# Enantioselective formal (3+3) cycloaddition of bicyclobutanes with nitrones enabled by asymmetric Lewis acid catalysis

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## Supplementary information

### Table of Contents

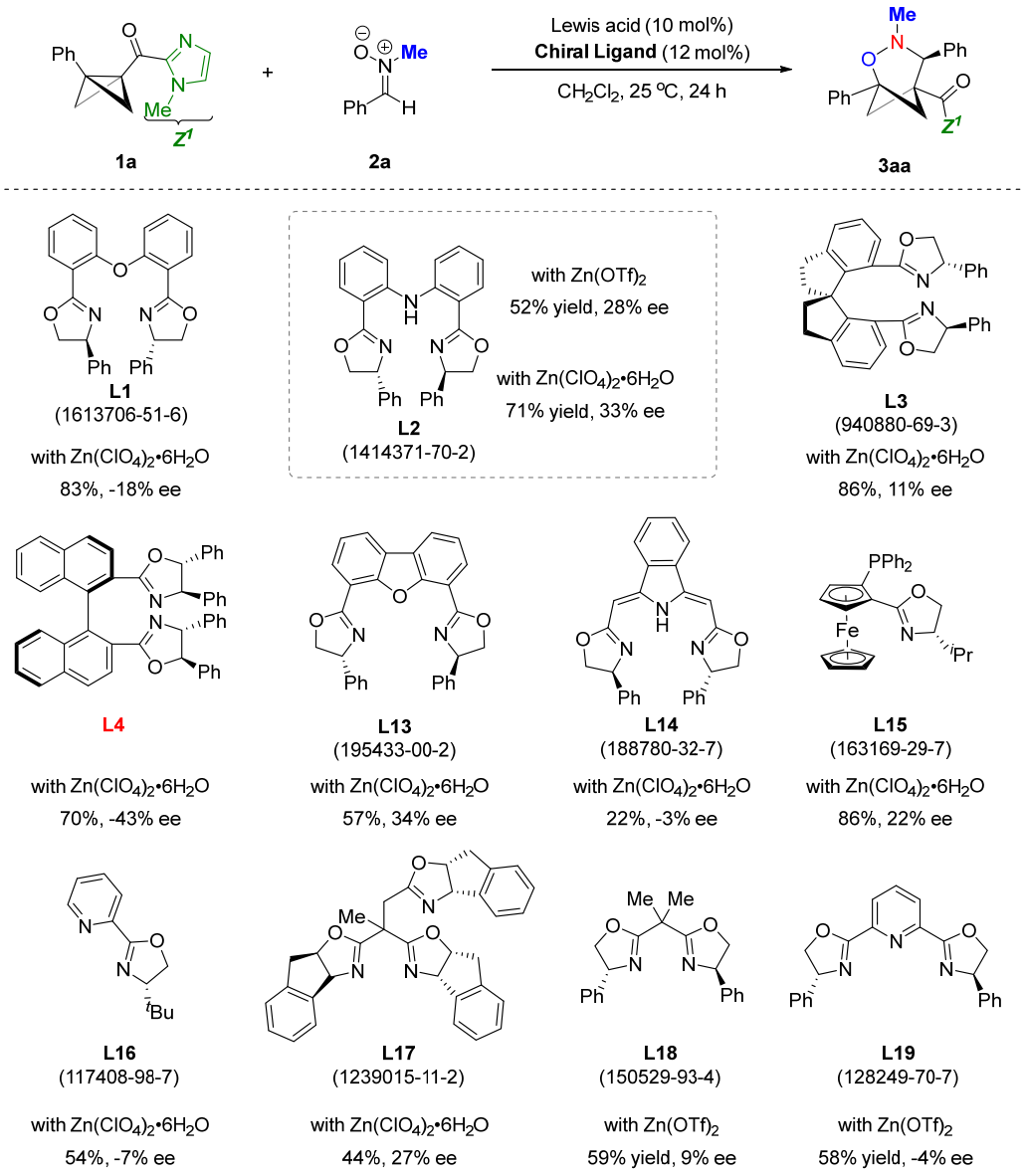
1. Supplementary Methods ..... S2
1.1 General Information ..... S2
1.2 Optimization Study ..... S3
1.3 General Procedure for the Enantioselective (3+3) Cycloadditions (GP1) ..... S7
1.4 General Procedure for the Synthesis of New Bicyclobutanes (GP2) ..... S7
1.5 Scale-Up Experiment ..... S8
1.6 Synthetic Transformations ..... S9
1.7 General Procedure for the Synthesis of Chiral Ligands ..... S13
2. Supplementary Discussion ..... S14
2.1 Unsuccessful BCB Substrates and Control Experiments ..... S14
2.2 Non-Linear Effect Study ..... S16
2.3 Proposed Catalytic Cycle and Computed Transition Structures ..... S17
2.4 Characterization Data of the New BCBs and Products ..... S18
3. X-Ray Crystallography ..... S73
4. Supplementary NMR and HPLC Spectra ..... S75
5. Supplementary Computational Details ..... S201
6. Supplementary References ..... S201

# 1. Supplementary Methods

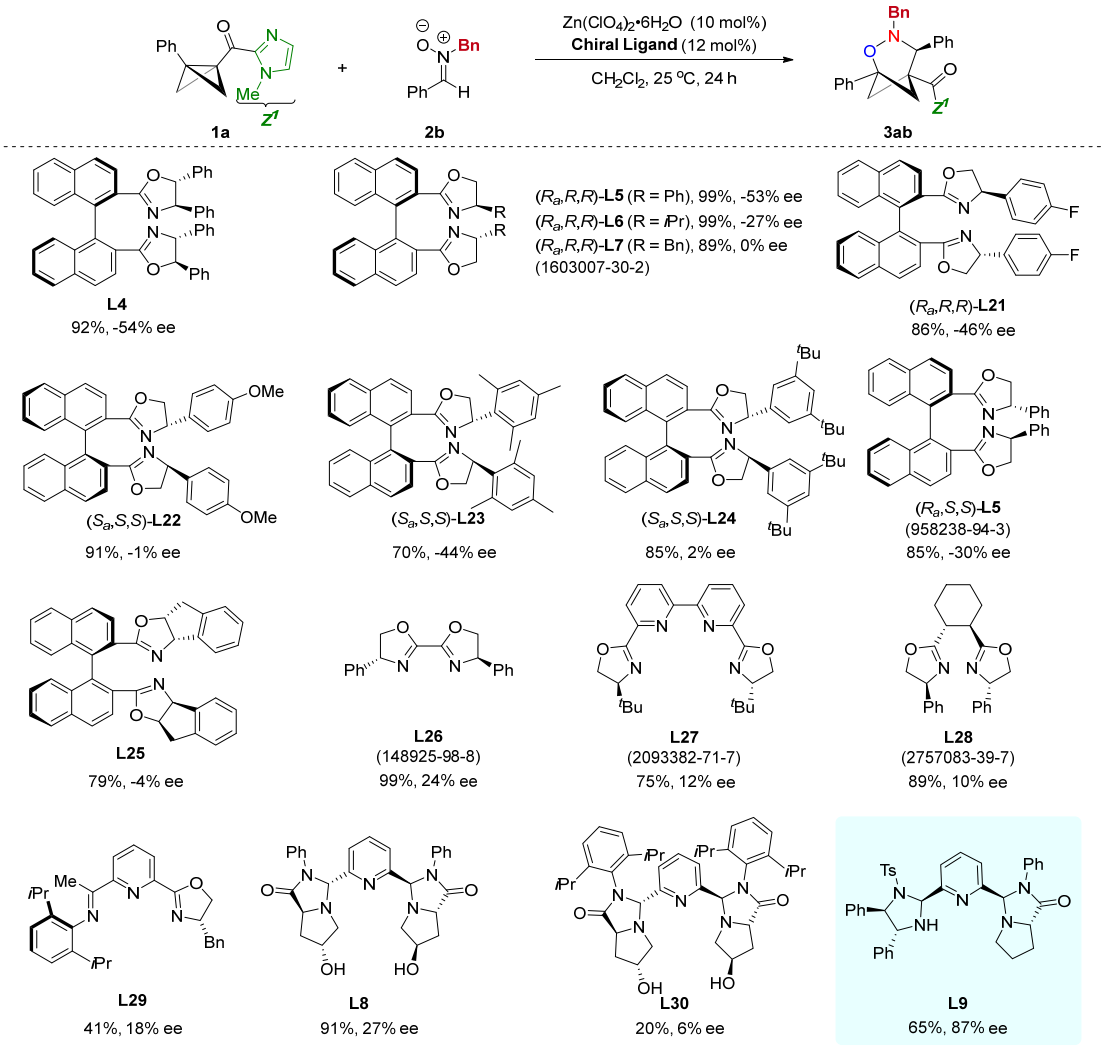
## 1.1 General Information

All reactions were performed in flame-dried glassware using conventional Schlenk techniques under a static pressure of nitrogen unless otherwise stated. Liquids and solutions were transferred with syringes. Bicyclo[1.1.0]butanes (BCBs)[1-4] and nitrones [5-6] were prepared according to reported procedures. $Co(OTf)_2$ (98%, *Bide* Chemical Company) and other commercially available reagents were purchased from *Leyan*, *Energy Chemical* and *Bide* Chemical Company and used as received. The solvents ($CH_2Cl_2$, 1,2-dichloroethane, $Et_2O$, THF and toluene *etc*.) were dried and purified following standard procedures. PhCl and Ethyl acetate (EtOAc) were purchased from *Energy Chemical* (99%, Extra Dry) and used as received. Technical grade solvents for extraction or chromatography (Petroleum ether, $CH_2Cl_2$, and ethyl acetate) were distilled prior to use. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 glass plates by *Merck*. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by *Grace* using the indicated solvents. $^1H$, $^{13}C$ NMR spectra were recorded in $CDCl_3$ on Bruker AV400 or 600 instruments. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent resonance as the internal standard ($CDCl_3$: δ = 7.26 ppm for $^1H$ NMR and $CDCl_3$: δ = 77.0 ppm for $^{13}C$ NMR). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplett, q = quartet, m = multiplet), coupling constants (Hz), and integration. The full-scan mass spectra were taken on a hybrid quadrupole-orbitrap mass spectrometer equipped with a heated electrospray ionization source (ThermoFischer Scientific, Bremen, Germany). Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel chiral columns at 35 $^oC$ and a mixture of HPLC-grade hexanes and isopropanol as eluent. Acknowledgement: the $^1H$, $^{13}C$ NMR spectra, single crystal X-ray diffraction and HRMS (ESI) were performed at Analytical Instrumentation Center of Hunan University. The absolute configuration was determined by single crystal X-ray diffraction analysis on Rigaku XtaLAB PRO MM003-DS dual system with a Cu micro-focus source. Diffraction data was collected at 173 K on a Rigaku XtaLAB PRO MM003-DS dual System with a Cu micro-focus source.

## 1.2 Optimization Study

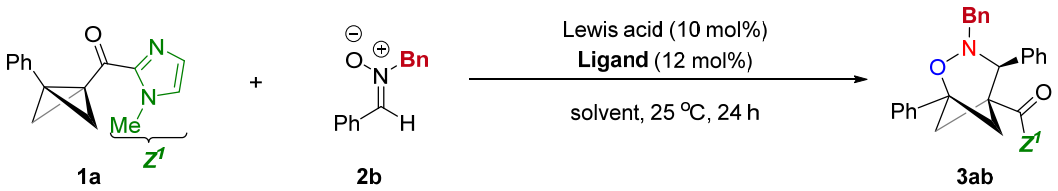



**Supplementary Figure 1.** Screening of chiral ligands for the enantioselective (3+3) cycloaddition of BCB **1a** and nitrone **2a**[a]. [a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv), **2a** (0.12 mmol, 1.2 equiv), Lewis acid (10 mol%) and Ligand (12 mol%), $CH_2Cl_2$ (2 mL), 25 °C, under $N_2$ for 24 h. The yields of **3aa** was determined by $^1H$ NMR with $CH_2Br_2$ as an internal standard. The *ee* value was determined by chiral HPLC with hexane/2-propanol. The CAS number of the ligand is in parentheses. [b] The ligands **L1-4** and **L13-19** were purchased from *Bide* Chemical Company and used as received.



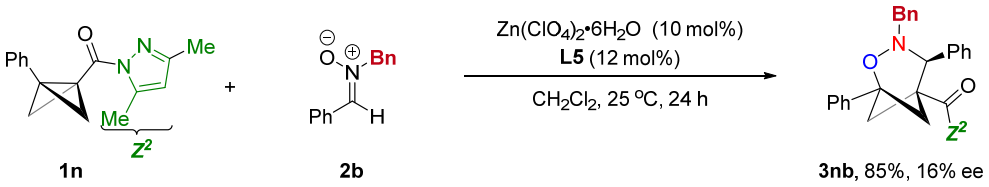

**Supplementary Figure 2.** Screening of chiral ligands for the enantioselective (3+3) cycloaddition of BCB **1a** and nitrone **2b**[a]. [a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv), **2b** (0.12 mmol, 1.2 equiv), $Zn(ClO_4)_2 \cdot H_2O$ (10 mol%) and Ligand (12 mol%), $CH_2Cl_2$ (2 mL), 25 °C, under $N_2$ for 24 h. The yields of **3ab** was determined by $^1H$ NMR with $CH_2Br_2$ as an internal standard. The ee value was determined by chiral HPLC with hexane/2-propanol. The CAS number of the ligand is in parentheses. [b] The ligands **L4-9** and **L22-28** were purchased from *Bide* Chemical Company and used as received. The ligands **L29** was synthesized according to the literature[7]. The ligands **L8** and **L30** were synthesized according to the literature[8]. The ligands **L9-12** were synthesized according to the literature[9-10]

**Supplementary Table 1.** Screening of Lewis acid and solvent for the enantioselective (3+3) cycloaddition of BCB **1a** and nitrone **2b**[a]

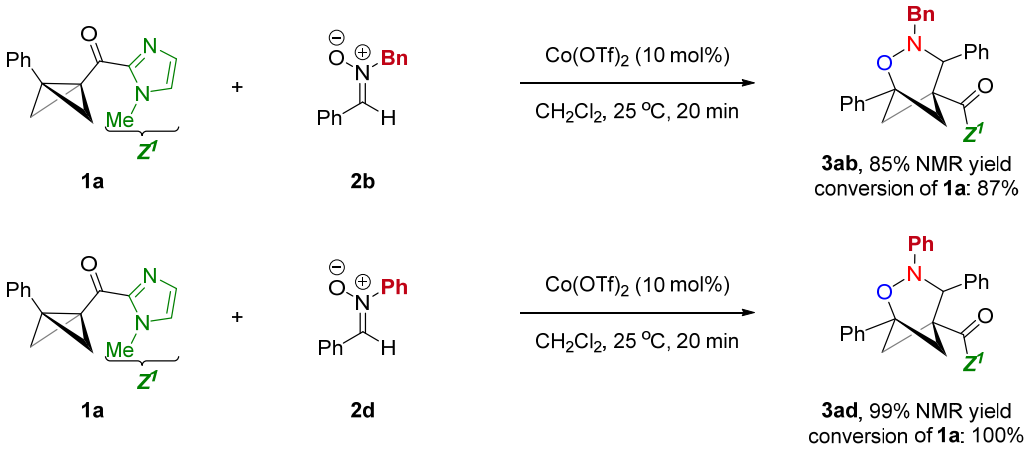



| Entry | Lewis acid | Ligand | solvent | Yield (%)[b] | *ee* (%)[c] |
|---|---|---|---|---|---|
| 1 | $Eu(OTf)_3$ | **L9** | $CH_2Cl_2$ | 90 | 2 |
| 2 | $Ga(OTf)_3$ | **L9** | $CH_2Cl_2$ | 99 | 0 |
| 3 | $Sc(OTf)_3$ | **L9** | $CH_2Cl_2$ | 66 | 17 |
| 4 | $Zn(OTf)_2$ | **L9** | $CH_2Cl_2$ | 51 | 90 |
| 5 | $Ni(OTf)_2$ | **L9** | $CH_2Cl_2$ | 95 | 80 |
| 6 | $Cu(OTf)_2$ | **L9** | $CH_2Cl_2$ | 89 | 65 |
| 7 | $Fe(OTf)_3$ | **L9** | $CH_2Cl_2$ | 84 | 14 |
| 8 | $Mg(OTf)_2$ | **L9** | $CH_2Cl_2$ | 45 | 23 |
| 9 | $Co(OTf)_2$ | **L9** | $CH_2Cl_2$ | 95 | 93 |
| 10 | $Co(OTf)_2$ | **L9** | EtOAc | 96 | 92 |
| 11 | $Co(OTf)_2$ | **L9** | toluene | 87 | 81 |
| 12 | $Co(OTf)_2$ | **L9** | THF | 82 | 91 |
| 13 | $Co(OTf)_2$ | **L9** | 1,4-dioxane | 92 | 84 |
| 14 | $Co(OTf)_2$ | **L9** | DCE | 93 | 91 |
| 15 | $Co(OTf)_2$ | **L9** | $CH_3CN$ | 60 | 59 |
| 16 | $Co(OTf)_2$ | **L9** | PhCl | 85 | 94 |
| 17 | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$ | 98 | 99 |
| 18[d] | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$ | 88 | 99 |
| 19[e] | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$ | 99 | 99 |
| 20 | $Co(OTf)_2$ | **L10** | $CHCl_3$ | 90 | 99 |
| 21 | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$:HFIP (3:1, v/v) | 15 | 96 |
| 22[f] | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$ | 99 | 97 |
| 23[g] | $Co(OTf)_2$ | **L10** | $CH_2Cl_2$ | 75 | 97 |
| 24 | $Co(OTf)_2$ | - | $CH_2Cl_2$ | 99 | - |
| 25 | - | **L10** | $CH_2Cl_2$ | No reaction | |
| 26 | - | - | $CH_2Cl_2$ | No reaction | |
| 27 | $Co(OTf)_2$ | *ent*-**L10** | $CH_2Cl_2$ | 98 | -99 |

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv), **2b** (0.12 mmol, 1.2 equiv), Lewis acid (10 mol%) and ligand (12 mol%), solvent (2 mL), 25 °C, under $N_2$ for 24 h. [b] Determined by $^1H$ NMR with $CH_2Br_2$ as an internal standard. [c] Determined by chiral HPLC with hexane/2-propanol. [d] At 0 °C. [e] At 40 °C. [f] 4 ÅMS (50 mg) was added. [g] $H_2O$ (5 μL) was added.

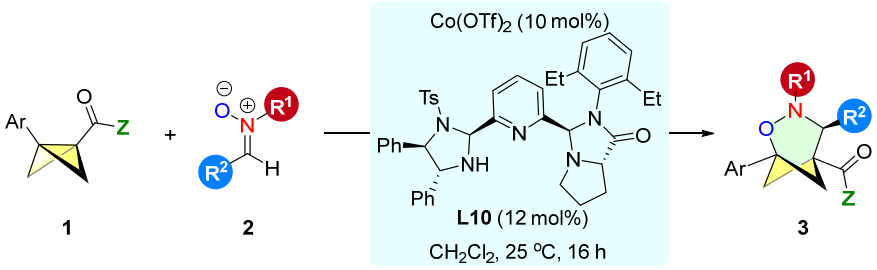



**Supplementary Figure 3.** Enantioselective cycloaddition of BCB **1n** and nitrone **2b**[a]. [a] Reaction conditions: **1n** (0.10 mmol, 1.0 equiv), **2b** (0.12 mmol, 1.2 equiv), $Zn(ClO_4)_2 \cdot H_2O$ (10 mol%) and **L5** (12 mol%), $CH_2Cl_2$ (2 mL), 25 °C, under $N_2$ for 24 h. The yield of **3nb** was determined by $^1H$ NMR with $CH_2Br_2$ as an internal standard. The *ee* value was determined by chiral HPLC with hexane/2-propanol.



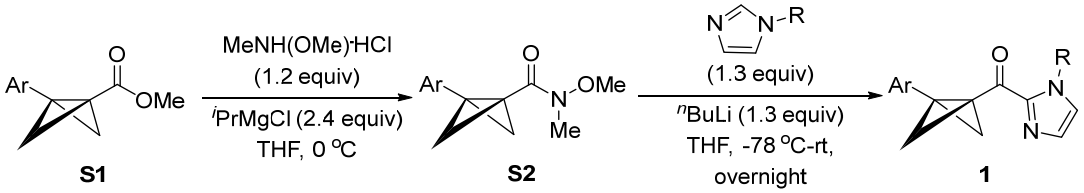

**Supplementary Figure 4.** Influence of $R^1$ substituents in nitrones on background reaction [a]. [a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv), **2b** or **2d** (0.12 mmol, 1.2 equiv), $Co(OTf)_2$ (10 mol%), $CH_2Cl_2$ (2 mL), 25 °C, under $N_2$ for 20 min. The yields of **3ab** or **3ad** were determined by $^1H$ NMR with $CH_2Br_2$ as an internal standard.

## 1.3 General Procedure for the Enantioselective (3+3) Cycloadditions (GP1)




Under an atmosphere of $N_2$, to a 25 mL oven-dried Schlenk tube were added $Co(OTf)_2$ (7.1 mg, 0.020 mmol) and **L10** (17.1 mg, 0.024 mmol), followed by 2.0 mL of anhydrous $CH_2Cl_2$. The solution was stirred at 25 °C for 0.5 h, and then the BCBs **1** (0.20 mmol, 1.0 equiv) and nitrones **2** (0.24 mmol, 1.2 equiv) were added. Then the resulting mixture was stirred at room temperature for 16 h till full conversion of **1** by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using PE/EtOAc (4:1, v/v) as the eluent, to afford the desired product **3**.

## 1.4 General Procedure for the Synthesis of New Bicyclobutanes (GP2)



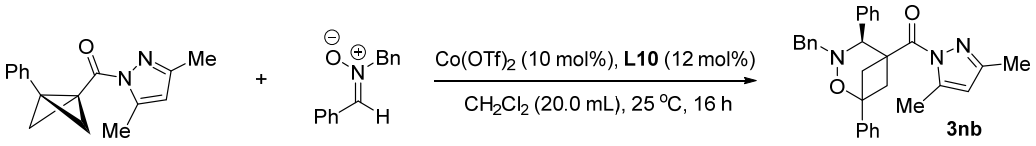

BCB esters **S1** were prepared according to literature procedures.[1-4] Weinreb amide derived BCBs **S2** were synthesized as following: An oven-dried 100 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with $N_2$ (x 3) and capped with a septum, BCB esters **S1** (5.00 mmol, 1.0 equiv) and THF (25.0 mL) were added. The reaction was cooled to 0 °C. MeNH(OMe)·HCl (585.0 mg, 6.00 mmol, 1.2 equiv) and $^{i}$PrMgCl (6.0 mL, 2.0 M in THF, 12.00 mmol, 2.4 equiv) were sequentially added to the solution. After stirred at the same temperature for 12 h, the reaction was quenched by saturated $NH_4Cl$ solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (25 mL),

dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The crude Weinreb amide derived BCBs **S2** was directly used in next reaction.

An oven-dried 100 mL round bottom flask equipped with a stir bar was cooled under vacuum. After backfilled with $N_2$ (x 3) and capped with a septum, *N*-substituted imidazole derivatives (6.50 mmol, 1.3 equiv) and THF (20.0 mL) were added. The reaction was cooled to -78 °C. $^n$BuLi (2.6 mL, 2.5 M in THF, 6.50 mmol, 1.3 equiv) was added to the solution. After stirred at the same temperature for 20 min, **S2** dissolved in THF (5.0 mL) was added. Next, the reaction was warm to room temperature and stirred overnight. Then, the reaction was quenched by saturated $NH_4Cl$ solution (20 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 5/1) to afford a new kind of BCB **1**.

**NOTE:** the bicyclo[1.1.0]butanes (**1n-p**) equipped with an acyl pyrazole group were synthesized according to the literature[11-12].

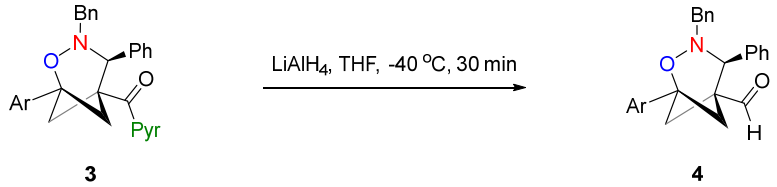
## 1.5 Scale-Up Experiment




Under an atmosphere of $N_2$, to a 100 mL oven-dried Schlenk tube were added $Co(OTf)_2$ (35.7 mg, 0.10 mmol, 10 mol%) and **L10** (85.0 mg, 0.12 mmol, 12 mol%), followed by 20.0 mL of anhydrous $CH_2Cl_2$. The solution was stirred at 25 °C for 0.5 h. Then the BCB **1n** (252.0 mg, 1.00 mmol, 1.0 equiv) and nitrone **2b** (253.2 mg, 1.20 mmol, 1.2 equiv) were added. The resulting mixture was stirred at room temperature for 16 h till full conversion of **1n** by TLC analysis. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography

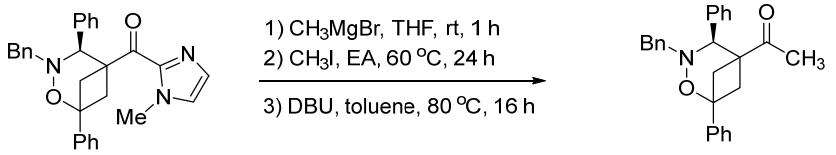
purification using PE/EtOAc (20:1, v/v) as the eluent, to afford the desired product **3nb** (458.4 mg, 99% yield, 99% ee).

## 1.6 Synthetic Transformations




**3** **4**

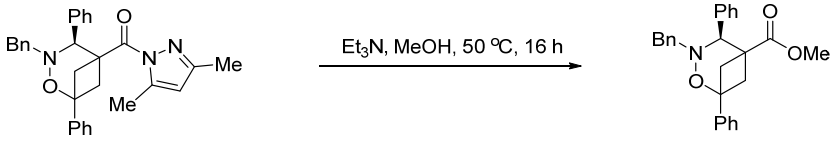
**General Procedure for the conversion of 3nb or 3qb to aldehyde (GP3):** The solution of $LiAlH_4$ (5.7 mg, 0.15 mmol, 1.5 equiv) in THF (2.0 mL) was cooled to -40 °C, and then a solution of **3** (0.10 mmol, 1.0 equiv) in THF (1.0 mL) was charged into the solution at -40 °C. After TLC analysis showed the starting material was consumed (30 min), HCl (aq. 1.0 M) was added at -40 °C and stirred for 15 min. The reaction mixture was directly filtered through celite, washed and extracted with EtOAc. The mixture was extracted with EtOAc (3 × 5 mL). Filtered and concentrated on rotavapor under reduced pressure. The residue was purification by flash chromatography on silica gel using petroleum ether/ethyl acetate (10/1) to afford **4** as a colorless oil.




**3ab** **5,** 75% yield, 99% ee

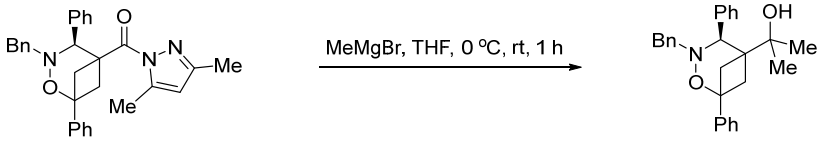
**Synthesis of (5):** In a flame dried Schlenk flask, MeMgBr (3.0 M in $Et_2O$, 0.1 mL, 0.30 mmol, 3.0 equiv) was added portionwise to a solution of the **3ab** (44.9 mg, 0.10 mmol, 1.0 equiv) in dry THF (1.0 mL) at room temperature. The reaction was stirred for 1 hours, and monitored by TLC. Then aqueous saturated $NH_4Cl$ solution (5 mL) was added to quench the reaction. The solution was extracted with ethyl acetate, washed with brine, dried over $Na_2SO_4$, filtered and concentrated on rotavapor under reduced pressure. The intermediate was dissolved with dry ethyl acetate (2.0 mL) and MeI (141.9 mg, 1.00 mmol, 10.0 equiv) was added. The reaction was heated at 60°C for 24 hours. And then, it was cooled down to room temperature and concentrated to

dryness. The residue was taken up in dry toluene (1.0 mL) and DBU (106.4 mg, 0.70 mmol, 7.0 equiv) was added. The mixture was heated at 80°C for 16 hours. The crude residue was purified by silica gel column chromatography (PE/EtOAc = 5:1) to afford **5** (28.7 mg, 75%, 99% ee) as a colorless oil.



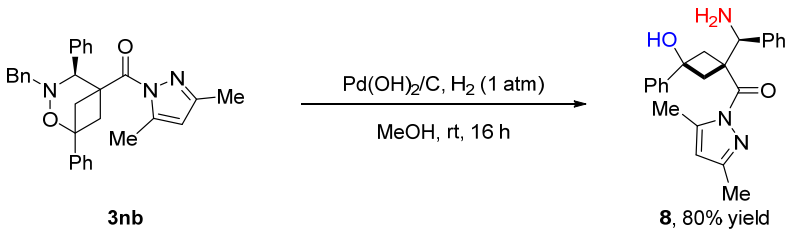

**3nb** **6**, 99% yield, 99% ee

**Synthesis of (6):** To a solution of **3nb** (46.3 mg, 0.10 mmol, 1.0 equiv) in MeOH (2.0 mL) was added $Et_3N$ (30 μL, 0.40 mmol, 2.0 equiv). The mixture was then stirred at 50 °C for 16 hour, and monitored by TLC. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification (PE/EtOAc = 20:1) as the eluent to afford **6** (41.0 mg, 99% yield, 99% ee) as a colorless oil.

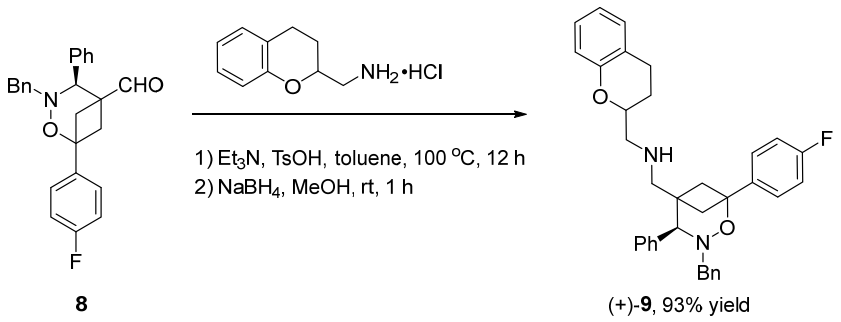



**3nb** **7,** 80% yield, 98% ee

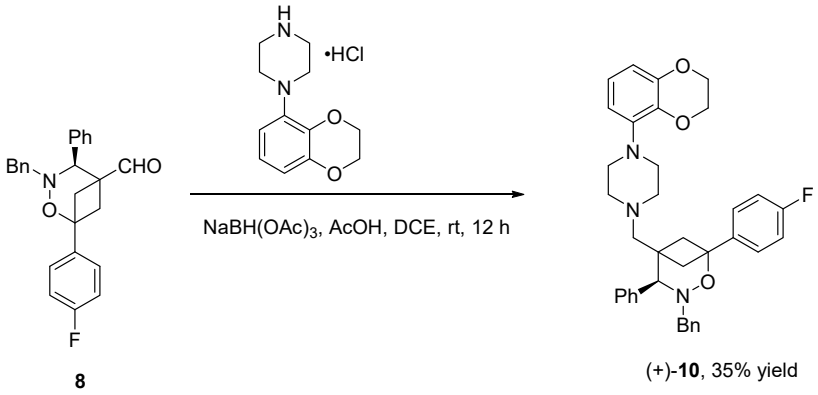
**Synthesis of (7):** In a flame dried Schlenk flask, **3nb** (46.3 mg, 0.10 mmol, 1.0 equiv) was stirred in anhydrous THF (2.0 mL). The solution was cooled to 0 °C and MeMgBr (3.0 M in $Et_2O$, 0.1 mL, 0.30 mmol, 3.0 equiv) was added slowly. And then the reaction was stirred at room temperature for 1 hour. Finally, aqueous saturated $NH_4Cl$ solution (2.0 mL) was added to quench the reaction. The mixture was extracted with EtOAc (3 × 5 mL). Filtered and concentrated on rotavapor under reduced pressure. The residue was purification by flash chromatography on silica gel using petroleum ether/ ethyl acetate (10/1) to afford **7** as a colorless oil (32.0 mg, 80% yield, 98% ee).



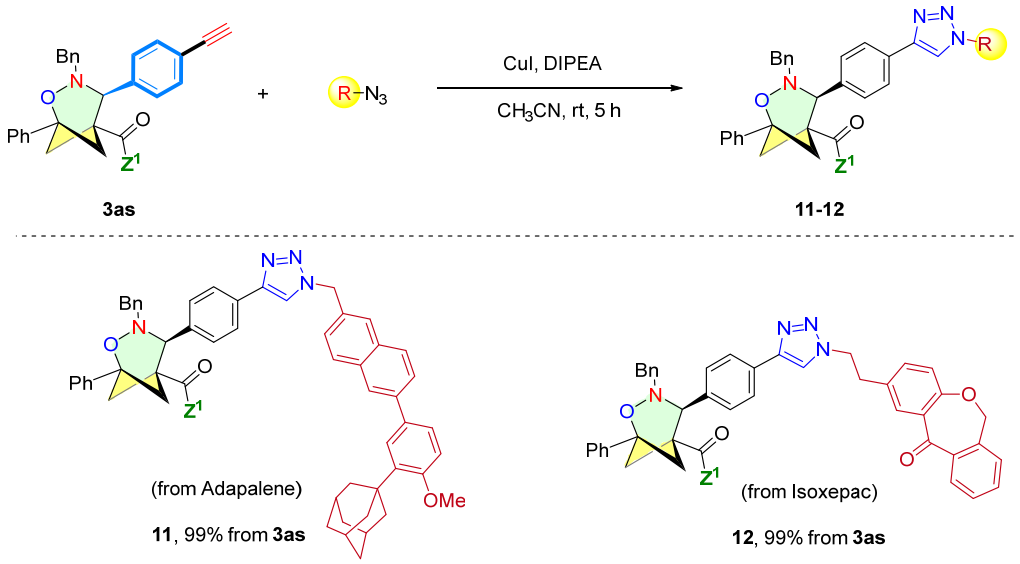

**Synthesis of (8):** To a solution of **3nb** (23.2 mg, 0.05 mmol, 1.0 equiv) in MeOH (5.0 mL) was added $Pd(OH)_2/C$ (10 wt%) (5.0 mg). This flask was in a vacuum and back-filled with $H_2$ (1 atm). After being stirred at room temperature for 16 hour, the reaction solution was filtered, and the filtered-cake was washed with EtOAc (5.0 mL). The filtrate was evaporated under vacuo, and purified by silica gel column chromatography using petroleum ether/ethyl acetate (2/1) as the eluent to give the product **8** in 80% yield (15.0 mg). $[\alpha]_D^{20}$ = +32.7 (*c* = 0.30, $CHCl_3$). The enantiomeric excess could not be determined using HPLC analysis with chiral stationary phases in our laboratory.




**Synthesis of (9):** To the solution of chroman-2-ylmethanamine hydrochloride (15.0 mg, 0.075 mmol) in toluene (1.0 mL) was added $Et_3N$ (7.6 mg, 0.075 mmol), and the mixture was stirred at 35 °C for 30 min. **8** (16.0 mg, 0.04 mmol), 4 Å MS (50 mg) and $TsOH \cdot H_2O$ (11.9 mg, 0.06 mmol) was added to the solution, and the mixture was stirred at 100 °C for 16 h. Then, the mixture was cooled to 0 °C. MeOH (1.0 mL) and $NaBH_4$ (2.3 mg, 0.06 mmol) was added to the solution, and the mixture was stirred for 1 h at room temperature. The resulting solution was quenched with $H_2O$ and extracted with EtOAc (3 × 5 mL). Filtered and concentrated on rotavapor under reduced pressure. The residue was purification by flash chromatography on silica gel using petroleum ether/ethyl acetate (3/1) to afford **9** as a colorless oil (20.0 mg, 93% yield).




**Synthesis of (10):** **8** (19.4 mg, 0.05 mmol) and 1-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)piperazine hydrochloride (12.9 mg, 0.05 mmol) were mixed in 1,2-dichloroethane (2 mL) and treated with $NaBH(OAc)_3$ (15.9 mg, 0.075 mmol) and HOAc (20 μL) under an atmosphere of argon. The reaction mixture was stirred at room temperature for 12 h. The resulting solution was quenched with 2 N NaOH (2.0 mL) and extracted with EtOAc (3 × 5 mL). Filtered and concentrated on rotavapor under reduced pressure. The residue was purification by flash chromatography on silica gel using petroleum ether/ethyl acetate (10/1) to afford **10** as a colorless oil (10.4 mg, 35% yield).

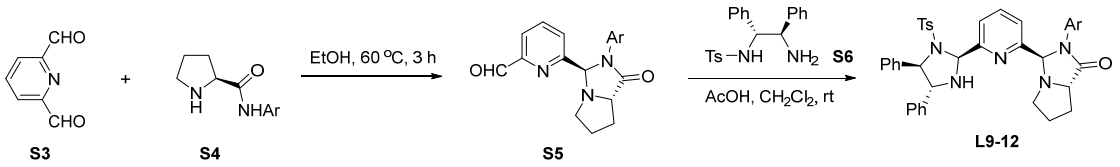



**General Procedure for Copper-Catalyzed Alkyne–Azide Cycloaddition (GP4):** A Schlenk tube is charged with **3as** (20.0 mg, 0.04 mmol, 1.0 equiv), CuI (0.8 mg, 0.004 mmol, 10 mol%), DIPEA (5.4 mg, 0.04 mmol, 1.0 equiv) and $CH_3CN$ (1.0 mL). Then azide compounds (0.06 mmol, 1.5 equiv) was added. The reaction mixture is stirred at

room temperature for 5 h. The mixture is then concentrated under reduced pressure, and purified by silica gel column chromatography to give the product **11-12**.

## 1.7 General Procedure for the Synthesis of Chiral Ligands

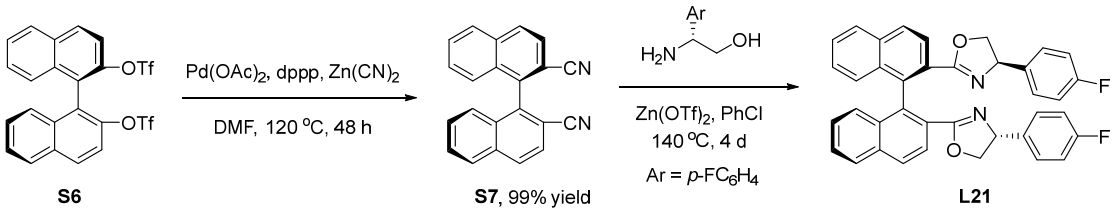
### 1.7.1 The synthesis of L9-12 (GP5)




To the solution of pyridine-2,6-dicarbaldehyde (2.70 g, 20 mmol, 2.0 equiv) in anhydrous ethanol (40 mL) was added *L*-prolinamides (10 mmol, 1.0 equiv), and the reaction was heated and stirred at 60 °C for 3 h. After that, the reaction mixture was concentrated in vacuo to remove ethanol. The residue was purified by flash column chromatography (PE/EtOAc, 10/1-1/1, v/v) to give compounds **S5**.

In a round-bottomed flask containing a stir bar, compound **S5** (6.9 mmol, 1,0 equiv), **S6** (6.9 mmol, 1.0 equiv) AcOH (0.6 mL, 10.5 mmol, 1.5 equiv) and $CH_2Cl_2$ (70 mL) were added. Then, the reaction was stirred at room temperature for 6-8 h. After that, the reaction mixture was quenched by saturated $NaHCO_3$ solution (20 mL). The organic layer was extracted with $CH_2Cl_2$ (3 × 20 mL). Filtered and concentrated on rotavapor under reduced pressure. The resulting residue was purified by silica gel column chromatography to give ligands **L9-12**.

### 1.7.2 The synthesis of L21



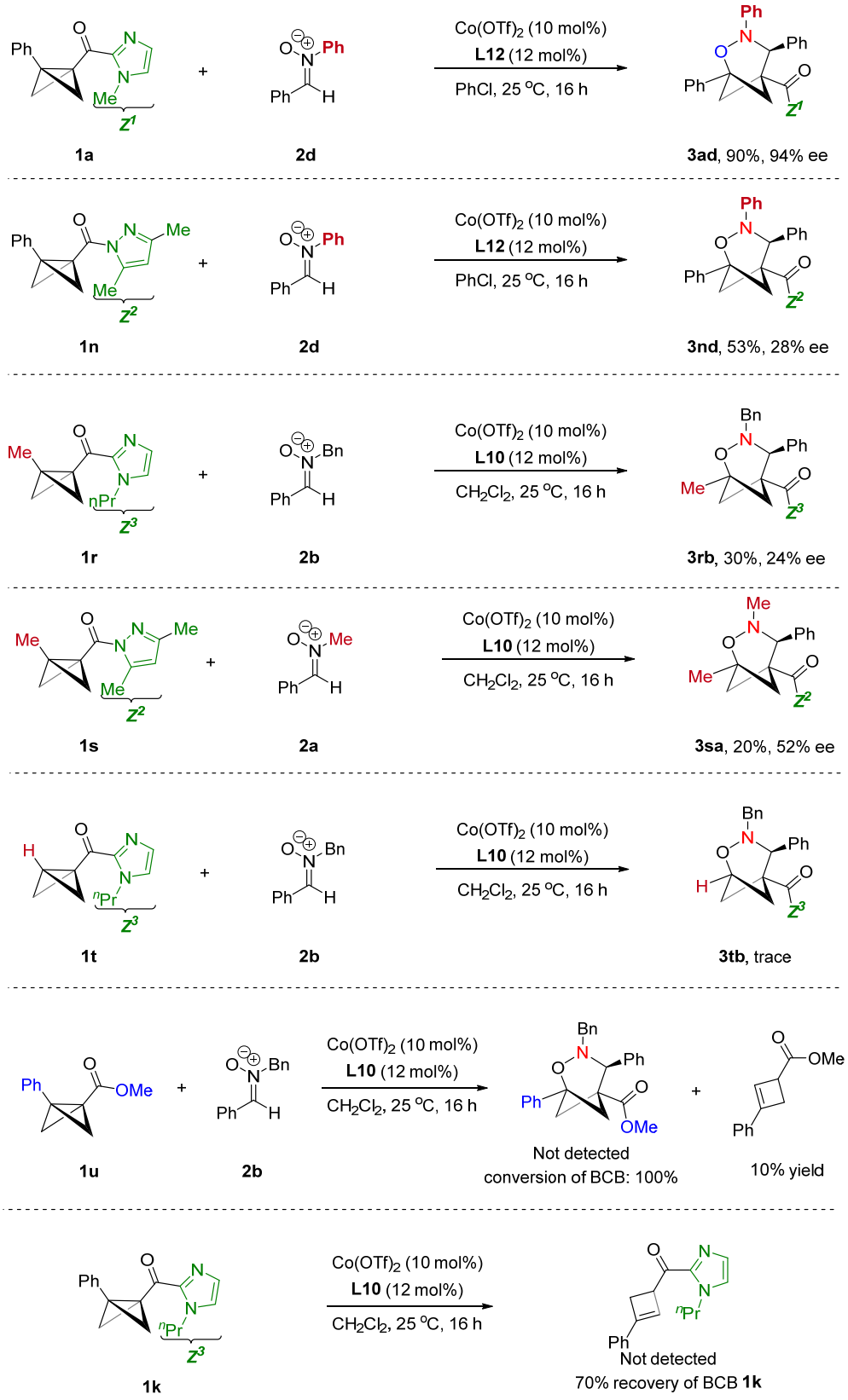
To the solution of BINOL-bistriflate **S6** (2.75 g, 5.0 mmol, 1.0 equiv) in DMF (20 mL) was added $Pd(OAc)_2$ (56.5 mg, 0.25 mmol, 5 mol%), dppp (162.0 mg, 0.5 mmol, 10 mol%) and $Zn(CN)_2$ (292.5 mg. 2.5 mmol, 5.0 equiv). Then the reaction was heated and stirred at 120 °C for 48 h. After the reaction was cooled to room temperature, the reaction mixture was diluted with ethyl acetate, and washed with $H_2O$ and brine. The mixture was then dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was further purified by flash chromatography (PE/EtOAc, 10/1, v/v) to give compounds **S7** (1.50 g, 99% yield).

To a 25 mL sealed tube were added $ZnCl_2$ (204.0 mg, 1.5 mmol, 5.0 equiv), **S7** (100.0 mg, 0.3 mmol, 1.0 equiv) and PhCl (3 mL). After the reaction mixture was stirred at room temperature for 10 min, (*R*)-2-amino-2-(4-fluorophenyl)ethan-1-ol (232.5 mg, 1.5 mmol, 5.0 equiv) was added to the tube. This tube was sealed and the reaction mixture was stirred at 120 °C for 4 days. The mixture was cooled to room temperature. $Et_2NH$ (1 mL) was added to the tube, and the mixture was stirred at room temperature for 1.0 h. The residue was further purified by flash chromatography (PE/EtOAc, 4/1, v/v) to give ligand **L21** as a colorless oil (69.6 mg, 40% yield).

## 2. Supplementary Discussion

### 2.1 Unsuccessful BCB Substrates and Control Experiments

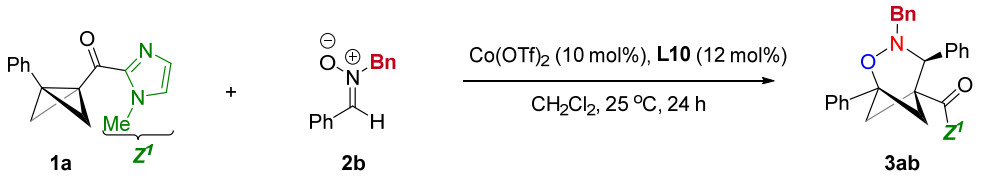
*The (3+3) reaction of **2n** with N-phenyl nitrone **2d** yields the desired **3nd** with 28% ee. In contrast, the cycloaddition of **1a** and **2d** produces **3ad** with 94% ee under identical reaction conditions. Unfortunately, the current reaction did not apply to methyl-substituted BCB substrate **1r** and mono-substituted BCB substrate **1t.** The ester-substituted BCB **1u** was used in the (3+3) cycloaddition but did not produce any cycloadduct, indicating that the chelation of bidentate group to Lewis acid catalyst is essential. In the absence of nitrone, the reaction of BCB 1k resulted in a 70% recovery of the starting material with no detectable cyclobutene, potentially excluding the presence of carbocation species.*




**Supplementary Figure 5.** Comparison of BCB with an acyl imidazole group and BCB with an acyl pyrazole moiety in stereocontrol and unsuccessful BCB substrates.

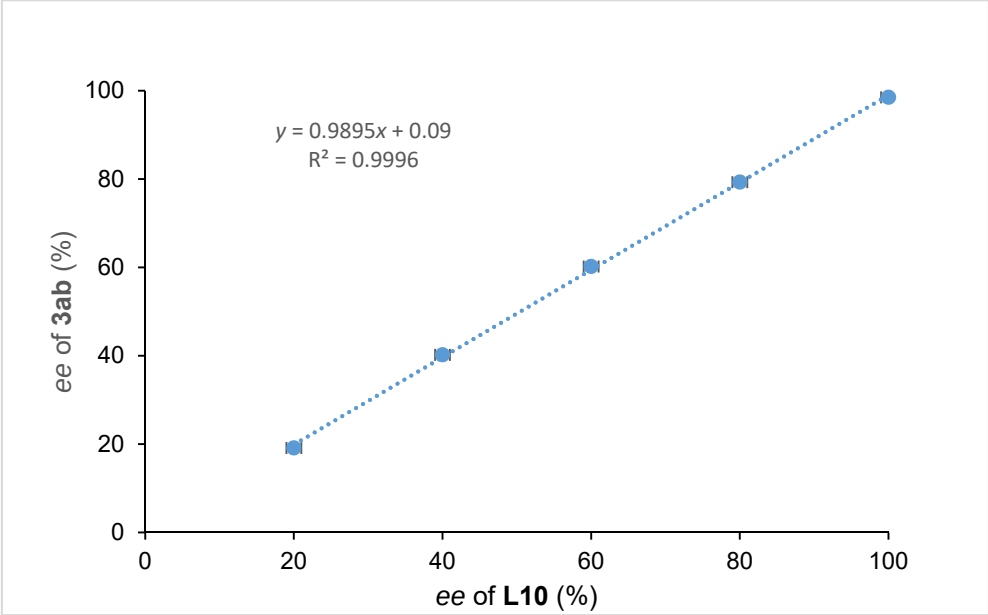
## 2.2 Non-Linear Effect Study

**Supplementary Table 2.** Tabulation of non-linear effects[a]



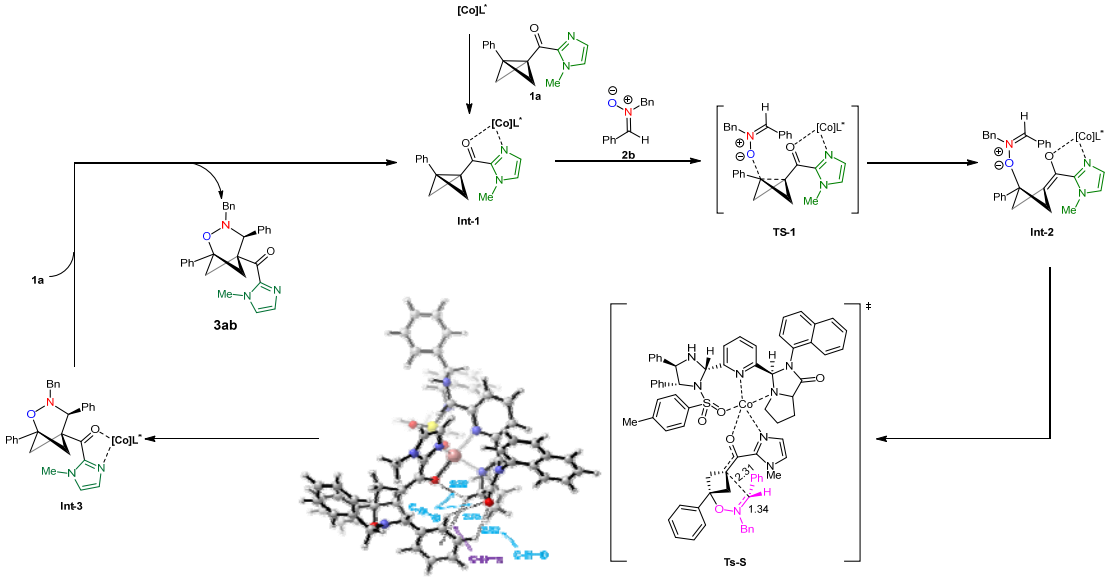

| Entry | **L10** ee (%)[b] | Product **3ab** ee (%) [b] | | | |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | average value |
| 1 | 20 | 19.0 | 19.1 | 19.1 | 19.1 |
| 2 | 40 | 40.4 | 40.1 | 40.2 | 40.2 |
| 3 | 60 | 60.2 | 60.4 | 60.0 | 60.2 |
| 4 | 80 | 79.2 | 79.4 | 79.2 | 79.3 |
| 5 | 100 | 98.5 | 98.6 | 98.5 | 98.5 |

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv), **2b** (0.12 mmol, 1.2 equiv), $Co(OTf)_2$ (10 mol%) and **L10** (12 mol%), $CH_2Cl_2$ (2 mL), 25 °C, under $N_2$ for 24 h. [b] Determined by chiral HPLC with hexane/2-propanol.




**Supplementary Figure 6**. Non-linear effect study.

## 2.3 Proposed Catalytic Cycle and Computed Transition Structures



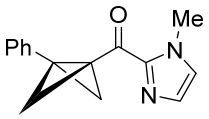

**Supplementary Figure 7.** Proposed catalytic cycle

To unravel the origin of enantiocontrol, density functional theory (DFT) calculations were performed at PBE0/6-31G(d)-SDD level of theory, using **1a** and **2b** as the model substrates along with the Co(II)−**L12** chiral system. As shown in Fig. 6 in the main text, transition states **Ts-S** and **Ts-R** leading to both products were located, in which divalent Co coordinated with two nitrogen and one oxygen atoms of **L12** as well as one oxygen and nitrogen atoms of **1a**, generating a square pyramidal geometry. The difference between the two activation barriers of the intramolecular nucleophilic cyclization for the two enantiomers was 2.2 kcal/mol, consistent with the excellent enantioselectivity experimentally observed. Moreover, noncovalent interactions between reactant fragment and **L12** in **Ts-S** and **Ts-R** were explored using independent gradient model based on Hirshfeld partition (IGMH) analysis. Three pairs of C–H•••O interaction existed in both **Ts-S** and **Ts-R**. Notably, in the favored transition state **Ts-S**, imidazolidone of **L12** engaged in C–H…π interaction with phenyl group of nitrone **2a**, likely dominating the preference for the nucleophilic attack of the enolate on the *Re*-face of nitrone **2a** to furnish the (*S*)-configuration of product **3ab**.

Based on the work of Deng[6], Xie, and Guo[5], as well as our DFT calculations, we have proposed a plausible catalytic cycle for the current (3+3) reaction. Initially, the

chiral Co(II)/**L12** catalyst coordinates with the acyl imidazole moiety, activating BCB **1a**. Subsequently, the concerted nucleophilic ring-opening pathway of **1a** with **2b** generates the key intermediate **int-2**. The carbanion is then generated in situ to attack the *Re* face of the C=N double bond in the nitrone via **Ts-S**, leading to the formation of **int-2**. Finally, ligand exchange releases the desired (*S*)-**3ab** and generates **int-1**.

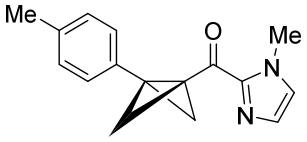
## 2.4 Characterization Data of the New BCBs and Products




**1a**
$C_{15}H_{14}N_2O$
M = 238.29 g/mol

**(1-methyl-1*H*-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone**: (**1a**) Prepared from methyl-3-phenylbicyclo[1.1.0]butane-1-carboxylate (1.88 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1a** as a white solid (1.53 g, 64% yield over 2 steps).

**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.28-7.26 (m, 2H), 7.24-7.16 (m, 3H), 7.07 (s, 1H), 6.85 (s, 1H), 3.63 (s, 2H), 3.60 (s, 3H), 1.90 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.7, 143.4, 133.3, 128.7, 128.2, 127.0, 126.0, 125.7, 40.4, 38.0, 35.7, 32.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{15}N_2O$: 239.1179; found: 239.1179.

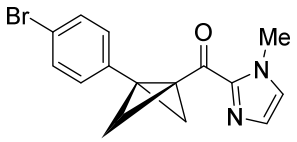



**1b**
$C_{16}H_{16}N_2O$
M = 252.32 g/mol

**(1-methyl-1*H*-imidazol-2-yl)(3-(*p*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone**: (**1b**) Prepared from methyl 3-(*p*-tolyl)bicyclo[1.1.0]butane-1-carboxylate (0.94 g, 5.00 mmol, 1.0 equiv)

according to the **GP2**. Purification by flash chromatography on silica gel afforded **1b** as a white solid (0.76 g, 60% yield over 2 steps).

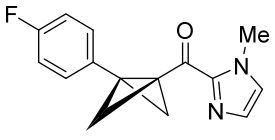
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.16 (d, *J* = 7.6 Hz, 2H), 7.07 (s, 1H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.85 (s, 1H), 3.61 (s, 5H), 2.27 (s, 3H), 1.88 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.8, 143.4, 136.8, 130.0, 129.0, 128.6, 125.9, 125.7, 41.0, 38.0, 35.7, 32.8, 21.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O$: 253.1335; found: 253.1334.




**1c**
$C_{15}H_{13}BrN_2O$
M = 317.19 g/mol

**(3-(4-bromophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone**: (**1c**)
Prepared from methyl 3-(4-bromophenyl)bicyclo[1.1.0]butane-1-carboxylate (1.34 g, 5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1c** as a white solid (0.79 g, 50% yield over 2 steps).

**$R_f$** = 0.30 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.07 (s, 1H), 6.89 (s, 1H), 3.69 (s, 3H), 3.62 (s, 2H), 1.88 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.1, 143.2, 132.7, 131.4, 128.8, 127.6, 126.0, 120.9, 39.4, 38.0, 36.0, 33.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{14}BrN_2O$: 317.0284; found: 317.0282.

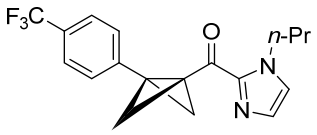



**1d**
$C_{15}H_{13}FN_2O$
M = 256.28 g/mol

**(3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**1d**)
Prepared from methyl 3-(4- fluorophenyl)bicyclo[1.1.0]butane-1-carboxylate (1.03 g,

5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1d** as a white solid (0.64 g, 50% yield over 2 steps).

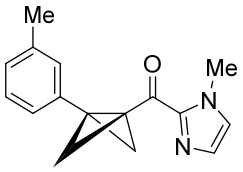
**$R_f$** = 0.30 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.27-7.23 (m, 2H), 7.07 (s, 1H), 6.94-6.88 (m, 3H), 3.68 (s, 3H), 3.61 (s, 2H), 1.89 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.4, 162.1 (d, *J* = 245 Hz), 143.4, 129.2 (d, *J* = 3 Hz), 128.9, 127.6 (d, *J* = 8 Hz), 125.9, 115.3 (d, *J* = 22 Hz), 39.7, 38.1, 35.9, 32.5 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.956 ppm. **HRMS** (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{15}H_{17}N_3O$: 274.1350; found: 274.1358.




**1e**
$C_{18}H_{17}F_3N_2O$
M = 334.13 g/mol

**(1-propyl-1H-imidazol-2-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl) methanone:** (**1e**)
Prepared from methyl 3-(4-(trifluoromethyl)phenyl) bicycle [1.1.0] butane-1-carboxylate (1.28 g, 5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1e** as a white solid (0.71 g, 52% yield over 2 steps).

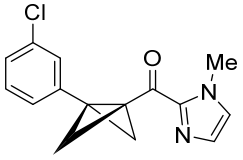
**$R_f$** = 0.36 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.09 (s, 1H), 6.92 (s, 1H), 4.07 (t, *J* = 7.2 Hz, 2H), 3.68 (s, 2H), 1.95 (s, 2H), 1.19 (q, *J* = 7.2 Hz, 2H), 0.53 (t, *J* = 7.6 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 184.8, 142.4, 138.1, 128.8 (q, *J* = 30 Hz), 125.7, 125.4, 125.2 (q, *J* = 4 Hz), 122.7, 123.4 (q, *J* = 70 Hz), 50.0, 38.2, 38.1, 33.8, 24.1, 10.5 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.539 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{18}F_3N_2O$: 335.1366; found: 335.1376.




**1f**
$C_{16}H_{16}N_2O$
M = 252.32 g/mol

**(1-methyl-1*H*-imidazol-2-yl)(3-(*m*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone**: (**1f**) Prepared from methyl 3-(*m*-tolyl)bicyclo[1.1.0]butane-1-carboxylate (1.01 g, 5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1f** as a white solid (0.50 g, 40% yield over 2 steps).

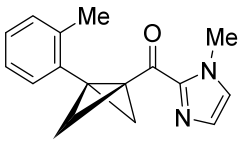
**$R_f$** = 0.25 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.11-7.04 (m, 4H), 6.98 (d, *J* = 6.8 Hz, 1H), 6.84 (s, 1H), 3.61 (s, 3H), 3.60 (s, 2H), 2.25 (s, 3H), 1.87 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.8, 143.4, 137.8, 133.1, 128.6, 128.1, 127.8, 126.8, 125.6, 123.0, 40.6, 38.0, 35.7, 32.8, 21.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O$: 253.1335; found: 253.1334.




**1g**
$C_{15}H_{13}ClN_2O$
M = 272.73 g/mol

**(3-(3-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1*H*-imidazol-2-yl)methanone**: (**1g**) Prepared from methyl 3-(3-chlorophenyl)bicyclo[1.1.0]butane-1-carboxylate (1.11 g, 5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1g** as a white solid (0.59 g, 43% yield over 2 steps).

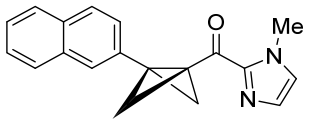
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.25 (s, 1H), 7.16-7.13 (m, 3H), 7.09 (s, 1H), 6.89 (s, 1H), 3.69 (s, 3H), 3.61 (s, 2H), 1.88 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.1, 143.2, 135.8, 134.2, 129.4, 128.8, 127.0, 126.2, 126.0, 124.2, 38.9, 38.0, 35.9, 33.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{14}ClN_2O$: 273.0789; found: 273.0787.




**1h**
$C_{16}H_{16}N_2O$
M = 252.32 g/mol

**(1-methyl-1*H*-imidazol-2-yl)(3-(*o*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone**: (**1h**) Prepared from methyl methyl 3-(*o*-tolyl)bicyclo[1.1.0]butane-1-carboxylate (0.61 g, 3.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1h** as a white solid (0.45 g, 59% yield over 2 steps).

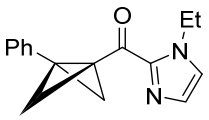
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.12-7.05 (m, 3H), 7.01-6.96 (m, 2H), 6.93 (s, 1H), 3.85 (s, 3H), 3.35 (s, 2H), 2.44 (s, 3H), 1.94 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 186.8, 143.7, 138.7, 132.3, 130.7, 128.8, 127.1, 126.0, 125.8, 125.6, 41.3, 38.6, 36.1, 30.3, 20.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O$: 253.1335; found: 253.1335.




**1i**
$C_{19}H_{16}N_2O$
M = 288.35 g/mol

**(1-methyl-1*H*-imidazol-2-yl)(3-(naphthalen-2-yl)bicyclo[1.1.0]butan-1-yl)methanone**: (**1i**) Prepared from methyl 3-(naphthalen-2-yl)bicyclo[1.1.0]butane-1-carboxylate (1.19 g, 5.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1i** as a white solid (0.72 g, 50% yield over 2 steps).

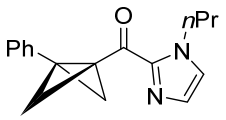
**$R_f$** = 0.30 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.44-7.36 (m, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.07 (s, 1H), 6.79 (s, 1H), 3.77 (s, 2H), 3.53 (s, 3H), 1.96 (s, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.4, 143.4, 133.2, 132.4, 131.1, 128.7, 127.8, 127.6, 127.5, 126.2, 125.8, 125.7, 125.6, 123.5, 40.8, 38.2, 35.8, 33.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{17}N_2O$: 289.1335; found: 289.1331.




**1j**
$C_{16}H_{16}N_2O$
M = 252.13 g/mol

**(1-ethyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone:** (**1j**) Prepared from methyl-3-phenylbicyclo[1.1.0]butane-1-carboxylate (1.88 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1j** as a white solid (1.35 g, 62% yield over 2 steps).

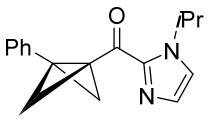
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.28-7.24 (m, 2H), 7.20 (t, *J* = 7.2 Hz, 2H), 7.16-7.12 (m, 1H), 7.08 (s, 1H), 6.91 (s, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.63 (s, 2H), 1.91 (s, 2H), 0.94 (t, *J* = 7.2 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.5, 142.5, 133.3, 128.8, 128.2, 126.9, 125.8, 124.1, 43.3, 40.1, 37.9, 33.0, 16.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{17}N_2O$: 253.1335; found: 253.1332.




**1k**
$C_{17}H_{18}N_2O$
M = 266.34 g/mol

**(3-phenylbicyclo[1.1.0]butan-1-yl)(1-propyl-1H-imidazol-2-yl)methanone**: (**1k**) Prepared from methyl-3-phenylbicyclo[1.1.0]butane-1-carboxylate (1.88 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1k** as a white solid (1.47 g, 55% yield over 2 steps).

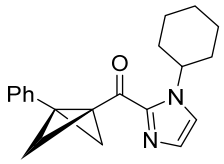
**$R_f$** = 0.30 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.27-7.15 (m, 5H), 7.09 (s, 1H), 6.90 (s, 1H), 4.02 (t, *J* = 7.2 Hz, 2H), 3.62 (s, 2H), 1.93 (s, 2H), 1.22-1.17 (m, 2H), 0.54 (t, *J* = 7.2 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 185.6, 142.6, 133.2, 128.6, 128.3, 126.9, 125.8, 125.0, 49.9, 40.2, 37.9, 33.1, 24.1, 10.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{19}N_2O$: 267.1492; found: 267.1487.




**1l**
$C_{17}H_{18}N_2O$
M = 266.34 g/mol

**(1-isopropyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone**: (**1l**) Prepared from methyl-3-phenylbicyclo[1.1.0]butane-1-carboxylate (1.88 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1l** as a white solid (1.36 g, 51% yield over 2 steps).

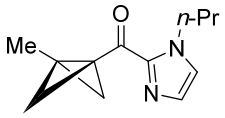
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.27-7.15 (m, 5H), 7.11 (s, 1H), 7.08 (s, 1H), 5.03-4.97 (m, 1H), 3.59 (s, 2H), 1.93 (s, 2H), 1.07 (d, *J* = 6.8 Hz, 6H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 186.1, 142.5, 133.3, 129.1, 128.3, 126.9, 125.8, 119.8, 48.6, 40.1, 38.0, 33.4, 23.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{19}N_2O$: 267.1492; found: 267.1488.




**1m**
$C_{20}H_{22}N_2O$
M = 306.17 g/mol

**(1-cyclohexyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone:** (**1m**) Prepared from methyl-3-phenylbicyclo[1.1.0]butane-1-carboxylate (1.88 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1m** as a white solid (1.10 g, 52% yield over 2 steps).

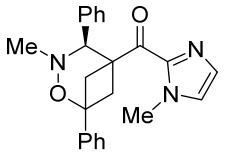
**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.27-7.14 (m, 5H), 7.09 (s, 1H), 7.06 (s, 1H), 4.55-4.49 (m, 1H), 3.57 (s, 2H), 1.93 (s, 2H), 1.67-1.63 (m, 3H), 1.51-1.49 (m, 2H), 1.26-1.15 (m, 4H), 1.09-1.02 (m, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 186.2, 142.6, 133.3, 129.0, 128.2, 126.8, 125.8, 122.2, 56.0, 40.1, 37.9, 34.1, 33.6, 25.5, 25.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{23}N_2O$: 307.1805; found: 307.1801.




**1q**
$C_{12}H_{16}N_2O$
M = 204.13 g/mol

**(3-methylbicyclo[1.1.0]butan-1-yl)(1-propyl-1H-imidazol-2-yl)methanone:** (**1q**) Prepared from benzyl 3-methylbicyclo[1.1.0]butane-1-carboxylate (2.02 g, 10.00 mmol, 1.0 equiv) according to the **GP2**. Purification by flash chromatography on silica gel afforded **1q** as a colorless oil (1.02 g, 50% yield over 2 steps).

$\mathbf{R_f}$ = 0.40 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.10 (s, 1H), 7.02 (s, 1H), 4.35 (t, *J* = 7.2 Hz, 2H), 2.89 (s, 2H), 1.84-1.74 (m, 2H), 1.57 (s, 3H), 1.53 (s, 2H), 0.91 (t, *J* = 7.2 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 188.2, 143.2, 128.7, 124.8, 50.3, 41.1, 36.0, 24.7, 23.1, 12.9, 11.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{12}H_{17}N_2O$: 205.1335; found: 205.1333.

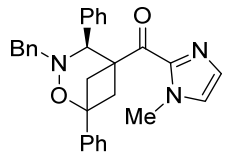



**3aa**
$C_{23}H_{23}N_3O_2$
M = 373.46 g/mol

**(*S*)-(3-methyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3aa**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-methyl-1-phenylmethanimine oxide (**2a**, 32.4 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3aa** as a white solid (64.2 mg, 86% yield).

**3aa**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 107-109 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 10.89 min, tr (minor) = 15.61 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +66.8 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 6.8 Hz, 2H), 7.39-

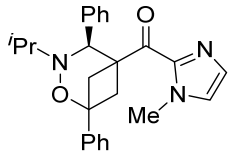
7.36 (m, 2H), 7.32-7.28 (m, 1H), 7.20 (s, 1H), 7.15-7.11 (m, 3H), 7.09-7.07 (m, 2H), 6.87 (s, 1H), 4.58 (s, 1H), 3.61 (t, *J* = 8.6 Hz, 1H), 3.40 (s, 3H), 2.90-2.84 (m, 2H), 2.62 (s, 3H), 2.47 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.55, 142.6, 141.1, 138.1, 129.1, 128.3, 128.1, 127.9, 127.8, 125.9, 125.9, 81.9, 77.3, 53.8, 49.9, 43.3, 35.1, 33.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{24}N_3O_2$: 374.1863; found: 374.1856.




**3ab**
$C_{29}H_{27}N_3O_2$
M = 449.55 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ab**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ab** as a white solid (72.4 mg, 85% yield).

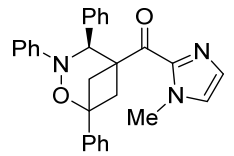
**3ab**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 113-115 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 15.00 min, tr (major) = 19.23 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +79.3 (*c* = 0.85, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.2 Hz, 2H), 7.30-7.24 (m, 9H), 7.14 (s, 5H), 6.87 (s, 1H), 4.85 (s, 1H), 3.99 (AB, *J* = 15.2 Hz, 1H), 3.86 (AB, *J* = 14.8 Hz, 1H), 3.65 (t, *J* = 9.4 Hz, 1H), 3.41 (s, 3H), 2.93 (d, *J* = 9.6 Hz, 1H), 2.81 (t, *J* = 9.2 Hz, 1H), 2.42 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 142.6, 141.3, 138.2, 138.1, 129.1, 128.6, 128.2, 128.11, 128.07, 127.9, 127.8, 127.5, 126.6, 125.9, 125.4, 81.7, 74.4, 58.5, 54.1, 49.7, 35.1, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{28}N_3O_2$: 450.2166; found: 450.2166.



**3ac**
$C_{25}H_{27}N_3O_2$
M = 401.51 g/mol

**(*S*)-(3-isopropyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ac**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-isopropyl-1-phenylmethanimine oxide (**2c**, 39.2 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ac** as a white solid (64.2 mg, 80% yield).

**3ac**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 143-145 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 5/95, 1.0 mL/min, 254 nm; tr (minor) = 6.79 min, tr (major) = 8.15 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +37.2 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.0 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.30-7.26 (m, 1H), 7.20 (s, 1H), 7.14-7.05 (m, 5H), 6.86 (s, 1H), 4.98 (s, 1H), 3.57 (t, *J* = 9.4 Hz, 1H), 3.38 (s, 3H), 2.94-2.90 (m, 1H), 2.87 (d, *J* = 9.6 Hz, 1H), 2.74 (t, *J* = 9.0 Hz, 1H), 2.37 (d, *J* = 10.0 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.4 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 192.1, 142.78, 142.0, 138.8, 129.0, 128.2, 127.9, 127.74, 127.71, 127.5, 125.7, 125.4, 80.8, 70.1, 53.9, 51.5, 49.3, 35.1, 34.4, 21.2, 14.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{28}N_3O_2$: 402.2176; found: 402.2176.

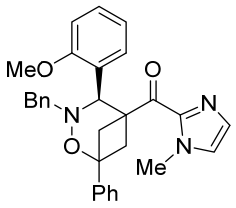


**3ad**
$C_{28}H_{25}N_3O_2$
M = 435.53 g/mol

**(*S*)-(1-methyl-1H-imidazol-2-yl)(1,3,4-triphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)methanone**: (**3ad**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-

yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*,1-diphenylmethanimine oxide (**2d**, 47.3 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ad** as colorless oil (78.4 mg, 90% yield).

**3ad**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 13.10 min, tr (major) = 20.54 min) gave the isomeric composition of the product: 94% ee. $[\alpha]_D^{20}$ = +66.8 (*c* = 1.38, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.36-7.31 (m, 1H), 7.18-7.14 (m, 8H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.97 (s, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.02 (s, 1H), 3.71 (s, 3H), 3.24-3.16 (m, 2H), 2.73 (d, *J* = 9.6 Hz, 1H), 2.65 (d, *J* = 9.2 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 190.8, 149.8, 142.1, 140.5, 138.6, 129.4, 128.5, 128.4, 128.1, 127.6, 127.5, 126.4, 125.9, 121.6, 117.0, 83.6, 71.1, 54.1, 45.4, 35.7, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{26}N_3O_2$: 436.2020; found: 436.2011.

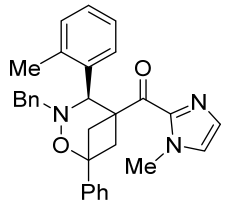



**3ae**
$C_{30}H_{29}N_3O_3$
M = 479.58 g/mol

**(*S*)-(3-benzyl-4-(2-methoxyphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ae**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(2-methoxyphenyl)methanimine oxide (**2e**, 57.9 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ae** as a white solid (89.2 mg, 93% yield).

**3ae**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 161-163 $^o$C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 8.97 min, tr (major) = 11.54 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ =

+96.0 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.32-7.21 (m, 7H), 7.19-7.09 (m, 3H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.81 (s, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 5.34 (s, 1H), 3.94 (AB, *J* = 14.8 Hz, 1H), 3.90 (AB, *J* = 14.8 Hz, 1H), 3.72 (t, *J* = 9.2 Hz, 1H), 3.47 (s, 3H), 3.40 (s, 3H), 2.99 (d, *J* = 9.6 Hz, 1H), 2.90 (t, *J* = 9.2 Hz, 1H), 2.46 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 192.3, 156.8, 142.7, 141.5, 138.7, 129.2, 128.9, 128.8, 128.4, 128.1, 127.7, 127.4, 126.4, 126.1, 125.43, 125.35, 120.6, 109.9, 81.7, 65.8, 58.4, 55.2, 53.9, 50.0, 35.8, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_3$: 480.2282; found: 480.2270.

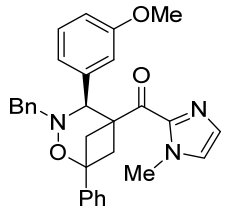



**3af**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-1-phenyl-4-(*o*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3af**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(*o*-tolyl)methanimine oxide (**2f**, 54.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3af** as a white solid (66.8 mg, 72% yield).

**3af**: **$R_f$** = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 175-177 °C. HPLC analysis (Chiralpak IC, $^i$PrOH/hexane = 15/85, 0.8 mL/min, 254 nm; tr (major) = 8.86 min, tr (minor) = 9.20 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +116.9 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 7.2 Hz, 2H), 7.28-7.20 (m, 8H), 7.15-7.10 (m, 2H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 5.06 (s, 1H), 3.90 (s, 1H), 3.92 (AB, *J* = 14.4 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.79 (t, *J* = 9.2 Hz, 1H), 3.37 (s, 3H), 3.02 (d, *J* = 9.6 Hz, 1H), 2.86 (t, *J* = 9.2 Hz, 1H), 2.50 (d, *J* = 10.0 Hz, 1H), 2.05 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 192.1, 142.7, 141.3, 138.5, 136.8, 135.9, 130.0, 128.9, 128.4, 128.2, 128.1, 127.8,

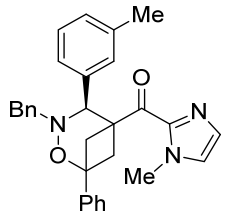
127.7, 127.5, 126.5, 126.2, 126.0, 125.4, 81.8, 69.3, 57.8, 54.2, 50.5, 36.1, 34.9, 19.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2324.




**3ag**
$C_{30}H_{29}N_3O_3$
M = 479.58 g/mol

**(*S*)-(3-benzyl-4-(3-methoxyphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ag**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3-methoxyphenyl)methanimine oxide (**2g**, 57.9 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ag** as colorless oil (57.5 mg, 60% yield).

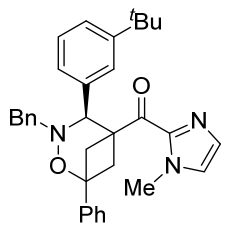
**3ag**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 0.8 mL/min, 254 nm; tr (minor) = 16.40 min, tr (major) = 17.12 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +63.7 (*c* = 1.38, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.30-7.27 (m, 6H), 7.23-7.20 (m, 3H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.91 (s, 1H), 6.76-6.67 (m, 3H), 4.83 (s, 1H), 4.01 (AB, *J* = 14.8 Hz, 1H), 3.86 (AB, *J* = 14.8 Hz, 1H), 3.65 (s, 3H), 3.62 (t, *J* = 9.6 Hz, 1H), 3.49 (s, 3H), 2.92 (d, *J* = 10.0 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 159.3, 142.8, 141.3, 139.6, 138.2, 129.2, 129.1, 128.7, 128.2, 127.9, 127.5, 126.6, 125.9, 125.4, 120.0, 114.2, 112.8, 81.7, 74.3, 58.7, 55.1, 54.1, 49.7, 35.2, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_3$: 480.2282; found: 480.2271.



**3ah**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-1-phenyl-4-(*m*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ah**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (Z)-N-benzyl-1-(m-tolyl)methanimine oxide (**2h**, 54.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ah** as a white solid (76.0 mg, 82% yield).

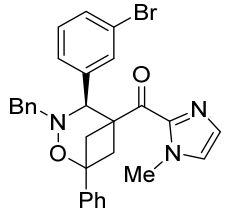
**3ah**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 111-113 °C. HPLC analysis (Chiralcel IC, $^i$PrOH/hexane = 10/90, 0.8 mL/min, 254 nm; tr (minor) = 8.18 min, tr (major) = 8.61 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +97.5 (*c* = 1.88, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30-7.26 (m, 6H), 7.24-7.19 (m, 3H), 7.04-7.01 (m, 1H), 6.97-6.93 (m, 2H), 6.87 (s, 2H), 4.78 (s, 1H), 4.00 (AB, *J* = 14.8 Hz, 1H), 3.84 (AB, *J* = 14.8 Hz, 1H), 3.64 (t, *J* = 9.4 Hz, 1H), 3.40 (s, 3H), 2.93 (d, *J* = 9.6 Hz, 1H), 2.80 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H), 2.19 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.7, 142.8, 141.4, 138.2, 138.0, 137.6, 129.0, 128.8, 128.6, 128.5, 128.1, 128.0, 127.8, 127.5, 126.6, 125.7, 125.4, 124.8, 81.7, 74.3, 58.6, 54.0, 49.7, 35.0, 34.9, 21.23 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2323.



**3ai**
$C_{33}H_{35}N_3O_2$
M = 505.66 g/mol

**(*S*)-(3-benzyl-4-(3-(tert-butyl)phenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ai**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3-(tert-butyl)phenyl)methanimine oxide (**2i**, 64.2 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ai** as colorless oil (87.0 mg, 86% yield).

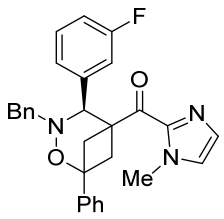
**3ai**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 11.76 min, tr (major) = 18.65 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +30.9 (*c* = 2.13, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.2 Hz, 2H), 7.31-7.25 (m, 6H), 7.23-7.18 (m, 4H), 7.16-7.11 (m, 2H), 6.98 (s, 1H), 6.84 (s, 1H), 4.85 (s, 1H), 4.02 (AB, *J* = 14.8 Hz, 1H), 3.86 (AB, *J* = 14.8 Hz, 1H), 3.66 (t, *J* = 9.4 Hz, 1H), 3.41 (s, 3H), 2.91 (d, *J* = 9.6 Hz, 1H), 2.81 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.4 Hz, 1H), 1.13 (s, 9H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 150.7, 142.7, 141.4, 138.3, 137.6, 129.0, 128.6, 128.12, 128.07, 127.8, 127.5, 126.6, 125.9, 125.5, 125.4, 124.9, 124.5, 81.7, 74.7, 58.6, 54.1, 49.8, 35.2, 35.0, 34.5, 31.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{36}N_3O_2$: 506.2802; found: 506.2792.




**3aj**
$C_{29}H_{26}BrN_3O_2$
M = 528.45 g/mol

**(*S*)-(3-benzyl-4-(3-bromophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3aj**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3-bromophenyl)methanimine oxide (**2j**, 69.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ai** as a white solid (81.4 mg, 77% yield).

**3aj**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 70-72 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 9.82 min, tr (minor) = 13.10 min) gave the isomeric composition of the product: 99.6% ee. $[\alpha]_D^{20}$ = +47.1 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.6 Hz, 2H), 7.30-7.23 (m, 11H), 7.07-7.03 (m, 2H), 6.95 (s, 1H), 4.83 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.87 (AB, *J* = 14.8 Hz, 1H), 3.56 (d, *J* = 9.4 Hz, 1H), 3.52 (s, 3H), 2.91 (d, *J* = 9.6 Hz, 1H), 2.78 (t, *J* = 9.4 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.1, 142.4, 141.1, 140.5, 137.7, 131.2, 131.1, 129.9, 129.3, 128.7, 128.2, 127.9, 127.6, 126.8, 126.4, 126.3, 125.4, 122.0, 81.7, 73.7, 58.9, 54.1, 49.5, 35.2, 34.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}BrN_3O_2$: 528.1281; found: 528.1271.

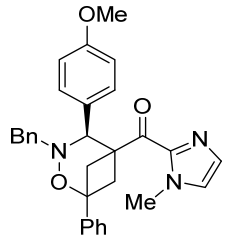



**3ak**
$C_{29}H_{26}FN_3O_2$
M = 467.54 g/mol

**(*S*)-(3-benzyl-4-(3-fluorophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ak**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3-fluorophenyl)methanimine oxide (**2k**, 55.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ak** as colorless oil (68.2 mg, 73% yield).

**3ak**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 10.03 min, tr (minor) = 10.55 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +86.1 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.6 Hz, 2H), 7.31-7.22 (m, 9H), 7.13-7.08 (m, 1H), 6.94-6.84 (m, 4H), 4.89 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.87 (AB, *J* = 14.8 Hz, 1H), 3.59 (t, *J* = 9.4 Hz, 1H), 3.53 (s, 3H), 2.90 (d, *J* = 10.0 Hz, 1H), 2.78 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.2,

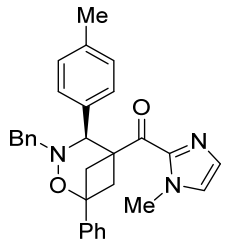
162.5 (d, *J* = 244 Hz), 142.4, 141.1, 140.8 (d, *J* = 7 Hz), 137.9, 129.6 (d, *J* = 8 Hz), 129.3, 128.7, 128.2, 127.9, 127.6, 126.8, 126.2, 125.4, 123.5 (d, *J* = 3 Hz), 115.0 (d, *J* = 18 Hz), 114.8 (d, *J* = 19 Hz), 81.7, 73.7 (d, *J* = 2 Hz), 58.8, 54.1, 49.6, 35.3, 34.9 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -112.755 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}FN_3O_2$: 468.2072; found: 468.2082.




**3al**
$C_{30}H_{29}N_3O_3$
M = 479.58 g/mol

**(*S*)-(3-benzyl-4-(4-methoxyphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3al**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-methoxyphenyl)methanimine oxide (**2l**, 57.9 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3al** as a white solid (76.7 mg, 80% yield).

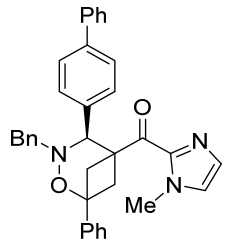
**3al**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 145-147 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 14.42 min, tr (minor) = 16.83 min) gave the isomeric composition of the product: 97% ee. $[\alpha]_D^{20}$ = +52.0 (*c* = 1.88, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.29-7.20 (m, 9H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.89 (s, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 4.82 (s, 1H), 3.96 (AB, *J* = 15.2 Hz, 1H), 3.83 (AB, *J* = 15.2 Hz, 1H), 3.72 (s, 3H), 3.63 (t, *J* = 9.4 Hz, 1H), 3.49 (s, 3H), 2.91 (d, *J* = 9.6 Hz, 1H), 2.78 (t, *J* = 9.2 Hz, 1H), 2.40 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.8, 159.2, 142.6, 141.4, 138.3, 130.2, 129.1, 129.0, 128.6, 128.1, 127.8, 127.5, 126.6, 125.9, 125.4, 113.5, 81.6, 73.7, 58.3, 55.1, 54.0, 49.7, 35.3, 34.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_3$: 480.2282; found: 480.2272.




**3am**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-1-phenyl-4-(*p*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3am**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(*p*-tolyl)methanimine oxide (**2m**, 54.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3am** as a white solid (69.5 mg, 75% yield).

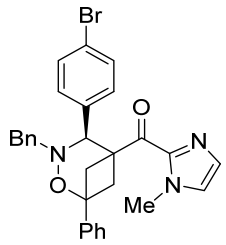
**3am**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 91-93 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 10.45 min, tr (minor) = 12.95 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +75.4 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.2 Hz, 2H), 7.29-7.20 (m, 9H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 2H), 6.89 (s, 1H), 4.82 (s, 1H), 4.00 (AB, *J* = 14.8 Hz, 1H), 3.83 (AB, *J* = 14.8 Hz, 1H), 3.64 (t, *J* = 9.2 Hz, 1H), 3.44 (s, 3H), 2.92 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.40 (d, *J* = 10.0 Hz, 1H), 2.23 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.8, 142.7, 141.4, 138.3, 137.7, 135.1, 129.1, 128.8, 128.6, 128.1, 127.8, 127.7, 127.5, 126.6, 125.9, 125.4, 81.6, 74.0, 58.4, 54.1, 49.7, 35.2, 35.0, 21.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2325.




**3an**
$C_{35}H_{31}N_3O_2$
M = 525.65 g/mol

**(*S*)-(4-([1,1'-biphenyl]-4-yl)-3-benzyl-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3an**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-1-([1,1'-biphenyl]-4-yl)-N-benzylmethanimine oxide (**2n**, 70.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3an** as a white solid (98.8 mg, 94% yield).

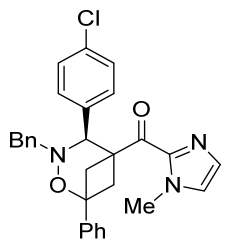
**3an**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 125-127 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 15.70 min, tr (minor) = 18.52 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +4.5 (*c* = 2.48, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.6 Hz, 2H), 7.42-7.37 (m, 6H), 7.33-7.27 (m, 7H), 7.24–7.20 (m, 5H), 6.88 (s, 1H), 4.90 (s, 1H), 4.05 (AB, *J* = 14.8 Hz, 1H), 3.89 (AB, *J* = 15.2 Hz, 1H), 3.69 (t, *J* = 9.4 Hz, 1H), 3.43 (s, 3H), 2.94 (d, *J* = 9.6 Hz, 1H), 2.82 (t, *J* = 9.0 Hz, 1H), 2.45 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 142.6, 141.3, 140.8, 140.5, 138.1, 137.2, 129.2, 128.8, 128.7, 128.3, 128.2, 127.9, 127.6, 127.3, 126.9, 126.7, 126.6, 125.9, 125.4, 81.7, 74.1, 58.6, 54.1, 49.8, 35.2, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{35}H_{32}N_3O_2$: 526.2489; found: 526.2475.



**3ao**
$C_{29}H_{26}BrN_3O_2$
M = 528.45 g/mol

**(*S*)-(3-benzyl-4-(4-bromophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ao**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-bromophenyl)methanimine oxide (**2o**, 69.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ao** as a white solid (87.7mg, 83% yield).

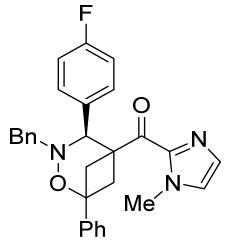
**3ao**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 125-127 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 12.33 min, tr (minor) = 13.94 min) gave the isomeric composition of the product: 99.6% ee. $[\alpha]_D^{20}$ = +26.9 (*c* = 2.10, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.6 Hz, 2H), 7.30-7.21 (m, 11H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.93 (s, 1H), 4.88 (s, 1H), 3.95 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.60 (t, *J* = 9.8 Hz, 1H), 3.55 (s, 3H), 2.89 (d, *J* = 9.6 Hz, 1H), 2.76 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.2, 142.3, 141.1, 137.8, 137.2, 131.3, 129.6, 129.3, 128.7, 128.2, 127.9, 127.6, 126.8, 126.2, 125.4, 122.0, 81.7, 73.6, 58.6, 54.0, 49.7, 35.4, 34.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}BrN_3O_2$: 528.1281; found: 528.1270.



**3ap**
$C_{29}H_{26}ClN_3O_2$
M = 484.00 g/mol

**(*S*)-(3-benzyl-4-(4-chlorophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ap**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-chlorophenyl)methanimine oxide (**2p**, 58.8 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ap** as a white solid (77.4 mg, 80% yield).

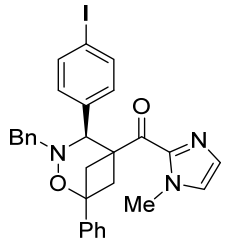
**3ap**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 107-109 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 12.08 min, tr (minor) = 14.57 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +44.8 (*c* = 1.88, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.6 Hz, 2H), 7.30-7.20 (m, 9H), 7.13-7.19 (m, 4H), 6.92 (s, 1H), 4.89 (s, 1H), 3.95 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.60 (t, *J* = 9.4 Hz, 1H), 3.54 (s, 3H), 2.89 (d, *J* = 9.6 Hz, 1H), 2.77 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.2, 142.3, 141.1, 137.9, 136.7, 133.8, 129.29, 129.26, 128.6, 128.3, 128.2, 127.9, 127.6, 126.7, 126.2, 125.4, 81.7, 73.6, 58.6, 54.0, 50.0, 35.4, 34.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}ClN_3O_2$: 484.1786; found: 484.1778.




**3aq**
$C_{29}H_{26}FN_3O_2$
M = 467.54 g/mol

**(*S*)-(3-benzyl-4-(4-fluorophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3aq**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-fluorophenyl)methanimine oxide (**2q**, 55.0 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3aq** as colorless oil (77.6 mg, 83% yield).

**3aq**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 11.00 min, tr (minor) = 14.11 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +68.1 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.8 Hz, 2H), 7.30-7.20 (m, 9H), 7.16-7.13 (m, 2H), 6.90 (s, 1H), 6.84 (t, *J* = 8.8 Hz, 2H), 4.89 (s, 1H), 3.96 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.61 (t, *J* = 9.4 Hz, 1H), 3.52 (s, 3H), 2.90 (d, *J* = 9.6 Hz, 1H), 2.78 (t, *J* = 9.0 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.4, 162.4 (d, *J* = 246 Hz), 142.4, 141.2, 138.0, 134.0 (d, *J* = 3 Hz), 129.6 (d, *J* = 8 Hz), 129.2, 128.6, 128.2, 127.9, 127.6, 126.7, 126.1, 125.4, 115.0 (d, *J* = 21 Hz), 114.9, 81.7, 73.5, 58.5, 54.0, 49.7, 35.3, 34.9 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$): δ -113.657ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}FN_3O_2$: 468.2082; found: 468.2073.

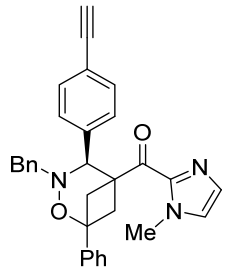



**3ar**
$C_{29}H_{26}IN_3O_2$
M = 575.45 g/mol

**(*S*)-(3-benzyl-4-(4-iodophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ar**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-iodophenyl)methanimine oxide (**2r**, 80.9 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ar** as a white solid (92.1 mg, 80% yield).

**3ar**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 155-157 $^{o}$C. HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 12.19 min, tr (minor) = 13.19 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +13.5 (*c* = 2.25, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.6

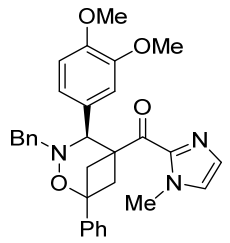
Hz, 2H), 7.29-7.23 (m, 8H), 7.20 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 3H), 4.86 (s, 1H), 3.95 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.59 (t, *J* = 9.4 Hz, 1H), 3.54 (s, 3H), 2.89 (d, *J* = 10.0 Hz, 1H), 2.76 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.2, 142.3, 141.1, 137.9, 137.8, 137.3, 129.8, 129.3, 128.6, 128.2, 127.9, 127.6, 126.7, 126.2, 125.4, 93.8, 81.7, 73.7, 58.6, 54.0, 49.6, 35.4, 34.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}IN_3O_2$: 576.1142; found: 576.1133.




