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Supporting Information

for

Synthesis of imidazo[1,5-*a*]pyridines via cyclocondensation of 2-(aminomethyl)pyridines with electrophilically activated nitroalkanes

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Synthetic procedures and characterization data for compounds 16c–f, 18b and 18d, 19aa, 19ab, 19ac, 19ag, 19bb, 19bg, 19ce, and 20 as well as ^{1}H NMR, ^{13}C NMR, and HRMS spectral charts for all new compounds

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Experimental procedures

1-(Quinolin-2-yl)butan-1-amine (**18b**): Intermediate 2-(1-bromobutyl)quinoline (**21b**) was prepared according to typical procedure 1 starting with commercially available 2-butylquinoline (**22b**, 2.78 g, 15.0 mmol). Purification was performed by preparative column chromatography, eluting with EtOAc/hexane 1:10–1:6. Yellow oil, R_f 0.63, (EtOAc/petroleum ether, 1:6). Yield 2.68 g (10.2 mmol, 68%). ^{1}H NMR (400 MHz, DMSO) δ 8.39 (d, *J* = 8.4 Hz, 1H), 8.03-7.94 (m, 2H), 7.76 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.60 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 5.38 (t, *J* = 7.5 Hz, 1H), 2.40–2.21 (m, 2H), 1.51-1.43 (m, 1H), 1.38–1.21 (m, 1H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, DMSO) δ 160.0, 146.6, 137.4, 130.0, 128.7, 127.8, 127.2, 127.0, 120.3, 56.3, 38.8, 20.8, 13.2; ATR-FTIR (ZnSe) *v* (cm^{-1}): 3062, 2970, 2934, 2876, 1626, 1604, 1566, 1505, 1469, 1433, 1380, 1310, 1187, 829, 757. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{13}H_{15}BrN$: 264.0382; Found: 264.0376. The title compound was obtained as yellow oil, R_f 0.54, (CH_2Cl_2/EtOH/NEt_3 80:20:1). Purification was performed by preparative column chromatography, eluting with CH_2Cl_2/EtOH/NEt_3 80:10:1–80:20:1. Yield 1.90 g (9.50 mmol, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H, 8-H), 8.04 (d, *J* = 8.5 Hz, 1H, 4-H), 7.76 (d, *J* = 8.1 Hz, 1H, 5-H), 7.69–7.64 (m, 1H, 7-H), 7.48 (t, *J* = 7.5 Hz, 1H, 6-H), 7.39 (d, *J* = 8.5 Hz, 1H, 3-H), 4.18 (t, *J* = 6.7 Hz, 1H, CH- 2-Bu), 2.61 (s, 2H, NH), 1.87–1.68 (m, 2H, CH_2- 2-Bu), 1.47–1.26 (m, 2H, CH_2- 2-Bu), 0.91 (t, *J* = 7.4 Hz, 3H, CH_3- 2-Bu). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 147.7, 136.6, 129.5, 129.2, 127.6, 127.4, 126.1, 119.4, 57.5, 40.7, 19.6, 14.1. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3370, 3062, 2964, 2976, 1619, 1601, 1563, 1502, 1429,1308, 1123. HRMS (ESI-TOF): m/z (M+Na)$^+$, Calcd. for $C_{13}H_{16}N_2Na$: 223.1206; Found: 223.1204.

(5-Bromo-6-methoxyquinolin-2-yl)methanamine (**18d**): Intermediate 5-bromo-2-(bromomethyl)-6-methoxyquinoline (**21d**) was prepared according to typical procedure 1 starting with commercially available 5-bromo-6-methoxy-2-methylquinoline (**22d**, 3.78 g, 15 mmol). Purification was performed by preparative column chromatography, eluting with EtAOAc/hexane, gradient 1:6–1:3. Yellow solid, mp 130-132 °C, R_f 0.37 (EtOAc/hexane, 1:3). Yield 4.47 g (13.5 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.8 Hz, 1H, 4-H), 8.07 (d, *J* = 9.3 Hz, 1H, 8-H), 7.61 (d, *J* = 8.8 Hz, 1H, 7-H), 7.51 (d, *J* = 9.3 Hz, 1H, 3-H), 4.71 (s, 2H, -CH_2-), 4.05 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 154.6, 143.3, 136.2, 130.0, 128.0, 122.7, 117.0, 107.5, 57.2, 33.8. ATR-FTIR (ZnSe) *v* (cm^{-1}): 2935, 1613, 1587, 1491, 1446, 1259, 1219, 1147, 1042. HRMS (ESI-TOF): m/z (M+Na)$^+$, Calcd. for $C_{11}H_{10}Br_2NO$: 329.9124; Found: 329.9118. The title compound was obtained as pale brown solid, mp 75-77 °C, R_f 0.30 (CH_2Cl_2/EtOH 5:1). Yield 3.06 g (11.5 mmol, 85%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (d, *J* = 8.8 Hz, 1H, 4-H), 8.02 (d, *J* = 9.3 Hz, 1H, 8-H), 7.73 (d, *J* = 9.3 Hz, 1H, 7-H), 7.70 (d, *J* = 8.8 Hz, 1H, 3-H), 4.04 (s, 2H, -CH_2-), 4.01 (s, 3H, -OCH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.5, 153.4, 142.8, 134.0, 129.6, 126.7, 121.8, 117.2, 106.1, 57.0, 46.8; ATR-FTIR (ZnSe) *v* (cm^{-1}): 3102, 2974, 2842, 1593, 1557, 1493, 1469, 1436, 1311, 1269, 1209, 1126, 1062. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{11}H_{12}BrN_2O$ 267.0128; Found: 267.0127.

3-Propylimidazo[1,5-*a*]pyridine (**16c**):[S1] The title compound was obtained according to the typical procedure 2 starting with 1-nitrobutane (**1c**, 206 mg, 2.00 mmol) and 2-picolylamine (**12**, 108 mg, 1.00 mmol). Yellow oil, R_f 0.27 (EtOAc/ petroleum ether, 1:1). Yield 94 mg (0.59 mmol, 59%). Alternatively, the same compound was prepared via typical procedure 3 starting with 4-methyl-*N*-(pyridin-2-ylmethyl)-benzenesulfonamide (**17**, 262 mg, 1.00 mmol) and 1-nitrobutane (**1c**, 206 mg, 2.00 mmol). Yield 107 mg (0.67 mmol, 67%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 7.2 Hz, 1H, 5-H), 7.48 (d, *J* = 9.0 Hz, 1H, 8-H), 7.25 (s, 1H, 1-H), 6.68 (dd, *J* = 9.0, 6.4 Hz, 1H, 7-H), 6.62–6.55 (m, 1H, 6-H), 2.92 (t, *J* = 7.4 Hz, 2H, -CH_2- 3-Pr), 1,90-1,44 (m, 2H, -CH_2- 3-Pr), 0.94 (t, *J* = 7.4 Hz, 3H, -CH_3- 3-Pr). ^{13}C NMR (101 MHz, DMSO-d_6) δ 138.5, 129.7, 121.6, 118.0, 117.84, 117.77, 111.8, 27.6, 20.11, 13.7. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3114, 2967, 1685, 1652, 1509, 1488, 1455, 1339, 1325, 1273. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{10}H_{13}N_2$: 161.1073; Found: 161.1070.

3-Pentylimidazo[1,5-*a*]pyridine (**16d**): The title compound was obtained according to the typical procedure 2 starting with 1-nitrohexane (**1d**, 262 mg, 2.00 mmol) and 2-picolylamine (**12**, 108 mg, 1.00 mmol). Yellow oil, R_f 0.61 (EtOAc/petroleum ether 1:1). Yield 105 mg (0.56 mmol, 56 %). Alternatively, the same compound was prepared via typical procedure 3 starting with 4-methyl-*N*-(pyridin-2-ylmethyl)benzenesulfonamide (**17**, 262 mg, 1.00 mmol), and 1-nitrohexane (**1d**, 262 mg, 2.00 mmol). Yield 120 mg (0.64 mmol, 64%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (d, *J* = 7.3 Hz, 1H, 5-H), 7.48 (d, *J* = 9.2 Hz, 1H, 8-H), 7.25 (s, 1H, 1-H), 6.68 (dd, *J* = 9.2, 6.1 Hz, 1H, 7-H), 6.59 (t, *J* = 6.7 Hz, 1H, 6-H), 2.93 (t, *J* = 7.5 Hz, 2H, -CH_2- 3-Am), 1.78–1.67 (m, 2H, -CH_2- 3-Am), 1.36–1.28 (m, 4H, -CH_2- 3-Am), 0.85 (t, *J* = 6.6 Hz, 3H, -CH_3- 3-Am).^{13}C NMR (101 MHz, DMSO-d_6) δ 138.6, 129.7, 121.6, 118.1, 117.84, 117.76, 111.8, 30.9, 26.4, 25.6, 21.9, 13.9.ATR-FTIR (ZnSe) *v* (cm^{-1}): 2953, 2927, 2868, 1698, 1650, 1557, 1504, 1458, 1363, 1326, 1272. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{12}H_{17}N_2$ + ([M+H]+): 189.1386, found: 189.1381 (*δ* =2.6 ppm).

Imidazo[1,5-*a*]pyridine (**16e**):[S2] The title compound was obtained via typical procedure 2 starting from nitromethane (**1e**, 122 mg, 2.00 mmol) and 2-picolylamine (**12**, 108 mg, 1.00 mmol). Light-brown solid, R_f 0.27 (EtOAc), mp 51-52, lit[S2] m.p. 52-54 °C ($CHCl_3$, hexane). Yield 73 mg (0.62 mmol, 62 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (s, 1H, 3-H), 8.32 (d, *J* = 7.0 Hz, 1H, 5-H), 7.52 (d, *J* = 9.1 Hz, 1H, 8-H), 7.34 (s, 1H, 1-H), 6.74 (dd, *J* = 8.9, 6.4 Hz, 1H, 7-H), 6.62 (t, *J* = 6.7 Hz, 1H, 6-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 129.6, 128.2, 123.2, 119.2, 119.0, 117.8, 112.2.ATR-FTIR (ZnSe) *v* (cm^{-1}): 3052, 2935, 2857, 1651, 1504, 1455, 1370, 1327, 1246, 1221, 1113. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_7H_7N_2$: 119.0604; Found: 119.0602.

3-Benzylimidazo[1,5-*a*]pyridine (**16f**):[S1] The title compound was obtained via typical procedure 2 starting from (2-nitroethyl)benzene (**1f**, 302 mg, 2.00 mmol) and 2-picolylamine (**12**, 108 mg, 1.00 mmol). Yellow solid, R_f 0.58 (EtOAc/petroleum ether, 1:1), mp 84-87 °C, lit[S1] yellow crystals mp 84-87 °C(cyclohexane). Yield 112 mg (0.54 mmol, 54%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (dd, *J* = 7.2, 1.1 Hz, 1H, 5-H), 7.52 (dt, *J* = 9.1, 1.2 Hz, 1H, 8-H), 7.32 (d, *J* = 1.0 Hz, 1H, 1-H), 7.30–7.25 (m, 2H, 2,6-H 3-Bn), 7.24–7.18 (m, 3H, 3,4,5-H 3-Bn), 6.71 (ddd, *J* = 9.1, 6.4, 1.0 Hz, 1H, 7-H), 6.59 (ddd, *J* = 7.4, 6.3, 1.2 Hz, 1H, 6-H), 4.41 (s, 2H, -CH_2- 2-Bn); ^{13}C NMR (101 MHz, DMSO-d_6) δ 137.26, 137.17, 130.1, 128.5 (2C), 128.3 (2C), 126.4, 121.5, 118.3, 118.1 (2C), 112.1, 32.0; ATR-FTIR (ZnSe) *v* (cm^{-1}): 3026, 2971, 2934, 1683, 1557, 1507, 1456, 1361, 1336, 1277. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{14}H_{13}N_2$: 209.1073; Found: 209.1075.

1-Methylimidazo[1,5-*a*]quinoline (**19aa**):[S3] The title compound was obtained via typical procedure 2 starting from nitroethane (**1a**, 150 mg, 2.00 mmol) and quinolin-2-ylmethanamine (**18a**, 158 mg, 1.00 mmol). Yellow oil, R_f 0.36 (EtOAc). Yield 111 mg (0.61 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H, 9-H), 7.51 (d, *J* = 7.7 Hz, 1H, 6-H), 7.39 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H, 7-H), 7.28 (t, *J* = 7.5 Hz, 1H, 8-H), 7.24 (s, 1H, 3-H), 7.13 (d, *J* = 9.4 Hz, 1H, 5-H), 6.80 (d, *J* = 9.4 Hz, 1H, 4-H), 2.98 (s, 3H, CH_3).^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 133.2, 130.3, 128.5, 127.6, 125.6, 124.8, 120.55, 120.52, 117.2, 116.1, 19.6. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3059, 1606, 1559, 1478, 1453, 1387, 1306, 1268, 1211. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{12}H_{11}N_2$: 183.0917; Found: 183.0918.

1-Ethylimidazo[1,5-a]quinoline (**19ab**):[S4] The title compound was obtained via typical procedure 2 starting from 1-nitropropane (**1b**, 178 mg, 2.00 mmol) and quinolin-2-ylmethanamine (**18a**, 158 mg, 1.00 mmol). Yellow oil, R_f 0.31, (EtOAc/petroleum ether, 1:4). Yield 90 mg (0.46 mmol, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 1H, 9-H), 7.63 (dd, *J* = 7.7, 1.7 Hz, 1H, 7-H), 7.52 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H, 8-H), 7.40 (dd, *J* = 7.5, 1.0 Hz, 1H, 6-H), 7.38 (s, 1H, 3-H), 7.23 (d, *J* = 2.4 Hz, 1H, 4-H), 6.96 (d, *J* = 9.3 Hz, 1H, 5-H), 3.45 (q, *J* = 7.4 Hz, 2H, CH_2 1-Et), 1.57 (t, *J* = 7.4 Hz, 3H, CH_3 1-Et); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 133.1, 130.4, 129.0, 128.2, 126.0, 125.4, 121.5, 119.5, 117.4, 116.8, 25.6, 12.0. ATR-FTIR (ZnSe) *v* (cm^{-1}): 2978, 2927, 1559, 1473, 1391, 1376, 1326, 1304, 1268, 1217, 1162, 1056. HRMS (ESI-TOF): Calcd. for m/z (M+H)$^+$, $C_{13}H_{13}N_2$ $^+$ 197.1073; Found: 197.1069.

1-Propylimidazo[1,5-*a*]quinoline (**19ac**):[S3] The title compound was obtained via typical procedure 2 starting from 1-nitrobutane (**1c**, 206 mg, 2.00 mmol) and quinolin-2-ylmethanamine (**18a**, 158 mg, 1.00 mmol). Colorless oil, R_f 0.42, (EtOAc/petroleum ether, 1:1). Yield 117 mg (0.56 mmol, 56%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (d, *J* = 8.5 Hz, 1H, 9-H), 7.79 (dd, *J* = 7.7, 1.4 Hz, 1H, 6-H), 7.62 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H, 7-H), 7.48–7.44 (m, 1H, 8-H), 7.42 (d, *J* = 9.4 Hz, 1H, 5-H), 7.34 (s, 1H, 3-H), 7.09 (d, *J* = 9.4 Hz, 1H, 4-H), 3.33 (t, 2H, -CH_2- 1-Pr), 1.98-1.80 (m, 2H, -CH_2- 1-Pr), 1.07 (t, *J* = 7.4 Hz, 3H, -CH_3- 1-Pr). ^{13}C NMR (101 MHz, DMSO-d_6) δ 143.6, 132.4, 129.8, 128.6, 128.2, 125.3, 125.0, 120.6, 120.3, 117.4, 116.7, 33.5, 20.1, 13.8.ATR-FTIR (ZnSe) *v* (cm^{-1}): 2967, 2890, 2810, 1665, 1477, 1453, 1391, 1264, 1211,1160. HRMS (ESI-TOF): m/z (M+H)$^+$, $C_{14}H_{15}N_2$: 211.1230; Found: 211.1228.

Imidazo[1,5-*a*]quinoline (**19ae**):[S5] The title compound was obtained via typical procedure 2 starting from nitromethane (**1e**, 122 mg, 2.00 mmol) and quinolin-2-ylmethanamine (**18a**, 158 mg, 1.00 mmol). Yellow solid, R_f 0.33, (EtOAc/petroleum ether, 1:1), m.p. 71-72 °C, lit[S4] yellow crystals mp 73-75 °C. Yield 139 mg (0.83 mmol, 83%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.53 (s, 1H, 1-H), 8.43 (d, *J* = 8.1 Hz, 1H, 9-H), 7.88 (d, *J* = 7.0 Hz, 1H, 5-H), 7.69 (dd, *J* = 8.4, 5.2 Hz, 2H, 7,3-H), 7.56 (dd, *J* = 8.1, 5.6 Hz, 2H, 8,6-H), 7.33 (d, *J* = 9.5 Hz, 1H, 4-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 130.3, 129.2, 128.9, 128.8, 128.1, 126.5, 123.8, 122.4, 119.4, 116.6, 115.9. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3125, 2927, 1740, 1555, 1478, 1451, 1240, 1217, 1142,1114. HRMS (ESI-TOF): m/z (M+H)$^+$, $C_{11}H_9N_2$: 169.0760; Found: 169.0761.

1-Phenylimidazo[1,5-a]quinoline (**19ag**):[S4] The title compound was obtained via typical procedure 4 starting from 2-nitro-1-phenylethan-1-one (**1h**, 330 mg, 2.00 mmol) and quinolin-2-ylmethanamine (**18a**, 158 mg, 1.00 mmol). Yellow solid, R_f 0.51 (EtOAc), mp 116-117 °C, lit[S5] yellow solid, mp 113-115°C. Yield 200 mg (0.84 mmol, 84%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (dd, *J* = 7.7, 1.6 Hz, 1H, 9-H), 7.63–7.57 (m, 5H, 1-Ph), 7.56 (s, 1H, 3-H), 7.53 (d, *J* = 9.4 Hz, 1H, 5-H), 7.43–7.33 (m, 2H, 6,8-H), 7.27 (ddd, *J* = 8.7, 7.0, 1.6 Hz, 1H, 7-H), 7.22 (d, *J* = 9.4 Hz, 1H, 4-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 141.7, 133.8, 131.7, 130.1, 129.51 (2C), 129.45, 128.99, 128.91 (2C), 127.6, 125.4, 125.2, 122.3, 121.4, 117.3, 116.53.ATR-FTIR (ZnSe) *v* (cm^{-1}): 3102, 2974, 2842, 1593, 1557, 1493, 1469, 1436, 1311, 1269, 1209, 1126, 1062 HRMS (ESI-TOF): m/z (M+H)$^+$, $C_{17}H_{13}N_2$: 245.1073; Found 245.1074.

1-Ethyl-3-propylimidazo[1,5-*a*]quinoline (**19bb**): The title compound was obtained via typical procedure 2 starting from 1-nitropropane (**1b**, 178 mg, 2.00 mmol) and 1-(quinolin-2-yl)butan-1-amine (**18b**, 200 mg, 1.00 mmol). Yellow oil, R_f 0.60, (EtOAc/petroleum ether, 1:4). Yield 150 mg (0.63 mmol, 63 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.5 Hz, 1H, 9-H), 7.54 (dd, *J* = 7.7, 1.3 Hz, 1H, 5-H), 7.43 (ddd, *J* = 8.6, 4.5, 0.7 Hz, 1H, 8-H), 7.30 (td, *J* = 7.4, 0.6 Hz, 1H, 7-H), 7.16 (d, *J* = 9.4 Hz, 1H, 6-H), 6.77 (d, *J* = 9.4 Hz, 1H, 4-H), 3.36 (q, *J* = 7.4 Hz, 2H, CH_2- 1-Et), 2.82–2.74 (m, 2H, CH_2- 3-Pr), 1.82–1.69 (m, 2H, CH_2- 3-Pr), 1.51 (t, *J* = 7.4 Hz, 3H, CH_3- 1-Et), 0.97 (t, *J* = 7.4 Hz, 3H, CH_3- 3-Pr). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 133.32, 133.31, 128.5, 127.5, 126.3, 126.1, 124.6, 118.9, 117.1, 116.5, 29.2, 25.6, 23.7, 14.1, 12.2. ATR-FTIR (ZnSe) *v* (cm^{-1}): 2960, 2876, 1887, 1696, 1625, 1557, 1480, 1455, 1389, 1374,1218, 1136,1114. HRMS (ESI-TOF): m/z (M+H)$^+$, $C_{16}H_{19}N_2$: 239.1543; Found: 239.1539.

3-Propylimidazo[1,5-*a*]quinoline (**19be**): The title compound was obtained via typical procedure 2 starting from nitromethane (**1e**, 122 mg, 2.00 mmol) and 1-(quinolin-2-yl)butan-1-amine (**18b**, 200 mg, 1.00 mmol). Yellow oil, R_f 0.38, (EtOAc/petroleum ether, 1:1). Yield 100 mg (0.48 mmol, 48%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H, 1-H), 8.29 (d, *J* = 8.3 Hz, 1H, 9-H), 7.79–7.73 (m, 1H, 6-H), 7.58 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, 7-H), 7.46–7.44 (m, 1H, 8-H), 7.42 (d, *J* = 8.1 Hz, 1H, 5-H), 7.05 (d, *J* = 9.5 Hz, 1H, 4-H), 2.76 (t, *J* = 7.3 Hz, 2H, -CH_2- 3-Pr), 1.96-1.44 (m, 2H, -CH_2- 3-Pr), 0.91 (t, *J* = 7.4 Hz, 3H, -CH_3- 3-Pr). ^{13}C NMR (101 MHz, DMSO-d_6) δ 134.7, 130.7, 128.5 (2C), 128.0, 125.3, 124.2, 123.7, 119.1, 116.6, 115.1, 28.4, 22.8, 13.7. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3114, 2964, 2868, 1683, 1557, 1489, 1458, 1378, 1339, 1225, 1129. HRMS (ESI-TOF): m/z (M+H)$^+$, Calcd. for $C_{14}H_{15}N_2$: 211.1230; Found: 211.1234.

1-Phenyl-3-propylimidazo[1,5-a]quinoline (**19bg**): The title compound was obtained via typical procedure 4 starting from 2-nitro-1-phenylethan-1-one (**1h**, 330 mg, 2.00 mmol) and 1-(quinolin-2-yl)butan-1-amine

(**18b**, 200 mg, 1.00 mmol). Yellow oil, R_f 0.34, (EtOAc/petroleum ether, 1:8). Yield 75 mg (0.26 mmol, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H, 2,6-H Ph), 7.57 (dd, *J* = 7.8, 1.6 Hz, 1H, 6-H), 7.52–7.48 (m, 3H, 3,4,5-H Ph), 7.46 (s, 1H, 9-H), 7.31–7.28 (m, 1H, 5-H), 7.28–7.24 (m, 1H, 7-H), 7.13 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, 8-H), 6.92 (d, *J* = 9.4 Hz, 1H, 4-H), 2.88 (t, 2H, CH_2- 3-Pr), 1.90-1.76 (m, 2H, CH_2- 3-Pr), 1.01 (t, *J* = 7.3 Hz, 3H, CH_3- 3-Pr). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.0, 135.1, 133.8, 132.6, 129.8 (2C), 129.3, 128.9 (2C), 128.6, 127.2, 126.7, 125.9, 125.1, 119.9, 117.5, 116.9, 29.3, 23.6, 14.2. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3062, 2956, 2872, 1601, 1553, 1486, 1455, 1374, 1317, 1253, 1213, 1145, 1076. HRMS (ESI-TOF): m/z $(M+H)^+$, Calcd. for $C_{20}H_{19}N_2$: 287.1543; Found: 287.1539.

6-Bromoimidazo[1,5-a]quinoline (**19ce**): The title compound was obtained via typical procedure 2 starting from nitromethane (**1e**, 122 mg, 2.00 mmol) and (6-bromoquinolin-2-yl)methanamine (**18c**, 237 mg, 1.00 mmol). Colorless solid, mp 152-153 °C, R_f 0.50, (EtOAc). Yield 144 mg (0.59 mmol, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H, 1-H), 7.83 (d, *J* = 8.8 Hz, 1H, 9-H), 7.80 (d, *J* = 2.2 Hz, 1H, 6-H), 7.64 (dd, *J* = 8.8, 2.2 Hz, 1H, 8-H), 7.48 (s, 1H, 3-H), 7.35 (d, *J* = 9.5 Hz, 1H, 4-H), 6.93 (d, *J* = 9.4 Hz, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.5, 131.2, 130.0, 128.6, 128.2, 126.1, 123.4, 120.1, 118.7, 118.3, 116.4. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3132, 1901, 1707, 1546, 1478, 1422, 1361, 1325, 1202, 1126,1107. HRMS (ESI-TOF): m/z $(M+H)^+$, Calcd. for $C_{11}H_8BrN_2$: 246.9865; Found: 246.9864.

Ethyl 2-oxo-2-((pyridin-2-ylmethyl)amino)acetate (**20**):[S6] The title compound was obtained via typical procedure 2 starting from ethyl 2-nitroacetate (**1i**, 266 mg, 2.00 mmol) and 2-picolylamine (**12**, 108 mg, 1.00 mmol). The reaction was carried out at 140 °C. Yellow powder, R_f 0.22, (EtOAc/ petroleum ether, 1:1), mp 57-59 °C, lit[S6] yellow crystals, mp 62-63.5 °C (EtOH). Yield 60 mg (0.29 mmol, 29%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (s, 1H, NH), 8.50 (d, *J* = 4.6 Hz, 1H, 6-H py), 7.76 (td, *J* = 7.7, 1.6 Hz, 1H, 4-H py), 7.30 (d, *J* = 4.1 Hz, 3-H py), 7.27 (t, *J* = 8.1 Hz, 2H, 5-H py), 4.44 (d, *J* = 6.1 Hz, 2H, CH_2), 4.26 (q, *J* = 7.1 Hz, 2H, CH_2), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.6, 157.3, 157.2, 148.9, 136.8, 122.3, 121.1, 62.1, 44.3, 13.8. ATR-FTIR (ZnSe) *v* (cm^{-1}): 3407, 2931, 1735, 1700, 1650, 1541, 1520, 1471, 1453, 1369,1206. HRMS (ESI-TOF): m/z $(M+Na)^+$, $C_{10}H_{12}N_2NaO_3$: 231.0740; Found: 231.0737.

Cited literature

S1. Li, M.; Xie, Y.; Ye, Y.; Zou, Y.; Jiang, H.; Zeng, W. *Org. Lett.* **2014,** *16*, 6232-6235.

S2. Catalan, J.; De Paz, J. L. G.; Yanez, M.; Amat-Guerri, F.; Houriet, R.; Rolli, E.; Zehringer, R.; Oelhafen, P.; Taft, R. W.; Anvia, F.; Qian, J. H. *J. Am. Chem. Soc.* **1988,** *110*, 2699-2705.

S3. Wang, Q., Zhang, S., Guo, F., Zhang, B., Hu, P., & Wang, Z. *J. Org. Chem*. **2012**, *72*, 11161–11166.

