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ORIGINAL ARTICLE

Facile synthesis and antimicrobial activity of a novel series of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-aryl-cyclopenta[*b*] pyrano-pyrimidine-4,6-5*H*-dione derivatives catalyzed by reusable silica-bonded *N*-propyl diethylenetriamine sulfamic acid

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KEYWORDS

Cyclopenta[*b*]pyrano pyrimidinones;
Silica-bonded *N*-propyl diethylenetriamine sulfamic acid;
Coumarin-3-carboxylic acid;
Antimicrobial activity

Abstract An efficient method for the synthesis of a novel series of cyclopenta[*b*]pyrano pyrimidinone derivatives with silica-bonded *N*-propyl diethylenetriamine sulfamic acid (SBPDSA) as catalyst has been achieved by the condensation of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives and coumarin-3-carboxylic acid under solvent free conditions. Antimicrobial studies showed all the target compounds processing good antibacterial and antifungal activities.

1. Introduction

Coumarins (2-oxo-2*H*-chromenes) are an old class of compounds, also known as benzopyranes, comprising a large class of cinnamic acid-derived phenolic compounds found in fungi, bacteria and plants, particularly in edible plants from different botanical families. Coumarins and their derivatives have attracted intense interest in recent years because of their diverse pharmacological properties such as anti-inflammatory (Witaicenis et al., 2014), antitumor (Avin et al., 2014), anticancer (Jashari et al., 2014; Zhang et al., 2014), acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) inhibitors (Asadipour et al., 2013), anti-proliferative (Zhao et al., 2014), antibacterial, antifungal and antioxidant (Renuka and Kumar, 2013), anti-osteoporotic (Sashidhara et al., 2013) and anti-tuberculosis activities (Kawate et al., 2013).

A considerable effort has been made for the synthesis of heterocyclic compounds containing coumarin moiety due to their wide pharmaceutical importance (Banothu and Bavanthula, 2012; Ghosh and Das, 2012; Augustine et al.,

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2012; Khoobi et al., 2011; Khan et al., 2011, 2012; Khurana and Kumar, 2009). However, these procedures are not entirely satisfactory and suffer from long reaction time or tedious work up. Hence, a method using a nonmetallic catalyst is desirable. Therefore, the introduction of new and efficient methods for this reaction is still necessary. Toward this goal, we were prompted to explore new methods for the synthesis of heterocyclic compounds containing coumarin moiety.

Silica-bonded *N*-propyl diethylenetriamine sulfamic acid has been reported as a novel catalyst for chemoselective synthesis of 1,1-diacetates (Sefat et al., 2011), and synthesis of α-aminonitriles (Rahi et al., 2012). However, to the best of our knowledge, there are no examples on the use of SBPDSA as catalyst for the synthesis of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-aryl-cyclopenta[*b*]pyrano-pyrimidine-4,6-5*H*-dione derivatives.

Considering the potential of developing new routes to the synthesis of heterocyclic compounds containing coumarin moiety due to their wide pharmaceutical importance (Ghashang et al., 2013, 2014a,b), we now describe the synthesis of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-cyclopenta[*b*]pyrano-pyrimidine-4,6-5*H*-dione derivatives by the condensation of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives and coumarin-3-carboxylic acid using SBPDSA as an efficient novel catalyst.

The synthesis of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives was achieved by the condensation of aldehydes **1**, malononitrile **2** and cyclopentane-1,3-dione **3**, using Alum ($KAl(SO_4)_2{\cdot}12H_2O$) as catalyst under solvent-free conditions (Scheme 1).

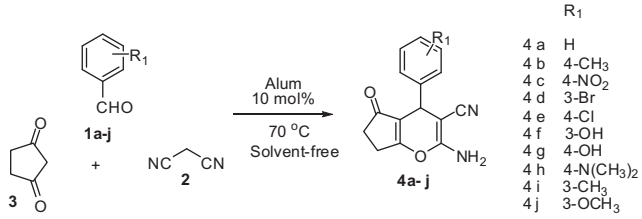
2. Experimental

2.1. Apparatus and analysis

Chemicals were purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products unless otherwise stated. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained using a Bruker DRX-500 Avance spectrometer at ambient temperature, using TMS as internal standard. FT-IR spectra were recorded as KBr pellets on a Shimadzu spectrometer. Mass spectra were determined on a Varian-Saturn 2000 GC/MS instrument. Elemental analysis was measured by means of a Perkin Elmer 2400 CHN elemental analyzer flowchart.

2.2. Preparation of silica-bonded N-propyl diethylenetriamine sulfamic acid (SBPDSA)

The catalyst was prepared as per the previously reported method (Sefat et al., 2011). The catalyst SBPDSA was obtained as a white powder. The content of S obtained from elemental analysis showed that typically a loading of 0.99 mmol/g H^+ was obtained (Rahi et al., 2012).



Scheme 1 Preparation of various 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta [*b*]pyran-3-carbonitrile derivatives.

2.3. General procedure to synthesis of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[b] pyran-3-carbonitrile derivatives using Alum ($KAl(SO_4)_2.12H_2O$) (10 mol%) as catalyst

A mixture of aldehydes **1** (1 mmol), malononitrile **2** (1 mmol), cyclopentane-1,3-dione **3** (1 mmol), and powdered Alum ($KAl(SO_4)_2{\cdot}12H_2O$) (10 mol%), under solvent-free conditions was stirred at 70 °C for appropriate time (Scheme 1). The progress of the reaction was monitored by TLC. After completion, the reaction was allowed to cool, ethanol (20 mL) was added and the catalyst was recovered to use subsequently by filtration. Concentration of the filtrate and recrystallization of the solid residue from hot ethanol afforded the crystals of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitriles in high yield. The recovered catalyst can be washed consequently with an aliquot of fresh CH_2Cl_2 (2 × 10 mL), water and then acetone. After drying, it can be reused without noticeable loss of reactivity. Compounds **4a–j** were identified by IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analysis.

2.4. Spectral data for the synthesized compounds (**4a–j**)

2.4.1. 2-Amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4a**)

IR (KBr, cm^{-1}): 3392, 3322, 3220, 2201, 1682, 1604, 1512, 1356, 1061, 683; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.22–2.34 (m, 2H, CH_2), 2.54–2.65 (m, 2H, CH_2), 4.24 (s, 1H, CH), 6.66 (s, 2H, NH_2), 7.18 (d, J = 7.2 Hz, 2H, ArH), 7.38 (m, 3H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.0, 35.2, 39.0, 49.2, 58.3, 112.0, 119.4, 126.3, 127.3, 129.0, 144.0, 157.9, 163.0, 195.6 ppm; MS(ESI): m/z 253 $(M+H)^+$; Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.76; N, 11.11%. Found: C, 71.36; H, 4.71; N, 11.10%.

