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# TBBDA CATALYZED ONE-POT PSEUDO FOUR-COMPONENT SYNTHESIS OF BENZIMIDAZOLYL CHROMENO [2,3-*D*] PYRIMIDINES AND THEIR ANTIMICROBIAL ACTIVITY

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## ABSTRACT

Multi component reactions (MCRs), because of their productivity, simple procedures, time-saving manner, convergence and facile execution, are one of the best tools in organic synthesis. MCRs, particularly those performed in environmentally friendly media, have been increasingly useful tools for the synthesis of biologically important compounds because of their environmentally friendly, atom economy, and green characteristics.

**KEYWORDS:** N, N N', N'- tetrabromobenzene-1,3- disulfonamide (TBBDA), one-pot *p*seudo four component synthesis, benzimidazolyl chromeno [2,3-*d*] pyrimidines, antimicrobial activity.

## INTRODUCTION

Multi- component reactions (MCRs) have proved to be highly successful in generating products in a one-pot synthetic operation.[1] The development of new multi-component reactions[2] is an area of considerable interest, because a large number of new products could be synthesized by these methods. High selectivity, high atom-economy, rapid and facility are central issues in MCRs. Chromeno pyrimidines are important pharmacophores that exhibit anti-inflammatory, anti aggregating, anti-platelet, analgesic and antithrombic and anticancer activities.[3,7] Benzimidazole derivatives are unique and possess broad spectrum pharmacological properties such as antihistaminic, antipyritic, anti-ulcerative, antiallergic and effective against the human cyto megalovirus (HCMY), and are also selective neuropeptide YY1 receptor antagonists.[8-11]

In view of the pharmaceutical importance of chromeno pyrimidines and benzimidazoles, we have developed a synthetic strategy in which both these phrmacophores are accomdated. Literature survey revealed that when one biodynamic heterocyclic system was coupled with another, a new analogue with enhanced biological activity was produced.[12-14] As a part of our research in organic synthesis, we herein report one-pot eco-friendly *p*seudo four-component synthesis of some new benzimidazolyl chromeno[2,3-*d*]pyrimidines catalyzed by N, N N', N'-tetrabromo –benzene -1,3-disulfanamide (TBBDA).

## EXPERIMENTAL METHOD

All the melting points were determined on a Cintex melting point apparatus and are uncorrected. Analytical TLC was performed on Merck precoated 60 $F_{254}$ silica gel plates. Visualization was done by exposing to iodine vapour. IR spectra (KBr pellet) were recorded on a Perkin- Elmer BX series FT-IR spectrometer. $^{1}$H NMR spectra were recorded on a Brukar 300 MHz spectrometer. $^{13}$C NMR spectra were recorded on a Bruker 75 MHz spectrometer. Chemical shift values are given in δ ppm with tetramethyl silane as an internal standard. ESI -MS spectra were recorded on a Agilent LC-MSD mass spectrometer. Elemental analyses were performed on a Carlo Erba 106 and Perkin-Elmer model 240 analyzers.

### General procedure for the synthesis of 2-(4-(1H-benzo[d]imidazol-1-yl)-5H-chromeno [2,3-d]pyrimidin-2-yl)phenols (4a-4k).

A mixture of salicylaldehyde **(2)** (2.0 mmol), malononitrile **(3)** (1.0 mmol), benzimidazole **(1)** (1.0 mmol), and TBBDA (1.10 mmol) were stirred in ethanol (10 mL) at room temperature for 12 h. The progress of the reaction was monitored by thin-layer chromatography [n-hexane/acetone (10:3)]. After completion of the reaction, the mixture was cooled to room temperature. Then, ethanol was added to the mixture. The solid product was collected by filtration, washed with ethanol, and purified by recrystallization from ethanol. After evaporation of the filtrate ethanol, cool methylene dichloride (2mL) was added, and the catalyst was recovered.