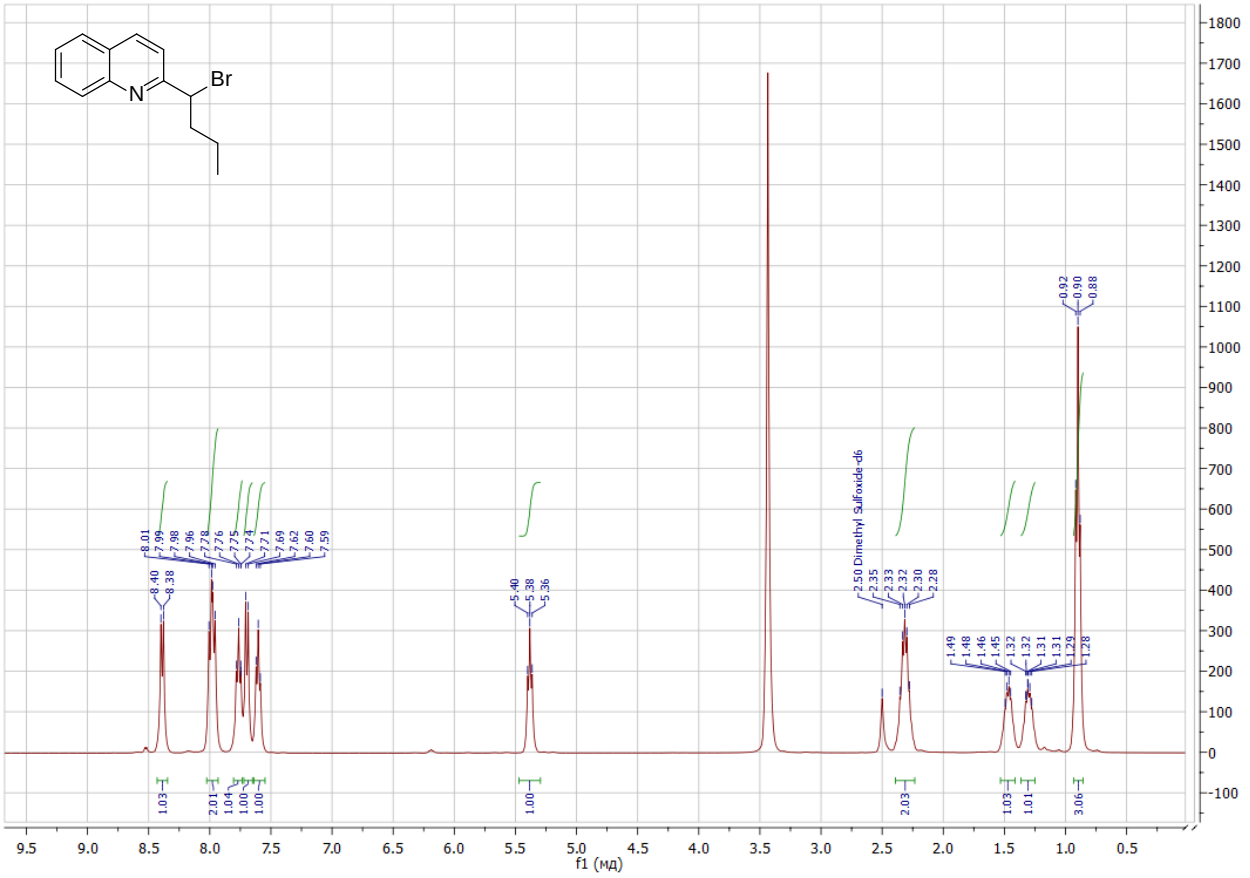
S4. Li, Z.; Wu, S.-S.; Luo, Z.-G.; Liu, W.-K.; Feng, C.-T.; Ma, S.-T. *J. Org. Chem.* **2016,** *81*, 4386-4392.

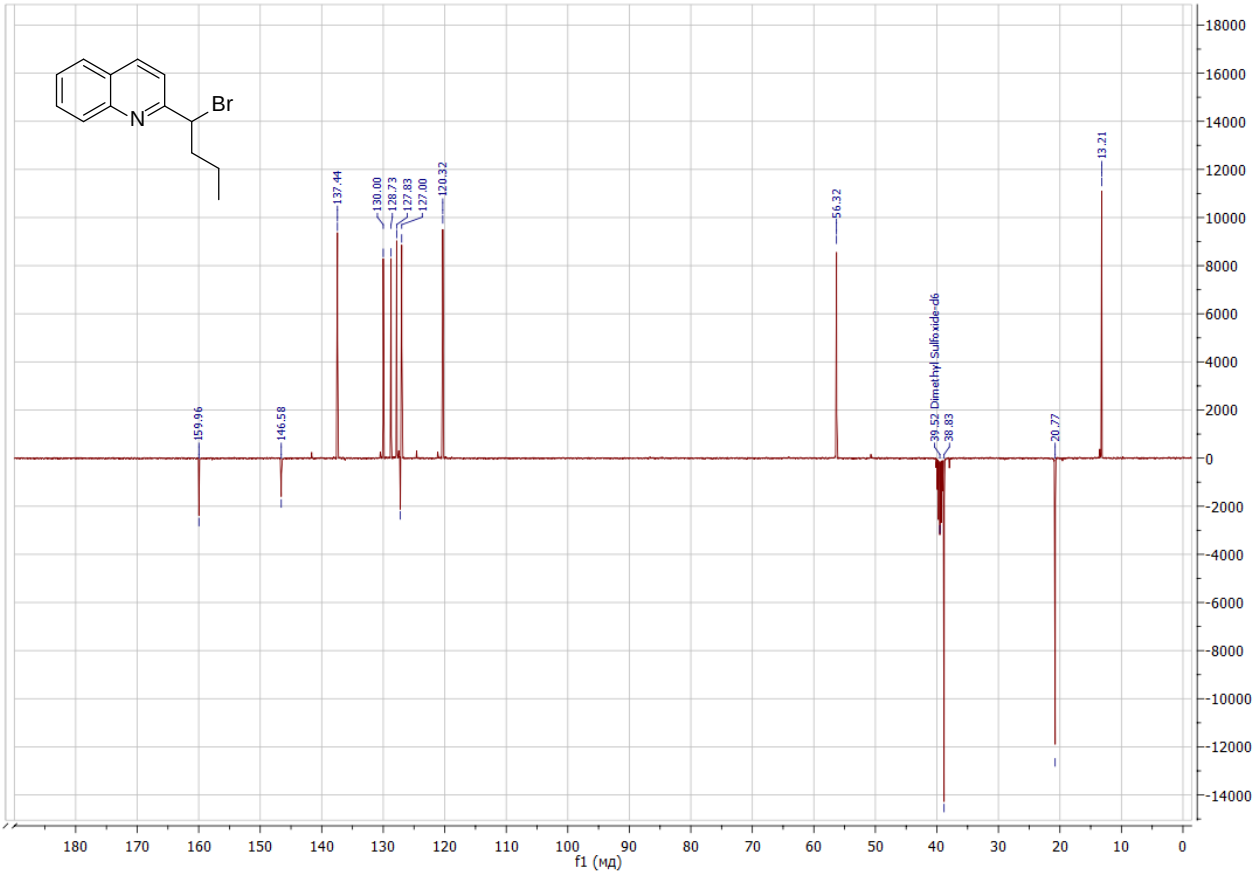
S5. Van Nispen, S. P. J. M.; Mensink, C.; Van Leusen, A. M. *Tetrahedron Lett.* **1980,** *21*, 3723-3726.

S6. Winterfeld, K.; Lampke, H.; Franzke, H. *Justus Liebigs Ann. Chem.* **1965,** *685*, 181-186.

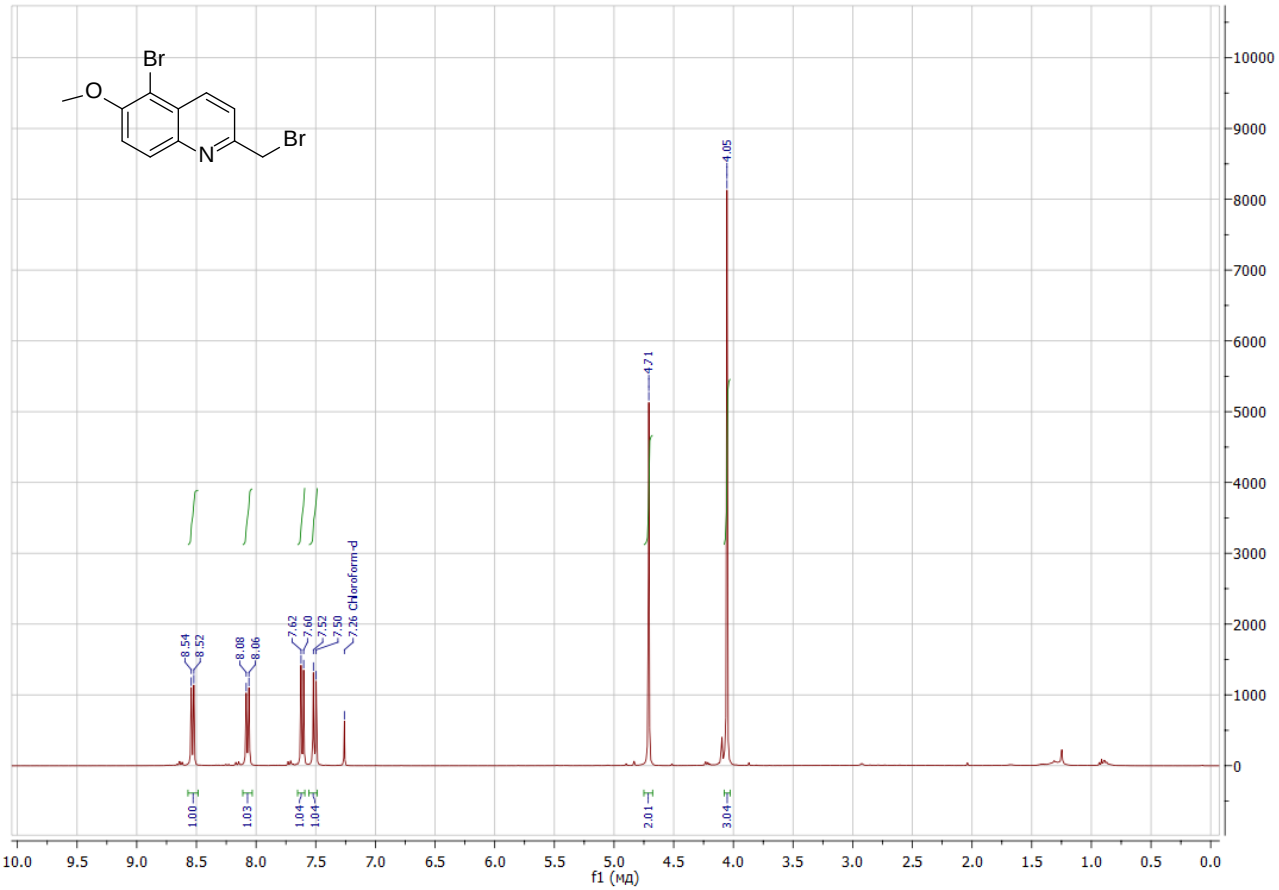
NMR spectral charts

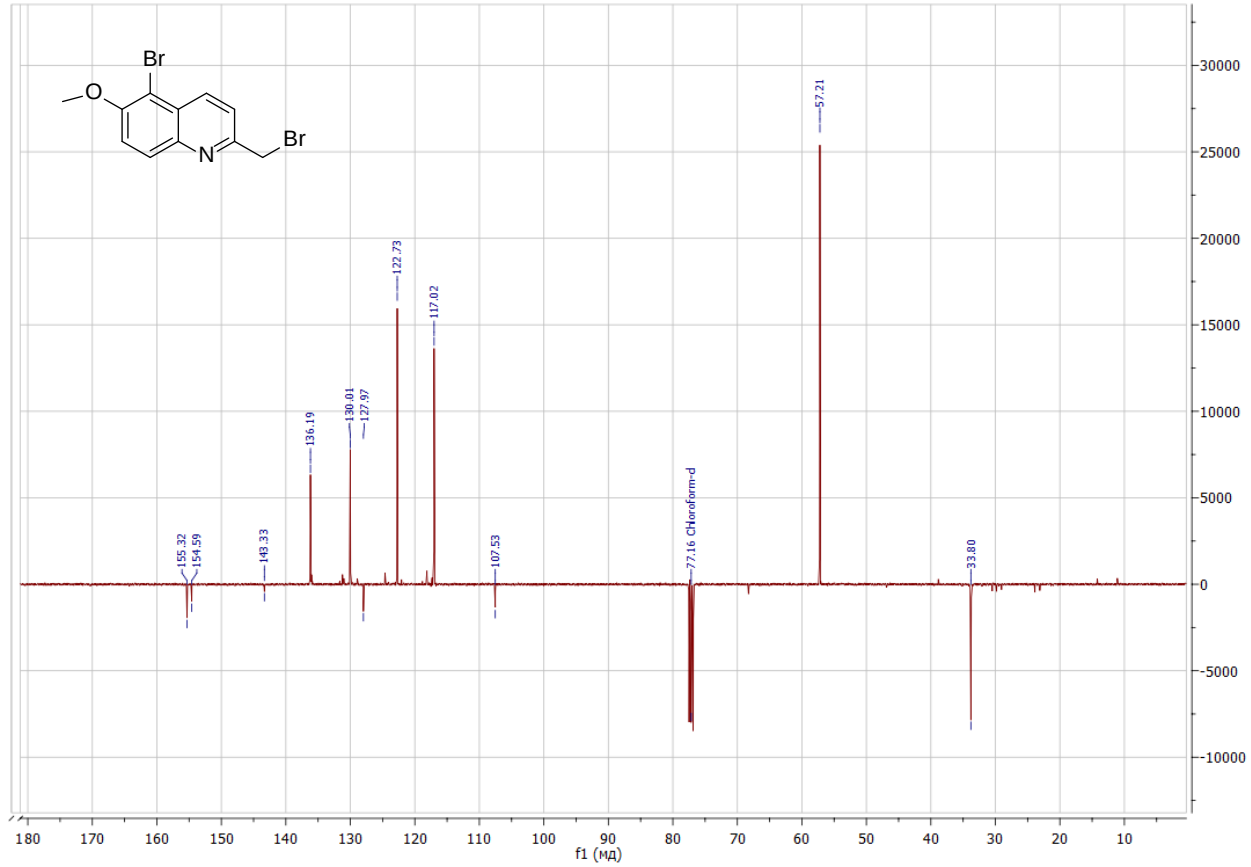
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **21b** in $CDCl_3$.



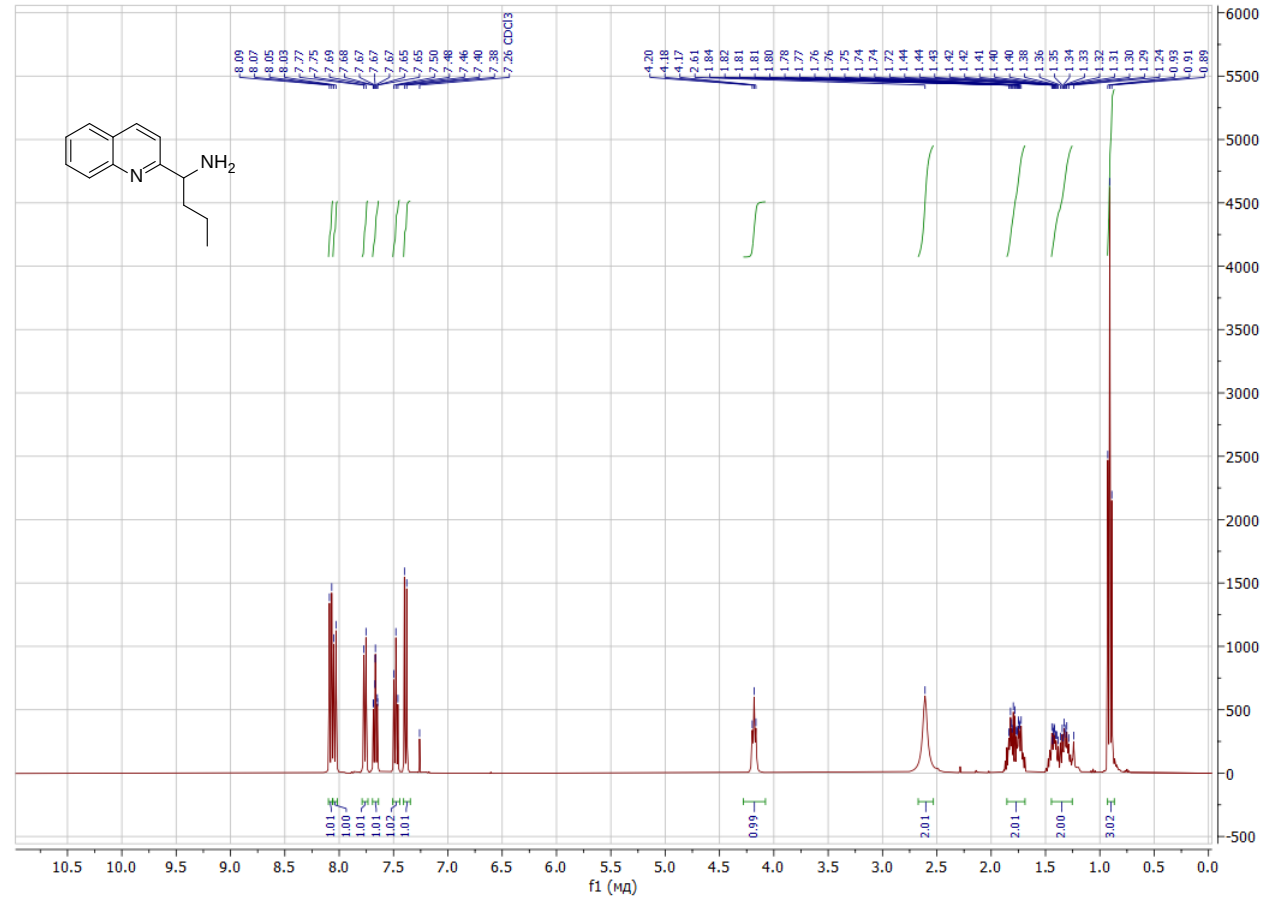


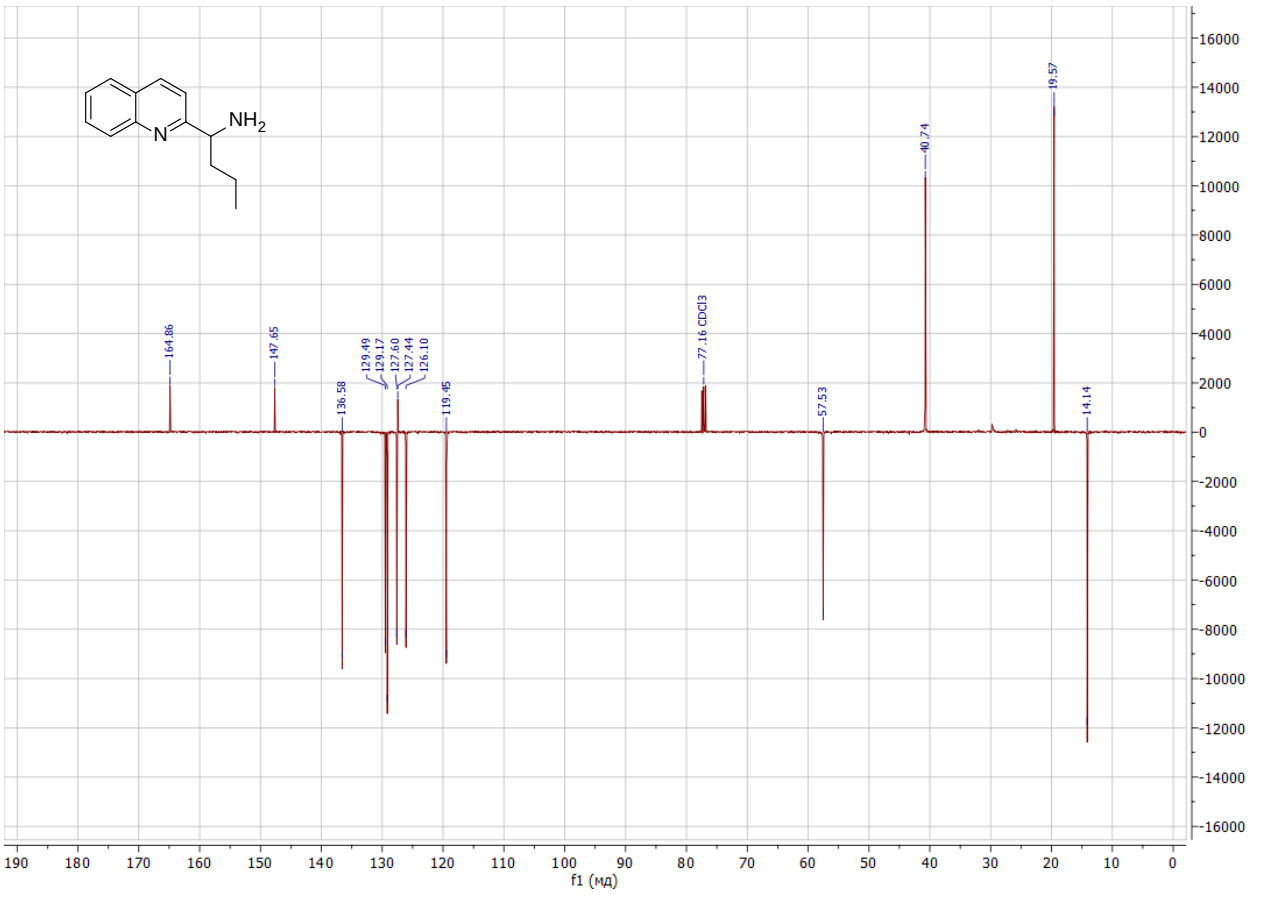
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **21d** in $CDCl_3$.



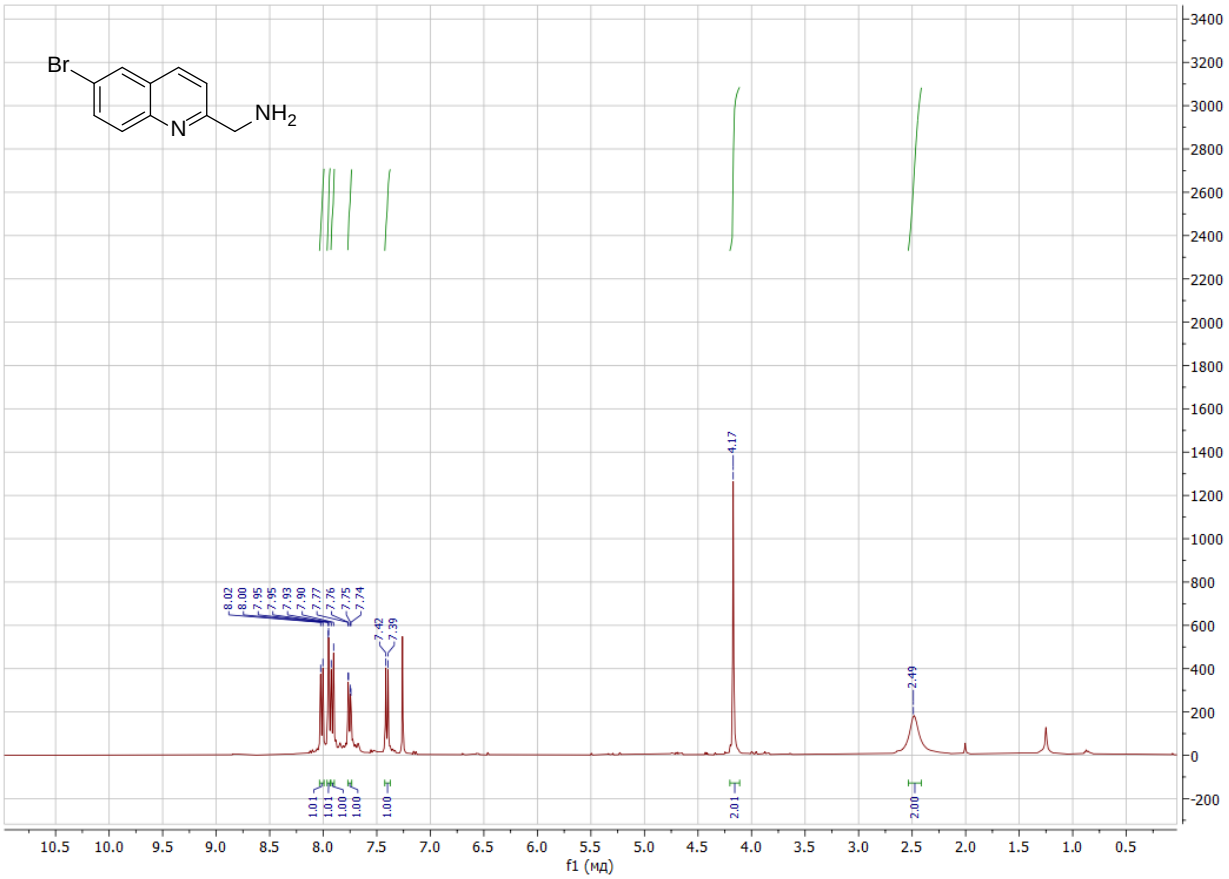


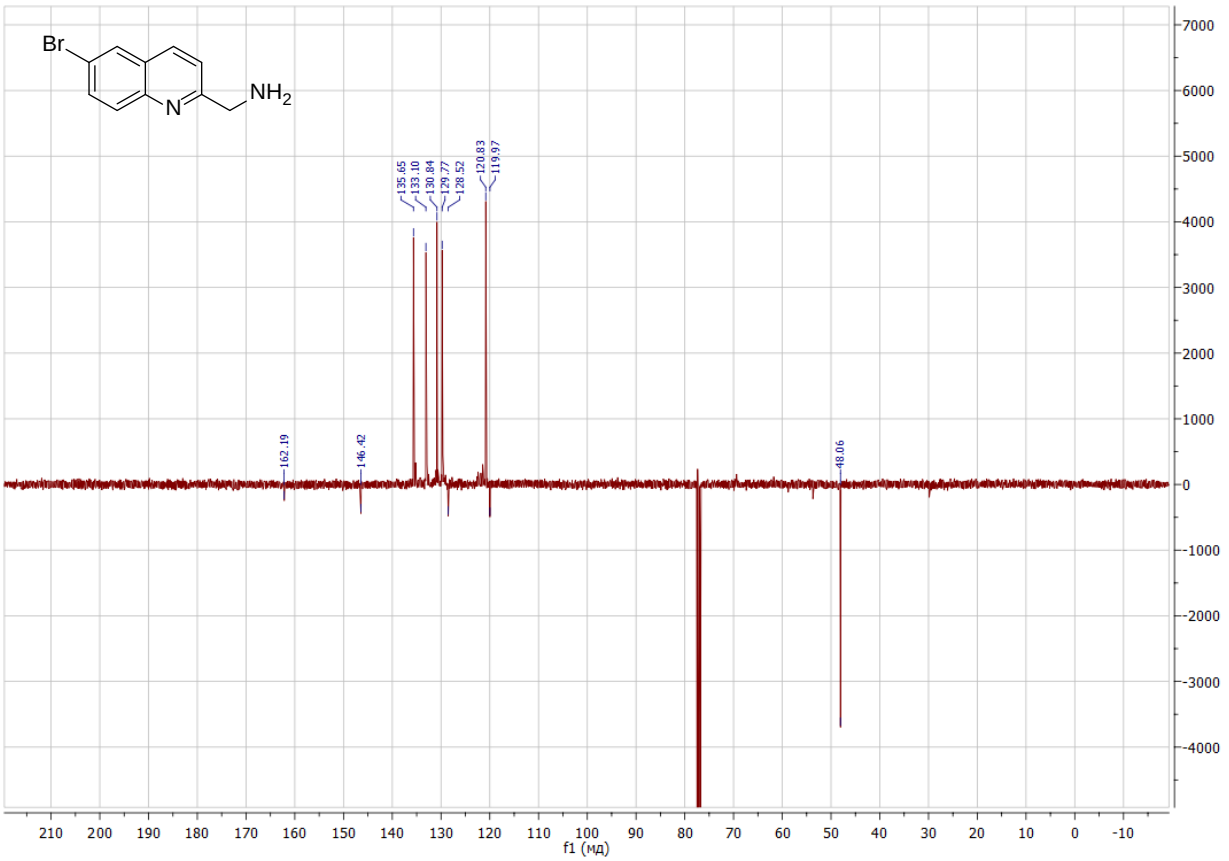
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **18b** in $CDCl_3$.



