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Microwave assisted synthesis of of quinolinyl thiazolidinones using Zeolite as an efficient and recyclable activation surface: SAR and Biological activity

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Abstract

*Zéolite 5A° has been used as an efficient and cost effective activating catalyst for the synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones starting from N-aryl-2-chloroquinolin-3-yl-azomethine and thioglycolic acid. The reactions were carried out under microwave irradiation. The catalyst could be recycled and used for several times. This reaction is scalable to multigram scale and the methodology has resulted in an efficient synthesis. Herein benign, environ friendly, efficient and extremely fast procedure for the synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones have been demonstrated. The produced thiazolidinone molecules were characterized on the basis of Elemental analysis, IR, Mass and ^{1}H-NMR. The synthesized moieties were screened for antibacterial activity against certain strains of test bacteria, Viz. Staphylococcus aureus (Gram positive), Pseudomonas vulgaris (Gram positive), Pseudomonas Aeruginosa (Gram negative) and Escherichia coli (Gram negative).Their antibacterial activities are reported (**Table 1**). The screening data suggest that compounds **4b**, **4c** and **4g** are highly active against two strains each of gram positive and gram negative bacteria showing the broadest spectrum of antibacterial activity.*

Keywords: Zeolites, microwave, thioglycolic acid, thiazolidinone, quinoline, catalyst.

INTRODUCTION

The synthesis of quinolines and their derivatives has been of considerable interest because a large number of natural products and drugs contain this heterocyclic moiety [1]. It is well known that quinolines exhibit a wide range of biological activities [2-5] and are valuable reagents for the synthesis of nano and mesostructures with enhanced electronic and photonic properties [6]. Consequently, various procedures such as the Skraup, Doebner-von Miller, and Friedlander and Combes syntheses have been developed for the synthesis of quinoline derivatives [7, 8].

Thiazolidinone and its derivative are known to possess a variety of physiological properties; viz. analgesic, local and spiral anaesthetics, antibacterial [9, 10] , anti inflammatory [11],

antituberculor [12], anticancer, anti HIV [13] and fungicidal [14] activities . In recent years, a large number of innovative drugs containing the thiazolidinone moiety have been developed, including hypoglycemic thiazolidinediones (pioglitazone and its analogs), dual COX-2/5-LOX inhibitors (darbufelon), new generation diuretics (etozolin), etc. [15]. Using modern technologies such as virtual and high-throughput screening, combinatorial chemistry, and molecular modeling, it was established that 4-thiazolidinones possess a high affinity to the PPAR-receptors family and are selective inhibitors of UDP-MurNAc/L-Ala ligase [16-20].

Numerous reports have appeared in the literature, which highlights their chemistry and use. A comprehensive review [21] has been written on thiazolidin-4-ones in 1961. Later, a review article [22] appeared that deals with the use of thiazolidinone derivatives as stabilizers for polymeric materials. Two reviews [23, 24] have been presented; one relates to the preparation of rhodanines (2- thioxothiazolidin-4-ones), and the other describes their uses as intermediates in organic synthesis. In recent years, several new methods for the preparation of thiazolidinone derivatives and reactions have been reported in the literature. However, these reactions suffered from drawbacks such as long reaction times, the use of high boiling solvents, low yields, and use of reactants with high toxicity, which limit their use for the synthesis of complex molecules. Thus a simple, solvent less, cost effective and efficient approach for the synthesis of functionalized 4-thiazolidinone is our interest.

Combination of the mineral supported and microwave irradiation has been used to carry out a wide range of reactions under solvent-free conditions [25]. Synthesis of organic compounds under solvent free conditions, especially adopted to microwave irradiation, leads to increased safety and environmental aspects [26]. For this purpose heterogeneous catalysis plays a fundamental role, mainly due to its economic and environmental advantages (i.e. minimum execution time, low corrosion, waste minimization, recycling of the catalyst, easy transport and disposal of catalysts) [27] . Another important goal in green chemistry is represented by the elimination of volatile organic solvents; in fact solvent-free organic reactions make synthesis simpler, save energy, and prevent solvent wastes, hazards, and toxicity. Of course the combination of heterogeneous catalysis with the use of solvent less conditions under microwaves represents a suitable way towards the so-called ideal synthesis. In conventional methodology the yield is sometimes lower than microwave protocols. Microwave irradiation facilitates the polarization of the molecule under irradiation causing rapid reaction to occur increase yield and so called atom economy.

