_2), 2.00–1.89 (m, 5H, 2×CH_2 + 1H from CH_2), 1.82–1.67 (m, 2H, CH_2), 1.63–1.47 (m, 3H, CH_2 + 1H from CH_2), 1.31 (m, 1H, CH_2), 1.26 (dd seen as t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 162.8 (d, $^1J_{CF}$ = 245.5 Hz, $C_{quat}F$), 155.9 (C=O), 145.7 (d, $^3J_{CF}$ = 8.4 Hz $C_{quat}N$), 126.9 (d, $^3J_{CF}$ = 10.4 Hz, CH_{ar}), 114.1 (d, $^2J_{CF}$ = 17.8 Hz, C_{quat}), 109.8 (d, $^4J_{CF}$ = 2.8 Hz, CH_{ar}), 108.0 (d, $^2J_{CF}$ = 23.3 Hz, CH_{ar}), 62.2 (CH_2O), 52.3 (CHN), 31.2 (d, $^3J_{CF}$ = 6.7 Hz, CH), 30.3 (CH_2), 29.8 (CH_2), 28.3 (CH_2), 27.5 (CH_2), 27.2 (CH_2), 26.8 (CH_2), 14.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –112.9; HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{23}FN_2O_2$ $[M+H]^{+\cdot}$ 307.1822 found, 307.1820.

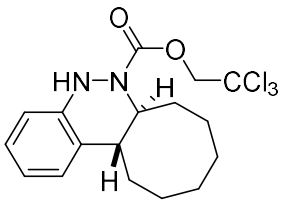


Ethyl (6a*S*,12a*R***)-6a,7,8,9,10,11,12,12a-octahydrobenzo[*h*]cycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3j)**. The general procedure was followed using aryldiazene carboxylate **2j** (114 mg, 0.5 mmol) and *trans*-cyclooctene (98 μL, 0.75 mmol), affording 135 mg of **3j** (80%) as a brown oil after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). FTIR (neat) ν_{max} (cm^{-1}) 3360, 3053, 2924, 2854, 1697; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.90 (d, $^3J_{HH}$ = 8.4, 1H, CH_{ar}), 7.77 (d, $^3J_{HH}$ = 8.3, Hz, 1H, CH_{ar}), 7.48 (m, 1H, CH_{ar}), 7.45–7.38 (m, 3H, 3×CH_{ar}), 6.96 (bs, 1H, NH), 4.67 (m, 1H, CHN), 4.19–4.06 (m, 2H, CH_2O), 3.01 (m, 1H, CH), 2.30 (m, 1H, CH_2), 2.09 (m, 1H, CH_2), 1.96–1.74 (m, 7H, 3×CH_2 + 1H from CH_2), 1.60 (m, 1H, CH_2), 1.52–1.40 (m, 2H, CH_2), 1.21 (dd seen as t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 139.9 ($C_{quat}N$), 131.8 (C_{quat}), 128.1 (CH_{ar}), 125.6 (CH_{ar}), 125.3 (CH_{ar}), 125.0 (CH_{ar}), 123.1 (CH_{quat}), 122.9 (CH_{quat}), 121.1 (CH_{ar}), 119.5 (CH_{ar}), 62.0 (CH_2O), 54.4 (CHN), 34.7 (CH), 32.2 (CH_2), 31.5 (CH_2), 27.6 (CH_2), 27.6 (CH_2), 25.6 (CH_2), 25.6 (CH_2), 14.4 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{21}H_{26}N_2O_2$ $[M+H]^{+\cdot}$ 339.2073, found 339.2059.

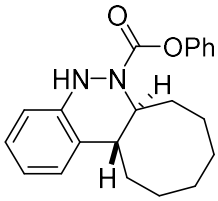


Tert*-butyl (6a*S,12a*R***)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3k)**. The general procedure was followed using aryldiazene carboxylate **2k** (103 mg, 0.5 mmol) and *trans*-cyclooctene (98 μL, 0.75 mmol), affording 122 mg (77%) of **3k** as an orange solid after 6 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 121–122 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3331, 2974, 2927, 2855, 1686; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.26 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH_{ar}), 7.06–7.02 (dd seen as t, $^3J_{HH}$ = 7.7 1H, CH_{ar}), 6.90 (dd seen as t, $^3J_{HH}$ =

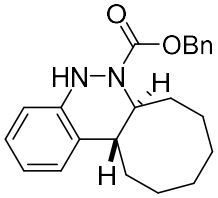
7.7, Hz, 1H, CH_{ar}), 6.77 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH_{ar}), 6.26 (bs, 1H, NH), 4.50 (m, 1H, CHN), 2.81 (m, 1H, CH), 2.25 (m, 1H, CH_2), 2.08 (m, 1H, CH_2), 1.86–1.74 (m, 5H, 3×CH_2 + 1H from CH_2), 1.73–1.57 (m, 3H, CH_2 + 1H from CH_2), 1.51–1.44 (m, 2H, CH_2), 1.39 (s, 9H, 3×CH_3); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.1 (C=O), 146.4 (C_{quat}N), 129.3 (C_{quat}), 126.8 (CH_{ar}), 125.7 (CH_{ar}), 121.5 (CH_{ar}), 114.4 (CH_{ar}), 80.9 (C_{quat}O), 55.5 (CHN), 34.9 (CH), 32.5 (CH_2), 32.2 (CH_2), 28.3 (3×CH_3), 27.6 (CH_2), 27.5 (CH_2), 25.0 (CH_2), 24.8 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{19}H_{28}N_2O_2$ $[M+Na]^{+\cdot}$ 339.2048, found 339.2050.



2,2,2-Trichloroethyl (6a*S,12a*R**)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3l)**. The general procedure was followed using aryldiazene carboxylate **2l** (141 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 130 mg (66%) of **3l** as a brown solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 82–84 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3320, 2923, 2853, 1702; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH_{ar}), 7.07 (dd seen as t, $^3J_{HH}$ = 7.7, Hz, 1H, CH_{ar}), 6.95 (dd seen as t, $^3J_{HH}$ = 7.7 Hz, 1H, CH_{ar}), 6.85 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH_{ar}), 6.42 (bs, 1H, NH), 4.82–4.70 (m, 2H, CH_2O), 4.65 (m, 1H, CHN), 2.90 (m, 1H, CH), 2.29 (m, 1H, CH_2), 2.17 (m, 1H, CH_2), 1.86–1.77 (m, 6H, 3×CH_2), 1.75–1.62 (m, 2H, CH_2), 1.54–1.45 (m, 2H, CH_2); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 153.2 (C=O), 145.6 (C_{quat}N), 129.0 (C_{quat}), 126.8 (CH_{ar}), 125.9 (CH_{ar}), 122.1 (CH_{ar}), 114.7 (CH_{ar}), 95.2 (CCl_3), 75.2 (CH_2O), 56.2 (CHN), 34.9 (CH), 32.5 (CH_2), 32.1 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 24.7 (CH_2), 24.4 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{21}Cl_3N_2O_2$ $[M+H]^+$ 391.0747, found 391.0749.

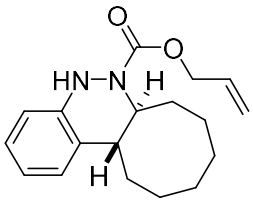


Phenyl (6a*S*,12a*R***)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3m)**. The general procedure was followed using aryldiazene carboxylate **2m** (113 mg, 0.5 mmol) and *trans*-cyclooctene (98 μL, 0.75 mmol), affording 129 mg (77%) of **3m** as a yellow solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 98:2). Mp: 96–97 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3340, 3062, 2925, 2851, 1708; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39–7.35 (m, 3H, 3×CH_{ar}), 7.22 (dd seen as t, $^3J_{HH}$ = 7.5, Hz, 1H, CH_{ar}), 7.18–7.09 (m, 3H, 3×CH_{ar}), 7.04 (m, 1H, CH_{ar}), 6.90 (d, $^3J_{HH}$ = 7.8 Hz, 1H, CH_{ar}), 6.54 (bs, 1H, NH), 4.74 (m, 1H, CHN), 2.99 (m, 1H, CH), 2.41–2.26 (m, 2H, CH_2), 1.99 (m, 1H, CH_2), 1.91–1.81 (m, 6H, 3×CH_2), 1.74 (m, 1H, CH_2), 1.66–1.53 (m, 2H, CH_2); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 153.7 (C=O), 150.9 ($C_{quat}O$), 145.9 ($C_{quat}N$), 129.4 (C_{quat}), 129.1 (2×CH_{ar}), 126.7 (CH_{ar}), 125.8 (CH_{ar}), 125.3 (CH_{ar}), 122.0 (CH_{ar}), 121.4 (2×CH_{ar}), 114.6 (CH_{ar}), 56.7 (CHN), 35.2 (CH), 32.7 (CH_2), 31.9 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 24.5 (CH_2), 24.4 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{21}H_{24}N_2O_2$ $[M+H]^{+\cdot}$ 337.1916, found 337.1907.

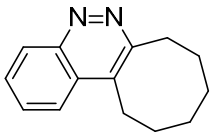


Benzyl (6a*S*,12a*R***)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3n)**. The general procedure was followed using aryldiazene carboxylate **2n** (120 mg, 0.5 mmol) and *trans*-cyclooctene (196 μL, 1.5 mmol, 3 equiv.), affording 91 mg (52%) of **3n** as a brown solid from after 7 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 89–90 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3326, 3032, 2923, 2854, 1697; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.40–7.28 (m, 6H, 6×CH_{ar}), 7.09 (dd seen as t, $^3J_{HH}$ = 7.5, Hz, 1H, CH_{ar}), 6.97 (dd seen as t, $^3J_{HH}$ = 7.5, 1H, CH_{ar}), 6.83 (d, $^3J_{HH}$ = 7.5 Hz, 1H, CH_{ar}), 6.36 (bs, 1H, NH), 5.15 (s,

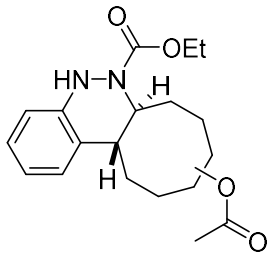
2H, CH_2O), 4.60 (m, 1H, CHN), 2.89 (m, 1H, CH), 2.29 (m, 1H, CH_2), 2.17 (m, 1H, CH_2), 1.87–1.75 (m, 6H, 3×CH_2), 1.74–1.63 (m, 2H, CH_2), 1.56–1.46 (m, 2H, CH_2); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.4 (C=O), 146.2 ($C_{quat}N$), 136.1 (C_{quat}), 129.4 (C_{quat}), 128.3 (2×CH_{ar}), 127.9 (CH_{ar}), 127.5 (2×CH_{ar}), 126.7 (CH_{ar}), 125.7 (CH_{ar}), 121.8 (CH_{ar}), 114.5 (CH_{ar}), 67.5 (CH_2O), 56.2 (CHN), 35.0 (CH), 32.6 (CH_2), 31.9 (CH_2), 27.4 (CH_2), 27.3 (CH_2), 24.6 (CH_2), 24.4 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{22}H_{26}N_2O_2$ $[M+H]^{+\cdot}$ 351.2073, found 351.2070.



Allyl (6a*S,12a*R**)-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (3o)**. The general procedure was followed using aryldiazene carboxylate **2o** (95 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 119 mg (79%) of **3o** as a brown solid after 4 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1). Mp: 74–76 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3320, 2929, 2852, 1694; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 7.06 (dd seen as t, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 6.93 (dd seen as t, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 6.83 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH_{ar}), 6.34 (bs, 1H, NH), 5.88 (m, 1H, =CH), 5.21 (d, $^3J_{HH}$ = 17.3 Hz, 1H, $=CH_2$), 5.18 (d, $^3J_{HH}$ = 10.5 Hz, 1H, $=CH_2$), 4.63–4.52 (m, 3H, CH_2O + CHN), 2.86 (m, 1H, CH), 2.29 (m, 1H, CH_2), 2.15 (m, 1H, CH_2), 1.85–1.74 (m, 6H, 3×CH_2), 1.72–1.59 (m, 2H, CH_2), 1.56–1.44 (m, 2H, CH_2); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.1 (C=O), 146.1 ($C_{quat}N$), 132.4 (=CH), 129.3 (C_{quat}), 126.6 (CH_{ar}), 125.7 (CH_{ar}), 121.8 (CH_{ar}), 117.3 ($=CH_2$), 114.5 (CH_{ar}), 66.3 (CH_2O), 56.0 (CHN), 35.0 (CH), 32.6 (CH_2), 31.9 (CH_2), 27.5 (CH_2), 27.3 (CH_2), 24.6 (CH_2), 24.5 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{24}N_2O_2$ $[M+H]^{+\cdot}$ 301.1916, found 301.1908.

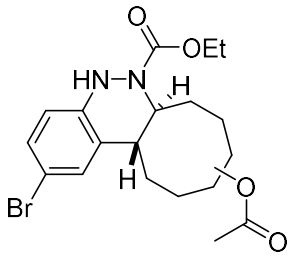


7,8,9,10,11,12-Hexahydrocycloocta[*c*]cinnoline (4a). The general procedure was followed using *N*-acetyl aryldiazene **2p** (111 mg, 0.75 mmol) or *N*-benzoyl aryldiazene **2q** (105 mg, 0.5 mmol) and *trans*-cyclooctene (98 µL, 0.75 mmol), affording 56 mg (70%) of **4** from **2p** after 0.5 h reaction or 22 mg (42%) of **4a** from **2q** after 6 h reaction as a yellow solid. Hexahydrocycloocta[*c*]cinnoline **4a** was also obtained in 98% yield by reaction of *N*-acetyl aryldiazene **2p** (37 mg, 0.25 mmol) with *trans*-cyclooctene (49 µL, 0.375 mmol, 1.5 equiv.) in refluxing chloroform for 30 h. Additionally, reaction of aryldiazene carboxylate **2a** (89 mg, 0.5 mmol) with cyclooctyne (81 mg, 0.75 mmol) afforded cinnoline derivative **4a** (32 mg, 30%) following the general procedure. Finally, compound **4a** (28 mg, 26%) was obtained following the general procedure with *N*-acetyl aryldiazene **2p** (74 mg, 0.5 mmol) and cyclooctyne (81 mg, 0.75 mmol) in a 2.5 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 85:15). Mp: 119–121 ºC; FTIR (neat) ν_{max} (cm^{-1}) 2925, 2851, 1636; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.45 (dd, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.5 Hz, 1H CH_{ar}), 7.99 (dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.5 Hz, 1H, CH_{ar}), 7.72–7.65 (m, 2H, 2×CH_{ar}), 3.42 (t, $^3J_{HH}$ = 6.3 Hz, 2H, CH_2), 3.22 (t, $^3J_{HH}$ = 6.5 Hz, 2H, CH_2), 1.92 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 1.46 (m, 2H, CH_2), 1.25 (m, 2H, CH_2); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 157.2 (C_{quat}N), 149.2 (C_{quat}N), 132.6 (C_{quat}), 130.6 (CH_{ar}), 130.4 (CH_{ar}), 128.8 (CH_{ar}), 125.1(C_{quat}), 122.6 (CH_{ar}), 33.6 (CH_2), 31.4 (CH_2), 30.1 (CH_2), 26.6 (CH_2), 25.6 (CH_2), 25.0 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{14}H_{16}N_2$ $[M+H]^{+\cdot}$ 213.1392, found 213.1383.



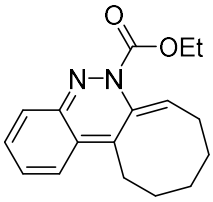
Ehyl (6a*S*,12a*R***)-9-acetoxy-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate and ehyl (6a*S***,12a*R***)-10-acetoxy-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (5a)**. The general procedure was followed using aryldiazene carboxylate **2a** (89 mg, 0.5 mmol) and (*E*)-cyclooct-4-en-1-yl acetate (126 mg, 0.75 mmol), affording 151 mg (87%) of **5a** as a brown solid after 9 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 90:10) obtaining an inseparable mixture of diastereo- and regioisomers. Mp: 59–62 ºC; FTIR (neat) ν_{max} (cm^{-1}) 3351, 2938, 2858, 1724; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.26–7.20 (m, 1H, CH_{ar}), 7.06–7.01 (m, 1H, CH_{ar}), 6.94–6.88 (m, 1H, CH_{ar}), 6.82–6.79 (m, 1H, CH_{ar}), 6.30 (bs, 1H, NH), 5.10–4.87 (m, 1H, CHN), 4.41–4.23 (m, 1H, HC-O), 4.13–4.01 (m, 2H, CH_2O), 2.85–2.63 (m, 1H, CH), 2.55–2.31 (m, 1H, CH_2), 2.25–2.06 (m, 2H, CH_2), 2.02–1.99 (m, 4H, CH_3CO + 1H from CH_2), 1.94–1.79 (m, 4H, 2×CH_2), 1.77–1.65 (m, 2H, CH_2), 1.20–1.15 (m, 3H, CH_3CH_2); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 170.1 (O=CCH_3), 170.1 (O=CCH_3), 170.0 (O=CCH_3), 169.9 (O=CCH_3), 155.7 (O=$COCH_2$), 155.4 (O=$COCH_2$), 155.4 (O=$COCH_2$), 155.3 (O=$COCH_2$), 147.0 ($C_{quat}N$), 146.9 ($C_{quat}N$), 146.8 ($C_{quat}N$), 146.6 ($C_{quat}N$), 129.7 (C_{quat}), 129.7 (C_{quat}), 129.6 (C_{quat}), 129.1 (C_{quat}), 126.1 (CH_{ar}), 125.9 (CH_{ar}), 125.8 (CH_{ar}), 125.8 (CH_{ar}), 125.8 (CH_{ar}), 125.8 (CH_{ar}), 125.8 (CH_{ar}), 125.7 (CH_{ar}), 122.0 (CH_{ar}), 122.0 (CH_{ar}), 121.9 (CH_{ar}), 121.9 (CH_{ar}), 114.6 (CH_{ar}), 114.5 (CH_{ar}) 114.4 (CH_{ar}), 114.4 (CH_{ar}), 74.6 (HC-O), 74.4 (HC-O), 73.3 (HC-O), 73.2 (HC-O), 61.9 (CH_2O), 61.9 (CH_2O), 61.9 (CH_2O), 61.8 (CH_2O), 58.1 (CHN), 57.7 (CHN), 56.7 (CHN), 56.5 (CHN), 37.3 (CH), 36.9 (CH), 35.8 (CH), 34.7 (CH), 33.7 (CH_2), 33.3 (CH_2), 32.6 (CH_2), 32.3 (CH_2), 32.3 (CH_2), 31.2 (CH_2), 31.2 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 29.5

(CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.2 (CH_2), 27.0 (CH_2), 26.3 (CH_2), 21.3 (CH_3CO), 21.3 (CH_3CO), 21.1 (CH_3CO), 21.0 (CH_3CO), 20.3 (CH_2), 20.3 (CH_2), 20.3 (CH_2), 19.9 (CH_2), 14.4 (CH_3CH_2), 14.4 (CH_3CH_2), 14.3 (CH_3CH_2), 14.3 (CH_3CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{19}H_{26}N_2O_4$ $[M+H]^{+\cdot}$ 347.1971, found 347.1968.

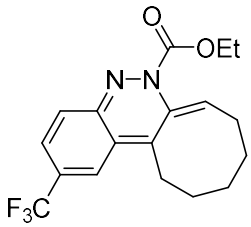


Ethyl (6a*S*,12a*R***)-9-acetoxy-2-bromo-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate and ethyl (6a*S***,12a*R***)-10-acetoxy-2-bromo-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (5f)**. The general procedure was followed using aryldiazene carboxylate **2e** (129 mg, 0.5 mmol) and (*E*)-cyclooct-4-en-1-yl acetate (126 mg, 0.75 mmol), affording 158 mg (74%) of **5f** as a brown oil after 10 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 95:10) obtaining an inseparable mixture of 4 diastereo- and regioisomers. FTIR (neat) ν_{max} (cm^{-1}) 3333, 2936, 2926, 1729, 1718, 1698; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.35–7.32 (m, 1H, CH_{ar}), 7.14–7.12 (m, 1H, CH_{ar}), 6.69–6.67 (m, 1H, CH_{ar}), 6.29 (bs, 1H, NH), 5.06–4.84 (m, 1H, CHN), 4.36–4.20 (m, 1H, HC-O), 4.09–4.04 (m, 2H, CH_2O), 2.81–2.57 (m, 1H, CH), 2.77–2.10 (m, 2H, CH_2), 2.05–1.96 (m, 4H, CH_3CO + 1H from CH_2), 1.93–1.50 (m, 7H, 3×CH_2 + 1H from CH_2), 1.21–1.15 (m, 3H, C*H*$_3$CH$_2$); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 170.2 (O=CCH_3), 170.2 (O=CCH_3), 170.0 (O=CCH_3), 170.0 (O=CCH_3), 155.8 (O=$COCH_2$), 155.6 (O=$COCH_2$), 155.6 (O=$COCH_2$), 155.4 (O=$COCH_2$), 146.2 ($C_{quat}N$), 146.1 ($C_{quat}N$), 146.0 ($C_{quat}N$), 145.8 ($C_{quat}N$), 132.1 (C_{quat}), 132.0 (C_{quat}), 131.5 (C_{quat}), 131.5 (C_{quat}), 129.4 (CH_{ar}), 129.1 (CH_{ar}), 129.1 (CH_{ar}), 129.0 (CH_{ar}), 128.7 (CH_{ar}), 128.6 (CH_{ar}), 128.6 (CH_{ar}), 128.6 (CH_{ar}), 116.2 (CH_{ar}), 116.1 (CH_{ar}), 116.0 (CH_{ar}), 116.0 (CH_{ar}), 114.6 ($C_{quat}Br$), 114.6 ($C_{quat}Br$), 114.5 ($C_{quat}Br$), 114.5 ($C_{quat}Br$), 74.5 (HC-O),

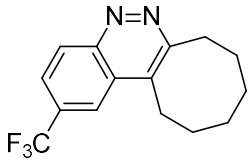
74.3 (HC-O), 73.2 (HC-O), 73.0 (HC-O), 62.2 (CH_2O), 62.1 (CH_2O), 62.1 (CH_2O), 62.1 (CH_2O), 57.8 (CHN), 57.5 (CHN), 56.5 (CHN), 56.4 (CHN), 37.3 (CH), 37.0 (CH), 36.0 (CH), 34.8 (CH), 33.8 (CH_2), 33.3 (CH_2), 32.6 (CH_2), 32.3 (CH_2), 32.3 (CH_2), 31.2 (CH_2), 31.2 (CH_2), 30.9 (CH_2), 30.5 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.8 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 27.0 (CH_2), 26.3 (CH_2), 21.3 (CH_3CO), 21.3 (CH_3CO), 21.2 (CH_3CO), 21.2 (CH_3CO), 20.9 (CH_2), 20.2 (CH_2), 20.2 (CH_2), 19.9 (CH_2), 14.4 (CH_3CH_2), 14.4 (CH_3CH_2), 14.4 (CH_3CH_2), 14.4 (CH_3CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{19}H_{25}BrN_2O_4$ $[M+H]^{+\cdot}$ 425.1076, found 425.1073.



Ethyl (*E*)-9,10,11,12-tetrahydrocycloocta[*c*]cinnoline-6(8*H*)-carboxylate (6a). The general procedure was followed using aryldiazene carboxylate **2a** (89 mg, 0.5 mmol) and cyclooctyne (81 mg, 0.75 mmol), affording 34 mg (24%) of **6a** as a yellow oil after 8 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 97:3) obtaining the instable compound **6a**, which was degraded after few hours. FTIR (neat) ν_{max} (cm^{-1}) 2956, 2850, 1712; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.02 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 0.8 Hz, 1H, CH_{ar}), 7.36 (dd, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.6 Hz, 1H, CH_{ar}), 7.27 (m, 1H, CH_{ar}), 7.15 (m, 1H, CH_{ar}), 6.13 (t, $^3J_{HH}$ = 8.9 Hz, 1H, =CH), 4.40 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.96 (t, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2), 2.61 (dt, $^3J_{HH}$ = 8.9 Hz, $^3J_{HH}$ = 6.7 Hz, 2H, CH_2), 1.82 (m, 2H, CH_2), 1.69 (m, 2H, CH_2), 1.60 (m, 2H, CH_2), 1.40 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 155.8 (C=O), 152.9 (C=N), 134.0 (C_{quat}), 128.0 (C_{quat}), 127.6 (CH_{ar}), 126.0 (C_{quat}), 125.6 (=CH), 125.4 (CH_{ar}), 123.0 (CH_{ar}), 119.4 (CH_{ar}), 62.9 (CH_2O), 34.4 (CH_2), 26.9 (CH_2), 26.1 (CH_2), 25.8 (CH_2), 23.8 (CH_2), 14.5 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{17}H_{20}N_2O_2$ $[M+H]^{+\cdot}$ 285.1603, found 285.1589.



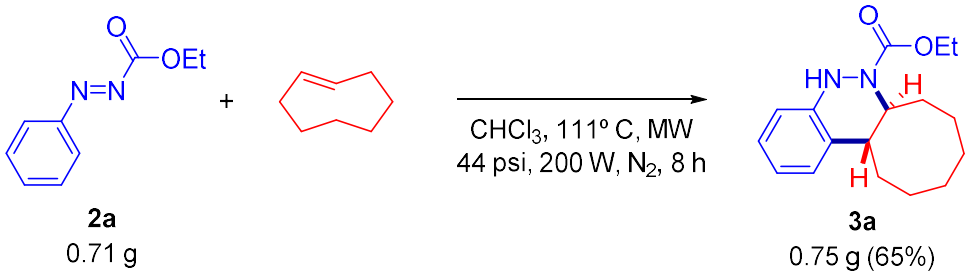
Ethyl (*E*)-2-(trifluoromethyl)-9,10,11,12-tetrahydrocycloocta[*c*]cinnoline-6(8*H*)-carboxylate (6e). The general procedure was followed using aryldiazene carboxylate **2e** (123 mg, 0.5 mmol) and cyclooctyne (81 mg, 0.75 mmol), affording 31 mg (18%) of **6e** as a yellow oil after 8 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 99:1) obtaining the instable compound **6e**, which was degraded after few hours. FTIR (neat) ν_{max} (cm^{-1}) 3362, 2930, 2852, 1724; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.16 (d, $^3J_{HH}$ = 8.9 Hz, $^4J_{HH}$ = 0.8 Hz, 1H, CH_{ar}), 7.59 (d, $^4J_{HH}$ = 2.4 Hz, 1H, CH_{ar}), 7.49 (m, 1H, CH_{ar}), 6.20 (t, $^3J_{HH}$ = 8.8 Hz, 1H, =CH), 4.41 (q, $^3J_{HH}$ = 7.1 Hz, 2H, CH_2O), 2.96 (t, $^3J_{HH}$ = 6.9 Hz, 2H, CH_2), 2.63 (dt, $^3J_{HH}$ = 8.8 Hz, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2), 1.83 (m, 2H, CH_2), 1.71 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 1.40 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 156.1 (C=O), 152.8 (C=N), 136.6 (C_{quat}), 127.6 (=CH), 127.4 (q, $^2J_{CF}$ = 32.8 Hz, C_{quat}), 127.2 (C_{quat}), 126.2 (C_{quat}), 124.4 (q, $^3J_{CF}$ = 3.6 Hz, CH_{ar}), 124.0 (q, $^1J_{CF}$ = 272.0 Hz, CF_3), 120.4 (q, $^3J_{CF}$ = 4.0 Hz, CH_{ar}), 119.8 (CH_{ar}), 63.3 (CH_2O), 34.2 (CH_2), 26.9 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 23.9 (CH_2), 14.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –62.3; HRMS (ESI-TOF) *m/z* calcd. for $C_{18}H_{19}F_3N_2O_2$ $[M+H]^{+\cdot}$ 353.1477, found 353.1480.



