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Fe_3O_4-MNPs promoted green synthesis of thiazole derivatives using alkyl bromides

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Abstract: In this research, magnetic iron oxide nanoparticles (Fe_3O_4-MNPs) were produced using green biosynthetic method by reduction of ferric chloride solution with *Clover Leaf* water extract. The nanoparticles generated using this procedure can potentially important in different purposes such as organic synthesis. A one-pot, efficient and high yielding procedure for the synthesis of thiazole derivatives is investigated. The procedure carried out *via* multicomponent reaction of isothiocyanate, alkyl bromides, *N*-methylthiazole and triphenylphosphine in the presence of bio-Fe_3O_4-MNPs as catalyst under solvent-free conditions at 50 ^oC. Easy, simple, rapid and clean procedure for the synthesis of thiazole derivatives are the advantages of this study.

Keywords: Isothiocyanate, Fe_3O_4-MNPs, Alkyl bromides, Green synthesis, Thiazole.

Introduction

In multicomponent reactions (MCRs), three or more reactants combine in a one-pot and generate one product. These reactions are interesting in last decade because of economically and environmentally advantageous towards multi-step methods [1-7]. Multi-step synthesis produce large amounts of waste due to separation steps of intermediate that commonly include employing of expensive, toxic and dangerous solvents in each step. MCRs are absolutely studied about combinatorial synthesis, and used in the discovery method for new drugs and agrochemicals [8]. MCRs have a great instrument toward the one-pot synthesis of different and complex compounds with small heterocycles.19approach to improve their synthetic utility. The nano catalyst display good catalytic activity compared to their bulk sized samples [9, 10] for the synthesis of some organic compounds. Nanoparticles are particles with very small sized along.

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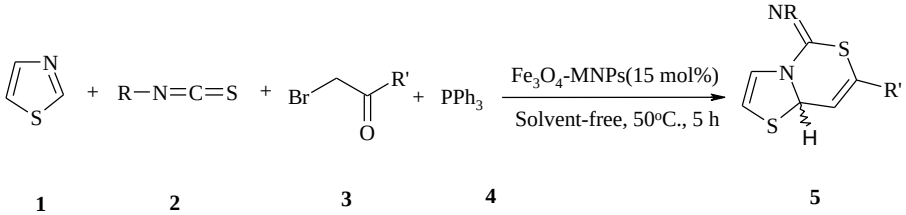
These compounds because of its large surface area to volume ratio have good catalytic reactivity, thermal conductivity, non-linear optical presentation and chemical steadiness [11]. Nanoparticles due to their antimicrobial activities [12] could be considered as nano antibiotics. Using plants with biomedical applications for biosynthesis of nanoparticles is a procedure of generating nanoparticles. This method is a cheap, bio friendly, safe, green procedure [13]. Green synthesis contains synthesis using plants, bacteria, fungi, algae etc. These methods investigated generation of bio-Fe3O4-MNPs with big scale without additional impurities [14]. Nanoparticles produced from plant show more catalytic activity without employing of expensive and toxic chemicals. These plants extract displaye some phytochemicals that play in both decreasing capping and stabilization agent. Currently, a great number of physical, chemical and biological procedure are available to generated different classes of nanoparticles [15]. The generated nanoparticles by using each methods display specific properties.

Conversely, at this time biosynthesis of metal nanoparticles by using of plants is under expansion.

Green nanotechnology has many important and involves a wide scale of procedures that decrease or remove toxic materials to restore the environment. Green chemistry methods are significant due to aim to protect resources and reducing costs [16–18]. In this research we investigate the synthesis of thiazole derivatives **5** *via* three-component reaction of thiazole **1**, isothiocyanates **2**, alkyl bromides **3** and triphenylphosphine **4** in the presence of catalytic amount of Fe_3O_4-MNPs nanoparticles under solvent-free conditions in good yield (Scheme **1**).



1 **2** **3** **4** **5**

2, 3, 5	R	R'	Yield % of **5**
a	Ph	CO_2Et	92
b	4-MeO-C_6H_4	CO_2Et	95
c	4-Me-C_6H_4	CO_2Et	92
d	4-NO_2-C_6H_4	CO_2Et	85
e	4-Br-C_6H_4	4-MeO-C_6H_4	90
f	4-Me-C6H4	4-MeO-C_6H_4	87
g	4-Me-C_6H_4	4-NO_2-C_6H_4	80
h	^{t}Bu	CO_2Et	97

Scheme 1. Synthesis of compound **5**.