2.4.2. 2-Amino-4-(4-methylphenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4b**)

IR (KBr, cm^{-1}): 3396, 3320, 3226, 2195, 1665, 1608, 1514, 1364, 1036, 798; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.18 (s, 3H, CH_3), 2.20–2.34 (m, 2H, CH_2), 2.55–2.67 (m, 2H, CH_2), 4.19 (s, 1H, CH), 6.74 (s, 2H, NH_2), 7.22 (d, J = 7.4 Hz, 2H, ArH), 7.40 (d, J = 7.4 Hz, 2H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.7, 35.3, 38.7, 49.4, 58.0, 112.6, 119.2, 126.4, 127.3, 129.3, 143.7, 158.3, 162.9, 196.0 ppm; MS(ESI): m/z 267 $(M+H)^+$; Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.18; H, 5.26; N, 10.52%. Found: C, 72.22; H, 5.25; N, 10.50%.

2.4.3. 2-Amino-4-(4-nitrophenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4c**)

IR (KBr, cm^{-1}): 3400, 3324, 3228, 2206, 1673, 1606, 1522, 1355, 1073, 836; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.18–2.27 (m, 2H, CH_2), 2.53–2.61 (m, 2H, CH_2), 4.22 (s, 1H, CH), 6.80 (s, 2H, NH_2), 7.26 (d, J = 7.0 Hz, 2H, ArH), 7.45 (d, J = 7.1 Hz, 2H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.4, 35.4, 39.4, 49.1, 57.9, 113.0, 118.9, 125.9, 127.3, 128.9, 143.8, 158.5, 163.8, 196.2 ppm; MS(ESI): m/z

298 $(M+H)^+$; Anal. Calcd for $C_{15}H_{11}N_3O_4$: C, 60.60; H, 3.70; N, 14.14%. Found: C, 60.50; H, 3.66; N, 14.10%.

*2.4.4. 2-Amino-4-(3-bromophenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4d**)*

IR (KBr, cm^{-1}): 3403, 3318, 3212, 2207, 1678, 1611, 1510, 1360, 1074, 845; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.09–2.18 (m, 2H, CH_2), 2.44–2.53 (m, 2H, CH_2), 4.26 (s, 1H, CH), 6.85 (s, 2H, NH_2), 7.31–7.44 (m, 4H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 27.0, 36.0, 38.7, 49.7, 58.6, 113.2, 118.8, 126.3, 127.3, 128.7, 144.4, 158.8, 164.0, 195.9 ppm; MS(ESI): m/z 331.9 $(M+H)^+$; Anal. Calcd for $C_{15}H_{11}BrN_2O_4$: C, 54.40; H, 3.32; N, 8.46%. Found: C, 54.42; H, 3.30; N, 8.44%.

*2.4.5. 2-Amino-4-(4-chlorophenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4e**)*

IR (KBr, cm^{-1}): 3394, 3331, 3214, 2208, 1669, 1600, 1515, 1362, 1071, 844; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.16–2.28 (m, 2H, CH_2), 2.51–2.63 (m, 2H, CH_2), 4.16 (s, 1H, CH), 6.74 (s, 2H, NH_2), 7.25 (d, J = 7.2 Hz, 2H, ArH), 7.38 (d, J = 7.2 Hz, 2H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.8, 36.1, 39.4, 49.4, 58.6, 112.8, 119.4, 126.5, 127.3, 128.4, 144.0, 158.6, 163.6, 196.1 ppm; MS(ESI): m/z 287 $(M+H)^+$; Anal. Calcd for $C_{15}H_{11}ClN_2O_2$: C, 62.84; H, 3.84; N, 9.77%. Found: C, 62.77; H, 3.80; N, 9.75%.

*2.4.6. 2-Amino-4-(3-hydroxyphenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4f**)*

IR (KBr, cm^{-1}): 3432, 3390, 3329, 3219, 2196, 1680, 1598, 1524, 1351, 1066, 856; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.11–2.23 (m, 2H, CH_2), 2.55–2.66 (m, 2H, CH_2), 4.21 (s, 1H, CH), 6.80 (s, 2H, NH_2), 7.34–7.49 (m, 4H, ArH), 9.48 (s, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 27.2, 35.7, 38.6, 50.0, 59.0, 113.4, 118.8, 125.7, 127.3, 129.0, 143.6, 158.4, 163.8, 195.7 ppm; MS(ESI): m/z 269 $(M+H)^+$; Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.48; N, 10.45%. Found: C, 67.10; H, 4.44; N, 10.40%.

*2.4.7. 2-Amino-4-(4-hydroxyphenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4g**)*

IR (KBr, cm^{-1}): 3466, 3401, 3333, 3289, 2194, 1677, 1596, 1525, 1358, 1074, 844; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.06–2.14 (m, 2H, CH_2), 2.43–2.56 (m, 2H, CH_2), 4.27 (s, 1H, CH), 6.82 (s, 2H, NH_2), 7.19 (d, J = 7.1 Hz, 2H, ArH), 7.35 (d, J = 7.2 Hz, 2H, ArH), 9.56 (s, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.5, 36.1, 39.3, 50.2, 58.4, 112.7, 118.7, 126.7, 127.3, 129.2, 144.2, 158.4, 163.0, 196.2 ppm; MS(ESI): m/z 269 $(M+H)^+$; Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.48; N, 10.45%. Found: C, 67.06; H, 4.45; N, 10.43%.

*2.4.8. 2-Amino-4-(4-N,N-dimethylaminophenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4h**)*

IR (KBr, cm^{-1}): 3398, 3320, 3210, 2199, 1672, 1604, 1516, 1364, 1033, 855; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.20–2.32 (m, 2H, CH_2), 2.50–2.61 (m, 2H, CH_2), 2.72 (s, 6H, $N(CH_3)_2$), 4.29 (s, 1H, CH), 6.78 (s, 2H, NH_2), 7.26 (d, J = 7.2 Hz, 2H, ArH), 7.41 (d, J = 7.2 Hz, 2H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 27.2, 37.3, 38.6, 49.6, 59.2, 112.9, 118.7, 126.3, 127.3, 129.3, 144.5, 158.0, 163.4, 196.1 ppm; MS(ESI): m/z 296 $(M+H)^+$; Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.15; H, 5.76; N, 14.23%. Found: C, 69.07; H, 5.71; N, 14.19%.

