

Supporting Information for:

Base-Mediated Regioselective [3 + 2] Annulation of Ketenimines and Isocyanides: Efficient Synthesis of 1,4,5-Trisubstituted Imidazoles

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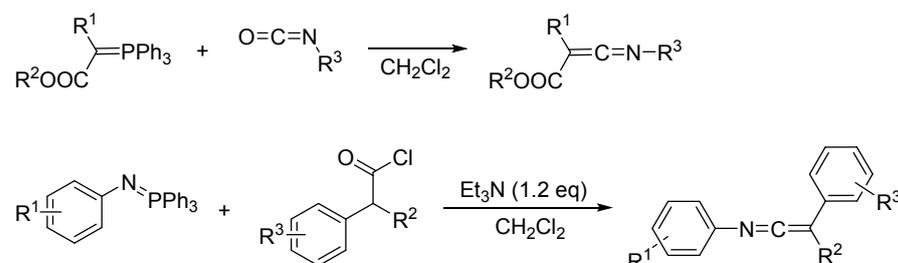
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1. General information

All chemicals which are commercially available were used without further purification unless otherwise noted. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash column chromatography was conducted on silica gel (300-400 mesh). ¹H NMR and ¹³C NMR spectra were recorded at 25 °C on a Varian 500 MHz and 125 MHz, respectively, and TMS as internal standard. Chemical shifts were reported in parts per million (ppm). High-resolution mass spectra (HRMS) were obtained using a Bruker microTOF II focus spectrometer (ESI). Melting points of all compounds were measured with a micro melting point apparatus. The compound with dimension 0.21 × 0.19 × 0.16 mm, was glued on a glass fiber. Data were collected at 283 K using graphite-monochromated Mo K α radiation ($\lambda = 0.71073\text{\AA}$) and Bruker APEX CCD area-detector in the range $3.090 < \theta < 25.00$.

2. Synthetic procedures of ketenimines 1

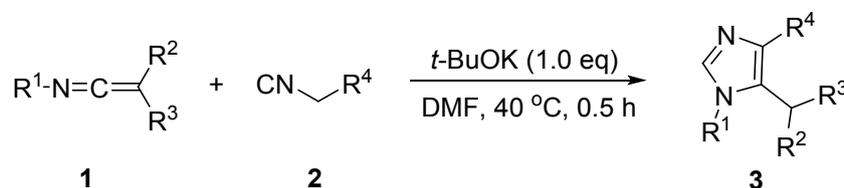
Ketenimines **1** were synthesized by following previously reported procedures.¹⁻⁵



References:

- (1) Zhou, X.; Jiang, Z.; Xue, L.; Lu, P.; Wang, Y. *Eur. J. Org. Chem.* **2015**, 2015, 5789.
- (2) Zhou, X. R.; Peng, Z. X.; Zhao, H. Y.; Zhang, Z. Y.; Lu, P.; Wan, Y. G. *Chem. Commun.* **2016**, 52, 10676.
- (3) Zhou, X. R.; Fan, Z. L.; Zhang, Z. Y.; Lu, P.; Wang, Y. G. *Org. Lett.* **2016**, 18, 4706.
- (4) Zhou, X. R.; Zhang, Z. Y.; Zhao, H. Y.; Lu, P.; Wan, Y. G. *J. Org. Chem.* **2017**, 82, 3787.
- (5) Zhou, X. R.; Li, Z. M.; Zhang, Z. Y.; Lu, P.; Wan, Y. G. *Org. Lett.* **2018**, 20, 1426.

3. Synthetic procedure and analytical data of compounds 3

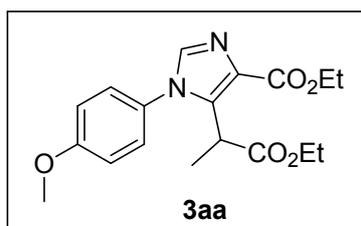


Typical synthetic procedure (with **3aa** as an example): To a solution of ethyl 3-((4-methoxyphenyl)imino)-2-methylacrylate (**1a**) (0.3 mmol, 69.9 mg) and ethyl isocyanoacetate (**2a**) (0.36 mmol, 0.039 mL) in DMF (2 mL) at 40 °C, *t*-BuOK (0.3 mmol, 33.7 mg) was added. After stirred for 30 min, substrate **1a** was completely consumed as indicated by TLC. The solution was cooled to room temperature, and poured into water (50 mL). The resulting mixture was extracted

by ethyl acetate (3 × 20 mL), the organic layer was combined and washed with brine (3 × 50 mL), dried over MgSO₄ and concentrated. Purification of the crude product with flash column chromatography (silica gel; petroleum ether: ethyl acetate = 5:1) gave **3aa** 89.3 mg, 86% yield as a yellow solid.

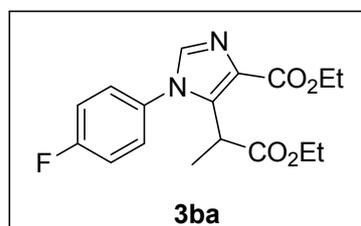
Analytical data of compounds of 3

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-methoxyphenyl)-1H-imidazole-4-carboxylate



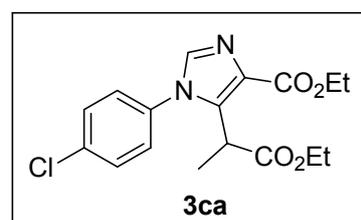
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 89.3 mg, 86 %, isolated as a yellow solid; m.p. 106-108 °C; ¹H NMR (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.43 (d, *J* = 7.2 Hz, 3H), 3.88 (s, 3H), 4.02 (q, *J* = 7.2 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 4.38 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 7.23 (d, *J* = 8.9 Hz, 2H), 7.52 (s, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 13.9, 14.2, 15.7, 35.5, 55.5, 60.3, 60.9, 114.7 (2C), 127.3, 128.0 (2C), 129.2, 137.3, 139.3, 160.3, 162.9, 171.2; HRMS (ESI-TOF) *m/z* calculated for C₁₈H₂₂N₂NaO₅⁺ ([M+Na]⁺): 369.1421, Found: 369.1430.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-fluorophenyl)-1H-imidazole-4-carboxylate



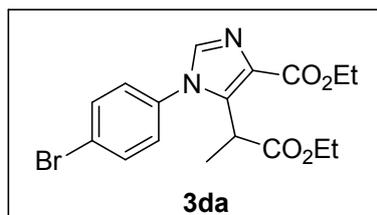
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 92.3 mg, 92 %, isolated as a yellow liquid; ¹H NMR (600 MHz, CDCl₃) δ 1.19 (t, *J* = 7.1 Hz, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.43 (d, *J* = 7.2 Hz, 3H), 4.03 (q, *J* = 7.2 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 4.39 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.24 (dd, *J* = 11.4, 5.4 Hz, 2H), 7.33 (dd, *J* = 8.6, 4.6 Hz, 2H), 7.54 (s, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 13.9, 14.2, 15.7, 35.5, 60.5, 61.1, 116.7, 116.8, 128.7, 128.8, 129.6, 130.8 (d, *J* = 3.0 Hz), 137.1, 139.0, 162.1 (d, *J* = 250.6 Hz), 162.9, 171.1; HRMS (ESI-TOF) *m/z* calculated for C₁₇H₁₉FN₂NaO₄⁺ ([M+Na]⁺): 357.1221, Found: 357.1232.

Ethyl 1-(4-chlorophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



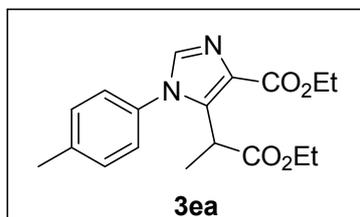
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 85.2 mg, 81 %, isolated as a light yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.19 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.44 (d, *J* = 7.2 Hz, 3H), 4.03 (q, *J* = 7.2 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 4.38 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.54 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.9, 14.3, 15.8, 35.6, 60.5, 61.1, 128.1 (2C), 129.8, 129.9, 133.3, 135.9, 136.9, 138.8, 162.8, 171.1; **HRMS** (ESI-TOF) *m/z* calculated for C₁₇H₂₀ClN₂O₄⁺ ([M+H]⁺): 351.1106, Found: 351.1115.

Ethyl 1-(4-bromophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



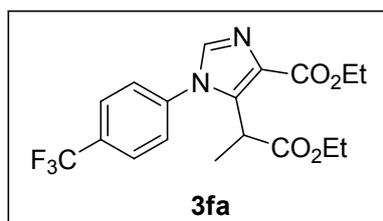
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 92.5 mg, 78 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.43 (d, *J* = 7.2 Hz, 3H), 4.02 (q, *J* = 7.1 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 4.39 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.21 (d, *J* = 7.7 Hz, 2H), 7.53 (s, 1H), 7.67 (d, *J* = 7.7 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 14.3, 15.8, 35.7, 60.6, 61.2, 124.1, 128.4 (2C), 129.9, 133.0 (2C), 133.9, 136.9, 138.9, 162.9, 171.1; **HRMS** (ESI-TOF) *m/z* calculated for C₁₇H₁₉BrN₂NaO₄⁺ ([M+Na]⁺): 417.0420, Found: 417.0429.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(p-tolyl)-1H-imidazole-4-carboxylate



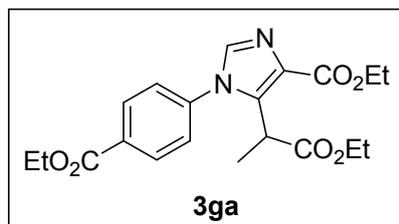
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 92.2 mg, 93 %, isolated as a light yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.2 Hz, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.44 (d, *J* = 7.2 Hz, 3H), 2.45 (s, 3H), 4.02 (q, *J* = 7.2 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 4.39 (dq, *J* = 7.8, 7.2 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.53 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.9, 14.2, 15.7, 21.0, 35.5, 60.3, 60.9, 126.5 (2C), 129.3, 130.2 (2C), 132.2, 137.0, 139.1, 139.9, 162.9, 171.2; **HRMS** (ESI-TOF) *m/z* calculated for C₁₈H₂₃N₂O₄⁺ ([M+H]⁺): 331.1652, Found: 331.1660.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-(trifluoromethyl)phenyl)-1H-imidazole-4-carboxylate



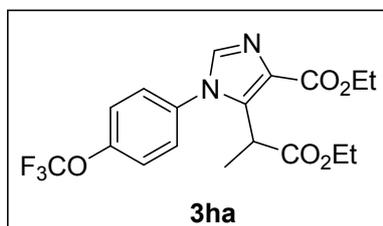
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 86.5 mg, 75 %, isolated as a light yellow liquid; **¹H NMR** (400 MHz, CDCl₃) δ 1.19 (t, *J* = 7.2 Hz, 3H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.47 (d, *J* = 7.2 Hz, 3H), 4.02 (q, *J* = 7.2 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 4.40 (dq, *J* = 8.4, 7.2 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.57 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 14.3, 15.8, 35.7, 60.6, 61.2, 123.2 (q, *J* = 270.3 Hz), 127.0 (q, *J* = 3.5 Hz), 127.3 (2C), 130.1, 132.0 (q, *J* = 33.0 Hz), 136.7, 138.0, 138.7, 162.8, 171.0; **HRMS** (ESI-TOF) *m/z* calculated for C₁₈H₂₀F₃N₂O₄⁺ ([M+H]⁺): 385.1370, Found: 385.1381.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-(ethoxycarbonyl)phenyl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 65.3 mg, 56 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.19 (t, *J* = 7.0 Hz, 3H), 1.42 (dt, *J* = 21.1, 6.8 Hz, 9H), 4.05 (dd, *J* = 14.4, 7.2 Hz, 1H), 4.09 (dd, *J* = 13.8, 6.8 Hz, 2H), 4.33–4.41 (m, 2H), 4.44 (dd, *J* = 14.1, 7.0 Hz, 2H), 7.42 (d, *J* = 7.9 Hz, 2H), 7.59 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 14.2, 14.3, 15.8, 35.6, 60.6, 61.2, 61.5, 126.7 (2C), 130.0, 131.1 (2C), 131.8, 136.8, 138.5, 138.8, 162.8, 165.0, 171.0; **HRMS** (ESI-TOF) *m/z* calculated for C₂₀H₂₅N₂O₆⁺ ([M+H]⁺): 389.1707, Found: 389.1717.

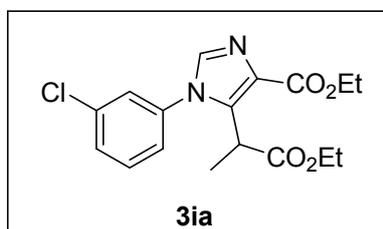
Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-(trifluoromethoxy)phenyl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 102.1 mg, 85 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.19 (t, *J* = 7.1 Hz, 3H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.46 (d, *J* = 7.2 Hz, 3H), 4.03 (q, *J* = 7.2 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 4.39 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.41 (s, 4H), 7.56 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.9, 14.2, 15.8, 35.6, 60.5, 61.1, 120.1 (q, *J* = 258.8 Hz), 122.0 (2C), 128.5 (2C), 129.8, 133.2, 136.9, 138.9,

149.8, 162.8, 171.0; **HRMS** (ESI-TOF) m/z calculated for $C_{18}H_{19}F_3N_2NaO_5^+([M+Na]^+)$: 423.1138, Found: 423.1154.

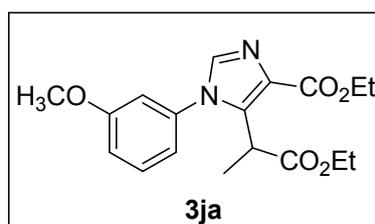
Ethyl 1-(3-chlorophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 76.8 mg, 73 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.20 (t, $J = 7.2$ Hz, 3H), 1.41 (t, $J = 7.2$ Hz, 3H), 1.45 (d, $J = 7.2$ Hz, 3H), 4.06 (q, $J = 7.2$ Hz, 1H), 4.11 (q, $J = 7.2$ Hz, 2H), 4.39 (dq, $J = 7.2, 6.6$ Hz, 2H), 7.25 (d, $J = 7.8$ Hz, 1H), 7.36 (s, 1H), 7.49 (t, $J = 7.8$ Hz, 1H), 7.53 (s, 1H), 7.55 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 14.2, 15.8, 35.6, 60.5, 61.1, 125.0, 127.1, 129.8, 130.0, 130.7, 135.4, 135.9, 136.8, 138.8, 162.8, 171.0; **HRMS** (ESI-TOF) m/z calculated for $C_{17}H_{20}ClN_2O_4^+([M+H]^+)$: 351.1106, Found: 351.1116.

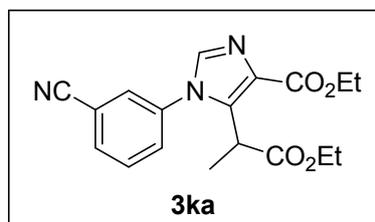
E

ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(3-methoxyphenyl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 90.4 mg, 87 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, $J = 7.1$ Hz, 3H), 1.40 (t, $J = 7.1$ Hz, 3H), 1.46 (d, $J = 7.2$ Hz, 3H), 3.85 (s, 3H), 4.05 (q, $J = 7.2$ Hz, 1H), 4.10 (q, $J = 7.0$ Hz, 2H), 4.38 (dq, $J = 7.2, 7.1$ Hz, 2H), 6.85 (s, 1H), 6.90 (d, $J = 7.7$ Hz, 1H), 7.06 (d, $J = 8.3$ Hz, 1H), 7.43 (t, $J = 8.1$ Hz, 1H), 7.56 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.9, 14.2, 15.7, 35.5, 55.4, 60.3, 60.9, 112.6, 115.1, 118.6, 129.4, 130.4, 135.8, 136.8, 138.9, 160.3, 162.9, 171.2; **HRMS** (ESI-TOF) m/z calculated for $C_{18}H_{23}N_2O_5^+([M+H]^+)$: 347.1601, Found: 347.1608.

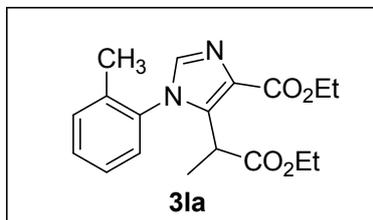
Ethyl 1-(3-cyanophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 73.7 mg, 72 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.21 (t, $J = 7.1$ Hz, 3H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.44 (d, $J = 7.2$ Hz, 3H), 4.05 (q, $J = 7.1$ Hz, 1H), 4.11 (q, $J = 7.0$ Hz, 2H), 4.39 (dq, $J = 7.2, 7.1$ Hz, 2H), 7.56 (s, 1H), 7.62 (d, $J = 8.0$ Hz, 1H), 7.67 (s, 1H), 7.71 (t, $J = 7.9$ Hz,

1H), 7.86 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 13.9, 14.1, 15.7, 35.5, 60.6, 61.2, 114.1, 116.7, 130.1, 130.2, 130.8, 131.2, 133.3, 135.8, 136.7, 138.5, 162.6, 170.8; HRMS (ESI-TOF) m/z calculated for $\text{C}_{18}\text{H}_{19}\text{N}_3\text{NaO}_4^+$ ($[\text{M}+\text{Na}]^+$): 364.1268, Found: 364.1259.

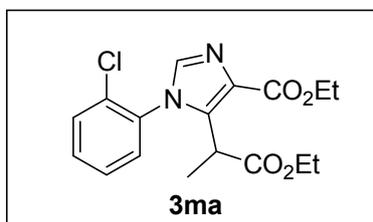
Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(o-tolyl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 84.2 mg, 85 %, isolated as a light yellow liquid, mixture of diastereoisomers; ^1H NMR (600 MHz, CDCl_3) δ 1.17 (t, $J = 7.2$ Hz, 3H), 1.40 (d, $J = 6.6$ Hz, 4.8H), 1.46 (d, $J = 7.2$ Hz, 1.2H), 2.13 (d, $J = 10.8$ Hz, 3H), 3.58 (q, $J = 7.2$ Hz, 0.6H), 3.68 (q, $J = 7.2$ Hz, 0.4H), 4.05–4.14 (m, 2H), 4.33–4.44 (m, 2H), 7.17 (d, $J = 7.8$ Hz, 0.6H), 7.26 (d, $J = 7.2$ Hz, 0.4H), 7.34 (t, $J = 7.2$ Hz, 1H), 7.40 (d, $J = 6.6$ Hz, 1H), 7.44–7.48 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 13.9 (d, $J = 9.8$ Hz), 14.3, 15.6 (d, $J = 4.7$ Hz), 17.0, 17.2, 35.6 (d, $J = 20.1$ Hz), 60.4, 60.9, 127.0 (d, $J = 5.7$ Hz), 127.8, 128.4, 129.0, 129.2, 130.1, 130.3, 131.3 (d, $J = 11.5$ Hz), 133.6 (d, $J = 10.7$ Hz), 135.7, 136.4, 136.6, 136.8, 139.1, 139.3, 162.9, 171.0; HRMS (ESI-TOF) m/z calculated for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_4^+$ ($[\text{M}+\text{H}]^+$): 331.1652, Found: 331.1660.

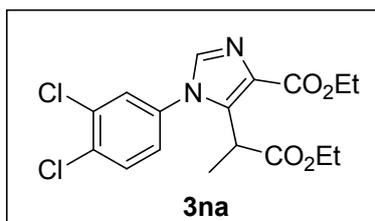
(d, $J = 24.2$ Hz)

Ethyl 1-(2-chlorophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



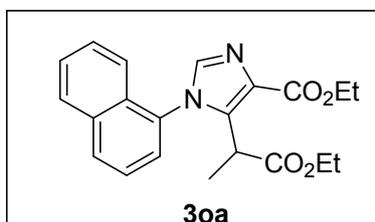
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 80.0 mg, 76 %, isolated as a light yellow liquid, mixture of diastereoisomers; ^1H NMR (600 MHz, CDCl_3) δ 1.18 (t, $J = 6.6$ Hz, 3H), 1.35 (d, $J = 7.2$ Hz, 1.5H), 1.41 (s, 3H), 1.51 (d, $J = 6.6$ Hz, 1.5H), 3.58 (q, $J = 7.2, 6.6$ Hz, 0.5H), 4.04 (q, $J = 7.2, 6.6$ Hz, 0.5H), 4.09 (q, $J = 6.6, 6.0$ Hz, 2H), 4.38–4.44 (m, 2H), 7.35 (d, $J = 7.8$ Hz, 0.5H), 7.40 (d, $J = 7.8$ Hz, 0.5H), 7.42–7.52 (m, 3H), 7.61 (t, $J = 7.2$ Hz, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 14.0 (d, $J = 12.4$ Hz), 14.3, 15.3 (d, $J = 13.0$ Hz), 35.7 (d, $J = 15.9$ Hz), 60.5, 61.0 (d, $J = 7.2$ Hz), 127.7, 127.9, 129.2, 129.5, 129.6, 130.0, 130.7 (d, $J = 9.4$ Hz), 131.5, 132.4, 132.6, 132.7, 132.9, 136.9, 137.3, 138.9, 139.2, 162.8, 163.0, 170.9, 171.2; HRMS (ESI-TOF) m/z calculated for $\text{C}_{17}\text{H}_{20}\text{ClN}_2\text{O}_4^+$ ($[\text{M}+\text{H}]^+$): 351.1106, Found: 351.1114.

Ethyl 1-(3,4-dichlorophenyl)-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



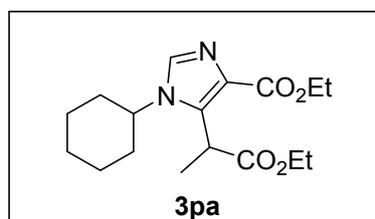
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 95.9 mg, 83 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.20 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.44 (d, *J* = 7.2 Hz, 3H), 4.07 (dd, *J* = 14.1, 6.7 Hz, 1H), 4.11 (dd, *J* = 14.0, 6.9 Hz, 2H), 4.38 (dq, *J* = 7.2, 7.1 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 1H), 7.48 (s, 1H), 7.53 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 14.2, 15.8, 35.6, 60.6, 61.3, 126.1, 128.8, 130.1, 131.4, 133.9, 134.1, 134.6, 136.8, 138.7, 162.8, 170.9; **HRMS** (ESI-TOF) *m/z* calculated for C₁₇H₁₉Cl₂N₂O₄⁺ ([M+H]⁺): 385.0716, Found: 385.0724.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(naphthalen-1-yl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 83.5 mg, 76 %, isolated as a yellow liquid, mixture of diastereoisomers; **¹H NMR** (600 MHz, CDCl₃) δ 1.12 (t, *J* = 7.2 Hz, 1.2H), 1.18 (t, *J* = 7.2 Hz, 1.8H), 1.37 (d, *J* = 7.2 Hz, 1.8H), 1.40 (d, *J* = 7.2 Hz, 1.2H), 1.42–1.45 (m, 3H), 3.61 (q, *J* = 7.2 Hz, 0.6H), 3.72 (q, *J* = 7.2 Hz, 0.4H), 3.83–3.89 (m, 0.4H), 3.95–3.98 (m, 0.4H), 4.06–4.09 (m, 1.2H), 4.37–4.48 (m, 2H), 7.29 (d, *J* = 8.4 Hz, 0.4H), 7.45 (q, *J* = 8.4 Hz, 1.2H), 7.51–7.55 (m, 1.4H), 7.59–7.64 (m, 3H), 7.98 (q, *J* = 7.8 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.8 (d, *J* = 6.3 Hz), 14.2, 15.8 (d, *J* = 8.6 Hz), 35.6 (d, *J* = 23.2 Hz), 60.4, 60.8, 121.6, 122.3, 124.9 (d, *J* = 11.8 Hz), 125.6, 126.1, 127.1 (d, *J* = 13.6 Hz), 127.8 (d, *J* = 14.5 Hz), 128.0, 128.2, 129.1 (d, *J* = 13.4 Hz), 130.3, 130.4, 130.5, 130.6, 130.7, 130.8, 133.9, 137.7 (d, *J* = 5.9 Hz), 140.2, 140.3, 162.8, 170.8 (d, *J* = 16.2 Hz); **HRMS** (ESI-TOF) *m/z* calculated for C₂₁H₂₂N₂NaO₄⁺ ([M+Na]⁺): 389.1472, Found: 389.1467.

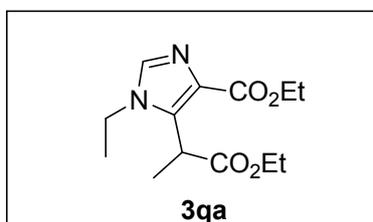
Ethyl 1-cyclohexyl-5-(1-ethoxy-1-oxopropan-2-yl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 79.3 mg, 82 %, isolated as a light yellow liquid; **¹H NMR** (400 MHz, CDCl₃) δ 1.21 (t, *J* = 7.1 Hz, 3H), 1.24–1.29 (m, 1H), 1.29–1.46 (m, 5H), 1.51 (d, *J* = 7.3 Hz, 3H), 1.66 (qd, *J* = 12.4, 3.3 Hz, 2H), 1.77 (d, *J* = 12.7 Hz, 1H), 1.93 (d, *J* = 14.0 Hz, 2H), 1.99 (d, *J* = 12.6 Hz, 1H), 2.06 (d, *J* = 12.7

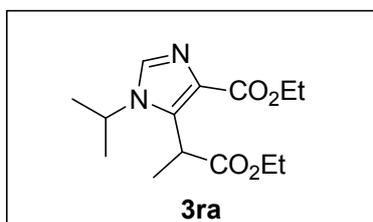
Hz, 1H), 3.75 (tt, $J = 12.0, 3.5$ Hz, 1H), 4.15 (qq, $J = 10.8, 7.1$ Hz, 2H), 4.36 (dq, $J = 7.3, 7.1$ Hz, 2H), 4.85 (q, $J = 7.2$ Hz, 1H), 7.54 (s, 1H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 13.9, 14.2, 16.0, 24.9, 25.6, 34.1, 34.8, 35.0, 55.4, 60.2, 61.2, 128.4, 134.4, 136.8, 163.4, 172.1; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{17}\text{H}_{26}\text{N}_2\text{NaO}_4^+$ ($[\text{M}+\text{Na}]^+$): 345.1785, Found: 345.1790.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-ethyl-1H-imidazole-4-carboxylate



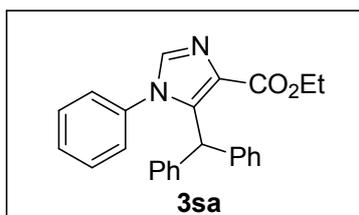
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 69.2 mg, 86 %, isolated as a light yellow liquid; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 1.19 (t, $J = 7.1$ Hz, 3H), 1.39 (t, $J = 7.1$ Hz, 3H), 1.45 (t, $J = 7.3$ Hz, 3H), 1.53 (d, $J = 7.3$ Hz, 3H), 3.95 (q, $J = 7.3$ Hz, 2H), 4.15 (q, $J = 7.1$ Hz, 2H), 4.35 (dq, $J = 7.3, 7.1$ Hz, 2H), 4.60 (q, $J = 7.3$ Hz, 1H), 7.49 (s, 1H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 13.9, 14.2, 15.7, 16.0, 35.0, 40.1, 60.2, 61.1, 129.2, 136.1, 137.3, 163.2, 171.7; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{13}\text{H}_{20}\text{N}_2\text{NaO}_4^+$ ($[\text{M}+\text{Na}]^+$): 291.1315, Found: 291.1317.

Ethyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-isopropyl-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 64.4 mg, 76 %, isolated as a light yellow liquid; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.21 (t, $J = 7.1$ Hz, 3H), 1.39 (t, $J = 7.1$ Hz, 3H), 1.48 (d, $J = 6.7$ Hz, 3H), 1.51 (d, $J = 4.8$ Hz, 3H), 1.52 (d, $J = 5.4$ Hz, 3H), 4.08–4.21 (m, 2H), 4.25 (dd, $J = 13.4, 6.7$ Hz, 1H), 4.35 (dq, $J = 7.1, 6.7$ Hz, 2H), 4.84 (q, $J = 7.2$ Hz, 1H), 7.58 (s, 1H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 14.0, 14.3, 15.9, 23.4, 24.0, 34.5, 47.6, 60.2, 61.2, 128.5, 133.9, 136.8, 163.4, 172.0; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{14}\text{H}_{22}\text{N}_2\text{NaO}_4^+$ ($[\text{M}+\text{Na}]^+$): 305.1472, Found: 305.1450.

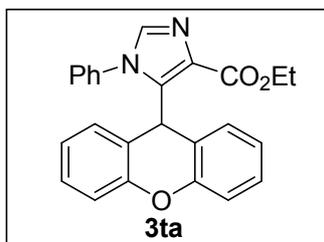
Ethyl 5-benzhydryl-1-phenyl-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 86.1 mg, 75 %, isolated as a yellow liquid; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 1.24 (t, $J = 7.1$ Hz, 3H), 4.20 (q,

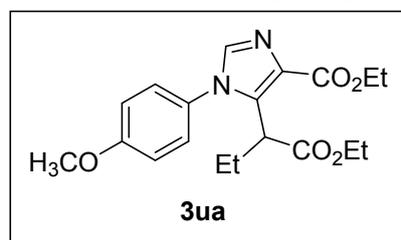
$J = 7.1$ Hz, 2H), 6.29 (s, 1H), 6.89 (d, $J = 7.9$ Hz, 2H), 6.95–7.06 (m, 4H), 7.11–7.19 (m, 6H), 7.22 (t, $J = 7.7$ Hz, 2H), 7.33 (t, $J = 7.4$ Hz, 1H), 7.53 (s, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 14.1, 46.2, 60.3, 126.4 (2C), 127.3 (2C), 127.9 (4C), 128.9, 129.0 (4C), 129.1, 130.7, 135.4, 138.0, 140.0, 140.2, 162.9; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{25}\text{H}_{22}\text{N}_2\text{NaO}_2^+$ ($[\text{M}+\text{Na}]^+$): 405.1573, Found: 405.1587.

