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Synthesis in Dry Media Coupled with Microwave Irradiation : Application to the Preparation of Enaminoketones.

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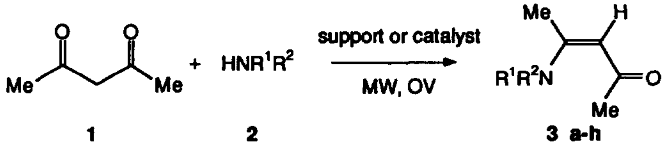
Keywords : microwaves, dry media, enaminoketones, acylamines.

Abstract : β-diketones react with a variety of amines and aminoesters over clay K_{10} or silica under microwave irradiation in open vessels to give within a few minutes, the corresponding enaminoketones with good yields. According to the reaction conditions acylamines may also result.

Organic synthesis in dry media, eventually under microwave irradiation is actually under extensive examination[1-6]. As part of our program related to the study of the reactivity of dicarbonyl compounds in heterogeneous media[7,8], we report now a very fast and simple procedure for the synthesis of enaminoketones and acylamines, starting from β-diketones and primary or secondary amines and aminoesters.

The experimental procedure is particularly simple : the β-diketone (10^{-2} mol) is mixed with the amino compound (10^{-2} mol) and the mixture is either adsorbed over the appropriate inorganic solid (montmorillonite clay K_{10} or silica, 3g) or added over a catalytic amount of PTSA (para toluene sulphonic acid, 2.10^{-4} mol) and submitted to irradiation in a domestic microwave oven[9] (MW). The reaction may be run in an open vessel (OV) or in a closed Teflon vessel (CV). The resulting product is treated with CH_2Cl_2 for filtration and subsequent evaporation and purification.



For instance, acetylacetone **1** reacts with a variety of amines **2** to give the following results (Table 1).

3	R^1	R^2	Support or catalyst	MW power (Watts)	Time (min)	isolated yield %	mp °C or bp °C / Torr
a	H	Bu	K_{10}	200	1	99	70 / 3.5 10^{-2}
b	H	Bz^i	"	100	3	97	160 / 2.5 10^{-2}
c	H	Ph	"	250	2	98	102
d	- $(CH_2)_4$ -		-	-	10	98	115
e	- $(CH_2)_5$ -		SiO_2	300	3	87^{ii}	50
f	Bu	Bu	PTSA	300	10	35	110 / 3.10^{-2}
g	Bu	Me	"	300	5	53	80 / 3.2 10^{-2}
h	Bz	Bz	"	400	10	53	160 / 3.6 10^{-2}

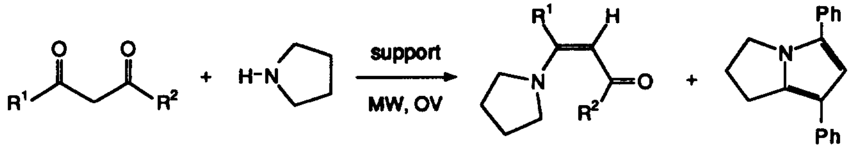
i : Bz = CH_2Ph

ii : over PTSA, 2 minutes at 300 Watts, yield : 69%.

Table 1

The stereochemistry of compounds **3** is Z with primary amines, as shown by the intramolecular hydrogen bond and the stereochemistry is not assigned in the case of secondary amines.

In the same way, we checked the reactivity of various dicarbonyl compounds with pyrrolidine as a model reaction (Table 2).



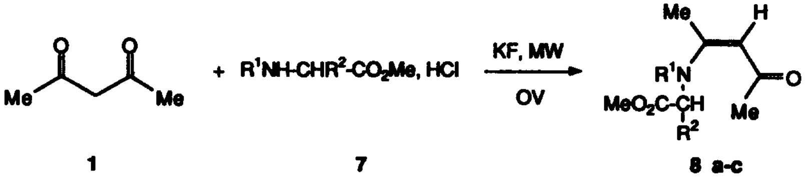
4	R^1	R^2	support	MW (Watts)	Time (min)	5 isolated yield %	mp °C or bp °C / Torr
a	Me	Ph	SiO_2	300	3	89	166
b	Ph	Ph	SiO_2	200	20	79^i	150 / 3.10^{-2}
c	Me	OMe	K_{10}	100	1	95	67

i : in this case the side product **6b** resulting from the condensation of the CH_2 in α position of nitrogen with the carbonyl group is formed and characterized by spectroscopic data (^1H, MNR and mass spectrum yield 15%).

Table 2

The protection of aminoacids by enamine formation has been mentioned in the literature[10] and we extended the scope of our procedure to aminoesters in the following way : aminoesters hydrochlorides (10^{-2} mol) react with acetylacetone (10^{-2} mol) (over previously dried KF, 2g, dried at

400 Watts during 15 minutes in the microwave oven) to give after microwave irradiation the corresponding enamines (Table 3).

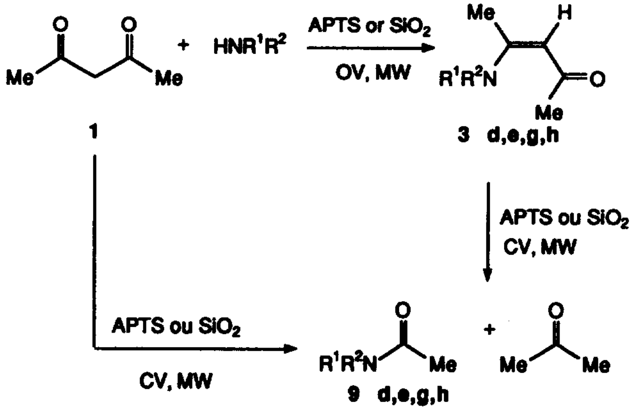


8	R¹	R²	MW (Watts)	Time (min)	isolated yield %	mp °C bp °C / Torr
a	H	H	200	2	97	62
b^i	H	Me	200	1	95	130 / 4.8 10^{-2}
c	- $(CH_2)_3$ -		250	1	97	120 / 3.4 10^{-2}

i : the experiment was run with L derivative and the rotation is not lost in the reaction.

Table 3

In an attempt to optimize the yields of some of the enaminoketones (i.e 3g and 3h) we tried to



operate in a closed Teflon vessel and we observed the unexpected formation of N-substituted acetamide 9 together with acetone elimination (Table 4).

9	R^1	R^2	Support or catalyst	MW (Watts)	Time (min)	isolated Yield %	mp °C or bp°C / Torr
d	- $(CH_2)_4$ -		SiO_2	300	12	90	115
e	- $(CH_2)_5$ -		SiO_2	300	15	71	50
g	Bu	Me	APTS	300	20	18	80 / 0.03
h	Bz	Bz	APTS	400	10	20	95 / 0.03

Table 4

It seems reasonable to assume that starting from the β-dicarbonyl compound and the amine in an open vessel the enaminoketone **3** is formed and the condensation water is eliminated in the microwave oven. But in a closed vessel, the water remains giving rise *in situ* to an hydrolysis of the enaminoketone by the mechanism of Stork [11]. In the last step, the acyl group in β position favours the cleavage of the C-C bond and stabilizes the resulting carbanion leading to acetone elimination. Starting from the isolated **3** in a closed vessel with non dried SiO_2, we also obtained **9** but if SiO_2 is previously dried, this transformation hardly takes place.

As a conclusion, it is noteworthy to mention that this procedure affords enaminoketones in shorter reaction-times and with better yields than the classical homogeneous reactions in benzene with continuous azeotropic elimination of water [12-14]. Extension to the reactions of dicarbonyl compounds with diamines and aminoalcohols is actually under progress.

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