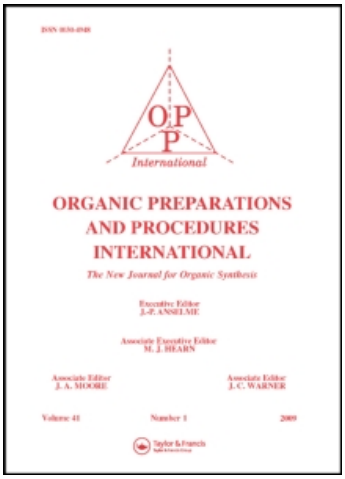

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EFFECT OF METAL IONS IN ORGANIC SYNTHESIS. PART XII
A NEW SYNTHESIS OF N-(α-CHLOROBENZYLIDENE)-N'-PHENYLHYDRAZINE BY REACTION OF PHENYLAZOSTILBENE AND COPPER(II) CHLORIDE

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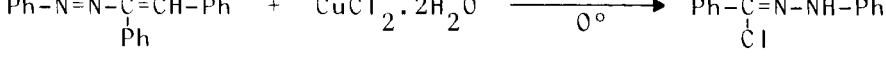
In recent years considerable attention has been devoted to the activity of transition metals in organic chemistry. We have previously investigated the effects of copper and iron ions in certain organic reactions,[1] and in particular on some reactivities of the azo-ene system of arylazoalkene derivatives.[2] We have now studied the synthesis of N-(α-chlorobenzylidene)-N'-phenylhydrazine by reaction of phenylazostilbene with copper(II) chloride dihydrate.

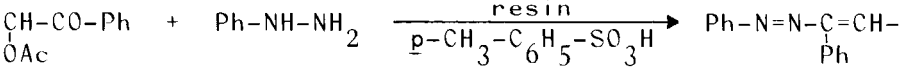
N-(α-Chlorobenzylidene)-N'-phenylhydrazine represents a very important intermediate in the chemistry of the 1,3-dipolar cycloadditions, whereas its basic treatment (generally triethylamine) easily generates, by 1,3-elimination of hydrogen chloride, diphenylnitrilimine ($Ph-\overset{+}{C}=N-\bar{N}-Ph \leftrightarrow Ph-C\equiv\overset{+}{N}-\bar{N}-Ph$). This latter compound, produced <u>in situ</u>, readily reacts with several 1,3-dipolarophile reagents, providing very interesting heterocyclic compounds.[3] At present, N-(α-chlorobenzylidene)-N'-phenylhydrazine is generally prepared according to Huisgen's

or Wolkoff's methodologies.[4]

Treatment of phenylazostilbene with copper(II) chloride dihydrate in acetone at 0° readily affords N-(α-chlorobenzylidene)-N'-phenylhydrazine in high yields (95% by hplc analysis, 85% after column chromatography and crystallization). The mild conditions used and good yields obtained may make our method simple and advantageous over other similar methods.[4] Furthermore, N-(α-chlorobenzylidene)-N'-phenylhydrazine prepared with our method can be employed without complicated procedures for its isolation and purification. In fact, the reaction mixture, after extraction with benzene and aqueous hydrogen chloride, affords N-(α-chlorobenzylidene)-N'-phenylhydrazine in good purity. This latter product was successfully utilized by us in some typical 1,3-dipolar cycloadditions, without further purification. This possibility is also noteworthy in consideration of the fact that this product is a serious irritant and occasional contact with contaminated articles causes severe dermatitis.



In order to make the present method even more convenient we considered the possibility to increase the yields of the phenylazostilbene synthesis (lit. 43-55%),[5] and the possibility of the conversion of acetoxydeoxybenzoin to N-(α-chlorobenzylidene)-N'-phenylhydrazine, without isolation of the pure phenylazostilbene intermediate. The first problem was solved by reaction of acetoxydeoxybenzoin and phenylhydrazine in the presence of p-toluenesulfonic acid and a strong acid cation exchanger resin, producing phenylazostilbene in 80% yields.



The crude reaction product obtained can be treated with copper(II) chloride dihydrate, as above-described, providing N-(α-chlorobenzylidene)-N'-phenylhydrazine in 65% yields.

EXPERIMENTAL SECTION

Phenylazostilbene from Acetoxydeoxybenzoin.- Phenylhydrazine (1.6 ml, 1.76 g, 1.63 mmol) was added to a solution of acetoxydeoxybenzoin (2 g, 0.79 mmol) in benzene (100 ml). After addition of strong acid cation exchanger resin (Merck LAB I; 0.5 g), the reaction mixture was heated under reflux for 0.5 hr. with a water separator described by Natelson and Gottfried.[6] The p-toluenesulfonic acid was added (0.05 g, 0.026 mmol), and the reflux was continued for 0.5 hr. A second portion of p-toluenesulphonic acid (0.05 g) was again added and after a further 0.5 hr. reflux, the reaction mixture was cooled and washed first with saturated aqueous sodium hydrogen carbonate (5 x 100 ml) and then with water (5 x 100 ml). The organic phase was dried over sodium sulfate and evaporated under reduced pressure. The red oily residue was chromatographed on a silica gel column (at first elution with cyclohexane and then with cyclohexane-ethyl acetate mixtures, gradually increasing the amount of ethyl acetate to a 90/10 (v/v) ratio). The crude product obtained was crystallized from n-pentane, affording 1.8 g (80%) of phenylazostilbene, as mixture of two (EE) and (ZE) isomers.[5b]

N-(α-Chlorobenzylidene)-N'-phenylhydrazine from Phenylazostilbene.- A solution of phenylazostilbene (1 g, 0.35 mmol) in acetone (50 ml) was added dropwise to a stirred solution of copper(II) chloride dihydrate (1.2 g, 0.7 mmol), cooled in an ice-bath. The mixture was stirred magnetically at 0° during 1 hr. until the reaction was completed (monitored by silica gel tlc). The mixture was then concentrated under reduced pressure and benzene (50 ml) is poured in the residue. The organic so-

lution was washed first with 5% aqueous hydrogen chloride (3 x 35 ml) and then with water (3 x 35 ml). The organic phase was dried over sodium sulfate, and evaporated under reduced pressure. The crude N-(α-chlorobenzylidene)-N'-phenylhydrazine obtained in good purity (95% by hplc analysis), can be further purified by chromatography column with cyclohexane-benzene 70/30 (v/v) as eluent. The collected fractions were concentrated under reduced pressure and the residue was crystallized, affording 0.69 g (85%) of pure product, mp. 129-131°, lit.[4] 129.5-130.5° (128-131°). Alternatively the crude product may be successfully used for 1,3-cycloaddition reactions, without further purification.

N-(α-Chlorobenzylidene)-N'-phenylhydrazine from Acetoxydeoxybenzoin.- Acetoxydeoxybenzoin was reacted with phenylhydrazine and the reaction mixture was treated as described above in detail for synthesis of phenylazostilbene from acetoxydeoxybenzoin. The red oil obtained was solved in acetone (50 ml) and added dropwise to a stirred solution of copper(II) chloride dihydrate (2.15 g, 1.27 mmol), cooled in an ice-bath. Afterward the reaction was treated as above described in detail for synthesis of N-(α-chlorobenzylidene)-N'-phenylhydrazine from phenylazostilbene, providing 1.18 g (65%) of N-(α-chlorobenzylidene)-N'-phenylhydrazine.

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