Silica-bonded *S*-sulfonic Acid as a Recyclable Catalyst for Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-ones

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2,3-Dihydroquinazolin-4(1*H*)-one derivatives were synthesized via a one-pot, three component reaction of isatoic anhydride and an aromatic aldehyde with ammonium acetate or primary amine catalyzed by silica-bonded *S*-sulfonic acid in ethanol at 80 ℃. The reaction work-up is simple and the catalyst is easily separated from the products by filtration. The heterogeneous catalyst was recycled for ten runs upon the condensation reaction of isatoic anhydride and 4-chlorobenzaldehyde with ammonium acetate without losing its catalytic activity.

Keywords silica-bonded *S*-sulfonic acid, aldehydes, 2,3-dihydroquinazolin-4(1*H*)-one, isatoic anhydride, amines

Introduction

2,3-Dihydroquinazolinones are a class of heterocycles that attracted much attention because they have been reported to possess a wide range of pharmaceutical activities including antifertility, antibacterial, antitumor, antifungle, and mono amine oxidize inhibition.[1-4] Several synthetic methods for the preparation of 2,3-dihydroquinazolinones have been reported. Among them, the most direct procedure includes condensation of aryl, alkyl, and heteroaryl aldehydes with anthranilamide in the presence of *p*-toluenesulfonic acid as a catalyst.[5,6] The synthesis of 2,3-dihydroquinazolinones was also achieved by reductive cyclisation of *o*-nitrobenzaldehyde or *o*-azidobenzamide.[7,8] Some of the recently reported methods include isatoic anhydride, and aldehydes with ammonium acetate or primary amine in the presence of different reagents or catalysts, namely *p*-toluenesulfonic acid,[9] amberlyst-15 microwaved-assisted,[10] montmorillonite K-10,[11] ionic liquid,[12] silica sulfuric acid,[13] $Zn(PFO)_2$,[14] ceric ammonium nitrate,[15] and MCM-41-SO_3H.[16]

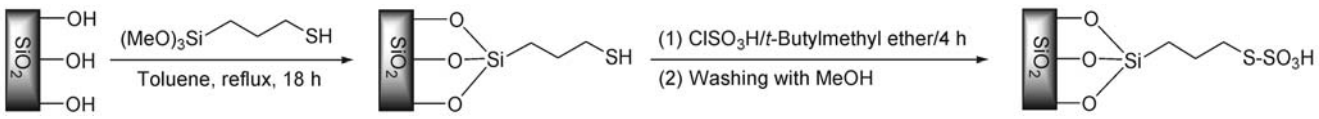
In recent years, the use of solid acidic catalysts has offered important advantages in organic synthesis, for example, operational simplicity, environmental compatibility, non-toxicity, reusability, low cost, and ease of isolation.[17,18] A tremendous upsurge of interest in various chemical transformations processes by catalysts under heterogeneous conditions has occurred. Silica bonded *S*-sulfonic acid (SBSSA) is a versatile catalyst that makes reaction processes convenient, more economic, and environmentally benign[19] (Scheme 1). Owing to the numerous advantages associated with this non-expensive and non-hazardous reagent, SBSSA has been explored as a powerful catalyst for various organic transformations under mild conditions.[20-25]

Experimental

General

Chemicals were purchased from Merck, Fluka and Aldrich chemical companies. IR spectra were run on a Perkin Elmer FT-IR Spectrum BX. The NMR spectra were run on Bruker Ultrashield 400 (400 MHz). Melting points were recorded on a Melting Point SMP1 apparatus in open capillary tubes and are uncorrected. With TLC using silica gel SILG/UV 254 plates the progress of reaction was followed. All of the products are characterized by comparison of their spectral (IR, ^{1}H NMR), TLC and physical data with those reported in the literature.[11-16] Silica bonded *S*-sulfonic acid (SBSSA) was prepared according to our previously reported procedure.[19-25]

Scheme 1 Preparation of silica-bonded *S*-sulfonic acid (SBSSA)



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General procedure for synthesis of 2,3-dihydroquinazolinone derivatives

To a mixture of isatoic anhydride (1 mmol), aromatic aldehyde (1 mmol), and ammonium acetate or primary amine (1 mmol) in 5 mL ethanol was added 0.005 g silica-bonded *S*-sulfonic acid (SBSSA) and heated at 80 ℃ in an oil bath. After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and remaining washed with warm ethanol (5 mL×2). After cooling, the corresponding 2,3-dihydroquinazolinone products were obtained and they were purified by recrystallization from hot ethanol. The recovered catalyst was dried and reused for subsequent runs.

