Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information for:

Construction of Chiral Chroman Skeletons *via* Catalytic Asymmetric [4+2] Cyclization of *ortho*-Hydroxyphenyl-Substituted *para*-Quinone Methides Catalyzed by Chiral-at-Metal Rhodium Complex

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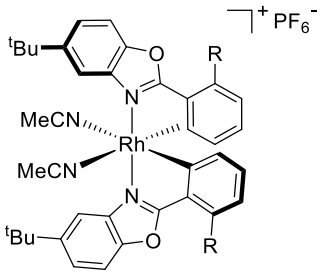
Contents

1. General Information

All non-aqueous reactions were performed in oven-dried glassware and standard Schlenk tubes under an atmosphere of argon. Dichloromethane (DCM) and 1,2-dichloroethane (DCE) were distilled from CaH_2 under inert atmosphere. Tetrahydrofuran (THF) and toluene were distilled from sodium and benzophenone under inert atmosphere. All other solvents and reagents were used as received unless otherwise noted. Thin layer chromatography was performed using silica gel 60 F-254 precoated plates (0.2~0.3 mm) and visualized by short-wave UV (254 nm) irradiation, potassium permanganate, or iodine stain. Column chromatography was performed with silica gel (200-300 mesh, Yantai Jiangyou Silica Gel Development Co., Ltd). The ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained in $CDCl_3$ using a Bruker-BioSpin AVANCE III HD 400 NMR spectrometer, respectively. Chemical shifts (δ) for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, and integration. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (δ 77.00 ppm) as the internal standard. The infrared spectra were recorded on a VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in cm^{-1}. Optical rotation was recorded on INESA SGW-1 polarimeter at concentrations of 0.5 g/100 mL or 1.0 g/100 mL. Enantiomeric excess was determined by HPLC analysis on Chiralpak column (Daicel Chemical Industries, LTD) on Shimadzu LC-20AD. High-resolution mass spectra were recorded on a Bruker Impact II UHR TOF LC/MS Mass Spectrometry.

2. Synthesis of Catalysts

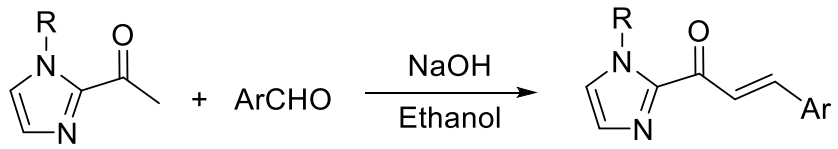


Δ-**Rh1** R = 3,5-$Me_2C_6H_3$
Δ-**Rh2** R = 3,5-$(CF_3)_2C_6H_3$
Δ-**Rh3** R = H

Racemic rhodium catalyst ***rac*-Rh3** and chiral catalyst **Δ-Rh3**, **Λ-Rh3** were prepared according to reported procedures developed by Meggers' group.[1] **Δ-Rh1**[2], **Δ-Rh2**[3] were synthesized following recently published procedures.

3. Synthesis of Substrates

3.1 Synthesis of α,β-unsaturated 2-acylimidazoles



α,β-unsaturated 2-acylimidazoles **1** were prepared by *Aldol* reaction according to a reported procedure.[3] 2-acetyl-imidazole (10.0 mmol, 1.0 eq.) and ethanol (50 mL) were added to a 100 mL round-bottom flask followed by the aromatic aldehyde (12 mmol, 1.2 eq.) and NaOH (5 mmol, 0.5 eq.). The solution was stirred at room temperature until the substrates consumption (detected by TLC). The reaction mixture was then quenched with saturated aqueous NH_4Cl and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with 50 mL brine and dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by a flash column chromatography on silica gel to afford the desired product **1**.

Alkyl *α,β*-unsaturated 2-acyl imidazole **1n** was prepared following aforesaid method in 80 °C overnight. **1o** was prepared according to published procedures.[4] **1r** was prepared according to published procedures.[5]

3.2 Synthesis of *para*-quinone methides

The *para*-quinone methides **2** were prepared according to a reported method.[6]

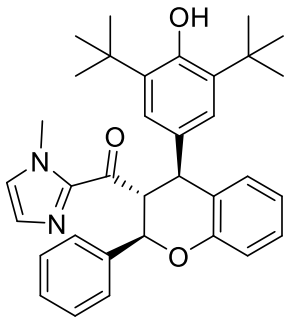
4. Asymmetric [4+2] Cyclization Reactions

4.1 Synthesis of racemic products as HPLC references

General Procedure: A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazoles **1** (0.20 mmol), *para*-quinone methides (*p*-QMs) **2** (0.24 mmol), K_2CO_3 (0.24 mmol) and racemic catalyst *rac*-**Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford racemic products as HPLC reference for determination of enantiomeric excess.

4.2 Substrate Scope

General Procedure: A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazoles **1** (0.20 mmol), *para*-quinone methides (*p*-QMs) **2** (0.24 mmol), K_2CO_3 (0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral products.



3a

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

Following **General Procedure**, a dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3a** as pale yellow oil (101.4 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 93%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 5.764 min, t_r(minor) = 6.517 min;

$[\alpha]_D^{25}$ = +127.1° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3418, 2966, 1642, 1451, 1485, 1431, 1410 cm^{-1};

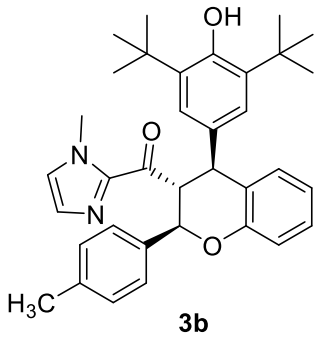
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.46 (m, 2H), 7.24 – 7.08 (m, 4H), 6.96 – 6.90 (m, 3H), 6.84 – 6.77 (m, 3H), 6.61 (s, 1H), 5.43 (d, *J* = 9.9 Hz, 1H), 4.97 (s, 2H), 4.61 (d, *J* = 11.4 Hz, 1H), 3.54 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.13, 154.67, 152.45, 143.76, 138.44, 135.45, 130.74, 129.41, 129.10, 128.40, 128.23, 127.85, 127.56, 126.41, 125.88, 120.45, 116.45, 81.02, 48.28, 35.62, 34.21, 30.35;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{38}N_2O_3Na^+$ $[M+Na]^+$: 545.2775, found: 545.2775.

In addition, when **Λ-Rh3** was used (3.0 mol %) instead of **Δ-Rh3** under the optimal conditions, the reaction also proceeded smoothly to afford the desired product **3a'** (the enantiomer of **3a**) as pale yellow oil (99.6 mg, yield: 95%). Enantiomeric excess was determined by HPLC analysis, *ee* = 93%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 5.776 min, t_r(major) = 6.399 min. $[\alpha]_D^{25}$ = -122.4° (*c* = 1.0, $CHCl_3$).

In the scale-up synthesis, a dried 25 mL flask was charged with α,β-unsaturated 2-acylimidazole **1a** (424.5 mg, 2.0 mmol), *para*-quinone methides (*p*-QMs) **2a** (745.1 mg, 2.4 mmol), K_2CO_3 (331.7 mg, 2.4 mmol) and chiral catalyst **Δ-Rh3** (49.8 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3a** as pale yellow oil (993.3 mg, yield: 95%). Enantiomeric excess was determined by HPLC analysis, *ee* = 93%.



3b

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(*p*-tolyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

Following **General Procedure**, a dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1b** (45.3 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3b** as pale yellow oil (104.2 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 93%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 5.309 min, t_r(minor) = 6.301 min;

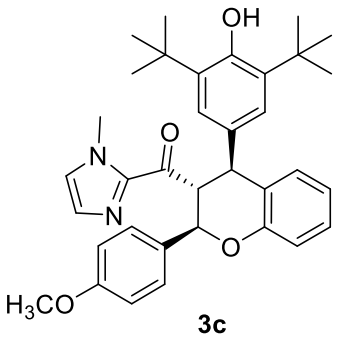
$[\alpha]_D^{25}$ = +94.82° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3626, 3450, 3145, 3102, 2958, 2885, 1662, 1614, 1580, 1518, 1483, 1447, 1407, 1364 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 – 7.36 (m, 2H), 7.15 – 7.08 (m, 1H), 7.04 (d, *J* = 7.8 Hz, 2H), 6.96 – 6.89 (m, 3H), 6.85 – 6.76 (m, 3H), 6.62 (s, 1H), 5.41 (d, *J* = 9.9 Hz, 1H), 5.04 – 4.80 (m, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 3.55 (s, 3H), 2.23 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.31, 154.80, 152.42, 143.79, 138.09, 135.47, 135.42, 130.78, 129.36, 129.10, 128.97, 127.87, 127.53, 126.40, 126.31, 125.88, 120.33, 116.45, 80.81, 48.59, 35.63, 34.20, 30.34, 21.22;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_3Na^+$ $[M+Na]^+$: 559.2931, found: 559.2932.



3c

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(4-methoxyphenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1c** (48.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3c** as pale yellow oil (98.0 mg, yield: 89%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 97%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 6.459 min, t_r(minor) = 8.318 min;

$[\alpha]_D^{25}$ = +115.6° (*c* = 1.0, $CHCl_3$);

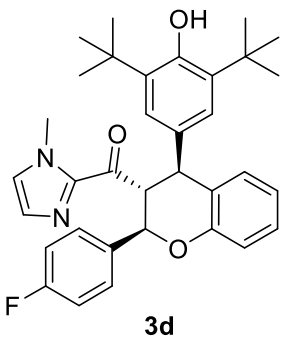
IR (KBr) ν_{max}: 3641, 2989, 2813, 1698, 1666, 1605, 1534, 1497, 1441, 1408, 1374 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.6 Hz, 2H), 7.17 – 7.08 (m, 1H), 6.97 – 6.89 (m, 3H), 6.87 – 6.73 (m, 5H), 6.66 (s, 1H), 5.39 (d, *J* = 10.2 Hz, 1H), 5.05 – 4.85 (m, 2H), 4.58 (d, *J* = 11.4 Hz, 1H), 3.72 (s, 3H), 3.58 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.34, 159.53, 154.78, 152.40, 143.78, 135.40, 130.77, 130.66, 129.37, 129.24, 129.10, 127.51, 126.39, 126.36, 125.85, 120.33, 116.43, 113.64, 80.54, 55.20, 48.54, 35.65, 34.18, 30.31;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_4Na^+$ $[M+Na]^+$: 575.2880, found: 575.2877.

In addition, when **Λ-Rh3** was used (3.0 mol %) instead of **Δ-Rh3** under the optimal conditions, the reaction also proceeded smoothly to afford the desired product **3c'** (the enantiomer of **3c**) as pale yellow oil (102.0 mg, yield: 92%). Enantiomeric excess was determined by HPLC analysis, *ee* = 98%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 6.660 min, t_r(major) = 8.343 min. $[\alpha]_D^{25}$ = -103.2° (*c* = 1.0, $CHCl_3$).



3d

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(4-fluorophenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1d** (46.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3d** as pale yellow oil (102.0 mg, yield: 94%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 93%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.548 min, t_r(minor) = 6.735 min;

$[\alpha]_D^{25}$= +299.2° (*c* = 1.0, $CHCl_3$);

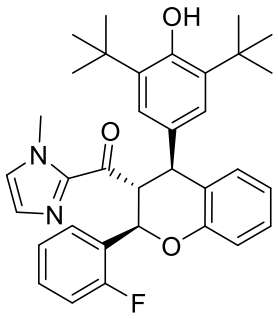
IR (KBr) ν_{max}: 3630, 3579, 2964, 1653, 1611, 1584, 1447, 1260 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 – 7.45 (m, 2H), 7.17 – 7.10 (m, 1H), 6.96 – 6.88 (m, 5H), 6.85 – 6.80 (m, 3H), 6.67 (s, 1H), 5.42 (d, *J* = 10.1 Hz, 1H), 5.03 – 4.81 (m, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 3.59 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.03, 162.6 (d, *J* = 246.3 Hz, 1C), 154.52, 152.47, 143.67, 135.47, 134.39, 134.35, 130.59, 129.67 (d, *J* = 8.4 Hz, 1C), 129.42, 129.20, 127.60, 126.44 (d, *J* = 23.4 Hz, 2C), 125.83, 120.55, 116.40, 115.12 (d, *J* = 21.3 Hz, 2C), 80.23, 48.27, 35.65, 34.19, 30.31;

^{19}F NMR (376 MHz, $CDCl_3$) δ = -113.60;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}FN_2O_3Na^+$ $[M+Na]^+$: 563.2680, found: 563.2679.



3e

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(2-fluorophenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1e** (46.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3e** as pale yellow oil (95.2 mg, yield: 88%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 99%, Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 5.182 min, t_r(minor) = 8.206 min;

$[\alpha]_D^{25}$ = +225.3° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3625, 3458, 2962, 2920, 2864, 1661, 1617, 1582, 1488, 1452, 1433, 1410 cm^{-1};

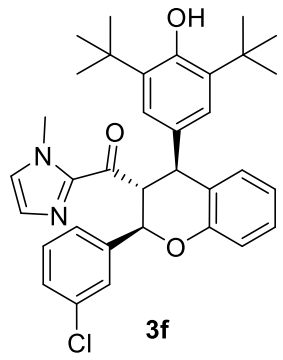
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (td, *J* = 7.5, 1.8 Hz, 1H), 7.20 – 7.10 (m, 2H), 7.06 (td, *J* = 7.5, 1.2 Hz, 1H), 6.97 – 6.90 (m, 4H), 6.84 – 6.78 (m, 3H), 6.65 (s, 1H), 5.79 (d, *J* = 10.2 Hz, 1H), 5.05 (t, *J* = 10.8 Hz, 1H), 4.97 (s, 1H), 4.62 (d, *J* = 11.4 Hz, 1H), 3.59 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.50, 160.22 (d, *J* = 248.8 Hz, 1C), 154.55, 152.46, 143.68, 135.45, 130.63, 130.05 (d, *J* = 8.3 Hz, 1C), 129.66, 129.62 (d, *J* = 3.4 Hz, 1C), 129.42, 129.18, 127.57, 126.46, 126.33, 125.89, 125.60 (d, *J* = 13.0 Hz, 1C),

124.24 (d, *J* = 3.6 Hz, 1C), 120.55, 116.40, 115.20 (d, *J* = 22.1 Hz, 1C), 73.72 (d, *J* = 3.4 Hz, 1C), 48.28, 35.62, 34.19, 30.32;

^{19}F NMR (376 MHz, $CDCl_3$): δ = -117.62;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}FN_2O_3Na^+$ $[M+Na]^+$: 563.2680, found: 563.2682.



3f

((2*R*,3*R*,4*S*)-2-(3-chlorophenyl)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1f** (49.4 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3f** as pale yellow oil (107.0 mg, yield: 96%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 96%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.945 min, t_r(minor) = 5.735 min;

$[\alpha]_D^{25}$= +80.2° (*c* = 1.0, $CHCl_3$);

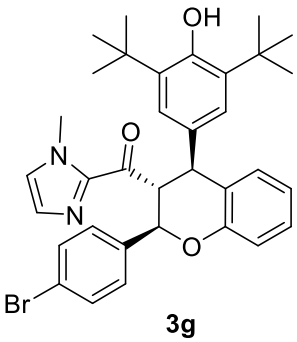
IR (KBr) ν_{max}: 3444, 2959, 1663, 1581, 1483.47, 1444, 1408, 1363 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.45 (m, 1H), 7.39 (dt, *J* = 6.9, 1.9 Hz, 1H), 7.19 – 7.11 (m, 3H), 6.97 – 6.89 (m, 3H), 6.84 – 6.80 (m, 3H), 6.67 (s, 1H), 5.41 (d, *J*

= 9.9 Hz, 1H), 5.02 – 4.83 (m, 2H), 4.61 (d, *J* = 11.4 Hz, 1H), 3.60 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.69, 154.33, 152.50, 143.65, 140.54, 135.49, 133.95, 130.58, 129.54, 129.45, 129.26, 128.49, 128.01, 127.65, 126.63, 126.26, 125.90, 125.85, 120.66, 116.41, 80.20, 47.92, 35.66, 34.21, 30.33;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}ClN_2O_3Na^+$ $[M+Na]^+$: 579.2385, found: 579.2390.



3g

((2*R*,3*R*,4*S*)-2-(4-bromophenyl)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1g** (58.2 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3g** as pale yellow oil (115.0 mg, yield: 96%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 97%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 7.082 min, t_r(minor) = 9.389 min;

$[\alpha]_D^{25}$ = +67.3° (*c* = 1.0, $CHCl_3$);

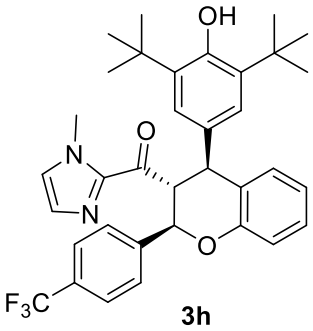
IR (KBr) ν_{max}: 3518, 2832, 1677, 1596, 1487, 1402, 1289 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 – 7.58 (m, 2H), 7.56 – 7.51 (m, 2H), 7.19 – 7.13 (m, 1H), 6.97 – 6.93 (m, 1H), 6.88 (s, 2H), 6.85 – 6.79 (m, 3H), 6.70 (s, 1H), 5.49 (d, *J* = 9.9 Hz, 1H), 5.01 – 4.80 (m, 2H), 4.59 (d, *J* = 11.3 Hz, 1H), 3.61 (s, 3H), 1.30 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.91, 154.44, 152.47, 143.61, 137.59, 135.47, 131.39, 130.50, 129.63, 129.40, 129.26, 127.63, 126.61, 126.26, 125.81, 122.38, 120.59, 116.39, 80.18, 48.35, 35.69, 34.18, 30.31;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}BrN_2O_3Na^+$ $[M+Na]^+$: 623.1880, found: 623.1884.

In addition, when **Λ-Rh3** was used (3.0 mol %) instead of **Δ-Rh3** under the optimal conditions, the reaction also proceeded smoothly to afford the desired product **3g'** (the enantiomer of **3g**) as pale yellow oil (112.0 mg, yield: 93%). Enantiomeric excess was determined by HPLC analysis, *ee* = 98%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 25 °C, t_r(minor) = 6.100 min, t_r(major) = 7.980 min. $[\alpha]_D^{25}$ = -66.9° (*c* = 1.0, $CHCl_3$).



3h

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(4-(trifluoromethyl)phenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1h** (56.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column

chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3h** as pale yellow oil (114.2 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* > 99%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.744 min, t_r(minor) =6.311 min;

$[\alpha]_D^{25}$ = +197.8° (*c* = 1.0, $CHCl_3$);

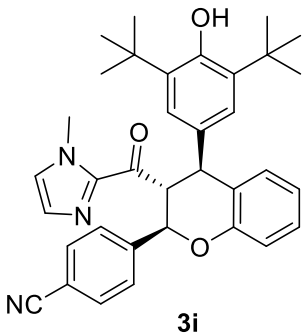
IR (KBr) ν_{max}: 3643, 3452, 3147, 2956, 1663, 1623, 1581, 1484, 1452, 1435, 1408, 1361, 1326 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 50.9, 8.1 Hz, 4H), 7.17 – 7.11 (m, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.90 (s, 2H), 6.85 – 6.79 (m, 3H), 6.66 (s, 1H), 5.51 (d, *J* = 10.0 Hz, 1H), 5.03 – 4.85 (m, 2H), 4.60 (d, *J* = 11.3 Hz, 1H), 3.58 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.72, 154.31, 152.54, 143.58, 142.54, 135.54, 130.44, 130.37 (q, *J* = 32.4 Hz, 1C), 129.44, 129.30, 128.20, 127.71, 126.67, 126.24, 125.82, 125.20 (q, *J* = 3.8 Hz, 2C), 124.03 (d, *J* = 272.2 Hz, 1C), 120.74, 116.40, 80.16, 48.21, 35.65, 34.20, 30.31;

^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.61;

HRMS (ESI, m/z) calcd. for $C_{35}H_{37}F_3N_2O_3Na^+$ $[M+Na]^+$: 613.2637, found: 613.2650.



3i

4-((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-3-(1-methyl-1*H*-imidazole-2-carbonyl)chroman-2-yl)benzonitrile

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1i** (47.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol),

K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 4:1) to afford chiral product **3i** as white solid (103.0 mg, yield: 94%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 85%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 10.950 min, t_r(minor) = 14.342 min;

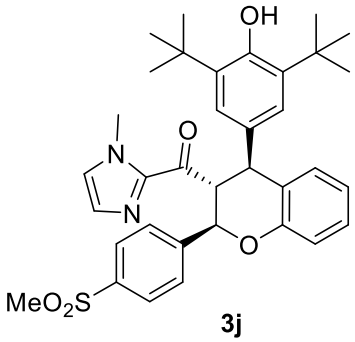
$[\alpha]_D^{25}$= +253.3° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3616, 3445, 3148, 3102, 2961, 2913, 2869, 2230, 1662, 1617, 1579, 1511, 1482, 1454, 1433, 1408, 1369, 1333 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (ddd, 4H), 7.19 – 7.14 (m, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.90 – 6.86 (m, 2H), 6.86 – 6.80 (m, 3H), 6.71 (s, 1H), 5.49 (d, *J* = 10.0 Hz, 1H), 5.00 – 4.80 (m, 2H), 4.58 (d, *J* = 11.3 Hz, 1H), 3.61 (s, 3H), 1.30 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.49, 154.06, 152.55, 143.87, 143.46, 135.53, 132.08, 130.23, 129.44, 129.38, 128.46, 127.76, 126.85, 126.12, 125.77, 120.88, 118.75, 116.36, 112.04, 79.95, 47.98, 35.72, 34.18, 30.28;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{37}N_3O_3Na^+$ $[M+Na]^+$: 570.2727, found: 570.2727.



3j

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(*p*-tolyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1j** (58.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 5:1 to 2:1) to afford chiral product **3j** as colorless oil (97.1 mg, yield: 81%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 91%, Chiralpak column AD-H, λ = 220 nm, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 14.629 min, t_r(minor) = 28.338 min;

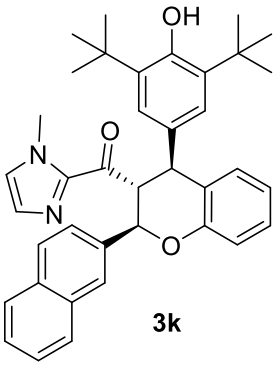
$[\alpha]_D^{25}$ = +241.8° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3582, 3452, 3148, 3105, 2956, 1925, 1662, 1609, 1580, 1484, 1438, 1403, 1364 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 – 7.70 (m, 4H), 7.18 – 7.12 (m, 1H), 6.96 – 6.92 (m, 1H), 6.89 (s, 2H), 6.86 – 6.82 (m, 2H), 6.80 (s, 1H), 6.69 (s, 1H), 5.54 (d, *J* = 10.0 Hz, 1H), 5.00 (s, 1H), 4.91 (s, 1H), 4.60 (d, *J* = 11.4 Hz, 1H), 3.61 (s, 3H), 2.96 (s, 3H), 1.30 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.42, 154.11, 152.56, 144.81, 143.46, 140.14, 135.58, 130.24, 129.46, 129.39, 128.83, 127.75, 127.37, 126.89, 126.18, 125.78, 120.88, 116.34, 79.95, 48.16, 44.46, 35.72, 34.19, 30.30;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_5SNa^+$ $[M+Na]^+$: 623.2550, found: 623.2551.



3k

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(naphthalen-2-yl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

.

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1k** (52.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3k** as pale yellow solid (111.2 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 96%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 7.116 min, t_r(minor) = 9.573 min;

$[\alpha]_D^{25}$ = +142.2° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3673, 3190, 3102, 2960, 2873, 1649, 1624, 1575, 1503, 1483, 1447 1421, 1307 cm^{-1};

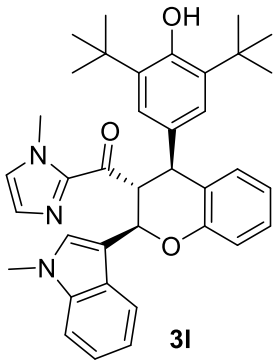
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1H), 7.80 – 7.67 (m, 4H), 7.42 – 7.36 (m, 2H), 7.15 (ddd, *J* = 8.5, 7.1, 2.1 Hz, 1H), 7.00 – 6.91 (m, 3H), 6.88 – 6.79 (m, 2H), 6.76 (s, 1H), 6.51 (s, 1H), 5.62 (d, *J* = 10.0 Hz, 1H), 5.17 – 4.93 (m, 2H), 4.66 (d, *J* = 11.4 Hz, 1H), 3.47 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.02, 154.66, 152.40, 143.61, 135.83, 135.39, 133.33, 132.92, 130.67, 129.39, 129.03, 128.16, 128.12, 127.56, 127.53, 127.39,

126.36, 125.99, 125.85, 125.82, 125.41, 120.43, 116.42, 81.11, 48.43, 35.49, 34.15, 30.28;

HRMS (ESI, *m*/*z*) calcd. for $C_{38}H_{40}N_2O_3Na^+$ $[M+Na]^+$: 595.2931, found: 595.2934.

In addition, when **Λ-Rh3** was used (3.0 mol %) instead of **Δ-Rh3** under the optimal conditions, the reaction also proceeded smoothly to afford the desired product **3k'** (the enantiomer of **3k**) as pale yellow solid (105.2 mg, yield: 92%). Enantiomeric excess was determined by HPLC analysis, *ee* = 90%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 6.805 min, t_r(major) = 9.573 min. $[\alpha]_D^{25}$ = -157.2° (*c* = 1.0, $CHCl_3$).



3l

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(1-methyl-1*H*-indol-3-yl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1l** (53.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 4:1) to afford chiral product **3l** as pale yellow oil (94.5 mg, yield: 82%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 93%, Chiralpak column IB, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 6.715 min, t_r(major) = 7.221 min;

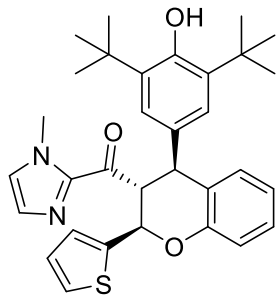
$[\alpha]_D^{25}$ = +274.8° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3610, 3393, 2913, 1662, 1512, 1505, 1479, 1439, 1407, 1303 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.43 (s, 1H), 7.18 – 7.08 (m, 4H), 6.97 – 6.89 (m, 3H), 6.88 – 6.76 (m, 3H), 6.60 (s, 1H), 5.87 (d, *J* = 10.5 Hz, 1H), 5.11 (s, 1H), 4.96 (s, 1H), 4.66 (d, *J* = 11.2 Hz, 1H), 3.61 (s, 3H), 3.45 (s, 3H), 1.32 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.35, 154.95, 152.39, 143.84, 136.67, 135.43, 131.06, 129.39, 128.90, 128.69, 127.46, 127.13, 126.42, 126.24, 125.90, 121.73, 120.21, 119.49, 116.54, 112.57, 109.10, 73.25, 48.95, 35.57, 34.21, 32.81, 30.35;

HRMS (ESI, *m*/*z*) calcd. for $C_{37}H_{41}N_3O_3Na^+$ $[M+Na]^+$: 598.3040, found: 598.3037.



3m

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(thiophen-2-yl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1m** (43.7 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3m** as pale yellow oil (82.2 mg, yield: 78%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 91%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 6.505 min, t_r(minor) = 6.989 min;

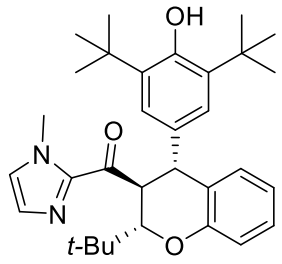
$[\alpha]_D^{25}$ = +164.8° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3671, 2923, 1667, 1596, 1504, 1478, 1447, 1410, 1355 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.97 – 6.93 (m, 1H), 6.91 – 6.86 (m, 3H), 6.84 – 6.78 (m, 3H), 6.70 (s, 1H), 5.77 (d, *J* = 10.2 Hz, 1H), 5.02 – 4.83 (m, 2H), 4.57 (d, *J* = 11.4 Hz, 1H), 3.62 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.83, 154.27, 152.49, 143.68, 141.47, 135.47, 130.44, 129.30, 127.63, 126.52, 126.44, 126.35, 126.17, 125.87, 125.81, 120.63, 116.48, 75.99, 48.51, 35.73, 34.20, 30.32;

HRMS (ESI, *m*/*z*) calcd. for $C_{32}H_{36}N_2O_3SNa^+$ $[M+Na]^+$: 551.2339, found: 551.2339.



3n

((2*S*,3*S*,4*R*)-2-(*tert*-butyl)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)chroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1n** (38.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3n** as colorless oil (95.6 mg, yield: 95%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 99%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 3.514 min, t_r(minor) = 5.295 min;

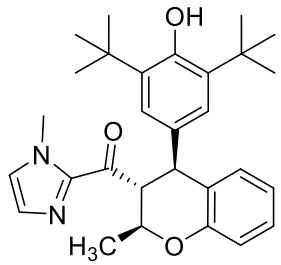
$[\alpha]_D^{25}$ = +104.1° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3625, 3440, 2961, 2913, 2869, 1673, 1584, 1489, 1456, 1434, 1408, 1363 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.12 (td, *J* = 7.6, 1.7 Hz, 1H), 6.98 (s, 1H), 6.93 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.87 (s, 2H), 6.77 – 6.71 (m, 2H), 6.68 – 6.64 (m, 1H), 4.99 (s, 1H), 4.60 (t, *J* = 10.7 Hz, 1H), 4.45 (d, *J* = 10.3 Hz, 1H), 4.24 (d, *J* = 10.9 Hz, 1H), 3.60 (s, 3H), 1.32 (s, 18H), 1.04 (s, 9H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.43, 154.96, 152.34, 144.36, 135.26, 129.19, 127.86, 127.47, 127.46, 126.48, 126.24, 119.65, 115.88, 86.17, 49.01, 36.40, 35.61, 34.15, 30.34, 26.61;

HRMS (ESI, *m*/*z*) calcd. for $C_{32}H_{42}N_2O_3Na^+$ $[M+Na]^+$: 525.3088, found: 525.3086.



3o

((2*S*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-methylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1o** (30.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3o** as colorless oil (86.0 mg, yield: 93%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 74%, Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 99.5:0.5, flow rate: 0.5 mL/min, 30 °C, t_r(minor) = 15.069 min, t_r(major) = 17.045 min;

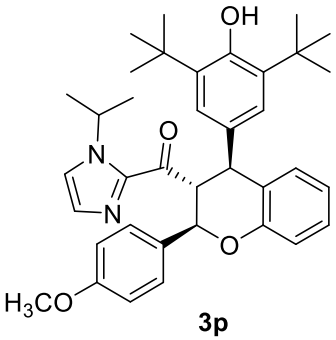
$[\alpha]_D^{25}$ = +98.0° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3634, 3421, 2958, 2886, 1665, 1585, 1483,1454, 1435, 1409, 1361 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.10 (ddd, *J* = 8.2, 5.2, 3.7 Hz, 1H), 6.99 (d, *J* = 0.9 Hz, 1H), 6.90 – 6.83 (m, 4H), 6.77 – 6.73 (m, 2H), 4.96 (s, 1H), 4.56 – 4.48 (m, 2H), 4.43 – 4.34 (m, 1H), 3.75 (s, 3H), 1.41 – 1.37 (m, 3H), 1.30 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.32, 154.36, 152.33, 144.22, 135.42, 131.12, 129.38, 129.33, 127.41, 126.88, 126.33, 125.75, 120.04, 116.11, 74.45, 47.63, 35.84, 34.18, 30.32, 19.81;

HRMS (ESI, *m*/*z*) calcd. for $C_{29}H_{36}N_2O_3Na^+$ $[M+Na]^+$: 483.2618, found: 483.2618.



3p

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(4-methoxyphenyl)chroman-3-yl)(1-isopropyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1p** (54.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column

chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3p** as pale yellow oil (78.0 mg, yield: 67%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 89%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.320 min, t_r(minor) = 5.456 min;

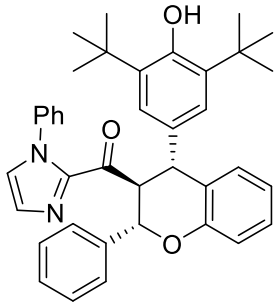
$[\alpha]_D^{25}$ = +94.2° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3452, 2961, 1668, 1639, 1516, 1483, 1437, 1406, 1241 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.3 Hz, 2H), 7.15 – 7.08 (m, 1H), 6.99 – 6.88 (m, 5H), 6.81 – 6.71 (m, 4H), 5.39 (d, *J* = 9.8 Hz, 1H), 5.22 – 5.00 (m, 2H), 4.96 (s, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 3.72 (s, 3H), 1.29 (s, 18H), 1.13 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.35, 159.52, 154.59, 152.45, 143.24, 135.39, 130.68, 130.30, 129.59, 129.40, 129.21, 127.46, 126.90, 126.20, 120.63, 120.26, 116.32, 113.58, 81.12, 55.19, 48.70, 34.17, 30.28, 26.93, 23.55, 22.71;

HRMS (ESI, *m*/*z*) calcd. for $C_{37}H_{44}N_2O_4Na^+$ $[M+Na]^+$: 603.3193, found: 603.3190.



3q

((2*S*,3*S*,4*R*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-phenyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1q** (54.1 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After

cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3q** as pale yellow oil (64.3 mg, yield: 55%).

Enantiomeric excess was determined by HPLC analysis, ee = 92%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 96:4, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 7.232 min, t_r(major) = 7.759 min;

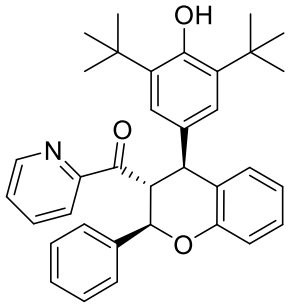
$[\alpha]_D^{25}$= -239.8° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3454, 2963, 1642, 1485, 1454, 1437, 1406 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.6 Hz, 2H), 7.40 – 7.22 (m, 6H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.08 – 7.01 (m, 3H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.88 – 6.79 (m, 2H), 6.77 – 6.71 (m, 1H), 6.58 (d, *J* = 7.5 Hz, 2H), 5.41 (s, 1H), 5.07 (s, 1H), 4.60 (s, 1H), 1.37 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 191.43, 154.40, 152.68, 143.52, 138.35, 138.00, 135.68, 130.17, 129.75, 129.15, 128.73, 128.52, 128.43, 128.27, 128.16, 127.58, 126.76, 126.43, 126.29, 125.30, 120.42, 116.36, 81.29, 48.34, 34.29, 30.39;

HRMS (ESI, *m*/*z*) calcd. for $C_{39}H_{40}N_2O_3Na^+$ $[M+Na]^+$: 607.2931, found: 607.2932.



3r

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(pyridin-2-yl)methanone

A dried 25 mL Schlenk tube was charged with **1r** (41.9 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2a** (74.5 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C

for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **3r** as pale yellow oil (92.8 mg, yield: 89%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 90%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 96:4, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 6.975 min, t_r(minor) = 7.620 min;

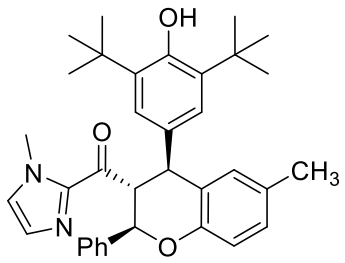
$[\alpha]_D^{25}$ = +209.8° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3629, 3453, 2958, 1689, 1649, 1582, 1486, 1437, 1366 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 4.7 Hz, 1H), 7.52 – 7.42 (m, 4H), 7.21 – 7.10 (m, 5H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.92 – 6.78 (m, 4H), 5.48 – 5.33 (m, 2H), 4.91 – 4.85 (m, 1H), 4.59 (d, *J* = 11.0 Hz, 1H), 1.25 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 203.33, 154.80, 153.09, 152.33, 148.31, 138.40, 135.99, 135.34, 130.90, 129.46, 128.34, 128.17, 127.96, 127.56, 126.33, 126.27, 125.81, 121.40, 120.46, 116.51, 81.05, 48.52, 34.12, 30.24;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{47}NO_3Na^+$ $[M+Na]^+$: 542.2666, found: 542.2663.



