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MICROWAVE-ASSISTED SYNTHESIS OF POLYHYDROQUINOLINE IN THE ABSENCE OF SOLVENT

Mark Castillo, Mitchell Ortiz and Bimal K. Banik*

Department of Chemistry, The University of Texas-Pan American, 1201 West University Drive, Edinburg, TX 78539, USA; E-mail: banik@utpa.edu

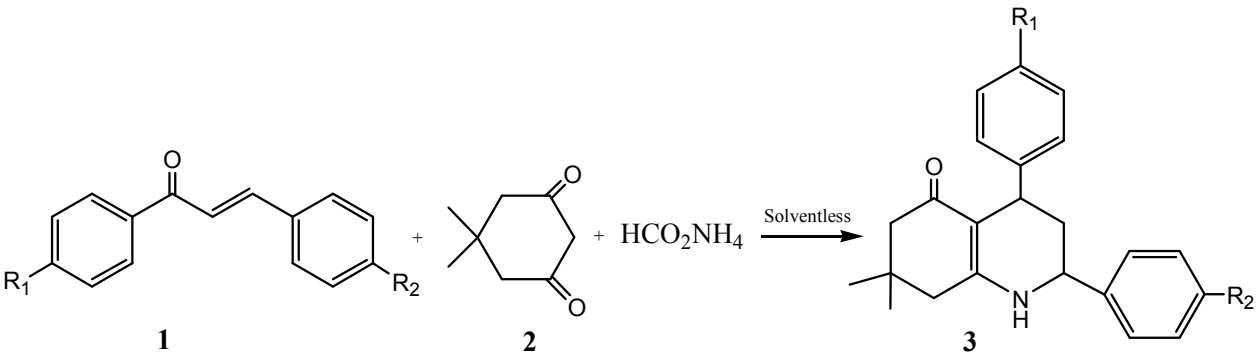
Abstract:
Microwave-assisted synthesis of polyhydroquinoline has been performed by the reaction of α, β-unsaturated ketone with demedone in the presence of ammonium formate. This reaction products product in excellent yield when performed under the solventless conditions

Keywords: Microwave, Unsaturated Ketone, Demedone, Polyhydroquinoline

Introduction:
The preparation of polyhydroquinoline is an important target in organic synthesis. The 1,4-dihydropyridines present in these types of molecules have numerous medicinal activities. Most of the reported procedures have limitations. The use of organic solvents and long reaction time are the main limitations. We report herein a microwave-induced method for the preparation of ploy hydroquinoline in the absence solvent by reacting unsaturated ketone with demedone.

Results and Discussion:
In our earlier reactions, we have reported the use of ammonium formate in microwave-induced reactions and identified it to be a versatile reagent in organic synthesis.[1] Our research on microwave-induced chemistry has culminated in a variety of procedures.[2,3] Reactions without using catalyst and solvent would be very important from the stand point of green chemistry.[4]
Several unsaturated ketones and demedone are commercially available. Reaction of **1** with **2** in the presence of ammonium formate in ethanol at reflux temperature produced polyhydroquinoline in 40% yield after 3h. Reaction of these reactant mixtures in a domestic microwave oven was difficult to accomplish since ethanol began to boil within 2 minutes of microwave irradiation. This problem was avoided by keeping a beaker of water (250 mL water in a 500 mL beaker). Using these conditions, irradiation in the microwave was possible and after 5 minutes, the yield of the product could be increased to 60%. These experiments have prompted us to investigate the reaction in the absence of solvent. Microwave irradiation of **1** and **2** in the presence of ammonium formate after 5 minutes using a heat sink produced polyhydroquinoline in about 80% yield. The reaction did not proceed in the absence of ammonium formate. This reaction required stoichiometric amounts of reagents and ammonium formate. The reaction, however, produced comparable yield when ethylene glycol was used as the solvent (**Scheme 1**).

