Support Information

Synthesis of imidazo[1,2-a][1,3,5]triazines by NBS mediated coupling of 2-amino-1,3,5-triazines with 1,3-dicarbonyl compounds

Zexi Pan, Chan Song, Chen Zhang, Wei Zhou, and Dong-Mei Cui

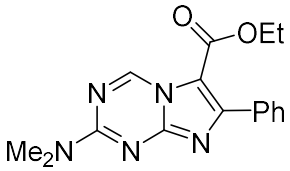
Experimental Section

Under otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin layer chromatography (TLC) was performed using silica gel 60 F_{254} and visualized using UV light. Column chromatography was performed with silica gel (mesh 300-400). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 500 MHz spectrometer in $CDCl_3$ with Me_4Si as an internal standard. Data were reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad and m = multiplet), coupling constant in Herts (Hz) and integration. IR spectra were recorded on an FT-IR spectrometer, and only major peaks are reported in cm^{-1}. HRMS and mass data were recorded by ESI on a TOF mass spectrometer.

General procedure for the preparation of imidazo[1,2-a][1,3,5]triazines

To a mixture of 2-amino-1,3,5-triazine **1** (1.0 mmol) and 1,3-dicarbonyl compound **2** (0.5 mmol) in NMP (3 mL) was added NBS (0.5 mmol). The resulting mixture was stirred at 80 ºC under N_2 atmosphere. After completion**,** the reaction mixture was cooled to room temperature, added H_2O and extracted with ethyl acetate (3×15 mL). The organic phase was dried over anhydrous Na_2SO_4. The mixture was evaporated under vacuum, and the residue was purified by flash chromatography with petroleum ether/ethyl acetate (2:1 (v/v)) to give the pure product.

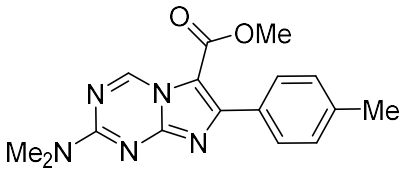
Ethyl 2-(dimethylamino)-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3a**)



Yellow solid, 133.4 mg, 90% yield; mp: 127-128 ºC; ^1H NMR (500 MHz, $CDCl_3$): δ 9.70 (s, 1H),

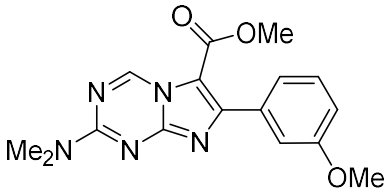
7.95-7.88 (m, 2H), 7.43-7.41(m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 3.34 (s, 3H), 3.29 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 158.7, 155.1, 152.6, 147.8, 133.1, 130.4, 129.3, 127.4, 108.0, 60.7, 37.4, 37.1, 14.1; IR (KBr, cm^{-1}): 2927, 1699, 1627, 1595, 1504, 1410, 1348, 1130, 755, 695. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}N_5O_2$ 312.1460, found 312.1458.

Methyl 2-(dimethylamino)-7-(p-tolyl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3b**)



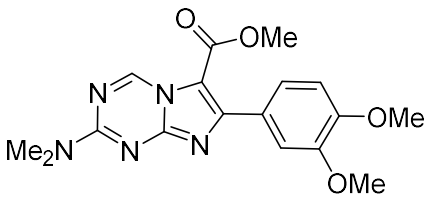
Yellow solid, 123.0 mg, 83% yield; mp: 171-172 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.67 (s, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 3.84 (s, 3H), 3.33 (s, 3H), 3.28 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7, 158.7, 155.4, 152.6, 147.8, 139.5, 130.2, 130.1, 128.4, 107.5, 51.4, 37.4, 37.2, 21.5; IR (KBr, cm^{-1}): 2949, 1697, 1633, 1592, 1409, 1344, 1157, 1131, 1006, 783. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}N_5O_2$ 312.1460, found 312.1463

Methyl 2-(dimethylamino)-7-(3-methoxyphenyl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3c**)



White solid, 132.3 mg, 85% yield; mp: 153-154 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.68 (s, 1H), 7.49-7.45 (m, 2H), 7.32 (t, J = 8.0 Hz, 1H), 6.99-6.96 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.33 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7, 159.0, 158.7, 154.9, 152.6, 147.8, 134.3, 128.5, 122.9, 115.9, 115.0, 107.8, 55.4, 51.4, 37.4, 37.2; IR (KBr, cm^{-1}): 1683, 1628, 1506, 1472, 1407, 1361, 1197, 762. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{18}N_5O_3$ 328.1410, found 328.1411

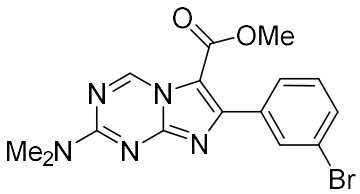
Methyl 7-(3,4-dimethoxyphenyl)-2-(dimethylamino)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3d**)



Yellow solid, 144.3 mg, 83% yield; mp: 175-176 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.66 (s, 1H),

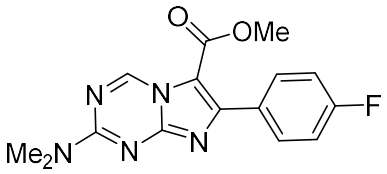
7.61(d, *J* = 2.0 Hz, 1H), 7.58(dd, *J* = 8.3, 2.0 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.87 (s, 3H), 3.34 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7, 158.7, 155.1, 152.6, 150.3, 148.2, 147.9, 125.5, 123.8, 113.5, 110.1, 107.3, 56.0, 55.9, 51.4, 37.4, 37.2; IR (KBr, cm^{-1}): 2960, 1679, 1623, 1536, 1424, 1355, 1267, 1132, 1046, 1020, 766. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}N_5O_4$ 358.1515, found 358.1514.

Methyl 7-(3-bromophenyl)-2-(dimethylamino)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3e**)



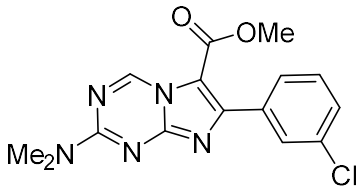
Yellow solid, 128.3 mg, 71% yield; mp: 152-153 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.68 (s, 1H), δ 8.09 (t, *J* = 1.8 Hz, 1H), 7.86 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.56 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.29 (dd, *J* = 8.0, 7.9 Hz, 1H), 3.86 (s, 3H), 3.35 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.4, 158.8, 153.3, 152.7, 147.8, 135.1, 133.3, 132.3, 129.2, 128.9, 121.7, 108.1, 51.6, 37.5, 37.2; IR (KBr, cm^{-1}): 1687, 1625, 1593, 1471, 1409, 1362, 1195, 1153, 782. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{15}N_5O_2Br$ 376.0409, found 376.0404.

Methyl 2-(dimethylamino)-7-(4-fluorophenyl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3f**)



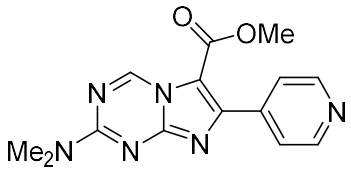
White solid, 118.4 mg, 75% yield; mp: 180-181 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.66 (s, 1H), 7.93-7.90 (m, 2H), 7.13-7.10 (m, 2H), 3.85 (s, 3H), 3.34 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 163.5 (d, *J* = 247.9 Hz), 160.5, 158.7, 154.2, 152.6, 147.8, 132.3 (d, *J* = 8.2 Hz), 129.1 (d, *J* = 3.1 Hz), 114.6 (d, *J* = 21.7 Hz), 107.7, 51.4, 37.4, 37.2; IR (KBr, cm^{-1}): 1698, 1628, 1586, 1412, 1371, 1132, 1040, 850, 765. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{15}FN_5O_2$ 316.1210, found 316.1206.

Methyl 7-(3-chlorophenyl)-2-(dimethylamino)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3g**)



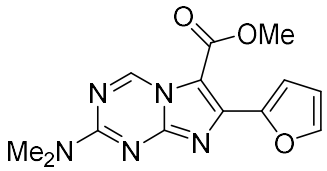
White solid, 124.9 mg, 75% yield; mp: 153-154 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.67 (s, 1H), 7.93 (t, J = 1.7 Hz, 1H), 7.79 (dt, J = 8.0, 1.7 Hz, 1H), 7.39(dt, J = 8.0, 1.7 Hz, 1H), 7.35(t, J = 8.0, 1H), 3.86 (s, 3H), 3.34 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 158.7, 153.4, 152.6, 147.8, 134.8, 133.5, 130.4, 129.4, 128.9, 128.4, 108.0, 51.5, 37.4, 37.2; IR (KBr, cm^{-1}): 948, 1676, 1583, 1462, 1410, 1316, 1250, 1180, 1049, 807, 770. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{15}ClN_5O_2$ 332.0914, found 332.0917.

Methyl 2-(dimethylamino)-7-(pyridin-4-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3h**)



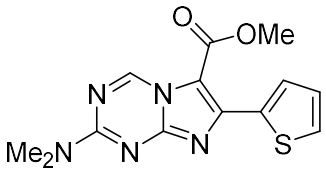
Yellow solid, 68.0 mg, 46% yield; mp: 195 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.67 (s, 1H), 8.69 (dd, J = 4.6, 1.7 Hz, 2H), 7.79 (dd, J = 4.6, 1.7 Hz, 2H), 3.86 (s, 3H), 3.35 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 158.7, 152.8, 151.9, 149.4, 147.8, 140.9, 124.4, 108.8, 51.6, 37.5, 37.2; IR (KBr, cm^{-1}): 1700, 1634, 1591, 1407, 1359, 1185, 1138, 764. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{15}N_6O_2$ 299.1256, found 299.1255.

Methyl 2-(dimethylamino)-7-(furan-2-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3i**)



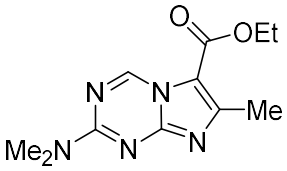
Yellow solid, 144.3mg, 90% yield; mp: 219-220 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.59 (s, 1H), 7.62 (dd, J = 3.5, 0.4 Hz, 1H), 7.48 (dd, J = 3.5, 0.4 Hz 1H), 6.56 (dd, J = 3.5, 3.5 Hz, 1H), 3.97 (s, 3H), 3.31 (s, 3H), 3.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 158.7, 152.7, 147.7, 147.2, 144.4, 115.4, 111.9, 106.4, 51.5, 37.3, 37.1; IR (KBr, cm^{-1}): 1684, 1633, 1407, 1372, 1194, 1147, 767. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{14}N_5O_3$ 288.1097, found 288.1099.

Methyl 2-(dimethylamino)-7-(thiophen-2-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3j**)



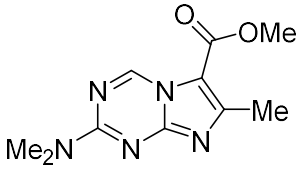
Yellow solid, 142.0mg, 93% yield; mp: 209 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.25 (dd, J = 3.8, 1.1 Hz, 1H), 7.51 (dd, J = 5.1, 1.1 Hz, 1H), 7.14 (dd, J = 5.0, 3.8 Hz, 1H), 3.99 (s, 3H), 3.32 (s, 3H), 3.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 158.8, 152.3, 148.5, 147.7, 135.9, 131.2, 129.9, 127.6, 106.1, 51.5, 37.5, 37.2; IR (KBr, cm^{-1}): 1693, 1632, 1590, 1405, 1176, 1120, 763. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{14}N_5O_2S$ 304.0868, found 304.0868.