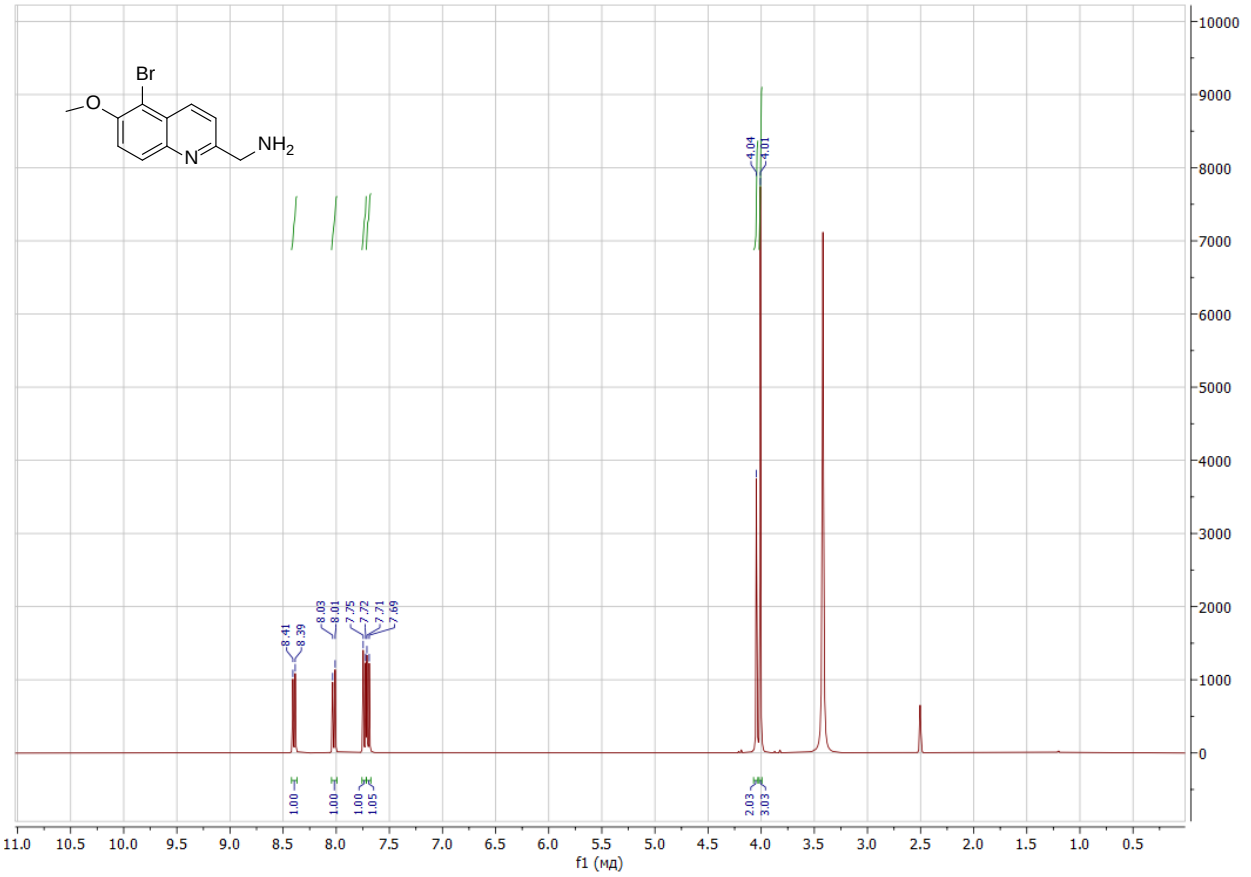


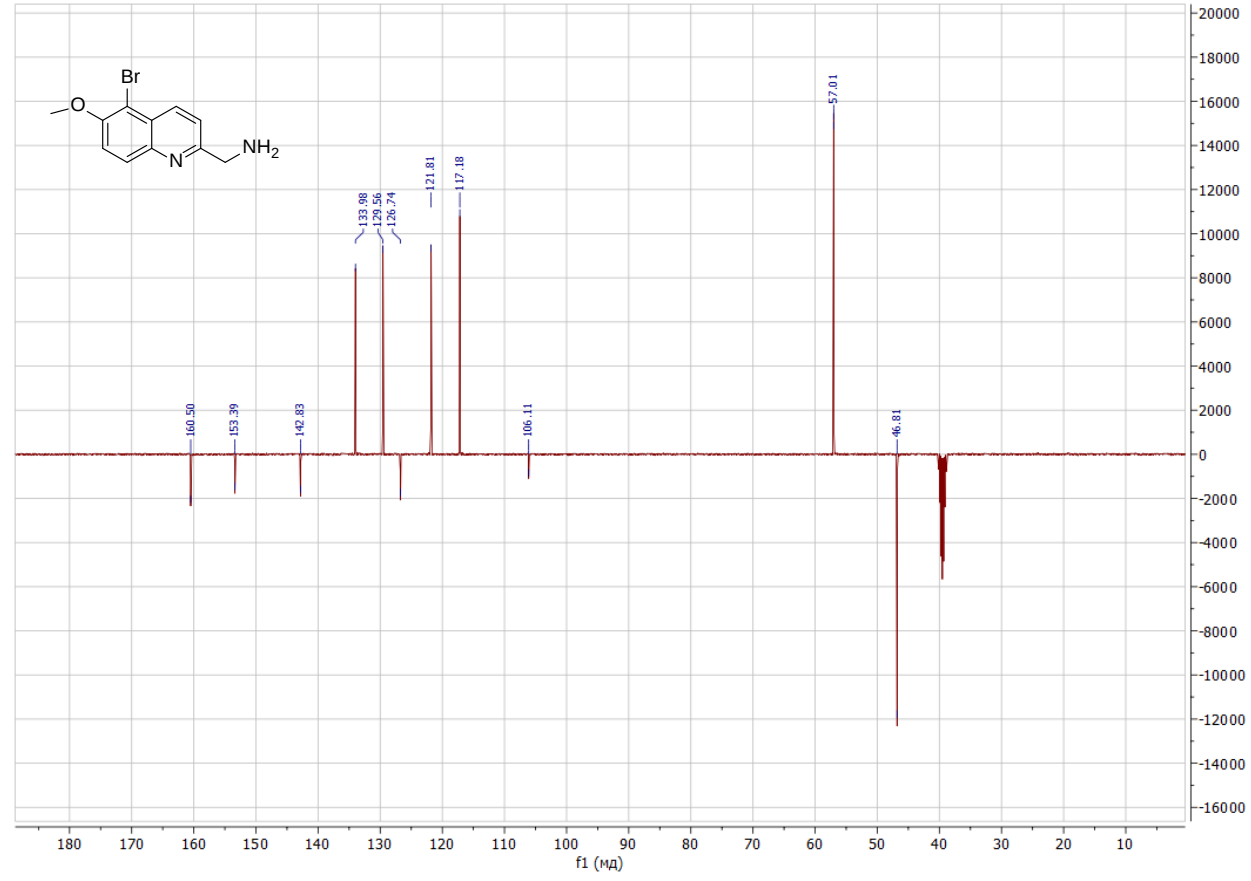
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **18c** in $CDCl_3$.



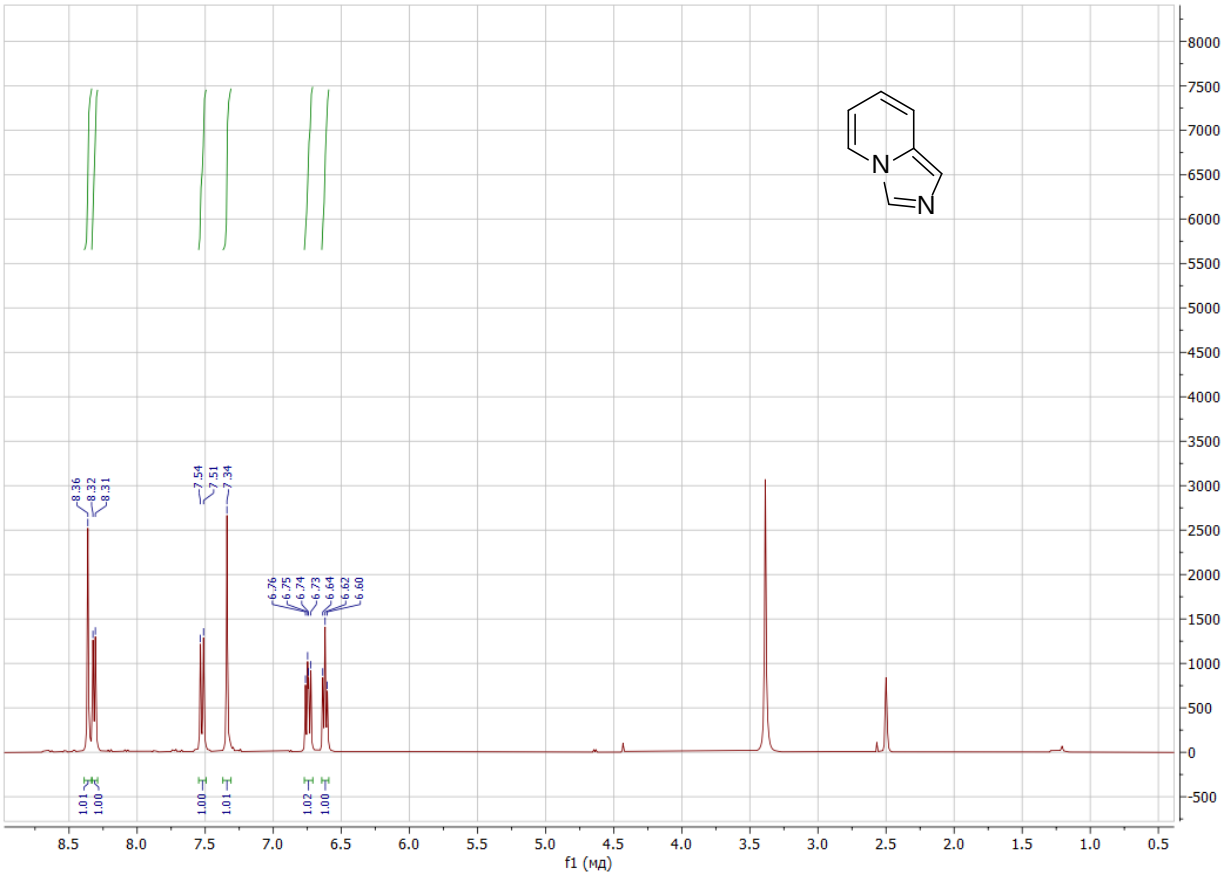


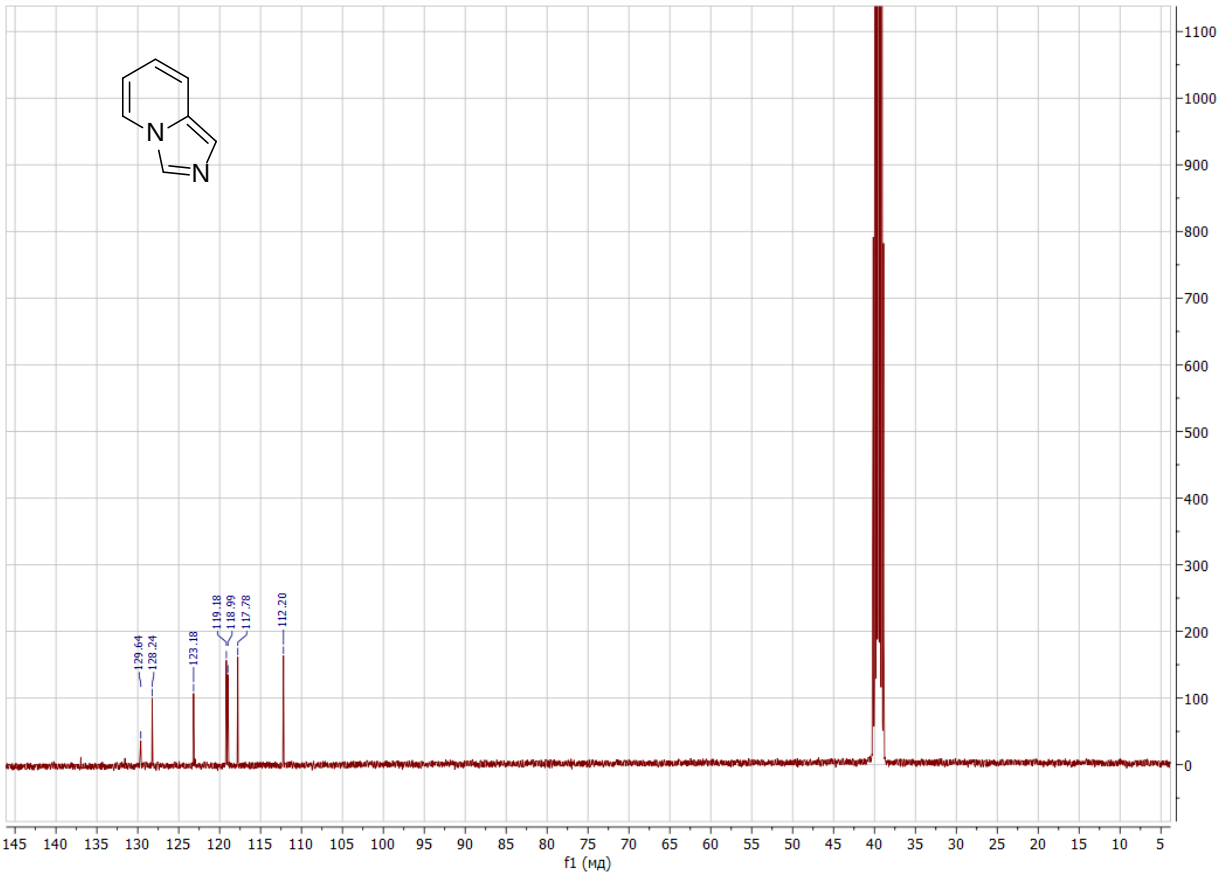
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **18d** in DMSO-d_6.



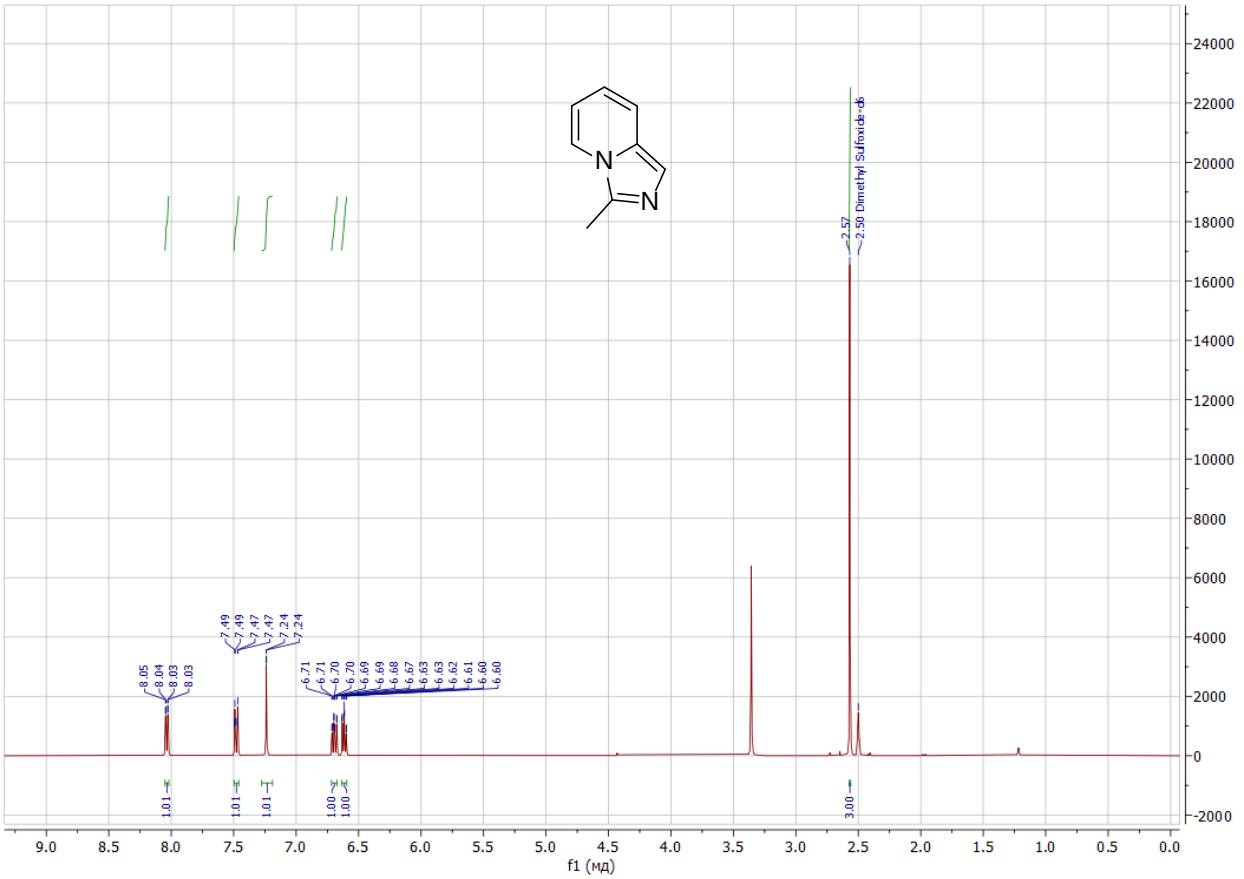


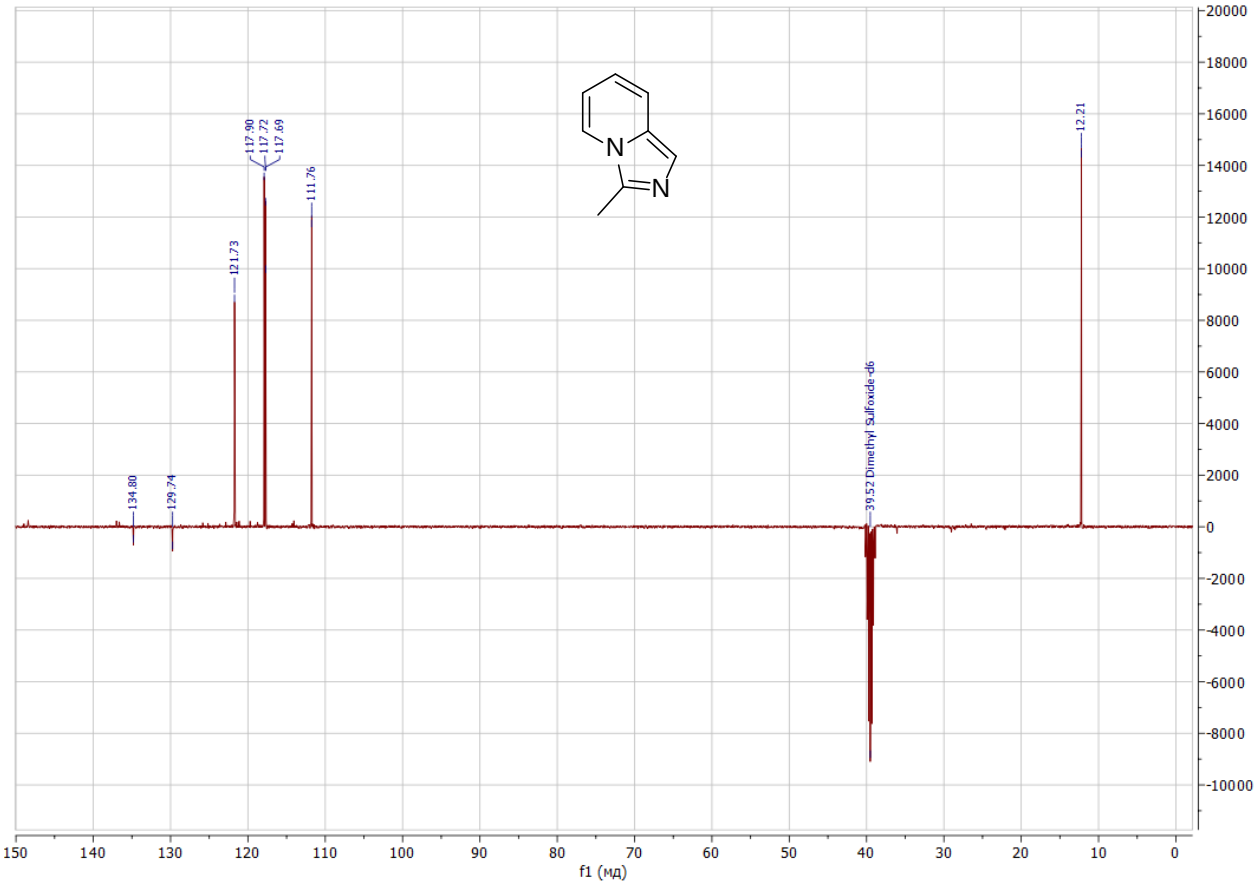
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16e** in DMSO-d_6.



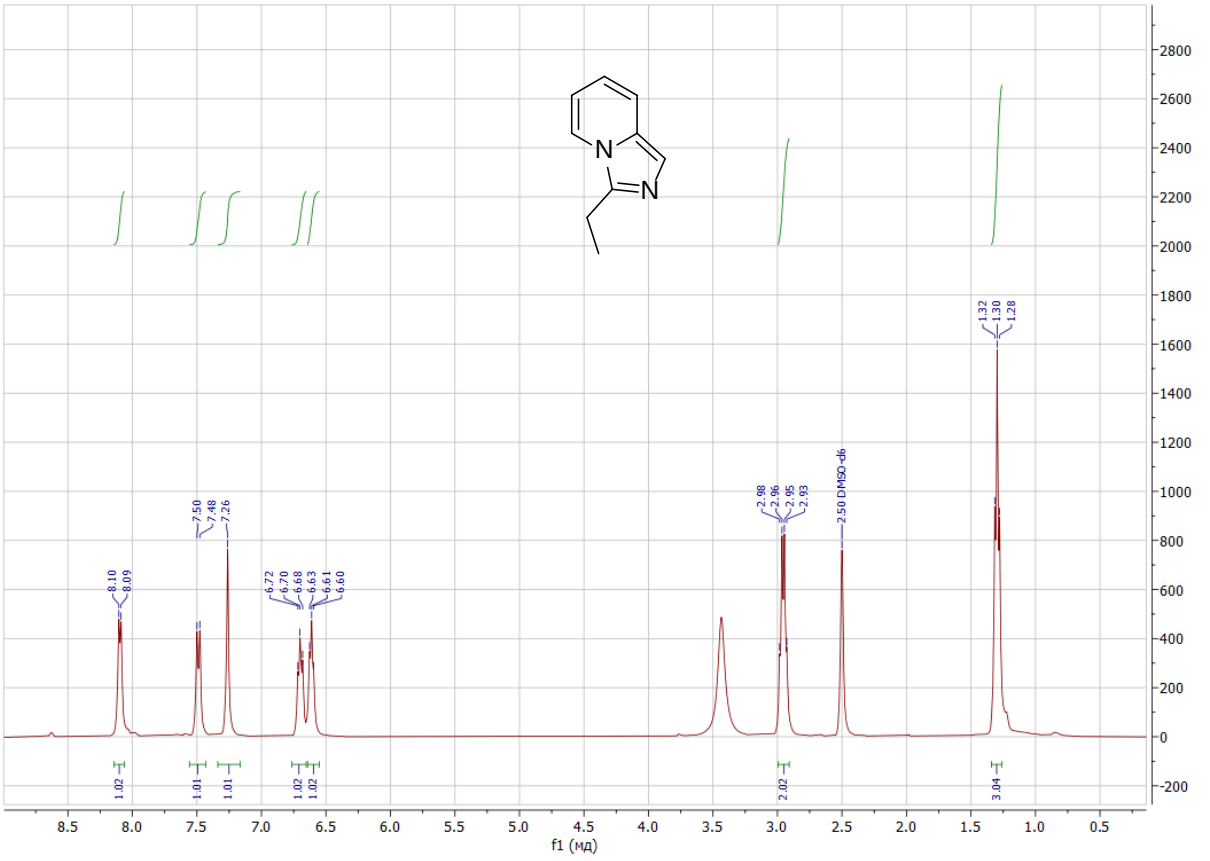


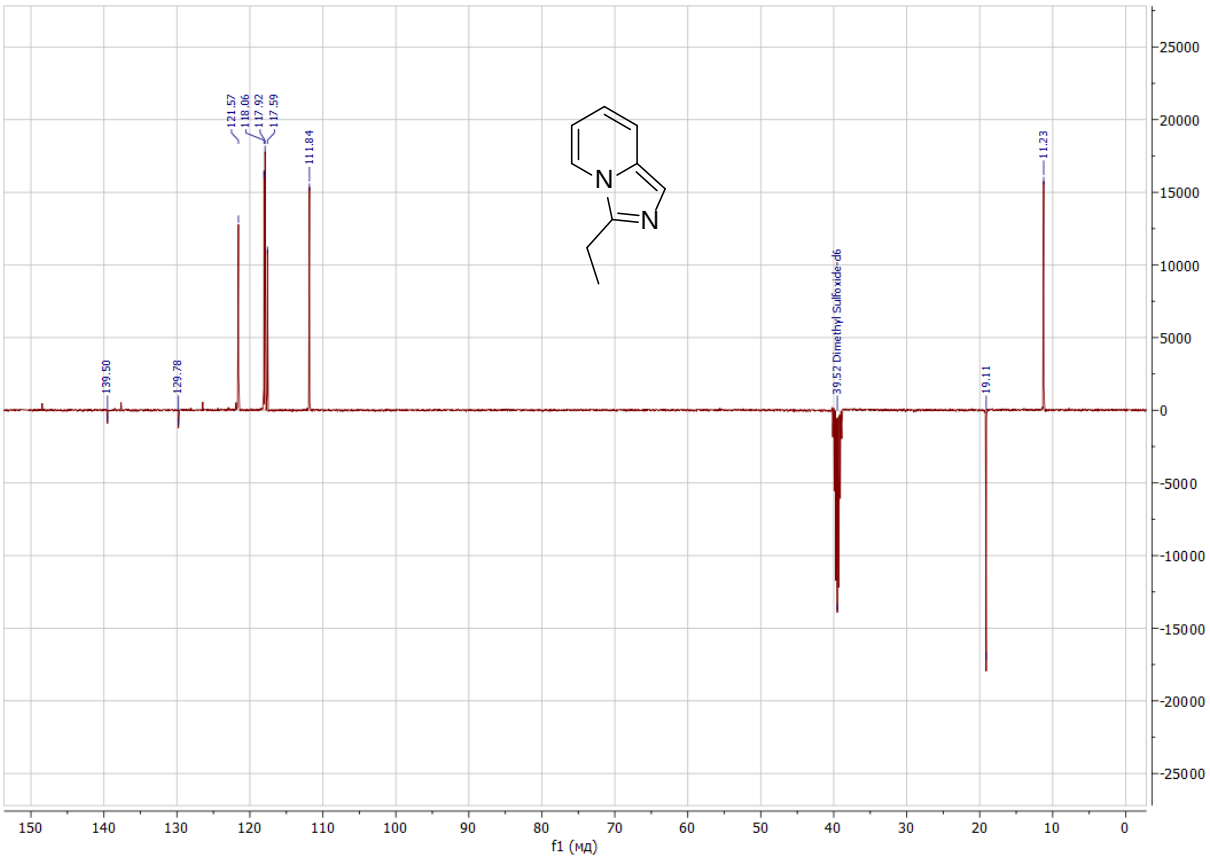
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16a** in DMSO-d_6.



