AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

An Efficient, green synthesis of sulfonamidino-thiocarabamide in absence of catalyst and their biological studies

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ABSTRACT

A clean and efficient route was established to synthesize sulfonamido-thiocarbamides via one-pot reactions in aqueous medium without use of a catalyst and/or organic solvent. The reaction with stoichiometric molar portion could be carried out in an open atmosphere to offer sulfonamido-thocarbamides in good to excellent yields and purities. The novel and clean methodology offers the advantages including short reaction time, excellent yields, operational simplicity, less leaks and environmentally benign path. The identity of newly synthesized compounds is based on elemental and spectral data. They have been further screened for their microbiological activities.

Keywords: Thiocarbamide, Antibacterial and anti-fungal activity, sulfonamido-thiocarbamides.

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Received 07 February 2014, Accepted 26 February 2014

Please cite this article in press as: Bhaskar CS. *et al* An Efficient, green synthesis of sulfonamidino-thiocarabamide in absence of catalyst and their biological studies. American Journal of PharmTech Research 2014.

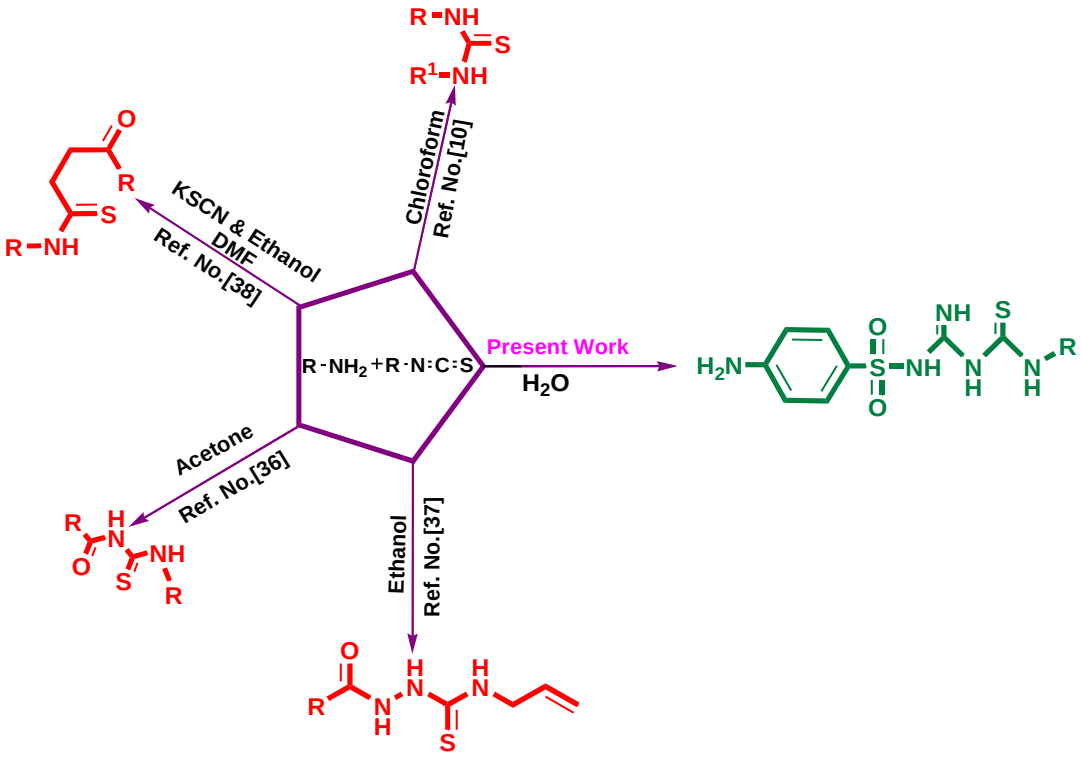
INTRODUCTION

Isothiocyanates are structural distinctive, well known chemical building blocks and found in many biological and pharmaceutically active compounds and have been used as important class of compound in organic chemistry[1-3]. They are used in synthesis of heterocyclic derivatives [4-6] and for the simple and convenient synthesis of alkyl, aryl and amino acid isothiocyanates using different synthetic methods [7]. 1,3-Disubstituted thiocarbamides and their derivatives exhibits a wide range of efficient guanylating agent both in solution [8,9] and on solid support [10-12]. The application of thiocarbamides is to synthesize many heterocyclic scaffold such as 1,3-thiazines [13], 1,3-diazines[14], 1,3-quinazolines[15], 1,2,4-triazines[16] and 1,3,5-triazines [17]. Acyl thiocarbamides are valuable starting materials for various organic transformations and have been used for synthesis of four [18], five [19-22], six [23] and seven [24] membered heterocyclic systems. Recently the advent of thiocarbamide have been considered for the use of increasing technologies for plasma membrane proteomics [25] and remarkable direct enantioselective aldol reactions catalyzed by proline-thiourea host guest relationship [26,27]. The synthesis of thiocarbmide have been gained importance due to diverse patent activities such as antidibatic [28], antiarhritic [29], antineoplastic [30] and anticoagulant [31] and also for treatment of cognitive problems [32], like prostate disorder [33,34]. Furthermore, many thiocarbamides are well known to possess a wide range of bioactivities such as fungicidal, antiviral and regulating activities for plant protection in agriculture [35-37]. Some of them are engaged as commercial insecticides [38], herbicides [39, 40] and fungicides [41, 42].

