

CONDENSATION OF SOME HETARYL SUBSTITUTED DIKETONES WITH AROMATIC DIAMINE

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The condensation of 1,2-di(quinolyl-2)-1,2-ethanedione and 1,2-di(6-methylquinolyl-2)-1,2-ethanedione with 4-methyl-1,2-phenylenediamine in the presence of acetic acid results in the formation of 2,3-di(quinolyl-2)-6-methylquinoxaline and 2,3-di(6-methylquinolyl-2)-6-methylquinoxaline, respectively.

The biological activities of the nitrogen containing conjugated heterocyclic compounds have been found to draw the attentions of the researchers of modern times. Such compounds are considerably used pharmaceutically as antiulcer, antimalarial, tuberculocidal and sedatives besides their uses as dyes in the textile industry, pesticides, stabilizers and inhibitors (Cheeseman & Werstuck 1978 and Cheeseman 1963).

Quinoxalines are the heterocyclic compounds that differ by the presence of a tertiary nitrogen atom in place of carbon at the fourth position in the heterocyclic ring of quinoline, are normally synthesized by the condensation of an aromatic *o*-diamine and ∞ -dicarbonyl compound. These compounds are considered to have significant biological activity. Their reactions as well as their pharmacological actions, continue to stimulate many investigations for example 2-methylquinoxaline N,N-dioxides substituted in the 3-position (e.g., with amide, amidino and ester groups) are potent bacteriocides (Ley, Eholzer, Metzger and Fritsche 1969, and 1970; Kasubick and Robertson 1972). Antibiotics of the triostin and quinomycin series, isolated from the cultures of *Streptomyces aureus*, have been shown by degradative study to contain a quinoxaline-2-carboxylic acid residue (Cheeseman & Werstuck 1978). Keeping this in view, the present research was conducted to add some other compounds to this class.

2,3-Di(quinolyl-2)-6-methyl quinoxaline (**1a**) and 2,3-di(6-methylquinolyl-2)-6-methyl quinoxaline (**1b**) were

synthesized by condensation followed by ring closure reaction, when 1,2-di(quinolyl-2)-1,2-ethanedione and/or 1,2-di(6-methylquinolyl-2)-1,2-ethanedione was treated with methyl substituted *o*-phenylenediamine respectively. The structures of the newly synthesized compounds have been determined and characterized by ultraviolet, infrared, nuclear magnetic resonance and mass spectral data whereas confirmed by elemental analysis.

Melting points were measured in open capillaries with an Electrothermal IA 9100 digital melting point apparatus.

All infrared spectra were recorded on a Phillips PU9714 Spectrophotometer using infrared grade potassium bromide. Nuclear magnetic resonance (^1H & ^{13}C) spectra were determined on "Varian 200MHz Gemini", "Bruker AC-200MHz FT-NMR" and "Bruker AM-500MHz FT-NMR spectrometers in deuteriochloroform and are reported in parts per million downfield from tetramethyl silane (TMS) as the internal standard (δ scale). Mass spectra were obtained with E1 MAT 312, Varian MAT 111, Varian MAT 112 and Hewlett Packard GC/MS 5890 spectrometer. Chemical analysis were performed in Austria and Germany and all new compounds gave satisfactory elemental analysis.

For the purpose of column chromatography silica gel 60 (70-230 mesh) from D. Merck AG was used. Eastman Kodak chromogram 13181 silica gel sheets with fluorescent indicator was used for thin layer chromatography (TLC).

The required 1,2-di(quinolyl-2)-1,2-ethanedione and 1,2-di(6-methylquinolyl-2)-1,2-ethanedione were prepared by the oxidation of 1,2-di(quinolyl-2)-1,2-ethenediol and 1,2-di(6-methylquinolyl-2)-1,2-ethenediol respectively, which were synthesized by the condensation reactions of the quinoline-2-carboxaldehyde and 6-methylquinoline-2-carboxaldehyde respectively. Quinoline-2-carboxaldehyde and 6-methylquinoline-2-carboxaldehyde in turn were prepared according to the literature procedure by the reaction of SeO_2 with the starting material i.e. 2-methylquinoline and 2,6-dimethylquinoline (Kaplan 1941) respectively. The obtained heterocyclic carboxaldehydes were found to have properties similar to that given in the literature. SeO_2 for the reaction was freshly prepared just before use by the method given by researchers (Blatt 1966).

