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$CO_{0.9}SM_{0.05}FE_{2.05}O_4$ NANOPARTICLES CATALYZED ONE POT SYNTHESIS OF 4-ARYL-2-AMINOTHIAZOLES IN WATER

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ABSTRACT: 2-amino-4-arylthiazoles are biologically important molecules and important motif of various natural products. Cobalt ferrite ($Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$) nanomaterial synthesized by sol-gel combustion method. Nano Cobalt ferrite efficiently used for the one-pot synthesis of 2-aminothiazoles by the reactions of *in-situ* prepared alpha-amino acetophenones and thiourea. Cobalt ferrite (NPs) found to be an effective catalyst for the present protocol which offered high reaction rate, simple and economic procedure and excellent yield of the thaizole.

KEYWORDS: $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ (NPs)**,** 2-amino thaizole, water, *in-situ* acetophenones, NBS (N-Bromosuccinimide)

INTRODUCTION

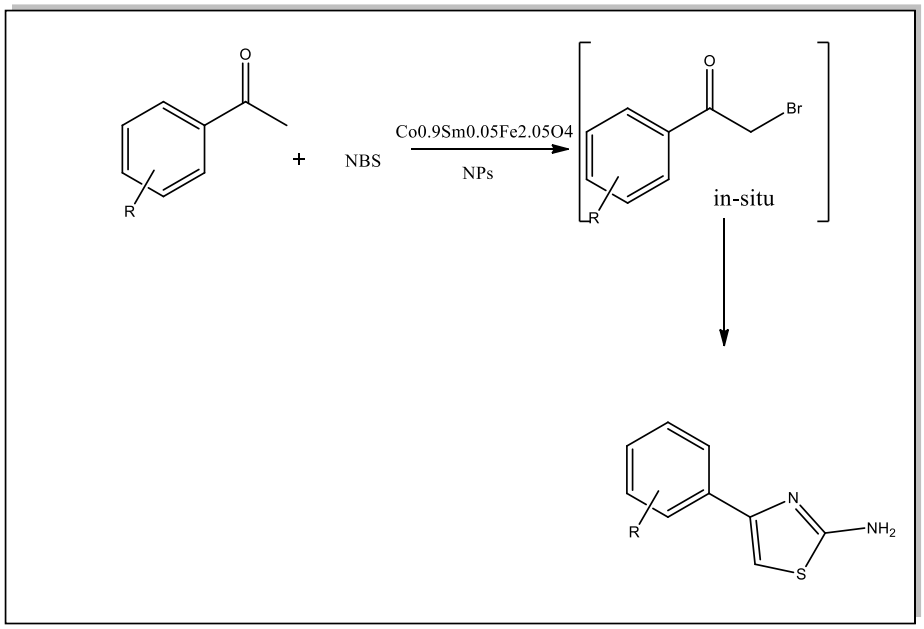
Thiazole and its derivatives are found to be an active precursor of valuable marked drugs required for ailment of inflammation (Clemence et al. 1988) and possess antibacterial (Tsuji and Ishikawa 1944) and immunosuppressant activity.[i-ii]

Thiazoles show wide application in the field of rubber vulcanization,[iii] sunscreens,[iv] sensors,[v] protosencitizers,[vi] liquid crystals,[vii] dyes[viii] and pigments.[ix] Moreover thiazoles and its derivatives occupy a prominent position in recent medicine due to their numerous applications in medicinal chemistry such as antidepresents,[x] antiulcer,[xi] antiHIV,[xii] antiimflammetory [xiii] and anticancer. [xiv]

Nanocatalyst, as one of the most important sustainable materials, have emerged as effiecient catalyst because of their small size, large surface area, selectivity and ability to recover and recycle without significant loss of catalytic activity. Cobalt ferrite Nano catalyst and heterogeneous catalyst have been extensively used in organic synthesis. Recently various organic transformations were achieved by using cobalt ferrites nanocatalyst such as oxidation,[xv] synthesis of pyrroles,[xvi] imidazoles and oxazoles,[xvii] thiazolidimanes,[xviii] pyridines,[xix] pyranes[xx] and N-formylation[xxi]. It attracted our interest to design cobalt ferrite catalyses synthesis of thiazoles.