4a

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-6-methyl-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2b** (77.9 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction

mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4a** as white solid (89.0 mg, yield: 83%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 91%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 3.731 min, t_r(major) = 5.062 min;

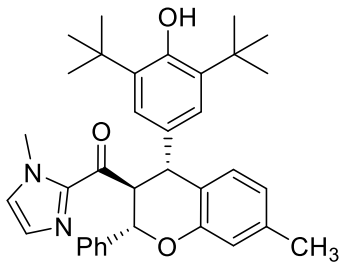
$[\alpha]_D^{25}$ = +135.4° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3673, 3412, 3102, 2815, 1800, 1664, 1609, 1580, 1518, 1483, 1403, 1321 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52 – 7.45 (m, 2H), 7.28 – 7.13 (m, 4H), 6.98 – 6.79 (m, 5H), 6.64 (d, *J* = 3.9 Hz, 2H), 5.38 (d, *J* = 10.0 Hz, 1H), 4.96 (s, 1H), 4.90 (s, 1H), 4.58 (d, *J* = 11.4 Hz, 1H), 3.58 (s, 3H), 2.17 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.28, 152.60, 152.39, 143.74, 138.55, 135.35, 130.92, 129.56, 129.51, 129.07, 128.31, 128.23, 128.19, 127.82, 126.33, 125.88, 125.86, 116.23, 80.88, 48.26, 35.65, 34.20, 30.34, 20.66.

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_3Na^+$ $[M+Na]^+$: 559.2931, found: 559.2932.



4b

((2*S*,3*S*,4*R*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-7-methyl-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2c** (77.9 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube

was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4b** as pale yellow oil (86.0 mg, yield: 80%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 96%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 15.912 min, t_r(major) = 19.574 min;

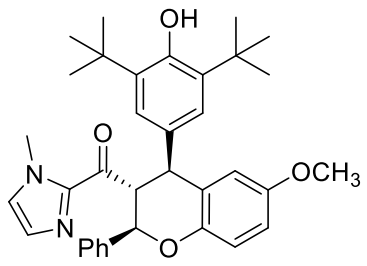
$[\alpha]_D^{25}$ = -87.5° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3615, 3450, 3197, 2977, 2816, 1740, 1602, 1571, 1545, 1483,1404 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.53 – 7.45 (m, 2H), 7.28 – 7.21 (m, 3H), 7.21 – 7.14 (m, 1H), 6.92 (s, 2H), 6.83 – 6.76 (m, 2H), 6.71 – 6.60 (m, 3H), 5.40 (d, *J* = 10.3 Hz, 1H), 4.99 – 4.80 (m, 2H), 4.56 (d, *J* = 11.4 Hz, 1H), 3.57 (s, 3H), 2.29 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.29, 154.42, 152.38, 143.77, 138.52, 137.48, 135.34, 130.84, 129.14, 129.07, 128.33, 128.20, 127.82, 126.33, 125.83, 123.33, 121.41, 116.81, 80.97, 48.09, 35.65, 34.19, 30.32, 21.10.

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_3Na^+$ $[M+Na]^+$: 559.2937, found: 559.2931.



4c

((2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-6-methoxy-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2d** (81.7 mg, 0.24 mmol),

K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4c** as white solid (96.2 mg, yield: 87%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 96%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.868 min, t_r(minor) = 6.069 min;

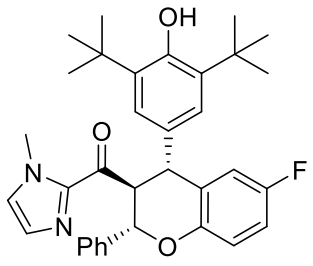
$[\alpha]_D^{25}$ = +111.9° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3591, 2959, 2885, 1659, 1611, 1492, 1459, 1434, 1409 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.45 (m, 2H), 7.28 – 7.12 (m, 3H), 6.94 – 6.87 (m, 3H), 6.83 (s, 1H), 6.72 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.64 (s, 1H), 6.38 – 6.34 (m, 1H), 5.37 (d, *J* = 10.0 Hz, 1H), 4.96 (s, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 3.63 (s, 3H), 3.57 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.19, 153.32, 152.47, 148.90, 143.73, 138.49, 135.44, 130.53, 129.05, 128.33, 128.18, 127.80, 127.18, 126.35, 125.82, 116.98, 114.48, 113.29, 81.00, 55.74, 48.36, 35.63, 34.19, 30.33;

HRMS (ESI, *m*/*z*) calcd. for $C_{35}H_{40}N_2O_4Na^+$ $[M+Na]^+$: 575.2880, found: 575.2877.



4d

((2*S*,3*S*,4*R*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-6-fluoro-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2e** (78.8 mg, 0.24 mmol),

K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4d** as pale yellow oil (104.8 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 99%, Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 5.182 min, t_r(minor) = 8.206 min;

$[\alpha]_D^{25}$ = -131.5° (*c* = 1.0, $CHCl_3$);

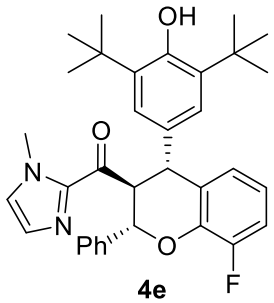
IR (KBr) ν_{max}: 3617, 3455, 2962, 2362, 1668, 1490, 1457, 1438, 1408, 1364 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 7.3 Hz, 2H), 7.25 – 7.20 (m, 2H), 7.19 – 7.13 (m, 1H), 6.93 – 6.86 (m, 3H), 6.86 – 6.79 (m, 2H), 6.62 (s, 1H), 6.53 (dd, *J* = 9.6, 3.0 Hz, 1H), 5.39 (d, *J* = 10.0 Hz, 1H), 5.00 (s, 1H), 4.92 (s, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 3.54 (s, 3H), 1.32 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.79, 158.09, 155.73, 152.66, 150.71 (d, *J* = 1.9 Hz, 1C), 143.65, 138.17, 135.66, 130.13, 129.14, 128.47, 128.23, 127.88, 127.80, 126.50, 125.76, 117.38 (d, *J* = 7.9 Hz, 1C), 115.25 (d, *J* = 23.7 Hz, 1C), 114.39 (d, *J* = 23.5 Hz, 1C), 81.14, 48.24, 35.60, 34.21, 30.31;

^{19}F NMR (376 MHz, $CDCl_3$): δ = -123.44;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}FN_2O_3Na^+$ $[M+Na]^+$: 563.2680, found: 563.2677.



4e

((2*S*,3*S*,4*R*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-8-fluoro-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2f** (78.8 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4e** as pale yellow oil (97.7 mg, yield: 90%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 90%, Chiralpak column ID, λ = 254 nm, *n*-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 9.096 min, t_r(major) = 10.637 min;

$[\alpha]_D^{25}$ = -81.0° (*c* = 1.0, $CHCl_3$);

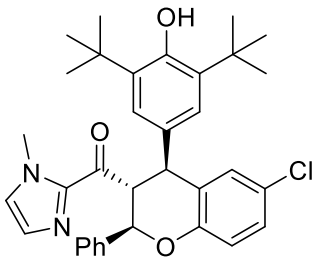
IR (KBr) ν_{max}: 3626, 2961, 2910, 1670, 1587, 1478, 1435, 1403 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.45 (m, 2H), 7.27 – 7.20 (m, 2H), 7.20 – 7.14 (m, 1H), 6.99 – 6.92 (m, 1H), 6.90 (s, 2H), 6.83 (s, 1H), 6.72 (td, *J* = 8.0, 4.9 Hz, 1H), 6.65 (s, 1H), 6.61 – 6.56 (m, 1H), 5.47 (d, *J* = 9.6 Hz, 1H), 4.98 (s, 2H), 4.63 (d, *J* = 11.4 Hz, 1H), 3.58 (s, 3H), 1.31 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.60, 152.55, 150.09, 143.60, 143.13, 143.02, 137.79, 135.49, 130.33, 129.09, 128.47, 128.21, 127.84 (d, *J* = 270.0 Hz, 1C), 127.83, 125.79, 124.33 (d, *J* = 3.4 Hz, 1C), 119.59 (d, *J* = 7.3 Hz, 1C), 113.96 (d, *J* = 17.8 Hz, 1C), 81.30, 48.01 (d, *J* = 2.5 Hz, 1C), 35.66, 34.20, 30.30;

^{19}F NMR (376 MHz, $CDCl_3$): δ = -136.74;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}FN_2O_3Na^+$ $[M+Na]^+$: 563.2686, found: 563.2684.



4f

((2*R*,3*R*,4*S*)-6-chloro-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2g** (82.8 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Δ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4f** as white solid (108.1 mg, yield: 97%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 96%, Chiralpak column AD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 5.341 min, t_r(minor) = 10.197 min;

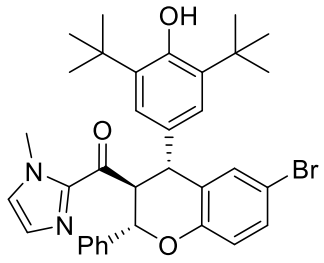
$[\alpha]_D^{25}$ = +106.9° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3618, 3431, 2959, 1668, 2921, 2875, 1631, 1599, 1572, 1476, 1456, 1439, 1405, 1364 cm^{-1};

^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.44 (m, 2H), 7.26 – 7.16 (m, 3H), 7.09 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.92 – 6.86 (m, 3H), 6.85 – 6.78 (m, 2H), 6.66 (s, 1H), 5.40 (d, *J* = 10.1 Hz, 1H), 4.99 (s, 1H), 4.89 (s, 1H), 4.57 (d, *J* = 11.4 Hz, 1H), 3.57 (s, 3H), 1.32 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.62, 153.35, 152.67, 143.60, 138.00, 135.65, 129.92, 129.17, 128.89, 128.51, 128.25, 128.11, 127.78, 127.63, 126.49, 125.75, 125.26, 117.91, 81.14, 48.12, 35.64, 34.20, 30.29;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}ClN_2O_3Na^+$ $[M+Na]^+$: 579.2385, found: 579.2386.



4g

((2*S*,3*S*,4*R*)-6-bromo-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2h** (93.4 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4g** as pale yellow oil (115.5 mg, yield: 96%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 98%, Chiralpak column IG, λ = 254 nm, *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 6.724min, t_r(minor) = 10.096 min;

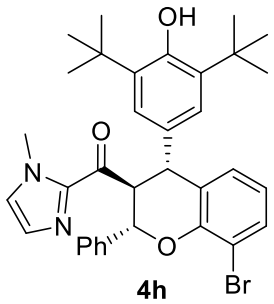
$[\alpha]_D^{25}$ = -84.2° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3603, 3537, 2872, 1633, 1596, 1536, 1506, 1485, 1480, 1439, 1272 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 – 7.43 (m, 2H), 7.27 – 7.14 (m, 3H), 7.09 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.92 – 6.86 (m, 3H), 6.86 – 6.77 (m, 2H), 6.66 (s, 1H), 5.40 (d, *J* = 10.1 Hz, 1H), 4.99 (s, 1H), 4.89 (s, 1H), 4.57 (d, *J* = 11.4 Hz, 1H), 3.57 (s, 3H), 1.32 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.62, 153.35, 152.67, 143.60, 138.00, 135.65, 129.92, 129.17, 128.89, 128.51, 128.25, 128.11, 127.78, 127.63, 126.49, 125.75, 125.26, 117.91, 81.14, 48.12, 35.64, 34.20, 30.29;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}BrN_2O_3Na^+$ $[M+Na]^+$: 623.1880, found: 623.1878.



4h

((2*S*,3*S*,4*R*)-8-bromo-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2i** (93.4 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for indicated time (monitored by TLC) under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral product **4h** as pale yellow oil (81.0 mg, yield: 67%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 95%, Chiralpak column OD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 98:2, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 5.877 min, t_r(major) = 9.131 min;

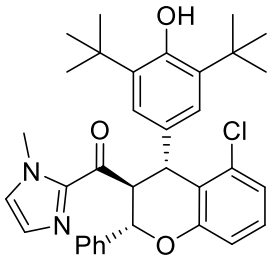
$[\alpha]_D^{25}$ = -107.3° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 2360, 2340, 1868, 1843, 1828, 1791, 1772, 1716, 1699, 1683, 1670, 1653, 1647, 1635, 1616, 1575, 1569, 1558, 1540, 1521, 1506, 1496, 1489, 1473, 1458, 1437, 1419, 1396, 1386 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 7.27 – 7.21 (m, 2H), 7.20 – 7.14 (m, 1H), 6.89 (s, 2H), 6.81 (s, 1H), 6.75 (dt, *J* = 7.8, 1.4 Hz, 1H), 6.70 – 6.64 (m, 2H), 5.54 (d, *J* = 10.0 Hz, 1H), 4.98 (s, 1H), 4.87 (s, 1H), 4.63 (d, *J* = 11.4 Hz, 1H), 3.59 (s, 3H), 1.30 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 192.51, 152.52, 151.10, 143.61, 138.06, 135.49, 131.27, 130.16, 129.18, 128.60, 128.29, 128.26, 128.12, 127.48, 126.47, 125.84, 120.93, 110.53, 81.49, 48.07, 35.63, 34.17, 30.27;

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}BrN_2O_3Na^+$ $[M+Na]^+$: 623.1880, found: 623.1882.



4i

((2*S*,3*S*,4*R*)-5-chloro-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchroman-3-yl)(1-methyl-1*H*-imidazol-2-yl)methanone

A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazole **1a** (42.5 mg, 0.20 mmol), *para*-quinone methides (*p*-QMs) **2j** (82.8 mg, 0.24 mmol), K_2CO_3 (33.2 mg, 0.24 mmol) and chiral catalyst **Λ-Rh3** (5.0 mg, 3.0 mol%). The tube was purged with argon, then anhydrous toluene (0.6 mL) was added. The reaction mixture was stirred at 50°C for 48 hours under argon. After cooling to room temperature, the mixture was purified by flash column chromatography on silica gel (dichloromethane as eluent) to afford chiral product **4i** as pale yellow oil (19.4 mg, yield: 17%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 98%, Chiralpak column ID, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(minor) = 12.955 min, t_r(major) = 15.404 min;

$[\alpha]_D^{25}$ = -145.3° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3615, 3450, 3197, 2977, 2816, 1740, 1602, 1571, 1545, 1483,1404 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.21 (m, 4H), 7.20 – 7.14 (m, 1H), 7.13 – 6.91 (m, 6H), 6.83 – 6.75 (m, 1H), 5.24 (dd, *J* = 9.2, 5.8 Hz, 1H), 3.99 (ddd, *J* = 17.7,

9.2, 3.1 Hz, 1H), 3.92 (d, *J* = 3.3 Hz, 3H), 3.73 (dd, *J* = 17.5, 6.2 Hz, 1H), 1.31 (s, 9H), 1.19 (s, 9H);

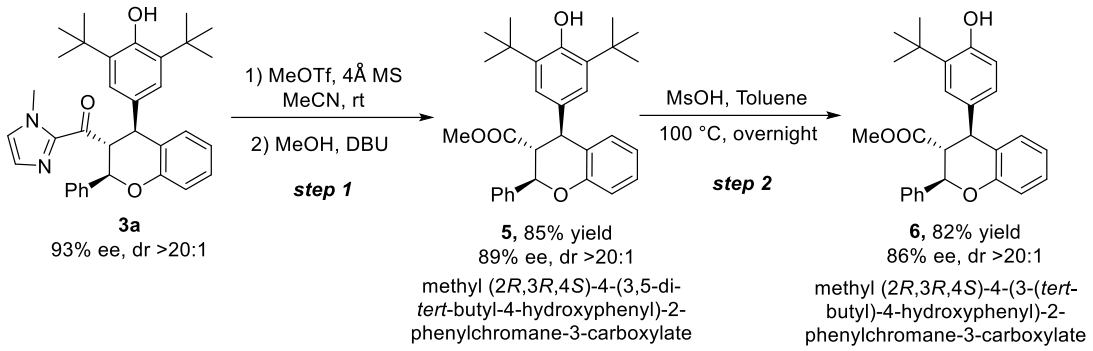
^{13}C NMR (101 MHz, $CDCl_3$):

Major, δ = 189.73, 186.62, 152.65, 149.24, 148.13, 142.61, 142.44, 135.17, 134.05, 133.99, 133.85, 129.66, 128.84, 128.53, 128.07, 127.16, 121.76, 114.79, 44.28, 41.40, 36.30, 35.32, 29.45;

Minor, δ = 189.61, 186.66, 152.91, 148.99, 148.02, 142.50, 142.38, 135.38, 134.11, 133.89, 133.80, 129.61, 128.75, 128.62, 128.04, 126.56, 121.89, 114.71, 44.42, 41.30, 36.34, 35.30, 29.50.

HRMS (ESI, *m*/*z*) calcd. for $C_{34}H_{37}ClN_2O_3Na^+$ $[M+Na]^+$: 579.2385, found: 579.2384.

5. Synthetic Transformations



3a
93% ee, dr >20:1

5, 85% yield
89% ee, dr >20:1
methyl (2*R*,3*R*,4*S*)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenylchromane-3-carboxylate

6, 82% yield
86% ee, dr >20:1
methyl (2*R*,3*R*,4*S*)-4-(3-(*tert*-butyl)-4-hydroxyphenyl)-2-phenylchromane-3-carboxylate

Step 1:

The directing imidazole moiety was cleaved according to a reported procedure with slight modification.[7] 4 Å MS (172 mg, 100 mg/0.1 mmol of **3a**) was added to a solution of **3a** (90.0 mg, 0.172 mmol) in dry CH_3CN (1.7 mL) under argon atmosphere. The suspension was stirred vigorously under a positive pressure of argon for 2 hours at 25°C. Then methyl trifluoromethansulfonate (78 uL, 0.688 mmol, 4.0 eq.) was added. After being stirred at 25°C for 12 hours, MeOH (1.0 mL) and DBU (39 uL, 0.258 mmol, 1.5 eq.) were subsequently added. After being stirred at 25 °C for 40 min, the reaction mixture was concentrated and the residue was subjected to a silica gel flash chromatography (petroleum ether/ EtOAc = 20:1 to 10:1) to afford products **5** as pale yellow oil (69.0 mg, yield: 85%).

Enantiomeric excess was determined by HPLC analysis, *ee* = 89%, Chiralpak column OD-H, λ = 254 nm, *n*-hexane/*i*-PrOH = 99:1, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.723 min, t_r(minor) = 6.018 min;

$[\alpha]_D^{25}$ = +176.0° (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3564, 2848, 1731, 1601, 1534, 1425, 1400, 1289 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.43 (m, 2H), 7.40 – 7.31 (m, 3H), 7.18 – 7.12 (m, 1H), 6.95 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.91 – 6.82 (m, 4H), 5.20 (d, *J* = 10.1 Hz, 1H), 5.11 (s, 1H), 4.54 (d, *J* = 11.4 Hz, 1H), 3.21 (s, 3H), 3.11 (dd, *J* = 11.4, 10.1 Hz, 1H), 1.38 (s, 18H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.33, 154.69, 152.81, 138.45, 135.89, 131.71, 129.81, 128.75, 128.55, 127.73, 127.05, 125.24, 124.97, 120.88, 116.65, 79.84, 55.62, 51.39, 46.92, 34.33, 30.40;

HRMS (ESI, *m*/*z*) calcd. for $C_{31}H_{36}O_4Na^+$ $[M+Na]^+$: 495.2506, found: 495.2505.

Step 2:

To a solution of **5** (47.2 mg, 0.1 mmol) in anhydrous toluene (2 mL) was added methanesulfonic acid (144.2 mg, 1.5 mmol) at ambient temperature, then stirred at 100 °C overnight and monitored by TLC. The reaction was quenched with the addition of H_2O (10 mL) and the mixture was then extracted with EtOAc. The combined organic layer was concentrated in vacuum and the residue purified by flash column chromatography on silica gel chromatography (petroleum ether/EtOAc = 8:1) to afford product **6** as white solid (34.2 mg, 82% yield). The racemic reaction was carried out in the same conditions.

Enantiomeric excess was determined by HPLC analysis, *ee* = 86%, Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 95:5, flow rate: 1.0 mL/min, 30 °C, t_r(major) = 4.601 min, t_r(minor) = 6.443 min;

$[\alpha]_D^{25}$ = +231.8^o (*c* = 1.0, $CHCl_3$);

IR (KBr) ν_{max}: 3513, 2792, 1702, 1643, 1534, 1490, 1432, 1376, 1325, 1288 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.41 (m, 2H), 7.41 – 7.31 (m, 3H), 7.19 – 7.09 (m, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.87 – 6.79 (m, 3H), 6.55 (d, *J* = 8.1 Hz, 1H), 5.18 (d, *J* = 10.1 Hz, 1H), 4.99 (s, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 3.21 (s, 3H), 3.14 (dd, *J* = 11.5, 10.1 Hz, 1H), 1.36 (s, 9H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.42, 154.67, 153.36, 138.28, 136.09, 133.13, 129.77, 128.83, 128.57, 127.91, 127.83, 127.05, 126.75, 124.91, 120.99, 116.93, 116.73, 79.74, 55.67, 51.54, 46.52, 34.54, 29.64;

HRMS (ESI, *m*/*z*) calcd. for $C_{27}H_{28}O_4Na^+$ $[M+Na]^+$: 439.1880, found: 439.1882.

6. ^{1}H NMR and ^{13}C NMR Spectra

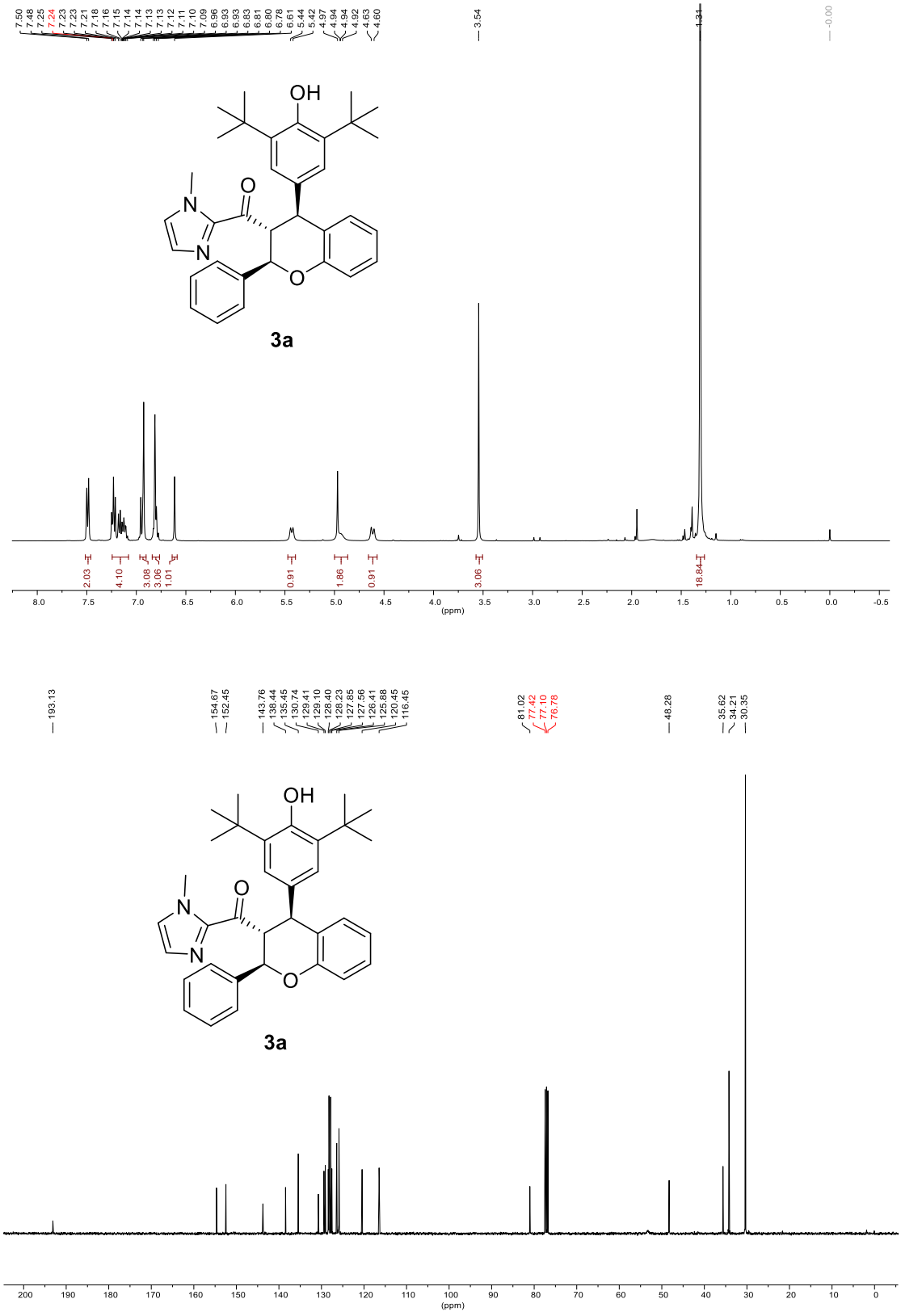


Figure S1. ^{1}H and ^{13}C NMR spectrum of **3a**.

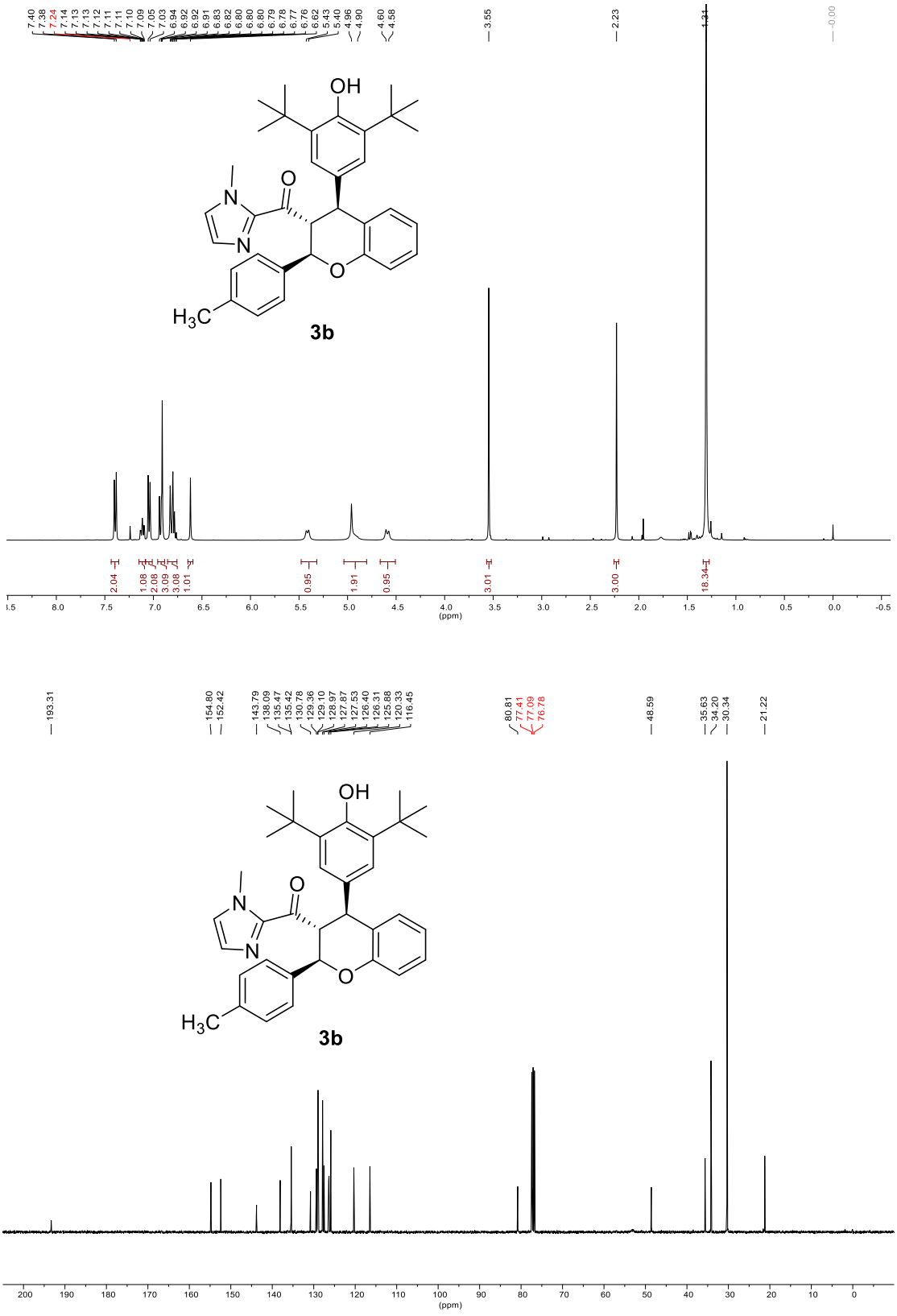


Figure S2. ^{1}H and ^{13}C NMR spectrum of **3b**.

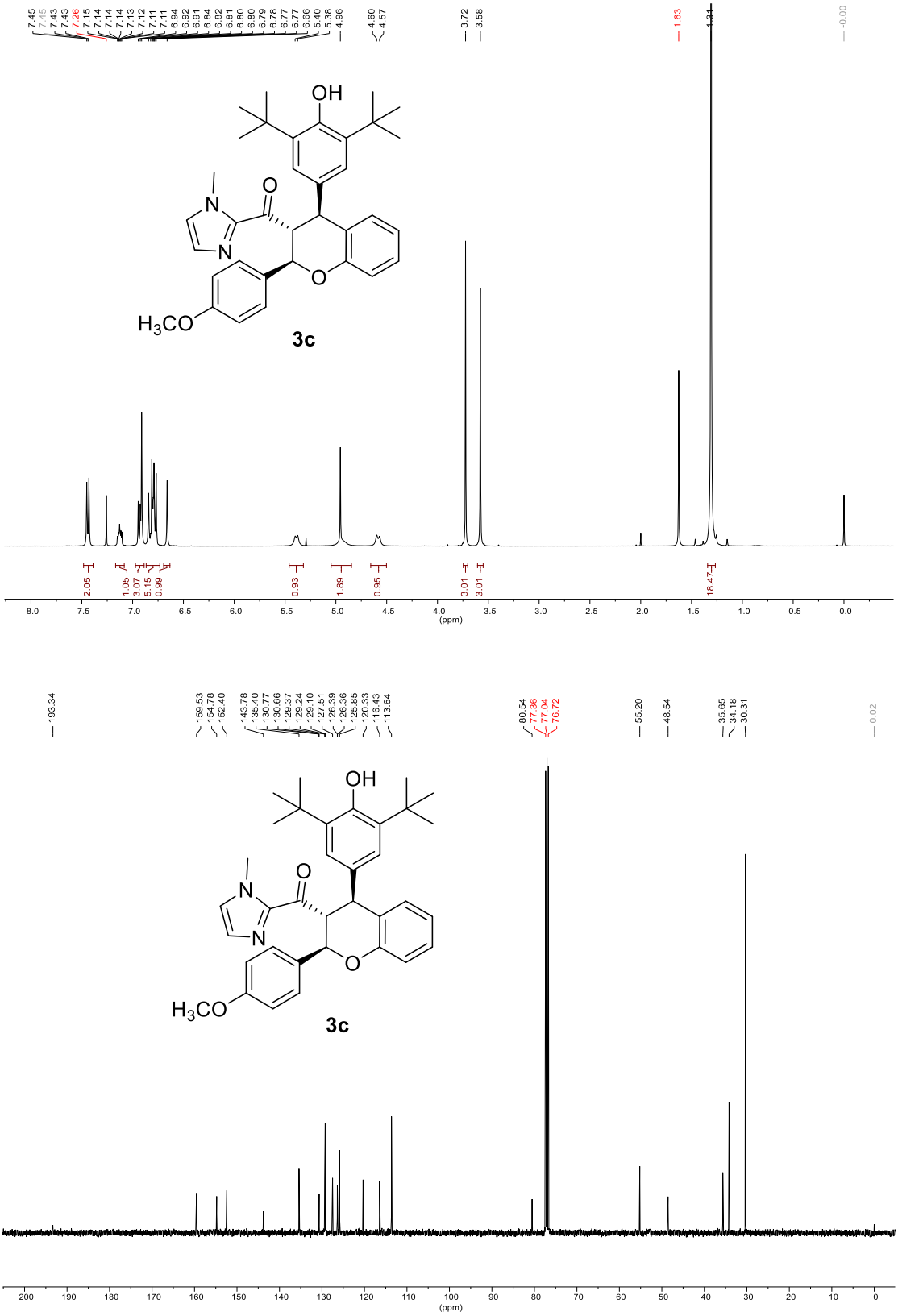
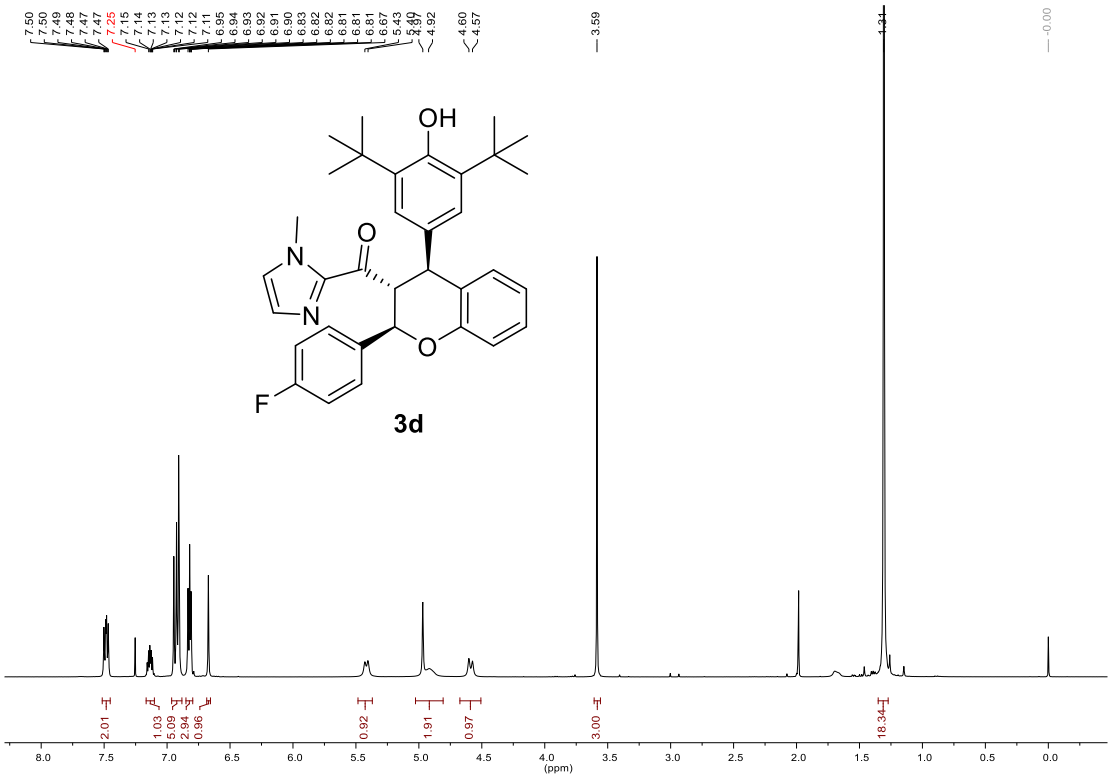
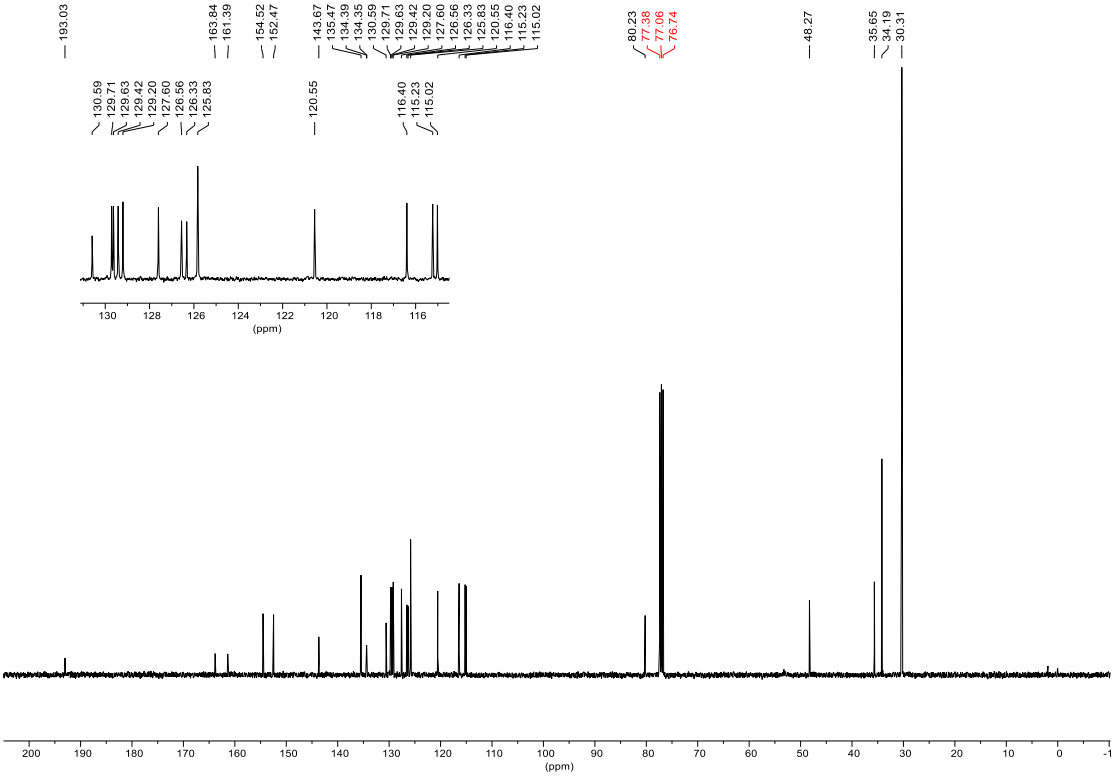


Figure S3. ^{1}H and ^{13}C NMR spectrum of **3c**.


