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SYNTHESIS OF 3-AMINO-1,2,3,4-TETRAHYDRO-QUINAZOLINE-2,4-DIONE

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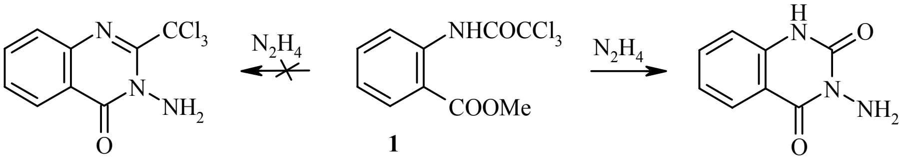
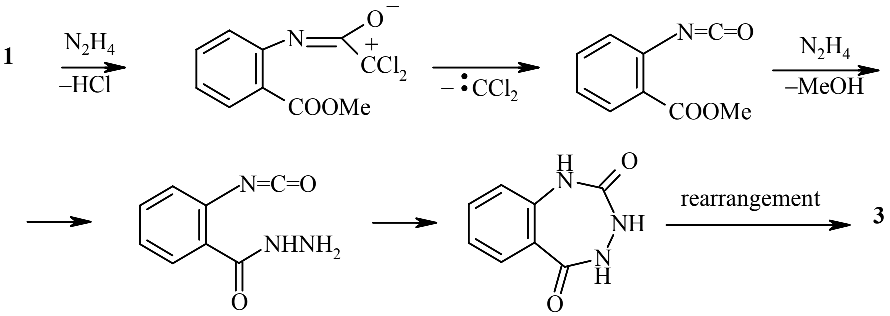
We expected that methyl N-trichloroacetylanthranilate (**1**), by analogy with methyl anthranilates acylated by aliphatic acids [1], would react with hydrazine to give 3-amino-2-trichloromethyl-3,4-dihydro-4-quinazolinone (**2**). However, 3-amino-1,2,3,4-tetrahydroquinazoline-2,4-dione (**3**) was isolated in about 30% yield in the case of an equimolar reagent ratio and in 65% yield with a 1:2 amide–hydrazine reagent ratio.



2 **1** **3**

We propose that hydrazine acts as a strong base to remove HCl from the trichloroacetamide group, which converts to an isocyanate group through subsequent loss of dichlorocarbene. In parallel, a hydrazide group is generated from the ester group by the action of excess hydrazine. The hydrazide group undergoes intramolecular nucleophilic addition to the isocyanate group to give seven-membered heterocycle **4**, which rearranges under the reaction conditions to give **3**.



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The ^{1}H NMR spectra of the products were taken on a Varian Gtshen-300 spectrometer at 300 MHz.

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Methyl N-Trichloroacetylanthranilate (1). A mixture of trichloroacetyl chloride (30 ml, 0.26 mol) and methyl anthranilate (34.5 ml, 0.26 mol) in toluene (250 ml) was heated at reflux until the onset of HCl liberation and complete dissolution of the amine hydrochloride suspension. Then, 200 ml solvent was distilled off the reaction mixture and petroleum ether (150 ml) was added to the residue. The mixture was cooled to -11°C and the yellow needle precipitate of amide **1** was filtered off to give 67.8 g (88%) of **1**; mp 85-87°C (heptane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.79 (3H, s, CO_2CH_3); 7.13-7.88 (4H, m, arom protons); 10.62 (1H, s, $N\underline{H}$). Found, %: C 40.72; H 2.60; N 4.54. $C_{10}H_8Cl_3NO_3$. Calculated, %: C 40.50; H 2.72; N 4.72.

3-Amino-1,2,3,4-tetrahydro-2,4-quinazolinedione (3). A mixture of amide **1** (29.6 g, 0.10 mol) and 98% hydrazine hydrate (11.0 ml, 0.20 mol) in methanol (250 ml) was heated at ~100°C. After 2 h, 200 ml of solvent was distilled off the suspension formed and the residue was cooled to 0°C. The precipitate formed was filtered off, washed on a filter with three 50-ml water portions, and dried at 100°C to give 11.5 g (65%) of **3** as colorless crystals; mp 287-289°C (1:4 DMF–methanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.50 (2H, s, $N\underline{H}_2$). 7.22-7.94 (4H, m, arom protons); 11.6 (1H, s, $N\underline{H}$). Found, %: C 54.01; H 4.11; N 23.98. $C_8H_7N_3O_2$. Calculated, %: 54.24; H 3.98; N 23.72.

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