Owing to this remarkable biological profile, the recent decade has witnessed a considerable growth in the decoration of the entire active and reactive site of thiocarbamides. Among all the active site and its literature survey reveals that, there is a great synthetic challenge for the C-N bond formation due to the nucleophilicity of NH_2 group and easily available electron for electrophilic carbon of N=C=S in aqueous medium. Water as a solvent is inexpensive, environmentally begin and offer better yields with completely new reactivity [43, 44]. Non-toxic, non-corrosive, non-flammable nature and relatively high vapour pressure as compared to organic solvents are favorable individually to render water as sustainable alternative [45, 46]. This is the reason why safer and eco-friendly reaction was carried out in aqueous medium with catalyst free condition.

The isothiocyanate is most reactive and play key role for the synthesis of thiocarbamide, furthermore various isothiocyanates have different biological activities. The highly reactive central electrophilic carbon atom of isothiocyanate (N=C=S) reacts rapidly with amino group of

sulphaguinidine which act as a nucleophile to give various thiocarbamides. It was observed that, the various active amines react rapidly with different isothiocyanates to give thiocarbamides. Literature review reveals that, the various amines react with diverse types of isothiocynates in a choice of organic solvents under appropriate condition to give thiocarbamide derivatives [17, 47-49] (Scheme 1).



Scheme 1 earlier and present work on amino compounds and isothiocyanates

The already reported methods have some weakness like organic solvents; expensive procedure, longer reaction time for completion of reaction and poor yields. More imprudent and biologically active sulphaguanidine has gained a renewed interest in C-N bond formation reaction with most reactive aryl isothiocyanates. To best of our knowledge simple nucleophilic addition reaction between sulphaguanidine and aryl isothiocyanates in aqueous medium is not yet reported. Here, we are reporting studies on the simple nucleophilic addition of sulphaguanidine with various aryl isothiocyanates in aqueous medium to give excellent yield of thiocarbamides.

MATERIALS AND METHODS

General Remark

Melting points were taken in open capillary tube and are uncorrected. Unless otherwise indicated, 1H NMR (400 MHz) spectra were recorded on a Bruker DSX-300/AV-III 400L NMR Spectrometer from DMSO-d6 solution with TMS as an internal reference. Chemical shift are

recorded as ppm on the δ scale. The MS spectra were recorded using QUATRO MICRO APIWATER mass spectrometer. IR spectra were recorded on a Shimadzu (4000-450 cm-1) FTIR Spectrophotometer. Thin layer chromatography (TLC) was performed with E. Merck pre-coated TLC plates, aluminium silica Gel60 F254, and spots were located with ultra violet (UV) light or Iodine vapors and by charring with suitable charring agent. All other reagents, solvents were used without further purification.

