SYNTHESIS OF SOME NOVEL 2-(2-CHLORO-3-QUINOLYL)-5-PHENYL-2, 3-DIHYDRO-1, 3,4 – OXADIAZOLES.

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Abstract: Various acetanilides **1** were treated with DMF and $POCl_3$ complex (Vilsmeier's reagent) to obtain 2-chloro-3-quinolinecarboxaldehydes **2**, which on treatment with aromatic acid hydrazides **3** in alcohol gave quinoline-3-substitutedhydrazones **4**. The latter, on reaction with acetic anhydride at reflux, yield oxadiazolines flanked by quinoline and substituted benzene moieties, i.e., 2-(2-chloro-3-quinolyl)-5-phenyl-2,3-dihydro-1,3,4-oxadiazole (**5**). The structures of **5** are supported by spectral data.

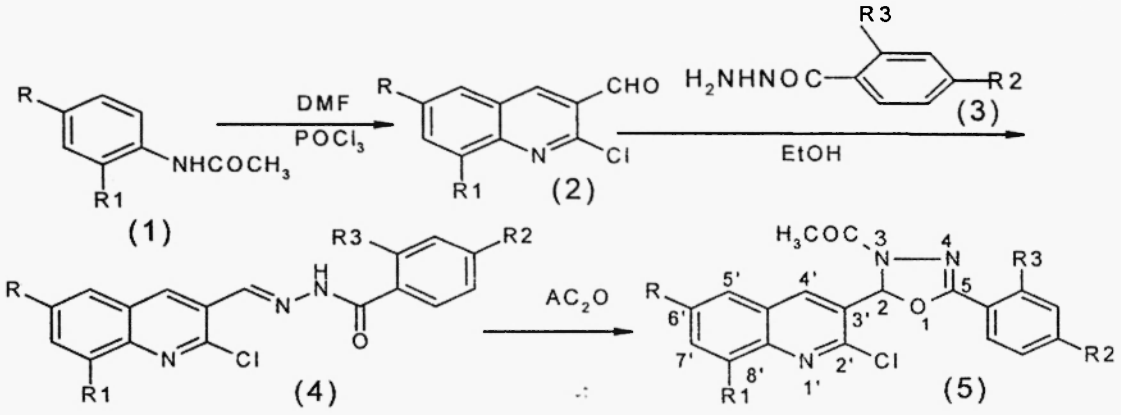
Introduction: In recent years the chemistry of quinolines[1-3] and their derivatives has gained increasing attention, due to the fact that substituted quinolines are associated with different types of biological activities[4-18]. Likewise a dihydrooxadiazole system flanked by various quinoline and substituted benzene moieties may also be found to be associated with wide range of biological activities. We report herein the synthesis of 2-(2-chloro-3-quinolyl)-5-Phenyl-2,3-dihydro-1,3,4–oxadiazole (5), incorporating two biologically active moieties-quinoline and oxadiazole - in a single molecule. The title compounds will be evaluated for their biological activities in course of time, the results of which will be published elsewhere.

Results and discussion:

Substituted acetanilides 1 were treated with dimethylformamide and phosphorus oxychloride (Vilsmeier's reagent) to obtain the known[19] 2-chloro-3-quinolinecarboxaldehydes 2. The latter, on treatment with substituted benzoic acid hydrazides 3 in alcohol at reflux temperature, gave the corresponding benzoic acid hydrazone 4 (Table-I). Heating 4a (i.e., 4, R=R1=R2=R3=H) with acetic anhydride at reflux temperature followed by simple workup of the reaction mixture gave 5a (i.e., 5, R= R1=R2=R3=H) containing the novel substituted oxadiazoline system. The structure of the compound 5a was established on the basis of its spectral data. Thus, in its IR (KBr) spectrum, peak was observed at 1680 cm^{-1} due to carbonyl function different from that at

1710 cm^{-1} which was found due to the aldehyde function in 2. In its ^{1}H-NMR spectrum, signals 5a showed at δ 2.5 (s,3H,3-CO-CH_3), 7.45 (s,1H,2-H), 8.20 (s,1H,4′-H), 8.00(d,J=8Hz,1H,8′-H), 7.60(dd,J=8/3Hz,1H,7′-H), 7.70(d,J=8Hz1H,5′-H), 7.80 (dd,J=8/3Hz,1H,6′-H), 7.50 (m,5H,ph-H). Its mass spectrum showed the molecular ion peak at M^+ 351 and the other peaks at m/z 309,275,274,216,140,105,77,43. The same reaction has been extended to several substituted 4 and the products obtained have all been assigned structure 5 on the basis of spectral data (Table-II). All the above reactions are briefly summerised in the scheme. Similar sequence of reactions was done on a different substrate[20-23] earlier by Belgian researchers to prepare substituted dihydrooxadiazoles.

