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Synthesis, Characterization and Antimicrobial Activities of 1,2,4-Triazole /Isatin Schiff bases and their Mn(II), Co(II) Complexes

SUNITA BAJROLIYA, G. S. KALWANIA*, SAVITA CHOUDHARY and S. CHOMAL

Department of Chemistry, S. K. Government P. G. College Sikar - 332001, India
*Corresponding author E-mail: gskalwania@gmail.com

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ABSTRACT

Mn(II) and Co(II) metal complexes have been synthesized with newly synthesized Schiff bases derived from isatin/5-nitroisatin and 3-substituted-4-amino-5-mercapto-1,2,4-triazole by new environmental benign microwave irradiation method as well as conventional method. Reaction achieved by microwave irradiation technique, require drastically reduced reaction time and provide high yield with improved selectivity as compared to conventional method. The synthesized compounds were characterized by elemental analysis as well as spectral studies. The elemental analysis were clearly indicated that ML_2 type complexes have 1:2 stoichiometry (M=metal, L=ligand). The synthesized Schiff bases and their metal complexes screened for antimicrobial activities against selected bacteria and fungi.

Keywords: Schiff bases, 1,2,4-Triazole, Isatin, 5-Nitroisatin, Microwave irradiation, Antimicrobial, Complexes.

INTRODUCTION

The chemistry of 1,2,4-triazole and its derivatives is particularly interesting because of their potential application in medicinal, agricultural and industrial fields[1-4]. Derivatives of 1,2,4-triazoles show variety of biological activities such as antimicrobial[5] anticonvulsant[6], anticancer[7], analgesic[8], anti HIV[9], and anti-inflammatory[10] properties. Similarly, Isatin and Schiff bases of isatin derivatives are reported to show diverse biological activities like antibacterial[11], antifungal[12], anticonvulsant[13], anti-HIV[14], antidepressant[15] and anti-inflammatory[16] activities. It is well known that the heterocyclic compounds containing both 1,2,4-triazole and isatin rings have broad spectrum of pharmacologic properties[2-8,11-15,17-18]. Some metal complexes derived from isatin and 1,2,4-triazole Schiff bases have reported to exhibit antimicrobial activities[19]. These diverse biological applications of schiff bases and their precursors have inspired us to synthesize a new series of [Mn(II), Co(II)] metal complexes with Schiff bases containing isatin/5-nitroisatin and 3-substituted-4-amino-5-mercapto-1,2,4-triazole.

In recent years Microwave assisted reactions have attracted researchers much interest because of simplicity of operation, enhanced reaction rates, high yields, improved selectivity[20-21] and environmental friendly reaction condition[22-24]. The reactions, which are not possible under normal conditions,can be overcome by high-energy microwave irradiation.Thereforwe have made efforts to develop and optimize anew environmentally benign method using microwave irradiation in our laboratory and finally 3-substituted-4-amino-5-mercapto-1,2,4-triazole[25]and isatin derivatives have been synthesized. These compounds were also prepared by conventional methods[26] to compare their results with new microwave irradiation method. The newly synthesized compounds were characterized by spectral as well as elemental analysis and screened for their biological activities.

EXPERIMENTAL

The melting point of synthesized compounds were determined on open aluminum block and not corrected. Purity was checked by TLC (thin layer of silica gel) using Merck Silica gel G-60. Infrared (IR) spectra of all the synthesized compounds recorded using KBr from Shimadzu FTIR, Affinity-1. The NMR spectra has taken by Varian Gemini 400 spectrometer (300MHz) using TMS as an internal standard. Elemental data obtained from all the synthesized compounds were found satisfactory.