Ethyl 2-(dimethylamino)-7-methylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3k**)



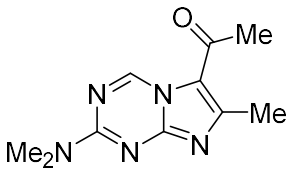
White solid, 96.0 mg, 77% yield; mp: 143 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.53 (s, 1H), 4.38 (q, J = 7.2, 2H), 3.30 (s, 3H), 3.25 (s, 3H), 2.60 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6, 158.6, 155.4, 152.6, 147.0, 108.8, 60.4, 37.3, 37.0, 16.1, 14.4; IR (KBr, cm^{-1}): 2995, 1682, 1627, 1581, 1405, 1384, 1197, 1096, 1014, 762. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{11}H_{16}N_5O_2$ 250.1304, found 250.1307.

Methyl 2-(dimethylamino)-7-methylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3l**)



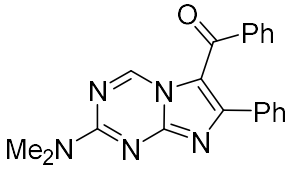
Yellow solid, 69.4mg, 61% yield; mp: 187-188 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.52 (s, 1H), 3.92 (s, 3H), 3.30 (s, 3H), 3.25 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1, 158.7, 155.6, 152.8, 147.1, 108.7, 51.4, 37.4, 37.1, 16.2; IR (KBr, cm^{-1}): 1697, 1633, 1594, 1385, 1195, 1091, 758. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{10}H_{14}N_5O_2$ 236.1147, found 236.1147.

1-(2-(Dimethylamino)-7-methylimidazo[1,2-a][1,3,5]triazin-6-yl)ethan-1-one (**3m**)



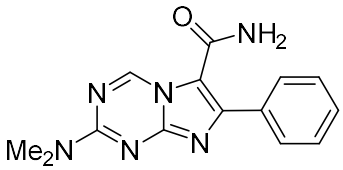
Yellow solid, 75.4mg, 69% yield; mp: 162-163 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.89 (s, 1H), 3.30 (s, 3H), 3.25 (s, 3H), 2.66 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.2, 159.0, 155.50, 152.9, 148.1, 119.1, 37.4, 37.0, 29.1, 17.7; IR (KBr, cm^{-1}): 2931, 1636, 1594, 1413, 1386, 1170, 1070, 787. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{10}H_{14}N_5O$ 220.1198, found 220.1200.

(2-(Dimethylamino)-7-phenylimidazo[1,2-a][1,3,5]triazin-6-yl)(phenyl)methanone (**3n**)



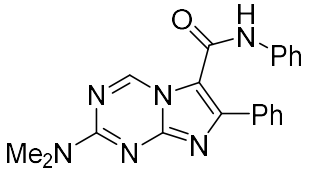
Yellow solid, 156.0 mg, 91% yield; mp: 207-208 ºC, [lit][1]: 209-210 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.48-7.45 (m, 2H), 7.34-7.32 (m, 2H), 7.29-7.26 (m, 1H), 7.16-7.13 (m, 1H), 7.11-7.04 (m, 4H), 3.38 (s, 3H), 3.33 (s, 3H).

2-(Dimethylamino)-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxamide (**3o**)



Yellow solid, 102.2 mg, 71% yield; mp: 257-258 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.93 (s, 1H), 7.77-7.71 (m, 2H), 7.58-7.45 (m, 3H), 5.73 (br, 1H), 5.36 (br, 1H), 3.35 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.8 158.2, 150.7, 148.5, 147.1, 133.8, 129.4, 129.3, 128.9, 112.0, 37.5, 37.0; IR (KBr, cm^{-1}): 3109, 1658, 1630, 1590, 1405, 1364, 1151, 786. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{15}N_6O$ 283.1307, found 283.1303.

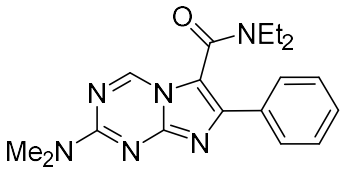
2-(Dimethylamino)-N,7-diphenylimidazo[1,2-a][1,3,5]triazine-6-carboxamide (**3p**)



Yellow solid, 136.2mg, 76% yield; mp: >300 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.93 (s, 1H),

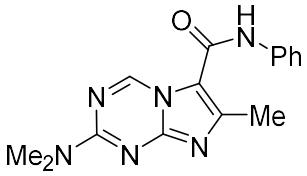
7.79-7.78 (m, 2H), 7.59 (s, 1H), 7.58- 7.52 (m, 3H), 7.31-7.26 (m, 4H), 7.09-7.06 (m, 1H), 3.35 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 158.1, 152.3, 149.9, 148.1, 137.5, 133.1, 130.2, 129.8, 129.2, 129.1, 124.3, 119.4, 111.2, 37.5, 37.2; IR (KBr, cm^{-1}): 2923, 1653, 1633, 1586, 1374, 1151, 770, 694. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{19}N_6O$ 359.1620, found 359.1615.

2-(Dimethylamino)-N,N-diethyl-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxamide (**3q**)



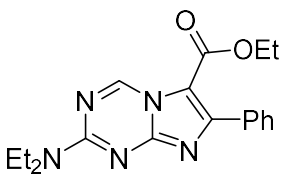
Yellow solid, 102.8mg, 61% yield; mp: 143-144 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.82-7.74 (m, 2H), 7.43-7.35 (m, 3H), 3.60-3.51 (m, 2H), 3.29 (s, 3H), 3.25 (s, 3H), 3.11-3.01 (m, 2H), 1.35-1.15 (m, 3H), 0.91-0.65 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5, 158.2, 151.1, 146.2, 145.0, 133.2, 129.1, 128.5, 128.3, 109.9, 43.0, 39.0, 37.4, 37.2, 13.9, 12.4; IR (KBr, cm^{-1}): 2959, 2930, 1636, 1613, 1590, 1405, 1127, 777, 698. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{23}N_6O$ 339.1933, found 339.1936.

2-(Dimethylamino)-7-methyl-N-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxamide (**3r**)



Yellow solid, 97.9mg, 66% yield; mp: 263ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.60 (s, 1H), 7.73-7.70 (m, 2H), 7.37-7.34 (m, 2H), 7.13-7.10(m, 1H), 3.32 (s, 3H), 3.27 (s, 3H), 2.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5, 157.9, 148.0, 144.3, 138.1, 133.3, 129.0, 123.9 120.0, 119.4, 37.5, 37.3, 8.4; IR (KBr, cm^{-1}): 2910, 1678, 1640, 1595, 1510, 1439, 1305, 1234, 1076, 756, 693. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{17}N_6O$ 297.1464, found 297.1460.

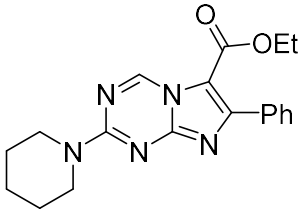
Ethyl 2-(diethylamino)-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3s**)



Yellow solid, 137.1mg, 82% yield; mp: 109-110 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.69 (s, 1H),

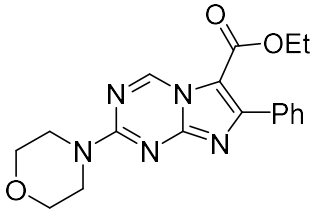
7.93-7.88 (m, 2H), 7.44-7.39 (m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 3.76-3.71 (m, 4H), 1.31-1.24 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 157.8, 155.2, 152.9, 148.0, 133.3, 130.5, 129.4, 127.5, 108.0, 60.7, 42.9, 42.4, 14.1, 13.6, 12.5; IR (KBr, cm^{-1}): 2987, 1670, 1625, 1567, 1381, 1351, 1153, 1086, 1045, 761, 697; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{22}N_5O_2$ 340.1773, found 340.1771.

Ethyl 7-phenyl-2-(piperidin-1-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3t**)



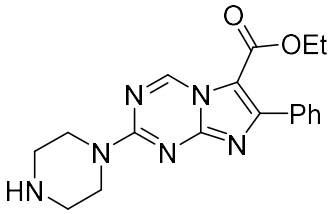
White solid, 150.6mg, 72% yield; mp: 106-107 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.66 (s, 1H), 7.93-7.88 (m, 2H), 7.42-7.41 (m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 3.95-3.93 (m, 4H), 1.72-1.66 (m, 6H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 157.6, 155.1, 152.8, 148.0, 133.2, 130.4, 129.3, 127.4, 108.1, 60.65, 45.8, 45.0, 26.1, 25.5, 24.6, 14.1; IR (KBr, cm^{-1}): 1682, 1623, 1567, 1377, 1191, 757, 657. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{22}N_5O_2$ 352.1773, found 352.1768.

Ethyl 2-morpholino-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3u**)



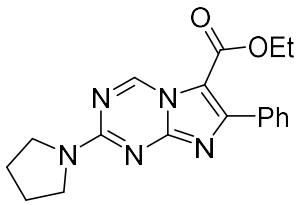
White solid, 160.6mg, 76% yield; mp: 139 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.66 (s, 1H), 7.90 (dd, J = 6.0, 2.3 Hz, 2H), 7.46-7.39 (m, 3H), 4.33 (q, J = 7.1 Hz, 2H), 3.99 (t, J = 4.9 Hz, 4H), 3.78（t, J = 4.9 Hz, 4H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 157.9, 155.1, 152.3, 148.3, 132.9, 130.4, 129.4, 127.5, 108.4, 66.7, 66.5, 60.8, 44.9, 44.2, 14.0; IR (KBr, cm^{-1}): 2992, 1674, 1622, 1557, 1402, 1383, 1242, 1154, 757, 684. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{20}N_5O_3$ 354.1566, found 354.1561.

Ethyl 7-phenyl-2-(piperazin-1-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3v**)



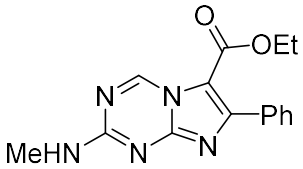
Yellow solid, 129.6mg, 73% yield; mp: 225-226 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.75 (s, 1H), 8.15 (s, 1H), 7.91-7.87 (m, 2H), 7.43-7.41 (m, 3H), 4.33 (q, J = 7.1 Hz, 2H), 4.06-3.99 (m, 4H), 3.68-3.64 (m, 2H), 3.50-3.46 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.9, 160.2, 157.8, 155.2, 152.1, 148.6, 132.8, 130.4, 129.6, 127.6, 108.5, 60.9, 45.2, 44.5, 39.9, 39.3, 14.0; IR (KBr, cm^{-1}): 3416, 2923, 1687, 1667, 1622, 1551, 1446, 1344, 1230, 1147, 707. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{18}H_{21}N_6O_2$ 353.1726, found 353.1725.

Ethyl 7-phenyl-2-(pyrrolidin-1-yl)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3w**)



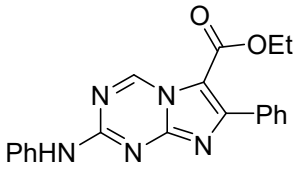
White solid, 131.0mg, 79% yield; mp: 155-157 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.70 (s, 1H), 7.92-7.90 (m, 2H), 7.43 -7.39 (m, 3H), 4.32 (q, J = 7.1 Hz, 2H), 3.74-3.68 (m, 4H), 2.05-2.01 (m, 4H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 156.6, 155.1, 152.6, 147.9, 133.2, 130.5, 129.3, 127.5, 107.9, 60.7, 47.4, 47.0, 25.5, 25.2, 14.1; IR (KBr, cm^{-1}): 2993, 1699, 1633, 1574, 1496, 1452, 1342, 1134, 786, 699. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{18}H_{20}N_5O_2$ 338.1617, found 338.1617.

