Supporting Information

Organocatalytic Enantioselective C–H Allenylation of Carbazoles with Propargylic Alcohols via Remote 1,8-Conjugate Addition

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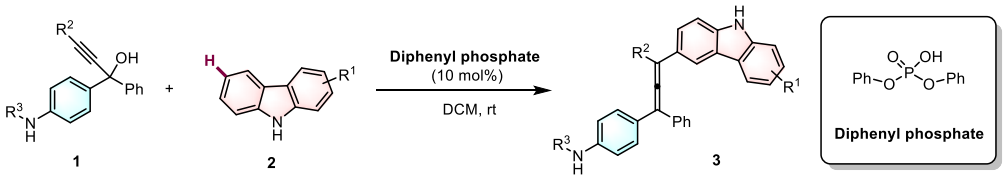
1. General Information

All reactions were carried out in oven-dried reaction vessel unless otherwise noted and solvents were dried according to established procedures. Reactions were monitored by thin layer chromatography (TLC). Purification of reaction product was carried out by flash chromatography using Qing Dao Sea Chemical Reagent silica gel (200-300 mesh). ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker 400 MHz or 500 MHz spectrometer in $CDCl_3$ unless otherwise noted. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm, δ) downfield from the internal standard Me_4Si (TMS, δ = 0 ppm). Chemical shifts in ^{13}C NMR spectra are reported relative to the central line of the chloroform signal (δ = 77.0 ppm). Data are presented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). HPLC analyses were conducted on an Agilent instrument using Daicel Chiralpak IA, IG, Chiralcel AD-H columns. High resolution mass spectra were obtained with a Shimadzu LCMS-IT-TOF mass spectrometer. Substrates **1**[1a] and **2**[1b] were synthesized according to the literature method.

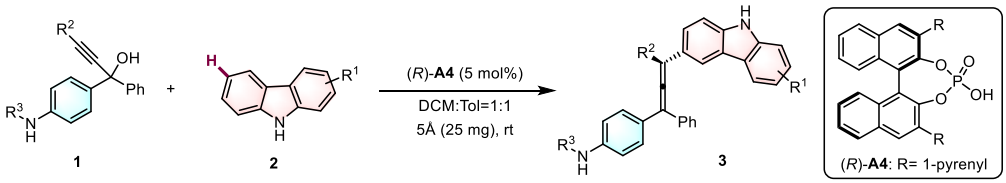
2. Experimental Procedure and Characterization of Products

a. General Procedure to Prepare Racemic Products 3



To a solution of *α*-(4-aminophenyl)propargylic alcohols **1** (0.10 mmol, 1.0 equiv.), and catalyst diphenyl phosphate (0.01 mmol, 10 mol%) in DCM (1 mL) was added carbazoles **2** (0.12 mmol, 1.2 equiv.). The mixture was stirred at room temperature until the reaction was completed (monitored by TLC analysis). The crude product was purified directly by flash column chromatography on silica gel (petroleum ether/ ethyl acetate = 15:1~5:1) to give the desired racemic products **3**.

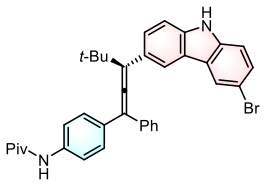
b. General Procedure to Prepare Enantioenriched Products 3



To a solution of *α*-(4-aminophenyl)propargylic alcohols **1** (0.05 mmol, 1.0 equiv.), 5Å (25 mg), and catalyst (*R*)-**A4** (0.0025 mmol, 5 mol%) in DCM:Tol (v:v = 1:1, 1 mL) was added carbazoles **2** (0.06 mmol, 1.2 equiv.). The mixture was stirred at room temperature until the reaction was completed (monitored by TLC analysis). The crude product was purified directly by flash column chromatography on silica gel (petroleum ether/ ethyl acetate = 15:1~5:1) to give the desired enantioenriched products **3**.

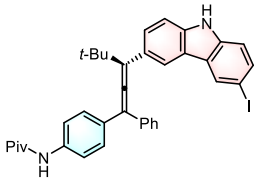
c. Analytical Data for Products 3

(*R*)-N-(4-(3-(6-bromo-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3a**)



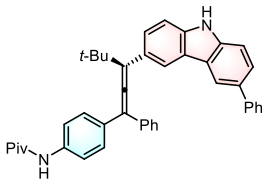
white foam, 20 h, 92% yield, 94% *ee*, $[a]_D^{20}$ = -82.13 (c = 0.33, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.14 (d, *J* = 1.8 Hz, 1H), 7.89 (s, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.43 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.39 – 7.29 (m, 9H), 7.27 – 7.21 (m, 2H), 1.33 (s, 9H), 1.25 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.43, 176.83, 139.01, 138.51, 137.79, 136.77, 133.96, 128.94, 128.86, 128.57, 128.49, 128.23, 126.95, 125.16, 123.19, 122.13, 120.97, 120.21, 118.94, 112.20, 110.35, 108.75, 39.75, 36.19, 29.97, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{36}H_{35}BrN_2O$ [M-H]$^-$: 589.1860; found: 589.1838. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IA column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 12.4 min, t_{minor} = 16.0 min.

(*R*)-N-(4-(3-(6-iodo-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3b**)



white foam, 20 h, 90% yield, 93% *ee*, $[a]_D^{20}$ = -137.33 (c = 0.15, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 1.5 Hz, 1H), 8.20 (s, 1H), 7.89 (d, *J* = 1.2 Hz, 1H), 7.60 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.39 – 7.30 (m, 9H), 7.27 – 7.23 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 1.33 (s, 9H), 1.25 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.42, 176.79, 139.01, 138.65, 137.80, 136.79, 134.14, 133.94, 129.32, 128.99, 128.95, 128.54, 128.49, 128.24, 126.95, 125.95, 121.88, 120.96, 120.18, 118.92, 112.77, 110.27, 108.77, 82.01, 39.76, 36.20, 29.98, 27.80. **HRMS** (ESI): *m/z* calcd. for $C_{36}H_{35}IN_2O$ [M-H]$^-$: 637.1721; found: 637.1721. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IA column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 11.7 min, t_{minor} = 16.0 min.

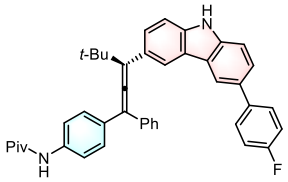
(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-phenyl-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3c**)



white foam, 20 h, 73% yield, 94% *ee*, $[a]_D^{20}$ = -101.18 (c = 0.17, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 1.6 Hz, 1H), 8.13 (s, 1H), 8.01 (s, 1H), 7.71 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.63 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.48 – 7.41 (m, 3H), 7.41 – 7.30 (m, 10H), 7.26 – 7.23 (m, 1H), 1.32 (s, 9H), 1.27 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.42, 176.73, 142.24, 139.41, 139.13, 137.94, 136.77, 134.04, 133.09, 128.99, 128.86, 128.64, 128.46, 128.27, 128.06, 127.48, 126.88, 126.57, 125.58, 123.95, 123.26, 120.94, 120.11,

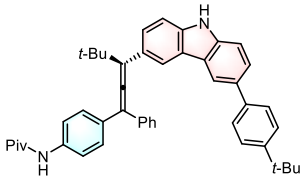
119.07, 119.03, 110.96, 110.25, 108.67, 39.75, 36.23, 30.01, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{40}N_2O$ [M-H]$^-$: 587.3068; found: 587.3061. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 14.1 min, t_{minor} = 9.5 min.

(*R*)-N-(4-(3-(6-(4-fluorophenyl)-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3d**)



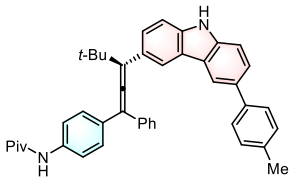
white foam, 16 h, 68% yield, 95% *ee*, $[a]_D^{20}$ = -152.50 (c = 0.12, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.17 (s, 1H), 8.01 (s, 1H), 7.65 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.57 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.33 (m, 10H), 7.29 – 7.24 (m, 1H), 7.15 (t, *J* = 8.7 Hz, 2H), 1.34 (s, 9H), 1.29 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.41, 176.77, 162.17 (d, *J* = 245.1 Hz), 139.33, 139.14, 138.37 (d, *J* = 3.0 Hz), 137.92, 136.77, 134.03, 132.12, 128.99, 128.94, 128.88, 128.67, 128.46, 128.27, 128.12, 126.90, 125.40, 123.94, 123.15, 120.94, 120.13, 119.04, 118.91, 115.71, 115.54, 111.00, 110.27, 108.67, 39.75, 36.23, 30.00, 27.79. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -117.20. **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{39}FN_2O$ [M-H]$^-$: 605.2974; found: 605.2973. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 23.6 min, t_{minor} = 15.9 min.

(*R*)-N-(4-(3-(6-(4-(tert-butyl)phenyl)-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3e**)



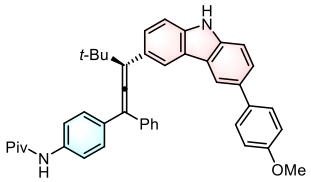
white foam, 12 h, 87% yield, 92% *ee*, $[a]_D^{20}$ = -103.75 (c = 0.16, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 1.6 Hz, 1H), 8.11 (s, 1H), 8.00 (s, 1H), 7.68 – 7.61 (m, 3H), 7.55 – 7.47 (m, 4H), 7.43 – 7.31 (m, 10H), 7.26 – 7.23 (m, 1H), 1.39 (s, 9H), 1.32 (s, 9H), 1.27 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.44, 176.71, 149.51, 139.34, 139.27, 139.12, 137.94, 136.76, 134.04, 132.96, 128.98, 128.58, 128.46, 128.26, 127.97, 127.08, 126.88, 125.80, 125.50, 123.91, 123.28, 120.92, 120.11, 119.08, 118.86, 110.91, 110.22, 108.65, 39.74, 36.23, 34.62, 31.57, 30.01, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{46}H_{48}N_2O$ [M+H]$^+$: 645.3839; found: 645.3841. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 21.1 min, t_{minor} = 8.9 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(p-tolyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3f**)



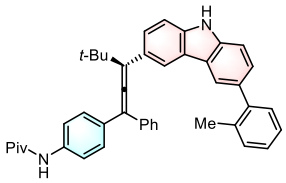
white foam, 16 h, 80% yield, 92% *ee*, $[a]_D^{20}$ = -87.89 (c = 0.19, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.12 (s, 1H), 8.00 (s, 1H), 7.61 (dd, *J* = 10.7, 4.5 Hz, 3H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.42 – 7.31 (m, 10H), 7.27 – 7.24 (m, 3H), 2.41 (s, 3H), 1.32 (s, 9H), 1.27 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.43, 176.72, 139.36, 139.26, 139.13, 137.94, 136.76, 136.21, 134.05, 133.03, 129.58, 128.98, 128.57, 128.45, 128.27, 127.98, 127.29, 126.87, 125.46, 123.92, 123.27, 120.93, 120.11, 119.08, 118.76, 110.92, 110.22, 108.64, 39.74, 36.22, 30.01, 27.79, 21.21. **HRMS** (ESI): *m/z* calcd. for $C_{43}H_{42}N_2O$ $[M+H]^+$: 603.3370; found: 603.3389. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 28.1 min, t_{minor} = 10.0 min.

(*R*)-N-(4-(3-(6-(4-methoxyphenyl)-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl) pivalamide (**3g**)



white foam, 12 h, 68% yield, 92% *ee*, $[a]_D^{20}$ = -90.77 (c = 0.13, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.10 (s, 1H), 8.00 (s, 1H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.43 – 7.31 (m, 10H), 7.26 – 7.23 (m, 1H), 7.01 (d, *J* = 8.6 Hz, 2H), 3.87 (s, 3H), 1.32 (s, 9H), 1.27 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.43, 176.71, 158.73, 139.13, 139.07, 137.95, 136.77, 134.93, 134.04, 132.82, 128.99, 128.58, 128.45, 128.27, 128.00, 126.88, 125.34, 123.96, 123.28, 120.95, 120.09, 119.08, 118.57, 114.33, 110.91, 110.20, 108.66, 55.53, 39.75, 36.24, 30.02, 27.80. **HRMS** (ESI): *m/z* calcd. for $C_{43}H_{42}N_2O_2$ $[M+H]^+$: 619.3319; found: 619.3320. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 70/30, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 17.9 min, t_{minor} = 8.5 min.

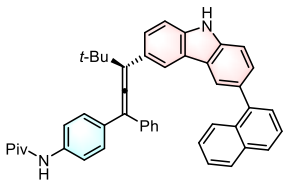
(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(o-tolyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3h**)



white foam, 18 h, 76% yield, 92% *ee*, $[a]_D^{20}$ = -104.74 (c = 0.19, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.99 (s, 1H), 7.95 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.41 – 7.22 (m, 16H), 2.31 (s, 3H), 1.32 (s, 9H), 1.26 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.49, 176.72, 142.84, 139.06, 138.89, 137.91, 136.75, 135.91, 134.02, 133.53, 130.49, 130.33, 128.96, 128.58, 128.44, 128.24, 127.91, 127.41, 127.00, 126.86, 125.80, 123.33,

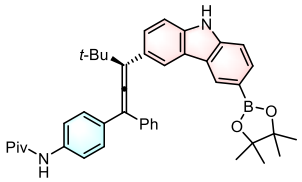
123.16, 120.93, 120.88, 120.12, 119.09, 110.20, 108.64, 39.73, 36.21, 30.01, 27.79, 20.85. **HRMS** (ESI): *m/z* calcd. for $C_{43}H_{42}N_2O$ $[M+H]^+$: 603.3370; found: 603.3377. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IA column (hexane/*i*-PrOH = 92/8, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 17.4 min, t_{minor} = 22.2 min.

(*R*)-N-(4-(4,4-dimethyl-3-(6-(naphthalen-1-yl)-9H-carbazol-3-yl)-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3i**)



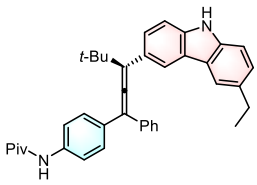
white foam, 15 h, 90% yield, 94% *ee*, $[a]_D^{20}$ = -100.45 (c = 0.22, MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.19 (s, 1H), 8.00 (t, *J* = 3.9 Hz, 2H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.89 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.59 – 7.48 (m, 7H), 7.46 – 7.29 (m, 10H), 7.27 – 7.22 (m, 1H), 1.33 (s, 9H), 1.28 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.47, 176.71, 141.19, 139.24, 139.11, 137.87, 136.73, 134.00, 133.98, 132.38, 132.17, 128.95, 128.64, 128.44, 128.33, 128.25, 128.22, 128.02, 127.53, 127.32, 126.86, 126.58, 126.03, 125.77, 125.55, 123.49, 123.11, 121.85, 120.96, 120.13, 119.08, 110.40, 110.26, 108.65, 39.72, 36.21, 30.00, 27.77. **HRMS** (ESI): *m/z* calcd. for $C_{46}H_{42}N_2O$ $[M+H]^+$: 639.3370; found: 639.3379. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 15.7 min, t_{minor} = 18.3 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3j**)



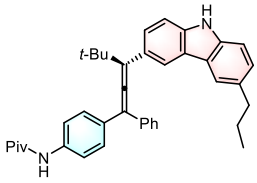
white foam, 16 h, 90% yield, 96% *ee*, $[a]_D^{20}$ = -107.92 (c = 0.24, MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.28 (s, 1H), 8.03 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.29 (m, 10H), 7.24 (t, *J* = 7.1 Hz, 1H), 1.39 (s, 12H), 1.32 (s, 9H), 1.25 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.34, 176.69, 142.16, 138.59, 137.88, 136.73, 134.01, 132.45, 128.96, 128.73, 128.46, 128.23, 128.00, 127.85, 126.84, 123.18, 123.13, 121.11, 120.13, 119.02, 110.20, 110.12, 108.66, 83.75, 39.73, 36.21, 29.95, 27.79, 25.07. **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{47}N_2O_3B$ $[M-H]^-$: 637.3614; found: 637.3597. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IG column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 9.3 min, t_{minor} = 19.6 min.

(*R*)-N-(4-(3-(6-ethyl-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3k**)



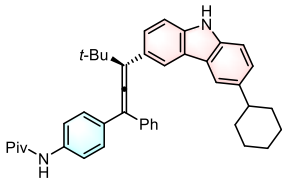
white foam, 12 h, 65% yield, 97% *ee*, $[a]_D^{20}$ = -121.93 (c = 0.19, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.95 (s, 1H), 7.89 (s, 1H), 7.54 – 7.50 (m, 2H), 7.41 – 7.31 (m, 10H), 7.27 – 7.24 (m, 2H), 2.82 (q, *J* = 7.6 Hz, 2H), 1.36 – 1.32 (m, 12H), 1.27 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.46, 176.68, 139.00, 138.33, 138.01, 136.76, 135.64, 134.08, 129.00, 128.43, 128.28, 127.65, 126.84, 126.32, 123.56, 123.13, 120.85, 120.04, 119.24, 119.15, 110.49, 110.02, 108.57, 39.76, 36.23, 30.03, 29.12, 27.81, 16.71. **HRMS** (ESI): *m/z* calcd. for $C_{38}H_{40}N_2O$ [M-H]$^-$: 539.3068; found: 539.3048. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 16.8 min, t_{minor} = 30.4 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-propyl-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3l**)



white foam, 12 h, 89% yield, 94% *ee*, $[a]_D^{20}$ = -120.92 (c = 0.11, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.95 (s, 1H), 7.87 (s, 1H), 7.54 – 7.50 (m, 2H), 7.42 – 7.30 (m, 10H), 7.27 – 7.25 (m, 1H), 7.23 (dd, *J* = 8.2, 1.6 Hz, 1H), 2.80 – 2.72 (m, 2H), 1.78 – 1.70 (m, 2H), 1.34 (s, 9H), 1.28 (s, 9H), 0.99 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.46, 176.68, 138.98, 138.36, 138.01, 136.75, 134.09, 133.98, 129.00, 128.43, 128.28, 128.25, 127.64, 126.84, 123.50, 123.11, 120.83, 120.04, 119.90, 119.15, 110.37, 110.01, 108.56, 39.75, 38.30, 36.23, 30.03, 27.80, 25.54, 14.05. **HRMS** (ESI): *m/z* calcd. for $C_{39}H_{42}N_2O$ [M+H]$^+$: 555.3370; found: 555.3385. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 8.1 min, t_{minor} = 13.4 min.

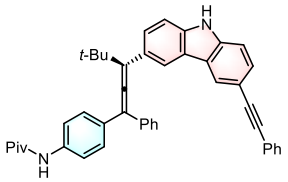
(*R*)-N-(4-(3-(6-cyclohexyl-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3m**)



white foam, 18 h, 78% yield, 95% *ee*, $[a]_D^{20}$ = -147.00 (c = 0.10, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.94 (s, 1H), 7.89 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.29 (m, 10H), 7.26 – 7.23 (m, 2H), 2.66 (t, *J* = 11.8 Hz, 1H), 1.97 (d, *J* = 12.5 Hz, 2H), 1.88 (d, *J* = 12.6 Hz, 2H), 1.77 (d, *J* = 12.1 Hz, 1H), 1.56 – 1.50 (m, 2H), 1.48 – 1.39 (m, 3H), 1.32 (s, 9H), 1.26 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.43, 176.69, 139.68, 139.02, 138.44, 138.03, 136.75, 134.11, 129.01, 128.43, 128.29, 128.21, 127.63, 126.82, 125.38, 123.44, 123.23, 120.77, 120.05, 119.16, 118.11, 110.43, 110.01, 108.54, 44.86, 39.75, 36.24, 35.39, 35.36, 30.03, 27.80, 27.28,

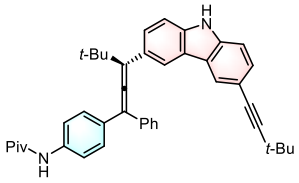
26.43. **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{46}N_2O$ $[M+H]^+$: 595.3683 found: 595.3704. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 7.8 min, t_{minor} = 16.6 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)pivalamide (**3n**)



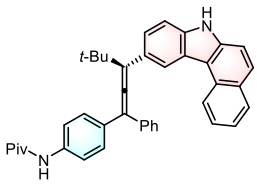
white foam, 20 h, 86% yield, 95% *ee*, $[a]_D^{20}$ = -107.93 (c = 0.19, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.30 (s, 1H), 7.99 (s, 1H), 7.61 – 7.53 (m, 5H), 7.43 – 7.33 (m, 13H), 7.29 – 7.25 (m, 1H), 1.34 (s, 9H), 1.28 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.45, 176.79, 139.61, 138.98, 137.83, 136.77, 133.98, 131.60, 129.58, 128.97, 128.95, 128.48, 128.46, 128.28, 128.24, 127.91, 126.93, 124.19, 124.02, 123.45, 122.68, 121.02, 120.18, 118.99, 113.97, 110.85, 110.33, 108.75, 90.93, 87.71, 39.74, 36.21, 29.98, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{40}N_2O$ $[M-H]^-$: 611.3068; found: 611.3068. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 15.6 min, t_{minor} = 8.1 min.

(*R*)-N-(4-(3-(6-(3,3-dimethylbut-1-yn-1-yl)-9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3o**)



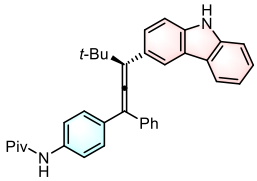
white foam, 15 h, 82% yield, 92% *ee*, $[a]_D^{20}$ = -111.05 (c = 0.19, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.13 (s, 1H), 7.94 (s, 1H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.42 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.40 – 7.30 (m, 9H), 7.29 – 7.23 (m, 2H), 1.36 (s, 9H), 1.32 (s, 9H), 1.25 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.41, 176.75, 139.11, 138.94, 137.87, 136.75, 134.00, 129.64, 128.95, 128.74, 128.46, 128.25, 128.13, 126.89, 123.92, 123.33, 122.77, 120.97, 120.14, 118.99, 114.89, 110.57, 110.21, 108.70, 96.45, 79.97, 39.74, 36.20, 31.41, 29.96, 28.11, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{44}N_2O$ $[M-H]^-$: 591.3381; found: 591.3366. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 95/5, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 30.2 min, t_{minor} = 25.4 min.

(*R*)-N-(4-(3-(7H-benzo[c]carbazol-10-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3p**)



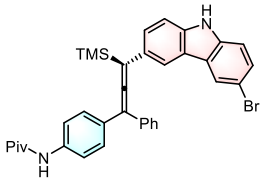
white foam, 18 h, 56% yield, 92% *ee*, $[a]_D^{20}$ = -73.81 (c = 0.21, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.3 Hz, 1H), 8.51 (s, 1H), 8.46 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.49 – 7.35 (m, 10H), 7.28 (t, *J* = 7.3 Hz, 1H), 1.35 (s, 9H), 1.34 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.92, 176.73, 138.02, 137.63, 137.56, 136.80, 134.07, 130.03, 129.41, 129.35, 129.32, 129.00, 128.49, 128.33, 127.55, 127.06, 126.91, 126.08, 123.88, 123.25, 123.06, 122.86, 120.11, 119.53, 115.46, 112.76, 110.54, 108.66, 39.76, 36.22, 30.21, 27.80. **HRMS** (ESI): *m/z* calcd. for $C_{40}H_{38}N_2O$ $[M-H]^-$: 561.2911; found: 561.2897. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 10.4 min, t_{minor} = 9.3 min.

(*R*)-N-(4-(3-(9H-carbazol-3-yl)-4,4-dimethyl-1-phenylpenta-1,2-dien-1-yl)phenyl)pivalamide (**3q**)



white foam, 12 h, 72% yield, 93% *ee*, $[a]_D^{20}$ = -131.67 (c = 0.18, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.99 (s, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.42 – 7.33 (m, 11H), 7.28 – 7.25 (m, 1H), 7.24 – 7.21 (m, 1H), 1.34 (s, 9H), 1.29 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.50, 176.73, 139.93, 138.65, 137.95, 136.76, 134.05, 128.98, 128.48, 128.44, 128.26, 127.76, 126.86, 125.96, 123.38, 123.12, 120.93, 120.48, 120.09, 119.48, 119.13, 110.75, 110.07, 108.60, 39.74, 36.20, 30.03, 27.79. **HRMS** (ESI): *m/z* calcd. for $C_{36}H_{36}N_2O$ $[M+H]^+$: 513.2900; found: 513.2912. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 16.0 min, t_{minor} = 10.9 min.

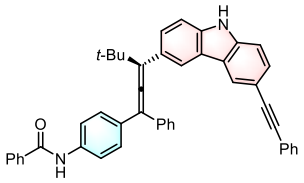
(*R*)-N-(4-(3-(6-bromo-9H-carbazol-3-yl)-1-phenyl-3-(trimethylsilyl)propa-1,2-dien-1-yl)phenyl)pivalamide (**3r**)



white foam, 24 h, 93% yield, 90% *ee*, $[a]_D^{20}$ = -65.60 (c = 0.25, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.12 (s, 1H), 7.97 (s, 1H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 – 7.35 (m, 6H), 7.35 – 7.27 (m, 3H), 7.26 – 7.19 (m, 2H), 1.31 (s, 9H), 0.34 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.37, 176.90, 138.99, 138.57, 137.04, 136.70, 133.22, 128.71, 128.64, 128.59, 128.10, 128.00, 127.06, 126.91, 125.06, 123.03, 122.75, 120.46, 119.29, 112.31, 112.19, 111.28, 106.21, 104.10, 39.72, 27.77, 0.22. **HRMS** (ESI): *m/z* calcd. for $C_{35}H_{35}BrN_2OSi$ $[M+H]^+$: 607.1775; found: 607.1736. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IA column (hexane/*i*-PrOH = 90/10, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major}

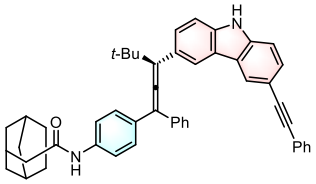
= 11.2 min, t_{minor} = 17.4 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)benzamide (**3s**)



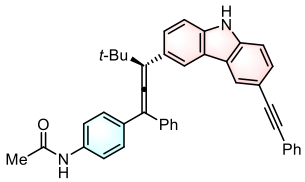
white foam, 18 h, 80% yield, 96% *ee*, $[a]_D^{20}$ = -129.44 (c = 0.21, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.25 (s, 1H), 8.00 (s, 1H), 7.93 (s, 1H), 7.88 (d, *J* = 7.4 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.59 – 7.52 (m, 4H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.5 Hz, 4H), 7.40 – 7.31 (m, 8H), 7.28 (t, *J* = 7.3 Hz, 1H), 1.30 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.51, 165.97, 139.59, 138.98, 137.79, 136.67, 135.10, 134.32, 131.99, 131.59, 129.59, 129.00, 128.94, 128.51, 128.45, 128.31, 127.91, 127.15, 126.98, 124.20, 124.00, 123.46, 122.70, 121.02, 120.39, 119.08, 114.00, 110.84, 110.35, 108.77, 90.91, 87.74, 36.23, 30.01. **HRMS** (ESI): *m/z* calcd. for $C_{46}H_{36}N_2O$ $[M-H]^-$: 631.2755; found: 631.2725. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IG column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 15.9 min, t_{minor} = 11.6 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)adamantane -1-carboxamide (**3t**)



white foam, 16 h, 82% yield, 96% *ee*, $[a]_D^{20}$ = -108.07 (c = 0.25, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.29 (s, 1H), 7.99 (s, 1H), 7.62 – 7.52 (m, 5H), 7.43 – 7.31 (m, 13H), 7.28 – 7.25 (m, 1H), 2.11 (s, 3H), 2.00 (s, 6H), 1.77 (q, *J* = 12.4 Hz, 6H), 1.67 (s, 1H), 1.28 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.45, 176.30, 139.63, 138.99, 137.85, 136.79, 133.88, 131.59, 129.56, 128.96, 128.93, 128.47, 128.45, 128.28, 128.25, 127.90, 126.91, 124.18, 124.02, 123.45, 122.68, 121.01, 120.17, 118.97, 113.94, 110.85, 110.34, 108.76, 90.95, 87.70, 41.63, 39.42, 36.55, 36.20, 29.98, 28.25. **HRMS** (ESI): *m/z* calcd. for $C_{50}H_{46}N_2O$ $[M+H]^+$: 691.3683; found: 691.3678. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 12.5 min, t_{minor} = 19.8 min.

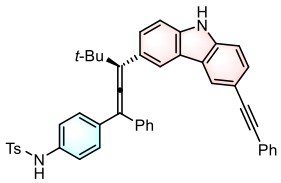
(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)acetamide (**3u**)



white foam, 16 h, 68% yield, 91% *ee*, $[a]_D^{20}$ = -89.21 (c = 0.18, MeOH). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.19 (s, 1H), 7.98 (s, 1H), 7.60-7.55 (m, 3H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.41-7.32 (m, 14H), 7.27 (s, 1H),

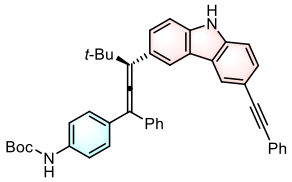
2.18 (s, 3H), 1.28 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.36, 168.36, 139.47, 138.85, 137.69, 136.50, 133.90, 131.49, 130.31, 129.49, 128.92, 128.79, 128.37, 128.35, 128.19, 127.82, 127.18, 126.84, 124.10, 123.89, 123.37, 122.60, 120.92, 119.90, 118.91, 113.95, 110.71, 110.20, 108.64, 99.75, 90.75, 87.63, 36.10, 30.95, 29.89, 24.61. **HRMS** (ESI): *m/z* calcd. for $C_{41}H_{34}N_2O$ $[M+H]^+$: 571.2744; found: 571.2733. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 85/15, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 12.7 min, t_{minor} = 8.3 min.