RESULTS AND DISCUSSION

The focus of the present work was on the synthesis of some new Schiff bases and their Mn (II), Co (II) metal complexes by microwave irradiation (Scheme 1). These compounds were also synthesized by conventional method[26]. In microwave method, the reaction time reduced from 6 hrs.to 3-5 minutes (3a-h) and from4 hrs.to 4-7 minutes (4a-p). The yield obtained from microwave method was better as compared to conventional method.The purity of the compounds was checked by TLC. The compounds were characterized with the help of spectral data (IR, ^{1}H NMR) and elemental analysis. All data were found in accordance with the proposed structures of synthesized compounds. The IR spectroscopic data have indicated the formation of 3a-h by disappearance of the NH_2 band at 3400 cm^{-1} (2a-d) and appearance of C=N band at about 1608-1643 cm^{-1}, The stretching vibrational N-H band at about 3201-3271 cm^{-1} and C=O band at about 1707-1738 cm^{-1}confirm the presence of indole ring in compounds 3a-h. A characteristic strong band at 2690–2716 cm^{-1}clearly indicate the presence of S-H group intriazole and another band around at 1098- 1112 cm^{-1} is assigned to ν(C=S)[27]. These observations indicate that the Schiff bases exhibit thiol–thionetautomerism.

All the metal complexes exhibited the band of ν(C=N) in the region 1592–1630 cm^{-1}, showing the shift of this band to lower wave numbers, as compared with the spectra of the Schiff bases. This shift indicates that the nitrogen is coordinated to the metal ion[28-30]. The band of ν(C=O) in the region 1702–1730 cm$^{"1}$ in the complexes, showing the shift to lower wave numbers compared with Schiff bases confirms that the carbonyl oxygen is also coordinated to the metal ion [31-32]. The new bands in the region of 460–472 cm^{-1} in the spectra of the metal complexes are assigned to stretching frequencies of (M–N) bonds. The absence of a band around at 2700 cm$^{"1}$ in all the metal complexes and new band in the region 358–380 cm$^{"1}$ in far IR-spectra indicate the formation of metal-sulfur bonds. All the infrared frequencies of metal complexes are summarized in Table 2.The comparison of ^{1}H NMR spectroscopic data of Schiff bases and their precursors also indicate the formation of 3a-h by the appearance of signal corresponding of two different NH protons at about 11.10-12.50 ppm and the disappearance of the NH_2 protons in the 2a-d at about 5.00 ppm.

All the Schiff bases (3a-h) and their metal complexes (4a-p)along with some standard antibiotics and antifungal drugs were screened for their antimicrobial activities against selected bacteria and fungus. All the antimicrobial activity results are summarized in Table 3. The nitro derivatives of Schiff bases (3e-h) were found more active as compared to others. Co (II) complexes (4i-p) show higher antimicrobial activity in comparison to respective Schiff bases against selected bacteria and fungi.

Table 1: Physical properties and analytical data of metal complexes (4a-p)