2-(Trifluoromethyl)-7,8,9,10,11,12-hexahydrocycloocta[*c*]cinnoline (4e). The general procedure was followed using aryldiazene carboxylate **2e** (123 mg, 0.5 mmol) and cyclooctyne (81 mg, 0.75 mmol), affording 46 mg (33%) of **4e** as a yellow solid after 8 h reaction. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 85:5). Mp: 127–130 ºC; FTIR (neat) ν_{max} (cm^{-1}) 2927, 2856; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.59 (d, $^3J_{HH}$ = 8.9 Hz, 1H, CH_{ar}), 7.30 (s, 1H, CH_{ar}), 7.87

(d, $^{3}J_{HH}$ = 8.9 Hz, 1H, CH_{ar}), 3.47 (m, 2H, CH_2), 3.27 (m, 2H, CH_2), 1.98–1.86 (m, 4H, 2×CH_2), 1.48 (m, 2H, CH_2), 1.27 (m, 2H, CH_2); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 158.6 ($C_{quat}N$), 149.2 ($C_{quat}N$), 133.7 (C_{quat}), 132.1 (CH_{ar}), 131.9 (q, $^{2}J_{CF}$ = 32.6 Hz, C_{quat}), 124.5 (q, $^{3}J_{CF}$ = 2.7 Hz, CH_{ar}), 124.2 (C_{quat}), 123.6 (q, $^{1}J_{CF}$ = 272.5 Hz, CF_3), 121.0 (q, $^{3}J_{CF}$ = 4.5 Hz, CH_{ar}), 33.6 (CH_2), 31.4 (CH_2), 30.3 (CH_2), 26.5 (CH_2), 25.5 (CH_2), 25.1 (CH_2); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm): –63.0; HRMS (ESI-TOF) *m/z* calcd. for $C_{15}H_{15}F_3N_2$ $[M+H]^{+\cdot}$ 281.1266, found 281.1272.

Gram-scale synthesis of 3a

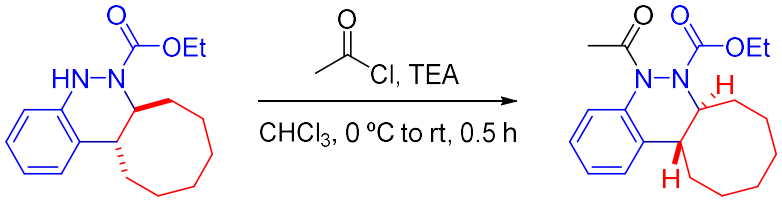


2a
0.71 g

3a
0.75 g (65%)

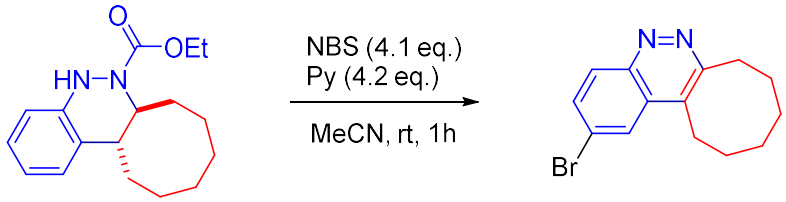
To a stirred solution of aryldiazene carboxylate **2a** (0.71 g, 4 mmol) in $CHCl_3$ (8 mL), *trans*-cyclooctene (784 µL, 6 mmol, 1.5 equiv.) was added under a nitrogen atmosphere. The reaction mixture was stirred in a microwave reactor and heated to 111 ºC under a pressure of 44 psi with a microwave power of 200 W for 8 h. The crude product was purified by column chromatography (SiO_2, hexanes/AcOEt 97:3) to afford 0.75 g (65%) of cinnoline **3a**.

Structural elaborations of 3a



3a **7**

Synthesis of ethyl (6a*S,12a*R**)-5-acetyl-6a,7,8,9,10,11,12,12a-octahydrocycloocta[*c*]cinnoline-6(5*H*)-carboxylate (7)**: To a 0 ºC solution of **3a** (29 mg, 0.1 mmol) and triethylamine (16 µL, 0.115 mmol) in $CHCl_3$ (1 mL), acetyl chloride (8 µL, 0.11 mmol) was added. The reaction mixture was stirred at room temperature for 0.5 h, then diluted with CH_2Cl_2 (10 mL), washed with 1M HCl (10 mL) and the organic layer was dried over anhydrous $MgSO_4$. After filtration and solvent removal under vacuum, compound **7** was obtained as a brown solid (27 mg 81%). Mp: 74–76 ºC; FTIR (neat) ν_{max} (cm^{-1}) 2926, 2853, 1724, 1686; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.69 (d, $^3J_{HH}$ = 7.6, Hz, 1H, CH_{ar}), 7.31 (d, $^3J_{HH}$ = 7.6, 1H, CH_{ar}), 7.19 (m, 1H, CH_{ar}), 7.13 (m, 1H, CH_{ar}), 4.67 (m, 1H, CHN), 4.16–3.99 (m, 2H, CH_2O), 2.76 (m, 1H, CH), 2.23 (s, 3H, CH_3), 2.00–1.60 (m, 10H, 5×CH_2), 1.53 (m, 1H, CH_2), 1.44 (m, 1H, CH_2), 1.15 (dd seen as t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3);^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 171.7 (C=O), 156.6 (C=O), 138.7 ($C_{quat}N$), 133.6 (C_{quat}), 126.0 (CH_{ar}), 125.7 (CH_{ar}), 125.7 (CH_{ar}), 122.8 (CH_{ar}), 62.8 (CH_2O), 59.5 (CHN), 35.3 (CH), 33.7 (CH_2), 31.0 (CH_2), 29.6 (CH_2), 27.5 (CH_2), 26.9 (CH_2), 24.3 (CH_2), 21.0 (CH_3), 14.3 (CH_3); HRMS (ESI-TOF) *m/z* calcd. for $C_{19}H_{26}N_2O_3$ $[M+H]^{+\cdot}$ 331.2022, found 331.2007.

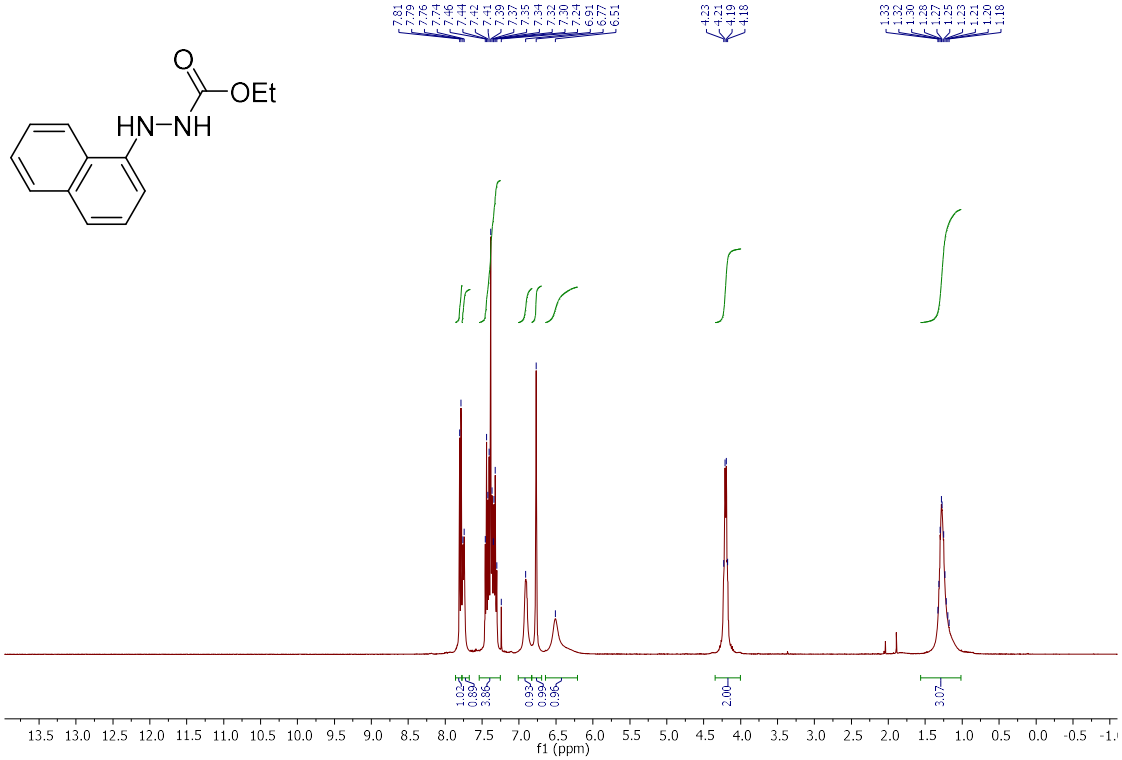


3a **8**

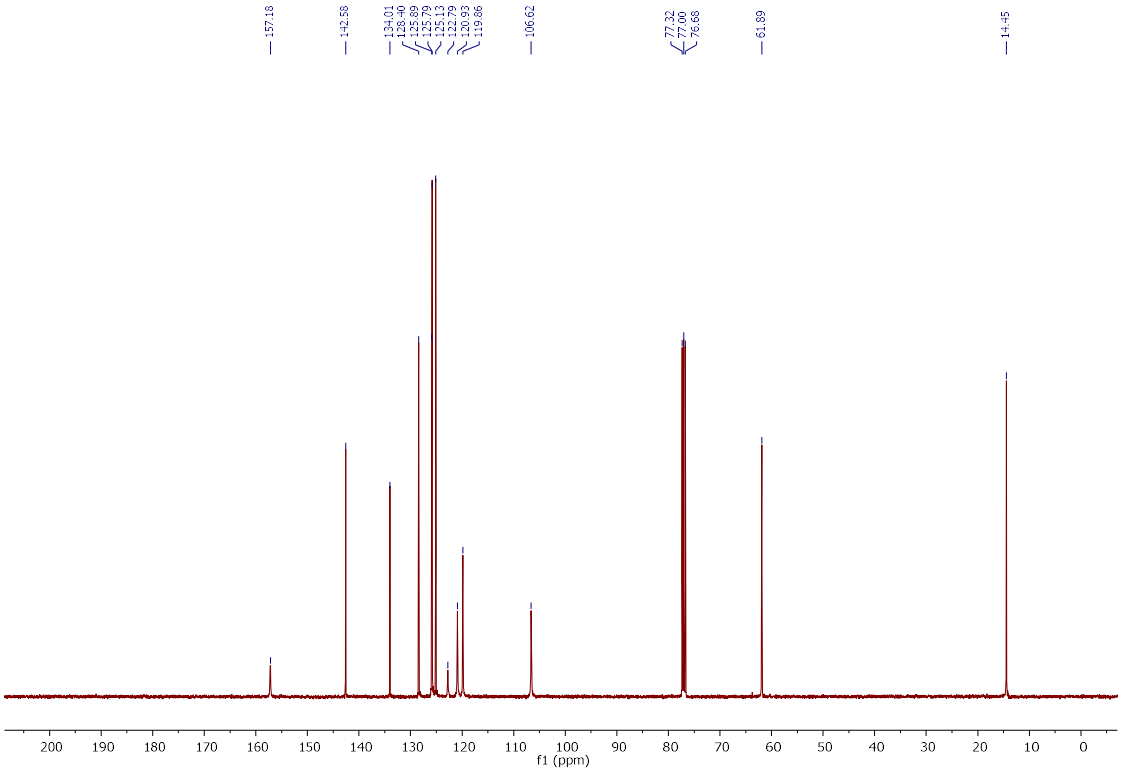
Synthesis of 2-bromo-7,8,9,10,11,12-hexahydrocycloocta[*c*]cinnoline (8): To a stirred solution of **3a** (58 mg, 0.2 mmol, 1 equiv.) and pyridine (69 µL, 0.84 mmol, 4.2 equiv.) in acetonitrile (6 mL), *N*-bromosuccinimide (NBS, 149 mg, 0.82 mmol, 4.1 equiv.) was added portion-wise under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 1 h, then washed with aqueous HCl (1.5 M, 4 mL), Na_2SO_3 (1.5%, 2 mL), saturated aqueous $NaHCO_3$ (4 mL), and brine (4 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated to dryness under vacuum. The crude product was purified by flash-column chromatography (SiO_2, hexanes/AcOEt 98:2) to give **9** (25 mg, 43%) as a yellow solid. Mp: 167–169 ºC; FTIR (neat) ν_{max} (cm^{-1}) 2920, 2844, 1730, 1603, 1467, 837; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.32 (d, $^3J_{HH}$ = 9.0 Hz, 1H, CH_{ar}), 8.15 (d, $^4J_{HH}$ = 2.0 Hz, 1H, CH_{ar}), 7.77 (dd, $^3J_{HH}$ = 9.0 Hz, $^4J_{HH}$ = 2.0 Hz, 1H, CH_{ar}), 3.42 (t, $^3J_{HH}$ = 6.1 Hz, 2H, CH_2), 3.17 (t, $^3J_{HH}$ = 6.4 Hz, 2H, CH_2), 1.93 (m, 2H, CH_2), 1.85 (m, 2H, CH_2), 1.47 (m, 2H, CH_2), 1.27 (m, 2H, CH_2); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ (ppm): 157.9 ($C_{quat}N$), 147.7 ($C_{quat}N$), 132.6 (CH_{ar}), 132.3 (CH_{ar}), 131.6 (C_{quat}), 126.2 ($C_{quat}Br$), 125.6 (C_{quat}), 125.0 (CH_{ar}), 33.6 (CH_2), 31.4 (CH_2), 30.1 (CH_2), 26.5 (CH_2), 25.6 (CH_2), 25.0 (CH_2); HRMS (ESI-TOF) *m/z* calcd. for $C_{14}H_{15}BrN_2$ $[M+H]^{+\cdot}$ 291.0497, found 291.0485.

NMR spectra of all target compounds

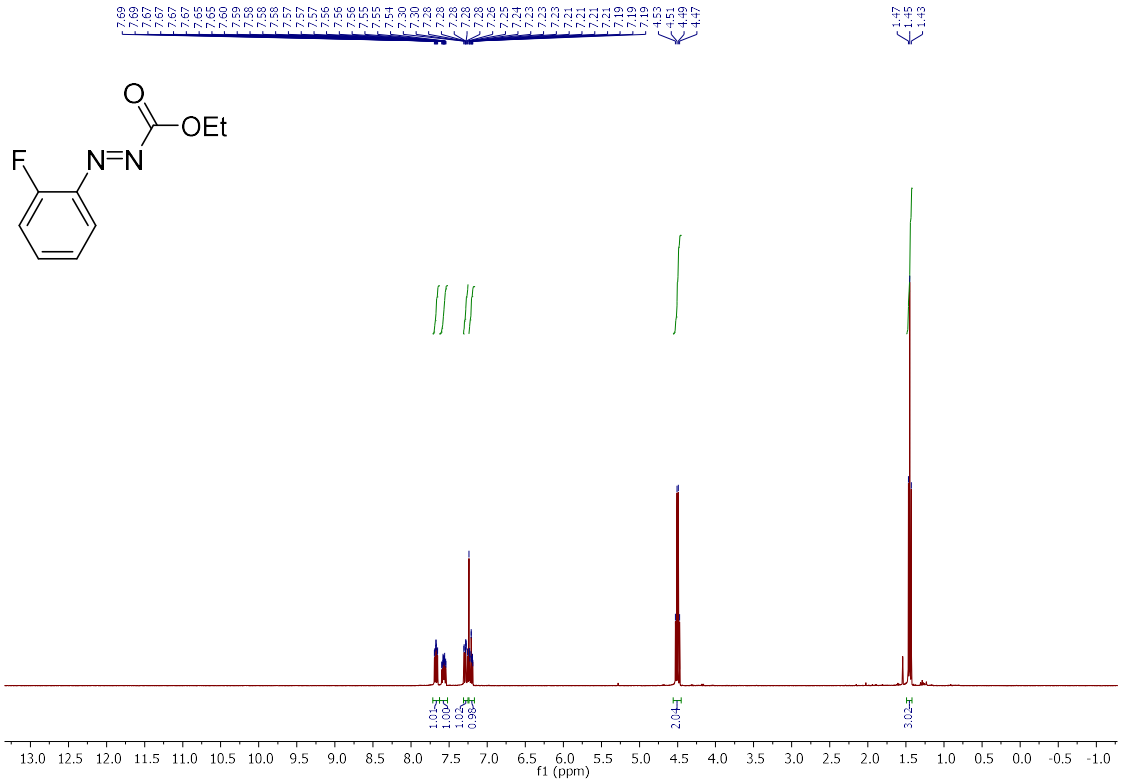
^{1}H NMR (400 MHz, $CDCl_3$) of functionalised hydrazine **1j**



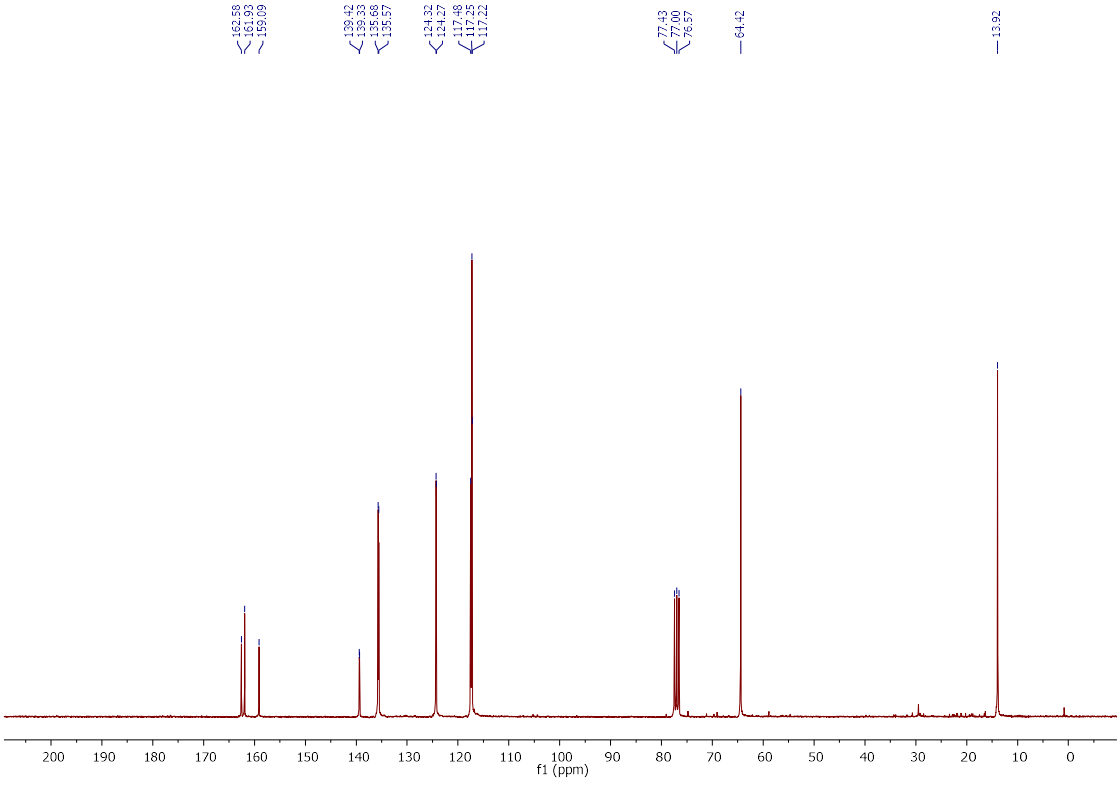
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of functionalised hydrazine **1j**



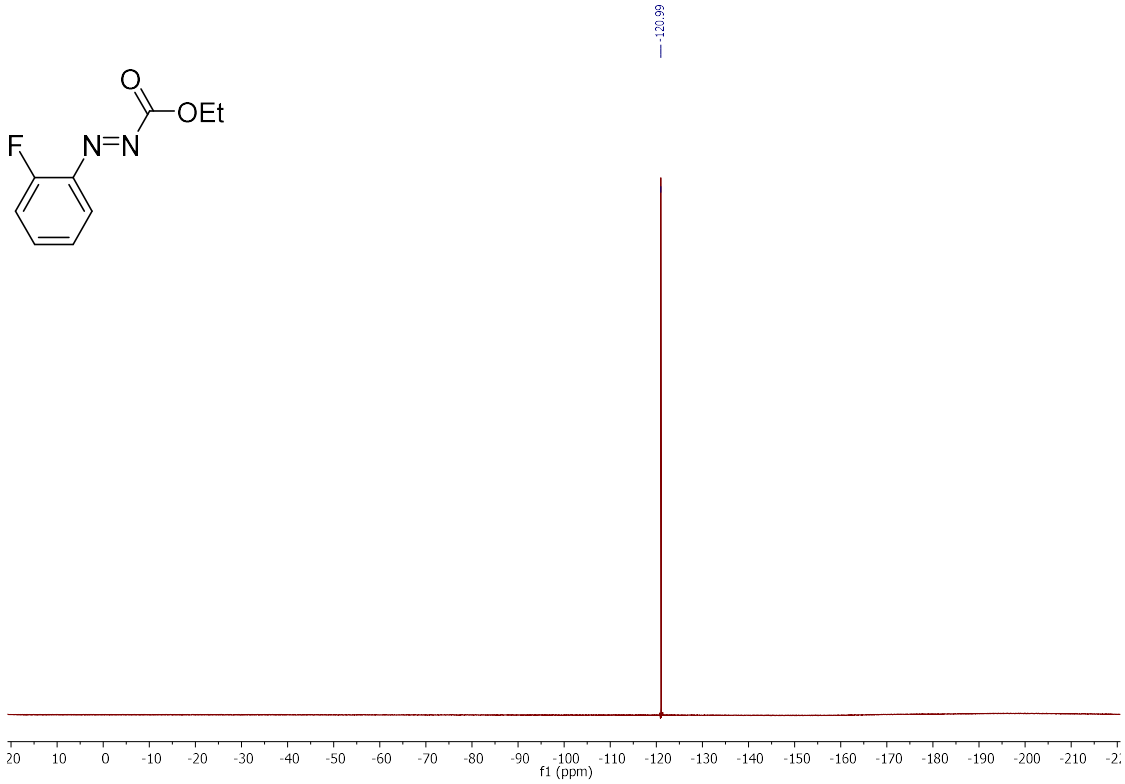
^{1}H NMR (400 MHz, $CDCl_3$) of aryldiazene carboxylate **2h**



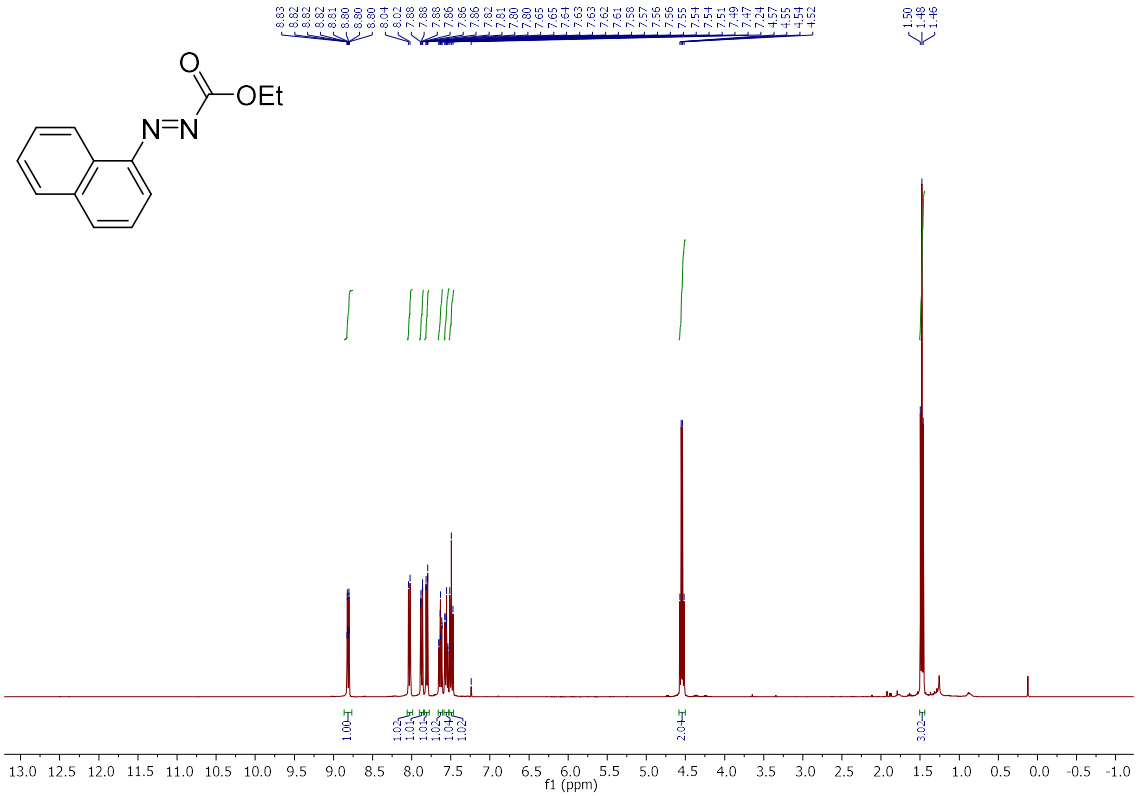
^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) of aryldiazene carboxylate **2h**



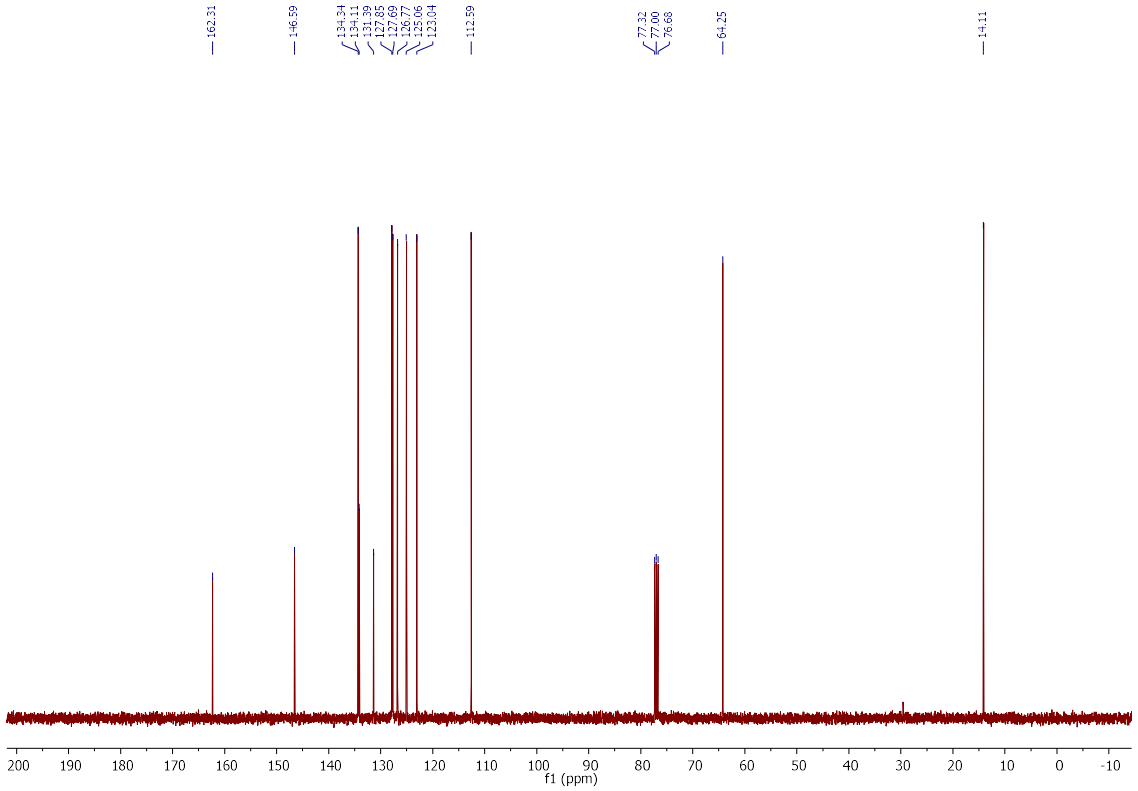
^{19}F (282 MHz, $CDCl_3$) of aryldiazene carboxylate **2h**



