Supporting Information

For

Ruthenium -Catalyzed Synthesis of tri-substituted 1,3,5-Triazines from alcohols and Biguanides

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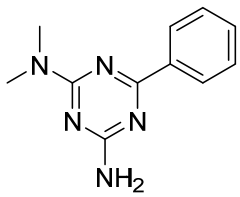
Experimental Section

Under otherwise noted, materials were obtained from commercial suppliers and used without further purification. *t*-BuOK (98% purity) was purchased from Aladdin Industrial Corporation. Thin layer chromatography (TLC) was performed using silica gel 60 F254 and visualized using UV light. Column chromatography was performed with silica gel (mesh 300-400). ^{1}H NMR and ^{13}C NMR spectrawere 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 parts per million (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, and m = multiplet), coupling constant in Hertz (Hz) and integration.

General Procedure for Synthesis of 1, 3, 5-triazines:

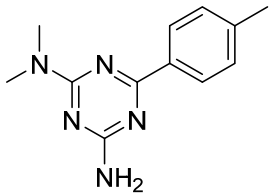
To a mixture of alcohols (1.0 mmol), biguanides hydrochloride (1.0 mmol), and *t*-BuOK (2.0 mmol) in dioxane (5 mmol) was added $RuCl_2$(COD) (2 mol%). The resulting mixture was then sealed and stirred for 12 h at 100 ℃. After completion of the reaction**,** the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4. The crude residue was obtained after evaporation of the solvent in vacuum**,** and the residue was purified by flash chromatography with CH_2Cl_2 and CH_3OH as the eluent to give the pure product.

***N*^{2}, *N*^{2}-dimethyl-6-phenyl-1,3,5-triazine-2,4-diamine (3a)**



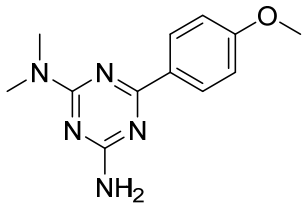
White solid; Mp: 165-167℃(lit.[1] 166℃); IR (KBr, cm^{-1}): 3336, 3189, 2920, 1661, 1574, 1511, 1382, 1289, 980, 825, 782; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38-8.37(m, 2H), 7.52-7.47 (m, 1H), 7.47-7.43 (m, 2H), 5.37 (s, 2H), 3.31 (s, 3H), 3.17 (s, 3H).

***N*^{2}, *N*^{2}-dimethyl-6-(p-tolyl)-1,3,5-triazine-2,4-diamine (3b)**[2]



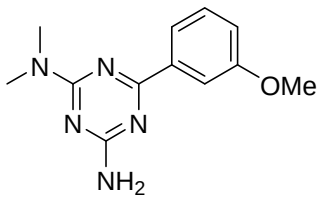
White solid; Mp: 191-192℃; IR (KBr, cm^{-1}): 3428, 2915, 1660, 1651, 1633, 1614, 1574, 1549, 1517, 1386; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 5.13 (s, 2H), 3.30 (s, 3H), 3.17 (s, 3H), 2.42 (s, 3H).

6-(4-methoxyphenyl)-N^2, N^2-dimethyl-1,3,5-triazine-2,4-diamine (3c)[2]



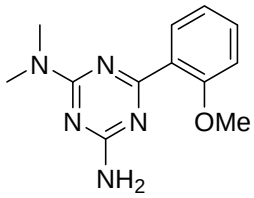
White solid; Mp: 195-197℃; IR (KBr, cm^{-1}): 3342, 3176, 1661, 1573, 1530, 1506, 1407, 1380, 1253, 1029, 980, 817; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 5.18 (s, 2H), 3.87 (s, 3H), 3.29 (s, 3H) 3.17 (s, 3H).

6-(3-methoxyphenyl)-N^2, N^2-dimethyl-1,3,5-triazine-2,4-diamine (3d)



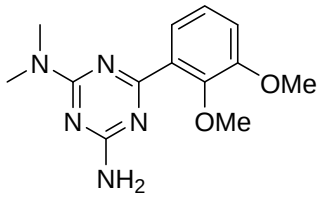
White solid; Mp: 199-200℃; IR (KBr, cm^{-1}): 3444, 3184, 1661, 1652, 1614, 1557, 1404, 1384, 1224, 1047; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 2.1 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.05 (dd, J = 7.9, 2.1 Hz, 1H), 5.10 (s, 2H), 3.90 (s, 3H), 3.30 (s, 3H), 3.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.8, 167.3, 165.6, 159.6, 138.7, 129.2, 120.8, 117.5, 113.1, 55.4, 36.3, 36.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{12}H_{16}N_5O$ 246.1355, found 246.1340

