An efficient nickel/silver co-catalyzed remote C−H amination of 8-aminoquinolines with azodicarboxylates at room temperature

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Supporting Information

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Experimental Section

Instrumentation and chemicals

^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard, operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Melting points were

measured by SGW X-4A microscopic apparatus. The X-ray crystallography was measured on Bruker D8 VENTURE PHOTON instrument. HRMS-ESI were measured by Q Exactive LC/HRMS spectrometer. Dichloromethane, ethyl acetate and hexane were used for column chromatography without further purification. All solvents and chemicals were obtained from commercial sources and used as received unless otherwise noted. All the *N*-(8-quinolyl)amides (**1**) were synthesized through the coupling between corresponding aryl or alkyl acids and 8-aminoquinoline as our previous work.[1]

Experimental procedures

General procedure for the nickel/silver co-catalyzed C−H amination of 8-aminoquinoline. A mixture of N-(8-quinolinyl)amide (0.2 mmol), azodicarboxylate (0.4 mmol), $AgNO_3$ (3 mol%) and $Ni(acac)_2$ (3 mol%) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then acetone (2 mL) was introduced. The resulting mixture was stirred at 25 °C for 12 h. After the reaction was complete, the mixture was added into H_2O (25 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous $MgSO_4$ and filtered. After removal of the solvent in vacuo, the residue was purified by column chromatography (ethyl acetate/hexane) to afford the pure product.

Characterization Data

Diethyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3aa)

White solid, mp 130–132 °C; 1H NMR (400 MHz, CDCl3): δ 9.83 (s, 1H), 8,81 (dd, J = 4.28 Hz, J = 1.60 Hz, 1H), 8.74 (d, J = 8.32 Hz, 1H), 8.58 (s, 1H), 7.63 (d, J = 8.36 Hz, 1H), 7.51 (dd, J = 8.56 Hz, J = 4.20 Hz, 1H), 7.45 (s, 1H), 4.23–4.17 (m, 4H), 2.35 (s, 3H), 1.29–1.23 (m, 6H); 13C NMR (100 MHz, CDCl3): δ 168.9, 148.4, 138.3, 134.9, 132.6, 131.9, 126.6, 125.4, 122.1, 115.8, 63.2, 62.3, 25.1, 14.4. HRMS-ESI(m/z): calcd for $C_{17}H_{20}N_4O_5$ ($M+H^+$): 361.1512, found 361.1515.

Diethyl 1-(8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ba)

White solid, mp 152–153 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1H), 8,80 (dd, *J* = 4.32 Hz, *J* = 1.64 Hz, 1H), 8.75 (d, *J* = 8.32 Hz, 1H), 8.58 (s, 1H), 7.66–7.63 (m, 2H), 7.50 (dd, *J* = 8.52 Hz, *J* = 4.16Hz, 1H), 4.22–4.16 (m, 4H), 2.63–2.57 (m, 2H), 1.33 (t, *J* = 7.56 Hz, 3H), 1.26–1.05 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 156.5, 156.2, 148.3, 138.4, 134.9, 132.6, 131.8, 126.6, 125.4, 122.1, 115.7, 63.3, 62.3, 31.3, 14.4, 9.7. HRMS-ESI(m/z): calcd for $C_{18}H_{22}N_4O_5$ ($M+H^+$): 375.1668, found 375.1670.

Diethyl 1-(8-butyramidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ca)

White solid, mp 149–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.85 (s, 1H), 8,81 (dd, *J* = 4.32 Hz, *J* = 1.68 Hz, 1H), 8.76 (d, *J* = 8.32 Hz, 1H), 8.59–8.57 (m, 1H), 7.66–7.61 (m, 2H), 7.50 (dd, *J* = 8.48 Hz, *J* = 4.16Hz, 1H), 4.23–4.16 (m, 4H), 2.54 (t, *J* = 7.64 Hz, 2H), 1.88–1.81 (m, 2H) , 1.34–1.22 (m, 6H), 1.05 (t, *J* = 7.40 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 156.5, 156.1, 148.3, 138.4, 134.9, 132.6, 131.8, 126.6, 125.4, 122.1, 115.7, 63.2, 62.3, 40.1, 19.1, 14.4, 13.8. HRMS-ESI(m/z): calcd for $C_{19}H_{24}N_4O_5$ ($M+H^+$): 389.1825, found 389.1827.

Diethyl 1-(8-(3-phenylpropanamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3da)

yellow solid, mp 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.79–8.75 (m, 2H), 8.57 (s, 1H), 7.64 (d, *J* = 8.36 Hz, 1H), 7.52–7.45 (m, 2H), 7.30–7.27 (m, 4H), 7.22–7.17 (m, 1H), 4.23–4.17 (m, 4H), 3.16–3.12 (m, 2H), 2.92–2.87 (m, 2H), 1.29–1.23 (m, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 156.5, 156.2, 148.3, 140.6, 138.3, 134.8, 132.5, 131.9, 128.6, 128.4, 126.6, 126.3, 125.4, 122.1, 115.8, 63.3, 62.3, 39.7, 31.4, 14.4. HRMS-ESI(m/z): calcd for $C_{24}H_{26}N_4O_5$ ($M+H^+$): 451.1981, found 451.1983.

Diethyl 1-(8-isobutyramidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ea)

yellow solid, mp 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.94 (s, 1H), 8,81 (dd, *J* = 4.28 Hz, *J* = 1.56Hz, 1H), 8.76 (d, *J* = 8.40 Hz, 1H), 8.59 (s, 1H), 7.68–7.63 (m, 2H), 7.50 (dd, *J* = 8.48 Hz, *J* = 4.16Hz, 1H), 4.23–4.15 (m, 4H), 2.82–2.73 (m, 1H), 1.38–1.18 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 156.5, 156.1, 148.4, 138.5, 135.0, 132.6, 131.8, 126.7, 125.4, 122.1, 115.8, 63.2, 62.3, 37.1, 19.7, 14.4. HRMS-ESI(m/z): calcd for $C_{19}H_{24}N_4O_5$ ($M+H^+$): 389.1825, found 389.1828.

Diethyl 1-(8-pivalamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3fa)

Light yellow solid, mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.31 (s, 1H), 8,82 (dd, *J* = 4.28 Hz, *J* = 1.68 Hz, 1H), 8.77 (d, *J* = 8.32 Hz, 1H), 8.57 (s, 1H), 7.64 (d, *J* = 8.36 Hz, 1H), 7.53–7.46 (m, 2H), 4.22–4.16 (m, 4H), 1.42 (s, 9H), 1.29–1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 156.4, 155.3, 152.3, 148.4, 138.8, 135.1, 132.5, 131.8, 126.6, 125.4, 122.0, 115.5, 64.1, 63.2, 62.5, 62.3, 40.4, 27.7, 14.4, 14.1. HRMS-ESI(m/z): calcd for $C_{20}H_{26}N_4O_5$ ($M+H^+$): 403.1981, found 403.1980.

Diethyl 1-(8-(cyclohexanecarboxamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ga)

White solid, mp 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.83–8.81 (m, 1H), 8.77 (d, *J* = 8.36 Hz, 1H), 8.58 (s, 1H), 7.63 (d, *J* = 8.32 Hz, 1H), 7.51 (dd, *J* = 8.56 Hz, *J* = 4.24 Hz, 1H), 7.43 (s, 1H), 4.24–4.14 (m, 4H),

2.52–2.43 (m, 1H), 2.11–2.03 (m, 2H), 1.91–1.84 (m, 2H), 1.77–1.69 (m, 2H), 1.68–1.57 (m, 2H), 1.44–1.36 (m, 2H), 1.26–1.07 (m, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 156.4, 148.3, 138.6, 135.1, 132.6, 131.7, 126.6, 125.4, 122.1, 115.7, 63.2, 62.3, 46.9, 29.7, 25.8, 25.7, 14.4. HRMS-ESI(m/z): calcd for $C_{22}H_{28}N_4O_5$ ($M+H^+$): 429.2138, found 429.2140.

Diethyl 1-(8-(cyclopropanecarboxamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ha)

Yellow solid, mp 212–214 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.06 (s, 1H), 8.85–8.82 (m, 1H), 8.72 (d, *J* = 8.32 Hz, 1H), 8.57 (s, 1H), 7.61 (d, *J* = 8.32 Hz, 1H), 7.55–7.51 (m, 1H), 7.21 (s, 1H), 4.25–4.17 (m, 4H), 1.85–1.77 (m, 1H), 1.29–1.23 (m, 6H), 1.17–1.15 (m, 2H), 0.95–0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 148.3, 138.3, 135.2, 132.5, 131.6, 126.6, 125.4, 122.1, 115.7, 63.2, 62.4, 16.3, 14.4, 8.3. HRMS-ESI(m/z): calcd for $C_{19}H_{22}N_4O_5$ ($M+H^+$): 387.1668, found 387.1665.

Diethyl 1-(8-methacrylamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ia)

Yellow solid, mp 154–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H), 8.84–8.79 (m, 2H), 8.59 (s, 1H), 7.66 (d, *J* = 8.36 Hz, 1H), 7.54–7.50 (m, 2H), 6.05 (s, 1H), 5.57 (d, *J* = 1.8 Hz, 1H), 4.24–4.16 (m, 4H), 2.18 (s, 1H), 1.28–1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 156.5, 148.5, 140.6, 138.8, 134.9, 132.6, 132.1, 126.6, 125.5, 122.1, 120.9, 115.8, 63.2, 62.3, 18.7, 14.4. HRMS-ESI(m/z): calcd for $C_{19}H_{22}N_4O_5$ ($M+H^+$): 387.1668, found 387.1670.

Diethyl 1-(8-benzamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ja)

Yellow solid, mp 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.79 (s, 1H), 8.92 (d, *J* = 8.32 Hz, 1H), 8.87–8.85 (m, 1H), 8.63–8.60 (m, 1H), 8.10–8.06 (m, 2H), 7.73–7.63 (m, 2H), 7.61–7.51 (m, 4H), 4.22–4.18 (m, 4H), 1.28–1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 156.5, 156.0, 148.5, 138.8, 135.0, 134.9, 132.6, 132.0, 128.9, 127.3, 126.7, 125.5, 122.2, 115.9, 63.2, 62.3, 14.4. HRMS-ESI(m/z): calcd for $C_{22}H_{22}N_4O_5$ ($M+H^+$): 423.1668, found 423.1670.

Diethyl 1-(8-(2-methylbenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ka)

White solid, mp 59–62 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.26 (s, 1H), 8.93 (d, *J* = 8.36 Hz, 1H), 8.80–8.77 (m, 1H), 8.61–8.58 (m, 1H), 7.73–7.66 (m, 2H), 7.59 (s, 1H), 7.51 (dd, *J* = 8.56 Hz, *J* = 4.16 Hz, 1H), 7.43–7.38 (m, 1H), 7.35–7.30 (m, 2H), 4.26–4.15 (m, 4H), 2.59 (s, 3H), 1.27–1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 156.5, 148.5, 138.7, 136.8, 136.4, 135.1, 132.6, 132.2, 131.5, 130.5, 127.3, 126.6, 126.1, 125.5, 122.2, 115.8, 63.3, 62.3,

20.2, 14.4. HRMS-ESI(m/z): calcd for $C_{23}H_{24}N_4O_5$ ($M+H^+$): 437.1825, found 437.1824.

Diethyl 1-(8-(4-methylbenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3la)

Yellow solid, mp 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.76 (s, 1H), 8.91 (d, *J* = 8.36 Hz, 1H), 8.88–8.85 (m, 1H), 8.61 (s, 1H), 7.99–7.96 (m, 2H), 7.70 (d, *J* = 8.36 Hz, 1H), 7.56–7.51 (m, 2H), 7.34 (d, *J* = 8.00 Hz, 2H), 4.26–4.17 (m, 4H), 2.45 (s, 3H), 1.27–1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 156.4, 148.5, 142.6, 138.8, 135.1, 132.6, 132.1, 129.5, 127.4, 126.7, 125.5, 122.2, 115.8, 63.2, 62.3, 21.6, 14.4, 14.2. HRMS-ESI(m/z): calcd for $C_{23}H_{24}N_4O_5$ ($M+H^+$): 437.1825, found 437.1826.

Diethyl 1-(8-(4-methoxybenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ma)

White solid, mp 204–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.72 (s, 1H), 8.90 (d, *J* = 8.32 Hz, 1H), 8.86 (dd, *J* = 4.28 Hz, *J* = 1.64 Hz, 1H), 8.60 (s, 1H), 8.08–8.03 (m, 2H), 7.69 (d, *J* = 8.40 Hz, 1H), 7.56–7.52 (m, 1H), 7.41 (s, 1H), 7.06–7.02 (m, 2H), 4.24–4.17 (m, 4H), 3.90 (s, 3H), 1.27–1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 162.7, 148.4, 138.8, 135.2, 132.6, 131.9, 129.2, 127.2, 126.7, 125.5, 122.2, 115.7, 114.1, 63.2, 62.4, 55.5, 14.4. HRMS-ESI(m/z): calcd for $C_{23}H_{24}N_4O_6$ ($M+H^+$): 453.1774, found 453.1775.

Diethyl 1-(8-(4-fluorobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3na)

White solid, mp 127–129 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.74 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 8.12–8.06 (m, 2H), 7.70 (d, *J* = 8.32 Hz, 1H), 7.57–7.53 (m, 1H), 7.46–7.43 (m, 1H), 7.25–7.19 (m, 2H), 4.25–4.17 (m, 4H), 1.28–1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 164.4, 163.9, 148.6, 138.8, 134.9, 132.7, 132.2, 131.1 (d, *J* = 3.11 Hz), 129.8, 129.7, 126.6, 125.5, 122.3, 116.0 (d, *J* = 21.87 Hz), 115.9, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for $C_{22}H_{21}FN_4O_5$ ($M+H^+$): 441.1574, found 441.1578.

Diethyl 1-(8-(4-chlorobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3oa)

White solid, mp 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.75 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 8.03–7.99 (m, 2H), 7.70 (d, *J* = 8.40Hz, 1H), 7.57–7.50 (m, 4H), 4.26–4.17 (m, 4H), 1.27–1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 156.5, 148.6, 138.8, 138.4, 134.7, 133.3, 132.7, 132.3, 129.1, 128.8, 126.6, 125.5, 122.3, 116.0, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for $C_{22}H_{21}ClN_4O_5$ ($M+H^+$): 457.1279, found 457.1280.

Diethyl 1-(8-(4-bromobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3pa)

White solid, mp 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.75 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 7.96–

7.92 (m, 2H), 7.71–7.66 (m, 3H), 7.55 (dd, J = 7.76 Hz, J = 4.20 Hz, 1H), 7.39 (s, 1H), 4.25–4.19 (m, 4H), 1.29–1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 156.4, 148.6, 138.8, 134.8, 133.8, 132.7, 132.4, 132.1, 128.9, 126.8, 126.6, 125.5, 122.3, 116.0, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for $C_{22}H_{21}BrN_4O_5$ ($M+H^+$): 501.0774, found 501.0775.

Diethyl 1-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3qa)

White solid, mp 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.82 (s, 1H), 8.91–8.86 (m, 2H), 8.62 (s, 1H), 8.18 (d, J = 8.04 Hz, 2H), 7.82 (d, J = 8.20 Hz, 2H), 7.72 (d, J = 8.32 Hz, 1H), 7.58–7.51 (m, 2H), 4.26–4.17 (m, 4H), 1.29–1.09(m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 156.4, 155.9, 148.7, 138.8, 138.2, 134.5, 133.7 (q, J = 32.57 Hz), 132.6, 127.8, 126.6, 126.0 (q, J = 3.64 Hz), 125.5, 125.0, 122.3, 116.1, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for $C_{23}H_{21}F_3N_4O_5$ ($M+H^+$): 491.1542, found 491.1541.

Diethyl 1-(2-methyl-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ra)

Yellow solid, mp 165–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H), 8.73 (d, J = 8.28 Hz, 1H), 8.45 (s, 1H), 7.55 (d, J = 8.32 Hz, 1H), 7.44 (s, 1H), 7.38 (d, J = 8.60 Hz, 1H), 4.24–4.17 (m, 4H), 2.74 (s, 3H), 2.61 (dd, J = 15.12 Hz, J = 7.52 Hz, 2H), 1.37–1.23 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 157.5, 156.4, 137.8, 134.3, 132.6, 131.8, 125.5, 123.5, 123.0, 115.7, 63.1, 62.3, 31.2, 25.2, 14.4, 9.7. HRMS-ESI(m/z): calcd for $C_{19}H_{24}N_4O_5$ ($M+H^+$): 389.1825, found 389.1828.

Diethyl 1-(4-chloro-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3sa)

Yellow solid, mp 92–95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91–9.88(m, 1H), 8.86–8.82 (m, 1H), 8.66–8.61 (m, 1H), 8.08–8.05 (m, 1H), 7.58–7.54 (m, 1H), 7.01–6.92 (m, 1H), 4.23–4.15 (m, 4H), 2.62–2.54 (m, 2H), 1.32–1.31 (m, 3H), 1.28–1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 156.3, 155.7, 155.5, 152.3, 147.1, 140.4, 140.2, 139.4, 139.2, 136.1, 135.9, 132.6, 132.1, 129.2, 124.8, 122.8, 122.5, 116.8, 64.1, 63.1, 62.5, 62.2, 31.3, 14.5, 14.4, 9.6. HRMS-ESI(m/z): calcd for $C_{18}H_{21}ClN_4O_5$ ($M+H^+$): 409.1279, found 409.1277.

Diethyl 1-(6-methoxy-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ta)

White solid, mp 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 8.86–8.77 (m, 2H), 8.64–8.62 (m, 1H), 7.49–7.45 (m, 1H), 7.35 (s, 1H), 4.24–4.07 (m, 4H), 4.00 (s, 3H), 2.63–2.57 (m, 2H), 1.33–1.28 (m, 3H), 1.25–1.01 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 156.9, 156.3, 153.5, 153.1, 146.2, 136.5, 133.4, 132.6, 126.8, 122.8, 117.2, 103.3, 63.0, 62.2, 62.0, 56.4, 31.2, 14.4, 9.5. HRMS-ESI(m/z): calcd for $C_{19}H_{24}N_4O_6$ ($M+H^+$): 405.1774, found

405.1778.

Diisopropyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ab)

Yellow solid, mp 189–190 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.83 (s, 1H), 8.81–8.79 (m, 1H), 8.73 (d, *J* = 8.36Hz, 1H), 8.57 (s, 1H), 7.61 (d, *J* = 8.40Hz, 1H), 7.52–7.48 (m, 1H), 7.29 (s, 1H), 5.02–4.96 (m, 2H), 2.35 (s, 3H), 1.26–1.04 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 156.1, 148.3, 138.3, 134.8, 132.7, 132.1, 126.5, 125.4, 122.0, 115.8, 71.1, 70.2, 25.1, 22.0, 21.8. HRMS-ESI(m/z): calcd for $C_{19}H_{24}N_4O_5$ ($M+H^+$): 389.1825, found 389.1827.

