Short Communication

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SYNTHESIS OF 2, 3-DI (QUINOL-8-YL) 6-METHYLQUINOXALINE

Seniz Kaban [a] ***and Nasir Ansar****[b]

[a]*Yildiz Technical University, Department of Chemistry, Istanbul, Turkey*

[b]*Department of Chemistry, Adamjee Government Science College, Karachi, Pakistan.*

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Quninoxalines are considered to have significant biological activity. Their reactions as well as their pharmacological actions continue to stimulate many investigations. Thus 2-methyl quinoxalines N,N-dioxides substituted in the 3-position (e.g., with amide, amidino, hydrazinocarbonyl and ester groups) are potent bacteriocides (Cheeseman 1963; Cheeseman and Werstiuk 1978). 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.

In the absence of chelation, formation of more stable benzoin **1** form rather than enediol takes place as in the case with quinoline-8-carboxaldehyde. This is characterized by its IR (3560-3300 cm^{-1} representing the presence of -OH group) and a band at 1670 cm^{-1} due to the C = O group of the synthesi-zed benzoin.

In the ^{1}H NMR spectrum a wide singlet at 7.1 ppm is appropriately due to the single hydrogen belonging to the -OH group of the benzoin skeleton (Bhacca Johnson and Shooly 1962). In addition many peaks were observed between 7.29-8.98 ppm due to the heterocyclic rings protons.

In the ^{13}C NMR spectrum the presence of a peak at 77.94 ppm in between the peaks for the solvent (chloroform) and 204.97 ppm (for the carbonyl carbon), due to the quarternary carbon of benzoin clearly mentions the presence of CH (OH) C=O group (Parikh 1974; Dyke, Floyd, Sainsbury and Theobald 1978; Pavia, Lampman and Kria 1979; Silverstein Bassler and Morrill 1981; Dean 1987; Williams and Fleming 1987; Erdik 1993). The structure was further con-firmed by its mass spectrum (moleculer ion peak at m/z 314).

The synthesized benzoin was then oxidized using air as oxidizing agent to respective l, 2-diketone **(2)** (C=O bond in Het-COCO-Het at 1700-1660 cm^{-1}) in the IR spectrum (Pavia, Lampman and Kria 1979). The fall of the vibration band towards low energy in 1,2-Di(quinol-8-yl)-1,2 ethanedione is certainly due to the presence of hetaryl groups facilitating conjugation in the compound (Bellamy 1960; Dean 1987).

The diketone was then condensed with 4-methyl-o-phenylenediamine in the presence of glacial acetic acid to give hetaryl and methyl substituted quinoxaline (3). The structure of quinoxaline **(3)** was characterized by the absence of the C=O peak of the 1,2-diketone in the IR spectrum as well as its mass and NMR spectra which completely support the assigned structure. The entire transformation is as given in the illustration.

Melting points are uncorrected and were measured in open capillaries with an electrothermal IA 9100 digital melting point apparatus.

Infrared spectra were recorded on a Phillips PU 9714 spectrometer using infrared grade potassium bromide. Nuclear magnetic resonance (^{1}H and ^{13}C) spectra were determined on Varian 200 MHz, Gemini, Bruker AC-200 MHz FT-NMR and Bruker AM-500MHz FT-tetramethylsilane (TMS) as the internal standard (d scale). Mass spectra were obtained with EIMAT 312, Varian MAT 111, Varian MAT 112 and Hewlett Packard GC/MS 5890 spectromter. Chemical analysis were performed in Austria and Germany and all new compounds gave satisfactory elemental analysis.

In column chromatography silica gel 60 (70-230 mesh) from E-Merck AG was used. Thin layer chromatography (TLC) was performed on Eastman Kodak chromagram 13181 silica gel sheets with fluorescent indicator.

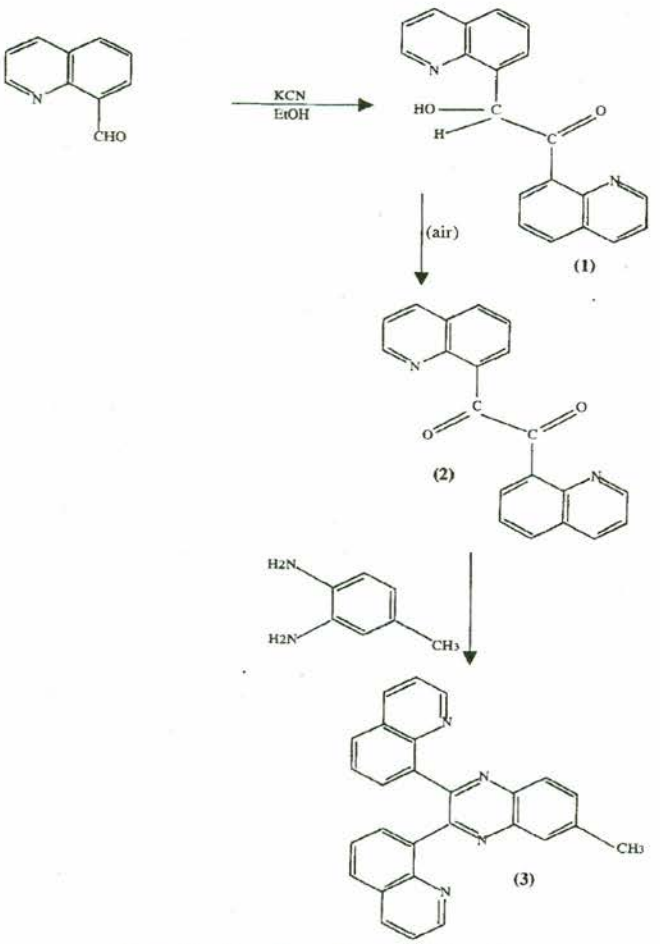
The required heterocyclic carboxaldehyde was prepared according to the procedure cited in literature using SeO_2 and 8-methyl quinoline as starting material (Radionov and Berkengeim 1945). The properties of the heterocyclic carboxaldehyde agreed with the reported values.