Ethyl 2-(methylamino)-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3x**)



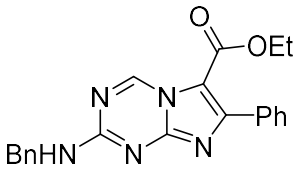
White solid, 76.5mg, 52% yield; mp: 131-132 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.66 (s, 1H), 7.91-7.89 (m, 2H), 7.44-7.41 (m, 3H), 5.84 (q, J = 5.1 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 3.12 (d, J = 5.1 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 159.5, 154.6, 152.4, 148.2, 133.0, 130.4, 129.4, 127.5, 108.7, 60.8, 28.3, 14.0; IR (KBr, cm^{-1}): 3436, 1704, 1659, 1379, 1195, 760, 696. HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{15}H_{16}N_5O_2$ 298.1304, found 298.1301.

Ethyl 7-phenyl-2-(phenylamino)imidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3y**)



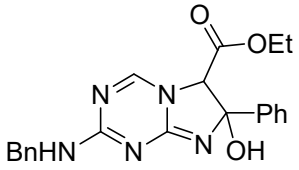
Yellow solid, 71.0mg, 40% yield; mp: 189-190 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.80 (s, 1H), 7.91-7.88 (m, 4H), 7.72 (br, 1H), 7.48-7.42 (m, 3H), 7.37 (m, 2H), 7.14 (t, J = 7.4 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 156.4, 155.0, 151.3, 148.5, 137.5, 132.8, 130.4, 129.5, 129.1, 127.6, 124.2, 119.9, 109.2, 61.0, 14.0; IR (KBr, cm^{-1}): 3443, 2923, 1672, 1633, 1599, 1558, 1401, 1377, 1152, 1048, 757, 691. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{18}N_5O_2$ 360.1460, found 360.1461.

Ethyl 2-(benzylamino)-7-phenylimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3z**)



Yellow solid, 78.2 mg, 52% yield; mp: 189-190 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.65 (s, 1H), 7.90-7.89 (m, 2H), 7.45-7.41 (m, 3H), 7.39-7.38 (m, 2H), 7.36-7.27 (m, 3H), 6.21 (t, J = 5.6 Hz, 1H), 4.74 (d, J = 5.6 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 158.7, 154.7, 152.1, 148.5, 137.4, 132.9, 130.4, 129.4, 128.7, 128.0, 127.7, 127.5, 108.8, 60.8, 45.4, 14.0; IR (KBr, cm^{-1}): 3250, 2987, 1685, 1643, 1479, 1376, 1350, 1192, 1154, 1050, 761, 694. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{20}N_5O_2$ 374.1617, found 374.1614.

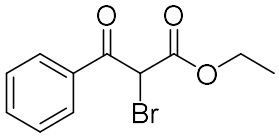
Ethyl 2-(benzylamino)-7-hydroxy-7-phenyl-6,7-dihydroimidazo[1,2-a][1,3,5]triazine-6-carboxylate (**3z'**)



White solid; mp: 123-124 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.42 (s, 1H), 9.33 (s, 1H), 8.64 (t, J = 5.6 Hz, 1H), 8.47 (s, 1H), 7.93-7.92 (m, 2H), 7.47-7.34 (m, 8H), 7.33-7.28 (m, 1H), 4.64 (d, J = 5.6 Hz, 2H), 4.30 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.6, 160.1, 151.4, 150.5, 144.8, 137.7, 133.3, 129.2, 128.8, 128.4, 127.8, 127.6, 113.0, 60.6,

44.9, 14.3; IR (KBr, cm^{-1}): 3315, 2929, 1703, 1634, 1538, 1382, 1149, 698. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{22}N_5O_3$ 392.1723, found 392.1725.

Ethyl 2-bromo-3-oxo-3-phenylpropanoate (**4**)[2]



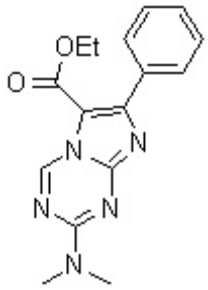
Yellow oil liquid; ^1H NMR (500 MHz, $CDCl_3$): δ 8.01-8.00 (m, 2H), 7.65-7.63 (m, 1H), 7.52-7.50 (m, 2H), 5.67 (s, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H).

Ref.

(1) Li, J. J.; Song, C.; Cui, D.-M.; Zhang, C. *Org. Biomol. Chem.,* **2017***, 15*, 5564- 5570

(2) Khan, A. T.; Ali, M. A; Goswami, P.; Choudhury L. H. *J. Org. Chem*., **2006**, *71*, 8961-8963.

170502
sc171426 CDCl3 0502



3a

170503
SC170426 CDCl3 0503

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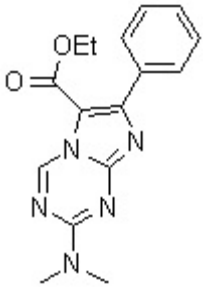
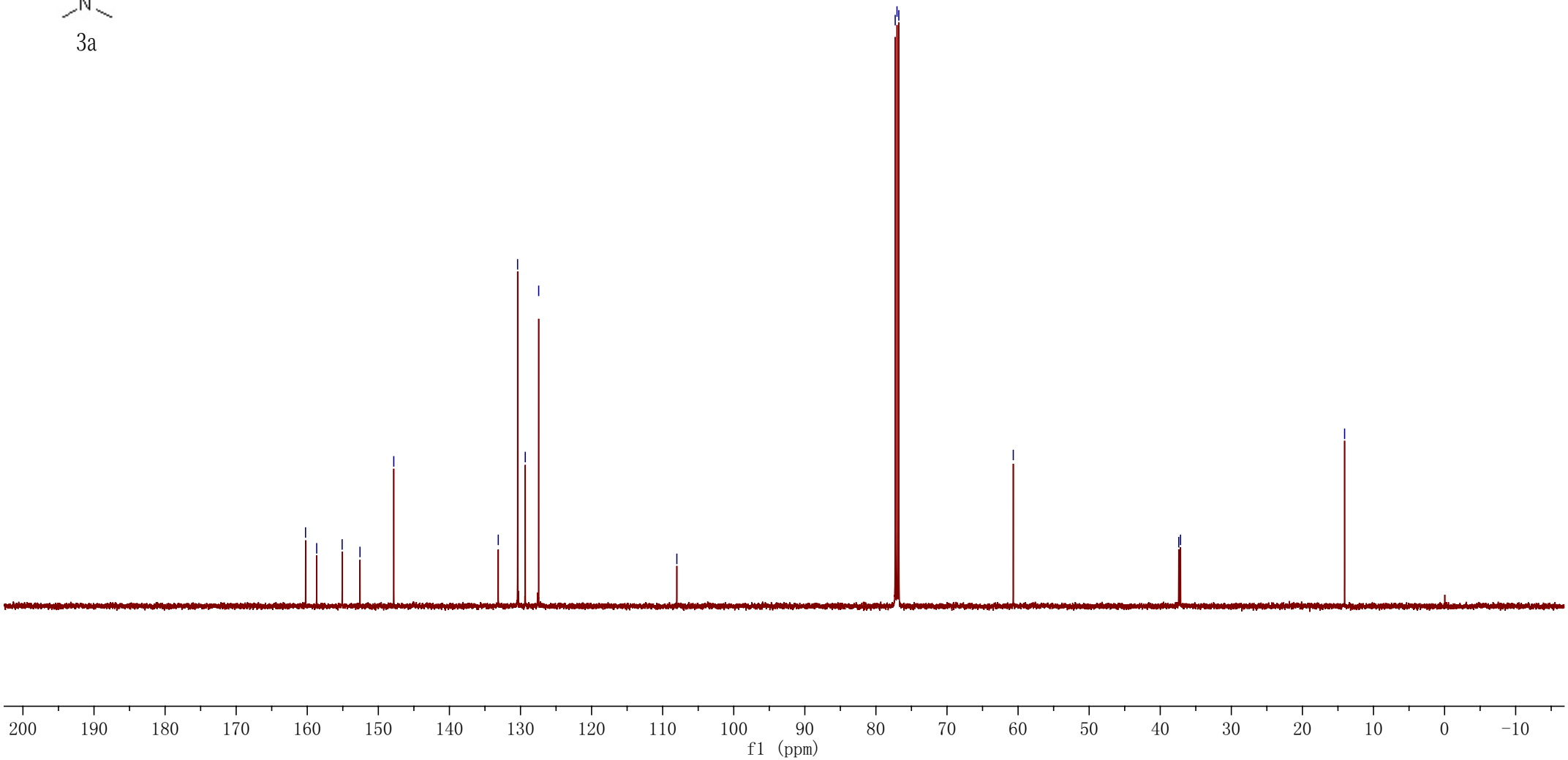
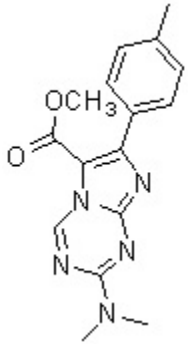
77.0327
76.7786
60.6748
37.3985
37.1501
14.0651



3a



170913
SC170620A CDC13 0913



3b

170918
SC160620A CDCl3 0918

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51.3632
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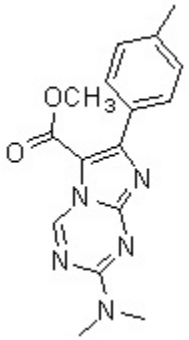
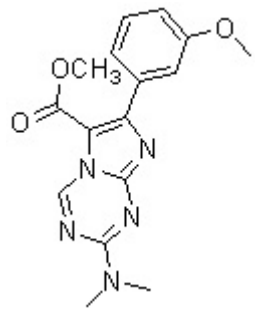


3b

170609
SC170608A CDCl3 0609



3c

170612
SC170608A CDCl3 0612

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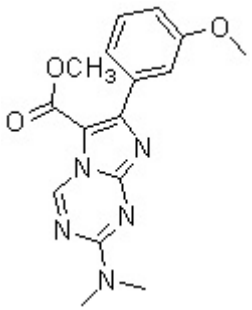
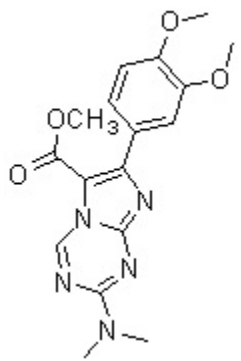
77.08
76.83
55.35
51.43
37.42
37.16