Ethyl 1-phenyl-5-(9H-xanthen-9-yl)-1H-imidazole-4-carboxylate



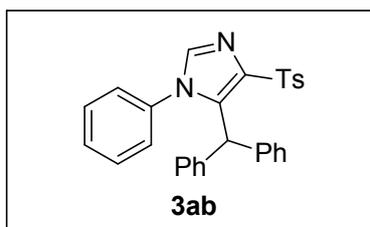
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 76.1 mg, 64 %, isolated as a yellow solid; m.p. 144–146 °C; ^1H NMR (600 MHz, CDCl_3) δ 1.49 (t, $J = 6.0$ Hz, 3H), 4.51 (q, $J = 6.0$ Hz, 2H), 6.25 (s, 2H), 6.67 (d, $J = 7.8$ Hz, 2H), 6.85 (s, 1H), 6.94 (t, $J = 7.2$ Hz, 2H), 6.99 (t, $J = 7.2$ Hz, 2H), 7.05–7.13 (m, 4H), 7.23 (t, $J = 7.2$ Hz, 1H), 7.34 (s, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 14.4, 32.3, 60.7, 116.0 (2C), 119.9, 122.9 (2C), 127.0 (2C), 128.3 (2C), 128.4, 128.8, 129.4, 130.0, 134.6, 138.4, 142.5, 150.2, 163.8; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{NaO}_3^+$ ($[\text{M}+\text{Na}]^+$): 419.1366, Found: 419.1374.

Ethyl 5-(1-ethoxy-1-oxobutan-2-yl)-1-(4-methoxyphenyl)-1H-imidazole-4-carboxylate



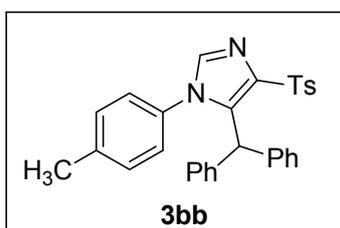
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 85.4 mg, 79 %, isolated as a light yellow liquid; ^1H NMR (600 MHz, CDCl_3) δ 0.68 (t, $J = 7.5$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H), 1.40 (t, $J = 7.1$ Hz, 3H), 1.67–1.97 (m, 1H), 2.04–2.25 (m, 1H), 3.88 (d, $J = 6.1$ Hz, 3H), 3.90 (dd, $J = 9.8, 5.5$ Hz, 1H), 4.08 (dq, $J = 7.2, 6.6$ Hz, 2H), 4.39 (dq, $J = 8.4, 7.2$ Hz, 2H), 7.00 (d, $J = 8.7$ Hz, 2H), 7.21 (d, $J = 8.7$ Hz, 2H), 7.53 (s, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 12.0, 14.0, 14.2, 23.1, 42.6, 55.5, 60.3, 60.8, 114.6 (2C), 127.5, 128.3 (2C), 129.7, 137.5, 137.9, 160.3, 163.0, 170.9; **HRMS** (ESI-TOF) m/z calculated for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{NaO}_5^+$ ($[\text{M}+\text{Na}]^+$): 383.1577, Found: 383.1586.

5-benzhydryl-1-phenyl-4-tosyl-1H-imidazole



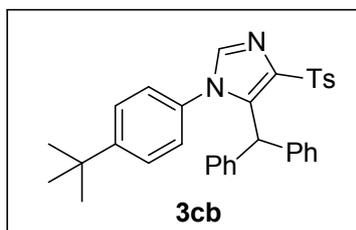
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 90.6 mg, 65 %, isolated as a yellow solid; m.p. 194-195 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.37 (s, 3H), 6.71 (d, *J* = 8.0 Hz, 2H), 6.78 (s, 1H), 6.88 (d, *J* = 7.5 Hz, 4H), 7.05–7.13 (m, 6H), 7.15 (t, *J* = 7.6 Hz, 4H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.47 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 21.4, 45.3, 126.5 (2C), 127.3 (2C), 127.7 (2C), 128.0 (4C), 128.8 (2C), 129.1, 129.2 (4C), 129.3, 135.2, 137.1, 138.3, 138.5, 139.1, 139.2, 143.6; HRMS (ESI-TOF) *m/z* calculated for C₂₉H₂₄N₂NaO₂S⁺ ([M+Na]⁺): 487.1451, Found: 487.1461.

6-benzhydryl-1-(p-tolyl)-4-tosyl-1H-imidazole



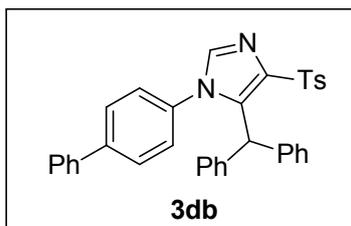
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 111.9 mg, 78 %, isolated as a white solid; m.p. 204-206 °C; ¹H NMR (600 MHz, CDCl₃) δ 2.28 (s, 3H), 2.36 (s, 3H), 6.59 (d, *J* = 8.2 Hz, 2H), 6.72 (s, 1H), 6.89 (t, *J* = 7.7 Hz, 6H), 7.05–7.21 (m, 8H), 7.45 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 20.9, 21.4, 45.3, 126.5 (2C), 127.1 (2C), 127.8 (2C), 127.9 (4C), 129.2, 129.3 (4C), 129.4 (2C), 132.6, 137.2, 138.3, 138.4, 139.2, 139.3, 143.6; HRMS (ESI-TOF) *m/z* calculated for C₃₀H₂₆N₂NaO₂S⁺ ([M+Na]⁺): 501.1607, Found: 501.1614.

5-benzhydryl-1-(4-(tert-butyl)phenyl)-4-tosyl-1H-imidazole



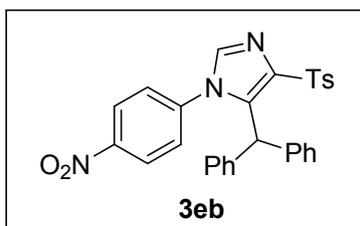
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 118.7 mg, 76 %, isolated as a white solid; m.p. 228-229 °C; ¹H NMR (600 MHz, CDCl₃) δ 1.24 (s, 9H), 2.36 (s, 3H), 6.63 (d, *J* = 8.5 Hz, 2H), 6.82 (s, 1H), 6.87 (d, *J* = 7.4 Hz, 4H), 7.06 (d, *J* = 8.6 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 4H), 7.14 (dd, *J* = 11.9, 4.5 Hz, 4H), 7.46 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 21.4, 31.0, 34.5, 45.3, 125.7 (2C), 126.4 (2C), 126.8 (2C), 127.7 (2C), 127.9 (4C), 129.2 (4C), 129.3, 132.5, 137.2, 138.3, 138.4, 139.2, 139.3, 143.6, 152.4; HRMS (ESI-TOF) *m/z* calculated for C₃₃H₃₂N₂NaO₂S⁺ ([M+Na]⁺): 543.2077, Found: 543.2090.

1-([1,1'-biphenyl]-4-yl)-5-benzhydryl-4-tosyl-1H-imidazole



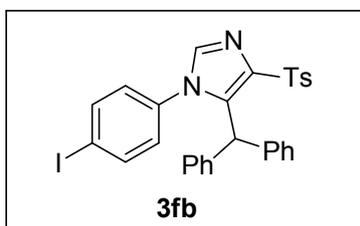
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 111.9 mg, 69 %, isolated as a yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 2.29 (s, 3H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.78 (s, 1H), 6.83 (d, *J* = 7.5 Hz, 4H), 7.03 (t, *J* = 7.5 Hz, 4H), 7.08 (dd, *J* = 12.4, 7.5 Hz, 4H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.29 (t, *J* = 7.1 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 2H), 7.43 (s, 1H), 7.53 (d, *J* = 8.2 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 21.5, 45.3, 126.6 (2C), 127.0 (2C), 127.4 (2C), 127.7 (2C), 127.8 (2C), 128.0 (4C), 128.0, 128.9 (2C), 129.3 (4C), 129.4, 134.3, 137.3, 138.3, 138.6, 139.2, 139.3, 139.4, 142.1, 143.7; **HRMS** (ESI-TOF) *m/z* calculated for C₃₅H₂₈N₂NaO₂S⁺ ([M+Na]⁺): 563.1764, Found: 563.1781.

6-benzhydryl-1-(4-nitrophenyl)-4-tosyl-1H-imidazole



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 71.9 mg, 47 %, isolated as a brown liquid; **¹H NMR** (600 MHz, CDCl₃) δ 2.38 (s, 3H), 6.85 (d, *J* = 7.6 Hz, 4H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.98 (s, 1H), 7.11 (t, *J* = 7.6 Hz, 4H), 7.17 (dd, *J* = 16.8, 8.0 Hz, 4H), 7.48 (s, 1H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 21.5, 45.0, 123.9 (2C), 126.9 (2C), 127.7 (2C), 128.3 (4C), 128.5 (2C), 129.1 (4C), 129.4, 137.2, 137.9, 138.7, 138.7, 139.4, 140.6, 144.1, 147.5; **HRMS** (ESI-TOF) *m/z* calculated for C₂₉H₂₃N₃NaO₄S⁺ ([M+Na]⁺): 532.1301, Found: 532.1306.

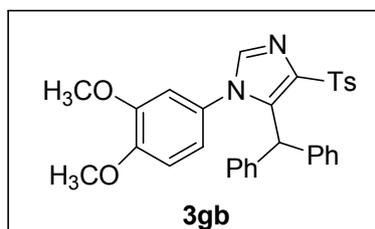
5-benzhydryl-1-(4-iodophenyl)-4-tosyl-1H-imidazole



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 139.9 mg, 79 %, isolated as a light brown solid; m.p. 212-213 °C; **¹H NMR** (600 MHz, CDCl₃) δ 2.37 (s, 3H), 6.42 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 7.7 Hz, 4H), 6.87 (s, 1H), 7.13 (dd, *J* = 14.6, 7.3 Hz, 6H), 7.18 (t, *J* = 7.3 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.43 (s, 1H), 7.60 (d, *J* = 8.1 Hz, 2H); **¹³C NMR** (151 MHz, CDCl₃) δ 21.4, 45.1, 94.8, 126.6 (2C), 127.7 (2C), 128.1 (4C), 129.0 (2C),

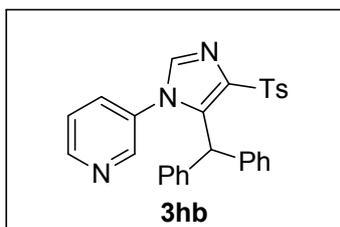
129.1 (4C), 129.3 (2C), 134.9, 137.1, 137.9, 138.1, 138.7, 138.9, 138.9, 143.8; **HRMS** (ESI-TOF) m/z calculated for $C_{29}H_{23}IN_2NaO_2S^+([M+Na]^+)$: 613.0417, Found: 613.0423.

5-benzhydryl-1-(3,4-dimethoxyphenyl)-4-tosyl-1H-imidazole



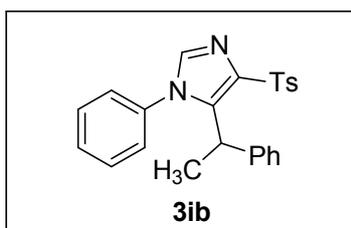
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 91.3 mg, 58 %, isolated as a brown solid; m.p. 155-157 °C; **¹H NMR** (600 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.41 (s, 3H), 3.84 (s, 3H), 6.05 (d, $J = 2.1$ Hz, 1H), 6.42 (dd, $J = 8.6, 2.1$ Hz, 1H), 6.59 (d, $J = 8.5$ Hz, 1H), 6.81 (s, 1H), 6.92 (d, $J = 7.3$ Hz, 4H), 7.16 (dt, $J = 14.5, 3.7$ Hz, 6H), 7.19 (d, $J = 4.5$ Hz, 2H), 7.49 (s, 1H), 7.66 (d, $J = 8.0$ Hz, 2H); **¹³C NMR** (151 MHz, $CDCl_3$) δ 21.4, 45.1, 55.3, 56.0, 110.2, 110.6, 119.5, 126.4, 127.7 (2C), 127.8 (4C), 127.9 (4C), 129.2 (2C), 129.3, 137.2, 138.3, 138.4, 139.1, 139.3, 143.6, 148.5, 149.5; **HRMS** (ESI-TOF) m/z calculated for $C_{31}H_{28}N_2NaO_4S^+([M+Na]^+)$: 547.1662, Found: 547.1662.

3-(5-benzhydryl-4-tosyl-1H-imidazol-1-yl)pyridine



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 90.8 mg, 65 %, isolated as a white solid; m.p. 188-190 °C; **¹H NMR** (600 MHz, $CDCl_3$) δ 2.38 (s, 3H), 6.85 (d, $J = 7.4$ Hz, 4H), 6.89–6.94 (m, 1H), 6.94–6.98 (m, 1H), 6.99 (s, 1H), 7.12 (t, $J = 7.6$ Hz, 4H), 7.14–7.20 (m, 4H), 7.45 (s, 1H), 7.63 (d, $J = 7.6$ Hz, 2H), 8.05 (s, 1H), 8.39–8.49 (m, 1H); **¹³C NMR** (151 MHz, $CDCl_3$) δ 21.5, 45.0, 123.2, 126.8, 127.7 (2C), 128.2 (4C), 129.0 (4C), 129.4 (2C), 132.4, 134.5, 137.4, 137.9, 138.8, 139.1, 139.2, 143.9, 147.8, 149.9; **HRMS** (ESI-TOF) m/z calculated for $C_{28}H_{23}N_3NaO_2S^+([M+Na]^+)$: 488.1403, Found: 488.1419.

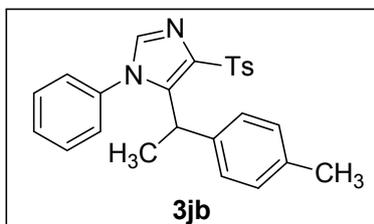
1-phenyl-5-(1-phenylethyl)-4-tosyl-1H-imidazole



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 88.1 mg, 73 %, isolated as a light yellow liquid; **¹H NMR** (600 MHz, $CDCl_3$) δ 1.55 (d, $J = 7.4$ Hz, 3H), 2.43 (s, 3H), 5.29 (q, $J = 7.3$ Hz, 1H), 6.74 (d, $J = 7.6$ Hz, 2H), 6.89 (d, $J = 7.1$ Hz, 2H), 7.07–7.16

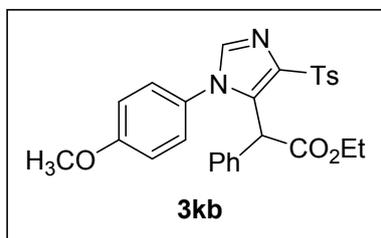
(m, 3H), 7.22 (t, $J = 7.8$ Hz, 2H), 7.32 (d, $J = 8.2$ Hz, 2H), 7.36 (t, $J = 7.6$ Hz, 1H), 7.38 (s, 1H), 7.89 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 17.5, 21.5, 32.9, 126.2, 127.3 (2C), 127.4 (2C), 127.7 (2C), 128.0 (2C), 128.9 (2C), 129.4, 129.5 (2C), 135.0, 137.3, 138.5, 138.8, 140.5, 140.8, 143.8; HRMS (ESI-TOF) m/z calculated for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{NaO}_2\text{S}^+$ ($[\text{M}+\text{Na}]^+$): 425.1294, Found: 425.1305.

1-phenyl-5-(1-(p-tolyl)ethyl)-4-tosyl-1H-imidazole



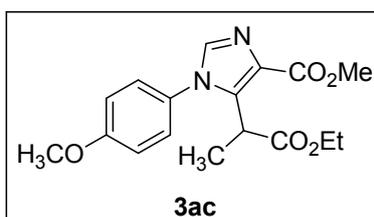
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 77.5 mg, 62 %, isolated as a light yellow liquid; ^1H NMR (600 MHz, CDCl_3) δ 1.52 (d, $J = 7.4$ Hz, 3H), 2.29 (s, 3H), 2.43 (s, 3H), 5.22 (q, $J = 7.2$ Hz, 1H), 6.77 (d, $J = 7.9$ Hz, 4H), 6.88–6.97 (m, 2H), 7.23 (t, $J = 7.8$ Hz, 2H), 7.31 (d, $J = 8.2$ Hz, 2H), 7.36 (d, $J = 7.6$ Hz, 1H), 7.38 (s, 1H), 7.88 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 17.6, 20.8, 21.5, 32.7, 127.2 (2C), 127.5 (2C), 127.8 (2C), 128.6 (2C), 128.8 (2C), 129.4, 129.5 (2C), 135.1, 135.8, 137.3, 137.9, 138.5, 138.9, 140.7, 143.8; HRMS (ESI-TOF) m/z calculated for $\text{C}_{25}\text{H}_{24}\text{N}_2\text{NaO}_2\text{S}^+$ ($[\text{M}+\text{Na}]^+$): 439.1451, Found: 439.1462.

Ethyl 2-(1-(4-methoxyphenyl)-4-tosyl-1H-imidazol-5-yl)-2-phenylacetate



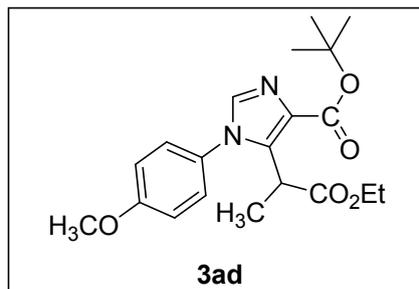
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 115 mg, 78%, isolated as a white solid; m.p. 168–169 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, $J = 6.8$ Hz, 3H), 2.42 (s, 3H), 3.79 (s, 3H), 4.19 (dq, $J = 7.2, 6.8$ Hz, 2H), 6.24 (s, 1H), 6.71 (d, $J = 8.8$ Hz, 2H), 6.80 (d, $J = 8.8$ Hz, 2H), 6.86 (d, $J = 7.2$ Hz, 2H), 7.03–7.19 (m, 3H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.42 (s, 1H), 7.94 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 13.9, 21.5, 46.2, 55.4, 61.6, 113.9 (2C), 126.9, 127.2, 127.7 (2C), 128.0 (2C), 128.7 (2C), 128.7 (2C), 129.5 (2C), 133.7, 134.7, 138.1, 138.4, 139.4, 144.0, 160.2, 169.4; HRMS (ESI-TOF) m/z calculated for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{NaO}_5\text{S}^+$ ($[\text{M}+\text{Na}]^+$): 513.6012, Found: 513.6018.

methyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-methoxyphenyl)-1H-imidazole-4-carboxylate



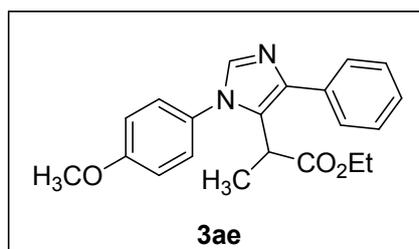
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 67.8 mg, 68 %, isolated as a light yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.42 (d, *J* = 7.0 Hz, 3H), 3.88 (s, 3H), 3.90 (s, 3H), 4.03 (q, *J* = 7.3 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.51 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.0, 15.8, 35.6, 51.5, 55.6, 61.1, 114.8 (2C), 127.4, 128.1 (2C), 129.0, 137.4, 139.6, 160.4, 163.5, 171.3; **HRMS** (ESI-TOF) *m/z* calculated for C₁₇H₂₀N₂NaO₅⁺ ([M+Na]⁺): 355.1264, Found: 355.1266.

tert-butyl 5-(1-ethoxy-1-oxopropan-2-yl)-1-(4-methoxyphenyl)-1H-imidazole-4-carboxylate



Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 84.2 mg, 75 %, isolated as a light yellow liquid; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.1 Hz, 3H), 1.43 (d, *J* = 7.2 Hz, 3H), 1.61 (s, 9H), 3.87 (s, 3H), 4.02 (q, *J* = 7.2 Hz, 1H), 4.04–4.10 (m, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 7.49 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 13.9, 15.7, 28.2, 35.4, 55.4, 60.9, 80.9, 114.6, 126.5 (2C), 128.0, 130.2 (2C), 137.1, 138.4, 160.3, 162.4, 171.4; **HRMS** (ESI-TOF) *m/z* calculated for C₂₀H₂₆N₂NaO₅⁺ ([M+Na]⁺): 397.1734, Found: 397.1743.

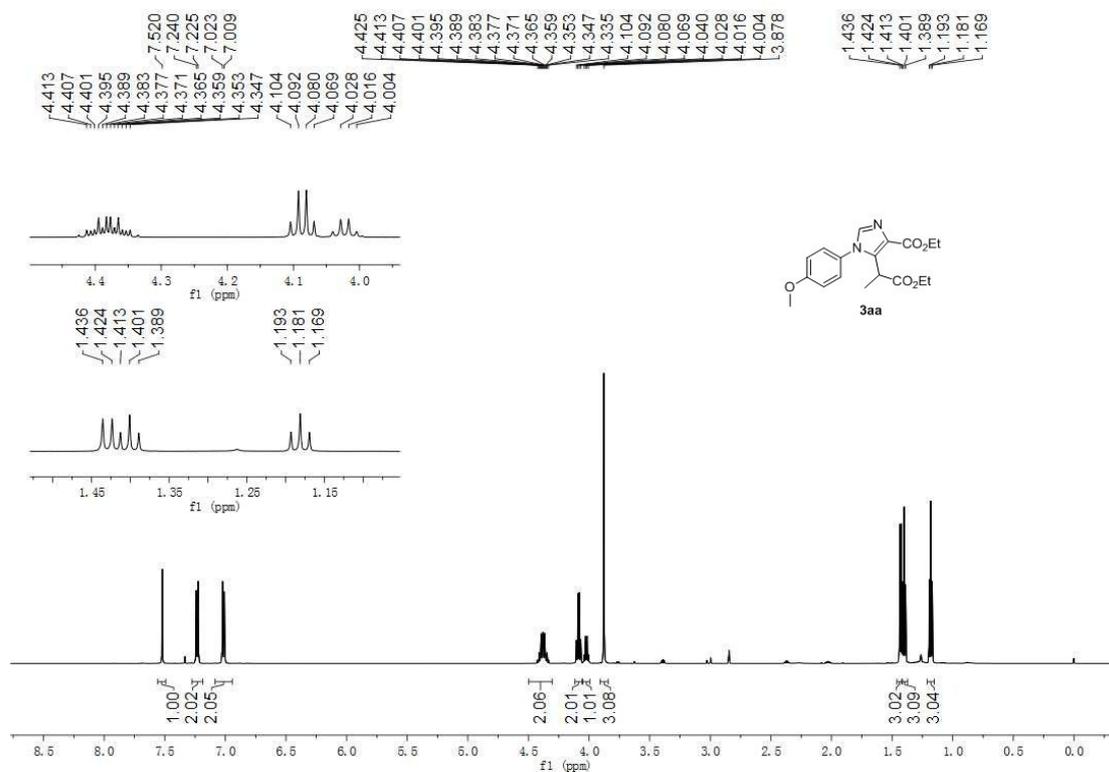
ethyl 2-(1-(4-methoxyphenyl)-4-phenyl-1H-imidazol-5-yl)propanoate



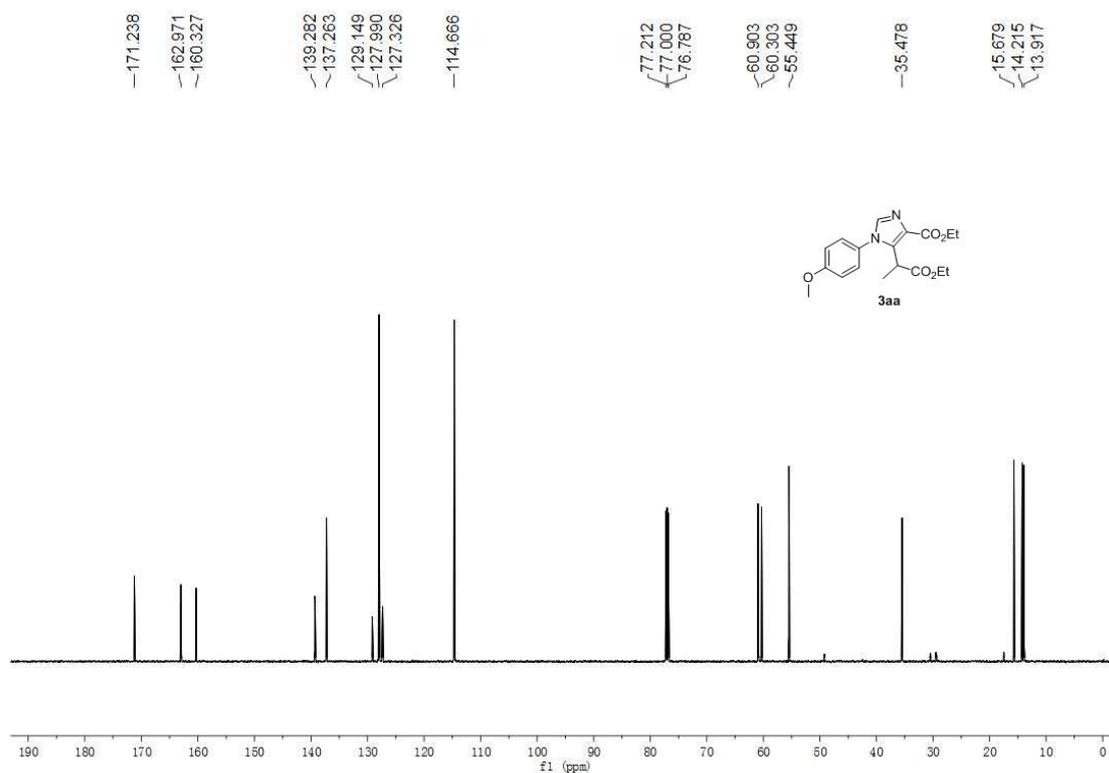
Conditions: 40 °C for 0.5 h. Purification: Flash chromatography (PE/EtOAc, 5:1). Yield: 65.2 mg, 62 %, isolated as a yellow solid; m.p. 87–89 °C; **¹H NMR** (600 MHz, CDCl₃) δ 1.18 (t, *J* = 7.2 Hz, 3H), 1.40 (d, *J* = 7.2 Hz, 3H), 1.42 (t, *J* = 7.2 Hz, 3H), 3.88 (s, 3H), 4.02 (q, *J* = 7.3 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 4.37 (dq, *J* = 7.3, 7.2 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 9.0 Hz, 2H), 7.52 (s, 1H); **¹³C NMR** (151 MHz, CDCl₃) δ 14.1 (d, *J* = 43.3 Hz), 15.7, 35.5, 60.5, 61.1, 116.7 (d, *J* = 23.1 Hz), 128.7, 128.8, 129.6, 130.8, 130.9, 137.1, 139.0, 162.1, 162.9, 163.8, 171.1; **HRMS** (ESI-TOF) *m/z* calculated for C₂₁H₂₃N₂O₃⁺ ([M+H]⁺): 351.1703, Found: 351.1712.

