International Journal of Computational and Experimental Science and ENgineering (IJCESEN)

Vol. 12-No.3 (2026) pp. 370-378
http://www.ijcesen.com

ISSN: 2149-9144

Research Article

Microwave-assisted synthesis of bis-Schiff bases of isatin derivatives catalyzed by Maghnite-H^+ as a green acid catalyst

Boumadiene Benlahreche[1,2*], Assya Taleb[3], Khaled Briki[4,5], Mouna Souad Abbassi[6,7], Abdelkader Brahimi[8], Saliha Brahimi[9], Mokhtar B. Lahrech[10] and Salih Hacini[11]

[1]Laboratory of Fine Chemicals (LCF), Department of Chemistry, Faculty of Exact and Applied Sciences, Université Oran1 Ahmed Ben Bella, BP-1524-Menouar, 31000- Oran, Algeria.
[2]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
*** Corresponding Author Email:** b.benlahrech2017@gmail.com-**ORCID:** 0009-0002-2390-0119

[3]Laboratory of Fine Chemicals (LCF), Department of Chemistry, Faculty of Exact and Applied Sciences, Université Oran1 Ahmed Ben Bella, BP-1524-Menouar, 31000- Oran, Algeria
Email: assyatab@yahoo.com-**ORCID:** 0000-0001-6230-194X

[4]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
[5]Laboratoire de recherches appliquées aux sciences du végétal, University Ziane Achour, Djelfa, Algeria.
Email: brkhch28@live.fr-**ORCID:** 0009-0003-2217-4626

[6]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
[7]Applied Chemical and Physical Sciences Laboratory, Ecole Normale Supérieure, Laghouat 03000, Algeria
Email: mouna0717@live.fr-**ORCID:** 0000-0002-3479-1053

[8]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
Email: abdelkader.brahimi@unv-djalfa.dz - **ORCID:** 0000-0002-5247-1150

[9]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
Email: saliha.brahimi@unv-djalfa.dz - **ORCID:** 0000-0002-5207-8850

[10]Laboratory of Organic Chemistry and Natural Substances, Faculty of Exact Sciences and Informatics, Ziane Achour University, Djelfa, Algeria.
Email: lahrechmokhtarboualem@yahoo.fr-**ORCID:** 0000-0002-5234-6543

[11]Laboratory of Fine Chemicals (LCF), Department of Chemistry, Faculty of Exact and Applied Sciences, Université Oran1 Ahmed Ben Bella, BP-1524-Menouar, 31000- Oran, Algeria
Email: s_hacini@hotmail.com- **ORCID:** 0000-0002-4111-3584

Article Info:

DOI: 10.22399/ijcesen.5483
Received: 05 April 2025
Revised: 14 March 2026
Accepted: 10 May 2026

Keywords

Green synthesis
Bis-Schiff bases of isatin
Maghnite-H^+
Microwave-assisted

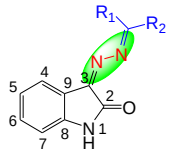
Abstract:

In the present study, we describe a microwave-assisted solvent free synthesis of *bis*-Schiff bases of isatin derivatives catalyzed by Maghnite-H^+. Treatment of isatin with hydrazine monohydrate gives in a first step 3-hydrazonoindolin-2-one, that is isolated and condensed with appropriate aldehydes or ketones in the second step. The major advantages of this unconventional *bis*-Schiff bases of isatin synthesis are short reaction time, operational simplicity, high yield, easy workup and environment friendly procedure. In addition, the green catalyst could be removed from the reation mixture by simple filtration. The chemical structures of the synthesized compounds were characterized by IR, ^{1}H-NMR and ^{13}C-NMR spectral data and compared with literature results.

1. Introduction

Isatin **1** and its derivatives are versatile substrates, which can be used for the synthesis of numerous heterocyclic compounds [1,2]. They also have a particular interest because of their applications in medicinal chemistry [3,4].A number of bis-Schiff bases of isatin have been reported with various pharmacological and biological properties including antibacterial [5,6], antifungal [7,8], anti cancer [9], antiviral [9], CNS depressant [9], anticonvulsant [10,11], anti-inflammatory [12], antiglycation [1,13], anti-HIV [14,15], anti-oxidant [16,17], cytotoxicity[18], antiproliferative [19], antitubercular [20], anti malarial [21] and analgesic [22]. It should be noted that other isatin hydrazone derivatives acta as efficient corrosion inhibitors [23,24].

Bis-Schiff bases which also called azines [25,26], >C=N-N=CR_1R_2 have attracted growing attention in organic synthesis as they are good synthons for access to heterocyclic compounds such as pyrazoles, purines and pyrimidines [27]. *Bis*-Schiff bases of isatin are usually prepared by acid catalyzed condensation of isatin hydrazones with aldehydes or ketones to yield respectively isatin aldazines (R_1 or R_2 = H) or isatin ketazines (R_1 and $R_2 \neq$ H) [28]. Other *bis*-Schiff bases of isatin catalyzed synthesis methods, based mainly on conventional heating, have been developed.



F*igure 1:* *Structure of bis-Schiff bases of isatin.*

They involve a variety of catalysts such as acetic acid[29,30], HCl [31,32], $CH_3CO_2Na/CaCl_2$ [33,34], $FeCl_3.6H_2O$ [35], nanocrystalline alumina powder [36], sulphated titania acid [37,38], triethylamine [39] or molecular iodine [40]. Therefore, there is a need to develop a simple and eco-friendly effective method under mild conditions for the preparation of *bis*-Schiff bases of isatin.

The green chemistry is one of the major challenges of the twenty-first century. The media make this title one of their most recurrent subjects to try to minimize the impact of chemical products and processes on the environment [41].

Nowadays, the organic synthesis is more and more oriented towards the respect of the principles of the green chemistry, such as: the nature and the quantity of solvents used, the choice of less harmful reagents, the use of renewable raw materials and simple efficient catalysts, the improved energy efficiency [42,43].

Homogeneous chemical catalysts present environmental problems due to the difficulty of reusing, separating, and purifying the reaction products. Therefore, the search for more environmentally friendly heterogeneous catalysts in organic synthesis has intensified. The montmorillonite clay catalyst obtained from North West Algeria, known as Maghnite.

The maghnite containing both Brønsted and Lewis acid sites can form highly active acid catalysts when exchanged protons. Algerian montmorillonite has higher SiO_2 and lower Al_2O_3 contents than other clays, and that proton exchange alters its composition and physicochemical properties (Table **1**). These changes enhance its effectiveness in acid-catalyzed reactions [44].

Furthermore, the use of microwave irradiation technique has rapidly developed in synthesis as a very interesting simple operational procedure, with less or no solvent requirements, respect for environment, reduced reaction times, high reaction yields and good products purity [45,46].