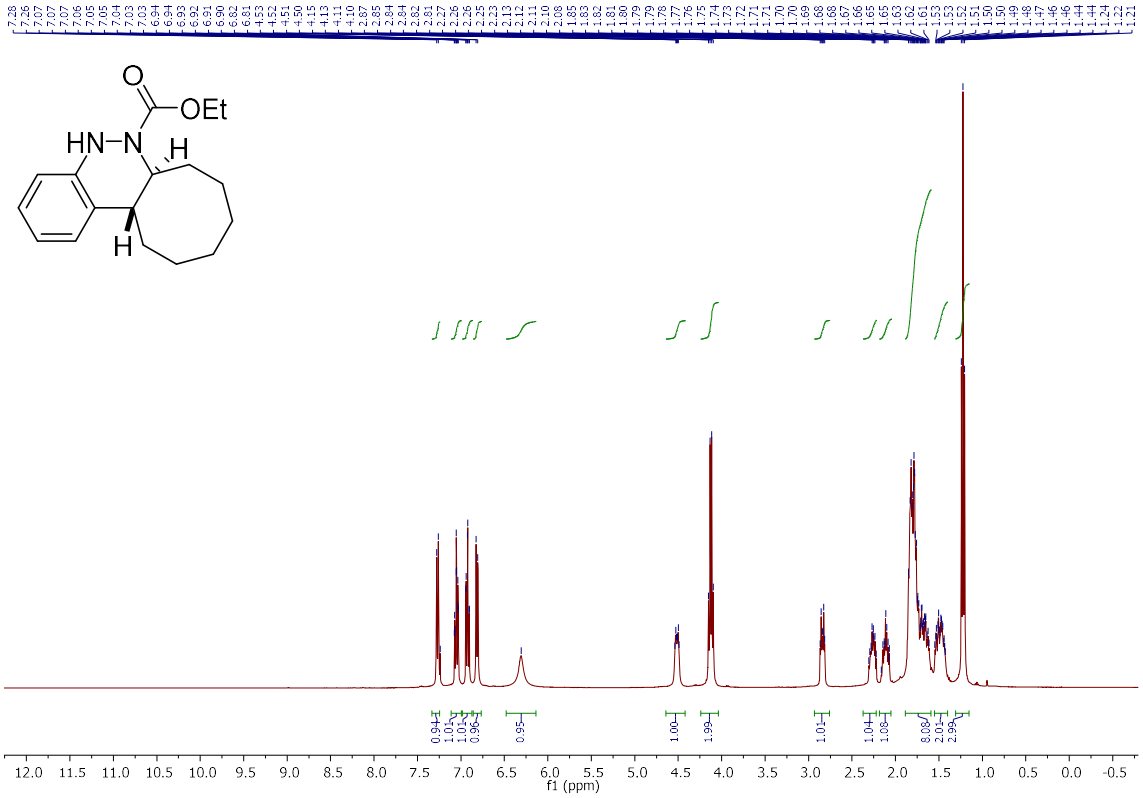
^{1}H NMR (400 MHz, $CDCl_3$) of aryldiazene carboxylate **2j**



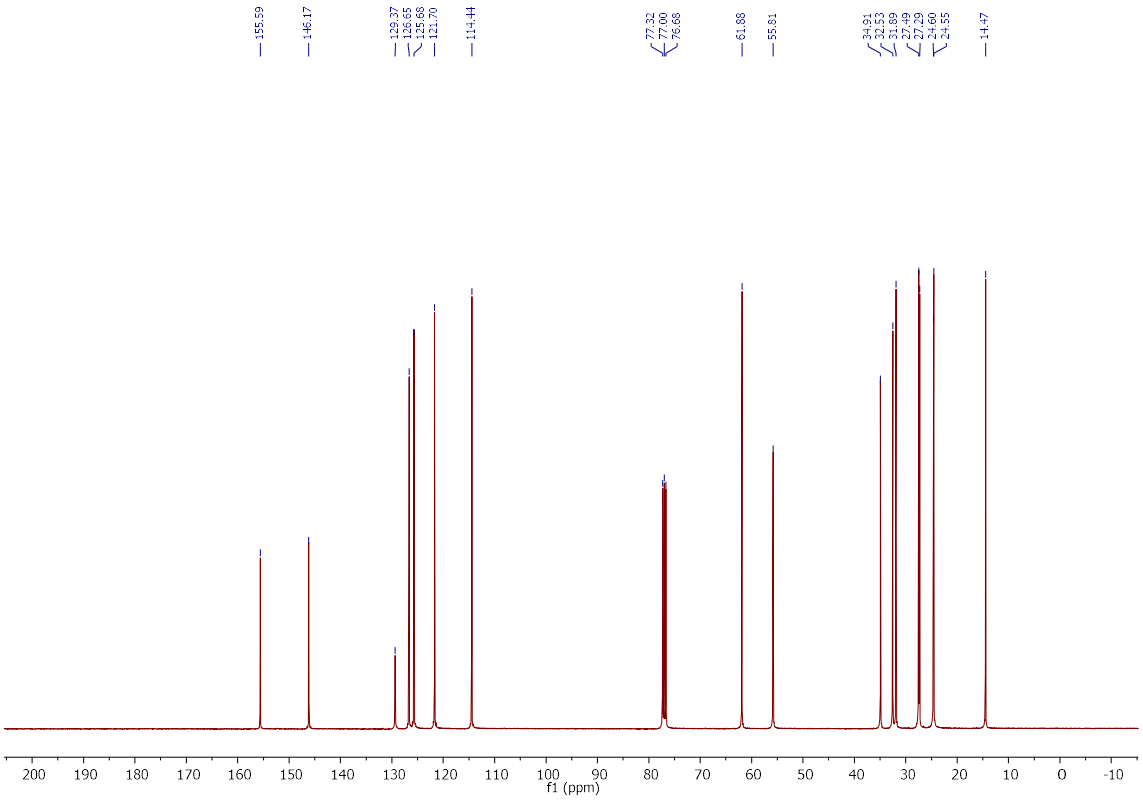
^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) of aryldiazene carboxylate **2j**



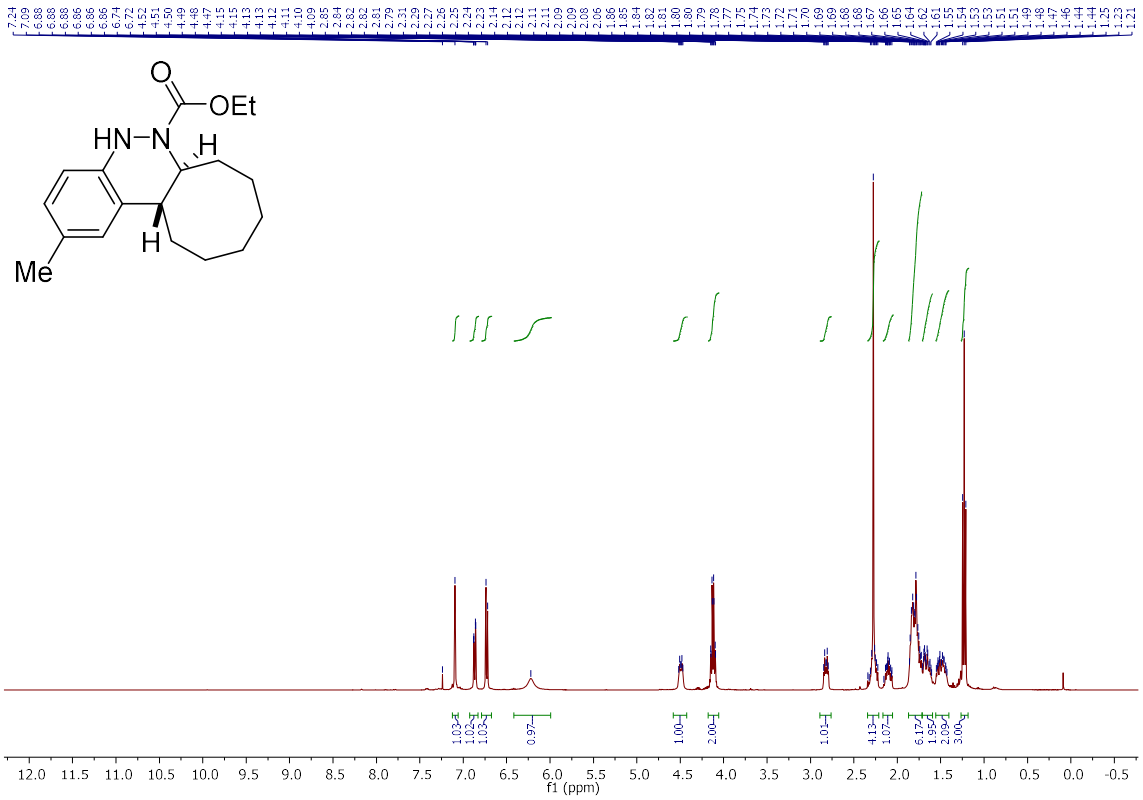
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3a**



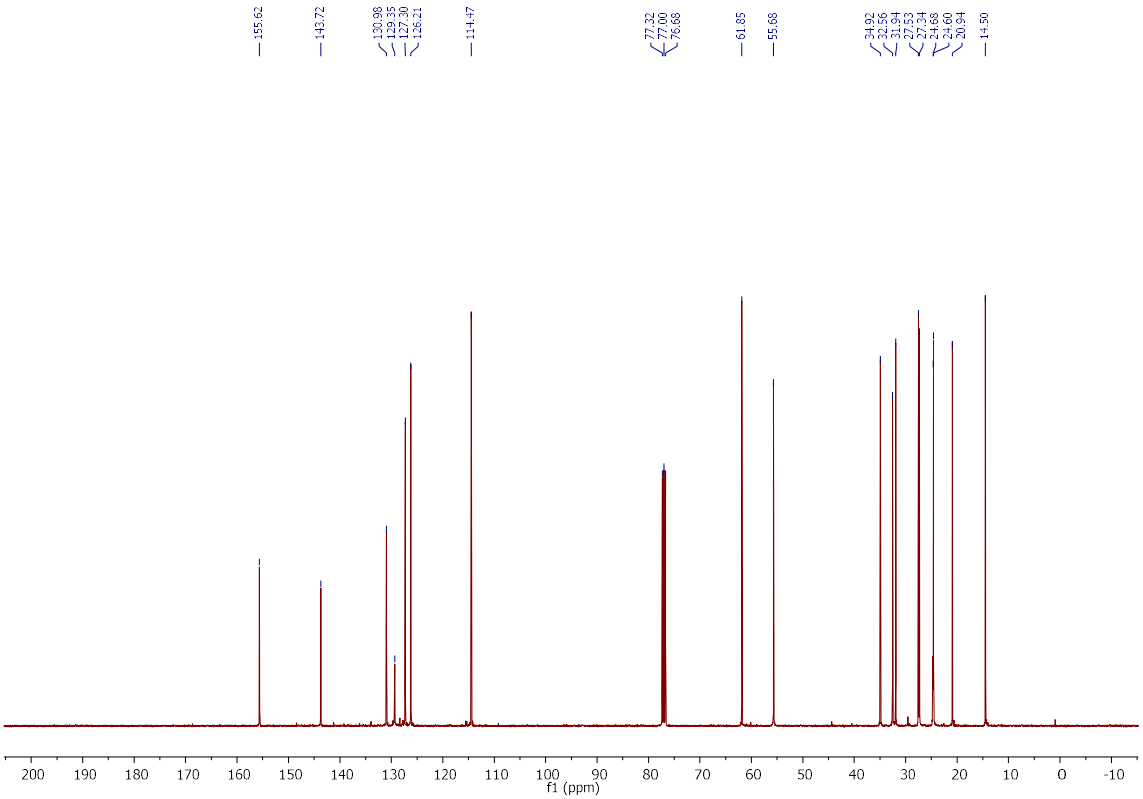
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3a**



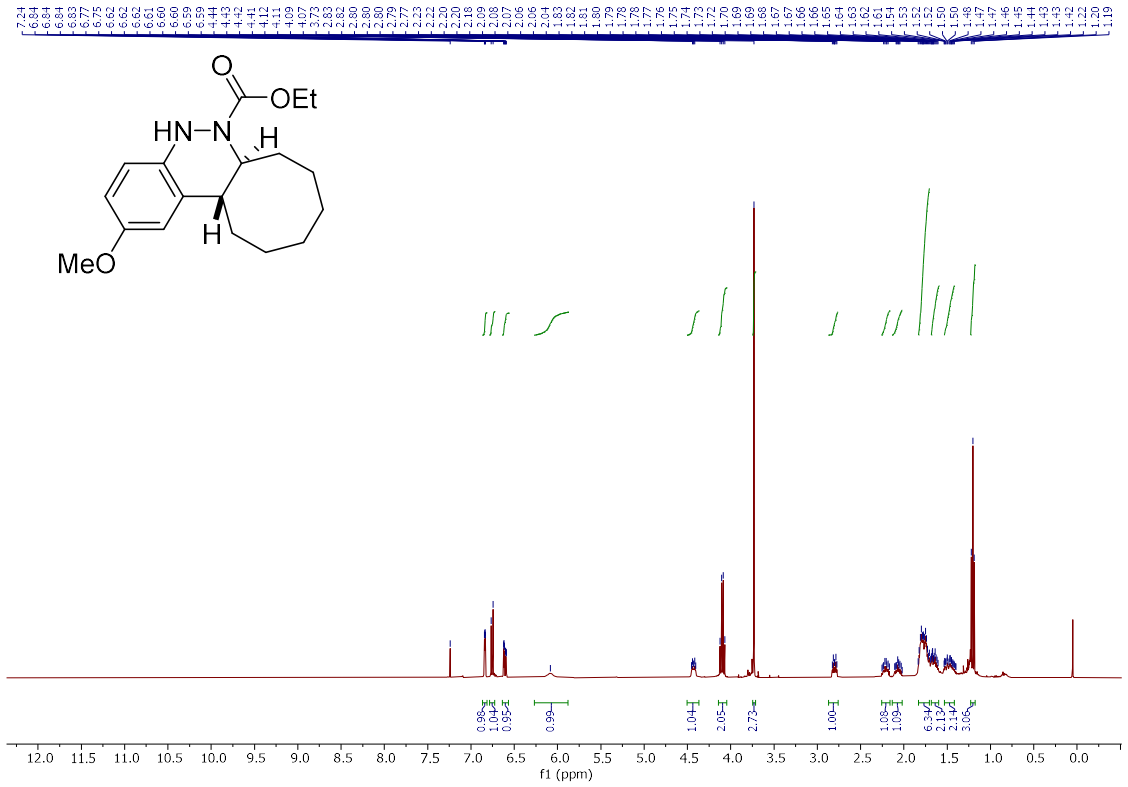
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3b**



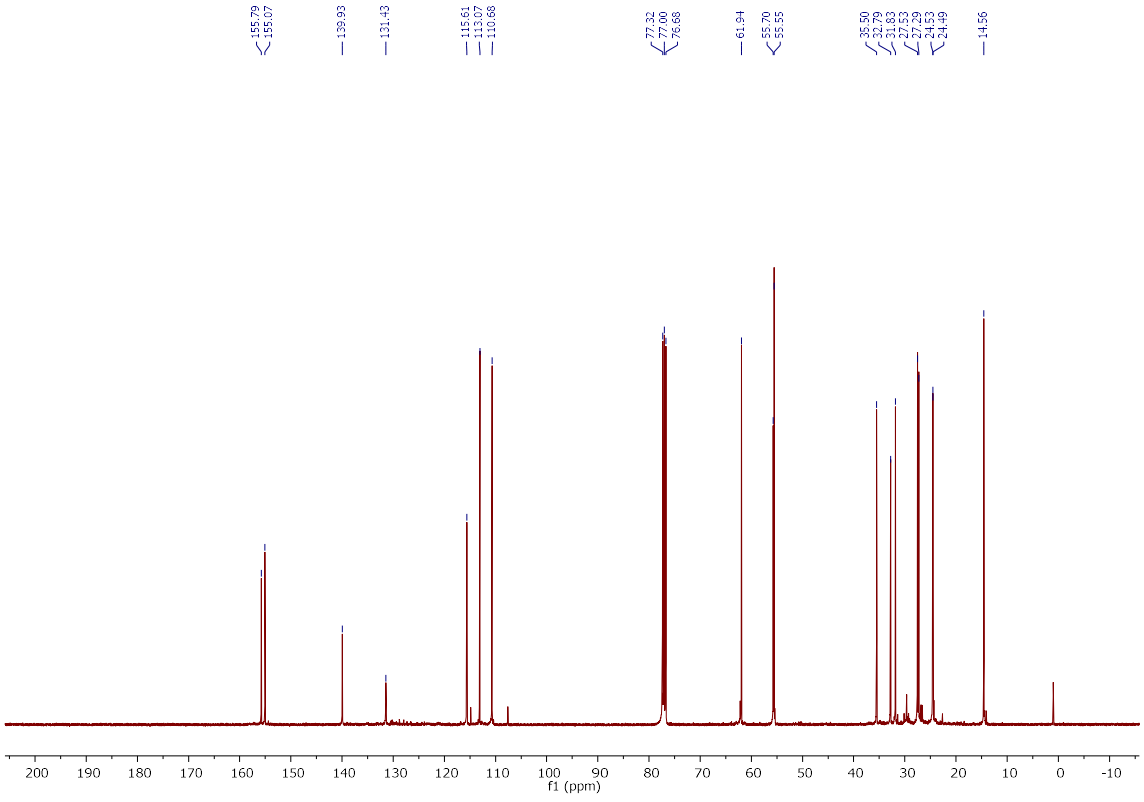
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3b**



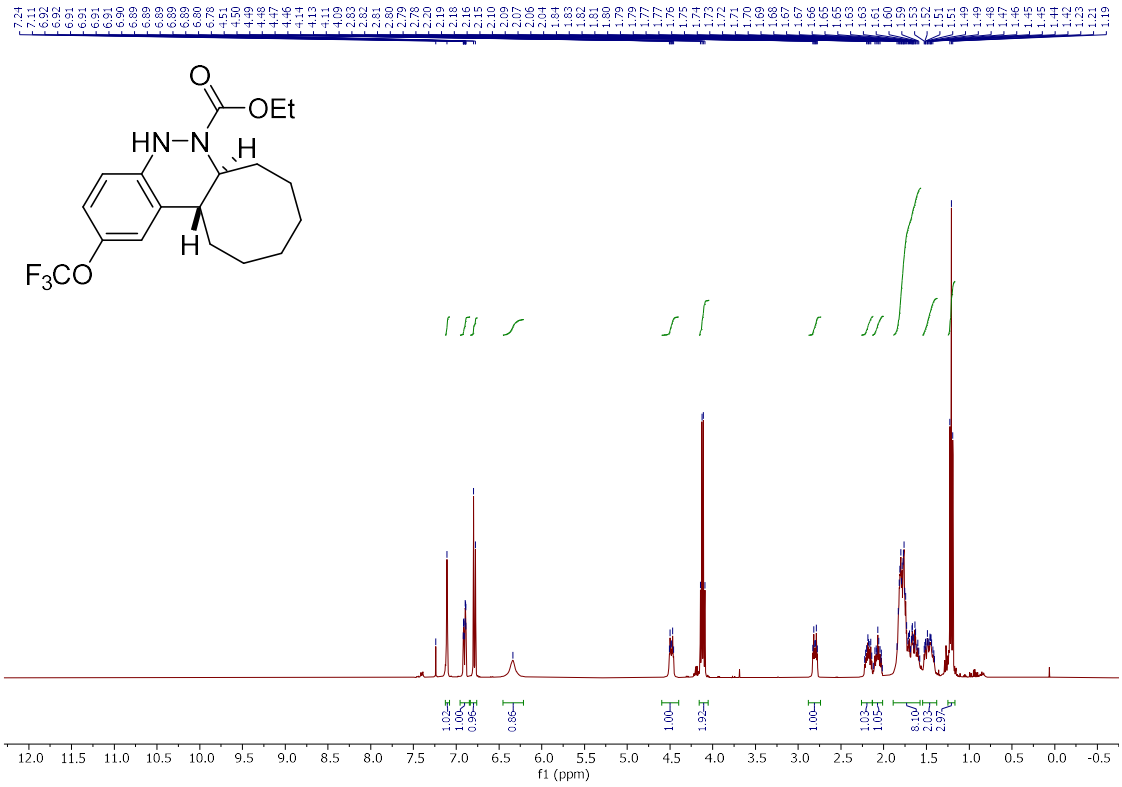
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3c**



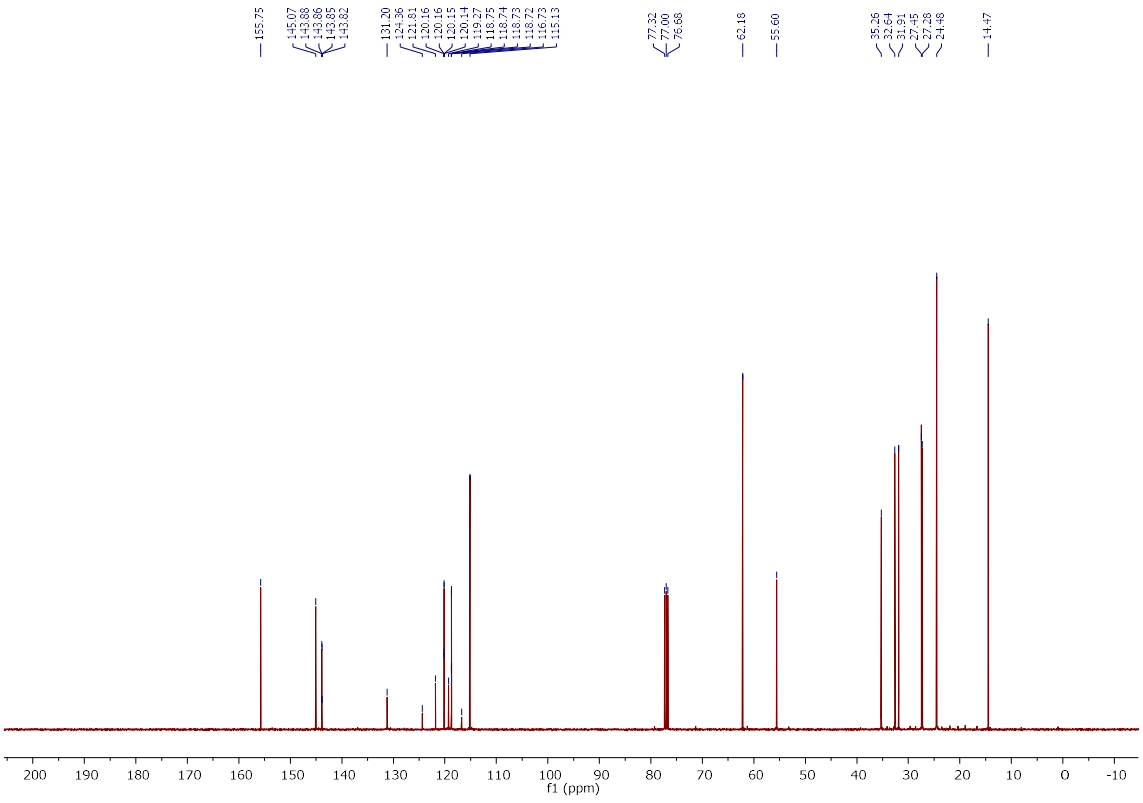
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3c**



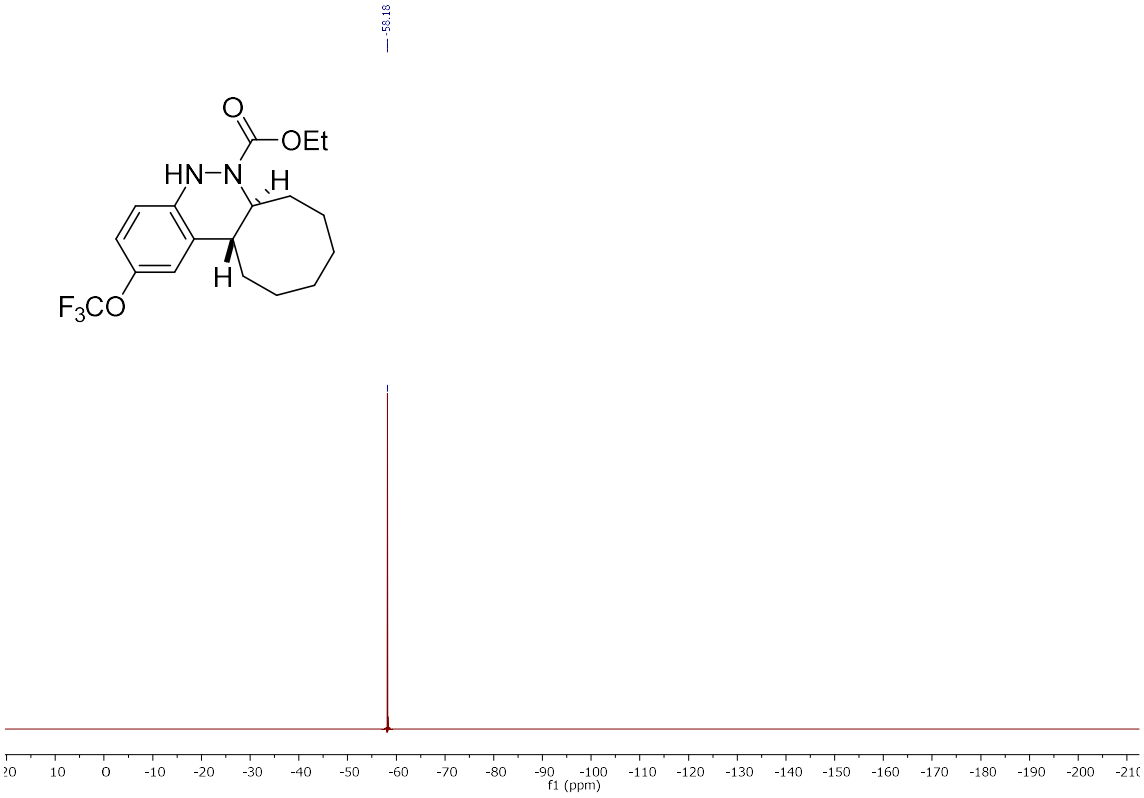
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3d**



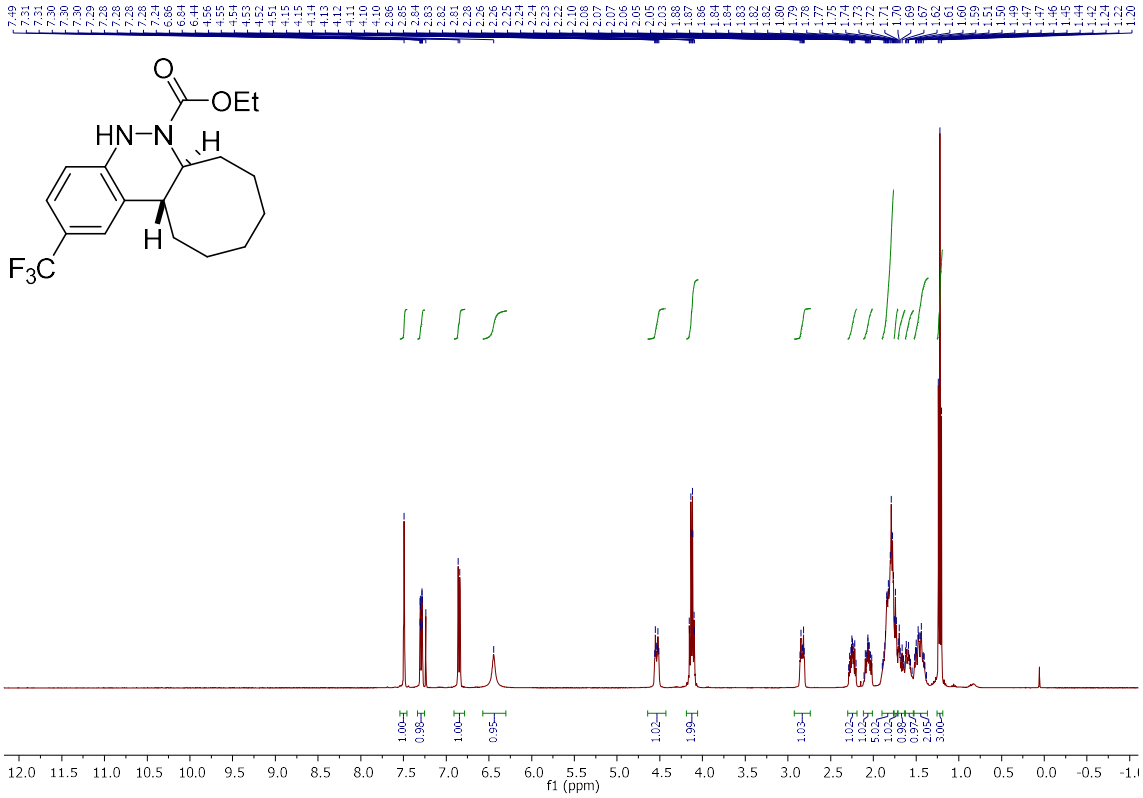
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3d**