1. Copies of ^1H NMR and ^{13}C NMR spectra of compounds 3

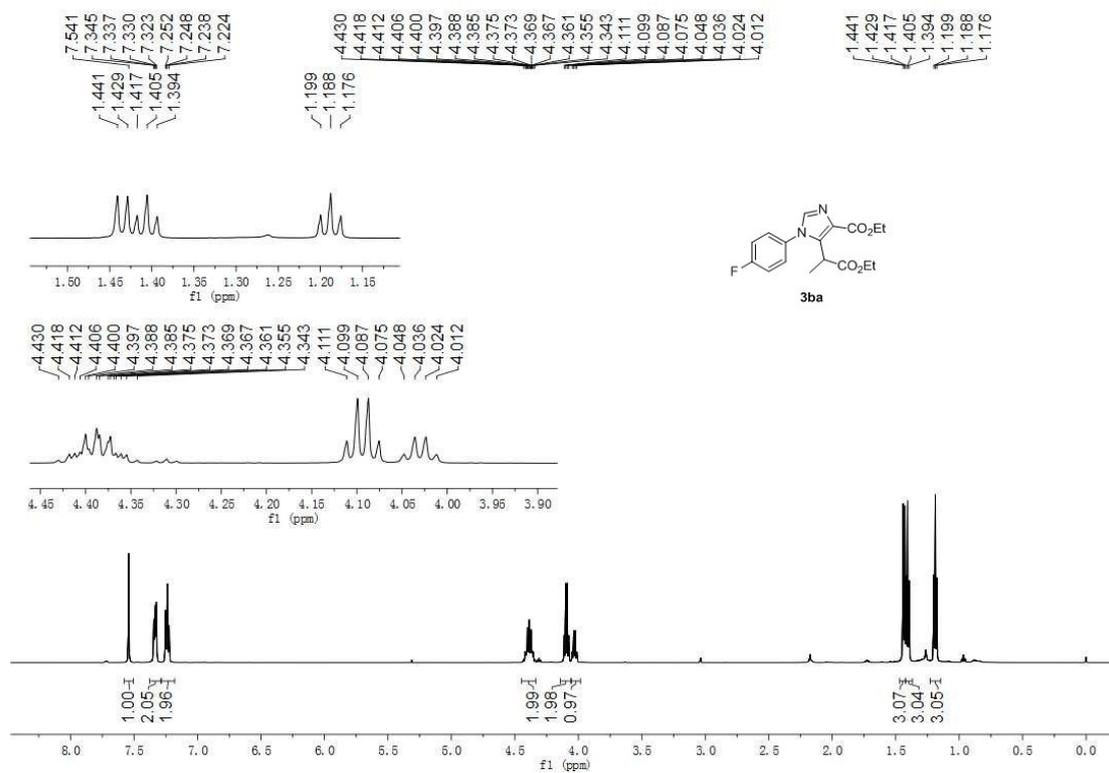
^1H NMR (600 MHz, CDCl_3) for 3aa



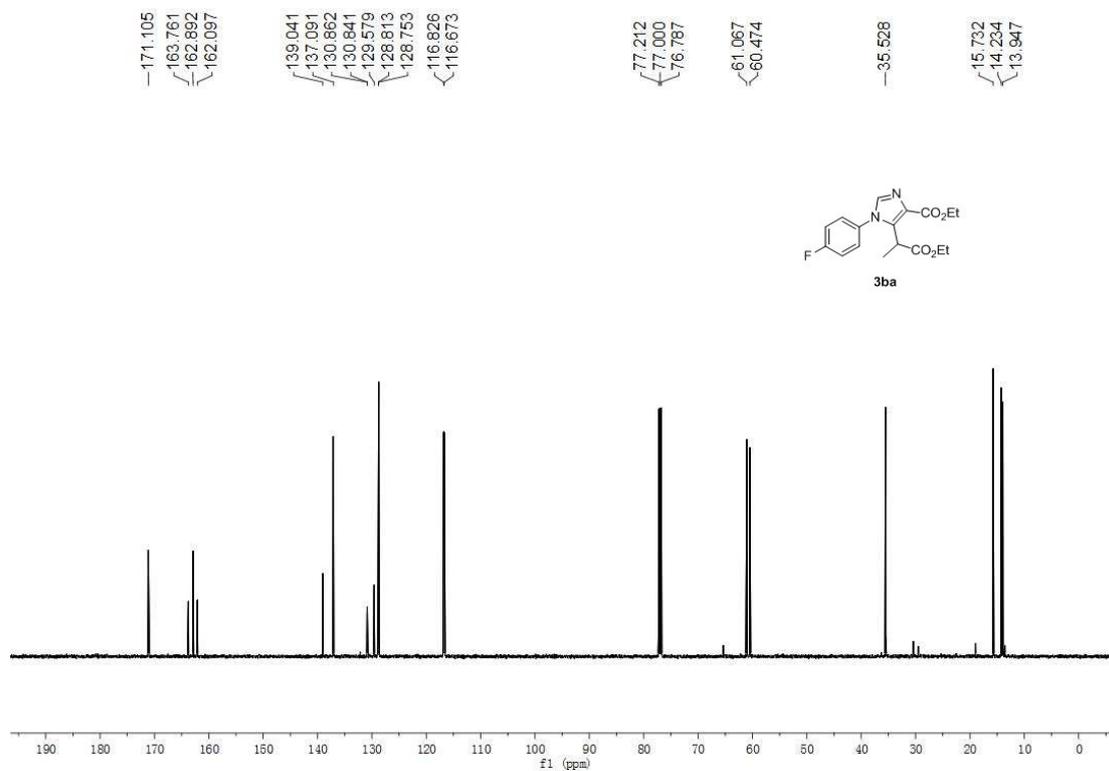
^{13}C NMR (151 MHz, CDCl_3) for 3aa



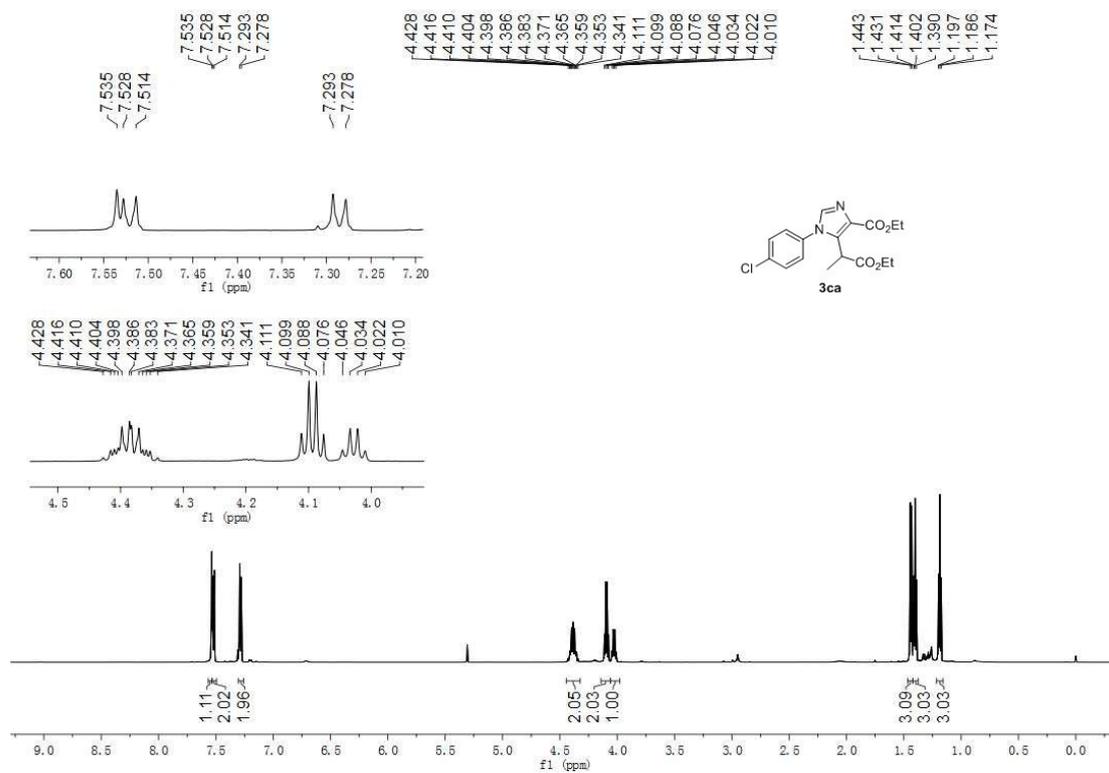
¹H NMR (600 MHz, CDCl₃) for 3ba



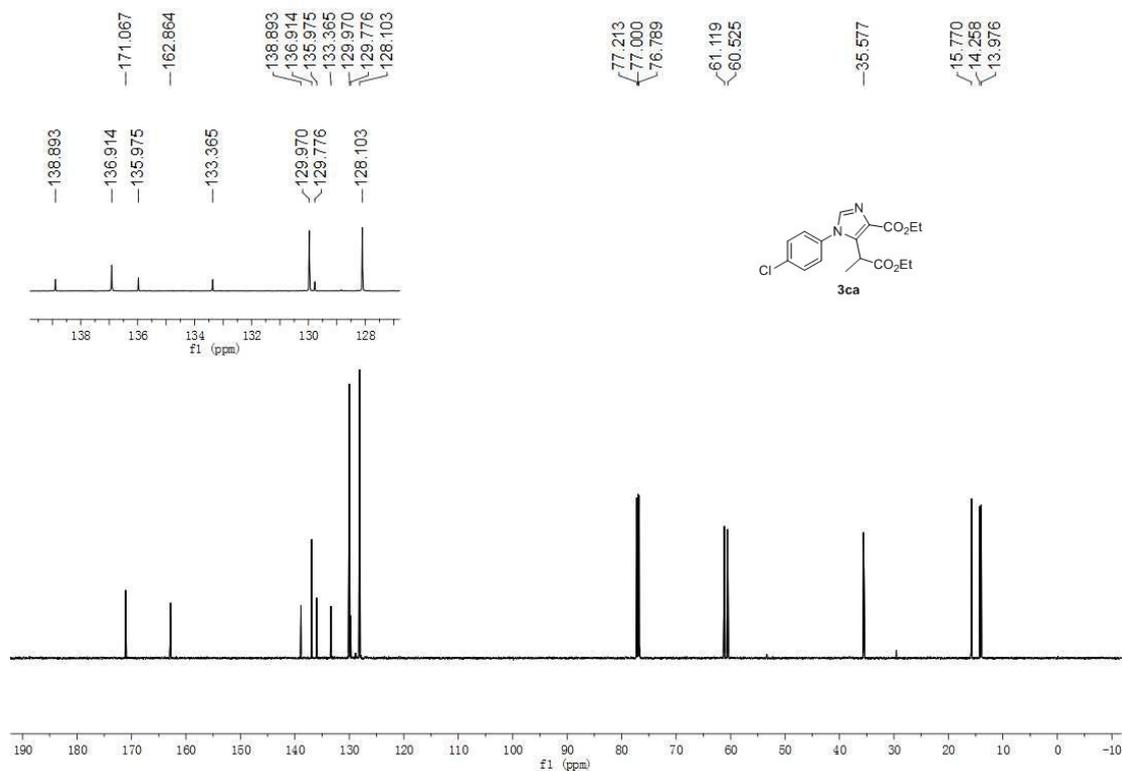
¹³C NMR (151 MHz, CDCl₃) for 3ba



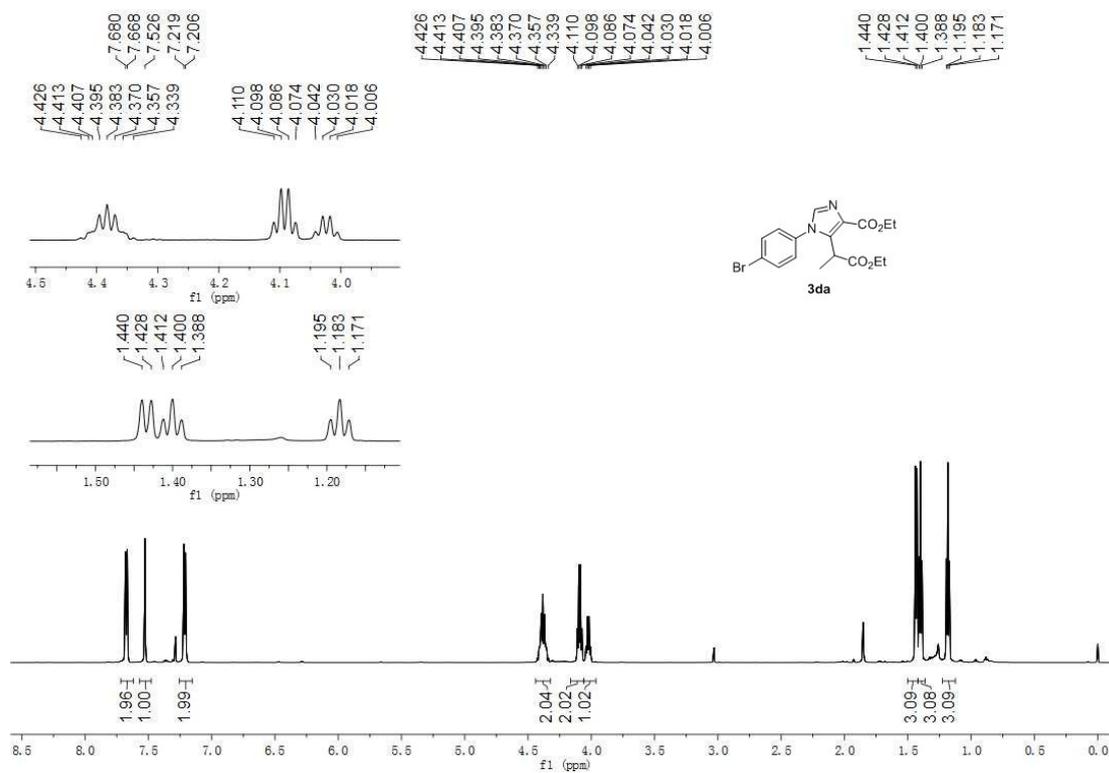
¹H NMR (600 MHz, CDCl₃) for 3ca



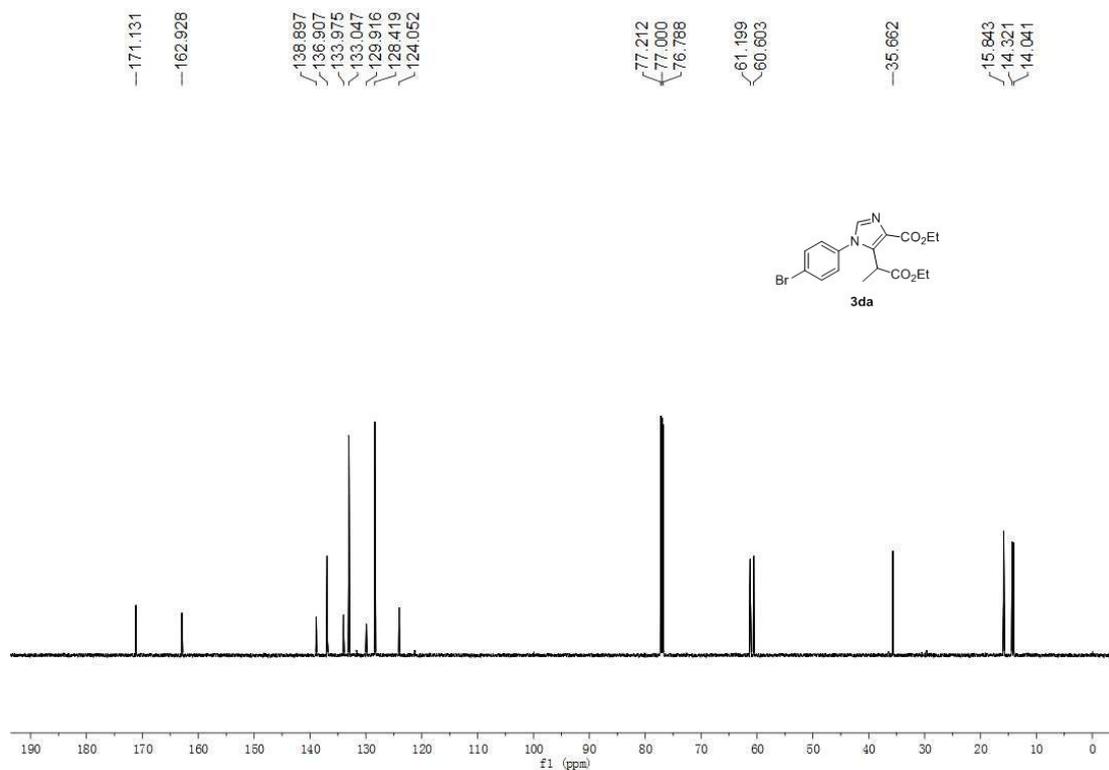
¹³C NMR (151 MHz, CDCl₃) for 3ca



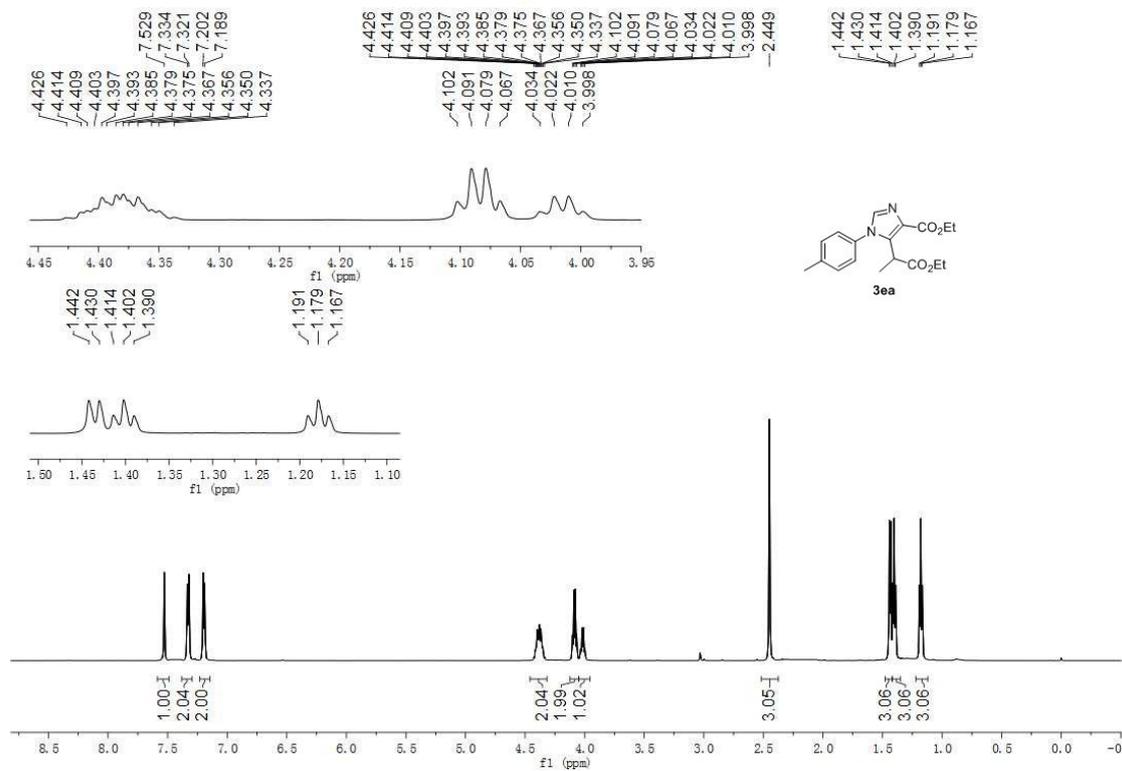
¹H NMR (600 MHz, CDCl₃) for 3da



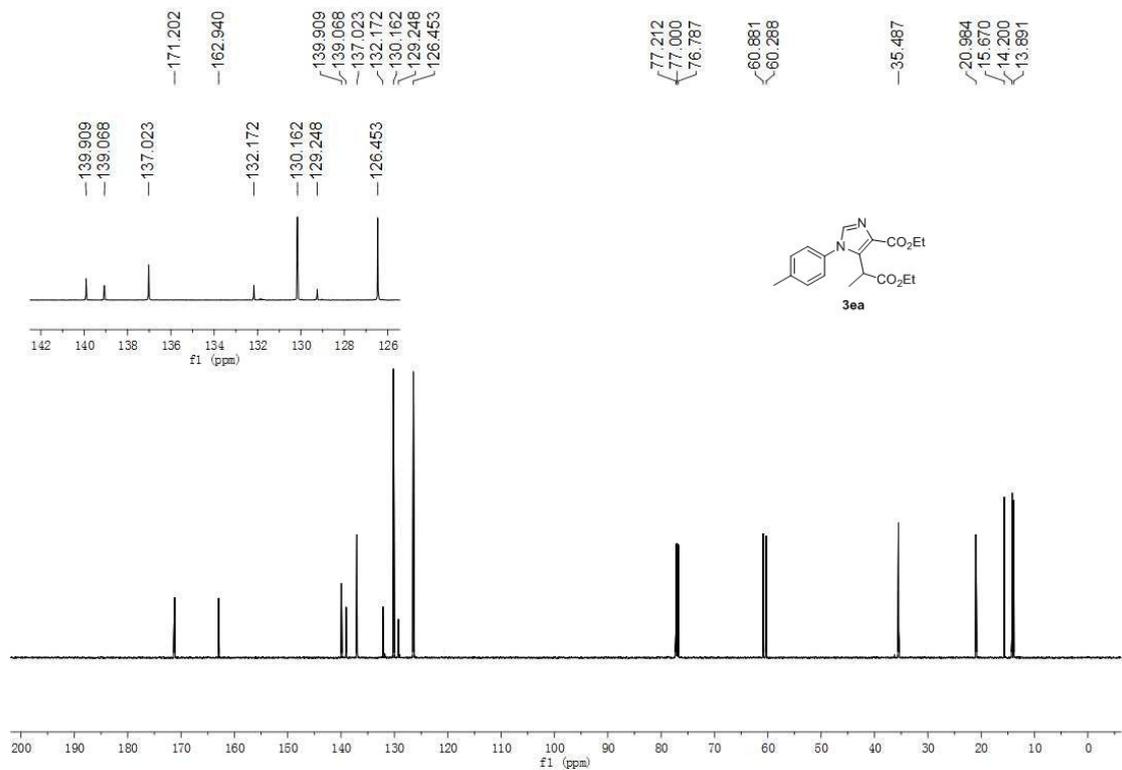
¹³C NMR (151 MHz, CDCl₃) for 3da



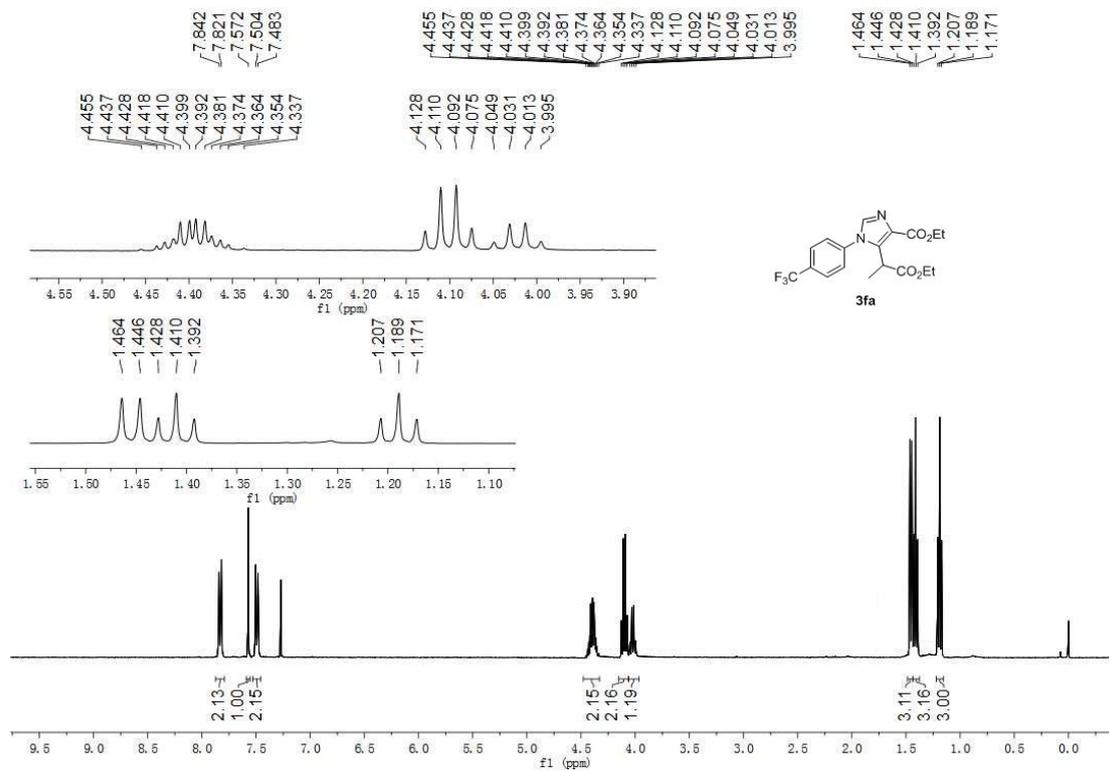
¹H NMR (600 MHz, CDCl₃) for 3ea



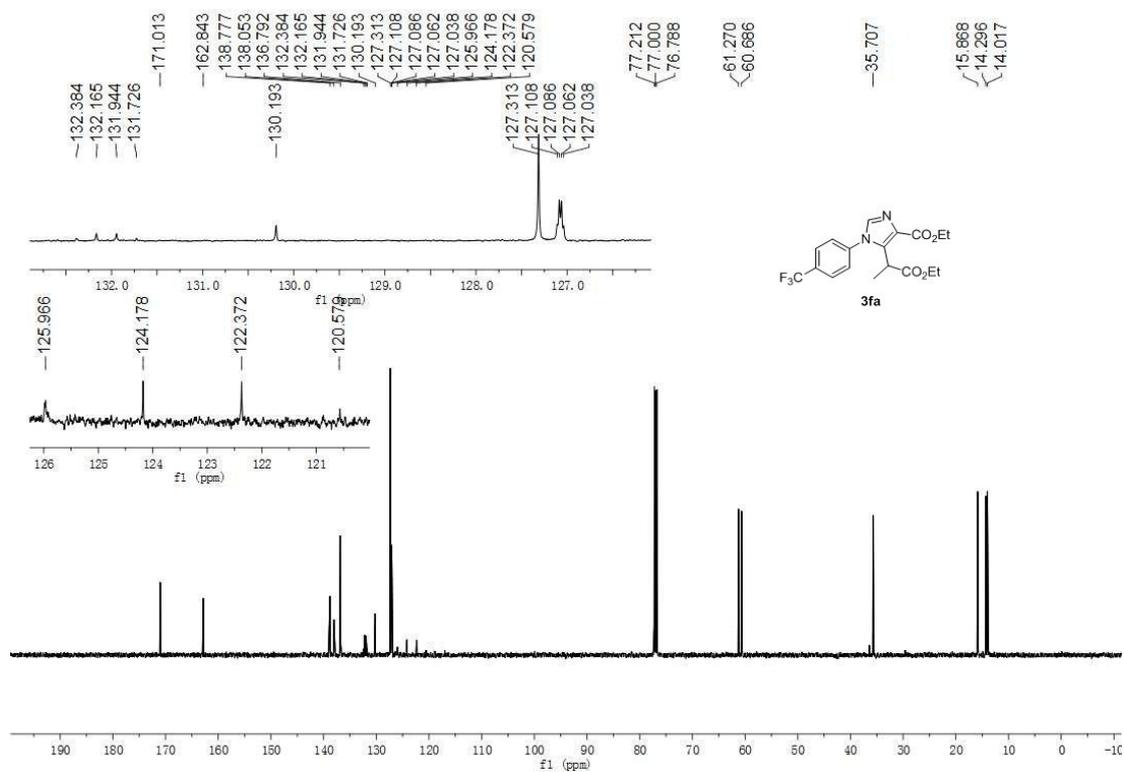
¹³C NMR (151 MHz, CDCl₃) for 3ea



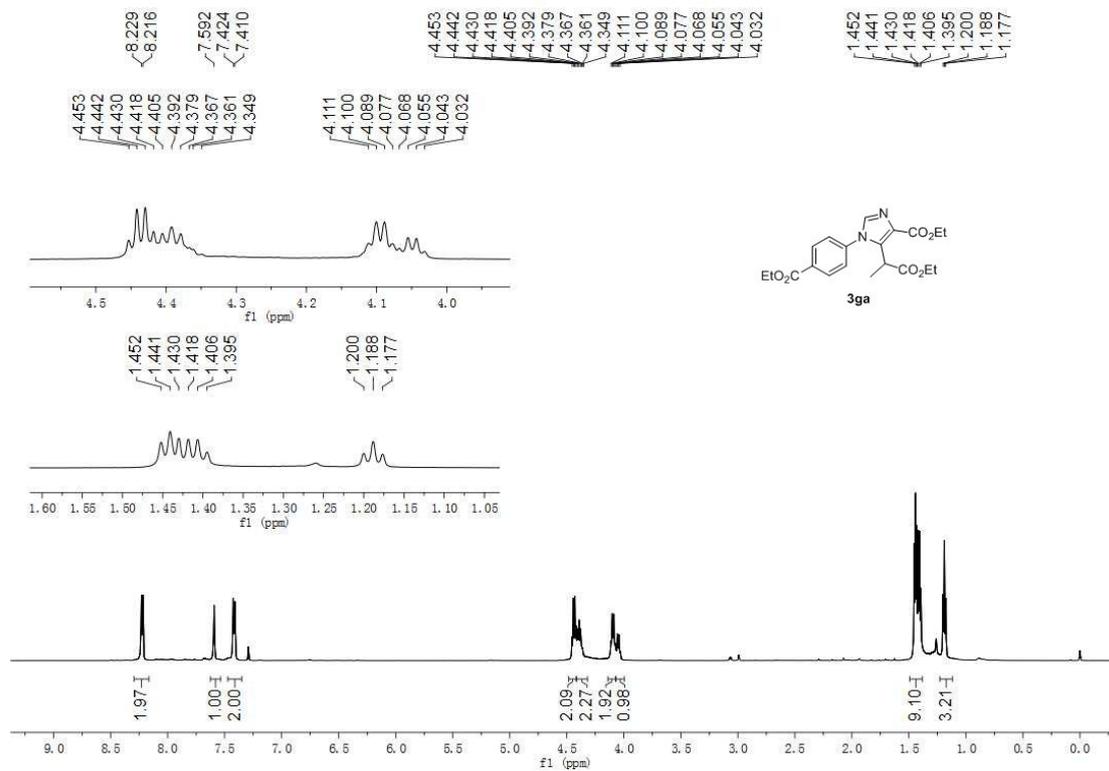