Di-tert-butyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ac)

Yellow solid, mp 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 8.79 (dd, *J* = 4.24 Hz, *J* = 1.64 Hz, 1H), 8.73 (d, *J* = 8.32Hz, 1H), 8.56–8.54 (m, 1H), 7.60 (d, *J* = 8.32Hz, 1H), 7.51 (dd, *J* = 8.48 Hz, *J* = 4.20 Hz, 1H), δ 7.03 (s, 1H), δ = 2.34 (s, 3H), 1.52–1.26 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 154.5, 148.2, 138.2, 134.5, 132.8, 126.1, 125.4, 121.8, 115.8, 82.4, 29.7, 28.2, 28.1, 25.1. HRMS-ESI(m/z): calcd for $C_{21}H_{28}N_4O_5$ ($M+H^+$): 417.2138, found 417.2137.

Dibenzyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ad)

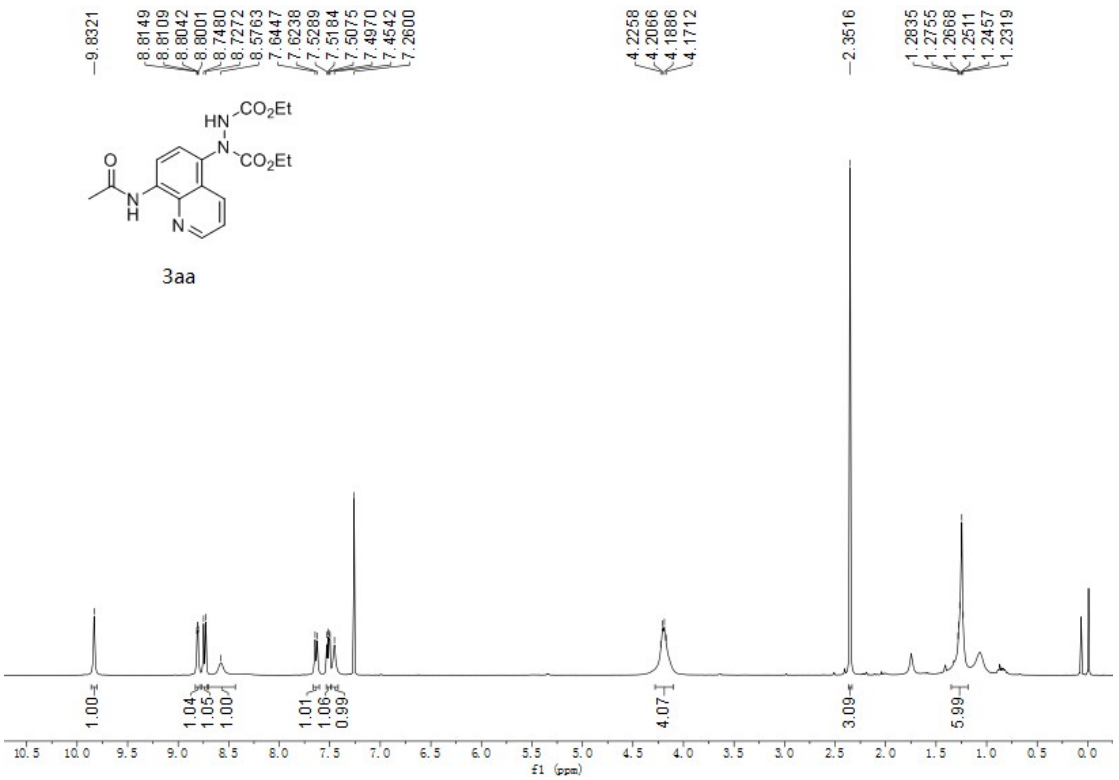
White solid, mp 68–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.78 (d, *J* = 4.16Hz, 1H), 8.72 (d, *J* = 8.40Hz, 1H), 8.51 (s, 1H), 7.63–7.43 (m, 3H), 7.31–7.05 (m, 10H), 5.15 (s, 4H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 156.2, 155.8, 148.3, 138.3, 135.4, 135.1, 132.5, 131.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 126.6, 125.3, 122.1, 115.7, 68.6, 68.0, 25.1. HRMS-ESI(m/z): calcd for $C_{27}H_{24}N_4O_5$ ($M+H^+$): 485.1825, found 485.1825.

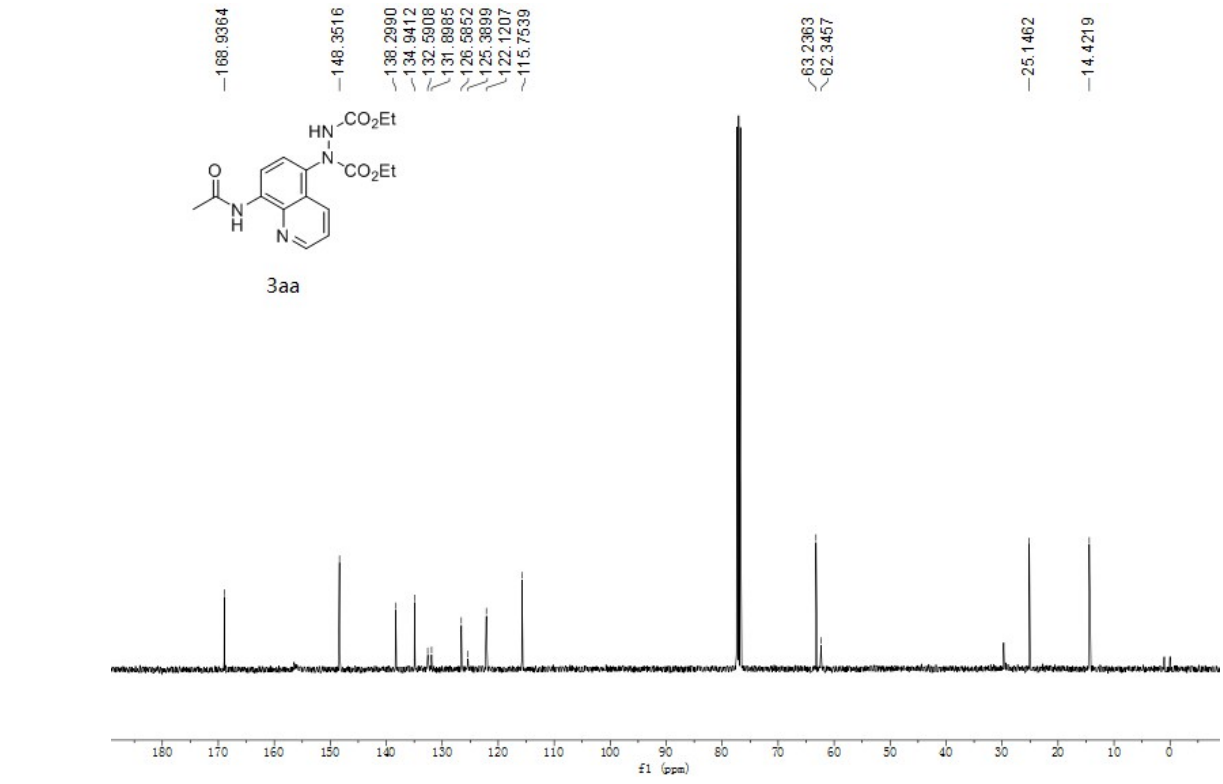
Bis(4-chlorobenzyl) 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ae)

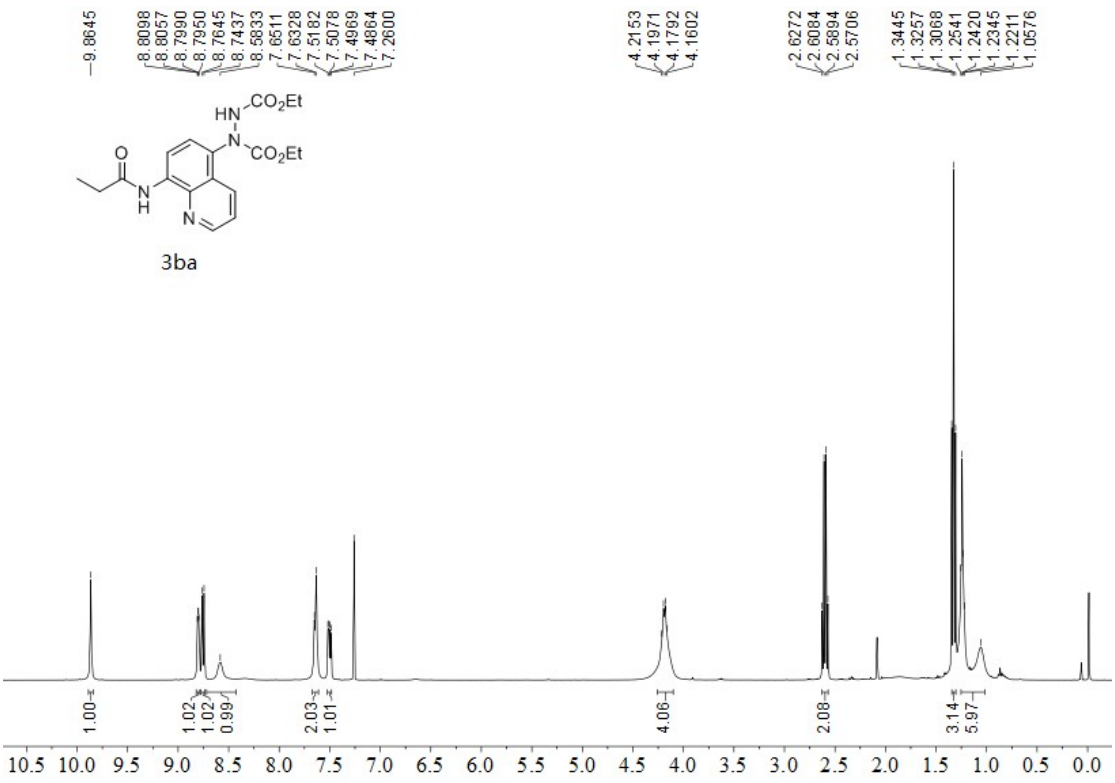
White solid, mp 160–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.81–8.78 (m, 1H), 8.72 (d, *J* = 8.32Hz, 1H), 8.47 (s, 1H), 7.62–7.44 (m, 3H), 7.29–7.26 (m, 2H), 7.22–6.97 (m, 6H), 5.10 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 156.0, 148.4, 138.3, 137.5, 135.2, 134.4, 133.9, 132.3, 131.4, 129.6, 129.4, 128.8, 128.7, 126.7, 125.3, 122.2, 115.7, 67.8, 67.2, 25.1. HRMS-ESI(m/z): calcd for $C_{27}H_{22}Cl_2N_4O_5$ ($M+H^+$): 553.1046, found 553.1047.

[1] Y. Wang, Y. Wang, K. Jiang, Q. Zhang and D. Li, *Org. Biomol. Chem.* 2016, **14**, 10180.

