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HETEROGENOUS CATALYTIC METHOD FOR THE SYNTHESIS OF BIQUINOLINES AND BIPYRIDINES

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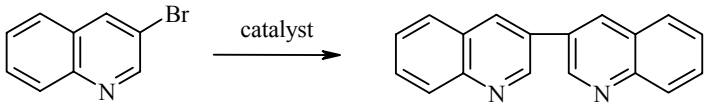
A method has been developed for the synthesis of 2,2'- and 3,3'-biquinolines and of 4,4'-bipyridine based on the coupling of 2- and 3-bromoquinoline or 4-bromopyridine using a Pd/C-hydrazine-KOH catalytic system.

Keywords: 2,2'-biquinoline, 3,3'-biquinoline, 4,4'-bipyridine, 4-bromopyridine, 2-bromoquinoline, 3-bromoquinoline, palladium on carbon, coupling.

A series of methods for the synthesis of 3,3'-biquinoline (**2**) is known [1-4]. These methods are based on the cross coupling of 3-bromoquinoline (**1**) under the action of different metals but have a number of deficiencies. The method [1] using equimolar amounts of 3-bromoquinoline and catalyst employs the expensive metallic palladium. Despite the fact that in method [2] a catalytic amount of metallic palladium is involved it cannot be used repeatedly. The deficiencies of methods [3] and [4] using a catalytic system based on Ni(0) are the need for chromatographic separation of the reaction mixture which impedes work up of large quantities of the 3,3'-biquinoline. Hence we decided to develop a more efficient synthesis of compound **2**.



1 **2**

We have attempted to develop a method allowing a repeated use of the palladium catalyst based on the work in [1]. It was found that 10% Pd/C can be used in place of palladium black. It can be regenerated using the system hydrazine–KOH. The yield is virtually unchanged at 46%.

It was further shown that the catalyst can be regenerated in the course of the reaction by gradual addition to the reaction mixture of a solution of alkali in hydrazine hydrate. This permits use of a catalytic amount of palladium and repeated use of the catalyst. However, the yield in this case decreases to 28%.

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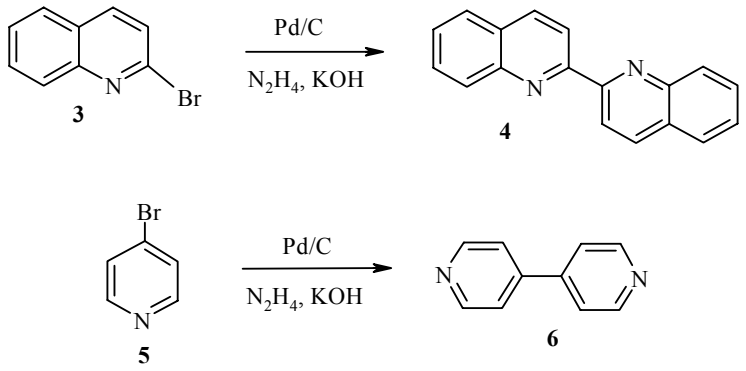

This method can be used in the synthesis of other biquinolines and bipyridines, e.g. 2,2'-biquinoline (**4**) ad 4,4'-bipyridine (**6**).

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WP-200 (200 MHz) instrument using TMS as internal standard. Monitoring of the reaction course and purity of the synthesized compounds was carried out on Silufol UV-254 plates with ethyl acetate as solvent.

General Method. A solution of KOH (0.67 g, 12 mmol) and 88% hydrazine hydrate (1.14 g, 20 mmol) in ethyl alcohol (3 ml) was added dropwise over 2 h to a mixture of the corresponding halo derivative (10 mmol) and Pd/C (0.51 g, 0.5 mmol) in refluxing ethanol (10 ml). Solvent was evaporated and the residue was recrystallized from DMF, separating the catalyst and KBr on a plaited filter. The catalyst was washed with water, dried, and used repeatedly.

3,3'-Biquinoline (2). Yield 0.72 g (28%) with mp 269-271ºC (alcohol) (mp 217ºC [1]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.63 (2H, ddd, $J_{5,6}$ = 8.1, $J_{6,7}$ = 6.9, $J_{6,8}$ = 1.2, H-6,6'); 7.77 (2H, ddd, $J_{6,7}$ = 6.9, $J_{7,8}$ = 8.4, $J_{5,7}$ = 1.5, H-7,7'); 7.94 (2H, dd, $J_{5,6}$ = 8.1, $J_{5,7}$ = 1.5, H-5,5'); 8.18 (2H, dd, $J_{7,8}$ = 8.4, $J_{6,8}$ = 1.2, H-8,8'); 8.46 (2H, d, $J_{2,4}$ = 2.4, H-4,4'); 9.29 (2H, d, $J_{2,4}$ = 2.4, H-2,2'). Found, %: C 84.71; H 4.58; H 10.71. $C_{18}H_{12}N_2$. Calculated, %: C 84.37; H 4.69; N 10.94.

2,2'-Biquinoline (4, $C_{18}H_{12}N_2$). Yield 1 g (39%), mp 197-198ºC (alcohol) (mp 196-198ºC [5]). A sample mixed with a known sample (commercially available) did not give a melting point depression. The ^{1}H NMR spectrum was identical to that given in [5].

4,4'-Bipyridine (6, $C_{10}H_8N_2$). Yield 0.53 g (34%) with mp 112-114ºC (water) (mp 112-114ºC [5]). A sample mixed with a known sample (commercially available) did not give a melting point depression. The ^{1}H NMR spectrum was identical to that given in [5].

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