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Research Article

Ultrasonication Mediated Time Saving, High Yield & High Purity Organic Reactions- An Emerging Strategy in Green Chemistry

B. B.Chavan*[1], P. P. Mehta[1], A.R. Chabukswar[2]
1. JSPM's Jayawantrao Sawant College of Pharmacy & Research, Hadapsar, Pune.
2. Maharashtra Institute of Pharmacy, Kothrud, Pune.

ABSTRACT
The characteristic feature of ultrasonicator is that the mechanical energy in the form of high intensity, high- frequency sound waves is transferred to the reaction mixture. This results in the generation & the collapse of large number of minute bubbles throughout the mixture. This effect, which is known as cavitation, is responsible for the quick & through stirring of reaction mixture.
The present work describes the comparison of ultrasonic waves mediated organic syntheses with the conventional methods in respect of % age yield, time for completion of the reaction & the purity of product. The reactions are selected which requires more stirring time for completion & carried out at ambient temperature. It concluded that the ultrasonic waves mediated organic reactions requires less time, gives high % age yield & high purity as compared to the conventional methods. In the present study, the organic reactions requiring maximum stirring at ambient temperature (without ice cold conditions) by conventional methods were compared with the ultrasonic mediated organic reactions.
Keywords: Ultrasonication, Cavitation, Yield, Purity, Time, Organic reactions

QR Code for Mobile Users

Address for Correspondence:
B. B. Chavan
JSPM's Jayawantrao Sawant College of Pharmacy & Research, Hadapsar, Pune.
E-mail: bhagwat.chavan@gmail.com
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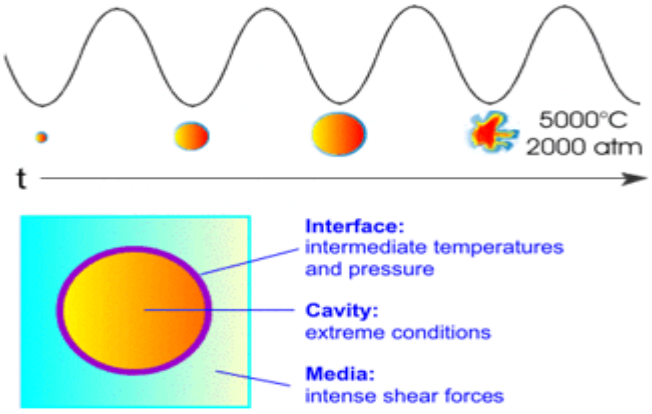
INTRODUCTION
The use of ultrasound in chemical reactions in solution provides specific activation based on a physical phenomenon: acoustic cavitation. Cavitation is a process in which mechanical activation destroys the attractive forces of molecules in the liquid phase. Applying ultrasound, compression of the liquid is followed by rarefaction (expansion), in which a sudden pressure drop forms small, oscillating bubbles of gaseous substances. These bubbles expand with each cycle of the applied ultrasonic energy until they reach an unstable size; they can then collide and/or violently collapse.
For example, sonolysis of $Fe(CO)_5$ in decane under argon produces amorphous iron upon decarbonylation instead of crystalline iron, which shows that both very high temperatures and also rapid cooling rates ($\sim 10^6$ K s^{-1}) are involved, the more volatile pentane yields $Fe_3(CO)_{12}$, indicating a somewhat slower collapse.



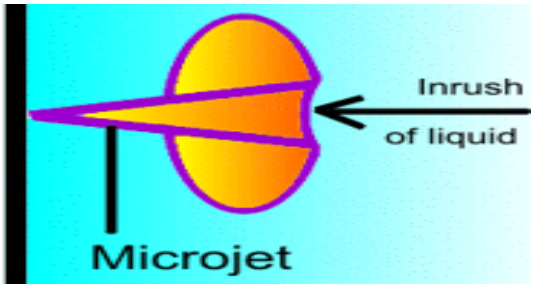
It has been estimated and calculated that the pressure within a bubble in water can rise to more than one thousand atmospheres, and the

temperature can reach several thousand degrees during a collapse, as heat conduction cannot keep up with the resulting adiabatic heating. As these bubbles are small and rapidly collapse, they can be seen as microreactors that offer the opportunity of speeding up certain reactions and also allow mechanistically novel reactions to take place in an absolutely safe manner.

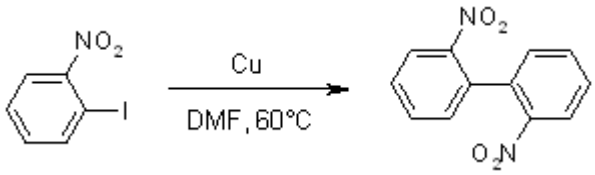
Many reactions can be conducted even in a simple ultrasonic cleaning bath, although the amount of energy that reaches the reaction is only between 1 and 5 W cm^{-2}, and temperature control is normally poor. Large-scale reactions can be better conducted using immersible ultrasonic probes that circumvent the transfer of the energy through water and the reaction vessel. The applied energies in this case can be several hundred times higher. Laboratory equipment uses frequencies between 20 kHz and 40 kHz, but cavitation can be generated well above these frequencies and recent research uses a much broader range.

Ultrasound in synthetic organic chemistry[2]

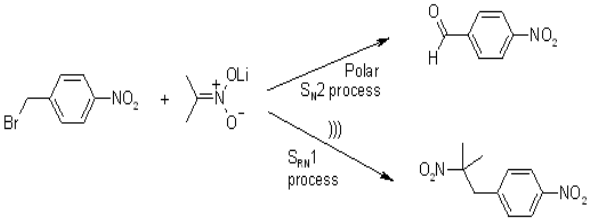
There are two types of effects mediated by ultrasound: chemical and physical. When the quantity of bubbles is low - using standard laboratory equipment - it is mainly physical rate acceleration that plays a role. For example, a specific effect is the asymmetric collapse near a solid surface, which forms microjets. This effect is the reason why ultrasound is very effective in cleaning, and is also responsible for rate acceleration in multiphasic reactions, since surface cleaning and erosion lead to improved mass transport.



