Supporting Information

Chitosan: An efficient, reusable and biodegradable catalyst for green synthesis of heterocycles

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Experimental Protocols

General

The ^{1}H NMR spectra were measured by BRUKER AVANCE II 400 NMR spectrometer with tretramethylsilane as an internal standard at 20-25 ^{o}C; data for ^{1}H NMR are reported as follow: chemical shift (ppm), integration, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and br, broad), coupling constant (Hz). IR spectra were recorded by SHIMADZU; IR spectrometer of sample dispersed in KBr pellet or nujol and is reported in terms of frequency of absorption (cm^{-1}). E-Merck pre-coated TLC plates, RANKEM silica gel G for preparative thin-layer chromatography were used. Melting points were determined in open capillaries and was uncorrected. 2-Amino benzothiazole was purchased from Sigma Aldrich and other chemical were purchased from Himedia, Mumbai India and used without any purifications.

Typical procedure for synthesis

A mixture of aldehydes (5 mmol), dicarbonyl (5 mmol) and urea/thiourea/2-amino benzothiazole/3-amino-1,2,4-triazole (5 mmol) was refluxed at 60-65 ^{o}C in the presence chitosan catalyst in 10 mL aqueous solution of 2% acetic acid. The reaction was monitored by TLC. After completion the reaction, mixture was filtered. The residue was purified via column chromatography on silica gel using DCM:Touluene (3:2). The heterocyclic derivatives were collected as solid and filtrate has chitosan catalyst reused as such for next run.

Characterization Data

Ethyl-2-methyl-4-(phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1a).

Pale-yellow crystals, mp 178-180 ^{o}C, R_f = 0.47 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3043 (C-H_{str}), 2968 (C-H_{str} in CH_2CH_3), 1670 (C=O_{str}), 1589 (C=N_{str}), 1462 (C=C_{str}), 744 (C-H_{def}); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.29 (3H, t, J_{HH} = 7.12 Hz, $CH_2\underline{CH_3}$), 2.46 (3H, s, $\underline{CH_3}$), 4.17 (2H, m, $\underline{CH_2}CH_3$), 6.39 (1H, s, -$\underline{CH}$), 7.07-7.43 (9H, m, $\underline{ArH}$); ^{13}C NMR (100 MHz, DMSO): 165.44, 162.59, 154.04, 141.26, 137.43, 128.26, 126.79, 122.22, 111.65, 102.56, 59.35, 56.82, 23.17, 13.99; ESI-MS: m/z Calculated for $C_{20}H_{18}N_2O_2S$ 350.44, Found $[M+H]^+$ 351.2; C, H and N analyses Calculated for C 68.48, H 5.13, N 7.98, Found C 68.78, H 5.38, N 7.89.

Ethyl-2-methyl-4-(4-hydroxy-3-methoxy phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1b).

Pale-yellow powder, mp 192-194 ^{o}C, R_f = 0.53 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3360 (OH^{str}), 3059 (C-H_{str}), 2983 (C-H_{str} in CH_2CH_3), 1703 (C=O_{str}), 1597 (C=N_{str}), 1504 (C=C_{str}), 740 (C-H_{def}); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.31 (3H, t, J_{HH} = 7.12 Hz, $CH_2\underline{CH_3}$), 2.47 (3H, s, $\underline{CH_3}$), 3.8 (3H, s, Ar-O$\underline{CH_3}$), 4.12-4.19 (2H, m, $\underline{CH_2}CH_3$), 6.36 (1H, s, -$\underline{CH}$), 6.78 (1H, d, J_{HH} = 5.6 Hz, $\underline{ArH}$), 6.89-6.92 (2H, m, $\underline{ArH}$), 7.13-7.31 (4H, m, $\underline{ArH}$), 9.80 (1H, s, $\underline{OH}$); ^{13}C NMR (100 MHz, DMSO): 165.60, 162.34, 153.51, 147.12, 146.42, 137.61, 132.52, 126.37, 122.21, 115.18, 111.92, 110.88, 59.28, 55.43, 23.09, 14.08; ESI-MS: m/z Calculated for $C_{21}H_{20}N_2O_4S$ 396.49, Found $[M+H]^+$ 397.2; C, H and N analyses Calculated for C 63.55, H 5.04, N 7.06, Found C 63.68, H 5.16, N 7.13.