**3as**
$C_{31}H_{27}N_3O_2$
M = 473.58 g/mol

**(*S*)-(3-benzyl-4-(4-ethynylphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3as**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(4-ethynylphenyl)methanimine oxide (**2s**, 56.5 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3as** as a white solid (66.3 mg, 70% yield).

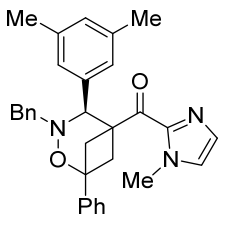
**3as**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 93-95 °C. HPLC analysis (Chiralpak IC, $^i$PrOH/hexane = 5/95, 0.8 mL/min, 254 nm; tr (minor) = 10.68 min, tr (major) = 11.58 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +19.2 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 7.6 Hz, 2H), 7.30-7.21 (m, 11H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.90 (s, 1H), 4.89 (s, 1H), 3.94 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.61 (t, *J* = 9.4 Hz, 1H), 3.50 (s, 3H), 3.03 (s, 1H), 2.90 (d, *J* = 9.6 Hz, 1H), 2.78 (t, *J* = 9.2 Hz, 1H), 2.42 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.2, 142.4, 141.2, 139.0, 137.9, 131.9, 129.2, 128.7, 128.2, 128.0, 127.9, 127.6, 126.7, 126.1, 125.4, 121.8, 83.3, 81.7, 77.5, 74.0, 58.7, 54.1, 49.7, 35.3, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{28}N_3O_2$: 474.2176; found: 474.2169.




**3at**
$C_{31}H_{31}N_3O_4$
M = 509.61 g/mol

**(*S*)-(3-benzyl-4-(3,4-dimethoxyphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3at**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3,4-dimethoxyphenyl)methanimine oxide (**2t**, 65.1 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3at** as a white solid (87.7 mg, 86% yield).

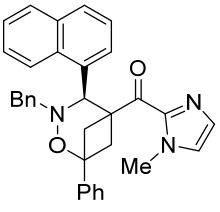
**3at**: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 1/1). Mp: 159-161 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 13.12 min, tr (minor) = 16.81 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +51.2 (*c* = 2.10, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 7.6 Hz, 2H), 7.30-7.22 (m, 9H), 6.91 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.58 (s, 1H), 4.83 (s, 1H), 4.02 (AB, *J* = 14.8 Hz, 1H), 3.86 (AB, *J* = 14.8 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.62 (t, *J* = 9.4 Hz, 1H), 3.53 (s, 3H), 2.90 (d, *J* = 9.6 Hz, 1H), 2.77 (t, *J* = 9.2 Hz, 1H), 2.40 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 148.5, 148.2, 142.7, 141.3, 138.3, 130.6, 129.0, 128.6, 128.1, 127.8, 127.5, 126.6, 125.9, 125.4, 119.8, 111.1, 110.9, 81.6, 73.9, 58.5, 55.7, 55.6, 54.1, 49.7, 35.4, 34.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_4$: 510.2387; found: 510.2378.




**3au**
$C_{31}H_{31}N_3O_2$
M = 477.61 g/mol

**(*S*)-(3-benzyl-4-(3,5-dimethylphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3au**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(3,5-dimethylphenyl)methanimine oxide (**2u**, 57.4 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3au** as colorless oil (82.1 mg, 86% yield).

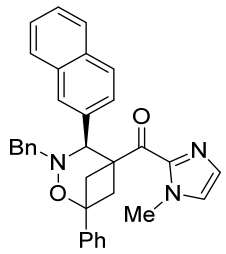
**3au**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 7.52 min, tr (minor) = 9.74 min) gave the isomeric composition of the product: 97% ee. $[\alpha]_D^{20}$ = +85.3 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.30-7.21 (m, 9H), 6.88 (s, 1H), 6.78 (s, 1H), 6.69 (s, 2H), 4.72 (s, 1H), 4.01 (AB, *J* = 14.8 Hz, 1H), 3.83 (AB, *J* = 14.8 Hz, 1H), 3.62 (t, *J* = 9.4 Hz, 1H), 3.40 (s, 3H), 2.93 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.40 (d, *J* = 10.0 Hz, 1H), 2.15 (s, 6H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.8, 143.0, 141.4, 138.3, 137.9, 137.4, 129.6, 129.0, 128.7, 128.1, 127.8, 127.5, 126.6, 125.6, 125.5, 125.4, 81.7, 74.3, 58.6, 54.0, 49.6, 34.9, 34.8, 21.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_2$: 478.2489; found: 478.2478.




**3av**
$C_{33}H_{29}N_3O_2$
M = 499.61 g/mol

**(*S*)-(3-benzyl-4-(naphthalen-1-yl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3av**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(naphthalen-1-yl)methanimine oxide (**2v**, 62.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3av** as a white solid (86.9 mg, 87% yield).

**3av**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 180-182 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 11.64 min, tr (minor) = 16.06 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +165.5 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.36-7.28 (m, 7H), 7.26-7.18 (m, 5H), 7.04 (s, 1H), 6.50 (s, 1H), 5.60 (s, 1H), 3.98-3.82 (m, 3H), 3.09 (d, *J* = 10.0 Hz, 1H), 2.99 (t, *J* = 9.4 Hz, 1H), 2.83 (s, 3H), 2.45 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.7, 142.5, 141.3, 138.0, 133.6, 133.4, 130.9, 128.8, 128.7, 128.4, 128.24, 128.17, 127.8, 127.6, 126.6, 125.8, 125.7, 125.5, 125.1, 124.9, 123.0, 81.7, 67.4, 58.6, 54.7, 49.9, 35.9, 34.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{30}N_3O_2$: 500.2333; found: 500.2323.

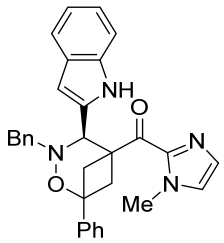



**3aw**
$C_{33}H_{29}N_3O_2$
M = 499.61 g/mol

**(*S*)-(3-benzyl-4-(naphthalen-2-yl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3aw**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(naphthalen-2-yl)methanimine oxide (**2w**, 62.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3aw** as a white solid (82.9 mg, 83% yield).

**3aw**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 173-175 °C. HPLC analysis (Chiralpak IC, $^i$PrOH/hexane = 10/90, 0.8 mL/min, 254 nm; tr (minor) = 9.06 min, tr (major) = 9.91 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +51.8 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.75-7.72 (m, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.63-7.61 (m, 1H), 7.45-7.34 (m, 6H), 7.32-7.18 (m, 9H), 6.84 (s, 1H), 5.03

(s, 1H), 4.03 (AB, *J* = 14.8 Hz, 1H), 3.89 (AB, *J* = 14.8 Hz, 1H), 3.74 (t, *J* = 9.4 Hz, 1H), 3.19 (s, 3H), 2.96 (d, *J* = 10.0 Hz, 1H), 2.85 (t, *J* = 9.0 Hz, 1H), 2.47 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 142.7, 141.3, 138.1, 135.7, 133.2, 133.0, 129.2, 128.7, 128.2, 127.94, 127.85, 127.6, 127.5, 127.4, 126.7, 126.0, 125.9, 125.44, 125.35, 81.8, 74.4, 58.7, 54.2, 49.8, 35.1, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{30}N_3O_2$: 500.2333; found: 500.2323.

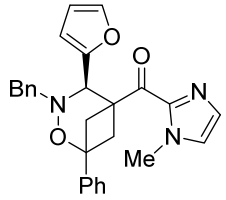



**3ax**
$C_{31}H_{28}N_4O_2$
M = 488.59 g/mol

**(*R*)-(3-benzyl-4-(1H-indol-2-yl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ax**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(1H-indol-2-yl)methanimine oxide (**2x**, 60.1 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ax** as a white solid (30.3 mg, 31% yield).

**3ax**: **$R_f$** = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 188-190 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 14.81 min, tr (major) = 28.58 min) gave the isomeric composition of the product: 95% ee. $[\alpha]_D^{20}$ = +18.1 (*c* = 0.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.37-7.22 (m, 12H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.92 (s, 1H), 5.88 (s, 1H), 5.24 (s, 1H), 4.10 (AB, *J* = 14.8 Hz, 1H), 3.96 (AB, *J* = 14.8 Hz, 1H), 3.57 (t, *J* = 9.4 Hz, 1H), 3.51 (s, 3H), 2.86 (d, *J* = 9.6 Hz, 1H), 2.75 (t, *J* = 9.2 Hz, 1H), 2.50 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 190.5, 142.4, 141.0, 137.5, 135.8, 134.9, 129.2, 129.0, 128.3, 128.0, 127.7, 126.9, 126.3, 125.4, 121.9, 120.2,

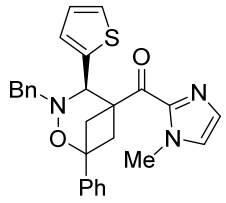
119.7, 111.1, 101.4, 81.8, 68.1, 59.2, 53.4, 49.0, 35.5, 34.8 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{29}N_4O_2$: 489.2275; found: 489.2275.




**3ay**
$C_{27}H_{25}N_3O_3$
M = 439.52 g/mol

**(*R*)-(3-benzyl-4-(furan-2-yl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ay**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(furan-2-yl)methanimine oxide (**2y**, 48.3 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ay** as a white solid (52.7 mg, 60% yield).

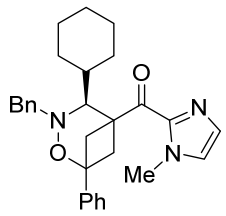
**3ay**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 107-109 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 14.63 min, tr (minor) = 19.42 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +56.4 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.32-7.21 (m, 10H), 7.05 (s, 1H), 6.97 (s, 1H), 6.18 (s, 1H), 5.01 (s, 1H), 4.11 (AB, *J* = 14.8 Hz, 1H), 3.89 (AB, *J* = 14.8 Hz, 1H), 3.73 (s, 3H), 3.50 (t, *J* = 9.4 Hz, 1H), 2.83 (d, *J* = 9.6 Hz, 1H), 2.71 (t, *J* = 9.2 Hz, 1H), 2.38 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.3, 143.0, 142.3, 141.3, 140.4, 138.2, 129.2, 128.6, 128.2, 127.9, 127.5, 126.7, 126.2, 125.4, 122.5, 109.1, 81.7, 66.2, 58.6, 53.4, 49.1, 35.6, 34.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{26}N_3O_3$: 440.1969; found: 440.1965.



**3az**
$C_{27}H_{25}N_3O_2S$
M = 455.58 g/mol

**(*R*)-(3-benzyl-1-phenyl-4-(thiophen-2-yl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3az**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-(thiophen-2-yl)methanimine oxide (**2z**, 52.2 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3az** as a white solid (72.9 mg, 80% yield).

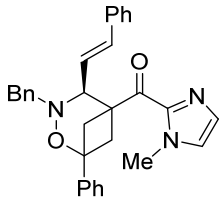
**3az**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 91-93 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 12.91 min, tr (major) = 14.54 min) gave the isomeric composition of the product: 99.7% ee. $[\alpha]_D^{20}$ = +71.2 (*c* = 1.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.32-7.21 (m, 9H), 7.17 (d, *J* = 5.2 Hz, 1H), 6.97 (s, 1H), 6.74 (t, *J* = 4.2 Hz, 1H), 6.35 (s, 1H), 5.37 (s, 1H), 4.12 (AB, *J* = 14.8 Hz, 1H), 3.89 (AB, *J* = 14.8 Hz, 1H), 3.64 (s, 3H), 3.59 (t, *J* = 9.4 Hz, 1H), 2.87 (d, *J* = 9.6 Hz, 1H), 2.76 (t, *J* = 9.2 Hz, 1H), 2.37 (d, *J* = 10.4 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 190.7, 142.4, 141.14, 141.09, 138.0, 129.2, 128.7, 128.2, 127.9, 127.6, 126.7, 126.2, 125.8, 125.7, 125.4, 124.9, 81.7, 69.8, 58.7, 54.1, 48.6, 35.5, 34.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{26}N_3O_2S$: 456.1740; found: 456.1735.



**3aaa**
$C_{29}H_{33}N_3O_2$
M = 455.60 g/mol

**(*S*)-(3-benzyl-4-cyclohexyl-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3aaa**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-cyclohexylmethanimine oxide (**2aa**, 52.2 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3aaa** as a white solid (54.7 mg, 60% yield).

**3aaa**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 131-133 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (major) = 7.40 min, tr (minor) = 8.31 min) gave the isomeric composition of the product: 70% ee. $[\alpha]_D^{20}$ = +67.1 (*c* = 1.38, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 5.0 Hz, 2H), 7.24 (s, 5H), 7.20-7.19 (m, 2H), 7.01 (s, 1H), 4.44 (AB, *J* = 14.8 Hz, 1H), 4.27 (AB, *J* = 14.8 Hz, 1H), 4.12 (s, 1H), 4.00 (s, 3H), 3.07 (t, *J* = 9.4 Hz, 1H), 2.78 (t, *J* = 9.4 Hz, 1H), 2.60 (d, *J* = 10.8 Hz, 1H), 2.49 (d, *J* = 10.2 Hz, 1H), 1.84 (d, *J* = 12.6 Hz, 1H), 1.65-1.54 (m, 5H), 1.17-1.11 (m, 1H), 1.07-0.96 (m, 3H), 0.78-0.74 (m, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 192.9, 142.1, 141.4, 139.0, 129.2, 128.8, 128.1, 128.0, 127.4, 126.7, 126.3, 125.4, 81.4, 73.2, 63.2, 52.4, 48.5, 43.0, 36.6, 36.2, 29.9, 29.3, 27.2, 27.1, 26.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{34}N_3O_2$: 456.2646; found: 456.2638.

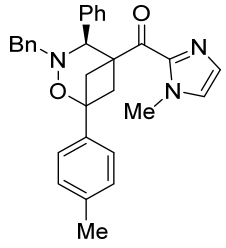



**3abb**
$C_{31}H_{29}N_3O_2$
M = 475.59 g/mol

**(*S*,*E*)-(3-benzyl-1-phenyl-4-styryl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3abb**) Prepared from ((1-methyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1a**, 47.6 mg, 0.20 mmol) and (1*Z*,2*E*)-*N*-benzyl-3-phenylprop-2-en-1-imine oxide (**2bb**, 57.0 mg, 0.24 mmol) according to the

**GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3abb** as a white solid (73.2 mg, 77% yield).

**3abb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 141-143 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 13.50 min, tr (major) = 14.24 min) gave the isomeric composition of the product: 97% ee. $[\alpha]_D^{20}$ = +12.3 (*c* = 1.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.6 Hz, 2H), 7.30-7.27 (m, 6H), 7.22-7.18 (m, 6H), 7.15-7.13 (m, 2H), 6.90 (s, 1H), 6.19-6.08 (m, 2H), 4.50 (d, *J* = 8.2 Hz, 1H), 4.28 (AB, *J* = 14.8 Hz, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.69 (s, 3H), 3.50 (t, *J* = 9.2 Hz, 1H), 2.83 (d, *J* = 9.6 Hz, 1H), 2.71 (t, *J* = 9.0 Hz, 1H), 2.39 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.9, 142.5, 141.3, 138.1, 136.3, 133.9, 129.3, 128.7, 128.4, 128.1, 127.9, 127.8, 127.5, 126.6, 126.4, 126.2, 125.8, 125.4, 81.6, 72.8, 58.8, 52.5, 48.7, 35.6, 34.8 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{30}N_3O_2$: 476.2333; found: 476.2324.

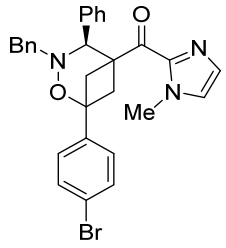



**3bb**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-4-phenyl-1-(*p*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3bb**) Prepared from (1-methyl-1H-imidazol-2-yl)(3-(p-tolyl)bicyclo[1.1.0]butan-1-yl)methanone (**1b**, 50.5 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3bb** as colorless oil (83.4 mg, 90% yield).

**3bb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 10.34 min, tr (major) = 21.60 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +90.2 (*c* = 2.00,

$CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.6 Hz, 2H), 7.28-7.23 (m, 2H), 7.21-7.18 (m, 4H), 7.13-7.08 (m, 7H), 6.86 (s, 1H), 4.83 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.84 (AB, *J* = 14.8 Hz, 1H), 3.63 (t, *J* = 9.4 Hz, 1H), 3.40 (s, 3H), 2.90 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.0 Hz, 1H), 2.39 (d, *J* = 10.0 Hz, 1H), 2.29 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.7, 142.6, 138.5, 138.2, 137.2, 129.1, 128.8, 128.6, 128.1, 128.0, 127.9, 127.8, 126.6, 125.8, 125.3, 81.6, 74.3, 58.5, 54.1, 49.8, 35.1, 34.9, 21.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2323.

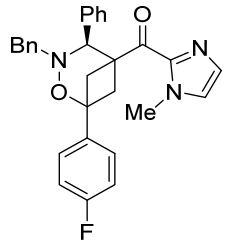



**3cb**
$C_{29}H_{26}BrN_3O_2$
M = 528.45 g/mol

**(*S*)-(3-benzyl-1-(4-bromophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3cb**) Prepared from (3-(4-bromophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1H-imidazol-2-yl)methanone (**1c**, 63.4 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3cb** as colorless oil (100.4 mg, 95% yield).

**3cb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 11.66 min, tr (major) = 28.74 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +82.1 (*c* = 1.25, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.30-7.25 (m, 3H), 7.23-7.20 (m, 2H), 7.16-7.14 (m, 7H), 6.89 (s, 1H), 4.83 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.83 (AB, *J* = 14.8 Hz, 1H), 3.62 (t, *J* = 9.2 Hz, 1H), 3.43 (s, 3H), 2.88 (d, *J* = 9.6 Hz, 1H), 2.78 (t, *J* = 9.2 Hz, 1H), 2.38 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.4, 142.6, 140.4, 138.1, 137.9, 131.3, 129.2, 128.6, 128.2, 127.89, 127.86, 127.2, 126.7, 126.0, 121.6, 81.2, 74.4, 58.6, 54.0, 49.8, 35.2,

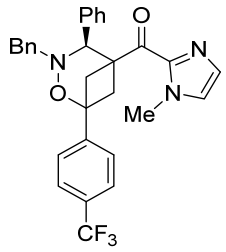
35.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}BrN_3O_2$: 528.1281; found: 528.1271.




**3db**
$C_{29}H_{26}FN_3O_2$
M = 467.54 g/mol

**(*S*)-(3-benzyl-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3db**) Prepared from (3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1H-imidazol-2-yl)methanone (**1d**, 51.2 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3db** as colorless oil (87.6 mg, 94% yield).

**3db**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 10.27 min, tr (major) = 17.57 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +89.7 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.0 Hz, 2H), 7.30-7.20 (m, 6H), 7.14 (s, 5H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.88 (s, 1H), 4.83 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.83 (d, *J* = 14.8 Hz, 1H), 3.63 (t, *J* = 9.4 Hz, 1H), 3.42 (s, 3H), 2.89 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.38 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 162.2 (d, *J* = 245 Hz), 142.6, 138.1 (d, *J* = 11 Hz), 137.3 (d, *J* = 3 Hz), 129.2, 128.6, 128.2, 128.1, 127.9, 127.23, 127.15, 126.7, 125.9, 115.0 (d, *J* = 22 Hz), 81.3, 74.4, 58.6, 54.0, 49.8, 35.12, 35.06 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.912 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}FN_3O_2$: 468.2082; found: 468.2073.



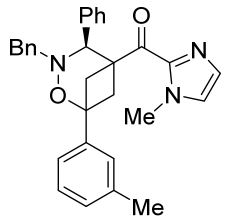

**3eb**

$C_{30}H_{26}F_3N_3O_2$

M = 517.55 g/mol

**(S)-(3-benzyl-4-phenyl-1-(4-(trifluoromethyl)phenyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3eb**) Prepared from (1-methyl-1H-imidazol-2-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1e**, 61.2 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3eb** as colorless oil (86.6 mg, 84% yield).

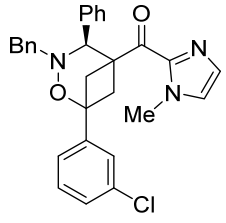
**3eb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 9.51 min, tr (major) = 23.71 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +93.9 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.39-7.35 (m, 4H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.25-7.21 (m, 2H), 7.18-7.14 (m, 5H), 6.91 (s, 1H), 4.86 (s, 1H), 4.00 (AB, *J* = 14.8 Hz, 1H), 3.84 (AB, *J* = 14.8 Hz, 1H), 3.65 (t, *J* = 9.6 Hz, 1H), 3.45 (s, 3H), 2.93 (d, *J* = 9.6 Hz, 1H), 2.82 (t, *J* = 9.2 Hz, 1H), 2.43 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 191.3, 145.1, 142.5, 138.0, 137.8, 129.7 (q, *J* = 32 Hz), 129.2, 128.6, 128.23, 128.21, 127.9, 127.8, 126.8, 126.0, 125.7, 125.2 (q, *J* = 4 Hz), 124.1 (q, *J* = 270 Hz), 81.2, 74.5, 58.7, 54.1, 49.9, 35.2 ppm. **$^{19}$F NMR** (565 MHz, $CDCl_3$) δ -62.520 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{30}H_{26}F_3N_3O_2K$: 556.1609; found: 556.1603.



**3fb**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-4-phenyl-1-(*m*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3fb**) Prepared from (1-methyl-1H-imidazol-2-yl)(3-(*m*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone (**1f**, 50.5 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3fb** as a white solid (79.7 mg, 86% yield).

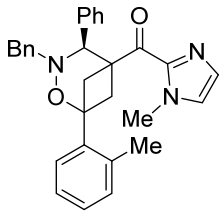
**3fb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 121-123 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 5.06 min, tr (major) = 6.24 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +84.9 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.23-7.17 (m, 3H), 7.16-7.08 (m, 7H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.87 (s, 1H), 4.83 (s, 1H), 3.99 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.64 (t, *J* = 9.4 Hz, 1H), 3.41 (s, 3H), 2.92 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.40 (d, *J* = 10.0 Hz, 1H), 2.28 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.7, 142.6, 141.3, 138.2, 138.1, 137.7, 129.1, 128.7, 128.3, 128.10, 128.06, 127.9, 127.8, 126.6, 126.2, 125.9, 122.4, 81.7, 74.4, 58.5, 54.1, 49.7, 35.1, 35.1, 21.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2326.



**3gb**
$C_{29}H_{26}ClN_3O_2$
M = 484.00 g/mol

**(*S*)-(3-benzyl-1-(3-chlorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3gb**) Prepared from (3-(3-chlorophenyl)bicyclo[1.1.0]butan-1-yl)(1-methyl-1H-imidazol-2-yl)methanone (**1g**, 54.5 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3gb** as a white solid (90.0 mg, 93% yield).

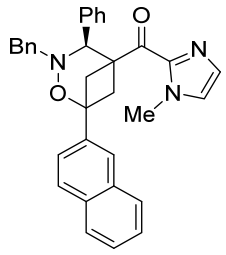
**3gb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 137-139 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 8.06 min, tr (major) = 11.52 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +84.3 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.2 Hz, 2H), 7.31-7.27 (m, 3H), 7.24-7.19 (m, 4H), 7.14 (s, 6H), 6.88 (s, 1H), 4.84 (s, 1H), 3.99 (AB, *J* = 14.8 Hz, 1H), 3.84 (AB, *J* = 14.8 Hz, 1H), 3.62 (t, *J* = 9.4 Hz, 1H), 3.42 (s, 3H), 2.89 (d, *J* = 10.0 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.39 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.3, 143.3, 142.5, 138.0, 137.9, 134.1, 129.5, 129.2, 128.7, 128.2, 127.9, 127.8, 127.6, 126.8, 126.0, 125.9, 123.5, 81.2, 74.4, 58.6, 54.0, 49.9, 35.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}ClN_3O_2$: 484.1786; found: 484.1778.




**3hb**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-4-phenyl-1-(*o*-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3hb**) Prepared from (1-methyl-1H-imidazol-2-yl)(3-(*o*-tolyl)bicyclo[1.1.0]butan-1-yl)methanone (**1h**, 50.5 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3hb** as colorless oil (83.4 mg, 90% yield).

**3hb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 10.12 min, tr (major) = 15.60 min) gave the isomeric composition of the product: 94% ee. $[\alpha]_D^{20}$ = +111.5 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 7.2 Hz, 2H), 7.24-7.22 (m, 3H), 7.19-7.09 (m, 9H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.87 (s, 1H), 4.82 (s, 1H), 3.93 (AB, *J* = 14.4 Hz, 1H), 3.88 (t, *J* = 9.0 Hz, 1H), 3.74 (AB, *J* = 14.4 Hz, 1H), 3.39 (s, 3H), 2.98-2.91 (m, 2H), 2.36 (d, *J* = 10.0 Hz, 1H), 2.19 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 142.7, 138.5, 138.3, 138.2, 130.9, 129.1, 129.0, 128.2, 128.12, 128.06, 127.9, 127.7, 126.66, 126.65, 125.8, 125.2, 82.9, 74.3, 58.7, 54.0, 49.2, 35.1, 33.4, 19.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2325.

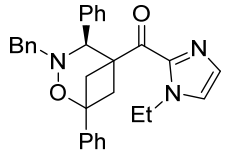



**3ib**
$C_{33}H_{29}N_3O_2$
M = 499.61 g/mol

**(*S*)-(3-benzyl-1-(naphthalen-2-yl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone**: (**3ib**) Prepared from (1-methyl-1H-imidazol-2-yl)(3-(naphthalen-2-yl)bicyclo[1.1.0]butan-1-yl)methanone (**1i**, 57.7 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3ib** as a white solid (83.9 mg, 84% yield).

**3ib**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 123-125 °C. HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 9.25 min, tr (major) = 28.45 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +115.5 (*c* = 2.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.78-7.71 (m, 4H), 7.45-7.39 (m, 5H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.25-7.23 (m, 2H), 7.16 (s, 5H), 6.88 (s, 1H), 4.89 (s, 1H), 4.02 (AB, *J* = 14.6 Hz, 1H), 3.88 (AB, *J* = 14.8 Hz, 1H), 3.72 (t, *J* = 9.4 Hz, 1H), 3.42 (s, 3H), 3.05

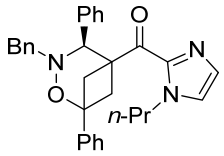
(d, *J* = 8.4 Hz, 1H), 2.90 (t, *J* = 9.1 Hz, 1H), 2.49 (d, *J* = 10.0 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 142.6, 138.7, 138.2, 138.1, 133.0, 132.8, 129.2, 128.8, 128.2, 128.1, 127.92, 127.90, 127.86, 127.5, 126.7, 125.94, 125.92, 125.88, 124.4, 123.6, 81.8, 74.5, 58.7, 54.2, 49.8, 35.1, 35.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{33}H_{30}N_3O_2$: 500.2333; found: 500.2322.




**3jb**
$C_{30}H_{29}N_3O_2$
M = 463.58 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-ethyl-1H-imidazol-2-yl)methanone**: (**3jb**) Prepared from ((1-ethyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1j**, 50.4 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3jb** as a white solid (74.1 mg, 80% yield).

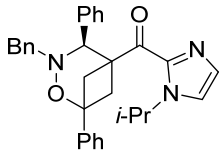
**3jb**: $\mathbf{R}_f$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 107-109 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 8.56 min, tr (major) = 16.27 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +78.1 (*c* = 1.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30-7.21 (m, 9H), 7.16-7.13 (m, 5H), 6.95 (s, 1H), 4.90 (s, 1H), 4.16-4.08 (m, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.86 (AB, *J* = 15.2 Hz, 1H), 3.80-3.73 (m, 1H), 3.67 (t, *J* = 9.4 Hz, 1H), 2.94 (d, *J* = 9.6 Hz, 1H), 2.82 (t, *J* = 9.0 Hz, 1H), 2.42 (d, *J* = 10.4 Hz, 1H), 0.87 (t, *J* = 7.0 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.4, 141.7, 141.4, 138.3, 138.2, 129.3, 128.6, 128.20, 128.15, 128.0, 127.8, 127.5, 126.6, 125.4, 124.5, 81.7, 74.5, 58.5, 54.2, 50.0, 43.2, 35.1, 15.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2331.




**3kb**
$C_{31}H_{31}N_3O_2$
M = 477.61 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-propyl-1H-imidazol-2-yl)methanone**: (**3kb**) Prepared from ((1-propyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1k**, 53.2 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3x** as a white solid (77.4 mg, 81% yield).

**3kb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 115-117 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 8.04 min, tr (major) = 15.44 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{26}$ = +61.4 (*c* = 1.88, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30-7.26 (m, 6H), 7.25-7.21 (m, 3H), 7.19-7.17 (m, 2H), 7.13-7.12 (m, 3H), 6.93 (s, 1H), 4.92 (s, 1H), 4.19-4.12 (m, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.86 (AB, *J* = 14.8 Hz, 1H), 3.70-3.60 (m, 2H), 2.93 (d, *J* = 9.6 Hz, 1H), 2.81 (t, *J* = 9.0 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H), 1.26-1.12 (m, 2H), 0.64 (t, *J* = 7.4 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.3, 141.7, 141.4, 138.3, 138.2, 129.1, 128.6, 128.22, 128.15, 128.1, 128.0, 127.8, 127.5, 126.6, 125.42, 125.40, 81.7, 74.5, 58.5, 54.2, 50.0, 49.8, 35.2, 23.7, 10.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_2$: 478.2489; found: 478.2484.

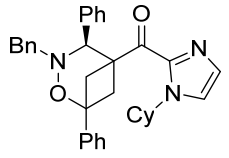



**3lb**
$C_{31}H_{31}N_3O_2$
M = 477.61 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-isopropyl-1H-imidazol-2-yl)methanone**: (**3lb**) Prepared from ((1-isopropyl-1H-imidazol-2-yl)(3-

phenylbicyclo[1.1.0]butan-1-yl)methanone (**1l**, 53.2 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3lb** as a white solid (69.7 mg, 73% yield).

**3lb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 101-103 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 6.65 min, tr (major) = 21.65 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +37.3 (*c* = 1.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.32-7.28 (m, 9H), 7.19-7.11 (m, 6H), 4.91-4.85 (m, 2H), 3.97 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.66 (t, *J* = 9.2 Hz, 1H), 2.95 (d, *J* = 9.6 Hz, 1H), 2.83 (t, *J* = 9.2 Hz, 1H), 2.43 (d, *J* = 10.0 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 5.6 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 141.7, 141.4, 138.3, 129.6, 128.6, 128.2, 128.13, 128.06, 127.9, 127.8, 127.5, 126.6, 125.4, 120.3, 81.7, 74.6, 58.4, 54.5, 50.2, 48.6, 35.1, 23.2, 23.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_2$: 478.2489; found: 478.2487.

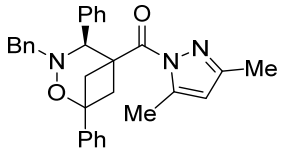



**3mb**
$C_{34}H_{35}N_3O_2$
M = 517.67 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-cyclohexyl-1H-imidazol-2-yl)methanone**: (**3mb**) Prepared from ((1-cyclohexyl-1H-imidazol-2-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1m**, 58.8 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3mb** as a white solid (72.0 mg, 71% yield).

**3mb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 3/1). Mp: 125-127 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 15/85, 1.0 mL/min, 254 nm; tr (minor) = 6.51 min, tr (major) = 25.27 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ =

+27.5 (*c* = 1.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30-7.21 (m, 9H), 7.16-7.11 (m, 6H), 4.90 (s, 1H), 4.43-4.35 (m, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.66 (t, *J* = 9.6 Hz, 1H), 2.95 (d, *J* = 9.6 Hz, 1H), 2.83 (t, *J* = 9.2 Hz, 1H), 2.43 (d, *J* = 10.0 Hz, 1H), 1.98 (d, *J* = 10.4 Hz, 1H), 1.77 (d, *J* = 12.0 Hz, 1H), 1.62 (d, *J* = 11.6 Hz, 2H), 1.40-1.26 (m, 2H), 1.17-1.06 (m, 4H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.7, 141.8, 141.4, 138.2, 129.4, 128.6, 128.2, 128.1, 128.0, 127.84, 127.81, 127.5, 126.6, 125.4, 120.8, 81.7, 74.6, 58.4, 56.2, 54.5, 50.2, 35.1, 34.0, 33.8, 25.40, 25.36, 25.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{34}H_{36}N_3O_2$: 518.2802; found: 518.2796.




**3nb**

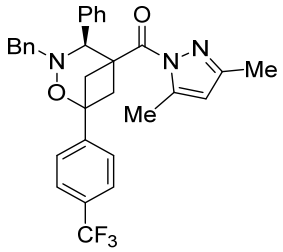
$C_{30}H_{29}N_3O_2$

M = 463.58 g/mol

**(*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone**: (**3nb**) Prepared from (3,5-dimethyl-1H-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1n**, 50.5 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3nb** as a white solid (91.9 mg, 99% yield).

**3nb**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). Mp: 103-105 °C. HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 2/98, 1.0 mL/min, 254 nm; tr (major) = 9.53 min, tr (minor) = 13.49 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +62.8 (*c* = 0.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.31-7.27 (m, 6H), 7.24-7.20 (m, 2H), 7.17 (s, 5H), 5.84 (s, 1H), 4.81 (s, 1H), 4.02 (AB, *J* = 14.8 Hz, 1H), 3.84 (AB, *J* = 14.8 Hz, 1H), 3.72 (t, *J* = 9.6 Hz, 1H), 2.96 (d, *J* = 9.6 Hz, 1H), 2.74 (t, *J* = 9.4 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H), 2.30 (s, 3H), 2.05 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.6, 151.9, 144.0, 141.2, 138.1, 137.7, 128.7, 128.3, 128.2, 128.1, 127.8, 127.53, 127.47, 126.7, 125.3, 110.2, 81.5, 73.6, 58.7, 51.7, 50.0,

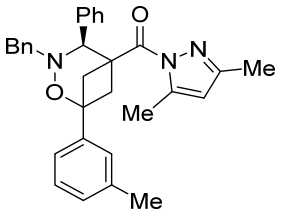
35.9, 13.9, 13.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_2$: 464.2333; found: 464.2319.




**3ob**
$C_{31}H_{28}F_3N_3O_2$
M = 531.58 g/mol

**(*S*)-(3-benzyl-4-phenyl-1-(4-(trifluoromethyl)phenyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone**: (**3ob**) Prepared from (3,5-dimethyl-1H-pyrazol-1-yl)(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1o**, 64.0 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3ob** as a colorless oil (89.0 mg, 84% yield).

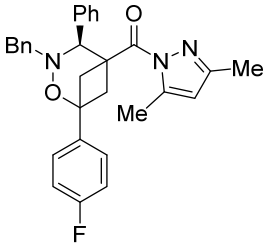
**3ob**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak OD-H, $^i$PrOH/hexane = 2/98, 0.8 mL/min, 254 nm; tr (major) = 5.83 min, tr (minor) = 6.52 min) gave the isomeric composition of the product: 92% ee. $[\alpha]_D^{20}$ = +49.0 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 4H), 7.31 (d, *J* = 7.2 Hz, 2H), 7.26-7.23 (m, 1H), 7.20-7.16 (m, 5H), 5.86 (s, 1H), 4.82 (s, 1H), 4.02 (AB, *J* = 14.4 Hz, 1H), 3.84 (AB, *J* = 14.4 Hz, 1H), 3.72 (t, *J* = 9.6 Hz, 1H), 2.97 (d, *J* = 10.0 Hz, 1H), 2.76 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H), 2.31 (s, 3H), 2.06 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.3, 152.2, 144.9, 144.1, 137.9, 137.4, 129.7 (q, *J* = 32 Hz), 128.7, 128.41, 128.38, 127.9, 127.4, 126.8, 125.7, 125.2 (q, *J* = 4 Hz), 124.1 (q, *J* = 270 Hz), 110.4, 81.1, 73.7, 58.8, 51.8, 50.2, 36.1, 13.9, 13.5 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.528 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{28}F_3N_3O_2$: 532.2206; found: 532.2213.



**3pb**
$C_{31}H_{31}N_3O_2$
M = 477.61 g/mol

**(*S*)-(3-benzyl-4-phenyl-1-(m-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone**: (**3pb**) Prepared from (3,5-dimethyl-1H-pyrazol-1-yl)(3-(m-tolyl)bicyclo[1.1.0]butan-1-yl)methanone (**1p**, 53.2 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3pb** as a colorless oil (95.4 mg, 99% yield).

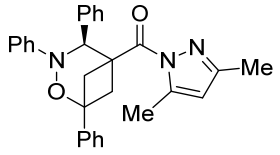
**3pb**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 2/98, 1.0 mL/min, 254 nm; tr (major) = 6.69 min, tr (minor) = 9.00 min) gave the isomeric composition of the product: 99.5% ee. $[\alpha]_D^{20}$ = +58.0 (*c* = 1.25, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.16-7.11 (m, 2H), 7.08 (s, 5H), 7.02-6.95 (m, 3H), 5.75 (s, 1H), 4.72 (s, 1H), 3.94 (AB, *J* = 14.8 Hz, 1H), 3.76 (AB, *J* = 14.8 Hz, 1H), 3.62 (t, *J* = 9.6 Hz, 1H), 2.88 (d, *J* = 10.0 Hz, 1H), 2.65 (t, *J* = 9.2 Hz, 1H), 2.31 (d, *J* = 10.0 Hz, 1H), 2.22 (s, 3H), 2.20 (s, 3H), 1.97 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.6, 151.9, 144.0, 141.1, 138.1, 137.74, 137.69, 128.8, 128.3, 128.2, 128.1, 127.8, 127.5, 126.7, 126.2, 122.4, 110.2, 81.5, 73.5, 58.7, 51.8, 49.9, 36.0, 21.4, 13.9, 13.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_2$: 478.2489; found: 478.2501.



**3qb**
$C_{30}H_{28}FN_3O_2$
M = 481.57 g/mol

**(*S*)-(3-benzyl-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone**: (**3qb**) Prepared from (3,5-dimethyl-1H-pyrazol-1-yl)(3-(4-fluorophenyl)bicyclo[1.1.0]butan-1-yl)methanone (**1q**, 54.0 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.7 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3qb** as a colorless oil (93.4 mg, 97% yield).

**3qb**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 1/99, 1.0 mL/min, 254 nm; tr (major) = 12.55 min, tr (minor) = 16.69 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +56.7 (*c* = 1.50, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 6.8 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.26-7.22 (m, 3H), 7.16 (s, 5H), 6.96 (t, *J* = 8.8 Hz, 2H), 5.85 (s, 1H), 4.80 (s, 1H), 4.01 (AB, *J* = 14.8 Hz, 1H), 3.83 (AB, *J* = 14.8 Hz, 1H), 3.70 (t, *J* = 9.6 Hz, 1H), 2.93 (d, *J* = 10.0 Hz, 1H), 2.73 (t, *J* = 9.4 Hz, 1H), 2.37 (d, *J* = 10.4 Hz, 1H), 2.31 (s, 3H), 2.05 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.4, 162.2 (d, *J* = 244 Hz), 152.0, 144.1, 138.0, 137.6, 137.1 (d, *J* = 3 Hz), 128.7, 128.3, 127.9, 127.5, 127.1 (d, *J* = 8 Hz), 126.7, 115.0 (d, *J* = 22 Hz), 110.3, 81.1, 73.6, 58.7, 51.7, 50.0, 36.0, 13.9, 13.5 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.853 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{29}FN_3O_2$: 482.2238; found: 482.2227.



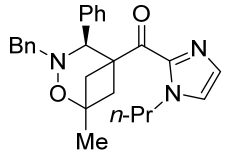

**3nd**

$C_{29}H_{27}N_3O_2$

M = 449.55 g/mol

**(*S*)-(3,5-dimethyl-1H-pyrazol-1-yl)(1,3,4-triphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)methanone**: (**3nd**)[3a] Prepared from (3,5-dimethyl-1H-pyrazol-1-yl)(3-phenylbicyclo[1.1.0]butan-1-yl)methanone (**1n**, 50.5 mg, 0.20 mmol) and (*Z*)-N,1-diphenylmethanimine oxide (**2d**, 47.3 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3nd** as a white solid (48.0 mg, 53% yield).

**3nd**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 2/98, 1.0 mL/min, 254 nm; tr (major) = 9.29 min, tr (minor) = 10.91 min) gave the isomeric composition of the product: 28% ee. $[\alpha]_D^{20}$ = +14.9 (*c* = 1.20, $CHCl_3$).**$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.50-7.48 (m,2H), 7.43-7.40 (m, 2H), 7.36-7.35 (m, 1H), 7.21-7.16 (m, 7H), 7.07-7.05 (m, 2H), 6.89-6.86 (m, 1H), 5.94 (s, 2H), 3.25 (t, *J* = 9.4 Hz, 1H), 3.18 (t, *J* = 9.4 Hz, 1H), 2.77 (d, *J* = 10.0 Hz, 1H), 2.58 (d, *J* = 10.4 Hz, 1H), 2.31 (s, 3H), 2.25 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.0, 152.4, 150.0, 144.30, 140.29, 138.3, 128.9, 128.5, 128.4, 128.3, 128.2, 127.1, 125.9, 121.5, 116.7, 110.7, 83.5, 70.2, 51.8, 45.3, 36.6, 13.97, 13.91 ppm.

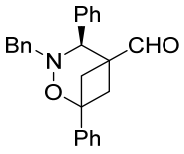



**3rb**
$C_{26}H_{29}N_3O_2$
M = 415.54 g/mol

**(*S*)-(3-benzyl-1-methyl-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-propyl-1H-imidazol-2-yl)methanone**: (**3rb**) Prepared from (3-methylbicyclo[1.1.0]butan-1-yl)(1-propyl-1H-imidazol-2-yl)methanone (**1r**, 40.8 mg, 0.20 mmol) and (*Z*)-*N*-benzyl-1-phenylmethanimine oxide (**2b**, 50.6 mg, 0.24 mmol) according to the **GP1** at rt for 16 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) afforded **3rb** as a colorless oil (25.0 mg, 30% yield).

**3rb**: $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 3/1). HPLC analysis (Chiralpak AD-H, $^{i}$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 5.67 min, tr (major) = 14.57 min) gave the isomeric composition of the product: 24% ee. $[\alpha]_D^{20}$ = +5.1 (*c* = 0.51, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.37-7.31 (m, 2H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.21-7.18 (m, 2H), 7.12-7.09 (m, 5H), 6.90 (s, 1H), 4.77 (s, 1H), 4.14-4.07 (m, 1H), 3.89 (AB, *J* = 14.8 Hz, 1H), 3.75 (AB, *J* = 14.8 Hz, 1H), 3.64-3.57 (m, 1H), 3.30 (t, *J* = 9.4 Hz, 1H), 2.51 (t, *J* = 9.2 Hz, 1H), 2.32 (d, *J* = 9.6 Hz, 1H), 2.10 (d, *J* = 10.0 Hz, 1H), 1.27 (s, 3H), 1.21-1.11 (m, 2H), 0.63 (t, *J* = 7.4 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.6, 141.7, 138.4, 138.4, 129.0, 128.6, 128.1, 128.0, 127.82, 127.80, 126.5, 125.2,

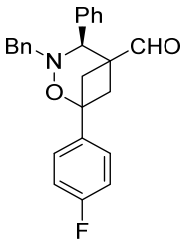
79.1, 74.3, 58.5, 54.6, 51.3, 49.8, 33.6, 23.7, 23.4, 10.9 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{26}H_{29}N_3O_2Na$: 438.2152; found: 438.2158.




**4nb**
$C_{25}H_{23}NO_2$
M = 369.46 g/mol

**(*S*)-3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-5-carbaldehyde** (**4nb**): Prepared from (*S*)-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (**3nb**, 46.3 mg, 0.1 mmol) according to the **GP3** at -40 °C for 30 min. Purification by flash chromatography on silica gel using petroleum ether/ethyl acetate (10/1) afforded **4nb** as a colorless oil (20.0 mg, 54% yield).

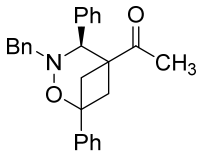
**4nb**: $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 2/98, 1.0 mL/min, 254 nm; tr (minor) = 7.54 min, tr (major) = 8.66 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +99.0 (*c* = 0.50, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 9.23 (s, 1H), 7.53-7.52 (m, 2H), 7.40-7.38 (m, 2H), 7.36-7.33 (m, 3H), 7.32-7.28 (m, 6H), 7.27-7.23 (m, 2H), 4.29 (s, 1H), 4.13 (AB, *J* = 14.8 Hz, 1H), 3.81 (AB, *J* = 14.8 Hz, 1H), 3.53 (t, *J* = 9.6 Hz, 1H), 2.69 (d, *J* = 9.6 Hz, 1H), 2.30 (d, *J* = 9.6 Hz, 1H), 2.06 (t, *J* = 9.0 Hz, 1H) ppm. **$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 200.5, 140.7, 137.28, 137.25, 129.2, 129.1, 128.9, 128.3, 128.0, 127.94, 127.89, 127.0, 125.3, 81.7, 72.0, 58.1, 52.2, 45.8, 35.1 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{25}H_{23}NO_2Na$: 392.1621; found: 392.1624.




**4qb**
$C_{25}H_{22}FNO_2$
M = 387.45 g/mol

**(*S*)-3-benzyl-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-5-carbaldehyde** (**4qb**): Prepared from (*S*)-(3-benzyl-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (**3qb**, 48.1 mg, 0.1 mmol) according to the **GP3** at -40 °C for 30 min. Purification by flash chromatography on silica gel using petroleum ether/ethyl acetate (10/1) afforded **4qb** as a colorless oil (23.3 mg, 60% yield).

(**4qb**): $\mathbf{R_f}$ = 0.4 (petroleum ether/EtOAc = 10/1). $[\alpha]_D^{20}$ = +133.6 (*c* = 0.70, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 9.22 (s, 1H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.41-7.28 (m, 7H), 7.26-7.22 (m, 3H), 6.98 (t, *J* = 8.6 Hz, 2H), 4.28 (s, 1H), 4.11 (AB, *J* = 14.8 Hz, 1H), 3.79 (AB, *J* = 14.8 Hz, 1H), 3.51 (t, *J* = 9.2 Hz, 1H), 2.66 (d, *J* = 9.2 Hz, 1H), 2.26 (d, *J* = 9.6 Hz, 1H), 2.05 (t, *J* = 9.2 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 200.4, 162.4 (d, J = 146 Hz), 137.2 (d, *J* = 7 Hz), 136.6 (d, *J* = 3 Hz), 129.2, 129.0, 128.0, 127.2, 127.1, 127.0, 115.1 (d, *J* = 21 Hz), 81.2, 72.0, 58.1, 52.1, 45.8, 35.3 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.222 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{23}FNO_2$: 388.1707; found: 388.1702.



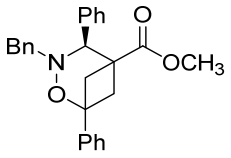

**5**

$C_{26}H_{25}NO_2$

M = 383.49 g/mol

**(*S*)-1-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)ethan-1-one** (**5**): $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (minor) = 5.06 min, tr (major) = 6.24 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +53.2 (*c* = 0.58, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.37-7.23 (m, 13H), 4.25 (s, 1H), 4.09 (AB, *J* = 14.8 Hz, 1H), 3.79 (d, *J* = 14.8 Hz, 1H), 3.60 (t, *J* = 9.4 Hz, 1H), 2.59 (d, *J* = 9.6 Hz, 1H), 2.29 (d, *J* = 10.0 Hz, 1H), 2.21 (t, *J* = 9.2 Hz, 1H), 1.68 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 208.8, 140.8, 137.5, 137.4, 129.0, 128.9, 128.8, 128.3, 128.2,

127.9, 127.8, 126.9, 125.3, 80.6, 73.2, 58.3, 54.4, 47.4, 35.3, 26.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{26}NO_2$: 384.1958; found: 384.1950.

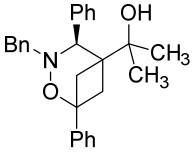



**6**

$C_{26}H_{25}NO_3$

M = 399.49 g/mol

**Methyl (*S*)-3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-5-carboxylate** (**6**): $\mathbf{R_f}$ = 0.6 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 2/98, 1.0 mL/min, 254 nm; tr (minor) = 9.25 min, tr (major) = 10.40 min) gave the isomeric composition of the product: 98% ee. $[\alpha]_D^{20}$ = +65.4 (*c* = 1.00, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 6.4 Hz, 2H), 7.36-7.22 (m, 13H), 4.24 (s, 1H), 4.09 (AB, *J* = 14.8 Hz, 1H), 3.80 (AB, *J* = 14.8 Hz, 1H), 3.58 (t, *J* = 9.6 Hz, 1H), 3.31 (s, 3H), 2.72 (d, *J* = 9.4 Hz, 1H), 2.37 (d, *J* = 10.0 Hz, 1H), 2.22 (t, *J* = 9.2 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 172.7, 140.8, 137.9, 137.4, 129.0, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 126.9, 125.3, 81.3, 73.1, 58.6, 51.3, 48.6, 47.7, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{26}NO_3$: 400.1907; found: 400.1901.



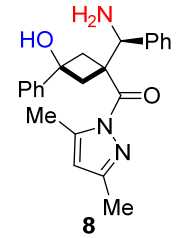

**7**

$C_{27}H_{29}NO_2$

M = 399.53 g/mol

**(*S*)-2-(3-benzyl-1,4-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)propan-2-ol** (**7**): $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). HPLC analysis (Chiralpak AD-H, $^i$PrOH/hexane = 5/95, 0.8 mL/min, 254 nm; tr (minor) = 12.11 min, tr (major) = 12.63 min) gave the isomeric composition of the product: 99% ee. $[\alpha]_D^{20}$ = +22.0 (*c* = 0.75, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.38-7.21 (m, 14H), 4.09 (s, 1H), 3.98 (AB, *J* = 14.6 Hz, 1H), 3.66 (d, *J* = 14.8 Hz, 1H), 3.32 (t, *J* = 9.2 Hz, 1H), 2.82 (d, *J* = 9.6 Hz, 1H), 2.22 (d, *J* = 10.0 Hz, 1H), 1.79 (t, *J* = 9.0 Hz, 1H), 1.12 (s, 3H), 0.65 (s, 3H) ppm. **$^{13}$C NMR**

(100 MHz, $CDCl_3$): δ 142.1, 140.0, 138.0, 130.0, 129.1, 128.6, 128.1, 127.8, 127.4, 126.7, 125.4, 80.0, 74.9, 72.0, 58.4, 50.7, 43.8, 33.2, 26.4, 25.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{30}NO_2$: 400.2271; found: 400.2263.

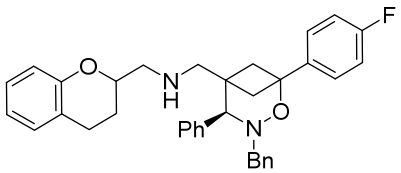



**8**

$C_{23}H_{25}N_3O_2$

M = 375.47 g/mol

**(*S*)-(1-(amino(phenyl)methyl)-3-hydroxy-3-phenylcyclobutyl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone** (**8**): $\mathbf{R_f}$ = 0.5 (petroleum ether/EtOAc = 1/1). $[\alpha]_D^{20}$ = +32.7 (*c* = 0.30, $CHCl_3$). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.4, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.22-7.20 (m, 4H), 6.93-6.91 (m, 2H), 5.87 (s, 1H), 5.06 (s, 1H), 3.48 (d, *J* = 14.0 Hz, 1H), 3.26 (d, *J* = 14.4 Hz, 1H), 3.04 (dd, *J* = 14.4, 4.4 Hz, 1H), 2.85 (dd, *J* = 14.4, 4.0 Hz, 1H), 2.26 (s, 3H), 2.17 (s, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 174.5, 151.5, 146.1, 144.5, 143.1, 128.6, 128.1, 127.8, 126.6, 125.8, 125.0, 110.2, 71.2, 57.6, 50.4, 50.3, 40.3, 14.02, 13.95 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{23}H_{25}N_3O_2K$: 414.1578; found: 414.1582.



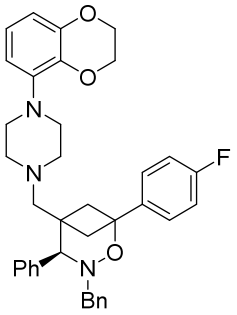

**9**

$C_{35}H_{35}FN_2O_2$

M = 534.68 g/mol

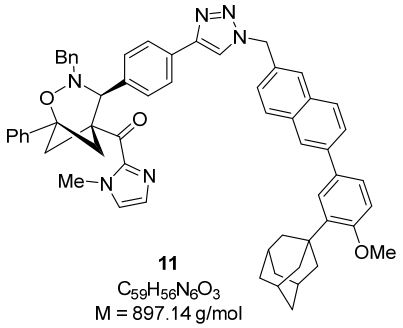
***N*-(((*S*)-3-benzyl-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)methyl)-1-(chroman-2-yl)methanamine** (**9**): $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 3/1). $[\alpha]_D^{20}$ = +50.8 (*c* = 0.25, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.2 Hz, 2H), 7.35-7.30 (m, 5H), 7.28-7.25 (m, 4H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.10-7.07 (m, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.97 (t, *J* = 8.4 Hz, 2H), 6.83 (t, *J* = 7.8 Hz, 1H), 6.78 (t, *J* = 9.0 Hz, 1H), 4.08 (s, 1H), 4.04-3.92 (m, 2H), 3.76-3.73 (m, 1H), 3.35-3.31 (m, 1H), 2.84-2.78 (m, 1H), 2.72-

2.69 (m, 1H), 2.60-2.53 (m, 1H), 2.50-2.46 (m, 1H), 2.30-2.22 (m, 2H), 1.98-1.94 (m, 1H), 1.89-1.83 (m, 2H), 1.74-1.65 (m, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 162.2 (d, *J* = 244 Hz) 154.6, 139.1, 139.0, 138.1, 137.9, 129.6, 129.5, 128.9, 128.50, 128.45, 128.12, 128.09, 127.8, 127.21, 127.18, 127.15, 127.13, 126.7, 122.0, 120.1, 116.7, 116.6, 115.0, 114.8, 81.9, 81.8, 75.3, 75.3, 75.1, 74.9, 59.1, 55.0, 54.73, 54.68, 54.6, 46.0, 45.9, 43.6, 43.5, 36.7, 36.5, 25.5, 25.4, 24.6 ppm. **$^{19}$F NMR** (565 MHz, $CDCl_3$) δ -115.186 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{35}H_{35}FN_2O_2$: 535.2755; found: 535.2744.




**10**
$C_{37}H_{38}FN_3O_3$
M = 591.73 g/mol

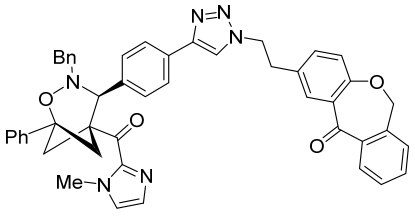
**(*S*)-3-benzyl-5-((4-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)piperazin-1-yl)methyl)-1-(4-fluorophenyl)-4-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane** (**10**): **$R_f$** = 0.2 (petroleum ether/EtOAc = 10/1). $[\alpha]_D^{20}$ = +24.5 (*c* = 0.20, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.58 (d, *J* = 6.6 Hz, 2H), 7.35-7.31 (m, 4H), 7.29-7.20 (m, 6H), 6.96 (t, *J* = 9.0 Hz, 2H), 6.78 (t, *J* = 7.8 Hz, 1H), 6.59 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.54 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.29-4.28 (m, 2H), 4.23-4.22 (m, 2H), 4.16 (s, 1H), 4.03 (AB, *J* = 14.8 Hz, 1H), 3.75 (AB, *J* = 14.8 Hz, 1H), 3.32 (t, *J* = 9.0 Hz, 1H), 2.98 (s, 4H), 2.56 (s, 2H), 2.50 (d, *J* = 9.0 Hz, 1H), 2.14-2.06 (m, 4H), 1.98 (d, *J* = 13.2 Hz, 1H), 1.79 (d, *J* = 9.6 Hz, 1H) ppm. **$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 162.1 (d, *J* = 243 Hz), 144.1, 141.9, 139.2, 138.3, 137.9 (d, *J* = 5 Hz), 136.4, 129.4, 128.8, 127.9, 127.8, 127.7, 127.1 (d, *J* = 9 Hz), 126.6, 120.6, 114.9 (d, *J* = 21 Hz), 111.8, 110.5, 82.5, 75.6, 64.3, 63.9, 63.6, 59.1, 54.1, 50.9, 48.5, 43.1, 37.3 ppm. **$^{19}$F NMR** (565 MHz, $CDCl_3$) δ -115.24 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{37}H_{38}FN_3O_3Na$: 614.2789; found: 614.2775.




**11**
$C_{59}H_{56}N_6O_3$
M = 897.14 g/mol

**((4*S*)-4-(4-(1-((6-(3-(adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)methyl)-1H-1,2,3-triazol-4-yl)phenyl)-3-benzyl-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone** (**11**): Prepared from (*S*)-(3-benzyl-4-(4-ethynylphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone (**3as**, 20.0 mg, 0.042 mmol) and 1-(5-(6-(azidomethyl)naphthalen-2-yl)-2-methoxyphenyl)adamantane (26.7 mg, 0.063 mmol) according to the **GP4** at rt for 5 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (4/1) afforded **11** as a white solid (37.7 mg, 99% yield).

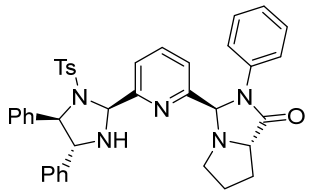
**11**: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 2/1). $[\alpha]_D^{20}$ = +0.9 (*c* = 1.00, $CHCl_3$). Mp: 141-143 °C. **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.87 (t, *J* = 9.8 Hz, 2H), 7.78-7.76 (m, 2H), 7.62-7.57 (m, 4H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.38-7.33 (m, 3H), 7.29-7.24 (m, 7H), 7.20-7.17 (m, 4H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.89 (s, 1H), 5.70 (d, *J* = 4.0 Hz, 2H), 4.89 (s, 1H), 3.98 (AB, *J* = 14.8 Hz, 1H), 3.89 (s, 3H), 3.85 (AB, *J* = 14.8 Hz, 1H), 3.63 (t, *J* = 9.4 Hz, 1H), 3.45 (s, 3H), 2.90 (d, *J* = 9.6 Hz, 1H), 2.79 (t, *J* = 9.2 Hz, 1H), 2.41 (d, *J* = 10.0 Hz, 1H), 2.18 (s, 6H), 2.10 (s, 3H), 1.80 (s, 6H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.4, 158.8, 147.8, 142.5, 141.3, 140.0, 139.0, 138.2, 138.0, 133.4, 132.6, 131.9, 131.4, 130.3, 129.3, 129.2, 128.7, 128.4, 128.24, 128.16, 127.84, 127.55, 127.2, 126.7, 126.6, 126.1, 125.9, 125.6, 125.6, 125.44, 125.40, 124.8, 119.5, 112.1, 81.7, 74.0, 58.6, 55.2, 54.5, 54.1, 49.7, 40.6, 37.1, 35.3, 34.9, 29.1 ppm. **HRMS** (ESI) *m/z*: $[M-H]^-$ calcd. for $C_{59}H_{55}N_6O_3$: 895.4341; found: 895.4353.



**12**
$C_{47}H_{40}N_6O_4$
M = 752.88 g/mol

**(*S*)-2-(2-(4-(4-(3-benzyl-5-(1-methyl-1H-imidazole-2-carbonyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-4-yl)phenyl)-1H-1,2,3-triazol-1-yl)ethyl)dibenzo[b,e]oxepin-11(6H)-one** (**12**): Prepared from (*S*)-(3-benzyl-4-(4-ethynylphenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone (**3as**, 20.0 mg, 0.042 mmol) and 2-(2-azidoethyl)dibenzo[b,e]oxepin-11(6H)-one (17.6 mg, 0.063 mmol) according to the **GP4** at rt for 5 h. Purification by flash chromatography on silica gel using EtOAc afforded **12** as a colorless oil (31.6 mg, 99% yield).

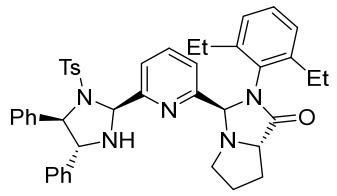
**12**: $\mathbf{R_f}$ = 0.2 (petroleum ether/EtOAc = 1/1). $[\alpha]_D^{20}$ = +10.0 (*c* = 0.50, $CHCl_3$). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 8.07 (d, *J* = 2.4 Hz, 1H), 7.87 (d, *J* = 7.8, 1H), 7.58-7.55 (m, 3H), 7.50-7.47 (m, 2H), 7.37-7.36 (m, 3H), 7.31-7.28 (m, 5H), 7.26-7.16 (m, 7H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.90 (s, 1H), 5.18 (s, 2H), 4.90 (s, 1H), 4.62 (t, *J* = 7.2 Hz, 2H), 4.01 (AB, *J* = 14.8 Hz, 1H), 3.87 (AB, *J* = 14.8 Hz, 1H), 3.65 (t, *J* = 9.0 Hz, 1H), 3.46 (s, 3H), 3.26 (t, *J* = 7.2 Hz, 2H), 2.92 (d, *J* = 9.6 Hz, 1H), 2.81 (t, *J* = 9.0 Hz, 1H), 2.43 (d, *J* = 9.6 Hz, 1H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 191.5, 190.9, 160.4, 147.2, 142.5, 141.3, 140.3, 138.12, 138.06, 135.8, 135.5, 132.9, 131.6, 130.6, 130.3, 129.5, 129.3, 129.2, 128.7, 128.4, 128.2, 127.9, 127.6, 126.7, 126.1, 125.5, 125.4, 125.3, 121.3, 119.8, 81.7, 74.0, 73.6, 58.6, 54.1, 51.5, 49.7, 35.7, 35.3, 35.0 ppm. **HRMS** (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{47}H_{40}N_6O_3K$: 791.2743; found: 791.2746.



**L9**
$C_{39}H_{37}N_5O_3S$
M = 655.82 g/mol

**(3*R*,7a*S*)-3-(6-((2*S*,4*R*,5*R*)-4,5-diphenyl-1-tosylimidazolidin-2-yl)pyridin-2-yl)-2-phenylhexahydro-1H-pyrrolo[1,2-c]imidazol-1-one:** (**L9**) Prepared from (*S*)-*N*-phenylpyrrolidine-2-carboxamide (247.3 mg, 1.3 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **L9** as a white solid (385 mg, 45% yield over 2 steps).

**$R_f$** = 0.5 (petroleum ether/EtOAc = 1/3). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.6 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.38-7.33 (m, 3H), 7.22-7.06 (m, 10H), 7.01 (d, *J* = 7.2 Hz, 2H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 7.2 Hz, 2H), 5.87 (s, 1H), 5.75 (s, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.14-4.08 (m, 2H), 3.49-3.40 (m, 2H), 2.92 (q, *J* = 8.4 Hz, 1H), 2.42 (s, 3H), 2.22-2.15 (m, 2H), 1.91-1.86 (m, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 174.6, 158.9, 157.6, 143.8, 139.2, 138.9, 138.3, 137.4, 134.0, 129.5, 128.8, 128.3, 128.1, 127.9, 127.5, 127.4, 127.2, 126.9, 125.0, 123.5, 121.2, 120.4, 84.2, 77.6, 71.9, 69.4, 64.8, 56.3, 27.8, 24.9, 21.5 ppm.

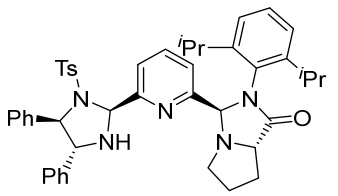



**L10**
$C_{43}H_{45}N_5O_3S$
M = 711.93 g/mol

**(3*R*,7a*S*)-2-(2,6-diethylphenyl)-3-(6-((2*S*,4*R*,5*R*)-4,5-diphenyl-1-tosylimidazolidin-2-yl)pyridin-2-yl)hexahydro-1H-pyrrolo[1,2-c]imidazol-1-one:** (**L10**) Prepared from (*S*)-*N*-(2,6-diethylphenyl)pyrrolidine-2-carboxamide (1.88 g, 10.0 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **L10** as a white solid (1.10 g, 52% yield over 2 steps).

**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.83 (t, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.25-7.15 (m, 8H), 7.06 (d, *J* = 7.6 Hz, 2H), 6.98-6.93 (m, 3H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 5.52 (s, 1H), 5.40 (s, 1H), 4.62 (d, *J* = 4.4 Hz, 1H), 4.29-4.26 (m, 1H), 4.10 (d, *J* = 4.4 Hz, 1H), 3.51-3.45 (m, 1H), 3.12-3.06 (m, 1H), 2.66-2.56 (m, 2H), 2.53-2.44 (m, 1H),

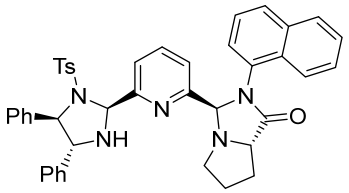
2.36 (s, 3H), 2.33-2.27 (m, 1H), 2.26-2.18 (m, 1H), 2.05-1.94 (m, 2H), 1.84-1.75 (m, 1H), 1.26-1.18 (m, 1H), 1.13 (t, *J* = 7.6 Hz, 3H), 0.72 (t, *J* = 7.6 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 173.8, 158.0, 157.2, 143.4, 142.7, 141.2, 140.5, 140.1, 137.8, 134.2, 132.0, 129.3, 128.3, 128.2, 128.0, 127.6, 127.3, 127.1, 127.0, 126.5, 126.2, 126.1, 123.8, 121.3, 85.4, 78.2, 71.1, 69.4, 65.0, 56.9, 29.0, 25.5, 24.9, 22.7, 21.5, 14.6, 13.5 ppm.




**L11**
$C_{45}H_{49}N_5O_3S$
M = 739.98 g/mol

**(3*R*,7a*S*)-2-(2,6-diisopropylphenyl)-3-(6-((2*S*,4*R*,5*R*)-4,5-diphenyl-1-tosylimidazolidin-2-yl)pyridin-2-yl)hexahydro-1H-pyrrolo[1,2-c]imidazol-1-one:** (**L11**) Prepared from (*S*)-*N*-(2,6-diisopropylphenyl)pyrrolidine-2-carboxamide (274.4 mg, 1.0 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **L11** as a white solid (273.5 mg, 37% yield over 2 steps).

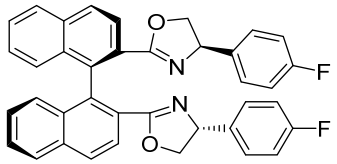
**$R_f$** = 0.4 (petroleum ether/EtOAc = 1/3). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.86 (t, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.20-7.09 (m, 10H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.94-6.86 (m, 4H), 5.62 (s, 1H), 5.31 (s, 1H), 4.47 (d, *J* = 6.0 Hz, 1H), 4.35-4.32 (m, 1H), 4.15 (d, *J* = 6.4 Hz, 1H), 3.44-3.38 (m, 1H), 3.07-3.01 (m, 1H), 2.93-2.88 (m, 1H), 2.83 (s, br, 1H), 2.41 (s, 3H), 2.33-2.26 (m, 1H), 2.24-2.15 (m, 2H), 2.04-1.90 (m, 2H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.21 (d, *J* = 6.8 Hz, 3H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 174.1, 158.2, 157.8, 147.9, 146.0, 143.7, 139.7, 139.6, 138.0, 133.9, 129.9, 129.5, 128.9, 128.2, 128.1, 127.8, 127.4, 127.3, 127.2, 126.7, 123.9, 123.7, 123.5, 121.7, 87.1, 77.8, 71.7, 69.5, 65.2, 56.9, 29.3, 29.0, 28.8, 25.4, 25.0, 24.8, 23.2, 22.6, 21.5 ppm.



**L12**
$C_{43}H_{39}N_5O_3S$
M = 705.88 g/mol

**(3*R*,7a*S*)-3-(6-((2*S*,4*R*,5*R*)-4,5-diphenyl-1-tosylimidazolidin-2-yl)pyridin-2-yl)-2-(naphthalen-1-yl)hexahydro-1H-pyrrolo[1,2-c]imidazol-1-one:** (**L12**) Prepared from (*S*)-*N*-(naphthalen-1-yl)pyrrolidine-2-carboxamide (576.7 mg, 2.4 mmol, 1.0 equiv) according to the **GP5**. Purification by flash chromatography on silica gel afforded **L12** as a white solid (241.0 mg, 14% yield over 2 steps).

**$R_f$** = 0.35 (petroleum ether/EtOAc = 5/1). **$^1$H NMR** (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.64-7.56 (m, 4H), 7.38-7.32 (m, 3H), 7.21-7.13 (m, 8H), 7.06 (d, *J* = 7.6 Hz, 3H), 6.86 (d, *J* = 7.2 Hz, 3H), 5.69 (s, 1H), 5.62 (s, 1H), 4.53 (d, *J* = 6.4 Hz, 1H), 4.45-4.42 (m, 1H), 4.05 (d, *J* = 6.4 Hz, 1H), 3.57-3.52 (m, 1H), 3.25-3.19 (m, 1H), 3.06 (s, br, 1H), 2.42 (s, 3H), 2.34-2.27 (m, 2H), 2.10-2.01 (m, 2H) ppm. **$^{13}$C NMR** (100 MHz, $CDCl_3$): δ 175.1, 158.7, 156.0, 143.8, 139.6, 139.0, 138.0, 134.3, 133.9, 132.3, 130.0, 129.5, 128.6, 128.4, 128.3, 128.2, 127.9, 127.5, 127.4, 127.0, 126.9, 126.7, 126.2, 125.3, 123.7, 121.9, 121.2, 86.6, 77.7, 71.7, 69.5, 65.1, 56.9, 28.4, 25.4, 21.5 ppm.



**L21**
$C_{38}H_{26}F_2N_2O_2$
M = 580.63 g/mol

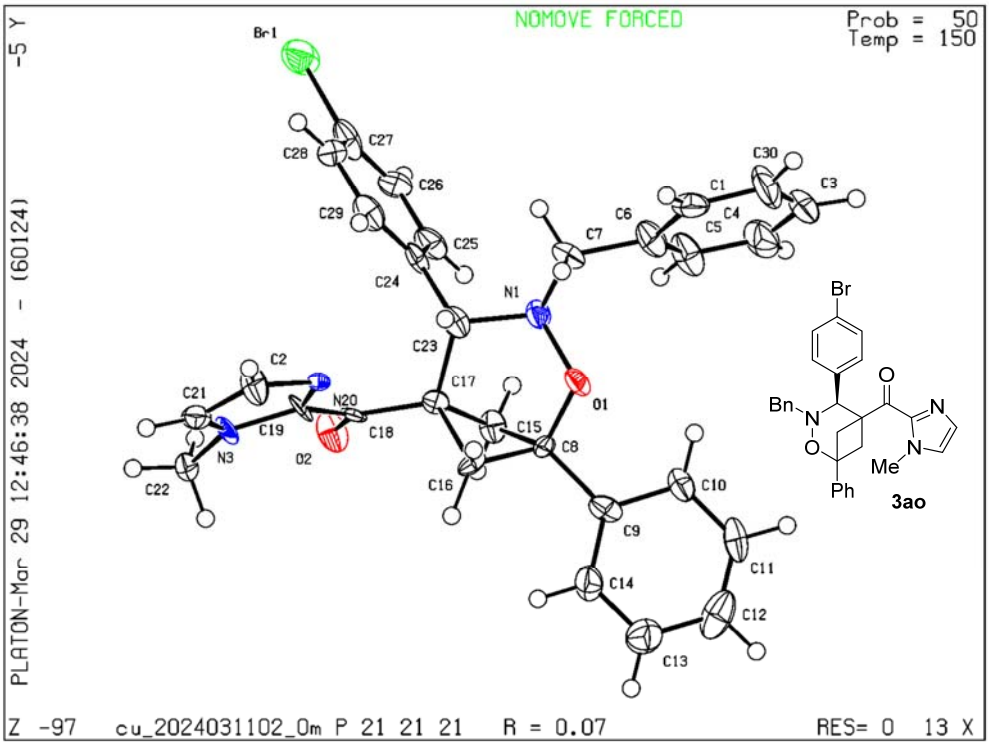
**$R_f$** = 0.3 (petroleum ether/EtOAc = 2/1). **$^1$H NMR** (600 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.98-7.95 (m, 4H), 7.55-7.52 (m, 2H), 7.31-7.25 (m, 4H), 6.72 (t, *J* = 8.6 Hz, 4H), 6.53 (dd, *J* = 8.6, 5.6 Hz, 4H), 5.04 (dd, *J* = 10.0, 8.2 Hz, 2H), 4.24 (dd, *J* = 10.2, 8.4 Hz, 2H), 3.67 (t, *J* = 8.4 Hz, 2H) ppm. **$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 165.0, 161.8

(d, *J* = 243 Hz), 138.2, 138.1, 134.5, 132.9, 127.93 (d, *J* = 6 Hz), 127.86, 127.8, 127.1, 127.0, 126.7, 126.1, 125.6, 115.0 (d, *J* = 21 Hz), 74.3, 69.3 ppm. **$^{19}$F NMR** (565 MHz, $CDCl_3$) δ -115.87 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{38}H_{27}F_2N_2O_2$: 581.2035; found: 581.2032.

## 3. X-Ray Crystallography

**Supplementary Table 3. Crystal data and structure refinement of compound 3ao**

Crystallographic files (CDCC: 2345666). There are no A-alerts and B-alerts, see CIF/checkCIF). The crystals are grown by slow solvent ($CH_2Cl_2$/$Et_2O$/*n*-Hexane) evaporation at room temperature. CCDC number of (*S*)-(3-benzyl-4-(4-bromophenyl)-1-phenyl-2-oxa-3-azabicyclo[3.1.1]heptan-5-yl)(1-methyl-1H-imidazol-2-yl)methanone **3ao** (>99% *ee*) is 2345666. Flack parameter of **3ao:** 0.116(7)



## Datablock: cu_2024031102_0m

Bond precision: C-C = 0.0133 A Wavelength=1.54178

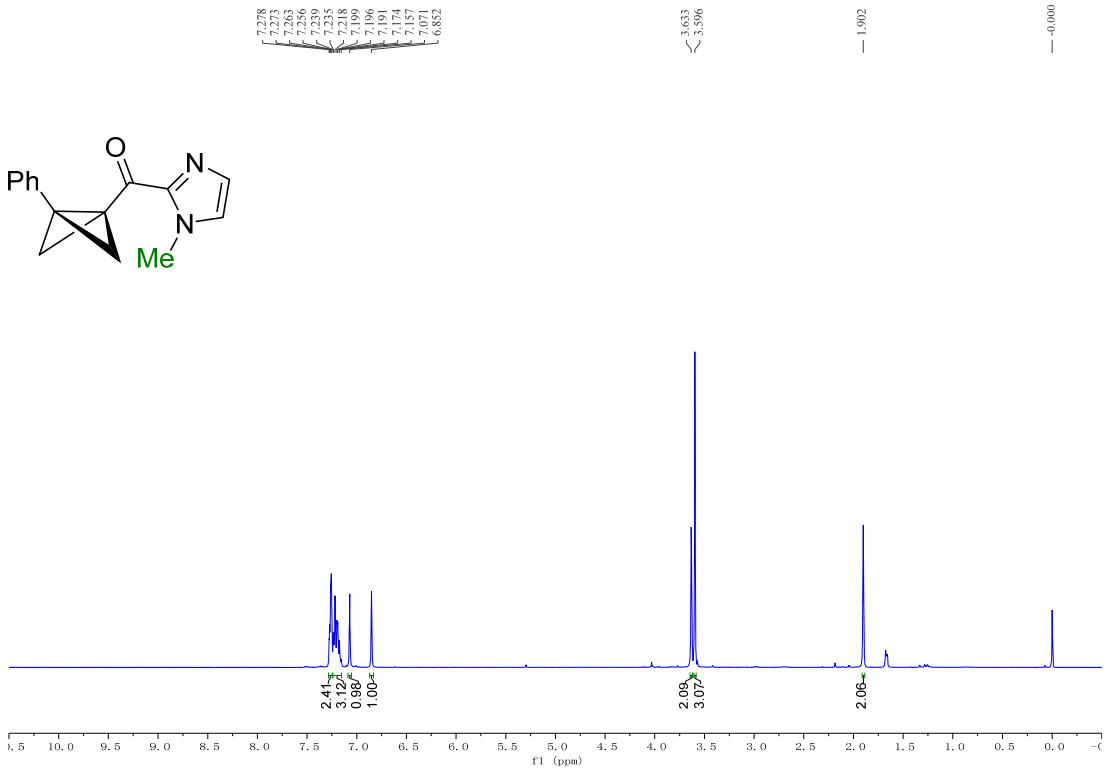
Cell: a=10.0277(2) b=10.9571(3) c=26.1879(7)
alpha=90 beta=90 gamma=90
Temperature: 150 K

| | Calculated | Reported |
|---|---|---|
| Volume | 2877.38(12) | 2877.38(12) |
| Space group | P 21 21 21 | P 21 21 21 |
| Hall group | P 2ac 2ab | P 2ac 2ab |
| Moiety formula | C29 H26 Br N3 O2 [+ solvent] | C29 H26 Br N3 O2 |
| Sum formula | C29 H26 Br N3 O2 [+ solvent] | C29 H26 Br N3 O2 |
| Mr | 528.43 | 528.44 |
| Dx,g cm-3 | 1.220 | 1.220 |
| Z | 4 | 4 |
| Mu (mm-1) | 2.162 | 2.162 |
| F000 | 1088.0 | 1088.0 |
| F000' | 1087.99 | |
| h,k,lmax | 12,13,31 | 12,13,31 |
| Nref | 5262[ 2994] | 5247 |
| Tmin,Tmax | 0.802,0.933 | 0.539,0.753 |
| Tmin' | 0.467 | |

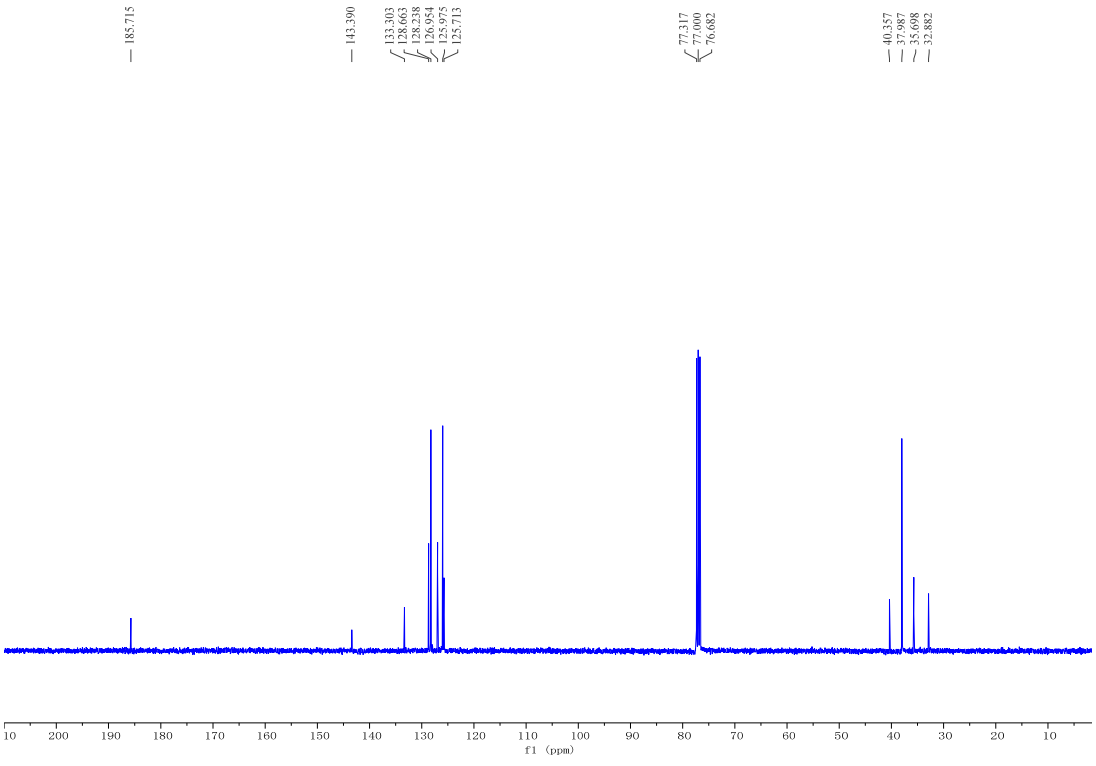
Correction method= # Reported T Limits: Tmin=0.539 Tmax=0.753
AbsCorr = MULTI-SCAN

Data completeness= 1.75/1.00 Theta(max)= 68.329

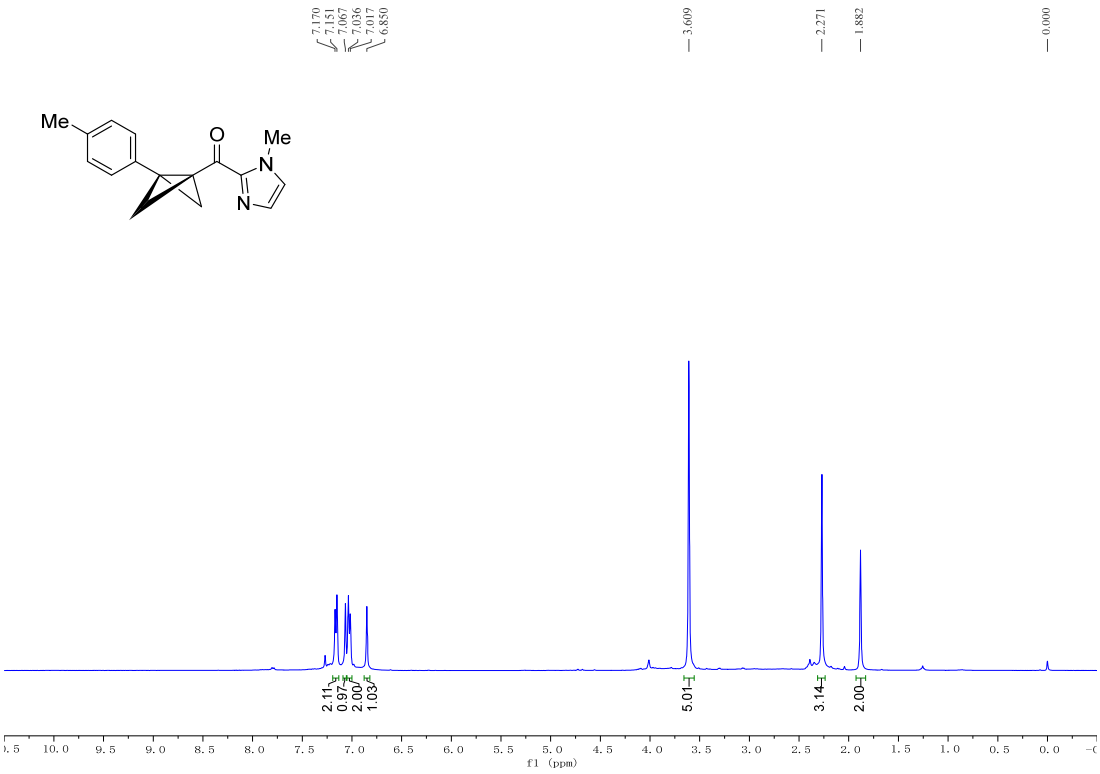
## 4. Supplementary NMR and HPLC Spectra



