SHORT PAPER

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Microwave-assisted efficient one-pot synthesis of nitriles in dry media†

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A rapid and efficient procedure is reported for the synthesis of nitriles by condensation of aldehydes with hydroxylamine hydrochloride in the presence of dibutyltin oxide supported on Al_2O_3 under microwave irradiation

Keywords: nitriles, aldehydes

Introduction

Conversion of aldehydes into nitriles is an important functional group transformation in organic synthesis.[1] Aromatic and aliphatic nitriles are versatile intermediates[2] in the synthesis of biologically active molecules such as thiazoles, 2-oxazolines, tetrazoles, imidazoles, triazoles and benzamidines. Nitriles can be prepared by dehydration of aldoximes formed from the aldehydes and hydroxylamine hydrochloride. In most cases, the aldoxime is prepared initially by condensation of aldehyde with hydroxylamine hydrochloride and then dehydrated by a wide variety of reagents.[3–4] Several, one-pot procedures have also been reported[5,6] to effect this transformation. However, most of these one-pot procedures are limited to aromatic aldehydes and often give unsatisfactory yields. Methods which have been developed for both aromatic and aliphatic aldehydes often involve expensive reagents[5] (hydroxylamine-*O*-sulphonic acid and 2,4-dinitrophenylhydroxylamine), corrosive[6] (formic acid) or hazardous[7a] (SeO_2) reagents and oxidising[7b] (Oxone®) agents. In recent years, there has been increasing interest in surface mediated solid state reactions coupled with microwaves[8] due to their enhanced selectivity improved reaction rates, operational simplicity and ease of product isolation. There is an advantage in developing a truly catalytic process for the conversion of aldehydes into nitriles using inexpensive reagents, which can effect the transformation under mild and neutral conditions.

Results and discussion

In continuation of our interest on solid supported reagents associated with microwaves,[9] herein we report a rapid and highly efficient procedure for the preparation of nitriles from aldehydes and hydroxylamine hydrochloride using a catalytic amount of dibutyltin oxide supported on alumina in dry media. The reaction proceeded rapidly on the surface of solid reagent system, n-Bu_2SnO–Al_2O_3 under microwave irradiation. A variety of aromatic, aliphatic and heterocyclic aldehydes were smoothly converted into the corresponding nitriles in high yields. The reactions were carried out in solvent-free conditions using a BPL, BMO-700T microwave oven operating at 450 W. The reaction temperature was controlled in a microwave oven by pulsed irradiation technique (1 min with 20 s. intervals). The temperature was measured at the end of each irradiation. The lowest observed temperature was 90°C after 1 min irradiation at 450 W and the highest observed temperature was 120°C after 5-min. irradiation at the same power. The products were isolated in 75–90% yield, when 1 equiv. of aldehyde, 1.2 equiv. of $NH_2OH.HCl$ and 0.15 equiv. of dibutyltin oxide were admixed with alumina (1 g) in a Pyrex test tube and exposed to microwave irradiation at 450 W for 3–7 min. These reactions, however, require approximately 8–12 h of heating at 120°C (highest temperature observed during microwave irradiation) to achieve yields comparable with those obtained by microwave irradiation. The conventional heating at 120°C and long reaction time (8-12 hrs) are totally avoided using microwave irradiation which is becoming an alternative heating source. In general, polar media or polar reactants absorb more microwave energy and generate heat energy as required to promote the reaction. As both alumina and catalyst are polar so they absorb microwaves effectively and complete the reaction in a short time. Further, the reactions proceeded only to a minor extent (10–15%) when the reactants were subjected to microwave irradiation for a long time (10–15 min.) in the absence of catalyst. The oximes were exclusively formed in good yields, when the reactants were irradiated in the presence of Al_2O_3. This clearly indicates the catalytic effect of dibutyltin oxide in this transformation. Different metal oxides like ZrO_2, MgO, ZnO, V_2O_5 and CeO_2 were doped on Al_2O_3 matrix for their effect. Dibutyltin oxide–Al_2O_3 is found to be more effective in terms of conversion and reaction times than others.

$$R\text{–}CHO + NH_2OH\cdot HCl \xrightarrow[\text{microwave irradiation}]{n\text{-}BU_2SnO\text{-}Al_2O_3} R \equiv CN$$

Scheme 1

In conclusion, we have developed a rapid and highly efficient procedure for the synthesis of nitriles from aldehydes and hydroxylamine hydrochloride using *n*-butyltin oxide supported on Al_2O_3 under microwave irradiation. The method offers several advantages like mild reaction conditions, inexpensive reagents, improved yields, enhanced reaction rates, cleaner reaction products and simple product isolation procedures which makes it a useful addition to the existing methods.