6-(2-methoxyphenyl)-N^2, N^2-dimethyl-1,3,5-triazine-2,4-diamine (3e)



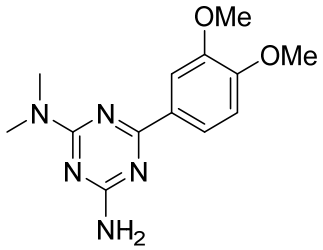
White solid; Mp: 242-244℃ (lit.[3] 223-224℃); IR (KBr, cm^{-1}): 3472, 3301, 3139, 1640, 1606, 1588, 1552, 1514, 1483, 1390, 822, 773; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.5, 1.8 Hz, 1H),δ 7.38 (ddd, J = 8.3, 7.5, 1.8 Hz, 1H), 7.02 (td, J = 7.5, 1 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 5.25 (s, 2H), 3.87 (s, 3H), 3.22 (s, 3H), 3.15 (s, 3H).

6-(2,3-dimethoxyphenyl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (3f)



White solid; Mp: 199-202℃; IR (KBr, cm^{-1}): 3417, 3294, 3162, 3006, 2935, 1637, 1561, 1516, 1469, 1396, 1262, 1080, 1004, 773, 755; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (dd, J = 8.0, 1.5 Hz, 1H), 7.11 (t, J = 8.0 Hz, 1H), 6.99 (dd, J = 8.0, 1.5 Hz, 1H), 5.25 (s, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.22 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 166.8, 165.6, 153.3, 147.7, 133.6, 123.8, 122.2, 113.7, 61.6, 56.0, 36.4, 36.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{18}N_5O_2$ 276.146, found 276.1473

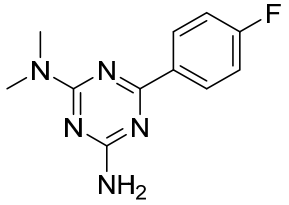
6-(3,4-dimethoxyphenyl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (3g)



White solid; Mp: 205-207℃; IR (KBr, cm^{-1}): 3425, 1659, 1650, 1644, 1574, 1566, 1510, 1484, 1415, 1377, 1026, 808; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.5

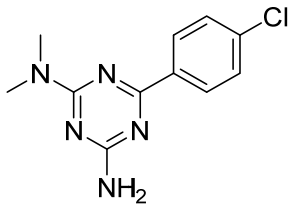
Hz, 1.9 Hz, 1H), 7.96 (d, J = 1.9 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 5.23 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 3.29 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 167.2, 165.9, 151.8, 148.6, 129.9, 121.8, 111.0, 110.4, 56.0, 55.9, 36.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{18}N_5O_2$ 276.146, found 276.1469

6-(4-fluorophenyl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (3h)



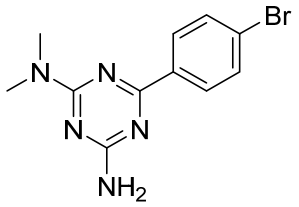
White solid; Mp: 184-185℃; IR (KBr, cm^{-1}): 3493, 3348, 3236, 1651, 1608, 1557, 1537, 1390, 835, 790; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54-8.27 (m, 2H), 7.15-7.07 (m, 2H), 5.26 (s, 2H), 3.29 (s, 3H), 3.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 167.26, 165.9, 165.0 (d, J = 249.2 Hz), 133.3 (d, J = 2.5 Hz), 130.5 (d, J = 8.7 Hz), 115.1 (d, J = 21.5 Hz), 36.3, 36.2. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{11}H_{13}FN_5$ 234.1155, found 234.1168

6-(4-chlorophenyl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (**3i**)[2]



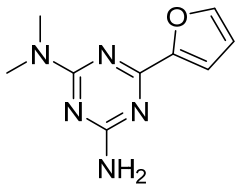
White solid; Mp: 192-193℃; IR (KBr, cm^{-1}): 3484, 3343, 3235, 1650, 1644, 1558, 1537, 1505, 1390, 1085, 1018, 809; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 5.12 (s, 2H), 3.30 (s, 3H), 3.17 (s, 3H).

6-(4-bromophenyl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (3j)[2]



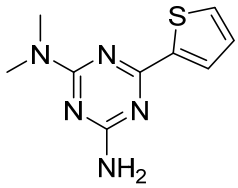
White solid; Mp: 190-192℃; IR (KBr, cm^{-1}): 3340, 3189, 2925, 1662, 1586, 1530, 1513, 1389, 981, 810; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30-8.19 (m, 2H), 7.60-7.53 (m, 2H), 5.21 (s, 2H), 3.29 (s, 3H), 3.17 (s, 3H).