Optimization the reaction conditions is the first step in these reactions. The reaction of *N*-methylthiazole **1**, phenylisothiocyanate **2a**, ethyl bromopyruvate **3a** and triphenylphosphine **4** was selected as the model reaction (Scheme1). This reaction has low yield without catalyst and mixture of reaction is very busy. We employed some nano catalysts such as ZnO-NPs, TiO_2-NPs, KF/CP NPs and CuO-NPs in the model reaction. Among them bio-Fe_3O_4-MNPs is the best because of green synthesis, easy separation of catalyst from the mixture of reaction and easy purification of product. Also several solvents and solvent-free conditions are employed for this reaction. The yield of reaction under solvent-free conditions and 50 ^oC is the good. The results of our optimization are showed in Table **1**.

Table 1. Optimization of reaction condition for the synthesis of compound **5a.**

Entry	Catalyst	Temperature ^oC	Solvent	Yield, % of **5a**
1	None	r.t.	None	-----
2	None	50	None	15
3	KF/CP NPs	r.t.	CH_2Cl_2	45
4	KF/CP NPs	50	CH_3CN	55
5	TiO_2-NPs	50	CH_3CN	65
6	TiO_2-NPs	50	None	68
7	TiO_2-NPs	80	Toluene	72
8	Fe_3O_4-MNPs	r.t.	CH_2Cl_2	54
9	Fe_3O_4-MNPs	50	CH_3CN	87
10	Fe_3O_4-MNPs	80	CH_3CN	87
11	**Fe_3O_4-MNPs**	**50**	**None**	**92**
12	CuO-NPs	r.t.	CH_2Cl_2	35

Bio-Fe_3O_4-MNPs were prepared by using the aqueous extract of *Clover Leaf*. For confirming the structure of bio-Fe_3O_4MNPs, field emission scanning electron microscopy (FESEM) (Figure 1) and XRD (Figure 2) spectra are given for nanostructure. FESEM analysis of the magnetic nanoparticles showed uniform-sized particles with spherical morphology.

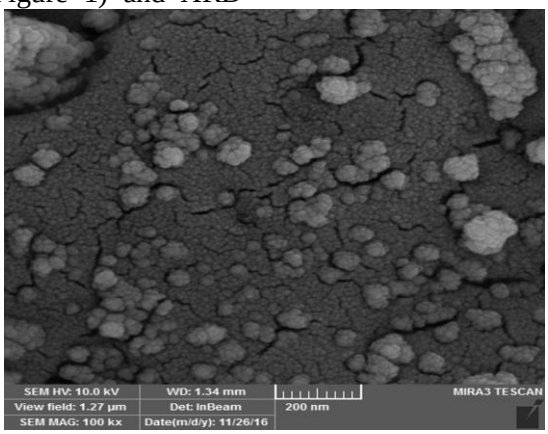


Figure 1. FESEM images of Fe_3O_4-MNPs.

Figure **2** shows the XRD spectra of the Fe_3O_4-MNPs. The diffraction peaks at 2θ = 29.7°, 35.6°, 42.9°, 57.3° and 62.7° can be indexed to (220), (311), (400), (511) and (440) planes of cubic Fe_3O_4 (JCPDS 19-0629). The average size of the Fe_3O_4-MNPs is calculated 14 nm.

