International Journal of Modern Agriculture, Volume 9, No. 4, 2020
ISSN: 2305-7246

CATALYST-FREE SYNTHESIS OF SYNTHESIS OF BIOLOGICAL ACTIVE FUNCTIONALIZED QUINOLONES

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Abstract

Quinolones and fluoroquinolones are synthesized in the metal catalysed 2-methylquinoline 1a and benzaldehyde 2a were chosen as the model substrates and subjected to the reactions under the catalyst-free conditions (1). The reaction proceed at 140 ^{0}C

1. Introduction:

Quinolones are large number of biologically active substances such as pharmaceuticals, agrochemicals, and natural products.[1]Among them, 2-alkenylquinoline cores are privileged structural motifs and spread over a variety of bioactive molecules such as chimanine.

Moreover, 2-alkenylquinoline itself contains an embedded imine and alkene, which might be exploited as a versatile synthetic precursor to access a wide range of functionalized heterocycles.[2] Therefore, direct olefination of quinolines has a great significance

in organic synthesis and great efforts have been devoted to develop efficient methods to construct such motifs.[3]

The newer fluoroquinolones have retained much of the activity of ciprofloxacin and ofloxacin against enteric gram-negative bacteria, but none is more potent than ciprofloxacin against these pathogens or against *Pseudomonas aeruginosa*. Levofloxacin is the active stereoisomer of the racemic mixture of the 2 stereoisomers that make up ofloxacin and thus is generally 2-fold more potent than ofloxacin Trovafloxacin and, to a lesser extent, levofloxacin generally have gram-negative coverage similar to that of ciprofloxacin, but both may be less active against some strains of *P. aeruginosa*.

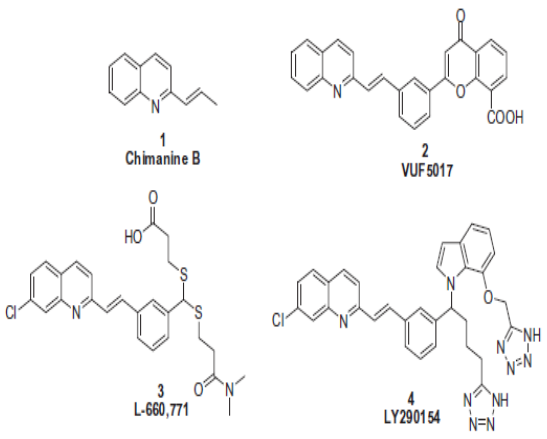

Figure 1. Biologically active 2-alkenlyazaarene derivatives.

Quinolones are a type of antibiotic[4]. Antibiotics kill or inhibit the growth of bacteria.There are five different quinolone classes. In addition, another class of antibiotic, called fluoroquinolones, were derived from

International Journal of Modern Agriculture, Volume 9, No. 4, 2020
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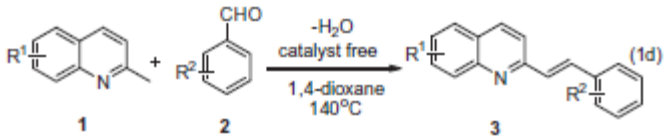
quinolones by modifying their structure with fluorine[5]. Quinolones and fluoroquinolones have many things in common, but also a few differences such as what organisms they are effective against[6]. Some people use the words quinolones and fluoroquinolones interchangeably[7]. Quinolones and fluoroquinolones detrimentally affect the function of two enzymes produced by bacteria, topoisomerase IV and DNA gyrase[8], so that they can no longer repair DNA or help in its manufacture[9,10].

2. Experimental section

Quinolones and fluoroquinolones are considered broad-spectrum antibiotics. This means that they are effective against a wide range of bacteria[11]. However, because of their risk of serious side effects, the FDA has advised that they are not suitable for common conditions such as sinusitis, bronchitis, and uncomplicated urinary tract infections, and should only be considered when treatment with other, less toxic antibiotics, has failed.



2-methylquinoline 1a and benzaldehyde 2a were chosen as the model substrates and subjected to the reactions under the catalyst-free conditions (1). The reaction did not proceed at 80 ^{0}C and almost no reaction at 100 _^{0}C. To our delight, this reaction proceeded smoothly at 140^{0}C in dioxane and the desired product was obtained in 51% yield.Theoretically, the mechanism of this tandem process might be rationalized as follows : the enamine intermediate B generated from 1 via tautomerization attacks the carbonyl group of aromatic aldehyde through the transition state C in which the intermediate B and the aldehyde 1 aggregate together by hydrogen bonding, furnishing the alcohol intermediate D. Because of the H-bonding interaction between nitrogen atom and oxygen atom in D and the steric hindrance between quinoline moiety and aromatic ring in the intermediate E, the equilibrium between D and E is more likely shifted to the left. Thus after subsequent dehydration, the (E)-configured 3 is finally afforded.

3. Conclusions

In summary, we have developed a facile synthesize of quinoline derivatives for the first time. This approach offers organic chemists a novel atom-economic pathway to directly functionalize C–H bond of 2-alkylquinolines and (E)-2-alkenylquinoline derivatives can be further employed as synthetic precursors to build a wide range of functionalized heterocycles. Further researches of building new C–C bond with this green approach are in due course in our laboratory.

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ISSN: 2305-7246

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