2-(4-Methylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (**3a**) m.p. 227—228 ℃ (Lit.[11] 233—234 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 3H), 5.72 (s, 1H), 6.67 (dt, J_1=7.3 Hz, J_2=1.0 Hz, 1H), 6.75 (dd, J_1=8.2 Hz, J_2=0.5 Hz, 1H), 7.06 (s, 1H), 7.19 (d, J=7.8 Hz, 2H), 7.24 (dt, J_1=7.3 Hz, J_2=1.5 Hz, 1H), 7.38 (d, J=8.1 Hz, 2H), 7.62 (dd, J_1=7.7 Hz, J_2=1.5 Hz, 1H), 8.25 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 20.73, 66.36, 114.39, 114.98, 117.05, 126.79, 127.32, 128.79, 133.24, 137.24, 137.70, 138.64, 147.90, 163.63; IR ν_{max}: 3310.62, 3190.28, 3015.10, 1667.15, 1655.22, 1606.59, 1507.08, 1482.62, 1382.76, 1296.48, 1180.47, 907.91, 749.54 cm^{-1}.

2-(4-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (**3b**) m.p. 179—180 ℃ (Lit.[9] 178—180 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.83 (s, 3H), 5.79 (s, 1H), 6.76 (dt, J_1=7.4 Hz, J_2=1.0 Hz, 1H), 6.83 (d, J=7.6 Hz, 1H), 7.04 (dt, J_1=8.6 Hz, J_2=2.0 Hz, 2H), 7.10 (s, 1H), 7.30—7.35 (m, 1H), 7.51 (dt, J_1=8.6 Hz, J_2=2.0 Hz, 2H), 7.70 (dd, J_1=7.8 Hz, J_2=1.8 Hz, 1H), 8.28 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 55.16, 66.29, 113.61, 114.39, 114.98, 117.07, 127.33, 128.20, 133.22, 133.43, 148.00, 159.40, 163.69; IR ν_{max}: 3296.30, 3174.22, 2832.14, 1650.64, 1608.28, 1503.15, 1482.92, 1386.55, 1301.71, 1240.53, 1173.37, 1030.28, 834.03, 791.93, 754.81 cm^{-1}.

2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3c) m.p. 203—205 ℃ (Lit.[11] 198—200 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.77 (s, 1H), 6.68 (dt, J_1=7.4 Hz, J_2=0.5 Hz, 1H), 6.75 (d, J=8.1 Hz, 1H), 7.15 (s, 1H), 7.25 (dt, J_1=7.8 Hz, J_2=1.5 Hz, 1H), 7.46 (d, J=8.6 Hz, 2H), 7.51 (d, J=8.8 Hz, 2H), 7.61 (dd, J_1=7.8 Hz, J_2=1.3 Hz, 1H), 8.34 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 65.73, 114.43, 114.92, 117.27, 127.34, 128.29, 128.74, 132.94, 133.38, 140.65, 147.63, 163.46; IR ν_{max}: 3307.85, 3186.90, 3025.09, 1667.20, 1651.54, 1607.30, 1504.47, 1483.08, 1383.22, 1292.59, 1133.67, 1091.92, 1015.63, 835.74, 751.04 cm^{-1}.

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3d) m.p. 201—203 ℃;[10] ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.76 (s, 1H), 6.69 (dt, J_1=7.2 Hz, J_2=1.0 Hz, 1H), 6.75 (d, J=8.07 Hz, 1H), 7.15 (s, 1H), 7.25 (dt, J_1=7.7 Hz, J_2=1.5 Hz, 1H), 7.45 (d, J=8.6 Hz, 2H), 7.58—7.62 (m, 3H), 8.35 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 65.79, 114.44, 114.92, 117.28, 121.55, 127.35, 129.06, 131.22, 133.39, 141.08, 147.61, 163.46; IR ν_{max}: 3307.94, 3188.80, 3025.12, 1665.97, 1651.50, 1605.61, 1504.15, 1480.89, 1430.38, 1382.00, 1292.03, 1132.94, 1072.04, 1012.00, 833.85, 750.48 cm^{-1}.