### Spectral data of compounds (4a-k)

**2-(4-(1H-Benzo[d]imidazol-1-yl)-5H-chromeno [2,3-d]pyrimidin-2-yl)phenol 4a**

yield. 85%, m.p. 202-04$^{o}$C. IR (KBr, cm$^{-1}$) : 3259 (OH), 1534 (-C=N)1130 (C-O-C); $^{1}$H NMR(300 MHz, $CDCl_3$, ppm): δ 3.91 (s, 2H, $CH_2$), 6.89-7.32 (m, 12 H, Ar-H), 8.08 (1H, benzimidazole-ring-H), 13.05 (bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$,

ppm): δ 23.63, 107.58, 115.31, 115.80, 116.39, 118.53, 121.20, 121.93, 123.05, 123.19, 124.63, 126.83, 128.83, 129.78, 130.10, 130.23, 135.25, 138.95, 143.30, 150.11, 155.32, 160.73, 169.65, 172.74. MS (ESI): *m/z* 393 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{16}N_4O_2$ . C, 73.46; H, 4.08; N, 14.28; Found : C, 73.44; H,4.11; N, 14.30%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-9-methyl-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-methylphenol 4b**: Yield. 89%, m.p. 210-12 $^oC$; IR (KBr, $cm^{-1}$): 3245 (OH), 1539 (-C=N), 1138 (C-O-C); $^1H$ NMR (300MHz, $CDCl_3$, ppm): δ 2.35 (s, 6H, $CH_3$), 3.94 (s, 2H, $CH_2$), 6.85-7.39 (m, 10 H, Ar-H), 8.10 (1H, benzimidazolering-H), 13.08 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm) δ: 23.63, 24.48, 24.52, 107.62, 115.35, 115.92, 116.34, 118.65, 121.43, 121.99, 123.11, 123.26, 124.68, 126.88, 128.92, 129.87, 130.16, 130.34, 135.29, 138.98, 143.39, 150.24, 155.52, 160.81, 169.70, 172.79. MS(ESI): *m/z* 421 $[M+H]^+$. Anal. Calcd. for $C_{26}H_{20}N_4O_2$ . C, 74.28; H, 4.76; N, 13.33. Found: C, 74.26; H, 4.77; N, 13.36%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-9-methoxy-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-methoxyphenol 4c**: Yield, 87%, m.p. 215-17 $^oC$; IR (KBr, $cm^{-1}$): 3240 (OH), 1541 (-C=N), 1139 (C-O-C); $^1H$ NMR(300 MHz, $CDCl_3$, ppm): δ 3.85 (s, 6H, $OCH_3$), 3.96 (s, 2H, $CH_2$), 6.88-7.45 (m, 10 H, Ar-H), 8.13 (1H, benzimidazole ring-H), 13.01 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm) δ : 23.61, 63.44, 63.54, 107.68, 115.39, 115.98, 116.40, 118.75, 121.48, 121.91, 123.21, 123.30, 124.76, 126.93, 128.99, 129.89, 130.21, 130.39, 135.32, 139.01, 143.41, 150.25, 155.59, 160.89, 169.75, 172.85. MS (ESI): *m/z* 453 $[M+H]^+$, Anal. Calcd. for $C_{26}H_{20}N_4O_4$ . C, 69.02; H, 4.42; N, 12.38. Found: C, 69.05; H, 4.45; N, 12.41%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-9-chloro-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-chlorophenol *(*4d*)*:** Yield: 80%, m.p. 230-32 $^oC$; IR (KBr, $cm^{-1}$): 3263 (OH), 1545 (-C=N), 1139 (C-O-C); $^1H$ NMR(300 MHz, $CDCl_3$, ppm): δ 3.95 (s, 2H, $CH_2$), 6.95-7.54 (m, 10 H, Ar-H), 8.16 (1H, benzimidazole ring-H), 13.10 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, CDCl3): δ 23.69, 107.67, 115.40, 115.89, 116.42, 118.58, 121.28, 121.99, 123.08, 123.29, 124.69, 126.91, 128.88, 129.81, 130.17, 130.26, 135.35, 139.02, 143.39, 150.18, 155.38, 160.78, 169.73, 172.81. MS (ESI): *m/z* 461 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{14}Cl_2N_4O_2$ .C, 62.60; H, 3.04; N, 12.17. Found: C, 62.57; H,3.08; N, 12.20.