Thus, to eliminate all the discussed drawbacks, an efficient and extremely fast procedure for the synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones **4(a-i)** by the reaction of N-aryl-2-chloroquinolin-3-yl-azomethine and thioglycolic acid in the presence of Zeolite 5A˚ as an activator under microwave irradiation has been demonstrated. A considerable increase in the reaction rate has been observed with better yield in microwave technique.

MATERIALS AND METHODS

Experimental

All reagents, solvents and catalyst are analytical grade from a commercial source and used directly. All the melting points were determined in open capillaries and are uncorrected. The purity of compounds was checked routinely by TLC (0.5mm thickness) using silica gel-G coated Al-plates (Merck) and spots were visualized by exposing the dry plates in iodine vapours. IR spectra (υ_{max} in cm^{-1}) were recorded on a Shimadzu FT-IR 8300 spectrophotometer using KBr technique; ^{1}H-NMR spectra on a Bruker Avance 400MHz NMR instrument using DMSO-*d*6 as

solvent and TMS as internal reference (chemical shifts in δ, ppm) and Mass spectra on a Jeol JMS D-300 spectrometer operating at 75 eV. The elemental analysis (C, H, N, and S) of compounds was performed on Carlo Erba-1108 elemental analyzer. The results were found to be in good agreement with the calculated values. Elemental analyses were carried out using a Perkin-Elmer; CHN elemental analyzer model 2400. The MW assisted synthesis of titled compounds was carried out in a CEM – 908010, bench mate model, 300 watts laboratory MW reactor. Before each reaction, same zeolite 5A° was dried at 120°c and reutilized.

Microwave mediated general synthesis of N-aryl-2-chloroquinolin-3-yl-azomethine.

N-aryl-2-chloroquinolin-3-yl-azomethine was obtained by the condensation of 2-chloroquinoline-3-carbaldehyde and aromatic amines. In a typical solvent less preparation, mixture of 2-chloroquinoline-3-carbaldehyde (**1**) (7.86 mmol) and aniline (7.28 mmol) without solvent were taken in a flask capped with funnel placed in a microwave oven and irradiated at 200 watt for 20 secs. Reaction was monitored by TLC. After completion of the reaction, the resultant mixture was allowed to attain the room temperature. After cooling, the resultant solid was crushed, washed with cold ethanol, filtered and dried under vacuum to give the crude Product. The crude product was recrystallized from methanol. Same method was followed for the production of other quinoline-imines.

Yield: 95%. M.P.171°C. Anal. Calc. For: $C_{16}H_{11}ClN_2$, C, 72.03; H, 4.14; N, 10.10 %. Found: C, 72.04; H, 4.18; N, 9.69 %. IR (cm^{-1}, KBr): 1620 (-C=N), 1683 (-C=O). ^{1}H-NMR (ppm, $CDCl_3$-d_6): 9.6 (s, 1H, -CH=N), 7.7-8.2 (m, 10H). MS (m/z) 266.6 (100%), 268.3 (32%).

Microwave mediated zeolite catalyzed general synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones 4(a-i):

A mixture of N-aryl-2-chloroquinolin-3-yl-azomethine **(3)** (3.93 mmol), $SHCH_2COOH$ (thioaceticacid) (3.63 mmol) and zeolite 5A° (0.10 g) was taken in a conical flask capped with a funnel placed in a microwave oven and irradiated (400W) for 30-60 secs. The reaction was monitored by TLC. After completion of reaction, the pasty solid obtained was allowed to cool. To that, 15 ml acetone was added and stirred for five minutes up to the dissolution of pasty solid. The zeolite was filtered out of the mother liquor for the other reaction. The mother liquor was poured into the crushed ice and the pH of the solution was set to 10 by 10% $NaHCO_3$ solution. Reaction mass was then stirred, filtered and washed with cold water. The crude product was recrystallized from methanol. Same process was used for the production of other thiazolidinones.

Yield: 92%. M.P.200°C. IR (cm^{-1}, KBr): 1672 (-C=O), 754, (C-S-C), 1619 (C=N, str, quinoline moiety), 775 (C-Cl) . ^{1}H-NMR (ppm, DMSO-d_6): 4.59 (s, 2H, $-CH_2$-thiazolidinone), 5.50 (s, 1H, -S-CH), 7.3-8.4(m, 10H). MS (m/z) 354.6 (100%), 356.3 (37%) Anal. Calc. For: $C_{19}H_{15}ClN_2OS$, C, 64.31; H, 4.26; N, 7.89; S, 9.04 %. Found: C, 64.34; H, 4.28; N, 7.90; S, 9.08 %.