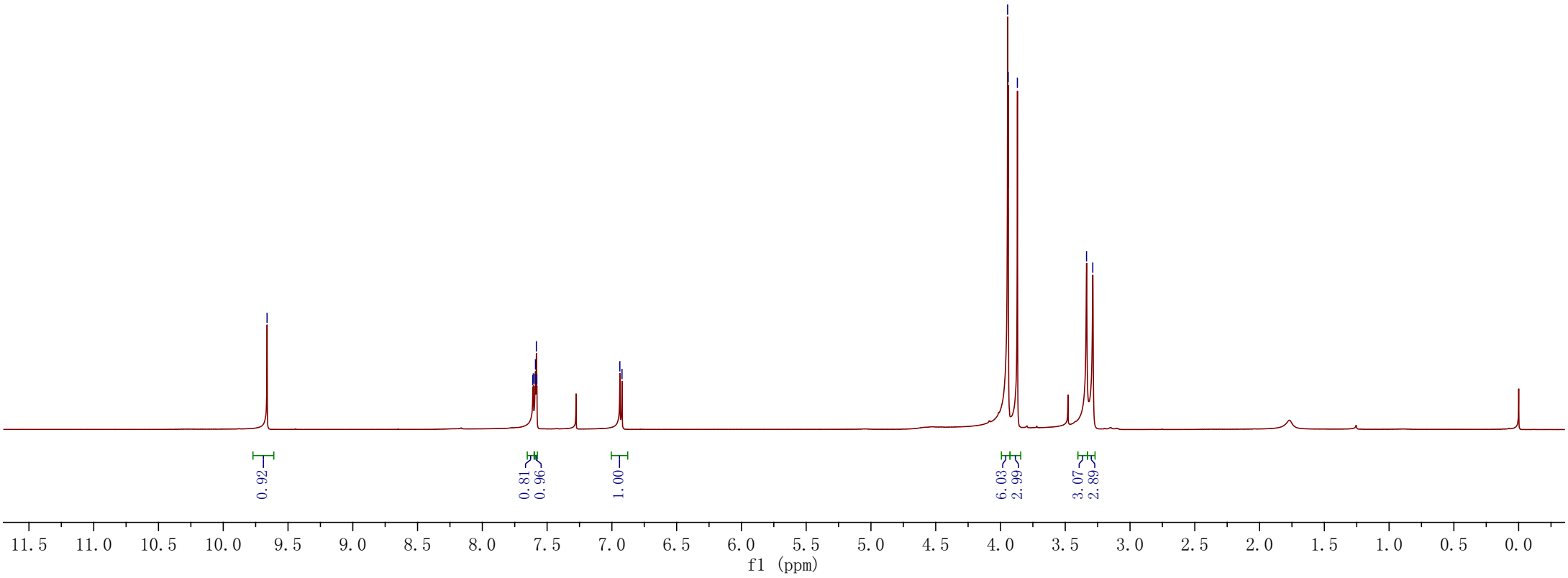


3c

170913
SC170629A CDC13 0913



3d



170918
SC170629A CDCl3 0918

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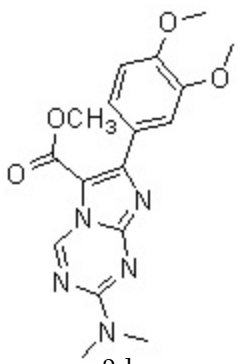
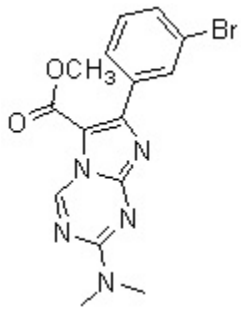
55.8903
51.4040
37.4314
37.1904



3d

170913
SC170712A CDC13 0913



3e

170918
SC170712A CDCl3 0918

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77.0812
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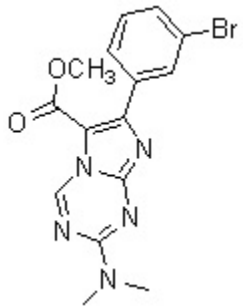
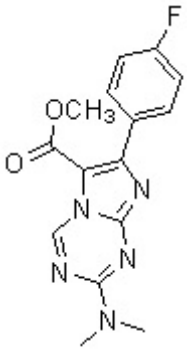
37.4938
37.2303



3e

170619
SC170612A CDC13 0619



3f

170620
SC170612A CDCl3 0620

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129.1514
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77.0334
76.7793
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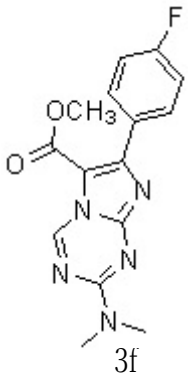
37.1585



3f

170609
SC170605B CDCl3 0609

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7.4018
7.3923
7.3889
7.3858
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7.3564
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7.2759
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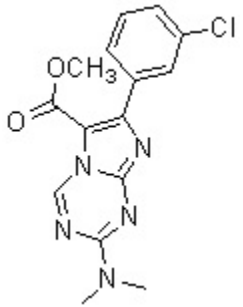
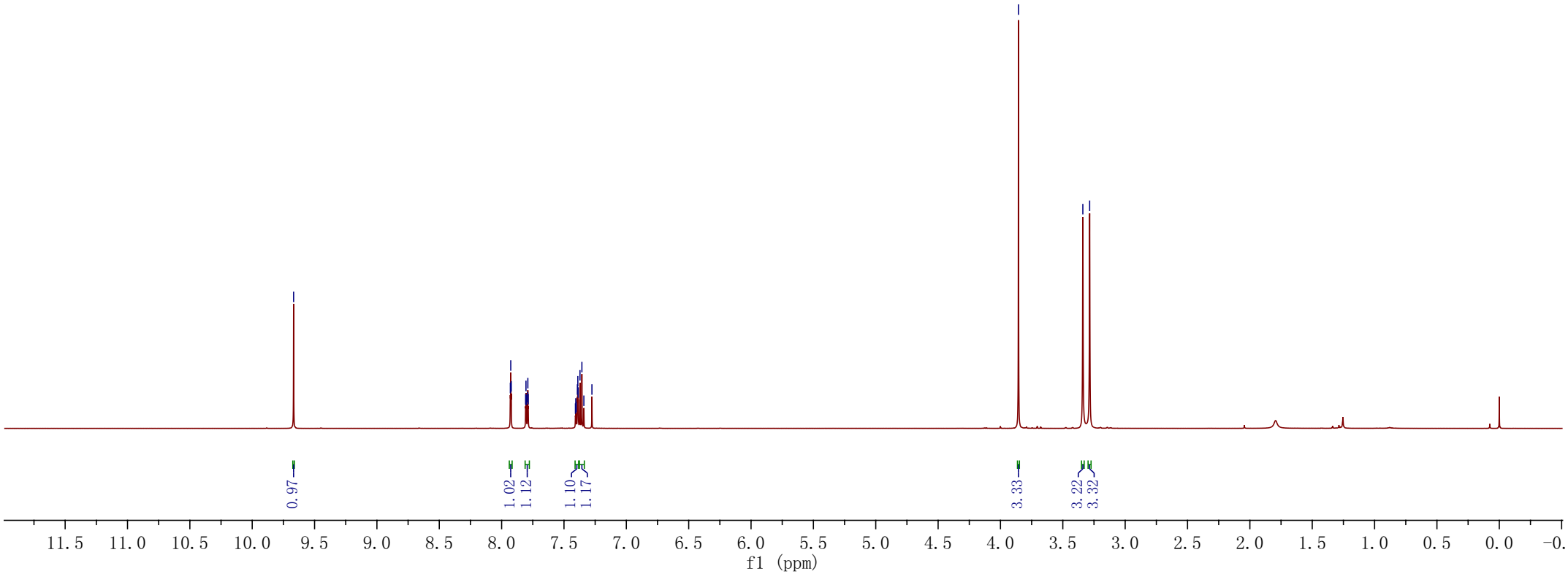
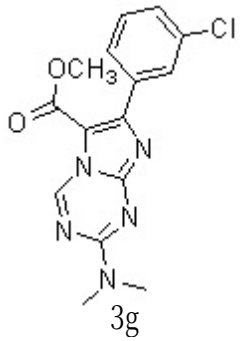
3.3394
3.2848



3g

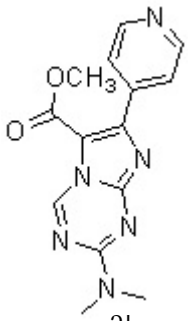


170612
SC170605B CDCl3 0612



3g

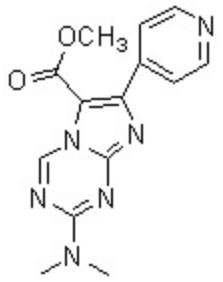
171031
SC170717B CDCl3 1030



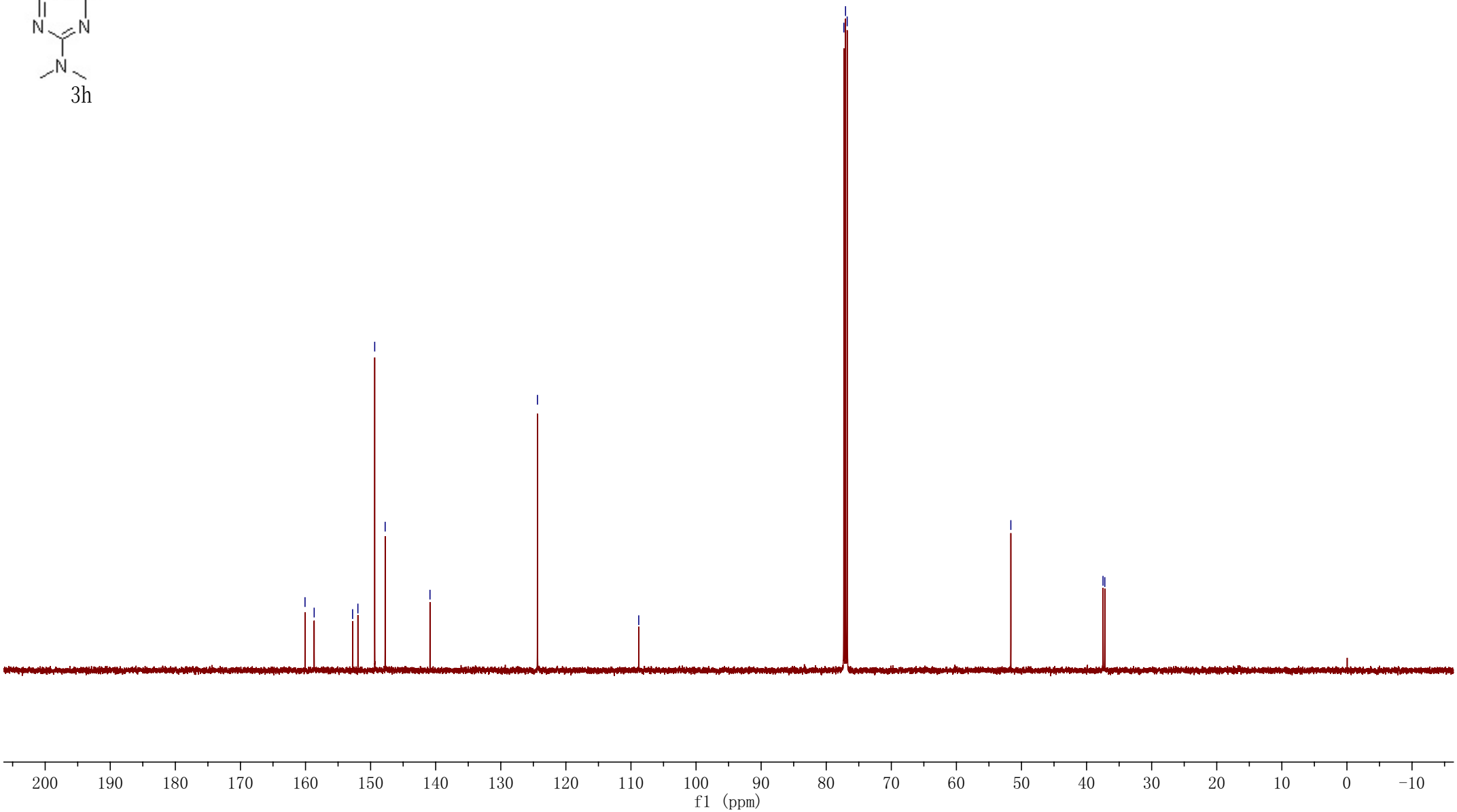
3h

171101
SC170717B CDCl3 1101

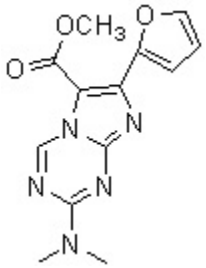
160.0760
158.6706
152.7655
151.9528
149.3707
147.7644
140.8771
124.3656
108.8046
77.2868
77.0325
76.7785
51.6332
37.4726
37.1982



