An elegant synthesis of quino[2,3-\(\alpha\)]carbazoles and their antibacterial studies

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Acid-catalysed condensation of 1-oxo-1,2,3,4-tetrahydrocarbazoles 1a-e with \(\alpha\)-aminobenzonitrile 2 affords quino[2,3-\(\alpha\)]carbazoles 3a-e in good yield. A plausible mechanism for the formation of 3a-e and the mass spectral fragmentation pattern of 3a are proposed. The titled compounds have been screened for \textit{in vitro} antibacterial activity.

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Many carbazole alkaloids with novel structure and useful biological activities were isolated from natural sources over the past decades. In general, pyranocarbazole and benzo-carbazole derivatives were reported to have prominent pharmacological properties like antihistamine, anti-inflammatory, antibiotic and antimicrobial activities. Pyridocarbazoles are known to have antitumor properties. To our knowledge there is no report on the synthesis of quinocarbazoles. Because of its interesting properties and promising pharmacological activity we have aimed to devise an elegant one-pot preparative method for the synthesis of quino[2,3-\(\alpha\)]carbazoles 3a-e, substituted pyridocarbazole derivatives, from 1-oxo-1,2,3,4-tetrahydrocarbazoles 1a-e.

Results and Discussion

To achieve our targeted compound, 1-oxo-1,2,3,4-tetrahydrocarbazole 1 was chosen as synthon which underwent condensation with \(\alpha\)-aminobenzonitrile 2 under acidic conditions as in the synthesis of quinolinones. 8-Methyl-1-oxo-1,2,3,4-tetrahydrocarbazole on condensation with \(\alpha\)-aminobenzonitrile 2 in toluene in the presence of a catalytic amount of \(p\)-toluenesulphonic acid, gave a single product 3 (Scheme I). The IR spectrum of the product showed strong absorptions at 1585, 1644 and 3246 cm\(^{-1}\) ascribable to C=N, C=O and N-H stretching vibrations, respectively. A strong band at 3365 cm\(^{-1}\) attests for the OH stretching vibration. The \(\textsuperscript{1}H\) NMR spectrum exhibited doublets at \(\delta\) 7.13, 7.49 and 8.47 assignable to C-9-H, C-10-H and C-11-H with J values 8.03 Hz, 8.15 Hz and 8.40 Hz, respectively. A broad singlet at \(\delta\) 8.60 was accountable for the quinolone-NH of the keto form. The OH proton resonated at \(\delta\) 11.39 as a broad singlet. A close look at the \(\textsuperscript{1}H\) NMR spectrum of the compound revealed that it exists in the keto and enolic forms with the ratio 1:1. Further, in the mass spectrum, the molecular ion peak appeared at m/z 298 (100%). The elemental analysis also agreed well with the molecular formula, C\(_{20}\)H\(_{14}\)N\(_2\)O. On the basis of the aforesaid data, structure of the product was proved to

![Scheme I](image-url)
be 6-hydroxy-12-methylquino[2,3-a]carbazole 3a (Scheme II).

A similar series of compounds 3b, 3c, 3d and 3e were obtained from 1b, 1c, 1d and 1e, respectively. The structures of the realised products were attested by IR, $^1$H NMR and mass spectra. The physical and spectral data of these compounds are given in Table I.

The plausible mechanism for the formation of the product 3 is as follows. The compound 1 underwent acid-catalysed condensation with $o$-aminobenzonitrile 2, to give an intermediate I, which on intramolecular electrophilic substitution at the second position of the carbazole derivative, with the $o$-nitrite group afforded the intermediate III. On subsequent protonation, hydrolysis and aromatisation, III yielded 6-hydroxyquino[2,3-a]carbazole 3 (keto and enol forms) (Chart I).

**Experimental Section**

Melting points were determined with a Boetius micro heating table and are uncorrected. IR spectra were recorded on a Shimadzu FTIR-8000 infra red spectrometer using KBr; $^1$H NMR spectra on a Varian AMX 400 FT-NMR spectrometer using tetramethylsilane as internal reference in DMSO-$d_6$ (chemical shifts in $\delta$, ppm); and mass spectra on a Jeol-JMS-D-300 mass spectrometer. Microanalyses were done on

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Scheme II—Mass spectral fragmentation pattern of 3a.
General procedure for the synthesis of quino-[2,3-α]carbazoles 3a-e. A mixture of 1-oxo-1,2,3,4-tetrahydrocarbazole (1, 1 mmole) and α-amino-benzonitrile (2, 1 mmole) was taken in 10 mL of dry toluene and added a catalytic amount of p-toluene-sulphonic acid. The reaction mixture was refluxed on an oil-bath for 6 hr. The completion of the reaction was checked by TLC. After the completion of the reaction, the excess solvent was removed under reduced pressure and the mixture was poured into ice cold water. The ice cold reaction mixture was neutralised with 5% NaHCO₃ solution and extracted with ethyl acetate (3×50 mL). The organic layer was dried with anhydrous sodium sulphate and the excess solvent was removed by distillation to give the crude product. The crude residue was purified by column chromatography over silica gel (pet. ether-ethyl acetate mixture, 75:25).

Antibacterial studies
All the newly synthesized compounds 3a-e, were screened for their in vitro antibacterial activities against Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and Bacillus subtilis according to the disc diffusion method. The minimal inhibitory concentration (MIC) values were determined by serial dilution technique using dimethyl sulphoxide as a solvent. Furacin was used as a standard drug for comparison in antibacterial screening studies. The results are given in Table II.

The antibacterial screening studies indicate that the compound 3e carrying chloro group showed an excellent antibacterial activity against E. coli,
The compounds 3a and 3e also possessed good antibacterial activities against B. subtilis and S. aureus. The antibacterial activities of the remaining compounds were comparable with that of furacin especially against S. aureus and B. subtilis.

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References