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-9-bromo-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-bromophenol 4e:** Yield, 80%, m.p. 242-44$^{o}$C; IR (KBr, cm-$^{1}$): 3271 (OH), 1549 (-C=N), 1145 (C-O-C); $^{1}$H NMR(300 MHz, $CDCl_3$, ppm): δ 3.97 (s, 2H, $CH_2$), 6.98-7.59 (m, 10 H, Ar-H), 8.19 (1H, benzimidazole ring-H), 13.15 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm) δ: 23.71, 107.71, 115.49, 115.92, 116.48, 118.61, 121.32, 122.01, 123.12, 123.31, 124.67, 126.97, 128.91, 129.89, 130.19, 130.32, 135.45, 139.11, 143.47, 150.23, 155.42, 160.81, 169.78, 172.93.MS(ESI): *m/z* 549 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{14}Br_2N_4O_2$. Anal. Calcd. for C, 52.55; H, 2.55; N, 10.21. Found: C, 52.58; H, 2.57; N, 10.24.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-9-nitro-5H-chromeno[2,3-d]pyrimidin-2-yl)-6-nitrophenol 4f:** Yield, 80%, m.p. 238-40$^{o}$C; IR (KBr, cm$^{-1}$): 3292 (OH), 1556 (-C=N), 1149 (C-O-C); $^{1}$H NMR(300 MHz, $CDCl_3$, ppm) δ : 3.99 (s, 2H, $CH_2$), 6.98-7.70 (m, 10 H, Ar-H), 8.21 (1H, benzimidazole ring-H), 13.19 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm): δ 23.75, 107.78, 115.51, 115.98, 116.49, 118.69, 121.38, 122.11, 123.23, 123.41, 124.71, 126.99, 128.98, 129.85, 130.21, 130.38, 135.51, 139.25, 143.51, 150.28, 155.49, 160.88, 169.81, 173.21. MS (ESI): *m/z* 483 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{14}N_6O_6$. C, 59.75; H, 2.90; N, 17.42; Found: C, 59.78; H,2.93; N, 17.46%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-7-methoxy-5H-chromeno[2,3-d]pyrimidin-2-yl)-4-methoxyphenol 4g:** Yield, 85%, m.p. 220-22$^{o}$C; IR (KBr, cm$^{-1}$): 3262 (OH), 1539 (-C=N) 1143 (C-O-C); $^{1}$H NMR(300 MHz, $CDCl_3$, ppm) δ: 3.88 (s, 6H, $OCH_3$), 3.92 (s, 2H, $CH_2$), 6.82-7.51 (m, 10H, Ar-H), 8.18 (1H, benzimidazole ring-H), 13.09 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm): δ 23.66, 63.42, 63.59, 107.71, 115.35, 115.89, 116.47, 118.79, 121.51, 121.98, 123.25, 123.36, 124.79, 126.99, 128.90, 129.93, 130.28, 130.44, 135.37, 139.07, 143.47, 150.29, 155.66, 160.94, 169.82, 172.93. MS (ESI): *m/z* 453 $[M+H]^+$, Anal. Calcd. for $C_{26}H_{20}N_4O_4$. C, 69.02; H, 4.42; N, 12.38. Found: C, 69.04; H, 4.26; N, 12.36%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-7-chloro-5H-chromeno[2,3-d]pyrimidin-2-yl)-4-chlorophenol 4h:** Yield, 78%, m.p. 235-37$^{o}$C; IR (KBr, cm$^{-1}$): 3268 (OH), 1547 (-C=N), 1142 (C-O-C); $^{1}$H NMR(300 MHz, $CDCl_3$, ppm) δ: 3.99 (s, 2H, $CH_2$), 6.97-7.58 (m, 10 H, Ar-H), 8.19 (1H, benzimidazole ring-H), 13.14 (bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm): δ 23.71, 107.73, 115.45, 115.91, 116.48, 118.61, 121.35, 122.02, 123.11, 123.34, 124.63, 126.98, 128.90, 129.88, 130.22, 130.29, 135.45, 139.11, 143.32,