*2.4.9. 2-Amino-4-(3-methylphenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4i**)*

IR (KBr, cm^{-1}): 3388, 3322, 3222, 2204, 1675, 1607, 1514, 1362, 1077, 790; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.12–2.19 (m, 2H, CH_2), 2.24 (s, 3H, CH_3), 2.42–2.53 (m, 2H, CH_2), 4.12 (s, 1H, CH), 6.76 (s, 2H, NH_2), 7.30–7.45 (m, 4H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 26.4, 35.7, 38.3, 50.2, 58.3, 112.9, 118.9, 125.8, 127.3, 128.8, 143.8, 157.9, 163.6, 196.0 ppm; MS(ESI): m/z 267 $(M+H)^+$; Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.18; H, 5.26; N, 10.52%. Found: C, 72.12; H, 5.22; N, 10.48%.

*2.4.10. 2-Amino-4-(3-methoxyphenyl)-5-oxo-4,5,6,7-tetrahydrocyclopenta[b]pyran-3-carbonitrile (**4j**)*

IR (KBr, cm^{-1}): 3405, 3326, 3216, 2195, 1681, 1597, 1523, 1355, 1031, 849, 762; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.13–2.24 (m, 2H, CH_2), 2.38–2.50 (m, 2H, CH_2), 3.58 (s, 3H, OCH_3), 4.17 (s, 1H, CH), 6.69 (s, 2H, NH_2), 7.19–7.33 (m, 4H, ArH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 27.4, 36.4, 38.7, 49.7, 59.3, 113.5, 118.2, 125.6, 127.3, 129.4, 144.0, 158.2, 163.7, 195.8 ppm; MS(ESI): m/z 283 $(M+H)^+$; Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 4.96; N, 9.92%. Found: C, 68.00; H, 4.94; N, 9.88%.

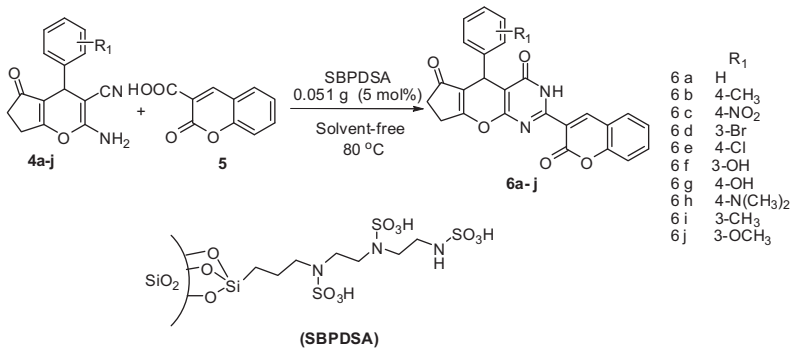
2.5. General procedure to synthesis of 7,8-dihydro-2-(2-oxo-2H-chromen-3-yl)-5-phenyl-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione derivatives using SBPDSA as catalyst

A mixture of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile **4a**–**j** (1 mmol), coumarin-3-carboxylic acid **5** (1 mmol) and SBPDSA (0.051 g/5 mol%) was heated at 80 °C for about 4–6 h (Scheme 2). After completion of the reaction (TLC), 2 mL of water was added, and the reaction mixture was stirred at room temperature for 20 min. The resulting precipitate was filtered. The crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 80:20) to provide the pure products. Compounds **6a**–**j** were identified by IR, ^1H NMR, ^{13}C NMR, mass and elemental analysis.

*2.6. Spectral data for the synthesized compounds (**6a**–**j**)*

*2.6.1. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-phenyl-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6a**)*

IR (KBr, cm^{-1}): 3411, 1713, 1659, 1620, 1599, 1211, 1066, 701; ^1H NMR (500 MHz, DMSO-d_6) δ: 2.04–2.15 (m, 2H, CH_2), 2.44–2.56 (m, 2H, CH_2), 4.44 (s, 1H, CH), 7.12 (d, J = 7.2 Hz, 2H, ArH), 7.44–7.51 (m, 3H, ArH), 7.66–7.78 (m, 4H, ArH), 8.46 (s, 1H, Coumarin), 9.48 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.5, 20.3, 26.7, 35.9, 37.2, 100.0, 113.2, 115.9, 118.2, 118.9, 124.9, 129.3, 131.0, 134.0, 136.5, 152.5, 154.6, 156.9, 164.7, 195.4 ppm; MS(ESI): m/z 425 $(M+H)^+$; Anal. Calcd for $C_{25}H_{16}N_2O_5$: C, 70.75; H, 3.77; N, 6.60%. Found: C, 70.70; H, 3.75; N, 6.58%.



Scheme 2 Preparation of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-aryl-cyclopenta[*b*] pyrano-pyrimidine-4,6-5*H*-diones.

*2.6.2. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-methylphenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6b**)*

IR (KBr, cm^{-1}): 3406, 1700, 1660, 1622, 1603, 1205, 1044, 788; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.11–2.21 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 2.52–2.64 (m, 2H, CH_2), 4.50 (s, 1H, CH), 7.22 (d, J = 7.2 Hz, 2H, ArH), 7.51 (d, J = 7.2 Hz, 2H, ArH), 7.60–7.77 (m, 4H, ArH), 8.40 (s, 1H, Coumarin), 9.40 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.6, 20.4, 26.5, 35.7, 36.9, 101.0, 113.8, 115.7, 117.9, 118.4, 124.3, 129.3, 130.5, 134.2, 137.0, 153.0, 154.0, 157.1, 163.9, 194.9 ppm; MS(ESI): m/z 439 $(M+H)^+$; Anal. Calcd for $C_{26}H_{18}N_2O_5$: C, 71.23; H, 4.11; N, 6.39%. Found: C, 71.13; H, 4.09; N, 6.36%.

*2.6.3. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-nitrophenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6c**)*

IR (KBr, cm^{-1}): 3400, 1704, 1664, 1624, 1605, 1202, 1063, 844; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.16–2.32 (m, 2H, CH_2), 2.58–2.70 (m, 2H, CH_2), 4.51 (s, 1H, CH), 7.19 (d, J = 7.2 Hz, 2H, ArH), 7.44 (d, J = 7.2 Hz, 2H, ArH), 7.62–7.75 (m, 4H, ArH), 8.33 (s, 1H, Coumarin), 9.39 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.6, 20.3, 26.6, 36.2, 37.2, 100.2, 113.1, 116.4, 118.4, 118.9, 124.9, 129.3, 130.3, 134.3, 136.4, 153.1, 154.0, 156.3, 163.5, 194.5 ppm; MS(ESI): m/z 470 $(M+H)^+$; Anal. Calcd for $C_{25}H_{15}N_3O_7$: C, 63.96; H, 3.20; N, 8.95%. Found: C, 63.88; H, 3.20; N, 2.90%.