Comp. No.	Formula	R	R'	R"	m.p. (de. Point)°C	Yield (%) Conv. Method	Micro Method	Elemental analyses found (calculated) M	C	H	N
(4a).	$Mn(C_{16}H_{10}N_5OS)_2$	H	H	H	240-245	76	90	7.81 (7.86)	54.62 (54.63)	2.84 (2.83)	19.91 (19.94)
(4b).	$Mn(C_{16}H_{10}N_5OS)_2$	H	H	OH	234-238	66	85	7.64 (7.62)	53.41 (53.49)	2.78 (2.79)	19.47 (19.49)
(4c).	$Mn(C_{16}H_{10}N_5OS)_2$	H	OH	H	>260	65 93	7.63	53.42 (7.66)	2.77 (53.40)	19.48 (2.78)	(19.46)
(4d).	$Mn(C_{16}H_9N_5OSBr)$	H	Br	H	>260	58	89	6.38 (6.35)	44.61 (44.68)	2.09 (2.09)	16.26 (16.23)
(4e).	$Mn(C_{16}H_9N_6O_3S)_2$	NO_2	H	H	>290	76	94	6.92 (6.93)	48.42 (48.39)	2.27 (2.28)	21.18 (21.25)
(4f).	$Mn(C_{16}H_9N_6O_3S)_2$	NO_2	H	OH	>290	65	92	6.65 (6.71)	46.54 (46.54)	2.18 (2.16)	12.10 (12.15)
(4g).	$Mn(C_{16}H_9N_6O_3S)_2$	NO_2	OH	H	>290	67	88	6.62 (6.66)	46.53 (46.50)	2.17 (2.18)	12.12 (12.10)
(4h).	$Mn(C_{16}H_8N_6O_3SBr)_2$	NO_2	Br	H	>290	63	91	5.77 (5.80)	40.39 (40.35)	1.68 (1.69)	17.67 (17.71)
(4i).	$Co(C_{16}H_{10}N_5OS)_2$	H	H	H	>290	75	96	8.33 (8.30)	54.31 (54.31)	2.82 (2.81)	19.80 (19.88)
(4j).	$Co(C_{16}H_{10}N_5O_2S)$	H	H	OH	>290	70	87	8.15 (8.26)	53.11 (53.10)	2.76 (2.75)	19.36 (19.36)
(4k).	$Co(C_{16}H_{10}N_5O2S)$	H	OH	H	>290	68	90	8.17 (8.20)	53.08 (53.13)	2.76 (2.74)	19.29 (19.30)
(4l).	$Co(C_{16}H_9N_5OSBr)_2$	H	Br	H	>290	62	92	6.81 (6.85)	44.40 (44.39)	2.08 (2.10)	16.19 (16.20)
(4m).	$Co(C_{16}H_9N_6O_3S)$	NO_2	H	H	>290	80	96	7.39 (7.42)	48.18 (48.20)	2.25 (2.24)	21.08 (21.10)
(4n).	$Co(C16H9N6O_4S)_2$	NO_2	H	OH	>290	69	90	7.10 (7.17)	46.32 (46.30)	2.17 (2.20)	20.26 (20.26)
(4o).	$Co(C_{16}H_9N_6O_4S)_2$	NO_2	OH	H	>290	70	92	7.12 (7.09)	46.30 (46.36)	2.18 (2.16)	20.24 (20.19)
(4p).	$Co(C_{16}H_8N_6O_3SBr)_2$	NO_2	Br	H	>290	64	86	6.17 (6.20)	40. 22 (40.20)	1.67 (1.67)	17.59 (17.60)

General Method for the Synthesis of Schiff bases

All the Schiff bases were synthesized by both conventional and microwave assisted methods. The latter method provided reproducible results and analytical data related to the products obtained from both methods were found coherent.

Conventional Method

The equimolar quantity of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (10 mmol) and isatin/5-nitroisatin (10 mmol) containing 3-4 drops concentrated HCl in hot methanol (40 ml) was refluxed for 6 hrs. After completion of reaction, the reaction mixture was cooled at room temperature. This solid obtained was filtered, washed with cold methanol, dried and recrystallized from methanol.

Microwave Assisted Method

A mixture of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (1 m mol) and isatin/5-nitroisatin (1 mmol) in methanol (10 ml) containing concentrated HCl (3-4 drops) was subjected to microwave irradiation intermittently at 30 seconds for 3-5 minutes. After completion of reaction as monitored by TLC, the reaction mixture was cooled at room temperature.The solid separated out on cooling was filtered, washed with cold methanol, dried and recrystallized from methanol.

The analytical data for all the synthesizes Schiff bases are summarized here. The yield obtained by microwave -assisted method is represented in bracket.

3-[3-Phenyl-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin

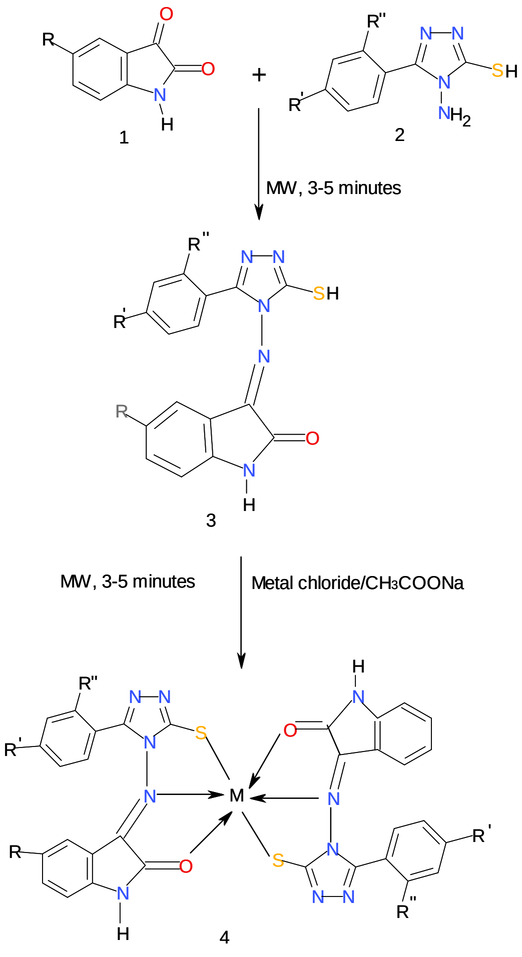
Yield 72%, (95%); m.p. 221°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1728 (>C=O), 1614 (C=N), 3211(N-H, isatin), 3187 (N-H, triazole), 2715 (S-H), 1104 (C=S); ^{1}H-NMR (DMSO-d$_6$, ´ ppm): 6.96-7.80 (Ar-9H, m), 11.98 (isatin, N-H, 1H, s), 11.14 (triazole, N-H, 1H, s), 11.20 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{11}N_5OS$; C: 59.82, H: 3.41, N: 21.80; Found (%); C: 59.81, H: 3.40, N: 21.80.

