SJIF 2012: 2.545

UIF 2013: 1.075

Received on:

7th February 2015

Revised on:

10th March 2015

Accepted on:

11th March 2015

Published on:

1st April 2015

Volume No.

Online & Print

9 (2015)

Page No.

20 to 25

SYNTHESIS AND BIOLOGICAL STUDY OF 5-(((4,5-DIPHENYL-4H-1,2,4-TRIAZOL-3-YL)THIO)METHYL)QUINOLIN-8-OL AND ITS METAL COMPLEXES

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ABSTRACT:

A novel ligand namely compound of 5-(((4,5-diphenyl-4h-1,2,4-triazol-3-yl)thio)methyl)quinolin-8-ol (THQ), derived in a good yield by condensation of from 4,5-diphenyl-4H-1,2,4-triazole-3-thiol with 5-chloromethyl-8-quinolinol (HQ). It was characterized by elemental analysis and spectral analysis. Various transition metal complexes of 5-(((4,5-diphenyl-4h-1,2,4-triazol-3-yl)thio)methyl)quinolin-8-ol(THQ) metal ions were prepared by treatment of THQ and metal salt of stoichiometric ratio. All the resultant metal complexes were characterized by metal ligand ratio, spectral and magnetic properties. All the samples i.e. THQ and its complexes were screened for their antimicrobial activity.

KEY WORD: *8-Hydroxyquinoline, Thiol, 1,2,4-Triazole.*

INTRODUCTION:

8-Hydroxyquinoline (HQ) has long been employed as analytical and separating agents due to its universal chelating ability offered by the heterocyclic N and phenolate O atoms and fluorescent property possessed by the conjugate system. The tailorability arising from the activation of positions 5 and 7 further expands HQ family and leads to numerous HQ-based derivatives [1–6]. Alternations in the substituents produce HQ-based compounds showing diverse properties and thus achieve desired functionalities. These

functionalities comprise both non-biological and biological activities. It was recently reported that HQ itself and Cu^{2+} synergistically showed anti-agiogenic activity via inhibiting proteasome [7]. It has also been reported that combination of two or more heterocyclic and non heterocyclic systems enhances the biological properties many-fold over the parent molecule [8, 9]. Furthermore, presence of a sulfur atom at the 3-position of 1, 2, 4-triazole is essential to enhance various types of biological activities [10]. Because of conclusive evidences on significant biological activities of pyridyl
group bearing 5-subtituted 1,2,4-triazole-3-thiones synthesis of the substituted derivatives of 1,2,4-triazole-3thione have been of interest [11]. Tetrazole, thiadiazole, quinoline, indole and triazole derivatives are well known for their significant biological activities [12-14]. 1,2,4-Triazole nucleus has been incorporated into a wide variety of therapeutically interesting compounds includingH1/H2 histamine receptor molecules, cholinesterase active agents, anti-anxiety agents and sedatives.[15]. Recently we have reported [16], the merge of compounds having 8-HQ and 4-phenyl-5-(pyridine-4-yl)-4,5-dihydro-3H-1,2,4-triazole-3thiol and their metal complexes has been reported. So, in extention of this work[16] the present work is in connection with work shown in the scheme I.

MATERIALS AND METHOD:

4,5-diphenyl-4H-1,2,4-triazole-3-thiol was prepeared by reported method.[17]. CMQ was prepared and used as starting materials for the synthesis of novel ligand L (Scheme. 1) by the method reported in the literature [18]. All other chemicals were used of laboratory grade.

MEASUREMENTS

^{1}H NMR spectrum of ligand THQ was recorded on Brucker spectrophotometer (400 MHz) in DMSO-d_6 using TMS as an internal standard (chemical shifts are expressed in d, ppm). The FT-IR spectra, all the samples were recorded on Perkin Elmer Spectrum GX spectrophotometer using KBr pellets. Melting points were taken in open glass capillary tubes by using Thiel's tube containing liquid paraffin and were uncorrected. The elemental analyses were performed by Vario EL CHN elemental analyzer. Metal containts of complexes were determine by Voge's method. [20]

SYNTHESIS OF LIGAND

To a solution of the compound 4,5-diphenyl-4H-1,2,4-triazole-3-thiol in DMSO, 5-chloromethyl-8-hydroxyquinoline hydrochloride(CMQ) was added slowly in portions at room temperature and reflux for 2.5 hours. The green solid which was filtered and washed with water. Yield 82%, Melting point 258 ^{0}C.