*2.6.4. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-bromophenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6d**)*

IR (KBr, cm^{-1}): 3415, 1699, 1661, 1618, 1600, 1206, 1070, 840; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.04–2.12 (m, 2H, CH_2), 2.32–2.46 (m, 2H, CH_2), 4.46 (s, 1H, CH), 7.25–7.42 (m, 4H, ArH), 7.78–7.90 (m, 4H, ArH), 8.44 (s, 1H, Coumarin), 9.45 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.7, 20.4, 26.0, 36.3, 37.1, 100.4, 113.6, 116.0, 118.4, 119.0, 124.8, 129.3, 131.0, 134.2, 136.4, 152.8, 153.8, 156.8, 163.8, 194.9 ppm; MS(ESI): m/z 503.9 $(M+H)^+$; Anal. Calcd for $C_{25}H_{15}BrN_2O_5$: C, 59.65; H, 2.98; N, 5.56%. Found: C, 59.55; H, 2.95; N, 5.54%.

*2.6.5. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-chlorophenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6e**)*

IR (KBr, cm^{-1}): 3424, 1708, 1658, 1619, 1607, 1208, 1073, 853; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.18–2.30 (m, 2H, CH_2), 2.62–2.73 (m, 2H, CH_2), 4.39 (s, 1H, CH), 7.10 (d, J = 7.2 Hz, 2H, ArH), 7.28 (d, J = 7.2 Hz, 2H, ArH), 7.73–7.86 (m, 4H, ArH), 8.38 (s, 1H, Coumarin), 9.50 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.0, 20.0, 26.2, 35.9, 37.7, 101.3, 113.9, 115.7, 118.2, 118.8, 124.8, 129.3, 130.7, 133.8, 137.0, 153.4, 154.1, 156.7, 164.4, 195.4 ppm; MS(ESI): m/z 459.45 $(M+H)^+$; Anal. Calcd for $C_{25}H_{15}ClN_2O_5$: C, 65.43; H, 3.27; N, 6.11%. Found: C, 65.40; H, 3.25; N, 6.10%.

*2.6.6. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(3-hydroxyphenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6f**)*

IR (KBr, cm^{-1}): 3455, 3403, 1698, 1669, 1622, 1596, 1210, 1043, 846; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.02–2.12 (m, 2H, CH_2), 2.33–2.44 (m, 2H, CH_2), 4.55 (s, 1H, CH), 7.24–7.46 (m, 4H, ArH), 7.77–7.88 (m, 4H, ArH), 8.42 (s, 1H, Coumarin), 9.52 (s, 1H, NH), 9.66 (s, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.4, 20.3, 26.1, 36.4, 38.0, 100.5, 113.4, 116.3, 118.2, 118.6, 124.6, 129.3, 130.7, 134.4, 136.4, 153.2, 154.1, 157.1, 164.5, 195.5 ppm; MS(ESI): m/z 441 $(M+H)^+$; Anal. Calcd for $C_{25}H_{16}N_2O_6$: C, 68.18; H, 3.63; N, 6.36%. Found: C, 68.11; H, 3.60; N, 6.34%.

*2.6.7. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-hydroxyphenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6g**)*

IR (KBr, cm^{-1}): 3458, 3410, 1714, 1664, 1625, 1602, 1216, 1073, 840; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.21–2.28 (m, 2H, CH_2), 2.49–2.57 (m, 2H, CH_2), 4.52 (s, 1H, CH), 7.20 (d, J = 7.2 Hz, 2H, ArH), 7.38 (d, J = 7.2 Hz, 2H, ArH), 7.70–7.82 (m, 4H, ArH), 8.50 (s, 1H, Coumarin), 9.43 (s, 1H, NH), 9.72 (s, 1H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.6, 19.9, 26.8, 36.3, 38.2, 100.1, 113.3, 116.5, 118.1, 118.9, 124.8, 129.3, 130.8, 134.3, 136.4, 153.1, 154.3, 157.5, 164.0, 195.8 ppm; MS(ESI): m/z 441 $(M+H)^+$; Anal. Calcd for $C_{25}H_{16}N_2O_6$: C, 68.18; H, 3.63; N, 6.36%. Found: C, 68.20; H, 3.65; N, 6.33%.

*2.6.8. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-N,N-dimethylaminophenyl)-cyclopenta [b]pyrano-pyrimidine-4,6-5H-dione (**6h**)*

IR (KBr, cm^{-1}): 3402, 1712, 1661, 1622, 1601, 1213, 1053, 845; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.15–2.22 (m, 2H, CH_2), 2.55–2.62 (m, 2H, CH_2), 2.68 (s, 6H, $N(CH_3)_2$), 4.48 (s, 1H, CH), 7.16 (d, J = 7.2 Hz, 2H, ArH), 7.42 (d, J = 7.2 Hz, 2H, ArH), 7.65–7.79 (m, 4H, ArH), 8.55 (s, 1H, Coumarin), 9.40 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 15.9, 19.9, 26.6, 36.4, 37.0, 100.9, 113.4, 116.0, 118.1, 118.9,

124.7, 129.3, 131.2, 134.3, 136.3, 152.8, 153.9, 156.8, 164.3, 194.6 ppm; MS(ESI): *m/z* 468 $(M+H)^+$; Anal. Calcd for $C_{27}H_{21}N_3O_5$: C, 69.38; H, 4.49; N, 8.99%. Found: C, 69.31; H, 4.46; N, 8.97%.

*2.6.9. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(3-methylphenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6i**)*

IR (KBr, cm^{-1}): 3418, 1703, 1657, 1617, 1607, 1209, 1070, 796; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.17–2.29 (m, 2H, CH_2), 2.34 (s, 3H, CH_3), 2.52–2.64 (m, 2H, CH_2), 4.50 (s, 1H, CH), 7.11–7.31 (m, 4H, ArH), 7.73–7.87 (m, 4H, ArH), 8.41 (s, 1H, Coumarin), 9.38 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.2, 20.0, 26.2, 36.1, 37.1, 100.8, 113.7, 115.6, 117.9, 118.7, 124.8, 129.3, 131.4, 135.0, 137.2, 153.4, 154.1, 156.9, 164.0, 195.5 ppm; MS(ESI): *m/z* 439 $(M+H)^+$; Anal. Calcd for $C_{26}H_{18}N_2O_5$: C, 71.23; H, 4.11; N, 6.39%. Found: C, 71.20; H, 4.07; N, 6.33%.

