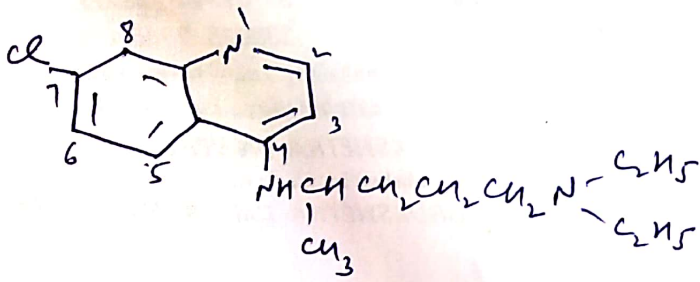
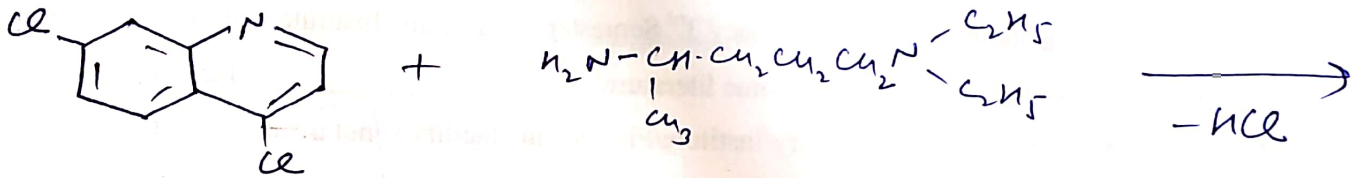


Chloroquine



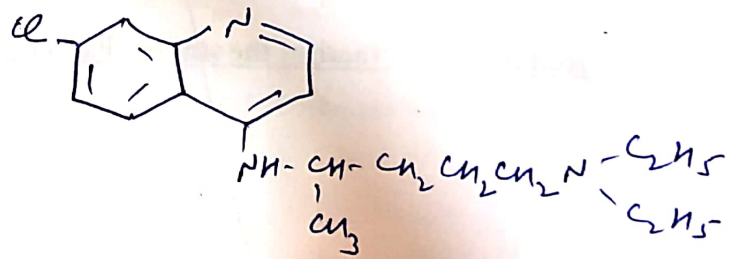
(RS)-7-Chloro-4-(4-diethyl-
-amino-1-methylbutylamino)-
-quinoline

Synthesis:-



4,7-Dichloro-
-quinoline

2-Amino-5-diethyl-
aminopentane

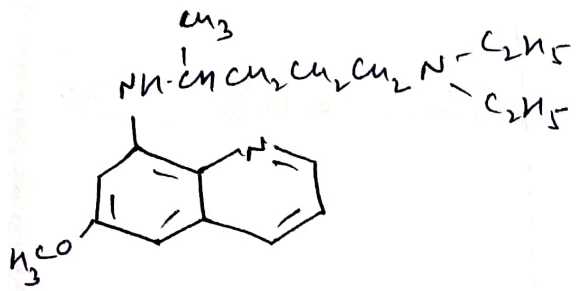


Chloroquine

MOA:- It acts by interaction with DNA. There is intercalation of chloroquine with guanine containing double stranded DNA. It has been reported to inhibit DNA polymerase markedly.

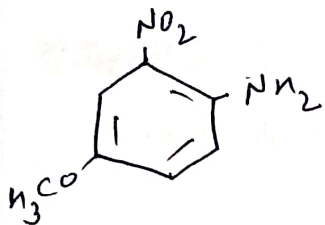
Uses:- It is used for the prophylaxis and treatment of malaria. It has a rapid schizontocidal effect. It kills the erythrocytic forms of malaria parasites at all stages of development.

