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Microwave Assisted Synthesis of N-Benzylenaminones Catalyzedby Chloroacetic acid

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Abstract

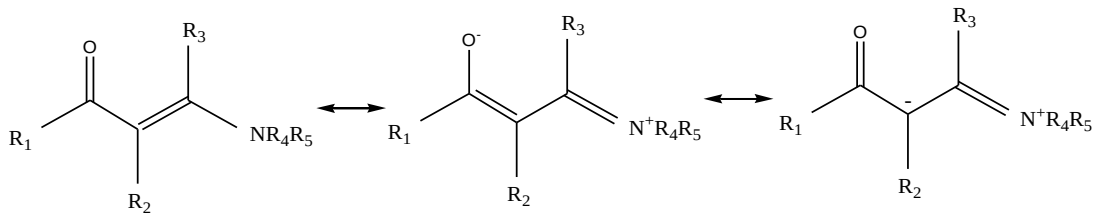
Benzylaminoalkenones and benzylaminoalkenoates 3 were synthesized from reaction of benzylamine with corresponding 1,3-diketones and 1,3-ketoesters in the presence of catalytic amount of chloroacetic acid under microwave radiation. This method offers several advantages including high yield of products, recyclable of the catalyst and easy experimental work-up procedure.

Keywords: β-Enaminones, Microwave Synthesis, 1,3-Diketones, 1,3-Ketoesters, Benzylamine, Chloroacetic acid.

1. Introduction

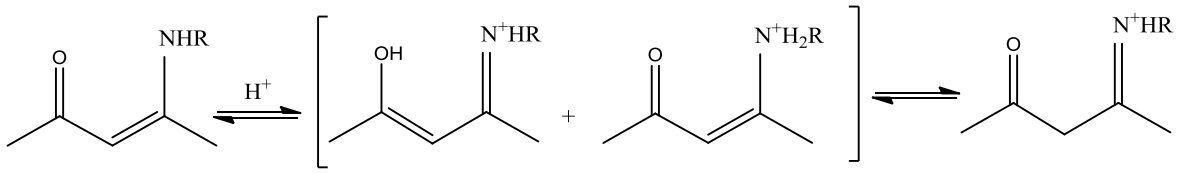
β-Enaminones contain the conjugated system O=C-C=C-N and are capable of reacting with a wide variety of both electrophilic and nucleophilic reagents (scheme 1).

The enaminone unit has three nucleophilic centers namely the hard oxygen as well as softer nitrogen and α-carbon [1].



Scheme 1. Resonance Structures of β-Enaminones

In the case reaction with a proton (hard electrophile), protonation in the kinetically driven stage occurs at oxygen (in a smaller extent also at nitrogen) and subsequently, in the thermodynamically driven stage, protonation takes place at carbon (scheme 2)[2].



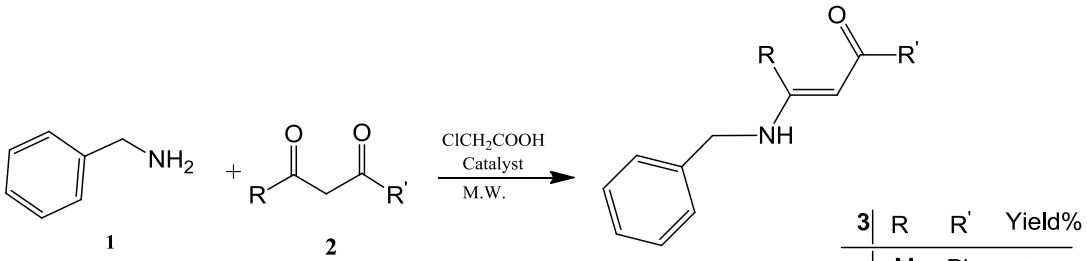
Scheme 2. Protonation of β-Enaminones

β-Enaminones have been greatly used as key intermediates in organic synthesis. In particular, they have been employed as synthetic building block of awide variety of heterocycles and pharmaceutical compounds [3, 4].

Despite their wide range of pharmacological activity and synthetic applications, the synthesis of enaminones has received little attention. Several improved precedures have been reported including the reaction of amines and 1,3-dicarbonyl compounds using $Zn(OAc)_2.2H_2O$, $COCl_2$-$6H_2O$, $Bi(OTf)_3$, $HClO_4$-SiO_2, silicagel, clay K_{10}/ultra-sound, Cu-nanoparticle and $NaAuCl_4$. Recently these compounds have been prepared in water as solvent [5, 6].

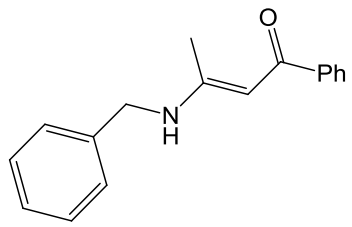
However, some of these methodes suffer from drawbacks such as long reaction times, unsatisfactory yields, low selectivity or the use expensive catalysts [7].

As part of our current studies on the development of new routes in approach to the synthesis of organonitrogen compounds [8, 9], we describe an efficient synthesis of enaminone derivatives from reaction of benzylamine with 1,3-diketones and 1,3-ketoesters by cloroacetic acid catalysis under microwave radiation (scheme 3, 4).

