

A Rapid and Convenient Synthesis of Oximes in Dry Media under Microwave Irradiation†

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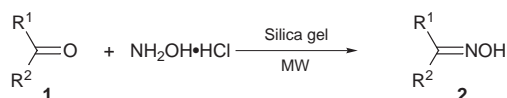
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In a novel method, the reaction of hydroxylamine hydrochloride with a number of aldehydes and ketones under microwave irradiation and solventless 'dry' condition gave oximes in excellent yield.

Oximes are highly crystalline and the oximation is a very efficient method for characterisation and purification of carbonyl compounds. These compounds not only represent a convenient series of derivatives of carbonyl compounds but also may be used as intermediates for the preparation of amides by the Beckmann rearrangement,¹ nitrones,² hydroximinoyl chlorides,³ nitrile oxide³ and chiral α -sulfinyl oximes.⁴ The usual method for the preparation of oximes involves treatment of carbonyl compounds with hydroxylamine hydrochlorides in a basic aqueous medium with adjustment of pH. Because of improper levels of solvent or reactant being used some oximes are liquid or oil-out and the operating conditions of this method are difficult.

Since the early articles of Gedye and Giguere,⁵ application of the microwave heating technique has been currently under intensive investigation and has been recently reviewed.⁶ The effects usually observed are: (a) decreased reaction time and (b) cleaner reaction with easier work-up. Especially interesting was the coupling with dry media conditions which allowed reaction on a preparative scale and open vessels (avoiding the risk of high pressures and explosions).⁷

We report here that silica gel, without any base, could be a useful catalyst for the preparation of oximes in dry media coupled with microwave irradiation. Hydroxylamine hydrochlorides were reacted with several aliphatic and aromatic aldehydes and ketones (Scheme 1) affording the desired oximes.



Scheme 1 Preparation of oximes **2**

In order to evaluate the synergy between dry media and microwave irradiation in this reaction, several experiments were tried. As shown in Table 1, the reaction of benzaldehyde and hydroxylamine hydrochloride without irradiation was

unsuccessful and the aldehyde was recovered unchanged after 60 min grinding in a mortar (entry 2). When silica gel was used as catalyst in aqueous solution (2 h, reflux), the corresponding oxime was obtained in 63% yield (entry 4). The reaction of benzaldehyde and hydroxylamine hydrochloride in the presence of silica gel without irradiation was unsuccessful and the yield of corresponding oxime after 30 min grinding in a mortar at 70 °C was only 20% (entry 3). Similarly when we used irradiation without silica gel for 6 min the condensation proceeded in only 20% yield (entry 5). Only in the case of dry media coupled with microwave irradiation, taking advantage of the synergy between both methodologies was the oxime produced in excellent yield (entry 1).

The ability of silica gel in dry media coupled with microwave irradiation was demonstrated using various aldehydes and ketones with hydroxylamine hydrochloride in the absence of any base, and the resulting data are summarised in Table 2. Aliphatic, aromatic and α , β -unsaturated aldehydes were converted to the corresponding oximes in > 76% yield in < 4 min (entries a–j). For ketones reactions were more difficult and lower yields were obtained (entries k–q). The less reactive benzophenone was also found to condense with hydroxamine hydrochloride in 50% yield in 6 min (entry k). The purity of the products were determined by ¹H NMR, IR spectra and melting point. It is very interesting that in these reactions nitriles were not formed, and in the IR spectra the CN group was not observed around 2200 cm⁻¹. In all ¹H NMR spectra the OH group of oximes appeared around δ 8.0–9.8 as a broad singlet and in IR spectra the OH and C=NOH group were observed around 3300–3500 and 1640–1690 cm⁻¹ respectively.

Another noteworthy feature of the method lies in the exclusive reaction of aldehydes with hydroxylamine hydrochloride irrespective of the presence of ketones. When we treated one equivalent of aldehydes in the presence of one equivalent of ketones with two equivalents of hydroxylamine hydrochloride only the aldehydes were selectively converted

Table 1 Condensation of benzaldehyde with hydroxylamine hydrochloride

Entry	Catalyst	<i>T</i> or <i>MW</i> power	Time/min	Solvent	Oxime ^a (%)
1	silica gel	800 W	1	None	96
2	silica gel	r.t.	60	None	0
3	silica gel	70 °C	30	None	20
4	silica gel	100 °C	120	Water	63
5	none	800 W	6	None	20

^aEvaluated by TLC analysis.