150.22, 155.47, 160.83, 169.79, 172.92. MS (ESI): *m/z* 461 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{14}Cl_2N_4O_2$ . C, 62.60; H, 3.04; N, 12.17. Found: C, 62.59; H,3.01; N, 12.15%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-7-bromo-5H-chromeno[2,3-d]pyrimidin-2-yl)-4-bromophenol (4i):** Yield: 77%, m.p. 249-51$^oC$; IR (KBr, $cm^{-1}$): 3277 (OH), 1561 (-C=N), 1153 (C-O-C); 1H NMR(300 MHz, $CDCl_3$, ppm) δ: 3.98 (s, 2H, $CH_2$), 6.99-7.61 (m, 10 H, Ar-H), 8.21 (1H, benzimidazole ring-H), 13.12 (bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm) δ: 23.62, 107.77, 115.52, 115.98, 116.51, 118.67, 121.38, 122.09, 123.18, 123.37, 124.72, 127.02, 128.96, 129.91, 130.21, 130.36, 135.51, 139.16, 143.51, 150.28, 155.48, 160.88, 169.83, 172.82.MS (ESI): *m/z* 549 $[M+H]^+$, Anal. Calcd. for: $C_{24}H_{14}Br_2N_4O_2$: Anal. Calcd. (%) For C, 52.55; H, 2.55; N, 10.21. Found: C, 52.56; H, 2.54; N, 10.19%.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-7,9-dichloro-5H-chromeno[2,3-d]pyrimidin-2-yl)-4,6-dichlorophenol 4j:** Yield, 76%, m.p. 256-58$^0C$; IR (KBr, cm-1): 3275 (OH), 1559 (-C=N), 1155 (C-O-C); $^1$H NMR(300 MHz, CDCl3, ppm) δ: 3.99 (s, 2H, $CH_2$), 6.97-7.63 (m, 9 H, Ar-H), 8.20 (1H, benzimidazole ring-H), 13.17 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$ CNMR (75MHz, $CDCl_3$, ppm) δ: 23.79, 107.87, 115.51, 115.98, 116.51, 118.68, 121.41, 122.11, 123.19, 123.43, 124.69, 127.02, 128.98, 129.91, 130.27, 130.31, 135.51, 139.22, 143.38, 150.28, 155.53, 160.89, 169.86, 172.98. MS(ESI): *m/z* 529 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{12}Cl_4N_4O_2$. C, 54.54; H, 2.27; N, 10.60. Found: C, 54.58; H, 2.30; N, 10.62.

**2-(4-(1H-Benzo[d]imidazol-1-yl)-7,9-dibromo-5H-chromeno[2,3-d]pyrimidin-2-yl)-4,6-dibromophenol 4k:** Yield, 77%, m.p. 262-70 $^oC$; IR (KBr, $cm^{-1}$): 3277 (OH), 1561 (-C=N), 1153 (C-O-C); $^1$H NMR (300 MHz, CDCl3, ppm) δ: 3.98 (s, 2H, $CH_2$), 6.99-7.61 (m, 10 H, Ar-H), 8.21 (1H, benzimidazole ring-H), 13.12 ( bs, 1H, OH, $D_2O$ exchangeable); $^{13}$CNMR (75MHz, $CDCl_3$, ppm) δ: 23.62, 107.77, 115.52, 115.98, 116.51, 118.67, 121.38, 122.09, 123.18, 123.37, 124.72, 127.02, 128.96, 129.91, 130.21, 130.36, 135.51, 139.16, 143.51, 150.28, 155.48, 160.88, 169.83, 172.82. MS (ESI): *m/z* 705 $[M+H]^+$, Anal. Calcd. for $C_{24}H_{12}Br_4N_4O_2$ . C, 40.90; H, 1.70; N, 7.98; Found: C, 40.87; H, 1.74; N, 7.95%.

