NEW ALKYLATIONS OF QUINOLINE N-OXIDES

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In the course of studies of phase-transfer catalyzed reaction of 4-chloroquinoline 1-oxide (1) with carbanions, we happened to find interesting alkylating reactions of 1 and 3-bromoquinoline 1-oxide (2) with active methylene compounds by means of 50% sodium hydroxide (A) or powdered sodium hydroxide (B).

(I) Reaction of 1 with Aliphatic Ketones: Treatment of a dichloromethane solution of 1 with an excess of acetone in the presence of excess A at room temperature gave 2-acetonyl-4-chloroquinoline 1-oxide in 58% yield, the 4-chloro group being inert. A similar result was obtained from the reaction with di-iso-propyl ketone, and reactions with diethyl and di-n-butyl ketones gave the respective deacylation products, the 2-ethyl- and 2-n-butyl derivatives. From the reaction with methylethyl ketone, 4-chloro-2-(2-oxo-n-butyl)- and 4-chloro-2-ethyl-quinoline 1-oxides.

(II) Reaction of 1 with ArCOR: While acetophenone (3) resisted the reaction described in (I), refluxing a benzene solution of 1 and 3 in the presence of B caused the displacement of the 4-chloro group to afford 4-phenacylquinoline 1-oxide in a small yield of 18%. Similar reactions of 1 with propiophenone and benzylphenyl ketone produced 4,4′-(1,1-ethylene)diquinoline 1-oxide and 4-benzylquinoline 1-oxide, respectively.

(III) Reaction of 1 with ArCH$_2$CN: The reaction of 1 with phenylacetonitrile in the presence of A or B also resulted in the displacement of the 4-chloro group to give 4-(phenylcyanomethyl)- (4) and 4-benzoyl-quinoline 1-oxides (5). When the reaction was carried out in boiling benzene under nitrogen or oxygen, 4 or 5 was obtained as the sole product, respectively, in high yield (87 and 86%). This reaction is fairly general and very promising for the route to 4-aroylquinoline 1-oxides.

(IV) Reaction of 2 with Active Methylenes: Treatment of a dimethylsulfoxide of 2 with phenylacetonitrile at 50° in the presence of B afforded 3-(phenylcyanomethyl)quinoline 1-oxide in 32% yield. Similar reactions with α-phenylbutyronitrile and benzylphenyl ketone gave the corresponding 3-substituted products (32 and 38%). It seems most likely that the reaction proceeds by S_{RN} mechanism.