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



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4.06
2.08
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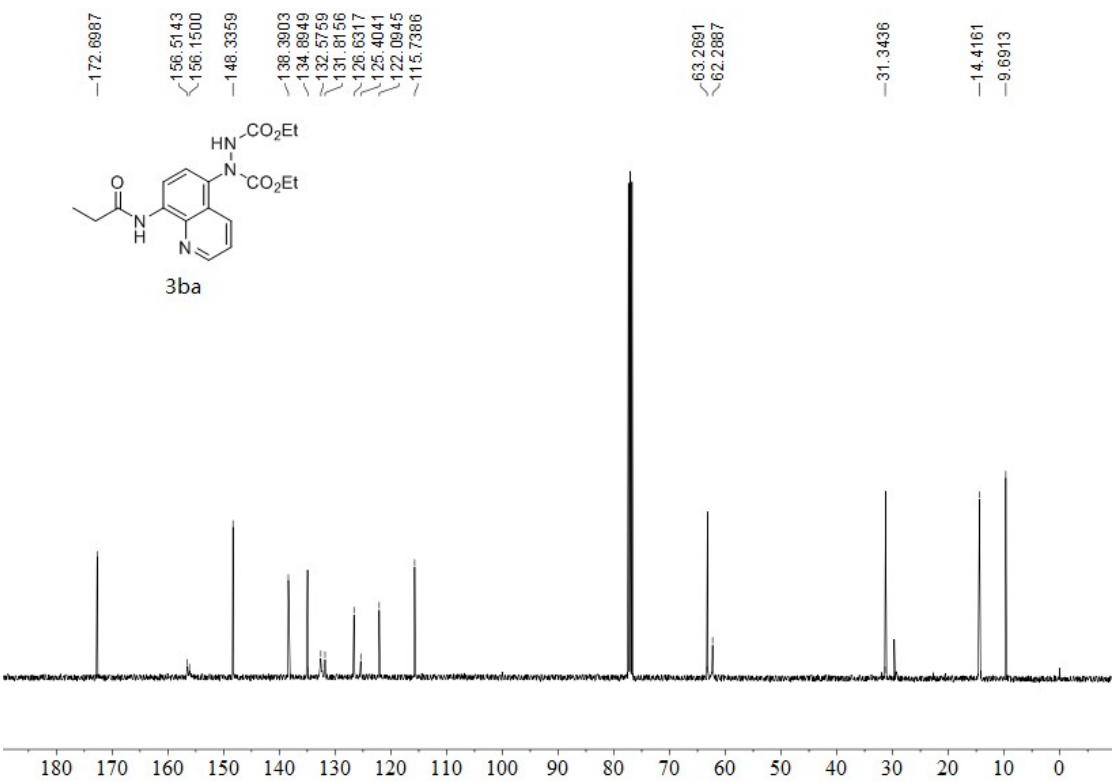
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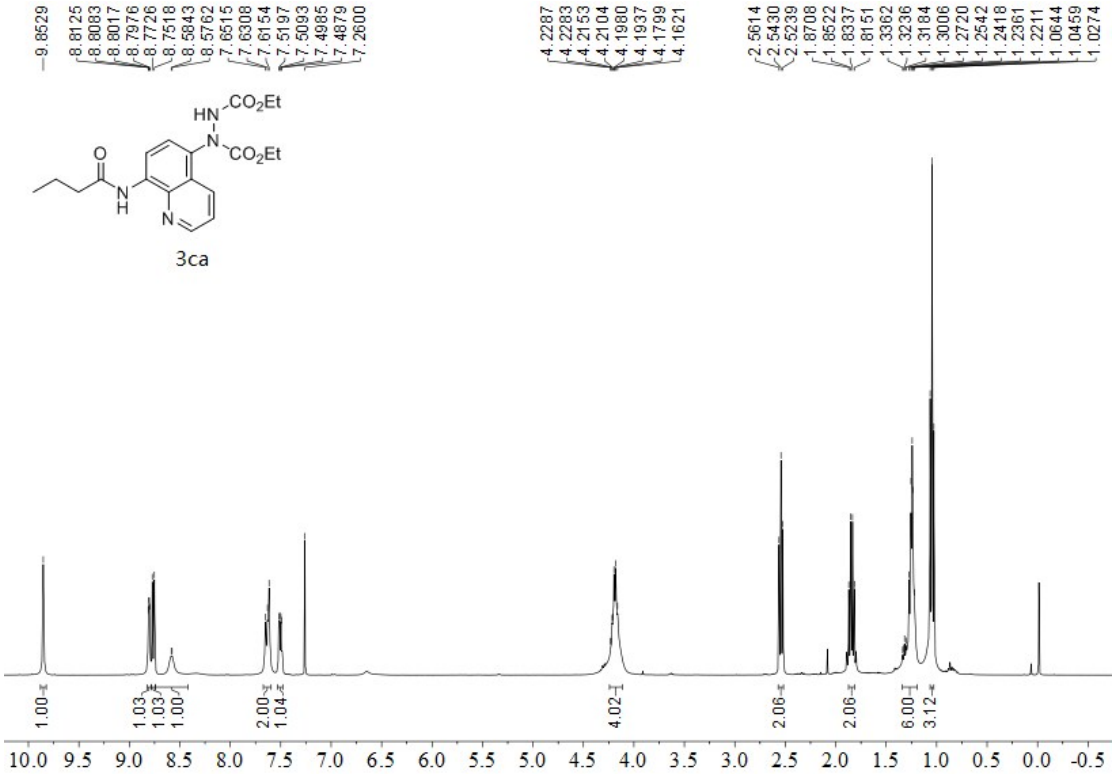
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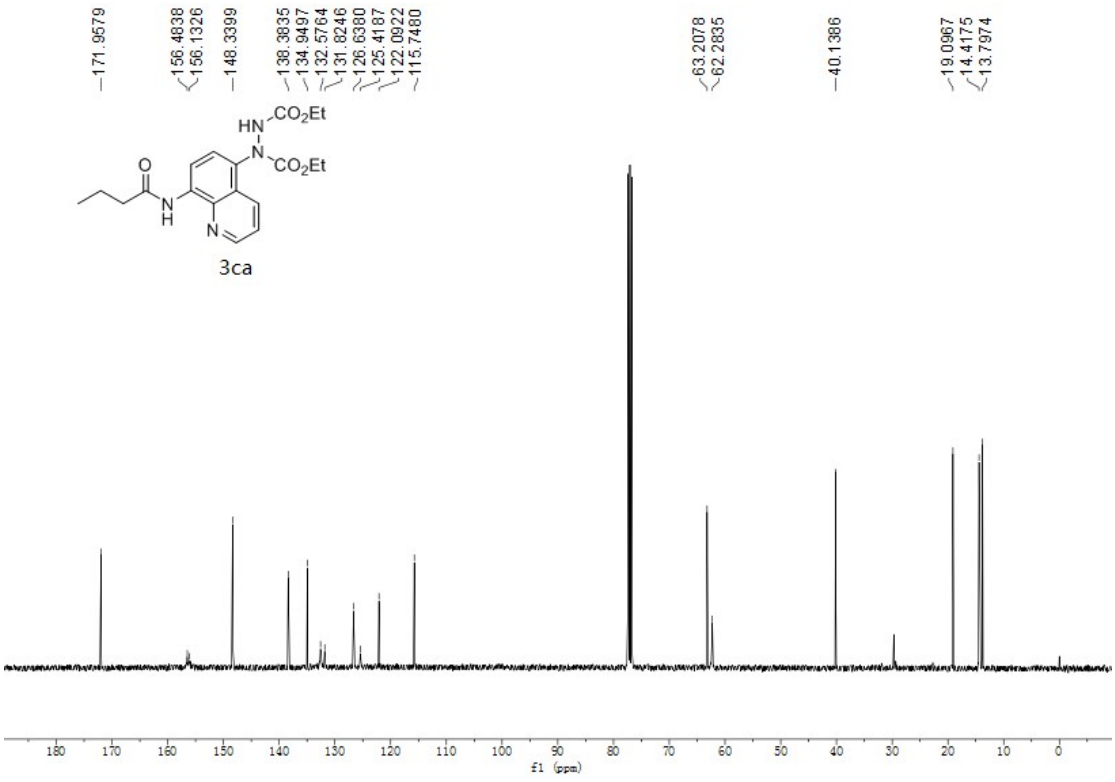
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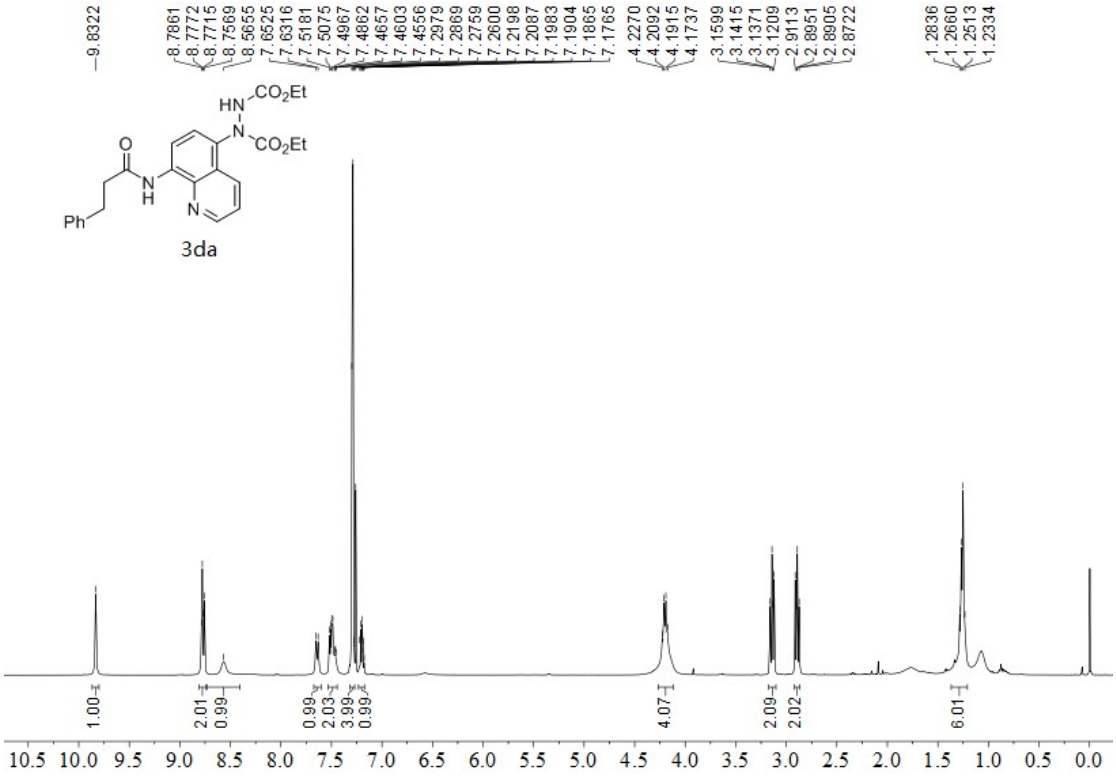
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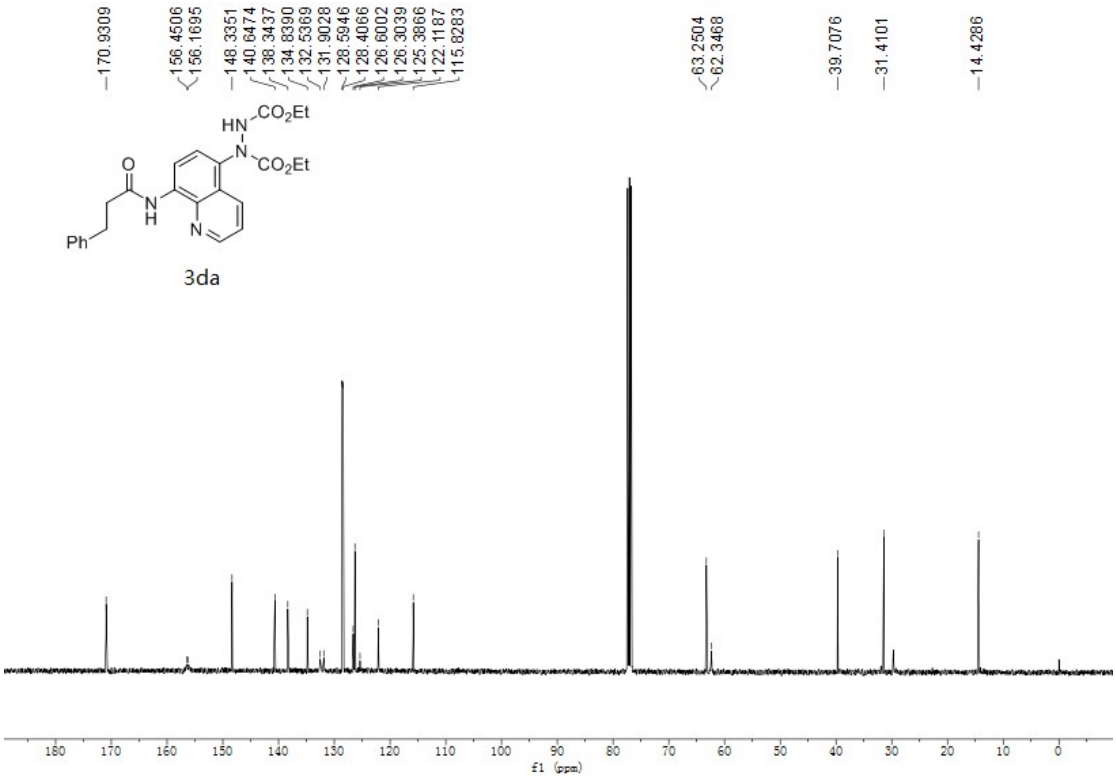
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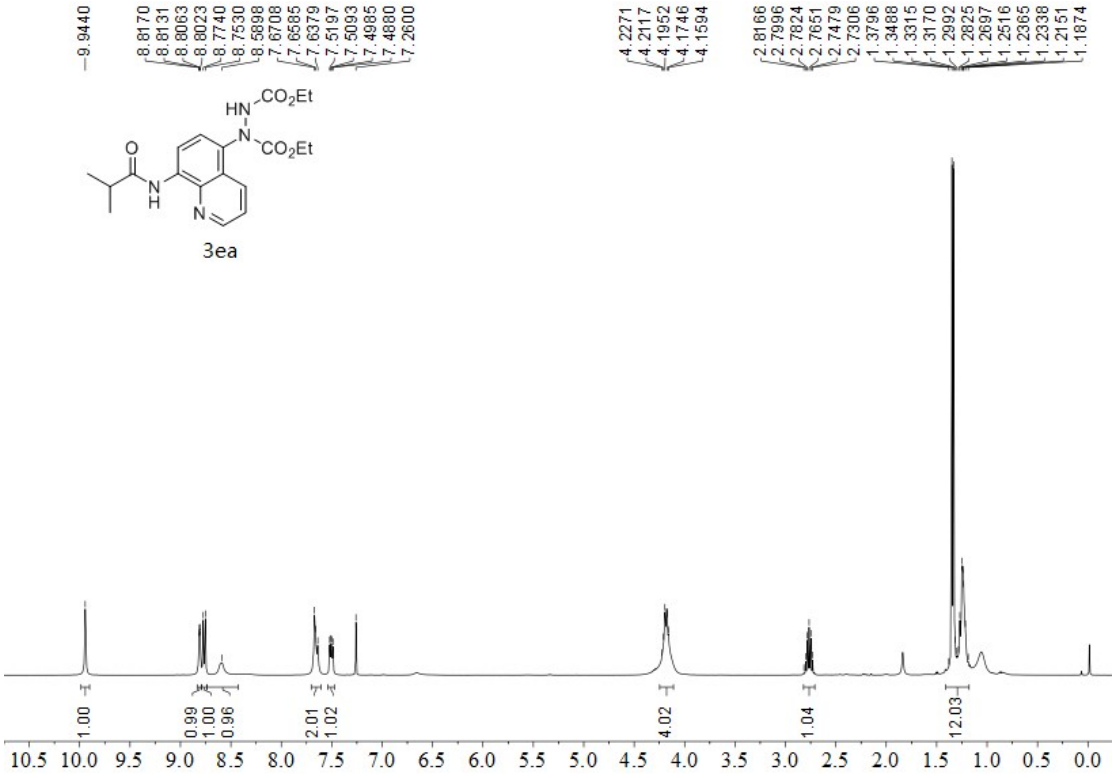
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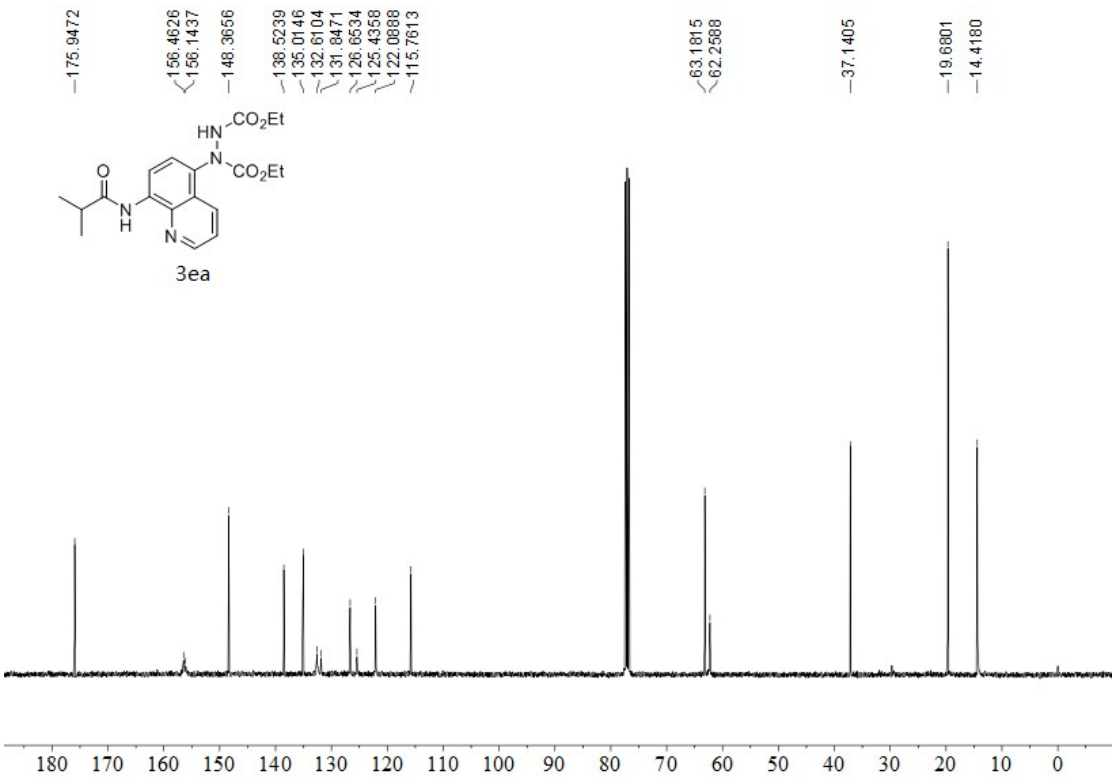
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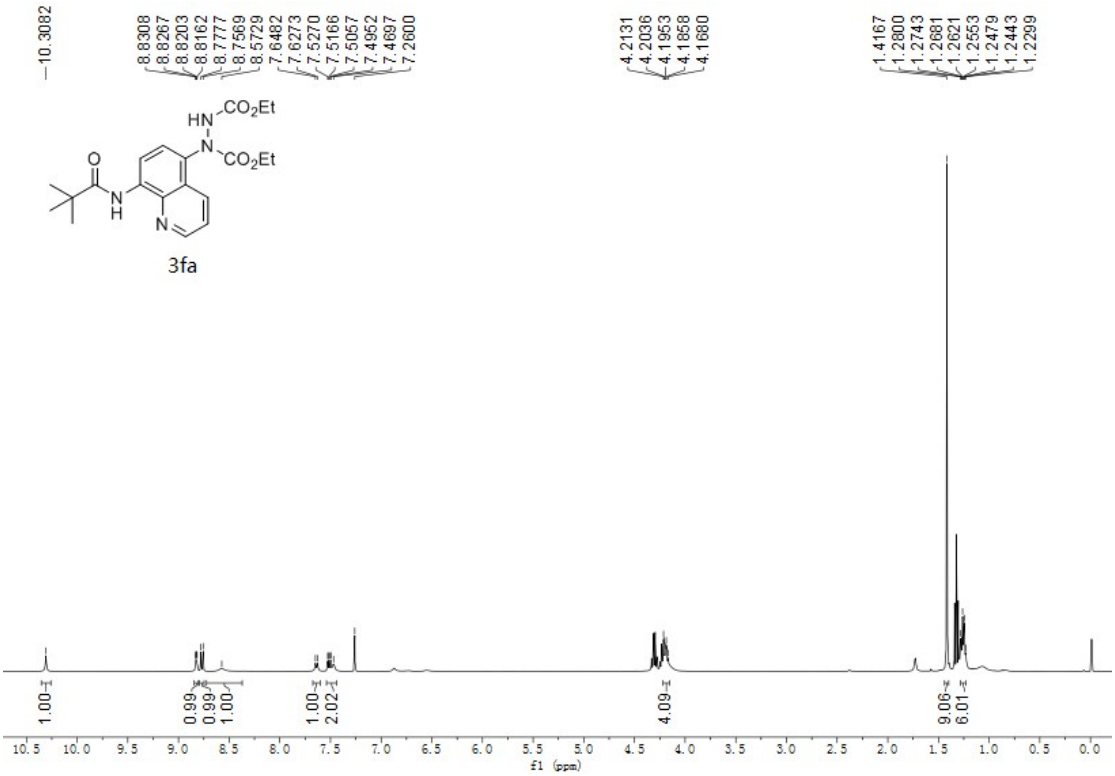