2-(4-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3e) m.p. 194—197 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.78 (s, 1H), 6.69 (dt, J_1=7.4 Hz, J_2=1.0 Hz, 1H), 6.76 (dd, J_1=8.3 Hz, J_2=0.5 Hz, 1H), 7.11 (s, 1H), 7.20—7.28 (m, 3H), 7.52—7.57 (m, 2H), 7.62 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H), 8.30 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 65.92, 114.43, 114.93, 114.98, 115.19, 117.24, 127.35, 128.99, 129.07, 133.35, 137.78, 147.78, 163.30, 163.55; IR ν_{max}: 3297.82, 3176.42, 3025.14, 1665.90, 1651.05, 1609.67, 1503.95, 1482.63, 1436.20, 1385.28, 1299.35, 1227.22, 1156.24, 1013.18, 864.95, 839.49, 791.97, 744.04 cm^{-1}.

2,3-Dihydro-2-(thiophen-2-yl)quinazolin-4(1*H*)-one (3f) m.p. 216—219 ℃ (Lit.[26] 213—216 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.87 (s, 1H), 6.55 (t, J=7.3 Hz, 1H), 6.60 (d, J=8.1 Hz, 1H), 6.81—6.84 (m, 1H), 6.96—6.98 (m, 1H), 7.08—7.12 (m, 2H), 7.30 (d, J=4.5 Hz, 1H), 7.46 (d, J=7.3 Hz, 1H), 8.30 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 62.54, 114.68, 115.09, 117.50, 125.69, 125.88, 126.44, 127.29, 133.35, 146.39, 147.21, 163.09; IR ν_{max}: 3287.72, 3168.38, 3035.76, 1650.43, 1606.77, 1513.82, 1487.23, 1437.91, 1371.93, 1295.86, 1171.54, 1133.18, 855.62, 804.71, 762.48, 709.83, 682.78 cm^{-1}.

2,3-Dihydro-3-phenyl-2-(4-methylphenyl)quinazolin-4(1*H*)-one (3g) m.p. 223—226 ℃;[27] ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.22 (s, 3H), 6.24 (d, J=2.5 Hz, 1H), 6.71 (dt, J_1=7.6 Hz, J_2=1.0 Hz, 1H), 6.76 (dd, J_1=8.1 Hz, J_2=0.5 Hz, 1H), 7.10 (d, J=7.8 Hz, 2H), 7.16—7.21 (m, 1H), 7.25—7.35 (m, 7H), 7.61 (d, J=2.7 Hz, 1H), 7.74 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 20.62, 72.44, 114.80, 115.40, 117.44, 125.92, 126.09, 126.48, 127.94, 128.58, 128.91, 133.70, 137.56, 137.80, 140.88, 146.56, 162.28; IR ν_{max}: 3296.14, 3015.10, 1633.11, 1611.42, 1586.33, 1505.80, 1486.97, 1392.11, 1312.22, 1262.68, 1161.73, 1112.32, 1022.90, 872.50, 821.29, 787.82, 749.83 cm^{-1}.

2,3-Dihydro-3-phenyl-2-(4-methoxyphenyl)quinazolin-4(1*H*)-one (3h) m.p. 205—207 ℃ (Lit.[14] 204—205 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.68 (s, 3H), 6.24 (d, J=2.5 Hz, 1H), 6.72 (dt, J_1=7.4 Hz, J_2=1.0 Hz, 1H), 6.77 (d, J=8.8 Hz, 1H), 6.85 (dt, J_1=8.8 Hz, J_2 = 2.0 Hz, 2H), 7.16—7.20 (m, 1H), 7.24—7.35 (m, 7H), 7.57 (d, J=2.5 Hz, 1H), 7.74 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 55.02, 72.32, 113.65, 114.78, 115.33, 117.42, 125.95, 126.29, 127.91, 128.56, 132.60, 133.69, 140.83, 146.66, 159.10, 162.32; IR ν_{max}: 3292.89, 3017.10, 2842.14, 1631.59, 1609.33, 1586.96, 1504.46, 1485.67, 1385.99, 1297.78, 1248.75, 1180.83, 1170.43, 1027.73, 834.06, 792.24, 748.50, 693.68 cm^{-1}.

