SIMPLE METHOD FOR THE SYNTHESIS OF 2-TRICHLOROMETHYL-4-QUINAZOLONES

M. V. Vovk and L. I. Samarai

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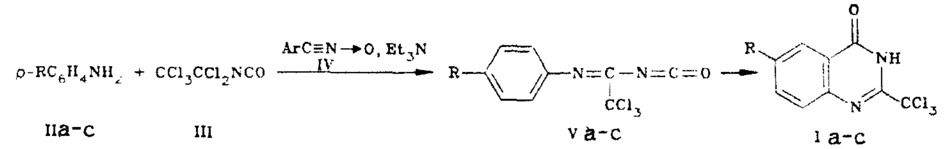
We have previously suggested several approaches to the synthesis of 4-quinazolones I based on the thermolysis of imidazoline-4,5-dione hydrochlorides [1], the reaction of N-arylimino carboxylic acid chlorides with silver cyanate [1], and the phosgenation of N-arylamidines [2].

We have found a new preparatively simple method for the synthesis of 2-trichloromethyl-4-quinazolones Ia-c that proceeds in virtually one step. It consists in the reaction of aromatic amines IIa-c with perchloroethyl isocyanate (III) in the presence of equimolar amounts of 2,4,6-trimethylbenzonitrile oxide (IV). The role of nitrile oxide IV consists in its unique blocking, in the initial stage of the reaction, of the heterocumulene group of isocyanate III [1]; nitrile oxide IV can be recovered in almost quantitative yield after completion of the process. It was established by IR spectroscopy that the reaction actually proceeds through a step involving the previously postulated [2] N-arylimino carboxylic acid isocyanates Va-c (see [3]), which undergo intramolecular cyclization on refluxing in benzene.



I, II, V a R=H; b $R=CH_3$; c R=Br; IV $Ar=2,4,6-(CH_3)_3C_6H_2$

A solution of 0.01 mole of nitrile oxide IV and three to four drops of triethylamine were added to a solution of 0.01 mole of isocyanate III in 20 ml of benzene, and the mixture was allowed to stand for 10-12 h. A solution of 0.01 mole of amines IIa-c and 0.02 mole of triethylamine in 15 ml of benzene was then added with stirring, and the precipitated triethylamine hydrochloride was removed by filtration. Intense absorption bands of N=C=O (2260 cm^{-1}) and C=N (1640 cm^{-1}) groups of isocyanates Va-c were observed in the IR spectra of the filtrates. The filtrates were refluxed for 1 h and evaporated, 10 ml of diethyl ether was added to the residue, and the undissolved quinazolones Ia-c were removed by filtration. After evaporation, 95-97% of the starting nitrile oxide IV was isolated from the filtrates.

2-Trichloromethyl-4-quinazolone (Ia). This compound had mp 210-211°C [4]. IR spectrum (KBr): 1665 (C=O), 3240 cm^{-1} (N—H). PMR spectrum [in $(CD_3)_2O$]: 10.94 (1H, s, NH), 7.37-7.73 ppm (4H, m, H_{arom}). The yield was 81%.

2-Methyl-2-trichloromethyl-4-quinazolone (Ib). This compound had mp 229-230°C [5]. IR spectrum (KBr): 1670 (C=O), 3190 cm^{-1} (N—H). PMR spectrum [in $(CD_3)_2CO$]: 11.67 (1H, s, NH), 7.73-7.96 (3H, m, H_{arom}), 2.46 ppm (3H, s, CH_3). The yield was 79%.

6-Bromo-2-trichloromethyl-4-quinazolone (Ic, $C_9H_4BrCl_3N_2O$). This compound had mp 249-250°C (from acetone). IR spectrum (KBr): 1675 (C=O), 3260 cm^{-1} (N—H). PMR spectrum [in $(CD_3)_2CO$]: 11.31 (1H, s, NH), 7.23-7.41 ppm (3H, m, H_{arom}). The yield was 84%.

The results of elementary analysis were in agreement with the calculated values.

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