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Synthesis and Characterization of Novel 4-[3,5-bis(trifluoromethyl)phenyl]-6-(Substituted phenyl)-1,6-dihydropyrimidine-2-thiol

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ABSTRACT

Synthesis of various dihydropyrimidine-2-thiol from (E)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(substituted)phenylprop-2-en-1-one and thiourea in presence of NaOH. The structures of the synthesized compounds were confirmed on the basis of spectral and elemental analysis.

KEYWORDS

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

INTRODUCTION

Chalcones are biogenetic precursors of flavonoids in higher plants. Also known chemically as chalcones, they consist of open-chain flavonoids in which the two aromatic rings are joined by a three carbon chain[1]. They display a wide range of pharmacological properties, including cytotoxity towards cancer cell lines[2,3], antimitotic[4], antimutagenic[5] and antitumor-promoting activities; antibacterial[6], antiviral[7], anti-inflammatory[8], antiulcerative[9] and hepatoprotective activities[10]. They are also useful in materials science fields such as non-linear optics (NLO)[11], optical limiting[12], electrochemical sensing[13], Langmuir films and photo initiated polymerization[14]. Various chalcone derivatives are notable materials for their second harmonic generation (SHG)[15]. They are well known intermediates for synthesizing various heterocyclic compounds. Cyclization of chalcones, leading to thiazines, pyrimidines, pyrazoline has been a developing field within the realm of heterocyclic chemistry for the past several years because of their ready accessibility and the broad spectrum of biological activity of the products as antibacterial, antifungal, antiprotozoal, antiinflammatory substances. A survey of literature in the recent past reveals that some pyrazoline derivatives possess antibacterial[16], anti-inflammatory[17], and antifungal effects[18]. Thiazine derivatives play a vital role in many biological processes and in the synthesis of drugs[19]. Pyrimidine derivatives occur in natural products like nucleic acids and vitamin B1 and they have remarkable pharmaceutical importance because of their biological activity as anti HIV, antitubercular, andantidiabetic compounds[20,21].

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MATERIAL 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.

General Method for Synthesis of 4-[3,5-bis(trifluoromethyl)phenyl]-6-(Substituted phenyl)-1,6-dihydropyrimidin-2-thiol: A mixture of (2*E*)-1-[3,5-bis(trifluoromethyl)phenyl]-3-(substituted phenyl)prop-2-en-1-one, (0.02mol), thiourea (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.

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

MS; m/z 432; mp 239ºC; Anal. Calcd. For $C_{19}H_{14}F_6N_2OS$; C, 52.78; H, 3.23; F, 26.36; N, 6.48; O, 3.70; S, 7.42; Found; C, 52.56; ; H, 3.13; F, 26.27; N, 6.39; O, 3.59; S, 7.38; IR (cm-1); 3049 (C-H stretching of aromatic ring); 1012 (C-F starching); 1078 (C-H in plane deformation of aromatic 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)

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

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

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2S$; C, 49.49; H, 2.54; Cl, 8.12; F, 26.10; N, 6.41; S, 7.34; Found; C, 52.38 ; H, 2.46; Cl, 8.07; F, 26.03; N, 6.37; S, 7.27; MS; m/z 436.

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

Anal. Calcd. For $C_{18}H_{11}F_7N_2S$; C, 51.43; H, 2.64; F, 31.64; N, 6.66; S, 7.63; Found; C, 51.38; ; H, 2.56; F, 31.46; N, 6.52; S, 7.54; MS; m/z 420.

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

Anal. Calcd. For $C_{18}H_{11}BrF_6N_2S$; C, 44.92; H, 2.30; Br,16.60; F, 23.69; N, 5.82; S, 6.66; Found; C, 44.87; H, 2.18; Br,16.48; F, 23.58; N, 5.71; S, 6.59; MS; m/z 479.

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

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2S$; C, 49.49; H, 2.54; Cl, 8.12; F, 26.10; N, 6.41; S, 7.34; Found; C, 52.38 ; H, 2.46; Cl, 8.07; F, 26.03; N, 6.37; S, 7.27; MS; m/z 436.

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

Anal. Calcd. For $C_{19}H_{14}F_6N_2OS$; C, 52.78; H, 3.23; F, 26.36; N, 6.48; O, 3.70; S, 7.42; Found; C, 52.56; ; H, 3.13; F, 26.27; N, 6.39; O, 3.59; S, 7.38; MS; m/z 432.

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

Anal. Calcd. For $C_{20}H_{16}F_6N_2O_2S$; C, 51.95; H, 3.49; F, 24.65; N, 6.06; O, 6.92; S, 6.93; Found; C, 51.88; H, 3.39; F, 24.57; N, 6.01; O, 6.89; S, 6.86; MS; m/z 462.

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

Anal. Calcd. For $C_{18}H_{10}Cl_2F_6N_2S$; C, 45.88; H, 2.14; Cl, 15.05; F, 24.19; N, 5.94; S, 6.80; Found; C, 45.79; H, 2.07; Cl, 15.02; F, 24.11; N, 5.85; S, 6.72; MS; m/z 462.

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

Anal. Calcd. For $C_{18}H_{11}ClF_6N_2S$; C, 49.49; H, 2.54; Cl, 8.12; F, 26.10; N, 6.41; S, 7.34;

Found; C, 52.30 ; H, 2.43; Cl, 8.06; F, 26.01; N, 6.34; S, 7.25; MS; m/z 436.

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

Anal. Calcd. For $C_{18}H_{11}F_7N_2S$; C, 51.43; H, 2.64; F, 31.64; N, 6.66; S, 7.63; Found; C, 51.34; H, 2.59; F, 31.45; N, 6.54; S, 7.57; MS; m/z 420.

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

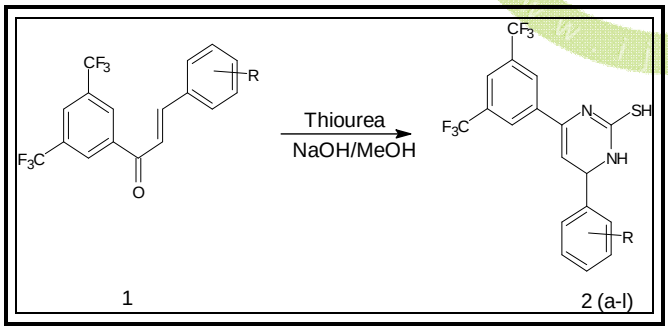
Anal. Calcd. For $C_{18}H_{11}BrF_6N_2S$; C, 44.92; H, 2.30; Br,16.60; F, 23.69; N, 5.82; S, 6.66; Found; C, 44.85; H, 2.15; Br,16.44; F, 23.56; N, 5.73; S, 6.58, MS; m/z 479.

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

Anal. Calcd. For $C_{20}H_{16}F_6N_2S$; C, 55.81; H, 3.75; F, 26.48; N, 6.51; S, 7.45; Found; C, 55.78; H, 3.68; F, 26.42; N, 6.43; S, 7.37, MS; m/z 430.

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 4-[3,5-bis(trifluoromethyl)phenyl]-6-(Substituted phenyl)-1,6-dihydropyrimidin-2-thiol were synthesised by the condensation of (2*E*)-1-[3,5-bis(trifluoromethyl)phenyl]-3-(substituted phenyl)prop-2-en-1-one and thiourea 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), 1651 (C=O stretching), 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) confirms of making Dihydropyrimidinthiol.

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