2,3-Dihydro-3-phenyl-2-(4-chlorophenyl)quinazolin-4(1*H*)-one (3i) m.p. 216—218 ℃ (Lit.[9] 216

—217 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.33 (d, J=2.7 Hz, 1H), 6.74 (dt, J_1=7.4 Hz, J_2=1.0 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 7.18—7.22 (m, 1H), 7.25—7.29 (m, 3H), 7.31—7.42 (m, 6H), 7.67 (d, J= 2.5 Hz, 1H), 7.73 (dd, J_1=7.8 Hz, J_2=1.3 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 71.93, 114.85, 115.28, 117.71, 126.12, 126.25, 128.00, 128.38, 128.52, 128.67, 132.90, 133.85, 139.67, 140.59, 146.41, 162.15; IR ν_{max}: 3294.11, 3025.11, 1631.02, 1613.60, 1506.60, 1486.18, 1414.12, 1385.87, 1312.74, 1160.81, 1088.42, 1014.52, 833.14, 787.94, 754.04, 693.82 cm^{-1}.

2,3-Dihydro-3-phenyl-2-(4-bromophenyl)quinazolin-4(1*H*)-one (3j) m.p. 219—223 ℃ (Lit.[14] 222—225 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.31 (d, J=2.5 Hz, 1H), 6.71—6.78 (m, 2H), 7.18—7.22 (m, 1H), 7.25—7.29 (m, 3H), 7.31—7.36 (m, 4H), 7.52 (dt, J_1=8.6 Hz, J_2=2.0 Hz, 2H), 7.67 (d, J=2.8 Hz, 1H), 7.73 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 71.96, 114.85, 115.29, 117.71, 121.52, 126.11, 126.19, 128.00, 128.68, 128.83, 131.31, 133.86, 140.10, 140.60, 146.37, 162.13; IR ν_{max}: 3292.59, 3059.72, 1631.15, 1612.28, 1505.74, 1484.31, 1412.02, 1385.56, 1312.64, 1160.08, 1114.22, 1070.57, 1011.20, 827.21, 751.95, 694.06 cm^{-1}.

2,3-Dihydro-3-phenyl-2-(4-fluorophenyl)quinazolin-4(1*H*)-one (3k) m.p. 235—238 ℃;[10] ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.33 (d, J=2.5 Hz, 1H), 6.74 (dt, J_1=7.6 Hz, J_2=1.0 Hz, 1H), 6.78 (d, J=7.8 Hz, 1H), 7.10—7.21 (m, 3H), 7.24—7.30 (m, 3H), 7.31—7.35 (m, 2H), 7.40—7.45 (m, 2H), 7.63 (d, J= 2.5 Hz, 1H), 7.74 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 72.03, 114.81, 115.07, 115.24, 115.29, 117.64, 126.12, 126.42, 127.98, 128.63, 128.78, 128.86, 133.82, 136.86, 140.60, 146.55, 160.64, 162.24, 163.07; IR ν_{max}: 3291.98, 3020.12, 1628.56, 1611.78, 1504.33, 1485.78, 1384.85, 1311.20, 1223.52, 1151.94, 1023.93, 840.10, 791.82, 752.57, 693.83 cm^{-1}; Mass *m*/*z* (%): 320 (M^++2, 27), 319 (M^++1, 79), 318 (M^+, 74), 316 (25), 264 (30), 243 (85), 155 (52), 118 (41), 98 (39), 82 (80), 57 (base peak).