All crude reaction products were examined by thin layer chromatography with chloroform as developing solvent and compared with the starting material and reagents to follow the progress of the reactions.

The ir, nmr, ms and analytical data alongwith the purification procedures are given in each experiment separately.

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Procedure and analytical data: 2,3-di(quinolyl-2)-6-methyl quinoxaline (1a). To a solution of 2.0 mmole (0.2440 gm) of 4-methyl 1,2-phenylenediamine in 20 ml acetic acid 2.0 mmoles of 1,2-di(quinolyl-2)-1,2-ethanedione (synthesized by the oxidation of 1,2-di-(quinolyl-2)-1,2-ethenediol which was obtained as a result of the condensation reaction of quinoline-2-carboxaldehyde (in the presence of potassium cyanide) was added and refluxed in an oil bath for one hour. The reactive mixture was cooled and 100 ml of water was added into it which resulted in the formation of a beige coloured emulsion which was treated by adding 20% sodium hydroxide solution and the resulting precipitates were filtered. The impure product was then dissolved in alcohol and heated with active charcoal, filtered and reprecipitated with water and crystallized using ethyl alcohol yielding 0.5028 gm (69%), m.p 233.4°C.

IR (Potassium bromide): 3000-3080 (aromatic, = C - H) 2920-3000 (methyl C - H cm^{-1}) $^1\text{H NMR}$ (chloroform-D): δ 2.64 (s, CH_3 , 3H) 7.41- 8.22 (m, aromatic, 15H).

ms: m/z (relative intensity) 400(M+2,2), 399 (M+1,22) 398 (M+,91), 397(M-1,100), 199(22), 154(2), 128(10), 101(2).

UV (chloroform): λ_{max} 259.6, 399.2 nm.

Elemental analysis: Calculated for $\text{C}_{27}\text{H}_{18}\text{N}_4$; C = 81.38, H = 4.55, N = 14.06 found C = 81.30, H = 4.89, N = 14.19.

2,3-di(6-methylquinolyl-2)-6-methyl quinoxaline (1b). To a solution of 2.0 mmole (0.2440 gm) of 4-methyl 1,2-phenylenediamine in 20 ml acetic acid, 2.0 mmoles of 1,2-di (6-methylquinolyl-2)-1,2-ethanedione (synthesized by the oxidation of 1,2-di (6-methylquinolyl-2)-1,2-ethenediol which was obtained as a result of the condensation reaction of 6-methylquinoline-2-carboxaldehyde (in the presence of potassium cyanide) was added & refluxed in an oil bath for one hour. The reactive mixture was cooled and 100 ml of water was added into it which resulted in the formation of a beige coloured emulsion which was destroyed by adding 20% sodium hydroxide solution and the resulting precipitates were filtered. The impure product was then dissolved in alcohol & heated with active charcoal, filtered and reprecipitated with water and crystallized using ethyl alcohol yielding 0.5030 gm (59%) m.p 152-3°C (Scheme 1).

IR (Potassium bromide): 2980-3070 (aromatic, = C - H) 2870-2980 (methyl C-H) cm^{-1} 1350 and 1430 (methyl, asymmetric and symmetric C-H).