6-(furan-2-yl)-*N*^{2}, *N*^{2}-dimethyl-1,3,5-triazine-2,4-diamine (**3k**)[4]



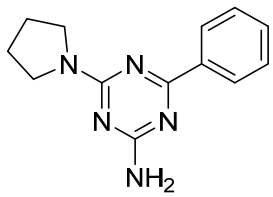
White solid; Mp: 219-220℃; IR (KBr, cm^{-1}): 3334, 3172, 1650, 1601, 1555, 1515, 1496, 1401, 1369, 1009, 810; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, J = 1.6, 0.8 Hz, 1H), 7.28 (dd, J = 3.4, 0.8 Hz, 1H), 6.51 (dd, J = 3.4, 1.6 Hz, 1H), 5.68 (s, 2H), 3.23 (s, 3H), 3.12 (s, 3H).

***N*^{2}, *N*^{2}-dimethyl-6-(thiophen-2-yl)-1,3,5-triazine-2,4-diamine** (**3l**)



White solid; Mp: 210-211℃; IR (KBr, cm^{-1}): 3328, 3195, 1644, 1572, 1528, 1510, 1432, 1386, 1014, 809, 715; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J = 3.7, 1.2 Hz, 1H), 7.46 (dd, J = 5.0, 1.2 Hz, 1H), 7.12 (dd, J = 5.0, 3.7 Hz, 1H), 5.20 (s, 2H), 3.26 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 166.9, 165.6, 143.0, 129.9, 129.4, 127.8, 36.2, 36.1. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_9H_{12}N_5S$ 222.0813, found 222.0808

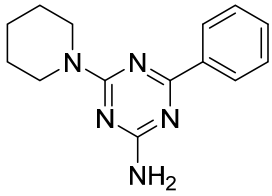
4-phenyl-6-(pyrrolidin-1-yl)-1,3,5-triazin-2-amine (**3m**)



White solid; Mp: 243-245℃ [lit.[5] 230℃]; IR (KBr, cm^{-1}): 3341, 3190, 2903, 2792, 1658, 1633, 1592, 1556, 1531, 1506, 983, 783, 703; ^{1}H NMR (500 MHz, $CDCl_3$) δ

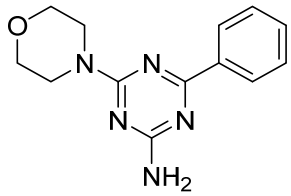
8.45-8.30 (m, 2H), 7.50-7.43 (m, 3H), 5.17 (s, 2H), 3.81-3.74 (m, 2H), 3.60-3.55 (m, 2H), 2.09-1.92 (m, 4H).

4-phenyl-6-(piperidin-1-yl)-1,3,5-triazin-2-amine (**3n**)



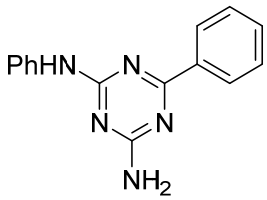
White solid; Mp: 146-147℃ [lit.[6] 154-156℃]; IR (KBr, cm^{-1}): 3434, 2935, 1658, 1654, 1589, 1548, 1515, 1392, 1286; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39-8.31 (m, 2H), 7.52-7.43 (m, 3H), 5.21 (s, 2H), 3.96-3.81 (m, 4H), 1.75-1.57 (m, 6H).

4-morpholino-6-phenyl-1,3,5-triazin-2-amine (3o)



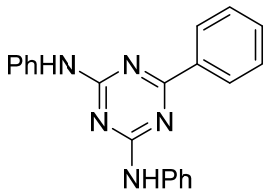
White solid; Mp: 133-134℃ [lit.[7] 121-123℃]; IR (KBr, cm^{-1}): 3428, 1651, 1635, 1580, 1548, 1520, 1446, 1392, 1344, 1110; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42-8.30 (m, 2H), 7.55-7.48 (m, 1H), 7.45 (t, J = 7.4 Hz, 2H), 5.22 (s, 2H), 4.11-3.85 (m, 4H), 3.83-3.63 (m, 4H).