2,3-Dihydro-3-phenyl-2-(thiophen-2-yl)quinazolin-4(1*H*)-one (3l) m.p. 197—200 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.54 (d, J=2.5 Hz, 1H), 6.79 (dt, J_1=7.6 Hz, J_2=1.0 Hz, 1H), 6.84 (d, J=7.8 Hz, 1H), 6.88 (dd, J_1=5.0 Hz, J_2=3.5 Hz, 1H), 6.97 (d, J= 3.5 Hz, 1H), 7.22—7.27 (m, 1H), 7.31—7.40 (m, 6H), 7.70 (d, J=2.8 Hz, 1H), 7.75 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 69.46, 115.24, 115.56, 118.05, 125.91, 126.33, 126.35, 126.39, 126.50, 127.94, 128.69, 133.81, 140.44, 144.58, 146.33, 161.54; IR ν_{max}: 3285.57, 3024.17, 1631.48, 1608.48, 1503.89, 1483.82, 1387.92, 1366.69, 1318.02, 1257.82, 1190.50, 1157.93, 1070.09, 837.02, 793.49, 754.12, 714.14, 694.28 cm^{-1}. Anal. calcd for $C_{18}H_{14}N_2OS$: C 70.56, H 4.61, N 9.14, S 10.47; found C 70.39, H 4.48, N 9.02.

2,3-Dihydro-3-phenethyl-2-(4-methylphenyl)quinazolin-4(1*H*)-one (3m) m.p. 151—154 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.26 (s, 3H), 2.70—2.77 (m, 1H), 2.85—2.98 (m, 2H), 3.98—4.04 (m, 1H), 5.80 (d, J=1.8 Hz, 1H), 6.61—6.77 (m, 2H), 7.15—7.29 (m, 11H), 7.65 (d, J=7.6 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 20.66, 33.60, 46.12, 70.28, 114.17, 114.76, 117.00, 126.17, 126.23, 127.36, 128.35, 128.58, 129.05, 133.15, 137.80, 138.05, 139.03, 146.46, 162.24; IR ν_{max}: 3282.06, 3027.47, 1628.10, 1609.15, 1583.56, 1506.09, 1485.13, 1408.10, 1311.22, 1173.21, 822.25, 750.40, 693.83 cm^{-1}; Mass *m*/*z* (%): 343 (M^++1, 18), 342 (M^+, 61), 341 (29), 320 (37), 291 (15), 264 (25), 237 (29), 217 (31), 155 (68), 118 (68), 82 (base peak), 57 (77). Anal. calcd for $C_{23}H_{22}N_2O$: C 80.67, H 6.48, N 8.18; found C 80.49, H 6.38, N 8.01.

2-(4-Chlorophenyl)-2,3-dihydro-3-phenethylquinazolin-4(1*H*)-one (3n) m.p. 156—158 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.69—2.78 (m, 1H), 2.87—3.01 (m, 2H), 4.01—4.08 (m, 1H), 5.89 (d, J=2.5 Hz, 1H), 6.62 (d, J=8.1 Hz, 1H), 6.67 (dt, J_1=7.6 Hz, J_2= 1.0 Hz, 1H), 7.17—7.23 (m, 4H), 7.26—7.30 (m, 2H), 7.34—7.38 (m, 3H), 7.41—7.45 (m, 2H), 7.65 (d, J= 7.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 33.57, 46.10, 69.57, 114.26, 114.75, 117.26, 126.21, 127.41, 128.08, 128.36, 128.61, 132.98, 133.31, 134.84, 140.10, 162.09; IR ν_{max}: 3282.50, 3015.10, 2983.12, 2881.16, 1627.48, 1606.11, 1582.06, 1507.09, 1484.60, 1433.27, 1402.09, 1358.90, 1310.08, 1228.17, 1174.75, 1089.19, 1002.14, 849.17, 829.33, 788.50, 755.55, 693.59 cm^{-1}; Mass *m*/*z* (%): 364 (M^++2, 18), 363 (M^++1, 28), 362 (M^+, 84), 361 (80), 360 (17), 321 (25), 291 (23), 264 (47), 244 (70), 237 (58), 155 (55), 118 (38), 98 (35), 82 (81), 57 (base peak). Anal. calcd for $C_{22}H_{19}ClN_2O$: C 72.82, H 5.28, Cl 9.77, N 7.72; found C 72.63, H 5.19, N 7.54.