Table 1. *Chemical compositions of Maghnite raw and Maghnite-H^+ [44].*

Sample	SiO_2	Al_2O_3	Fe_2O_3	MgO	CaO	Na_2O	K_2O	TiO_2	SO_3	As	Water loss at 110°C
Alg-Maghnite raw (%)	69.39	14.67	1.16	1.07	0.3	0.5	0.79	0.16	0.91	0.05	11
Alg-Maghnite-H^+ (%)	71.7	14.03	0.71	0.8	0.28	0.21	0.77	0.15	0.34	0.01	11

In continuation of our previous work on environmentally benign methods, we present a new green approach for the synthesis of *bis*-Schiff bases of isatin derivatives catalyzed by Maghnite-H^+ under solvent-free conditions using microwave irradiation.

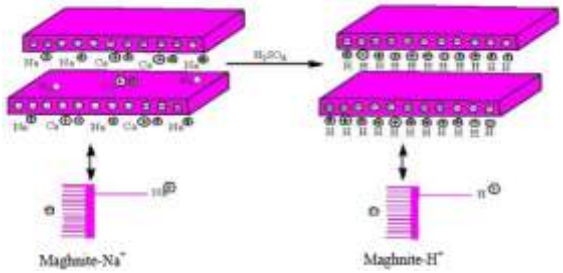
2. Material and Methods

2.1.General

All commercial reagents and solvents were used as supplied without further purification : isatin (98%, Alfa Aesar), 4-Hydroxybenzaldehyde (98%,Sigma-Aldrich), Furfural (99%, Sigma-Aldrich), 2-Hydroxybenzaldehyde (98%,Sigma-Aldrich), 4-Chlorobenzaldehyde (97%, Sigma-Aldrich), 4-Nitrobenzaldehyde (98%, Sigma-Aldrich), Hydra zine hydrate (80%, Sigma-Aldrich) and Ethanol (96%, Sigma-Aldrich). Followup of the reactions and checking the purity of the compounds were made by TLC on precoated Silica gel-aluminum plates (E. Merck Kieselgel 60 F-254) and were visualized by exposure to UV-light at 254 nm or iodine vapor for few seconds. The melting points were measured on a Stuart SMP10/120V/60 with the help of an open capillary tube. FT-IR spectra were recorded on a Bruker ATR spectrometer and the values are expressed in cm^{-1}. The ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker AQS-AVANCE spectrometer at 400 MHz using DMSO with TMS as internal standard and the following multiplicity abbreviations were used: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet. The microwave irradiated synthesis was performed in domestic microwave oven (Condor, CMW-A2602, 0-900W). All the reactions were carried out at power level-3, which corresponds to 300W. Algerian montmorillonite clay (Maghnite) was procured from "BENTAL" (Algerian Society of Bentonite).

2.2. Preparation of Maghnite-H^+

Maghnite-H^+ was prepared according to the literature [44,47,48]. Raw-Maghnite (20g) was crushed for 20 min and oven dried at 105°C for 2 hours. The Maghnite was then weighted and placed in an erlenmeyer flask together with 500ml of distilled water. The maghnite/water mixture was stirred using a magnetic stirrer and combined with 500 ml sulphuric acid solution (0,5M) until saturation was achieved after two days at room temperature. The mineral was washed with distilled water until became sulphate free and then dried at 105°C. The maghnite-H^+ thus prepared is ready to be used directly to catalyze our reactions.



Scheme 1. *Activated forms of Maghnite under sulfuric acid (H_2SO_4).*

2.3. General procedure for the synthesis of 3-Hydrazonoindolin-2-one 3a-b

A mixture of isatin **1a-b** (1 mmol) and hydrazine monohydrate **2** (80%, 2 mmol) with catalytic amount of maghnite-H^+ (10%wt) was irradiated in a domestic microwave oven at an emitted power of 300W for 3 min under solvent free conditions. When the yellowish product was observed and the reaction completed (monitored by TLC), the crude product was dissolved in hot ethanol and then filtered to remove the solid catalyst. The filtrate was cooled to give the solid product. The crystalline powder was filtered, washed with cold water, ethanol and dried at 60-70°C to afford compounds **3a-b** which was used for next step without any further purification .

2.4. General procedure for preparation of *bis*-Schiff bases of isatin 5a-j

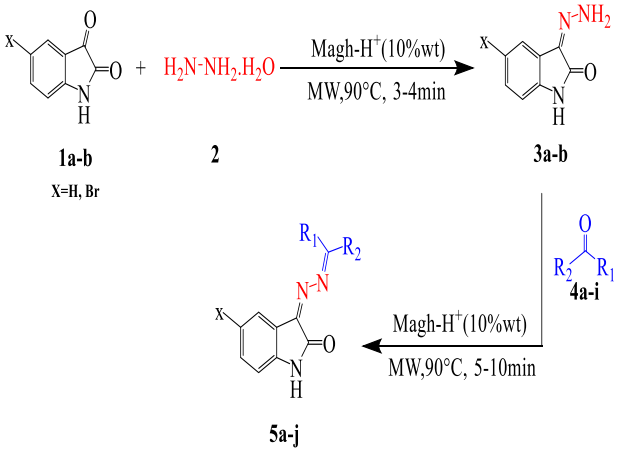
A mixture of 3-Hydrazonoindolin-2-one derivatives **3a-b** (1mmol) and arylaldehydes or ketones **4a-i** (1mmol) with catalytic amount of maghnite-H^+ (10%wt) was irradiated by microwave for 5-8 min at an emitted power of 300W under solvent free conditions. The progress of reaction was monitored by TLC. The crude product was dissolved in hot ethanol and then filtered to remove the solid catalyst. The filtrate was cooled to give the solid product. The crystalline powder was filtered, washed with ethanol and dried at 60-70°C to afford compounds **5a-j** (Scheme **2**). The spectral data IR, ^{1}H-NMR and ^{13}C-NMR, were used to determine the structures of all compounds.

2.5. Spectroscopic information of the synthesized compounds

3-hydrazono-indoline-2-one (3a)

Yellow powder; Yield: 93%; IR (cm^{-1}): 3354 (N-H), 3151 (N-H Isatin), 1655 (C=O), 1602 (C=N), 1549

(aromatic C=C); ^{1}H NMR (400MHz, DMSO-d_6): δ ppm 10.70 (s, 1H, NH), 10.54 (d, *J* = 14.5 Hz, 1H, -NHR_2), 9.56 (d, *J* = 14.6 Hz, 1H , -NHR_2), 7.36 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.15 (t, *J* = 7.7 Hz, 1H, Ar-H), 6.97 (t, *J* = 7.0 Hz, 1H, Ar-H), 6.86 (d, *J* = 7.7 Hz, 1H, Ar-H); ^{13}C NMR (75MHz, DMSO-d_6): δ ppm 110.43, 117.91, 121.82, 126.65, 127.50, 139.10, 163.24, 206.99 (C=O).



Scheme 2. Synthesis of *bis*-Schiff bases of isatin derivatives **5a-j**.