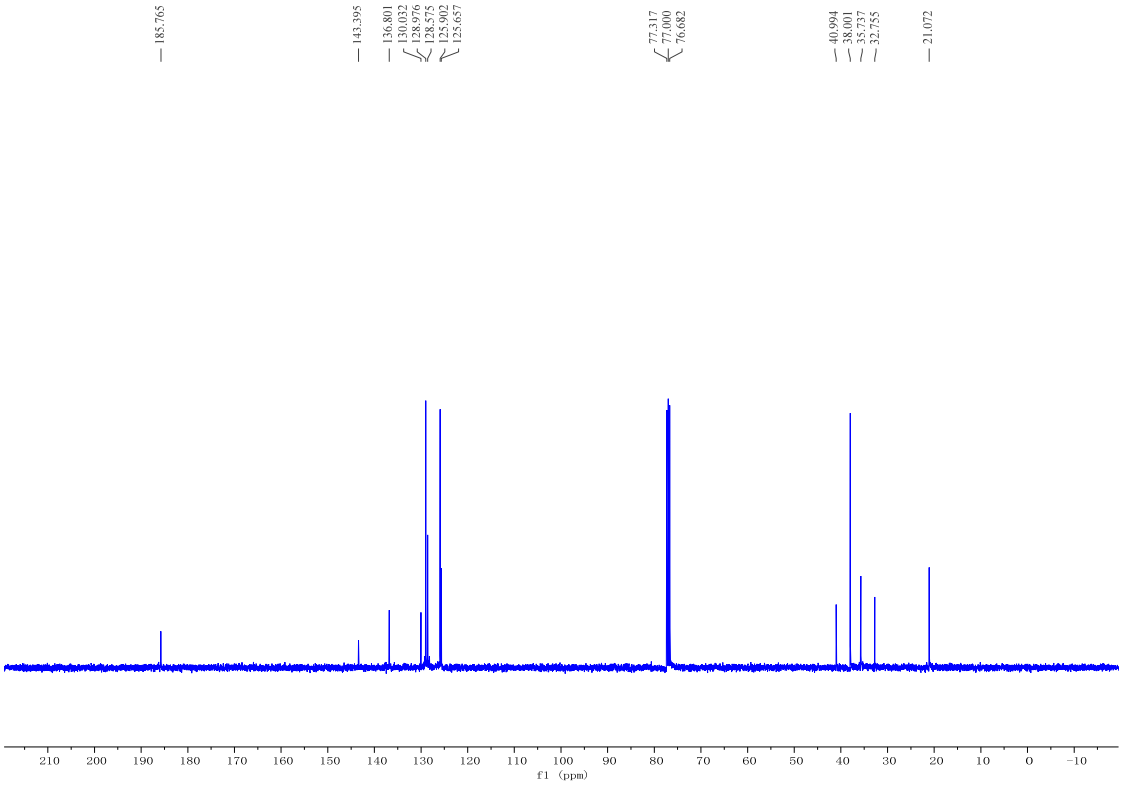

**Supplementary Figure 8.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1a**



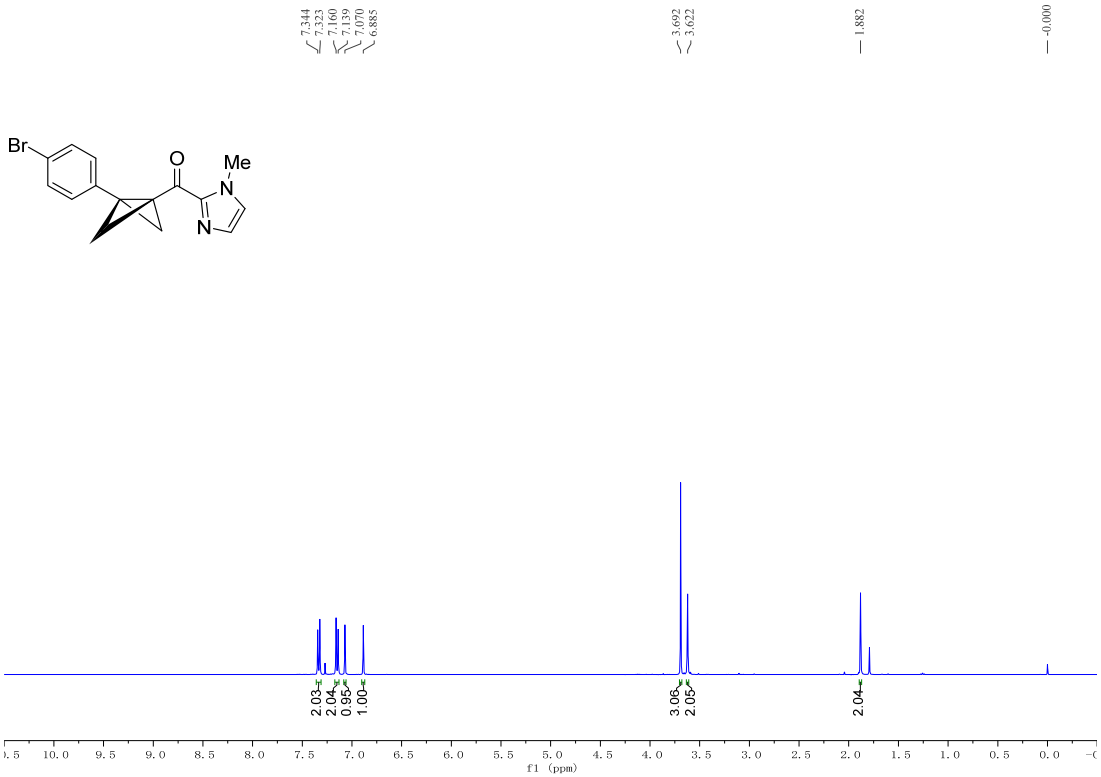

**Supplementary Figure 9.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1a**



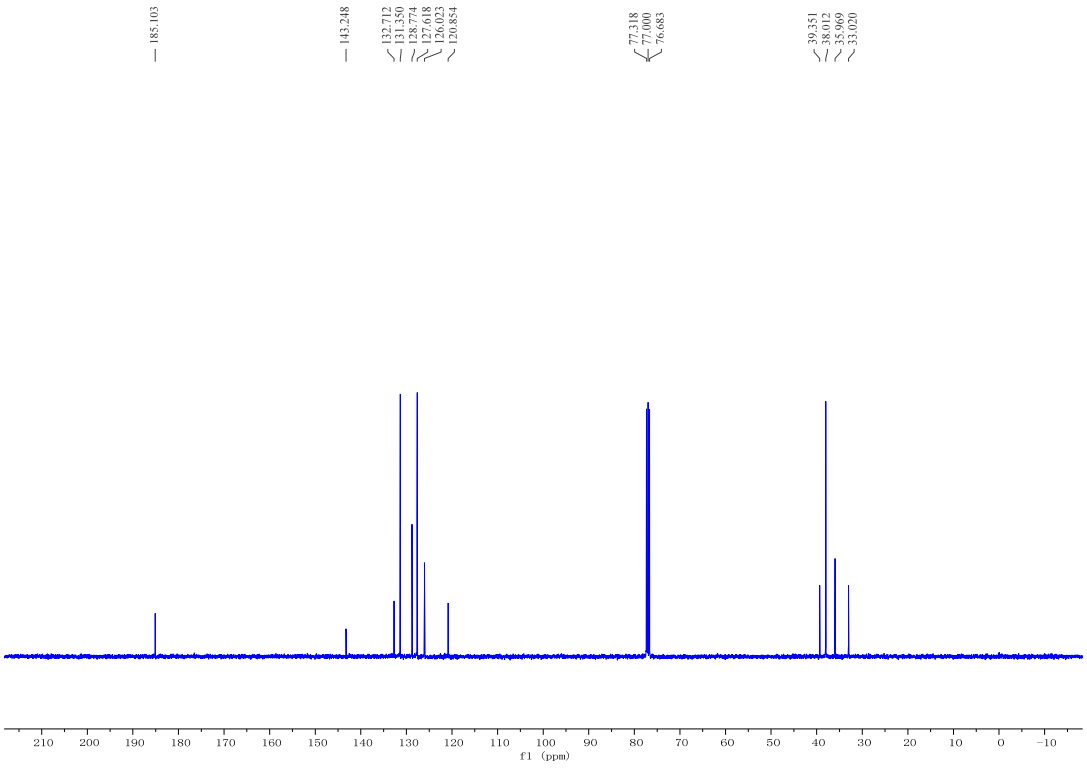

**Supplementary Figure 10.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1b**



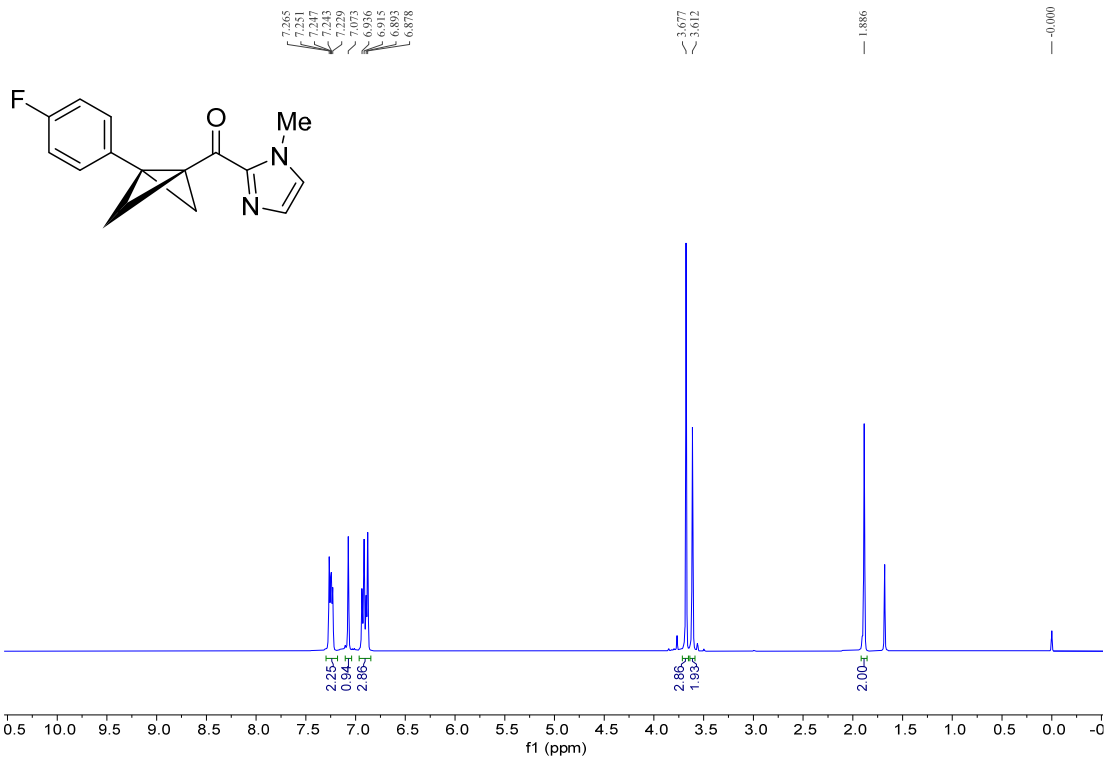

**Supplementary Figure 11.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1b**



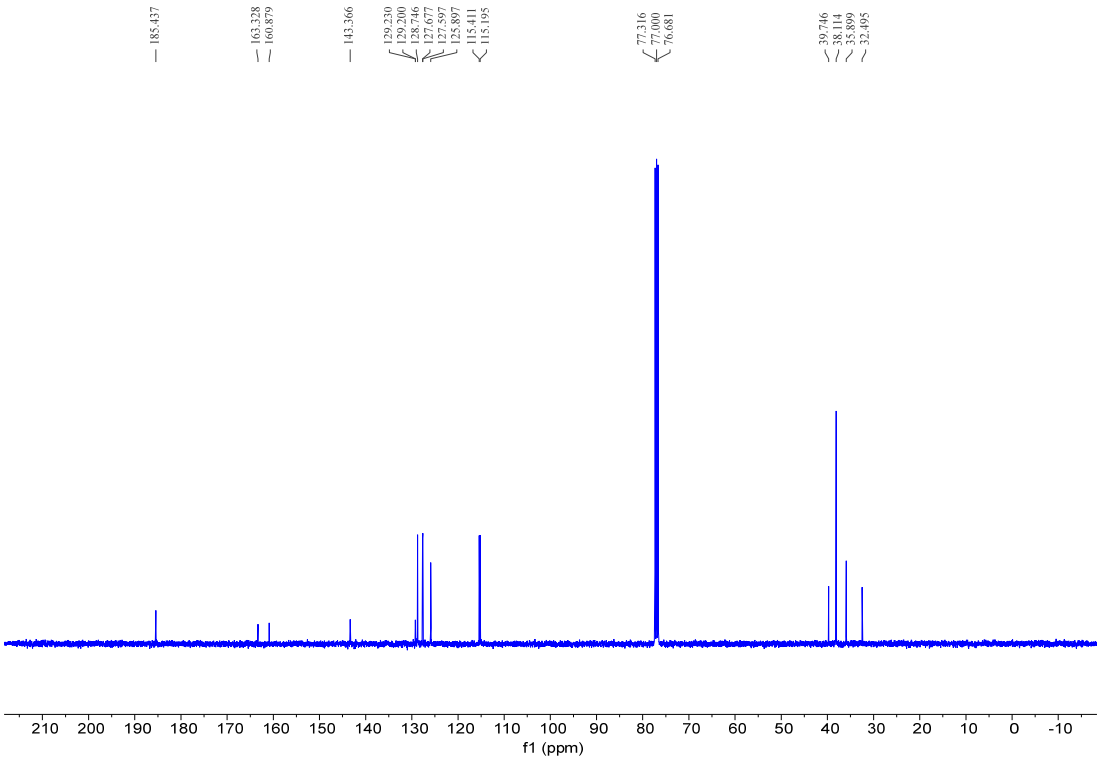

**Supplementary Figure 12.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1c**



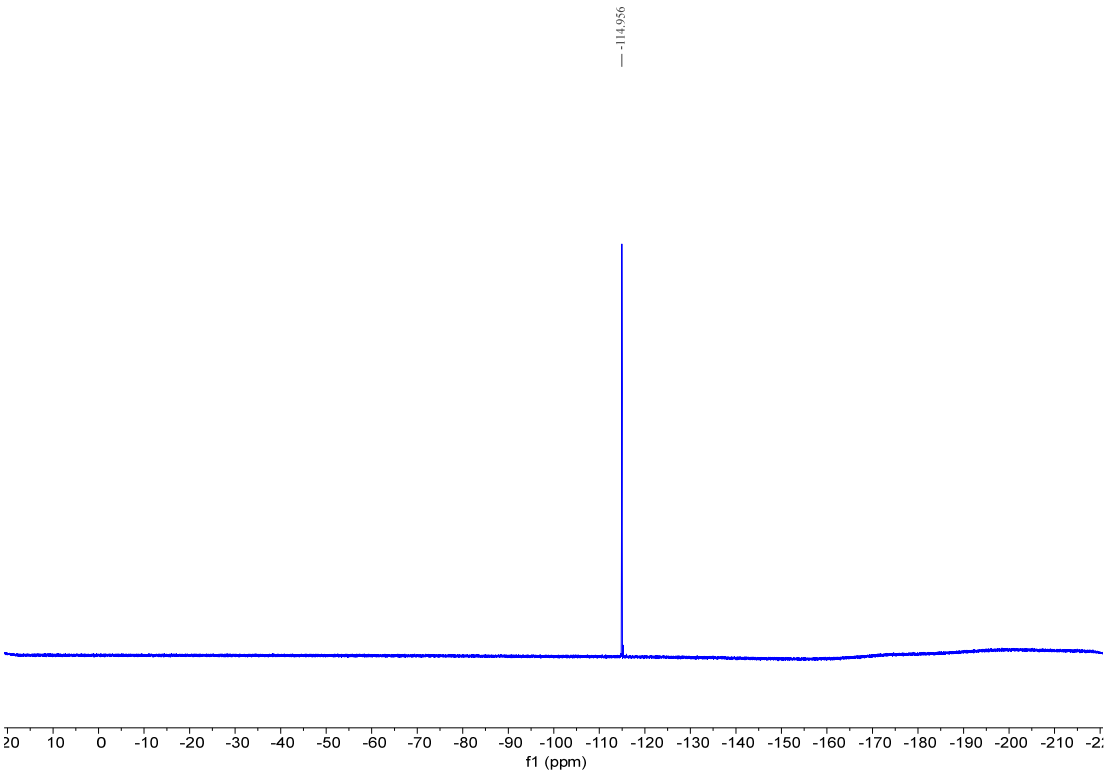

**Supplementary Figure 13.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1c**



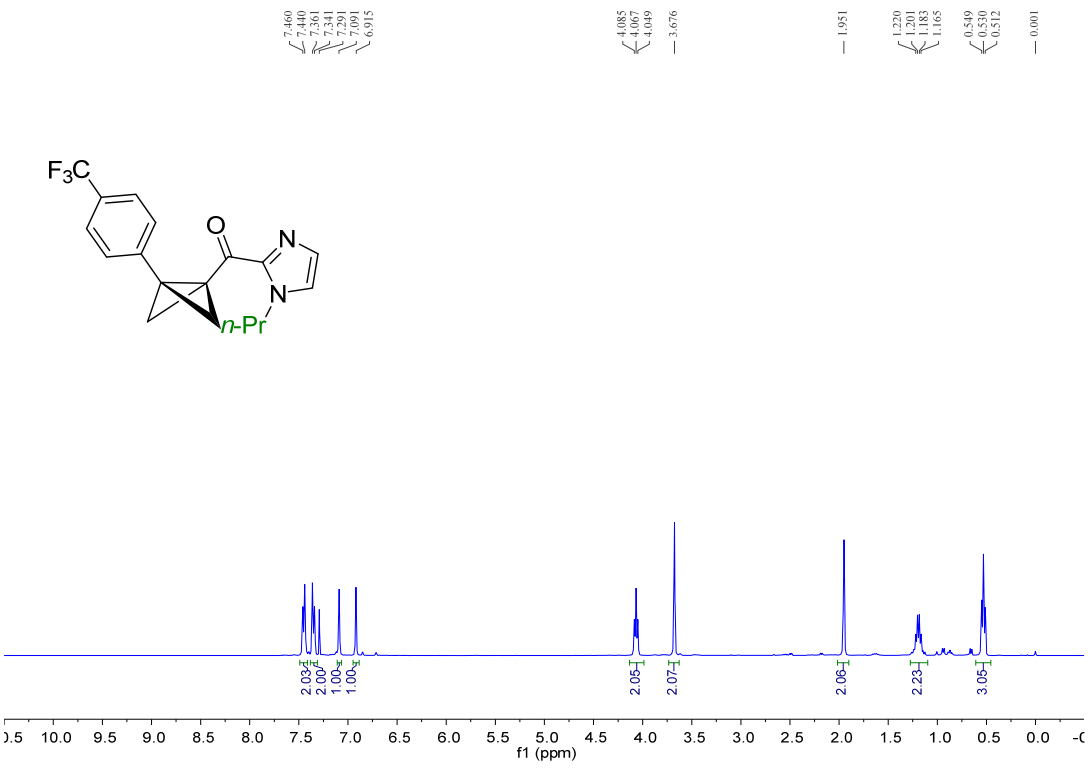

**Supplementary Figure 14.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1d**



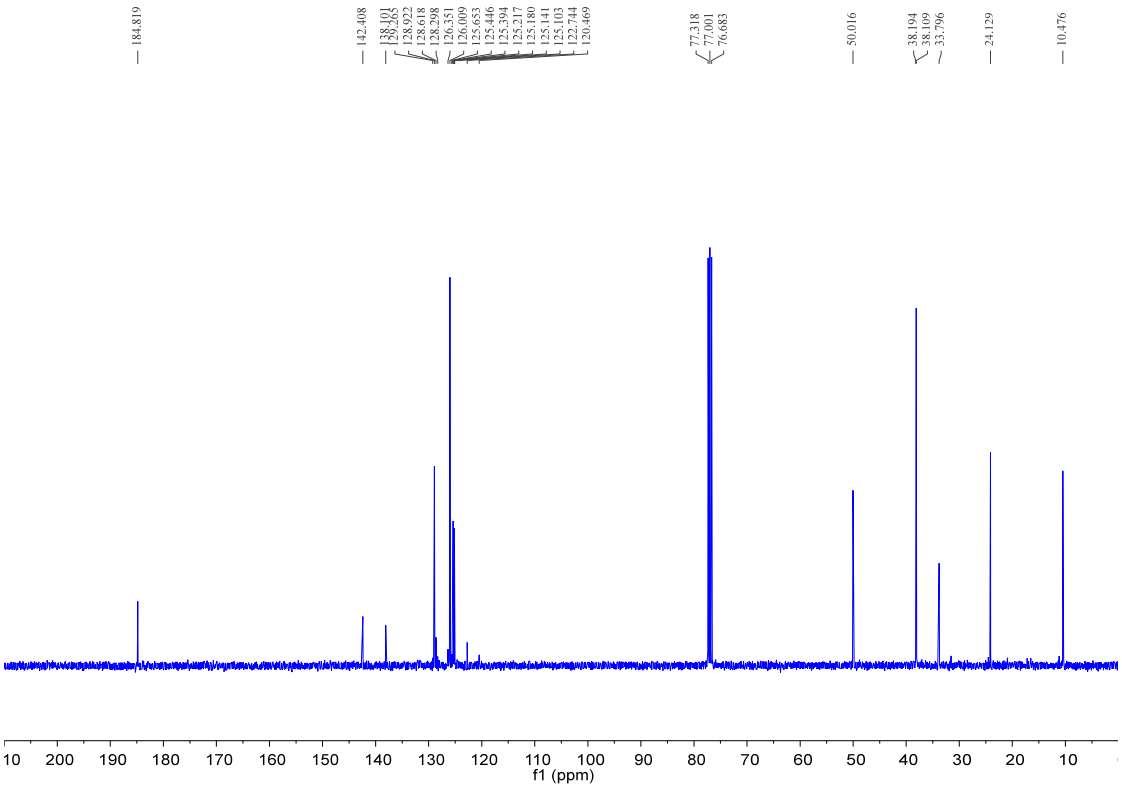

**Supplementary Figure 15.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1d**



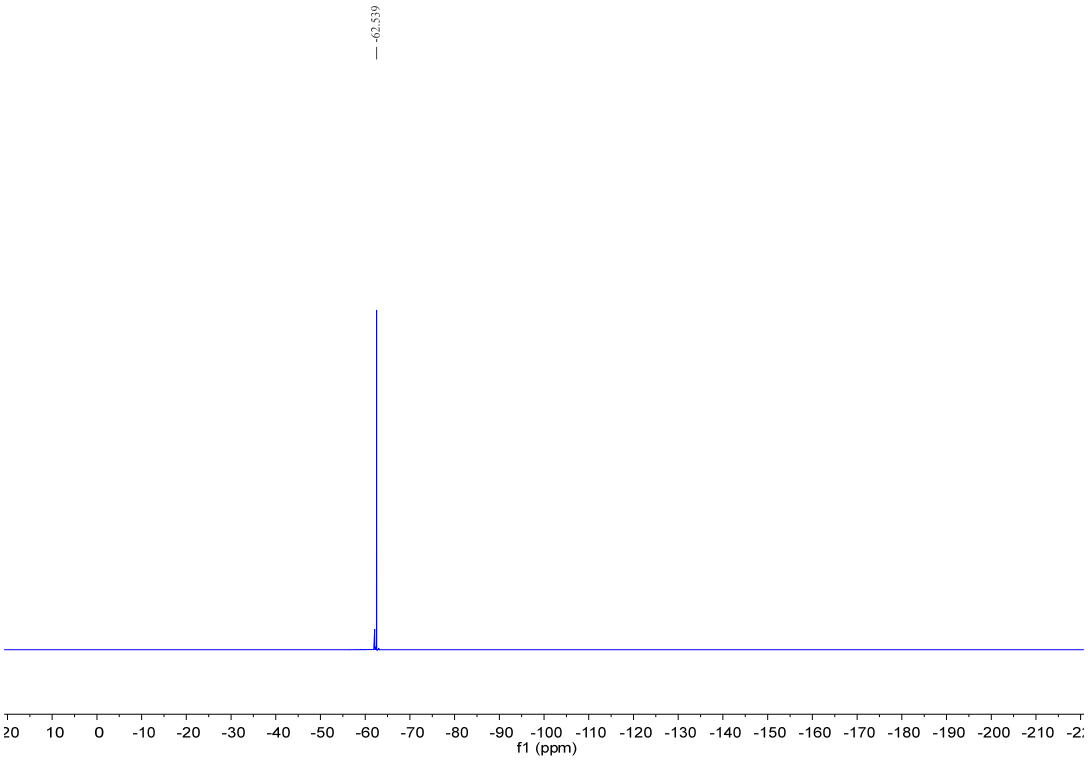

**Supplementary Figure 16.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **1d**



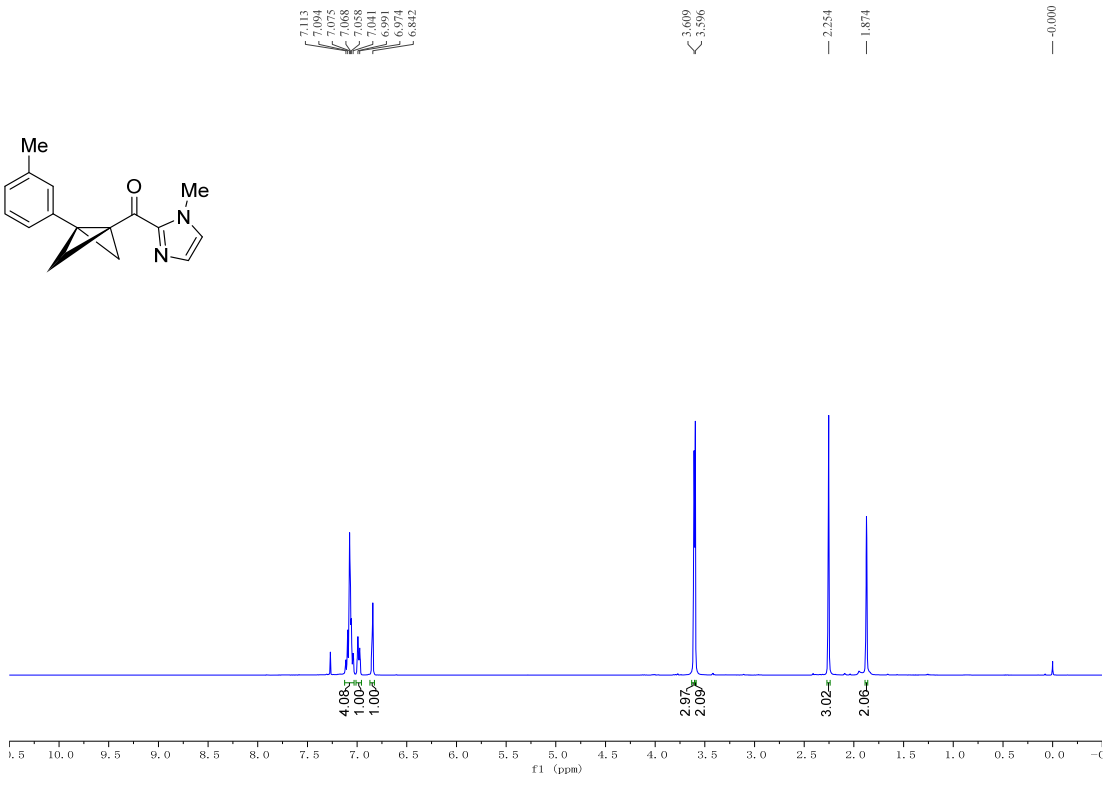

**Supplementary Figure 17.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1e**



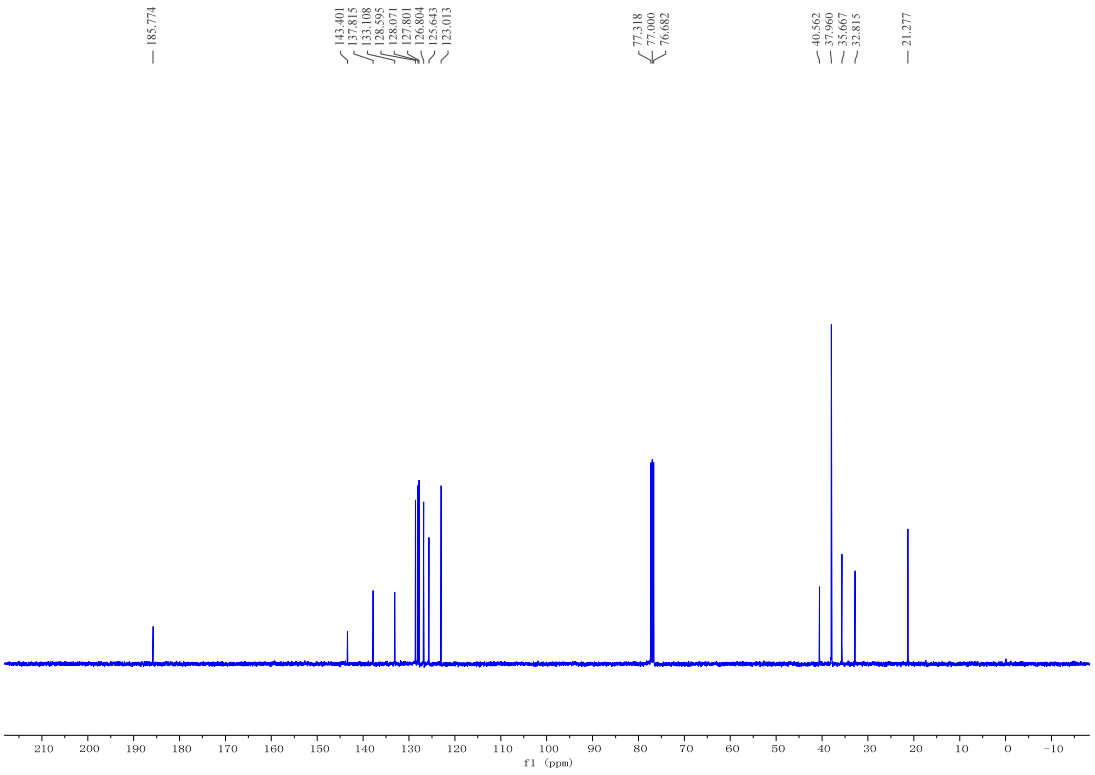

**Supplementary Figure 18.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1e**



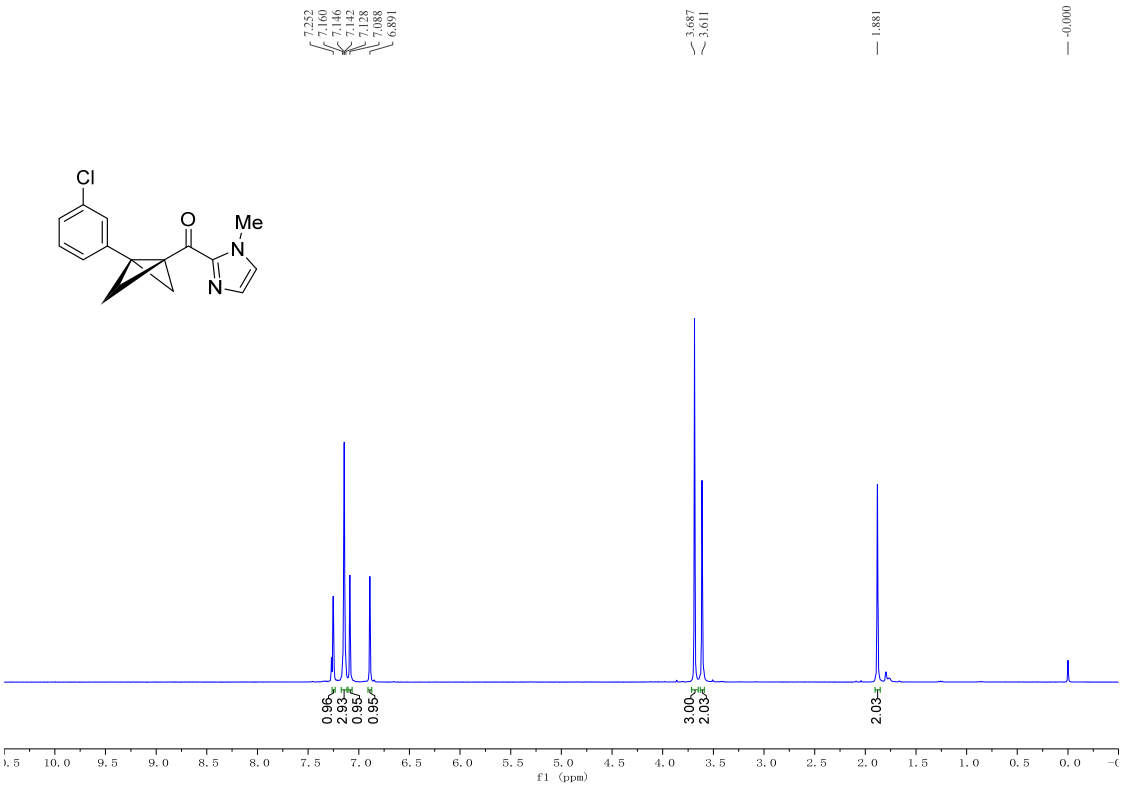

**Supplementary Figure 19.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **1e**



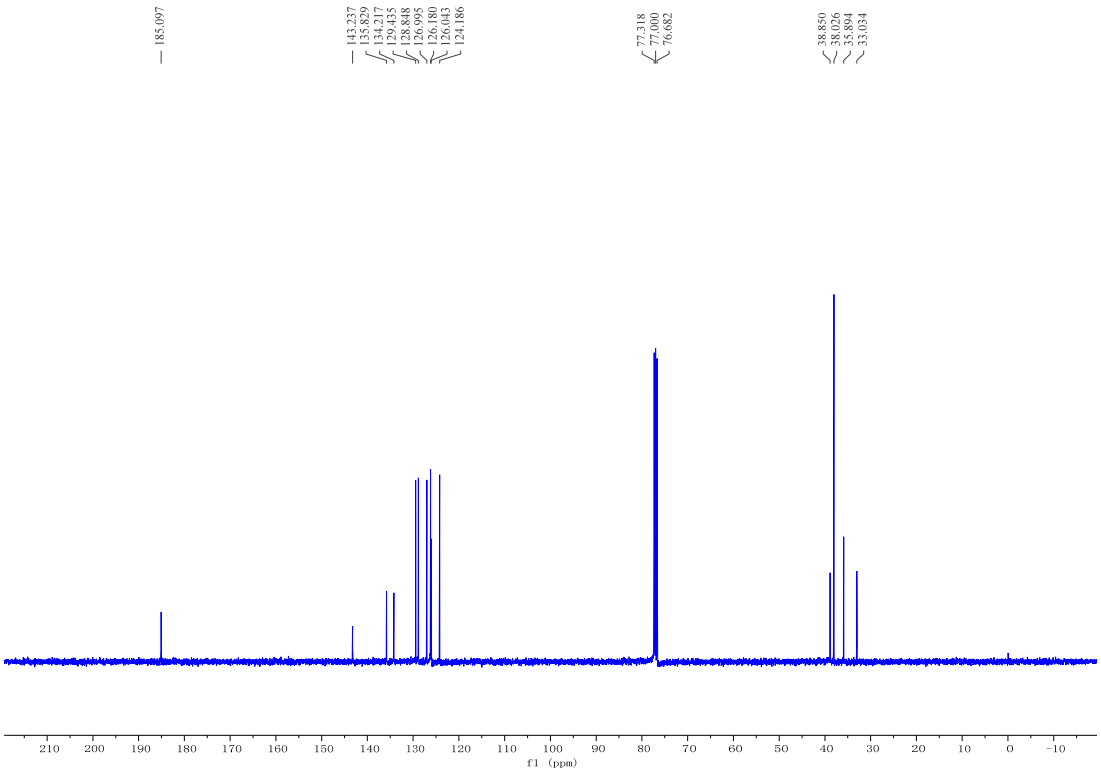

**Supplementary Figure 20.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1f**



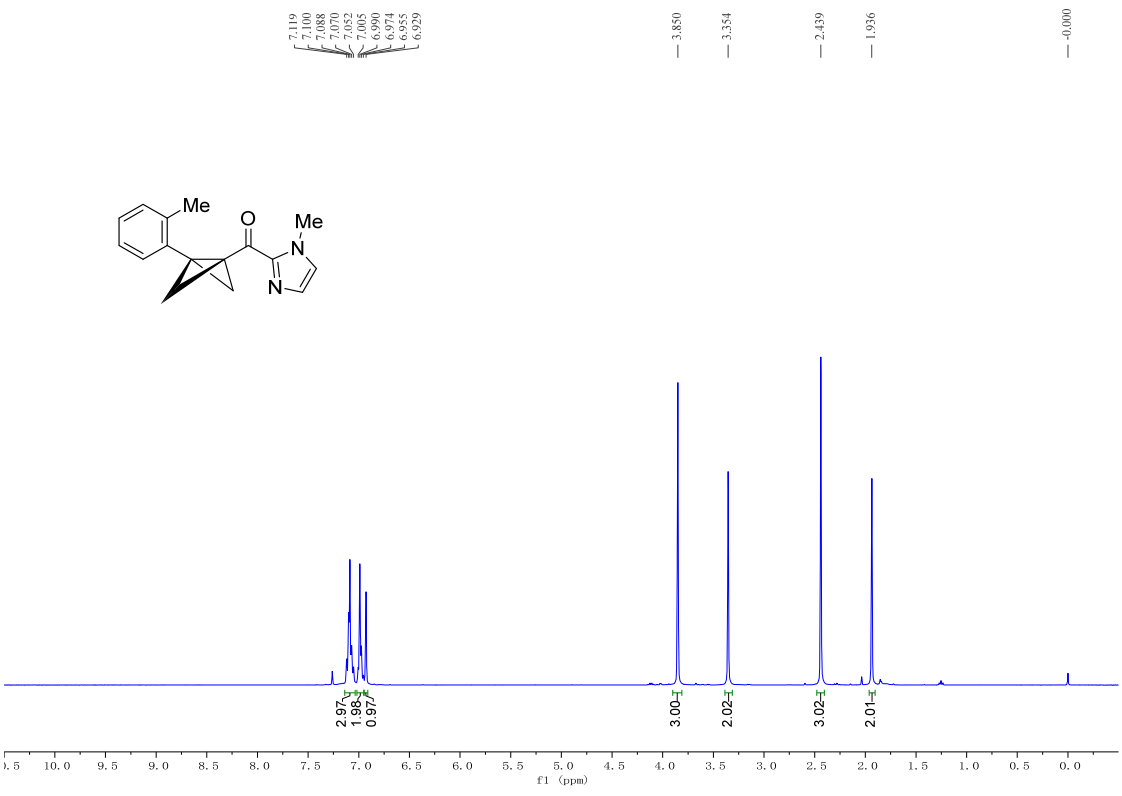

**Supplementary Figure 21.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1f**



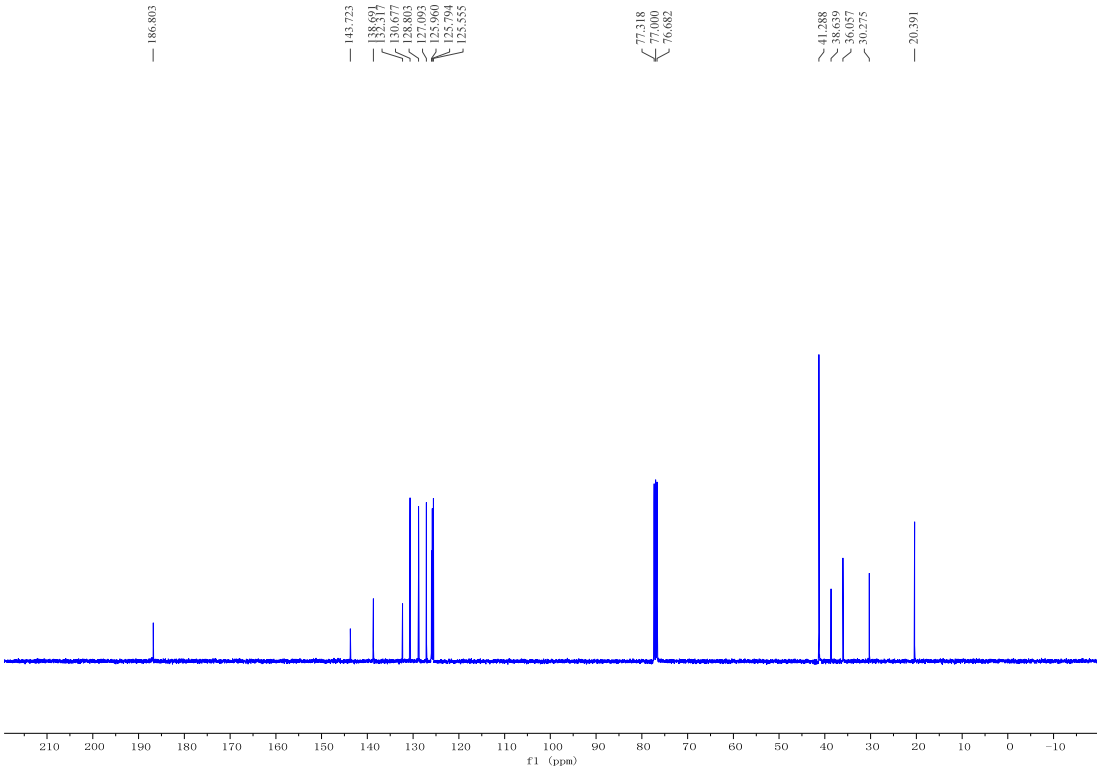

**Supplementary Figure 22.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1g**



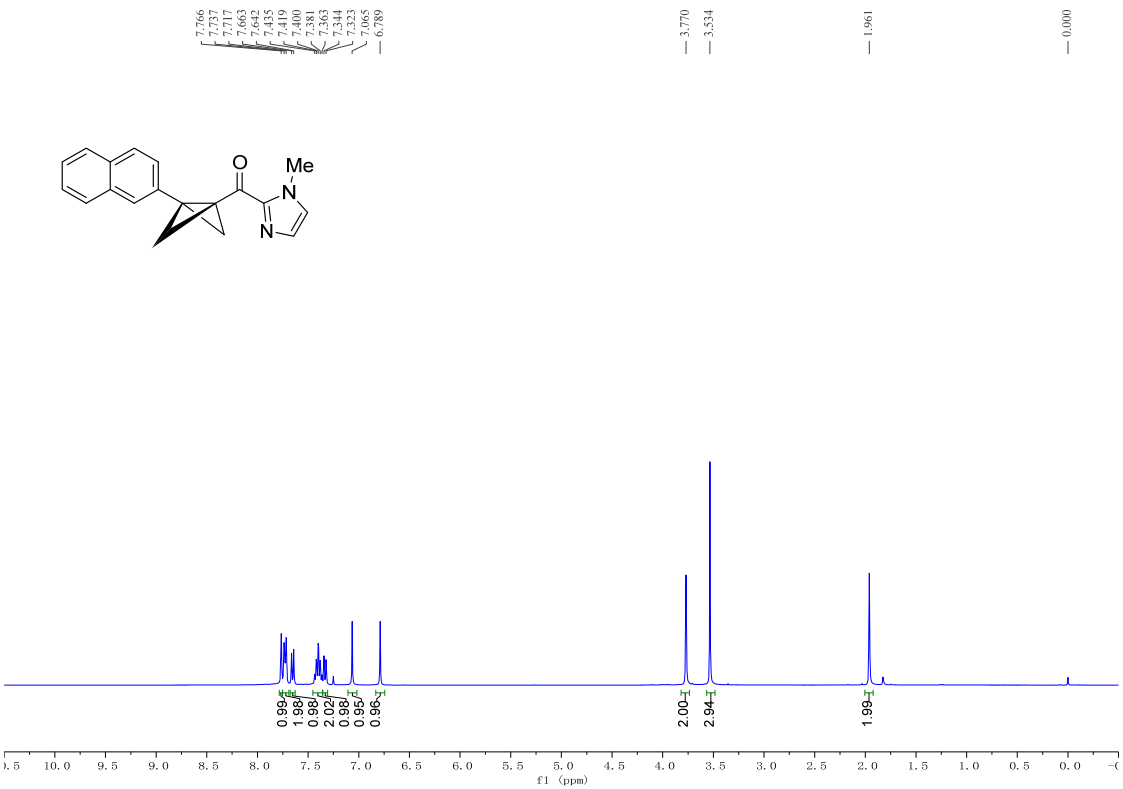

**Supplementary Figure 23.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1g**



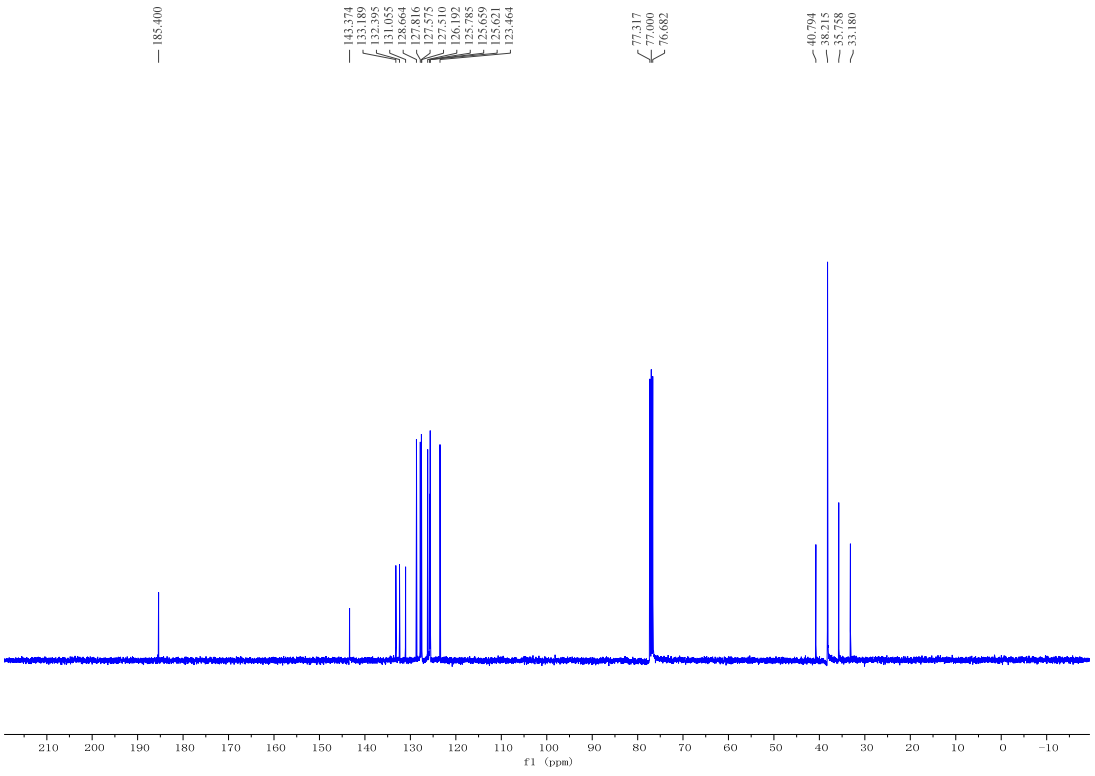

**Supplementary Figure 24.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1h**



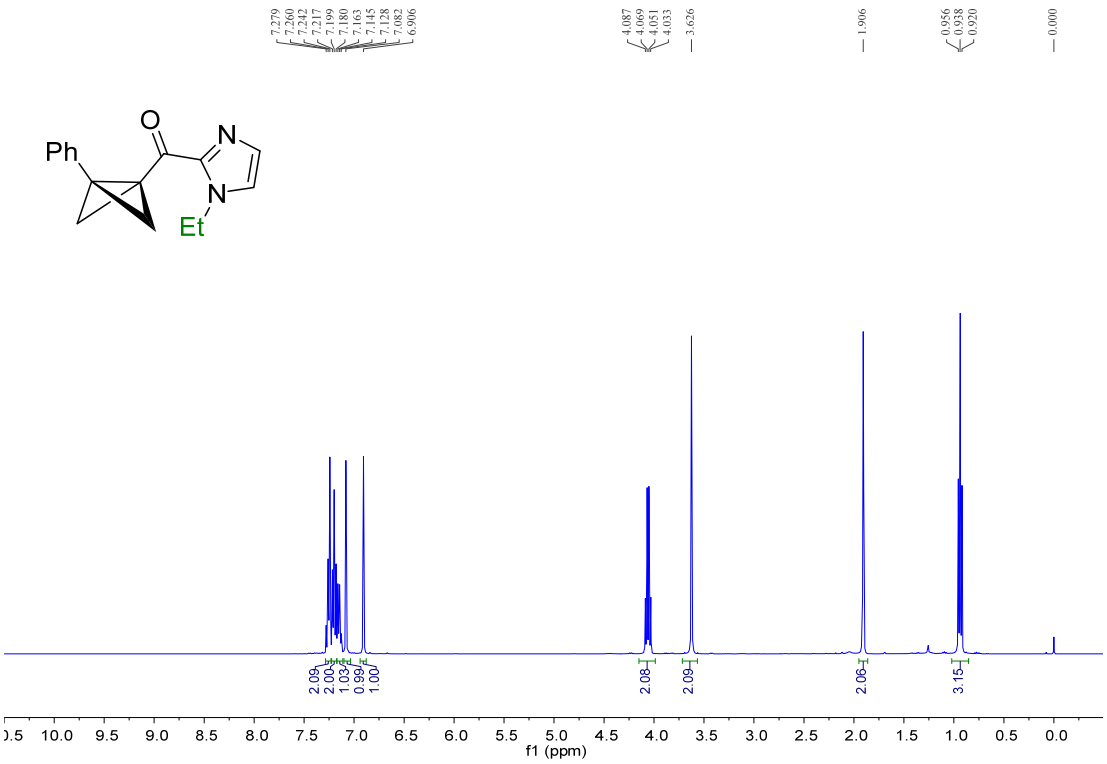

**Supplementary Figure 25.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1h**



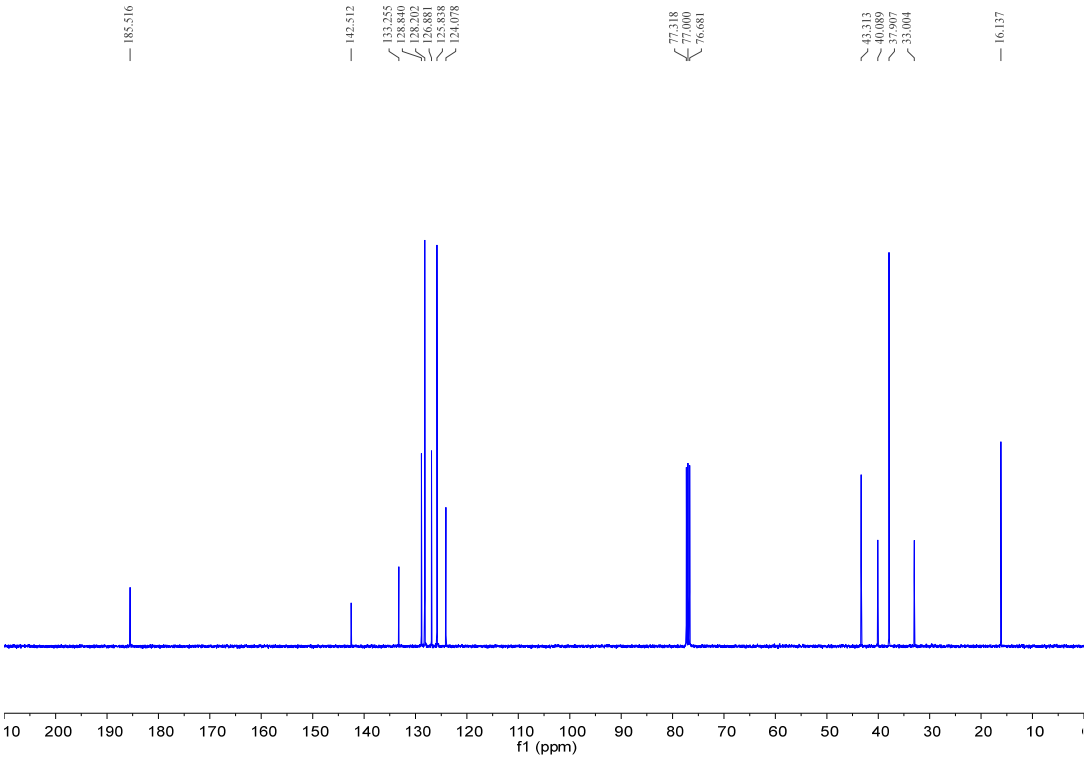

**Supplementary Figure 26.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1i**



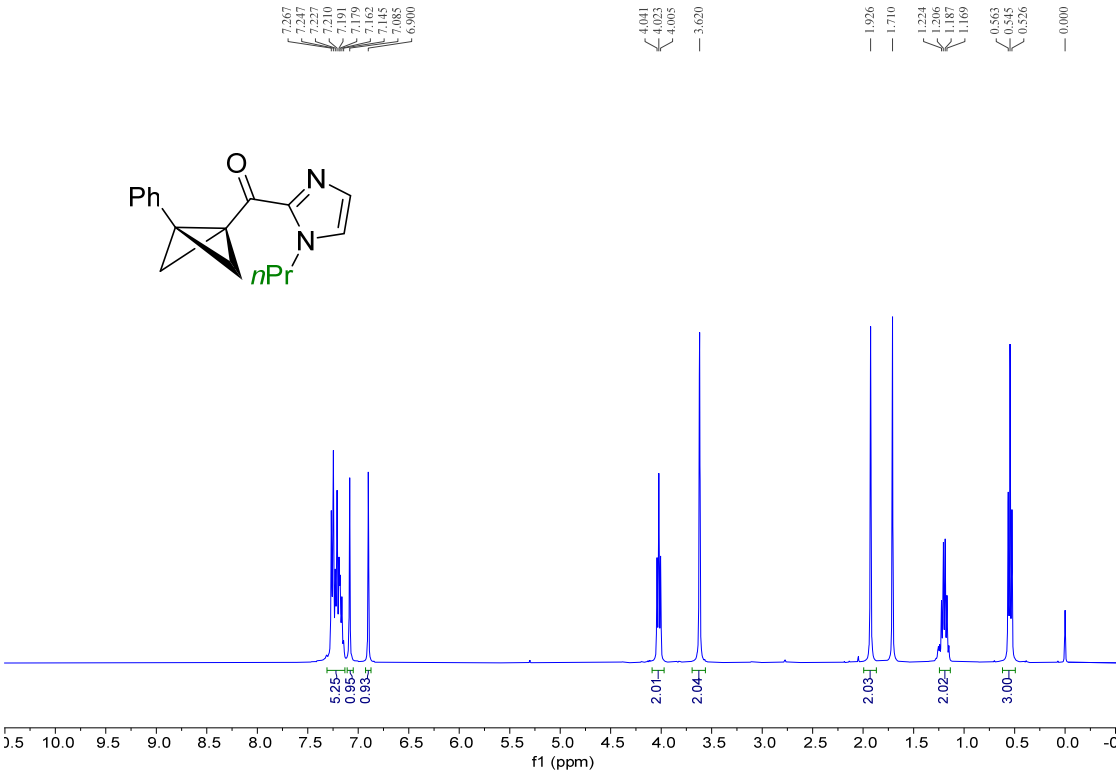

**Supplementary Figure 27.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1i**



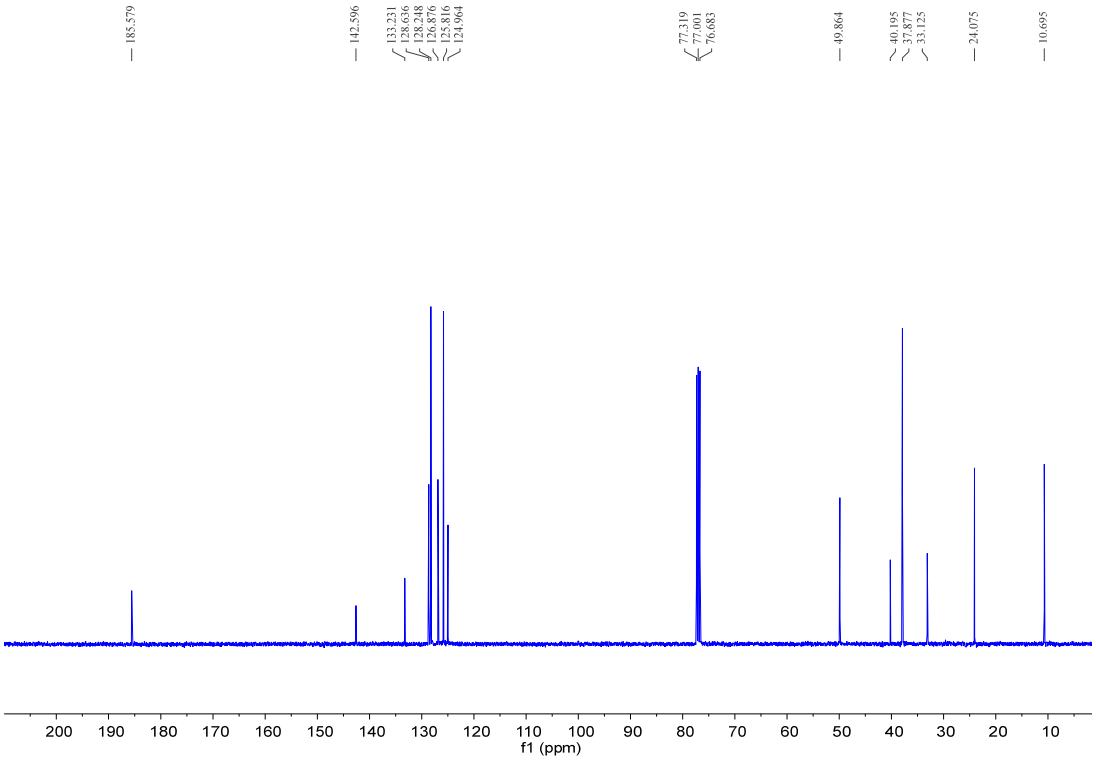

**Supplementary Figure 28.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1j**



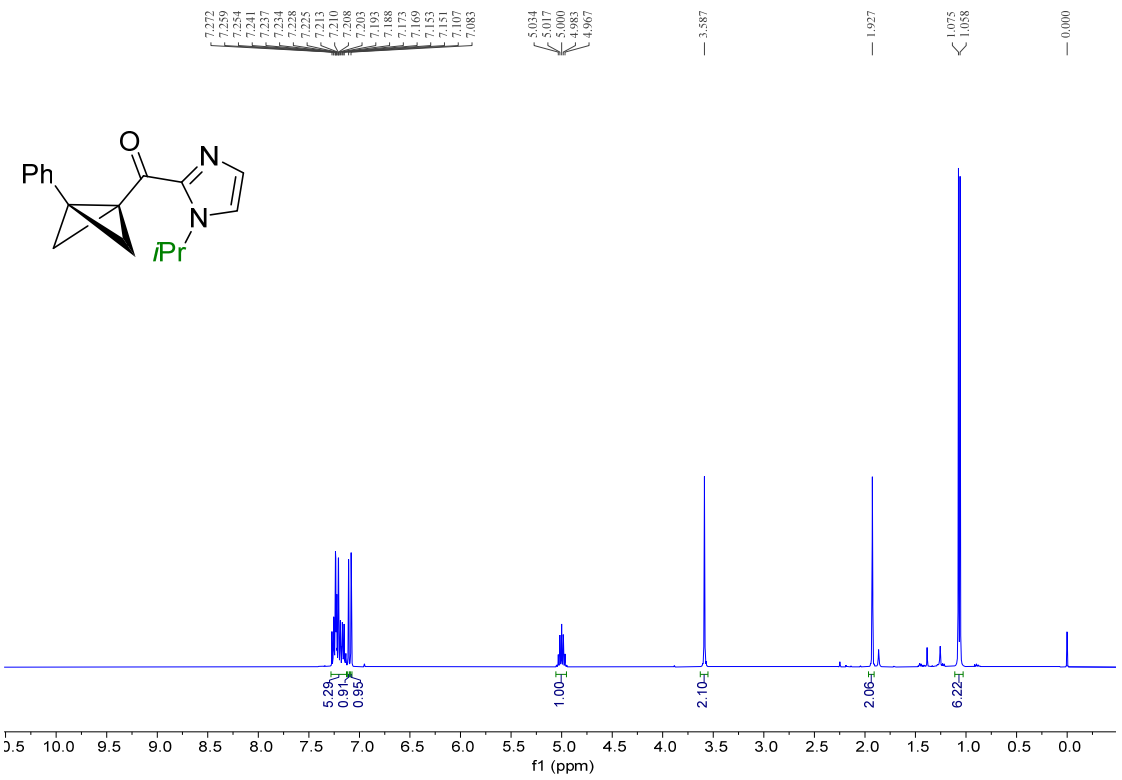

**Supplementary Figure 29.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1j**



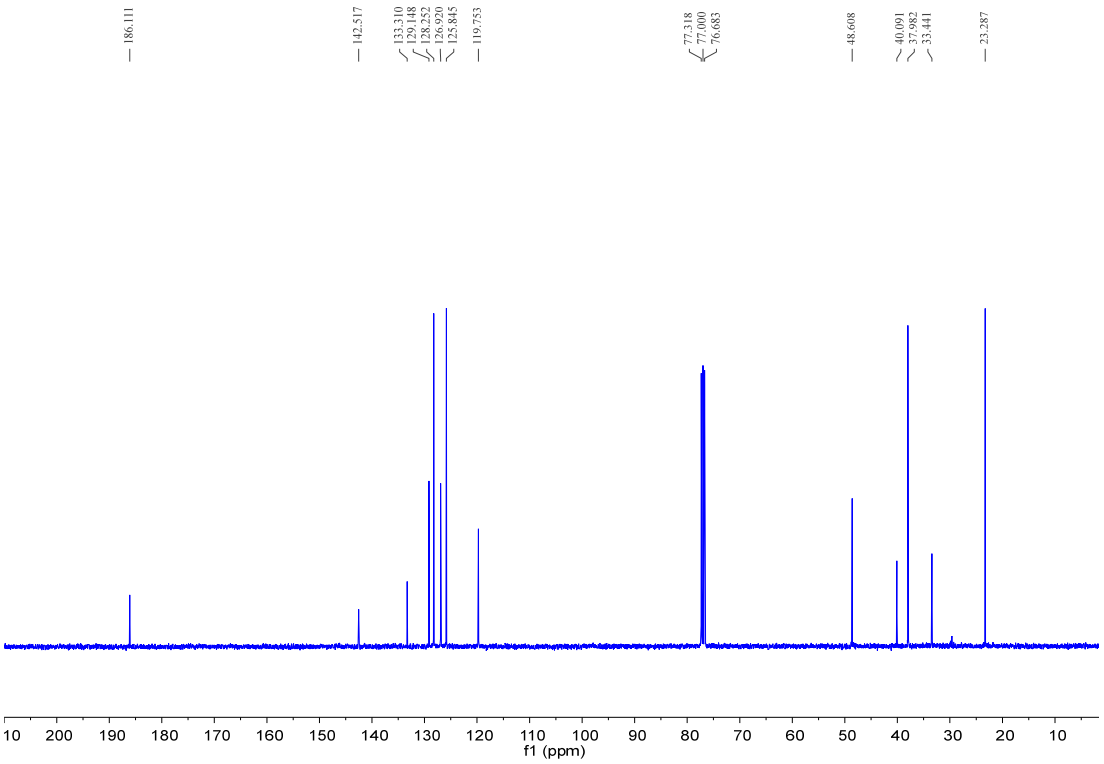

**Supplementary Figure 30.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1k**



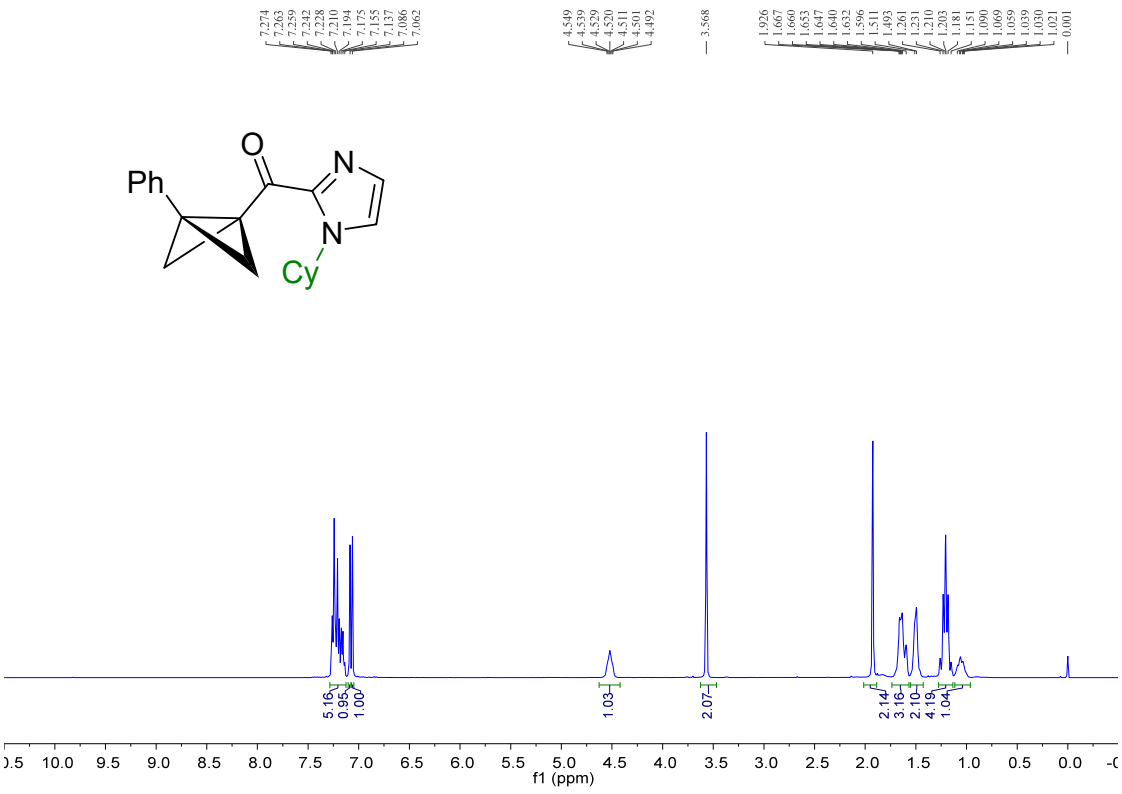

**Supplementary Figure 31.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1k**



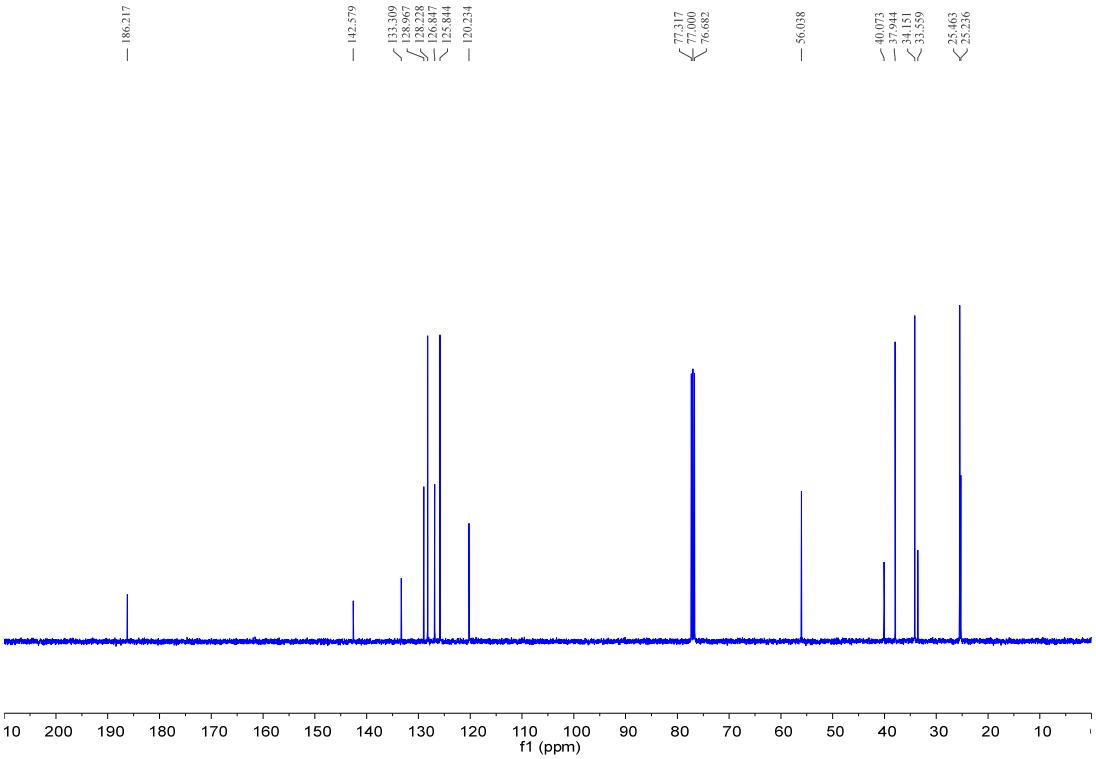

**Supplementary Figure 32.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1l**



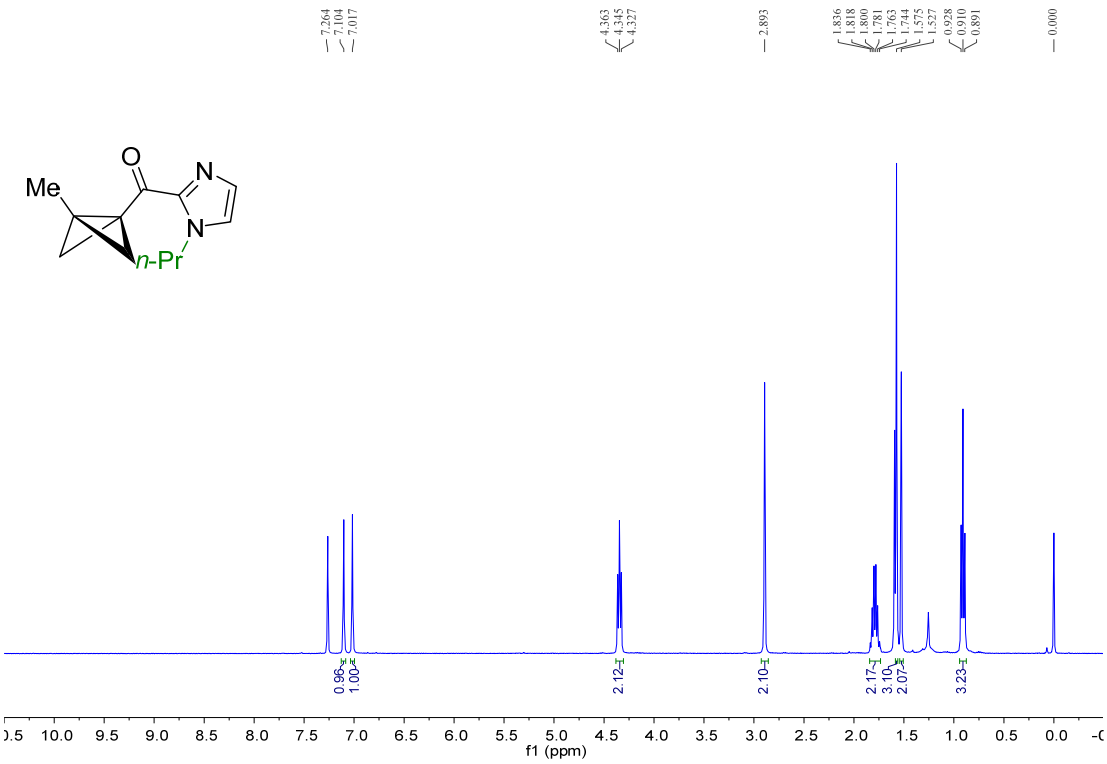

**Supplementary Figure 33.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1l**



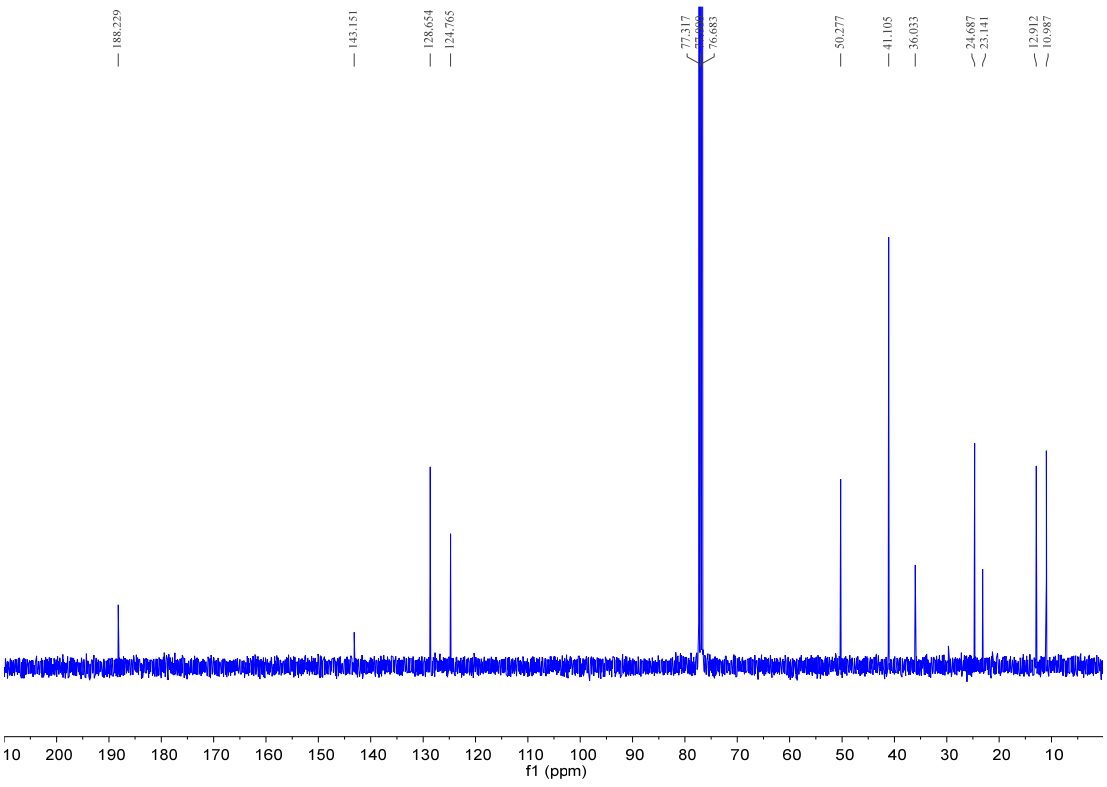

**Supplementary Figure 34.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **1m**



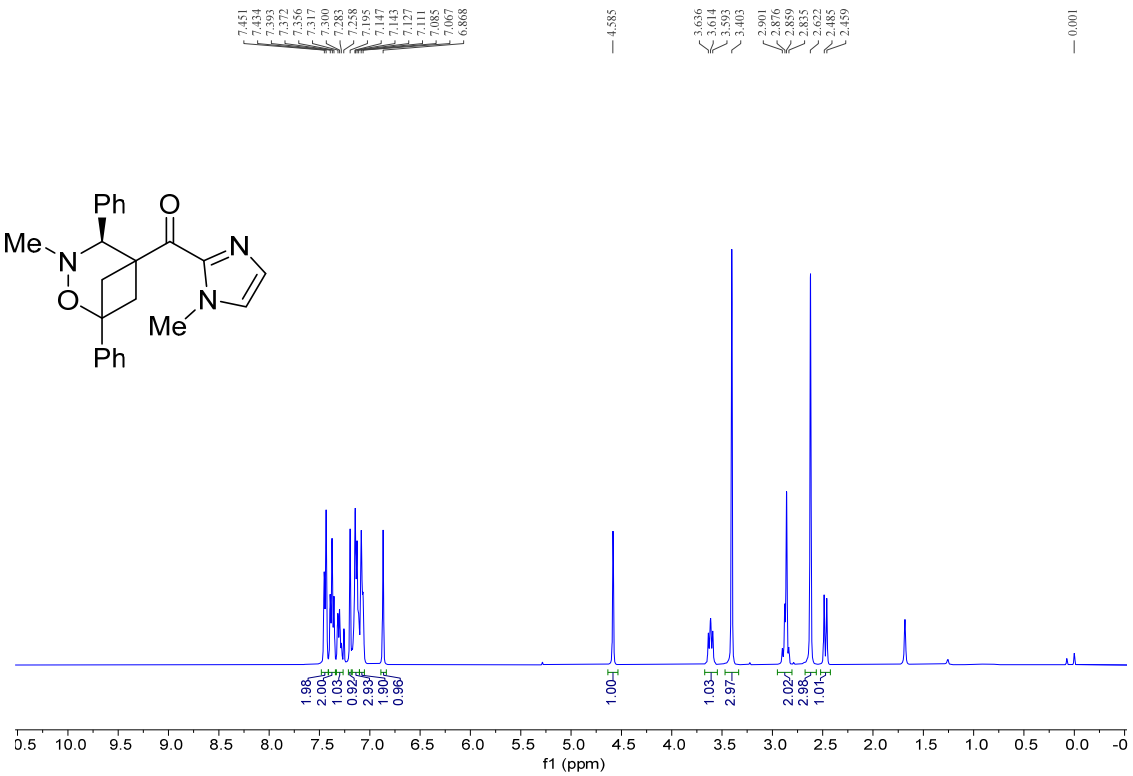

**Supplementary Figure 35.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **1m**



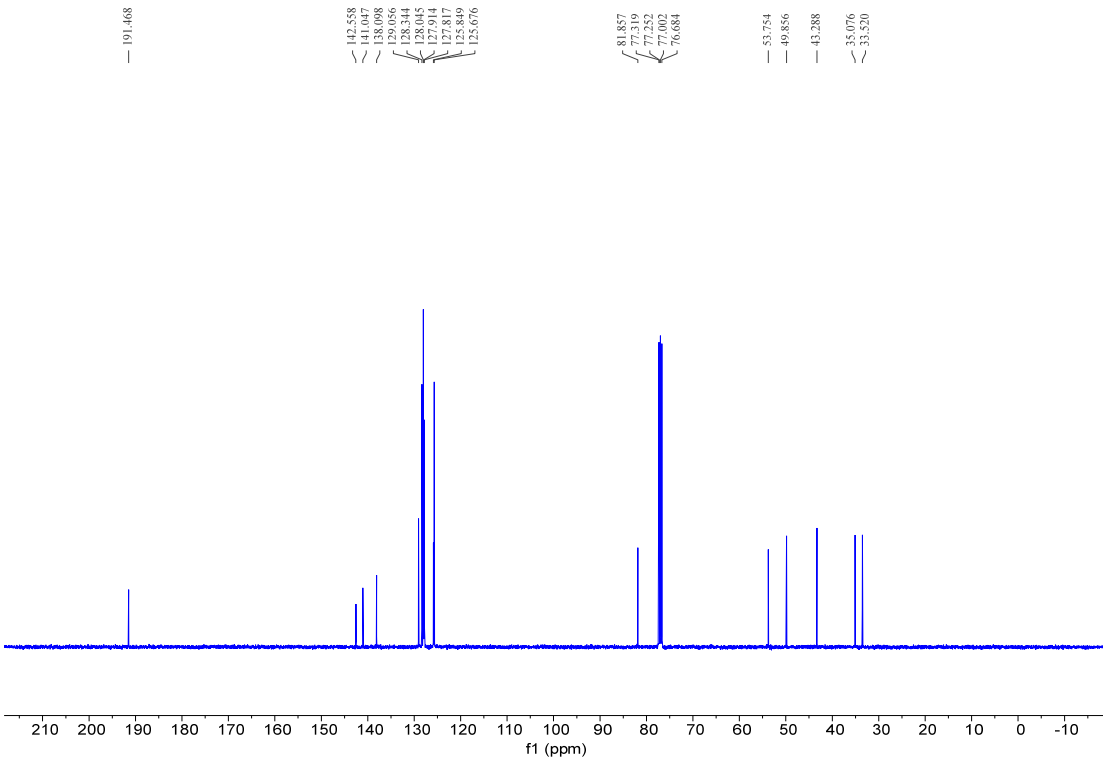

