Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information for

Mechanistic insights into NH_4OAc-promoted imine dance in Rh-catalysed multicomponent double C−H annulations through N-retention/-exchange dual channel

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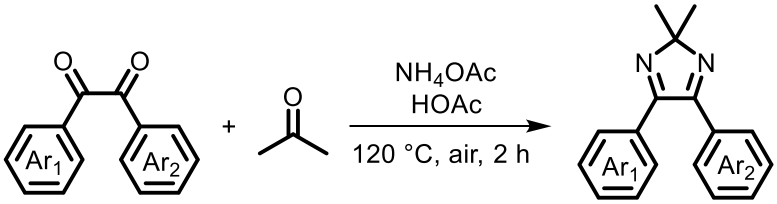
1 General remarks

NMR spectra were recorded on a BRUKER Ascend 500. The ^{1}H NMR (500 MHz) chemical shifts were measured relative to $CDCl_3$ or DMSO-d_6 as the internal reference ($CDCl_3$: δ = 7.26 ppm; DMSO-d_6: δ = 2.50 ppm). The ^{13}C NMR (125 MHz) chemical shifts were given using $CDCl_3$ or DMSO-d_6 the internal standard ($CDCl_3$: δ = 77.16 ppm; DMSO-d_6: δ = 39.52 ppm). High-resolution mass spectra (HRMS) were obtained with a BRUKER solanX 70 FT-MS (ESI$^+$). Melting points were determined with SGW® X-4 and are uncorrected. The diffraction data of crystals were collected on a Bruker APEX-II CCD with Ga- Ka radiation, λ = 1.34139 Å) at 260 K. at Shiyanjia lab (www.Shiyanjia.com).

All reagents were obtained from commercial suppliers and used without further purification. All reaction mixtures were heated with aluminum heating blocks and detected by TLC (thin layer chromatography) with silica gel-coated plates. $[(Cp^*RhCl_2)_2]$[1], alkynes **2**[2], furoxan **9**,[3] hexahydroquinoxaline **10**,[4] and cyclic iodoniums **12**[5] were prepared according to the literature procedures.

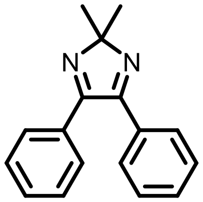
2 General procedure for the syntheses

2.1 General procedure A (GP A) for the synthesis of 2*H*-imidazoles 1



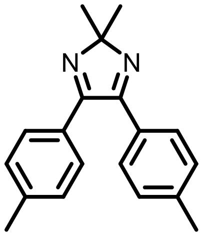
A solution of benzil (1 mmol), acetone (1.03 mmol, 1.03 equiv), NH_4OAc (504 mg, 7 mmol, 7 equiv) in glacial acetic acid (2 mL) was reacted at 120 °C for 2 h under air. After reaction completed, the reaction mixture was cooled to room temperature, then extracted with ethyl acetate. The combine organic phase was washed with saturated aq. $NaHCO_3$, dried with $MgSO_4$ and concentrated under vacuum to obtain crude products. The crude products were eluted by flash chromatography with petroleum ether/ethyl acetate (10/1) to afford the 2*H*-imidazole products **1**.

2,2-dimethyl-4,5-diphenyl-2*H*-imidazole (1a)



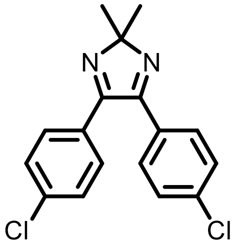
Brown solid (208.2 mg, 84% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 10/1, v/v). M.p.: 65.0–67.0 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.51 (d, J = 7.0 Hz, 4H), 7.45 (t, J = 7.3 Hz, 2H), 7.36 (t, J = 7.5 Hz, 4H), 1.67 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 164.3, 132.8, 130.3, 129.0, 128.4, 101.7, 24.3 ppm. Data in accordance with the literature.[6]

2,2-dimethyl-4,5-di-*p*-tolyl-2*H*-imidazole (1b)



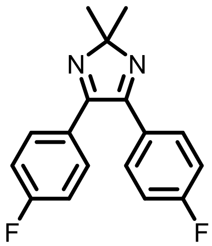
Brown solid (173.5 mg, 81% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 10/1, v/v). M.p.: 131.0–133.0 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.41 (d, J = 8.0 Hz, 4H), 7.16 (d, J = 7.5 Hz, 4H), 2.38 (s, 6H), 1.64 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 164.3, 140.4, 130.1, 129.1, 129.0, 101.3, 24.4, 21.6 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{19}H_{21}N_2$ ($[M+H]^+$) 277.1699, found 277.1694.

4,5-bis(4-chlorophenyl)-2,2-dimethyl-2*H*-imidazole (1c)



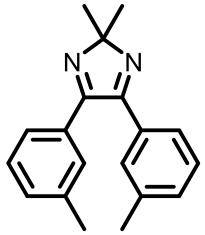
Brown solid (175 mg, 55% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 20/1→10/1, v/v). M.p.: 157–159 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.44 (d, J = 8.5 Hz, 4H), 7.36 (d, J = 8.0 Hz, 4H), 1.64 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 163.0, 136.8, 131.0, 130.3, 128.9, 102.2, 24.2 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{17}H_{15}Cl_2N_2$ ($[M+H]^+$) 317.0607, found 317.0608.

4,5-bis(4-fluorophenyl)-2,2-dimethyl-2*H*-imidazole (1d)



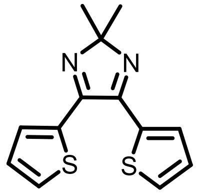
Brown solid (137 mg, 48% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 10/1, v/v). M.p.: 108–110 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.51–7.49 (m, 4H), 7.07 (t, J = 8.5 Hz, 4H), 1.64 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 164.1 (d, J_{C-F}= 249.5 Hz), 163.1, 131.1 (d, $J_{C\text{-}F}$= 8.6 Hz), 128.8 (d, $J_{C\text{-}F}$= 3.1 Hz), 115.7 (d, $J_{C\text{-}F}$= 21.8 Hz), 101.8, 24.2 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{17}H_{15}N_2F_2$ ($[M+H]^+$) 285.1198, found 285.1195.

2,2-dimethyl-4,5-di-*m*-tolyl-2*H*-imidazole (1e)



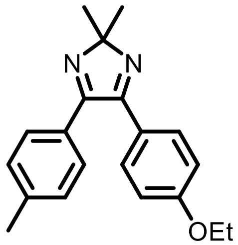
Brown oil (181.1 mg, 65% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 20/1→10/1, v/v). **^{1}H NMR (500MHz, $CDCl_3$):** δ = 7.50 (s, 2H), 7.29 (d, J = 2.5 Hz, 2H), 7.26–7.25 (m, 4H, cover the solvent), 2.39 (s, 6H), 1.71 (s, 6H) ppm. **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 164.5, 138.3, 132.8, 131.1, 129.6, 128.1, 126.2, 101.5, 24.4, 21.5 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{19}H_{21}N_2$ ($[M+H]^+$) 277.1699, found 277.1697.

2,2-dimethyl-4,5-di(thiophen-2-yl)-2*H*-imidazole (1f)



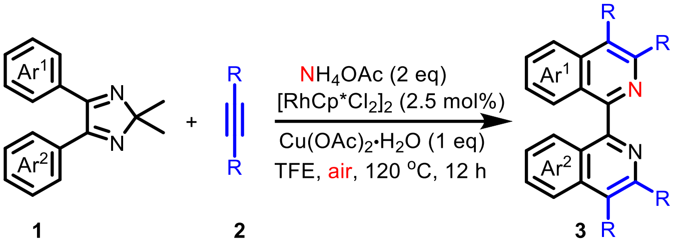
Brown solid (131.4 mg, 50% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 20/1→10/1, v/v). M.p.: 120–122 ºC. **^{1}H NMR (500MHz, $CDCl_3$):** δ = 7.50 (d, J = 4.5 Hz, 2H), 7.41 (d, J = 3.0 Hz, 2H), 7.08 (t, J = 4.3 Hz, 2H), 1.63 (s, 6H) ppm. **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 157.4, 134.9, 130.4, 129.6, 127.6, 101.7, 24.5 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{13}H_{13}N_2S_2$ ($[M+H]^+$) 261.0515, found 261.0514.

4-(4-ethoxyphenyl)-2,2-dimethyl-5-(*p*-tolyl)-2*H*-imidazole (1g)



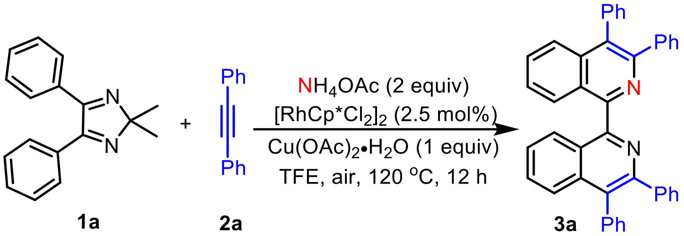
Brown oil (236.5 mg, 77% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 10/1→2/1, v/v). **^{1}H NMR (500MHz, $CDCl_3$):** δ = 7.46 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 7.5 Hz, 2H), 7.16 (d, J = 7.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 4.04 (q, J = 7.0 Hz, 2H), 2.38 (s, 3H), 1.63 (s, 6H), 1.41 (t, J = 7.0 Hz, 3H) ppm. **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 164.4, 163.8, 160.6, 140.3, 130.7, 130.2, 129.1, 128.9, 125.0, 114.2, 101.1, 63.6, 24.4, 21.6, 14.8 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{20}H_{23}N_2O$ ($[M+H]^+$) 307.1805, found 307.1805.

2.2 General procedure B (GP B) for the four-component reaction to synthesize 1,1′-BIQs



The mixture of 2*H*-imidazole **1** (0.1 mmol), alkyne **2** (0.2 mmol, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 8/1, v/v) to afford products **3**.

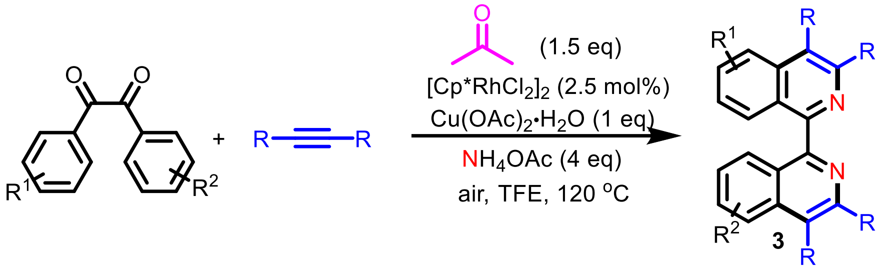
Table S1. *Optimization of the four-component reaction conditions*[a]



entry	variation from the standard conditions	yield (%)[b]
1	**none**	**93**
2	without NH$_4$OAc	26
3	NH$_4$OAc (1 equiv)	74
4	NH$_4$Cl or (NH$_4$)$_2$CO$_3$ instead of NH$_4$OAc	trace
5	RhCl$_3$·3H$_2$O as catalyst	n.d.
6	Cp*Co(CO)I$_2$ as catalyst	n.d.
7	[Ru(*p*-cymene)Cl$_2$]$_2$ as catalyst	trace
8	without Cu(OAc)$_2$·H$_2$O	35
9	under N$_2$	42
10	without Cu(OAc)$_2$·H$_2$O under N$_2$	18
11	Cu(OAc)$_2$·H$_2$O (0.5 equiv)	67
12	Cu(OAc)$_2$·H$_2$O (2 equiv)	89
13	Cu(OAc)$_2$·H$_2$O (2 equiv) under N$_2$	85
14	Ag$_2$CO$_3$ or AgOTf as oxidant	72, 54
15	HFIP as solvent	82
16	MeOH as solvent	12
17	DCE as solvent	trace
18	1,4-dioxane as solvent	n.d.

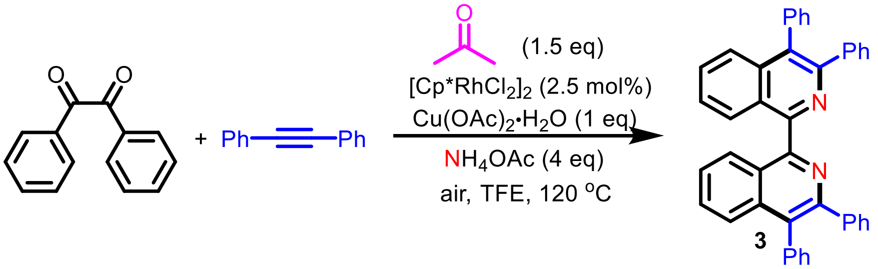
[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), NH_4OAc (2 equiv), $[Cp^*RhCl_2]_2$ (2.5 mol%) and $Cu(OAc)_2\cdot H_2O$ (1 equiv) in TFE (2 mL) at 120 °C for 12 h under air. [b]Isolated yield. TFE = trifluoroethanol, HFIP = hexafluoroisopropanol, DCE = 1,2-dichloroethane. n.d. = not detected.

2.3 General procedure C (GP C) for the six-component reaction to synthesize 1,1′-BIQs



The mixture of benzil (0.1 mmol), alkyne (0.2 mmol, 2 equiv), acetone (8.7 mg, 0.15 mmol, 1.5 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol%), $Cu(OAc)_2\cdot H_2O$ (20 mg, 0.1 mmol, 1 equiv), NH_4OAc (30.8mg, 0.4 mmol, 4 equiv) and TFE (2 mL) was stirred at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 8/1, v/v) to afford compounds **3**.

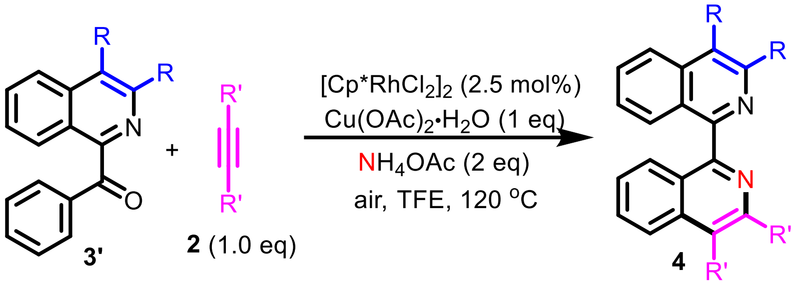
***Table S2**. Optimization of the six-component reaction conditions*



entry	acetone	NH_4OAc	yield (%)[b]
1	none	2 equiv	n.d.
2	1.5 equiv	2 equiv	25%
3	1.5 equiv	4 equiv	52%

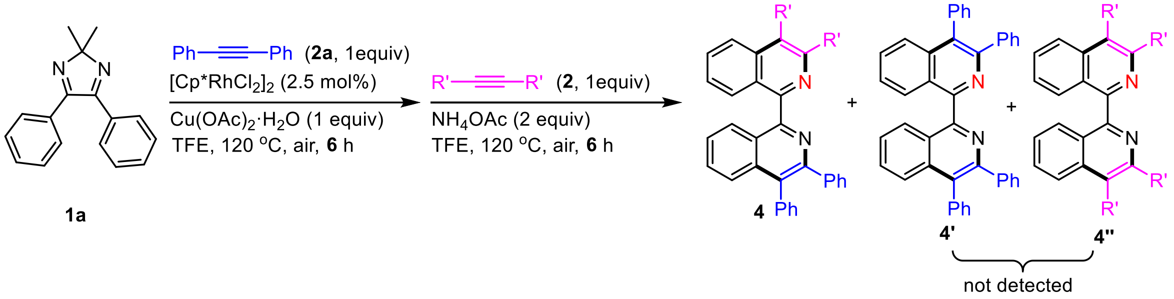
[a]Reaction conditions: benzil (0.1 mmol), alkyne **2a** (0.2 mmol), acetone (x equiv), NH_4OAc (y equiv), $[Cp^*RhCl_2]_2$ (2.5 mol%) and $Cu(OAc)_2\cdot H_2O$ (1 equiv) in TFE (2 mL) at 120 °C for 12 h under air. [b]Isolated yield. TFE = trifluoroethanol, n.d. = not detected.

2.4 General procedure D (GP D) for the synthesis of non-symmetric 1,1'-BIQs



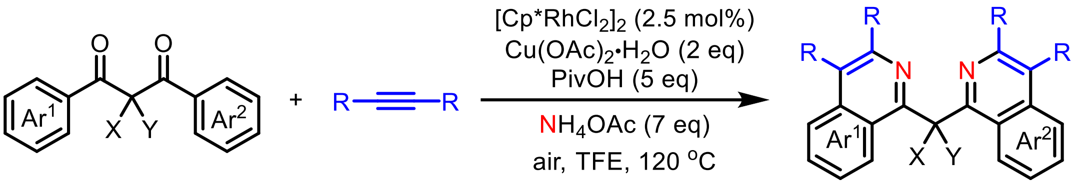
The mixture of **3′** (0.1 mmol), alkyne **2** (0.1 mmol, 1 equiv), [$(Cp^*RhCl_2)_2$] (1.6 mg, 2.5 mol%), $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 0.1 mmol, 1 equiv), NH_4OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 8/1, v/v) to afford non-symmetric products **4**.

2.5 General procedure E (GP E) for one-pot, two-step synthesis of non-symmetric 1,1'-BIQs



A solution of **1a** (24.8 mg, 0.1 mmol), alkyne **2a** (17.8 mg, 0.1 mmol, 1 equiv), [$(Cp^*RhCl_2)_2$] (1.6 mg, 2.5 mol%), $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 0.1 mmol, 1 equiv) and TFE (2 mL) was reacted at 120 °C for 6 h under air, then another molecule of alkyne **2** (0.1 mmol, 1 equiv) and NH_4OAc (15.4 mg, 0.2 mmol, 2 equiv) were added to the reactor. The resulting mixture was stirred at 120 °C for another 6 h under air. After reaction complete, the reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 8/1, v/v) to afford non-symmetric products **4**. (Notably, this reaction shows high chemo-selectivity, giving **4** solely without generation of **4′** and **4″**).

2.6 General procedure F (GP F) for the synthesis of C-bridged 1,1'-bisisoquinolines

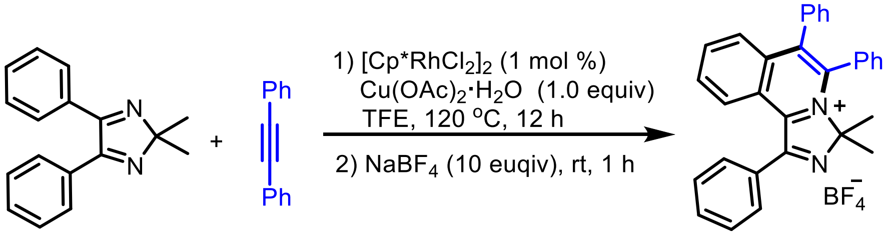


5

The mixture of 1,3-diketone (0.1 mmol), alkyne (0.2 mmol, 2 equiv), NH_4OAc (54 mg, 0.7 mmol, 7 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol%), $Cu(OAc)_2{\cdot}H_2O$ (40 mg, 0.2 mmol, 2 equiv), PivOH (102 mg, 0.5 mmol, 5 equiv) and TFE (2 mL) was stirred at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by flash chromatography with petroleum ether/ethyl acetate (80/1 → 40/1, v/v) to afford compounds **5**.

3 Control experiments for mechanistic studies

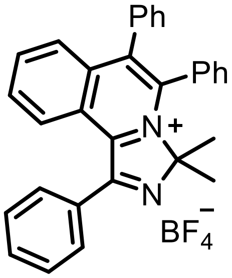
3.1 Synthesis of compound Int-C



1a (1 equiv) **Int-C**, 90%

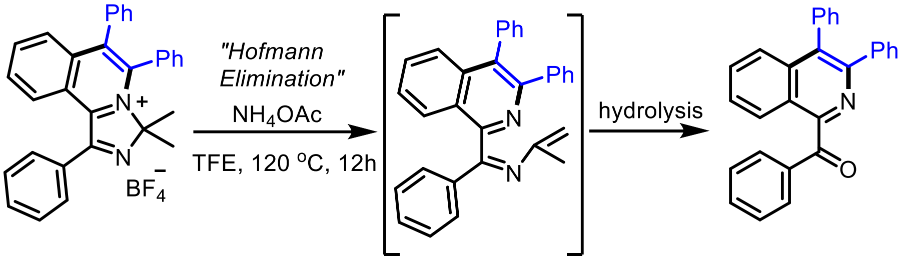
A solution of **1a** (24.8 mg, 0.1 mmol), alkyne **2a** (17.8 mg, 0.1 mmol, 1 equiv), $[(Cp^*RhCl_2)_2]$ (0.6 mg, 1 mol%), $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 0.1 mmol, 1 equiv) and TFE (2 mL) was reacted at 120 °C for 12 h under air. Then $NaBF_4$ (110 mg, 1 mmol, 10 equiv) was added to the reaction mixture for reacting at room temperature for another 1h. The reaction mixture was concentrated under vacuum and the residue was purified by a silica gel (100−200 mesh) column, eluting with CH_2Cl_2/CH_3OH (80/1 → 10/1, v/v) to afford **Int-C** as a yellow solid.

3,3-dimethyl-1,5,6-triphenyl-3*H*-imidazo[5,1-*a*]isoquinolin-4-ium tetrafluoroborate (Int-C)



Yellow solid (46.3mg, 90% yield). M.p.: >250 °C. **^{1}H NMR (500MHz, DMSO-*d*$_6$):** δ = 8.19 (t, J = 7.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.97 (t, J = 7.5 Hz, 1H), 7.89–7.87 (m, 2H), 7.81–7.78 (m, 3H), 7.62–7.58 (m, 3H), 7.48–7.36 (m, 6H), 7.24 (d, J = 6.5 Hz, 2H), 1.77 (s, 6H) ppm. **^{13}C NMR (125 MHz, DMSO-*d*$_6$):** δ = 162.3, 146.3, 142.8, 139.6, 139.3, 136.8, 133.2, 132.6, 132.6, 131.3, 131.2, 130.5, 130.0, 129.6, 129.3, 128.7, 128.6, 128.3, 127.4, 127.0, 126.3, 122.1, 104.0, 24.5 ppm. **^{19}F NMR (470 MHz, DMSO-*d_6*):** δ = -148.35, -148.45 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{31}H_{25}N_2$ ([M−BF_4^-]$^+$ 425.2012, found 425.2010.

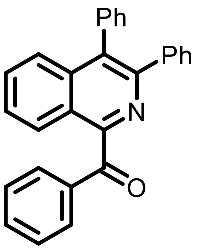
3.2 Hofmann elimination proof (converting Int-C to 3a′)



Int-C **Int-C'** **3a'**, 92%

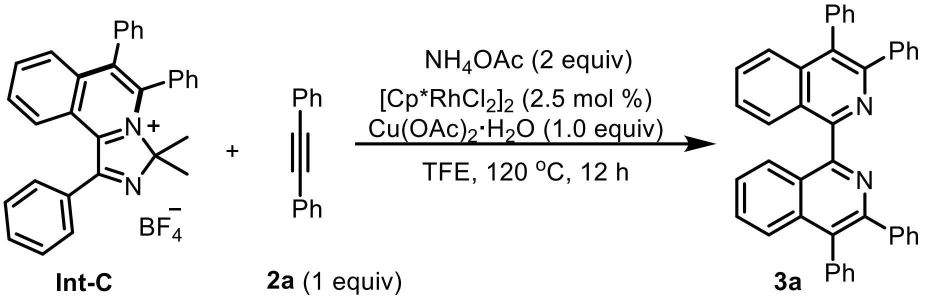
A solution of **In-C** (51.2 mg, 0.1 mmol), NH_4OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a silica gel (100−200 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 80/1, v/v) to afford **3a′** as a white solid (35.6 mg, 92% yield).

(3,4-diphenylisoquinolin-1-yl)(phenyl)methanone (3a′)



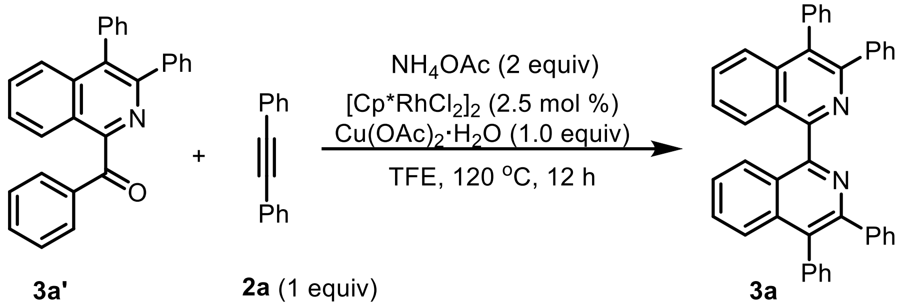
Yellow solid (36.5 mg, 95% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 100/1→80/1, v/v). **^{1}H NMR (500MHz, $CDCl_3$):** δ = 8.25 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 7.0 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.66–7.58 (m, 3H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.43–7.37 (m, 5H), 7.32–7.31 (m, 2H), 7.18–7.17 (m, 3H) ppm. **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 194.9, 155.9, 149.0, 140.2, 137.2, 137.1, 136.8, 133.8, 132.5, 131.3, 131.1, 130.8, 130.5, 128.6, 128.6, 127.8, 127.4, 126.4, 126.1, 125.2 ppm. The NMR data are consistent with the literature.[7]

3.3 Synthesis of 3a from Int-C



A solution of **Int-C** (51.2 mg, 0.1 mmol), alkyne **2a** (17.8 mg, 0.1 mmol, 1 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at 120 °C for 12 h under air. The reaction gave **3a** as a white solid (39.2 mg, 70% yield) by purifying through a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 80/1, v/v).

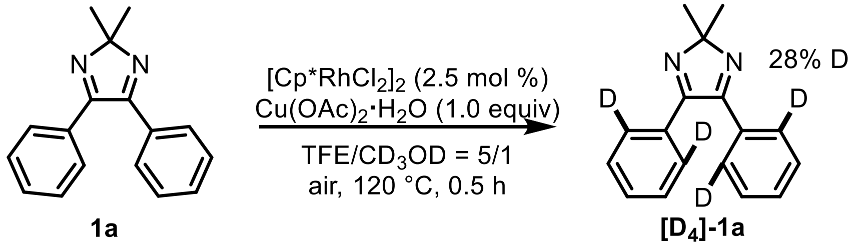
3.4 Synthesis of 3a from 3a′



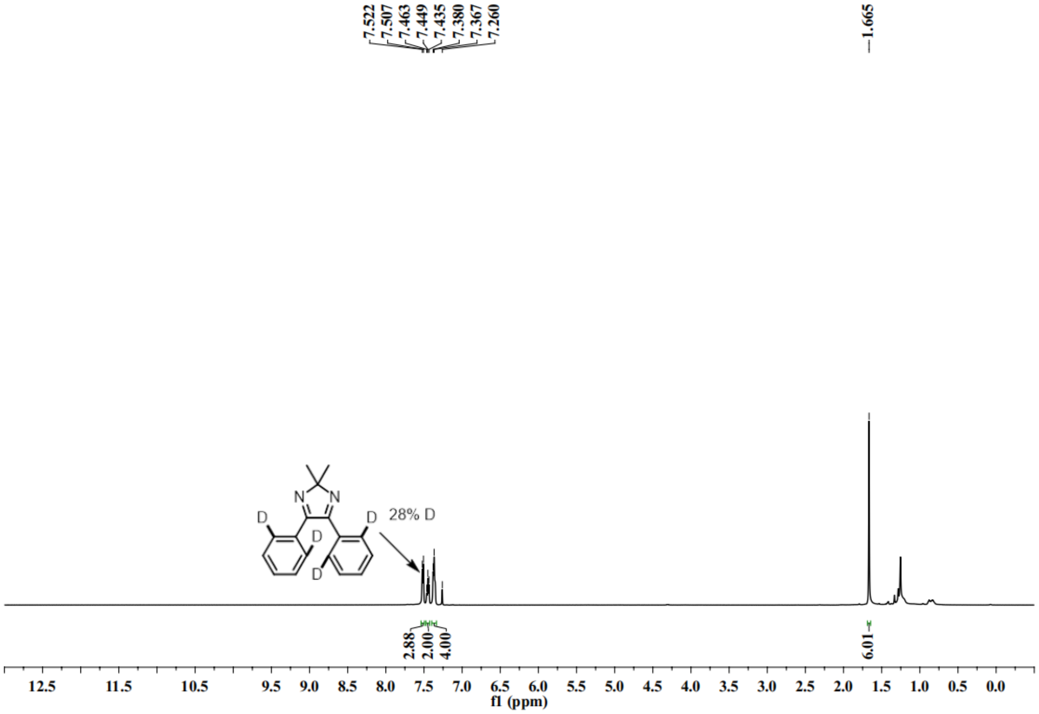
The reaction of **3a′** (38.5 mg, 0.1 mmol), alkyne **2a** (17.8 mg, 0.1 mmol, 1 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) at 120 °C for 12 h under air afforded **3a** as a white solid (55 mg, 98% yield).

4 Isotope labeling experiments

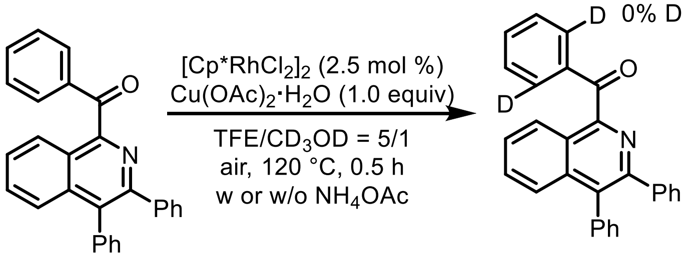
4.1 H/D exchange experiments



The mixture of **1a** (12.4 mg, 0.05 mmol), [(Cp*RhCl$_2$)$_2$] (0.8 mg, 2.5 mol %), Cu(OAc)$_2$·H$_2$O (10 mg, 0.05 mmol, 1 equiv) in TFE (1 mL) and CD$_3$OD (0.2 mL) was reacted at 120 °C for 0.5 h under air. After the reaction was cooled down, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with petroleum ether/EtOAc (10/1 → 5/1, v/v) to afford **[D$_4$]-1a**. ^{1}H NMR analysis showed that (4-2.88)/4=28% hydrogen at the *ortho* positions of the phenyl ring was deuterated.

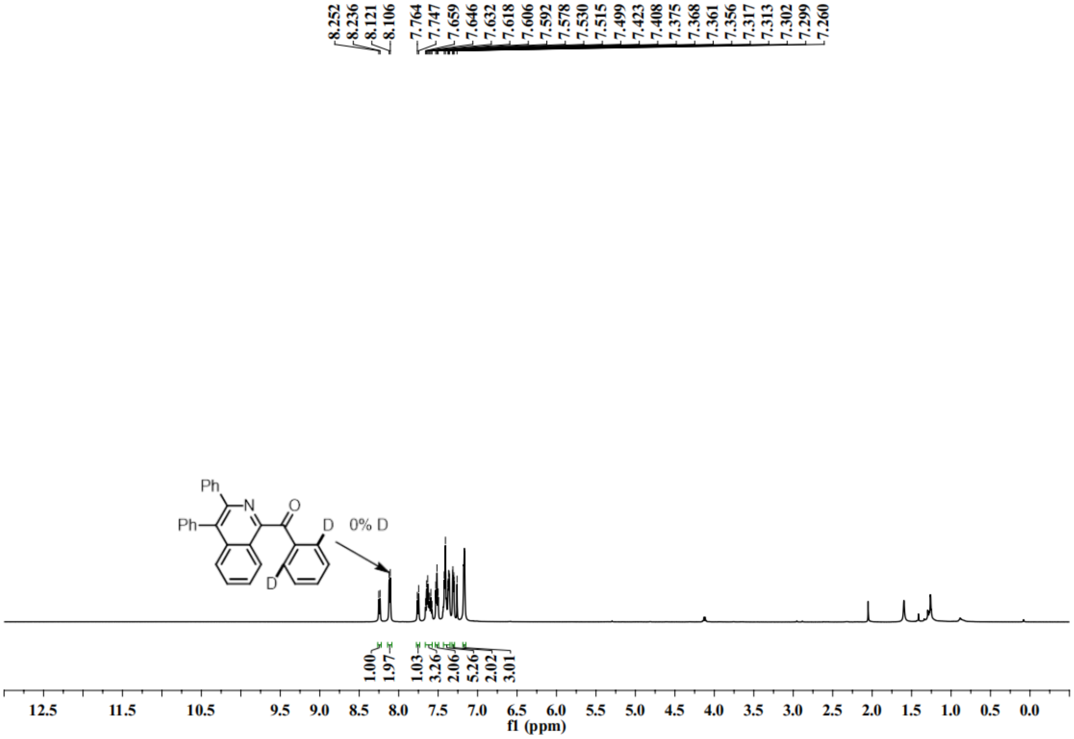


^{1}H NMR (500 MHz, CDCl$_3$) of **[D$_4$]-1a**

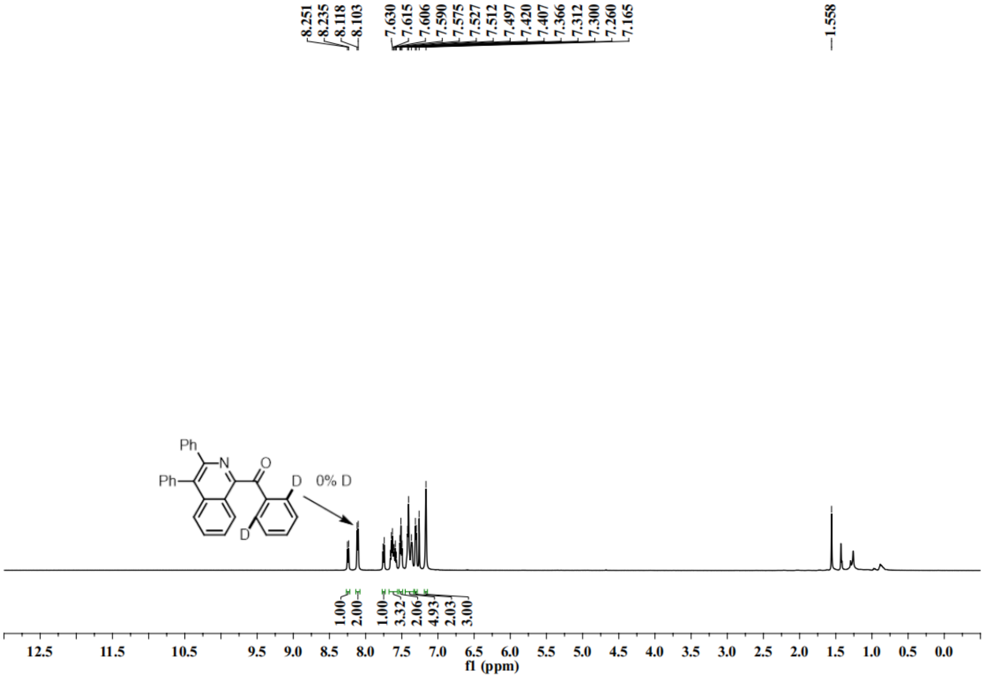


3a' **[D$_2$]-3a'**

The mixture of **3a′** (19.3 mg, 0.05 mmol), [(Cp*RhCl$_2$)$_2$] (0.8 mg, 2.5 mol %), Cu(OAc)$_2$·H$_2$O (10 mg, 0.05 mmol, 1 equiv), with or without NH$_4$OAc (7.7 mg, 0.1 mmol, 2 equiv) in TFE (1 mL) and CD$_3$OD (0.2 mL) was reacted at 120 °C for 0.5 h under air. After the reaction was cooled down, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel, eluting with petroleum ether/EtOAc (10/1 → 5/1, v/v) to afford **[D$_2$]-3a′**. ^{1}H NMR analysis showed that 0% hydrogen at the *ortho* positions of the phenyl ring was deuterated.



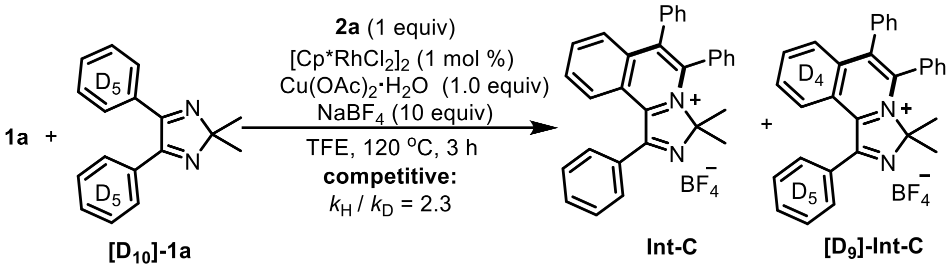
^{1}H NMR (500 MHz, $CDCl_3$) of **[D$_2$]-3a′** (with NH_4OAc)



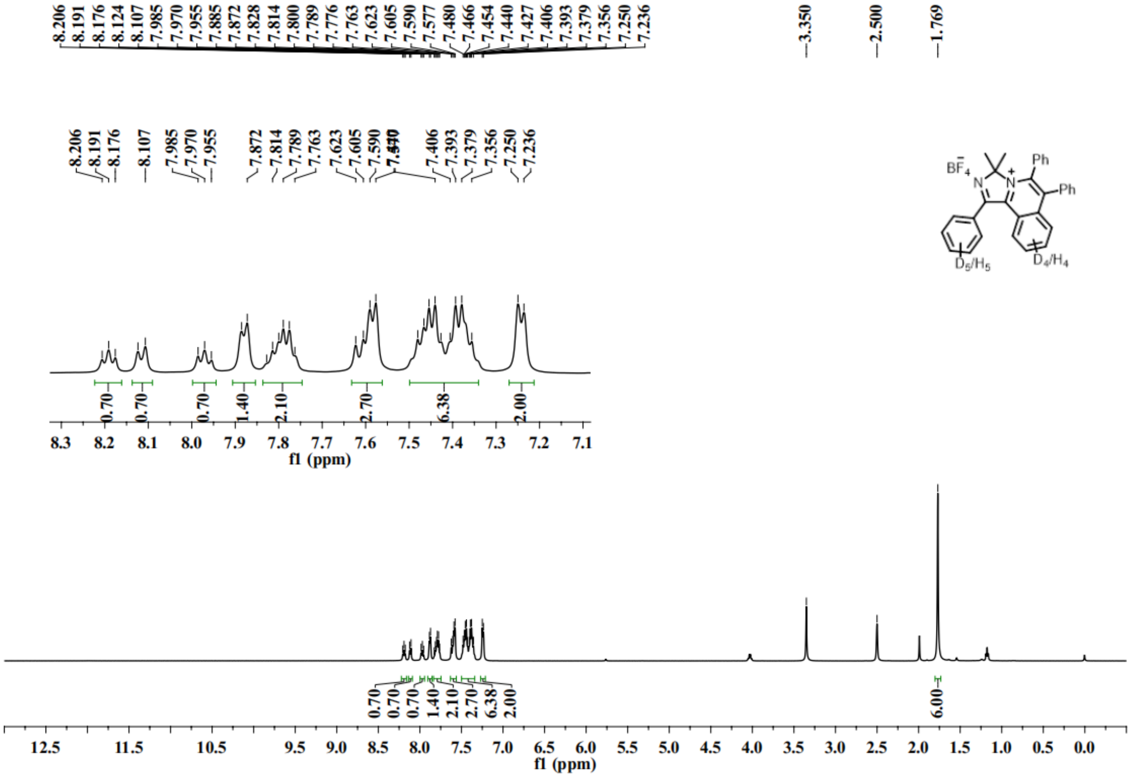
^{1}H NMR (500 MHz, $CDCl_3$) of **[D$_2$]-3a′** (without NH_4OAc)

4.2 Kinetic isotope effect (KIE) studies

KIE of the first C-H activation

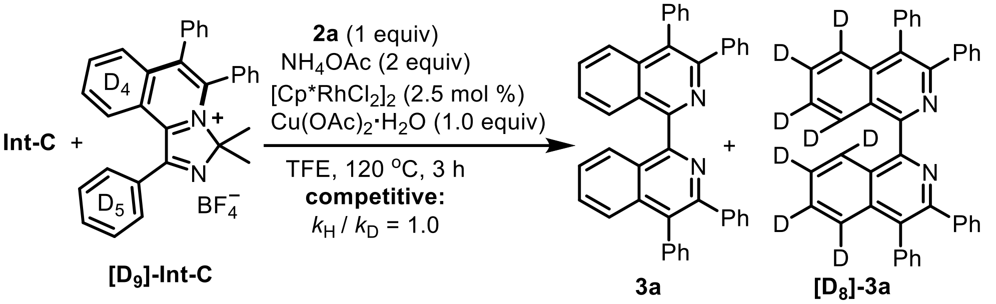


The mixture of **1a** (12.4 mg, 0.05 mmol), **[D$_{10}$]-1a** (12.9 mg, 0.05 mmol), **2a** (0.05 mmol, 8.9 mg, 1 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol %), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.05 mmol, 1 equiv) and TFE (2 mL) was reacted at 120 °C for 3 h under air. After the reaction was cooled down the solvent was evaporated under reduced pressure and the residue was purified by a silica gel (100−200 mesh) column, eluting with CH_2Cl_2/CH_3OH (80/1 → 10/1, v/v) to afford the mixture of **Int-C** and **[D$_9$]-Int-C**. The ratio of **Int-C/([D$_9$]-Int-C**) was determined to be 2.3 ($k_H/k_D \approx 0.7/[1-0.7] = 2.3$) by ^{1}H NMR.

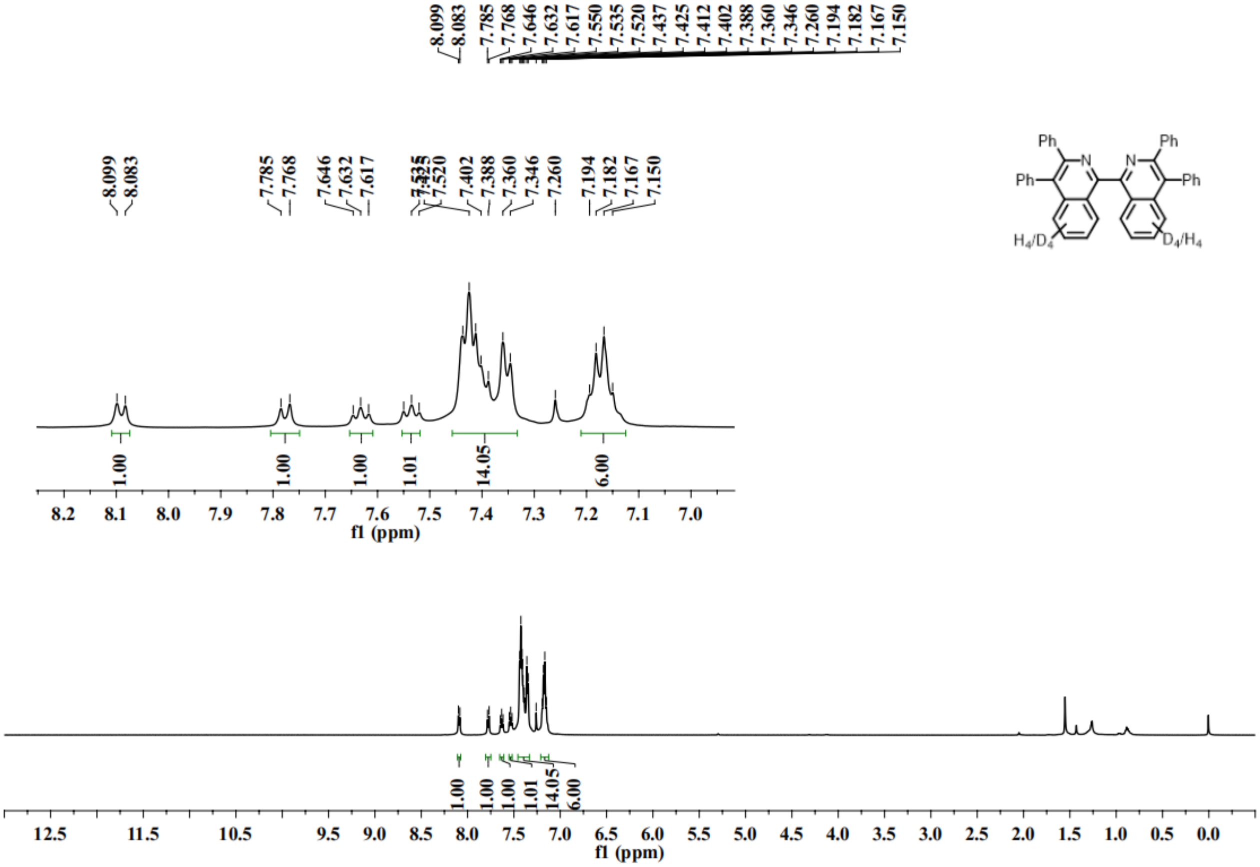


^{1}H NMR (500 MHz, DMSO-d_6) of **Int-C** and **[D$_9$]-Int-C**

KIE of the second C-H activation

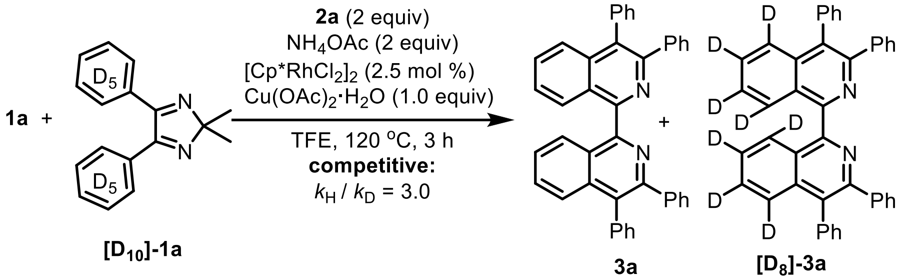


The mixture of **Int-C** (25.6 mg, 0.05 mmol), **[D$_9$]-Int-C** (26.1 mg, 0.05 mmol), **2a** (0.05 mmol, 8.9 mg, 1 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol %), Cu(OAc)$_2$·H$_2$O (20 mg, 0.05 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.1 mmol, 2 equiv) and TFE (2 mL) was reacted at 120 °C for 3 h under air. After the reaction was completed, the solvent was evaporated and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 60/1, v/v) to afford the mixture of **3a** and **[D$_8$]-3a**. The ratio of **3a**/(**[D$_8$]-3a**) was determined to be 1.0 ($k_H/k_D \approx 1/[2-1] = 1.0$) by ^{1}H NMR.

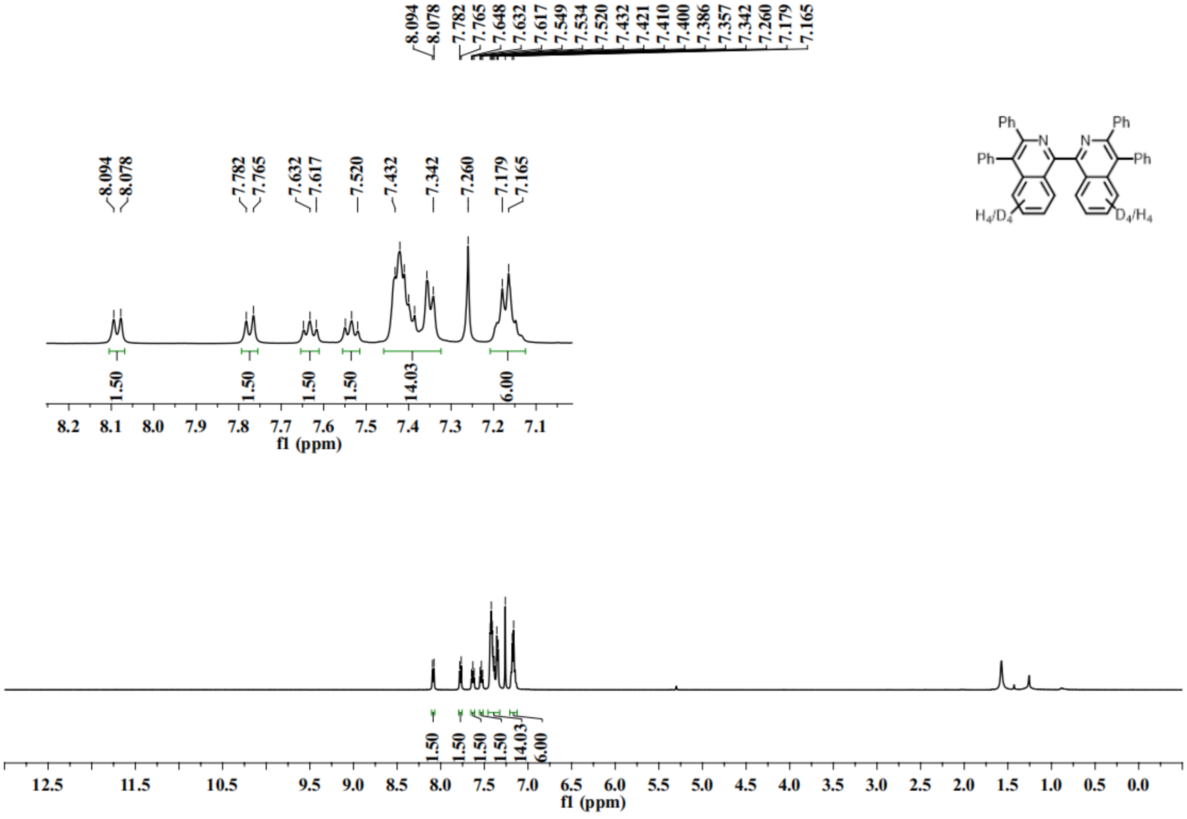


^{1}H NMR (500 MHz, CDCl$_3$) of **3a** and **[D$_8$]-3a**

KIE of the double C-H activation

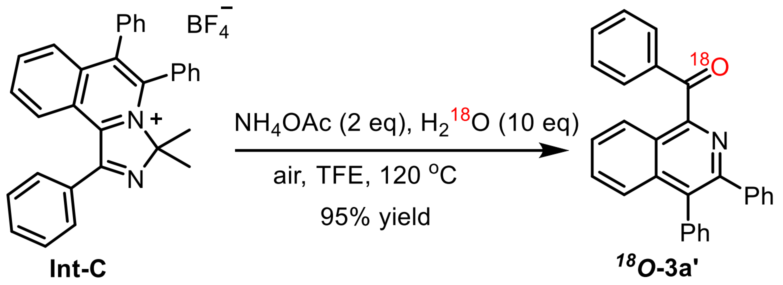


The mixture of **1a** (12.4 mg, 0.05 mmol), **[D$_{10}$]-1a** (12.9 mg, 0.05 mmol), **2a** (0.1 mmol, 17.8 mg, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol %), Cu(OAc)$_2$·H$_2$O (20 mg, 0.05 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.1 mmol, 2 equiv) and TFE (2 mL) was reacted at 120 °C for 3 h under air. The reaction was cooled down before the solvent was evaporated under reduced pressure. The residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 50/1, v/v) to afford the mixture of **3a** and **[D$_8$]-3a**. The ratio of **3a**/(**[D$_8$]-3a**) was determined to be 3.0 ($k_H/k_D \approx 1.5/[2\text{-}1.5]=3.0$) by ^{1}H NMR.



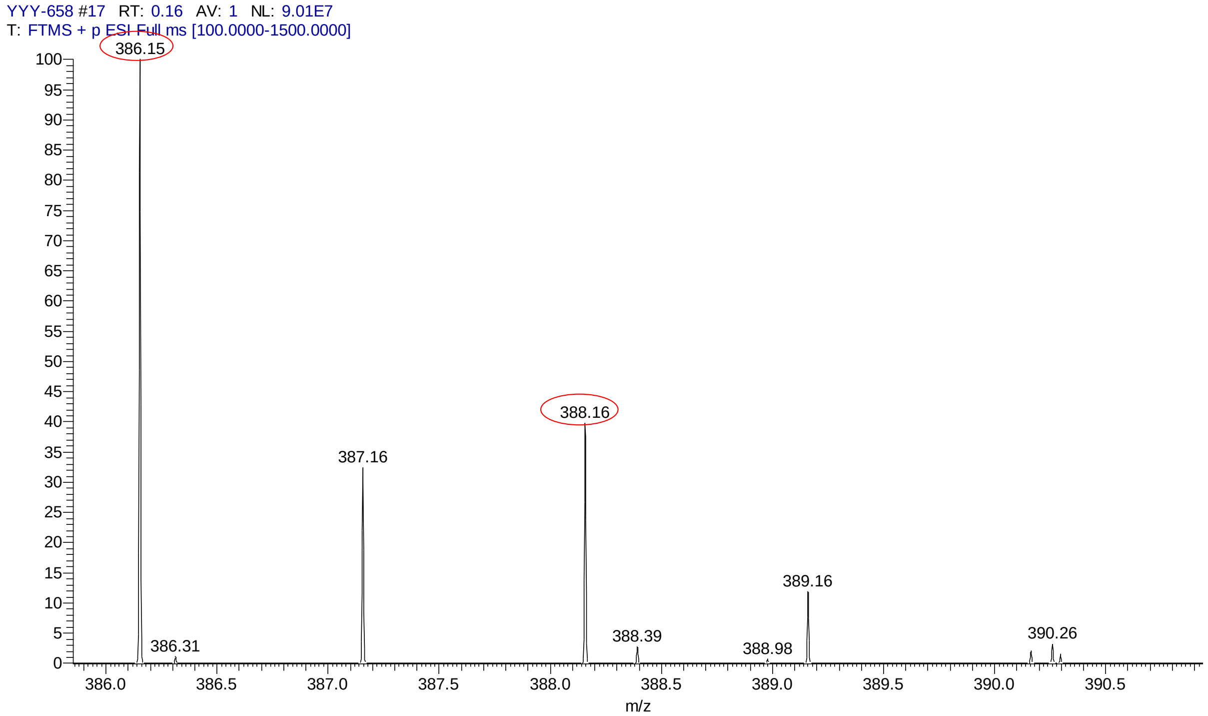
^{1}H NMR (500 MHz, CDCl$_3$) of **3a** and **[D$_8$]-3a**

4.3 ^{18}O labeling experiment



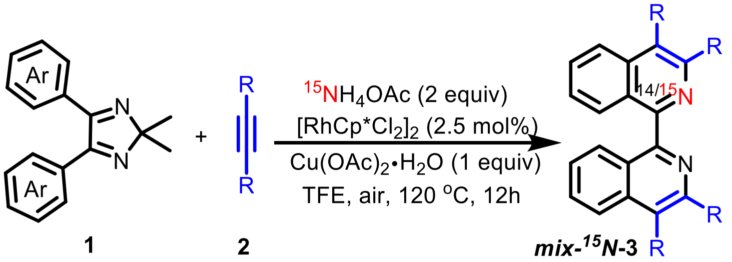
The mixture of **Int-C** (51.2 mg, 0.1 mmol), NH_4OAc (15.4 mg, 0.2 mmol, 2 equiv), $H_2{}^{18}O$ (18 µL, 1 mmol, 10 equiv) and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was purified by a silica gel (100−200 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 40/1, v/v) to afford ***^{18}O*-3a′** as a yellow solid (36.6 mg, 95% yield).