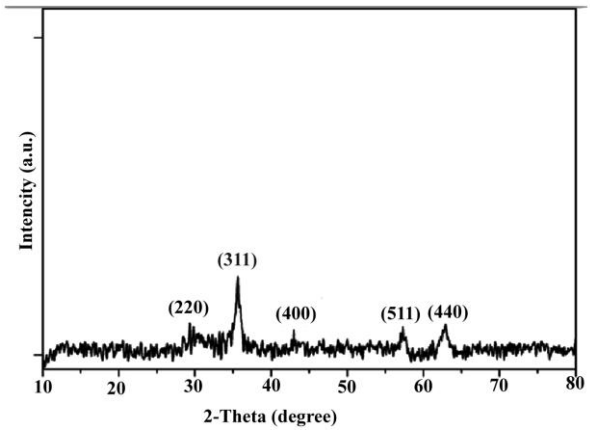


Figure 2. XRD powder pattern of Fe_3O_4-MNPs

The UV-visible spectrum of the green synthesized Fe_3O_4-MNPs employing as a capping agent has been shown in Figure 3. This spectrum shows a broad bond at 365 nm which is characteristic of the Surface Plasmon Resonance (SPR) of Fe_3O_4-MNPs in solution.

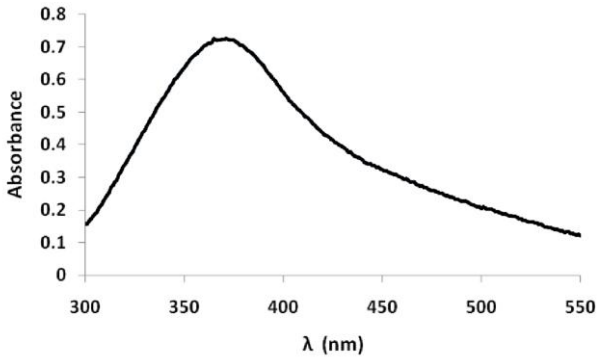


Figure 3. UV-visible spectrum of Fe_3O_4-MNPs

Figure 4 shows the FT-IR spectra of the *Clover Leaf* extract and Fe_3O_4 nanoparticles.The FT-IR spectrum of the extract (a) represented some peaks at 3500 to 3000, 1634, 1412, 1300 to 1100 cm^{-1}. These peaks could be attributed to the functional groups of flavonoids and other phenolic compounds in the *Clover Leaf* extract that are answerable for the decrease of the metal ions and capping of the bio-decreased nanoparticles. The characteristic band of Fe–O in the FT-IR spectra of the Fe_3O_4-MNPs (b) is located at 588 cm^{-1}.

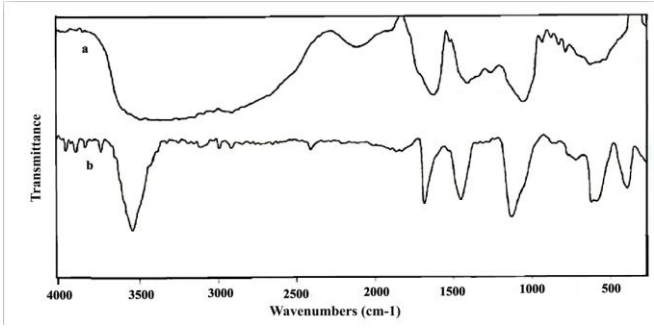
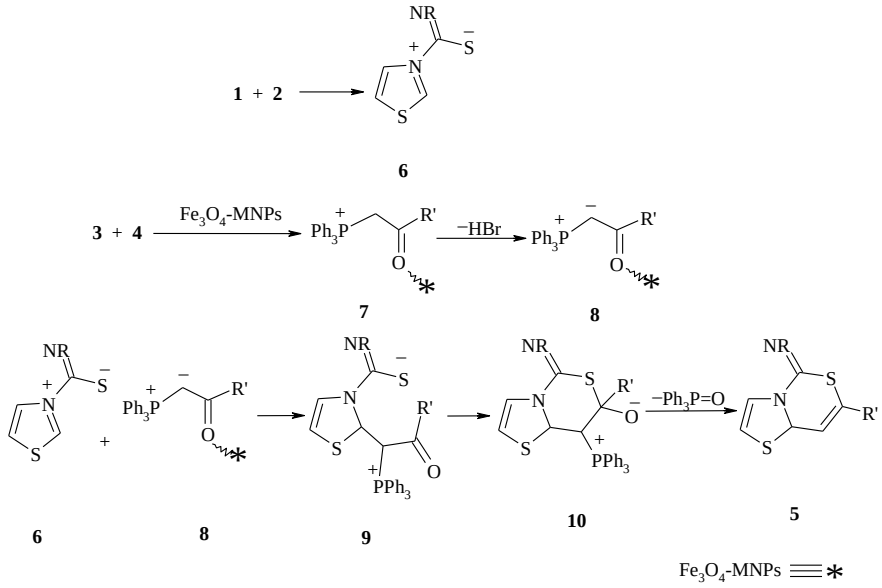