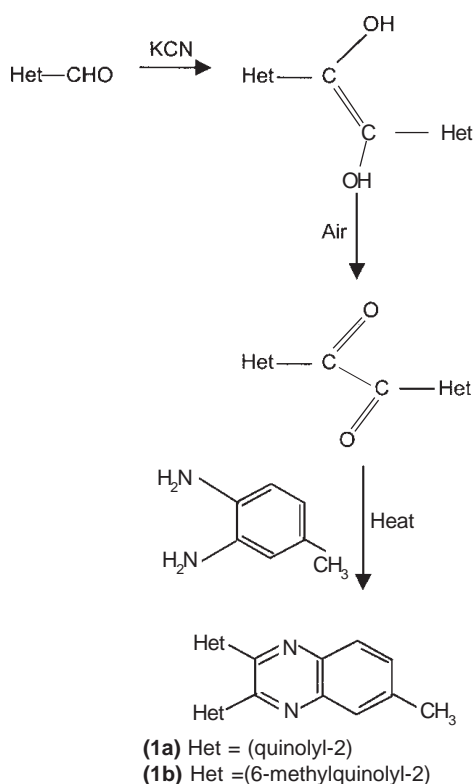
$^1\text{H NMR}$ (chloroform-D): δ 2.48 (s, 2CH_3 , 3H), 2.65 (s, CH_3 , 3H) and 7.32-8.18 (m, aromatic, 13H)

MS: m/z (relative intensity) 428(M^{+2} ,2), 427(M^{+1} ,34), 426(M^{+} ,88), 425(M^{-1} ,100), 411 (M-15,80), 272(20),213(12), 168(2), 167(6), 142(2), 141(4), 115(8).

UV (chloroform): λ_{max} 259.2, 342.4 nm.

Elemental analysis: Calculated for $\text{C}_{29}\text{H}_{22}\text{N}_4$; C = 81.66, H = 5.20, N = 13.13 found C = 81.46, H = 5.33, N = 12.90.

The formation of both quinoxalines i.e., 2,3-di(quinolyl-2)-6-methyl quinoxaline (**1a**) as well as 2,3-di(6-methylquinolyl-2)-6-methyl quinoxaline (**1b**) as a result of condensation reaction between 4-methyl 1,2-phenylenediamine and the respective hetaryl substituted 1,2-ethanedione was confirmed after comparing the UV, IR, $^1\text{H NMR}$ and MS spectra of the starting materials with that of the synthesized products. Upon observation of the IR spectra of both the hetaryl and methyl substituted quinoxalines the absence of the characteristic C=O absorption band of the 1,2-dicarbonyl compound i.e., in between 1700-1660 cm^{-1} and the bands at 3325 cm^{-1} and 3285 cm^{-1} representative of the symmetric and asymmetric N-H stretching vibrations of NH_2 group of the 4-methyl 1,2-phenylenediamine show the progress of the reaction whereas the presence of the absorption bands at 1585, 1540 and 1480 cm^{-1} due to C=C and C=N bonds of the heterocyclic ring besides the bands between 1440-1420 cm^{-1} due to the symmetric and asymmetric C-H bending vibrations and between 2980-2780 cm^{-1} due to



Scheme 1

the stretching vibrations in the spectra of both the compounds confirm the formation of the hetaryl and methyl substituted quinoxalines which was further supported by their ^1H NMR spectra. In the mass spectra of both the synthesized compounds, the appearance of a molecular ion peak at m/z 398 and other expected peaks at 199, 154, 128 and 101 in case of compound (**1a**) whereas a molecular ion peak at 426 and other expected peaks at 272, 168, 142 and 115 in case of compound (**1b**) confirm the structures of the synthesized compounds.

Key words: Condensation Diketones, Aromatic Diamine

References

- Blatt A H 1966 *Organic Synthesis*, Collective Volume II, John Willey and Sons, Inc., 12th Ed New York p 510.
- Cheeseman G W H 1963 Recent Advances in Quinoxaline Chemistry. In: *Advances Heterocyclic Chemistry*, vol **2**, A R Katritzky, ed Academic Press, New York, pp 203-243.
- Cheeseman G W H, Werstiuk E S G 1978 Quinoxaline Chemistry. In: *Advances in Heterocyclic Chemistry*, vol **22**, A R Katritzky and A J Boulton, ed, Academic Press, New York, pp 367-431.
- Kasubick R V, Robertson R L 1972 Fr Demande 2, 132, 378 *Chem. Abstr* **78** 159673.
- Ley K, Eholzer U, Metzger K G, Fritsche D 1969 *S African Patent*, 6806, 099. *Chem Abstr* **71** 91528.
- Ley K, Eholzer U, Metzger K G, Fritsche D 1970 *S African Patent*, 6906, 094. *Chem Abstr* **72** 3508.