***^{18}O*-3a′** was dissolved in methanol and filtered with a cotton pad, and the filtrate was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap). HRMS analysis showed that the abundance of ^{18}*O* in **3a′** was 27%.



m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	100	100	73
[M+H] + 2	4.4	41.2	36.8	**27**

4.4 ^{15}N labeling experiments



Synthesis: The mixture of **1** (0.1 mmol), **2** (0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol %), $Cu(OAc)_2·H_2O$ (20 mg, 0.1 mmol, 1 equiv), $^{15}NH_4OAc$ (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was reacted at 120 °C for 10 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 40/1, v/v) to afford product **mix-^{15}N-3**.

^{15}N test: mix-^{15}N-3 was dissolved in methanol and filtered with a cotton pad, and the filtrate was diluted with the methanol and analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap).

Determination of ^{15}N Incorporation: Percent ^{15}N isotope incorporation was determined by comparison of the mass spectral patterns of ^{15}N-labeled product versus ^{14}N-counterpart and calculated by the expressions below.[8]

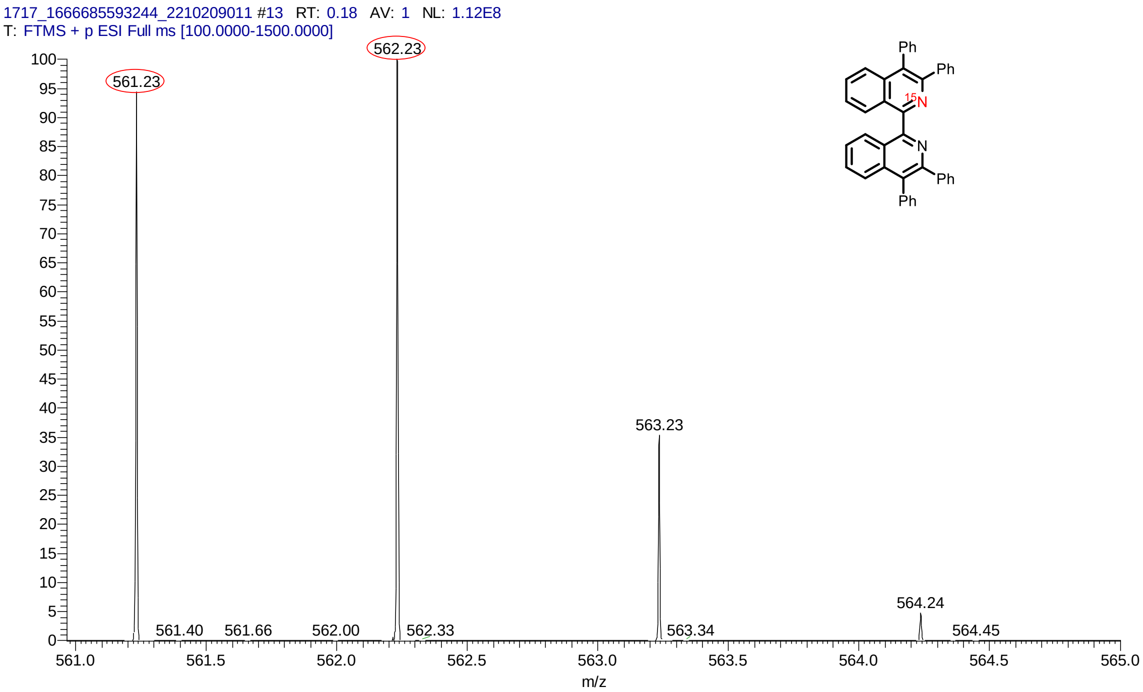
% ^{15}N incorp. = [(Corrected abundance of ^{15}N) / (Corrected abundance of ^{15}N + Observed abundance of ^{14}N], where observed abundance of ^{14}N is obtained from the mass signal intensities at [M] (*m/z*).

Corrected Abundance of ^{15}N = Observed abundance of ^{15}N – (Observed abundance of ^{14}N × Relative natural abundance of ^{15}N / 100), where observed abundance of ^{15}N is obtained from the mass signal intensities at [M+1] (*m/z*).

Representative Example (mix-^{15}N-3a):

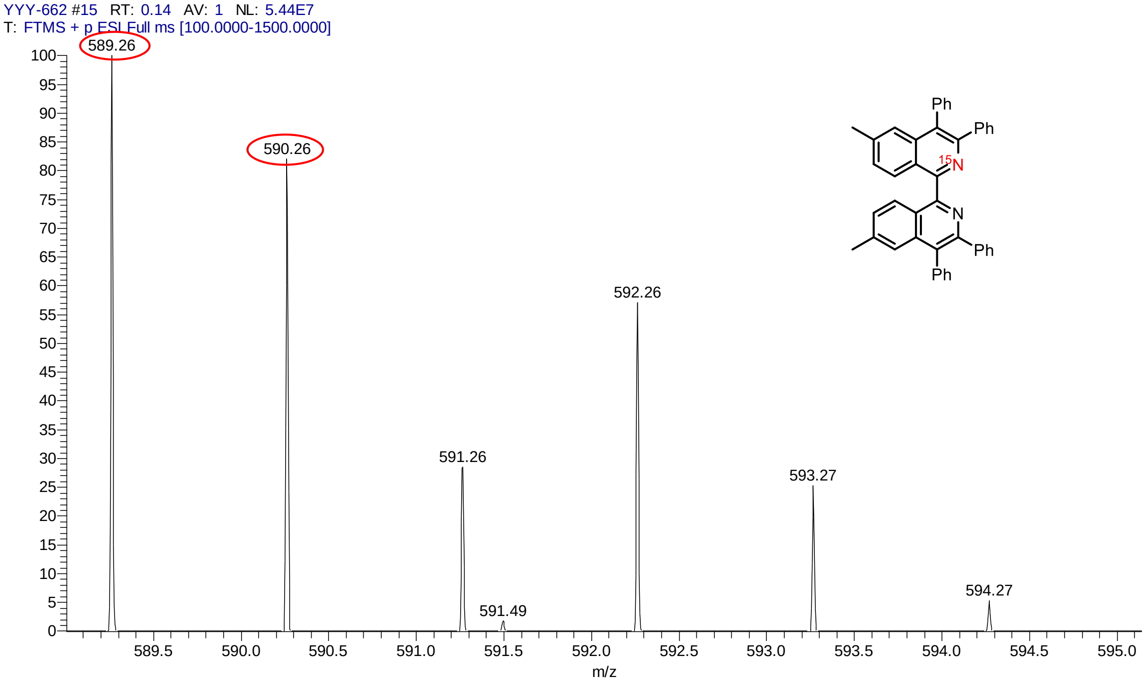
Corrected abundance of ^{15}N of **3a** = 100 – (91.19 × 45.4/100) = 100 – 41.4 = 58.6%

% ^{15}N incorp. of **3a** = 58.6/ (58.6+91.19) = 58.6/149.79 = 39 %



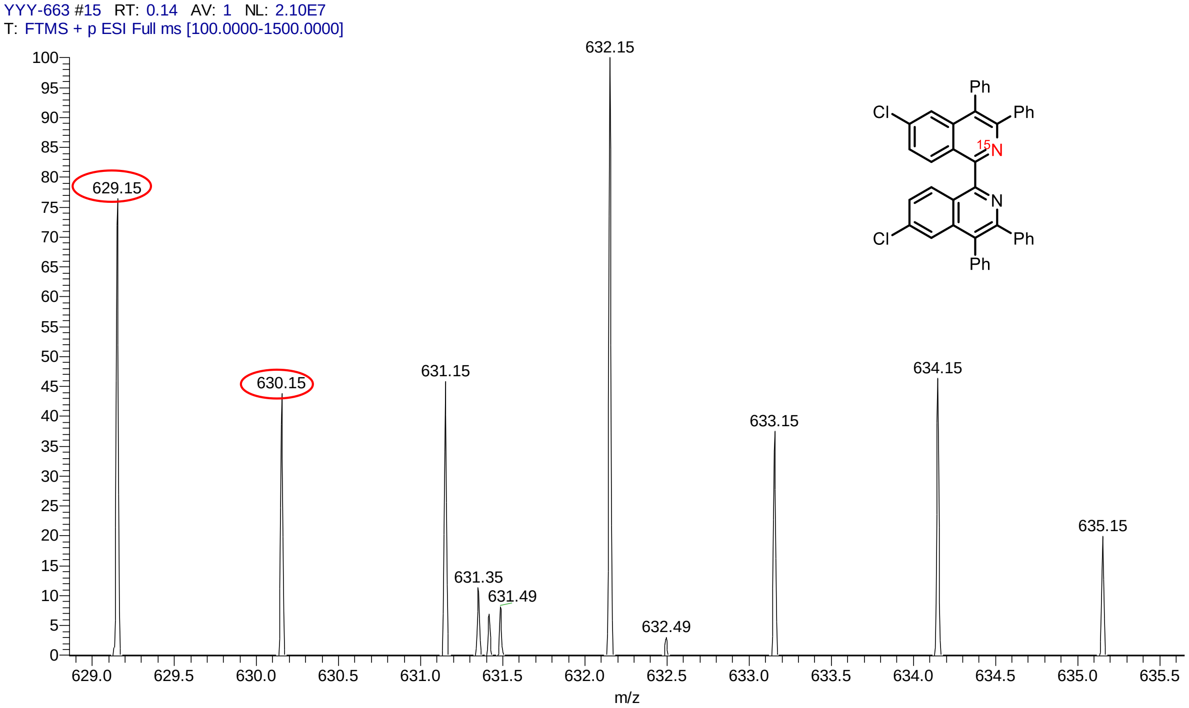
m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	91.19	91.19	61
[M+H] + 1	45.4	100	58.6	**39**

According to above procedure, **mix-^{15}N-3a** was obtained as with solid (51.6 mg, 92% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3a** was 39%.



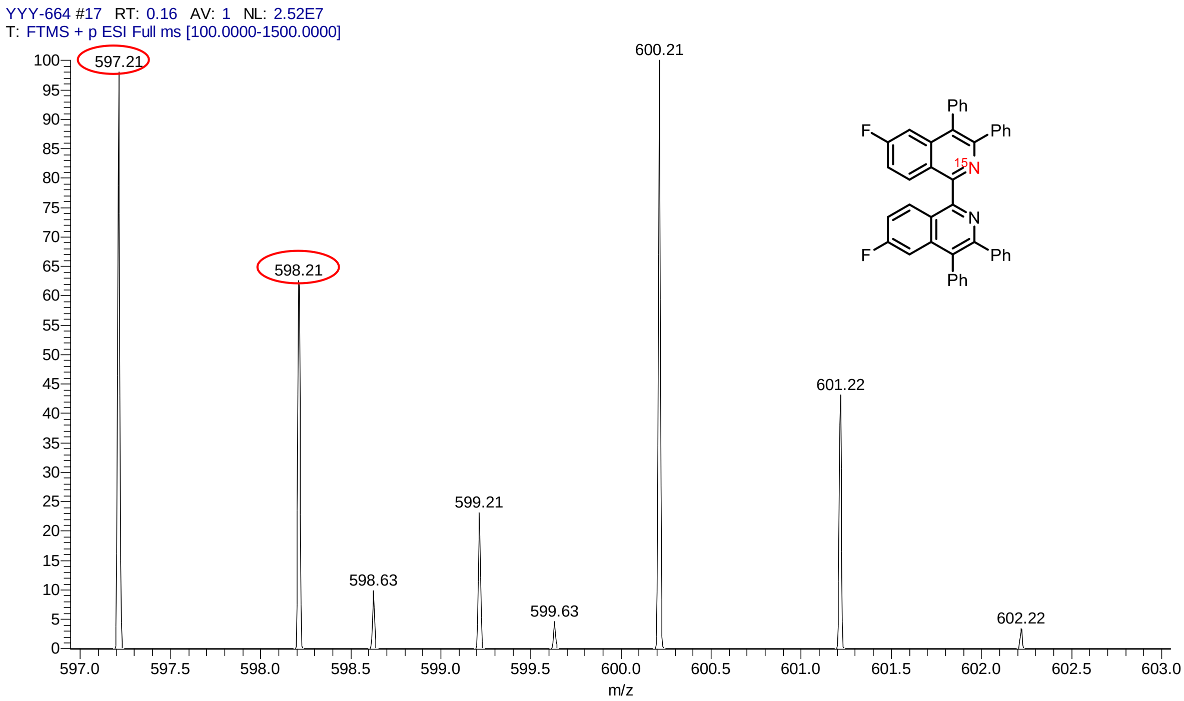
m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	100	100	70
[M+H] + 1	47.6	89.54	41.94	**30**

According to above procedure, **mix-^{15}N-3b** was obtained as with solid (33.4 mg, 57% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3b** was 30%.



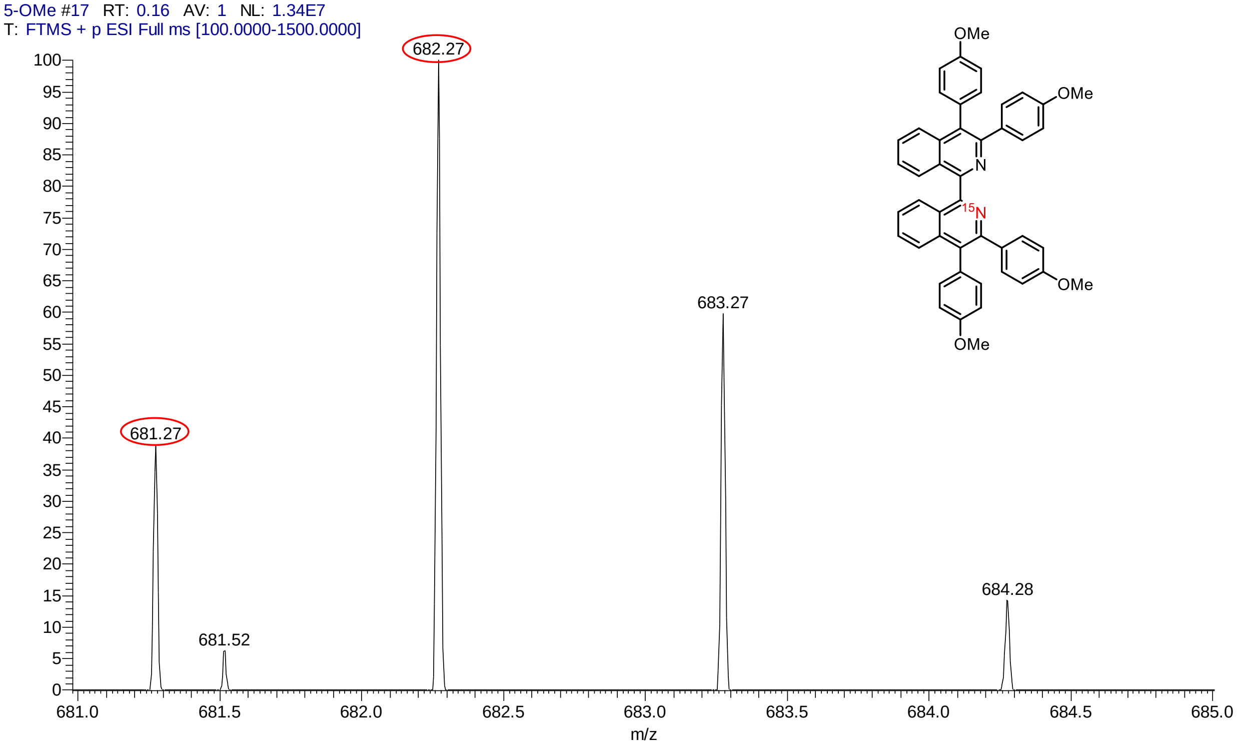
m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	78.73	78.73	91
[M+H] + 1	45.4	43.97	8.23	**9**

According to above procedure, **mix-^{15}N-3c** was obtained as with solid (46.9 mg, 77% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3c** was 9%.



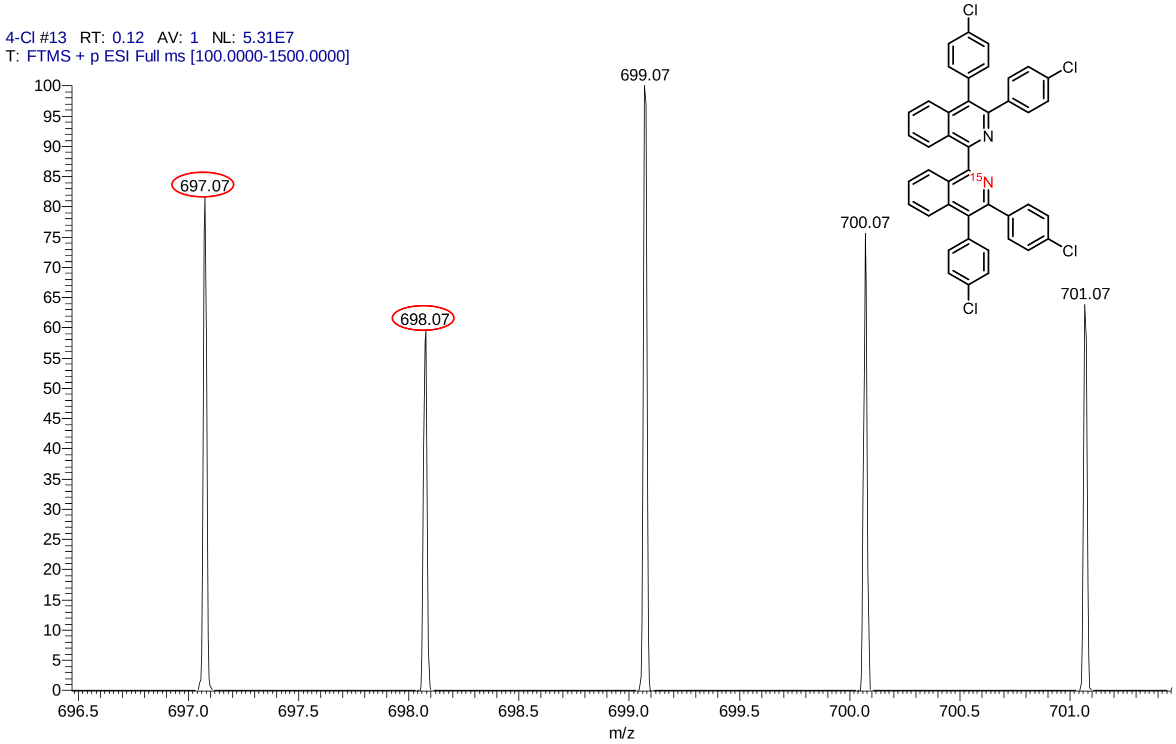
m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	100	100	84
[M+H] + 1	45.4	64.93	19.53	**16**

According to above procedure, **mix-^{15}N-3d** was obtained as with solid (24.3 mg, 41% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3d** was 16%.



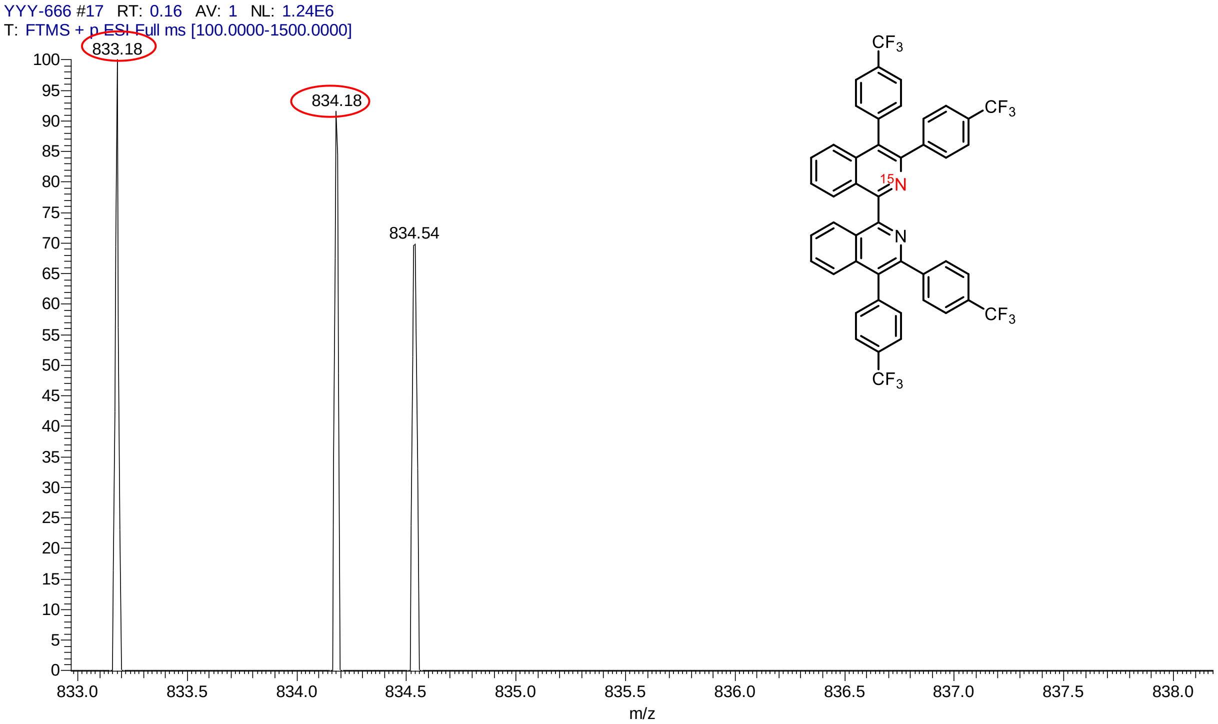
m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	39.17	39.17	33
[M+H] + 1	49.8	100	80.49	**67**

According to above procedure, **mix-^{15}N-3j** was obtained as with solid (32.7 mg, 48% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3j** was 67%.



m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	78.2	80.22	80.22	72
[M+H] + 1	35.5	59.44	30.96	**28**

According to above procedure, **mix-^{15}N-3k** was obtained as with solid (44.6 mg, 64% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3k** was 28%.

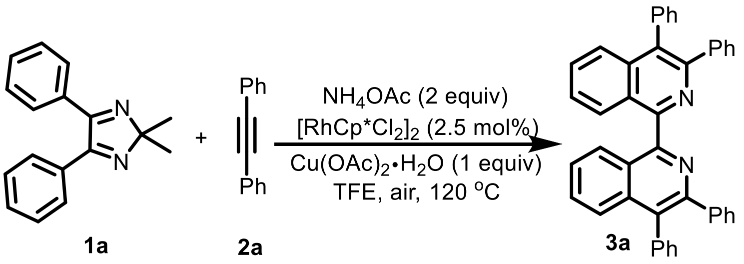


m/z	Relative Natural Abundance (%)	Observed Abundance (%)	Corrected Abundance (%)	Isotopic Enrichment Relative (%)
[M+H] + 0	100	100	100	70
[M+H] + 1	49.8	93.03	43.23	**30**

According to above procedure, **mix-^{15}N-3m** was obtained as with solid (60.8 mg, 73% yield), and HRMS analysis showed that the abundance of ^{15}N in **mix-^{15}N-3m** was 30%.

5 ESI-MS studies

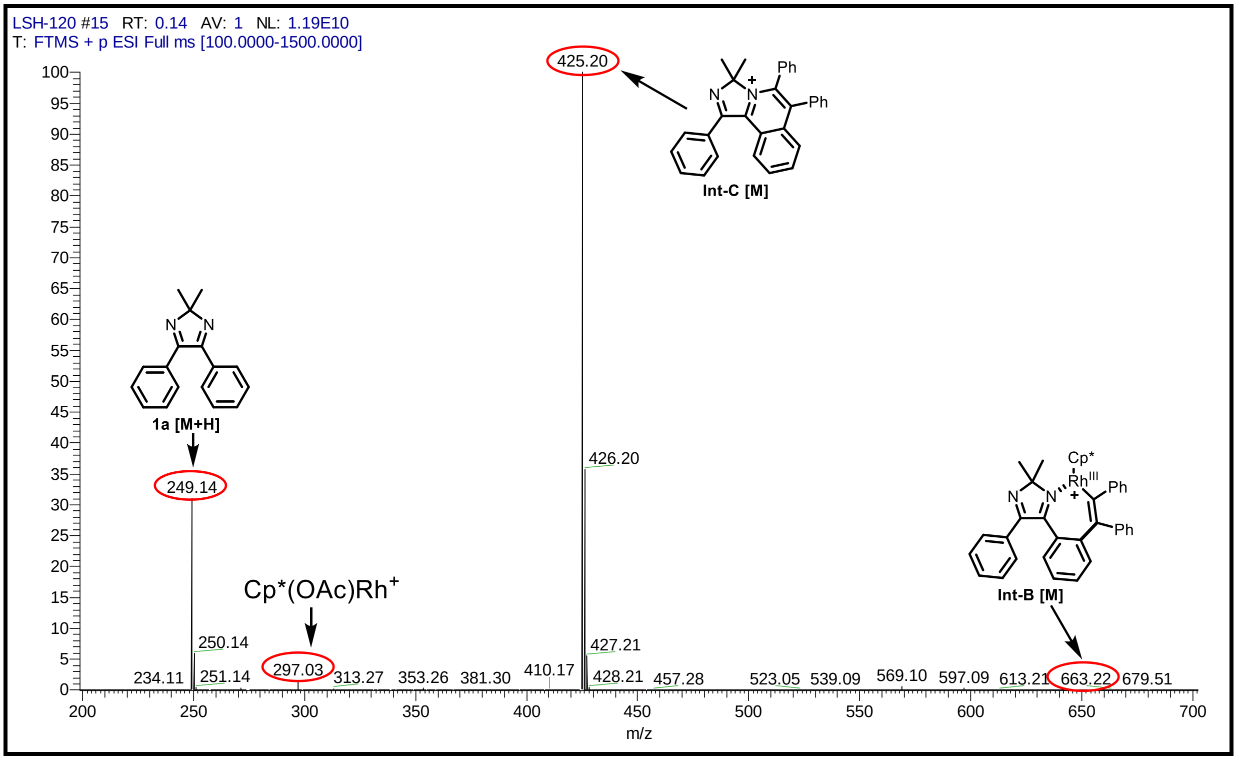
5.1 Detecting the four-component reaction mixture at 30 min

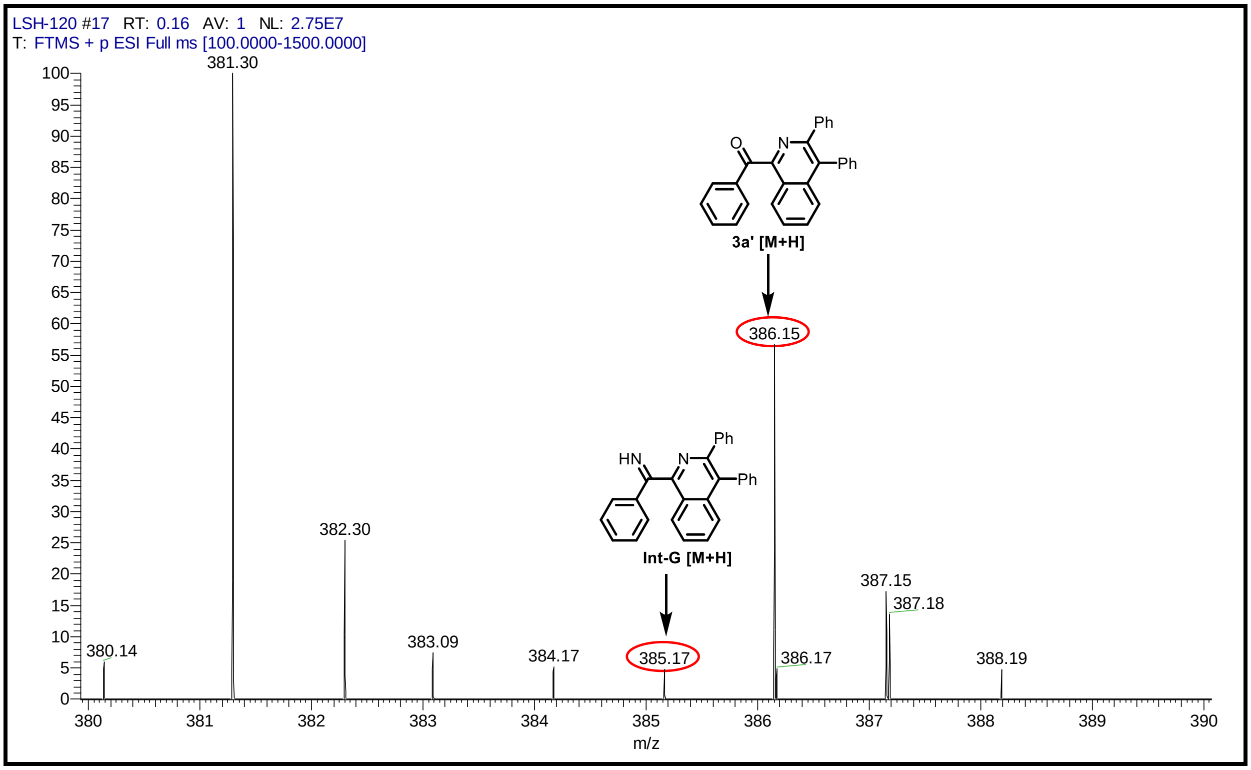


The mixture of **1a** (0.1 mmol), **2a** (0.2 mmol, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 1 equiv), NH$_4$OAc (15.4 mg, 2 equiv) and TFE (2 mL) was stirred at 120 °C for 0.5 h under air. After 0.5 h, the reaction mixture was filtered with a cotton pad, and the filtrate was diluted with the methanol and analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The HRMS spectrum clearly displays the intermediates, **Cp*(OAc)Rh**$^+$, **Int-A**, **Int-B**, **Int-C**, **Int-F**, **Int-G**, **3a′**, and **3a.**

Table S3 *ESI-MS data found at 30 min*

Intermediates	Formula	Calculated	Observed
Cp*(OAc)Rh$^+$ [M]$^+$	$C_{12}H_{18}O_2Rh$	297.04	297.03
Int-A [M]$^+$	$C_{27}H_{30}N_2Rh$	485.15	485.14
Int-B [M]$^+$	$C_{41}H_{40}N_2Rh$	663.22	663.22
Int-C [M]$^+$	$C_{31}H_{25}N_2$	425.20	425.20
Int-F [M]$^+$	$C_{45}H_{33}N_2$	601.26	601.26
Int-G [M + H]$^+$	$C_{28}H_{21}N_2$	385.17	385.17
3a′ [M + H]$^+$	$C_{28}H_{20}NO$	386.15	386.15
3a [M + H]$^+$	$C_{42}H_{29}N_2$	561.23	561.23

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382.30
383.09
384.17
380.14
385.17
386.15
386.17
387.15
387.18
388.19
O
N
Ph
Ph
3a' [M+H]
HN
N
Ph
Ph
Int-G [M+H]
100
95
90
85
80
75
70
65
60
55
50
45
40
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25
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15
10
5
0
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384
385
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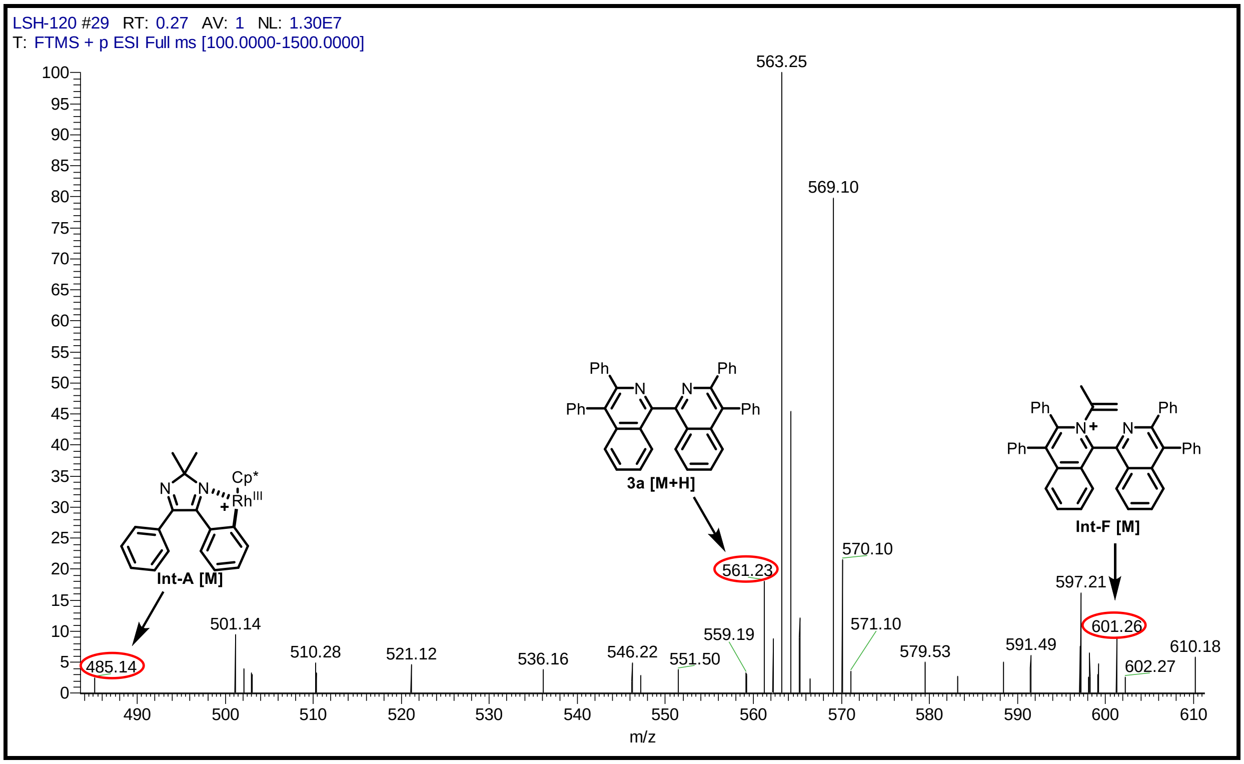
387
388
389
390
m/z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485.14
579.53
591.49
597.21
601.26
602.27
610.18
N
N
Cp*
Rh^{III}
+
Int-A [M]
Ph
N
Ph
N
Ph
Ph
3a [M+H]
Ph
Ph
N+
N
Ph
Ph
Int-F [M]
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85
80
75
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60
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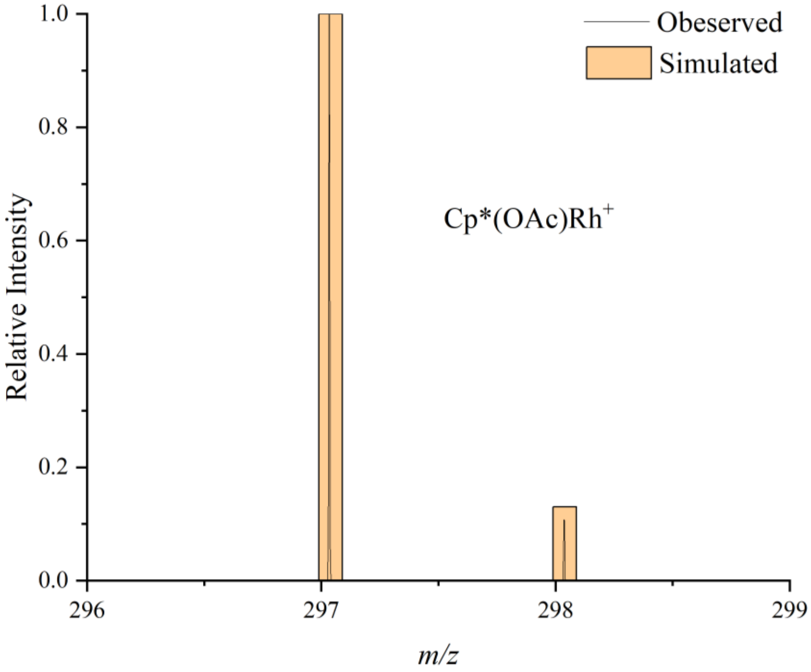


Figure S1 *Isotopic distribution vs the mass spectrum simulated for* ***Cp*(OAc)Rh***$^+$

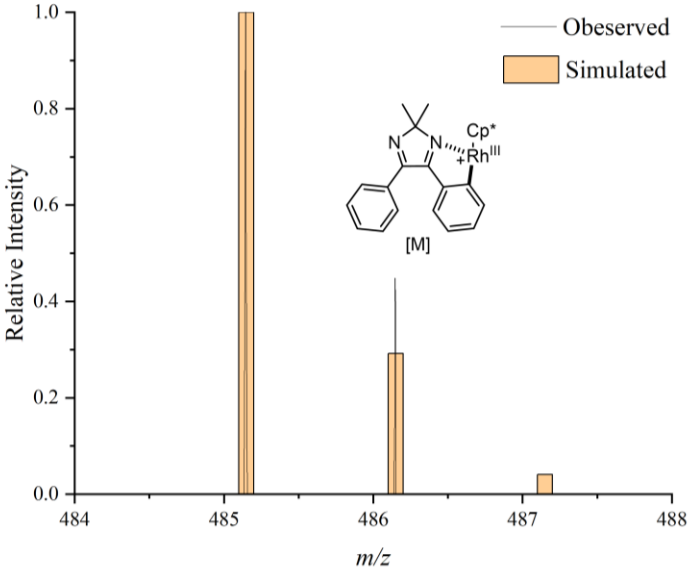


Figure S2 *Isotopic distribution vs the mass spectrum simulated for* ***Int-A***

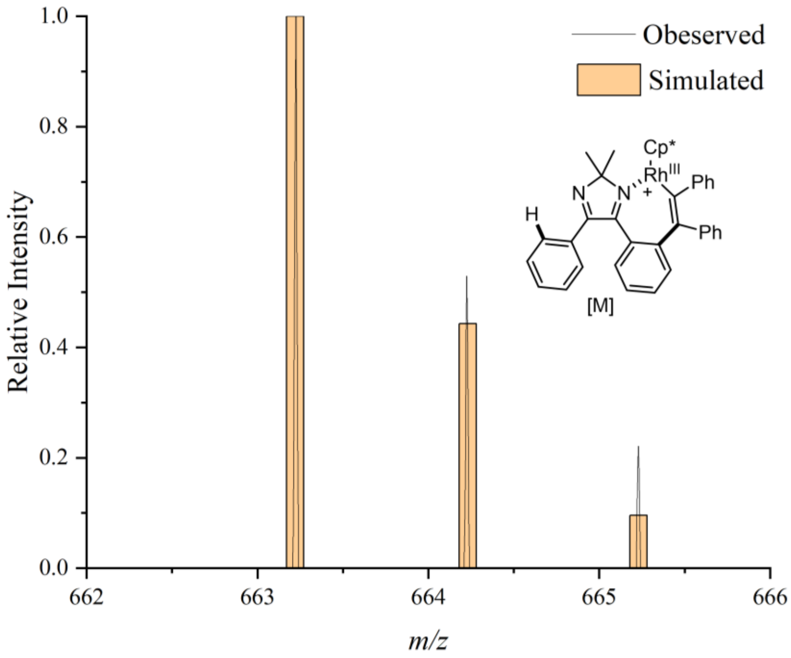


Figure S3 *Isotopic distribution vs the mass spectrum simulated for* ***Int-B***

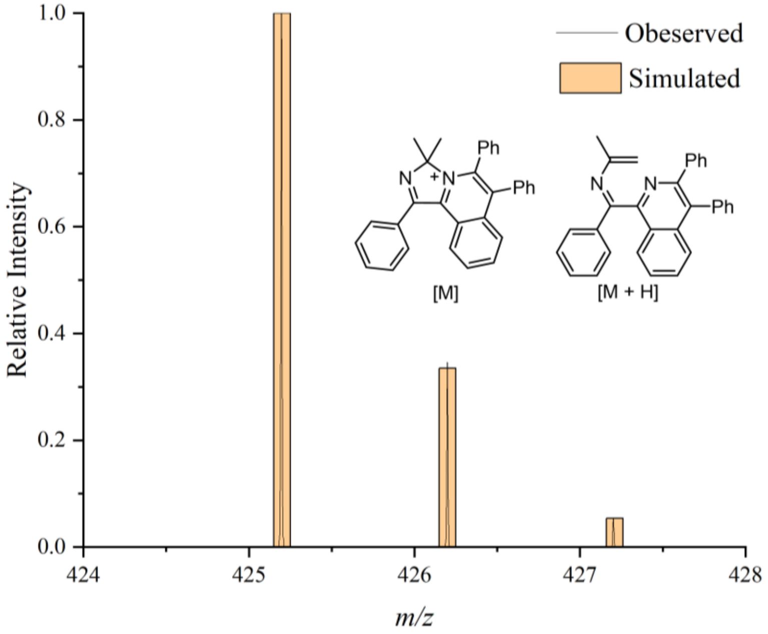


Figure S4 *Isotopic distribution vs the mass spectrum simulated for* ***Int-C/ Int-C′***

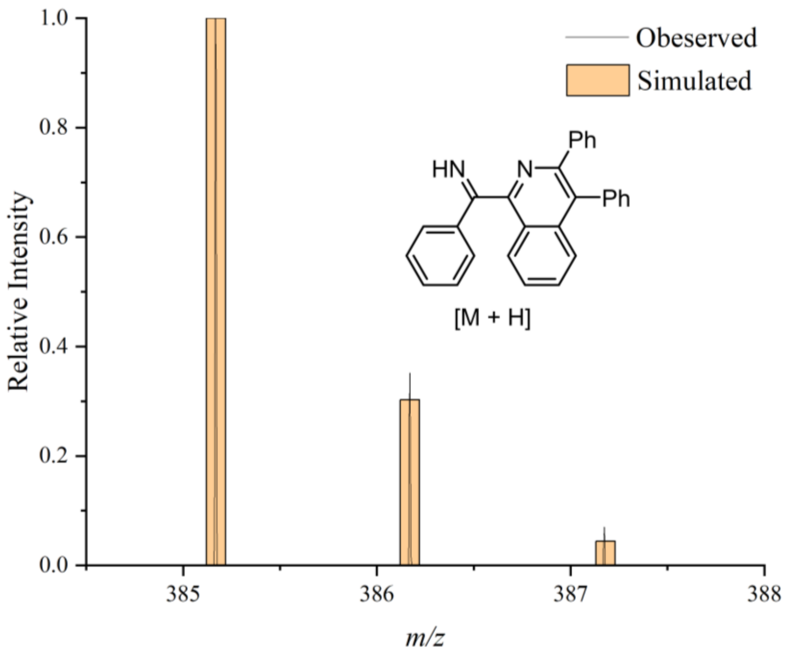


Figure S5 *Isotopic distribution vs the mass spectrum simulated for* ***Int-G***

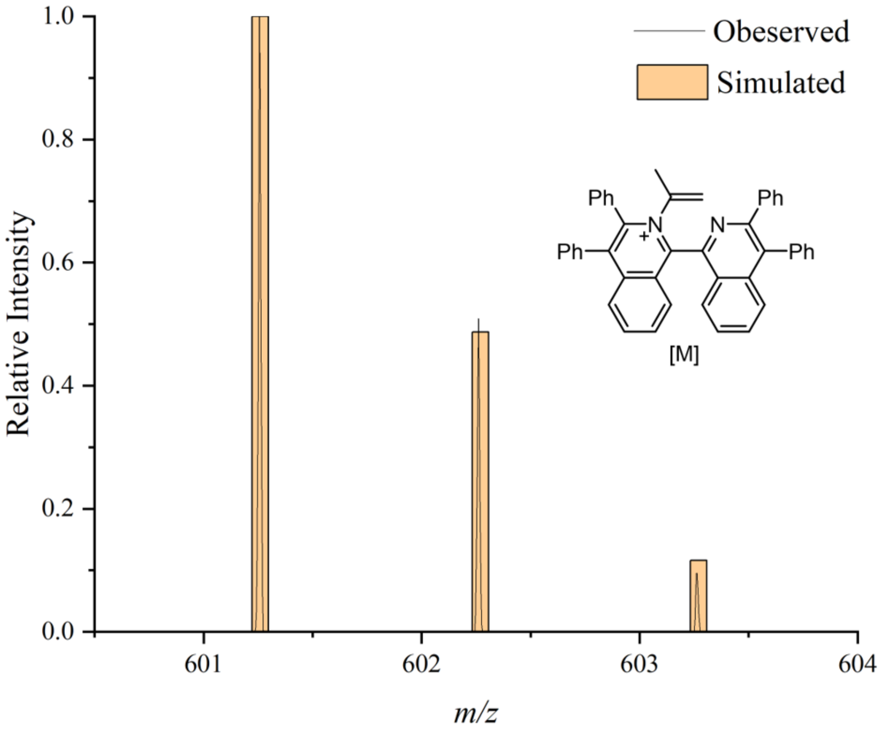


Figure S6 *Isotopic distribution vs the mass spectrum simulated for* ***Int-F***

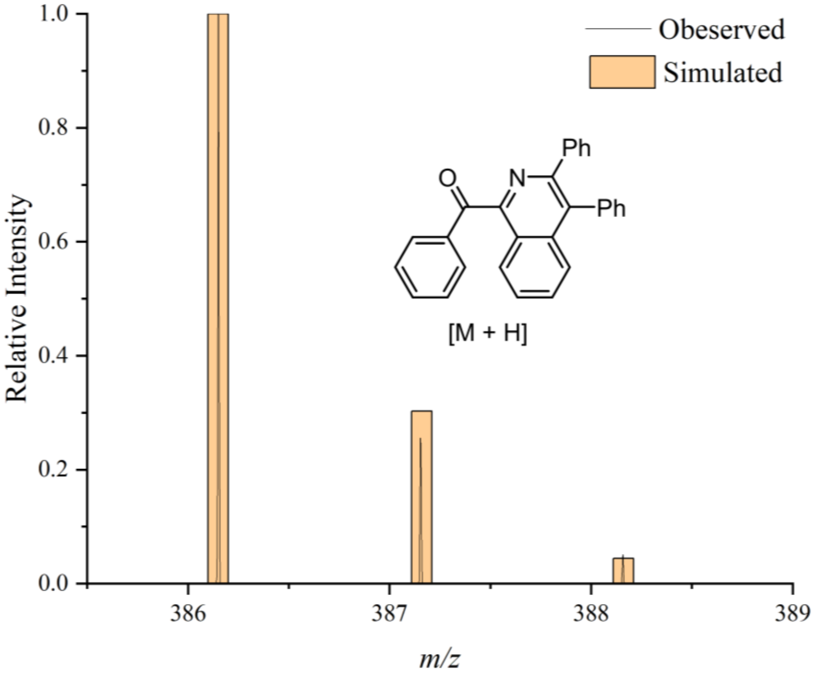


Figure S7 *Isotopic distribution vs the mass spectrum simulated for* ***3a'***

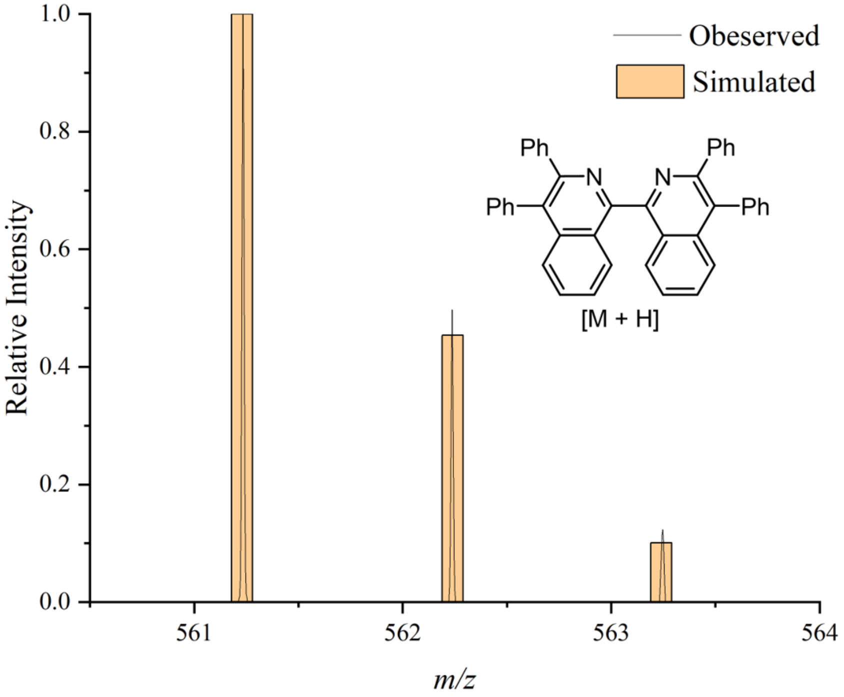
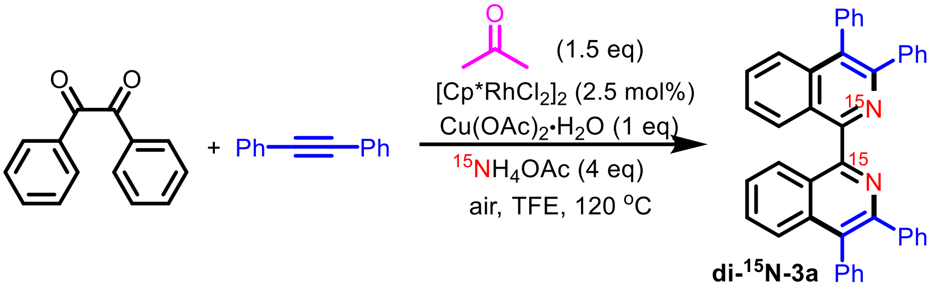


Figure S8 *Isotopic distribution vs the mass spectrum simulated for* ***3a***

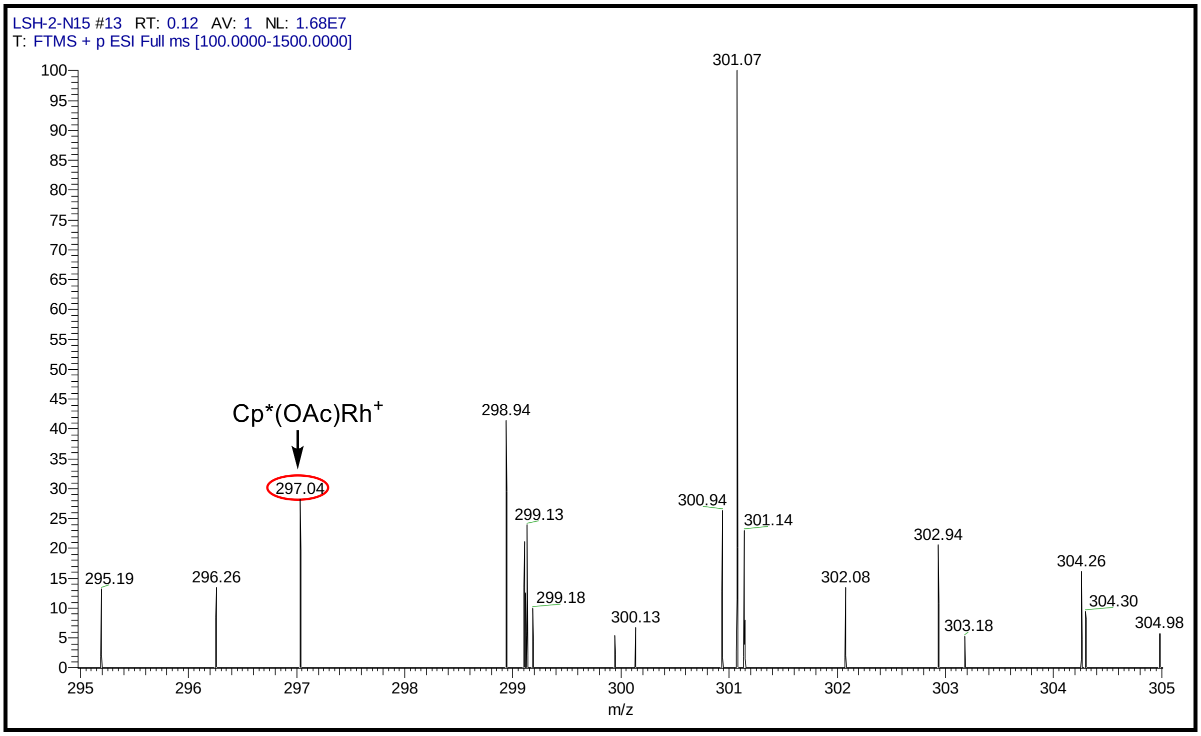
5.2 Detecting the six-component reaction mixture in the presence of $^{15}NH_4OAc$

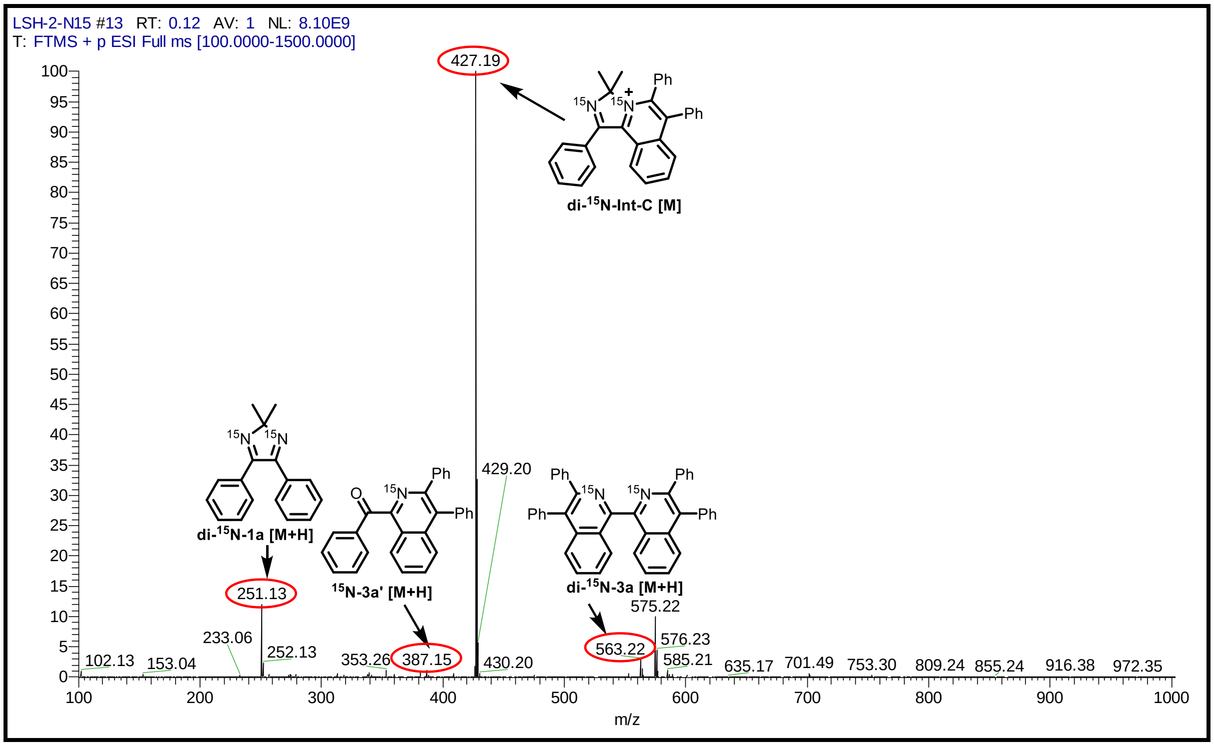


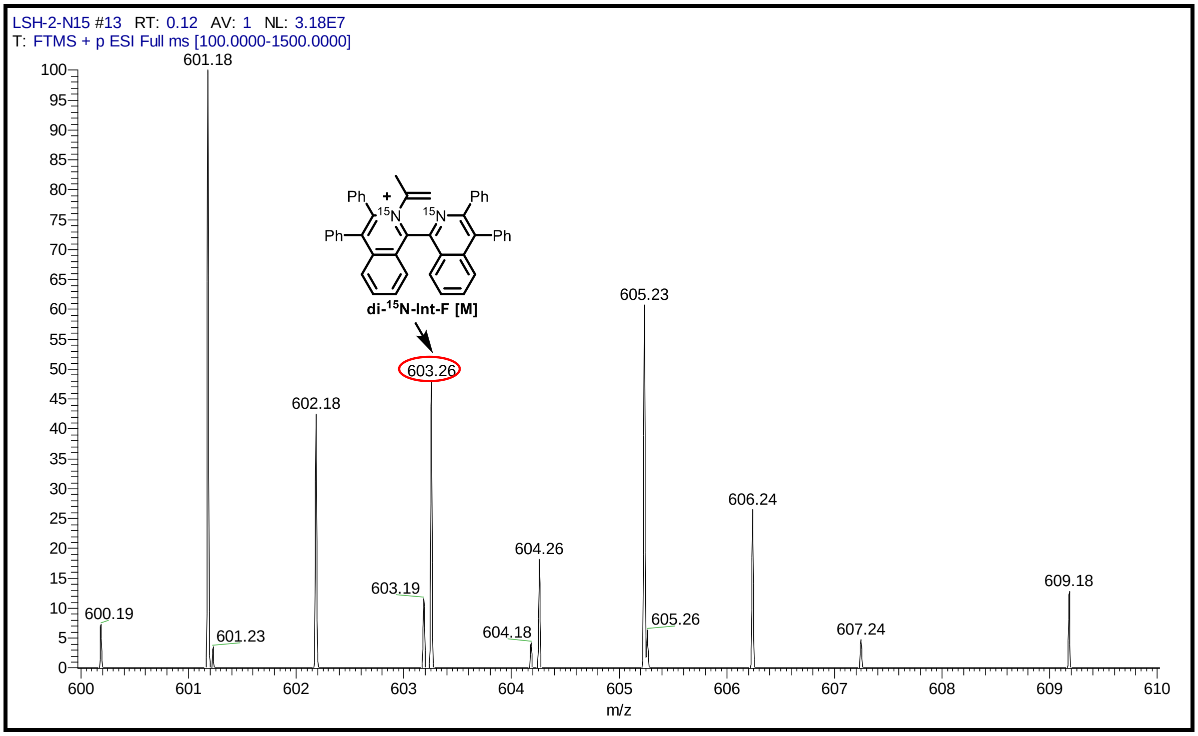
The mixture of benzil (10.5 mg, 0.05 mmol), diphenylacetylene (17.8 mg, 0.1 mmol, 2 equiv), acetone (0.075 mmol, 1.5 equiv), $[(Cp^*RhCl_2)_2]$ (0.8 mg, 2.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol, 1 equiv), NH_4OAc (15.4 mg, 0.2 mmol, 4 equiv) and TFE (1 mL) was stirred at 120 °C for 5 h under air. After 5 h, the reaction mixture was filtered with a cotton pad, and the filtrate was diluted with the methanol and analysed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The HRMS spectrum clearly displays the intermediates, $Cp^*(OAc)Rh^+$, ***di-^{15}N*-1a**, ***di-^{15}N*-Int-C**, ***^{15}N*-3a′**, ***di-^{15}N*-Int-F,** and ***di-^{15}N*-3a**.