General Procedure:

4-Amino-N-carbamimidoyl benzene sulfonamide (**1**, 2 mmol) was dissolved in hot water (15mL) in two necks RB flask and attached with reflux condenser then drop wise aryl isothiocyanates (2a-i, 2 mmol) was added through serine with continuous stirring. The reaction was started within 15-20 minutes after the complete addition of aryl isothiocyanates. The reaction mixture was then refluxed with stirring for 2-3 hours. The completion of reaction was monitored by thin layer chromatography. The products were work up by simple filtration, and then washed several times with hot water to remove the excess of sulphaguanidine followed by petroleum ether to give pure products (3a-i). The identities of newly synthesized compounds were based on spectroscopic comparison like IR, ^{1}H NMR and Mass spectral data. IR[50-51], ^{1}H NMR[52-53] and Mass spectra's of all the newly synthesized compounds (3a-i) are shown in results and discussion section.

RESULTS AND DISCUSSION

In sulphaguinidine moiety having two active groups, one is sulphoxyimino group which is more reactive than other amino group, therefore, sulphoxyimino group react faster with highly reactive isothiocyantates under catalyst free condition, simple reflux in aqueous medium to give excellent yield. The simple nucleophilic addition reaction monitored by TLC and completion of reaction indicated that, the single spot was observed. The reaction product workup by simple method and identity of product was checked by two ways, first reaction took place on sulphoxyimino group. It was further confirmed by positive dye test means other amino group was intact while alkaline plumbite test of the product showed positive result for C=S group which indicated that, free sulphur is present in thiocarbamide. The same reaction was optimized in aqueous medium along with various organic solvents such as ethanol and acetone. The optimized results of reaction conditions are summarized in Table 1 and graphical representation shown in figure 1.

After the successful optimization of reactions in three different solvents, it was clearly indicated that, water is sustainable alternative of greener type without any pollution to give excellent yields

compared to that of ethanol and acetone (Table 2, entry 1-5). Furthermore, we investigated that electron donating (entry 3) and electron withdrawing (entry 5) substituent at C-4 position of aryl group of isothiocyanate has better yield of product but the electron donating (entry 2) and electron withdrawing (entry 4) substituent at C-3 position of aryl group of isothiocyanate has not much encouraging yield of product.

Table 2 Optimization of reaction with different solvents

Entry	Product	Yield (%)C_2H_5OH	Yield (%)H_2O	Yield (%) CH_3COCH_3
1	3a	90.10	92.02	90.42
2	3b	75.32	90.32	93.60
3	3c	91.02	93.41	92.27
4	3g	71.25	78.42	72.50
5	3h	71.31	95.02	90.07