^1H NMR (600 MHz, CDCl_3) for 3fa



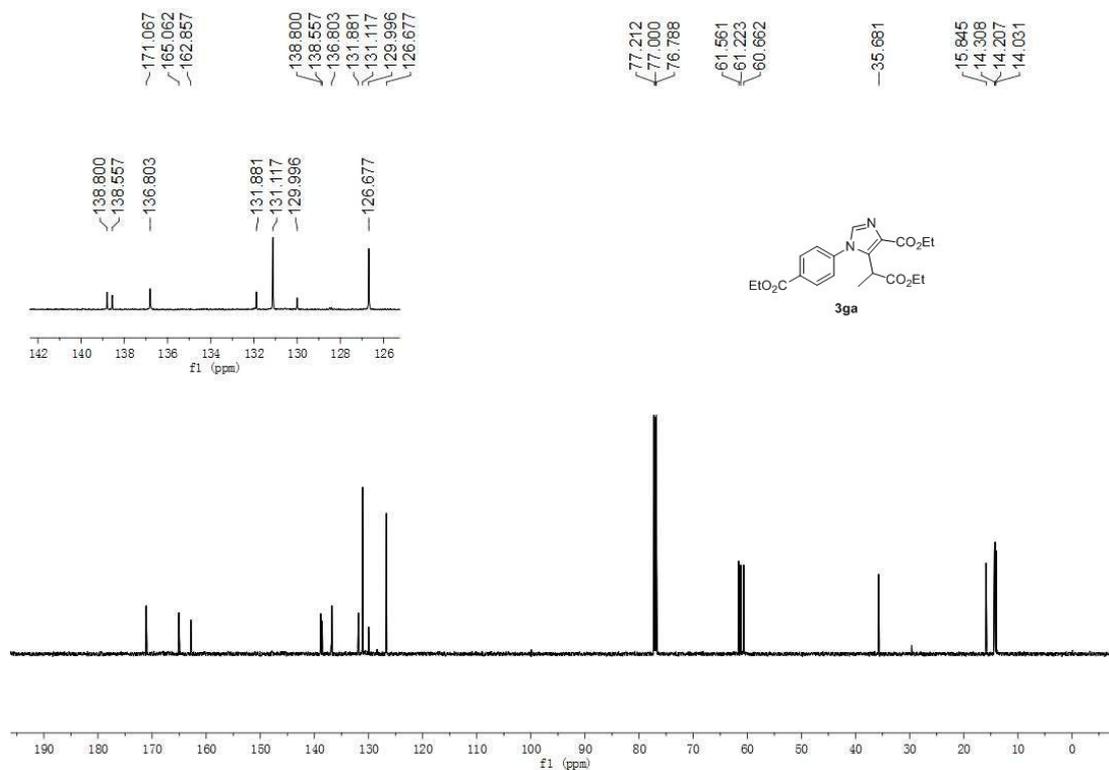
^{13}C NMR (151 MHz, CDCl_3) for 3fa



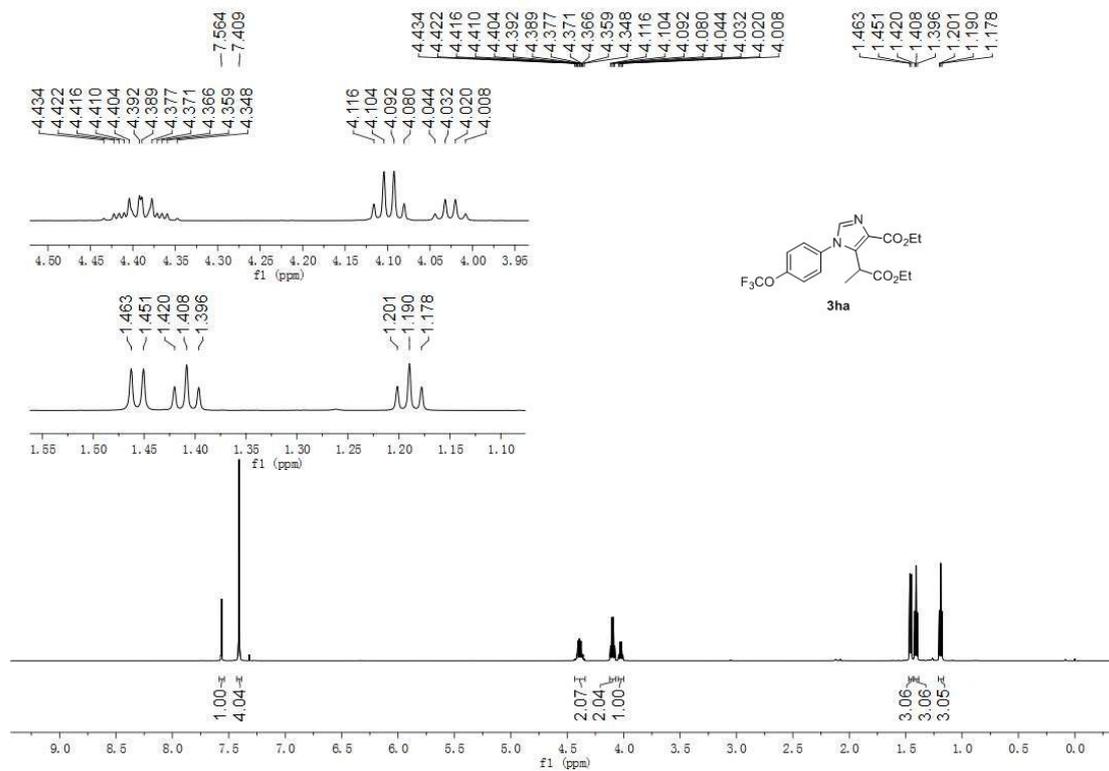
¹H NMR (600 MHz, CDCl₃) for 3ga



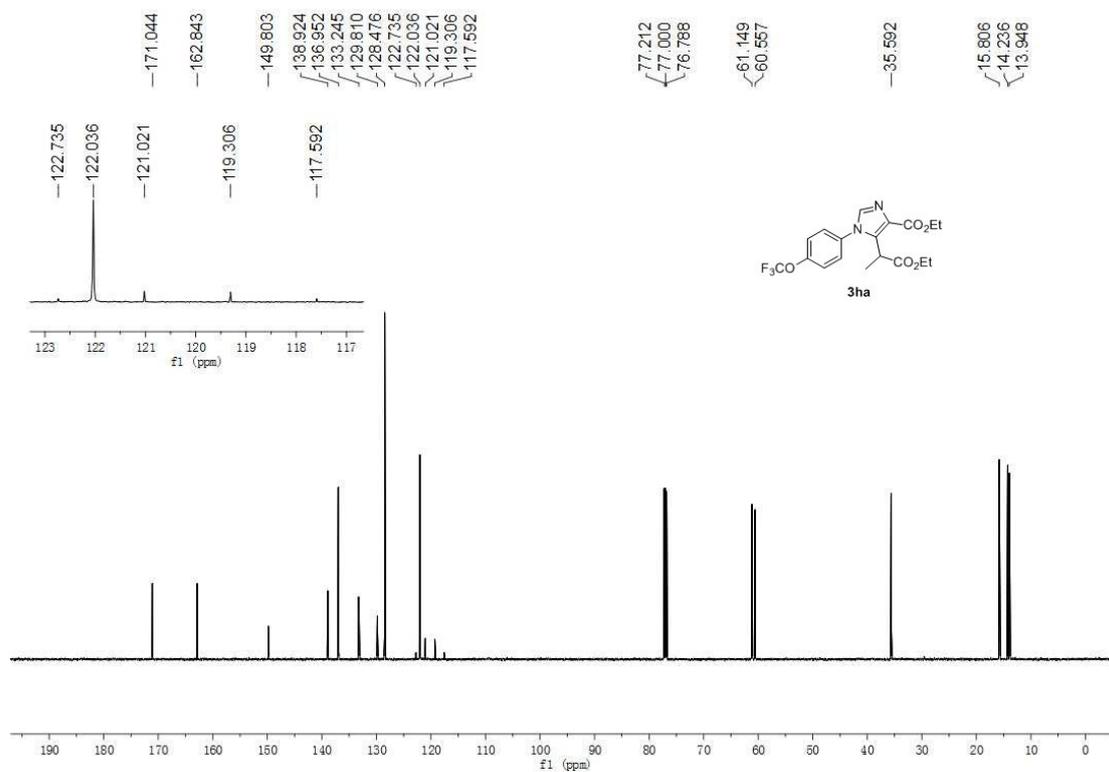
¹³C NMR (151 MHz, CDCl₃) for 3ga



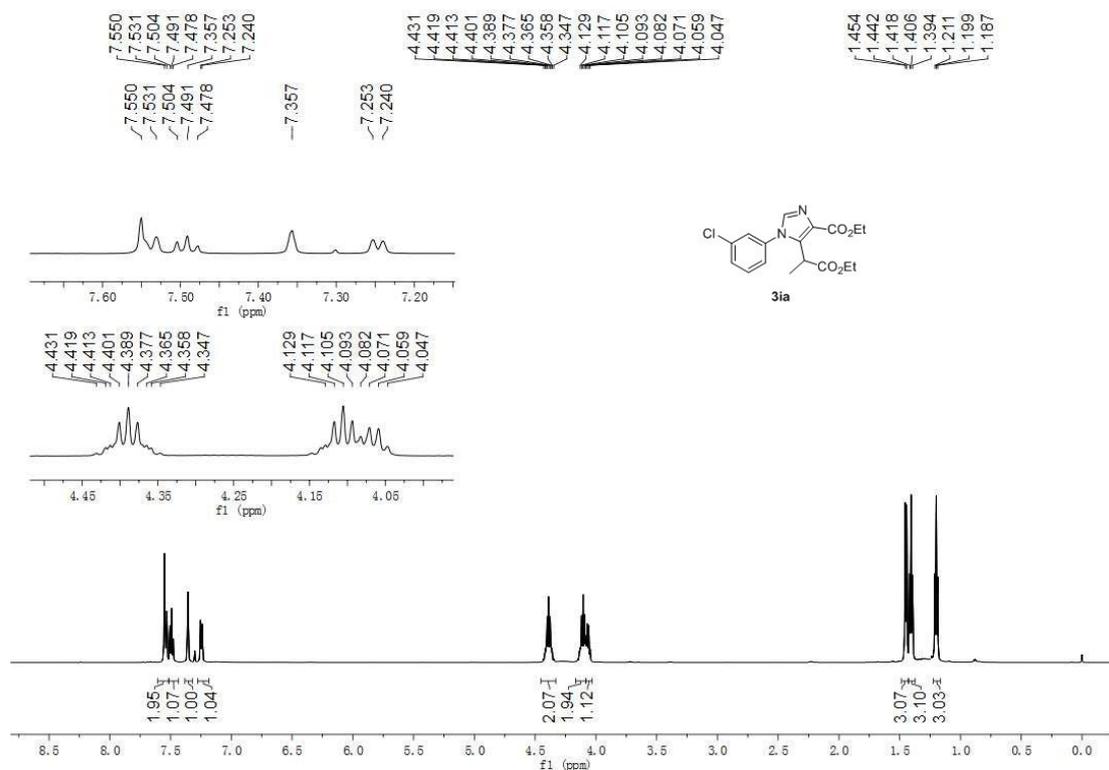
¹H NMR (600 MHz, CDCl₃) for 3ha



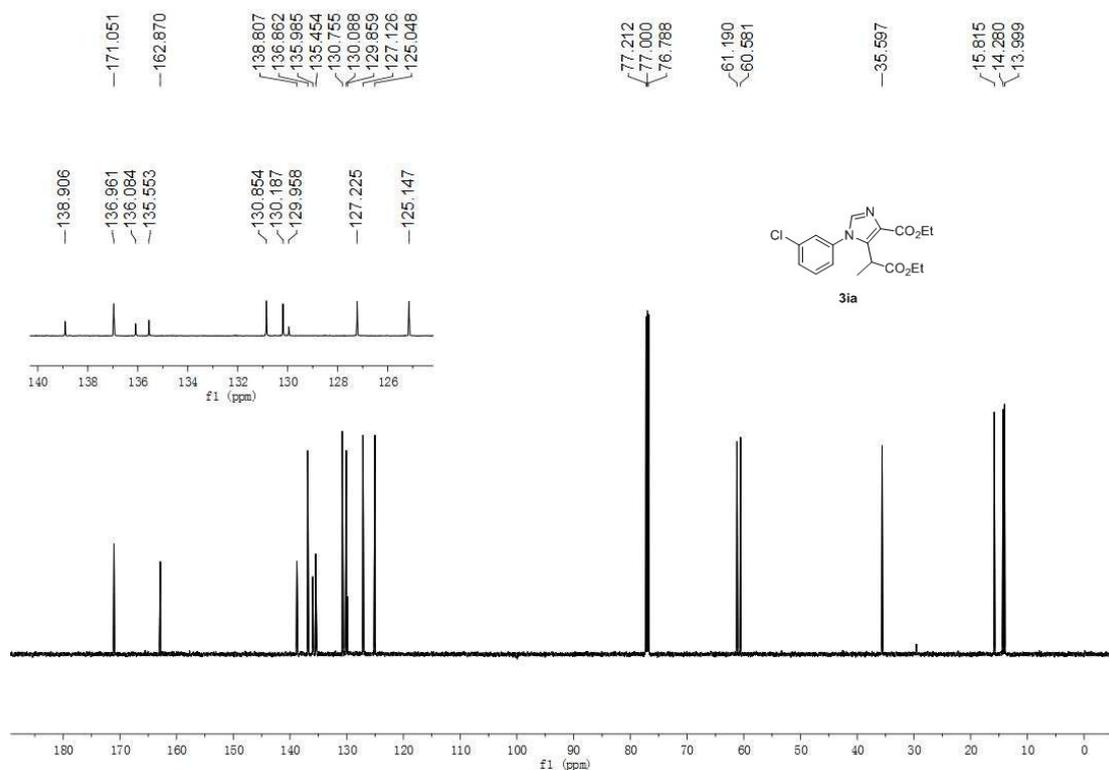
¹³C NMR (151 MHz, CDCl₃) for 3ha



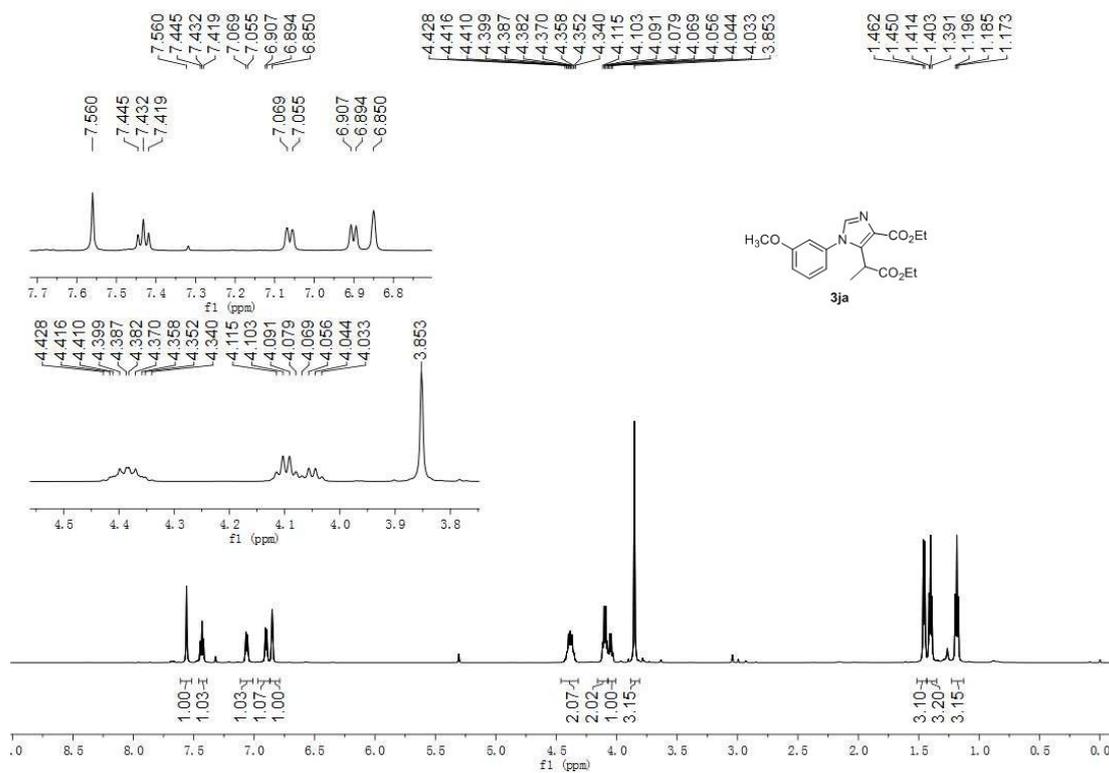
¹H NMR (600 MHz, CDCl₃) for 3ia



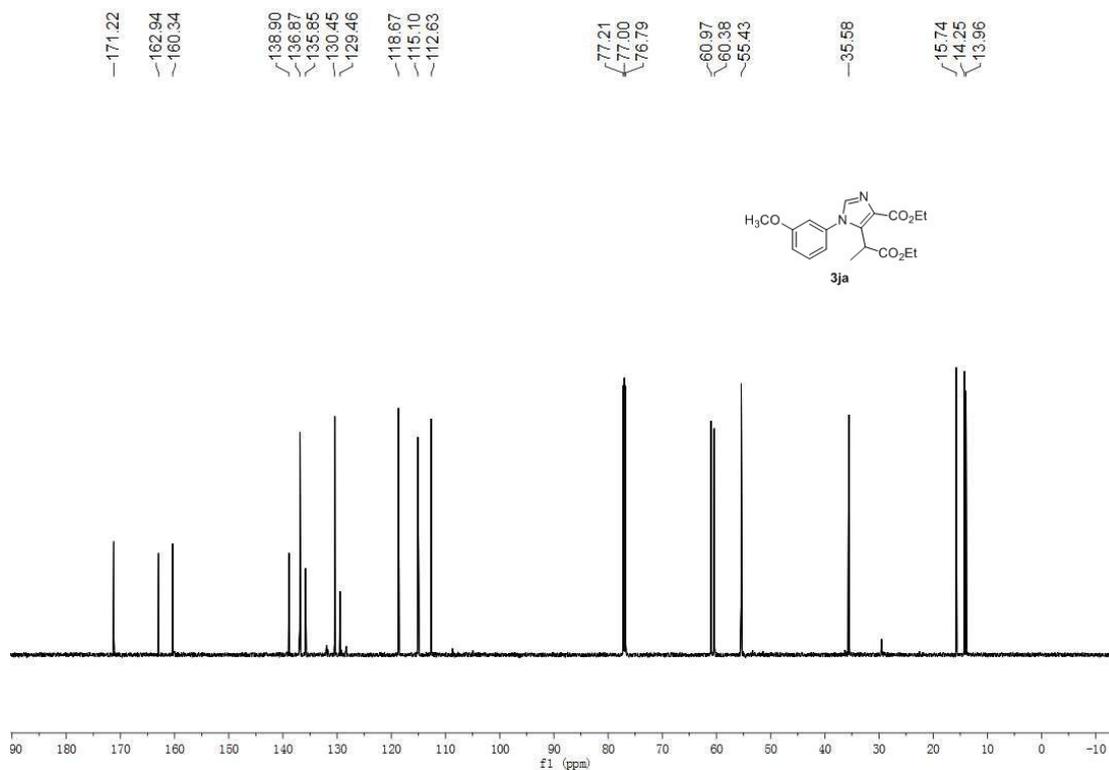
¹³C NMR (151 MHz, CDCl₃) for 3ia



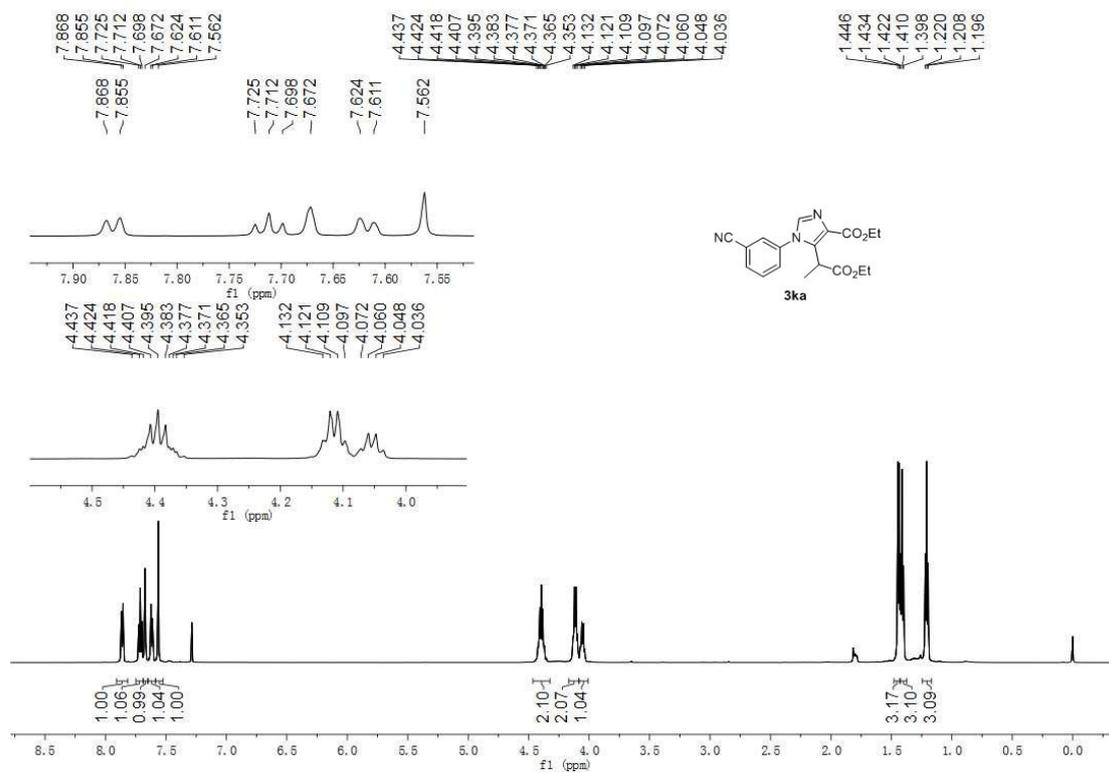
¹H NMR (600 MHz, CDCl₃) for 3ja



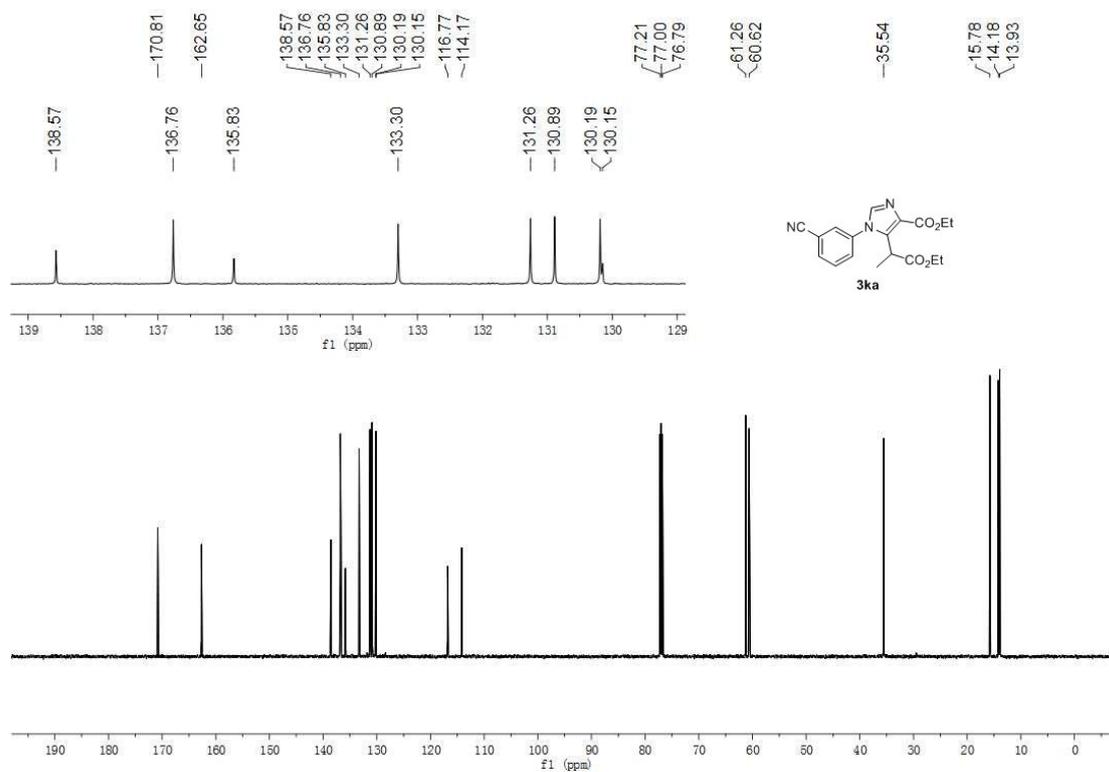
¹³C NMR (151 MHz, CDCl₃) for 3ja



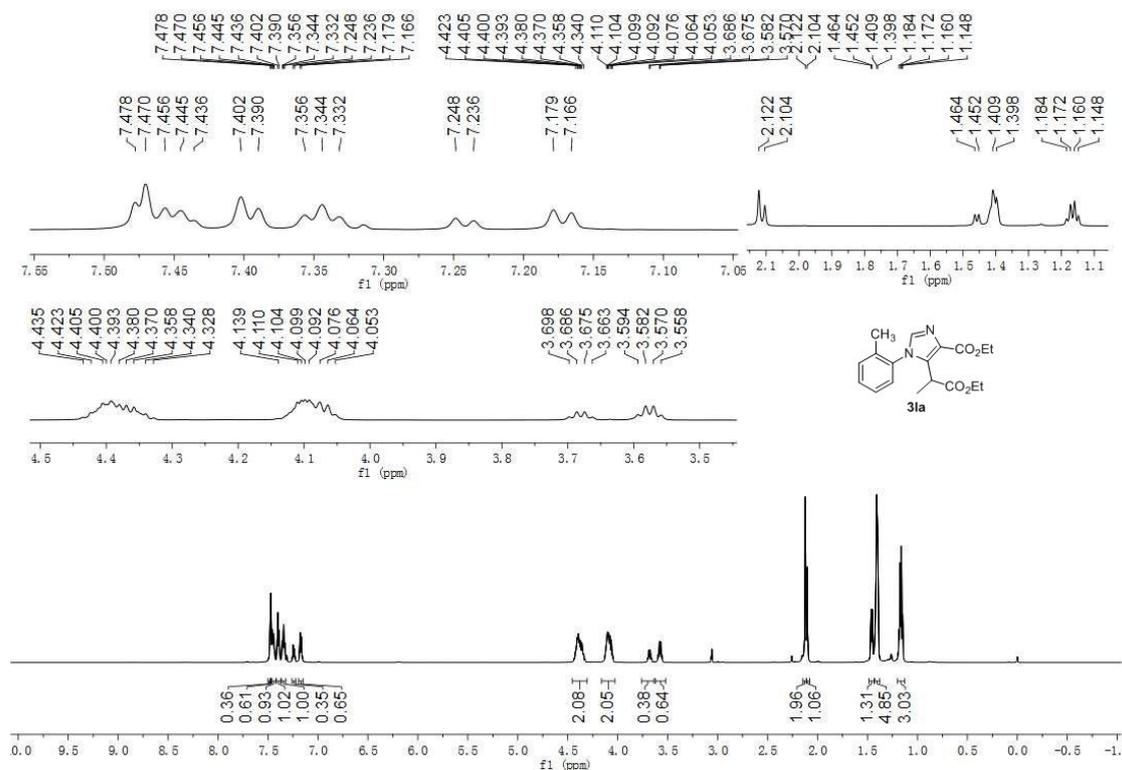
¹H NMR (600 MHz, CDCl₃) for 3ka



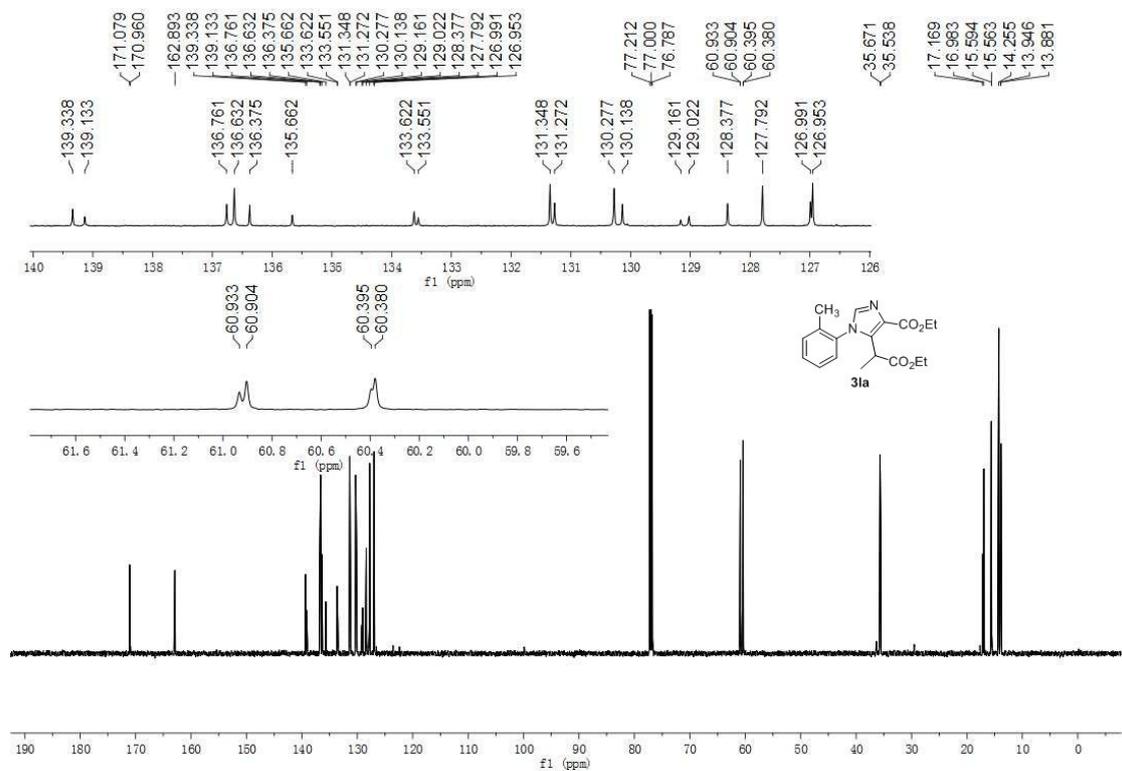