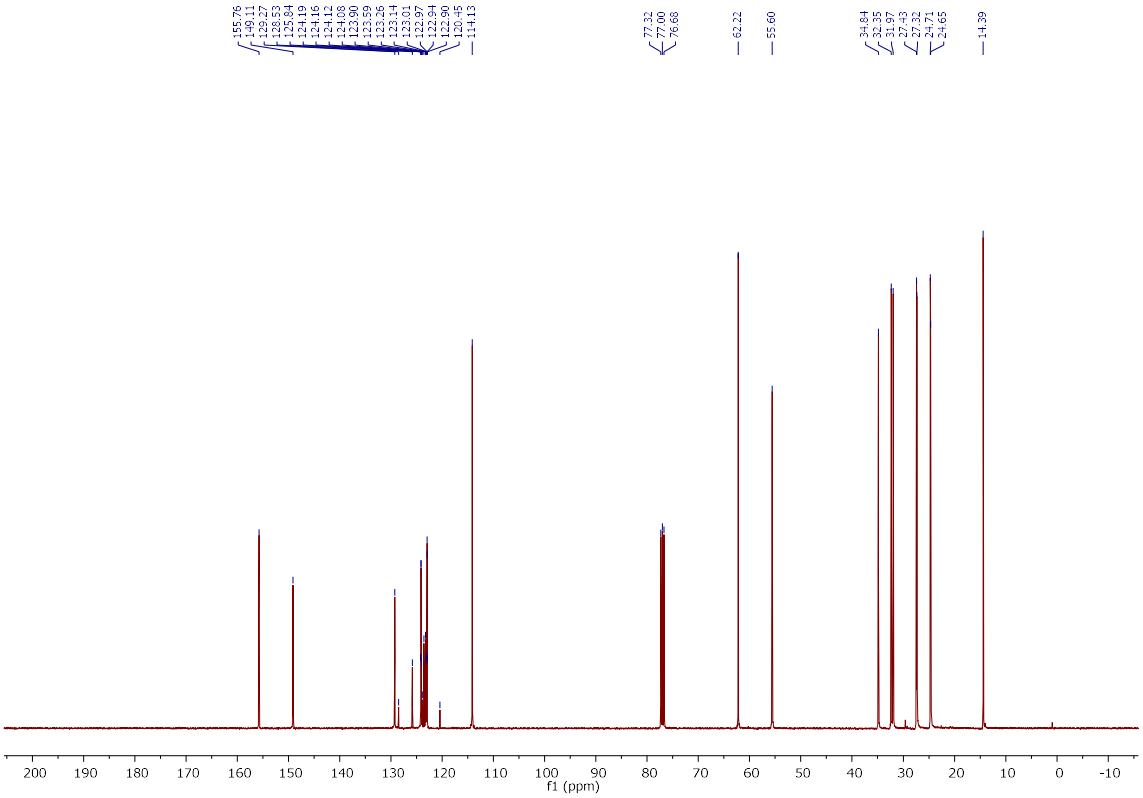
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3d**



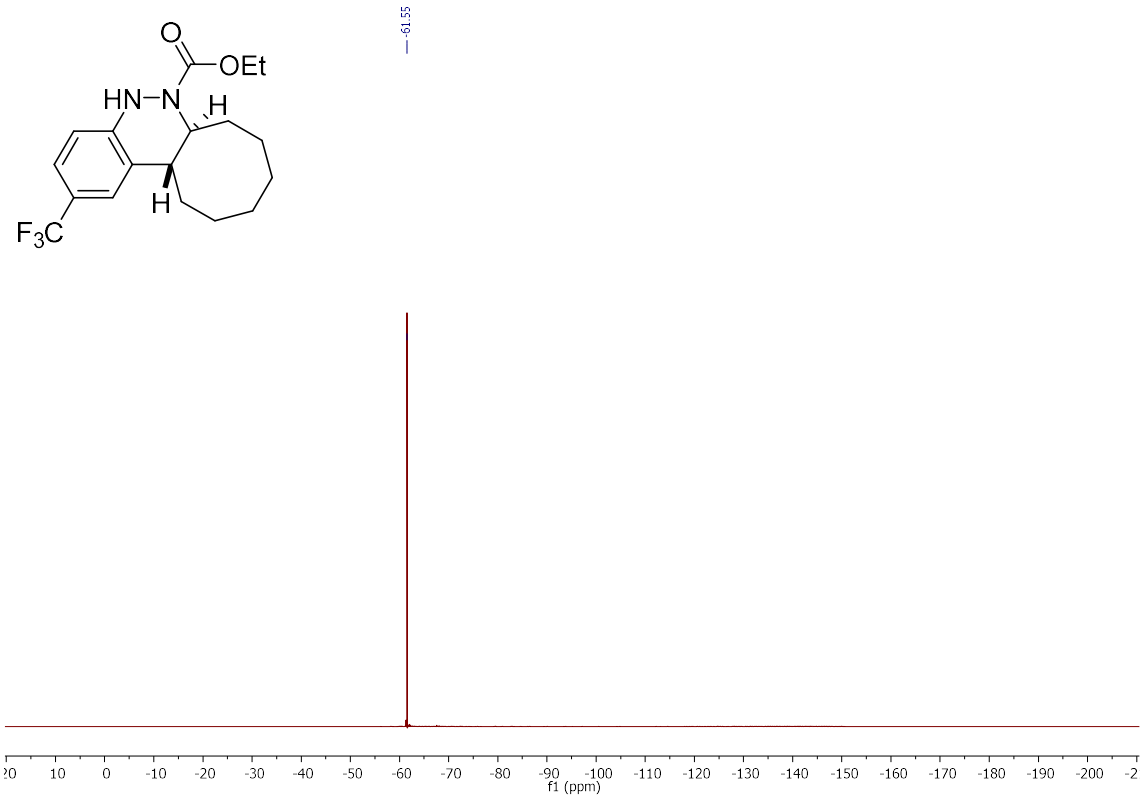
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3e**



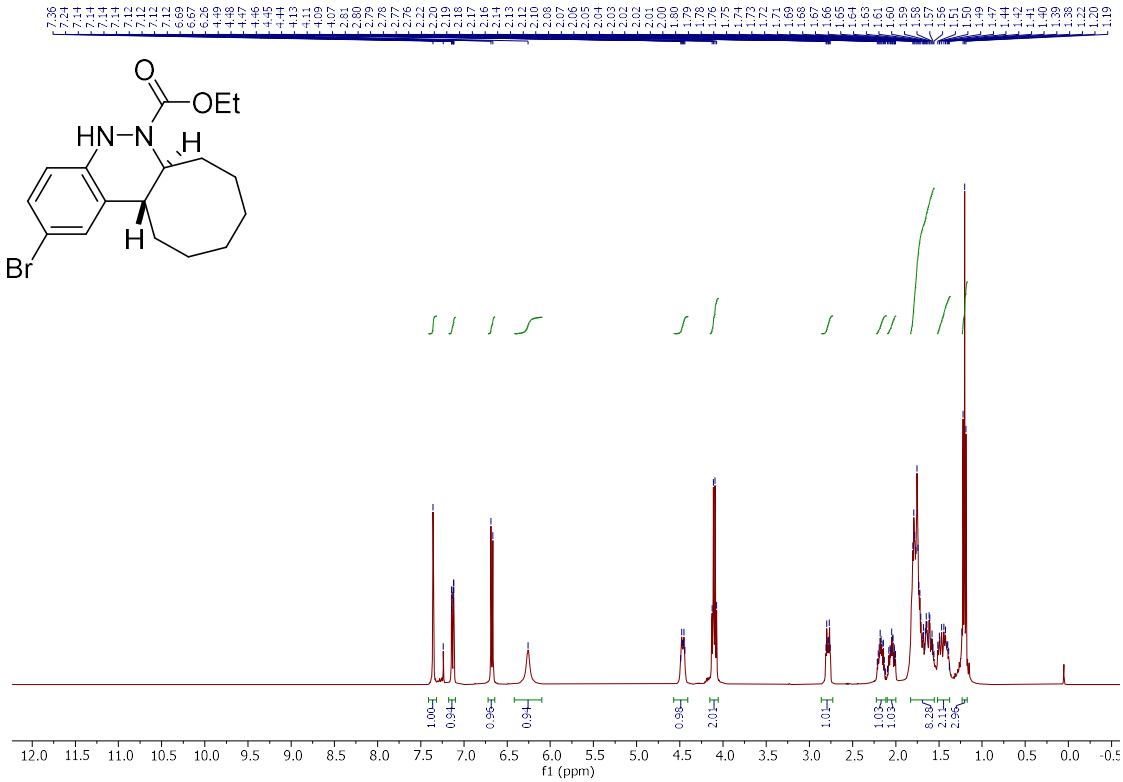
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3e**



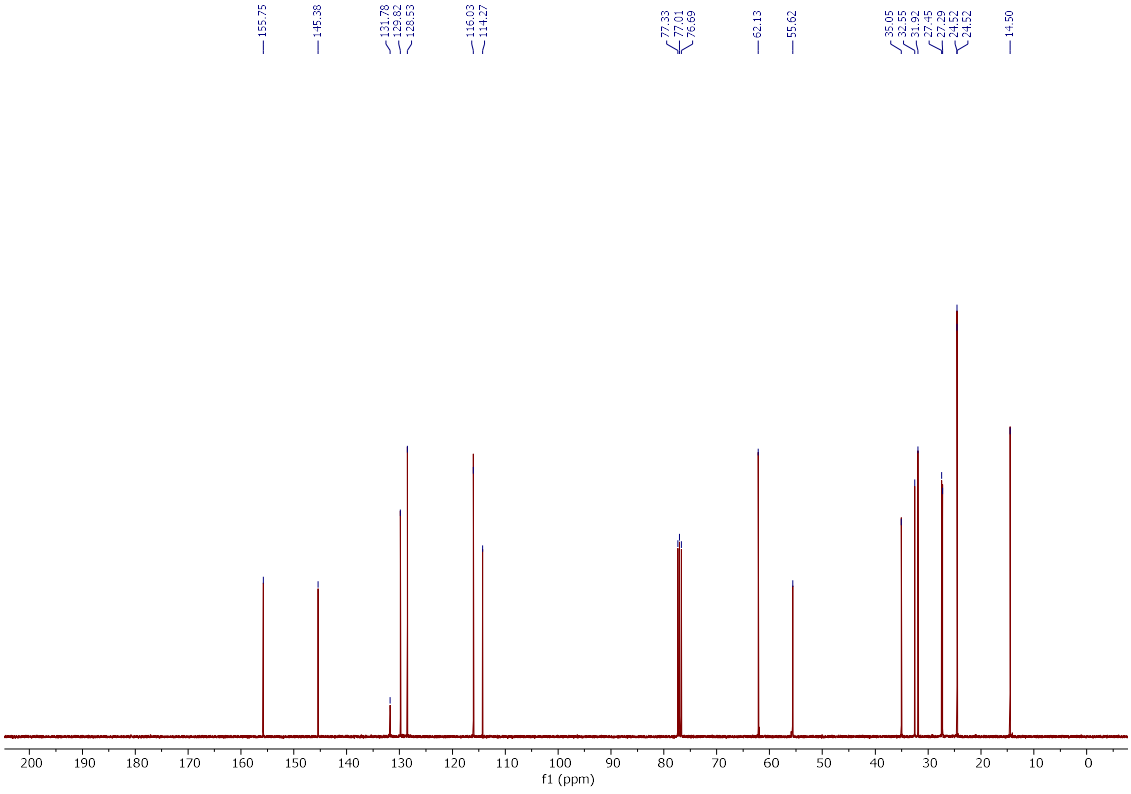
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3e**



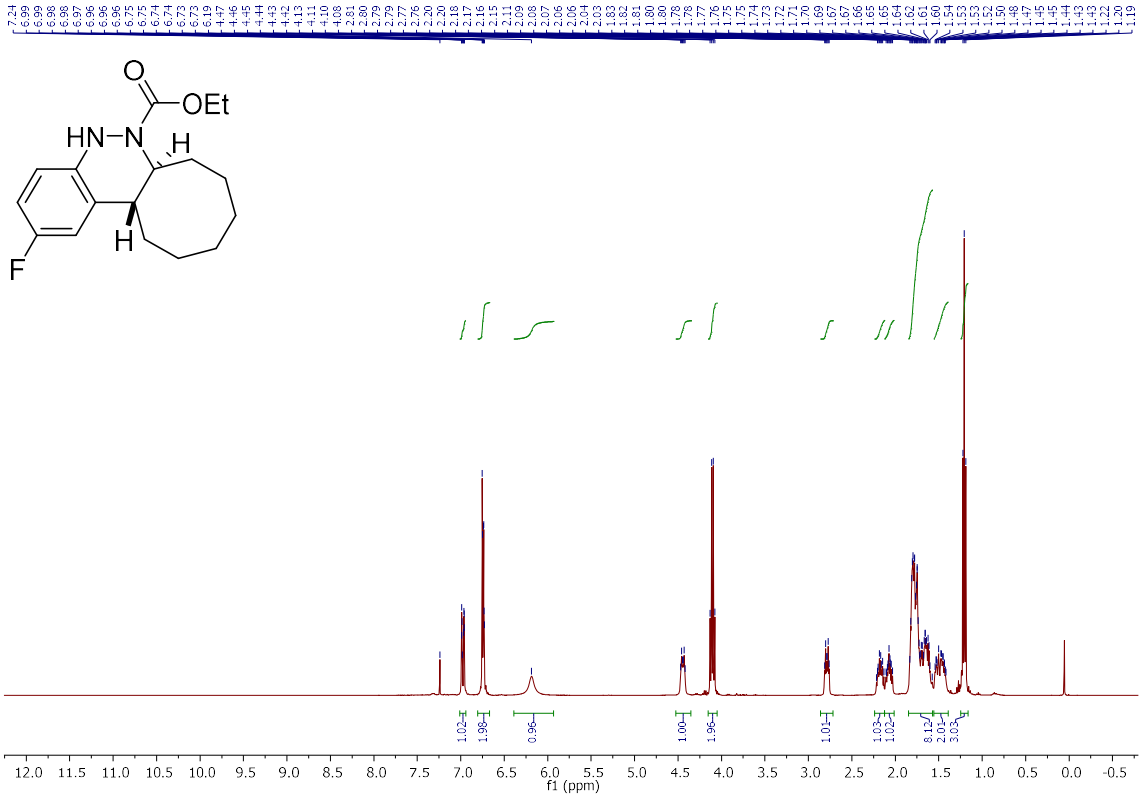
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3f**



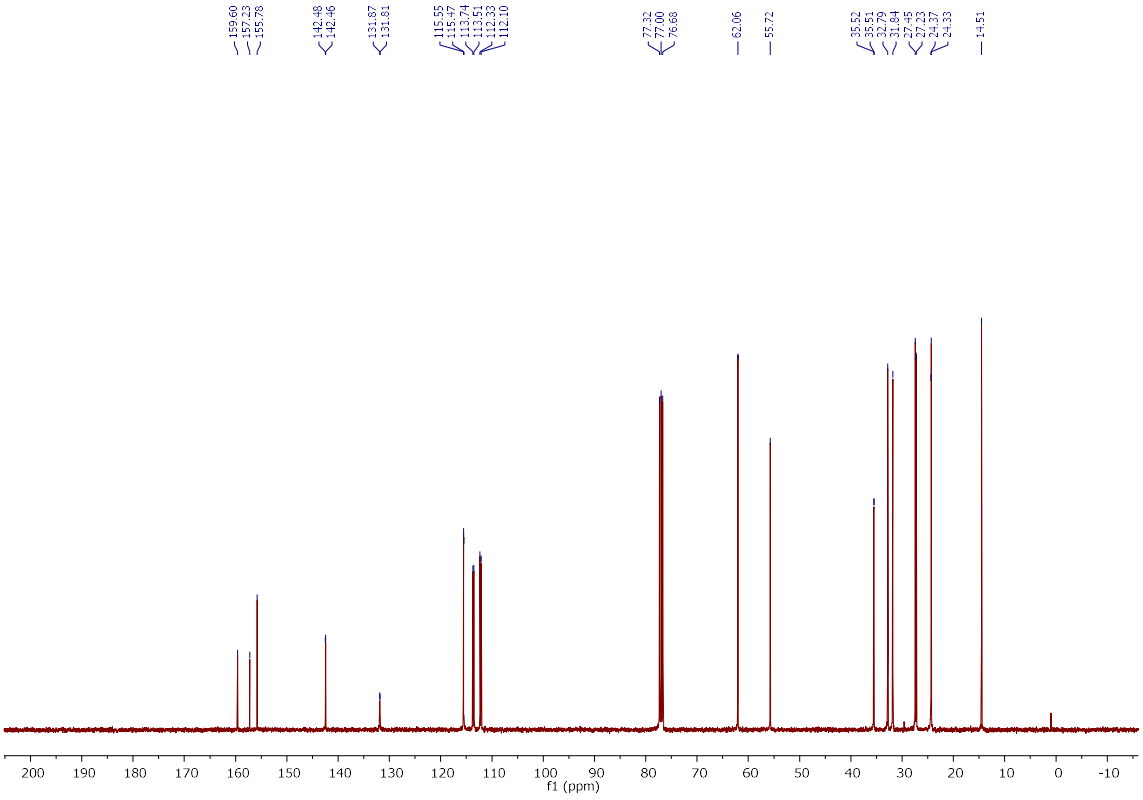
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3f**



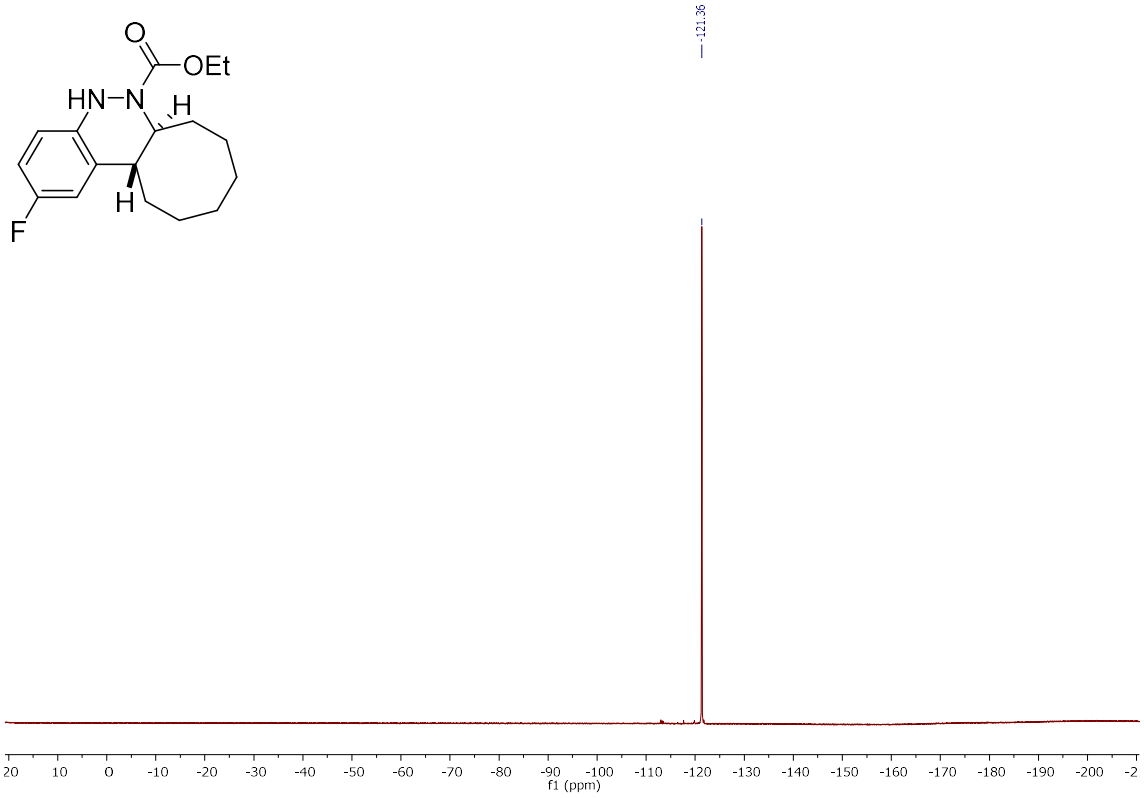
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3g**



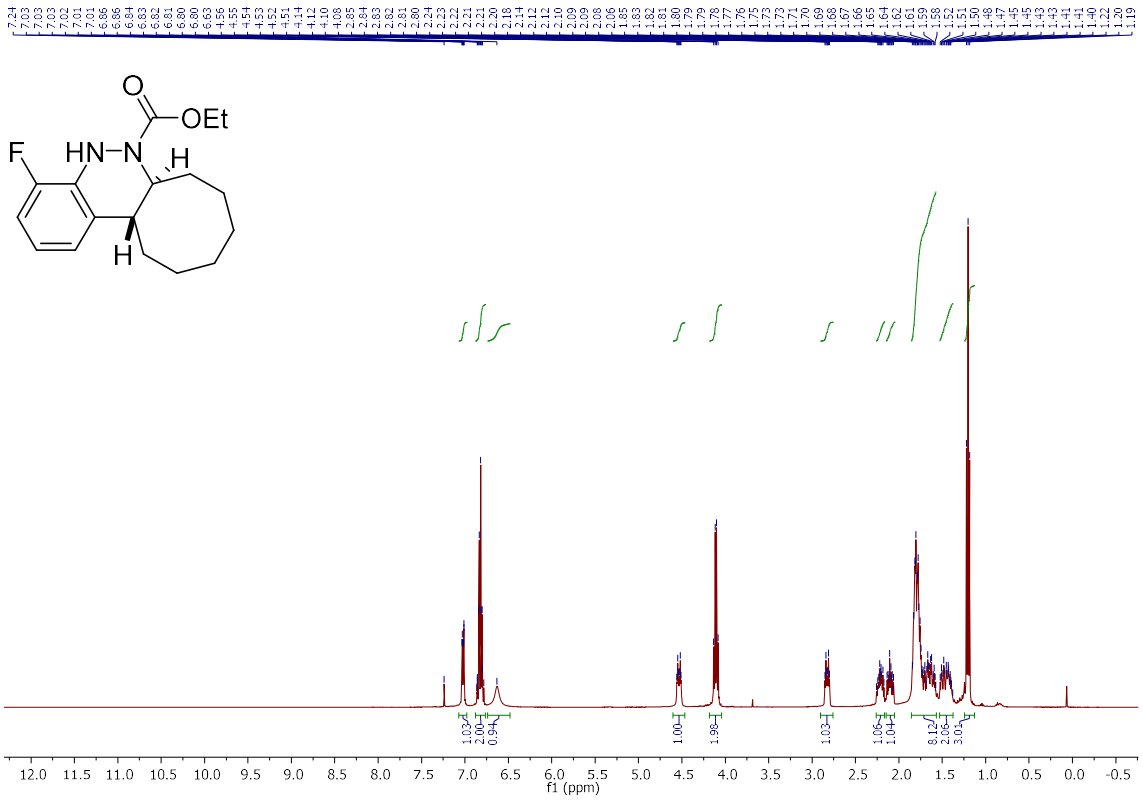
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3g**



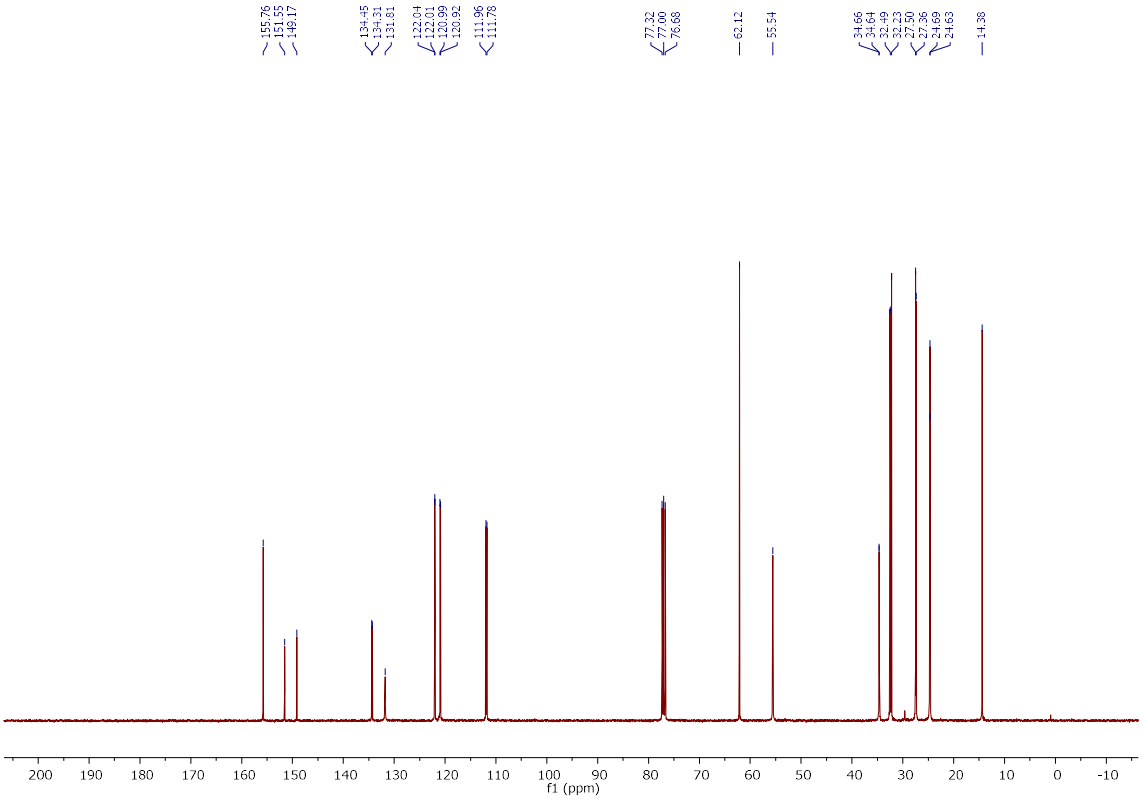
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3g**



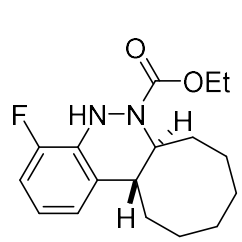
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3h**



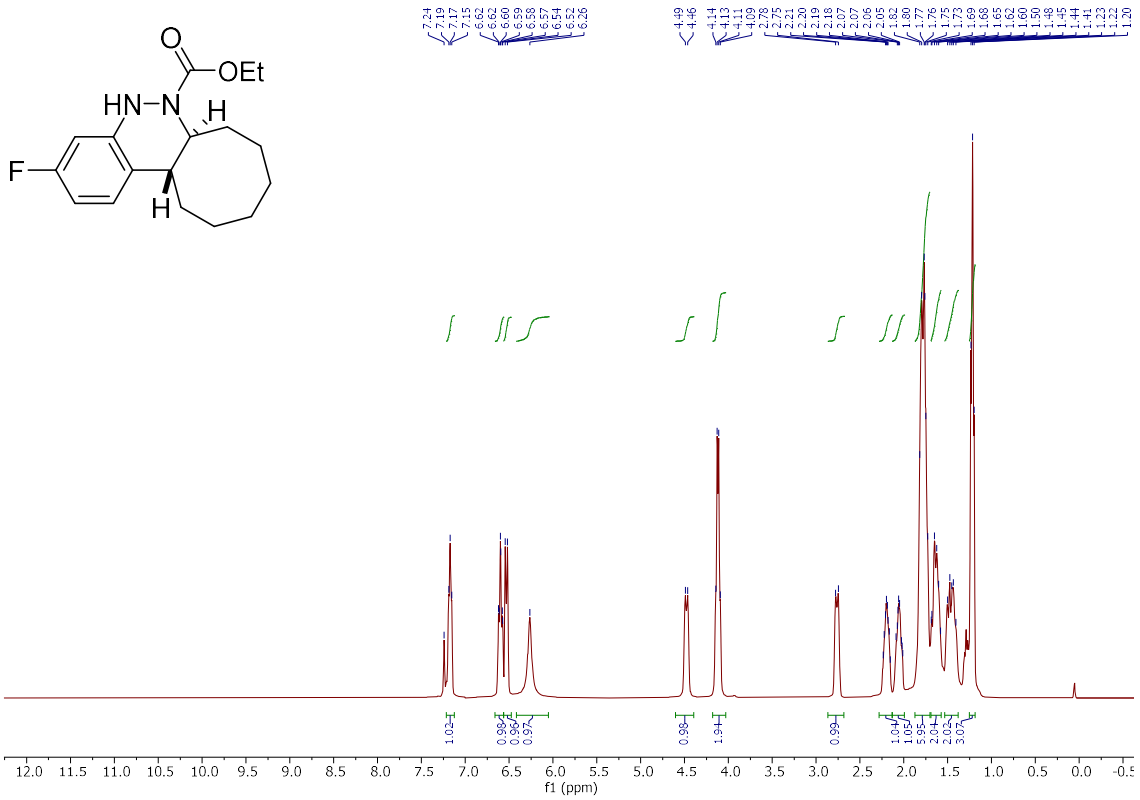
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3h**