(*R*)-N-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl)-4-methylbenzenesulfonamide (**3v**)



white foam, 18 h, 65% yield, 70% *ee*, $[a]_D^{20}$ = -49.78 (c = 0.12, MeOH)**. ^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.19 (s, 1H), 7.98 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.64 – 7.56 (m, 3H), 7.42 – 7.33 (m, 10H), 7.31 – 7.28 (m, 3H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.88 (s, 1H), 2.36 (s, 3H), 1.29 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.32, 143.94, 139.44, 138.84, 137.45, 136.19, 135.05, 134.96, 131.47, 129.69, 129.56, 128.94, 128.74, 128.40, 128.37, 128.21, 128.11, 127.86, 127.28, 126.94, 124.05, 123.83, 123.33, 122.61, 121.60, 120.89, 119.07, 114.02, 110.75, 110.22, 108.40, 90.69, 87.72, 36.11, 29.86, 21.53. **HRMS** (ESI): *m/z* calcd. for $C_{46}H_{38}N_2O_2S$ $[M+H]^+$: 683.2727; found: 683.2736. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 17.4 min, t_{minor} = 14.2 min.

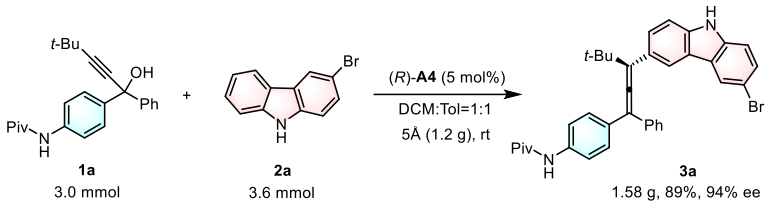
tert-butyl (*R*)-(4-(4,4-dimethyl-1-phenyl-3-(6-(phenylethynyl)-9H-carbazol-3-yl)penta-1,2-dien-1-yl)phenyl) carbamate (**3w**)



light brown foam, 20 h, 90% yield, 80% *ee*, $[a]_D^{20}$ = -124.08 (c = 0.21, MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.12 (s, 1H), 7.97 (s, 1H), 7.57 (d, J = 6.1 Hz, 3H), 7.46 – 7.28 (m, 15H), 6.50 (s, 1H), 1.52 (s, 9H), 1.26 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.3, 152.9, 139.5, 138.8, 137.8, 137.0, 132.6, 131.5, 129.5, 129.1, 128.9, 128.3, 128.3, 128.2, 127.8, 126.8, 124.1, 123.9, 123.4, 122.6, 120.9, 118.8, 118.6, 114.0, 110.7, 110.2, 108.7, 90.8, 87.6, 36.1, 29.9, 28.4. **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{40}N_2O_2$ $[M+H]^+$: 629.3163; found: 629.3176. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak AD-H column (hexane/*i*-PrOH = 80/20, flow rate 1 mL·min^{-1}, λ = 254 nm): t_{major} = 9.9 min, t_{minor} = 5.6 min.

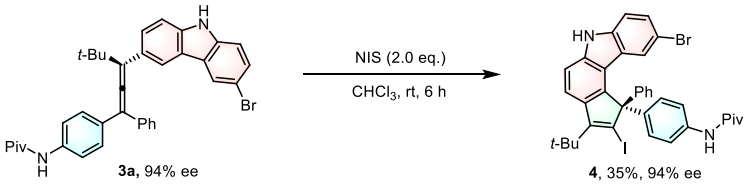
3. The scale-up experiment and transformation of 3a

a. The scale-up experiment of 3a



To a solution of *α*-(4-aminophenyl)propargylic alcohol **1a** (3.0 mmol, 1.0 equiv.), 5Å (1.2 g), and catalyst (*R*)-**A4** (0.15 mmol, 5 mol%) in DCM:Tol (v:v = 1:1, 50 mL) was added **2a** (3.6 mmol, 1.2 equiv.). The mixture was stirred at room temperature until the reaction was completed (monitored by TLC analysis). The crude product was purified directly by flash column chromatography on silica gel (petroleum ether/ ethyl acetate = 15:1~5:1) to give the desired chiral product **3a**.

b. The transformation of 3a to compound 4



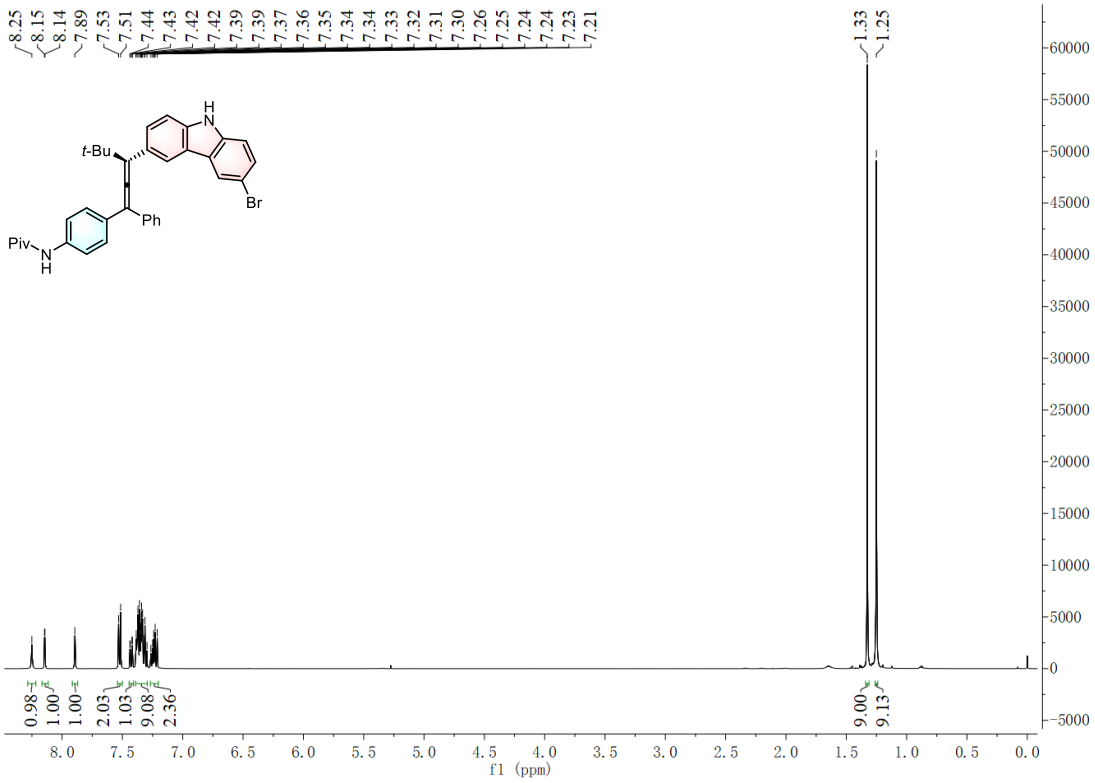
To a solution of (R)-**3a** (0.1 mmol, 1.0 equiv) in $CHCl_3$ (1 mL) was slowly added the $CHCl_3$ (1.5 mL) solution of NIS (0.2 mmol, 2.0 equiv) using a syringe. The mixture was stirred at room temperature until the reaction was completed (monitored by TLC analysis). The crude product was purified directly by flash column chromatography on silica gel (petroleum ether/ ethyl acetate = 10:1) to give the desired chiral product **4**.

(*S*)-N-(4-(9-bromo-3-(tert-butyl)-2-iodo-1-phenyl-1,6-dihydrocyclopenta[c]carbazol-1-yl)phenyl)pivalamide (**4**)

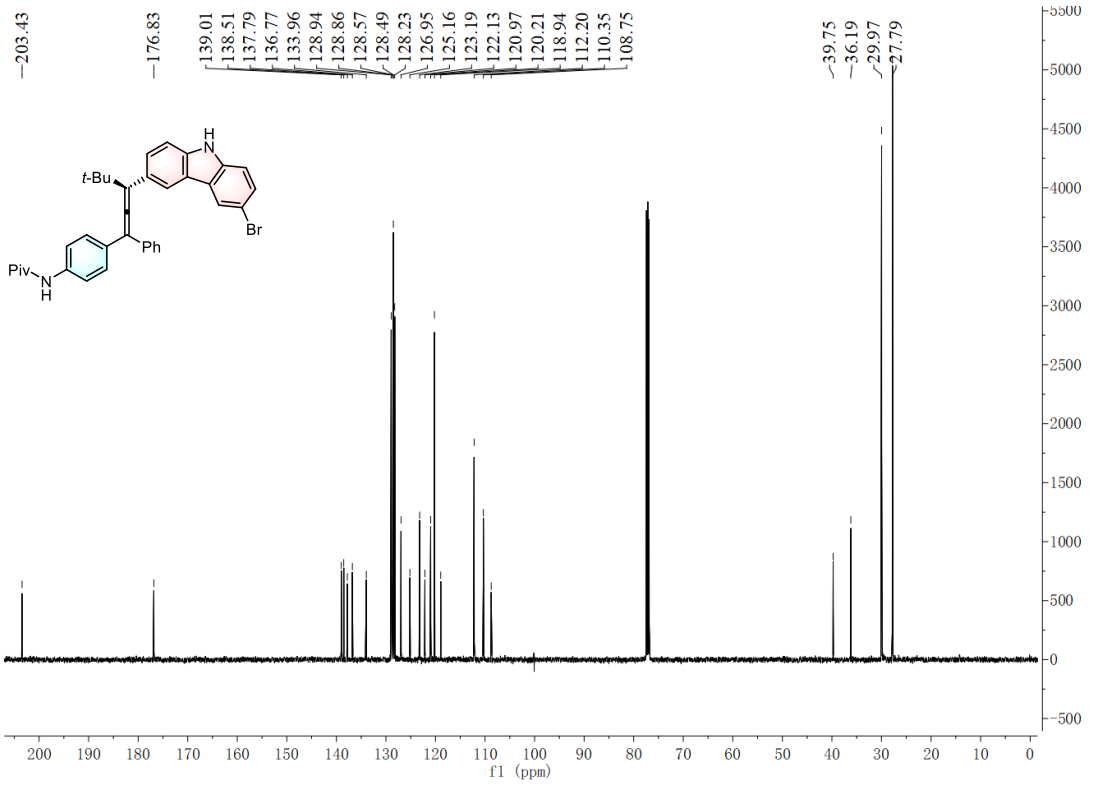
White solid, 6 h, 35% yield, 94% *ee*, $[a]_D^{20}$ = -209.35 (c = 0.12, MeOH). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.39 (s, 1H), 8.23 (s, 1H), 8.02 (s, 1H), 7.47 (d, J = 8.7 Hz, 2H), 7.26 (s, 1H), 7.22 (t, J = 6.5 Hz, 1H), 7.17 – 7.07 (m, 5H), 6.88 (d, J = 8.6 Hz, 2H), 6.42 (s, 1H), 6.35 (d, J = 8.6 Hz, 1H), 1.78 (s, 9H), 1.26 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.0, 154.7, 150.8, 142.4, 138.4, 138.2, 137.8, 137.5, 136.9, 130.5, 129.0, 128.4, 128.3, 128.2, 128.2, 126.9, 123.9, 123.0, 119.4, 118.2, 115.2, 114.2, 110.5, 108.5, 106.6, 100.0, 77.2, 70.7, 39.8, 35.9, 31.4, 27.7. **HRMS** (ESI): *m/z* calcd. for $C_{36}H_{34}BrIN_2O$ $[M+H]^+$: 717.0972; found: 717.0979. **HPLC analysis:** The enantiomeric excess was determined by HPLC with Chiralpak IA column (hexane/*i*-PrOH = 80/20, flow rate 0.8 mL·min^{-1}, λ = 254 nm): t_{major} = 5.2 min, t_{minor} = 6.2 min.

4. Copies of NMR Spectra

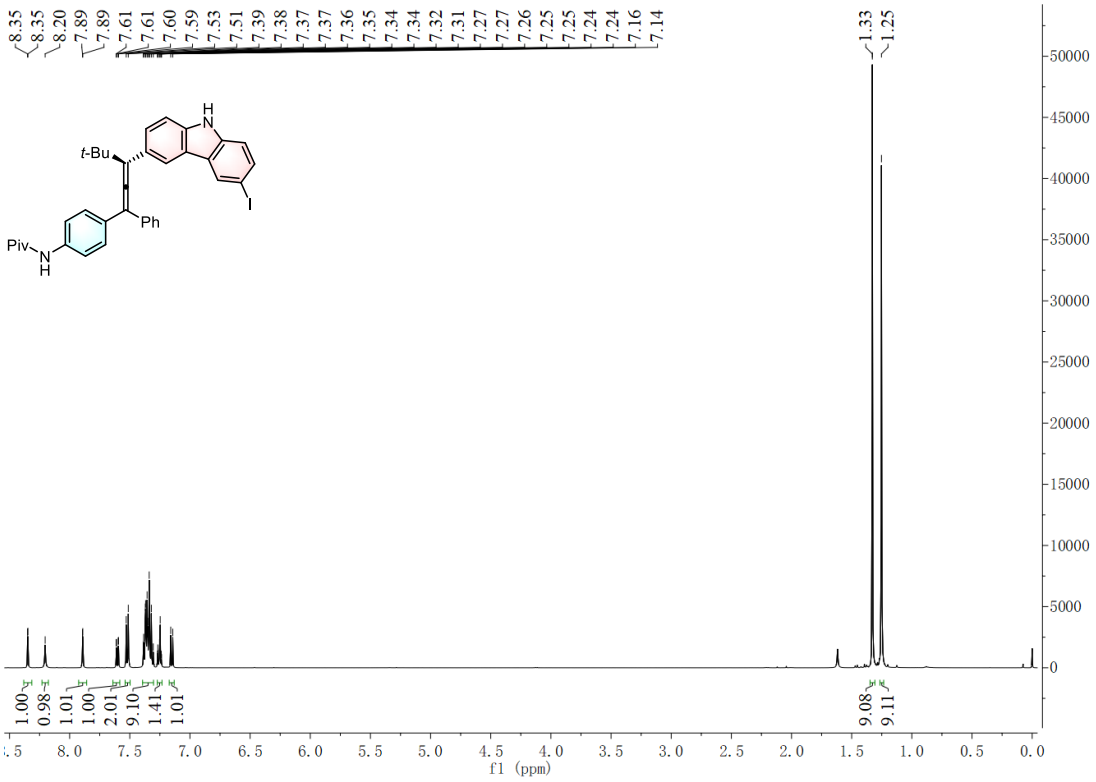
^{1}H NMR of compound 3a (in $CDCl_3$)



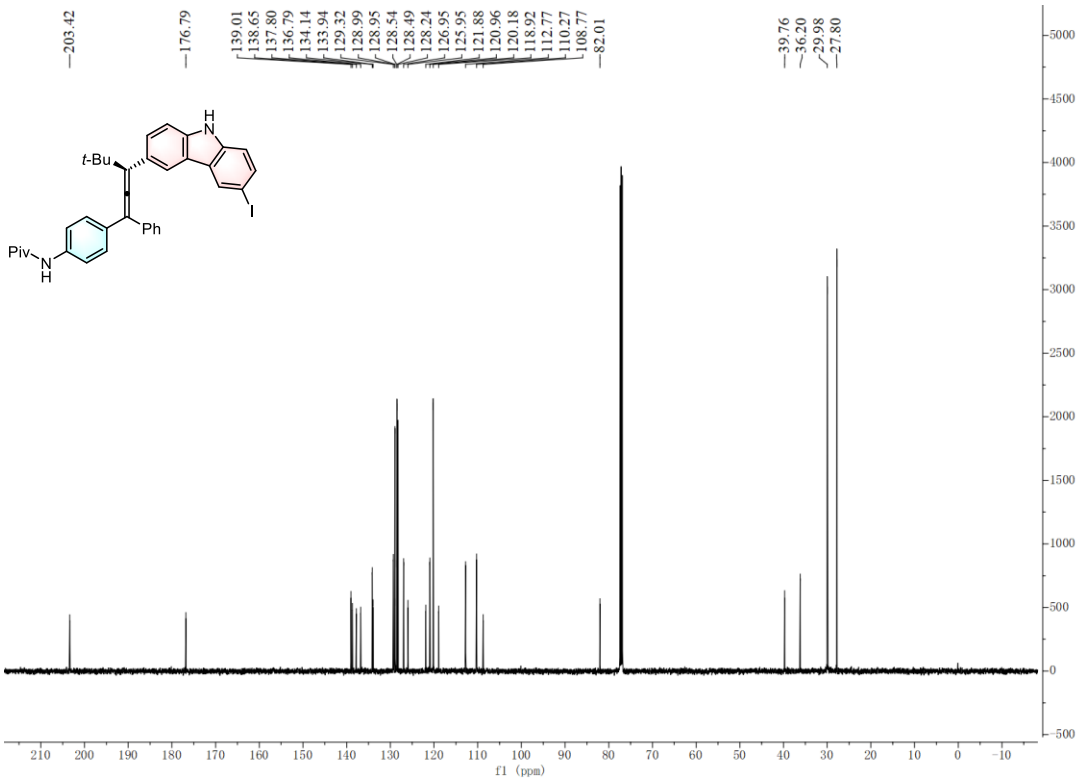
^{13}C NMR of compound 3a (in $CDCl_3$)



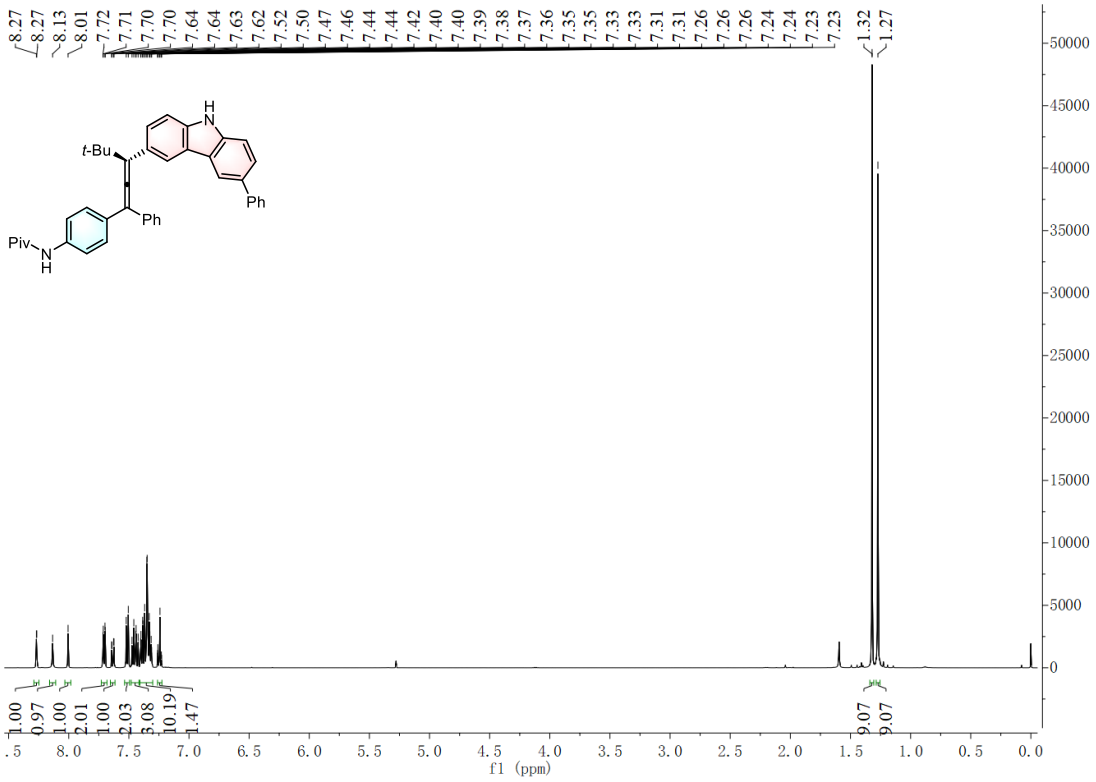
^{1}H NMR of compound 3b (in $CDCl_3$)



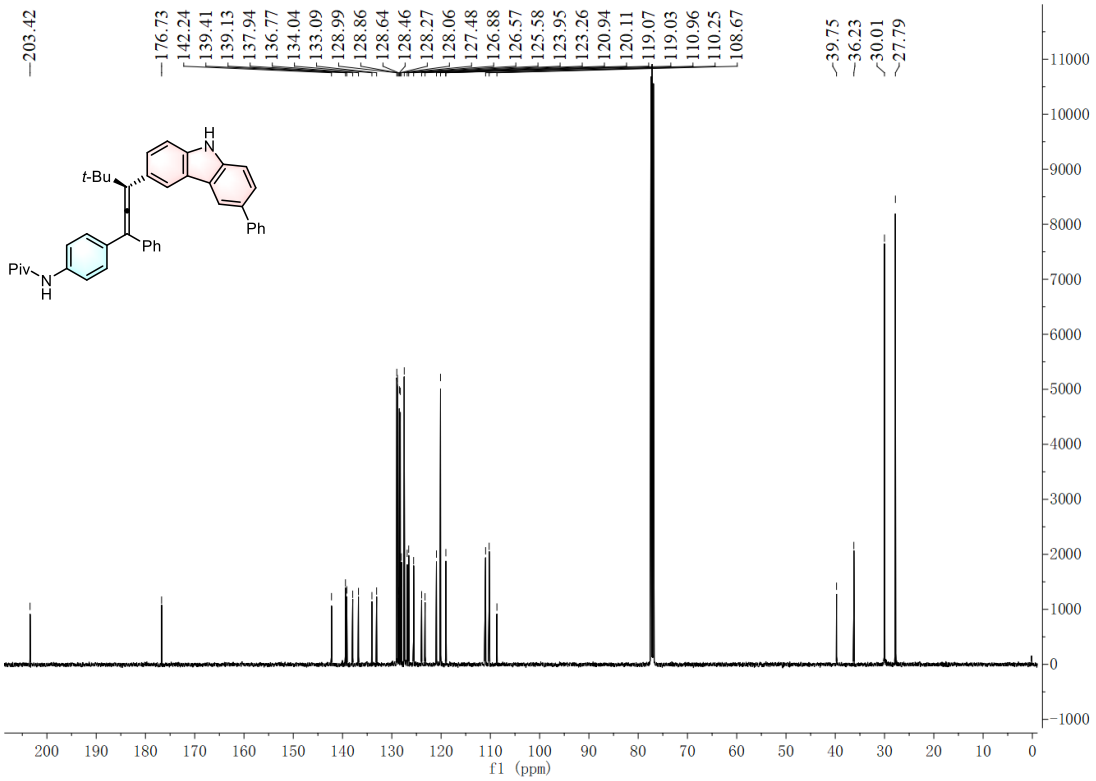
^{13}C NMR of compound 3b (in $CDCl_3$)



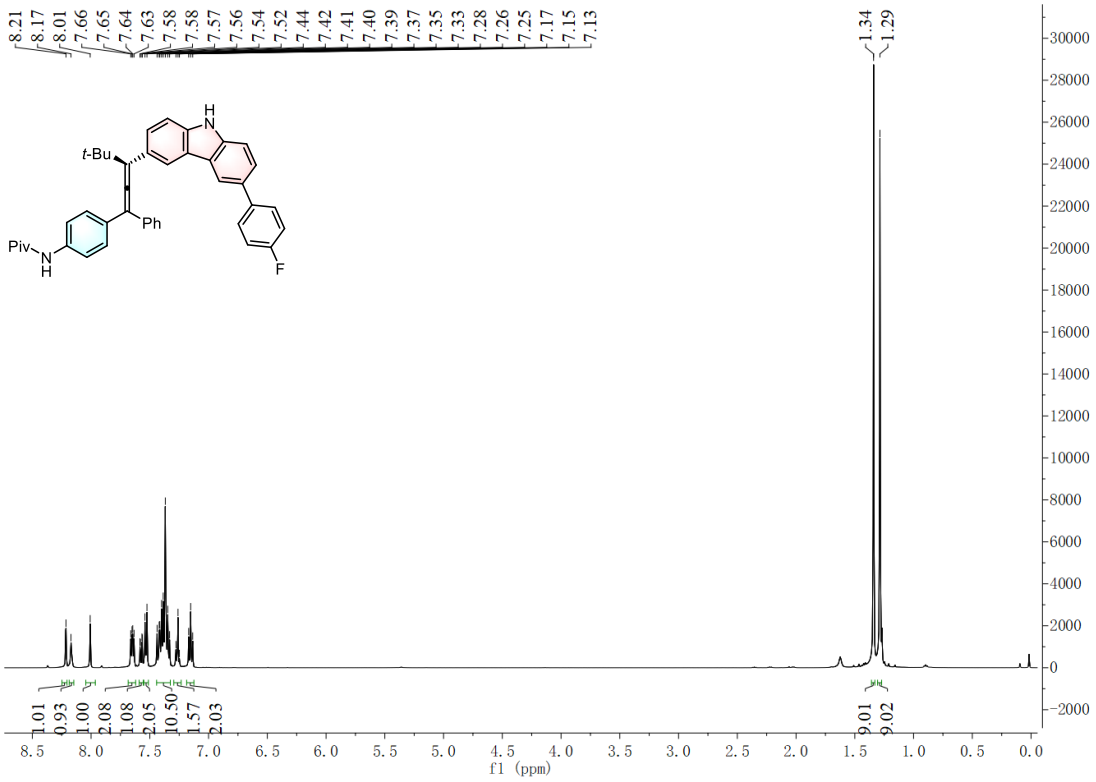
^{1}H NMR of compound 3c (in $CDCl_3$)



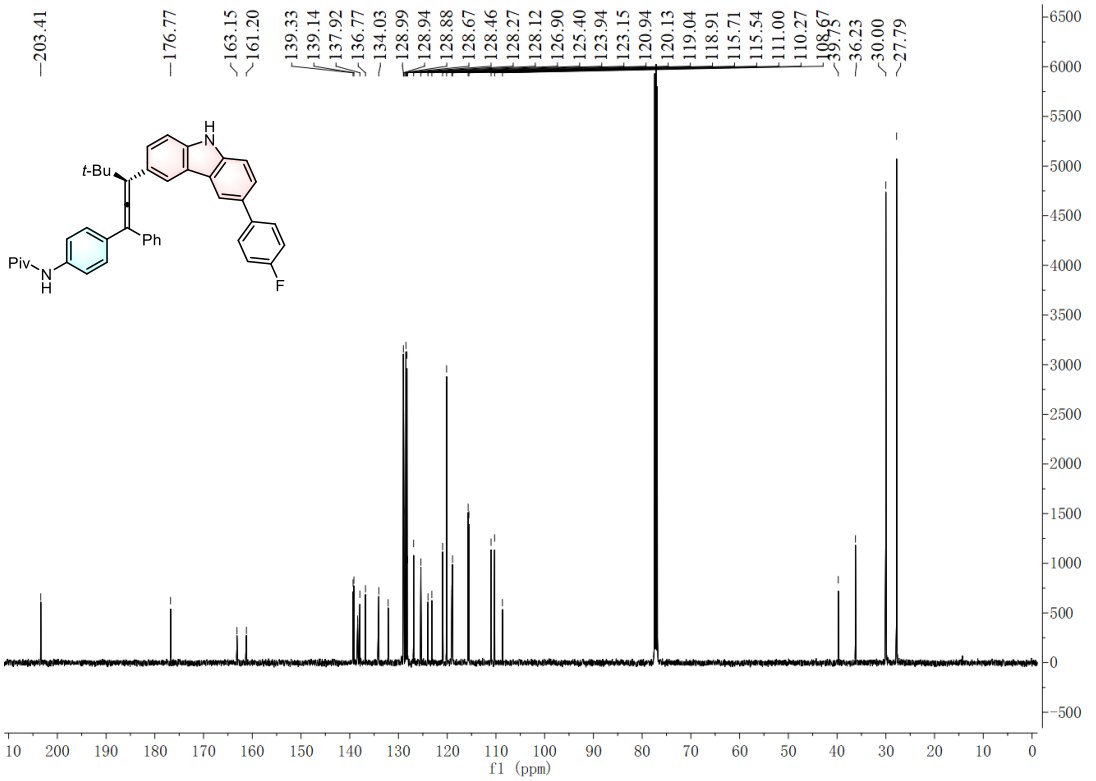
^{13}C NMR of compound 3c (in $CDCl_3$)