3h

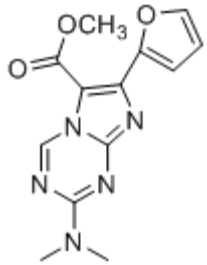


170619
SC170612B CDCl3 0619



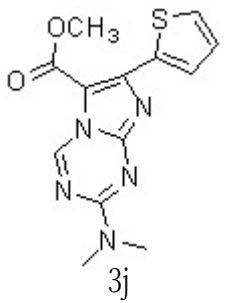
3i

170620
SC170612B CDCl3 0620



3i

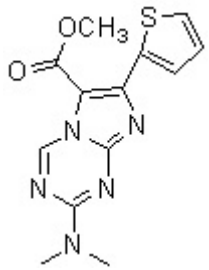
170913
SC170623 CDC13 0913



3j

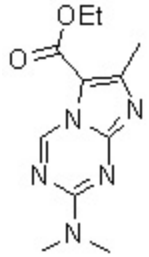
170918
SC170623 CDCl3 0918

160.2305
158.7596
152.2600
148.4631
147.7121
135.9424
131.2278
129.8519
127.5732
106.1407
77.3371
77.0829
76.8285
51.4585
37.4486
37.2371



3j

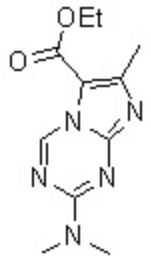
161010
LJJ161008-134-P CDCl3 1016



3k

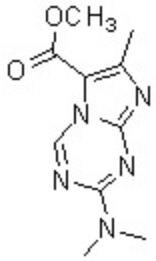
171031
SC170719 CDCl3 1031

160.6411
158.6090
155.4058
152.6084
147.0407
108.7652
77.2851
77.0307
76.7766
60.3745
37.3147
37.0342
16.1408
14.4432



3k

170913
SC170628A CDC13 0913



3l

170918
SC170628A CDC13 0918

161.0714
158.7098
155.5935
152.7786
147.0704
108.6956
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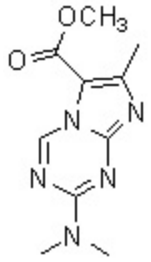
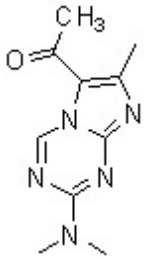
77.0814
76.8273
51.3998
37.3892
37.0983
16.1677



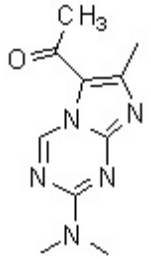
3l

170619
SC170602A CDC13 0619



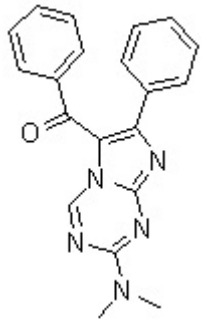
3m

170620
SC170602A CDCl3 0620



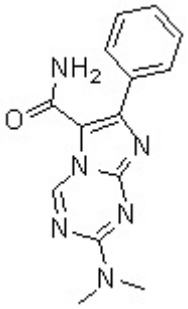
3m

170913
SC170717A CDCl3 0913



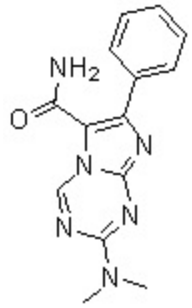
3n

171113
SC171109 CDCl3 1113



3o

SC171109



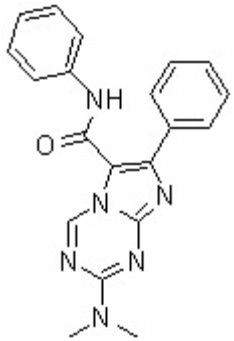
3o

161.82
158.24
150.68
148.49
147.12
133.77
129.43
129.36
128.89
111.97
40.47
40.30
40.13
39.97
39.80
39.63
39.47
37.46
37.03

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

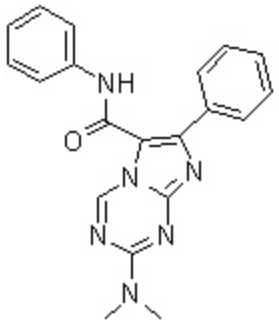
Desktop


NH
O
N
N
N
N
N

3p

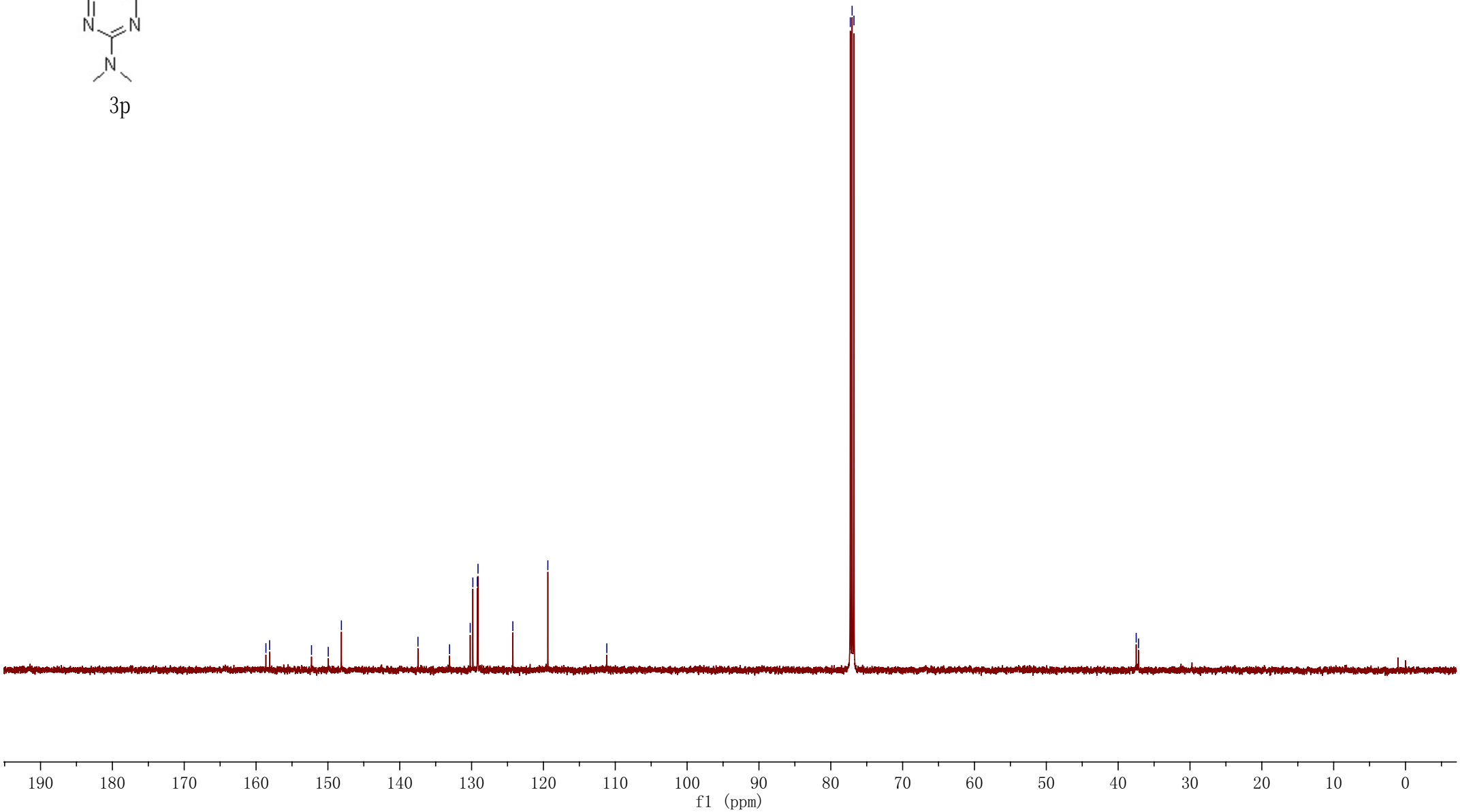
9.93
7.79
7.78
7.59
7.56
7.55
7.55
7.30
7.29
7.27
7.26
7.10
7.08
7.07
3.35
3.28
1.00
2.00
1.00
3.04
4.06
1.06
3.02
3.07
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

SC171123

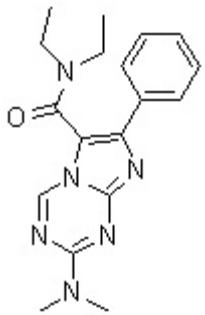


3p

158.63
158.12
152.28
149.95
148.12
137.47
133.07
130.19
129.83
129.20
129.11
124.26
119.39
111.18
77.28
77.03
76.78
37.49
37.16



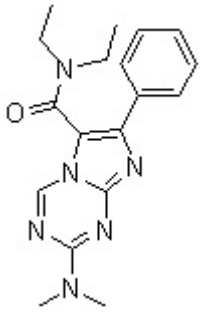
171205
SC171125A 17-12-05



3q

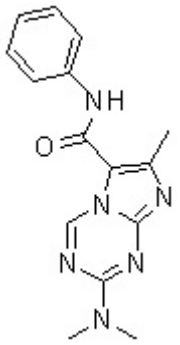
171218
SC171125A CDCl3 1218

161.4478
158.2407
151.0716
146.1532
145.0000
133.1692
129.0806
128.4769
128.2601
109.9423
77.2894
77.0353
76.7808
43.0396
38.9978
37.3685
37.1650
13.8923
12.3797



3q

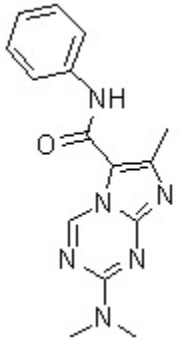
171205
SC171125B 17-12-05



3r

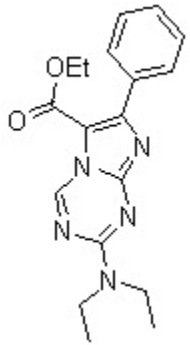
SC171225B碳+17A171132
SC171125B CDCl3 1212

161.45
157.95
148.01
144.33
138.11
133.32
128.98
123.94
120.02
119.44
77.29
77.04
76.78
37.51
37.30
8.35



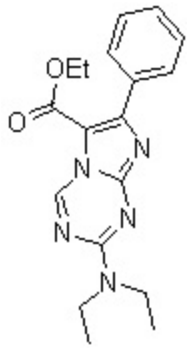
3r

171018
sc171016 CDCl3 1018



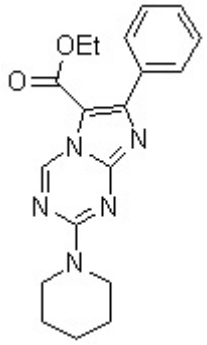
3s

171019
SC171016 CDCl3 1019



3s

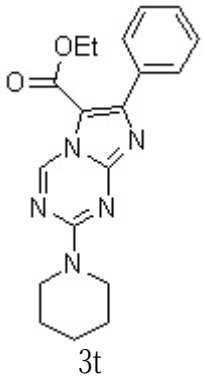
170602
SC170510B CDCl3 0602



3t

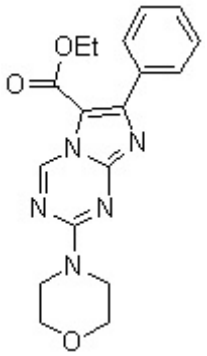
170607
SC170510B CDCl3 0607

160.23
157.63
155.14
152.83
148.04
133.17
130.39
129.31
127.44
108.14
77.29
77.03
76.78
60.65
45.78
44.97
26.13
25.48
24.57
14.07