5-bromo-3-hydrazonoindolin-2-one (3b)

Yellow powder (yield 96%); FT-IR (ν_{max} in cm^{-1}): 3395 (N-H), 3231 (N-H Isatin), 1665 (C=O), 1560 (C=N), 1551 (aromatic C=C); ^{1}H NMR (400 MHz, DMSO-d_6, δ in ppm): 10.82 (s, 1H, NH), 10.68 (d, *J* = 14.2 Hz, 1H, -NH_2), 9.89 (d, *J* = 14.2 Hz, 1H, -NH_2), 7.45 (s, *J* = 7.8 Hz, 1H, H_4 of isatin), 7.32 (d, *J* = 7.8 Hz, 1H, H_7 of isatin), 7.29 (d, *J* = 7.5 Hz, 1H, H_6 of isatin); ^{13}C NMR (100MHz, DMSO-d_6, δ in ppm): 112-137 (aromatic C-H), 162 (C=O).[28]

3-((4-Chlorobenzylidene)hydrazono)indolin-2-one (5a)

Orange powder (yield 95%); IR (cm^{-1}): 3276 (NH), 3053 (aromatic C-H),1718 (C=O), 1611 (C=N), 1590 (aromatic C=C), 749 (C-Cl); ^{1}H NMR (400MHz, DMSO-d_6): δ ppm 10.86 (s, 1H,-NH-), 8.62 (s,1H, -N=CH), 8.00 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.87 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.65 (d, *J* = 7.6 Hz, 1H, H_7 of isatin), 7.41 (t, *J* = 7.7, 1H, H_6 of isatin), 7.03 (t, *J* = 7.6 Hz, 1H, H_5 of isatin), 6.91 (d, *J* = 7.8 Hz, 1H, H_4 of isatin). ^{13}C NMR (75MHz, DMSO-d_6): δ ppm 111.38, 111.98, 116.79, 122.87, 129.26, 129.84, 130.91, 132.77, 134.33, 137.17, 141.72, 145.60, 150.80, 159.29, 164.88 (C=O).

3-((4-Nitrobenzylidene)hydrazono)indolin-2-one (5b)

Orange powder (yield 92%); IR (cm^{-1}): 3277 (NH), 3052 (aromatic C-H), 1719 (C=O), 1612 (C=N), 1591 (aromatic C=C), 1327 (C-NO_2); ^{1}H NMR (400MHz,DMSO-d_6): δ ppm 10.90 (s, 1H,-NH-), 8.67(s, 1H, N=CH), 8.39 (d, *J* = 8.6 Hz, 2H, Ar-H), 8.21 (d, *J* = 8.6 Hz, 2H, Ar-H), 7.74 (d, *J* = 7.6 Hz, 1H, H_7 of isatin), 7.42 (t, *J* = 7.7 Hz, 1H, H_6 of isatin), 7.02 (t, *J* = 7.6 Hz, 1H, H_5 of isatin), 6.92 (d, *J* = 7.8 Hz, 1H, H_4 of isatin). ^{13}C NMR (75 MHz, DMSO-d_6): δ ppm 111.50, 111.85, 116.54, 122.29,122.94, 124.75, 129.21, 130.16, 134.61, 139.58, 145.78, 149.51, 150.18, 156.77, 164.63 (C=O).

3-(2-(2-hydroxybenzylidene)hydrazono)indolin-2-one(5c)

Red powder (yield 84%); IR (cm^{-1}): 3395 (OH), 3179 (NH), 3081 (aromatic C-H), 1712 (C=O), 1673 (C=N), 1536 (aromatic C=C); ^{1}H NMR (400MHz,DMSO-d_6): δ ppm 11.11(s,1H,-NH-), 10.98 (s, 1H, -OH),9.00 (s, 1H, N=CH), 7.70(d, *J* = 7.6 Hz, 1H, H_7 of isatin), 7.52 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.42 (t, *J* = 7.7 Hz, 1H, H_6 of isatin), 7.42 (t, *J* = 7.7 Hz, 1H,Ar-H), 7.08 (t, *J* = 7.9 Hz, 1H,Ar-H). 7.03 (d, *J* = 7.6 Hz, 1H,Ar-H), 6.98 (t, *J* = 7.6 Hz, 1H, H_5 of isatin),6.93 (d, *J* = 7.8 Hz, 1H, H_4 of isatin). ^{13}C NMR (75 MHz, DMSO-d_6): δ ppm 111.67, 116.26, 117.01, 118.67, 120.08, 123.03, 128.66, 131.32, 133.70, 134.89, 145.23, 145.67, 159.11, 163.25, 163.89 (C=O).

3-((Furan-2-ylmethylene)hydrazono)indolin-2-one (5d)

Yellow powder (yield 83%); IR (cm^{-1}): 3276 (NH), 3054 (aromatic C-H), 1720 (C=O), 1613 (C=N), 1590 (aromatic C=C); ^{1}H NMR (400MHz, DMSO-d_6): δ ppm 10.82 (s, 1H,-NH-),8.50 (s, 1H, N=CH), 8.08 (d, *J* = 8.1 Hz, 2H,Ar-H), 7.40 (t, *J* = 7.7 Hz, 1H, H_6 of isatin), 7.34 (d, *J* = 7.6 Hz, 1H, H_7 of isatin), 7.04 (t, *J* = 7.6 Hz,1H,H_5 of isatin), 6.90 (d, *J* = 7.8 Hz, 1H, H_4 of isatin), 6.80 (d, *J* = 1.7 Hz,1H, Ar-H). ^{13}C NMR (75 MHz, DMSO-d_6): δ ppm 111.25, 113.64, 117.18, 120.17, 122.76, 129.51, 134.16, 145.39, 148.52, 149.55, 151.24, 151.80, 165.13 (C=O).

3-(2-(4-hydroxybenzylidene)hydrazono)indolin-2-one(5e)

Orange powder (yield 93%); IR (cm^{-1}): 3397 (OH), 3149 (NH), 3047 (aromatic C-H), 1680 (C=O), 1614 (C=N), 1541 (aromatic C=C), 1092 (C-O); ^{1}H NMR (400MHz, DMSO-d_6): δ ppm 10.79 (s, 1H,-NH-),10.36 (s, 1H, -OH), 8.61 (s, 1H, N=CH), 8.10 (d, *J* = 7.6 Hz, 1H, H_7 of isatin), 7.87 (d, *J* = 8.5 Hz, 2H,Ar-H), 7.39 (t, *J* = 7.7 Hz, 1H, H_6 of isatin), 7.05 (t, *J* = 7.6 Hz, 1H, H_5 of isatin), 6.96 (d, *J* = 8.5 Hz, 2H,Ar-H), 6.90 (d, *J* = 7.8 Hz, 1H, H_4 of isatin); ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm: 111.15, 116.66, 116.67, 117.23, 122.75, 125.05, 129.38, 131.87, 131.88, 133.78, 145.22, 151.16, 162.10, 163.47, 165.33 (C=O).

