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Enamines Preparation Under Solvent-free Conditions Catalyzed by $LiClO_4$

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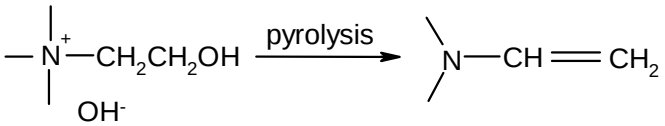
Abstract

A simple, efficient, and novel method has been developed for the synthesis of enamines in presence of lithium perchlorate as a catalyst under solvent-free conditions accelerated by microwave irradiation. This method is remarkable by its mildness and by its easily work-up operation.

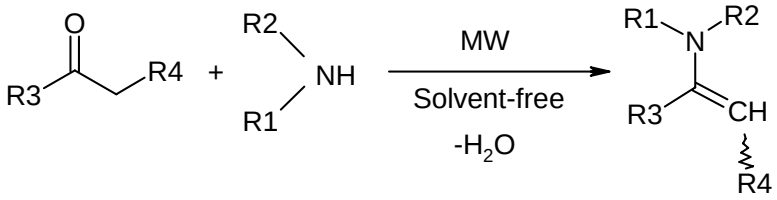
Introduction

Enamines have been intensively studied in organic synthesis in wide variety of ways following Stork's report on the application of enamines in the alkylation and acylation of carbonyl compounds[1]. Weidinger *et al* have reported that 1,3-diaza-1,3-butadiene have been shown to participate in [4+2] cycloaddition reaction with 1-[4-morpholino]cyclohexene[2]. Enamines have been used in natural product synthesis, for example total synthesis of fabianine[3] and quaipyridines[4] including heteroaromatic azadiene *Diels-Alder* reaction.
The simplest enamine of carbonyl compounds was prepared long ago by Mayer and Hopf [5] who made *N*,*N*-dimethylvinylamine (the enamine of acetaldehyde) by pyrolysis of choline (scheme 1).

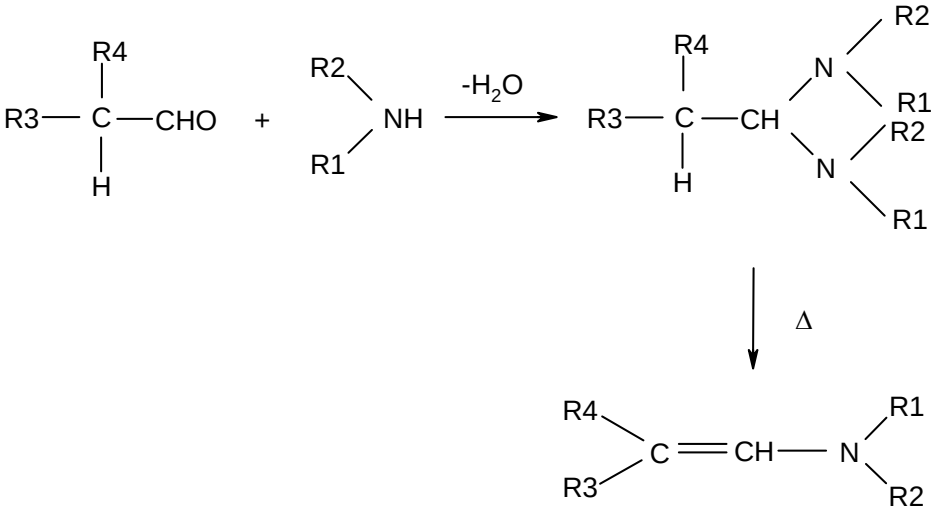


Scheme 1. Pyrolysis of choline

This is obviously not a general method and it remained for Mannich and Davidsen[6] to provide the synthesis which with some modification of details is still the one used today: reaction of an aldehyde or ketone with a secondary amine, in presence of dehydrating agents such as anhydrous potassium carbonate. Under these conditions ketones are converted into their enamines directly (scheme 2-a) while aldehydes are transformed into their nitrogen analog of an acetal (aminal) which is then decomposed, on distillation, to enamine and secondary amine (scheme 2-b).



(a)



(b)

Scheme 2. General method for the preparation of enamines from (a) ketones (b) aldehydes

In many works the practice has been to use azeotropic distillation with benzene, toluene, or xylene depending on the rate of the reaction for cyclic ketones and disubstituted acetones. In some cases *p*-toluenesulfonic acid may be added to the mixture[1]. Recently, for environmental and economic reasons, attention has been focused on catalytic reactions under solvent-free conditions[7-9]. Lithium perchlorate has been effectively employed as a Lewis acid catalyst for various reactions like aminoalkylation of electron-rich aromatic compounds[10], selective *Michael* addition of active methylene compounds[11], and regioselective ring opening of epoxides[12].
In continuation of our previous researches on solvent-free reactions, we herein describe the preparation of enamines under microwave irradiation conditions. Lithium perchlorate is added to the mixture as a *Lewis* acid. Furthermore, it plays another role as a dehydrating agent too.

Result and Discussion

The preparation of enamines was generally carried out by treatment of 2.0 mmol of a ketone and 2.5 mmol of a secondary amine in presence of 0.2 mmol $LiClO_4$ as catalyst. The rate of enamine formation is affected, not unexpectedly, by two factors, the basicity and the nature and environment of the secondary amino group and the nature and environment of the carbonyl group.
As shown in Table 1, pyrrolidine gives a higher reaction rate than the weaker basic morpholine (K_b (pyrrolidine)= 1.3×10^{-3}, K_b (morpholine)= 2.4×10^{-6})[1], while cyclic

amines generally produce enamines faster than open-chain ones. This is also confirmed by literature. [1]
The presence of $LiClO_4$ as a Lewis acid enhanced the reactivity of carbonyl functional group. It has also played a role as a dehydrating agent.

Table 1. Solvent-free preparation of enamines with high to quantitative yield

Entry	Ketone	Amine	Time (min)	Convert (%)	Isolated yield (%)
1	Cyclohexanone	Pyrrolidine	5	>99	85
2	Cyclohexanone	Morpholine	6	>99	80
3	Cyclohexanone	Diethylamine	7	>99	60
4	Acetophenone	Pyrrolidine	8.5	>99	78
5	Acetophenone	Morpholine	20	>99	80
6	Acetophenone	Diethylamine	19	>99	68
7	Diethylketone	Pyrrolidine	6	>99	82
8	Diethylketone	Morpholine	11	>99	73

Experimental

Typical experimental procedure for the preparation of enamines:

A mixture of a secondary amine (2.5 mmol) and a ketone (2.0 mmol) and $LiClO_4$ (0.042g, 0.2 mmol) in a 25 mL round bottom flask was subjected to microwave irradiation for 5-20 min, with 10-30 sec intervals for cooling. The power of irradiation was fixed on 70% of the full power of 1000 W.
The reaction progress was monitored by TLC. After completion of the reaction, the mixture was diluted by about 5 mL dichloromethane and filtered for separating the catalyst. The produced water and remained amine was distillated out by bulb-to-bulb distillation. The products were obtained with good to high isolated yields (60-85%) (Table 1).

Conclusion

In summary, this paper describes a general method for the synthesis of enamines using catalytic amount of $LiClO_4$. The efficiency and operational simplicity of the method as well as mild reaction conditions and easier work-up procedure make it a useful method for the synthesis of enamines.

Acknowledgment

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