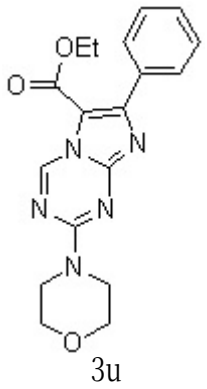
3t

170602
SC170513B CDCl3 0602



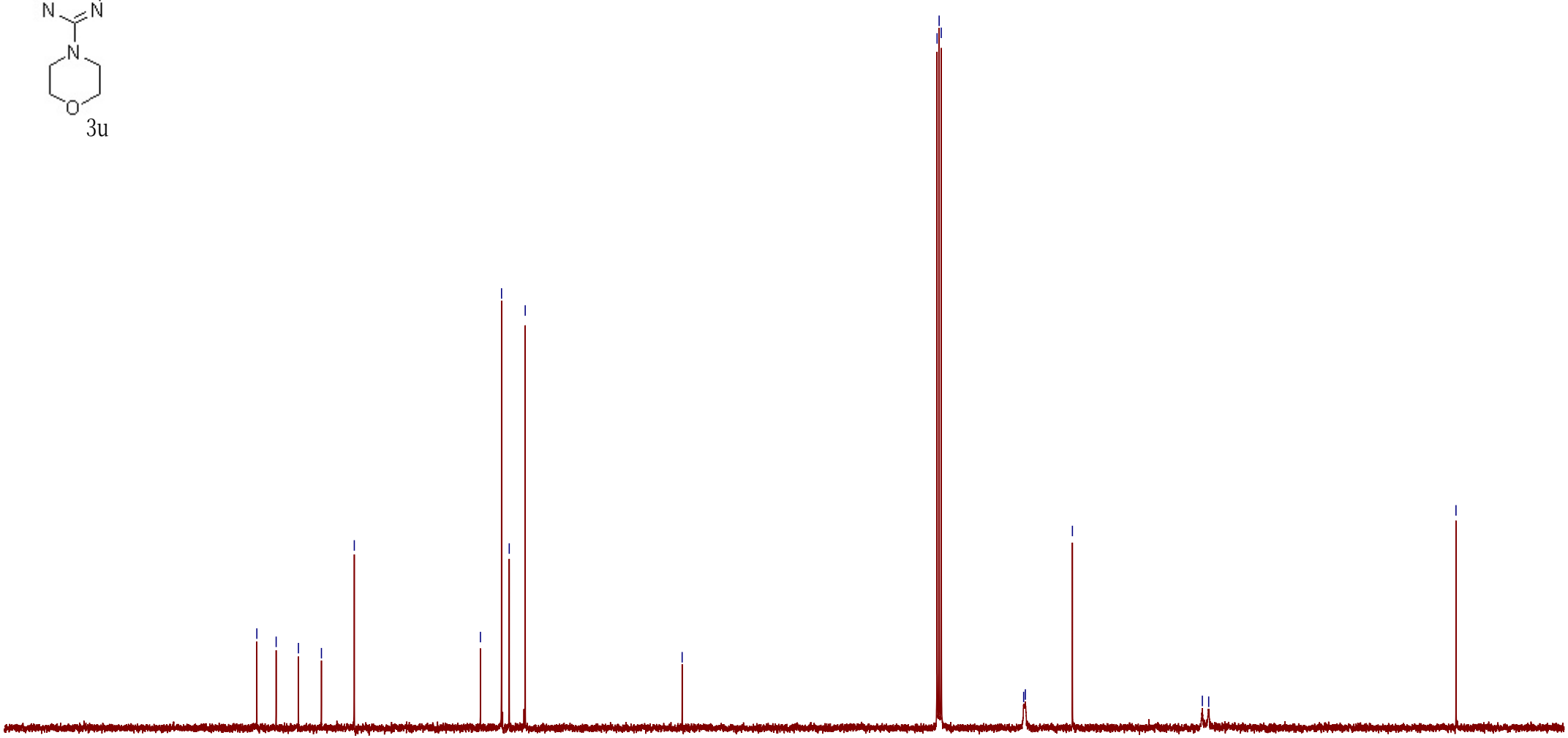
3u

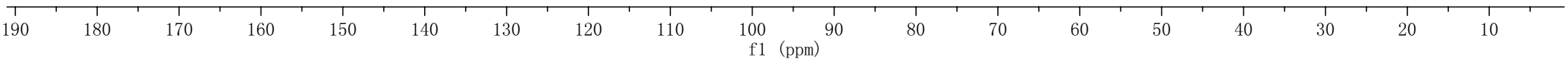
170607
SC170513B CDC13 0607



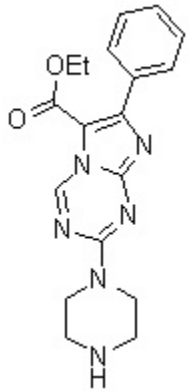
3u

160.2029
157.8492
155.1331
152.3312
148.3239
132.9469
130.3750
129.4362
127.4899
108.3601
77.2871
77.0330
76.7788
66.7328
66.5230
60.7889
44.9492
44.1769
14.0310





170913
SC170712B CDC13 0913



3v

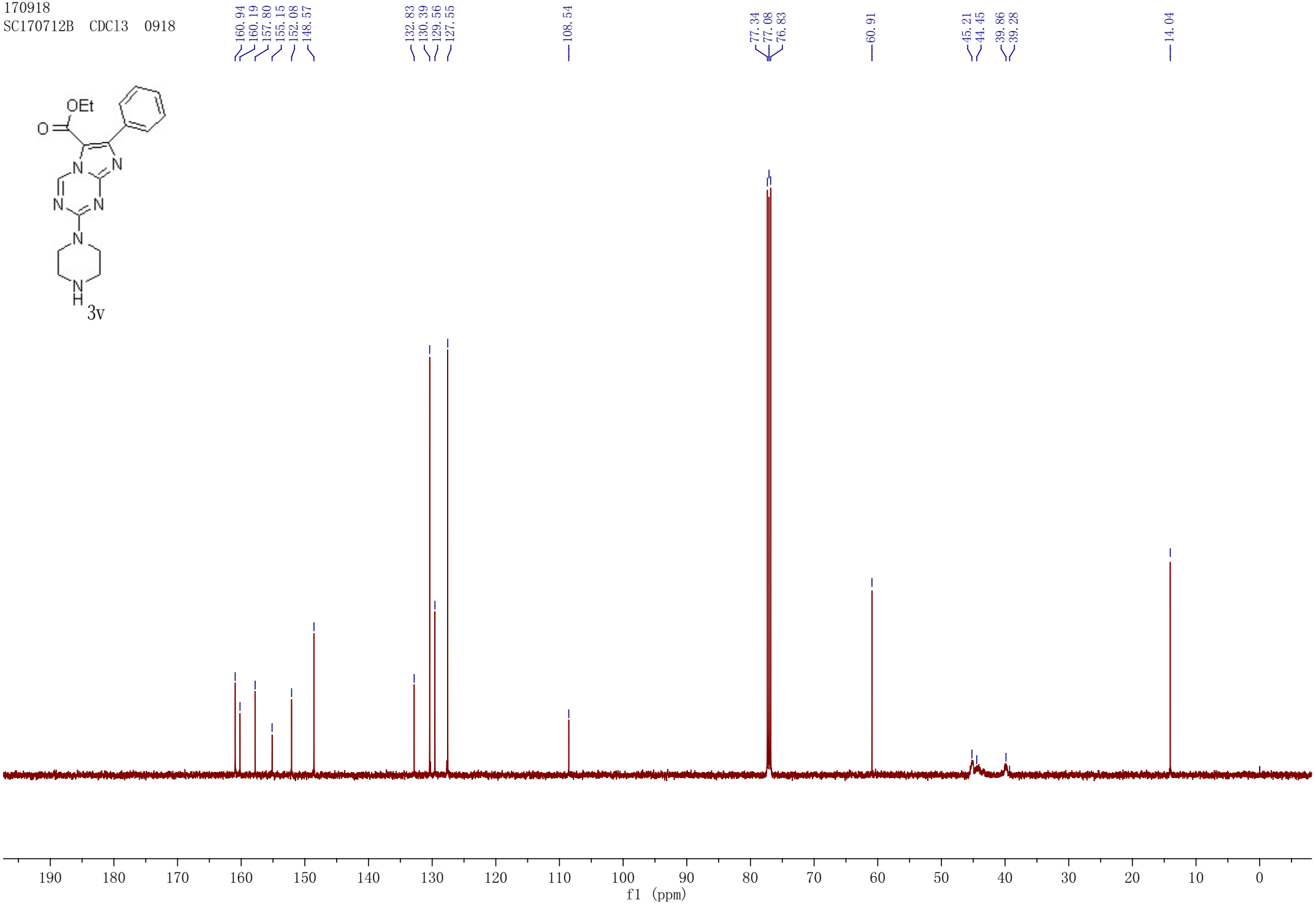
9.7503
8.1470
7.8964
7.8899
7.8813
7.8317
7.4273
7.4206
7.4180
7.2758
4.3515
4.3372
4.3230
4.3087
4.0441
4.0070
3.6716
3.6607
3.6505
3.4947
3.4843
3.4742
1.3031
1.2888
1.2745

1.00 1.07 2.16 3.23 2.14 2.06 2.12 2.18 2.10 3.10

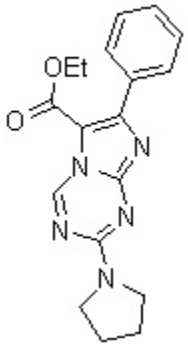
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

