

## New Route to Metformin Hydrochloride (*N,N*-dimethylimidodicarbonimidic diamide hydrochloride) Synthesis

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**Abstract:** In this work, microwave (MW) assisted synthesis of metformin hydrochloride was performed on thin layer chromatography (TLC) plates. This versatile, simple and economical green methodology is readily amendable to parallel synthesis of metformin hydrochloride libraries.

**Keywords:** metformin hydrochloride, microwave heating, solvent free condition

### Introduction

Metformin hydrochloride (*N,N*-dimethylimidodicarbonimidic diamide hydrochloride) is an oral antihyperglycemic drug used in the management of diabetes. It is usually prepared from the reaction between dimethylamine hydrochloride and dicyano diamide at 120-140 °C in 4 hrs time with 69% yield [1]. In designing ecofriendly synthesis of the target molecule, the starting materials are made to react by modifying the reaction conditions in such a way that the by-products and wastes are eliminated and also the use of organic solvents is minimized [2-4]. Thin layer chromatography (TLC) has been reported as a tool for reaction optimization in microwave assisted synthesis [5]. This method has been used to modify a conventional procedure for an efficient synthesis of metformin hydrochloride by simply spotting of the reaction mixture on a TLC plate and then subjecting it to microwave irradiation.

### Experimental

In a typical experiment, a test reaction was carried out on a 5×20 cm TLC plate, a spot of solution of dicyanodiamide **1** (0.42 g) and dimethylamine hydrochloride **2** (0.4 g) in 5 ml ethanol was placed on a TLC plate and subjected to MWI at 540 W at an interval of 40 seconds intermittently for 5 min. Then, the TLC plate was run in an appropriate system. A prominent spot of metformin hydrochloride **3** was seen and the *r<sub>f</sub>* value of which was consistent with that of the standard sample. In order to get an appreciable yield of pure product, the reaction was carried out on a preparative TLC plate. An array of spots of reactants for the synthesis of metformin hydrochloride was put on a preparative TLC plate along with a reference TLC with two spots (one of the reactants and other of expected product). Both the plates were subjected to MWI intermittently at an interval of 40 s at 540 powers for 5 min. The reference TLC was viewed in an iodine chamber and accordingly that portion of silica gel containing the product was scratched from the preparative TLC plate and the product was extracted in EtOH. Evaporation of the solvent afforded 0.82 g (92% yields) of the desired product.

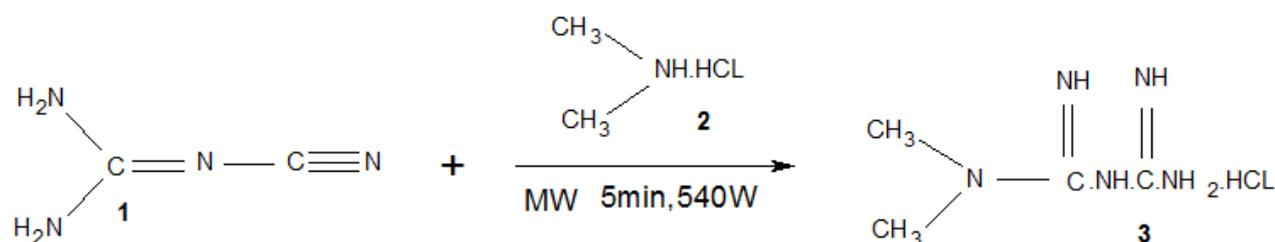
Melting point: 224-225°C

IR (KBr cm<sup>-1</sup>): 1580, 1620, 1063, 1075, 935, 740

UV (Methanol, λ<sub>max</sub>): 236 nm

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ (ppm): 2.92 (s, 6H, CH<sub>3</sub>); 6.77 (s, 4H, amide); 7.19 (s, 2H, imine)

<sup>13</sup>C-NMR (125 MHz, D<sub>2</sub>O): δ (ppm): 160.6, 158.9, 38.1.



## Results and Discussion

The yield of metformin hydrochloride by this ecofriendly method was 92% and the reaction time was 5 min. The viability and uniqueness of this method can serve as a useful tool for rapid reaction optimization in metformin hydrochloride synthesis.

The advantages of this ecologically safe protocol includes a simple reaction set up that does not requires specialized equipment, shorter reaction time, reduction of solvent, clean product, optimum use of energy and usage of only few milligrams of reactants in a few drops of solvent .

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