## ANTIBACTERIAL ACTIVITY

The ready-made nutrient broth medium (Himedia, 24 g) was suspended in distilled water (100 mL) and heated until it dissolved completely. The medium and test tubes were autoclaved at a pressure of 15 lb/inc2 for 20 min. A set of sterilized test tubes with nutrient

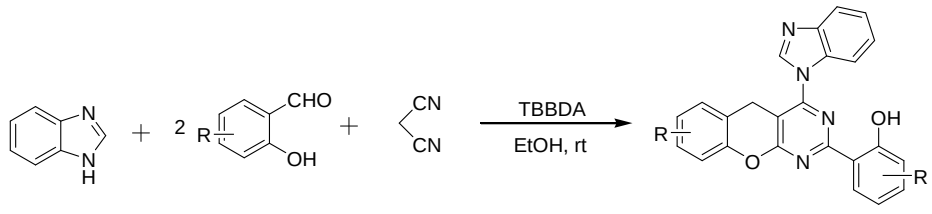
broth medium was capped with cotton plugs. The test compound was dissolved in acetone and a concentration of 100µg/mL of the test compound was added in the first test tube, which was serially diluted. A fixed volume of 0.5 mL of overnight culture was added in all the test tubes which were incubated at 37 $^0$C for 24 h. After 24 h these tubes were measured for turbidity.

## ANTIFUNGAL ACTIVITY

For the antifungal assay, the ready-made potato dextrose agar medium (Himedia, 39 g) was suspended in distilled water (100 mL) and heated until it dissolved completely. The medium and glass petri dishes were autoclaved at a pressure of 15 lb/in C2 for 20 min. The medium was poured into sterile petri dishes under aseptic conditions in a Laminar flow chamber. When the medium in the plates solidified, 0.5 mL of the culture (one-week-old) of fungal spore suspension was inoculated and uniformly spread over the agar surface with a sterile L-shaped rod. Solutions were prepared by dissolving test compound in acetone. After inoculation, cups were scooped out with 6-mm sterile cork borer and the lids of the dishes were replaced. To each cup, different concentrations of test solution were added. Controls were maintained with acetone and *fluconazole*. The treated and the controls were kept at room temperature for 72–96 h. Three to four replicates were maintained for each treatment.

## RESULTS AND DISCUSSION

The one-pot pseudo four-component reaction of benzimidazole **(1)** (1 mmol), salicylaldehyde **(2)** **(**2 mmol), and malononitrile **(3)** (1mmol) in presence of TBBDA in ethanol at room temperature afforded 2-(4-(*1H-benzo[d]imidazol-1-yl)-5H-chromeno[2,3-d]pyrimidine-2-yl)phenol* ***(*4).**