Ethyl-2-methyl-4-(4-dimethylamino phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1c).

Pale-yellow powder, mp 230-232 ^{o}C, R_f = 0.57 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3059 (C-H_{str}), 2897 (C-H_{str} in CH_2CH_3), 1612 (C=O_{str}), 1581 (C=N_{str}), 1431 (C=C_{str}), 815-754 (C-H_{def}); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.29 (3H, t, J_{HH} = 7.12 Hz, $CH_2\underline{CH_3}$), 2.86 (3H, s, $\underline{CH_3}$), 3.06 (6H, s, $N(\underline{CH_3})_2$), 4.15 (2H, m, $\underline{CH_2}CH_3$), 6.71-7.5 (4H, m, ArH), 7.71-7.92 (4H, m, ArH); ^{13}C NMR (100 MHz, DMSO): 166.39, 165.44, 153.95, 152.63, 133.43, 127.71, 125.91, 124.45, 121.63, 120.57, 23.13, 13.60; ESI-MS: m/z Calculated for $C_{22}H_{23}N_3O_2S$ 393.54, Found $[M+H]^+$ 394.2; C, H and N analyses Calculated for C 67.08, H 5.84, N 10.67, Found C 67.16, H 5.98, N 10.75.

Ethyl-2-methyl-4-(4-nitro phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1d).

Yellow powder, mp 148-149 ^{o}C, R_f = 0.52 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3348 (C-H_{str}), 2933 (C-H_{str} in CH_2CH_3), 1625 (C=O_{str}), 1510 (NO_{2str}), 1267 (C=C_{str}), 962-812 (C-H_{def}); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.31 (3H, s, $CH_2\underline{CH_3}$), 2.46 (3H, s, $\underline{CH_3}$), 4.15 (2H, m, $\underline{CH_2}CH_3$), 6.52 (1H, s, -CH), 7.03-7.63 (8H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): 166.25, 163.56, 155.83, 147.95, 147.62, 137.44, 128.06, 126.88, 124.43, 124.01, 123.73, 122.47, 111.36, 102.01, 60.42, 57.03, 23.97, 14.40; ESI-MS: m/z Calculated for $C_{20}H_{17}N_3O_4S$ 395.46, Found $[M+H]^+$ 396.4; C, H and N analyses Calculated for C 60.69, H 4.29, N 10.62, Found C 60.78, H 4.35, N 10.70.

Ethyl-2-methyl-4-(2-hydroxy phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1e).

Pale-yellow powder, mp 210-212 ^{o}C, R_f = 0.59 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3288 (OH_{str}), 3059 (C-H_{str}), 2897 (C-H_{str} in CH_2CH_3), 1612 (C=O_{str}), 1581 (C=N_{str}), 1431 and 1377 (C=C_{str}), 815-754 (C-H_{def}); ^{1}H NMR (400 MHz , $CDCl_3$): δ_H 1.25 (3H, t, J_{HH} = 4.76 Hz,

$\underline{CH_3}CH_2$), 2.35 (3H, s, $\underline{CH_3}$), 4.04-4.12 (m, 2H, $CH_3\underline{CH_2}$), 6.30 (1H, s, $\underline{-CH}$), 6.66 (2H, d, J_{HH} = 8.40 Hz, ArH), 7.13-7.59 (4H, m, ArH), 7.59 (1H, d, J_{HH} = 7.76 Hz, ArH), 9.26 (1H, s, OH); ^{13}C NMR (100 MHz, DMSO): 165.55, 162.27, 157.22, 153.46, 137.56, 131.95, 128.13, 126.34, 123.57, 122.94, 122.20, 115.02, 111.80, 102.96, 59.27, 56.37, 23.09, 14.03; ESI-MS: m/z Calculated for $C_{20}H_{18}N_2O_3S$ 367.34, Found $[M]^+$ 367.2; C, H and N analyses Calculated for C 65.49, H 4.91, N 7.64, Found C 65.51, H 4.95, N 7.62.