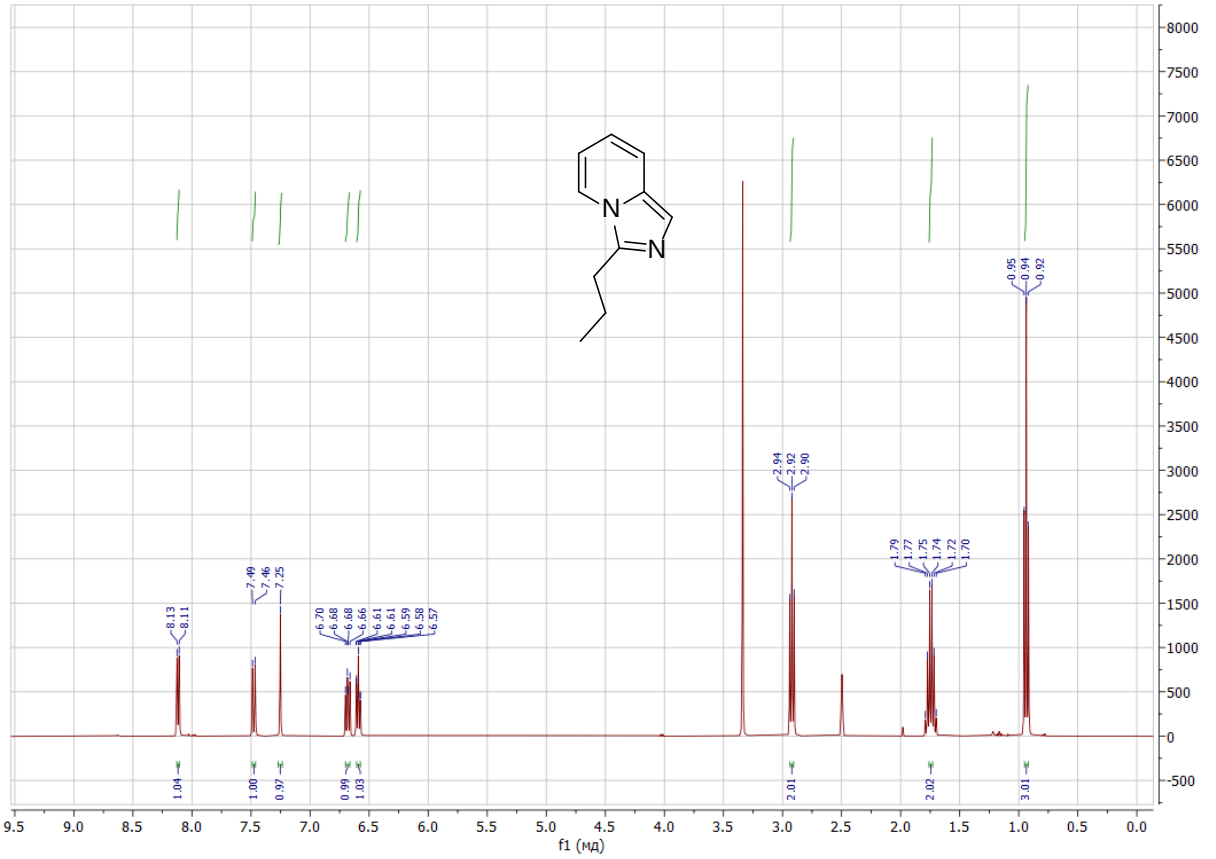


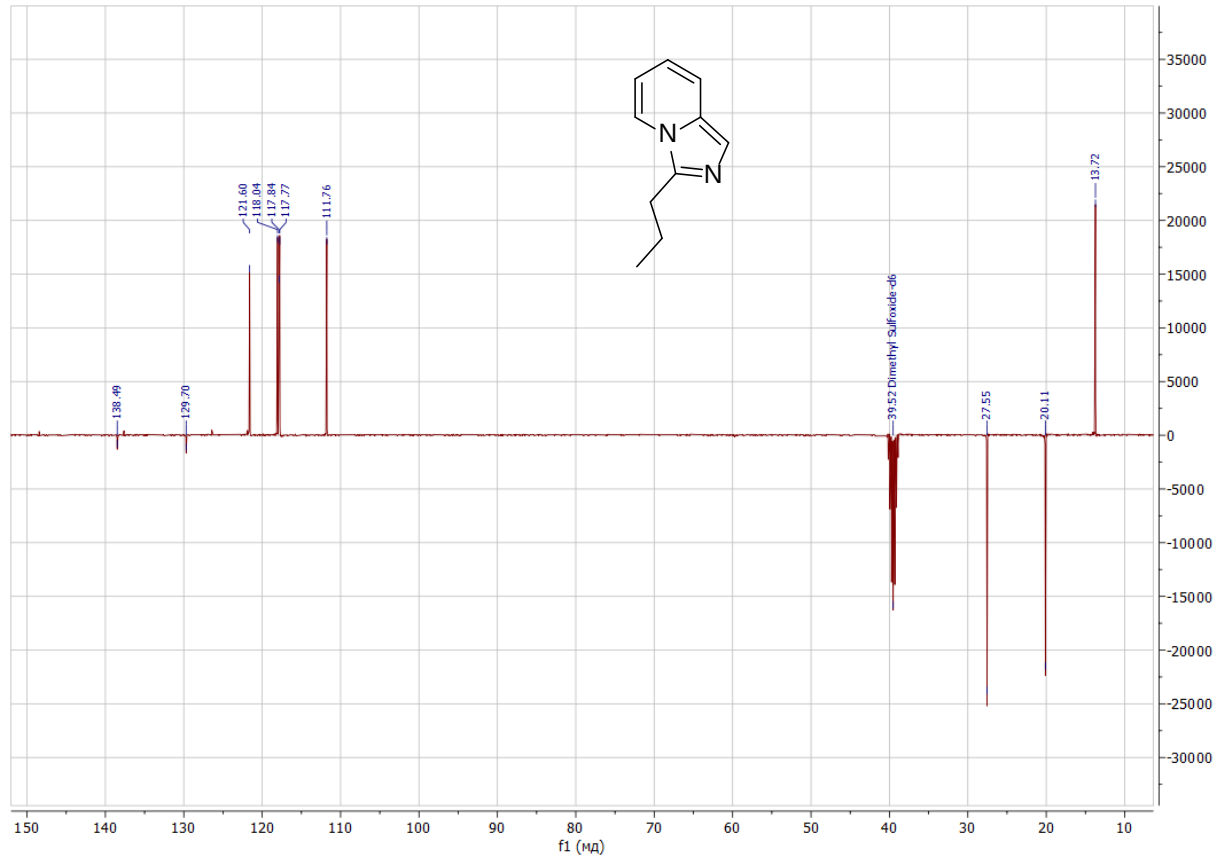
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16b** in DMSO-d_6.



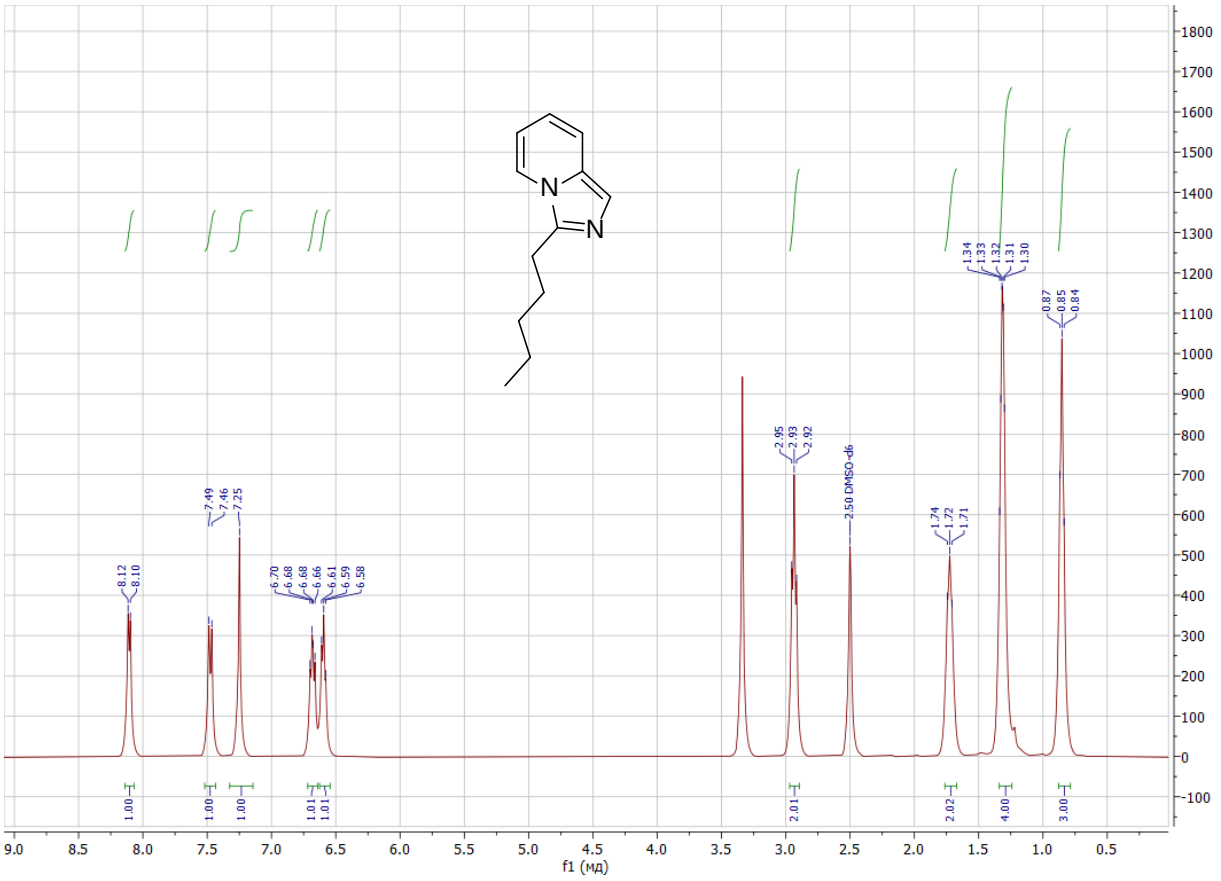


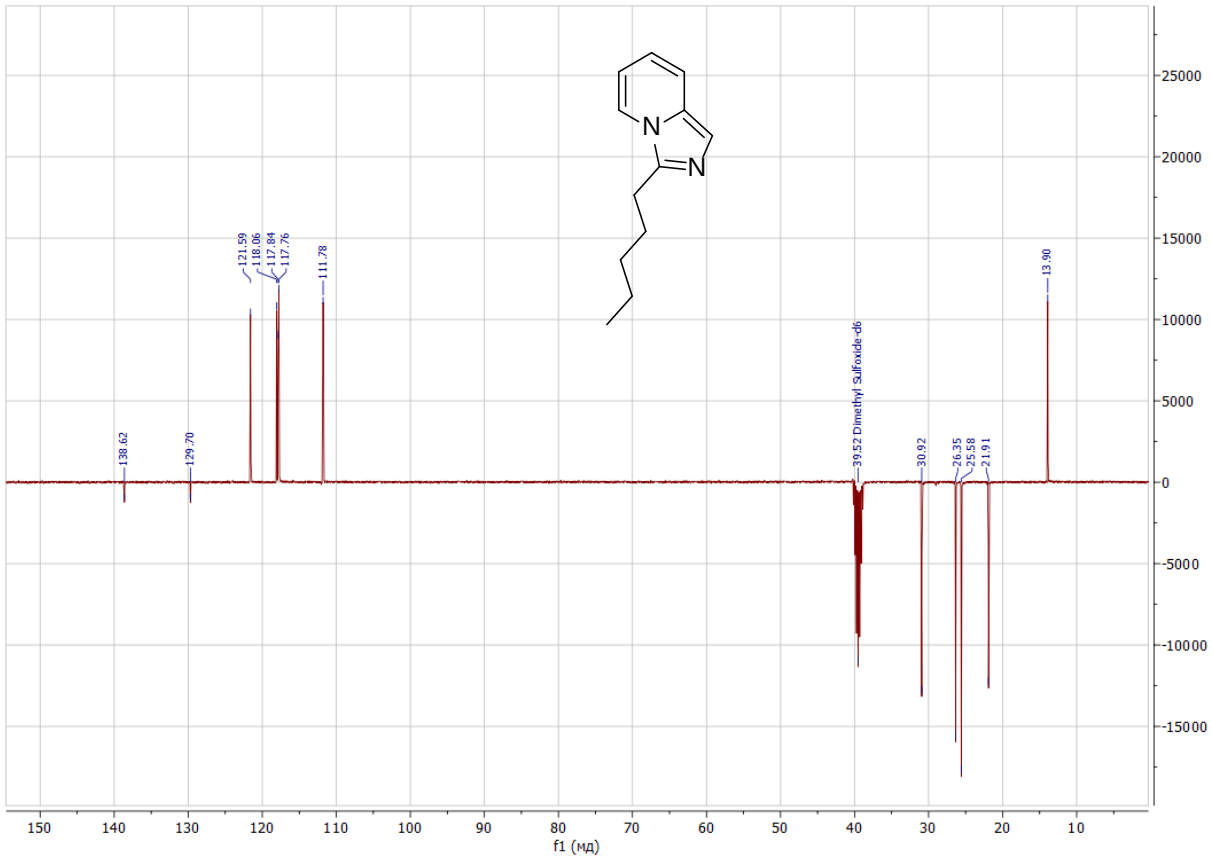
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16c** in DMSO-d_6.



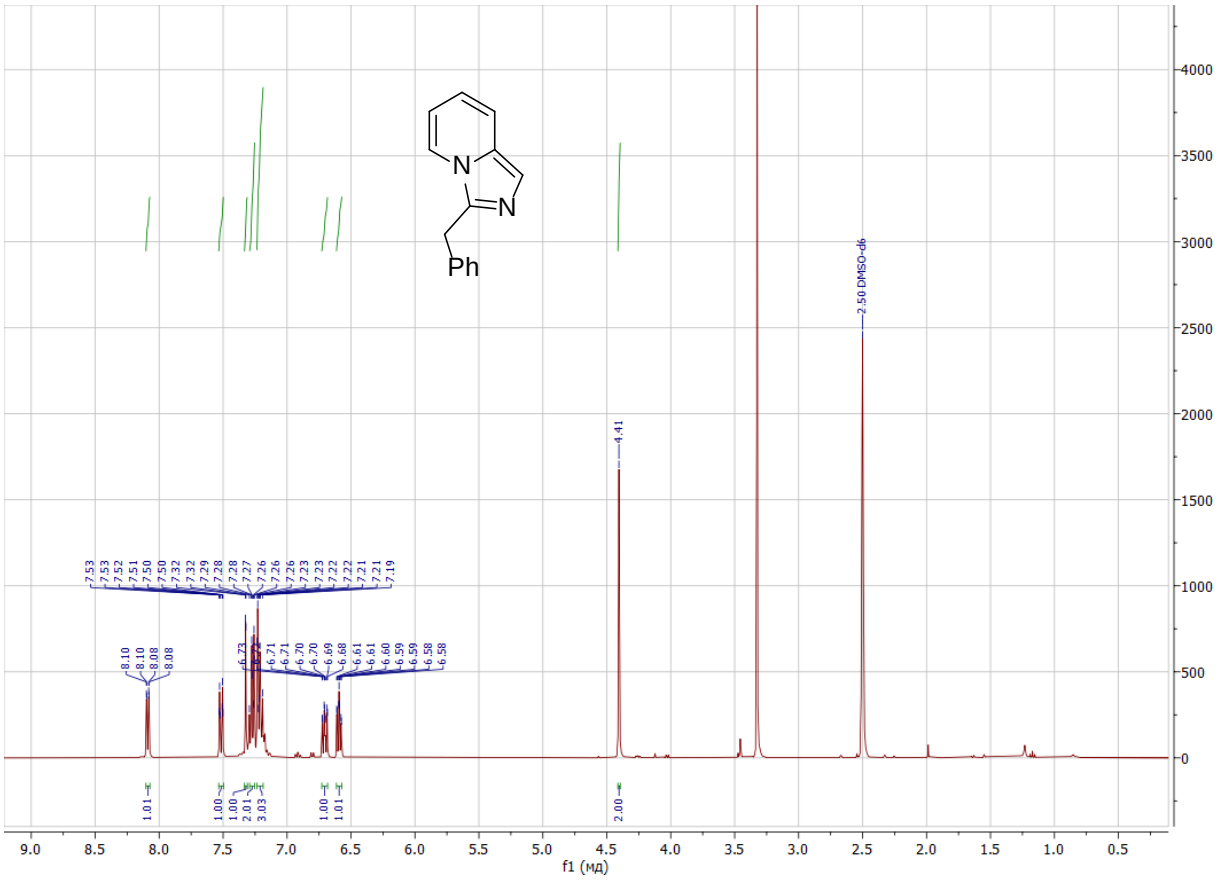


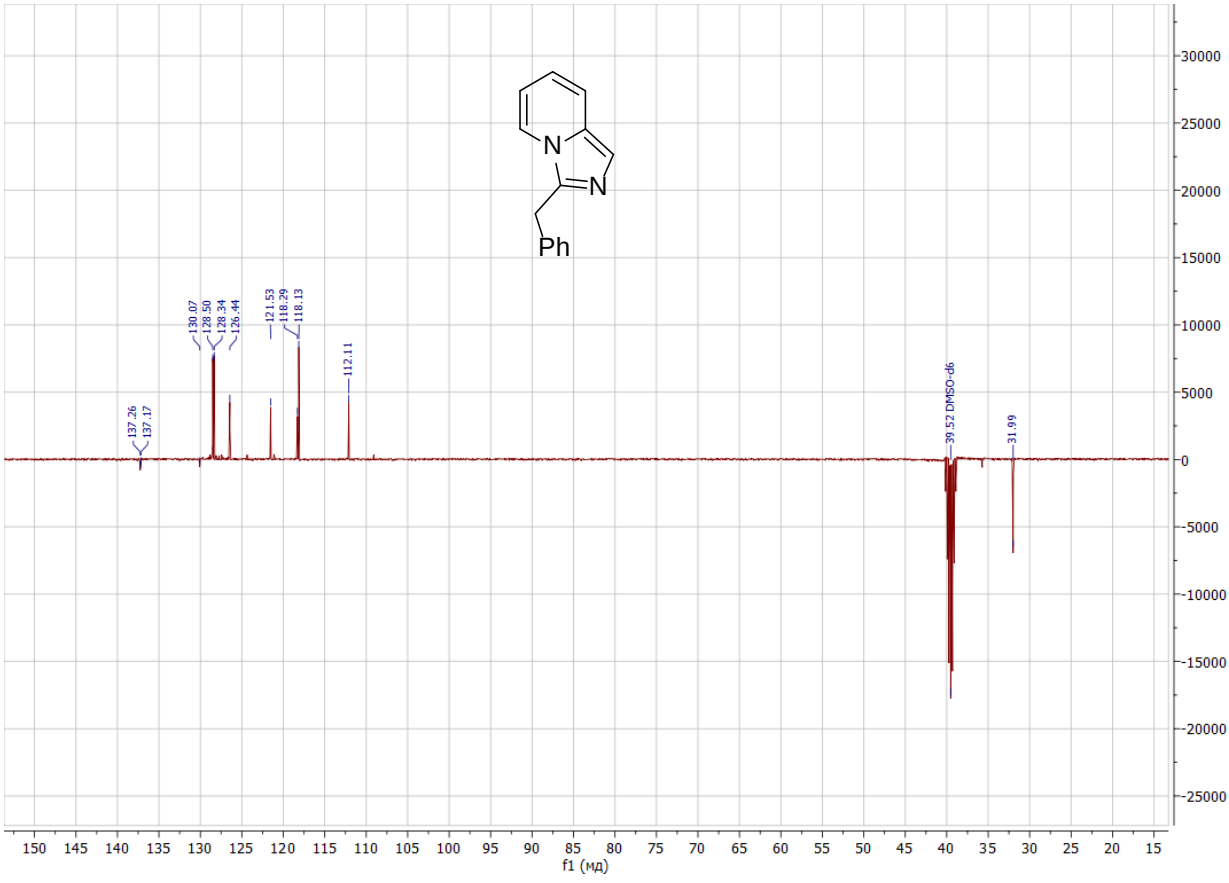
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16d** in DMSO-d_6.



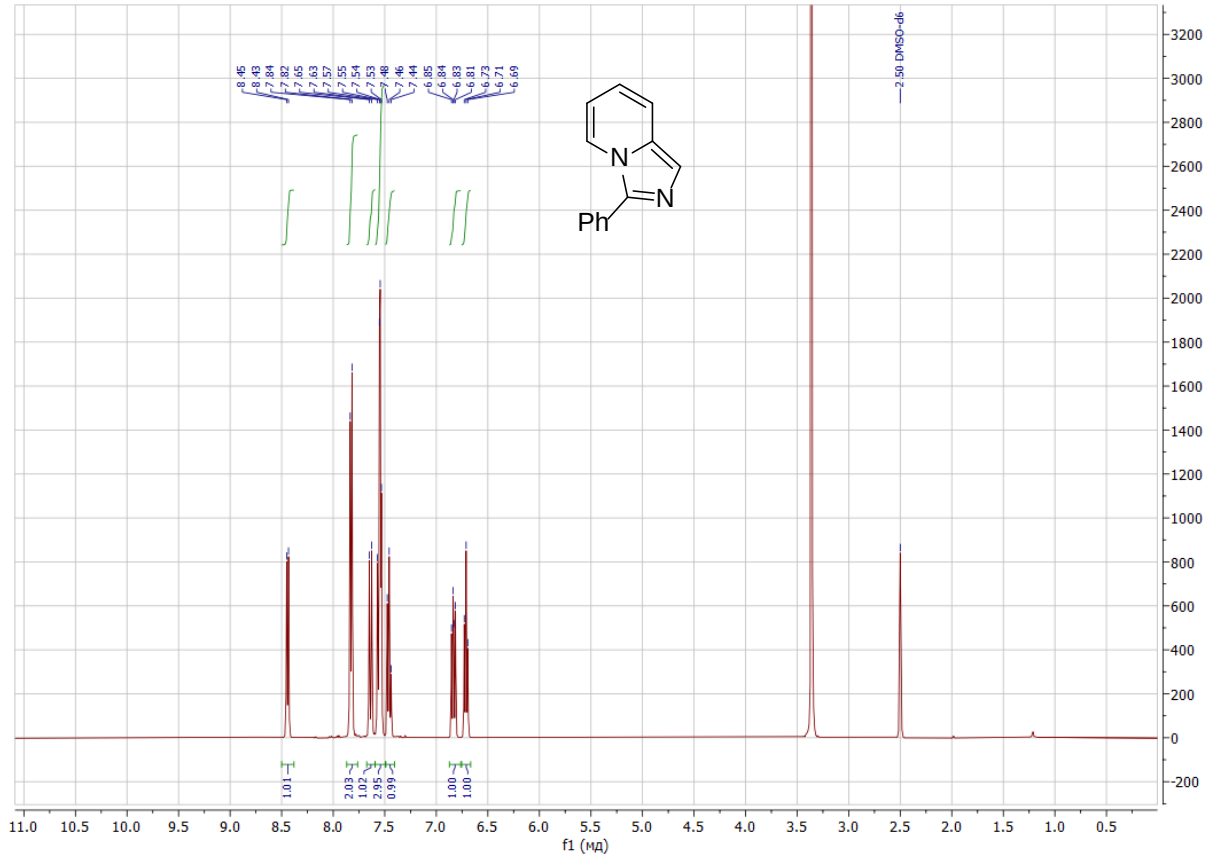


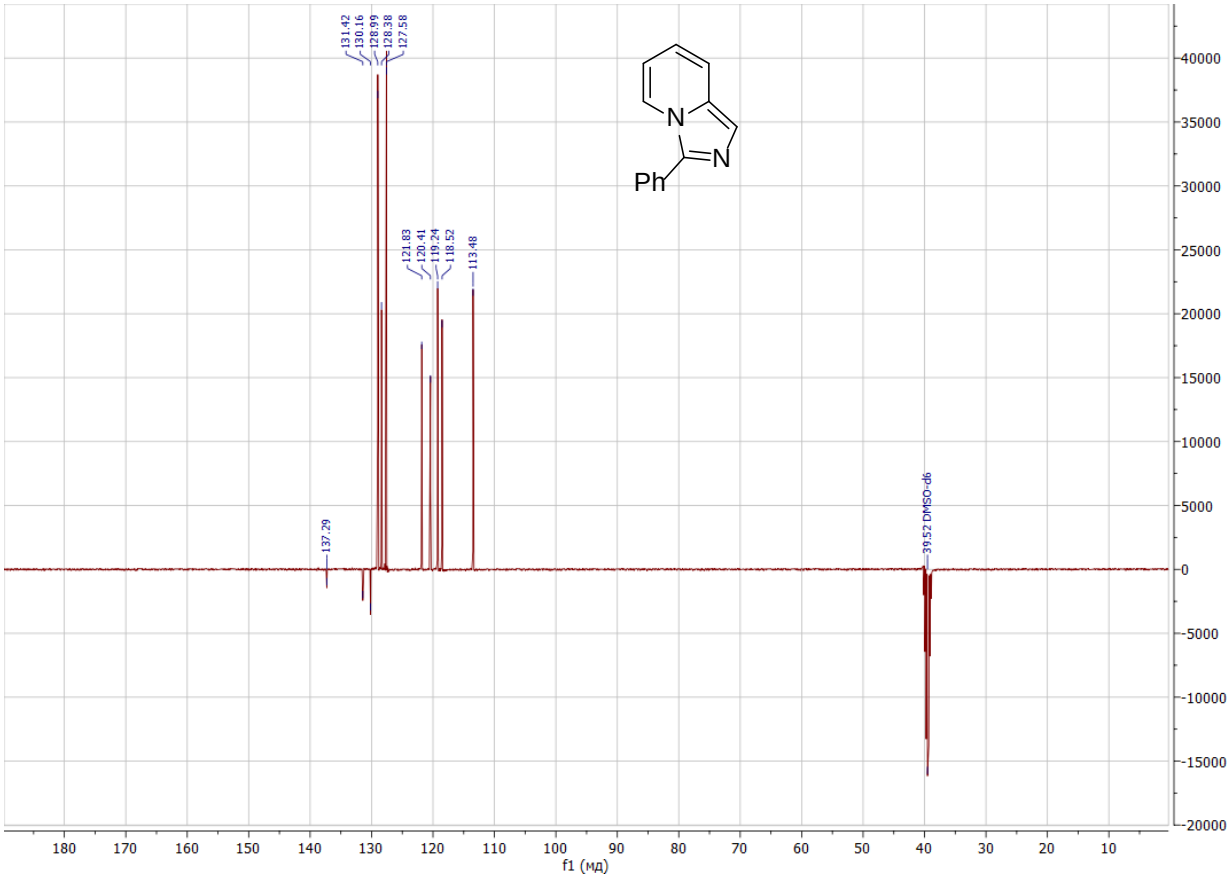
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16f** in DMSO-d_6.