Herein, $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ nanoparticals use as an efficient catalyst for the one-pot synthesis of 2-amino thiazoles. The primary protocol involves reacting acetophenones with N-

bromosuccinimide in water to synthesize phenacyl bromides. On completion of reaction, thiourea was added into same pot containing *in-situ* prepared phenacylbromide to obtained 4-aryl-2-amino thiazoles.



Scheme 1 $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ catalysed synthesis of 2-amino thiazoles

Experimental:

Materials and methods

Melting points were taken in open capillary and are un-corrected. ^{1}H NMR was recorded in $CDCl_3$ solvent on a Bruker AC 400 MHz spectrometer. Characterization of synthesized cobalt ferrite achieved by XRD, TEM, etc.

General procedure for the synthesis of 4-aryl-2-aminothiazoles

A mixture of acetophenone (1 mmol), N-Bromosuccinimide (1 mmol), and $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ (10 mol%) in water (5 mL) was stirred at 85-90^{0}C and the formation of α-bromoketones was monitored by thin-layer chromatography (TLC). On completion of the bromination, thiourea (1 mmol) was added to the reaction mixture and stirred at same temperature. After completion of the reaction, the reaction mass was poured in ice-cold water and basified by 10% aqueous ammonia; the solid obtained was filtered, washed with cold water and recrystallized from proper solvents.

Spectral data of synthesized compounds

2-(4-Chlorophenyl)amino-4-(4-chlorophenyl)thiazole 3a ^{1}H NMR (400 MHz, $CDCl_3$): d 6.72 (1H, s, NH D_2O exchangeable); 6.79–7.85 (9H, m, Ar–H and thiazole proton). Analytically calculated (%) for $C_{15}H_{10}Cl_2N_2S$: C, 56.13; H, 3.29; N, 8.62; found C, 55.77; H, 3.13; N, 8.78; m/z 323 (M+2). 2-**(4-Fluorophenyl)amino-4-(4-chlorophenyl)thiazole 4m** 1H NMR (400 MHz, $CDCl_3$): d 6.69 (1H, s, NH D_2O exchangeable); 7.12–7.88 (9H, m, Ar–H and thiazole proton at 5). Analytically calculated (%) for $C_{15}H_{10}ClFN_2S$: C, 56.22; H, 3.44; N, 9.01; found C, 56.16; H, 3.33; N, 9.20; m/z 306 (M+2).

2-(4-Methylphenyl)amino-4-(4-methylphenyl)thiazole 4n ^{1}H NMR (400 MHz, $CDCl_3$): d 2.29(3H, s, CH3); 6.49(1H, s, NH); 7.5–7.7 (9H, m, Ar–H and H- of thiazole). Analytically calculated (%) for $C_{17}H_{16}N_2S$: C, 72.85; H, 5.77; N, 9.97; found C, 72.72; H, 5.65; N, 9.86;

2-(4-Chlorophenyl)amino-4-(4-bromophenyl)thiazole 4q 1H NMR (400 MHz, $CDCl_3$): d 6.62 (1H, s, NH D_2O exchangeable); 7.28–7.81 (9H, m, Ar–H and thiazole proton). Analytically calculated (%) for $C_{15}H1_0BrClN_2S$: C, 49.33; H, 2.81; Br, 21.88; N, 7.68; found C, 49.25; H, 2.52; N, 7.56; m/z 366 (M+).

4-Phenylthiazol-2-amine (3a). ^{1}HNMR: 5.15 ppm (br singlet, 2H, for NH_2, D2O exchange), 6.86 ppm (s, 1H, thiazolyl proton) and 7.21–7.84 (m, 5H,for aromatic proton of benzene ring) .

