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Potential anti-bacterial agents: Montmorillonite Clay catalyzed synthesis of novel 2-(3, 5-substituted-1H-pyrazol-1-yl)-3-substituted quinolones and their in-silico molecular docking studies

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A series of 2-(3,5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines 5(a-g), were obtained from 2-chloro-3-(1,3-dioxolan-2-yl)quinolines 2(a-c) and diketones 3(a-c) in great yields by utilizing Montmorillonite clay K-10 as a catalyst through eco-friendly methodology. All the synthesized compounds were characterized by FTIR, 1H-NMR, 13C-NMR and HRMS spectral techniques. Antibacterial screening of the compounds revealed that some of the compounds demonstrate moderate to good results. Amongst all, compound 2c displayed good inhibitory profile against P. aeruginosa and B. subtilis while compound 5e exhibited remarkable activity against S. aureus, B. subtilis and P. aeruginosa with an MIC value of 25µg/mL and moreover against E. coli and K. pneumonia the compound 5c was representing a MIC value of 50µg/mL which was comparable to that of the standard. In addition, the compound 5f was demonstrating good viability against S. aureus and P. aeruginosa with a MIC value of 25µg/mL. The compounds 2c and 5f however showed relatively moderate inhibition against S. aureus, while the later had a moderate activity against B. subtilis respectively. To further display the antibacterial efficacy of 2c, 5c and 5f molecular docking studies were done which confirmed that compound 5c possess good binding interaction with that of peptide deformylase protein with a binding energy of -8.1 Kcal/mol which was more prominent than standard Ampicillin (-7.5 Kcal/mol) while the compounds 2c and 5f have moderate binding affinity.

1 Introduction

Heterocyclic compounds particularly, the functionalized quinolines have exhibited considerable attention owing to their biological properties such as anti-asthmatic, antibacterial, anti-inflammatory and anti-hypertensive properties. The functionalized quinolines are widespread in many natural products and find their applications in the synthesis of pharmaceuticals and biologically active molecules. Subsequently, various procedures have been proposed for developing highly functionalized quinoline frameworks which has always been a fascinating theme to numerous organic and medicinal chemists. In addition, late literature survey on heterocyclic systems either annulated or substituted quinoline frame were signifying different biological activities. For example, the mono triazolyl substituted quinolines possess anti-cancer activity, quinoline-based azetidine and thiazolidinone analogues were promising antimicrobial and antitubercular activity, 4-arylchalconegen-7-choquinolines presented good antioxidant activity, isoxazolopyrimido[4,5-b]quinolines and isoxazolochromeno[2,3-d]pyrimidin-4-ones exhibited good antimicrobial, anti-inflammatory and analgesic activity. Particularly, the 2-substituted quinoline ring systems were reported to be possessing diversified therapeutic activities. The C-2 pyridinyl and pyridinyl vinyl substituted quinolones were reported to possess very good anti-fungal activity and an introduction of an aryl or indole moiety at C-2 of quinoline ring resulted in potent PDE4 inhibitory properties. Likewise, pyrazoles then again are heterocyclic targets of considerable importance and are available in an extensive number of biologically active molecules relevant to the pharmaceutical and agrochemical sectors. They have shown broad spectrum of pharmacological and biological activities such as anti-microbial, anti-tumor, anti-fungal, anti-tubercular, anti-leukemia, anti-depressant, anti-convulsant and anti-hyperglycemic properties.

Compounds incorporating the pyrazolyl structural unit are being developed in a wide variety of therapeutic areas. Pyrazolo[3,4-b]quinoline derivatives are significant for their pharmacological activities. Particularly, they display potential antiviral, antimalarial and anti-inflammatory properties. As of late, the utilization of solid supported reagents has gained considerable significance in organic synthesis attributable to their simplicity of handling, reaction rates, greater selectivity, simple work-up and reusability of the catalyst. The effectiveness of Montmorillonite K-10 catalysis in organic synthesis has been demonstrated by their advantages of high atom efficiency, simplified isolation of product, easy recovery and recyclable of the catalysts. By considering all the above aspects in continued quinoline research interests, we were intrigued to synthesize novel molecules having substituted pyrazole ring in the 2nd position of quinoline moiety by green chemistry approach utilizing MK-10 catalyst.