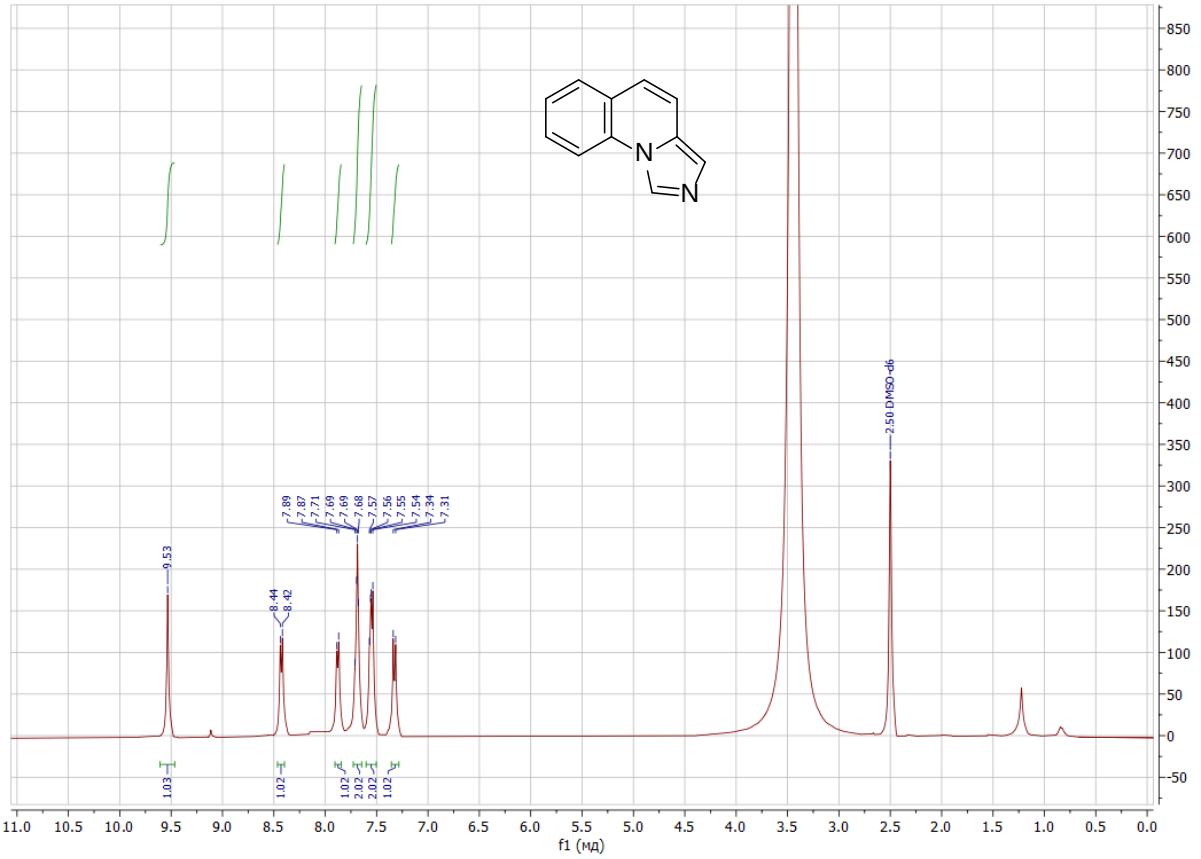


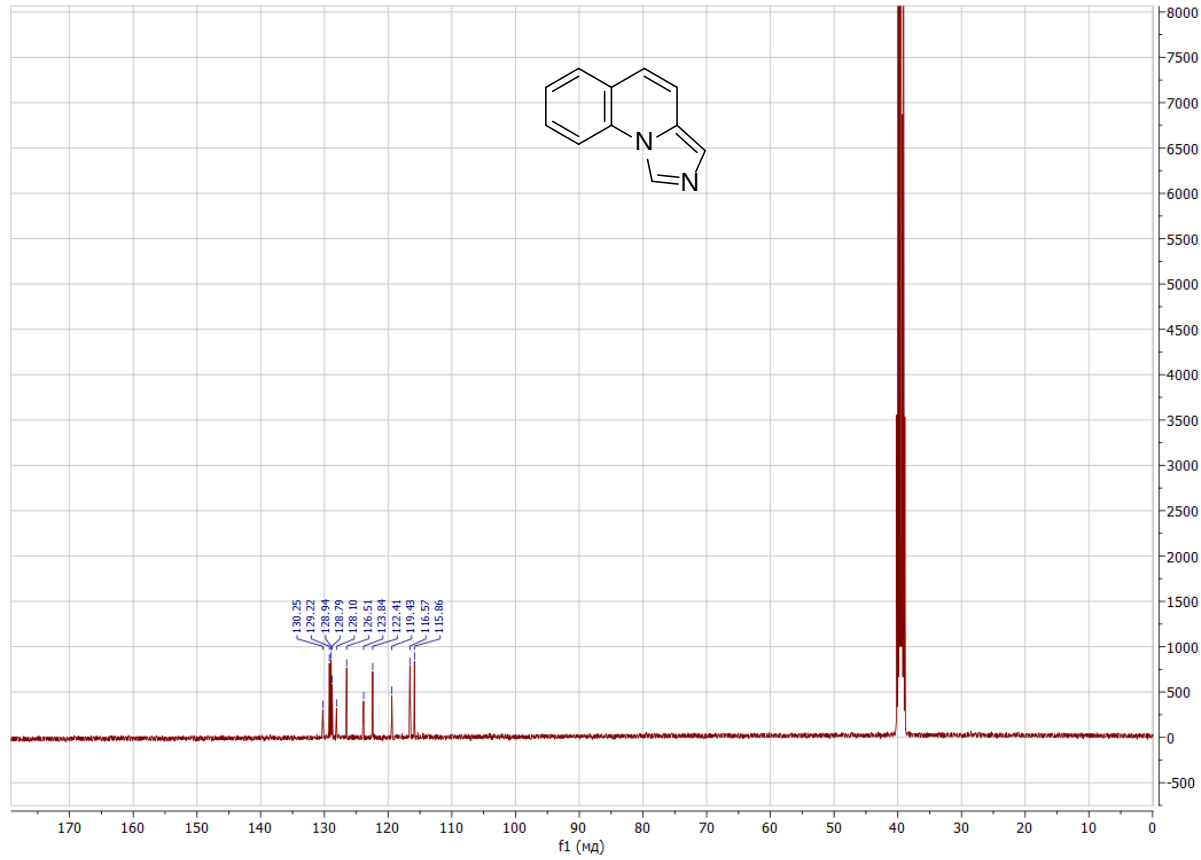
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **16g** in DMSO-d_6.



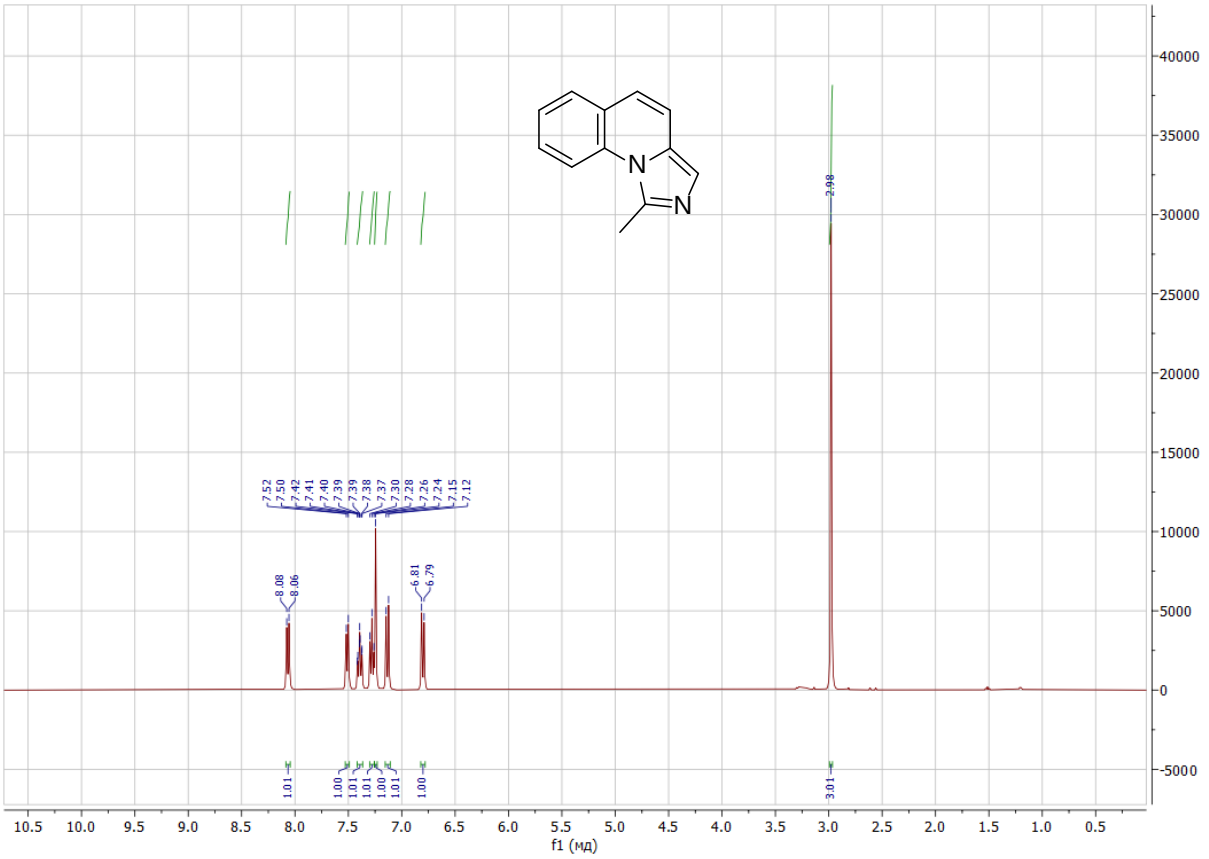


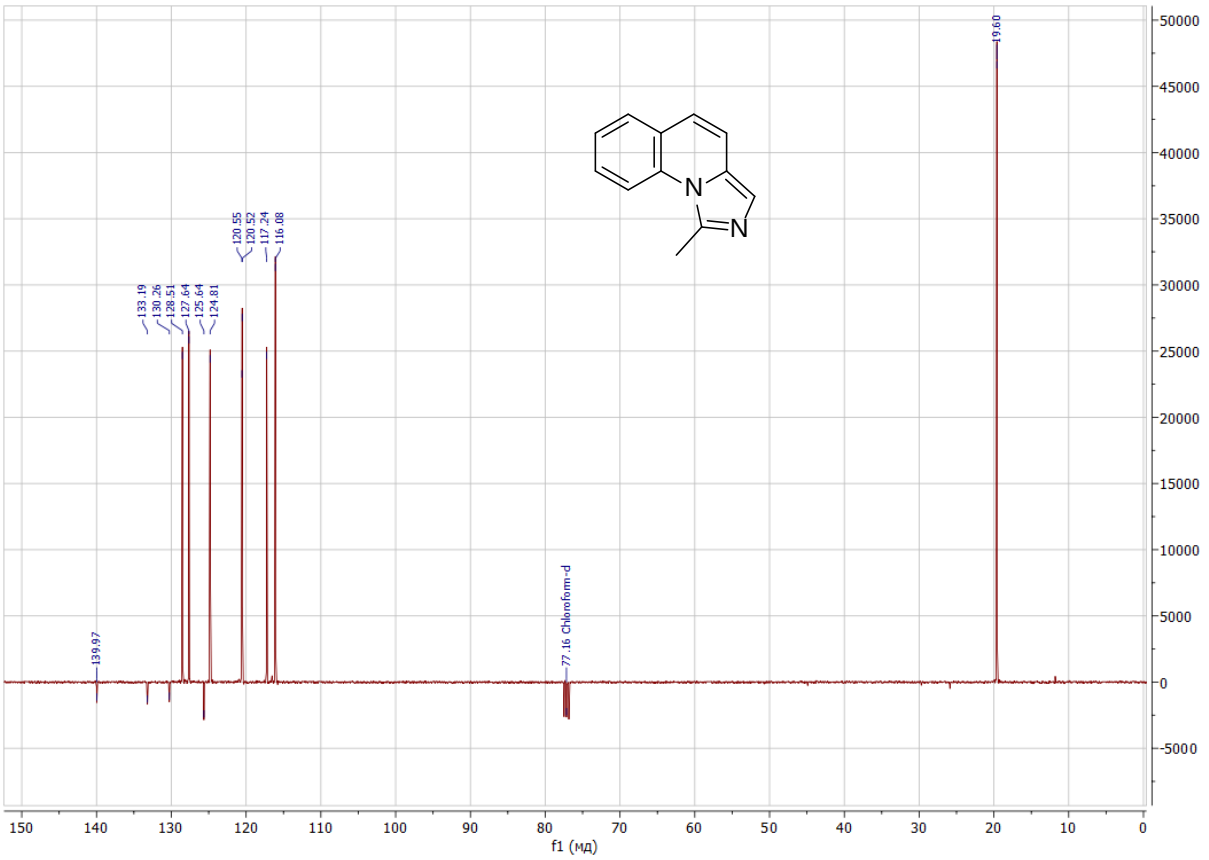
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19ae** in DMSO-d_6.



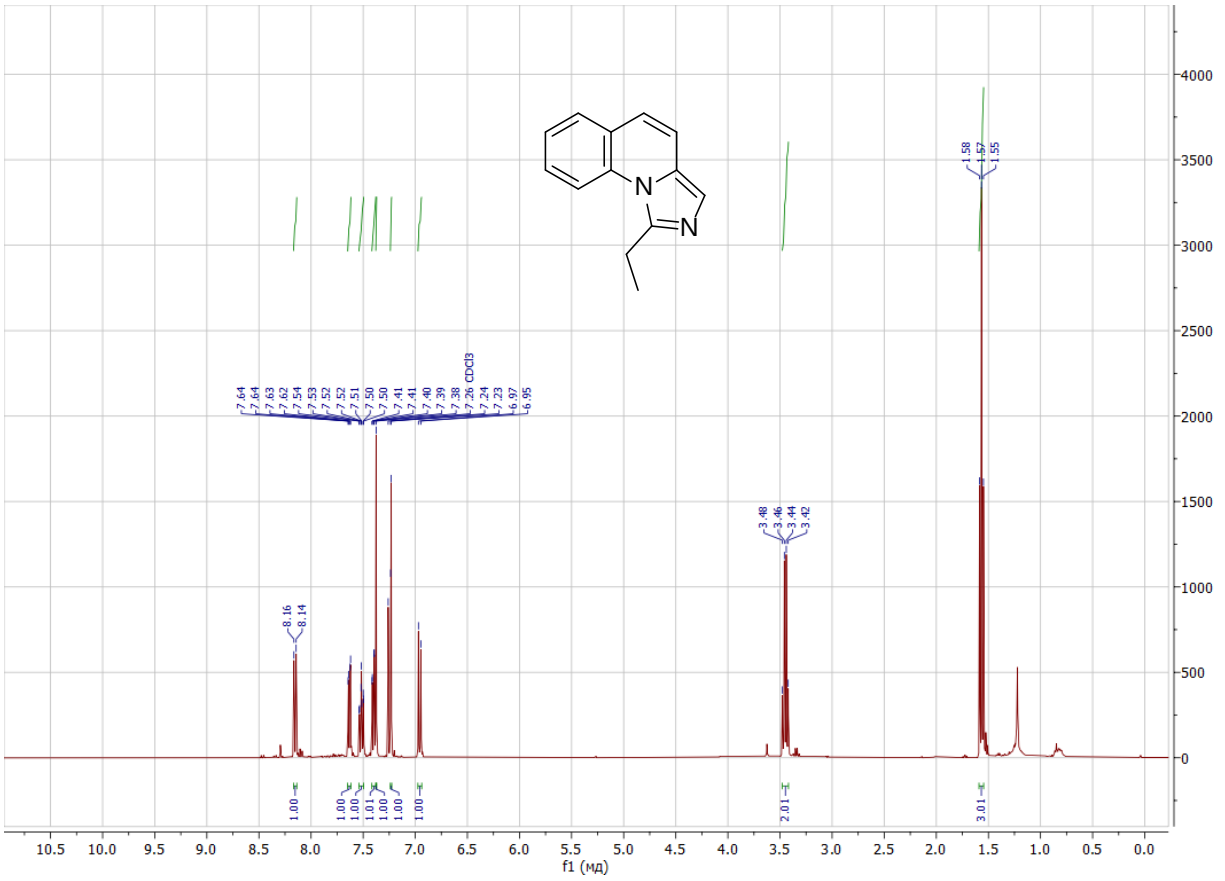


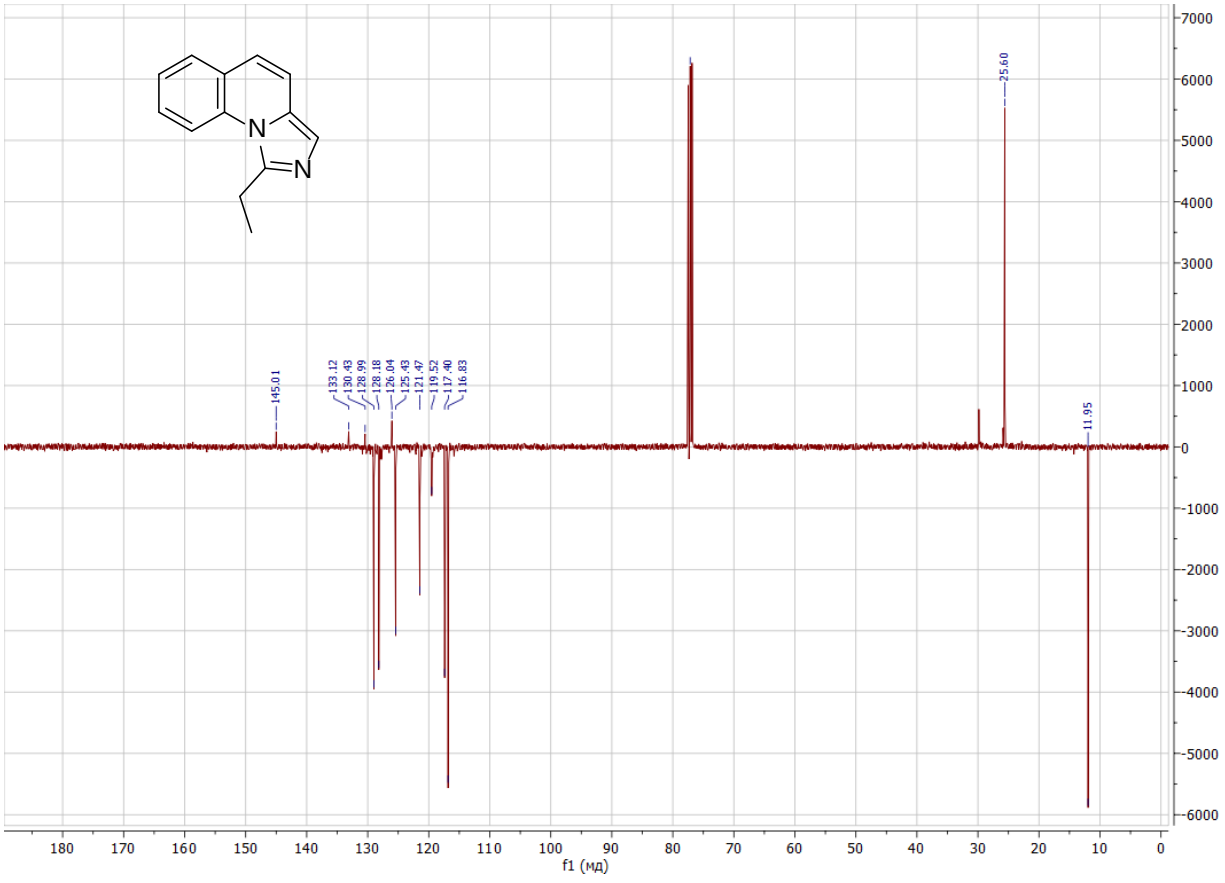
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19aa** in $CDCl_3$.



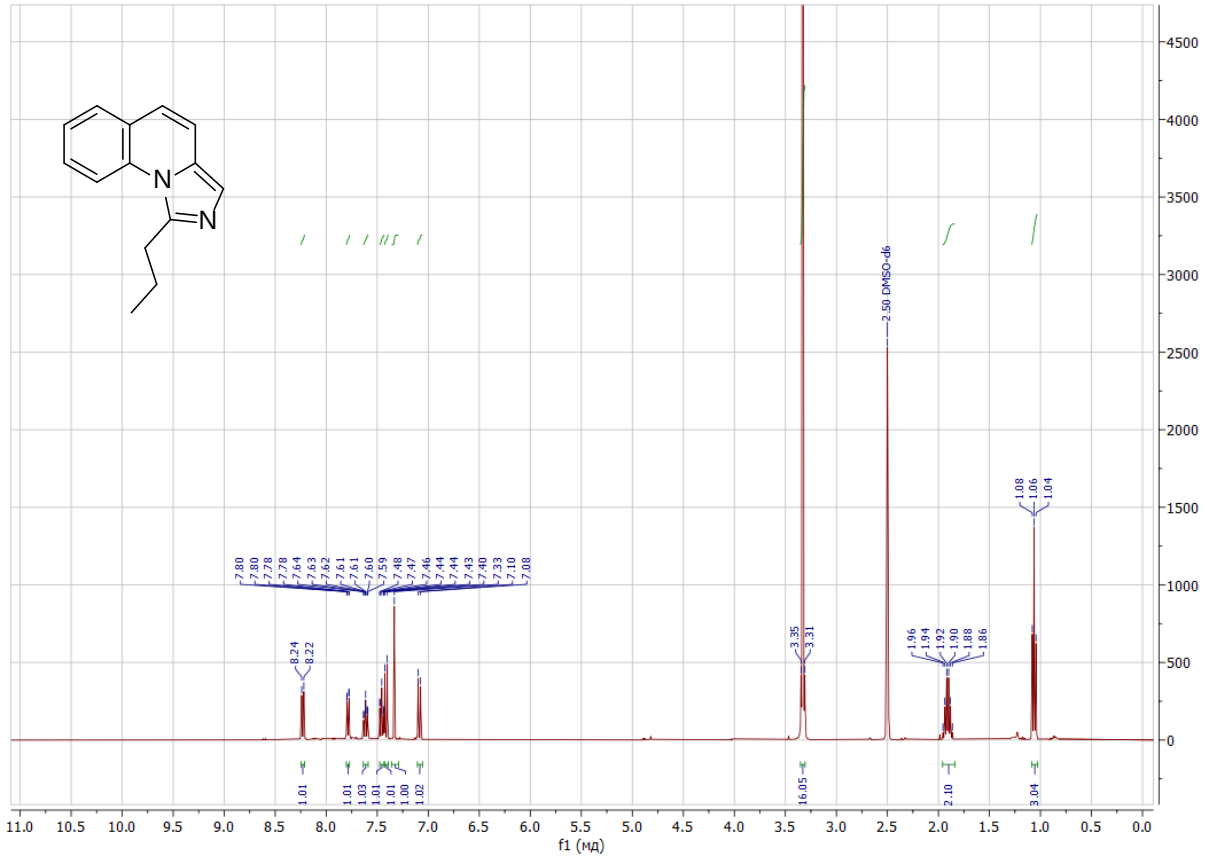


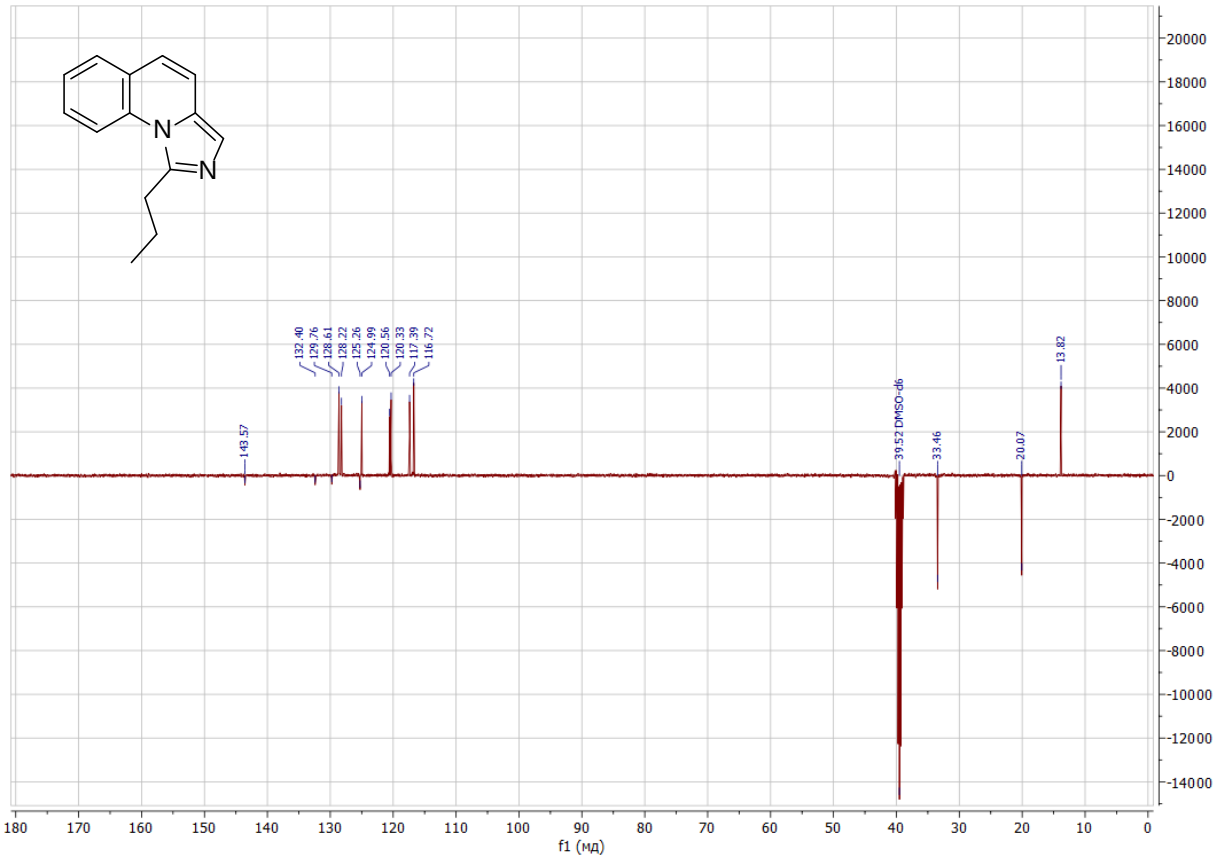
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19ab** in $CDCl_3$.



