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# Synthesis and Characterization of novel 6-[3,5-bis(trifluoromethyl)phenyl]-4-(substitutedphenyl)-1,4-dihydropyrimidin-2-ol

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## ABSTRACT

Synthesis of various pyrimidines 3(a-o) from (E)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(substituted)phenylprop-2-en-1-one and Urea in presence of NaOH. The structures of the synthesized compounds were confirmed on the basis of spectral and elemental analysis. The synthesized compounds were screened for antimicrobial activity.

## KEYWORDS

Chalcones; (E)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(substituted)phenylprop-2-en-1-one; urea, dihydropyrimidine-2-ol compounds.

## INTRODUCTION

In recent years pyrimidine derivatives have received significant attention owing to their diverse range of biological properties particularly being antifungal[1], antitubercular[2], antibacterial[3,4], antiviral[5–8], anticancer[9] and antioxidant[10]. 2,5-Disubstituted-1,3,4-thiadiazoles represent one of the most active classes of compounds possessing wide spectrum of biological activities. 2,5-Disubstituted-1,3,4-thiadiazole derivatives exhibit in vitro antimycobacterial[11], antibacterial[12], anticancer[13,14] and antioxidant[15] properties. Considering the above facts, the goal of the present study was to combine disubstituted pyrimidines with 1,3,4-thiadiazole residues in order to develop hybrid molecules with potential of enhanced activity and to test their antioxidant and antitumor activities. Earliear we have reported[16] the synthesis of some novel chalcones of (E)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(substituted)phenylprop-2-en-1-one and as an extension of that work now we wish to report some novel pyrimidine derivatives synthesized by condensation of Urea and Chalcones in presence of Sodium hydroxide.

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## MATERIALS AND METHODS

The solvents and reagents used in the synthetic work were of analytical grade obtained from Hi-media and were purified by distillation or crystallization where necessary and their boiling or melting points were compared with the available literature values. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded FTIR Unicorn Maltson 1000 spectrophotometer**.**1H-NMR spectra were recorded on Bruker Ac-80 (80 MHz) spectrometer (300MHz in DMSO-d6) using TMS as internal standard and chemical shifts are indicated in δ (ppm). The progress of the reaction was monitored on precoated silica gel 60 F 254 plates (Merck) using different solvent systems and visualizing the spots under ultraviolet light and iodine chamber. Elemental analyses for C, H and N were carried out using a Perkin -Elmer C, H, and N analyzer.

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**General method for the preparation of 6-[3,5-bis(trifluoromethyl)phenyl]-4-(substitutedphenyl)-1,4-dihydropyrimidin-2-ol:** A mixture of (2*E*)-1-[3,5-bis(trifluoromethyl)phenyl]-3-(substituted phenyl)prop-2-en-1-one, (0.02mol), urea (0.02 mol) were dissolved in ethanolic sodium hydroxide (10ml) was stirred about 2-3 hours with a magnetic stirrer. This was then poured into 400 ml of cold water with continuous stirring for an hour and then kept in refrigerator for 24 hours. The precipitate obtained was filtered, washed and recrystallized. The completion of the reaction was monitored by TLC.

**2(a) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(2-Methoxy phenyl)-1,4-dihydropyrimidin-2-ol**

MS; m/z 416; mp 285$^{o}$C; Anal. Calcd. For $C_{19}H_{14}F_6N_2O_2$; C, 54.81; H, 3.39; F, 27.38; N, 6.73; O, 7.69; Found; C, 54.71; H, 3.26; F, 27.24; N, 6.64; O, 7.54; IR (cm-1); 3049 (C-H stretching of aromatic ring); 1012 (C-F starching); 1078 (C-H in plane deformation of aromatic ring); 3215 -3450 (b, -OH on ring), 1H NMR (DMSO-d6) ppm: 6.7 to 6.9 (m, 4H aromatic), 3.86 (s, 3H, -$OCH_3$), 7.52-7.58 (m, 3H aromatic fluorinated ring), 6.75 (w, 1H ethylene pyrimidine ring), 2.01 (w, 1H, alcohol).

Similarly remaining compounds were confirmed by element analysis and their mass spectra.

**2(b) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(2-Chloro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2O$; C, 51.38; H, 2.64; Cl, 8.43; F, 27.09; N, 6.66; O, 3.80; Found; C, 51.26; H, 2.59; Cl, 8.34; F, 27.01; N, 6.53; O, 3.72; MS; m/z 420.

**2(c) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(2-Fluoro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}F_7N_2O$; C, 53.48; H, 2.74; F, 32.90; N, 6.93; O, 3.96; Found; C, 53.39; H, 2.62; F, 32.81; N, 6.87; O, 3.84; MS; m/z 404.

**2(d) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(3-Bromo phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}BrF_6N_2O$; C, 46.47; H, 2.38; Br, 17.18; F, 24.50; N, 6.02; O, 3.44; Found; C, 46.34; H, 2.27; Br, 17.06; F, 24.38; N, 6.01; O, 3.32; MS; m/z 464.

**2(e) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(3-Chloro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2O$; C, 51.38; H, 2.64; Cl, 8.43; F, 27.09; N, 6.66; O, 3.80; Found; C, 51.25; H, 2.54; Cl, 8.38; F, 27.08; N, 6.58; O, 3.72; MS; m/z 420.

