Convenient method for the synthesis of 2-phenyl-4-chloro-3-formylquinoline and its utility for the synthesis of Thieno(3,2-c)-4-phenylquinoline-2-carboxylic acid

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Abstract 2-phenyl-4-chloro-3-formyl quinoline **2** was obtained by the reaction of **1** with $POCl_3$/DMF in CTAB medium. The newly synthesized aldehyde was then converted to acrylic ester **4** via its acid **3** which was then brominated and chlorinated to get the trihalocompound **7** . The trihalocompound thus obtained was treated with thiourea to get the titled compound **8**.

Introduction Varoius quinoline aldehydes were synthesised extensively by using Vilsmeir reagent with micellar medium(**1**). In continuation,herein we report a new method for the synthesis of hitherto new aldehyde 2-phenyl-4-chloro-3-formyl quinoline **2** using $POCl_3$/DMF and CTAB(Cetyl Triethyl Ammonium Bromide) as phase transfer catalyst. The newly synthesized aldehyde was utilized to prepare new angular thienoquinolines

Experimental Melting points were determined on the mettler FP 51 instrument and are uncorrected. IR spectra were recorded on shimazdu FT-IRP (s) 8201 spectrophotometer as KBr pellets. ^1H NMR spectra were recorded on an AMX 400 spectrophotometer in $CDCl_3$. Elemental analyses were performed by Perkin Elmer model 1240 B CHNS analyser and the values are within the permissible limits (± 0.5). Proceedings of the reaction were monitored by using TLC with silicagel-G. Petroleum ether and ethyl acetate were used as irrigant and spots were visualized with iodine.

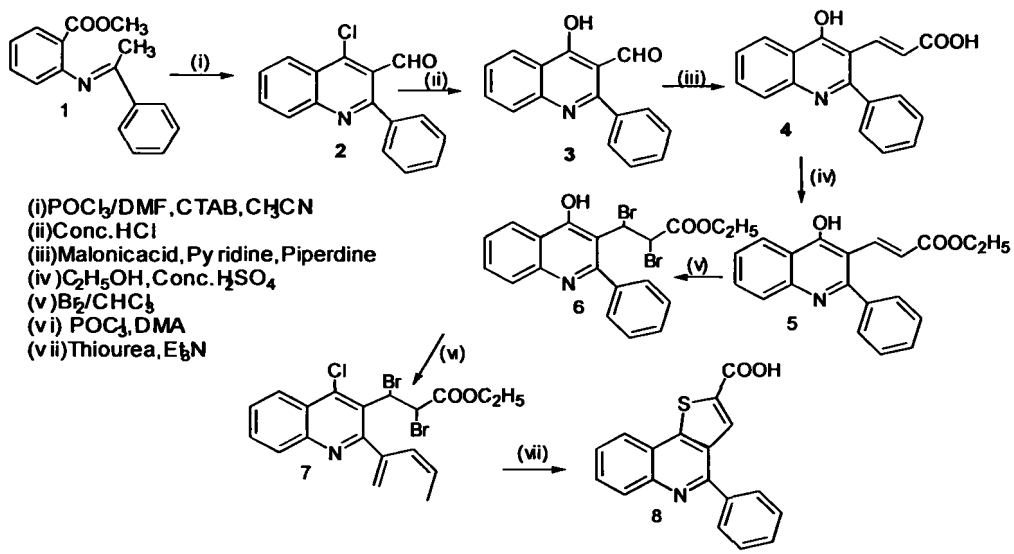
Typical procedure: 2-(1-phenylethylidineamino) methyl benzoate 1
Acetophenone(0.0388mole,4.5mL),Methylanthranilate (0.0388, 5mL) ,3 drops of Conc.HCl is added and the mixtuire was kept aside for 3days . The product **1** crystallizes out. Melting point: 109-111°C IR(KBr)(cm^{-1}) 1737,1620(C=O,C=N).

Typicalprocedure:2-Phenyl-4-chloro-3-formylquinoline 2 To a solution of compound **1** (2.965mmol, 0.750g) in 20mL of acetonitrile was added 0.1mL of CTAB and the solution was stirred under ice cold condition . To this the Vilsmeir adduct (3/2.6mL) $POCl_3$/DMF was added drop by drop and the stirring was continued for ½ an hour and the reaction mixture was further heated for 30 minutes. After the completion of the reaction, the reaction mixture was poured into crushed ice, filtered, dried and purified by column chromatography using petroleumether:ethylacetate(93:7)

Typical procedure: 1-(4-chloro-2-phenyl-(1H) -3-quinolyl-1,2dibromoacrylic ethyl ester
The aldehyde thus obtained was converted to 4-oxo **3**, acrylic acid **4** and then to acrylic ester **5** . The acrylic ester thus obtained was brominated and then chlorinated with $POCl_3$ **7** (**2**).

Typical procedure: Thieno(3,2-c)-4-phenylquinoline-2-carboxylic acid 8 To the solution of 1-(4-chloro-2-oxo-(1H)-3-quinolyl)1,2-dichloroacrylic ethylester (0.00168mol,0.500g) and thiourea (0.00168mol, 0.320g) and 4 drops of triethylamine in 30 mL abs.ethanol was refluxed in a water bath for 6-8 hrs. After the removal of excess solvent, the organic layer was extracted with chloroform and washed with water. Column chromatography of the residue with petroleum ether : ethylacetate furnished a white amorphous compound .

Results and discussion: 2-phenyl-4-chloro-3-formyl quinoline was obtained by the formylation of compound **1** with $POCl_3$/DMF in CTAB medium IR(KBr cm^{-1}) 1685,1033(C=O,C-Cl), ^{1}H-NMR($CDCl_3$) δ10.2(s,CHO), δ(6.8-7.3)(m,9H),Mass m/z 303. The aldehyde thus obtained was converted to 4-oxo derivative by treating with HCl IR(KBr)1685,3360(C=O,OH).and to acrylicacid **4** with malonicacid (0.2g0.0052mol),pyridine(2mL) and piperdine (3drops). IR(KBrcm^{-1})1707(COOH),and then to acrylic ester IR (KBr cm^{-1})1727, 3350(COO,OH), ^{1}H-NMR(DMSO) δ 2.1(t,3H), δ 3.2(q,2H), δ 4.1(d,1H) δ 4.8(d,1H), δ 6.8-7.6(m,9H) Mass m/z=318. The acrylic ester thus obtained was brominated with bromine in $CHCl_3$ and then chlorinated with $POCl_3$(12mL)and DMA(3drops).The product **8** was obtained by refluxing a solution of 1-(4-chloro-2-oxo-(1H)-3-quinolyl)1,2-dbromoacrylic ethylester (0.00168mol) and thiourea(0.00168mol) and 4 drops of triethylamine in 30 mL of abs ethanol in a water bath for 6-8 hrs. After the removal of excess solvent, the organic layer was extracted with chloroform and washed with water. Column chromatography of the residue with petroleum ether: ethylacetate furnished awhiteamorphouscompound.IR(KBrcm^{-1})1727,3350(COO,OH),^{1}H-NMR($CDCl_3$) δ 11.1(s,COOH) δ 9(m,ArH) δ5.5(s,C_3H)Mass m/z=305. **(Scheme-1)** Which was identified as thieno(3,2-c)-4-phenylquinoline-2-carboxylic acid.



Scheme-1

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