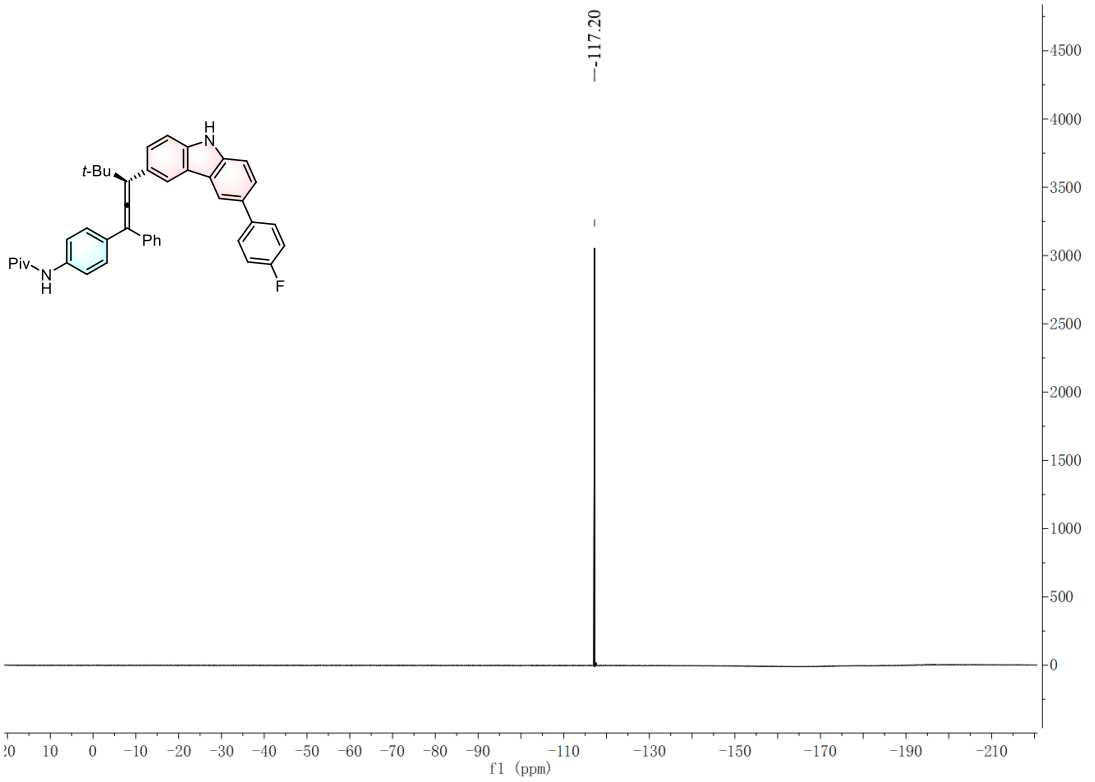
^{1}H NMR of compound 3d (in $CDCl_3$)



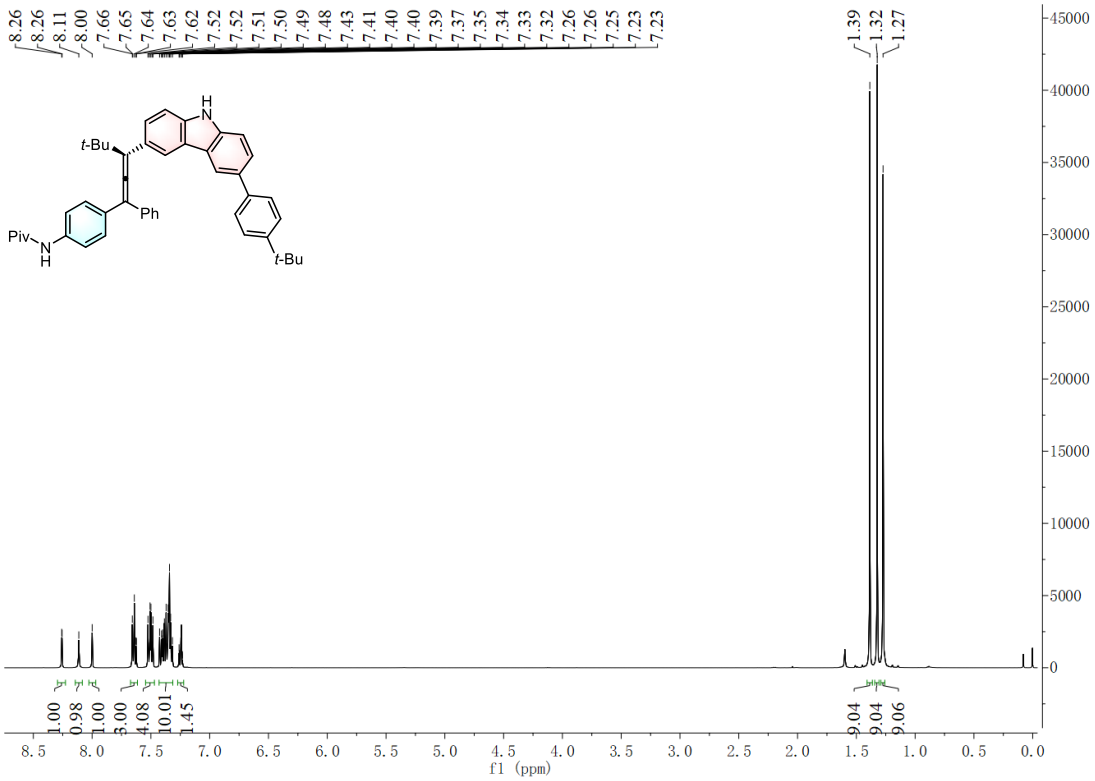
^{13}C NMR of compound 3d (in $CDCl_3$)



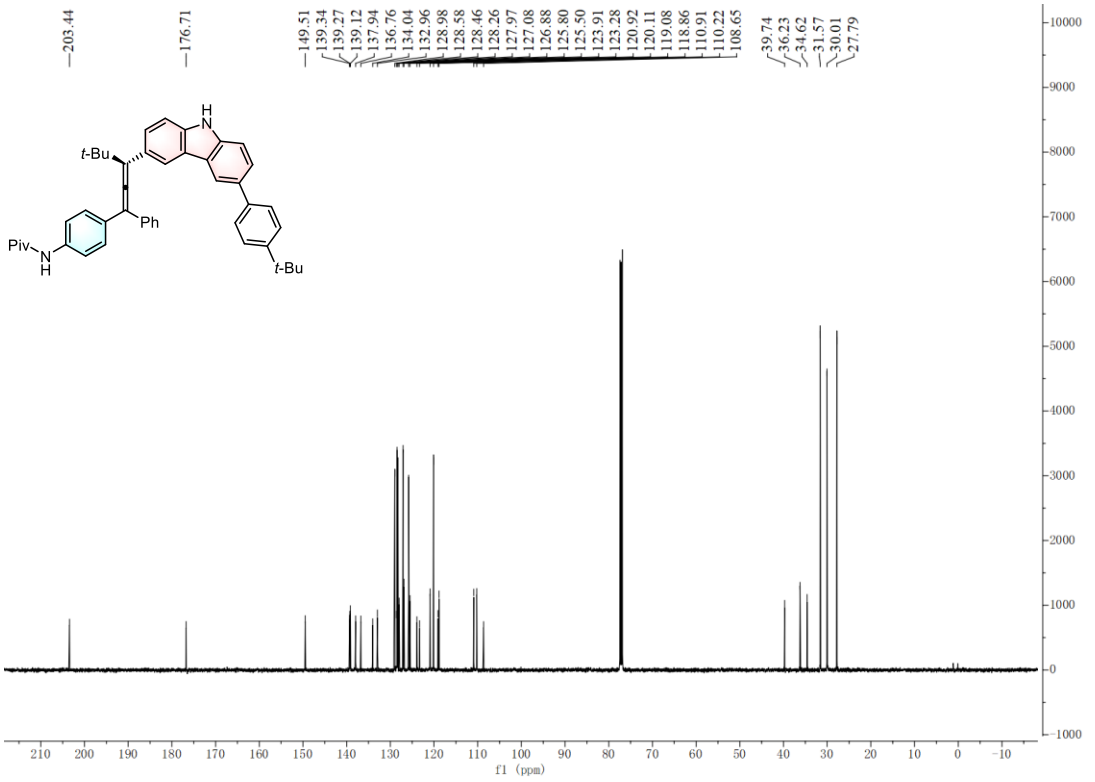
^{19}F NMR of compound 3d (in $CDCl_3$)



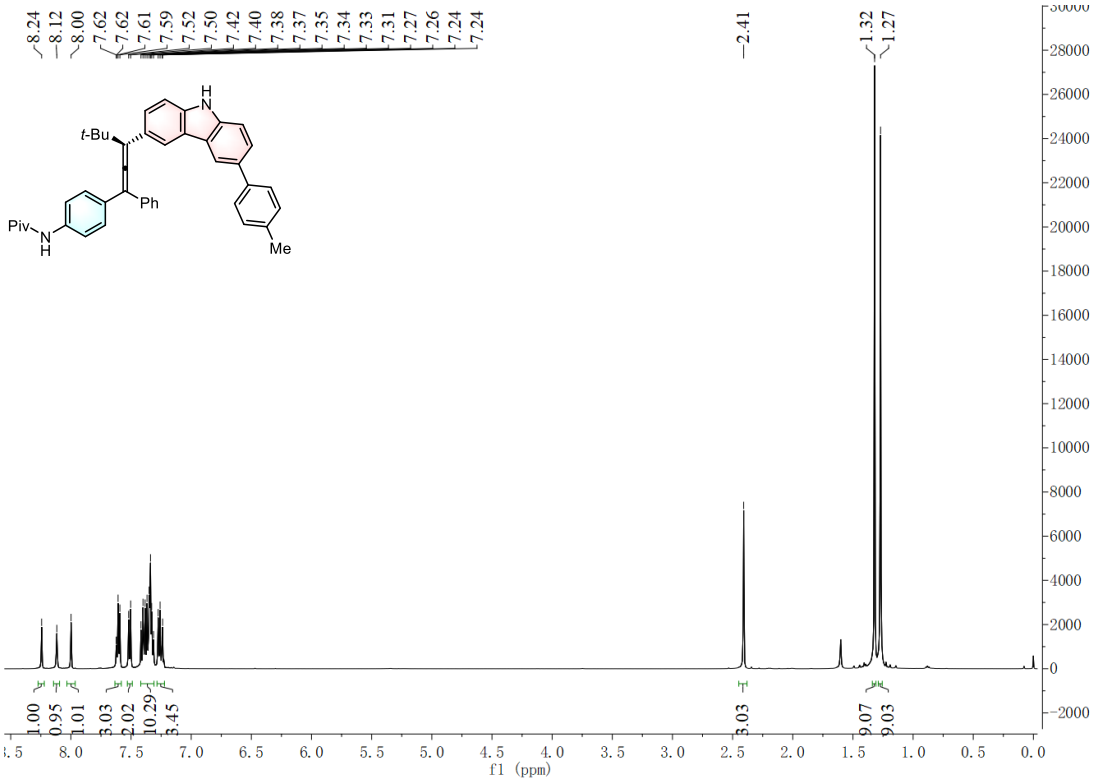
^{1}H NMR of compound 3e (in $CDCl_3$)



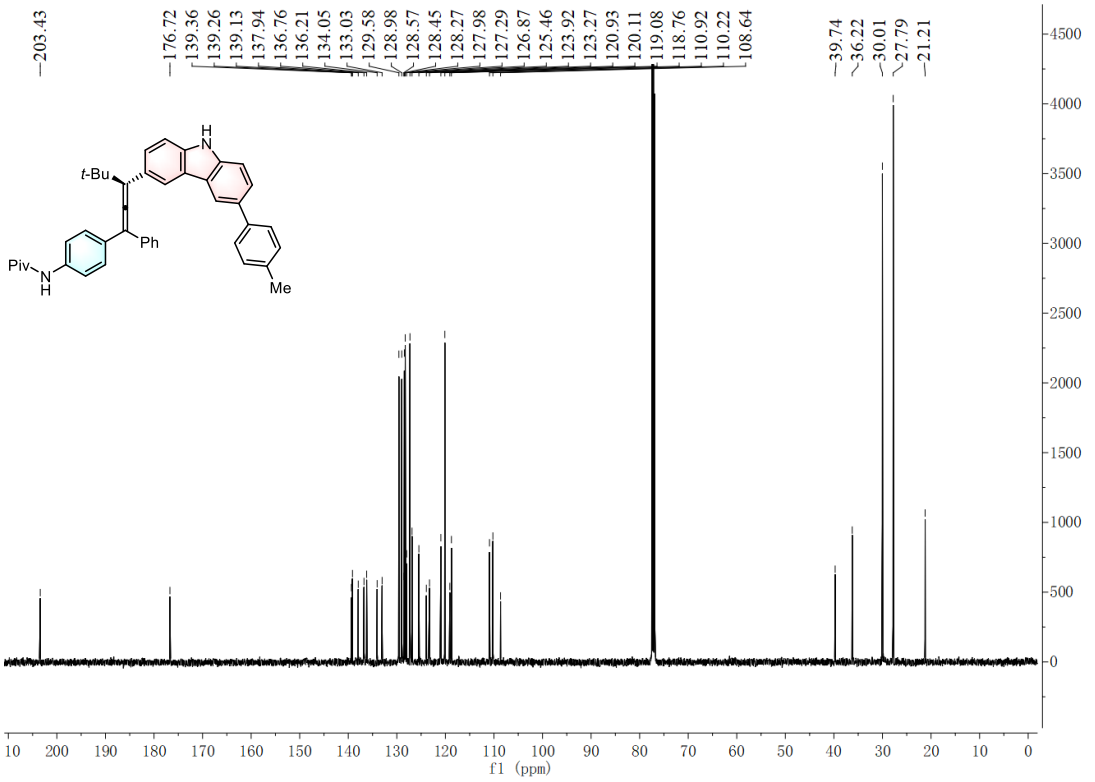
^{13}C NMR of compound 3e (in $CDCl_3$)



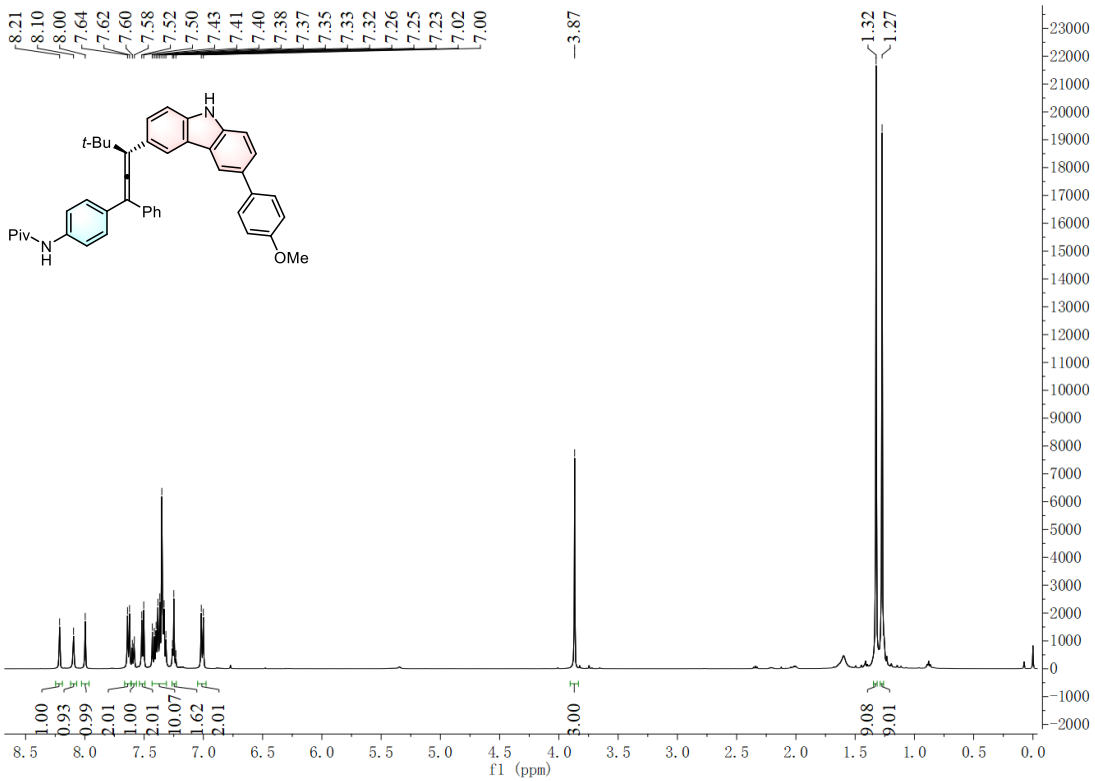
^{1}H NMR of compound 3f (in $CDCl_3$)



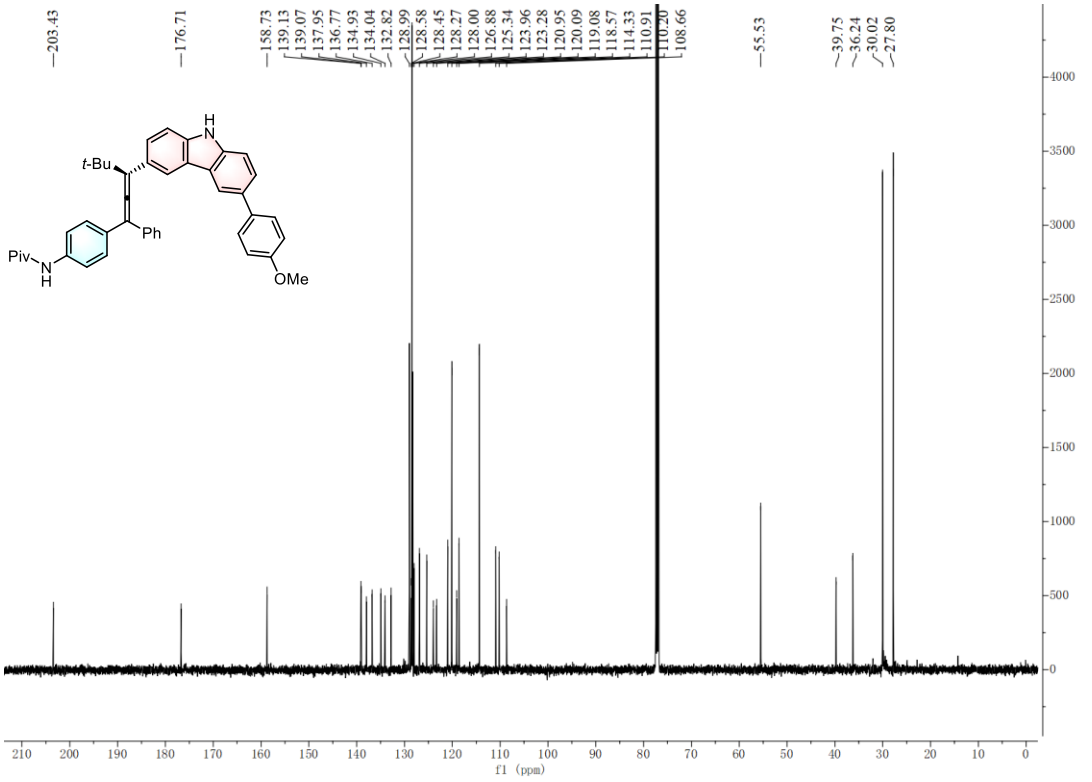
^{13}C NMR of compound 3f (in $CDCl_3$)



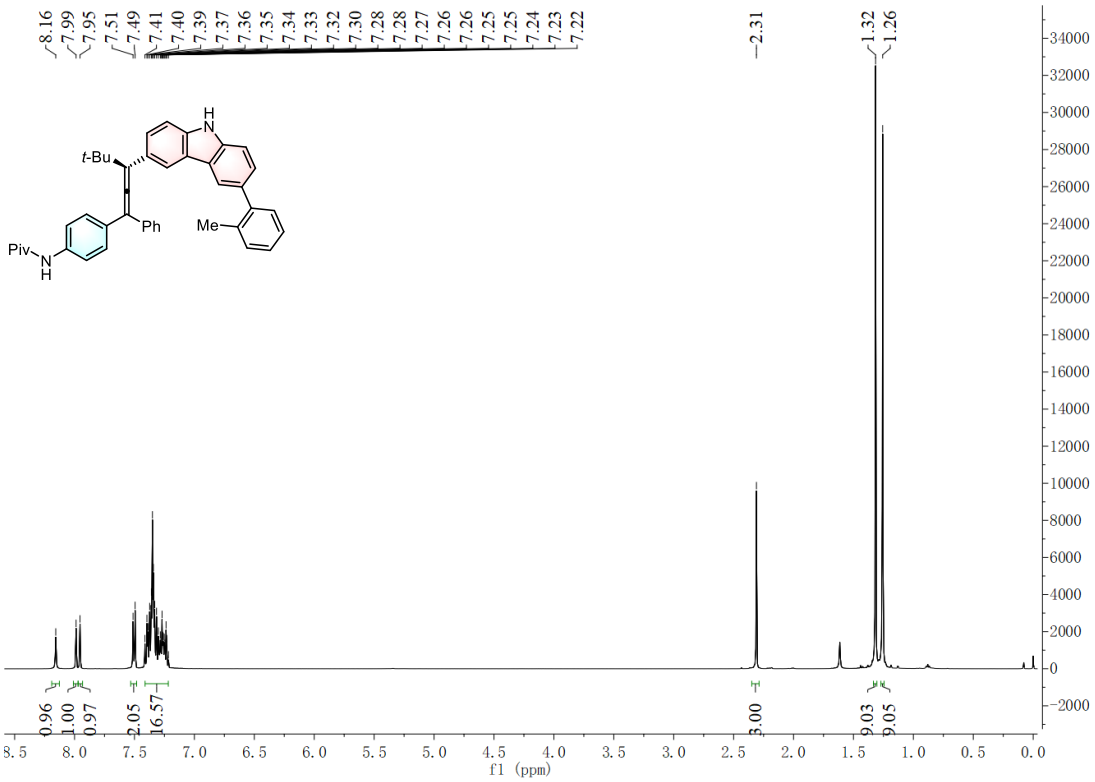
^{1}H NMR of compound 3g (in $CDCl_3$)



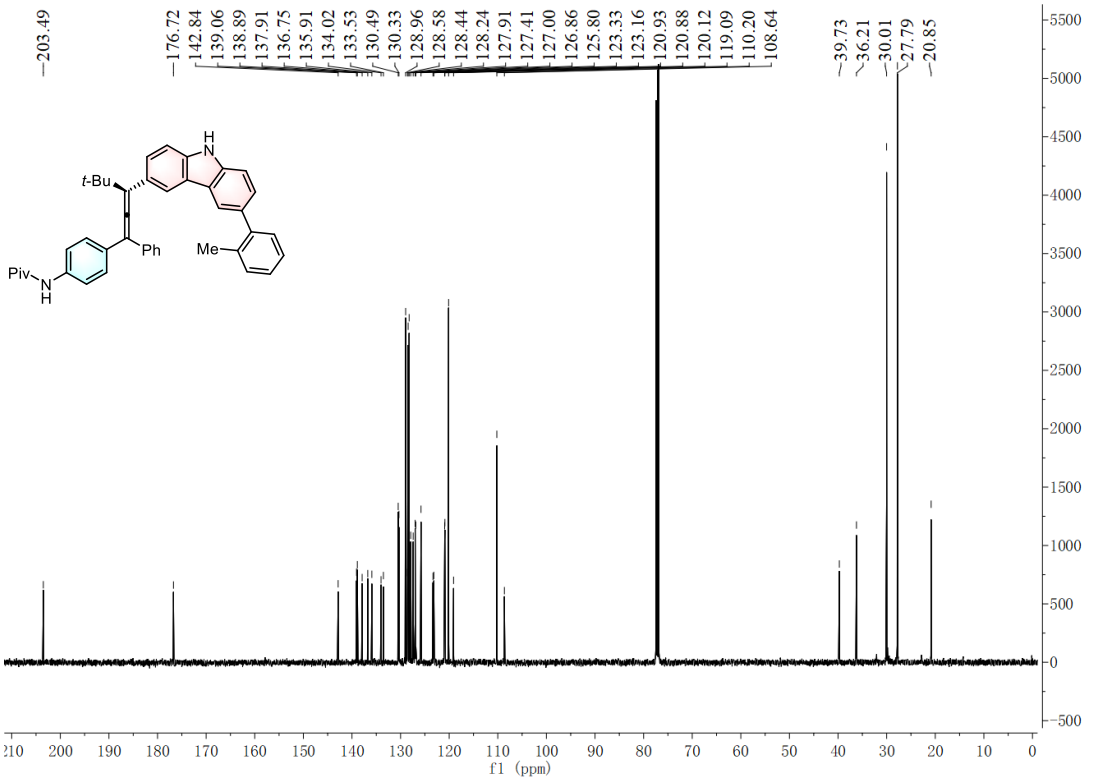
^{13}C NMR of compound 3g (in $CDCl_3$)



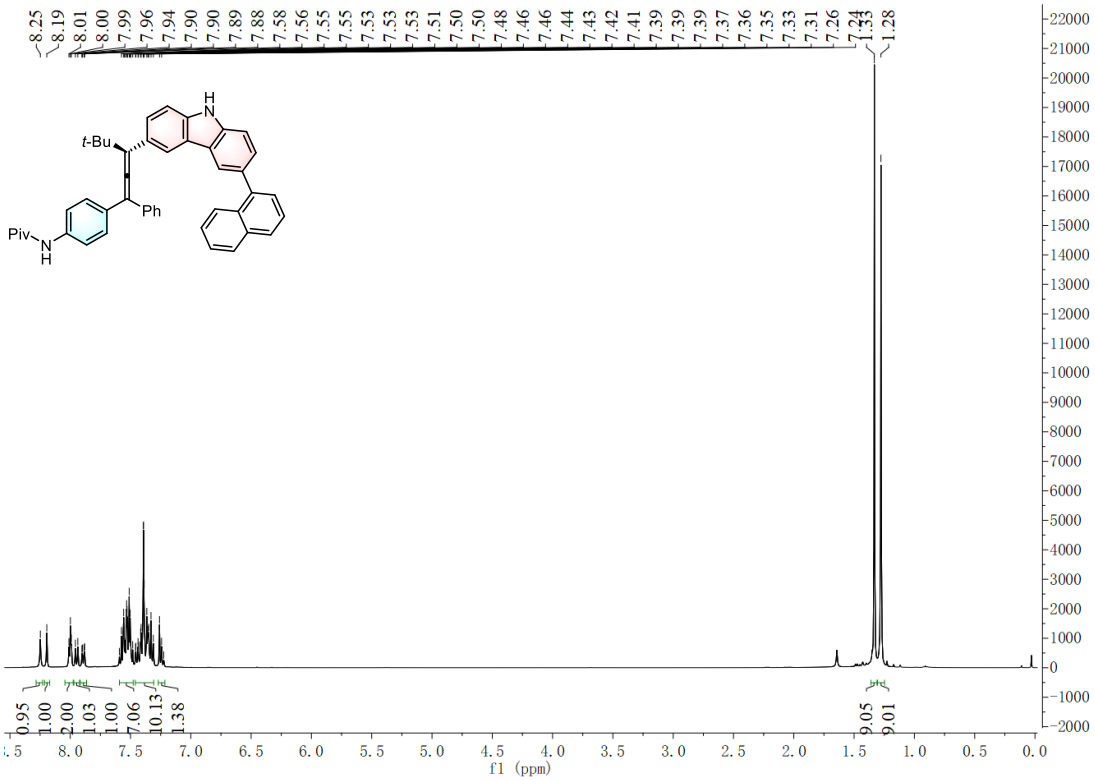
^{1}H NMR of compound 3h (in $CDCl_3$)



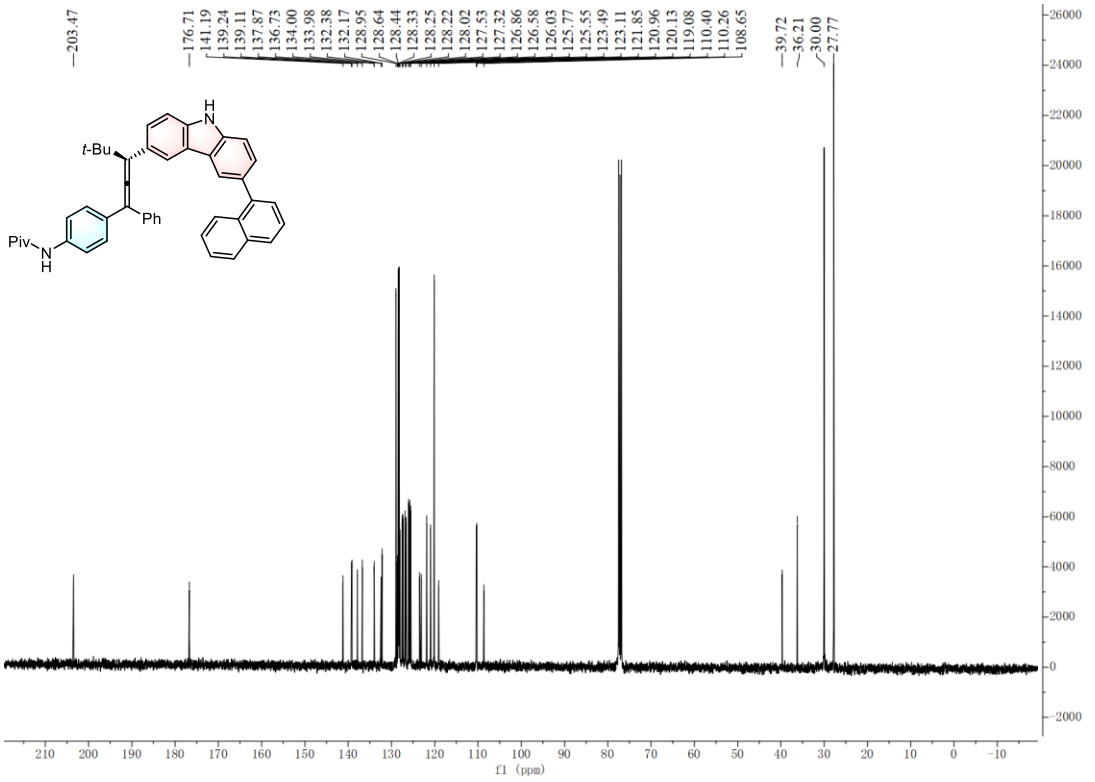
^{13}C NMR of compound 3h (in $CDCl_3$)



