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*SHORT COMMUNICATION*

# Rapid Solvent-free Synthesis of Aromatic Hydrazides under Microwave Irradiation

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**ABSTRACT**

A variety of aromatic hydrazides has been synthesised by solvent-free hydrazinolysis of corresponding esters with hydrazine hydrate under microwave irradiation.

**Keywords :** Aromatic hydrazides, microwave irradiation, solvent-free synthesis, hydrazides

## 1. INTRODUCTION

Over the past few years, there has been growing interest in the synthesis of organic compounds under microwave irradiation because of increasing environmental consciousness. The feasibility of microwave-assisted synthesis has been demonstrated in various transformations like protection and deprotection[1], condensation[2], cycloaddition[3], alkylation[4], oxidation[5], reduction[6], synthesis of various heterocyclic compounds[7-9], and in many other chemical reactions. The salient features of these transformations are the enhanced reaction rates, greater selectivity, and the experimental ease of manipulation[10] leading to an efficient, environment-friendly and cost-effective pathway to several synthetically useful compounds. Acyl derivatives of hydrazines are called acid hydrazides or hydrazides. These constitute an important class of biologically active organic compounds. The therapeutic uses of hydrazides are well-documented in the literature. Hydrazides and their condensation products are also reported to possess a wide range of biological activities such as antibacterial activity[11-13] and tuberculostatic properties[14].

Some of the hydrazides and corresponding hydrazones are psychopharmacological agent, eg, monoamine oxidase (MAO) inhibitor and serotonine antagonists[15]. Hydrazides are commonly prepared by the hydrazinolysis of esters with hydrazine hydrate[16]. The reaction usually takes place at room temperature but sometimes it is necessary to heat the reaction mixture on steam bath for periods varying from 5 min to several days. In some cases, however, the reaction proceeds with great difficulty after heating for several days or even under pressure in a sealed tube. When the reaction is carried out by heating in a sealed tube, partial decarboxylation may also take place[17]. In addition, by the classical method, there is always a possibility for the formation of dihydrazides (R*CONHNHCO*R) as by-product.

## 2. EXPERIMENTAL PROCEDURE

Methyl or ethyl ester of aromatic carboxylic acid (0.1mol) was dissolved in hydrazine hydrate (99-100 %, 0.1 mol) in a glass tube and was placed in Samsung CK138F domestic microwave oven. After irradiation for a specified period, the solid

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product was obtained on cooling at room temperature and purified by recrystallisation from ethanol. The compounds were characterised by mixed melting points and IR spectral analysis using Nicolet IMPACT410 FT-IR spectrophotometer.

Salicylic acid hydrazide: mp 150-51°C; IR (*KBr*): 3320 $cm^{-1}$, 3269 $cm^{-1}$, 2929 $cm^{-1}$, 1647 $cm^{-1}$, 1587 $cm^{-1}$, 1532 $cm^{-1}$, 1485 $cm^{-1}$, 1367 $cm^{-1}$, 1239 $cm^{-1}$, 963 $cm^{-1}$, 761 $cm^{-1}$, $^1H$ NMR ($CDCl_3$): δ 1.5 (s, 2*H*, $NH_2$), 4.2(s, 1*H*, *OH*), 6.9-7.8 (m, 4*H*, *Ar*), 8.0 (s, 1*H*, *CONH*); MS: m/z (%) = 152 $[M]^+$ (38), 121 $[M-31]^+$ (100), 93 $[M-59]^+$ (18), 65(12).

## 3. RESULTS AND DISCUSSION

A rapid, single-step and solvent-free microwave approach has been described for the synthesis of a variety of aromatic acid hydrazides:

$$Ar-COOR' \xrightarrow[MW]{99\%\, NH_2-NH_2H_2O} Ar-CONHNH_2$$

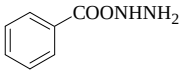
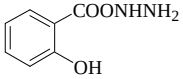
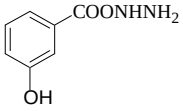
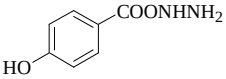
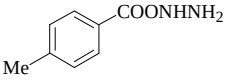
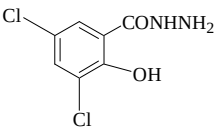
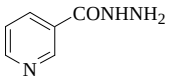
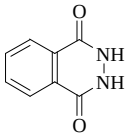
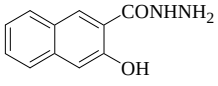
As a classical example, the hydrazinolysis of methyl salicylate, methyl nicotinate, ethyl phthalate, ethyl 3-hydroxynaphthoate were carried out both by conventional method as well as by solvent-free microwave irradiation to establish the importance of the above microwave irradiations over the classical methods. The results are shown in Table 1. High yield and less reaction time of the hydrazides (Table 1) clearly indicate the importance of solvent-free microwave method over the conventional method.

**Table 1. Hydrazinolysis of aromatic esters**

| Product | Microwave irradiation technique (450 W) | | Conventional method* | |
|---|---|---|---|---|
| | Time (s) | Yield (%) | Time (h) | Yield (%) |
| Salicylic acid hydrazide | 120 | 90 | 1 | 65 |
| Nicotinic acid hydrazide | 30 | 87 | 4 | 65 |
| Phthalic acid hydrazide | 60 | 89 | 4 | 40 |
| 3-Hydroxynaphthoic acid hydrazide | 40 | 85 | 2 | 30 |

* In refluxing ethanol

**Table 2. Microwave-assisted solvent-free synthesis of acid hydrazides**

| Hydrazide | mp (°C) | Microwave irradiation | | |
|---|---|---|---|---|
| | | Power (W) | Reaction time (s) | Yield (%) |
|  **1** | 110-11 | 450 | 180 | 86 |
|  **2** | 150-51 | 450 | 120 | 90 |
|  **3** | 156-68 | 900 | 30 | 85 |
|  **4** | 265 (d) | 450 | 90 | 85 |
|  **5** | 114-16 | 900 | 30 | 88 |
|  **6** | 199-200 | 300 | 20 | 87 |
|  **7** | 159-60 | 300 | 30 | 87 |
|  **8** | > 300 | 450 | 60 | 89 |
|  **9** | 208-210 | 900 | 40 | 85 |

Melting points and spectral data of all the compounds were matching with the authentic samples.

Similar microwave-assisted solvent-free experiments were also carried with a variety of aromatic esters including heterocyclic and naphthyl ester using equimolar mixture of the corresponding ester and hydrazine hydrate in the absence of any solvent, catalyst and solid support. The data presented in Table 2 again shows the efficiency of microwave irradiation method.

## 4. CONCLUSION

Easy experimental procedure and quantitative yield of the products make it a useful synthetic method for the synthesis of hydrazides.

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