



## Atom efficient grinding technique for the synthesis of hydrazones catalyzed by citric acid

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### ABSTRACT

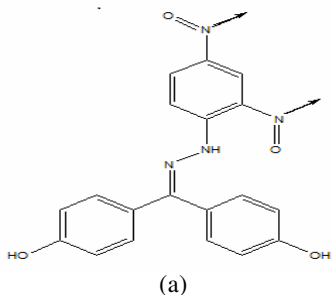
A highly efficient and expedient protocol for the synthesis of hydrazones catalyzed by citric acid is investigated via reaction of hydrazine hydrate with different carbonyl compounds. The use of inexpensive, non-hazardous easily available citric acid as a catalyst for the synthesis hydrazones employing grinding technique is reported. The structures of the synthesized compounds are established on the basis of physical, chemical and spectral data.

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### Introduction

In recent decades various diseases threatened the world with their hazardous effects like Cancer, Malaria, AIDS and Tuberculosis. More than 50 million peoples are affected by malaria causing approximately 2 million deaths per year. Tuberculosis claims over 2 million lives worldwide each year. Researchers are involved in the business to synthesize the molecules of biological interest which can provide relief to the world from these hazardous diseases. Hydrazones have been emerged as one of the fruitful product of their efforts.

L.R. Morgan *et al.* explored the studies of anticancer agent 4,4'-dihydroxybenzophenone-2,4-dinitrophenylhydrazone (a) by preparing its stable double salts showing improved in vitro anticancer activity than its precursor alone [1].



In addition to this, various substituted hydrazones exhibit antimicrobial [2], antimalarial [3], anti-inflammatory [4], anti-HIV [5], anticonvulsant [6], anti-hyperalgesic [7] and other pharmacological potencies [8-10]. On the other fold, hydrazones have been utilized in synthetic chemistry for protection of carbonyl compounds [11] and as chemical intermediate which can act as electrophile and as nucleophile in mannich type reaction, asymmetric syncyanation and allylation reactions [12]. Variety of hydrazones has been employed as ligands for preparing various bioactive complexes [13-16]. Apart from these we must discuss the use of hydrazones in medical biotechnology

in coupling methods. They are used to couple with certain drugs. The hydrazones based bond is stable at neutral pH (in the blood) but it is rapidly destroyed in acidic environment of lysosomes and the drug become free for its action [17].

Classical method for the synthesis of hydrazones is the reaction of hydrazine with slight excess of carbonyl compounds in refluxing conditions using ethanol or toluene as a solvent. Recently RS Varma utilized the polystyrene sulphonic acid as a catalyst for the synthesis of hydrazones under microwave conditions [18]. DJ Brondani reported the synthesis of some aryl hydrazones in aqueous media under ultrasound irradiation [19]. And the very recent development in the synthetic methods is the use of Ball-Mill for the solvent free synthesis of hydrazones by F Lamaty [12].

These days, variety of acid catalysts has been employed in synthetic chemistry. Competing with the huge range of catalyst citric acid played a vital role in organic synthesis [20-21] due to its non toxic nature, easy availability and for simple work up procedure. Efficiency and selectivity of solid state reactions are more fruitful than solution reaction [22], the reason lies in the regular and tight arrangement of molecules in a crystal.

In persuasion to develop neat methodologies and exploring the green chemistry goals [23] we offer the synthesis of hydrazones by reacting various halo substituted aldehydes and ketones with hydrazine hydrate catalyzed by citric acid via grinding technique.

### Experimental:

#### Methods and Analysis:

All chemicals were purchased from S. D. fine Chemicals (India). Melting points were recorded using open capillary method and are uncorrected. The progress of the reaction was monitored by thin layer chromatography technique. IR spectra were recorded on Perkin-Elmer 237 spectrometer. <sup>1</sup>H NMR spectra on Bruker Avance DPX400 MHz spectrometer with