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Synthesis, Characterization and Comparative Microbial Screening of Some 5-AlkoxyMethyl-8-Quinolinol

Ketan B Patel[1, 2] and Kiran S Nimavat[1]

[1]Government Science College, Department of Chemistry, Gandhinagar, Gujarat, India
[2]Research scholar of JJT University, Rajasthan

ABSTRACT

5-Alkoxymethyl-8-quinolinol compounds have been prepared. Structural, spectroscopic and thermal properties have been studied on the basis of infrared spectra, Mass spectra, NMR spectra, electronic spectra, and elemental analyses. The compounds, control and standard drug were tested for their antimicrobial activity. The compounds exhibit good activity against Bacterial strains Gram +ve and Gram –ve and fungal strains compared with parental compounds and moderate compared with the standard drugs.

Keywords: Oxine, Spectral studies, Magnetic moment and Antimicrobial activity.

Corresponding author

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INTRODUCTION

The antibacterial activity of 8-hydroxyquinoline and its derivatives is long-known. The drugs from this group are used as chemotherapeutics in medicine for more than 120 years [1-4], and in analytical chemistry as chelators [5-6].Some newly synthesized derivatives of 8-Quinolinol were shown to exhibit a higher microbiological activity [7-9].

8-Hydroxyquinoline (8-HQ) moiety has received continuous attention as a platform for the construction of a number of selective and efficient ionophores [10]. The most interesting feature of 8-HQ is its very low quantum yield in aqueous or organic solutions but the fluorescence enhancement occurred from cation binding and many metal chelates of 8-HQ exhibit intense fluorescences[11-12]. Although the selectivity of 8-HQ and its simple derivative is rather poor, it can be improved by appropriate substitution on the phenolic oxygen atom or aromatic rings [13].

Heterocycles containing the quinoline ring constitute a wide variety of biologically active compounds [14]. Clioquinol is an antifungal drug and antiprotozoal drug. It is neurotoxic in large doses. It is a member of a family of drugs called hydroxyquinolines. The drugs have been found to have activity against both viral and protozoal infections [15].

Previously, Kharadi et al. have synthesized a series of 8-hydroxyquinoline derivatives and their transition metal complexes [16-17]. We are also synthesized three compound (methoxy, ethoxy and n-propoxy) [18-19] new derivatives of same series. Hence, in this paper, we report remaining eight compounds of 5-alkoxymethyl-8-hydroxyquinolinols Synthesis, biological aspects and spectroscopic studies.

EXPERIMENTAL

Reagent and solvents

All the chemicals and reagents used for the preparation of compounds were commercial products (E. Merck Ltd, India) and used without further purification. Clioquinol was purchased from Atul Ltd., Agro Chemical Division, Atul, Valsad (India). Luria broth and agar- agar were purchased from SRL, India. The organic solvents were purified by recommended method [20].

Physical measurements

Elemental analysis was carried out using Perkin Elmer, USA 2400-II CHN analyzer. The IR spectra were recorded on a FT-IR Nicolet 400D Spectrophotometer using KBr pellets. NMR spectra were recorded on a model Bruker Avance (400MHz).

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Preparation of compounds

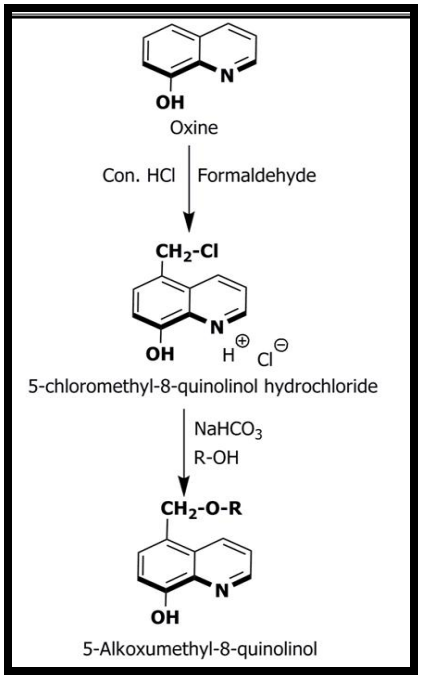
Synthesis of 5-chloromethyl-8-Quinolinol (CMQ)

5-chloromethyl-8-quinolinol (CMQ) was prepared by chloromethylation of 8-hydroxyquinoline (Oxine) according to the method reported in literature[17]. The detail of the procedure is given below.

