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GREEN SYNTHESIS AND CHARACTRISATION OF NOVEL TRIAZOLES DERIVATIVES OF 2-MERCAPTOBENZOTHIAZOLE

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ABSTRACT: Novel 2-Mercaptobenzothiazole deriveties synthesized from 2- Mercaptobenzothiazole reacted with ethyl chloroacetate to get ester derivatives **(3)** using Green method. These ester converted to hydrazids **(4)** by reaction with hydrazine hydrate under MWI. 5-substituted 1,3,4-oxadiazole **(5a-g)** synthesized from hydrazide, substituted benzoic acid and phosphprous oxochloried by Microwave irradiation as reported in literature.1,3,4- Triazoles **6a-g** synthesized from above oxadiazole **5a-g**. The structure of newly synthesized compound was established by physico-chemical and spectral data analysis.

KEY WORDS: 2-Mercaptobenzothiazole, hydrazine hydrate, substituted 1,3,4-Triazole, Substituted benzoic acid, Microwave irradiation.

INTRODUCTION

A review of the recent literature revealed that many effective antimicrobial agents show a heterocyclic moiety within their structure[1] and, in particular, that substituted benzimidazole, benzoxazole, and benzothiazole derivatives bring different biological properties such as chemotherapeutical, antibacterial, antifungal, and antiviral activities, with a low toxicity for the antimicrobial therapeutic use in man[2–4] Structure- activity relationship (SAR) studies carried out on these types of heterocycles have shown that positions 2 and 6 are crucial for

antibacterial activity against Grampositive and Gram-negative bacteria strains[5]. It has been found that 2-substituted benzothiazole have good potential to exhibit anticancer Activity[6]

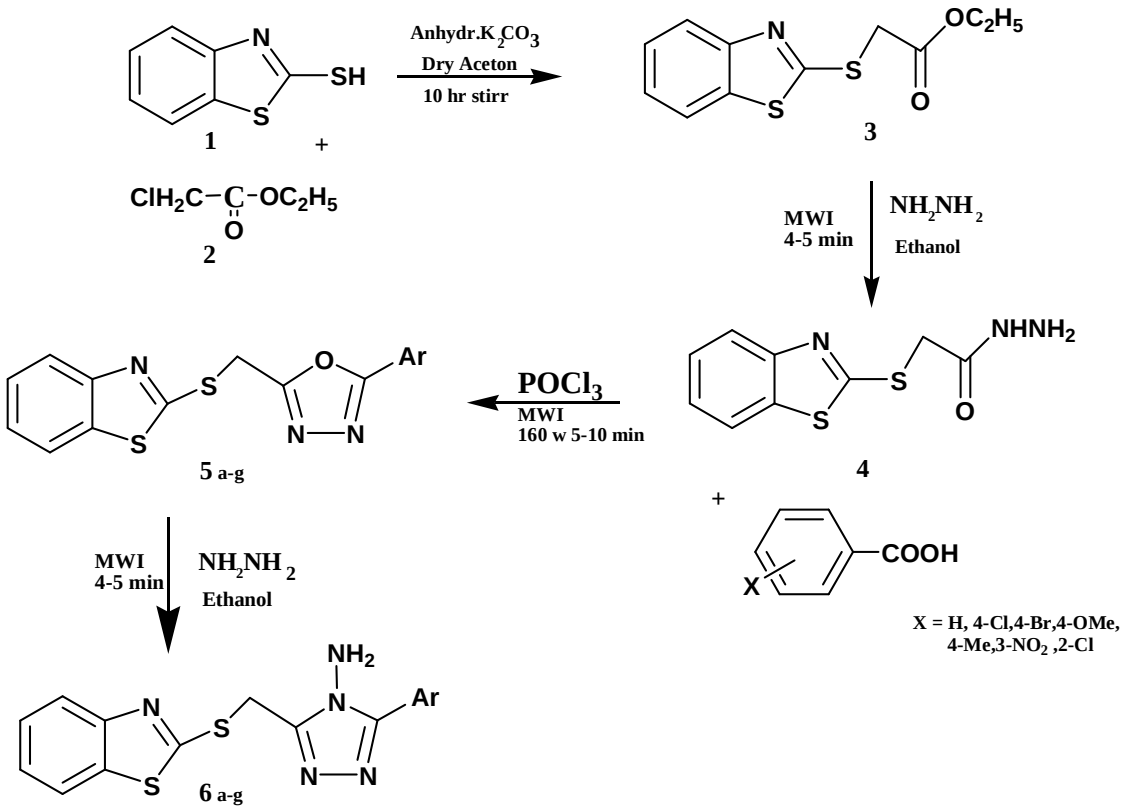
In recent years the remarkable efficiency of compounds having 1,3,4-triazole nucleus have been demonstrated including antibacterial, antifungal, antiviral, antimicrobial activities. 1,3,4-triazole related compounds have attracted much attention due to their inspirable role in medicine, agriculture and industry[7].

