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A CONVINIENT SYNTHESIS OF THIAZOLO PYRIMIDO BENZOTHIAZOLE DERIVATIVES

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ABSTRACT

The 6-Cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine on reaction with substituted 2-amino benzothiazoles in presence of weak base anhydrous K_2CO_3 and N,N-dimethyl formamide as solvent afford 6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*] benzothiazoles. The newly synthesized compounds were confirmed on the basis of Mass Spectroscopy, Infrared Spectroscopy and ^{1}HNMR Spectroscopy.

KEYWORDS: 6-Cyano-5-oxo-7-(methylthio)-5*H*-thiazolo [3,2-*a*]pyrimidine, 2-amino benzothiazole, K_2CO_3, N,N-dimethyl formamide.

INTRODUCTION

Benzothiazole is pharmacologically active bicyclic ring possessing group like nitrogen, sulphur as hetero atom and formed by thiazole ring fused with benzene ring which act as weak base, the hetrocyclic compounds having benzothiazole ring have different biological application and which behave as chemical drug in different places of pharmaceutics time to time.[1] The thiazolo pyrimido benzothiazole heterocycles made up of three heterocyclic ring of benzothiazole, thiazole and pyrimidine fusion. These structural fusion exhibit versatile chemical and biological properties to the resulting compounds, making them important scaffold for the development of new chemical drugs and bioactive molecules. Fused benzothiazole, thiazolo pyrimidine compounds exhibit different type of activity like antimicrobial activity[2,3,4], anti-inflammatory activity[5], antioxidant potential[6],

antitubercular agent[7,8], antiproliferative agent[9] and insecticidal activity.[10] Based on the reported literature on the significance of thiazolo pyrimido benzothiazole in medicinal chemistry, chemist has sustained the attention of preparing thiazolo pyrimido benzothiazole compounds.

In the present paper, we reported synthesis of substituted 6-imino-5-oxo thiazolo[2,3-*b*] pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles by condensation reaction of 6-Cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine with selected nucleophile like substituted 2-amino benzothiazole compounds in N,N-dimethyl formamide (DMF) as reaction solvent and anhydrous potassium carbonate as weak base. The synthesized compounds were characterized by IR, ^{1}HNMR and Mass spectroscopy. The present work provides significant method include simple, inexpensive experimental procedure, short reaction time, and good yield.

EXPERIMENTAL

All the chemicals used in present works are from analytical grade and used without further refinement. Melting points of the products were determined in open capillary tubes on an electro thermal melting point apparatus and were uncorrected. The development of reactions and the purity of the isolated compounds were monitored by thin layer chromatography (TLC) on Ultra Violet active silica gel plate (Merck). Infrared spectra were recorded on Shimadzu FT-IR spectrophotometer, ^{1}HNMR spectra were obtained on Bruker advance spectrophotometer 500 MHz in DMSO-d_6 using tetramethyl silane (TMS) as an internal standard. Mass spectrums were analyzed on GC-MS spectrometer using the electron spray ionization technique.

GENERAL PROCEDURE

Synthesis of 6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles

A mixture of 6-cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine (1) (0.223 g, 0.001 mol) and substituted 2-amino benzothiazoles (2a-f) (0.001 mol) in 15 ml of N,N-dimethyl formamide as solvent and weak carbonate base anhydrous K_2CO_3 (10 mg) as catalyst was refluxed for 4-5 hours. The reaction mixture was cooled to room temperature and poured into ice cold water containing crushed ice. The separated solid mass of product was filtered, washed with ice cold water and recrystallized using absolute ethanol to give pure 6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles (3a-3f).(Scheme 1).

6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazole (3a)

Brown powder, Yield 75%, M.P. 276°C (dec.). IR (KBr/cm^{-1}) 3433, 3390 (=NH stretch), 1722 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 6.68-7.63 (m, 6H, Ar-H & thiazolic-H), 8.21-8.34 (s, 1H, =NH), Mass spectrum: m/z 325 [M^+].

6-imino-5-oxo-10-methyl thiazolo [2,3-*b*] pyrimido [5,6-*e*] pyrimido [2,3-*b*] benzothiazole (3b)

Brown powder, Yield 78%, M.P. 297°C (dec.). IR (KBr/cm^{-1}) 3390, 3320 (=NH stretch), 1707 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 2.602 (s,3H, CH_3), 6.78-7.85 (m, 5H, Ar-H & thiazolic-H), 8.23-8.49 (s, 1H, =NH), Mass spectrum: m/z 339 [M^+].