Figure 4. FT-IR spectra of (a) *Clover Leaf* extract (b) Fe_3O_4-MNPs

The amount of catalyst is 15 mol% in optimized condition. We used 10-30 mol% catalyst for selecting best amount of catalyst. By increasing the amount of catalyst from 15 mol%, isn't seen any change in the yield of reaction. After each run, the catalyst was separated from the mixture of reaction and washed with ethylacetate, then dried under vacuum at room temperature.

The structure of compounds **5a-h** was confirmed by ^{1}H-NMR, ^{13}C-NMR, IR and mass spectroscopy. For example, the ^{1}H-NMR of compound **5a** displays one singlet for NMe protons at 2.85 ppm, one doublet at 5.26 (d, ^3J = 6.8 Hz) ppm for -CH protone, three doublets for three =CH proton at 6.56 (d, ^3J = 6.5 Hz), 6.75 (d, ^3J = 6.5 Hz), 7.03 (d, ^3J = 6.8 Hz) ppm along with signals for aromatic moiety. The ^{13}C NMR spectra of **5a** show resonance of C=N group and carbonyl at 157.2 (C=N), 165.3 (C=O) ppm respectively.

Although we have not confirmed the mechanism of the reaction in the presence of Fe_3O_4-MNPs, a possible examination is proposed in Scheme 2. In one pot the reaction of *N*-methylthiazole **1** and isothiocyanate **2** produce intermediate **6**. In another pot, the reaction of α-bromo ketones **3** and triphenylphosphine **4** produce intermediate **7** that in the presence of Fe_3O_4 magnetic nanoparticles (MNPs) is converted to intermediate **8** by elimination of HBr. The intermediate **6** react with intermediate **8** to produce zwitterionic species **9**. Finally, intermolecular cyclization of intermediate **9** generates intermediate 10 that followed by elimination of triphenyl phosphin oxide produce compounds **5** (Scheme 2).



Scheme 2. Proposed mechanism for the synthesis of **5**.

Conclusion

In summary, thiazole derivatives were prepared *via* multicomponent reaction of *N*-methylthiazole, isothicyanates, alkyl bromides and triphenylphosphine in the presence of catalytic amounts of Fe_3O_4-MNPs under solvent-free condition at 50^{o}C in good yield.

These procedures have some advantages such as easy separation of product, green conditions, and reusability and easy separation of catalyst.

Experimental

All chemicals used in this work were prepared from Fluka and were employed without further purification. IR spectra (KBr medium) were recorded on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DRX-500 AVANCE spectrometer at 500 and 125 MHz, respectively, in $CDCl_3$ using TMS as internal standard. Mass spectra (electron impact ionization) were recorded on a Finnigan MAT 8430 spectrometer operating at an ionization potential 70 eV. Elemental analyses were performed using a Heraeus CHN–O-Rapid analyzer.

Preparation of Fe_3O_4 MNPs:

Dried *Clover Leaf* (10gr) was drench in water (200 mL) at 80^{o}C. After 2 h, the mixture was filtered and water essential oil was used for preparation of Fe_3O_4-MNPs as following.
100 ml water extract of *Clover Leaf* was taken in a 250 two-neck round bottom flask, and $FeCl_3$ (2 mmol), $FeCl_2$ (1 mmol) were added. Then, the solution of NH_4OH (9 M, 10 ml) was then injected drop wise into the mixture with vigorous stirring under N_2 atmosphere for 1 h at room temperature. The resultant solution was a black color precipitate. The precipitate was separated by applying external magnetic field and washed with water for several times as well as dried in oven at 80 ^{o}C for 24 h.