2 Results and discussion

2.1 Chemistry

In the present study, synthesis of novel 2-(3, 5-substituted-1H-pyrazol-1-yl)-3-quinolines, 4, 5(a-g) is reported following the schemes depicted in Scheme 1. At first, the 2-chloro-3-(1, 3-dioxolan-2-yl) quinoline derivatives, 1(a-f) acquired from the corresponding chloroformyl derivatives, were reacted with an
excess of hydrazine hydrate in ethanolic solution in the presence of catalytic amount of ammonia under reflux condition to offer the 2-hydradino-3-(1,3-dioxolan-2-yl)quinolines, 2(a-f) in quantitative yields in a short reaction time (1-2 h) than the reported procedure\(^\text{16}\) (Table 1). One of the compounds, 2b was crystallized, analysed successfully and reported\(^\text{17}\).

Compounds 2 were then reacted with diketones, 3(a-c) in ethanolic medium by utilizing different catalysts to offer the 2-(3,5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines, 5(a-g). The reaction conditions were optimized by conducting the model reaction of 2b and acetic anhydride, 3a and by utilizing different catalysts, for example, conc. H\(_2\)SO\(_4\), anhydrous AlCl\(_3\), SnCl\(_2\cdot 2\)H\(_2\)O and MK-10 under reflux conditions in EtOH. The results are listed in Table 2. The reaction did not continue in the absence of catalyst; while, the reaction did proceed with a 57-83\% yields in the presence of catalysts. On examining different catalysts, the MK-10 was chosen as the best catalyst for the synthesis of 2-(3,5-dimethyl-1H-pyrazol-1-yl)-3-(1,3-dioxolan-2-yl)-7-methyl quinolines, 5d. The catalyst loading of MK-10 has been screened from 20 mg to 140 mg and proposed that 100 mg of the catalyst reaction was essential for the completion of the reaction. The 2-(3,5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines 5(a-g) were isolated in excellent yields (Table 3). It is observed, that in the presence of conc. H\(_2\)SO\(_4\), the destruction of methyl protecting group have resulted in the formation of 2-(3,5-dimethyl-1H-pyrazol-1-yl)-7-methylquinoline-3-carbaldehyde, 4. The plausible mechanism of formation of the desired compound, 5d is delineated in Fig. 1.

The structures of all the compounds, 4, 5(a-g) were confirmed by the FT-IR, \(^1\)H-NMR, \(^13\)C-NMR and mass and HRMS spectra. The mass spectrum of 5d demonstrated a molecular ion peak at \(m/z\) 310 [M + H]\(^+\), which indicates the adduction reaction of the acyclic anhydride, 3a to the 1-(3-(1,3-dioxol-2-yl)-2)-methylquinolin-2-yl)hydrazine, 2b. The appearance of three methyl protons at \(\delta 2.32\) ppm is attributable to the CH\(_2\) group at 7 position of the quinoline system. The three methyl protons appeared as singlet each at \(\delta 2.43\) ppm and \(\delta 2.47\) ppm attributable to the two methyl groups in the pyrazole moiety. Likewise, the existence of four methylene protons at \(\delta 4.08\) ppm indicates the dioxalan-1-yl moiety and the peaks observed at \(\delta 5.97\), \(\delta 6.13\), \(\delta 7.45\), \(\delta 7.79\) and \(\delta 7.82\) ppm are attributable to the five aromatic protons in \(^1\)H-NMR spectrum. The \(^13\)C-NMR spectrum of compound 5d demonstrated peaks carbons at \(\delta 10.9\), \(\delta 17.3\), \(\delta 22.7\) and \(\delta 66.4\) ppm attributable to the aliphatic and peaks from \(\delta 101.6\) to \(\delta 160\) ppm are attributable to the aromatic carbons.

### 2.2 Anti-bacterial evaluation

The structural activity relationship investigations of 2-hydradino-3-(1,3-dioxolan-2-yl)quinolines, 2(a-c) and 2-pyrazololquinolin-3-(1,3-dioxolan-2-yl)quinolines, 5(a-f) were performed for their antimicrobial activity against five separate bacterial organisms.

The antibacterial effect of the compounds was assessed utilizing ampicillin as a standard and reported as minimum inhibitory concentration (MIC) values. Graphical representation of the antibacterial trend followed could be seen in Fig. 2. In the 2-hydradino-3-(1,3-dioxolan-2-yl)quinoline series, from compound 2a to 2c the number of methyl groups was found to be increasing at positions 7 and 8 and therefore amongst 2(a-c) the antibacterial effects were found to be higher for compound 2c, against all the tested bacteria. The compound 2c exhibited MIC value of 25µg/mL which is comparable to the standard employed against P. aeruginosa and B. subtilis. This may be ascribed to the existence of methyl groups at position 7 and 8 of quinoline nucleus which may expect to increase lipophilicity of the molecule.