OH
O
N
N
O
F
3d
7.50
7.50
7.49
7.48
7.48
7.47
7.47
7.25
7.15
7.14
7.13
7.13
7.12
7.12
7.11
6.95
6.94
6.93
6.92
6.91
6.90
6.83
6.82
6.82
6.81
6.81
6.81
6.67
5.43
5.40
4.92
4.60
4.57
3.59
1.31
0.00
2.01
1.03
5.09
2.94
0.96
0.92
1.91
0.97
3.00
18.34
(ppm)


193.03
163.84
161.39
154.52
152.47
143.67
135.47
134.39
134.35
130.59
129.71
129.63
129.42
129.20
127.60
126.56
126.33
125.83
120.55
116.40
115.23
115.02
80.23
77.38
77.06
76.74
48.27
35.65
34.19
30.31
(ppm)

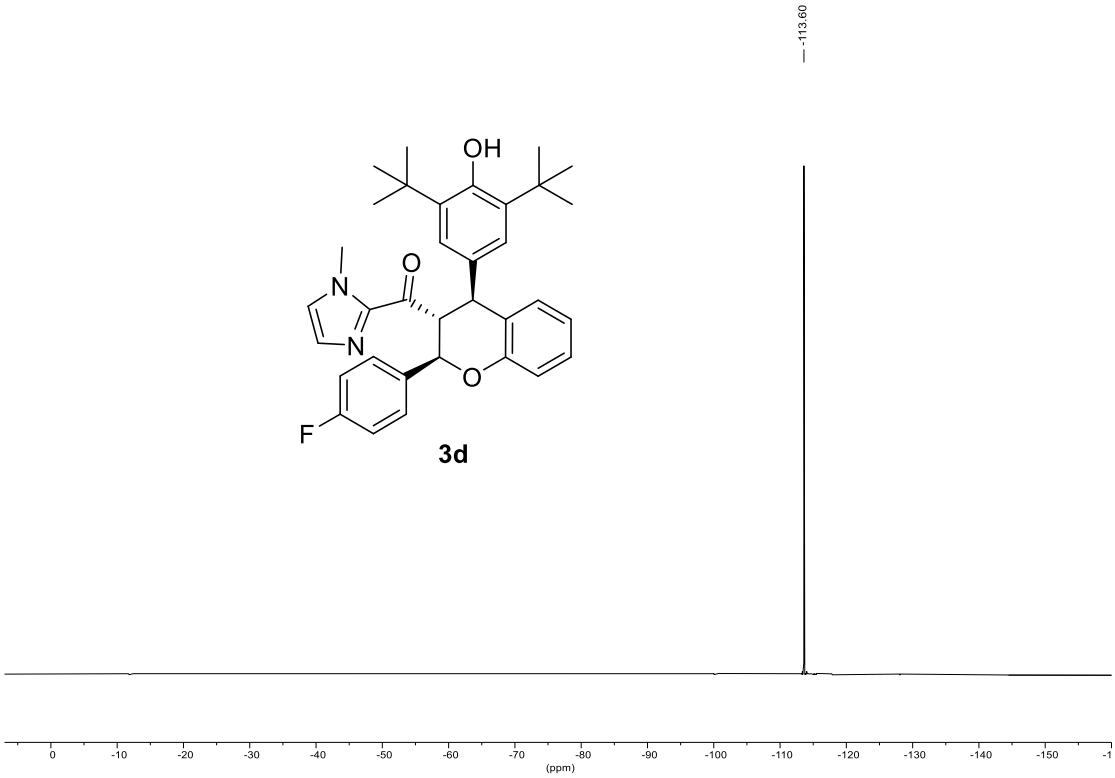
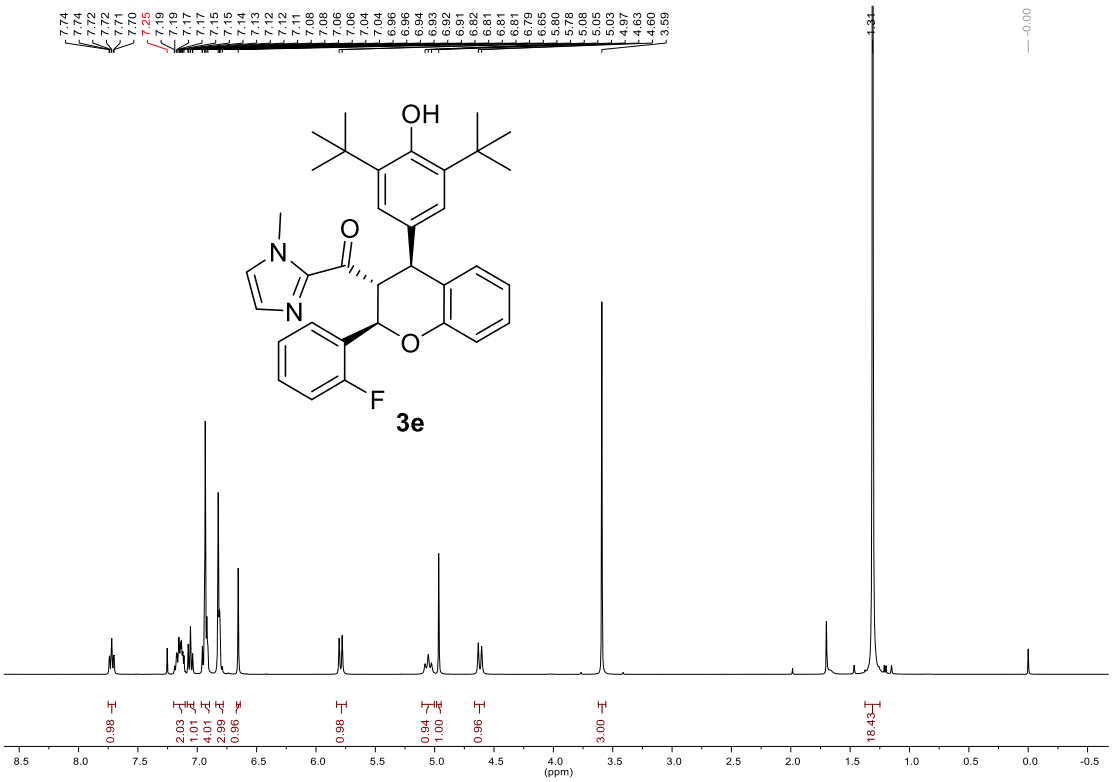


Figure S4. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **3d**.


OH
O
N
N
O
F
3e

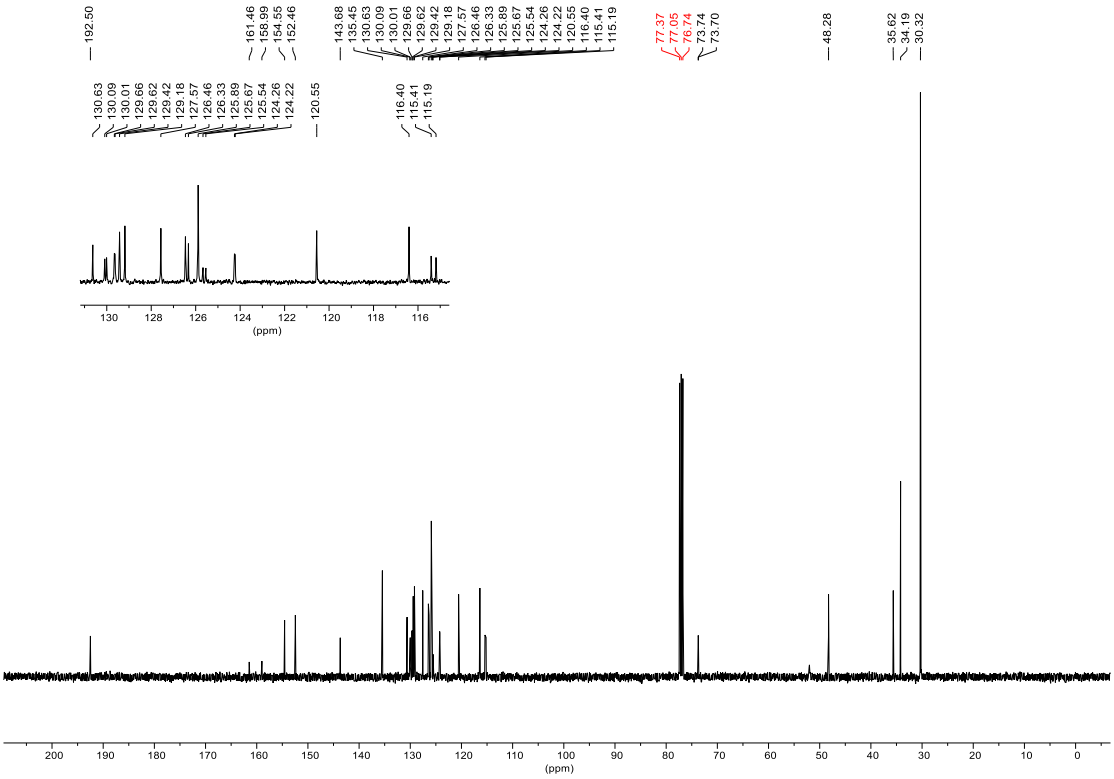


Figure S5. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **3e**.

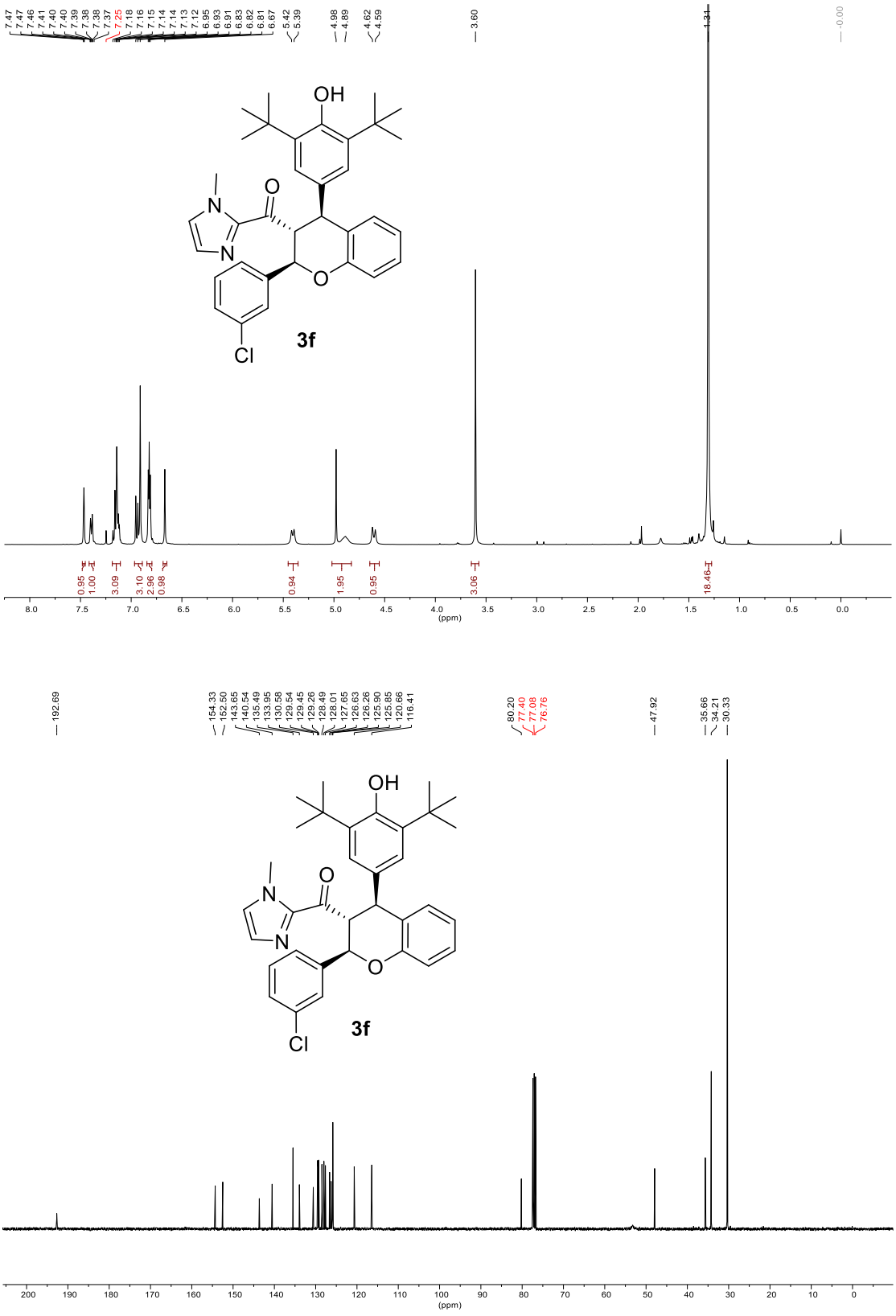


Figure S6. ^{1}H and ^{13}C NMR spectrum of **3f**.

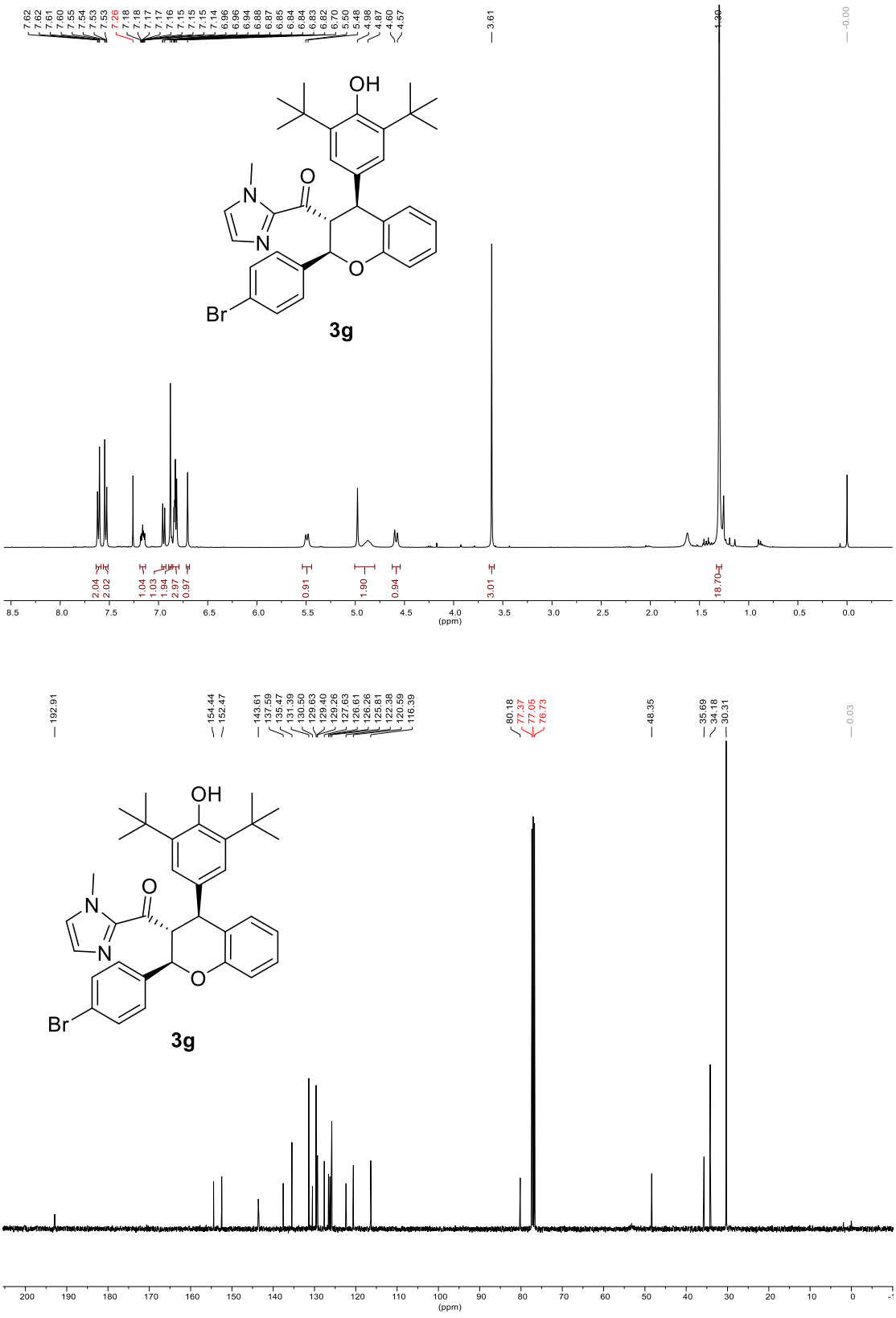
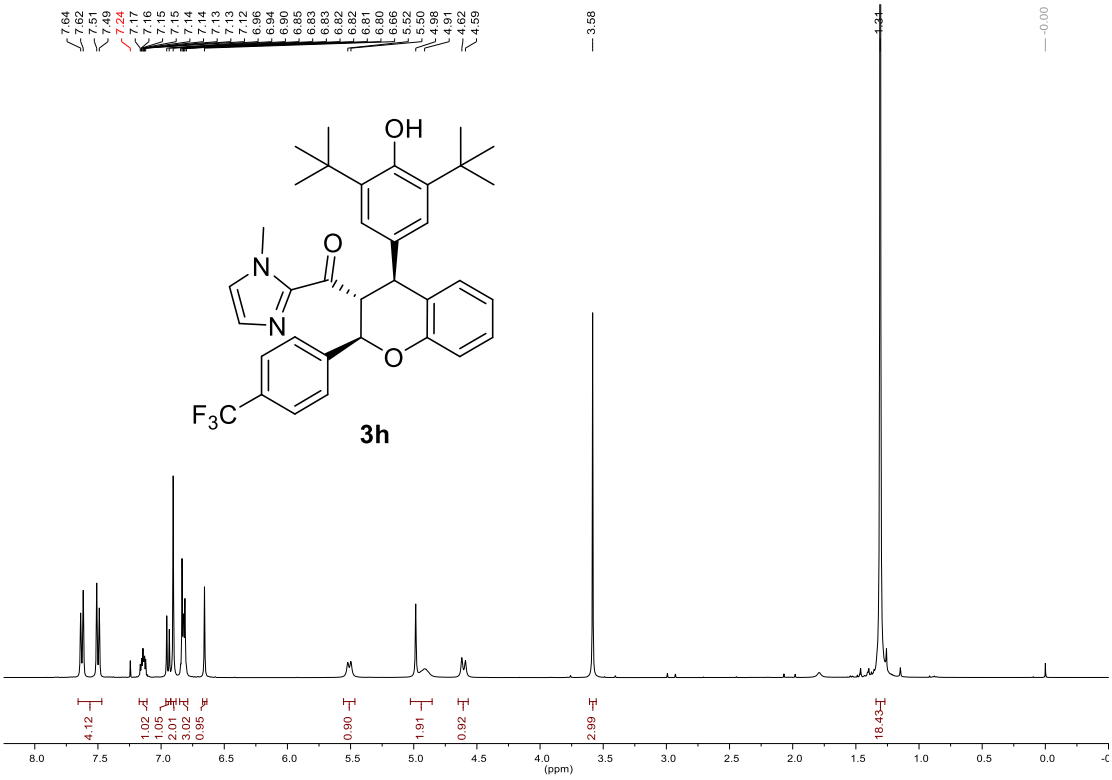
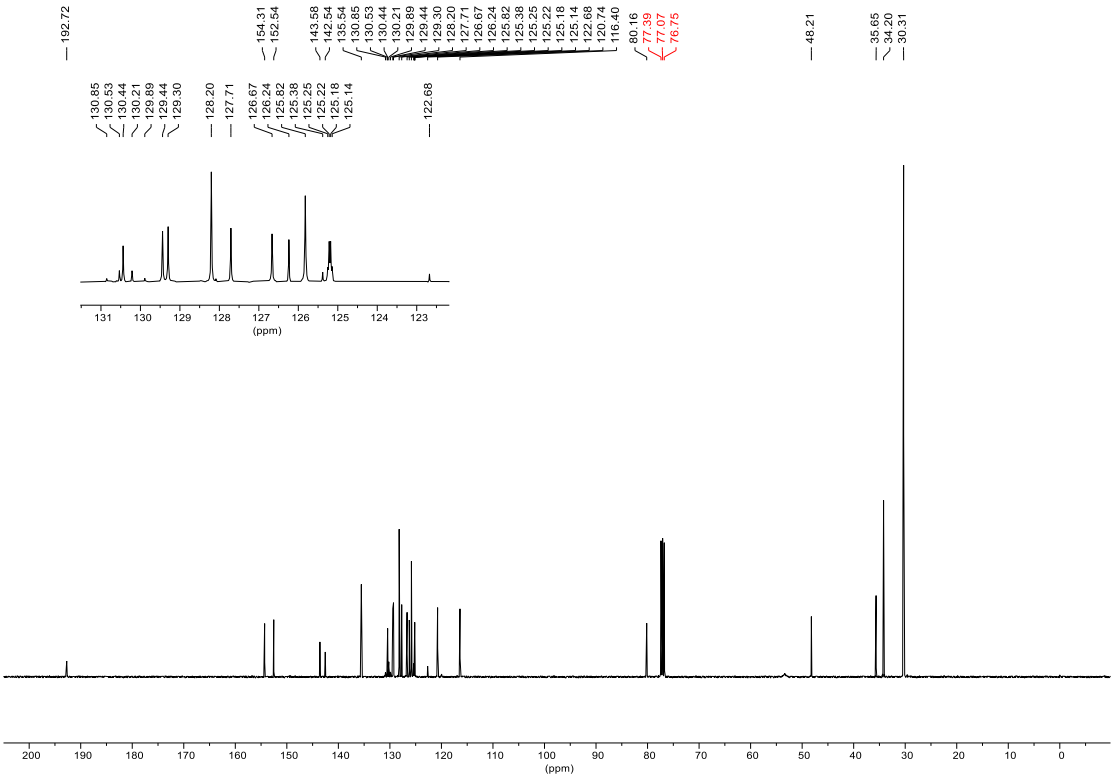


Figure S7. ^{1}H and ^{13}C NMR spectrum of **3g**.


OH
O
N
N
O
F3C
3h
7.64
7.62
7.51
7.49
7.24
7.17
7.16
7.15
7.15
7.14
7.14
7.13
7.13
7.12
6.96
6.94
6.90
6.85
6.83
6.82
6.82
6.81
6.80
6.66
5.52
5.50
4.98
4.81
4.62
4.59
3.58
1.31
0.00
4.12
1.02
1.05
2.01
3.02
0.95
0.90
1.91
0.92
2.99
18.43
(ppm)


192.72
154.31
152.54
143.58
142.54
135.54
130.85
130.53
130.44
130.21
129.89
129.44
129.30
128.20
127.71
126.67
126.24
125.82
125.38
125.25
125.22
125.18
125.14
122.68
120.74
116.40
80.16
77.39
77.07
76.75
48.21
35.65
34.20
30.31
(ppm)

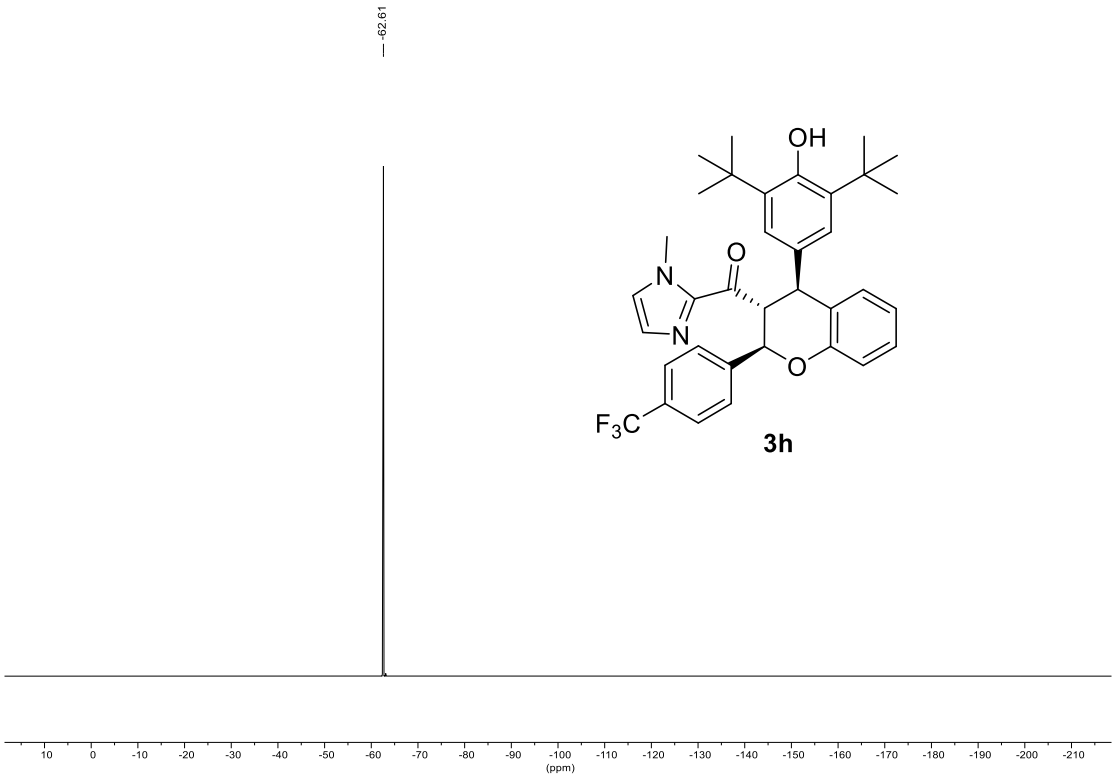


Figure S8. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **3h**.

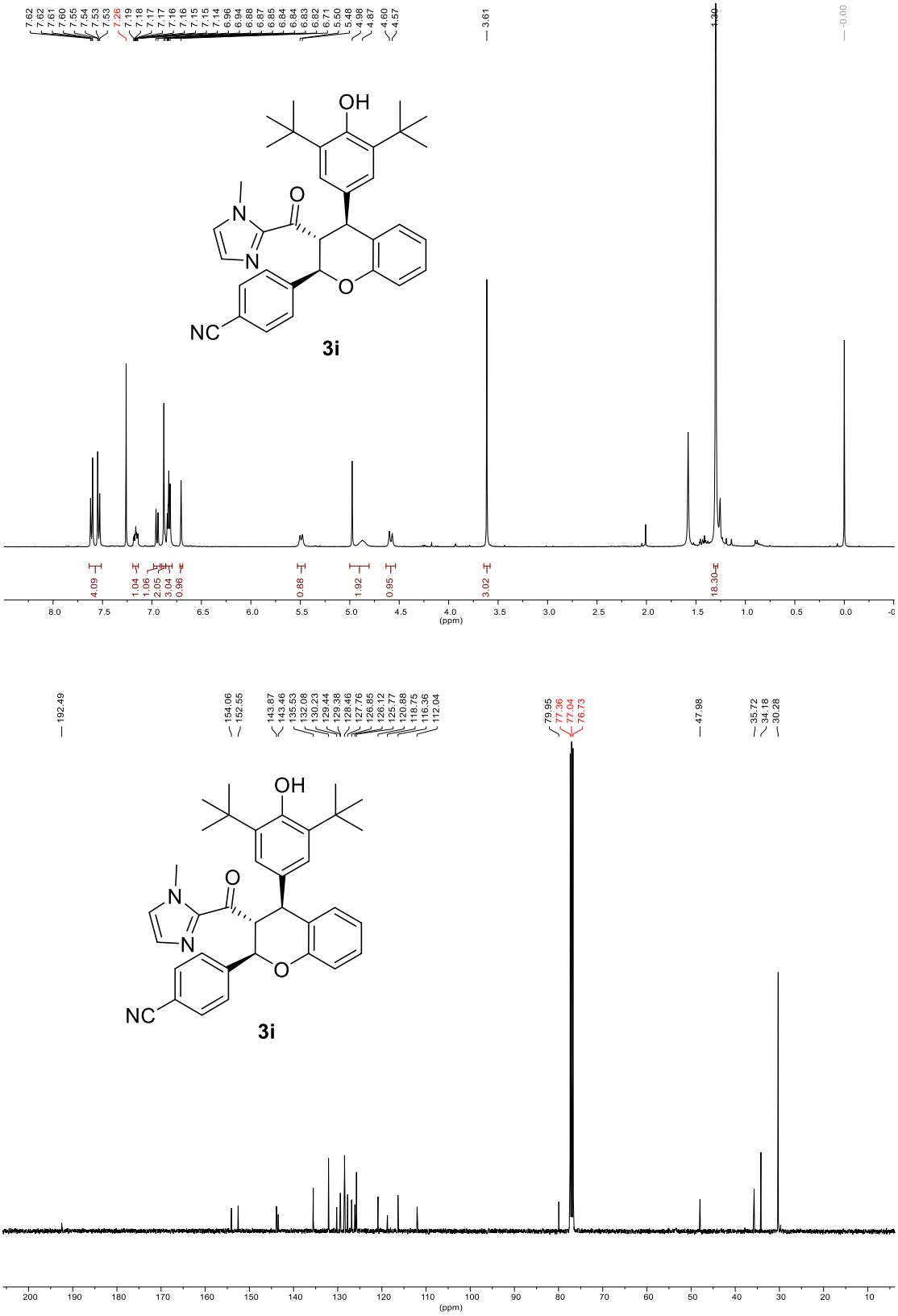


Figure S9. ^{1}H and ^{13}C NMR spectrum of **3i**.

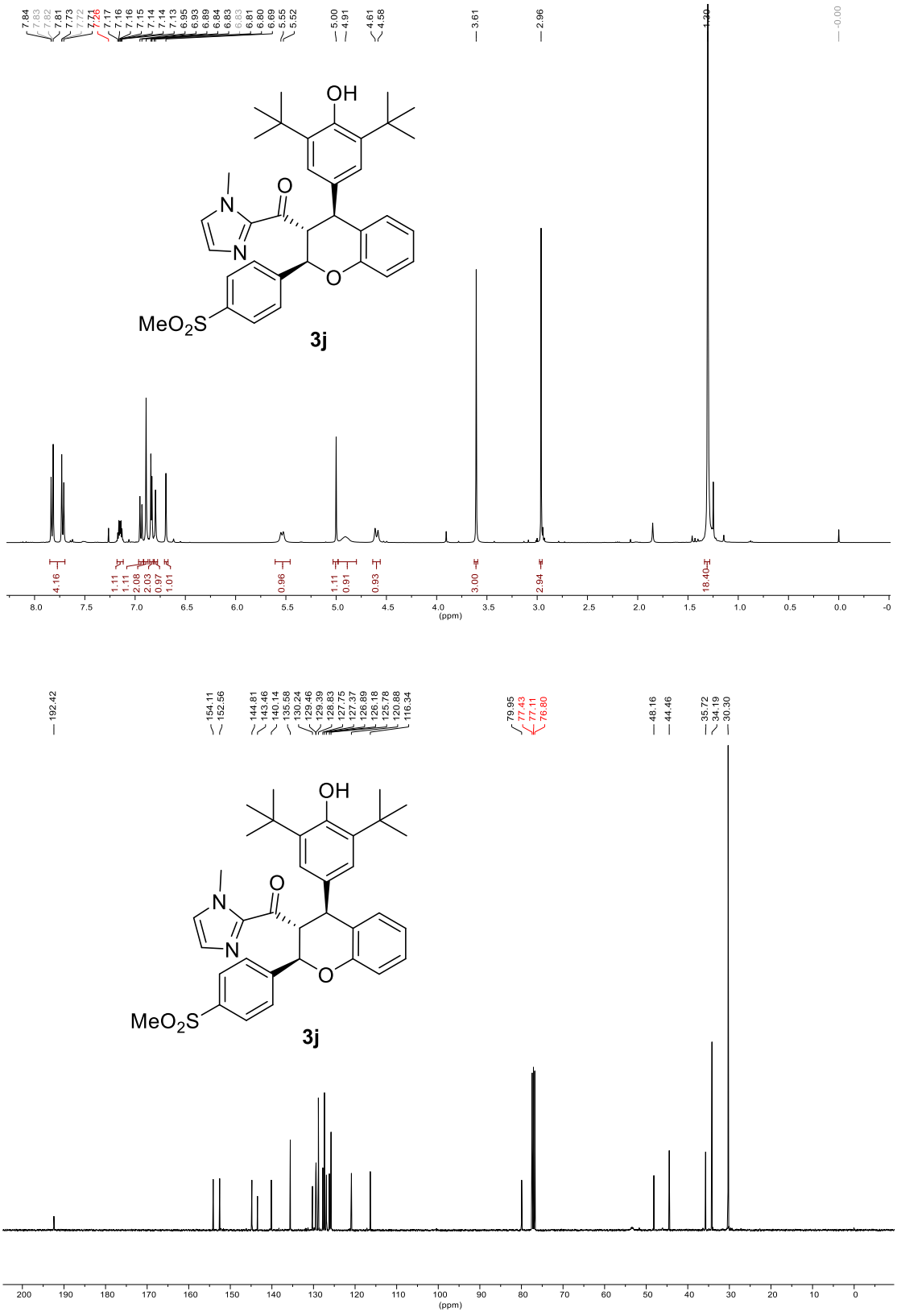


Figure S10. ^{1}H and ^{13}C NMR spectrum of **3j**.