**1** **2** **3** **4**

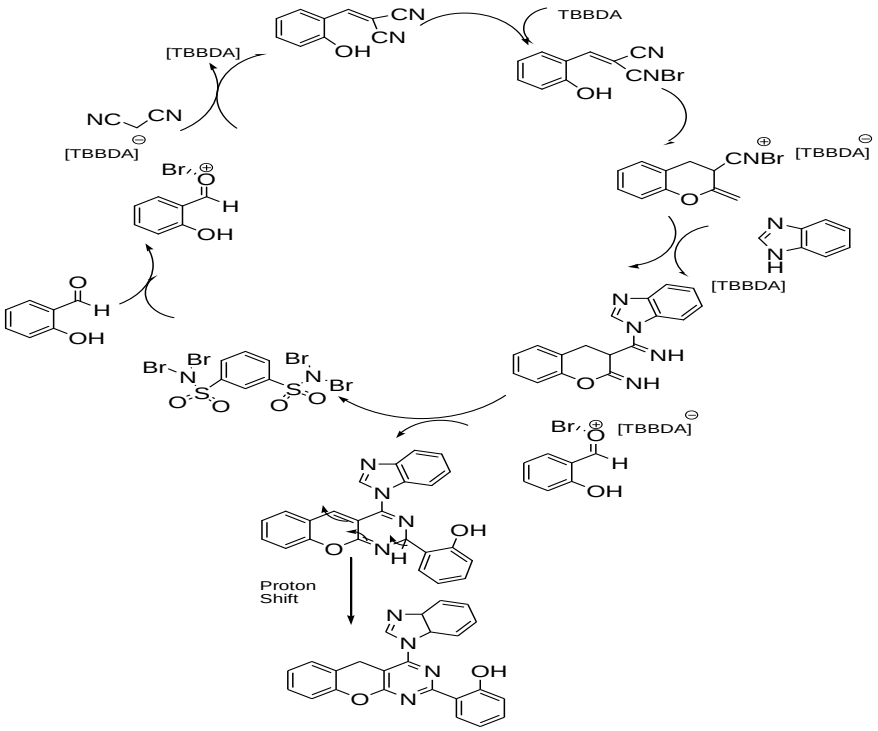
4a, R= H; 4b, R=3-$CH_3$ ; 4c, R=3-$OCH_3$ ; 4d, R=3-Cl
4e, R= 3-Br; 4f, R=3-$NO_2$ ; 4g, R= 5-$OCH_3$ ; 4h, R= 5-Cl
4i, R= 5- Br; 4j, R= 3,5 –$Cl_2$ ; 4k, R =3,5- $Br_2$ .

**Scheme1: Synthesis of 2-(4-(*1H-benzo [d] imidazol-1-yl) -5H – chromeno [2, 3 - d] pyrimidine-2-yl) phenol*s.**

To establish the feasibility of the strategy, optimize reaction conditions, different solvents such as ethyl acetate, dichloromethane, acetonitrile, $H_2O$, THF and EtOH in presence of TBBDA were screened. The best result was obtained with ethanol solvent.

The scope and generality of this one-pot pseudo four-component synthesis of benzimidazolyl chromeno [2,3-*d*] pyrimidines (4) is illustrated by conducting the reaction with substituted salicylaldehydes. In each case, the corresponding product was isolated in excellent yield (75-85%) (Scheme I).The great advantage of present procedure using TBBDA in the synthesis of benzimidazolyl chromeno[2,3-*d*]pyrimidines is the mild condition, high yield, simple experimental set-up and work up. Besides this, the reaction is equally efficient and is comparable with different functional groups *viz*.,electron releasing and electron attracting groups on salicylaldehyde ring, and the approach proved to be general applicability.

Mechanistically, it is likely that TBBDA release bromonium ion *in situ*, which acts as an electrophilic species.[15-16]. The plausible mechanism for the synthesis of benzimidazolyl chromeno[2,3-*d*] pyrimidines is shown in Scheme 2.




**Scheme 2: Suggested mechanism for the synthesis of 2-(4-(1H-benzo [*d*] imidazol-1-yl) -5H – chromeno [2, 3 - *d*] pyrimidine-2-yl)phenols.**

## ANTIMICROBIAL ACTIVITY

### ANTIBACTERIAL ACTIVITY

The newly synthesized title compounds 4a–g were evaluated for their *in vitro* antibacterial activity against Gram-*positive bacteria viz., Bacillus subtilis (Bs), Bacillus sphaericus (Bsp), and Staphylococcus aureus (Sa) and Gram-negative bacteria viz., Pseudomonas aeruginosa* (Pa), *Klobsinella aerogenes* (Ka), and *Chromobacterium violaceum* (Cv) at 100 µg/mL concentration. The *in vitro* antibacterial activity of the tested compounds was assessed by MIC using broth dilution method.[17] *Ciprofloxacin* was used as standard drug for comparison. The results of antibacterial screening (Table 1) reveal that the compounds 4a–g displayed a better activity and were more active than the standard *Ciprofloxacin*. Compounds 4b, 4c and 4g carrying methyl and methoxy substituents on the benzene ring showed better activity. Compounds 4d, 4e, and 4f carrying chloro, bromo and substitutions on benzene ring did not exhibit much activity. Compound 4a showed least activity because it has no substituent on the benzene ring. However, the degree of inhibition varied both with the test compound and with the bacteria used in the present investigation. In conclusion, compounds 4b, 4c and 4g showed maximum activity by inhibiting the growth of all the bacteria under investigation compared to standard *Ciprofloxacin*, hence can be exploited for the formulation of bacteriocides after further studies.