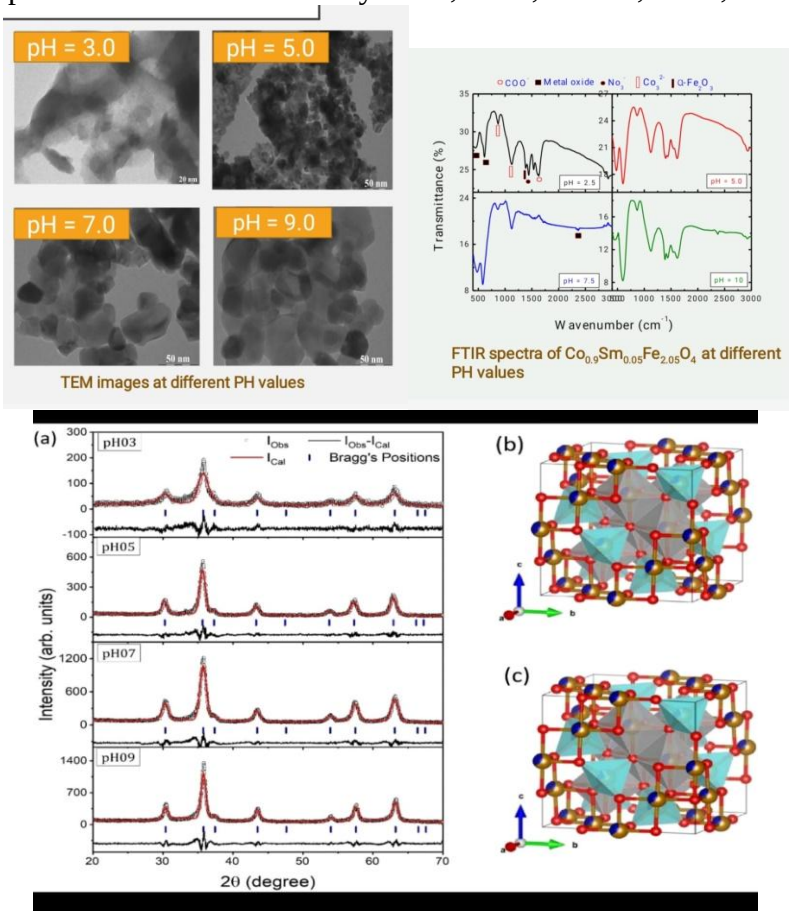
4-(4-cholo-Phenyl)thiazol-2-amine (3c). 5.33 ppm (br singlet, 2H, for NH_2, D_2O exchange), 6.69 (s, 1H, thiazolyl proton), 7.37 (d, 2H, J=8.67 Hz, aromatic proton of benzene ring) and 7.81 (d, 2H, J=8.65 Hz, aromatic proton of benzene ring).

4-(4-Bromo-Phenyl)thiazol-2-amine (3e): 5.34 ppm (br singlet, 2H, for NH_2 , D_2O exchange), 6.77 (s, 1H, thiazolyl proton), 7.47 (d, 2H, J=7.6 Hz aromatic proton of benzene ring) and 7.65 (d, 2H, J=8.6Hz, aromatic proton of benzene ring).

4-(4-methyl-Phenyl)thiazol-2-amine (3f): 2.48 ppm (s, 3H, for CH_3 group), 5.48 (br singlet, 2H, for NH_2, D_2O exchange), 6.67(s, 1H, thiazolyl proton), 7.37 (d, 2H, d, 2H, J=7 Hz, aromatic proton of benzene ring).

RESULT AND DISCUSSION:

Most of the literature survey reveals that, nanoferrite can be used as a catalyst for the formation of C-C bond, and synthesis of various biologically active heterocyclic compounds.[22] Hence, initially pure and substituted magnetic ferrite were prepared by sol-gel combustion method. Synthesized sample are well characterised by XRD, SEM, EDAX, TEM, etc techniques. fig.1



XRD of **$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$**

Fig.1 Spectral images of $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$

Fe-rich cobalt ferrite nanoparticles with a chemical formula $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ were synthesized by a chemical route vix.sol-gel auto combustion method. These nanoparticles were

synthesized from the corresponding precursor solutions of varying pH values ranging from 3-9. These synthesized nanoparticles used as a catalyst for the synthesis of biologically active 2-amino thiazoles. Initially reaction of acetophenone with N-Bromo succinimide carried out in the presence of 10 mole precent Fe-rich cobalt ferrite in water. Furthermore, thiourea was added in the same pot to achieve the synthesis of 2-amino thiazoles. Reaction was optimized by varying various amount of catalyst such as 2mol%, 5mol%, 10 mol% and 15mol% and result were depicted in **table 1**. It was observed that reaction could be possible in all proportions of catalyst but in 10 mol% found to be give high yield.