2-(2-chloroquinoline-3-yl)-3- phenyl thiazolidin-4-ones 4(a).

Yield: 94%. M.P. 200°C. IR (cm^{-1}, KBr): 1672 (-C=O), 754, (C-S-C), 1619 (C=N, str, quinoline moiety), 775 (C-Cl) . ^{1}H-NMR (ppm, DMSO-d_6): 4.59 (s, 2H, $-CH_2$-thiazolidinone), 5.50 (s, 1H, -S-CH), 7.3-8.4(m, 10H). MS (m/z) 354.6 (100%), 356.3 (37%). Anal. Calc. For: $C_{19}H_{15}ClN_2OS$, C, 64.31; H, 4.26; N, 7.89; S, 9.04 %. Found: C, 64.34; H, 4.28; N, 7.90; S, 9.08 %.

3-(2-chlorophenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(b).

Yield: 95%. M.P.215°C. IR (cm^{-1}, KBr): 1676 (-C=O), 754, (C-S-C), 1619 (C=N, str, quinoline moiety), 787 (C-Cl). ^{1}H-NMR (ppm, DMSO-d_6): 4.56 (s, 2H, $-CH_2$-thiazolidinone), 5.51 (s, 1H, -S-CH), 7.3-8.4(m, 9H). MS (m/z) 388.2 (100%), 390.5 (69%). Anal. Calc. For: $C_{19}H_{14}Cl_2N_2OS$, C, 58.62; H, 3.63; N, 7.22; S, 8.24 %. Found: C, 58.65; H, 3.67; N, 7.26; S, 8.27 %.

3-(4-chlorophenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(c)
.Yield: 89%. M.P.225˚C. IR (cm^{-1}, KBr): 1680 (-C=O), 754, (C-S-C), 1617 (C=N, str, quinoline moiety), 788 (C-Cl). ^{1}H-NMR (ppm, DMSO-d_6): 4.57 (s, 2H, −CH_2-thiazolidinone), 5.56 (s, 1H, -S-CH), 7.3-8.4(m, 9H). MS (m/z) 388.4 (100%), 390.3 (69%). Anal. Calc. For: $C_{19}H_{14}Cl_2N_2OS$, C, 58.64; H, 3.65; N, 7.25; S, 8.23 %. Found: C, 58.66; H, 3.68; N, 7.28; S, 8.25 %.

3-(2-methoxyphenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(d).
Yield: 96%. M.P.218˚C. IR (cm^{-1}, KBr): 1688 (-C=O), 745 (C-S-C), 1619 (C=N, str, quinoline moiety), 1158 (-OCH_3), 785 (C-Cl), . ^{1}H-NMR (ppm, DMSO-d_6): 4.53 (s, 2H, −CH_2-thiazolidinone), 5.56 (s, 1H, -S-CH), 3.84 (s, 3H, -OCH_3) ,6.9-8.2(m, 9H). MS (m/z) 384.0 (100%), 386.1 (37%). Anal. Calc. For: $C_{20}H_{17}ClN_2O_2S$, C, 62.42; H, 4.43; N, 7.26; S, 8.32 %. Found: C, 62.45; H, 4.46; N, 7.28; S, 8.36 %.

3-(3,4-dimethoxyphenyl)-2-(2-chloroquinolin-3-yl)thiazolidine-4-one 4(e).
Yield: 92%. M.P.228˚C. IR (cm^{-1}, KBr): 1682 (-C=O), 740 (C-S-C), 1619 (C=N, str, quinoline moiety), 1153 (-OCH_3), 785 (C-Cl), . ^{1}H-NMR (ppm, DMSO-d_6): 4.56 (s, 2H, −CH_2-thiazolidinone), 5.58 (s, 1H, -S-CH), 3.97 (s, 6H,-OCH_3) ,7.2-8.2(m, 8H). MS (m/z) 414.8 (100%), 416.1 (37%). Anal. Calc. For: $C_{21}H_{19}ClN_2O_3S$, C, 60.74; H, 4.63; N, 6.75; S, 7.73 %. Found: C, 60.74; H, 4.67; N, 6.78; S, 7.75 %.