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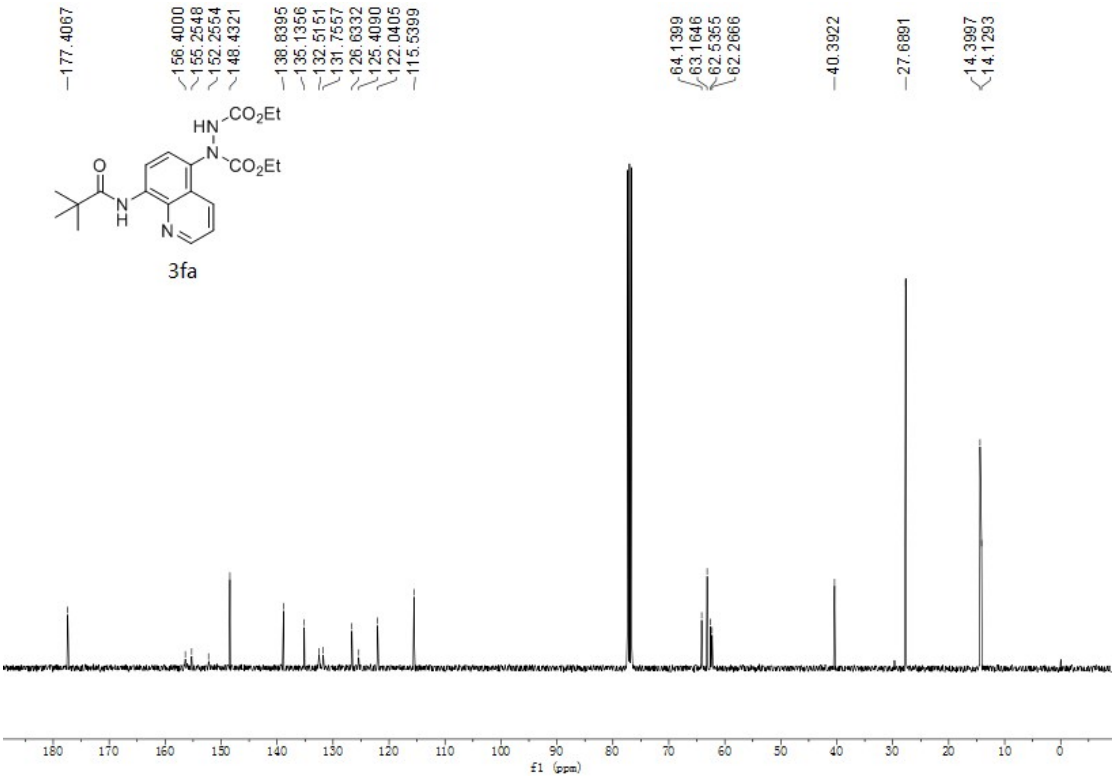
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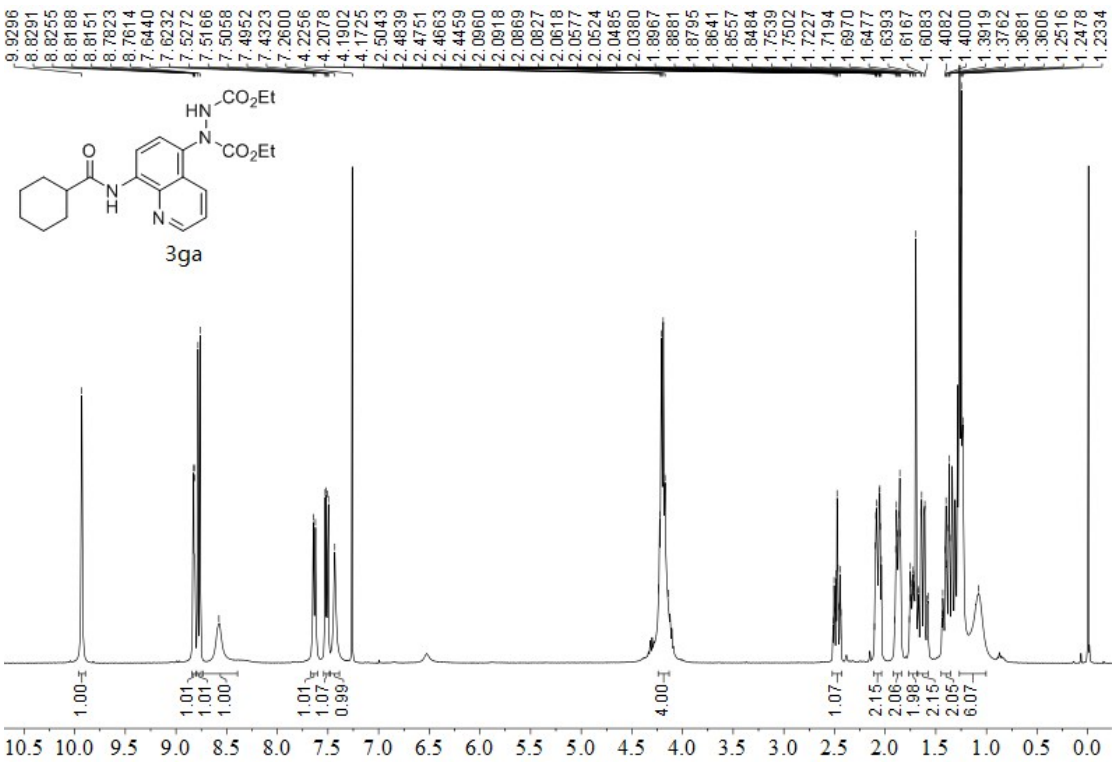
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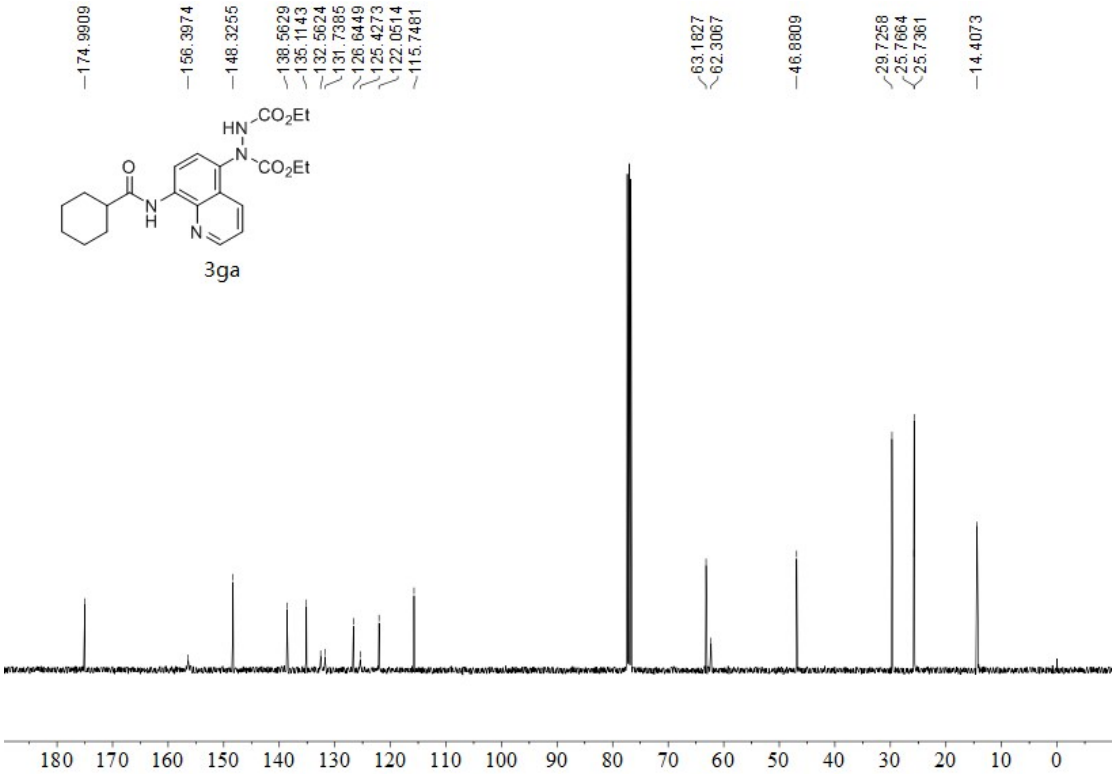
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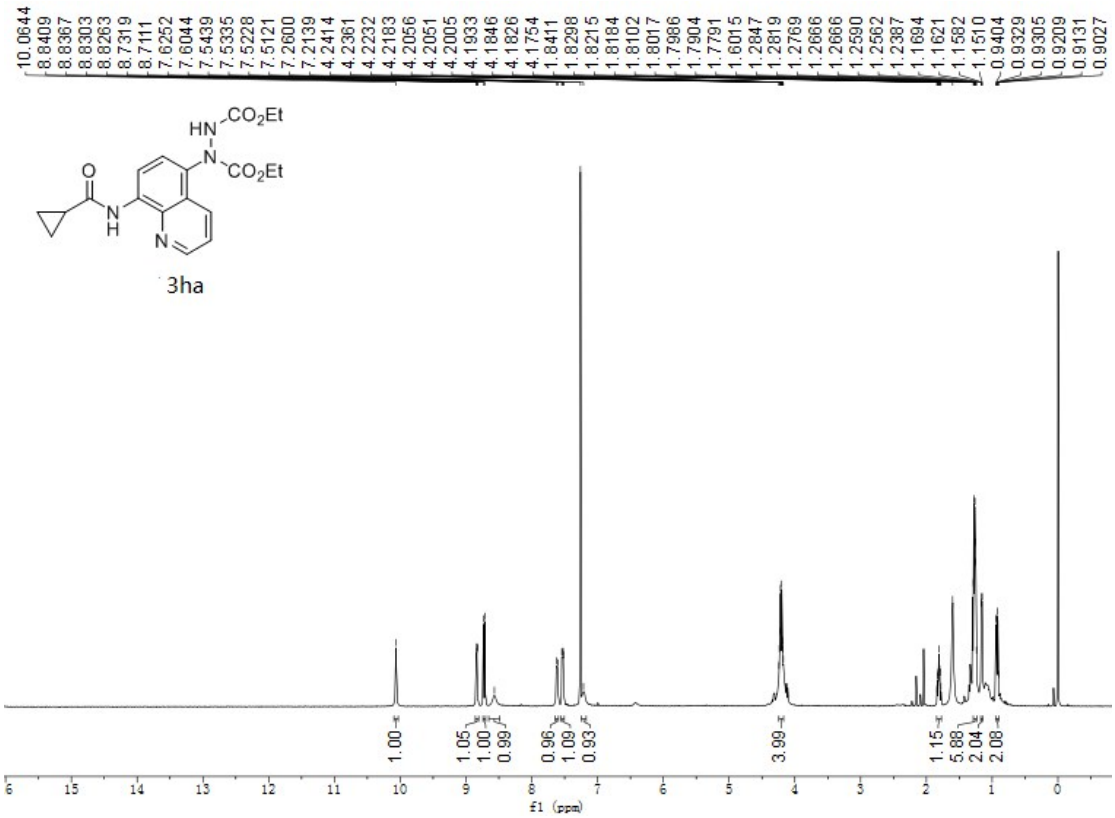
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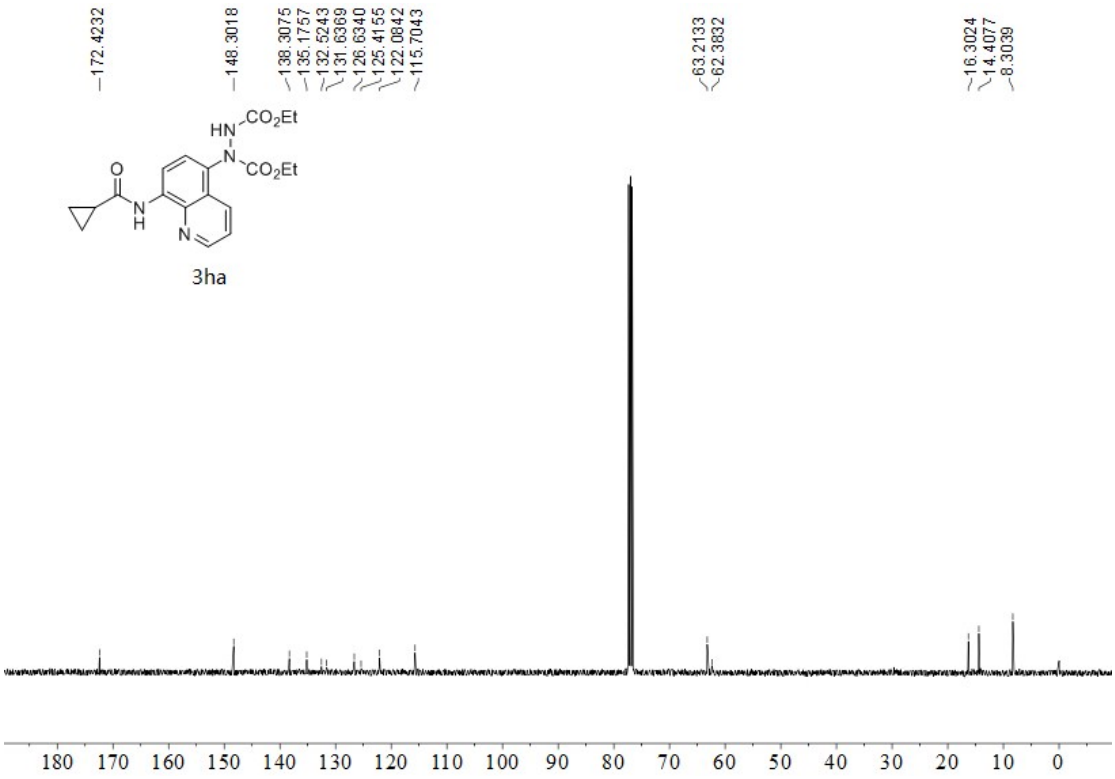
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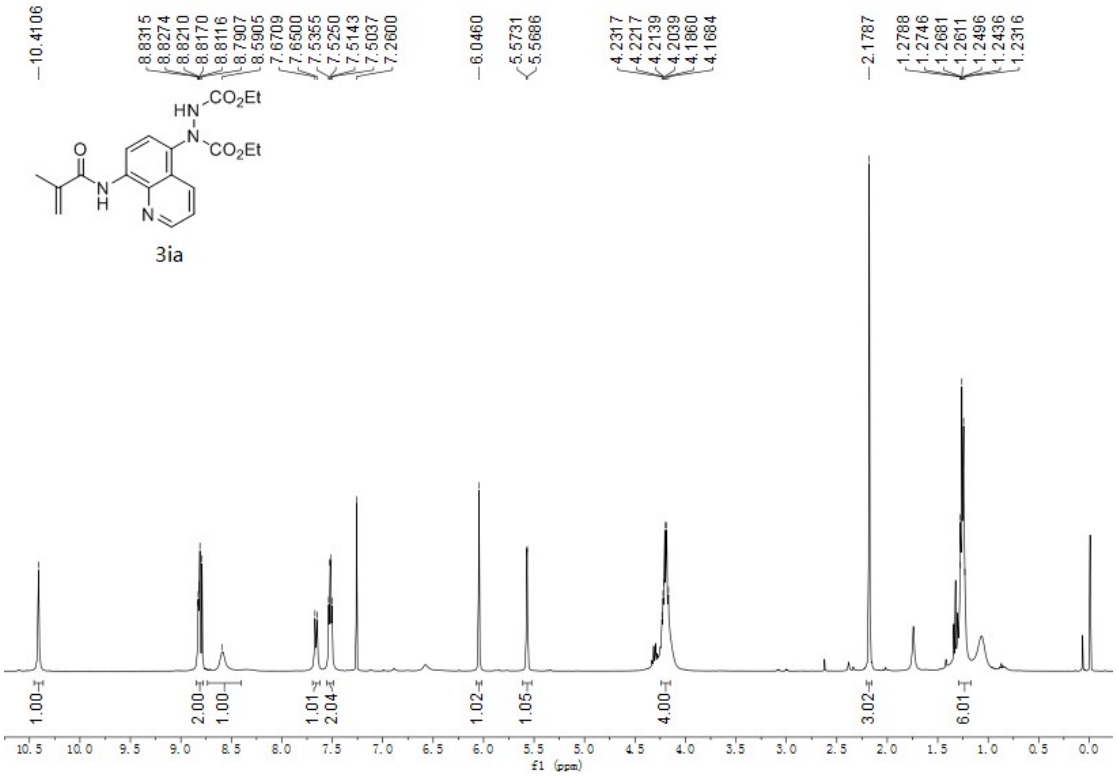
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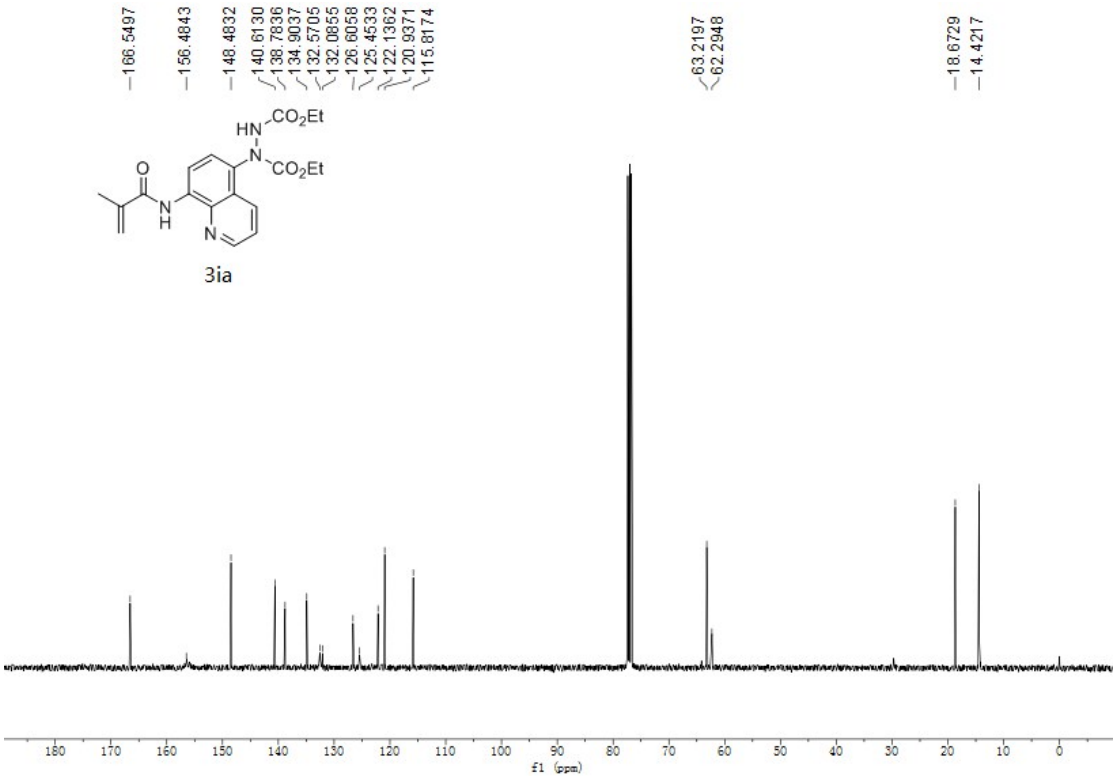
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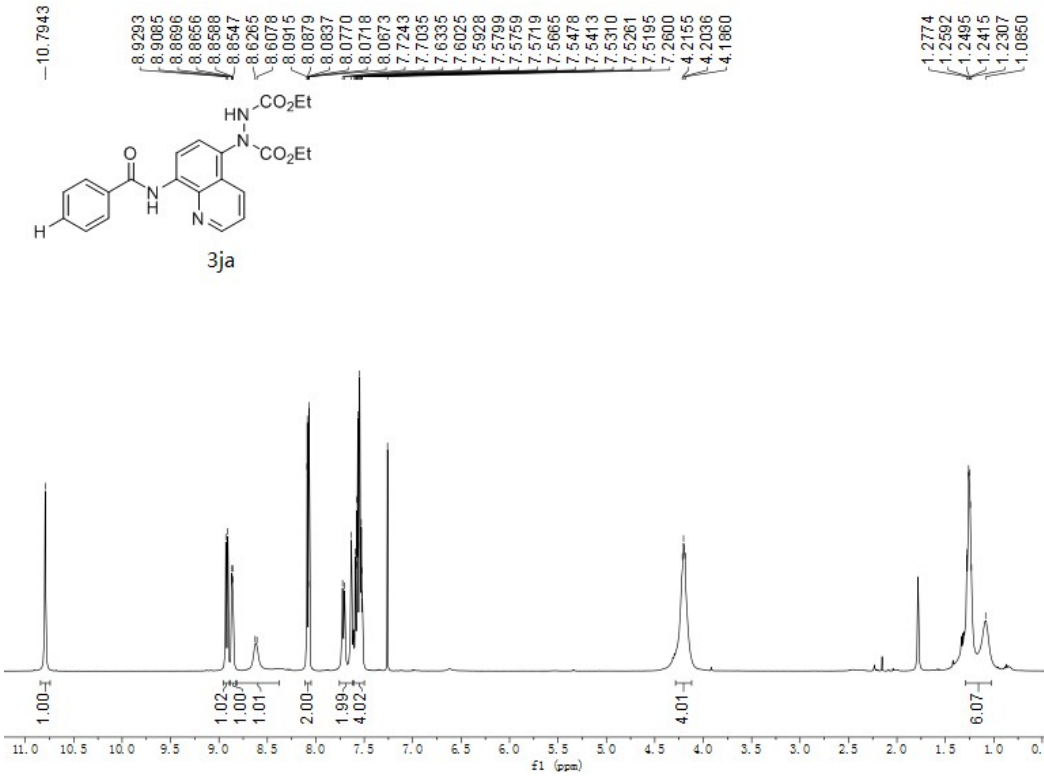
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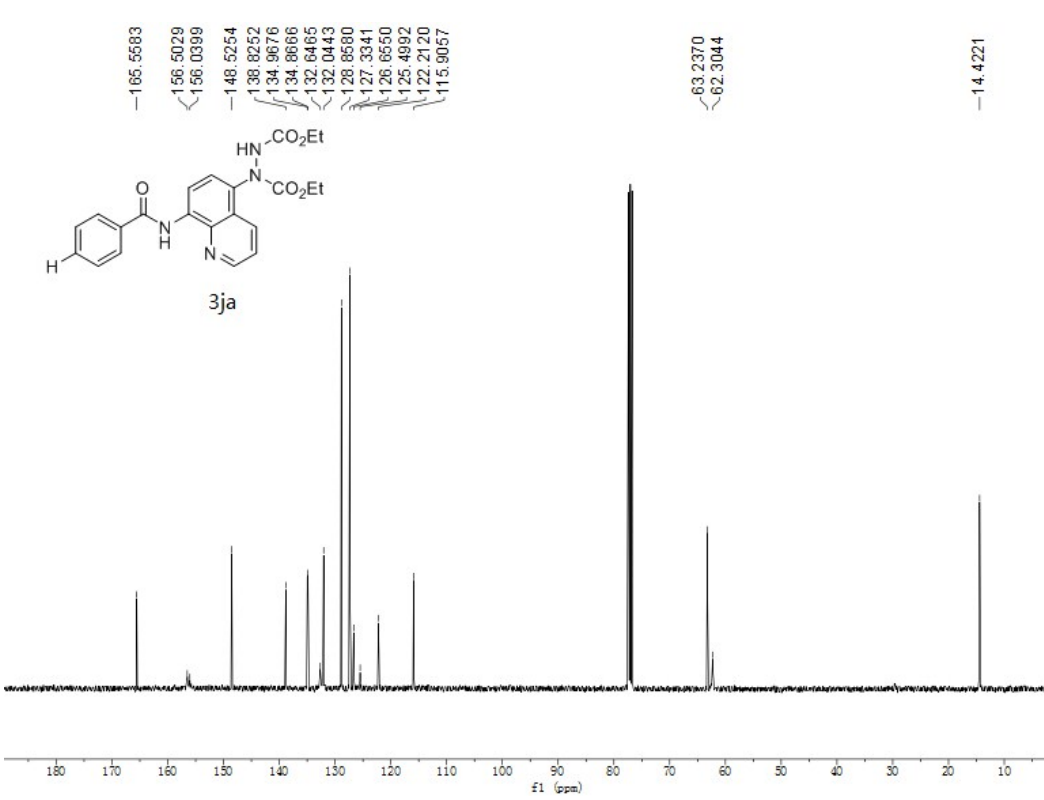
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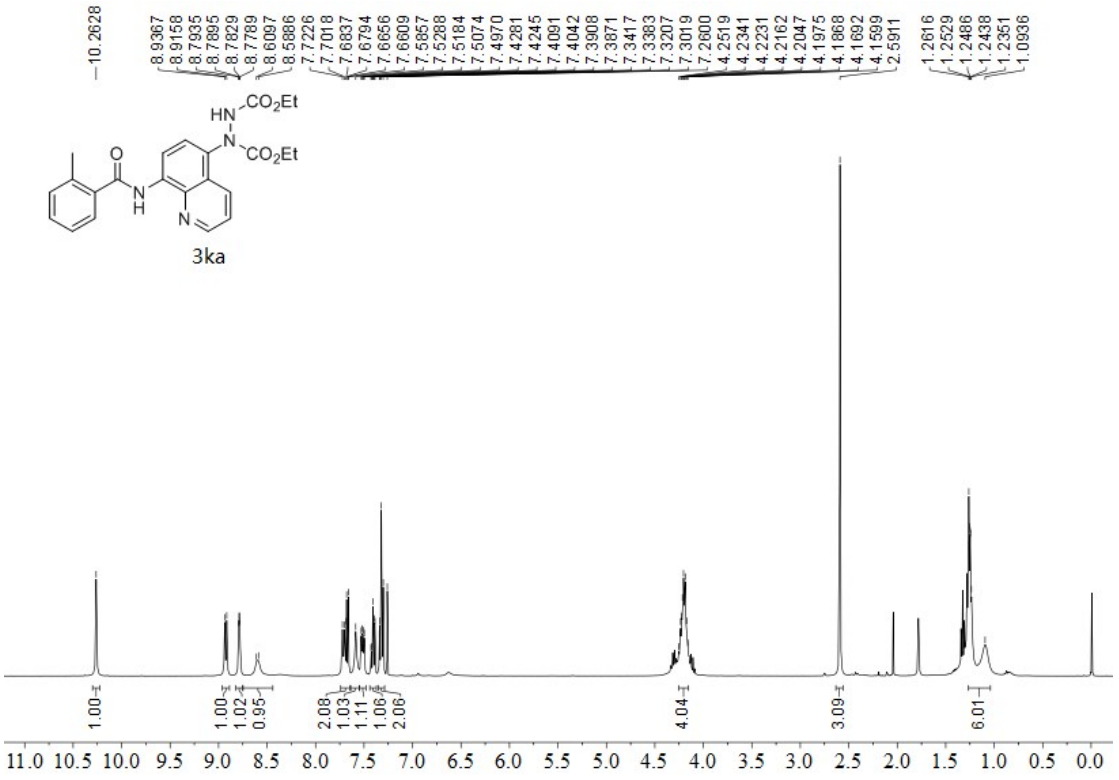