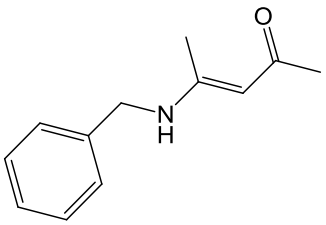


3	R	R'	Yield%
a	Me	Ph	85
b	Me	Me	82
c	Ph	Ph	90
d	Me	OEt	81

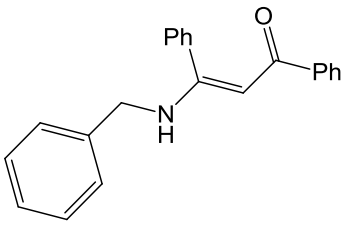
Scheme 3: Catalytic Synthesis of β-Enaminones 3a-d under microwave radiation



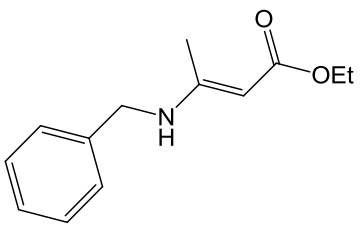
3a: 3-(benzylamino)-1-phenylbut-2-en-1-one



3b: 4-(benzylamino)pent-3-en-2-one



3c: 3-(benzylamino)-1,3-diphenylprop-2-en-1-one



3d: ethyl 3-(benzylamino)but-2-enoate

Scheme 3: Structures of β-Enaminones 3a-d

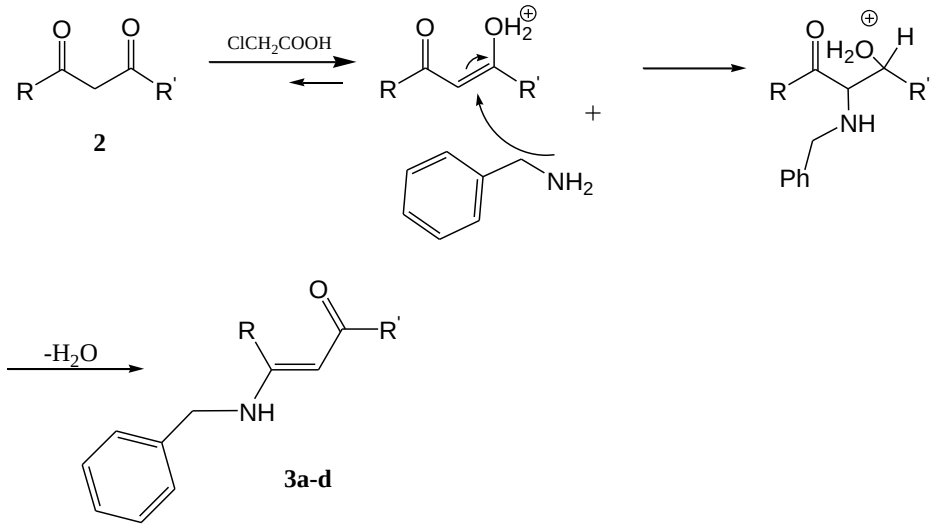
2. Experimental

A mixture of benzylamine (0.1g, 1mmol) and 1,3-diketone (1mmol) was irradiated by microwave with catalytic amount of chloroacetic acid (9 mg 0.01mmol) at 180^{o}C for 2 minutes. After irradiation, the crude reaction product was subjected to dry-flash column chromatography using 20% EtOAc in n-hexane as eluent to isolatepure products **3**.

3. Results

β- Enaminones **3a-d** were synthesized from reaction of benzylamine **1** with 1,3-diketones or 1,3-ketoesters **2**. Firstly, we examined the efficiency of different reaction media for the condensation reactions of benzyl amine and 1,3-diketones. Significant rate enhancementand improved yields were observed using chloroacetic acid as a catalyst and microwave radiation as reaction media. In here, β-enaminones were prepared in the presence of chloroacetic acid adopting two procedures either via heating the reactants under reflux in toluene for 24 h to produce 65-70% yieldsor under solvent-free condition and microwave radiation within a few minutes giving 80-90% yields. The latter method was preferred than the former one due to it afforded pure product with higher yield in shorter time.The structures of compounds **3a–d** were confirmed from their IR, ^{1}H NMR and ^{13}C NMR spectra. For example, the ^{1}H NMR spectrum of **3b** in CCl_3 exhibited two singlets for methyl groups (δ = 1.93, 2.05 ppm), a doublet (δ = 4.48 ppm) for CH_2N, and a broad singlet for NH in δ = 11.18 ppm along with multiplets(δ = 7.26-7.37 ppm) for the aromatic region. The proton-decoupled ^{13}C NMR spectrum of **3b** showed 10 distinct resonances in agreement with the proposed structure. The IR spectrum of **3b** displayed characteristic carbonyl and C=C bands (1692, 1580). The ^{1}H NMR and ^{13}C NMR spectra of **3d** were similar to those for **3b** except for the ester moiety, which exhibited characteristic resonances in the appropriate regions of the spectrum.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation under acid catalyst (Scheme 4).



Scheme 4:Proposed mechanism for the formation of compounds **3**

4. Conclusion

In summary we describe an efficient solvent free synthesis of enaminone in the presence of of chloroacetic acid catalyst under microwave radiation. The advantage of the presentprocedure is that the reaction is performed by simple mixing of the starting materials using an inexpensive and available catalyst in a short time. So the products **3** are prepared in good yields according to a green chemistry procedure.This method was successfully applied to enamination of β-diketones and β-ketoesters.

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