¹³C NMR (151 MHz, CDCl₃) for 3ka



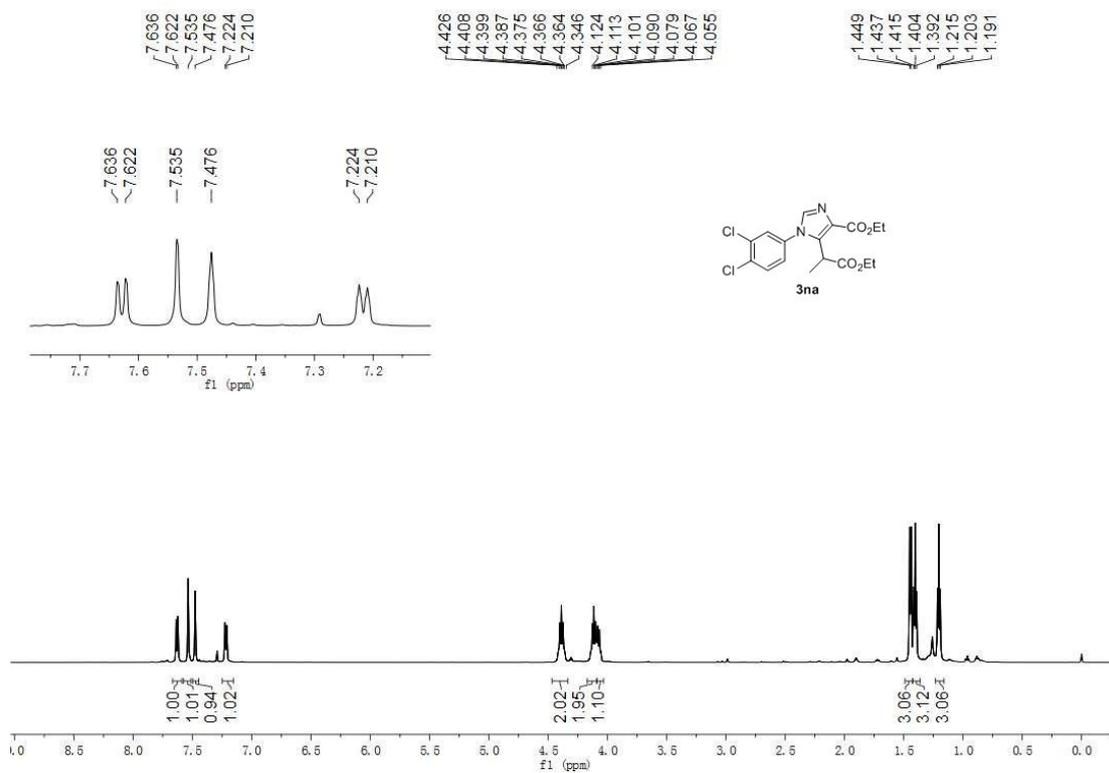
¹H NMR (600 MHz, CDCl₃) for 3la



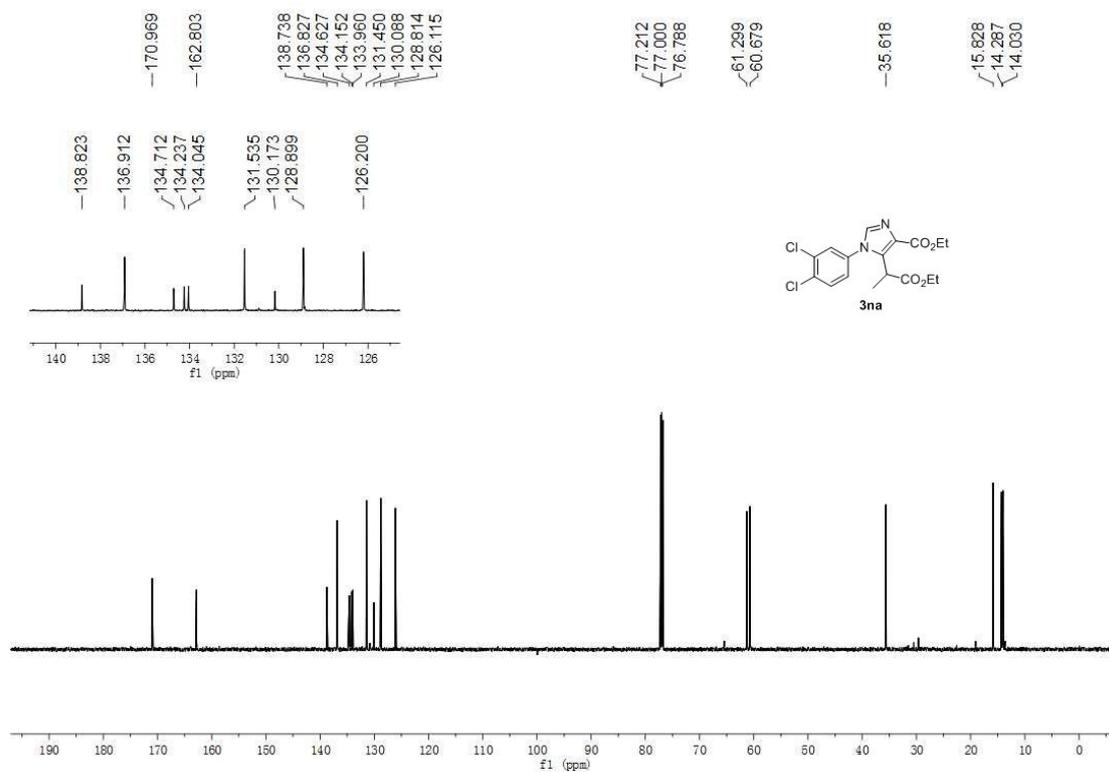
¹³C NMR (151 MHz, CDCl₃) for 3la



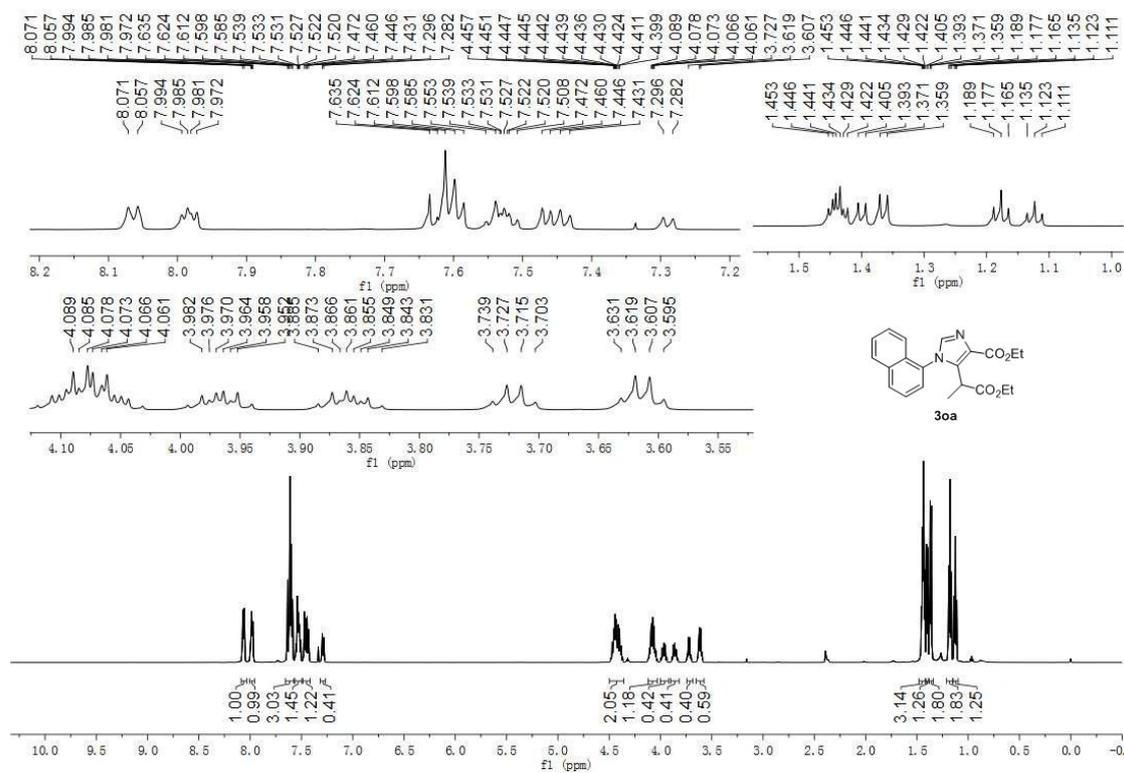
¹H NMR (600 MHz, CDCl₃) for 3na



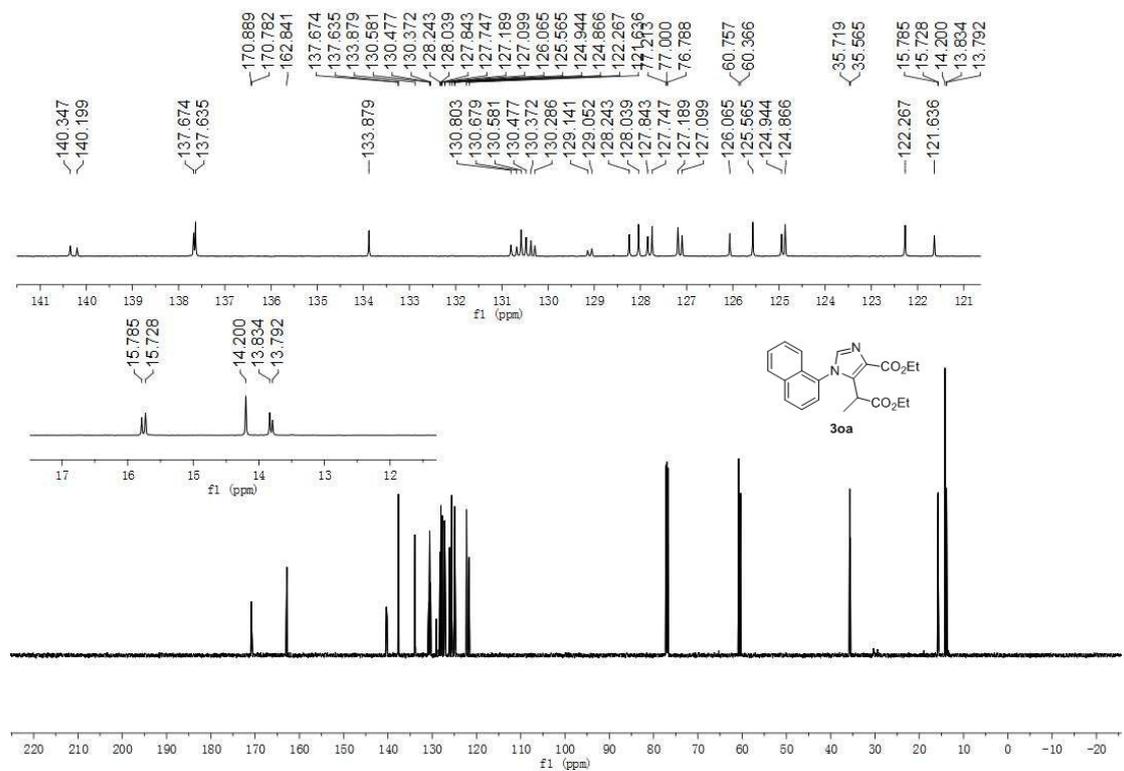
¹³C NMR (151 MHz, CDCl₃) for 3na



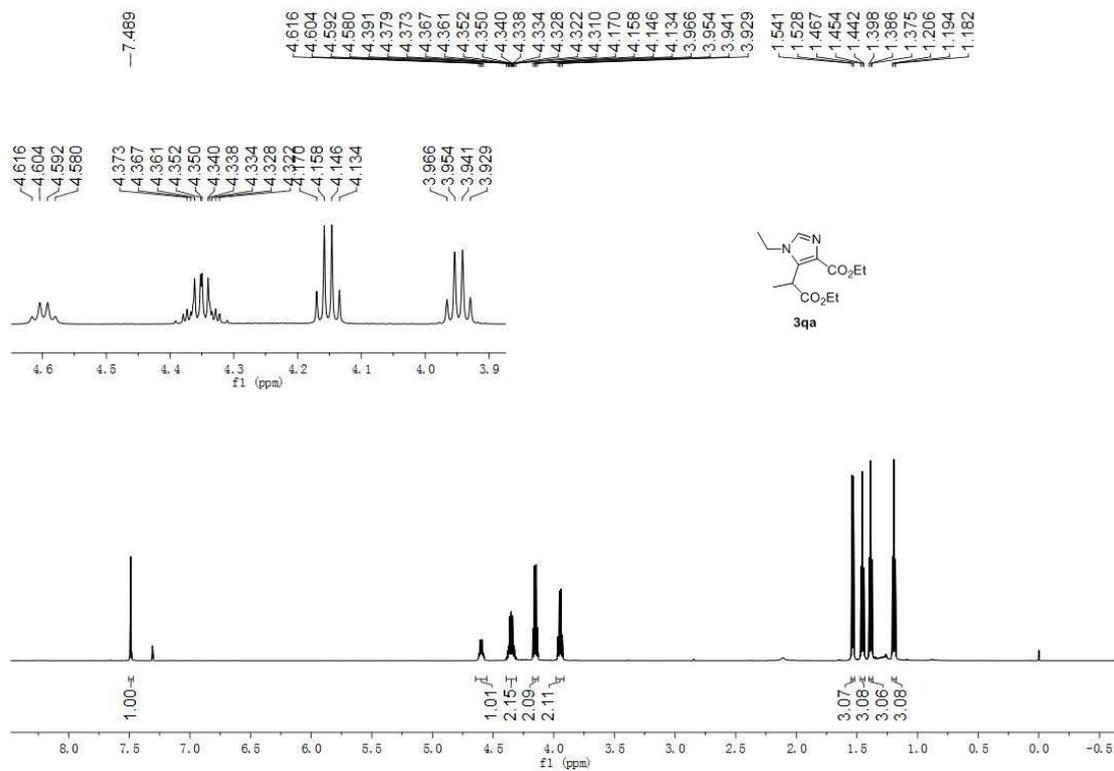
¹H NMR (600 MHz, CDCl₃) for 30a



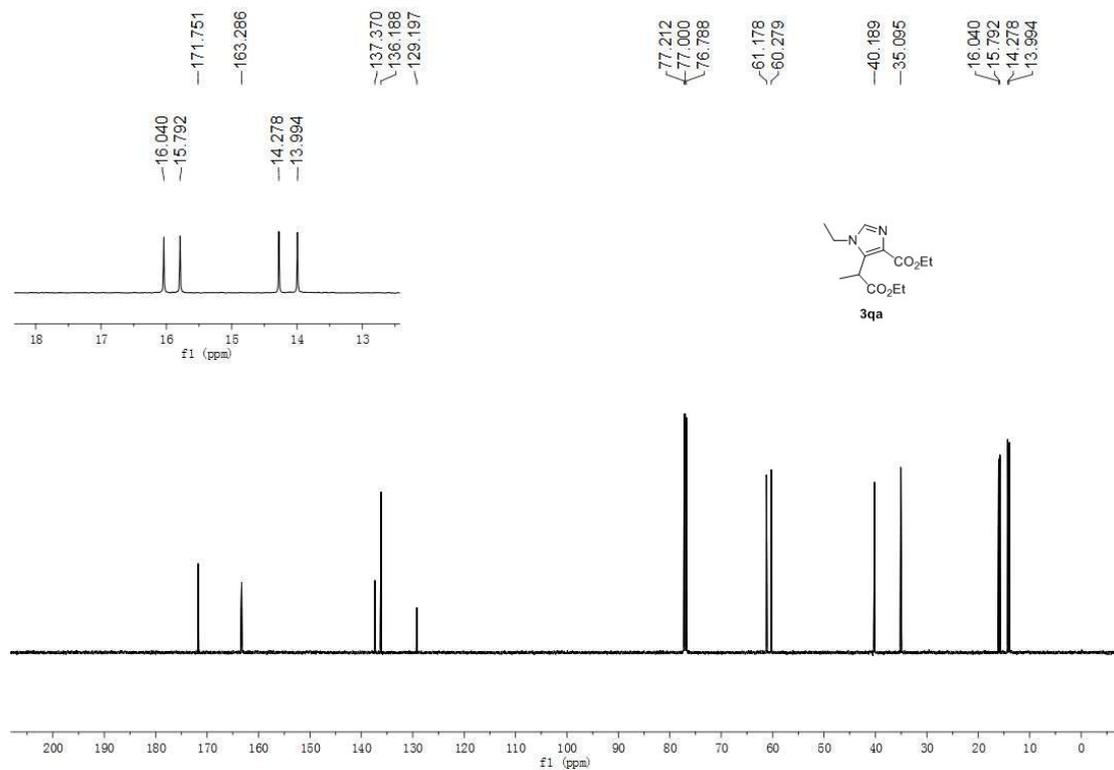
¹³C NMR (151 MHz, CDCl₃) for 30a



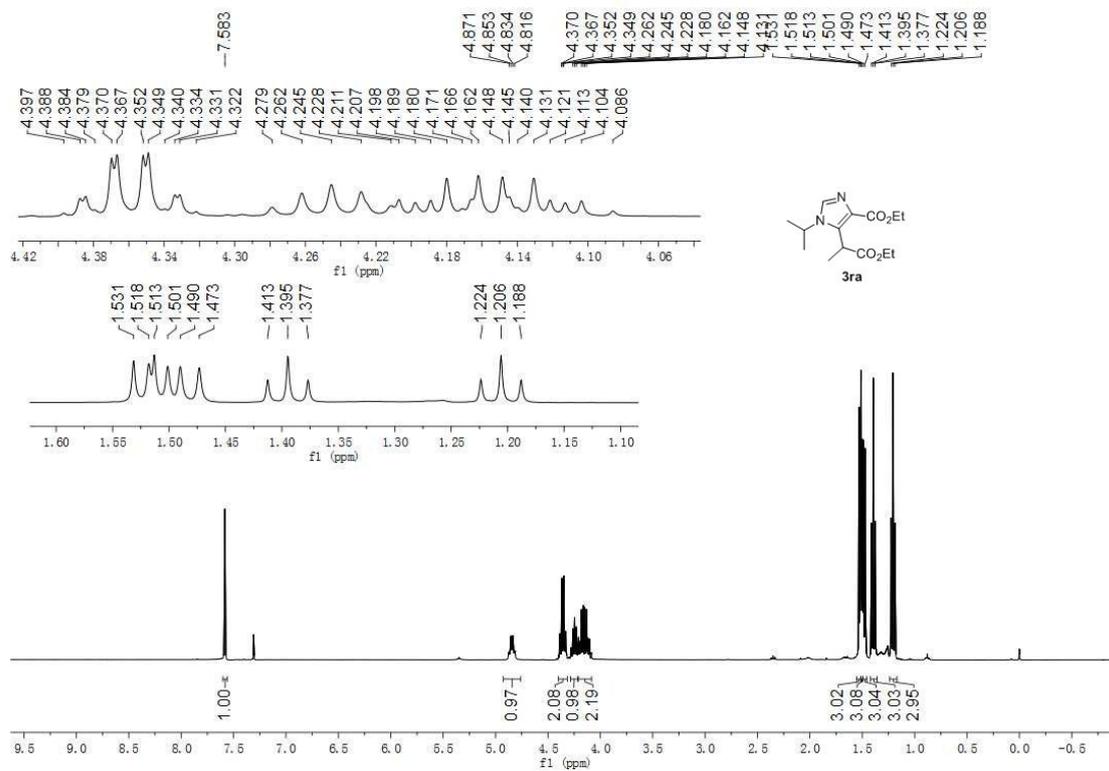
¹H NMR (600 MHz, CDCl₃) for 3qa



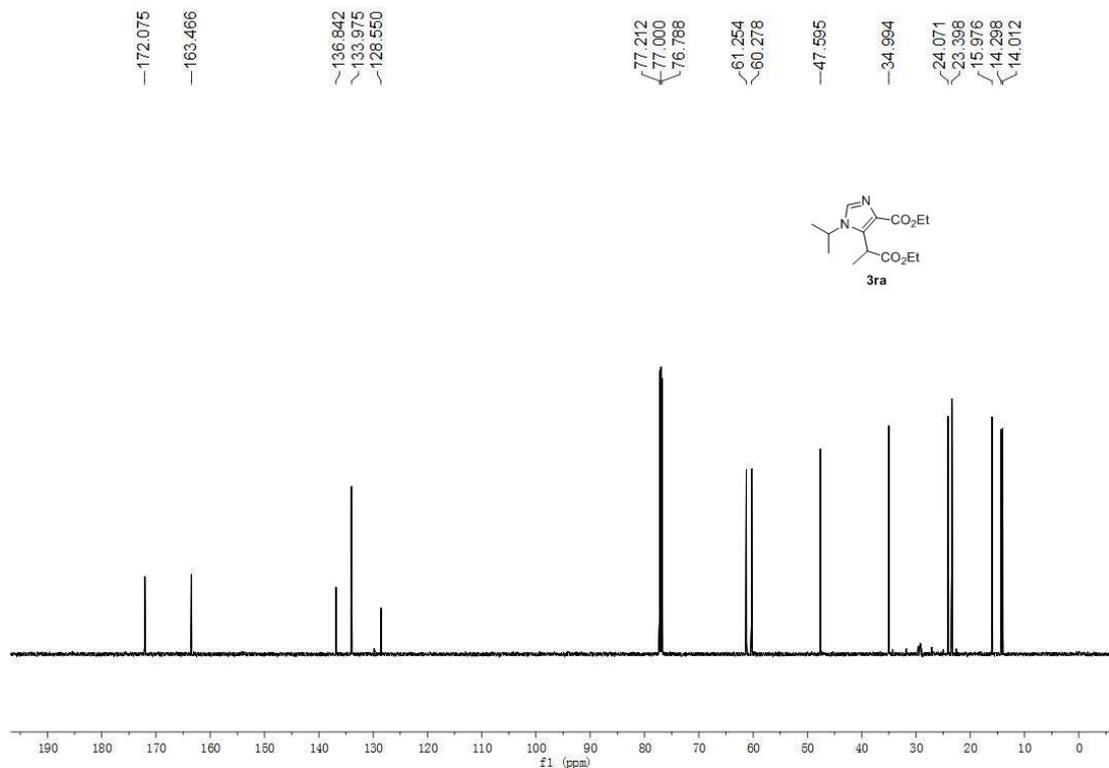
¹³C NMR (151 MHz, CDCl₃) for 3qa



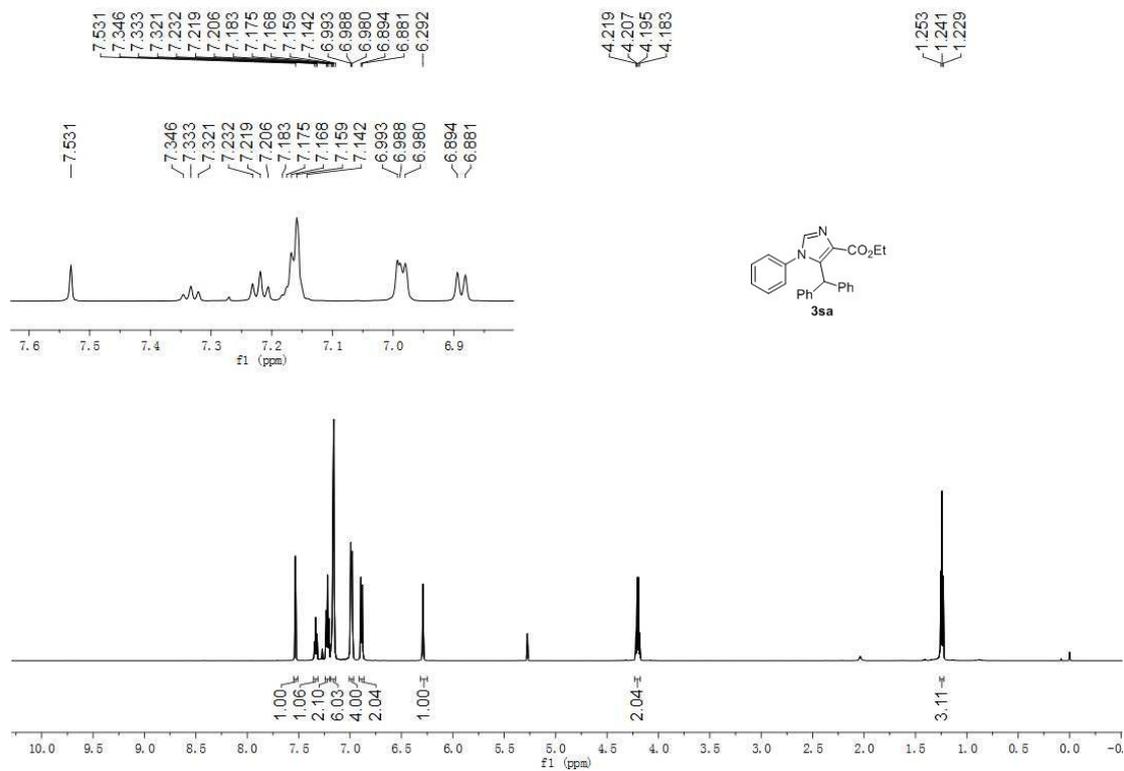
¹H NMR (400 MHz, CDCl₃) for 3ra



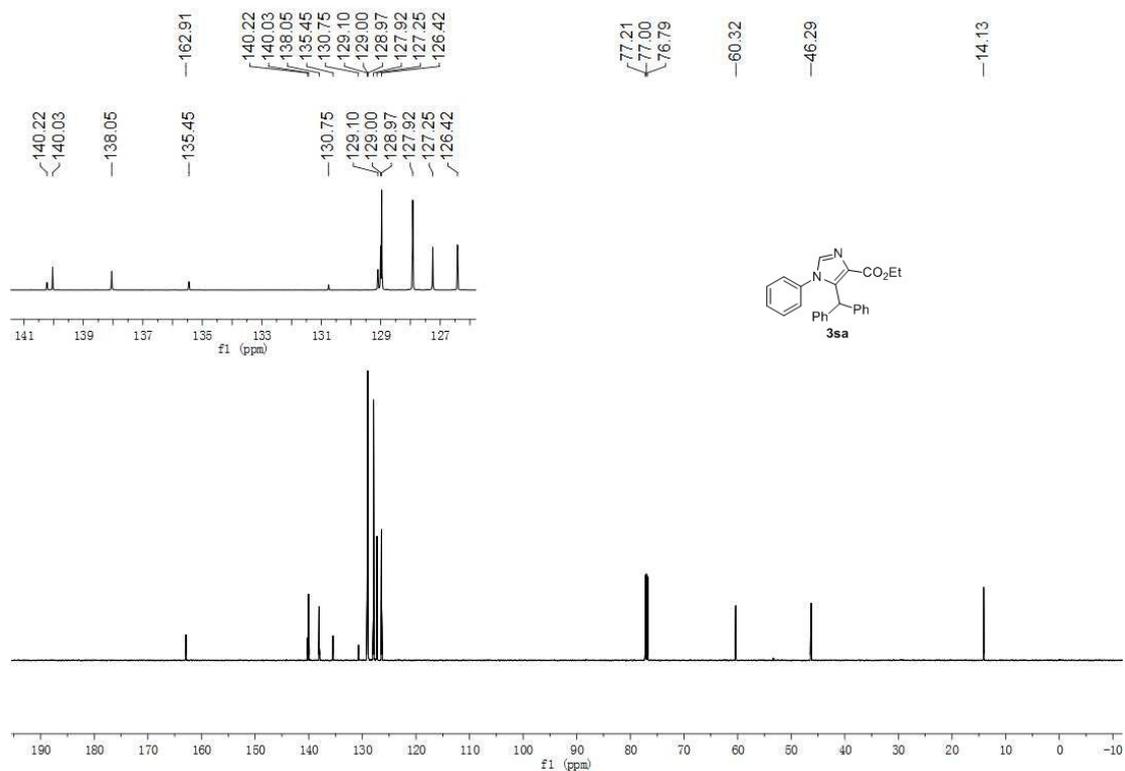
¹³C NMR (151 MHz, CDCl₃) for 3ra



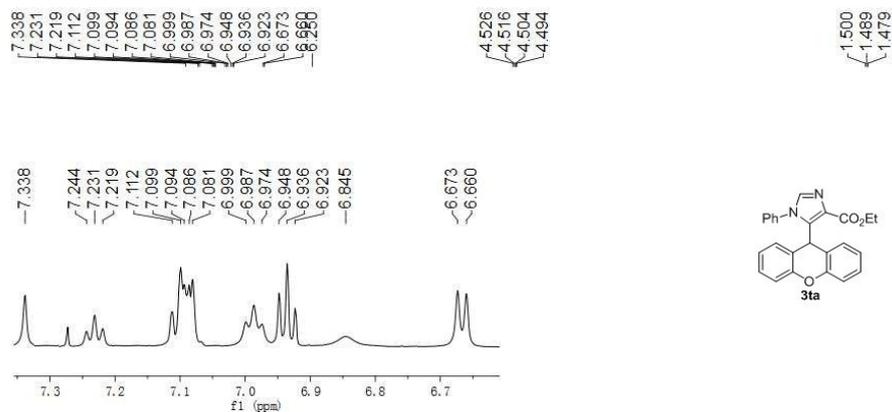
¹H NMR (600 MHz, CDCl₃) for 3sa