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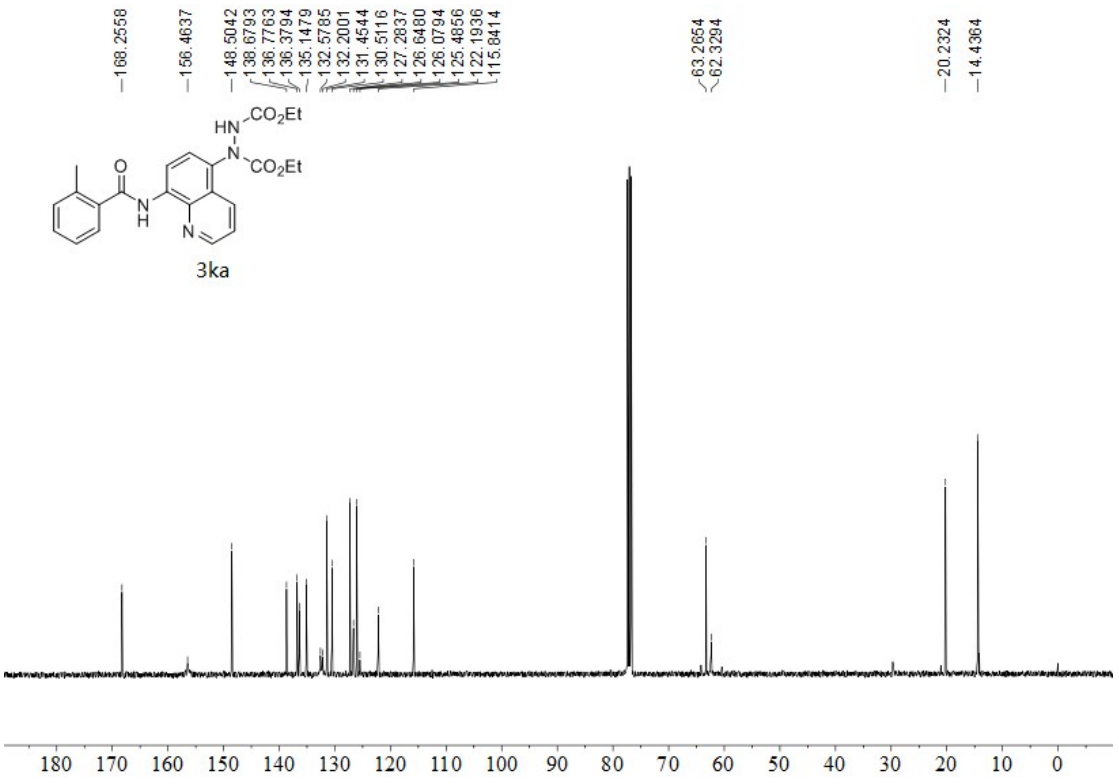
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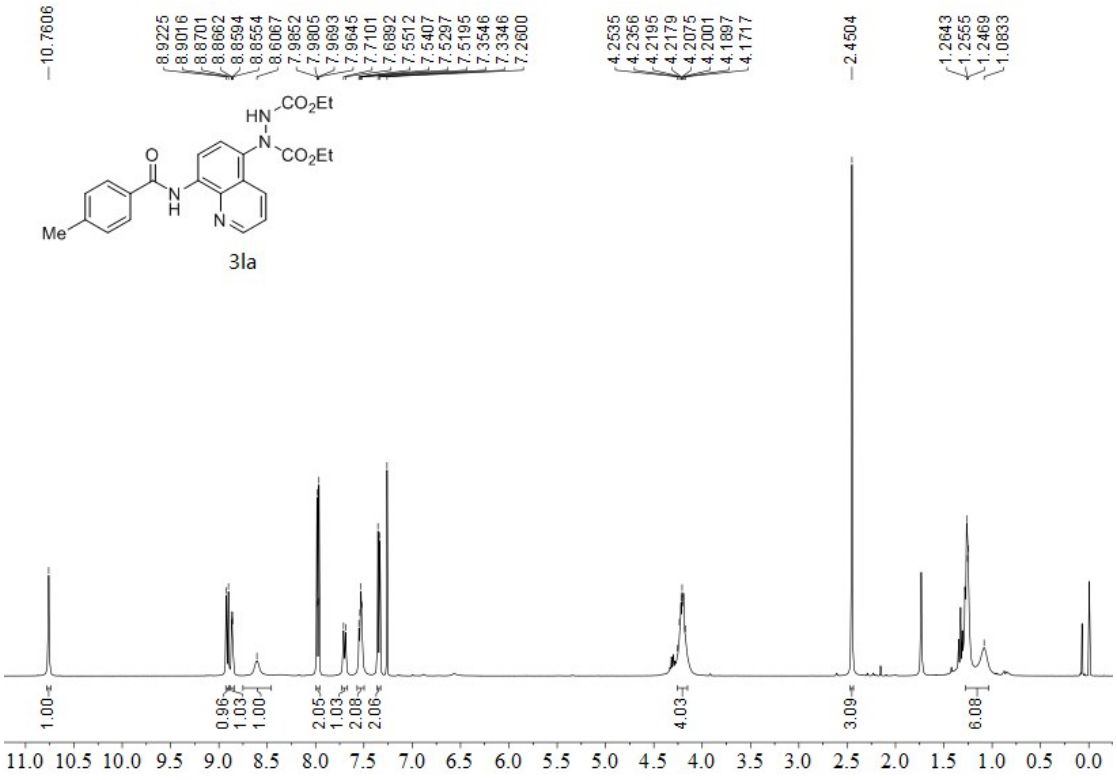
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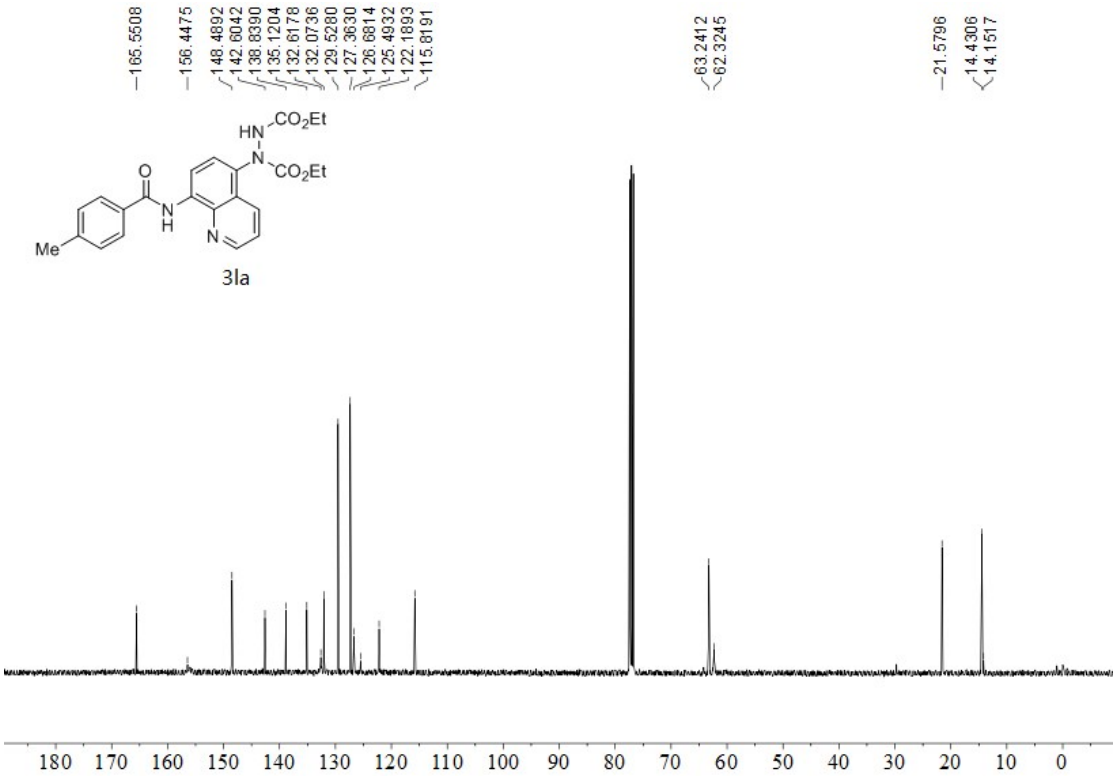
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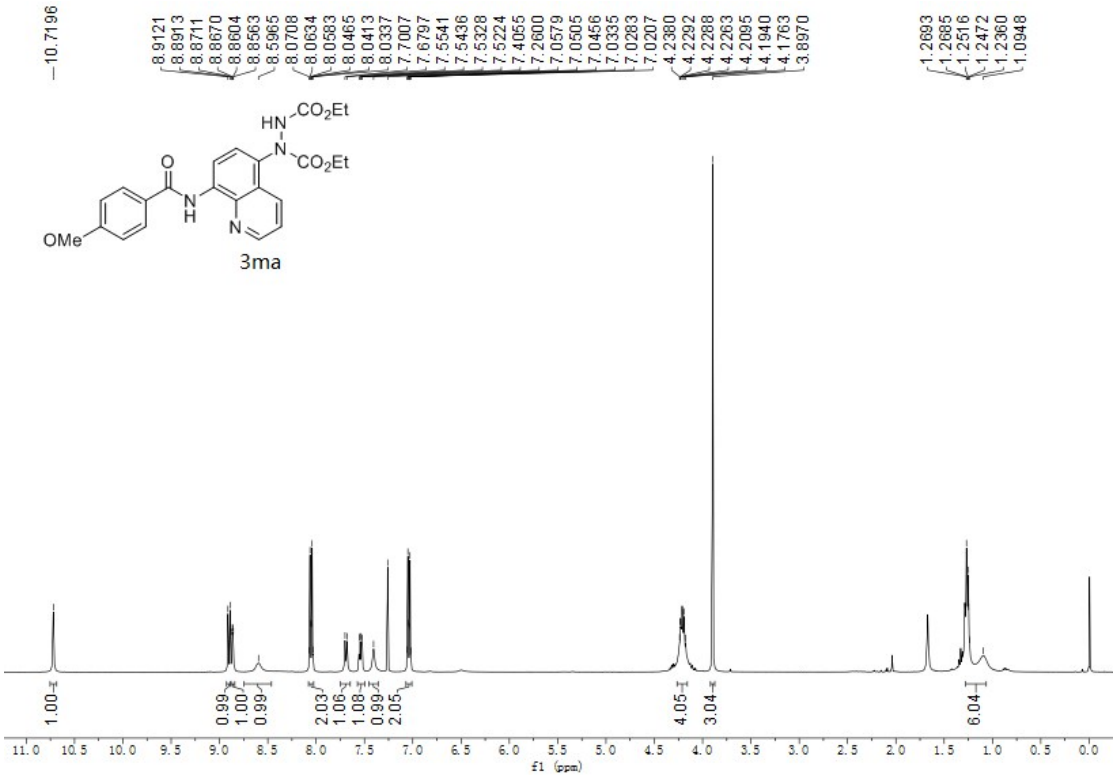
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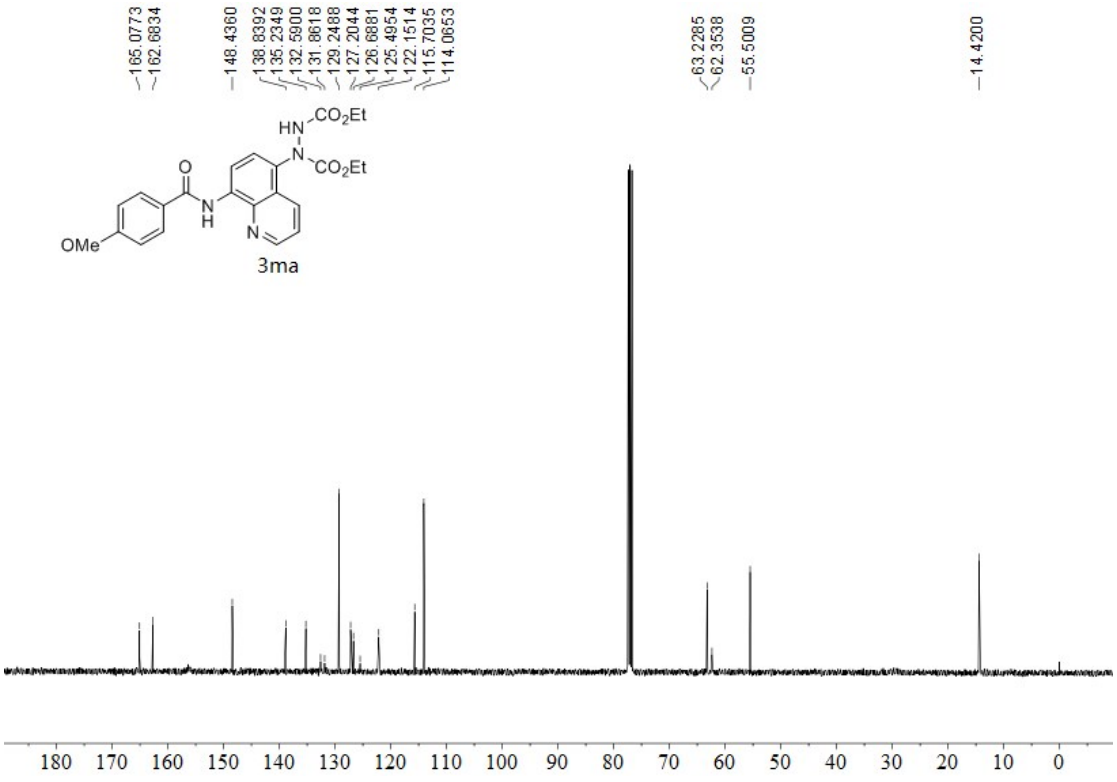
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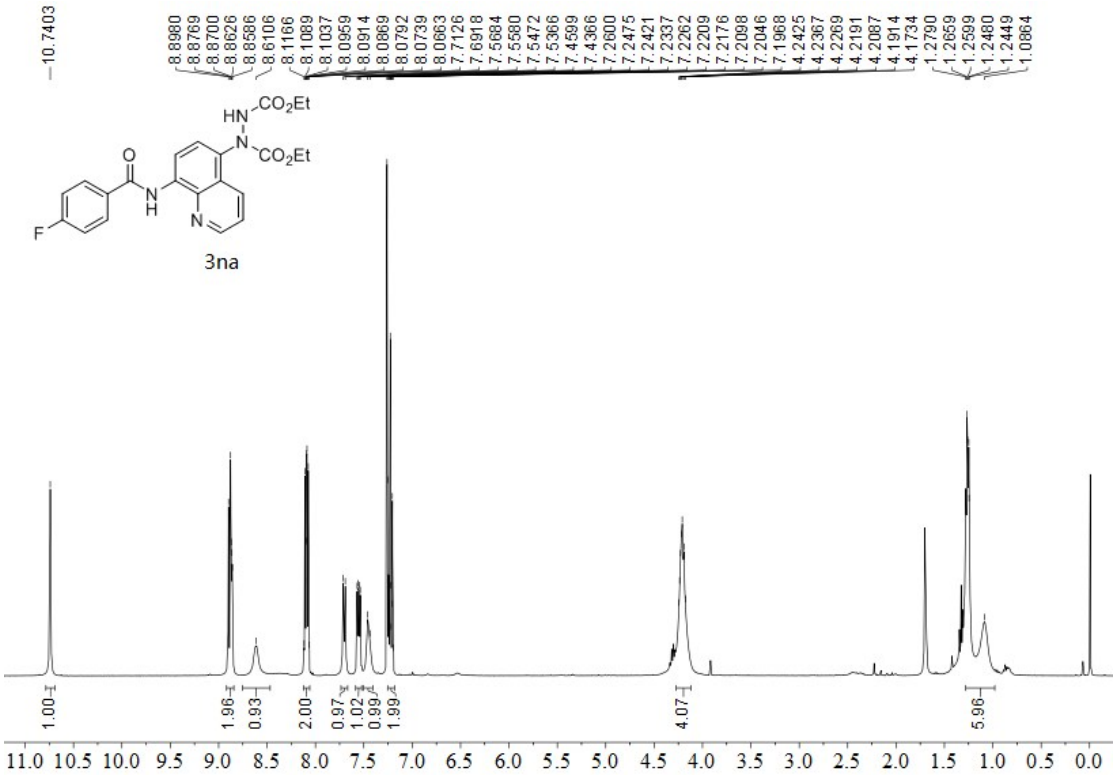
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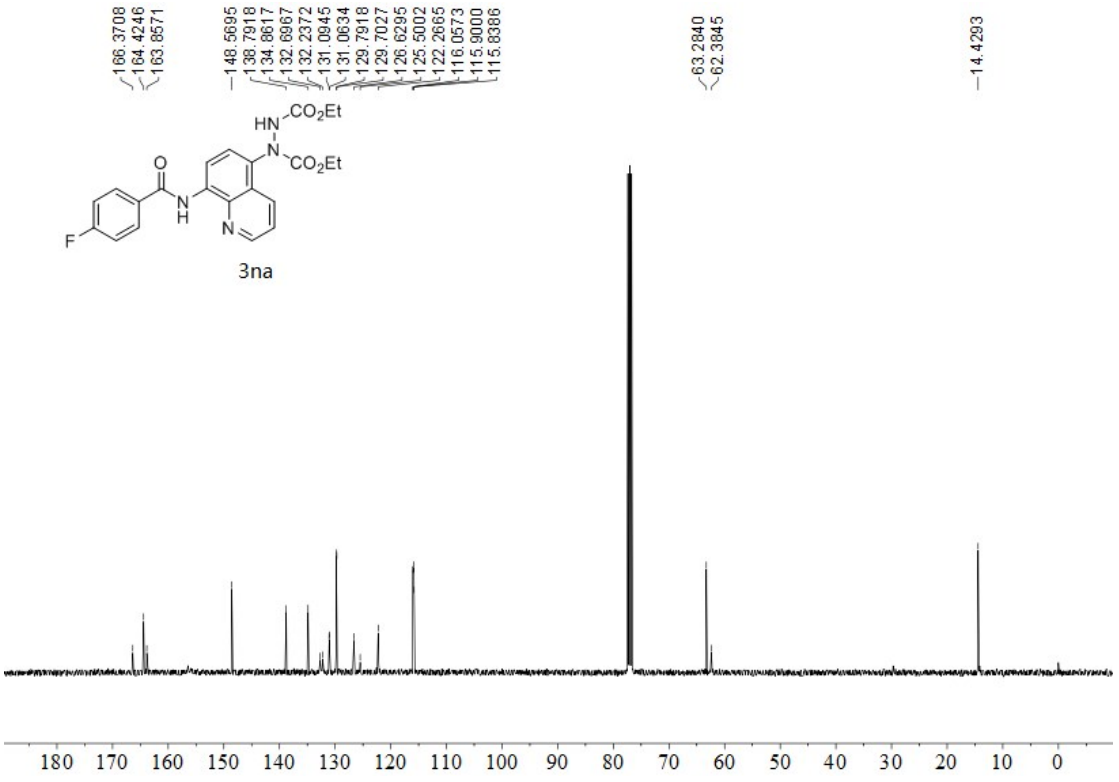
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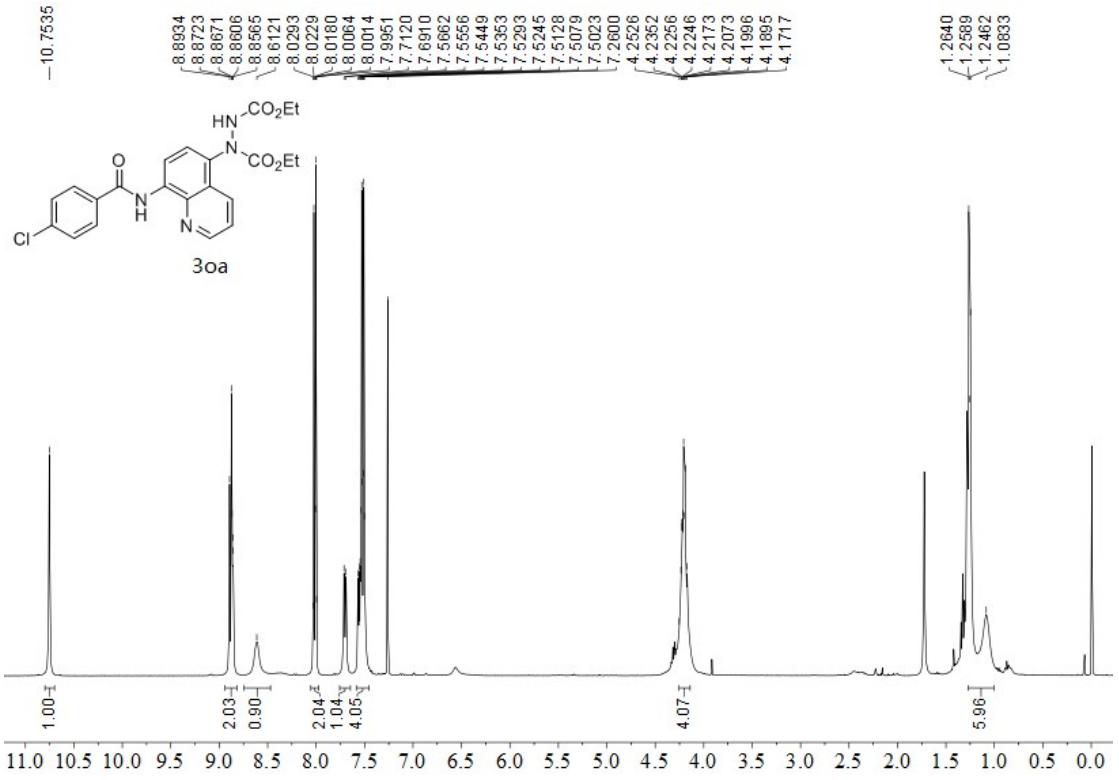
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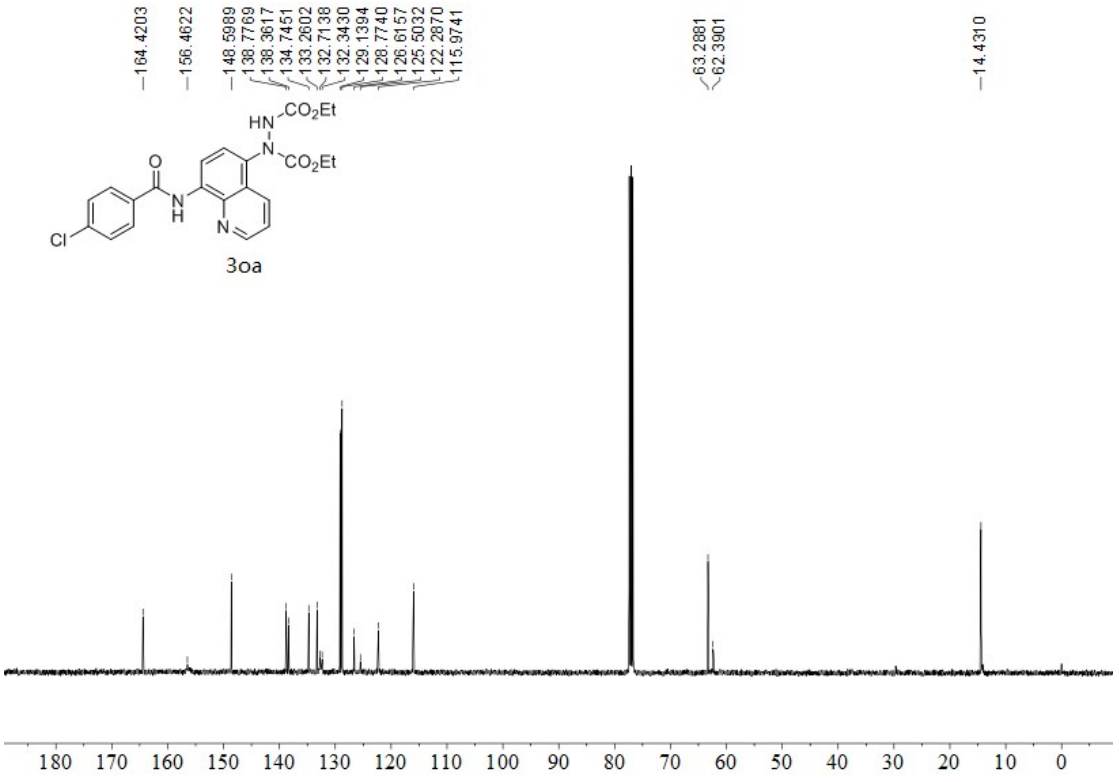