Table S4 *ESI-MS data found for six-component reaction in the presence of $^{15}NH_4OAc$*

Intermediates	Formula	Calculated	Observed
Cp*(OAc)Rh$^+$ $[M]^+$	$C_{12}H_{18}O_2Rh$	297.04	297.04
***di-^{15}N*-1a** $[M + H]^+$	$C_{17}H_{17}{}^{15}N_2$	251.13	251.13
***di-^{15}N*-Int-C** $[M]^+$	$C_{31}H_{25}{}^{15}N_2$	427.20	427.19
***^{15}N*-3a′** $[M + H]^+$	$C_{28}H_{20}{}^{15}NO$	387.15	387.15
***di-^{15}N*-Int-F** $[M]^+$	$C_{45}H_{33}{}^{15}N_2$	603.26	603.26
***di-^{15}N*-3a** $[M + H]^+$	$C_{42}H_{29}{}^{15}N_2$	563.23	563.22


LSH-2-N15 #13 RT: 0.12 AV: 1 NL: 1.68E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]
Cp*(OAc)Rh+
297.04
295.19
296.26
298.94
299.13
299.18
300.13
300.94
301.07
301.14
302.08
302.94
303.18
304.26
304.30
304.98
m/z


LSH-2-N15 #13 RT: 0.12 AV: 1 NL: 8.10E9
T: FTMS + p ESI Full ms [100.0000-1500.0000]
427.19
di-15N-Int-C [M]
di-15N-1a [M+H]
251.13
15N-3a' [M+H]
387.15
di-15N-3a [M+H]
563.22
102.13
153.04
233.06
252.13
353.26
429.20
430.20
575.22
576.23
585.21
635.17
701.49
753.30
809.24
855.24
916.38
972.35
m/z



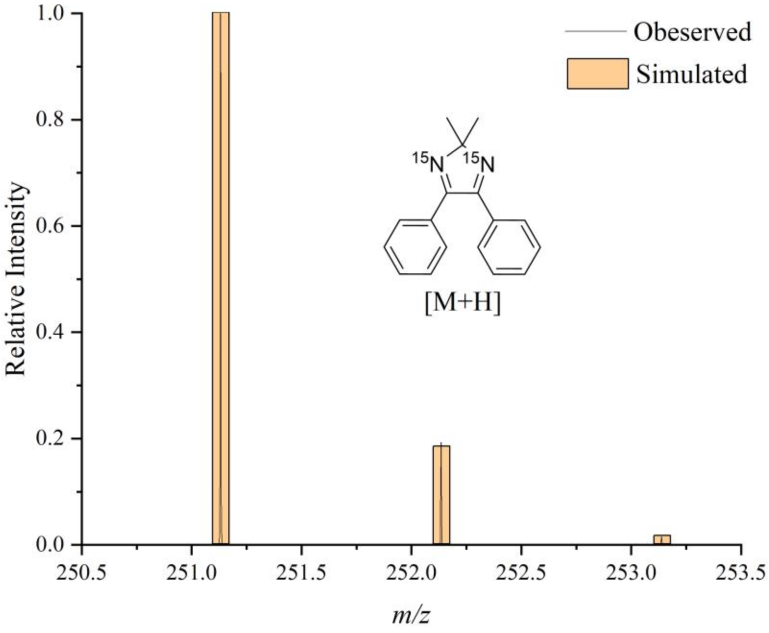


Figure S9 *Isotopic distribution vs the mass spectrum simulated for* ***di-^{15}N-1a***

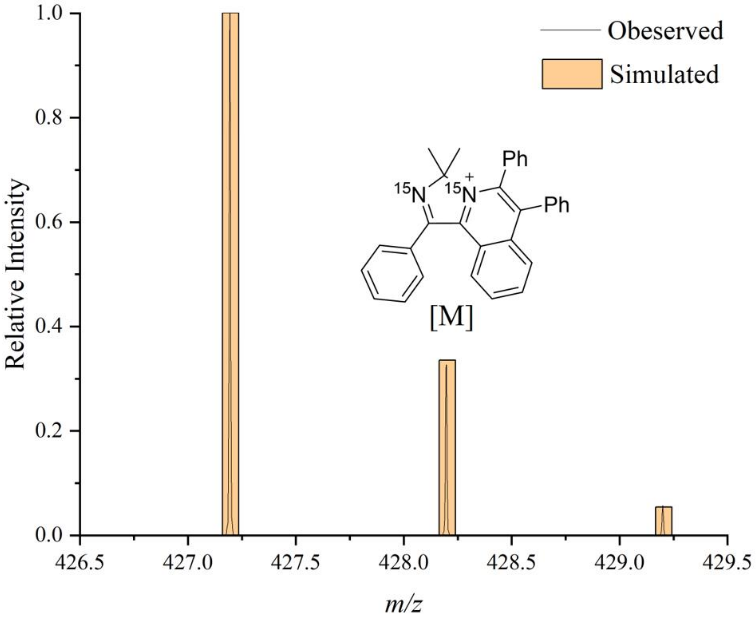


Figure S10 *Isotopic distribution vs the mass spectrum simulated for* ***di-^{15}N-Int-C***

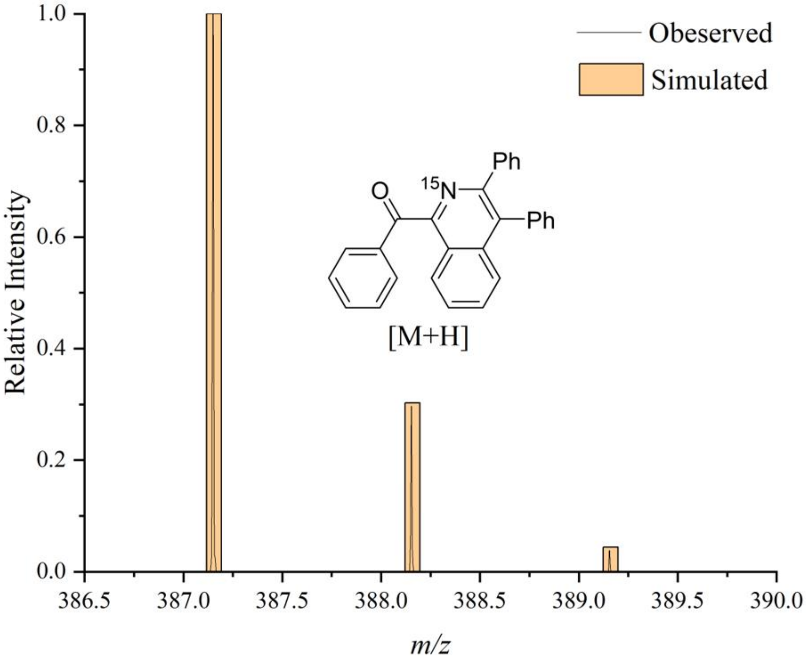


Figure S11 *Isotopic distribution vs the mass spectrum simulated for* ***^{15}N-3a'***

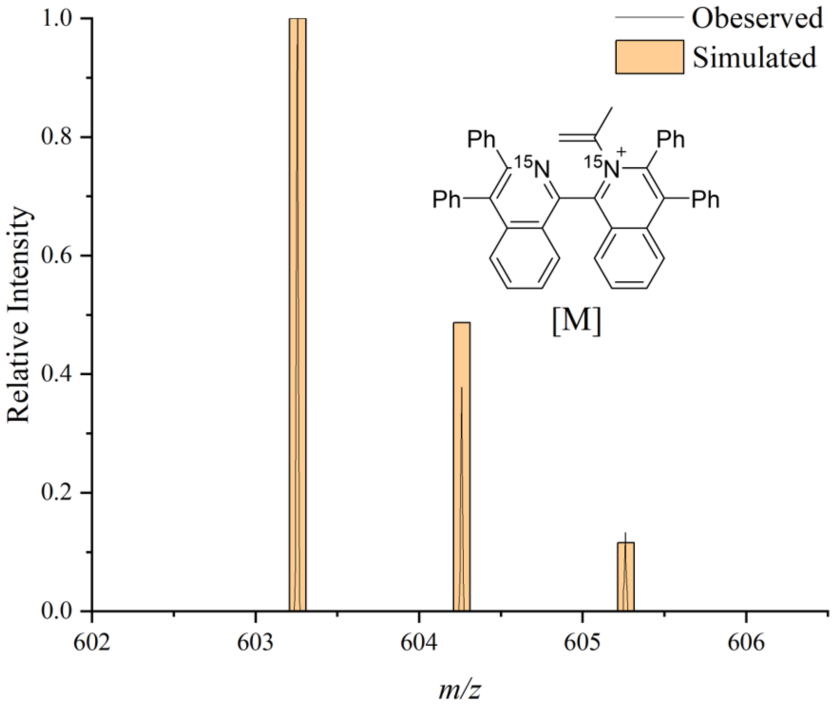


Figure S12 *Isotopic distribution vs the mass spectrum simulated for* ***di-^{15}N-Int-F***

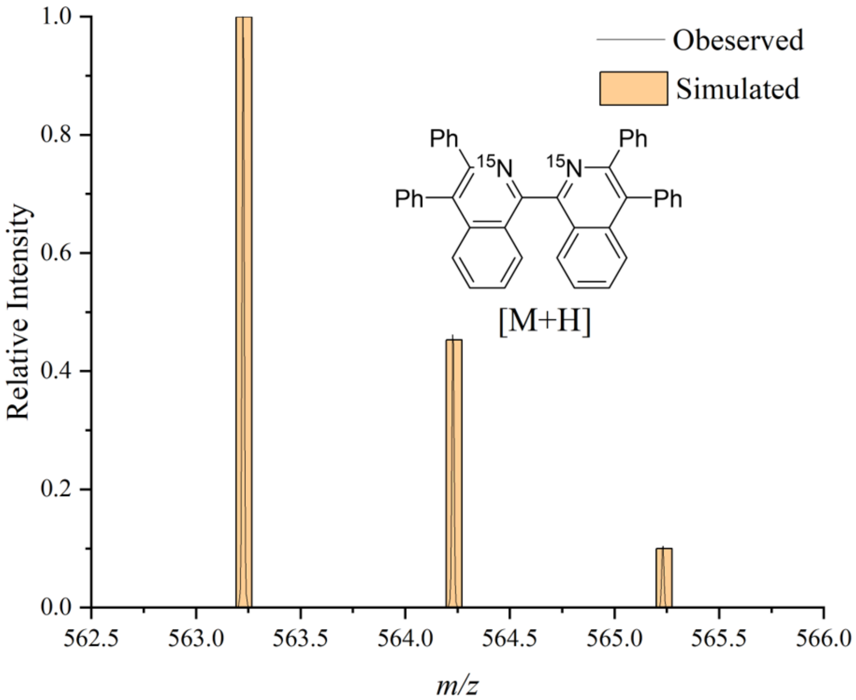
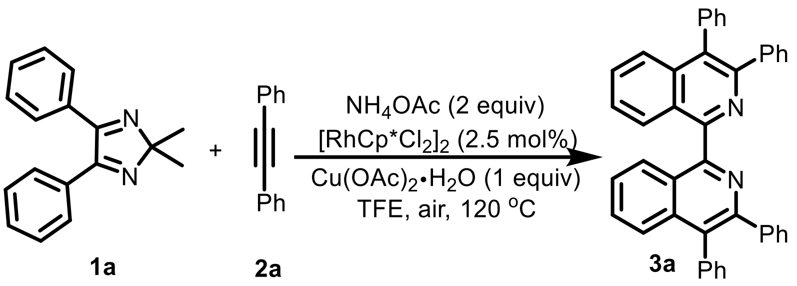


Figure S13 *Isotopic distribution vs the mass spectrum simulated for* ***di-^{15}N-3a***

5.3 Time-dependent ESI-MS to monitor the reaction process

(1) In neutral system:

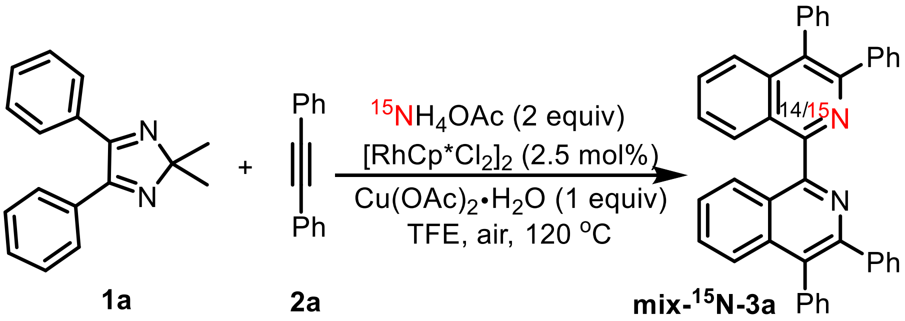


The mixture of **1a** (24.8 mg, 0.1 mmol), **2a** (35.6 mg, 0.2 mmol, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), NH$_4$OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at room temperature for 5 min under air, then moved to heat at 120 °C. At the reaction time of 5 min (rt), 0.5 h (120 °C), 2 h (120 °C), 6 h (120 °C), 10 h (120 °C) and 12 h (120 °C), the reaction mixture was extracted with a micro injector. The reaction mixture was diluted with methanol and filtered by cotton pad, and the filtrate was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The Time-dependent ESI-MS spectrum clearly showed the change trend in the relative intensity of intermediates (Table S5).

Table S5 *Intensity of the intermediates according to time in ESI-MS*

	5 min	0.5 h	2 h	6 h	10 h	12 h
1a	8659657728	3711735296	628686144	147309856	79096224	78157600
Int-A	3228962.5	192570.4	133243	25267.8	20237.8	19962.7
Int-B	4197236	1869430.4	Not found	Not found	Not found	Not found
Int-C/C'	4948361216	11091359744	14646522880	11478876160	6540953088	6532972032
Int-F	Not found	6585557.5	32953764	63775988	104018872	101017182
Int-G	2418946.8	890194.1	1707117	1274590.9	840716.5	983024.1
3a'	32065688	16364353	17705166	17394136	11195047	11828096
3a	Not found	18205718	238285584	314316960	355185088	495769408

5.4 Time-dependent ESI-MS in the synthesis of mix-^{15}N-3a

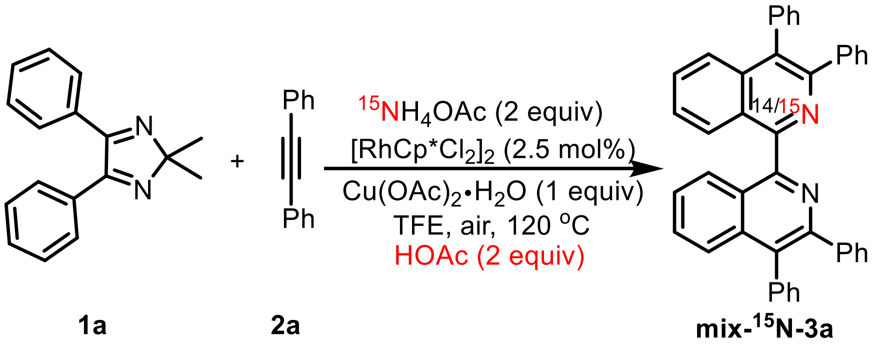


The mixture of **1a** (24.8 mg, 0.1 mmol), **2a** (35.6 mg, 0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol%), $Cu(OAc)_2·H_2O$ (20 mg, 0.1 mmol, 1 equiv), $^{15}NH_4OAc$ (15.6 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at room temperature for 5 min under air, then moved to heat at 120 °C. At the reaction time of 5 min, 2 h, 4 h, 6 h, 8 h, 10 h, and 12 h, the reaction mixture was extracted with a micro injector. The reaction mixture was diluted with methanol and filtered by cotton pad, and the filtrate was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The ^{15}N-labeling ratio of **3a** was clearly tracked by the time-dependent ESI-MS.

Table S6. *Intensity of the peak ([M+H] and [M+H+1]) according to time in ESI-MS*

	5 min	2 h	4 h	6 h	8 h	10 h	12 h
Intensity **[M+H]**	41763176 561.23	114854160 561.23	259384320 561.23	302288096 561.23	348470784 561.23	428523776 561.23	449511648 561.23
Intensity **[M+H+1]**	47364584 562.23	128923232 562.23	273356576 562.23	320238272 562.23	389003424 562.23	340005760 562.23	526074144 562.23
^{15}N ratio	40.5%	40.1%	37.5%	37.7%	39.8%	41.4%	41.7%

(2) In acidic system:

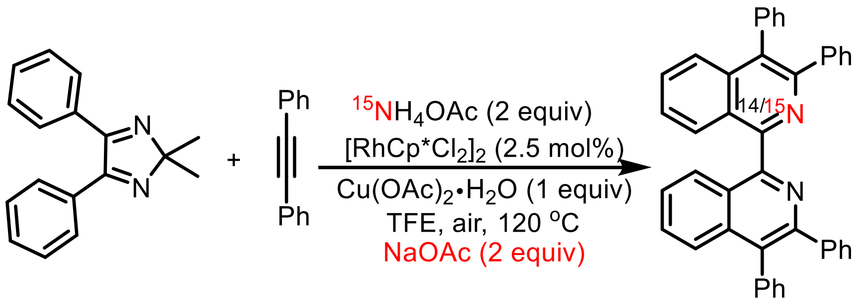


The mixture of **1a** (24.8 mg, 0.1 mmol), **2a** (35.6 mg, 0.2 mmol, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), ^{15}NH$_4$OAc (15.6 mg, 0.2 mmol, 2 equiv), HOAc (11μl, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at room temperature for 5 min under air, then moved to heat at 120 °C. At the reaction time of 5 min, 2 h, 4 h, 6 h, 8 h, 10 h, and 12 h, the reaction mixture was extracted with a micro injector. The reaction mixture was diluted with methanol and filtered by cotton pad, and the filtrate was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The ^{15}N-labeling ratio of **3a** was clearly tracked by the time-dependent ESI-MS.

Table S7. *Intensity of the peak ([M+H] and [M+H+1]) according to time in ESI-MS when adding HOAc*

	5 min	2 h	4 h	6 h	8 h	10 h	12 h
Intensity **[M+H]**	17051444 561.23	27897696 561.23	48938864 561.23	56579532 561.23	5178050.5 561.23	79532904 561.23	90193704 561.23
Intensity **[M+H+1]**	13669079 562.23	17924206 562.23	34024300 562.23	49847268 562.23	4290084.5 562.23	74332088 562.23	103594040 562.23
^{15}N ratio	41.3%	35.1%	37.3%	43.8%	42.1%	45.5%	50.8%

(3) In basic system:



1a **2a** **mix-^{15}N-3a**

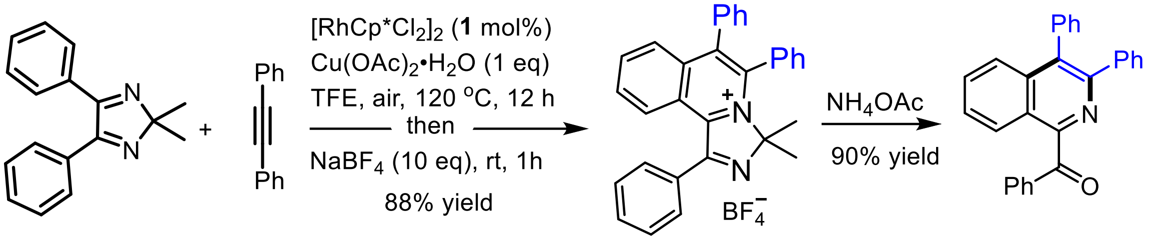
The mixture of **1a** (24.8 mg, 0.1 mmol), **2a** (35.6 mg, 0.2 mmol, 2 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), ^{15}NH$_4$OAc (15.6 mg, 0.2 mmol, 2 equiv), NaOAc (16.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at room temperature for 5 min under air, then moved to heat at 120 °C. At the reaction time of 5 min, 2 h, 4 h, 6 h, 8 h, 10 h, and 12 h, the reaction mixture was extracted with a micro injector. The reaction mixture was diluted with methanol and filtered by cotton pad, and the filtrate was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. The ^{15}N-labeling ratio of **3a** was clearly tracked by the time-dependent ESI-MS.

Table S8. *Intensity of the peak ([M+H] and [M+H+1]) according to time in ESI-MS when adding NaOAc*

	5 min	2 h	4 h	6 h	8 h	10 h	12 h
Intensity **[M+H]**	6533618.5 561.23	4917115.5 561.23	10278779 561.23	33717960 561.23	26260442 561.23	30985018 561.23	31880254 561.23
Intensity **[M+H+1]**	2505176.3 562.23	2001445.8 562.23	34024300 562.23	19582682 562.23	18282992 562.23	18008446 562.23	18475614 562.23
^{15}N ratio	22.0%	23.4%	27.1%	37.3%	32.4%	32.4%	32.4%

6 Synthetic applications

6.1 Scale-up reactions (1 mmol)

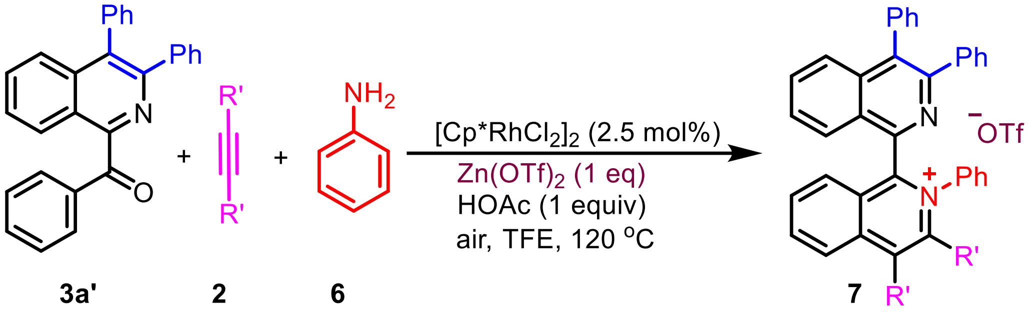


1a (1 mmol) **2a** (1 mmol) **Int-C** **3a'**

Synthesis of Int-C. The mixture of 2*H*-imidazole **1a** (248 mg, 1 mmol), alkyne **2a** (178 mg, 1 mmol, 1equiv), [(Cp*$RhCl_2$)$_2$] (6 mg, 1 mol%), $Cu(OAc)_2\cdot H_2O$ (200 mg, 1 mmol, 2 equiv), and TFE (10 mL) was stirred at 120 °C for 12 h under air. Then, $NaBF_4$ (110 mg, 2 mmol, 10 equiv), was added to the reaction mixture, stir at room temperature for 1 h. After reaction completed, the mixture was concentrated under vacuum and the residue was purified by a silica gel (100−200 mesh) column, eluting with CH_2Cl_2/CH_3OH (80/1 → 10/1, v/v) to afford **Int-C** as a yellow solid (451 mg, 88% yield).

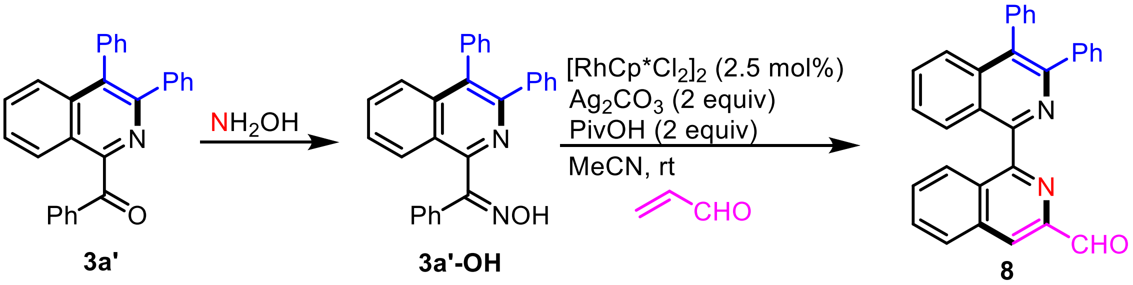
Synthesis of 3a′. A solution of **In-C** (451 mg, 0.88 mmol), NH_4OAc (136 mg, 1.76 mmol, 2 equiv) and TFE (9 mL) was reacted at 120 °C for 12 h under air. The solvent was removed under vacuum and the residue was purified by a silica gel (100−200 mesh) column, eluting with petroleum ether/EtOAc (100/1 → 80/1, v/v) to afford **3a′** as a white solid (305 mg, 90% yield).

6.2 General procedure for the synthesis of 1,1'-biisoquinolinium salts 7



The mixture of **3a′** (38.5 mg, 0.1 mmol), alkyne **2** (0.1 mmol, 1 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol%), aniline **6** (14 mg, 1.5 mmol, 1.5 equiv), Zn(OTf)$_2$ (36.4 mg, 0.1 mmol, 1 equiv), HOAc (6 µL, 0.1 mmol, 1 equiv) and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a silica gel (200−300 mesh) column, eluting with CH_2Cl_2/CH_3OH (80/1 → 8/1, v/v) to afford salts **7**.

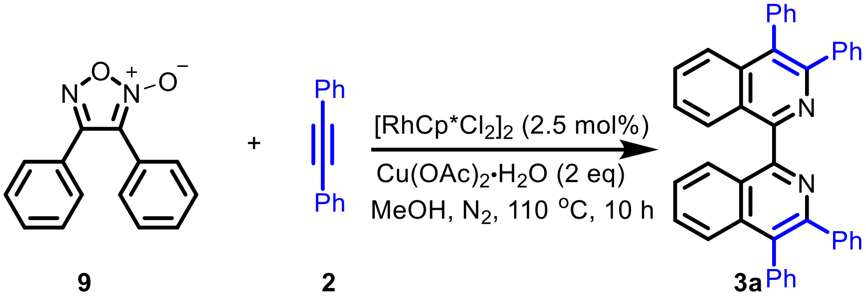
6.3 Synthesis of trisubstituted 1,1'-biisoquinoline 8



To a dry Schlenk tube with a magnetic stir bar was added **3a′** (77.1 mg, 0.2 mmol), NH_2OH • HCl (34.7 mg, 0.5 mmol, 2.5 equiv), pyridine (23.7 mg, 0.3 mmol, 1.5 equiv) and EtOH (2 mL). The mixture was stirred at 90 °C for 10 h. After cooling down to room temperature, a large amount of solid is precipitated. The precipitate was collected by filtration and washed with EtOH (2 mL) to afford (3,4-diphenylisoquinolin-1-yl)(phenyl)methanone oxime **3a′-OH** as a white solid (73.6 mg, 92% yield).

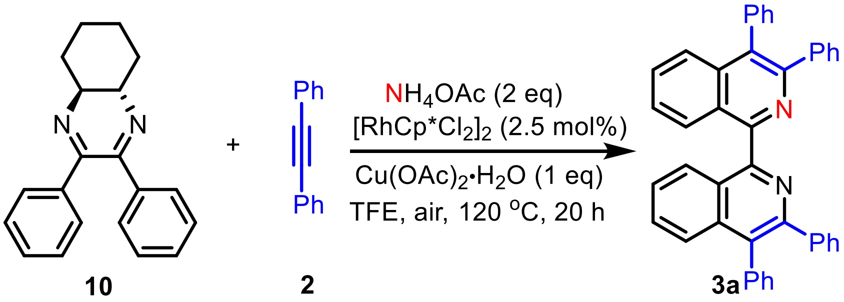
Then, **3a′-OH** (40 mg, 0.1 mmol), acrolein (16.8 mg, 0.3 mmol, 3 equiv), [(Cp*RhCl$_2$)$_2$] (1.3 mg, 2.0 mol%), Ag_2CO_3 (55.1 mg, 2 equiv), PivOH (20.4 mg, 2 equiv) and MeCN (1 mL) were added to a dry Schlenk tube for stirring at room temperature for 18 h under air. The residue was purified by a silica gel (100−200 mesh) column, eluting with petroleum ether/EtOAc (10/1, v/v) to afford **8** as a yellowish solid (20.1 mg, 46%).

6.4 Synthesis of 3a from furoxan 9



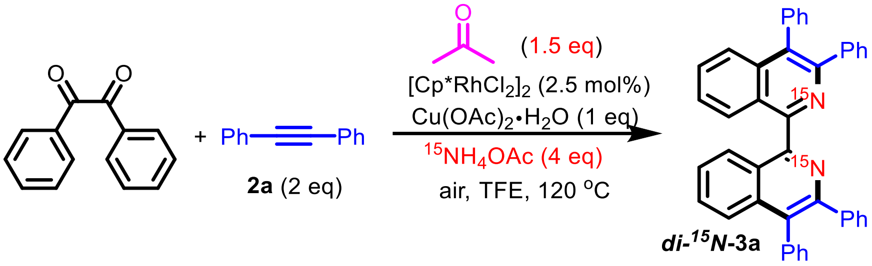
To a dry Schlenk tube with a magnetic stir bar was added furoxan **9** (23.8 mg, 0.1 mmol), alkyne **2a** (35.6 mmol, 0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (40 mg, 0.2 mmol, 2 equiv), and MeOH (2 mL). The reaction mixture was stirred at 110 °C for 10 h under nitrogen atmosphere before concentrated under vacuum. The residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (40/1 → 8/1, v/v) to afford **3a** as a white solid (47.6 mg, 84%).

6.5 Synthesis of 3a from diimine 10



The mixture of **10** (28.8 mg, 0.1 mmol), alkyne **2a** (35.6 mmol, 0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol%), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol, 1 equiv), NH_4OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was stirred at 120 °C for 20 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (40/1 → 8/1, v/v) to afford **3a** as a white solid (17.0 mg, 30% yield). While **3a** was not detected when NH_4OAc was absent.

6.5 Synthesis of di-^{15}N-3a with full ^{15}N-labeling



The mixture of benzil (21 mg, 0.1 mmol), **2a** (35.6 mmol, 0.2 mmol, 2 equiv), acetone (1.5 mmol, 1.5 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol %), $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 0.1 mmol, 1 equiv), $^{15}NH_4OAc$ (30.8 mg, 0.4 mmol, 4 equiv) and TFE (2 mL) was reacted at 120 °C for 12h under air. The reaction mixture was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 8/1, v/v) to afford **di-^{15}N-3a** as a white solid (28 mg, 50% yield). The ^{15}N ratio was determined by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap). HRMS analysis showed that the abundance of ^{15}N in **3a** was close to 100%.

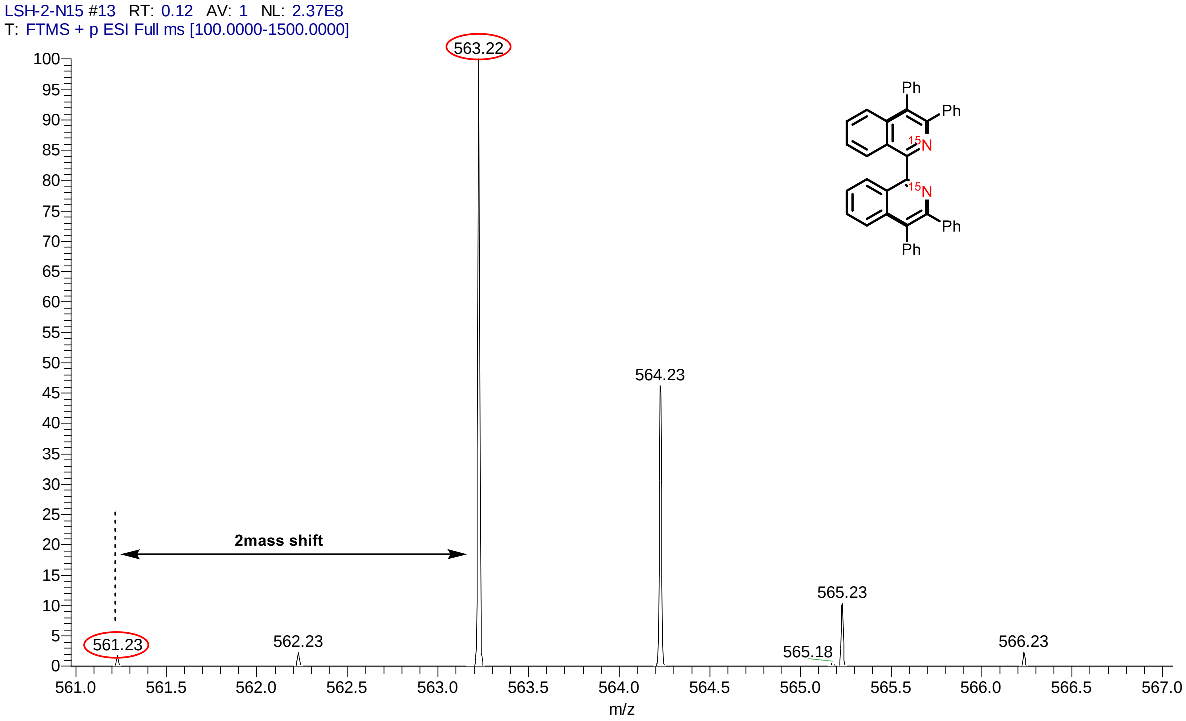
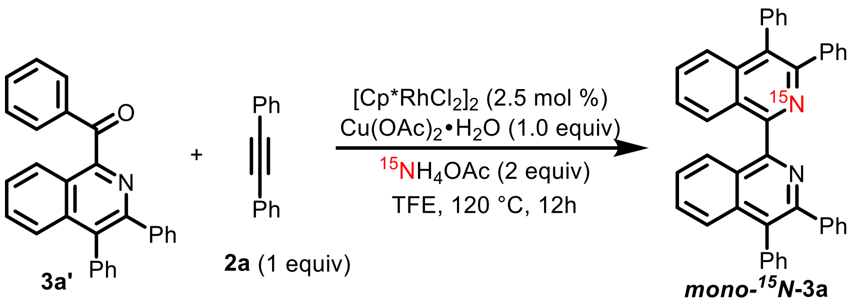


Figure S14 *ESI-MS of* ***di-^{15}N-3a***

6.6 Synthesis of mono-^{15}N-3a with full ^{15}N-labeling



The mixture of **3a′** (38.5 mg, 0.1 mmol), **2a** (17.8 mg, 0.1 mmol, 1 equiv), [(Cp*RhCl$_2$)$_2$] (1.6 mg, 2.5 mol %), Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol, 1 equiv), ^{15}NH$_4$OAc (15.4 mg, 0.2 mmol, 2 equiv) and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was purified by a neutral aluminum oxide (200−300 mesh) column, eluting with petroleum ether/EtOAc (80/1 → 40/1, v/v) to afford ***mono-^{15}N*-3a** as a white solid (50.2 mg, 90% yield). The ^{15}N ratio was determined by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap). HRMS analysis showed that the abundance of ^{15}*N* in **3a** was 100%.

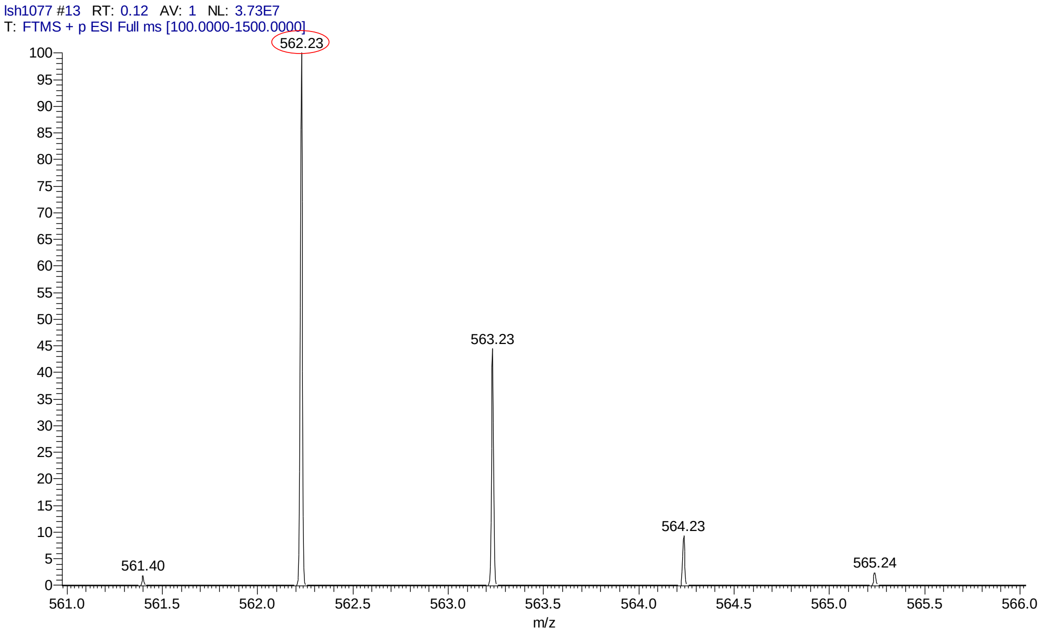
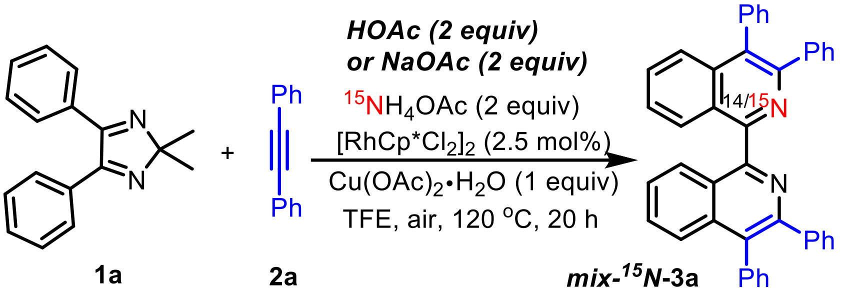


Figure S15 *ESI-MS of* ***mono-^{15}N-3a***

6.7 Adjusting the ^{15}N incorporation of mix-^{15}N-3a by reaction acidity



With acid HOAc: The mixture of **1** (0.1 mmol), **2** (0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol %), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol, 1 equiv), $^{15}NH_4OAc$ (15.4 mg, 0.2 mmol, 2 equiv), HOAc (11 μL, 0.2 mmol, 2 equiv), and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. HRMS analysis showed that the abundance of ^{15}N in **3a** was 58%.

With base NaOAc: The mixture of **1** (0.1 mmol), **2** (0.2 mmol, 2 equiv), $[(Cp^*RhCl_2)_2]$ (1.6 mg, 2.5 mol %), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol, 1 equiv), $^{15}NH_4OAc$ (15.4 mg, 0.2 mmol, 2 equiv), **NaOAc** (16.4 mg, 0.2 mmol, 2 equiv), and TFE (2 mL) was reacted at 120 °C for 12 h under air. The reaction mixture was analyzed by HRMS analysis using Vanquish-Exactive Plus liquid chromatography mass spectrometry (ion trap) without any purification. HRMS analysis showed that the abundance of ^{15}N in **3a** was 27%.

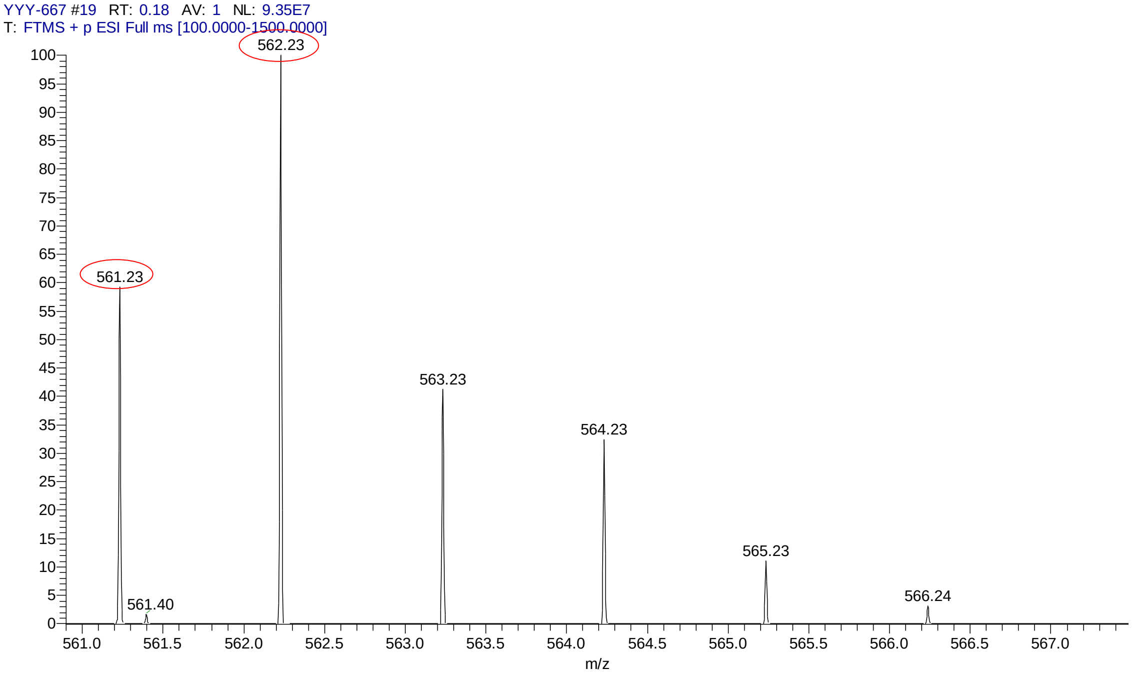


Figure S16 *ESI-MS of* ***mix-^{15}N-3a*** *in the presence of HOAc*

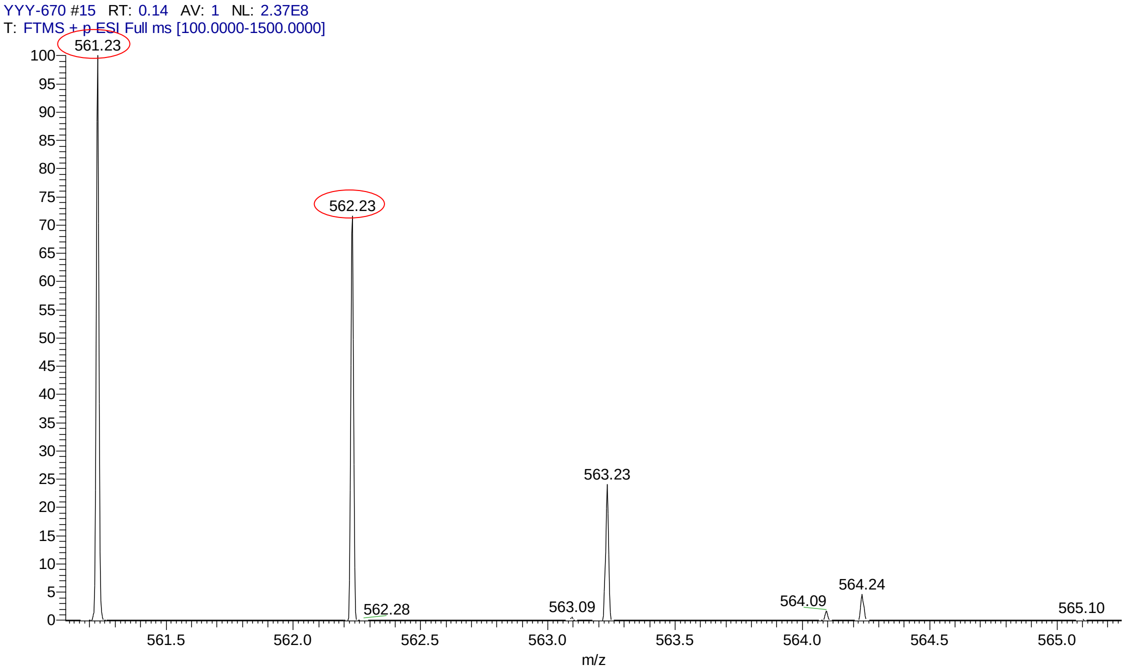
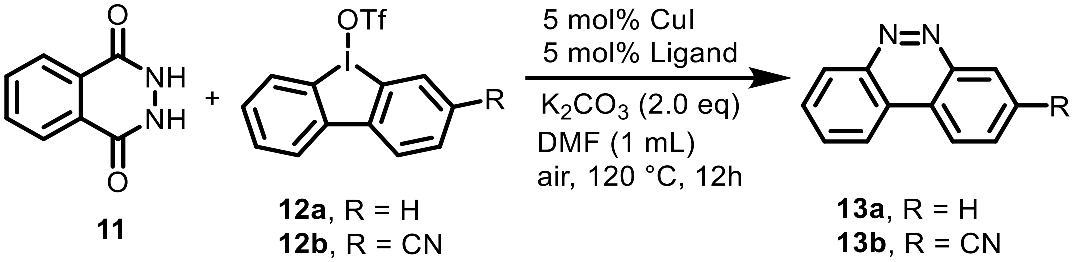


Figure S17 *ESI-MS of* ***mix-^{15}N-3a*** *in the presence of NaOAc*

7 Using 1,1′-BIQ as ligand in double *N*-arylation to synthesize benzo[*c*]cinnolines



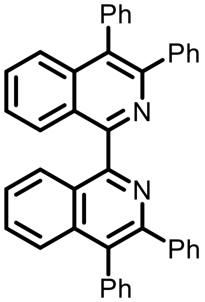
The mixture of phthalhydrazide **11** (32.4 mg, 0.2 mmol), **12** (0.25 mmol, 1.25 equiv), CuI (2 mg, 5 mol%), ligand (5 mol%), K_2CO_3 (55.2 mg, 0.4 mmol, 2 equiv) and DMF (1 mL) was stirred at 120 °C for 12 h under air. The reaction mixture was concentrated under vacuum and the residue was purified by a silica gel (100–200 mesh) column, eluting with petroleum ether/EtOAc (10/1 → 5/1, v/v) to afford **13a** or **13b**.