2,3-Dihydro-3-(4-hydroxyphenyl)-2-(4-methylphenyl)quinazolin-4(1*H*)-one (3o) m.p. 249—252 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.11 (s, 3H), 5.98 (d, J=2.5 Hz, 1H), 6.55—6.61 (m, 4H), 6.90 (dt, J_1=8.8 Hz, J_2 = 2.0 Hz, 2H), 6.98 (d, J = 8.1 Hz, 2H), 7.11—7.15 (m, 3H), 7.35 (d, J=2.3 Hz, 1H), 7.59 (dd, J_1=7.6 Hz, J_2=1.5 Hz, 1H), 9.33 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 20.63, 73.05, 114.56, 115.09, 115.37, 117.30, 126.52, 127.82, 127.87, 128.84, 132.15, 133.45, 137.49, 137.95, 146.58, 155.45, 162.24; IR ν_{max}: 3310.99, 3119.71, 3015.12, 2891.15, 2359.28, 1633.60, 1612.53, 1596.03, 1580.32, 1514.24, 1444.59, 1421.41, 1266.33, 1225.42, 1150.33, 1117.79, 1018.36, 869.90, 839.50, 806.42, 770.55, 752.30, 695.18 cm^{-1}; Mass *m*/*z* (%): 331 (M^++1, 9), 330 (M^+, 51), 329 (26), 328 (10), 254 (30), 217 (28), 155 (60), 118 (61), 82 (base peak), 57 (77). Anal. calcd for $C_{21}H_{18}N_2O_2$: C 76.34, H 5.49, N 8.48; found C 76.18, H 5.34, N 8.31.

2,3-Dihydro-2,3-di(4-methylphenyl)quinazolin-4(1*H*)-one (3p) m.p. 243—247 ℃;[27] ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.22 (s, 3H), 2.26 (s, 3H), 6.18 (d, J=2.8 Hz, 1H), 6.68—6.75 (m, 2H), 7.09—7.15 (m, 6H), 7.23—7.28 (m, 3H), 7.55 (d, J=2.5 Hz, 1H), 7.72 (dd, J_1=7.8 Hz, J_2=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6,

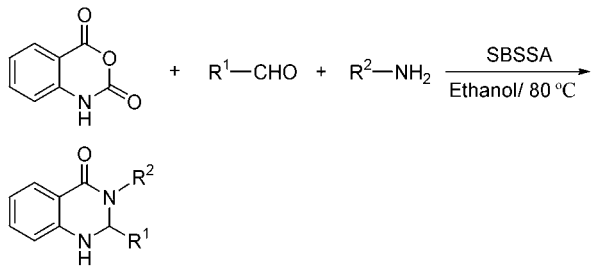
100 MHz) δ: 20.62, 72.56, 114.70, 115.38, 117.38, 126.05, 126.45, 127.88, 128.89, 129.05, 133.60, 135.18, 137.52, 137.90, 138.31, 146.53, 162.20; IR ν_{max}: 3299.19, 3015.11, 2892.16, 1634.01, 1607.98, 1583.17, 1505.12, 1485.01, 1387.10, 1313.90, 1262.37, 1159.48, 1107.52, 1024.63, 877.72, 816.18, 780.88, 764.52, 733.16, 694.37 cm^{-1}; Mass *m*/*z* (%): 329 (M^++1, 10), 328 (M^+, 51), 327 (19), 217 (27), 155 (60), 118 (58), 82 (base peak), 57 (80).