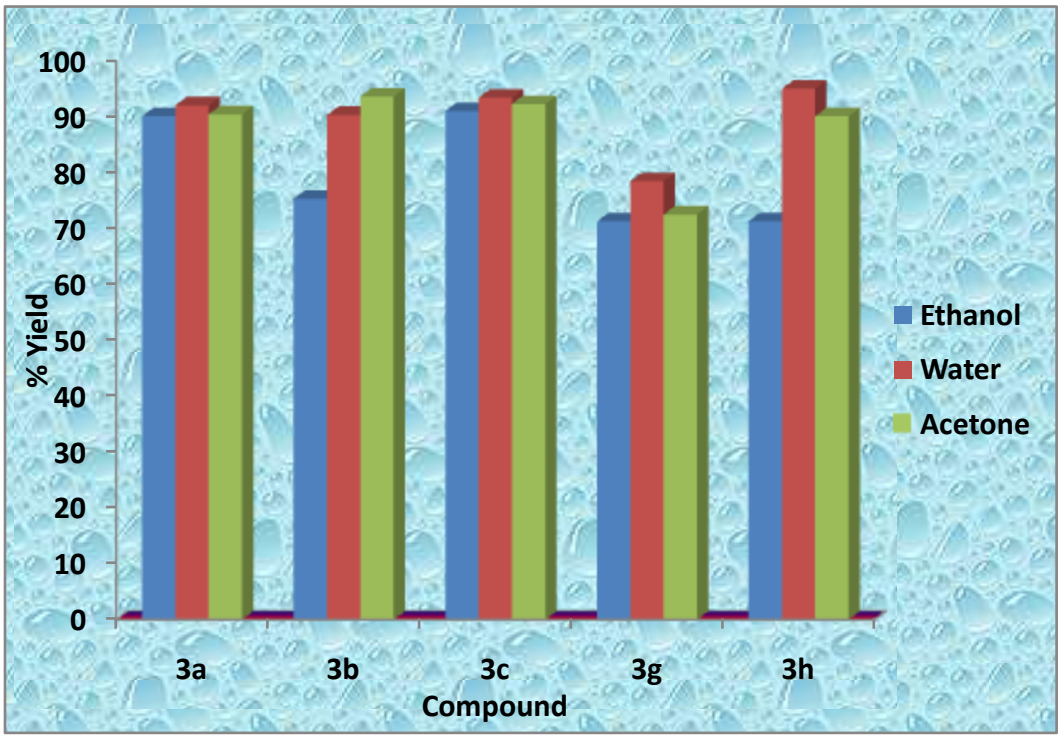
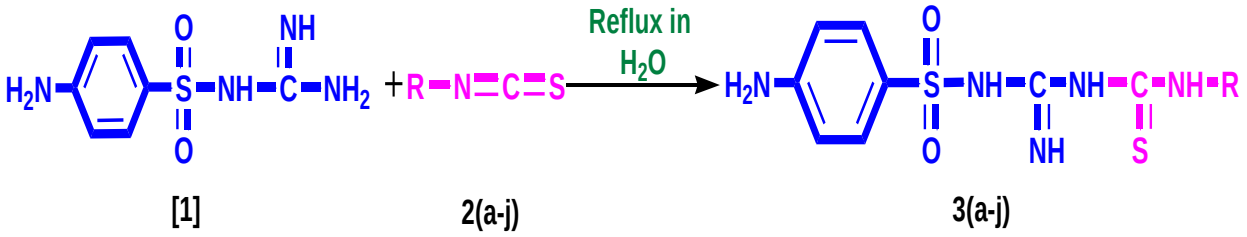
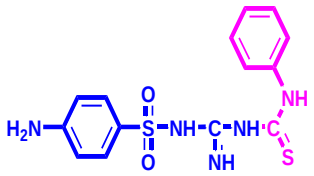
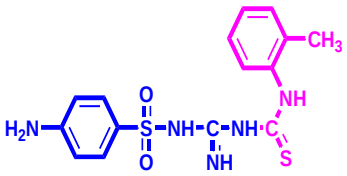


Figure 1 Graphical representation of optimized reaction with different solvents

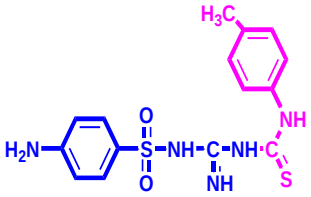




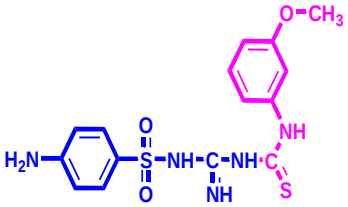
3a(Yield: 92.02%)



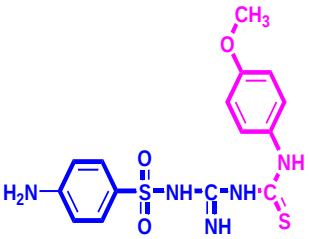
3b(Yield: 90.32%)



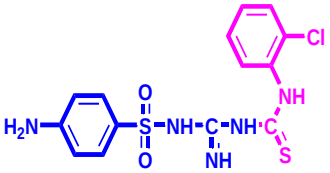
3c(Yield: 93.41%)



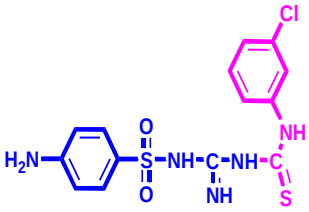
3d(Yield: 93.11%)



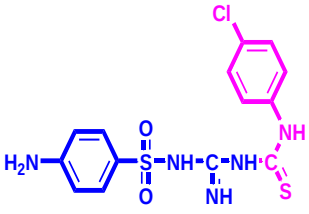
3e(Yield: 93.02%)



