AN ORIGINAL METHOD FOR THE SYNTHESIS OF QUINAZOLINES

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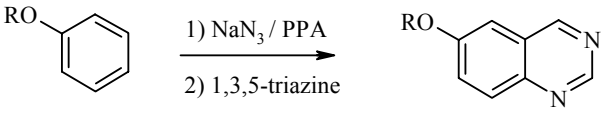
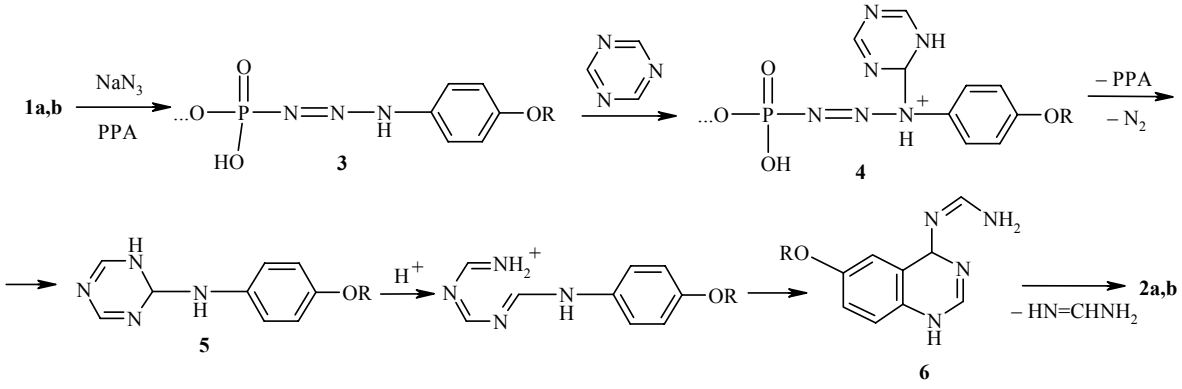
Quinazolines are a well-known class of heterocyclic compounds, for which quite a few methods of synthesis have been developed (see, for example, the work of Chilin et al. [1]). Nevertheless, methods involving the formation of the N(1)–C(8a) and C(4)–C(4a) bonds have not been reported. In the present work, we propose such a method based on the recently reported NaN_3/PPA reagent combination [3]*. The reaction of phenol **1a** or anisole **1b** (1 mmol) and NaN_3 (1.1 mmol) in PPA (2-3 g) at 55-60°C over 3 h monitored by thin-layer chromatography with subsequent addition of 1,3,5-triazine (1.5 mmol) and heating for an additional 4 h at 90-100°C leads to quinazoline **2a** in 49% yield or quinazoline **2b** in 54% yield.



1a,b **2a,b**

1, 2 a R = H, **b** R = Me

The reaction, evidently procedes trough the following stages sequence:



*The PPA sample used containing 86% P_2O_5 was prepared according to Uhlig [2].

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The reaction of sodium azide in PPA with the activated arene gives intermediate **3** [3], which reacts with 1,3,5-triazine to give compound **4**. The decomposition of **4** gives N-(arylamino)triazine **5**, which undergoes ring opening and subsequent intramolecular electrophilic substitution to give quinazoline derivative **6**. The loss of formamidine from compound **6** gives the desired quinazoline **2**.

The NMR spectra were taken on a Bruker WP-200 spectrometer at 200 MHz with TMS as the internal standard. The reaction course and purity of the products were monitored by thin-layer chromatography on Silufol UV-254 plates with ethyl acetate as the eluent.

The reaction mixture was treated with 50 ml water and filtered. The filtrate was extracted with three 50-ml portions of ethyl acetate. The aqueous layer was brought to pH 9-10 by adding ammonium hydroxide. The precipitate formed or oil was extracted by three 50-ml portions of ethyl acetate. The solvent was evaporated off and the products obtained were purified by recrystallization.

6-Hydroxyquinazoline (2a) was obtained in 49% yield (0.072 g); mp 237-239°C (water) (mp 239°C [1]). ^{1}H NMR spectrum in DMSO-d_6, δ, ppm (*J*, Hz): 7.61 (1H, dd, *J* = 9.1, *J* = 2.5, H-7); 7.99 (1H, d, *J* = 9.1, H-8); 8.14 (1H, d, *J* = 2.5, H-5); 9.18 (1H, s, H-4); 9.28 (1H, s, H-2). Found, %: C 65.71; H 4.17; N 19.14. $C_8H_6N_2O$. Calculated, %: C 65.75; H 4.14; N 19.17.

6-Methoxyquinazoline (2b) was obtained in 54% yield (0.086 g); mp 71-72°C (petroleum ether) (mp 71°C [1]). ^{1}H NMR spectrum in $CDCl_3$, δ, ppm (*J*, Hz): 3.95 (3H, s, OCH_3); 7.13 (1H, d, *J* = 2.5, H-5); 7.56 (1H, dd, *J* = 9.2, *J* = 2.5, H-7); 7.94 (1H, d, *J* = 9.2, H-8); 9.21 (1H, s, H-4); 9.29 (1H, s, H-2). Found, %: C 67.45; H 5.05; N 17.51. $C_9H_8N_2O$. Calculated, %: C 67.49; H 5.03; N 17.49.

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