GENERAL PROCEDURE FOR THE SYNTHESIS OF METAL COMPLEXES

A hot solution of metal(II) salt (2.5 mmol) in 50% aqueous formic acid (2.5 ml) was added drop-wisely with continuous stirring to the hot 20% aqueous formic acid solution (20 ml) of Ligand (L) (5 mmol). With the proper adjustment of the pH (~8.5) using 50% NH_4OH solution, the resultant mixture was further digested for 4 hours on steam bath. The obtained solid product was filtered, washed with hot water, and subsequently with small quantity of ethanol, acetonitrile, and dried in a vacuum desiccator. The Cu(II), Co(II), Mn(II),Ni(II) and Zn(II) metal complexes of THQ ligand were prepared.

RESULT AND DISCUSSION:

The structure of the products THQ was elucidated on the basis of their spectral (IR, And ^{1}H NMR) and elemental analysis. In a IR spectra, Ligand having broad band at 3810 cm^{-1} is due to phenolic OH group of 8-hydroxy quinoline moiety. The band at 1450 cm^{-1} is appeared due to CH_2 bending vibrations. The inflections around 2920 cm^{-1} and 2850 cm^{-1} are attributed to asymmetric and symmetric vibration of $-CH_2$. The band around 1560 to 1590 cm^{-1} attributed to –C=N- stretching vibrations. The bands around 1220 and 1020 cm^{-1} are mainly due to N-N bending vibrations. The weak bands due to out of plane deformation of 1,2,3 or 1,3 or 1,4-disubstituted benzene ring systems are appeared at 760,860, and 810 cm^{-1} respectively. In a NMR study, at 5.74 ppm shows singlet of phenolic –OH. The $-CH_2$ protons gives singlet at 3.72 ppm. Aromatic protons gives multiplate at 6.88 to 7.52 ppm. Comparing the IR spectra of metal complexes and ligand shows that the band of $-CH_2$ shifting 1450 to 1457 cm^{-1}, the band C-N shows at 1269 cm^{-1} and the broad band of υ^{OH} at 3500-2600 cm^{-1}.

ANTIMICROBIAL STUDIES OF METAL COMPLEXES

All the Complexes are toxic more or less to fungi. Cu^{+2} metal complexes are more toxic than others. This is expected because the copper salts are mostly used as fungicides. Most of the Complexes inhibit the growth of the belove organisms which cause decease in many plants.

The results of the magnetic moment value (Table 1) supported octahedral geometry for all the metal complexes [19]. Probable structure of the metal complex from the above analytical facts is given in Scheme I. The antimicrobial activity data of all the compounds are summarized in Table 2 and chart 1. The newly generated metal complexes have exerted significant inhibitory activity against the growth of the tested bacterial and fungal strains than the ligand itself

REFRENCES:

1. X.H. Ouyang, G.R. Wang, H.P. Zeng, W.M. Zhang, J. Li, J. Organomet. Chem. 694(2009) 3511.
2. J.A. Gonzalez-Vera, E. Lukovic, B. Imperiali, J. Org. Chem. 74 (2009) 7309.
3. L.H. Li, B. Xu, Tetrahedron 64 (2008) 10986.
4. B. Himmi, J.P. Joly, F. Hlimi, M. Soufiaoui, S. Kitane, A. Bahloul, A. Eddaif, A. Sebban, J. Heterocycl. Chem. 45 (2008) 1023.
5. X.H. Ouyang, H.P. Zeng, Y. Xie, Chin. J. Org. Chem. 27 (2007) 402.
6. A. Mishra, P.K. Nayak, N. Periasamy, Tetrahedron Lett. 45 (2004) 6265.
7. K.G. Daniel, D.J. Kuhn, A. Kazi, Q.P. Dou, Curr. Cancer Drug Targets 5 (2005) 529.
8. Chai B, Qian X, Cao S, Liu H, Song G (2003) ARKIVOC ii:141–145s.
9. Shaker RM (2006) ARKIVOC ix:59–112.
10. Al-Khawas MS, Hazaa BAA, Al-Din AS (1979) Sci Pharm 47:314–320.
11. Kurse LI, Finkelestein JA (1990) Eur Pat App Ep-395, 505 (Cl. C07 D401/60) Chem Abst (1990)113, 115311w.
12. Hullman, JW, Wu MJ, Lu J, *J. Org. Chem*. 1998: 63; 4510.
13. Stillings MR, Welbourn AP, Walter D, *J. Med. Chem*. 1986: 29; 2280.
14. Ibrahim A, Rahman, A.; Abdu, E.; Edity, B. Collect. Czech. *Chem. Commun*. 1991: 56; 1749.
15. Heindel ND, Reid JR. *J Heterocycl Chem*, 1980:17.
16. V. P. Prajapati, J. R. Limbachia, ISST Journal of Applied Chemistry, Vol. 4 No. 2, (JulyDecember 2013), p.p. 25-28
17. K.M. Daoud, A.W. Al-Obaydi, National Journal of Chemistry,2008, Volume 31, 531- 542.
18. K.K. Oza, D.H. Jani, H.S. Patel, Appl. Organomet. Chem. 25 (2011) 154.
19. F. A. Cot t on, G. Wi l ki nson, Advanced Inorganic Chemistry, 5th edn, Wiley Interscience, New York,1988.
20. B. N. Figgis, The magnetochemisty of complxes in modern coordination chemistry, Interscience, New yourk (1960).