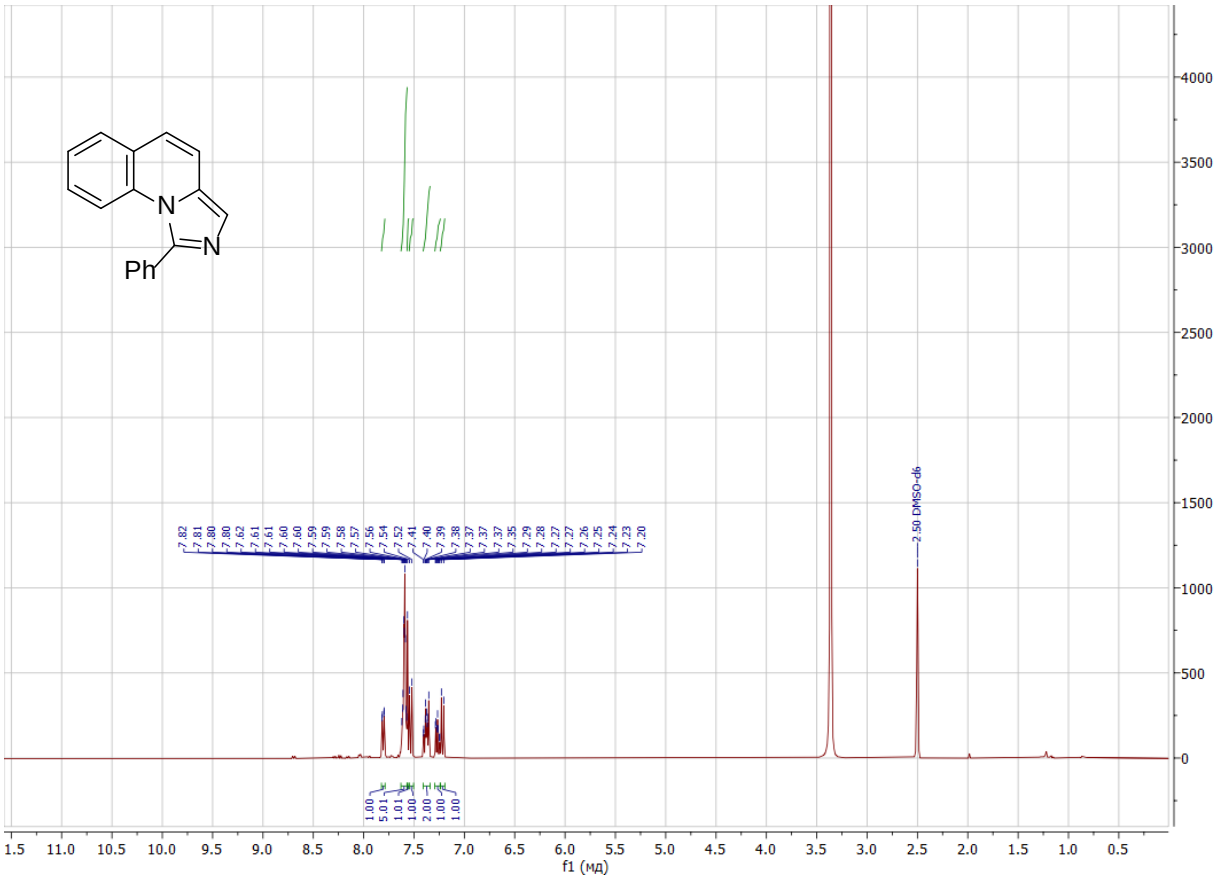


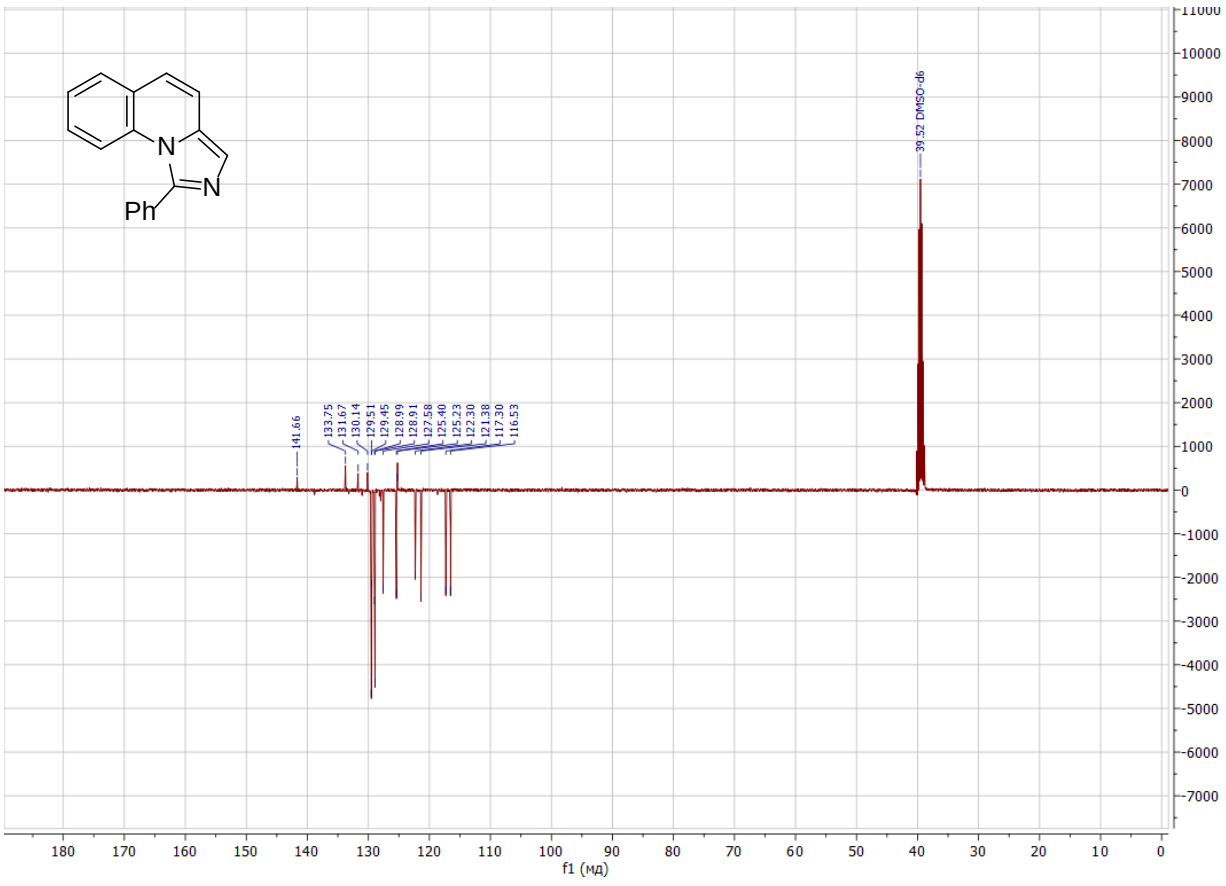
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19ac** in DMSO-d_6.



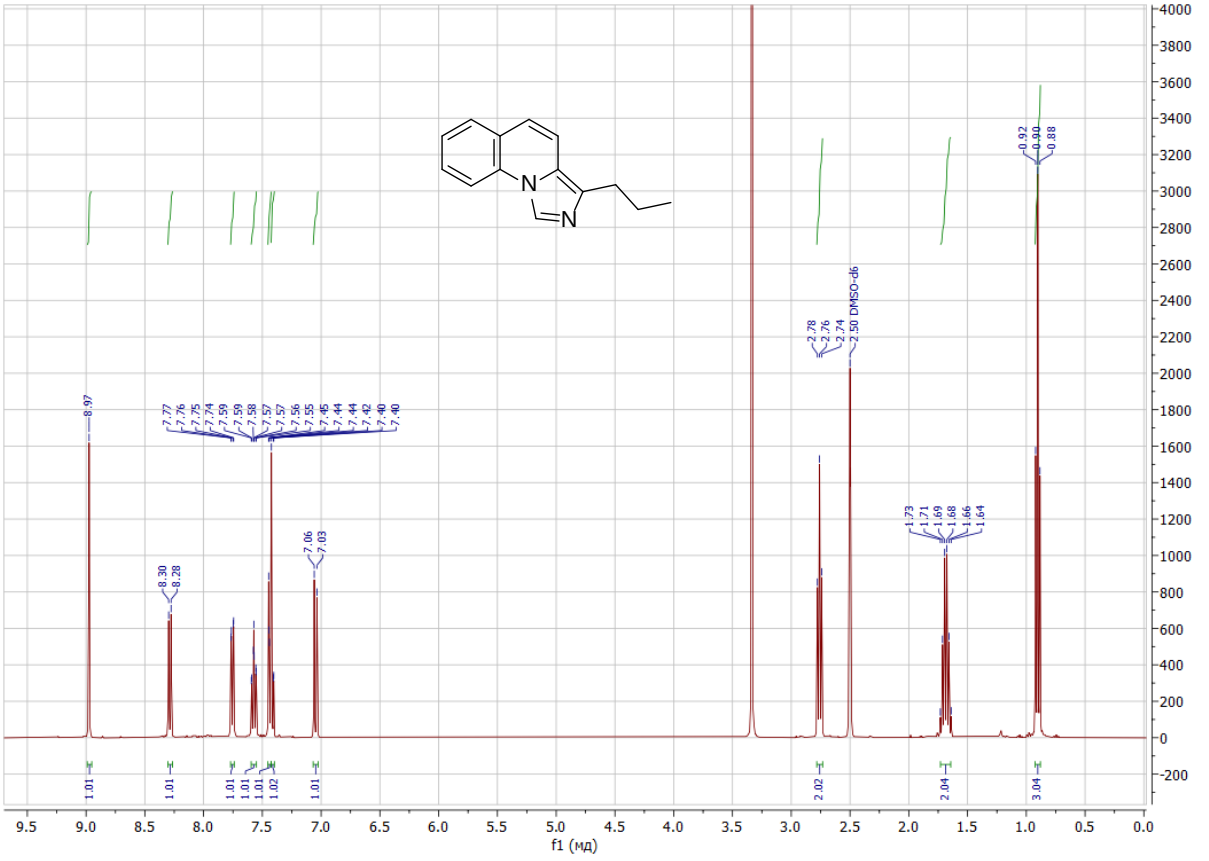


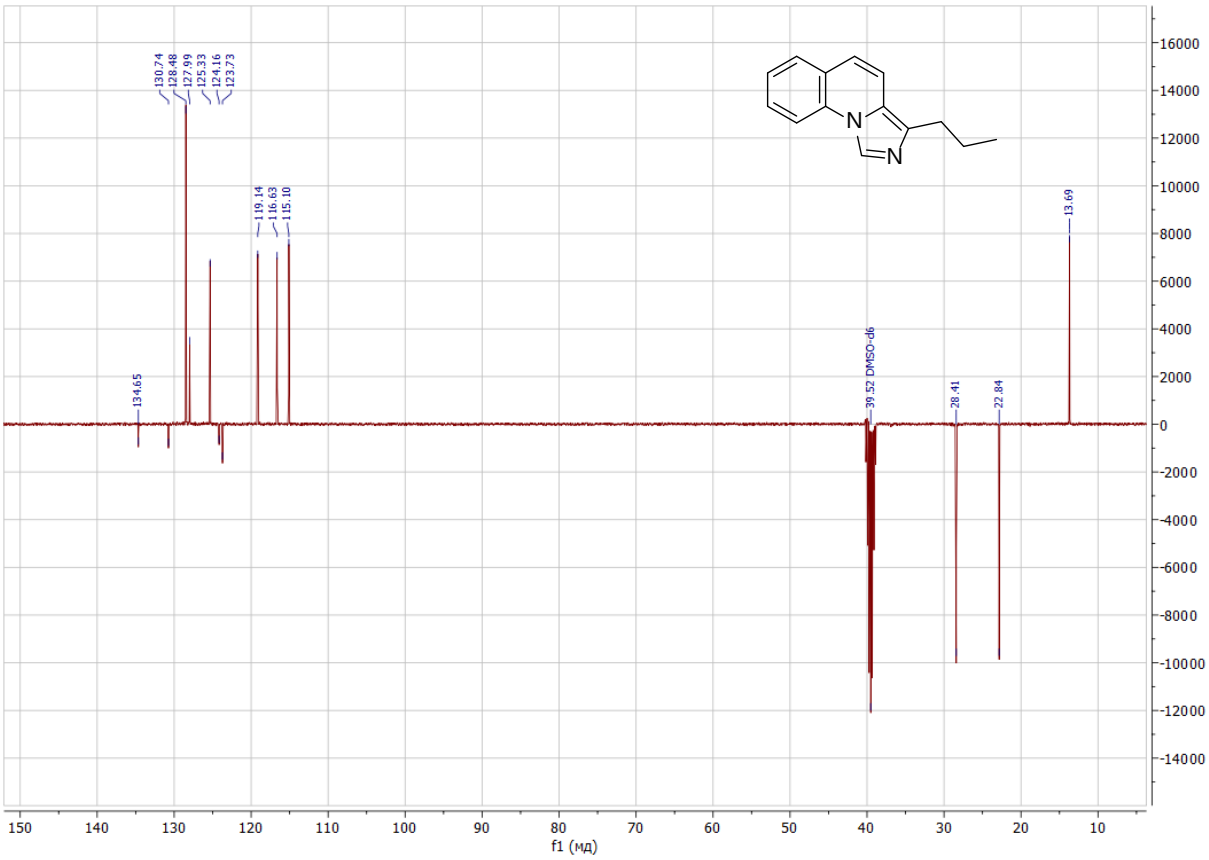
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19ag** in DMSO-d_6.



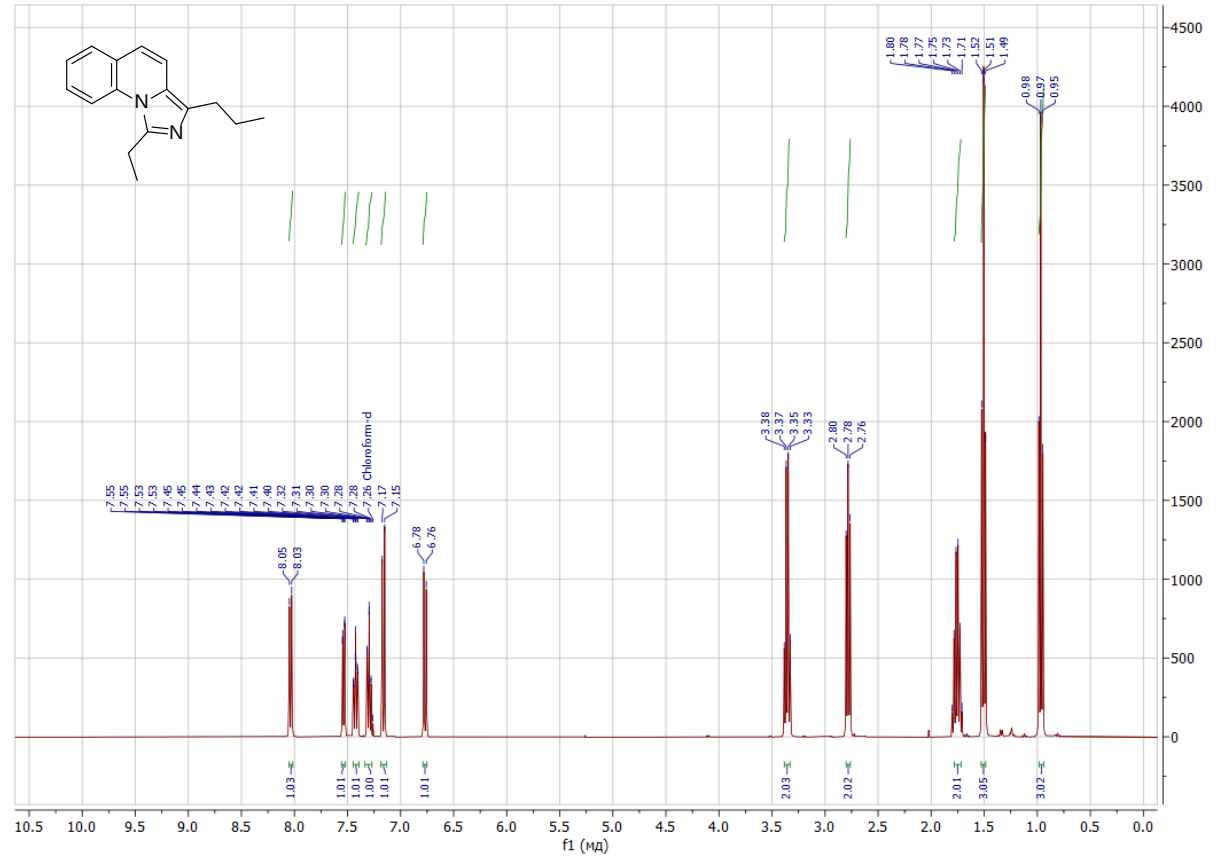


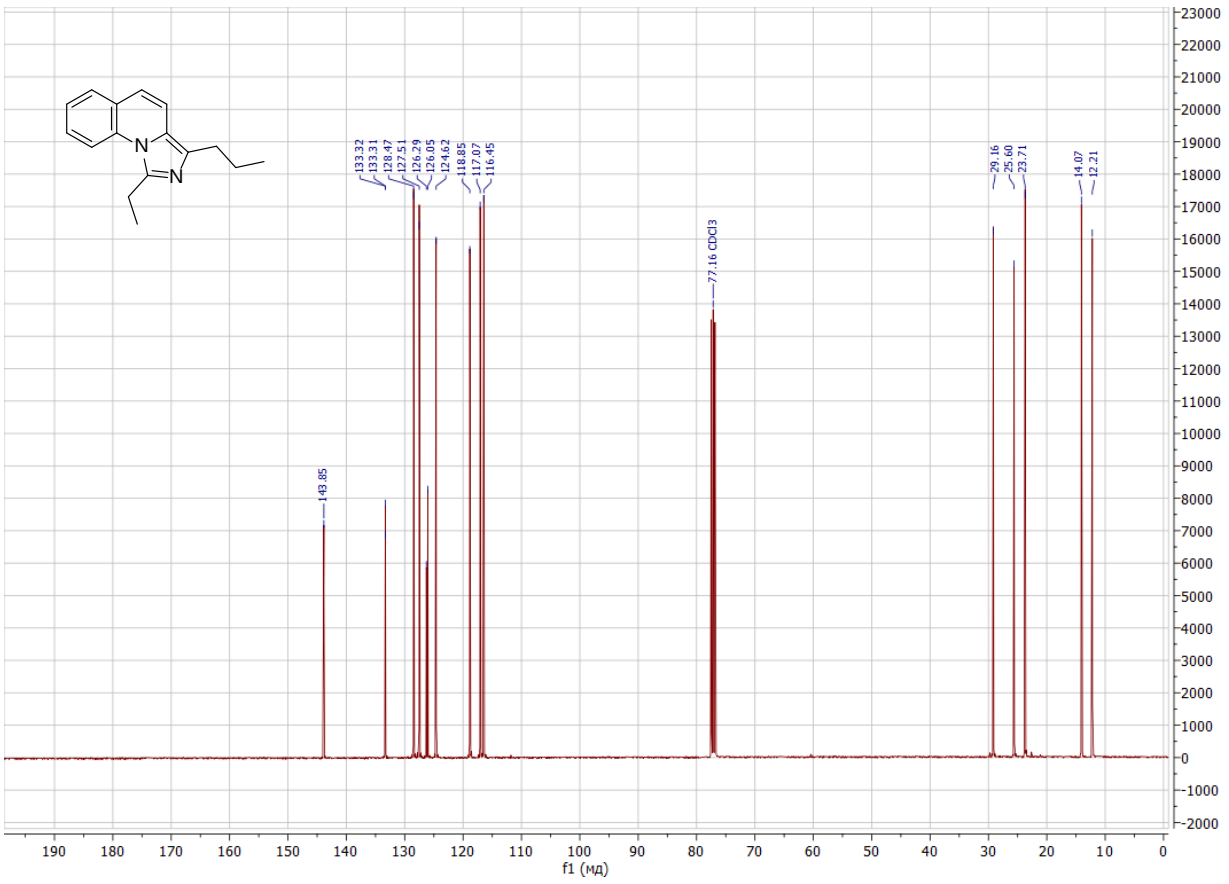
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19be** in DMSO-d_6.



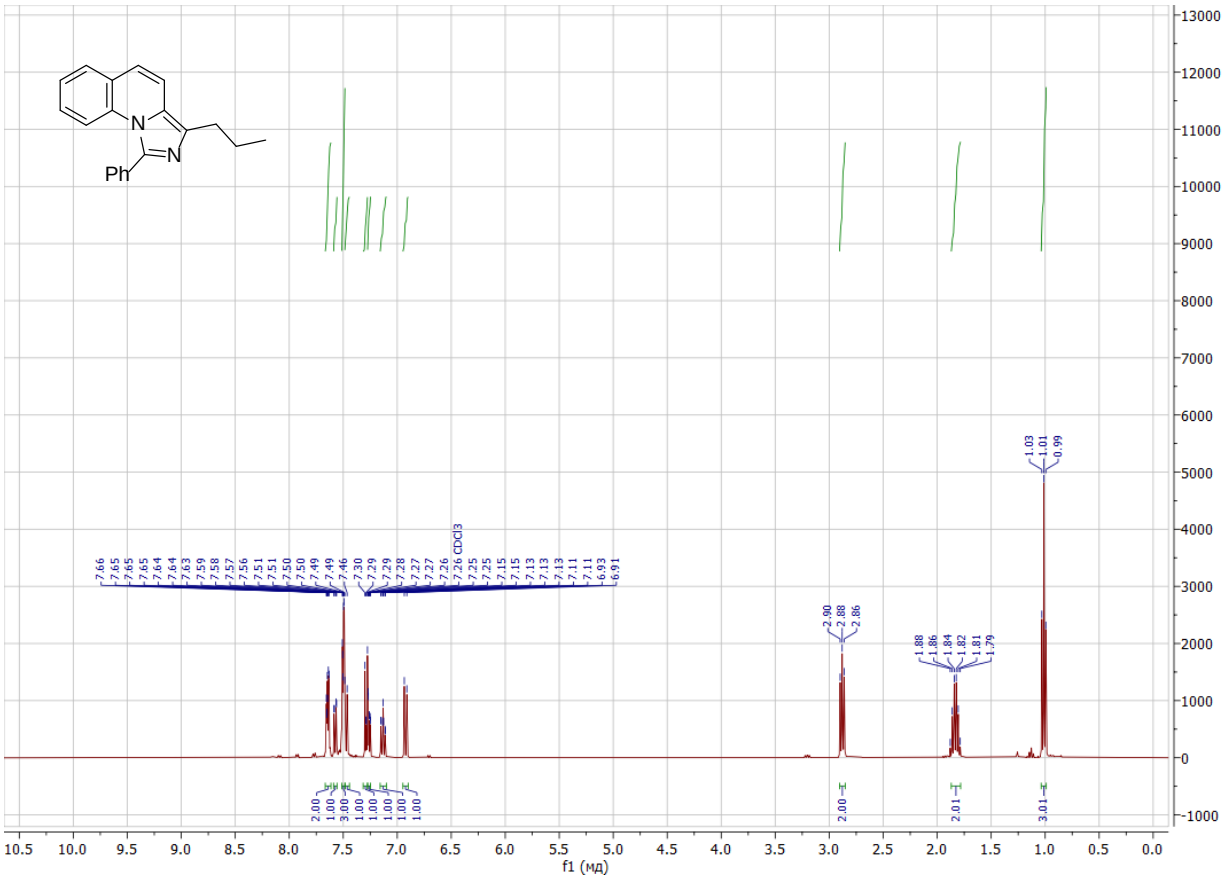


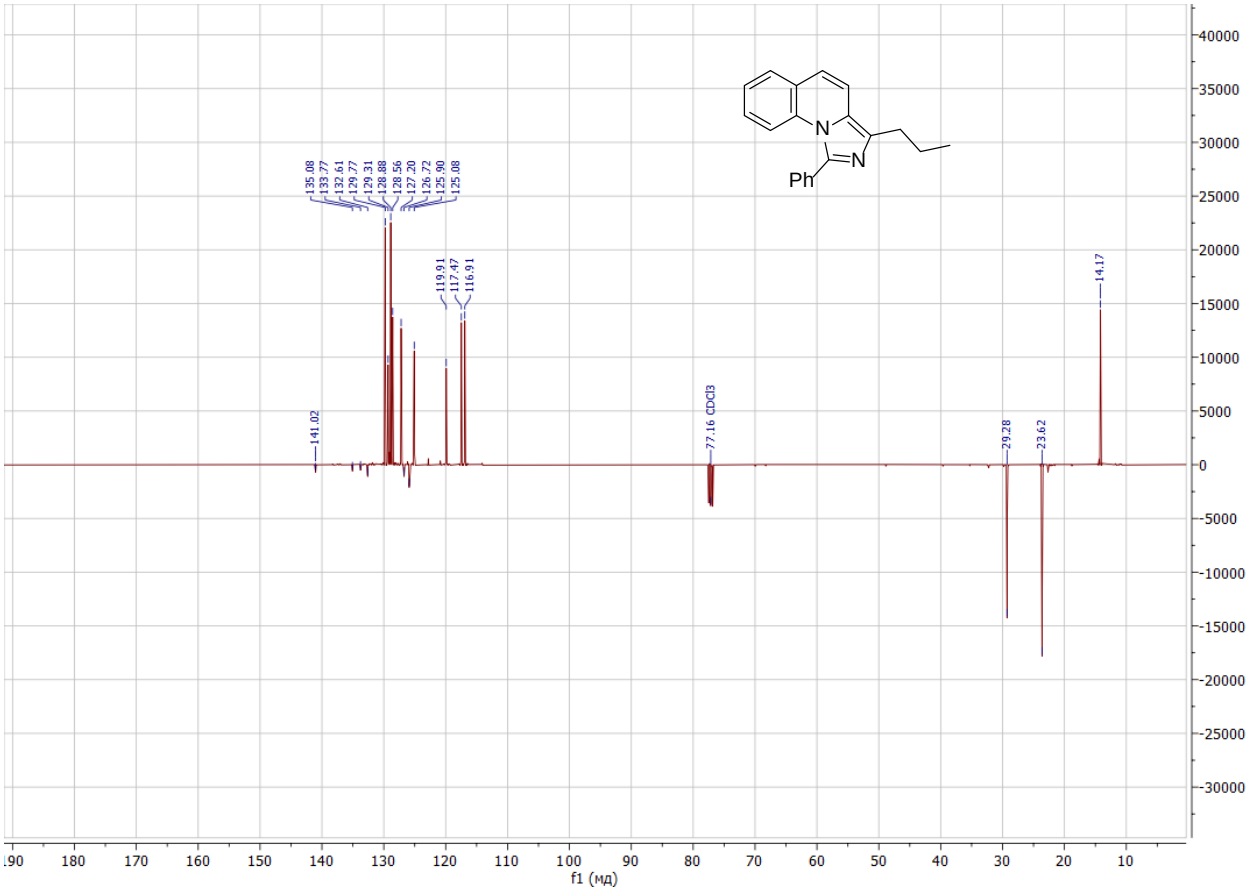
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19bb** in $CDCl_3$.



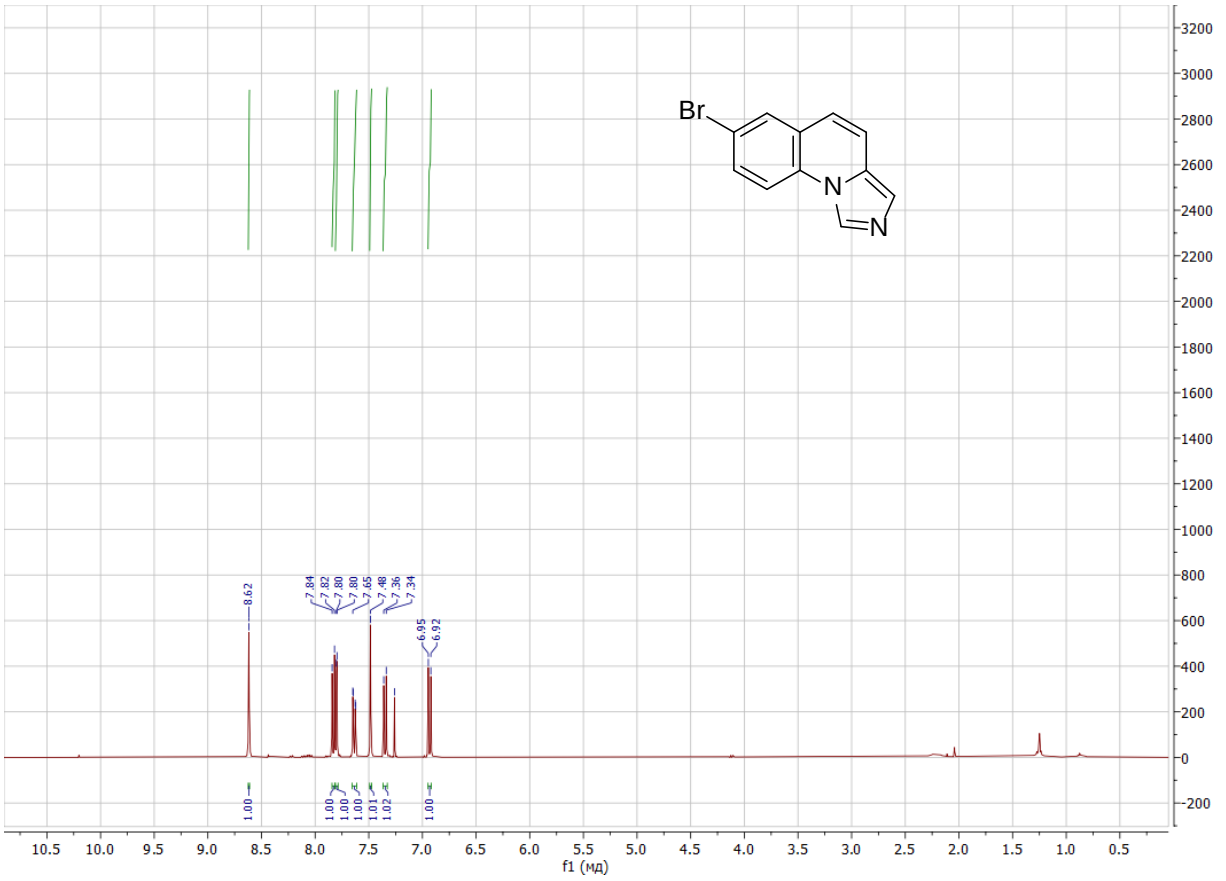


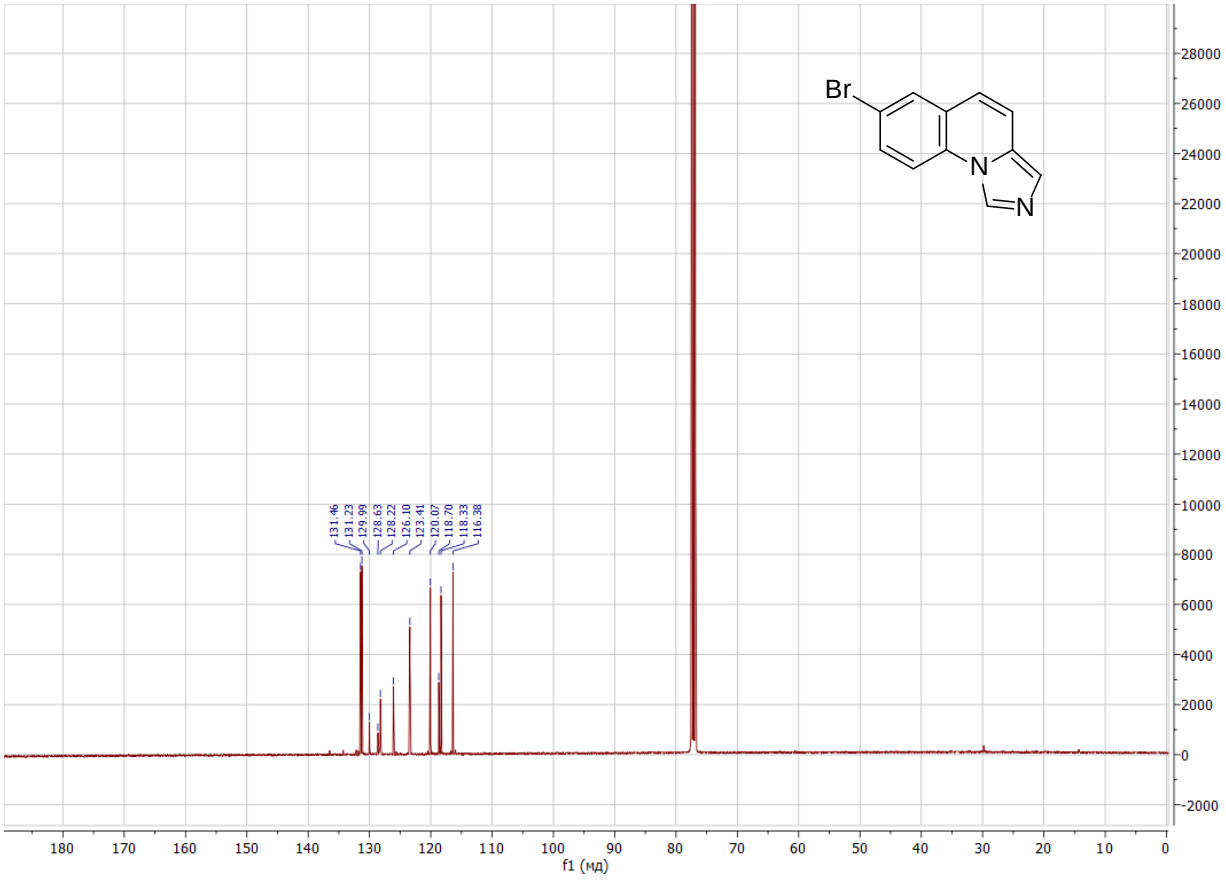
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19bg** in $CDCl_3$.