Ethyl-2-methyl-4-(4-hydroxy phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1f).

Pale-yellow powder, mp 210-212 ^oC, R_f = 0.59 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3288 (OH_{str}), 3059 ($C\text{-}H_{str}$), 2897 ($C\text{-}H_{str}$ in CH_2CH_3), 1612 ($C{=}O_{str}$), 1581 ($C{=}N_{str}$), 1431 and 1377 ($C{=}C_{str}$), 815-754 ($C\text{-}H_{def}$); ^{1}H NMR (400 MHz , $CDCl_3$): δ_H 1.25 (3H, t, J_{HH} = 14.16 Hz, $\underline{CH_3}CH_2$), 2.35 (3H, s, $\underline{CH_3}$), 4.04-4.12 (m, 2H, $CH_3\underline{CH_2}$), 6.30 (1H, s, $\underline{-CH}$), 6.66 (2H, d, J_{HH} = 8.40 Hz, ArH), 7.13-7.59 (5H, m, ArH), 7.59 (1H, d, J_{HH} = 7.76 Hz, ArH), 9.26 (1H, s, OH); ^{13}C NMR (100 MHz, DMSO): 165.55, 162.27, 157.22, 153.46, 137.56, 131.95, 128.13, 126.34, 123.57, 122.94, 122.20, 115.02, 111.80, 102.96, 59.27, 56.37, 23.09, 14.03; ESI-MS: m/z Calculated for $C_{20}H_{18}N_2O_3S$ 367.34, Found $[M]^+$ 367.2; C, H and N analyses Calculated for C 65.49, H 4.91, N 7.64, Found C 65.51, H 4.95, N 7.62.

Ethyl-2-methyl-4-(4-methoxy phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1g).

Pale-yellow powder, mp 130-132 ^oC, R_f = 0.53 (DCM:Toluene; 3:2); IR (KBr) (υ_{max}, cm^{-1}): 2941 ($C\text{-}H_{str}$ in CH_2CH_3), 1627 ($C{=}O_{str}$), 1508 ($C{=}N_{str}$), 1280 ($C{=}C_{str}$), 962-813 ($C\text{-}H_{def}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (3H, t, J_{HH} = 4.76 Hz, $\underline{CH_3}CH_2$), 2.45 (3H, s, $\underline{CH_3}$), 3.71 (3H, s, Ar-$O\underline{CH_3}$), 4.11-4.21 (2H, m, $CH_3\underline{CH_2}$), 6.34 (1H, s, $\underline{-CH}$), 6.78 (2H, d, J_{HH} = 8.64 Hz, ArH), 7.21-

7.58 (6H, m, ArH); ^{13}C NMR (100 MHz, DMSO): 166.67, 163.27, 159.42, 154.51, 152.07, 138.06, 133.81, 128.51, 126.57, 123.88, 123.82, 122.14, 120.89, 119.04, 113.90, 111.80, 103.24, 60.09, 57.20, 55.18, 23.73, 14.40; ESI-MS: m/z Calculated for $C_{21}H_{20}N_2O_2S$ 380.47, Found $[M+H]^+$ 381.3; C, H and N analyses Calculated for C 66.23, H 5.25, N 7.35, Found C 66.26, H 5.27, N 7.35.

Ethyl-2-methyl-4-(2, 6-dichloro phenyl)-4H-pyrimido[2,1-b][1,3]benzothiazole-3-carboxylate (1h).