**Supplementary Figure 36.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **1q**



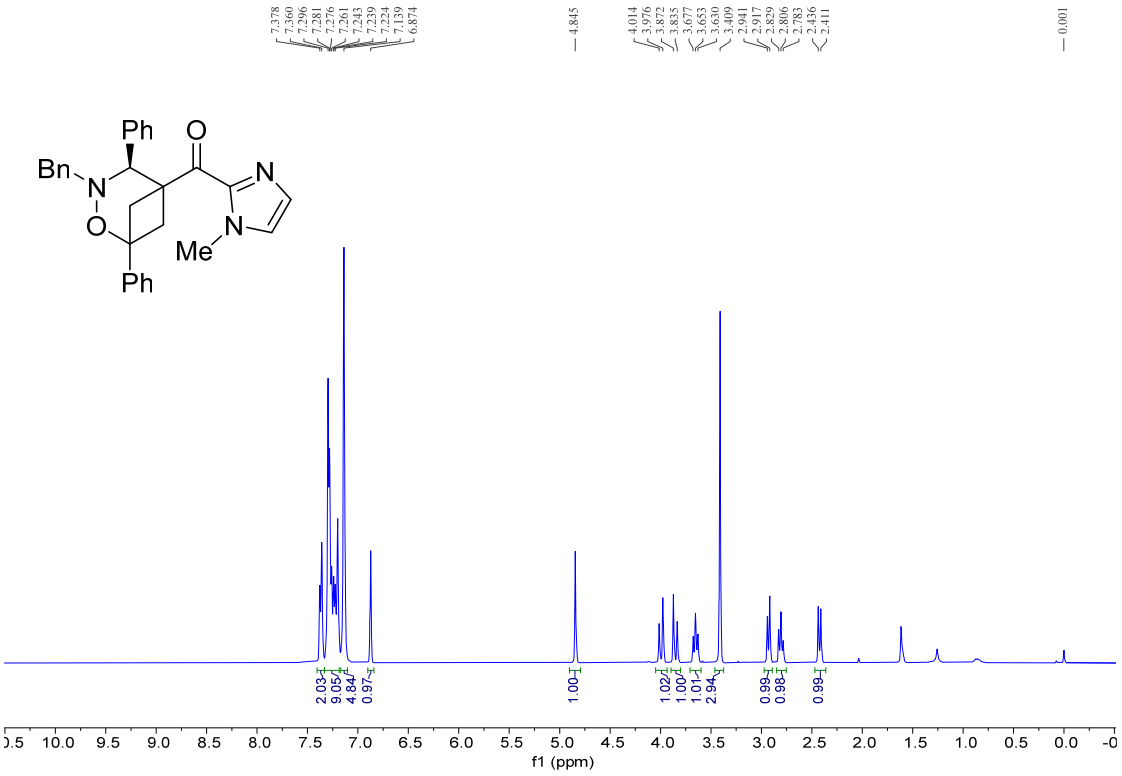

**Supplementary Figure 37.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **1q**



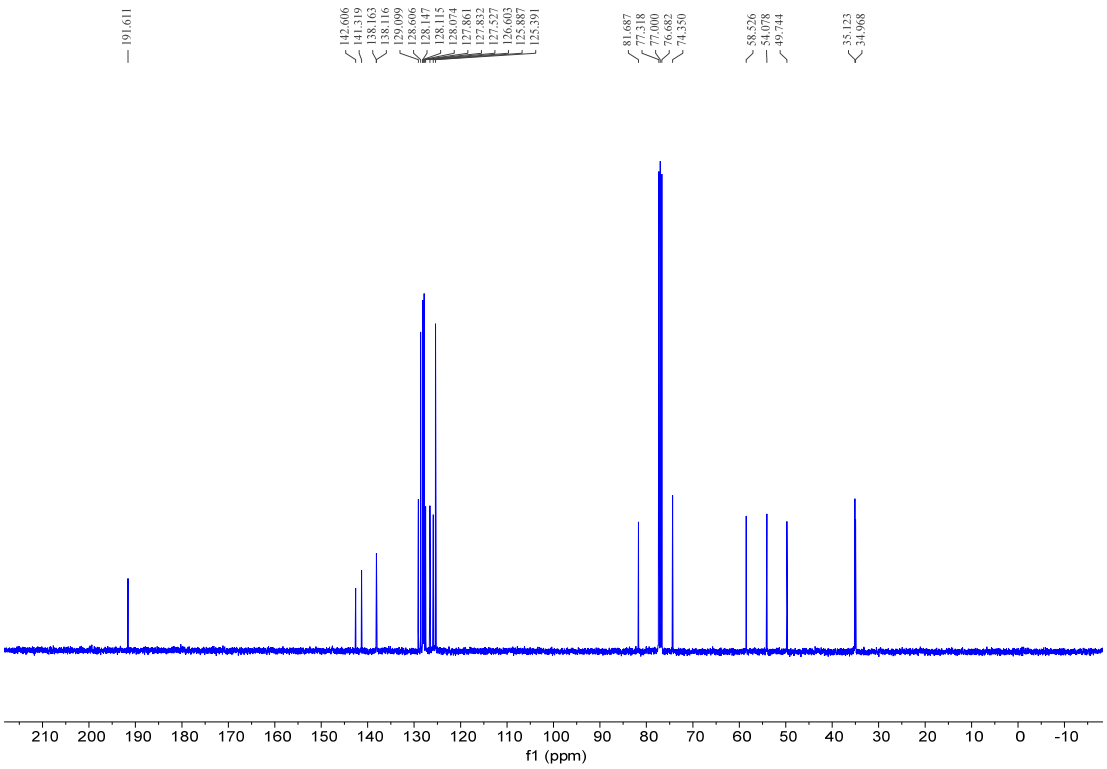

**Supplementary Figure 38.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3aa**



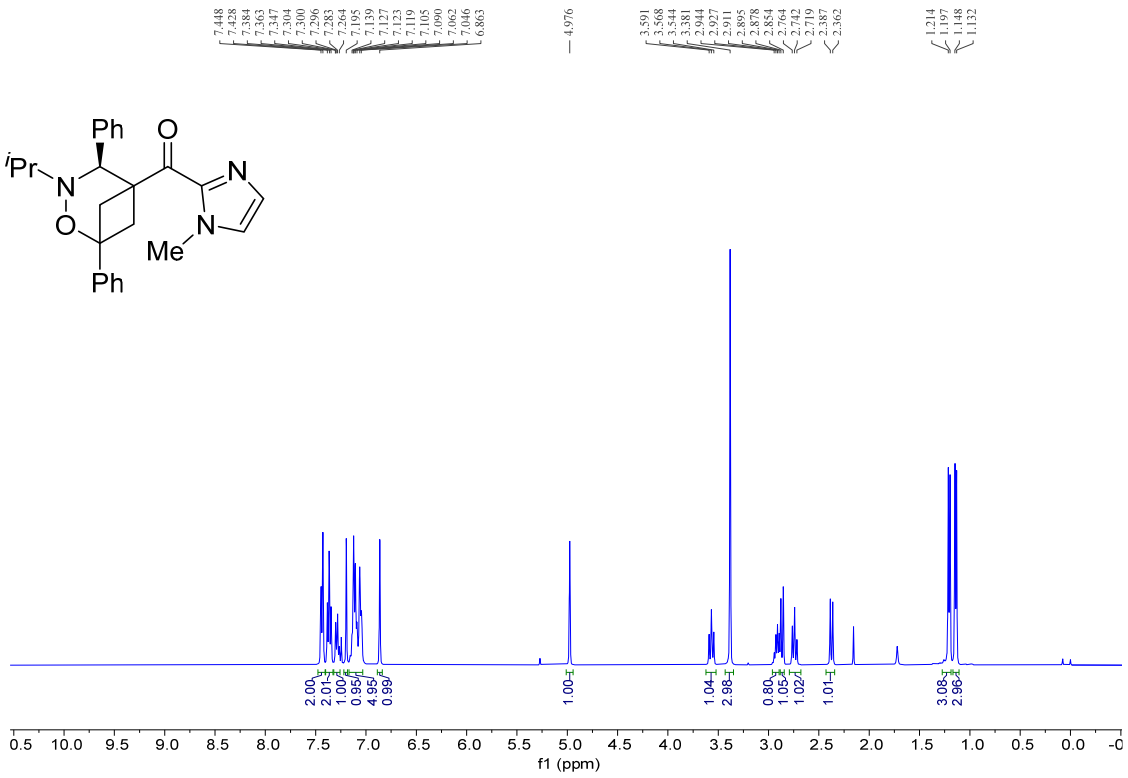

**Supplementary Figure 39.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3aa**



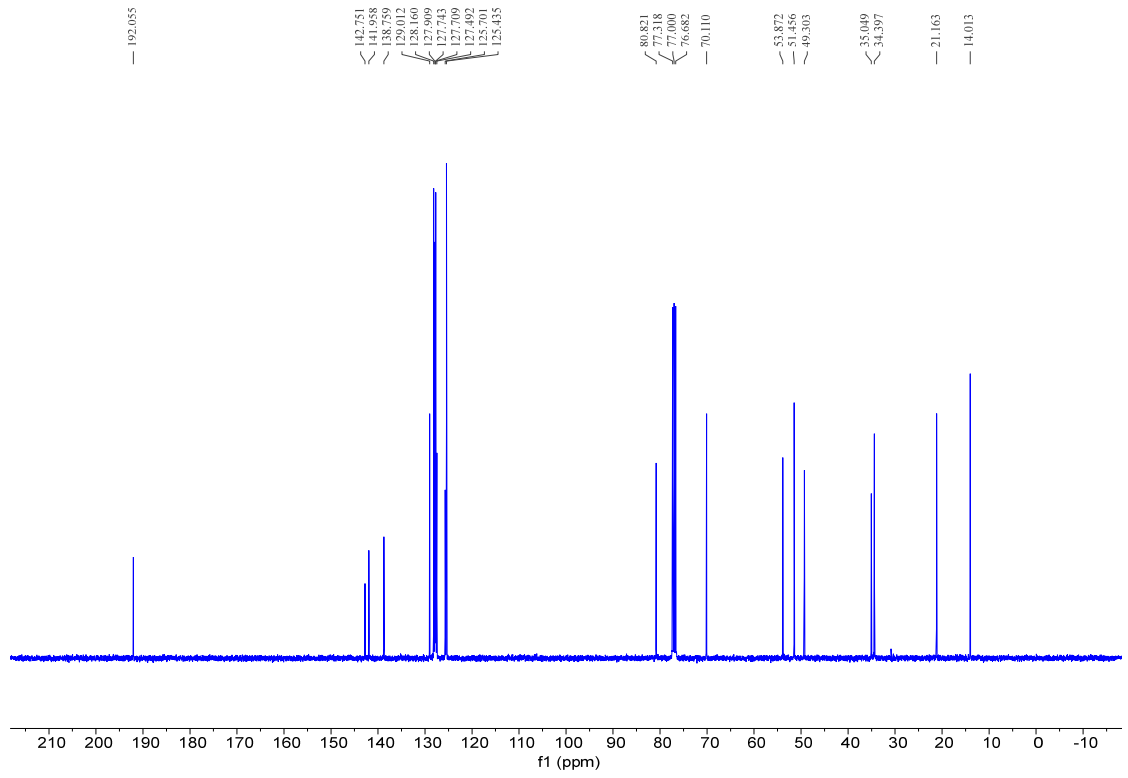

**Supplementary Figure 40.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ab**



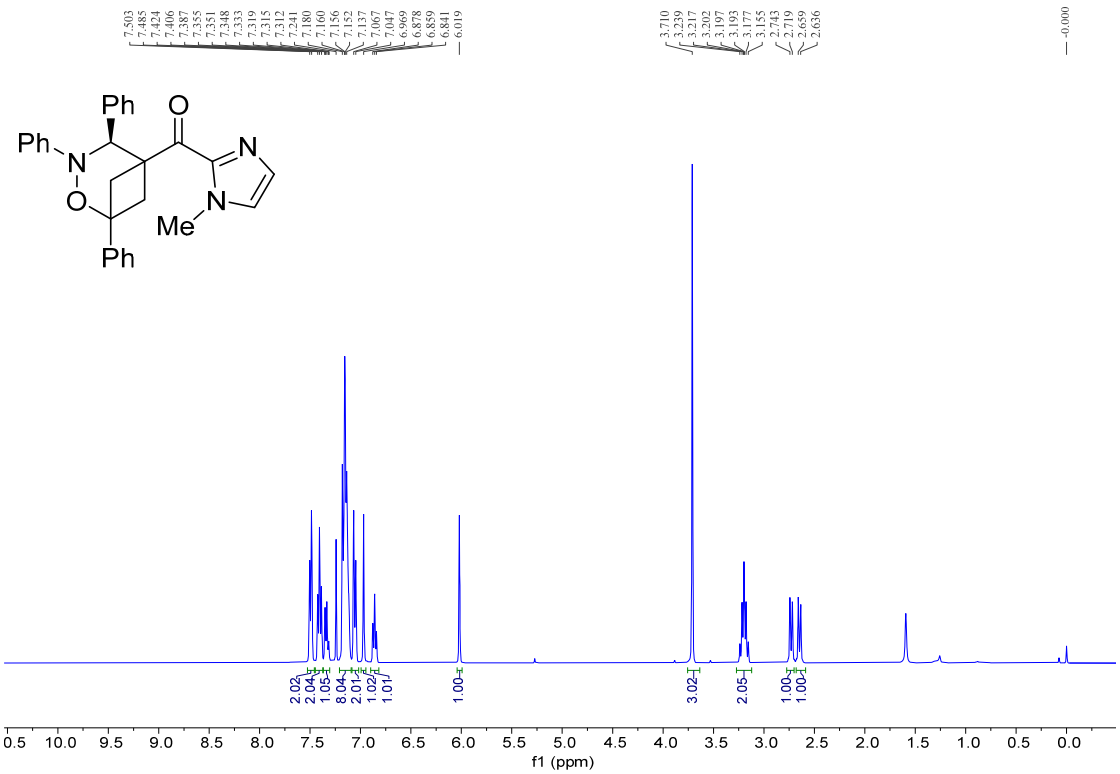

**Supplementary Figure 41.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ab**



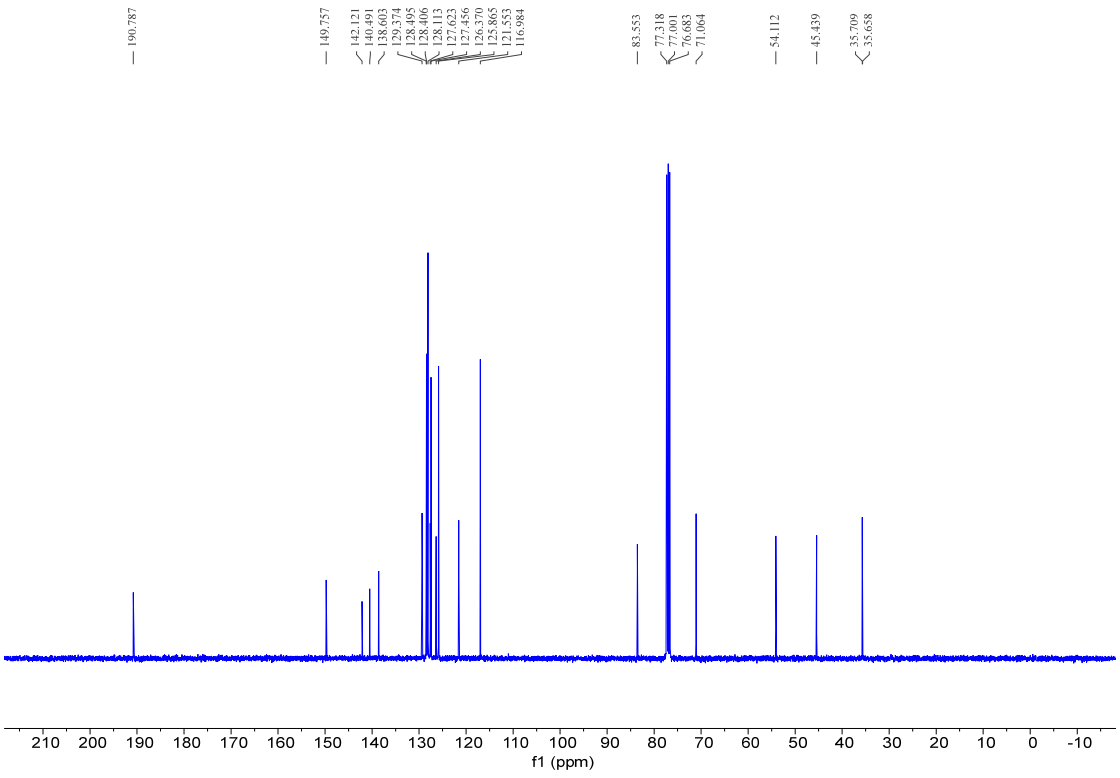

**Supplementary Figure 42.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ac**



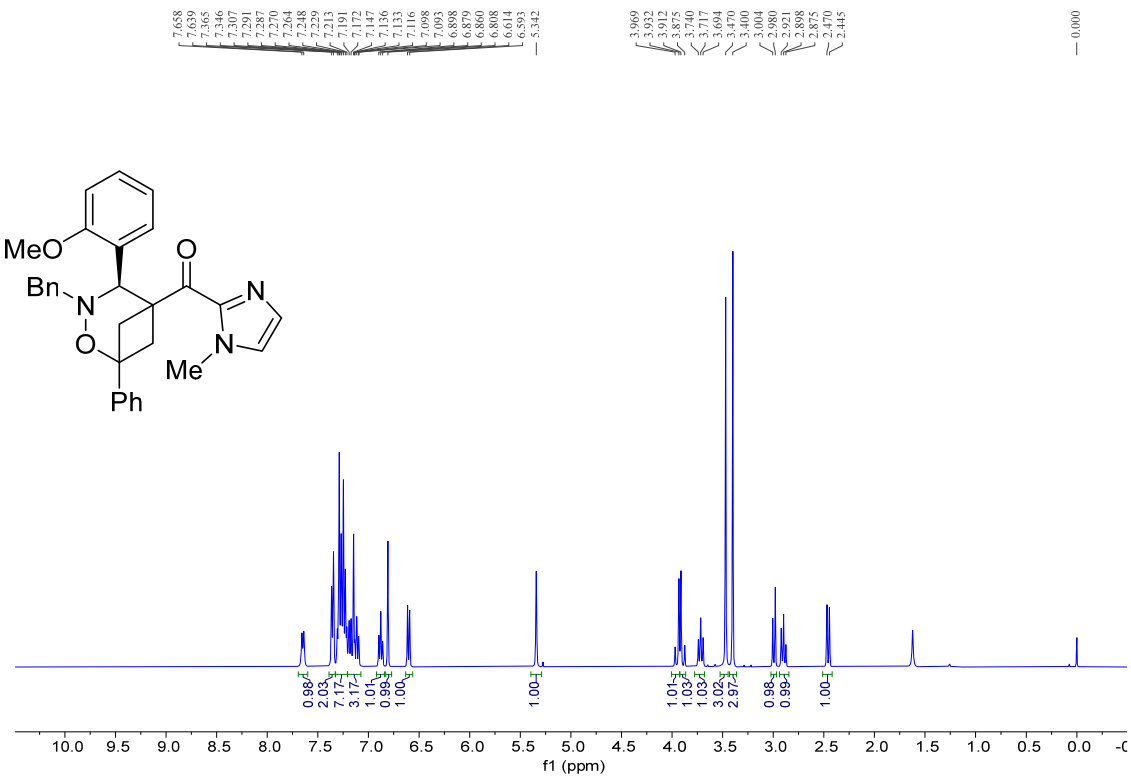

**Supplementary Figure 43.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ac**



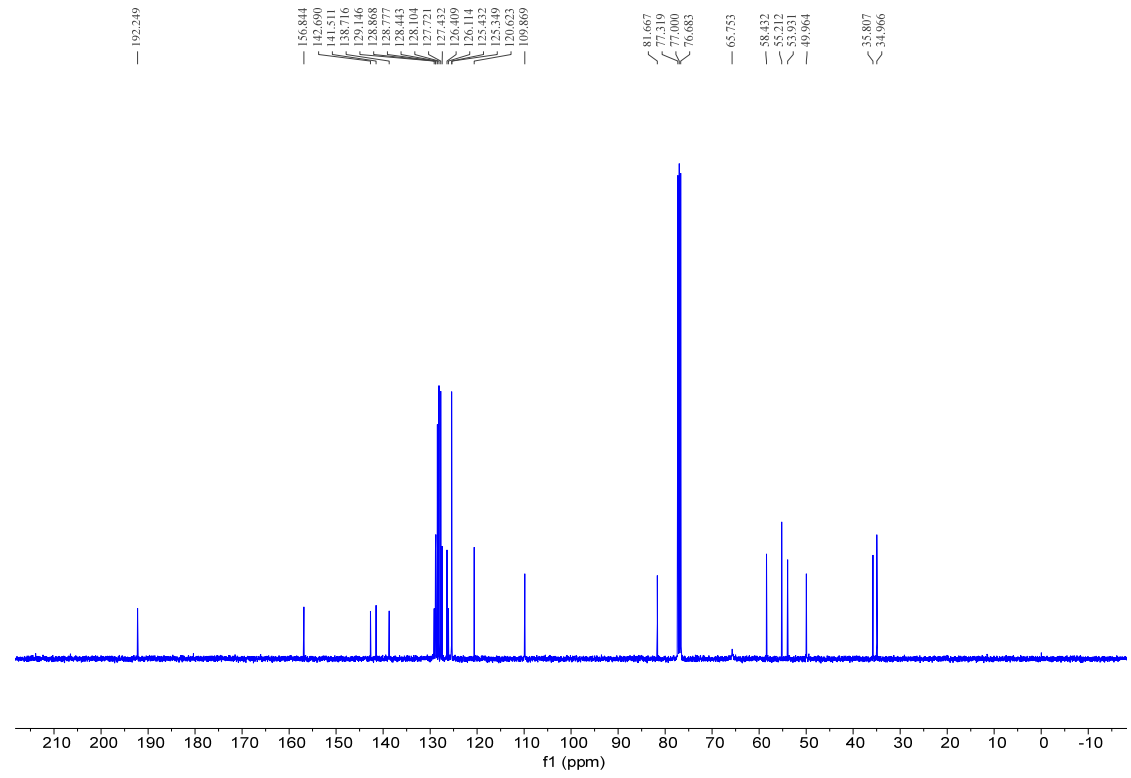

**Supplementary Figure 44.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ad**



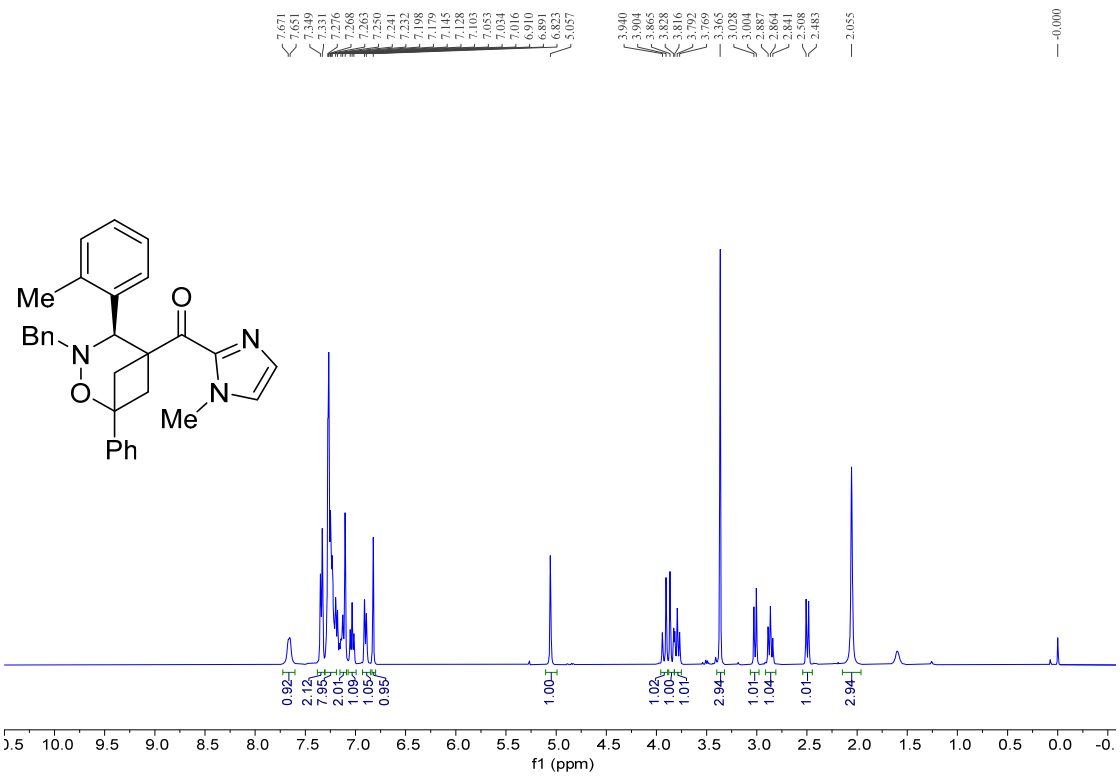

**Supplementary Figure 45.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ad**



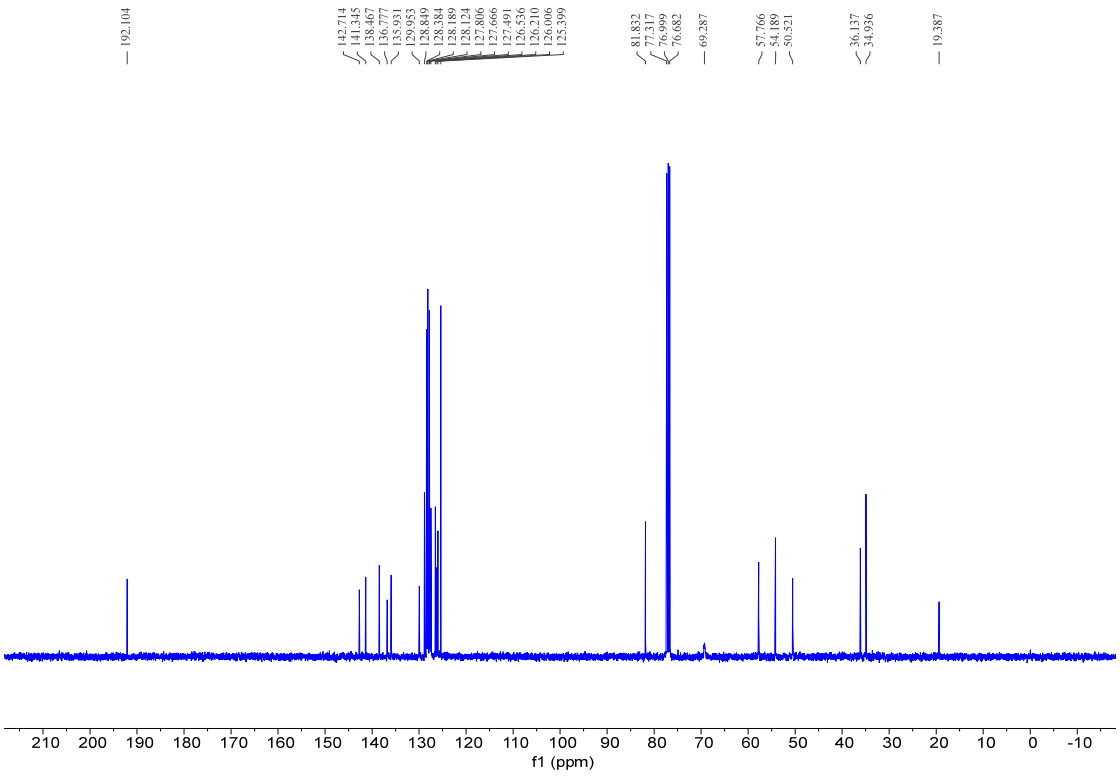

**Supplementary Figure 46.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ae**



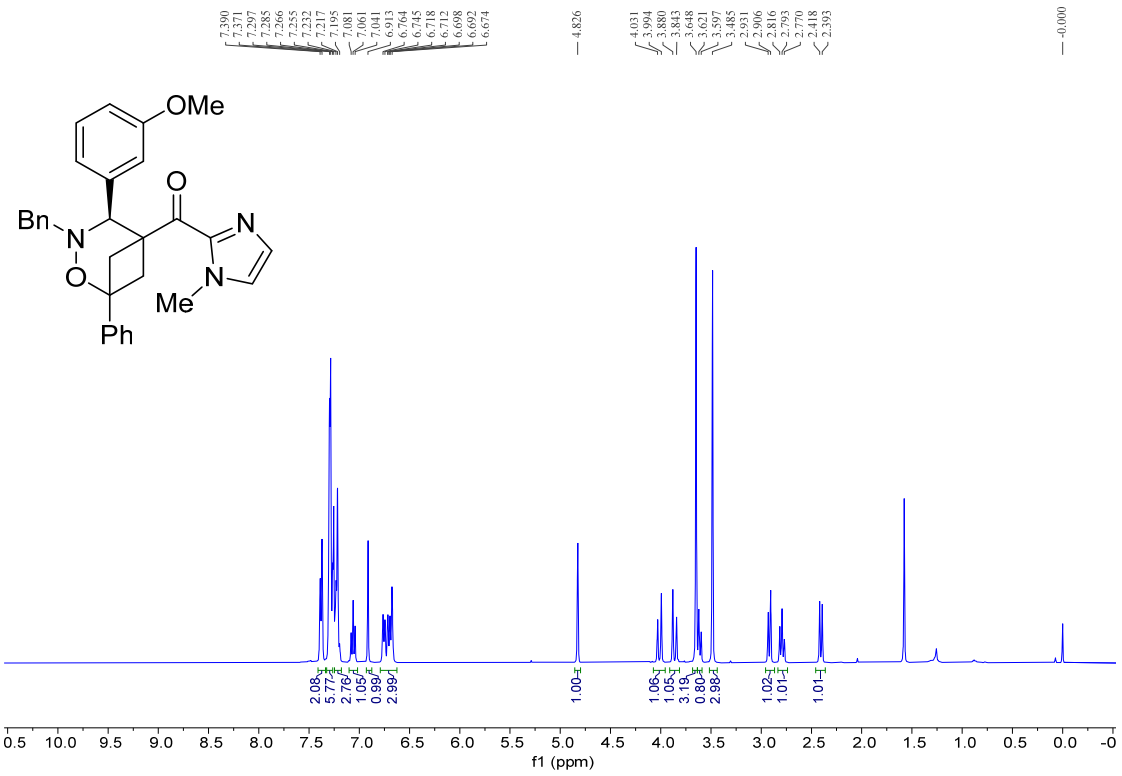

**Supplementary Figure 47.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ae**



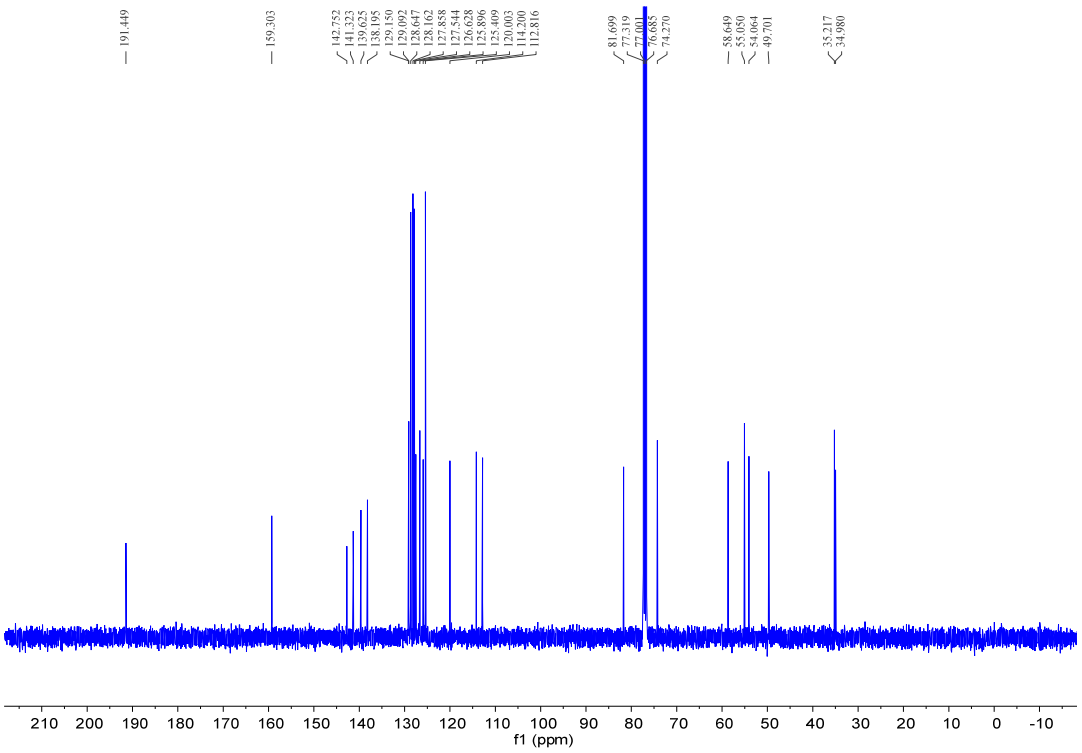

**Supplementary Figure 48.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3af**



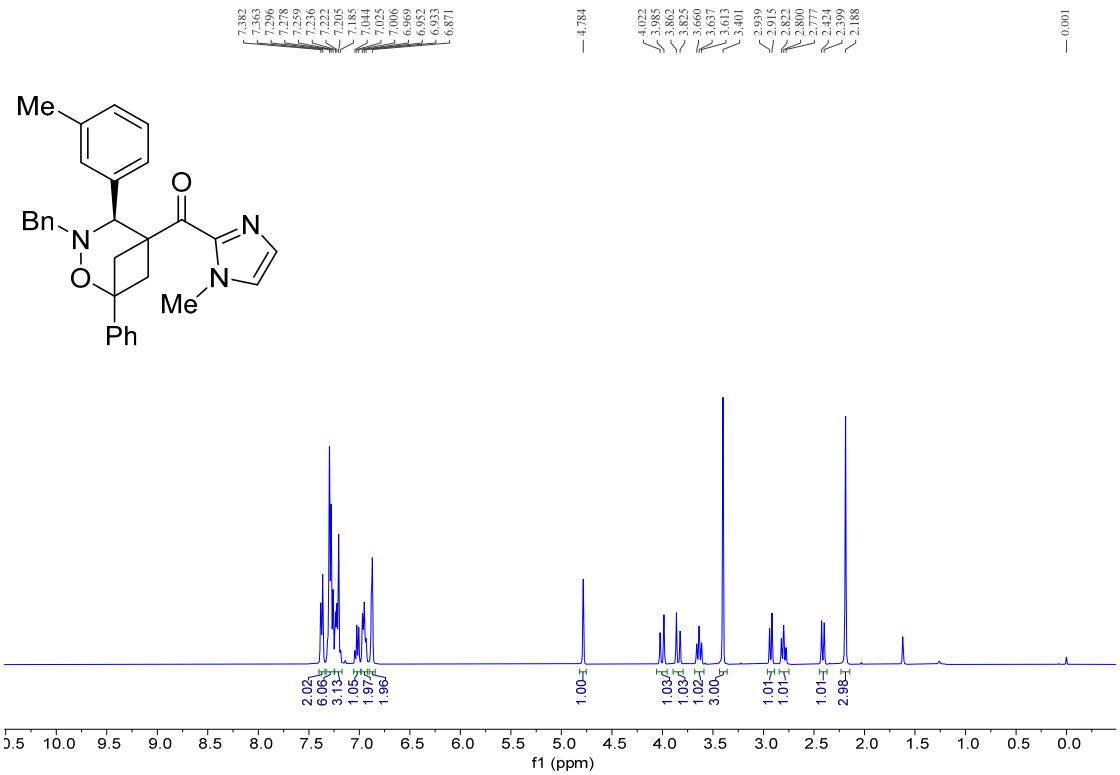

**Supplementary Figure 49.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3af**



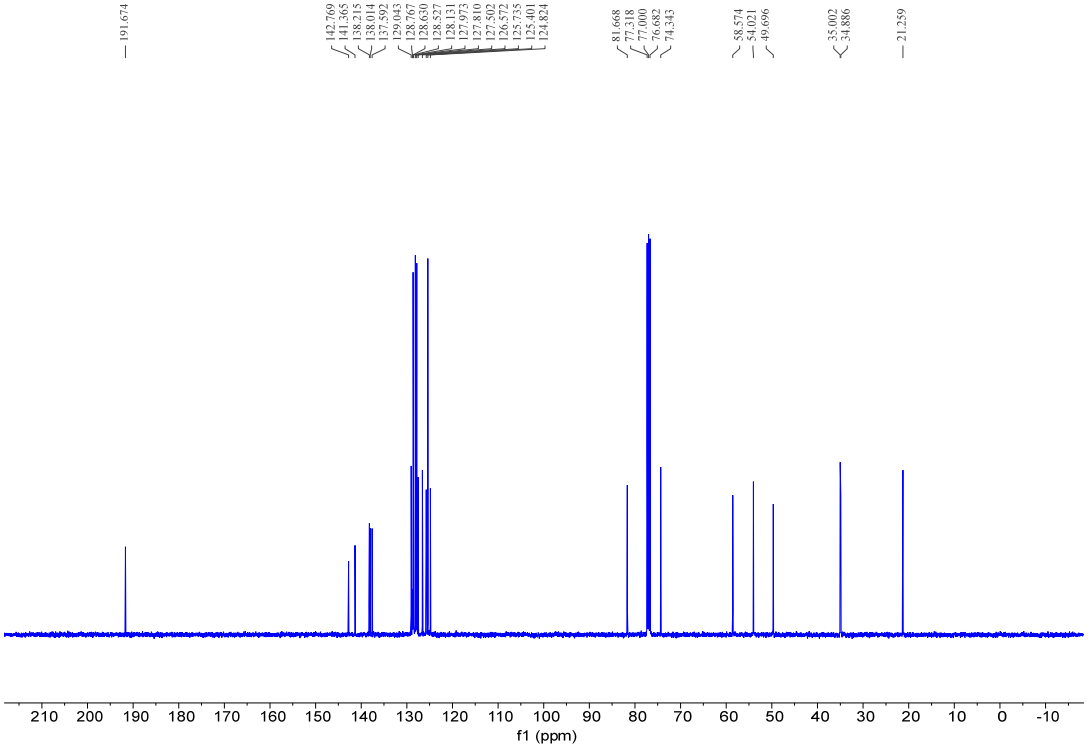

**Supplementary Figure 50.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ag**



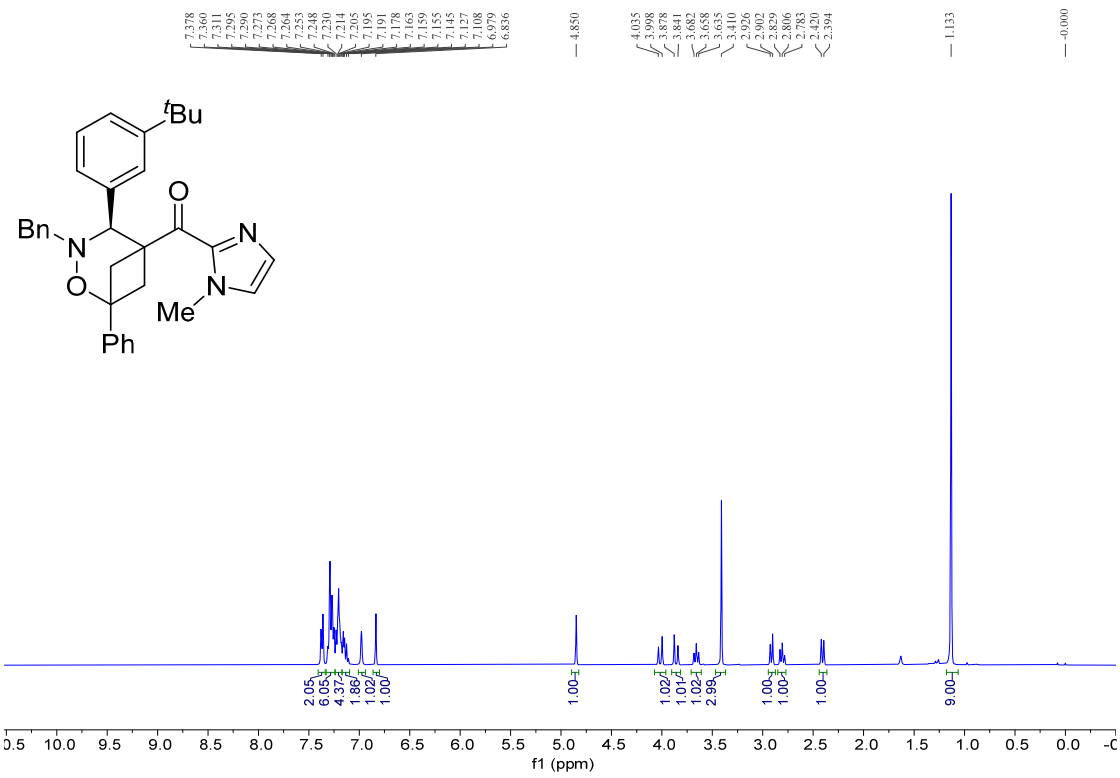

**Supplementary Figure 51.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ag**



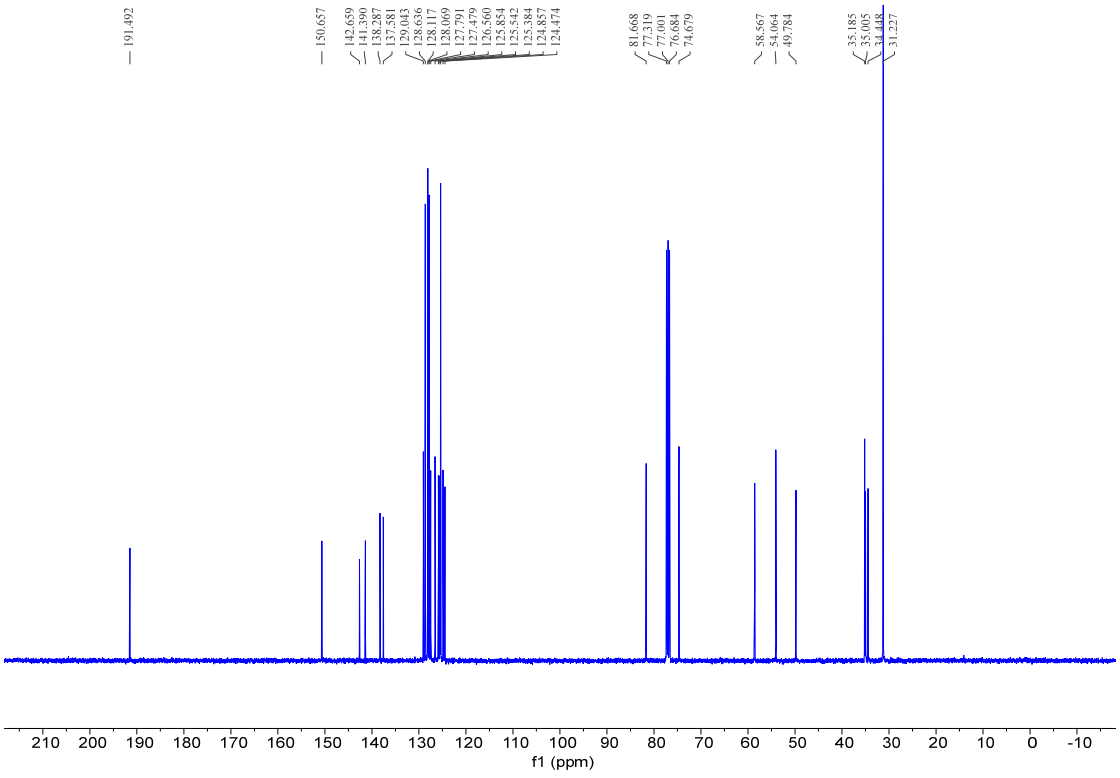

**Supplementary Figure 52.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ah**



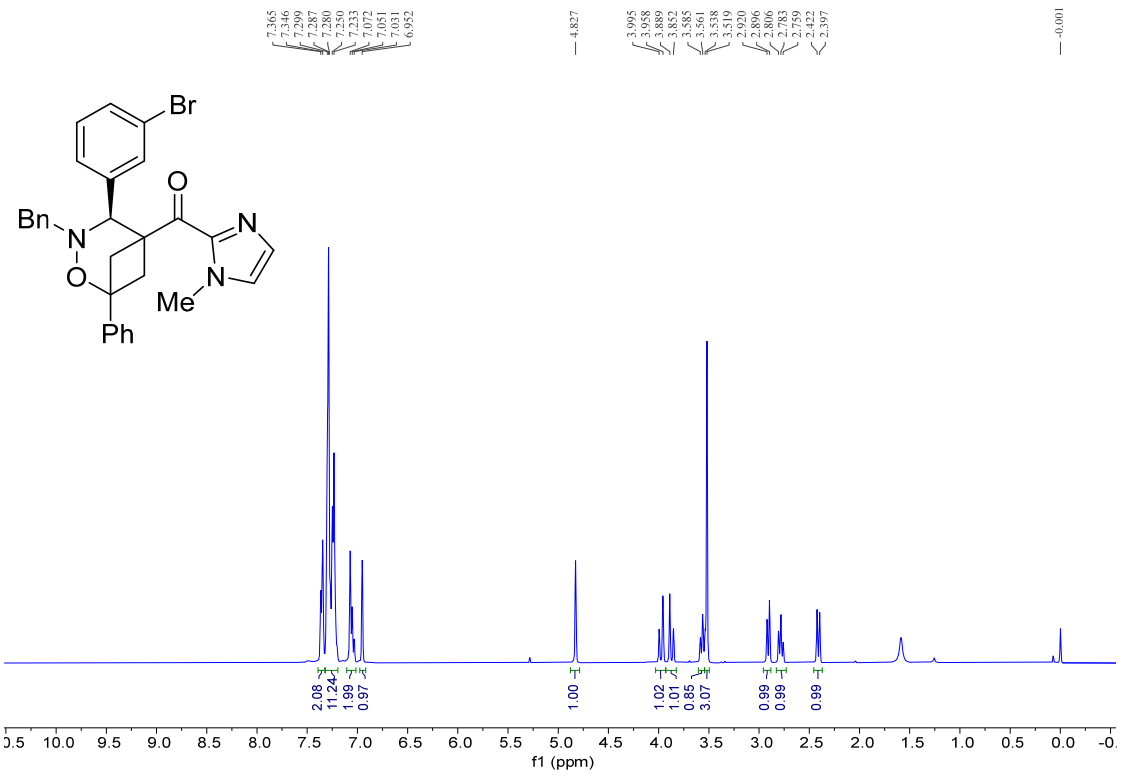

**Supplementary Figure 53.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ah**



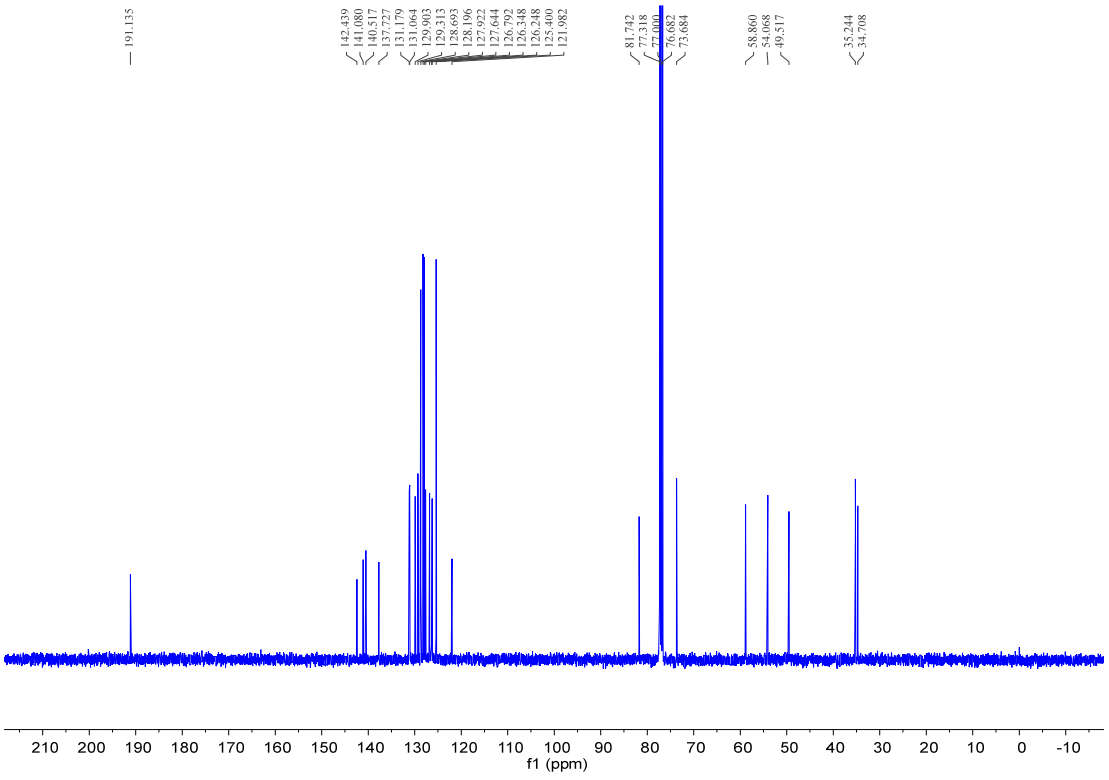

**Supplementary Figure 54.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ai**



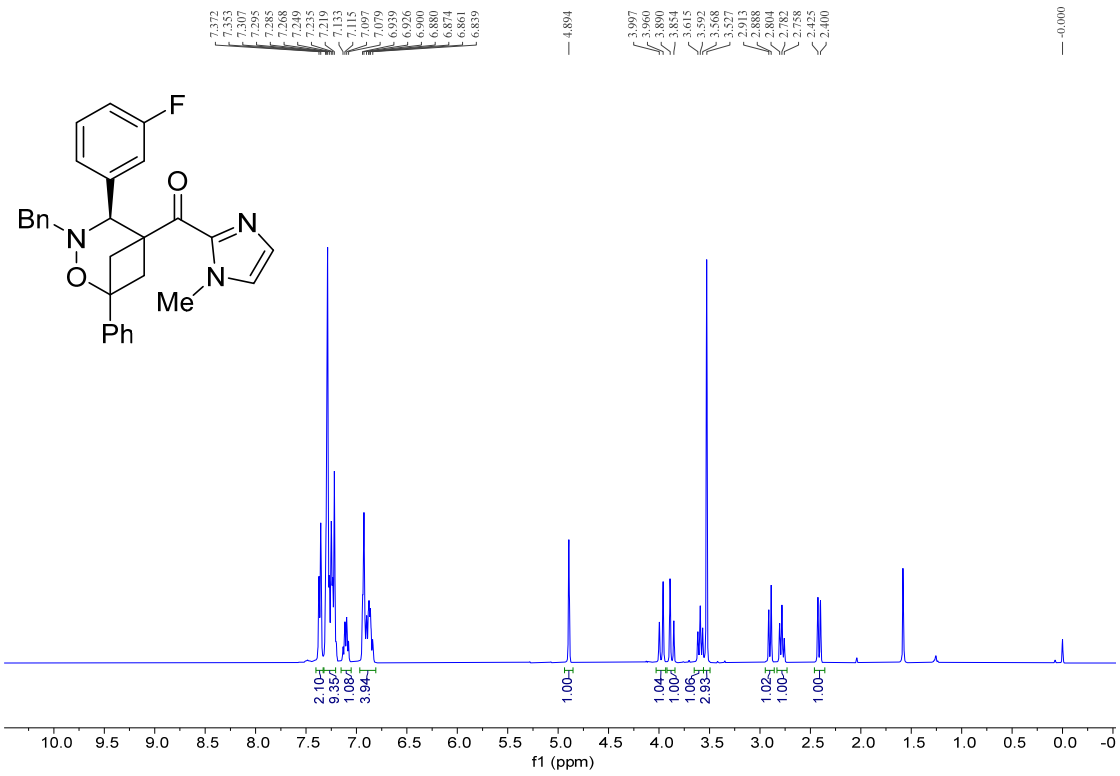

**Supplementary Figure 55.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ai**



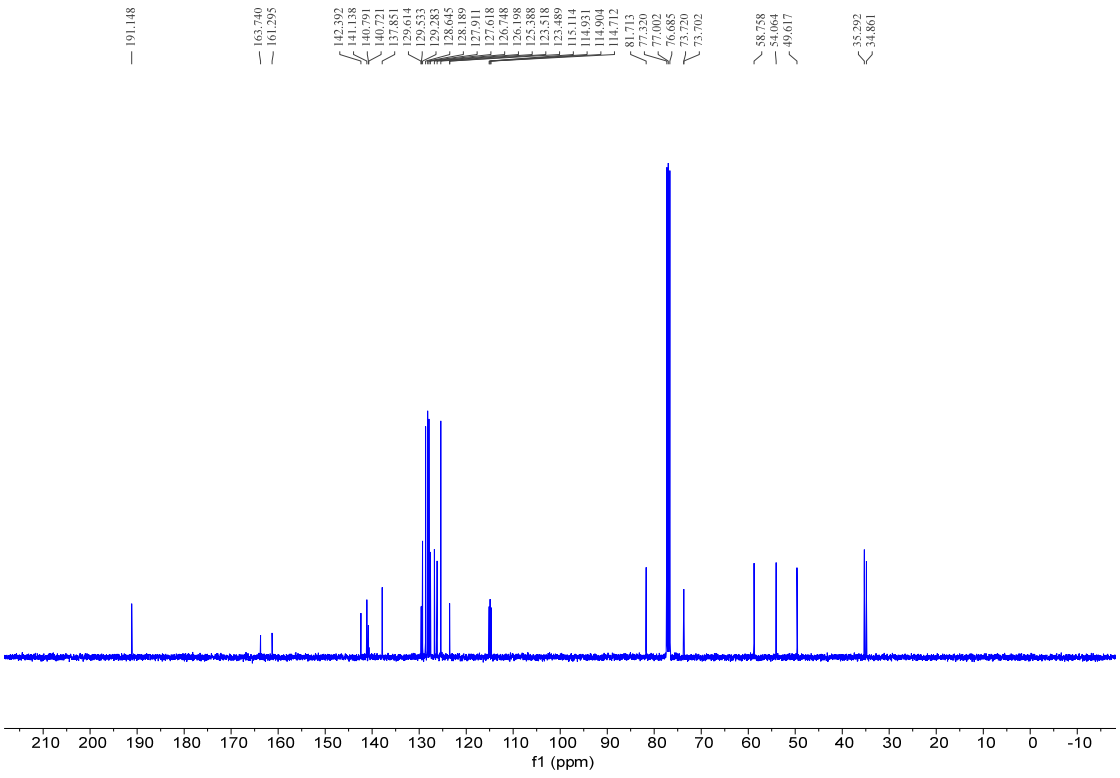

**Supplementary Figure 56.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3aj**



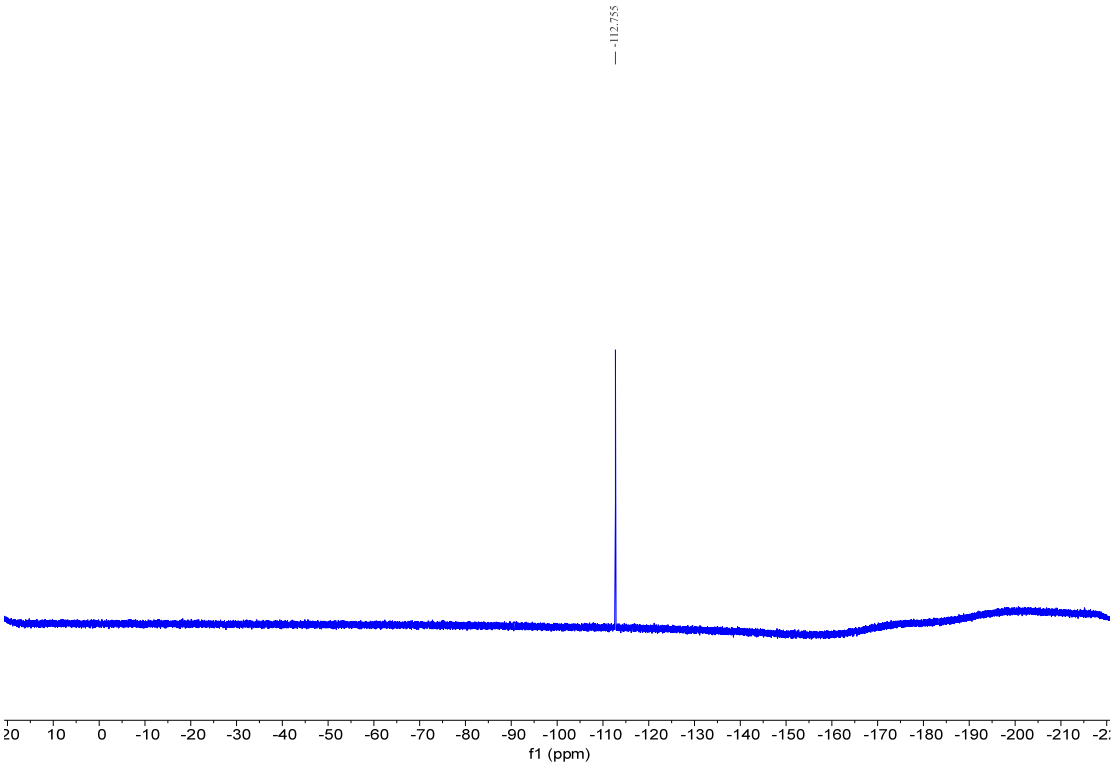

**Supplementary Figure 57.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3aj**



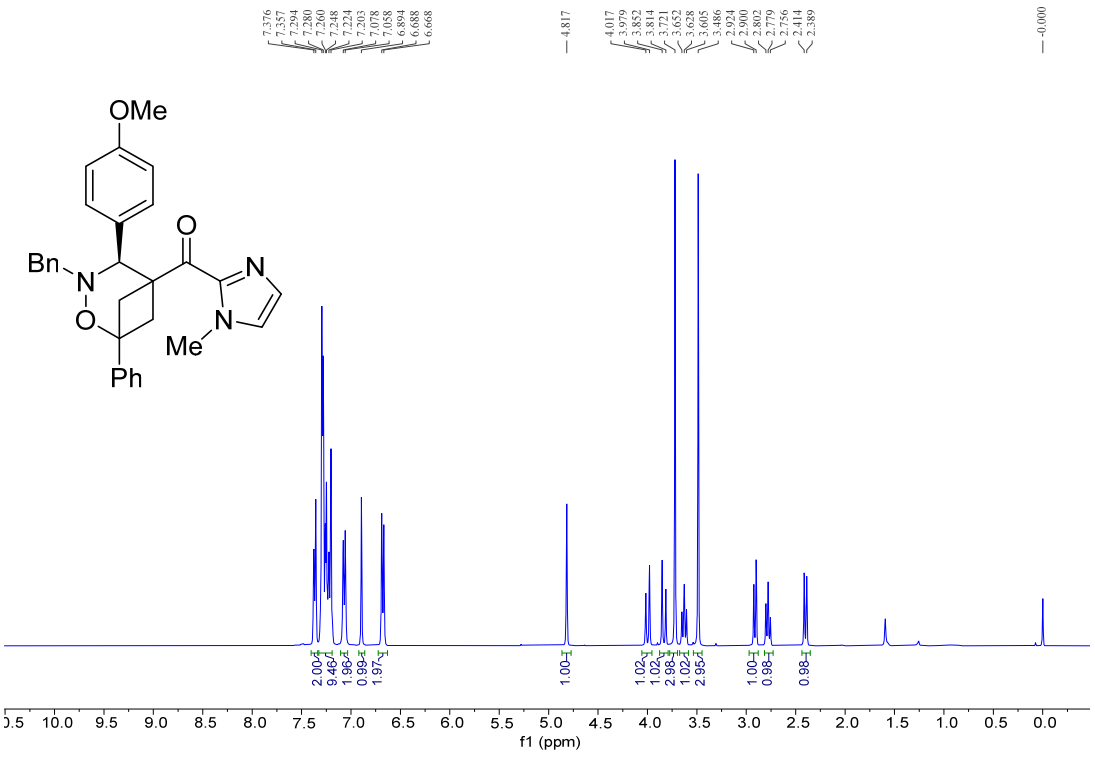

**Supplementary Figure 58.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ak**



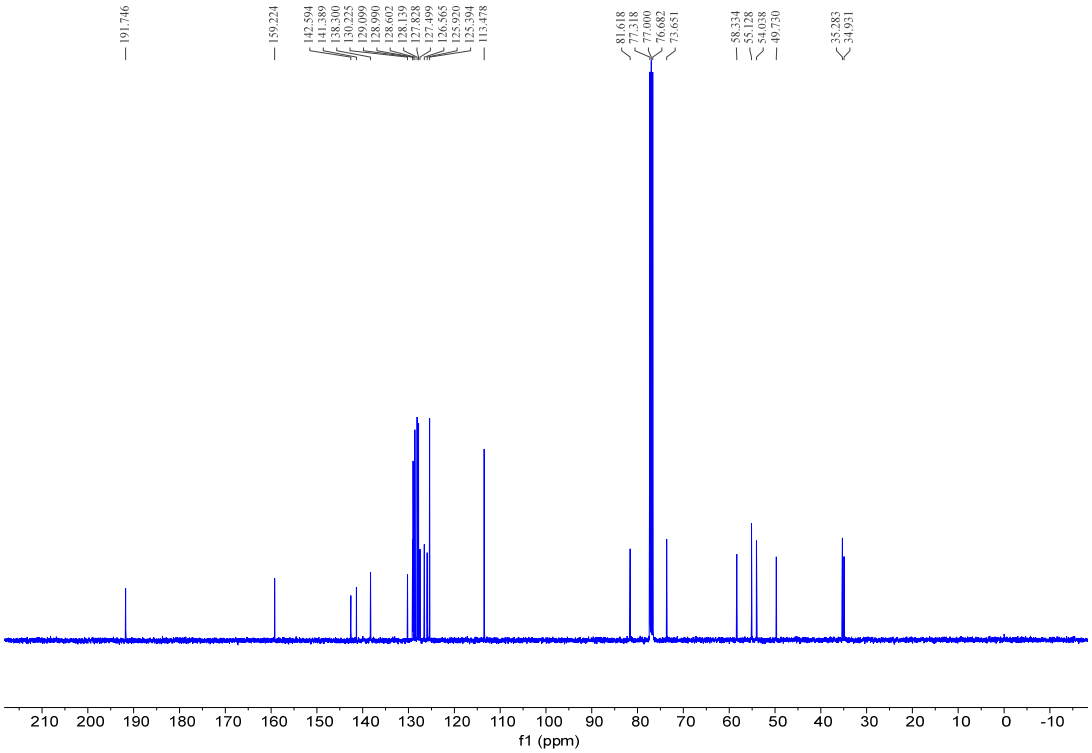

**Supplementary Figure 59.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ak**



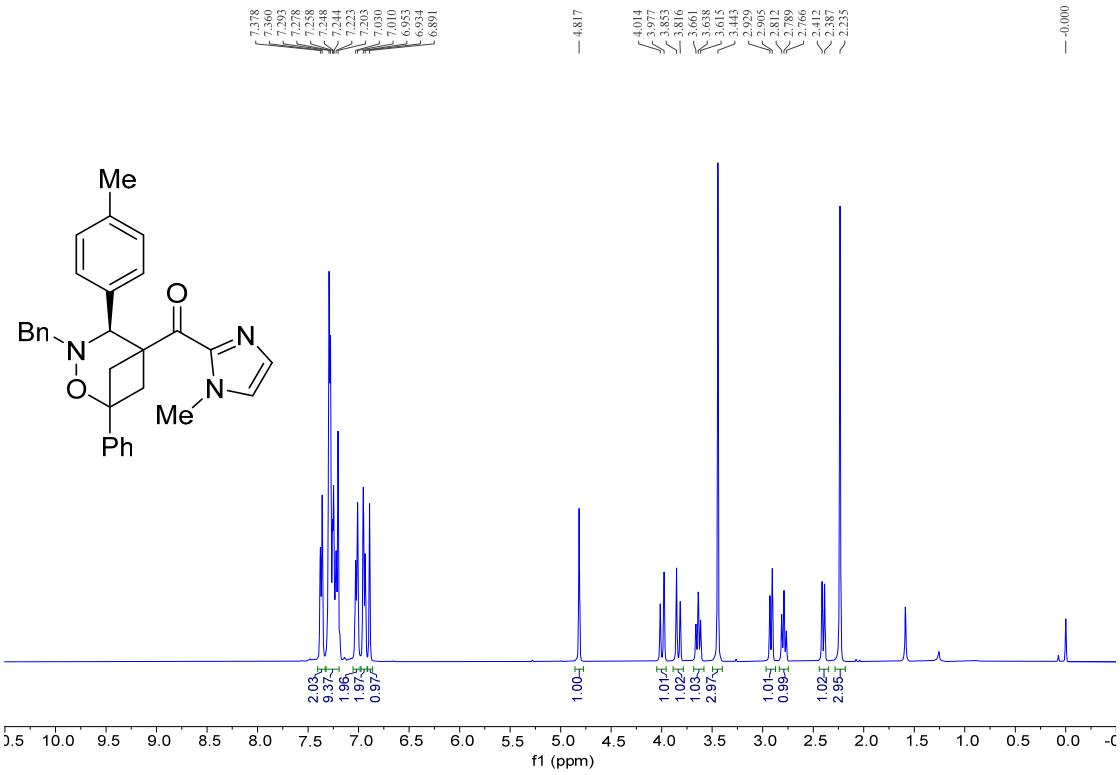

**Supplementary Figure 60.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **3ak**



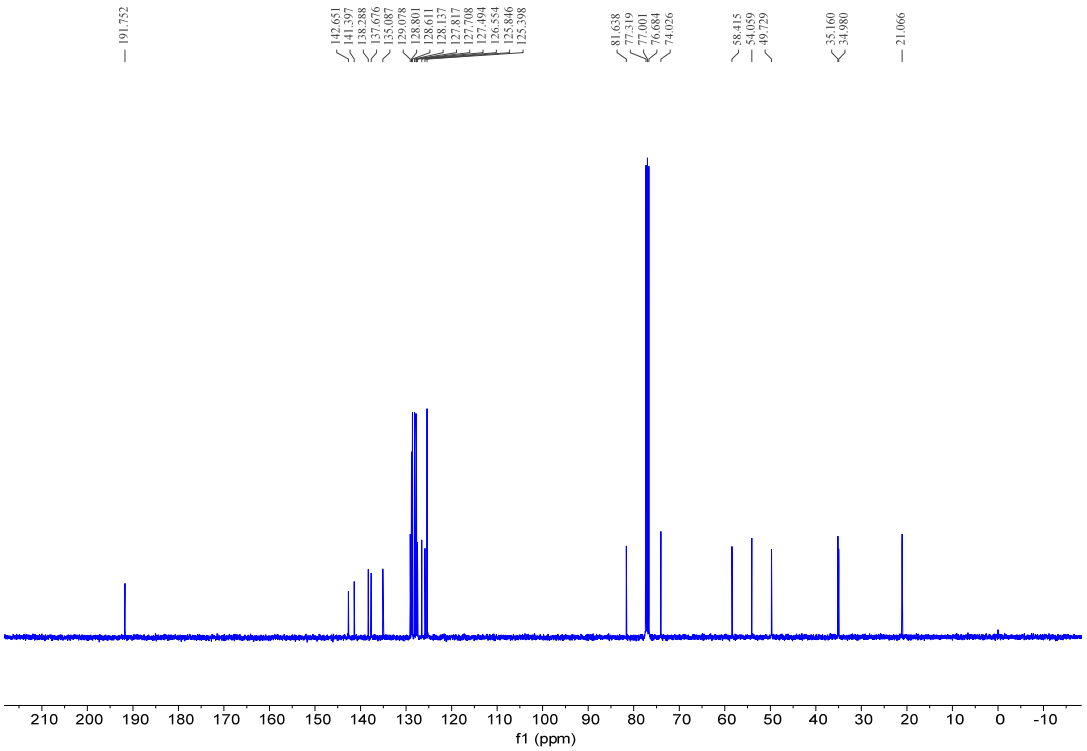

**Supplementary Figure 61.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3al**




**Supplementary Figure 62.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3al**

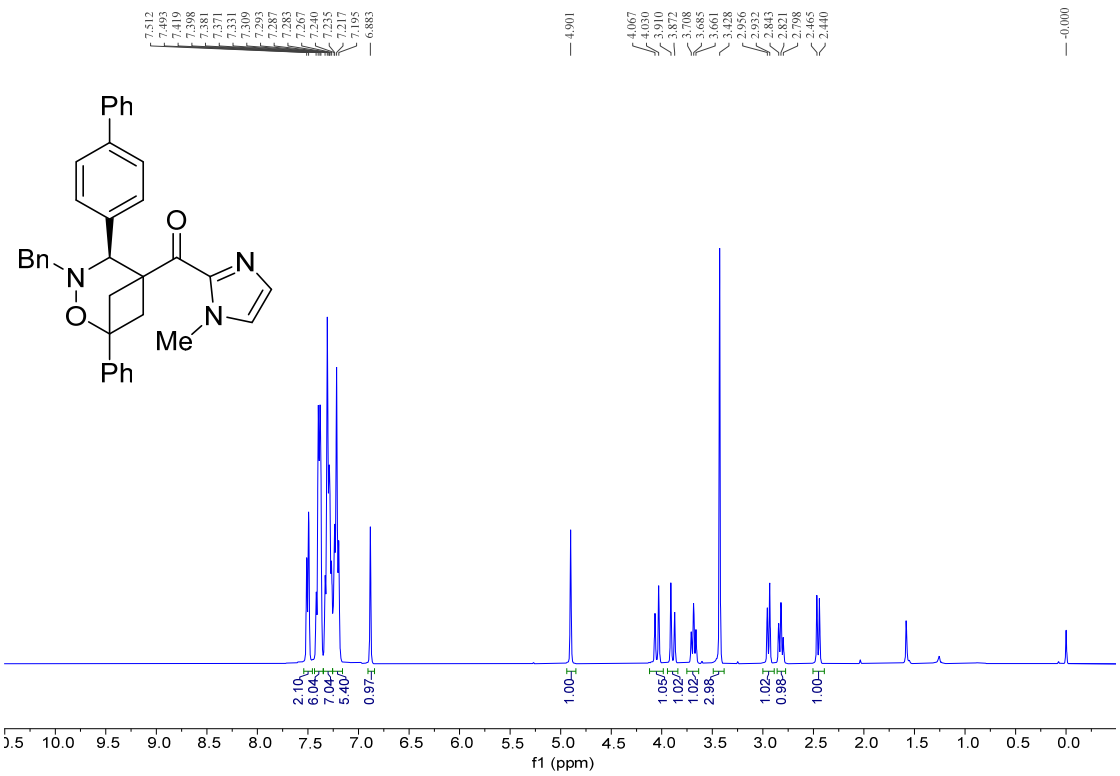



**Supplementary Figure 63.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3am**

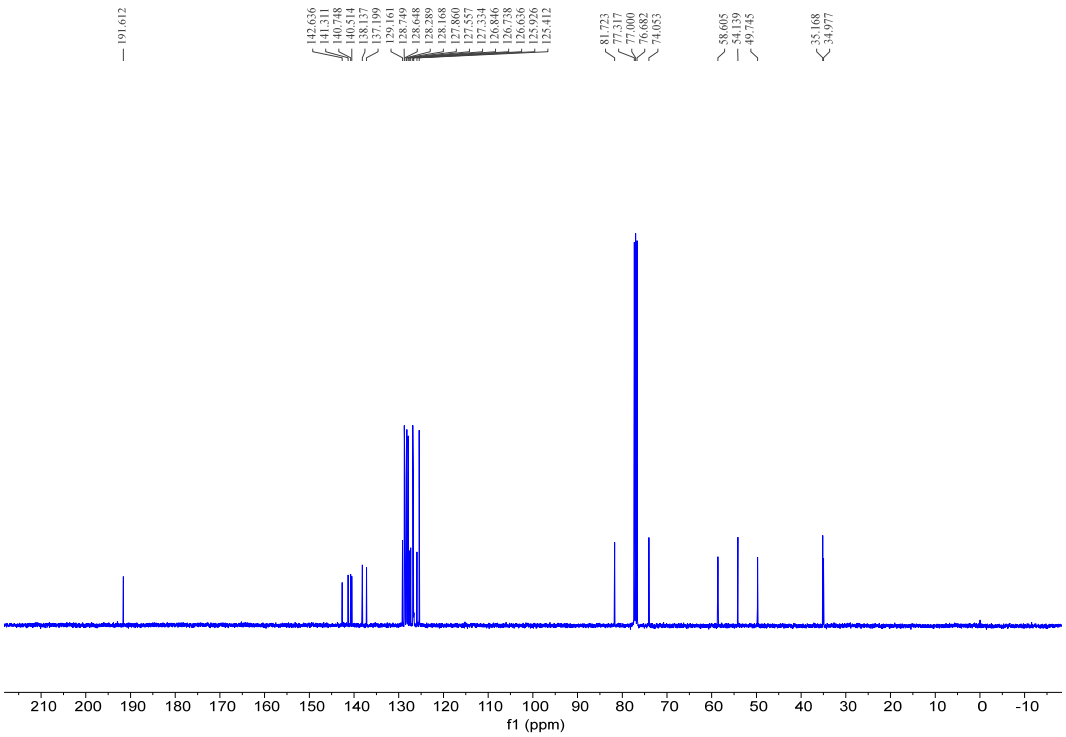



**Supplementary Figure 64.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3am**

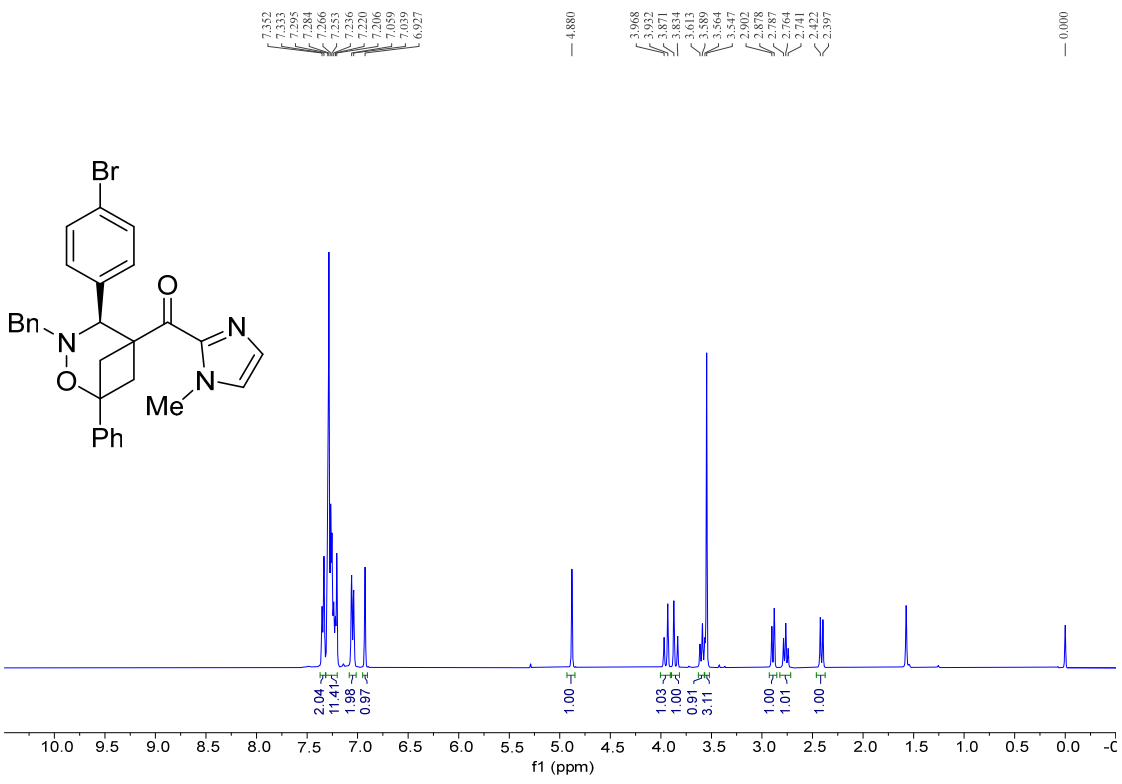
**$^{1}H$ and $^{13}C$ NMR Spectra for Compound 3an**:



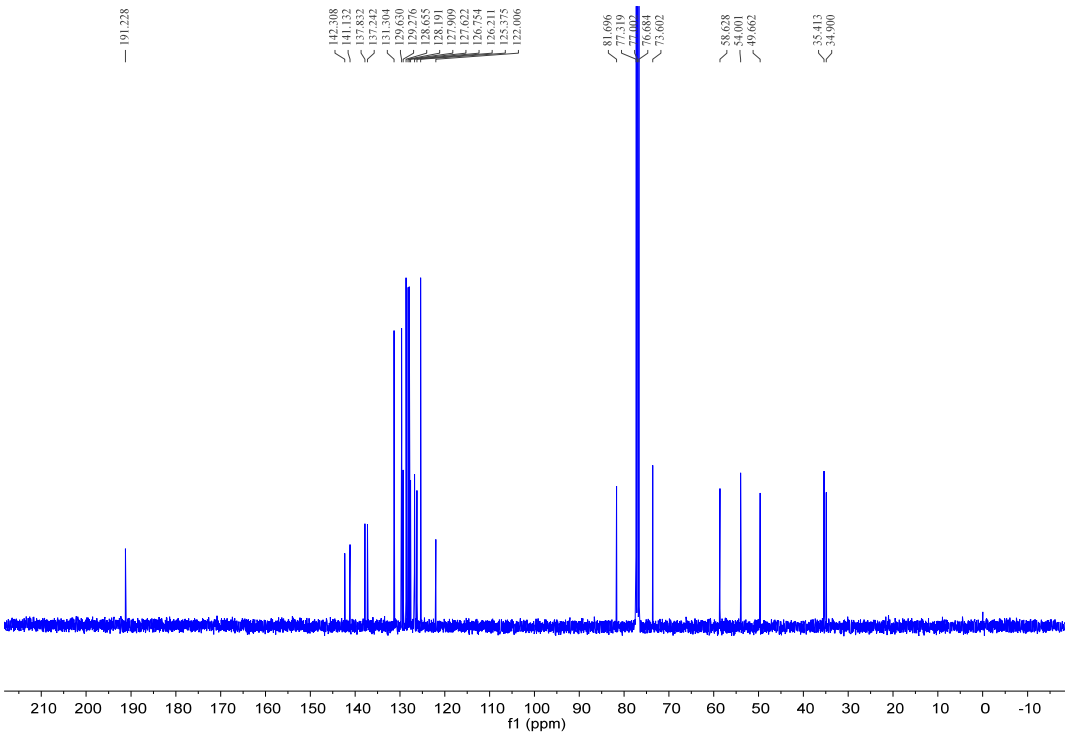

**Supplementary Figure 65.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3an**



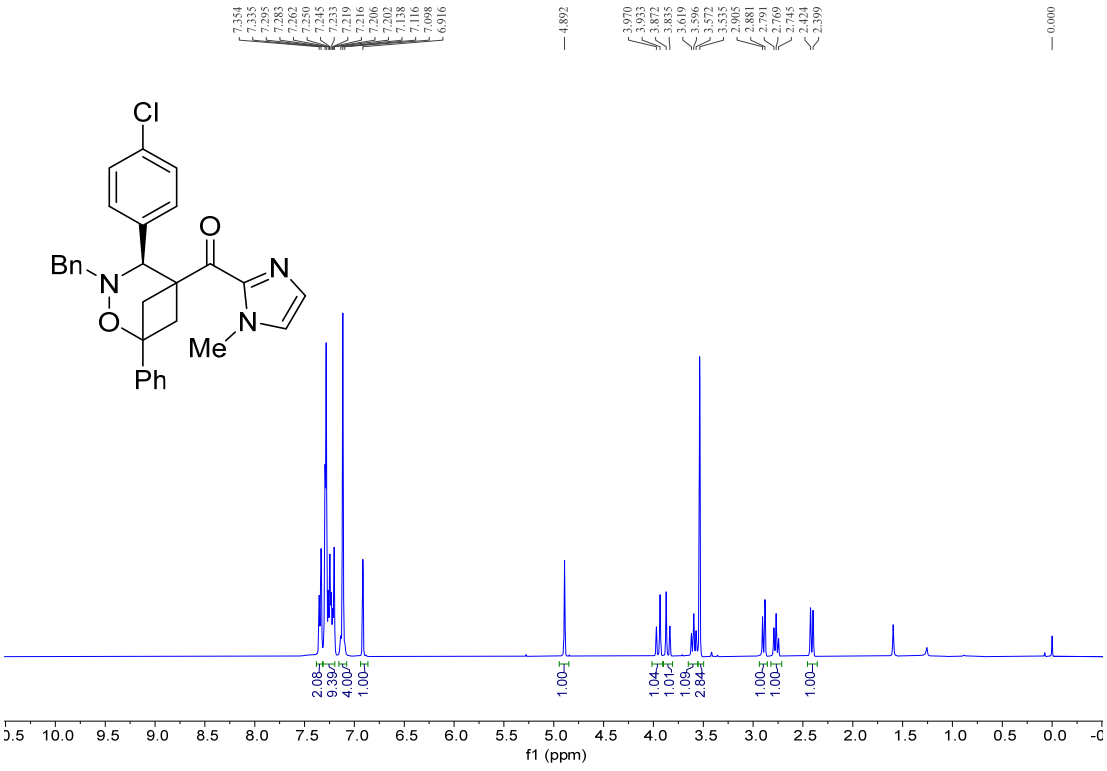

**Supplementary Figure 66.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3an**



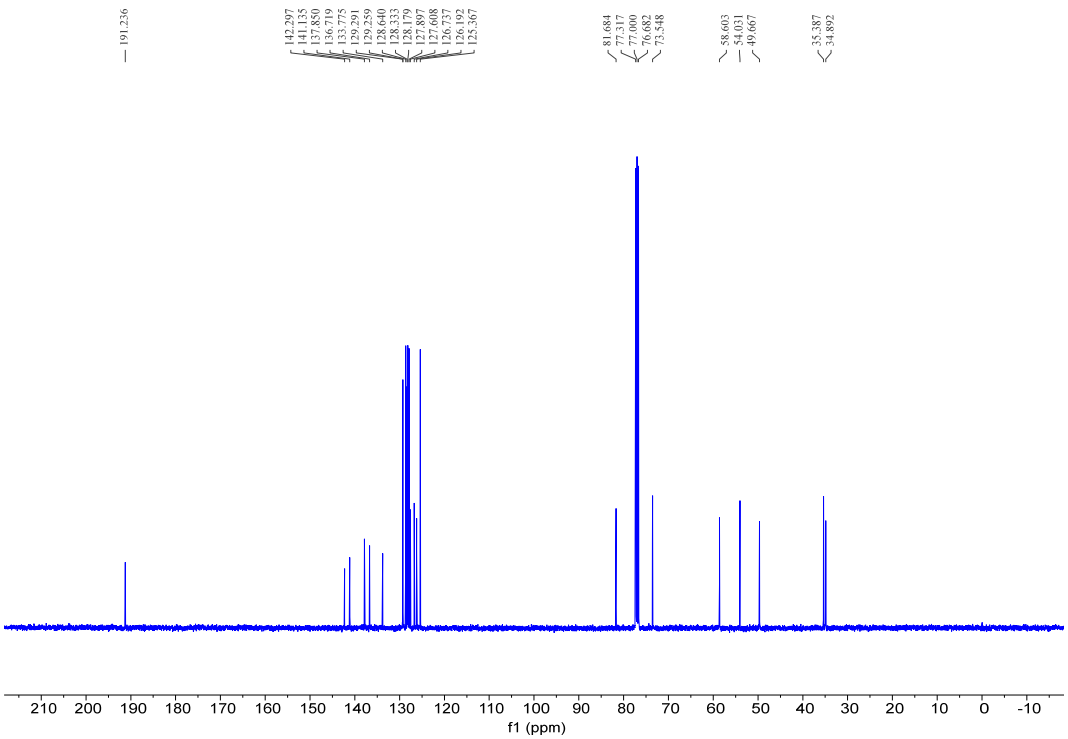

**Supplementary Figure 67.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3ao**



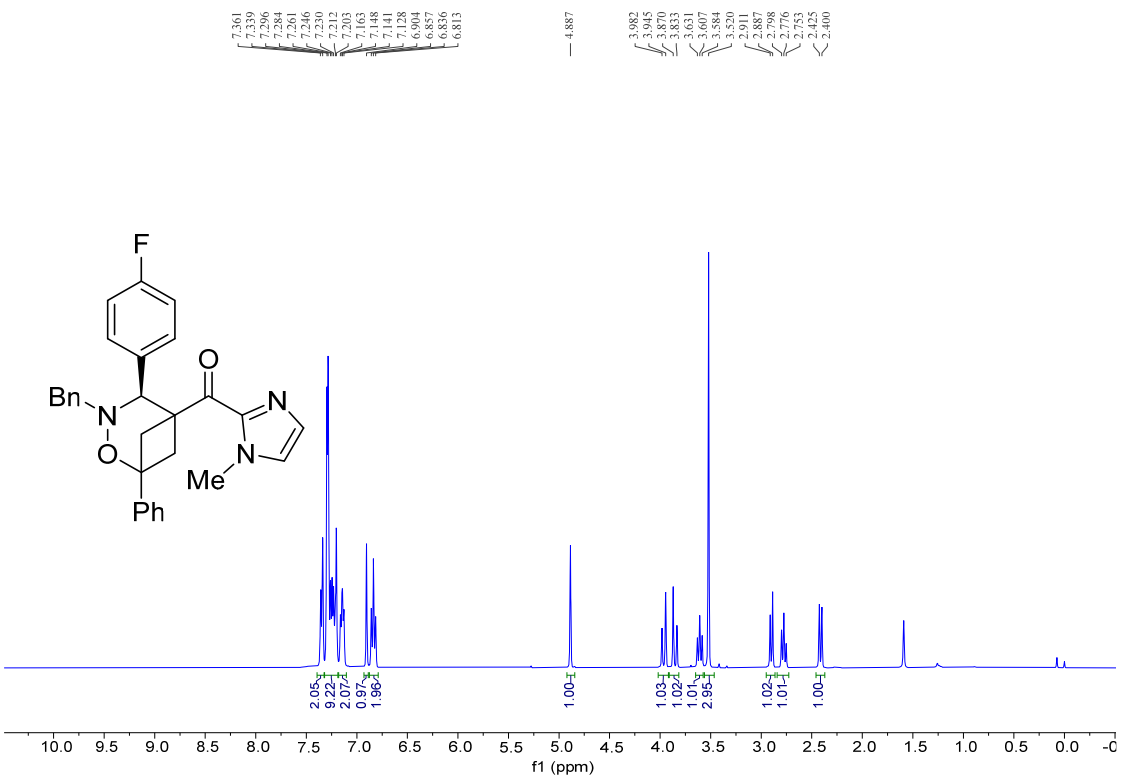

**Supplementary Figure 68.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ao**



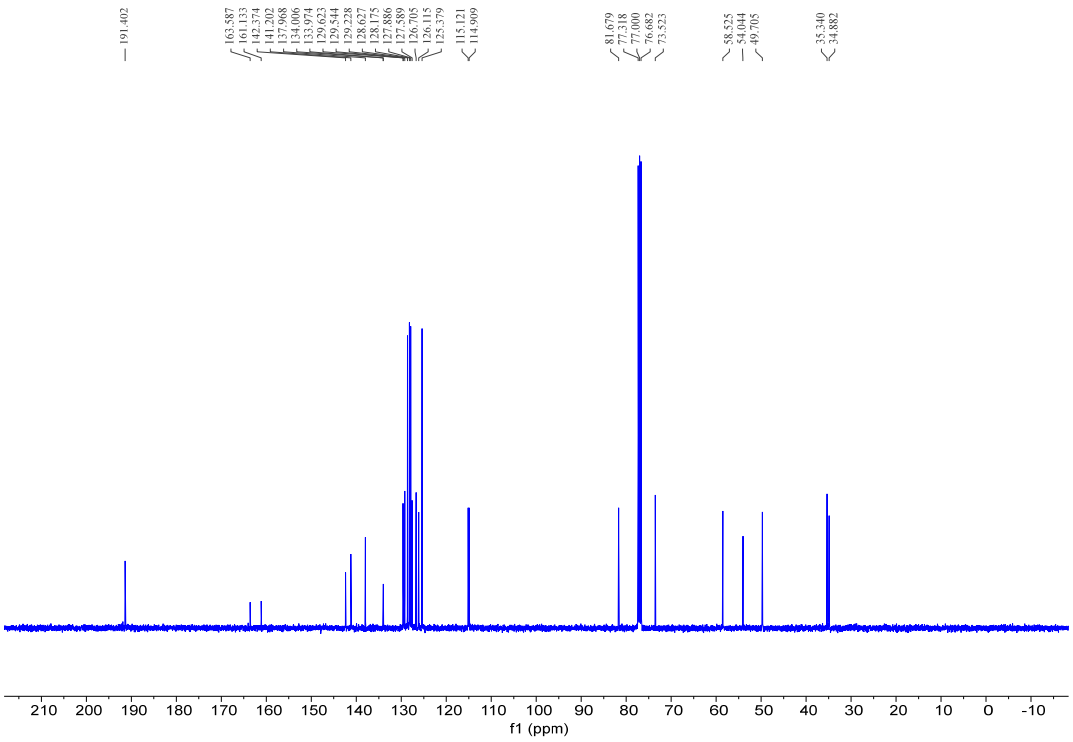

**Supplementary Figure 69.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3ap**



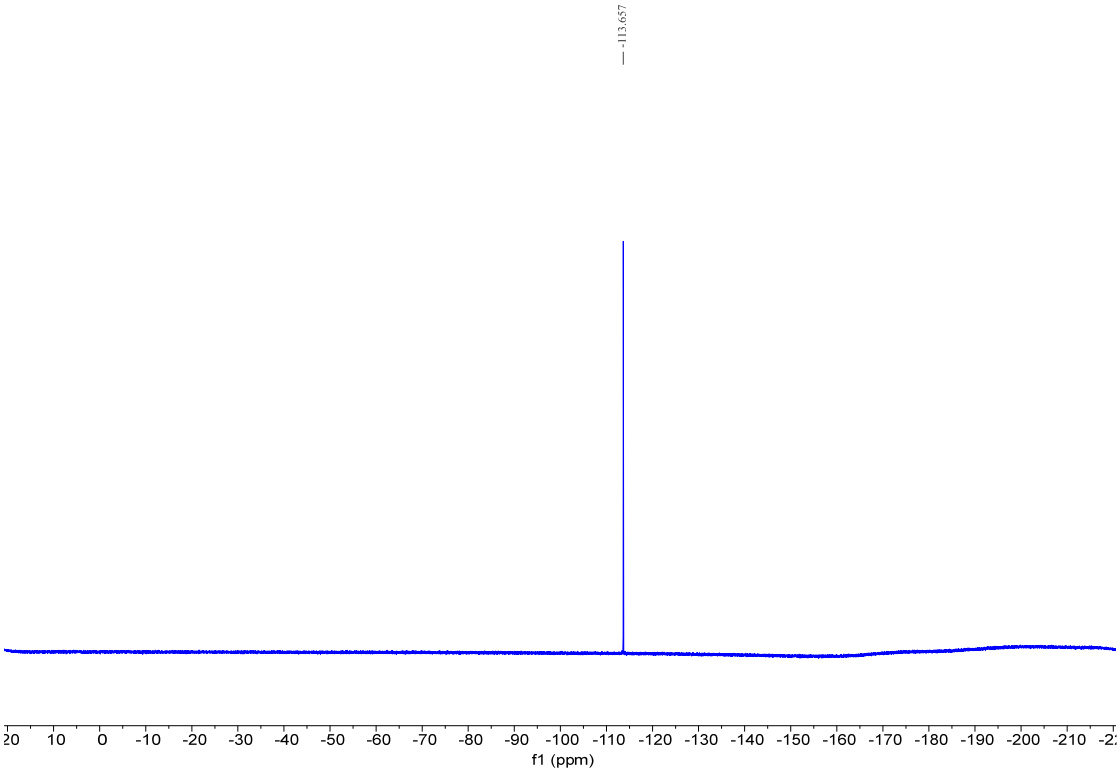

**Supplementary Figure 70.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ap**



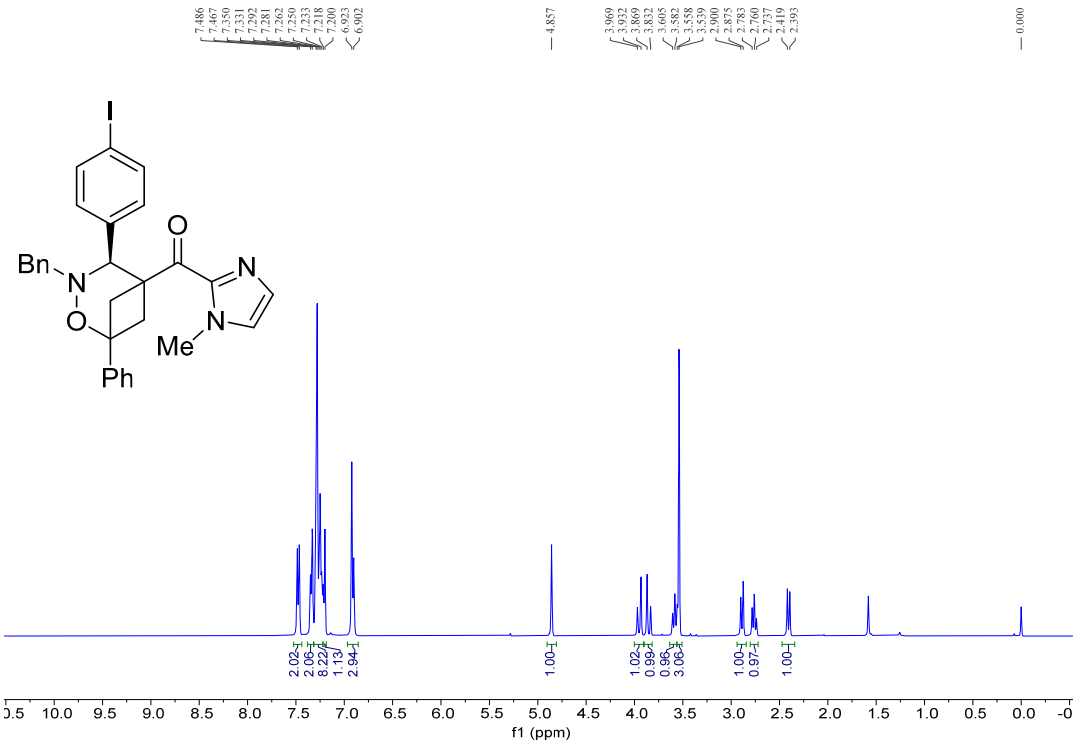

**Supplementary Figure 71.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3aq**



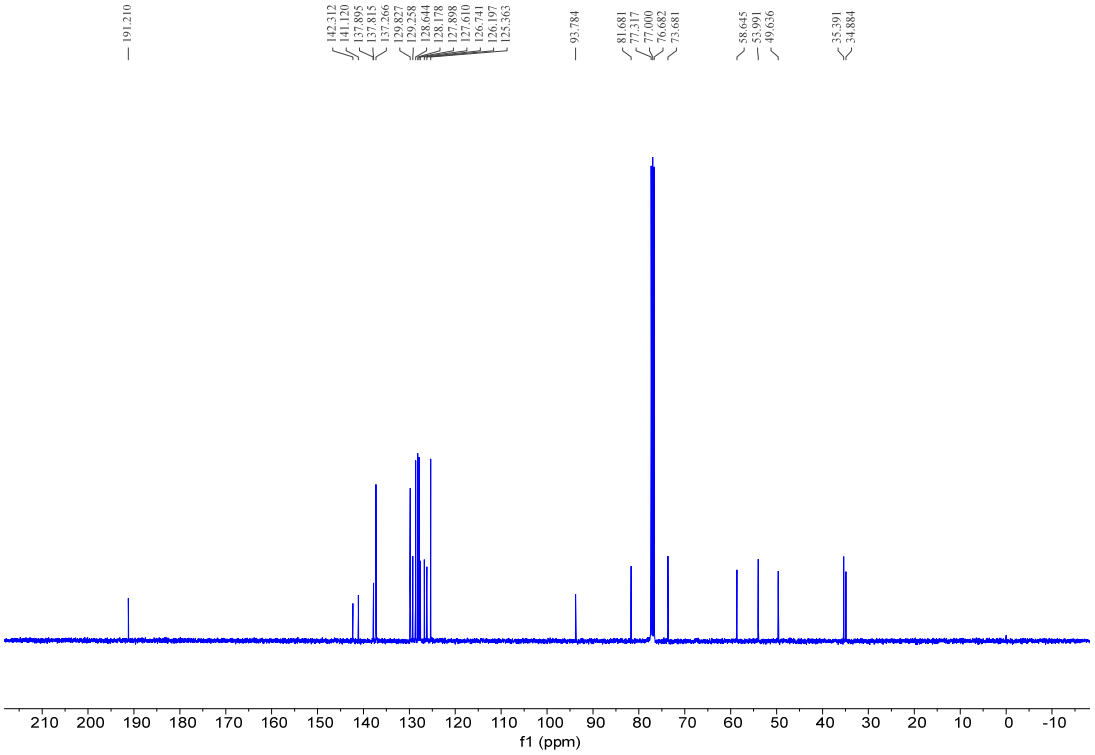

**Supplementary Figure 72.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3aq**



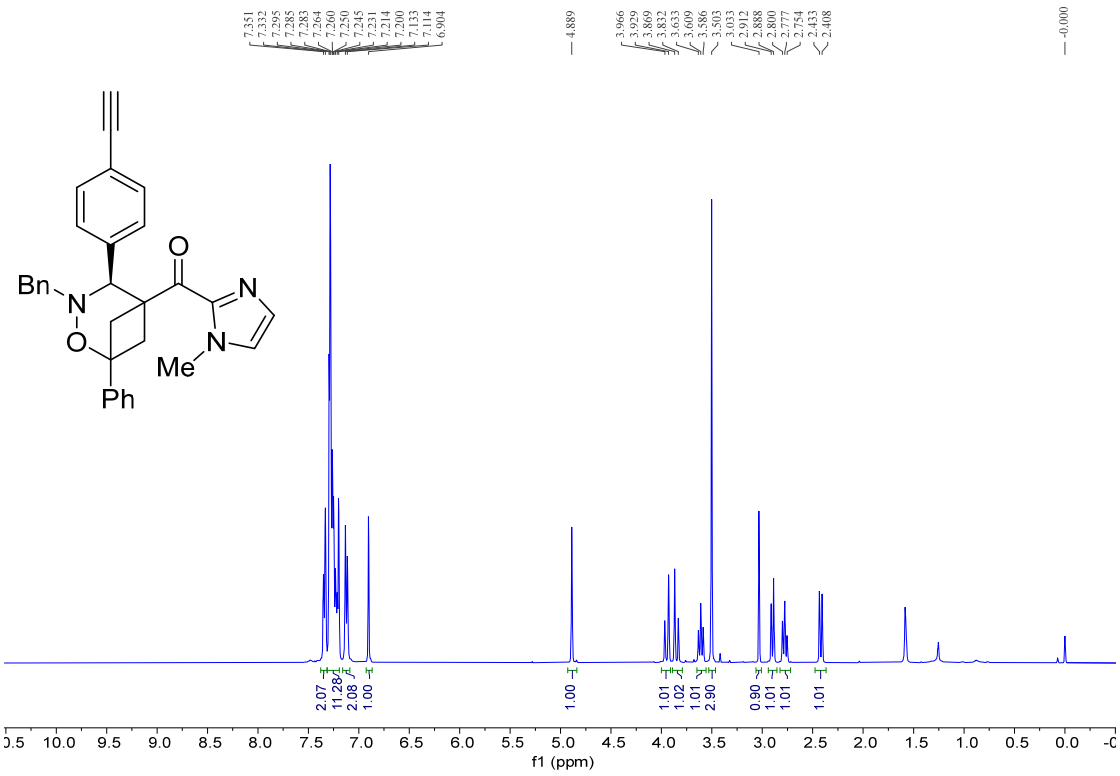

**Supplementary Figure 73.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **3aq**



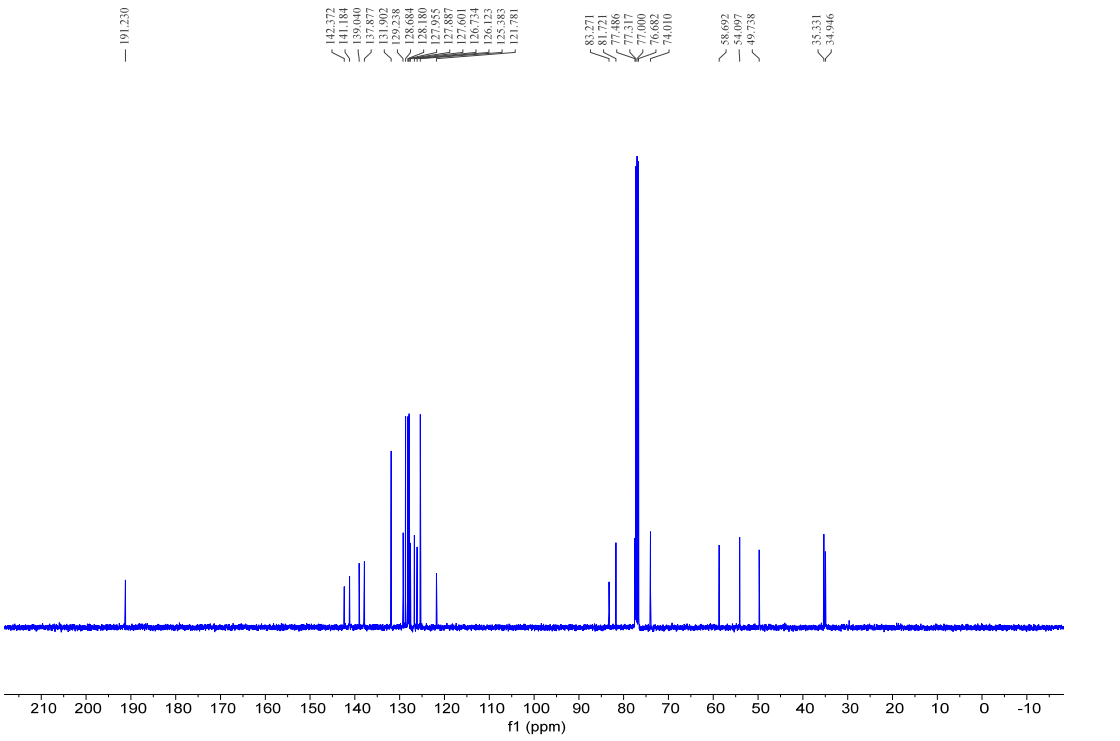

**Supplementary Figure 74.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ar**



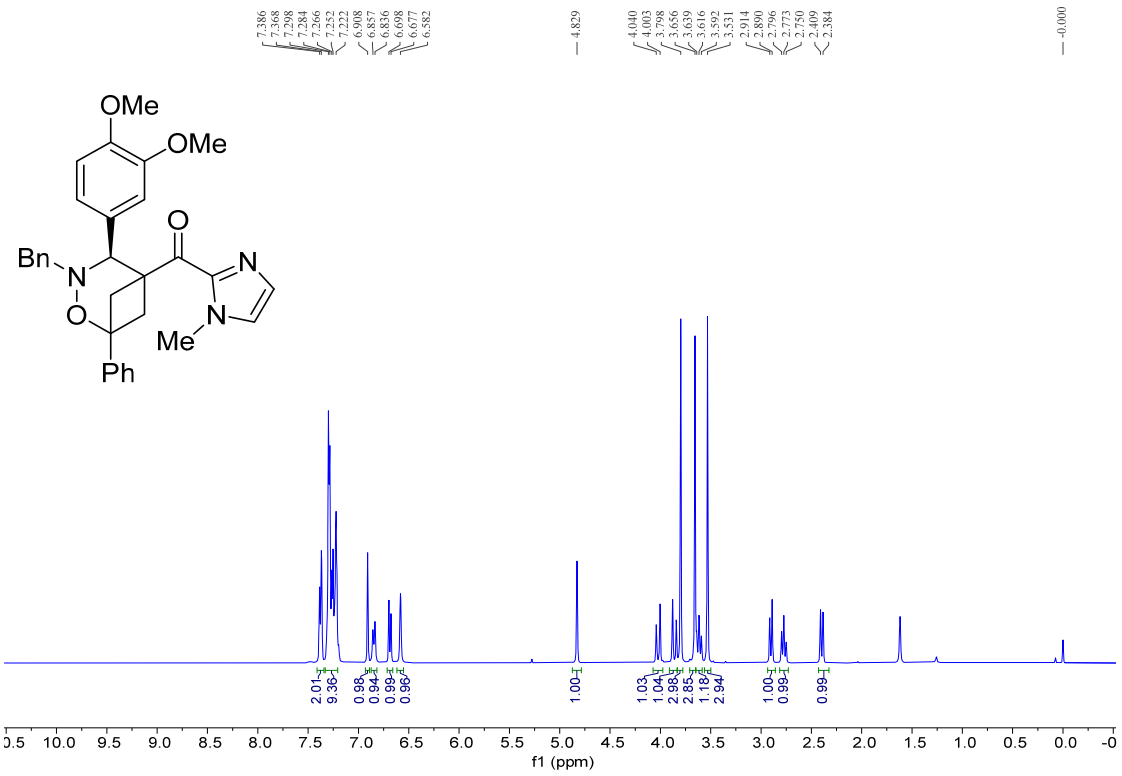

**Supplementary Figure 75.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ar**



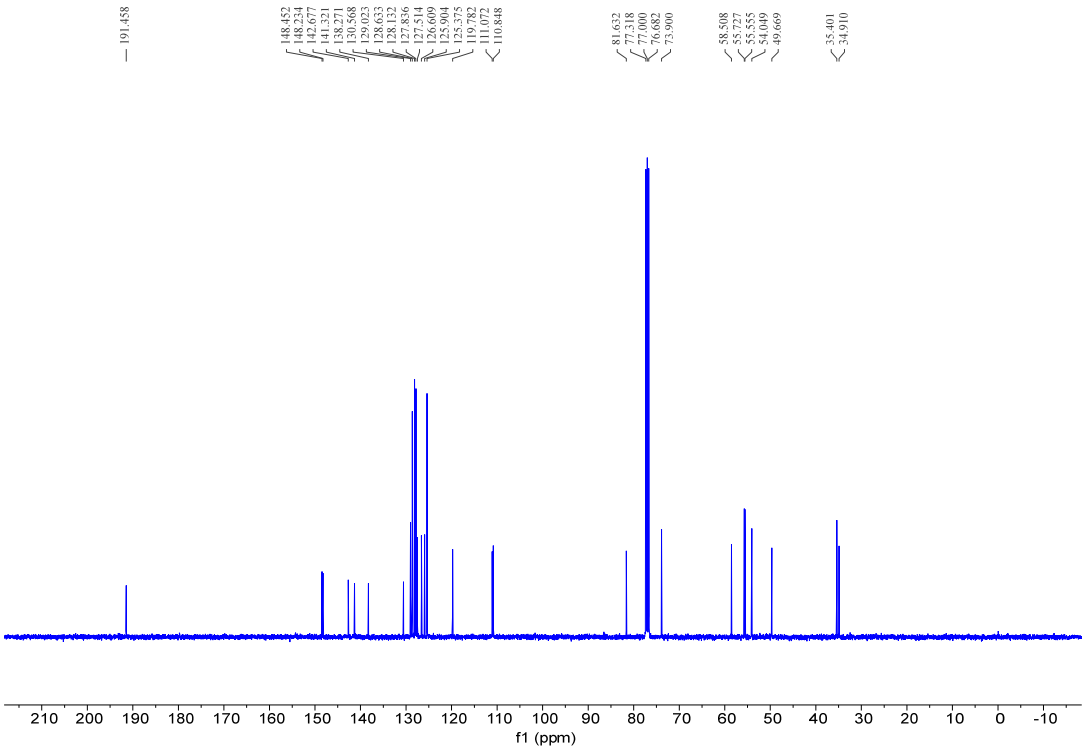

**Supplementary Figure 76.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3as**



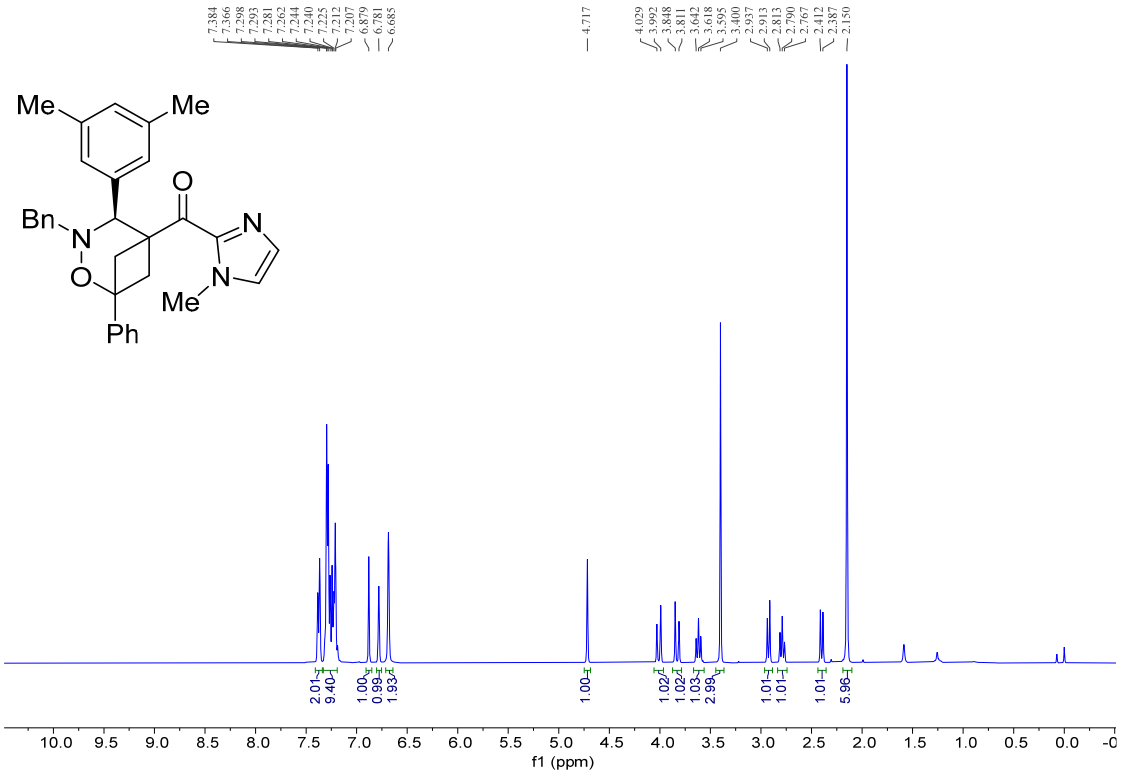

**Supplementary Figure 77.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3as**



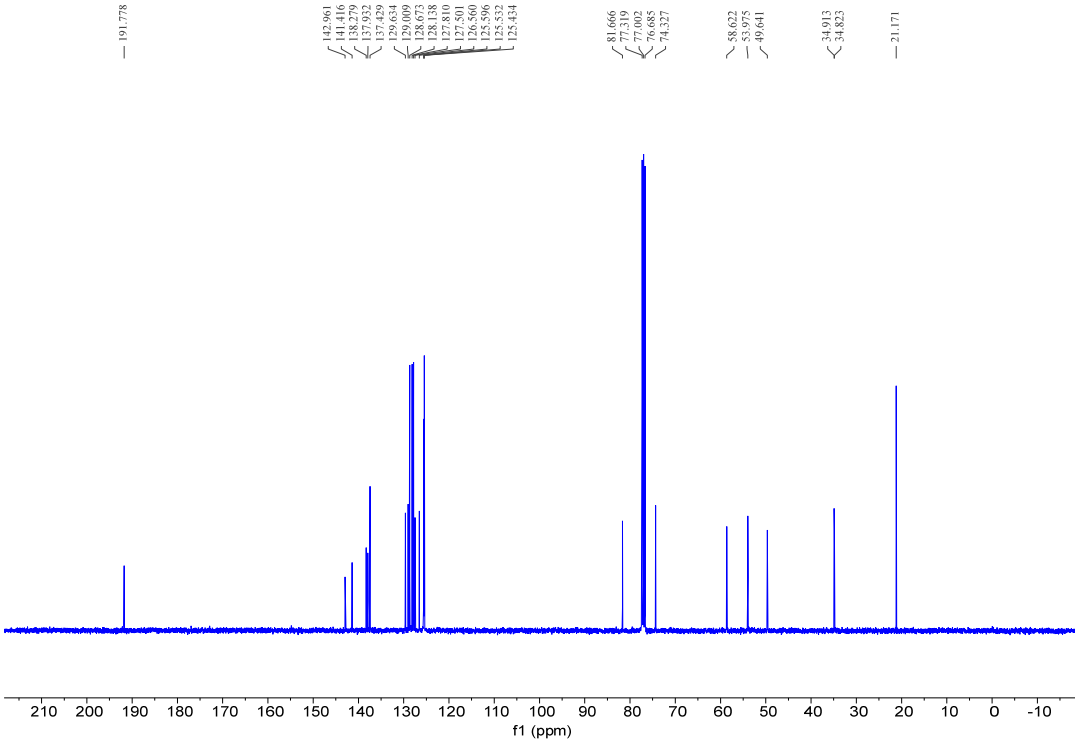

**Supplementary Figure 78.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3at**



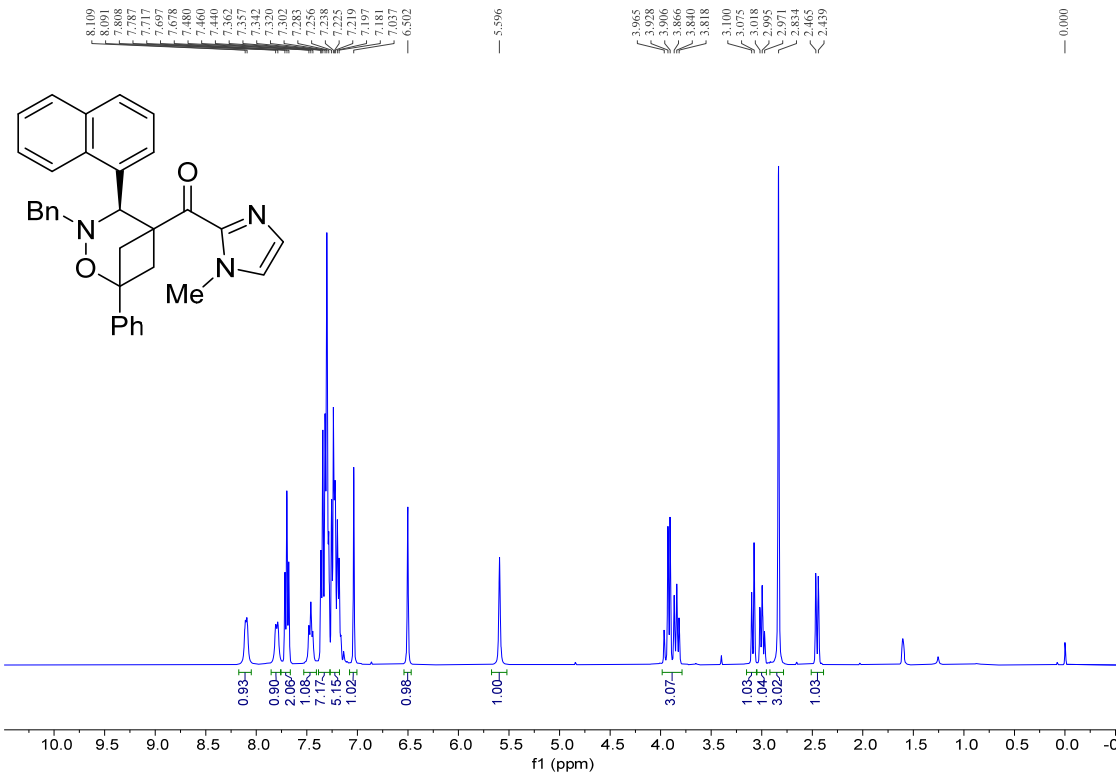

**Supplementary Figure 79.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3at**



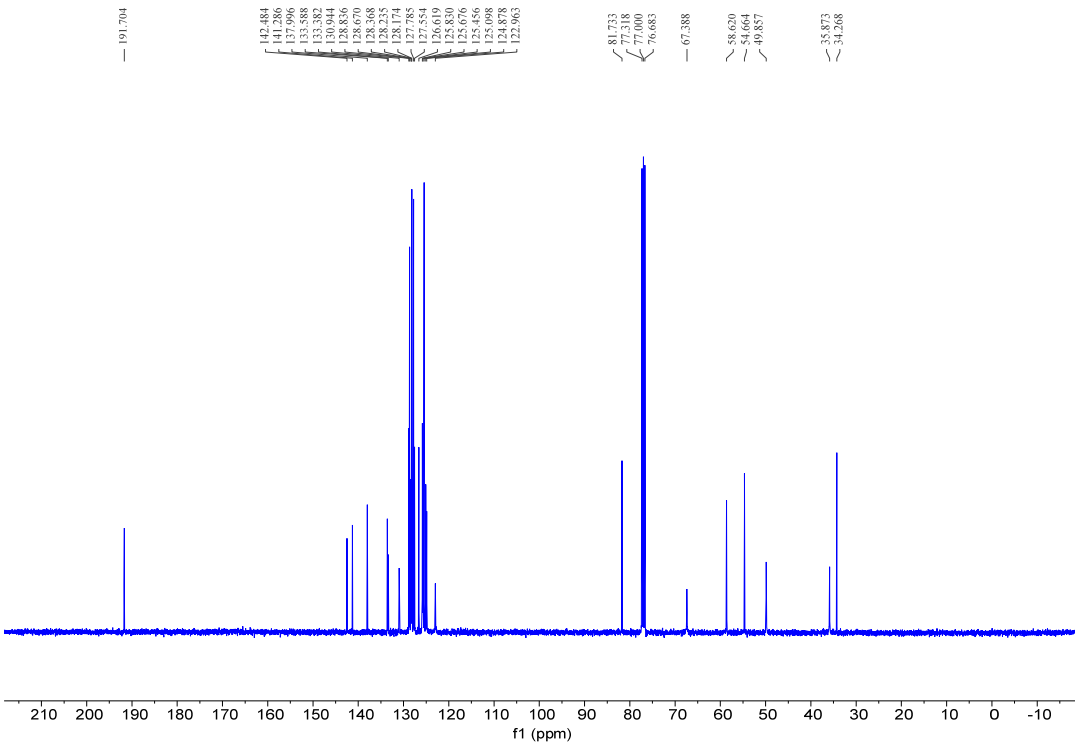

**Supplementary Figure 80.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3au**



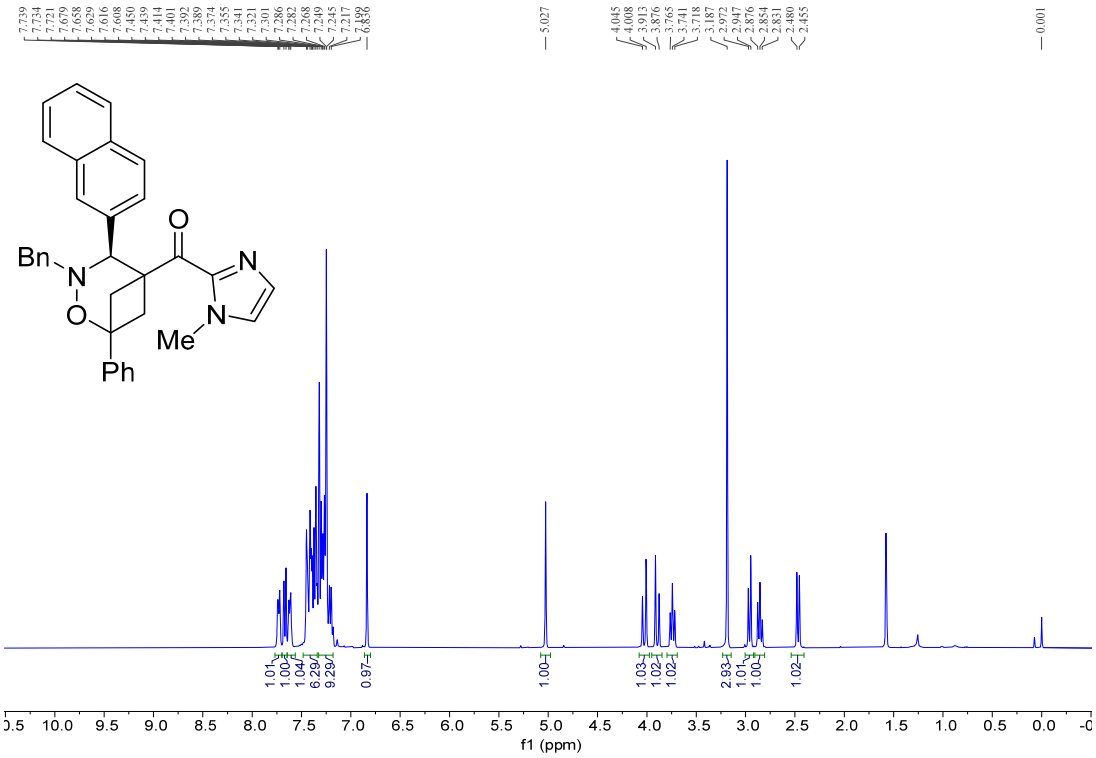

**Supplementary Figure 81.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3au**



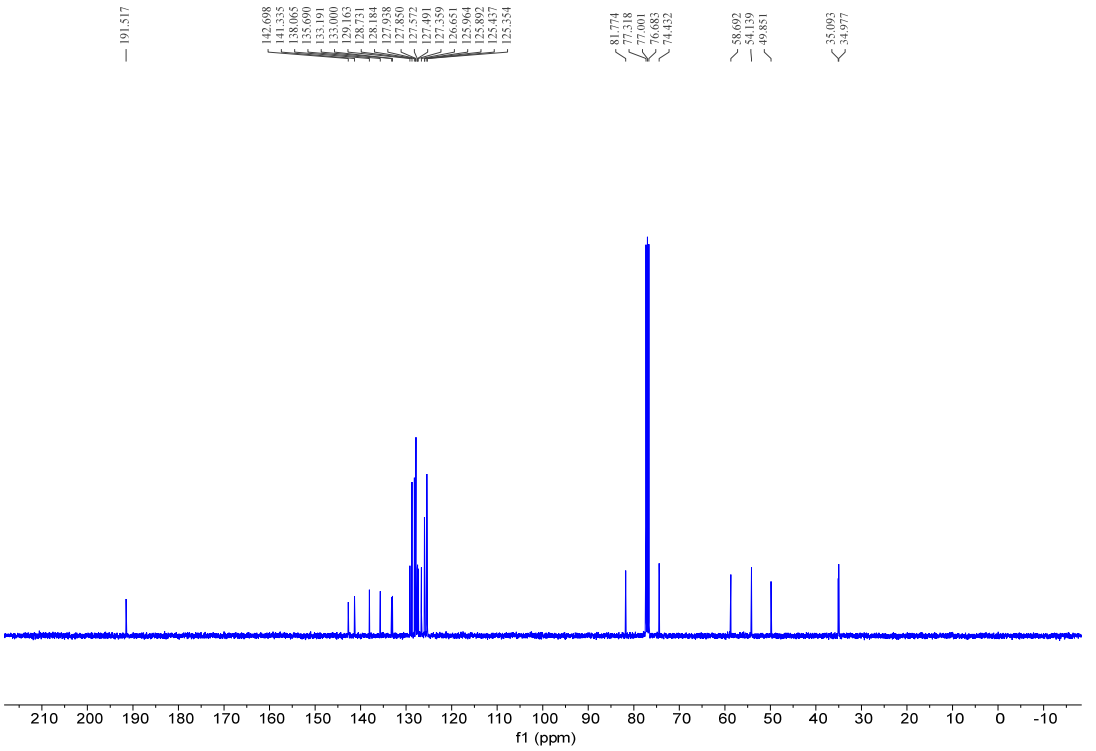

**Supplementary Figure 82.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3av**



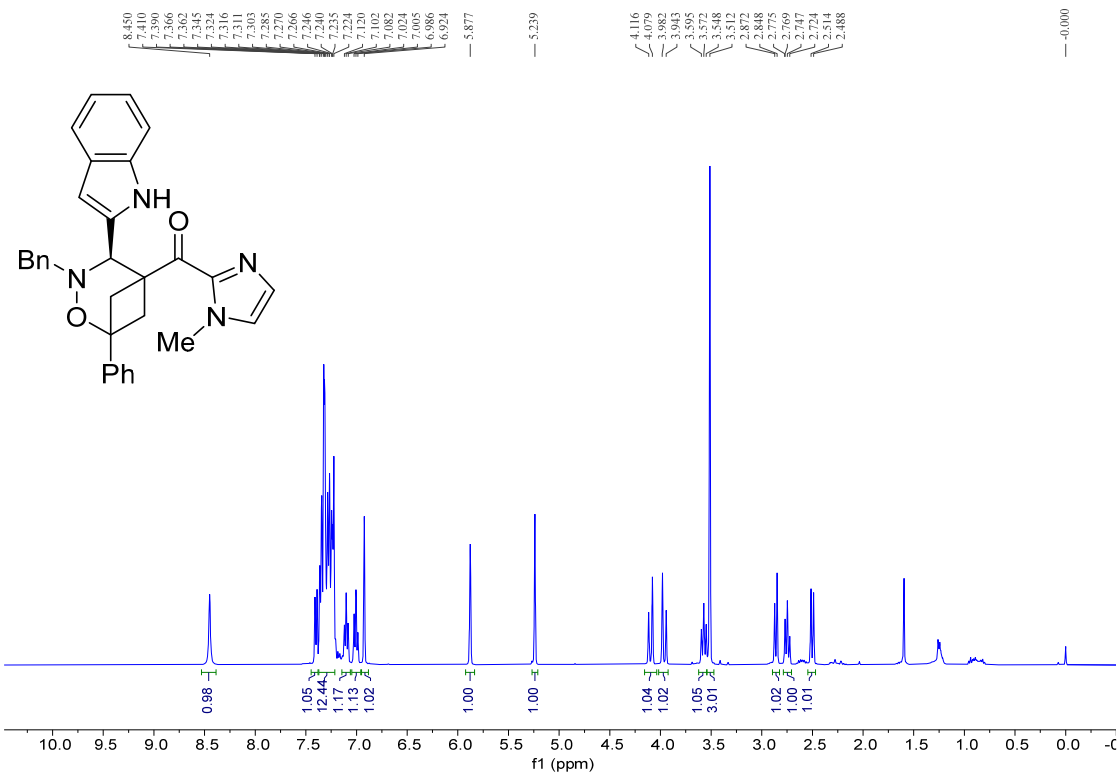

**Supplementary Figure 83.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3av**



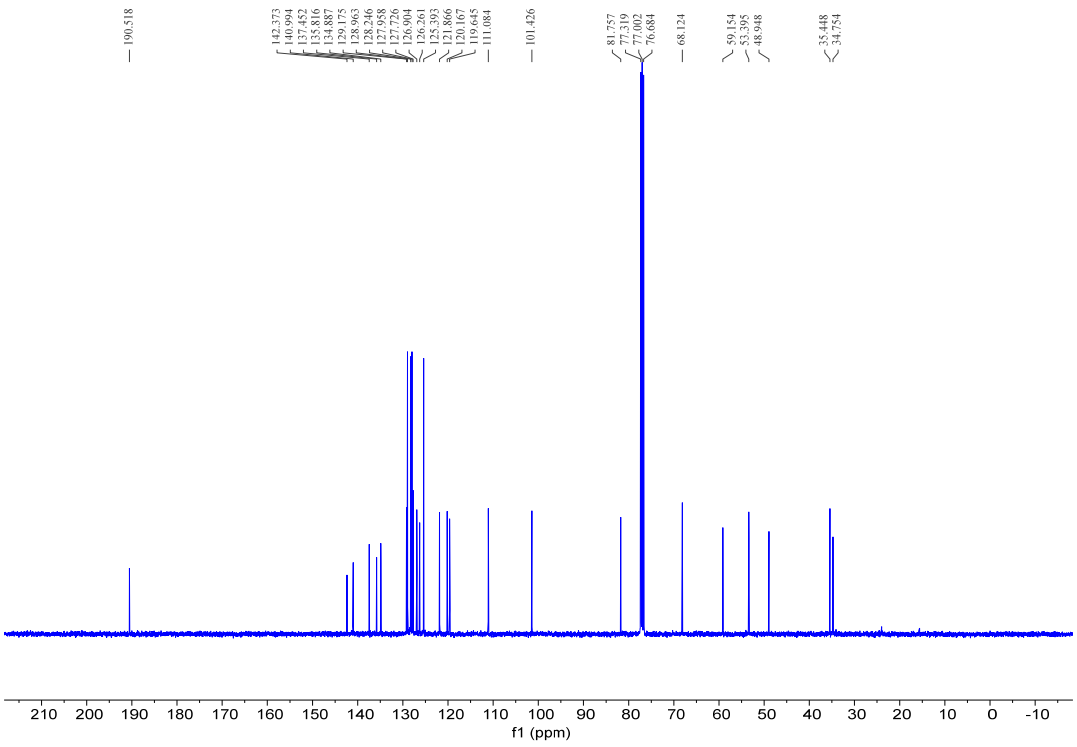

**Supplementary Figure 84.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3aw**



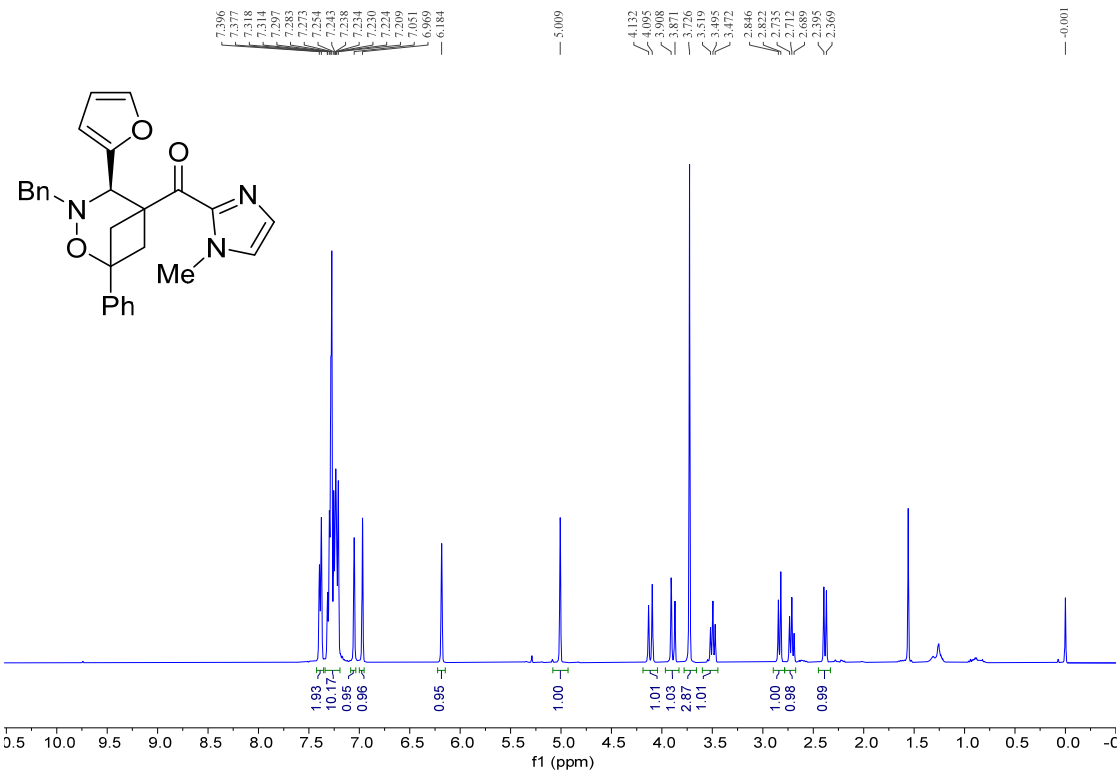

**Supplementary Figure 85.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3aw**



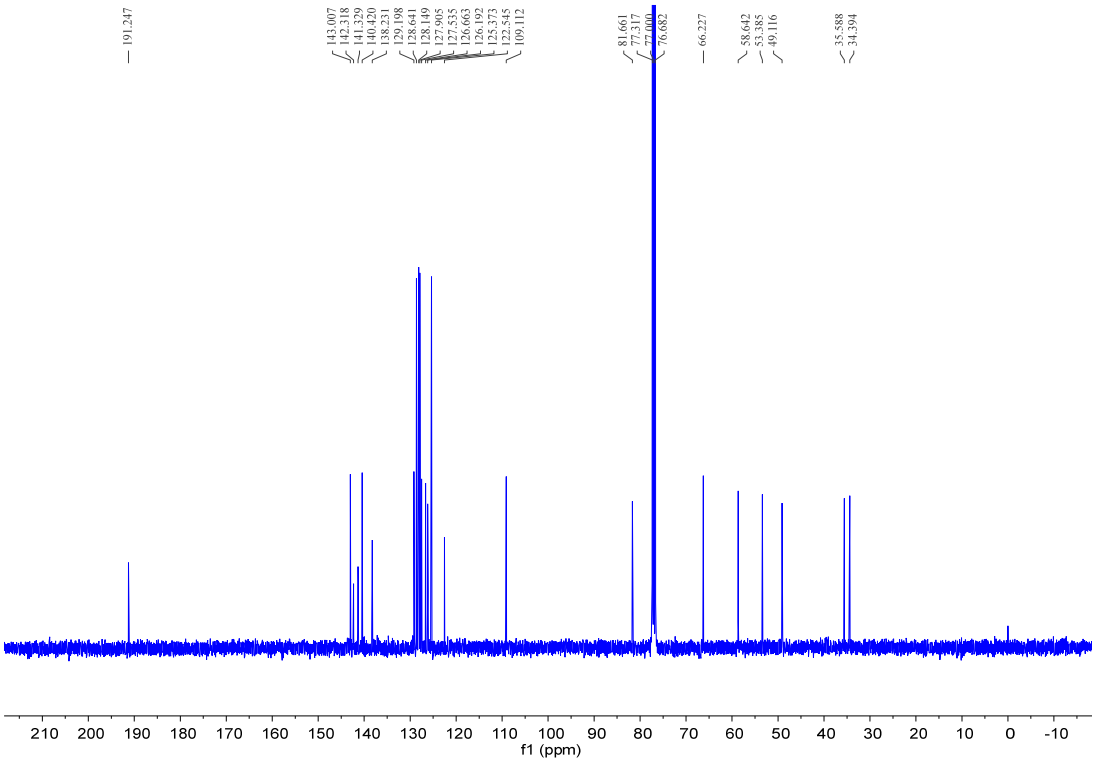

**Supplementary Figure 86.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ax**



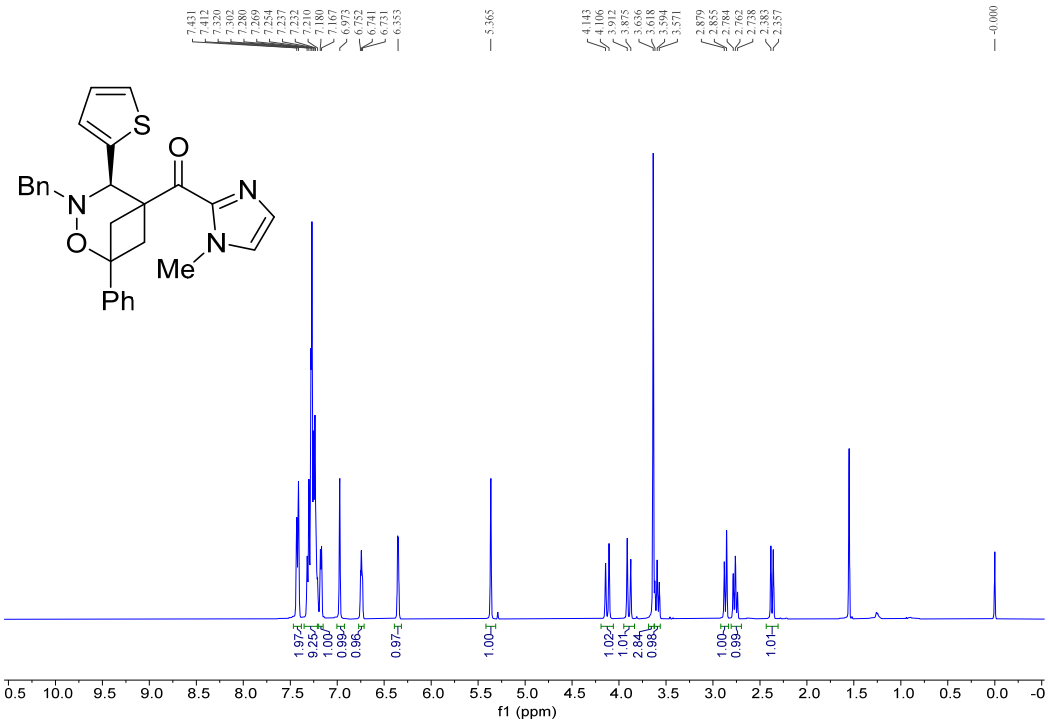

**Supplementary Figure 87.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ax**



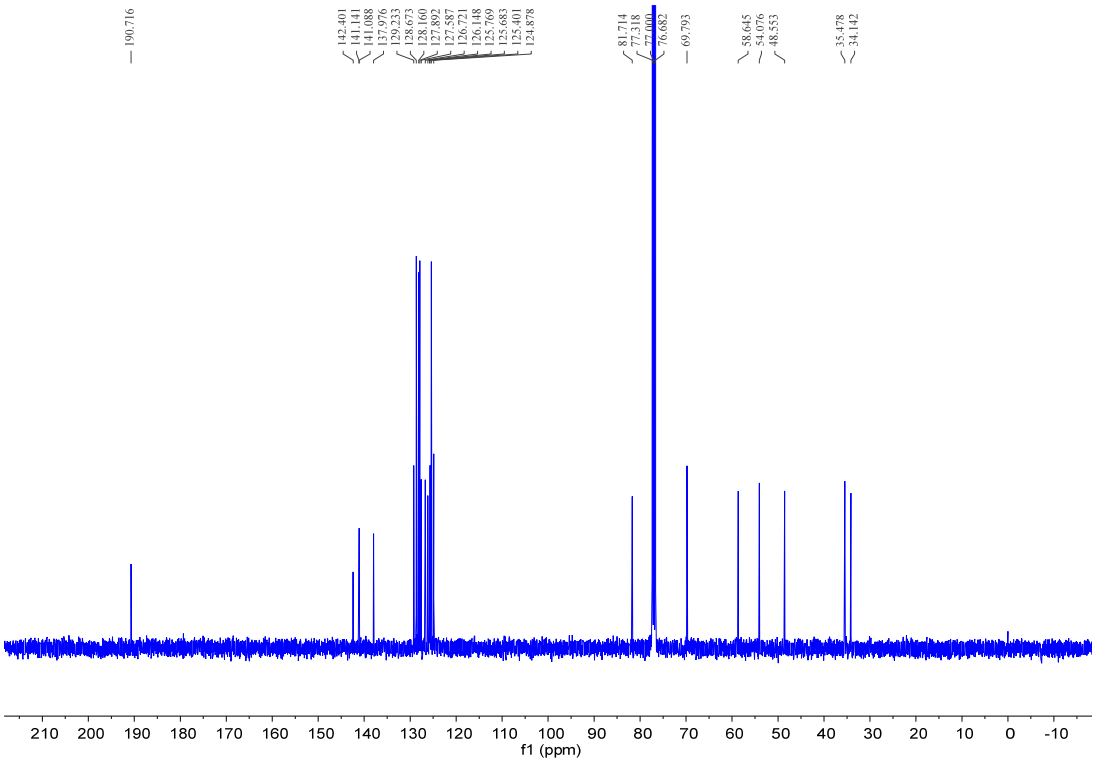

**Supplementary Figure 88.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3ay**



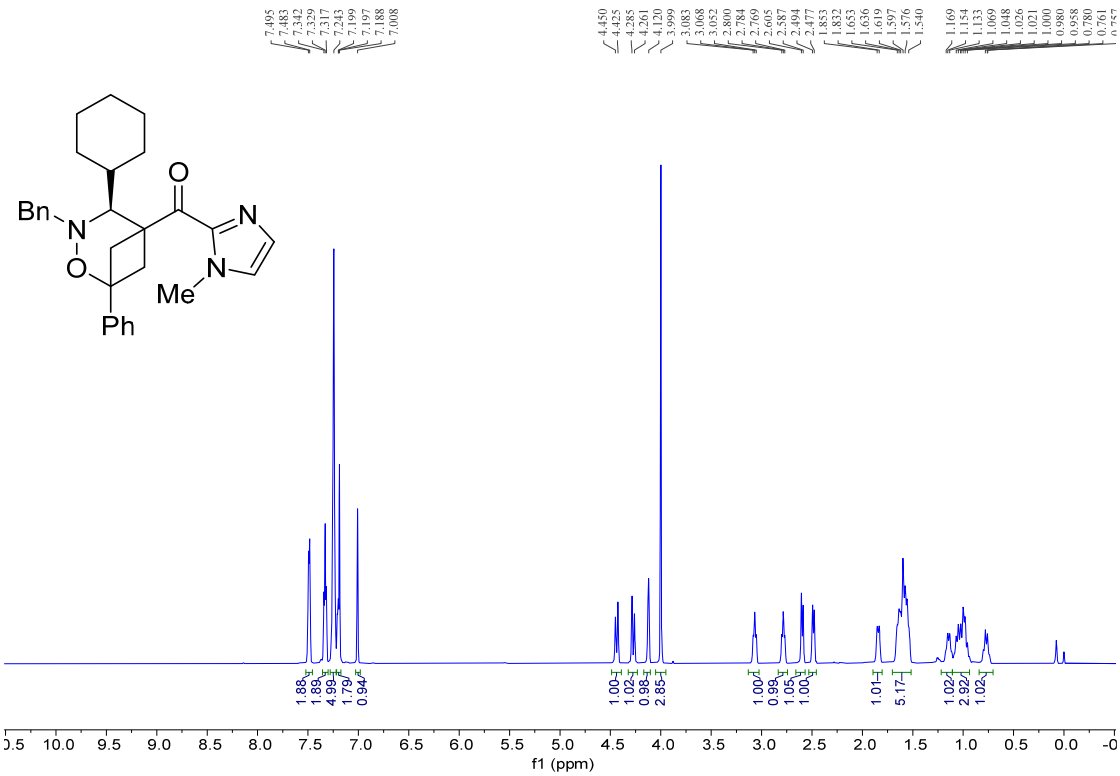

**Supplementary Figure 89.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ay**



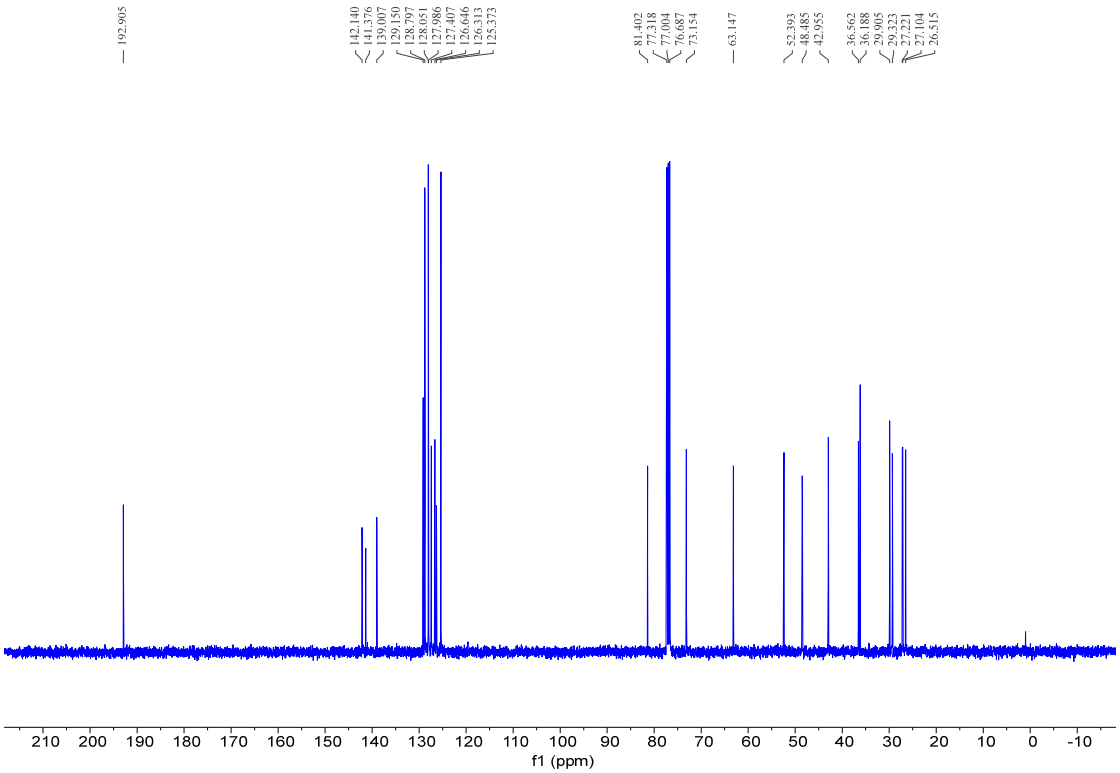

**Supplementary Figure 90.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3az**



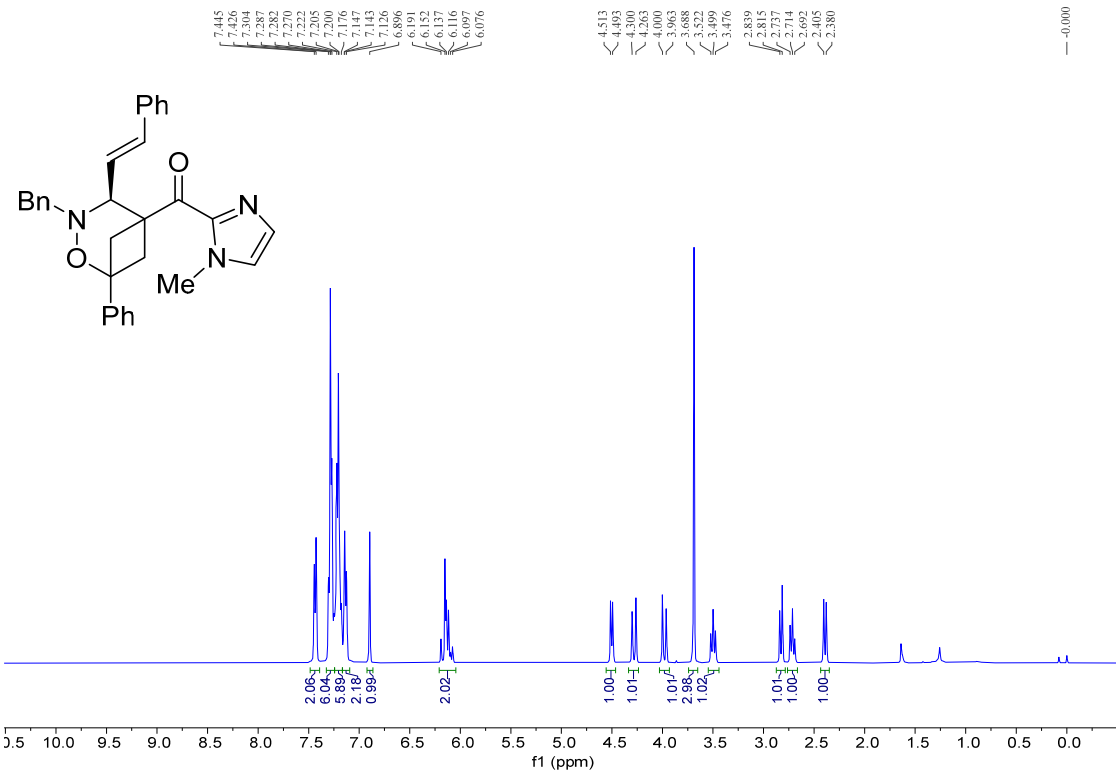

**Supplementary Figure 91.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3az**



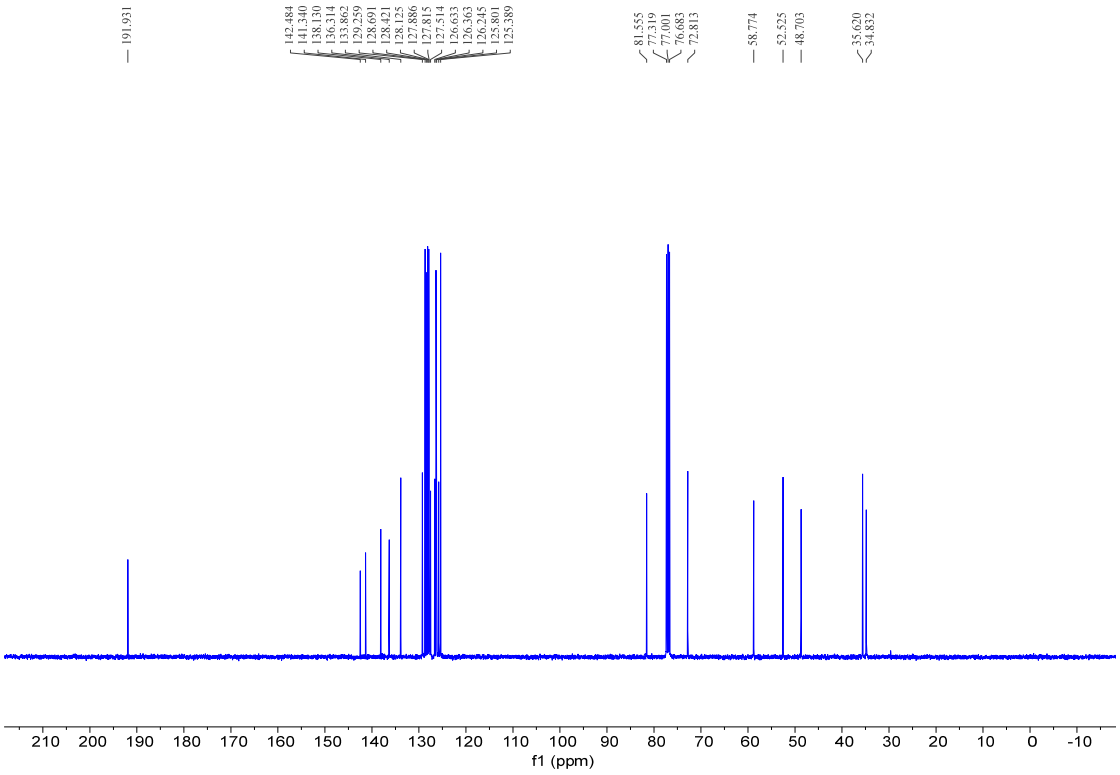

**Supplementary Figure 92.** $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **3aaa**



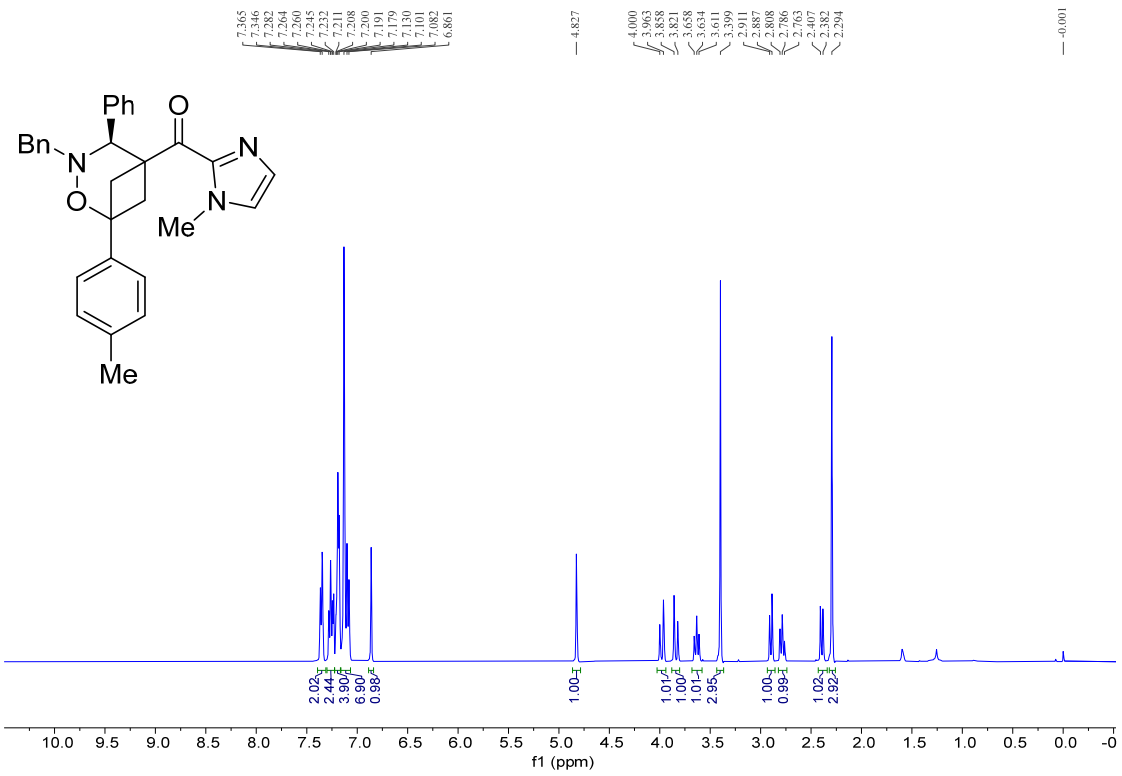

**Supplementary Figure 93.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3aaa**



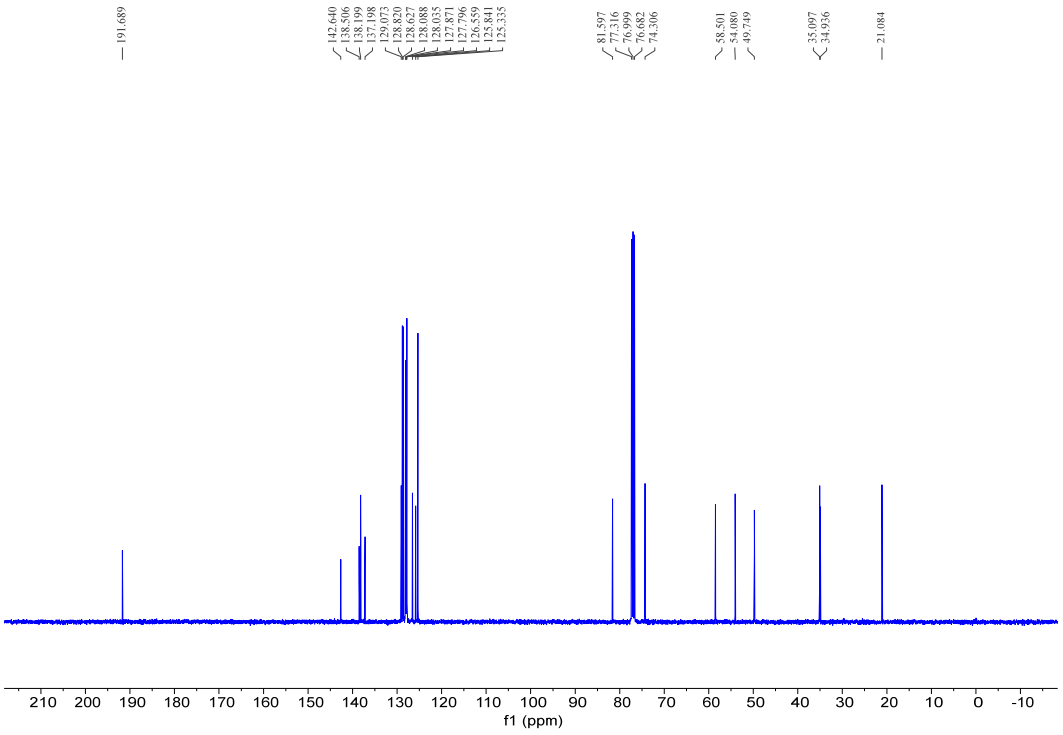

**Supplementary Figure 94.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3abb**



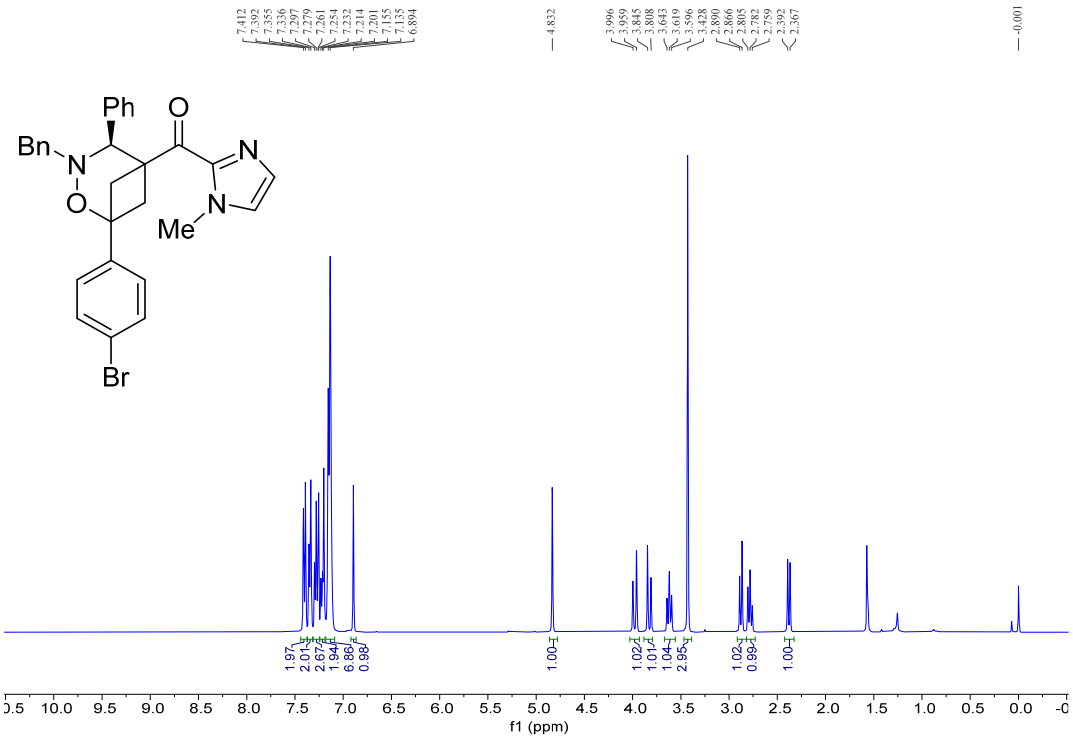

**Supplementary Figure 95.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3abb**



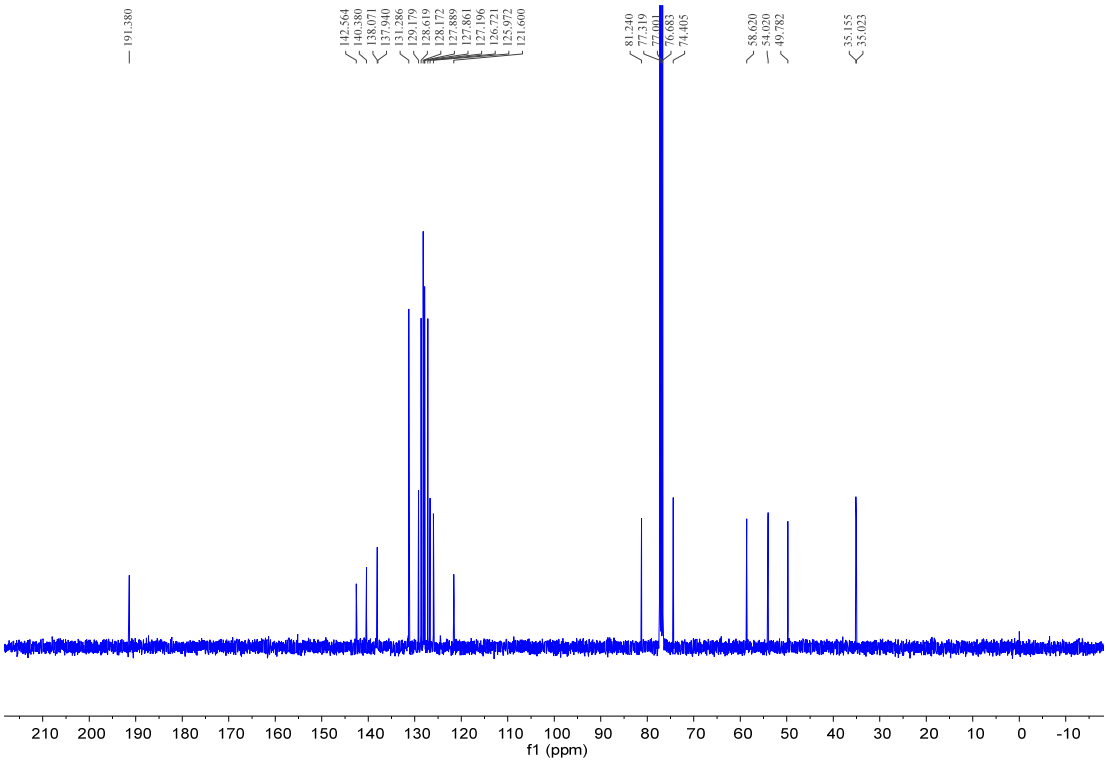

**Supplementary Figure 96.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3bb**



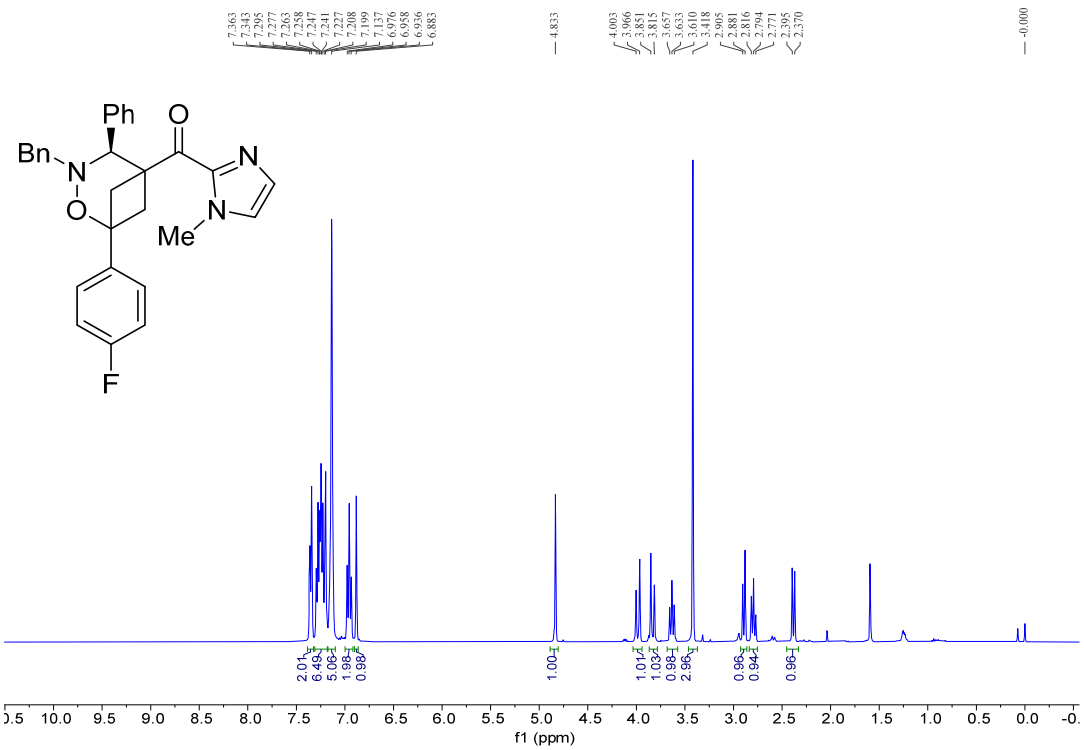

**Supplementary Figure 97.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3bb**



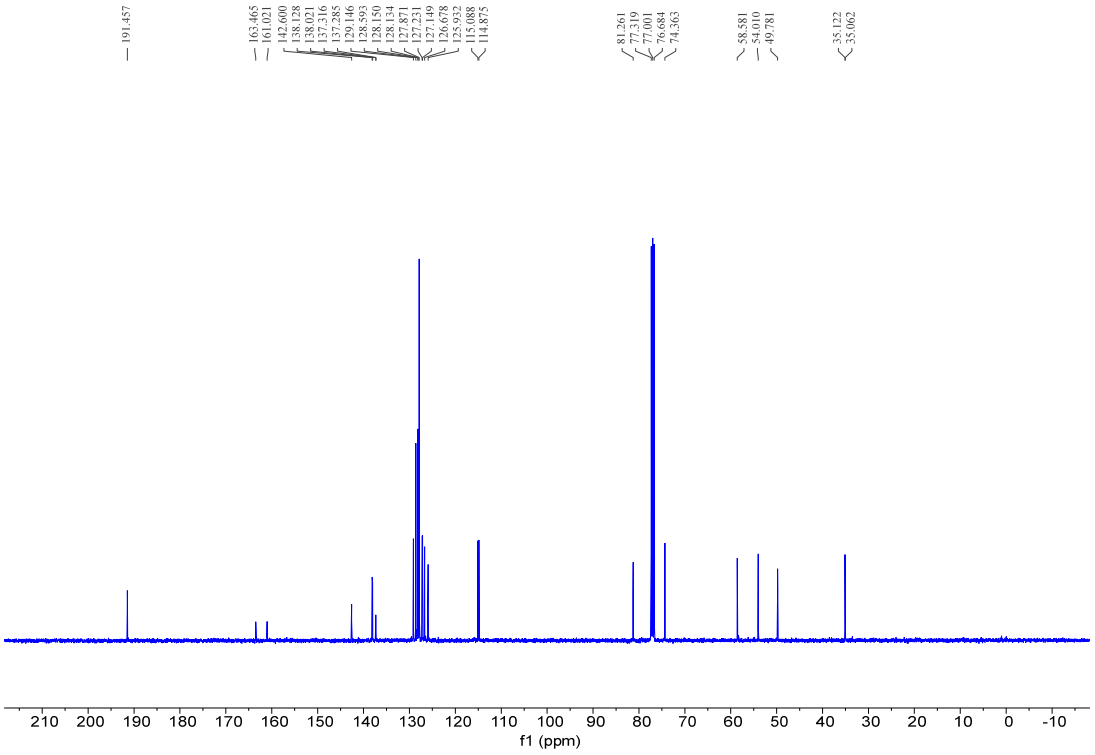

**Supplementary Figure 98.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3cb**



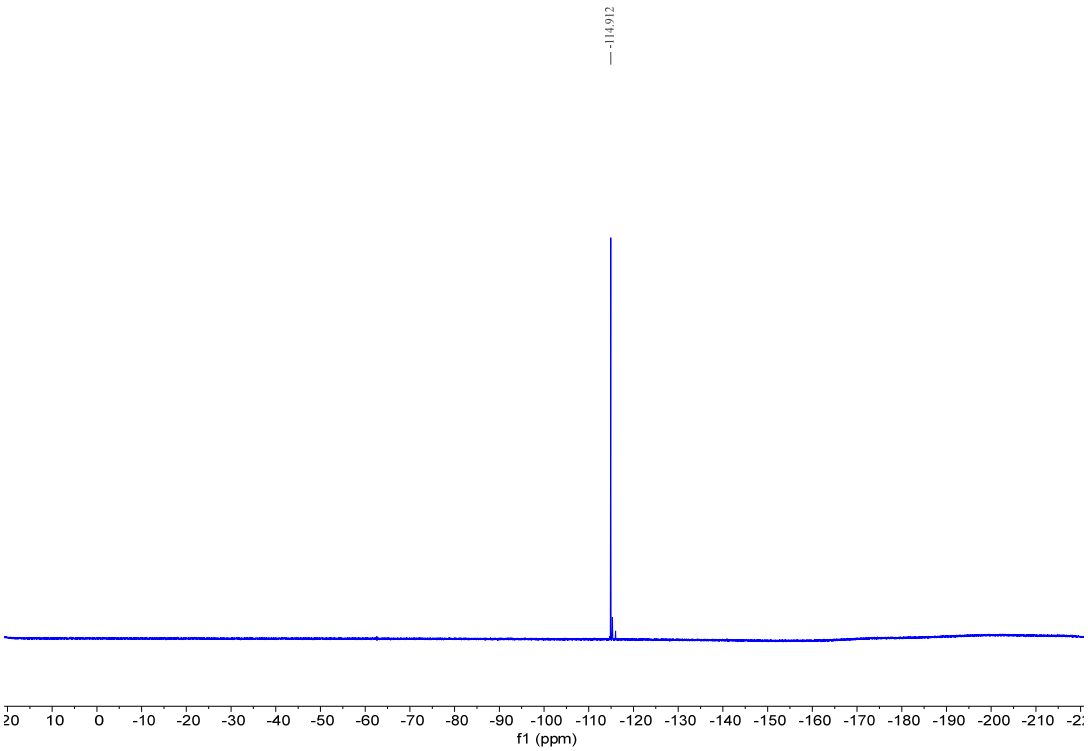

**Supplementary Figure 99.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3cb**



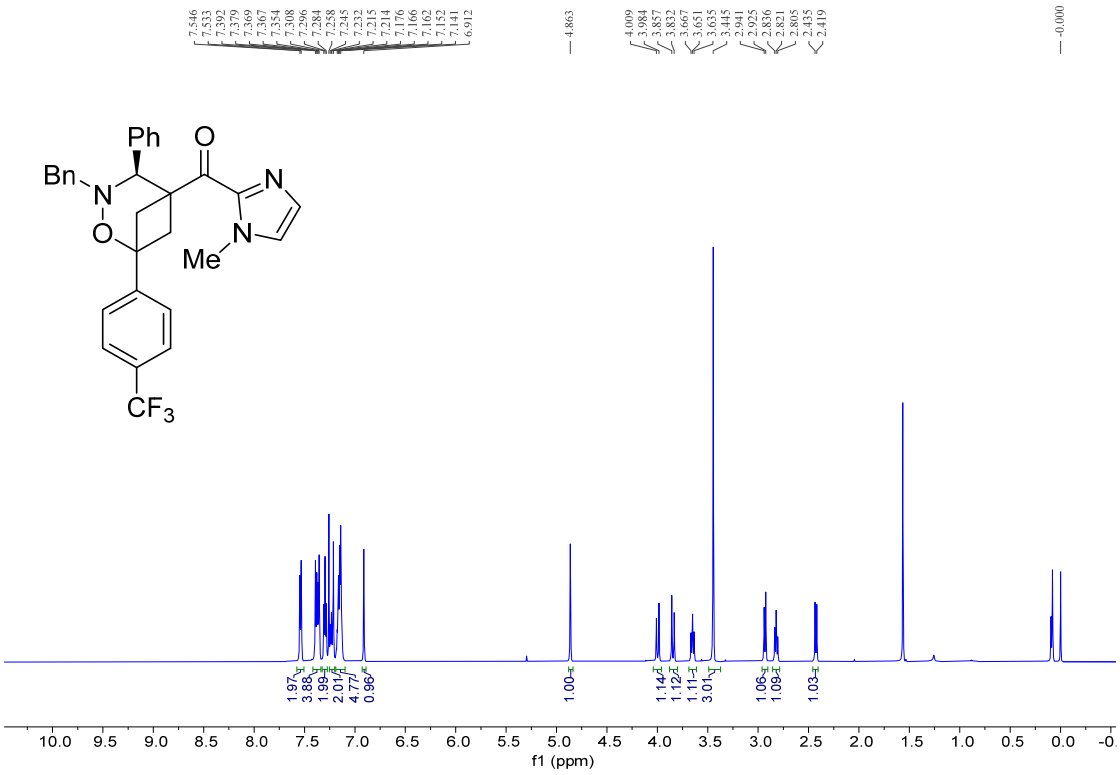

**Supplementary Figure 100.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3db**



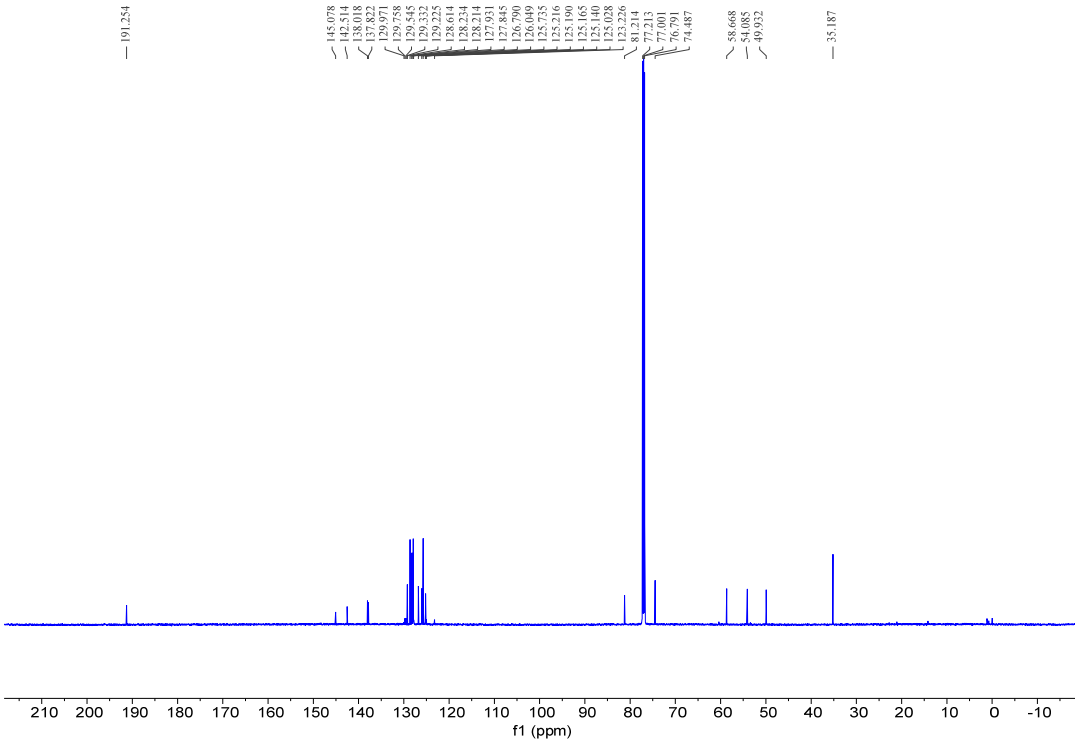

**Supplementary Figure 101.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3db**



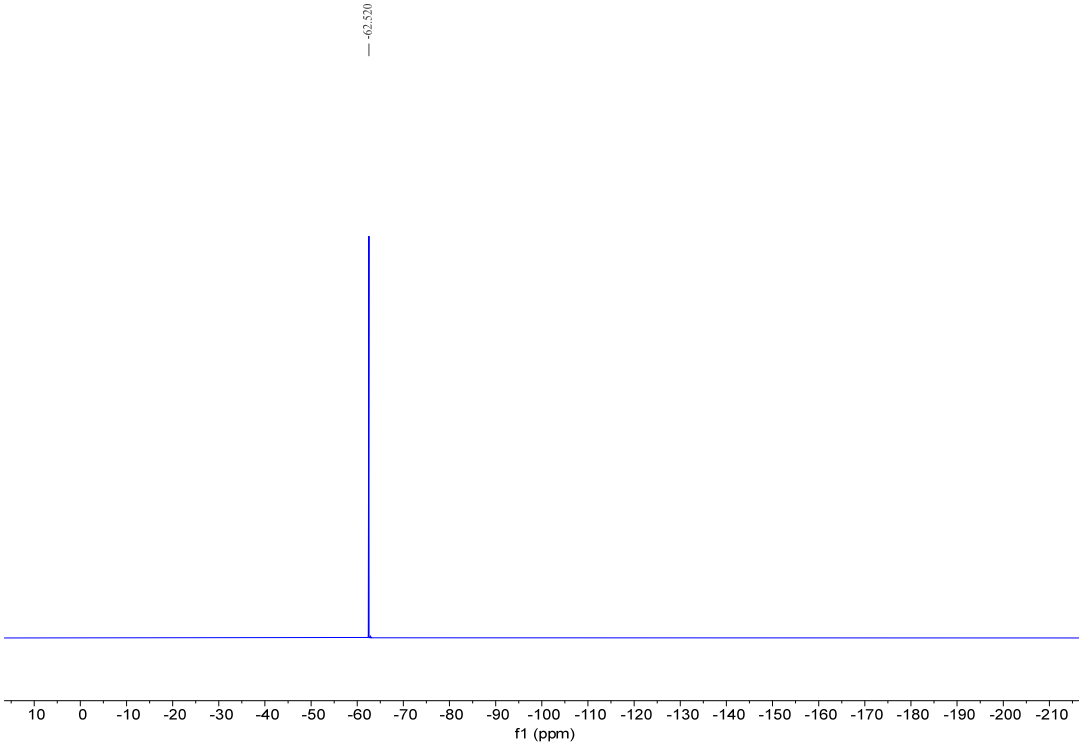

**Supplementary Figure 102.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **3db**



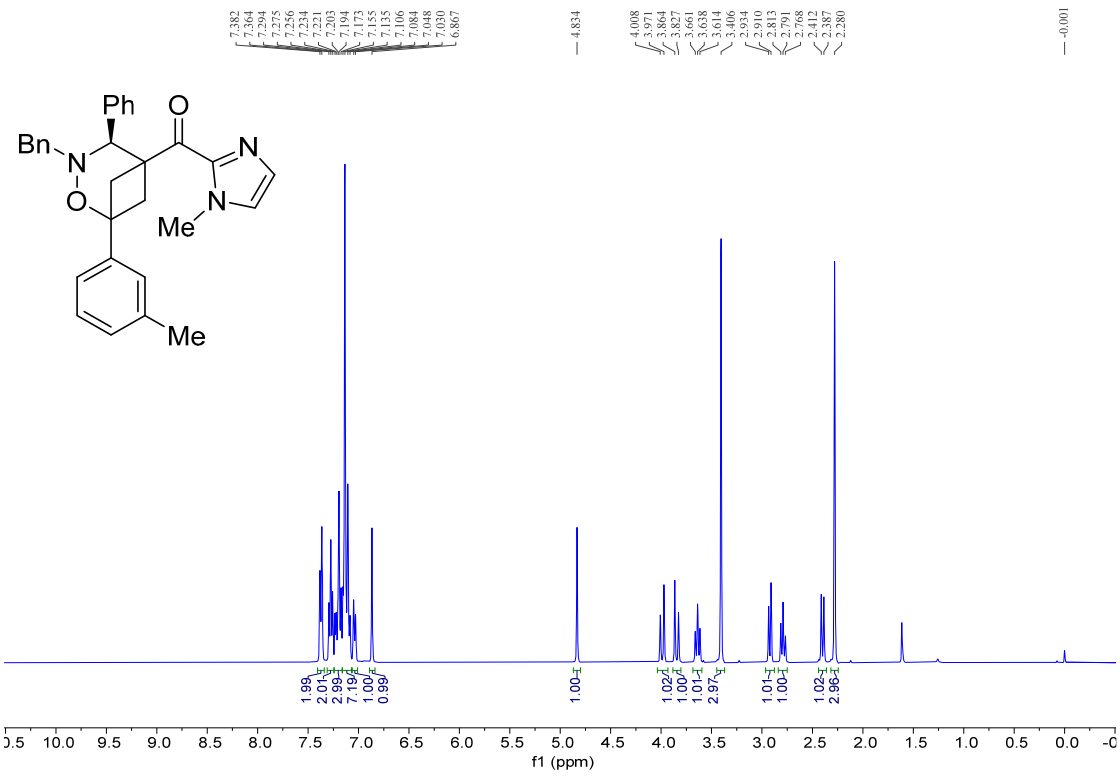

**Supplementary Figure 103.** $^{1}H$ NMR (600 MHz, $CDCl_3$) spectrum of compound **3eb**



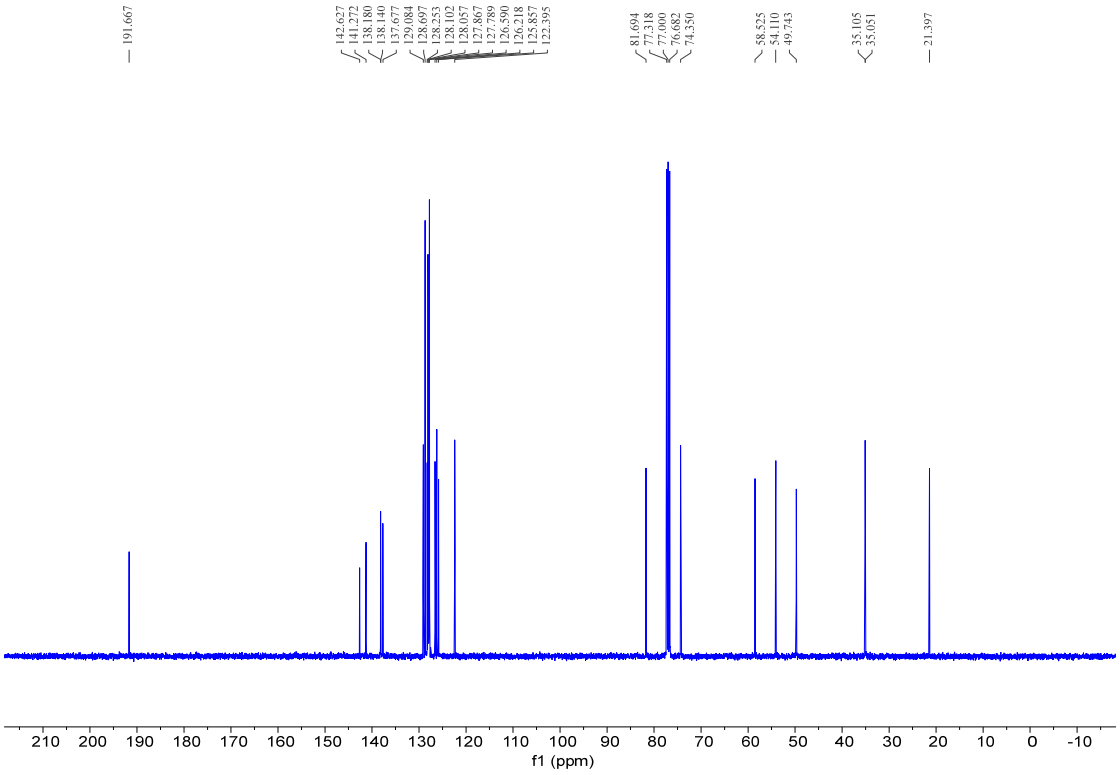

**Supplementary Figure 104.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3eb**



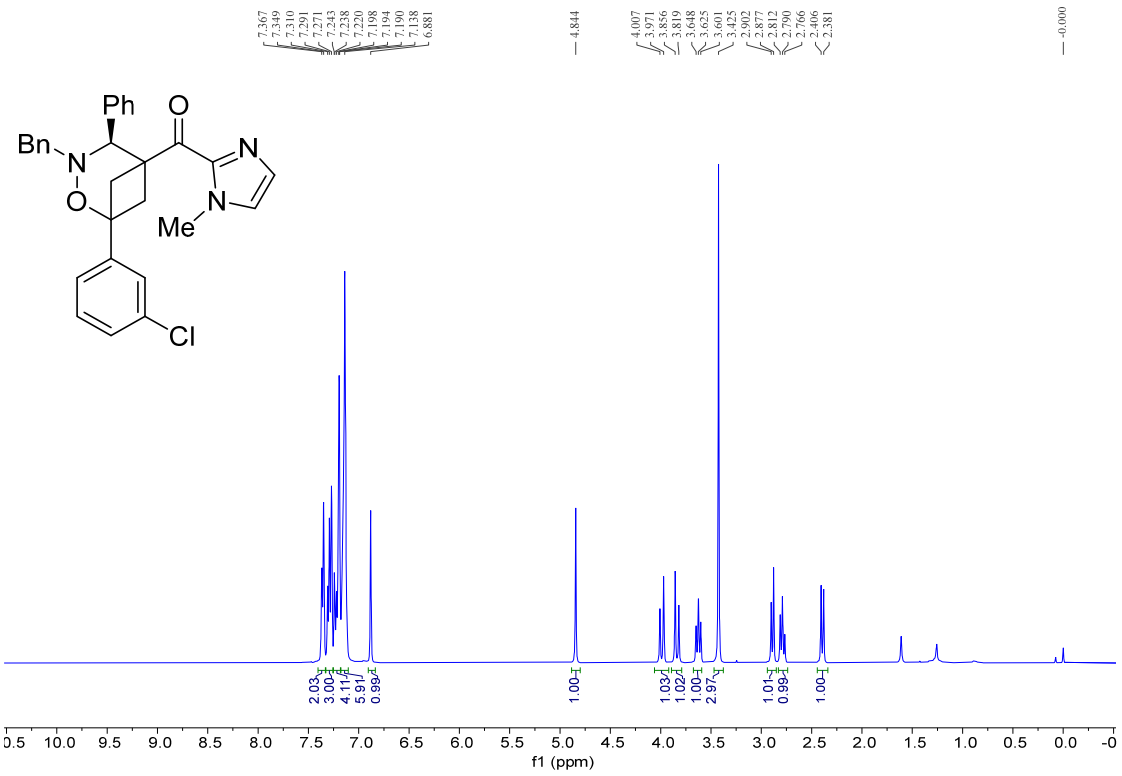

**Supplementary Figure 105.** $^{19}F$ NMR (565 MHz, $CDCl_3$) spectrum of compound **3eb**



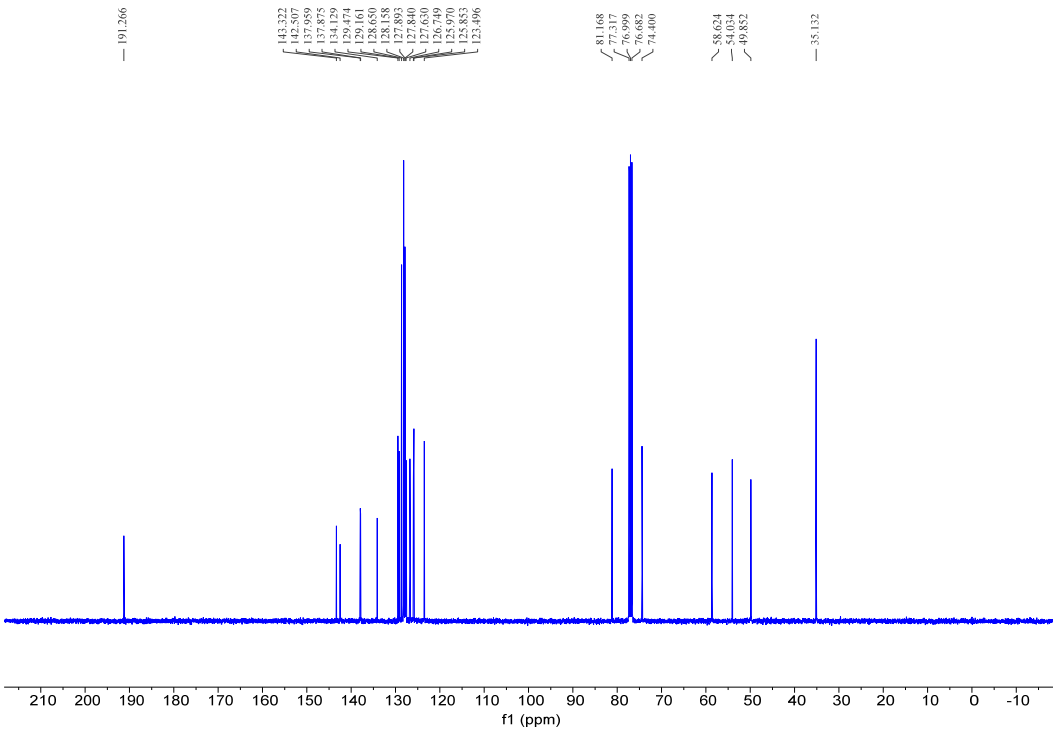

**Supplementary Figure 106.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3fb**



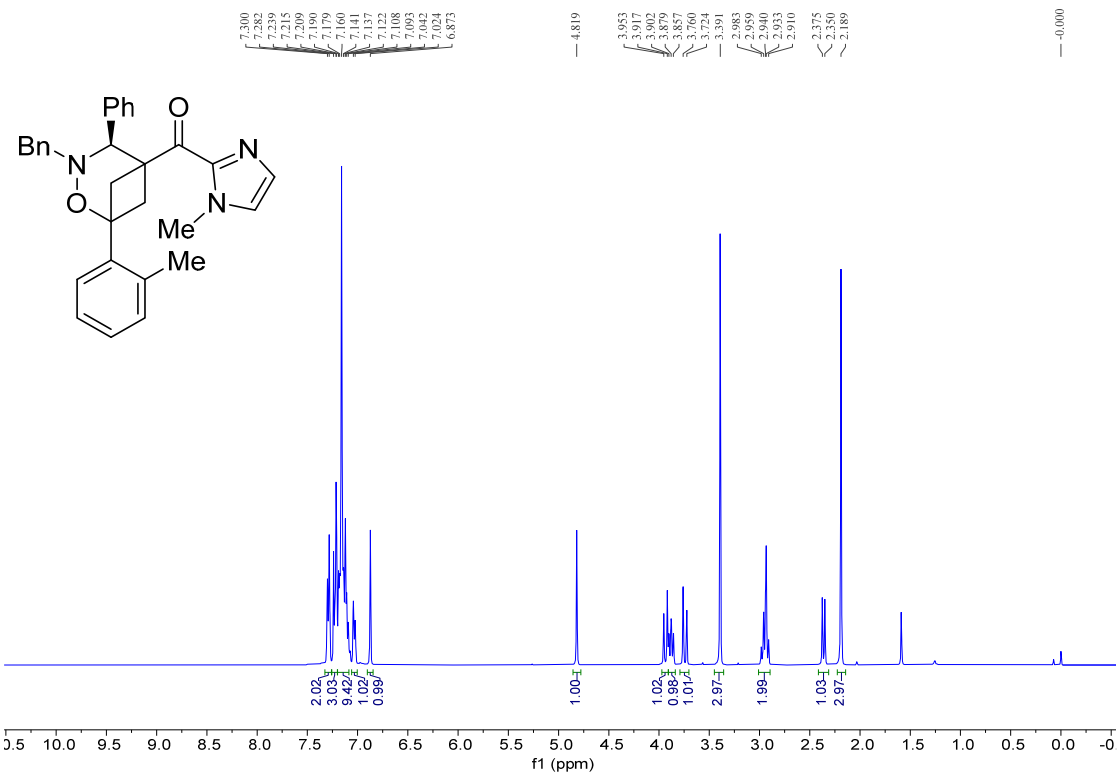

**Supplementary Figure 107.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3fb**



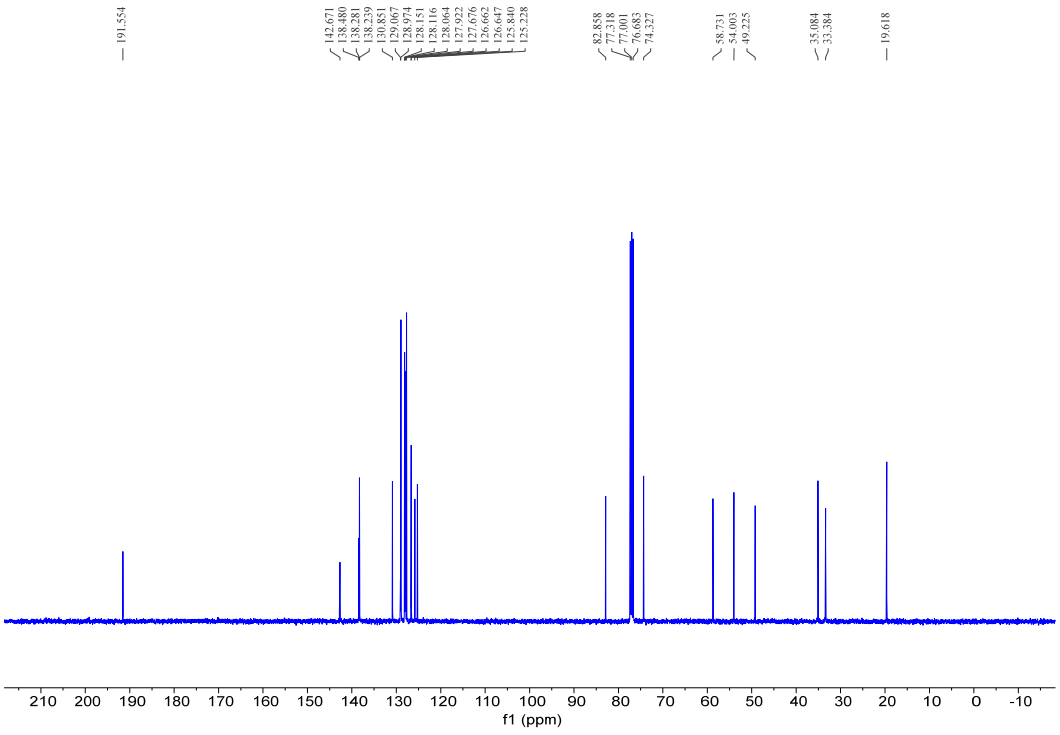

**Supplementary Figure 108.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3gb**



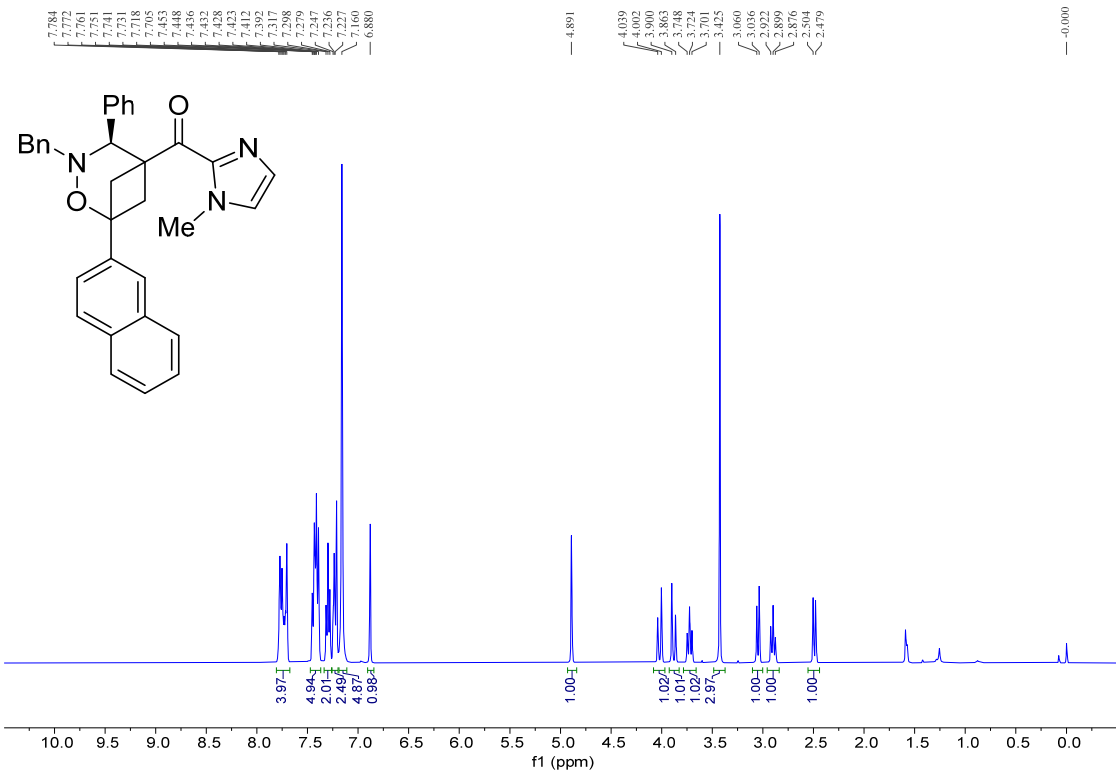

**Supplementary Figure 109.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3gb**



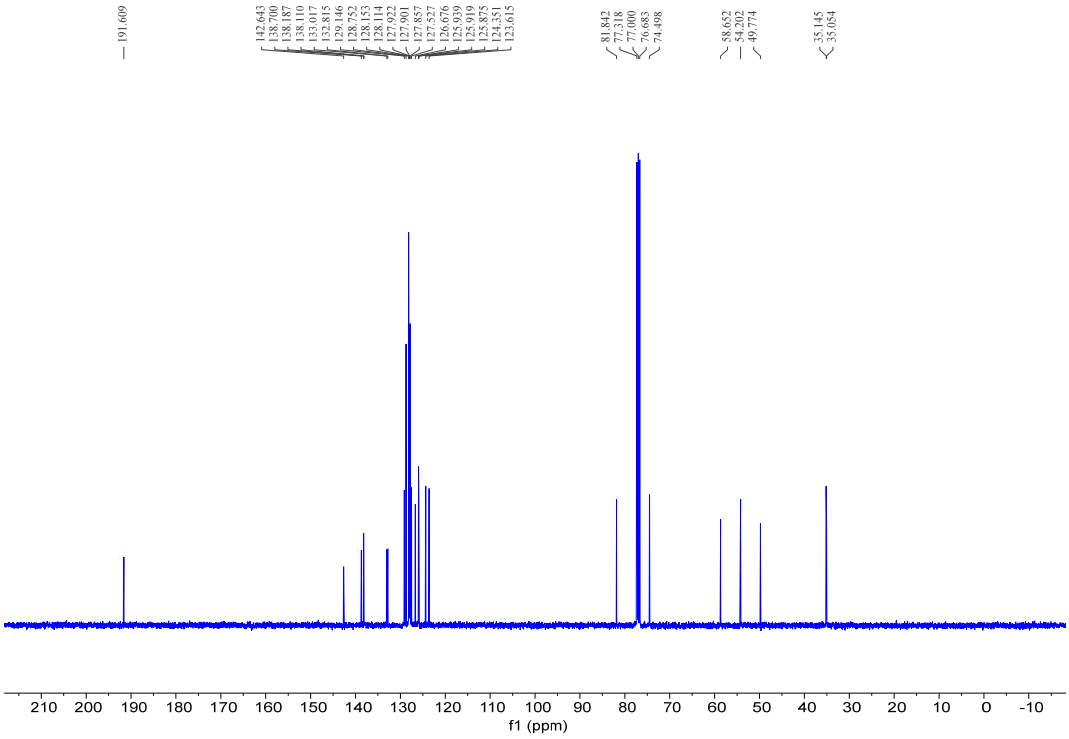

**Supplementary Figure 110.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3hb**



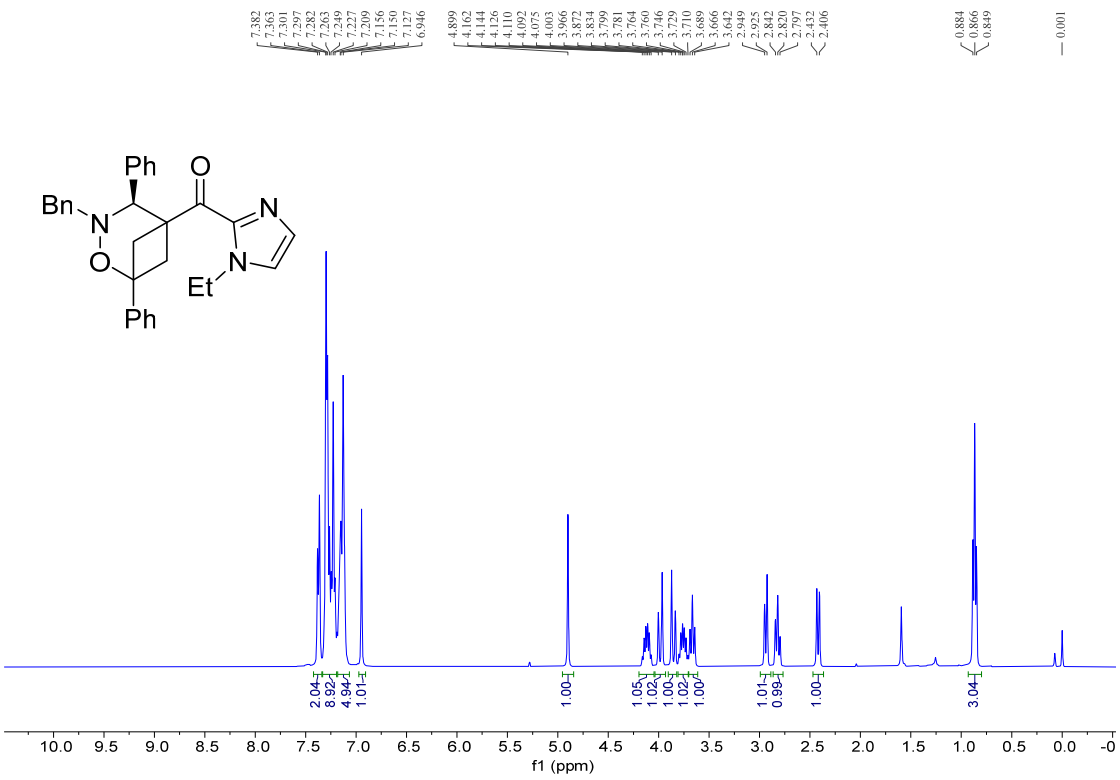

**Supplementary Figure 111.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3hb**



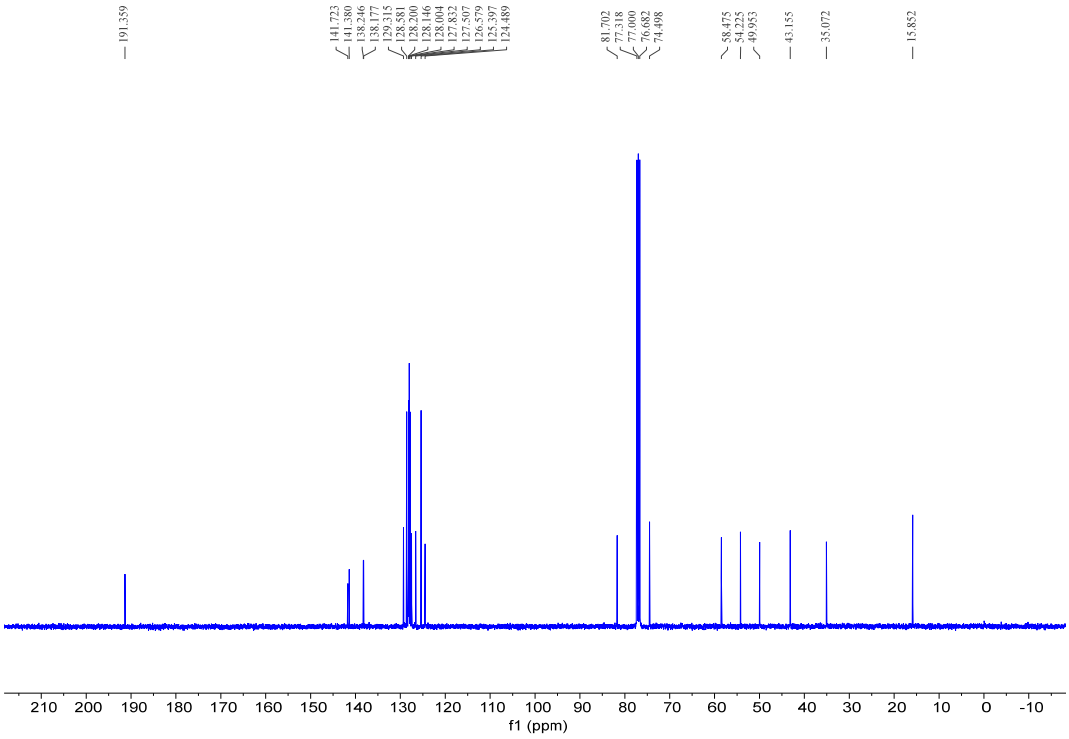

**Supplementary Figure 112.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3ib**



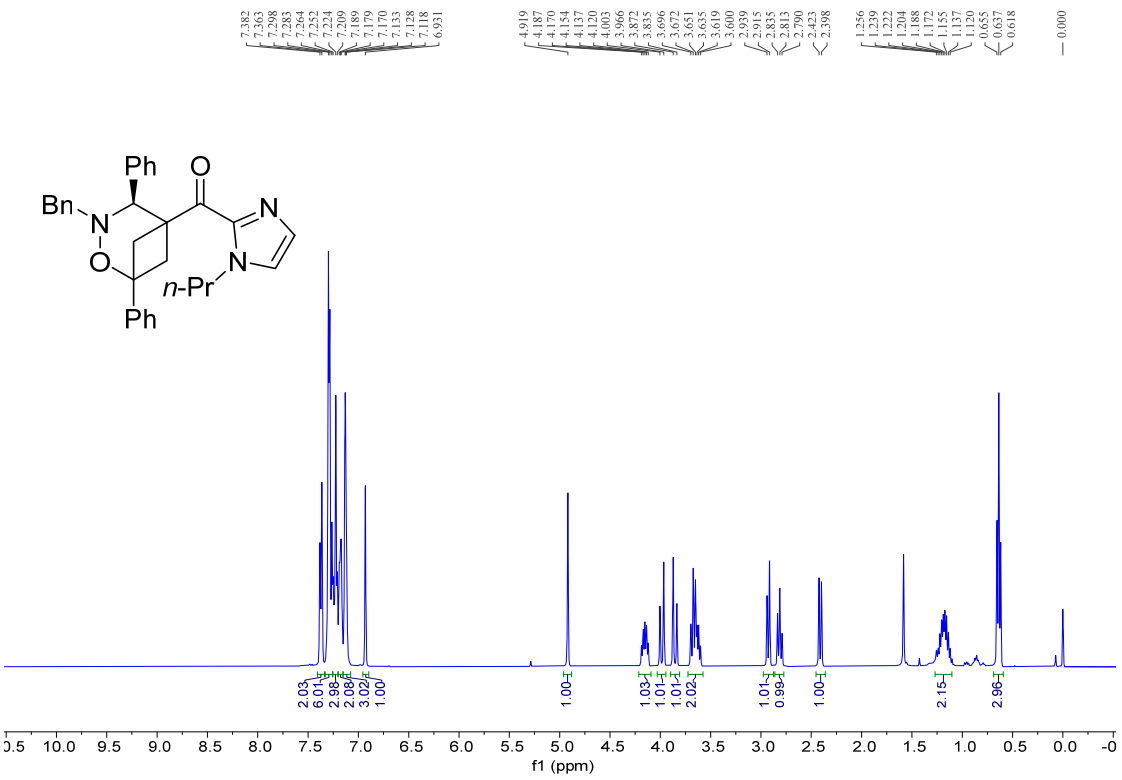

**Supplementary Figure 113.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3ib**



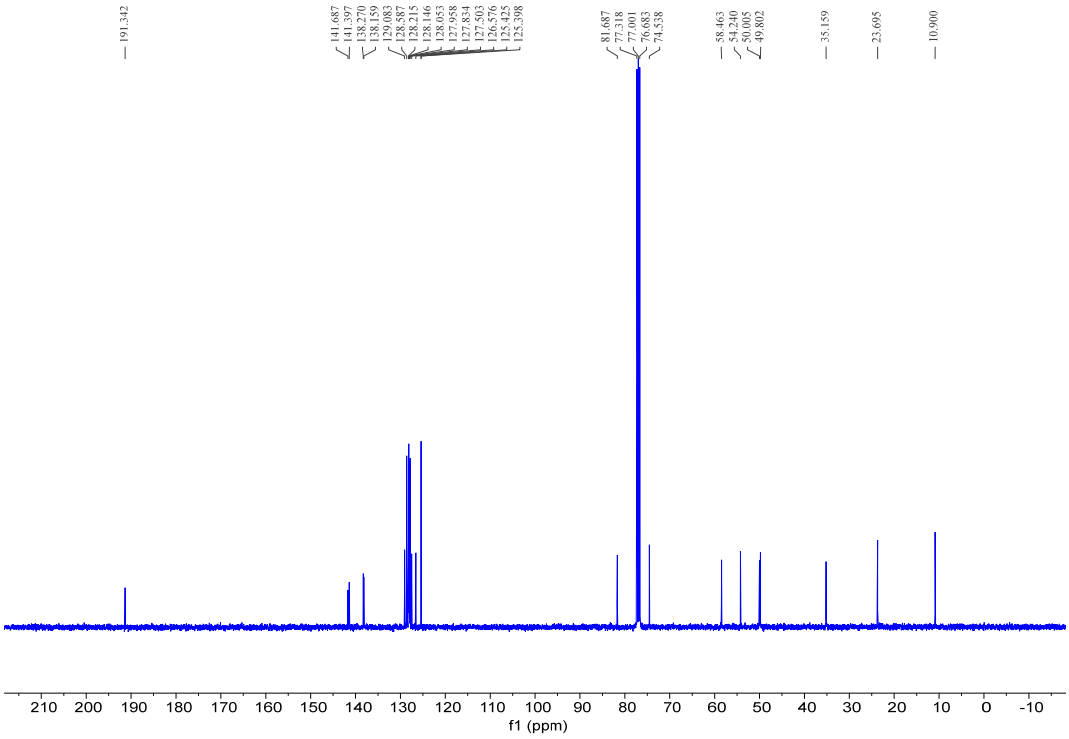

**Supplementary Figure 114.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3jb**



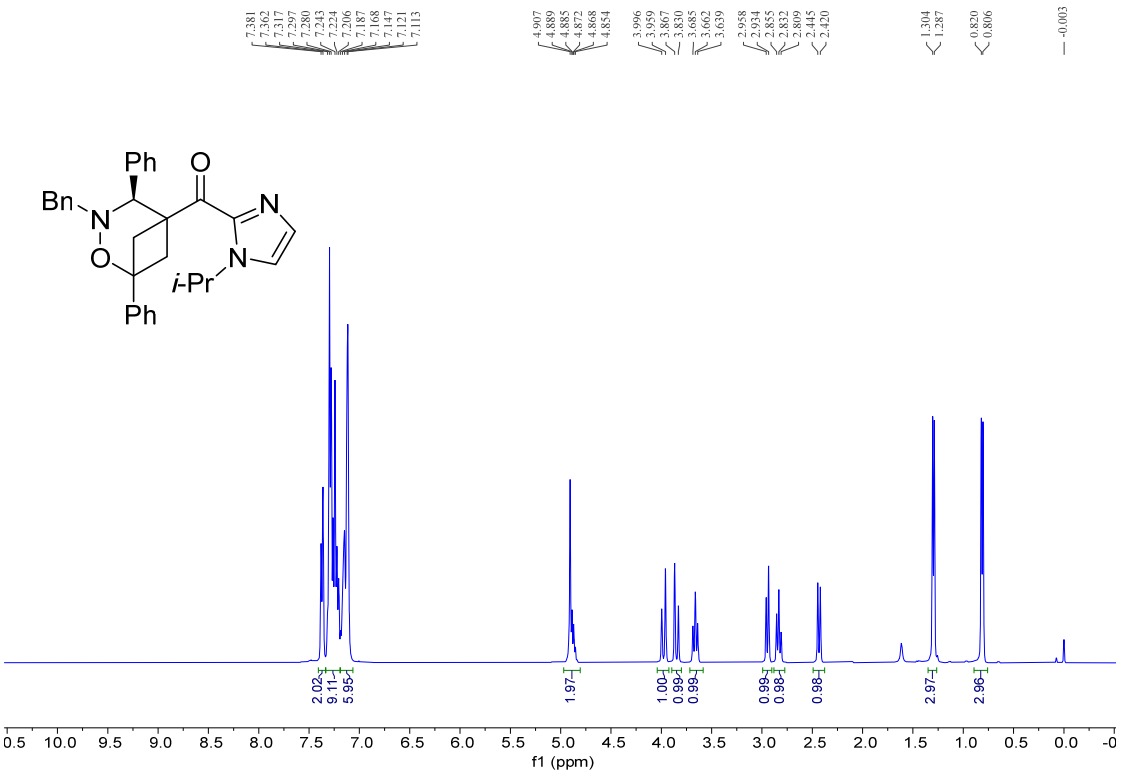

**Supplementary Figure 115.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3jb**



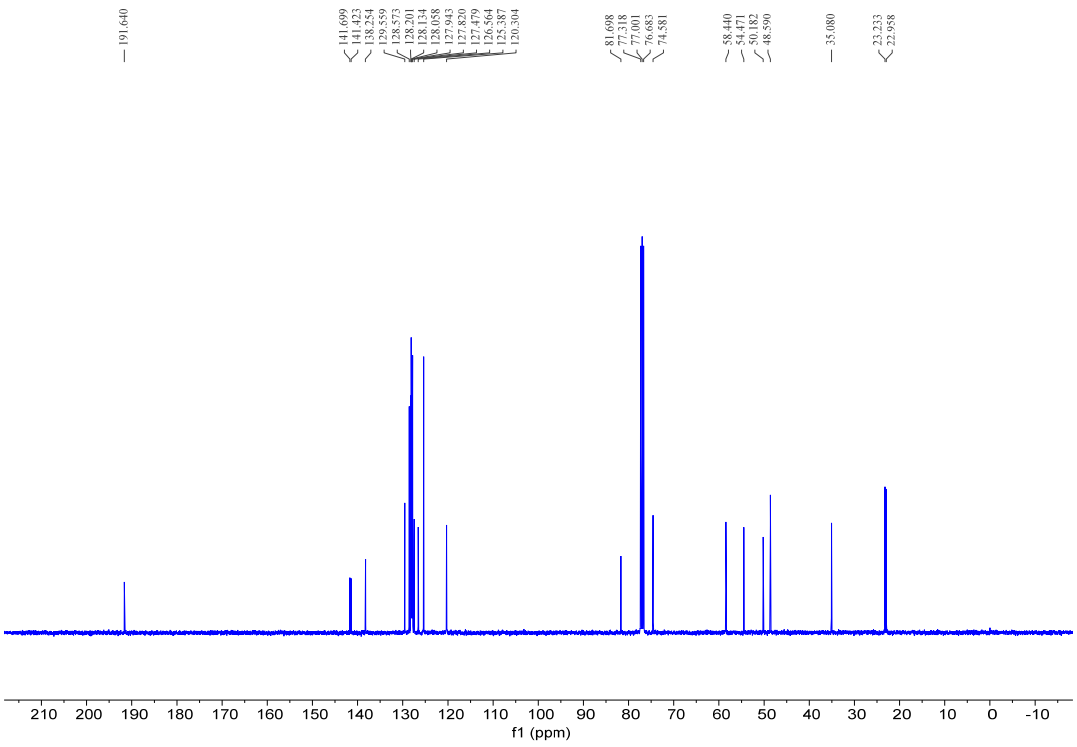

**Supplementary Figure 116.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3kb**



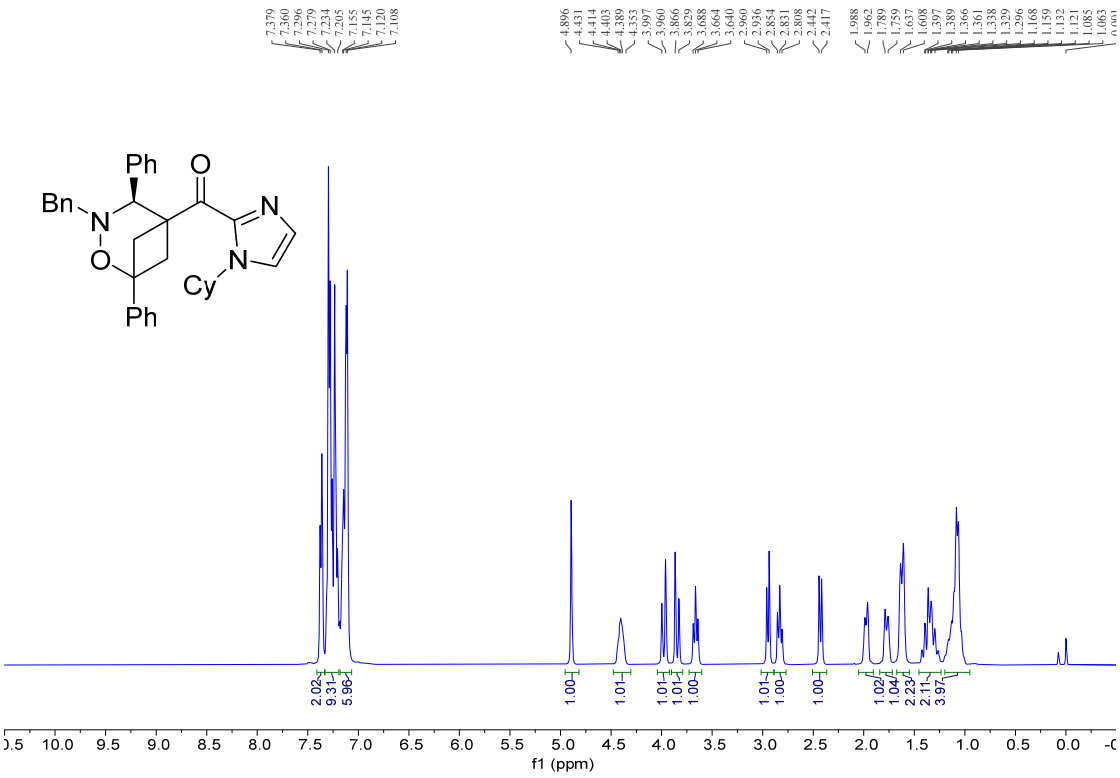

**Supplementary Figure 117.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3kb**



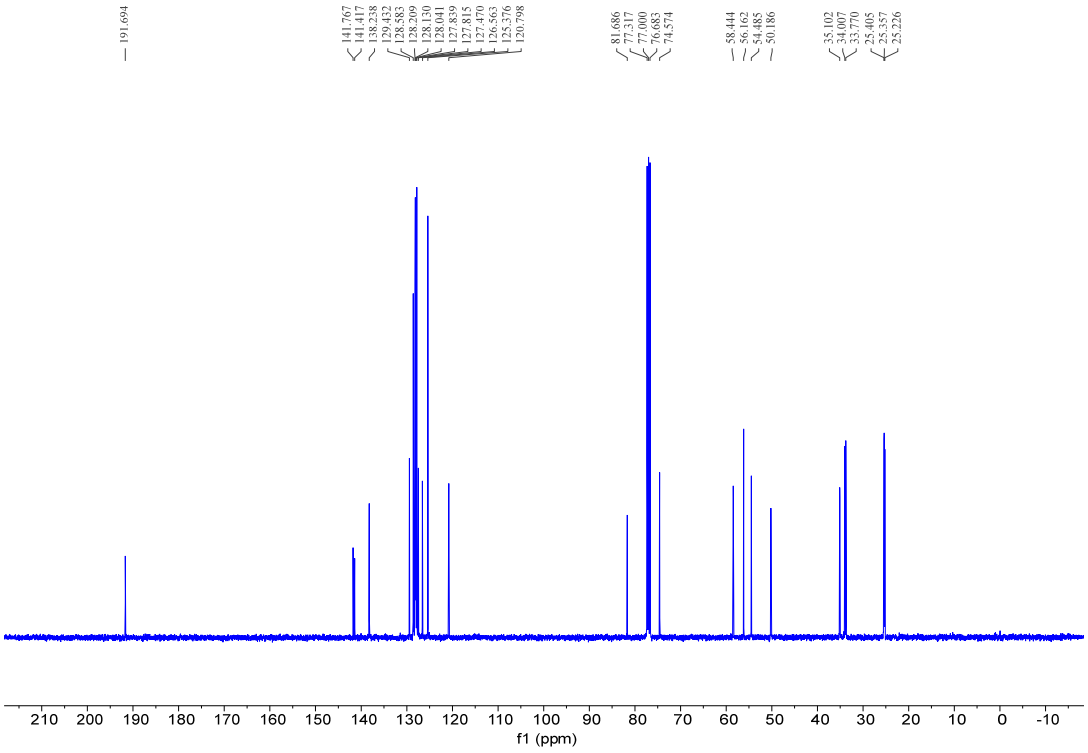

**Supplementary Figure 118.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3lb**



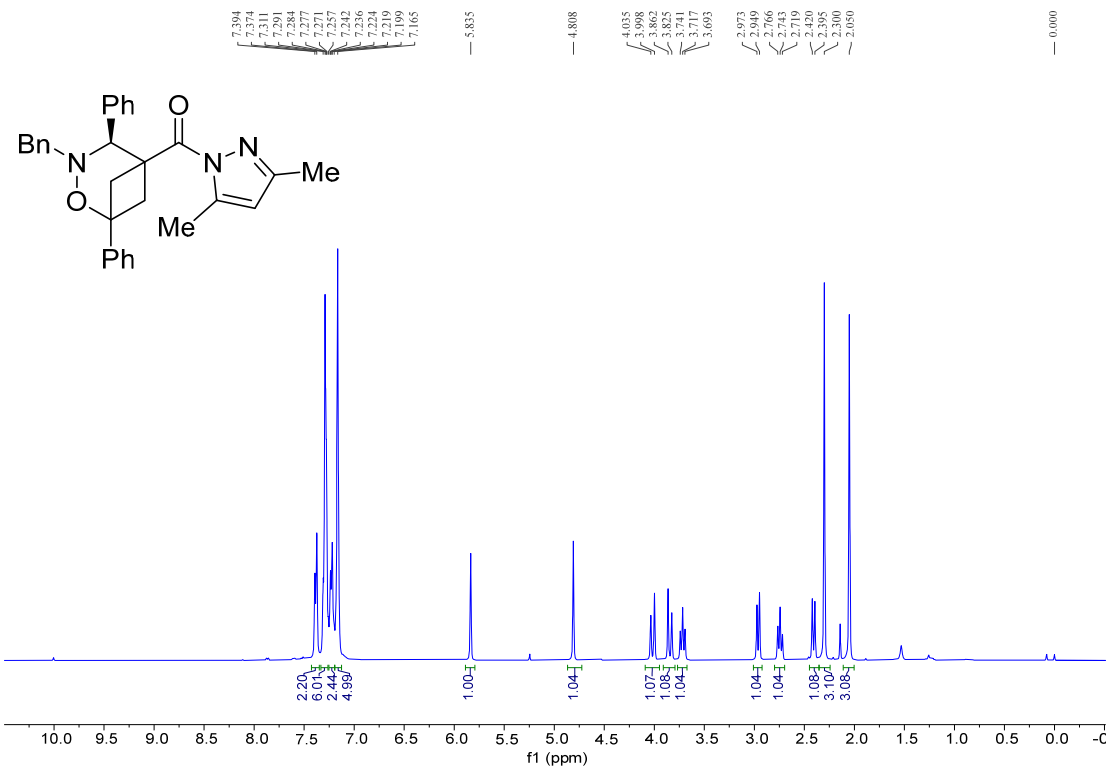

**Supplementary Figure 119.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3lb**



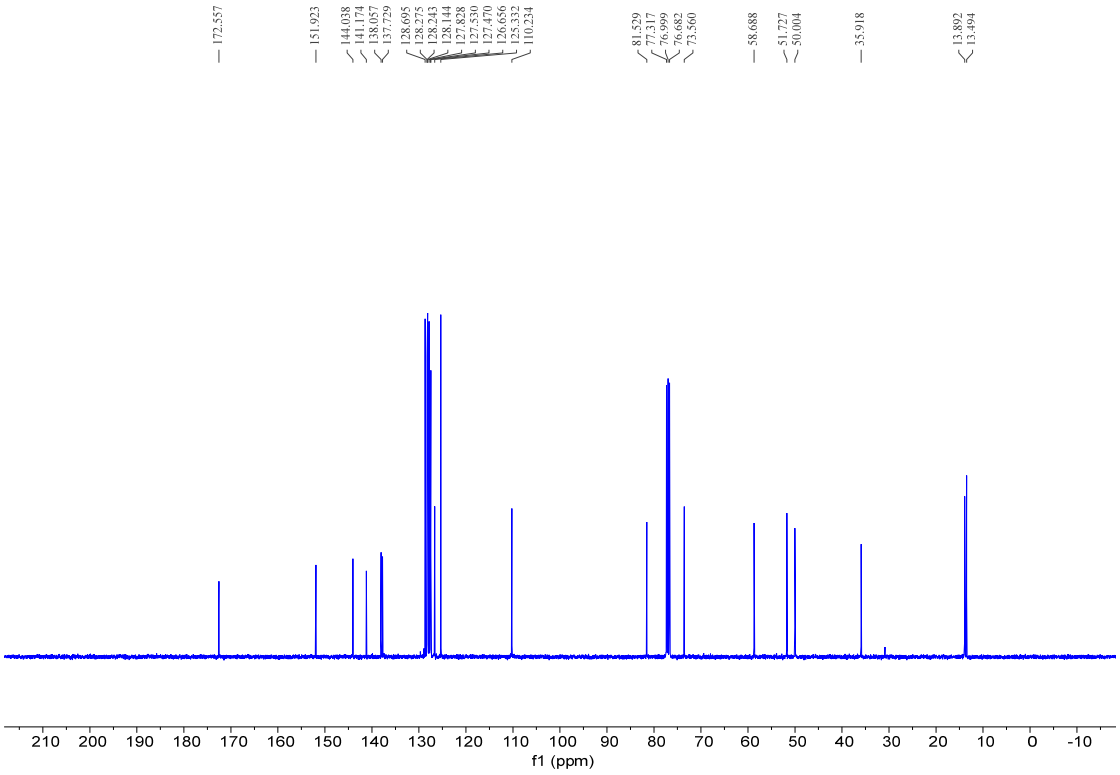

**Supplementary Figure 120.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3mb**



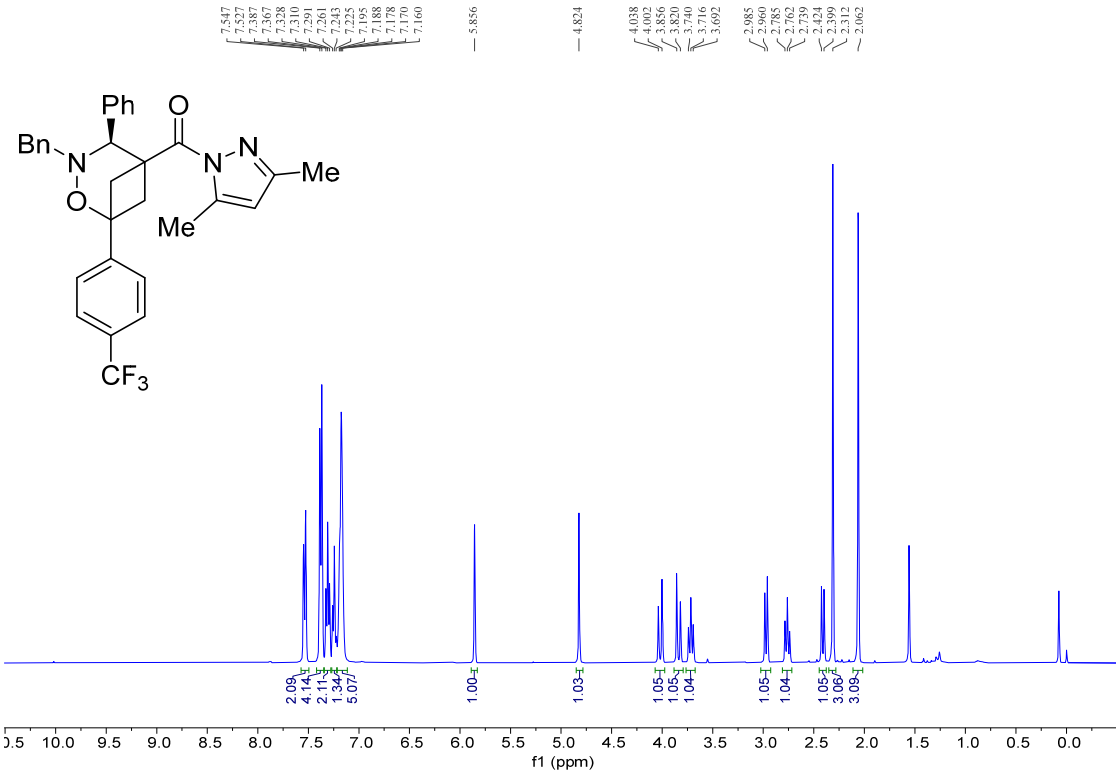

**Supplementary Figure 121.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3mb**



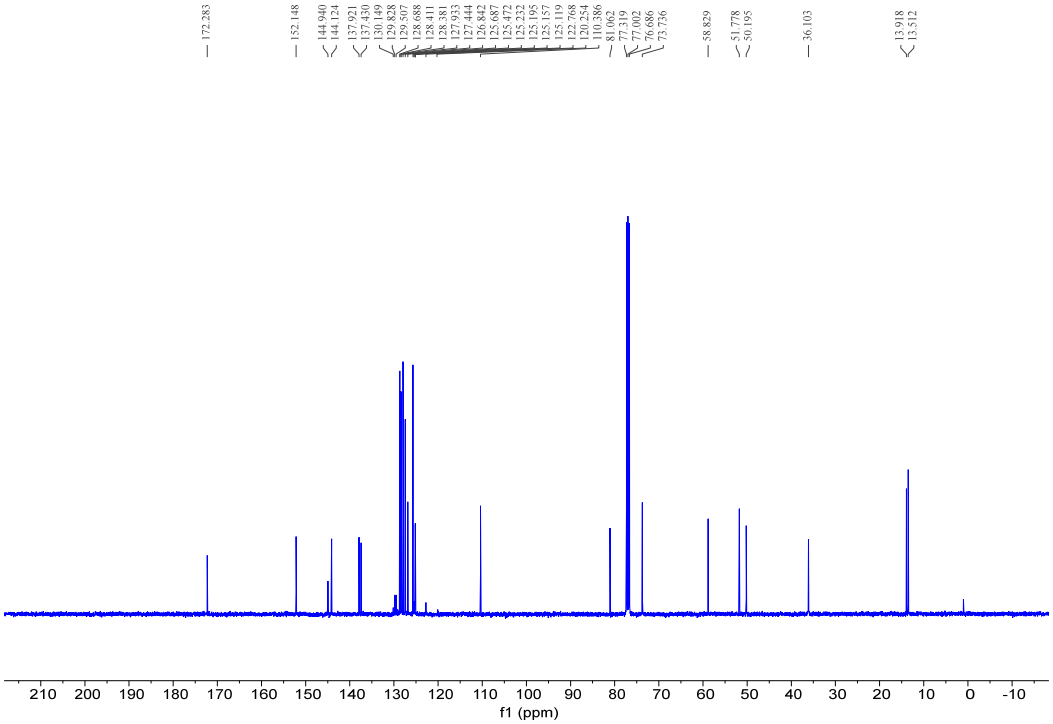

**Supplementary Figure 122.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3nb**



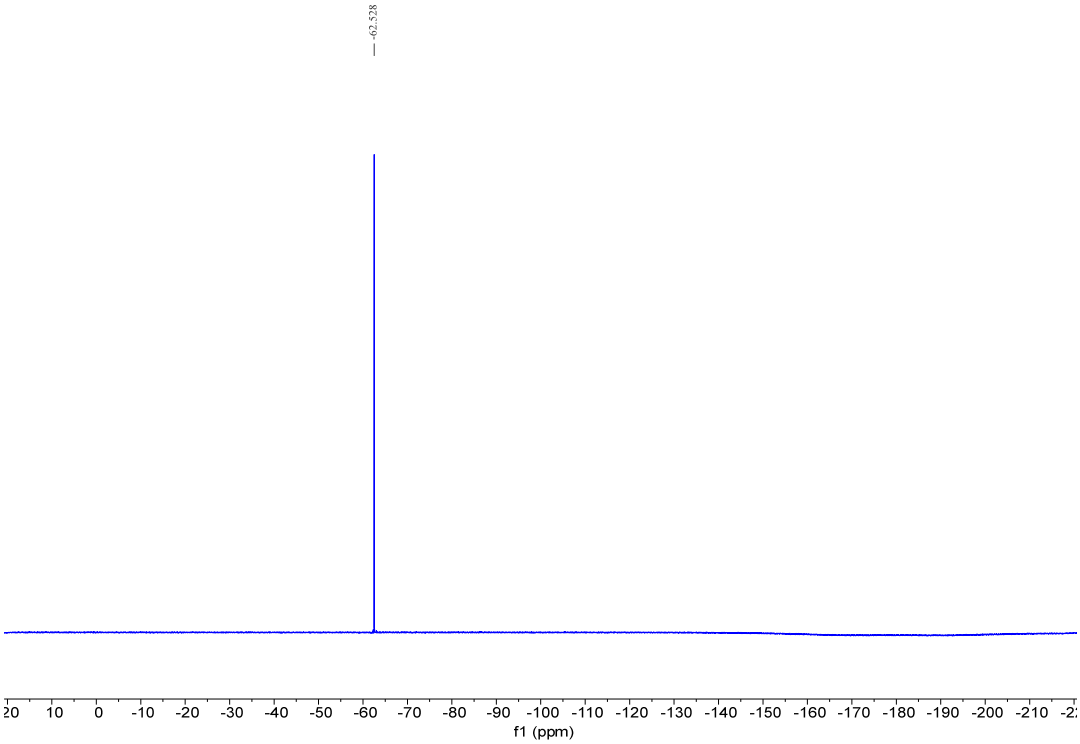

**Supplementary Figure 123.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3nb**



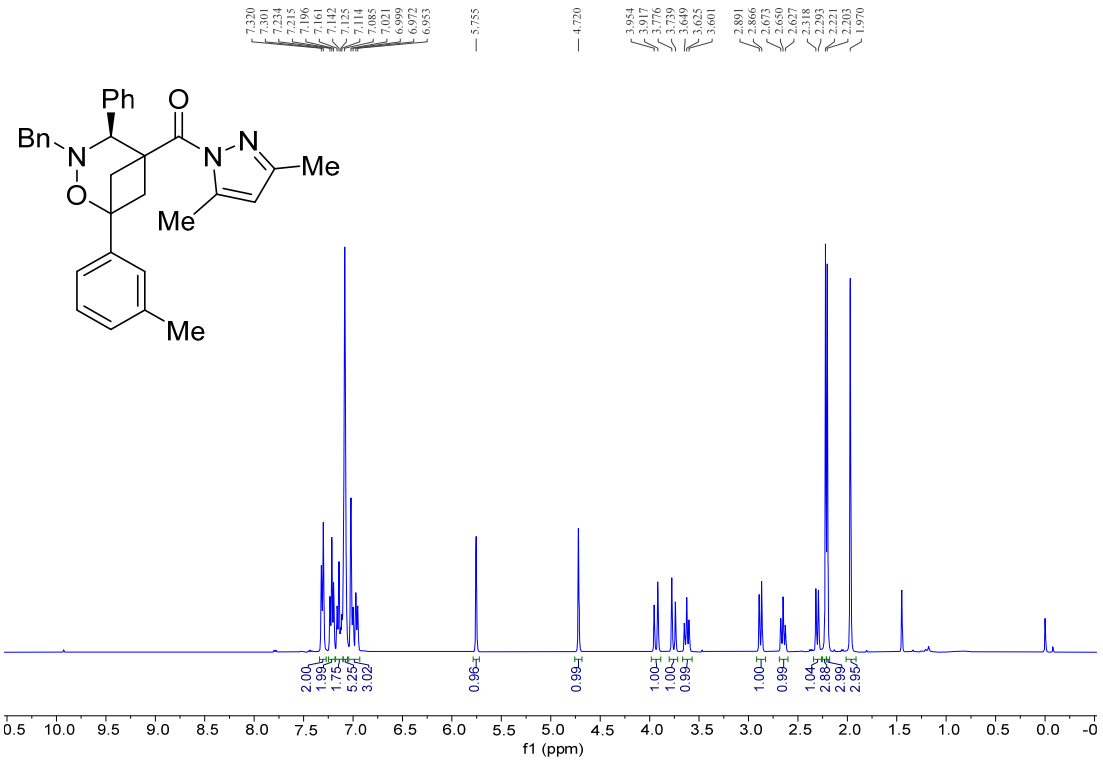

**Supplementary Figure 124.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3ob**



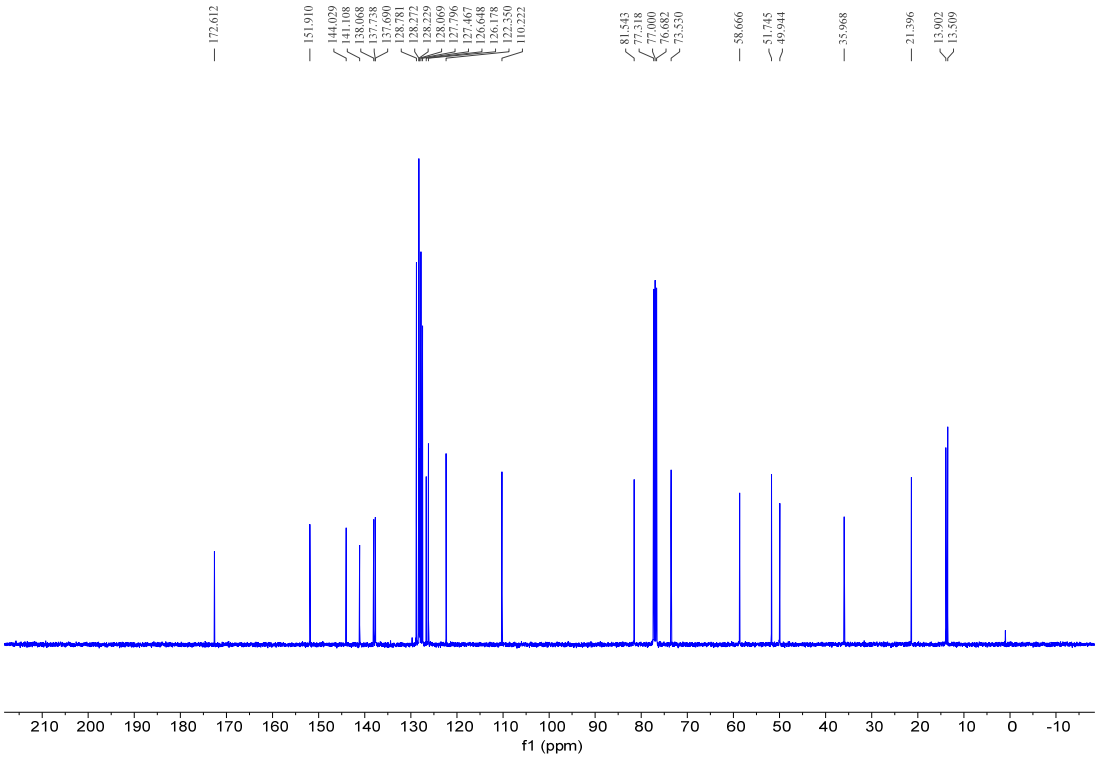

**Supplementary Figure 125.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3ob**



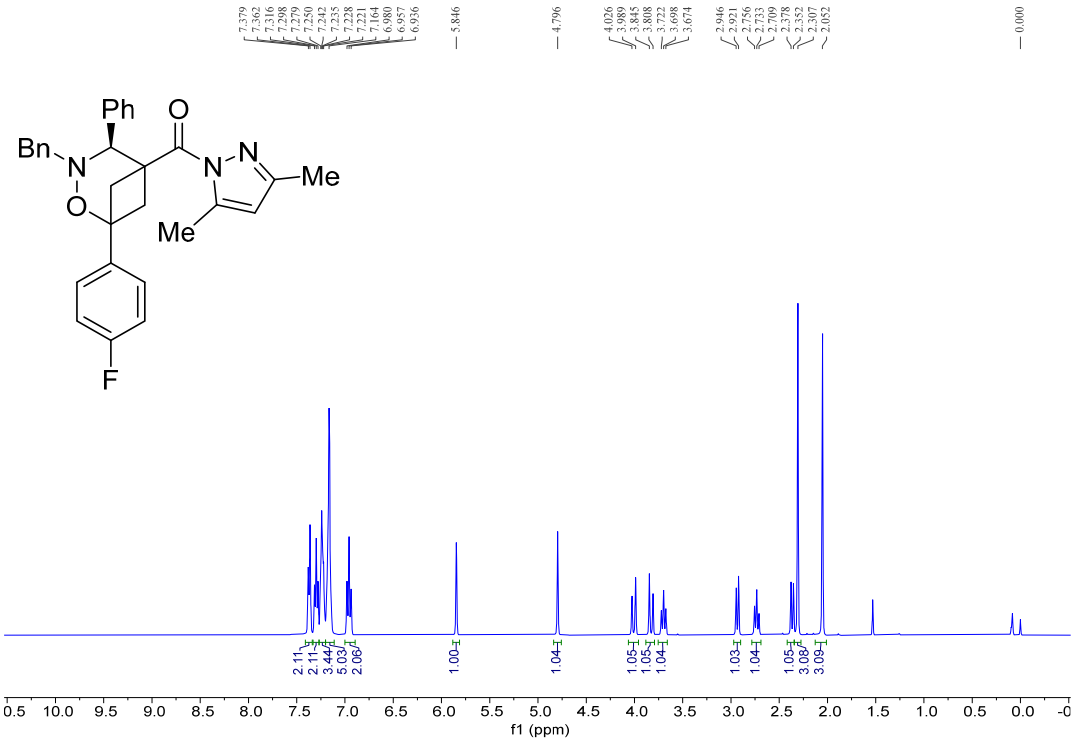

**Supplementary Figure 126.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **3ob**



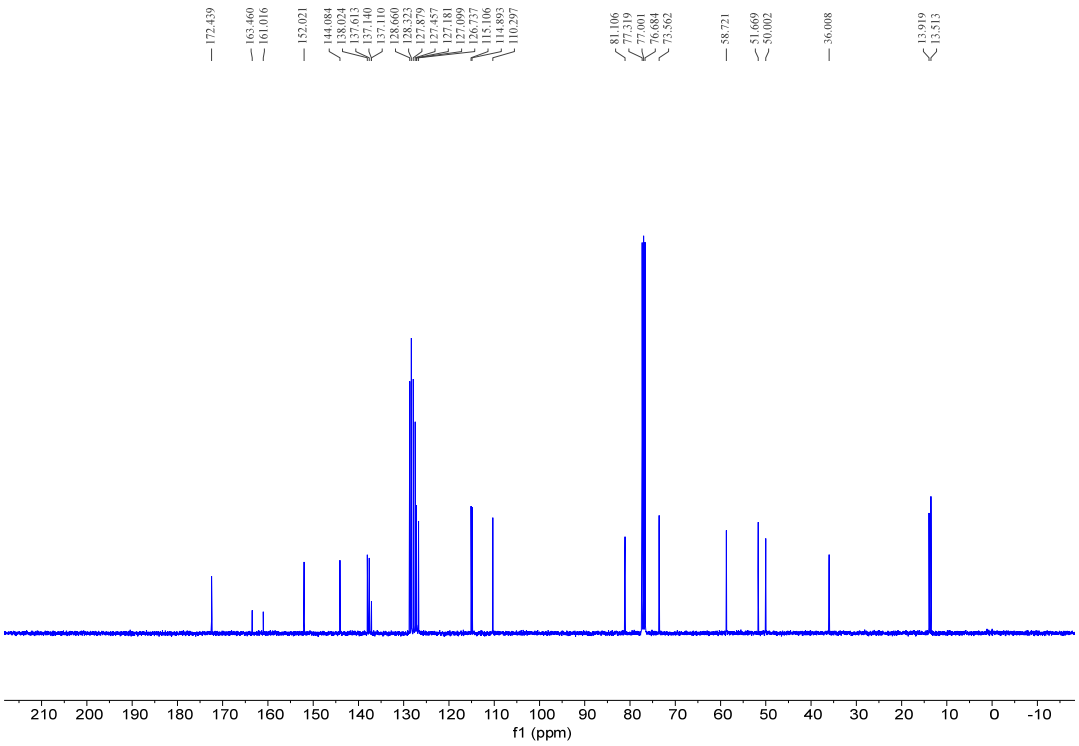

**Supplementary Figure 127.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3pb**



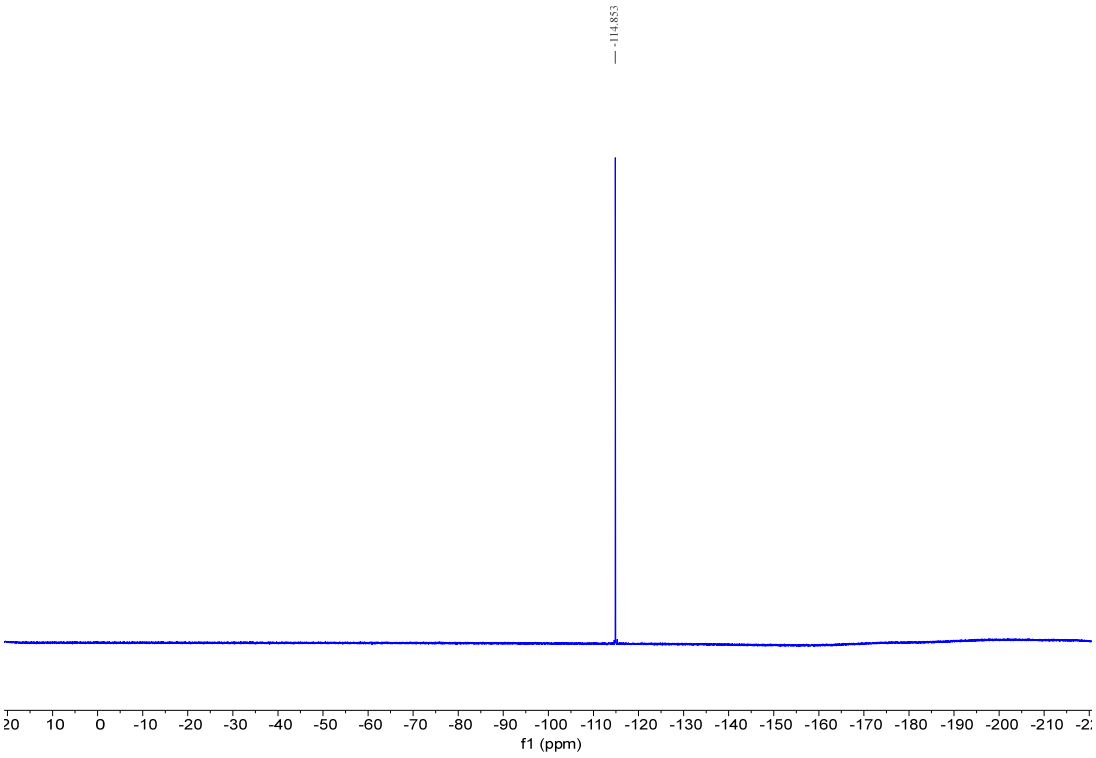

**Supplementary Figure 128.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3pb**



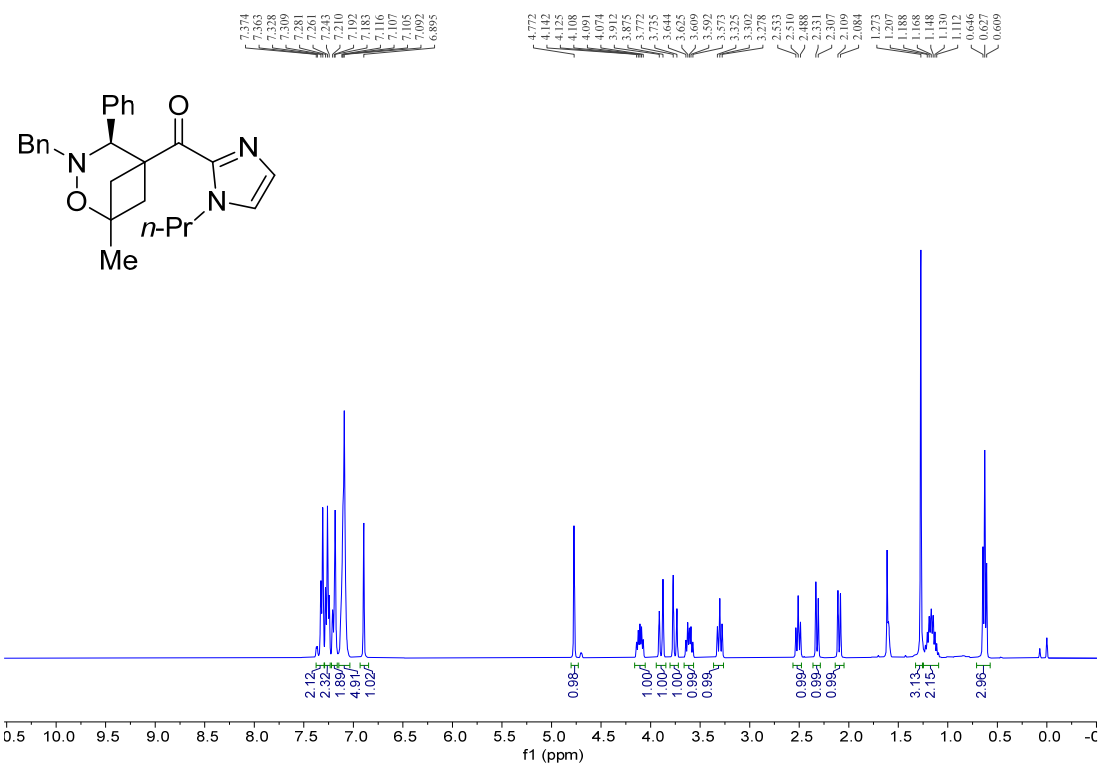

**Supplementary Figure 129.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **3qb**



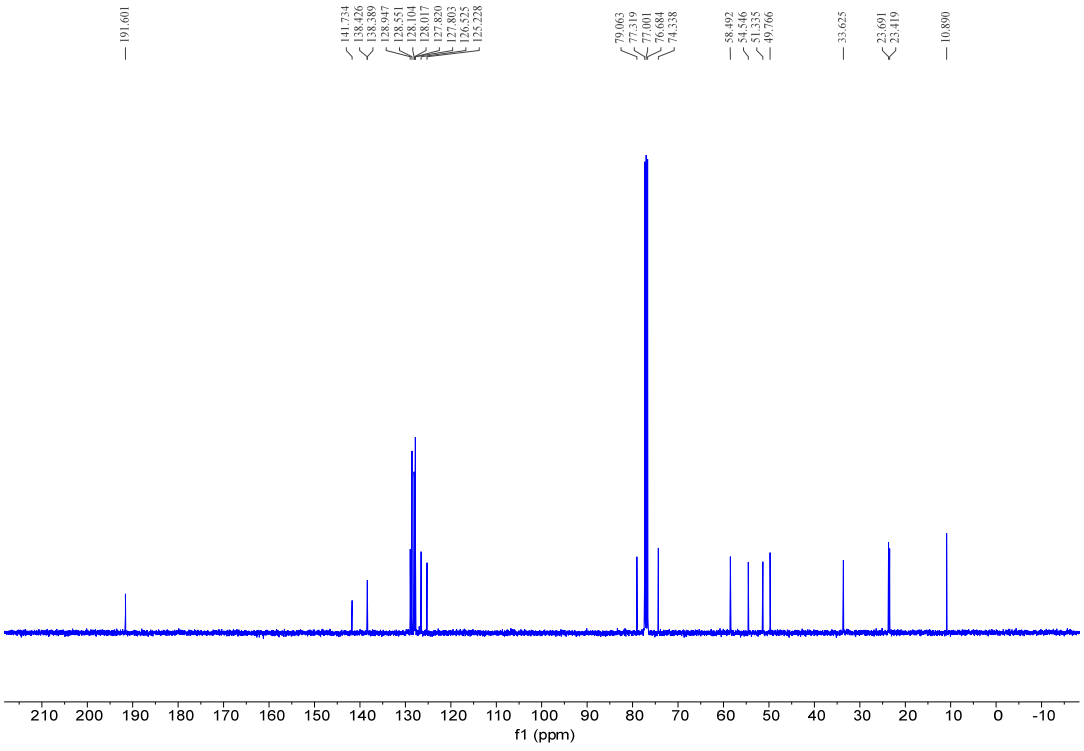

**Supplementary Figure 130.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **3qb**



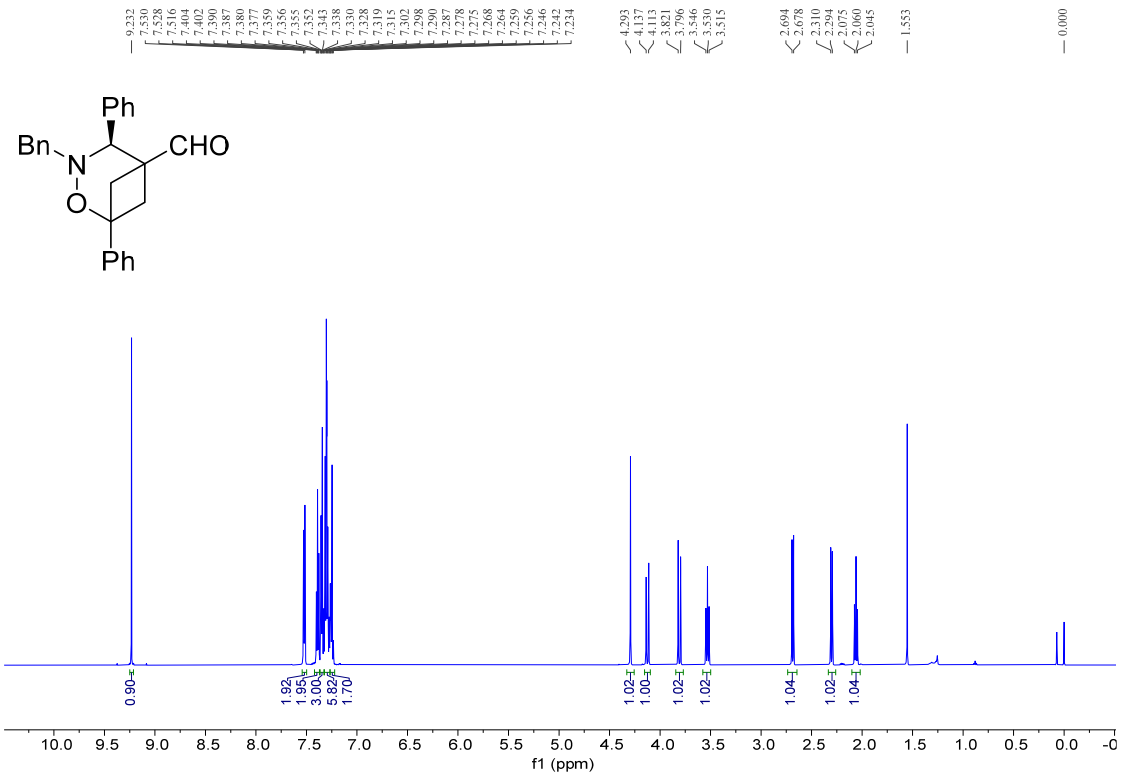

**Supplementary Figure 131.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **3qb**



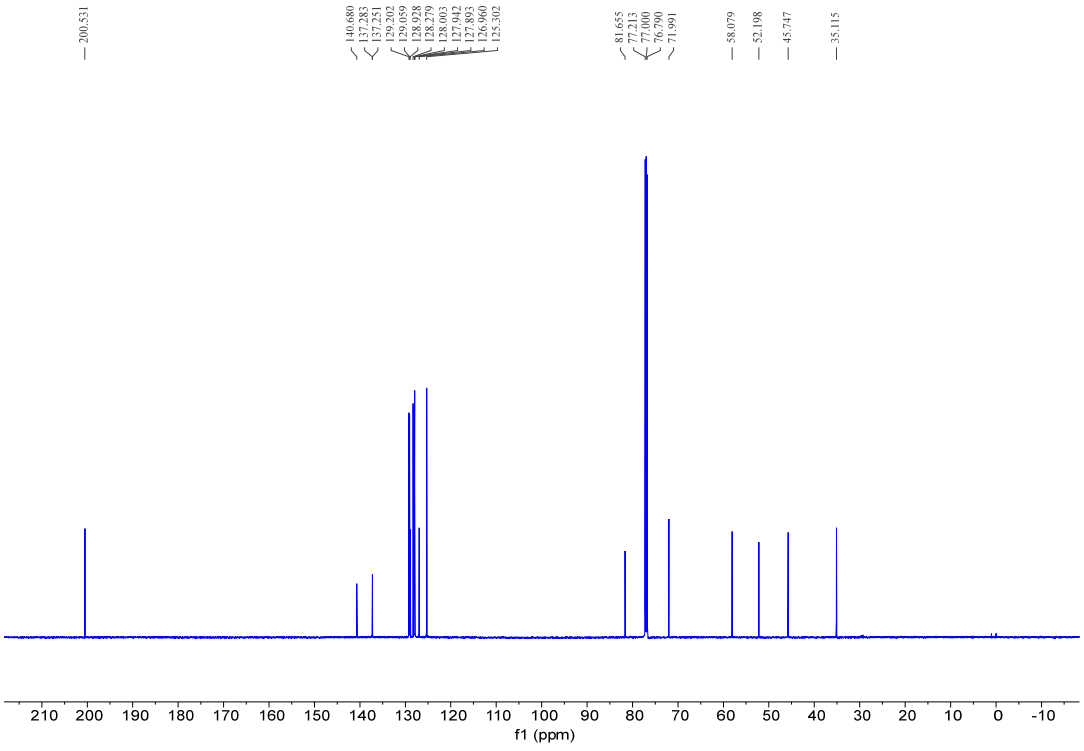

**Supplementary Figure 132.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **3rb**



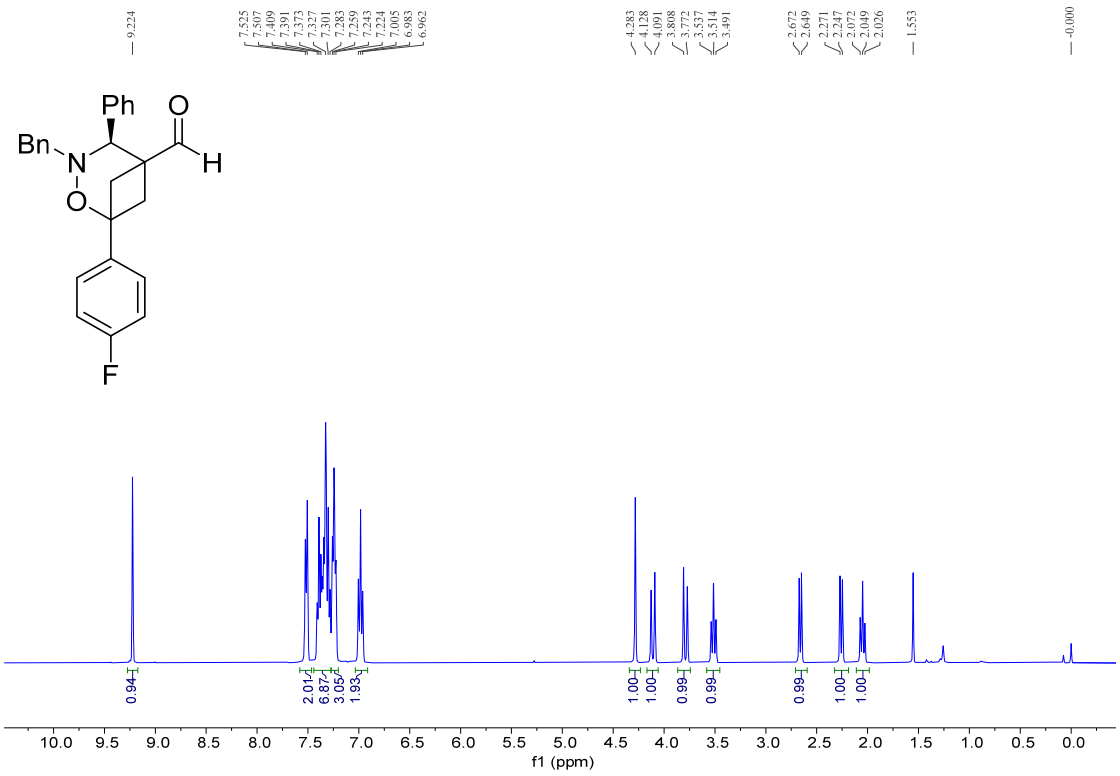

**Supplementary Figure 133.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **3rb**



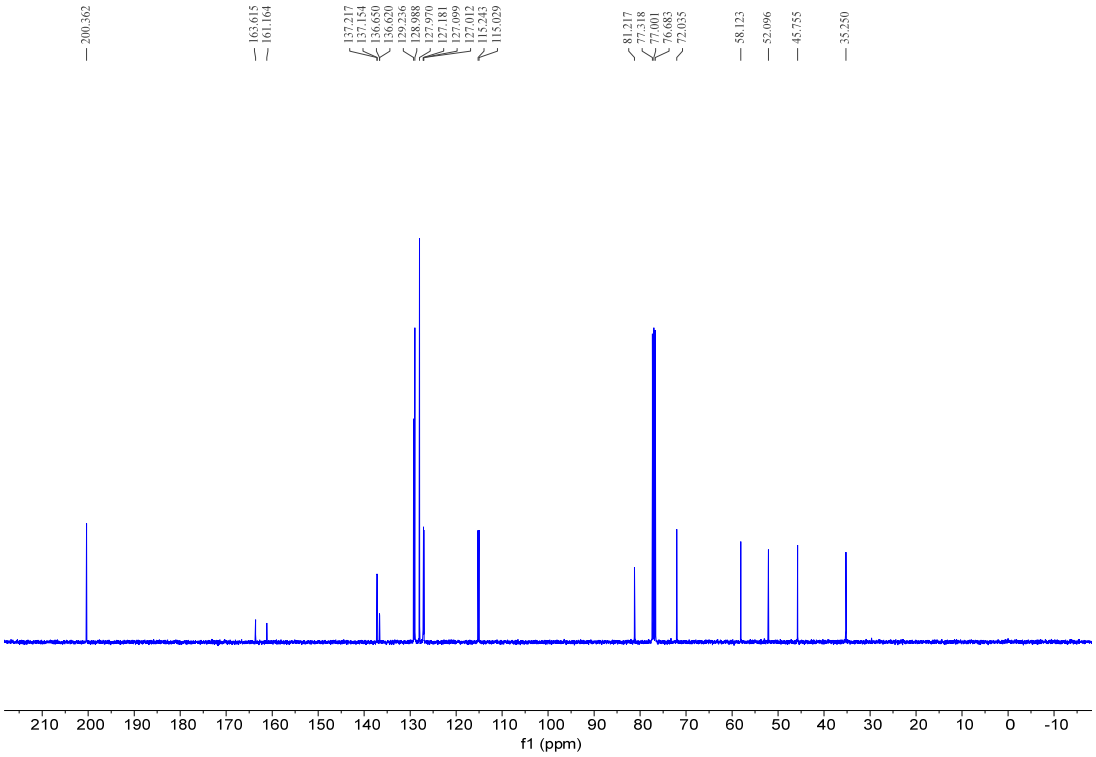

**Supplementary Figure 134.** $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **4nb**



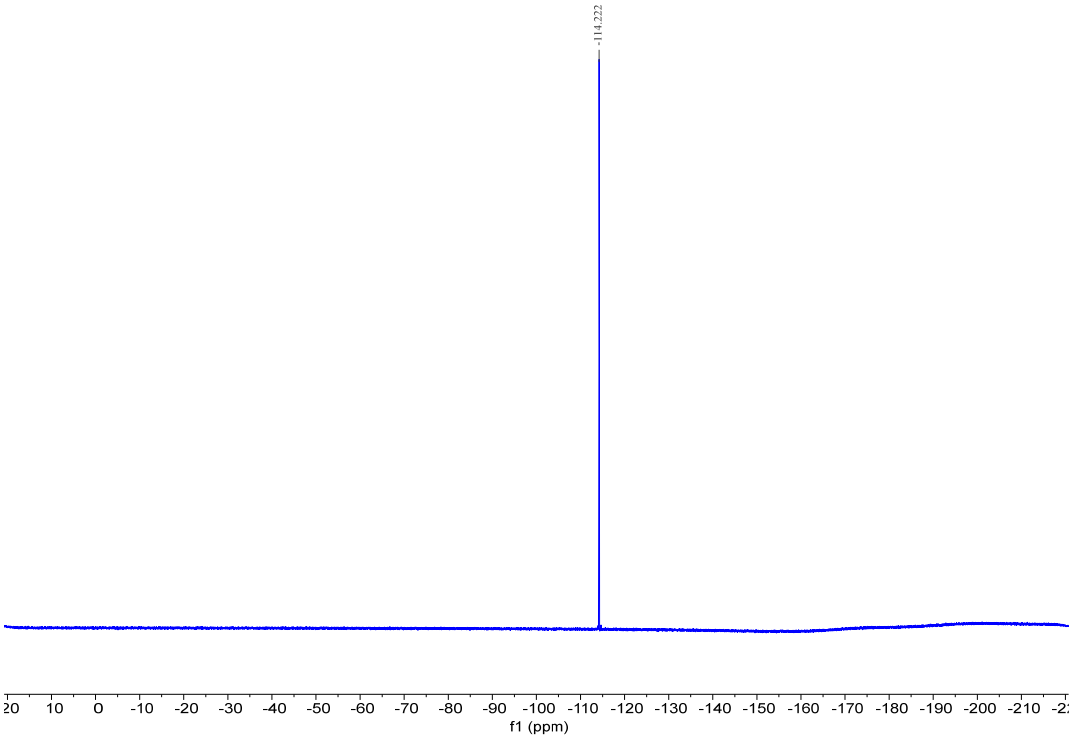

**Supplementary Figure 135.** $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **4nb**



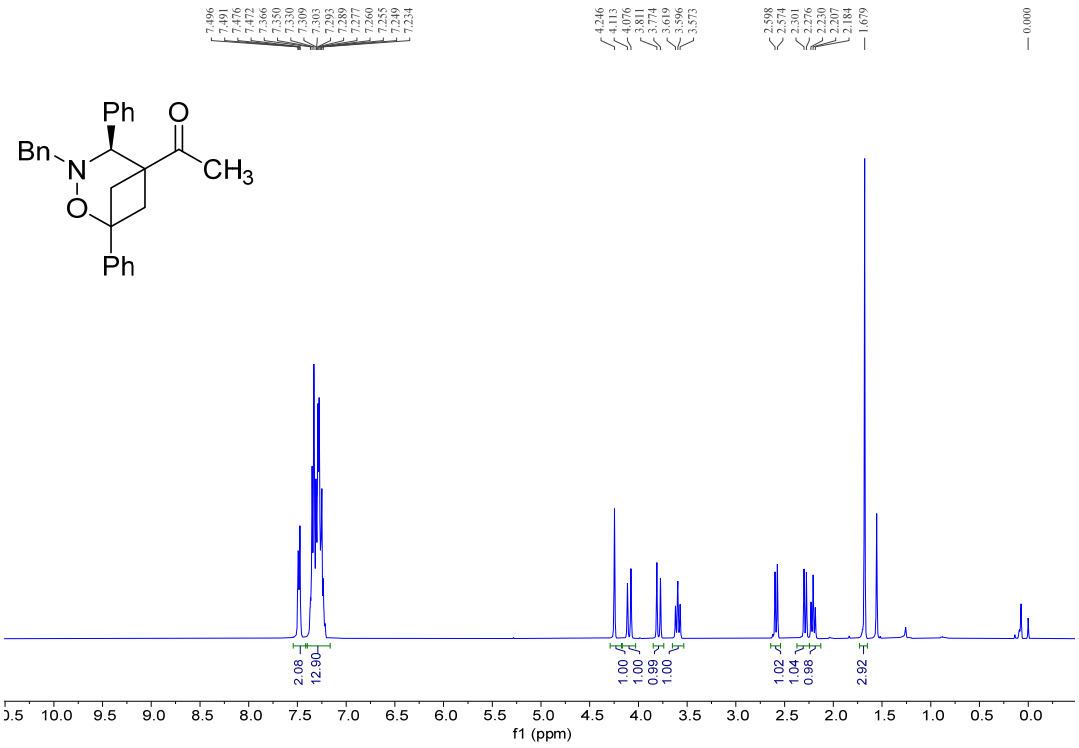

**Supplementary Figure 136.** $^{1}$H NMR (400 MHz, $CDCl_3$) spectrum of compound **4qb**



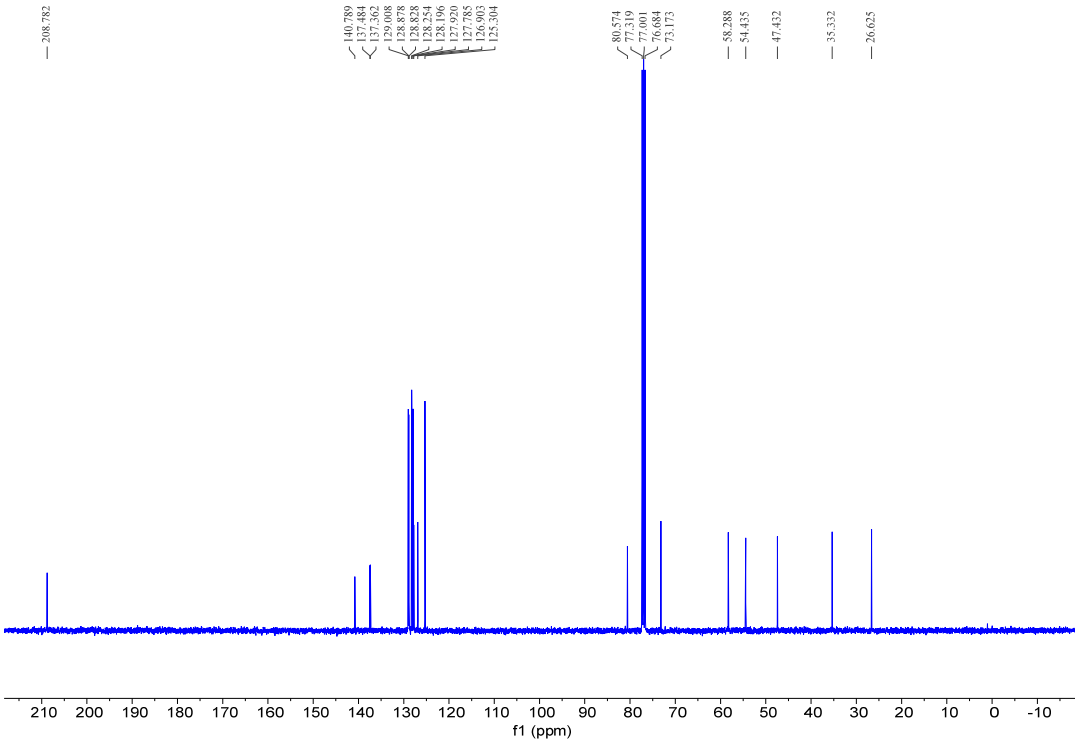

**Supplementary Figure 137.** $^{13}$C NMR (100 MHz, $CDCl_3$) spectrum of compound **4qb**



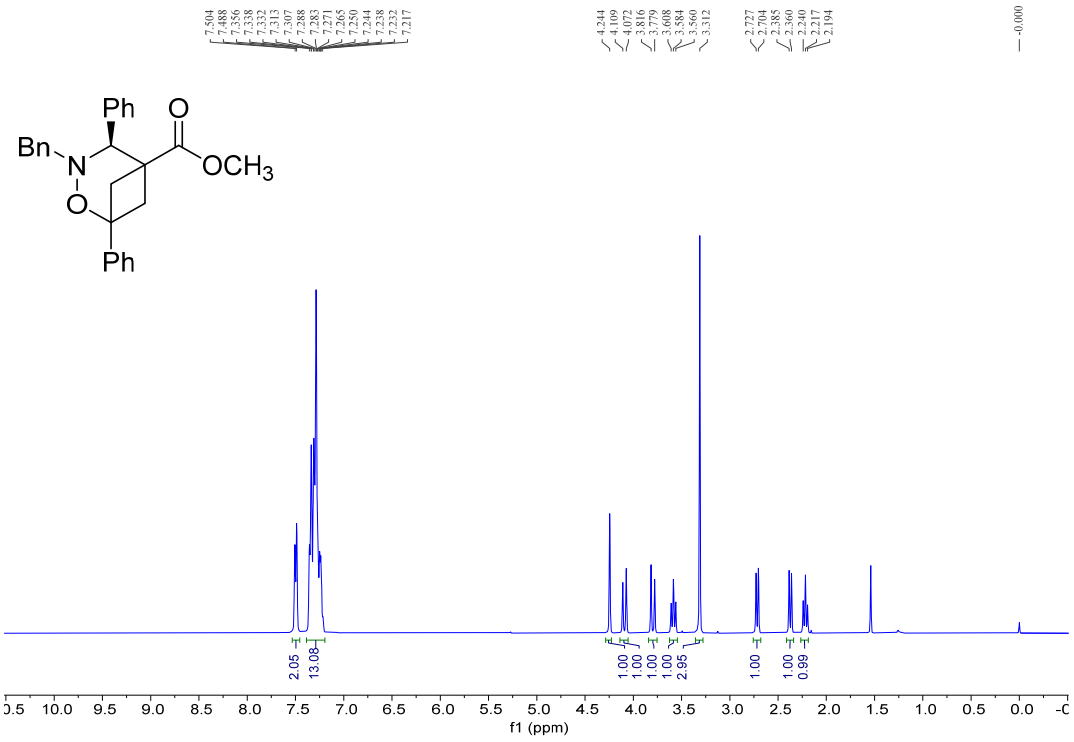

**Supplementary Figure 138.** $^{19}F$ NMR (376 MHz, $CDCl_3$) spectrum of compound **4qb**



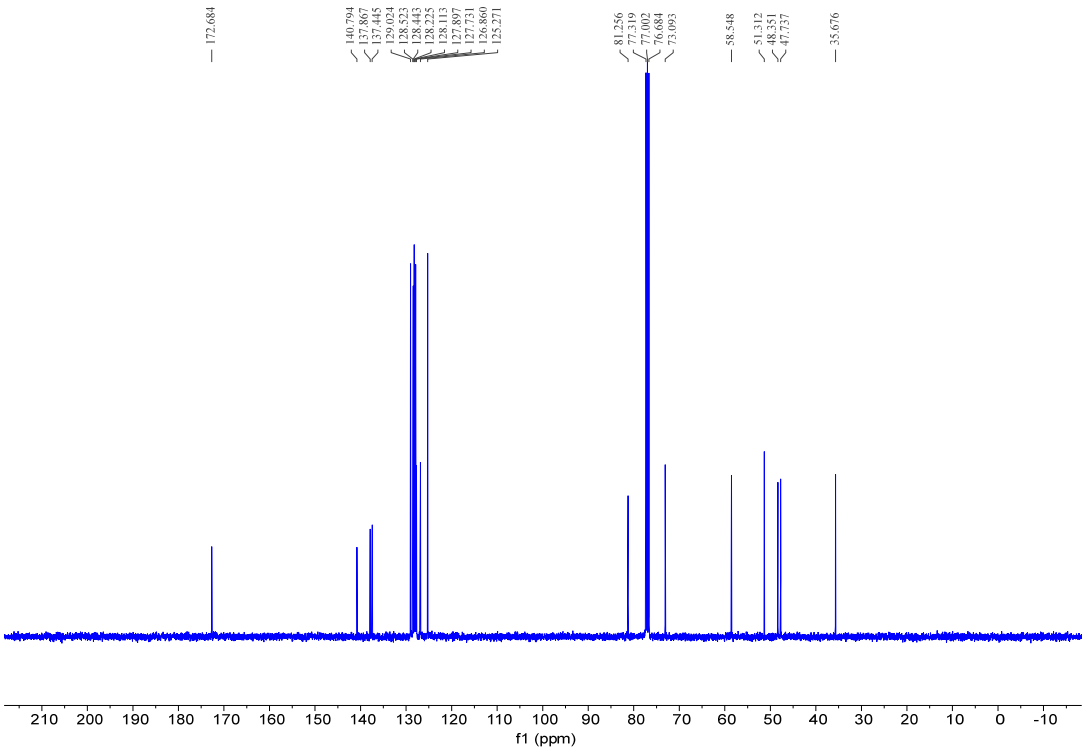

**Supplementary Figure 139.** $^1H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **5**



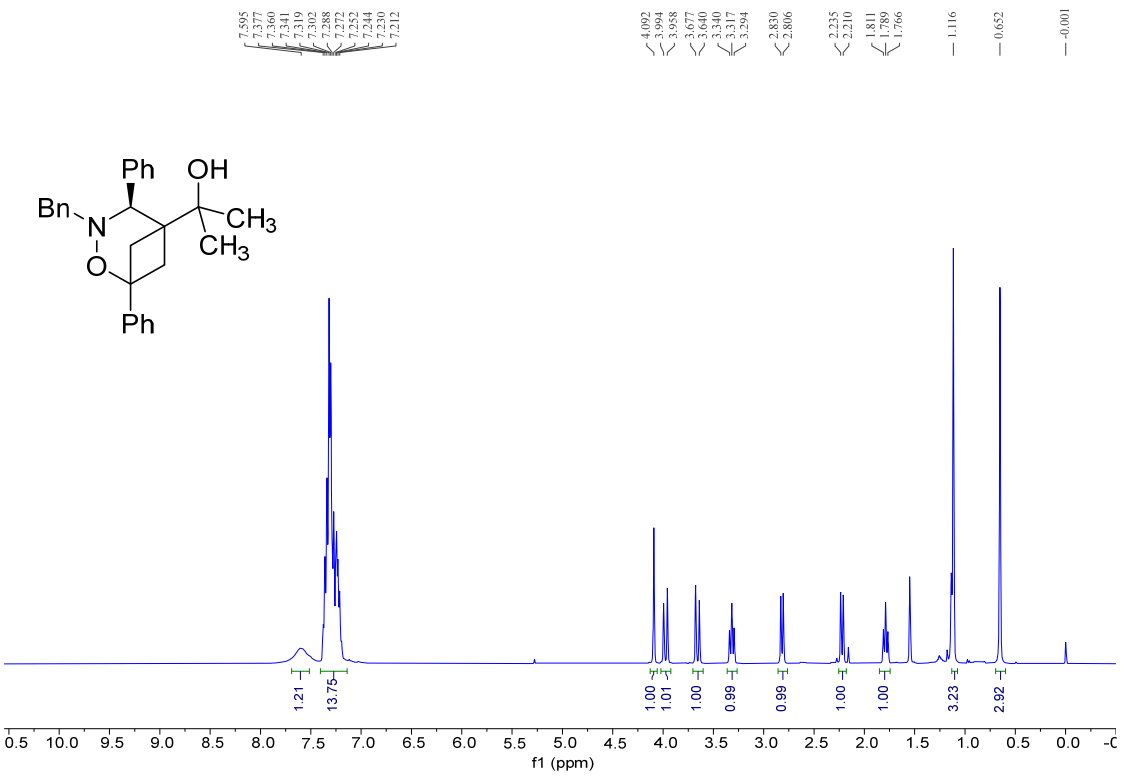

**Supplementary Figure 140.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **5**



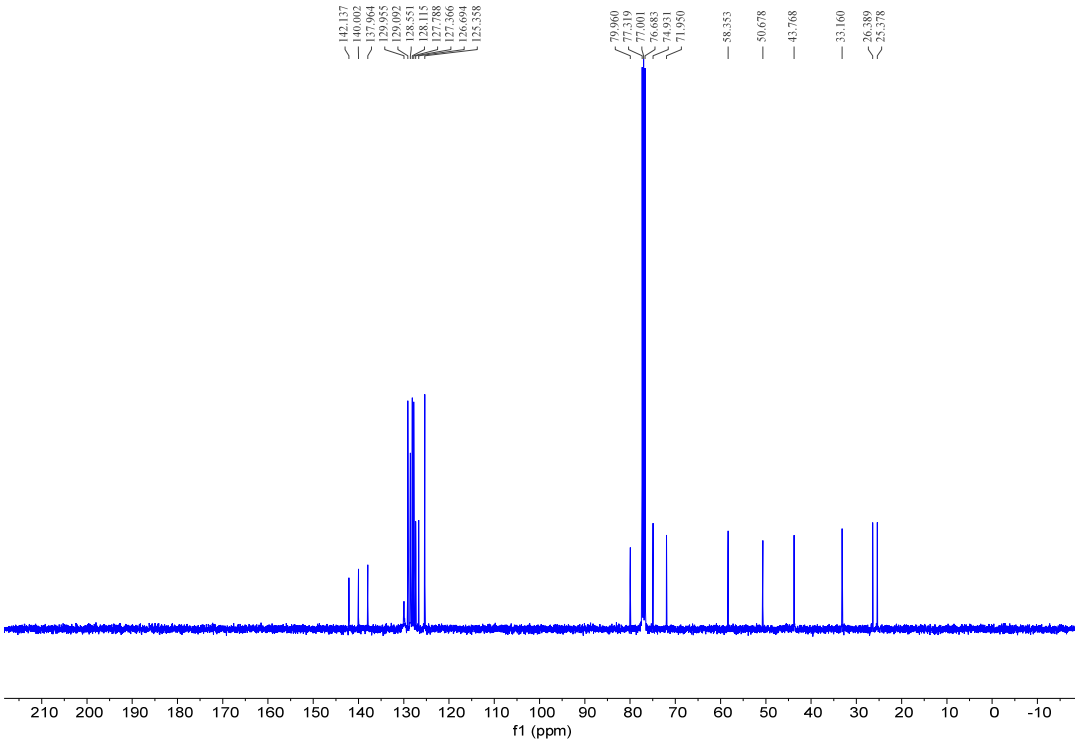

**Supplementary Figure 141.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **6**



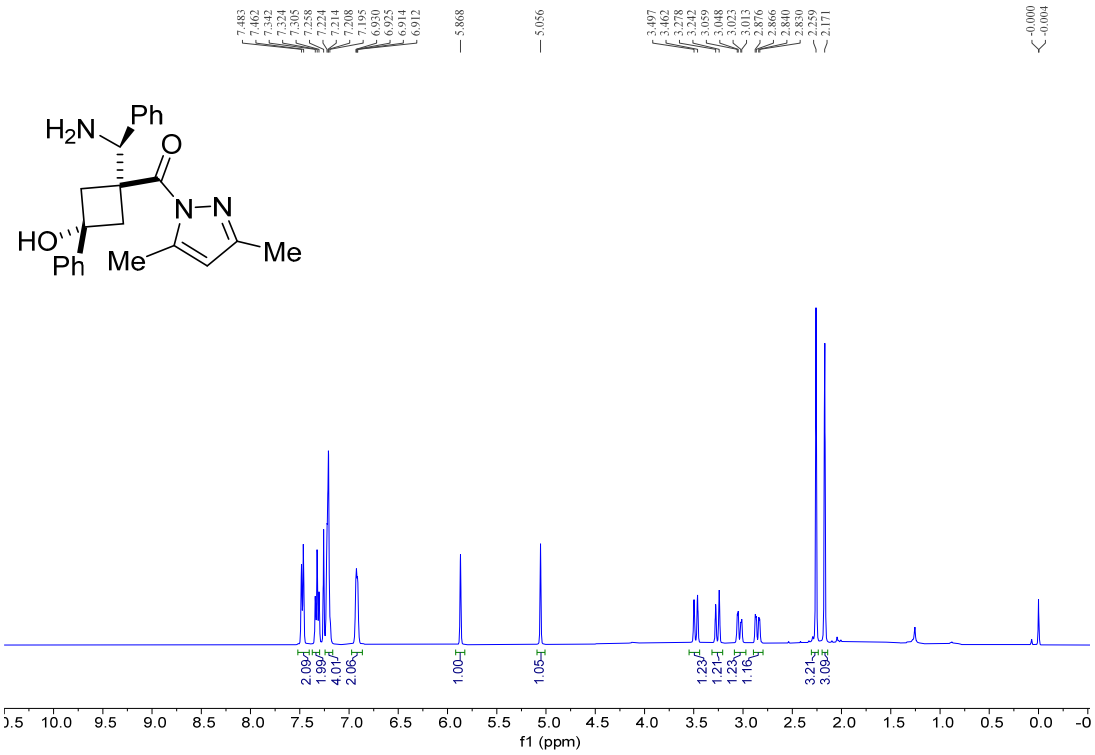

**Supplementary Figure 142.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **6**



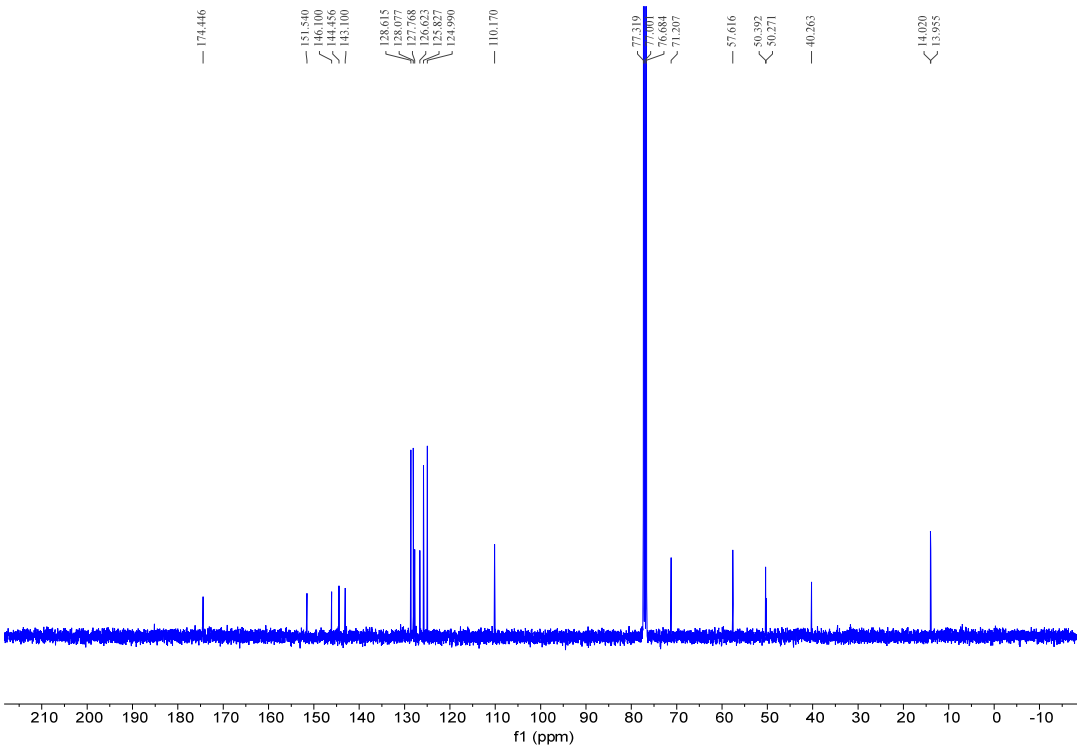

**Supplementary Figure 143.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **7**



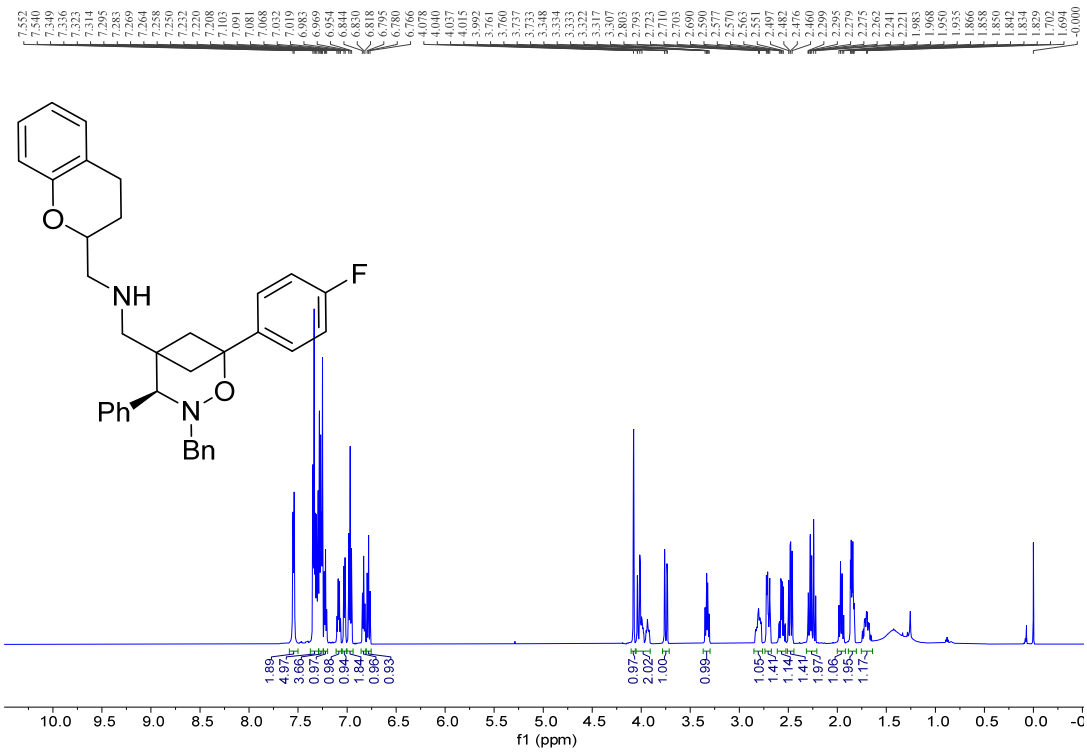

**Supplementary Figure 144.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **7**



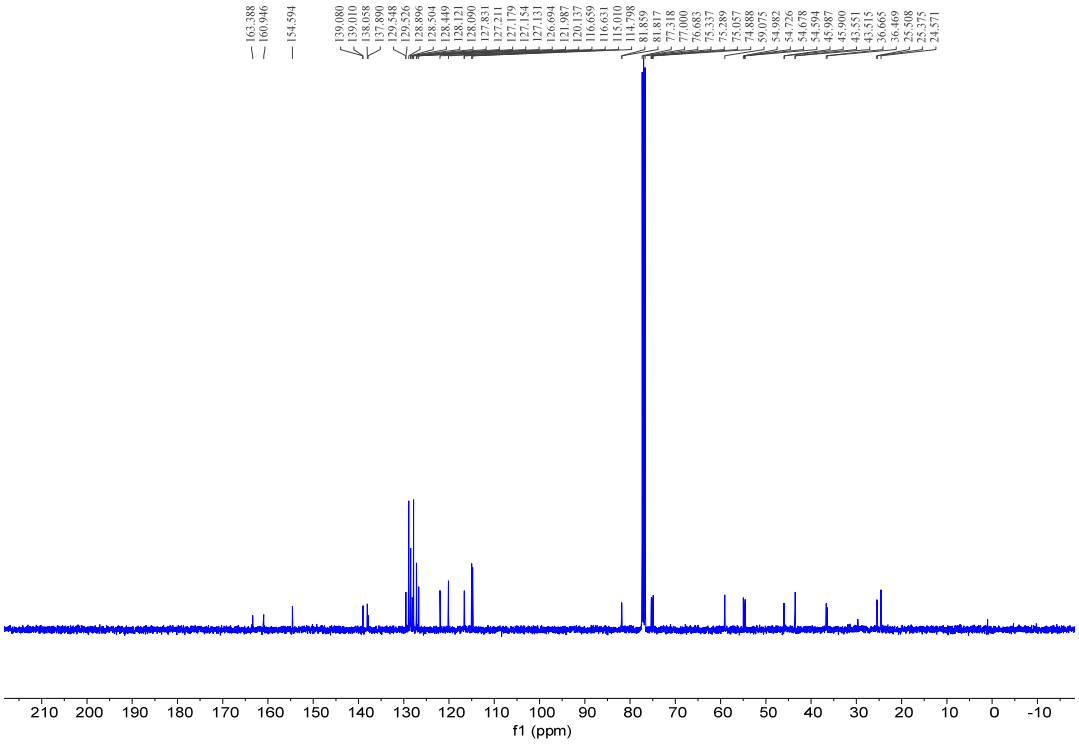

**Supplementary Figure 145.** $^{1}H$ NMR (400 MHz, $CDCl_3$) spectrum of compound **8**



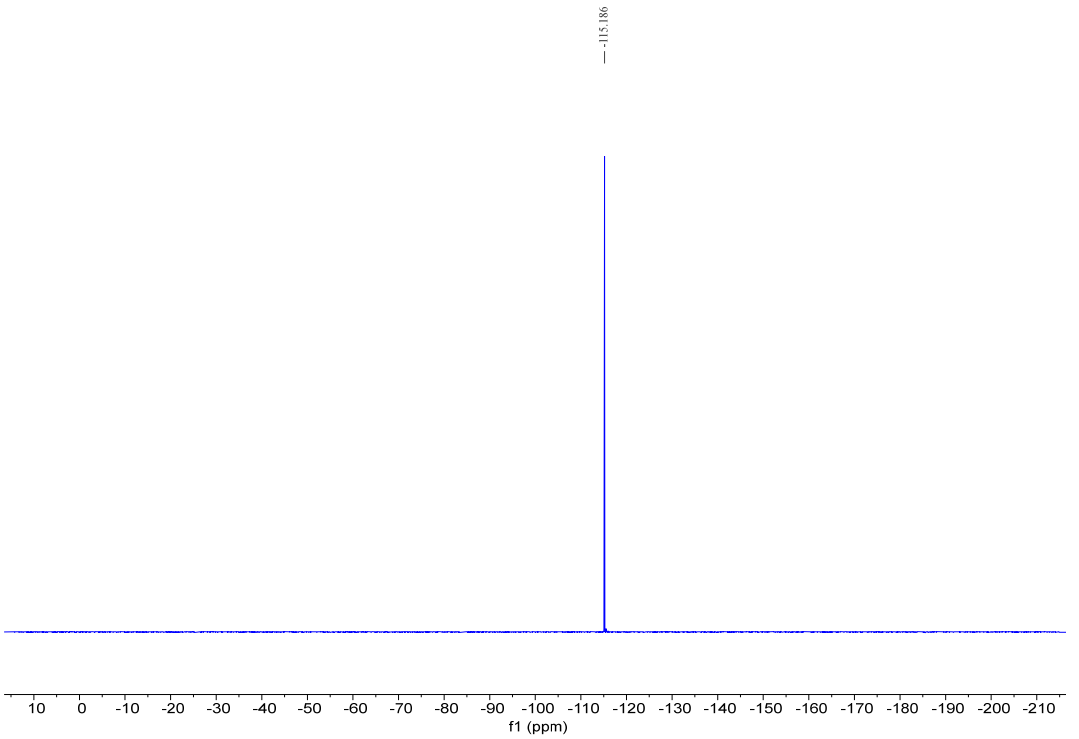

**Supplementary Figure 146.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **8**



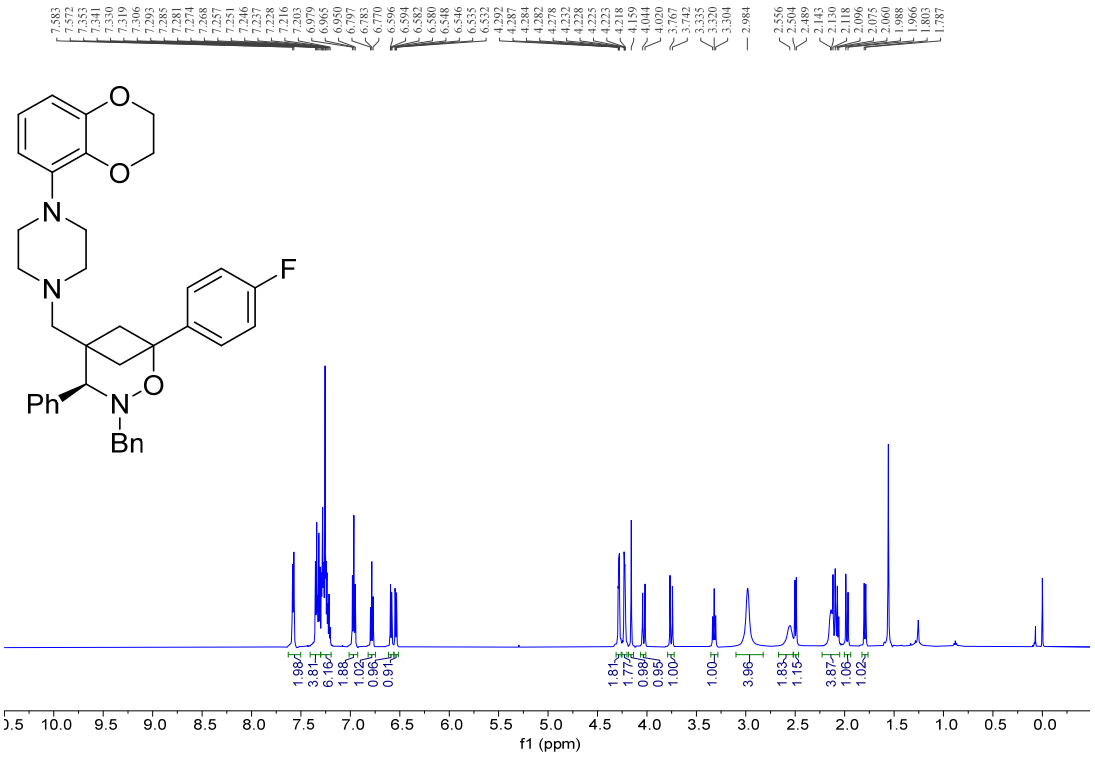

**Supplementary Figure 147.** $^{1}H$ NMR (600 MHz, $CDCl_3$) spectrum of compound **9**



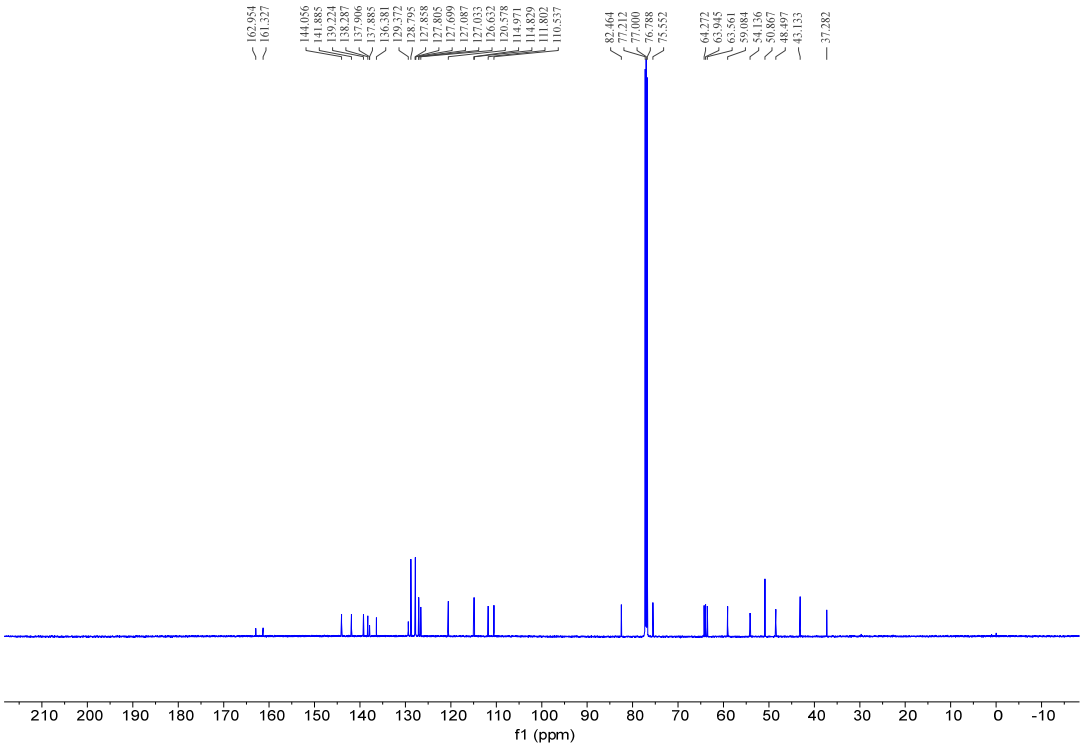

**Supplementary Figure 148.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **9**



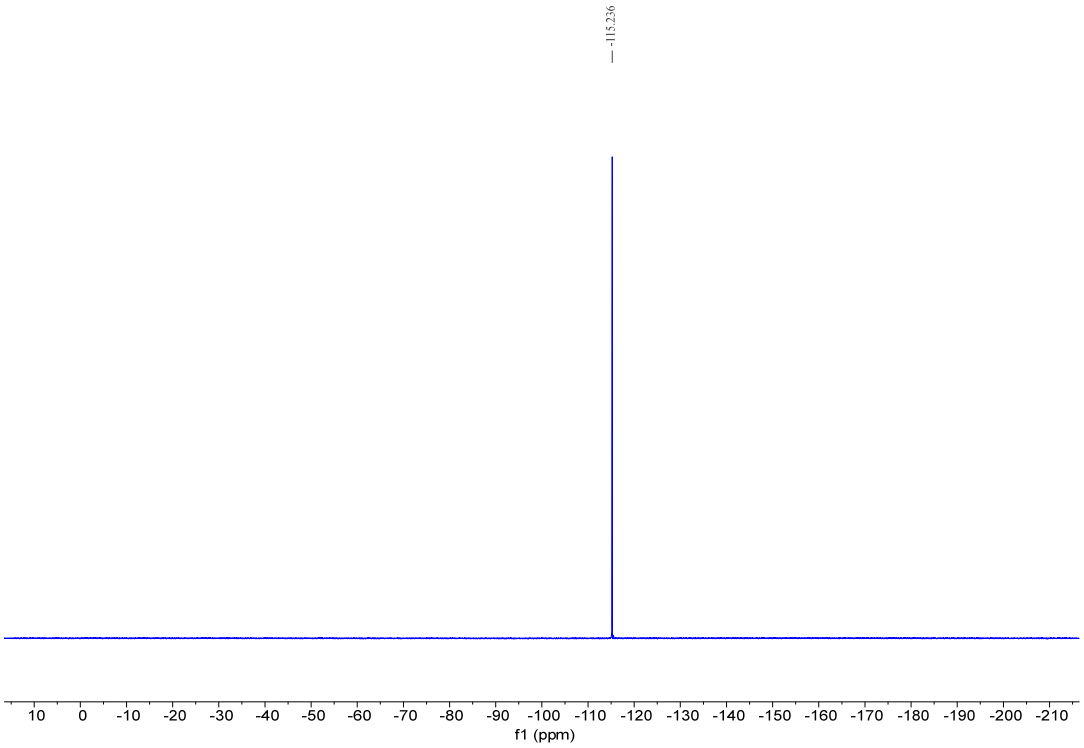

**Supplementary Figure 149.** $^{19}F$ NMR (565 MHz, $CDCl_3$) spectrum of compound **9**



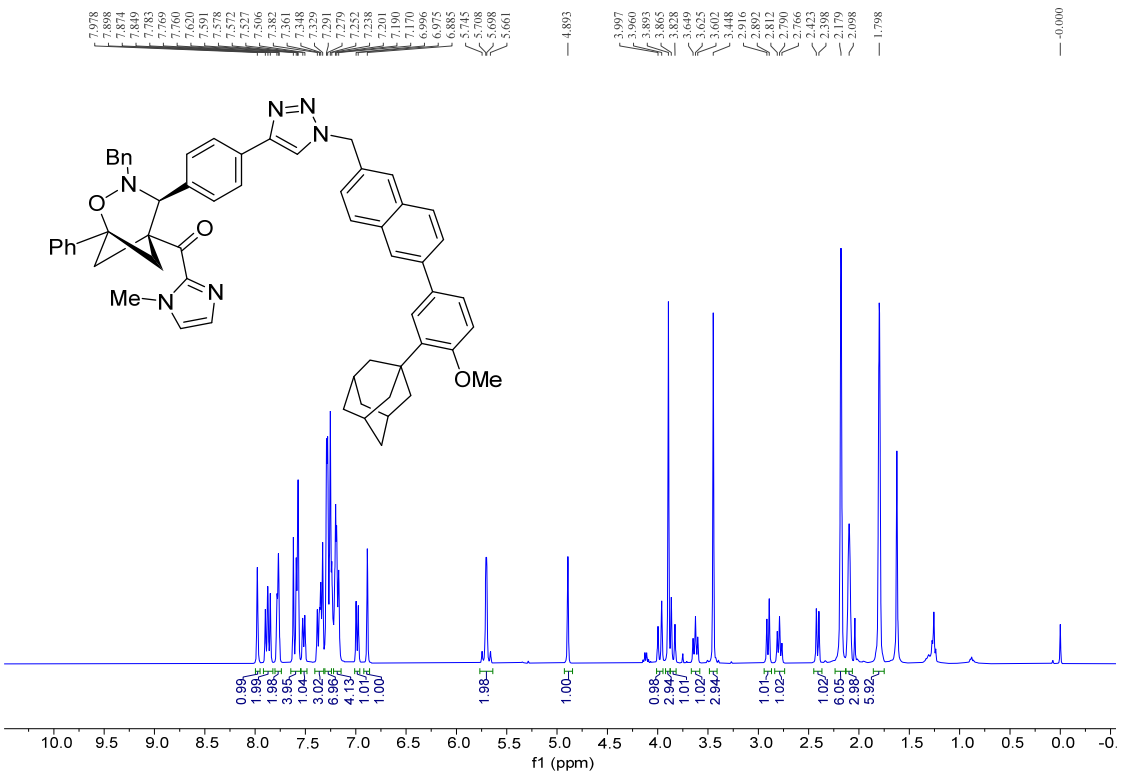

**Supplementary Figure 150.** $^{1}$H NMR (600 MHz, $CDCl_3$) spectrum of compound **10**



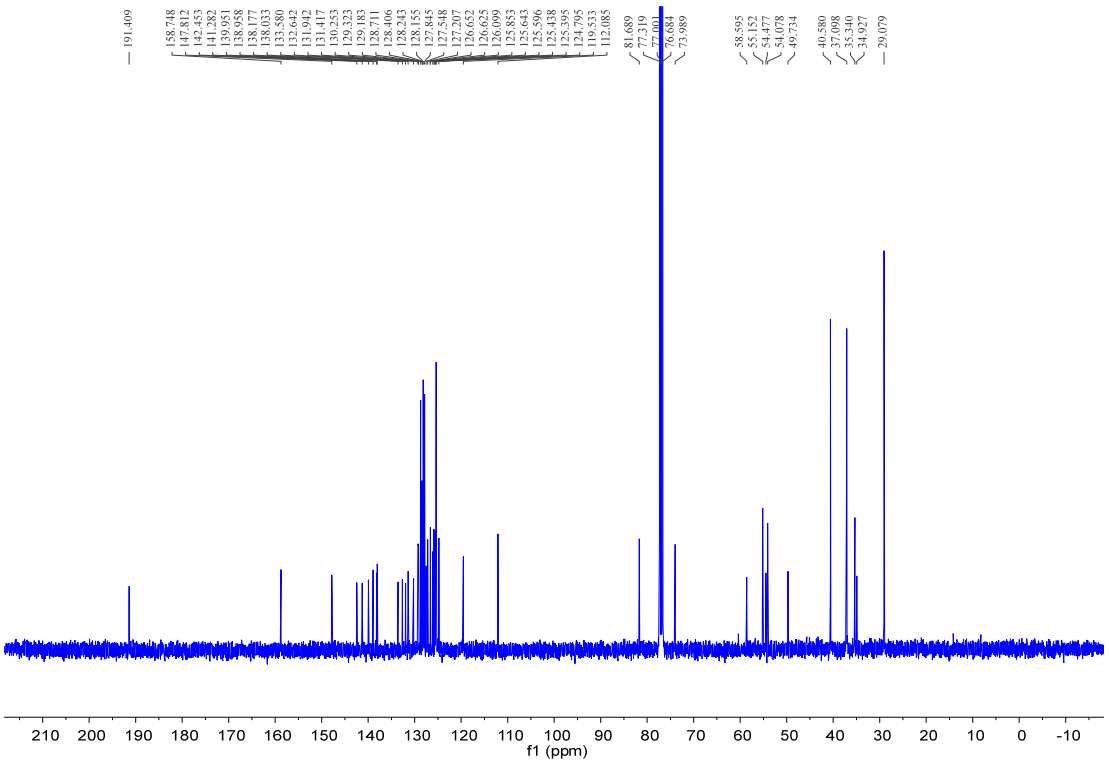

**Supplementary Figure 151.** $^{13}$C NMR (150 MHz, $CDCl_3$) spectrum of compound **10**



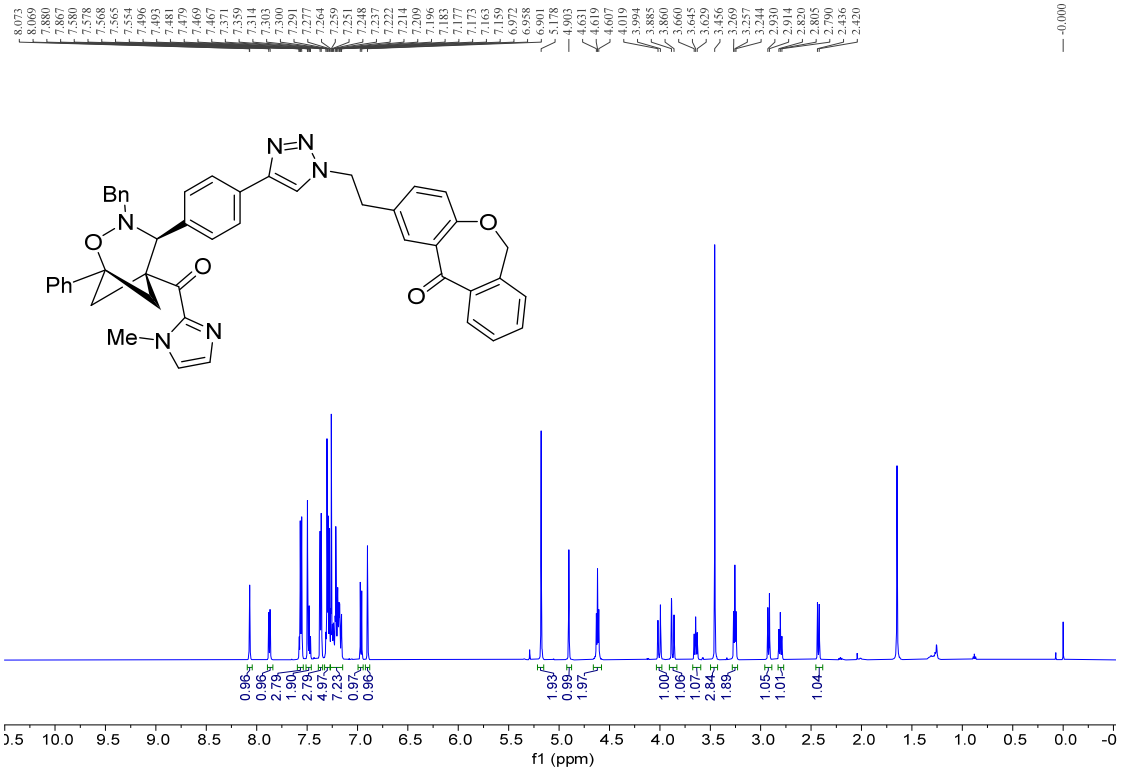

**Supplementary Figure 152.** $^{19}F$ NMR (565 MHz, $CDCl_3$) spectrum of compound **10**



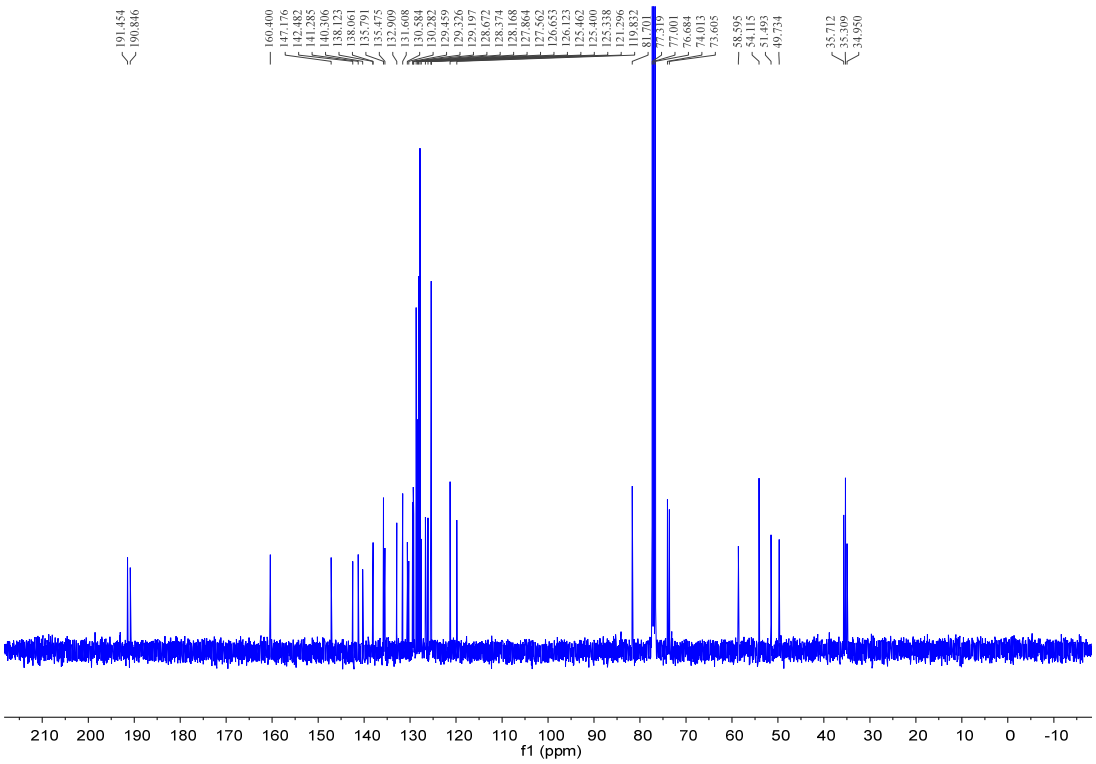

**Supplementary Figure 153.** $^1H$ NMR (600 MHz, $CDCl_3$) spectrum of compound **11**



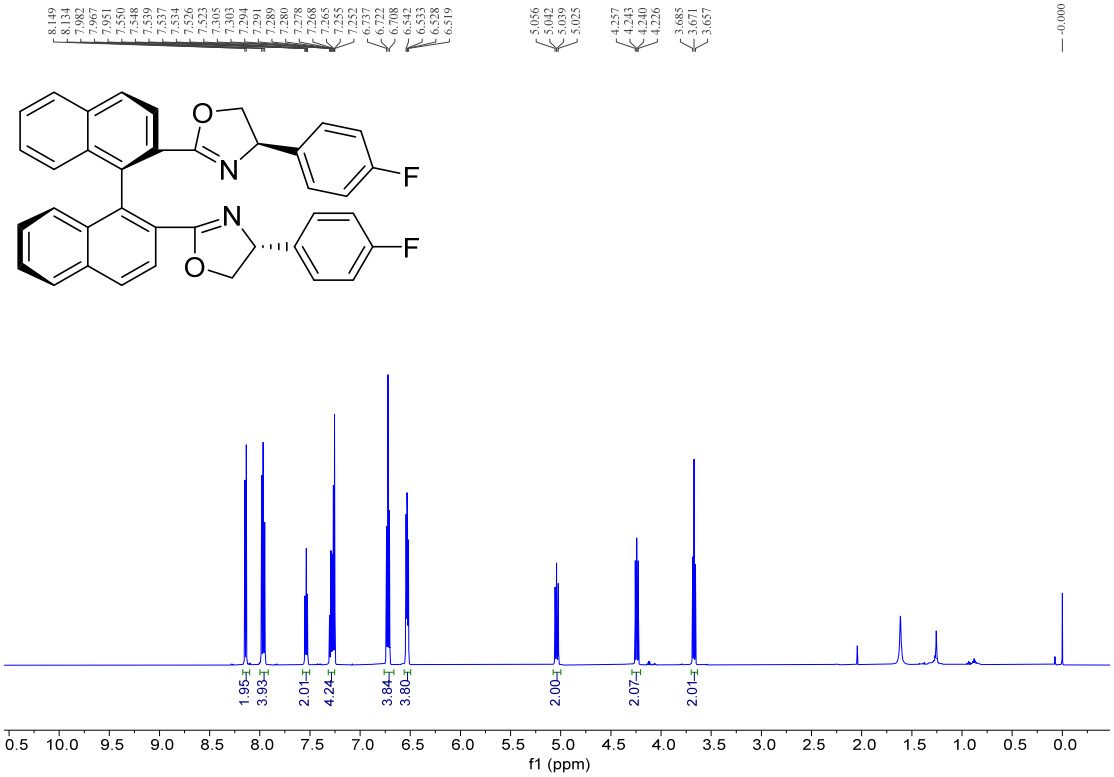

**Supplementary Figure 154.** $^{13}C$ NMR (150 MHz, $CDCl_3$) spectrum of compound **11**



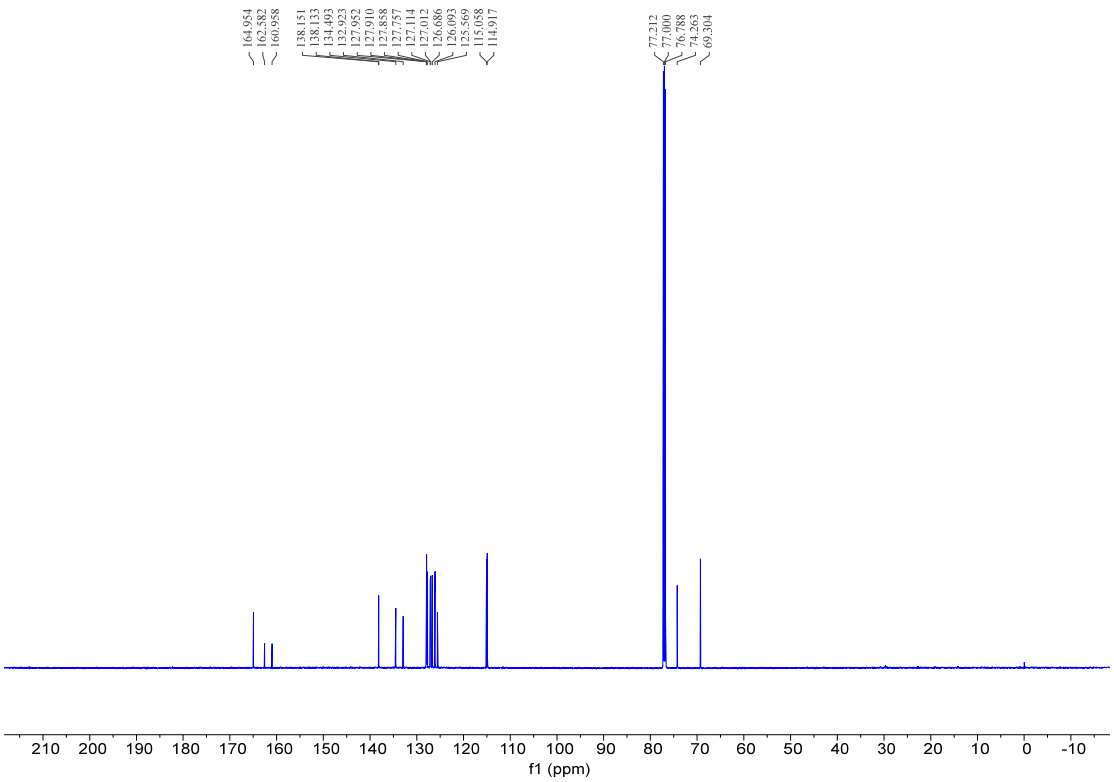

**Supplementary Figure 155.** $^{1}H$ NMR (600 MHz, $CDCl_3$) spectrum of compound **12**



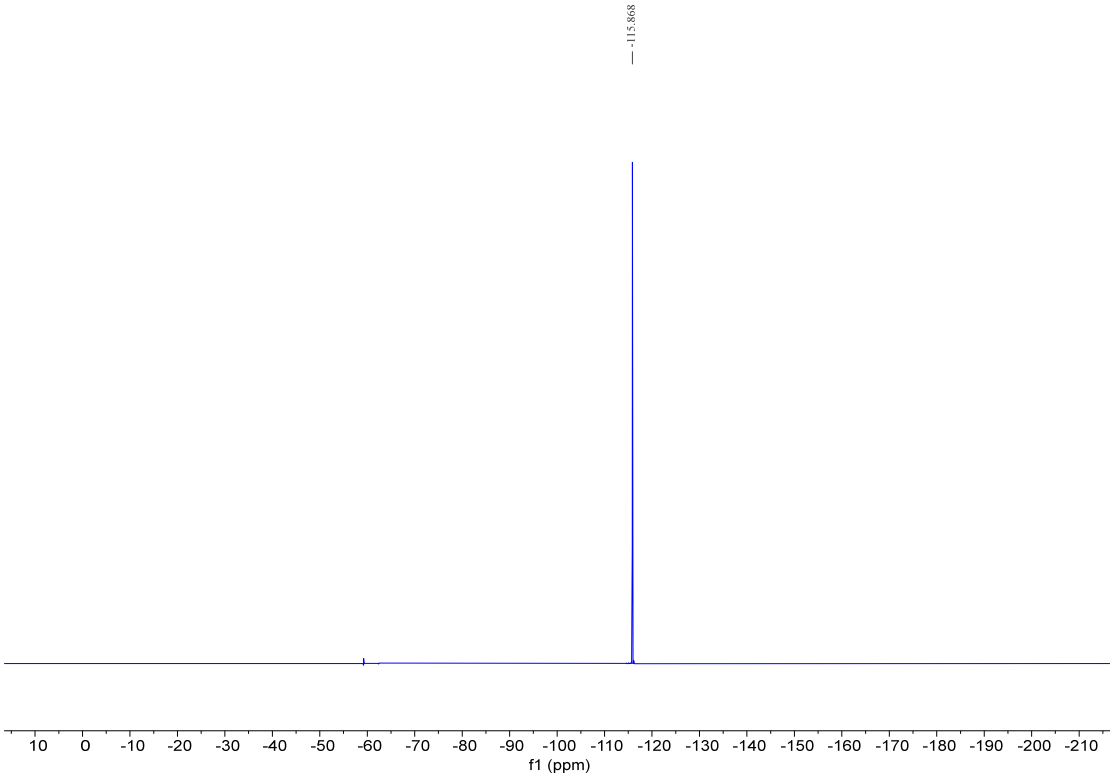