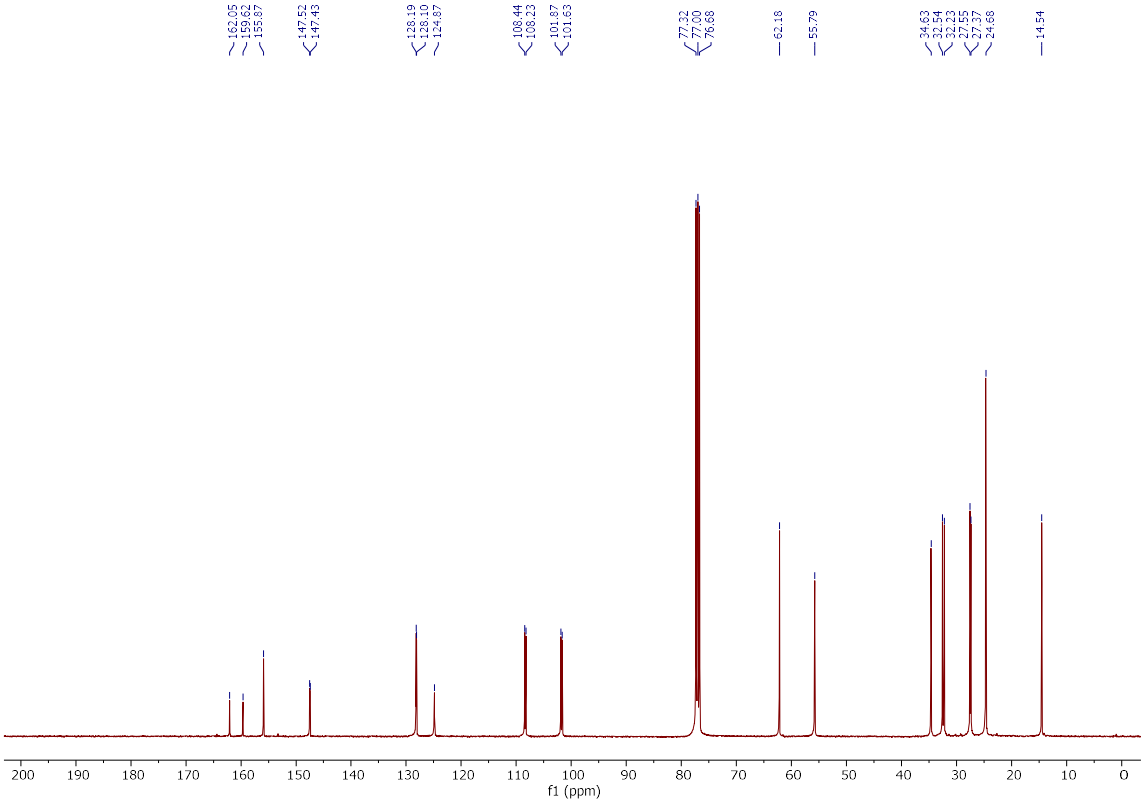
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3h**



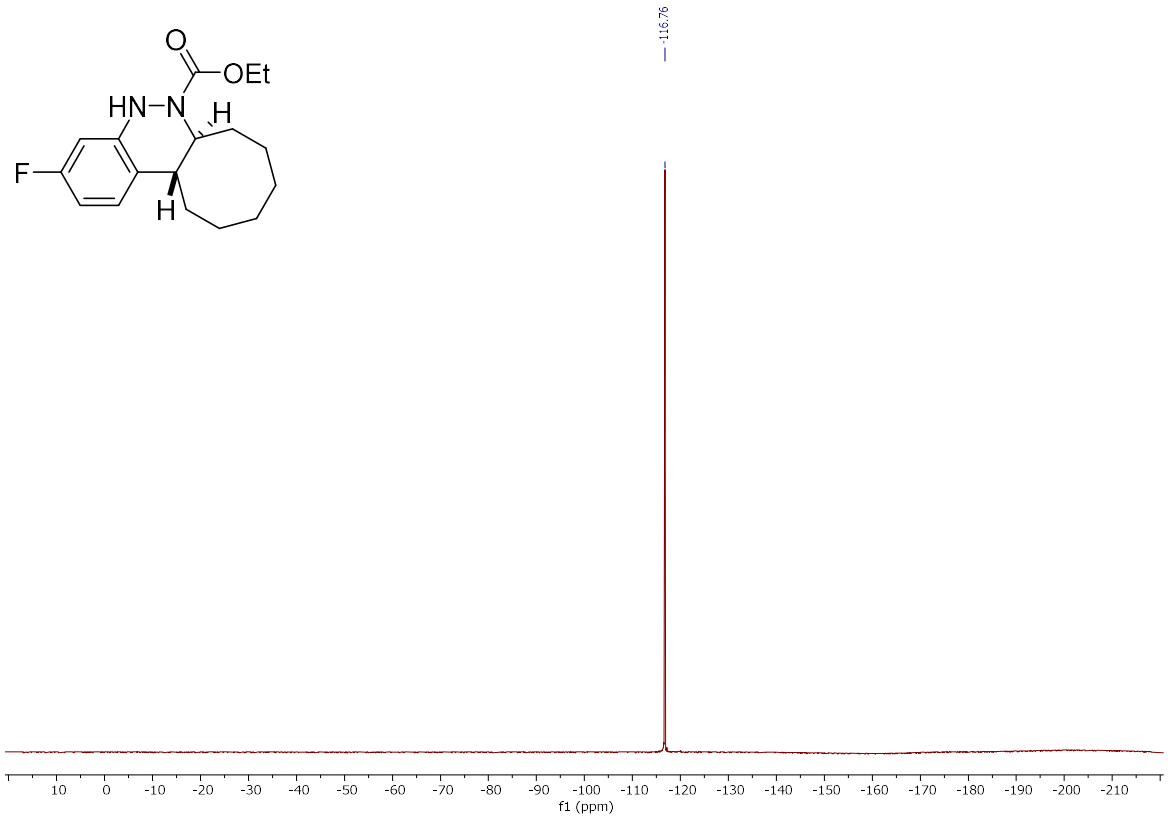
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3i$_1$**



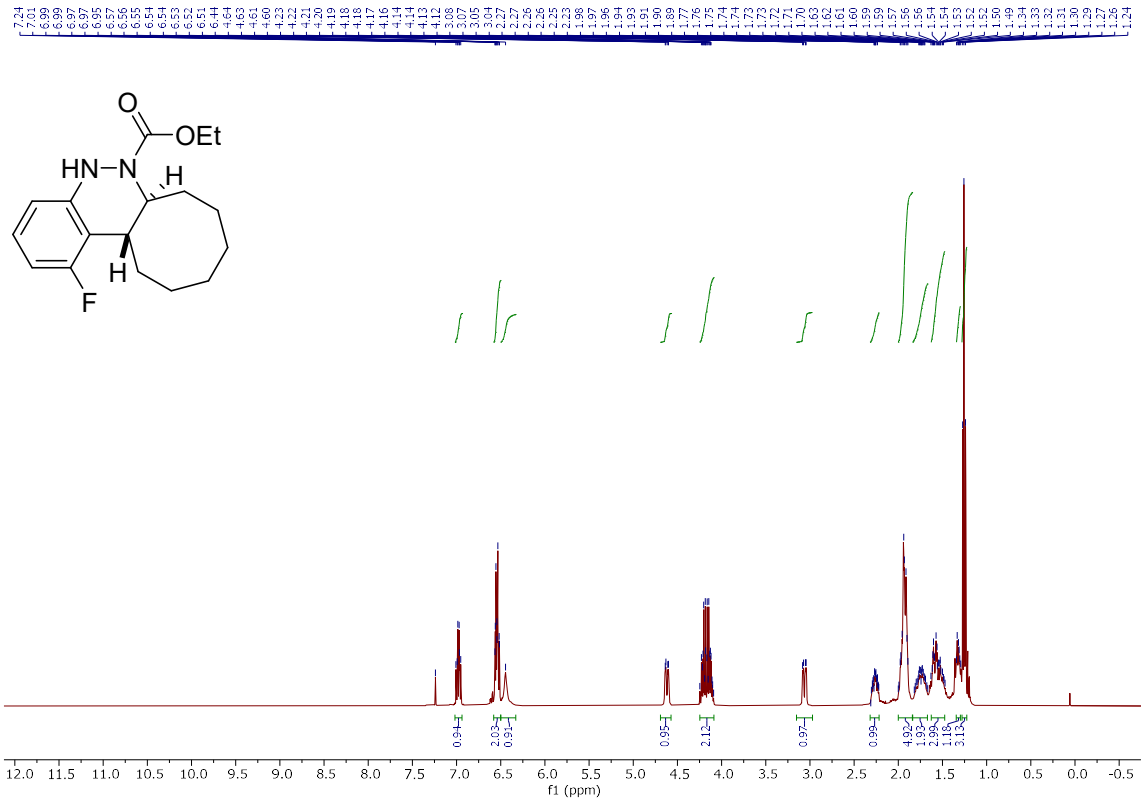
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3i$_1$**



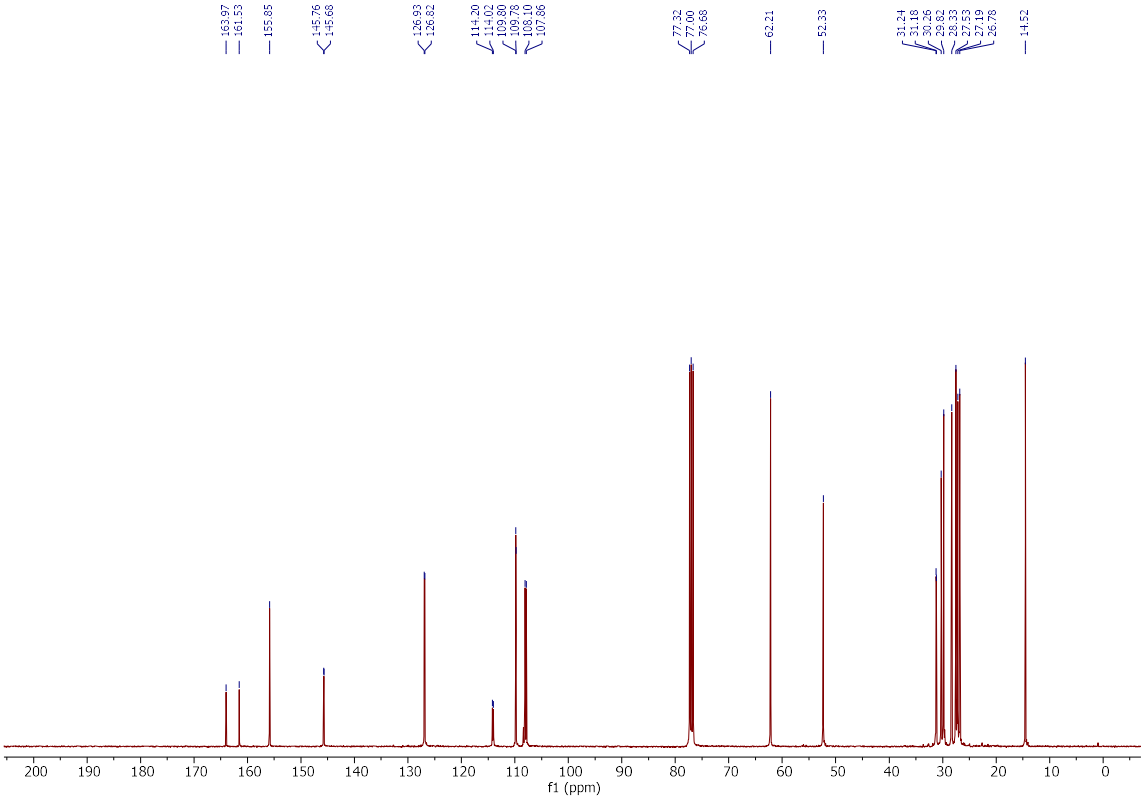
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3i$_1$**



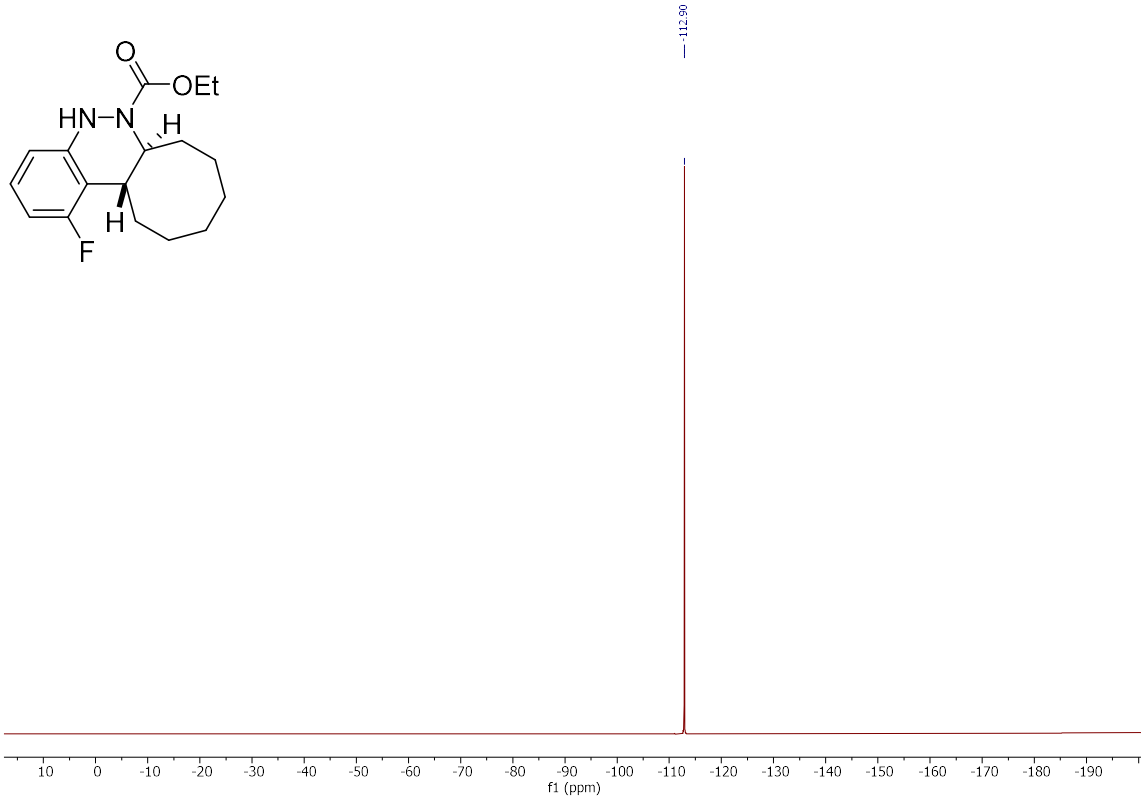
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3i2**



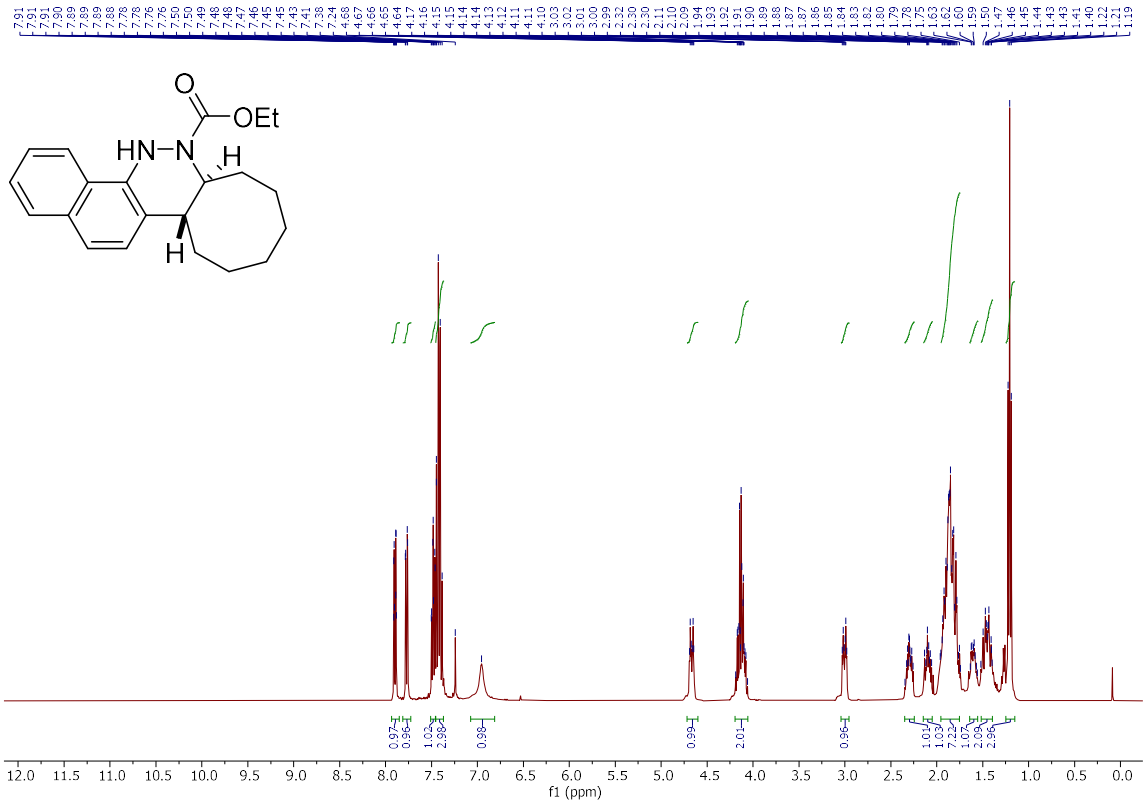
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3i2**



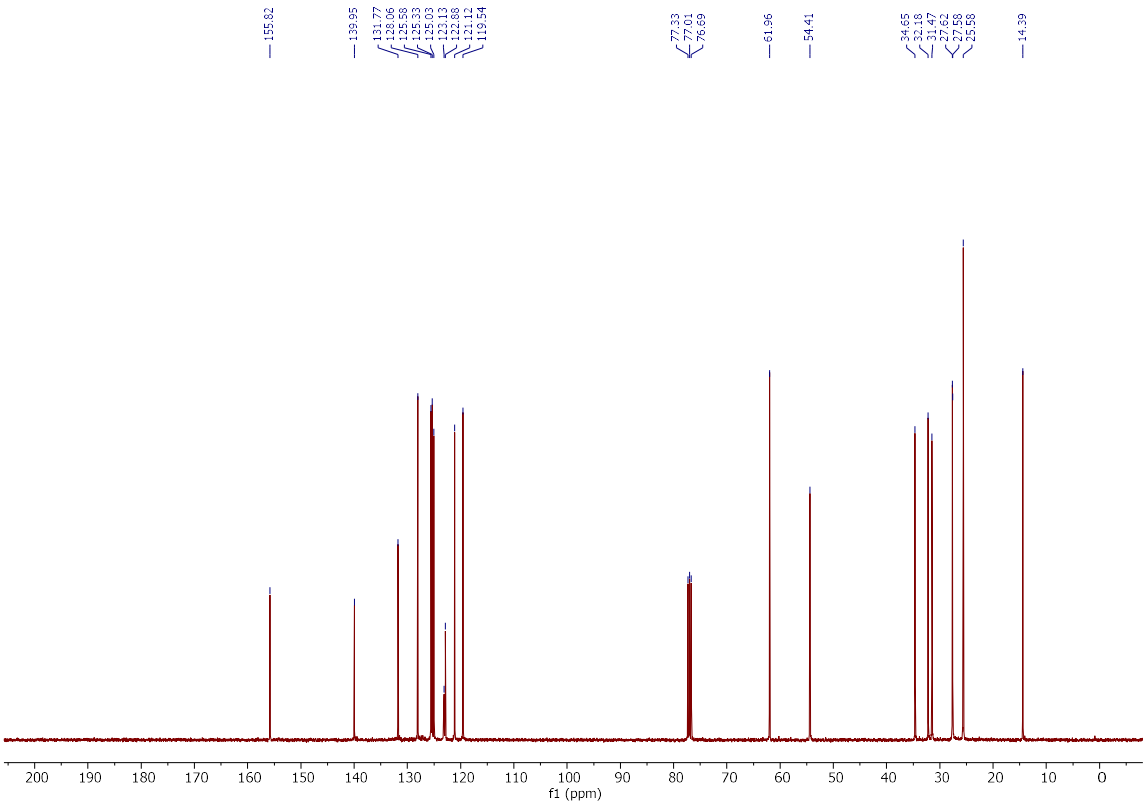
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **3i2**



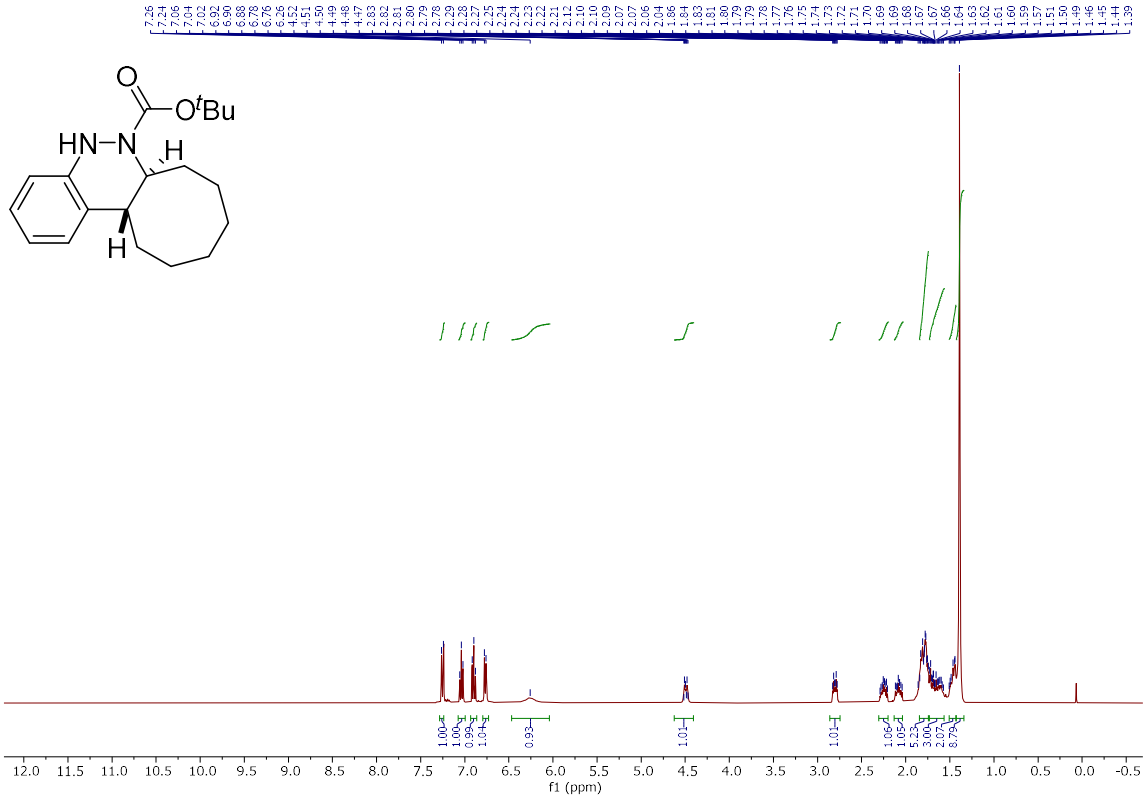
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3j**



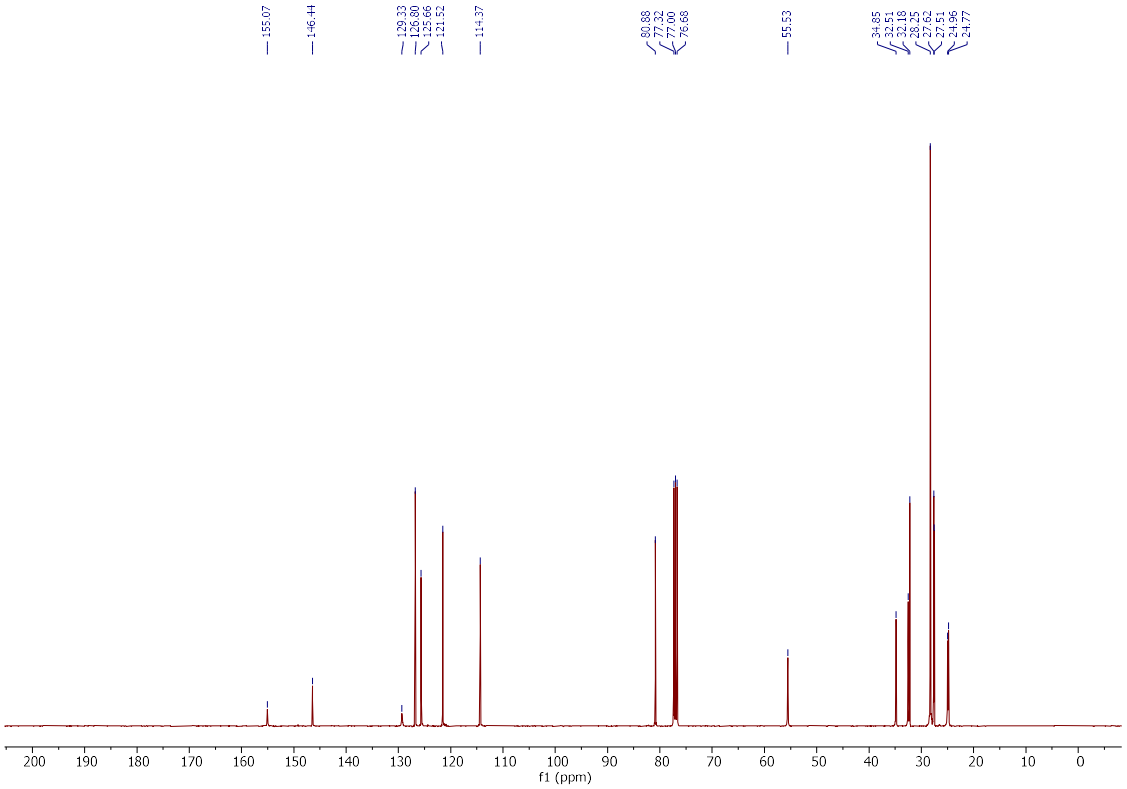
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3j**



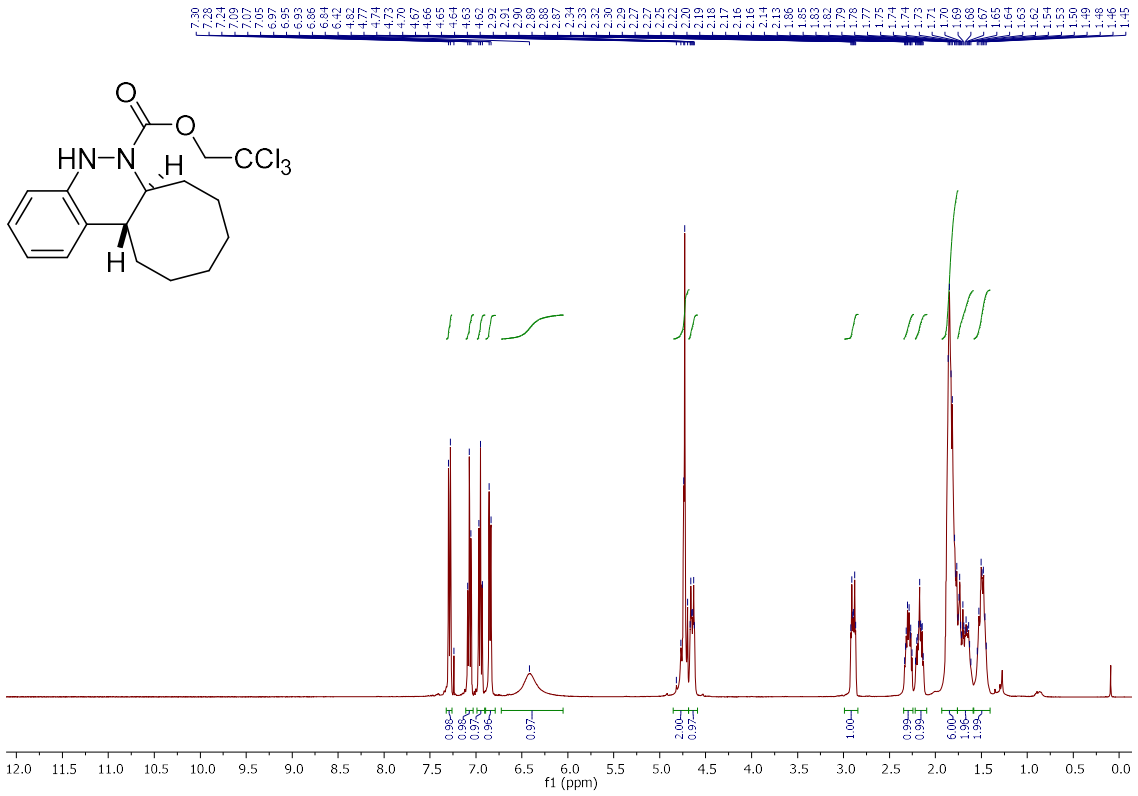
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3k**