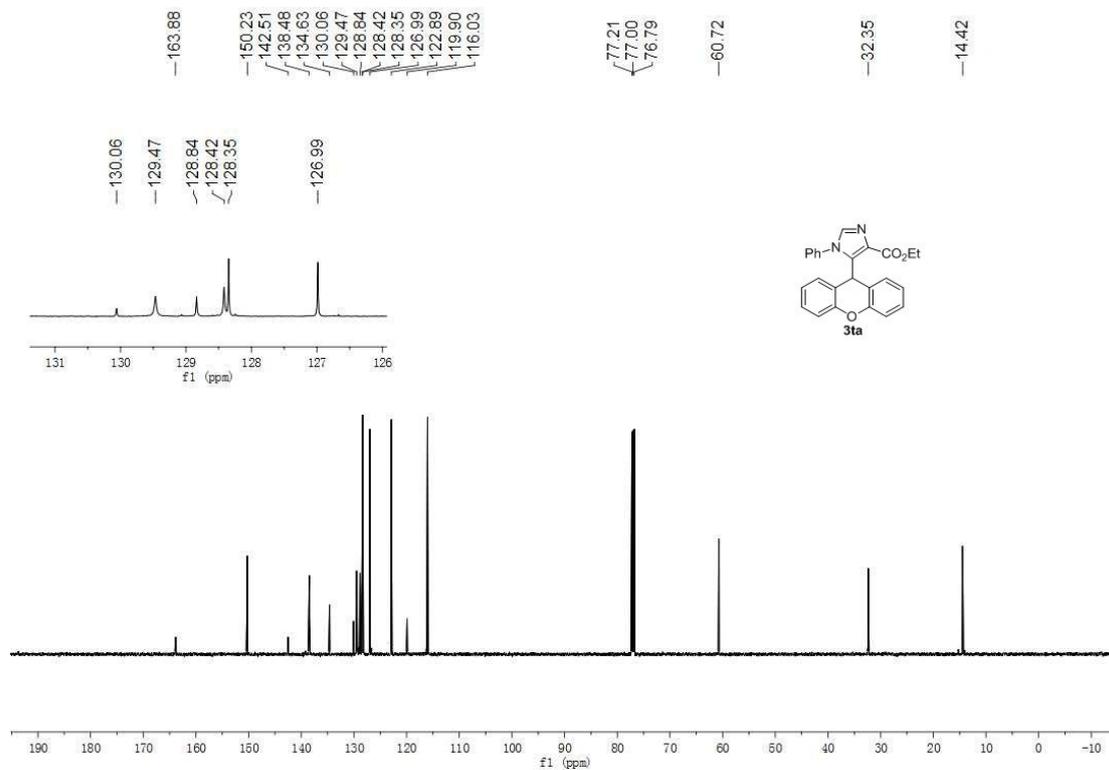
¹³C NMR (151 MHz, CDCl₃) for 3sa



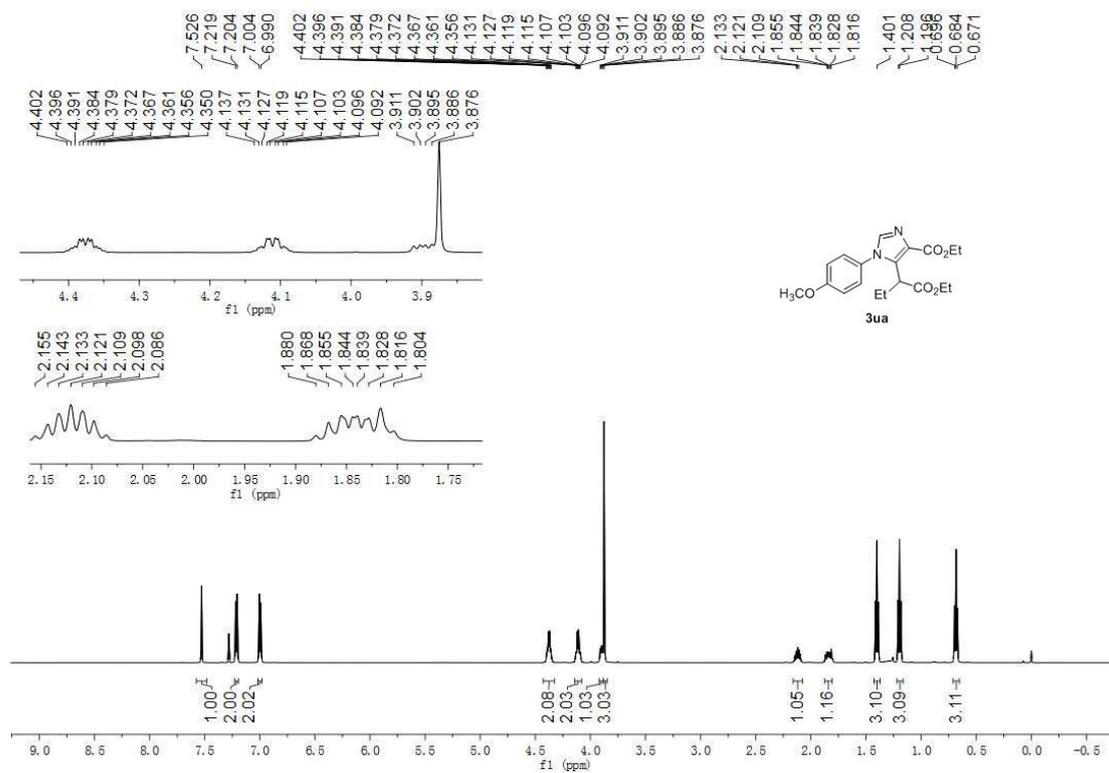
¹H NMR (600 MHz, CDCl₃) for 3ta



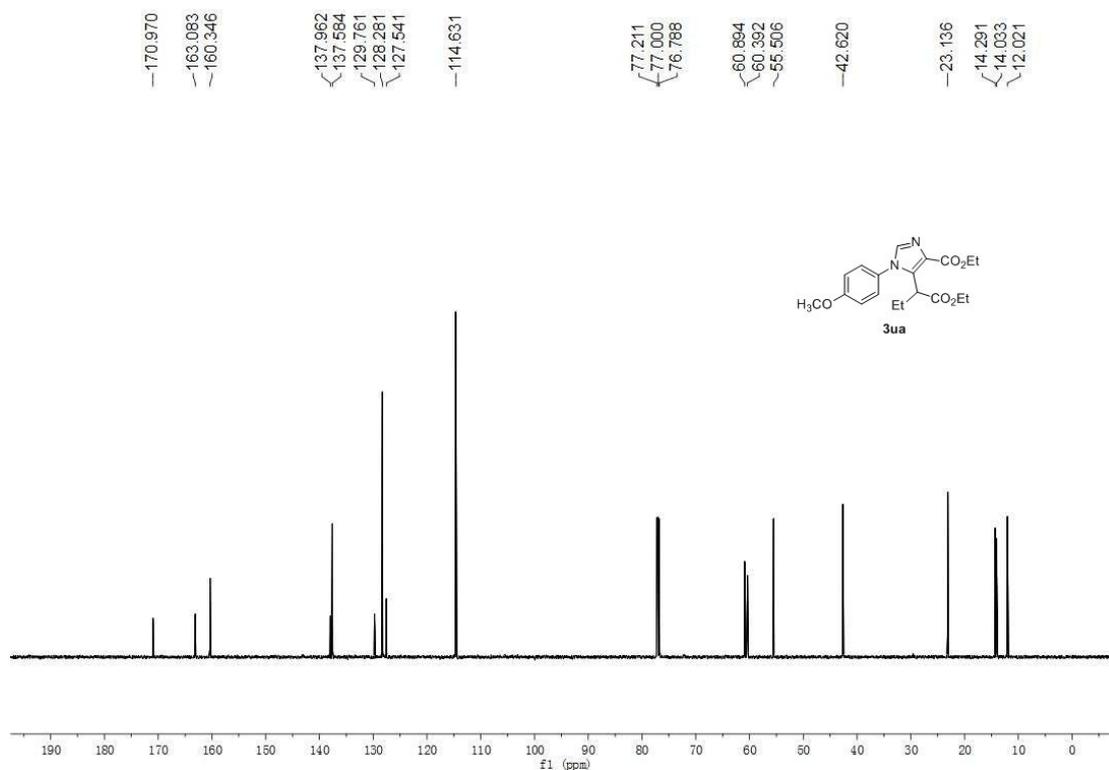
¹³C NMR (151 MHz, CDCl₃) for 3ta



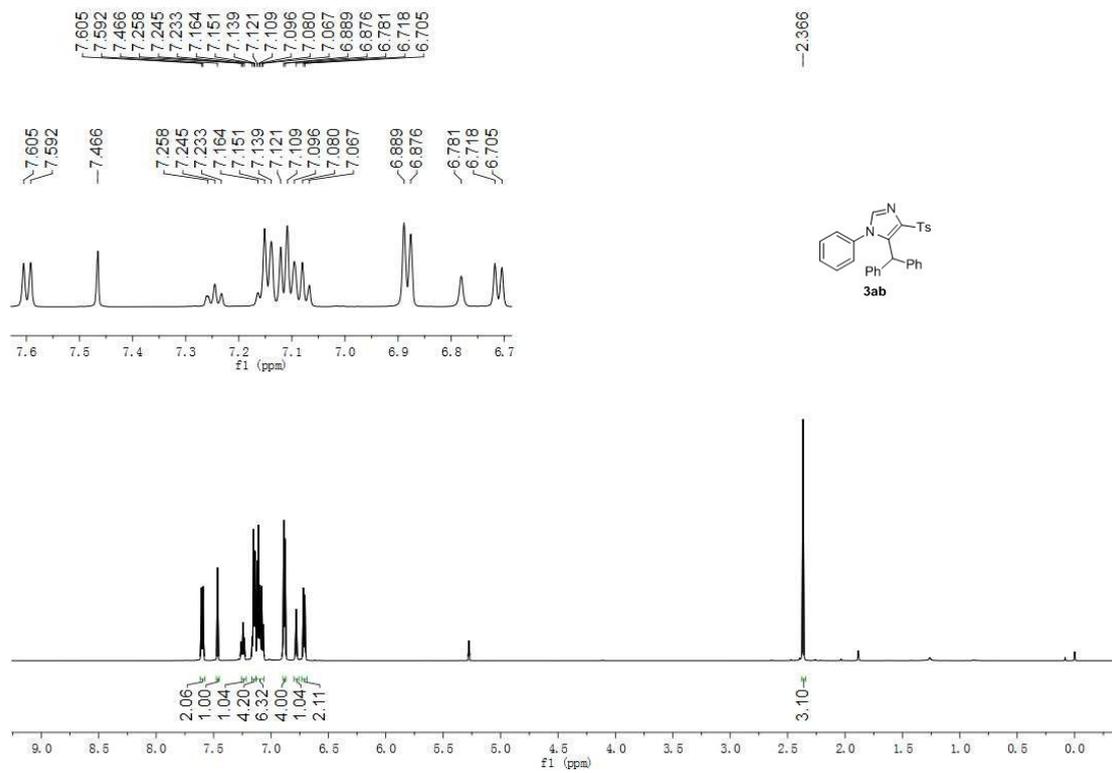
¹H NMR (600 MHz, CDCl₃) for 3ua



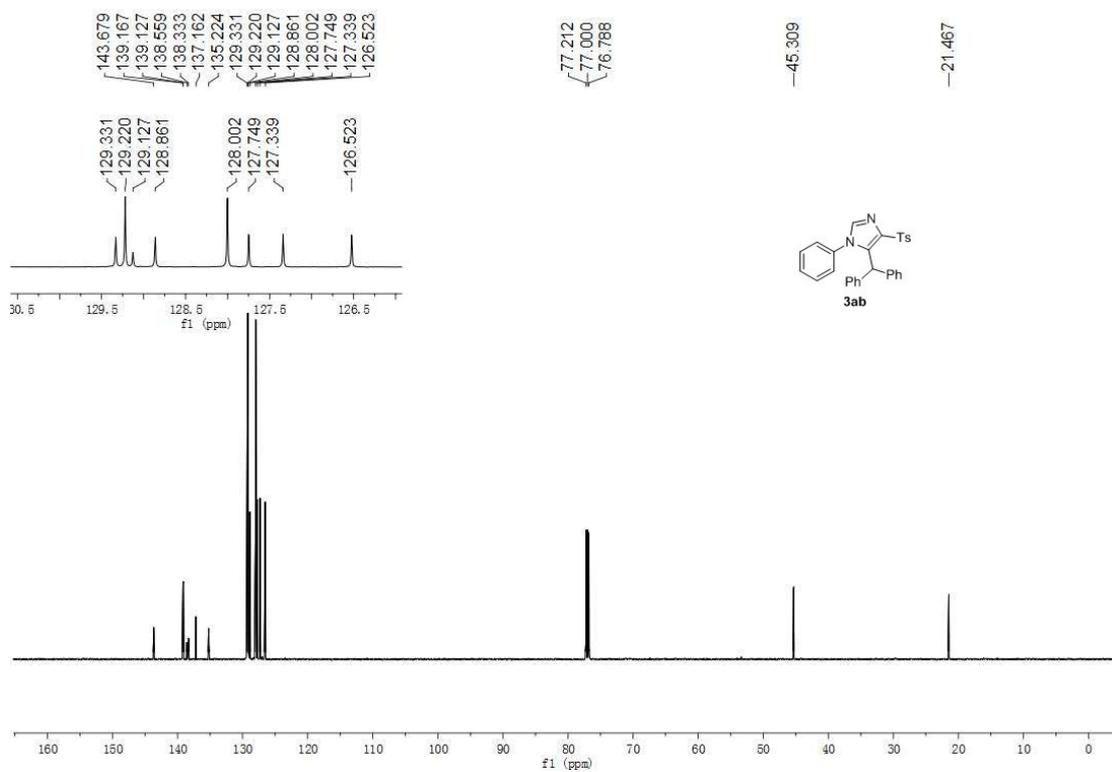
¹³C NMR (151 MHz, CDCl₃) for 3ua



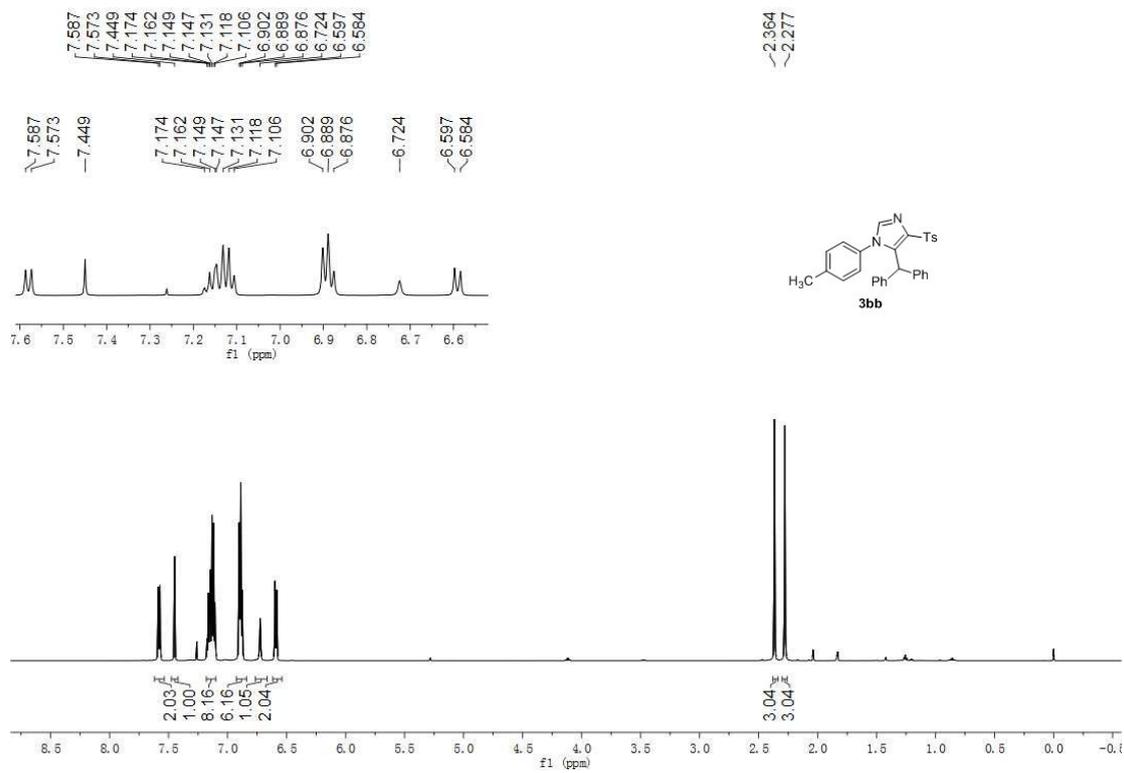
^1H NMR (600 MHz, CDCl_3) for 3ab



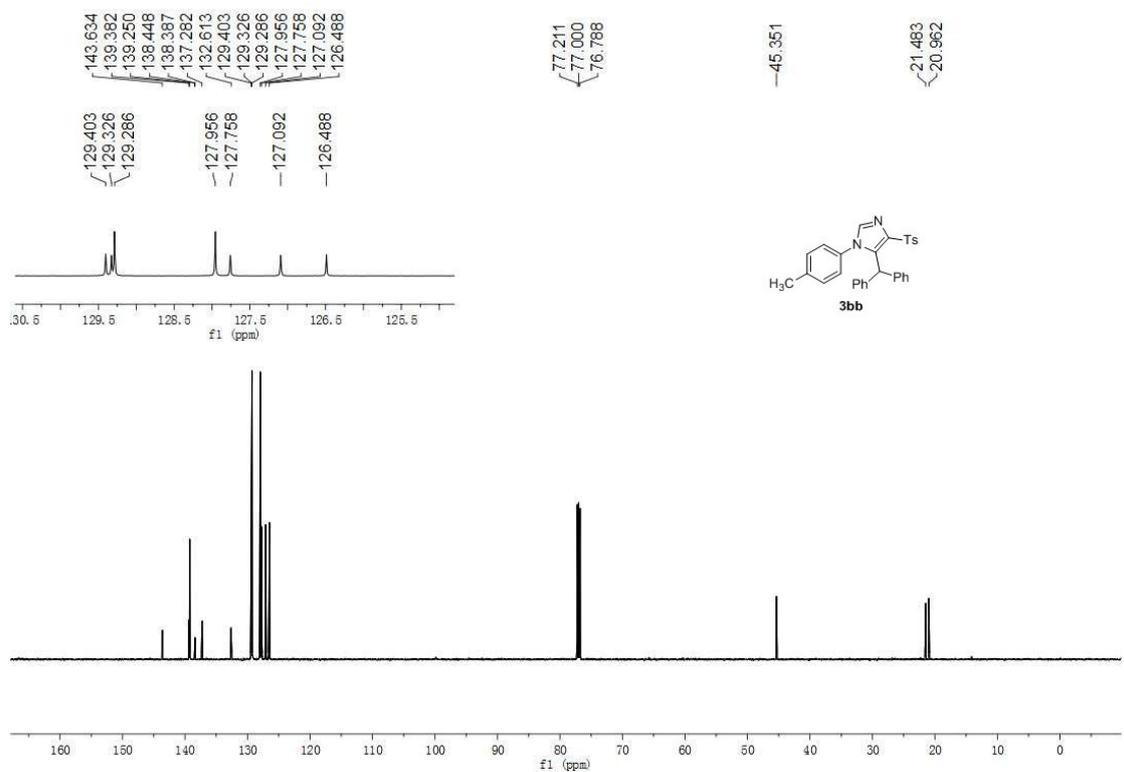
^{13}C NMR (151 MHz, CDCl_3) for 3ab



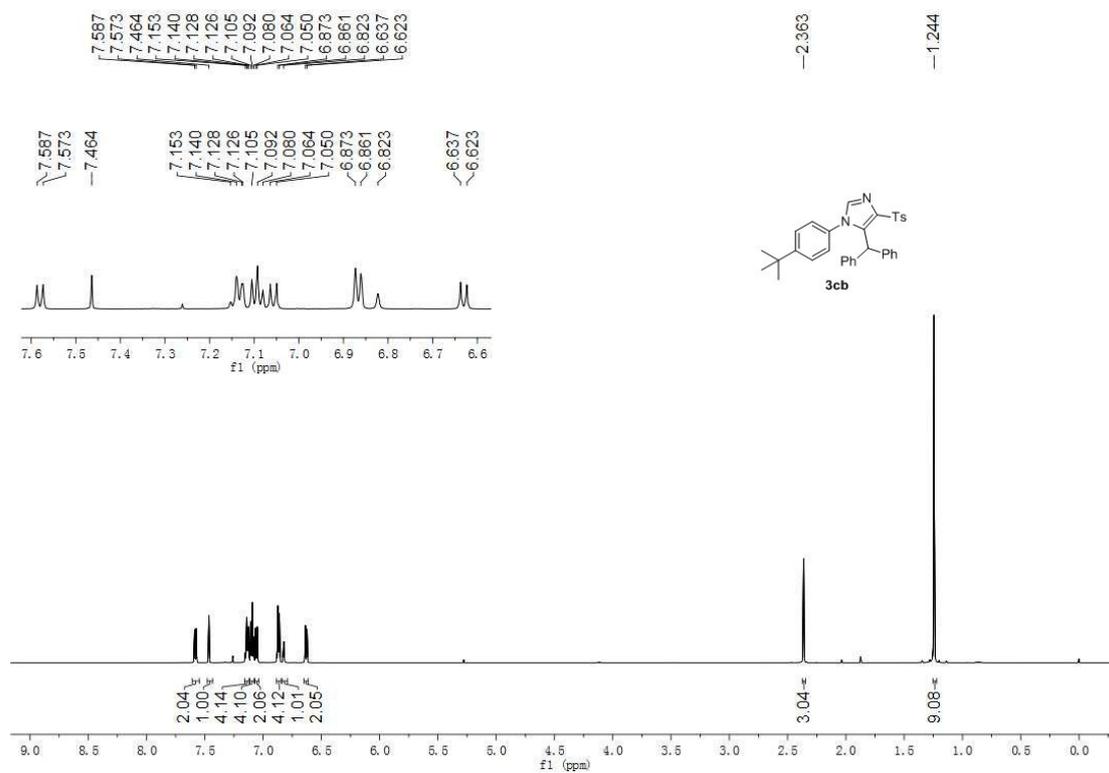
^1H NMR (600 MHz, CDCl_3) for **3bb**



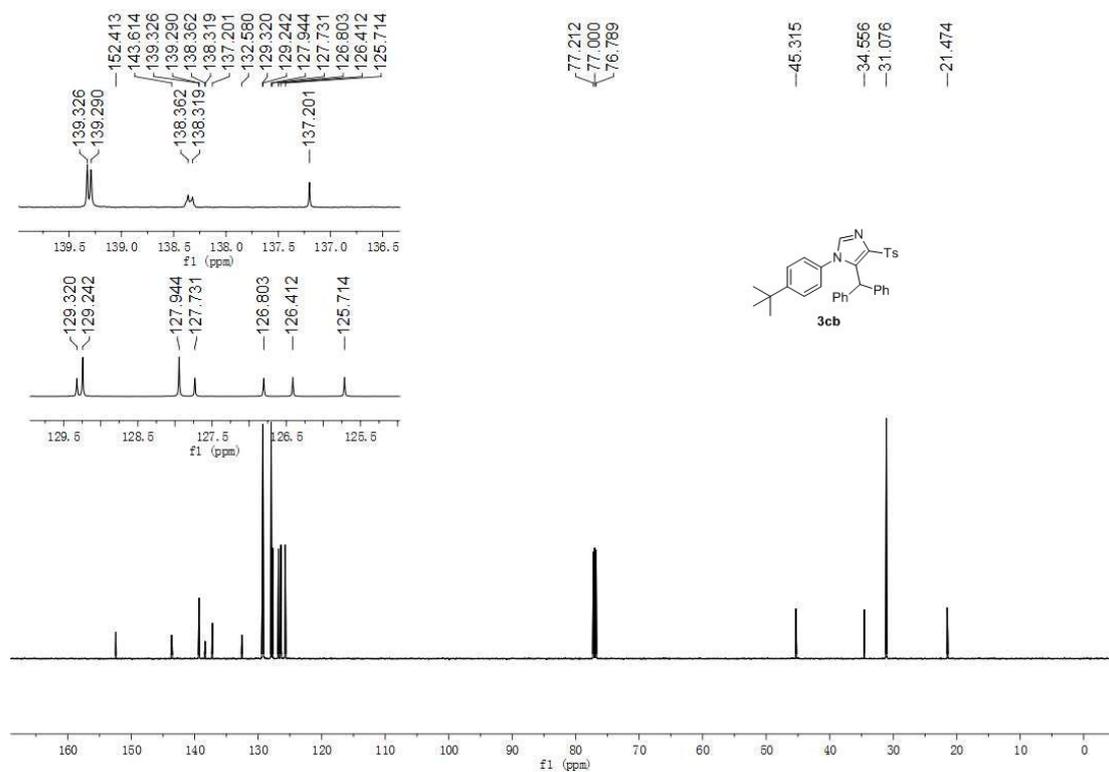
^{13}C NMR (151 MHz, CDCl_3) for **3bb**



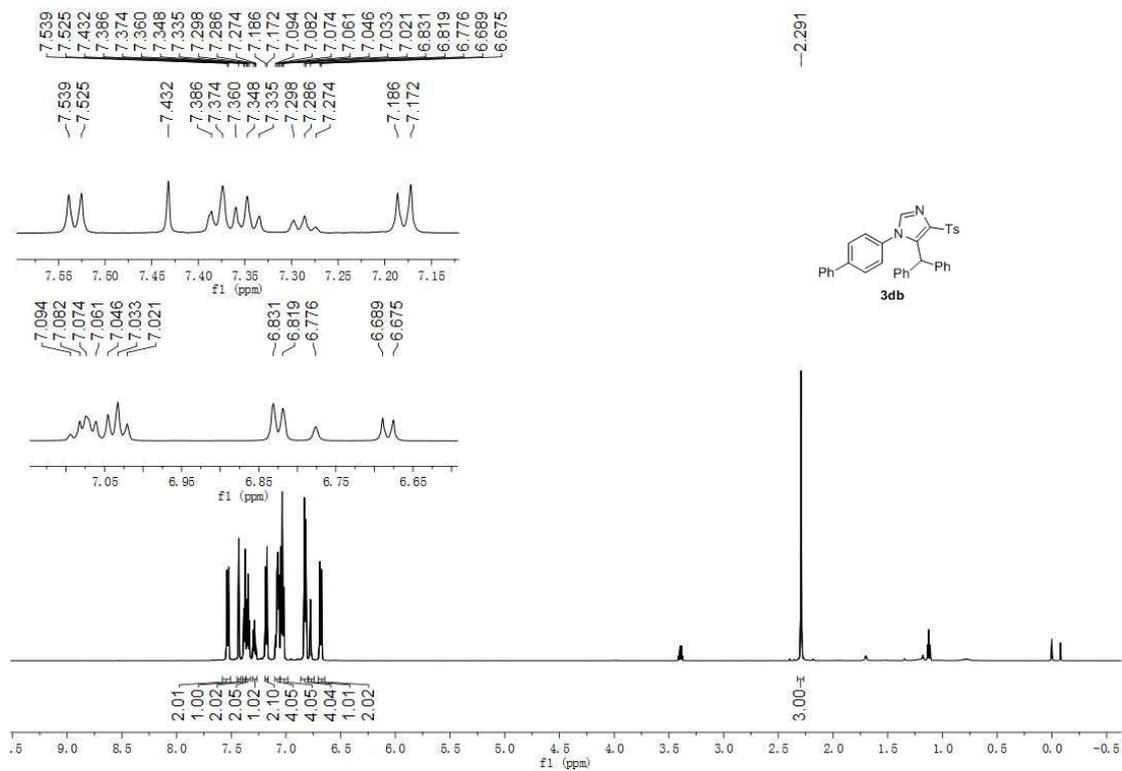
^1H NMR (600 MHz, CDCl_3) for **3cb**



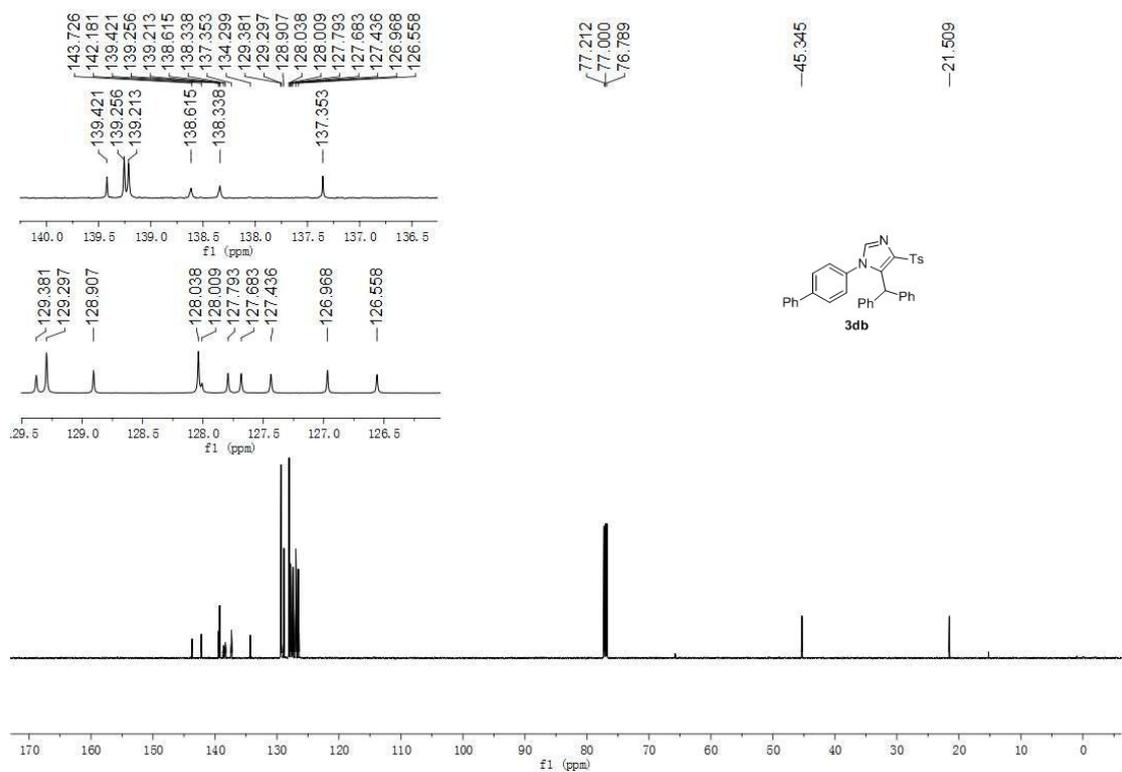
^{13}C NMR (151 MHz, CDCl_3) for **3cb**