Table S9. *Reaction data of* ***10*** *and* ***11***

Entry	Iodonium	Ligand	Yield (%)^b
1	**12a**	none	67 (**13a**)
2	**12a**	2,2′-Bipy	90 (**13a**)
3	**12a**	1,10-Phen	90 (**13a**)
4	**12a**	DMEDA	90 (**13a**)
5	**12a**	**3a**	95 (**13a**)
6	**12b**	2,2′-Bipy	35 (**13b**)
7	**12b**	**3a**	95 (**13b**)
8	**12b**	**3e**	80 (**13b**)
9	**12b**	**3j**	82 (**13b**)
10	**12b**	**3m**	78 (**13b**)
11	**12b**	**3o**	89 (**13b**)

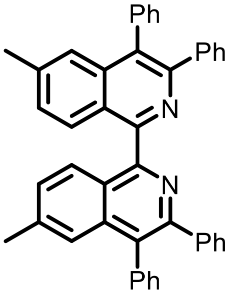
8 Experimental data for the described substances

3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3a)



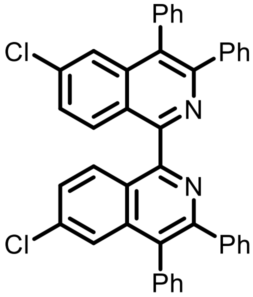
White solid (From GP B: 52.1 mg, 93% yield; From GP C, 29.0 mg, 52% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.09 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.44–7.35 (m, 14H), 7.20–7.14 (m, 6H) ppm. The NMR data are consistent with the literature.[9]

6,6'-dimethyl-3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3b)



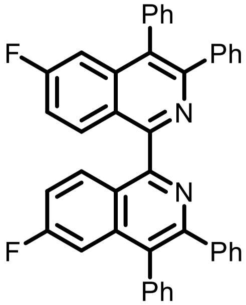
White solid (37.7 mg, 64% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→60/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.97 (d, *J* = 8.5 Hz, 2H), 7.51 (s, 2H), 7.43–7.33 (m, 16H), 7.18–7.12 (m, 6H), 2.45 (s, 6H) ppm. The NMR data are consistent with the literature.[9]

6,6'-dichloro-3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3c)



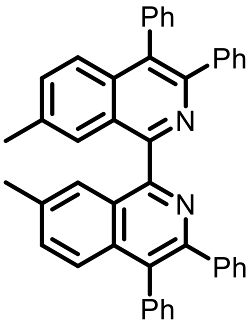
White solid (From GP B: 48.5 mg, 77% yield; From GP C, 30.4 mg, 48% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.09 (d, J = 8.0 Hz, 2H), 7.75 (s, 2H), 7.49 (d, J = 9.0 Hz, 2H), 7.46–7.38 (m, 10H), 7.32 (d, J = 7.0 Hz, 4H), 7.21–7.15 (m, 6H) ppm. The NMR data are consistent with the literature.[9]

6,6'-difluoro-3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3d)



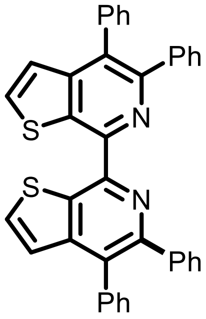
White solid (34.4 mg, 58% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.19–8.16 (m, 2H), 7.45–7.39 (m, 12H), 7.32–7.30 (m, 6H), 7.19–7.15 (m, 6H) ppm. The NMR data are consistent with the literature.[9]

7,7'-dimethyl-3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3e)



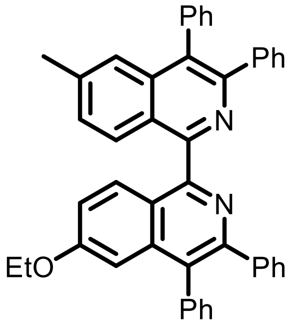
White solid (47.2 mg, 80% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.83 (s, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.48–7.46 (m, 2H), 7.44–7.35 (m, 14H), 7.20–7.13 (m, 6H), 2.47 (s, 6H) ppm. The NMR data are consistent with the literature.[9]

4,4',5,5'-tetraphenyl-3a,7a-dihydro-7,7'-bithieno[2,3-*c*]pyridine (3f)



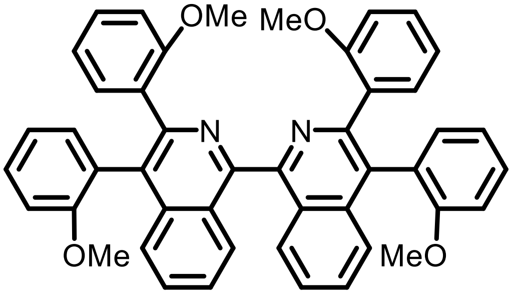
White solid (22.4 mg, 39% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→20/1, v/v). M.p.: >250 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 7.78 (d, J = 5.5 Hz, 2H), 7.67 (d, J = 7.0 Hz, 4H), 7.41–7.29 (m, 18H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 147.7, 139.9, 138.3, 136.4, 135.3, 131.0, 130.8, 128.4, 127.9, 127.8, 127.6, 127.4, 127.2, 125.4, 122.7 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{38}H_{25}N_2S_2$ ([M+H]$^+$) 573.1459, found 573.1458.

6-ethoxy-6'-methyl-3,3',4,4'-tetraphenyl-1,1'-biisoquinoline (3g)



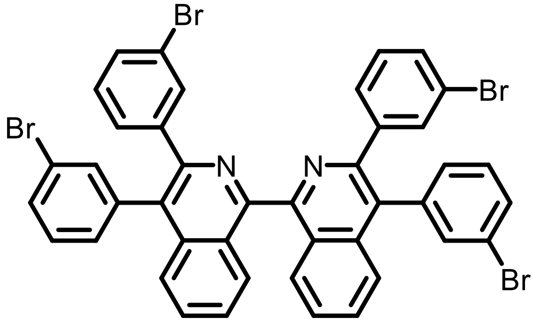
White solid (From GP B: 46.4 mg, 75% yield; From GP C, 36.6 mg, 59% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.00–7.97 (m, 2H), 7.52 (s, 1H), 7.42–7.35 (m, 15H), 7.17–7.14 (m, 7H), 7.00 (s, 1H), 3.96 (q, J = 7.0 Hz, 2H), 2.45 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm. The NMR data are consistent with the literature.[9]

3,3',4,4'-tetrakis(2-methoxyphenyl)-1,1'-biisoquinoline6 (3h)



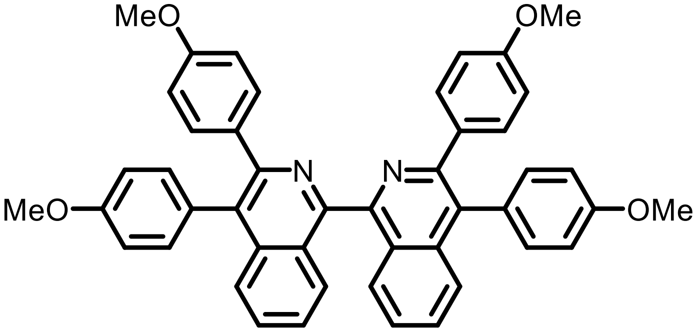
White solid (37.6 mg, 69% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 10/1→2/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.33 (s, 2H), 7.58–7.56 (m, 4H), 7.52–7.50 (m, 2H), 7.29–7.26 (m, 2H), 7.19–7.11 (m, 6H), 6.91–6.86 (m, 4H), 6.75 (s, 4H), 3.71 (s, 6H), 3.60 (s, 6H) ppm. The NMR data are consistent with the literature.[9]

3,3',4,4'-tetrakis(3-bromophenyl)-1,1'-biisoquinoline (3i)



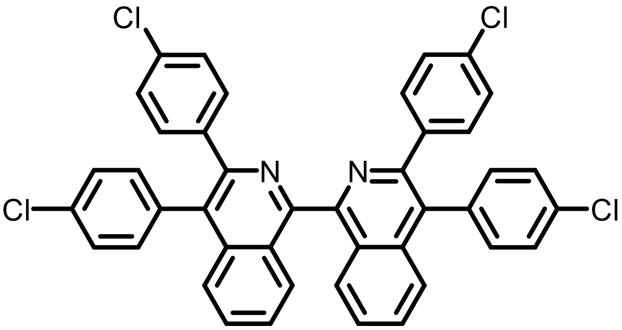
White solid (43.6 mg, 50% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→20/1, v/v). M.p.: >250 ºC . **^{1}H NMR (500MHz, $CDCl_3$):** δ = 7.98 (d, *J* = 8.5 Hz, 2H), 7.76–7.67 (m, 6H), 7.59–7.54 (m, 6H), 7.34–7.31 (m, 4H), 7.26–7.24 (m, 4H), 7.05 (t, *J* = 8.0 Hz, 2H) ppm. **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 157.9, 148.2, 142.3, 139.2, 136.9, 134.1, 133.5, 131.2, 131.1, 130.6, 130.3, 130.2, 130.1, 129.4, 129.1, 127.8, 127.5, 127.0, 125.9, 122.7, 122.2 ppm. The NMR data are consistent with the literature.[10]

3,3',4,4'-tetrakis(4-methoxyphenyl)-1,1'-biisoquinoline (3j)



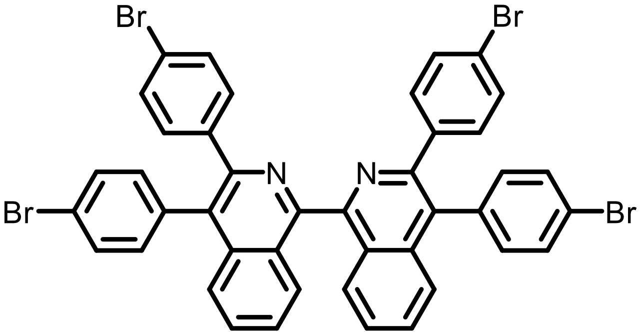
White solid (From GP B: 34.4 mg, 51% yield; From GP C, 31.6 mg, 46% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 20/1→8/1, v/v). **^{1}H NMR (500MHz, $CDCl_3$):** δ = 8.04 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 4H), 7.26–7.25 (m, 4H), 6.98 (d, *J* = 8.5 Hz, 4H), 6.72 (d, *J* = 8.5 Hz, 4H), 3.89 (s, 6H), 3.74 (s, 6H) ppm. The NMR data are consistent with the literature.[9]

3,3',4,4'-tetrakis(4-chlorophenyl)-1,1'-biisoquinoline (3k)



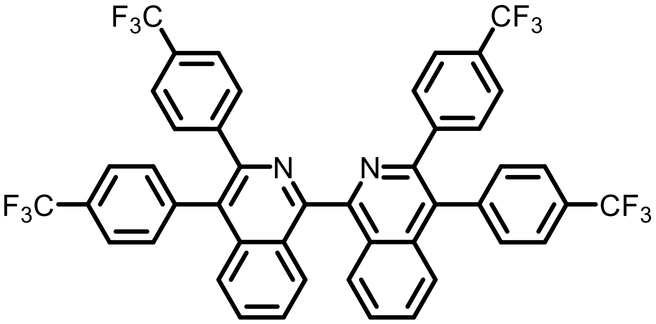
White solid (49.2 mg, 70% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 100/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.01 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.67 (t, J = 7.5 Hz, 2H), 7.55 (t, J = 7.0 Hz, 2H), 7.43 (d, J = 8.5 Hz, 4H), 7.33 (d, J = 8.5 Hz, 4H), 7.28–7.26 (m, 4H), 7.18 (d, J = 8.5 Hz, 4H) ppm. The NMR data are consistent with the literature.[9]

3,3',4,4'-tetrakis(4-bromophenyl)-1,1'-biisoquinoline (3l)



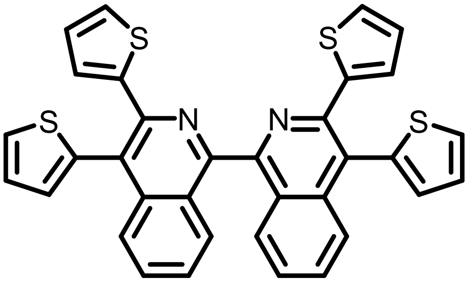
White solid (73.3 mg, 84% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 100/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.00 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.66 (t, J = 7.8 Hz, 2H), 7.60−7.53 (m, 6H), 7.34 (d, J = 7.0 Hz, 4H), 7.27 (d, J = 9.0 Hz, 4H, cover the solvent), 7.21 (d, J = 6.5 Hz, 4H) ppm. The NMR data are consistent with the literature.[9]

3,3',4,4'-tetrakis(4-(trifluoromethyl)phenyl)-1,1'-biisoquinoline (3m)



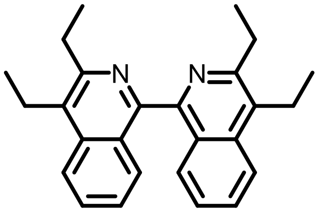
White solid (From GP B: 68.4 mg, 82% yield; From GP C, 43.3 mg, 52% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 100/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.07 (d, J = 8.0 Hz, 2H), 7.75−7.70 (m, 8H), 7.62 (t, J = 6.0 Hz, 2H), 7.52−7.46 (m, 12H) ppm. The NMR data are consistent with the literature.[10]

3,3',4,4'-tetra(thiophen-2-yl)-1,1'-biisoquinoline (3n)



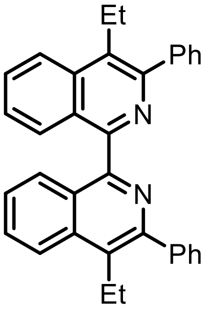
White solid (26.4 mg, 45% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.28 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 7.69−7.64 (m, 4H), 7.51 (t, J = 7.5 Hz, 2H), 7.35 (t, J = 3.8 Hz, 2H), 7.28−7.27 (m, 2H), 7.25−7.24 (m, 2H), 6.91 (t, J = 4.0 Hz, 2H), 6.82 (d, J = 3.0 Hz, 2H) ppm. The NMR data are consistent with the literature.[10]

3,3',4,4'-tetraethyl-1,1'-biisoquinoline (3o)

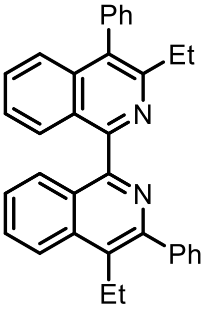


White solid (30.1 mg, 81% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 60/1→10/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** *δ* = 8.08 (d, *J* = 8.0 Hz, 2H), 7.67−7.63 (m, 4H), 7.33 (t, *J* = 8.0 Hz, 2H), 3.20 (q, *J* = 7.3 Hz, 4H), 3.10 (q, *J* = 7.7 Hz, 4H), 1.39 (t, *J* = 6.8 Hz, 12H) ppm. The NMR data are consistent with the literature.[9]

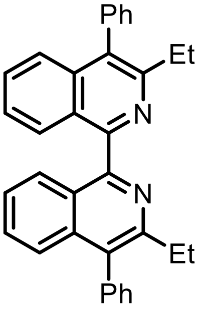
4,4'-diethyl-3,3'-diphenyl-1,1'-biisoquinoline (3p)



3p (major)



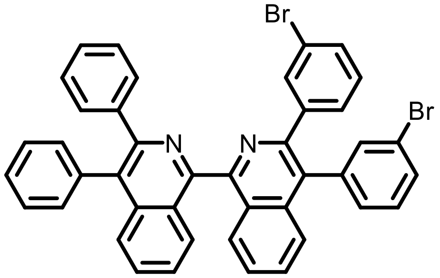
3p' (minor)



3p'' (none)

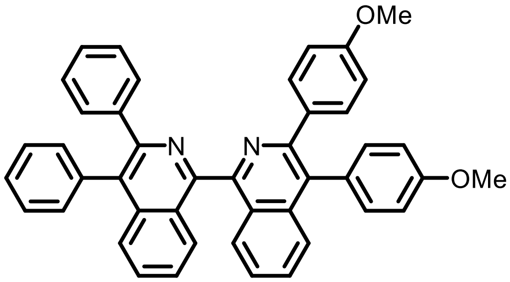
White solid (24.3 mg, 52% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 60/1→10/1, v/v) afforded the mixture of **3p**, **3p′** and **3p″** (**3p**:**3p′**:**3p″** = 3:1:0). **^{1}H NMR (500MHz, CDCl$_3$, major):** *δ* = 8.17 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.74 (t, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.0 Hz, 4H), 7.48–7.42 (m, 7H), 7.38–7.35 (m, 3H), 3.14 (q, *J* = 7.0 Hz, 4H), 1.34 (t, *J* = 7.3 Hz, 6H) ppm. The NMR data are consistent with the literature.[9]

3,4-bis(3-bromophenyl)-3',4'-diphenyl-4a,8a-dihydro-1,1'-biisoquinoline (4ai)



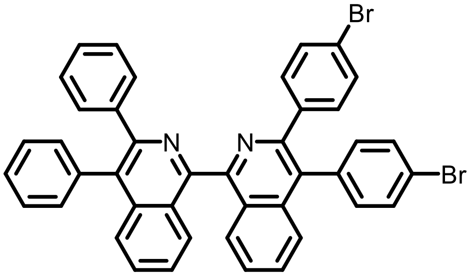
White solid (From GP D: 70.2 mg, 98% yield; From GP E, 25.1 mg, 35% yield), purification via a neutral aluminum oxide (200–300 mesh) column (petroleum ether/EtOAc = 80/1→20/1, v/v). M.p.: >250 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.10 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 7.74 (d, J = 8.5 Hz, 1H), 7.71–7.63 (m, 3H), 7.60–7.53 (m, 4H), 7.44–7.40 (m, 5H), 7.36 (d, J = 6.5 Hz, 2H), 7.32 (t, J = 7.8 Hz, 2H), 7.27–7.25 (m, 2H, cover the solvent), 7.21–7.16 (m, 3H), 7.06 (t, J = 7.8 Hz, 1H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 158.3, 157.1, 149.8, 148.2, 142.4, 140.8, 139.3, 137.4, 137.3, 136.9, 134.1, 133.5, 131.4, 131.1, 131.0, 130.6, 130.5, 130.5, 130.3, 130.1, 130.0, 129.3, 129.1, 128.5, 127.8, 127.7, 127.6, 127.6, 127.2, 127.2, 127.1, 126.8, 126.3, 125.8, 122.7, 122.2 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{42}H_{27}Br_2N_2$ ([M+H]$^+$) 717.0541, found 717.0540.

3,4-bis(4-methoxyphenyl)-3',4'-diphenyl-4a,8a-dihydro-1,1'-biisoquinoline (4aj)



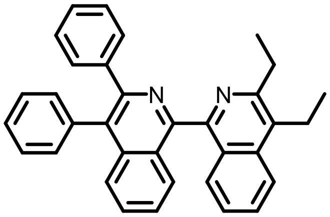
White solid (From GP D: 58.0 mg, 93% yield; From GP E, 24.6 mg, 40% yield), purification via a neutral aluminum oxide (200–300 mesh) column (petroleum ether/EtOAc = 20/1→2/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.09–8.04 (m, 2H), 7.77 (t, J = 7.8 Hz, 2H), 7.64–7.59 (m, 2H), 7.53–7.48 (m, 2H), 7.42–7.34 (m, 9H), 7.26–7.24 (m, 2H), 7.19–7.13 (m, 3H), 6.98 (d, J = 7.5 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 3.74 (s, 3H) ppm. The NMR data are consistent with the literature.[9]

3,4-bis(4-bromophenyl)-3',4'-diphenyl-4a,8a-dihydro-1,1'-biisoquinoline (4al)



White solid (From GP D: 70.1 mg, 97% yield; From GP E, 32.5 mg, 45% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→20/1, v/v). M.p.: 237–239 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** *δ* = 8.09 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.68–7.51 (m, 6H), 7.43–7.41 (m, 5H), 7.35 (d, *J* = 8.5 Hz, 4H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18–7.14 (m, 3H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** *δ* = 158.2, 157.2, 149.8, 148.4, 140.8, 139.5, 137.4, 137.3, 137.0, 136.2, 133.01, 132.2, 132.0, 131.4, 131.4, 131.1, 130.9, 130.6, 130.5, 130.0, 128.5, 127.8, 127.8, 127.6, 127.5, 127.3, 127.2 (2C), 127.0, 126.8, 126.3, 125.8, 122.1, 121.9 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{42}H_{27}Br_2N_2$ ($[M+H]^+$) 717.0541, found 717.0545.

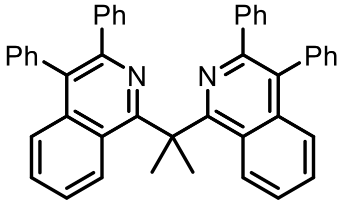
3,4-diethyl-3',4'-diphenyl-4a,8a-dihydro-1,1'-biisoquinoline (4ao)



White solid (45.0 mg, 97% yield), purification via a neutral aluminum oxide (200−300 mesh) column (petroleum ether/EtOAc = 80/1→20/1, v/v). M.p.: 164−166 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** *δ* = 8.11 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J*

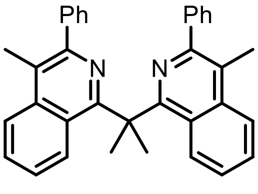
= 8.5 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.45–7.38 (m, 7H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.17–7.13 (m, 3H), 3.21 (q, *J* = 7.5 Hz, 2H), 3.11 (q, *J* = 7.5 Hz, 2H), 1.42–1.39 (m, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** *δ* = 158.0, 156.0, 149.7, 141.0, 137.7, 137.3, 136.3, 131.5, 130.6, 130.4, 130.0, 129.7, 128.5, 128.1, 127.7, 127.6, 127.5, 127.1, 127.0, 126.9, 126.8, 126.1, 125.9, 123.2, 28 8, 21.2, 15.4, 15.3 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{34}H_{29}N_2$ ([M+H]$^+$) 465.2331, found 465.2327.

1,1'-(propane-2,2-diyl)bis(3,4-diphenylisoquinoline) (5a)

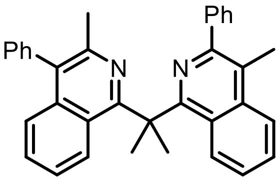


White solid (14.7 mg, 24% yield), purification via filtration. M.p.: >250 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** *δ* = 7.82 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 7.5 Hz, 4H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.43–7.36 (m, 6H), 7.32–7.28 (m, 12H), 7.08 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** *δ* = 165.9, 147.9, 141.4, 138.2, 137.5, 131.6, 130.8, 129.5, 129.1, 128.5, 127.7, 127.4, 127.2, 126.6, 126.2, 125.9, 125.5, 52.5, 30.9. ppm. **HRMS (ESI) *m/z*:** calcd for $C_{45}H_{35}N_2$ ([M+H]$^+$) 603.2800, found 603.2794.

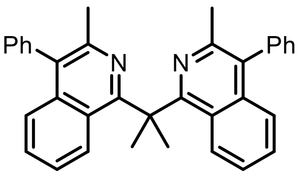
1,1'-(propane-2,2-diyl)bis(4-methyl-3-phenylisoquinoline) (5b)



5b (major)



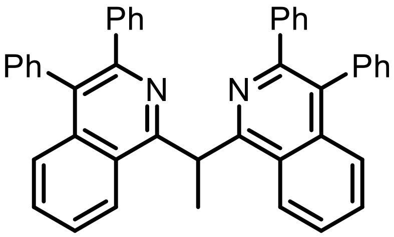
5b' (minor)



5b''(none)

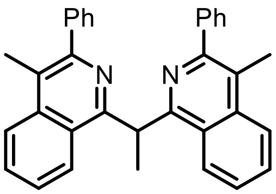
Light brown solid (8 mg, 17% yield), purification via filtration afforded the mixture of **5b**, **5b** and **5b″** (**5b**: **5b′**: **5b″** = 10:1:0). **^{1}H NMR (500MHz, CDCl$_3$, major):** *δ* = 8.01 (d, *J* = 9.0 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 4H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 4H), 7.48–7.42 (m, 4H), 7.04 (d, *J* = 7.8 Hz, 2H), 2.72 (s, 6H), 2.16 (s, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$, major):** δ = 164.4, 149.5, 142.1, 137.7, 130.7, 129.0, 128.1, 127.6, 126.7, 125.5, 125.4, 124.4, 122.5, 51.8, 30.9, 16.1 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{35}H_{31}N_2$ ([M+H]$^+$) 479.2487, found 479.2483.

1,1'-(ethane-1,1-diyl)bis(3,4-diphenylisoquinoline) (5c)

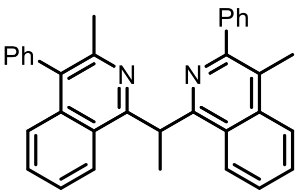


White solid (23.6 mg, 40% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 80/1→40/1, v/v). M.p.: >250 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.86 (d, *J* = 8.0 Hz, 2H), 7.63-7.61 (m, 2H), 7.48–7.46 (m, 8H), 7.37–7.35(m, 6H), 7.26–7.22(m, 10H, cover the solvent), 6.12 (q, *J* = 7.0 Hz, 1H), 2.32 (d, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 161.9, 148.7, 141.3, 138.0, 137.2, 131.5 (2C), 130.6, 129.6, 128.5, 128.4, 127.6, 127.3, 127.1, 126.5, 126.4, 126.3, 48.5, 19.4 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{44}H_{32}N_2Na$ ([M+Na]$^+$) 611.2463, found 611.2462.

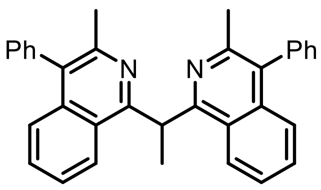
1,1'-(ethane-1,1-diyl)bis(3-methyl-4-phenylisoquinoline) (5d)



5d (major)



5d' (minor)

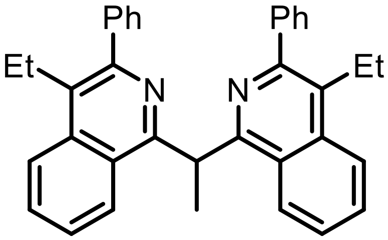


5d"(none)

Yellow oil (28.8 mg, 62% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 80/1→40/1, v/v) afforded the mixture of **5d**, **5d′** and **5d″** (**5d**: **5d′**: **5d″** = 4:1:0).**^{1}H NMR (500MHz, CDCl$_3$, major):** δ = 8.74 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 7.5 Hz, 2H), 7.69 (d, *J*

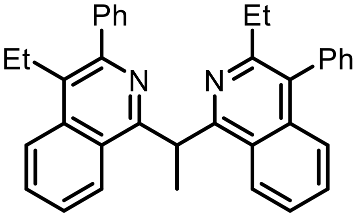
= 7.5 Hz, 4H), 7.59 (t, *J* = 7.8 Hz, 2H), 7.53(t, *J* = 7.5 Hz, 4H), 7.46–7.40 (m, 4H), 5.89 (q, *J* = 7.0 Hz, 1H), 2.61 (s, 6H), 2.18 (d, *J* = 7.9 Hz, 3H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$, major):** δ = 160.4, 150.2, 142.0, 137.3, 130.3, 129.5, 128.1, 127.5, 127.2, 126.3, 126.0, 124.3, 122.7, 49.2, 29.9, 19.4 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{34}H_{29}N_2$ ([M+H]$^+$) 465.2331, found 465.2328.

1,1'-(ethane-1,1-diyl)bis(4-ethyl-3-phenylisoquinoline) (5e)



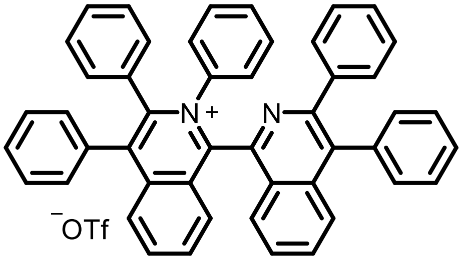
Yellow oil (24.7 mg, 50% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.84 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 7.5 Hz, 4H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 4H), 7.48–7.41(m, 4H), 5.90 (q, *J* = 7.2 Hz, 1H), 3.02 (q, *J* = 7.5 Hz, 4H) 2.18 (d, *J* = 7.0 Hz, 3H), 1.29 (t, *J* = 7.5 Hz, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 160.3, 150.3, 142.4, 136.2, 129.6, 129.4, 129.0, 128.2, 127.7, 127.5, 126.9, 125.9, 124.2, 49.5, 21.9, 19.3, 15.9 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{36}H_{33}N_2$ ([M+H]$^+$) 493.2644, found 493.2641.

3-ethyl-1-(1-(4-ethyl-3-phenylisoquinolin-1-yl)ethyl)-4-phenylisoquinoline (5e′)



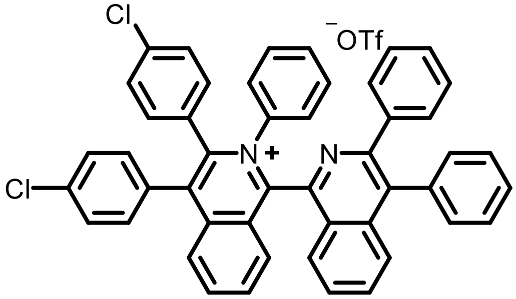
Yellow oil (8 mg, 16% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 80/1→40/1, v/v). **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.88 (d, *J* = 8.5 Hz, 1H), 8.78 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.50–7.40 (m, 6H), 7.38–7.34 (m, 2H), 7.31–7.28 (m, 2H), 5.91 (q, *J* = 7.2 Hz, 1H), 3.02 (q, *J* = 7.5 Hz, 2H), 2.77 (q, *J* = 7.5 Hz, 2H), 2.22 (d, *J* = 7.5 Hz, 3H), 1.31–1.28 (m, 6H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 161.6, 160.4, 152.4, 150.3, 142.4, 138.3, 137.0, 136.3, 130.5 (2C), 129.6, 129.4, 129.2, 129.0, 128.5 (2C), 128.3, 127.8, 127.5, 127.4, 126.9, 126.6, 126.0, 125.8, 125.4, 124.2, 49.4, 31.8, 29.0, 21.9, 19.3, 15.9 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{36}H_{33}N_2$ ([M+H]$^+$) 493.2644, found 493.2639.

2,3,3',4,4'-pentaphenyl-4a,8a-dihydro-[1,1'-biisoquinolin]-2-ium triflate (7a)



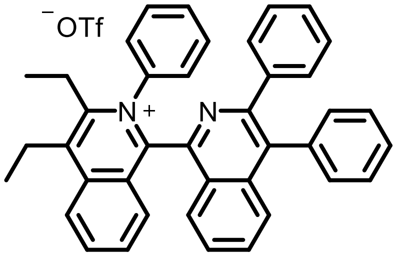
Yellow solid (55.1 mg, 70% yield), purification via a silica (100-200 mesh) gel column (CH_2Cl_2/CH_3OH = 100/1→60/1, v/v). M.p.: 151−153 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.49 (d, *J* = 8.0 Hz, 1H), 8.04 (t, *J* = 7.3 Hz, 1H), 7.95 (t, *J* = 7.3 Hz, 2H), 7.84–7.77 (m, 4H), 7.67–7.59 (m, 3H), 7.45–7.41 (m, 3H), 7.31–7.27 (m, 4H), 7.20 (s, 5H), 7.13 (d, *J* = 7.0 Hz, 1H), 7.07–7.02 (m, 3H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.94–6.89 (m, 3H), 6.84–6.79 (m, 2H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 156.5, 149.9, 149.6, 146.7, 140.5, 140.1, 140.0, 139.9, 137.2, 136.1, 135.9, 133.8, 133.2, 133.1, 132.2, 132.0, 131.9, 131.3, 131.1, 130.9, 130.4, 130.3, 130.1, 129.9, 129.7, 129.2, 129.0, 128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8(3C), 127.7, 127.3, 127.2, 127.0, 125.6 ppm. **^{19}F NMR (470 MHz, CDCl$_3$):** δ = −78.40 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{48}H_{33}N_2$ ([M−OTf $^-$]$^+$) 637.2638, found 637.2636.

3,4-bis(4-chlorophenyl)-2,3',4'-triphenyl-[1,1'-biisoquinolin]-2-ium triflate (7b)



Yellow solid (56.0 mg, 65% yield), purification via a silica (100-200 mesh) gel column (CH_2Cl_2/CH_3OH = 100/1→60/1, v/v). M.p.: 177−179 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.44 (d, J = 8.5 Hz, 1H), 8.07 (t, J = 7.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.83–7.77 (m, 4H), 7.64–7.59 (m, 3H), 7.43 (d, J = 8.0 Hz, 2H), 7.40–7.34 (m, 2H), 7.31-7.28 (m, 3H), 7.19 (br s, 5H) 7.07–7.06 (m, 3H), 7.00–6.94 (m, 2H), 6.83 (d, J = 8.0 Hz, 2H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 157.3, 149.9, 149.3, 145.5, 140.0, 139.8, 139.5, 137.6, 136.0, 135.9, 135.6, 135.2, 134.4, 133.5, 133.3, 132.3, 132.0, 131.6, 131.5, 131.1, 130.9, 130.6, 130.2, 130.1, 130.0, 129.9, 129.8, 129.2, 129.0, 128.7, 128.4, 128.3, 128.1 (2C), 127.9, 127.8, 127.6, 127.5, 127.4, 127.3, 125.7 ppm. **^{19}F NMR (470 MHz, CDCl$_3$):** δ = −78.46 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{48}H_{31}Cl_2N_2$ ([M−OTf $^-$]$^+$) 705.1859, found 705.1856.

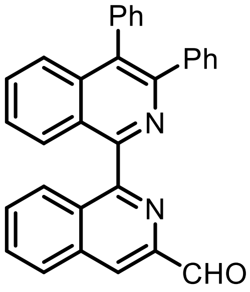
3,4-diethyl-2,3',4'-triphenyl-[1,1'-biisoquinolin]-2-ium (7c)



Yellow solid (42.2 mg, 61% yield), purification via a silica (100-200 mesh) gel column (CH_2Cl_2/CH_3OH = 100/1→60/1, v/v). M.p.: 110−112 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 8.45 (d, J = 9.0 Hz, 1H), 8.14 (t, J = 7.5 Hz, 1H), 8.02 (t, J = 7.0 Hz, 1H), 7.77 (t, J = 7.3 Hz, 1H), 7.71 (t, J = 7.5 Hz, 2H), 7.64–7.57 (m, 3H), 7.47–7.41 (m, 2H), 7.36–7.33 (m, 3H), 7.29 (t, J = 7.5 Hz, 1H), 7.25–7.24 (m, 1H), 7.19 (s, 5H), 7.08 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 7.0 Hz, 1H), 3.57–3.50 (m, 1H), 3.47–3.40 (m, 1H), 3.23–3.15 (m, 1H), 3.00–2.93 (m, 1H), 1.60 (t, J = 7.5 Hz, 3H), 1.23

(t, J = 7.8 Hz, 3H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ = 155.4, 149.8, 148.7, 140.0, 139.8, 139.3, 139.1, 136.9, 136.1, 135.8, 132.9, 132.1, 131.1, 130.9, 130.7, 130.6, 129.9, 129.8, 129.7, 128.7, 128.4, 128.0, 128.0, 127.9, 127.7, 127.7, 127.1, 127.0, 125.7, 124.8, 24.7, 22.6, 14.9, 13.9 ppm. **^{19}F NMR (470 MHz, CDCl$_3$):** δ = −78.42 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{40}H_{33}N_2$ ([M−OTf $^-$]$^+$) 541.2638, found 541.2637.

3',4'-diphenyl-[1,1'-biisoquinoline]-3-carbaldehyde (8)



Yellowish solid (20.1 mg, 46% yield), purification via a silica (100-200 mesh) gel column (petroleum ether/EtOAc = 20/1→10/1, v/v). M.p.: > 250 ºC. **^{1}H NMR (500MHz, CDCl$_3$):** δ = 10.35 (s, 1H), 8.57 (s, 1H), 8.16 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.84 (t, J = 7.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.43–7.40 (m, 5H), 7.35 (d, J = 6.0 Hz, 2H), 7.19–7.16 (m, 3H) ppm. **^{13}C NMR (125 MHz, CDCl$_3$):** δ =193.8, 159.4, 156.4, 150.0, 146.0, 140.6, 137.3, 136.7, 131.7, 131.5, 131.4, 130.7, 130.5, 130.4, 129.3, 128.6, 128.0, 127.8, 127.7, 127.4, 127.3, 126.9, 126.6, 126.4, 121.6 ppm. **HRMS (ESI) *m/z*:** calcd for $C_{31}H_{21}N_2O$ ([M+H]$^+$) 437.1649, found 437.1646.

9 References

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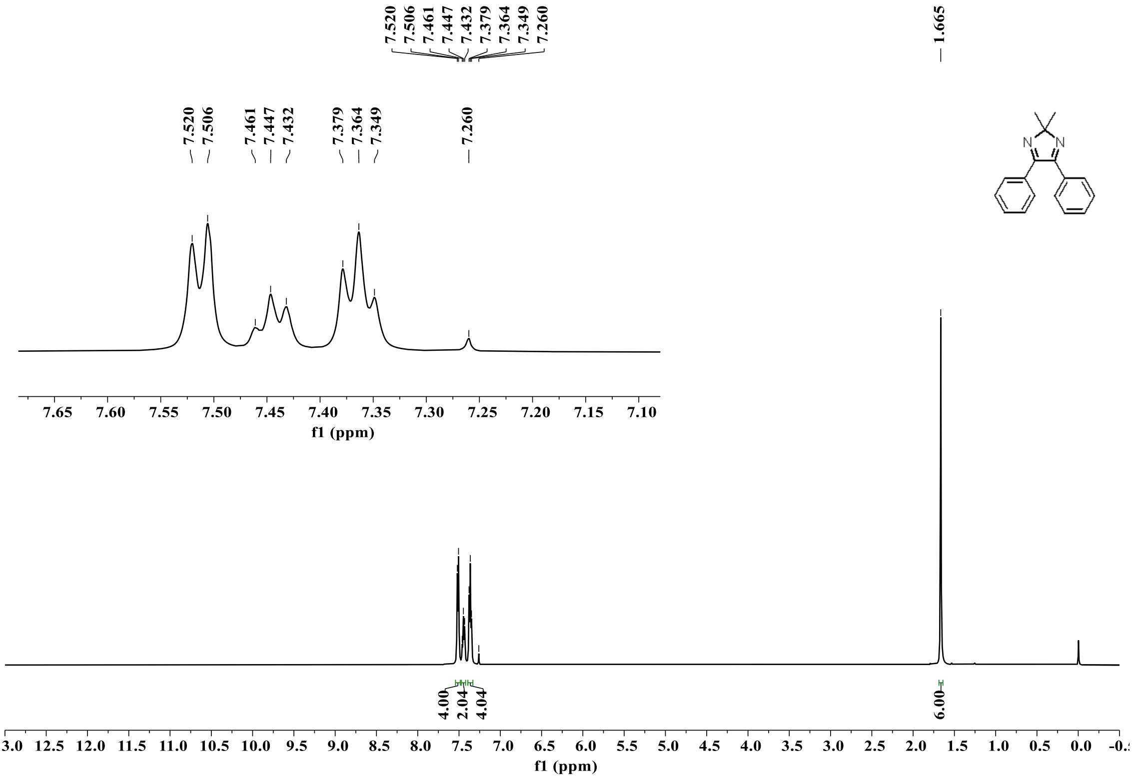
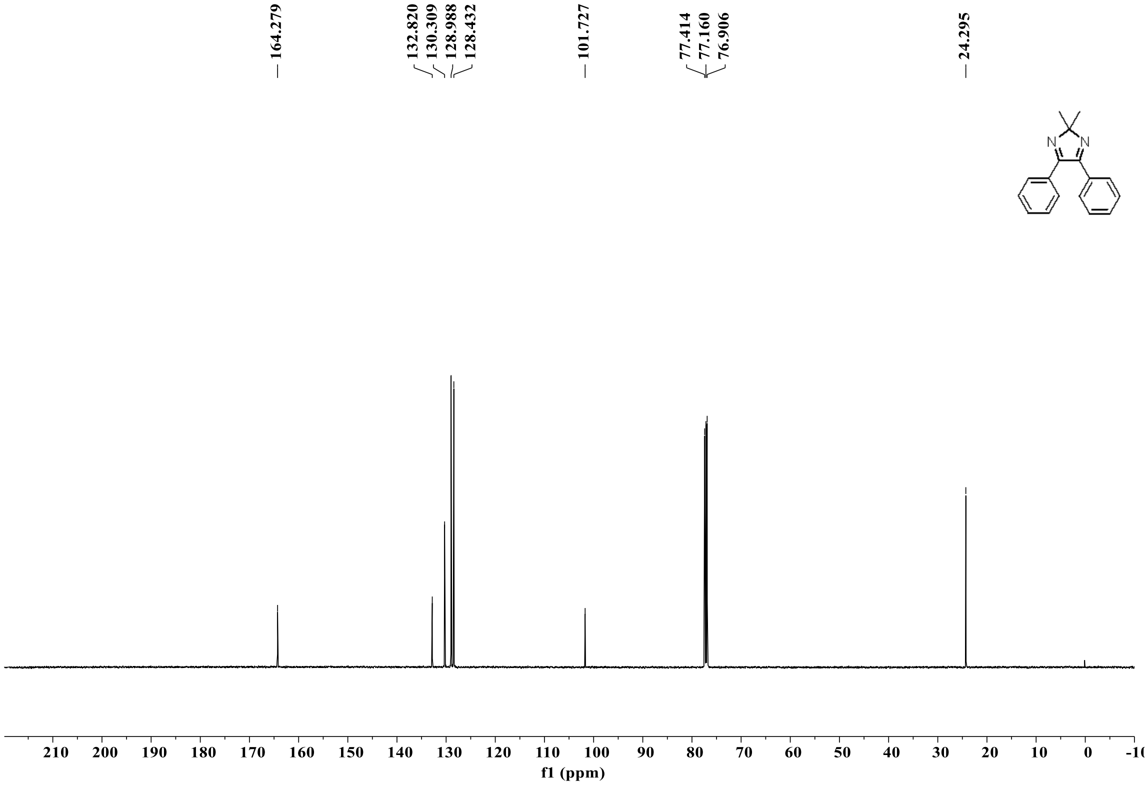
10 Copies of ^{1}H and ^{13}C and ^{19}F spectra

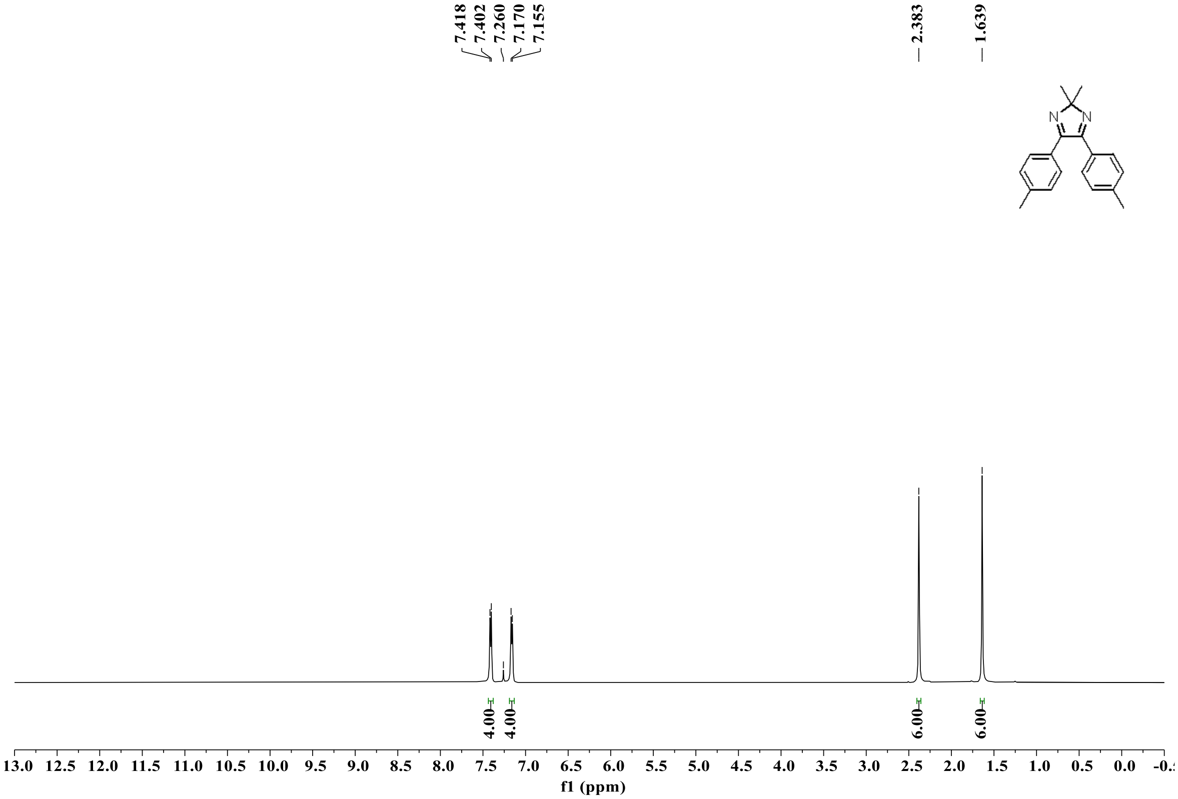
^{1}H NMR (500 MHz, $CDCl_3$) of **1a**



^{13}C NMR (500 MHz, $CDCl_3$) of **1a**



^{1}H NMR (500 MHz, CDCl$_3$) of **1b**



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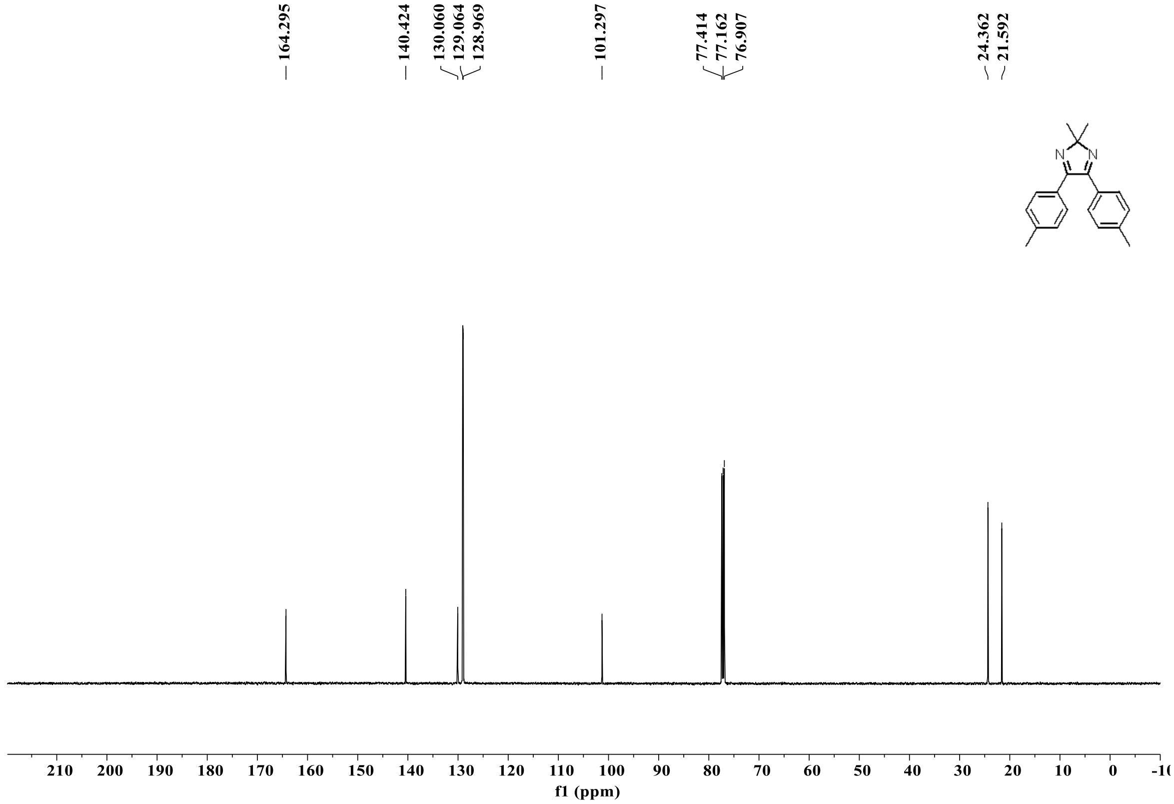
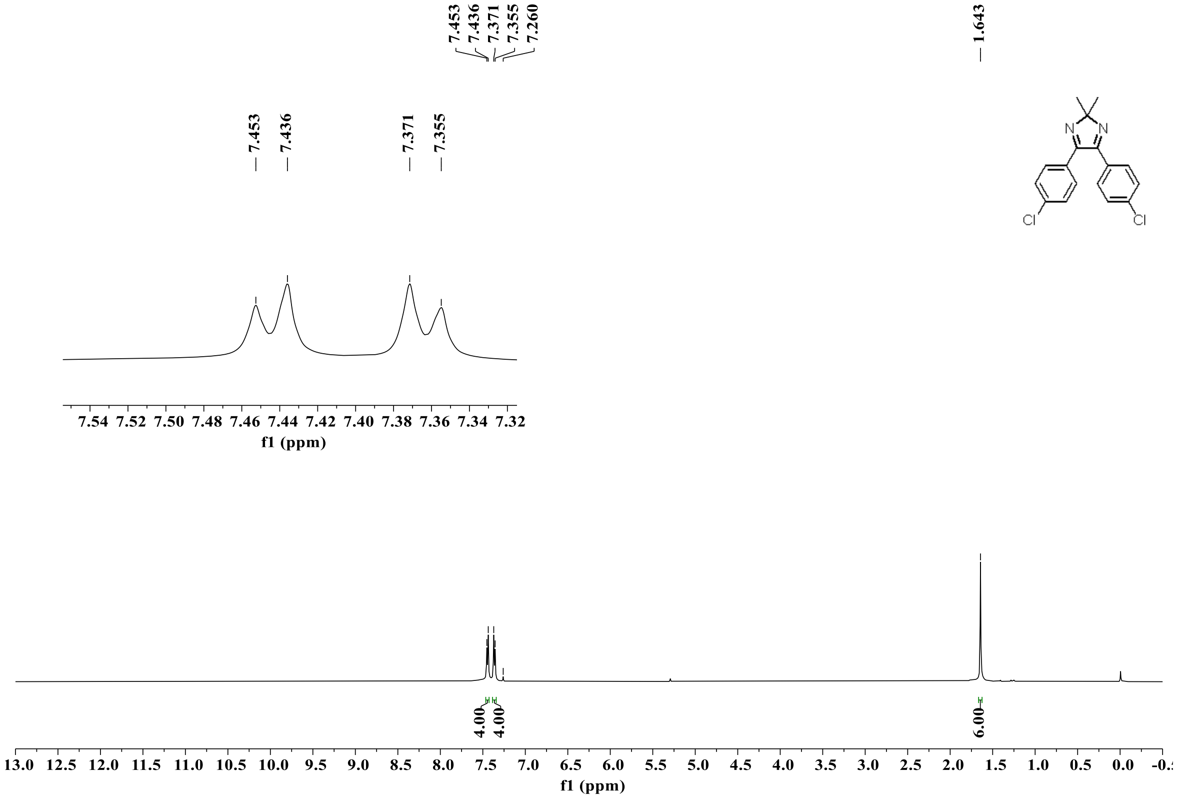
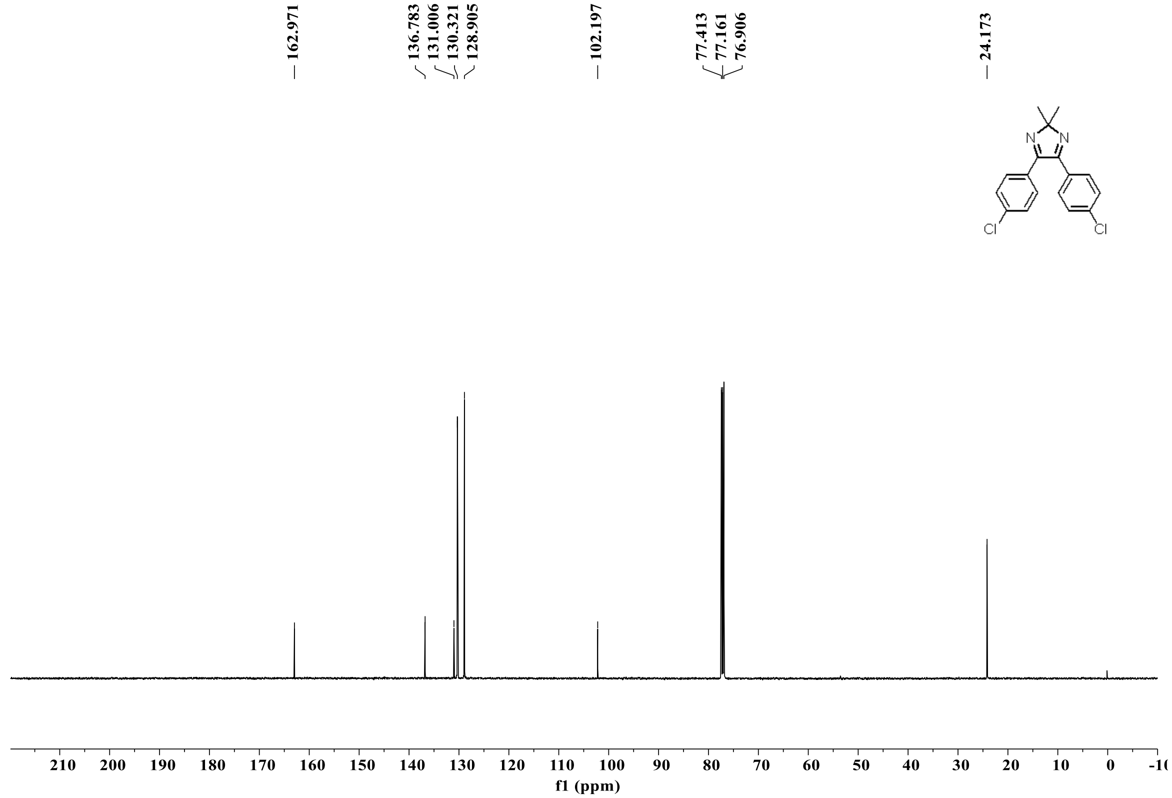