To a mixture of 7.3 gm. (0.05 mole) of 8-hydroxyquinoline (oxine), 8 ml. Conc. HCl and 8 ml. (0.05 mole) of 37 % formaldehyde dry HCL gas was passed at room temperature, till the yellow crystals fallout (about 2hours). The precipitates were filtered and air dried yield was 77% and m.p 180°c. (Uncorrected) [21].

Synthesis of 5-(Alkoxymethyl-8-Quinolinol)

The reaction of 5-chloromethyl-8-quinolinol (CMQ) with various alcohols has been adopted. The various 5-(alkoxymethyl)-8-hydroxy quinolinols were prepared by neucleophillic substitution reaction of 5-chloromethyl-8- quinolinol (CMQ) with various alcohols. The procedure already repotted in literature [20] for certain alcohol. To a suspension of 2.3 gm. (0.01 mole) of 5-chloromethyl-8-quinolinol (CMQ), alcohol (3 times.) and 0.84 gm. (0.01 mole) of sodium bicarbonate ($NaHCO_3$) added. The mixture was warmed on the steam bath with occasional shaking until most of the alcohol had been evaporated. The pale yellow solid was dissolved in water and made basic with 5 % ammonium hydroxide. The white solid was collected on a filter and dried. The reaction scheme is shown in Fig. 1. % Yield, MP, elemental analysis data and spectral data are tabulated in table. 1.



Antimicrobial studies

Antifungal activity

The antifungal activity of the standard fungicide (Flucanazone) and compounds were tested for their effect on the growth of microbial cultures and studied for their interaction with *Aspergillus niger and Trichothesium Sp.* using Czapek's agarmedium having the composition, glucose 20 g, starch 20 g, agar-agar 20 g and distilled water 1000 ml. To this medium was added requisite amount of the compounds after being dissolved in methanol so as to get the certain concentrations (50, 100 and 200 ppm). The medium then was poured into petri plates and the spores of fungi were placed on the medium with the help of inoculum's needle. These petri plates were wrapped in polythene bags containing a few drops of alcohol and were placed in an incubator at 30 °C. The controls were also run and three replicates were used in each case. The linear growth of the fungus was recorded by measuring the diameter of the fungal colony after 96 h and

The percentage inhibition was calculated by the equation: % Inhibition D (C – T/C) 100

Where C and T are the diameters of the fungal colony in the control and the test plates, respectively [22].

Antibacterial activity

Antibacterial activity was tested against Gram –ve (*Escherichia coli* and *Ps. Aeruginosa, Bacillus subtilis)* and Gram +ve (*Becillus megaterium* and *Staphylococcus aureus*) using the paper disc plate method [23, 24]. Each of the compounds was dissolved in methanol and solutions of the concentrations (500 and 1000 ppm) were prepared separately. Paper discs of Whatman filter paper (No. 42) of uniform diameter (2 cm) were cut and sterilized in an autoclave. The paper discs soaked in the desired concentration of the complex solutions were placed aseptically in the Petri dishes containing nutrient agar media (agar 20 g C beef extract 3g C peptone 5g) seeded with *E. coli* and *B. subtilis* bacteria separately. The Petri dishes were incubated at 37°C and the inhibition zones were recorded after 24 h of incubation. The antibacterial activity of common standard antibiotic Streptomycin was also recorded using the same procedure as above at the same concentrations and solvent. The %Activity Index for the complex was calculated by the formula as under:

% Activity Index = D Zone of inhibition by test compound x 100 /Zone of inhibition by standard

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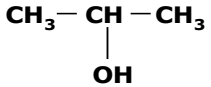
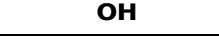
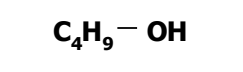
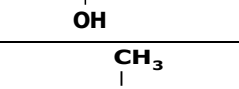
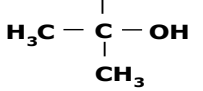
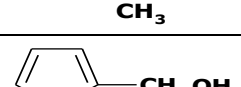
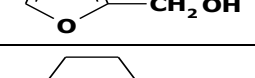
Table 1: Analytical, physical and spectral parameters of compounds:

Compounds	Molecular formula	R-OH	MP ^{0}C uncorrected	M. wt gm/mole	Yield %	Elemental analysis			FT-IR data of Compounds				
						% C	% H	% N	Frequencies Cm^{-1}				
						Found (Cal).	Found (Cal).	Found (Cal).	OH	Aromatic	8-HQ Moiety	C-N	CH_2
HL-4	$C_{13}H_{15}NO_2$		65	217	80	71.68 (71.88)	6.70 (6.91)	6.32 (6.45)	3800-2700	1599 1507 3026	1624,1578, 1507, 1470	1275-1298	2850,2940, 1450
HL-5	$C_{14}H_{17}NO_2$		47	231	75	72.65 (72.72)	7.28 (7.35)	5.93 (6.06)	3810 - 2710	1599 1507 3028	1634,1575, 1698, 1470	1275-1298	2850,2921, 1450
HL-6	$C_{14}H_{17}NO_2$		46	231	70	72.60 (72.72)	7.30 (7.35)	5.90 (6.06)	3800 - 2690	1599 1507 3028	1638,1575, 1698, 1470	1275-1298	2850,2920, 1450
HL-7	$C_{14}H_{17}NO_2$		50	231	67	72.65 (72.72)	7.28 (7.35)	5.95 (6.06)	3800-2600	1599 1507 3028	1638,1575, 1698, 1470	1275-1298	2849,2918, 1450
HL-8	$C_{16}H_{18}NO_2$		80	256	65	74.88 (75.00)	6.93 (7.03)	5.41 (5.46)	3800-2700	1599 1507 3028	1638,1575, 1698	1275-1298	2850,2910, 1450
HL-9	$C_{17}H_{15}NO_2$		82	265	60	76.81 (76.98)	5.54 (5.66)	5.19 (5.28)	3800-2600	1599 1507 3028	1638,1575, 1698	1275-1298	2850,2920, 1450
HL-10	$C_{15}H_{13}NO_3$		79	255	62	70.42 (70.58)	4.98 (5.09)	5.38 (5.49)	3800-2700	1599 1507 3028	1638,1575, 1698	1275-1298	2850,2920, 1450
HL-11	$C_{16}H_{21}NO_3$		83	275	55	69.69 (69.81)	7.55 (7.63)	5.02 (5.09)	3650-2700	1598 1507 3028	1638,1575, 1698	1275-1298	2850,2920, 1450

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RESULTS AND DISCUSSION

The toxic effect of all the compounds on fungi and bacteria are shown in Table 2. The results give the following conclusion. All the compounds are toxic more or less to fungi. The substitution of phenyl rings does not have more effect on the fungicidal activity of compounds.

Table 2: Antimicrobial activity of sample:

Sample	Zone of inhibition (in mm)					
	Antifungal activity		*Gram + Ve*		*Gram -Ve*	
	Trichothesium Sp.	*A. Niger*	*Becillus megaterium*	*S.taphylococcus aureus*	*Ps. Aeruginosa*	*E-Coli*
8HQ	45	52	10	13	12	15
DMSO	15	16	11	10	11	11
HL-4	62	59	21	17	18	21
HL-5	59	60	19	17	19	19
HL-6	67	65	22	21	19	22
HL-7	62	63	19	17	19	19
HL-8	79	80	22	21	19	22
HL-9	57	53	14	19	17	16
HL-10	63	63	17	21	17	11
HL-11	60	80	17	17	11	17

IR spectra

The analytical and physical data of the compounds are presented in Table 1. The compounds are White and stable in air. All the IR spectra comprise the broad band from 3600 to 2600 cm^{-1} with the inflections. The broad band is appeared due to phenolic OH group of 8-hydroxy quinoline moiety. The inflections around 2920 cm^{-1} and 2850 cm^{-1} are attributed to asymmetric and symmetric stretching vibration of -CH_2 of The supporting band at 1450 cm^{-1} is also appeared due to CH_2 bending vibrations. The bands around 1500 and 1600 cm^{-1} in the region of double bond are appeared, that might be raised from aromatic segment of 8-hydroxy quinoline. The weak band around 3030 cm^{-1} might be due to aromatic C-H stretching vibrations. The other bands in the fingerprint region are appeared at their respective position. The bands around 1220 and 1020 cm^{-1} are mainly due to C-N bending vibrations while the C=N stretching vibration features is appeared around 1690 and 1660 cm^{-1}. 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.

CONCLUSION

We have synthesized some 5-(Alkoxymethyl-8-Quinolinol) from parent compound 5-chloromethyl-8-quinolinol. The antimicrobial screening of the synthesized compounds showed moderate to good activity compared with the parent moiety 8-hydroxyquinoline, control (DMSO) and moderately same activity with each others.

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