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SYNTHESIS OF NOVEL N-{[2-(MORPHOLIN-4-YL)- QUINOLINE-3-YL] METHYL}2-[(4-AMINOPENTYL) (ETHYL) AMINO] ETHANOL DERIVATIVES

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ABSTRACT

2-(morpholin-4-yl)quinoline-3-carbaldehyde condensed with 2-[(4-aminopentyl)(ethyl)amino}ethanol in alcoholic solvent preferably in isopropyl alcohol to form imines intermediate which on further reduction with suitable reducing agent preferably sodium borohydride to gives corresponding amine derivatives of quinolone Formula-I i.e. N-{[2-(morpholine-4-yl)-quinoline-3-yl-methyl}2-[(4-aminopentyl)(ethyl)amino]ethanol as shown inFig-1.Substituted derivatives at 6^{th}& 7^{th} position of quinoline ring were synthesized.

Keywords: Amine, Quinoline, Imines, Morpholine, Synthesisetc.

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INTRODUCTION

Quinoline and their derivatives are very important in medicinal chemistry[1-3] because of their wide occurrence in natural products and drugs.The rapid and efficient generation of nitrogen-containing privileged structural motifs is a great challenge in biological, organic, and medicinal chemistry.

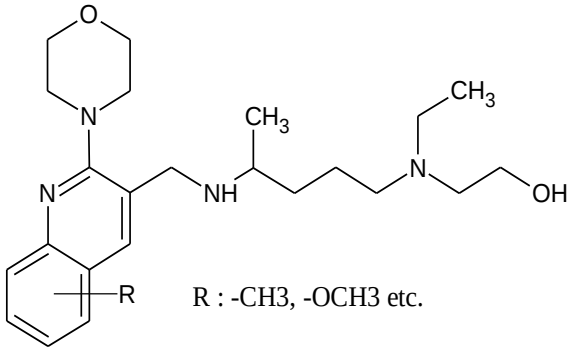

Fig-1: Formula

Quinoline shows interest of research for many years as a large number of natural products contain these heterocycles and they are found in numerous commercial products including pharmaceuticals, fragrances and dyes.Quinoline alkaloids such as quinine, chloroquine, mefloquine and amodiaquine are used as efficient drugs for the treatment of malaria. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmaceutical properties[4-7].Quinoline possess interesting physiological properties such as phthalide isoquinoline alkaloids play interesting roles such as non-narcotic cough suppressant and an effective antagonist of an inhibitory neurotransmitter g-aminobutyric acid (GABA). 2-[(4-aminopentyl)(ethyl)amino} ethanol skeleton used in varieties of biologically potential active hypertensive and antimalarial drugs available in market such as HCQS, Chloroquine phosphate.

MATERIALS AND METHODS

Reactions progress was monitored by thin layer chromatography (TLC) which was performed on 200 µm thick aluminum sheets having silica gel 60F254 as adsorbent. The solvent system used for developing the TLC plate was hexane:ethyl acetate (7:1).Spots were visualized under UV-light.Melting points were determined in open capillary tubes and are uncorrected.

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IR spectra have been recorded on Shimadzu FTIR spectrophotometer; model IR Prestige-21 (cm^{-1}, in KBr). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-400 (400 MHz FT-NMR) in DMSO-*d*6 and TMS was used as internal standard. Peak values are shown in ppm, in the δ scale. Mass spectra were recorded on a Waters micromass ZQ. Starting materials were obtained from S.D.fine&Spectrochem. All the solvents and reagents were of laboratory reagent grade and were dried in advance and redistilled before use whenever required. Column chromatography with silica gel & crystallization techniquewere used to purify the crude products.

EXPERIMENTAL

Synthesis of substitutedN-{[2-(morpholine-4-yl)-quinoline-3-yl-methyl}2-[(4-aminopentyl)(ethyl)amino]ethanol(Ia-c) from 2-(morpholin-4-yl)quinoline-3-carbaldehyde(1a-c)&2-[(4-aminopentyl) (ethyl) amino] ethanol (2) in two stage i.e. formation of imine which was taken insitu to next stage for reduction for corresponding amine.

Experimental procedure:

InRBF under nitrogen atmosphere charge 20 ml Isopropyl alcohol, 1.0gm2-(morpholin-4-yl) quinoline-3-carbaldehyde and 1.1gm2-[(4-aminopentyl)(ethyl) amino]ethanol was added. Heat reaction mass to reflux & maintained for 5 to 6hrs.Reaction progress was monitored with TLC, after reaction completion cooled reaction mass to 45-50^{0}C and distilled Isopropyl alcohol under vacuum to get imine product which was subjected to next stage for reduction. To this reaction mass containing imine product charged 12 ml methanol, 0.55eq Sodium borohydride 25-30^{0}C Maintained reaction mass temperature 60-65^{0}C for 5 to 6 hrs. Cool reaction mass and filtered precipitated product and dried in oven at 45-50^{0}C.