3-[3'-(2''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin

Yield 64%, (91%); m.p. 178°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1730 (>C=O), 1613 (C=N), 3208(N-H, isatin), 3165 (N-H, triazole), 2706 (S-H), 1106 (C=S), 756 (1,2-disubstitutedphenyl); ^{1}H-NMR (DMSO-d$_6$, ´ ppm): 6.93-7.78 (Ar-8H, m), 11.92 (isatin, N-H, 1H, s), 11.12 (triazole, N-H, 1H, s), 11.18 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{11}N_5O_2S$; C: 56.97, H: 3.26, N: 20.78; Found (%); C: 56.97, H : 3.26, N: 20.77.

3-[3'-(4''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin

Yield 66%, (92%); m.p. 249 °C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1731 (>C=O), 1614 (C=N), 3209(N-H, isatin), 3168 (N-H, triazole), 2705 (S-H), 1105 (C=S), 841 (1,4-disubstitutedphenyl); ^{1}H-NMR (DMSO-d$_6$, ´ ppm): 7.95-7.80 (Ar-8H, m), 11.91



R=H,NO$_2$; R'=H,OH,Br; R''=H,OH; M=Mn(II),Co(II)

Scheme 1: Synthesis pathway for the preparation of compounds

(isatin, N-H, 1H, s), 11.13 (triazole, N-H, 1H, s), 10.85 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{11}N_5O_2S$; C: 56.97, H: 3.27, N: 20.77; Found (%); C: 56.97, H : 3.26, N: 20.79.

3-[3'-(4''-Bromophenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin

Yield 62%, (88%); m.p. 260°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1726 (>C=O), 1608 (C=N), 3201 (N-H, isatin), 3134 (N-H, triazole), 2690 (S-H), 1098 (C=S), 845 (1,4-disubstitutedphenyl); ^{1}H-NMR (DMSO-d_6, ´ ppm): 7.08-7.90 (Ar-8H, m), 12.00 (isatin, N-H, 1H, s), 11.15 (triazole, N-H, 1H, s), 10.98 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{10}N_5OSBr$; C: 48.03, H: 2.50, N: 17.52; Found (%); C: 48.01, H : 2.50, N: 17.50.

3-[3'-Phenyl-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin

Yield 70%, (90%); m.p. 269°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1707 (>C=O), 1632 (C=N), 3265(N-H, isatin), 3121 (N-H, triazole), 2716 (S-H), 1106 (C=S), 1355 1541 (NO$_2$); ^{1}H-NMR (DMSO-d_6, ´ ppm): 7.12-8.40 (Ar-8H, m), 12.42 (isatin, N-H, 1H, s), 11.81 (triazole, N-H, 1H, s), 10.97 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{10}N_6O_3S$; C: 52.44, H: 2.73, N: 22.96; Found (%); C: 52.45, H: 2.73, N: 22.95.