3-(2-(4-bromobenzylidene)hydrazono)indolin-2-one (5f).

Yellow powder (yield 94%); IR spectrum, v, cm^{-1}: 3274 (NH), 3055 (aromatic C-H), 1719 (C=O), 1612 (C=N), 1590 (aromatic C=C), 750 (C-Br). ^{1}H NMR spectrum (400MHz, DMSO-*d6*), δ, ppm (*J*, Hz): 11.00 (s, 1H,-NH-); 8.64 (s,1H, -N=CH); 7.99 (d, *J* = 8.1Hz, 2H, Ar-H); 7.62 (d, *J* = 8.0 Hz, 2H, Ar-H); 8.00 (d, *J* = 7.6 Hz, 1H, H_7 of isatin); 7.60 (t, *J* = 7.7, 1H, H_6 of isatin); 7.57 (t, *J* = 7.6 Hz, 1H, H_5 of isatin); 6.87 (d, *J* = 7.8 Hz, 1H, H_4 of isatin). ^{13}C NMR spectrum (100MHz, DMSO-*d6*), δ, ppm: 113.59; 114.01; 118.17; 124.88; 130.13; 131.12; 136.80; 139.36; 144.91; 149.34; 149.68; 157.55; 164.17 (C=O).

3,3'-(Hydrazine-1,2-diylidene)diindolin-2-one (5g).

Red crystals (yield 97%); FT-IR (ν_{max} in cm^{-1}): 3275 (2N-H), 1718 (2C=O), 1631 (2C=N), 3051 (aromatic C-H), 1590 (aromatic C=C); ^{1}H NMR (400 MHz, DMSO-*d6*, δ in ppm): 11.02 (s, 2H,2NH), 7.53 (d, 2H, *J* = *7.8* Hz, H_4 of isatin), 7.42 (t, 2H, *J* =7.5 Hz, H_7 of isatin), 7.02 (t, 2H, *J* = 7.5 Hz, H_6 of isatin), 6.91 (d, 2H, *J* = 7.8 Hz, H_5 of isatin); ^{13}C NMR (100MHz, DMSO-*d6*, δ in ppm): 111.59, 116.25, 123.02, 128.68, 134.88, 145.23, 145.66, 163.90 (2C=O).

3-(2-(4-oxopentan-2-ylidene)hydrazono)indolin-2-one (5h).

Orange powder (yield 96%); FT-IR (ν_{max} in cm^{-1}): 3064 (N-H), 2978 (aromatic C-H),1698 (C=O), 1613 (C=N), 1543 (aromatic C=C); ^{1}H NMR (400 MHz, DMSO-*d6*, δ in ppm): 11.00 (s, 1H,-NH-), 7.46 (d, *J* = 7.5 Hz,1H, H_7 of isatin), 7.30 (t, *J* = 7.8 Hz, 1H, H_6 of isatin), 7.03 (t, *J* = 7.8 Hz, 1H, H_5 of isatin), 6.92 (d, *J* = 7.5 Hz, 1H, H_4 of isatin), 5.55 (s, 2H, CH_2), 2.25 (s, 3H, CH_3), 2.09 (s, 3H, CH_3); ^{13}C NMR (100MHz, DMSO-*d6*, δ in ppm): 18.17, 30.23, 101.71, 111.10, 120.32, 121.02, 122.40, 130.81, 133.22, 142.09, 141.72, 155.64, 161.78, 196.99 (C=O).

5-bromo-3-((z)-(-oxoindolinylidene)hydrazono) indolin-2-one (5i).

Red crystals (yield 96%); FT-IR (ν_{max} in cm^{-1}): 3133 (2N-H), 1722 (2C=O), 1607 (2C=N), 3079 (aromatic C-H), 1459 (aromatic C=C); ^{1}H NMR (400 MHz, DMSO-*d6*, δ in ppm): 11.13 (s, 1H, NH), 11.01 (s, 1H, NH), 7.67 (d, 1H, *J* = *7.8* Hz, H_4 of isatin), 7.45 (t, 1H, *J* =7.5 Hz, H_7 of isatin), 7.03 (t, 1H, *J* = 7.5 Hz, H_6 of isatin), 6.91 (d, 1H, *J* = 7.8 Hz, H_5 of isatin), 6.94 (s, 1H, H_4 of 5-bromoisatin), 7.54 (d, 1H, *J* = 7.5 Hz, H_6 of 5-bromoisatin), 7.64 (d, 1H, *J* = 7.8 Hz, H_7 of 5-bromoisatin); ^{13}C NMR (100MHz, DMSO-*d6*, δ in ppm): 111.62, 113.57, 114.14, 116.30, 118.00, 123.03, 127.24, 129.12, 130.84, 135.13, 137.04, 145.25, 145.95, 163.56 (2C=O).

5-bromo-3-((z)-(5-bromo-oxoindolin-3-ylidene) hydrazono)indolin-2-one (5j).

Red crystals (yield 95%), FT-IR (ν_{max} in cm^{-1}): 3134 (2N-H), 1742 (2C=O), 1632 (2C=N), 3085 (aromatic C-H), 1443 (aromatic C=C); ^{1}H NMR (400 MHz, DMSO-*d6*, δ in ppm): 11.13 (s, 2H,2NH), 7.67 (s, 2H, *J* = *7.8* Hz, H_4 of 5-bromoisatin), 7.64 (d, 2H, *J* =7.5 Hz, H_7 of 5-bromoisatin), 6.91 (d, 2H, *J* = 7.5 Hz, H_6 of 5-bromoisatin); ^{13}C NMR (100MHz, DMSO-*d6*, δ in ppm): 113.56, 114.14, 118.06, 131.22, 137.22, 145.11, 146.28, 163.60 (2C=O).

3. Results and Discussions

The reaction of isatin **1a-b** with hydrazine monohydrate **2** gives 3-Hydrazonoindolin-2-one **3a-b**, which is condensed with aromatic aldehydes or ketones **4a-i** to yield the desired products **5a-j** (Scheme **2**)**.** The modified clay catalyst used is obtained by treating of a local bentonite (also called maghnite) with sulphuric acid [48,49].

Experimentally, we observed that these reactions have advantages including shortless time with higher yields as shown by the results compared to

classical methods (Table **2**). Moreover, the catalyst could be removed from the reactionnal mixture and recycled up to three times without loss of catalytic activity. The structures of compounds **5a-j** have been well confirmed by the melting points and on basis of spectral data (IR, ^{1}H NMR and ^{13}C NMR) compared with the literature values.

