Phosphorus Pentoxide in Organic Synthesis. XXX.* New Synthesis of 4(3*H*)-Quinazolinones

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We have reported[2] that methyl *N*-acylanthranilates react with a mixture of hydrochlorides of aliphatic or aromatic primary amines, phosphorus pentoxide and *N,N*-dimethylcyclohexylamine at 180 °C to give 4(3*H*)-quinazolinones.

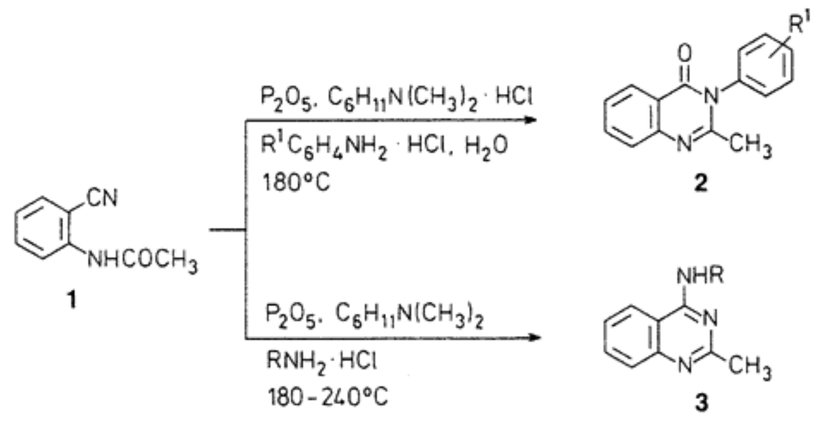
We now prepare 4(3*H*)-quinazolinones (**2**) by reaction of 2-acylaminobenzonitrile with arylamine hydrochlorides, phosphorus pentoxide, *N,N*-dimethylcyclohexylamine hydrochloride and water at 180 °C in 31–53 % yields. The reaction is finished within 20–40 min according to silica TLC used to follow the disappearance of starting material **1**.

This new method of preparing 4(3*H*)-quinozolinones can also be used for preparation of the hypnotic drugs[3] meclaqualone (**2**, R^1 = 2-Cl) and methaqualone (**2**, R^1 = 2-CH_3) in 31 % and 53 % yields, respectively.

Addition of water to the reaction mixture is decisive for obtaining the 4(3*H*)-quinazolinones (**2**). Previously, we have reported [4] that quinazolinamines (**3**) were isolated when **1** reacted at 180–240 °C with the same reagent mixture as in the present investigation, but without addition of water.

Experimental

*3-Aryl-2-methyl-4(3*H*)-quinazolinones. General Procedure.* The reagent was prepared by mixing P_2O_5 (8.5 g, 60 mmol), *N,N*-dimethylcyclohexylamine hydrochloride (9.8 g, 60 mmol), arylamine hydrochloride (60 mmol) and water (2.16 g, 120 mmol) in a flask fitted with a mechanical stirrer and a reflux condenser with a drying tube ($CaCl_2$). The mixture was heated in an oil bath at 200–220 °C (oil bath temperature) until a homogeneous mixture was achieved (ca. 0.5 h). The oil bath temperature was adjusted to 180 °C and the starting material **1** (15 mmol) was added and allowed to react for the specified reaction time. At 10 min intervals a small sample was withdrawn from the reaction mixture, dissolved in 2M NaOH and the solution was extracted with CH_2Cl_2. The extract was subjected to silica TLC [CH_2Cl_2/CH_3OH (19:1)] in order to follow the disappearance of **1**. The reaction mixture was allowed to cool to about 100 °C and 2M NaOH solution (250 ml) was added until alkaline reaction (pH 9–11). The mixture was stirred at room temperature until the reaction cake was digested. The alkaline aqueous solution was then extracted with CH_2Cl_2 (3 × 100 ml). CH_2Cl_2 was stripped off and *N,N*-dimethylcyclohexylamine was distilled off at 10 mmHg. The unreacted aniline derivative was distilled off at 1 mmHg at 100 °C. The crude products were recrystallized from methanol to give pure compounds with melting points in agreement with those reported in the literature.[2,5–7] The following compounds were prepared (R^1, yield/%, reaction period/min): H, 43, 20; 4-F, 37, 30; 3-F, 46, 30; 2-F, 53, 40; 4-Cl, 50, 35; 3-Cl, 38, 30; 2-Cl, 31, 40; 4-CH_3, 33, 20; 3-CH_3, 40, 30; 2-CH_3, 53, 25.



Scheme 1.

*Part XXIX, see Ref. 1.

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