Pale-yellow powder, mp 150-152 ^{o}C, R_f = 0.56 (DCM:Toluene; 3:2);); IR (KBr) (υ_{max}, cm^{-1}): 3012 (C-H_{str}), 2922 (C-H_{str} in CH_2CH_3), 1625 (C=O_{str}), 1500 (C=N_{str}), 1278 (C=C_{str}), 960-812 (C-H_{def}); ^{1}H NMR (400 MHz, DMSO): δ_H 1.09 (3H, t, J_{HH} = 4.76 Hz, $CH_2\underline{CH_3}$), 2.47 (3H, s, $\underline{CH_3}$), 4.04 (2H, m, $\underline{CH_2}CH_3$), 7.01-7.66 (7H, m, Ar-H); ^{13}C NMR (100 MHz, DMSO): 171.88, 165.92, 162.99, 151.33, 137.57, 133.73, 132.41. 129.14, 126.08, 125.57, 124.52, 122.97, 121.69, 117.66, 116.07, 59.26, 23.11, 14.04; ESI-MS: m/z Calculated for $C_{20}H_{16}N_2Cl_2O_2S$ 419.41, Found $[M]^+$ 419.6; C, H and N analyses Calculated for C 57.22, H 3.81, N 6.77, Found C 57.19, H 3.84, N 6.76.

6,6-dimethyl-9-phenyl-5,6,7,9-tetrahydro-4H-1,2,4-triazolo[5,1-b]quinazolin-8-one (2a)

White powder, mp 230-232 ^{o}C, R_f = 0.58 (DCM:Toluene 3:2); IR (KBr) (υ_{max}, cm^{-1}): 2850 (C-H_{str}), 1645 (C=O_{str}), 1587 (C-H_{def}), 1483 (C-H_{def}), 1454 (C=C_{str}), 1270 (C-N_{str}). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.96 (s, 3H, $\underline{CH_3}$), 1.05 (s, 3H, $\underline{CH_3}$), 2.17 (d, 1H, J_{HH} = 6.52 Hz, H-5), 2.19 (d, 1H, J_{HH} = 12.52 Hz, H-5'), 2.23-2.59 (m, 2H, H-7), 6.44 (s, 1H, H-9), 7.07-7.48 (m, 5H, ArH), 7.66 (s, 1H, H-2), 8.1 (s, 1H, NH); ESI-MS: m/z Calculated for $C_{17}H_{18}N_4O$ 294.34, Found $[M+H]^+$ 295; C, H and N analyses Calculated for C 69.30, H 6.11, N 19.02, Found C 69.46, H 6.19, N 19.09.

6,6-dimethyl-9-(2-hydroxy-phenyl)-5,6,7,9-tetrahydro-4H-1,2,4-triazolo[5,1-b]quinazolin-8-one (2b)

White powder, mp 112-114 ^{o}C, R_f = 0.56 (DCM:Toluene 3:2); IR (KBr) (υ_{max}, cm^{-1}): 2850 (C-H_{str}), 1625 (C=O_{str}), 1585 (C-H_{def}), 1510 (C-H_{def}), 1427 (C=C_{str}), 1269 (C-N_{str}), 864-1124 (C-H_{def}). NMR (400 MHz, $CDCl_3$): δ_H 0.98, (s, 3H, $\underline{CH_3}$), 1.02, (s, 3H, $\underline{CH_3}$), 2.33 (d, 1H, J_{HH} = 3.36 Hz, H-5), 2.4 (d, 1H, J_{HH} = 1.80 Hz, H-5'), 2.57-2.78 (m, 2H, H-7), 6.49 (s, 1H, H-9), 6.85-7.36 (m, 5H, ArH), 7.62 (s, 1H, H-2), 8.29 (s, 1H, $\underline{NH}$), 9.18 (s, 1H, OH); ESI-MS: m/z Calculated for $C_{17}H_{18}N_4O_2$ 310.3, Found $[M-H]^+$ 309; C, H and N analyses Calculated for C 65.74, H 5.80, N 18.04, Found C 65.89, H 5.76, N 18.16.