3-(2-hydroxyphenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(f).
Yield: 93%. M.P.146˚C. IR (cm^{-1}, KBr): 1685 (-C=O), 741 (C-S-C), 1619 (C=N, str, quinoline moiety), 3202 (-OH), 785 (C-Cl), . ^{1}H-NMR (ppm, DMSO-d_6): 4.56 (s, 2H, −CH_2-thiazolidinone), 5.58 (s, 1H, -S-CH), 10.08 (s, 1H, -OH), 7.4-8.2(m, 9H). MS (m/z) 370.1 (100%), 372.7 (36%). Anal. Calc. For: $C_{19}H_{15}ClN_2O_2S$, C, 61.52; H, 4.08; N, 7.56; S, 8.62 %. Found: C, 61.55; H, 4.10; N, 7.58; S, 8.66 %.

3-(4-hydroxyphenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(g).
Yield: 92%. M.P.123˚C. IR (cm^{-1}, KBr): 1686 (-C=O), 742 (C-S-C), 1620 (C=N, str, quinoline moiety), 3202 (-OH), 785 (C-Cl). ^{1}H-NMR (ppm, DMSO-d_6): 4.55 (s, 2H, −CH_2-thiazolidinone), 5.59 (s, 1H, -S-CH), 9.08 (s, 1H, -OH) ,7.6-8.2(m, 9H). MS (m/z) 370.3 (100%), 372.6 (36%). Anal. Calc. For: $C_{19}H_{15}ClN_2O_2S$, C, 61.54; H, 4.06; N, 7.58; S, 8.63 %. Found: C, 61.58; H, 4.09; N, 7.59; S, 8.64 %.

3-(2-nitrophenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(h).
Yield: 94%. M.P.225˚C. IR (cm^{-1}, KBr): 1685 (-C=O), 740 (C-S-C), 1619 (C=N, str, quinoline moiety), 1589 (-NO_2), 785 (C-Cl), . ^{1}H-NMR (ppm, DMSO-d_6): 4.56 (s, 2H, −CH_2-thiazolidinone), 5.58 (s, 1H, -S-CH), 7.8-8.2(m, 9H). MS (m/z) 399.4 (100%), 401.2 (36%). Anal. Calc. For: $C_{19}H_{14}ClN_3O_3S$, C, 57.01; H, 3.54; N, 10.51; S, 8.06 %. Found: C, 57.04; H, 3.66; N, 10.53; S, 8.08 %.

3-(4-nitrophenyl)-2-(2-chloroquinolin-3-yl) thiazolidine-4-one 4(i).
Yield: 94%. M.P.245˚C. IR (cm^{-1}, KBr): 1685 (-C=O), 745 (C-S-C), 1618 (C=N, str, quinoline moiety), 1588 (-NO_2), 787 (C-Cl), . ^{1}H-NMR (ppm, DMSO-d_6): 4.55 (s, 2H, −CH_2-thiazolidinone), 5.56 (s, 1H, -S-CH), 7.8-8.2(m, 9H). MS (m/z) 399.2 (100%), 401.4 (36%). Anal. Calc. For: $C_{19}H_{14}ClN_3O_3S$, C, 57.03; H, 3.52; N, 10.52; S, 8.04 %. Found: C, 57.05; H, 3.65; N, 10.57; S, 8.06 %.

Antibacterial activity

The agar cup plate method using Hi-Media agar medium was employed to study the antibacterial activity of **4(a-i)** against *S. aureus*, *P. vulgaris*, *P. aeruginosa* and *E. coli* . Preparation of nutrient broth, subculture, base layer medium, agar medium and peptone water was done as per the standard procedure. Each test compound (50 mg) was dissolved in dimethylformamide (50 ml, 1000 µg/ml), which was used as sample solution. Sample size for all the compounds was fixed at 0.1 ml. Using a sterilized cork borer, cups were scooped out of agar medium contained in a petri dish which was previously inoculated with the microorganisms. The test compound solution (0.1 ml) was added in the cups and the petri dishes were subsequently incubated at 37 °C for 48 h. Ampicillin and Streptomycin were used as reference drugs and dimethylformamide as a negative control. Zones of inhibition produced by each compound were measured in mm, and the results are listed in **Table 1**.