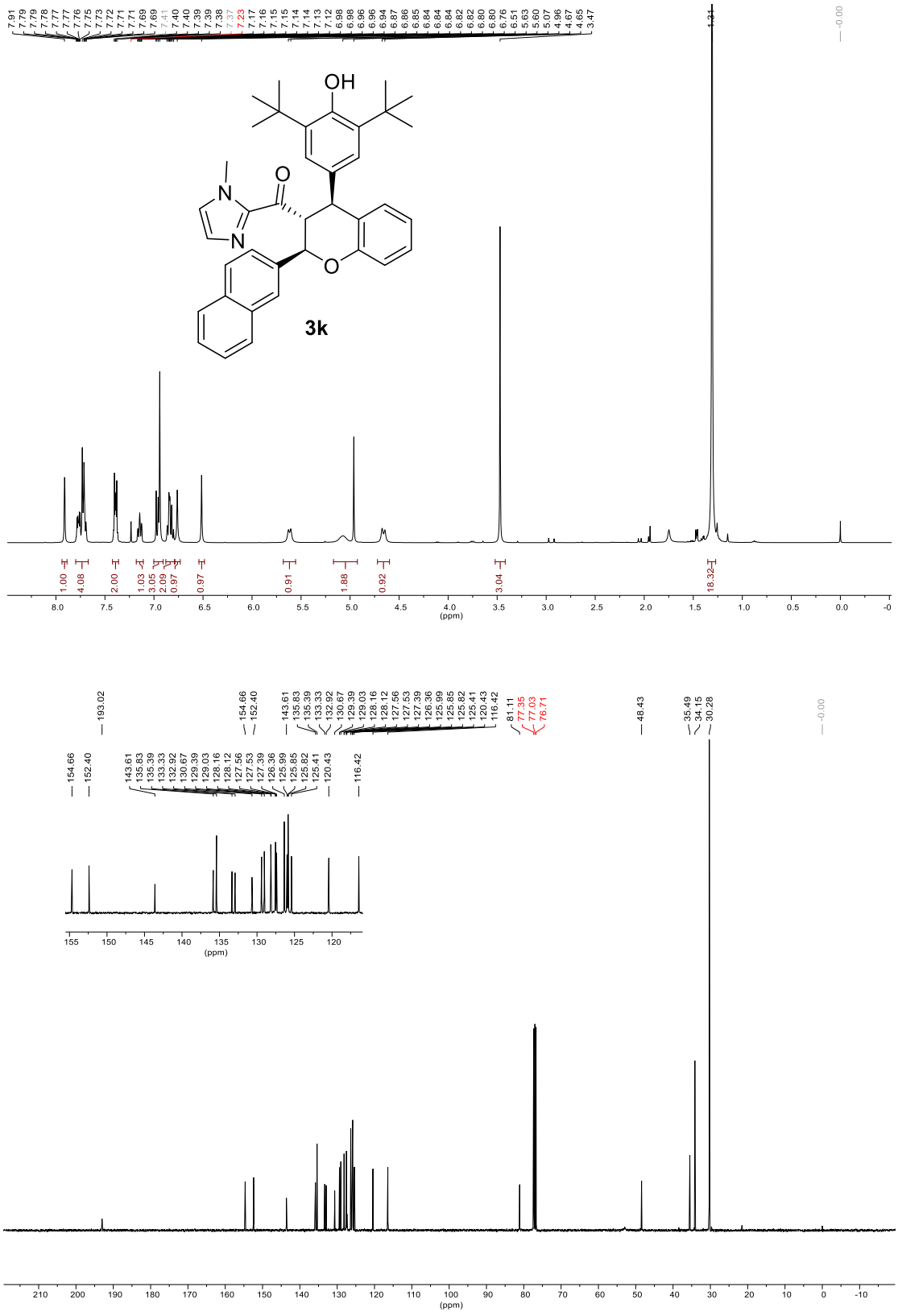


Figure S11. ^{1}H and ^{13}C NMR spectrum of **3k**.

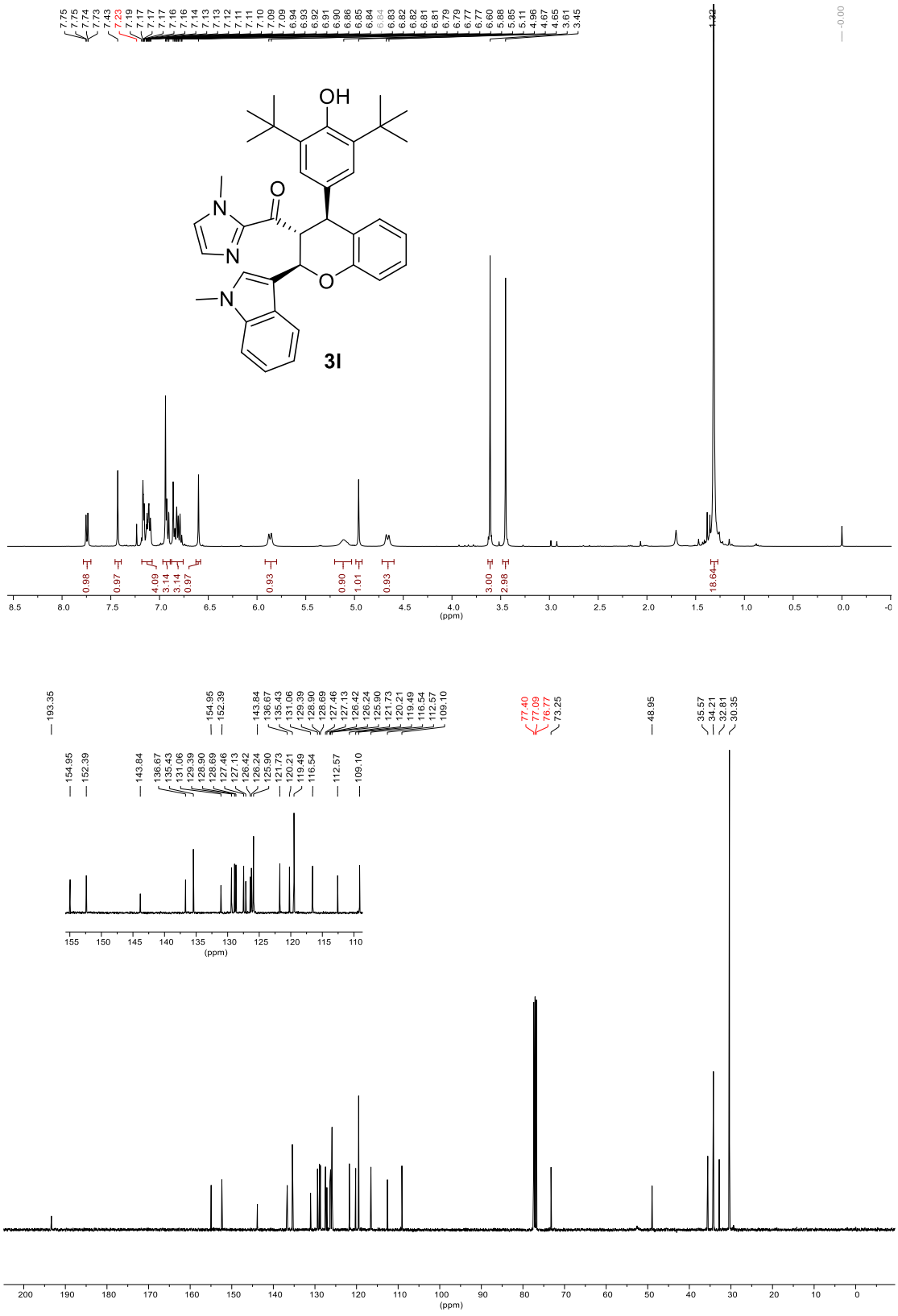


Figure S12. ^{1}H and ^{13}C NMR spectrum of **3l**.

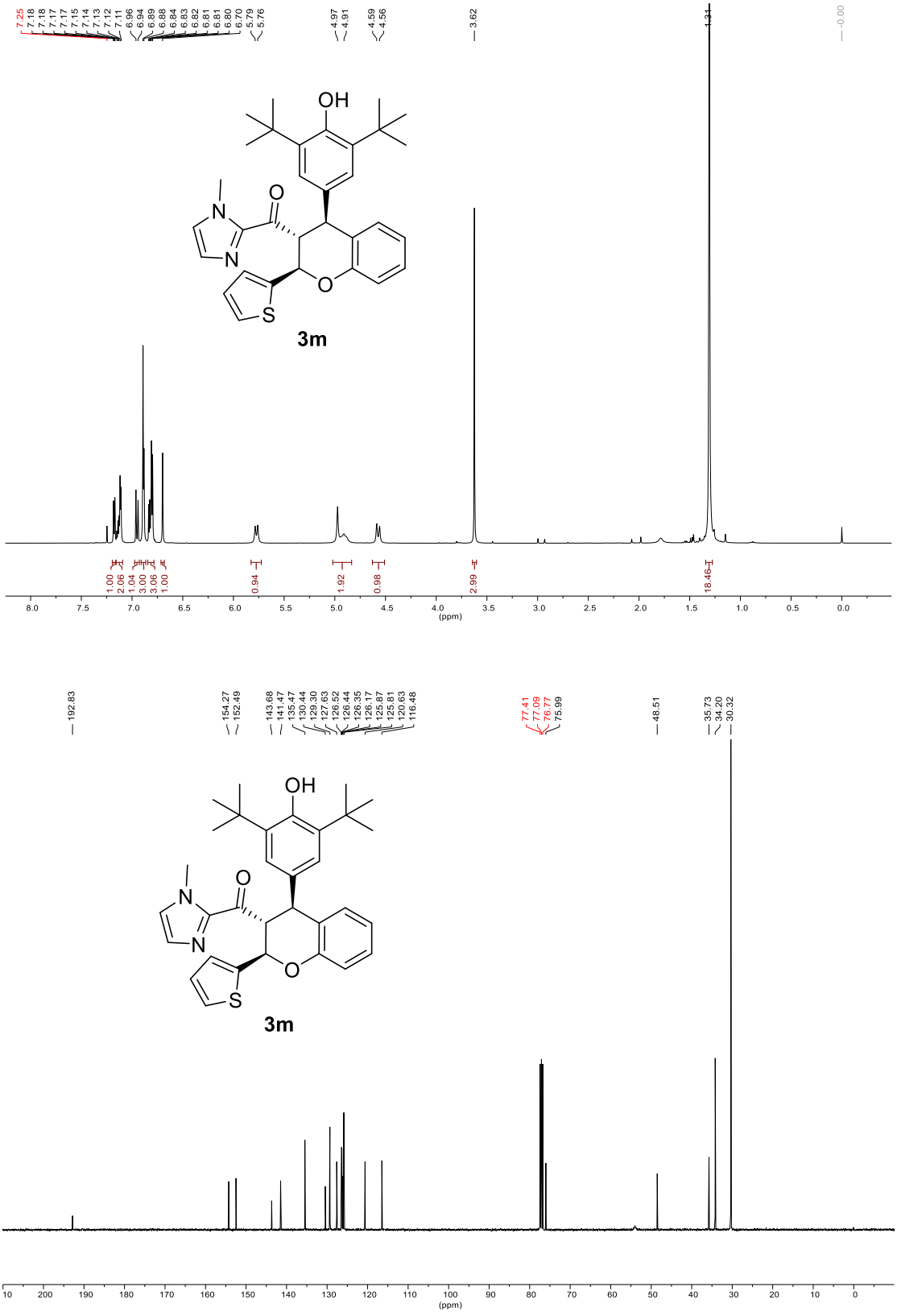


Figure S13. ^{1}H and ^{13}C NMR spectrum of **3m**.

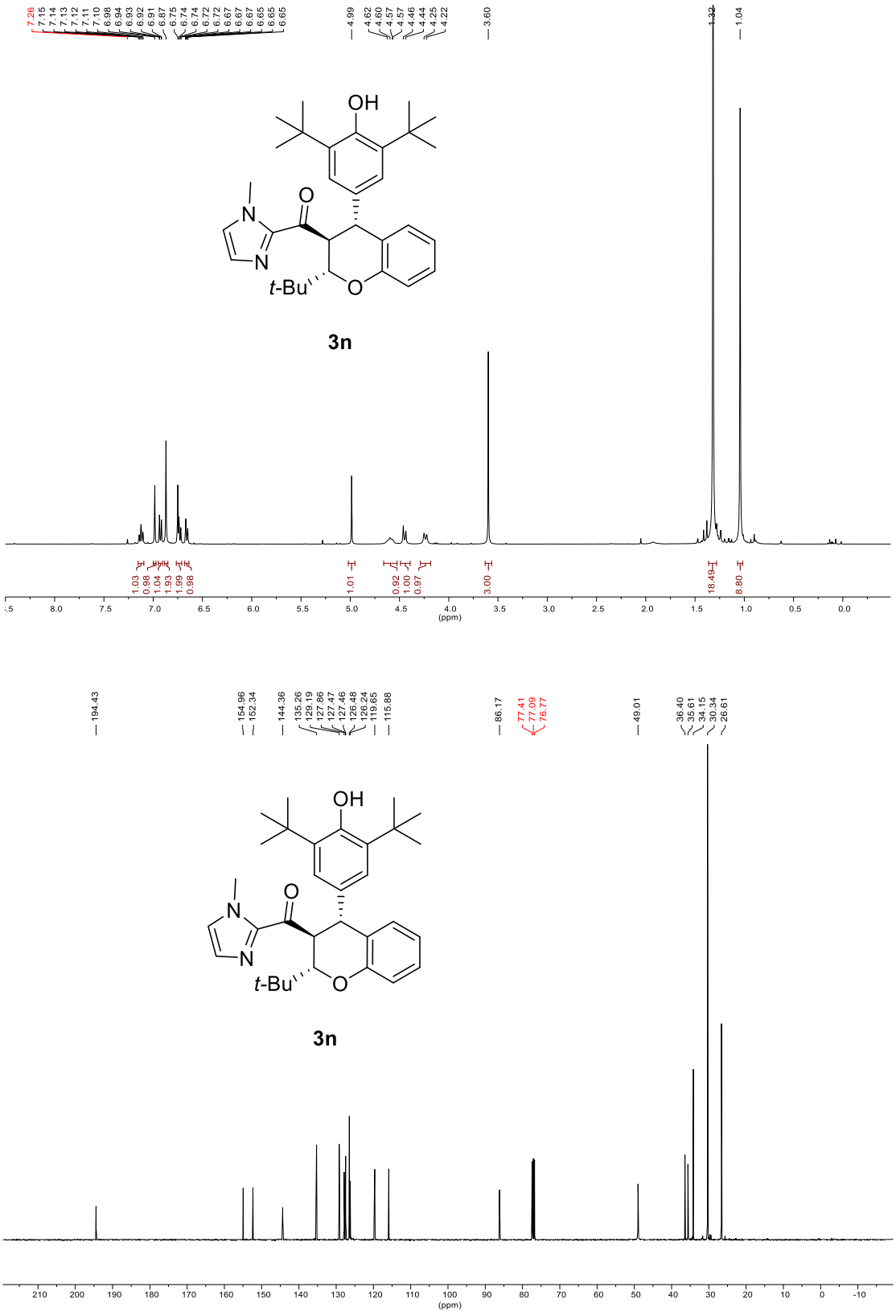


Figure S14. ^{1}H and ^{13}C NMR spectrum of **3n**.

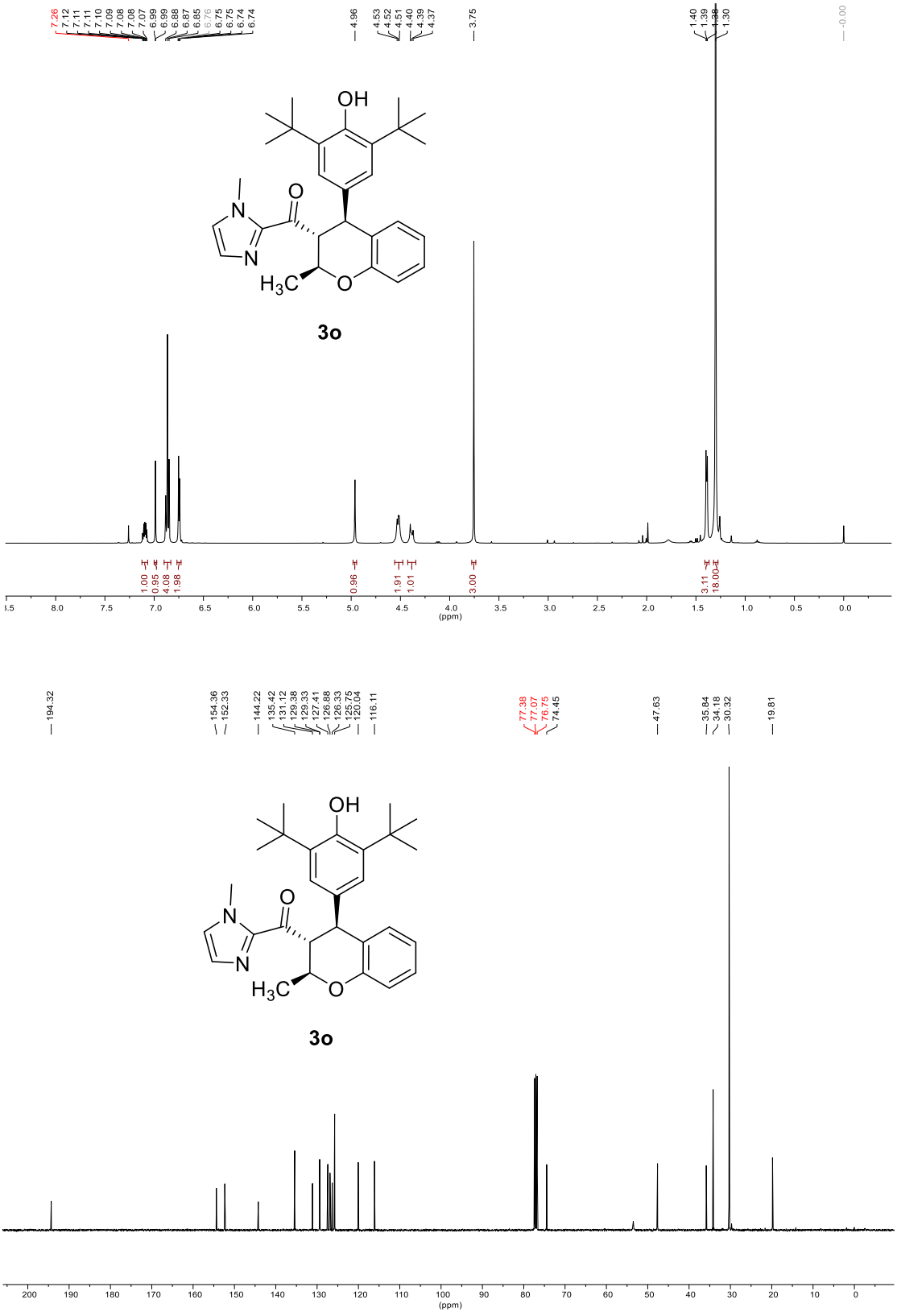


Figure S15. ^{1}H and ^{13}C NMR spectrum of **3o**.

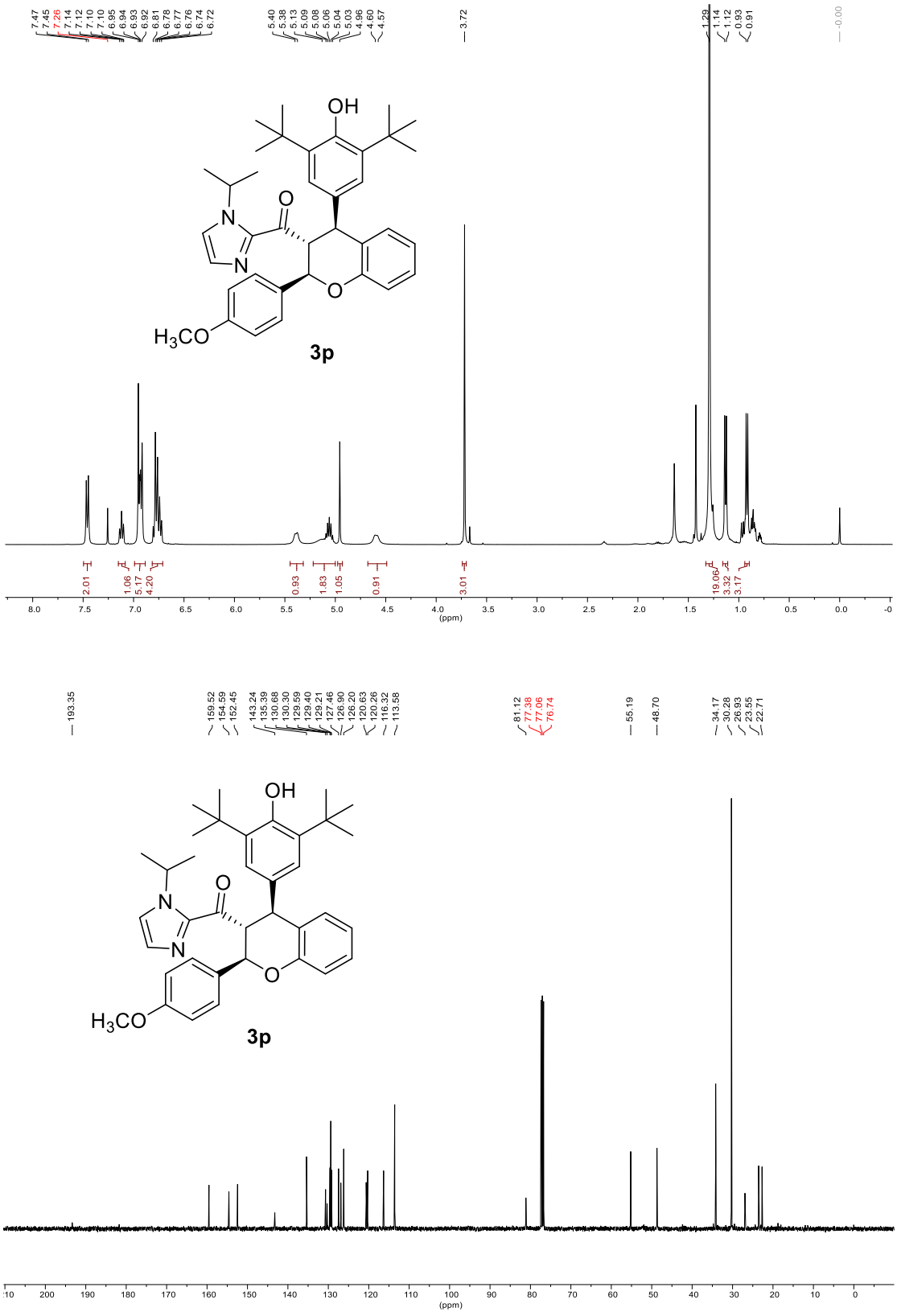


Figure S16. ^{1}H and ^{13}C NMR spectrum of **3p**.

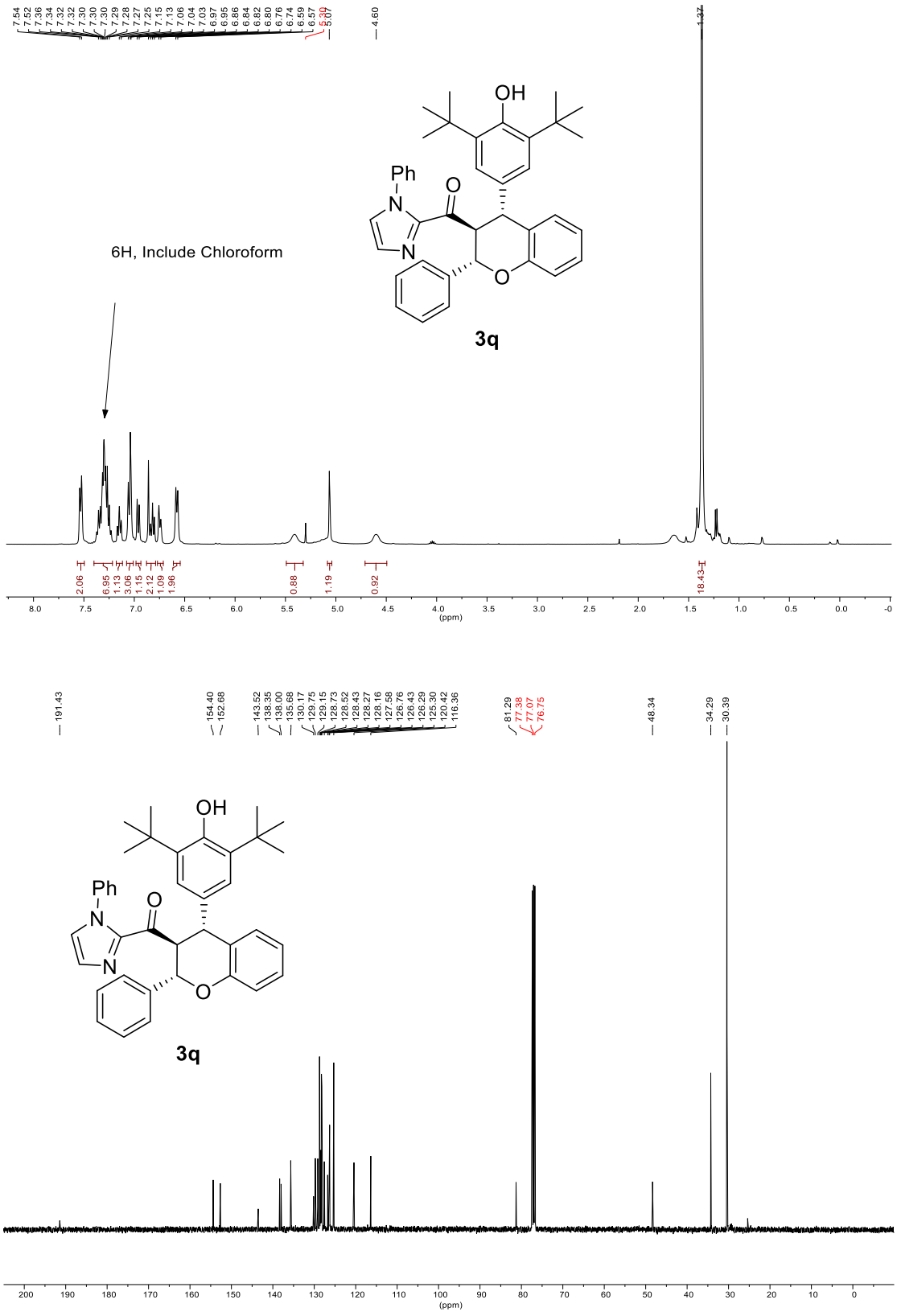


Figure S17. ^{1}H and ^{13}C NMR spectrum of **3q**.

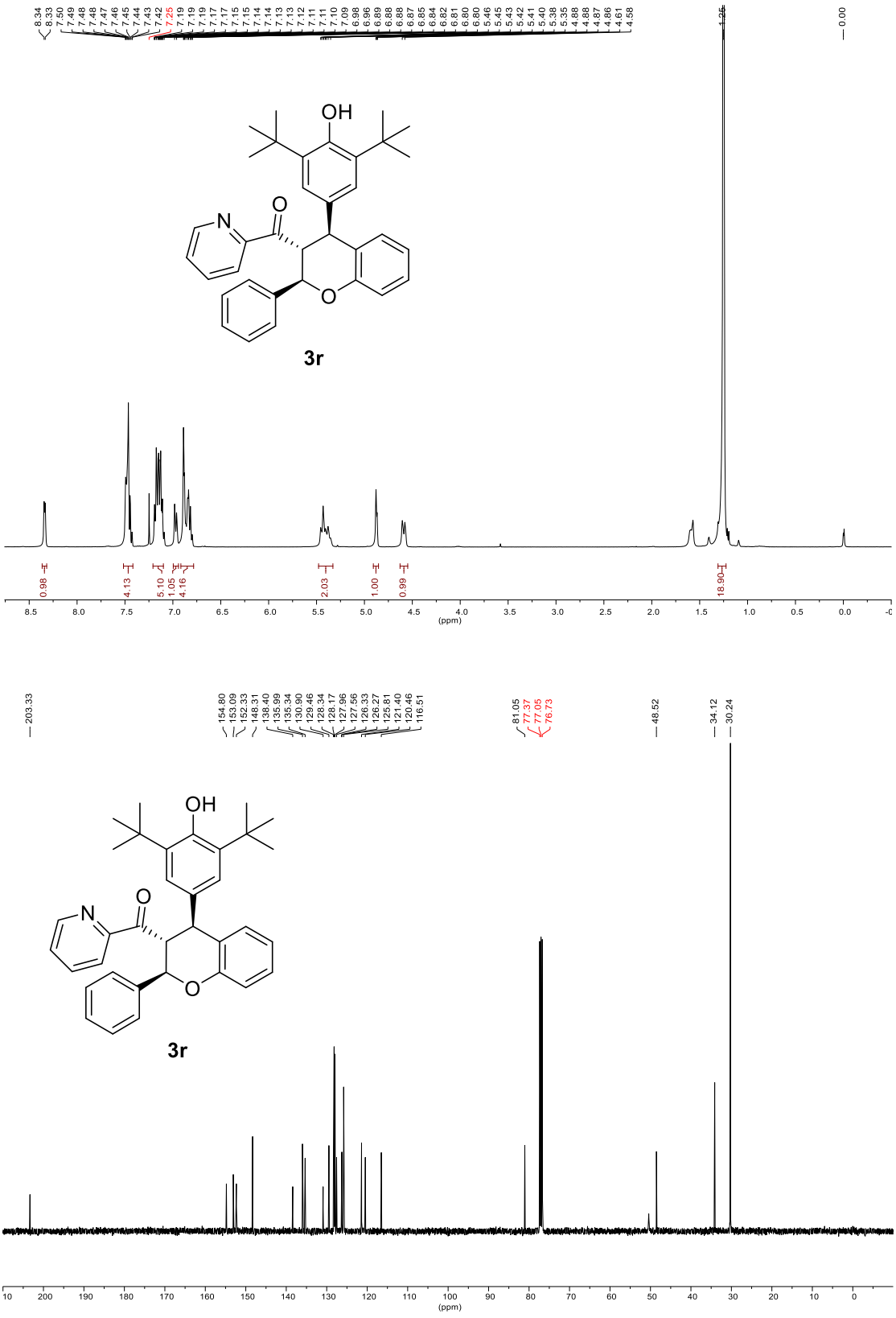


Figure S18. ^{1}H and ^{13}C NMR spectrum of **3r**.

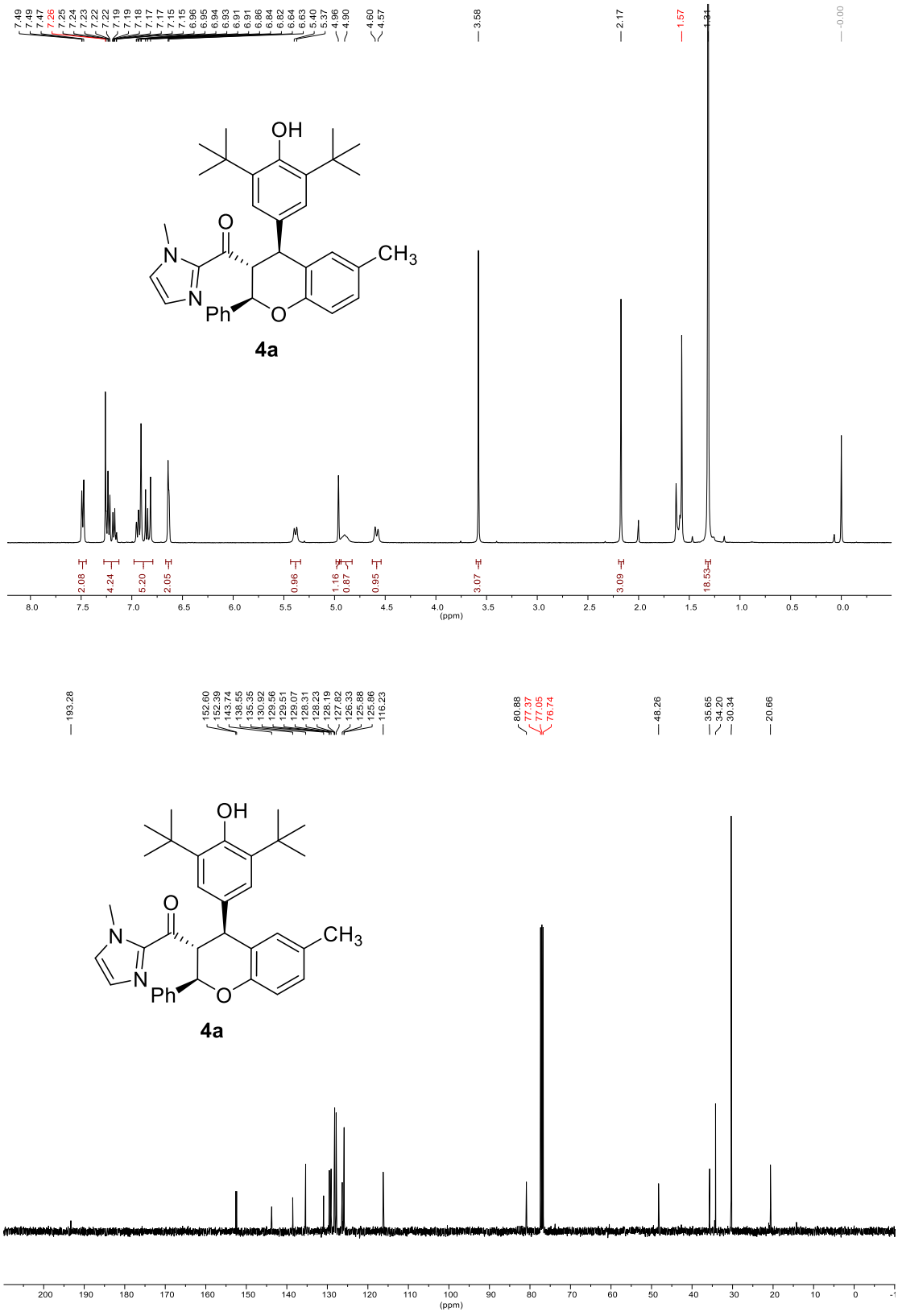


Figure S19. ^{1}H and ^{13}C NMR spectrum of **4a**.

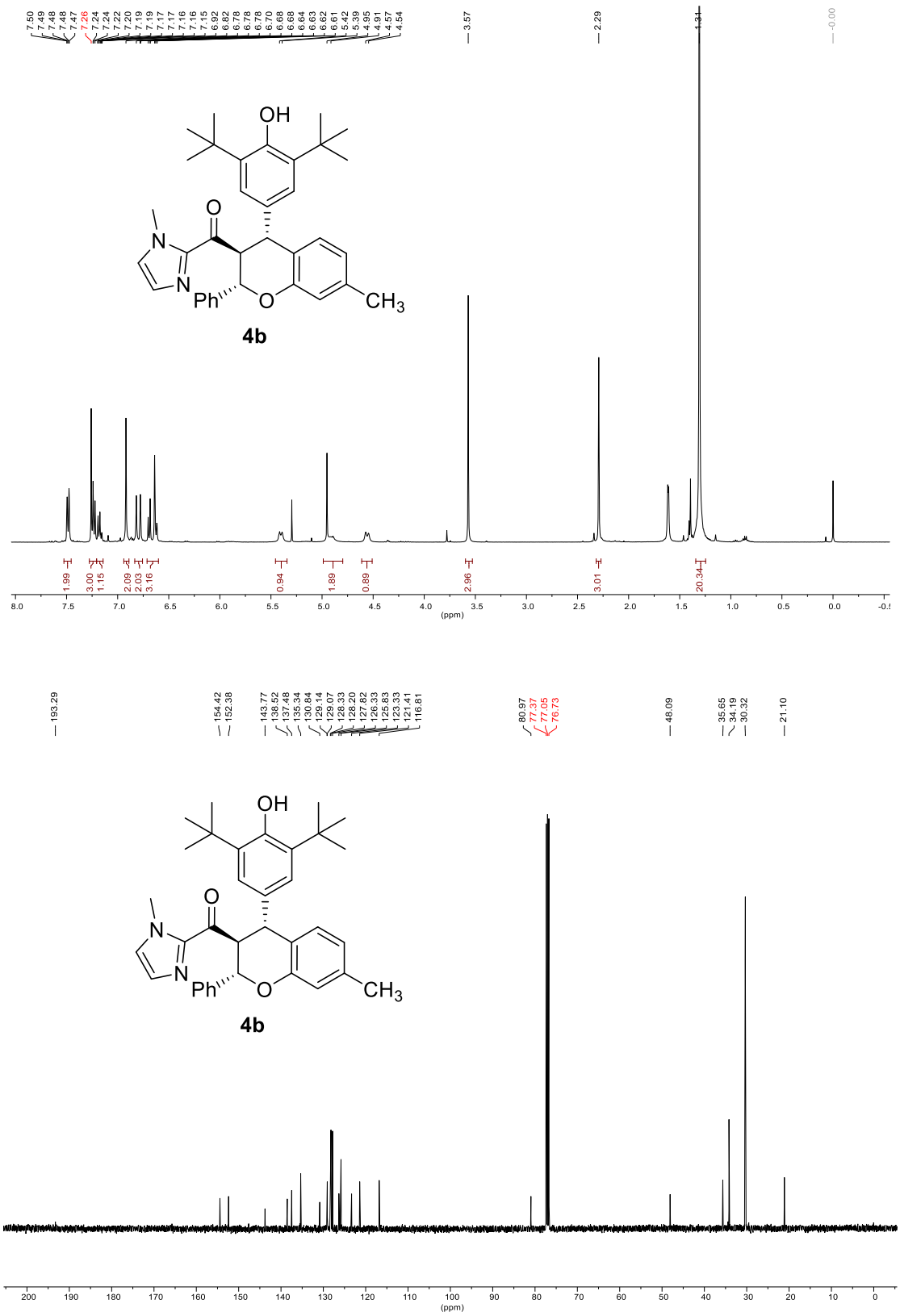


Figure S20. ^{1}H and ^{13}C NMR spectrum of **4b**.