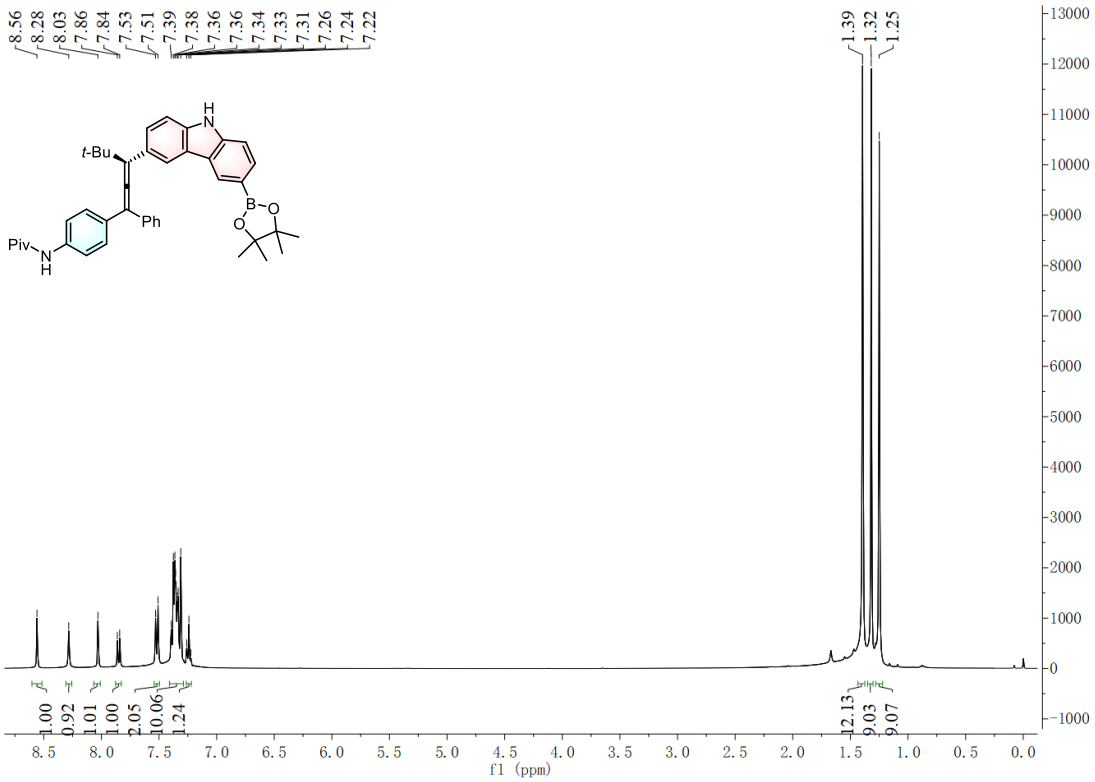
^{1}H NMR of compound 3i (in $CDCl_3$)



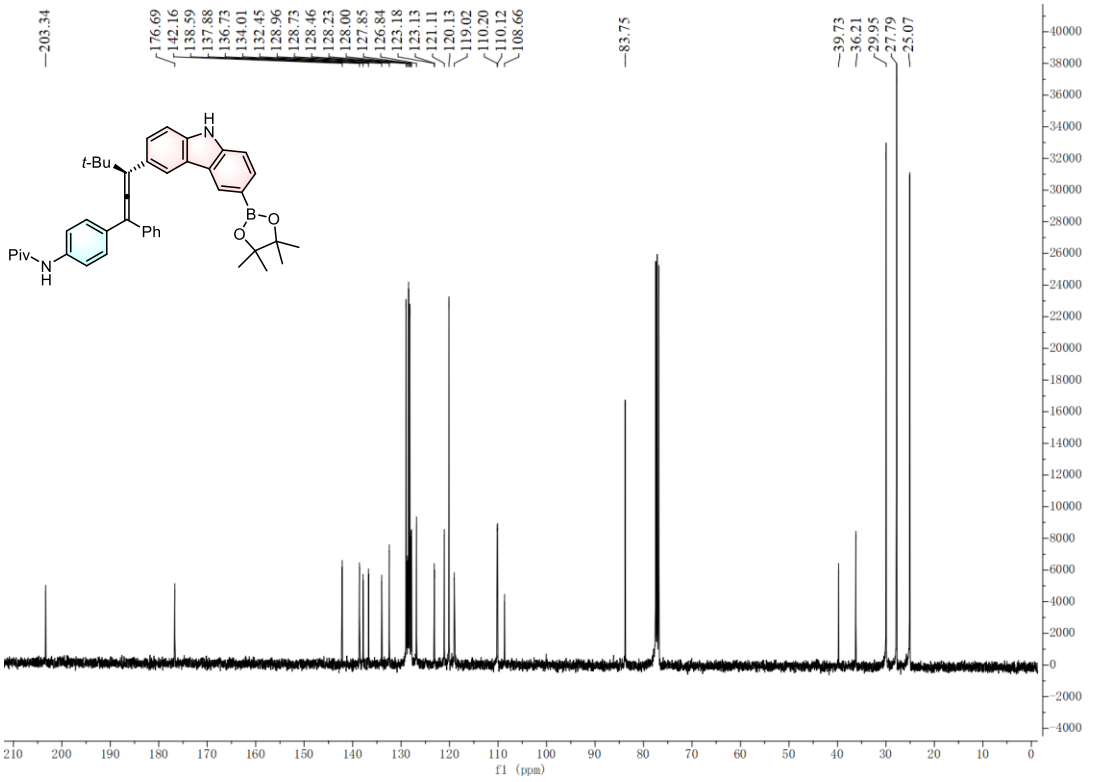
^{13}C NMR of compound 3i (in $CDCl_3$)



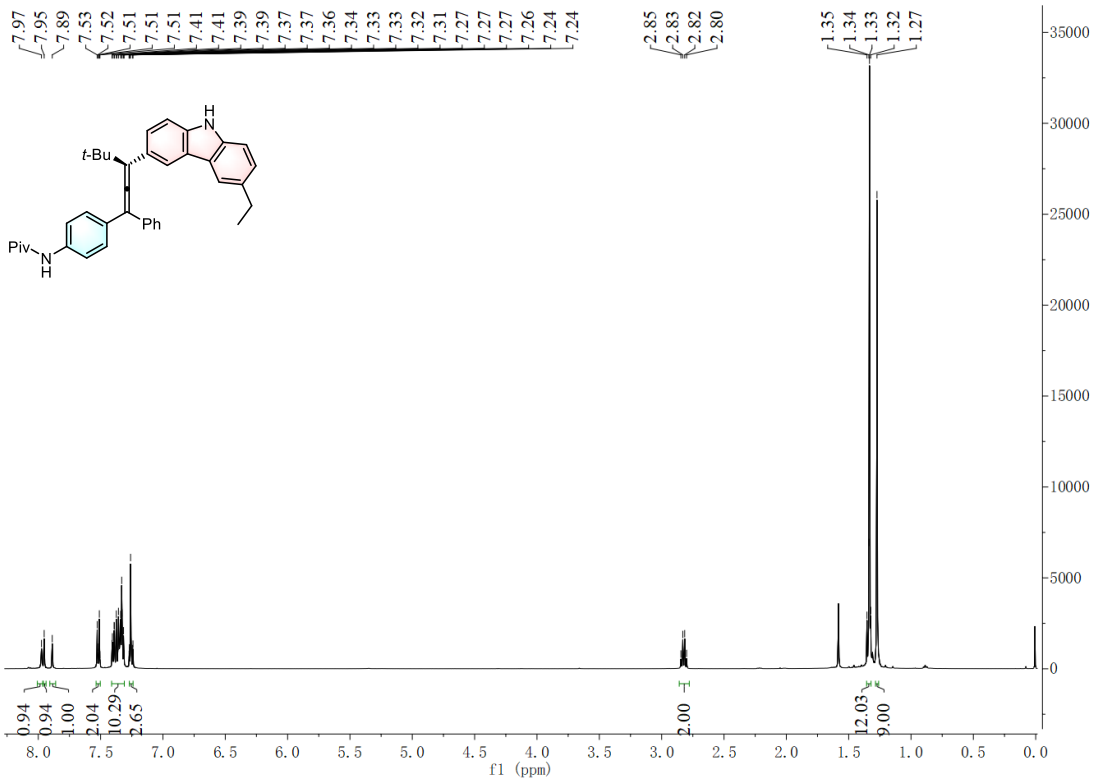
^{1}H NMR of compound 3j (in $CDCl_3$)



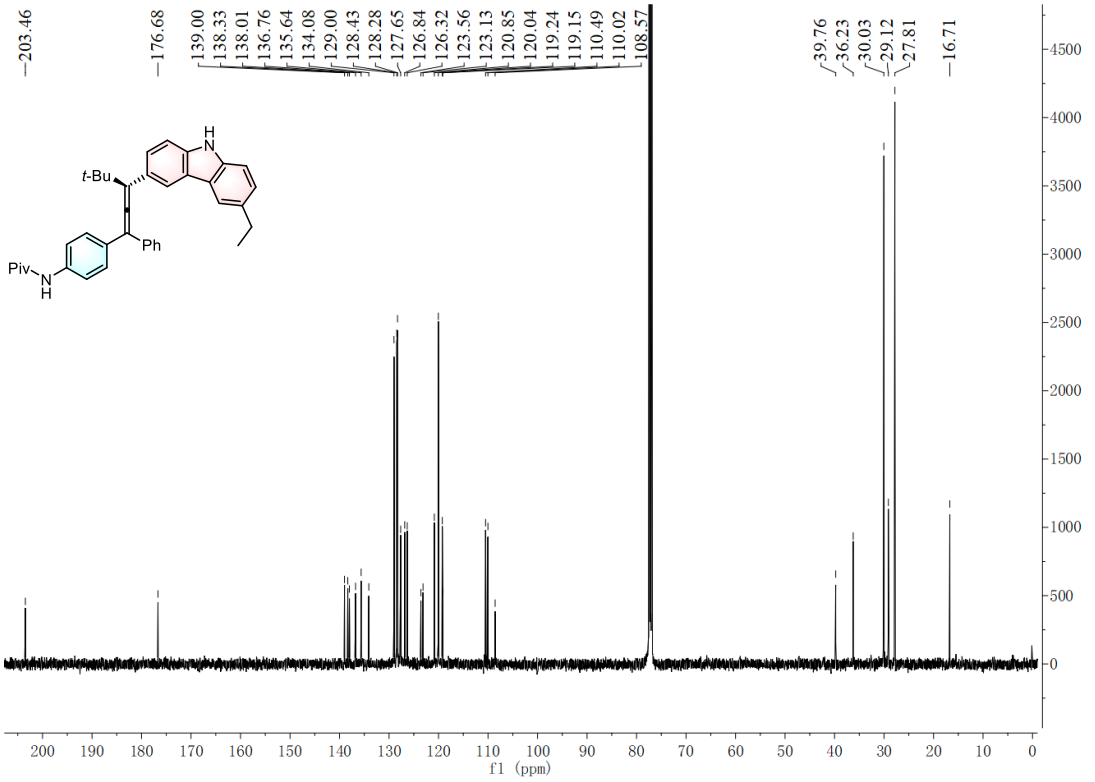
^{13}C NMR of compound 3j (in $CDCl_3$)



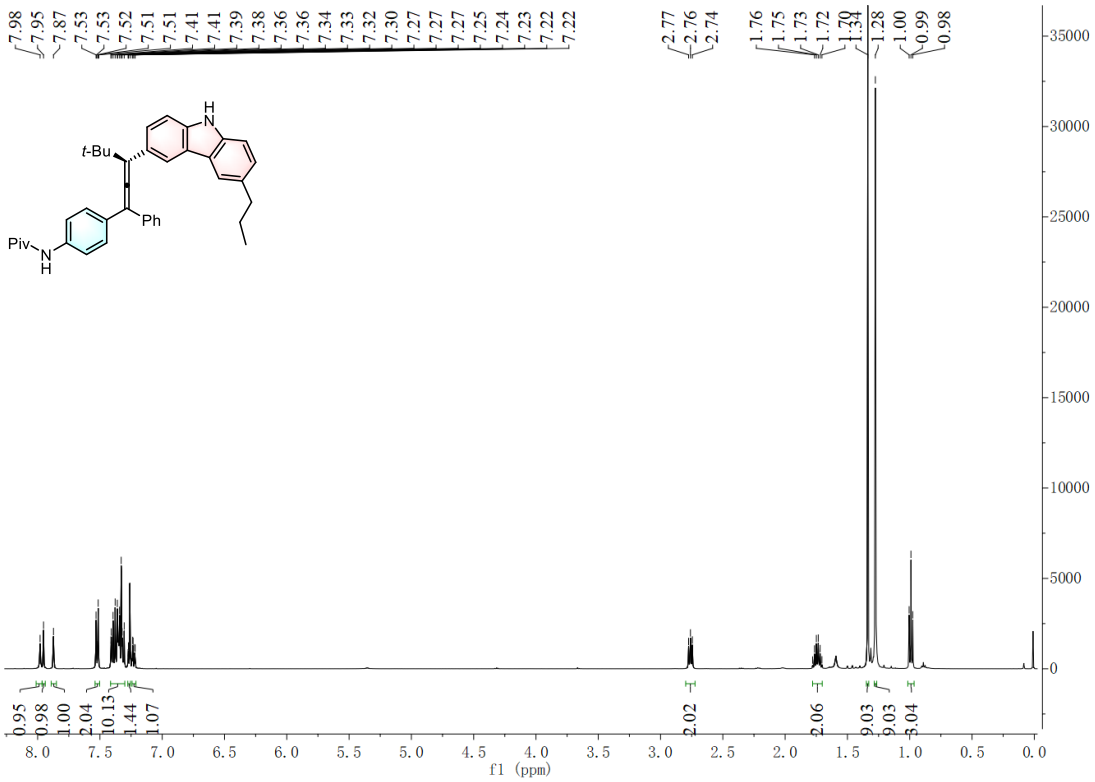
^{1}H NMR of compound 3k (in $CDCl_3$)



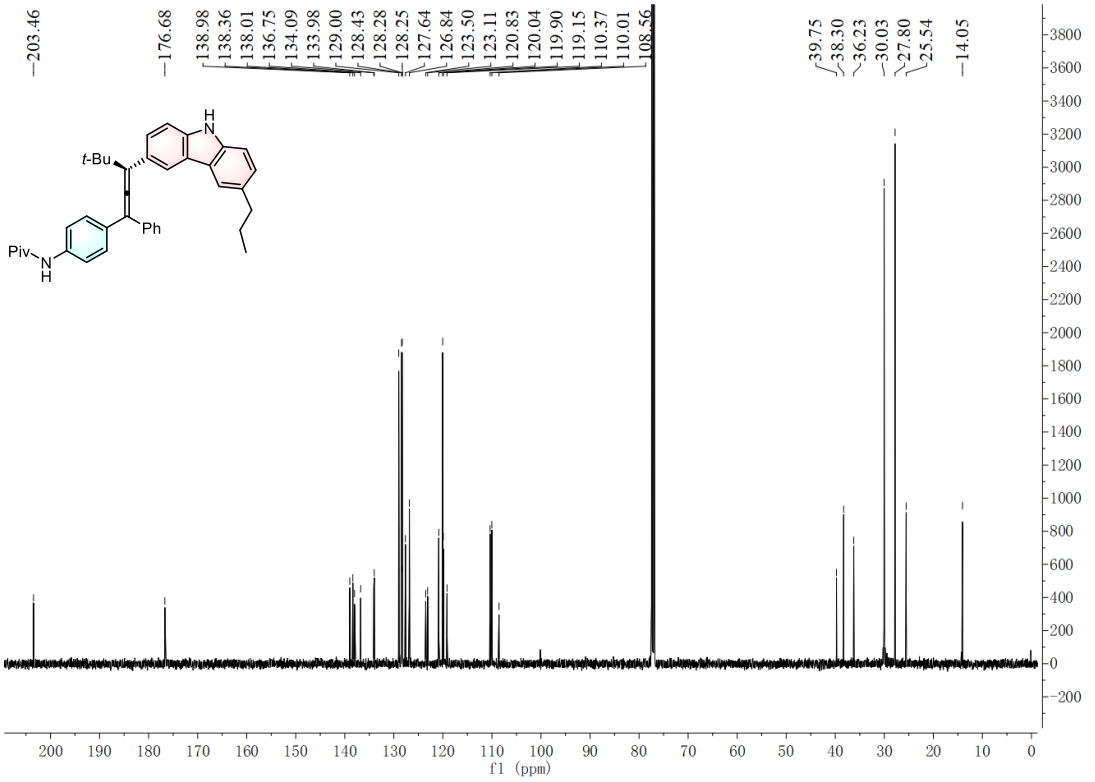
^{13}C NMR of compound 3k (in $CDCl_3$)



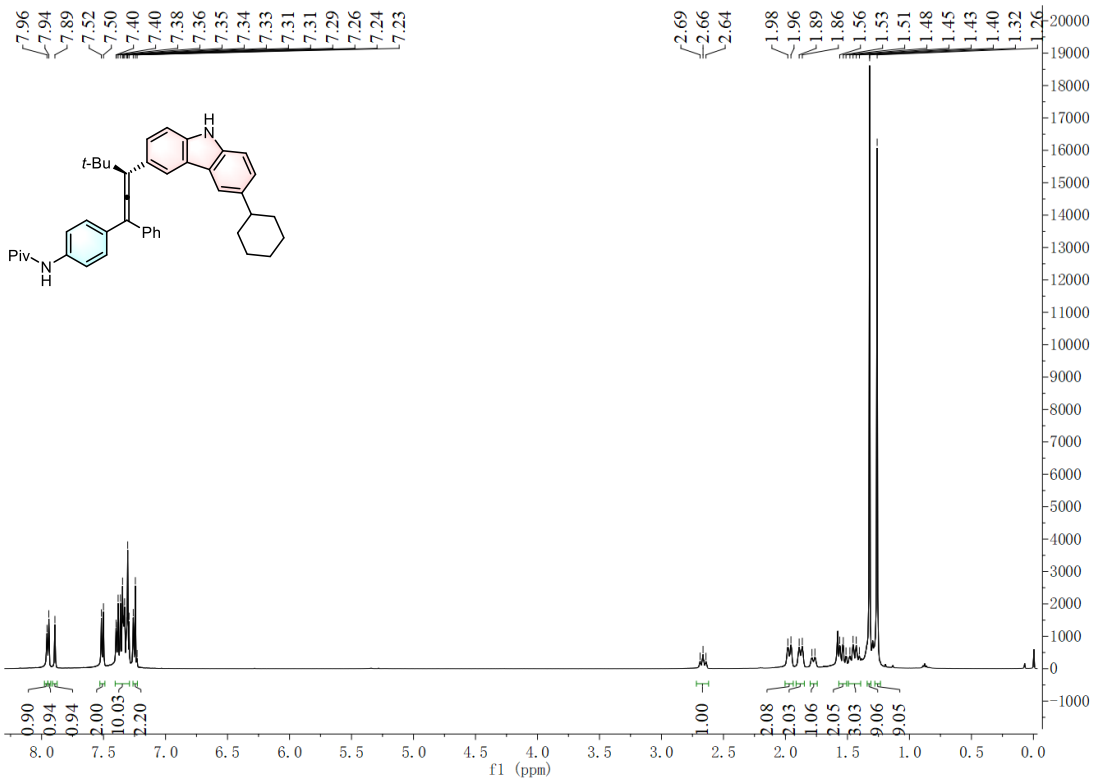
^{1}H NMR of compound 3l (in $CDCl_3$)



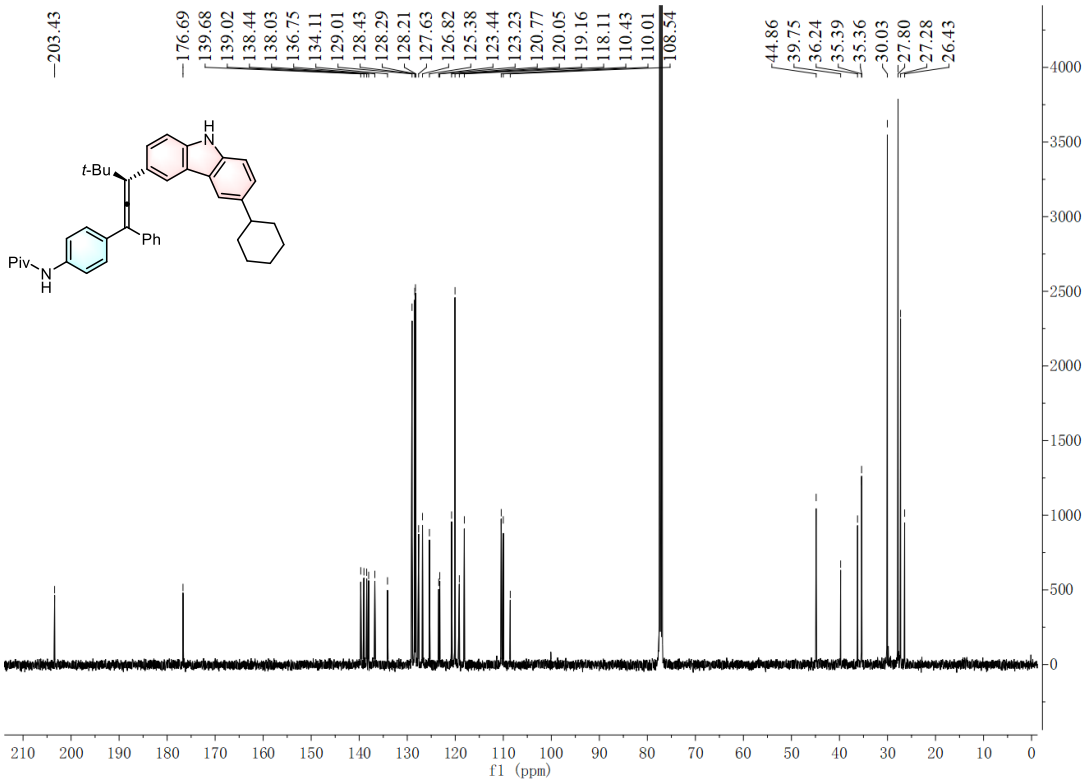
^{13}C NMR of compound 3l (in $CDCl_3$)



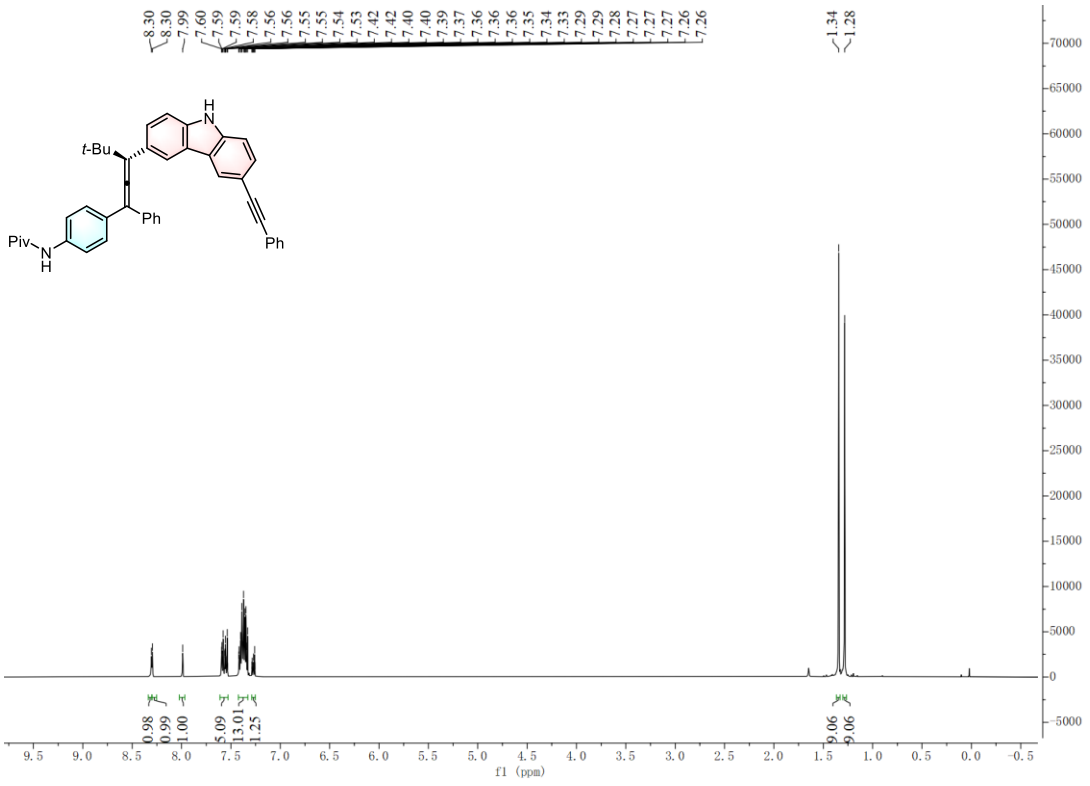
^{1}H NMR of compound 3m (in $CDCl_3$)



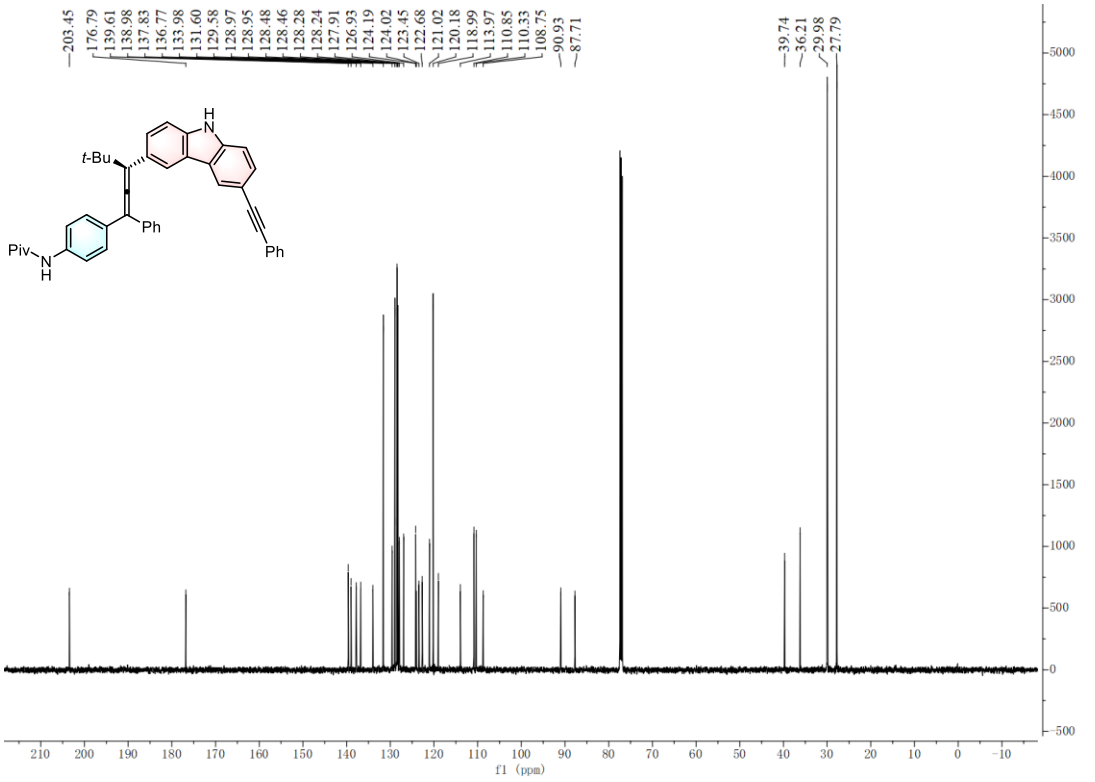
^{13}C NMR of compound 3m (in $CDCl_3$)