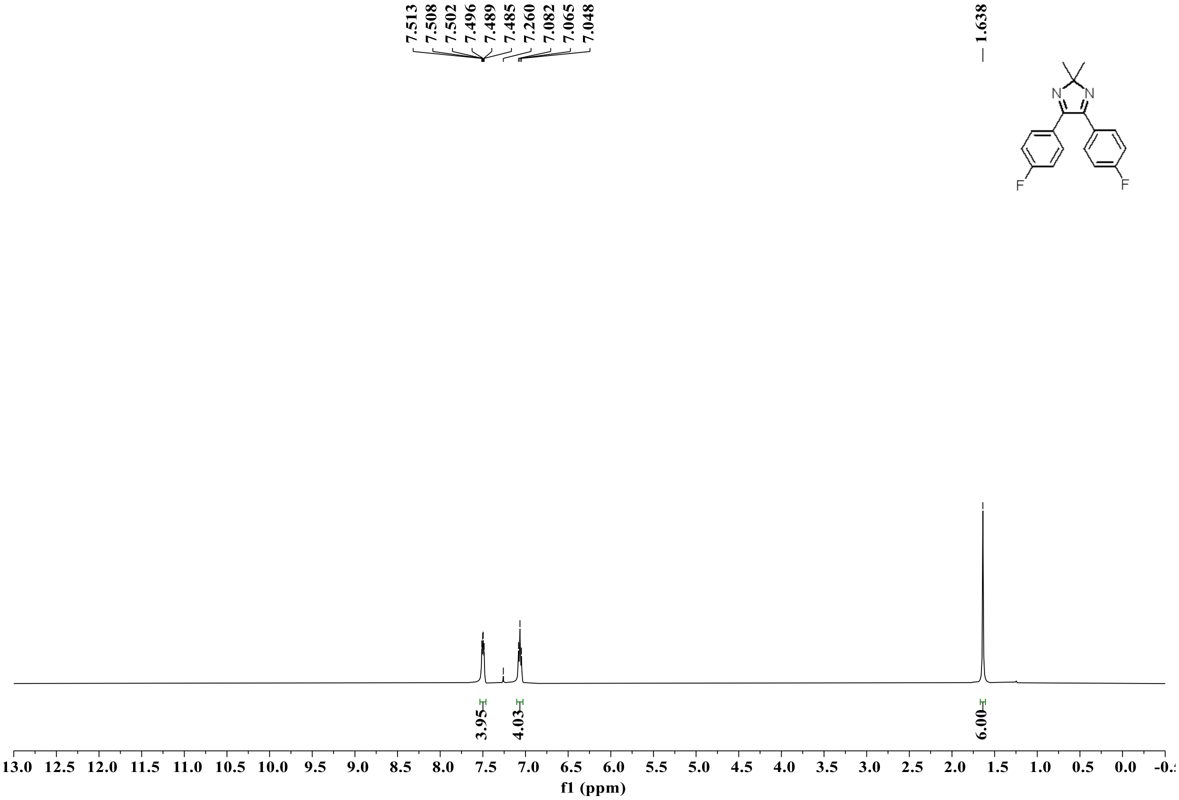
^{1}H NMR (500 MHz, CDCl$_3$) of **1c**



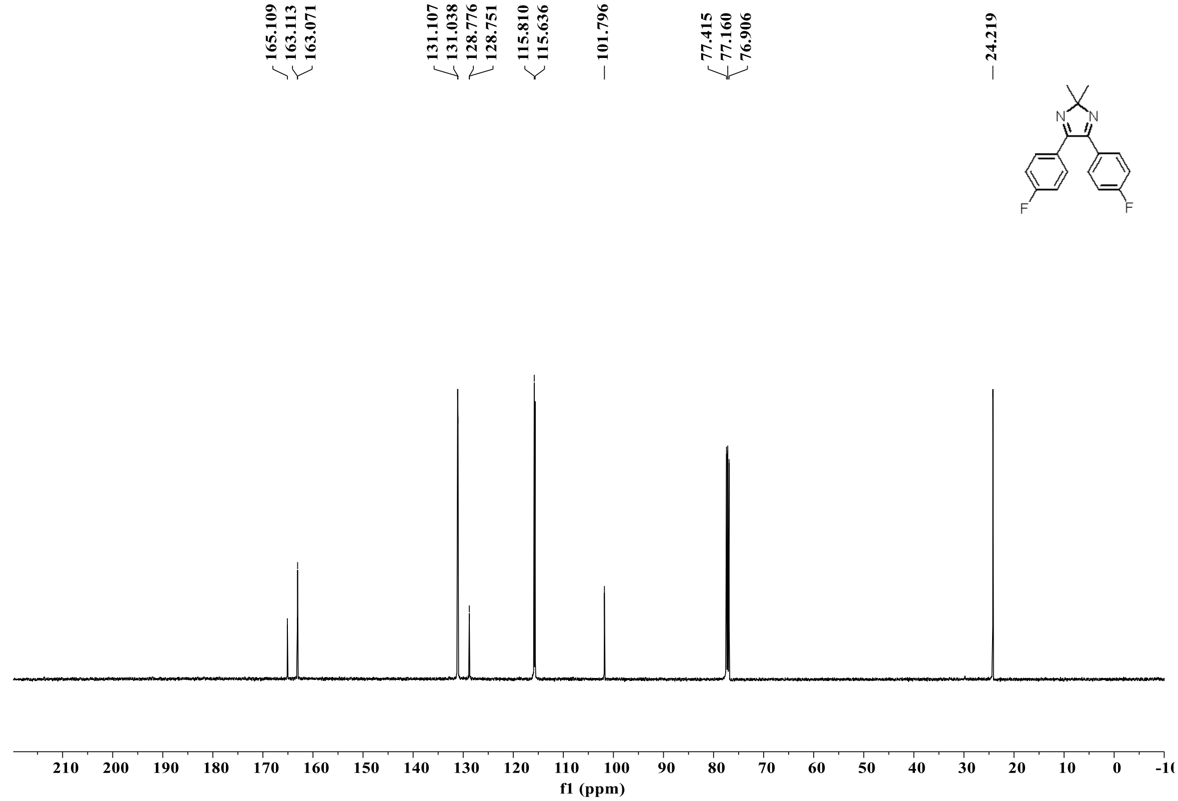
^{13}C NMR (500 MHz, CDCl$_3$) of **1c**



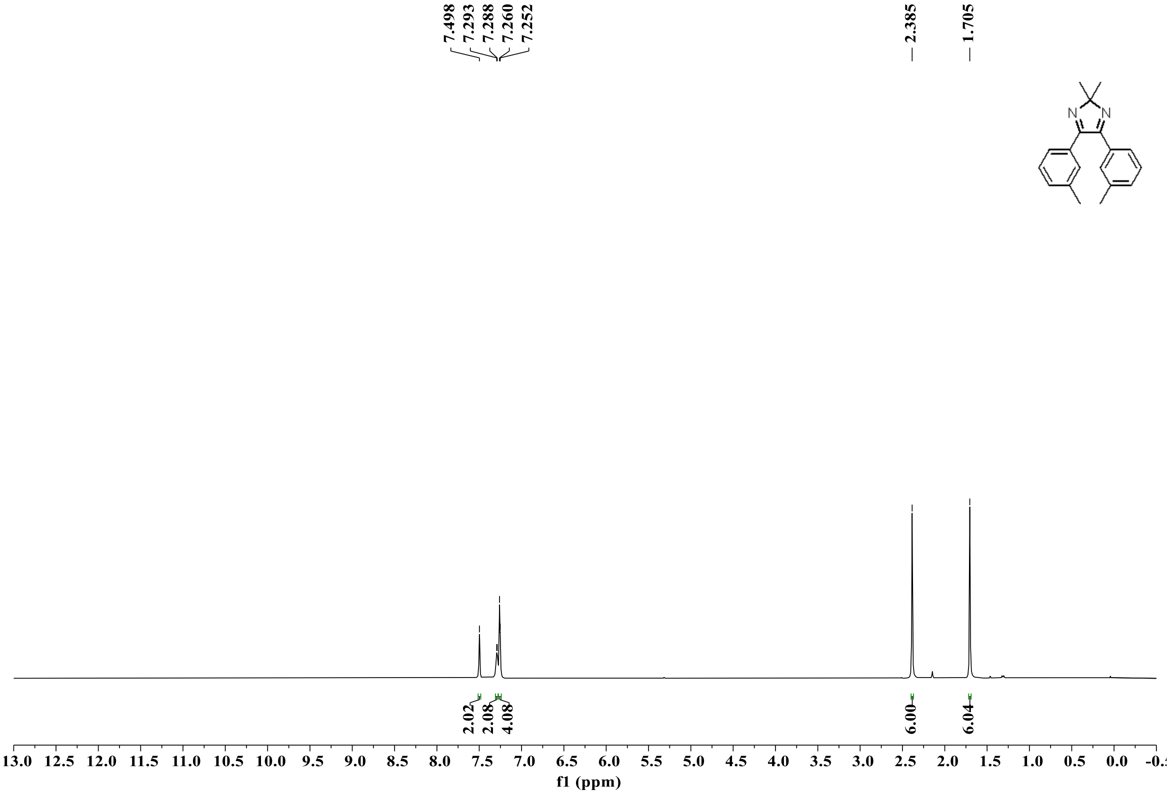
^{1}H NMR (500 MHz, CDCl$_3$) of **1d**



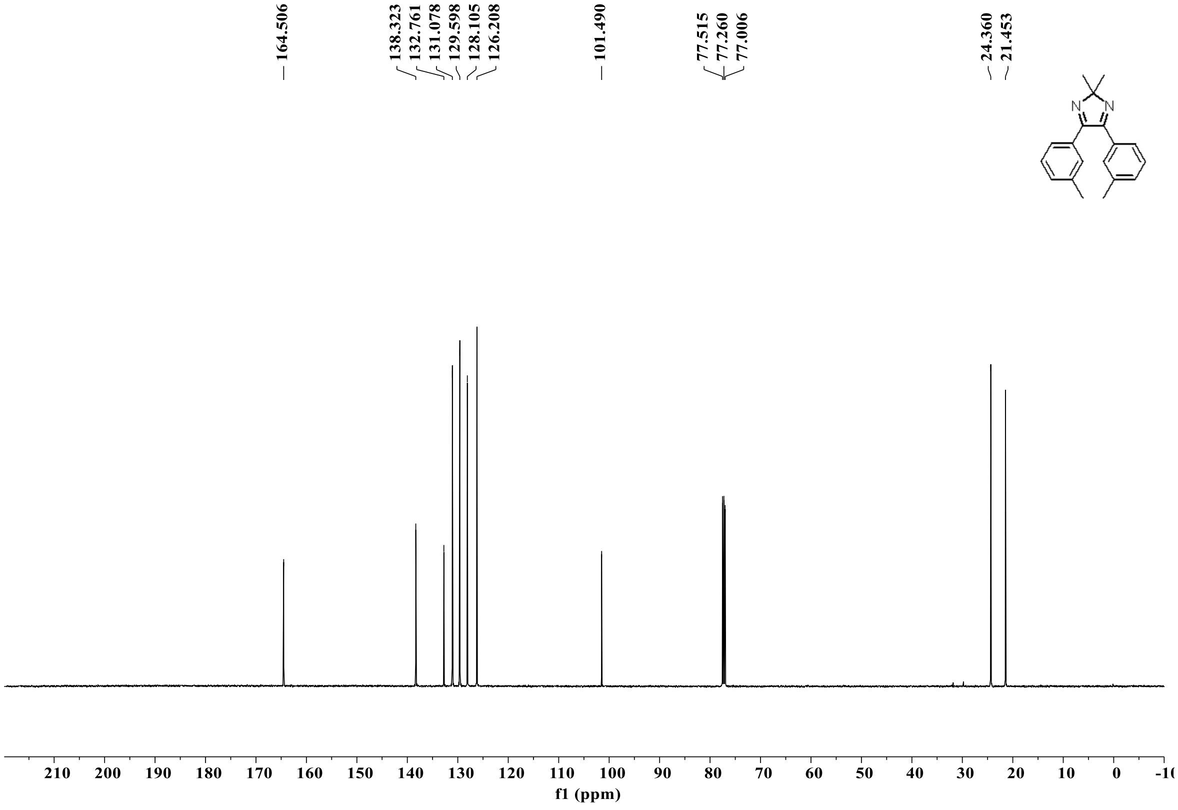
^{13}C NMR (500 MHz, CDCl$_3$) of **1d**



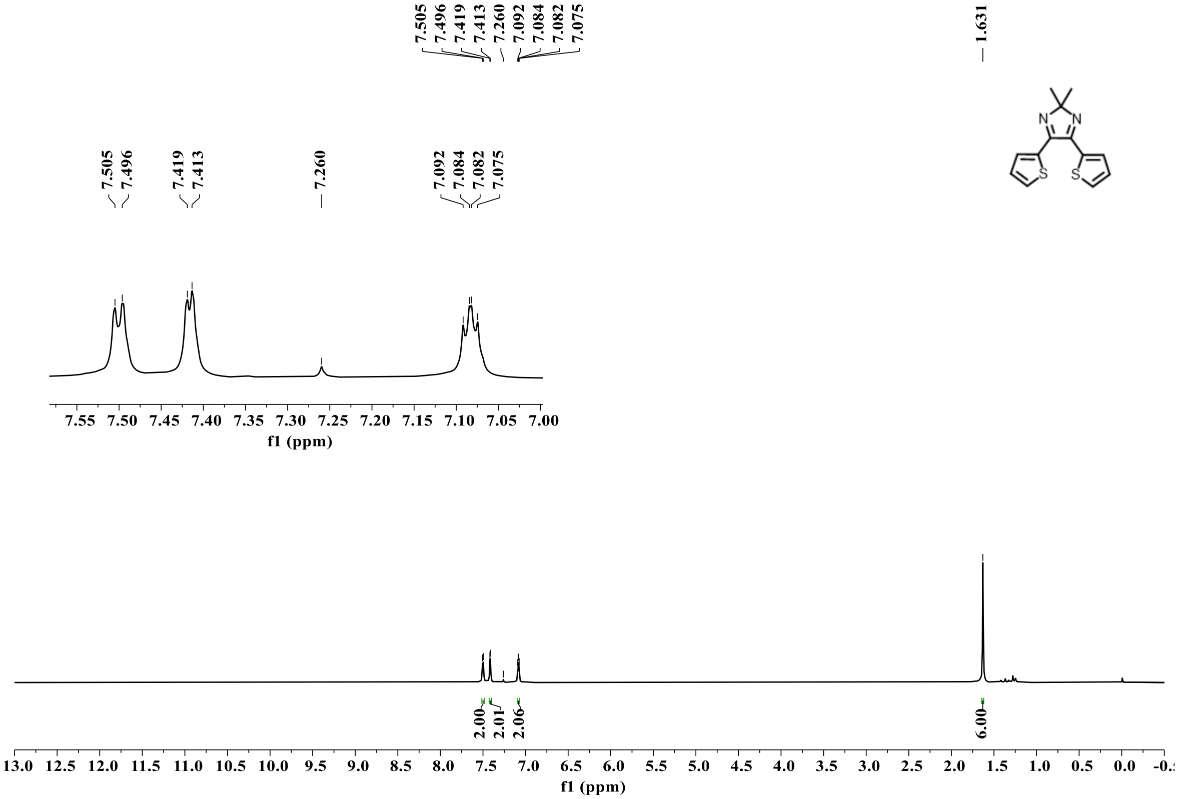
^{1}H NMR (500 MHz, CDCl$_3$) of **1e**



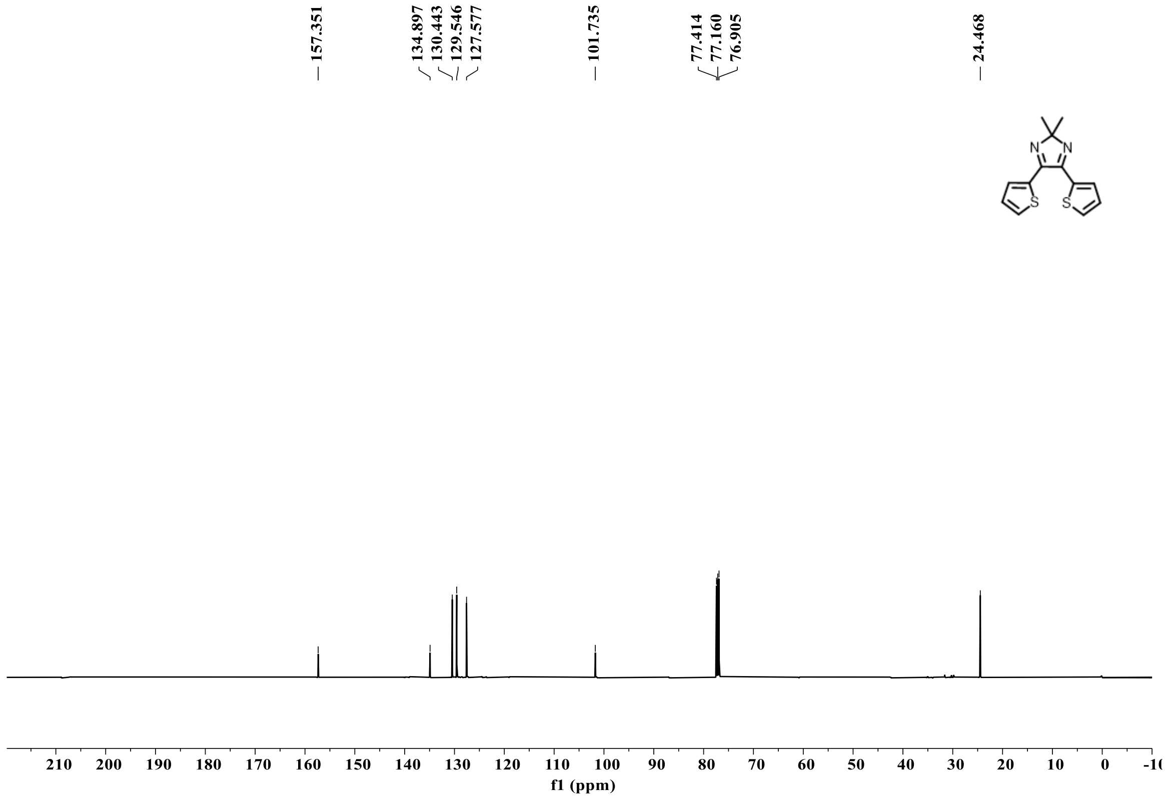
^{13}C NMR (500 MHz, CDCl$_3$) of **1d**



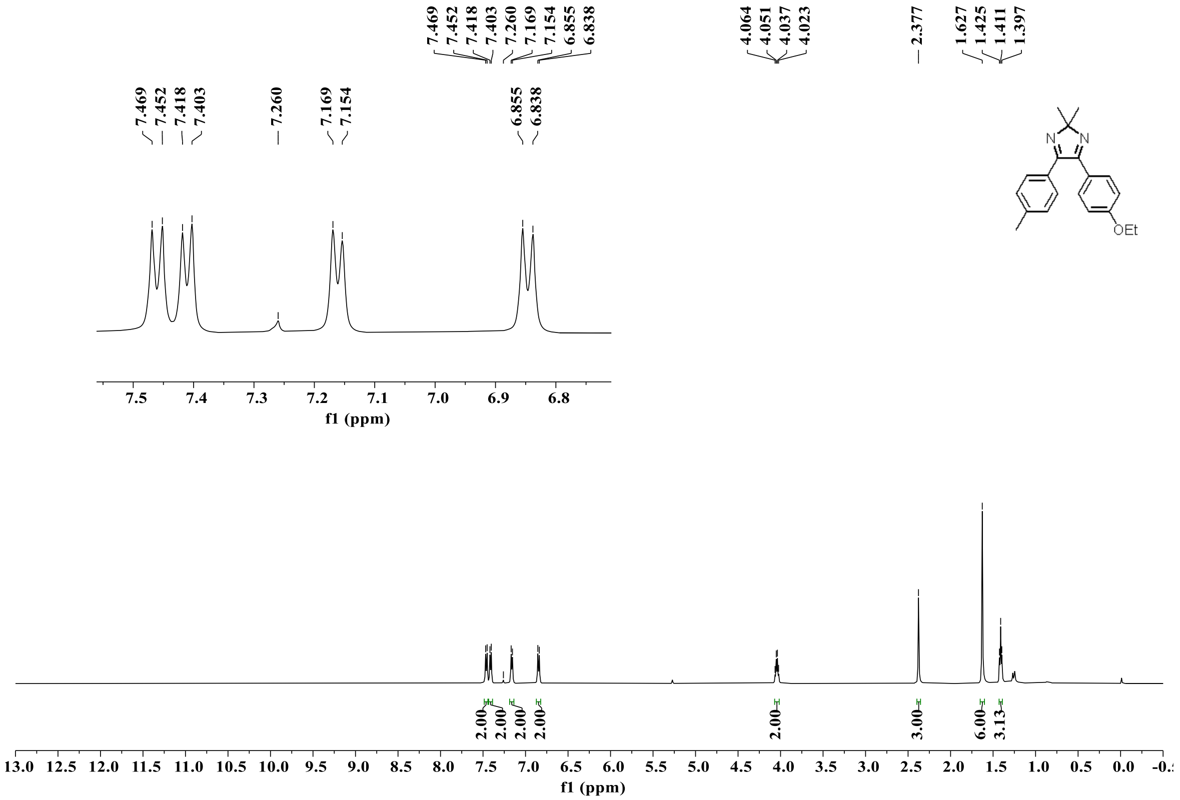
^{1}H NMR (500 MHz, $CDCl_3$) of **1f**



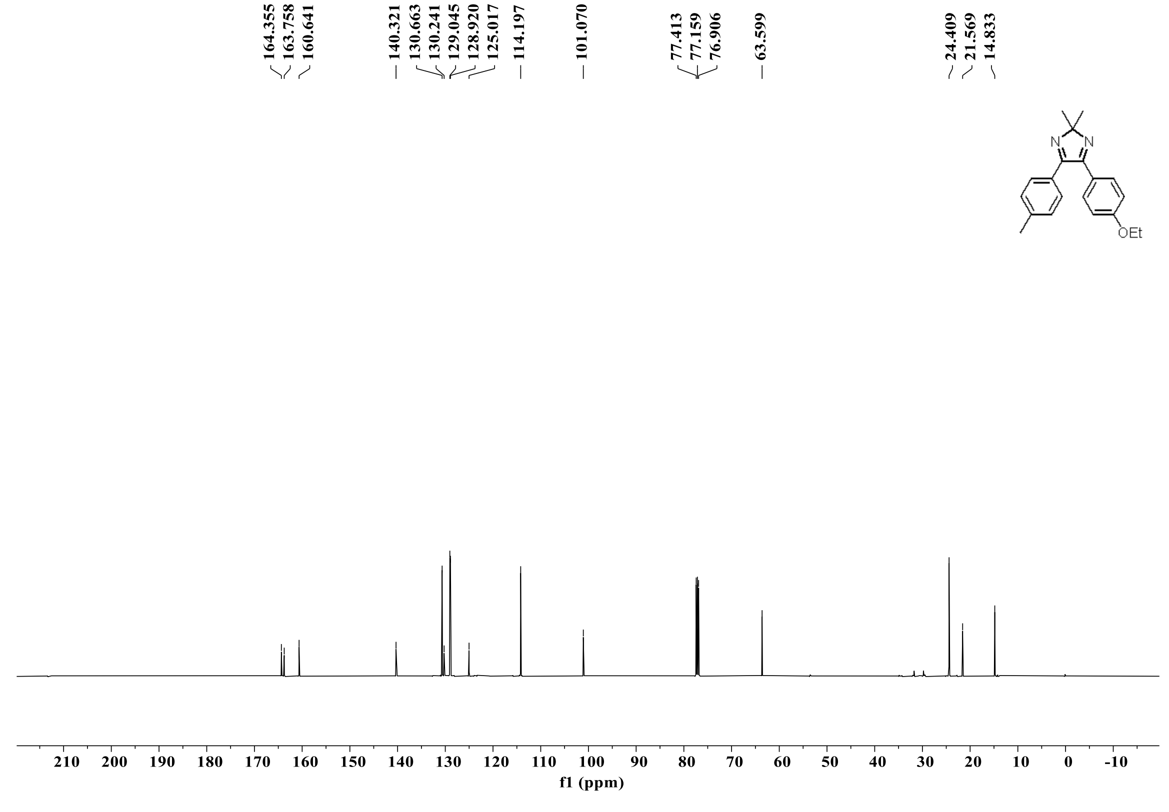
^{13}C NMR (500 MHz, $CDCl_3$) of **1f**



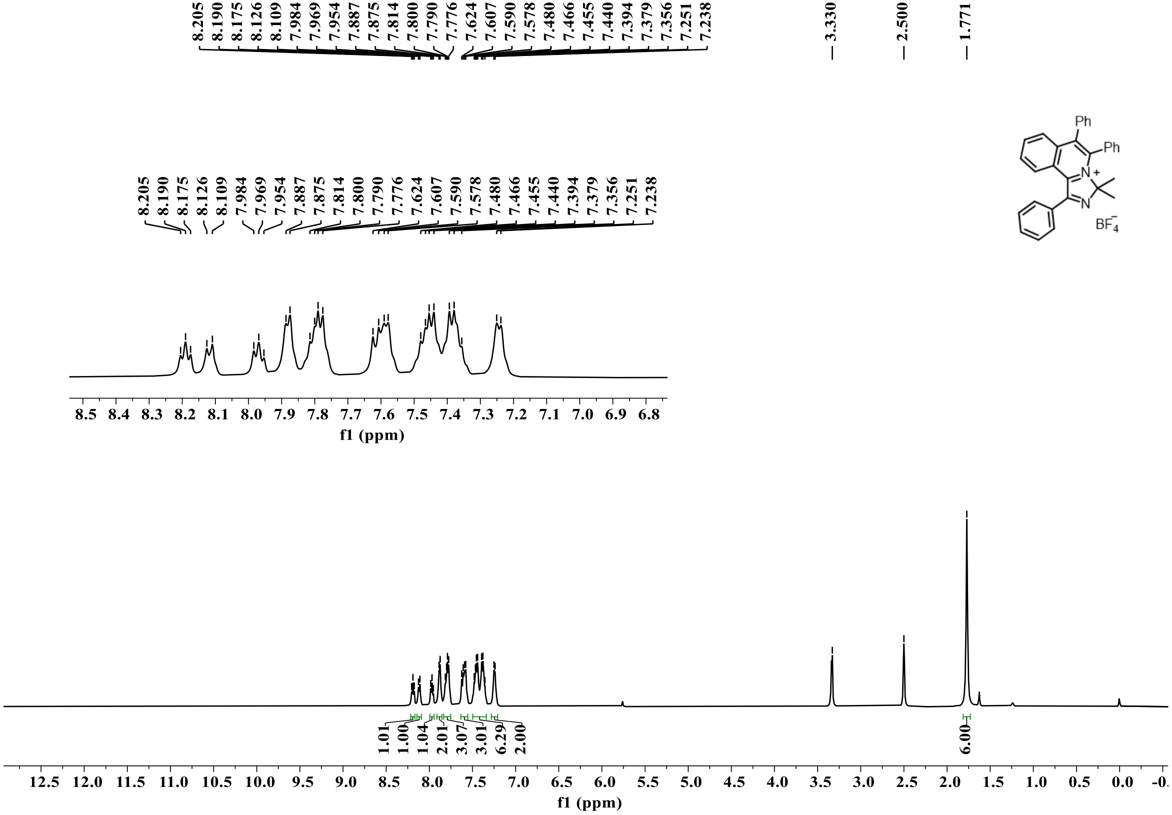
^{1}H NMR (500 MHz, CDCl$_3$) of **1g**



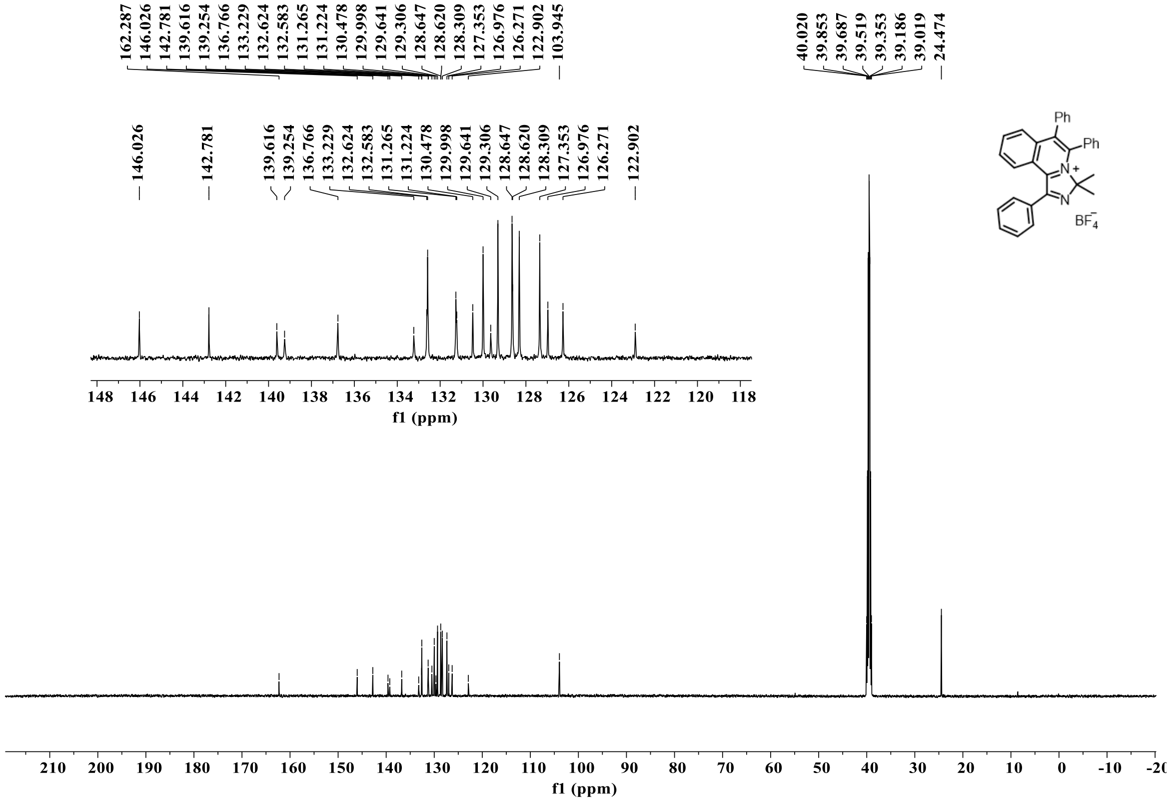
^{13}C NMR (500 MHz, CDCl$_3$) of **1g**



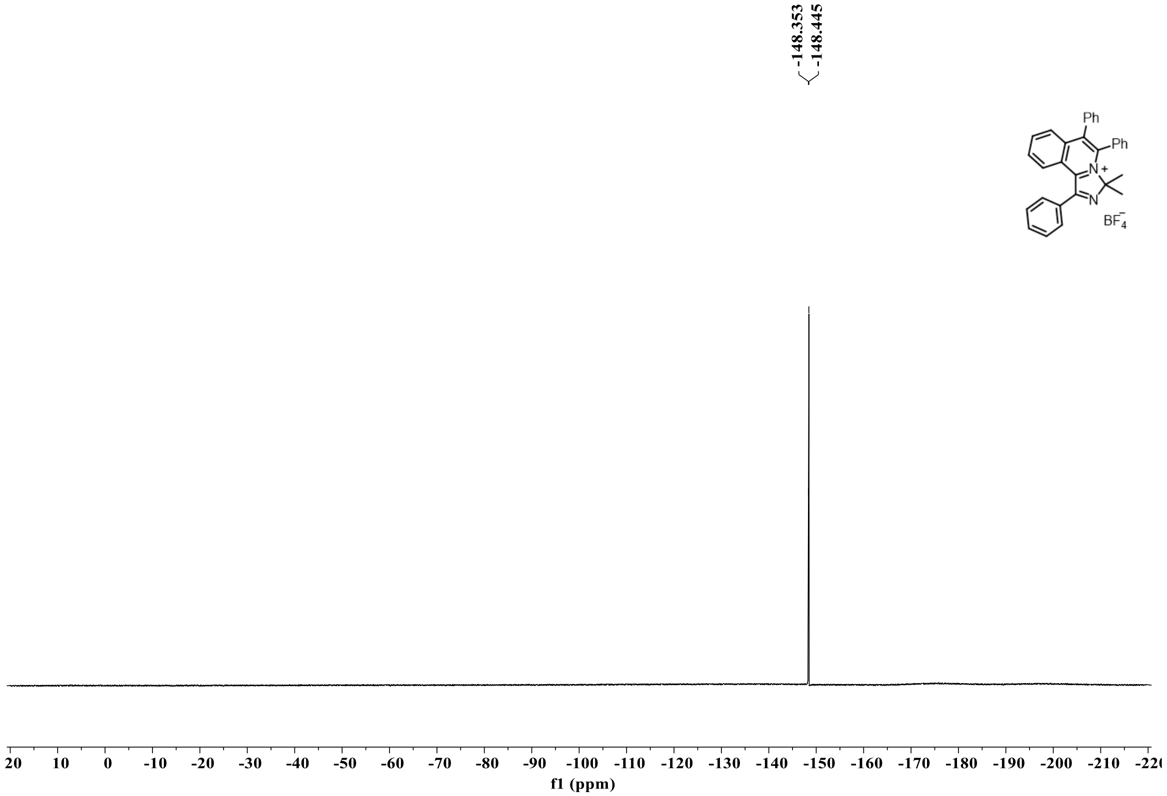
^{1}H NMR (500 MHz, DMSO-d_6) of **Int-C**



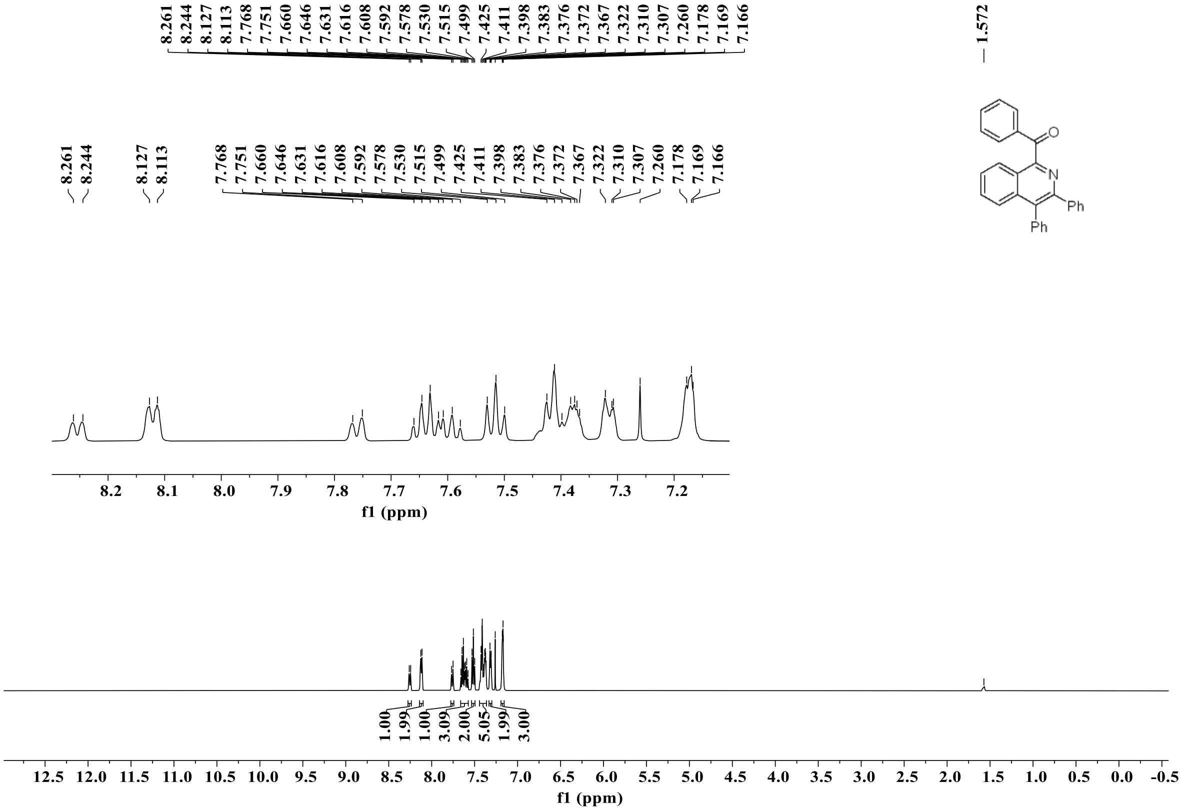
^{13}C NMR (125 MHz, DMSO-d_6) of **Int-C**



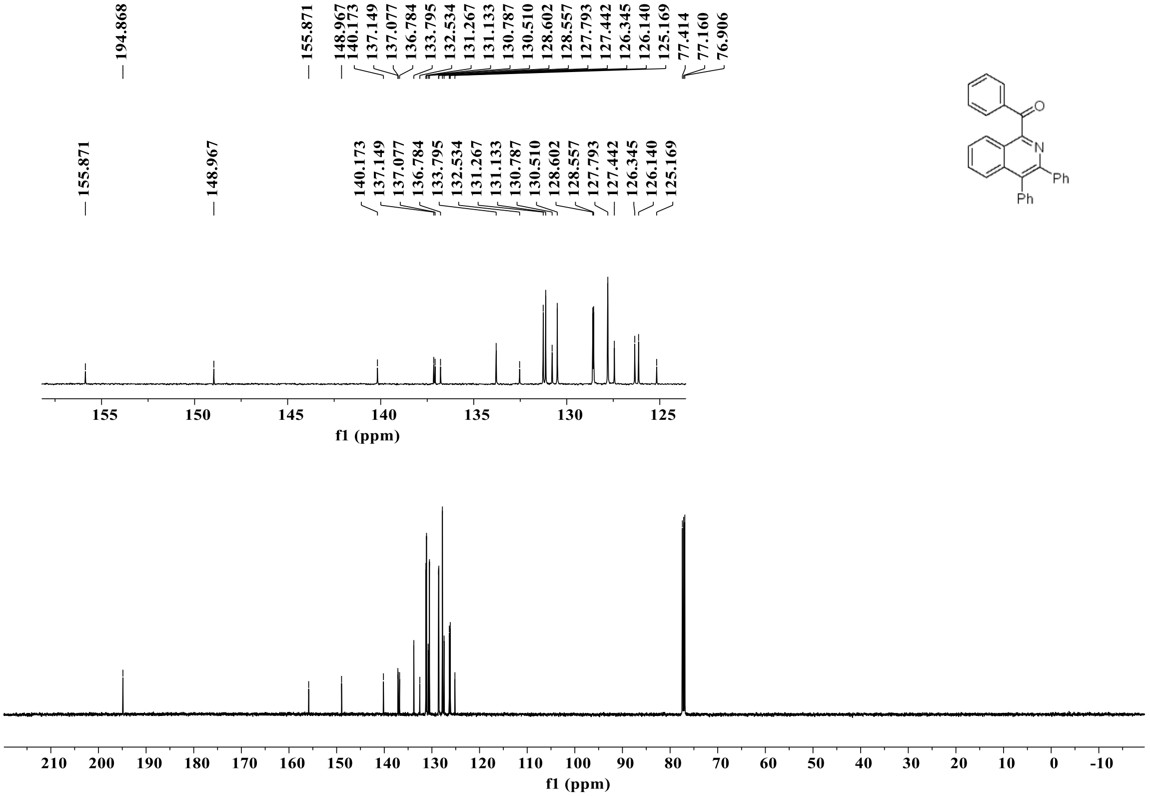
^{19}F NMR (470 MHz, DMSO-d_6) of **Int-C**



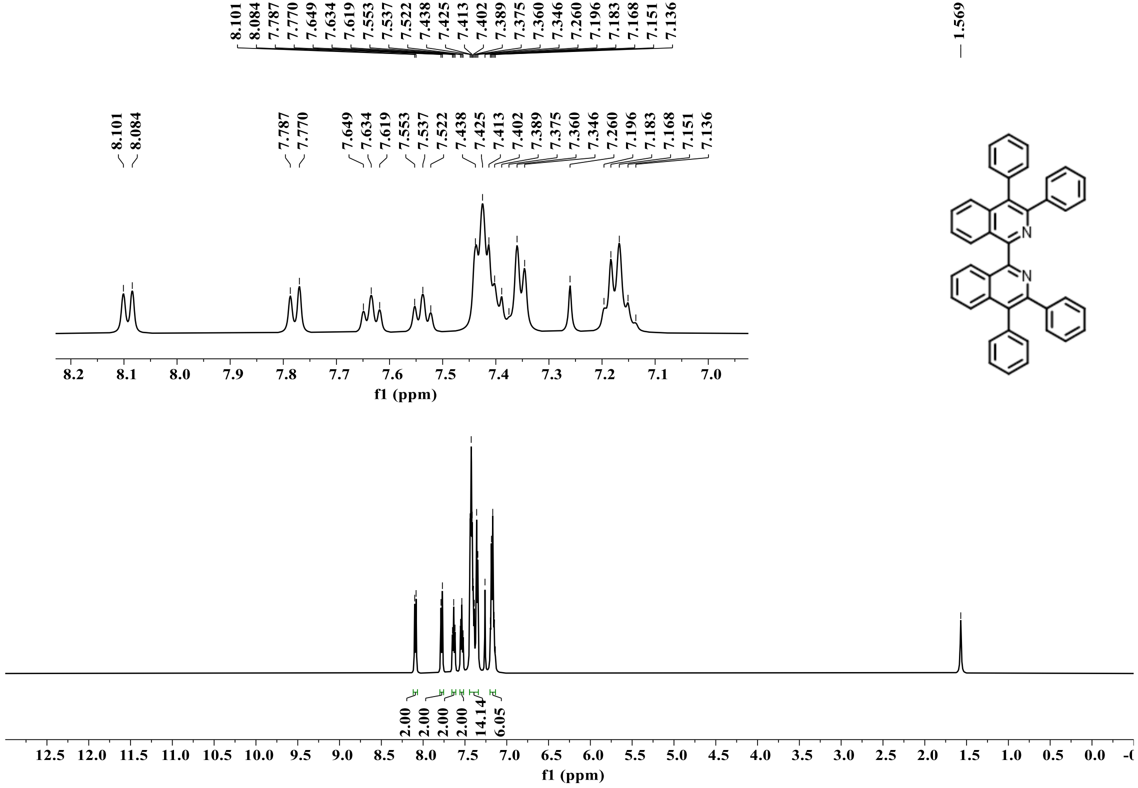
^{1}H NMR (500 MHz, CDCl$_3$) of **3a′**



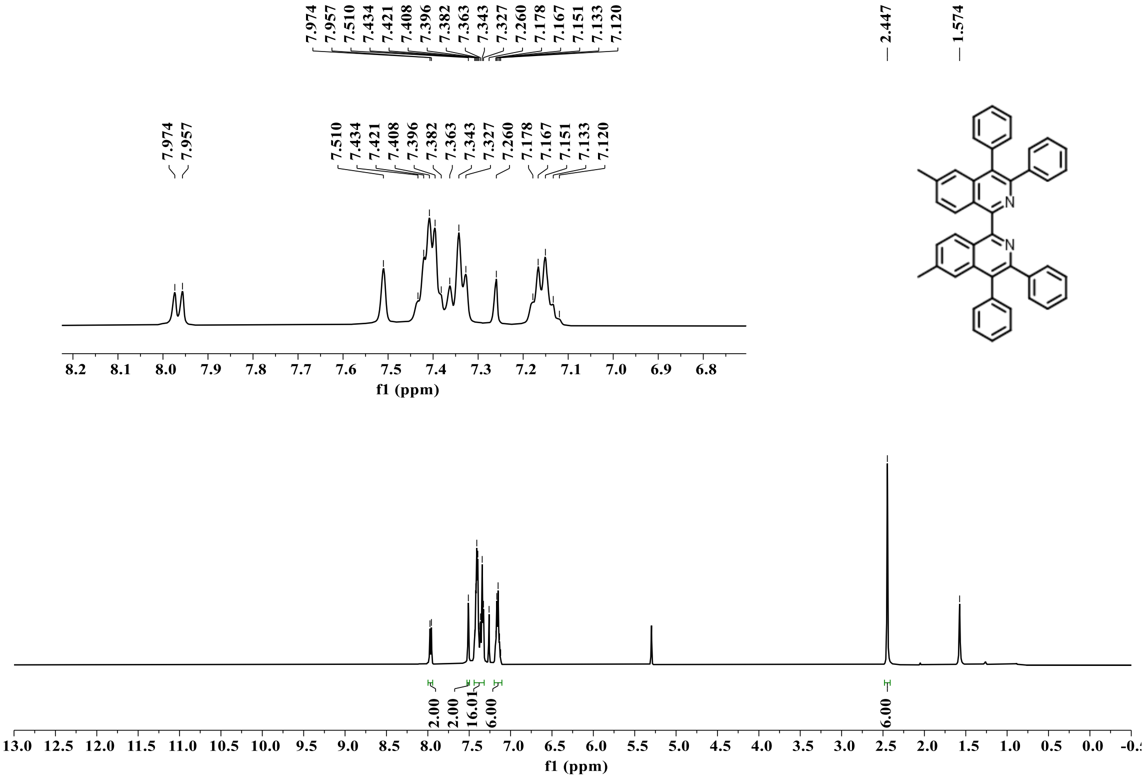
^{13}C NMR (125 MHz, CDCl$_3$) of **3a′**