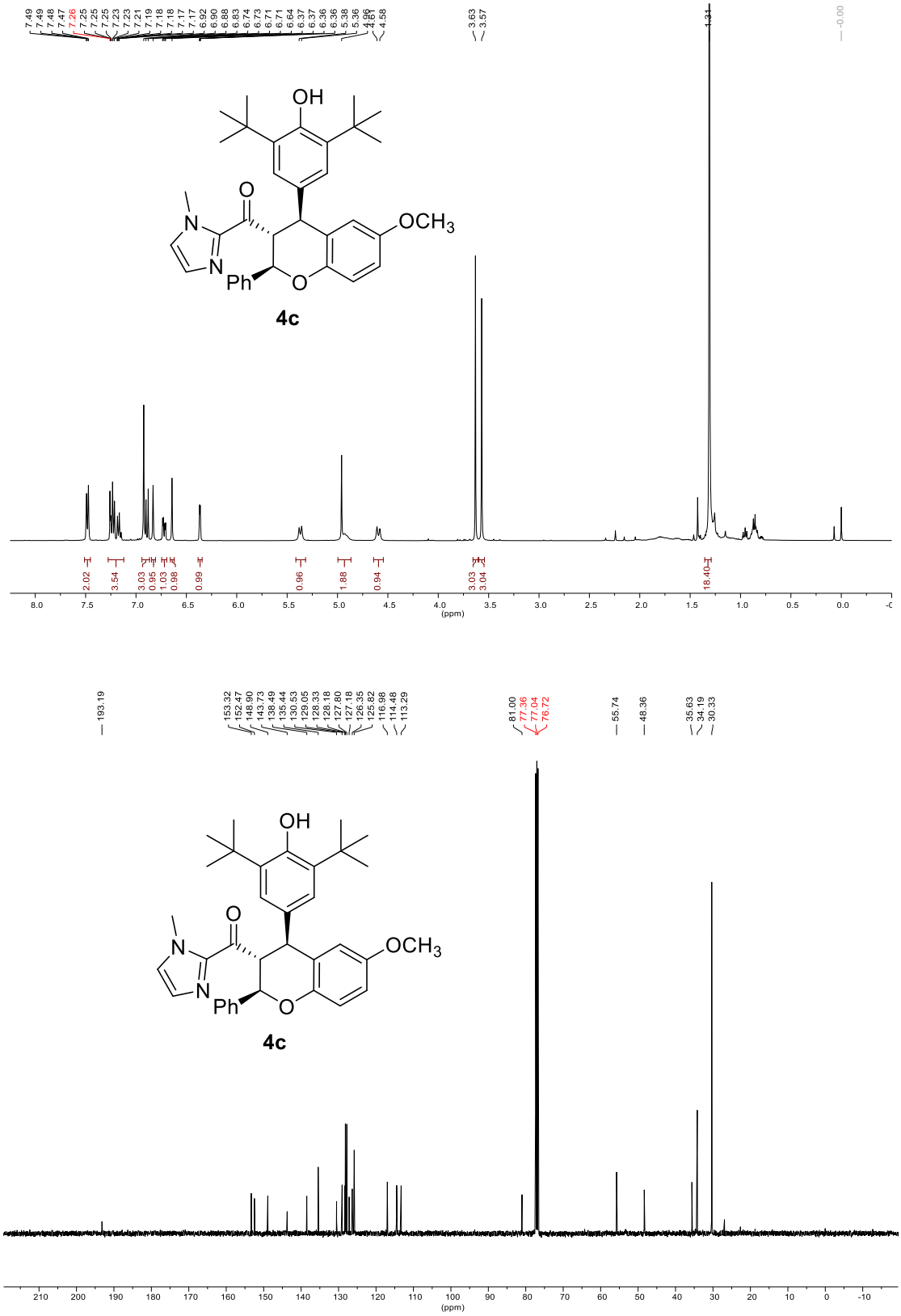
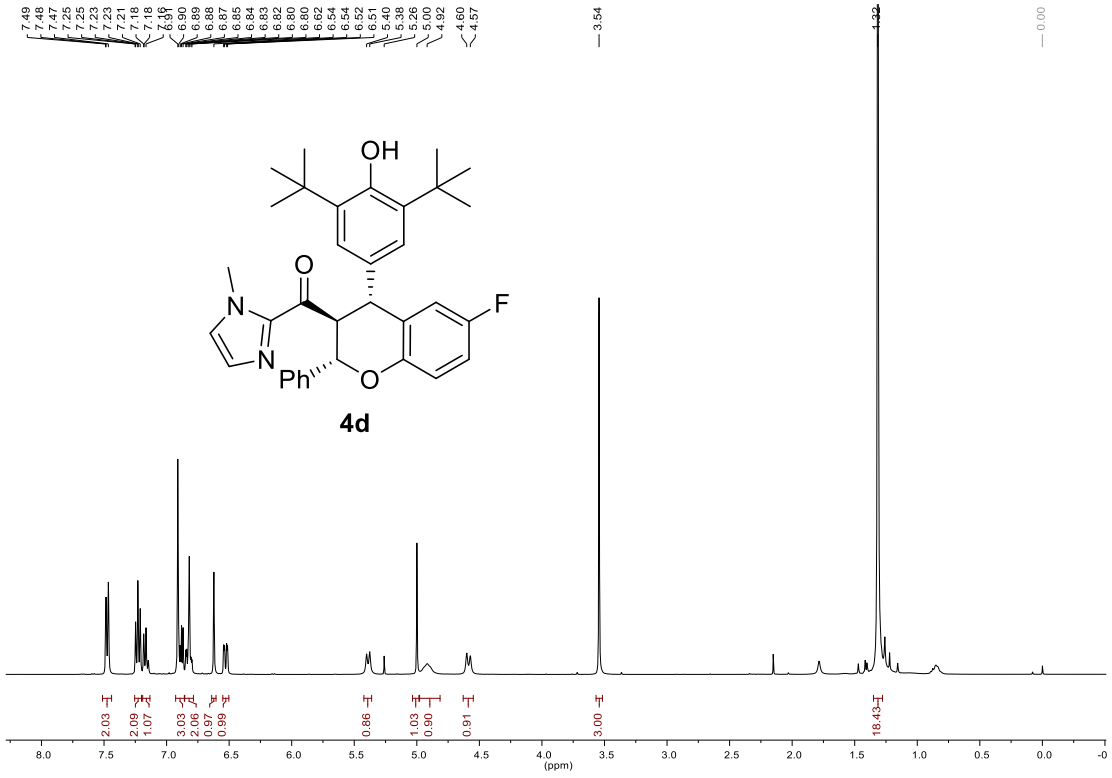


Figure S21. ^{1}H and ^{13}C NMR spectrum of **4c**.


7.49
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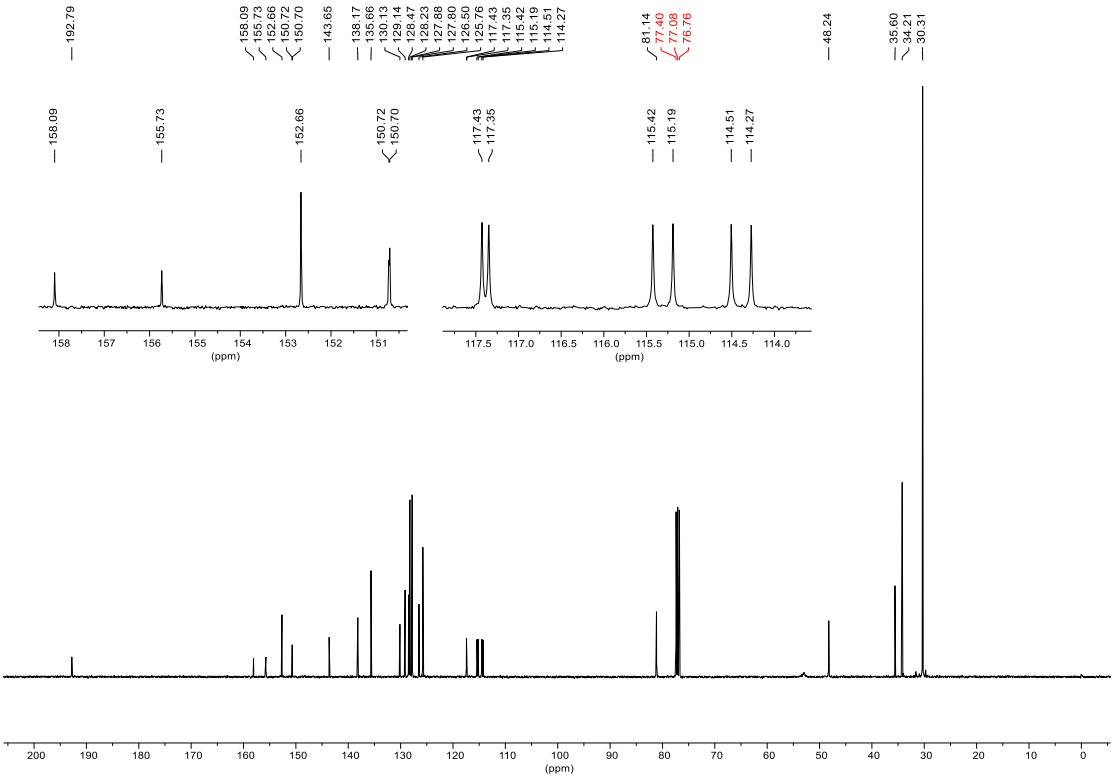
7.47
7.25
7.25
7.23
7.23
7.21
7.18
7.18
7.16
6.91
6.90
6.89
6.88
6.87
6.85
6.84
6.83
6.82
6.80
6.80
6.62
6.54
6.54
6.52
6.51
5.40
5.38
5.26
5.00
4.92
4.60
4.57
3.54
1.32
0.00
OH
O
N
N
Ph
O
F
4d
2.03
2.09
1.07
3.03
2.06
0.97
0.99
0.86
1.03
0.90
0.91
3.00
18.43
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
(ppm)


192.79
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152.66
150.72
150.70
143.65
138.17
135.66
130.13
129.14
128.47
128.23
127.88
127.80
126.50
125.76
117.43
117.35
115.42
115.19
114.51
114.27
81.14
77.40
77.08
76.76
48.24
35.60
34.21
30.31
158.09
155.73
152.66
150.72
150.70
117.43
117.35
115.42
115.19
114.51
114.27
158
157
156
155
154
153
152
151
(ppm)
117.5
117.0
116.5
116.0
115.5
115.0
114.5
114.0
(ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

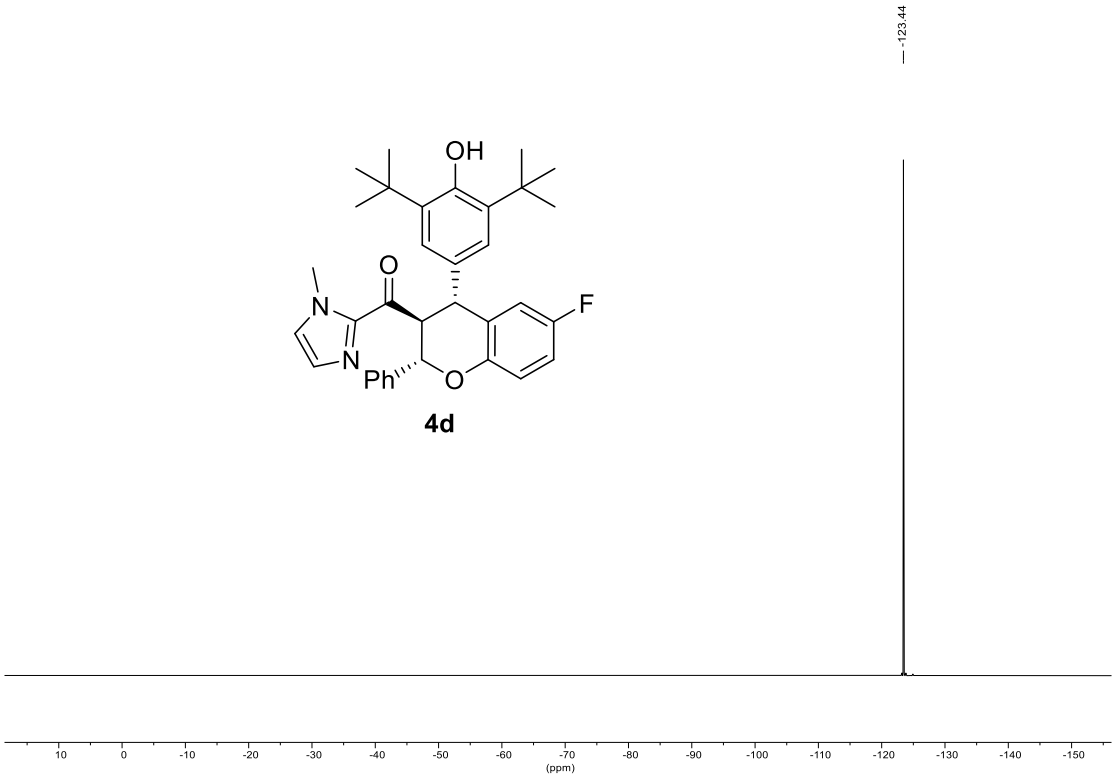
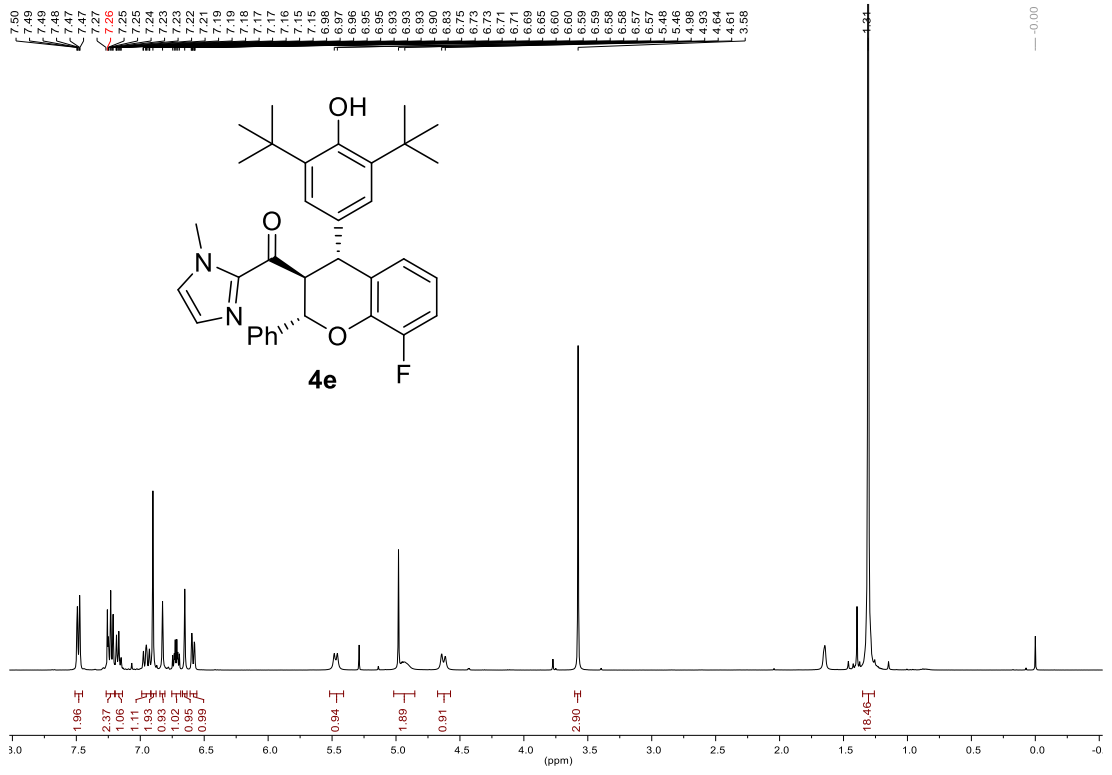
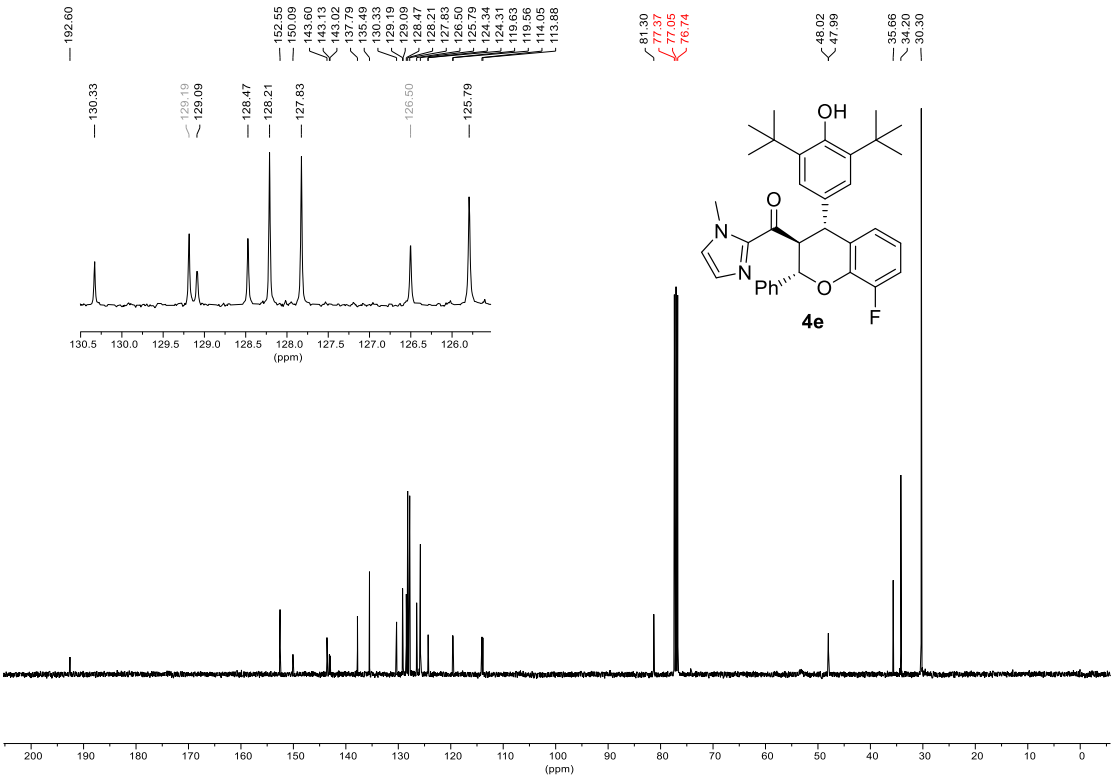


Figure S22. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **4d**.


OH
O
N
N
Ph
O
F
4e
(ppm)


OH
O
N
N
Ph
O
F
4e
(ppm)

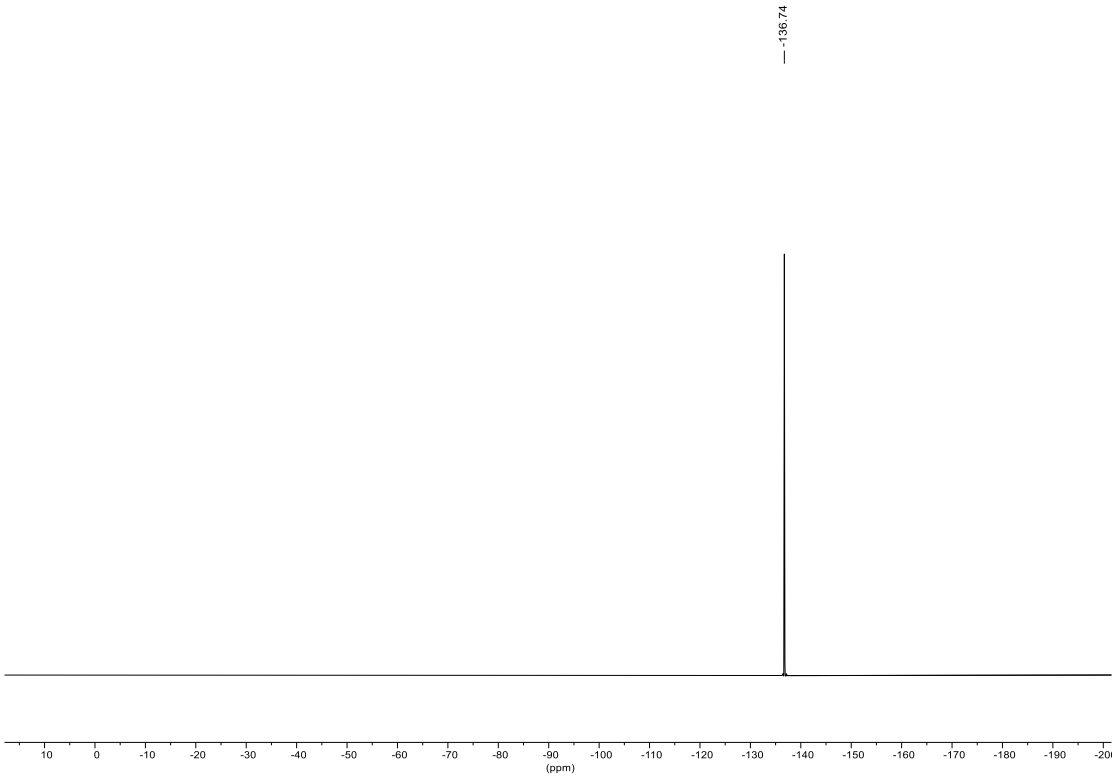


Figure S23. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **4e**.

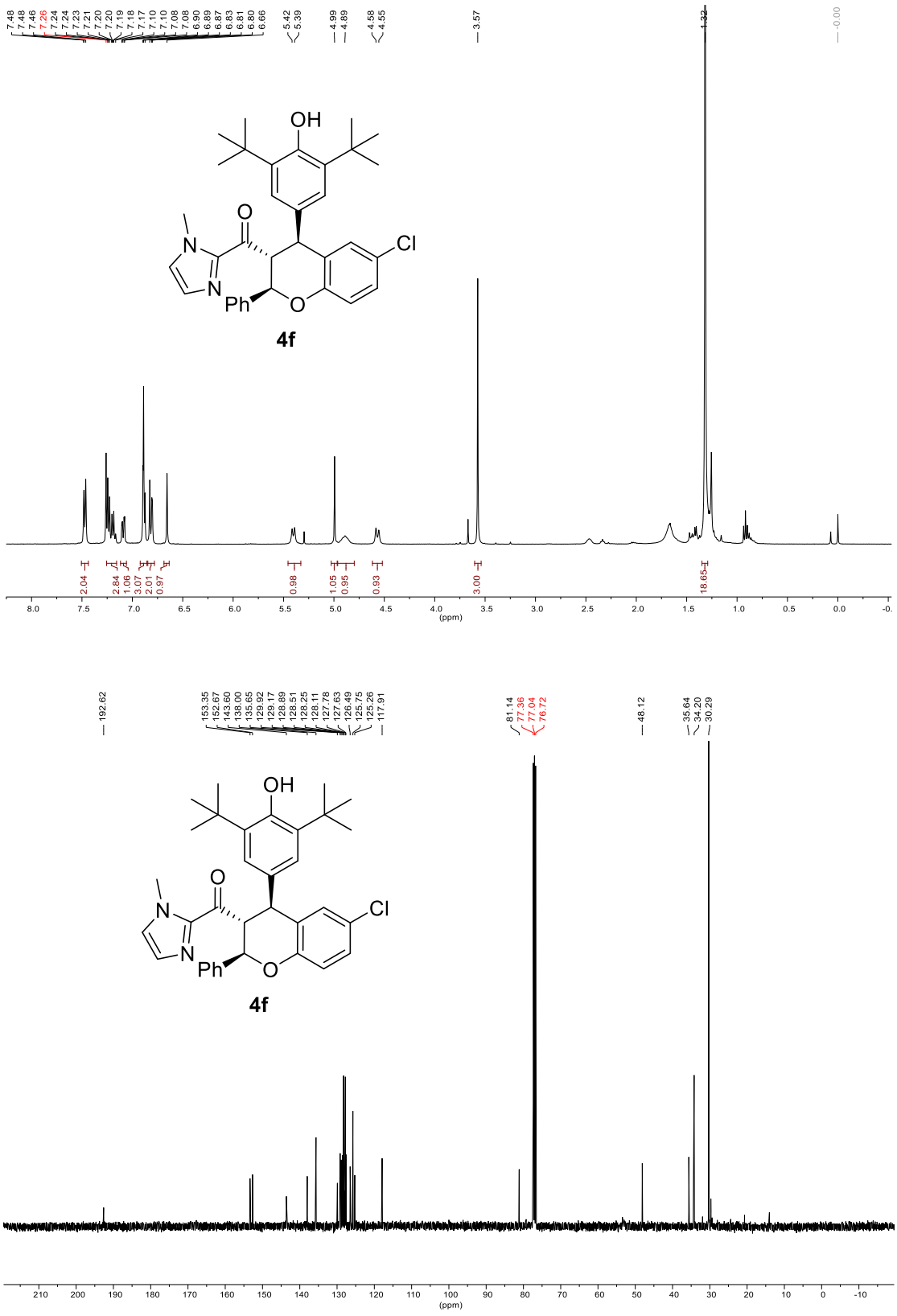


Figure S24. ^{1}H and ^{13}C NMR spectrum of **4f**.

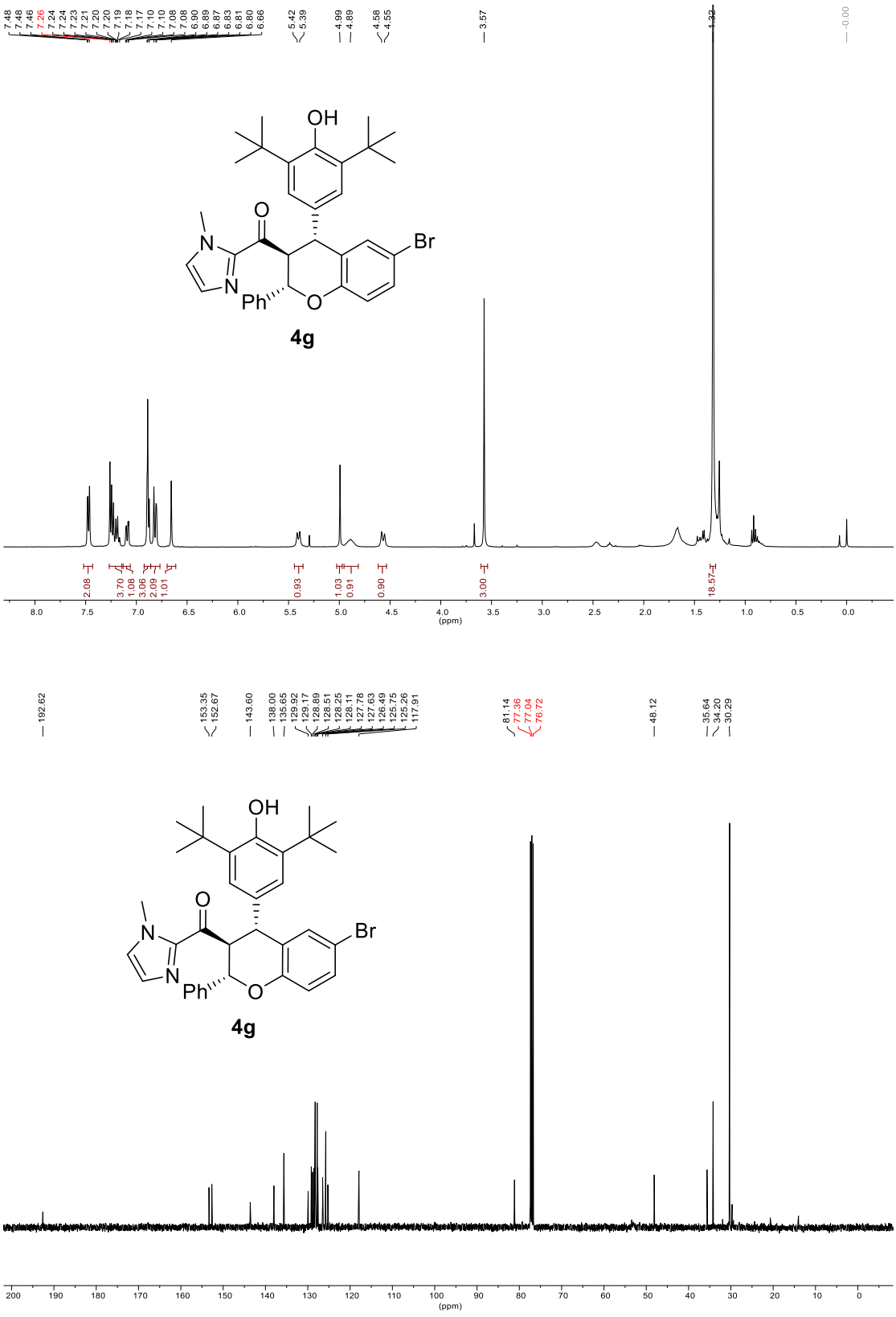


Figure S25. ^{1}H and ^{13}C NMR spectrum of **4g**.

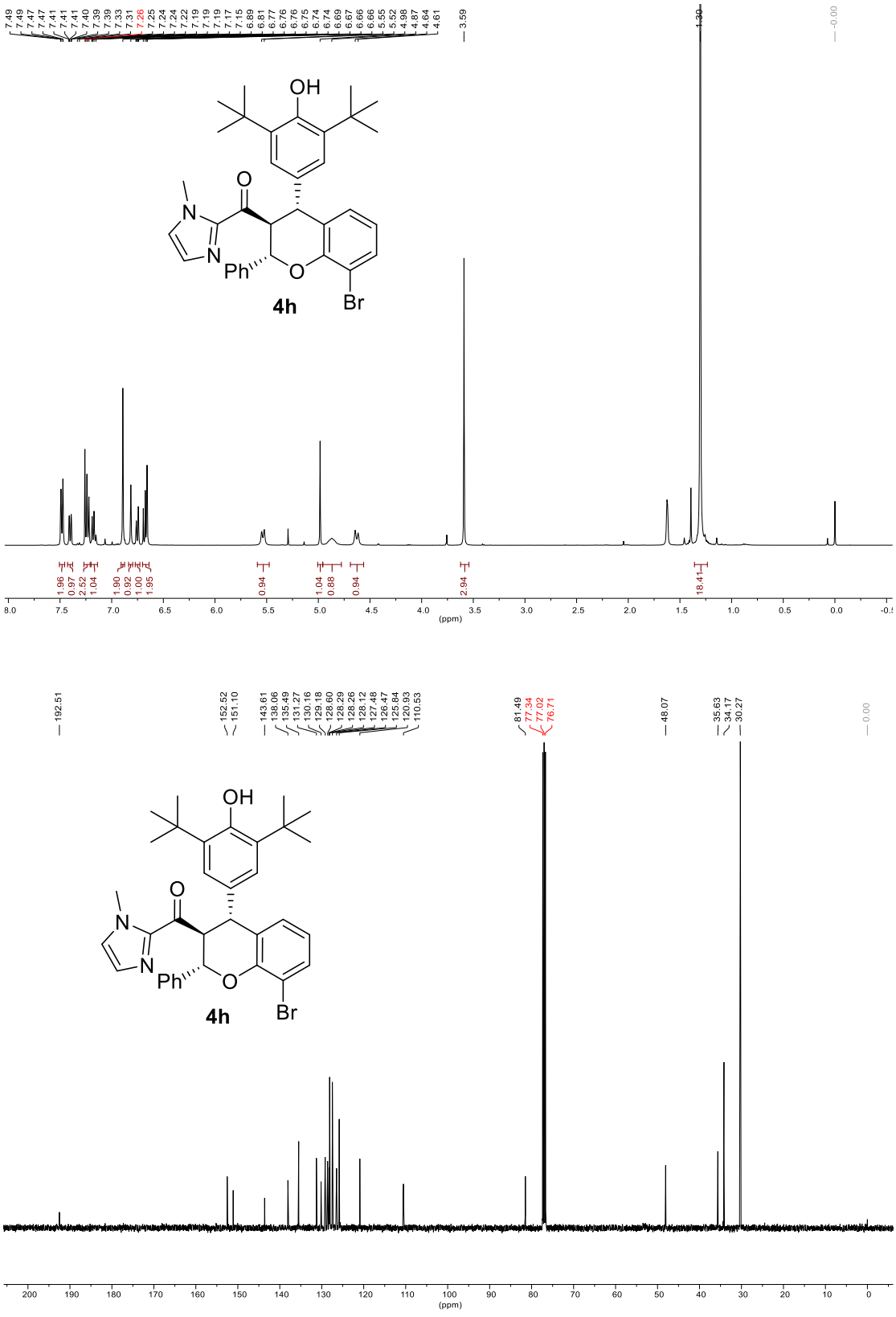


Figure S26. ^{1}H and ^{13}C NMR spectrum of **4h**.

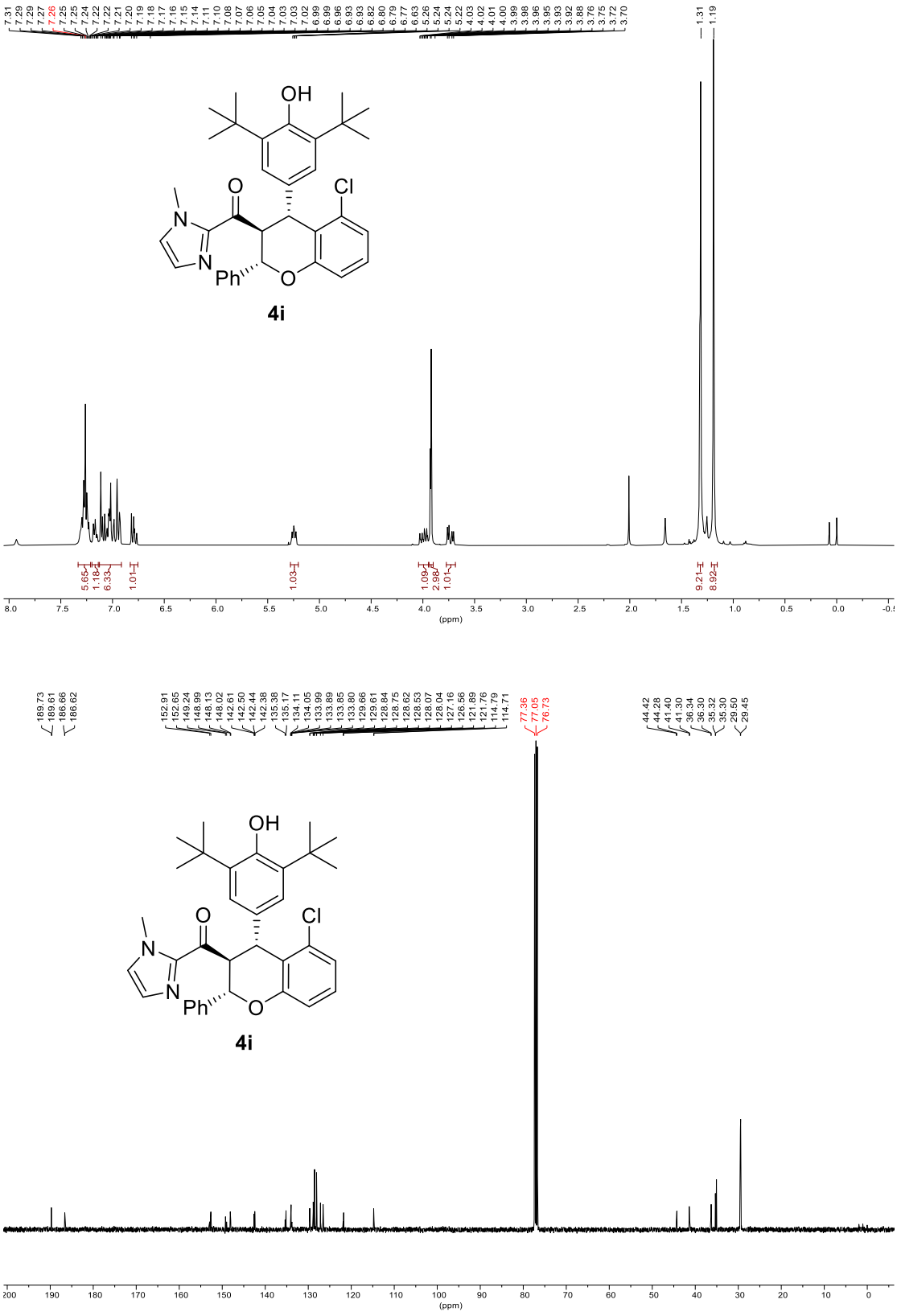


Figure S27. ^{1}H and ^{13}C NMR spectrum of **4i**.

