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## A novel method for the synthesis of 2-ketomethylquinolines under solvent-free conditions using microwave irradiation<sup>†</sup>

Hossein Loghmani-Khouzani,\* Majid M. Sadeghi, Javad Safari and Alireza Minaeifar

Department of Chemistry, Faculty of Sciences, University of Isfahan, Isfahan 81744, IR Iran Received 2 October 2000; accepted 27 April 2001

Abstract—Several 2-ketomethylquinolines are synthesized by heating 2-methylquinolines with acyl chlorides, in a conventional microwave oven. © 2001 Published by Elsevier Science Ltd.

The synthesis of 2-ketomethylquinolines is an important reaction in organic chemistry because of the applications of these compounds in heterocyclic synthesis and chemical transformations.<sup>1-6</sup> The ability of 2ketomethylquinolines to act as polydentate ligands to form stable complexes with different cations is well known.<sup>7</sup> Although the synthesis of 2-ketomethylquinolines has been extensively documented with a variety of methods being available, many of these have limitations in their general application.<sup>8–19</sup> Microwave irradiation has opened up new perspectives in synthetic organic chemistry, not only in terms of yield and selectivity, but also in ease of the reaction conditions.<sup>20–23</sup>

We report here that silica gel is a useful catalyst for the preparation of 2-ketomethylquinolines under solventfree conditions using microwave irradiation. 2Methylquinoline and 2,3-dimethylquinoline (1) were reacted with several acyl chlorides (2) affording the desired 2-ketomethylquinolines (3) (Scheme 1).

In order to evaluate the synergy between the solventfree medium and microwave irradiation in this reaction, several experiments were carried out, as shown in Table 1. The reaction of 2-methylquinoline and benzoyl chloride without irradiation at room temperature and at 200°C was unsuccessful and the 2-methylquinoline was recovered unchanged (entry 1, 2). Similarly the use of irradiation in the absence of silica gel for 4 min was unsuccessful (entry 3). Only under solvent-free conditions coupled with microwave irradiation, taking advantage of the synergy between both methodologies,



Scheme 1.

Table 1. Reaction of 2-methylquinoline with benzoyl chloride

| Run | Catalyst   | Temp. or MW Power | Time (min) | 2-Ketomethylquinoline (%) |
|-----|------------|-------------------|------------|---------------------------|
| 1   | Silica gel | rt                | 60         | 0                         |
| 2   | Silica gel | 200°C             | 60         | 0                         |
| 3   | None       | 900 W             | 4          | 0                         |
| 4   | Silica gel | 400 W             | 4          | 91                        |

Keywords: 2-ketomethylquinolines; silica gel; microwave irradiation; 2-methylquinoline.

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<sup>\*</sup> Corresponding author.

were the 2-ketomethylquinolines produced in excellent yields (entry 4). The reaction product is formed by loss of hydrogen chloride after 4 min. Next, we studied the reaction of 2-methylquinoline and benzoic acid or methyl benzoate in the presence of silica gel. No special reaction occurred.

The present procedure provides a useful and convenient method for the preparation of 2-ketomethylquinolines in the presence of silica gel.

General experimental procedure: The preparation of 1phenyl-2-(quinol-2-yl)-ethan-1-one **3a** (Table 2) is representative of the general procedure employed. To an equimolar (1 mmol) mixture of 2-methylquinoline (143 mg) and benzoyl chloride; (140 mg) placed in an open glass container, silica gel (silica gel 60, 230–240 mesh, Merck) (300 mg) was added and the reaction mixture was irradiated in a microwave oven at 400 W power for 4 min. Upon completion of the reaction, as followed by TLC examination, the product is extracted into dichloromethane (3×10 ml). The solvent was evaporated and the resulting crude material was purified on a silica gel plate (eluent;  $CCl_4/Et_2O$ ) affording the 1phenyl-2-(quinol-2-yl)-ethane-1-one (**3a**) in 91% yield (Table 2).

The ability of silica gel under solvent-free conditions coupled with microwave irradiation was demonstrated using various acyl chlorides with 2-methylquinoline and the resulting data are summarized in Table 2. Aromatic acyl chlorides were converted to the corresponding 2-ketomethylquinolines in good to excellent yields in less than 4 min. In all <sup>1</sup>H NMR spectra the NH group of the 2-ketomethylquinolines appeared around  $\delta$  14–16

 Table 2. Preparation of several 2-ketomethylquinoline (3)

 from acyl chlorides and 2-methylquinolines under

 microwave irradiation

| Entry | R <sup>2</sup>                    | $\mathbb{R}^1$ | Product <sup>a</sup> | Yield <sup>b</sup> (%) | Мр    |
|-------|-----------------------------------|----------------|----------------------|------------------------|-------|
| 1     | Ph                                | Н              | 3a                   | 91                     | 119   |
| 2     | 4-MeC <sub>6</sub> H <sub>4</sub> | Н              | 3b                   | 90                     | 171   |
| 3     | $4 - MeOC_6H_4$                   | Н              | 3c                   | 83                     | 154   |
| 4     | 4-ClC <sub>6</sub> H <sub>4</sub> | Н              | 3d                   | 77                     | 163   |
| 5     | $2-ClC_6H_4$                      | Н              | 3e                   | 53                     | 115   |
| 6     | $4-BrC_6H_4$                      | Н              | 3f                   | 89                     | 167   |
| 7     | 2-Pyridyl                         | Н              | 3g                   | 78                     | 152.5 |
| 8     | 1-Naphthyl                        | Н              | 3h                   | 80                     | 152   |
| 9     | Ph                                | Me             | 3i                   | 86                     | 100   |
| 10    | $\mathbf{B}\mathbf{u}^{t}$        | Н              | _c                   | _                      | _     |
| 11    | $\mathbf{B}\mathbf{u}^{t}$        | Me             | _c                   | _                      | _     |
| 12    | $\mathbf{Pr}^{i}$                 | Н              | _c                   | _                      | _     |
| 13    | $\Pr^i$                           | Me             | _c                   | -                      | -     |

<sup>a</sup> All products exhibited spectroscopic data (IR, <sup>1</sup>H NMR and MS) consistent with their structures.

<sup>b</sup> Yields refer to isolated and chromatographically pure products.

<sup>c</sup> No product was isolated after 15 min.

as a broad singlet<sup>2,3</sup> and in the IR spectra the C=O/C=C groups in CHCl<sub>3</sub> were observed around 1610–1640  $\rm cm^{-1}$ .

In conclusion, the reported method is an interesting, easy and novel method for the preparation of 2ketomethylquinolines. In addition, high yields of the products, short reaction times, ease of work-up conditions and low cost make the above method preferable to other existing methods.

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