3.1 Infrared Spectroscopy (FT-IR)

The IR spectra of all synthesized compounds show bands shared at 3354-3400, 3149-3277, 1680-1720 cm^{-1} and a weak band at 1611-1673 cm^{-1} assigned [9,14,15] respectively to -NH_2, N-H, C=O and C=N vibrations of the 3-Hydrazonoindolin-2-one ring **3a-b**, which confirms the condensation of hydrazine hydrate **2** on the carbonyl in position 3 of isatin **1a-b**. IR spectrum of *bis*-Schiff bases of isatin derivatives **5a-j** also exhibited some other strong bands like 1536-1591 and 1006-1027 cm^{-1} assigned [49] to aromatic (C=C) and hydrazinic (N-N) groups respectively.

The 3-(2-(4-hydroxybenzylidene)hydrazono)indolin-2-one **5e** and 3-(2-(2-hydroxybenzylidene)hydrazono)indolin-2-one **5c** show absorption large bands shared at 3400-3393 cm^{-1} assigned [1,10,13,16,20] to O-H stretching. The 3-((4-nitrobenzylidene)hydrazono)indolin-2-one **5b** shows strong band in the range of 1290-1330 cm^{-1} attributed to (N-O) stretching vibrations in nitro group, while the 3-((4-chlorobenzylidene) hydrazono)indolin-2-one **5a** exhibits its characteristics band at around 610-750 cm^{-1} attributed to (C-Cl) stretching vibrations.

In addition, the 3-((furan-2-ylmethylene)hydrazono)indolin-2-one **5d** shows absorption bands at 1283-1328 cm^{-1} attributed to (C-O) covalent bond. corresponding to azomethine[1,10,13,28] group-CH=N.

In addition, the absence of NH_2 signal of 3-Hydrazonoindolin-2-one derivatives **3a-b** (usually around 10.54-9.56 ppm) is further evidence of *bis*-Schiff bases of isatin **5a-j** formation. Products **5c** and **5e** have another signal appearing at δ 10.52-10.45 ppm for O-H

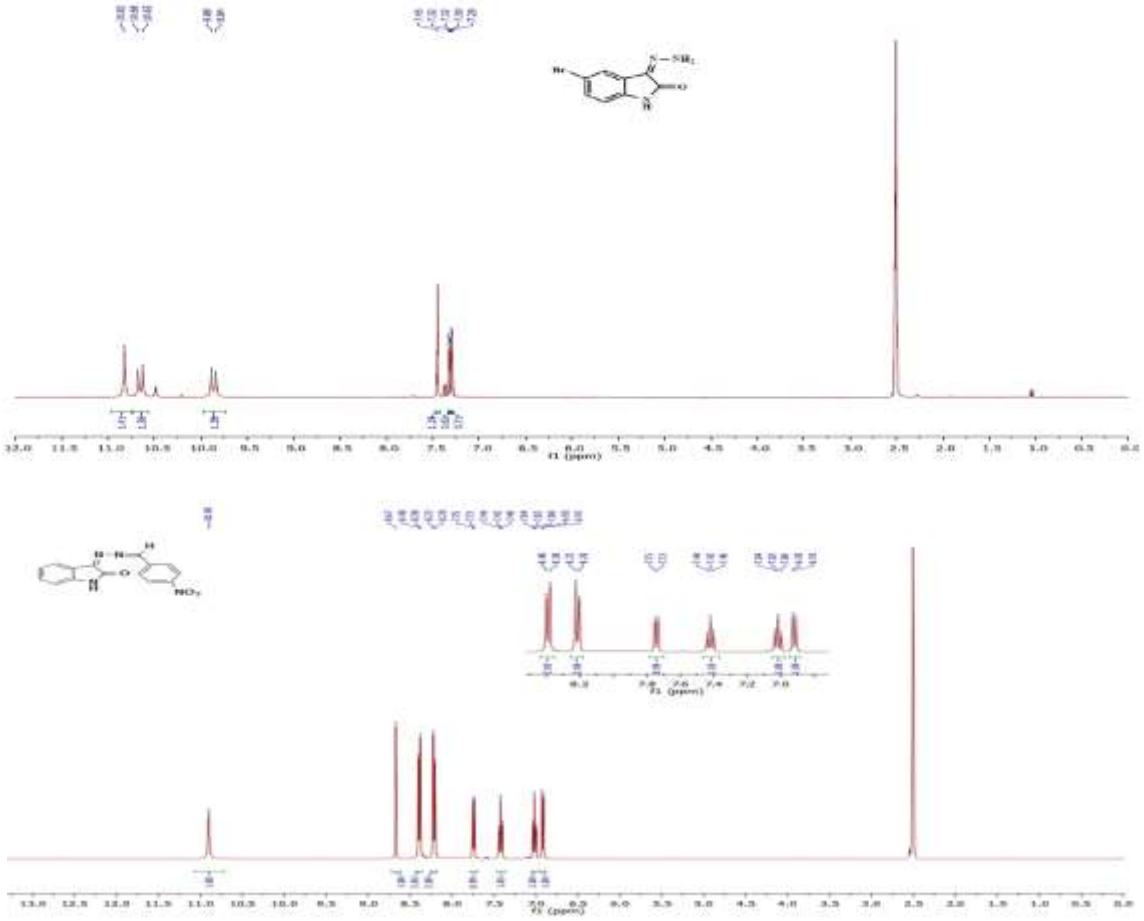
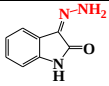
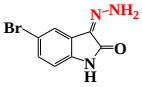
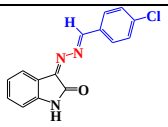
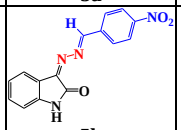
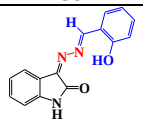
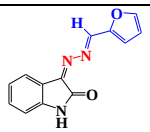
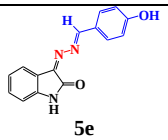
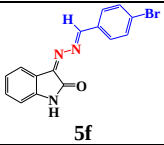
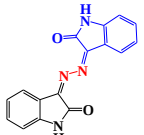
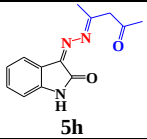
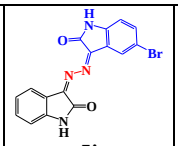
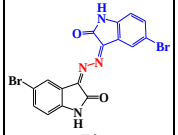


Figure 4: *^{1}H-NMR spectra of compounds **3b** and **5b** respectively.*

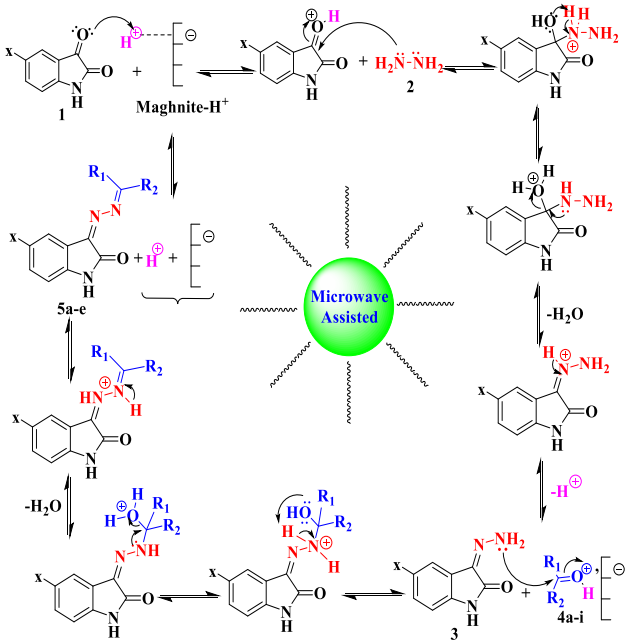
3.2 Nuclear Magnetic Resonance (NMR)