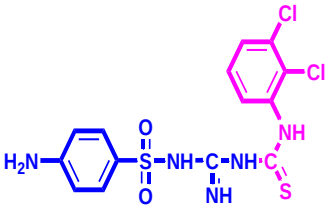
3f(Yield: 94.82%)



3g(Yield: 78.42%)



3h(Yield: 95.02%)



3i(Yield: 85.97%)

Reaction Scheme

Characterization data of (3a-i):

4-Amino-N-[N-(phenylcarbamothioyl) carbamimidoyl] benzenesulfonamide (3a):

Colorless Solid, Yield=92.02%, m.p. =174^{O}C. IR (cm^{-1}): 3500, 3452, 3356, 3282, 3226, 3014, 1651, 1620, 1408, 1323, 1134. NMR (400 MHz, DMSO-d6): δ 09.984 (s,1H,SO_2NH), δ 09.963 (s,1H,C=NH), δ 09.900 (s,1H, NH), δ 7.314-7.688 (m,9H,Ar-H), δ 3.331(s,2H, Ar-NH_2), δ 07.154 (s,1H,Ar-NH). MS: (m/z) (M+1), $[C_{14}H_{15}N_5O_2S_2]^{\cdot+}$ = 350,(M), $[C_{14}H_{15}N_5O_2S_2]^{\cdot+}$ =349, (M-1), $[C_{14}H_{14}N_5O_2S_2]^{\cdot+}$ = 348, $[C_6H_6NO_2S]^{\cdot+}$ =156, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_8N_3O_2S]^{\cdot+}$=198, $[C_7H_9N_4O_2S]^{\cdot+}$ =213, $[C_8H_9N_4O_2S_2]^{\cdot+}$ =257, $[C_8H_{10}N_5O_2S_2]^{\cdot+}$ =272. Analysis for $C_{14}H_{15}N_5O_2S_2$: 349: Calcd.: C,48.12; H,4.33; N,20.04; O,9.16; S,18.35; Found: C,48.15; H,4.34; N,20.09; O,9.19; S,18.39.

4-Amino-N-{N-[(3-methylphenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3b):

Colorless Solid, Yield=90.32%, m.p. =180^{O}C. IR (cm^{-1}):3450, 3332, 3242, 3196, 3159, 1651, 1633, 1404, 1309, 1141, 736, 694. NMR (400 MHz, DMSO-d6): δ 10.186 (s,1H,SO_2NH), δ

09.935 (s,1H,C=NH), δ 09.900 (s,1H, NH), δ 6.947-7.701 (m,8H,Ar-H), δ 3.315(s,2H, Ar-NH_2), δ 06.668 (s,1H,Ar-NH), δ 02.074 (s,3H,CH_3).MS: (m/z) (M+1), $[C_{15}H_{17}N_5O_2S_2]^{\cdot+}$ = 364,(M), $[C_{15}H_{17}N_5O_2S_2]^{\cdot+}$ =363, (M-1), $[C_{15}H_{16}N_5O_2S_2]^{\cdot+}$ = 362, $[C_6H_6NO_2S]^{\cdot+}$ =156, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_9H_{10}N_3S]^{\cdot+}$=192, $[C_7H_9N_4O_2S]^{\cdot+}$ =213, $[C_8H_9N_4O_2S_2]^{\cdot+}$ =257. Analysis for $C_{15}H_{17}N_5O_2S_2$: 363: Calcd.: C,49.57; H,4.71; N,19.27; O,8.80; S,17.64; Found: C,49.60; H,4.76; N,19.32; O,8.82; S,17.70.

