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Mild, Efficient, and Rapid Dehydration of Aldoximes to Nitriles Mediated by Phthalic Anhydride Under Microwave Irradiation

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Summary. Aldoximes can be efficiently and rapidly dehydrated to nitriles by treatment with phthalic anhydride under microwave irradiation.

Keywords. Aldoximes; Phthalic anhydride; Nitriles; Microwave Irradiation.

Introduction

Nitriles have been used in organic synthesis for a long time as precursors of biologically active compounds such as antipecurnavirus tetrazole analogues [1], 1,2-diarylimidazoles as potent anti-inflammatory agents [2], triazolo[1,5-*c*]primidines with potent antiasthma activity, and benzamidine with fibrinogen antiagonistic activity [4]. Another application of nitriles is their reaction with β-aminoalcohol in the presence of a catalyst to give 2-oxazolines, which are used as chiral auxiliaries in asymmetric synthesis [5]. The most common route to nitriles starts from aldehydes [6]. Very recently, aldehydes have been converted into nitriles using ammonia and hydrogen peroxides [7].

Oximes are extensively employed for the purification of carbonyl compounds [8]. In addition, oximes can be synthesized from non-carbonyl compounds [9]. Therefore, direct conversion of oximes to nitriles offers an alternative and promising route. In spite of this possibility, only few reports exist in literature dealing with this reaction. The use of trimethylsilyl iodide [10], 1,1′-oxalyldiimidazole [11], and carbon monoxide/water in the presence of a Rh carbonyl cluster [12] have been reported. Recently, a new enzymatic method for the conversion of aldoximes to nitriles has been described [13].

Results and Discussion

Microwave irradiation is a useful technique in organic synthesis [14]. In connection with our interest using microwave irradiation to implement and increase reaction

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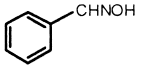
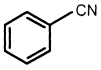
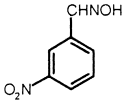
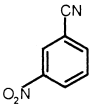
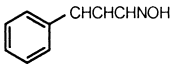
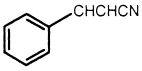
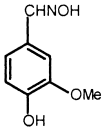
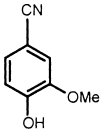
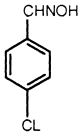
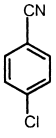
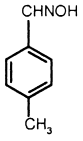
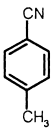
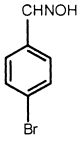
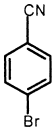
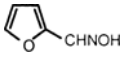
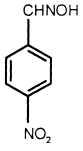
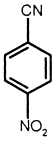
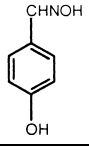
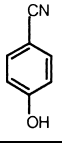
Table 1. Conversion of aldoximes to nitriles with phthalic anhydride under microwave irradiation

Entry	Oxime (**1**)[a]	Nitrile (**2**)	Reaction time (min)	M.p./°C or b.p./°C (torr)		Yield[b] %
				reported	found	
1			4	121 (100)	123.5 (100)	90
2			3	116	115–117	87
3			5	254 (760)	251–252 (760)	86
4			4	84	85–87	85
5			10	93	92–93	90
6			8	30	26–28	92
7			12	109	112–114	80
8			5	142 (760)	146–149 (760)	86
9			15	144	146–149	78
10			7	110	110–112	94

[a] Oximes were synthesized according to reported procedures

[b] Yields refer to isolated products

rates [15], in this communication we report that phthalic anhydride, an inexpensive and readily available reagent, can convert aldoximes to nitriles rapidly and efficiently in acetonitrile under microwave irradiation. When benzaldoxime and phthalic anhydride were dissolved in CH_3CN and treated with microwaves for less

than 4 min, benzonitrile was obtained almost quantitatively. To assess the generality of the method, a variety of aldoximes were converted to the corresponding nitriles in very short reaction times and high yields under the same conditions (Table 1).

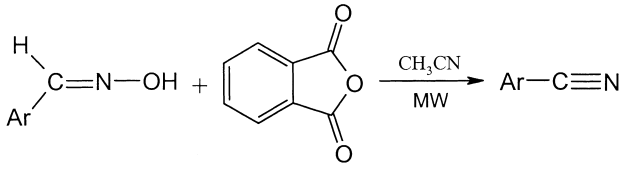
In conclusion, we have developed a mild, efficient, inexpensive, and rapid method for the direct conversion of aldoximes to nitriles.

Experimental

All products are known compounds; their physical data agreed with those of authentic samples.

General procedure

5 mmol of an appropriate oxime **1** and 5.05 mmol phthalic anhydride were added to 10 cm^3 of anhydrous acetonitrile. The resulting mixture was immediately placed into a microwave oven operating at medium to high power for the time indicated (Table 1). Then, the solvent was evaporated, and the resulting residue was extracted with $3 \times 30\,cm^3$ of CH_2Cl_2. The organic layer was washed with 5% NH_3 and an excess of H_2O to remove phthalic acid. The organic layer was dried over $MgSO_4$ and then evaporated. The residue was recrystallized from *n*-hexane/ethylacetate (Table 1, entries 2, 4–7, 9, 10) or purified by passing through a short silicagel column using $CHCl_3$ as eluent (Table 1, entries 1, 3, 8) to give pure nitrile **2**.



1 **2**

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