170918
SC170712B CDCl3 0918



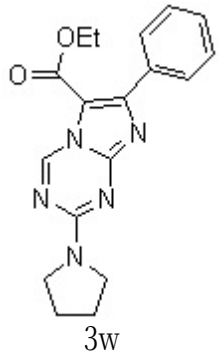
170913
SC170704A CDC13 0913



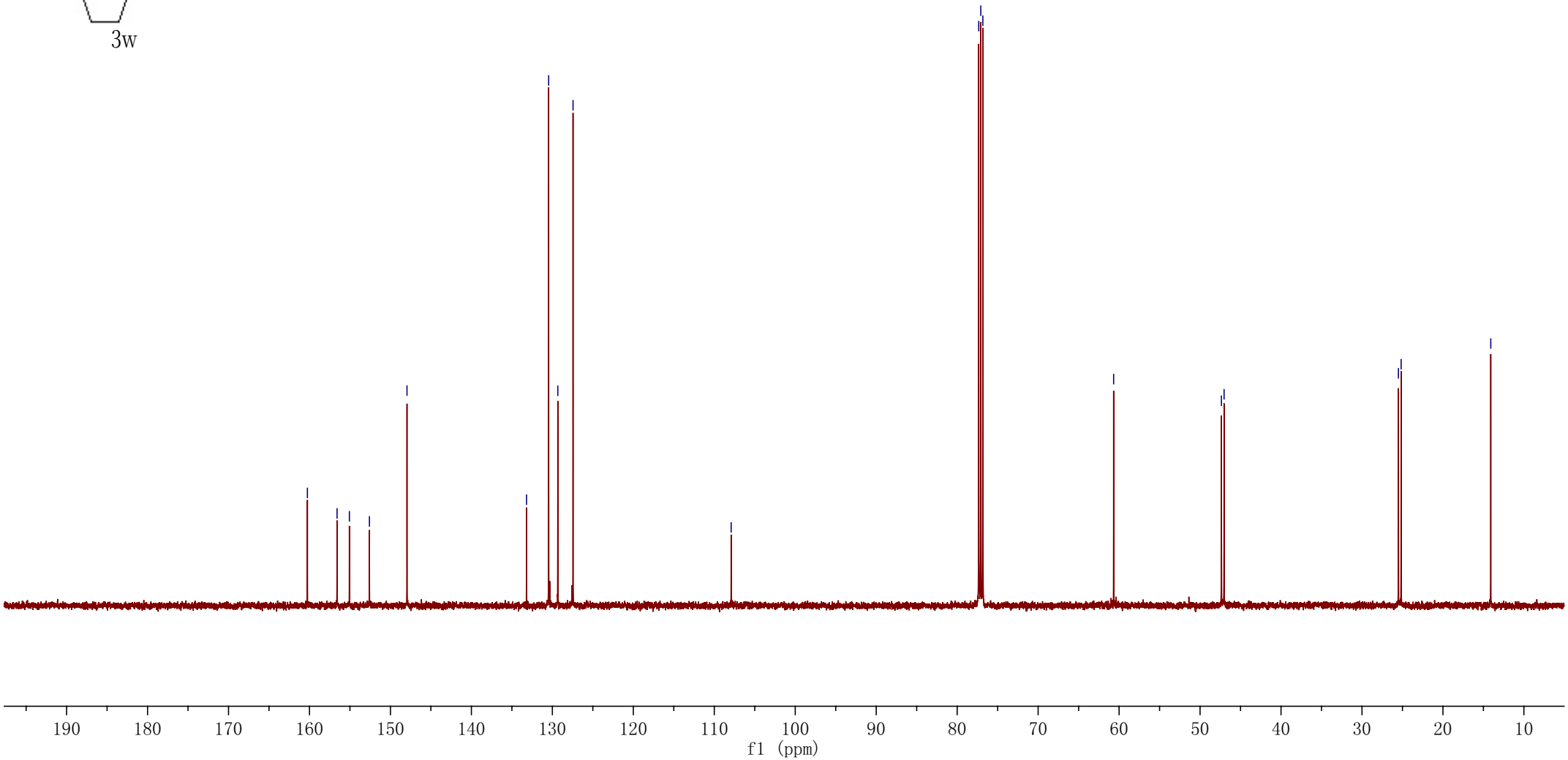
3w

170918
SC170704A CDCl3 0918

160.2566
156.5935
155.0709
152.5939
147.9547
133.1912
130.4558
129.3263
127.4457
107.9162
77.3371
77.0826
76.8284
60.6720
47.3608
47.0312
25.4970
25.1643
14.0911

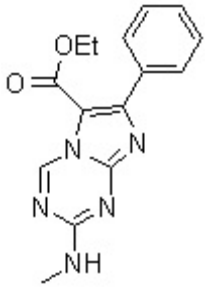


3w

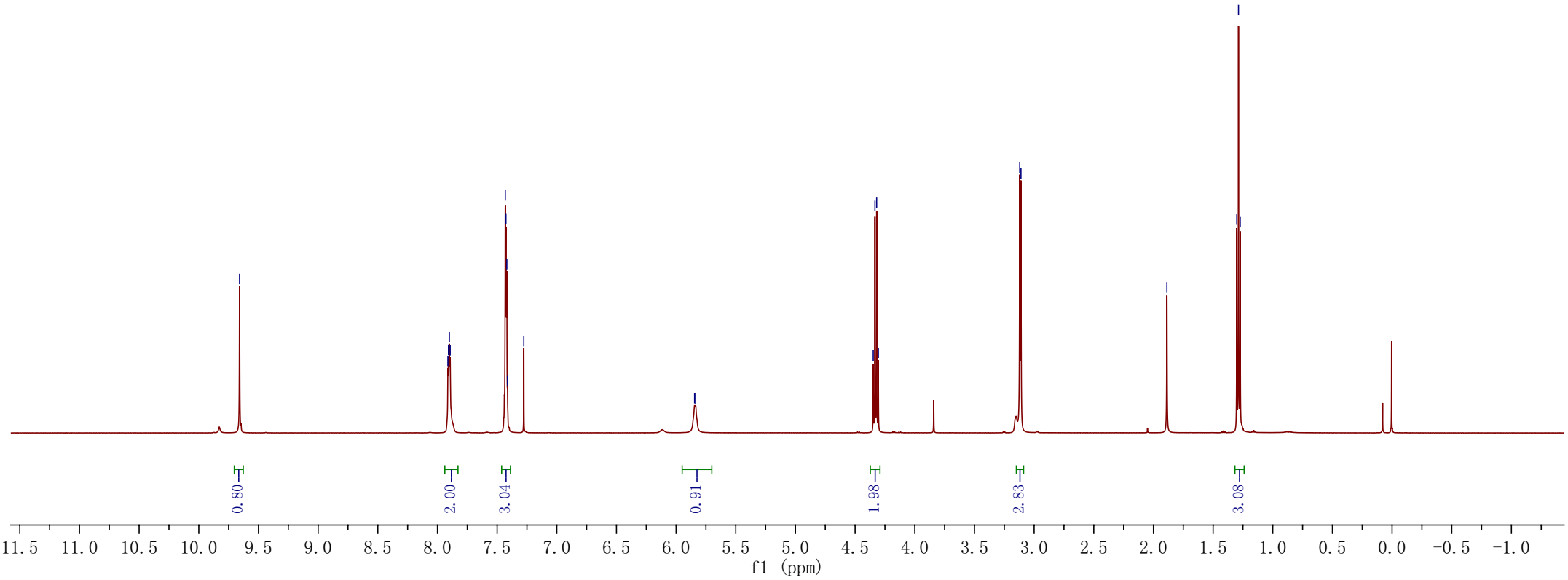


171011
SC170921B CDCl3 1011

9.6583
7.9123
7.9076
7.9004
7.8933
7.4316
7.4261
7.4187
7.4132
7.2763
5.8453
5.8367
4.3480
4.3338
4.3195
4.3053
3.1204
3.1102
1.8872
1.3015
1.2872
1.2730

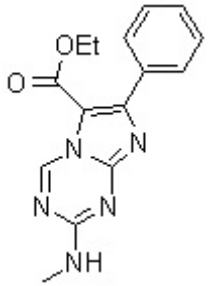


3x

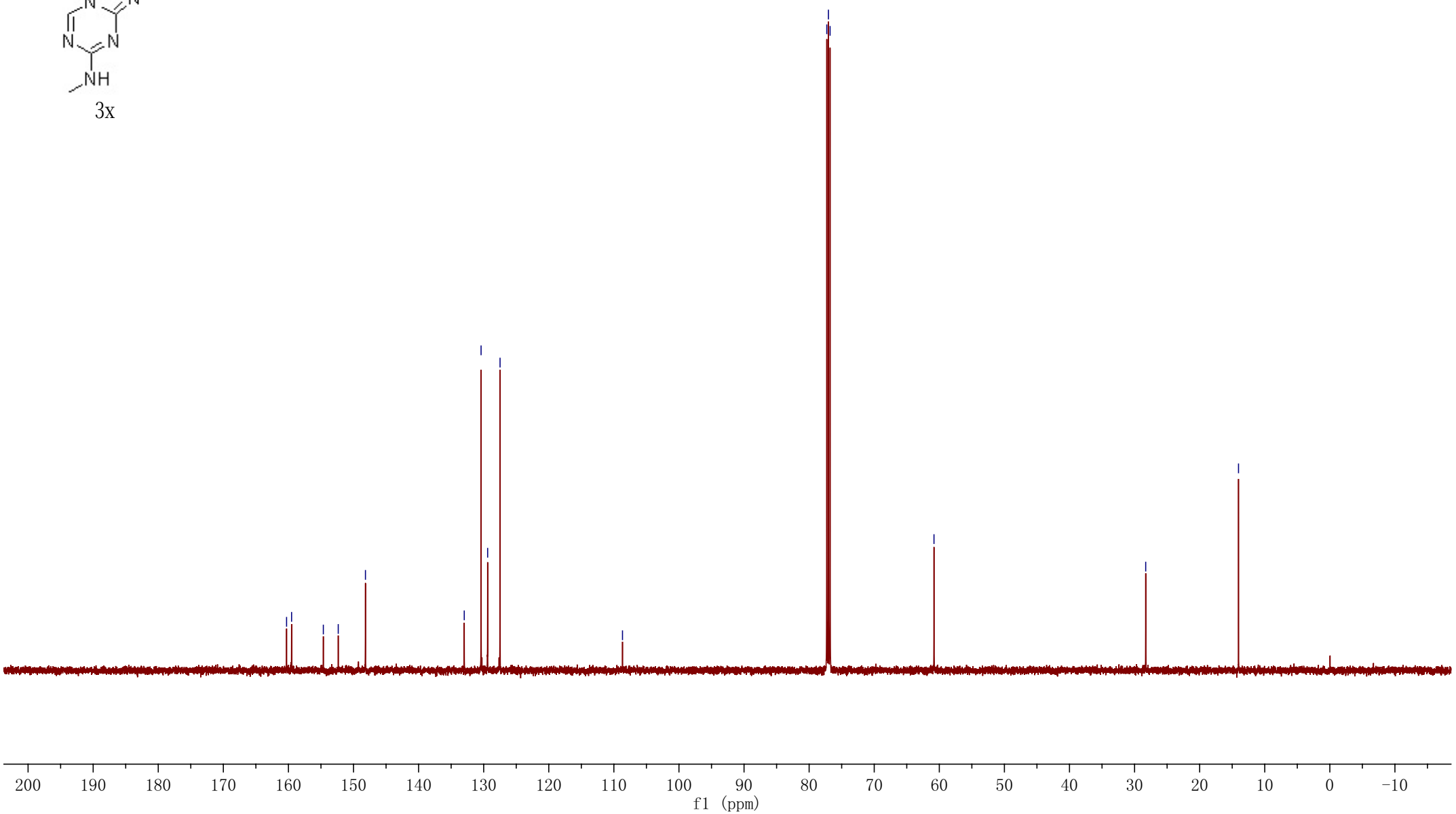


171013
sc170921B CDCl3 1013

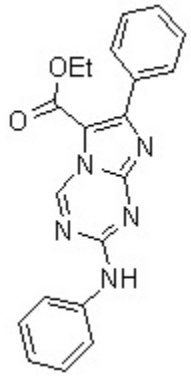
160.2848
159.5144
154.6365
152.3460
148.1658
132.9861
130.4025
129.3913
127.4866
108.6747
77.2886
77.0346
76.7805
60.8166
28.2893
14.0305



