

The Preparative Nonreflux Procedure on Disproportionation Reaction in Small-Scale Synthesis

Dini Rohmawati*, Sri Handayani*, Cornelia Budimarwanti*, Dista Arum Sari*, Diana Yuliyanti*, Muchammad Ikmal Abdillah*, Oktavia Pratiwi*, Tria Novita Anasriah*

* Department of Chemistry Education, Universitas Negeri Yogyakarta

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Corresponding Author:

Dini Rohmawati,
Department of Chemistry
Universitas Negeri Yogyakarta

Email: dini_rohmawati@uny.ac.id

ABSTRACT

Reactions with nonreflux procedures are based on the mechanical impact energy to promote the transformation process of chemicals. The simple procedures are grinding-milling, microwave-assisted, and ultrasonic-assisted. Generally, the procedures were undergoing nonsolvent or solventless reaction conditions also in effective and efficient processes, which corresponds to the principles of green chemistry. In its development, disproportionation reaction could also be undergone by applying these methods. This article discussed the preparative procedures of nonreflux with grinding, shaking, ultrasonic-assisted, and microwave-assisted in disproportionation reactions, which later could be used as standard procedures according to green chemistry and sustainable development goals (SDGs).

Keyword: nonreflux, ultrasonic, microwave, grinding, shaking, disproportionation,

1. INTRODUCTION

The disproportionation reaction of aldehyde without alpha hydrogen refers to the Cannizzaro reaction. This reaction is known because the result gave percent yields about 50% alcohol and 50% carboxylic acid in one single-step reaction. In the presence of a strong base such as NaOH, the carbon atom of carbonyl will undergo nucleophilic acyl substitution due to the abstract of hydroxy ion, which leads to the formation of alkoxide ion as an ionic mechanism (Suhail et al., 2020).

Due to the simplicity of the reaction, several methods have been developed for this procedure. Nonreflux procedures have been promoted in recent years due to the implementation of the principles of green chemistry and sustainable development goals (SDGs) as these procedures offer alternative energy sources (Espro *et al.*, 2021; Baig & Varma, 2012). The growth of the approaches is mostly due to the simple and easy procedures in the process. The most common advantage of these methods was the short reaction time which led to low energy consumption, the methods also were done in solventless or nonsolvent conditions. Hence, these conditions offered the solid-state reactions under the mechanochemical procedures. Compared to the conventional reaction process which consists of dissolving and refluxing for long hours and high energy consumption to complete the reaction.

In the organic compound reaction, a mechanical process could assist in the change of the chemicals. This process helps the collision of the molecules and later the formation of new

compounds. For example, the pressure on chemical solid forms will improve the surface area during grinding and then give better contact with the reactants as the particles pulverize and react (Fantozzi *et al.*, 2023). This led to the enhancement in the reaction rate and later, the more efficient and effective reaction time. In addition, it was also demonstrated that the reaction rate does not depend on the particle size; instead, it depends on surface activation. Further, the mechanochemical is also feasible in promoting molecular rearrangement during the reaction as in the benzil-benzilic acid rearrangement (Ardila-Fierro *et al.*, 2023).

Based on the mechanochemical-assisted process, several nonreflux methods have been introduced in the disproportionation reaction such as microwave-assisted (Varma, 1998; Sharifi, 1999; Pourjavadi, 2002; Janczewski, 2019), ultrasonic-assisted (Poláčková *et al.*, 1996; Enterazi & Shameli, 2000), grinding (Phonchaiya *et al.*, 2009; Rahman & Kadi, 2012), and friction (Melgar *et al.*, 2010; Subbiah *et al.*, 2013). All procedures could be achieved under various conditions with less reaction time and higher percent yield than the reflux method. By considering the benefit and effectiveness of the nonreflux techniques, these procedures become more commonly adopted in disproportionation reactions. Herein, the procedure for disproportionation reaction under microwave-assisted, ultrasonic-assisted, grinding, and friction was prepared with convenient requirements. These preparative procedures aim for simple yet efficient reactions for undergraduate experiments.

2. DISCUSSIONS

The reflux method is a convenient way to promote the collision between molecules of the starting materials. This procedure is commonly used in the laboratory to perform organic compound reactions with heating in the presence of solvents as a medium to serve the interaction. However, the procedure usually takes quite a long time to obtain the product. With the awareness of the environment in recent years, several drawbacks of the reflux procedure such as the long reaction time, the halogenated solvent, and the total reaction waste, have become considerations to use the method in organic synthesis.

Several methods have been investigated to overcome the boundaries. One common method is adopting mechanical-assisted procedures to increase the reaction efficiency (Andersen & Mack, 2018). Mechanical force could induce the chemical reaction by acting as a driving force in disrupting the chemical bond in starting materials. The act corresponds to the energy that impacts the molecules in a shorter time with intensified energy to start the collision between them and later give the targeted product with fewer byproducts (Espro & Rodríguez-Padrón, 2021). This type of energy could be from the physical or additional mechanical forces such as friction or wave energy. Therefore, this method was known as mechanochemical which has been adopted to pursue the efficient and effective chemical reaction. The mechanical-assisted procedure also allows the solventless or nonsolvent reaction which considerably promotes environmentally friendly chemical reactions. This work described adopting several mechano-assisted methods such as microwave-assisted, ultrasonic-assisted, and friction (as in grinding and shaking) in the disproportionation reaction.