### ANTIFUNGAL ACTIVITY

The title compounds 4a–g were also evaluated for their antifungal activity against *Fusarium oxysporum (Fo), Verticillium dahlia (Vd), Alternaria solani (As), Rhizoctonia solani(Rs), Colletotrichum capsici (Cc),* and *Pythium aphanidermatum(Pa)* in acetone by agar cup bioassay method[18] using *fluconazole* as the standard drug, and the values are recorded in µg/mL in MIC. The antifungal activity data (Table 1) reveals that compounds 4a–g are highly toxic toward all the fungi under investigation. Compounds 4b, 4c and 4g exhibited high antifungal activity by inhibiting the growth of fungi to a remarkable extent, when compared to standard drug *fluconazole* which may be due to the presence of methyl and methoxy substituents on the benzene ring. Compound 4a showed good activity. Compounds 4d, 4e, and 4f are moderately active. However, the degree of spore germination inhibition varied with the test compound as well as with the fungi under investigation. It is noteworthy that compounds 4b, 4c and 4g showed better activity, when compared with the standard drug *fluconazole*, hence, may be exploited for control of wilt diseases of different crops as fungicides after further studies.

**Table 1: Antimicrobial activity of 2-(4-(1*H*-benzo[*d*]imidazol-1-yl)-5*H*-chromeno [2,3-*d*]pyrimidin-2-yl) phenols (4a-g).**

| Compound | Minimum Inhibitory Concentration (MIC)[a,b] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Bacterial strains | | | | | | Fungal Strains | | | | | |
| | ***Bs*** | ***Bsp*** | ***Sa*** | ***Pa*** | ***Ka*** | ***Cv*** | ***Fo*** | ***Vd*** | ***As*** | ***Rs*** | ***Cc*** | ***Pas*** |
| **4a** | 15 | 18 | 22 | 20 | 18 | 18 | 15 | 14 | 15 | 12 | 13 | 13 |
| **4b** | 8 | 7 | 8 | 8 | 7 | 6 | 8 | 8 | 6 | 8 | 7 | 7 |
| **4c** | 6 | 6 | 8 | 9 | 8 | 6 | 6 | 7 | 8 | 8 | 11 | 10 |
| **4d** | 20 | 18 | 20 | 19 | 15 | 16 | 16 | 15 | 14 | 13 | 14 | 17 |
| **4e** | 16 | 19 | 18 | 22 | 16 | 15 | 13 | 14 | 13 | 14 | 16 | 18 |
| **4f** | 18 | 14 | 14 | 18 | 16 | 16 | 15 | 13 | 18 | 14 | 15 | 19 |
| **4g** | 8 | 6 | 8 | 7 | 8 | 6 | 10 | 8 | 11 | 9 | 12 | 10 |
| *Ciprofloxacin* | 20 | 22 | 26 | 25 | 20 | 22 | - | - | - | - | | - |
| *Fluconazole* | - | - | - | - | - | - | 16 | 16 | 20 | 16 | 18 | 22 |

[a]Negative control (acetone)- no activity.

[b]Concentration 100 µg/mL.

## CONCLUSION

In conclusion, the present procedure that uses TBBDA as a catalyst provides a highly efficient green methodology for the synthesis of benzimidazolyl chromeno [2,3-*d*] pyrimidines in one-pot reaction. The significant improvements noticed in this reaction are high yields, simple method, inexpensive catalyst and easy work-up. The products are isolated in pure form by recrystallization without intervention of chromatography, making the technology practical, easy to perform and facile.

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