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4-chloro-6-methoxy-2-styryl quinoline, its synthesis and antibacterial activity

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ABSTRRACT

P-anisidine on treatment with ethyl aceto acetate in ethanol refluxing for 4 hrs.gave ethyl-3-[4-methoxyphenyl) imino] butanol which is on thermal cyclization in hot propylene glycol at 100^0c gave 4-hydroxy-6-methoxy-2-methyl quinoline. The latter on heating with $POCl_3$ gave 4-chloro-6-methox-2-methyl quinoline which on treatment with benzaldehyde gave corresponding 4-chloro-6-methoxy-2-styryl quinoline. The product have been characterized based on the spectral data and have been evaluated for its antibacterial activity.

Keywords: P-ansidine, Quinoline, Anti bacterial activity, Propylene glycol, Benzaldehyde.

INTRODUCTION

Quinoline ring system is prevalent in a variety of pharmacologically active compounds as well as in natural products. A number of biological activities have been associated with quinoline-containing compounds such as Anti-inflammatory, Anti allergic, Anti-malarial, Anti-bacterial, Anti proliferative, Anticancer etc. Beside these, quinoline ring also occupies a unique position in the design and synthesis of novel biologically active compounds. Halogens containing quinolines are of particular interest, because the Halogen atom can play a crucial role in the compounds bioactive and provides an avenue for further structure elaboration. In view of these considerations it was considered worthwhile to synthesis new quinolines derivatives and evaluate them for their antibacterial activity.

MATERIALS AND METHODS

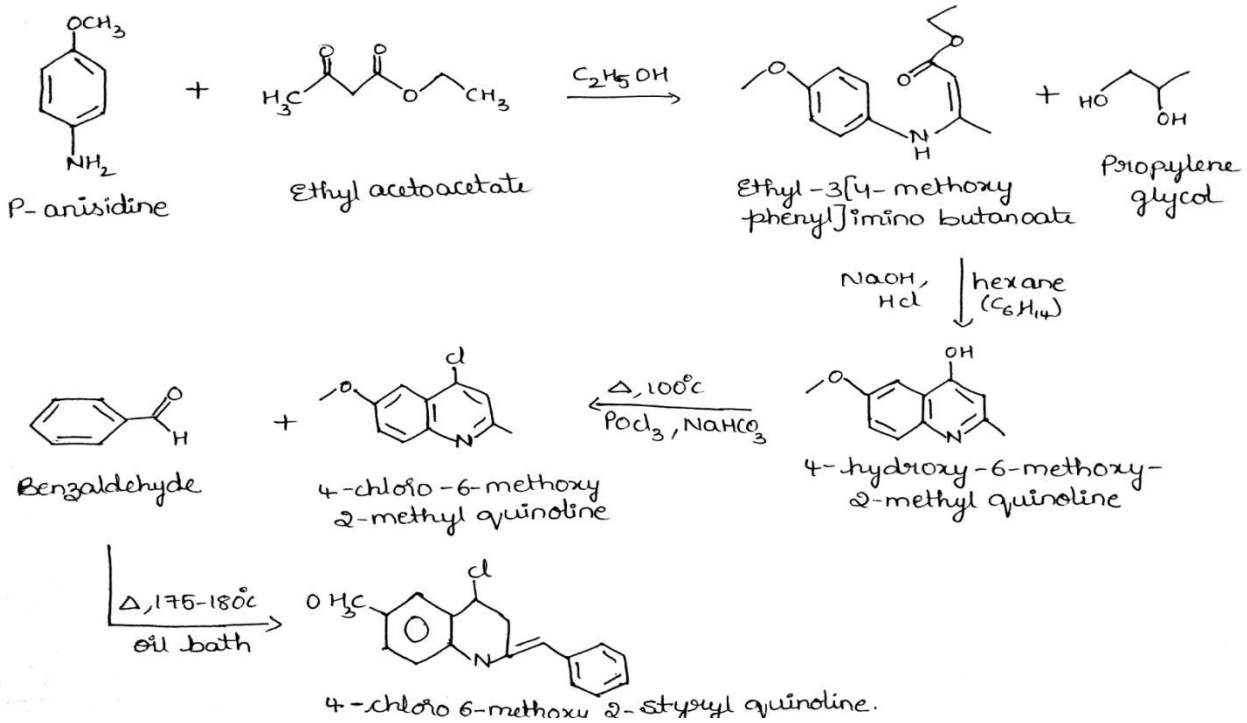
Chemicals used

P-ansidine, Ethyl aceto acetate, Ethanol, Propylene glycol, Hexane, sodium hydroxide, Hydrochloric acid, $POCl_3$, Sodium bicarbonate, Benzayldehyde.

Apparatus used

Soxhlet apparatus, Ice bath, Oil bath, Water bath.