**Supplementary Figure 156.** $^{13}C$ NMR (100 MHz, $CDCl_3$) spectrum of compound **12**




**Supplementary Figure 157.** $^{1}H$ NMR (600 MHz, $CDCl_3$) spectrum of compound **L21**




**Supplementary Figure 158.** $^{13}C$ NMR (150 MHz, $CDCl_3$) spectrum of compound **L21**




**Supplementary Figure 159.** $^{19}F$ NMR (565 MHz, $CDCl_3$) spectrum of compound **L21**

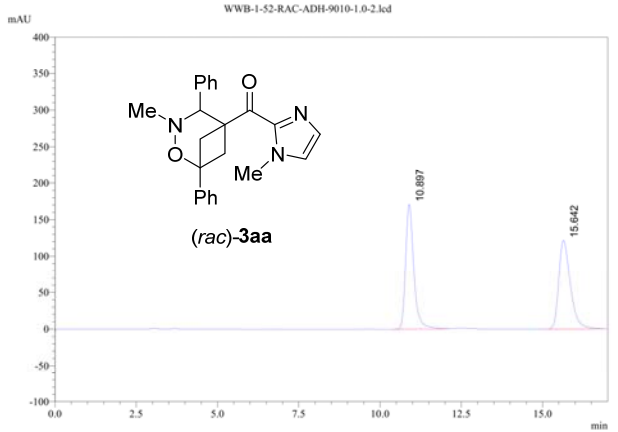
2024-03-19 11:21:33 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-52-RAC-ADH-9010-1.0-1 |
| Sample ID | : WWB-1-52-RAC-ADH-9010-1.0-1 |
| Data File | : WWB-1-52-RAC-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2023/10/8 10:12:50 |
| Date Processed | : 2023/10/8 10:32:29 |




(*rac*)-**3aa**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.897 | 10.392 | 170784 | 3015242 | 50.071 |
| 2 | 15.642 | 14.983 | 121756 | 3006637 | 49.929 |
| Total | | | 292540 | 6021879 | 100.000 |

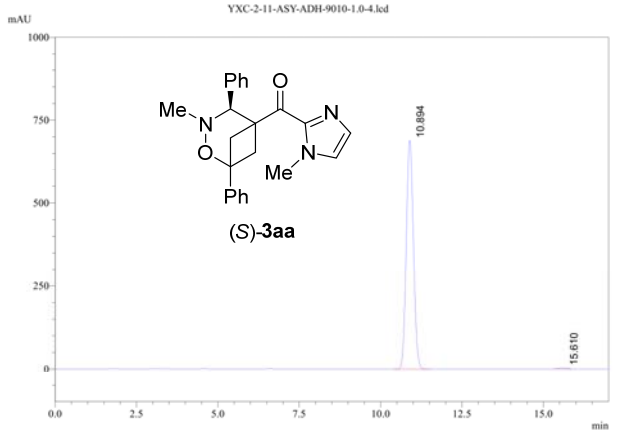
2024-03-19 11:21:10 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-11-ASY-ADH-9010-1.0-3 |
| Sample ID | : YXC-2-11-ASY-ADH-9010-1.0-3 |
| Data File | : YXC-2-11-ASY-ADH-9010-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/19 11:03:01 |
| Date Processed | : 2024/3/19 11:20:40 |




(*S*)-**3aa**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.894 | 10.375 | 688858 | 10553294 | 99.433 |
| 2 | 15.610 | 15.333 | 3333 | 60216 | 0.567 |
| Total | | | 692191 | 10613509 | 100.000 |

**Supplementary Figure 160.** HPLC spectra of (*rac*)-**3aa** and (*S*)-**3aa**

2024-02-29 16:10:16 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-189-RAC-ADH-9010-1.0-1 |
| Sample ID | : WWB-1-189-RAC-ADH-9010-1.0-1 |
| Data File | : WWB-1-189-RAC-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
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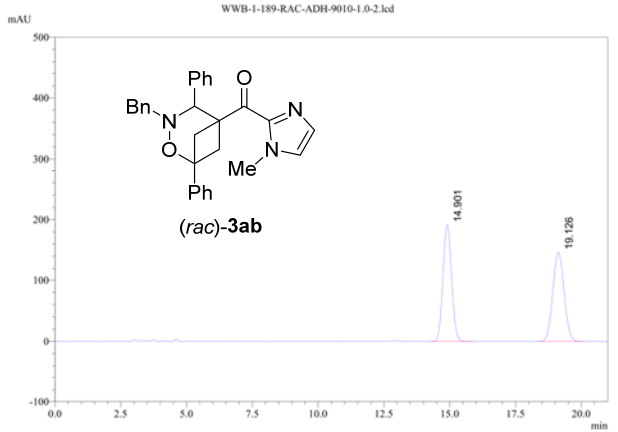


(*rac*)-**3ab**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.901 | 14.250 | 191912 | 4411046 | 50.191 |
| 2 | 19.126 | 18.325 | 147012 | 4377492 | 49.809 |
| Total | | | 338924 | 8788538 | 100.000 |

2024-02-29 16:09:55 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-189-2-ASY-ADH-9010-1.0-1 |
| Sample ID | : WWB-1-189-2-ASY-ADH-9010-1.0-1 |
| Data File | : WWB-1-189-2-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
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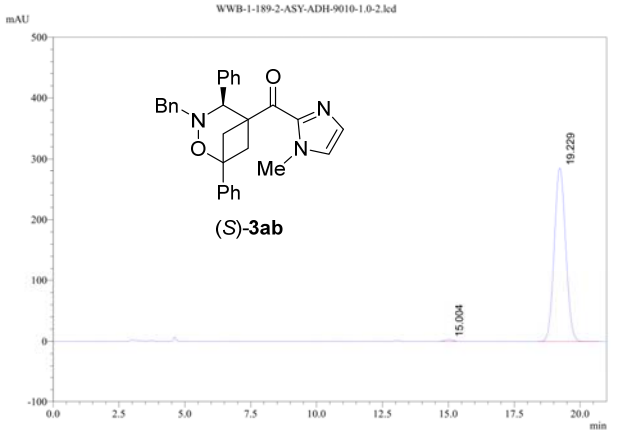
| Date Processed | : 2024/2/29 16:09:08 |




(*S*)-**3ab**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 15.004 | 14.650 | 2999 | 62987 | 0.726 |
| 2 | 19.229 | 18.317 | 285544 | 8609355 | 99.274 |
| Total | | | 288543 | 8672342 | 100.000 |

**Supplementary Figure 161.** HPLC spectra of (*rac*)-**3ab** and (*S*)-**3ab**

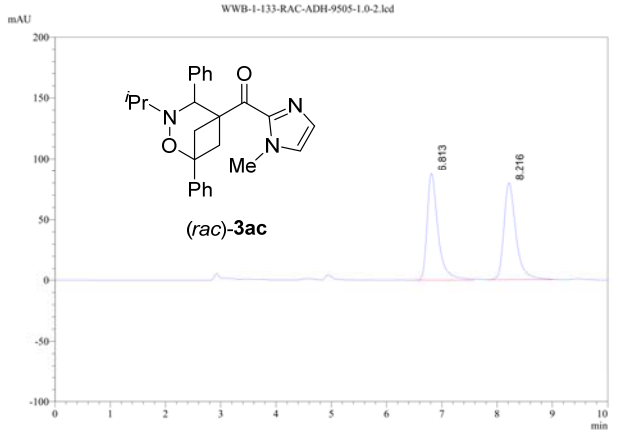
2024-03-25 19:39:22 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-133-RAC-ADH-9505-1.0-1 |
| Sample ID | : WWB-1-133-RAC-ADH-9505-1.0-1 |
| Data File | : WWB-1-133-RAC-ADH-9505-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2023/12/27 17:12:50 |
| Date Processed | : 2024/3/25 19:29:13 |




(*rac*)-**3ac**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.813 | 6.492 | 87700 | 1215130 | 50.064 |
| 2 | 8.216 | 7.817 | 79577 | 1212012 | 49.936 |
| Total | | | 167277 | 2427142 | 100.000 |

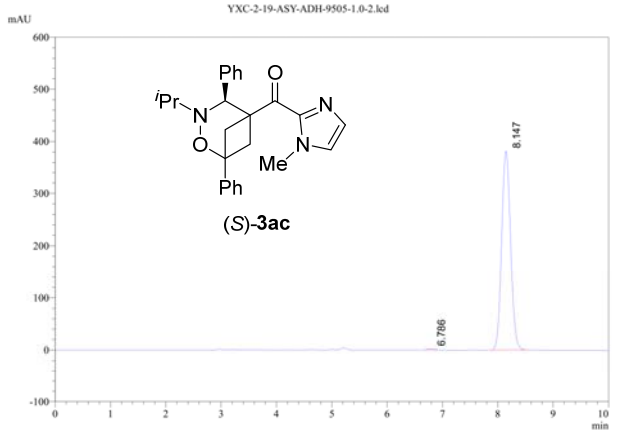
2024-03-25 19:40:30 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-19-ASY-ADH-9505-1.0-1 |
| Sample ID | : YXC-2-19-ASY-ADH-9505-1.0-1 |
| Data File | : YXC-2-19-ASY-ADH-9505-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 19:26:25 |
| Date Processed | : 2024/3/25 19:40:10 |




(*S*)-**3ac**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.786 | 6.683 | 2030 | 15116 | 0.352 |
| 2 | 8.147 | 7.883 | 381725 | 4274411 | 99.648 |
| Total | | | 383755 | 4289527 | 100.000 |

**Supplementary Figure 162.** HPLC spectra of (*rac*)-**3ac** and (*S*)-**3ac**

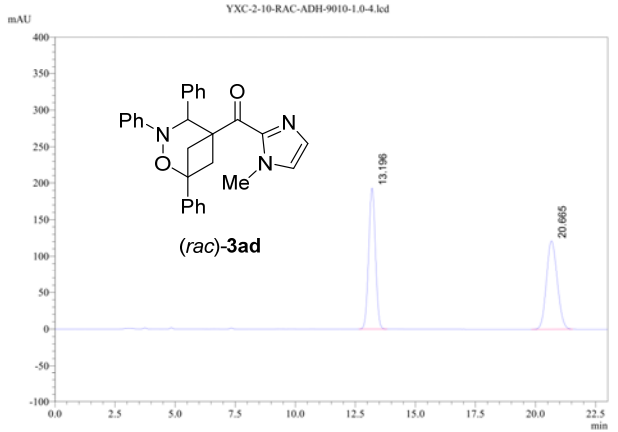
2024-03-19 10:42:32 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-10-RAC-ADH-9010-1.0-3 |
| Sample ID | : YXC-2-10-RAC-ADH-9010-1.0-3 |
| Data File | : YXC-2-10-RAC-ADH-9010-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/19 10:08:44 |
| Date Processed | : 2024/3/19 10:38:08 |




(*rac*)-**3ad**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.196 | 12.642 | 192865 | 3787653 | 49.943 |
| 2 | 20.665 | 19.825 | 121229 | 3796231 | 50.057 |
| Total | | | 314094 | 7583884 | 100.000 |

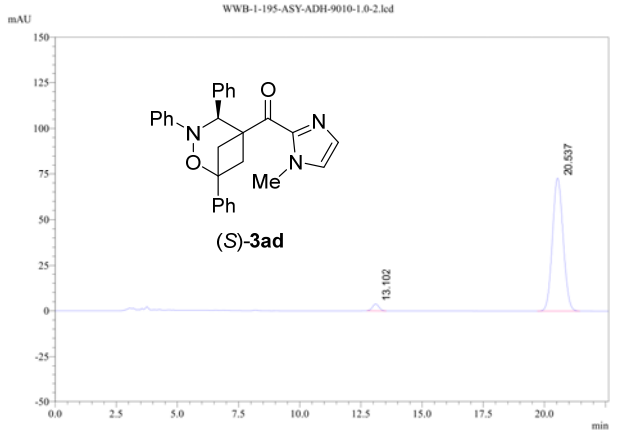
2024-03-20 10:08:07 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-195-ASY-ADH-9010-1.0-1 |
| Sample ID | : WWB-1-195-ASY-ADH-9010-1.0-1 |
| Data File | : WWB-1-195-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/20 9:43:58 |
| Date Processed | : 2024/3/20 10:07:20 |




(*S*)-**3ad**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.102 | 12.733 | 3707 | 68303 | 2.977 |
| 2 | 20.537 | 19.708 | 72778 | 2226030 | 97.023 |
| Total | | | 76485 | 2294333 | 100.000 |

**Supplementary Figure 163.** HPLC spectra of (*rac*)-**3ad** and (*S*)-**3ad**

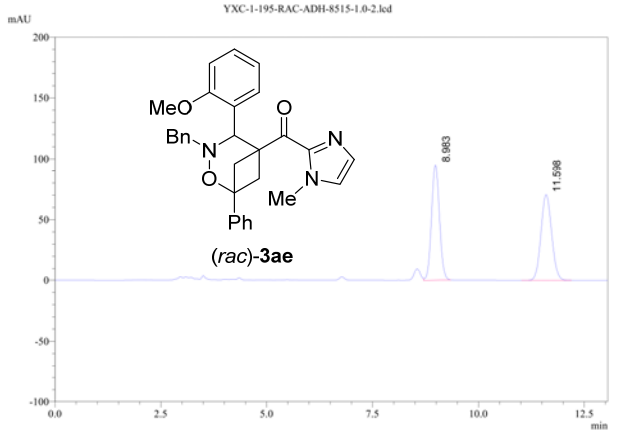
2024-03-14 10:36:44 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-195-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-195-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-195-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 10:20:15 |
| Date Processed | : 2024/3/14 10:34:04 |




(*rac*)-**3ae**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.983 | 8.700 | 95065 | 1247877 | 50.084 |
| 2 | 11.598 | 11.017 | 70505 | 1243670 | 49.916 |
| Total | | | 165570 | 2491547 | 100.000 |

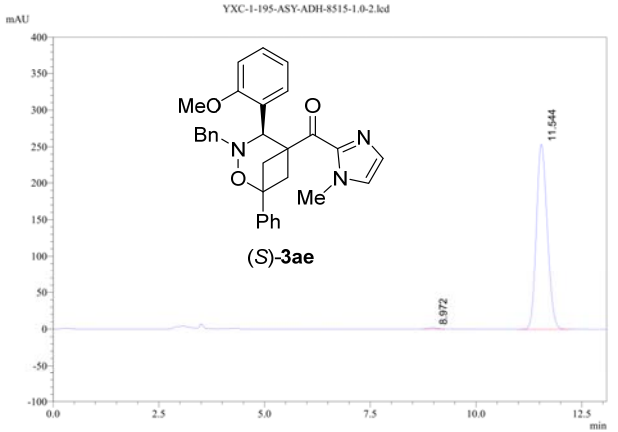
2024-03-14 10:51:49 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-195-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-195-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-195-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 10:34:59 |
| Date Processed | : 2024/3/14 10:51:26 |




(*S*)-**3ae**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.972 | 8.717 | 2025 | 26632 | 0.584 |
| 2 | 11.544 | 10.975 | 253743 | 4537244 | 99.416 |
| Total | | | 255767 | 4563875 | 100.000 |

**Supplementary Figure 164.** HPLC spectra of (*rac*)-**3ae** and (*S*)-**3ae**

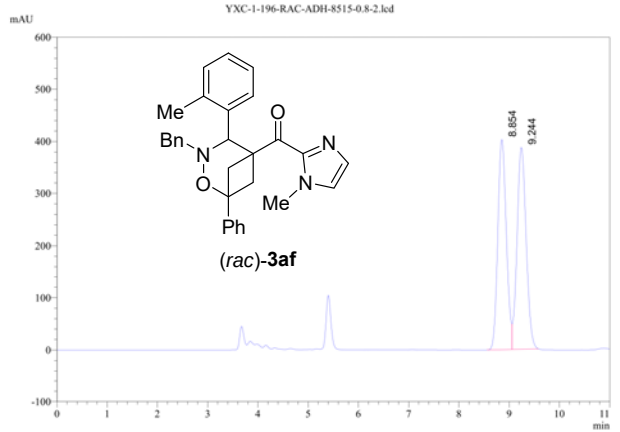
2024-03-14 17:27:47 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-196-RAC-ADH-8515-0.8-1 |
| Sample ID | : YXC-1-196-RAC-ADH-8515-0.8-1 |
| Data File | : YXC-1-196-RAC-ADH-8515-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 16:55:47 |
| Date Processed | : 2024/3/14 17:14:21 |




(*rac*)-**3af**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.854 | 8.558 | 402694 | 4768315 | 49.462 |
| 2 | 9.244 | 9.058 | 387074 | 4872079 | 50.538 |
| Total | | | 789768 | 9640394 | 100.000 |

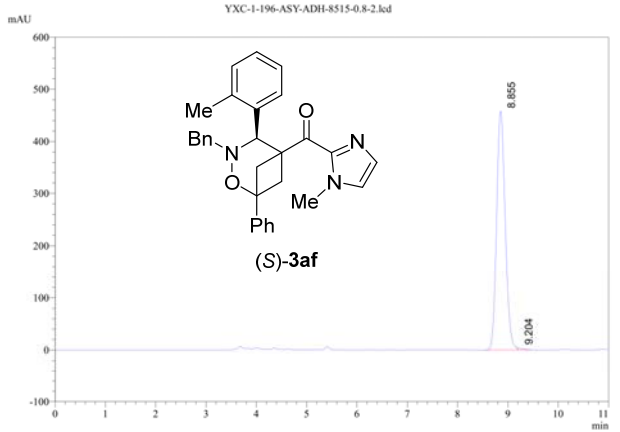
2024-03-14 17:27:58 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-196-ASY-ADH-8515-0.8-1 |
| Sample ID | : YXC-1-196-ASY-ADH-8515-0.8-1 |
| Data File | : YXC-1-196-ASY-ADH-8515-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 17:15:02 |
| Date Processed | : 2024/3/14 17:27:17 |




(*S*)-**3af**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.855 | 8.525 | 457725 | 5447201 | 99.500 |
| 2 | 9.204 | 9.192 | 4137 | 27348 | 0.500 |
| Total | | | 461861 | 5474549 | 100.000 |

**Supplementary Figure 165.** HPLC spectra of (*rac*)-**3af** and (*S*)-**3af**

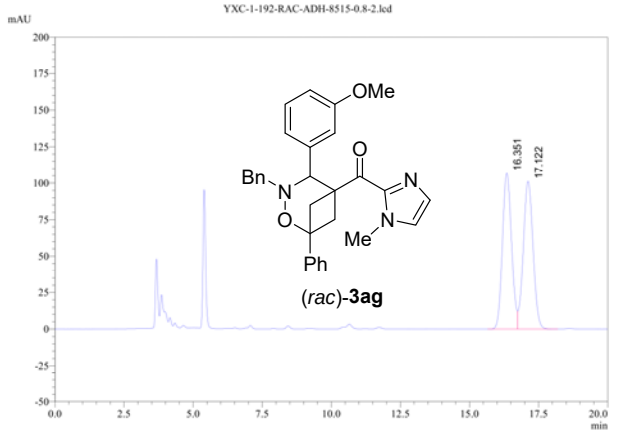
2024-03-14 16:30:29 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-192-RAC-ADH-8515-0.8-1 |
| Sample ID | : YXC-1-192-RAC-ADH-8515-0.8-1 |
| Data File | : YXC-1-192-RAC-ADH-8515-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 16:03:24 |
| Date Processed | : 2024/3/14 16:27:32 |




(*rac*)-**3ag**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 16.351 | 15.658 | 106713 | 2456846 | 49.695 |
| 2 | 17.122 | 16.742 | 101089 | 2486953 | 50.305 |
| Total | | | 207802 | 4943799 | 100.000 |

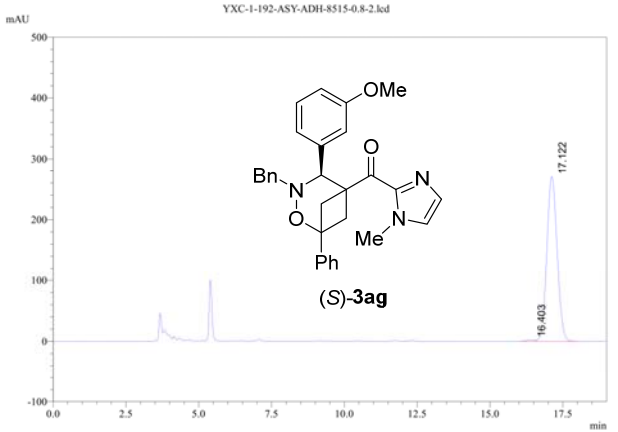
2024-04-16 15:48:02 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-192-ASY-ADH-8515-0.8-1 |
| Sample ID | : YXC-1-192-ASY-ADH-8515-0.8-1 |
| Data File | : YXC-1-192-ASY-ADH-8515-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 16:28:31 |
| Date Processed | : 2024/3/14 16:54:40 |

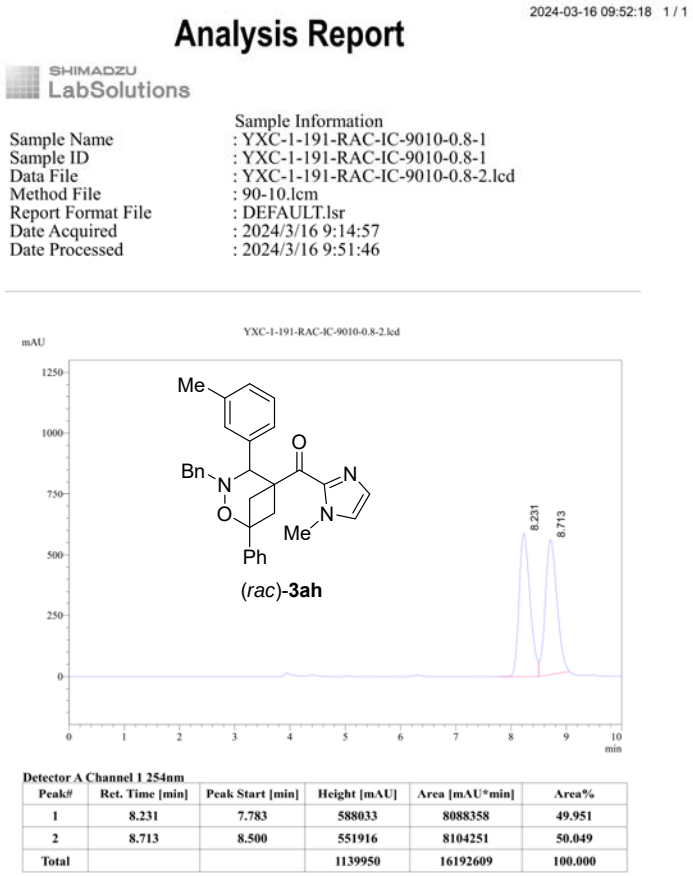



(*S*)-**3ag**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 16.403 | 15.958 | 2524 | 50867 | 0.757 |
| 2 | 17.122 | 16.567 | 270544 | 6665730 | 99.243 |
| Total | | | 273067 | 6716597 | 100.000 |

**Supplementary Figure 166.** HPLC spectra of (*rac*)-**3ag** and (*S*)-**3ag**



2024-03-16 09:52:18 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

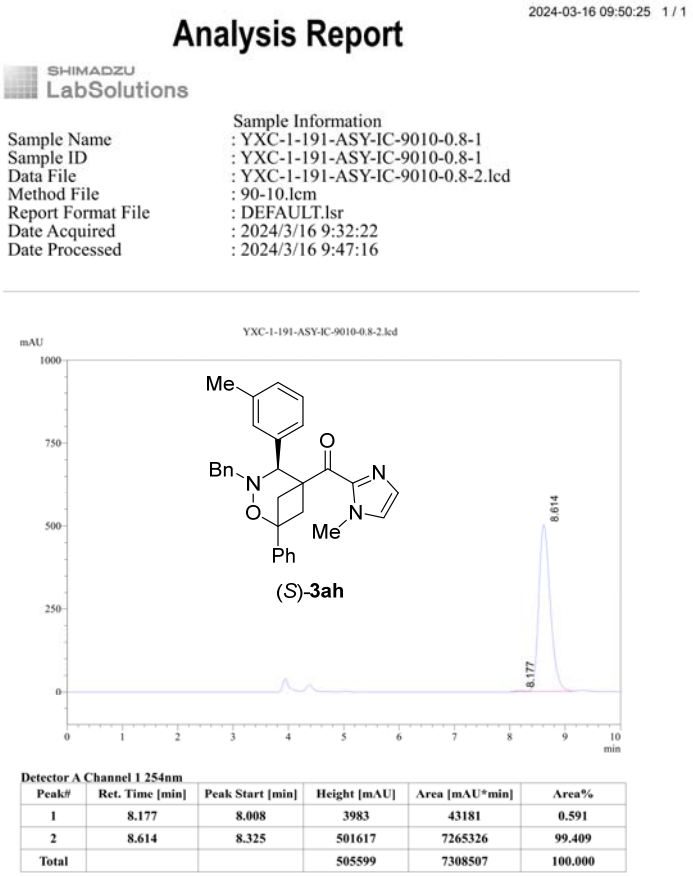
| | |
|---|---|
| Sample Name | : YXC-1-191-RAC-IC-9010-0.8-1 |
| Sample ID | : YXC-1-191-RAC-IC-9010-0.8-1 |
| Data File | : YXC-1-191-RAC-IC-9010-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 9:14:57 |
| Date Processed | : 2024/3/16 9:51:46 |



(*rac*)-**3ah**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.231 | 7.783 | 588033 | 8088358 | 49.951 |
| 2 | 8.713 | 8.500 | 551916 | 8104251 | 50.049 |
| Total | | | 1139950 | 16192609 | 100.000 |



2024-03-16 09:50:25 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-191-ASY-IC-9010-0.8-1 |
| Sample ID | : YXC-1-191-ASY-IC-9010-0.8-1 |
| Data File | : YXC-1-191-ASY-IC-9010-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 9:32:22 |
| Date Processed | : 2024/3/16 9:47:16 |



(*S*)-**3ah**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.177 | 8.008 | 3983 | 43181 | 0.591 |
| 2 | 8.614 | 8.325 | 501617 | 7265326 | 99.409 |
| Total | | | 505599 | 7308507 | 100.000 |

**Supplementary Figure 167.** HPLC spectra of (*rac*)-**3ah** and (*S*)-**3ah**

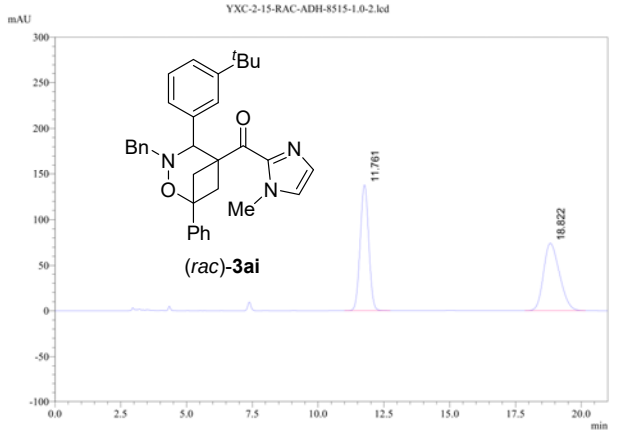
2024-03-25 20:50:28 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-15-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-15-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-2-15-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 20:01:59 |
| Date Processed | : 2024/3/25 20:28:09 |




(*rac*)-**3ai**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.761 | 11.000 | 137571 | 3114842 | 49.981 |
| 2 | 18.822 | 17.850 | 74020 | 3117169 | 50.019 |
| Total | | | 211591 | 6232010 | 100.000 |

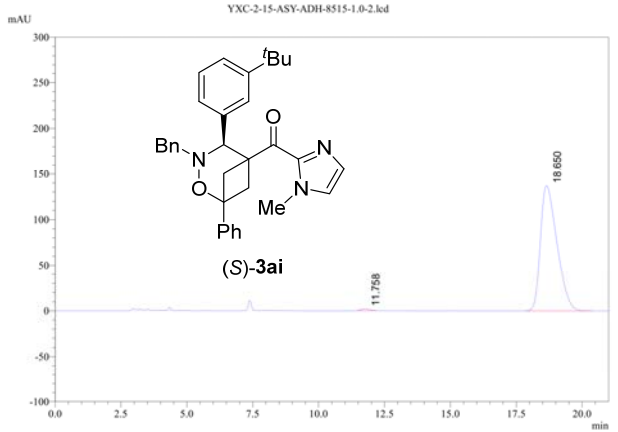
2024-03-25 20:51:37 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-15-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-15-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-2-15-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 20:29:08 |
| Date Processed | : 2024/3/25 20:51:10 |




(*S*)-**3ai**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.758 | 11.433 | 1993 | 41221 | 0.683 |
| 2 | 18.650 | 17.842 | 137169 | 5990055 | 99.317 |
| Total | | | 139162 | 6031276 | 100.000 |

**Supplementary Figure 168.** HPLC spectra of (*rac*)-**3ai** and (*S*)-**3ai**

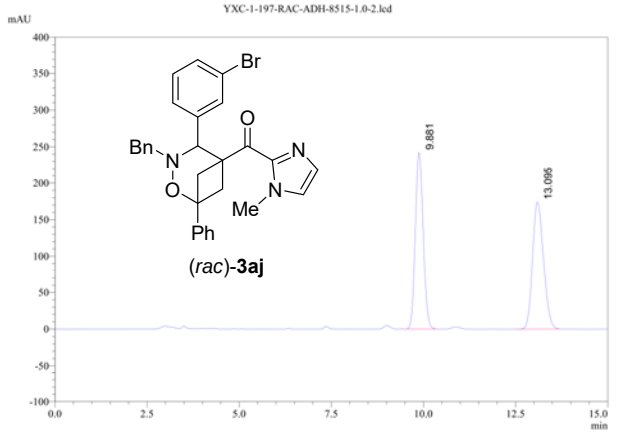
2024-03-14 11:06:32 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-197-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-197-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-197-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 10:03:12 |
| Date Processed | : 2024/3/14 10:19:28 |




(*rac*)-**3aj**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.881 | 9.467 | 241857 | 3589956 | 49.921 |
| 2 | 13.095 | 12.525 | 173776 | 3601361 | 50.079 |
| Total | | | 415634 | 7191317 | 100.000 |

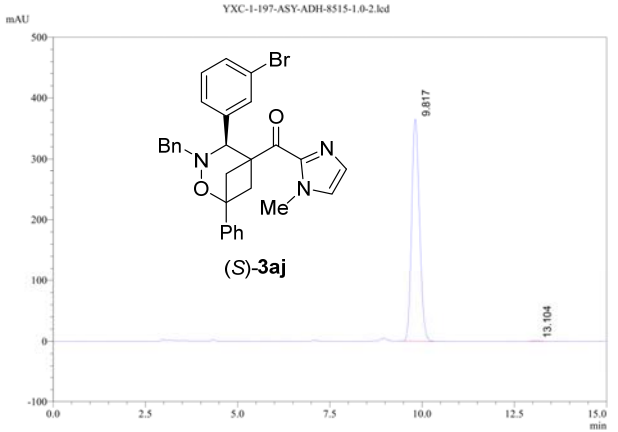
2024-03-14 11:06:52 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-197-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-197-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-197-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 10:48:59 |
| Date Processed | : 2024/3/14 11:05:58 |




(*S*)-**3aj**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.817 | 9.425 | 364823 | 5429670 | 99.812 |