3-[3'-(2''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'yl]imino-5-nitroisatin

Yield 65%, (86%); m.p. 290°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1714 (>C=O), 1641 (C=N), 3271(N-H, isatin), 3116 (N-H, triazole), 2710 (S-H), 1110 (C=S), 764 (1,2-disubstitutedphenyl), 1350 1542 (NO$_2$); ^{1}H-NMR (DMSO-d_6, ´ ppm): 7.39-8.16 (Ar-7H, m), 12.29 (isatin, N-H, 1H, s), 11.62 (triazole, N-H, 1H, s), 11.20 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{10}N_6O_4S$; C: 50.27, H: 2.61, N: 21.97; Found (%); C: 50.26, H : 2.61, N: 21.98.

3-[3'-(4''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin

Yield 67%, (94%); m.p. 280°C; IR (KBr, $\nu_{max.}$, cm^{-1}): 1718 (>C=O), 1640 (C=N), 3268 (N-H, isatin), 3168 (N-H, triazole), 2708 (S-H), 1110 (C=S), 844 (1,4-disubstitutedphenyl), 1350 1542 (NO$_2$); H-NMR (DMSO-d_6, ´ ppm): 7.35-8.18 (Ar-7H, m), 12.30 (isatin, N-H, 1H, s), 11.59 (triazole, N-H, 1H, s), 10.96 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_{10}N_6O_4S$; C: 50.27, H: 21.98, N: 20.77; Found (%); C: 50.27, H : 2.60, N: 21.99.

3-[3'-(4''-Bromophenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin

Yield 60%, (90%); m.p. 292°C; IR (KBr,

Table 2: Characteristic infrared vibrations (cm^{-1}) of metal complexes (4a-p)

Compound	Indole ring				
No.	ν(C=O)	ν(C=N)	ν(N-H)	ν(M-S)	ν(M-N)
4(a)	1718	1601	3210	364	465
4(b)	1721	1599	3206	359	468
4(c)	1716	1596	3210	361	466
4(d)	1711	1593	3203	376	463
4(e)	1704	1612	3217	365	464
4(f)	1705	1627	3198	358	470
4(g)	1703	1622	3211	363	464
4(h)	1727	1630	3197	374	462
4(i)	1720	1603	3213	367	464
4(j)	1722	1596	3207	358	466
4(k)	1719	1598	3211	363	467
4(l)	1709	1592	3198	379	461
4(m)	1702	1617	3216	371	465
4(n)	1709	1628	3201	365	463
4(o)	1707	1620	3210	360	468
4(p)	1730	1628	3202	378	460

$\nu_{max.}$, cm^{-1}): 1738 (>C=O), 1643 (C=N), 3230 (N-H, isatin), 3130 (N-H, triazole), 2702 (S-H), 1112 (C=S), 852 (1,4-disubstitutedphenyl), 1362 1540 (NO_2); ^{1}H-NMR (DMSO-d_6, ´ ppm): 7.23-8.65 (Ar-7H, m), 12.49 (isatin, N-H, 1H, s), 11.96 (triazole, N-H, 1H, s), 10.90 (S-H, 1H, s); Anal. Calculated (%) for $C_{16}H_9N_6O_3SBr$; C: 43.15, H: 2.04, N: 18.87; Found (%); C: 43.15, H : 2.02, N: 18.88.

General Method for the Synthesis of Metal Complexes

All the metal complexes were synthesized by both conventional and microwave assisted methods. The latter method provided reproducible results and analytical data related to the products obtained from both methods were found coherent.

Conventional method

A solution of metal chloride (1 mmol)in methanol **(**6 ml) and 2 mmol of sodium acetate were added to Schiff base (2 mmol)dissolved in Methanol (30 ml) and refluxed on water bath for 4 hrs. The reaction mixture was cooled at room temperature and solid separated out was filtered, washed thoroughly with methanol and water and dried.