Preparation of compounds 5a-h:

To a stirred mixture of *N*-methylthiazole **1** (2 mmol) mixed with isothiocyanate **2** (2 mmol) under solvent-free conditions was added mixture of alkyl bromides **3** (2 mmol) and triphenylphosphine **4** in the presence of Fe_3O_4-MNPs (15 mol%) after 45 min at 50 ^{o}C. After completion of the reaction (5 h; TLC control (hexane–AcOEt,1:3), 15 mL H2O was poured to mixture of reaction. Fe_3O_4-MNPs were separated by using external magnetic. After removing solvent, the residue was purified by column chromatography (3:1 hexane/EtOAc) to afforded pure title compounds.

Ethyl 1-methyl-5-(phenylimino)-1,8a-dihydroimidazo [1,2-c][1,3]thiazine-7-carboxylate (5a):

Yellow oil; Yield: 0.58 g (92%). IR (KBr) (ν_{max}/cm^{-1}): 1735, 1694, 1525, 1454, 1337 and 1229 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.28 (3 H, t, ^3J = 7.3 Hz, Me), 2.85 (3 H, s, NMe), 4.25 (2 H, q, ^3J = 7.3 Hz, CH_2O), 5.26 (1 H, d, ^3J = 6.8 Hz, CH), 6.56 (1 H, d, ^3J = 6.5 Hz, CH), 6.75 (1 H, d, ^3J = 6.5 Hz, CH), 7.03 (1 H, d, ^3J = 6.8 Hz, CH), 7.22 (2 H, t, ^3J = 7.5 Hz, 2 CH), 7.34 (1 H, t, ^3J = 7.5 Hz, CH), 7.43 (2 H, d, ^3J = 7.5 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.2 (Me), 38.3 (NMe), 62.4 (CH_2O), 81.2 (CH), 107.2 (CH), 121.6 (CH), 124.3 (C), 125.3 (2 CH), 130.4 (2 CH), 131.2 (CH), 133.4 (CH), 152.4 (C), 157.2 (C=N), 165.3 (C=O) ppm. MS, m/z (%): 315 (M^+, 15), 269 (82), 77 (68), 45 (100). Anal.Calcd for $C_{16}H_{17}N_3O_2S$ (315.39): C, 60.93; H, 5.43; N, 13.32. Found: C, 61.12; H, 5.62; N, 13.54.

Ethyl 1-methyl-5-(4-methoxyphenylimino)-1,8a-dihydroimidazo[1,2-c][1,3]thiazine-7-carboxylate (5b):

Yellow oil; Yield: 0.66 g (95%). IR (KBr) (ν_{max}/cm^{-1}): 1737, 1695, 1547, 1478, 1357 and 1286 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (3 H, t, ^3J = 7.4 Hz, Me), 2.86 (3 H, s, NMe), 3.87 (3 H, s, MeO), 4.27 (2 H, q, ^3J = 7.4 Hz, CH_2O), 5.26 (1 H, d, ^3J = 6.3 Hz, CH), 6.48 (1 H, d, ^3J = 6.2 Hz, CH), 6.67 (1 H, d, ^3J = 6.2 Hz, CH), 6.95 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.14 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.18 (1 H, d, ^3J = 6.3 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.8 (Me), 38.5 (NMe), 55.6 (MeO), 62.2 (CH_2O), 81.5 (CH), 106.8 (CH), 114.5 (2 CH), 124.5 (C), 126.7 (2 CH), 130.5 (CH), 133.4 (CH), 145.2 (C), 155.3 (C), 157.5 (C=N), 165.7 (C=O) ppm. MS, m/z (%): 345 (M^+, 10), 314 (84), 107 (88), 45 (100). Anal.Calcd for $C_{17}H_{19}N_3O_3S$ (345.42): C, 59.11; H, 5.54; N, 12.17. Found: C, 59.25; H, 5.72; N, 12.32.

