Comparison between mechanochemical and solution synthesis of ammonium-iminodiacetatedithiocarbamate

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Abstract : In this study, a comparison between the mechanochemical and conventional (solution) synthesis of ammonium-iminodiacetatedithiocarbamate is presented. The solution-based synthesis was carried out using methanol as the solvent, and the product was obtained after three hours. The mechanochemical synthesis method was chosen due to its alignment with the principles of green chemistry, particularly in reducing or eliminating the use of harmful organic solvents. The mechanochemical synthesis was conducted using iminodiacetic acid, ammonium carbonate, and carbon disulfide as starting materials and two types of ball mills: a vibratory ball mill (Fritsch Mini-Mill Pulverisette 23) and a planetary ball mill (Tmax ball mill). The mechanical energy provided by these mills enabled the reaction to proceed efficiently without the need for additional solvents or external heating. Compared to conventional solution-based methods, this approach significantly reduces solvent waste, shortens reaction times, and simplifies product isolation. Fourier transform infrared spectroscopy (FTIR) was used to monitor the progression of the reactions and to confirm the identity of the final products. The results suggest that mechanochemistry is a viable, sustainable, and environmentally friendly alternative for the synthesis of dithiocarbamate derivatives.

Keywords: mechanochemistry, syntheses, dithiocarbamate

1. Introduction

Mechanochemistry, recognized by IUPAC as a world-changing technology, has gained increasing attention within the framework of green chemistry. Mechanochemistry offers a solvent-free approach that not only reduces the use of harmful organic solvents, but also offers advantages such as improved selectivity, faster reactions, higher yields, and access to otherwise hard-to-obtain compounds [1]. This is particularly important considering that organic solvents are still widely used in laboratories and the chemical industry. Despite their usefulness in synthesis, purification, and processing, many of these solvents pose serious health and environmental risks. Their extensive and often uncontrolled use can lead to workplace

hazards and environmental pollution. This has led to an increasing focus on green chemistry and the promotion of safer, less toxic alternatives and improved solvent management [2].

Dithiocarbamates are known as sulfur donor ligands for their strong ability to form stable complexes with transition metals, making them valuable for a wide range of applications. Ammonium-iminodiacetatedithiocarbamate, $(NH_4)_3$idadtc, as a dithiocarbamate derivative, has potential applications as an enzyme inhibitor and has been explored for therapeutic use in the treatment of HIV, cancer, and other diseases, as well as for its antimicrobial, anti-inflammatory, and medical imaging properties [3]. Previously, $(NH_4)_3$idadtc was prepared using a conventional method that requires the use of significant amounts of methanol [4]. While the conventional synthesis involves reacting ammonium hydroxide with carbon disulfide in methanol, the solvent-free mechanochemical approach is increasingly being studied as a more sustainable and environmentally friendly alternative within the principles of green chemistry.

2. Experimental

The synthesis of $(NH_4)_3$idadtc via the solution route followed a previously reported method [4]. Iminodiacetic acid, ammonium carbonate, and carbon disulfide were milled mechanochemically using a vibratory ball mill (Fritsch Mini-Mill Pulverisette 23) and a planetary ball mill (Tmax ball mill). Figure 1 presents both synthesis routes.

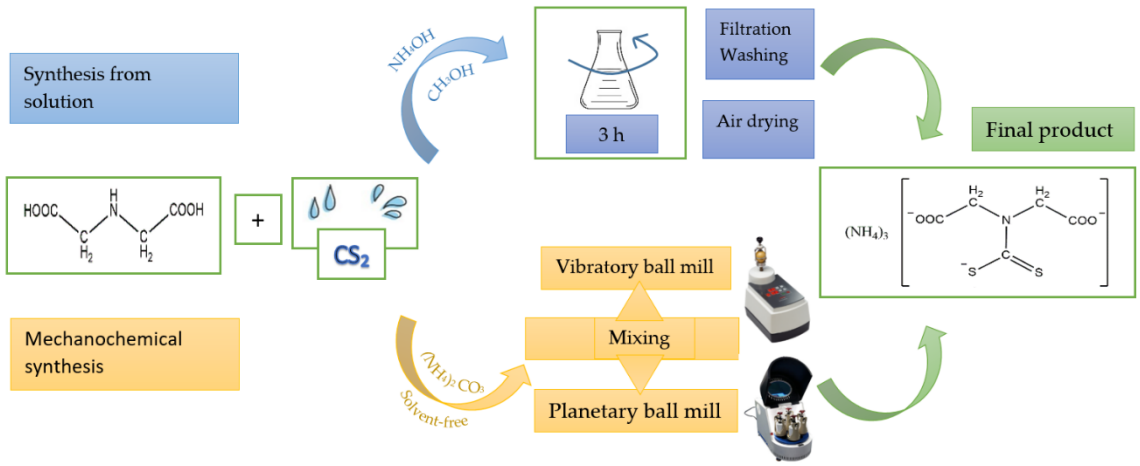

Figure 1. Synthesis routes for $(NH_4)_3$idadtc

Table 1 summarizes the different conditions applied for the syntheses in the respective mills.