Microwave Assisted Method

A solution of metal chloride (1 mmol)in methanol **(**3 ml) and 2 mmol of sodium acetate were added to Schiff base (2 mmol) dissolved in Methanol (10 ml) and subjected to microwave irradiation intermittently at 30 seconds for 4-7 minutes. After completion of the reaction as monitored by TLC, the

Table 3: Antimicrobial activities of schiff bases and their metal complexes

	Zone of Inhibition in mm					
Compd.No.	Antibacterial Activity			Antifungal Activity		
	E. coli	*P. aeruginosa*	*S. aureus*	*B. subtilis*	*A. niger*	*C. albicans*
3(a))	7	8	9	9	8	7
3(b)	6	7	8	7	7	7
3(c)	7	9	7	10	6	8
3(d)	8	9	7	6	9	7
3(e)	7	11	10	13	8	8
3(f)	8	10	11	15	10	9
3(g)	8	12	10	10	8	9
3(h)	10	9	12	13	11	10
4(a)	7	10	6	7	8	10
4(b)	8	8	10	9	6	7
4(c)	9	8	9	9	8	6
4(d)	7	9	7	8	6	6
4(e)	8	7	6	10	8	8
4(f)	6	11	8	8	8	9
4(g)	7	8	9	9	7	6
4(h)	8	10	12	6	10	9
4(i)	8	10	8	9	7	7
4(j)	9	9	7	9	8	11
4(k)	8	10	7	12	7	9
4(l)	7	8	8	9	8	8
4(m)	9	13	11	14	10	9
4(n)	11	10	13	16	10	11
4(o)	10	13	14	12	9	9
4(p)	12	11	16	15	9	10
Streptomycein	18	20	23	25	-	-
Fluconazole	-	-	-	-	23	22

hot reaction mixture was cooled at room temperature. The solid separated out was filtered, washed thoroughly with methanol and water and dried.

Antimicrobial activity

Antimicrobial activity of synthesized Schiff bases and their metal complexes were evaluated *in vitro by* using agar-plate diffusion technique[33] by measuring the zone of inhibition in mm. The antibacterial activity was evaluated against four bacterial strains *Escherichia coli* ATCC 25922(*E. coli*), *Pseudomonas aeruginosa* ATCC 27853 (*P. aeruginosa*), *Staphylococcus aureus ATCC* 25923 (s. *aureus*) and *Bacillus subtilis ATCC 6633* (*B. subtilis*) at 100¼g/mL concentration of samples with standard drugs Streptomycin. After completion of incubation period (18-24 h at 37 ^{0}C), the zone of inhibition of growth in the form of diameter in mm was measured (Table 3).

An antifungal activity was evaluated against *Aspergillus neiger* (*A. neiger*) and *Canadida albicans* (*C. albicans*) at 100 μg/mL concentration of samples using Fluconazole as standard drug. After completion of the incubation period (18-24 h at 37 ^{0}C), the zone of inhibition of growth in the form of diameter in mm was measured (Table 3).

CONCLUSION

The prepared Schiff bases behave as tridentate chelating agent with Mn(II), Co(II) metal ions and coordinated through N, O and S atoms. The elemental analysis were clearly indicated that ML_2 type complexes have 1:2 stoichiometry (M=metal, L=ligand). All the Schiff bases and their Mn(II), Co(II) metal complexes were synthesized by microwave irradiation as well as by conventional method to compare analytical data and confirm their structure. The studies revealed that Schiff bases containing nitro group were found more active against selected bacteria and fungi. It is also observed that Co (II) metal complexes have exhibited higher antimicrobial activity than the respective Schiff bases as cleared from data in table 3.