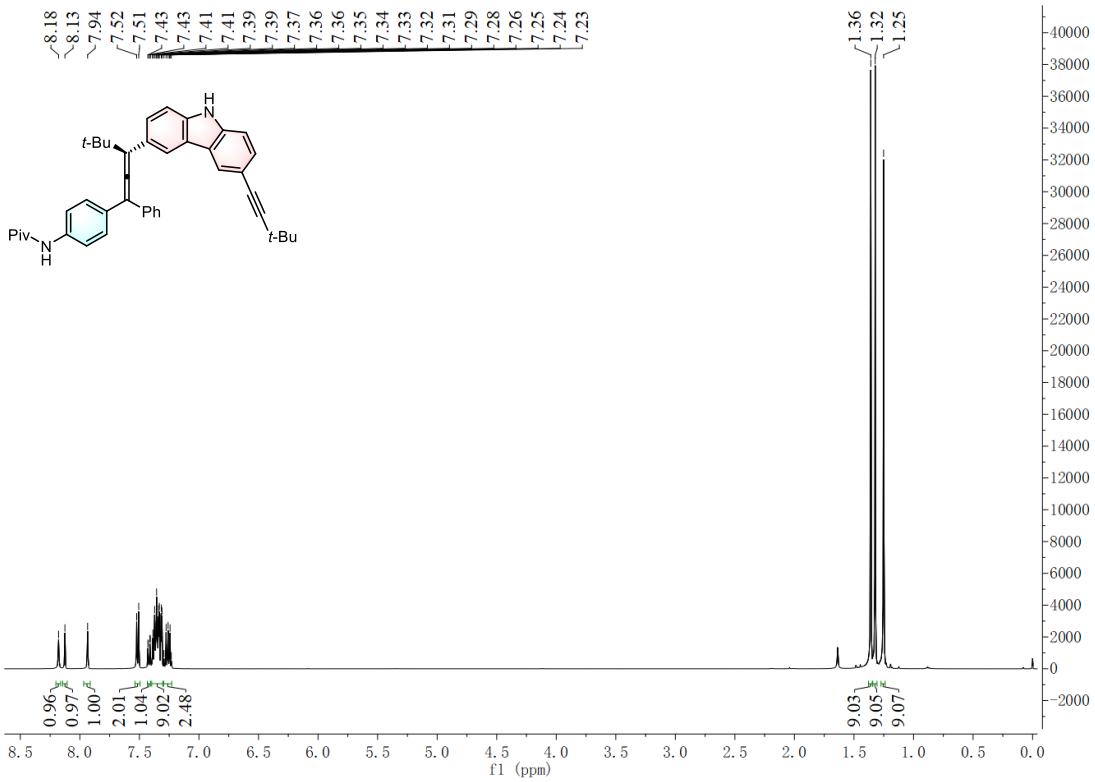
^{1}H NMR of compound 3n (in $CDCl_3$)



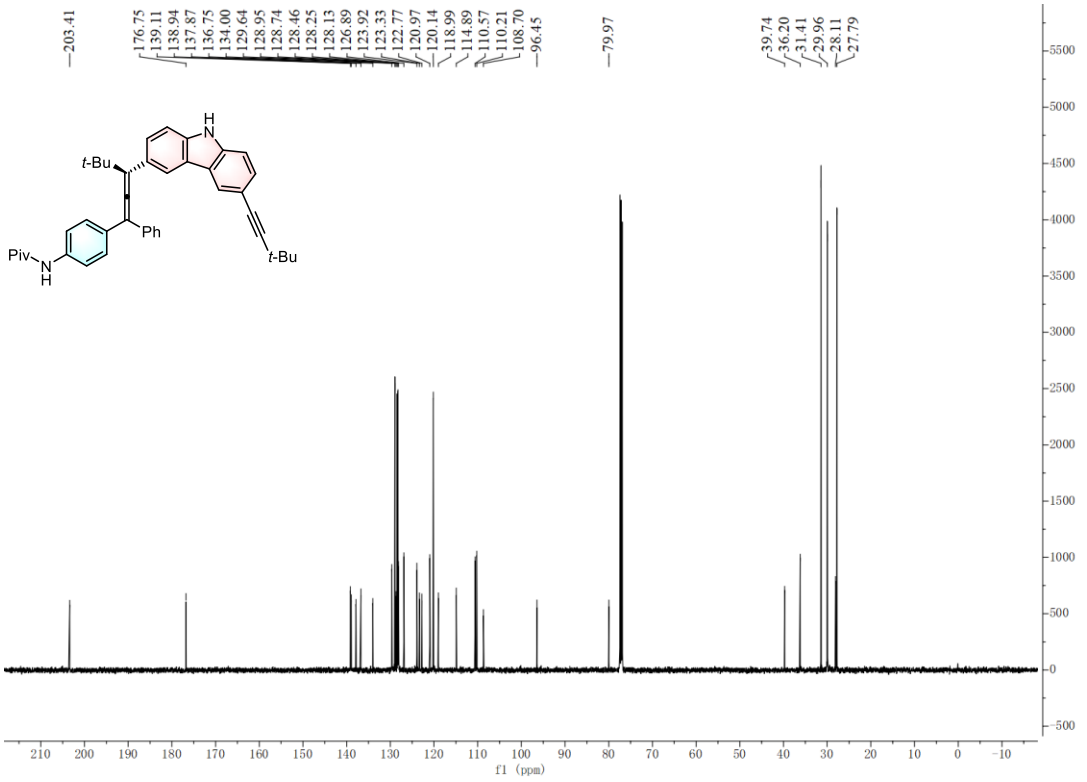
^{13}C NMR of compound 3n (in $CDCl_3$)



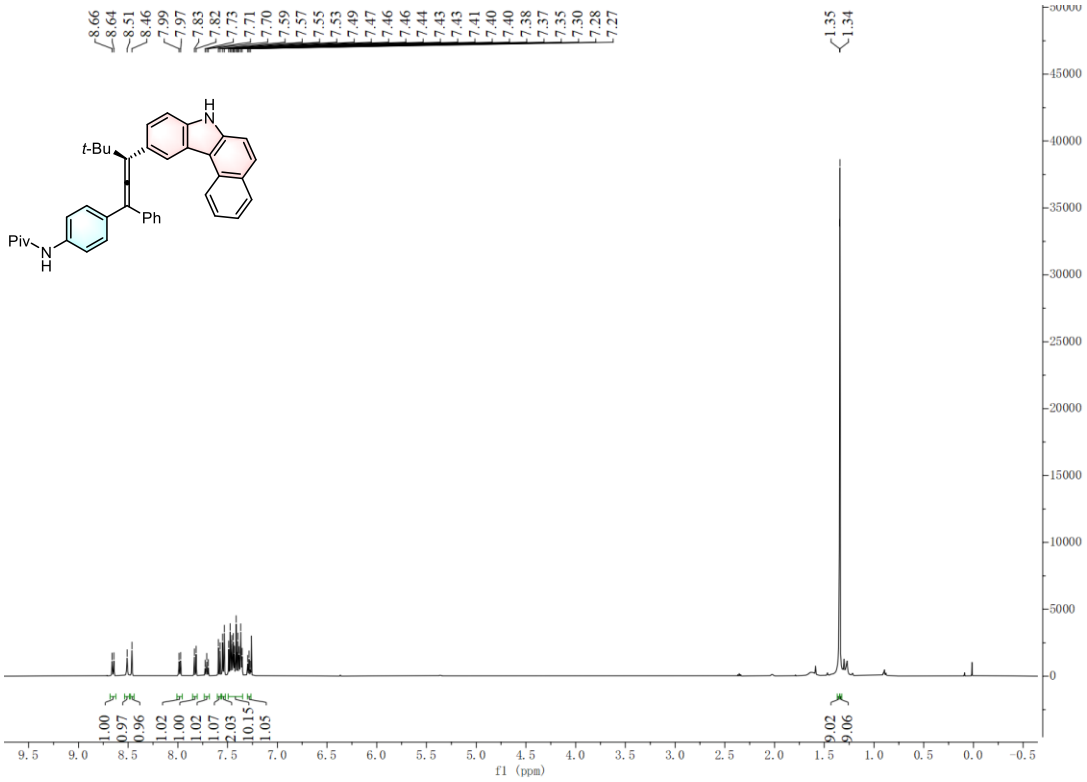
^{1}H NMR of compound 3o (in $CDCl_3$)



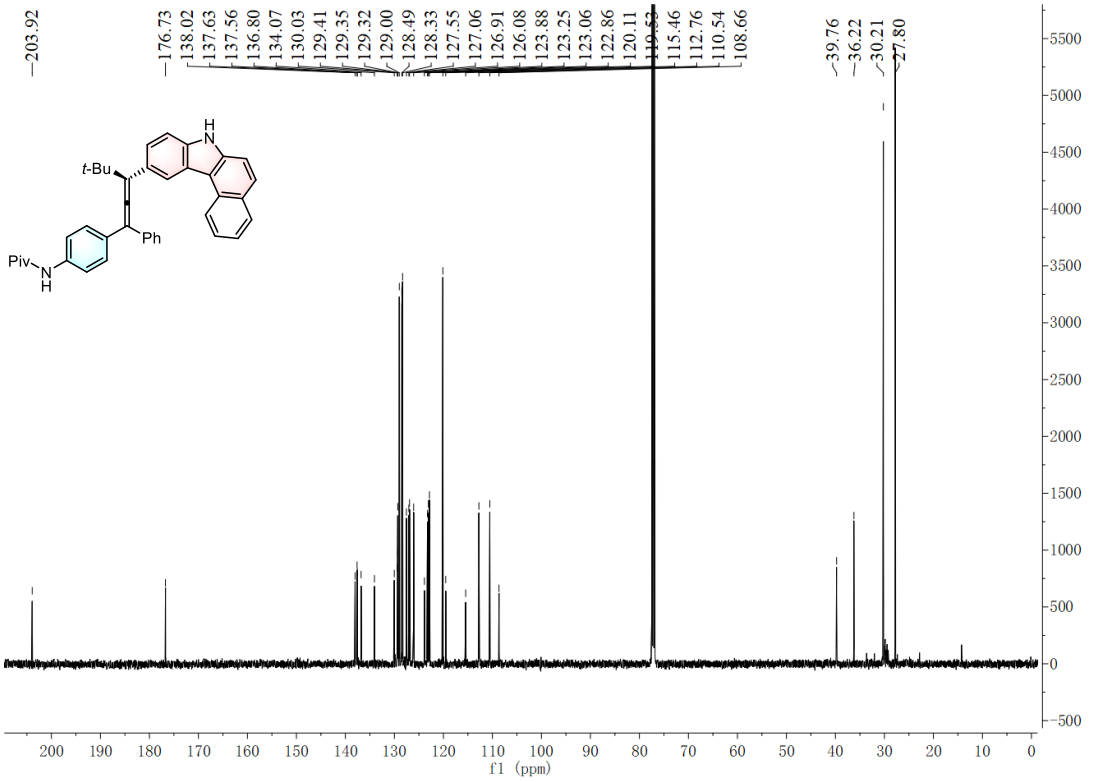
^{13}C NMR of compound 3o (in $CDCl_3$)



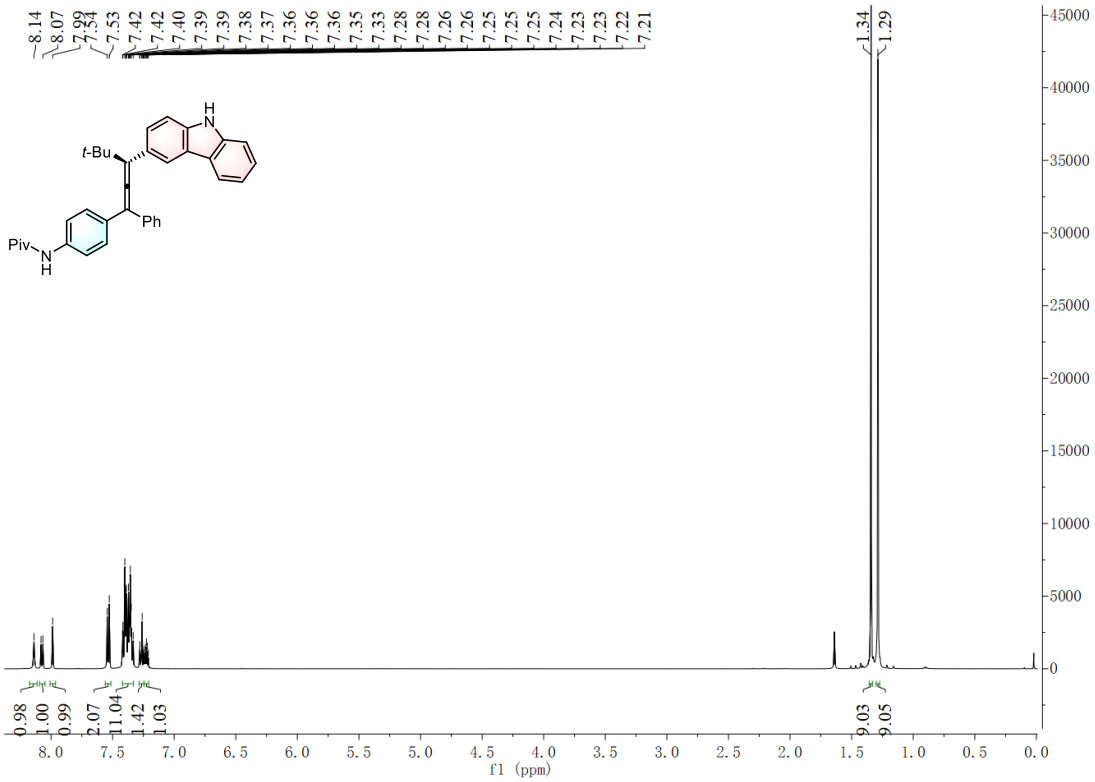
^{1}H NMR of compound 3p (in $CDCl_3$)



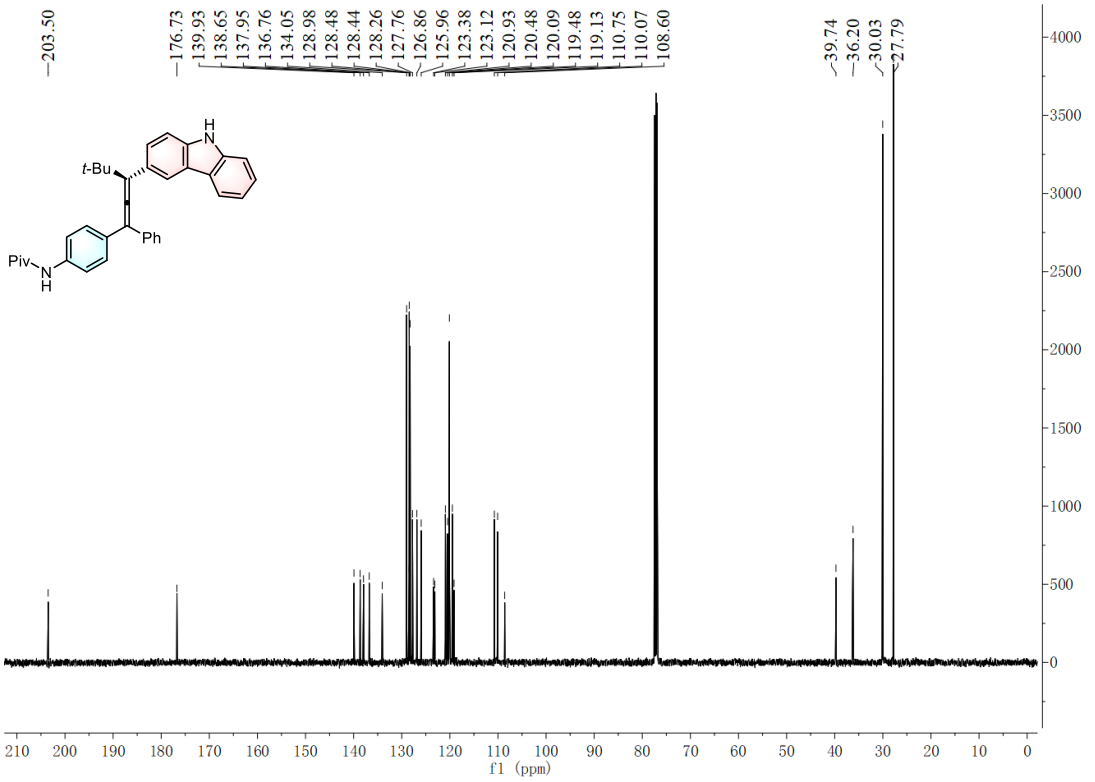
^{13}C NMR of compound 3p (in $CDCl_3$)



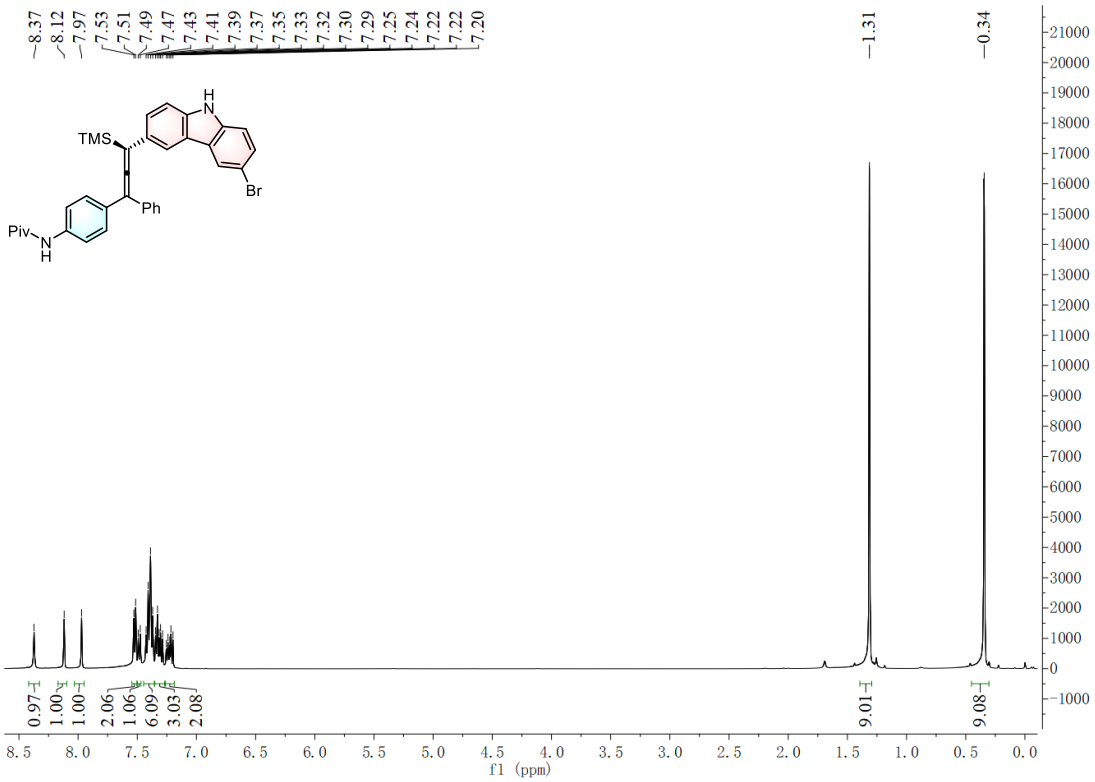
^{1}H NMR of compound 3q (in $CDCl_3$)



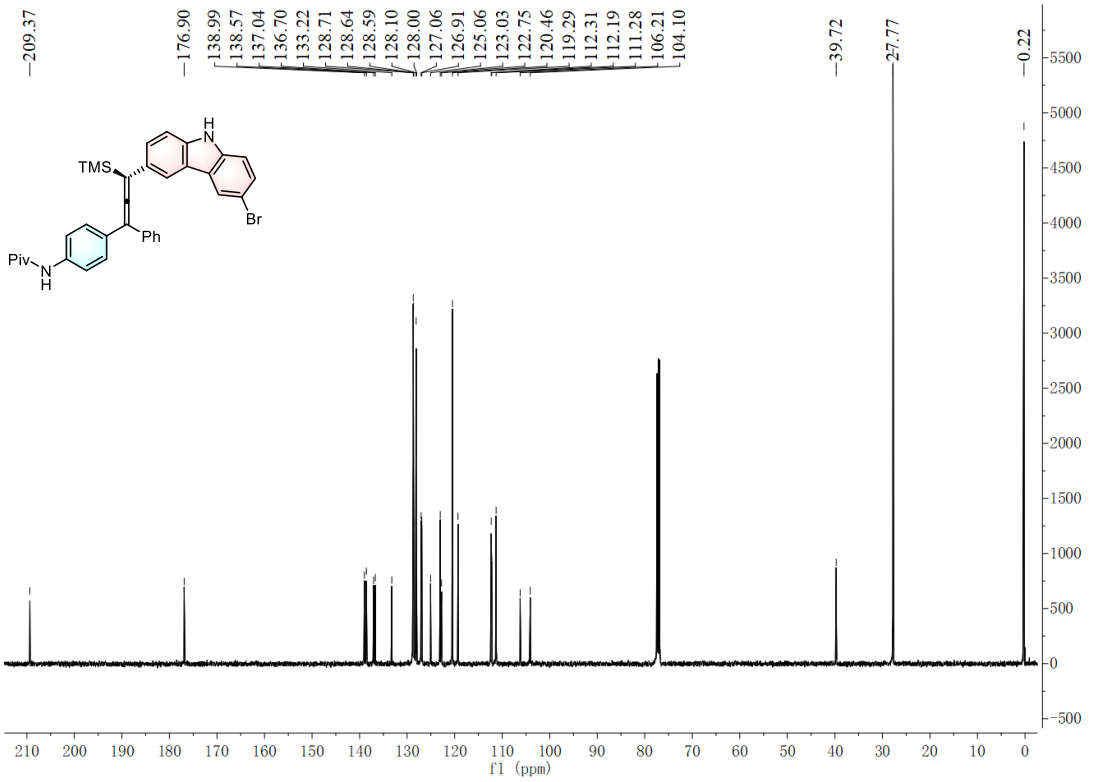
^{13}C NMR of compound 3q (in $CDCl_3$)



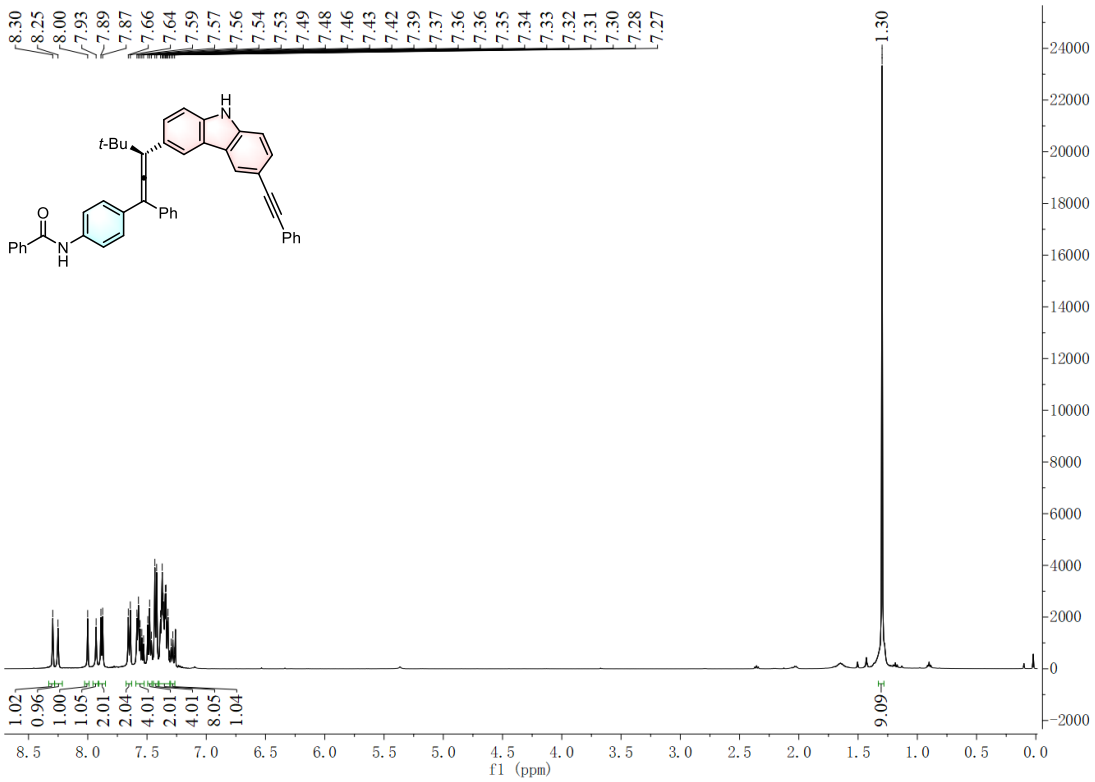
^{1}H NMR of compound 3r (in $CDCl_3$)



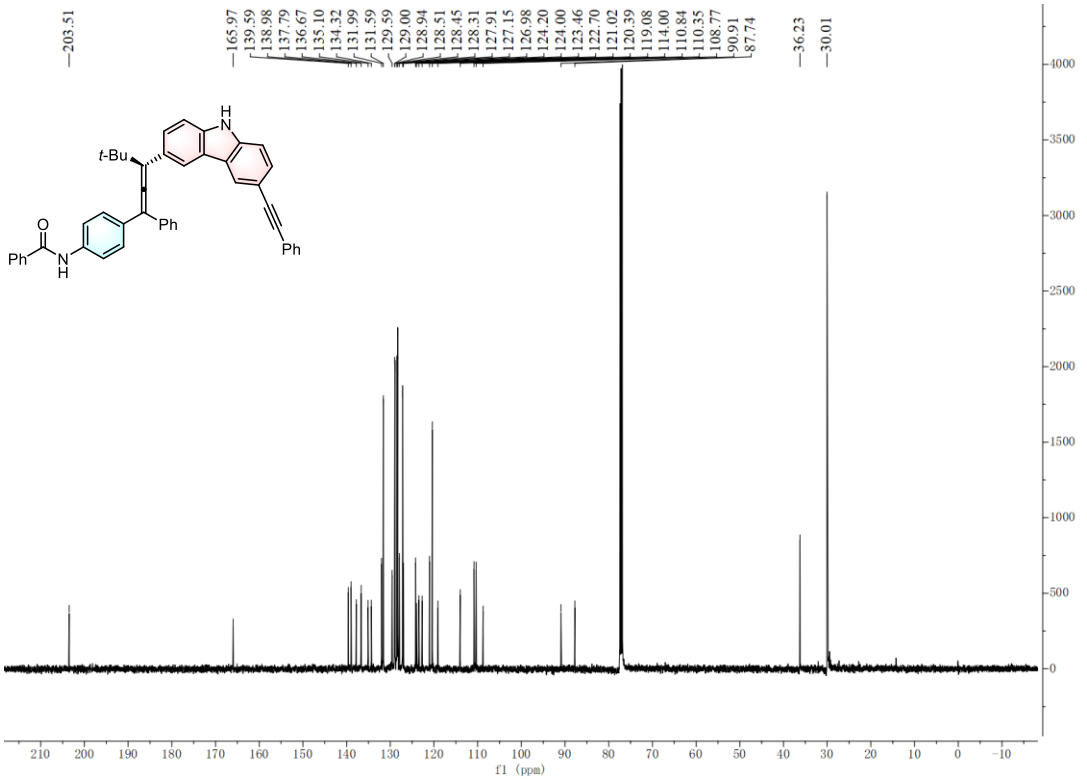
^{13}C NMR of compound 3r (in $CDCl_3$)



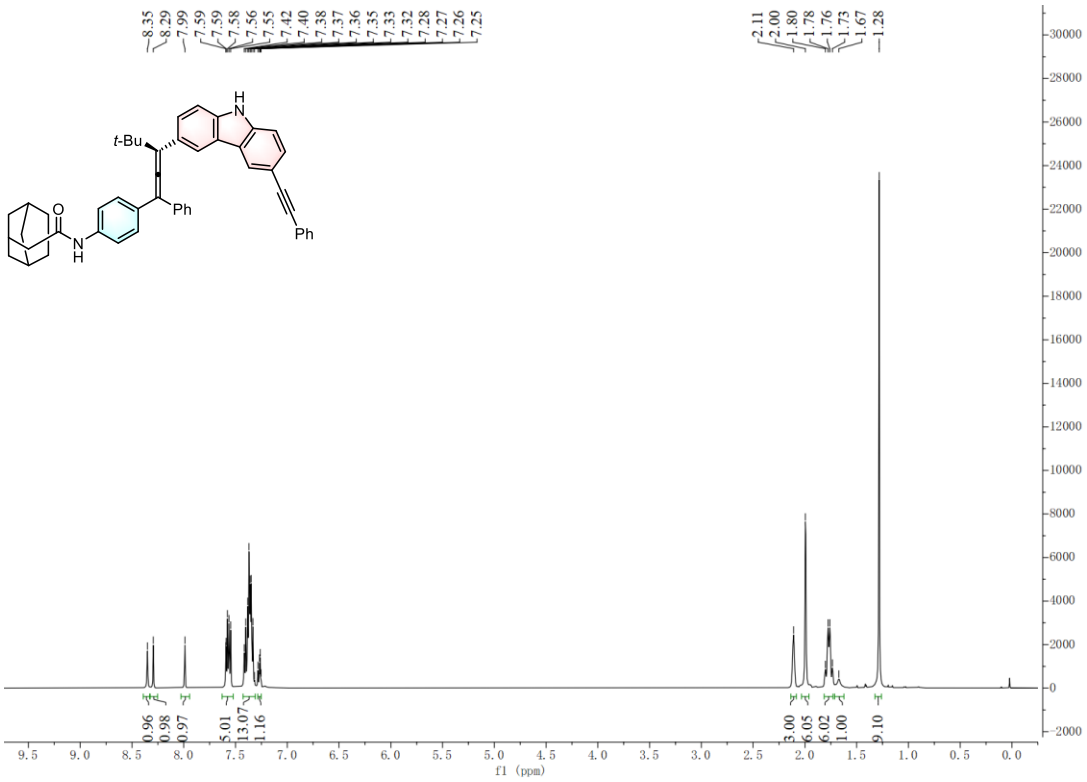
^{1}H NMR of compound 3s (in $CDCl_3$)