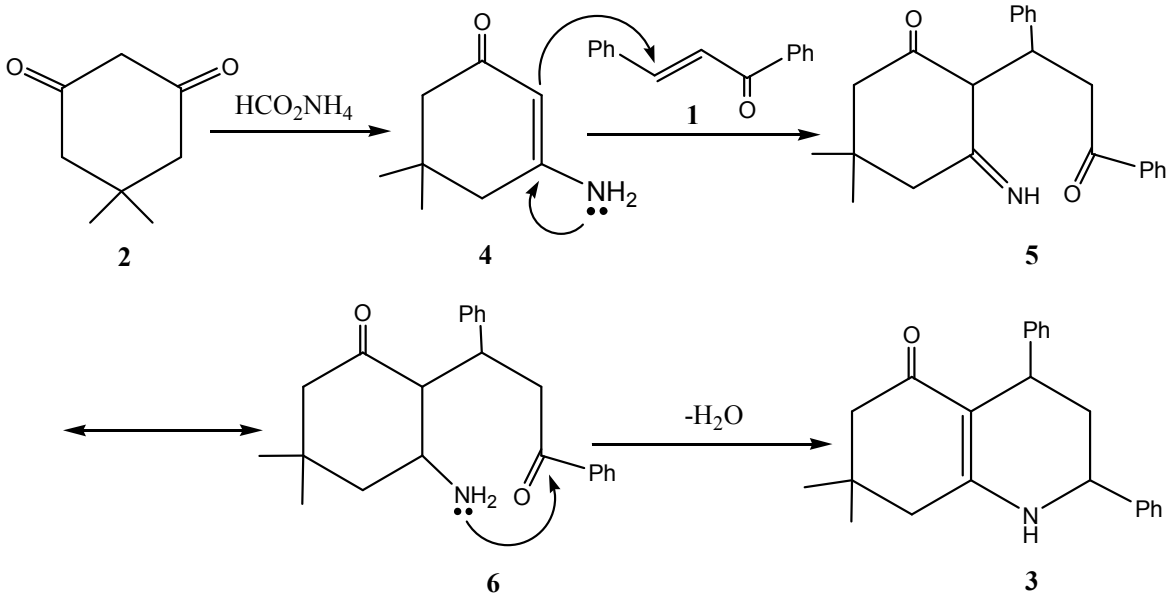
Scheme 1



a: R_1=R_2=H
b: R_1=Phenyl, R_2= *p*-Methoxyphenyl
c: R_1= *p*-Methoxyphenyl, R_2=Phenyl

The mechanism of this reaction has not been investigated. However, considering the nature of the starting materials, we believe this reaction proceeds through the formation of enamine **4**. The enamine can undergo a conjugate reaction and this process can form intermediates **5** and **6**. Subsequently, a dehydration reaction at high temperature seems feasible to form the product **3** (**Scheme 2**).

Scheme 2:



After the reaction, ethyl acetate was added to the reaction mixtures and the organic layer was filtered and evaporated. The pure product was isolated using column chromatography over silica gel.

Conclusion:
In conclusion, this method produces polyhydroquinolines in reasonably good yield following a very simple procedure. Our method using microwave-irradiation with ammomium formate is fascinating for the synthesis of these types of molecules.

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2. We have been engaged in microwave-induced reactions. For a few examples, see: (a) D. Bandyopadhyay and B.K. Banik, *Helv. Chim. Acta*. 298 (2010); (b) A. Kall, D. Bandyopadhyay and B.K. Banik, *Synthetic Communications*, **40**, 1730 (2010).

3. For some recent examples of microwave-induced reactions, see: (a) M.R. Baar, D. Falcone and C. Gordon, *J. Chem. Edn*. **87**, 84 (2010); (b) J. Bo, F. Shi, S.J. Tu, *Curr. Org. Chem*. **14**, 357 (2010); (c) A. De Cozar, M.C. Millan, C. Cebrian, P. Prieto, A. Diaz-Ortiz, A. De La Hoz and F.P. Cossio, *Org. & Biomol. Chem*. **8**, 1000 (2010); (d) J.A. Marafie and H.D. Moseley, *Org. & Biomol. Chem*. **8**, 2219 (2010); (e) K.C. Golden, B.T. Gregg and J.F. Quinn, *Tetrahedron Lett*. **51**, 4010 (2010);(f) J. McNutly, P. Das and D. McLeod, *Chemistry-A European J*. **16**, 6756 (2010).

4. We have been actively engaged in devising synthetic methods which are practical or ecologically friendly. For examples, see: (a) B.K. Banik, M. Suhendra, I. Banik and F.F. Becker, *Synth. Commun.* **30**, 3745 (2000); (b) B.K. Banik, I. Banik, L. Hackfeld, F.F. Becker, *Heterocycles*, **56**, 467 (2001); (c) B.K. Banik, L. Hackfeld and F.F. Becker, *Synth. Commun*. **31**, 129 (2001);(d) S. Samajdar, F.F. Becker and B.K. Banik, *Synth. Commun.* **31**, 2691 (2001); (e) C. Mukhopadhyay, F.F. Becker and B.K. Banik, *Synth. Commun*. **31**, 2399 (2001); (f) S.K. Dasgupta and Banik, B. K. *Tetrahedron Lett*. **43**, 9445 (2002); (g) B.K. Banik, S. Samajdar and I. Banik, *Tetrahedron Lett.* **44**, 1699 (2003); (h) N. Srivastava and B.K. Banik, *J. Org. Chem.* **68**, 2109 (2003).