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One pot Synthesis and Antibacterial activity of 3-substituted derivatives of14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole

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Abstract : 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*][1,3]benzothiazole(I) independently on condensation with 2-amino-6-substituted benzothiazole in the presence of DMF and catalytic amount of K_2CO_3 reflux for 5-6 hours to yield 3-substituted derivatives of 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*] pyrimido[5,6-*e*] pyrimido[2,1-*b*][1,3] benzothiazole (III-a-e).The synthesized compounds were characterized by elemental analysis and spectral data.
Key Words : 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*][1,3]benzothiazole, DMF, Potassium carbonate.

Introduction :

A one pot synthesis is a green approach towards the synthesis of various heterocyclic compounds and for a researcher there is lot of scope to change the reaction condition, to change the solvent, to change the catalyst or to modify the catalyst or even to develop various novel one pot chemical reactions. Pyrimidine, iminopyrimidine, pyrazole and fused benzothiazole heterocycles are reported to be effective pharmacophores [1-10]. A survey of literature made it evident that very little work has been carried out on the synthesis of fused pyrimidobenzothiazole possessing three to four rings which exhibit a wide spectrum of biological and pharmacological activities.

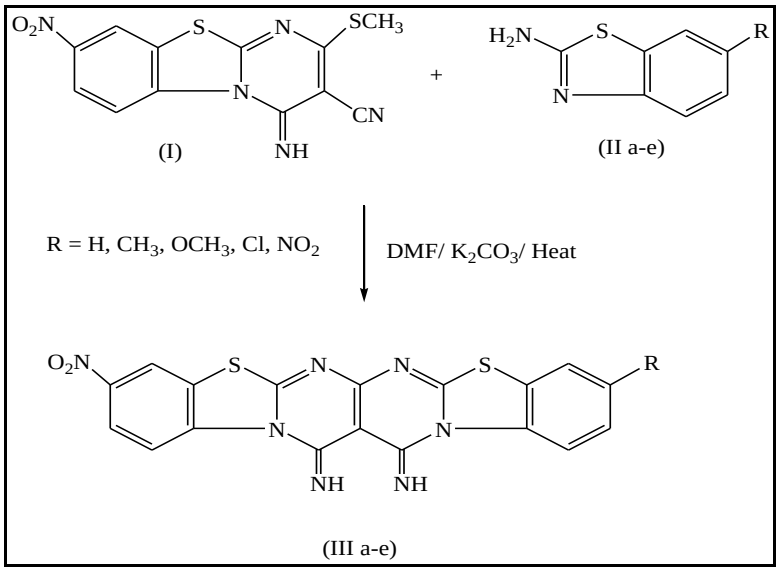
Pyrimido [2,1-*b*] benzothiazole and its 8-substitued derivatives were synthesized by Nair Mohan D. *et.al.*[11]by refluxing diethyl ethoxymethylenemalonate with respective 2-amino benzothiazoles. These derivatives were found to have antiviral activity.

A comprehensive review on the methods of preparation and reactions of iminopyrimidines has been published in the form of book, "The Pyrimidines" by Brown D.J.*et al.*[12-13]Imino compounds are known to possess some sedative and hypnotic actions. Denny W.A. *et al.*[14]reported fused pyrido, -imidazo, -pyrazolo, -pyrazino and -pyrolloheterocycles as topoisomerase-targeted anticancer agents. Jimonet Patrick and his research group [15] reported synthesis and pharmacological activity of 6-(trifluoromethoxy)-3-substituted-2-imino benzothiazolines. These compounds were found to be three times more potent than 6-(trifluoromethoxy) - 2-benzothiazolamine (Riluzole), a blocker of excitatory amino acid mediated neurotransmission. Erlenmeyer and Von Meyenburg [16] reported the preparation and moderate sedative activity of 5,5-dialkyl-2-imino-4-thiazolidones which is in marked contrast to the lack of activity of the iminobarbituric acids [17-20].

Experimental Section:

All melting points were determined in open capillary tube and were uncorrected. IR spectra were recorded with potassium bromide pellets technique, ^{1}H NMR spectra were recorded on AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra were recorded on a FT VG-7070 H Mass Spectrometer using EI technique at 70 eV. All the reactions were monitored by Thin layer chromatography.

Material and Methods :



General procedure :

Preparation of 3-substituted derivatives of 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-a-e).

It is prepared by condensation of 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3]benzothiazole (I) independently with 2-aminobenzothiazole(II-a), 2-amino-6-methyl benzothiazole(II-b), 2-amino-6-methoxy benzothiazole(II-c), 2-amino-6-chloro benzothiazole(II-d), and 2-amino-6-nitro benzothiazole(II-e)in the presence of DMF and catalytic amount of K_2CO_3reflux for 5-6 hours to get 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole and its 3-substituted derivatives(III-a-e).

1) Preparation of 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-a).