**2(f) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(3-Methoxy phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{19}H_{14}F_6N_2O_2$; C, 54.81; H, 3.39; F, 27.38; N, 6.73; O, 7.69; Found; C, 54.67; H, 3.35; F, 27.18; N, 6.54; O, 7.58; MS; m/z 416.

**2(g) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(3-4Dimethoxy phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{20}H_{16}F_6N_2O_3$; C, 53.82; H, 3.61; F, 25.54; N, 6.28; O, 7.69; Found; C, 53.63; H, 3.51; F, 25.17; N, 6.25; O, 10.54; MS; m/z 446.

**2(h) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(3,4-Dichloro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{10}Cl_2F_6N_2O$; C, 47.50; H, 2.21; Cl, 15.58; F, 25.04; N, 6.15; O, 3.51; Found; C, 47.28; H, 2.14; Cl, 15.38; F, 25.01; N, 6.02; O, 3.38; MS; m/z 454.

**2(i) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(4-Chloro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2O$; C, 51.38; H, 2.64; Cl, 8.43; F, 27.09; N, 6.66; O, 3.80; Found; C, 51.02; H, 2.42; Cl, 8.21; F, 26.99; N, 6.40; O, 3.32; MS; m/z 420.

**2(j) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(4-Fluoro phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{18}H_{11}F_7N_2O$; C, 53.48; H, 2.74; F, 32.90; N, 6.93; O, 3.96; Found; C,

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53.19; H, 2.45; F, 32.52; N, 6.67; O, 3.54; MS; m/z 404.

**2(k) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(4-Bromo phenyl)-1,4-dihydropyrimidin-2-ol**

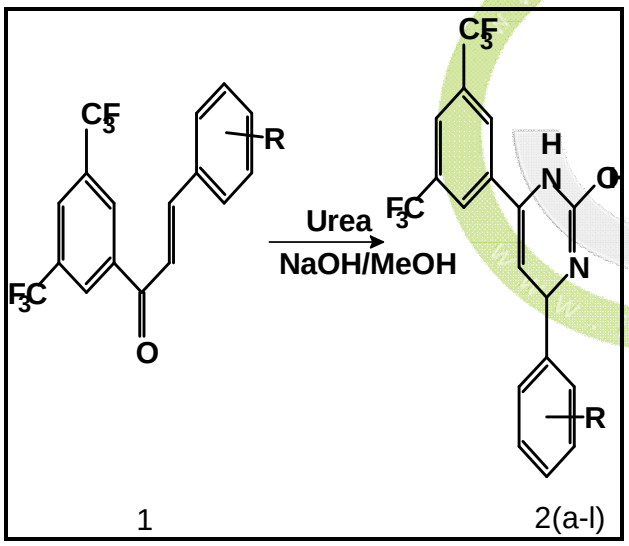
Anal. Calcd. For $C_{18}H_{11}BrF_6N_2O$; C, 46.47; H, 2.38; Br, 17.18; F, 24.50; N, 6.02; O, 3.44; Found; C, 46.21; H, 218; Br, 17.01; F, 24.26; N, 6.09; O, 3.21; MS; m/z 464.

**2(l) 6-[3,5-bis(trifluoromethyl)phenyl]-4-(2,4-Dimethyl phenyl)-1,4-dihydropyrimidin-2-ol**

Anal. Calcd. For $C_{20}H_{16}F_2N_2O$; C, 57.97; H, 3.89; F, 27.51; N, 6.76; O, 3.86; Found; C, 57.56; H, 3.54; F, 27.42; N, 6.68; O, 3.65; MS; m/z 414.

All the above compounds were purified by means of silica gel column and confirmed by 1H NMR, IR, Mass and Elemental analysis.

## REACTION SCHEME




## RESULTS AND DISCUSSION

The different 6-[3,5-bis(trifluoromethyl)phenyl]-4-(substitutedphenyl)-1,4-dihydropyrimidin-2-ol were synthesised by the condensation of (2*E*)-1-[3,5-bis(trifluoromethyl)phenyl]-3-(substituted phenyl)prop-2-en-1-one and urea in presence of NaOH. The M.P. of the synthesised compounds was checked by the given literatures. The purity of compounds was analyzed by TLC. The structures of the synthesized compounds 3(a-i) were confirmed on the basis of spectral and elemental analysis. The IR spectrum of these compounds exhibited bands due to 3049 (C-H stretching of aromatic ring), 3215-3450 (b, -OH on ring), 1622, 1564 and 1519 (C=C stretching of aromatic ring), 1078 (C-H in plane deformation of aromatic ring), 825 (C-H out of plane bending of 1,4-disubutituion), 1012 (C-F stretching). Further, in their 1H NMR (δ, ppm) spectrum, the appearance of signal at: 6.7 to 6.9 (m, 4H aromatic), 3.86 (s, 3H, -$OCH_3$), 7.52-7.58 (m, 3H aromatic fluorinated ring), 6.75 (w, 1H ethylene pyrimidine ring), 2.01 (w, 1H, alcohol) confirms of making Dihydropyrimidin-ol.

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