As above all derivatives Ia-c were synthesized & characterized with modern spectroscopic methods as mentioned above.

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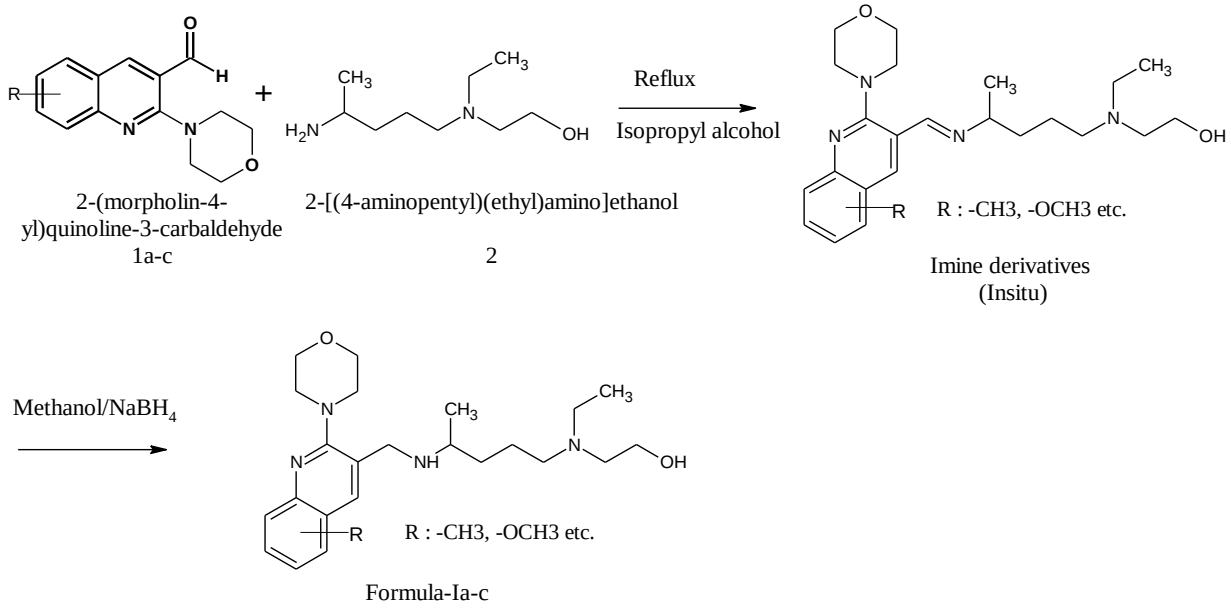
Reaction scheme:

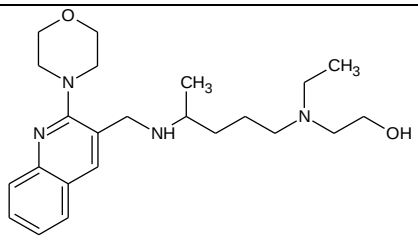
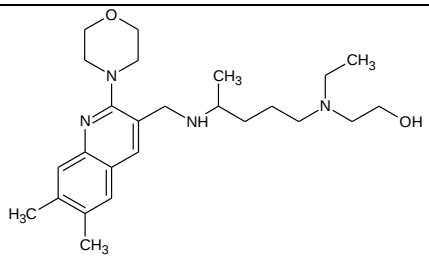
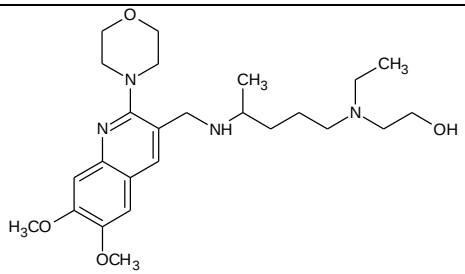


2-(morpholin-4-yl)quinoline-3-carbaldehyde
1a-c

2-[(4-aminopentyl)(ethyl)amino]ethanol
2

Imine derivatives
(Insitu)

Formula-Ia-c

Ia (R=H)	**Ib (R=6,7-CH_3)**	**Ic (R=6,7-OCH_3)**
		

RESULTS AND DISCUSSION

All synthesized compounds Ia-c were obtained with good yield and purity. Compound may exhibits antihypertensive, antimicrobial activities and study for the same is under progress. Quinoline condensed with such amine side chain (2-[(4-aminopentyl) (ethyl) amino] ethanol)exhibits potential activity in treatment of hypertension and antimalarial such as hydroxyl chloroquine sulfate (HCQS) Hydroxychloroquine phosphate (HCQP)& Chloroquine phosphate. These morphine substituted Ia-c new molecules will probably show good biological activities.

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