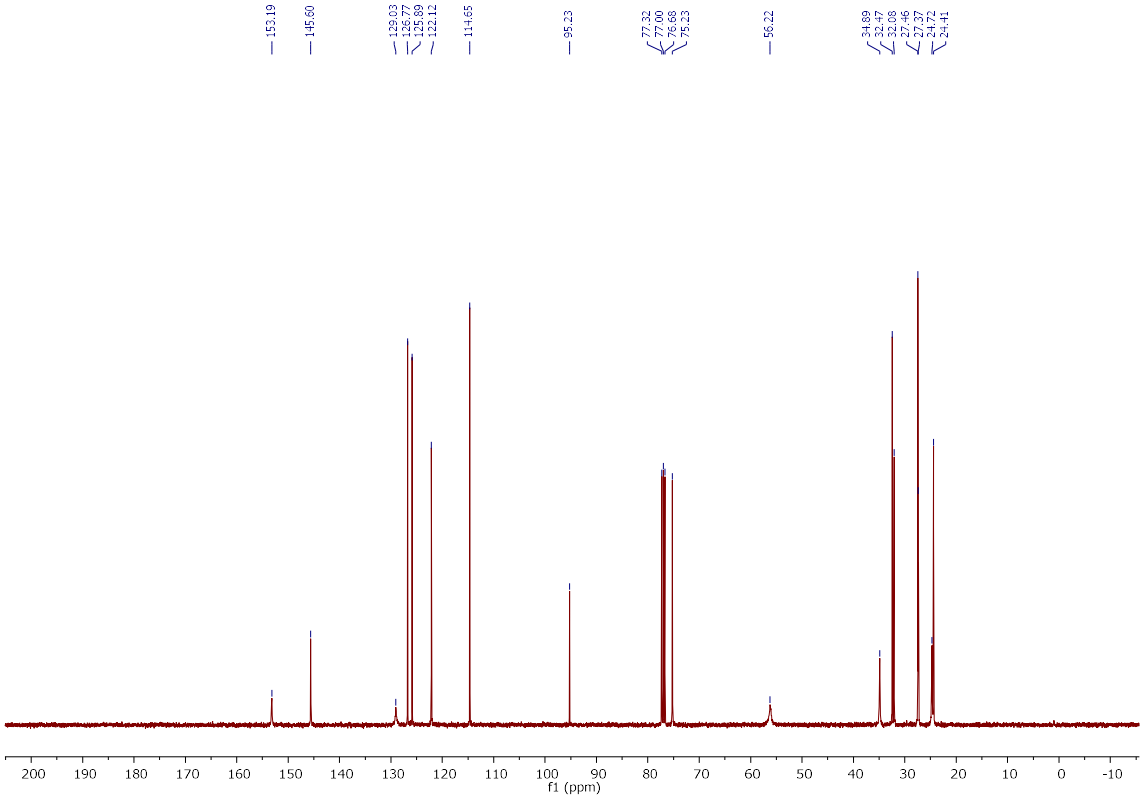
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3k**



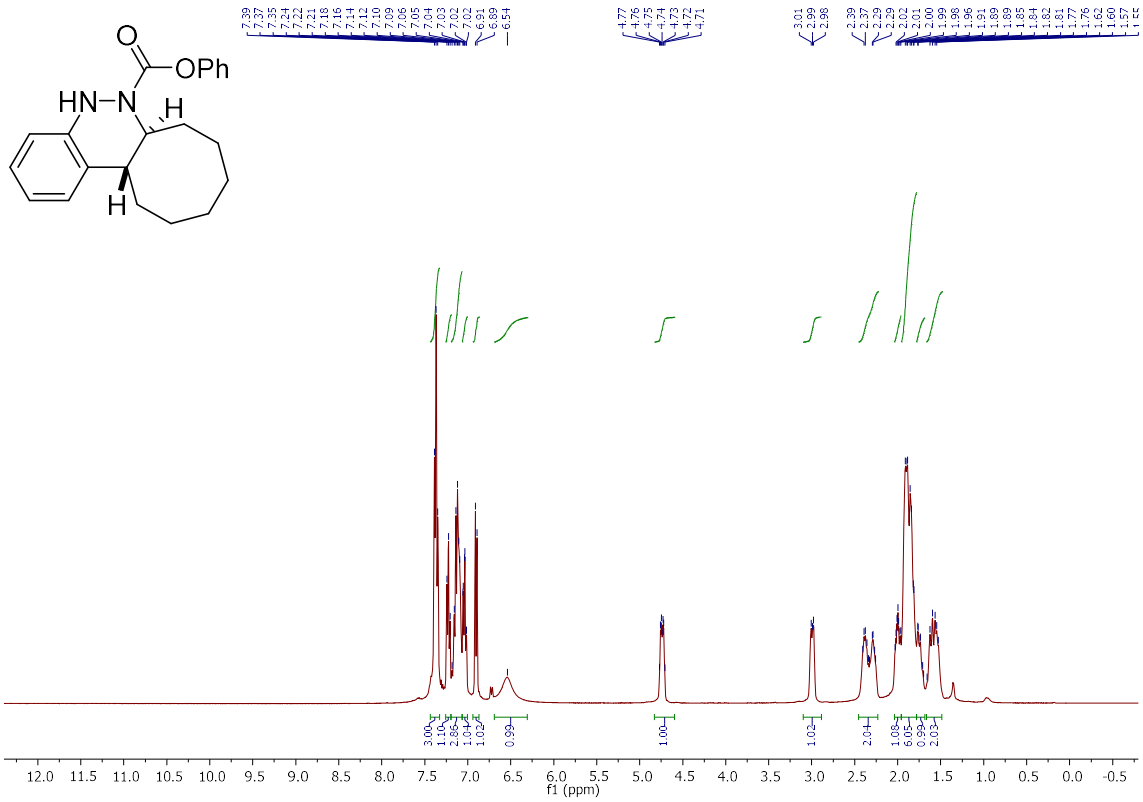
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3l**



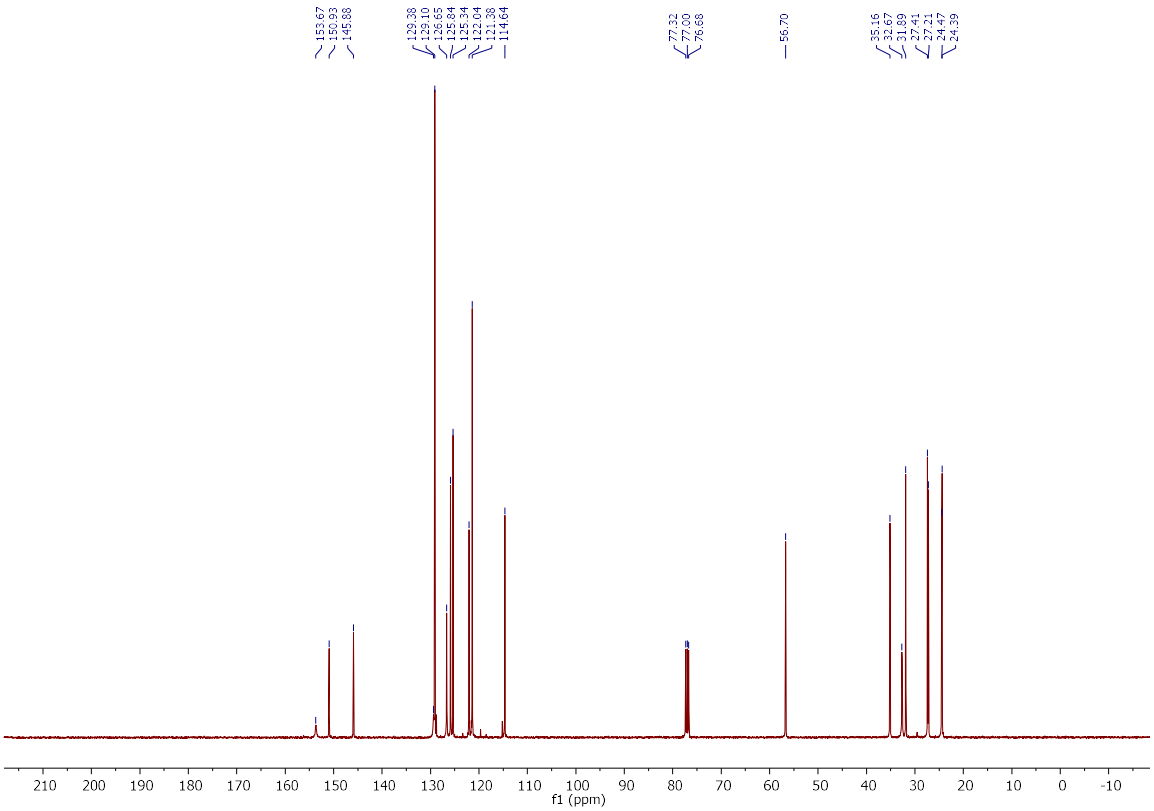
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3l**



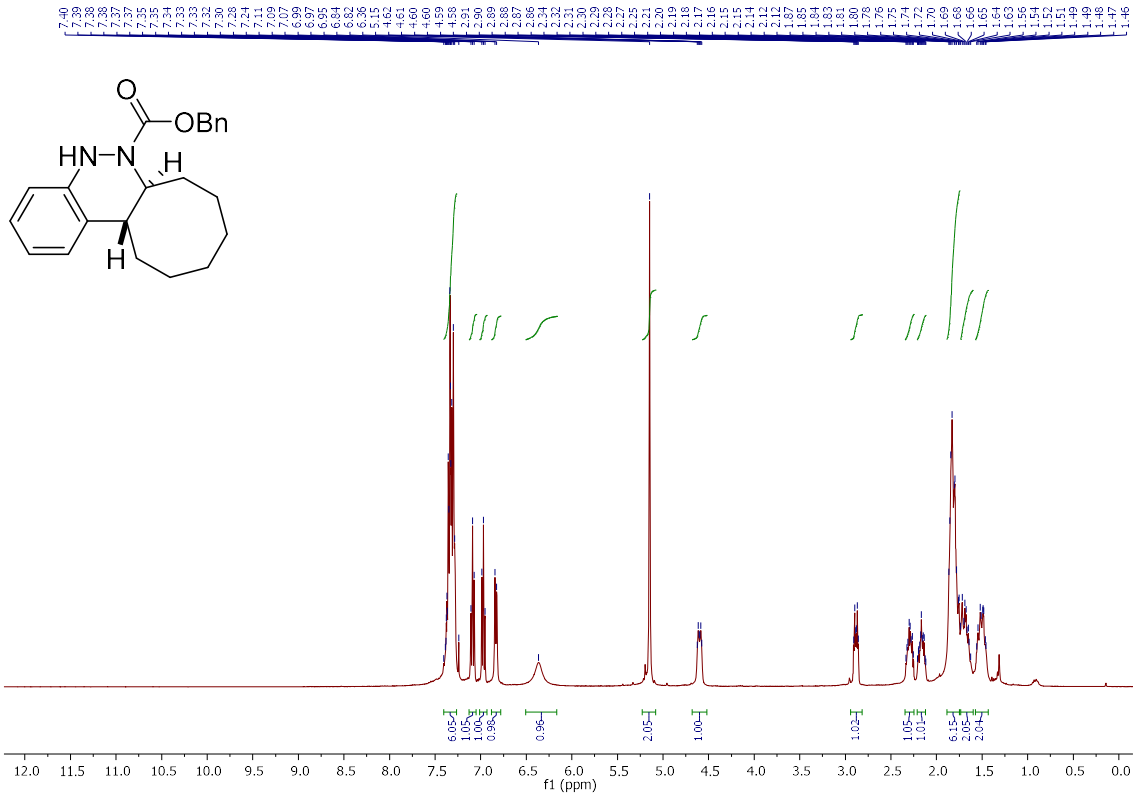
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3m**



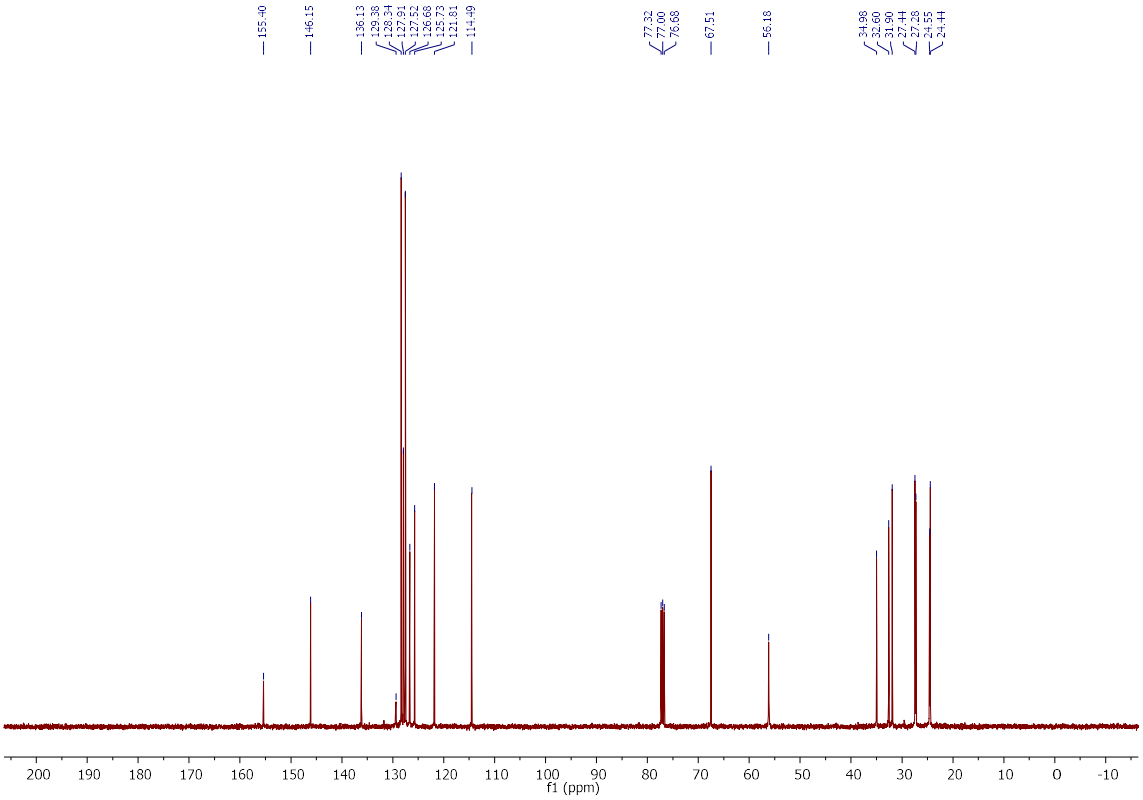
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3m**



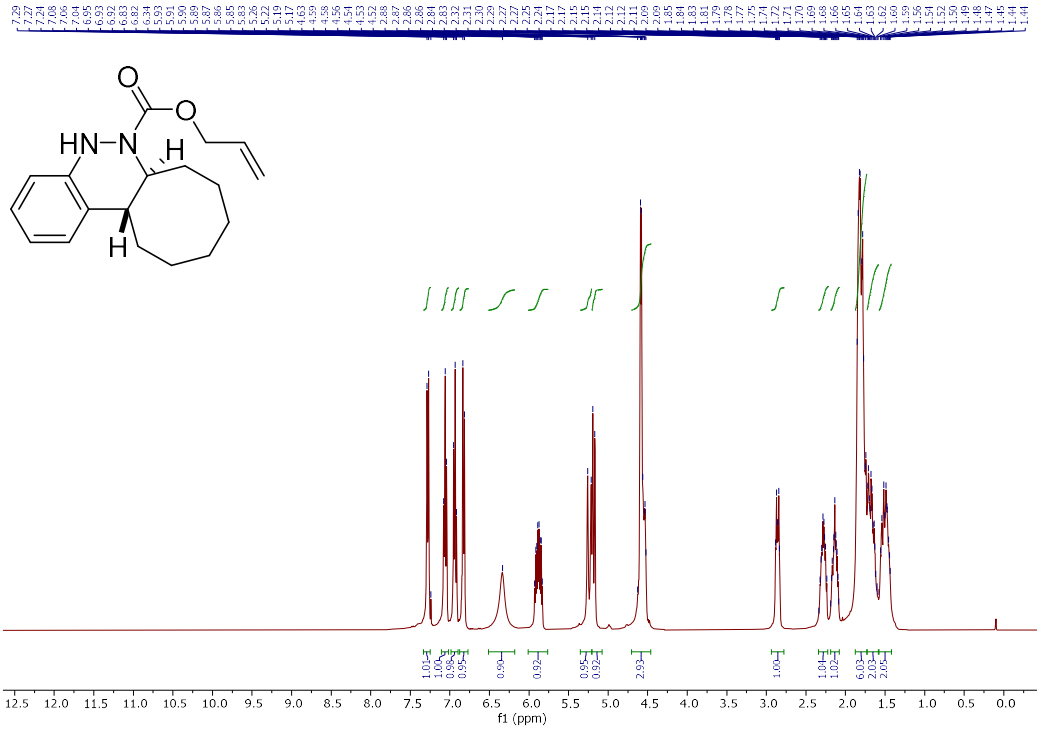
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3n**



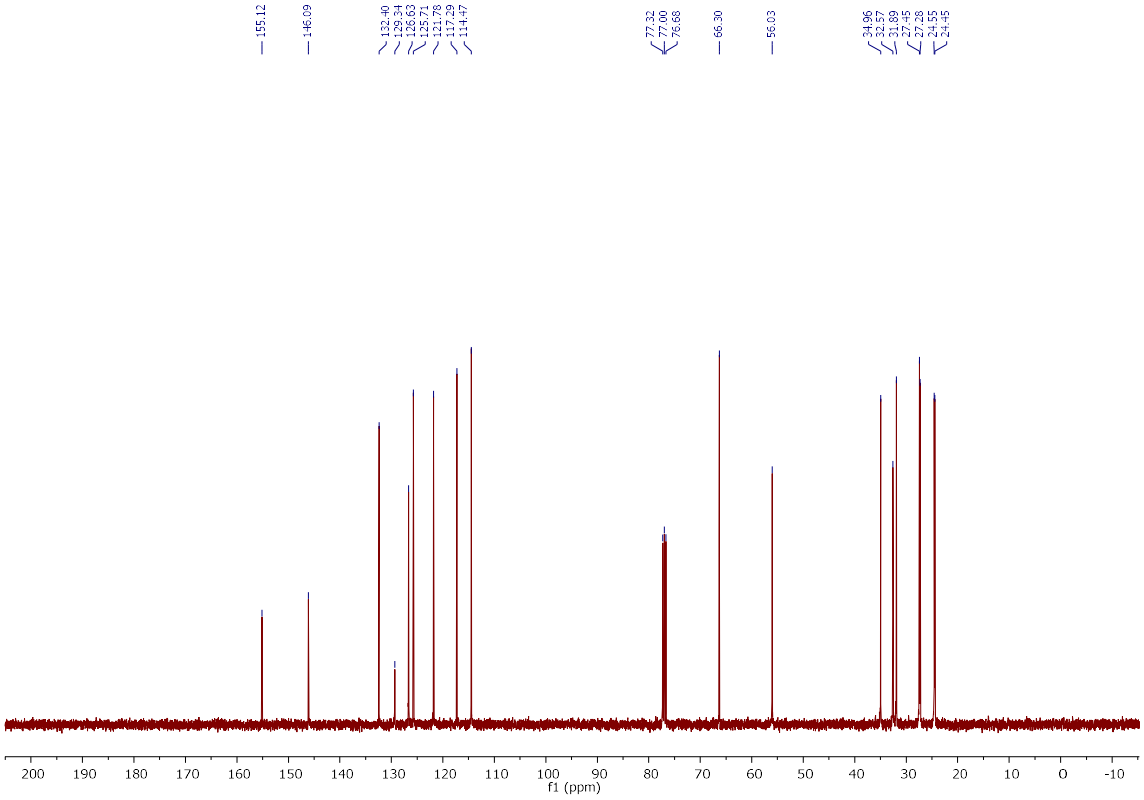
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3n**



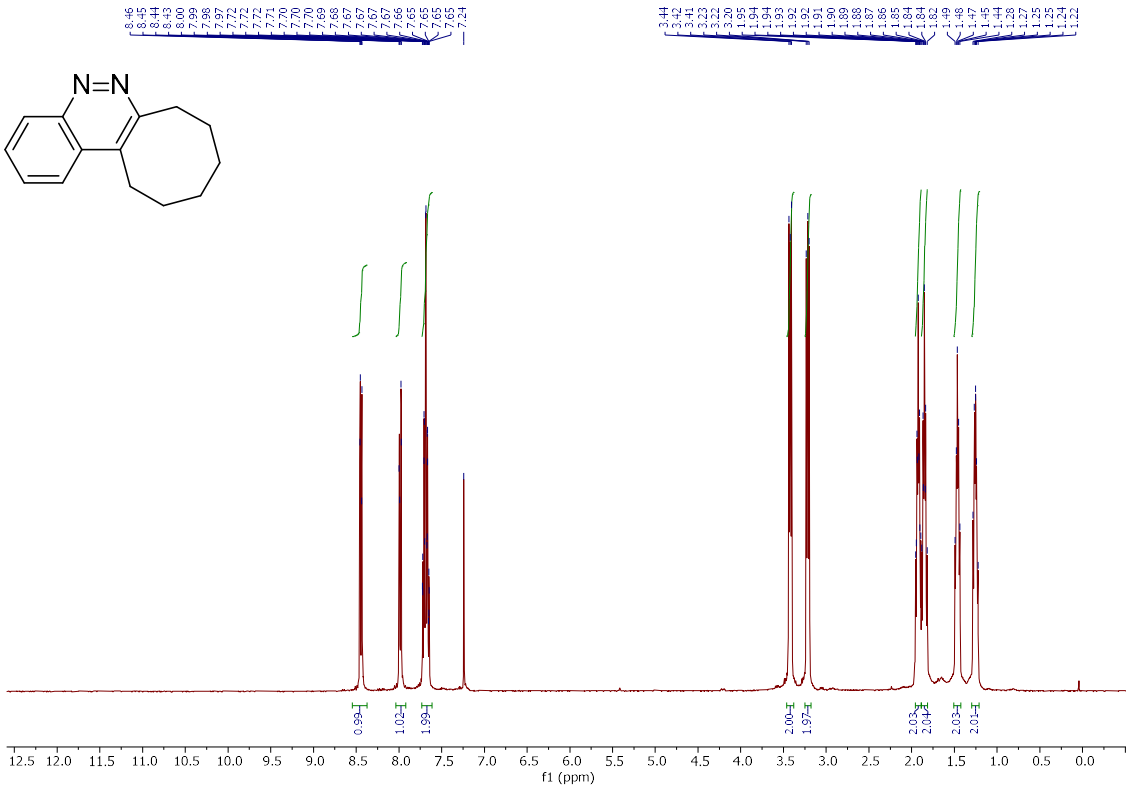
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **3o**



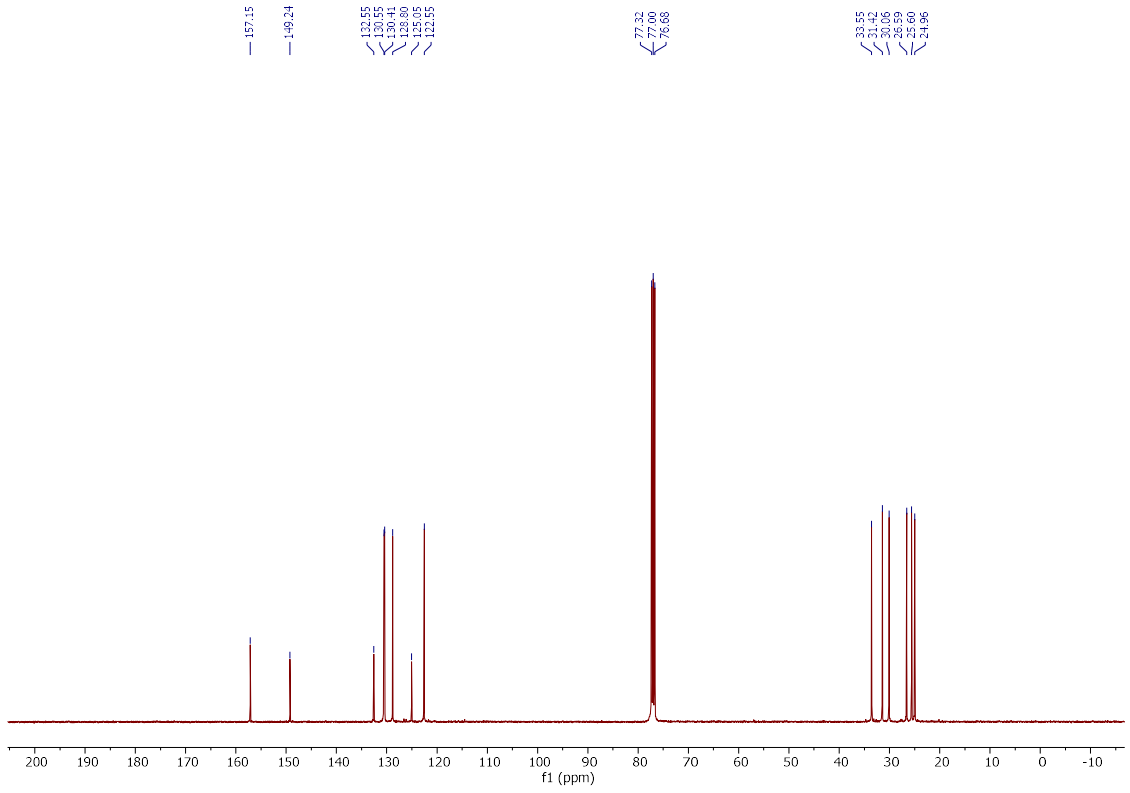
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **3o**



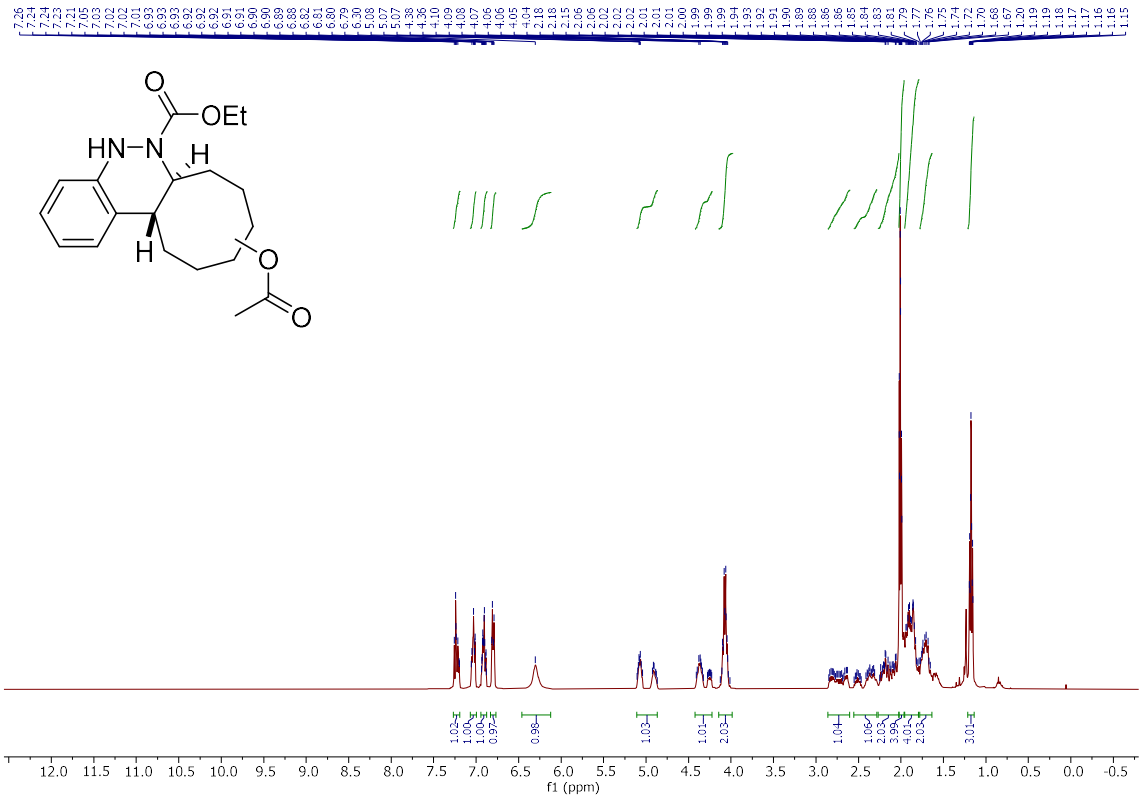
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **4a**