In ^{1}H-NMR spectra, all synthesized compounds have shown singlet at 10.79-11.11 ppm corresponding to secondary amino group (-NH-) of isatin skeleton. The aromatic protons resonate as multiplet in the region of δ 6.80-8.39 ppm. We also note for all compounds a signal at δ 8.50-9.00 ppm

Table 2. *physical data of the synthesized compounds* ***5a-j*** *by (MW = microwave irradiation).*

Entry	Structure	MW	Lit.Reflux	M.P(°C) Lit.(°C)
		Time / Yield (min) / (%)	Time / Yield (h) / (%)	
1	 **3a**	3 / 93	2 / 77.9 [15,16,44]	225-226 226-228
2	 **3b**	4/ 96	[32]	159-161
3	 **5a**	8 / 95	6 / 78 [28,44]	269-271 270-272
4	 **5b**	7 / 92	6 / 66 [28,44]	252-254 254-256
5	 **5c**	6 / 84	3 / 83 [1,16]	207-209 208 -211
6	 **5d**	5 / 83	6 / 55 [9,44]	209-211 209
7	 **5e**	6 / 93	4 / 60 [1,10, 13, 16,20,44]	261-263 261
8	 **5f**	9 / 94	-	200-202
9	 **5g**	10/ 97	4 / 46 [28]	> 300 > 300
10	 **5h**	9/ 96	4 / 46 [15]	228-230 > 300
11	 **5i**	9 / 96	-	220-222
12	 **5j**	8 / 96	6 / 78	269-271

A reactionnal mechanism is proposed in Scheme **3** to explain the formation of *bis*-Schiff bases of isatin **5a-j** from isatin **1a-b**. This two steps mechanism is based on the activation of carbonyl groups by the catalyst maghnit-H$^+$, which acts by increasing the electrophily of carbon. The first step involves a nucleophilic attack of the amino electrons of hydrazine hydrate **2** on the carbonyl group in position 3 of protonated isatin **1a-b**. This reaction leads to a hemiaminal, followed by dehydration to give 3-Hydrazonoindolin-2-one derivatives **3a-b**. In the second step, the reaction begins with a nucleophilic attack of terminal amino group of 3-Hydrazonoindolin-2-one derivatives **3a-b** on the protonated carbonyl of arylaldehydes or ketones **4a-i** , after removal of a molecule of water, the *bis*-Schiff bases of isatin derivatives **5a-j** are obtained.



Scheme 3: *Mechanism for the synthesis of bis-Schiff bases of isatin derivatives* ***5a-j.***

4. Conclusions

In conclusion, we have developed a green approach and highly efficient alternative for the synthesis of

bis-Schiff bases of isatin derivatives **5a-j** by condensation 3-Hydrazonoindolin-2-one deriva tives **3a-b** with different aromatic aldehydes or ketones **4a-i** using catalytic amount of maghnite-H^+ by performing microwave irradiation under solvent free conditions. This environment friendly process has the advantage of shorter reaction times, simple and mild reaction conditions, good to excellent yields and possible reuse of the catalyst without significant loss of activity.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper
- **Acknowledgement:** The authors declare that they have nobody or no-company to acknowledge.
- **Author contributions:** The authors declare that they have equal right on this paper.
- **Funding information:** The authors declare that there is no funding to be acknowledged.
- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.
- **Use of AI Tools:** The author(s) declare that no generative AI or AI-assisted technologies were used in the writing process of this manuscript.

References

[1] Khan, K.M., Khan, M., Ali, M., Taha, M.,Rasheed, S., Perveen, S., Choudhary, M.I. (2009). Synthesis of bis-Schiff bases of isatins and their antiglycation activity. Bioorg. Med. Chem.,17(22): 7795-7801, doi:10.1016/j.b mc.2009.09.028.

[2] Saxena, A., Das, D.R., Saxena, S. (2015). Synthesis, Anti TB, Antioxidant, Antimicrobial Activity of some Isatin-3-hydrazone derivatives. *Chem. Sci. Rev. Lett*., 4(14), 729-734.

[3] El-Sawi, E. A., Mostafa, T. B., & Radwan, H. A. (2011). Synthesis and biological activity of functionalized phosphorus derivatives of isatin imines. *European Journal of Chemistry*, *2*(4), 539-543, doi: 10.5155/eurjchem.2. 4.539-543.55

[4] Rabia, M. K., Mohamad, A. D. M., Ismail, N. M., & Mahmoud, A. A. (2013). Synthesis, characterization, anti-fungi and anti-bacterial activity of new [(2-pyridyl)-3-isatin]-bishydrazone. *Russian Journal of General Chemistry*, *83*(12), 2406-241, doi: 10.1134/S10703632 13120360.

[5] Kandile, N. G., Zaky, H. T., Mohamed, M. I., Ismaeel, H. M., & Ahmed, N. A. (2012). Synthesis, characterization and in vitro antimicrobial evaluation of new compounds incorporating oxindole nucleus. *Journal of Enzyme Inhibition and Medicinal Chemistry*, *27*(4), 599-608., doi: 10.3109/14756366.2011.576251.

[6] Shingade, S.G., Sanjaykumar, Bari, B., Waghmare, U.B. (2012). Synthesis and antimicrobial activity of 5-chloroindoline-2,3-dione derivatives. Med. Chem. Res., 21: 1302-1312, doi: 10.1007/s00044-011-9644-y.

[7] Vasanthi, R., Rajendraprasad, Y., Srinivas, B. (2013). Synthesis, Charac- terization, Antibacterial and Anti- fungal Activities of Isatin Derivatives. Int. J. Chem. Tech. Res., 5(6): 3015-3022.

[8] (a) Jarrahpour, A., Khalili, D., De Clercq, E., Salmi, C., & Brunel, J. M. (2007). Synthesis, antibacterial, antifungal and antiviral activity evaluation of some new bis-Schiff bases of isatin and their derivatives. *Molecules*, *12*(8), 1720-1730. doi:10.3390/12081720. (b)Jarrahpour , A., Sheikh, J., El Mounsi, I., Juneja, H., Ben Hadda, T. (2012). Computational evaluation and experimental in vitro antibacterial, antifungal and antiviral activity of bis-Schiff bases of isatin and its derivatives. Med. Chem. Res., 22(3): 1203-1211, doi:10.1007/s00044-012-0127-6.