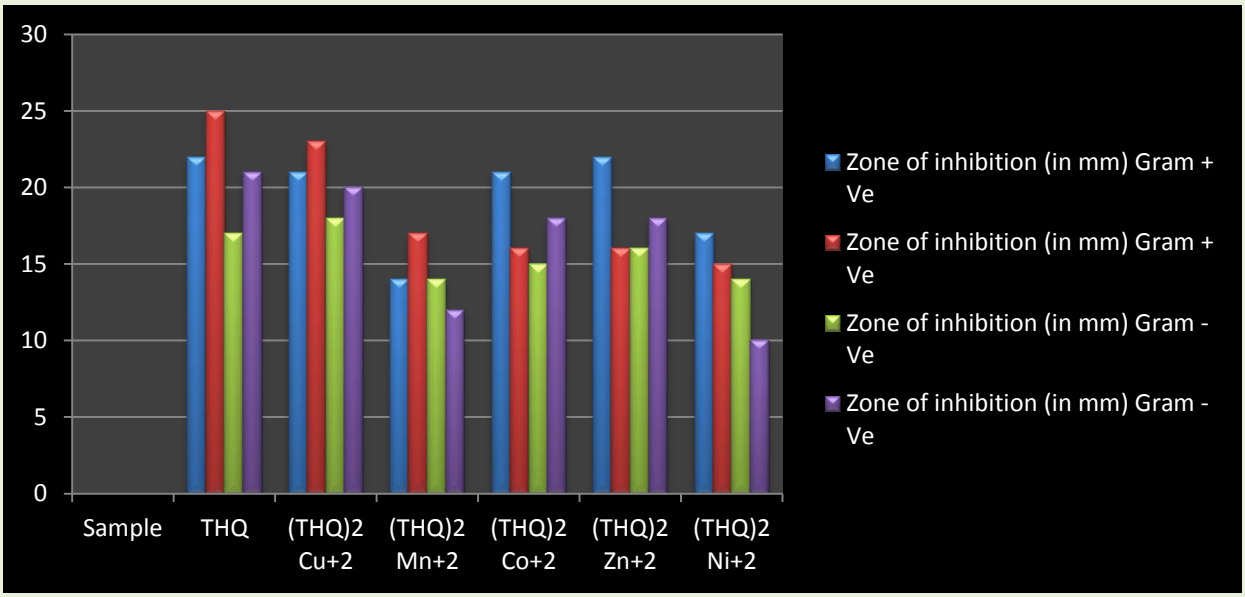
Table 1:Physical and Analytical Data of The Ligand and its Metal Complexes