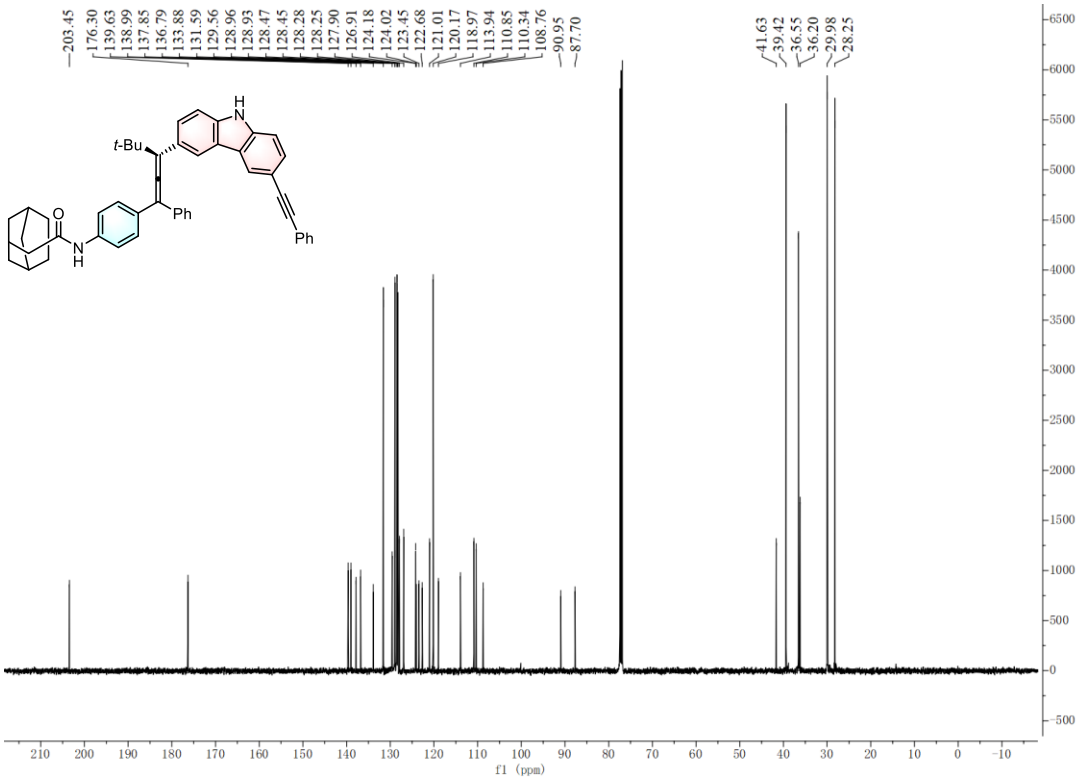
^{13}C NMR of compound 3s (in $CDCl_3$)



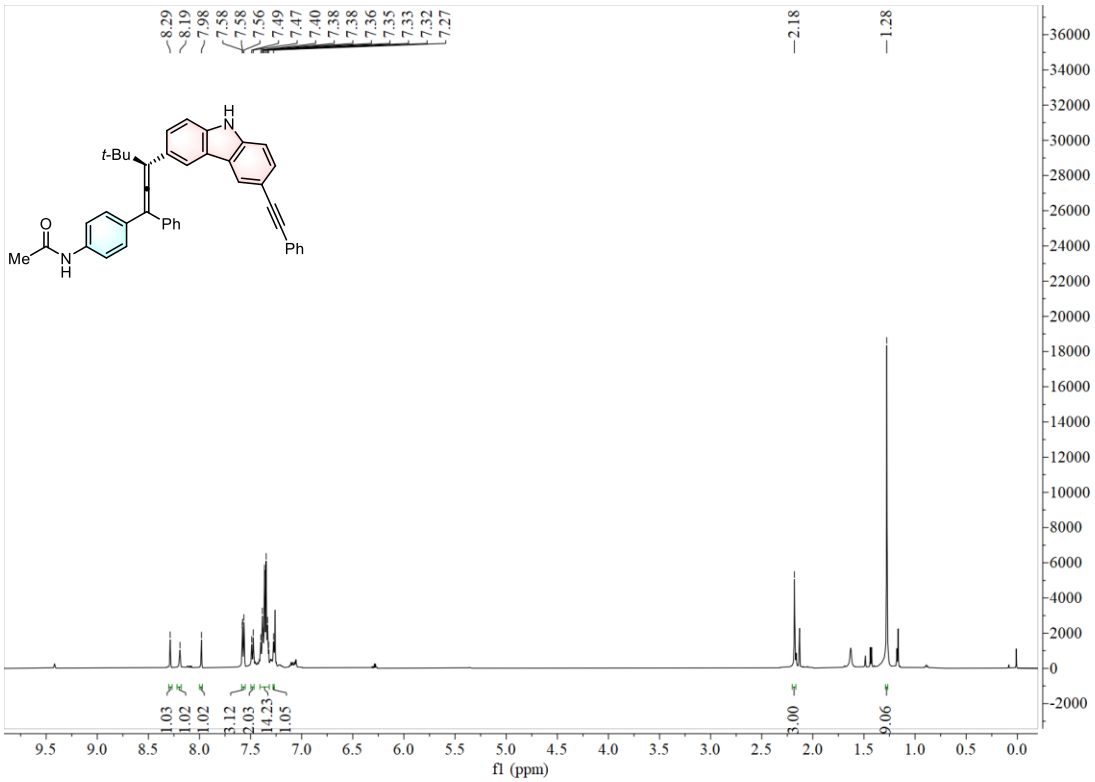
^{1}H NMR of compound 3t (in $CDCl_3$)



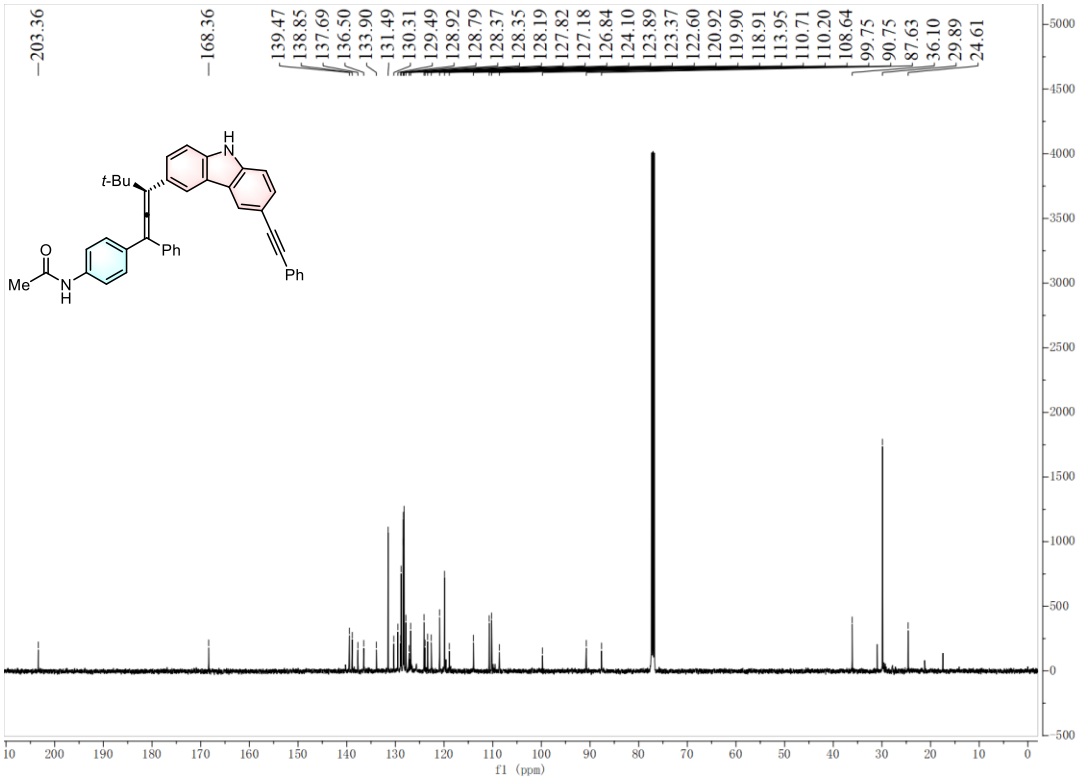
^{13}C NMR of compound 3t (in $CDCl_3$)



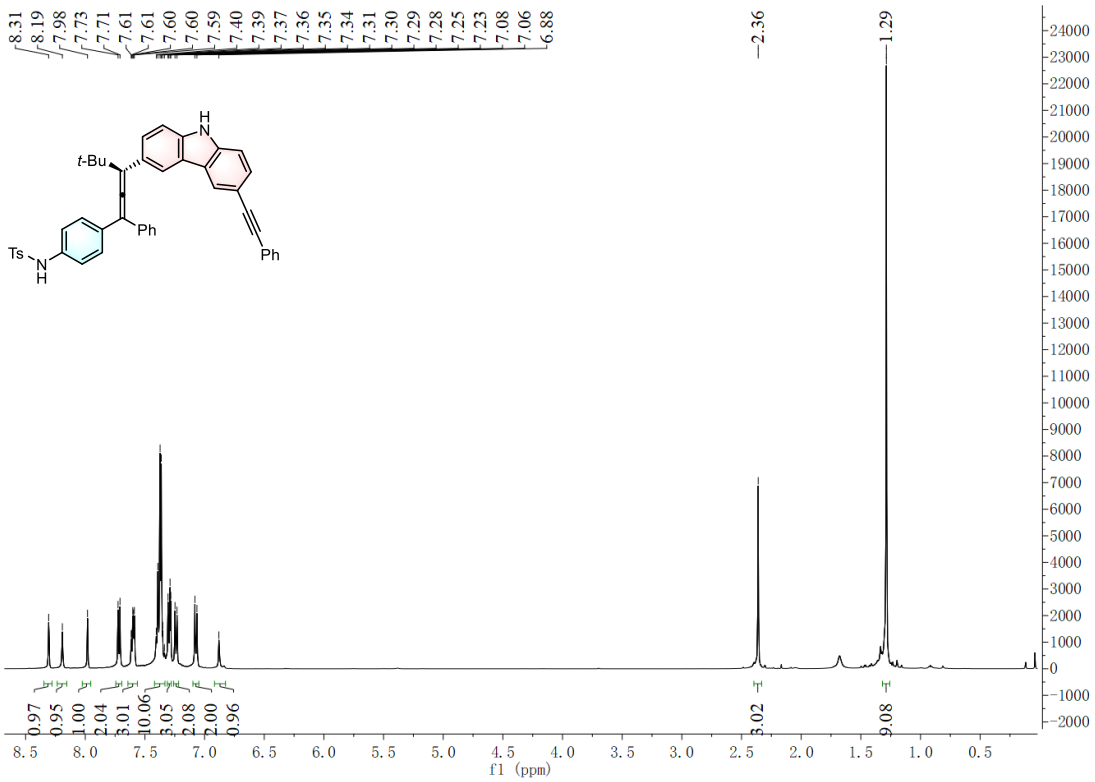
^{1}H NMR of compound 3u (in $CDCl_3$)



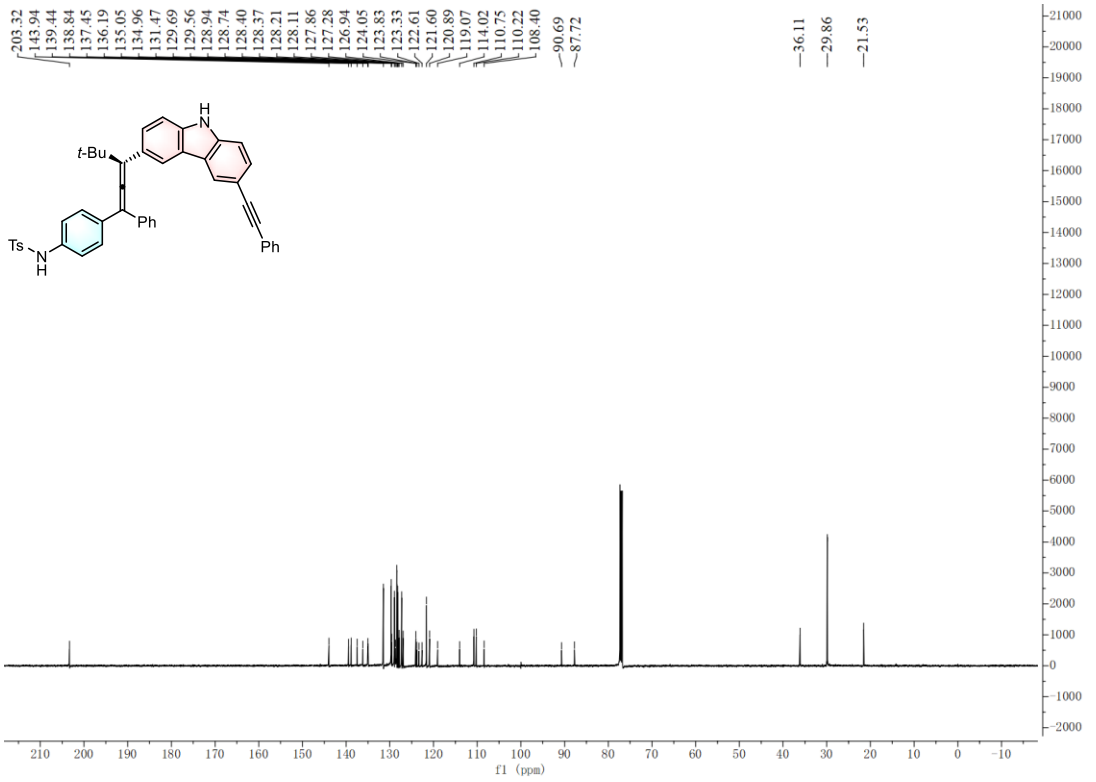
^{13}C NMR of compound 3u (in $CDCl_3$)



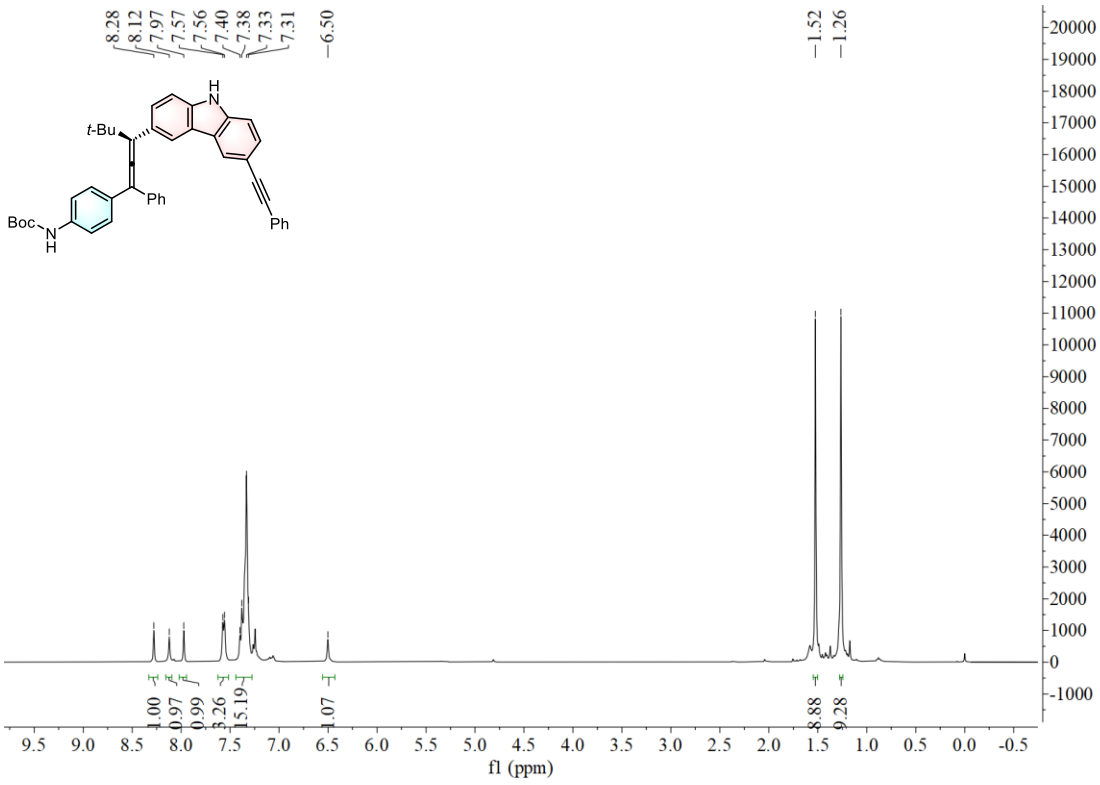
^{1}H NMR of compound 3v (in $CDCl_3$)



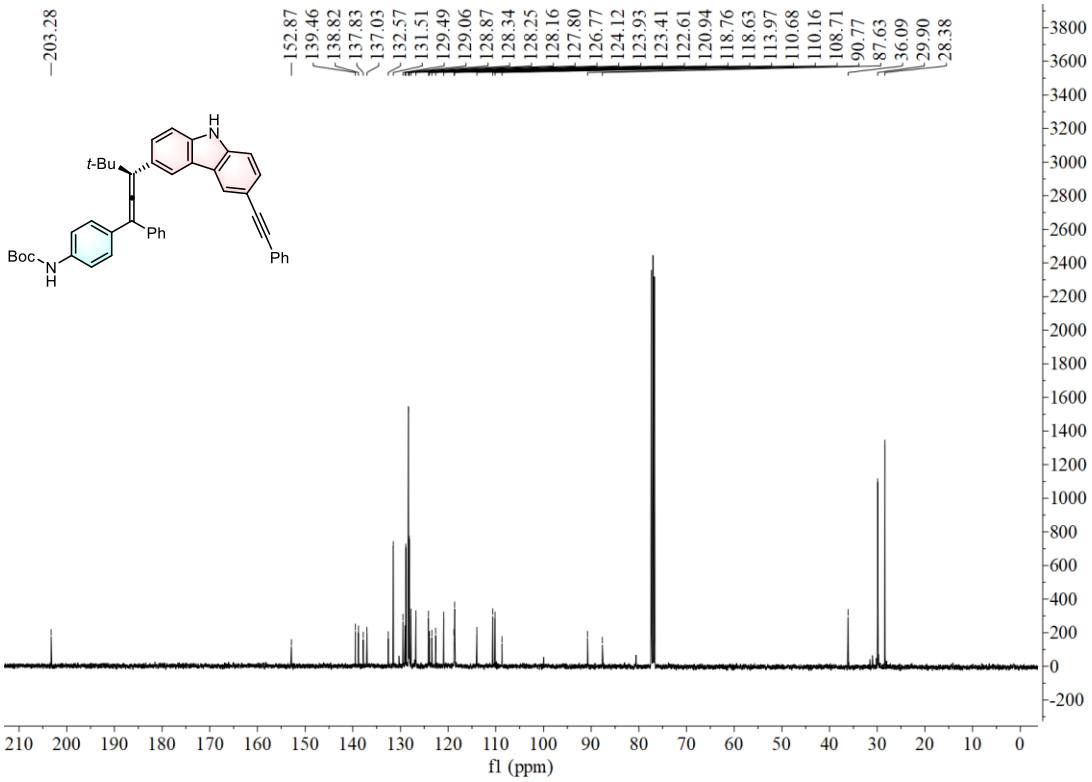
^{13}C NMR of compound 3v (in $CDCl_3$)



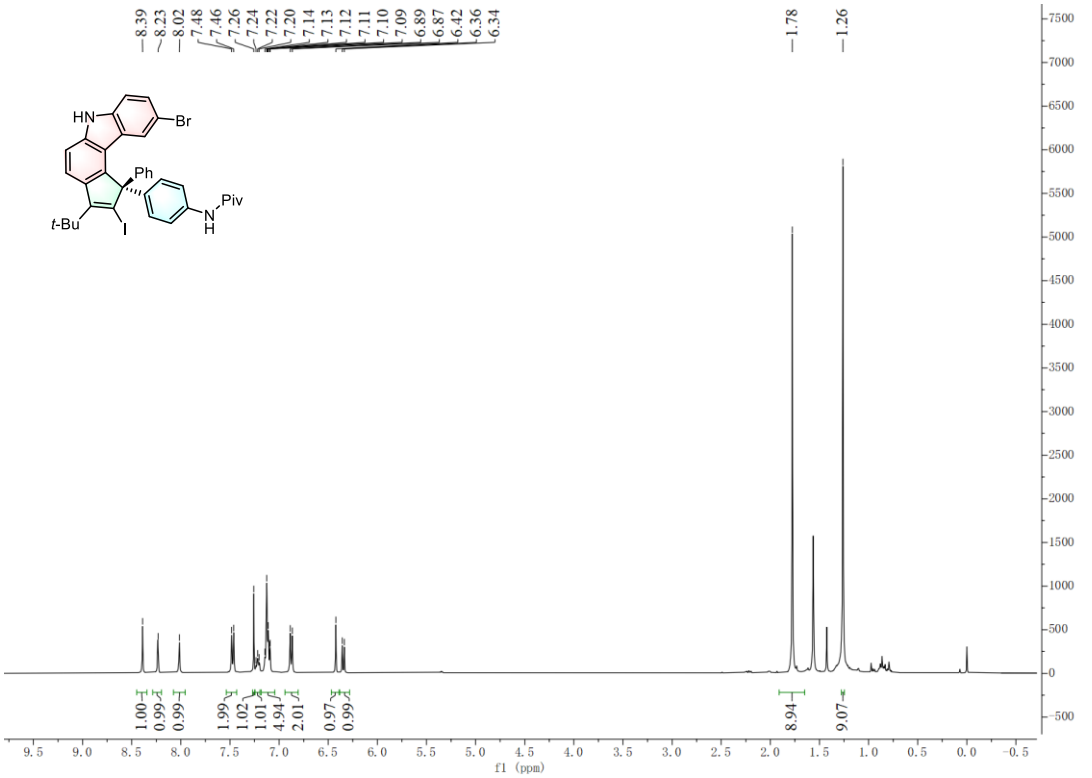
^{1}H NMR of compound 3w (in $CDCl_3$)



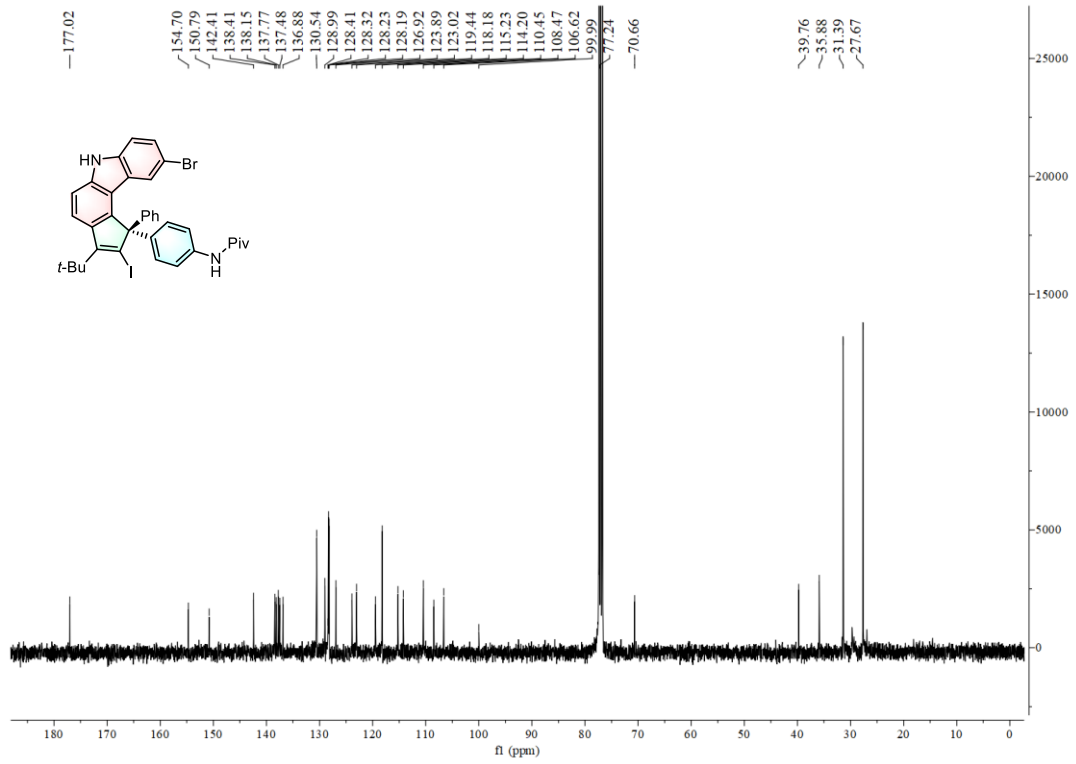
^{13}C NMR of compound 3w (in $CDCl_3$)



^{1}H NMR of compound 4 (in $CDCl_3$)

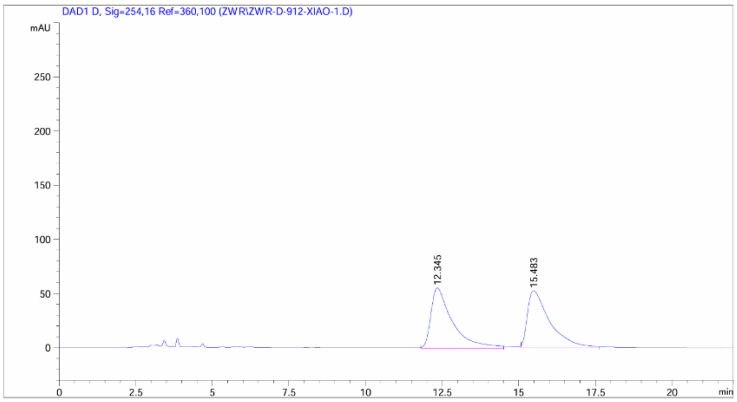


^{13}C NMR of compound 4 (in $CDCl_3$)



5. Copies of HPLC Spectra

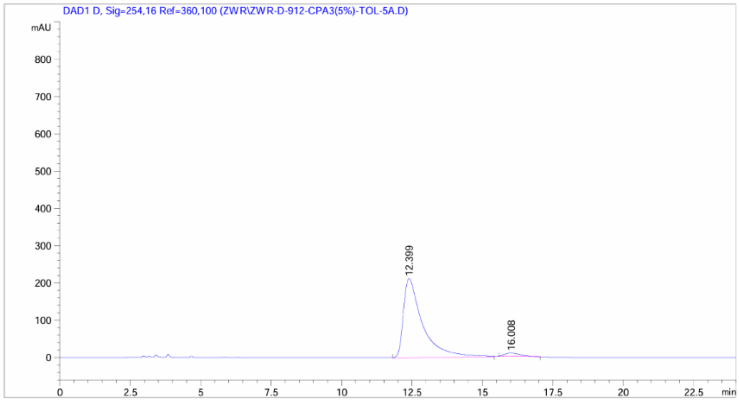
HPLC spectrum of the racemate 3a



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.345	MM R	0.8162	2726.29736	55.66949	50.3186
2	15.483	MM R	0.8497	2691.77832	52.79777	49.6814

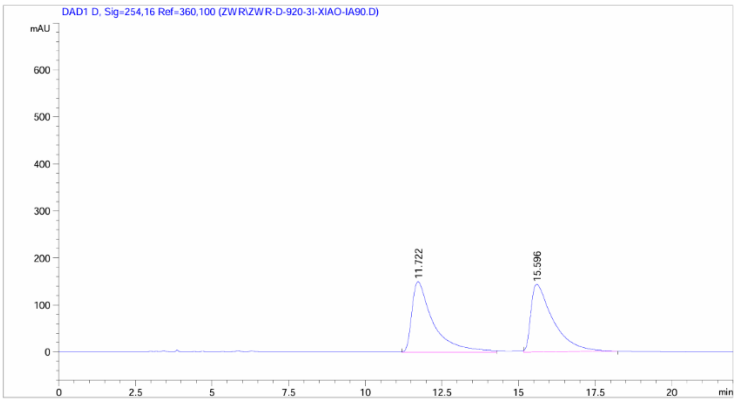
HPLC spectrum of the enantioenriched compound 3a



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.399	MM R	0.7923	1.01067e4	212.60239	96.9976
2	16.008	MM R	0.6355	312.83896	8.20505	3.0024

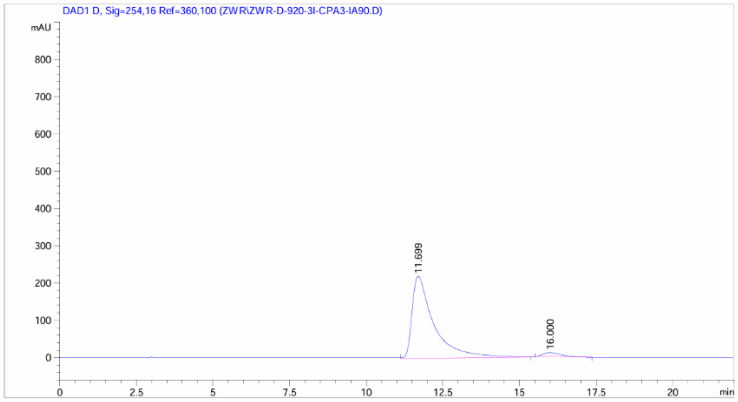
HPLC spectrum of the racemate 3b



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.722	MM R	0.8183	7395.21045	150.61432	50.2253
2	15.596	MM R	0.8459	7328.86084	144.39667	49.7747

