Synthesis of quinolines involving electrophilic amination of arenes with sodium azide in polyphosphoric acid

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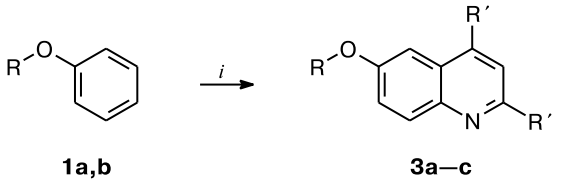
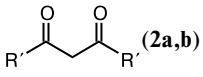
Quinolines are well-known compounds for which a considerable number of synthetic methods have been developed.[1] Nevertheless, no methods including the formation of the N(1)—C(8a) and C(4)—C(4a) bonds were known in the literature. In the present work, we proposed such a method, which is based on the recently found reagent combination NaN_3/polyphosphoric acid (PPA*).[3] We showed that the reactions of phenol (**1a**) and anisole (**1b**) with NaN_3 in PPA at 55—60 °C for 3 h followed by addition of 1,3-dicarbonyl compound **2a,b** and heating for additional 3 h at 120—130 °C afford quinolines **3a—c** in yields of 31—42% (Scheme 1).

Scheme 1



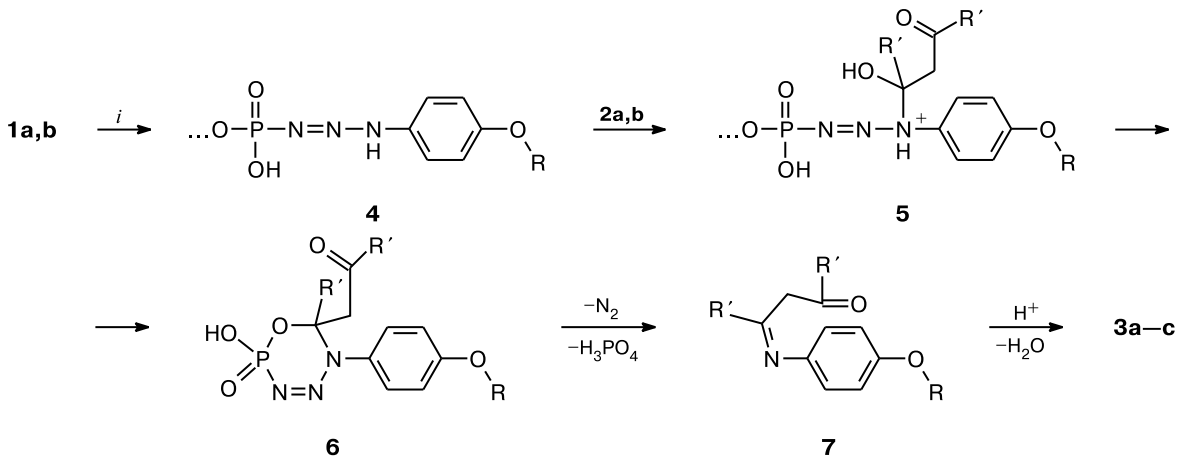
i. 1) NaN_3/PPA; 2) 

R = H (**1a**), Me (**1b**); R′= Me (**2a**), Ph (**2b**); R = H, R′ = Ph (**3a**), R = Me, R′= Ph (**3b**), R = R′ = Me (**3c**).

The proposed mechanism of this transformation includes the formation of triazene **4** according to the mechanism analogous to that given in Ref. 3, the electrophilic attack of **4** by 1,3-dicarbonyl compound, cyclization of intermediate **5** to compound **6**, and decomposition of the latter to yield azomethine **7**, whose intramolecular alkylation affords quinolines **3** (Scheme 2).

Thus, the consecutive reaction of sodium azide and a 1,3-dicarbonyl compound with an aromatic compound in PPA results in quinolines through the *one-pot* reaction. In future, we intend to study to what extent this reaction is general with respect to aromatic and heteroaromatic compounds.

Scheme 2



i. NaN_3, PPA.

* PPA containing 86% of P_2O_5, which has been prepared according to the published procedure,[2] was used.

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NMR spectra were recorded on a Bruker WP-200 (200 MHz) instrument using $SiMe_4$ as the internal standard. The course of the reaction and purity of the compounds synthesized were monitored by TLC on Silufol UV-254 plates using chloroform as a solvent.

Synthesis of compounds 3a—c (general procedure). A mixture of phenol (**1a**) or anisole (**1b**) (1 mmol) and NaN_3 (0.072 g, 1.1 mmol) in PPA (2—3 g) was thoroughly stirred at 55—60 °C for 3 h (TLC control). The temperature was then raised to 120—130 °C and the mixture was stirred for an additional 1 h. Then, the corresponding 1,3-dicarbonyl compound **2a**,**b** (1 mmol) was added and the mixture was stirred at the same temperature for additional 4 h. The reaction mixture was cooled to 80 °C, poured with stirring into cold water (30 mL), extracted with ethyl acetate (3×50 mL), alkalified with aqueous ammonia to pH ~8, and extracted with ethyl acetate (3×50 mL). This extract was concentrated. Compounds **3a,b** were purified by recrystallization and compound **3c** was purified by chromatography (the eluent was chloroform).

6-Hydroxy-2,4-diphenylquinoline (3a) was obtained in a yield of 0.131 g (34%), m.p. 222—223 °C (benzene—petroleum ether; *cf.* Ref. 4: m.p. 222—223 °C). Found (%): C, 84.95; H, 5.03; N, 4.67. $C_{21}H_{15}NO$. Calculated (%): C, 84.82; H, 5.08; N, 4.71. ^{1}H NMR (DMSO-d_6), δ: 7. 21 (m, 1 H); 7.3—7.6 (m, 9 H); 7.74 (s, 1 H); 8.1—8.2 (m, 3 H).

6-Methoxy-2,4-diphenylquinoline (3b) was obtained in a yield of 0.131 g (42%), m.p. 121—122 °C (chloroform—petroleum ether; *cf.* Ref. 5: m.p. 121—122 °C). Found (%): C, 85.05; H, 5.43; N, 4.57. $C_{22}H_{17}NO$. Calculated (%): C, 84.86; H, 5.50; N, 4.50. The ^{1}H NMR spectrum was analogous to that given in Ref. 5.

6-Methoxy-2,4-dimethylquinoline (3c) was obtained in a yield of 0.058 g (31%) as an oil (*cf.* Ref. 6: oil). Found (%): C, 76.79; H, 6.62; N, 7.09. $C_{12}H_{13}NO$. Calculated (%): C, 76.98; H, 7.00; N, 7.48. ^{1}H NMR ($CDCl_3$), δ: 2.78 (s, 3 H, Me(4)); 2.82 (s, 3 H, Me(2)); 3.87 (s, 3 H, OMe); 7. 58 (d.d, 1 H, H(7), J = 9.1 Hz, J = 2.5 Hz); 7.65 (s, 1 H, H (3)); 7.93 (d, 1 H, H(8), J = 9.1 Hz); 8.12 (d, 1 H, H(5), J = 2.5 Hz).

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