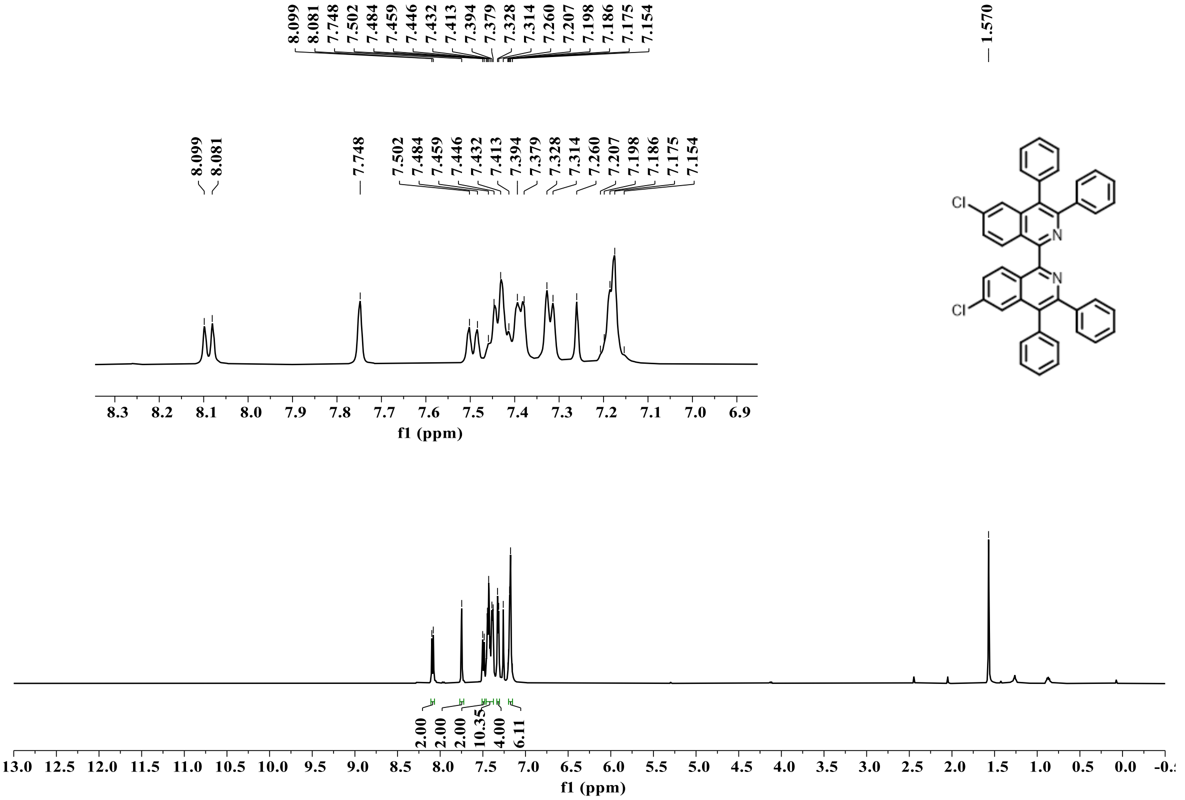
^{1}H NMR (500 MHz, CDCl$_3$) of **3a**



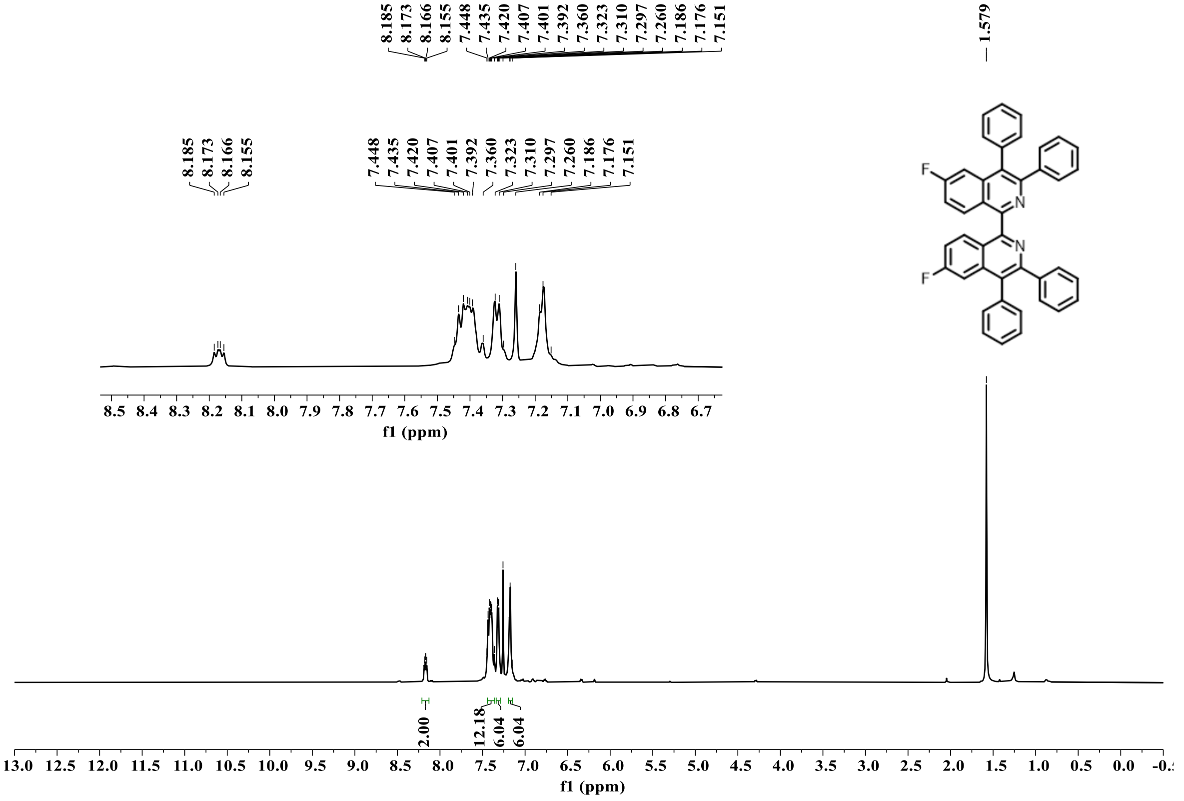
^{1}H NMR (500 MHz, CDCl$_3$) of **3b**



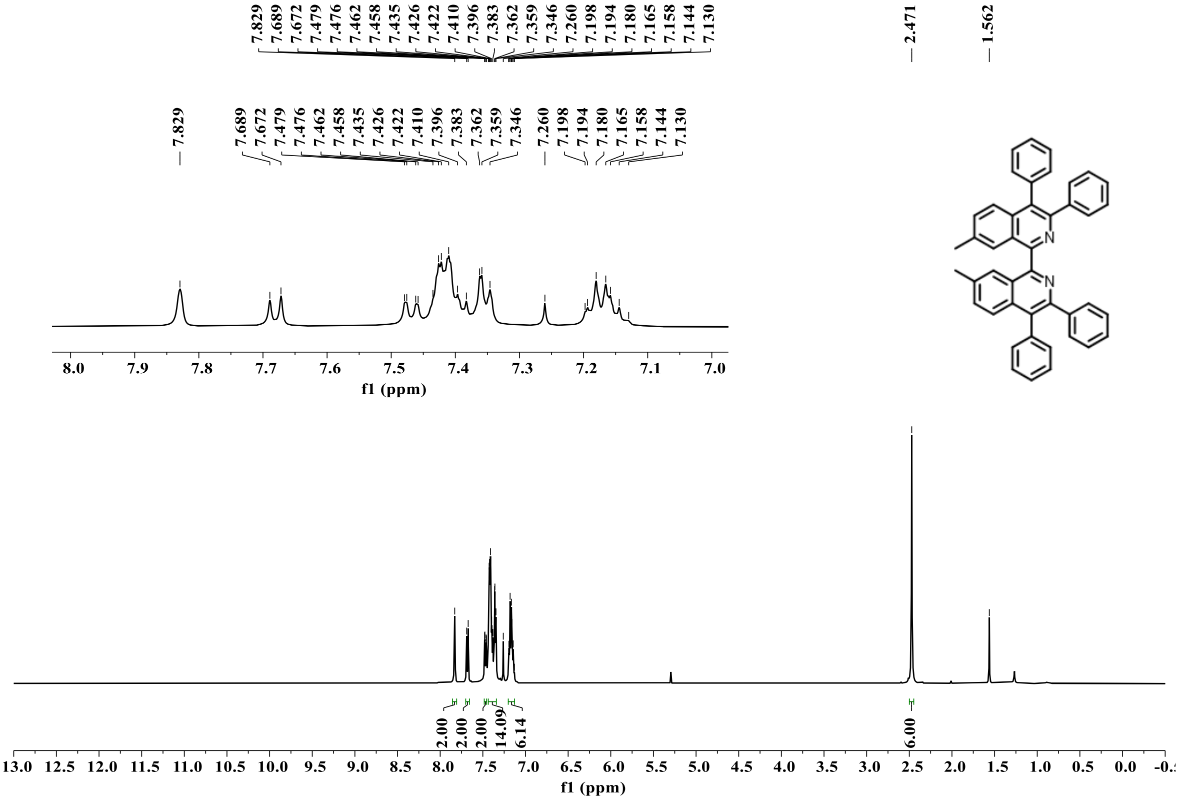
^{1}H NMR (500 MHz, CDCl$_3$) of **3c**



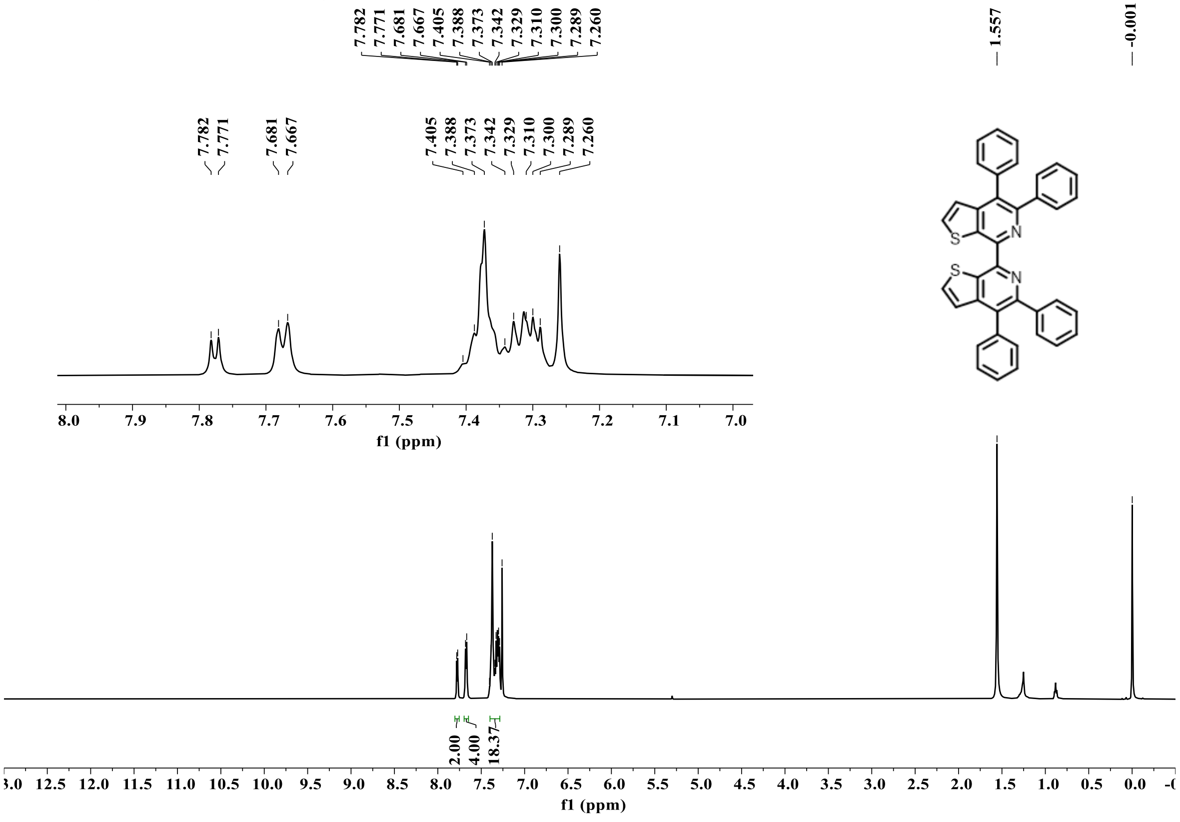
^{1}H NMR (500 MHz, CDCl$_3$) of **3d**



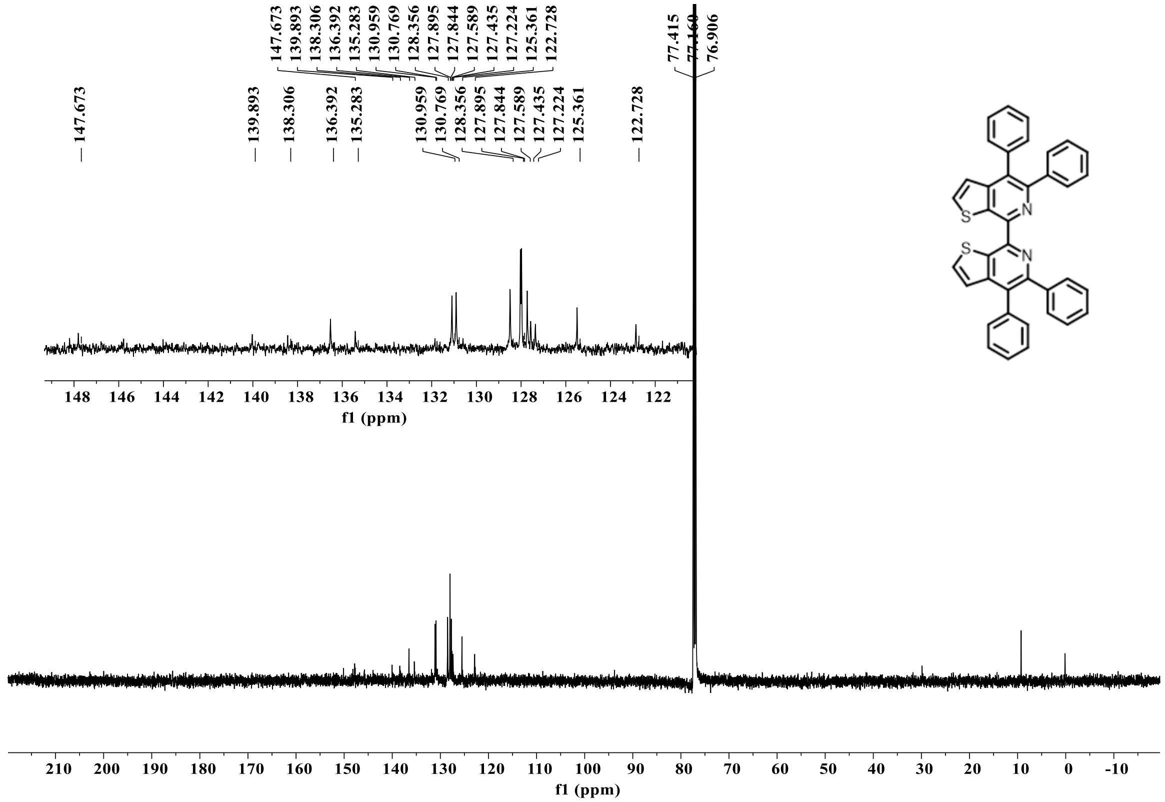
^{1}H NMR (500 MHz, CDCl$_3$) of **3e**



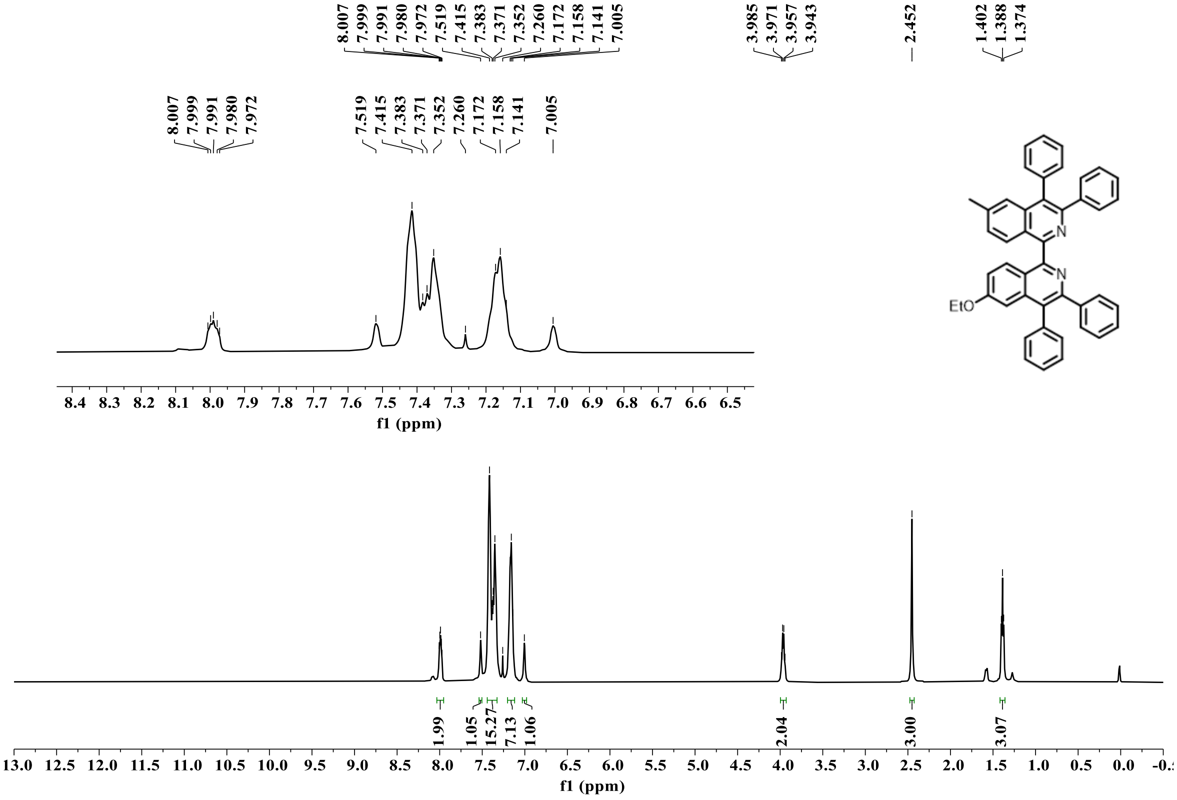
^{1}H NMR (500 MHz, CDCl$_3$) of **3f**



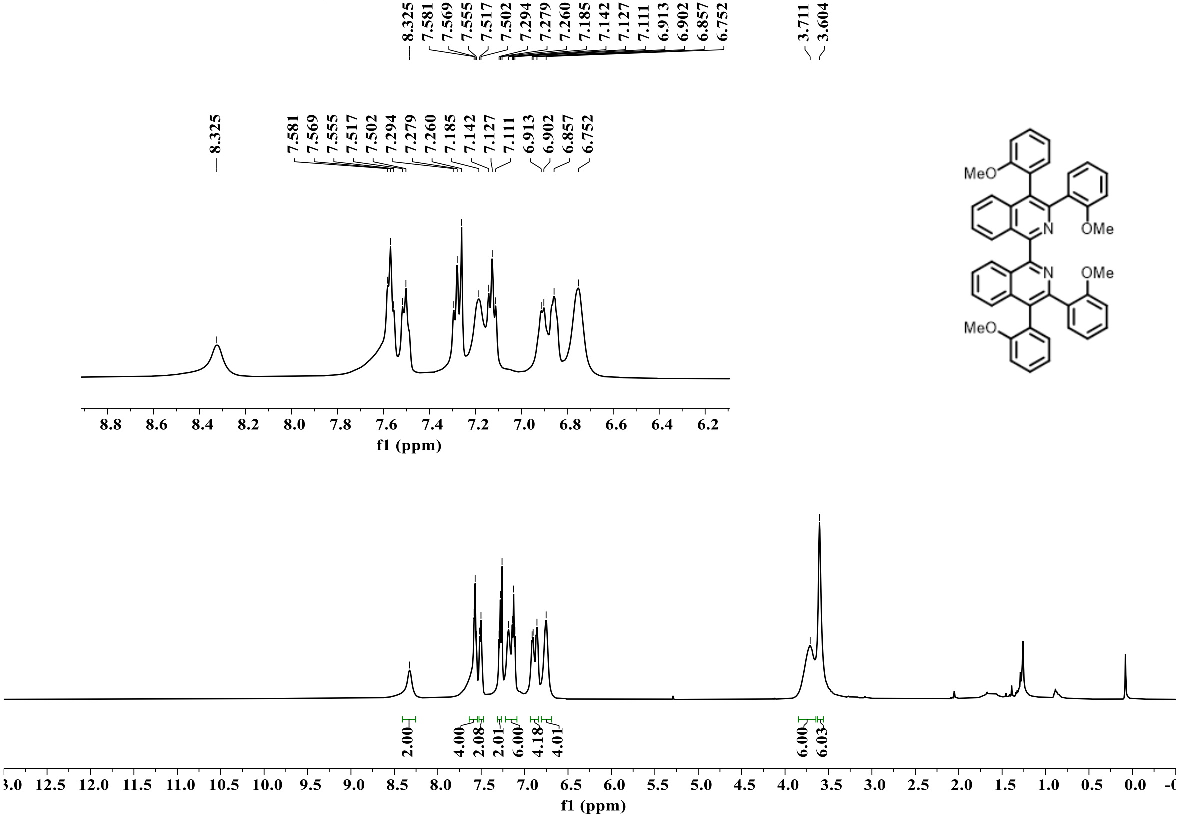
^{13}C NMR (125 MHz, CDCl$_3$) of **3f**



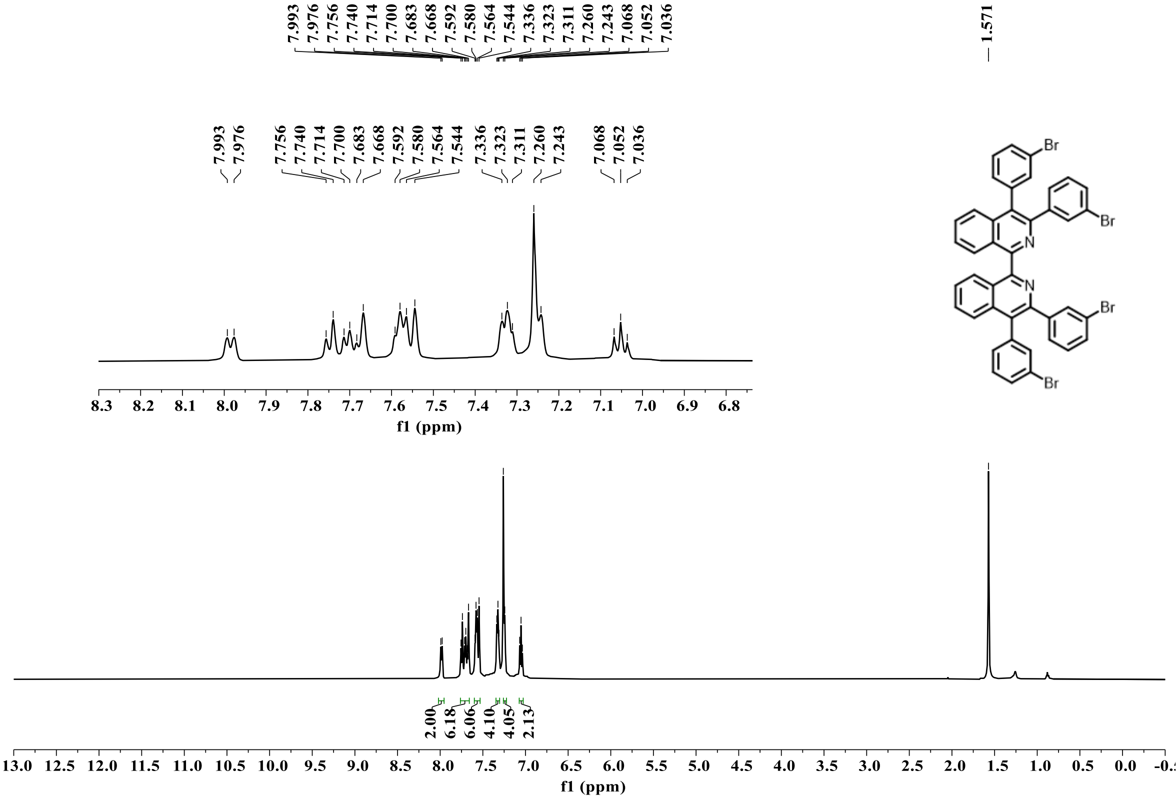
^{1}H NMR (500 MHz, CDCl$_3$) of **3g**



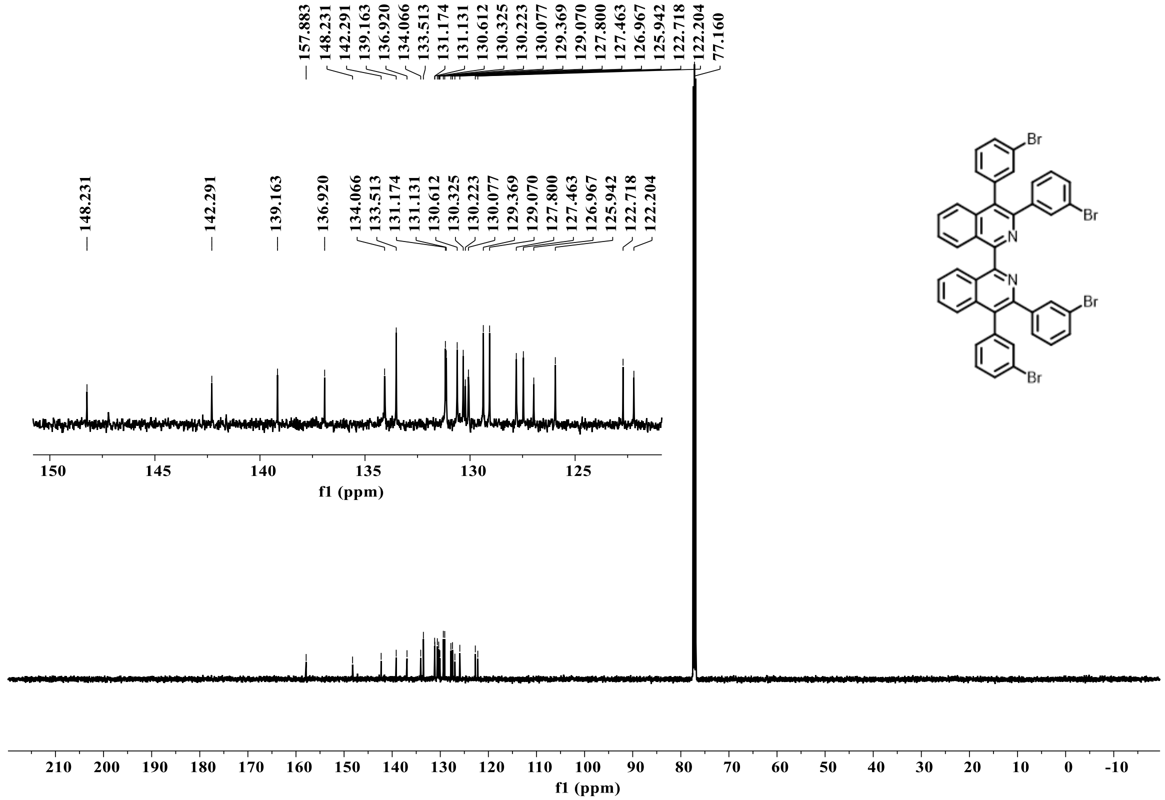
^{1}H NMR (500 MHz, CDCl$_3$) of **3h**



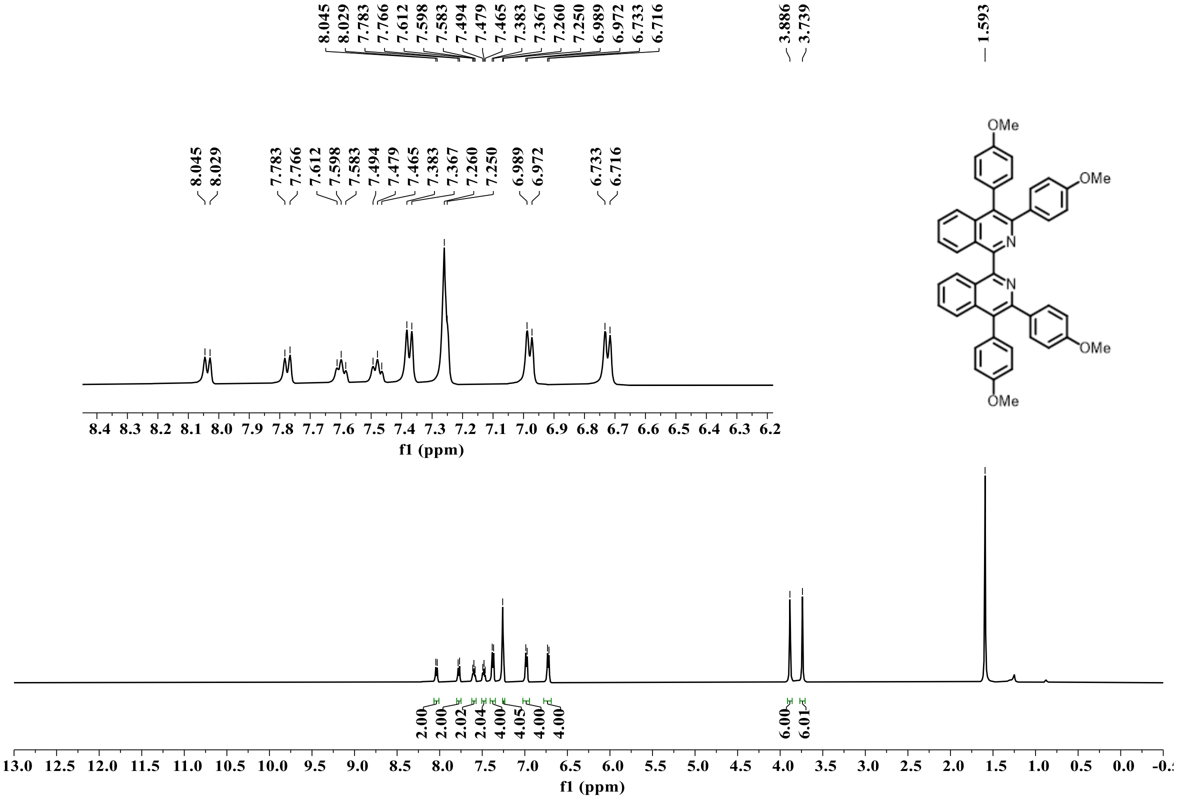
^{1}H NMR (500 MHz, CDCl$_3$) of **3i**



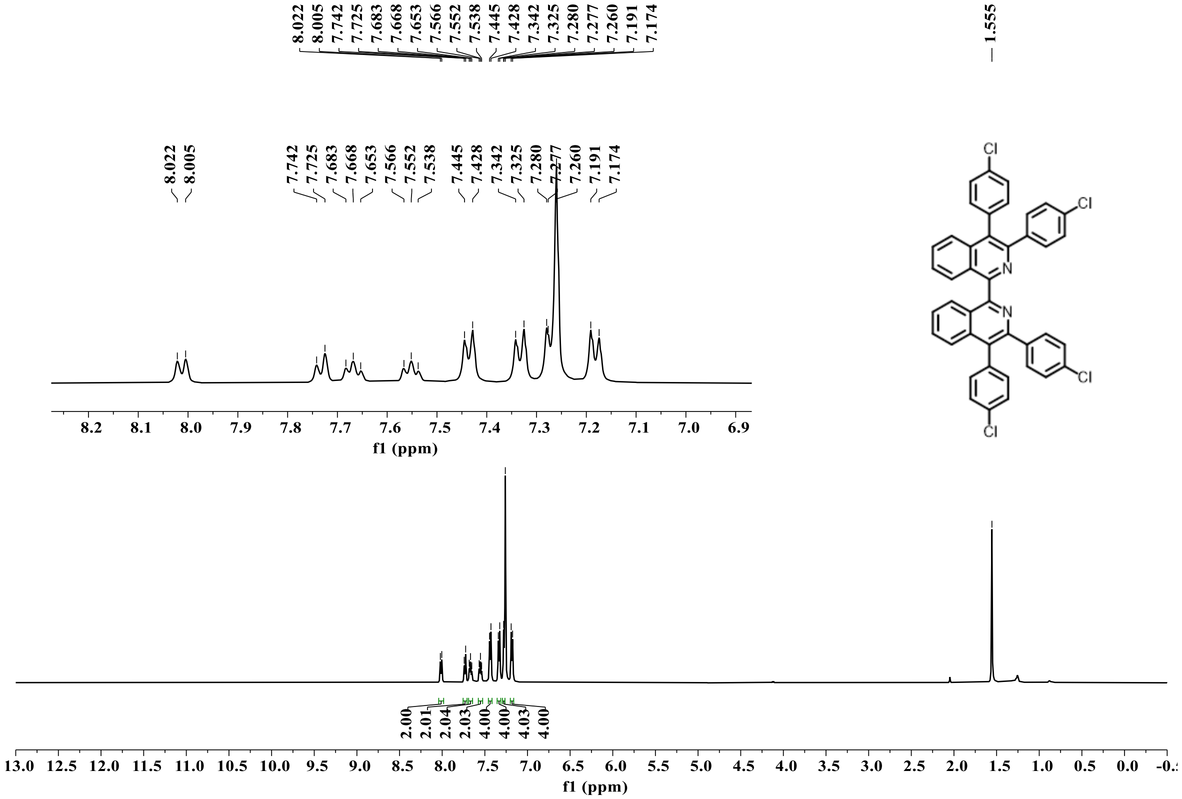
^{13}C NMR (125 MHz, CDCl$_3$) of **3i**



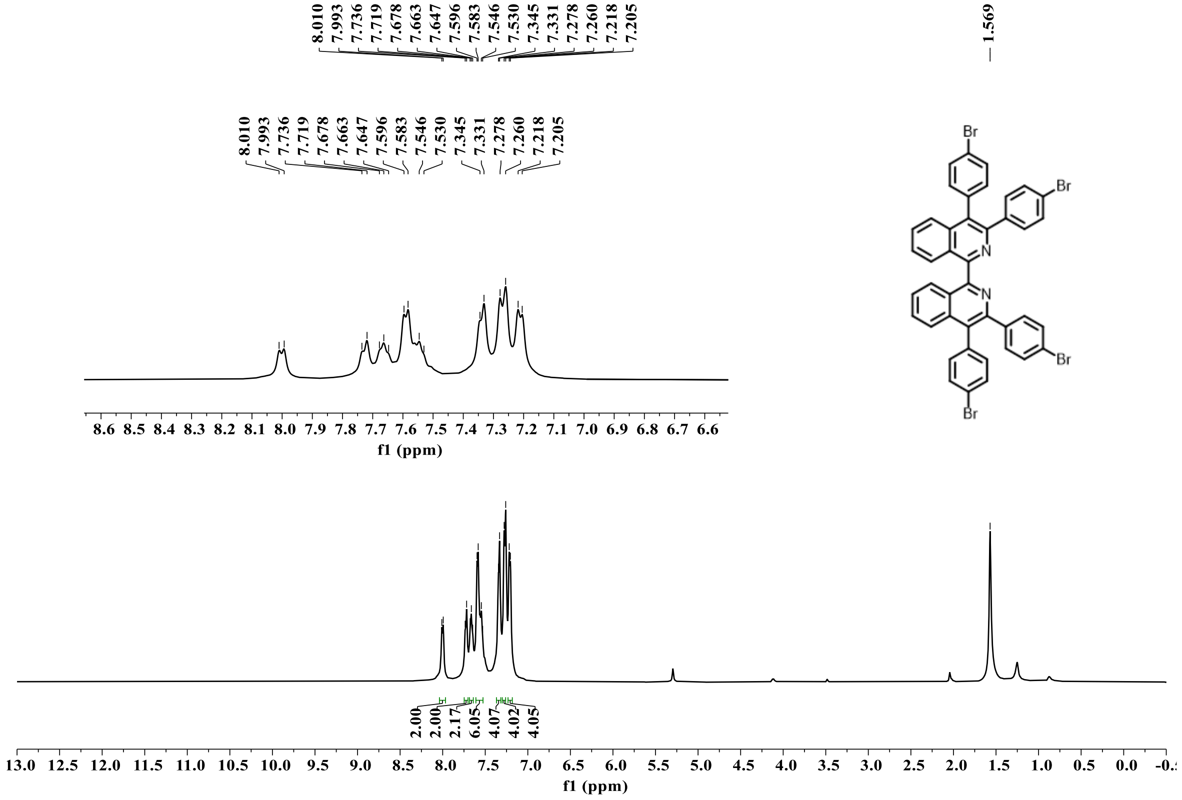
^{1}H NMR (500 MHz, CDCl$_3$) of **3j**



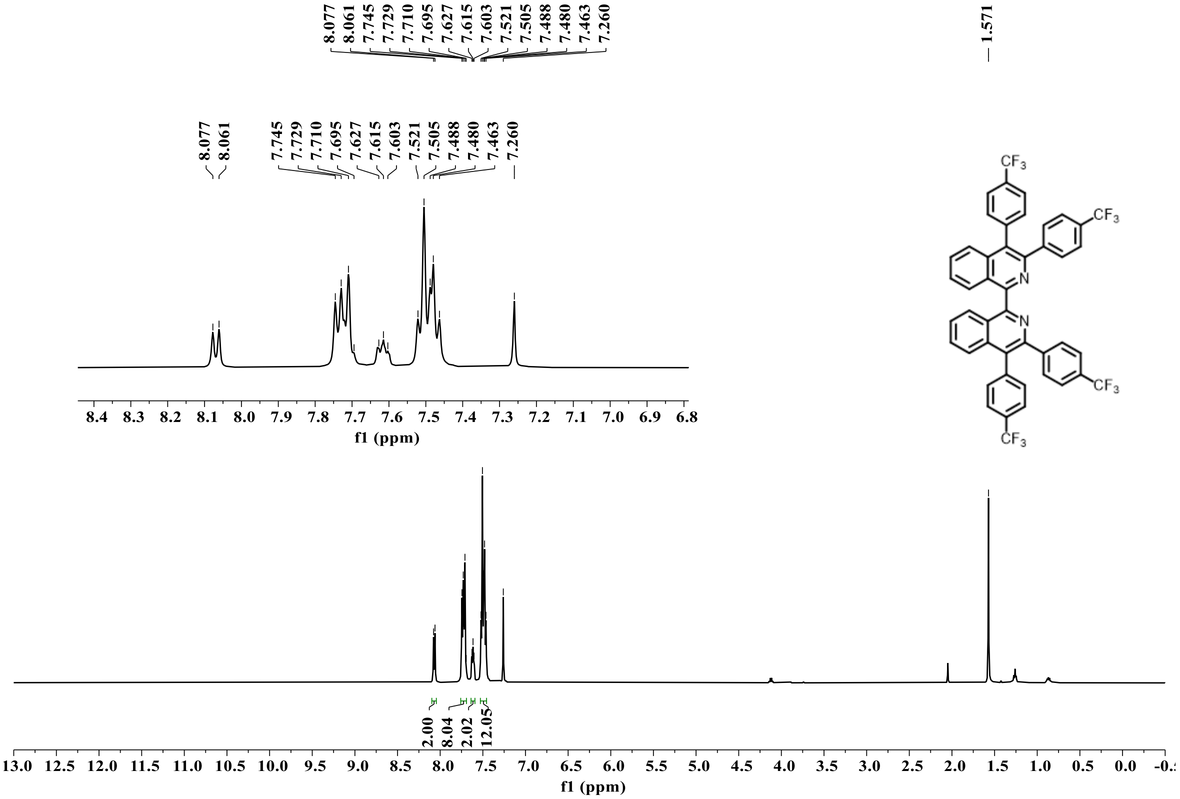
^{1}H NMR (500 MHz, CDCl$_3$) of **3k**



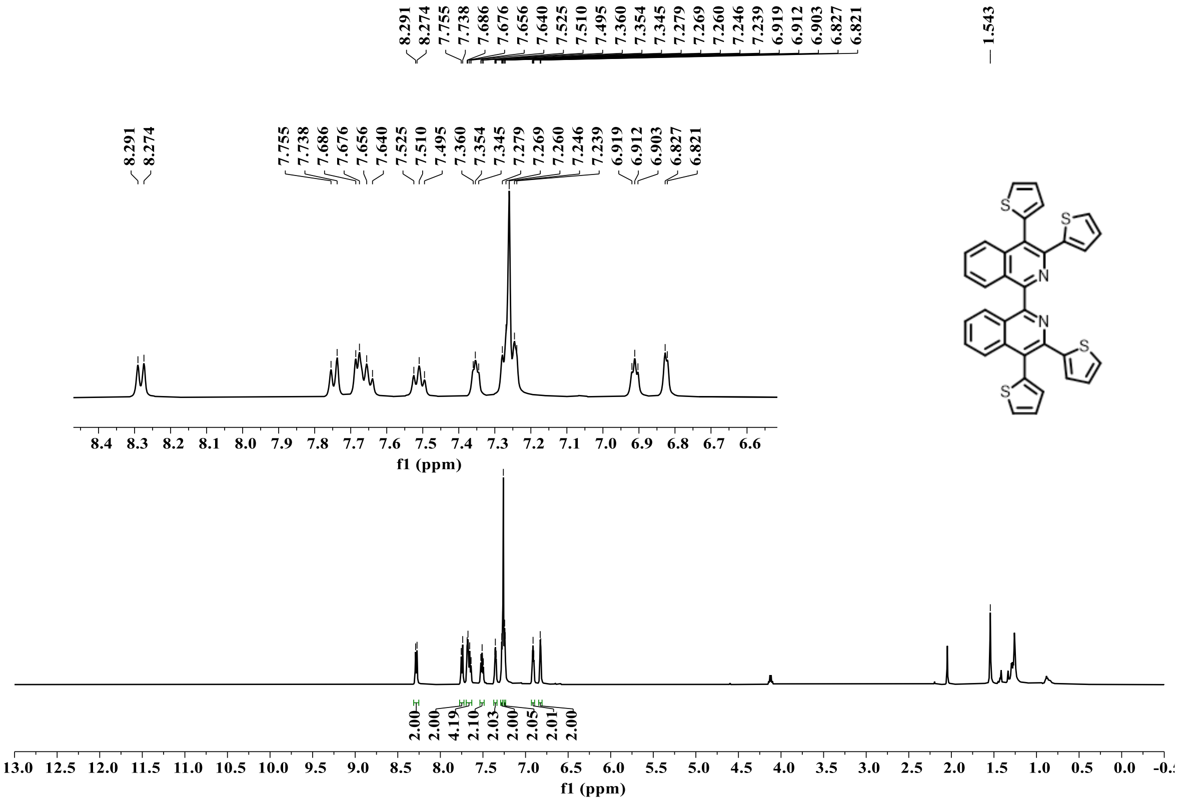
^{1}H NMR (500 MHz, CDCl$_3$) of **3l**



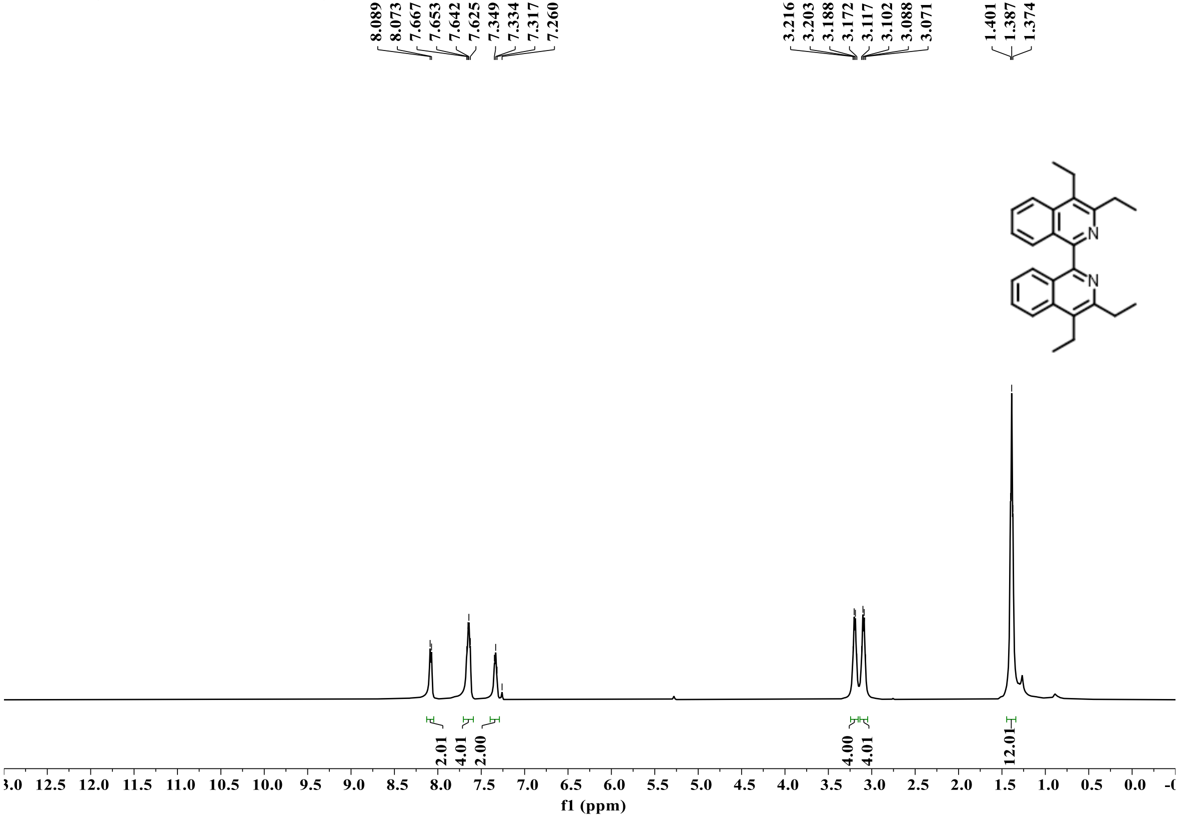
^{1}H NMR (500 MHz, CDCl$_3$) of **3m**



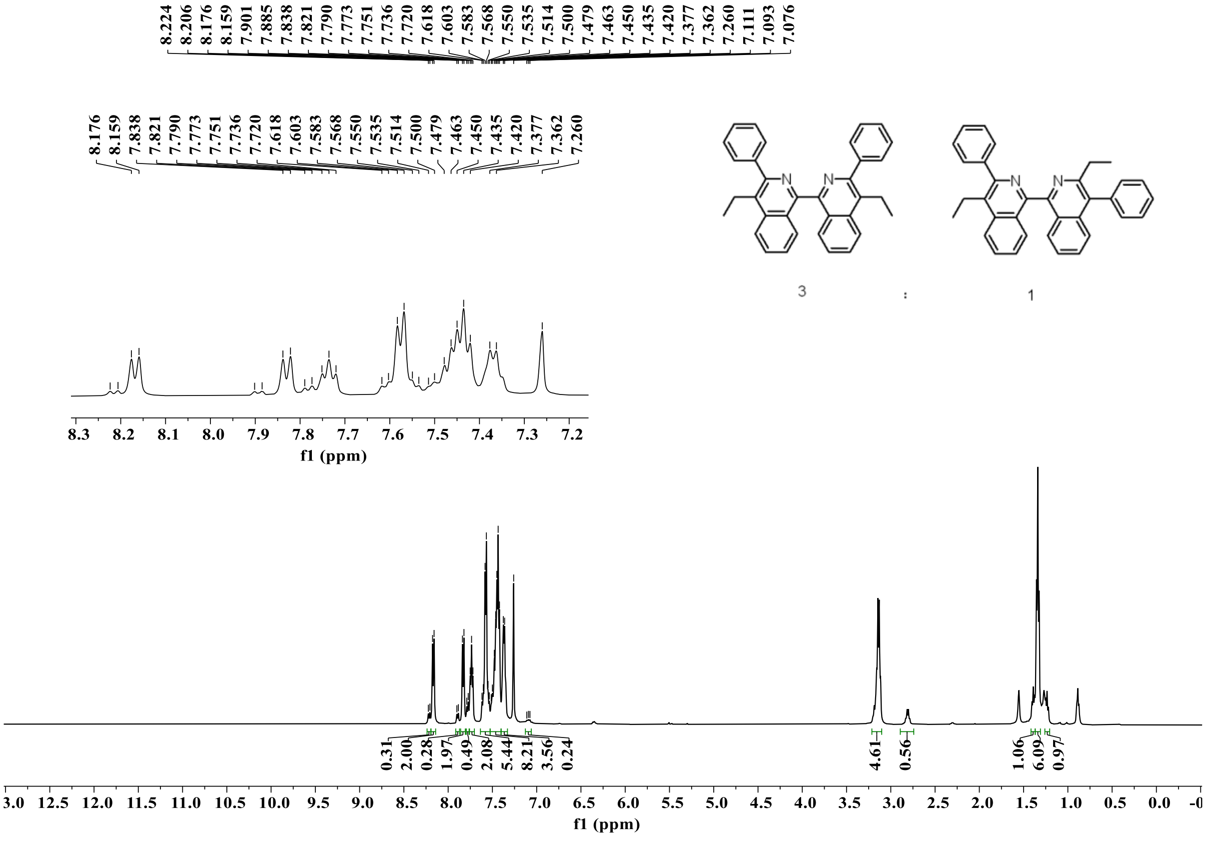
^{1}H NMR (500 MHz, CDCl$_3$) of **3n**



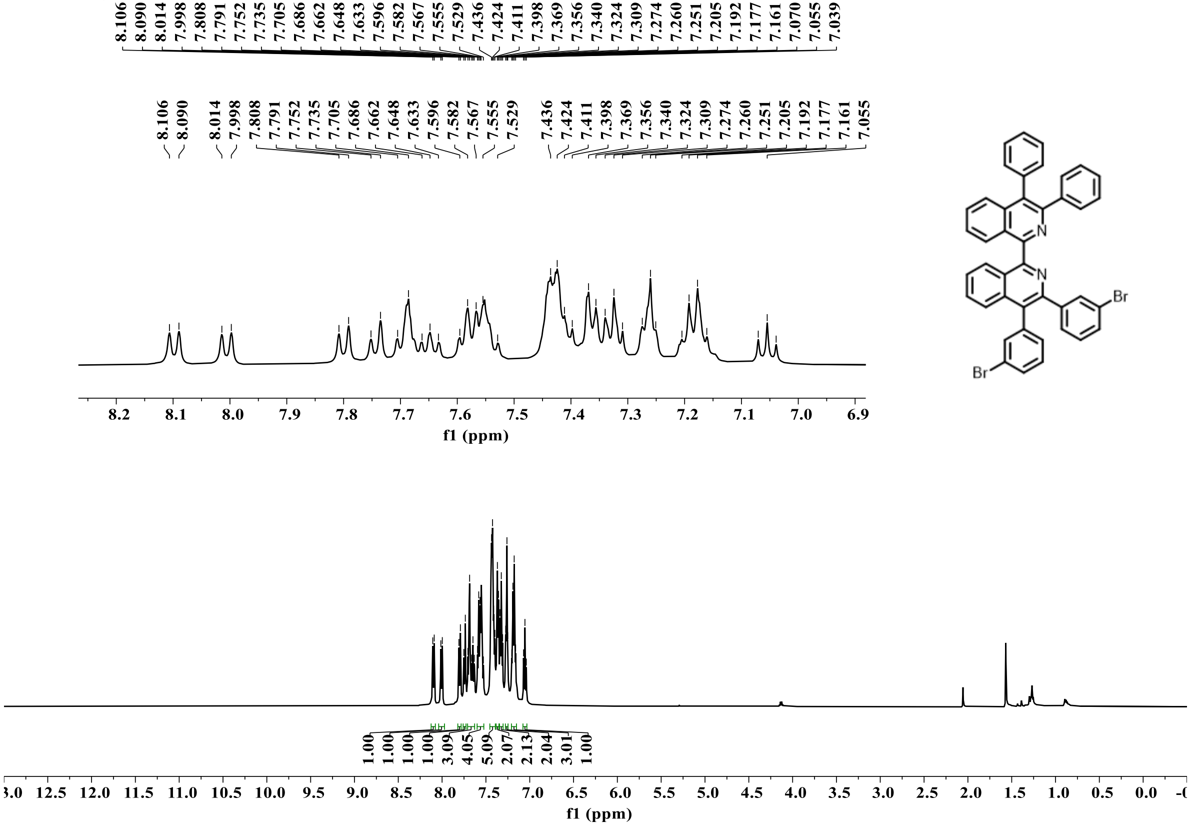
^{1}H NMR (500 MHz, CDCl$_3$) of **3o**



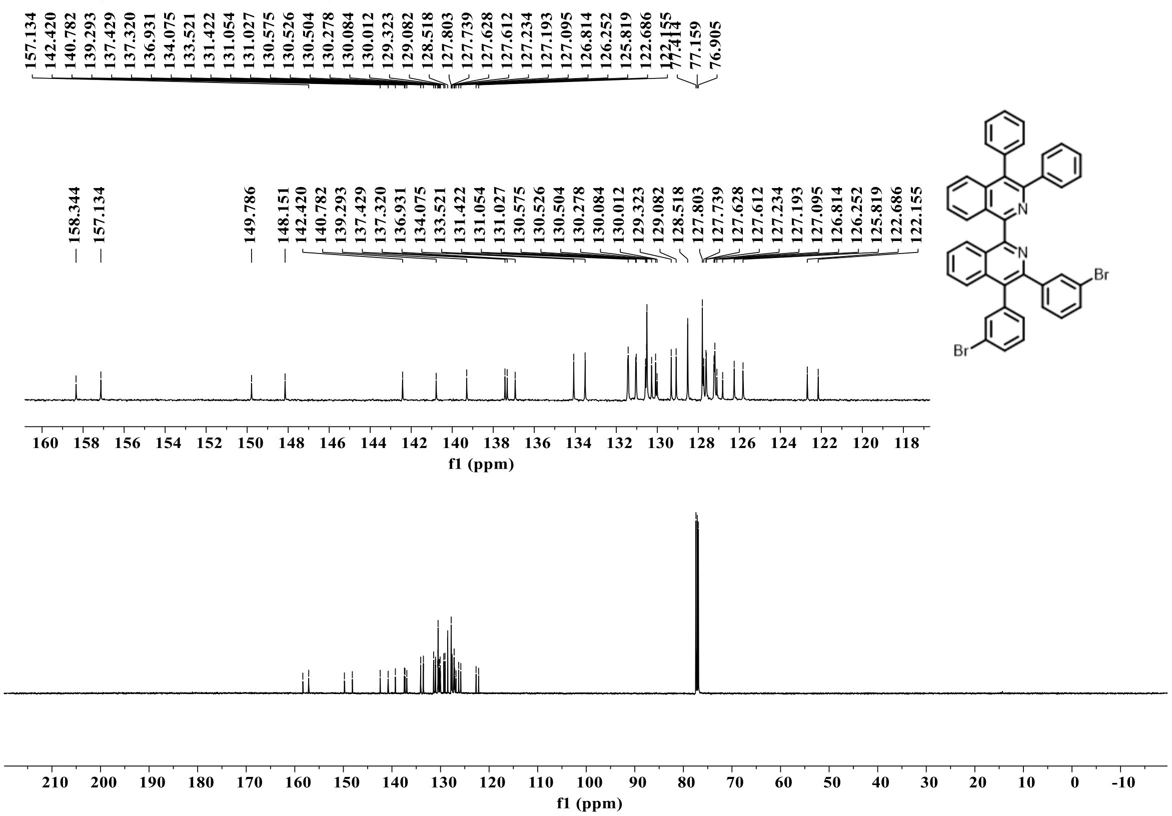
^{1}H NMR (500 MHz, CDCl$_3$) of **3p**



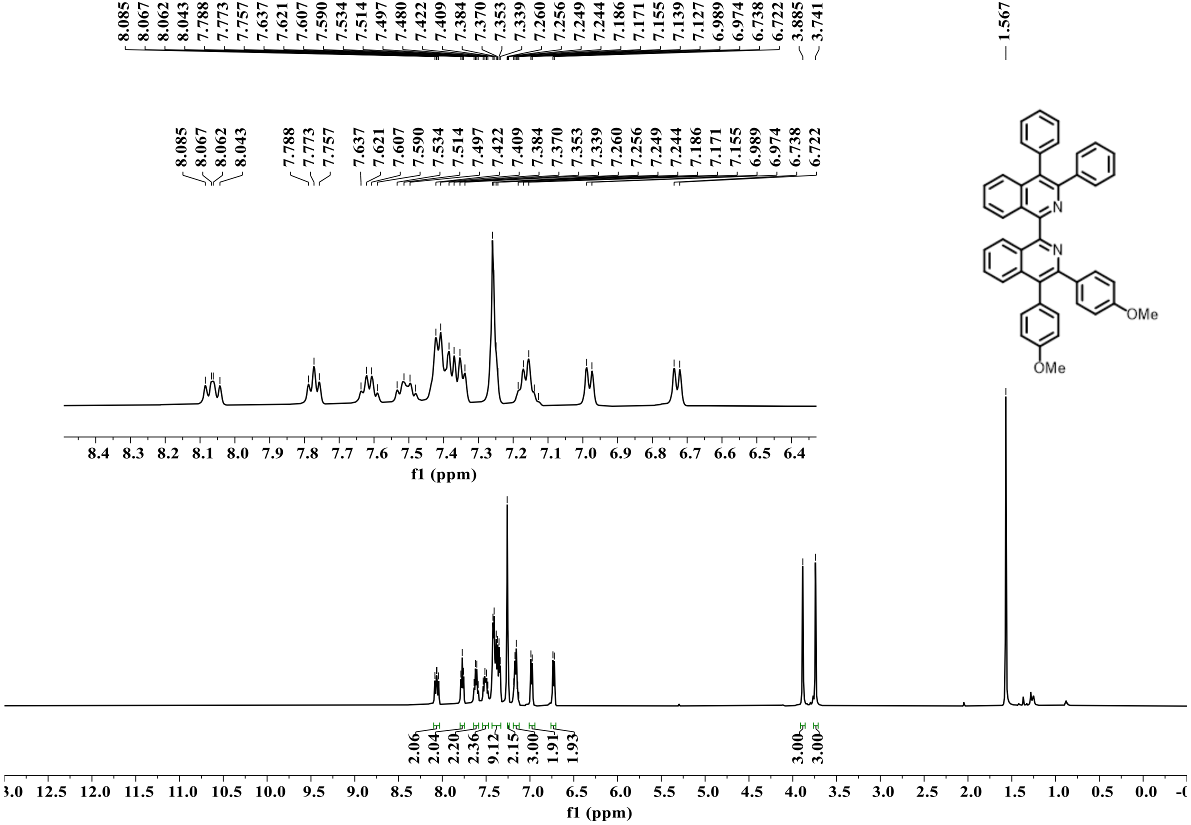
^{1}H NMR (500 MHz, CDCl$_3$) of **4ai**