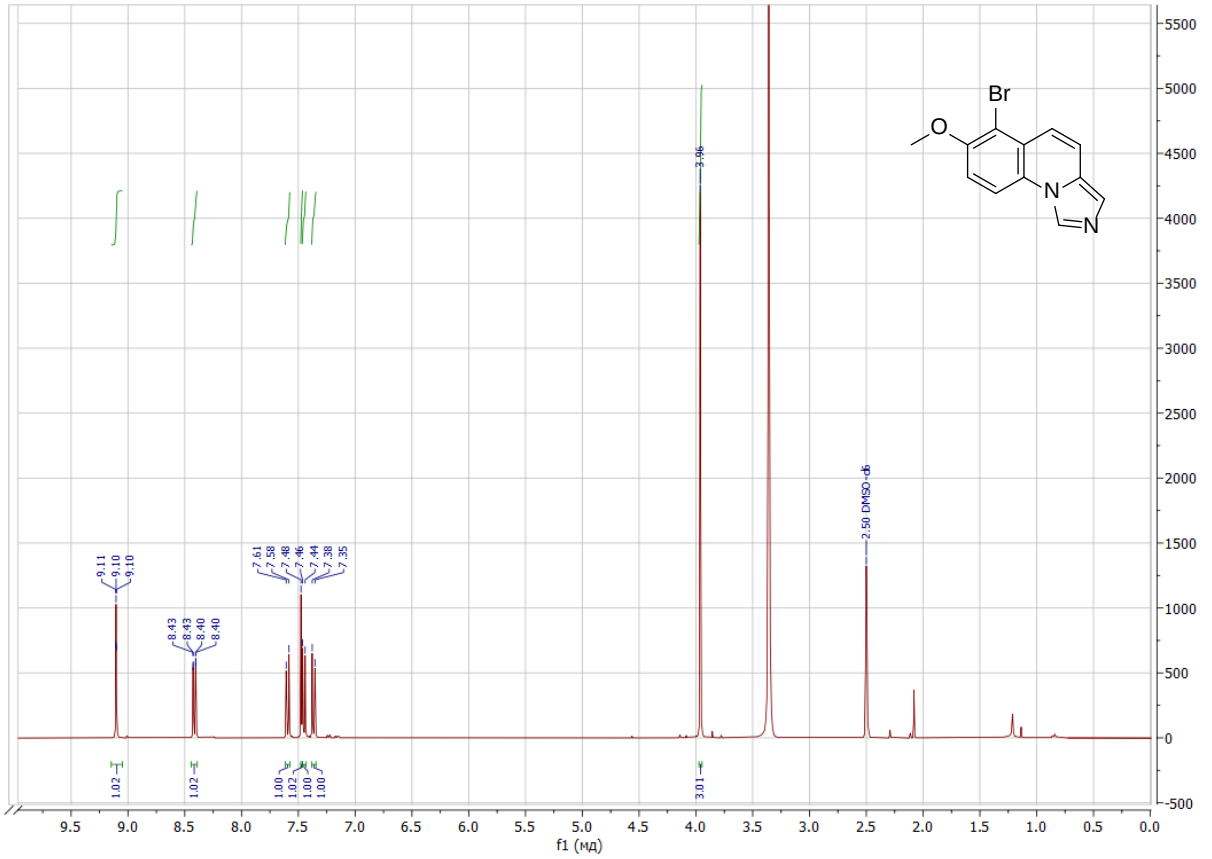


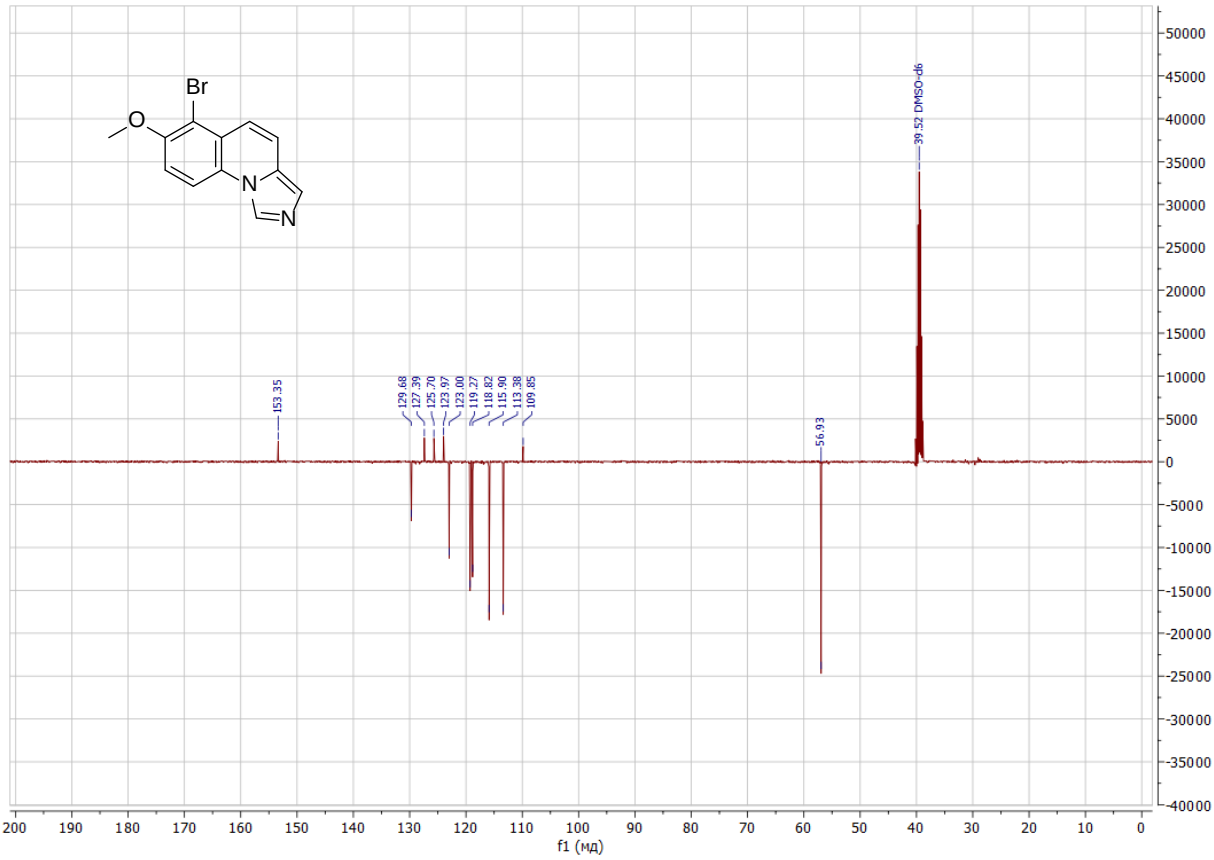
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19ce** in $CDCl_3$.



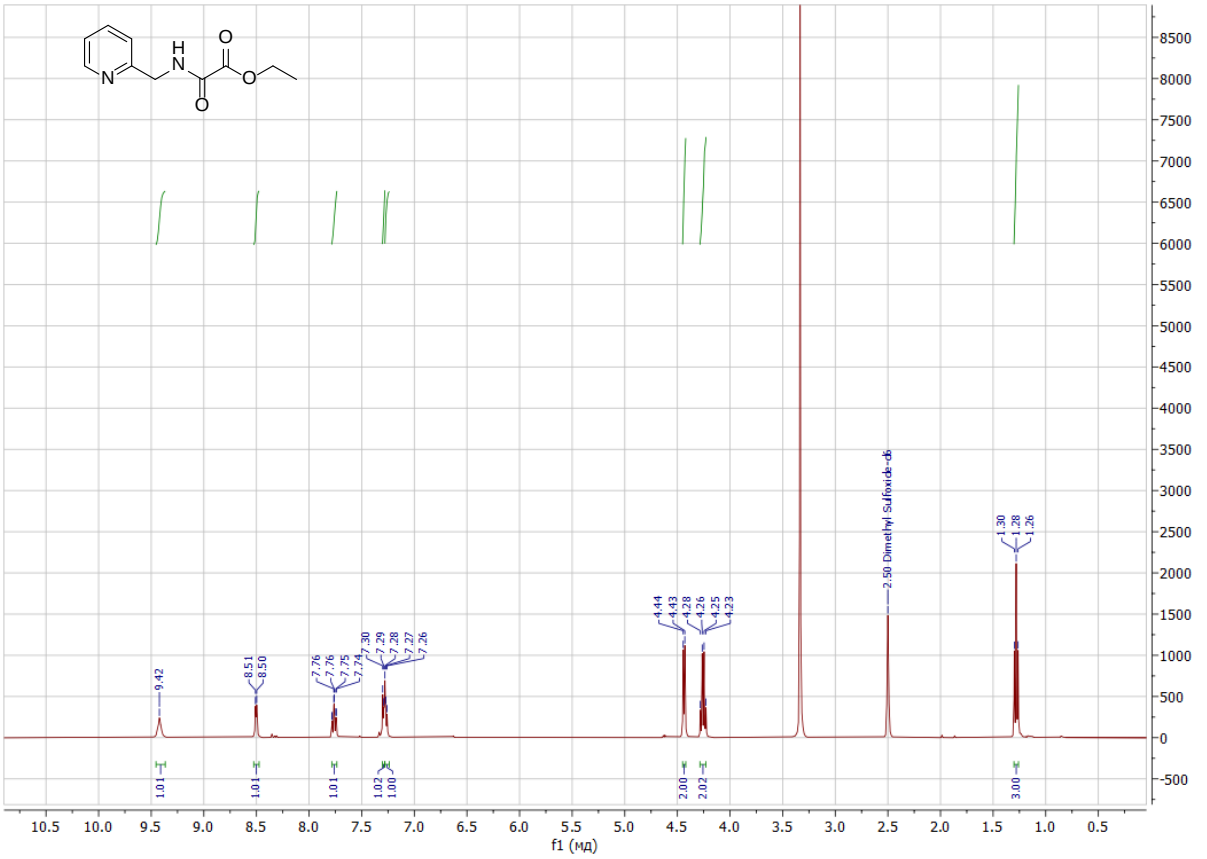


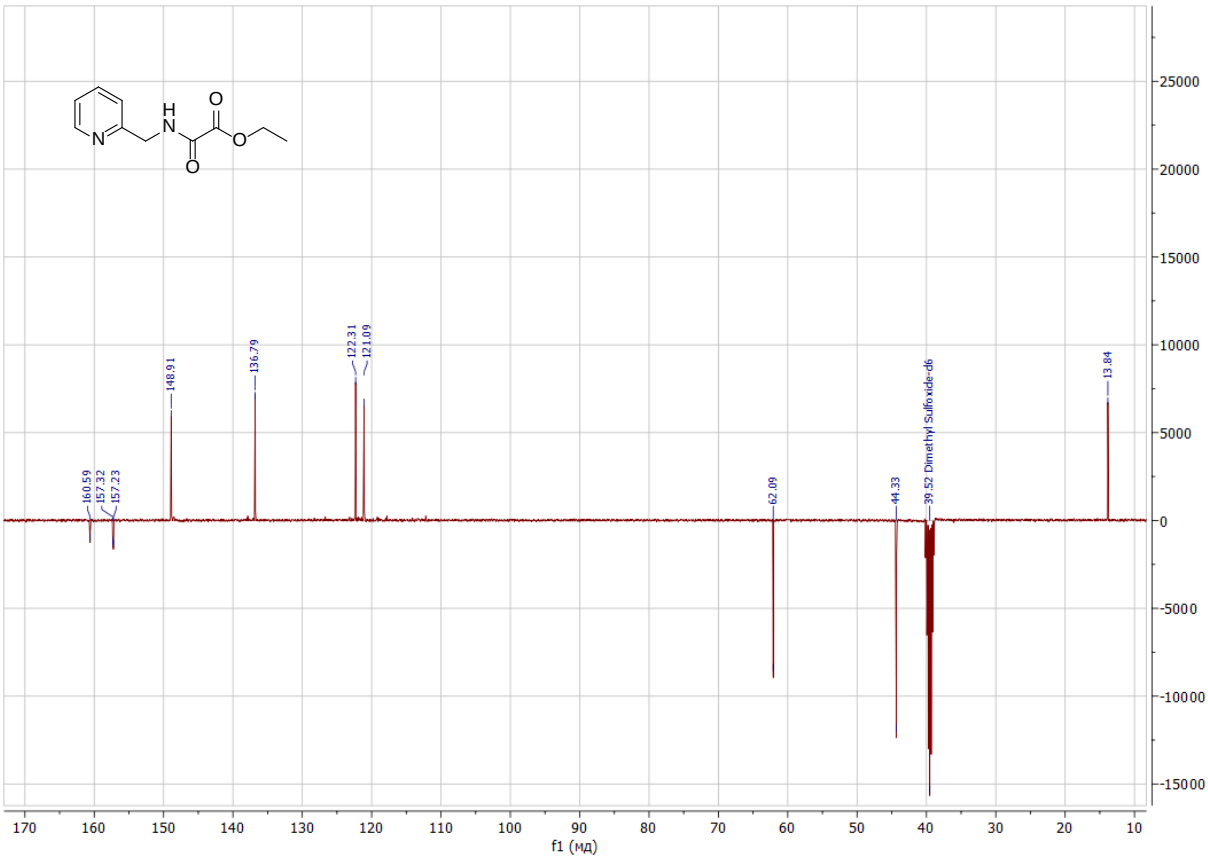
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **19de** DMSO-d_6.



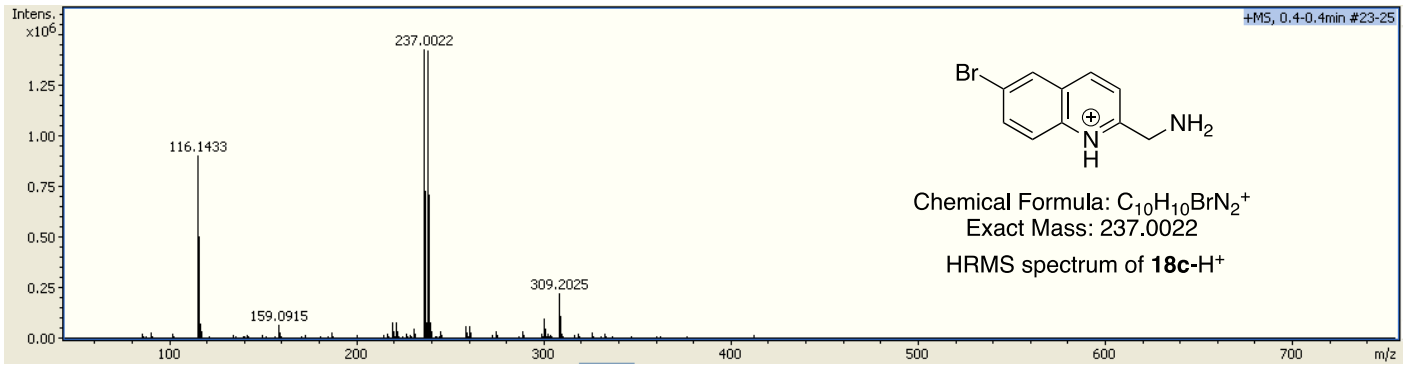


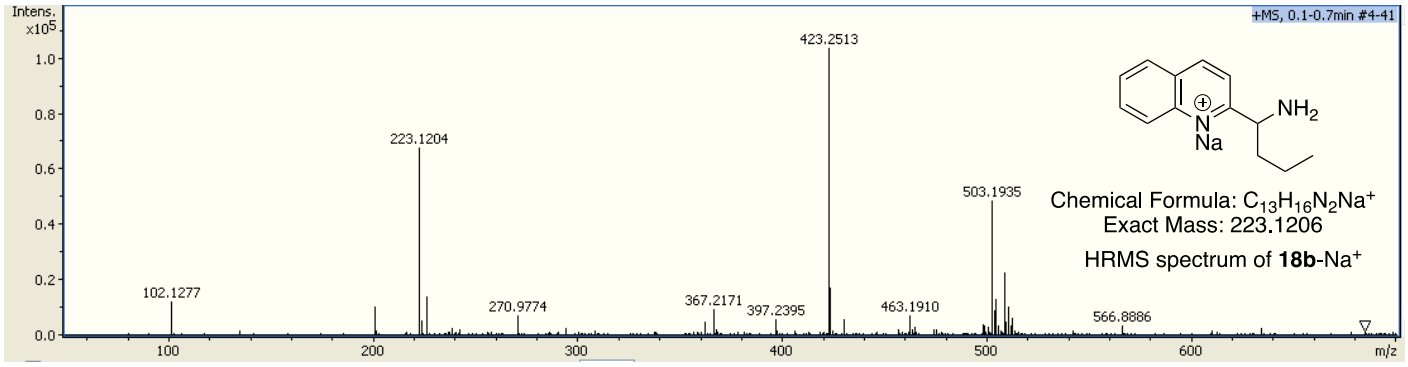
^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **20** DMSO-d_6.