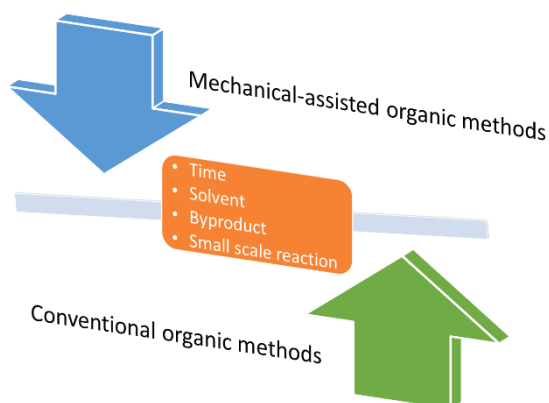


Figure 1. The conventional and mechanical-assisted organic reaction in comparison.

2.1. Mechanical-assisted method

Chemical reactions under the microwave-assisted procedure use microwave radiation (0.3 – 300 CHz) to accelerate the reaction rate. The common conception for the increase in reaction rate is related to the rise of temperature in the reaction medium by the microwave radiation field. As the reaction could occur due to the bond-breaking of the reactant and bond-making of the product, microwave radiation with its electromagnetic field will interact with the molecule and induce this process. The molecule absorbs radiation within microwave range and promotes the excitation state to a higher energy level. Following the excitation process, the relaxation also occurs from the resonance process and overall, the process leads to the activation of the new bond. The size of the molecule also gives different results, the smaller the molecule size typically the lower the energy transition within the range of 5 – 150 cm^{-1} . It was also hypothesized that the dielectric relaxation led to the infliction of heat (Dudley, Richert, & Stigman, 2015).

In another mechanical-assisted reaction system with friction, the reactant was physically milled manually by a mortar and pestle or mechanically by a milling device. Howard et al. (2018) described this type of reaction could be affected by several factors which were the energy to promote the collision, the energy transfer to the reactant, and the time of molecule to collide. Since kinetic energy was used in this procedure, the collision of the molecules occurred as a direct impact of the disruption process using instruments. During this period, several outcomes could be observed such as the homogeneity of the mixture during the milling/grinding process, the pressure on the reactant to form a powdered mixture, and the volume of the instrument. As this procedure uses kinetic energy to directly assist the contact between reactants, the reaction time could also be reduced significantly.

The third physical phenomenon that is adopted in organic synthesis is ultrasonic waves (20 KHz – 1 MHz) and the procedure is generally known as sonication (Nasir & Varma, 2012). In the ultrasonic-assisted reaction, the molecules in the medium were propagated and oscillated. As a result, the energy is transferred in the direction of propagation and transmitted in the form of longitudinal and transverse waves. In the process, due to the alternate area of high and low pressure from the longitudinal vibration of molecules, the cavitation phenomenon is observed. This phenomenon refers to the formation of cavities or bubbles under the low-pressure and the collapse of cavities or bubbles when the pressure is high. The cavitation could be affected by several factors including the frequency and the intensity of ultrasonic. Further, the organic reaction under sonication could be done in two types of reactions: homogeneous and heterogeneous. The homogeneous types are usually via radical or radical-ion intermediates in which cavities act as microreactors to break the chemical bonds. While heterogeneous types, the process is mechanically affected by cavitation such as the decrease in particle size and the enhancement in mass transfer.

2.2. Mechanical-assisted reaction as the nonreflux procedure in disproportionation reaction

In the disproportionation reaction, the common reactants are an aldehyde without H- α and a strong base in the presence of solvent. Therefore, benzaldehyde usually undergoes this type of reaction. Generally, the procedure of disproportionation in organic synthesis uses the reflux method, though the procedure could be done at room temperature and high temperature. Several studies in disproportionation reactions have been investigated under mechanical-assisted reactions (Figure 2).

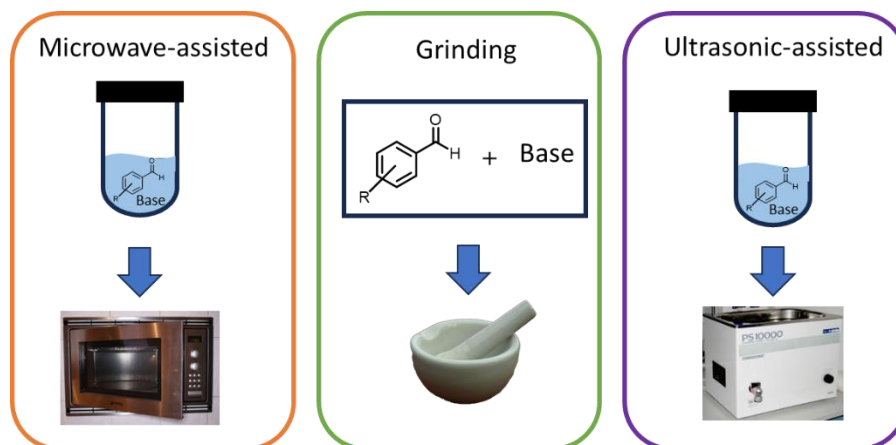
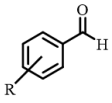
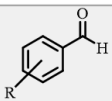


Figure 2. The three nonreflux procedures in disproportionation reaction.