Experimental

Piperonal (5 mmol) hydroxylamine hydrochloride (6 mmol), and *n*-dibutyltin oxide (0.5 mmol) were admixed with alumina (1 g) and exposed to microwave irradiation at 450 W (BPL, BMO-700T) for an appropriate time. After complete conversion, as indicated by TLC, the reaction mixture was filtered and the residue washed with dichloromethane (2 × 15 ml) which was then concentrated *in vacuo*. The resulting solid was recrystallised in ethanol to give 3,4-methylenedioxybenzonitrile in 92% yield as a white solid m.p. 68–70°C (68–69°C Lit.,). The liquid products were purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate-hexane, 1:9) to afford the corresponding nitriles in pure form.

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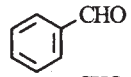
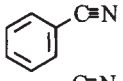
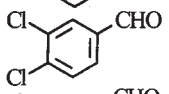
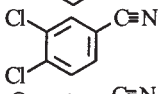
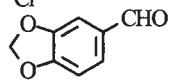
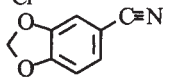
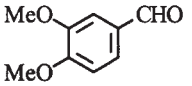
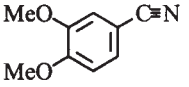
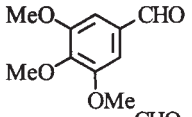
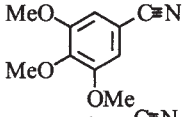
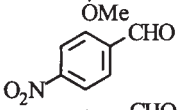
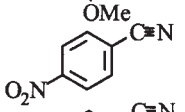
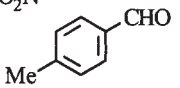
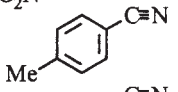
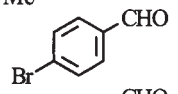
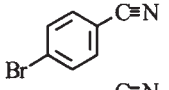
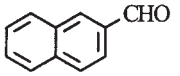
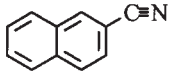
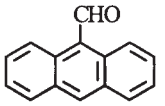
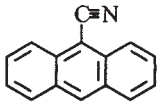
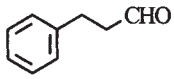
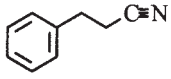
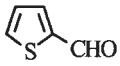
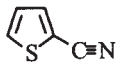
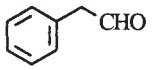
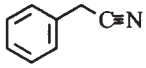
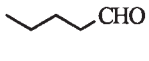
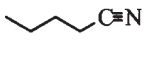
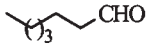
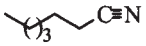
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Conversion of aldehydes into nitriles under microwave irradiation

Entry	Aldehyde	Nitrile[a]	Reaction time/min.	Yield/%[b]	m.p.°C or b.p.°C (mm) Found	Reported[2,4]
a)			4	88	189–190 (760)	190–191 (760)
b)			5	90	69–71	70–72
c)			3	92	68–70	68–69
d)			4	89	90–92	91–93
e)			5	85	91–93	92–94
f)			7	70	145–147	146–147
g)			5	87	216–218 (760)	216–217 (760)
h)			6	90	112–114	113–114
i)			7	78	65–65	64–66
j)			7	70	174–176	175–177
k)			4	76	254–256 (760)	254–255 (760)
l)			3	90	190–192 (760)	192 (760)
m)			4	87	100–102 (10)	101–103 (10)
n)			3	75	69–70 (10)	69–71 (10)
o)			5	78	198–200 (3)	197–199 (10)

[a]All products were characterised by ^{1}H NMR, IR and mass spectra. [b]Isolated yields after purification

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