REACTIONS OF AROMATIC N-OXIDES WITH HETEROCYCLIC ACTIVE METHYLENES IN THE PRESENCE OF ACETIC ANHYDRIDE

Seitaro Saeki, Mohammed M. Yousif, Kazuhisa Funakoshi and Masatomo Hamana
Faculty of Pharmaceutical Science, Kyushu University
Maidashi, Higashi-ku, Fukuoka 812, Japan

(I) Reactions with 3-arylrhodanines (A), 2-phenyl-2-oxazolin-5-one (B) and 2-phenyl-2-thiazolin-4-one (C): N-Oxides of quinoline and isoquinoline (1 and 2) reacted with A, B and C at 90° in the presence of Ac_2O, giving the correponding α-substituted products in the usual way. Pyridine N-oxide (3) similarly reacted with A, but not with C. 2-Phenyl-4-(2-pyridyl)-2-oxazolin-5-one was obtained by heating 3 with N-benzoylglycine, Ac_2O and AcONa at 80°.

(II) Preparation of α-CH_2SH and α-CH_2NH_2 derivatives of quinolines, isoquinoline and pyridine: Hydrolysis of 5-substituted-A or 5-substituted-C obtained in (I) with hot 48% HBr afforded 2-quinoline-, 1-isoquinoline- and 2-pyridine-methanethiols, and that of 4-substituted-B with hot 10% HCl gave α-aminomethyl-quinolines, -isoquinoline and -pyridine.

(III) Reactions with barbituric acid (D): The reaction of 1 with D produced not only 5-(2-quinolyl)barbituric acid (E) but also quinolinium 5-barbituric acid ylides (F), depending upon the nature of 1 and the reaction conditions[(a): at R.T. in Ac_2O (1.2 eq)-DMF. (b): at 90° in Ac_2O(1.2 eq)-DMF. (c): at 90° in Ac_2O]. The reactions of quinoline and lepidine N-oxides under the conditions (a) afforded F, whereas those under (b) and (c) gave E. The behavior of 4-methoxy- and 4-chloro-quinoline N-oxides was the very reverse with respect to the conditions (a) and (b); nevertheles, the reaction under (c) yielded also E. 4-Morpholino-, 3-bromo- and 3-acetamido-quinoline N-oxides gave only F, and 3-cyanoquinoline N-oxide did E, independently of the reaction conditions. The regioselectivities and yields were very high in all the cases.

(IV) Reactions with Meldrum's acid (G): Quinoline N-oxides 1 readily reacted with G to give the 2-substituted quinolines, which were converted to the hydrochlorides of 2-methyl, 2-carboxymethyl and 2-methoxycarbonylmethyl derivatives. The reaction with 5-alkyl-G followed by hydrolysis with HCl was proved to be a promising route to 2-alkylquinolines.