3x



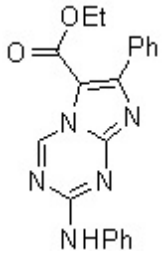
171031
SC171013 CDCl3 1030



3y

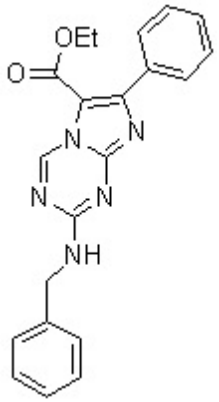
171101
SC171013 CDCl3 1101

160.20
156.35
154.99
151.29
148.52
137.53
132.81
130.42
129.54
129.07
127.58
124.20
119.93
109.16
77.29
77.03
76.78
61.02
14.03



3y

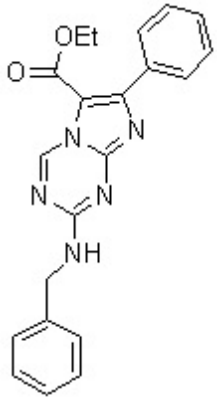
170928
SC170706-a CDCl3 0928



3z

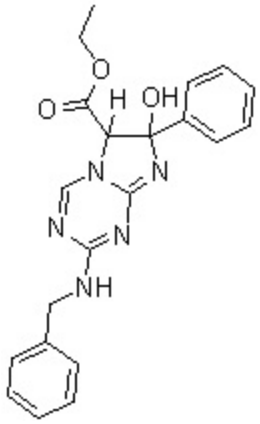
170929
SC170706-a CDC13 0929

160.2214
158.7214
154.6955
152.1304
148.4892
137.4631
132.9433
130.3958
129.4289
128.7278
127.9862
127.7114
127.5147
108.7898
77.2876
77.0333
76.7791
60.8438
45.4405
14.0353



3z

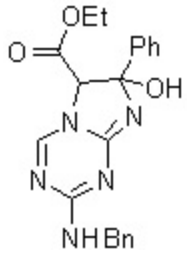
170913
SC170706-b CDCl3 0913



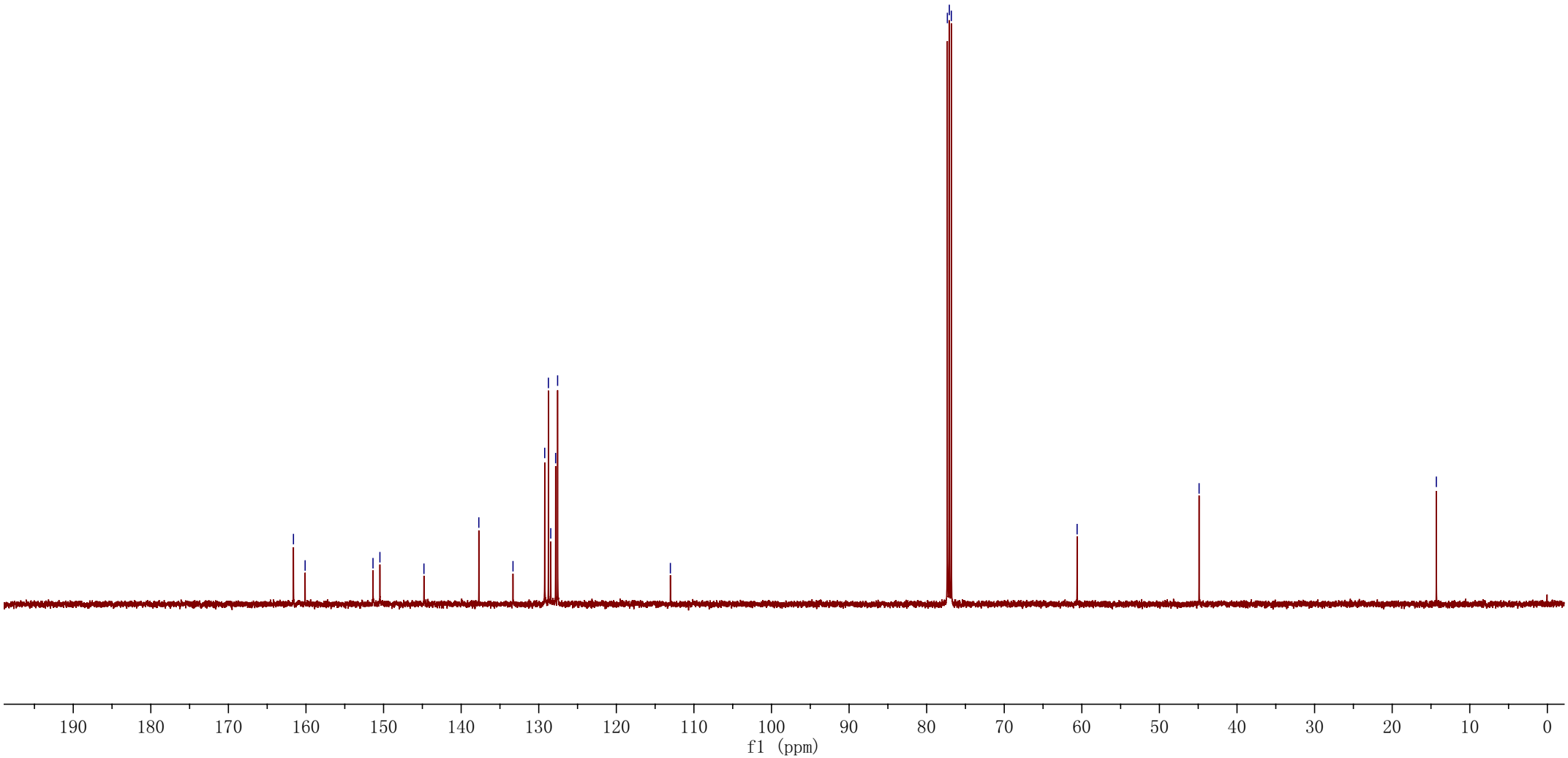
3z'

170918
SC170706-b CDCl3 0918

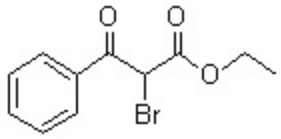
161.62
160.11
151.36
150.47
144.80
137.72
133.32
129.23
128.76
128.45
127.82
127.57
113.03
77.33
77.08
76.82
60.61
44.89
14.31



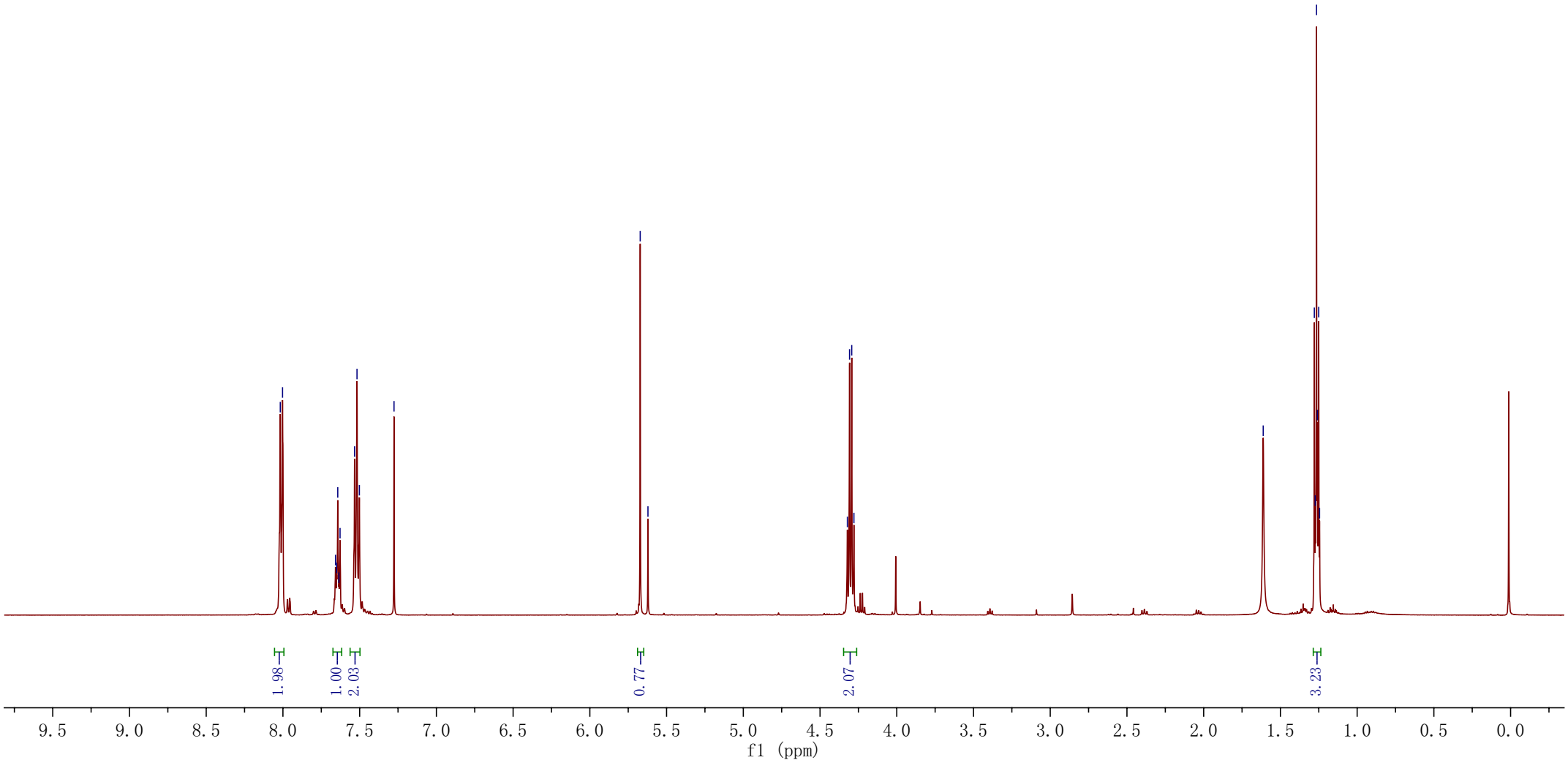
3z'



171018
SC171018-XIU CDCl3 1018



4



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 171130_sc171128

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 171130_sc171128

```
Bond precision:  C-C = 0.0030 A          Wavelength=0.71073

Cell:          a=7.1753(5)        b=10.1901(9)     c=11.0558(9)
               alpha=109.818(7)   beta=97.305(6)   gamma=100.110(6)
Temperature:   150 K
```

	Calculated	Reported
Volume	733.32(11)	733.32(11)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C16 H17 N5 O2	C16 H17 N5 O2
Sum formula	C16 H17 N5 O2	C16 H17 N5 O2
Mr	311.35	311.34
Dx,g cm-3	1.410	1.410
Z	2	2
Mu (mm-1)	0.098	0.098
F000	328.0	328.0
F000’	328.13	
h,k,lmax	8,12,13	8,12,13
Nref	2696	2690
Tmin,Tmax	0.953,0.965	0.858,1.000
Tmin’	0.953	

```
Correction method= # Reported T Limits: Tmin=0.858 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.998          Theta(max)= 25.347

R(reflections)= 0.0482( 2027)     wR2(reflections)= 0.1312( 2690)

S = 1.028                 Npar= 211
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          3 Report
PLAT978_ALERT_2_C Number C-C Bonds with Positive Residual Density.          0 Info
```

Alert level G

```
PLAT380_ALERT_4_G Incorrectly? Oriented X(sp2)-Methyl Moiety .....        C12 Check
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          3 Note
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   2 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   1 ALERT type 2 Indicator that the structure model may be wrong or deficient
   2 ALERT type 3 Indicator that the structure quality may be low
   1 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 09/11/2017; check.def file version of 08/11/2017

Datablock 171130_sc171128 - ellipsoid plot