^{13}C NMR (125 MHz, CDCl$_3$) of **4ai**



^{1}H NMR (500 MHz, CDCl$_3$) of **4aj**



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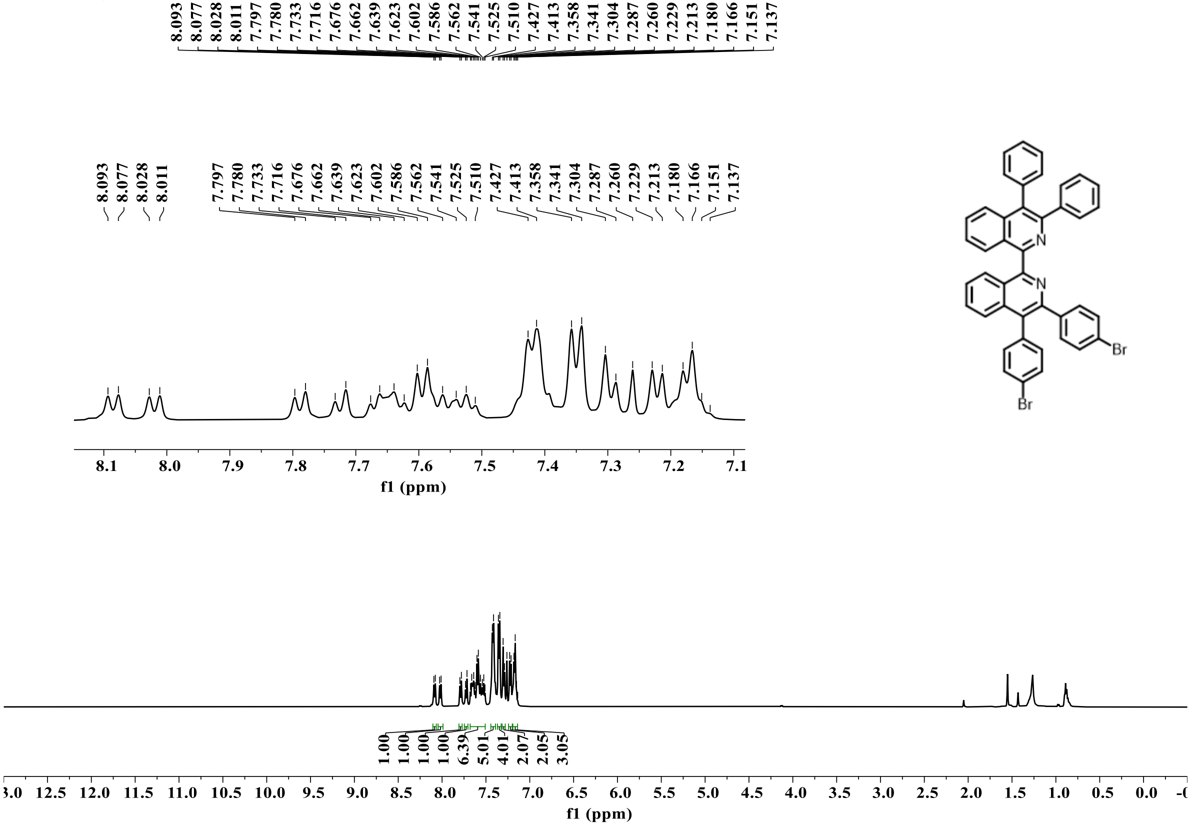
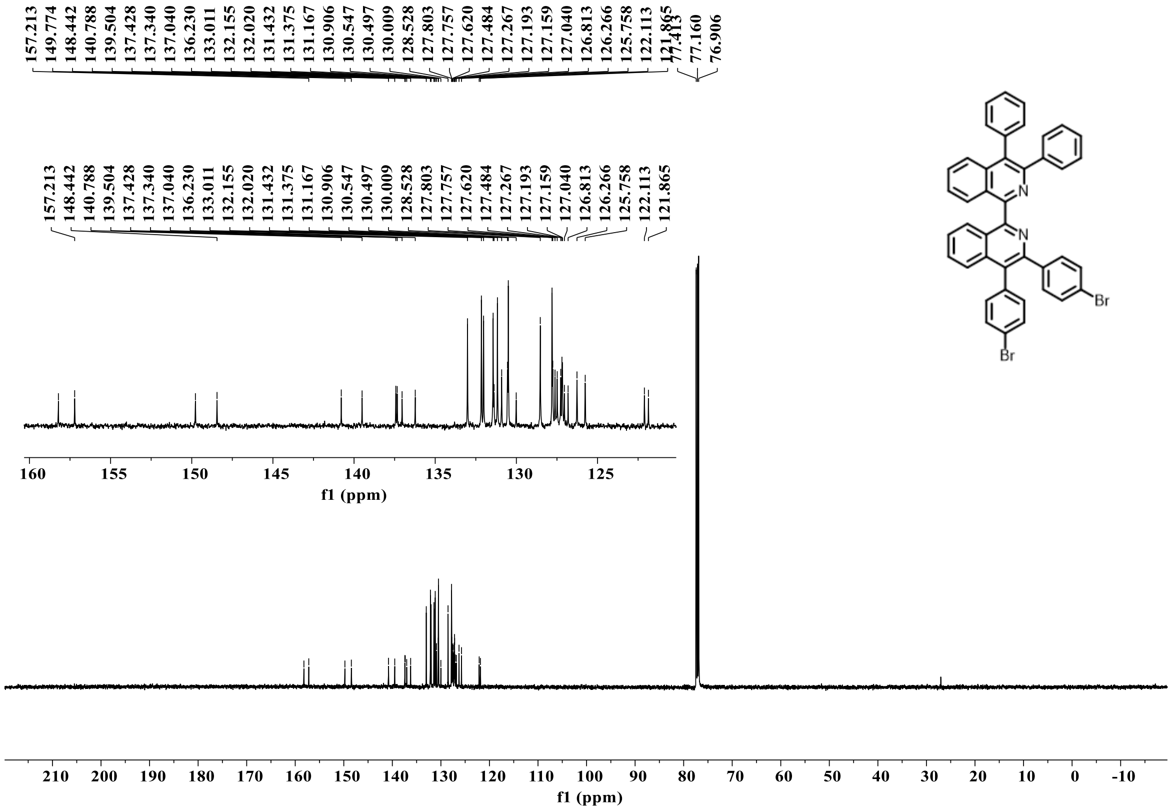


^{13}C NMR (125 MHz, $CDCl_3$) of **4al**



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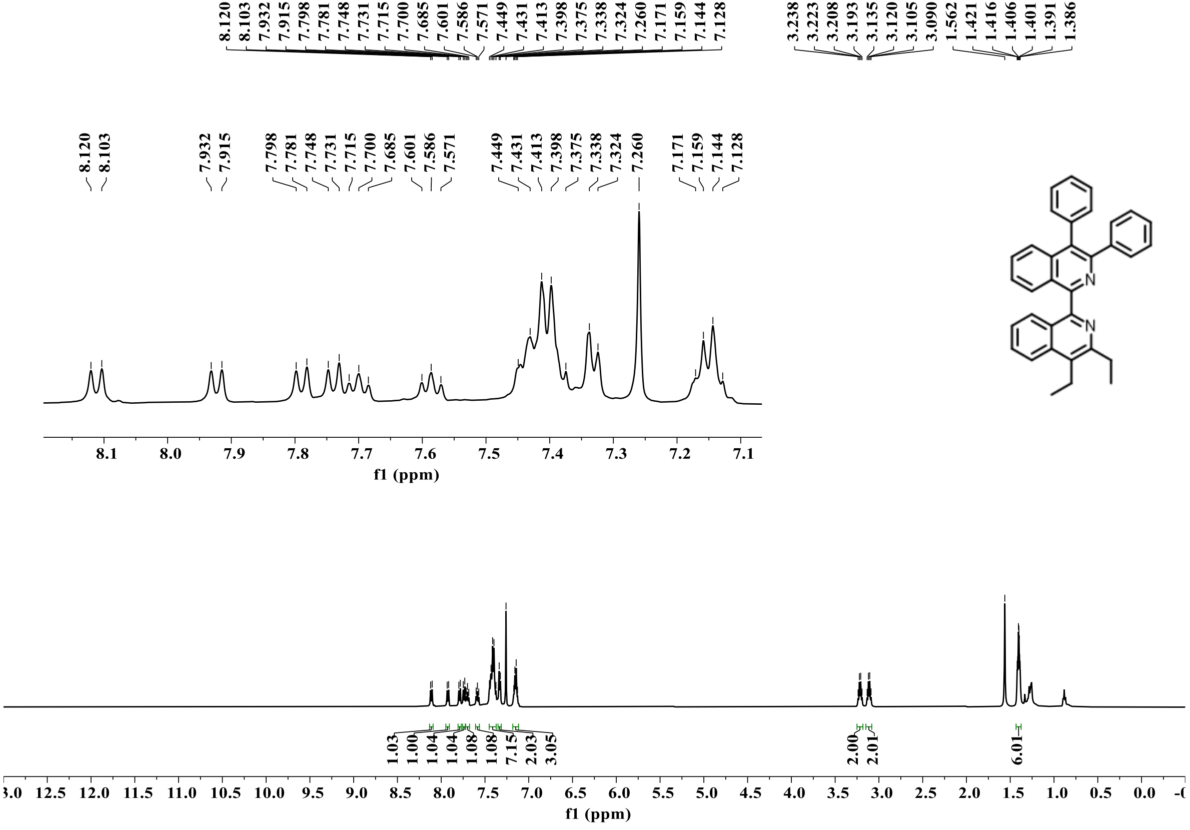

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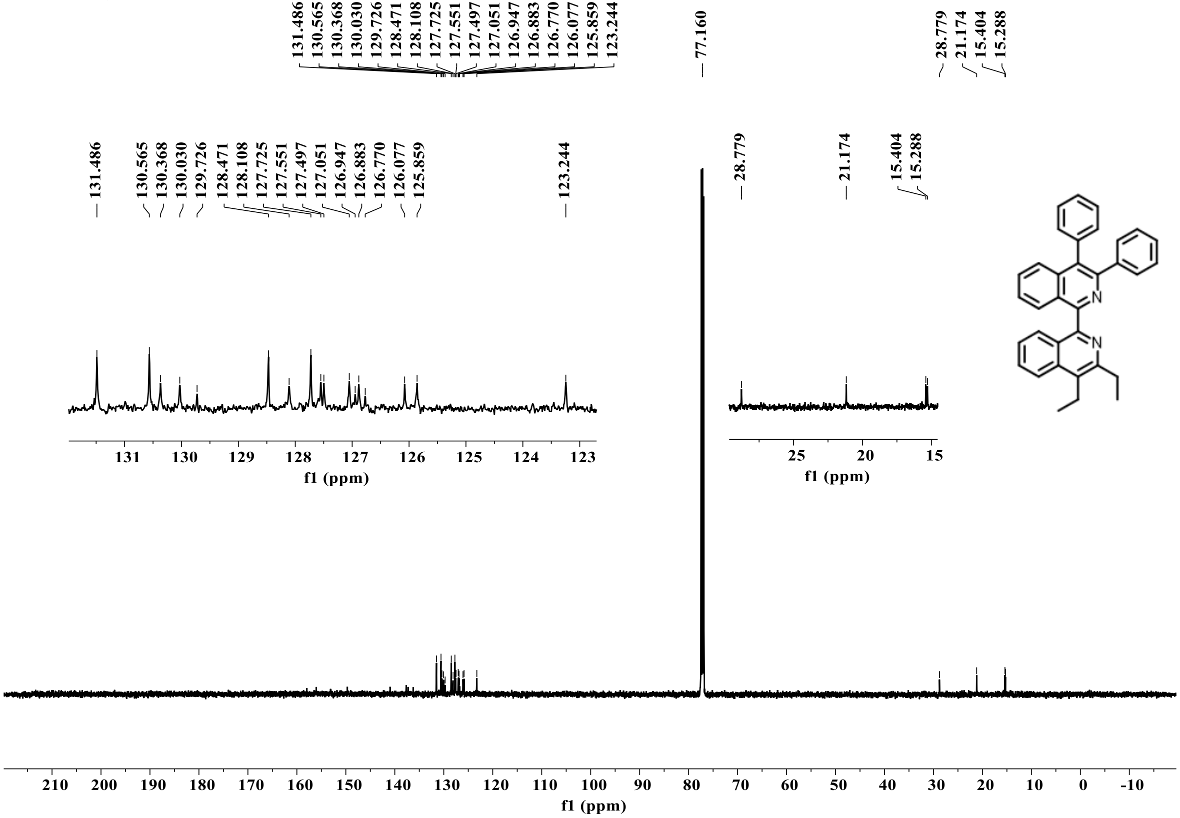

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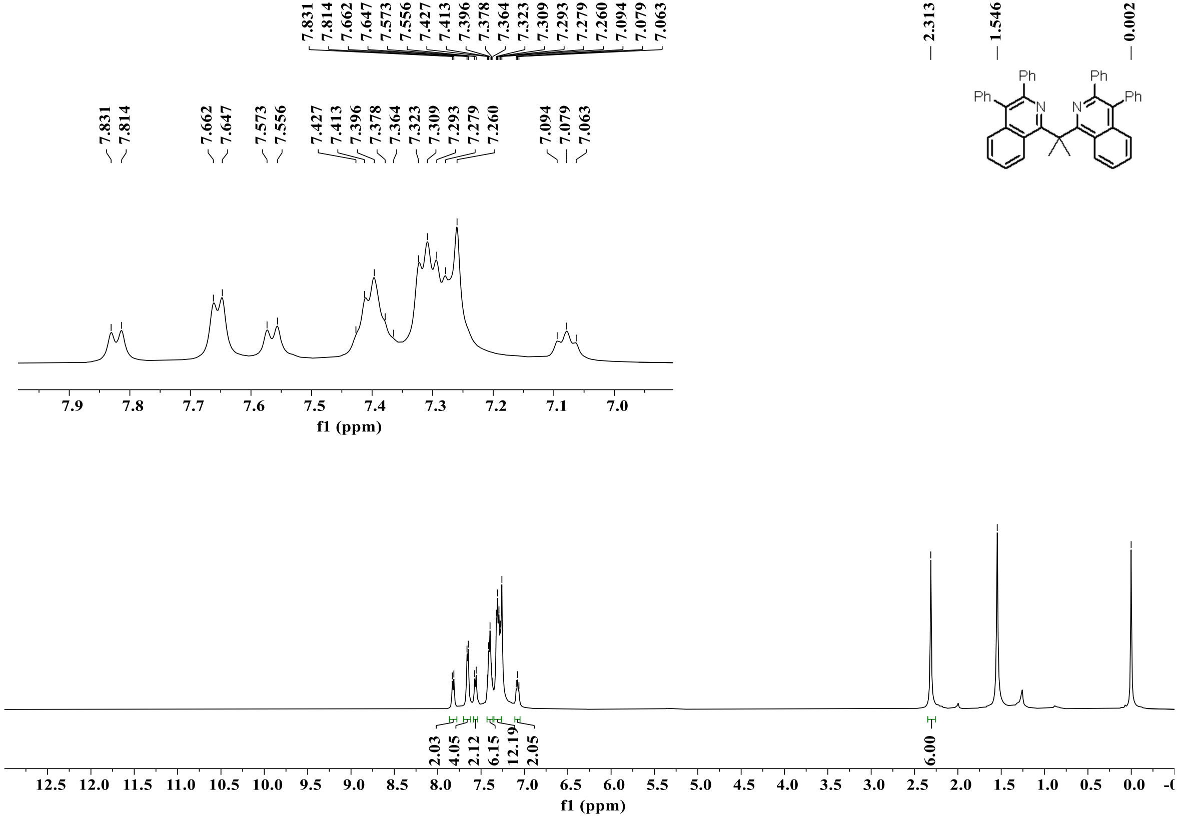

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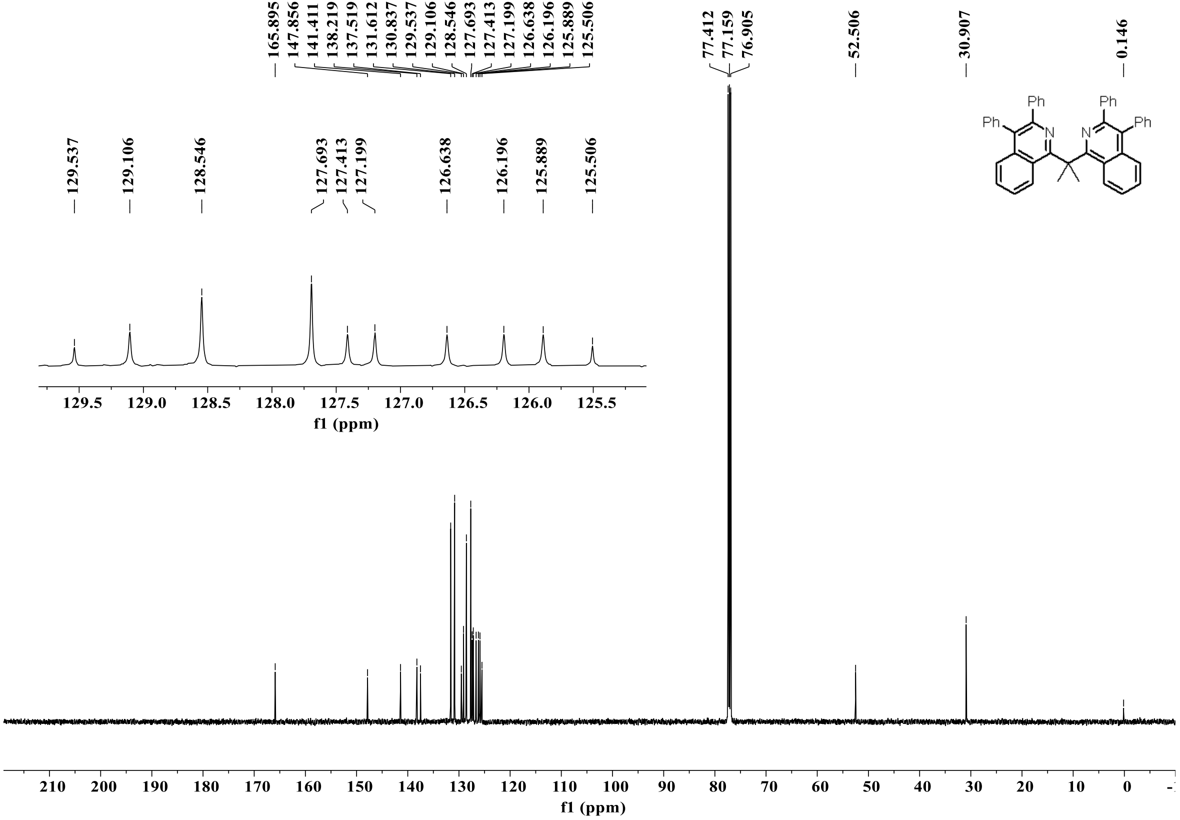

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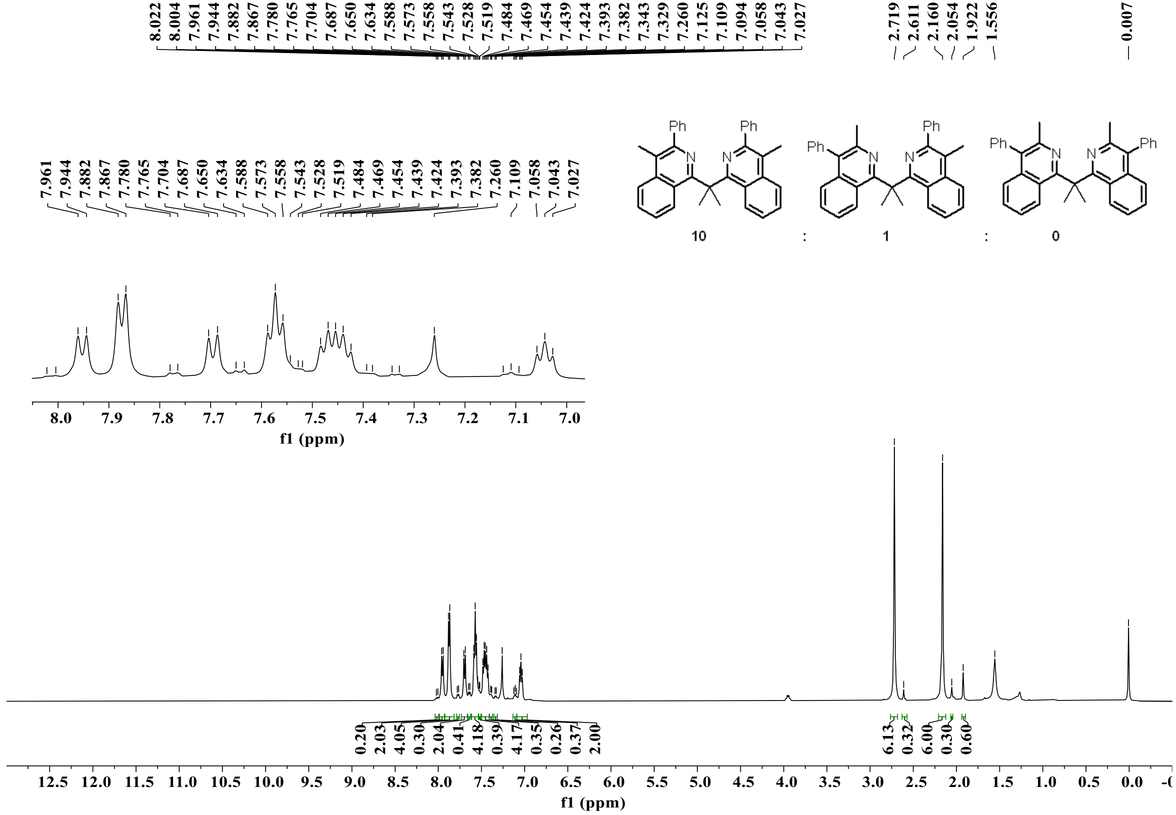

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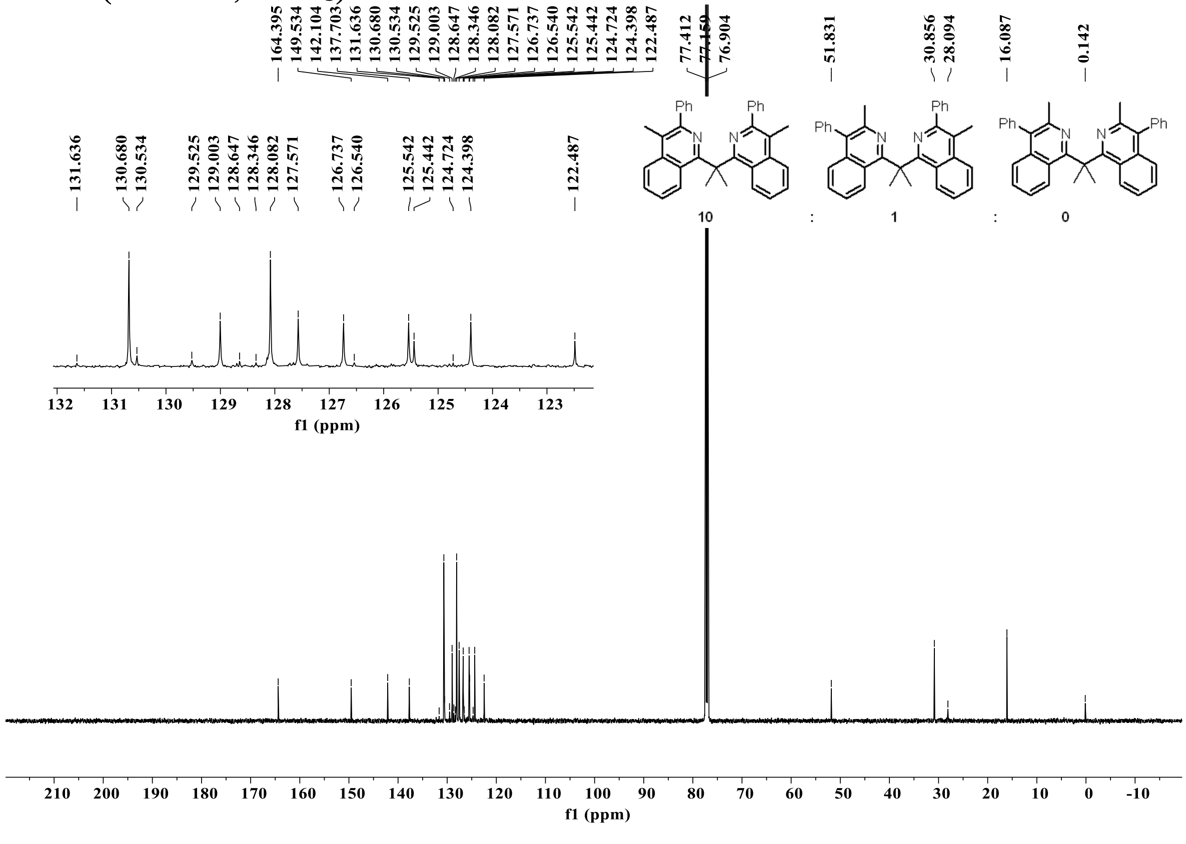

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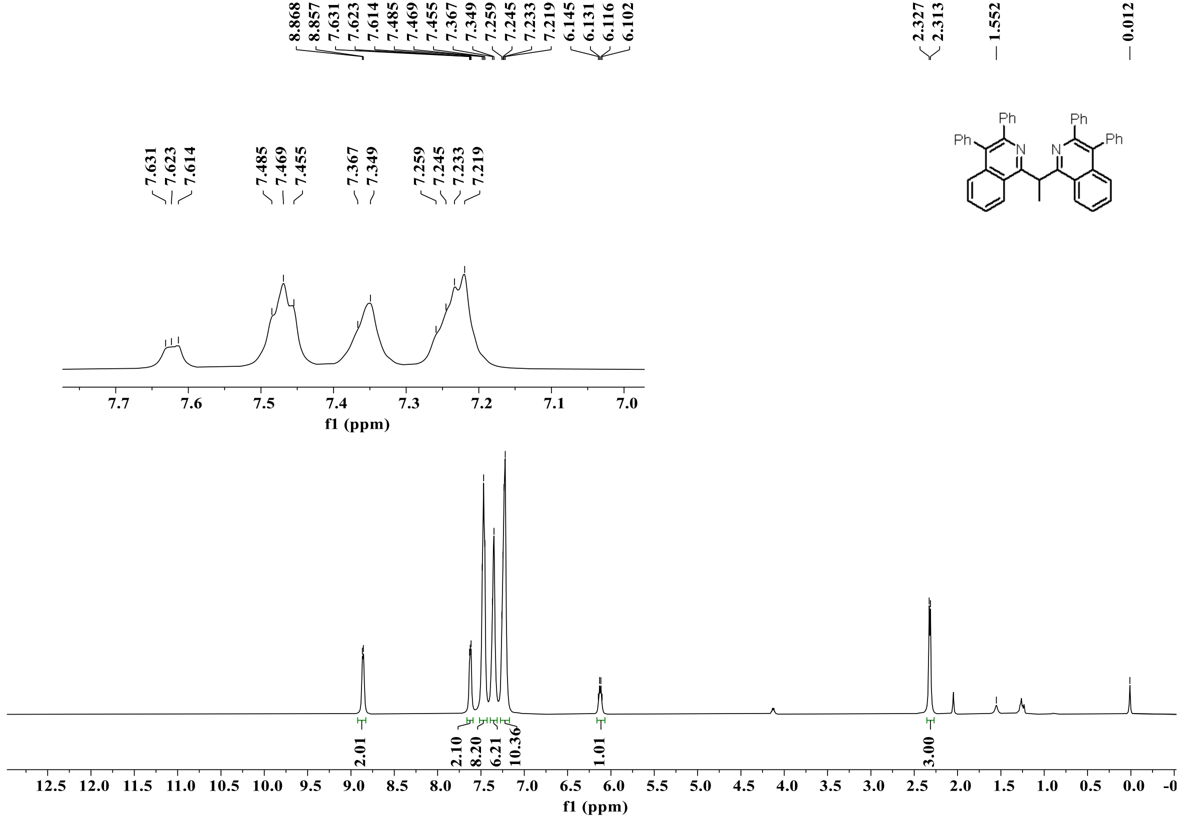

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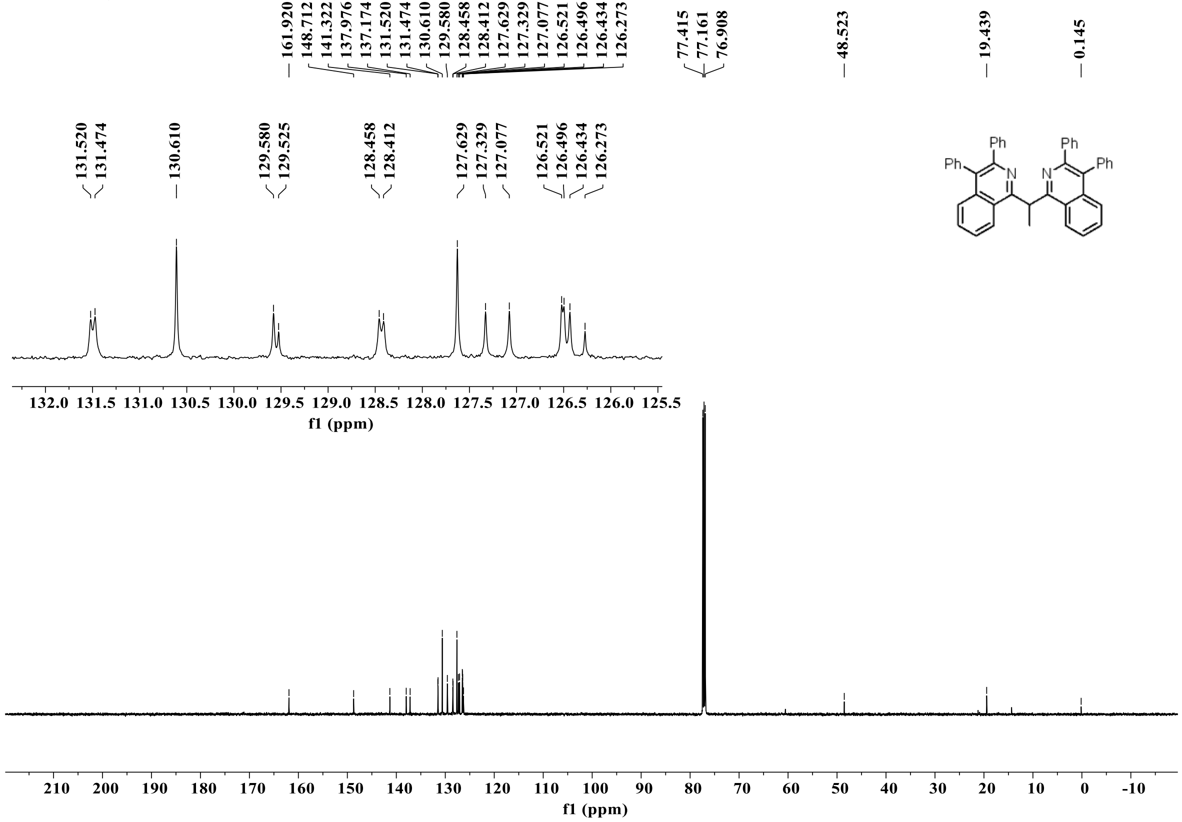

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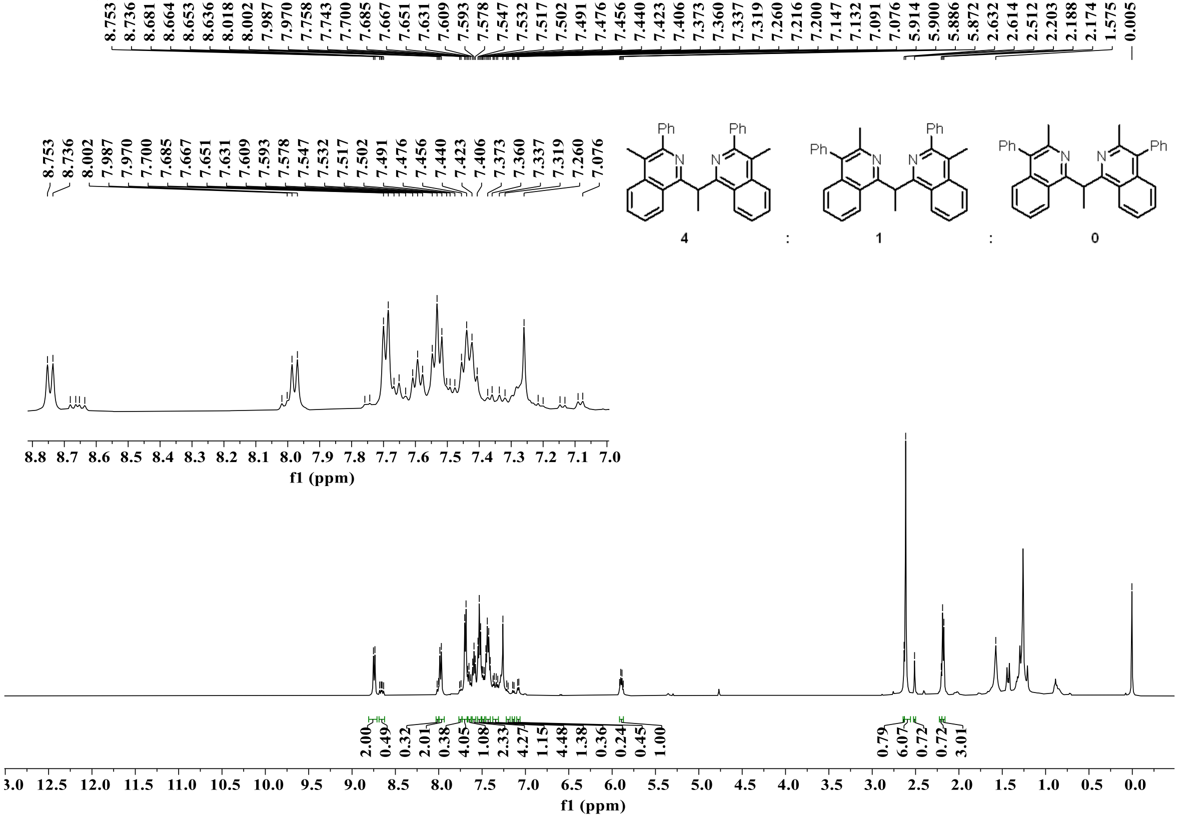

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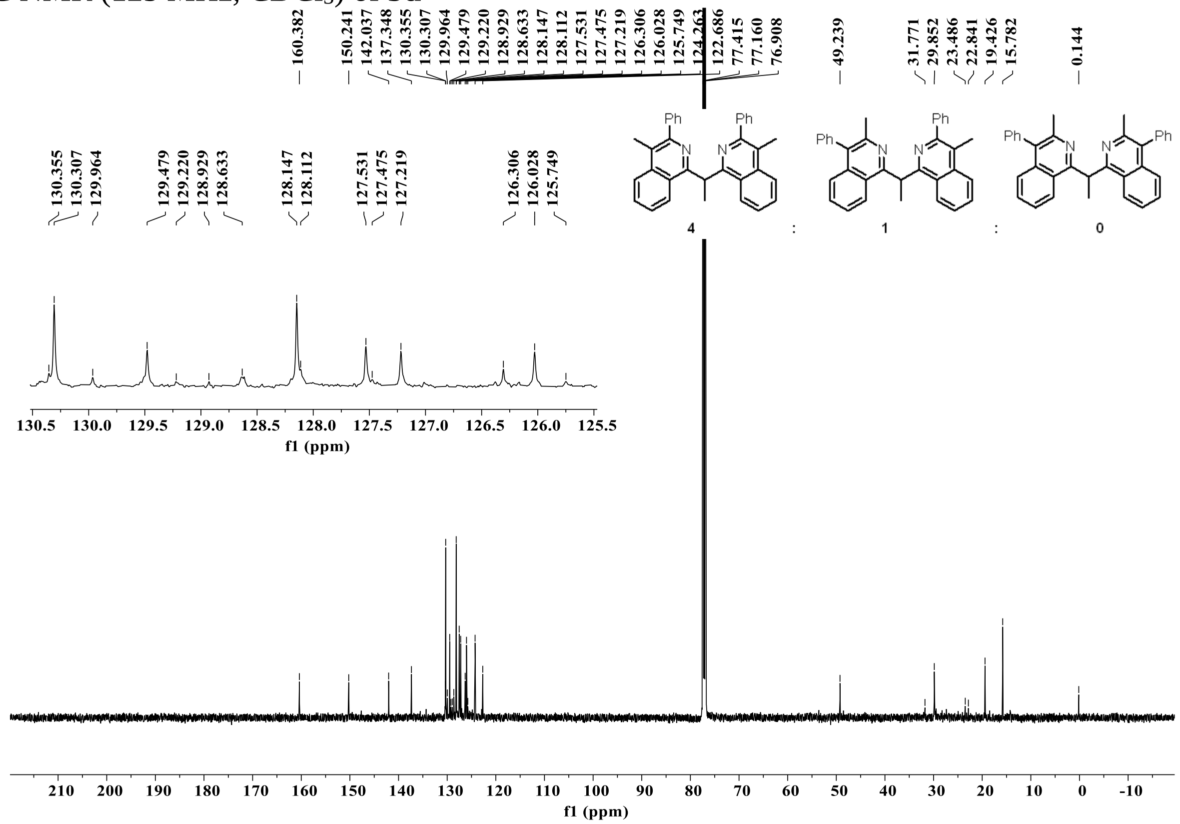

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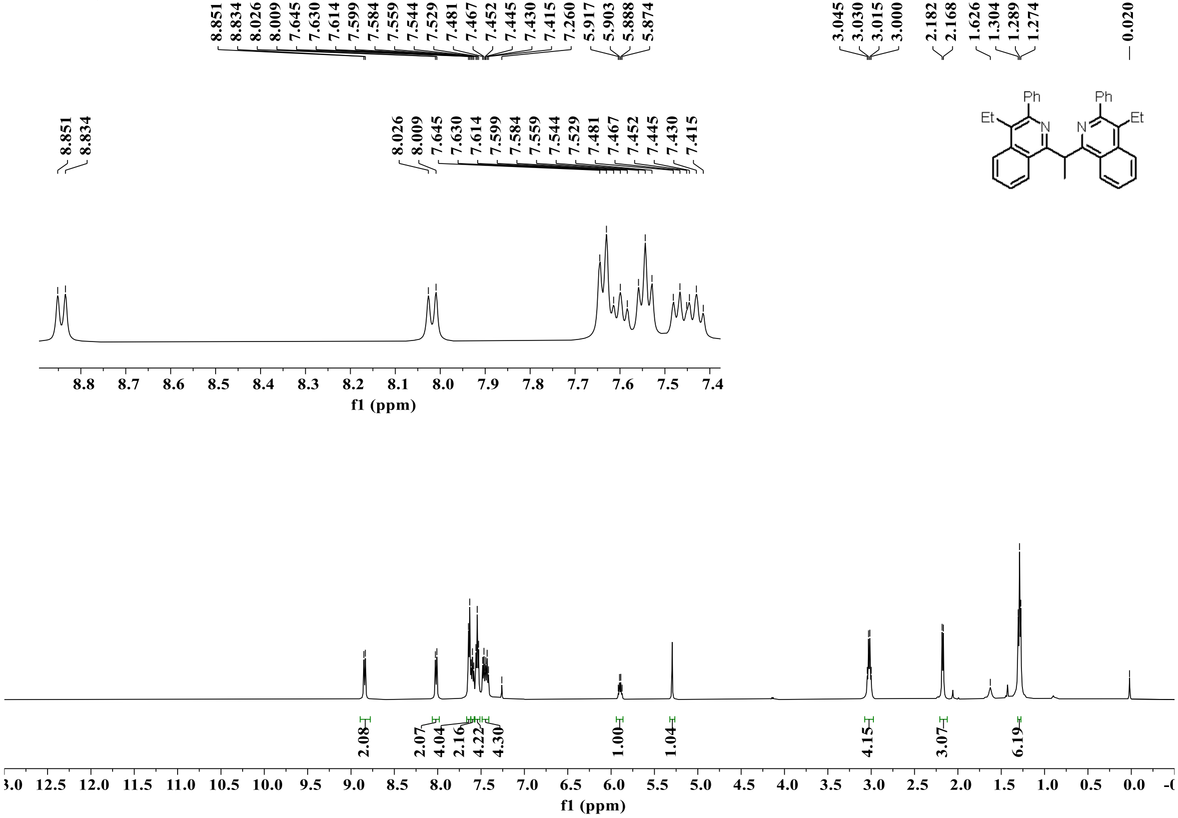

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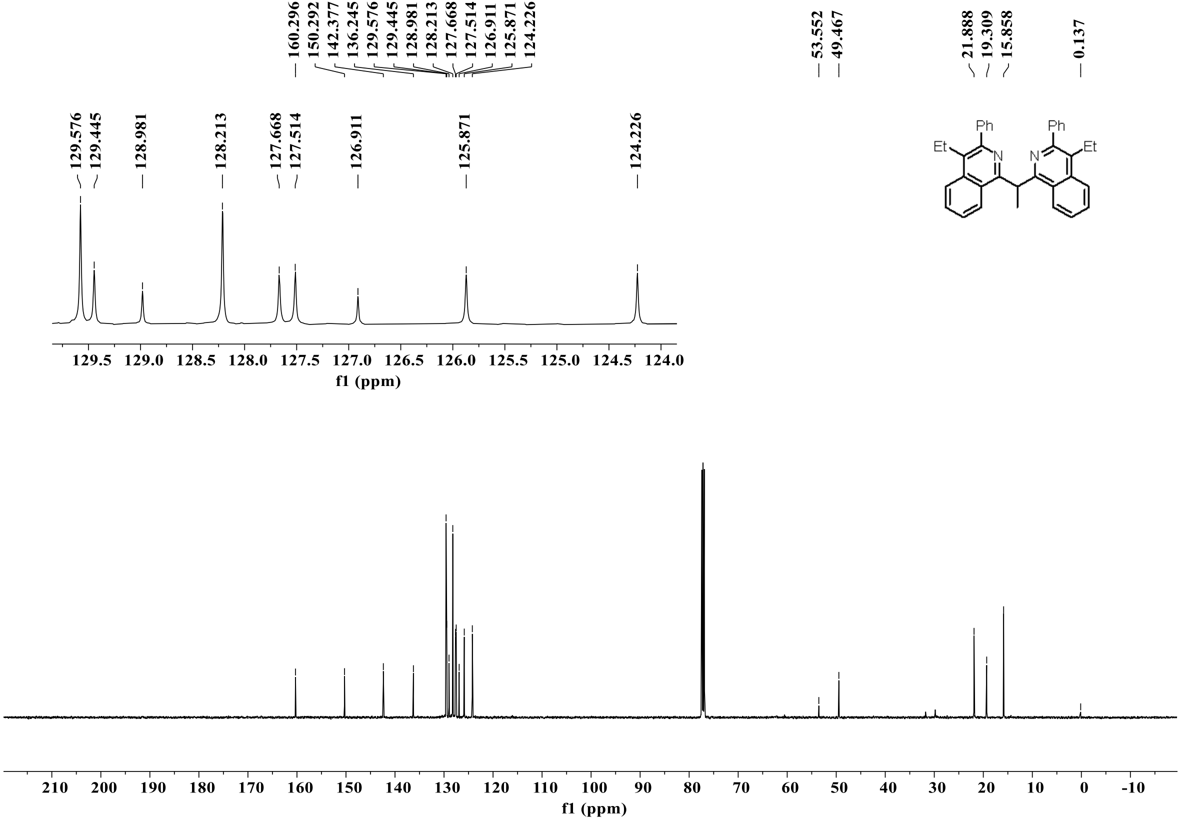

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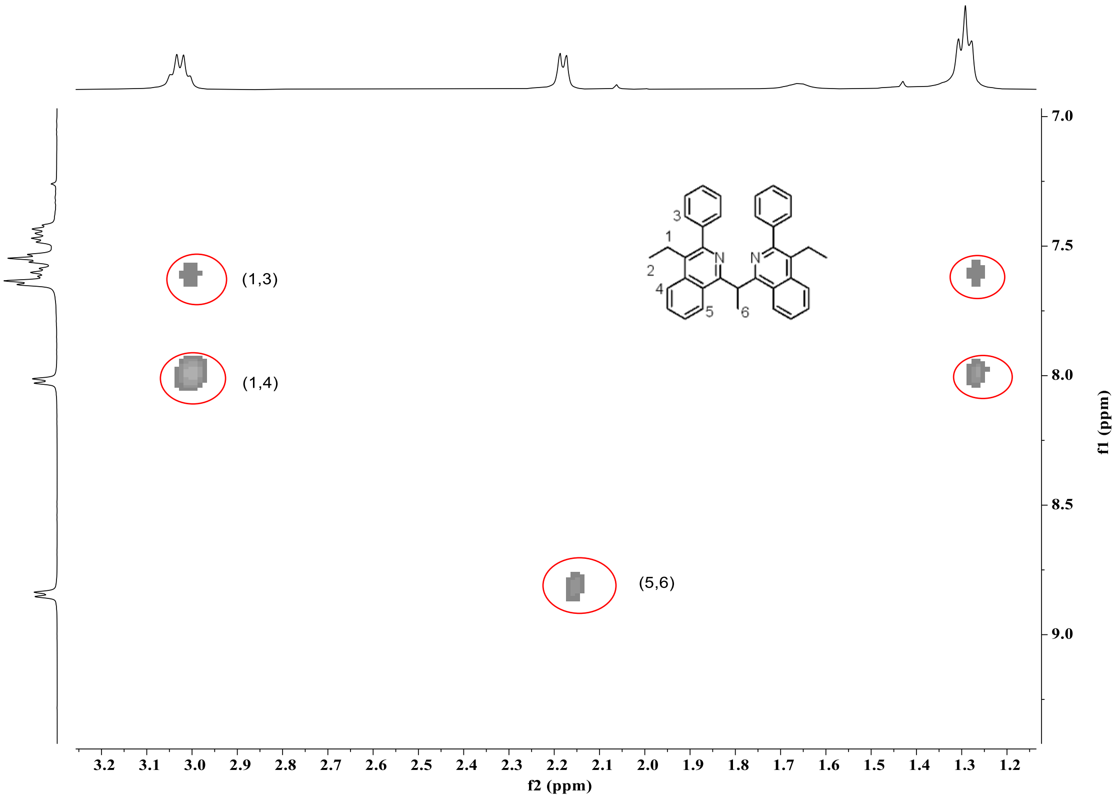

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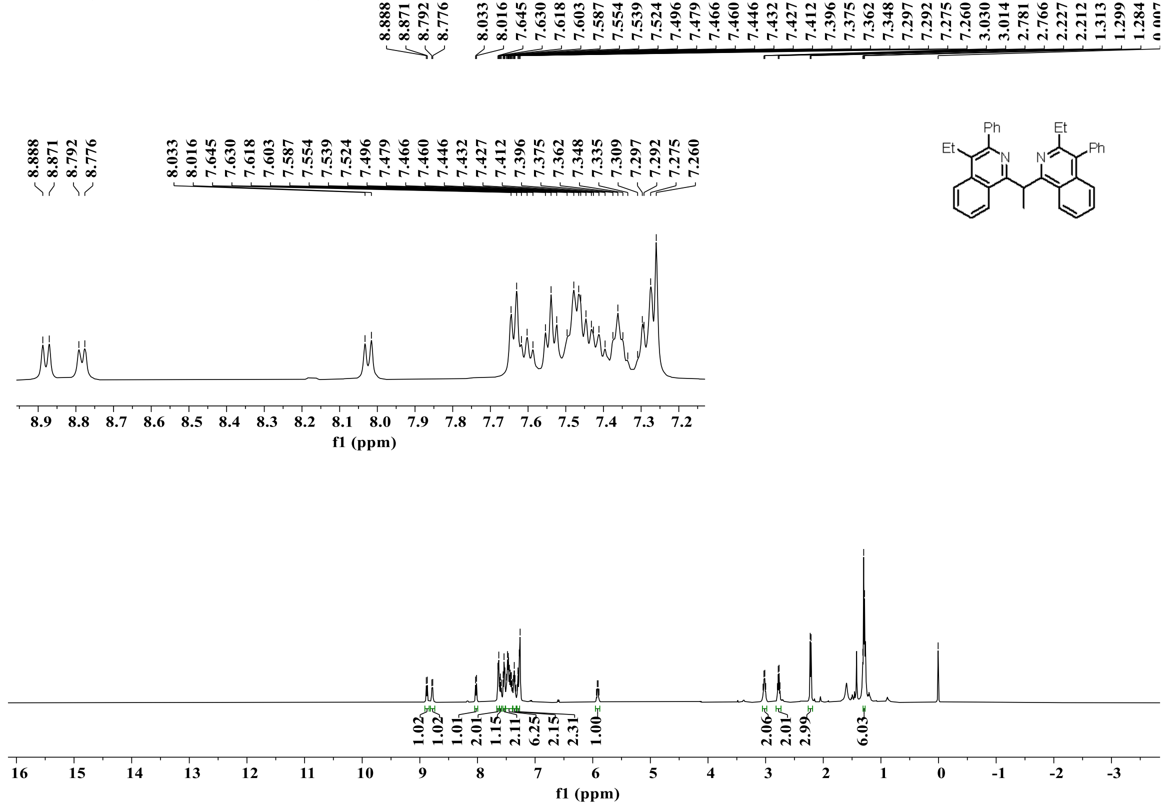

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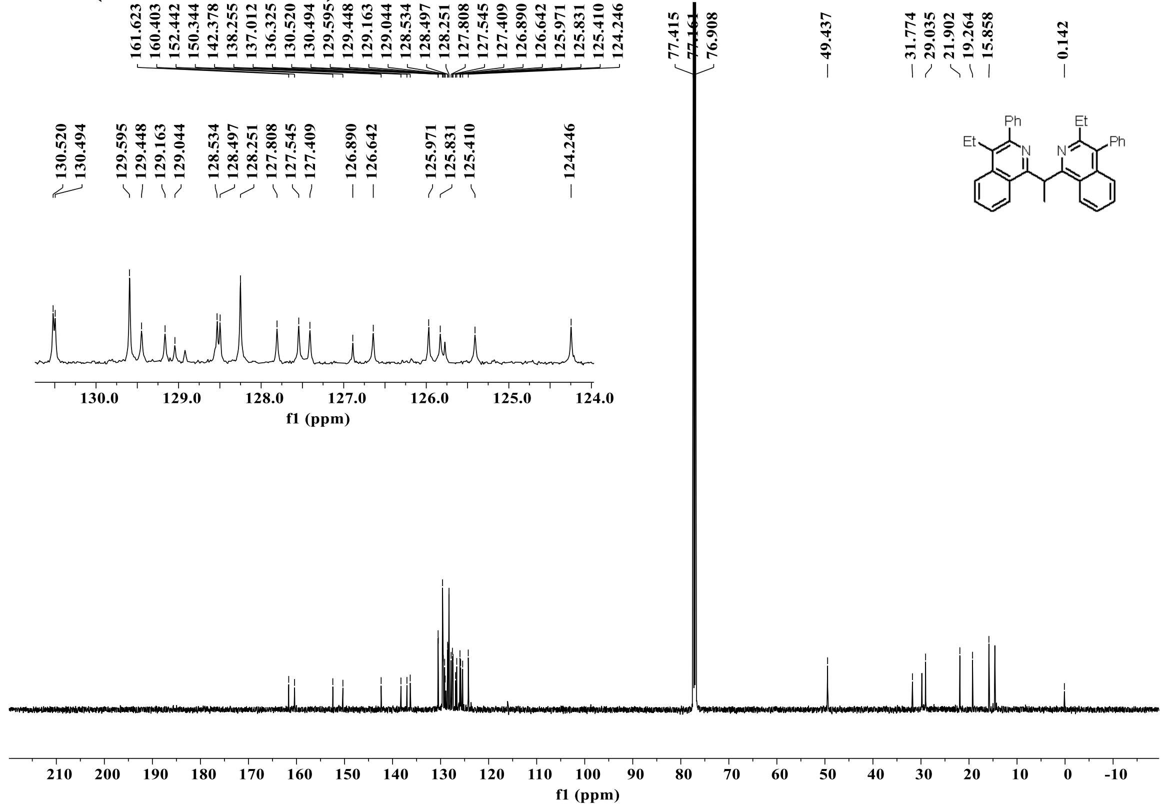
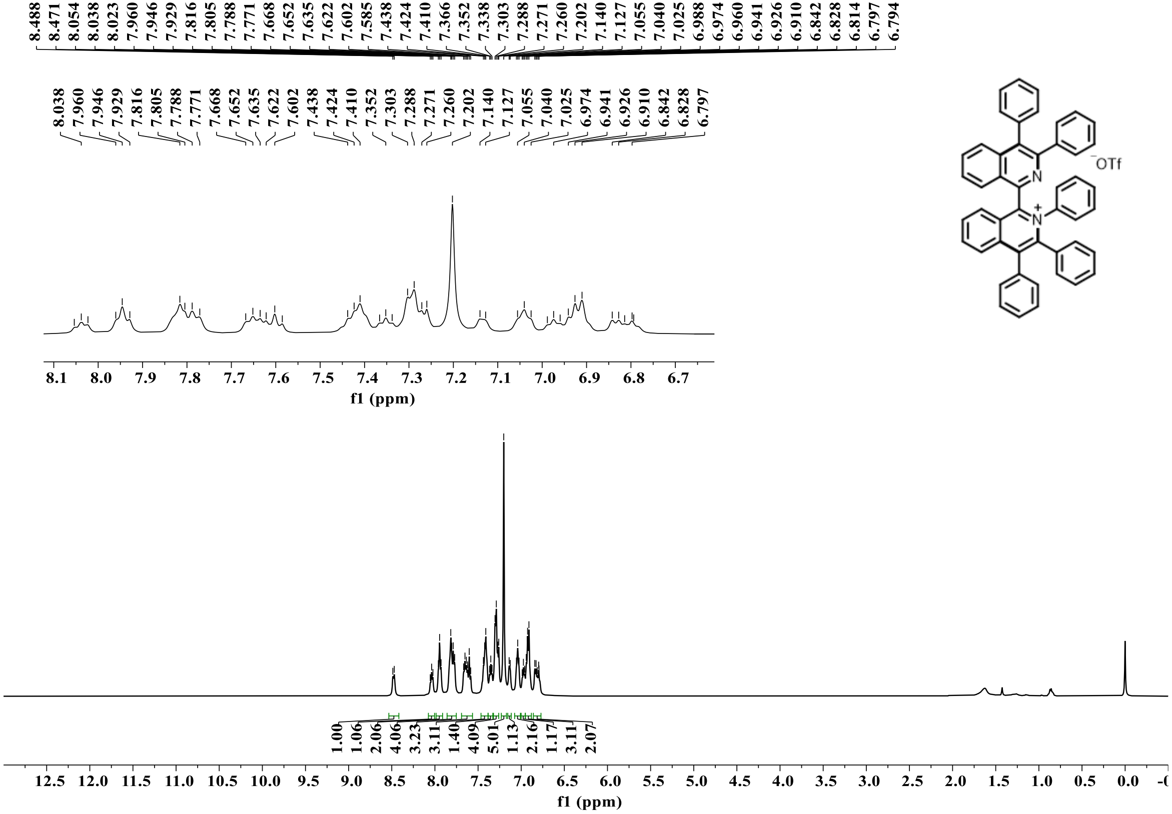