Table 1: Antibacterial activity of compounds 4(a-i)

Comp.	Gram positive bacteria		Gram negative bacteria	
	S.aureus	*P.vulgaris*	*E.coli*	*P.aeruginosa*
4a	+ + +	+ +	-	-
4b	+ + +	+ +	+ + +	+ + +
4c	+ +	+ +	+ +	-
4d	+ +	-	-	+
4e	+ + +	-	+ +	+ +
4f	+ + +	+ + +	+ + +	+ + +
4g	+ +	+	+ +	+ +
4h	+ +	-	-	+
4i	+ +	-	-	+
Ampicillin	+ + +	+ +	+ +	+ + +
Streptomycin	+ + +	+ + +	+ + +	+ + +

Key to symbols: Inactive = - (inhibition zone < 5 mm); Slightly active = + (inhibition zone 5-10 mm); Moderately active = + + (inhibition zone 10-15 mm); Highly active = + + + (inhibition zone > 15 mm).

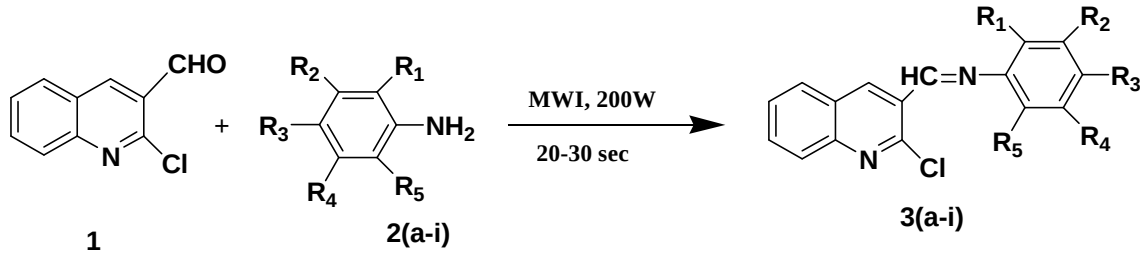
RESULTS AND DISCUSSION

Recently, there has been a growing interest in the use of inorganic solid acids in organic synthesis [26, 28]. Solid acids, compared to liquid acids, have many advantages such as simplicity in handling and environmental protection [29]. Among the reported solid acids, Zeolites have attracted an increasing attention because of their availability, suitable acidity and thermal stability. The use of zeolites also reveals some features such as reduction in the thermal degradation, better selectivity and easy work-up after reaction. Zeolite 5A˚ is an aluminosilicate zeolite mineral belonging to the pentasil family of zeolites. Its chemical formula is $Na_nAl_nSi_{96-n}O_{192}$•$16H_2O$ ($0<n<27$). Zeolite-5A˚ has high silicon to aluminum ratio. The high silica content yields high chemical resistance. It is stable until 500–600˚C. It can absorb small molecules such as water, hydrochloric acid, ammonia, methanol, or hydrogen sulfide. It has several advantages, including being environmentally friendly, nontoxic, inexpensive, recoverable, and reusable.

Therefore we decided to explore its suitability in heterocyclization reaction. Our synthetic approach is very clear. First, Schiff's bases N-aryl-2-chloroquinolin-3-yl-azomethine prepared from the reaction of 2-chloroquinoline-3-carbaldehyde and different aromatic amines using a

reported method by MORE technique [30] as shown in **Scheme 1.** Finally, quinoline- imines on heterocyclization with thioglycolic acid using zeolite 5A˚ under microwaves afforded 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones as shown in **Scheme 2**.

Scheme 1. Synthesis of N-aryl-2-chloroquinolin-3-yl-azomethine 3(a-i).



1 2(a-i) 3(a-i)

Scheme 2. Synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones 4(a-i).

3(a-i) 4(a-i)

	R_1	R_2	R_3	R_4	R_5
2a,3a,4a	-H	-H	-H	-H	-H
2b,3b,4b	-Cl	-H	-H	-H	-H
2c,3c,4c	-H	-H	-Cl	-H	-H
2d,3d,4d	$-OCH_3$	-H	-H	-H	-H
2e,3e,4e	-H	$-OCH_3$	$-OCH_3$	-H	-H
2f,3f,4f	-OH	-H	-H	-H	-H
2g,3g,4g	-H	-H	-OH	-H	-H
2h,3h,4h	$-NO_2$	-H	-H	-H	-H
2i,3i,4i	-H	-H	$-NO_2$	-H	-H

In all experiments a molar ratio 1:1 of two starting materials, i.e. quinoline- imines, thioglycolic acid and Zeolite 5A˚ (0.100 g) was irradiated under microwave irradiation. After each reaction the catalyst was recycled and used for the next reactions without any activity loss. The method is very easy and can be used for synthesis of different thiazolidinones **4(a-i)** depending on different substituted groups. The most important and salient feature of the present reaction is the recyclability of the catalyst and the scaleability of the reaction. It was observed that the catalyst could be reused at least seven times. Use of the recycled catalyst in the reaction had no effect either on the yield of the product or the quality of the product. Moreover no side products were observed in these reactions. Furthermore, the reaction can be scaled up to a multigram scale.

