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# A NOVEL ROUTE FOR SYNTHESIS OF 2-PHENYL-4-QUINOLONE DERIVATIVES USING DIACETOXY IODOBENZENE AND THEIR ANTIBACTERIAL ACTIVITY

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## ABSTRACT

As an alternative reagent to various traditional dehydrogenating reagents Diacetoxy iodo benzene is stable, non-hazardous, acidic and has been successfully used for dehydrogenation reactions.[1] Herein we report a new and ecofriendly route for synthesis of 2-phenyl-4-quinolone using diacetoxy iodo benzene and potassium hydroxide.[2] A series of 2,3-dihydro-2-phenyl-quinolones[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, DIB.

## INTRODUCTION

Quinolones4 are analogues of flavanones and thiaflavanones which are characterized by a fused benzoring and phenyl substituent.

Quinolones are broad-spectrum antibioties that play an important role in treatment of serious bacterial infectons, 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 concentra-tions in host inflammatory cells.

## 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 $ZnCl_2$. Substituted 2,3-dihydro-2-phenyl-4-quinolones were dehydrogenated using diacetoxy iodo benzene in 0.1 N KOH.

**Table No. 1: Physical Parameters And Elemental Analysis Of 2,3 dihydro 2-Phenyl 4-Quinolones.**

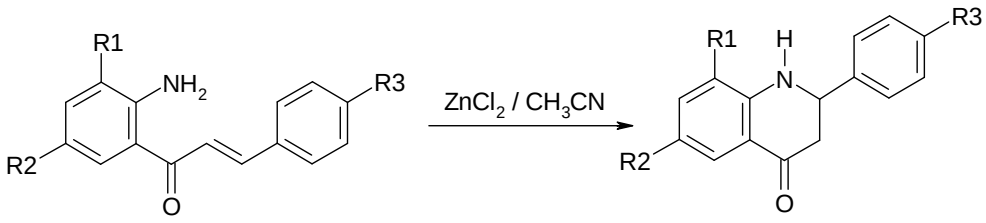
| Sr. No. | Compound | M.P. ($^0$C) | Mol. Weight | % Yield |
|---|---|---|---|---|
| 1. | 2-phenyl-8-chloro-4-quinolone | 242 | 258 | 87 |
| 2. | 2-phenyl-8-bromo-4-quinolone | 245 | 303 | 82 |
| 3. | 2-phenyl-8-iodo-4-quinolone | 248 | 350 | 80 |
| 4. | 2-phenyl-8-fluoro-4-quinolone | 251 | 242 | 70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

## EXPETIMENTAL

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. $^1$H NMR spectra were recorded at room temperature on a 300 MHz. Varian Inova Spectrometer in $CDCl_3$ 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**

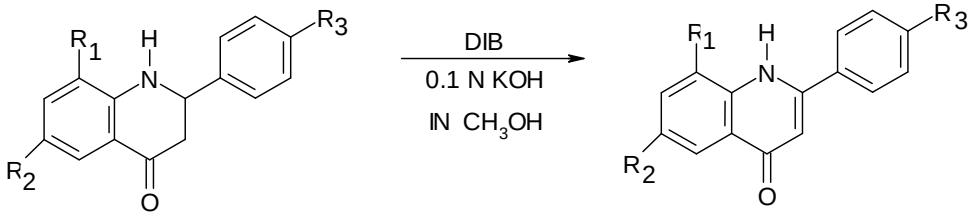



(4) (5)

A solution of substituted 1-(2'aminophenyl)-3-phenyl-2-propene-1-one (3.0 m moles) and Zinc chloride (1 M in $Et_2O$, 3.3 m mole) in $CH_3CN$ (12 ml) was heated to $80^0C$ for (24 hrs) after evaporation of $CH_3CN$ the mixture was poured into saturated solution of $NH_4Cl$ (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**




COMPOUND - V COMPOUND - VI

To compound 5 (2 m.mole) was added a solution of 0.1 N KOH in $CH_3OH$ (60 ml 6 m. mole) and Diacetoxy Iodo benzene (7.09 mg 2.2 m mole) at room temperature. The mixture was heated to $60^0C$ for 16 hrs. After evaporation of $CH_3OH$, 0.05 N HCl (50 ml) was slowly added to the mixture at $O^0C$. The resulting precipitate was separated by filtration washed with $H_2O$ and re-crystallized by $CH_3OH$.

## 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), 3064, 2964, 1632 (C=O, C=C), 1580, 1546, 1504, 1472, 1450, 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.

**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, 772cm.

**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 quinolene**

Literature survey reveals that number of 2-phenyl quinolone derivatives are significant due to their anti-bacterial[5], anti-fungal[6], antitumor[7], anti-convulsants[8], anti-oxidant[9], neuro-protectives[10], insecticides[11-12] 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-pehnyl quinolone were studied by the usual cup-plate-agar-diffusion method.[13-14] 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.[15]

**Antibacterial Activity of 2-phenyl quinolone 10 <: weak; > 10: moderate; > 16: significant.**

| Sample | Zone of inhibition in mm | | |
|---|---|---|---|
| **Compound** | **E. coli** | **S. typhi** | **S. aureus** |
| I | 12 | 10 | 06 |
| II | 1 | 11 | 07 |
| III | 17 | 13 | 09 |
| IV | 15 | 12 | 07 |
| Std. drug | 30 | 28 | 26 |

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