4-(2-hydroxy phenyl)-7,7-dimethyl-5-oxo-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione (3a)

White powder, mp 140-142 ^{o}C, R_f = 0.57 (DCM:Toluene 3:2)); IR (KBr) (υ_{max}, cm^{-1}): 3404 (OH_{str}), 2850 (C-H_{str}), 1615 (C=O_{str}), 1575 (C-H_{def}), 1510 (C-H_{def}), 1427 (C=C_{str}), 1269 (C-N_{str}), 864 (C-H_{def}). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.99 (s, 3H, $\underline{CH_3}$) 1.07 (s, 1H, $\underline{CH_3}$), 2.14 (s, 1H, $\underline{CH_2}$), 2.4 (s, 2H, $\underline{CH_2}$), 5.54 (s, 1H, $\underline{CH}$), 7.08-7.48 (m, 4H, ArH), 8.1 (broad band, 2H, $\underline{NH}$), 11.91 (s, 1H, OH); ESI-MS: m/z Calculated for $C_{16}H_{18}N_2O_3$ 286.36 Found $[M-H]^+$ 285.3; C, H and N analyses Calculated for C 67.04, H 6.28, N 9.77, Found C 67.16, H 6.22, N 9.91.

4-phenyl-7,7-dimethyl-5-oxo-1,2,3,4,5,6,7,8-octahydroquinazoline-2-thione (3b)

White powder, mp 162-164 ^{o}C, R_f = 0.56 (DCM:Toluene 3:2); IR (KBr) (υ_{max}, cm^{-1}): 2650 (C-H_{str}), 1645 (C=O_{str}), 1587 (C-H_{def}), 1554 (C-H_{def}), 1483 (C=C_{str}). NMR (400 MHz, $CDCl_3$): δ_H 0.98 (s, 3H, $\underline{CH_3}$), 1.10 (s, 3H, $\underline{CH_3}$), 2.22 (s, 1H, $\underline{CH_2}$), 2.46 (s, 1H, $\underline{CH_2}$), 4.74 (1H, s, $\underline{CH}$), 7.08-7.48 (m, 5H, ArH), 8.08 (broad band, 2H, $\underline{NH}$); ESI-MS: m/z Calculated for $C_{16}H_{18}N_2OS$

286.38 Found $[M-H]^+$ 285.3; C, H and N analyses Calculated for C 67.04, H 6.28, N 9.77, Found C 67.21, H 6.33, N 9.89

12-phenyl-substituted-2,3,4,12-tetrahydrobenzo[4,5]thiazolo[2,3-b]quinazolin-1-one (4a)

Pale yellow powder, mp 230-232 ^oC, R_f = 0.53 (DCM:Toluene 3:2); IR (KBr) (υ_{max}, cm^{-1}): 3007 ($C-H_{str}$), 2922 ($C-H_{str}$), 1625 ($C=O_{str}$), 1510 ($C-H_{def}$), 1267 ($C-H_{def}$), 1122 ($C=S_{str}$), 962-812 ($C-H_{str}$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 0.93 (s, 3H, $\underline{CH_3}$), 1.09 (s, 3H, $\underline{CH_3}$), 2.18-2.30 (m, 2H, $\underline{CH_2}$), 2.52 (s, 2H, $\underline{CH_2}$), 6.53 (s, 1H, C-H), 7.17-7.53 (m, 9H, ArH); ESI-MS: m/z Calculated for $C_{22}H_{20}N_2OS$ 360.42 Found $[M+H]^+$ 361.3; C, H and N analyses Calculated for C 73.24, H 5.54, N 7.76, Found C 73.29, H 5.65, N 7.83.

Knoevenagel intermediate

Off white powder, mp 78-80 ^oC, ^1H-NMR (400 MHz, $CDCl_3$): H ppm 1.29 (3H, t, J = 14.24 Hz, CH_2CH_3), 2.46 (3H, s, CH_3), 4.17 (2H, m, CH_2CH_3), 6.39 (1H, s, =CH), 7.07-7.43 (5H, m, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): 200.71, 164.16, 140.09, 137.16, 134.65, 134.01, 132.73, 129.49, 128.75, 61.29, 29.72, 13.71; ESI-MS: m/z Calculated for $C_{13}H_{14}O_3$ 218.3, Found $[M+H]^+$ 219.5.