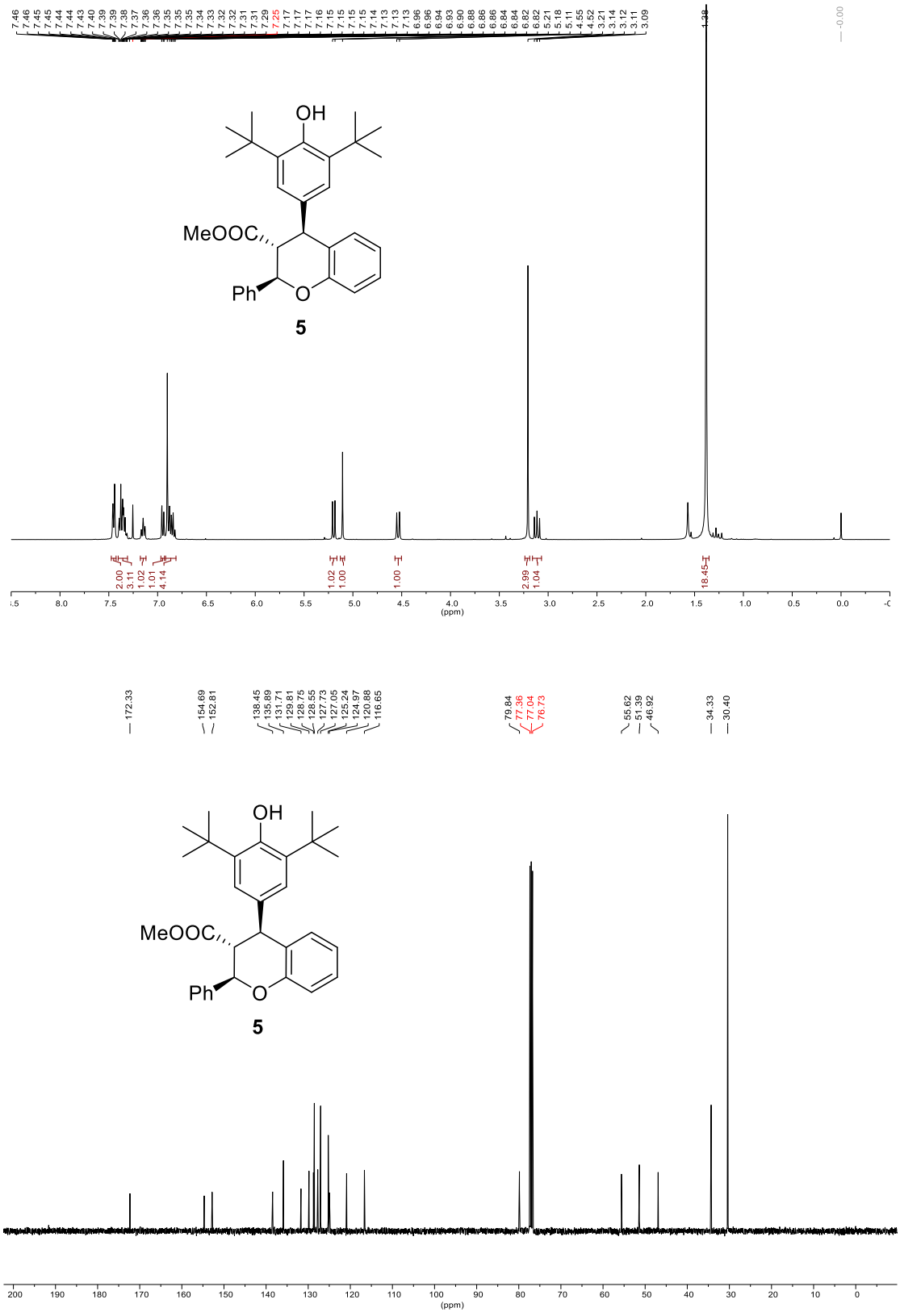


Figure S28. ^{1}H and ^{13}C NMR spectrum of **5**.

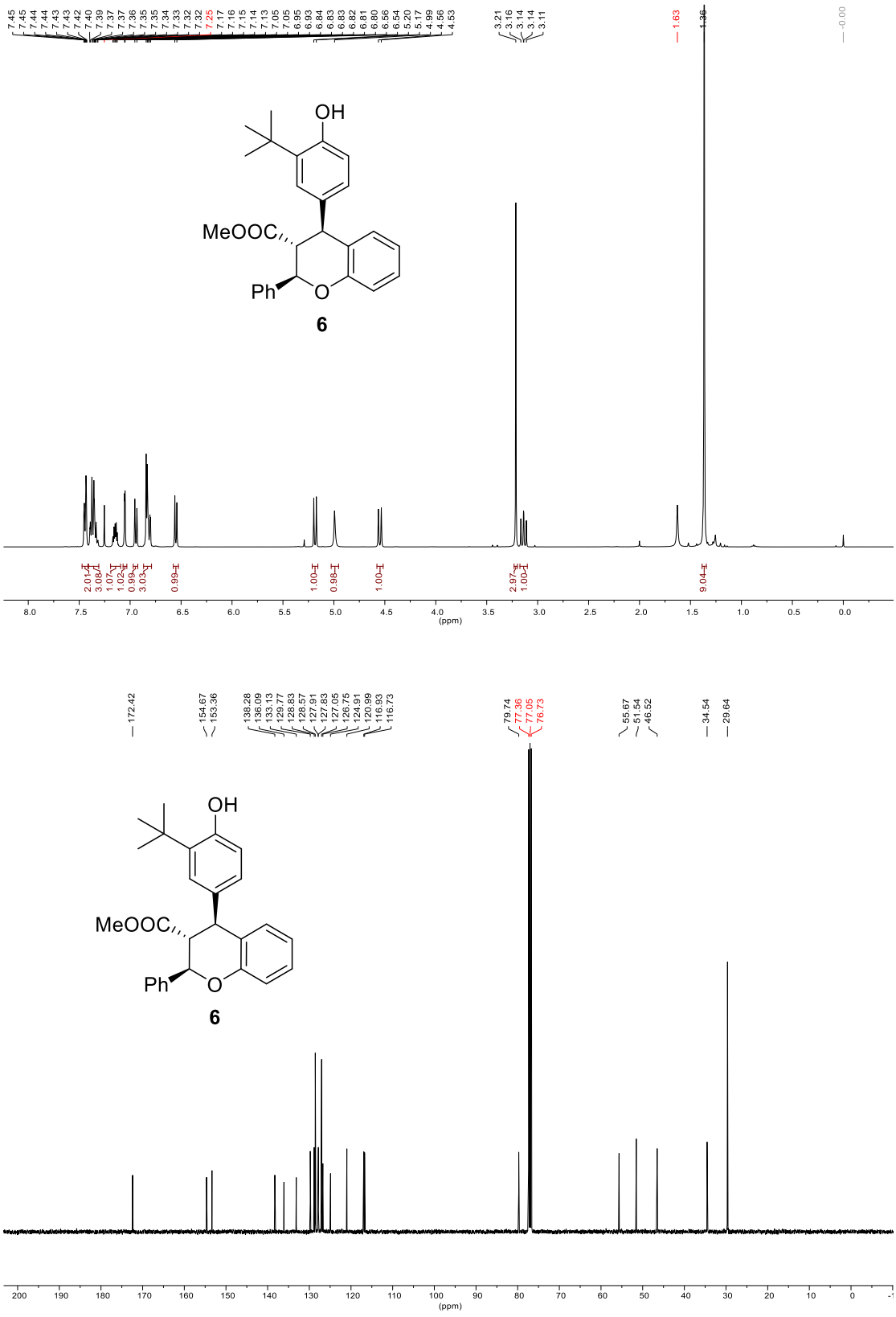
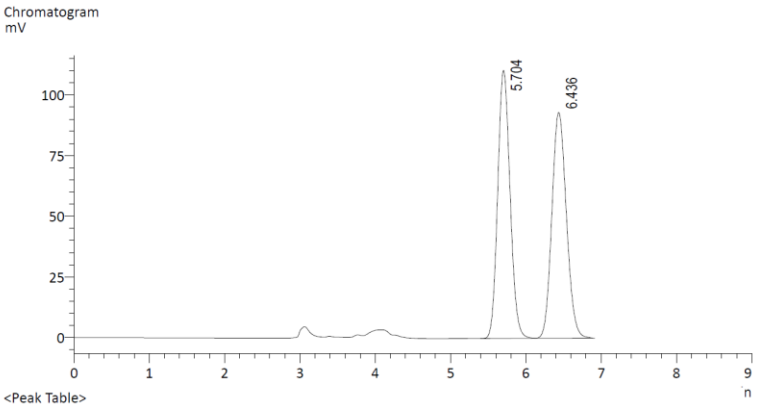


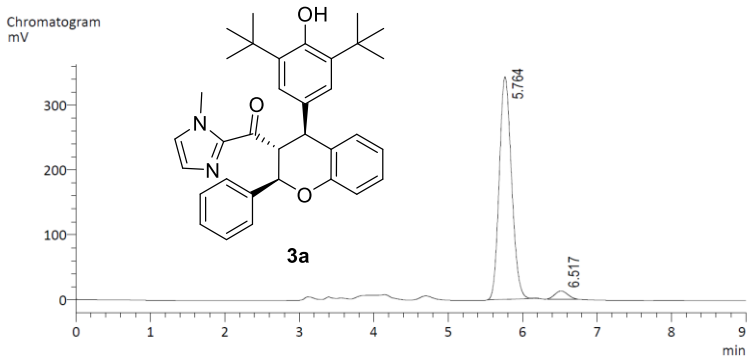
Figure S29. ^{1}H and ^{13}C NMR spectrum of **6**.

7. HPLC Traces on Chiral Stationary Phase



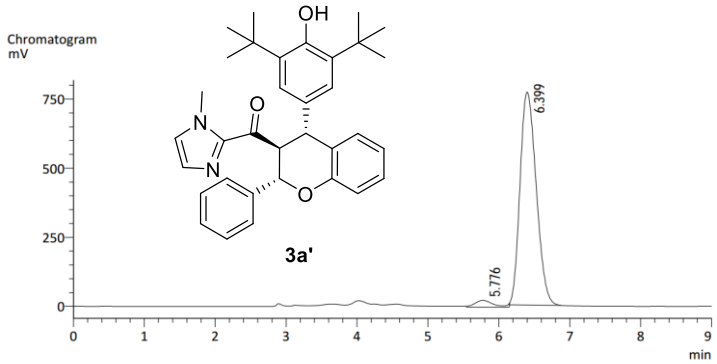
<Peak Table>
???A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.704	1259042	110442	50.276
2	6.436	1245196	93030	49.724
Total		2504238	203473	100.000



<Peak Table>
Detector A 254nm

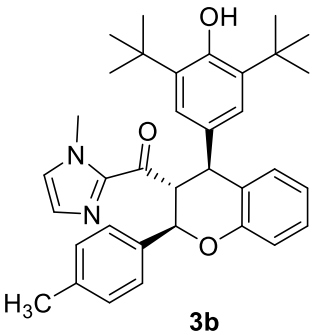
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.764	3942108	342546	96.490
2	6.517	143420	12253	3.510
Total		4085528	354799	100.000



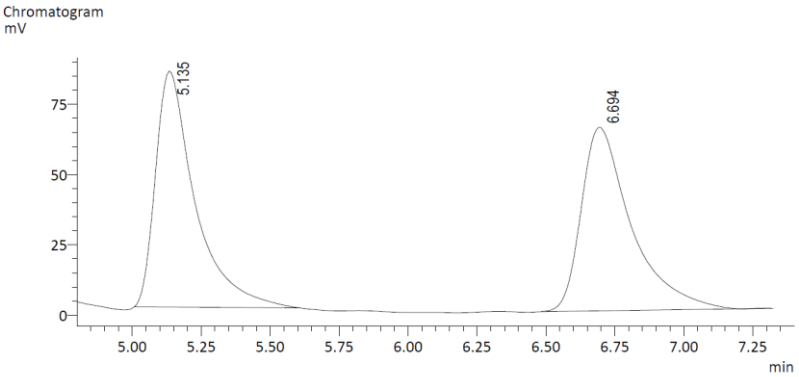
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.776	429813	23911	3.400
2	6.399	12210428	769797	96.600
Total		12640241	793708	100.000

Figure S30. HPLC traces of racemic (reference) and chiral **3a**, **3a'**. Area integration = 96.5: 3.5 (93% ee) and 3.4: 96.6 (93% ee).

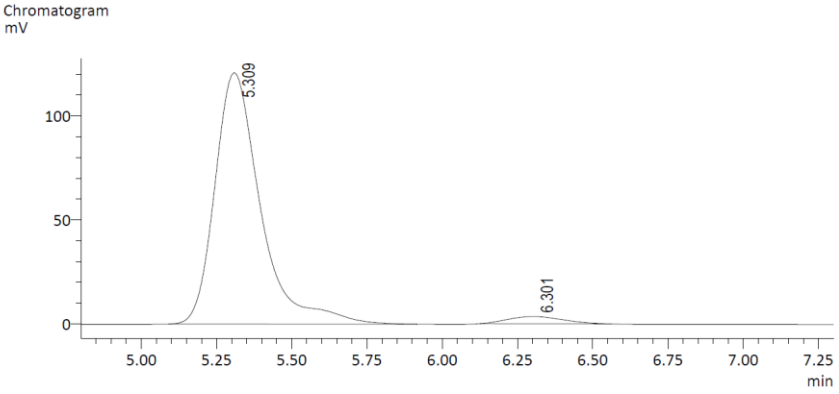


3b



<Peak Table>
???A 254nm

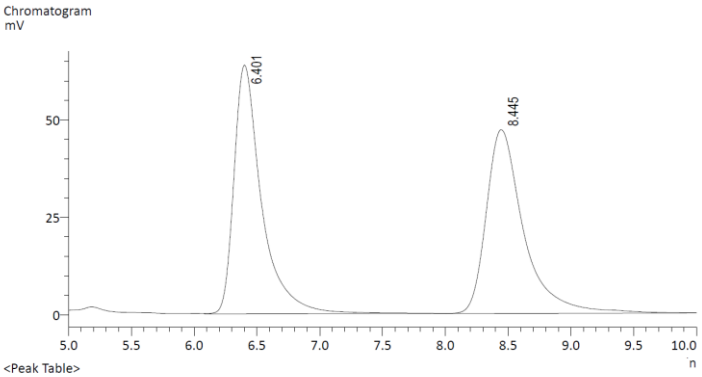
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.135	833992	83874	50.396
2	6.694	820877	65272	49.604
Total		1654869	149146	100.000



<Peak Table>
Detector A 254nm

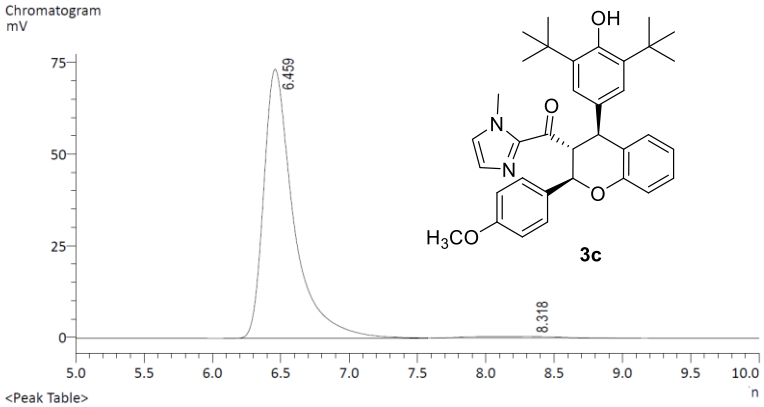
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.309	1277354	120980	96.664
2	6.301	44083	3476	3.336
Total		1321437	124456	100.000

Figure S31. HPLC traces of racemic **3b** (reference) and chiral **3b**. Area integration = 96.7:3.3 (93% ee).



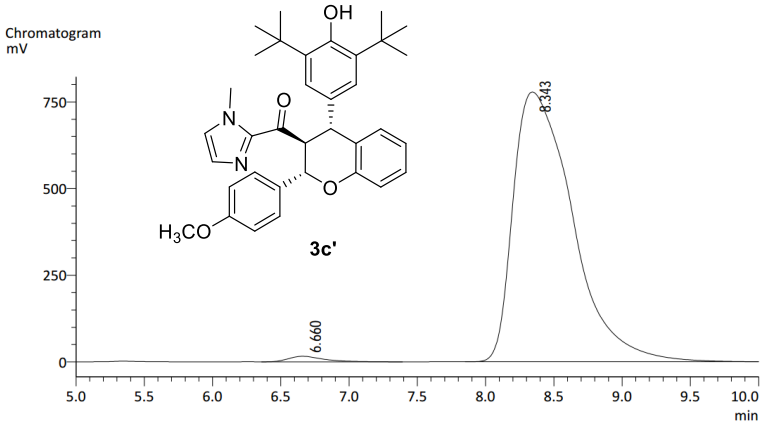
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.401	982179	63862	50.153
2	8.445	976196	47116	49.847
Total		1958375	110978	100.000



<Peak Table>
Detector A 254nm

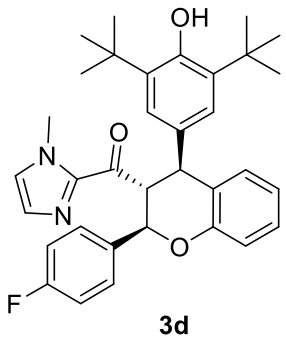
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.459	1128459	73495	98.410
2	8.318	18235	411	1.590
Total		1146694	73906	100.000



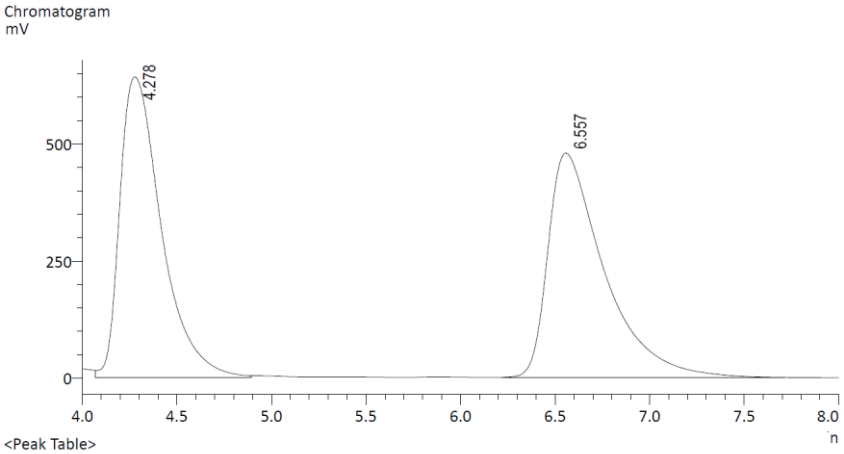
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.660	288274	15991	1.209
2	8.343	23551501	778165	98.791
Total		23839775	794156	100.000

Figure S32. HPLC traces of racemic (reference) and chiral **3c**, **3c'**. Area integration = 98.4:1.6 (97% ee) and 1.2: 98.8 (98% ee).

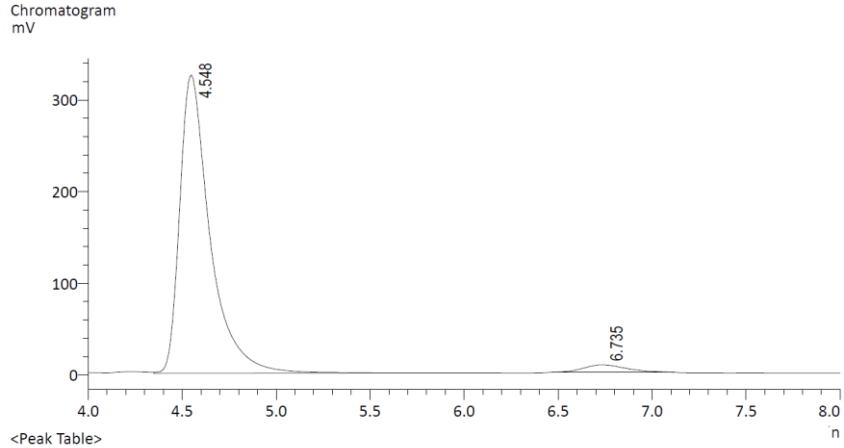


3d



<Peak Table>
Detector A 254nm

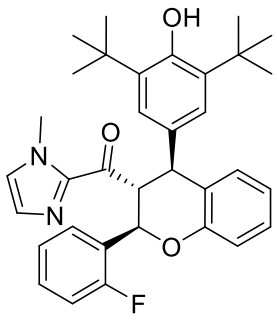
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.278	9860378	642865	49.896
2	6.557	9901591	479141	50.104
Total		19761969	1122005	100.000



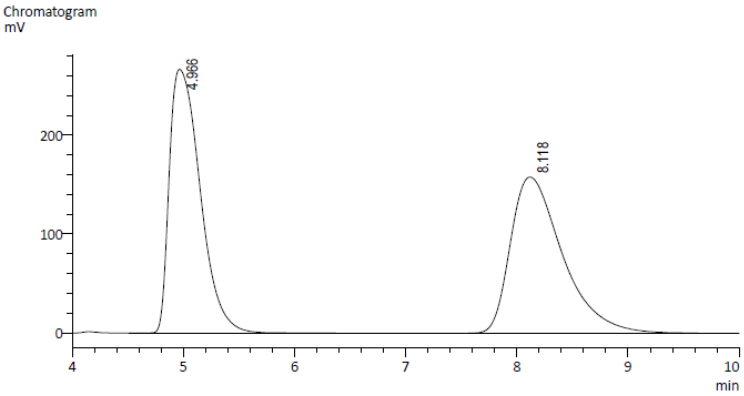
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.548	3642485	325217	96.526
2	6.735	131077	8151	3.474
Total		3773562	333368	100.000

Figure S33. HPLC traces of racemic **3d** (reference) and chiral **3d**. Area integration = 96.5:3.5 (93% ee).

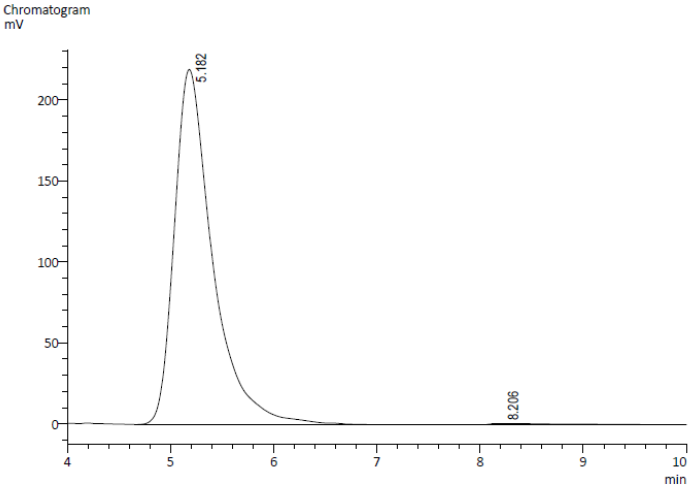


3e



<Peak Table>
Detector A 254nm

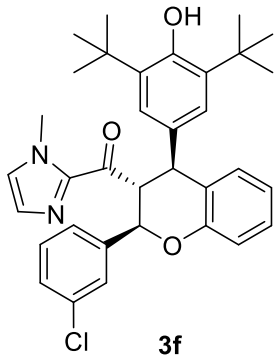
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.966	5155208	267034	50.073
2	8.118	5140224	157997	49.927
Total		10295432	425032	100.000



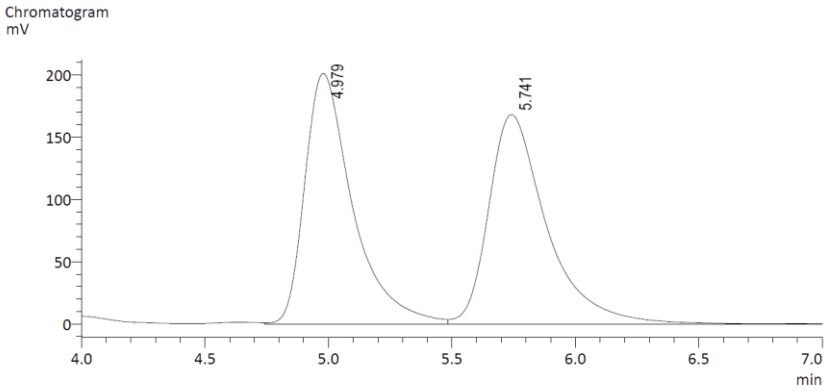
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.182	5660992	219239	99.496
2	8.206	28687	692	0.504
Total		5689679	219931	100.000

Figure S34. HPLC traces of racemic **3e** (reference) and chiral **3e**. Area integration = 99.5:0.5 (99% ee).

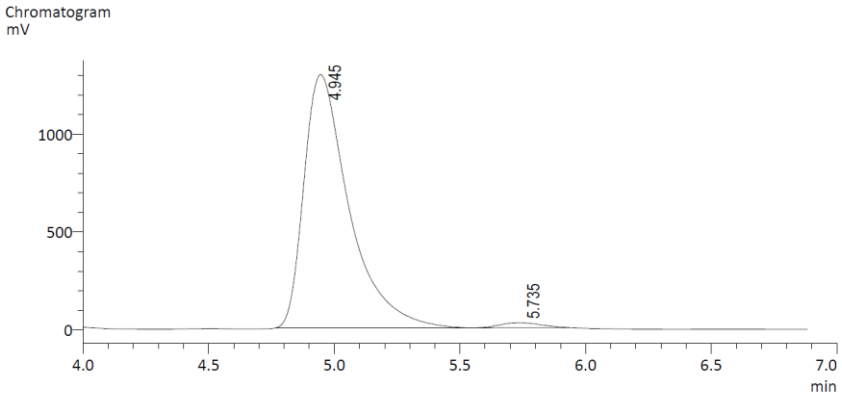


3f



<Peak Table>
Detector A 254nm

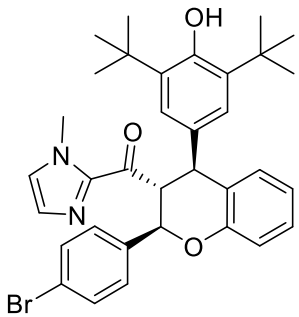
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.979	2715322	201180	49.515
2	5.741	2768550	168334	50.485
Total		5483873	369514	100.000



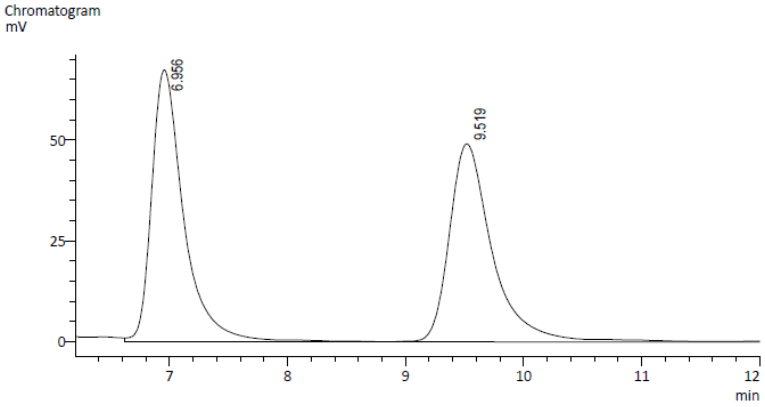
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.945	16219778	1295898	98.230
2	5.735	292303	26166	1.770
Total		16512081	1322063	100.000

Figure S35. HPLC traces of racemic **3f** (reference) and chiral **3f**. Area integration = 98.2:1.8 (96% ee).

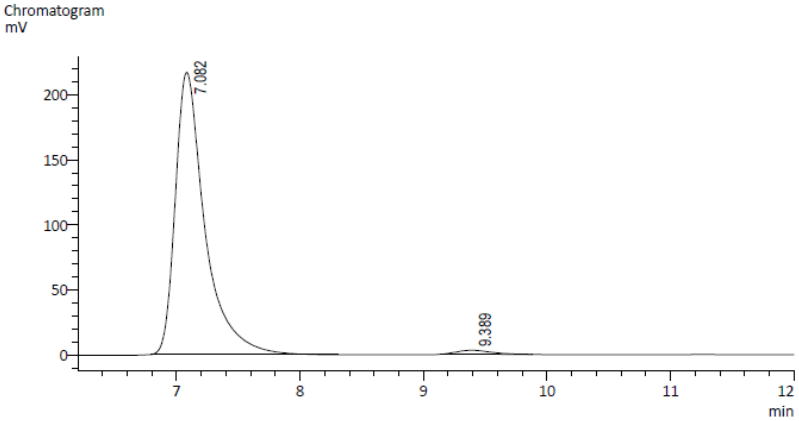


3g



<Peak Table>
Detector A 254nm

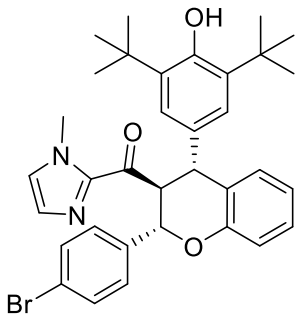
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.956	1281368	67368	50.465
2	9.519	1257762	49069	49.535
Total		2539130	116436	100.000



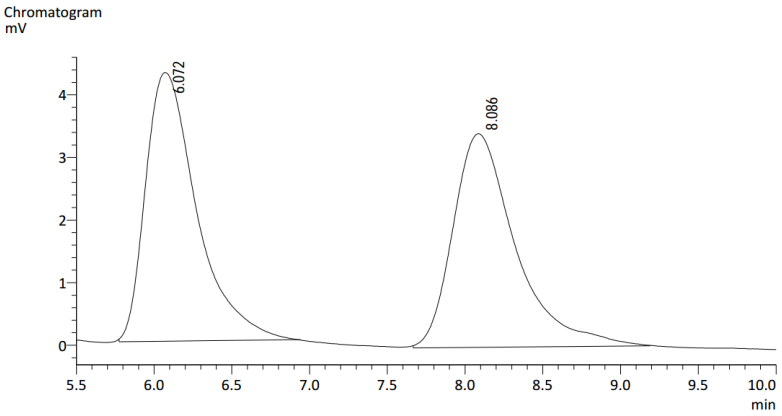
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	7.082	3620149	216884	98.523
2	9.389	54260	2930	1.477
Total		3674409	219814	100.000

Figure S36. HPLC traces of racemic **3g** (reference) and chiral **3g**. Area integration = 98.5:1.5 (97% ee).

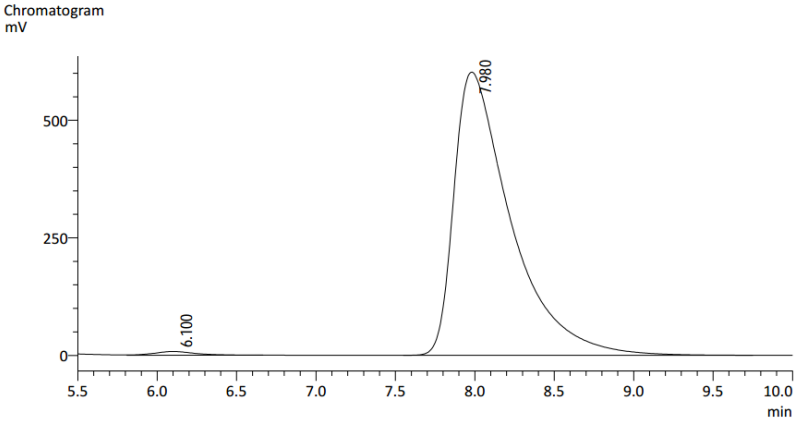


3g'



<Peak Table>
Detector A 254nm

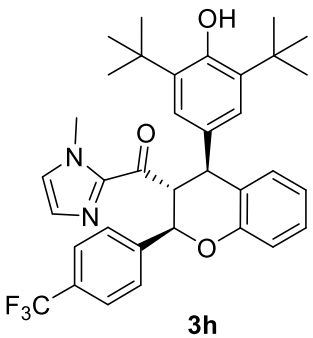
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.072	98194	4291	50.724
2	8.086	95390	3413	49.276
Total		193584	7704	100.000



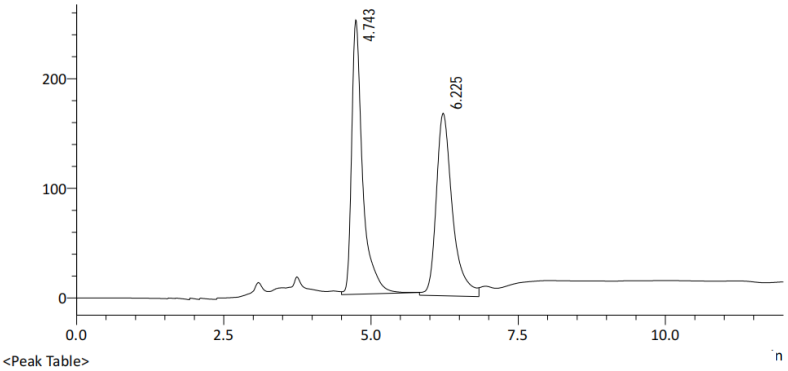
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.100	143012	7974	0.944
2	7.980	15000259	602192	99.056
Total		15143271	610166	100.000

Figure S37. HPLC traces of racemic (reference) and chiral **3g'**. Area integration = 0.9:99.1 (98% ee).

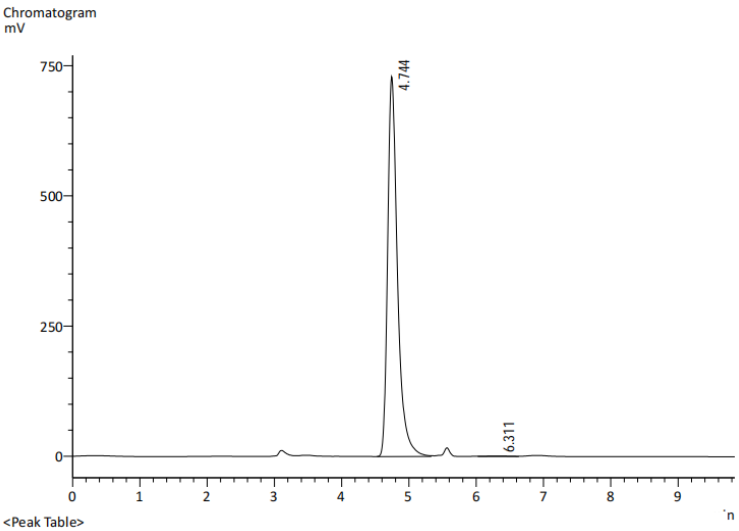


3h



<Peak Table>
Detector A 220nm

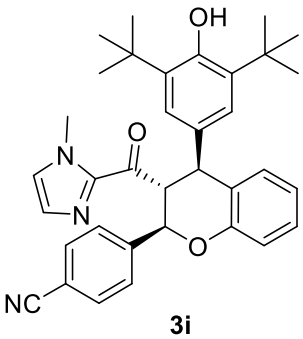
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.743	3256499	249963	50.399
2	6.225	3204958	166396	49.601
Total		6461457	416358	100.000



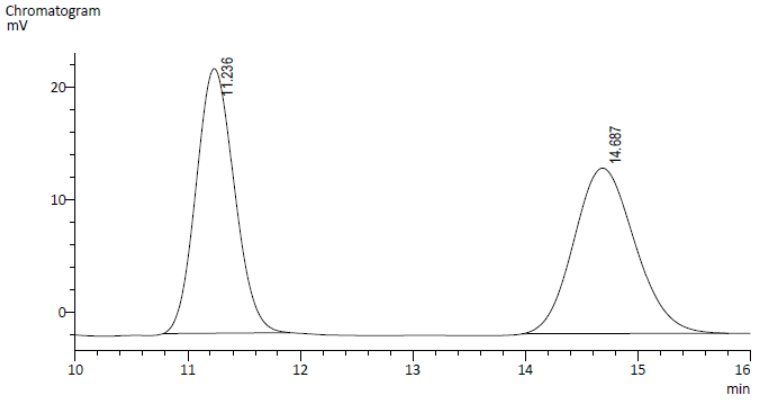
<Peak Table>
Detector A 220nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.744	7451424	729689	99.749
2	6.311	18752	831	0.251
Total		7470176	730520	100.000

Figure S38. HPLC traces of racemic **3h** (reference) and chiral **3h**. Area integration = 99.7:0.3 (99.4% ee).