Scheme of experiment



SYNTHESIS PROCEDURE

Preparation of Ethyl-3-[(4-methoxyphenyl) imino] butanol

A mixture of P-ansidine (12.3g, 100mmol), ethyl aceto acetate (13g, 100mmol) and ethanol (150ml) was refluxed on a hot water bath for 4hrs. At the end of this period, the mixture was distilled to half its volume by evaporation. The residual mixture was cooled in ice water bath at 0-5^{0}c when a crystalline solid separated out from the reaction mixture. The mixture was filtered and the insoluble solid was washed with cold ethanol (20ml) and dried, the crude product was re-crystallized from methanol.

Preparation of 4-hydroxy-6-methoxy-2-methyl Quinoline

Compound ethyl-3-[(4-methoxy phenyl) imino]butanol (17g, 80mmol) was added slowly to preheated propylene glycol at 100^{0}c in small lots. After completion of addition, was diluted with hexane and the reaction mixture was cooled to 0^{0}c ,the separated solid was filtered, washed with hexane (2*5ml) and dried. The solid obtained was dissolved in 10% NaOH (100ml), filtered and neutralized with dil.HCL (20%, 20mmol). The separated off white solid was filtered washed with water (2*10ml) and dried.

Preparation 4-chloro-6-methoxy-2-methyl Quinoline

A mixture of compound 4-hydroxy-6-methoxy-2-methyl quinoline (14.15g, 75mmol) and $POCl_3$ (8ml, 80mmol) in 1:3 ratio (w/v) was heated on a water bath at 100^{0}c for 1hr. The reaction mixture was cooled to room temperature, diluted with ice cold water (30ml) and neutralized with super saturated $NaHCO_3$ (20ml) solution. The separated solid was filtered, washed with water (2*20ml) and dried.

Synthesis of 4-chloro-6-methyl-2-styryl Quinoline

A mixture of compound 4-chloro-6-methoxy-2-methyl quinoline (0.52g, 2.5mmol) and benzaldehyde (7.5mmol) in 1:3 ratio (w/v) was heated in oil bath at 60-100^{0}c for about half an hour. When water elimination was observed by water drops appearing on the flask neck i.e after 0.5hrs of heating, the mixture was cooled to room temperature and washed with hexane (2*15ml) inorder to remove unreacted benzaldehyde. The residue was re-crystallized from ethanol to obtain final compound.

Antibacterial studies of 4-chloro-6-methoxy-2-styryl quinoline

The newly synthesized final compound was evaluated for its antibacterial activity against

staphylococcus aureus strains by a standardized suspension of the test bacterium which was inoculated and incubated for 16-18hrs at 37^0c. The minimum inhibitory concentration was noted by observing the area of zone of inhibition.

20ml of agar media was poured into each Petri dish and plates were dried by placing in an incubator at 37^0c for 1hr. Using an agar punch, wells were made and synthesised sample was placed and minimum inhibitory concentration was tested after 48 hrs. A control of amoxicillin was also prepared in the same way and tested for zone of inhibition at 37^0c after 48 hrs. Antibacterial activity was determined for both by measuring the diameter of inhibition zone.

4-choloro-6-methoxy-2-styryl quinoline

standard amoxicillin

Screening of 4-chloro-6-methoxy-2-styryl quinoline for antibacterial activity

s.no.	Organism	Zone of inhibition	
1	Staphylococcus aureus	Standard amoxicillin 7.5mm	4-choloro-6-methoxy-2-styryl quinoline 8mm

RESULTS AND DISCUSSION

p-anisidine was condensed with ethyl aceto acetate in refluxing ethanol to obtain ethyl 3-[(4-methoxy phenyl)imino] butanoate . The latter was thermally cyclized by heating at 100^0c in hot propylene glycol for 0.5hrs to obtain 4-hydroxy-6-methoxy-2-methyl quinoline, this compound on treatment with $POCl_3$ followed by aqueous $NaHCO_3$ treatment gave 4-chloro-6-methoxy-2-methyl quinolone. When this product was treated with benzaldehyde in 1:3 ratio (w/v) at 100^0c followed by simple processing, 4-chloro-6-methoxy-2-styryl quinoline was obtained as product whose structure was assigned based on its spectral characteristics.

4-choloro-6-methoxy-2-styryl quinoline

IR(KBr, $V_{max,}CM^{-1}$):2878 (C-H), 1498 (C-H); H NMR (400 MH_2, $CDCL_3$/TMS):δ PPM 3.81 (S, 3H, OCH_3), 7.01-7.95m(m, 10H, 8 aromattic + two styryl protons); LC/MS; M/Z 314 (M^+ + 1) and (M^+ +3)

REPORT

The antimicrobial screening of newly synthesiszed compounds against antibacterial strains exhibited moderate to very good activity at MIC 7.5_{mm} to 8.5_{mm}.

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