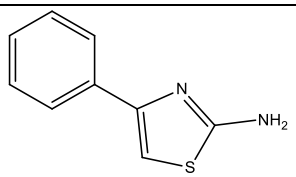
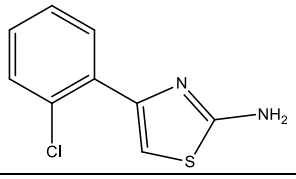
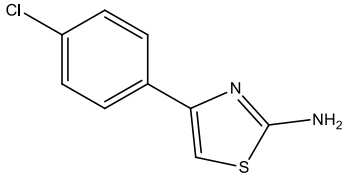
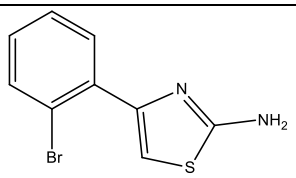
Table 1: Optimization of the catalyst for the synthesis of thiazoles

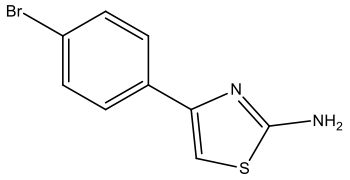
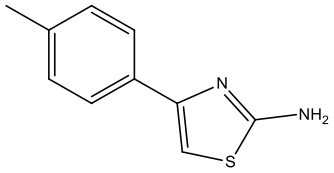
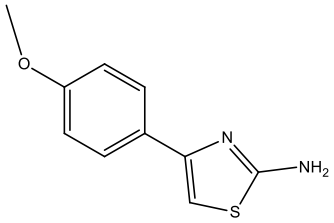
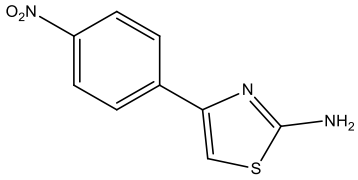
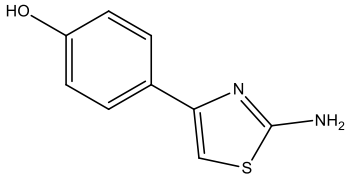
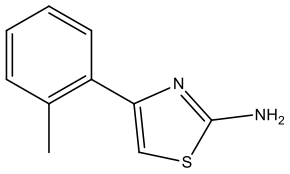
Entry	Catalyst	Mol %	Solvent	Time (min.)[b]	Yield[a]
1	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	2	Ethanol	10	79
2	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	5	Ethanol	12	81
3	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	10	Ethanol	12	81
4	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	15	Ethanol	12	79
5	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	10	Water	8	89
6	$Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$	5	Water	15	80
7	$CeZr_2O_4$	10	Ethanol	20	49

Reaction carried out using acetophenone (1mmol), thiurea(1mmol) and NBS(1mmol)
[a]Isolated yield
[b]Time for overall reaction

To generalize the scope above reaction differently substituted acetophenones, were used for the reaction and results are shown in **table 2**. All the synthesized 2-amino thiazoles derivatives were characterized by ^{1}H NMR, IR and Mass spectrometric techniques.

Table 2: Physical data of 2-amino thiazoles

Compound	Structure	Time (Min.)	Yield	Melting point(^{0}C)
3a		8	89	147
3b		7	92	188
3c		7	92	178-179
3d		8	90	165

3e		8	90	166-168
3f		9	88	135-136
3g		8	89	206-208
3h		7	92	285-287
3i		8	88	204
3j		8	88	146

CONCLUSION :

A novel and environmentally benign protocol designed for the synthesis of 4-aryl-2-aminothiazoles using $Co_{0.9}Sm_{0.05}Fe_{2.05}O_4$ catalyst and water as a green reaction medium. The main remarkable features of this approach are: rapid, mild reaction condition, atom and step economy, use of *in-situ* prepared lachrymatric and unstable α-bromoketones, high yields (89–92%) and green chemistry such as avoiding hazardous organic solvents, toxic catalysts and waste.

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CONFLICT OF INTEREST

All the authors do not have any potential conflict of interest.

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