4-Amino-N-{N-[(4-methylphenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3c):

Colorless Solid, Yield=93.41%, m.p. =152^{O}C. IR (cm^{-1}):3491, 3444, 3352, 3286, 3228, 3034, 1651, 1622, 1417, 1321, 1132. NMR (400 MHz, DMSO-d6): δ 10.186 (s,1H,SO_2NH), δ 09.888 (s,1H,C=NH), δ 09.874 (s,1H, NH), δ 7.127-7.678 (m,8H,Ar-H), δ 3.325(s,2H, Ar-NH_2), δ 06.535 (s,1H,Ar-NH), δ 02.073 (s,3H,CH_3).MS: (m/z) (M+1), $[C_{15}H_{17}N_5O_2S_2]^{\cdot+}$ = 364,(M), $[C_{15}H_{17}N_5O_2S_2]^{\cdot+}$ =363, (M-1), $[C_{15}H_{16}N_5O_2S_2]^{\cdot+}$ = 362, $[C_6H_6NO_2S]^{\cdot+}$ =156, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_8N_3O_2S]^{\cdot+}$=198, $[C_7H_9N_4O_2S]^{\cdot+}$ =213. Analysis for $C_{15}H_{17}N_5O_2S_2$: 363: Calcd.: C,49.57; H,4.71; N,19.27; O,8.80; S,17.64; Found: C,49.61; H,4.75; N,19.33; O,8.82; S,17.70.

4-Amino-N-{N-[(3-methoxylphenyl)carbamothioyl]carbamimidoyl}benzenesulfonamide (3d):

Colorless Solid, Yield=93.11%, m.p. =175^{O}C. IR (cm^{-1}): 3442, 3344, 3228, 3161, 1645, 1633, 1435, 1317, 1138, 825, 667. NMR (400 MHz, DMSO-d6): δ 10.187 (s,1H,SO_2NH), δ 09.883 (s,1H,C=NH), δ 09.863 (s,1H, NH), δ 7.164-7.701 (m,8H,Ar-H), δ 3.299(s,2H, Ar-NH_2), δ 06.678 (s,1H,Ar-NH), δ 03.728 (s,3H,OCH_3). MS: (m/z) (M+1), $[C_{15}H_{17}N_5O_3S_2]^{\cdot+}$ = 380,(M), $[C_{15}H_{17}N_5O_3S_2]^{\cdot+}$ =379, (M-1), $[C_{15}H_{16}N_5O_3S_2]^{\cdot+}$ = 378, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_9H_{11}N_4OS]^{\cdot+}$ =223, $[C_8H_9N_4O_2S_2]^{\cdot+}$ =257, $[C_9H_{11}N_4O_3S_2]^{\cdot+}$ =287,$[C_{14}H_{14}N_5O_2S_2]^{\cdot+}$ =348. Analysis for $C_{15}H_{17}N_5O_3S_2$: 379: Calcd.: C,47.48; H,4.52; N,18.46; O,12.65; S,16.90; Found: C,47.51; H,4.57; N,18.52; O,12.68; S,16.97.

4-Amino-N-{N-[(4-methoxylphenyl)carbamothioyl]carbamimidoyl}benzenesulfonamide (3e):

Colorless Solid, Yield=93.02%, m.p. =179^{O}C. IR (cm^{-1}):3485, 3427, 3350, 3319, 3259, 3024, 2958, 2839, 1651, 1622, 1417, 1323, 1136,731, 667. NMR (400 MHz, DMSO-d6): δ 09.826(s,1H,SO_2NH), δ 09.786 (s,1H,C=NH), δ 09.786 (s,1H, NH), δ 6.911-7.676(m,8H,Ar-H), δ 3.312(s,2H, Ar-NH_2), δ 06.894(s,1H,Ar-NH), δ 03.740 (s,3H,OCH_3). MS: (m/z) (M+1), $[C_{15}H_{17}N_5O_3S_2]^{\cdot+}$ = 380,(M), $[C_{15}H_{17}N_5O_3S_2]^{\cdot+}$ =379, (M-1), $[C_{15}H_{16}N_5O_3S_2]^{\cdot+}$ = 378,

$[C_6H_5NO_2S]^{\cdot+}$ =155, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_8H_9N_2OS]^{\cdot+}$ =181, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_9H_{11}N_4OS]^{\cdot+}$ =223. Analysis for $C_{15}H_{17}N_5O_3S_2$: 379: Calcd.: C,47.48; H,4.52; N,18.46; O,12.65; S,16.90; Found: C,47.51; H,4.58; N,18.54; O,12.68; S,16.88.