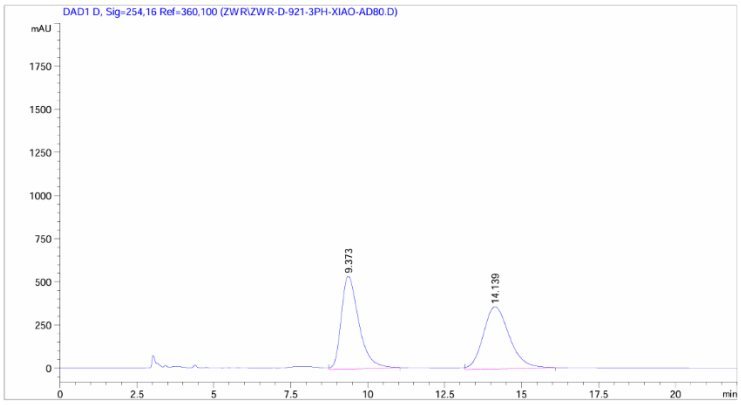
HPLC spectrum of the enantioenriched compound 3b



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.699	MM R	0.8240	1.08796e4	220.05493	96.5101
2	16.000	MM R	0.6301	393.41727	10.40657	3.4899

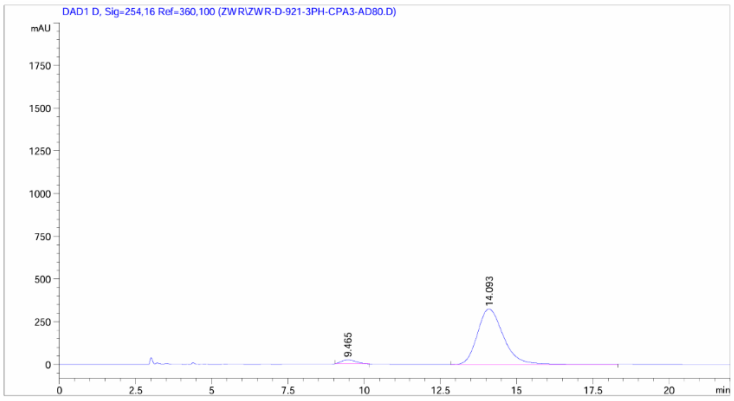
HPLC spectrum of the racemate 3c



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.373	MM R	0.6664	2.15328e4	538.53131	50.0834
2	14.139	MM R	0.9936	2.14611e4	359.99542	49.9166
总量 :				4.29939e4	898.52673	

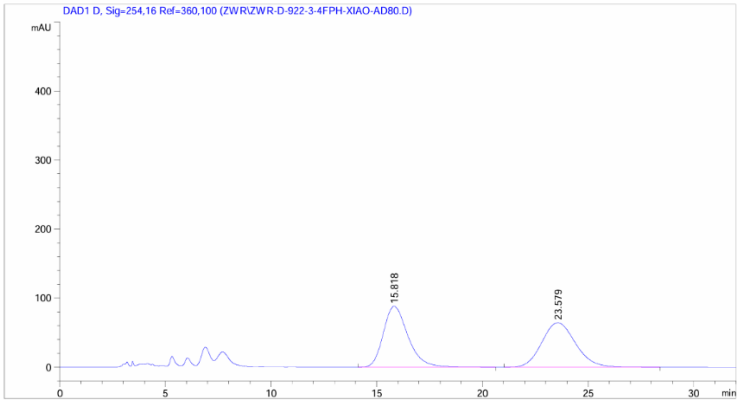
HPLC spectrum of the enantioenriched compound 3c



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.465	MM R	0.5104	646.12103	21.09683	3.1022
2	14.093	MM R	1.0286	2.01817e4	327.02151	96.8978

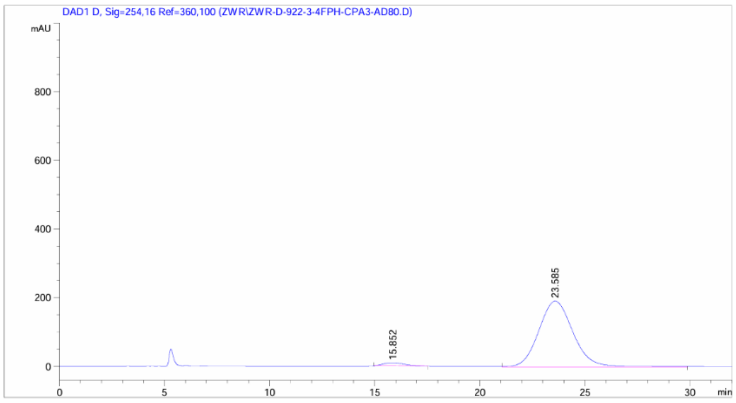
HPLC spectrum of the racemate 3d



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	15.818	BB	1.2200	7168.81152	88.22604	50.0186
2	23.579	BB	1.5919	7163.47217	64.29466	49.9814

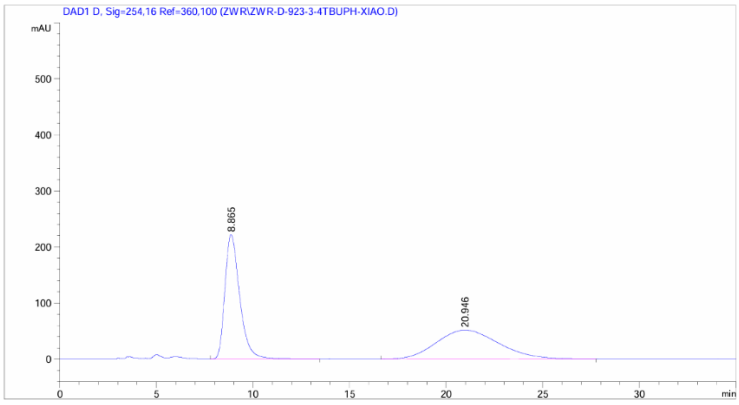
HPLC spectrum of the enantioenriched compound 3d



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	15.852	MM R	1.0561	556.96808	8.78939	2.4608
2	23.585	MM R	1.9150	2.20767e4	192.13411	97.5392

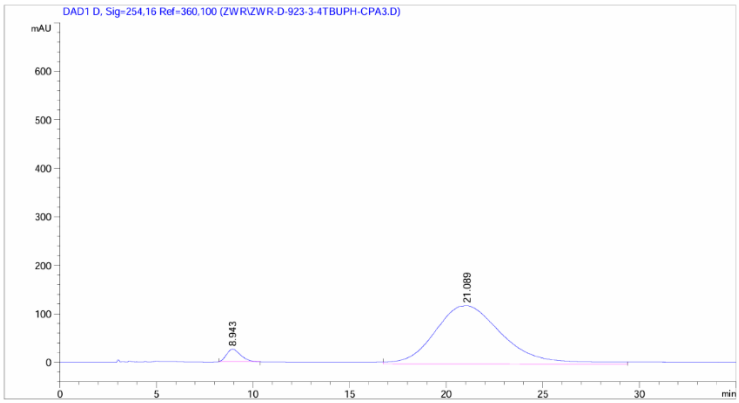
HPLC spectrum of the racemate 3e



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.865	BB	0.8117	1.18183e4	221.77623	50.2360
2	20.946	BB	2.6526	1.17073e4	51.68651	49.7640

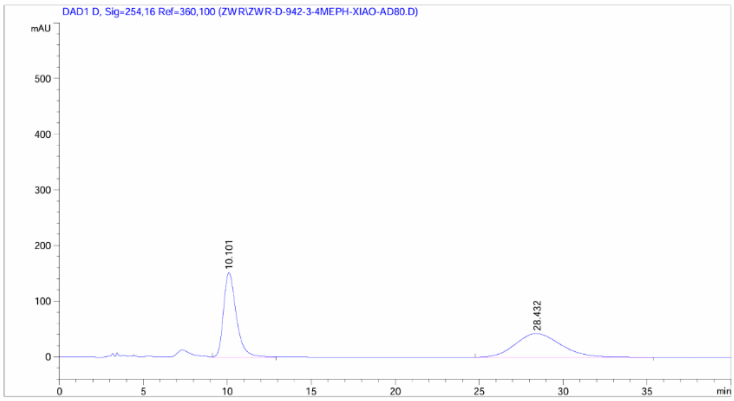
HPLC spectrum of the enantioenriched compound 3e



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.943	MM R	0.8110	1219.50500	25.06153	3.9611
2	21.089	MM R	4.1147	2.95679e4	119.76389	96.0389

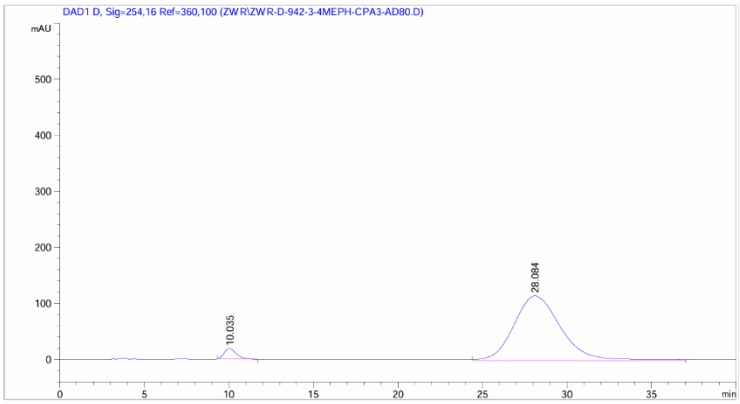
HPLC spectrum of the racemate 3f



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.101	MM R	0.8947	8196.48242	152.69258	49.9930
2	28.432	MM R	3.1938	8198.78516	42.78503	50.0070

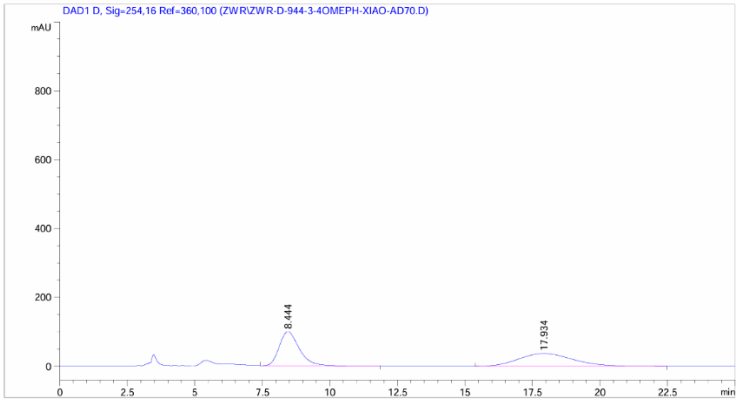
HPLC spectrum of the enantioenriched compound 3f



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.035	MM R	0.8107	894.79352	18.39662	3.9787
2	28.084	MM R	3.1464	2.15950e4	114.39114	96.0213

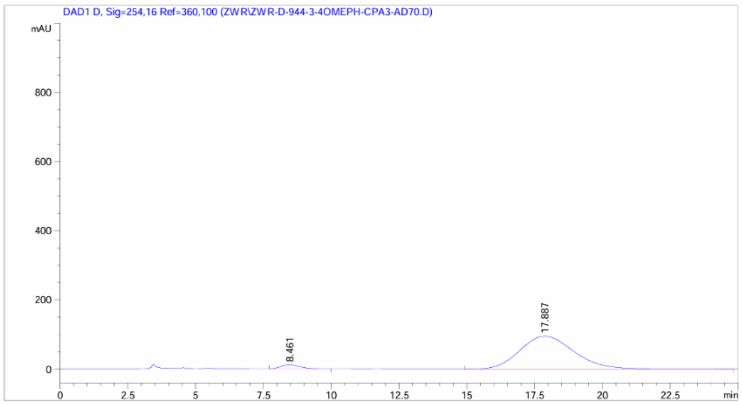
HPLC spectrum of the racemate 3g



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.444	MM R	0.8858	5319.47559	100.08861	50.1623
2	17.934	MM R	2.3618	5285.06299	37.29597	49.8377

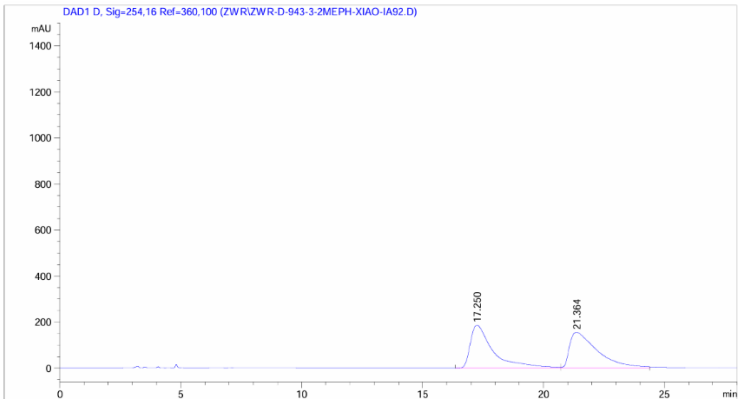
HPLC spectrum of the enantioenriched compound 3g



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.461	MM R	0.7891	538.50171	11.37434	3.7275
2	17.887	MM R	2.4067	1.39084e4	96.31864	96.2725

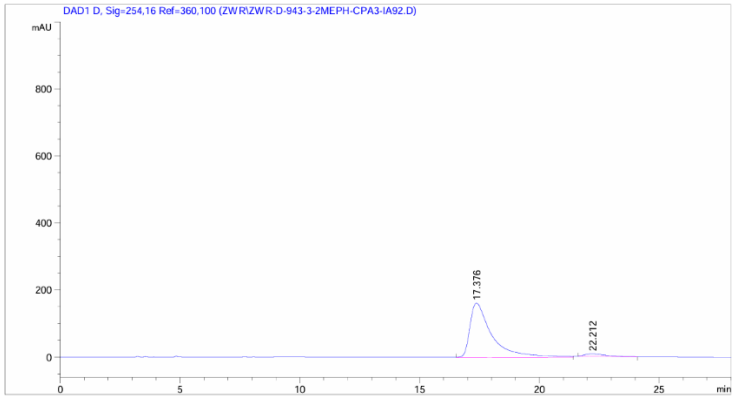
HPLC spectrum of the racemate 3h



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.250	BV	0.9455	1.22690e4	186.49519	49.5496
2	21.364	MF R	1.3389	1.24921e4	155.50197	50.4504

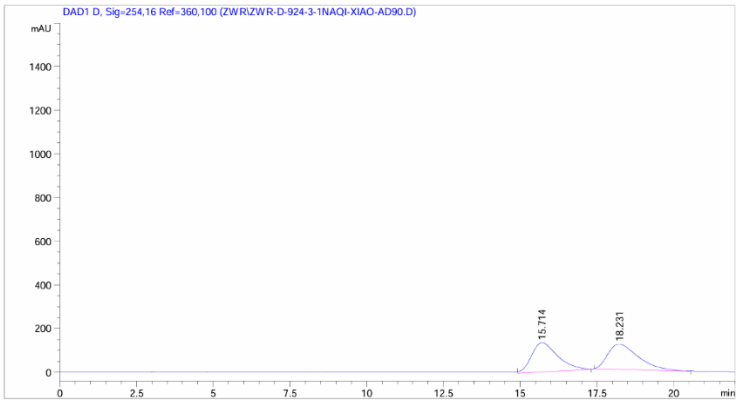
HPLC spectrum of the enantioenriched compound 3h



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	17.376	MM R	1.0615	1.03213e4	162.05214	96.0481
2	22.212	MM R	1.0024	424.66708	7.06088	3.9519

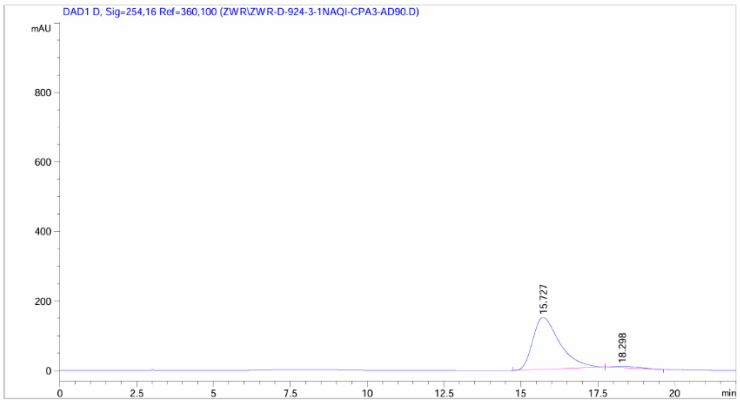
HPLC spectrum of the racemate 3i



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	15.714	MM R	1.0022	8046.00586	133.80852	50.1954
2	18.231	MM R	1.1546	7983.36865	115.24272	49.8046

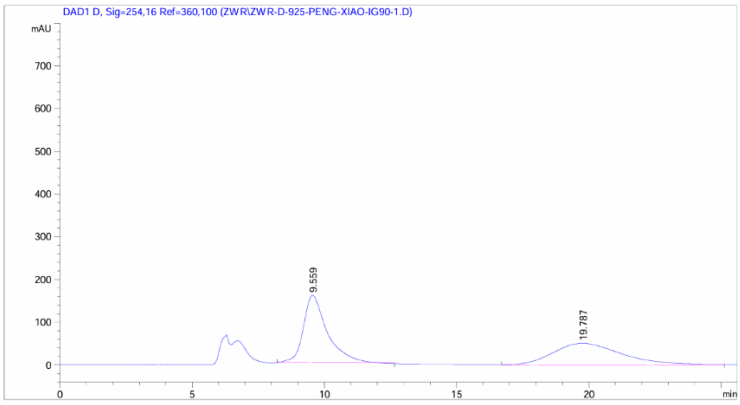
HPLC spectrum of the enantioenriched compound 3i



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	15.727	BB	0.9155	9071.80371	149.17780	97.3699
2	18.298	BBA	0.6428	245.03918	4.51755	2.6301

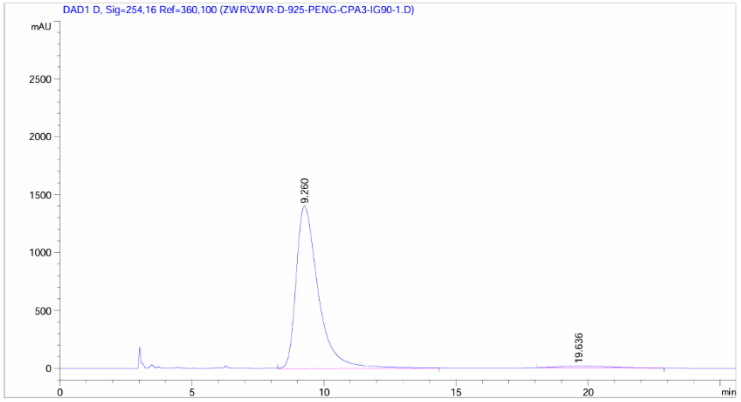
HPLC spectrum of the racemate5j



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.559	MM R	1.0395	9775.65918	156.73065	50.1107
2	19.787	MM R	3.1321	9732.48145	51.78964	49.8893

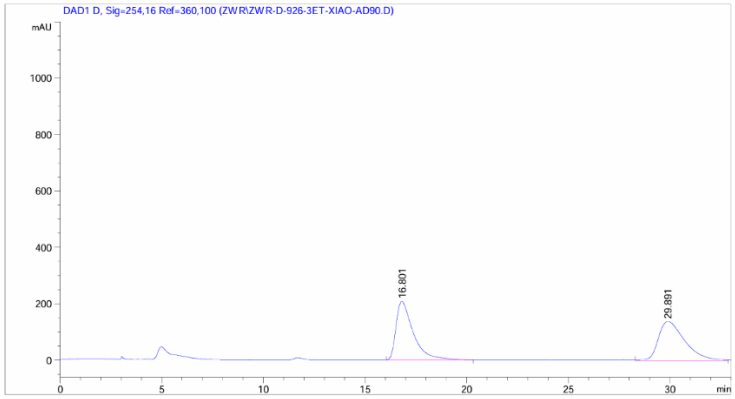
HPLC spectrum of the enantioenriched compound 3j



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.260	MM R	0.9774	8.23653e4	1404.48572	97.9211
2	19.636	MM R	2.2634	1748.64319	12.87595	2.0789

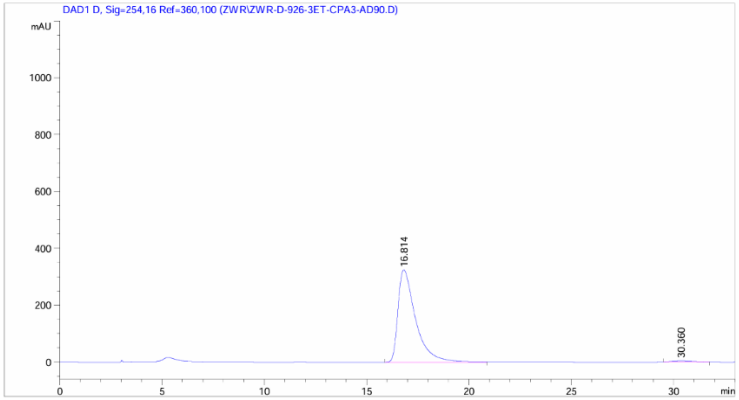
HPLC spectrum of the racemate 3k



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.801	MM R	0.9949	1.24915e4	209.26178	50.1044
2	29.891	MM R	1.5005	1.24394e4	138.17143	49.8956

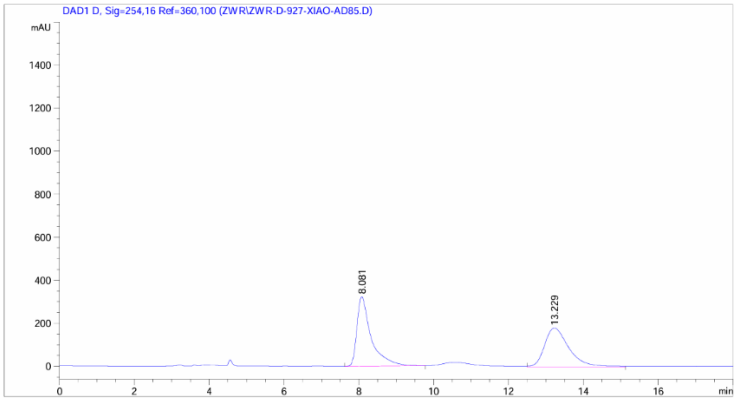
HPLC spectrum of the enantioenriched compound 3k



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	16.814	MM R	1.0046	1.96239e4	325.55090	98.7777
2	30.360	MM R	1.0900	242.82753	3.71294	1.2223

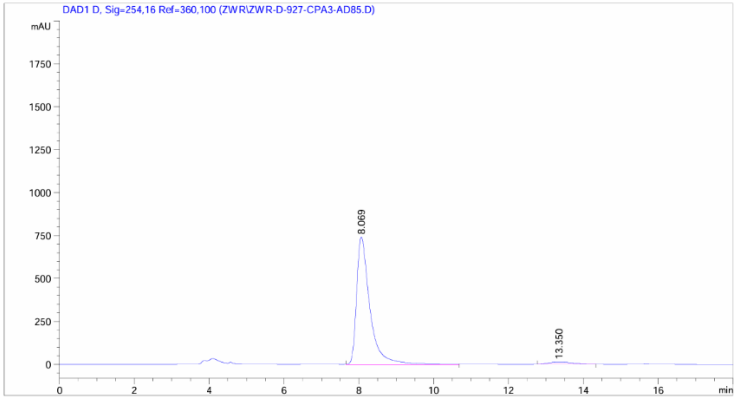
HPLC spectrum of the racemate 3l



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.081	BB	0.3824	8527.17480	322.61490	50.6091
2	13.229	MM R	0.7651	8321.91992	181.27296	49.3909

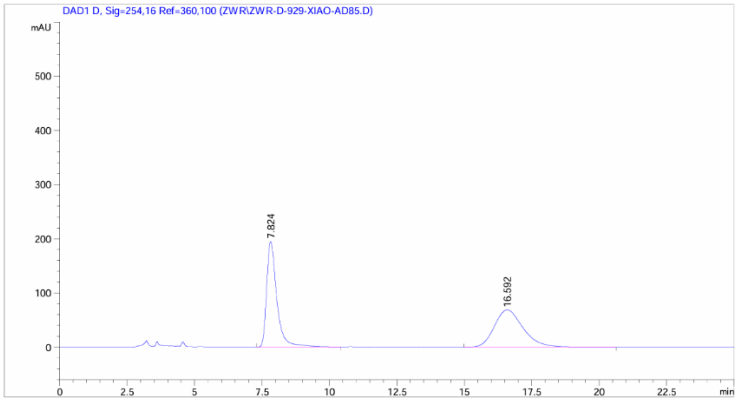
HPLC spectrum of the enantioenriched compound 3l



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.069	MM R	0.4159	1.85389e4	742.87463	97.2351
2	13.350	MM R	0.6677	527.16162	13.15801	2.7649

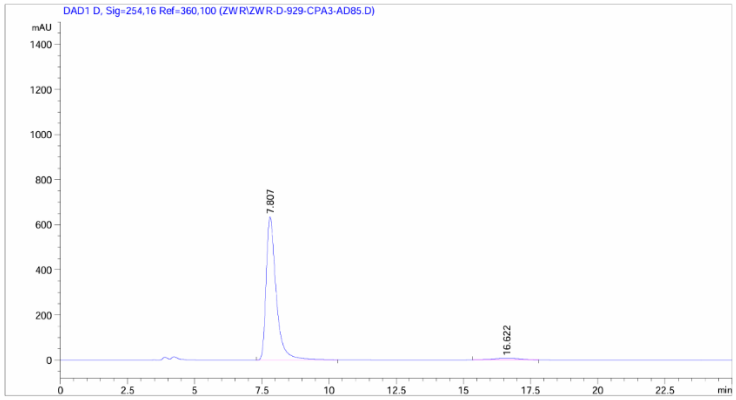
HPLC spectrum of the racemate 3m



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.824	BB	0.3919	5106.71387	194.79382	49.8529
2	16.592	BB	1.1066	5136.85498	68.99612	50.1471

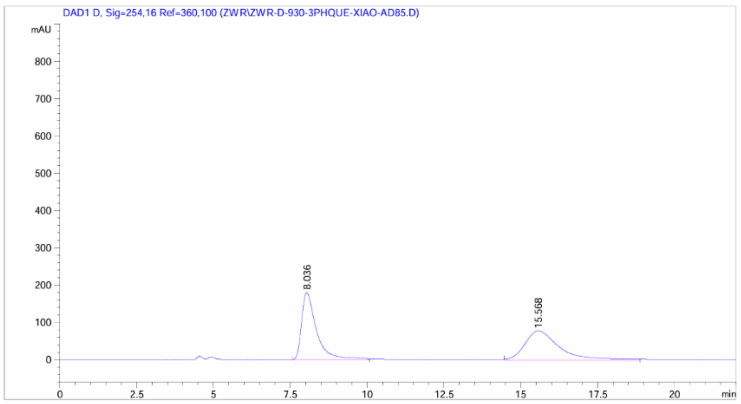
HPLC spectrum of the enantioenriched compound 3m



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.807	MM R	0.4434	1.69528e4	637.25336	97.6997
2	16.622	MM R	1.0415	399.15536	6.38722	2.3003

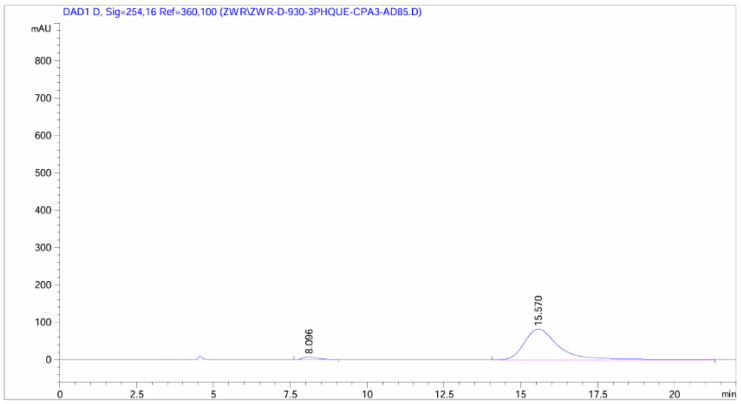
HPLC spectrum of the racemate 3n



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.036	MM R	0.5655	6125.90674	180.54611	50.1726
2	15.568	MM R	1.3001	6083.75635	77.99060	49.8274

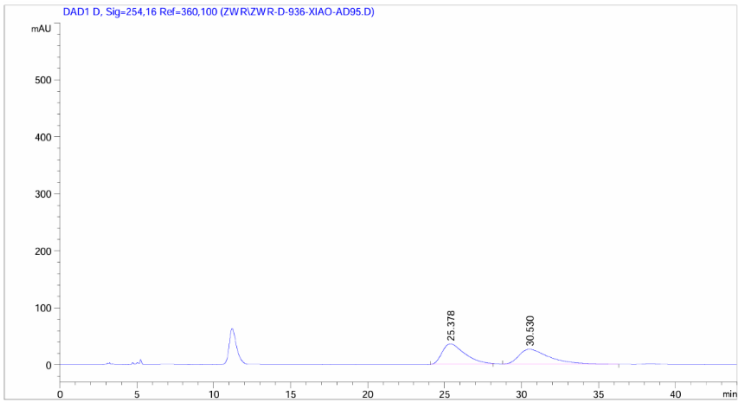
HPLC spectrum of the enantioenriched compound 3n



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.096	MM R	0.4449	171.90125	6.43991	2.4545
2	15.570	MM R	1.3666	6831.61133	83.31934	97.5455