| 2 | 13.104 | 12.867 | 671 | 10221 | 0.188 |
| Total | | | 365494 | 5439891 | 100.000 |

**Supplementary Figure 169.** HPLC spectra of (*rac*)-**3aj** and (*S*)-**3aj**

2024-03-13 19:11:35 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-193-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-193-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-193-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
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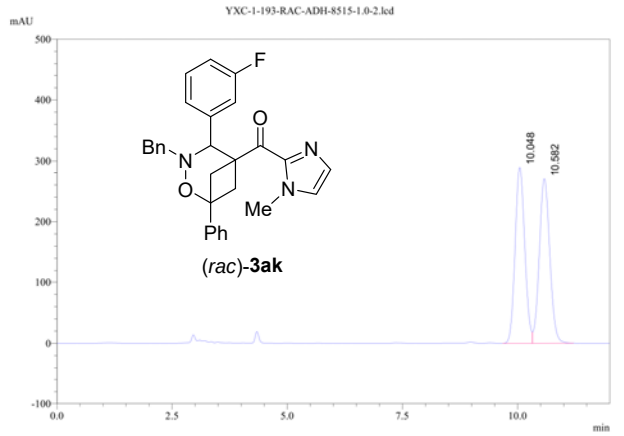
| Date Processed | : 2024/3/13 19:08:11 |




(*rac*)-**3ak**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.048 | 9.675 | 289500 | 4227893 | 49.724 |
| 2 | 10.582 | 10.325 | 270082 | 4274824 | 50.276 |
| Total | | | 559582 | 8502717 | 100.000 |

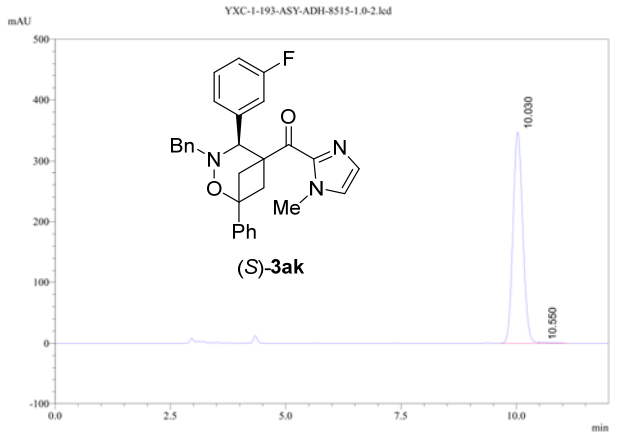
2024-03-13 19:25:30 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-193-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-193-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-193-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/13 19:09:17 |
| Date Processed | : 2024/3/13 19:22:48 |




(*S*)-**3ak**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.030 | 9.650 | 347617 | 5106310 | 99.327 |
| 2 | 10.550 | 10.492 | 1602 | 34591 | 0.673 |
| Total | | | 349219 | 5140901 | 100.000 |

**Supplementary Figure 170.** HPLC spectra of (*rac*)-**3ak** and (*S*)-**3ak**

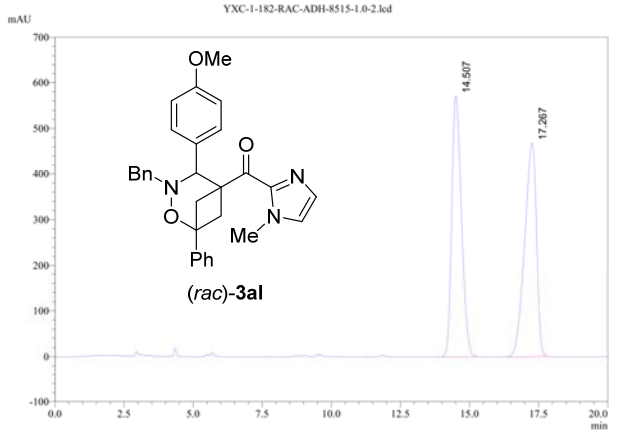
2024-03-08 14:53:15 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-182-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-182-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-182-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 14:29:32 |
| Date Processed | : 2024/3/8 14:50:37 |




(*rac*)-**3al**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.507 | 13.975 | 571643 | 13895029 | 50.013 |
| 2 | 17.267 | 16.292 | 468627 | 13887924 | 49.987 |
| Total | | | 1040270 | 27782953 | 100.000 |

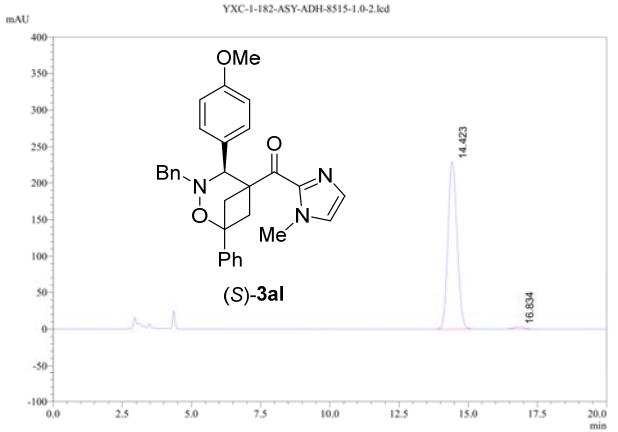
2024-03-08 15:14:25 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-182-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-182-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-182-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 14:51:28 |
| Date Processed | : 2024/3/8 15:14:05 |




(*S*)-**3al**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.423 | 13.833 | 230016 | 5278181 | 98.628 |
| 2 | 16.834 | 16.433 | 2972 | 73427 | 1.372 |
| Total | | | 232988 | 5351608 | 100.000 |

**Supplementary Figure 171.** HPLC spectra of (*rac*)-**3al** and (*S*)-**3al**

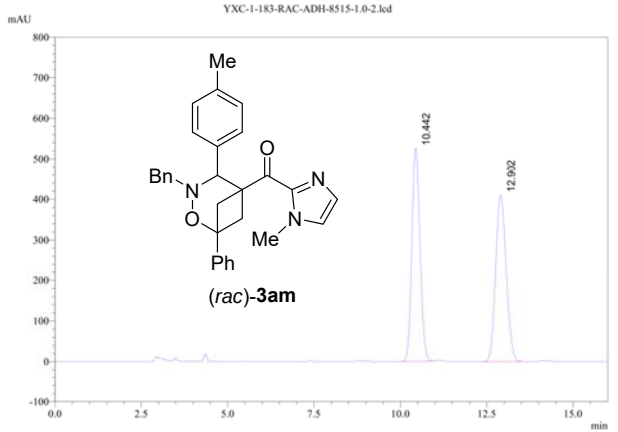
2024-03-08 15:40:34 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-183-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-183-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-183-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 15:16:00 |
| Date Processed | : 2024/3/8 15:37:43 |




(*rac*)-**3am**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.442 | 10.058 | 525678 | 8628731 | 49.861 |
| 2 | 12.902 | 12.392 | 411102 | 8676742 | 50.139 |
| Total | | | 936779 | 17305473 | 100.000 |

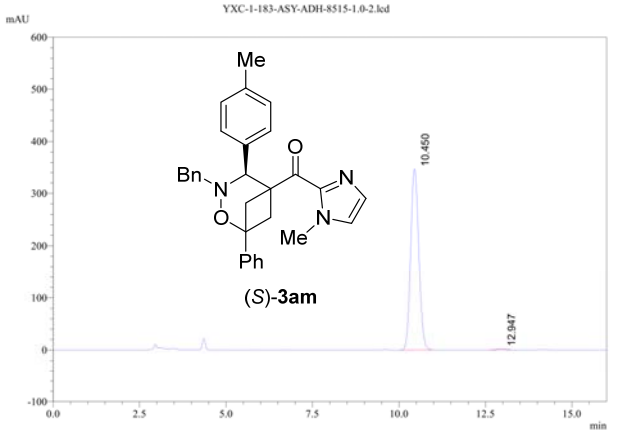
2024-03-08 16:28:10 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-183-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-183-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-183-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 15:38:36 |
| Date Processed | : 2024/3/8 16:01:53 |

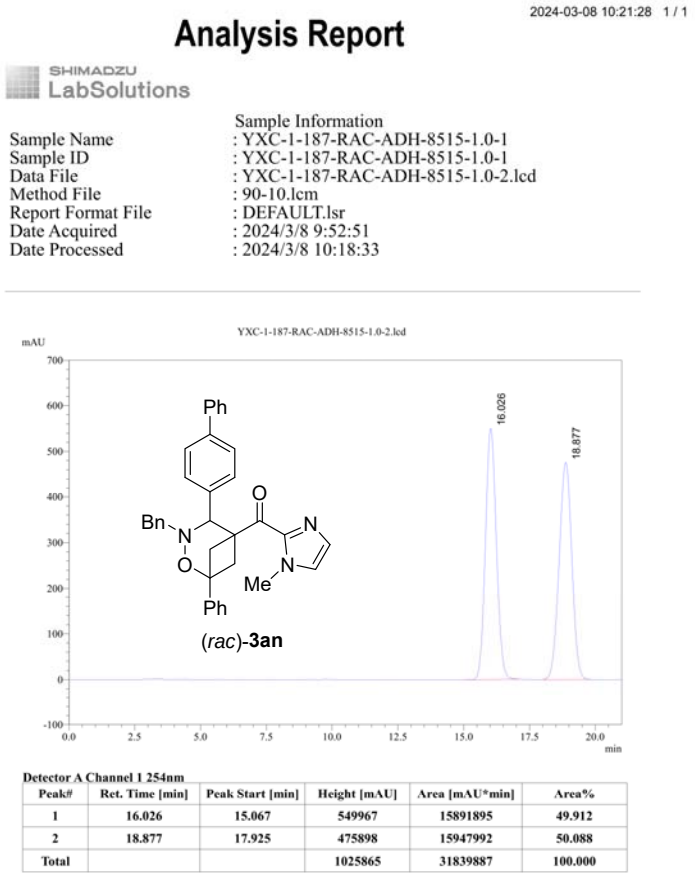



(*S*)-**3am**

Detector A Channel 1 254nm

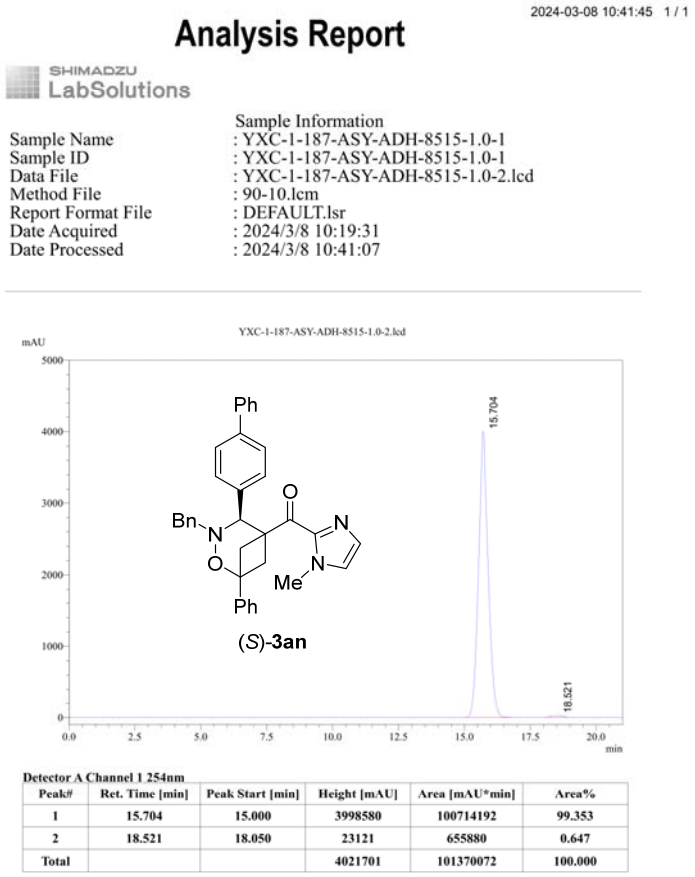
| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.450 | 10.017 | 347759 | 5679335 | 99.159 |
| 2 | 12.947 | 12.592 | 2471 | 48178 | 0.841 |
| Total | | | 350230 | 5727513 | 100.000 |

**Supplementary Figure 172.** HPLC spectra of (*rac*)-**3am** and (*S*)-**3am**




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 16.026 | 15.067 | 549967 | 15891895 | 49.912 |
| 2 | 18.877 | 17.925 | 475898 | 15947992 | 50.088 |
| Total | | | 1025865 | 31839887 | 100.000 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 15.704 | 15.000 | 3998580 | 100714192 | 99.353 |
| 2 | 18.521 | 18.050 | 23121 | 655880 | 0.647 |
| Total | | | 4021701 | 101370072 | 100.000 |

**Supplementary Figure 173.** HPLC spectra of (*rac*)-**3an** and (*S*)-**3an**

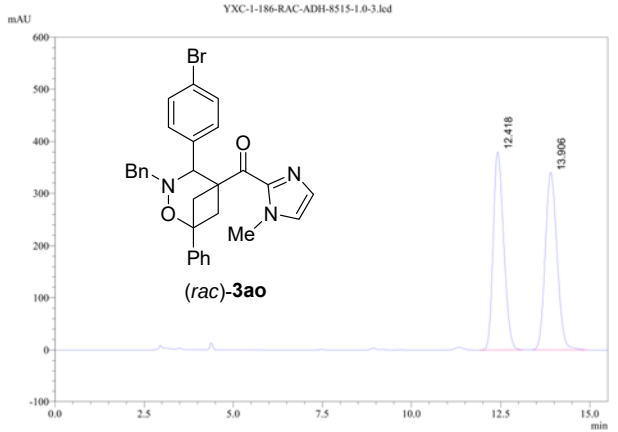
2024-03-06 21:42:33 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-186-RAC-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-186-RAC-ADH-8515-1.0-2 |
| Data File | : YXC-1-186-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 21:07:47 |
| Date Processed | : 2024/3/6 21:42:20 |




(*rac*)-**3ao**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.418 | 11.908 | 379652 | 7774863 | 49.728 |
| 2 | 13.906 | 13.383 | 339545 | 7859883 | 50.272 |
| Total | | | 719197 | 15634746 | 100.000 |

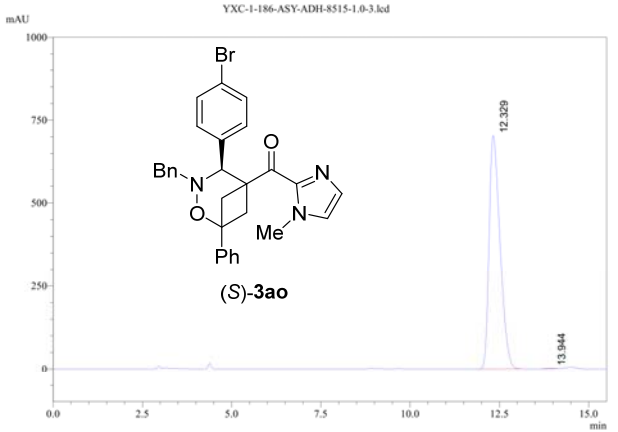
2024-03-06 21:43:45 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-186-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-186-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-186-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 21:24:51 |
| Date Processed | : 2024/3/6 21:43:26 |




(*S*)-**3ao**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.329 | 11.925 | 702846 | 14945422 | 99.813 |
| 2 | 13.944 | 13.650 | 1687 | 28046 | 0.187 |
| Total | | | 704533 | 14973468 | 100.000 |

**Supplementary Figure 174.** HPLC spectra of (*rac*)-**3ao** and (*S*)-**3ao**

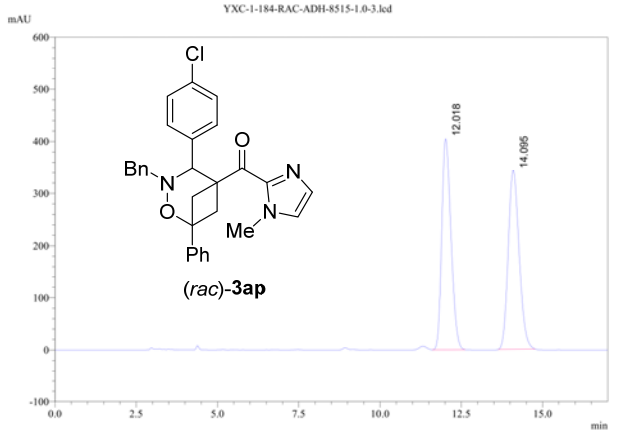
2024-03-06 21:10:49 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-184-RAC-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-184-RAC-ADH-8515-1.0-2 |
| Data File | : YXC-1-184-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 20:09:52 |
| Date Processed | : 2024/3/6 20:33:38 |




(*rac*)-**3ap**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.018 | 11.600 | 404519 | 7964018 | 49.828 |
| 2 | 14.095 | 13.633 | 342160 | 8019079 | 50.172 |
| Total | | | 746679 | 15983097 | 100.000 |

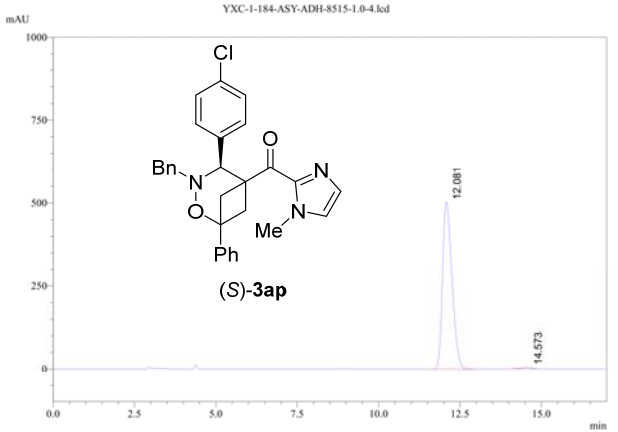
2024-03-06 21:09:52 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-184-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-184-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-184-ASY-ADH-8515-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 20:48:58 |
| Date Processed | : 2024/3/6 21:09:31 |

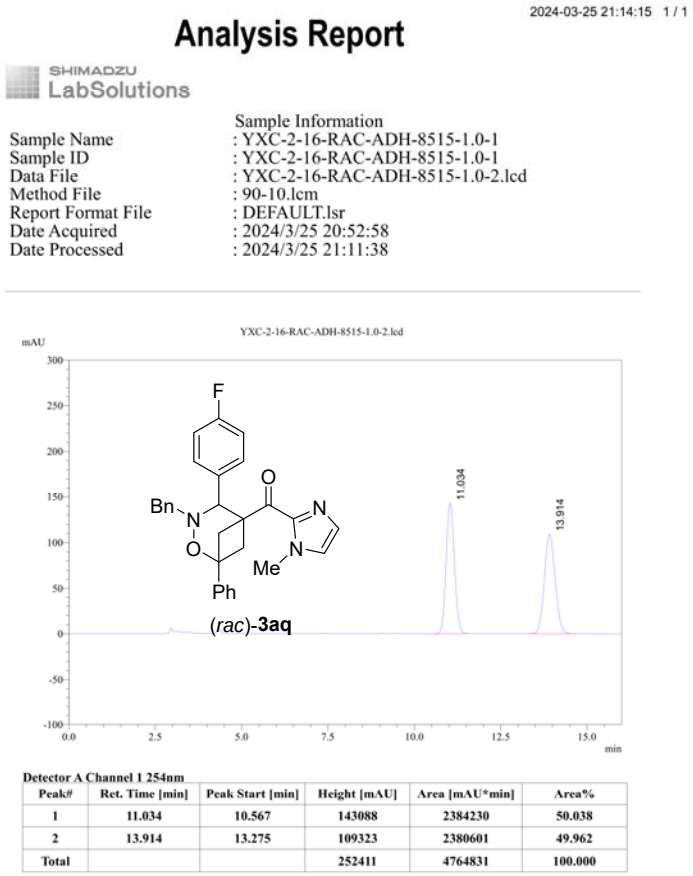



(*S*)-**3ap**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.081 | 11.658 | 502613 | 10151025 | 98.904 |
| 2 | 14.573 | 14.042 | 4749 | 112448 | 1.096 |
| Total | | | 507362 | 10263474 | 100.000 |

**Supplementary Figure 175.** HPLC spectra of (*rac*)-**3ap** and (*S*)-**3ap**



2024-03-25 21:14:15 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

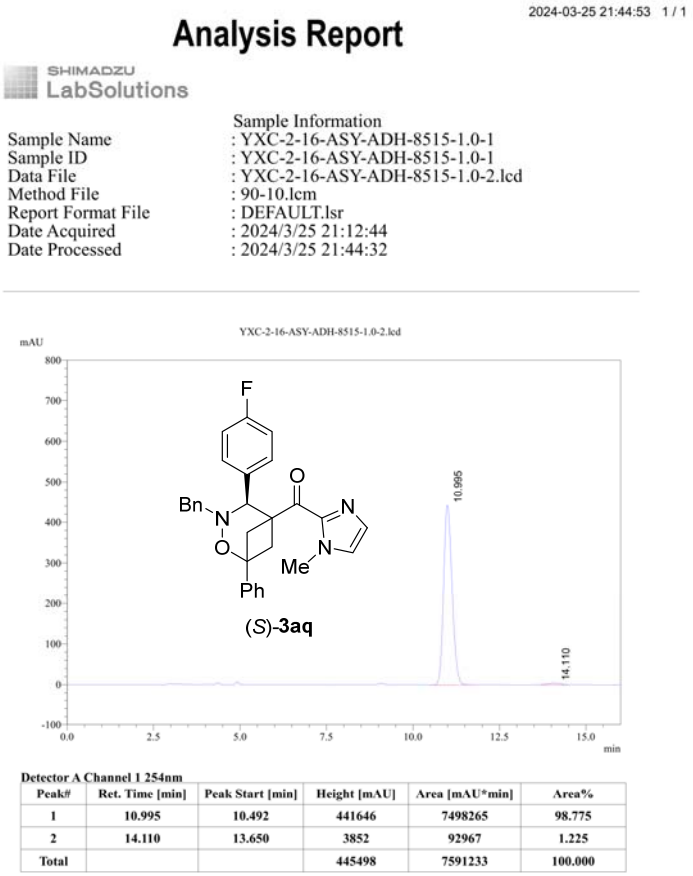
| | |
|---|---|
| Sample Name | : YXC-2-16-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-16-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-2-16-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 20:52:58 |
| Date Processed | : 2024/3/25 21:11:38 |



(*rac*)-**3aq**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.034 | 10.567 | 143088 | 2384230 | 50.038 |
| 2 | 13.914 | 13.275 | 109323 | 2380601 | 49.962 |
| Total | | | 252411 | 4764831 | 100.000 |



2024-03-25 21:44:53 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-16-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-16-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-2-16-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 21:12:44 |
| Date Processed | : 2024/3/25 21:44:32 |



(*S*)-**3aq**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.995 | 10.492 | 441646 | 7498265 | 98.775 |
| 2 | 14.110 | 13.650 | 3852 | 92967 | 1.225 |
| Total | | | 445498 | 7591233 | 100.000 |

**Supplementary Figure 176.** HPLC spectra of (*rac*)-**3aq** and (*S*)-**3aq**

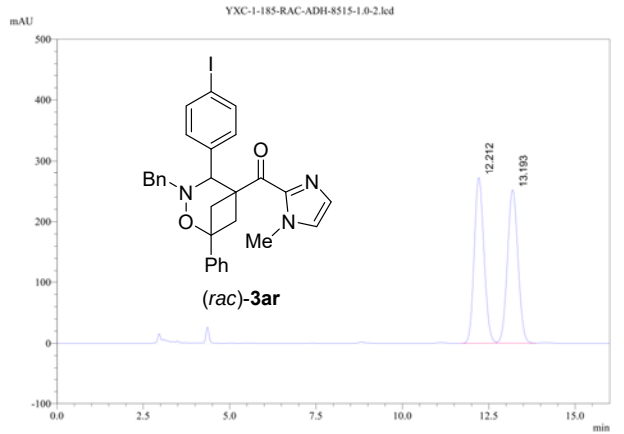
2024-03-08 16:28:49 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-185-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-185-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-185-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 16:02:59 |
| Date Processed | : 2024/3/8 16:25:40 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.212 | 11.692 | 272013 | 5350557 | 49.985 |
| 2 | 13.193 | 12.725 | 251800 | 5353826 | 50.015 |
| Total | | | 523814 | 10704383 | 100.000 |

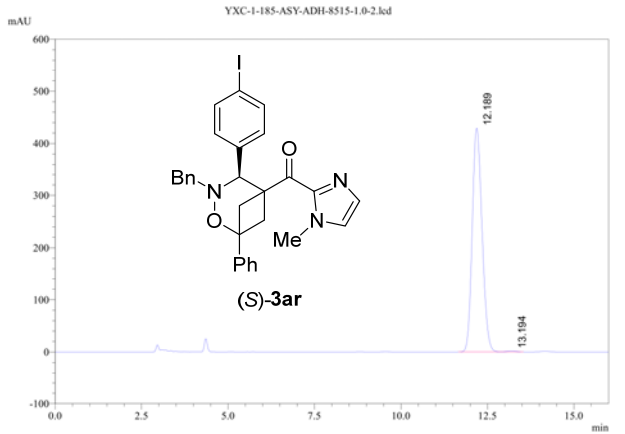
2024-03-08 16:43:39 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-185-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-185-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-185-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 16:26:41 |
| Date Processed | : 2024/3/8 16:43:18 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.189 | 11.658 | 429140 | 8481412 | 99.524 |
| 2 | 13.194 | 12.892 | 1959 | 40571 | 0.476 |
| Total | | | 431098 | 8521983 | 100.000 |

**Supplementary Figure 177.** HPLC spectra of (*rac*)-**3ar** and (*S*)-**3ar**

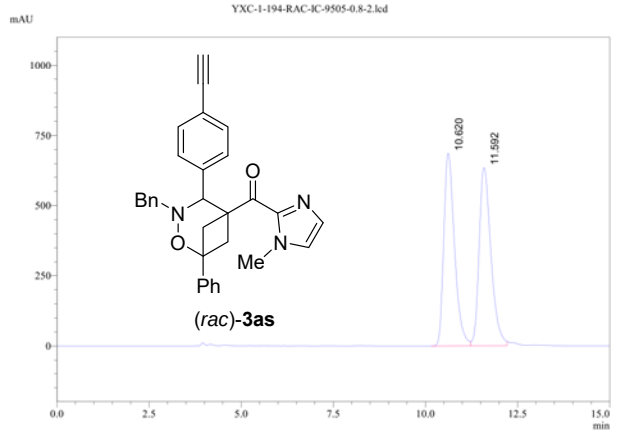
2024-03-16 10:37:42 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-194-RAC-IC-9505-0.8-1 |
| Sample ID | : YXC-1-194-RAC-IC-9505-0.8-1 |
| Data File | : YXC-1-194-RAC-IC-9505-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 10:17:55 |
| Date Processed | : 2024/3/16 10:35:31 |




(*rac*)-**3as**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.620 | 10.158 | 686376 | 13940064 | 49.657 |
| 2 | 11.592 | 11.225 | 635207 | 14132783 | 50.343 |
| Total | | | 1321583 | 28072847 | 100.000 |

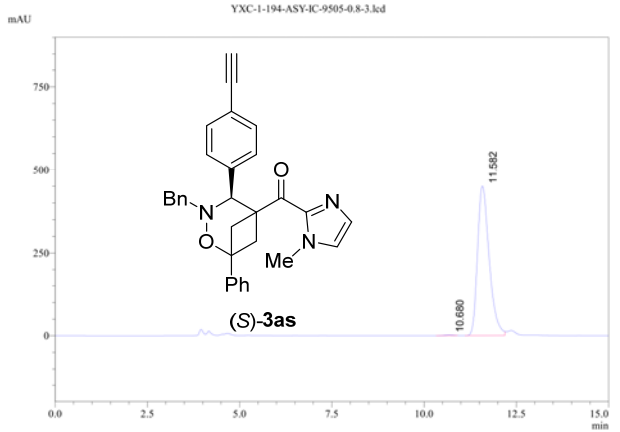
2024-03-16 11:20:11 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-194-ASY-IC-9505-0.8-1 |
| Sample ID | : YXC-1-194-ASY-IC-9505-0.8-1 |
| Data File | : YXC-1-194-ASY-IC-9505-0.8-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 10:54:53 |
| Date Processed | : 2024/3/16 11:19:44 |




(*S*)-**3as**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.680 | 10.325 | 1758 | 29106 | 0.293 |
| 2 | 11.582 | 11.108 | 449978 | 9896263 | 99.707 |
| Total | | | 451736 | 9925369 | 100.000 |

**Supplementary Figure 178.** HPLC spectra of (*rac*)-**3as** and (*S*)-**3as**

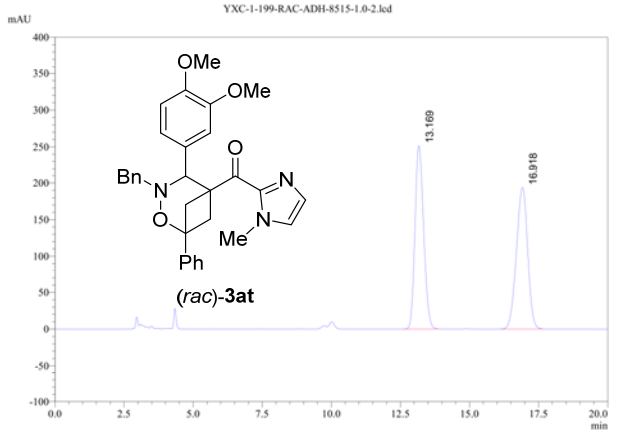
2024-03-14 15:47:51 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-199-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-199-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-199-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 14:59:45 |
| Date Processed | : 2024/3/14 15:23:40 |




(*rac*)-**3at**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.169 | 12.625 | 251515 | 5488511 | 50.000 |
| 2 | 16.918 | 16.133 | 193566 | 5488567 | 50.000 |
| Total | | | 445081 | 10977078 | 100.000 |

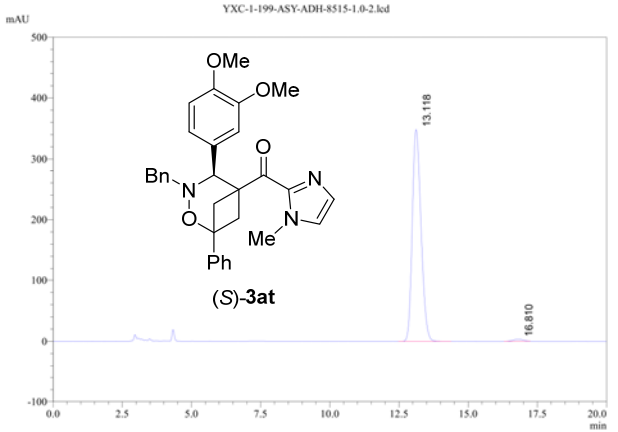
2024-03-14 15:48:15 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-199-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-199-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-199-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/14 15:24:40 |
| Date Processed | : 2024/3/14 15:47:07 |

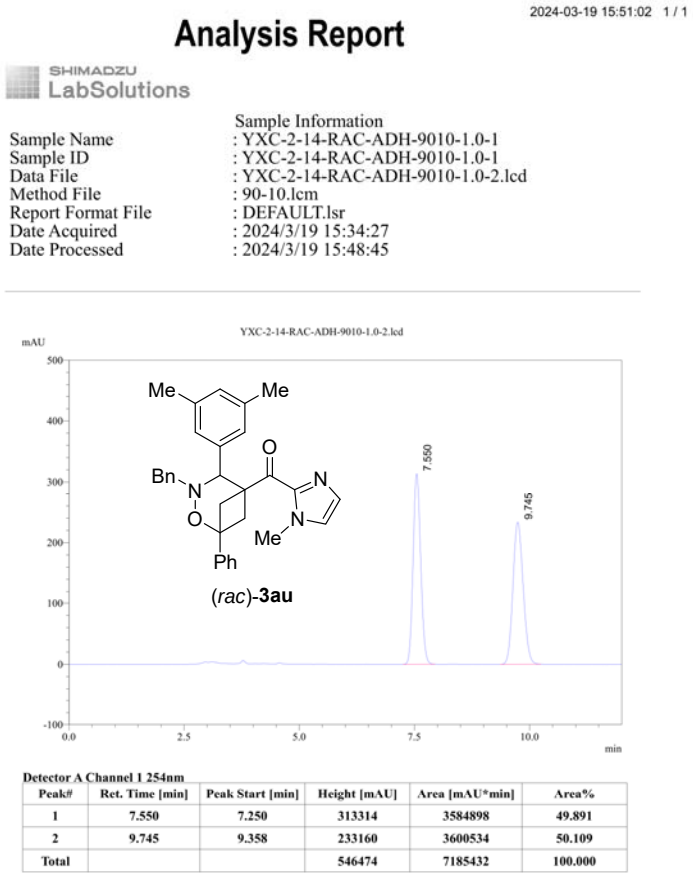



(*S*)-**3at**

Detector A Channel 1 254nm

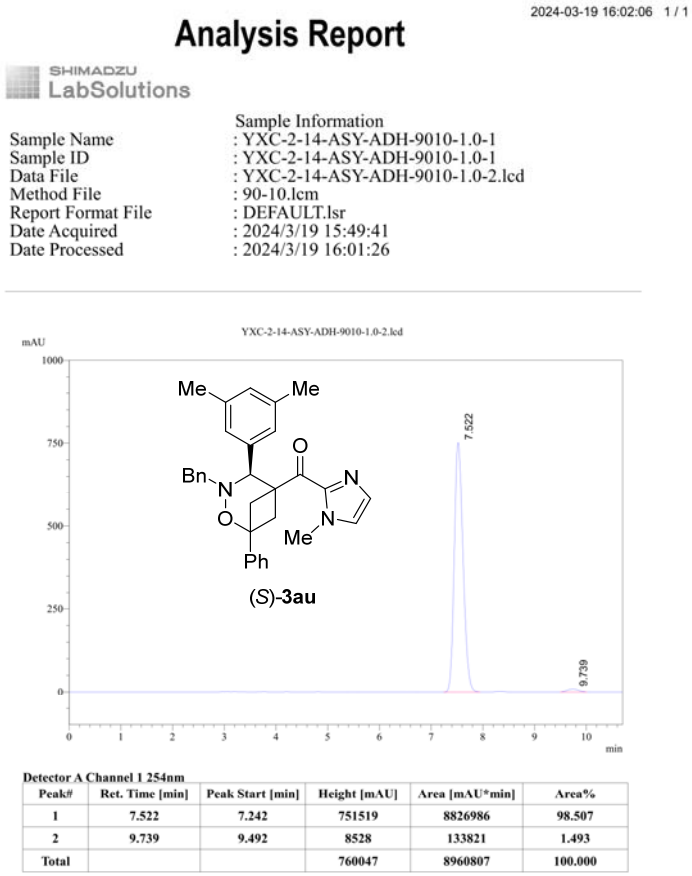
| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.118 | 12.475 | 348438 | 7667272 | 98.875 |
| 2 | 16.810 | 16.300 | 3319 | 87214 | 1.125 |
| Total | | | 351757 | 7754486 | 100.000 |

**Supplementary Figure 179.** HPLC spectra of (*rac*)-**3at** and (*S*)-**3at**




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.550 | 7.250 | 313314 | 3584898 | 49.891 |
| 2 | 9.745 | 9.358 | 233160 | 3600534 | 50.109 |
| Total | | | 546474 | 7185432 | 100.000 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.522 | 7.242 | 751519 | 8826986 | 98.507 |
| 2 | 9.739 | 9.492 | 8528 | 133821 | 1.493 |
| Total | | | 760047 | 8960807 | 100.000 |