Ethyl 1-methyl-5-(4-methylphenylimino)-1,8a-dihydroimidazo[1,2-c][1,3]-7-carboxylate (5c):

Yellow oil; Yield: 0.61 g (92%). IR (KBr) (ν_{max}/cm^{-1}): 1735, 1698, 1562, 1486, 1378 and 1295 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (3 H, t, ^3J = 7.4 Hz, Me), 2.23 (3 H, s, Me), 2.95 (3 H, s, NMe), 4.26 (2 H, q, ^3J = 7.4 Hz, CH_2O), 5.23 (1 H, d, ^3J = 5.8 Hz, CH), 6.63 (1 H, d, ^3J = 6.8 Hz, CH), 6.73 (1 H, d, ^3J = 6.8 Hz, CH), 6.97 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.15 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.18 (1 H, d, ^3J = 5.8 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.5 (Me), 21.5 (Me), 38.7 (NMe), 62.5 (CH_2O), 79.6 (CH), 107.2 (CH), 127.3 (2 CH), 129.5 (2 CH), 130.4 (CH), 131.4 (C), 132.5 (CH), 149.5 (C), 158.2 (C=N), 166.2 (C=O) ppm. MS, m/z (%): 329 (M^+, 15), 284 (82), 91 (68), 45 (100). Anal.Calcd for $C_{17}H_{19}N_3O_2S$ (329.42): C, 61.98; H, 5.81; N, 12.76. Found: C, 62.18; H, 5.96; N, 12.92.

Ethyl 1-methyl-5-(4-nitrophenylimino)-1,8a-dihydro imidazo[1,2-c][1,3]-7-carboxylate (5d):

Yellow oil; Yield: 0.61 g (85%). IR (KBr) (ν_{max}/cm^{-1}): 1737, 1696, 1573, 1494, 1389 and 1295 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26 (3 H, t, ^3J = 7.4 Hz, Me), 2.92 (3 H, s, NMe), 4.22 (2 H, q, ^3J = 7.4 Hz, CH_2O), 5.53 (1 H, d, ^3J = 6.3 Hz, CH), 6.58 (1 H, d, ^3J = 6.8 Hz, CH), 6.64 (1 H, d, ^3J = 6.8 Hz, CH), 7.16 (2 H, d, ^3J = 7.8 Hz, 2 CH), 7.22 (1 H, d, ^3J = 6.3 Hz, CH), 8.12 (2 H, d, ^3J = 7.8 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.6 (Me), 38.5 (NMe), 61.8 (CH_2O), 81.4 (CH), 107.4 (CH), 124.3 (C), 125.2 (2 CH), 127.5 (2 CH), 130.5 (CH), 133.6 (C), 142.6 (C), 154.7 (C), 159.4 (C=N), 165.8 (C=O) ppm. MS, m/z (%): 360 (M^+, 10), 315 (76), 45 (100). Anal.Calcd for $C_{16}H_{16}N_4O_4S$ (360.39): C, 53.32; H, 4.47; N, 15.55. Found: C, 53.46; H, 4.64; N, 15.76.

N-[7-(4-methoxyphenyl)-1-methyl-1,8a-dihydro imidazo[1,2-c][1,3]thiazine-5-ylidene]-N-(4-methylphenyl) amine (5e):

Yellow oil; Yield: 0.65 g (90%). IR (KBr) (ν_{max}/cm^{-1}): 1698, 1589, 1494, 1386 and 1296 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.24 (3 H, s, Me), 2.93 (3 H, s, NMe), 3.85 (3 H, s, MeO), 5.23 (1 H, d, ^3J = 5.9 Hz, CH), 6.65 (1 H, d, ^3J = 6.5 Hz, CH), 6.73 (1 H, d, ^3J = 6.5 Hz, CH), 6.83 (1 H, d, ^3J = 5.9 Hz, CH), 7.03 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.16 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.28 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.43 (2 H, d, ^3J = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 21.8 (Me), 39.2 (NMe), 55.3 (MeO), 82.6 (CH), 108.4 (CH), 113.8 (2 CH), 123.2 (CH), 126.2 (2 CH), 128.4 (2 CH), 130.7 (2 CH), 131.2 (CH), 131.8 (C), 133.4 (C), 134.6 (C), 149.3 (C), 154.8 (C=N), 161.4 (C) ppm. MS, m/z (%): 363 (M^+, 15), 272 (86), 107 (100). Anal.Calcd for $C_{21}H_{21}N_3OS$ (363.48): C, 69.39; H, 5.82; N, 11.56. Found: C, 69.52; H, 5.97; N, 11.72.

