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MGFE$_2$O$_4$ CATALYSED SYNTHESIS OF 3-METHYLBENZO[4,5]IMIDAZO[2,1-B]THIAZOL-2-YL)(PHENYL)METHANONES

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ABSTRACT: Synthesis of 3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanoneshas been achieved by the cyclization of 2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone and acetic anhydride in the presence of MgFe$_2$O$_4$ as a nanocatalyst. The synthesized 3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones are valuable scaffolds with potential bioactivities. Present method focus on the highly efficient and economic route for 3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones.

KEYWORDS:1*H*-Benzo[d]imidazole-2-thiol, MgFe$_2$O$_4$, acetic anhydride, ethanol.

INTRODUCTION

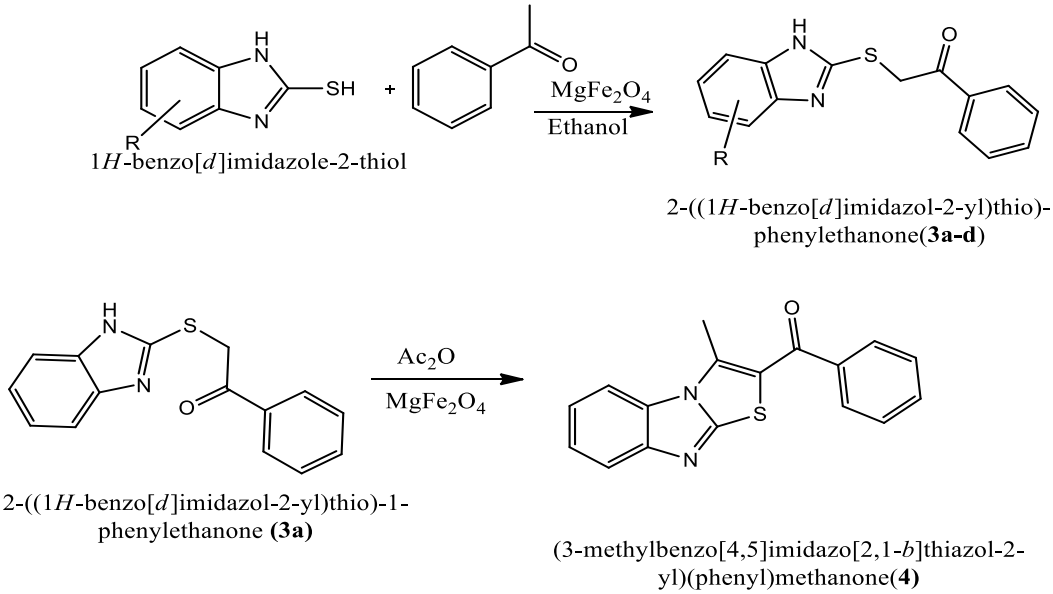
Nitrogen and sulphur containing heterocyclic compounds atoms occupy a prominent place in medicinal chemistry owing to their distinct biological and pharmacological properties. Among them, imidazothiazoles have attracted great deal of interest because of their structural similarity with nucleotides and alkaloids, in addition to this; they easily interact with biological macromolecules[i-ii]. The benzo[4,5]imidazo[2,1-b]thiazole motif represents a fused heterocyclecontains an imidazole and thiazole nucleus, enhancing electronic properties, and binding ability toward various biological targets[iii].

Imidazothiazoles derivatives exhibit a broad spectrum of pharmacological applications such as antimicrobial, antifungal, antimalarial, anti-inflammatory, antiviral, anticancer, and antiprotozoalactivitiesi[v-vi]. The involvement of methyl groups can modify lipophilicity, bioactivity, while benzoyl groups can improve π–π stacking interactions [vii].

Many improved approaches have been designed for the construction of benzo[4,5]imidazo[2,1-b]thiazoles derivatives including cyclocondensation reactions of 2-aminobenzothiazoles with α-haloketones, α-haloesters, or active methylene compounds under reflux or catalyst-assisted conditions[viii-ix],microwave-assisted and Transition-metal-catalyzedprotocols[x-xvii]. Most of these protocols suffer with one or more severe drawbacks such as low yield, harsh reaction condition, expensive, use of volatile and hazardous medium. Therefore there is urgent requirement of

environmentally benign economic approach for the synthesis of 3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanon**es.**

Herein, (3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanoneis synthesized in the presence of $MgFe_2O_4$ as a nanocatalyst. The present method involves the initial coupling of mercaptobenaimidazole with aromatic kenones to obtained 2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone (**3**) intermediate. 2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone(3) further treated with acetic anhydride in the presence of $MgFe_2O_4$ in ethanol to offered (3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones.