The same pattern was observed in biological effect for the series 5(a-g), where, the compounds 5c and 5f were found to be better active over all other members of the series. The compound 5e was found to have same or better MIC values over the standard utilized for the study. In the compounds 5a, 5b and 5e the position 7 on quinoline nucleus was unattributed while, two methyl groups existed in the 3' and 5' positions of the compound 5a. Likewise, in the compound 5e the methyl groups were replaced with aromatic system at 3' and 5' positions. Compound 5e was found to have potential and exceptional antibacterial character with a MIC value of 25µg/mL against S. aureus, P. aeruginosa, B. Subtilis and 50µg/mL against E. coli and K. pneumonia respectively. The compound 5f, having methyl groups at position 7 and 8 of quinoline nucleus and further more at 3' and 5' positions in pyrazole moiety has astounding activity against S. aureus, P. Aeruginosa with a MIC of 25 µg/mL. Remaining compounds were found to be not signifying any promising antibacterial activity. This indicated that the replacement of methyl to aromatic ring have resulted in compounds with better antibacterial property which makes the compound optimum lipophilic in nature.

The assessment of the docking results were carried out by simultaneously sorting the different complexes concerning the anticipated binding energies (Table 5), (Fig 3). From the results acquired from the docking analysis it was apparent that the compound 5e have good binding interaction with that of peptide deformylase with binding energy of -8.1 Kcal/mol which was more noteworthy than the standard Ampicillin (-7.5 Kcal/mol). The compounds 2c and 5f have moderate binding affinity with receptor possessing binding energies -7.3 and -6.9 Kcal/mol.

### 3 Experimental

The materials were purchased from Sigma-Aldrich, Merck and were utilized without any additional purification. All reactions were observed by TLC (Thin layer chromatography). Melting points were recorded on an Elchem digital melting point apparatus in open capillaries and are uncorrected. The \(^1\)H-NMR spectra was measured on a Bruker Avance-400 MHz instrument at room temperature. Chemical shifts \(\delta\) are in parts per million (ppm) measured in CDCl\(_3\), or DMSO-d6 as solvent and relative to TMS as the internal standard. Mass spectra were obtained using ESI, LCMS, and HRMS spectrometry.

#### 3.1 General procedure of the synthesis of 2-chloro-3-(1,3-dioxolan-2-yl)quinolines, 1(a-f)

A solution of 2-chloroquinoline-3-carbaldehydes, (10 mmol) in benzene (50 mL) containing ethylene glycol (1.78 g, 16 mL, 28.5 mmol) and a crystal of toluene-p-sulfonic acid was heated under reflux for 5 h utilizing a Dean-Stark apparatus until no more water collected in the side arm. The cooled solution was treated with saturated aqueous sodium carbonate (50 mL). Benzene layer was separated, dried and evaporated to afford 1(a-f) which were recrystallized from petroleum ether gave a yellowish solids. The products were characterized by NMR, mass spectral techniques.
2-Chloro-3-(1,3-dioxolan-2-yl)-7-methylquinolines,1b

Pale yellow powder, 85 % yield, mp 72-74 °C (Lit. 75-76 °C). IR (KBr pellets, cm⁻¹) ν: 3053, 2887, 1606, 1563, 1360, 1108, 781. ¹H NMR (CDCl₃, ppm, 300 MHz) δ: 2.54 (3H, s, CH₃), 2.72 (3H, s, CH₃), 4.10 (4H, m, CH₂), 6.22 (1H, s, CH), 7.44 (1H, d, J = 9 Hz, CH), 7.69 (1H, d, J = 8 Hz, CH), 8.65 (1H, s, CH). ¹³C NMR (CDCl₃, ppm, 75 MHz) δ: 13.3 (CH₃), 20.7 (CH₂), 2 x 65.4 (CH₂), 100.5 (CH=O), 124.8, 127.3, 127.6, 128.4, 129.5, 136.4, 136.7, 138.9, 146.9, 147.9 (C=N). Mol. formula: C₁₁H₁₃ClNO₂ requires 263.7; ESI-MS m/z: 264 (M+).

2-Chloro-3-(1,3-dioxolan-2-yl)-8-methylquinolines,1d

Pale yellow powder, 87 % yield, mp 86-88 °C (Lit. 88-90 °C). IR (KBr pellets, cm⁻¹) ν: 2932, 2883, 1614, 1597, 1330, 1101, 765. ¹H NMR (CDCl₃, ppm, 400 MHz) δ: 2.78 (3H, s, CH₃), 4.12 (4H, m, CH₂), 6.26 (1H, s, CH), 7.44 (1H, t, J = 8 Hz, CH), 7.58 (1H, d, J = 8 Hz, CH), 7.68 (1H, d, J = 8 Hz, CH), 8.37 (1H, s, CH). ¹³C NMR (CDCl₃, ppm, 100 MHz) δ: 18.0, 2 x 65.0 (CH₂), 101.5 (CH=O), 119.1, 121.7, 122.1, 122.6, 126.3, 130.4, 133.2, 135.2, 146.1, 155.4 (C=N). Mol. formula: C₁₁H₁₃ClNO₂ requires 249.7; LC-MS m/z: 250 (M+).
Bath for 2R4 h. On completion of the reaction, the solution was filtered to remove the catalyst, MKR10 and then the excess solvent was extracted using rotary evaporator to yield 2-(3,5-substituted-1H-pyrazol-1-yl)-1-(1,3-dioxolan-2-yl), 5(a-g) in good yields. At the commencement of our work, conventional approach of this synthesis was attempted by reacting compound 2b with acetyl isocyanate, 3a in the presence of conc. H2SO4 which resulted in deprotection of aldehyde group and 2-(3,5-dimethyl-1H-pyrazol-1-yl)quinoline-3-carboxylic, 4 was formed.

2-(3,5-dimethyl-1H-pyrazol-1-yl)-7-methylquinoline-3-carboxylic acid, 4 mp 227-229 °C, FTIR, ν/cm−1:2917, 2850, 1690, 1593, 1498. 1H NMR (CDCl3, 300 MHz, ppm), δ 2.32 (s, 3H, CH3), 2.5 (s, 3H, CH3), 2.62 (s, 3H, CH3), 6.15 (s, 1H, CH), 7.45-7.47 (d, 1H, J = 6 Hz, CH), 7.95 (m, 2H, CH), 8.75 s, (1H, CH), 10.20 (s, 1H, -CHO). 13C NMR (CDCl3, 75 MHz, ppm), δ 13.4, 22.1, 29.6, 108.9 (CH0), 123.2, 124.3, 127.8, 129.2, 129.7, 139.3, 142.8, 146.2, 148.1 (C=N), 163.2 (C=O). GC-MS m/z: 265 (M+). Mol. formula: C17H19N2O requires 245.12.

2-(3,5-Dimethyl-1H-pyrazol-1-yl)-7-methylquinoline, 5a mp >300 °C, FTIR, ν/cm−1:2923, 2849, 1687, 1621. 1H NMR (DMSO-d6, 400 MHz, ppm), δ 2.32 (s, 3H, CH3), 2.43 (s, 3H, CH3), 2.46 (s, 3H, CH3), 4.08 (m, 4H, CH2), 5.97 (s, 1H, CH), 6.13 (s, 1H, CH), 7.45-7.51 (m, 2H, CH), 7.79 (s, 1H, CH), 8.72 (s, 1H, CH). 13C NMR (DMSO-d6, 100 MHz, ppm), δ 10.9, 17.3, 22.7, 2 x 66.4 (CH2=CH2), 101.6 (CH-0), 105.4, 119.7, 2 x 122.9, 127.1, 2 x 127.9, 133.8, 137.8, 143.6, 144.7, 149.0, 161.0 (C=N). El-MS/m/z: 272 (M+1). Mol. formula: C19H19N2O2 requires 299.14. HRMS [El] calcd for C19H19N2O2 299.1477 [M]+, found 299.1473.

3-(3,5-dioxolan-2-yl)-7-methyl-2-(3-methyl-5-phenyl-1H-pyrazol-1-yl)quinoline, 5e mp >300 °C, FTIR, ν/cm−1:2929, 2840, 1690, 1628. 1H NMR (DMSO-d6, 500 MHz, ppm), δ 2.32 (s, 3H, CH3), 2.43 (s, 3H, CH3), 2.47 (s, 3H, CH3), 4.08 (m, 4H, CH2), 5.97 (s, 1H, CH), 6.13 (s, 1H, CH), 7.25-7.33 (m, 4H, CH), 7.51 (s, 2H, CH), 7.70-7.72 (d, 1H, J = 8, CH), 7.90 (m, 2H, CH). 13C NMR (DMSO-d6, 100 MHz, ppm), δ 12.8, 21.2, 2 x 65.8 (CH2=CH2), 101.2 (CH-0), 103.4, 118.6, 122.3, 125.9, 2 x 126.7, 127.8, 2 x 128.4, 2 x 129.1, 132.3, 137.7, 137.8, 141.5, 145.9, 147.1, 162.1 (C=N). LC-MS/m/z: 372 (M+1). Mol. formula: C21H19N2O2 requires 371.16. HRMS [El] calcd for C21H19N2O2 371.1477 [M]+, found 371.1473.

4 Antibacterial activity

Cultures of bacteria were grown on nutrient broth (Hi Media) at 37 °C for 12–14 h and were maintained on respective agar slants at 4 °C. All the compounds 2(a–c) and 5(a–g) were tested for
their minimum inhibition concentrations (MIC) by dissolving in 100% DMSO to obtain a concentration range of 25, 50, 75, 100 μg/cm² and screened for their antibacterial activities against Gram-positive S. aureus ATCC 700699, B. subtilis MTCC 430, and Gram-negative E. coli ATCC 11105, Klebsiella ATCC 10273 and P. aeruginosa ATCC 27853 by agar well technique. The standard antibacterial ampicillin was also tested under similar conditions for comparison.

4.1 Determination of minimum inhibitory concentration (MIC)

The concentration of test cultures was adjusted to 0.5 McFarland standards by using a spectrophotometer. Test organisms were grown in brain heart infusion broth (ID: 1BS6). Rapid energy evaluation was achieved by pre-incubation at 37°C for 24 h. The minimum concentration of each compound showing a zone of inhibition was considered to be MIC. The experiments were performed in triplicate (Table 4).

4.2 Molecular docking analysis for antibacterial efficacy

The binding affinity of compounds 1-(3-(1,3-Dioxolan-2-yl)-7,8-dimethyl quinolin-2-yl) hydrazine 2c, 3-(1,3-dioxolan-2-yl) 2-(3,5-diphenyl-1H-pyrazol-1-yl)quinoline 5e, 2-(3,5-dimethyl-1H-pyrazol-1-yl)-3(1,3 dioxy lan-2-yl)-7,8-dimethylquinoline 5f with peptide deformylase were calculated by using Autodock v.1.5.6. The peptide deformylase was taken from protein data bank (ID: 1BS6). Rapid energy evaluation was achieved by pre-calculated atomic affinity potential for each ligand separately and the energy of interaction of each atom in the ligand was encountered. Finally, grid maps were calculated for each ligand separately and docking analysis were carried out by using Lamarckian Genetic Algorithm. Autodock was run several times to get various docked confirmations which were used further for predicting docking energy. For each ligand 5 best poses were generated and scored by using Autodock 4.2 scoring functions. Peptide deformylase is an enzyme which involves in the deformylation of mitochondrial proteins in bacteria. Inhibition of peptide deformylase results in membrane delocalization which subsequently leads to bacterial death.

Conclusions

A facile and efficient method has been developed for the synthesis of 2-(3,5-disubstituted-1H-pyrazolyl)-3-(1,3-dioxolan-2yl)quinolines 5(a-g) by refluxing equimolar mixture of 2-hydrazone-3-(1,3-dioxolan-2-yl)quinolines, 2(a-c) and diketones, 3(a-c) in ethanol using Montmorillonite clay 10 as an efficient catalyst. Also the synthesis of 2-hydrazone-3(1,3-dioxolan-2-yl) quinolines, 2(a-c) has been achieved within lesser time using NH₃. The synthesized compounds were evaluated for in vitro antibacterial activity out of which 2c, 5c, 5f showed good to moderate efficacy against the tested strains when compared to that of standard ampicillin and in addition to this SAR analysis and docking studies were also in good agreement with the above results.

Notes and references

FIGURE CAPTIONS

Scheme 1: Scheme 1. Synthesis of 2-hydrazino-3-(1,3-dioxolan-2-yl)quinolines, 2(a-f)

Scheme 2: Synthesis of 2-(3, 5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines4 and 5(a-g)

Fig. 1: Plausible mechanism for the synthesis of 3-(1, 3-dioxolan-2-yl)-2-(3, 5-di methyl-1H-pyrazol-1-yl)-7-methyl quinoline, 5d

Fig. 2: Antimicrobial activity of compounds 2(a-c), 5(a-g) and S-Ampicillin (standard)

Fig3: The binding interactions of various ligands with peptide deformylase. [A] The binding affinity of 2c with receptor in ribbon view. [B] Interaction of 2c with the molecular surface of the receptor. [C] The binding affinity of 5c with receptor in ribbon view. [D] Interaction of 5c with the molecular surface of the receptor. [E] The binding affinity of 5f with receptor in ribbon view. [F] Interaction of 5f with the molecular surface of the receptor. [G] The binding affinity of Ampicillin with receptor in ribbon view. [H] Interaction of Ampicillin with the molecular surface of the receptor.
Reagents and Conditions: (i) \( \text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}, \text{EtOH/}\text{NH}_3\text{EtOH}, \text{reflux, 80 °C} \)

Scheme 1. Synthesis of 2-hydrazino-3-(1, 3-dioxolan-2-yl)quinolines, 2(a-f)
Scheme 2. Synthesis of 2-(3,5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines 4 and 5(a-g)

Reagents and Conditions: (i) Conc. H$_2$SO$_4$, EtOH, reflux, 80 °C  (ii) MK-10, EtOH, reflux, 80 °C
Fig. 1 Plausible mechanism for the synthesis of 3-(1, 3-dioxolan-2-yl)-2-(3, 5-di methyl-1H-pyrazol-1-yl)-7-methyl quinoline, 5d
Fig. 2 Antibacterial activity of compounds 2(a-c), 5(a-g) and S-Ampicillin (standard)
**Fig. 3:** The binding interactions of various ligands with peptide deformylase. [A] The binding affinity of 2c with receptor in ribbon view. [B] Interaction of 2c with the molecular surface of the receptor. [C] The binding affinity of 5c with receptor in ribbon view. [D] Interaction of 5c with the molecular surface of the receptor. [E] The binding affinity of 5f with receptor in ribbon view. [F] Interaction of 5f with the molecular surface of the receptor. [G] The binding affinity of Ampicillin with receptor in ribbon view. [H] Interaction of Ampicillin with the molecular surface of the receptor.

**Table 1.** Synthesis of 2-hydrazino-3-(1,3-dioxolan-2-yl)quinolines2(a-f)\(^a\)

<table>
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<th>S. No.</th>
<th>R</th>
<th>Product</th>
<th>Time / h</th>
<th>Reported Yield %</th>
<th>Experimental Yield(^b) %</th>
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<tr>
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<td>2f</td>
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<td>89</td>
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</table>

Reagents\(^a\): 1(a-f)-1 mmole, NH\(_2\)NH\(_2\).H\(_2\)O (excess), EtOH, 2-3 drops of NH\(_3\), 80 °C; \(^b\)isolated yield

**Table 2.** Screening of the catalyst and its amount of the cyclization reaction\(^a\)
### Table 3. Synthesis of 2-(3,5-substituted-1H-pyrazol-1-yl)-3-substituted quinolines, 5(a-g)\(^a\)

<table>
<thead>
<tr>
<th>S. No.</th>
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<th>R(_2)</th>
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<th>Time/ h</th>
<th>Yield(^b/)%</th>
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<td>CH(_3)</td>
<td>5g</td>
<td>3</td>
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</table>

Reagents\(^a\): 2(a-c) (1 mmole), 3(a-c) (1 mmole), MK-10 (100 mg), EtOH, 80 °C; \(^b\)isolated yield

### Table 4. Determination of minimum inhibitory concentration

<table>
<thead>
<tr>
<th>Test strains</th>
<th>MIC (µg cm(^{-3}))</th>
<th>2a</th>
<th>2b</th>
<th>2c</th>
<th>5a</th>
<th>5b</th>
<th>5c</th>
<th>5d</th>
<th>5e</th>
<th>5f</th>
<th>5g</th>
<th>S</th>
<th>N</th>
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<td>75</td>
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</tbody>
</table>

S-Standard (Ampicillin), N-Negative Control (DMSO)
Table 5. Binding affinity of synthesized ligands 2c, 5c and 5f and standard Ampicillin with peptide deformylase.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Binding Energies (kcal/mol)</th>
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<tr>
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<td>2c</td>
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<tr>
<td>5c</td>
<td>-7.3</td>
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<tr>
<td>5f</td>
<td>-6.4</td>
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<tr>
<td>Standard(^a)</td>
<td>-6.7</td>
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</tbody>
</table>

\(^a\)Ampicillin
Potential anti-bacterial agents: Montmorillonite Clay catalyzed synthesis of novel 2-(3, 5-substituted-1H-pyrazol-1-yl)-3-substituted quinolones and their in-silico molecular docking studies

Pasupala Pavan, R. Subashini*, K. R. Ethiraj and F. Nawaz Khan*

Graphical Abstract