6-imino-5-oxo-8,10-dimethyl thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazole (3c)

Brown powder, Yield 80%, M.P. 302°C (dec.). IR (KBr/cm^{-1}) 3420, 3390 (=NH stretch), 1712 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 2.91 (s,6H, $2CH_3$), 6.28-7.23 (m, 4H, Ar-H & thiazolic-H), 8.20-8.42 (s, 1H, =NH), Mass spectrum: m/z 353 [M^+].

6-imino-5-oxo -10-methoxy thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*] benzothiazole (3d)

Brown powder, Yield 82%, M.P. 284°C (dec.). IR (KBr/cm^{-1}) 3418, 3340 (=NH stretch), 1705 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 3.75-3.82 (s, 3H, -OCH_3), 6.91-7.80(m, 5H, Ar-H & thiazolic-H), 8.12-8.57 (s, 1H, =NH), Mass spectrum: m/z 355 [M^+].

10-Chloro-6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazole (3e)

Brown powder, Yield 83%, M.P. 289°C (dec.). IR (KBr/cm^{-1}) 3412, 3310 (=NH stretch), 1695 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 7.28-8.26 (m, 5H, Ar-H & thiazolic-H), 9.06 (s,1H, -N-H), Mass spectrum: m/z 359 [M^+].

6-imino-10-nitro-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*] benzothiazole (3f)

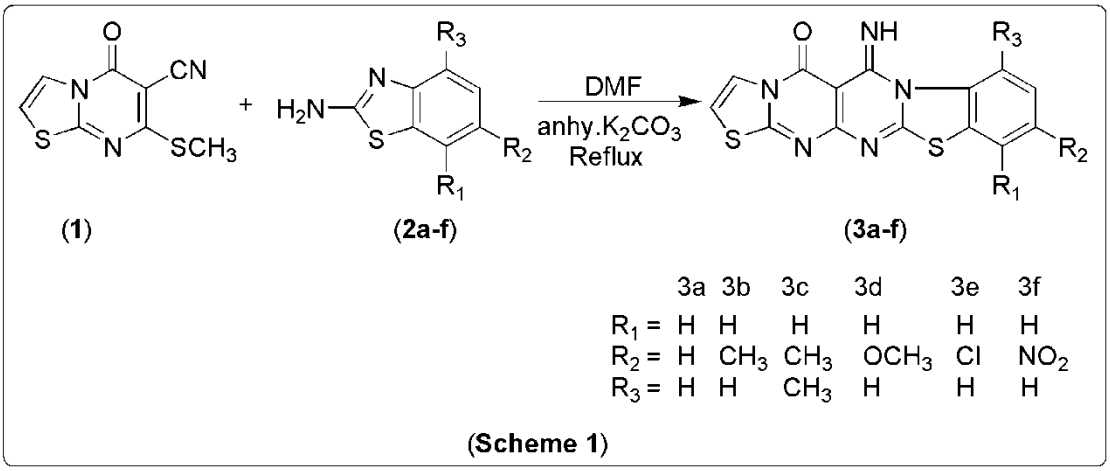
Brown powder, Yield 79%, M.P. 283°C (dec.). IR (KBr/cm^{-1}) 3394, 3271 (=NH stretch), 1718 (>C=O stretch), ^{1}H NMR spectrum: (DMSO-d_6, δ ppm) 7.32-8.18 (m, 5H, Ar-H & thiazolic-H), 8.95 (s,1H, -N-H), Mass spectrum: m/z 370 [M^+].

RESULT AND DISCUSSION

In present work, we reported simple process for preparation of 6-imino-5-oxo thiazolo[2,3-*b*]

pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles (3a-f) by reaction of 6-cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine (1) and substituted 2-amino benzothiazole compounds using K_2CO_3 as catalyst and DMF as reaction solvent (Scheme 1). The yield of these synthesized compounds in the range of 75% to 83% with simple separation procedure. The structure of these synthesized compounds was confirmed on the basis of Mass Spectroscopy, Infra Red Spectroscopy and Proton Magnetic Resonance Spectroscopy.

6-cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine (1) have a replaceable active thiomethyl group(-SCH_3) at the 7-position which is activated electron withdrawing cyano group (-CN) at 6-postion, which on reaction with selected nucleophile like substituted 2-amino benzothiazole independently in presence of catalytic amount (0.005 mol) of anhydrous potassium carbonate and N,N-dimethyl formamide as solvent with formation of 6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles (3a-3f).