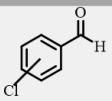
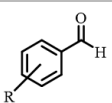

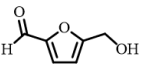
Varma et al (1998) studied the crossed disproportionation reaction on several aromatic aldehydes and paraformaldehyde with barium hydroxide as a base. In comparison, with the conventional method, the reaction under microwave-assisted was done in a shorter time (under 3 minutes). However, the product was obtained with alcohol derivatives as a major in a range of 80 – 99%. Microwave-assisted was also applied in disproportionation reaction by Sharifi et al (1999) with sodium hydroxide and basic alumina as bases. The reaction was assisted by water as the medium to facilitate the excitation and relaxation process. Similar results were also observed with higher products and shorter reaction times. Alumina has also been used as a base to transform aldehydes into the corresponding alcohol and acid by Pourjavadi et al (2002). Despite alumina being considered a weak base, the reaction occurred. It was proposed that the mechanism was carried out on the γ -alumina surface. Janczewski et al (2019) adopted similar conditions to investigate the disproportionation reaction of several aldehyde derivatives. The experiments were also done by optimizing reaction conditions such as reaction time, temperature, and power. The summary is presented in Table 1.

Table 1. Disproportionation reaction under the microwave-assisted procedure.

No	Compounds	Condition	Reference
1	RCHO + HCHO	Ba(OH) ₂ ·8H ₂ O Reaction time: 0.25-2 minutes	Varma et al. (1998)
2		Al ₂ O ₃ (basic), NaOH, H ₂ O Reaction time: 15 seconds	Sharifi et al. (1999)
3		γ-Al ₂ O ₃ Reaction time: 3-7 minutes	Pourjavadi et al. (2002)
4	RCHO	NaOH, Al ₂ O ₃ , H ₂ O Reaction time: 1-2 minutes Temperature: 100-160°C	Janczewski et al (2019)

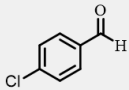
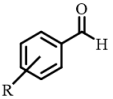
The mechano method via friction and grinding offered a simple procedure to achieve the targeted products as in Table 2. Phonchaiya et al (2009) prepared an experiment for undergraduates based on the disproportionation reaction of chlorobenzaldehyde. The reaction was done in solventless condition with the grinding method for 30 – 40 minutes. In comparison, Rahman and Kadi (2012) set up the experiment within 10 minutes. Despite the similar techniques, the required reaction time was different due to the distinct purposes. However, both experiments gave a simple procedure for the disproportionation reaction using the grinding technique. Another different procedure with the same methods was also displayed in the experiments by Melgar et al (2010) and Subbiah et al (2013).

Table 2. The mechano methods in disproportionation reaction.

No	Compounds	Condition	Reference
1		KOH Reaction time: 30-40 minutes grinding	Phonchaiya et al. (2009)
2		NaOH Reaction time: 10 minutes grinding	Rahman & Kadi (2012)
3		NaOH Reaction time: 10 minutes friction	Melgar et al (2010)
4		NaOH, H ₂ O Reaction time: 18 hours friction	Subbiah et al (2013)

Another mechano-assisted reaction was under ultrasonication. In the disproportionation reaction, several experiments were introduced as shown in Table 3. The procedure is commonly adopted in the presence of solvent, therefore a phase transfer catalyst was used to promote the interaction between the organic molecule and bases. Poláčková et al. (1996) investigated the reaction of several benzaldehyde derivatives with potassium hydroxide. The reaction was done with the least in 1 hour and the most in 6.5 hours. Interestingly, Enterazi and Shamel (2000) showed the shorter reaction time

Table 3. Ultrasonication methods in disproportionation reaction.

No	Compounds	Condition	Reference
1		KOH Reaction time: 1-6.5 hours Phase transfer catalyst: 18-Crown-6, Aliquat, TEBA	Poláčková et al. (1996)
2		KOH Reaction time: 40 minutes Phase transfer catalyst: TEBA	Enterazi & Shameli (2000)

3. CONCLUSION

Disproportionation reaction is generally done under conventional conditions in the presence of solvents. However, the study of mechano-assisted showed several procedures without using reflux conditions. Further, the method could also be applied in nonsolvent and solventless conditions. Three common procedures for disproportionation reactions are microwave-assisted, friction-assisted, and ultrasonic-assisted.

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