CHEMOTHERAPY OF MALARIA

IV. Synthesis of 4-(Guanidylphenylamino)quinolines

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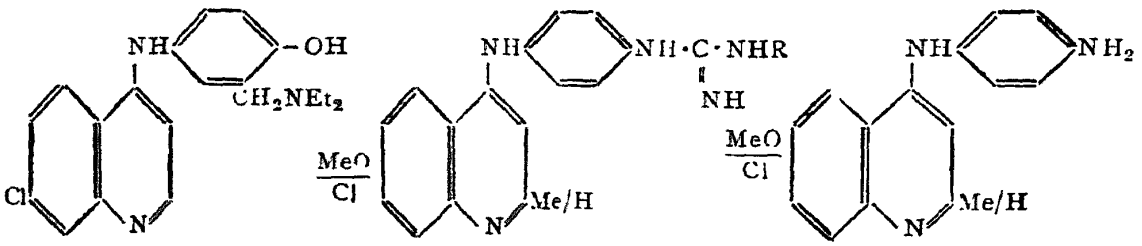
OF the hundreds of 4-aminoquinolines tried against malaria, two classes of compounds have been found to show good therapeutic action: (1) those having an aliphatic side chain terminating in an alkylamino group, such as chloroquin or oxychloroquin, and (2) those having a benzene ring bearing further basic substituents, such as "camoquin" (I). The compounds of second group are easier to synthesise and also manufacture, but the possibilities in this direction have not been fully explored. The attempts to synthesise quinoline derivatives with a guanidine or biguanide side chain at the position 4 having proved a failure as shown in the previous part, as the next best, the synthesis of 4-phenylaminoquinoline derivatives with a guanidine radical substituted in the benzene ring (II) was taken up. This paper records the attempts made to work out a general method of synthesis of compounds of type (II) which could be used to synthesise a variety of quinolines.



(I) (II) (III)

Since we wanted to introduce a variety of substituents (R) in the guanidine residue, attempts were made to synthesise the guanidine derivatives starting from the compound (III). By reacting 4-chloro-6-methoxyquinaldine with *p*-phenylenediamine at 130–40°, Slater[1] obtained 4-(*p*-aminoanilino)-6-methoxyquinaldine, which on acetylation furnished the corresponding acetamino compound. These two compounds have now been prepared by treating 4-chloro-6-methoxy quinaldine with acetphenylenediamine and then hydrolysing the resulting acetamino compound. Similarly, by using 4-chloro-8-methoxy-quinaldine, 4:6-dichloroquinaldine and