3-(5-Chloro-2-hydroxy-phenyl)-2-(4-chlorophenyl)-2,3-dihydro-1*H*-quinazolin-4-one (3q) m.p. 235—237 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.21 (d, J=1.3 Hz, 1H), 6.73—6.77 (m, 2H), 6.82 (d, J=8.6 Hz, 1H), 7.00 (d, J=2.5 Hz, 1H), 7.07 (dd, J_1=8.6 Hz, J_2=2.5 Hz, 1H), 7.29—7.37 (m, 4H), 7.42—7.54 (m, 2H), 7.70 (dd, J_1=7.8 Hz, J_2=1.3 Hz, 1H), 10.05 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 71.92, 114.46, 114.56, 118.75, 127.94, 128.17, 128.30, 129.24, 132.63, 141.30, 143.65, 152.37, 161.69; IR ν_{max}: 3333.85, 1608.07, 1577.56, 1501.08, 1482.80, 1417.00, 1353.45, 1257.61, 1190.15, 1159.49, 1117.21, 1087.49, 1014.02, 822.17, 756.46, 738.36, 709.90 cm^{-1}; Mass *m*/*z* (%): 384 (M^+, 40), 383 (27), 382 (15), 355 (11), 328 (28), 310 (28), 243 (35), 217 (67), 155 (76), 118 (34), 98 (30), 82 (83), 57 (base peak). Anal. calcd for $C_{20}H_{14}Cl_2N_2O_2$: C 62.35, H 3.66, Cl 18.41, N 7.27; found C 62.18, H 3.51, N 7.10.

Results and discussion

During our studies towards the development of new routes to the synthesis of highly substituted heterocycles and the usage of solid acid catalysts,[28-32] we wish to report a valid and an efficient procedure for synthesis of 2,3-dihydroquinazolinones via one-pot condensation of isatoic anhydride and aldehydes with NH_4OAc or primary amine in the presence of silica-bonded *S*-sulfonic acid (SBSSA) as an inexpensive solid acid catalyst (Scheme 2).

Scheme 2 SBSSA catalyzed synthesis of 2,3-dihydroquinazolinones



To study the effect of catalyst loading on the condensation of isatoic anhydride, aldehydes, and ammonium acetate as the corresponding 2,3-dihydroquinazolinones, the reaction of isatoic anhydride and 4-chlorobenzaldehyde with NH_4OAc was chosen as a model reaction in ethanol under heating conditions (Table 1). To illustrate the need of SBSSA for this condensation we examined the model reaction in the absence of SBBSA under heating at 80 ℃ (Table 1, Entriy 1). The results show clearly that SBSSA is an effective catalyst for this transformation and without SBSSA the reaction did not take place, even after 300 min. As indicated in Table 1, the best results have been obtained at 80 ℃ with 0.005 g (0.016 mol%) SBSSA and the yield of reaction with increasing the amount of SBSSA decreased.

Table 1 The reaction of isatoic anhydride and 4-chloro-benzaldehyde with ammonium acetate in the presence of different amounts of SBSSA at 80 ℃[a]

Entry	The amounts of catalyst/g	Time/min	Yield[b]/%
1	—	300	—
2	0.2	130	50
3	0.15	130	65
4	0.1	130	75
5	0.03	130	80
6	0.01	130	90
7	0.005	130	90

[a] The molar ratio of isatoic anhydride∶4-chlorobenzaldehyde∶NH_4OAc was used as followed 1∶1∶1 mmol respectively, in ethanol (5 mL) at 80 ℃. [b] Isolated yield.

The model reaction was also examined in various solvents in the presence of 0.005 g of SBSSA (Table 2). As shown in Table 2, condensation reaction in ethanol and methanol gave the best results in the case of yield, and we chose ethanol for environmental acceptance.

Table 2 The reaction of isatoic anhydride and 4-chlorobenzaldehyde with ammonium acetate catalyzed by SBSSA in different solvents at reflux conditions[a]

Entry	Solvent	Time/min	Yield[b]/%
1	Water	130[c]	65
2	Dichloromethane	130	25
3	Acetonitrile	130	15
4	Ethanol	130[c]	90
5	Methanol	130	90
6	Toluene	130[c]	—

[a] The molar ratio of isatoic anhydride∶4-chlorobenzaldehyde∶NH_4OAc was used as followed 1∶1∶1 mmol with SBSSA (0.016 mol%), respectively, in solvent (5 mL) at reflux conditions. [b] Isolated yield. [c] Reaction was performed at 80 ℃.

The generality of this process was demonstrated by the wide range of substituted and structurally divers aldehydes to synthesize the corresponding products in high to excellent yields (Table 3). Also, a series of aniline derivatives and 2-phenylethyl amine were employed and all 2,3-dihydroquinazolinones were obtained in high to excellent yields.

