Ecofriendly synthesis of 2-phenyl-4-quinolone derivatives using K10 clay catalyst and their antibacterial activity.

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ABSTRACT:

As an alternative reagent to various traditional dehydrogenating reagents K10 clay is stable, non-hazardous, acidic and has been successfully used for dehydrogenation reactions\(^{1-3}\). Herein we report a new and ecofriendly route for synthesis of 2-phenyl-4-quinolone using K10 clay.

A series of 2,3-dihydro-2-phenyl-quinolones \(^{1-3}\) has been synthesized using acid-catalyzed one-pot reaction quinolones were formed by heating of arylamines and ethyl benzolacetate in toluene. Similarly, the 6 (7 or 8)-substituted 2,3-dihydro-2-phenyl-quinolones were prepared from the para (ortho or meta)-substituted aniline.

KEYWORDS:

2,3-dihydro-2-phenyl-quinolones, 2-phenyl-4-quinolone, K10 clay.

INTRODUCTION:

Quinolones\(^4\) are analogues of flavanones and thiaflavanones which are characterized by a fused benzoring and phenyl substituent.

Quinolones are broad-spectrum antibiotics that play an important role in treatment of serious bacterial infections, especially hospital-acquired infections and others in which resistance to older antibacterial classes is suspected.

Quinolones are bactericidal agents that target the bacterial DNA gyrase enzyme. Many quinolones have pharmacody-namic properties that result in high intracellular concentrations in host inflammatory cells.

INTRODUCTION TO CLAYS IN CHEMISTRY:

In the most general sense, clays are a type of fine-grained earth, primarily composed of aluminum and silicate minerals. Montmorillonite clays\(^{1-3}\) are thought to have formed from volcanic ash during the Jurassic and later periods, and were named for the location of their discovery, Montmorillon, France, in the 1800s. These clays are now mined in regions all over the world, including Europe, Africa, Asia, South and North America, with U.S. mines in Florida, Georgia, Illinois and Texas. Montmorillonite clays have a wide variety of uses and have recently been found to have the ability to catalyze a wide range of chemical reactions. A catalyst is a chemical species that induces a chemical reaction to occur at a reasonable rate, without itself being consumed in the process; the catalyst\(^{1-3}\)can typically be recovered and reused. Development of naturally benign substances like clays as catalysts for chemical reactions constitutes an exciting breakthrough in Green Chemistry and promises to reduce the amount of hazardous waste associated with the synthesis of new drug compounds\(^4\).
RESULT AND DISCUSSION:

A series of novel substituted 2,3-dihydro-2-phenyl-4-quinolones were prepared by cyclisation of substituted 1-(2’aminophenyl)-3-phenyl-2-propene-1-one by using ZnCl₂. Substituted 2,3-dihydro-2-phenyl-4-quinolones were dehydrogenated using K10 clay Table No. 1

PHYSICAL PARAMETERS AND ELEMENTAL ANALYSIS OF 2,3DIHYDRO 2-PHENYL 4-QUINOLONES

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Compound</th>
<th>M.P. (⁰C)</th>
<th>Mol. Weight</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2-phenyl-8-chloro-4-quinolone</td>
<td>242</td>
<td>258</td>
<td>87</td>
</tr>
<tr>
<td>2.</td>
<td>2-phenyl-8-bromo-4-quinolone</td>
<td>245</td>
<td>303</td>
<td>82</td>
</tr>
<tr>
<td>3.</td>
<td>2-phenyl-8-iodo-4-quinolone</td>
<td>248</td>
<td>350</td>
<td>80</td>
</tr>
<tr>
<td>4.</td>
<td>2-phenyl-8-fluoro-4-quinolone</td>
<td>251</td>
<td>242</td>
<td>70</td>
</tr>
<tr>
<td>5.</td>
<td>2-phenyl-6,8-chloro-4-quinolone</td>
<td>232</td>
<td>293</td>
<td>86</td>
</tr>
<tr>
<td>6.</td>
<td>2-phenyl-6,8-bromo-4-quinolone</td>
<td>258</td>
<td>381</td>
<td>82</td>
</tr>
<tr>
<td>7.</td>
<td>2-phenyl-6,8-iodo-4-quinolone</td>
<td>230</td>
<td>475</td>
<td>72</td>
</tr>
<tr>
<td>8.</td>
<td>2-(4’chlorophenyl)-6,8-dichloro-4-quinolone</td>
<td>240</td>
<td>292</td>
<td>84</td>
</tr>
<tr>
<td>9.</td>
<td>2-(4’methoxyphenyl)-6,8-dichloro-4-quinolone</td>
<td>255</td>
<td>288</td>
<td>72</td>
</tr>
<tr>
<td>10.</td>
<td>2-(4’methoxyphenyl)-6,8-dichloro-4-quinolone</td>
<td>245</td>
<td>292</td>
<td>70</td>
</tr>
</tbody>
</table>

EXPERIMENTAL:

All the chemicals used were of S.D. Fine chemicals. All the solvent used were distilled previously. Clay was purchased from Aldrich chemicals.

Melting points were measured in open glass capillaries on a Perfit Electro-thermal melting-point apparatus and are uncorrected. ¹H NMR spectra were recorded at room temperature on a 300 MHz. Varian Inova Spectrometer in CDCl₃ using TMS as internal standard level for all the experiments. The reactions were monitored by TLC using pre-coated plates (Merck).
Preparation of 2,3-dihydro-2-phenyl-4-quinolone:

A solution of substituted 1-(2’aminophenyl)-3-phenyl-2-propene-1-one (3.0 m moles) and Zinc chloride (1 M in Et₂O, 3.3 m mole) in CH₃CN (12 ml) was heated to 80°C for (24 hrs) after evaporation of CH₃CN the mixture was poured into saturated solution of NH₄Cl (30 ml) and extracted with methylene chloride (3 x 20 ml).