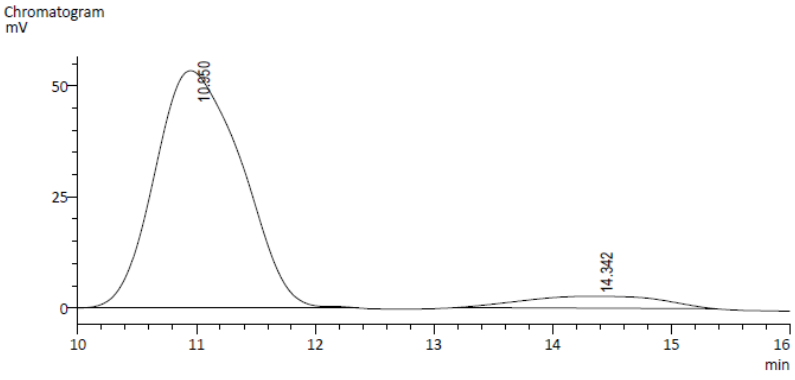


3i



<Peak Table>
Detector A 254nm

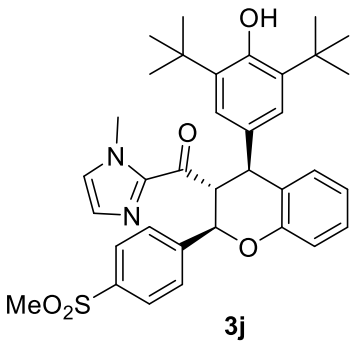
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	11.236	557264	23562	49.978
2	14.687	557745	14731	50.022
Total		1115009	38293	100.000



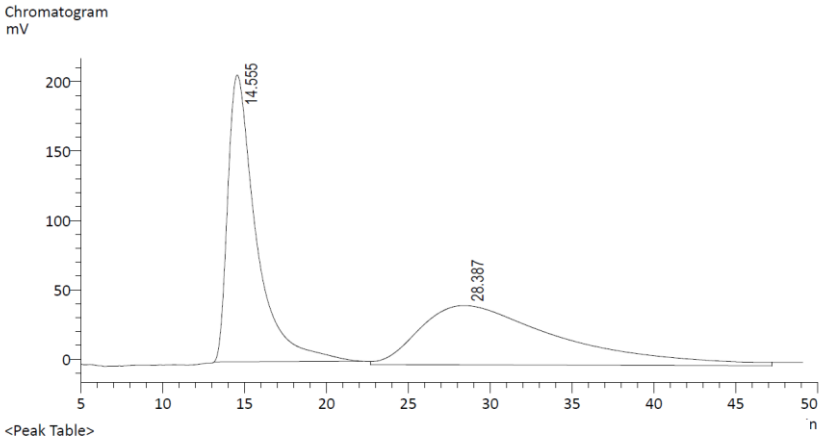
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	10.950	2713302	53415	92.691
2	14.342	213954	2636	7.309
Total		2927257	56050	100.000

Figure S39. HPLC traces of racemic **3i** (reference) and chiral **3i**. Area integration = 92.7:7.3 (85% ee).

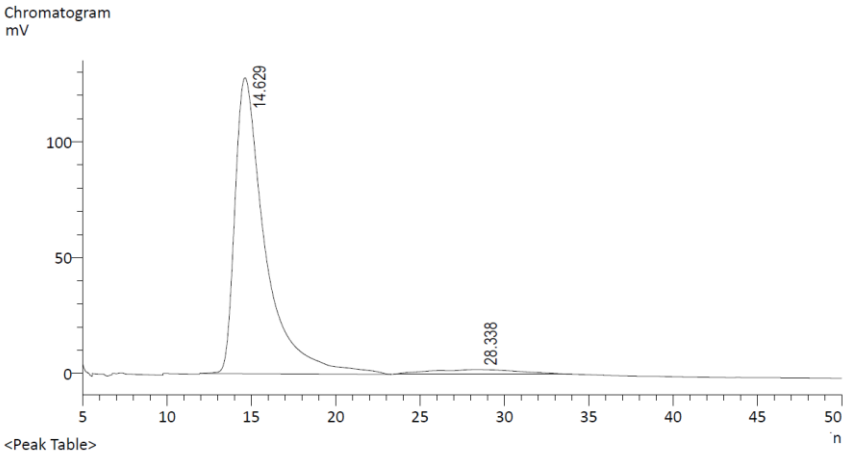


3j



<Peak Table>
Detector A 220nm

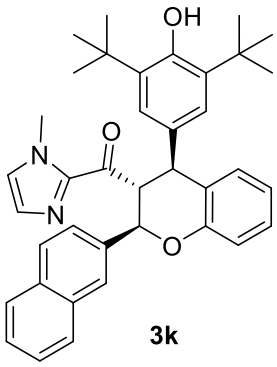
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	14.555	24977048	206722	49.609
2	28.387	25371164	42653	50.391
Total		50348212	249376	100.000



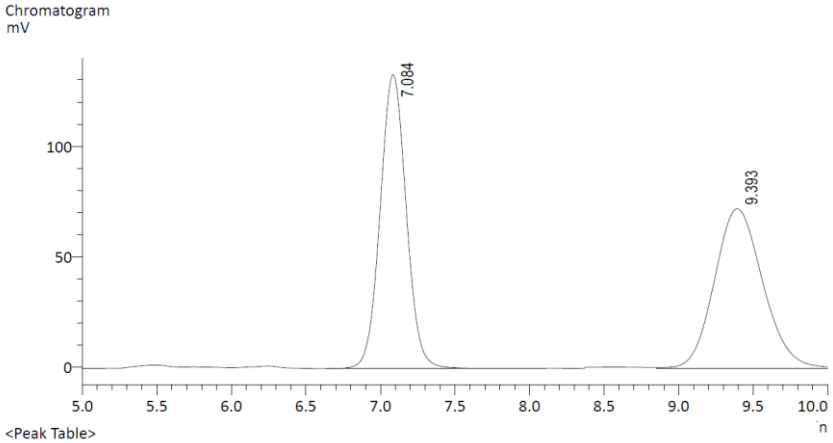
<Peak Table>
Detector A 220nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	14.629	15970279	127710	95.586
2	28.338	737434	2024	4.414
Total		16707713	129734	100.000

Figure S40. HPLC traces of racemic **3j** (reference) and chiral **3j**. Area integration = 95.6:4.4 (91% ee).

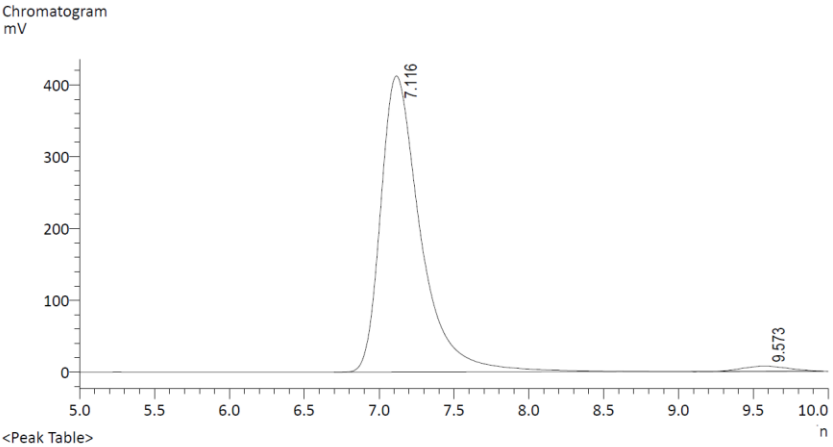


3k



<Peak Table>
Detector A 254nm

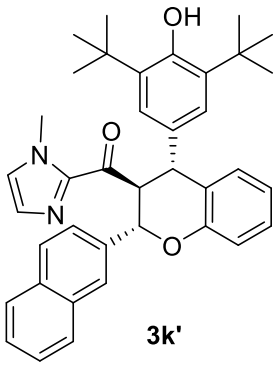
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	7.084	1623229	133108	49.642
2	9.393	1646609	72275	50.358
Total		3269839	205383	100.000



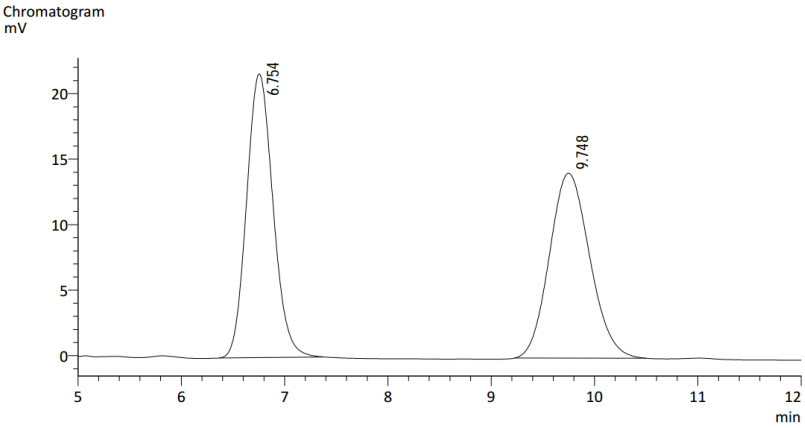
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	7.116	7639233	412419	97.928
2	9.573	161664	7306	2.072
Total		7800897	419725	100.000

Figure S41. HPLC traces of racemic **3k** (reference) and chiral **3k**. Area integration = 97.9:2.1 (96% ee).

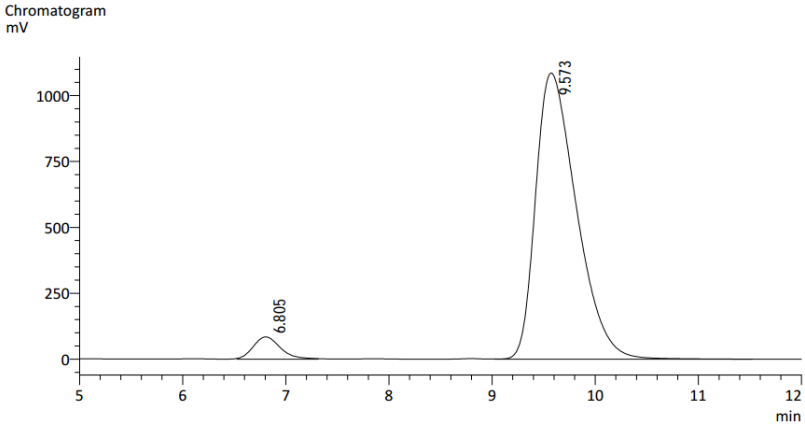


3k'



<Peak Table>
Detector A 254nm

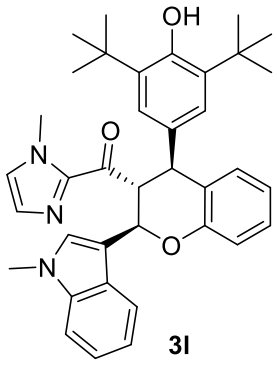
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.754	385358	21647	50.172
2	9.748	382720	14116	49.828
Total		768078	35763	100.000



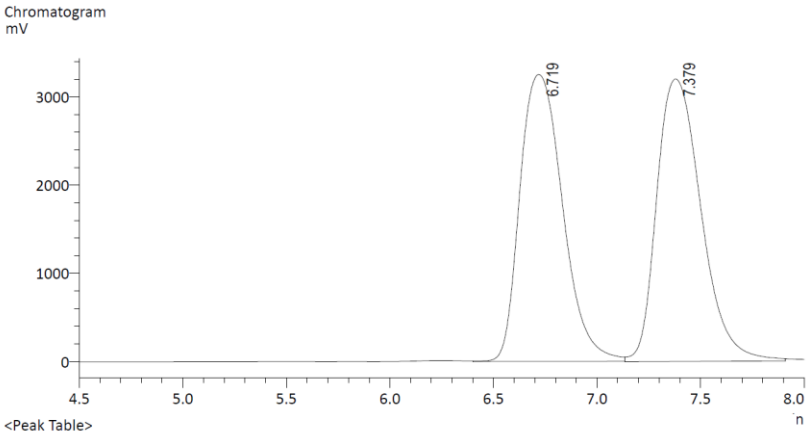
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.805	1542668	84277	4.915
2	9.573	29845358	1085784	95.085
Total		31388025	1170061	100.000

Figure S42. HPLC traces of racemic (reference) and chiral **3k'**. Area integration = 4.9:95.1 (90% ee).

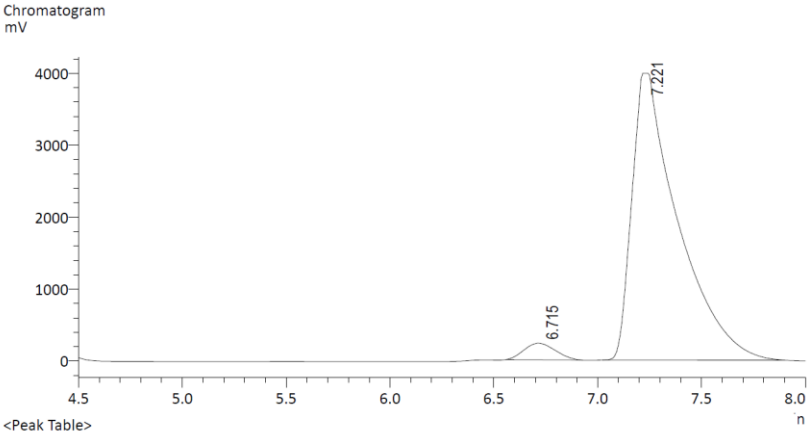


3l



<Peak Table>
Detector A 220nm

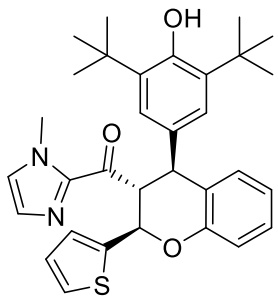
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.719	46775076	3254859	49.436
2	7.379	47842826	3201987	50.564
Total		94617902	6456845	100.000



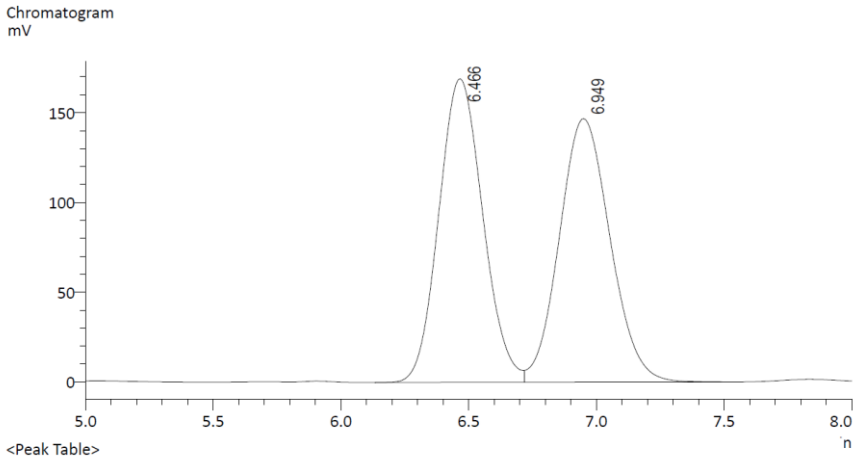
<Peak Table>
???A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.715	2386229	229154	3.737
2	7.221	61475282	3986507	96.263
Total		63861511	4215661	100.000

Figure S43. HPLC traces of racemic **3l** (reference) and chiral **3l**. Area integration = 3.7:96.3 (93% ee).

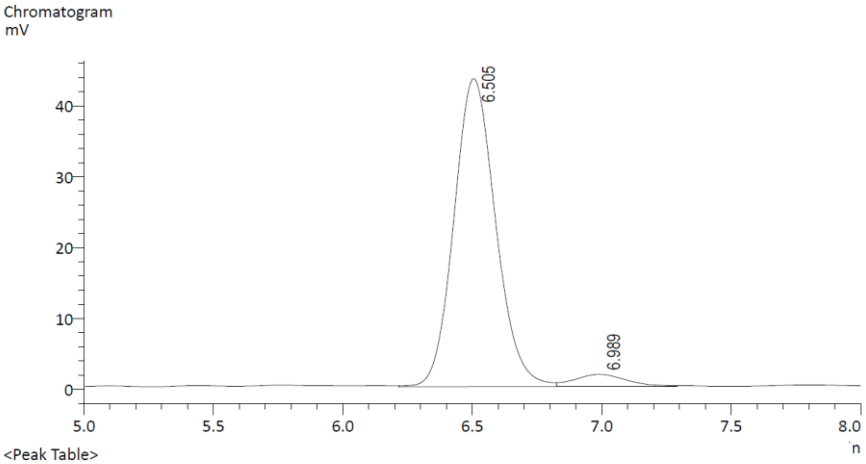


3m



<Peak Table>
Detector A 254nm

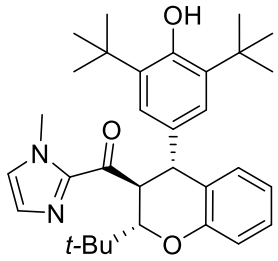
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.466	2031045	169159	50.024
2	6.949	2029076	146853	49.976
Total		4060121	316011	100.000



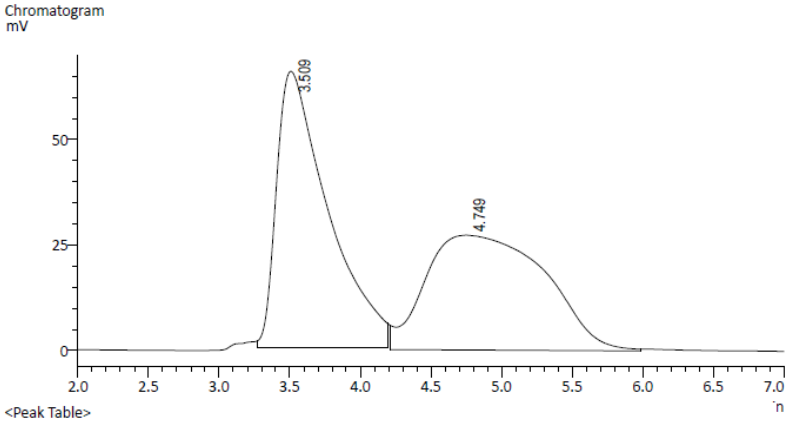
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.505	487620	43477	95.304
2	6.989	24027	1730	4.696
Total		511647	45207	100.000

Figure S44. HPLC traces of racemic **3m** (reference) and chiral **3m**. Area integration = 95.3:4.7 (91% ee).

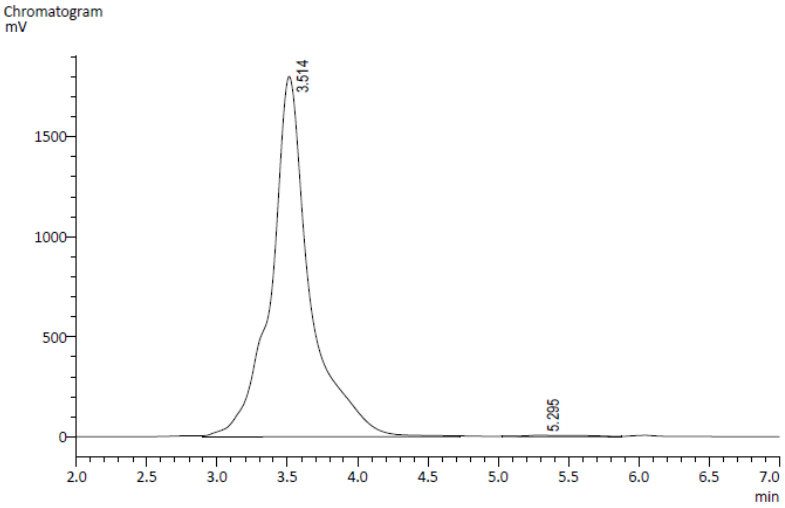


3n



<Peak Table>
Detector A 254nm

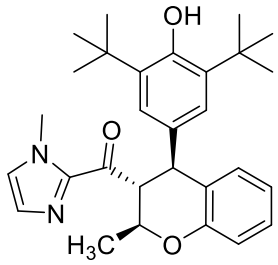
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	3.509	1664427	65650	50.734
2	4.749	1616265	27204	49.266
Total		3280692	92854	100.000



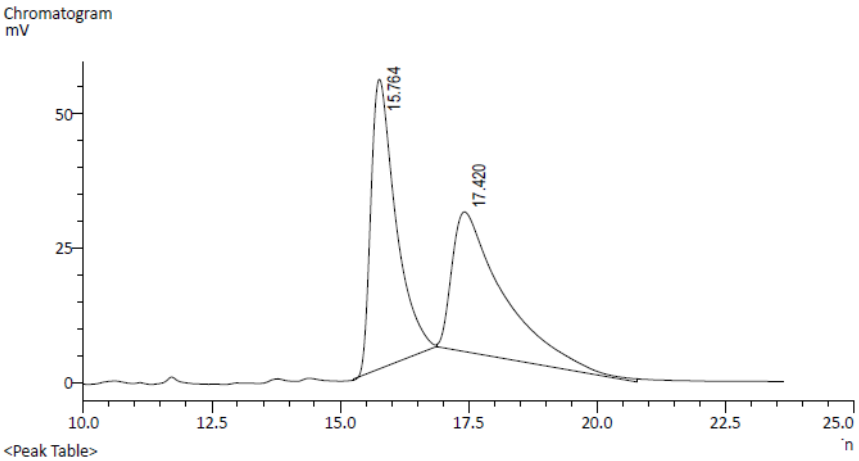
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	3.514	34605084	1801353	99.327
2	5.295	234545	6693	0.673
Total		34839629	1808045	100.000

Figure S45. HPLC traces of racemic **3n** (reference) and chiral **3n**. Area integration =99.3: 0.7 (99% ee).

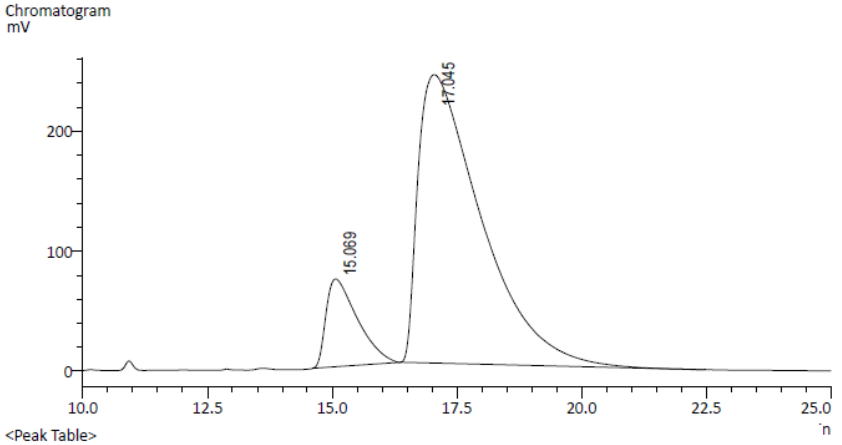


3o



<Peak Table>
Detector A 254nm

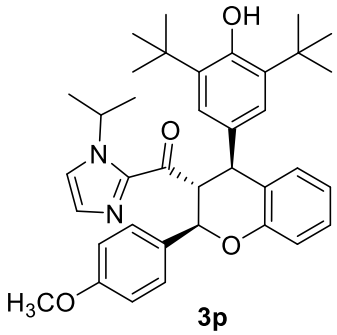
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	15.764	1821833	53880	49.899
2	17.420	1829227	25997	50.101
Total		3651060	79878	100.000



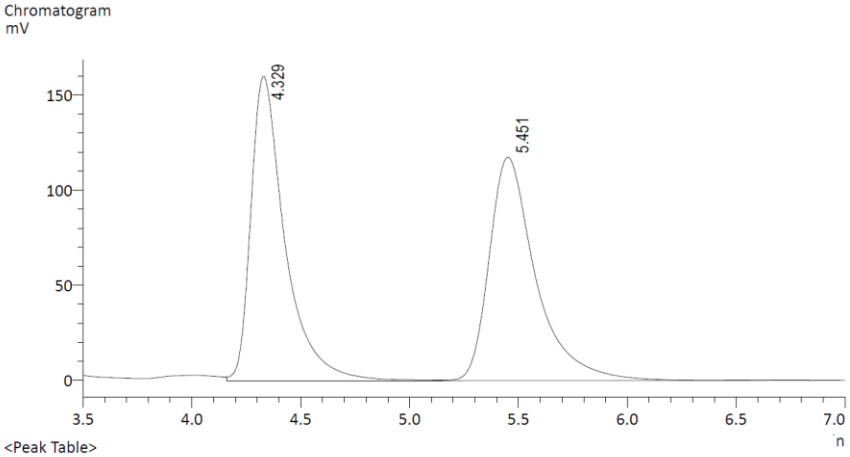
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	15.069	3200848	73181	13.101
2	17.045	21231226	240526	86.899
Total		24432074	313707	100.000

Figure S46. HPLC traces of racemic **3o** (reference) and chiral **3o**. Area integration = 13.1:86.7 (74% ee).

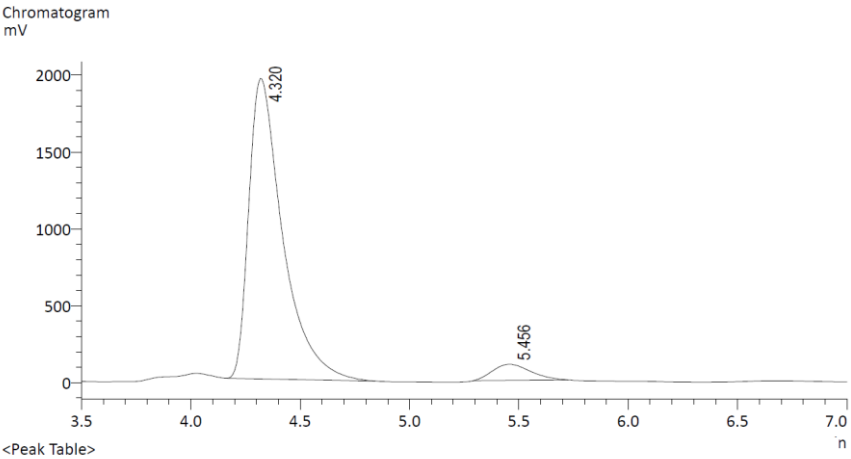


3p



<Peak Table>
Detector A 254nm

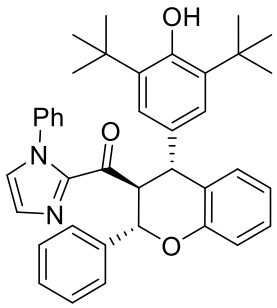
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.329	1743346	159947	49.921
2	5.451	1748857	117502	50.079
Total		3492203	277449	100.000



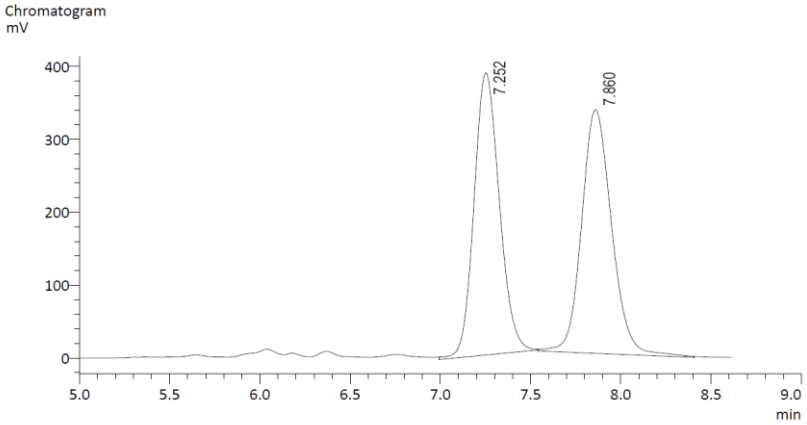
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.320	21104280	1953594	94.286
2	5.456	1279092	105396	5.714
Total		22383372	2058990	100.000

Figure S47. HPLC traces of racemic **3p** (reference) and chiral **3p**. Area integration = 94.3:5.7 (89% ee).

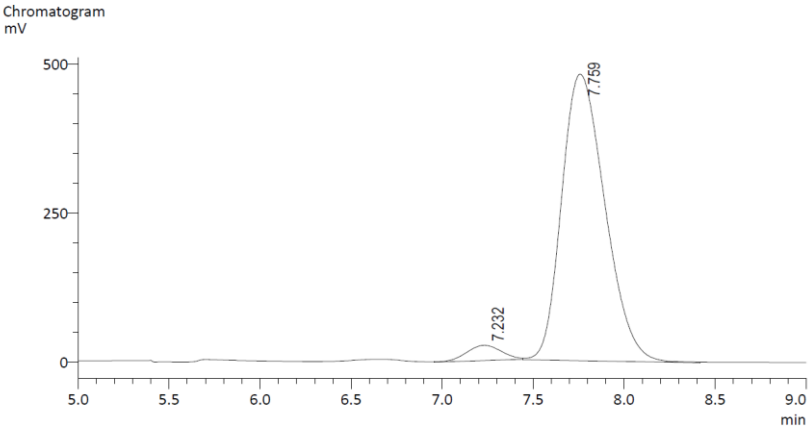


3q



<Peak Table>
Detector A 254nm

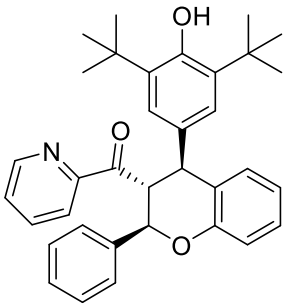
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	7.252	3778886	387173	49.405
2	7.860	3869865	334469	50.595
Total		7648751	721642	100.000



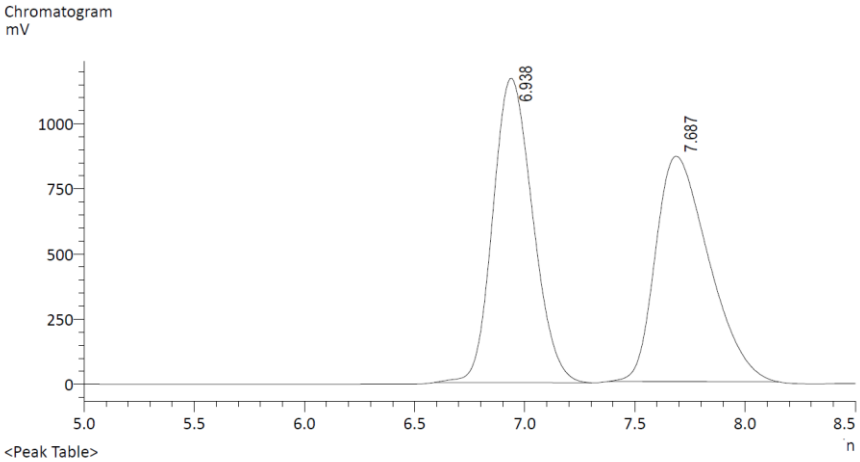
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	7.232	340806	25572	4.105
2	7.759	7962404	480851	95.895
Total		8303210	506423	100.000

Figure S48. HPLC traces of racemic **3q** (reference) and chiral **3q**. Area integration = 4.1:95.9 (92% ee).

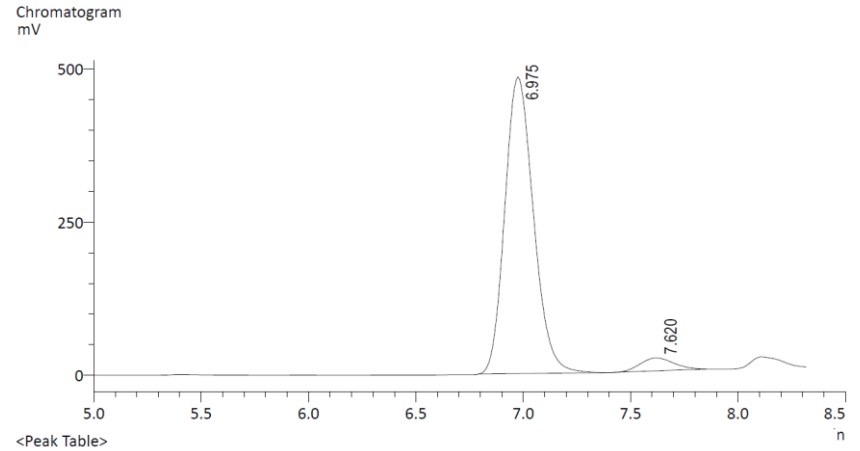


3r



<Peak Table>
???A 254nm

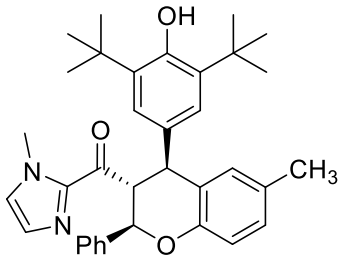
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.938	14715375	1168174	50.276
2	7.687	14554074	864915	49.724
Total		29269450	2033089	100.000



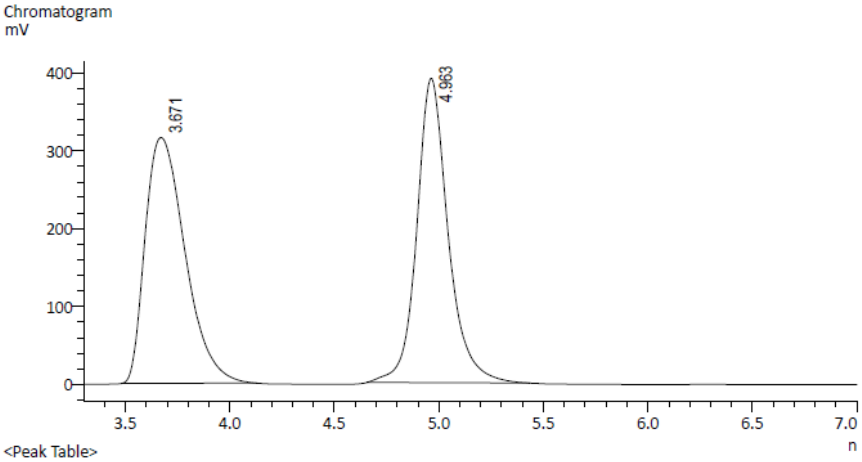
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.975	4501843	484530	95.118
2	7.620	231054	21023	4.882
Total		4732897	505553	100.000

Figure S49. HPLC traces of racemic **3r** (reference) and chiral **3r**. Area integration = 95.1: 4.9 (90% ee).