All these observations prompted us to start a research program for the synthesis of small molecules potentially useful as antimicrobial agents. After a careful screening of various hetero nuclei, we have chosen to focus our attention on benzothiazole derivatives. In particular, we synthesized 2-mercaptobenzothiazole derivatives carrying 1,3,4-triazole moiety.

In present work, syntheses of the compounds having these two biologically active rings is carried out by green methods[8-9] which overhead on conventional methods[10-13] and confirmed further by their spectral analysis.

RESULT AND DISCUSSION

The reaction between 2-Mercaptobenzothiazole[1] and ethylchloroacetate[2] in anhydrous K_2CO_3 and dry acetone medium followed by green method resulted in formation of ethyl-2-(benzothiazolylthio) acetate[3], which on reaction with hydrazine hydrate gave [(2-benzothiazolylthio) acetyl]-hydrazine[4]. The reaction of this comp.[4] with different substituted aromatic acids in presence of phosphorus oxychloride under microwave irradiation gave 5-(substituted phenyl-1.3.4–oxadiazol-2-yl)-2-mercaptobenthiazole[5] **(a-g)**. 1.3.4-triazoles **6(a-g)** synthesized from[5] **(a-g)** reacts with hydrazinhydrated under microwave irradiation. The structures of the newly synthesized compounds[5] **(a-g)** were established on the basis of spectral data. The synthetic route followed for obtaining the title compounds is outlined in **Scheme I**. The physical characterizations of **6(a-g)** given in **Table I.**



Scheme I

EXPERIMENTAL

All the chemicals were obtained from commercial suppliers and used after further purification. All the melting points were determined in open capillary tubes and are uncorrected. The IR spectra (ύ in cm^{-1}) were recorded on a perkin-Elmer spectrophotometer in KBr pellets. ^{1}HMR spectra were recorded on Varian Gemini (200 MHz) spectrometer using DMSO as solvent and TMS as an internal standard. All chemical shifts values are reported in δ scale downfield from TMS. Homogeneity of the compound was checked by TLC on silica gel plates.

General procedure for the synthesis Ethyl-2-(benzothiazolylthio) acetate [3]

Green Method

2-Mercaptobenzothiazole 1 (0.01 mole) and ethylchloroacetate (0.01 mole)[2] in ethanol and NaOH were stirred for 10 hr room temperature. The completion of the reaction was mentioned on T.L.C. The reaction mixture was poured on to the crushed ice. The solid precipitated was filtered, washed with water and recrystallised from cloroform. The obtained product was identified from comparing product obtained by conventional method and their melting point. mp. 45-47 ^oC, Yield- 80-90 %

IR (KBr): 3022, 1723, 1614, 696 cm-1.

^{1}**H-NMR**: δ (ppm): 1.23 (3H, t), 4.13 (2H, q), 4.46 (2H, s), 6.79-7.87 (4H, m).

Synthesis of [(2-benzothiazolylthio) acetyl]-hydrazine[4]

Green Method:

A mixture of Ethyl-2-(benzothiazolylthio) acetate[3] (1 mol,) and hydrazine hydrate (0.4 mol) and ethanol (40 ml) was taken RBF placed in microwave oven and irradiated for 4 min. After completion of reaction (monitored by TLC), mixture was cooled and the resulting solid was filtered, dried and recrystallized from ethanol to yield compound[4]**.**

Yield: 84 %, mp = 166-167 ^{o}C.

IR (KBr): 3022, 1722, 1612, 694 cm^{-1}.

^{1}**H-NMR:** δ (ppm)**:** 4.42 (2H, s), 4.80 (2H, s), 6.70-7.80 (4H, m), 7.89 (1H, s).

Synthesis of 5-(substituted phenyl-1,3,4–oxadiazol-2-yl)-2-mercaptobenthiazole(5a-g).

Green Method

The mixture of [(2-benzothiazolylthio) acetyl]-hydrazine[4] **(**0.02M), substituted aromatic acid Ar a-g (0.03M) and phosphorus-oxychloride (1ml) was ground to get homogeneous mixture and then heated in a beaker under microwave irradiation at 160W for 5-15 min. completion of reaction was monitored by TLC. The contents were cooled to room temp. and added to excess ice cold water. The solid product separated was collected by filtration and further purified by recrystllization from ethanol-DMF mixture (2:1).

mp. 170-215 ^{o}C, Yield= 85-90%.

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-phenyl (5a)

IR (KBr): 3027, 3080, 2937, 1620, 1612, 1600, 1527, 1065, 1022, 696 cm^{-1}.

^{1}**H-MNR:** δ (ppm) 4.60 (2H, S), 6.65-8.22(9H, m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(4-Chloro phenyl) (5b)

IR (KBr) : 3025, 3077,2939, 1612, 1630, 1685, 1530, 1072, 1033,690,730 cm^{-1}.

^{1}**H NMR:** δ (ppm) 4.65 (2H, s), 6.60-8.28 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(4-Br-phenyl) (5c)

IR (KBr) : 3029, 3081, 2936,1689, 1627, 1614,1533, 1076, 1035, 689, 722 cm^{-1}.