SCHEME



Experimental Section: IR spectra were recorded as KBr pellets on a Perkin Elmer System 2000 F.T. I.R. spectrometer. ^{1}H NMR spectra were recorded on a 100 MHz or 200 MHz Varian Instrument was using TMS as internal standard. Melting points are uncorrected and were determined in open capillaries. TLC was recorded on glass plates coated with silica Gel G and spotting was done using iodine chamber or UV lamp.

Preparation of 4: (General procedure): A mixture of **2** (0.01mole) and benzoic acid hydrazide **3** (0.01mole) in ethyl alcohol (20mL) was stirred under reflux for 3 hrs. The mixture was then cooled to R.T, the separated product filtered, washed with ethyl alcohol and recrystalised from methanol to obtain pure **4**.

Preparation of 5: (General procedure) A mixture of **4** (0.01mole) and acetic anhydride (15mL) was heated under reflux with constant stirring for 3 hrs. At the end of this period, the reaction mixture was cooled to RT and diluted with ice water. The separated solid was filtered, washed with water and dried to obtain crude **5**.The latter were recrystalised from a suitable solvent to obtain pure **5**.

Table I

Reaction of 2 with Acid hydrazides 3 to obtain 4

Sl No	Quinolines 2 Used	Aromatic acid hydrazides 3 used	Product 4 obtained	Yield (%)	M.P°c
a.	R=R1=H	R2=H R3=H	R=R1=R2=R3=H	82	202-05
b.	R=H R1=CH_3	R2=Cl R3=H	R1=CH_3,R2=Cl ,R= R3=H	81	244-46
c.	R=H R1=CH_3	R2=H R3=Cl	R1=CH_3,R3=Cl, R= R2=H	78	252-54
d.	R=H R1=CH_3	R2=OCH_3 R3=H	R1=CH_3,R2=OCH_3,R=R3=H	80	140-42
e.	R=CH_3 R1=H	R2=H R3=Cl	R=CH_3,R3=Cl, R= R2=H	82	258-60
f.	R=CH_3 R1=H	R2=OCH_3R3=H	R=CH_3,R2=OCH_3,R1=R3 =H	81	216-18
g.	R=OCH_3 R1=H	R2=Cl R3=H	R=OCH_3,R2=Cl,R1=R3=H	82	268-70
h.	R=OCH_3 R1=H	R2=H R3=Cl	R=OCH_3,R3=Cl ,R1=R2=H	84	250-52
i.	R=H R1=CH_3	R2=H R3=H	R1=R=CH_3, R2=R3=H	80	138-40

Table-II

Physical and spectral data of 5(a-i) obtained from 4(a-i)

Compd.,	Yield (%)	mp °C	^{1}H-NMR data
5a	75	178-80	2.5(s,3H,3-CO-CH_3),7.45(s,1H,2-H), 7.5(m,5H,ph-H), 7.60(dd,1H,7′-H), 7.70(d,1H,5′-H), 7.80(dd,1H,6′-H), 8.00(d,1H,8′-H),8.20(s,1H,4′-H).
5b	70	214-16	2.5(s,3H,3-CO-CH_3), 2.7(s,3H,8′-CH_3), 7.50(s,1H,2-H), 7.6-7.8(m,9H,ph-H).
5c	72	158-60	2.5(s,3H,3-CO-CH_3), 2.7(s,3H,8′-CH_3), 7.50(s,1H,2-H), 7.6-7.8(m,8H,ph-H).
5d	71	182-84	2.5(s,3H,3-CO-CH_3), 2.7(s,3H,8′-CH_3), 3.90(s,3H,ph-OCH_3),7.50(s,1H,2-H), 7.6-7.9(m,8H,ph-H).
5e	74	204-06	2.5(s,3H,3-CO-CH_3), 2.7(s,3H,6′-CH_3), 7.45(s,1H,2-H), 7.5-7.8(m,8H,ph-H).
5f	73	200-02	2.5(s,3H,3-CO-CH_3), 2.7(s,3H,6′-CH_3), 3.90(s,3H,ph-OCH_3), 7.50(s,1H,2-H), 7.6-7.9(m,8H,ph-H).
5g	69	218-20	2.5(s,3H,3-CO-CH_3), 3.90(s,3H,6′-OCH_3), 7.45(s,1H,2-H), 7.5-7.8(m,8H,ph-H).
5h	70	182-84	2.5(s,3H,3-CO-CH_3), 3.90(s,3H,6′-OCH_3), 7.50(s,1H,2-H), 7.6-7.9(m,8H,ph-H).
5i	72	152-54	2.5(s,3H,3-CO-CH_3), 2.70(s,3H,8′-CH_3), 7.45(s,1H,2-H), 7.5-7.8(m,10H,ph-H).

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