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REFERENCES

1. Legrand, C.; Ropaa, P.; Vulturescu, B.; Hogeac, A. M.; Surpateanu, G.G.; Cazier, F.; Woisel, P.; Surpateanu, G. *Progress in Organic Coatings* **2005***,* *53*, 106-111.
2. Ewiss, N. F.; Bahajaj, A. A.; Elsherbini, E. A. *J. Heterocycl. Chem.***1986**, *23*, 1451-1458.
3. Eweiss, N. F.; Bahajaj, A. A. *J. Heterocycl. Chem.***1987**, *24*, 1173-1182.
4. Prasad, A.; Ramalingam, R. J.; Rao, A. B.; Diwan, P. V.; Sattur, P. B. *Eur. J. Med.Chem*. **1989**, *24*, 199-201.
5. Turan-Zitouni, G.; Kaplanc1kl1, Z. A.; Y1ld1z, M. T.; Chevallet, P.; Kaya, D. *Eur. J. Med.Chem.***2005**, *40*, 607-613.
6. Chen, J.; Sun, Y.; Chai, K. Y.; Lee, J. S.; Song, M. S.; Quan, Z. S. *Bioorg. Med. Chem*. **2007**,*15*, 6775-6781.
7. Bekircan, O.; Gumrukcuoglu, N. *Indian J. Chem*. **2005**, *44B*, 2107-2113.
8. Turan-Zitouni, G.; Kaplanc1kl1, Z. A.; Erol, K.; Kilic, F. S. *Farmaco***1999**, *54*, 218-223.
9. Akhtar, T.; Hameed, S.; Al-Masoudi, N. A.; Khan, K. M. *Heteroatom. Chem*. **2007**, *18*, 316-322.
10. Turan-Zitouni, G.; Kaplancikli, Z. A.; Özdemir, A.; Chevallet, P. *Arch. Pharm. Chem. Life Sci* .**2007**,*340*,586-590.
11. Sarangapani, M.; Reddy, V. M.*Indian J. Pharm. Sci.***1994**,*56*, 174-177.
12. Pandeya, S. N.; Sriram, D.; Nath, G.; De Clercq, E. *Pharm. ActaHelv.***1999**, *74*, 11-17 .
13. Popp, F. D.; Parson, R.; Donigan, B. E. *J. Heterocycl. Chem*. **1980**, *17*, 1329-1330.
14. Pandeya, S. N.; Sriram D.; DeClercq, E.; Nath, G. *Eur. J. Pharm. Sci.***1999**,*9*, 25-31.
15. Singh, G. S.; Singh, T.; Lakhan, R. *Indian J. Chem.* **1997**, *36B*, 951-954.

16. Bhattacharya, S. K.; Chakrabarti, S. *Indian J. Exp. Biol*. **1998**, *36*, 118-121.
17. Islam, M. R.; Abedin, M. J.; Hossain, M. M.; Duddeck H. *J. Bangladesh Chem. Soc*.**1998**,*11*,71-78 .
18. Kahveci, B. *Molecules***2005**, *10*, 376-382.
19. Kulkarni, D.; Patil, S. A.; Badami, P. S. *Journal of Sulfur Chemistry* **2009**,*30(2)*, 145-159.
20. Chandak, S.*Tetrahedron***1995**, 51, 10403-10432.
21. Kidwa, M.; Sapra, P.; Bhushan, K. R.; Saxena, R. K.*Montash Chem*. **2000**, *113*, 85-90.
22. Kappe, C. O.*Curr.Opin.Chem. Biol.***2002**, *6*, 314-320.
23. Larhed, M.; Moberg, C.; Hallberg, A.*Acc. Chem. Res.* **2002**,*35*, 717-727.
24. Lidstrom, P.; Tirrey, J.; Wathey, B. Westman J., *Tetradedron***2001**, *57*, 9225-9283.
25. Kalwania, G. S.; Choudhary, S.; Chomal, S. *Chemical Science Transactions***2014,***3(3)*, 1147-1155.
26. Mathew, V.; Keshavayya,J.; Vaidya, V. P.*J Chem*. **2007**, *4(3)*,320-342.
27. Singh, G.; Singh, P. A.; Singh, K.; Singh, D. P.; Handa, R. N.; Dubey, S. N. *Proc. Nat. Acad. Sci. Ind.***2002**, *72A*,87-94
28. Hassaan, A. M. A. *Indian J. Chem.***1997,** *36***,**241-243.
29. Soliman, A. A.; Linert ,W. *Thermochim. Acta***1999,** *333*,67-75.
30. Nakamoto K. Infrared Spectra of Inorganic and Coordination Compounds*,* Wiley-Interscience.NewYork, (1970).
31. Cerchiaro, G.; Saboya, P. L.; Ferreira, A. M. C.; Tomazela, D. M.; Eberlin, M. N. *Transit.Met.Chem.***2004**,*29,* 495-504.
32. Murukan, B.; Bhageerethi, S. K.; Kochukittan, M.*J. Coord. Chem.***2007,***60*,1607-1617.
33. Turan-Zitouni, G.; Kaplancikli, Z. A.; Erol,K.; Kilic, F. S.*Farmaco***1999**,*54*, 218-223.