CONDENSATION OF QUINOLINE AND ISOQUINOLINE N-OXIDES WITH 3-AMINOCROTONIC ACID DERIVATIVES

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In order to introduce a carbon substituent to the 2-position of quinoline ring, the reactions of some isoxazoles and 3-aminocrotonic acid derivatives with quinoline N-oxide(1) were investigated.

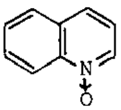
i) 3,5-Dimethyl-4-isoxazolylmagnesium bromide reacted with (1) to give (2) and its N-oxide. The catalytic reduction of (2) over Raney Ni gave rise to (3) which was hydrolyzed to 2-acetonylquinoline.

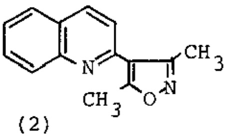
ii) 5-Amino-3-methylisoxazole reacted with (1) in the presence of benzoyl chloride to give (4), which was transformed into 2-quinolineacetamide by catalytic reduction and subsequent hydrolysis.

iii) As well as 5-amino-3-methylisoxazole, 3-methyl-5-isoxazolone was condensed with (1) in the presence of acetic anhydride to give (5). The chloride(6) obtained from (5) with $POCl_3$ was reacted with nucleophiles to give the corresponding products.

iv) Since 3-aminocrotonic acid and its derivatives are considered to be equivalent to the isoxazoles in the reactions described above, the condensation of (1) with such compounds was examined. While ethyl 3-aminocrotonate and the amide reacted with (1) to give the products(7a,b) as expected, the tricyclic compound(8) was obtained by the condensation of (1) with 3-aminocrotononitrile as a main product. The structural determination and the mechanism of the condensation will be discussed in this report.

With some exceptions, these reactions were applicable to the synthesis of isoquinoline derivatives from isoquinoline N-oxide.


(1)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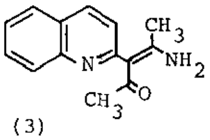
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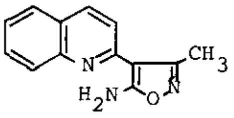
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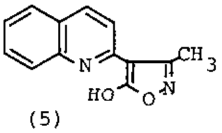
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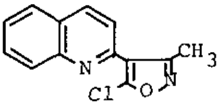
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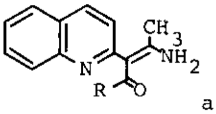
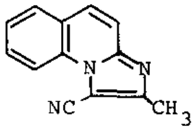

(7a,b)

a: $R=OC_2H_5$
b: $R=NH_2$


(8)