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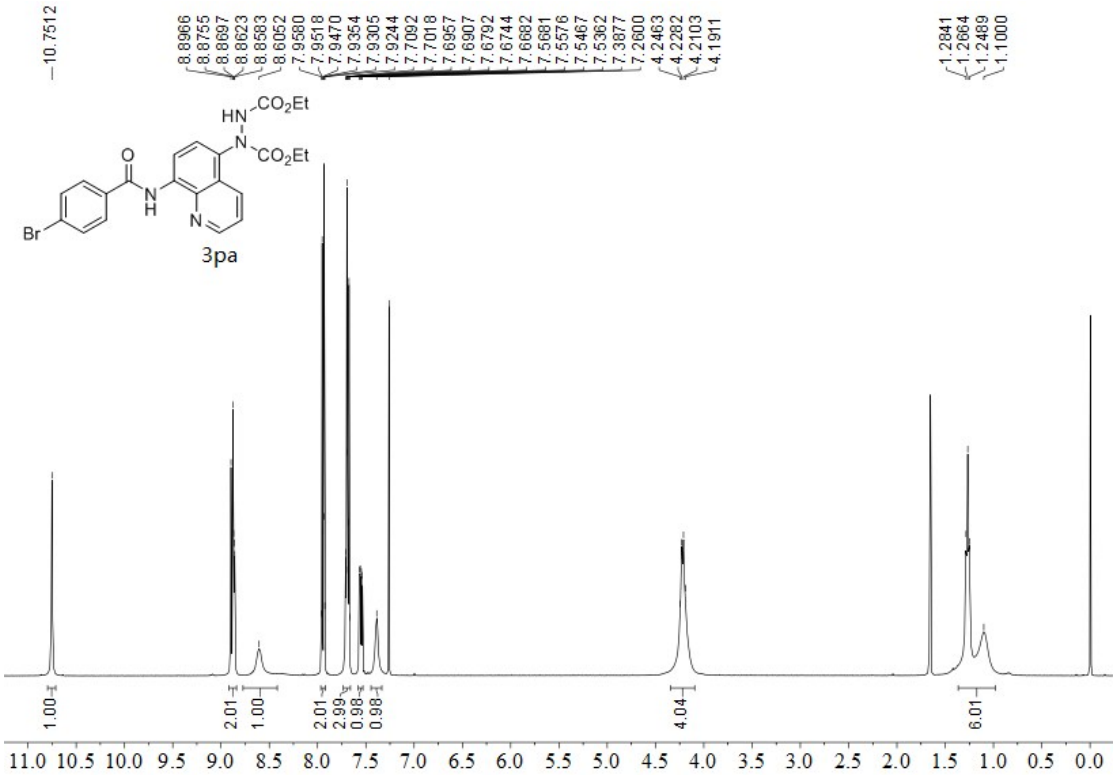
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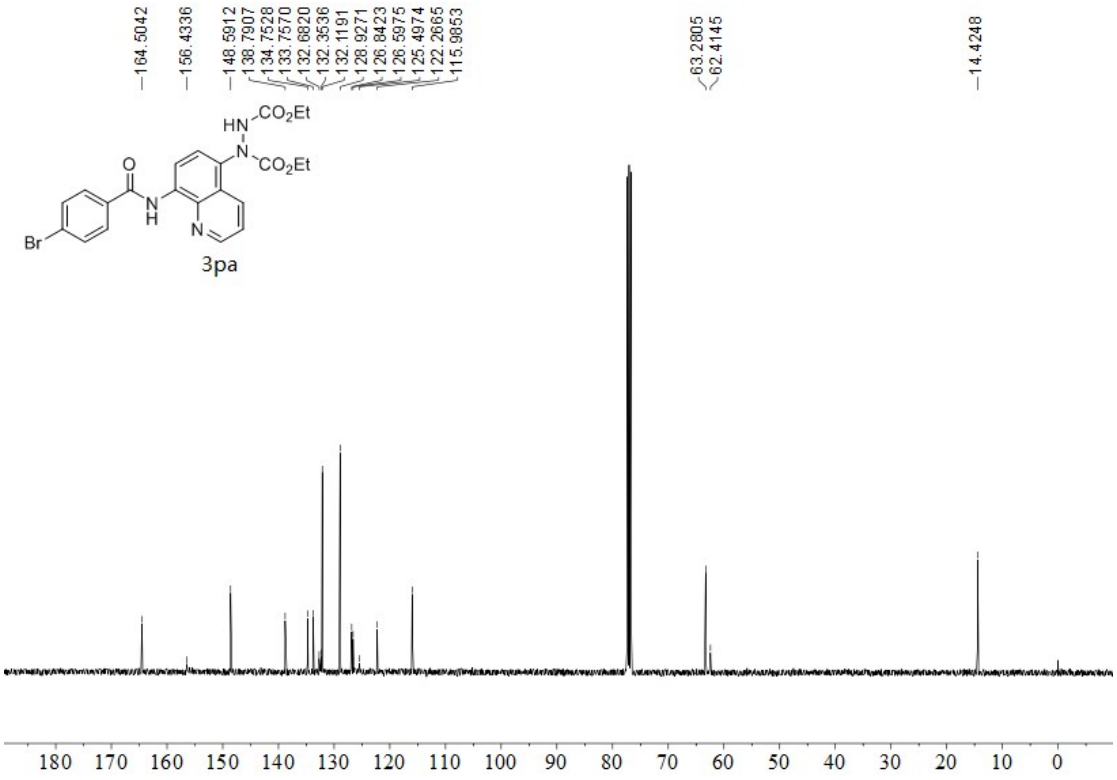
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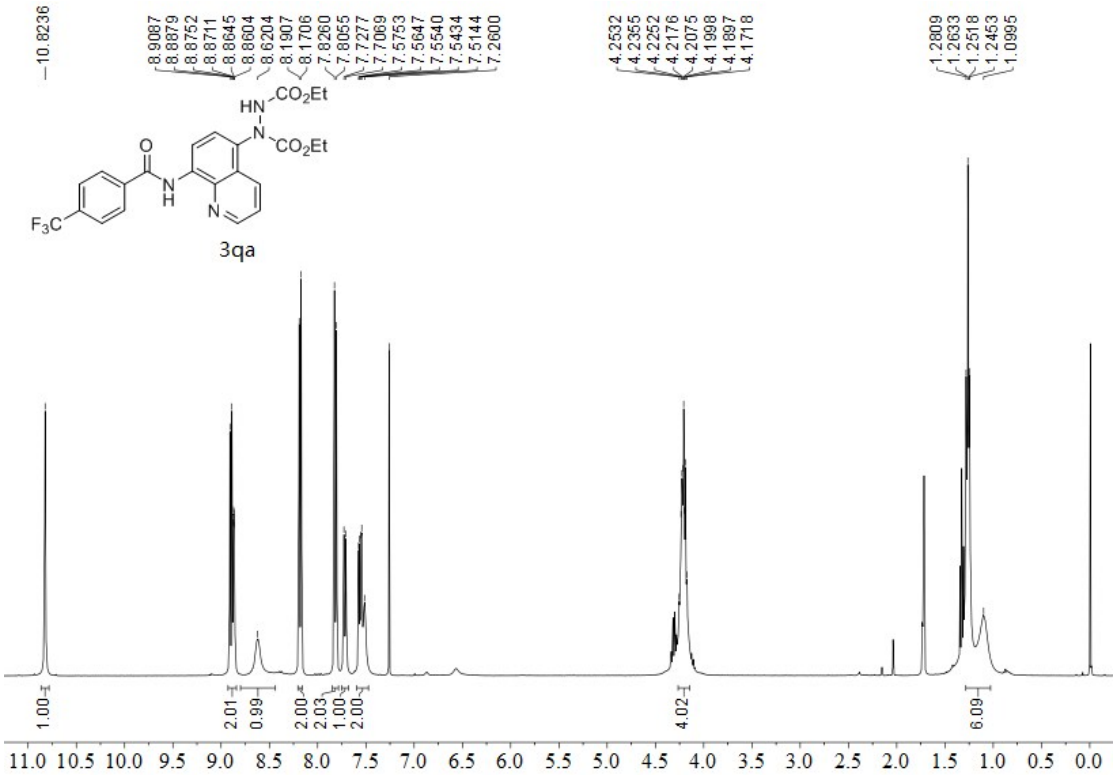
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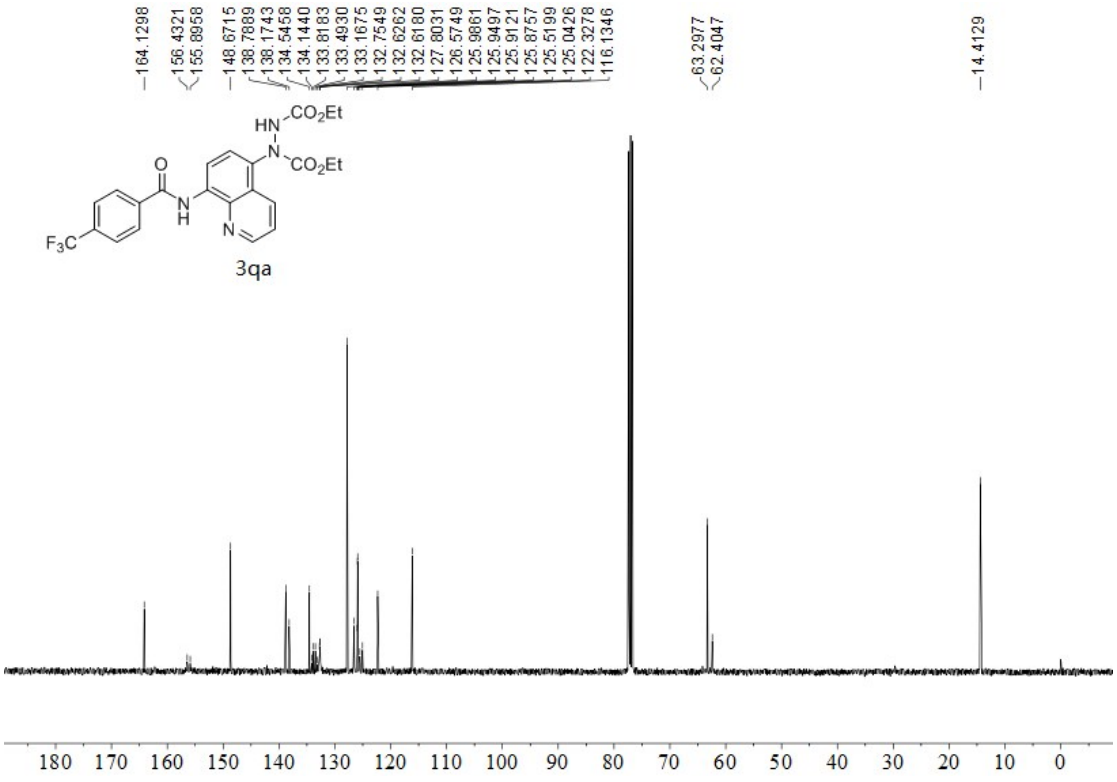
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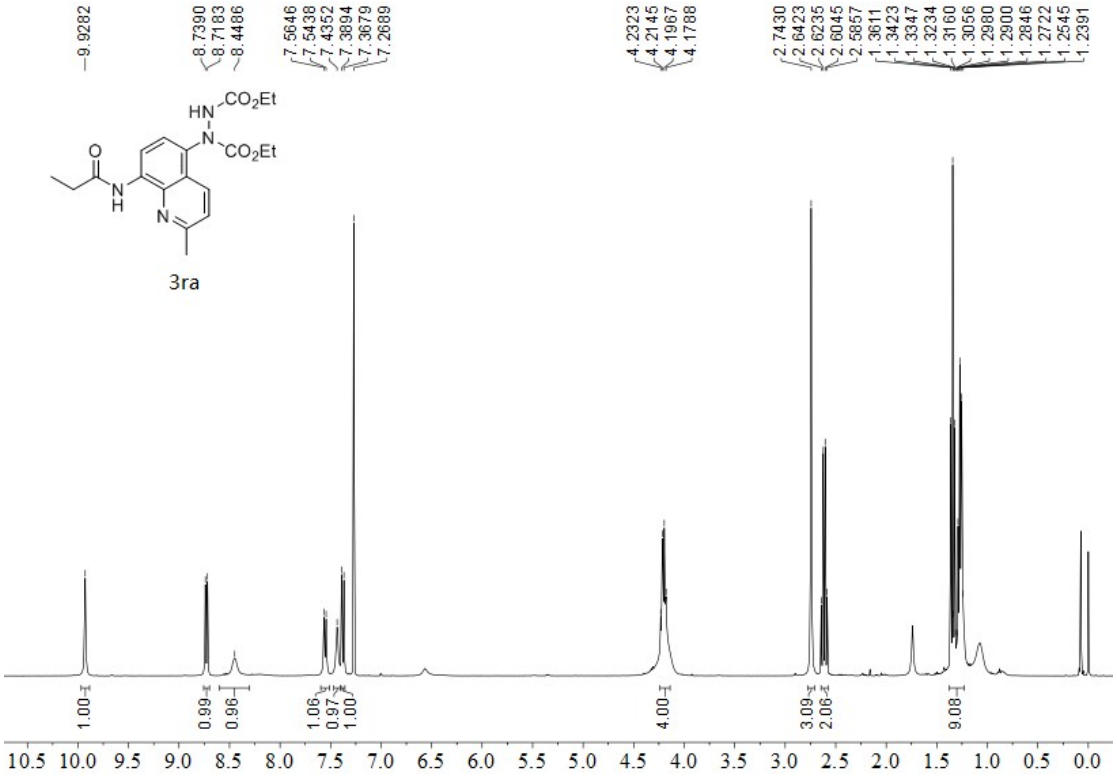
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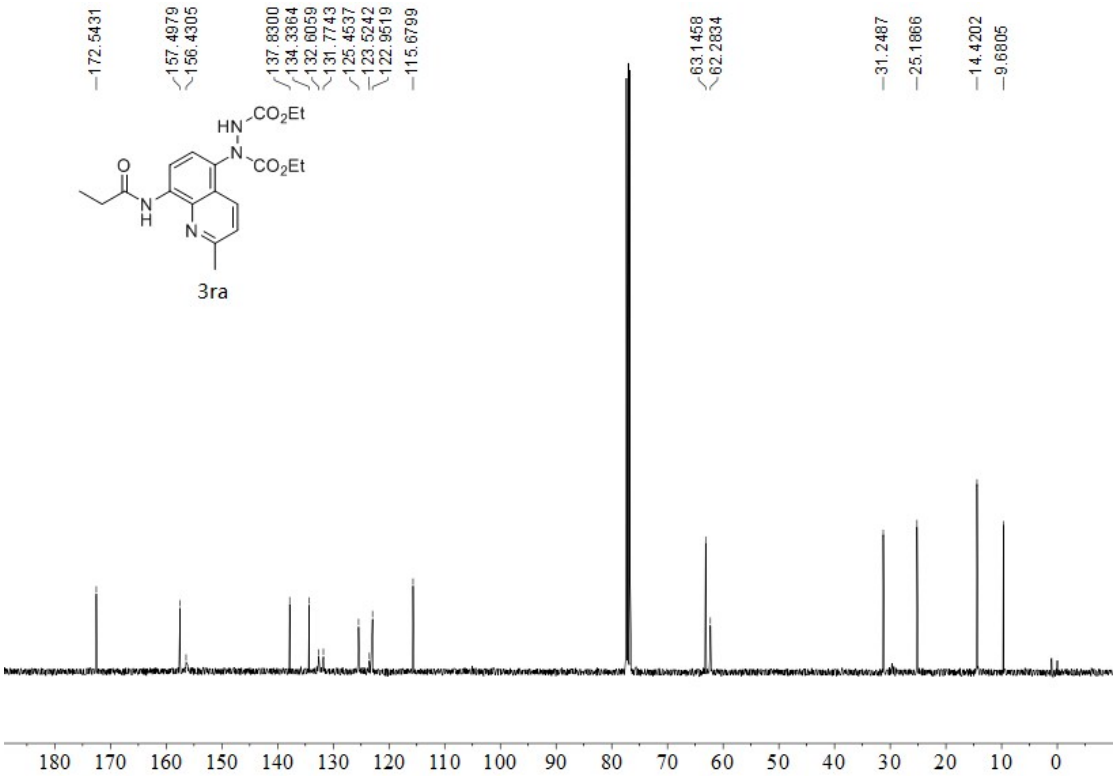
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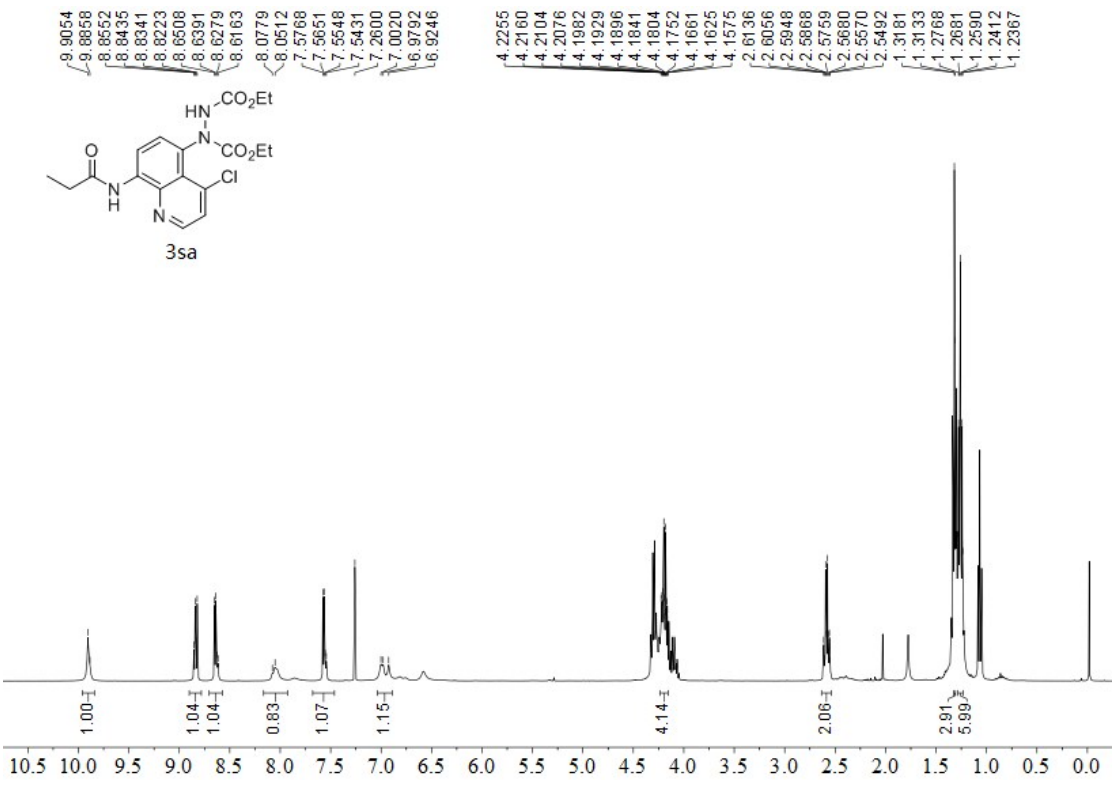
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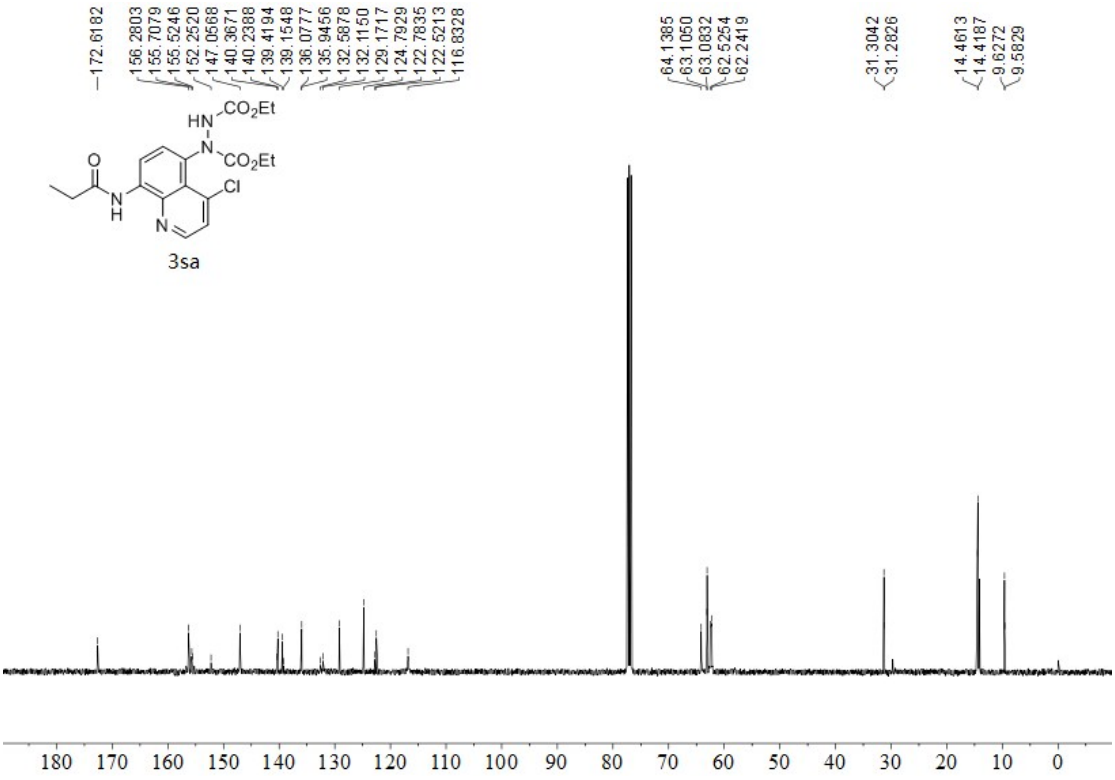
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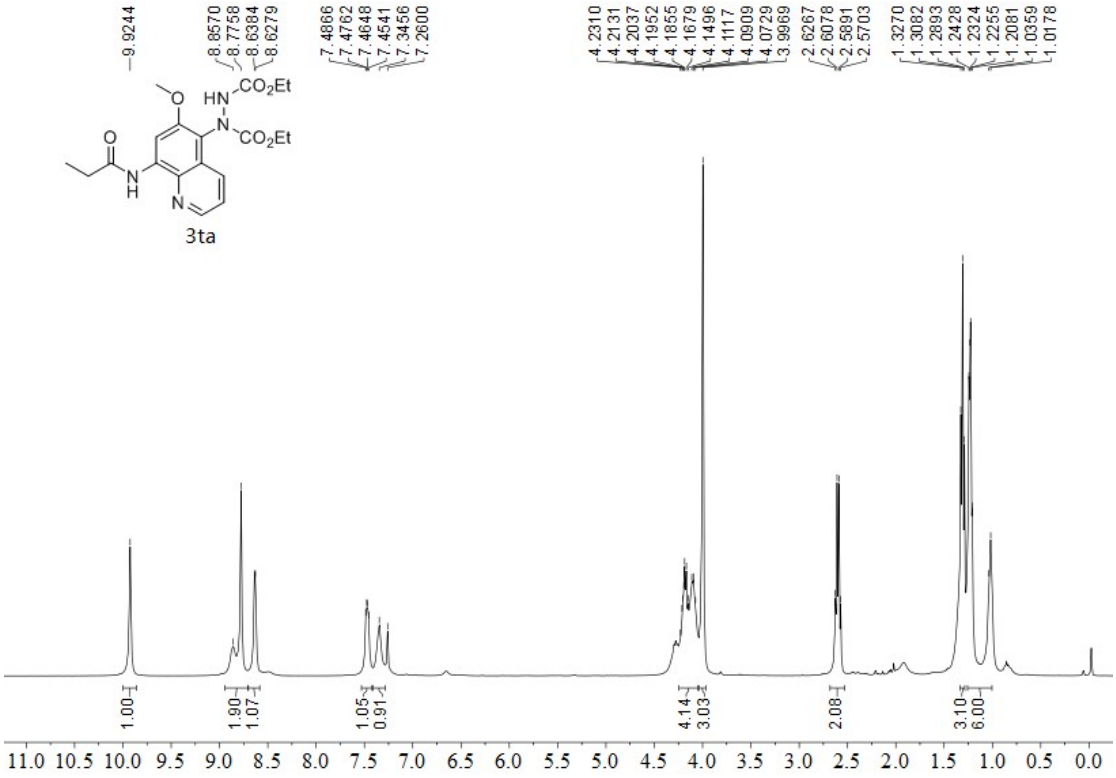
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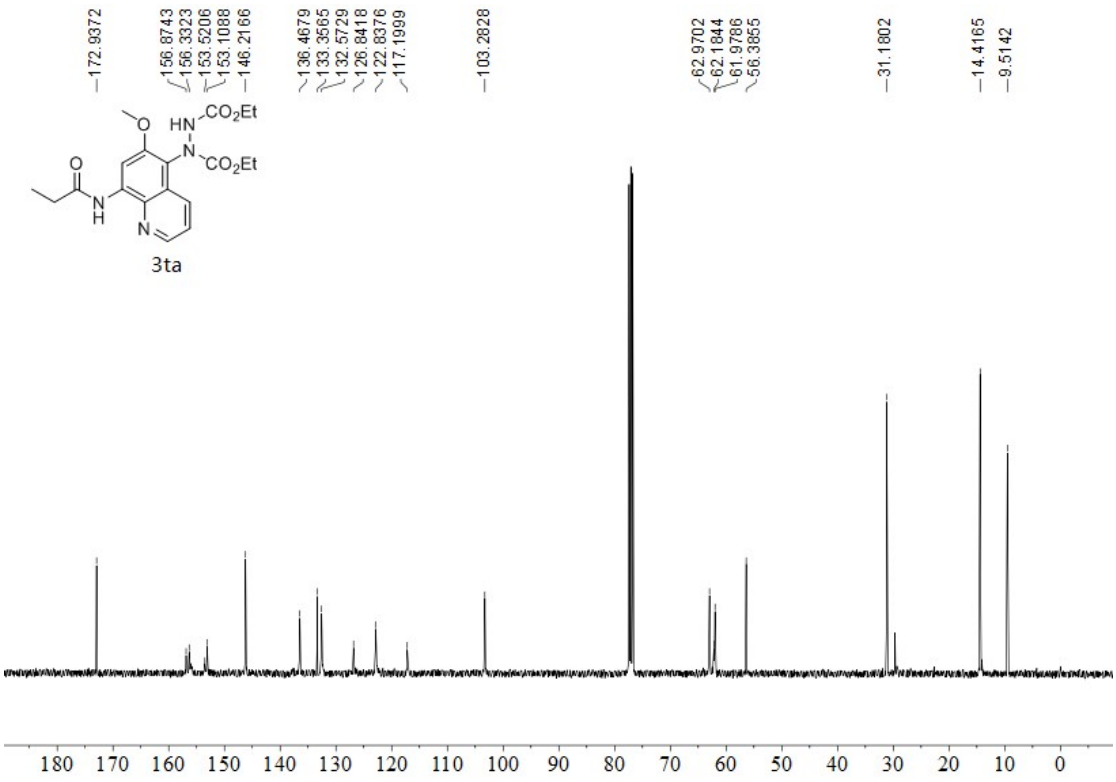