The SeO_2 was freshly prepared just before use according to the procedure given by Harry Kaplan (Kaplan 1941).

A detailed description of the experiment is given to illustrate the general procedure. All crude reaction products were examined by thin-layer chromatography with chloroform as developing solvent and compared against the starting materials and reagents to follow the progress of the reaction. The purification procedures and additional comments together with the IR, NMR, MS and analytical data are given in each experiment.

2-Hydroxy-1,2-di (quinolyl-8) ethanone (1a). Quinoline-8-carboxaldehyde 10.0 mmole was dissolved in 6ml 50% aqueous ethanol in 100ml round bottom flask. To it was added another solution of 4.0 mmoles of potassium cyanide in very

*Author for correspondence



Step-wise formation of methylquinoxaline

little water and then this reaction mixture was stirred for a few minutes, and then heated at about 105-10°C in oil bath. The colour of the solution changed to yellow after fifteen minutes, and then it was further heated for half an hour. This was cooled and the precipitates were filtered and washed with water, a few ml of methanol and diethyl ether; 2.29 (73%) of compound **3a** was obtained which was recrystallized using pyridine to give analytical sample, m.p: 157-8°C.

IR (potassium bromide): 3560-3300, 3100-2980, 1670, 1585, 1560, 1490, 1230, 1095, 1000, 870, 830, 810, 790 cm^{-1}.

^{1}H NMR (deuteriochloroform): d6.88 (s, CH, 1H), 7.10 (s, OH, 1H) 7.29-8.98 (m, aromatic, 12H).

13C NMR (deuteriochloroform): d77.94 (quaternary carbon), 121.47-150.65 (heteroaromatic), 204.97 (C=O).

UV(chloroform): d_{max} 240.1, 303. 2nm. *ms*: m/z (relative intensity): 314 (M^+,7), 158(100), 156(49), 129 (76), 128(32), 102(13). Anal calcd for $C_{20}H_{14}N_2O_2$ (314.3428), C; 76.41, H; 4.48 N; 8.91 found C;76.28, H; 4.57, N; 8.94.

1,2-Di (quinolyl-8)-1,2-ethandione (1b). 10.0 mmoles of 2-hydroxyl, 2-di(quinolyl-8) ethanone was dissolved in dioxane and heated in an electrical bath and then air was passed through the solution till dark brown colour changed to very light yellow.

After cooling water was added upto precipitation. 0.2820gm (90%) of 3b was obtained, which upon recrystallization with dioxane gave analytical sample, m.p 174-6°C.

IR (potassium bromide): 3120-3000, 1660, 1585, 1560, 1490, 1225, 1075, 865, 825 and 780cm^{-1}.

^{1}HNMR (deuterio-chloroform): d8.67.9.03 (m, aromatic, 12H).

UV (chloroform): 1_{max} 240.9.293.2nm. *ms*: *m/z* (relative intensity) 313 (M^+1,5), 312 (M^+,21), 255(9), 156(100), 126(44), 101 (17).

Anal calcd for $C_{20}H_{12}N_2O_2$; C;76.91,H;8.97; found C; 76, H;4.10 N;9.01.

2-3,-Di (quinolyl-8)-6-methylquinoxaline (1c): 2.0 mmoles (0.24gms) of 4-methyl 1,2-phenylenediamine was taken in a 100ml round bottomed flask. To it was added 2.0 ml glacial acetic acid and dissolved. To this solution 2.0mmoles of **1b** was added and refluxed for one hour. The solution was then cooled and poured into 100 ml of water to give an emulsion which was destroyed by adding 20% aqueous NaOH solution into it; the ppt thus obtained was filtered. The impure solid was then dissolved in ethanol and heated with activated charcoal and filtered. Water was added to the obtained filtrate to give the required product yielding 5.26g (66%), which was then recrystallized with diethyl ether to give analytical sample, m.p 229-30°C.

IR(potassium bromide): 3100-2960, 2960-2870, 1585, 1570, 1480, 1440, 1340, 1110, 1050, 990, 825, 785, 755cm^{-1}.

^{1}HNMR (deuteriochlorform): d2-62(s,CH_3, 3H), 7.12-8.63 (m, aromatic, 15H). *ms:* m/z(relative intensity) 398(M^+,68), 397(M-1,7), 270(100), 199(27), 154(25), 142(14), 128(13), 101(27).

Anal calcd. for $C_{27}H_{18}N_4$: (398.4660), C; 81.38, H; 4.55, N; 14.06; found: C; 81.22, H; 4.77, N; 13.98.

Key words: Synthesis, Methylquinoxaline.

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