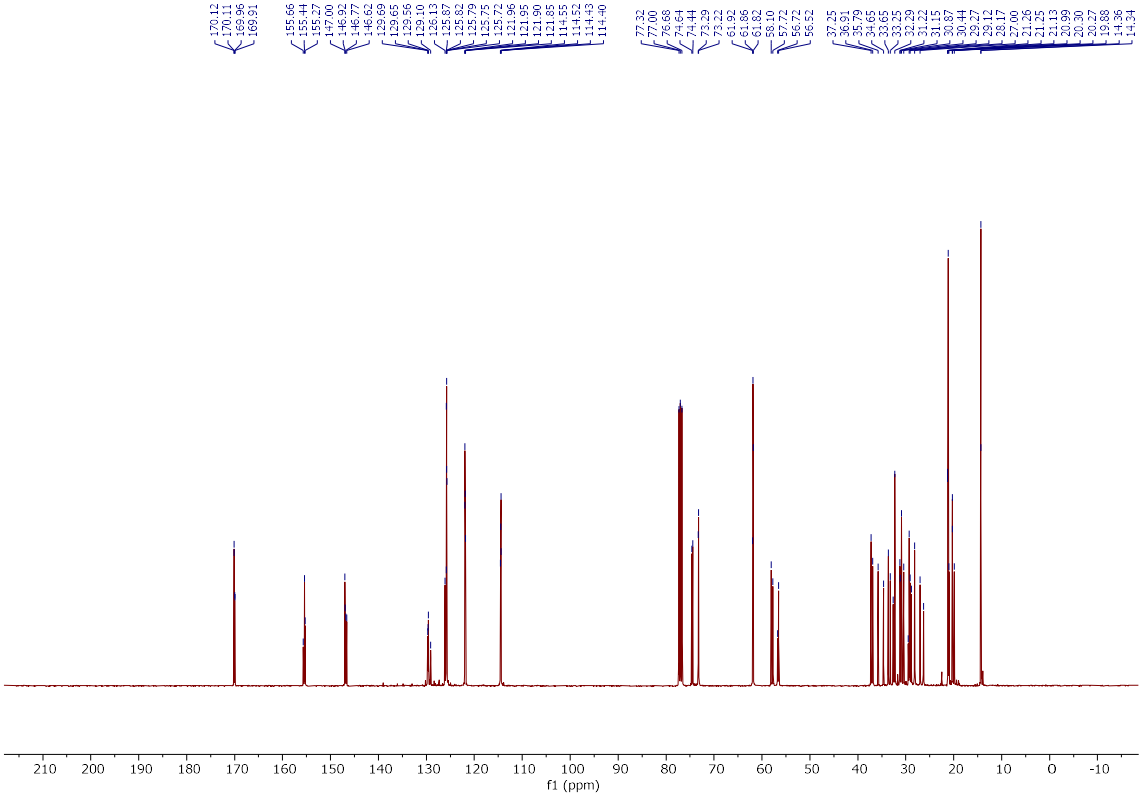
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **4a**



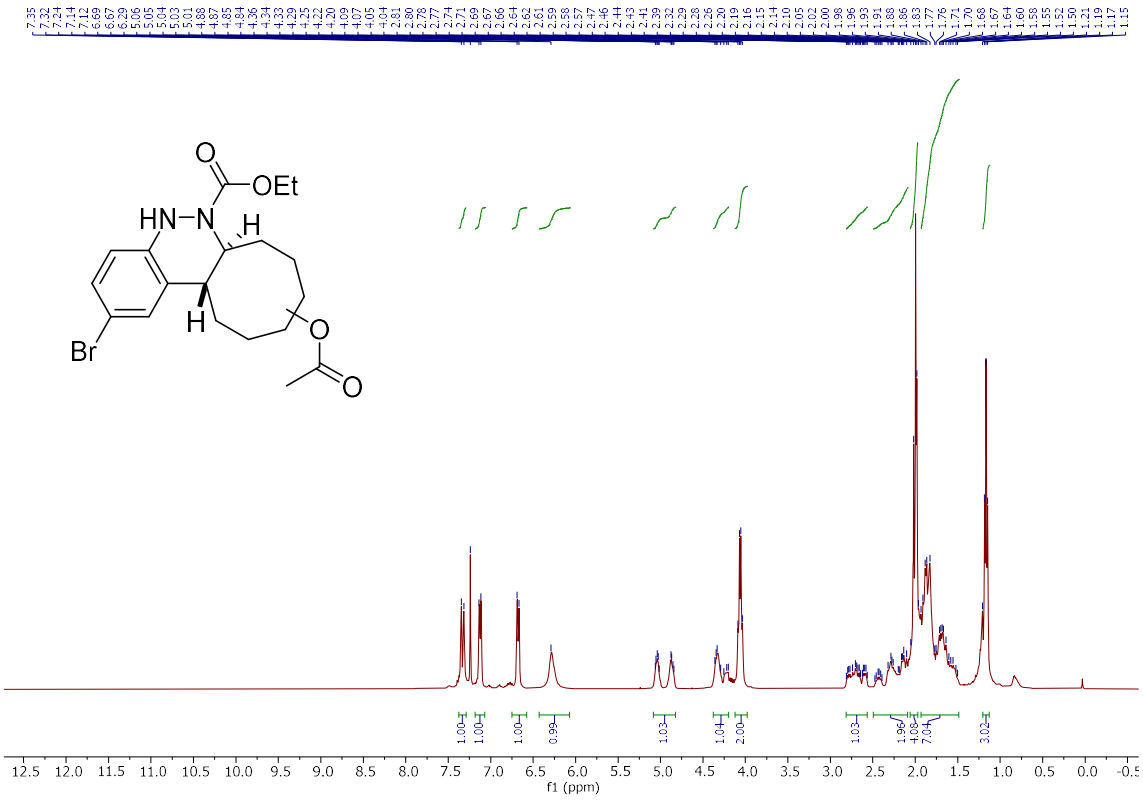
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **5a**



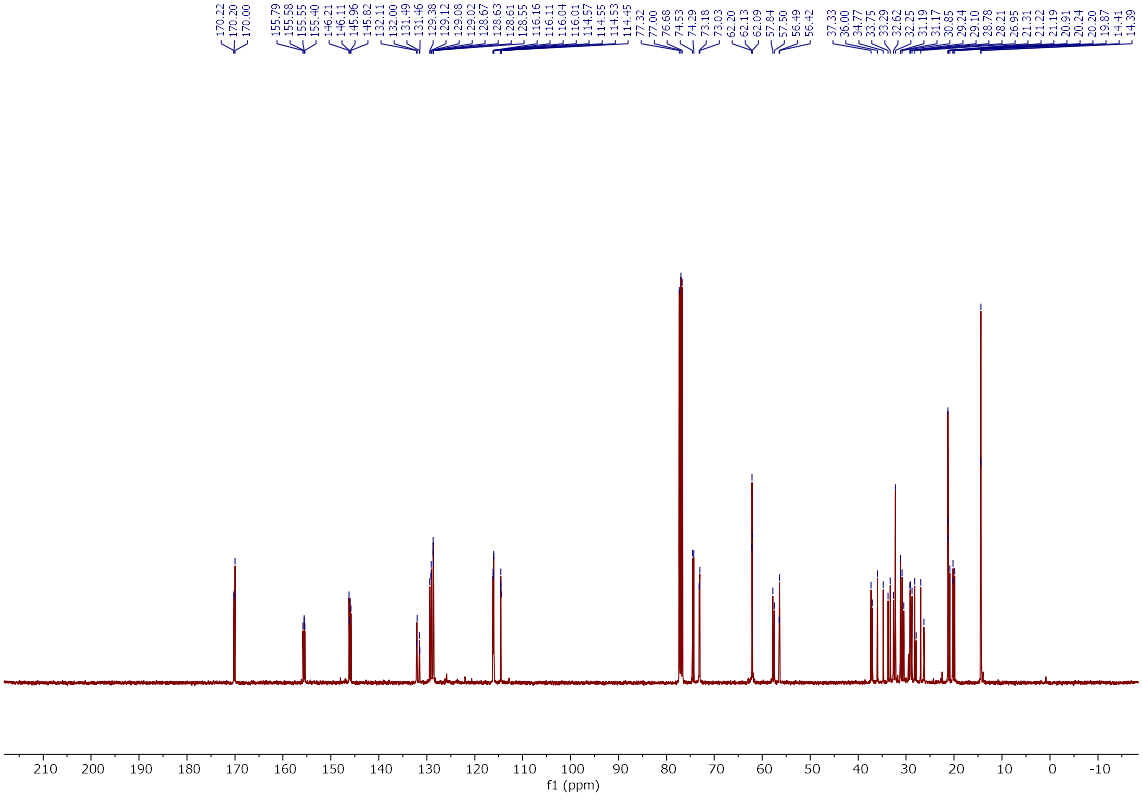
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **5a**



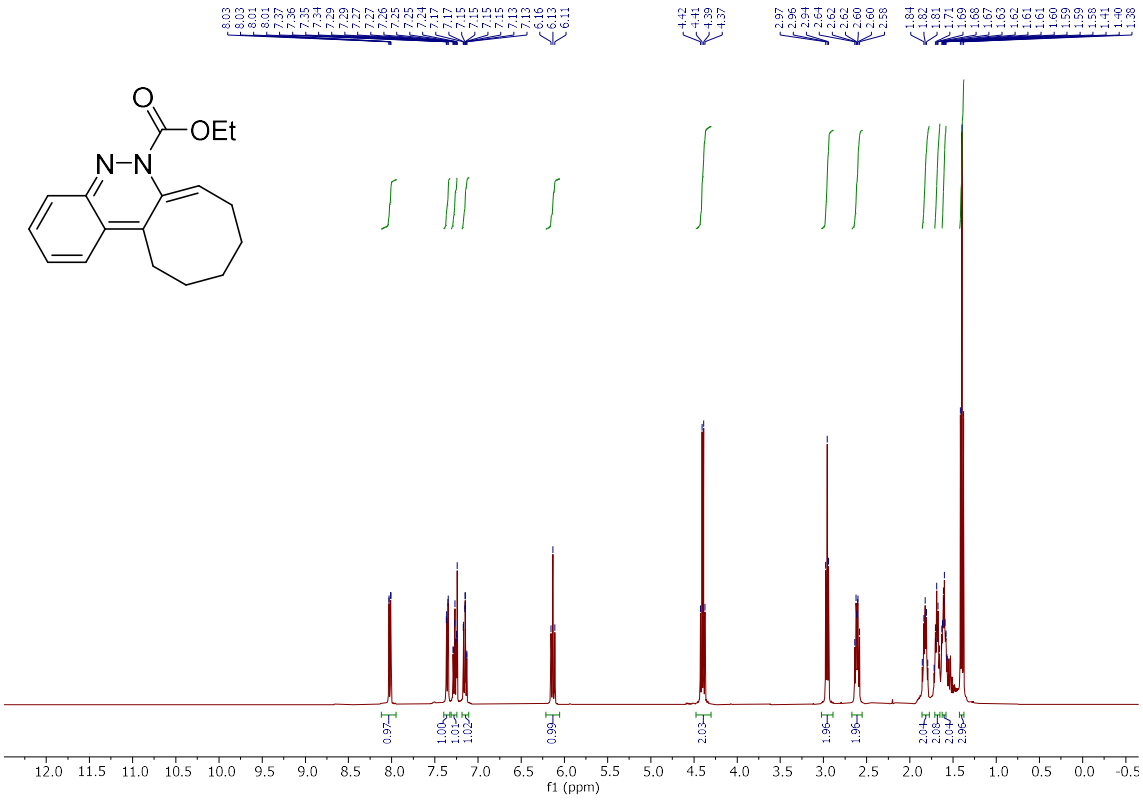
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **5f**



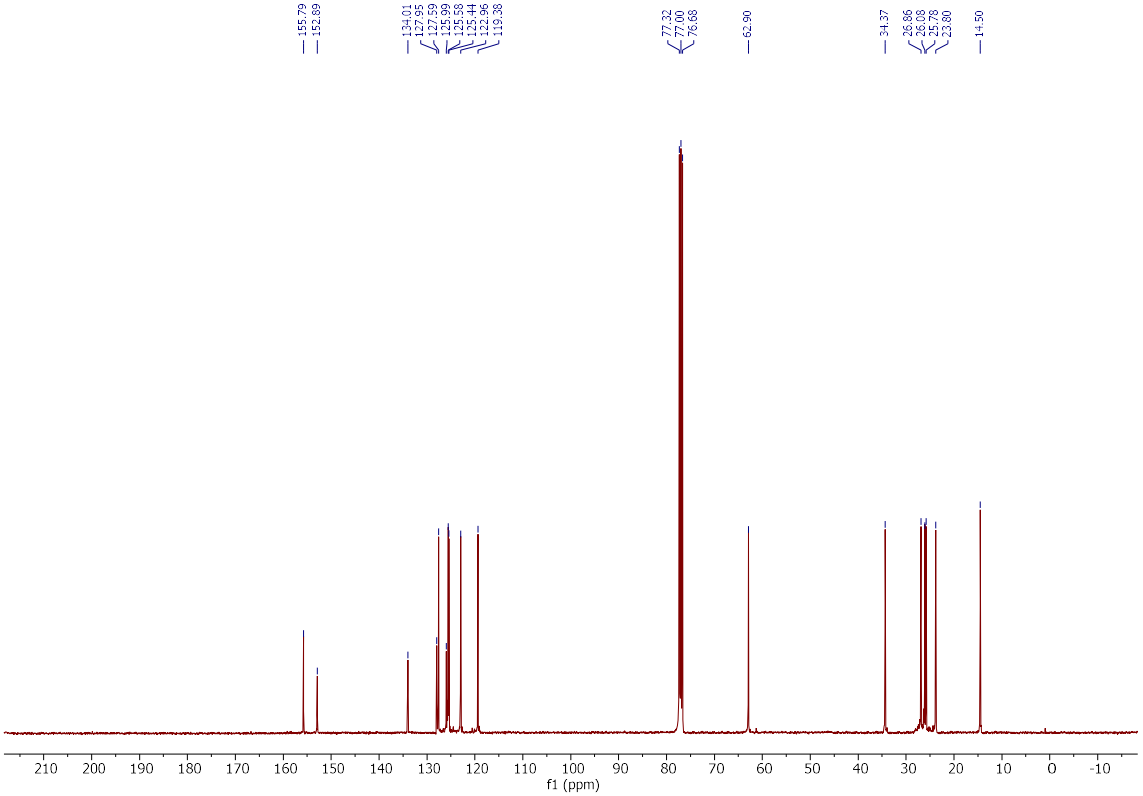
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **5f**



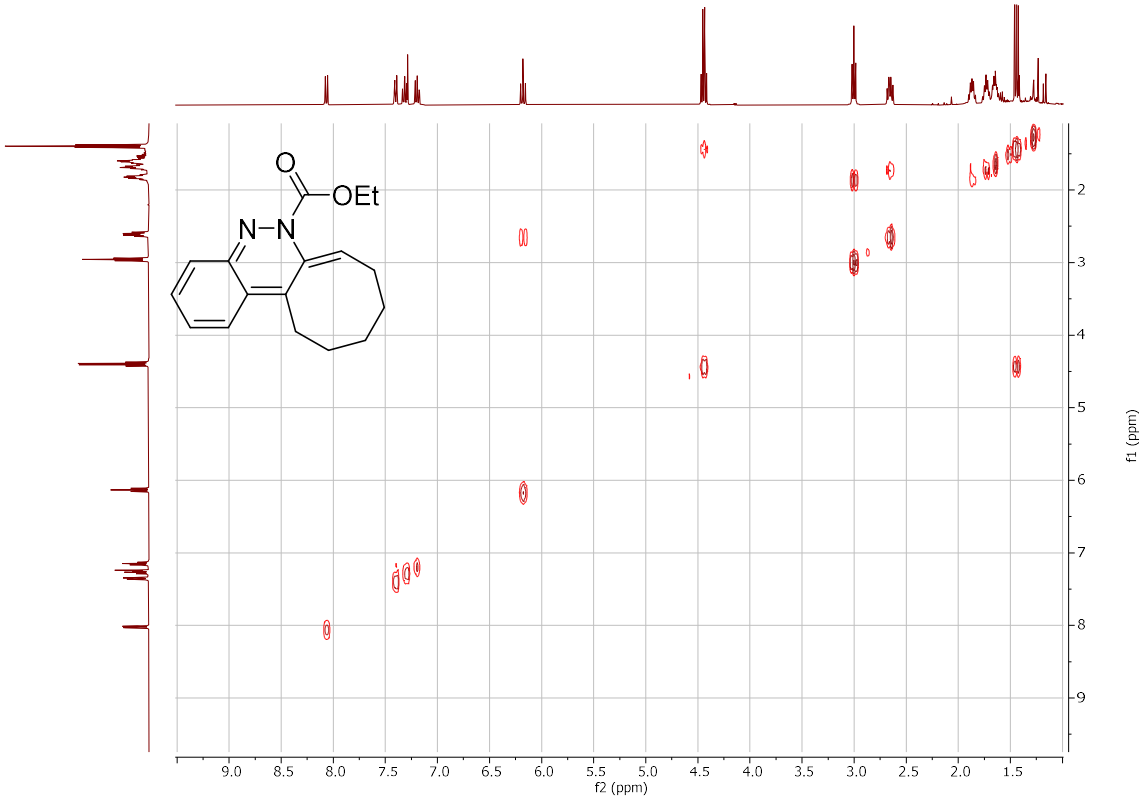
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **6a**



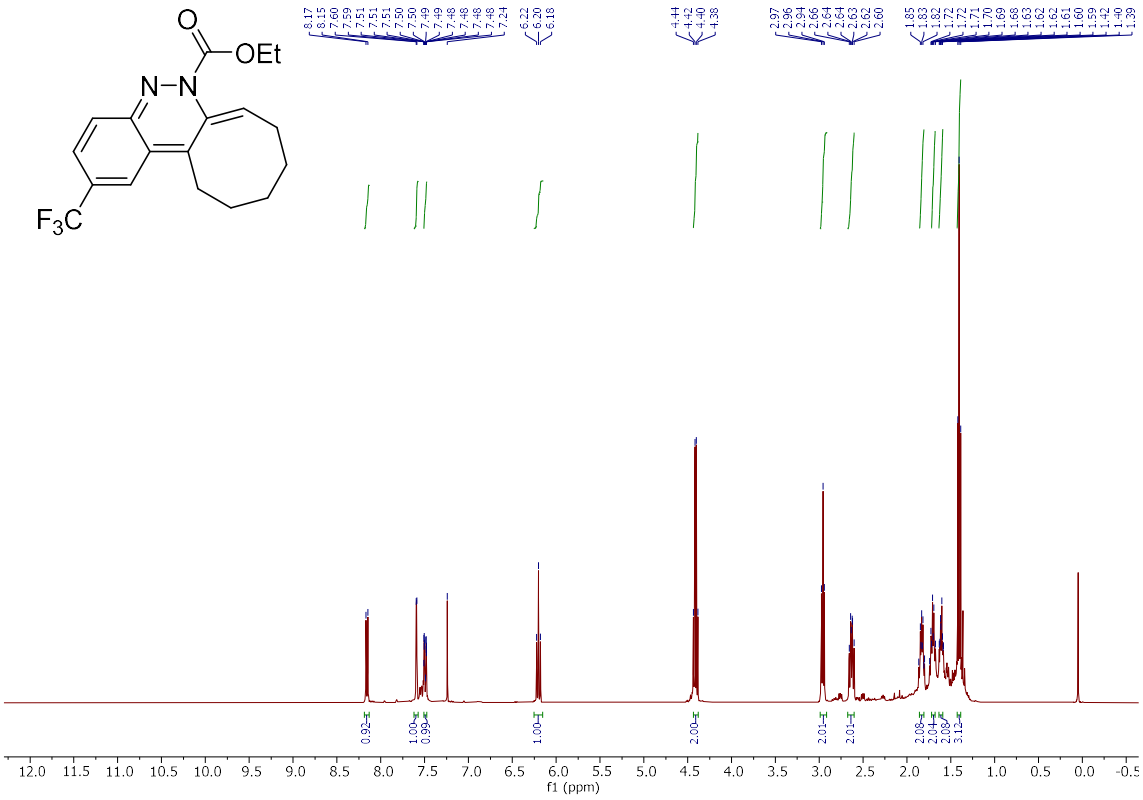
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **6a**



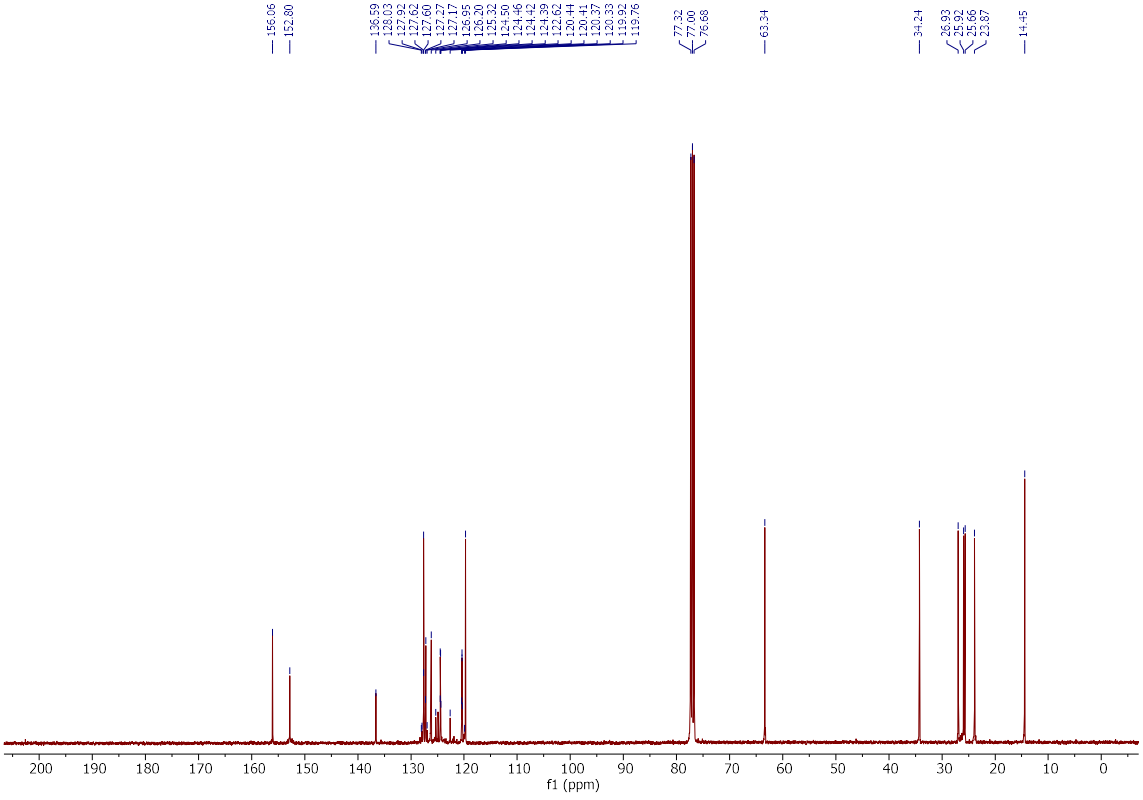
2D COSY NMR {^{1}H-^{1}H} (100 MHz, $CDCl_3$) of cinnoline derivative **6a**



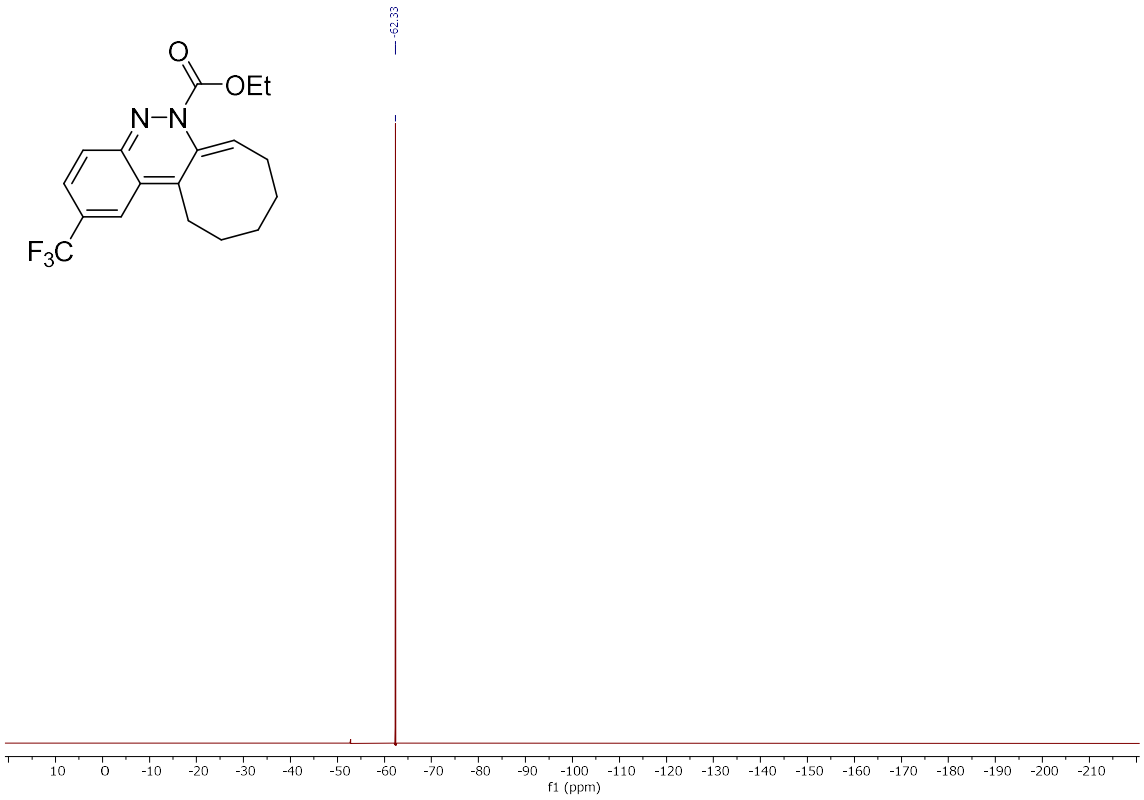
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **6e**



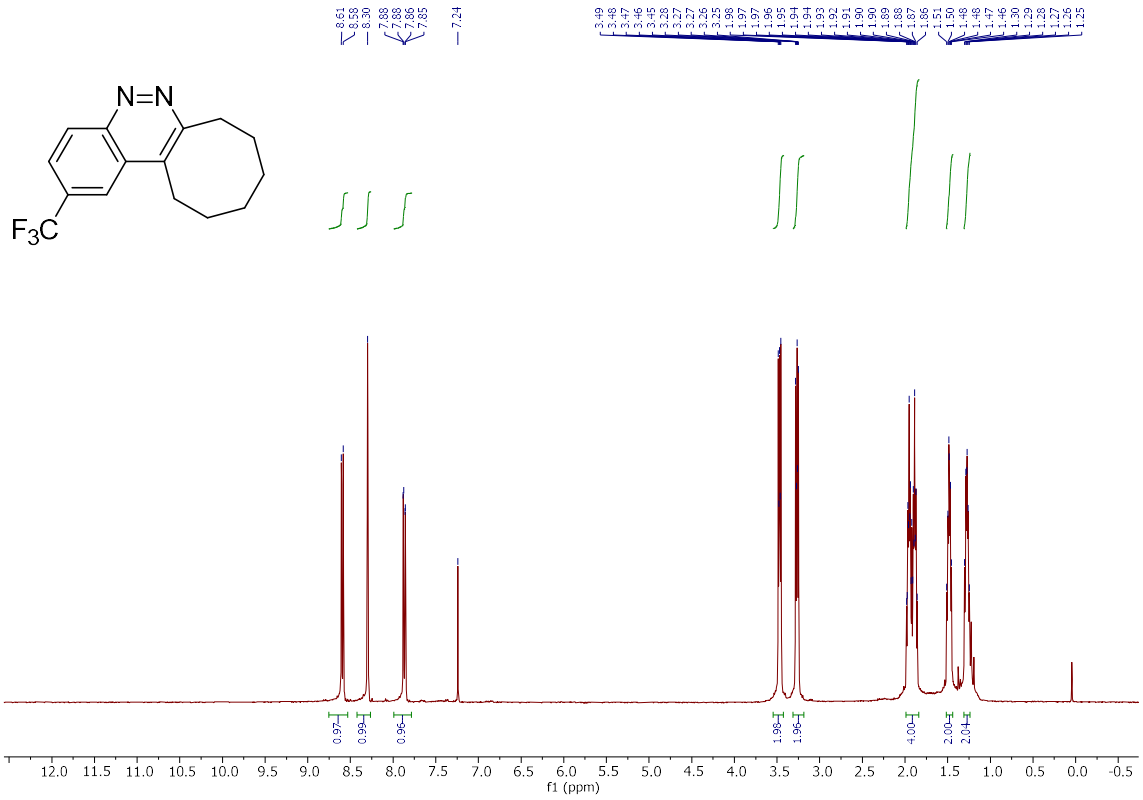
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **6e**



