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NOTE

Synthesis and Antimicrobial Activity of 2-(1,3-Benzothiazol-2-ylthio)-N-(6-substituted 1,3-Benzothiazol-2-yl)acetamide

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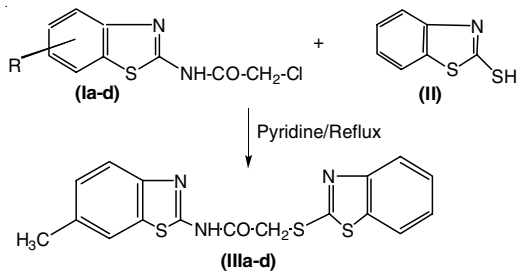
A mixture of 2-chloroacetylamino-6-substituted benzothiazole and pyridine was mixed properly then added to round-bottom flask containing a solution of 2-mercaptobenzothiazole in pyridine solution and the reaction mixture was refluxed for 5 h. After completion of the reaction, it was cooled to room temperature and the separated solid was filtered and dried. The products were recrystallized from alcohol. The synthesized compounds were characterized by elemental analysis and spectral data.

Keywords: 2-Chloroacetylamino-6-substituted benzothiazole, Pyridine, 2-Mercaptobenzothiazole.

A survey of literature reveals that less work has been carried out on synthesis of fused pyrimido benzothiazole exhibits activities like antiallergic [1], herbicidal [2], antiviral [3], antiparasitic [4,5], antiparkinsonian activity [6], anti-inflammatory [7,8], phosphodiesterase inhibition [9], fungicidal [10] and antitumor [11]. Benzothiazole derivatives are an important class of heterocyclic compounds that exhibit a wide range of biological properties in medicinal and agricultural chemistry [12-16]. Further industrial applications as antioxidants [17,18], vulcanization accelerators [19,20] and a dopant in a light emitting organic electroluminescent devices [21] have also been reported. Many reports have appeared in the literature describing the formation of benzothiazoles *via* one of the two major routes.

However, these methodologies suffer from one or more disadvantages, such as tedious workup, high temperature, prolonged reaction time and toxic organic solvents such as DMF and DMSO. Carrying out organic reactions in water has become highly desirable in recent years to meet environmental considerations. The use of water as a sole medium of organic reactions would greatly contribute to the development of environmentally friendly processes. It would be even more desirable to carry out catalytic organic reactions in water, which normally require delicate reaction conditions in order for the catalyst to be stable and yet reactive. In this note, we reported one pot synthesis of 2-[2-(1,3-benzothiazol-2-yl)hydrazino]-*N*-(6-substituted-1,3-benzothiazol-2-yl)acetamide.

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.



Synthesis of 2-(1,3-benzothiazol-2-ylthio)-*N*-(6-methyl-1,3-benzothiazol-2-yl)acetamide (IIIa): A mixture of 2-chloroacetylamino-6-methyl benzothiazole (0.1 mol) and pyridine was dissolved properly then added to the round bottom flask containing a solution of 2-mercaptobenzothiazole (0.1 mol) in pyridine solution and the reaction mixture was refluxed for 5 h. After completion of the reaction it was cooled to room temperature and the separated solid was filtered and dried. The product was recrystallized from alcohol. Yield: 57 %, IR (KBr, ν_{max}, cm^{-1}): 3410 (-NH), 1725 (CO), ^{1}H NMR: (DMSO): δ 2.35 (s 3H CH_3), δ 4.00 (s 2H CH_2), δ 8.00 (s 1H -NH), δ 7.60 (d 3H Ar-H), δ 7.55 (d 2H Ar-H), δ 8.20 (d 2H Ar-H), EI-MS: (*m/z* RA %): 372 (M+1), Elemental analysis: $C_{17}H_{13}N_3OS_3$, Calcd. (%): C 54.96, H 3.53, N 11.31, O 4.31, S 25.89; Found (%): C 54.93, H 3.50, N 11.27, O 4.28, S 25.85.