*2.6.10. 7,8-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(3-methoxyphenyl)-cyclopenta[b]pyrano-pyrimidine-4,6-5H-dione (**6j**)*

IR (KBr, cm^{-1}): 3406, 1709, 1662, 1626, 1600, 1214, 1029, 847, 769; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.18–2.29 (m, 2H, CH_2), 2.40–2.56 (m, 2H, CH_2), 3.66 (s, 3H, OCH_3), 4.47 (s, 1H, CH), 7.18–7.33 (m, 4H, ArH), 7.76–7.90 (m, 4H, ArH), 8.39 (s, 1H, Coumarin), 9.41 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 16.3, 20.2, 26.3, 35.7, 37.0, 101.2, 114.2, 116.0, 118.3, 118.8, 125.0, 129.3, 131.4, 134.2, 136.4, 152.8, 153.8, 157.4, 166.0, 196.0 ppm; MS(ESI): *m/z* 455 $(M+H)^+$; Anal. Calcd for $C_{26}H_{18}N_2O_6$: C, 68.72; H, 3.96; N, 6.16%. Found: C, 68.61; H, 3.93; N, 6.15%.

3. Results and discussion

The synthetic pathway of compounds (**6a–j**) was achieved *via* the intermediates 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives (**4a–j**). These compounds (**4a–j**) were obtained by the three component condensation of aldehydes **1**, malononitrile **2** and cyclopentane-1,3-dione **3** using Alum ($KAl(SO_4)_2{\cdot}12H_2O$) (10 mol%), under solvent-free conditions (Scheme 1). Due to its mild and reusable catalytic activity for the synthesis of pyran derivatives (Rajguru et al., 2013), we opted to use Alum [$KAl(SO_4)_2{\cdot}12H_2O$] as a non-toxic catalyst. The aromatic aldehydes **1** bearing electron-withdrawing and electron donating groups were found to be equally effective to produce 2-amino-4*H*-pyrans **4a–j** in very good yields (Table 1).

After the synthesis of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives **4**, we have synthesized compounds **6**. To optimize the reaction conditions, the effect of catalyst loading was investigated between compound **4a** and coumarin-3-carboxylic acid. The reaction was carried out under neat conditions at 80 °C without and with different acid catalysts (cellulose sulfuric acid, silica sulfuric acid, sulfamic acid, SBPDSA each 5 mol%). The maximum yield was obtained using SBPDSA. It can be seen that the reaction did not proceed even after 12 h in the absence of this catalyst (Table 2, entry 1). Although a lower catalyst loading of 3 or 2 mol% accomplished this condensation, 5 mol% of SBPDSA was optimal in terms of reaction time and isolated yield (Table 2, entries 5 and 6). Increasing the amount from 5 to 8 mol% has no effect on the product yield and reaction time (Table 2, entry 8).

Table 1 Preparation of various 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives.[a]

Entry	R1	Product	Time (h)	Yield (%)[b]	Mp (°C)
1	H	**4a**	2.0	93	204–206
2	4-CH_3	**4b**	2.0	90	206–208
3	4-NO_2	**4c**	2.0	88	201–203
4	3-Br	**4d**	1.5	89	220–222
5	4-Cl	**4e**	1.5	90	242–244
6	3-OH	**4f**	1.5	92	212–214
7	4-OH	**4g**	2.0	90	228–230
8	4-$N(CH_3)_2$	**4h**	2.0	89	236–238
9	3-CH_3	**4i**	1.5	89	198–200
10	3-OCH_3	**4j**	2.0	92	190–192

[a] Reaction conditions: cyclopentane-1,3-dione (1 mmol), aldehyde (1 mmol) and malononitrile (1 mmol) in the presence of Alum ($KAl(SO_4)_2{\cdot}12H_2O$) (10 mol%) in solvent-free conditions at 70 °C.
[b] Isolated yield.

To expand the generality of this novel catalytic method, various cyclopenta[*b*]pyrano pyrimidinone derivatives **6a–j** (Scheme 2) were synthesized under the optimized conditions and the results are presented in Table 3. After completion of the reaction the catalyst, SBPDSA was recovered by evaporating the aqueous layer, washed with acetone, dried and reused for subsequent reactions without significant loss in its activity (Fig. 1). All the structures of the synthesized compounds **6** were confirmed by their analytical and spectroscopic data.

A probable mechanism for the formation of **6a** as a model *via* the condensation reaction is outlined in Scheme 3. Firstly, the protonation of coumarin-3-carboxylic acid by SBPDSA as a solid acid occurred to form a cation intermediate (**a**). In continuation, the formation of (**b**) resulting from the amidation of (**a**) with **4a** was established. In the next step, the protonation of nitrile group of intermediate (**b**) following by a cyclo-addition reaction occurred to form the intermediate (**c**). In continuation the addition reaction of -SO_3^- followed by ring opening of the (**c**) to the intermediate (**d**) and (**e**) followed by ring closure of intermediate (**e**) results in the formation of intermediate (**f**) that converts to the (**6a**) as product by the de-protonation reaction. Interestingly, the formation of compound **6a**, obtained from the condensation of coumarin-3-carboxylic acid with **4a**, confirms the mechanism of the reaction which was rarely described in the literature as Dimroth rearrangement (Foucourt et al., 2010; Dimroth, 1909).

The possibility of recycling the catalyst was examined using the condensation reaction of compound **4a** with coumarin-3-carboxylic acid **5** in the optimized conditions. The catalyst was recovered from the aqueous phase (filtration), washed with acetone, dried and re-used for subsequent reactions without loss of activity and efficiency. The recycled catalyst could be reused five times without any additional treatment or appreciable reduction in catalytic activity (Fig. 1).

X-ray diffraction (XRD) for SBPDSA using powder X-ray diffraction measurements was performed using Advance diffractometer made by Bruker AXS company in Germany. Scans were taken with a 2θ step size of 0.04 and a counting

Table 2 Preparation of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-cyclopenta[*b*] pyrano-pyrimidine-4,6-5*H*-dione: Effect of catalyst.[a]

Entry	Catalyst	Amount of catalyst (mol%)	Time (h)	Yield (%)[b]
1	None	0	12.0	Trace
2	Cellulose sulfuric acid	5	6.0	70
3	Silica sulfuric acid	5	6.0	73
4	Sulfamic acid	5	8.0	59
5	SBPDSA	5 (0.051 g)	4.0	90
6	SBPDSA	8 (0.081 g)	4.0	90
7	SBPDSA	3 (0.031 g)	4.0	77
8	SBPDSA	2 (0.021 g)	4.0	69

[a] Reaction conditions: **4a** (1 mmol) and coumarin-3-carboxylic acid (1 mmol) at 80 °C.
[b] Isolated yield.