1*H*-benzo[*d*]imidazole-2-thiol

2-((1*H*-benzo[*d*]imidazol-2-yl)thio)-1-phenylethanone(**3a-d**)

2-((1*H*-benzo[*d*]imidazol-2-yl)thio)-1-phenylethanone **(3a)**

(3-methylbenzo[4,5]imidazo[2,1-*b*]thiazol-2-yl)(phenyl)methanone(**4)**

R= H,OCH_3,CH_3,Cl

Scheme 1: $MgFe_2O_4$ catalysedsynthesis of 3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones.

EXPERIMENTAL

Material and method

$MgFe_2O_4$ (x = 0.0–1.0) was synthesized using the sol-gel auto-combustion method, employing high-purity nitrates. Analytical reagent (A.R.) grade citric acid ($C_6H_8O_7 \cdot H_2O$), magnesium nitrate ($Mg(NO_3)_2 \cdot 6H_2O$), and iron nitrate ($Fe(NO_3)_3 \cdot 9H_2O$). $MgFe_2O_4$ ferrite was characterized by X-ray diffraction.

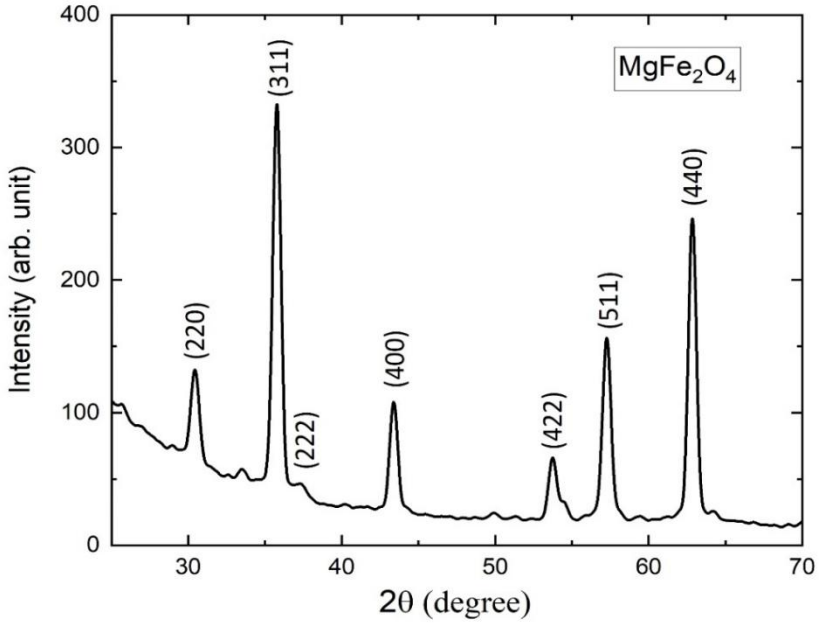


Figure 1: X-ray diffraction pattern of $MgFe_2O_4$ nanoparticles.

General procedure for the synthesis of 2-((1H-benzo[d]imidazol-2-yl)thio)-1-phenylethanone

The solution of compound 1 mercaptoimidazole and acetophenone was dissolve in ethanol. add 2 mol% $MgFe_2O_4$ and resulting reaction mixture was stirred for required time at 85°C. The reaction was monitored by TLC. On completion of reaction, reaction mass was poured on crushed ice. Separated solid of crude mercapto derivative of benzimidazoles was extracted by ethyl acetate (3x10),dried and recrystallized by ethanol. And catalyst recovered from aqueous phase used for further run.