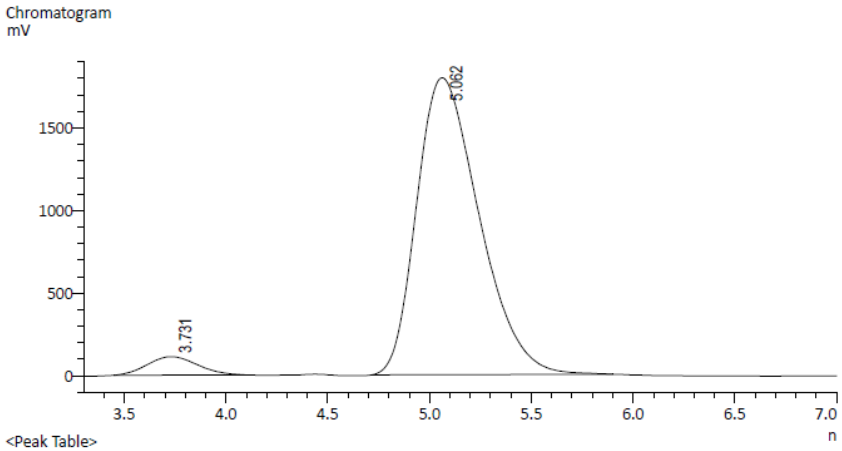


4a



<Peak Table>
Detector A 254nm

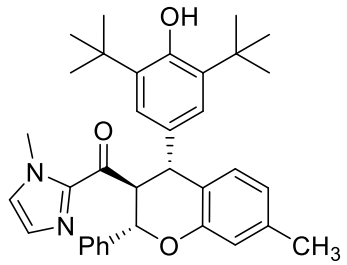
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	3.671	4186557	315292	50.612
2	4.963	4085275	390423	49.388
Total		8271832	705715	100.000



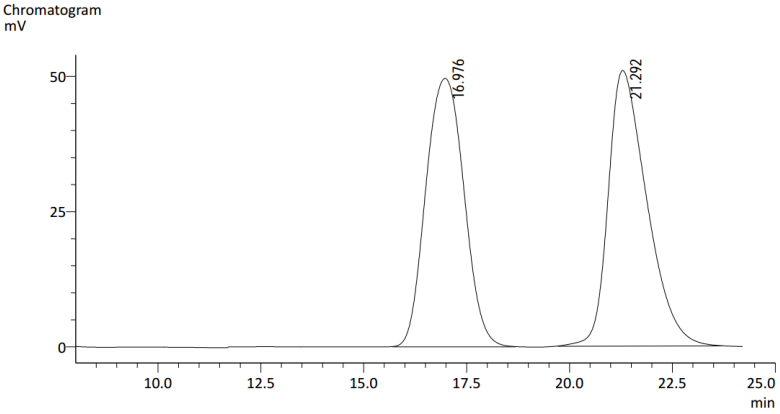
<Peak Table>
???A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	3.731	1903299	111553	4.722
2	5.062	38405687	1797854	95.278
Total		40308986	1909407	100.000

Figure S50. HPLC traces of racemic **4a** (reference) and chiral **4a**. Area integration = 4.7:95.3 (91% ee).

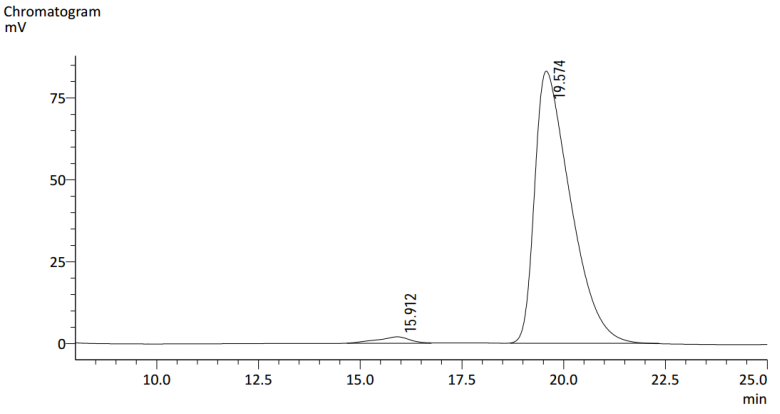


4b



<Peak Table>
Detector A 254nm

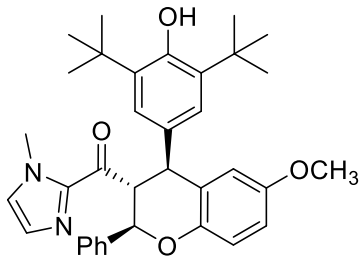
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	16.976	3208245	49629	49.056
2	21.292	3331700	50963	50.944
Total		6539945	100592	100.000



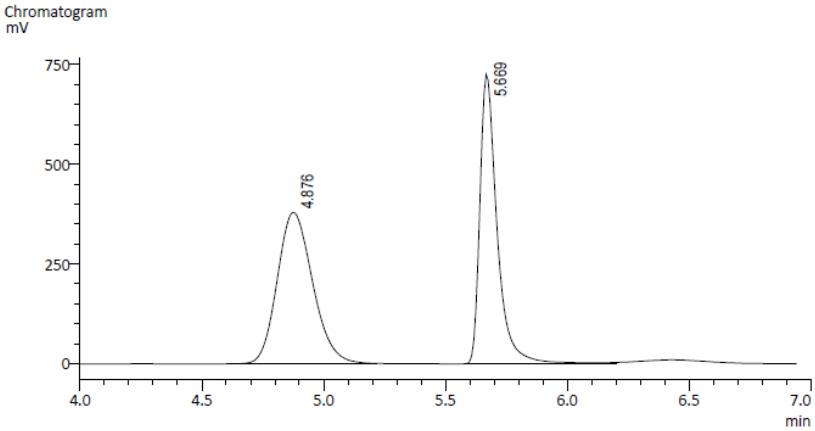
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	15.912	111497	1972	2.142
2	19.574	5094881	83052	97.858
Total		5206378	85024	100.000

Figure S51. HPLC traces of racemic **4b** (reference) and chiral **4b**. Area integration = 2.1:97.8 (96% ee).

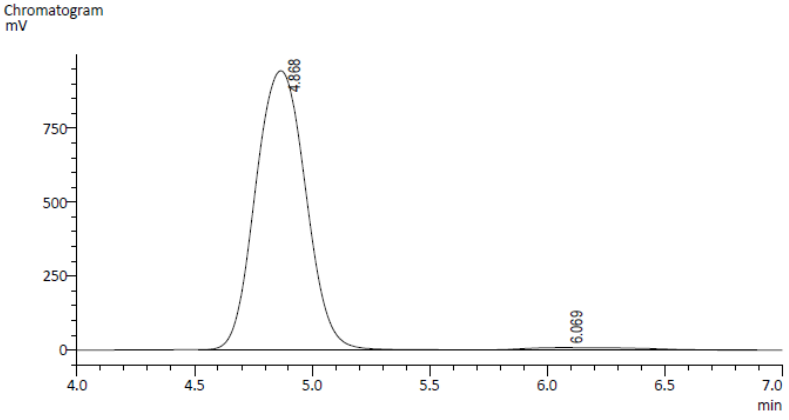


4c



<Peak Table>
Detector A 254nm

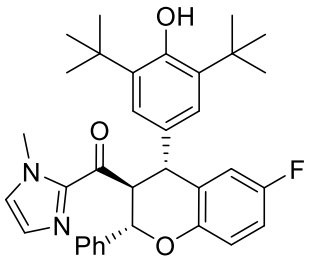
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.876	3804628	378724	51.420
2	5.669	3594492	725362	48.580
Total		7399120	1104086	100.000



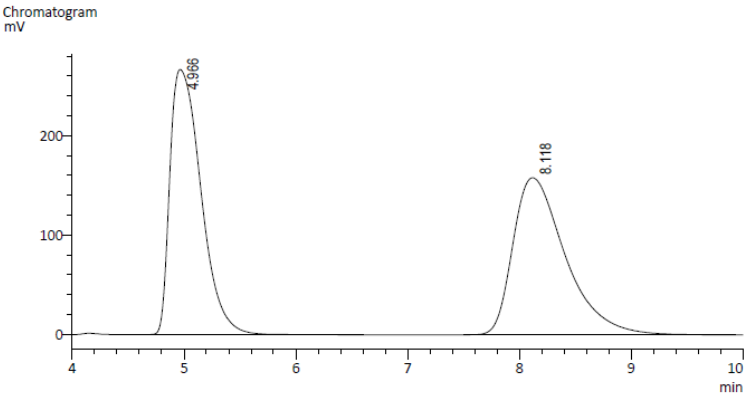
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.868	14005900	944191	98.010
2	6.069	284368	8279	1.990
Total		14290268	952470	100.000

Figure S52. HPLC traces of racemic **4c** (reference) and chiral **4c**. Area integration = 98.0:2.0 (96% ee).

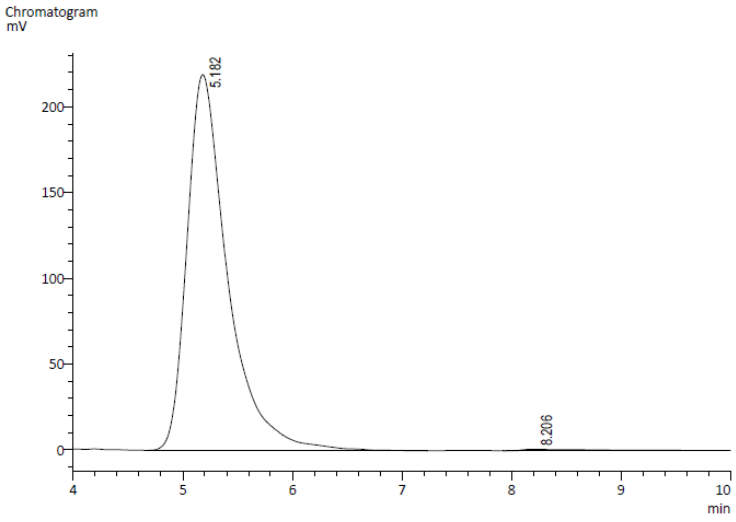


4d



<Peak Table>
Detector A 254nm

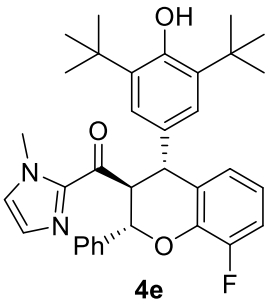
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.966	5155208	267034	50.073
2	8.118	5140224	157997	49.927
Total		10295432	425032	100.000



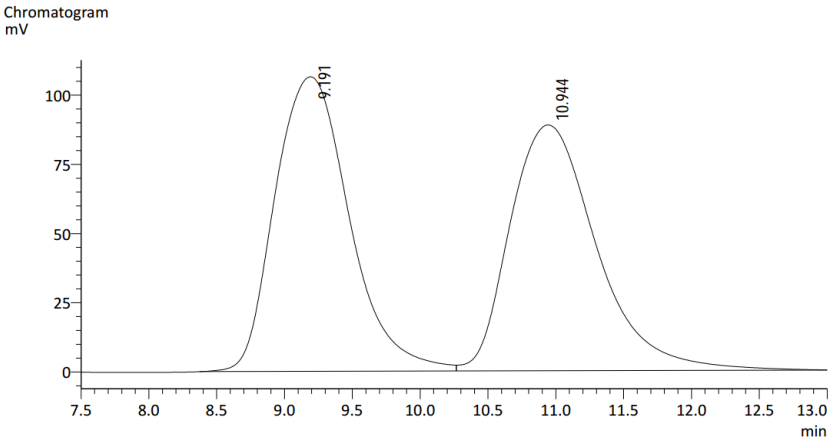
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.182	5660992	219239	99.496
2	8.206	28687	692	0.504
Total		5689679	219931	100.000

Figure S53. HPLC traces of racemic **4d** (reference) and chiral **4d**. Area integration = 99.5:0.5 (99% ee).

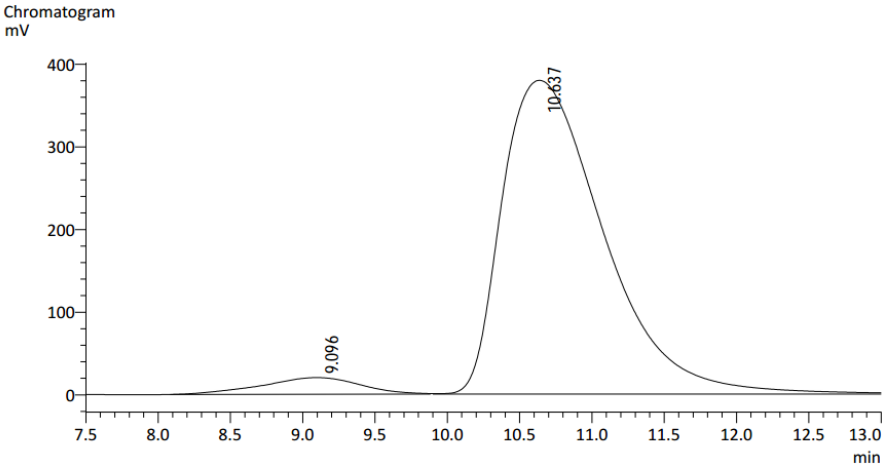


4e



<Peak Table>
Detector A 254nm

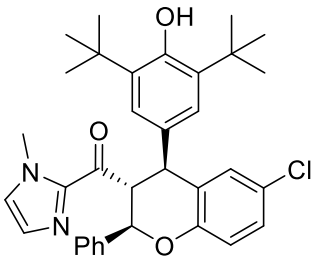
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	9.191	4060533	106389	50.697
2	10.944	3948830	88770	49.303
Total		8009364	195159	100.000



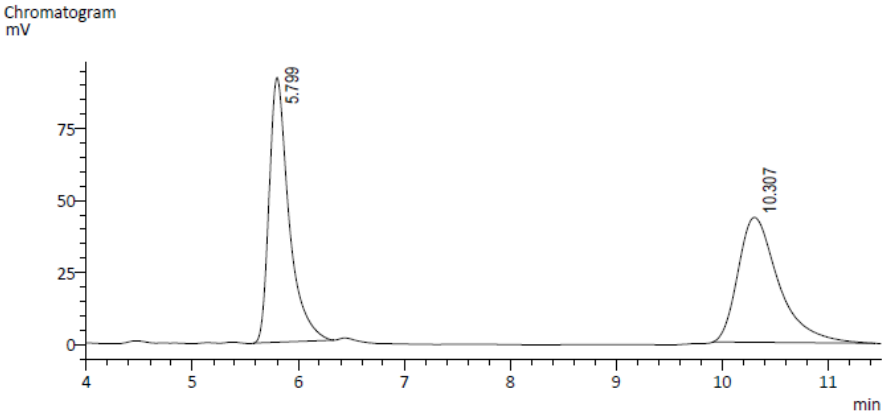
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	9.096	953861	20142	4.884
2	10.637	18576884	379544	95.116
Total		19530745	399686	100.000

Figure S54. HPLC traces of racemic **4e** (reference) and chiral **4e**. Area integration = 4.9:95.1 (90% ee).

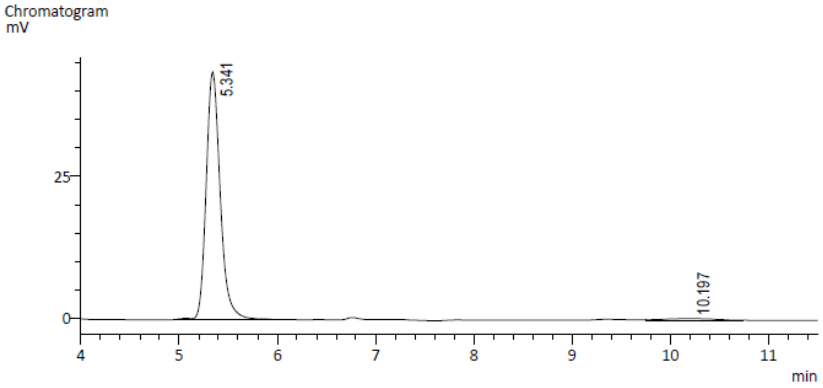


4f



<Peak Table>
Detector A 254nm

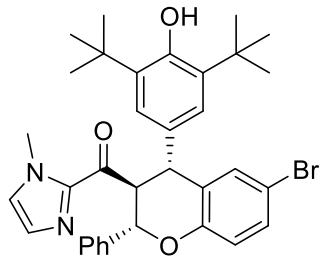
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.799	1192170	91850	50.827
2	10.307	1153374	43324	49.173
Total		2345544	135173	100.000



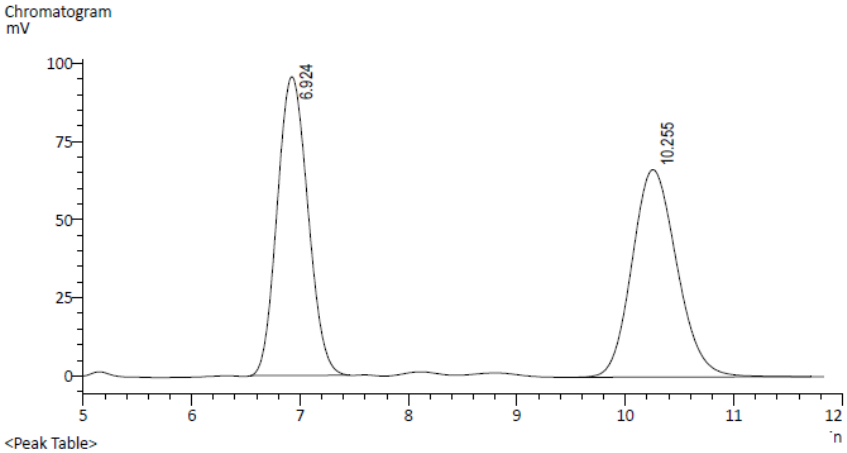
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.341	434930	43539	97.788
2	10.197	9836	293	2.212
Total		444767	43831	100.000

Figure S55. HPLC traces of racemic **4f** (reference) and chiral **4f**. Area integration = 97.8:2.2 (96% ee).

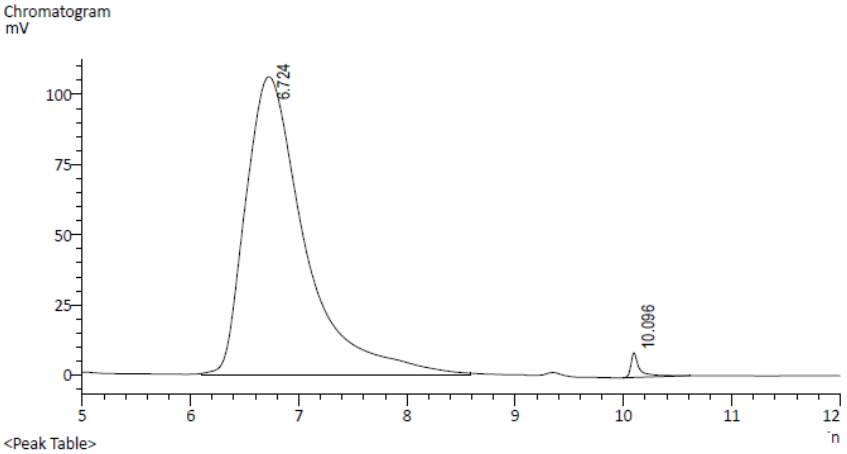


4g



<Peak Table>
Detector A 254nm

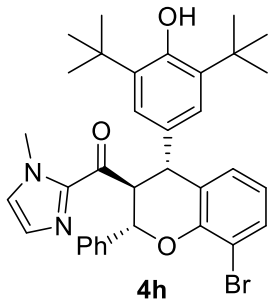
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.924	1881267	95603	49.569
2	10.255	1913991	66385	50.431
Total		3795257	161988	100.000



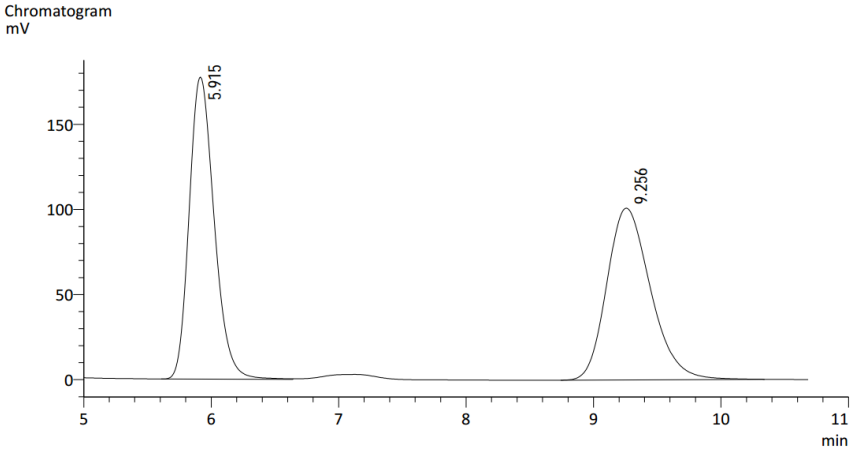
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	6.724	4067641	106346	98.759
2	10.096	51115	8715	1.241
Total		4118756	115061	100.000

Figure S56. HPLC traces of racemic **4g** (reference) and chiral **4g**. Area integration = 98.8:1.2 (98% ee).

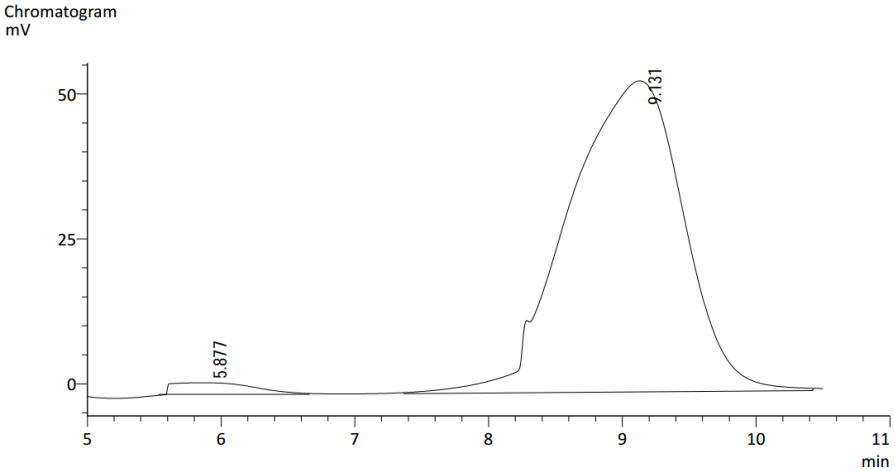


4h



<Peak Table>
Detector A 254nm

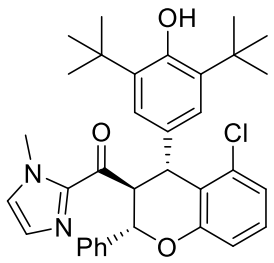
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.915	2413340	177438	50.030
2	9.256	2410414	100913	49.970
Total		4823754	278351	100.000



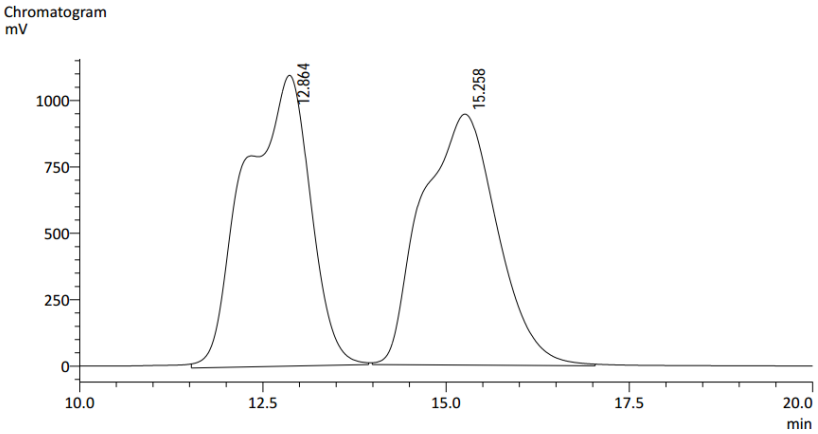
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	5.877	84633	1990	2.583
2	9.131	3192128	53648	97.417
Total		3276761	55638	100.000

Figure S57. HPLC traces of racemic **4h** (reference) and chiral **4h**. Area integration = 2.6:97.4 (95% ee).

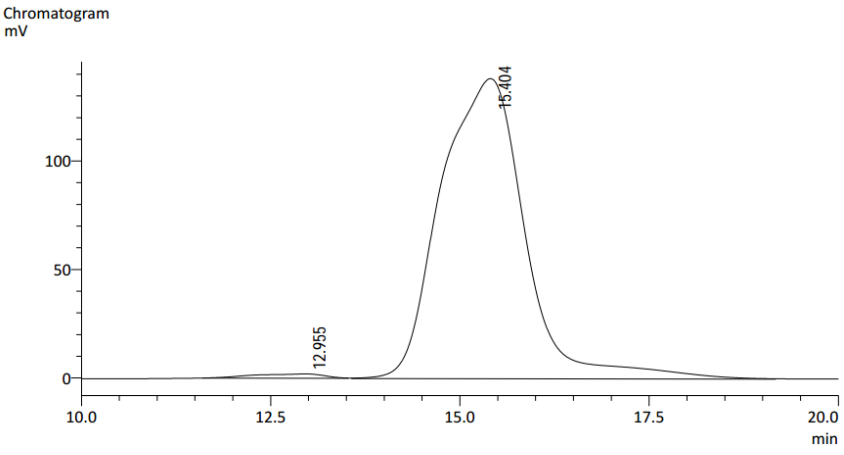


4i



<Peak Table>
Detector A 254nm

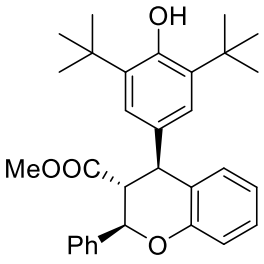
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	12.864	67772509	1095023	50.107
2	15.258	67483412	945096	49.893
Total		135255921	2040119	100.000



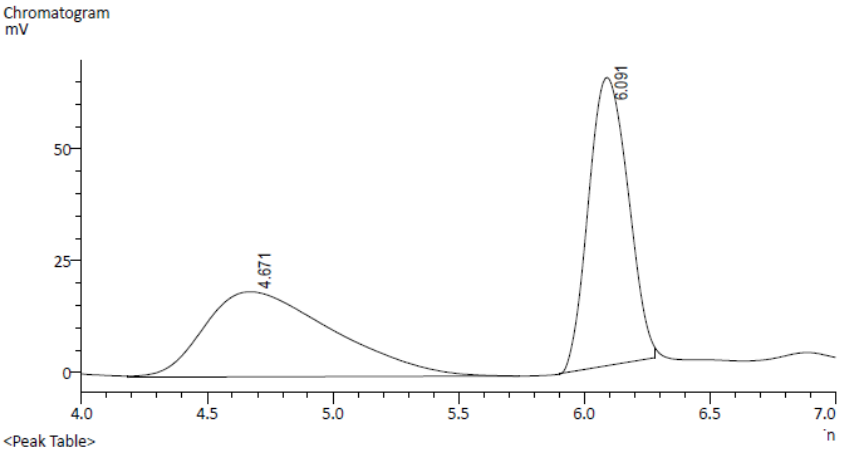
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	12.955	134051	2009	1.235
2	15.404	10719596	138320	98.765
Total		10853647	140329	100.000

Figure S58. HPLC traces of racemic **4i** (reference) and chiral **4i**. Area integration = 1.2:98.8 (98% ee).

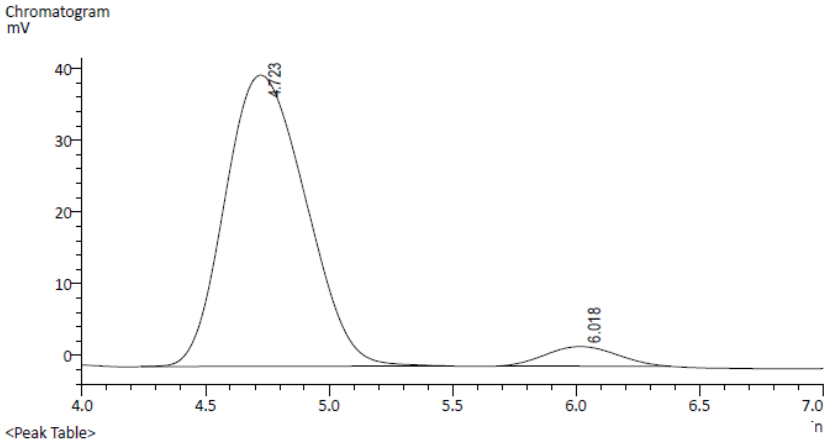


5



<Peak Table>
Detector A 254nm

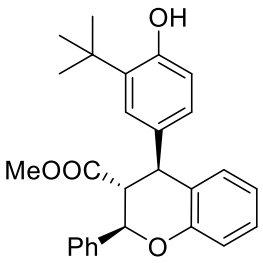
Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.671	681928	19047	49.073
2	6.091	707692	64573	50.927
Total		1389620	83619	100.000



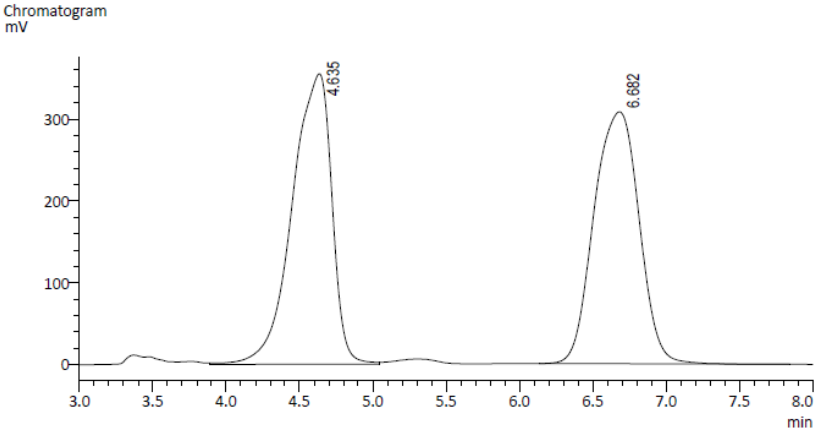
<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.723	919165	40628	94.351
2	6.018	55035	2733	5.649
Total		974200	43362	100.000

Figure S59. HPLC traces of racemic **5** (reference) and chiral **5**. Area integration = 94.4:5.6 (89% ee).

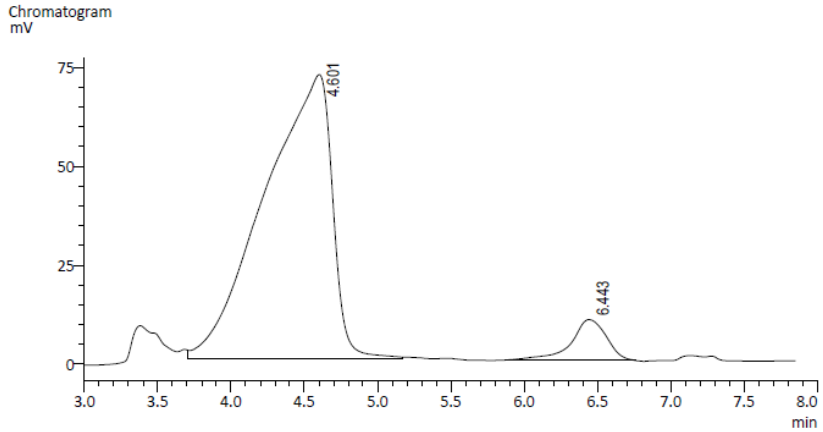


6



<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.635	6665766	354820	50.272
2	6.682	6593554	307819	49.728
Total		13259320	662638	100.000



<Peak Table>
Detector A 254nm

Peak#	Retention Time (min)	Area (mAU*min)	Height (mAU)	Area Ratio (%)
1	4.601	2303265	71801	92.905
2	6.443	175888	10344	7.095
Total		2479152	82145	100.000

Figure S60. HPLC traces of racemic **6** (reference) and chiral **6**. Area integration = 92.9:7.1 (86% ee).

8. Single Crystal X-Ray Diffraction Studies

The single crystal for compound **3k** was prepared from a mixture solvent of ethyl acetate and *n*-hexane (v/v = 3:1). The data were collected on a Bruker APEX-II CCD equipped with molybdenum micro-focus X-ray sources (λ = 0.71073 Å) at 299 K. The crystal structures were resolved by direct methods and all calculations were performed on the SHELXL-97 program package. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added in the riding model and refined with isotropic thermal parameters. The absolute configuration of **3k** was determined as (2*R*, 3*R*, 4*S*) based on its single crystal X-ray analysis. The structure is shown in **Figure S51**. The detailed information is listed in the **Table S1**. Crystallographic data for **3k** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number **CCDC 2118016**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

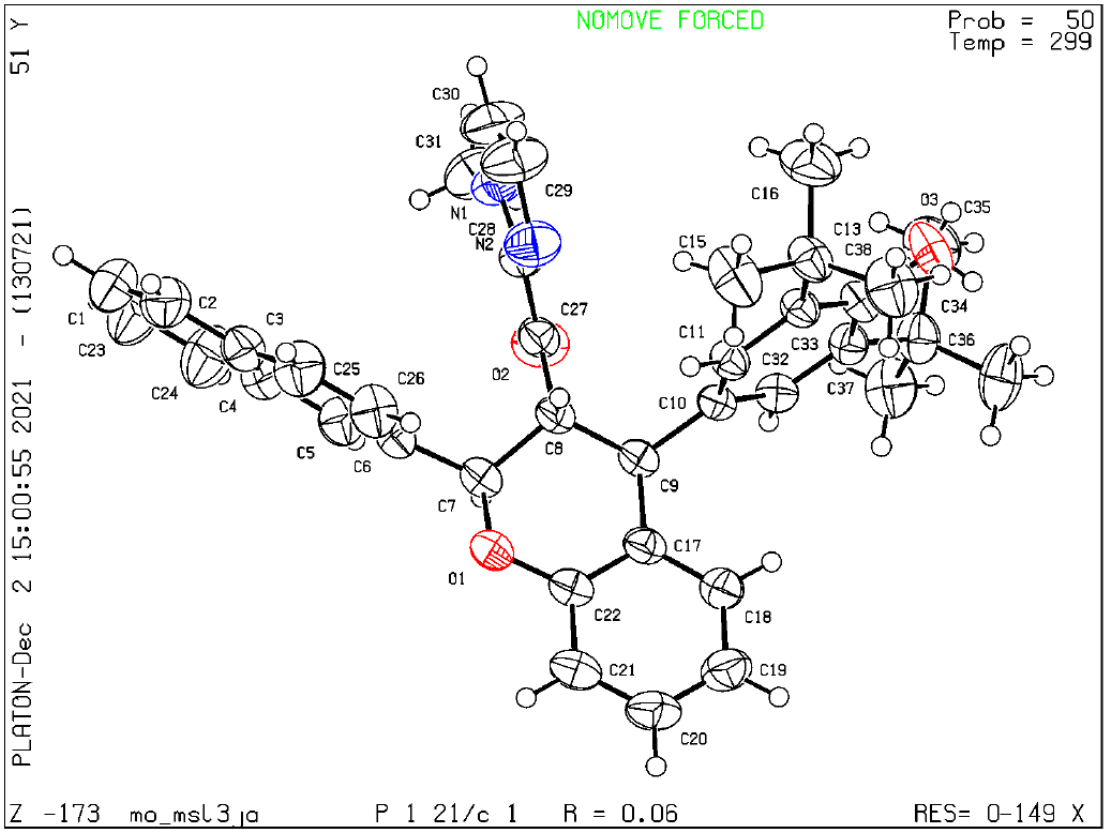


Figure S51. Crystal structure of **3k** to verify absolute configuration.

Table S1. Crystal data and structure refinement for compound **3k**.

Bond precision	**C-C = 0.0034 Å**	**Z**	**4**
Wavelength	0.71073 Å	**Mu (mm^{-1})**	0.075
Cell	a=10.3498(7) *α*=90	**F000**	1224.0
	b=22.0427(14) *β*=109.472(3)	**F000'**	1224.50
	c=14.8597(10) *γ*=90	**h,k,l_{max}**	13, 28, 19
Temperature	299 K	**N_{ref}**	7123
Volume	3196.2(4)	**T_{min},T_{max}**	0.657, 0.731
Space group	P21/c	**Data completeness**	0.994
Hall group	-P 2ybc	**θ (max)**	27.244
Moiety formula	$C_{38}H_{40}N_2O_3$	**R(reflections)**	0.0578(5221)
Sum formula	$C_{38}H_{40}N_2O_3$	**wR2(reflections)**	0.1731(7123)
Mr	572.72	**S**	1.053
Dx, g (cm^{-3})	1.190	**Npar**	395

9. References

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