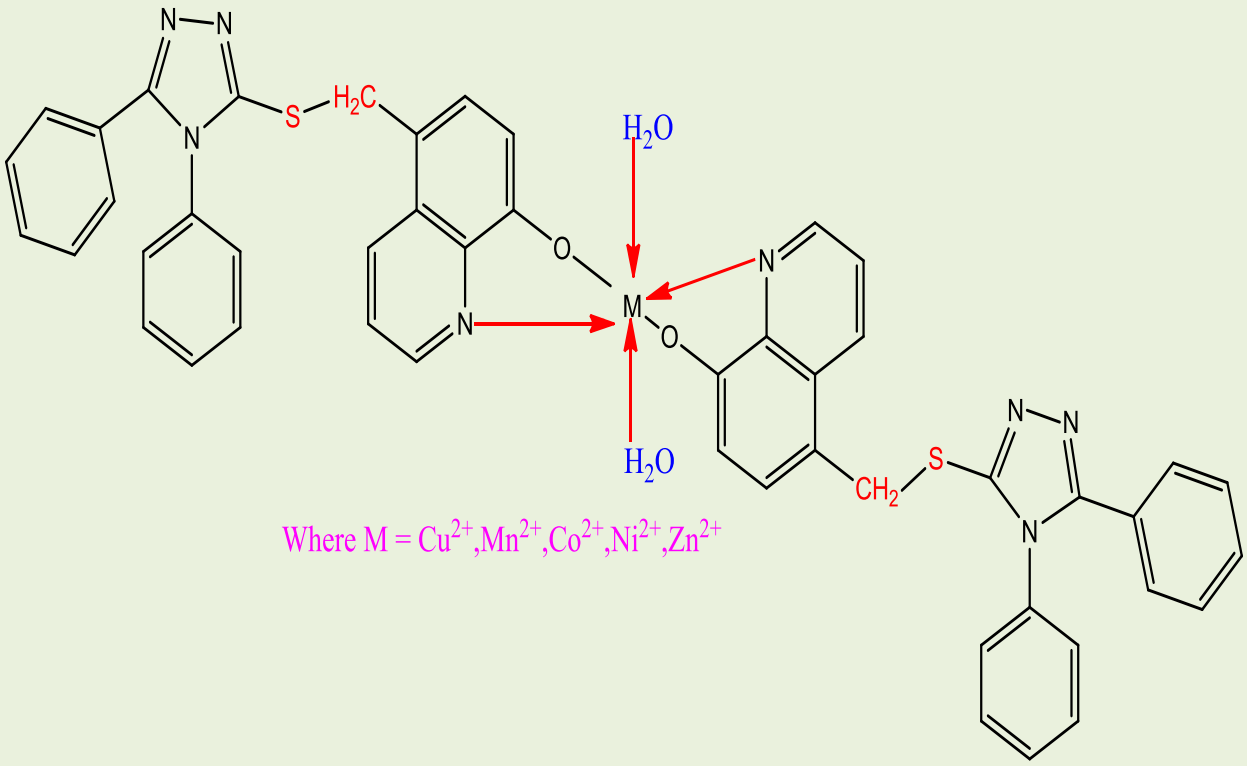
Sr. No.	Empirical Formula	Formula Weight g mol^{-1}	Colour Yield(%)	Melting Point .C	Elemental analysis Found% (Calculate %)				μ^{eff} (B.M.)
					C	H	N	M	
1	$C_{24}H_{18}N_4SO$	410	Green 80%	260-262	67.30 (70.24)	8.87 (70.24)	17.09 (17.08)	–	
2	$CuC_{48}H_{38}N_8S_2O_4$	918.10	Dark Green 75%	>300	60.05 (62.79)	3.95 (3.94)	15.22 (15.21)	6.92 (6.90)	2.1
3	$MnC_{48}H_{38}N_8S_2O_4$	909.49	Brown 70%	>300	60.60 (63.38)	3.96 (3.98)	15.38 (15.36)	6.01 (6.02)	3.8
4	$CoC_{48}H_{38}N_8S_2O_4$	913.49	Dark Brown 72%	>300	60.32 (63.10)	3.94 (3.96)	15.32 (15.29)	6.44 (6.43)	3.2
5	$NiC_{48}H_{38}N_8S_2O_4$	913.25	Green 64%	>300	60.35 (63.12)	3.96 (3.97)	15.31 (15.29)	6.44 (6.43)	5.7
6	$ZnC_{48}H_{38}N_8S_2O_4$	919.94	Yellow 68%	>300	59.91 (62.66)	3.95 (3.94)	15.19 (15.18)	7.09 (7.08)	D

Table 2: Antifungal activity of ligand THQ and their Metal Chelates

Sample	Zone of inhibition at 1000 ppm (%)				
	Penicillium Expansum	*Botrydepladia Thiobromine*	*Nigras Pora Sp.*	*Trichothesium Sp.*	*A. Niger*
THQ	58	67	68	61	60
$(THQ)_2\ Cu^{+2}$	75	88	82	82	80
$(THQ)_2\ Mn^{+2}$	58	58	56	64	54
$(THQ)_2\ Co^{+2}$	64	68	73	70	12
$(THQ)_2\ Zn^{+2}$	72	70	74	82	64
$(THQ)_2\ Ni^{+2}$	60	63	64	75	09

Chart 1: Antibacterial activity of ligands THQ and their Metal Chelates.





SCHEME 1