4-Amino-N-{N-[(2-chlorophenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3f):

Colorless Solid, Yield=94.82%, m.p. =193^{O}C. IR (cm^{-1}):3452, 3439, 3334, 3242, 3176, 3095, 1649, 1631, 1402, 1323, 1139,734, 665. NMR (400 MHz, DMSO-d6): δ 10.186(s,1H,SO_2NH), δ 10.186 (s,1H,C=NH), δ 09.621 (s,1H, NH), δ 7.266-7.702(m,8H,Ar-H), δ 3.312(s,2H, Ar-NH_2), δ 06.513(s,1H,Ar-NH). MS: (m/z) (M+1), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 384,(M), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 383, (M-1), $[C_{14}H_{13}ClN_5O_2S_2]^{\cdot+}$ = 382, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_5ClN_5]^{\cdot+}$=171, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_8H_7ClN_3S]^{\cdot+}$=213, $[C_8H_8ClN_4\ O_2S_2]^{\cdot+}$ =291, $[C_7H_6ClN_2S_2]^{\cdot+}$ =185 . Analysis for $C_{14}H_{14}ClN_5O_2S_2$: 383: Calcd.: C,43.80; H,3.68; Cl,9.24; N,18.24; O,8.34; S,16.71; Found: C,43.85; H,3.70; Cl,9.28; N,18.30; O,8.39; S,16.80.

4-Amino-N-{N-[(3-chlorophenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3g):

Colorless Solid, Yield=78.42%, m.p. =187^{O}C. IR (cm^{-1}):3464, 3334, 3317, 3286, 3250, 3072, 1631, 1612, 1402, 1371, 1141, 734, 696. NMR (400 MHz, DMSO-d6): δ 10.140 (s,1H,SO_2NH), δ 10.140 (s,1H,C=NH), δ 10.072 (s,1H, NH), δ 7.330-7.701 (m,8H,Ar-H), δ 3.313(s,2H, Ar-NH_2), δ 07.168 (s,1H,Ar-NH). MS: (m/z) (M+1), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 384,(M), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 383, (M-1), $[C_{14}H_{13}ClN_5O_2S_2]^{\cdot+}$ = 382, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_8N_3O_2S]^{\cdot+}$=198, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_8H_7ClN_3S]^{\cdot+}$=213, $[C_8H_8ClN_4\ S]^{\cdot+}$ =229, $[C_{14}H_{14}N_5S_2O_2]^{\cdot+}$ =348 . Analysis for $C_{14}H_{14}ClN_5O_2S_2$: 383: Calcd.: C,43.80; H,3.68; Cl,9.24; N,18.24; O,8.34; S,16.71; Found: C,43.85; H,3.71; Cl,9.23; N,18.29; O,8.38; S,16.79.

4-Amino-N-{N-[(4-chlorophenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3h):

Colorless Solid, Yield=95.02%, m.p. =172^{O}C. IR (cm^{-1}):3516, 3439, 3354, 3280, 3236, 3034, 1649, 1620, 1413, 1317, 1134, 732, 665. NMR (400 MHz, DMSO-d6): δ 10.062(s,1H,SO_2NH), δ 10.025 (s,1H,C=NH), δ 10.025 (s,1H, NH), δ 7.375-7.694(m,8H,Ar-H), δ 3.311(s,2H, Ar-NH_2), δ 07.370(s,1H,Ar-NH). MS: (m/z) (M+1), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 384,(M), $[C_{14}H_{14}ClN_5O_2S_2]^{\cdot+}$ = 383, (M-1), $[C_{14}H_{13}ClN_5O_2S_2]^{\cdot+}$ = 382, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_7H_5ClNS]^{\cdot+}$=170, $[C_8H_7ClN_3S]^{\cdot+}$=214, $[C_{14}H_{14}N_5S_2O_2]^{\cdot+}$ =348 . Analysis for $C_{14}H_{14}ClN_5O_2S_2$: 383: Calcd.: C,43.80; H,3.68; Cl,9.24; N,18.24; O,8.34; S,16.71; Found: C,43.88; H,3.65; Cl,9.29; N,18.32; O,8.39; S,16.79.