Table 3 Preparation of various 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-aryl-cyclopenta [*b*]pyrano-pyrimidine-4,6-5*H*-dione derivatives.[a]

Entry	Compound **4**	Product	Time (h)	Yield (%)[b]	Mp (°C)
1	**4a**	**6a**	4.0	90	266–268
2	**4b**	**6b**	4.0	88	224–226
3	**4c**	**6c**	3.5	91	258–260
4	**4d**	**6d**	3.5	91	234–236
5	**4e**	**6e**	3.5	90	238–240
6	**4f**	**6f**	4.0	90	246–248
7	**4g**	**6g**	4.0	92	254–256
8	**4h**	**6h**	4.0	88	262–264
9	**4i**	**6i**	4.0	89	244–246
10	**4j**	**6j**	4.0	89	272–274

[a] Reaction conditions: **4a–j** (1 mmol), and coumarin-3-carboxylic acid (1 mmol) in the presence of SBPDSA (5 mol%) at 80 °C.
[b] Isolated yield.

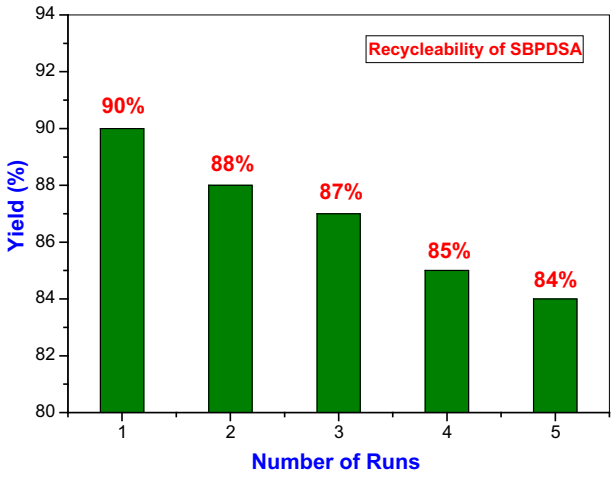


Figure 1 Recycling of catalyst SBPDSA for the synthesis of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-cyclopenta[*b*]pyrano-pyrimidine-4,6-5*H*-dione from **4a** and coumarin-3-carboxylic acid.

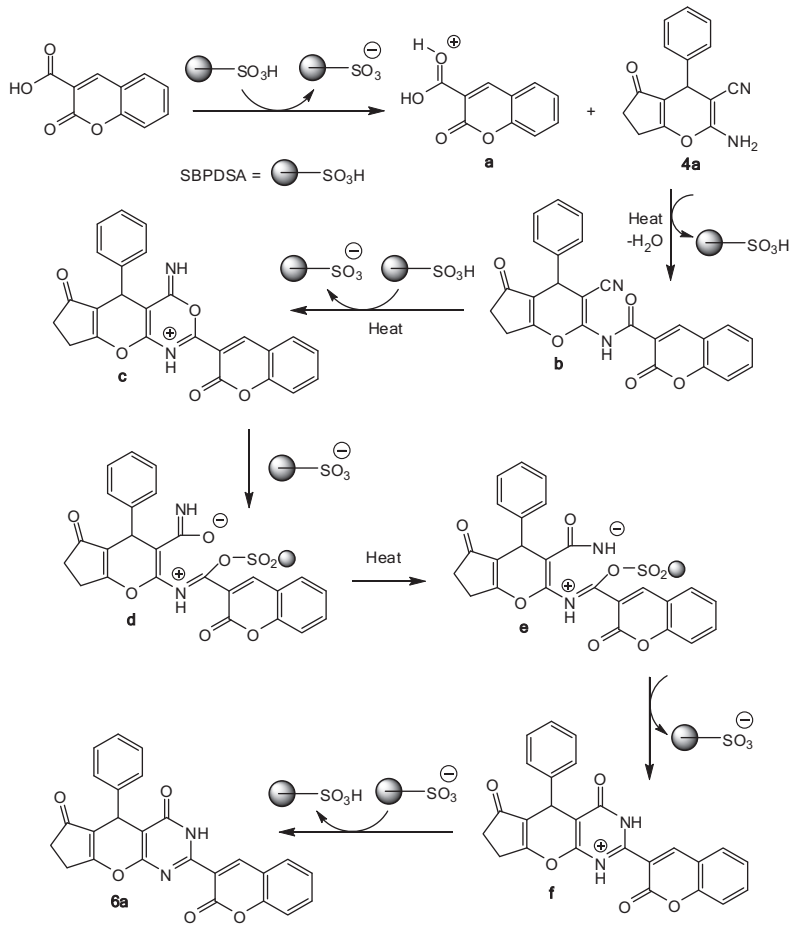
time of 30 s at room temperature. Specimens for XRD were prepared by compaction into a glass-backed aluminum sample holder. Data were collected over a 2θ range from 4° to 75°. The fresh catalyst and recovered catalyst were characterized by XRD and their pattern is presented in Fig. 2. As it is shown in Fig. 2 no significant change in the structure of catalyst was observed during the reaction.

3.1. Biological evaluations

Variously substituted on the aromatic ring, the compounds **6a–j** may be useful in understanding the influence of steric and electronic effects on biological activity. They were tested for their antibacterial and antifungal activity at different concentrations in DMSO. Ciprofloxacin and Amphotericin-B were used as the positive control drugs for antibacterial and antifungal tests, respectively. Inoculums of the bacterial and fungal cultures were also prepared. The minimum concentration at which no growth was observed was taken as the minimum inhibitory concentration (MIC) value.

3.2. Antibacterial activity

The newly synthesized compounds were screened for their *in vitro* antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* bacterial strains by the serial plate dilution method. Serial dilutions of the drug in Muller Hinton broth were taken in tubes and their *pH* was adjusted to 5.0 using phosphate buffer. A standardized suspension of the test bacterium was inoculated and incubated for 16–18 h at 37 °C. The MIC is the lowest concentration of the drug for which no growth is detected. The results are summarized in



Scheme 3 A possible mechanism for the formation of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-aryl-cyclopenta[*b*] pyrano-pyrimidine-4,6-5*H*-dione derivatives.

