REACTION OF SCHIFF BASES WITH α-HALO KETONES

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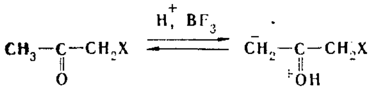
UDC 547.832.5'836:953.4

1-Halomethyl-3-arylbenzo[f]quinoline derivatives were obtained by condensation of Schiff bases with α-halo ketones.

In order to obtain benzo[f]quinoline derivatives with an active halogen in the side chain by condensation of Schiff bases with CH acid compounds we turned to a study of the reaction of arylidene-β-naphthylamines with halo ketones.

It is known [1] that under acid catalysis conditions the —I effect of the halogen atom of a halo ketone and protonation of the carbonyl group oxygen atom promote stabilization of the anion:



$$\mathrm{CH_3{-}\underset{\underset{O}{\|}}{C}{-}CH_2X \xrightleftharpoons{H^+,\ BF_3} \bar{C}H_2{-}\underset{\underset{^+OH}{\|}}{C}{-}CH_2X}$$

In conformity with this, in the reaction of azomethines with halo ketones the hydrogen atom of the methyl group in the ketone molecules should be more labile, and one might expect the formation of 1-halomethyl derivatives of benzo[f]quinoline as the main reaction products. However, when we carried out this reaction under the usual conditions for the condensation of azomethines with ketones (in ethanol; in the presence of hydrochloric acid or boron trifluoride etherate as the catalyst [2, 3]), we observed considerable resinification of the reaction mixture and isolated 1-methyl derivatives of benzo[f]quinolines; admixed 1-halomethylderivative was detected in only a few cases. However, when we carried out the condensation in aprotic solvents (dry benzene and dioxane) in the presence of boron trifluoride etherate we obtained 1-halomethyl-3-arylbenzo[f]quinolines as the major reaction products; admixtures of the corresponding 1-methyl-3-arylbenzo[f]quinolines were detected by thin-layer chromatography (TLC). The IR spectra of all of the synthesized benzo[f]quinoline derivatives containing a CH_2Cl group contained an absorption band at ~605-610 cm^{-1} corresponding to the stretching vibrations of the C—Cl bond. We established by means of IR spectroscopy that the percentage of the 1-methyl derivative of the corresponding benzo[f]quinoline in the reaction mixture increased when the heating time was increased. An appreciable decrease in the integral intensity of the band at 605 cm^{-1} is observed in the IR spectra of samples selected after heating at 90-95°C for 1 h. The 1-methyl derivative of benzo[f]quinoline was isolated as the only reaction product after heating for 2 h. The band at 605 cm^{-1} was absent in the IR spectrum of the latter product. This provides a basis for the assumption that the primary reaction product is the halomethyl derivative. Consequently, condensation of Schiff bases with halo ketones proceeds at the methyl group rather than at the methylene group. The methyl derivative of benzo[f]quinolines may be formed in this case as a result of reduction of the halomethyl group to a methyl group due to the hydrogen liberated from the dihydro derivative of benzo[f]quinoline. All of these observations enable us to imagine the hypothetical trend of the reaction by the scheme (see following page for scheme).

It is known that solvation is the most important factor determining the reactivities of carbanions. The isolation of halomethyl derivatives of benzo[f]quinoline when aprotic nonpolar solvents are used can be explained by the fact that these solvents, while weakly

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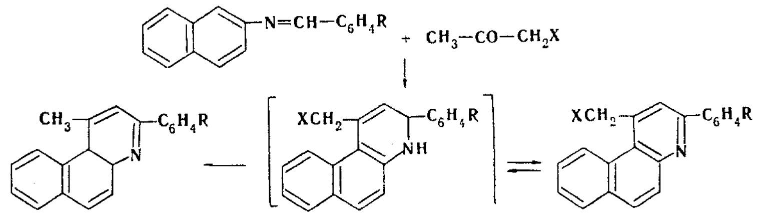
Institute of Physical Organic Chemistry, Academy of Sciences of the Belorussian SSR, Minsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 811-813, June, 1975. Original article submitted November 11, 1973; revision submitted August 15, 1974.