**Supplementary Figure 180.** HPLC spectra of (*rac*)-**3au** and (*S*)-**3au**

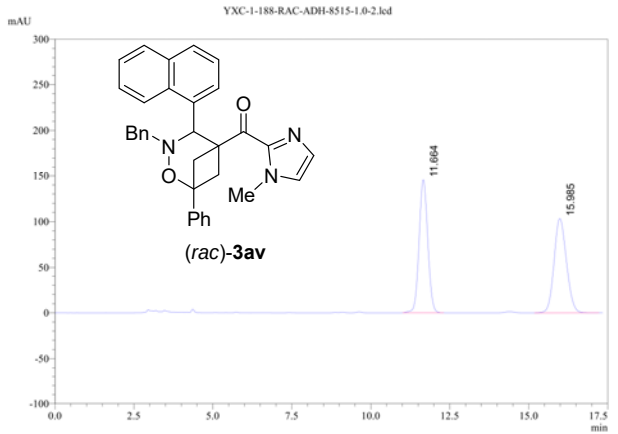
2024-03-08 11:05:09 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-188-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-188-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-1-188-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 10:43:19 |
| Date Processed | : 2024/3/8 11:04:40 |




(*rac*)-**3av**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.664 | 11.008 | 145567 | 2802690 | 49.799 |
| 2 | 15.985 | 15.183 | 103408 | 2825323 | 50.201 |
| Total | | | 248975 | 5628013 | 100.000 |

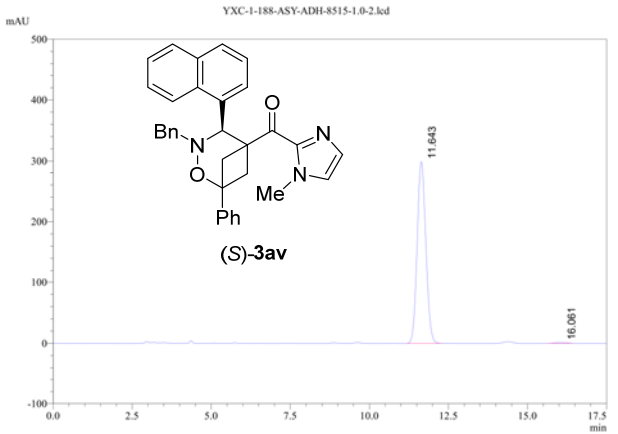
2024-03-08 11:20:13 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-188-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-1-188-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-1-188-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/8 11:01:39 |
| Date Processed | : 2024/3/8 11:19:59 |




(*S*)-**3av**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.643 | 11.158 | 299057 | 5705082 | 99.497 |
| 2 | 16.061 | 15.625 | 1163 | 28852 | 0.503 |
| Total | | | 300220 | 5733934 | 100.000 |

**Supplementary Figure 181.** HPLC spectra of (*rac*)-**3av** and (*S*)-**3av**

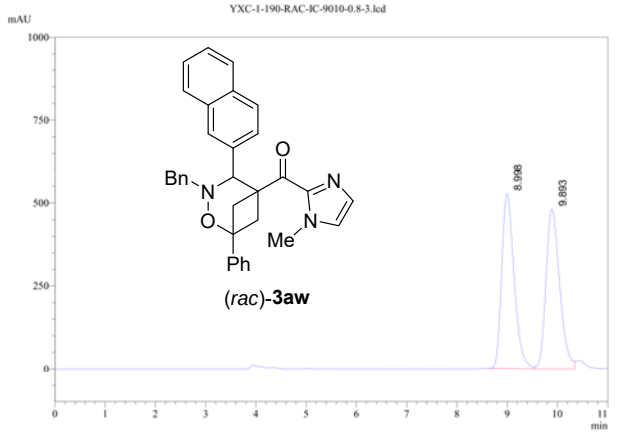
2024-03-15 22:03:09 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-190-RAC-IC-9010-0.8-1 |
| Sample ID | : YXC-1-190-RAC-IC-9010-0.8-1 |
| Data File | : YXC-1-190-RAC-IC-9010-0.8-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/15 21:50:51 |
| Date Processed | : 2024/3/15 22:02:50 |




(*rac*)-**3aw**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.998 | 8.642 | 527180 | 9050652 | 49.864 |
| 2 | 9.893 | 9.542 | 481278 | 9099950 | 50.136 |
| Total | | | 1008459 | 18150601 | 100.000 |

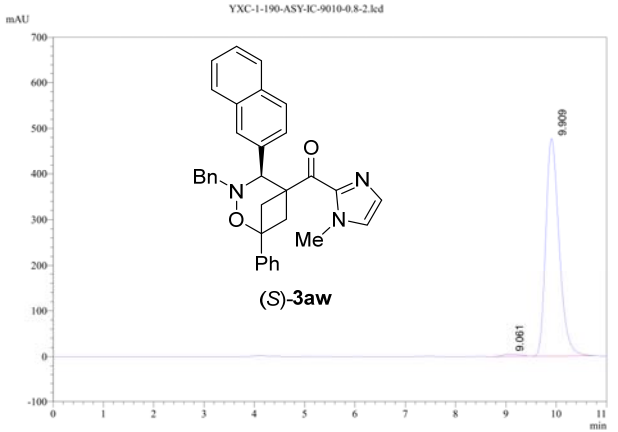
2024-03-15 21:52:58 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-190-ASY-IC-9010-0.8-1 |
| Sample ID | : YXC-1-190-ASY-IC-9010-0.8-1 |
| Data File | : YXC-1-190-ASY-IC-9010-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/15 21:36:17 |
| Date Processed | : 2024/3/15 21:52:27 |




(*S*)-**3aw**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.061 | 8.742 | 4897 | 101582 | 1.140 |
| 2 | 9.909 | 9.517 | 476848 | 8811454 | 98.860 |
| Total | | | 481745 | 8913036 | 100.000 |

**Supplementary Figure 182.** HPLC spectra of (*rac*)-**3aw** and (*S*)-**3aw**

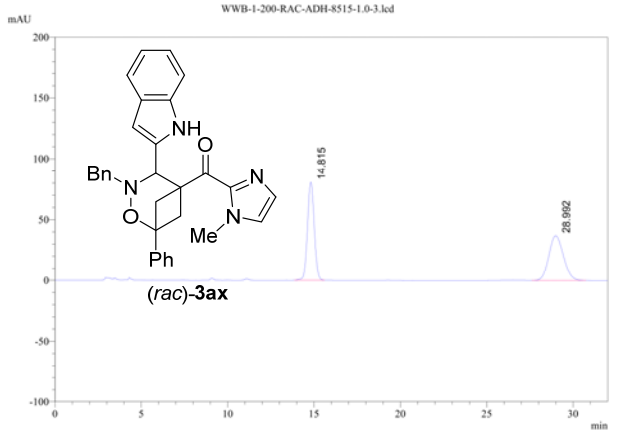
2024-03-28 10:09:52 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-200-RAC-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-200-RAC-ADH-8515-1.0-2 |
| Data File | : WWB-1-200-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 9:33:38 |
| Date Processed | : 2024/3/28 10:09:34 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.815 | 13.858 | 80685 | 2202970 | 50.342 |
| 2 | 28.992 | 27.608 | 36996 | 2173023 | 49.658 |
| Total | | | 117681 | 4375993 | 100.000 |

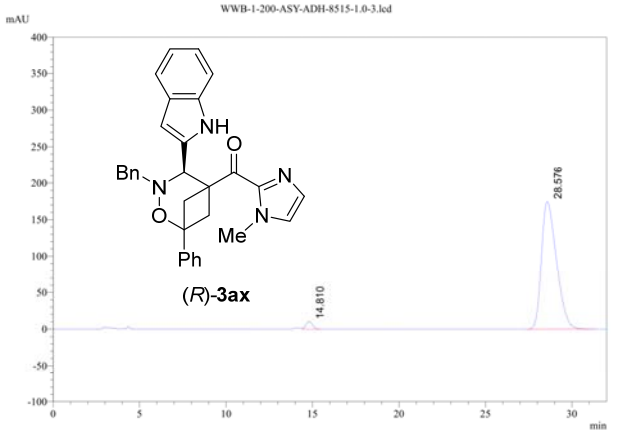
2024-03-28 10:42:08 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-200-ASY-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-200-ASY-ADH-8515-1.0-2 |
| Data File | : WWB-1-200-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 10:08:00 |
| Date Processed | : 2024/3/28 10:41:28 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.810 | 14.417 | 10410 | 277619 | 2.559 |
| 2 | 28.576 | 27.200 | 174527 | 10573168 | 97.441 |
| Total | | | 184938 | 10850787 | 100.000 |

**Supplementary Figure 183.** HPLC spectra of (*rac*)-**3ax** and (*R*)-**3ax**

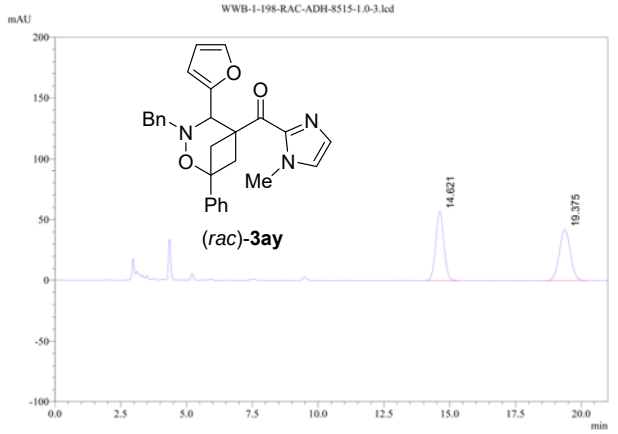
2024-03-27 21:55:49 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-198-RAC-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-198-RAC-ADH-8515-1.0-2 |
| Data File | : WWB-1-198-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/27 21:11:59 |
| Date Processed | : 2024/3/27 21:33:35 |




(*rac*)-**3ay**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.621 | 14.050 | 57087 | 1235613 | 50.064 |
| 2 | 19.375 | 18.600 | 42211 | 1232456 | 49.936 |
| Total | | | 99298 | 2468069 | 100.000 |

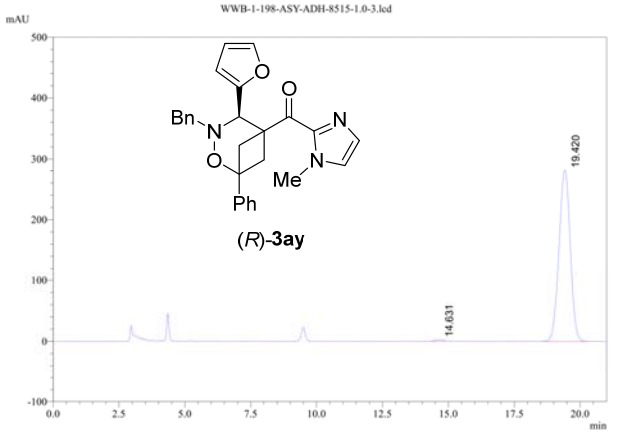
2024-03-27 21:56:43 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-198-ASY-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-198-ASY-ADH-8515-1.0-2 |
| Data File | : WWB-1-198-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/27 21:34:28 |
| Date Processed | : 2024/3/27 21:56:26 |




(*R*)-**3ay**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 14.631 | 14.342 | 2359 | 43221 | 0.515 |
| 2 | 19.420 | 18.567 | 281642 | 8352376 | 99.485 |
| Total | | | 284001 | 8395597 | 100.000 |

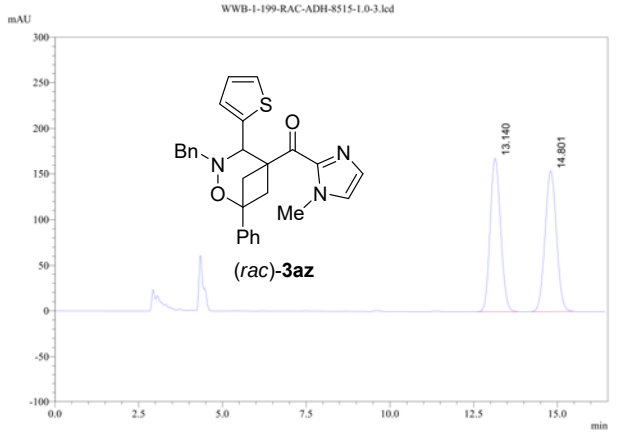
**Supplementary Figure 184.** HPLC spectra of (*rac*)-**3ay** and (*R*)-**3ay**

2024-03-28 09:15:31 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : WWB-1-199-RAC-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-199-RAC-ADH-8515-1.0-2 |
| Data File | : WWB-1-199-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 8:54:41 |
| Date Processed | : 2024/3/28 9:11:44 |




(*rac*)-**3az**

Detector A Channel 1 254nm

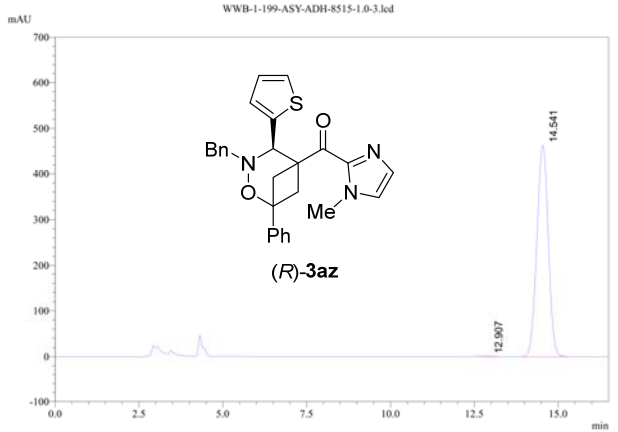
| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.140 | 12.600 | 168497 | 3655273 | 49.941 |
| 2 | 14.801 | 14.225 | 153936 | 3663928 | 50.059 |
| Total | | | 322434 | 7319201 | 100.000 |

2024-03-28 09:32:26 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : WWB-1-199-ASY-ADH-8515-1.0-2 |
| Sample ID | : WWB-1-199-ASY-ADH-8515-1.0-2 |
| Data File | : WWB-1-199-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 9:12:49 |
| Date Processed | : 2024/3/28 9:32:00 |




(*R*)-**3az**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.907 | 12.533 | 799 | 15858 | 0.145 |
| 2 | 14.541 | 13.842 | 463538 | 10925145 | 99.855 |
| Total | | | 464337 | 10941004 | 100.000 |

**Supplementary Figure 185.** HPLC spectra of (*rac*)-**3az** and (*R*)-**3az**

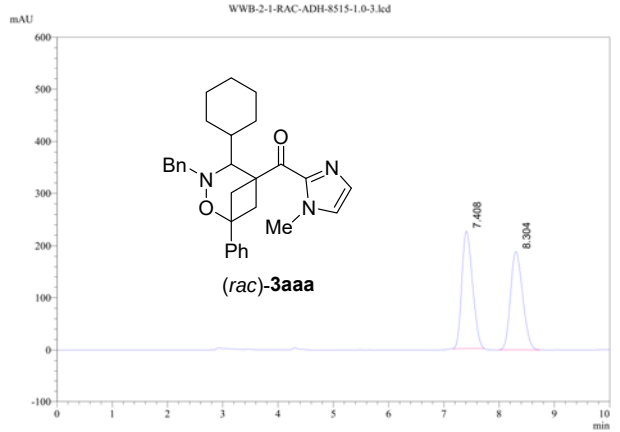
2024-04-24 10:27:16 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-1-RAC-ADH-8515-1.0-2 |
| Sample ID | : WWB-2-1-RAC-ADH-8515-1.0-2 |
| Data File | : WWB-2-1-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 10:43:10 |
| Date Processed | : 2024/3/28 11:02:12 |




(*rac*)-**3aaa**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.408 | 7.158 | 225273 | 3025053 | 51.303 |
| 2 | 8.304 | 7.992 | 188617 | 2871408 | 48.697 |
| Total | | | 413890 | 5896462 | 100.000 |

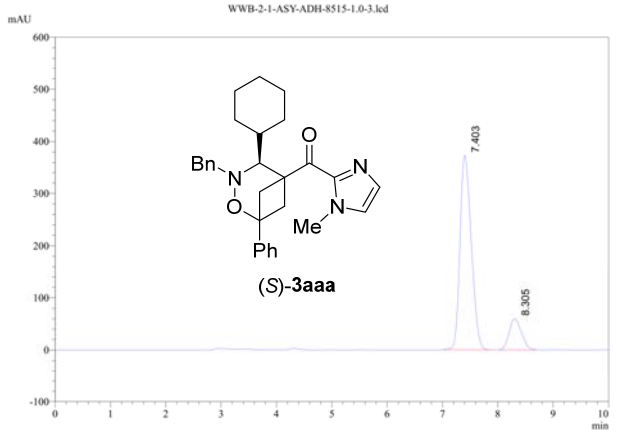
2024-04-24 10:27:30 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-1-ASY-ADH-8515-1.0-2 |
| Sample ID | : WWB-2-1-ASY-ADH-8515-1.0-2 |
| Data File | : WWB-2-1-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/28 11:03:03 |
| Date Processed | : 2024/3/28 11:14:58 |

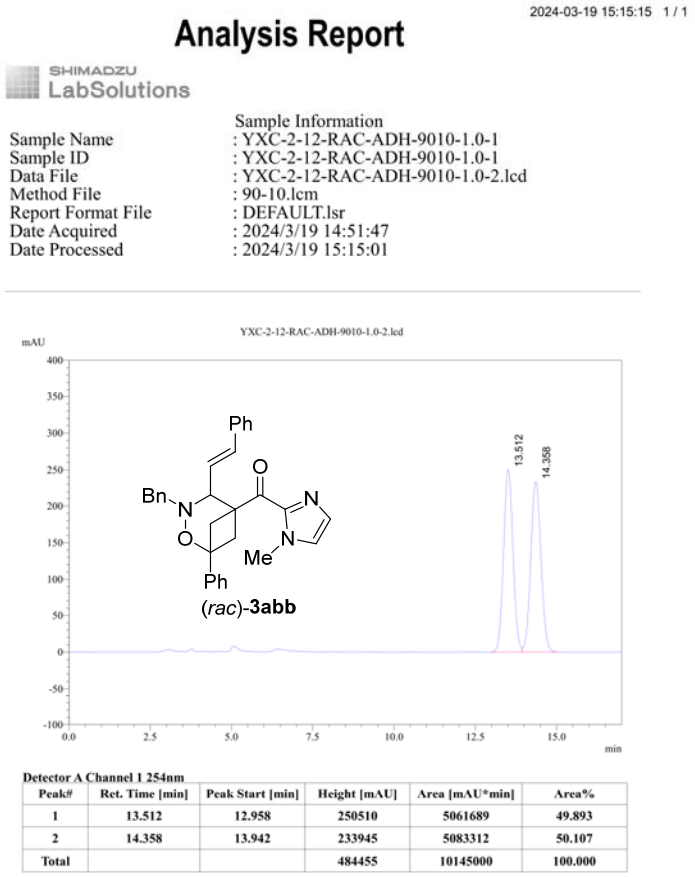



(*S*)-**3aaa**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.403 | 7.008 | 373312 | 5284383 | 85.203 |
| 2 | 8.305 | 8.017 | 59607 | 917696 | 14.797 |
| Total | | | 432919 | 6202079 | 100.000 |

**Supplementary Figure 186.** HPLC spectra of (*rac*)-**3aaa** and (*S*)-**3aaa**



2024-03-19 15:15:15 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

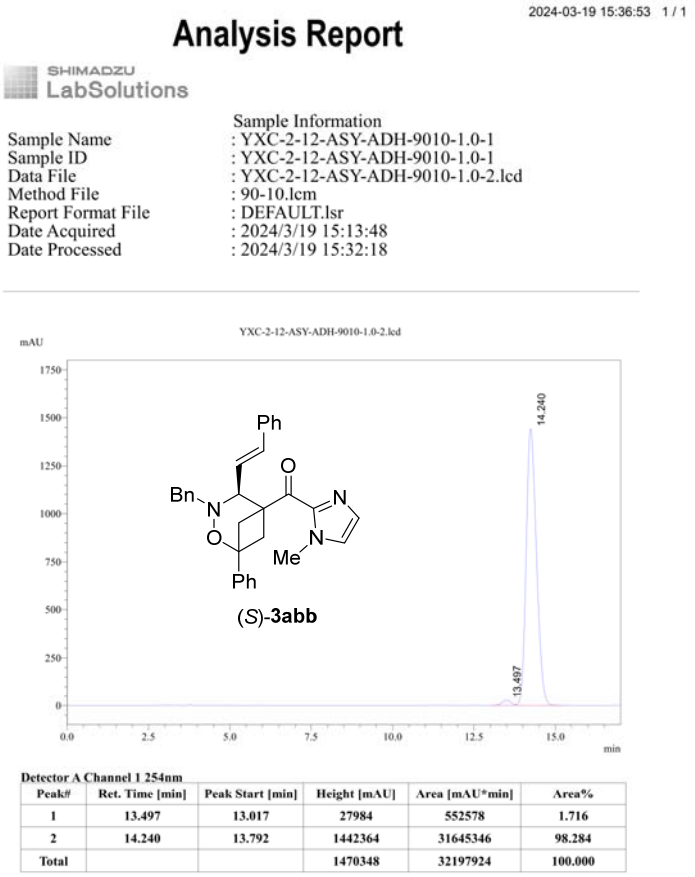
Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-12-RAC-ADH-9010-1.0-1 |
| Sample ID | : YXC-2-12-RAC-ADH-9010-1.0-1 |
| Data File | : YXC-2-12-RAC-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/19 14:51:47 |
| Date Processed | : 2024/3/19 15:15:01 |



Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.512 | 12.958 | 250510 | 5061689 | 49.893 |
| 2 | 14.358 | 13.942 | 233945 | 5083312 | 50.107 |
| Total | | | 484455 | 10145000 | 100.000 |



2024-03-19 15:36:53 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-12-ASY-ADH-9010-1.0-1 |
| Sample ID | : YXC-2-12-ASY-ADH-9010-1.0-1 |
| Data File | : YXC-2-12-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/19 15:13:48 |
| Date Processed | : 2024/3/19 15:32:18 |



Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 13.497 | 13.017 | 27984 | 552578 | 1.716 |
| 2 | 14.240 | 13.792 | 1442364 | 31645346 | 98.284 |
| Total | | | 1470348 | 32197924 | 100.000 |

**Supplementary Figure 187.** HPLC spectra of (*rac*)-**3abb** and (*S*)-**3abb**

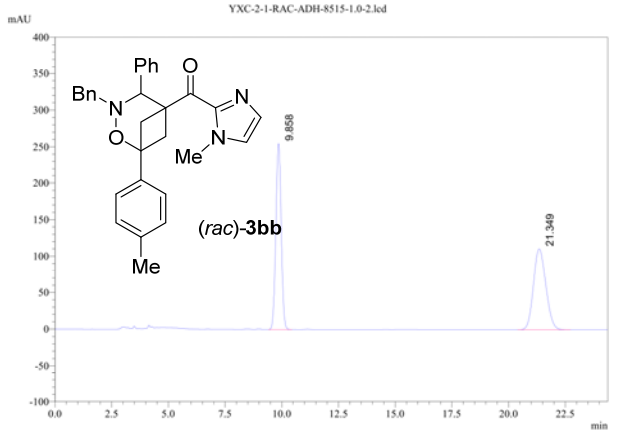
2024-03-20 18:43:49 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-1-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-1-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-2-1-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/20 14:31:36 |
| Date Processed | : 2024/3/20 14:57:27 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.858 | 9.408 | 254896 | 4205405 | 50.024 |
| 2 | 21.349 | 20.400 | 110903 | 4201438 | 49.976 |
| Total | | | 365799 | 8406843 | 100.000 |

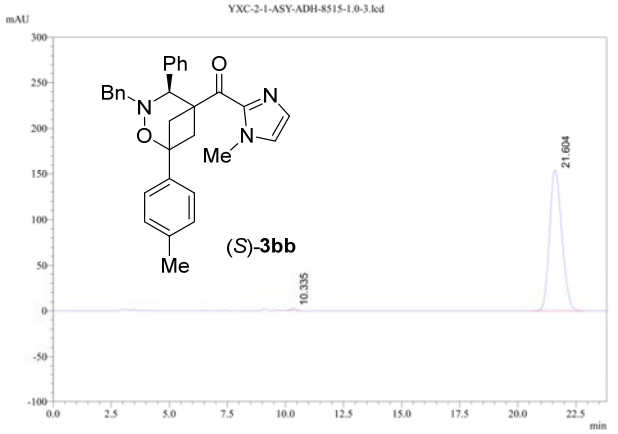
2024-03-20 18:44:18 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-1-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-1-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-2-1-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/20 17:50:04 |
| Date Processed | : 2024/3/20 18:14:48 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.335 | 10.058 | 2695 | 38841 | 0.677 |
| 2 | 21.604 | 20.625 | 154136 | 5697163 | 99.323 |
| Total | | | 156831 | 5736004 | 100.000 |

**Supplementary Figure 188.** HPLC spectra of (*rac*)-**3bb** and (*S*)-**3bb**

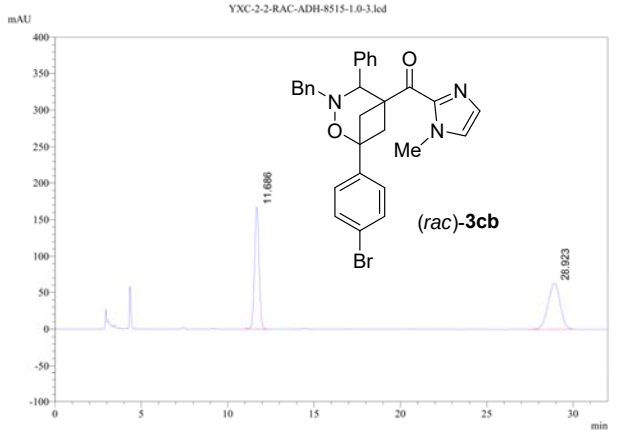
2024-03-18 20:50:39 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-2-RAC-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-2-RAC-ADH-8515-1.0-2 |
| Data File | : YXC-2-2-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/18 20:07:47 |
| Date Processed | : 2024/3/18 20:48:05 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.686 | 11.000 | 167007 | 3040222 | 50.060 |
| 2 | 28.923 | 27.583 | 62902 | 3032949 | 49.940 |
| Total | | | 229909 | 6073171 | 100.000 |

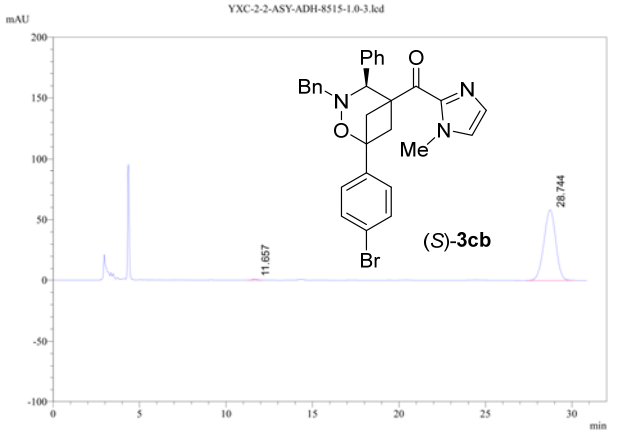
2024-03-18 21:20:40 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

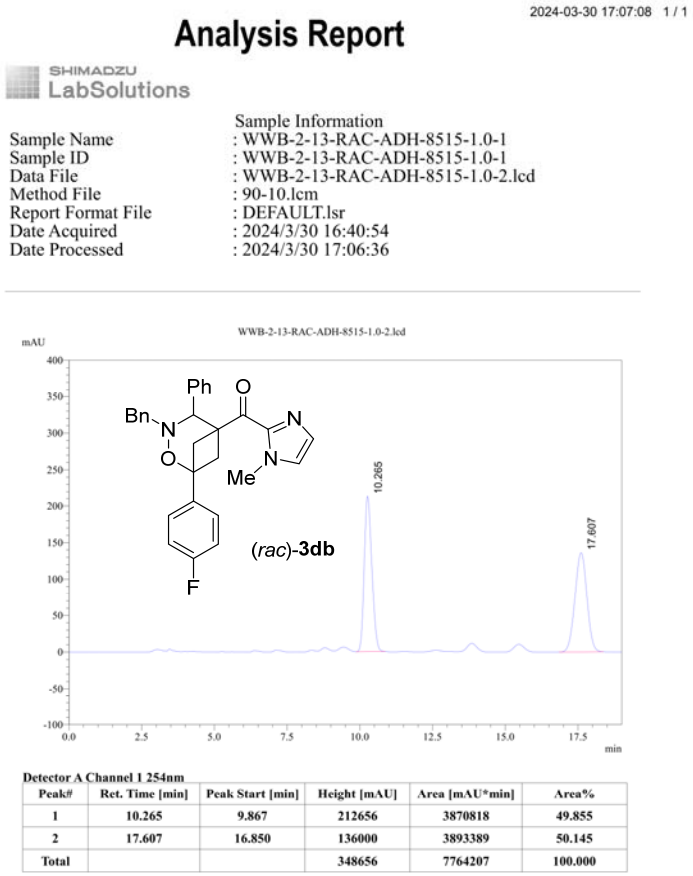
| | |
|---|---|
| Sample Name | : YXC-2-2-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-2-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-2-2-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/18 20:48:56 |
| Date Processed | : 2024/3/18 21:20:20 |

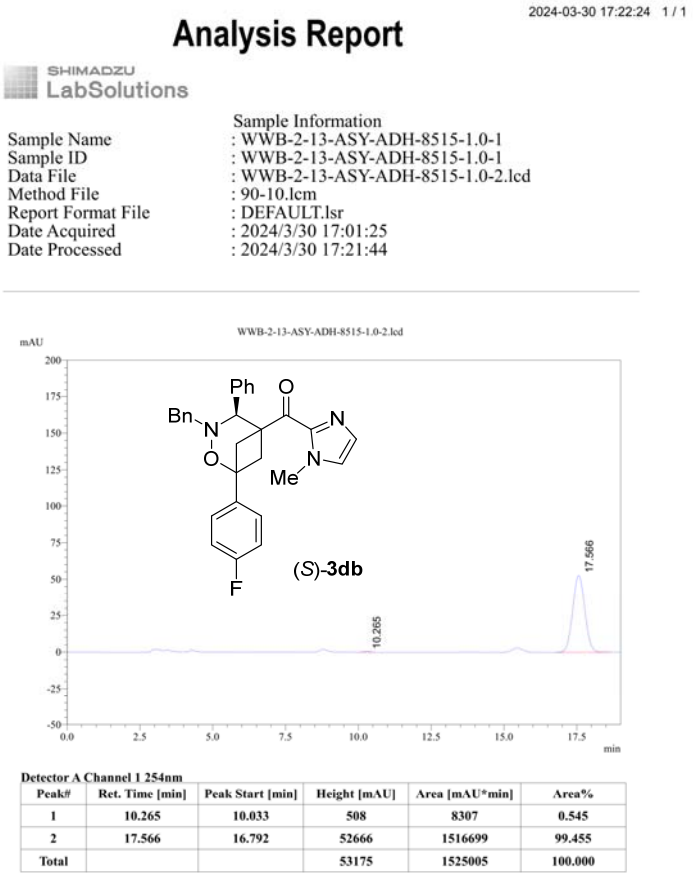



Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 11.657 | 11.217 | 863 | 16314 | 0.582 |
| 2 | 28.744 | 27.350 | 58084 | 2785904 | 99.418 |
| Total | | | 58947 | 2802218 | 100.000 |

**Supplementary Figure 189.** HPLC spectra of (*rac*)-**3cb** and (*S*)-**3cb**




**Supplementary Figure 190.** HPLC spectra of (*rac*)-**3db** and (*S*)-**3db**

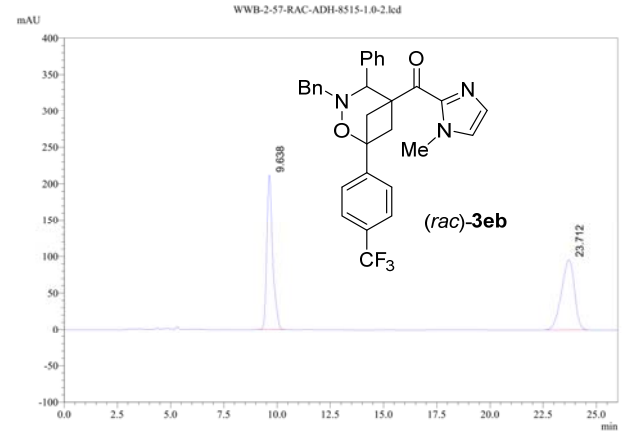
2024-05-07 16:10:29 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-57-RAC-ADH-8515-1.0-1 |
| Sample ID | : WWB-2-57-RAC-ADH-8515-1.0-1 |
| Data File | : WWB-2-57-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/5/7 14:54:53 |
| Date Processed | : 2024/5/7 16:09:54 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.638 | 9.067 | 211492 | 4045334 | 49.963 |
| 2 | 23.712 | 22.583 | 95526 | 4051254 | 50.037 |
| Total | | | 307019 | 8096588 | 100.000 |

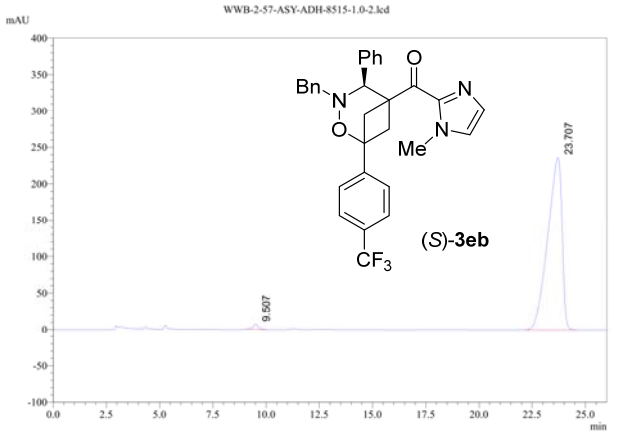
2024-05-07 16:10:43 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-57-ASY-ADH-8515-1.0-1 |
| Sample ID | : WWB-2-57-ASY-ADH-8515-1.0-1 |
| Data File | : WWB-2-57-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/5/7 15:40:44 |
| Date Processed | : 2024/5/7 16:09:31 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.507 | 9.050 | 6882 | 133805 | 1.203 |
| 2 | 23.707 | 22.108 | 236479 | 10990996 | 98.797 |
| Total | | | 243361 | 11124800 | 100.000 |

**Supplementary Figure 191.** HPLC spectra of (*rac*)-**3eb** and (*S*)-**3eb**

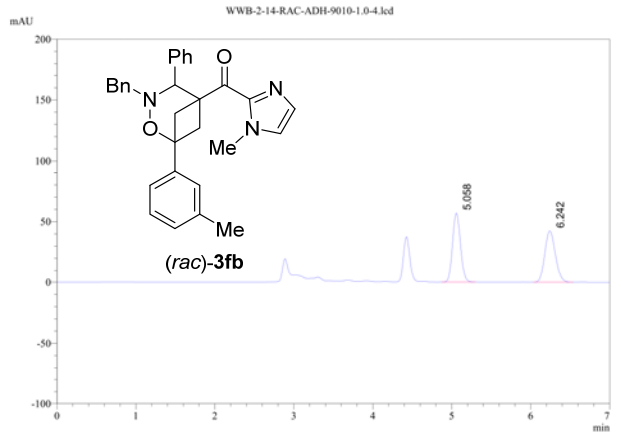
2024-04-02 15:21:37 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-14-RAC-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-14-RAC-ADH-9010-1.0-1 |
| Data File | : WWB-2-14-RAC-ADH-9010-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/2 15:11:08 |
| Date Processed | : 2024/4/2 15:21:00 |




(*rac*)-**3fb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.058 | 4.875 | 56902 | 399463 | 50.169 |
| 2 | 6.242 | 6.033 | 42483 | 396773 | 49.831 |
| Total | | | 99385 | 796236 | 100.000 |

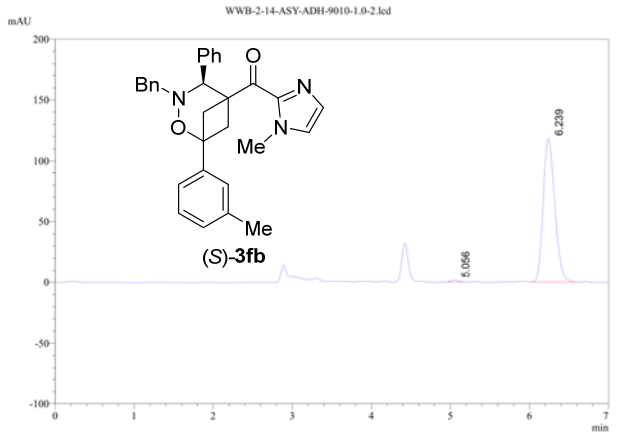
2024-04-02 15:27:43 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-14-ASY-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-14-ASY-ADH-9010-1.0-1 |
| Data File | : WWB-2-14-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/2 15:19:13 |
| Date Processed | : 2024/4/2 15:27:34 |




(*S*)-**3fb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.056 | 4.967 | 1444 | 8995 | 0.742 |
| 2 | 6.239 | 6.008 | 118292 | 1203188 | 99.258 |
| Total | | | 119736 | 1212183 | 100.000 |

**Supplementary Figure 192.** HPLC spectra of (*rac*)-**3fb** and (*S*)-**3fb**

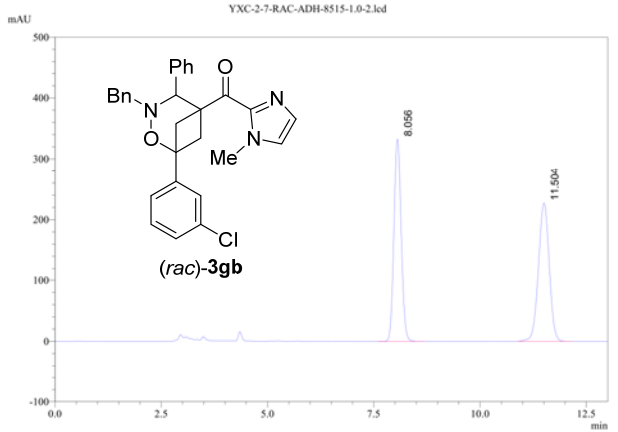
2024-03-20 18:45:08 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-7-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-7-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-2-7-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/20 14:56:49 |
| Date Processed | : 2024/3/20 15:17:10 |




(*rac*)-**3gb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.056 | 7.600 | 332645 | 3943502 | 49.607 |
| 2 | 11.504 | 10.867 | 227063 | 4006009 | 50.393 |
| Total | | | 559708 | 7949511 | 100.000 |

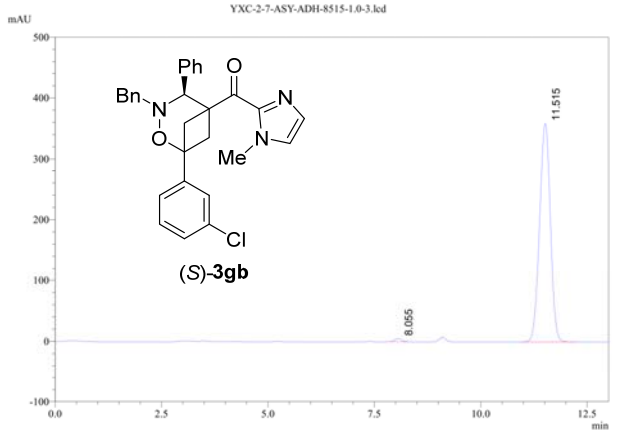
2024-03-20 18:59:40 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-7-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-7-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-2-7-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/20 18:41:20 |
| Date Processed | : 2024/3/20 18:59:31 |




(*S*)-**3gb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.055 | 7.867 | 5434 | 61607 | 0.964 |
| 2 | 11.515 | 10.942 | 359239 | 6328886 | 99.036 |
| Total | | | 364673 | 6390493 | 100.000 |

**Supplementary Figure 193.** HPLC spectra of (*rac*)-**3gb** and (*S*)-**3gb**

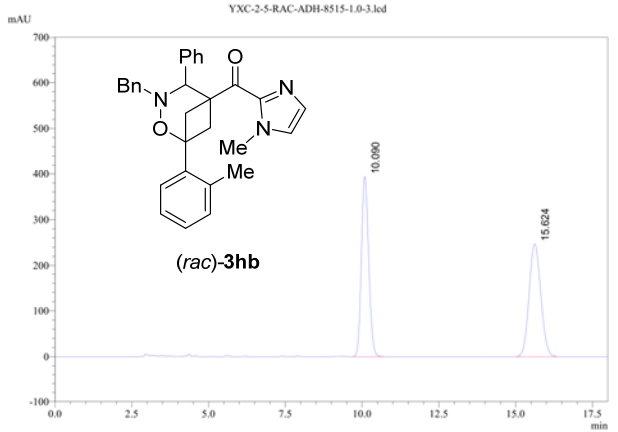
2024-03-18 21:45:14 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-5-RAC-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-5-RAC-ADH-8515-1.0-2 |
| Data File | : YXC-2-5-RAC-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/18 21:22:14 |
| Date Processed | : 2024/3/18 21:44:49 |




(*rac*)-**3hb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.090 | 9.642 | 394073 | 6504813 | 49.974 |
| 2 | 15.624 | 14.958 | 247342 | 6511606 | 50.026 |
| Total | | | 641415 | 13016419 | 100.000 |

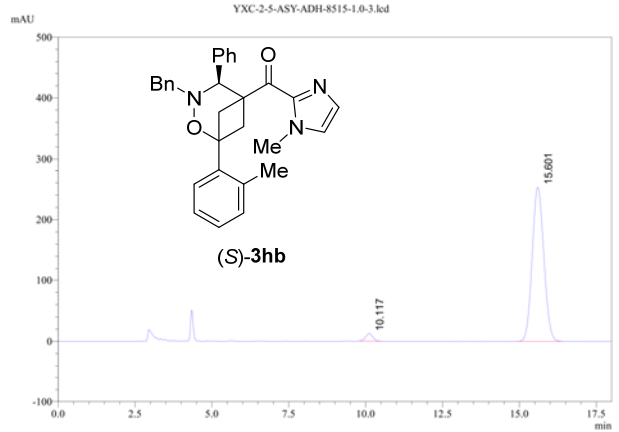
2024-03-18 22:02:41 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-5-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-2-5-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-2-5-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/18 21:43:29 |
| Date Processed | : 2024/3/18 22:02:21 |

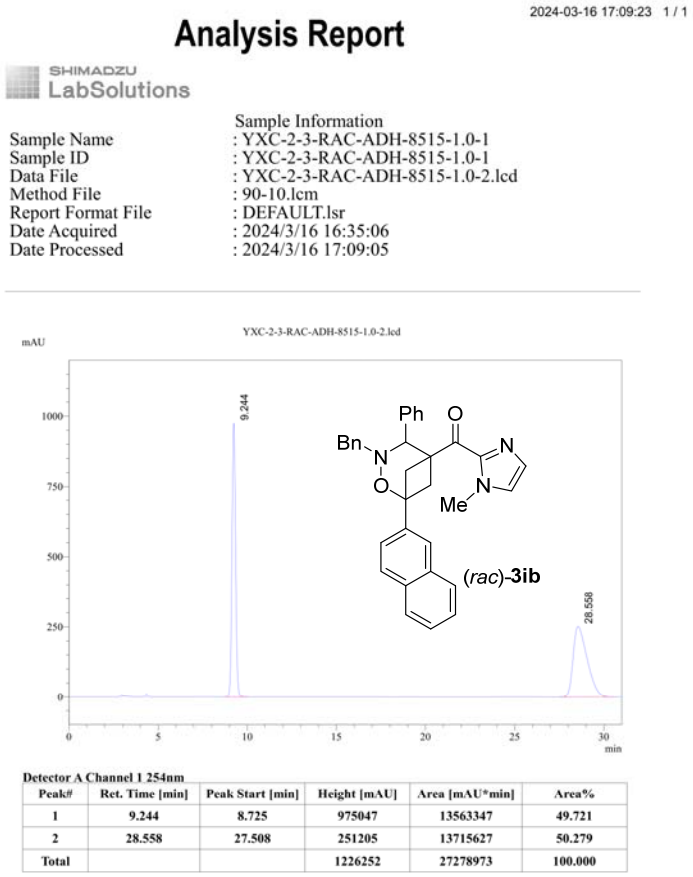



(*S*)-**3hb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 10.117 | 9.783 | 12243 | 198668 | 2.894 |
| 2 | 15.601 | 14.900 | 253099 | 6665021 | 97.106 |
| Total | | | 265342 | 6863688 | 100.000 |

**Supplementary Figure 194.** HPLC spectra of (*rac*)-**3hb** and (*S*)-**3hb**



2024-03-16 17:09:23 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

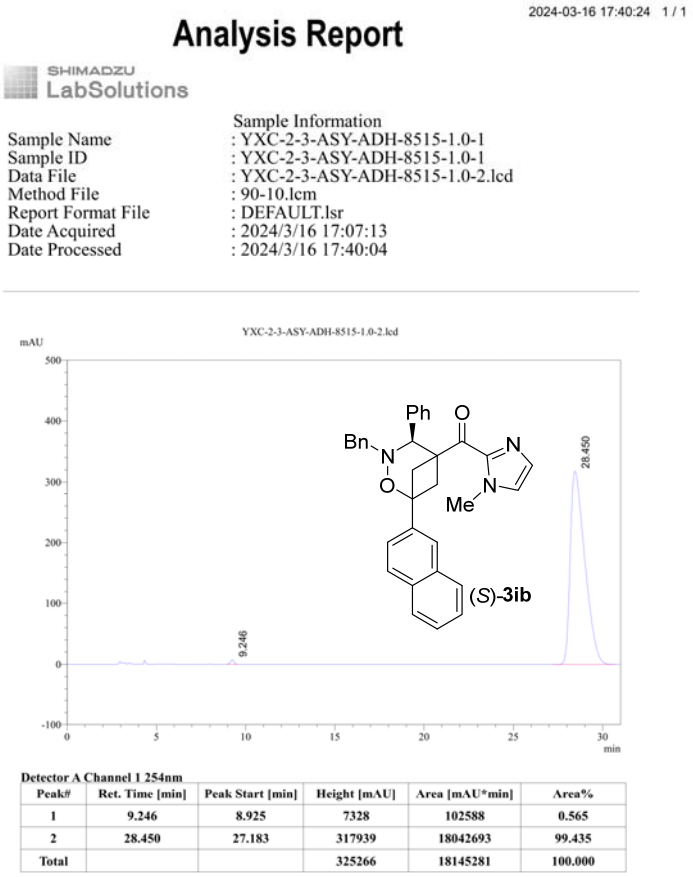
Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-3-RAC-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-3-RAC-ADH-8515-1.0-1 |
| Data File | : YXC-2-3-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 16:35:06 |
| Date Processed | : 2024/3/16 17:09:05 |



Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.244 | 8.725 | 975047 | 13563347 | 49.721 |
| 2 | 28.558 | 27.508 | 251205 | 13715627 | 50.279 |
| Total | | | 1226252 | 27278973 | 100.000 |



2024-03-16 17:40:24 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-2-3-ASY-ADH-8515-1.0-1 |
| Sample ID | : YXC-2-3-ASY-ADH-8515-1.0-1 |
| Data File | : YXC-2-3-ASY-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/16 17:07:13 |
| Date Processed | : 2024/3/16 17:40:04 |



Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.246 | 8.925 | 7328 | 102588 | 0.565 |
| 2 | 28.450 | 27.183 | 317939 | 18042693 | 99.435 |
| Total | | | 325266 | 18145281 | 100.000 |

**Supplementary Figure 195.** HPLC spectra of (*rac*)-**3ib** and (*S*)-**3ib**

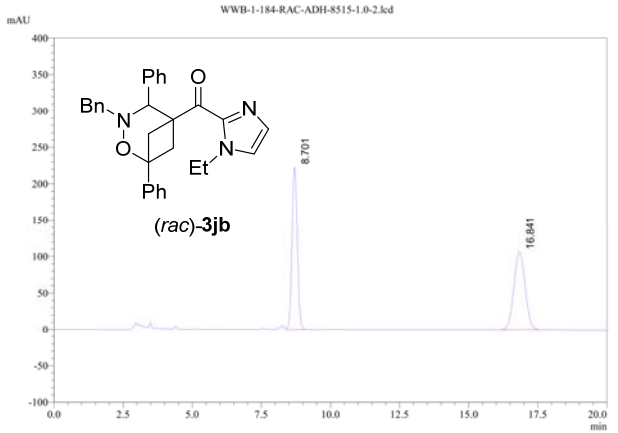
2024-02-28 14:19:44 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-184-RAC-ADH-8515-1.0-1 |
| Sample ID | : WWB-1-184-RAC-ADH-8515-1.0-1 |
| Data File | : WWB-1-184-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/2/28 10:36:28 |
| Date Processed | : 2024/2/28 10:58:30 |




(*rac*)-**3jb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.701 | 8.408 | 222841 | 2987634 | 49.968 |
| 2 | 16.841 | 16.150 | 106146 | 2991499 | 50.032 |
| Total | | | 328987 | 5979134 | 100.000 |

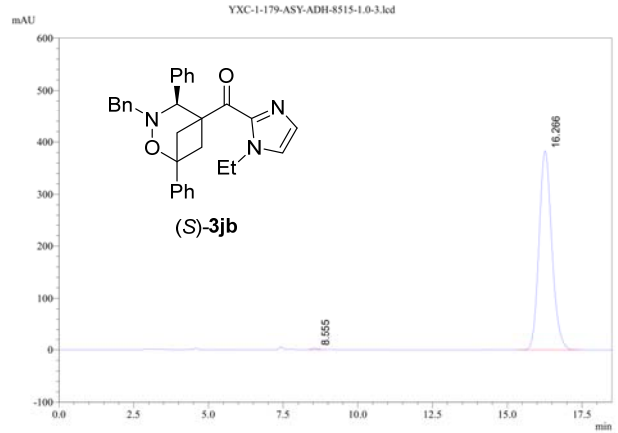
2024-03-06 17:27:55 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-179-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-179-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-179-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 17:07:40 |
| Date Processed | : 2024/3/6 17:27:06 |




(*S*)-**3jb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.555 | 8.333 | 3044 | 39418 | 0.343 |
| 2 | 16.266 | 15.367 | 382984 | 11453630 | 99.657 |
| Total | | | 386027 | 11493048 | 100.000 |

**Supplementary Figure 196.** HPLC spectra of (*rac*)-**3jb** and (*S*)-**3jb**

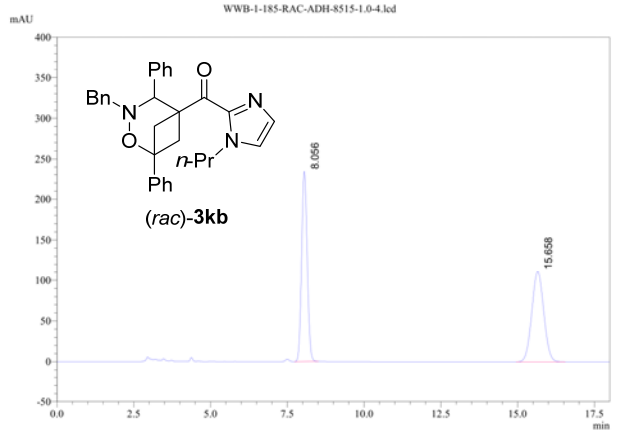
2024-02-28 15:55:12 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-185-RAC-ADH-8515-1.0-1 |
| Sample ID | : WWB-1-185-RAC-ADH-8515-1.0-1 |
| Data File | : WWB-1-185-RAC-ADH-8515-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/2/28 15:31:55 |
| Date Processed | : 2024/2/28 15:51:40 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.056 | 7.733 | 233959 | 2972618 | 49.765 |
| 2 | 15.658 | 14.950 | 110535 | 3000685 | 50.235 |
| Total | | | 344493 | 5973302 | 100.000 |

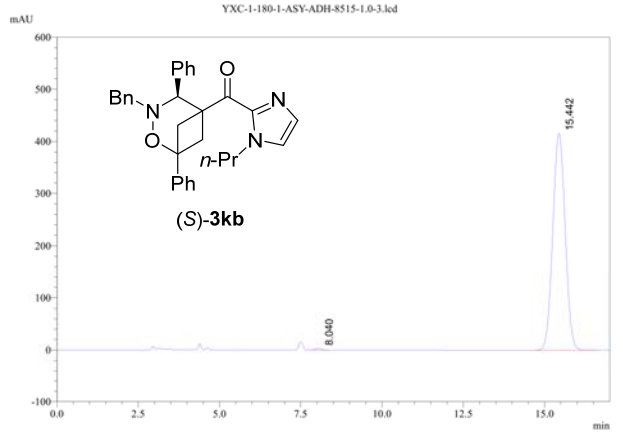
2024-03-06 19:07:58 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-180-1-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-180-1-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-180-1-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 18:48:59 |
| Date Processed | : 2024/3/6 19:07:23 |




Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 8.040 | 7.808 | 3758 | 45534 | 0.412 |
| 2 | 15.442 | 14.575 | 415868 | 10996378 | 99.588 |
| Total | | | 419626 | 11041912 | 100.000 |

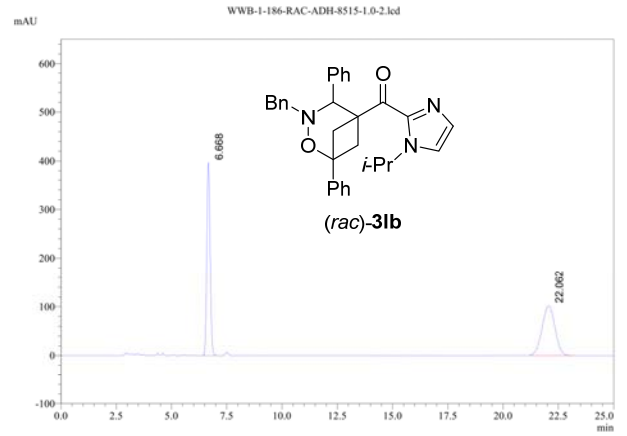
**Supplementary Figure 197.** HPLC spectra of (*rac*)-**3kb** and (*S*)-**3kb**

2024-02-28 16:52:30 1 / 1

## Analysis Report

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : WWB-1-186-RAC-ADH-8515-1.0-1 |
| Sample ID | : WWB-1-186-RAC-ADH-8515-1.0-1 |
| Data File | : WWB-1-186-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/2/28 15:52:28 |
| Date Processed | : 2024/2/28 16:18:53 |




(*rac*)-**3lb**

Detector A Channel 1 254nm

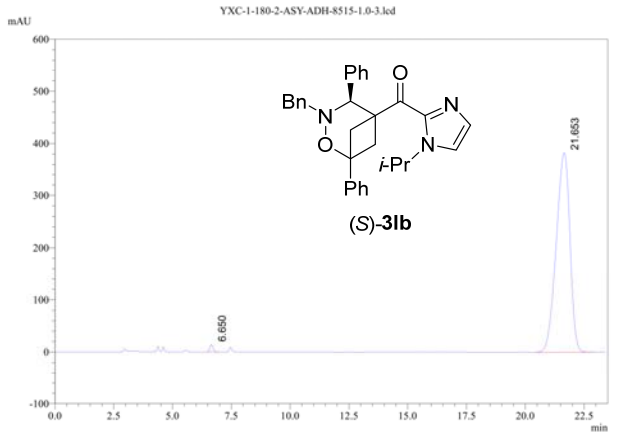
| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.668 | 6.375 | 396383 | 4130734 | 49.990 |
| 2 | 22.062 | 21.175 | 101756 | 4132374 | 50.010 |
| Total | | | 498140 | 8263108 | 100.000 |

2024-03-06 19:34:26 1 / 1

## Analysis Report

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : YXC-1-180-2-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-180-2-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-180-2-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 19:09:37 |
| Date Processed | : 2024/3/6 19:33:49 |




(*S*)-**3lb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.650 | 6.450 | 14209 | 144911 | 0.927 |
| 2 | 21.653 | 20.400 | 382571 | 15483960 | 99.073 |
| Total | | | 396780 | 15628871 | 100.000 |

**Supplementary Figure 198.** HPLC spectra of (*rac*)-**3lb** and (*S*)-**3lb**

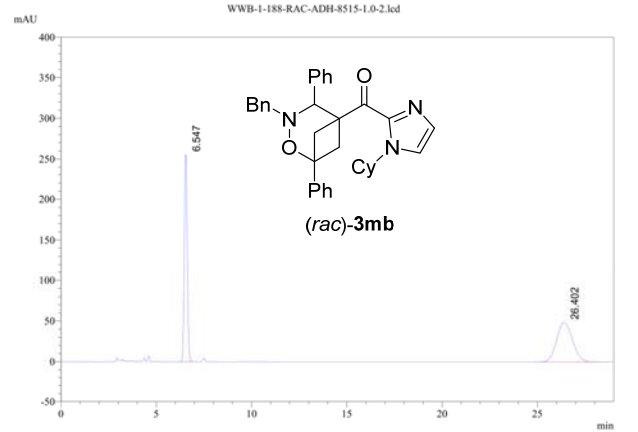
2024-02-28 18:30:18 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-1-188-RAC-ADH-8515-1.0-1 |
| Sample ID | : WWB-1-188-RAC-ADH-8515-1.0-1 |
| Data File | : WWB-1-188-RAC-ADH-8515-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/2/28 16:50:47 |
| Date Processed | : 2024/2/28 17:20:32 |




(*rac*)-**3mb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.547 | 6.183 | 255439 | 2746555 | 49.817 |
| 2 | 26.402 | 25.142 | 48448 | 2766750 | 50.183 |
| Total | | | 303887 | 5513306 | 100.000 |

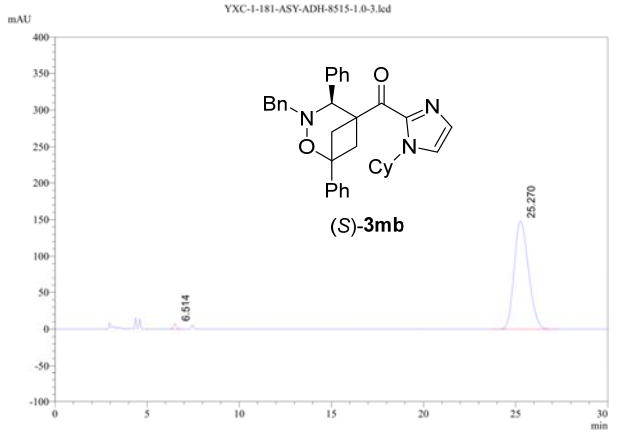
2024-03-06 20:08:11 1 / 1

## Analysis Report

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : YXC-1-181-ASY-ADH-8515-1.0-2 |
| Sample ID | : YXC-1-181-ASY-ADH-8515-1.0-2 |
| Data File | : YXC-1-181-ASY-ADH-8515-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/6 19:36:14 |
| Date Processed | : 2024/3/6 20:07:42 |




(*S*)-**3mb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.514 | 6.225 | 7080 | 72969 | 0.903 |
| 2 | 25.270 | 23.758 | 148442 | 8011080 | 99.097 |
| Total | | | 155522 | 8084050 | 100.000 |

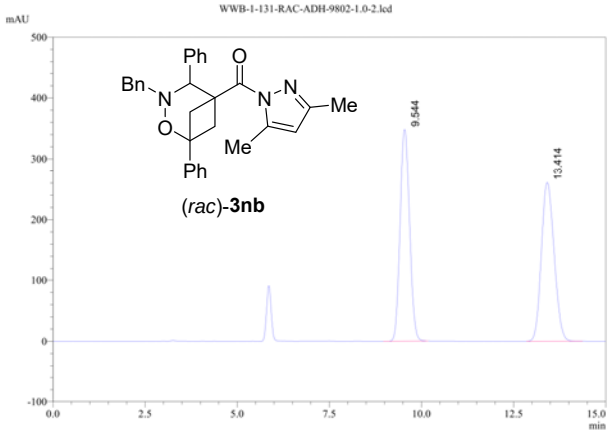
**Supplementary Figure 199.** HPLC spectra of (*rac*)-**3mb** and (*S*)-**3mb**

2024-03-25 19:12:50 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : WWB-1-131-RAC-ADH-9802-1.0-1 |
| Sample ID | : WWB-1-131-RAC-ADH-9802-1.0-1 |
| Data File | : WWB-1-131-RAC-ADH-9802-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2023/12/26 15:47:41 |
| Date Processed | : 2024/3/25 19:12:05 |




(*rac*)-**3nb**

Detector A Channel 1 254nm

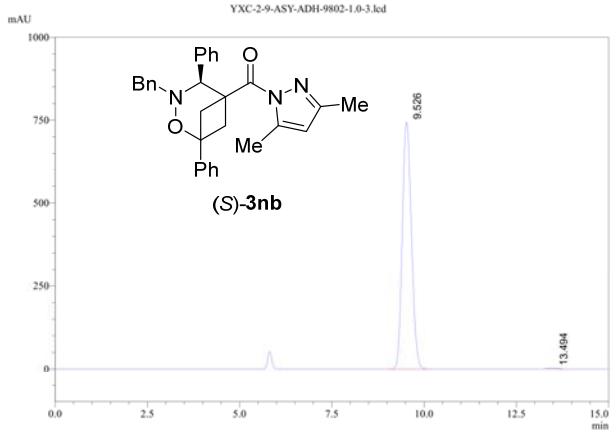
| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.544 | 8.967 | 348171 | 6236119 | 49.771 |
| 2 | 13.414 | 12.850 | 260692 | 6293387 | 50.229 |
| Total | | | 608863 | 12529506 | 100.000 |

2024-03-25 19:14:13 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

| Sample Information | |
|---|---|
| Sample Name | : YXC-2-9-ASY-ADH-9802-1.0-2 |
| Sample ID | : YXC-2-9-ASY-ADH-9802-1.0-2 |
| Data File | : YXC-2-9-ASY-ADH-9802-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/25 18:57:57 |
| Date Processed | : 2024/3/25 19:13:42 |




(*S*)-**3nb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.526 | 9.050 | 743690 | 12798511 | 99.604 |
| 2 | 13.494 | 13.250 | 2817 | 50840 | 0.396 |
| Total | | | 746507 | 12849351 | 100.000 |

**Supplementary Figure 200.** HPLC spectra of (*rac*)-**3nb** and (*S*)-**3nb**

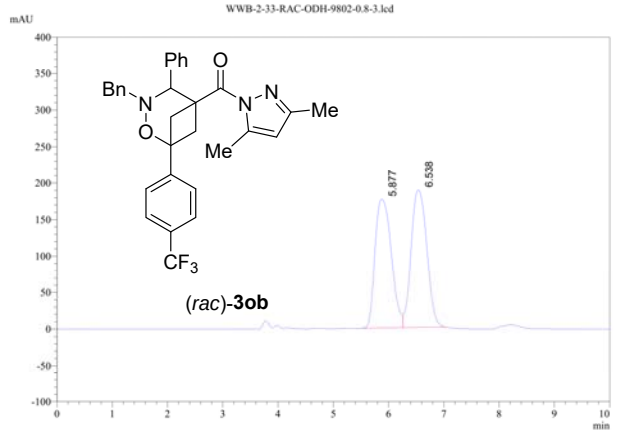
2024-04-18 16:23:17 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-33-RAC-ODH-9802-0.8-2 |
| Sample ID | : WWB-2-33-RAC-ODH-9802-0.8-2 |
| Data File | : WWB-2-33-RAC-ODH-9802-0.8-3.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/18 15:59:14 |
| Date Processed | : 2024/4/18 16:13:27 |




(*rac*)-**3ob**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.877 | 5.492 | 176209 | 3620315 | 49.375 |
| 2 | 6.538 | 6.258 | 188121 | 3711981 | 50.625 |
| Total | | | 364330 | 7332295 | 100.000 |

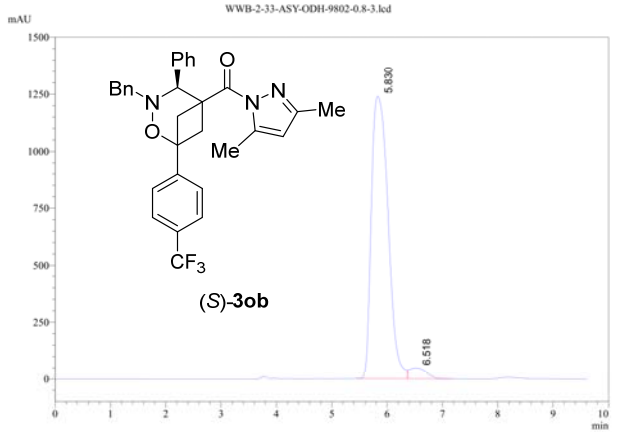
2024-04-18 16:23:34 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-33-ASY-ODH-9802-0.8-2 |
| Sample ID | : WWB-2-33-ASY-ODH-9802-0.8-2 |
| Data File | : WWB-2-33-ASY-ODH-9802-0.8-3.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/18 16:11:51 |
| Date Processed | : 2024/4/18 16:22:32 |




(*S*)-**3ob**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.830 | 5.433 | 1238764 | 25986508 | 96.127 |
| 2 | 6.518 | 6.367 | 47924 | 1047103 | 3.873 |
| Total | | | 1286688 | 27033610 | 100.000 |

**Supplementary Figure 201.** HPLC spectra of (*rac*)-**3ob** and (*S*)-**3ob**

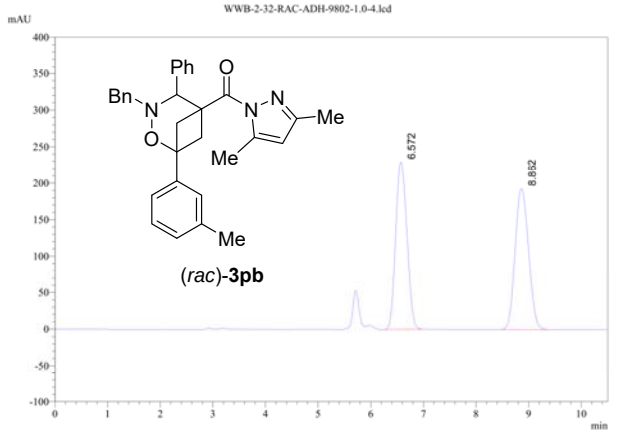
2024-04-22 11:20:21 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-32-RAC-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-32-RAC-ADH-9802-1.0-1 |
| Data File | : WWB-2-32-RAC-ADH-9802-1.0-4.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/22 11:06:23 |
| Date Processed | : 2024/4/22 11:17:22 |




(*rac*)-**3pb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.572 | 6.267 | 229194 | 3403634 | 49.882 |
| 2 | 8.862 | 8.475 | 192796 | 3419714 | 50.118 |
| Total | | | 421990 | 6823348 | 100.000 |

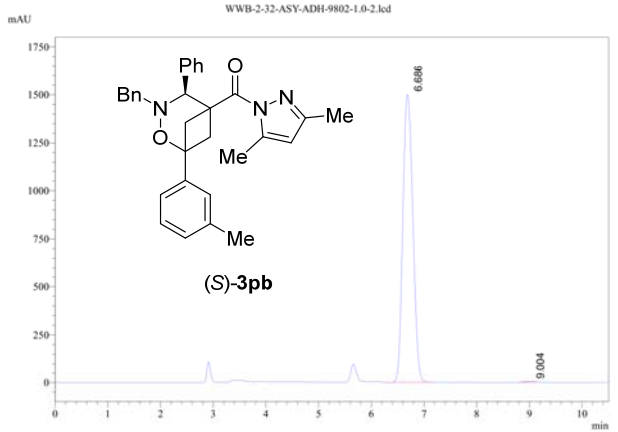
2024-04-22 11:30:14 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-32-ASY-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-32-ASY-ADH-9802-1.0-1 |
| Data File | : WWB-2-32-ASY-ADH-9802-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/22 11:18:27 |
| Date Processed | : 2024/4/22 11:29:45 |




(*S*)-**3pb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 6.686 | 6.342 | 1500103 | 19823799 | 99.753 |
| 2 | 9.004 | 8.825 | 4223 | 49039 | 0.247 |
| Total | | | 1504326 | 19872838 | 100.000 |

**Supplementary Figure 202.** HPLC spectra of (*rac*)-**3pb** and (*S*)-**3pb**

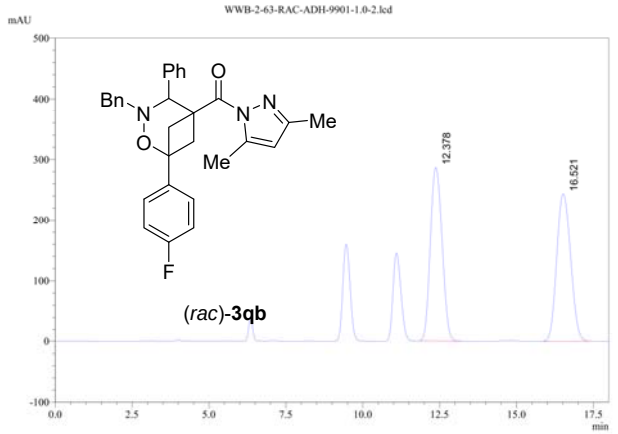
2024-05-10 11:05:17 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-63-RAC-ADH-9901-1.0-1 |
| Sample ID | : WWB-2-63-RAC-ADH-9901-1.0-1 |
| Data File | : WWB-2-63-RAC-ADH-9901-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/5/10 10:02:02 |
| Date Processed | : 2024/5/10 10:22:29 |




(*rac*)-**3qb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.378 | 11.858 | 286561 | 7636129 | 49.858 |
| 2 | 16.521 | 15.858 | 243812 | 7679759 | 50.142 |
| Total | | | 530373 | 15315888 | 100.000 |

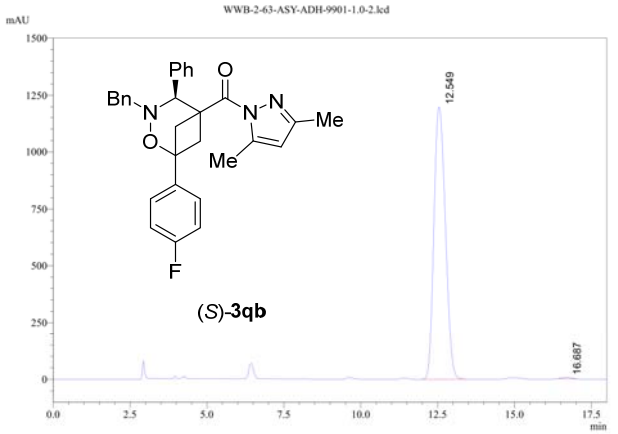
2024-05-10 11:05:35 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-63-ASY-ADH-9901-1.0-1 |
| Sample ID | : WWB-2-63-ASY-ADH-9901-1.0-1 |
| Data File | : WWB-2-63-ASY-ADH-9901-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/5/10 10:21:15 |
| Date Processed | : 2024/5/10 10:40:06 |




(*S*)-**3qb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.549 | 12.000 | 1198428 | 30917643 | 99.585 |
| 2 | 16.687 | 16.417 | 5994 | 128861 | 0.415 |
| Total | | | 1204422 | 31046505 | 100.000 |

**Supplementary Figure 203.** HPLC spectra of (*rac*)-**3qb** and (*S*)-**3qb**

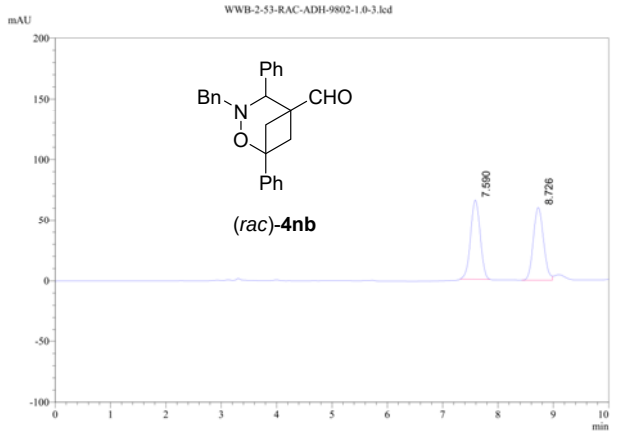
2024-04-29 20:15:20 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-53-RAC-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-53-RAC-ADH-9802-1.0-1 |
| Data File | : WWB-2-53-RAC-ADH-9802-1.0-3.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/29 19:51:46 |
| Date Processed | : 2024/4/29 20:02:25 |




(*rac*)-**4nb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.590 | 7.317 | 65377 | 786229 | 50.550 |
| 2 | 8.726 | 8.425 | 60167 | 769121 | 49.450 |
| Total | | | 125543 | 1555351 | 100.000 |

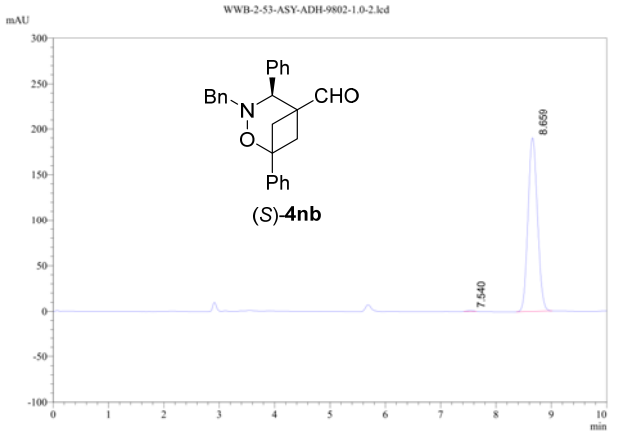
2024-04-29 20:15:41 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-53-ASY-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-53-ASY-ADH-9802-1.0-1 |
| Data File | : WWB-2-53-ASY-ADH-9802-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/29 20:03:15 |
| Date Processed | : 2024/4/29 20:14:23 |




(*S*)-**4nb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 7.540 | 7.417 | 922 | 7383 | 0.326 |
| 2 | 8.659 | 8.367 | 190471 | 2260587 | 99.674 |
| Total | | | 191393 | 2267970 | 100.000 |

**Supplementary Figure 204.** HPLC spectra of (*rac*)-**4nb** and (*S*)-**4nb**

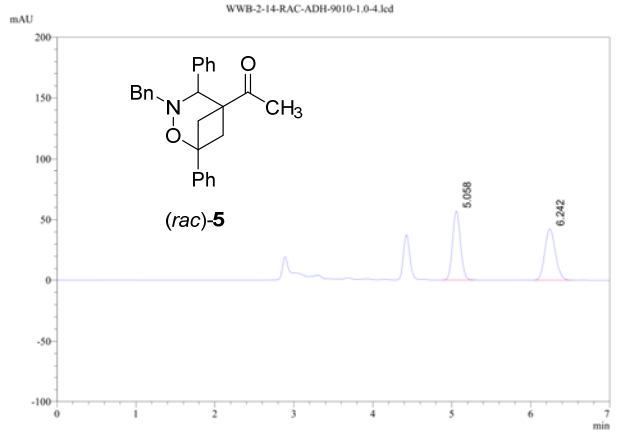
2024-04-02 15:21:37 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-14-RAC-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-14-RAC-ADH-9010-1.0-1 |
| Data File | : WWB-2-14-RAC-ADH-9010-1.0-4.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/2 15:11:08 |
| Date Processed | : 2024/4/2 15:21:00 |




(*rac*)-**5**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.058 | 4.875 | 56902 | 399463 | 50.169 |
| 2 | 6.242 | 6.033 | 42483 | 396773 | 49.831 |
| Total | | | 99385 | 796236 | 100.000 |

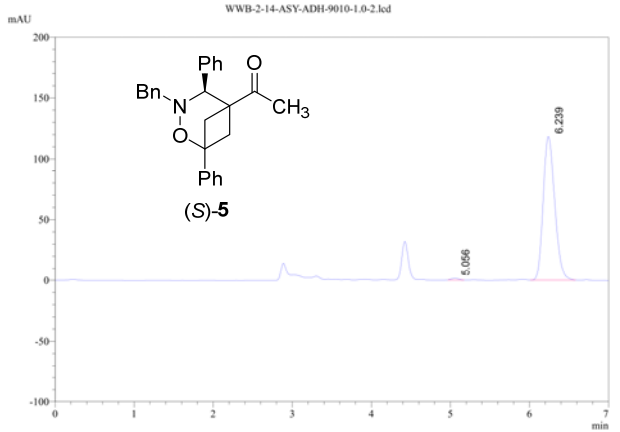
2024-04-02 15:27:43 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-14-ASY-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-14-ASY-ADH-9010-1.0-1 |
| Data File | : WWB-2-14-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/2 15:19:13 |
| Date Processed | : 2024/4/2 15:27:34 |




(*S*)-**5**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.056 | 4.967 | 1444 | 8995 | 0.742 |
| 2 | 6.239 | 6.008 | 118292 | 1203188 | 99.258 |
| Total | | | 119736 | 1212183 | 100.000 |

**Supplementary Figure 205.** HPLC spectra of (*rac*)-**5** and (*S*)-**5**

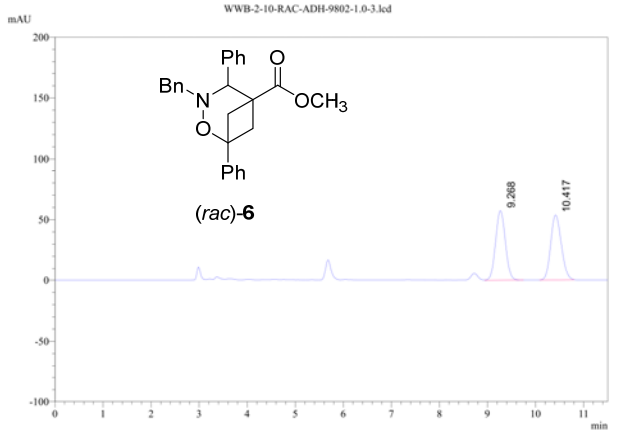
2024-03-29 21:59:57 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-10-RAC-ADH-9802-1.0-2 |
| Sample ID | : WWB-2-10-RAC-ADH-9802-1.0-2 |
| Data File | : WWB-2-10-RAC-ADH-9802-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/29 21:45:03 |
| Date Processed | : 2024/3/29 21:57:24 |




(*rac*)-**6**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.268 | 8.942 | 57347 | 816263 | 49.802 |
| 2 | 10.417 | 10.083 | 53482 | 822765 | 50.198 |
| Total | | | 110829 | 1639027 | 100.000 |

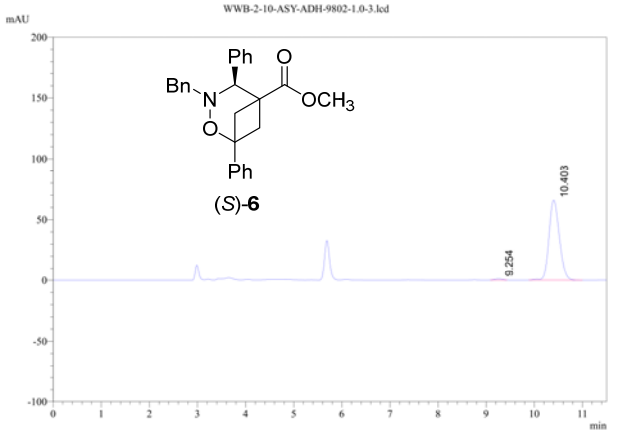
2024-03-29 22:12:52 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-10-ASY-ADH-9802-1.0-2 |
| Sample ID | : WWB-2-10-ASY-ADH-9802-1.0-2 |
| Data File | : WWB-2-10-ASY-ADH-9802-1.0-3.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/29 21:58:30 |
| Date Processed | : 2024/3/29 22:12:40 |

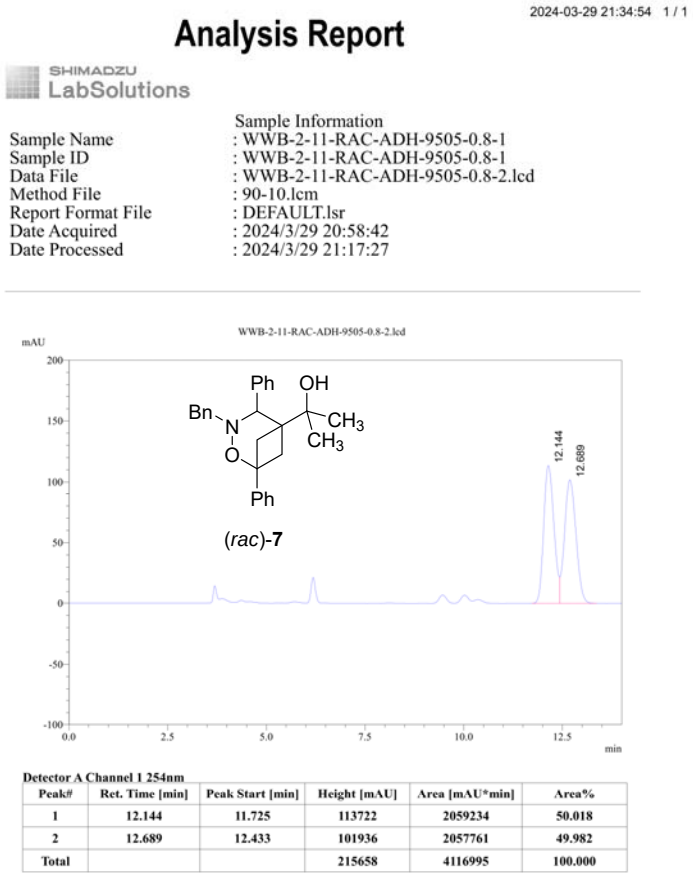



(*S*)-**6**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.254 | 9.083 | 968 | 10815 | 1.079 |
| 2 | 10.403 | 9.883 | 65743 | 991145 | 98.921 |
| Total | | | 66711 | 1001960 | 100.000 |

**Supplementary Figure 206.** HPLC spectra of (*rac*)-**6** and (*S*)-**6**



2024-03-29 21:34:54 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

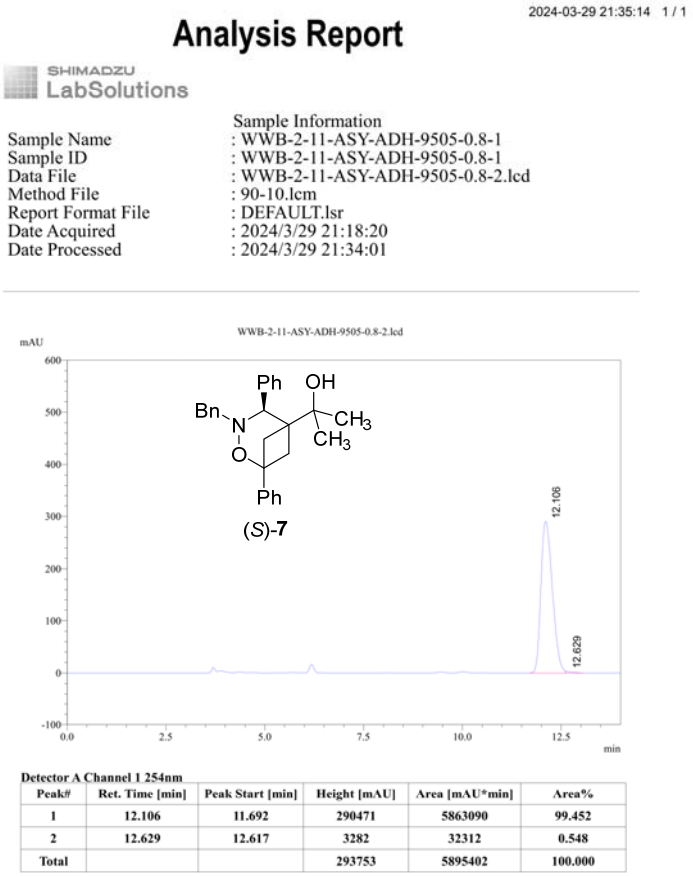
| | |
|---|---|
| Sample Name | : WWB-2-11-RAC-ADH-9505-0.8-1 |
| Sample ID | : WWB-2-11-RAC-ADH-9505-0.8-1 |
| Data File | : WWB-2-11-RAC-ADH-9505-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/29 20:58:42 |
| Date Processed | : 2024/3/29 21:17:27 |



(*rac*)-**7**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.144 | 11.725 | 113722 | 2059234 | 50.018 |
| 2 | 12.689 | 12.433 | 101936 | 2057761 | 49.982 |
| Total | | | 215658 | 4116995 | 100.000 |



2024-03-29 21:35:14 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-11-ASY-ADH-9505-0.8-1 |
| Sample ID | : WWB-2-11-ASY-ADH-9505-0.8-1 |
| Data File | : WWB-2-11-ASY-ADH-9505-0.8-2.lcd |
| Method File | : 90-10.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/3/29 21:18:20 |
| Date Processed | : 2024/3/29 21:34:01 |



(*S*)-**7**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 12.106 | 11.692 | 290471 | 5863090 | 99.452 |
| 2 | 12.629 | 12.617 | 3282 | 32312 | 0.548 |
| Total | | | 293753 | 5895402 | 100.000 |

**Supplementary Figure 207.** HPLC spectra of (*rac*)-**7** and (*S*)-**7**

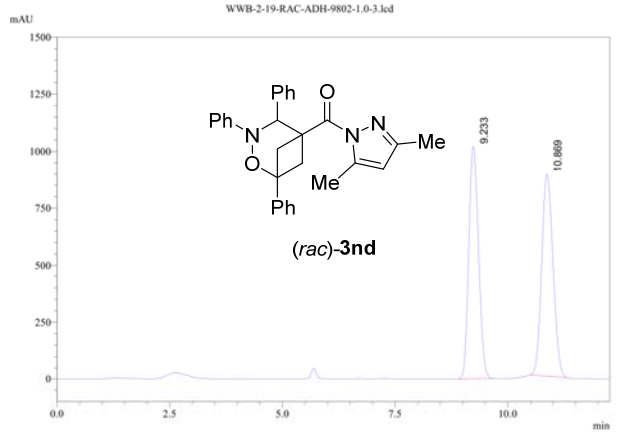
2024-04-16 15:46:20 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-19-RAC-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-19-RAC-ADH-9802-1.0-1 |
| Data File | : WWB-2-19-RAC-ADH-9802-1.0-3.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/5 15:23:39 |
| Date Processed | : 2024/4/5 15:36:36 |




(*rac*)-**3nd**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.233 | 8.858 | 1020268 | 15369146 | 49.775 |
| 2 | 10.869 | 10.500 | 884611 | 15507991 | 50.225 |
| Total | | | 1904879 | 30877137 | 100.000 |

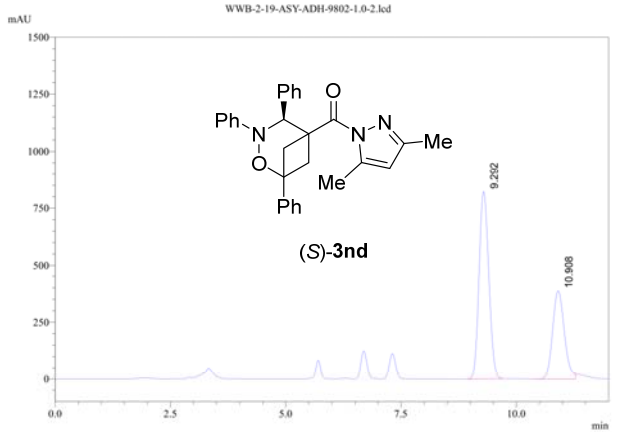
2024-04-16 15:46:36 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-19-ASY-ADH-9802-1.0-1 |
| Sample ID | : WWB-2-19-ASY-ADH-9802-1.0-1 |
| Data File | : WWB-2-19-ASY-ADH-9802-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
| Date Acquired | : 2024/4/5 15:37:15 |
| Date Processed | : 2024/4/5 15:51:25 |




(*S*)-**3nd**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 9.292 | 8.883 | 822236 | 12066117 | 63.749 |
| 2 | 10.908 | 10.433 | 386980 | 6861395 | 36.251 |
| Total | | | 1209215 | 18927512 | 100.000 |

**Supplementary Figure 208.** HPLC spectra of (*rac*)-**3nd** and (*S*)-**3nd**

2024-04-17 16:45:58 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-29-RAC-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-29-RAC-ADH-9010-1.0-1 |
| Data File | : WWB-2-29-RAC-ADH-9010-1.0-3.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
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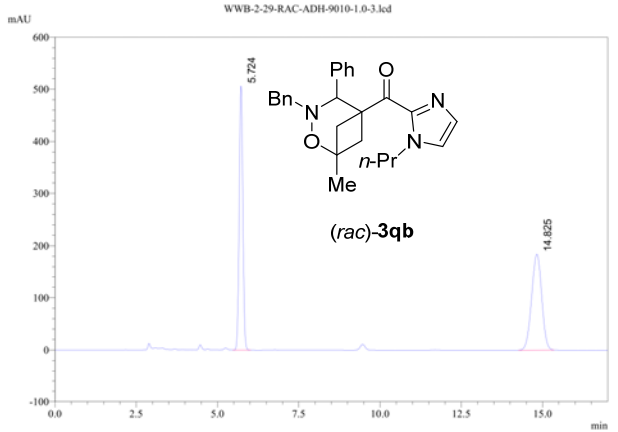
| Date Processed | : 2024/4/17 16:17:54 |




(*rac*)-**3qb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.724 | 5.467 | 505887 | 3939366 | 49.829 |
| 2 | 14.825 | 14.250 | 184001 | 3966392 | 50.171 |
| Total | | | 689888 | 7905758 | 100.000 |

2024-04-17 16:46:24 1 / 1

**Analysis Report**

SHIMADZU LabSolutions

Sample Information

| | |
|---|---|
| Sample Name | : WWB-2-29-ASY-ADH-9010-1.0-1 |
| Sample ID | : WWB-2-29-ASY-ADH-9010-1.0-1 |
| Data File | : WWB-2-29-ASY-ADH-9010-1.0-2.lcd |
| Method File | : 98-02.lcm |
| Report Format File | : DEFAULT.lsr |
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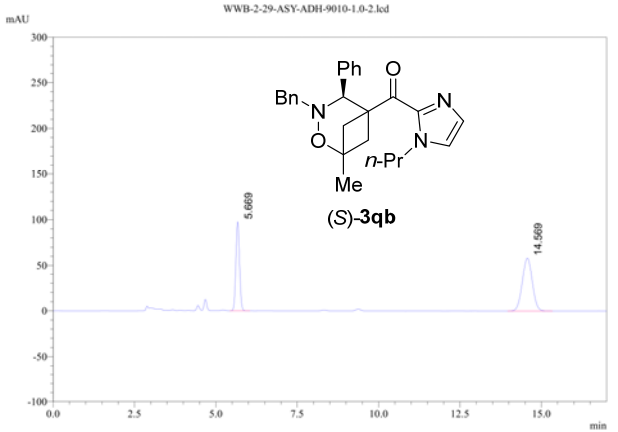


(*S*)-**3qb**

Detector A Channel 1 254nm

| Peak# | Ret. Time [min] | Peak Start [min] | Height [mAU] | Area [mAU*min] | Area% |
|---|---|---|---|---|---|
| 1 | 5.669 | 5.425 | 97440 | 765456 | 38.152 |
| 2 | 14.569 | 13.958 | 58199 | 1240886 | 61.848 |
| Total | | | 155639 | 2006343 | 100.000 |

**Supplementary Figure 209.** HPLC spectra of (*rac*)-**3qb** and (*S*)-**3qb**

## 5. Supplementary Computational Details

In order to understand the origin of enantioselectivity, density functional theory (DFT) calculations were carried out using the Gaussian 09 software package.[13-16] The spin-quartet state was calculated for the cobalt(II) complexes because of the high-spin state with lower energy. The stationary structures were optimized using PBE0 method and combined basis set. That is, SDD for Co atom, and 6-31G(d) basis set for all the other atoms.[17] Truhlar and coworkers' SMD solvation model was employed to consider the solvent effect of Dichloromethane.[18] The geometry optimizations were performed without symmetry constraints, and the nature of the extrema was checked by analytical frequency calculations. The intrinsic reaction coordinate (IRC)[19] pathways have been traced to verify two desired minima connected by the transition states. The independent gradient model based on Hirshfeld partition (IGMH) analysis was conducted with Multiwfn and VMD.[20-22] The 3-D images of the calculated structures were prepared using CYLview.[23]

Note: source data are provided with this paper

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