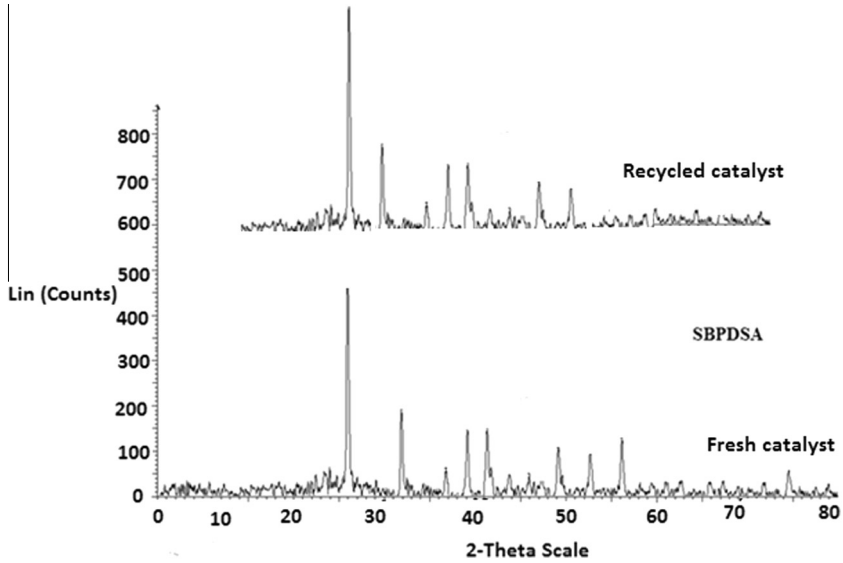


Figure 2 XRD pattern of fresh and recovered SBPDSA.

Table 4. The MIC values were evaluated at concentration range, 12.5–25 μg/mL. Upon exploration of the antibacterial activity data (Table 4), it has been observed that all compounds were found to have antibacterial activity against *E. coli*, *P. aeruginosa* and *K. pneumoniae*, and *Staphylococcus aureus* when compared with the employed standard drug.

Table 4 *In vitro* antibacterial and antifungal activities of compounds **6a–j**.

Compounds	Minimum inhibitory concentration (MIC) in μg/mL					
	Antibacterial activity			Antifungal activity		
	E. coli	*P. aeruginosa*	*K. pneumonia*	*A. flavus*	*R. schipperae*	*A. niger*
6a	150	100	150	150	150	150
6b	100	50	75	125	75	75
6c	25	25	25	50	25	50
6d	50	50	50	50	50	50
6e	75	50	75	100	75	100
6f	75	75	75	100	100	100
6g	150	150	150	150	150	150
6h	150	100	150	150	150	150
6i	75	75	75	100	75	100
6j	75	50	75	100	75	100
Ciprofloxacin	25	12.5	25	–	–	–
Amphotericin-B	–	–	–	50	25	50

3.3. Antifungal activity

Newly prepared compounds were also screened for their antifungal activity against *Aspergillus flavus*, *Rhizopus schipperae* and *Aspergillus niger* in DMSO by the serial plate dilution method. Sabourauds agar media were prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 mL) and adjusting the *pH* to 5.7. Normal saline was used to make a suspension of sore of fungal strains for lawning. Activity of each compound was compared with Amphotericin-B as standard. The results are summarized in Table 4. The MIC values were evaluated at concentration range, 25–50 μg/mL. The results given in Table 4 show that all compounds exhibited antifungal activity with MIC against *A. flavus*, *R. schipperae* and *A. niger* compared with Amphotericin-B as standard drug.

3.4. Influence of aromatic substituents

The results suggest that the antibacterial and antifungal activities are markedly influenced by the aromatic substituents. Compound **6a** without any substituent in the aryl moiety exhibits antibacterial activity *in vitro* at 150, 100 and 150 μg/ml against *E. coli*, *P. aeruginosa* and *K. pneumonia* respectively and also exhibits antifungal activity *in vitro* at 150, 150 and 150 μg/ml against *A. flavus*, *R. schipperae* and *A. niger*, respectively. Compounds **6c**, **6d** and **6e** with electron-withdrawing substituents in the aromatic ring show greater antibacterial activity than the other compounds against all the tested organisms. Also, compounds **6c** and **6d** show greater antifungal activity than all the other compounds against all the tested organisms. The aromatic substituents in **6c** and **6e** have positive values for the Hammett substituent constant σ_p [NO_2 (+0.78) and Cl (+0.23)] and the aromatic substituent in **6d** also has positive value for the Hammett substituent constant σ_m [Br (+0.40)]. The aromatic substituents in **6b** and **6h** have negative values for the Hammett substituent constant σ_p [CH_3 (−0.17) and $N(CH_3)_2$ (−0.205)] and the aromatic substituent in **6i** also has negative value for the Hammett substituent constant σ_m [CH_3 (−0.069)]. The Hammett substituent constant σ for the aromatic substituents in **6f** and **6g** is σ_m OH (+0.12) and σ_p OH (−0.37), respectively. Hence, **6f** is more active than **6g**.

3.5. Acute toxicity

The median lethal doses (LD_{50}) of the synthesized compounds **6a–j** were determined in mice (Sztaricskai et al., 1999). Groups of male adult mice, each of six animals, were injected i.p. with graded doses of each of the test compounds. The percentage of mortality in each group of animals was determined 24 h, after injection. Computation of LD_{50} was processed by a graphical method. The LD_{50} values for **6a–j** were 20–30 times higher than its MIC.

4. Conclusions

We have developed a green and simple protocol for the synthesis of 7,8-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-cyclopenta[*b*]pyrano-pyrimidine-4,6-5*H*-dione derivatives *via* the condensation of 2-amino-4-phenyl-5-oxo-4,5,6,7-tetrahydrocyclopenta[*b*]pyran-3-carbonitrile derivatives and coumarin-3-carboxylic acid using SBPDSA as an efficient novel catalyst. This procedure is a promising strategy and has advantages such as easy workup and eco-friendliness. It is expected that the present methodology will find application in organic synthesis. All the synthesized compounds were screened for their *in vitro* antimicrobial activity compared to the standard drug Ciprofloxacin and Amphotericin-B for antibacterial and antifungal activity respectively.

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References

Asadipour, A., Alipour, M., Jafari, M., Khoobi, M., Emami, S., Nadri, H., Sakhteman, A., Moradi, A., Sheibani, V., Moghadam, F.H., Shafiee, A., Foroumadi, A., 2013. Novel coumarin-3-carboxamides bearing *N*-benzylpiperidine moiety as potent acetylcholinesterase inhibitors. Eur. J. Med. Chem. 70, 623–630.

Augustine, J.K., Bombrun, A., Ramappa, B., Boodappa, C., 2012. An efficient one-pot synthesis of coumarins mediated by propylphos-

phonic anhydride (T3P) via the Perkin condensation. Tetrahedron Lett. 53, 4422–4425.

Avin, B.R.V., Thirusangu, P., Ranganatha, V.L., Firdouse, A., Prabhakar, B.T., Khanum, S.A., 2014. Synthesis and tumor inhibitory activity of novel coumarin analogs targeting angiogenesis and apoptosis. Eur. J. Med. Chem. 75, 211–221.