Synthesis of 2-(1,3-benzothiazol-2-ylthio)-*N*-(6-methoxy-1,3-benzothiazol-2-yl)acetamide (IIIb): A mixture of 2-chloroacetylamino-6-methoxy benzothiazole (0.1 mol) and pyridine was dissolved properly then added to the round bottom flask containing a solution of 2-mercapto benzothiazole (0.1 mol) in pyridine solution and the reaction mixture was refluxed for 5 h. After completion of the reaction, it was cooled to room temperature and the separated solid was filtered and dried. The product was recrystallized from alcohol. Yield: 67 %, IR (KBr, ν_{max}, cm^{-1}): 3445 (-NH), 1717 (CO), ^{1}H NMR: (DMSO): δ 3.73 (s 3H OCH_3), δ 4.17 (s 2H CH_2), δ 8.00 (s 1H -NH), δ 8.12 (d 3H Ar-H), δ 7.55 (d 2H Ar-H), δ 8.15 (d 2H Ar-H), EI-MS: (*m/z* RA %): 388 (M+1), Elemental analysis: $C_{17}H_{13}N_3O_2S_3$, Calcd. (%): C 52.69, H 3.38, N 10.84, O 8.26, S 24.82; Found (%): 52.65, H 3.34, N 10.80, O 8.24, S 24.80.

Synthesis of 2-(1,3-benzothiazol-2-ylthio)-*N*-(6-chloro-1,3-benzothiazol-2-yl)acetamide (IIIc): A mixture of 2-chloroacetylamino-6-chloro benzothiazole (0.1 mol) and pyridine was dissolved properly then added to the round bottom flask containing a solution of 2-mercapto benzothiazole (0.1 mol) in pyridine solution and the reaction mixture was refluxed for 5 h. After completion of the reaction it was cooled to room temperature and the separated solid was filtered and dried. The product was recrystallized from alcohol. Yield: 55 %, IR (KBr, ν_{max}, cm^{-1}): 3395 (-NH), 1710 (CO), ^{1}H NMR: (DMSO): δ 4.17 (s 2H CH_2), δ 8.00 (s 1H -NH), δ 8.00 (d 3H Ar-H), δ 7.55 (d 2H Ar-H), δ 8.12 (d 2H Ar-H), EI-MS: (*m/z* RA %): 392 (M+1), Elemental analysis: $C_{16}H_{10}N_3OS_3Cl$, Calcd. (%): C 49.03, H 2.57, Cl 9.05, N 10.72, O 4.08, S 24.54; Found (%): C 49.01, H 2.55, Cl 9.00, N 10.70, O 4.08, S 24.51.

Synthesis of 2-(1,3-benzothiazol-2-ylthio)-*N*-(6-nitro-1,3-benzothiazol-2-yl)acetamide (IIId): A mixture of 2-chloroacetylamino-6-nitro benzothiazole (0.1 mol) and pyridine was dissolved properly then added to the round bottom flask containing a solution of 2-mercaptobenzothiazole (0.1 mol) in pyridine solution and the reaction mixture was refluxed for 5 h. After completion of the reaction it was cooled to room temperature and the separated solid was filtered and dried. The product was recrystallized from alcohol. Yield: 61 %, IR (KBr, ν_{max}, cm^{-1}): 3375 (-NH), 1742 (CO), 1350 & 1560 (NO_2) ^{1}H NMR: (DMSO): δ 4.18 (s 2H CH_2), δ 8.00 (s 1H -NH), δ 7.90 (d 3H Ar-H), δ 7.56 (d 2H Ar-H), δ 8.10 (d 2H Ar-H), EI-MS: (*m/z* RA %): 402 (M+1), Elemental analysis: $C_{16}H_{10}N_4O_3S_3$, Calcd. (%): C 47.75, H 2.50, N 13.92, O 11.93, S 23.90; Found (%): C 47.71, H 2.48, N 13.90, O 11.91, S 23.85.

All the synthesized compounds were screened for antibacterial activity studies at a concentration of 50 and 100 µg/mL using DMSO as a control against *Aspergillus niger* and *Penicillium* sp species by well diffusion method on nutrient agar media, ampicillin 50 and 100 µg/mL used as standard against Gram-positive and Gram-negative bacteria. Compounds **IIIb** and **IIId** shows good antibacterial activity against *Penicillium* sp species and compounds **IIIa** and **IIIc** shows good antibacterial activity against *Aspergillus niger* species.

Conclusion

Two moieties of substituted benzothiazoles are fused and screened for antibacterial studies showed a broad spectrum of antibacterial activity. They showed good activity against *Penicillium* sp. and *Aspergillus niger* species.

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