Table 3 Preparation of 2,3-dihydroquinazolinones catalyzed by SBSSA in ethanol at 80 ℃[a]

Entry	R^1	R^2	Product	Time/min	Yield[b]/%
1	4-$CH_3C_6H_4$	H	**3a**	90	87
2	4-$CH_3OC_6H_4$	H	**3b**	120	84
3	4-ClC_6H_4	H	**3c**	130	90
4	4-BrC_6H_4	H	**3d**	120	86
5	4-FC_6H_4	H	**3e**	120	84
6	2-thionyl	H	**3f**	150	78
7	4-$CH_3C_6H_4$	C_6H_5	**3g**	150	80
8	4-$CH_3OC_6H_4$	C_6H_5	**3h**	180	78
9	4-ClC_6H_4	C_6H_5	**3i**	150	80
10	4-BrC_6H_4	C_6H_5	**3j**	210	80
11	4-FC_6H_4	C_6H_5	**3k**	135	82
12	2-thionyl	C_6H_5	**3l**	210	75
13	4-$CH_3C_6H_4$	$PhCH_2CH_2$	**3m**	35	87
14	4-ClC_6H_4	$PhCH_2CH_2$	**3n**	40	88
15	4-$CH_3C_6H_4$	4-HO-C_6H_4	**3o**	240	75
16	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**3p**	90	80
17	4-ClC_6H_4	2-HO-5-ClC_6H_4	**3q**	120	75

[a] The molar ratio of isatoic anhydride∶aldehyde∶amine was used as followed 1∶1∶1 mmol with SBSSA (0.016 mol%), respectively in ethanol (5 mL) at 80 ℃. [b] Isolated yield.

The possibility of recycling the catalyst was examined. For this reason, the reaction of isatoic anhydride and 4-chlorobenzaldehyde with NH_4OAc in the presence of SBSSA was studied at 80 ℃ and under solvent-free conditions. Upon completion, the reaction mixture was filtered and washed with warm ethanol. The product was recrystallized from hot ethanol. The recycled catalyst could be reused ten times without any treatment. No observation of appreciable loss in its catalytic activities was shown (Figure 1).

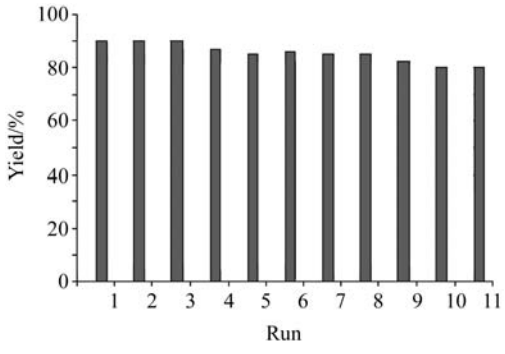


Figure 1 Recyclability of silica bonded *S*-sulfonic acid as catalyst in the condensation reaction of isatoic anhydride (1 mmol) and 4-chlorobenzaldehyde (1 mmol) with ammonium acetate (1 mmol) in ethanol (5 mL) at 80 ℃. Reaction time＝130 min.

Finally, a comparative study of SBSSA with other recently reported catalysts for the synthesis of 2-(4-methylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (**3a**), as a model compound was made which revealed that SBSSA is equally efficient, but much cheaper and reusable (Table 4).

Table 4 Comparison of the efficiency of SBSSA with some of the reported catalyst on the reaction of 4-methylbenzaldelyde with isatoic anhydride and ammonium acetate

Catalyst	Catalyst loading/g	Time/min	Yield[a]/%	Ref.
p-Ts-OH	0.5 mol	120	80	9
Montmorillonite K-10	0.3	300	73	11
[bmim]BF_4	0.2	120	92	12
Silica sulfuric acid	0.08	240	79	13a
Silica sulfuric acid	0.11	210	90	13c
MCM-41-SO_3H	0.005	15	90	16
SBSSA	0.005	90	87	Present Work

[a] Isolated yield.

Conclusion

In conclusion, heterogeneous conditions, easy and clean work-up, high yields and recovery of the catalyst make this method practical for multi-component reactions. We believe that the present methodology could become an important addition to the existing methodologies.

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