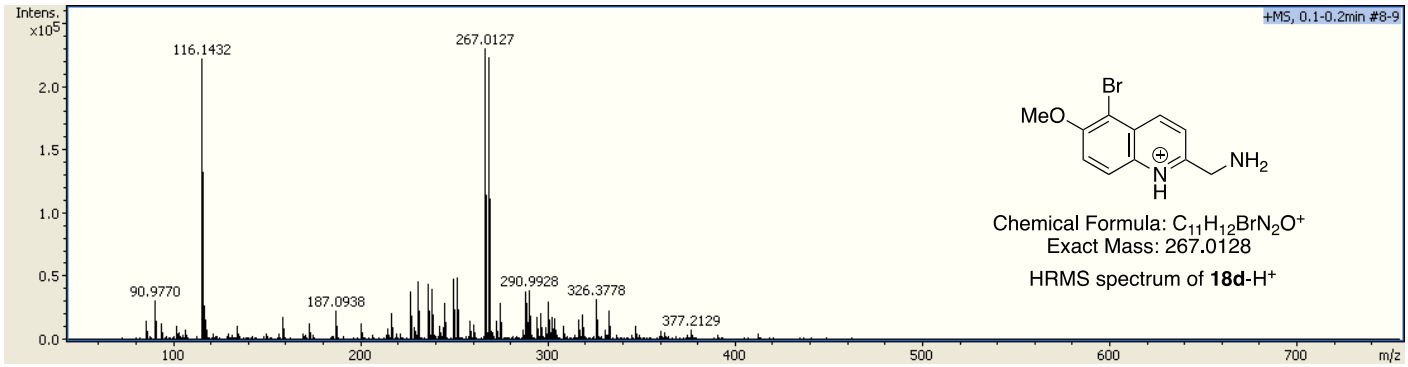


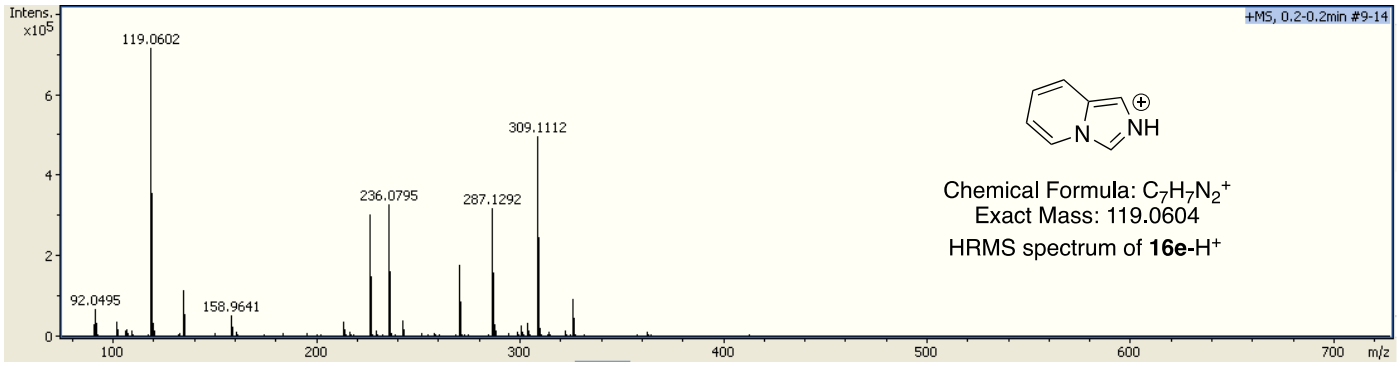


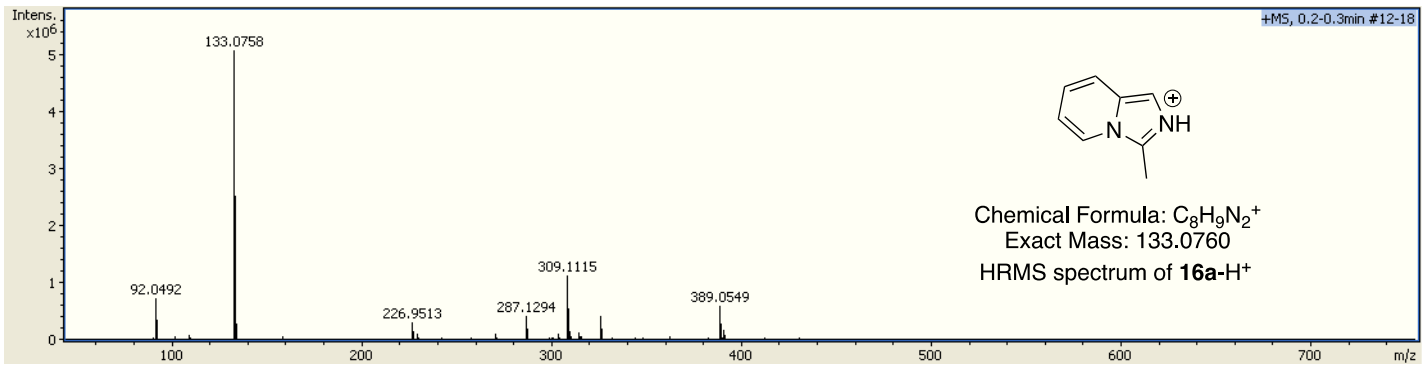
HRMS spectral charts

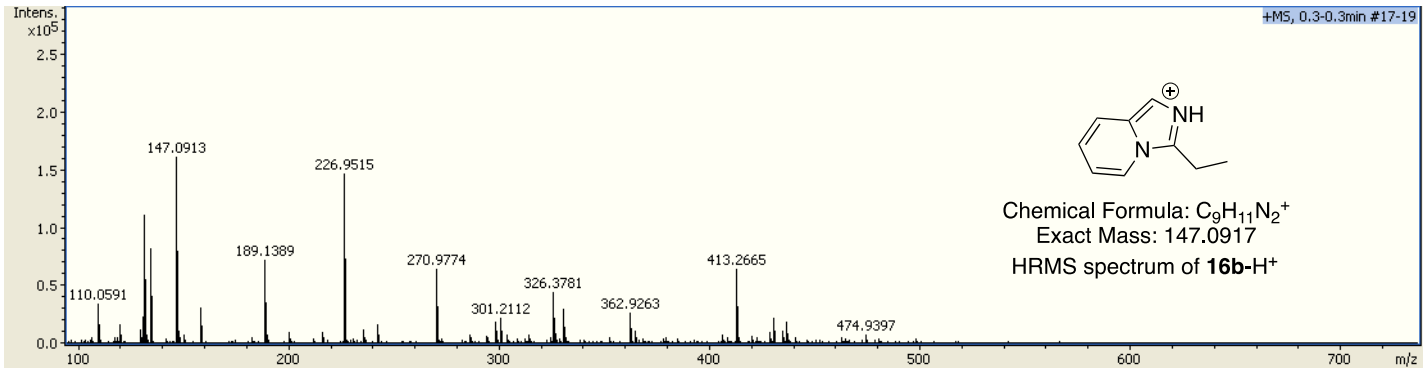


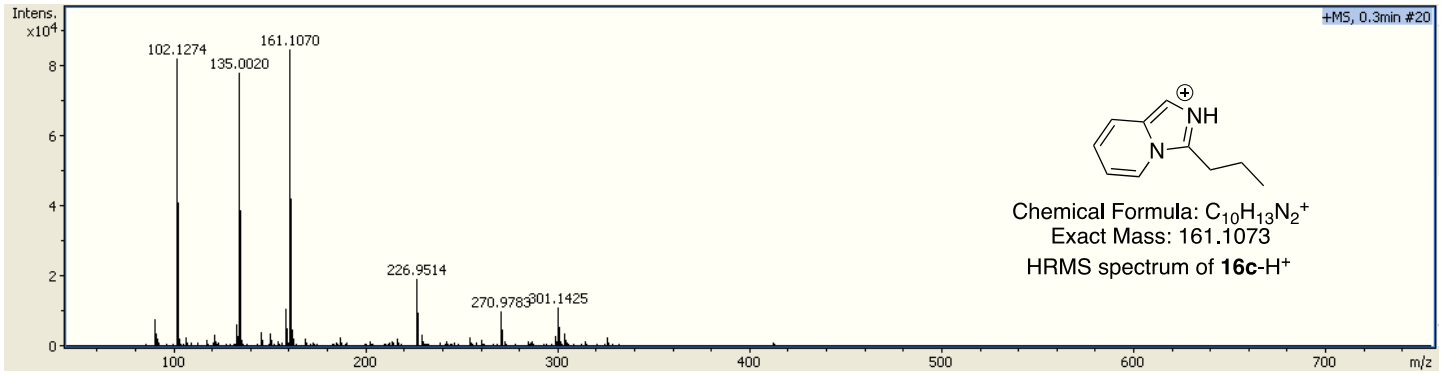


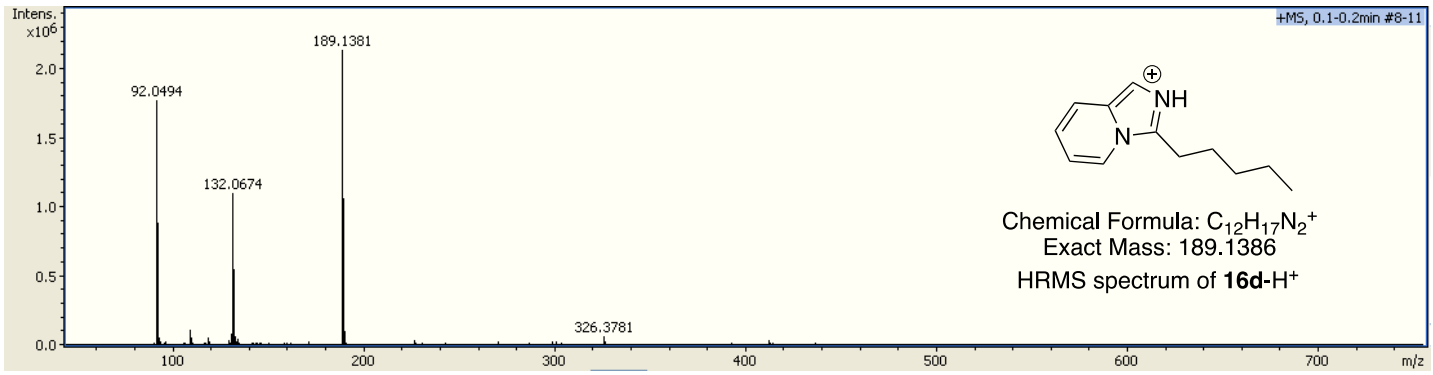


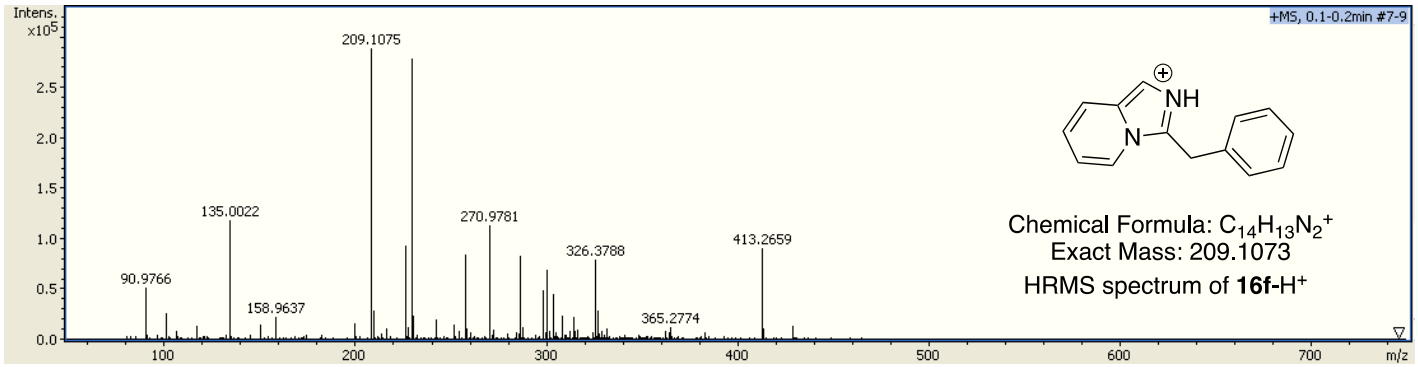


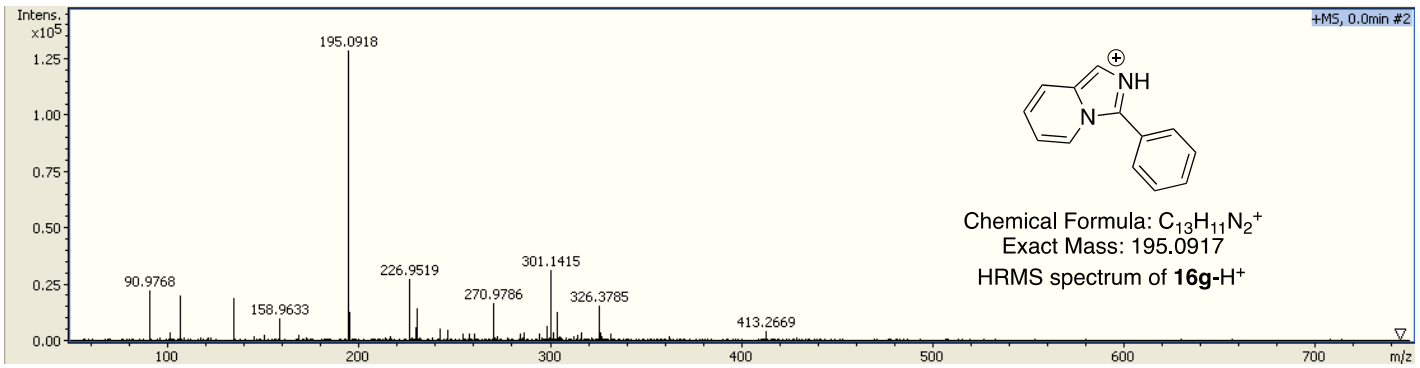

Intens.
x10^6
+MS, 0.2-0.3min #12-18
133.0758
92.0492
226.9513
287.1294
309.1115
389.0549
NH
N
Chemical Formula: C8H9N2+
Exact Mass: 133.0760
HRMS spectrum of 16a-H+
m/z

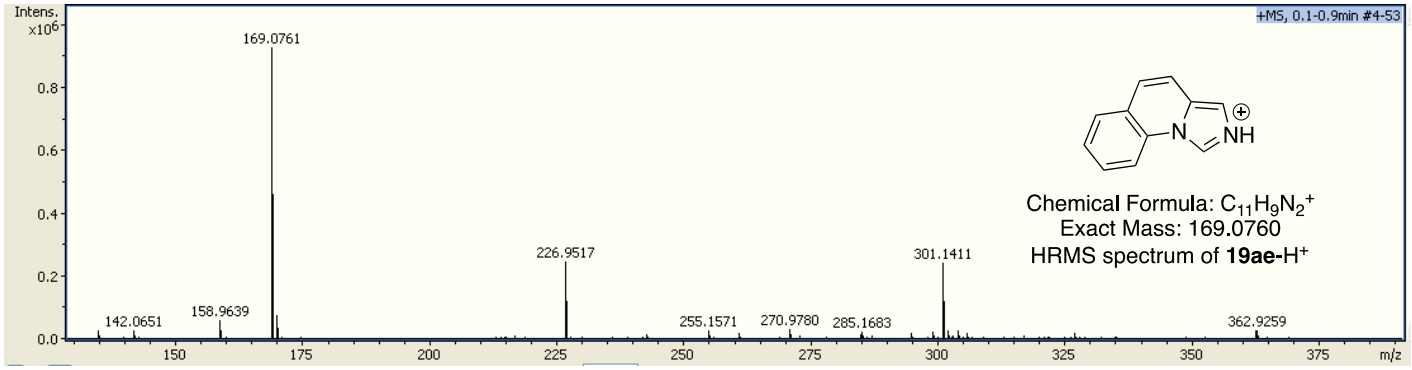

Intens.
x10^5
+MS, 0.3-0.3min #17-19
147.0913
226.9515
189.1389
270.9774
326.3781
413.2665
110.0591
301.2112
362.9263
474.9397
NH
N
Chemical Formula: C9H11N2+
Exact Mass: 147.0917
HRMS spectrum of 16b-H+
m/z

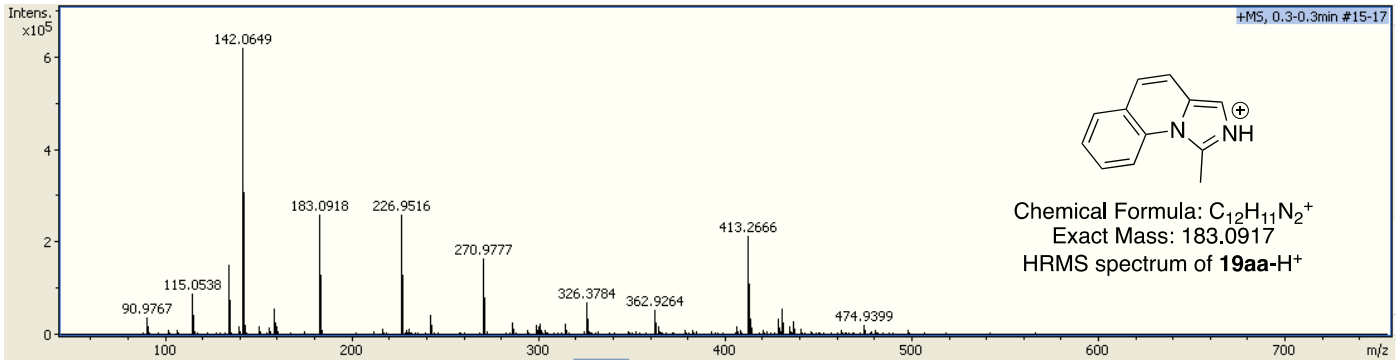

Intens.
x10^4
+MS, 0.3min #20
102.1274
135.0020
161.1070
226.9514
270.9783
301.1425
NH
N
Chemical Formula: C10H13N2+
Exact Mass: 161.1073
HRMS spectrum of 16c-H+
m/z

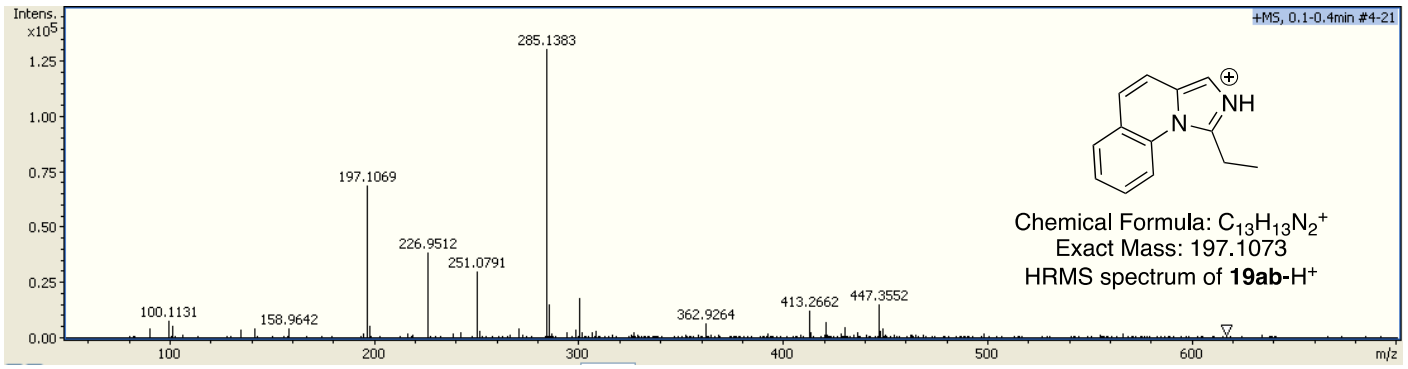

Intens.
x10^6
+MS, 0.1-0.2min #8-11
189.1381
92.0494
132.0674
326.3781
NH
N
Chemical Formula: C12H17N2+
Exact Mass: 189.1386
HRMS spectrum of 16d-H+
m/z

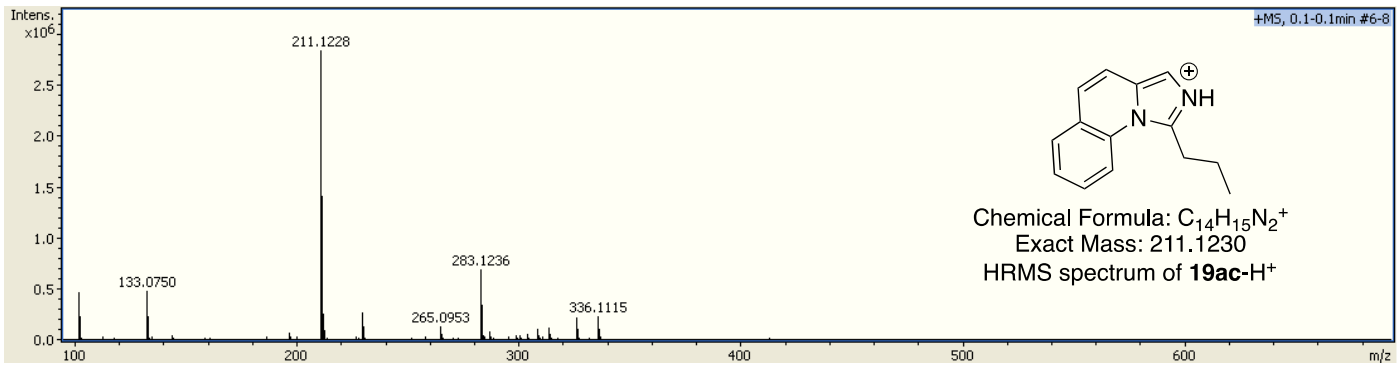

Intens.
x10^5
+MS, 0.1-0.2min #7-9
209.1075
135.0022
270.9781
326.3788
413.2659
90.9766
158.9637
365.2774
NH
N
Chemical Formula: C14H13N2+
Exact Mass: 209.1073
HRMS spectrum of 16f-H+
m/z

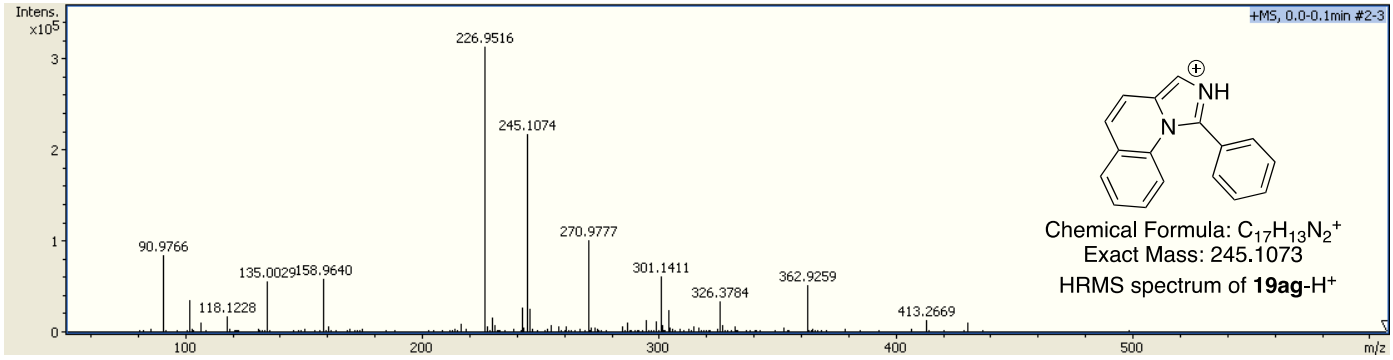

+MS, 0.0min #2
Intens.
x10^5
195.0918
90.9768
158.9633
226.9519
270.9786
301.1415
326.3785
413.2669
m/z
Chemical Formula: C13H11N2+
Exact Mass: 195.0917
HRMS spectrum of 16g-H+

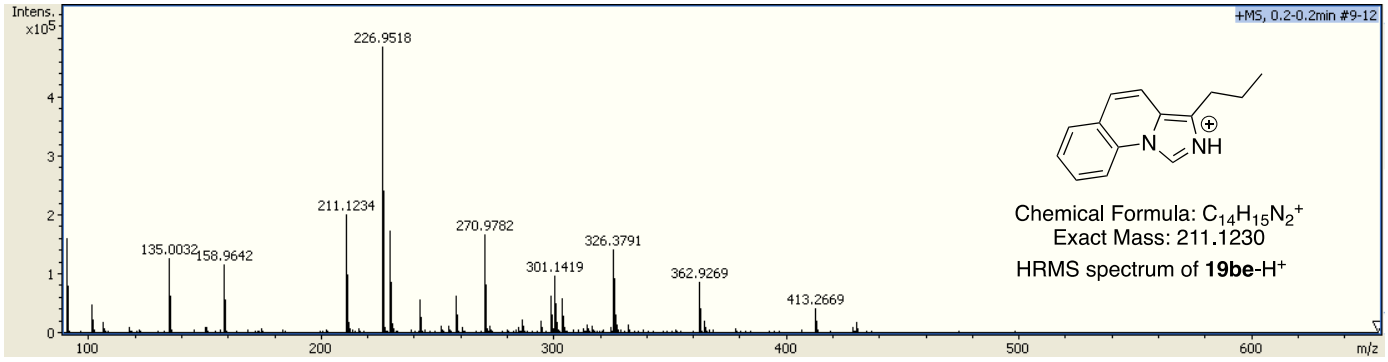

+MS, 0.1-0.9min #4-53
Intens.
x10^6
169.0761
142.0651
158.9639
226.9517
255.1571
270.9780
285.1683
301.1411
362.9259
m/z
Chemical Formula: C11H9N2+
Exact Mass: 169.0760
HRMS spectrum of 19ae-H+

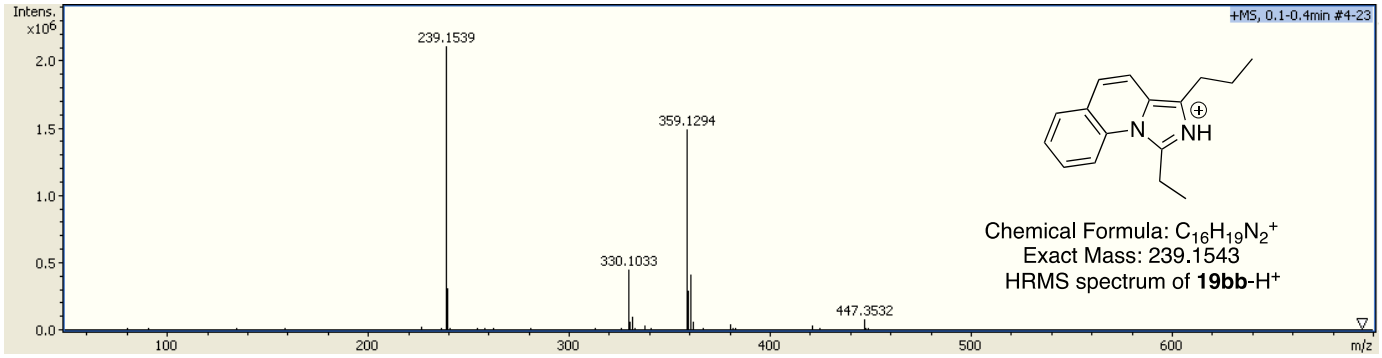

+MS, 0.3-0.3min #15-17
Intens.
x10^5
142.0649
90.9767
115.0538
183.0918
226.9516
270.9777
326.3784
362.9264
413.2666
474.9399
m/z
Chemical Formula: C12H11N2+
Exact Mass: 183.0917
HRMS spectrum of 19aa-H+

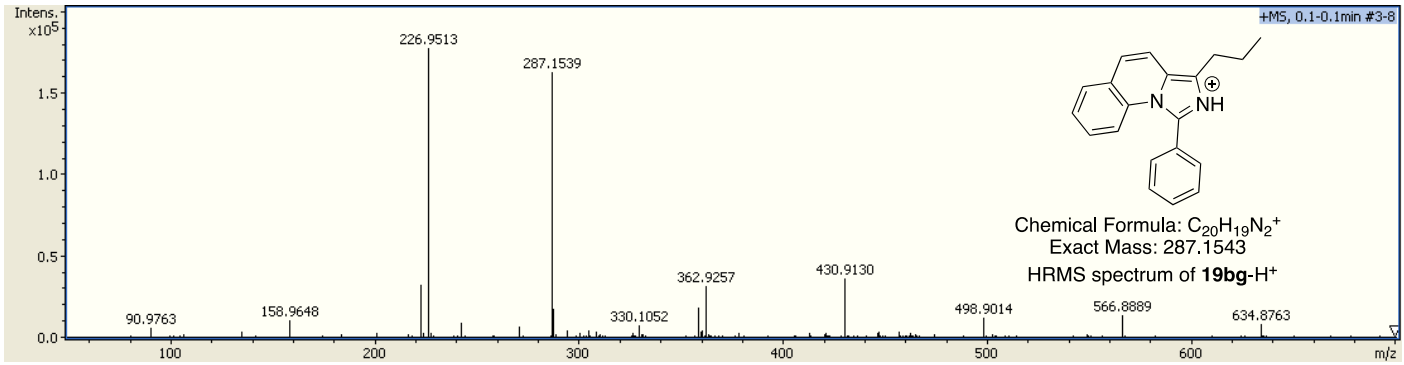

+MS, 0.1-0.4min #4-21
Intens.
x10^5
285.1383
197.1069
100.1131
158.9642
226.9512
251.0791
362.9264
413.2662
447.3552
m/z
Chemical Formula: C13H13N2+
Exact Mass: 197.1073
HRMS spectrum of 19ab-H+

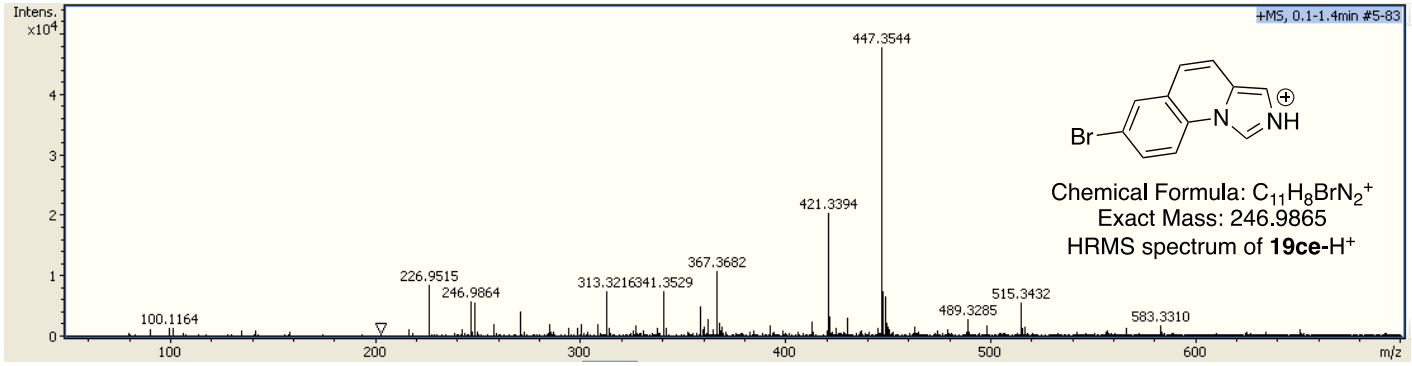

+MS, 0.1-0.1min #6-8
Intens.
x10^6
211.1228
133.0750
265.0953
283.1236
336.1115
m/z
Chemical Formula: C14H15N2+
Exact Mass: 211.1230
HRMS spectrum of 19ac-H+

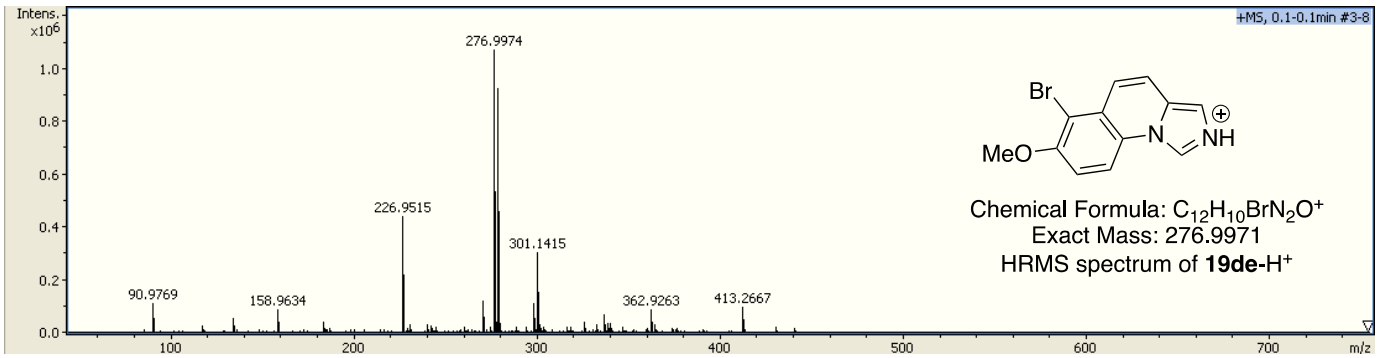

Intens.
x10^5
+MS, 0.0-0.1min #2-3
226.9516
245.1074
270.9777
90.9766
135.0029
158.9640
118.1228
301.1411
326.3784
362.9259
413.2669
m/z
NH
N
Chemical Formula: C17H13N2+
Exact Mass: 245.1073
HRMS spectrum of 19ag-H+


Intens.
x10^5
+MS, 0.2-0.2min #9-12
226.9518
211.1234
270.9782
135.0032
158.9642
301.1419
326.3791
362.9269
413.2669
m/z
N
NH
Chemical Formula: C14H15N2+
Exact Mass: 211.1230
HRMS spectrum of 19be-H+

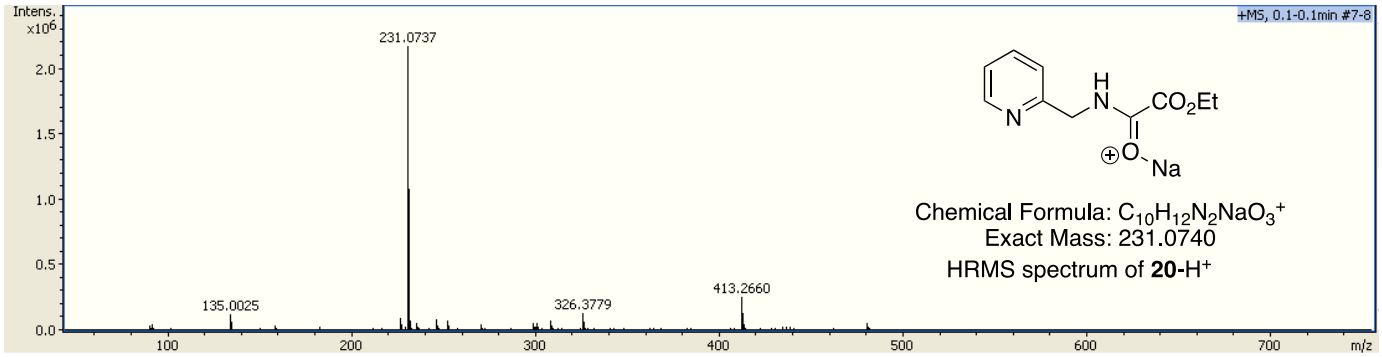

Intens.
x10^6
+MS, 0.1-0.4min #4-23
239.1539
359.1294
330.1033
447.3532
m/z
N
NH
Chemical Formula: C16H19N2+
Exact Mass: 239.1543
HRMS spectrum of 19bb-H+


Intens.
x10^5
+MS, 0.1-0.1min #3-8
226.9513
287.1539
362.9257
430.9130
90.9763
158.9648
330.1052
498.9014
566.8889
634.8763
m/z
N
NH
Chemical Formula: C20H19N2+
Exact Mass: 287.1543
HRMS spectrum of 19bg-H+


Intens.
x10^4
+MS, 0.1-1.4min #5-83
447.3544
421.3394
367.3682
226.9515
246.9864
313.3216341.3529
515.3432
489.3285
583.3310
100.1164
m/z
Br
N
NH
Chemical Formula: C11H8BrN2+
Exact Mass: 246.9865
HRMS spectrum of 19ce-H+



Chemical Formula: $C_{12}H_{10}BrN_2O^+$
Exact Mass: 276.9971
HRMS spectrum of **19de**-H^+



Chemical Formula: $C_{10}H_{12}N_2NaO_3^+$
Exact Mass: 231.0740
HRMS spectrum of **20**-H^+