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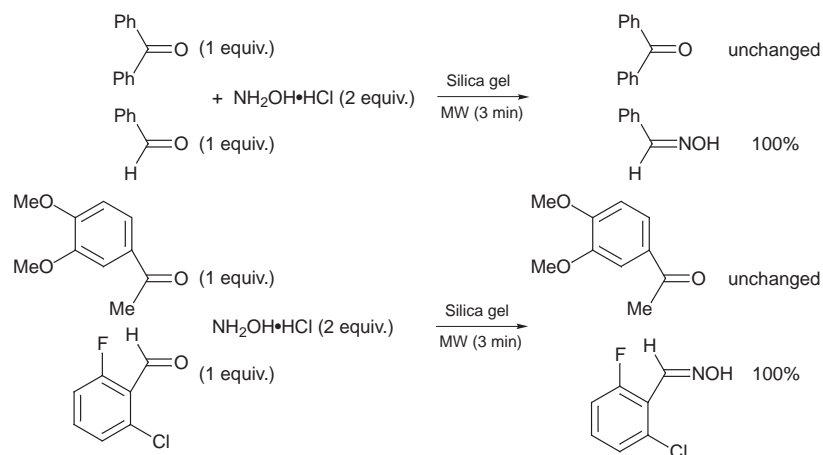
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to the corresponding oximes and ketones did not react at all (Scheme 2). Therefore this methodology could be used selectively for preparation of aldioximes of the compounds that contain both aldehyde and ketone functional groups.

Table 2 Reaction of carbonyl compounds **1** with hydroxylamine hydrochloride

Entry	R ¹	R ²	Power ^a /W	Time/s	Yield ^{b,c} (%)	Mp/°C
a	Ph	H	800	50	90	33–35
b	2-MeOC ₆ H ₄	H	800	160	94	88–90
c	4-BrC ₆ H ₄	H	800	220	88	111–113
d	4-ClC ₆ H ₄	H	800	210	92	105–107
e	4-NO ₂ C ₆ H ₄	H	800	180	87	128–130
f	4-MeOC ₆ H ₄	H	800	140	79	63–65
g	4-Me ₂ NC ₆ H ₄	H	800	120	76	138–140
h	2-C ₁ , 6-FC ₆ H ₃	H	800	180	98	126–127
i	PhCH=CH	H	800	240	84	136–138
j	3,4-(MeO) ₂ C ₆ H ₃	H	800	120	86	92–94
k	Ph	Ph	800	360	50	138–140
l	3,4-(MeO) ₂ C ₆ H ₃	Me	800	270	37	139–141
m	PhCO	Ph	900	480	21	—
n	Ph	Me	900	240	73	56–58
o	PhCH(OH)	Ph	900	480	0	—
p		–[CH ₂] ₅ –	900	360	0	—
q		–[CH ₂] ₆ –	900	480	0	—

^aIrradiations were carried out in a domestic microwave oven (Samsung 2450 MHz, 900 W), for an optimised time and power. The temperature of reaction reached 80–90 °C. ^bEvaluated by weight of isolated oxime after purification. ^cAll products are known compounds and exhibit satisfactory spectroscopic data (¹H NMR and IR).

**Scheme 2**

To the best of our knowledge, this is the first example for silica gel catalysis of this reaction. In conclusion, the reported procedure is an interesting, easy and novel method for the preparation of oximes. These reactions are fast, the procedure simple and of low cost, and it was possible to work under mild neutral conditions.

Experimental

General Method.—Preparation of **2**. In a typical experiment, a mixture of 0.106 g (1 mmol) of benzaldehyde and (2 mmol, 0.140 g) of hydroxylamine hydrochloride was ground thoroughly in a mortar and supported on silica gel (silica gel 60, 230–400 mesh, Merck) (1 g). The mortar was covered with a watch glass and put inside a Samsung microwave (2450 MHz, 900 W). The compound was irradiated for 2 min (Table 1) and the completion of the reaction is monitored by TLC examination. After completion of the reaction, the mortar was removed from the oven and the mixture was cooled to room temperature, 10 ml of 5% aqueous HCl were added and the solution was extracted with CH₂Cl₂ (2 × 5 ml). The extracts were combined, dried (CaCl₂) and evaporation of solvent under vacuum gave benzaldehyde oxime, which was ≥ 98 pure, (TLC, ¹H NMR, IR and melting point). The product could be further purified by recrystallization from *n*-hexane.

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