SYNTHESIS OF 8-HYDROXY-2,5,7-TRIMETHYL-4-PHENYLQUINAZOLINE

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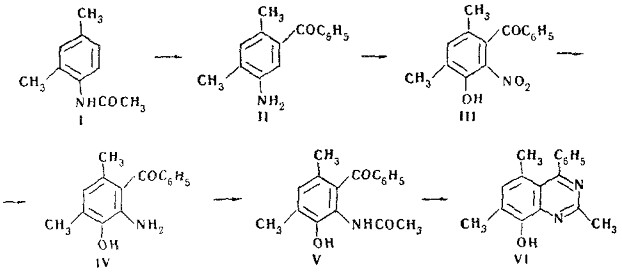
The synthesis of 8-hydroxy-2,5,7-trimethyl-4-phenylquinazoline (VI) starting from 2,4-dimethylacetanilide (I) and the color reactions of VI with cations are described.

Derivatives of 8-hydroxyquinazoline are known as highly selective chelating agents [1]. In the present paper we describe the synthesis of the previously unknown 8-hydroxy-2,5,7-trimethyl-4-phenylquinazoline (VI) by the following route:



5-Amino-2,4-dimethylbenzophenone (II) was obtained, in contrast to the method described by Chardonnens [2], by the direct acylation of 2,4-dimethylacetanilide (I). Compounds III–VI were obtained in a similar manner to the acetophenone derivatives synthesized previously [3].

Compound VI gives color reactions with copper (II), zinc, cadmium, mercury (I, II) silver, cobalt (II), and palladium (II) ions, while 8-hydroxy-2,4,5-tetramethylquinazoline reacts only with copper (II), zinc, mercury (II), thalium (I), and lead [4]. The coupling of 2-methylquinazolines with diazonium salts in an acid medium has been described [5]. However, compound VI does not react even with p-nitrobenzenediazonium chloride in an acid medium. In an alkaline medium, VI couples with p-nitro- and o-carboxybenzenediazonium chlorides with the formation of colored compounds.

EXPERIMENTAL

5-Amino-2,4-dimethylbenzophenone (II). With stirring, 125 g (0.9 mole) of anhydrous aluminum chloride was added gradually to 48.5 g (0.3 mole) of 2,4-dimethylacetanilide in 250 ml of carbon disulfide at a temperature not exceeding 40°C. At the same temperature, 71.0 g (0.5 mole) of benzoyl chloride was added over 2 hr to the pink-red mass formed. The mixture was boiled for another 2 hr and the carbon disulfide was distilled off. The residue was poured onto 300 g of ice. The resinous product was separated off and boiled with 200 ml of 18% hydrochloric acid for 2 hr. The precipitate that separated after cooling was dissolved in 120–150 ml of water and the pH was brought to 8–10 with saturated sodium carbonate solution. The precipitate that deposited was washed with water, dried, and recrystallized from aqueous ethanol (1:1). Yield 42.0 g (63%), mp 101°C (according to the literature [2], 103–104°C).

5-Hydroxy-2,4-dimethyl-6-nitrobenzophenone (III). At 0–10°C, a solution of 2.5 g (0.034 mole) of sodium nitrite in 14 ml of water was added to 5.0 g (0.022 mole) of II in 10 ml of nitric acid (d 1.34) and 30 ml of water and the mixture was filtered from a small amount of resin, kept at room temperature for 2 hr, heated at 50° C for 3 hr, and cooled to room temperature. The precipitate formed was filtered off and was twice recrystallized from ethanol. This gave 2.6 g (43%) of III. Yellow crystals, mp 119.5–120°C. Readily soluble in ethanol benzene, chloroform, and 2 N NaOH; sparingly soluble in water. Found, %: C 66.19; H 4.98. Calculated for $C_{15}H_{13}NO_4$, %: C 66.41; H 4.83.

6-Amino-5-hydroxy-2,4-dimethylbenzophenone (IV). With stirring, 50.0 g (0.30 mole) of sodium hydrosulfite in 80 ml of water was added to a suspension of 10.0 g (0.036 mole) of III in 100 ml of water and 25 ml of ethanol, and the mixture was heated to 60–70°C and stirred for 30 min, after which it was extracted with benzene (4 × 100 ml). The benzene extracts were evaporated in vacuum at 50–60°C to ~30 ml. The crystals that deposited on cooling were filtered off, washed with 10 ml of cooled benzene, and recrystallized from benzene. Yield 6.0 g (80%). Light yellow crystals, mp 125° C. Soluble in benzene, ethanol, acetone, chloroform, and water. Found, %: C 74.27; H 6.20; N 5.76. Calculated for $C_{15}H_{15}NO_2$, %: C 74.67; H 6.27; N 5.80.

6-Acetylamino-5-hydroxy-2,4-dimethylbenzophenone (V). To a solution of 2.5 g (0.011 mole) of IV in 20 ml of acetic acid were added 1.85 g of sodium acetate and, slowly, in drops, 0.9 g (0.012 mole) of acetyl chloride. The mixture was heated to 50° C, stirred for 15–20 min, poured into water, and left overnight. The product was recrystallized from ethanol. Yield 2.5 g (86%). White scales, mp 150° C. Soluble in ethanol, acetone, dimethylformamide, chloroform, benzene, and alkali; insoluble in water and hydrochloric acid. Found, %: C 72.50; H 6.04; N 4.85%. Calculated for $C_{17}H_{16}NO_3$, %: C 72.33; H 5.72; N 4.96.

8-Hydroxy-2,5,7-trimethyl-4-phenylquinazoline (VI). 14.0 g (0.05 mole) of V was added to a melt of 420 g of ammonium acetate. Ammonia was passed through the mixture at 150–160°C for 3 hr 30 min. The cooled mass was diluted with water (~1000 ml). The resinous precipitate that deposited was recrystallized from 75% ethanol. Yield 10.2 g (67.1%). Gray powder, mp 84° C. After vacuum sublimation—yellow needles, mp 84° C. Soluble in benzene, acetone, carbon tetrachloride, ethanol, acetic acid, alkali, and hydrochloric acid; insoluble in water. Found, %: C 76.96; H 6.28; N 10.59. Calculated for $C_{17}H_{16}N_2O$, %: C 77.24; H 6.11; N 10.60.

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