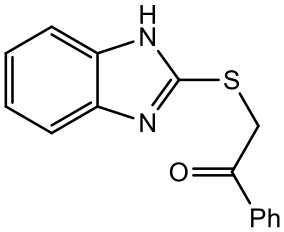
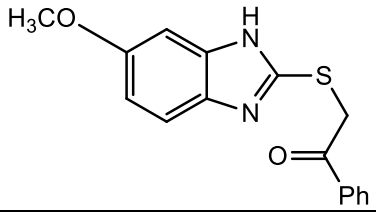
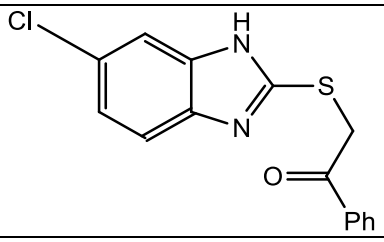
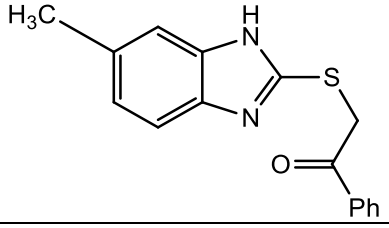
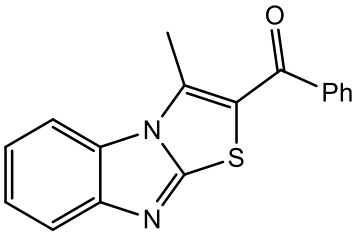
General procedure for the synthesis of (3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones

A mixture of 2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone (3) (1 mmol) and acetic anhydride (12 mL) was heated at 85°C in the presence 5 mol% $MgFe_2O_4$. After the completion of the reaction, acetic anhydride was distilled off completely. Separated solid was extracted by ethyl acetate (3x10), dried and recrystallized by ethanol.catalyst was recovered from aqueous phase used for further run

RESULTS AND DISCUSSION

(3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanonewas synthesized by two-step sequence starting from 1*H*-Benzo[d]imidazole-2-thioland aromatic keones.condensation of 2-mercaptobenzimidazole with substituted acetophenone afforded the 2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone**(3a-d)**in the presence of $MgFe_2O_4$ in ethanol (**table 1**).The second step, intermediate (**3**) reacted with acetic anhydride in the presence of $MgFe_2O_4$ nanoferrite as a heterogeneous catalyst led to cyclocondensation, generating the (3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanone(**Table 1**). $MgFe_2O_4$ provides Lewis acidic sites to activate the carbonyl group and expedites cyclization under mild conditions.

Table 1: Physical data of Synthesized Compounds..

Compounds	structure	Time (min.)	Yield (%)	Melting point
3a		**21**	97	195-197
3b		20	95	184-185
3c		20	96	156-158
3d		23	97	175-176
4		35	87	124

Structure of the products was confirmed through various spectroscopic techniques. IR spectra showed a strong band around ~1672 cm^{-1} indicating the benzoyl carbonyl (C=O) group, while ^{1}H NMR spectra confirmed the presence of a methyl substituent on aromatic ring(singlet at ~δ 2.2 ppm). The ^{13}C NMR spectrum exhibited signals for the carbonyl carbon (~δ 191 ppm), aromatic carbons, and the methyl-substituted heteroaromatic carbons.

The recyclability of $MgFe_2O_4$ nanoparticles was also evaluated (**Table 2**). The catalyst maintained high activity over three consecutive cycles, with yields ranging from 87% in the first run to 81% in the third, and catalyst recovery above 90%. This recyclability highlights the potential of $MgFe_2O_4$ NPs as a sustainable and eco-friendly catalyst for heterocyclic synthesis.

Table 2:Recyclability of catalyst ($MgFe_2O_4$).

Catalyst	Cycle	Yield %
$MgFe_2O_4$	1^{st}	87
$MgFe_2O_4$	2^{nd}	85
$MgFe_2O_4$	3^{rd}	82

Spectral data of synthesized compounds

2-((1H-Benzo[d]imidazol-2-yl)thio)-1-phenylethanone (**3a**).

Melting point: 195-197^{O}C. Mass: $[ES]^+$: Calculated – 270.19, Found – 269.12. ^{1}H NMR (400 MHz, DMSO, δ ppm): 4.83 (s, 2H,), 5.1 (s, 1H), 7.21 (d, 2H), 7.55 (d, 2H), 7.558 (d, 2H), 7.61 (d, 1H) ,7.97 (d, 2H),. ^{13}C NMR (400 MHz, DMSO, δ ppm): 37.07, 115.41, 122.23, 128.65, 128.31, 133.51, 135.38,138,46, 146.18, 193.41.