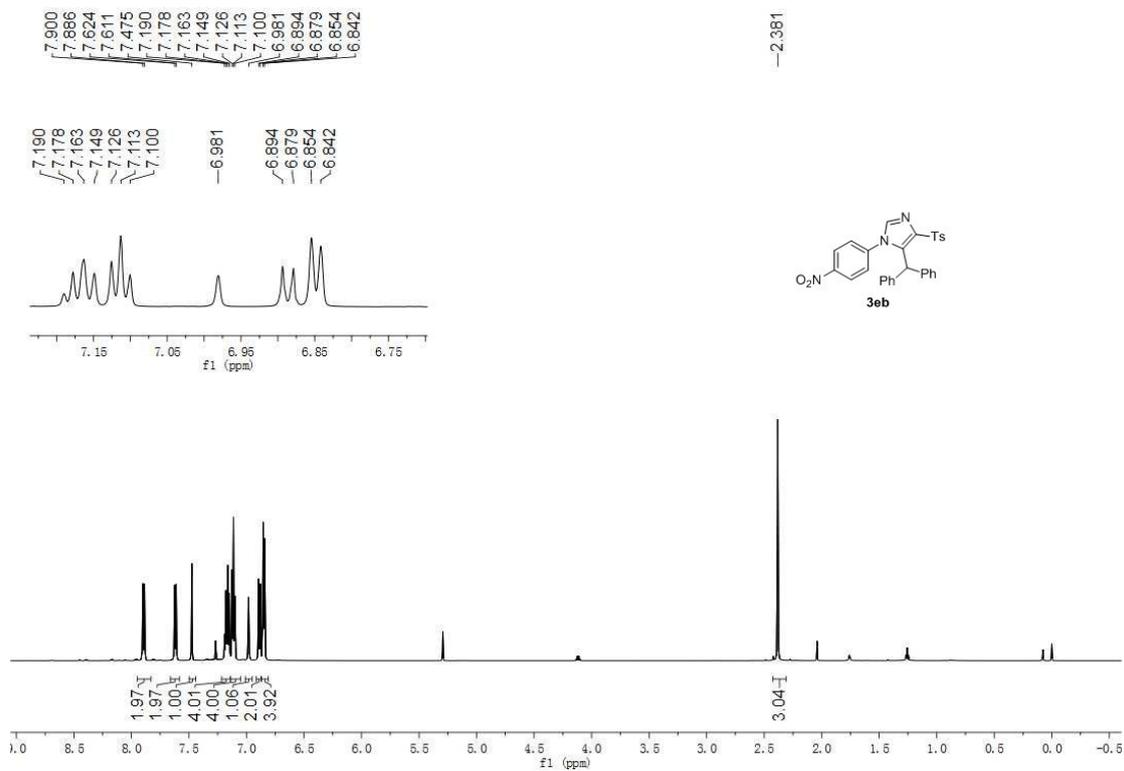
¹H NMR (600 MHz, CDCl₃) for 3db



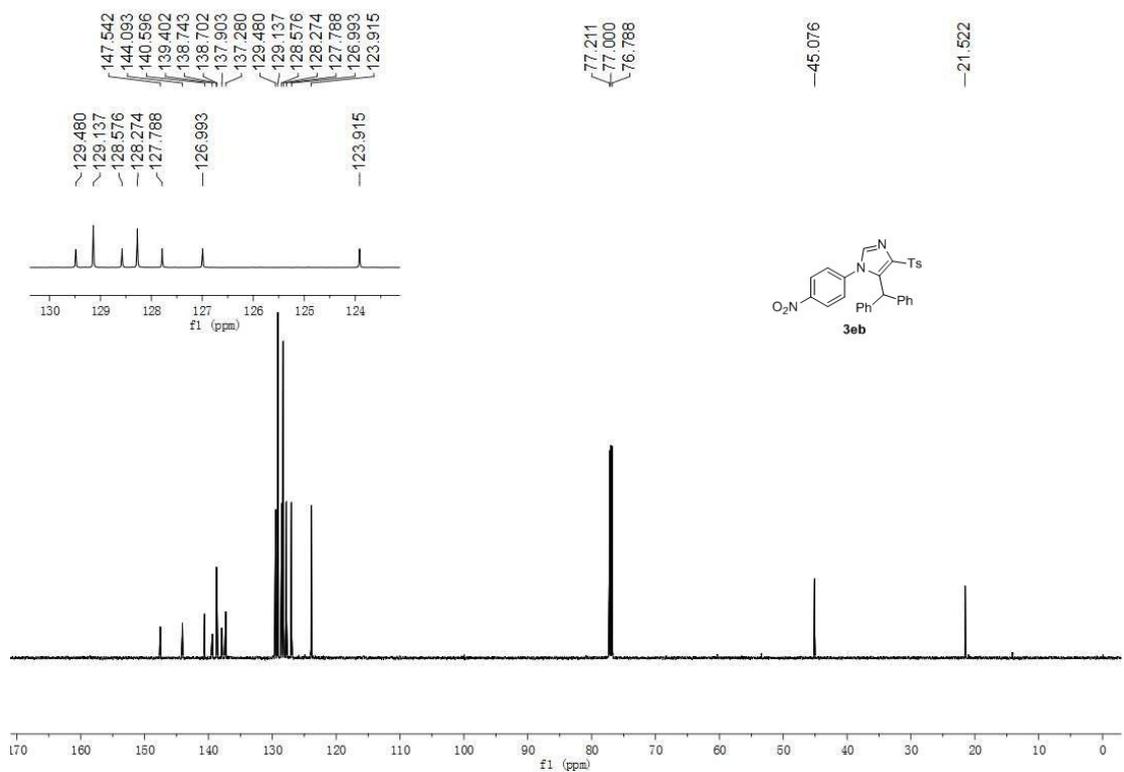
¹³C NMR (151 MHz, CDCl₃) for 3db



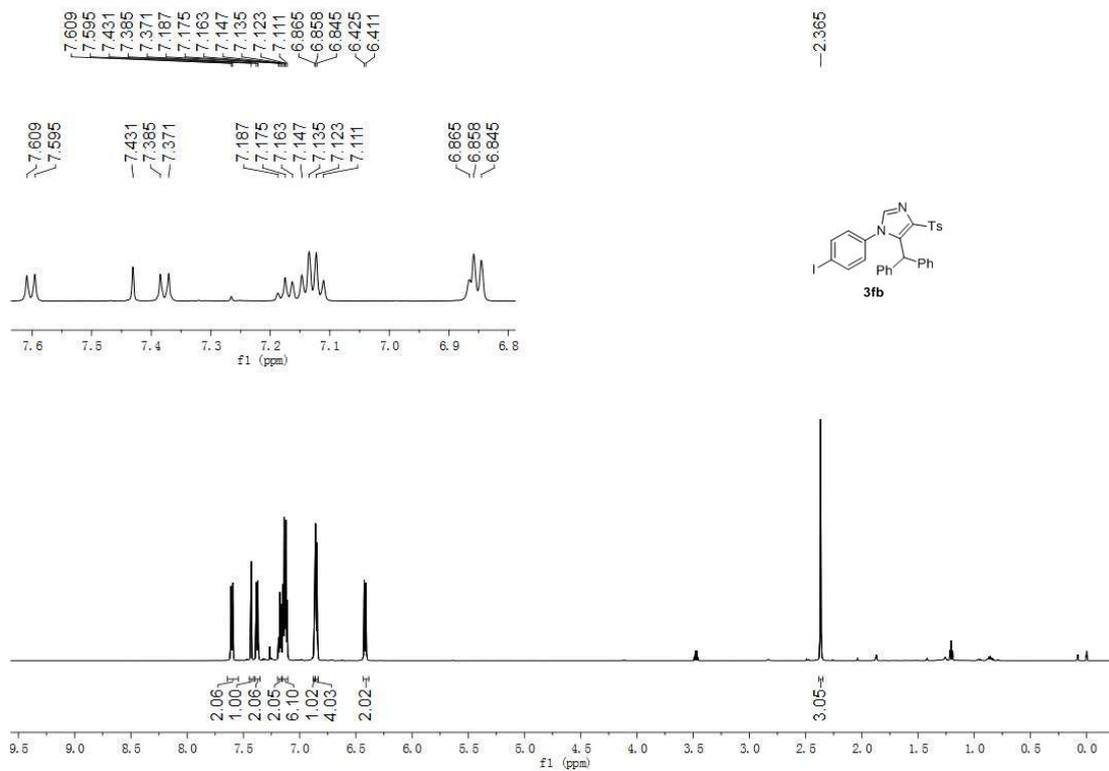
¹H NMR (600 MHz, CDCl₃) for 3eb



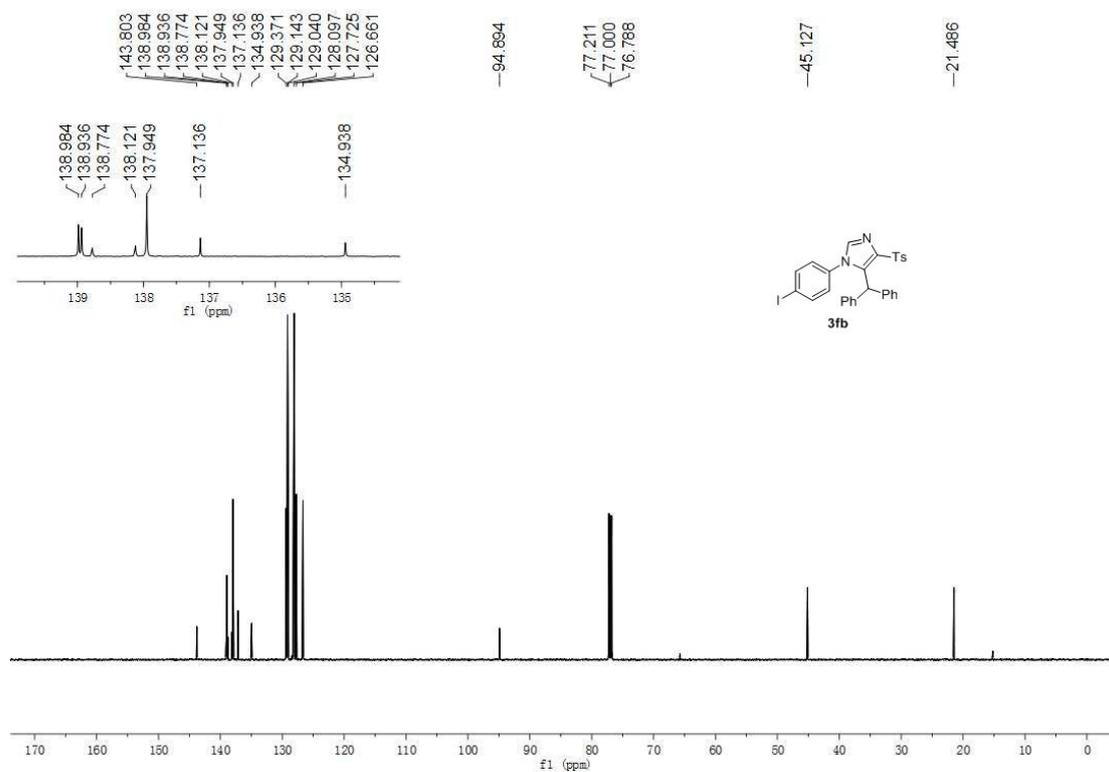
¹³C NMR (151 MHz, CDCl₃) for 3eb



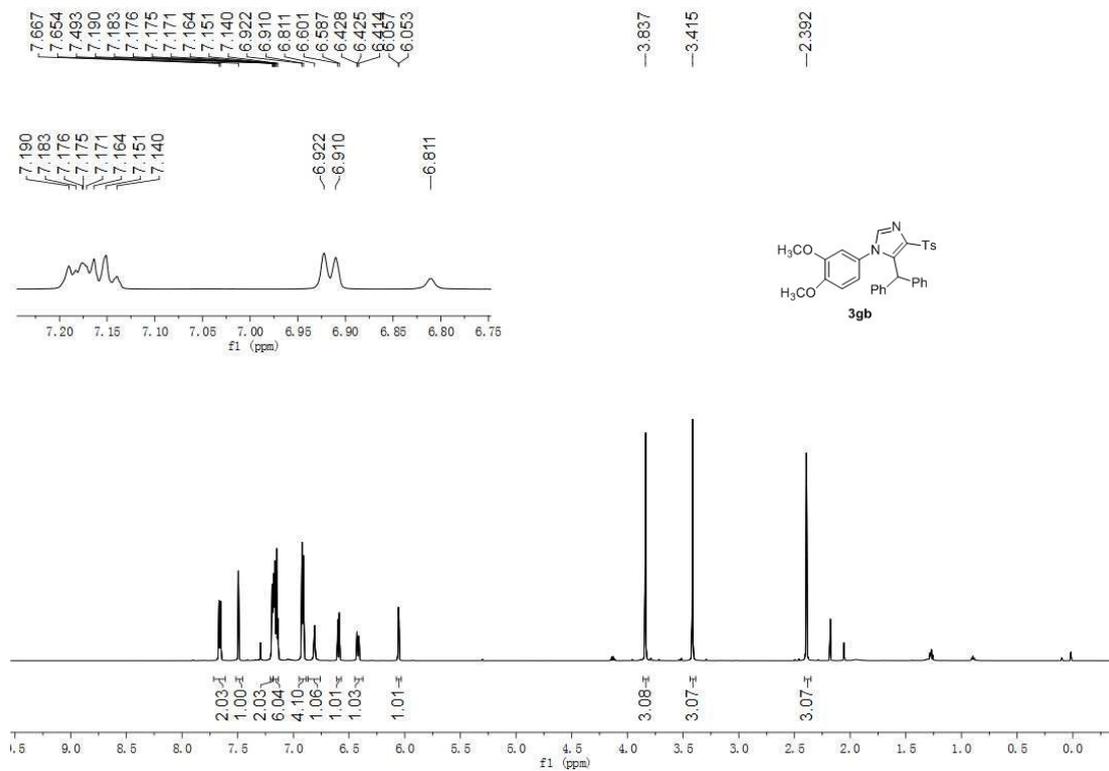
¹H NMR (600 MHz, CDCl₃) for 3fb



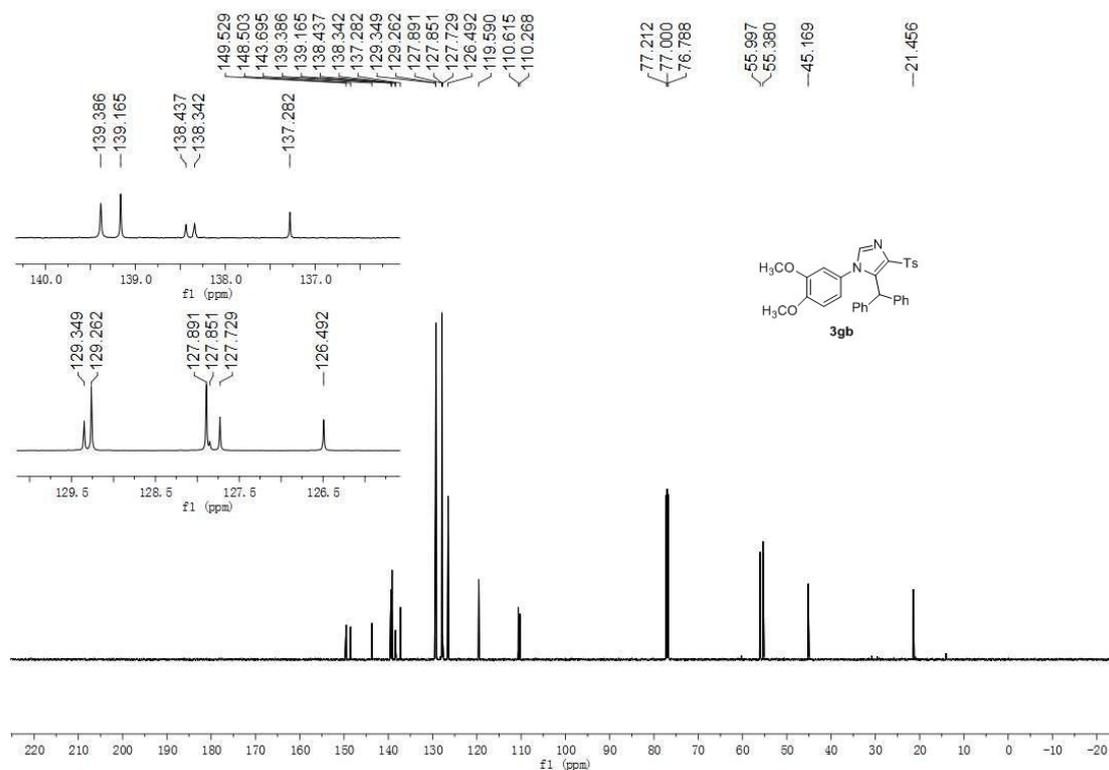
¹³C NMR (151 MHz, CDCl₃) for 3fb



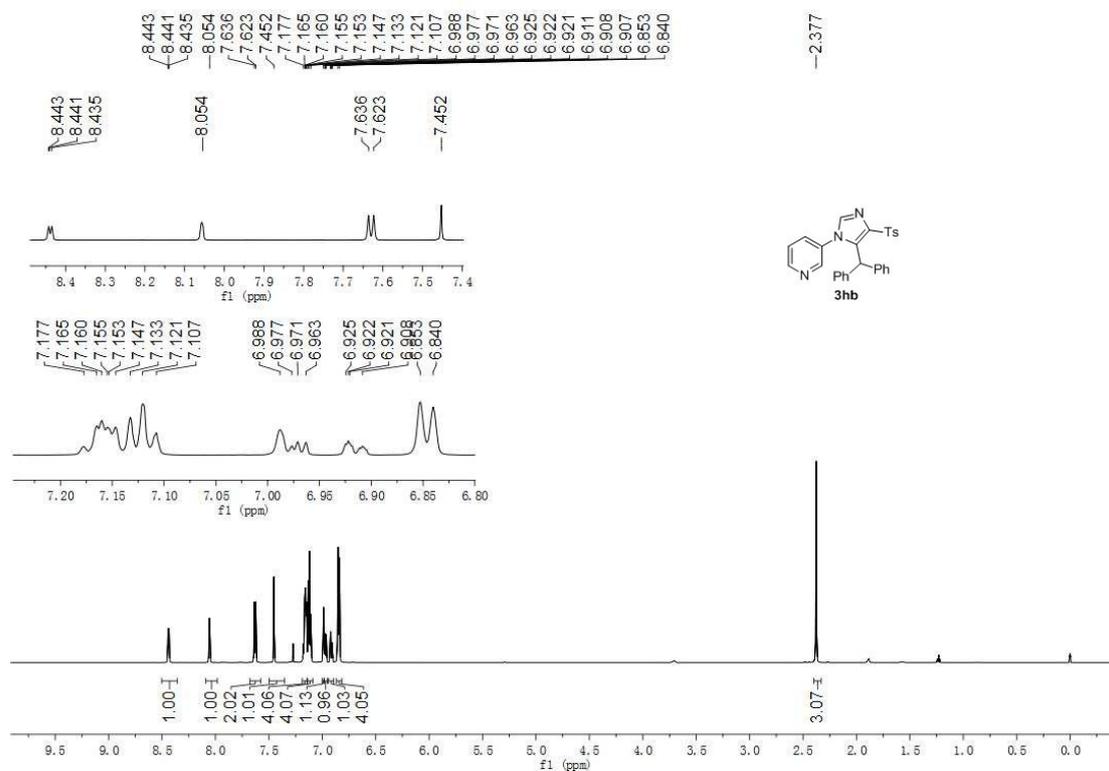
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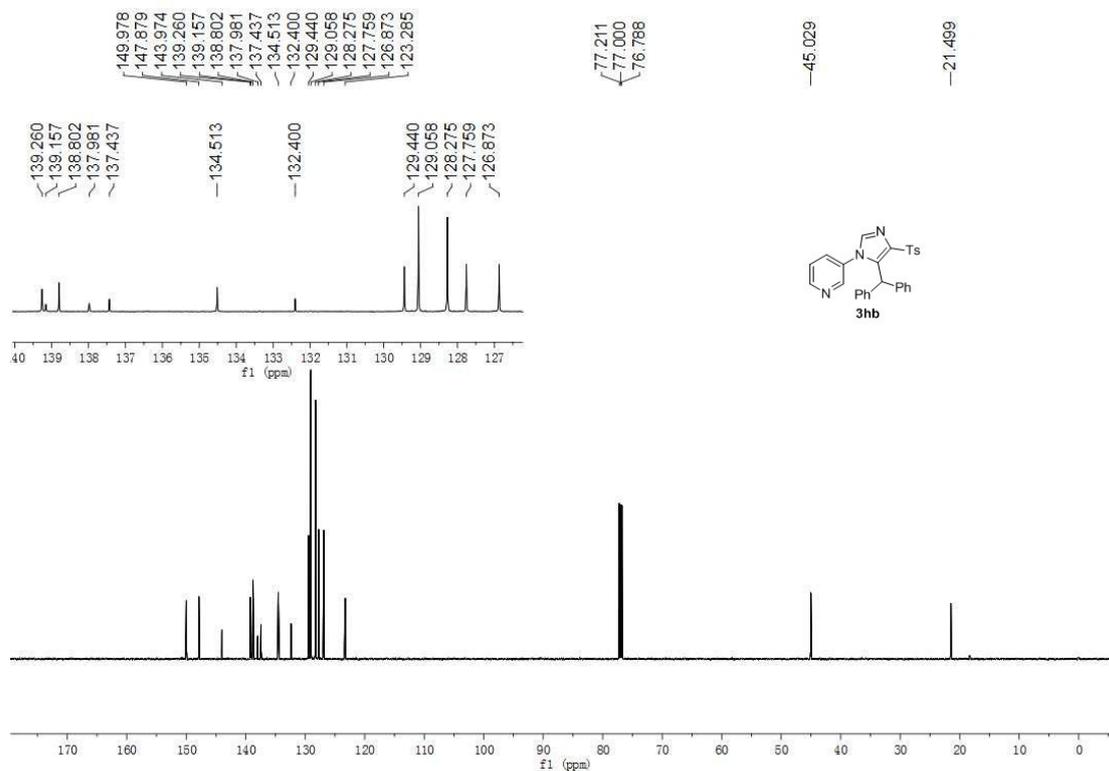
¹³C NMR (151 MHz, CDCl₃) for 3gb