Structural features of the synthesized azomethine and thiazolidinones were obtained from FTIR, ELEMENTAL Analyses, ^{1}H-NMR and Mass spectral studies. In the IR spectra of the N–((2-chloroquinolin-3-yl) methylene) substituted phenyl, the characteristic absorption around 1620 cm^{-1} is assigned to (-C=N) azomethine linkages which are absent in the spectra of the thiazolidinones confirmed the heterocyclization. The ^{1}H-NMR spectrum of the N–((2-chloroquinolin-3-yl) methylene) benzamine in DMSO-d_6 at room temperature using TMS as an internal standard showed the following signals: -CH=N- around 9.6 ppm (s, 1H) and aromatic protons as multiplet around 7.7-8.2 ppm (m, 10H). One singlet around 5.5 ppm which account for one methylene protons on the S-C-H in the spectra of quinoline thiazolidinones, confirmed the cyclization.

Structure Activity Relationship

A perusal of antibacterial screening data indicates that all the compounds under investigation were moderately active to the test bacteria. The structure of synthesized thiazolidinones **4(a-i)** for ease of analysis can be divided into into three parts, Viz., thiazolidinones skeleton, quinoline side chain at C-2 of thiazolidinone skeleton, and substituted phenyl ring at N-1 of thiazolidinone skeleton. We have fixed the former two parts and varied the latter one by attaching the phenyl ring with several functional groups such as 2-NO_2, 3-NO_2, 4-OMe, 3, 4-di-OMe, 2-OH, 4-OH and 2-Cl. These modifications in the thiazolidinone skeleton followed by the analysis of resulting molecules, structure have resulted in the following findings:

The unsubstituted phenyl ring at N-1 is non effective against gram negative strains and moderately effective against gram positive ones in compound **4a**. The introduction of halogen group on the N-1 phenyl ring shows good result in case of **4b** and **4c**. The introduction of electron withdrawing substituent like nitro at position 2 and 3 on the N-1 phenyl ring masked the potency in case of compounds **4h** and **4i** as compared with **4a**.

On the other hand, compounds **4f** and **4g** had an activity quite comparable to the commercial antibiotics (Ampicillin and Streptomycin) tested under similar conditions. This activity was probably due to the presence of a strong polar substituent -OH at position 2 of the phenyl ring on the thiazolidinone moiety as compared to the similar substitution at position 4 in compound **4f** which has shown moderate activity. In both the cases the oxygen can act as a hydrogen bond acceptor and the hydrogen can act as a hydrogen bond donor. One or all of these interactions may be important in binding the molecules to the binding site. Thus in both the cases, the hydroxyl group may be involved in some H-bonding, which increases the affinity of the molecule for the active site of the enzyme. So 2-OH is necessary for high activity of the compound **4g**. Conversion of OH to methyl ether or substitution of 4-OMe on the ring has reduced the activity as compared to Compound **4g**. However, substituted 3, 4-di-OMe has shown some moderate activity.

Further investigation of compound **4g** on a wider range of bacteria as well as with higher dilution is desirable. As far as molecular masses of **4g** is concerned, the compound have mass around 370 Dalton. Optimizing compounds for high activity on a biological target almost often goes along with increased molecular weights. However, compounds with higher weights are less likely to be absorbed and therefore to ever reach the place of action and less active. Although an attempt was made to combine various groups in these molecules with the hope of achieving compounds of better potency, the results are not very encouraging in all the cases, except compounds **4f** and **4g**.

CONCLUSION

In conclusion, we have developed à zeolite-catalyzed, simple, solvent-free, cost effective, and environmentally benign technique for the synthesis of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones. This reaction is scalable to multigram scale. These compounds have been synthesized in high yield by using zeolite 5A˚ and avoiding the use of any solvent under microwaves. In addition the catalyst can be recovered by filtration, drying and utilized at least seven times without lowering its activity. The results of present biological investigation suggested antibacterial activity of 2-(2-chloroquinoline-3-yl)-3-substituted phenyl thiazolidin-4-ones. It has been suggested that some functional groups present in these compounds displayed moderate to good biological activity, compounds **4b**, **4c**, **4g** are found to be most active.

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