Pamaquine

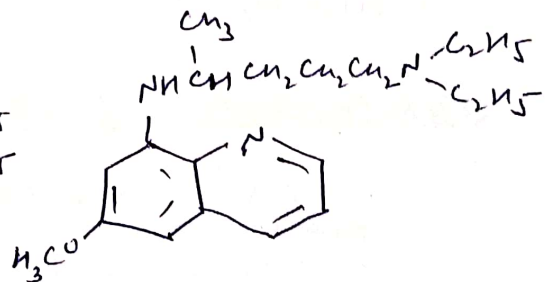
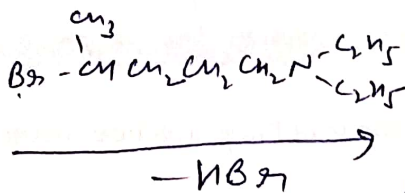
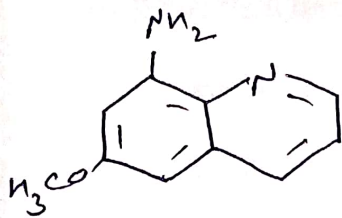
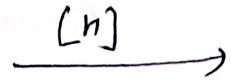
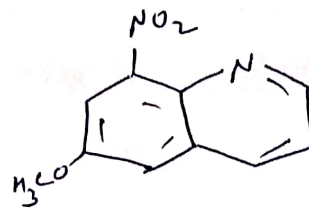
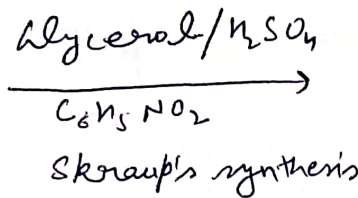


8-(4-Diethylamino-1-methylbutylamino)-6-methoxyquinoline.

Synthesis:-



4-methoxy-2-nitro-aniline



Pamaquine.

MOA:-

It kills the intrahepatic form of Plasmodium vivax and Plasmodium ovale, and thereby prevents the development of the erythrocytic forms that are responsible for relapses.

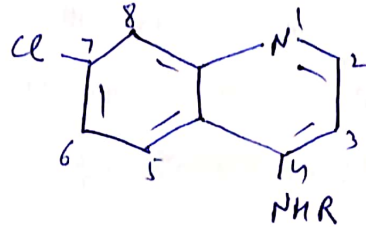
Uses:-

In the treatment of malaria caused by Plasmodium vivax and p. ovale.

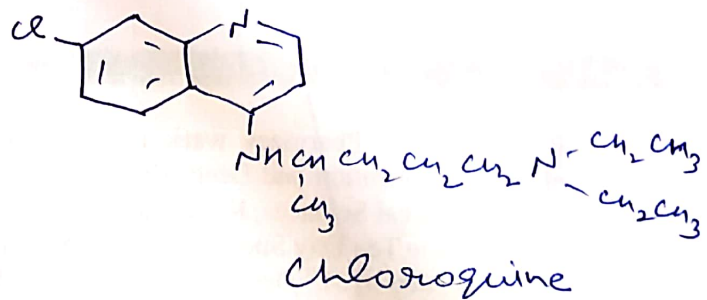
SAR of Antimalarial drugs (Quinolines)

Prototype drug:- Quinine.