3ta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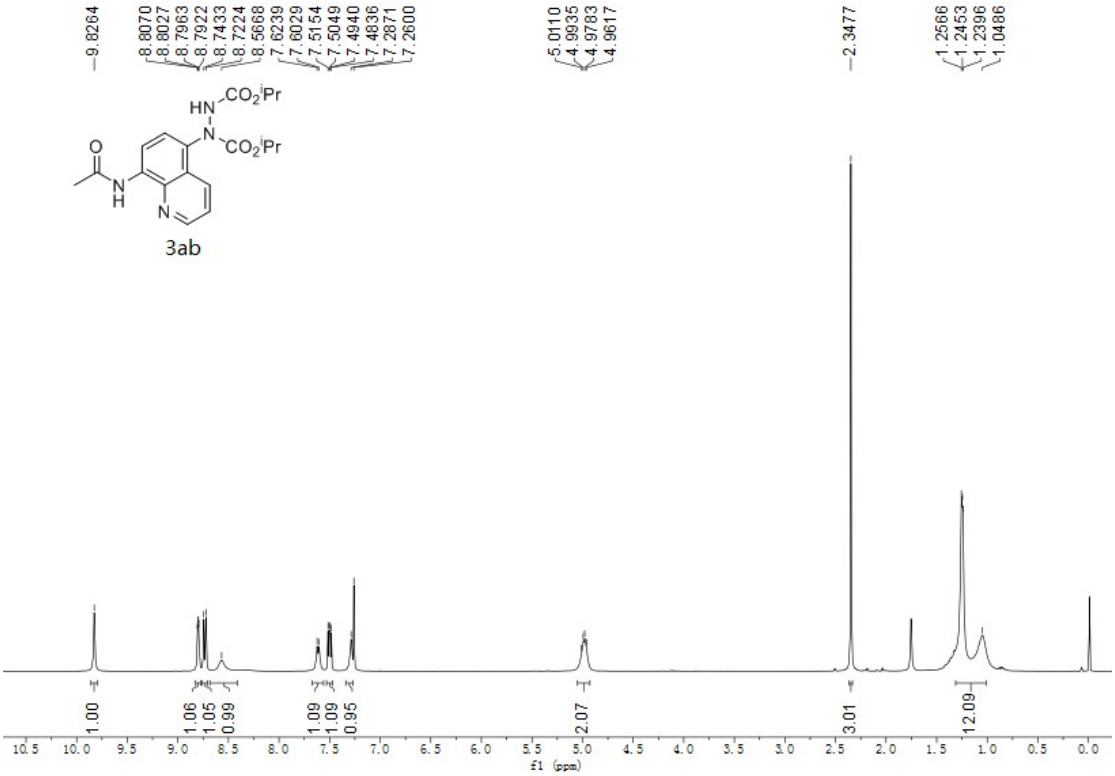
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7.2600
5.0110
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4.9783
4.9617
2.3477
1.2566
1.2453
1.2396
1.0486
HN
CO2iPr
N
CO2iPr
O
N
H
N
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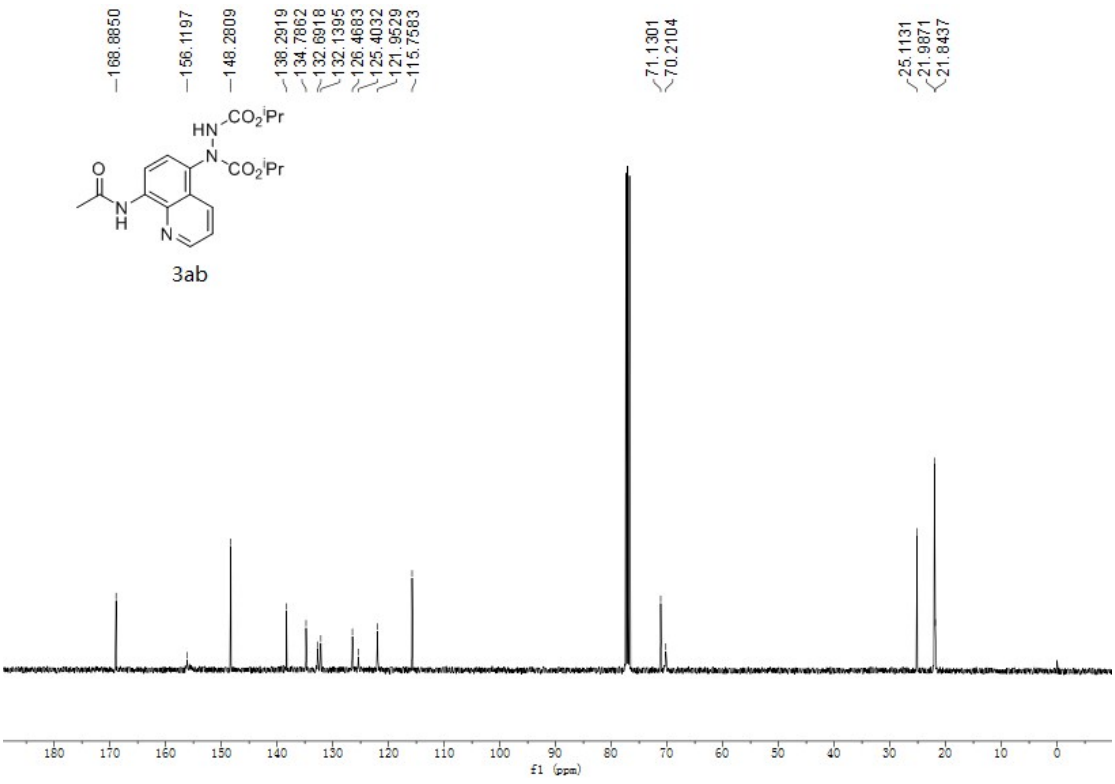
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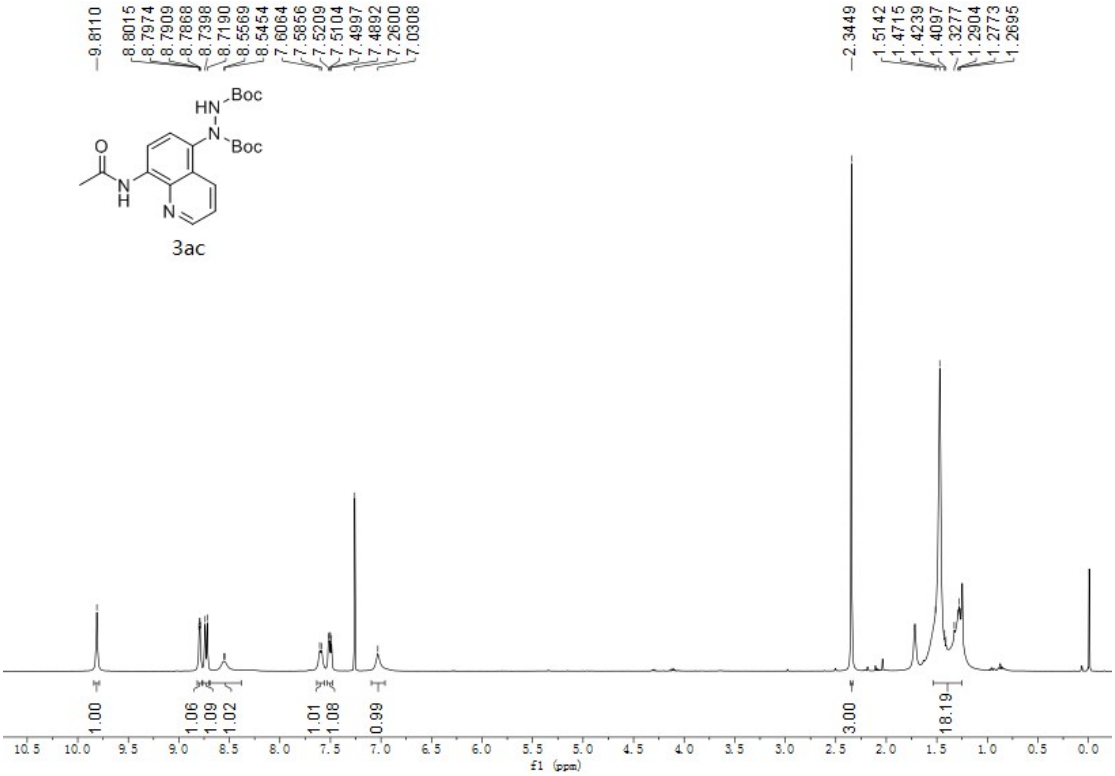
O
N
H
N
3ab
f1 (ppm)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Boc
N
Boc
O
N
H
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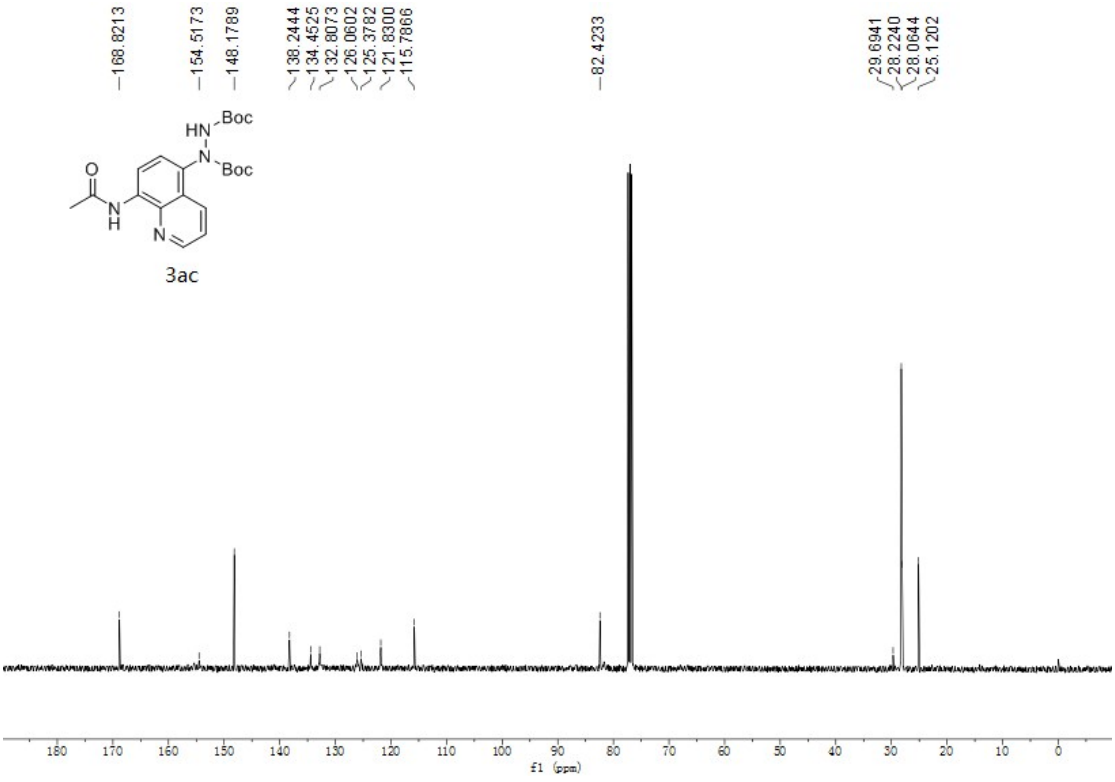
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N
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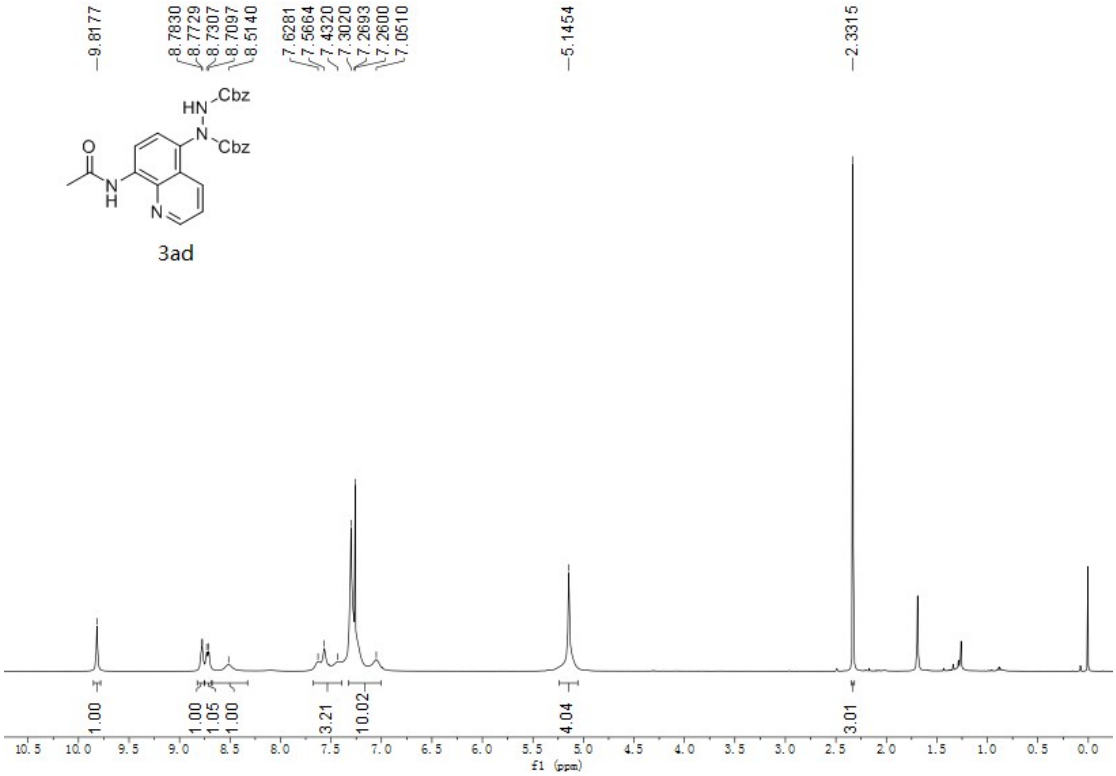
N
3ac
f1 (ppm)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7.2600