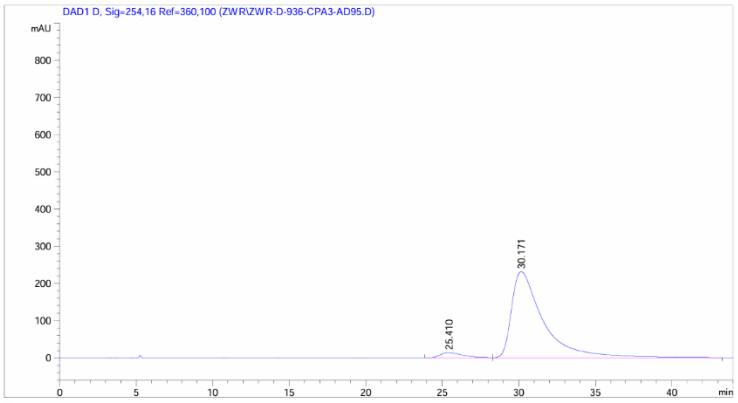
HPLC spectrum of the racemate 3o



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	25.378	MM R	1.7382	3736.89331	35.83047	49.9687
2	30.530	MM R	2.3548	3741.56787	26.48165	50.0313

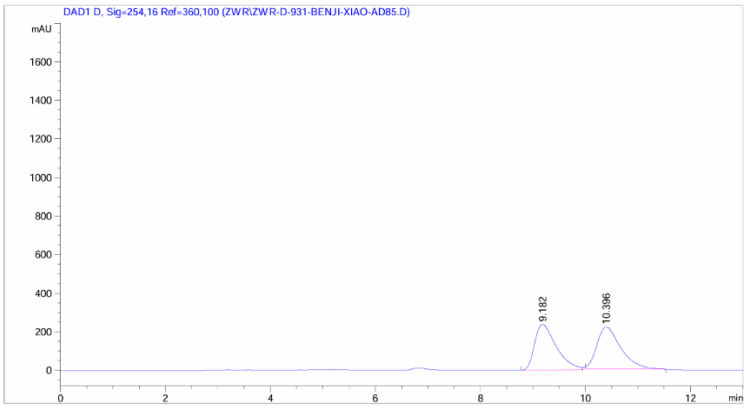
HPLC spectrum of the enantioenriched compound 3o



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	25.410	BB	1.1581	1367.13123	13.91653	3.9697
2	30.171	BB	2.0758	3.30717e4	230.52086	96.0303

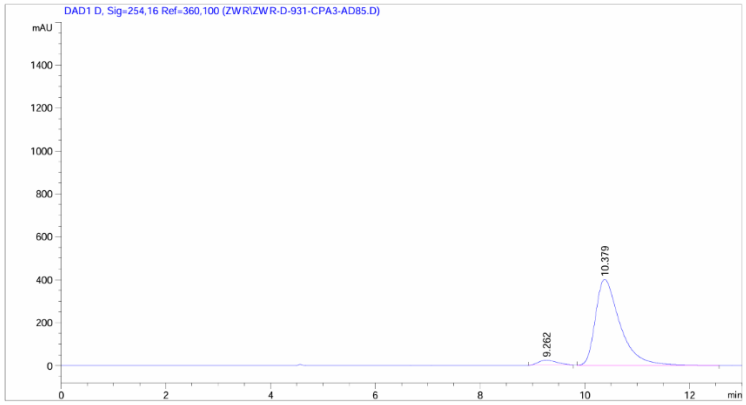
HPLC spectrum of the racemate 3p



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.182	MM R	0.4817	6853.86377	237.15517	49.8190
2	10.396	MM R	0.5274	6903.67139	218.15767	50.1810

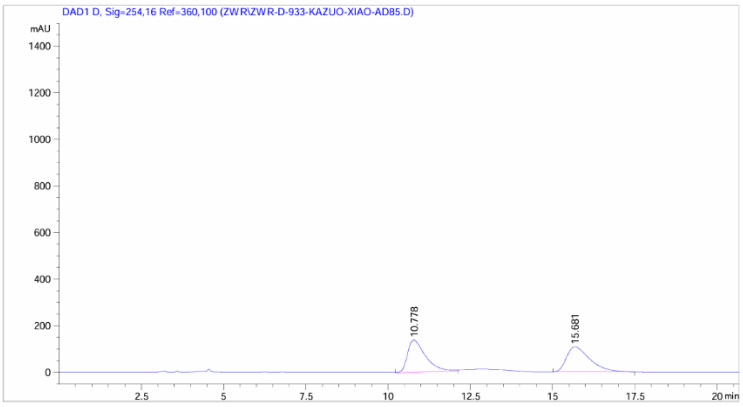
HPLC spectrum of the enantioenriched compound 3p



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	9.262	MM R	0.3931	522.28040	22.14271	3.7794
2	10.379	MF R	0.5511	1.32970e4	402.15225	96.2206

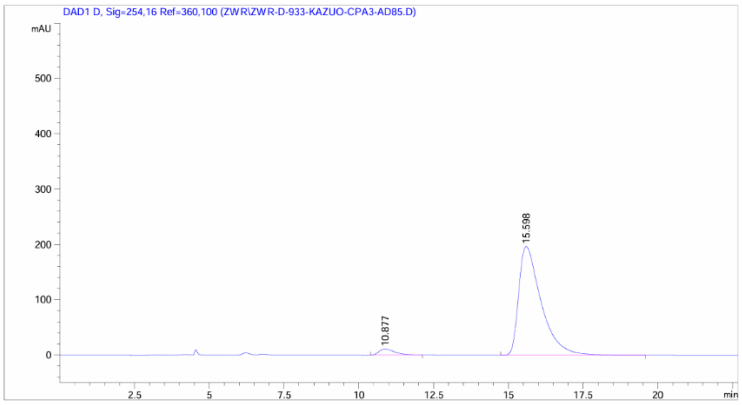
HPLC spectrum of the racemate 3q



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.778	MM R	0.6322	5236.23242	138.03337	50.2364
2	15.681	MM R	0.8125	5186.95020	106.40298	49.7636

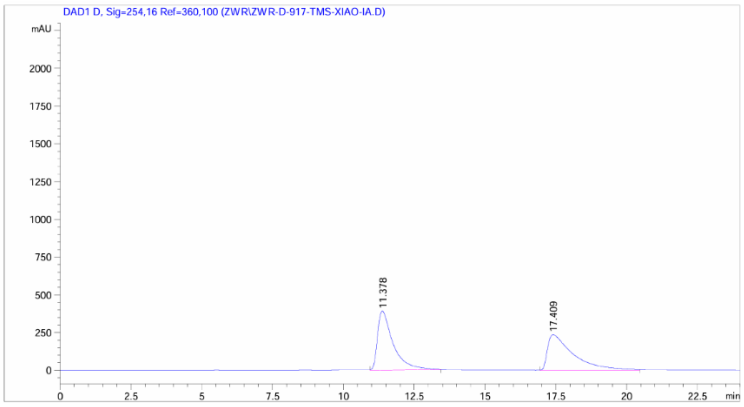
HPLC spectrum of the enantioenriched compound 3q



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	10.877	MM R	0.5687	363.67001	10.65861	3.4178
2	15.598	MM R	0.8717	1.02767e4	196.48283	96.5822

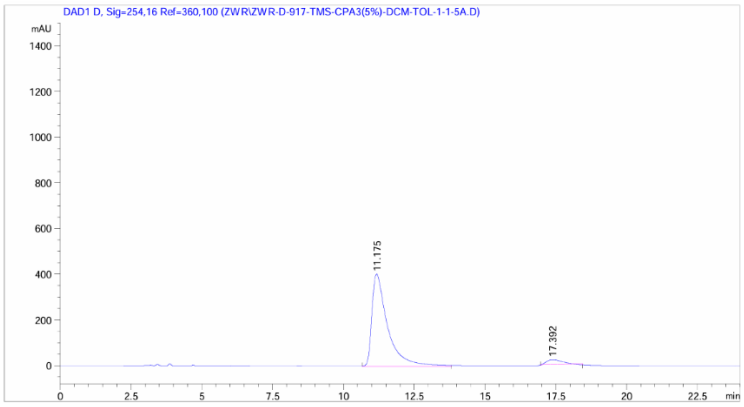
HPLC spectrum of the racemate 3r



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.378	MM R	0.6378	1.49779e4	391.41553	49.8456
2	17.409	MM R	1.0638	1.50706e4	236.11235	50.1544

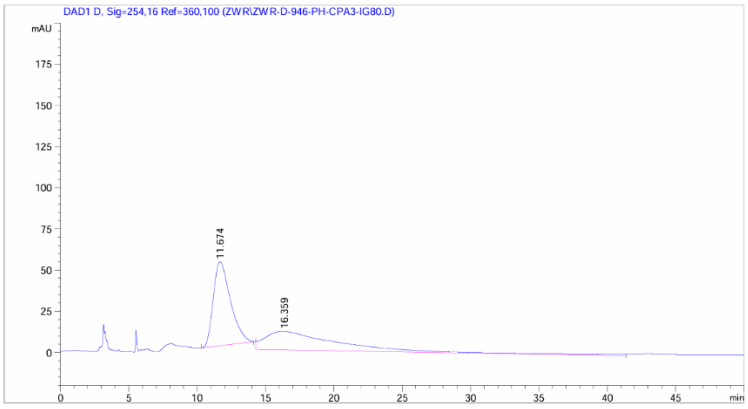
HPLC spectrum of the enantioenriched compound 3r



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.175	MM R	0.6555	1.59427e4	405.33401	95.3087
2	17.392	MM R	0.6182	784.73370	21.15584	4.6913

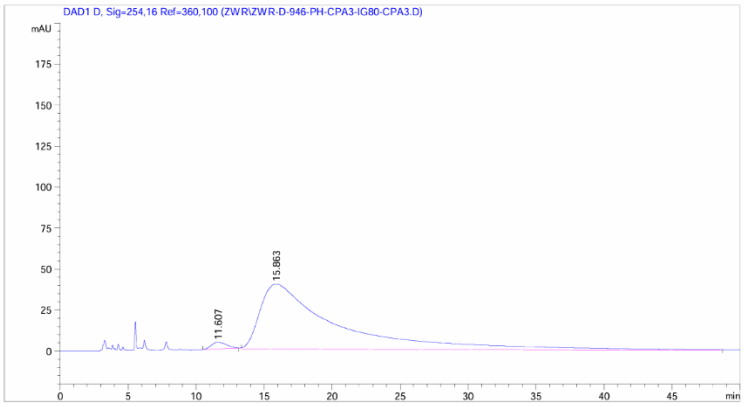
HPLC spectrum of the racemate 3s



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.674	BB	1.2583	4446.56543	50.94206	50.8206
2	16.359	MM R	6.3079	4302.96533	11.36920	49.1794

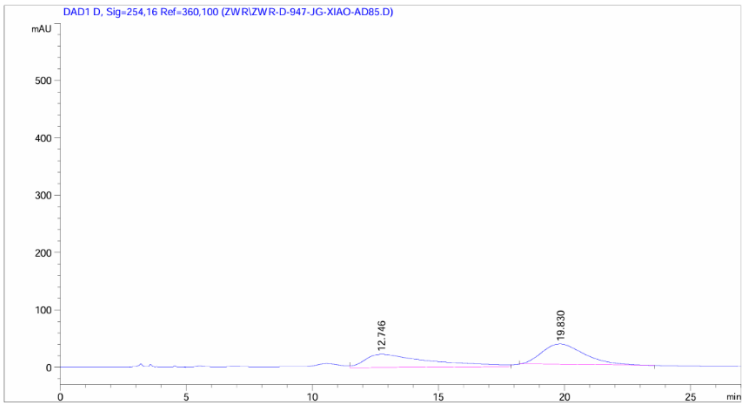
HPLC spectrum of the enantioenriched compound 3s



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.607	MM R	1.2758	308.58264	4.03111	1.9134
2	15.863	MM R	6.6298	1.58191e4	39.76742	98.0866

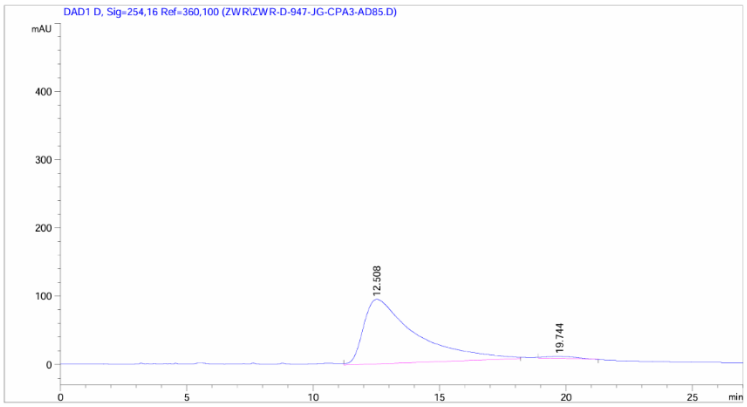
HPLC spectrum of the racemate 3t



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.746	MM R	3.0199	4143.35938	22.86679	50.5550
2	19.830	MM R	1.9212	4052.38818	35.15425	49.4450

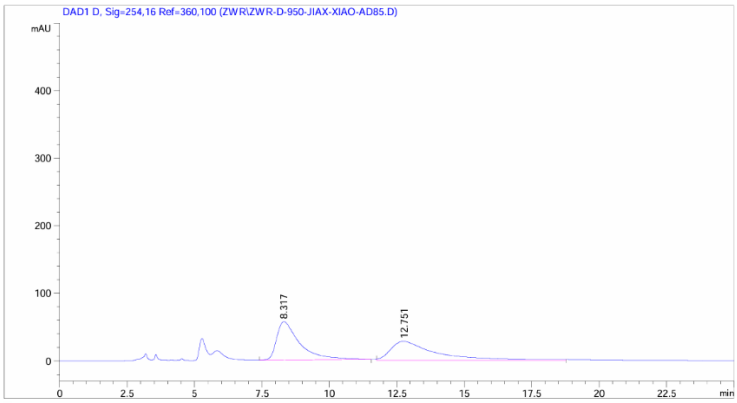
HPLC spectrum of the enantioenriched compound 3t



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	12.508	MM R	2.3942	1.36060e4	94.71665	98.1559
2	19.744	MM R	1.3940	255.61588	3.05617	1.8441

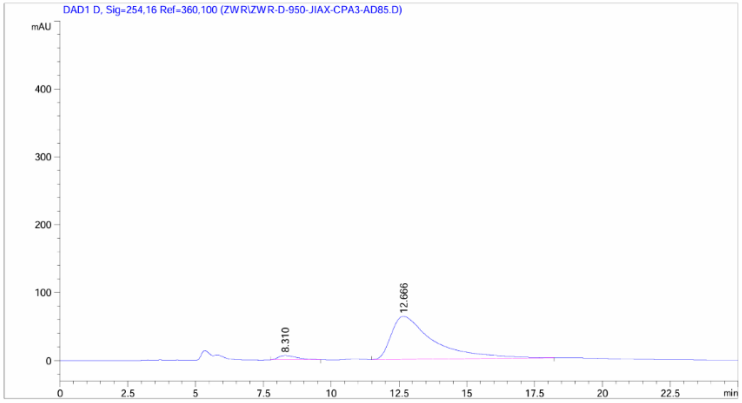
HPLC spectrum of the racemate 3u



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.317	BB	0.8533	3373.16260	56.60118	49.8272
2	12.751	MM R	2.0031	3396.55322	28.26086	50.1728

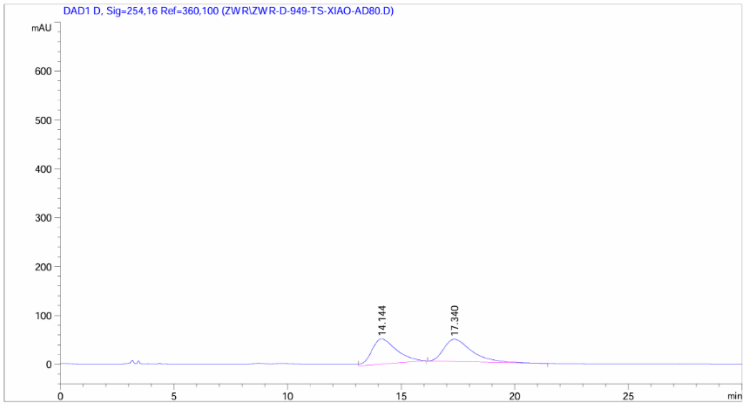
HPLC spectrum of the enantioenriched compound 3u



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	8.310	MM R	0.8063	308.35788	6.37408	4.3169
2	12.666	BB	1.4785	6834.68701	63.26110	95.6831

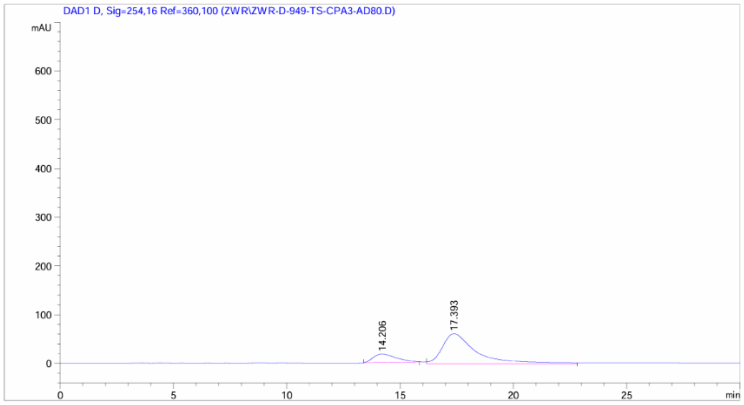
HPLC spectrum of the racemate 3v



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	14.144	MM R	1.2607	3893.13623	51.46910	49.9664
2	17.340	BB	1.2626	3898.37598	45.45398	50.0336

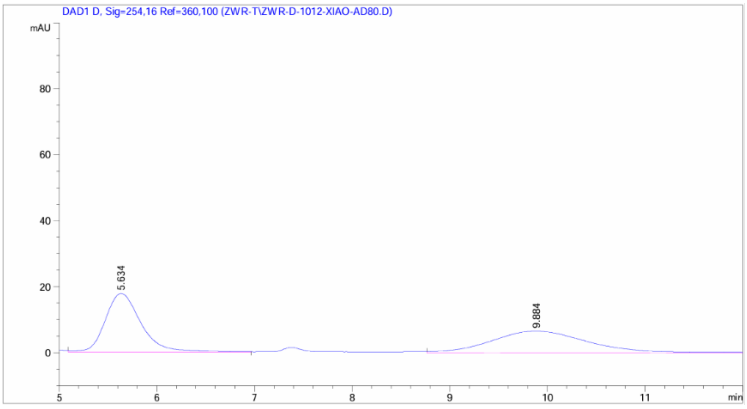
HPLC spectrum of the enantioenriched compound 3v



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	14.206	MM R	1.1596	1184.48694	17.02378	15.4339
2	17.393	MM R	1.7580	6490.08691	61.53027	84.5661

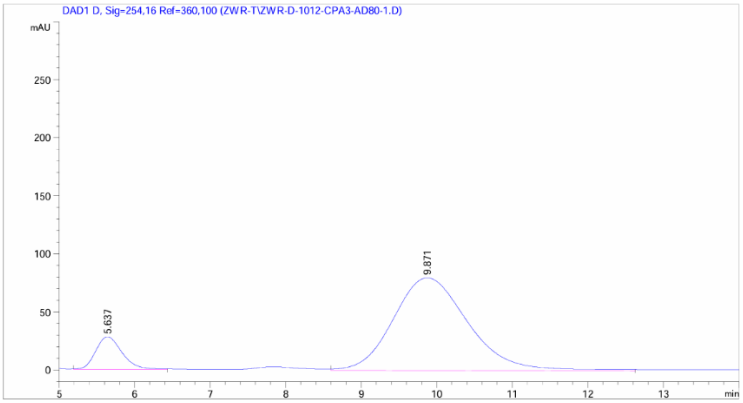
HPLC spectrum of the racemate 3w



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	5.634	MM R	0.4248	452.45154	17.75208	49.9719
2	9.884	MM R	1.1426	452.96094	6.60711	50.0281

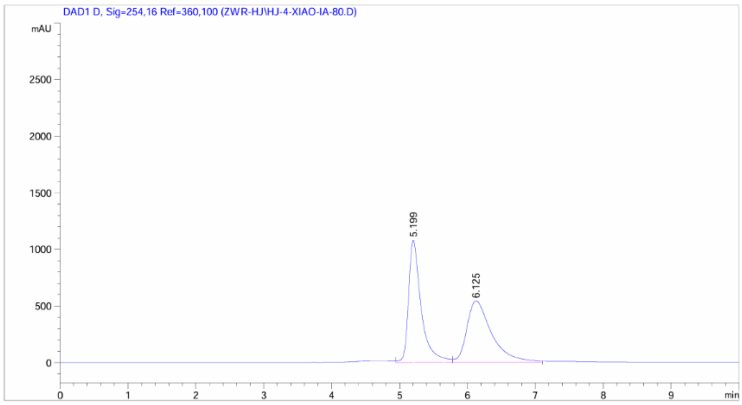
HPLC spectrum of the enantioenriched compound 3w



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	5.637	MM R	0.4038	680.04626	28.06696	10.9564
2	9.871	MM R	1.1533	5526.77148	79.86871	89.0436

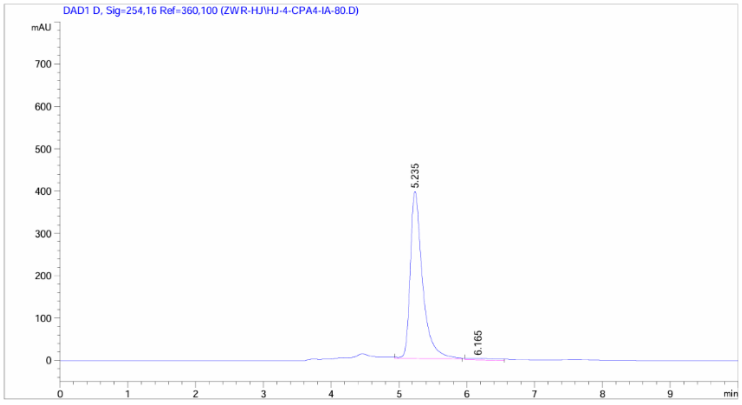
HPLC spectrum of the racemate 4



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	5.199	VV	0.1912	1.40113e4	1081.12573	50.1921
2	6.125	MF R	0.4263	1.39040e4	543.63312	49.8079

HPLC spectrum of the enantioenriched compound 4



信号 1: DAD1 D, Sig=254,16 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	5.235	MM R	0.2095	4963.60742	394.79053	97.6326
2	6.165	MM R	0.4976	120.36034	4.03110	2.3674

6. Determination of the absolute configuration of 3a

The software Crest [2] was used to explore the conformational space of potential structures within the GFN0 [3, 4] theoretical framework. The structure was optimized at the GFN2-xTB [4] level with a 4 kcal/mol energy threshold to exclude high-energy conformers. Geometry optimization and vibrational frequency calculations for the conformer were performed at the B3LYP-D3(BJ)/TZVP (IEFPCM, MeOH)) level of theory. Theoretical ECD spectrum were calculated by time-dependent density functional theory (TDDFT) at the B3LYP/TZVP (IEFPCM, MeOH) level. The ECD spectrum of compound **3a** was generated by Boltzmann averaging based on Gibbs free energy and simulated using SpecDis V1.71 [5], with a sigma/gamma value of 0.35 eV. All calculations were carried out using the Gaussian 09 [6] software package.

Compound **3a** was dissolved in methanol at a concentration of 0.01352 mM, and circular dichroism (CD) measurement was conducted in a 10 mm pathlength quartz cuvette. The UV and CD spectra were recorded using a JASCO J-1500 spectrophotometer with the following parameters: scanning range of 400–190 nm, step size of 0.2 nm, bandwidth of 4 nm, 2 s data integration time per point, and a scanning rate of 100 nm/min. A single spectral scan was performed for the sample, and the spectrum was smoothed to enhance data stability and accuracy.

The calculated spectrum of (*R*)-**3a** exhibited excellent agreement with the experimental data, thereby unequivocally confirming the absolute *R*-configuration of compound **3a**. (Fig. S1).

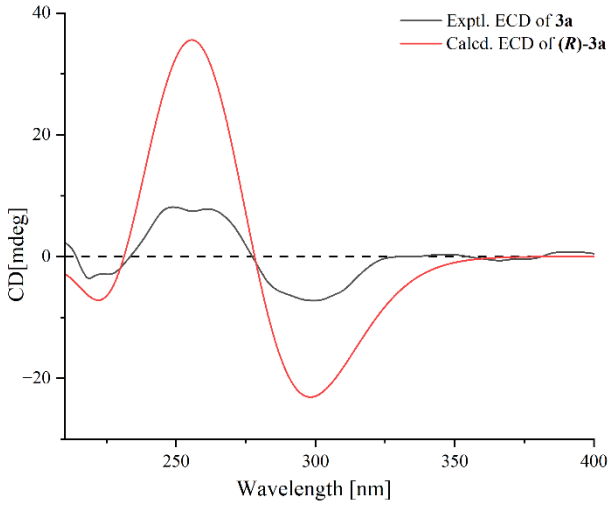


Fig. S1. Comparison of the calculated ECD of (*R*)-**3a** with the experimental one of **3a**.

Atomic coordinates (Å) of 3a obtained at the B3LYP-D3BJ/TZVP level of theory in methanol.

(*R*)-**3a**

delta G = 0.0000 kcal/mol

population = 30.95 %

C 4.589064 0.644095 -1.153225

C 5.238161 -0.152486 -0.206020

C 4.590165 -0.422732 1.006656

C 3.332320 0.089203 1.264687

C 2.667841 0.888044 0.325872

C 3.324630 1.151336 -0.878707

C 1.296307 1.394236 0.586770

N 6.515885 -0.709959 -0.387412

C 0.842831 2.675894 -0.022118

C 0.468167 0.723748 1.357306

C -0.370204 0.060014 2.099047

C -1.273929 -0.927466 1.422086

C -2.501520 -0.518086 0.911696

C -3.323706 -1.445329 0.272754

C -2.897935 -2.792222 0.147861

C -1.667920 -3.212505 0.646126

C -0.871474 -2.268941 1.278728

C -4.623806 -1.364091 -0.355673

C -4.928382 -2.666486 -0.832346

N -3.877964 -3.506039 -0.518368

C -5.533094 -0.323529 -0.549128

C -6.713681 -0.613547 -1.210723

C -7.018409 -1.894915 -1.682555

C -6.121720 -2.938410 -1.495509

Br -7.995681 0.798528 -1.495367

C -0.470356 0.256511 3.621855

C -0.461145 2.806540 -0.510661

C -0.906372 4.014107 -1.035127

C -0.052987 5.113217 -1.084273

C 1.248418 4.992968 -0.604331

C 1.693745 3.784753 -0.080483

C -1.906427 0.669988 3.985619

C -0.128929 -1.065202 4.330027

C 0.498632 1.348715 4.086265

C 7.376245 -0.596755 -1.444435

C 8.707759 -1.357472 -1.271389

O 7.114135 0.057516 -2.446284

C 9.474733 -0.788195 -0.062421

C 8.432415 -2.859104 -1.064785

C 9.549797 -1.169346 -2.536426

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H 5.084905 -1.032724 1.753635

H 2.853825 -0.130244 2.209836

H 2.837793 1.759237 -1.629435

H 6.834675 -1.272910 0.385581

H -2.810788 0.514502 1.010382

H -1.339176 -4.238269 0.540941

H 0.093448 -2.567298 1.666615

H -3.832425 -4.486244 -0.741987

H -5.322532 0.675707 -0.194022

H -7.953431 -2.074302 -2.193892

H -6.351925 -3.931285 -1.858734

H -1.122534 1.950052 -0.480394

H -1.918376 4.095070 -1.412273

H -0.397667 6.053672 -1.495323

H 1.918545 5.843201 -0.634782

H 2.705412 3.701752 0.294731

H -2.627635 -0.094559 3.695833

H -1.985210 0.818115 5.064926

H -2.180666 1.604400 3.491725

H -0.197868 -0.933620 5.412308

H 0.885927 -1.387723 4.088858

H -0.818072 -1.859727 4.042341

H 1.534022 1.082832 3.868010

H 0.284363 2.299468 3.595179

H 0.406218 1.491963 5.164561

H 9.643061 0.284283 -0.175936

H 8.949991 -0.951158 0.880362

H 10.446985 -1.278402 0.014020

H 7.897361 -3.064537 -0.136147

H 9.380397 -3.398321 -1.021390

H 7.846965 -3.267072 -1.890734

H 10.495491 -1.702079 -2.422896

H 9.036623 -1.560894 -3.414842

H 9.766185 -0.116119 -2.714358

7. References

[1] (a) Chen, M.; Qian, D.; Sun, J. *Org. Lett.* **2019**, *21*, 8127; (b) Xia, W.; An, Q.-J.; Xiang, S.-H.; Li, S.; Wang, Y.-B.; Tan, B. *Angew. Chem. Int. Ed.* **2020**, *59*, 6775.

[2] Pracht, P.; Bohle, F.; Grimme, S. *Phys. Chem. Chem. Phys.* **2020**, *22*, 7169.

[3] Grimme, S.; Bannwarth, C.; Shushkov, P. *J. Chem. Theory Comput.* **2017**, *13*, 1989.

[4] Bannwarth, C.; Ehlert, S.; Grimme, S. *J. Chem. Theory Comput.* **2019**, *15*, 1652.

[5] Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. *Chirality* **2013**, *25*, 243.

[6] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr., Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 09, Revision A.02; Gaussian, Inc.,: Wallingford, CT, 2016.