N-[7-(4-methoxyphenyl)-1-methyl-1,8a-dihydro imidazo[1,2-c][1,3]thiazine-5-ylidene]-N-(4-bromophenyl) amine (5f):

Yellow oil; Yield: 0.74 g (87%). IR (KBr) (ν_{max}/cm^{-1}): 1696, 1585, 1497, 1389 and 1295 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.87 (3 H, s, NMe), 3.87 (3 H, s, MeO), 5.56 (1 H, d, ^3J = 6.3 Hz, CH), 6.62 (1 H, d, ^3J = 6.8 Hz, CH), 6.74 (1 H, d, ^3J = 6.8 Hz, CH), 6.96 (1 H, d, ^3J = 6.3 Hz, CH), 7.12 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.23 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.45 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.57 (2 H, d, ^3J = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 38.5 (NMe), 55.6 (MeO), 81.8 (CH), 106.8 (CH), 113.2 (2 CH), 114.6 (C), 123.5 (CH), 126.2 (2 CH), 128.4 (2 CH), 130.2 (CH), 132.4 (2 CH), 133.4 (C), 134.2 (C), 151.2 (C), 155.3 (C=N), 160.4 (C) ppm. MS, m/z (%): 428 (M^+, 15), 321 (58), 107 (100). Anal.Calcd for $C_{20}H_{18}BrN_3OS$ (428.35): C, 56.08; H, 4.24; N, 9.81. Found: C, 56.23; H, 4.42; N, 9.95.

N-[7-(4-methylphenyl)-1-methyl-1,8a-dihydro imidazo[1,2-c][1,3]thiazine-5-ylidene]-N-(4-nitrophenyl) amine (5g):

Yellow oil; Yield: 0.60 g (80%). IR (KBr) (ν_{max}/cm^{-1}): 1695, 1589, 1496, 1387 and 1292 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 2.25 (3 H, s, Me), 2.93 (3 H, s, NMe), 5.52 (1 H, d, ^3J = 5.9 Hz, CH), 6.67 (1 H, d, ^3J = 6.5 Hz, CH), 6.78 (1 H, d, ^3J = 6.5 Hz, CH), 6.92 (1 H, d, ^3J = 5.9 Hz, CH), 7.15 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.24 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.82 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.93 (2 H, d, ^3J = 7.6 Hz, 2 CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 21.4 (Me), 38.9 (NMe), 81.6 (CH), 107.4 (CH), 123.5 (CH), 125.3 (2 CH), 127.3 (2 CH), 128.6 (2 CH), 130.4 (2 CH), 131.2 (CH), 134.3 (C), 146.3 (C), 148.4 (C), 150.4 (C), 156.4 (C=N) ppm. MS, m/z (%): 378 (M^+, 15), 287 (62), 91 (100). Anal.Calcd for $C_{20}H_{18}N_4O_2S$ (378.45): C, 63.47; H, 4.79; N, 14.80. Found: C, 63.62; H, 93; N, 14.94.

Ethyl 1-methyl-5-(tert-butylimino)-1,8a-dihydro imidazo[1,2-c][1,3]thiazine-7-carboxylate (5h):

Yellow oil; Yield: 0.57 g (97%). IR (KBr) (ν_{max}/cm^{-1}): 1734, 1563, 1476, 1345 and 1242 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (3 H, t, ^3J = 7.3 Hz, Me), 1.28 (9 H, s, Me_3C), 2.87 (3 H, s, NMe), 4.23 (2 H, q, ^3J = 7.3 Hz, CH_2O), 5.27 (1 H, d, ^3J = 6.4 Hz, CH), 6.63 (1 H, d, ^3J = 6.7 Hz, CH), 6.82 (1 H, d, ^3J = 6.7 Hz, CH), 7.15 (1 H, d, ^3J = 6.4 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.3 (Me), 30.2 (Me_3C), 38.2 (NMe), 62.5 (CH_2O), 80.6 (CH), 107.8 (CH), 123.4 (C), 130.2 (CH), 133.4 (CH), 156.2 (C=N), 165.6 (C=O) ppm. MS, m/z (%): 295 (M^+, 20), 238 (86), 57(100), 45 (88). Anal.Calcd for $C_{14}H_{21}N_3O_2S$ (295.40): C, 56.92; H, 7.17; N, 14.22. Found: C, 57.12; H, 7.35; N, 14.40.

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