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A Novel Method for the Synthesis of 2-Ketomethylquinolines

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Abstract

Several 2-ketomethylquinolines were synthesized by heating, 2-methyl quinoline with acyl chloride in the presence of $AlCl_3$ Contrary to reported procedures, this method was accomplished at a short time obtaining good results.

Keywords: 2-Ketomethylquinolines; 2-Methylquinoline; $AlCl_3$

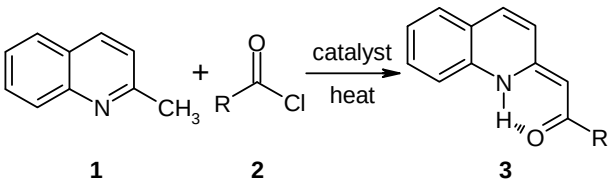
Introduction

2-Ketomethylquinolines are important heterocycles in organic synthesis, which can undergo further transformations and applications. 2-ketomethyl-quinolines acts as polydentate ligands to form stable complexes with different cations. Although the synthesis of 2-ketomethylquinolines has been extensively documented, such methods possess important limitations that prevent their general application. During the last decades, different methods for the preparation of quinaldine derivatives have been reported [1-11]. Among the different derivatives of quinaldine, major efforts have been done on 2-ketomethyquinolines.

In this research, the useful and new methods for the preparation of 2-ketomethyquinolines are considered. The belief is that the new methods have advantages of simplicity, facilitating preparation and mild conditions. The results of this study will be useful for the evaluation of the application of these methods in different contexts.

The structures of products have also been identified using ultra violet-visible, IR, ^{1}H NMR and ^{13}C NMR spectra data. These compounds take the most stable forms of enaminone, ketimine and iminol depending on their kind of substitution and functional group.

We report here that $AlCl_3$ is a useful catalyst for the preparation of 2-ketomethylquinolines under thermal conditions. 2-methylquinoline (1) were reacted with several acyl chlorides (2) affording the desired 2-ketomethylquinolines (3) (Scheme 1).



1 **2** **3**

R = alkyl or aryl

Scheme 1

Results and Discussion

The present procedure provides a useful and convenient method for the preparation of 2-ketomethyl-quinolines in the presence of $AlCl_3$. The first, 2-ketomethylquinolines (3) were obtained with various Lewis acids and equimolar mixture of 2-methyl-quinoline (1 mL, 1.09 g) and benzoyl chloride (1 mL, 1.21 g) (Table 1).

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Table 1. Preparation of 2-ketomethylquinolines (3) with various Lewis acids

Entry	Lewis acid	Cat. mmol	Yield %
1	$AlCl_3$	1.5	90
2	$SnCl_2$	1.6	5
3	BF_3/EtO_2	16	10
4	$BiCl_3$	1.6	50
5	$ZrCl_4$	1.7	60
6	CuCl (I)	1.7	–

According to Table 1, $AlCl_3$ was the best catalyst for preparation of 2-ketomethylquinolines derivatives.

Then the synthesis of compounds (3) takes place in two ways:

(i) A mixture of 2-methylquinoline (1), acyl chloride (2) and $AlCl_3$ in dry petroleum benzine was refluxed for 3-5 h and the products on purification as above furnished compounds (90%) (Table 2).

(ii) A mixture of 2-methylquinoline (1), acyl chloride (2) was refluxed for 10 h and the products on purification as above furnished compounds (0-5%) (Table 2).

The constitution of (3) was confirmed by ^{1}H NMR, ^{13}C NMR and IR spectra data. Aryl chlorides were converted to the corresponding 2-ketomethylquinolines in good to excellent yields. The 2-phenyl-1-(2-quinolyl)-1-ethanon (Entry 8, 3i) was low yield because, that can give Micheal addition, (2-chlorophenyl)(2-quinolyl)methanone (Entry 4, 3e) lower yield than (4-chloro phenyl)(2-quinolyl)methanone (Entry 3, 3d) because (2-chlorophenyl)(2-quinolyl)methanone has steric hindrance and yield. In all ^{1}H NMR spectra NH group of the 2-ketomethylquinolines appeared around δ 14-16 as a broad singlet and in the IR spectra the C=O/C=C groups were observed around 1610-1640 cm^{-1}. Proton vinillic appeared around δ 5-6 as a singlet and in IR spectra the C=C/C=O groups 1500-1600 cm^{-1}.

A new experimental technique by combining catalyst and without catalyst has been established to carry out in good yields for synthesis of 2-ketomethylquinolines. The reaction time is sharply decreased from 10 h to 3-4 h with an increase in product yield (Table 2).

Experimental

Chemicals were purchased from Merck (Germany) and were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded ($CDCl_3$, CD_3CN AND DMSO-d_6 solvent) by a Bruker DRX-400 Avance spectrometer, respectively, with tetramethylsilane (TMS) as an internal reference. A Magna-550 Nicolet recorded IR spectra was used. Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected.

Table 2. Preparation of several 2-ketomethylquinolines (3) from acyl chlorides (2) and 2-methyl quinoline

Entry	R	Product[a]	Time/h	Yield[b] (%)	Yield[c] (%)	m. p. /°C	m. p. /°C Reported[d]
1	Ph	3a	3	90	5	115-117	113
2	4-MeC_6H_4	3b	3	80	4	170-172	169
3	4-ClC_6H_4	3d	3	70	0	161-163	162
4	2-ClC_6H_4	3e	3.5	50	0	114-116	117
5	4-$MeOC_6H_4$	3f	4	80	3	153-155	153
6	4-BrC_6H_4	3g	3	85	0	164-167	164
7	4-$O_2NC_6H_4$	3h	3	40	0	178-180	177-178
8	C_6H_5CH=CH	3i	5	15	0	168-170	169[e]
9	$C_6H_5CH_2$	3j	5	35	0	82-84	81-83
10	CH_3	3k	5	0	0	–	–

[a] All products exhibited spectroscopic data (IR, ^{1}H NMR) consisted with their structures.

[b] Yields refer to isolated and chromatographically pure products by $AlCl_3$.

[c] Yields refer to isolated and chromatographically pure products without catalyst.

[d] [12]

[e] [13]

General Procedure

(i) An equimolar mixture of new distilled 2-methylquinoline (1 mL, 1.09 g) and new distilled benzoyl chloride (1 mL, 1.21 g), $AlCl_3$ (1.5 mmol) in dry pet. ether (80°C, 15 mL) was refluxed with stirring for 3 h, upon completion of the reaction, as followed by TLC. The solvent was evaporated then the aqueous solution of sodiunm bicarbonat was added and was filtered. The solid residue was chromatographed over a silica gel column petroleum benzine (60°C): ethyl acetate, 4:1 v/v) or some of the light yellow product was obtained by crystallization it from aqueous ethanol (90%). Reaction yields and melting points of the products are given in Table 2.

(ii) An equimolar mixture of new distilled 2-methylquinoline (1 mL, 1.09 g) and new distilled benzoyl chloride (1 mL, 1.21 g) in dry petroleum benzine (80°C, 15 mL) was refluxed with stirring for 10 h, upon completion of the reaction, as followed by TLC examination and the yellow product part was separated and recognizing (5%) (Table 2).

The reported method is an interesting, easy and novel method, high yields of the products, ease of work-up conditions and low cost make the above method preferable to other existing methods.

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