***N*^{2}, 6-diphenyl-1,3,5-triazine-2,4-diamine (3p)**[8]



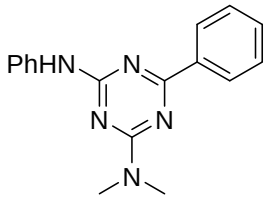
White solid; Mp: 205-207℃; IR (KBr, cm^{-1}): 3455, 1636, 1600, 1598, 1526, 1488, 1443, 1397, 1233; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 7.3 Hz, 2H), 7.66 (d, J = 7.9 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.25 (s, 1H), 7.12 (t, J = 7.4 Hz, 1H), 5.36 (s, 2H).

***N*^{2}, *N*^{4}, 6-triphenyl-1,3,5-triazine-2,4-diamine (3q)**



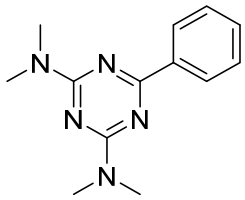
White solid; Mp: 217-220℃ [lit.[9] 216-218℃]; IR (KBr, cm^{-1}): 3417, 3252, 3152, 3108, 1616, 1511, 1441, 1337, 1287, 1216, 988, 823; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, J = 7.3 Hz, 2H), 7.68 (d, J = 7.7 Hz, 4H), 7.58-7.55 (m, 1H), 7.53-7.49 (m, 2H), 7.39 (t, J = 7.9 Hz, 4H), 7.28 (br, 2H), 7.17-7.11 (m, 2H).

N^2, N^2-dimethyl-N^4, 6-diphenyl-1,3,5-triazine-2,4-diamine (3r)[10]



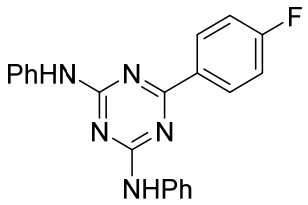
White solid; Mp: 135-137℃; IR (KBr, cm^{-1}): 3258, 3199, 3059, 2927, 1613, 1583, 1529, 1496, 1449, 1406, 820, 757; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48-8.41 (m, 2H), 7.71 (dd, J = 8.6, 1.0 Hz, 2H), 7.55 –7.48 (m, 3H), 7.39-7.35 (m, 2H), 7.20 (br, 1H), 7.09-7.06 (m, 1H), 3.36 (s, 3H), 3.26 (s, 3H).

N^2, N^2, N^4, N^4-tetramethyl-6-phenyl-1,3,5-triazine-2,4-diamine (3s)



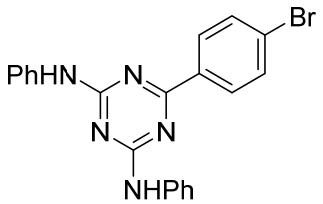
White solid; Mp: 92-95℃ [lit.[11] 103-105℃]; IR (KBr, cm^{-1}): 3444, 3065, 2925, 2864, 1589, 1548, 1384, 1039, 1207, 962, 779, 699; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48-8.42 (m, 2H), 7.51-7.40 (m, 3H), 3.25 (br, 12H).

6-(4-fluorophenyl)-N^2, N^4-diphenyl-1, 3, 5-triazine-2, 4-diamine (3t)



White solid; Mp: 167-169℃; IR (KBr, cm^{-1}): 34187, 3262, 1604, 1574, 1538, 1510, 1492, 1441, 1412, 1366, 1293, 812, 753; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47-8.44 (m, 2H), 7.63 (d, J = 7.6 Hz, 4H), 7.53 (br, 2H), 7.37 (t, J = 7.6 Hz, 4H), 7.21-7.09 (m, 4H); ^{13}C NMR (125MHz, $CDCl_3$) δ 170.7, 165.3 (d, J = 250.3 Hz), 164.6, 138.2, 132.5 (d, J = 2.46 Hz), 130.7 (d, J = 8.8 Hz), 128.8, 123.6, 120.7, 115.5 (d, J = 21.7 Hz) . HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{17}FN_5$ 358.1468, found 358.1481.

6-(4-bromophenyl)-*N*^{2}, *N*^{4}-diphenyl-1, 3, 5-triazine-2, 4-diamine (3u)



White solid; Mp: 199-200℃; IR (KBr, cm^{-1}): 3409, 3382, 1606, 1583, 1504, 1439, 1397, 1379, 1341, 801; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 7.8 Hz, 4H), 7.66-7.58 (m, 2H), 7.40 (t, J = 7.8 Hz, 4H), 7.21 (br, 2H), 7.17-7.10 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 138.2, 135.4, 131.7, 130.1, 128.9, 128.5, 126.7, 123.7, 120.7. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{17}BrN_5$ 418.0667, found 418.0675

Reference

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