^{1}**H NMR :** δ (ppm) 4.63 (2H,S); 6.62-8.28 (8H,m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(4-OMe-phenyl) (5d)

IR (KBr) : 3023,3070,2935,1683,1632,1615,1529,1074,1031,690,725 cm^{-1}.

^{1}**H NMR :** δ (ppm) 4.58 (2H,S) ; 6.58-8.17 (8H,m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(4-Me-phenyl) (5e)

IR (KBr) : 3021,3075,2933,1680,1629,1616,1528,1073,1030,690,735 cm^{-1}.

^{1}H NMR : δ (ppm) 4.56 (2H,S); 6.49-7.94 (8H,m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(2-Cl-phenyl) (5f)

IR (KBr) : 3033,3085,2936,1685,1635,1615,1529,1075,1032,692,737 cm^{-1}.

^{1}H NMR : δ (ppm) 4.70 (2H,S); 6.66-8.34 (8H,m).

2-(benzo[d]thiazol-2-ylthio-1.3,4-oxadiazoles-2-(3-NO_2-phenyl) (5g)

IR (KBr) : 3032,3082,201688,1637,1613,1530,1077,1033,694,740 cm^{-1}.

^{1}H NMR : δ (ppm) 4.68 (2H,S); 6.67-8.32 (8H,m).

Synthesis of 5-(substituted phenyl-1.3.4–Triazol-2-yl)-2-mercapto benthiazole(6a-g).

Green Method

5-(substituted phenyl-1.3.4–oxadiazol-2-yl)-2-mercaptobenthiazole[5] (1 mol,) and hydrazine hydrate (0.4 mol) and ethanol (40 ml) was taken RBF placed in microwave oven and irradiated for 4 min. After completion of reaction (monitored by TLC), mixture was cooled and the resulting solid was filtered, dried and recrystallized from ethanol to yield compound[6]**.** The melting point and yields are summarized in **Table I**

Spectral details for few compounds from **6a-g** are given below:

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-phenyl (6a)

IR (KBr): 3213, 3038, 1575, 1515, 1465, 1255, 1070, 682, 723.

^{1}H-MNR: δ (ppm) 8.37(dd, 1H), 7.61(m, 1H), 7.89(m, 1H), 4.10(s, 2H).

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-(4-Chloro phenyl) (6b)

IR (KBr): 3160, 3120, 1572, 1525, 1470, 1262, 1073, 685, 730.

^{1}H NMR: δ (ppm) 3.82(2H, S), 4.65 (2H, s), 6.60-8.28 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3.4-Triazoles-2-(4-Br-phenyl) (6c)

IR (KBr): 3308, 3029, 3081, 1689, 1627, 1614, 1533, 1076, 689, 734.

^{1}H NMR: δ (ppm) 4.12(s, 2H), 4.63 (2H, S); 6.62-8.28 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-(4-OMe-phenyl) (6d)

IR (KBr) : 3250, 3023,3070,1683,1632,1615,1529,1074,690,725.

^{1}H NMR: δ (ppm) 3.89(2H, S), 3.20(3H, S), 4.58 (2H, S), 6.58-8.17 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-(4-Me-phenyl) (6e)

IR (KBr) : 3330, 3021,3075,1680,1629,1616,1528,1073,690,735.

^{1}H NMR: δ (ppm) 3.96(2H, S), 3.29(3H.S), 4.56 (2H, S), 6.49-7.94 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-(2-Chloro-phenyl) (6f)

IR (KBr) : 3325, 3033,3085,1685,1635,1615,1529,1075,692,737.

^{1}H NMR: δ (ppm) 3.65(2H, S) 4.70 (2H, S), 6.66-8.34 (8H, m).

2-(benzo[d]thiazol-2-ylthio-1.3.4 -Triazoles-2-(3-NO_2-phenyl) (6g)

IR (KBr) : 327, 03032,3082,1688,1637,1613,1530,1077,694,740.

^{1}H NMR: δ (ppm) 3.42(2H,S), 4.68 (2H, S), 6.67-8.32 (8H, m).

Table- I. Physical Data of Compounds 6a-g

Sr. No.	Ar	Molecular Formula	% Yield	mp in ^{0}C
6a	Ph	$C_{16}H_{11}N_5S_2$	83	210-212
6b	4-Cl-Ph	$C_{16}H_{10}N_5ClS_2$	84	255-257
6c	4-Br-Ph	$C_{16}H_{10}N_5BrS_2$	85	262-265
6d	4-Ome-Ph	$C_{17}H_{13}N_5OS_2$	82	180-182
6e	4-Me-Ph	$C_{17}H_{13}N_5S_2$	80	200-202
6f	2-Cl-Ph	$C_{16}H_{10}N_5ClS_2$	85	148-150
6g	3-NO_2-Ph	$C_{16}H_{10}N_6O_2S_2$	83	160-163

CONCLUSION

The heterocyclic moieties of 5- substituted Triazole derivatives of 2-marcapto benzothiazole even though have many biological activities but their synthesis involves non-green approach along with some hazardous outputs. The present work tried to synthesis heterocyclic compound carrying such biological activities and minimizes these along with minimal time consumption by the use of green method like stirring, grinding, and microwave chemistry.

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