Banothu, J., Bavanthula, R., 2012. Brønsted acidic ionic liquid catalyzed highly efficient synthesis of chromeno pyrimidinone derivatives and their antimicrobial activity. Chin. Chem. Lett. 23, 1015–1018.

Dimroth, O., 1909. Ueber intramolekulare Umlagerungen. Umlagerungen in der Reihe des 1, 2, 3-triazols. Justus Liebigs Ann. Chem. 364, 183–226.

Foucourt, A., Dubouilh-Benard, C., Chosson, E., Corbiere, C., Buquet, C., Iannelli, M., Leblond, B., Marsais, F., Besson, T., 2010. Microwave-accelerated Dimroth rearrangement for the synthesis of 4-anilino-6-nitroquinazolines. Application to an efficient synthesis of a microtubule destabilizing agent. Tetrahedron 66, 4495–4502.

Ghashang, M., Mansoor, S.S., Aswin, K., 2013. Synthesis and in vitro microbiological evaluation of novel series of 8-hydroxy-2-(2-oxo-2H-chromen-3-yl)-5-phenyl-3H-chromeno[2,3-d]pyrimidin-4(5H)-one derivatives catalyzed by reusable silica-bonded *N*-propylpiperazine sulfamic acid. Res. Chem. Intermed. http://dx.doi.org/10.1007/s11164-013-1419-2.

Ghashang, M., Aswin, K., Mansoor, S.S., 2014a. An eco-friendly catalytic route for one-pot synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives by silica-supported perchloric acid ($HClO_4$–SiO_2) under solvent-free conditions. Res. Chem. Intermed. 40, 1135–1145.

Ghashang, M., Mansoor, S.S., Aswin, K., 2014b. Pentafluorophenylammonium triflate (PFPAT) catalyzed facile construction of substituted chromeno[2,3-d]pyrimidinone derivatives and their antimicrobial activity. J. Adv. Res. 5, 209–218.

Ghosh, P.P., Das, A.R., 2012. Nano crystalline ZnO: a competent and reusable catalyst for one pot synthesis of novel benzylamino coumarin derivatives in aqueous media. Tetrahedron Lett. 53, 3140–3143.

Jashari, A., Imeri, F., Ballazhi, L., Shabani, A., Mikhova, B., Drager, G., Popovski, E., Huwiler, A., 2014. Synthesis and cellular characterization of novel isoxazolo- and thiazolo hydrazinylidene-chroman-2,4-diones on cancer and non-cancer cell growth and death. Bioorg. Med. Chem. 22, 2655–2661.

Kawate, T., Iwase, N., Shimizu, M., Stanley, S.A., Wellington, S., Kazyanskaya, E., Hung, D.T., 2013. Synthesis and structure–activity relationships of phenyl-substituted coumarins with antitubercular activity that target FadD32. Bioorg. Med. Chem. Lett. 23, 6052–6059.

Khan, A.T., Lal, M., Ali, S., Khan, M.M., 2011. One-pot three-component reaction for the synthesis of pyran annulated heterocyclic compounds using DMAP as a catalyst. Tetrahedron Lett. 52, 5327–5332.

Khan, A.T., Das, D.K., Islam, K., Das, P., 2012. A simple and expedient synthesis of functionalized pyrido[2,3-*c*]coumarin derivatives using molecular iodine catalyzed three-component reaction. Tetrahedron Lett. 53, 6418–6422.

Khoobi, M., Ramazani, A., Foroumadi, A.R., Hamadi, H., Hojjati, Z., Shafiee, A., 2011. Efficient microwave-assisted synthesis of 3-benzothiazolo and 3-benzothiazolino coumarin derivatives catalyzed by heteropoly acids. J. Iran. Chem. Soc. 8, 1036–1042.

Khurana, J.M., Kumar, S., 2009. Tetrabutylammonium bromide (TBAB): a neutral and efficient catalyst for the synthesis of biscoumarin and 3,4-dihydropyrano[*c*]chromene derivatives in water and solvent-free conditions. Tetrahedron Lett. 50, 4125–4127.

Rahi, T., Baghernejad, M., Niknam, K., 2012. Silica-bonded *N*-propyl diethylenetriamine sulfamic acid as a recyclable solid acid catalyst for the synthesis of α-aminonitriles. Chin. J. Catal. 33, 1095–1100.

Rajguru, D., Keshwal, B.S., Jain, S., Bhagwat, V.W., 2013. Alum [$KAl(SO_4)_2 \cdot 12H_2O$]: a green and efficient catalyst for synthesis of pyrano[4,3-*b*]pyrans in water under conventional and microwave conditions. Monatsh. Chem. 144, 1411–1416.

Renuka, N., Kumar, K.A., 2013. Synthesis and biological evaluation of novel formyl-pyrazoles bearing coumarin moiety as potent antimicrobial and antioxidant agents. Bioorg. Med. Chem. Lett. 23, 6406–6409.

Sashidhara, K.V., Modukuri, R.K., Choudhary, D., Rao, K.B., Kumar, M., Khedgikar, V., Trivedi, R., 2013. Synthesis and evaluation of new coumarine pyridine hybrids with promising anti-osteoporotic activities. Eur. J. Med. Chem. 70, 802–810.

Sefat, M.N., Deris, A., Niknam, K., 2011. Preparation of silica-bonded propyl-diethylene-triamine-*N*-sulfamic acid as a recyclable catalyst for chemoselective synthesis of 1,1-diacetates. Chin. J. Chem. 29, 2361–2367.

Sztaricskai, F., Takacs, E.I., Pusztai, F., Szabo, G., Csipo, I., 1999. Antiulcer effect of 5-amino salicylic acid. Arch. Pharm. Med. Chem. 332, 321–326.

Witaicenis, A., Seito, L.N., da Silveira Chagas, A., de Almeida Jr., L.D., Luchini, A.C., Rodrigues-Orsi, P., Cestari, S.H., Di Stasi, L.C., 2014. Antioxidant and intestinal anti-inflammatory effects of plant-derived coumarin derivatives. Phytomedicine 21, 240–246.

Zhang, W., Li, Z., Zhou, M., Wu, F., Hou, X., Luo, H., Liu, H., Han, X., Yan, G., Ding, Z., Li, R., 2014. Synthesis and biological evaluation of 4-(1,2,3-triazol-1-yl)coumarin derivatives as potential antitumor agents. Bioorg. Med. Chem. Lett. 24, 799–807.

Zhao, L., Yao, Y., Li, S., Lv, M., Chen, H., Li, X., 2014. Cytotoxicity and DNA binding property of triphenylethylene-coumarin hybrids with two amino side chains. Bioorg. Med. Chem. Lett. 24, 900–904.