[9] Dweedar, H.E., Mahrous, H., Ibrahim, H.S.,Abdel-Aziz, H.A. (2014). Analogue-based design, synthesis and biological evaluation of 3-substituted-(methylene hydrazono)indolin-2-ones as anticancer agents. *Eur. J. Med. Chem*., 78: 275-280, doi: 10.1016/j.ejmech.2014. 03.058.

[10]Afsah, E.M., Elmorsy, S.S., Abdelmageed, S.M., Zaki, Z.E. (2015). Synthesis of some new mixed azines, Schiff and Mannich bases of pharmaceutical interest related to isatin. Z. Naturforsch., 70(6)b: 393-402, doi:10.1515/znb-2014-0262.

[11] Prakash, C. R., Raja, S., & Saravanan, G. (2010). Synthesis, characterization and anticonvulsant activity of novel Schiff base of isatin derivatives. *Int J Pharm Pharm Sci*, *2*(4), 177-181.

[12] Panneerselvam, P., Reddy, R. S., Murali, K., & Kumar, N. R. (2010). Synthesis, analgesic, anti-inflammatory and antimicrobial activities of some novel Schiff's bases of 5-subsituted Isatin. *Der Pharma Chemica*, *2*(1), 28-37.

[13] Gholamzadeh, P., Ziarani, G.M., Badiel, A.(2016). Application of SBA-Pr-SO3H in the green synthesis of isatinhydrazone derivatives: Characterization, UV-Vis investigation and computational studies. J. Chil. Chem. Soc., 61(2): 2935-2939, doi: 10.40 67/ S0717-9707 2016000200017.

[14] Oguntoye, O.S., Hamid, A.A., Iloka, G.S., Bodede, S.O., Owalude, S.O., Tella, A.C. (2016). Synthesis and spectroscopic analysis of Schiff Bases of Imesatin and Isatin derivatives. J. Appl. Sci. Environ. Manage., 20 (3): 653-657, doi: 10.4314/jasem.v20i3.20.

[15] (a) Sunday, I.G., Christiana, K.A., Sunday, B., Olubunmi, O.S. (2016). Synthesis and Spectroscopic analysis of Schiff bases of Isatin and Imesatin derivatives. I.J.S.E.A.S., 2(4):381-388.(b) Kandile, N. G., Zaky, H. T., Mohamed, M. I., Ismaeel, H. M., & Ahmed, N. A. (2012). Synthesis, characterization and in vitro antimicrobial evaluation of new compounds incorporating oxindole nucleus. *Journal of Enzyme Inhibition and Medicinal Chemistry*, *27*(4), 599-608, doi: 10.3109/14756366.2011.576251.

[16] Khan, K.M., Khan, M., Ambreen, N., Rahim, F., Muhammad, B., Ali, S., Haider, S.M., Perveenb, S., Choudhary, M.I. (2011). Bis-Schiff Bases of Isatins: A New Class of Anti-oxidant. J. Pharm. Res., 4(10): 3402-3404.

[17] Khan, Z., Maqsood, Z.T., Tanoli, M.A.K., Khan, K.M., Iqbal, L., Lateef, M. (2015). Synthesis, Characterization, In-Vitro Antimicrobial and Antioxidant Activities of Co+2, Ni+2, Cu+2 and Zn+2 Complexes of 3-(2-(2-hydroxy-3-methoxybenzylid ene)hydrazono)indolin-2-one. J. Basic. Appl. Sci. 11: 125-130, doi: 10.6000/1927-5129.2015.11.1718.

[18] Ibrahim, H. S., Abou-Seri, S. M., Ismail, N. S., Elaasser, M. M., Aly, M. H., & Abdel-Aziz, H. A. (2016). Bis-isatin hydrazones with novel linkers: Synthesis and biological evaluation as cytotoxic agents. *European Journal of Medicinal Chemistry*, *108*, 415-422., doi:10.1016/j.ejme ch.20 15.11.047.

[19] Fares, M., Eldehna, W. M., Abou-Seri, S. M., Abdel-Aziz, H. A., Aly, M. H., & Tolba, M. F. (2015). Design, synthesis and in vitro antiproliferative activity of novel isatin-quinazoline hybrids. *Archiv der Pharma zie*, *348*(2), 144-154., doi:10.1002/ardp.201400 337.

[20] Suresh, A. J., Lakshmi, S. G., Kumar, V. S., Madhuraj, M., Durga, V., & Surya, P. R. (2018). Design, synthesis, characterization, and biological evaluation of some novel antitubercular agents targeting thymidylate synthetase, enoyl-ACP reductase, and l, d-trans peptidase-2. *J. Pharm. Res*, *12*(3), 332-339.

[21] Akhaja, T. N., & Raval, J. P. (2012). Design, synthesis and in vitro evaluation of tetrahydropyrimidine–isatin hybrids as potential antitubercular and antimalarial agents. *Chinese Chemical Letters*, *23*(7), 785-788., doi: 10.1016/j.ccl et.2012.05.004.

[22]Chinnasamy, R. P., Sundararajan, R., & Govindaraj, S. (2010). Synthesis, characterization, and analgesic activity of novel schiff base of isatin derivatives. *Journal of advanced pharmaceutical technology & research*, *1*(3), 342-347., doi:10.4103/0110- 5558.72428.

[23]]Swathy, S. S., Joseyphus, R. S., Nisha, V. P., Subhadrambika, N., & Mohanan, K. (2016). Synthesis, spectroscopic investigation and antimicrobial activities of some transition metal complexes of a [(2-hydroxyacetophenone)-3-isatin]-bishydrazone. *Arabian Journal of Chemistry*, *9*, S1847-S1857., doi: 10.101 6/j.arabjc.2012.05.004.

[24] Ansari, K. R., & Quraishi, M. A. (2014). Bis-Schiff bases of isatin as new and environmentally benign corrosion inhibitor for mild steel. *Journal of Industrial and Engineering Chemistry*, *20*(5), 2819-2829., doi: 10.10 16/j.jiec.2013.11.014.

[25] Ravi, K., Krishnakumar, B., & Swaminathan, M. (2012). An Efficient Protocol for the Green and Solvent-Free Synthesis of Azine Derivatives at Room Temperature Using BiCl3-Loaded Montmorillonite K10 as a New Recyclable Heterogeneous Catalyst. *International Scholarly Research Notices*, (1), 595868., doi:10.5402/ 2012/595868.

[26] Safari, J., & Gandomi-Ravandi, S. (2014). Structure, synthesis and application of azines: a historical perspective. *RSC advances*, *4*(86), 46224-46249., doi : 10.1039/c4ra04870a.

[27] Krishnakumar, B., & Swaminathan, M. (2011). An expeditious and solvent free synthesis of azine derivatives using sulfated anatase–titania as a novel solid acid catalyst. *Catalysis Communications*, *16*(1), 50-55., doi:10. 1016/j.catcom. 2011.08.029.