GENERAL PROCEDURE:

Dehydrogenation of 2,3-dihydro-2-phenyl-4-quinolone to 2-phenyl-4-quinolone :

To compound 5 (2 m.mole) was added a solution of K-10 clay and dry benzene (0.1 m mol)at room temperature. The mixture was heated to 60°C for 16 hrs. After evaporation of CH₃OH, 0.05 N HCl (50 ml) was slowly added to the mixture at 0°C. The resulting precipitate was separated by filtration washed with H₂O and re-crystallized by CH₃OH.

SPECTRAL ANALYSIS:

The structures of the products were confirmed from NMR, IR and LCMS. The representative spectral analysis for few of the products is given below. The observed values are in accordance with the literature values.

**Compound – I**

PMR : 4.0 (1H,s), 7.21(5H,m), 4.44(1H,t), 3.07 (2H,d), 7.55 (1H,d), 6.60 (1H,dd), 7.23 (1H,d).

IR : 3432 (NH), 3068, 2960, 1630 (C=O, C=C), 1580, 1546, 1504, 1470, 1452, 1432, 1256, 1140, 770 cm.

**Compound – II**

PMR : 4.0 (1H,s), 7.18 (5H,m), 4.40 (1H,t), 3.02 (2H,d) 7.61 (1H,d)6.55 (1H,dd) 7.39 (1H,d).

IR: 3430 (NH), 3068, 2960, 1630 (C=O, C=C), 1580, 1546, 1500, 1470, 1452, 1432, 1142, 768 cm.
Compounds III, IV, and V were characterized by proton NMR (PMR) and infrared (IR) spectroscopy. The PMR spectra showed the following resonances:

**Compound III PMR**: 4.02 (1H, s), 7.20 (5H, m), 4.42 (1H, t), 3.04 (2H, d), 7.66 (1H, d), 6.43 (1H, dd), 7.60 (1H, d). **IR**: 3436 (NH), 3065, 2963, 1628 (C=O, C=C), 1578, 1540, 1502, 1474, 1455, 1432, 1250, 1140, 766 cm.  

**Compound IV PMR**: 4.04 (1H, s), 7.16 (5H, m), 4.40 (1H, t), 3.05 (2H, d), 7.39 (1H, d), 6.66 (1H, dd), 6.98 (1H, d). **IR**: 3436 (NH), 3068, 2966, 1636 (C=O, C=C), 1588, 1548, 1508, 1478, 1458, 1436 1255, 1140, 772 cm.  

**Compound V PMR**: 4.02 (1H, s), 7.12 (5H, m), 4.40 (1H, t), 3.06 (2H, d), 7.52 (1H, s), 7.20 (1H, s). **IR**: 3436 (NH), 3068 2960, 1630 (C=O, C=C), 1588, 1548, 1506, 1470, 1448, 1436, 1258, 772 cm.

**Antibacterial Activity of 2-Phenyl quinolone**:  
Literature survey reveals that number of 2-phenyl quinolone derivatives are significant due to their anti-bacterial5, anti-fungal6, antitumor7, anti-convulsants8, anti-oxidant9, neuro-protectives10, insecticides11-12 actives.  

The synthesized compound were screened in vitro for their antibacterial activity against gram positive (Staphylococcus aureus) and gram negative (Escherichia coli and Salmonella typhi) bacteria.

**Experimental**:  
The antibacterial activities of 2-phenyl quinolone were studied by the usual cup-plate-agar-diffusion method13-14. The compounds were screened for their antibacterial activity against Gram-negative (E-coli and S-typhi) and Gram-positive (S-aureus) bacteria.  

The following steps involves in cup-plate-agar-diffusion method.  

a) Preparation of media, sterilization, and tubing.  
b) Sterilization of the cleaned glass apparatus.  
c) Pouring of the seeded medium into sterilized petri-dishes.  
d) Pouring of the dilute solution of the compound into tubes.  
e) Incubation at a particular temperature.  
f) Determination of the zones of inhibition.  

In addition to the composition of the test media, its pH is a factor which may directly or indirectly influence the activity of a drug. The pH of the test media taken for S-aureus and E-coli was adjusted in the range 7.6 ± 0.1. The composition of the basal media used in the experiments was
(i) sodium chloride = 6.0 gm, (ii) peptone = 10.0 gm, (iii) beef extract = 3.0 gm, (iv) yeast extract = 2.0 gm, (v) sucrose = 1.5 gm, (vi) agar-agar = 3.0%, and (vii) distilled water = 1.0 liter.

Procedure:

The test sample solution of particular dilution (1 mg/mL in DMSO) was introduced. The plates were incubated immediately at 27 cm for 20 hours. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Growth inhibition was compared with standard drug. Separate studies were carried out with the solutions alone of DMSO and they showed no activity against any bacterial strains. Growth inhibition was compared with the standard Ampicillin trihydrate as antibacterial agent.

Result and Discussion:

A number of authors were interested to investigate the biological and medicinal properties of 2-phenyl quinolone inhibit enzyme production.  

Antibacterial Activity of 2-phenyl quinolone

<table>
<thead>
<tr>
<th>Sample</th>
<th>Zone of inhibition in mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
</tr>
<tr>
<td>Compound</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>12</td>
</tr>
<tr>
<td>II</td>
<td>1</td>
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<tr>
<td>III</td>
<td>17</td>
</tr>
<tr>
<td>IV</td>
<td>15</td>
</tr>
<tr>
<td>Std. drug</td>
<td>30</td>
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</table>
REFERENCES:


