SYNTHESIS OF 4-PHENYLPYRROLO[2,3-*b*]QUINOLINE DERIVATIVES BY HANTZSCH APPROACH

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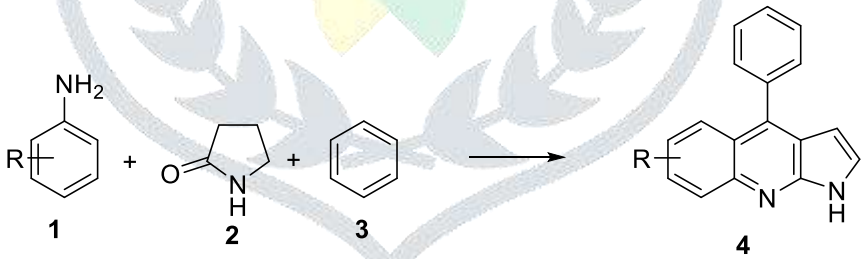
Abstract: *In the present investigative programme we synthesised new nitrogen heterocyclic compounds namely substituted 4-phenylpyrrolo[2,3-b]quinolines, using substituted aniline, benzaldehyde and 2-pyrrolidone by multicomponent one step Hantzsch approach.*

Key words *:* 4-phenylpyrrolo[2,3-b]quinolines, Pyrrrolo quinolines, Hantzsch approach

1. Introduction

Heterocyclic compounds have great applicability in pharmaceutics because they have specific chemical reactivity and provide false synthons in biosynthetic process or block the normal functioning of biological receptors. Most of the alkaloids, pigments (such as indigo, haemoglobin, anthocyanin etc.), some well known drugs (like penicillin, streptomycin, sulphathiazole, pyrenthrin, rotenmone, strychnine, reserpine, etc.) consists of heterocyclic ring system. Many workers have been reported the application of heterocyclic compounds[1-5]. These compounds are useful in the field of medicine and used as a starting material for the synthesis of new drugs[6-12]. The view of this in mind we concentrate the most convenient process to make heterocycic moiety, leads the synthesis of 4-phenylpyrrolo[2,3-*b*]quinoline by multicomponent Hantzsch approach.

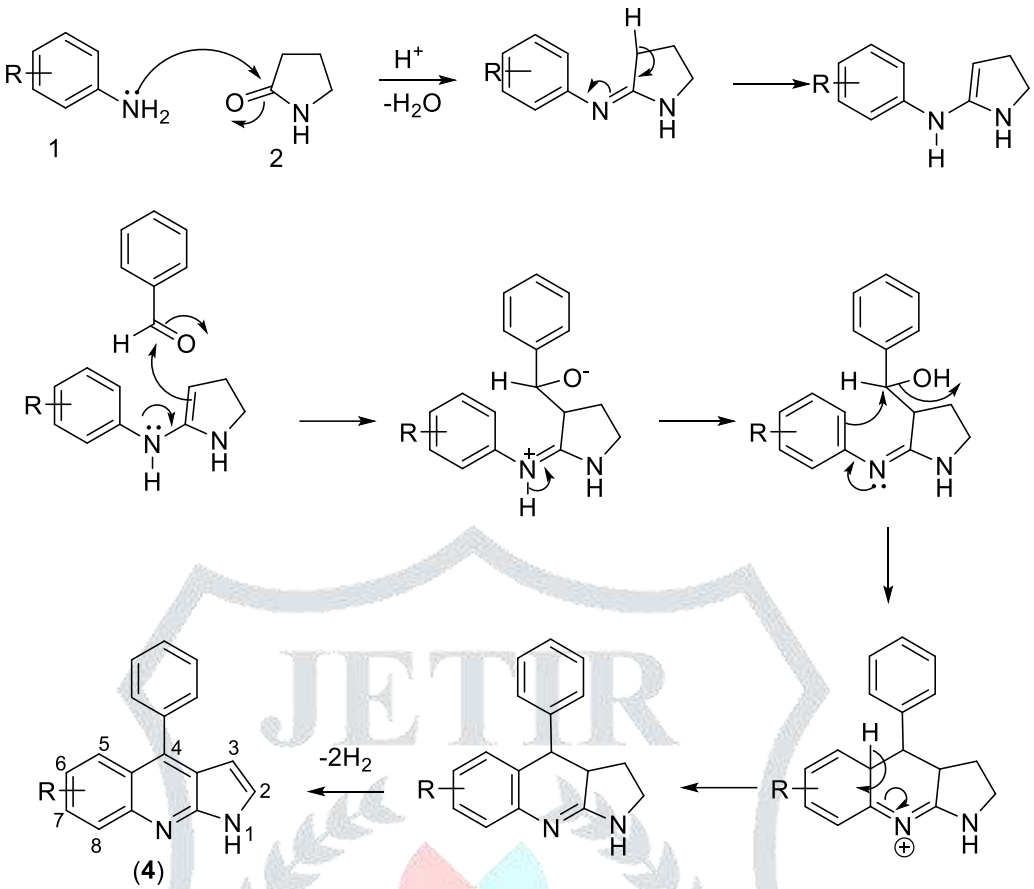


Scheme 1. Synthesis of 4-phenylpyrrolo[2,3-b]quinoline

2. Results and discussion

In the present study the substituted aniline were used and treated with 2-pyrrolidone and benzaldehyde. In this one step multicomponent process, Hantzsch approach, equal molar above mentioned reactants were taken and shaked well. Then, the reaction mixture was refluxed to 120-125 ^{o}C for 6 hrs. At that time of formation of titled compound **4,** the colour of the solution was changed yellow to brown. The formed intermediate from the condensation, aniline with 2-pyrrolidone, attacks the carbonyl carbon of benzaldehyde led to the formation of 4-phenylpyrrolo[2,3-*b*]quinoline by the removal of water.

The plausible mechanism of the reaction is



Scheme 2. Proposed mechanism for the formation of 4

3. Materials and Methods

The solvents and reagents used for the synthesis were of reagent grade and were purified by standard methods. Petroleum ether used was at boiling range 60-80 ºC. Anhydrous sodium sulphate was used to dry the solutions of organic solvents. Melting points were determined on Raaga melting point apparatus and were uncorrected. They are expressed in degree centigrade. IR spectrum was recorded on Shimadzu FTIR 8201 (PC) spectrometer using KBr pellets, and the absorption frequencies are expressed in reciprocal centimeters (cm^{-1}). ^1H NMR spectra were recorded on BRUKER 400 (MHz) spectrometer using tetramethylsilane (TMS) as an internal standard. The chemical shifts are expressed in parts per million (PPM).

3.1 Preparation of 4-phenylpyrrolo[2,3-*b*]quinoline (4)

Accordingly 0.0658 mole of substituted aniline was dissolved in acetic acid. To this, equal moles of pyrolidine and benzaldehyde were added. After adding the reagents, the reaction mixture was shaken well up to 5 min then it was refluxed to 120-125 ºC for 6 hrs. The reaction mixture was monitored by TLC. The reaction mixture was poured into crushed ice and kept it aside without disturbance for 1 hr. Then it was filtered and washed with cold water. Then the precipitate was allowed to dry. The dried precipitate was chromatographed over silica gel using petroleum ether: ethyl acetate (94:6) as eluent, furnishing the pure compound 6-chloro-4-phenylpyrrolo[2,3-*b*]quinoline **(4).**

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3.1.1 6-Chloro-4-phenyl-pyrrolo[2,3-b]quinoline (4a)

Yield 69 %, mp 204 - 206 ºC, IR (KBr, υ_{max}) cm^{-1}: 3240 (–NH), 1488 (C=N-), 1082 (C-Cl), ^1H NMR ($CDCl_3$) [δ ppm]: 6.4-8.7 (m, 10H, Ar-H) and 10.3 (bs, 1H, NH),CHN analysis for $C_{17}H_{11}ClN_2$ (278.74) (%): Calcd. C 73.25, H 3.98, Cl 12.72, N 10.05, Found C 73.12, H 3.56, Cl 12.54, N 9.95.

3.1.2 7-Chloro-4-phenyl-pyrrolo[2,3-b]quinoline (4b)

Yield 54 %, mp 216 - 218 ºC, IR (KBr, υ_{max}) cm^{-1}: 3244 (–NH), 1482 (C=N-), 1078 (C-Cl), ^1H NMR ($CDCl_3$) [δ ppm] : 6-8 (m, 10H, Ar-H) and 10.2 (bs, 1H, NH), CHN analysis for $C_{17}H_{11}ClN_2$ (278.74) (%): Calcd. C 73.25, H 3.98, Cl 12.72, N 10.05, Found C 73.18, H 3.66, Cl 12.64, N 9.98.

3.1.3 8-Chloro-4-phenyl-pyrrolo[2,3-b]quinoline (4c)
Yield 82 %, mp 228 - 230 ºC, IR (KBr, υ_{max}) cm^{-1} : 3248 (–NH), 1486 (C=N-), 1087 (C-Cl) ^1H NMR ($CDCl_3$) [δ ppm] 6.2-8.4 (m, 10H, Ar-H) and 10.3 (bs, 1H, NH), CHN analysis for $C_{17}H_{11}ClN_2$ (278.74) (%): Calcd. C 73.25, H 3.98, Cl 12.72, N 10.05, Found C 73.22, H 3.46, Cl 12.65, N 9.99.

3.1.4 6-nitro-4-phenyl-pyrrolo[2,3-b]quinoline (4d)
Yield 74 %, mp 208 - 210 ºC, IR (KBr, υ_{max}) cm^{-1}:3359 (–NH), 1514 cm^{-1} (–NO_2), ^1H NMR ($CDCl_3$) [δ ppm] 6.6-8.3 (m, 10H, Ar-H) and 10.5 (bs, 1H, NH), CHN analysis for $C_{17}H_{11}N_3O_2$ (289.29) (%): Calcd. C 70.58, H 3.83, N 14.53, Found C 70.12, H 3.56, N 14.25.

3.1.5 7-nitro-4-phenyl-pyrrolo[2,3-b]quinoline (4e)
Yield 65 %, mp 234 - 236 ºC, IR (KBr, υ_{max}) cm^{-1}: 3365 (–NH), 1534 cm^{-1} (–NO_2), ^1H NMR ($CDCl_3$) [δ ppm] 6.4-8.2 (m, 10H, Ar-H) and 10.5 (bs, 1H,NH). CHN analysis for $C_{17}H_{11}N_3O_2$ (289.29) (%): Calcd. C 70.58, H 3.83, N 14.53, Found C 70.39, H 3.76, N 14.45.

3.1.6 8-nitro-4-phenyl-pyrrolo[2,3-b]quinoline (4f)
Yield 92 %, mp 262 - 264 ºC, IR (KBr, υ_{max}) cm^{-1}:3353 (–NH), 1529 cm^{-1} (–NO_2), ^1H NMR ($CDCl_3$) [δ ppm] 6.3-8.2 (m, 10H, Ar-H) and 10.5 (bs, 1H, NH). CHN analysis $C_{17}H_{11}N_3O_2$ (289.29) (%): Calcd.C 70.58, H 3.83, N 14.53, Found C 70.34, H 3.58, N 14.47.

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