[28] Ibrahim, H. S., Abdelhadi, S. R., & Abdel-Aziz, H. A. (2015). Hydrolysis and Hydrazinolysis of Isatin-Based Ald-and Ketazines. *J. Chem.*, (1), 826489, doi: 10.11 55/2015/826489.

[29] Shingade, S. G., Bari, S. B., & Waghmare, U. B. (2012). Synthesis and antimicrobial activity of 5-chloroindoline-2, 3-dione derivatives. *Medicinal Chemistry Research*, *21*(7), 1302-1312., doi:10.1007/s00044-011-9644-y.

[30] Saxena, A., Das, D.R., Saxena, S. (2015). Synthesis, Anti TB, Anti oxidant, Antimicrobial Activity of some Isatin-3-hydrazone derivatives. Chem. Sci. Rev. Lett., 4(14), 729-734.

[31] Rabia, M. K., Mohamad, A. D. M., Ismail, N. M., & Mahmoud, A. A. (2013). Synthesis, characterization, anti-fungi and anti-bacterial activity of new [(2-pyridyl)-3-isatin]-bishydrazone. *Russian Journal of General Chemistry*, *83*(12), 2406-2412.

[32] Siddappa, K., & Mayana, N. S. (2014). Synthesis, Spectroscopic Characterization, and Biological Evaluation Studies of 5-Bromo-3-(((hydroxy-2-methylquinolin-7-yl) methylene) hydrazono) indolin-2-one and Its Metal (II) Complexes. *Bioinorganic chemistry and applications*, *2014*(1), 483282., doi: 10.1155/2014/483 282.

[33] Loghmani-Khouzani, H., Sadeghi, M. M., Safari, J., Abdorrezaie, M. S., & Jafarpisheh, M. (2001). A convenient synthesis of azines under solvent-free conditions using microwave irradiation. *Journal of Chemical Research*, (2), 80-81.

[34] Lasri, J., Aly, M. M., Eltayeb, N. E., & Babgi, B. A. (2018). Synthesis of symmetrical and asymmetrical azines from hydrazones and/or ferrocenecarboxaldehyde as potential antimicrobial–antitumor agents. *Journal of Molecular Structure*, *1164*, 1-8., doi: 10.1016/j.molstruc. 2018.03.0 30.

[35] Eshghi, H., & Hosseini, M. (2008). Selective and Convenient Protection of Aldehydes as Azines under Solvent-Free Conditions. *Journal of the Chinese Chemical Society*, *55*(3), 636-638., doi: 10.1002/jccs .200800093.

[36] Sadjadi, S., Rasouli, S. (2011). An efficient synthesis of imidazo[1,2-a]azine using nanocrystalline alumina powder. Int. J. Nano.Dim., 1(3): 177-186.

[37] Krishnakumar, B., & Swaminathan, M. (2011). An expeditious and solvent free synthesis of azine derivatives using sulfated anatase–titania as a novel solid acid catalyst. *Catalysis Communications*, *16*(1), 50-55., doi:10.1016/j.catcom.2011.08.029.

[38] Arun, V., and K. R. Sankaran. "Characterization and Computational analysis of unsymmetrical azines." *Can. J. Trans* 3.3 (2015): 319-326., doi: 10.13179/canchemtrans. 2015.03.03.0224.

[39] Safari, J., Gandomi-Ravandi, S. (2011). Highly efficient practical procedure for the synthesis of azine derivatives under solvent-free conditions. *Synth. Commun*., 41: 645-651, doi:10.1080 /00 3 9791100362952340.

[40] Nanjundaswamy, H.M., Pasha, M.A. (2007). Rapid, Chemoselective and Facile Synthesis of Azines by Hydrazine/I2. Synth. Commun., 37: 3417-3420, doi: 10.1080/00397 910701483837.

[41] Anastas, P.T., Warner, J.C. (1998). Green Chemistry: Theory and Practice. Oxford University Press: New York, p. 30. *ISBN*. 9780198502340.

[42] Dehbi, O., Ishak, E. A., Bakht, M. A., Geesi, M. H., Alshammari, M. B., Chagnault, V., & Riadi, Y. (2018). Water-mediated synthesis of disubstituted 5-aminopyrimidines from vinyl azides under microwave irradiation. *Green chemistry letters and reviews*, *11*(2), 62-66., doi:10.1080/175182 53.2018.1437225.

[43] Ghasemzadeh, M. A., Abdollahi-Basir, M. H., & Mirhosseini-Eshkevari, B. (2018). Multi-component synthesis of spiro [diindeno [1, 2-b: 2′, 1′-e] pyridine-11, 3′-indoline]-triones using zinc terephthalate metal-organic frameworks. *Green. Chem. Lett. Rev*, *11*(1), 47-53. doi:10.1080/17518253.2018.1434565.

[44] Benlahreche, B., Taleb, A., Lahrech, M. B., & Hacini, S. (2019). Isatin Aldazines Synthesis using A Proton Exchanged Algerian Montmorillonite Clay as Acid Eco-friendly Catalyst. *Bulletin of Chemical Reaction Engineering & Catalysis*, *14*(3), 551-558., doi: 10.976 7/bcrec.14.3.4 574.551-558 .

[45] Bekdemir, Y., & Efil, K. (2014). Microwave Assisted Solvent-Free Synthesis of Some Imine Derivatives. *Organic Chemistry International*, *2014*(1), 816487., 1-5, doi: 10.12966/jsmr.12.04.2014.

[46] Panda, J., Patro, V. J., Sahoo, B. M., & Mishra, J. (2013). [Retracted] Green Chemistry Approach for Efficient Synthesis of Schiff Bases of Isatin Derivatives and Evaluation of Their Antibacterial Activities. *Journal of Nanoparticles*, *2013*(1), 549502., doi : 10.1155/2013 /549502.

[47] Belbachir, M., Bensaoula, A. (2006). Composition and method for catalysis using bentonites. U. S. Pat., US 7,09 4,823 B2.

[48] Alali, K., Lebsir, F., Amri, S., Rahmouni, A., Srasra, E., Besbes, N. (2019). Algerian Acid Activated Clays as Efficient Catalysts for a Green Synthesis of Solketal by Chemo- selective Acetalization of Glycerol with Acetone. Bull. Chem. React. Eng. Catal., 14 (1): 130-141, doi:10.9767/ bcrec.14.1.2445.130-141.

[49] Tanoli, M.A.K., Khan, Z., Maqsood, Z.T., Iqbal, L., Lateef, M., Hussain, Z., Kamal, T.(2014). Copper (II) Complexes of Bishydrazone Derivatives: Synthesis, Characterization and Urease Inhibition Studies, Middle. East. J. Sci. Res., 22 (5): 698-703, doi: 10.5829/idosi.me jsr.2014.22.05.21942.