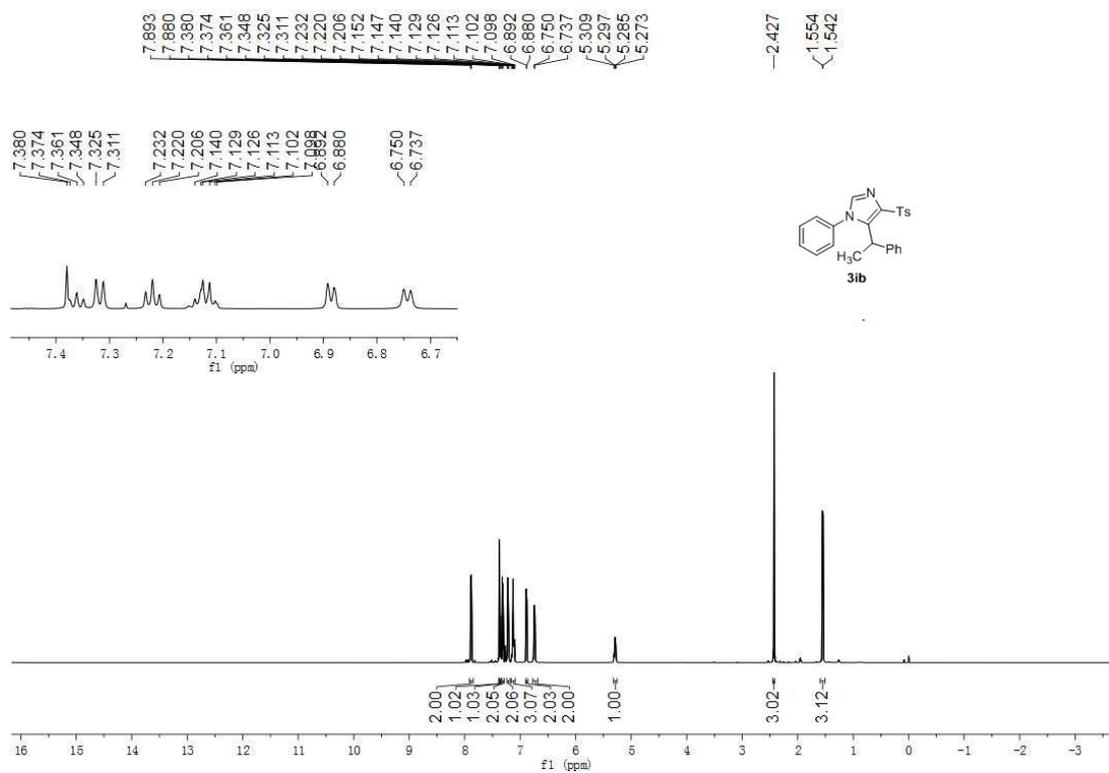
¹H NMR (600 MHz, CDCl₃) for 3hb



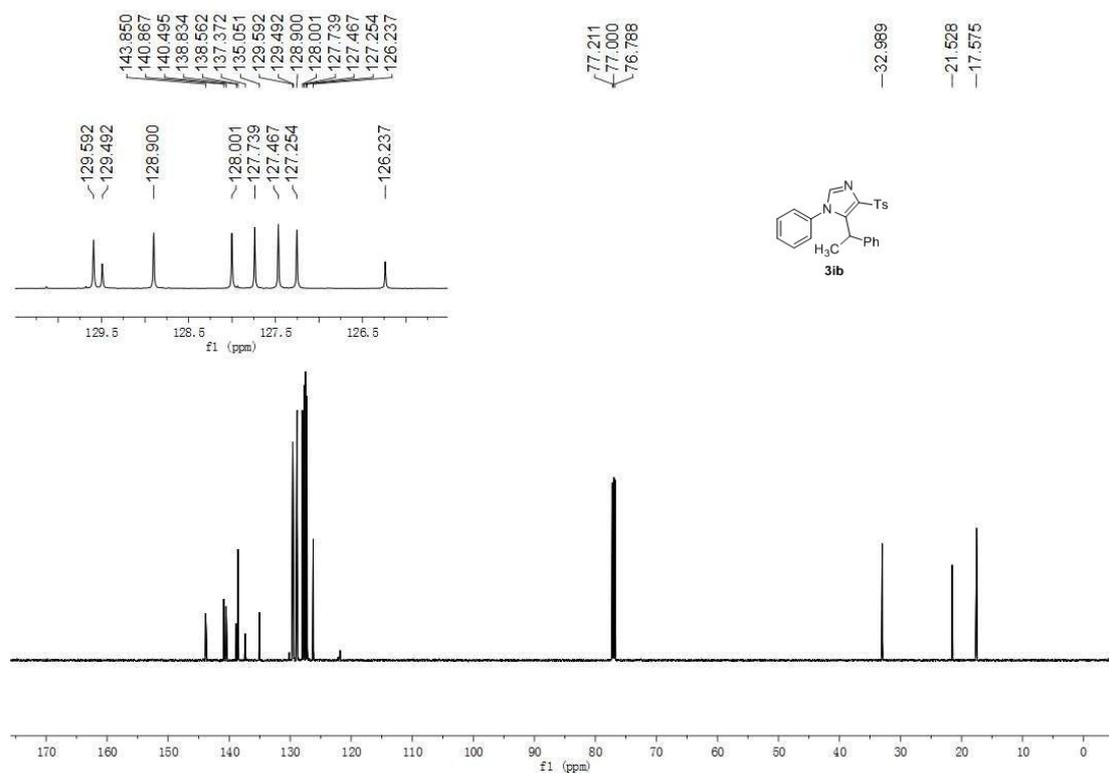
¹³C NMR (151 MHz, CDCl₃) for 3hb



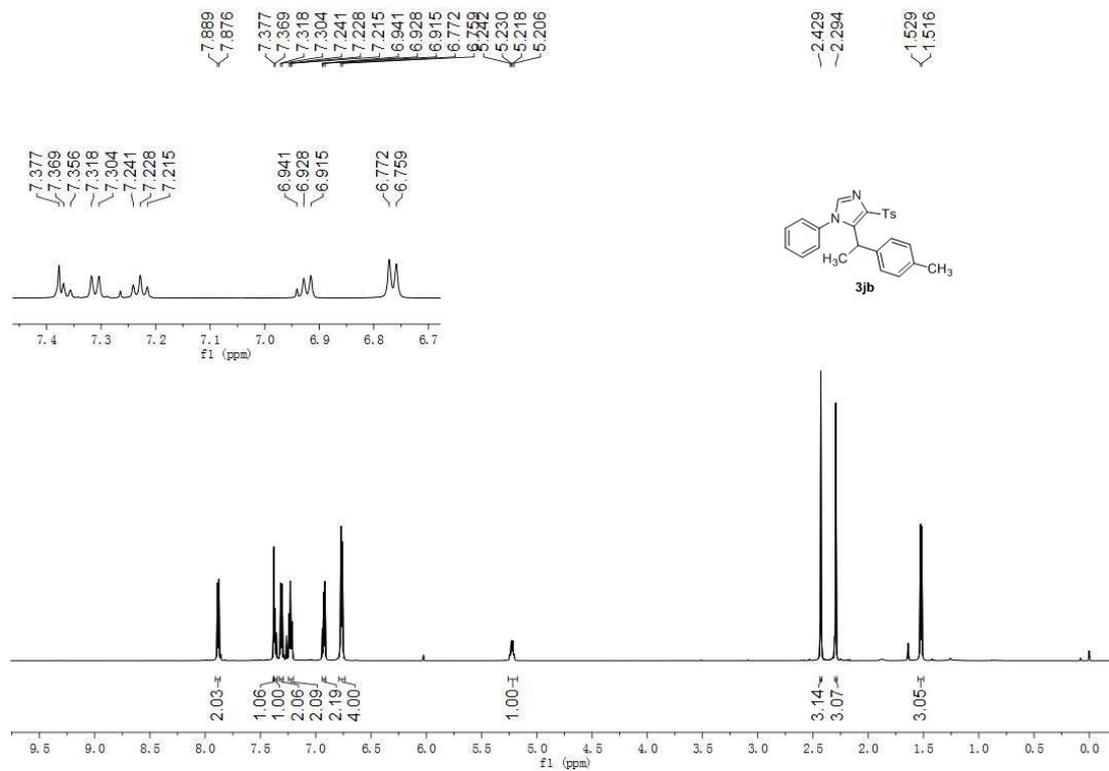
¹H NMR (600 MHz, CDCl₃) for 3ib



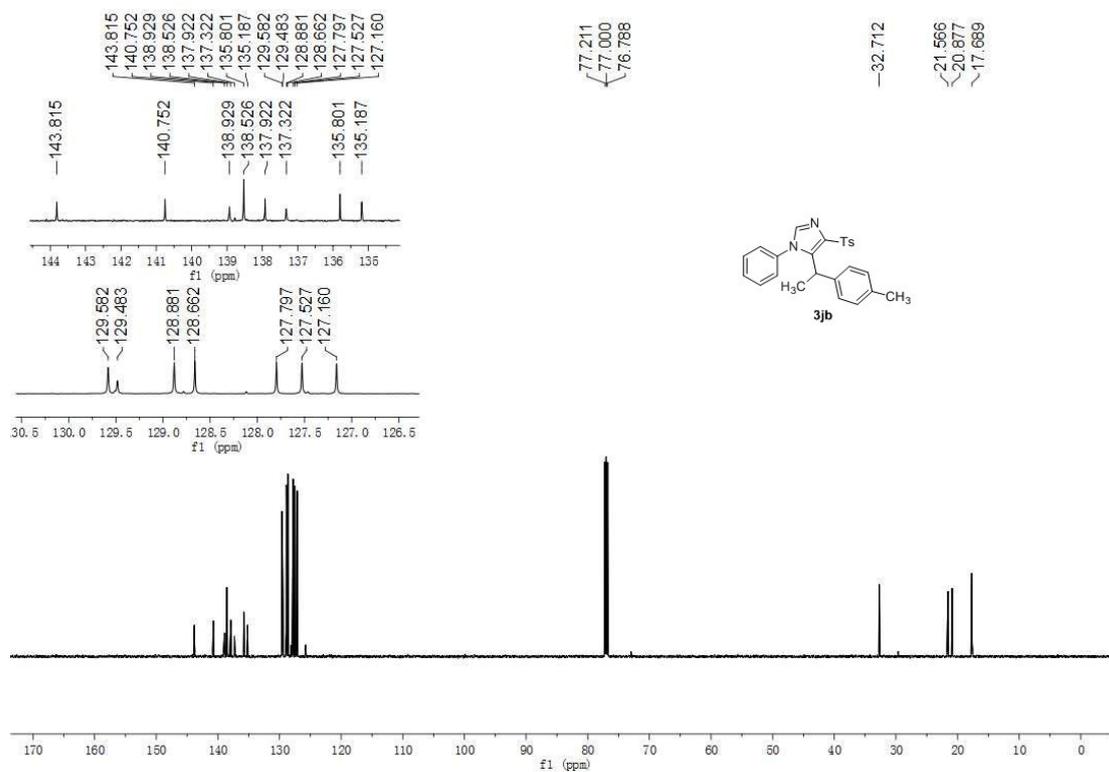
¹³C NMR (151 MHz, CDCl₃) for 3ib



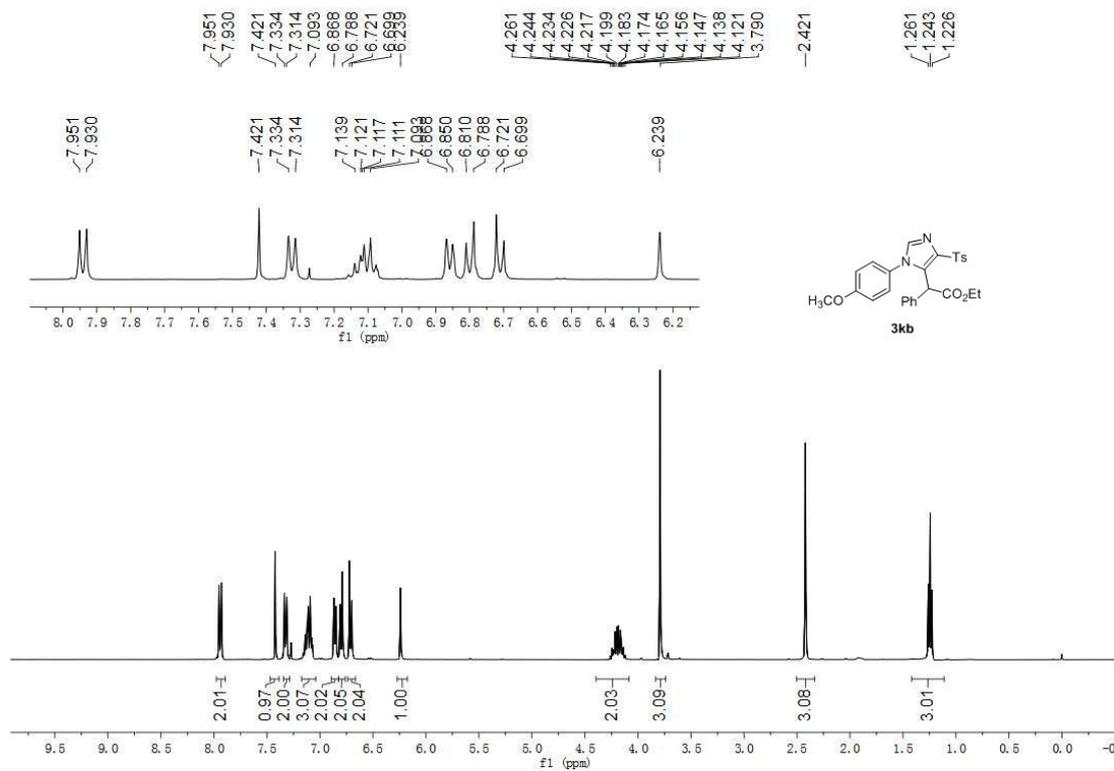
¹H NMR (600 MHz, CDCl₃) for 3jb



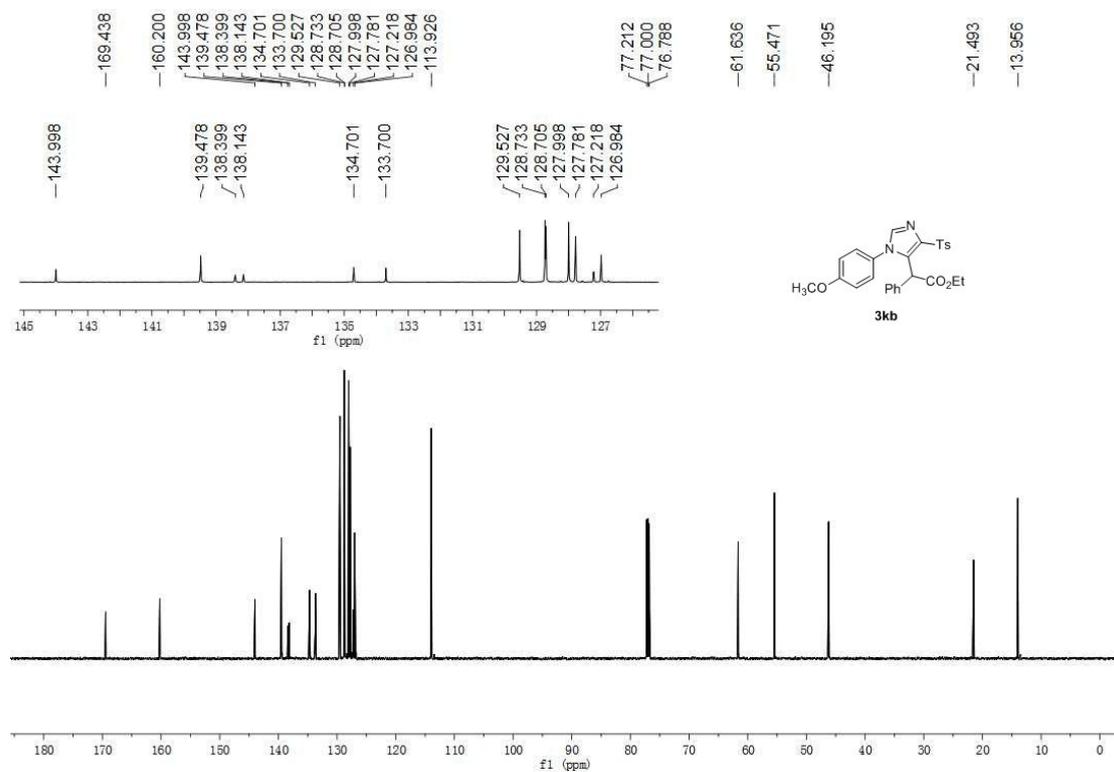
¹³C NMR (151 MHz, CDCl₃) for 3jb



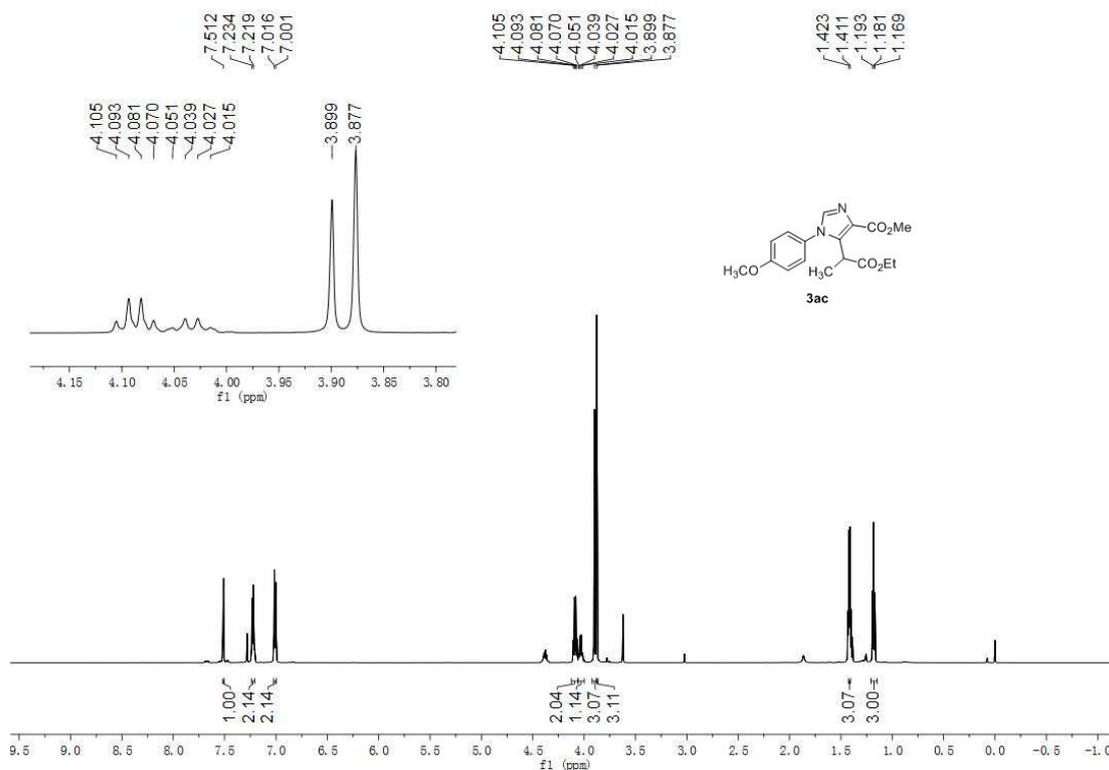
¹H NMR (400 MHz, CDCl₃) for 3kb



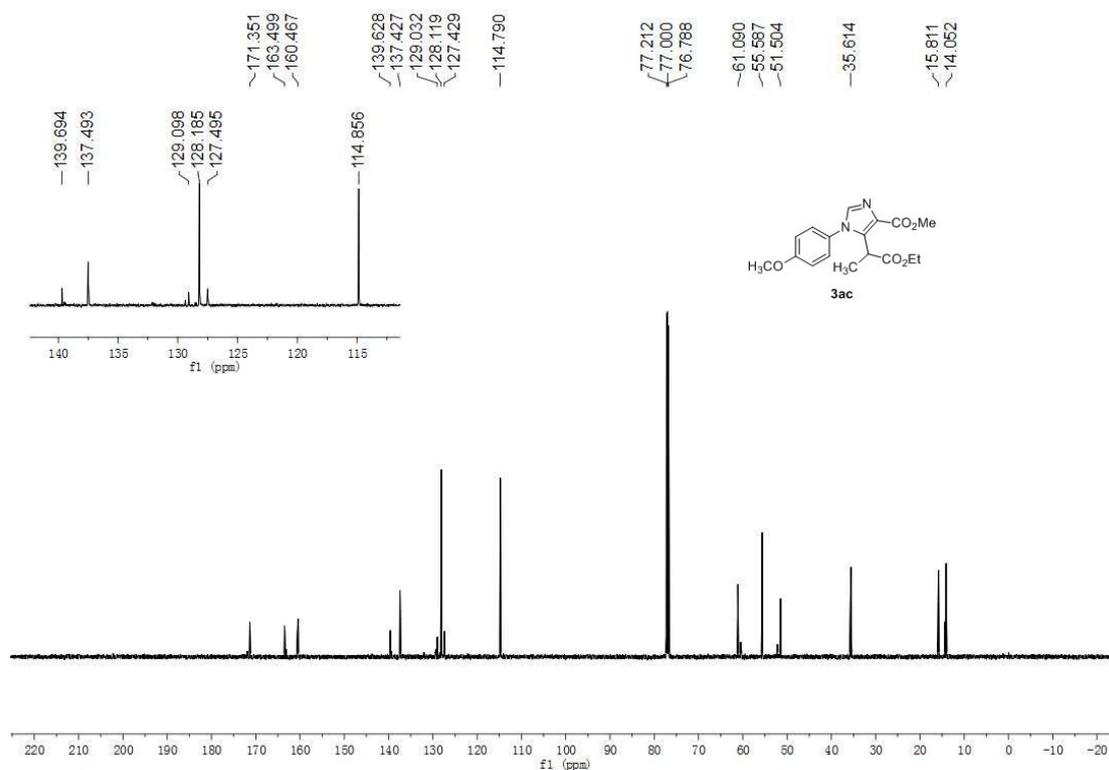
¹³C NMR (151 MHz, CDCl₃) for 3kb



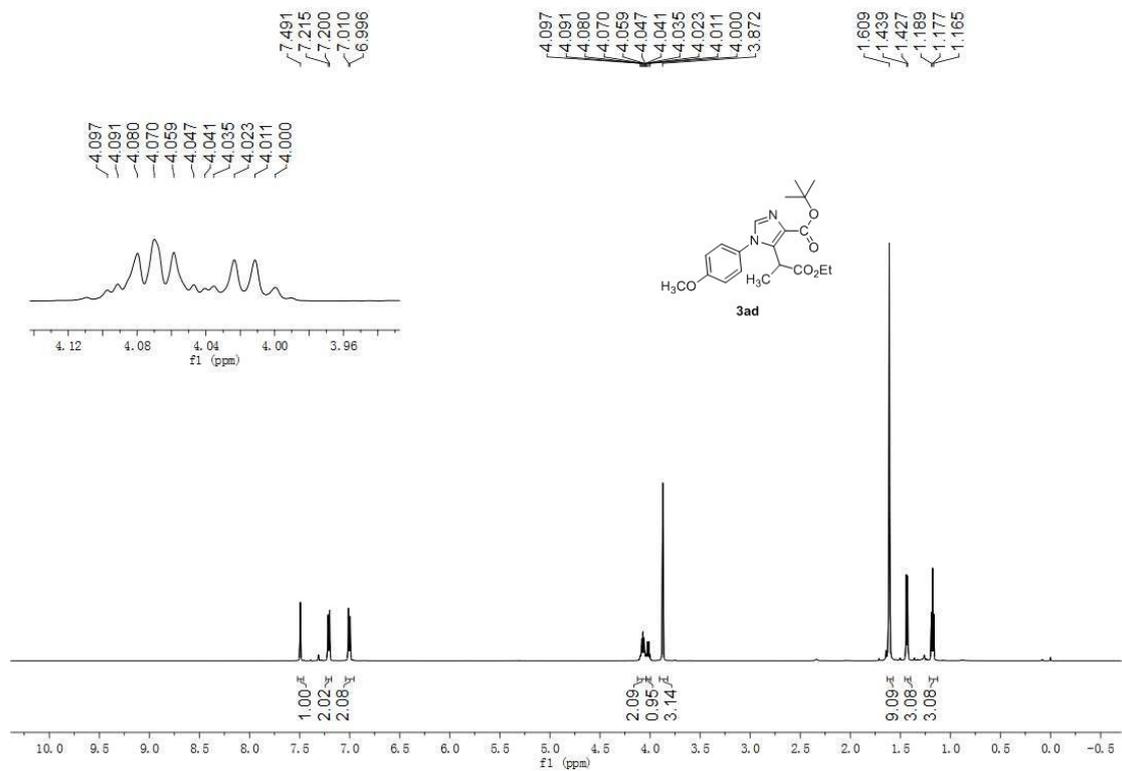
¹H NMR (600 MHz, CDCl₃) for 3ac



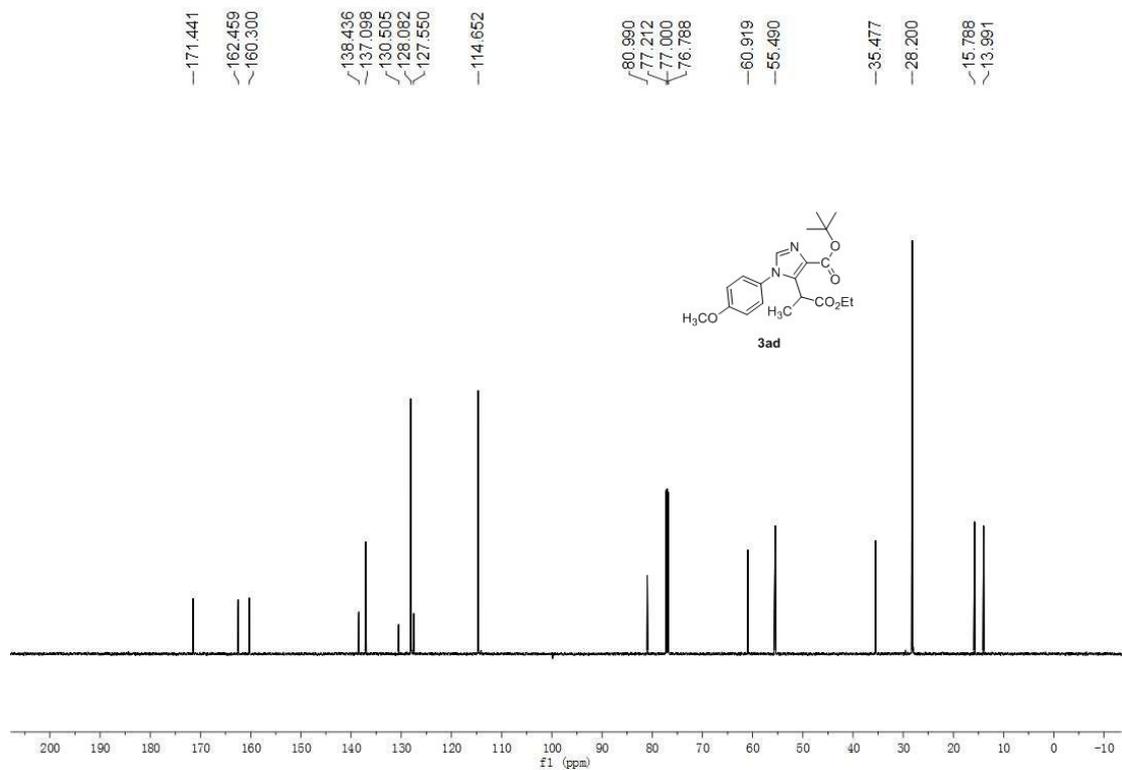
¹³C NMR (151 MHz, CDCl₃) for 3ac



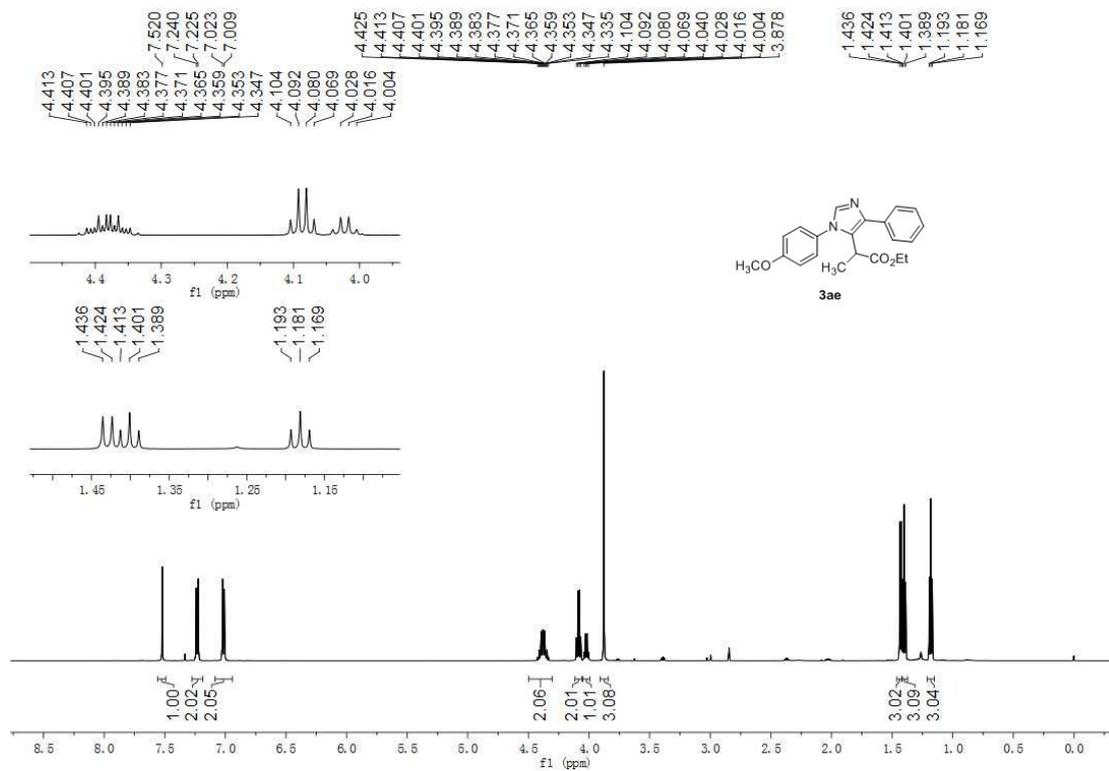
¹H NMR (600 MHz, CDCl₃) for 3ad



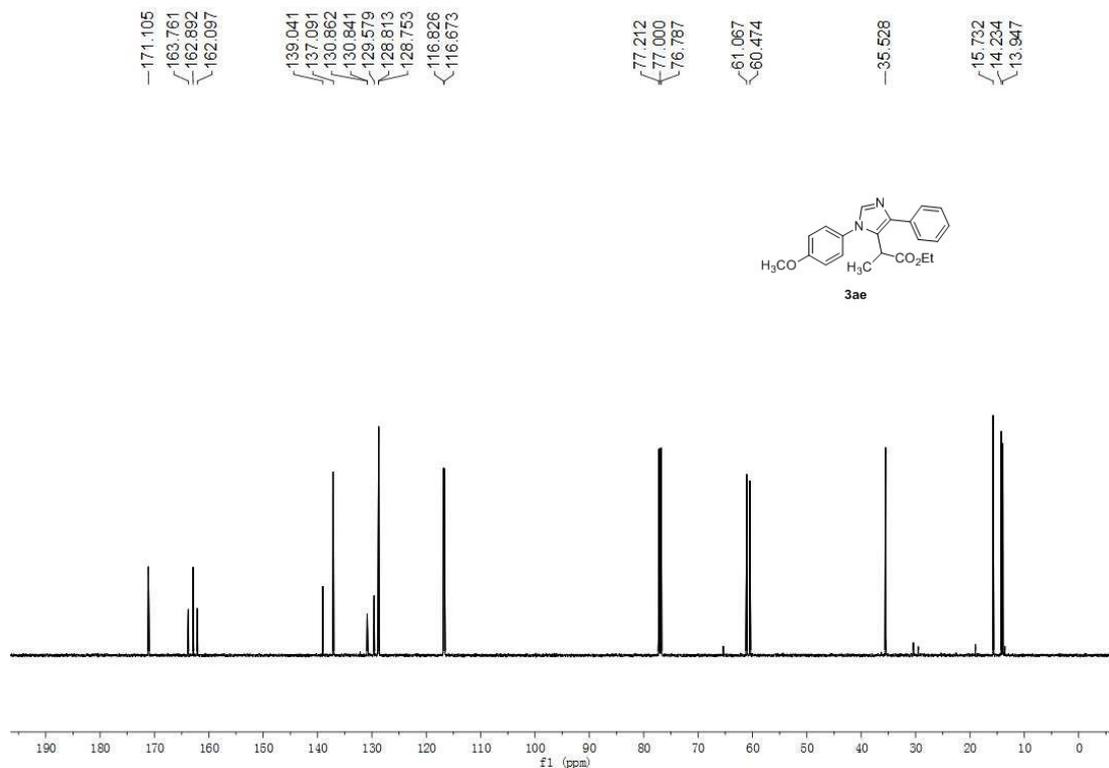
¹³C NMR (151 MHz, CDCl₃) for 3ad



¹H NMR (600 MHz, CDCl₃) for 3ae



¹³C NMR (151 MHz, CDCl₃) for 3ae



5. X-ray Crystallographic Data of compounds 3fb

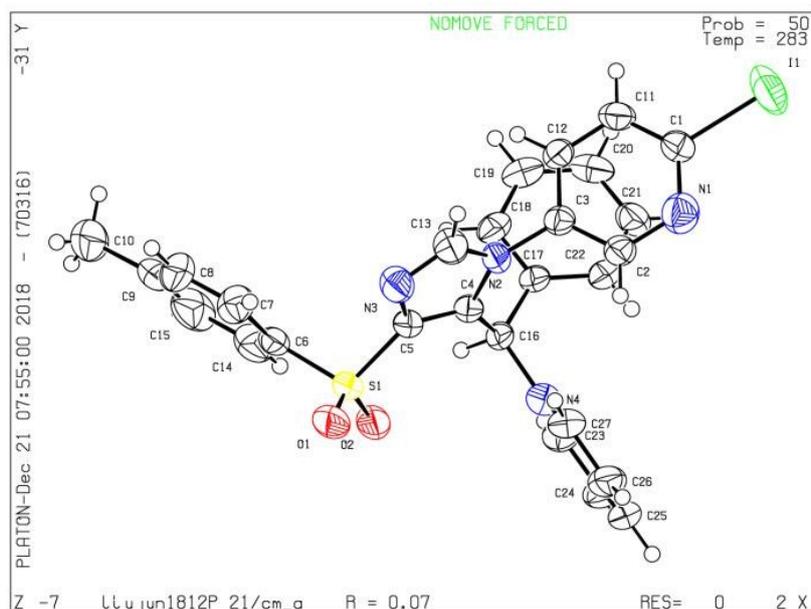
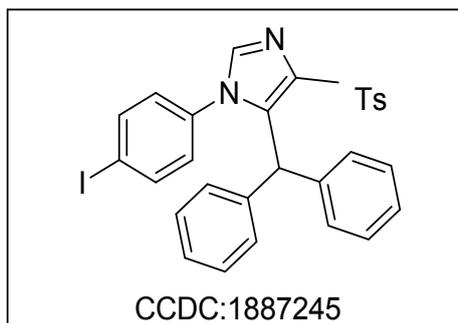


Table 1. Crystal data and structure refinement for liujun181221_1_0m_a.

Identification code	liujun181221_1_0m_a
Empirical formula	C ₂₉ H ₂₃ IN ₂ O ₂ S
Formula weight	590.45
Temperature	283(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
space group	P2(1)/c
Unit cell dimensions	a = 12.861(7) Å a = 90 ° b = 15.356(9) Å b = 107.411(15) ° c = 13.575(7) Å g = 90 °
Volume	2558(2) Å ³
Z	4
Calculated density	1.533 mg/m ³
Absorption coefficient	1.362 mm ⁻¹
F(000)	1184.0
Crystal size	0.21 x 0.19 x 0.16 mm

Theta range for data collection	2.65 to 26.09 °
Limiting indices	-15<=h<=15, -19<=k<=18, -16<=l<=14
Reflections collected	35806
Unique	5046 [R(int) = 0.0640]
Completeness to theta = 25.00	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8115 and 0.7629
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5046 / 0 / 317
Goodness-of-fit on F ²	1.111
Final R indices [I>2sigma(I)]	R1 = 0.0652, wR2 = 0.1640
R indices (all data)	R1 = 0.0974, wR2 = 0.2022
Extinction coefficient	0.0263(18)
Largest diff. peak and hole	1.160 and -1.295 e. Å ⁻³