2-((6-Methoxy-1H-benzo[d]imidazol-2-yl)thio)-1-phenylethanone (**3b**)

Melting point: 184-185^{O}C. Mass: $[ES]^+$: Calculated – 298.33, Found – 298.34. ^{1}H NMR (400 MHz, DMSO, δ ppm): 4.11(s, 3H, -CH_3), 4.72 (s, 2H), 4.78 (s, 1H,), 7.24(d, 1H), 7.52 (d, 1H),7.55 (d, 1H), 7.59 (d, 2H), 7.68 (d, 1H) ,8.00 (d, 2H). ^{13}C NMR (400 MHz, DMSO, δ ppm 35.71, 58.14, 101.79, 112.11, 116.91, 128.71, 129.34, 131.66, 133.89, 139.00,147.14, 153.40, 194.14.

2-((6-Methyl-1H-benzo[d]imidazol-2-yl)thio)-1-phenylethanone(**3d**)

Melting point: 175-176^{O}C. **Mass:** $[ES]^+$: Calculated – 283.45 Found – 283.03. **^{1}H NMR** (400 MHz, DMSO, δ ppm): 2.13 (s, 3H, -CH_3), 4.751 (s, 2H, -CH_2), 4.93 (s, 1H, -NH), 7.44(d, 1H, Ar-H), 7.51 (d, 1H, Ar-H),7.56 (d, 1H, Ar-H), 7.59 (d, 2H, Ar-H), 7.66 (d, 1H, Ar-H),7.97 (d, 2H, Ar-H),. **^{13}C NMR** (400 MHz, DMSO, δ ppm): 22.11, 35.33, 113.49, 114.22, 126.19, 128.6,128.8, 132.33,133.44,134.11,137.31, 138.13, 139.88, 194,6.

(3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanones(**4)**

^{1}H NMR (400 MHz, DMSO) 2.43 (s,3H), 7.22 (d, 2H,), 7.59 (d, 1H), 7.64 (s, 12H,), 7.73 (s, 1H,), 7.89 (s, 2H) 7.91 (s, 1H); mass spectrum: MF $C_{17}H13N_2OS$, calculated m/z 292.28, observed m/z 293.0746 (m+1).

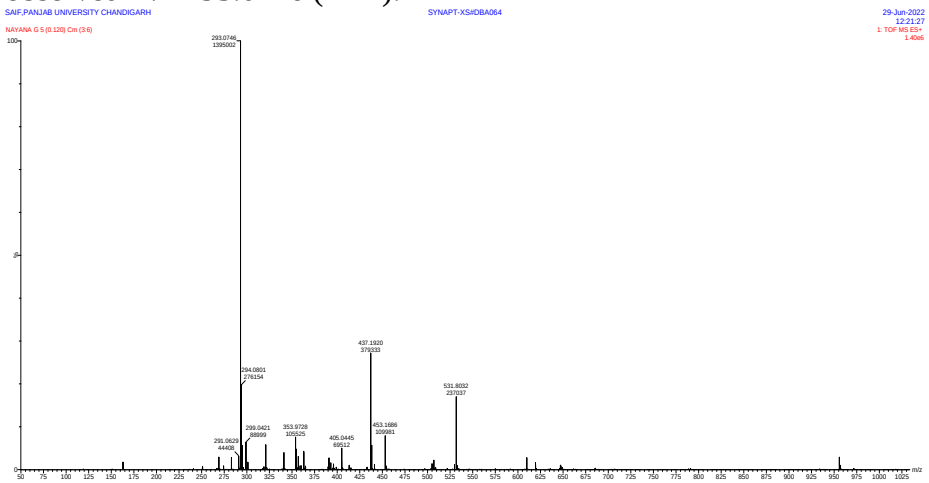


Fig.2 Mass spectrum of compound 4

CONCLUSION

The present methodology provides an efficient and green route for the synthesis of (3-Methylbenzo[4,5]imidazo[2,1-b]thiazol-2-yl)(phenyl)methanonederivatives. The use of a magnetically recoverable $MgFe_2O_4$ nanoferrite not only enhance reaction rate but also yield of

the products. The significant features of this route are operational simplicity, efficient and follow the principles of green chemistry by allowing catalyst recovery.

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