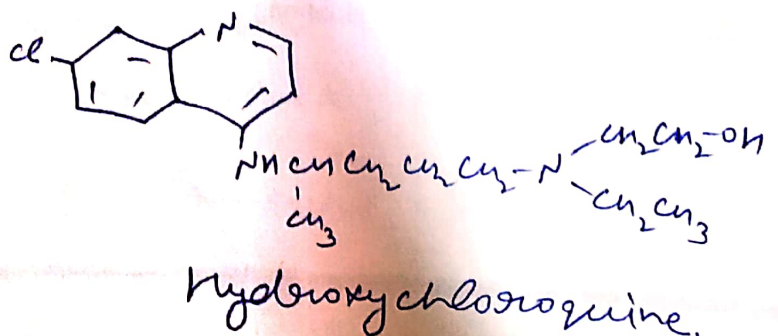
4-Aminoquinolines:-



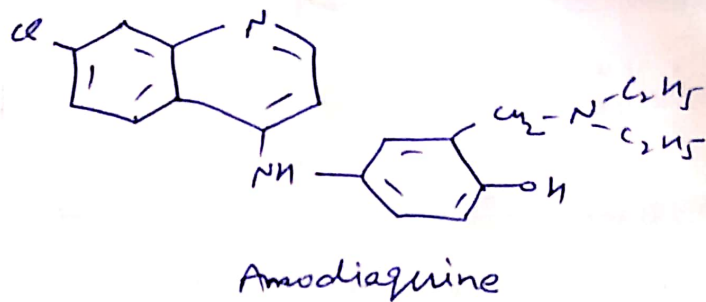
→ At C-4 position, the dialkylaminoalkyl side chain has 2-5 carbon atoms between the nitrogen atoms, which is optimum for activity. e.g. Chloroquine, quinacrine.



→ The substitution of a hydroxyl group on one of the ethyl groups on the tertiary amine reduces toxicity. e.g. Hydroxychloroquine.



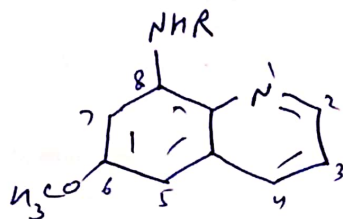
→ Incorporation of an aromatic ring in the side chain, gives a compound with reduced toxicity.
~~and active~~ e.g. Amodiaquine.



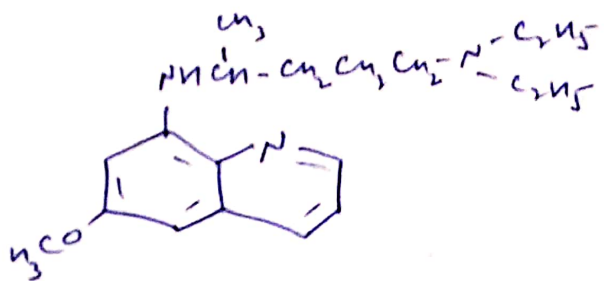
→ The tertiary amine in the side chain is essential for activity.

→ The 7-chloro group in the quinoline nucleus is optimal.

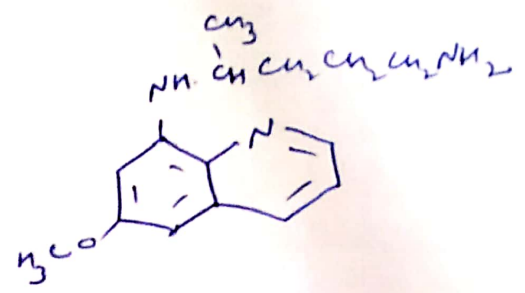
8-Aminoquinolines:-



→ If the dialkylaminoalkyl side chain is attached at 8th position, it gives derivatives of 8-aminoquinolines, e.g. Pamaquine, Primaquine, Quinocide.



Pamaquine

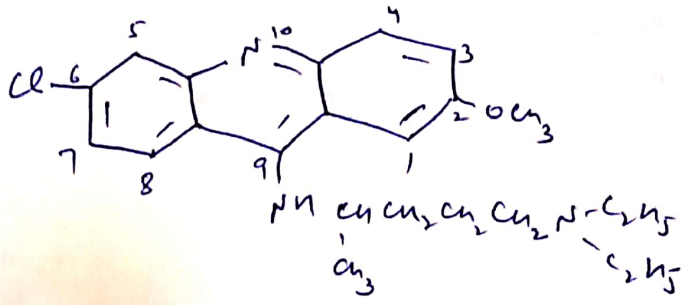


Primaquine

- In this category, tertiary amine is not essential for activity. e.g. Primaquine.
- Methoxy group at position 6 is optimum for activity.

9- Aminoacridines :-

The fusion of an aromatic ring with quinoline nucleus results in the production of an active drug, i.e. Quinacrine.



Quinacrine.