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An efficient method for the α-phenylhydrazation of heterocyclic systems under mild and heterogeneous conditions

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Abstract

A combination of silica modified sulfuric acid and aryldiazonium salt was used as an agent for the α-phenylhydrazation of 2-ketomethylquinoline under mild and heterogeneous conditions to provide moderate to excellent yield.

Keywords: α-Phenylhydrazation; 2-Ketomethylquinoline; Heterogeneous conditions

1. Introduction

Diazonium salts are occasionally used to introduce groups other than fluorine into an aromatic ring. For example, the diazonium salt group may be replaced by different groups such as the acetoxyl, nitro, nitrile, hydrogen, halogen, methyl, vinyl, arsenic, mercury and copper. Numerous methods are available for the reduction of arenediazonium salts [1]. The reactions of arenediazonium salts with various carbon nucleophiles such as Grignard reagents, enamines, enolether, lithium enolates of ketones or esters, and ketene silyl acetals [2] lead to the formation of azo or hydrazo compounds. The structure of azo-coupling products is obtained from the investigation of amines, phenoxides, and anions of C-acids. This problem has been satisfactorily solved as late as after applying the methods of nuclear magnetic resonance [3–5].

The carbon in aliphatic azo compounds is attached to a hydrazone, which is the product of the reaction.

In the current research we decided to choose a new system. Our goal, in undertaking this line of work, was three-fold: (a) to overcome the limitations and drawbacks of the reported methods such as tedious work-up and low yields; (b) to replace labour-extensive trial and error improvements with a rational design; and moreover (c) to constrain a reaction to the surface of solid habitually allowing exposure to milder conditions and increasing its reactivity [6].

In this study, we wish to report a one-pot heterogeneous procedure for α-phenylhydrazation of 2-ketomethylquinoline by aryldiazonium salt and sodium nitrite.

2. Results and discussion

2-Ketomethylquinolines are important components in organic chemistry because of the applications of these compounds in heterocyclic synthesis and chemical transformations [7–12]. Different kinds of 2-ketomethylquinolines (**1**) were subjected to α-phenylhydrazation reaction in the presence of sodium nitrite, derivatives of aniline and silica modified sulfuric acid (I) in dichloromethane (Scheme 1). α-Phenylhydrazation reaction was performed under mild and completely heterogeneous condition and gave moderate to excellent yields (Table 1). When reactions occur at the methylene group, the azo compound formed initially rapidly rearranges to form the α-hydrazokethones (**3**) [13].

The reported α-phenylhydrazation reaction can be readily carried out simply by placing sodium nitrite, derivatives of aniline, silica modified sulfuric acid (I), 2-ketomethylquinoline (**1**), and CH_2Cl_2 as inert solvents in a reaction vessel and efficiently stirring the resultant heterogeneous mixture at 5 °C for 30 min.

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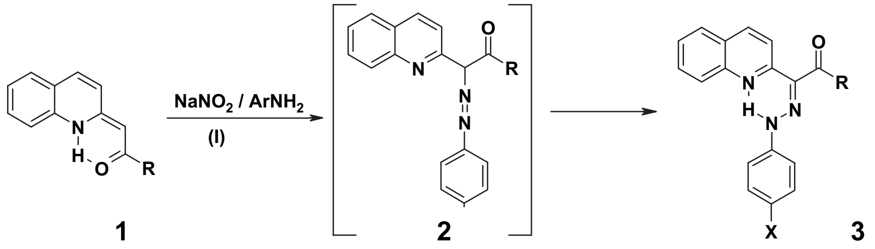

R	CO$_2$Et, C$_6$H$_5$, C(CH$_3$)$_3$, 2-C$_6$H$_4$N,
X	Br, NO$_2$, CH$_3$

Scheme 1. Synthesis of derivatives of α-phenylhydrazo-2-ketomethylquinolines.

The initial azo products were converted to the corresponding α-hydrazokethones immediately and the products can be isolated by simple filtration and evaporation of the solvent. The results and reaction conditions are given in Table 1. Although the azo coupling also occurs in the absence of silica modified sulfuric acid, the reaction time is very long with lower yield. Therefore, we think that the silica modified sulfuric acid acts as a reaction medium providing a heterogeneous effective surface area for in situ generation of HNO$_2$ in low concentrations. It also makes work-up easy.

Similarly, this new system generates HNO$_2$ and NO$^+$, in situ, and thus acts as an N$_2$O$_4$ equivalent because a number of reactions are known in which nitrogen tetroxide (N$_2$O$_4$ ⇔ NO$^+$ NO$_3$) is involved in the formation diazonium salts. Therefore, in this paper we show that in situ generation of NO$^+$ is an effective factor for the azo coupling.

In conclusion, the low cost and the availability of the reagents, easy and clean work-up and high yield make this an attractive method for organic synthesis. This simple procedure is highly selective and contamination by products is avoided. We believe that the present methodology is an important addition to existing methodologies.

3. Experimental

In a typical procedure, chemical reagent was purchased from Merck chemical company. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded by Bruker DRX 500 Avance spectrometer. Multiplicities of proton resonance were designated as singlet (s), doublet (d), and triplet (t). Tetramethylsilane (TMS) was used as an internal reference. A Magna-550 Nicolet recorded FT-IR spectra. Spectra of hydrazone were obtained with KBr pellet and CH$_2$Cl$_2$ solvent. Vibrational transition frequencies were reported as wave numbers (cm^{-1}). A mass spectrum was recorded by QP 1100EX Shimadzu spectrometer. Solid compound reported in this paper gave satisfactory C, H, N microanalyses with a Perkin−Elmer Model 240 analyzer. Melting point obtained with an electrothermal micromelting point apparatus is uncorrected.

In the first stage, a mixture of (0.3 g) silica sulfuric acid and 1 mmol (0.069 g) of sodium nitrite was cooled in an ice bath. Then 1 mmol (0.139 g) of 4-nitroanilin was slowly added to the mixture with stirring in an ice bath for half an hour. Then, 1 mmol of 2-ketomethylquinoline derivative was rapidly added to the previous mixture with continued stirring for 30 min under 5 °C. On completion of the reaction, the products were filtered off, washed with water until acid-free, and dried at 50 °C in an oven to give hydrazone compounds **3**(**a**−**i**), which were recrystallised from suitable solution.

Table 1
Comparing yield in homogeneous & hetrogeneous reactions

Entry	3	R	X	% Yield in homogenous reaction [14]	% Yield in heterogeneous reaction
1	**a**	CO$_2$Et	Br	75	82
2	**b**	C$_6$H$_5$	Br	73	80
3	**c**	C(CH$_3$)$_3$	Br	82	93
4	**d**	2-C$_6$H$_4$N	NO$_2$	85	95
5	**e**	CO$_2$Et	NO$_2$	99.9	99.9
6	**f**	C$_6$H$_5$	NO$_2$	99	99.9
7	**g**	C(CH$_3$)$_3$	NO$_2$	91	98
8	**h**	C(CH$_3$)$_3$	CH$_3$	63	75
9	**i**	C$_6$H$_5$	CH$_3$	68	79

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