4-Amino-N-{N-[(2, 3-dichlorophenyl)carbamothioyl] carbamimidoyl} benzenesulfonamide (3i):

Colorless Solid, Yield=85.97%, m.p. =191^{O}C. IR (cm^{-1}):3439, 3332, 3223, 3203, 3194, 3170,

1624, 1589, 1402, 1321, 1139, 732, 673. NMR (400 MHz, DMSO-d6): δ 10.244(s,1H,SO_2NH), δ 10.187 (s,1H,C=NH), δ 09.749 (s,1H, NH), δ 7.342-7.711(m,7H,Ar-H), δ 3.301(s,2H, Ar-NH_2), δ 06.974(s,1H,Ar-NH). MS: (m/z) (M+1), $[C_{14}H_{13}Cl_2N_5O_2S_2]^{\cdot+}$=420,(M), $[C_{14}H_{13}Cl_2N_5O_2S_2]^{\cdot+}$=419, $[C_6H_7N_2O_2S]^{\cdot+}$=171, $[C_7H_7N_2O_2S]^{\cdot+}$=183, $[C_7H_8N_3O_2S]^{\cdot+}$=198, $[C_7H_9N_4O_2S]^{\cdot+}$=213, $[C_8H_6Cl_2N_3S]^{\cdot+}$ =248, $[C_8H_7\ Cl_2\ N_4S_2O_2]^{\cdot+}$ =329, $[C_{14}H_{13}\ Cl\ N_5S_2O_2]^{\cdot+}$ =382 . Analysis for $C_{14}H_{13}Cl_2N_5O_2S_2$: 418: Calcd.: C,40.20; H,3.13; Cl,16.95; N,16.74; O,7.65; S,15.33; Fd: C,40.26; H,3.19; Cl,16.99; N,16.80; O,7.69; S,15.40.

Antimicrobial screening:

The synthesized compounds (3a-i) were screened for their antibacterial activity using cup plate method[Ref.]. The bacterial organisms used included both gram-positive as well as gram-negative strains like E. coli, S. aureus, B. Subtilis, Pseudomonas, S. typhi. Sensativity plates were seeded with bacterial innoculum of $1x10^6$ CIUμg mL^{-1} and each well (diameter 10mm) was loaded with 0.1mL of test compound solution in DMSO, so that concentration of each compound was 100μg mL^{-1}. The zones of inhibition were recorded after incubation for 24hrs at 37°C, using vernier caliper. Inhibition zone record of the compounds clearly indicated that 3d; 3f, 3g and 3i were highly active and 3b, 3c and 3h are moderately active intermediate against B. Subtilis. Compounds 3b, 3e, 3f are weakly active against S. aureus and 3g, 3h; 3i are moderately active against S. aureus. All compounds did not show any activity against E. coli, Pseudomonas and S. typhi.

Table 1: Antimicrobial activities of sulfonamido-thiocarbamides

Organism	3a	3b	3c	3d	3e	3f	3g	3h	3i	Control
E. coli	---	---	---	---	---	---	---	---	---	---
S. aureus	---	+	---	---	+	+	++	++	++	---
B. Subtilis	---	++	++	+++	---	+++	+++	++	+++	---
Pseudomonas	---	---	---	---	---	---	---	---	---	---
S. typhii	---	---	---	---	---	---	---	---	---	---

(---) => Inactive (12mm and less), (+): Weakly active (13-16mm,) (++): Moderately active (17-20mm), (+++): Highly active (21mm and above)

CONCLUSION

An efficient, green route has been established to synthesize sulfonamido-thiocarbamides in H_2O-medium without use of a catalyst and/or organic solvents. The novel development offers the advantages including short reaction time, excellent yields, operational simplicity, less leaks and environmentally benign path.

ACKNOWLEDGMENTS

Authors are thankful to UGC, New Delhi, India for providing financial assistance (File no.

89/2011-5/7/2011). The authors are also grateful to Shri Shivaji Science College, Akola, Indian Institute of Science, Bangalore and Vishnu Chemical, Hyderabad for recording the IR, NMR and Mass spectra. Authors also obliged to Dr. V. N. Charde, Department of Microbiology, Arts, Commerce and Science College, Koradi for antimicrobial activities. Thanks are also due to Dr. Mrs. S.B. Taywade, Principal, Arts, Commerce and Science College, Koradi for encouragement and providing necessary facilities.

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