3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3] benzothiazole (I) reflux with 2-amino benzothiazole (II-a) in the presence of DMF and catalytic amount of K_2CO_3 for 5-6 hours to yields 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole.

Yield : 61 %, IR:(KBr/cm^{-1}) : 3280 & 3320 (=NH), 3110 (Ar-H), 1615 (C=N), 1517 & 1350 (NO_2), ^{1}H-NMR: (DMSO): δ 4.00 (s 1H =NH), δ 4.10 (s 1H =NH), δ 6.95-7.10 (d 4H Ar-H), δ 7.12- 7.86 (d 3H Ar-H), EI-MS: (m/z:RA%): 420 (M+1), Elemental analysis : $C_{18}H_9N_7O_2S_2$, Calculated: (%) C 51.54, H 2.16, N 23.28, O 7.63, S 15.29 Found (%) : C 51.50, H 2.12, N 23.21, O 7.60, S 15.25

2) Preparation of 3-methyl-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-b).

Condensation of 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3] benzothiazole (I) and 2-amino-6-methylbenzothiazole (II-b) in the presence of DMF and small amount of potassium carbonate for 5 hours to give 3-methyl-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole.

Yield : 54 %, IR:(KBr/cm^{-1}) :3310 & 3325(=NH), 3111 (Ar-H), 1617 (C=N), 1520 & 1340 (NO_2),EI-MS: (m/z:RA%): 434 (M+1), Elemental analysis : $C_{19}H_{11}N_7O_2S_2$, Calculated: (%) C 52.65, H 2.56, N 22.62, O 7.38, S 14.79 Found (%) : C 52.60, H 2.51, N 22.60, O 7.32, S 14.76

3) Preparation of 3-methoxy-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-c).

It is prepared by reaction of3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3] benzothiazole (I) and 2-amino-6-methoxybenzothiazole (II-c) in the presence of Dimethyl formamide and potassium carbonate for 6 hours to get3-methoxy-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole.

Yield : 57 %, IR:(KBr/cm^{-1}) :3311 & 3315(=NH), 3100 (Ar-H), 1623 (C=N), 1515 & 1335 (NO_2),1162 (C-O), EI-MS: (m/z:RA%): 450 (M+1), Elemental analysis : $C_{19}H_{11}N_7O_3S_2$, Calculated: (%) C 50.77, H 2.47, N 21.81, O 10.68, S 14.27 Found (%) : C 50.71, H 2.45, N 21.77, O 10.63, S 14.24

4) Preparation of 3-chloro-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-d).

It is prepared by the condensation of 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3]benzothiazole(I) and 2-amino-6-chlorobenzothiazole (II-d) in the presence of Dimethyl formamide and potassium carbonate for 5 hours to produce3-chloro-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole.

Yield : 71 %, IR:(KBr/cm^{-1}) :3311 & 3281(=NH), 3112 (Ar-H), 1627 (C=N), 1519 & 1337 (NO_2),EI-MS: (m/z:RA%): 454 (M+1), Elemental analysis : $C_{18}H_8ClN_7O_2S_2$, Calculated: (%) C 47.63, H 1.78, Cl 7.81, N 21.60, O 07.05, S 14.13 Found (%) : C 47.60, H 1.75, Cl 7.75, N 21.55, O 07.00, S 14.11

5) Preparation of 3-nitro-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*] [1,3]benzothiazole (III-e).

It is prepared by the reaction of 3-cyano-4-imino-2-methylthio-8-nitro-4H-pyrimido[2,1-*b*] [1,3]benzothiazole(I) and 2-amino-6-nitrobenzothiazole (II-e) in presence of DMF and K_2CO_3 for 6 hours to produce 3-nitro-14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*]pyrimido[2,1-*b*][1,3]benzothiazole.

Yield : 65 %, IR:(KBr/cm^{-1}) :3300 & 3268(=NH), 3122 (Ar-H), 1620 (C=N), 1510 & 1355 (NO_2),EI-MS: (m/z:RA%): 465 (M+1), Elemental analysis : $C_{18}H_8N_8O_4S_2$, Calculated: (%) C 46.55, H 1.74,N 24.13, O 13.78, S 13.81 Found (%) : C 46.50, H 1.71,N 24.11, O 13.74, S 13.75

Results and Discussion :

One pot reactions constitute an especially attractive recent synthetic strategy since they provide easy and rapid access to large number of organic compounds with diverse substitution pattern. In present work, we report one pot synthesis of novel fused heterocyclic compound, 14,15-diimino-10-nitro-benzothiazolo[2,3-*b*]pyrimido[5,6-*e*] pyrimido[2,1-*b*][1,3]benzothiazole and its 3-substituted derivatives (III-a-e).

Conclusion :

In conclusion a facile one pot synthesis has been developed for the title compounds using readily available starting materials.All the newly synthesized compounds were screened for antibacterial activity. These compounds was found to possess a broad spectrum activity. However, the activities of the tested compounds are much less than those of standard antibacterial agents used.

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