^{1}H NMR (500 MHz, CDCl$_3$) of **7a**



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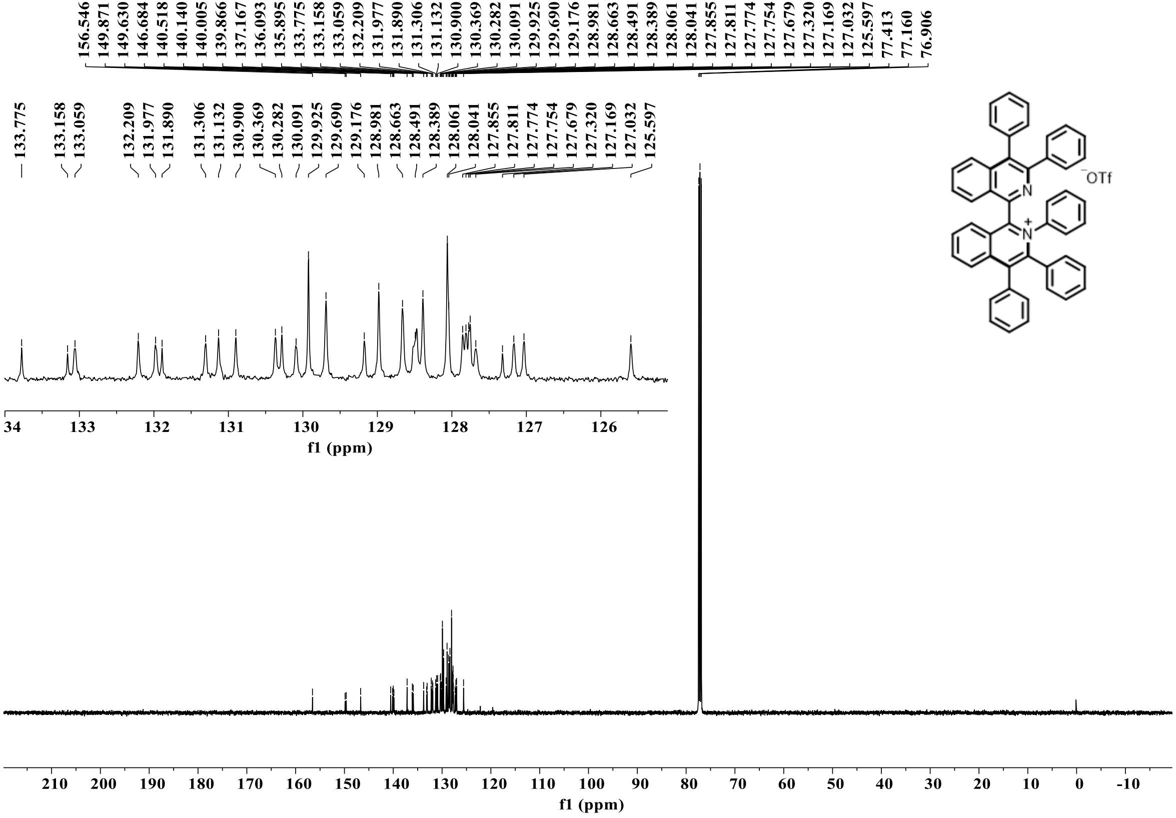
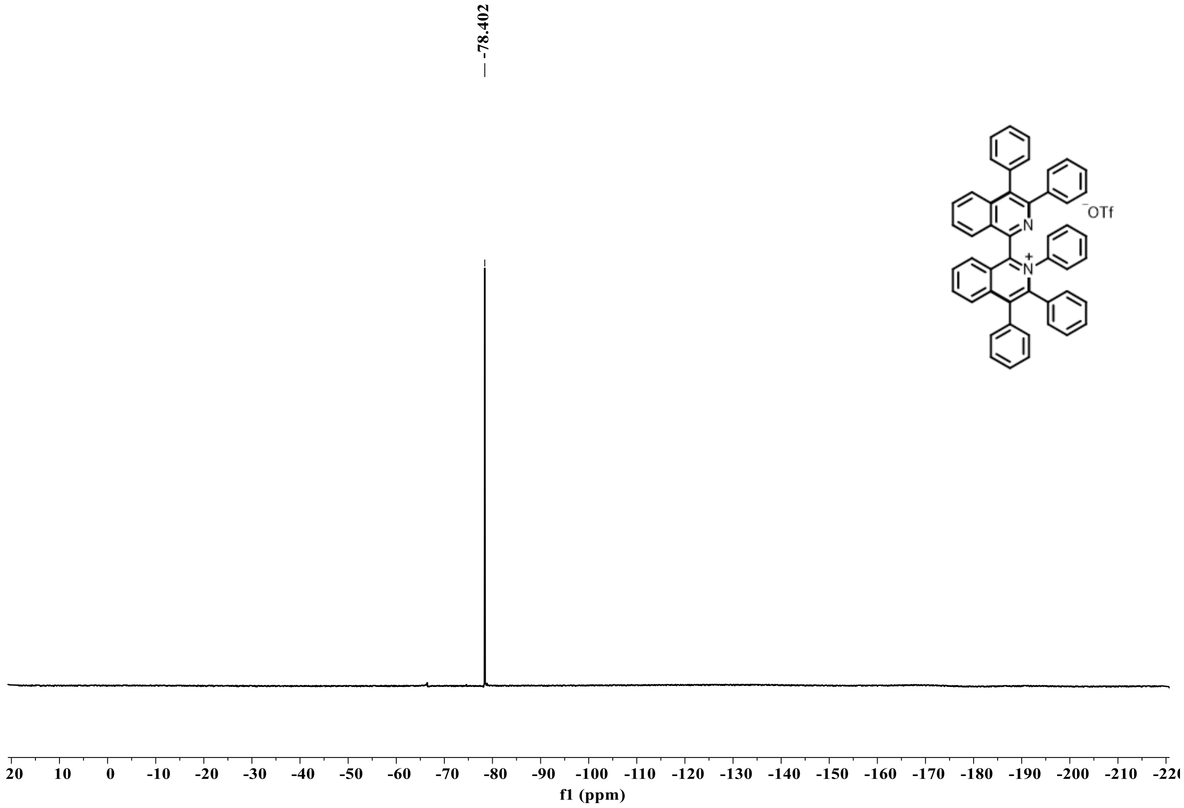
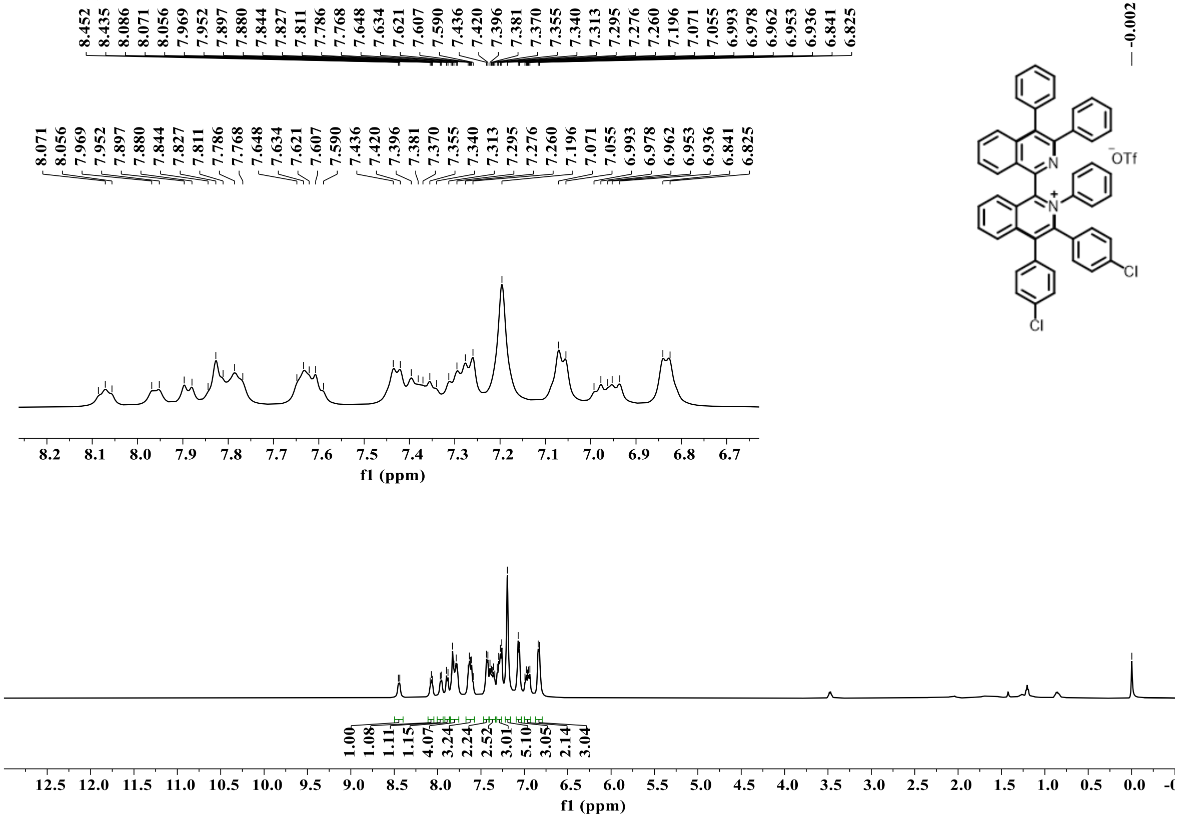


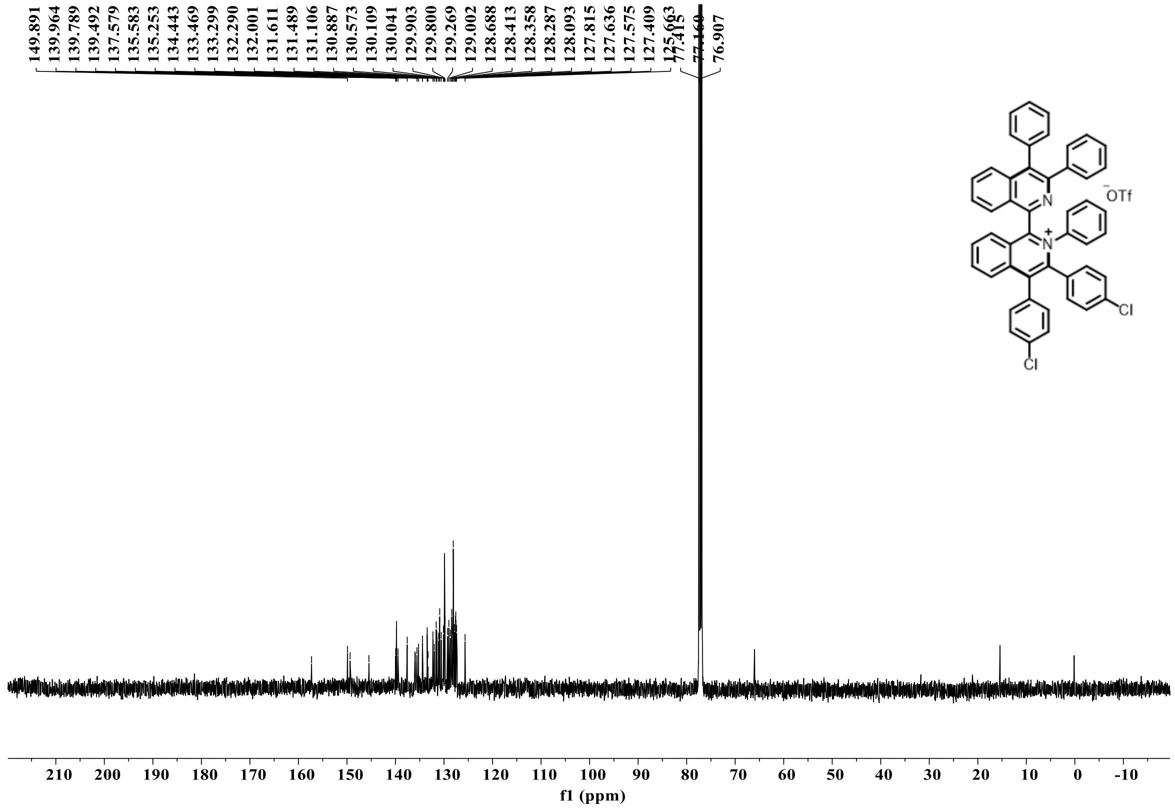
^{19}F NMR (470 MHz, $CDCl_3$) of **7a**



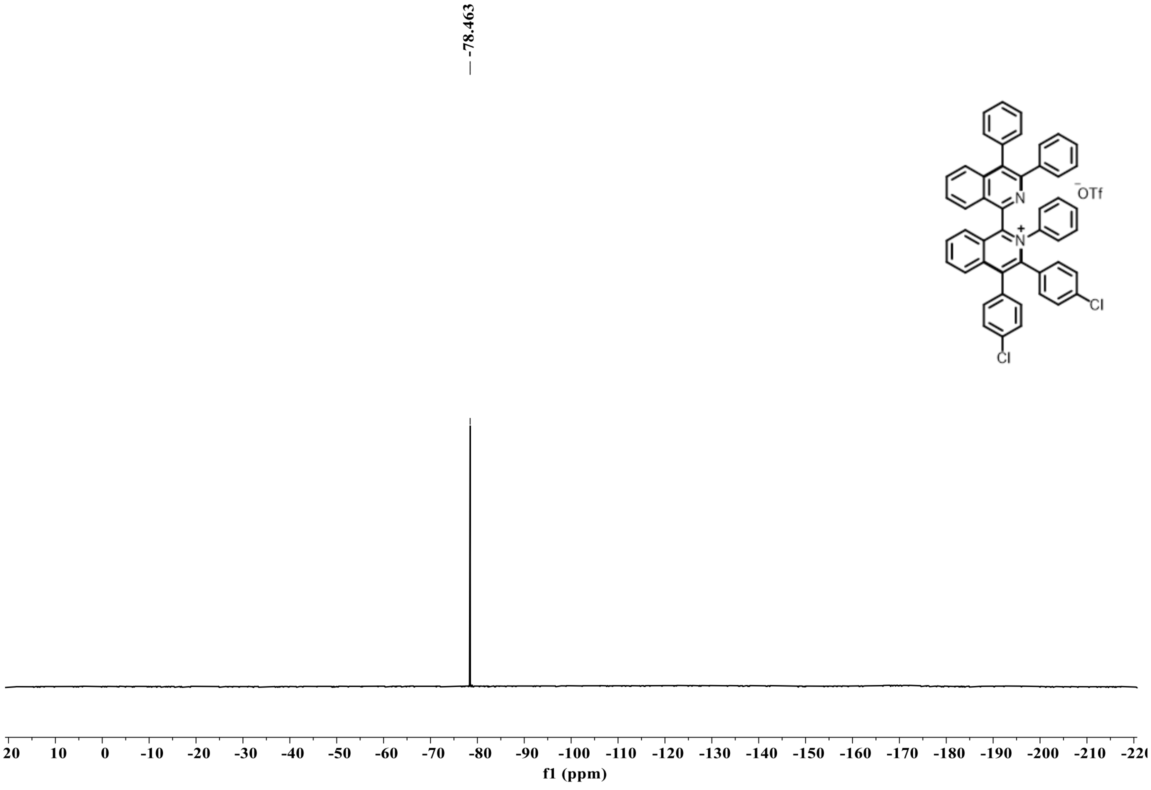
^{1}H NMR (500 MHz, CDCl$_3$) of **7b**



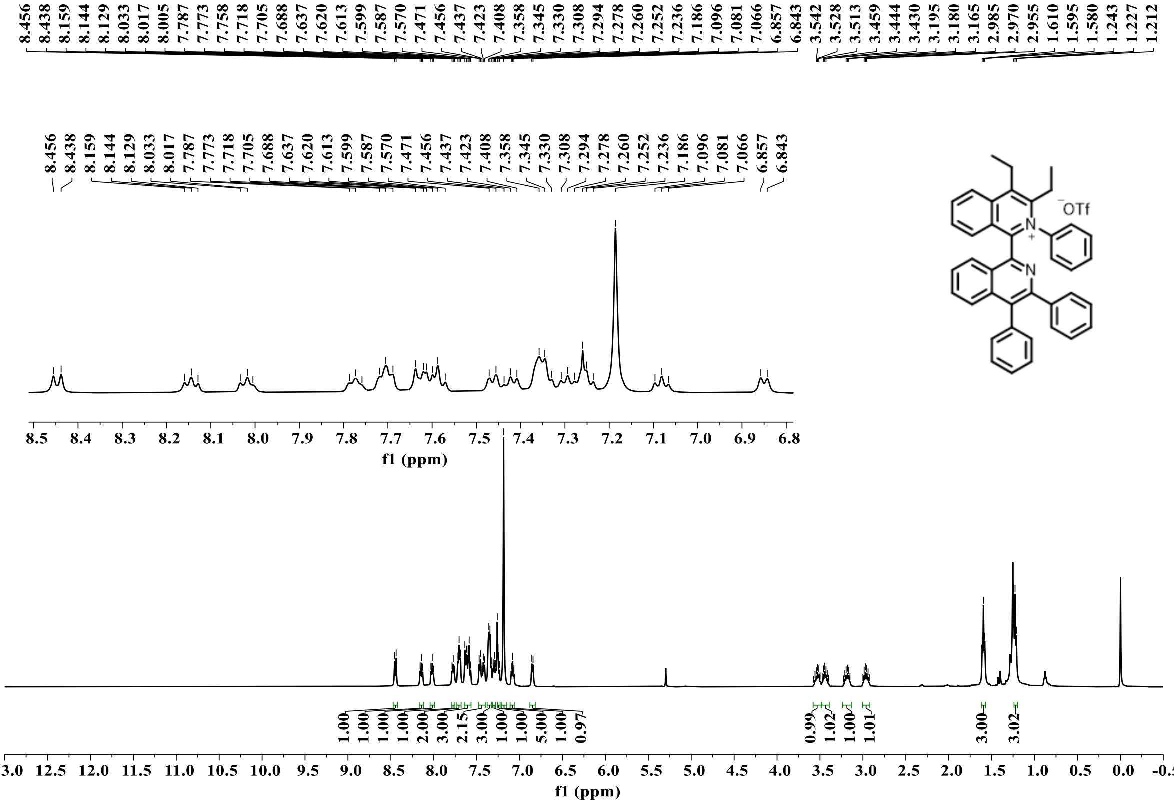
^{13}C NMR (125 MHz, CDCl3) of **7b**



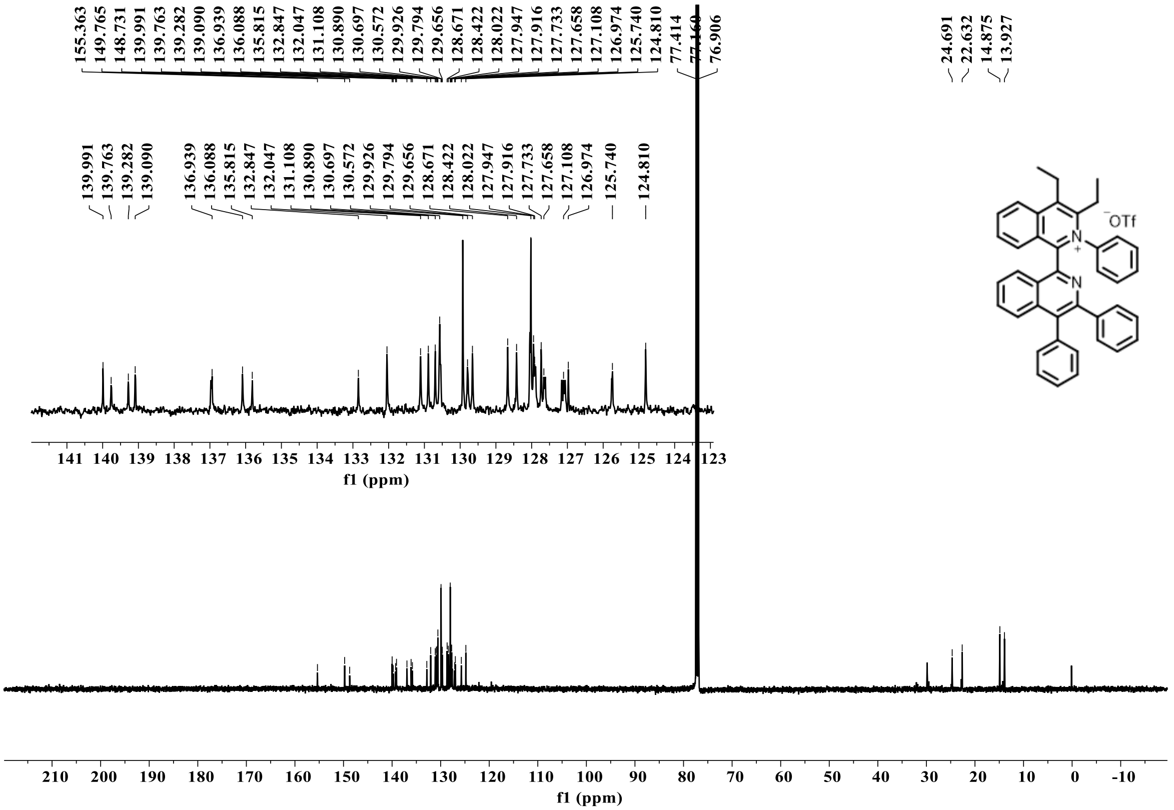
^{19}F NMR (470 MHz, CDCl$_3$) of **7b**



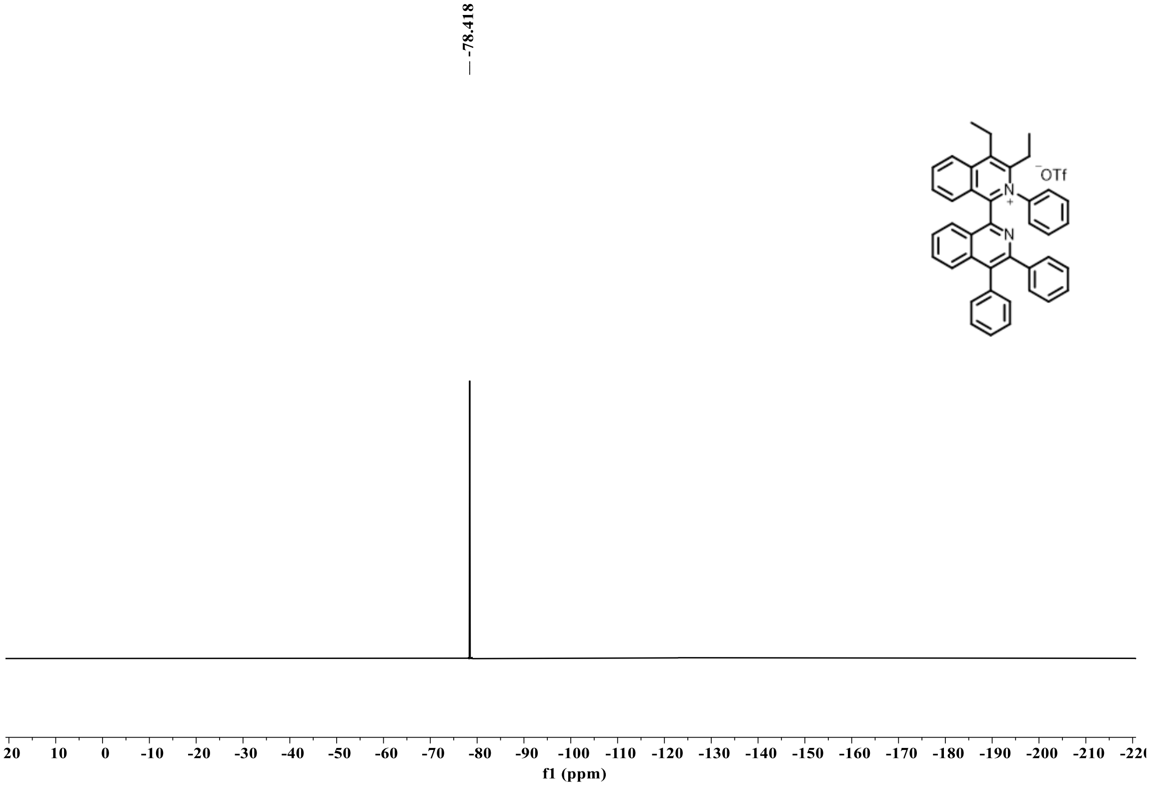
^{1}H NMR (500 MHz, $CDCl_3$) of **7c**



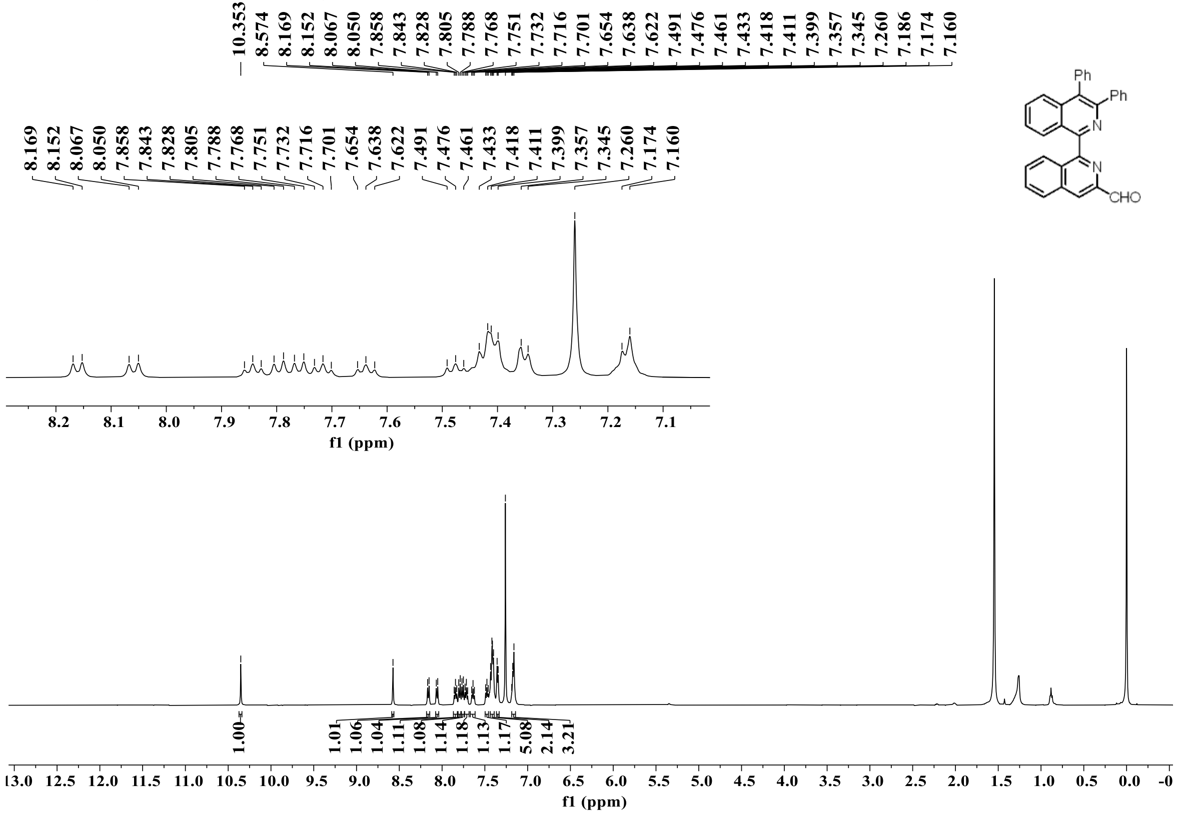
^{13}C NMR (125 MHz, CDCl3) of **7c**



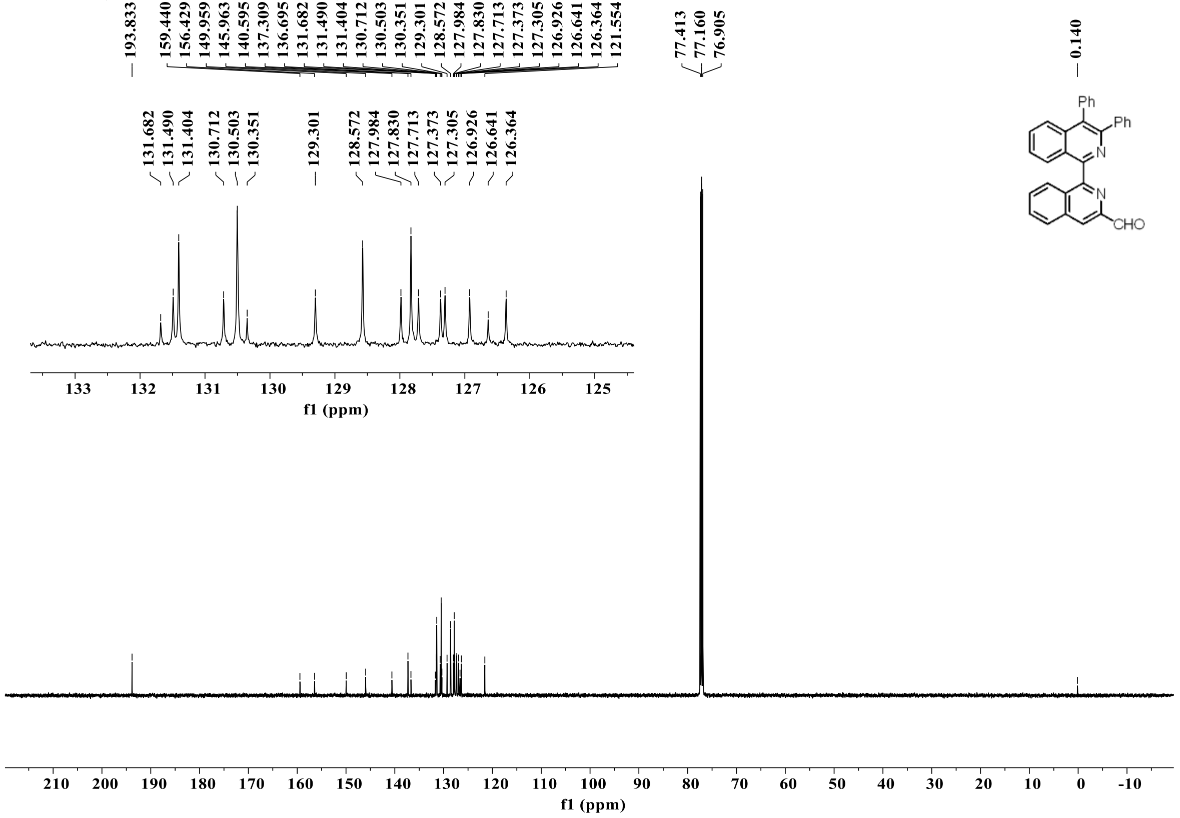
^{19}F NMR (471 MHz, CDCl$_3$) of **7c**



^{1}H NMR (500 MHz, $CDCl_3$) of **8**



^{13}C NMR (125 MHz, CDCl3) of **8**



11 X-ray crystallographic data

General crystal growing conditions of **Int-C**: X-ray quality single crystal of **Int-C** was grown from the co-solvent of DCM and *n*-hexane (10:1, v/v) at room temperature by slow evaporation for 3 days.

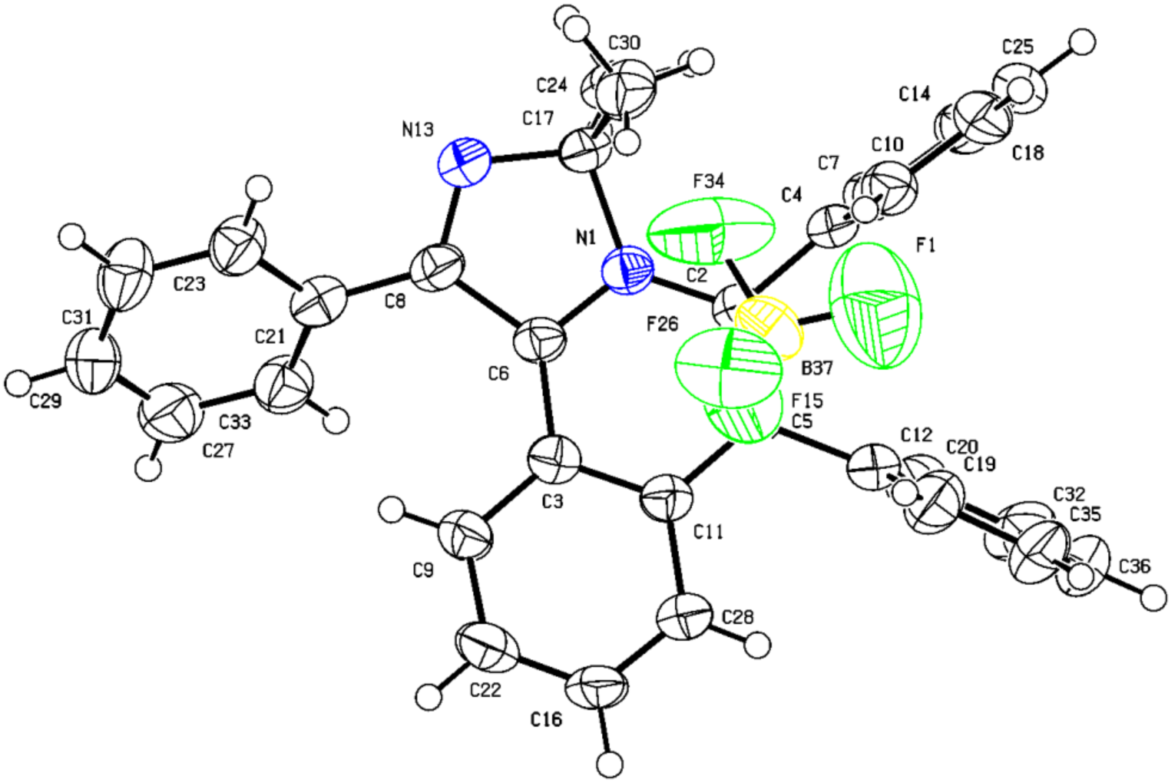


Figure S18 *The molecular structure of* ***Int-C*** *(CCDC 2266530). Thermal ellipsoids are shown at the 50% probability level.*

Table S10 Crystal data and structure refinement for 1_tw.

Identification code	1_tw
Empirical formula	$C_{31}H_{25}BF_4N_2$
Formula weight	512.34
Temperature/K	260.0
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	8.5802(9)
b/Å	19.2499(19)
c/Å	15.3566(17)
α/°	90
β/°	94.856(6)

γ/°	90
Volume/Å^3	2527.3(5)
Z	4
ρ_{calc}g/cm^3	1.347
μ/mm^{-1}	0.523
F(000)	1064.0
Crystal size/mm^3	0.03 × 0.02 × 0.01
Radiation	Ga Kα (λ = 1.34139)
2Θ range for data collection/	6.42 to 114.274
Index ranges	$-10 \leq h \leq 10$, $-24 \leq k \leq 24$, $-2 \leq l \leq 19$
Reflections collected	5143
Independent reflections	5143 [R_{int}= ?, R_{sigma}= 0.0630]
Data/restraints/parameters	5143/0/347
Goodness-of-fit on F^2	1.116
Final R indexes [I>=2σ (I)]	R_1= 0.1200, wR_2= 0.3367
Final R indexes [all data]	R_1= 0.1623, wR_2= 0.3513
Largest diff. peak/hole / e Å^{-3}	0.44/-0.44

Table S11 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 1_tw. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
N1	2734(7)	1386(3)	8347(4)	30.0(13)
C2	2870(8)	1071(3)	7545(4)	30.7(15)
C3	2948(8)	299(4)	9122(4)	31.1(15)
C4	2845(5)	1487(2)	6725(2)	32.1(15)
C7	1424(5)	1605(3)	6244(3)	38.3(17)
C14	1386(5)	1953(3)	5449(3)	47(2)
C25	2769(7)	2183(3)	5135(3)	51(2)
C18	4190(5)	2064(3)	5617(3)	49(2)
C10	4228(5)	1716(3)	6411(3)	39.5(18)
C5	3017(9)	364(4)	7528(5)	33.0(16)
C6	2714(8)	1023(3)	9093(5)	30.9(15)
C8	2446(9)	1555(4)	9779(5)	35.8(17)
C9	3090(10)	-100(4)	9901(5)	41.7(19)
C11	3125(9)	-37(4)	8307(5)	34.8(16)
N13	2471(8)	2172(3)	9474(4)	38.6(15)
F15	6810(70)	730(30)	7980(40)	96(16)
C16	3437(11)	-1131(4)	9068(6)	48(2)
C17	2647(10)	2157(4)	8546(5)	37.4(17)

Table S11 Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times10^3$) for 1_tw. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
C22	3310(10)	-798(4)	9868(5)	47(2)
C24	1195(11)	2491(4)	8098(6)	49(2)
F26	9150(60)	940(30)	8500(30)	98(13)
C28	3331(11)	-766(4)	8309(5)	46(2)
C30	4133(10)	2524(4)	8348(5)	47(2)
C33	1099(6)	918(3)	10919(3)	44.8(19)
C21	2129(6)	1434(3)	10698(2)	38.0(17)
C23	2865(6)	1853(2)	11346(3)	46(2)
C31	2571(7)	1757(3)	12214(3)	57(2)
C29	1541(7)	1241(3)	12434(3)	55(2)
C27	805(6)	822(3)	11787(3)	54(2)
F34	7700(70)	1651(19)	7720(90)	210(40)
C36	3089(9)	-791(3)	5157(3)	77(4)
C32	1678(7)	-563(3)	5437(4)	61(3)
C20	1666(5)	-175(3)	6200(4)	50(2)
C12	3065(6)	-14(2)	6681(3)	37.8(17)
C19	4476(5)	-242(3)	6400(4)	54(2)
C35	4488(7)	-631(3)	5638(4)	65(3)
B37	7989(14)	1048(6)	7909(8)	58(3)
F1	8030(50)	1260(20)	7055(18)	93(12)
F15A	6800(40)	548(17)	8082(17)	61(5)
F26A	9400(40)	847(12)	8360(30)	114(12)
F1A	8440(40)	830(40)	7129(18)	177(18)
F34A	7570(30)	1677(10)	8300(13)	87(7)

Table S12 Anisotropic Displacement Parameters ($Å^2\times10^3$) for 1_tw. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
N1	27(3)	29(3)	33(3)	-1(2)	1(2)	3(2)
C2	33(4)	29(3)	30(3)	-2(3)	3(3)	4(3)
C3	27(4)	32(3)	34(4)	3(3)	0(3)	2(3)
C4	40(4)	26(3)	31(4)	0(3)	4(3)	2(3)
C7	40(4)	40(4)	34(4)	4(3)	-5(3)	1(3)
C14	58(6)	45(5)	35(4)	7(3)	-6(4)	3(4)
C25	78(7)	39(4)	38(4)	7(3)	11(5)	1(4)
C18	59(6)	42(4)	48(5)	5(4)	15(4)	-5(4)
C10	39(4)	40(4)	39(4)	1(3)	4(3)	-3(3)
C5	36(4)	29(3)	35(4)	-1(3)	8(3)	1(3)

Table S12 Anisotropic Displacement Parameters (Å^2×10^3) for 1_tw. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
C6	28(4)	30(3)	34(4)	0(3)	2(3)	4(3)
C8	41(4)	32(4)	34(4)	-6(3)	3(3)	-3(3)
C9	48(5)	40(4)	38(4)	9(3)	10(4)	7(4)
C11	37(4)	32(4)	35(4)	1(3)	4(3)	6(3)
N13	46(4)	33(3)	38(3)	-7(3)	8(3)	-1(3)
F15	74(18)	100(30)	110(30)	49(17)	-20(16)	-42(17)
C16	61(6)	29(4)	55(5)	7(4)	12(4)	12(4)
C17	49(5)	28(3)	35(4)	-1(3)	0(3)	1(3)
C22	54(5)	39(4)	47(5)	18(4)	3(4)	8(4)
C24	57(5)	34(4)	55(5)	-4(4)	-6(4)	17(4)
F26	41(17)	150(30)	100(20)	-4(18)	-27(13)	10(16)
C28	63(6)	30(4)	46(4)	3(3)	18(4)	6(4)
C30	51(5)	47(5)	45(5)	-6(4)	7(4)	-15(4)
C33	39(5)	44(4)	53(5)	-9(4)	11(4)	-7(4)
C21	43(4)	33(4)	39(4)	-1(3)	9(3)	3(3)
C23	50(5)	46(4)	43(4)	-8(4)	5(4)	-8(4)
C31	63(6)	71(6)	39(5)	-18(4)	6(4)	-11(5)
C29	55(6)	64(6)	49(5)	0(4)	24(4)	0(5)
C27	57(6)	46(5)	62(6)	0(4)	27(5)	-4(4)
F34	120(40)	70(20)	400(110)	60(40)	-120(50)	20(20)
C36	134(11)	52(6)	45(5)	-13(4)	15(6)	0(7)
C32	75(7)	51(5)	53(5)	-14(4)	-17(5)	-3(5)
C20	61(6)	40(4)	49(5)	-5(4)	-2(4)	-3(4)
C12	50(5)	28(3)	35(4)	1(3)	4(3)	-1(3)
C19	59(6)	52(5)	53(5)	-13(4)	13(4)	-2(4)
C35	72(7)	65(6)	61(6)	-19(5)	23(5)	7(5)
B37	51(7)	57(7)	67(7)	14(6)	5(6)	-10(6)
F1	100(20)	150(30)	37(11)	15(14)	32(11)	-4(19)
F15A	55(8)	74(13)	54(8)	7(9)	9(6)	-24(9)
F26A	43(11)	51(9)	240(30)	29(12)	-29(14)	4(7)
F1A	130(20)	310(50)	91(13)	30(20)	55(13)	-30(30)
F34A	102(12)	60(8)	105(12)	2(8)	44(11)	8(7)

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
N1	C2	1.387(9)	C16	C28	1.356(11)
N1	C6	1.342(9)	C17	C24	1.514(11)
N1	C17	1.520(9)	C17	C30	1.511(11)
C2	C4	1.491(7)	F26	B37	1.31(4)
C2	C5	1.367(9)	C33	C21	1.3900

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C3	C6	1.408(9)	C33	C27	1.3900
C3	C9	1.418(10)	C21	C23	1.3900
C3	C11	1.428(10)	C23	C31	1.3900
C4	C7	1.3900	C31	C29	1.3900
C4	C10	1.3900	C29	C27	1.3900
C7	C14	1.3900	F34	B37	1.22(3)
C14	C25	1.3900	F34	F1	1.32(15)
C25	C18	1.3900	C36	C32	1.3900
C18	C10	1.3900	C36	C35	1.3900
C5	C11	1.420(10)	C32	C20	1.3900
C5	C12	1.493(8)	C20	C12	1.3900
C6	C8	1.501(9)	C12	C19	1.3900
C8	N13	1.278(9)	C19	C35	1.3900
C8	C21	1.479(8)	B37	F1	1.37(3)
C9	C22	1.359(11)	B37	F15A	1.44(3)
C11	C28	1.415(10)	B37	F26A	1.40(3)
N13	C17	1.446(9)	B37	F1A	1.36(4)
F15	B37	1.20(6)	B37	F34A	1.41(2)
C16	C22	1.398(12)			

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C2	N1	C17	127.9(6)	C24	C17	N1	112.1(6)
C6	N1	C2	122.6(6)	C30	C17	N1	111.1(6)
C6	N1	C17	109.4(5)	C30	C17	C24	112.7(7)
N1	C2	C4	121.3(5)	C9	C22	C16	120.4(7)
C5	C2	N1	117.8(6)	C16	C28	C11	120.9(8)
C5	C2	C4	120.9(6)	C21	C33	C27	120.0
C6	C3	C9	124.4(7)	C33	C21	C8	121.1(4)
C6	C3	C11	116.5(6)	C23	C21	C8	118.9(4)
C9	C3	C11	119.0(6)	C23	C21	C33	120.0
C7	C4	C2	119.1(4)	C31	C23	C21	120.0
C7	C4	C10	120.0	C23	C31	C29	120.0
C10	C4	C2	120.8(4)	C31	C29	C27	120.0
C4	C7	C14	120.0	C29	C27	C33	120.0
C7	C14	C25	120.0	B37	F34	F1	65(5)
C14	C25	C18	120.0	C32	C36	C35	120.0
C10	C18	C25	120.0	C20	C32	C36	120.0
C18	C10	C4	120.0	C12	C20	C32	120.0
C2	C5	C11	121.6(7)	C20	C12	C5	119.0(5)
C2	C5	C12	120.7(6)	C20	C12	C19	120.0
C11	C5	C12	117.7(6)	C19	C12	C5	120.8(5)

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
N1	C6	C3	122.0(6)	C12	C19	C35	120.0
N1	C6	C8	104.9(6)	C19	C35	C36	120.0
C3	C6	C8	133.1(7)	F15	B37	F26	117(4)
N13	C8	C6	111.7(6)	F15	B37	F34	111(4)
N13	C8	C21	120.4(6)	F15	B37	F1	109(3)
C21	C8	C6	127.9(6)	F26	B37	F1	129(3)
C22	C9	C3	120.5(7)	F34	B37	F26	117(4)
C5	C11	C3	119.2(6)	F34	B37	F1	61(8)
C28	C11	C3	118.1(7)	F26A	B37	F15A	108.7(19)
C28	C11	C5	122.7(7)	F26A	B37	F34A	105.5(18)
C8	N13	C17	110.4(6)	F1A	B37	F15A	102(2)
C28	C16	C22	120.9(7)	F1A	B37	F26A	93(3)
N13	C17	N1	103.2(5)	F1A	B37	F34A	138(3)
N13	C17	C24	106.8(7)	F34A	B37	F15A	106.7(15)
N13	C17	C30	110.4(6)	F34	F1	B37	54(3)

A	**B**	**C**	**D**	**Angle/°**	**A**	**B**	**C**	**D**	**Angle/°**
N1	C2	C4	C7	-90.9(7)	C6	C8	C21	C23	138.1(7)
N1	C2	C4	C10	93.2(7)	C8	N13	C17	N1	-0.3(9)
N1	C2	C5	C11	-3.7(11)	C8	N13	C17	C24	118.0(7)
N1	C2	C5	C12	176.0(6)	C8	N13	C17	C30	-119.1(7)
N1	C6	C8	N13	-6.2(9)	C8	C21	C23	C31	179.1(6)
N1	C6	C8	C21	171.8(7)	C9	C3	C6	N1	173.6(7)
C2	N1	C6	C3	4.9(11)	C9	C3	C6	C8	-4.8(13)
C2	N1	C6	C8	-176.3(6)	C9	C3	C11	C5	-178.7(7)
C2	N1	C17	N13	178.4(7)	C9	C3	C11	C28	4.2(11)
C2	N1	C17	C24	63.9(10)	C11	C3	C6	N1	-3.2(11)
C2	N1	C17	C30	-63.3(9)	C11	C3	C6	C8	178.3(8)
C2	C4	C7	C14	-175.9(5)	C11	C3	C9	C22	-3.4(12)
C2	C4	C10	C18	175.8(5)	C11	C5	C12	C20	96.9(7)
C2	C5	C11	C3	5.2(12)	C11	C5	C12	C19	-79.1(7)
C2	C5	C11	C28	-177.8(8)	N13	C8	C21	C33	135.1(6)
C2	C5	C12	C20	-82.8(8)	N13	C8	C21	C23	-44.0(9)
C2	C5	C12	C19	101.2(7)	F15	B37	F1	F34	104(4)
C3	C6	C8	N13	172.4(8)	C17	N1	C2	C4	-4.0(11)
C3	C6	C8	C21	-9.5(14)	C17	N1	C2	C5	176.4(7)
C3	C9	C22	C16	1.5(14)	C17	N1	C6	C3	-173.1(7)
C3	C11	C28	C16	-3.3(13)	C17	N1	C6	C8	5.7(8)
C4	C2	C5	C11	176.7(6)	C22	C16	C28	C11	1.5(14)
C4	C2	C5	C12	-3.6(11)	F26	B37	F1	F34	-102(5)
C4	C7	C14	C25	0.0	C28	C16	C22	C9	-0.5(15)

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
C7	C4	C10	C18	0.0	C33	C21	C23	C31	0.0
C7	C14	C25	C18	0.0	C21	C8	N13	C17	-174.3(7)
C14	C25	C18	C10	0.0	C21	C33	C27	C29	0.0
C25	C18	C10	C4	0.0	C21	C23	C31	C29	0.0
C10	C4	C7	C14	0.0	C23	C31	C29	C27	0.0
C5	C2	C4	C7	88.6(7)	C31	C29	C27	C33	0.0
C5	C2	C4	C10	-87.2(8)	C27	C33	C21	C8	-179.1(6)
C5	C11	C28	C16	179.7(8)	C27	C33	C21	C23	0.0
C5	C12	C19	C35	176.0(5)	C36	C32	C20	C12	0.0
C6	N1	C2	C4	178.3(6)	C32	C36	C35	C19	0.0
C6	N1	C2	C5	-1.3(11)	C32	C20	C12	C5	-176.0(5)
C6	N1	C17	N13	-3.7(8)	C32	C20	C12	C19	0.0
C6	N1	C17	C24	-118.2(7)	C20	C12	C19	C35	0.0
C6	N1	C17	C30	114.6(7)	C12	C5	C11	C3	-174.6(6)
C6	C3	C9	C22	179.8(8)	C12	C5	C11	C28	2.4(11)
C6	C3	C11	C5	-1.6(11)	C12	C19	C35	C36	0.0
C6	C3	C11	C28	-178.8(7)	C35	C36	C32	C20	0.0
C6	C8	N13	C17	3.9(9)	F1	F34	B37	F15	-101(5)
C6	C8	C21	C33	-42.8(10)	F1	F34	B37	F26	122(4)

Table S13 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 1_tw.

Atom	*x*	*y*	*z*	U(eq)
H7	498.22	1452.11	6453.51	46
H14	435.25	2032.79	5127.17	56
H25	2744.04	2415.43	4603.82	61
H18	5115.81	2217.39	5406.79	59
H10	5178.82	1636.71	6733.14	47
H9	3032.65	117.42	10437.7	50
H16	3595.69	-1608.38	9055.5	58
H22	3376.93	-1056.89	10381.41	56
H24A	1285.27	2510.91	7479.9	74
H24B	1084.81	2953.04	8320.42	74
H24C	292.82	2220.82	8210.52	74
H28	3394.4	-999.1	7782.74	55
H30A	5020.42	2252.53	8565.38	71
H30B	4178.44	2971.57	8625.46	71
H30C	4144.7	2581.85	7727.7	71
H33	607.07	638.1	10485.4	54
H23	3554.32	2198.48	11198.36	55
H31	3063.5	2037.02	12647.12	69

Table S13 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 1_tw.

Atom	***x***	***y***	***z***	**U(eq)**
H29	1344.46	1176.1	13015.03	66
H27	116.23	476.63	11934.18	65
H36	3097.03	-1051.12	4646.46	92
H32	742.49	-670.65	5115.29	73
H20	722.35	-22.17	6387.7	61
H19	5411.29	-134.62	6722.47	65
H35	5431.46	-783.1	5450.06	78

Atom	***Occupancy***	**Atom**	***Occupancy***	**Atom**	***Occupancy***
F15	0.39(6)	F26	0.39(6)	F34	0.39(6)
F1	0.39(6)	F15A	0.61(6)	F26A	0.61(6)
F1A	0.61(6)	F34A	0.61(6)		