7.0510
5.1454
2.3315
HN
Cbz
N
Cbz
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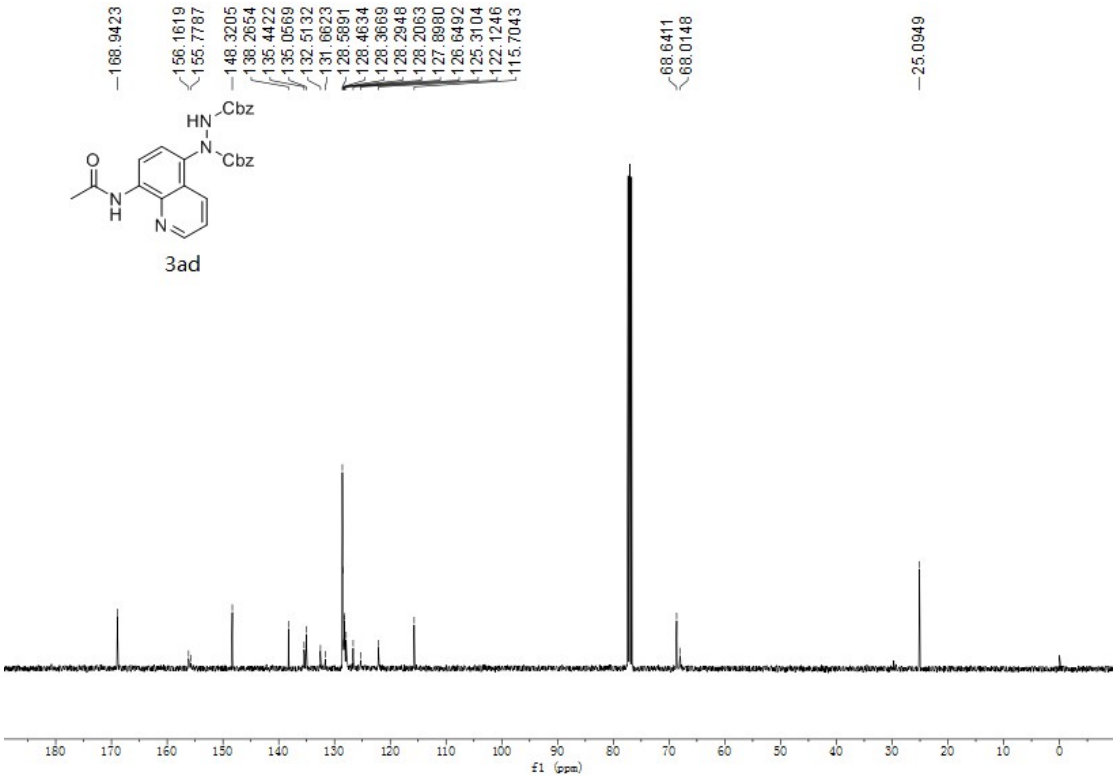
3.01
f1 (ppm)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125.3104
122.1246
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Cbz
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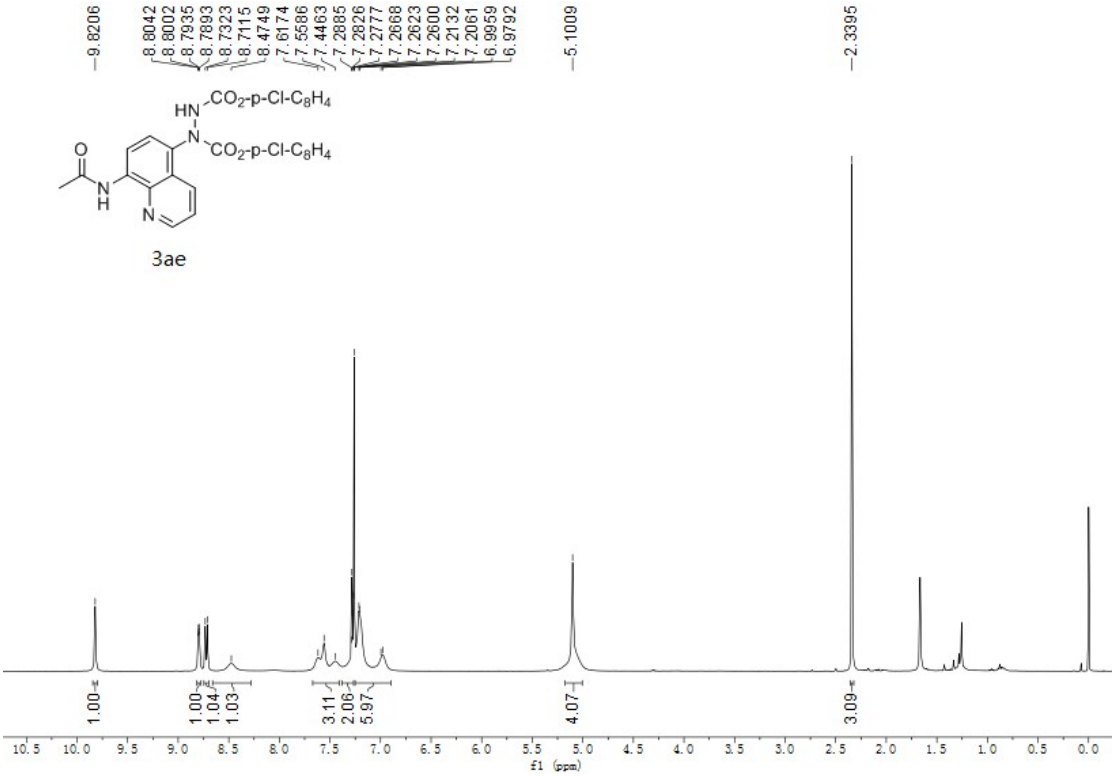
Cbz
O
N
H
N
3ad
f1 (ppm)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7.2826
7.2777
7.2668
7.2623
7.2600
7.2132
7.2061
6.9959
6.9792
5.1009
2.3395
HN
CO2-p-Cl-C8H4
N
CO2-p-Cl-C8H4
O
N
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1.00
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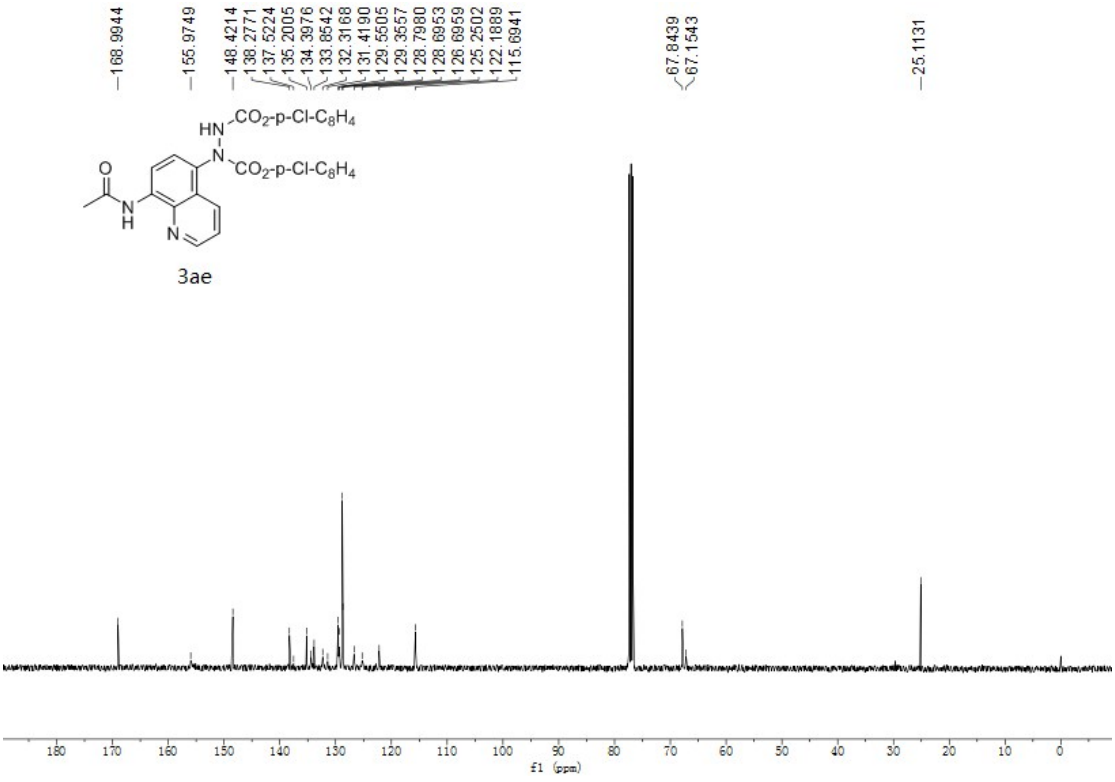
3.09
f1 (ppm)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125.2502
122.1889
115.6941
67.8439
67.1543
25.1131
HN
CO2-p-Cl-C8H4
N
CO2-p-Cl-C8H4
O
N
H
N
3ae
f1 (ppm)