Mechanochemical route	MH1	MH2	MH3	MH4	MH5	MH6
Mill Model	Fritisch Mini-Mill Pulverisette 23			Tmax Ball Mill		
Balls	1 × Ø 10 mm	7 × Ø 5 mm	5 × Ø 5 mm	80 × Ø 5 mm, 8 × Ø 7 mm, 8 × Ø 10 mm	80 × Ø 5 mm, 8 × Ø 7 mm, 8 × Ø 10 mm	8 × Ø 7 mm, 8 × Ø 10 mm

IDA : $(NH_4)_2CO_3$: CS_2 mmol	0,5 : 1 : 0,5	2 : 4 : 2	1 : 2 : 1	2 : 4 : 2	20 : 30: 20 (equimolar)	10: 20 :10
Mixing Time IDA+ $(NH_4)_2CO_3$ Add CS_2	5 min + 40 min	5 min + 3 h 55 min	Mixed together for 30 min	5 min+ 1h 55 min +1h	10 min+ 1h 50 min	5 min+ 1h 55 min
Conditions	45 Hz, RT	25 Hz, RT	45 Hz, RT	45 Hz, RT	45 Hz, RT	45 Hz, RT

Table 1. The different synthesis conditions

3. Results and discussion

The FTIR spectrum of $(NH_4)_3$idadtc obtained from solution (MHR) was used as a reference for comparison with the products of the mechanochemical syntheses (Figure 2). In the products MH1–MH3, which were synthesized in the vibratory ball mill without the use of solvents , the characteristic band around 989 cm^{-1}, which indicates the formation of the dithiocarbamate group, is either absent (MH1) or very weak (MH2). Its intensity increases with extended milling time. In contrast, the band is completely absent in one-pot synthesis (MH3), where all reagents are added at once, emphasizing the importance of the order of reagent addition. The presence of bands around 1700 cm^{-1} in MH1–MH3 suggests that the reactions did not lead to complete deprotonation of the carboxylic groups as observed in the reference sample.

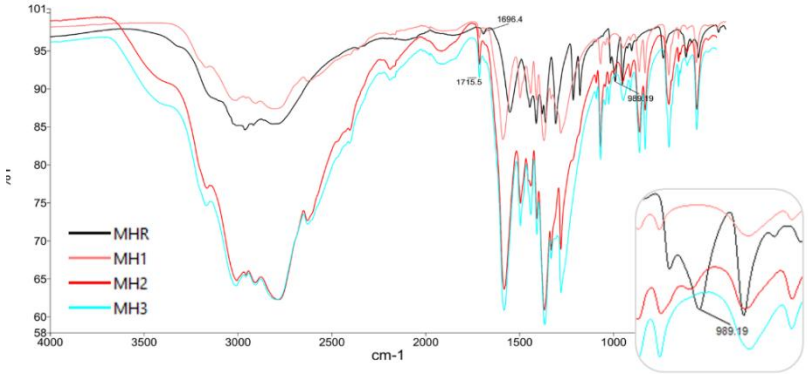

Figure 2. FTIR spectra of the reference compound (MHR) and the products obtained by vibrational milling (MH1–MH3)

In the case of sample MH4, extending the milling time from 2 to 3 hours led to the formation of a more pronounced band at 988 cm^{-1}, more uniform C–N vibrations, and a weakening of the band around 1700 cm^{-1}, indicating deprotonation of the carboxylic group. The spectrum (Figure 3) of this sample is closest to the reference. Samples MH5 and MH6 exhibit almost identical spectra to MH4. MH5 was obtained using equimolar amounts of reagents, suggesting that the addition of excess ammonium salt, as in the case of synthesis in solution, is not necessary for the formation of the desired product. MH6 was synthesized using the LAG method with the addition of a small amount of methanol, demonstrating that liquid-assisted grinding does not significantly affect the composition of the final product and is not required.

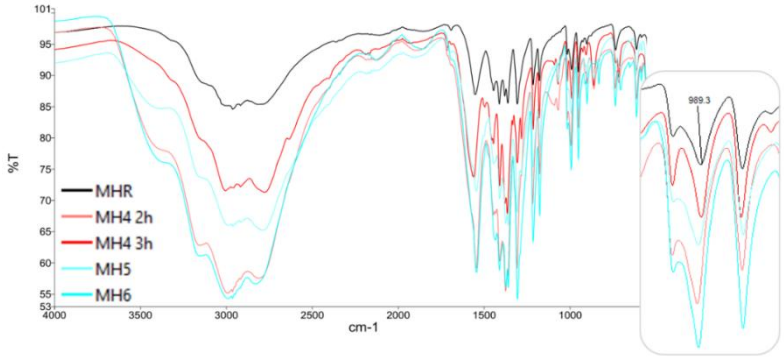

Figure 3. FTIR spectra of the reference compound (MHR) and the products obtained by planetary milling under different conditions (MH4–MH6)

4. Conclusions

This paper examines the differences between the synthesis of ammonium-iminodiacetatedithiocarbamate using a mechanochemical method and the conventional solution-based approach. The FTIR spectra of both methods and different mechanochemical protocols were compared to evaluate the effects of reaction conditions on product formation. The $(NH_4)_3$idadtc obtained in the planetary ball mill without solvents is of comparable quality to the product from the conventional solution-based synthesis, which consumes substantially more solvent.

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