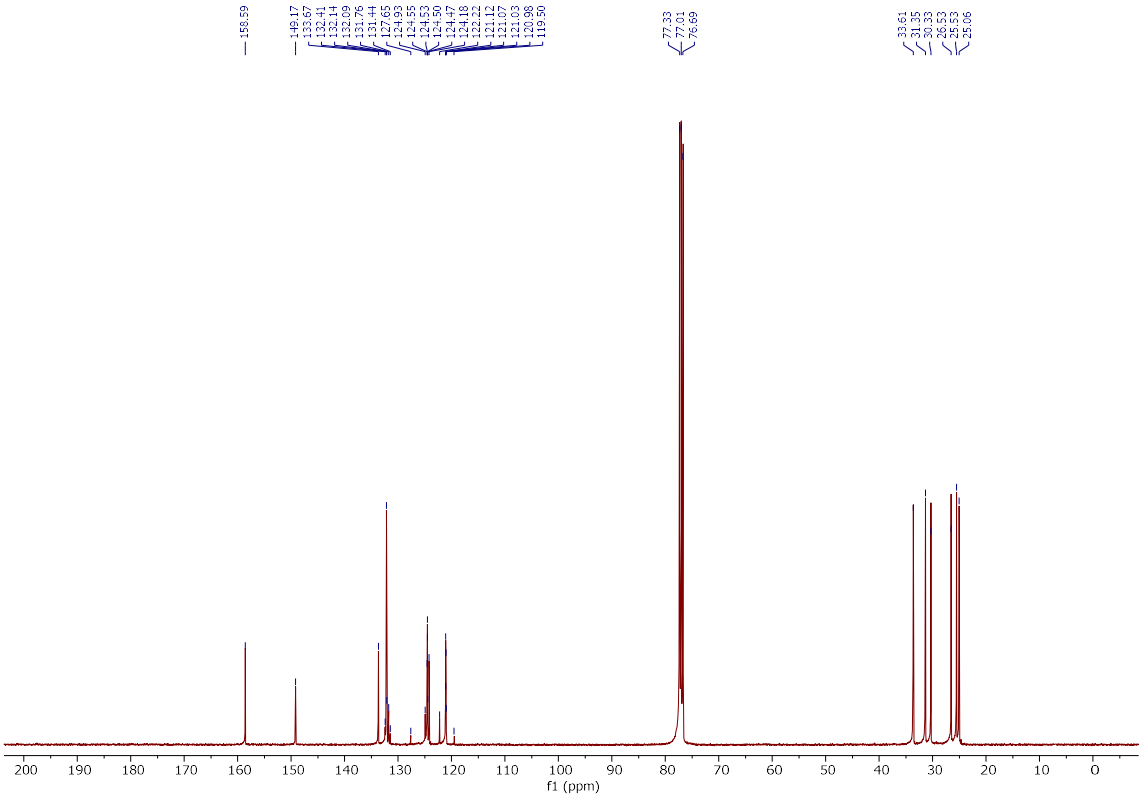
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **6e**



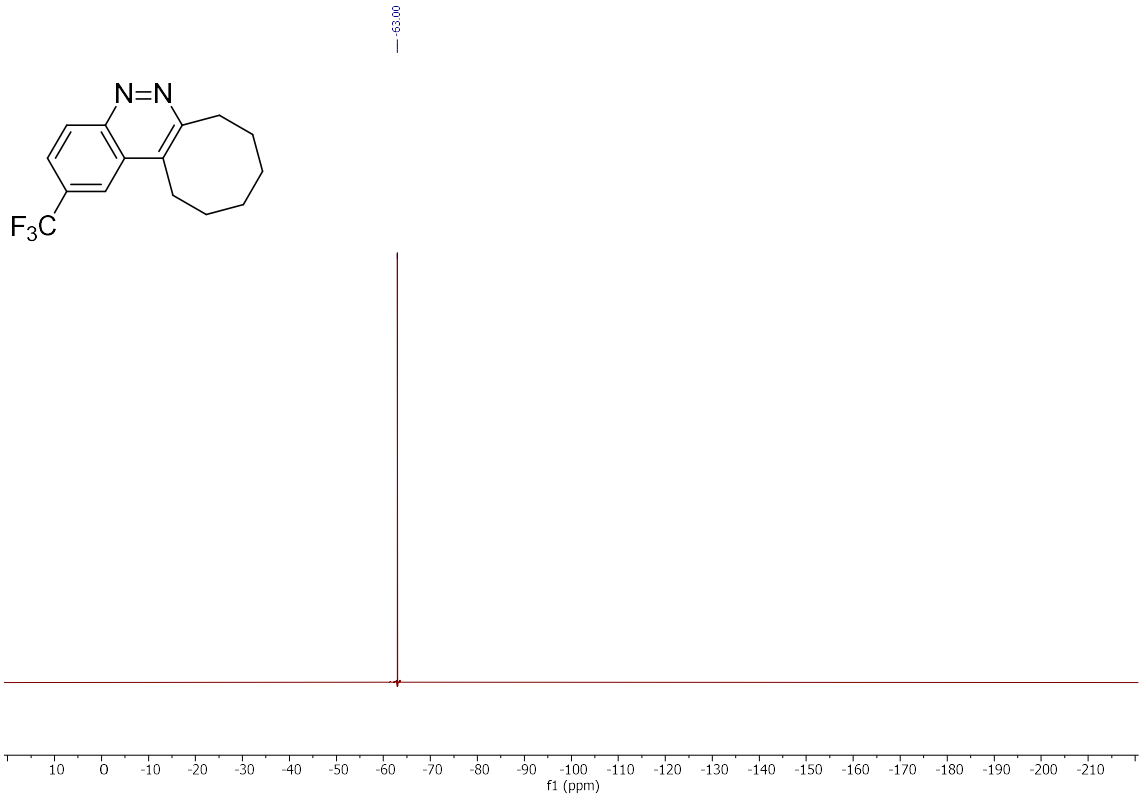
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **4e**



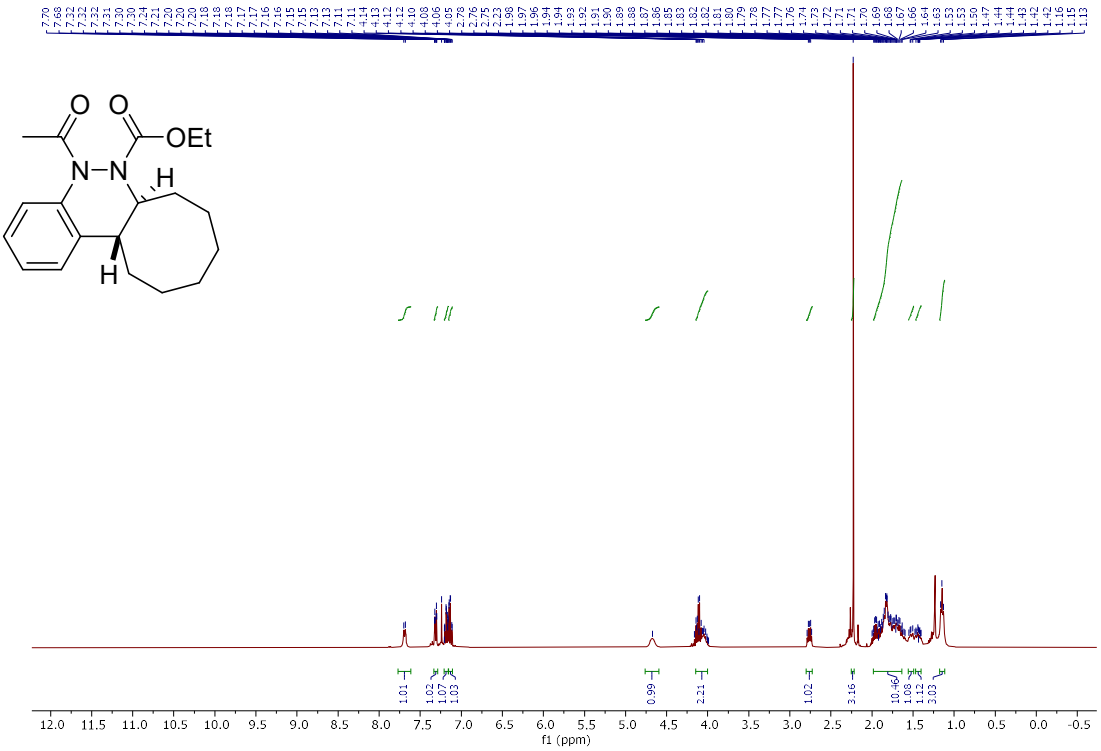
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **4e**



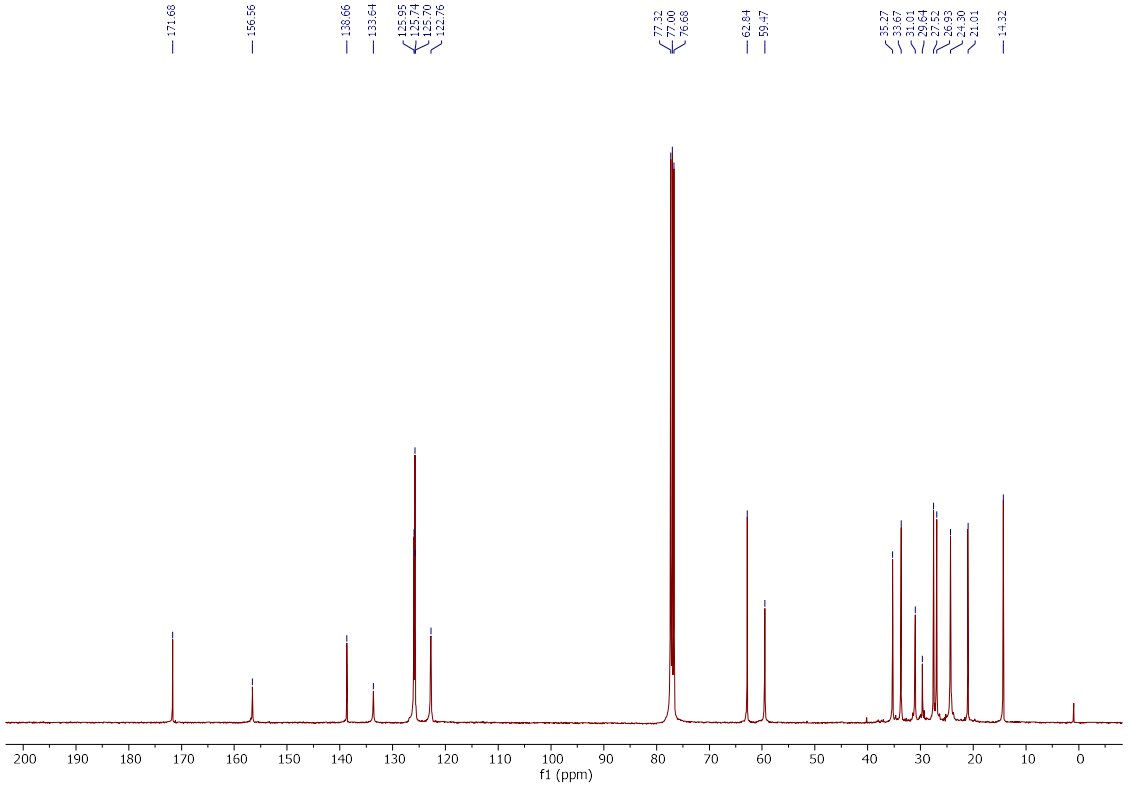
^{19}F (376 MHz, $CDCl_3$) of cinnoline derivative **4e**



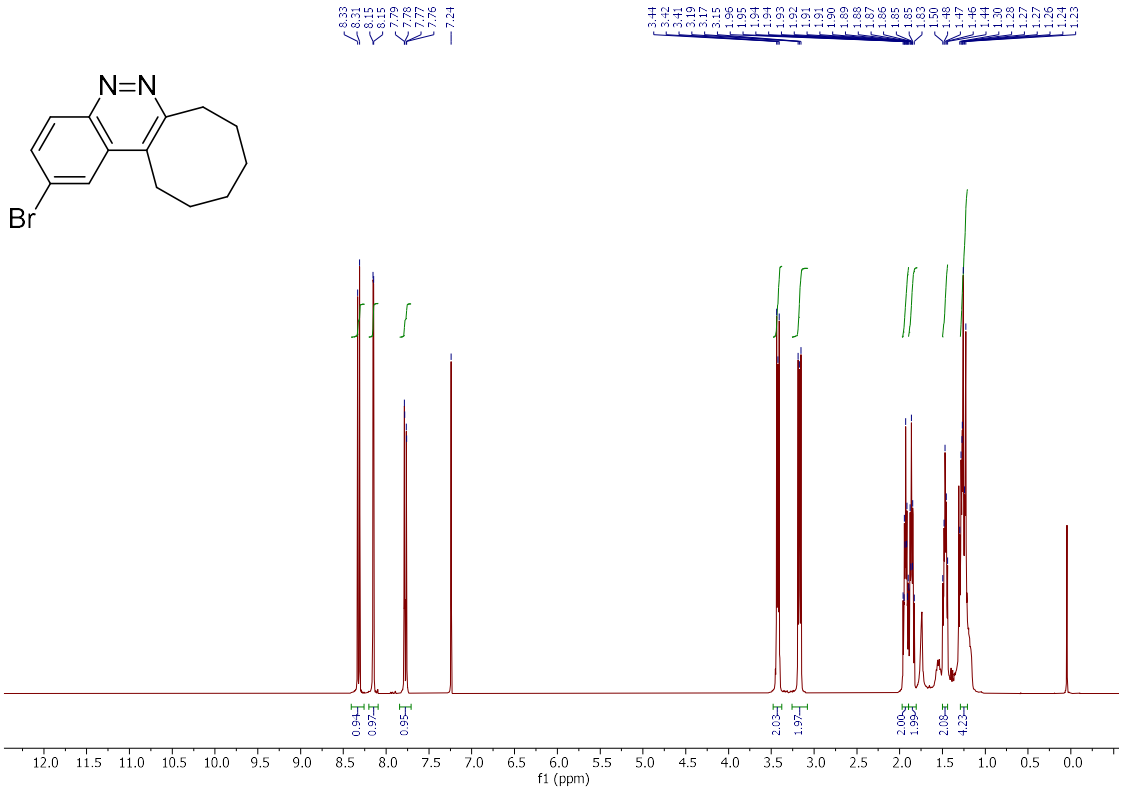
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **7**



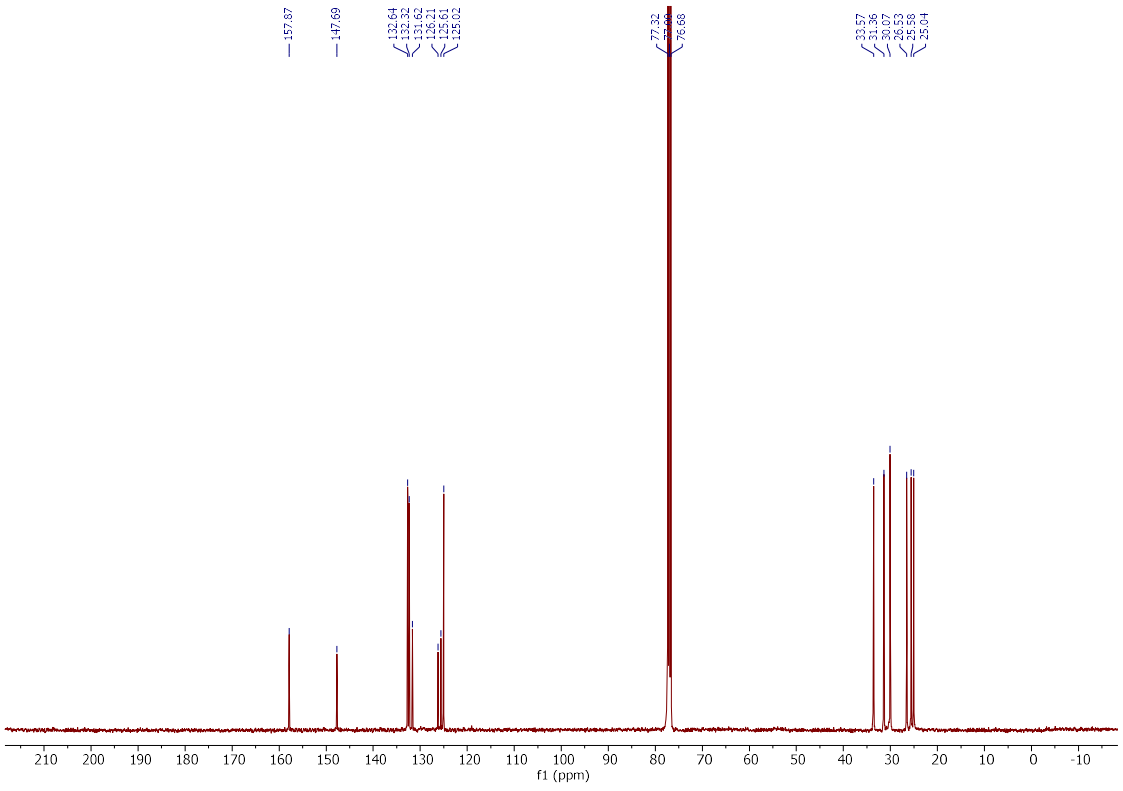
^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **7**



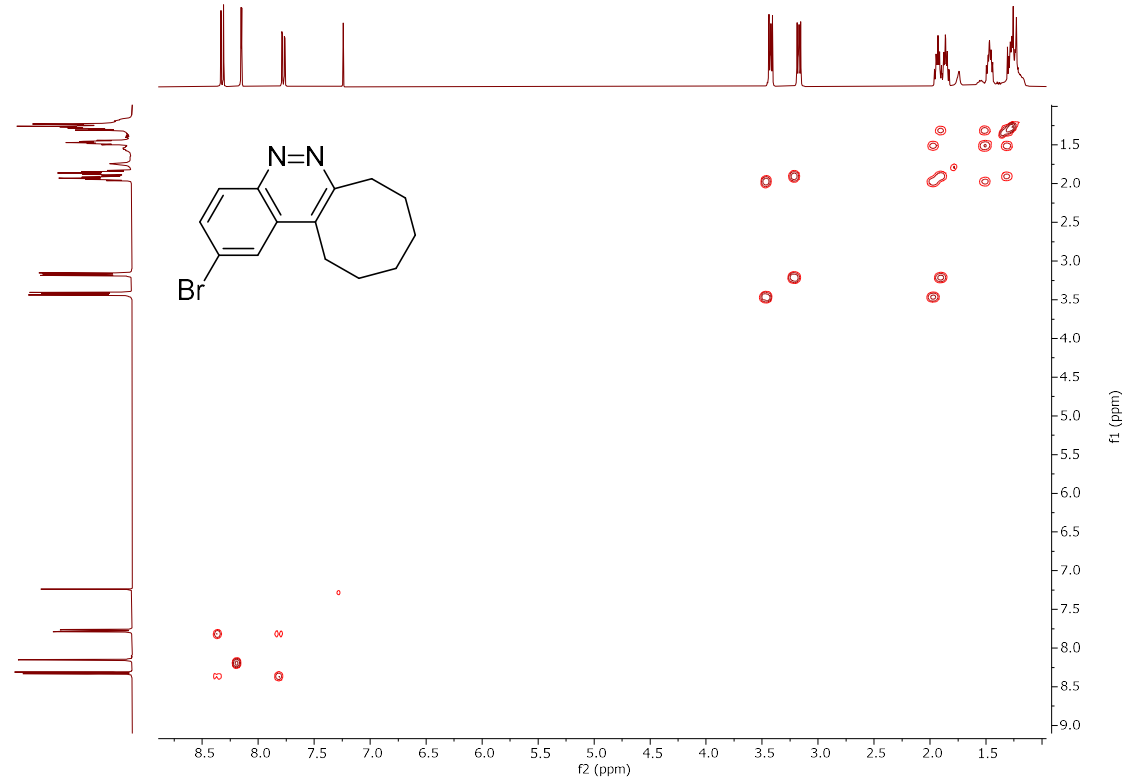
^{1}H NMR (400 MHz, $CDCl_3$) of cinnoline derivative **8**

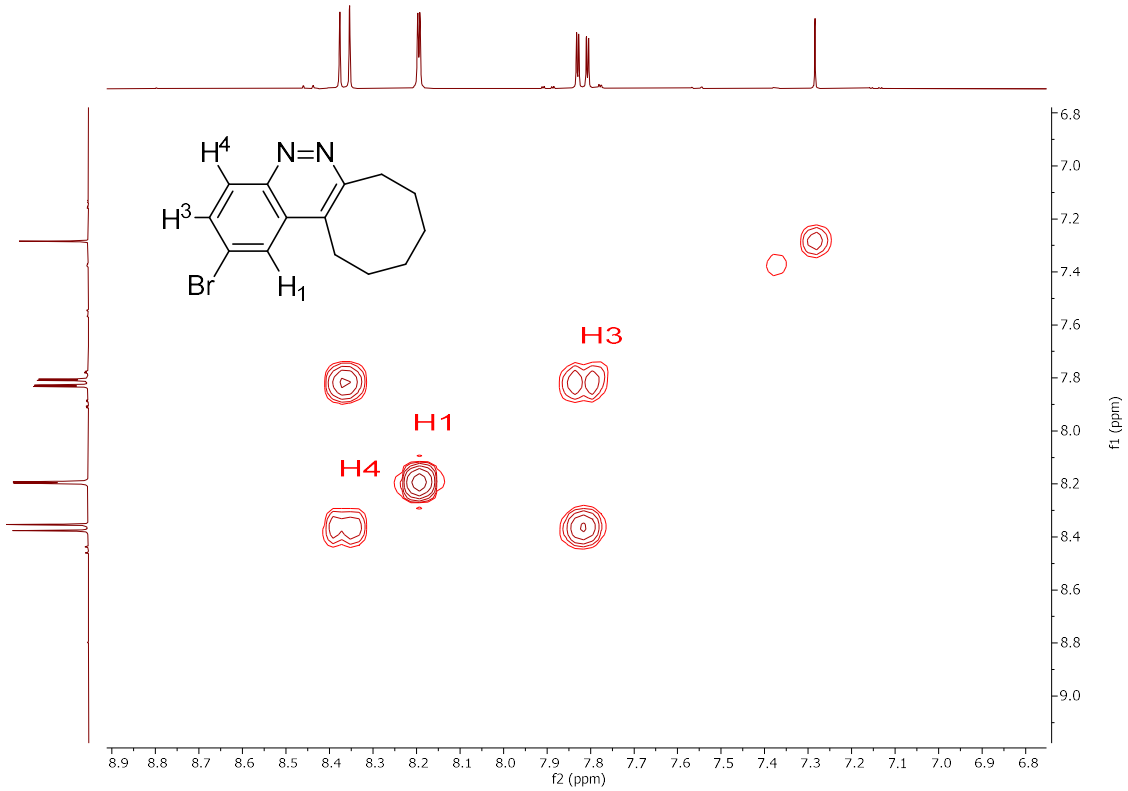


^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) of cinnoline derivative **8**



2D COSY NMR {^{1}H-^{1}H} (100 MHz, $CDCl_3$) of cinnoline derivative **8**





ORTEP drawing and X-ray crystallographic data for compound 3a

(CCDC deposition number 2343772)

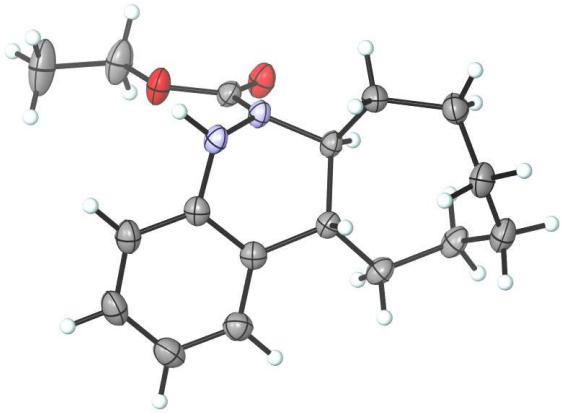


Figure S1. ORTEP diagram of compound **3a** with thermal displacement parameters drawn at 50% probability.

Single crystals of $C_{17}H_{24}N_2O_2$ **[3a]** were obtained. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, HyPix diffractometer. The crystal was kept at 181(16) K during data collection. Using Olex2,[10] the structure was solved with the SHELXS[11] structure solution program using Intrinsic Phasing and refined with the SHELXL[12] refinement package using Least Squares minimization.

Table S1. Crystal data and structure refinement for **3a**.

Empirical formula	$C_{17}H_{24}N_2O_2$
Formula weight	288.38
Temperature/K	181(16)
Crystal system	triclinic
Space group	P-1
a/Å	5.78458(12)
b/Å	7.85285(14)
c/Å	17.1515(2)
α/°	93.0396(13)
β/°	94.1142(14)
γ/°	101.4945(16)
Volume/Å^3	759.71(2)
Z	2
ρcalcg/cm^3	1.261
μ/mm^{-1}	0.656
F(000)	312.0
Crystal size/mm^3	0.507 × 0.386 × 0.211
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.178 to 147.672
Index ranges	$-7 \leq h \leq 7$, $-9 \leq k \leq 9$, $-21 \leq l \leq 18$
Reflections collected	14481
Independent reflections	2996 [R_{int} = 0.0467, R_{sigma} = 0.0274]
Data/restraints/parameters	2996/0/191
Goodness-of-fit on F^2	1.073
Final R indexes [I>=2σ (I)]	R_1 = 0.0453, wR_2 = 0.1173
Final R indexes [all data]	R_1 = 0.0473, wR_2 = 0.1193
Largest diff. peak/hole / e Å^{-3}	0.19/-0.18

References

1 X. Jiménez-Aberásturi, F. Palacios, J. M. de los Santos. $Sc(OTf)_3$-Mediated [4 + 2] Annulations of *N*-Carbonyl Aryldiazenes with Cyclopentadiene to Construct Cinnoline Derivatives: Azo-Povarov Reaction. *J. Org. Chem*. **2022**, *87*, 11583-11592.

2 D. Hirose, T. Taniguchi, H. Ishibashi, *Angew. Chem. Int. Ed*. **2013**, *52*, 4613-4617.

3 M. Fressancourt-Collinet, B. Hong, L., Leclercq, P. L. Alsters, J.-M. Aubry, V. Nardello-Rataj, *Adv. Synth. Catal*., **2013**, *355*, 409-420.

4 V. A. Stepanova, V. V. Dunina, I. P. Smoliakova, *Organometallics* **2009**, *28*, 6546-6558.

5 K. J. Shea, J. S. Kim, *J. Am. Chem. Soc*. **1992**, *114*, 3044-3051.

6 H. Stöckmann, A. A. Neves, H. A. Day, S. Stairs, K. M. Brindle, F. J. Leeper, *Chem. Commun*. **2011**, *47*, 7203-7205.

7 H. Zhan, H. de Jong, D. W. P. M. Löwik, *ACS Appl. Bio Mater*. **2019**, *2*, 2862-2871.

8 S. V. Facchini, J.-M. Neudörfl, L. Pignataro, M. Cettolin, C. Gennari, A. Berkessel, U. Piarulli, *ChemCatChem*, **2017**, *9*, 1461–1468.

9 W. Chen, D. Wang, C. Dai, D. Hamelberg, B. Wang, *Chem. Commun.*, **2012**, *48*, 1736–1738.

10 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann. *OLEX2*: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.

11 G. M. Sheldrick. A short history of *SHELX*. *Acta Cryst*. **2008**, *A64*, 112-122.

12 G. M. Sheldrick. Crystal structure refinement with *SHELXL*. *Acta Cryst*. **2015**, *C71*, 3-8.