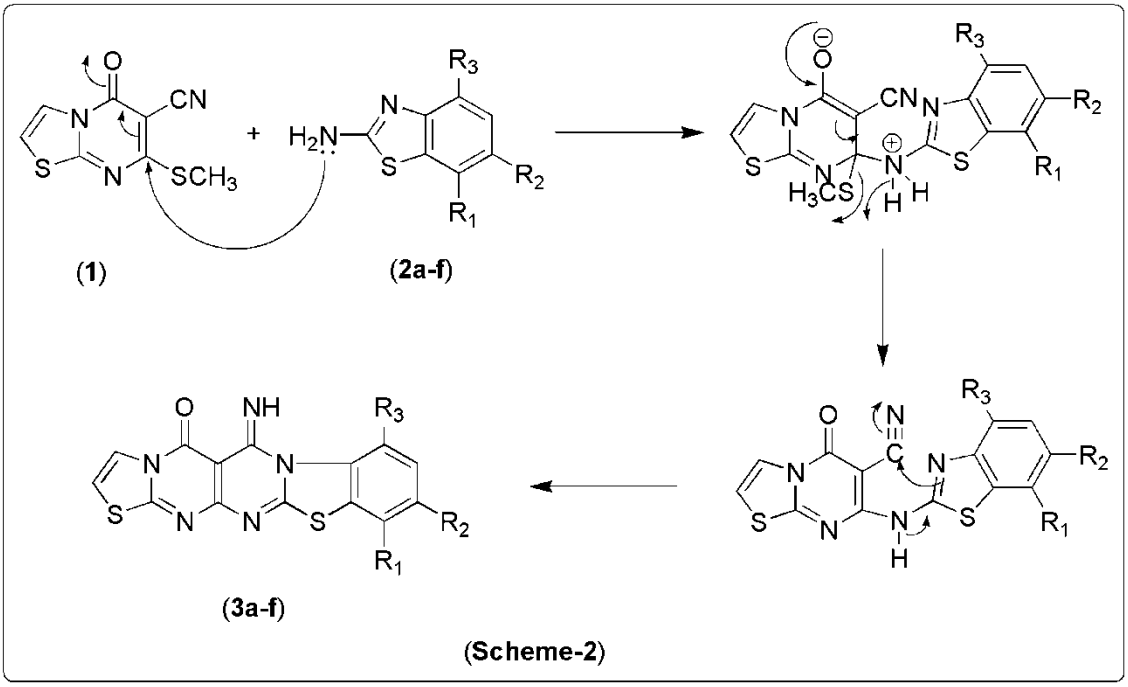
	3a	3b	3c	3d	3e	3f
R_1 =	H	H	H	H	H	H
R_2 =	H	CH_3	CH_3	OCH_3	Cl	NO_2
R_3 =	H	H	CH_3	H	H	H

(Scheme 1)

Mass spectrum of prepared compounds exhibit that molecular ion peak corresponds to molecular mass of respective compound which shows that formation of stable compounds 3a-f. Infrared spectra show absorption band in the range of 3433-3271 cm^{-1}, 1722-1695 cm^{-1} due to =N-H, >C=O stretching for compounds 3a–f respectively. The disappearance of band at 2205 cm^{-1} indicates -CN group undergo cyclization to gain six membered pyrimidine ring. Proton magnetic resonance spectral data also is in accord with structures assigned to compounds 3a-f.

^1H NMR spectra of these compounds showed absence of singlet at δ2.60 ppm due to thiomethyl protons indicates that cyclization took place. The new signals appears at δ8.12-9.06 ppm are due to =N-H proton.

The probable reaction mechanism for the formation of compound (3a-f) can be adduced as follows (Scheme 2).



(Scheme-2)

CONCLUSION

Herein we have reported a convenient and efficient method for the synthesis of 6-imino-5-oxo thiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,3-*b*]benzothiazoles by reaction of 6-cyano-5-oxo-7-(methylthio)-5*H*-thiazolo[3,2-*a*]pyrimidine and selected nucleophile like substituted 2-amino benzothiazole compounds using K_2CO_3 as catalyst and DMF as reaction solvent. This method provides special advantages, like the use of a reusable catalyst, affording high yields, employing a simple reaction procedure, and provides the simple isolation procedure. The synthesized compounds were confirmed on the basis of IR, ^{1}HNMR and Mass Spectroscopic analysis technique.

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