TABLE 1. 1-Halomethyl-3-arylbenzo[f]quinolines

Halogen	R	mp, °C	Empirical formula	Found, %				Calc., %				Yield, %
				C	H	N	halogen	C	H	N	halogen	
Cl	H	125—126	$C_{20}H_{14}ClN$	79,3	4,5	4,6	11,5	79,1	4,6	4,6	11,7	48
Cl	*p*-NO_2	200—201	$C_{20}H_{13}ClN_2O_2$	69,0	3,8	8,0	10,1	68,8	3,7	8,0	10,2	45
Cl	*m*-NO_2	186—187	$C_{20}H_{13}ClN_2O_2$	69,0	3,9	7,8	10,0	68,8	3,7	8,0	10,2	40
Cl	*p*-Cl	127—128	$C_{20}H_{13}Cl_2N$	71,0	4,0	3,7	20,7	71,0	3,8	4,1	21,1	65
Cl	*p*-OCH_3	146—147	$C_{21}H_{16}BrNO$	75,9	4,9	4,0	10,4	75,6	4.8	4,2	10,6	35
Br	H	160—161	$C_{20}H_{14}BrN$	69,0	4,1	3,7	22,7	69,0	4,0	4,0	23,0	50
Br	*p*-NO_2	212—213	$C_{20}H_{13}Br_2N$	61,5	3,4	7,1	20,2	61,1	3,3	7,1	20,4	46
Br	*p*-Br	166—167	$C_{20}H_{13}BrN_2O_2$	55,8	3,2	3,0	36,9	56,2	3,1	3,3	37,4	80
Br	*p*-OCH_3	151—152	$C_{21}H_{16}ClNO$	66,6	4,2	3,7	20,9	66,7	4,2	3,7	21,0	40



solvating the resulting anion, apparently do not suppress its nucleophilic activity, whereas boron trifluoride, owing to its electrophilic properties, stabilizes the anion. When the reaction is carried out in alcohol in the presence of hydrochloric acid, the first step apparently involves reduction of the resulting halomethyl derivative of benzo[f]quinoline.

The structures of the 1-halomethyl-3-aryl derivatives of benzo[f]quinoline were confirmed by means of the UV spectra, which have the form characteristic for benzo[f]quinolines, and by the results of elementary analysis. The purity of the products was confirmed by TLC. The physical characteristics of all of the compounds are presented in Table 1.

EXPERIMENTAL METHOD

Chloro- and bromoacetone were prepared by the method in [4]. The individuality of the substances was monitored by TLC on activity II Al_2O_3. The eluent was benzene, and the chromatograms were developed with iodine vapors. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer.

Reaction of Arylidene-β-naphthylamines with Halo Ketones in Dioxane.* A 2-ml sample of boron trifluoride etherate and 1 ml of halo ketone were added to a solution of 0.01 mole of the Schiff base in 20 ml of dry dioxane, and the mixture was heated with stirring at 90-95° for 30-40 min. The excess solvent was then removed by distillation, the residue was cooled, and the crystalline precipitate was removed by filtration and treated with cold NH_4OH. The corresponding 1-halomethyl-3-arylbenzo[f]quinoline derivatives were isolated by crystallization of the products from toluene and ethanol (Table 1).

Reaction of Arylidene-β-naphthylamines with Halo Ketones in Ethanol. A 1-ml sample of $C_6H_5NO_2$, 1 ml of halo ketone, and eight to 10 drops of concentrated HCl were added to a solution of 0.01 mole of the Schiff base in ethanol, and the mixture was heated in an ampul at 100-110° for 1 h. It was then cooled, and the precipitate was removed by filtration, treated with ammonium hydroxide, and crystallized from ethanol and toluene to give 1-methyl-3-arylbenzo[f]quinoline derivatives [R and yields (in %) given]: H 32, p-NO_2 50, and m-NO_2 62.

The benzo[f]quinoline derivatives were identified by means of genuine products (synthesized from acetone and the appropriate azomethine) by TLC and IR spectroscopy. No melting-point depressions were observed for mixtures of the products with genuine samples.

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*The yield of the target product was considerably lower in benzene, and pronounced resinification was observed.

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