For example, when ultrasound is applied to an Ullmann reaction that normally requires a 10-fold excess of copper and 48 h of reaction time, this can be reduced to a 4-fold excess of copper and a reaction time of 10 h. The particle size of the copper shrinks from 87 to 25 μm, but the increase in the surface area cannot fully explain the increase in reactivity. It was suggested that sonication also assists in the breakdown of intermediates and desorption of the products from the surface.



Typically, ionic reactions are accelerated by physical effects - better mass transport - which is also called "False Sonochemistry". If the extreme conditions within the bubble lead to totally new reaction pathways, for example via radicals generated in the vapor phase that would only have a transient existence in the bulk liquid, we speak about "sonochemical switching". Such a switch has been observed for example in the following Kornblum-Russel reaction where sonication favors an SET pathway:



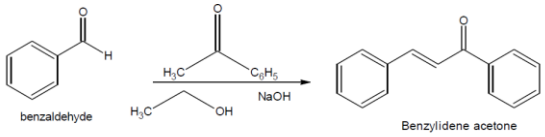
Applications for sonochemistry can be found in many areas, but sonochemical processes are most widely developed for heterogeneous reactions. Currently, sonochemistry is a multidisciplinary field in which chemists, physicists, chemical engineers and mathematicians must cooperate to develop a better understanding of the processes that take place within the collapsing bubbles to develop totally new applications. However, the potential for making improvements in many types of reaction suggests that every chemical laboratory should be equipped with at least one cleaning bath for simple trials.

Methods and Materials[2,3,4,5]**:**

Synthesis of Benzylidene acetophenone:

A solution of 2.18 gm of sodium hydroxide in 19.6 gm of water and 10.0 gm of 95 per cent alcohol are introduced into a bottle which is loosely covered with a perforated disk of cardboard, supplied with an effective stirrer, and supported in a larger vessel so as to permit cooling with cracked ice. Into the alkaline solution, 5.2 gm of pure acetophenone is poured, the bottle is rapidly surrounded with cracked ice, and the stirrer started; 4.6 gm of benzaldehyde is then added at once. The temperature of the mixture should not be below 15° and it should not be allowed to rise above 30° during the reaction. If it tends to do so, the stirring is not sufficiently vigorous.

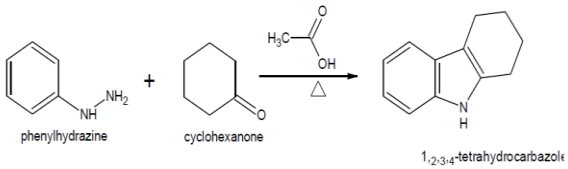
It is advantageous, though not essential, to inoculate the mixture with a little powdered benzalacetophenone after stirring for one-half hour. After two to three hours, the mixture becomes so thick that the stirring is no longer effective. The stirrer is then removed and the mixture left to itself in an ice box for about ten hours. The mixture now is a thick paste composed of small shot-like grains suspended in an almost colorless liquid. It is cooled in a freezing mixture and then either centrifuged or filtered on a large Büchner funnel, washed with water until the washings are neutral to litmus, and finally washed with 200 cc of 95 per cent alcohol, which has previously been cooled to 0°. After thorough drying in the air, the crude product weighs about 8.8 gm (97 per cent of the theoretical amount) and melts at 50–54°. It is sufficiently pure for most purposes but tenaciously holds traces of water. It is most readily purified by recrystallization from four to four and one-half times its weight of 95 per cent alcohol. Eight hundred and eighty grams of crude product give 7.7 gm (85 per cent of the theoretical amount) of light yellow material (m. p. 55–57°) and 0.4–0.5 gm that require recrystallization.



Synthesis of 1,2,3,4-Tetrahydrocarbazole:

A mixture of 9.8 gm of cyclohexanone and 36 gm of acetic acid contained in a three-necked round-bottomed flask equipped with a reflux condenser, a slip-sealed stirrer, and a dropping funnel is heated under reflux and stirred while 10.8 gm of phenylhydrazine is added during 1 hour.

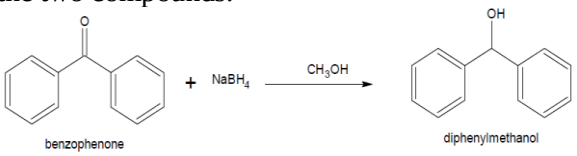
The mixture is heated under reflux for an additional hour and poured into a beaker and stirred by hand while it solidifies. It is then cooled to about 5° and filtered with suction, the filtrate being cooled in ice and refiltered through the filter cake. The final filtrate is discarded. The filter cake is washed with 10 ml. of water and finally with 10 ml. of 75% ethanol. Each wash is allowed to soak into the filter cake before it is sucked dry. The crude solid is air-dried overnight and crystallized from 70 ml of methanol after treatment with decolorizing carbon; yield 12–13.5 gm of 1,2,3,4-tetrahydrocarbazole, m.p. 115–116°. The mother liquor is concentrated to one-fourth of its original volume and yields an additional 1 gm of product (total yield 76–85%).



Synthesis of Benzhydrol:

Dissolve the benzophenone 3.64 mg (2 mmol) in 5 mL ethanol in a 25 mL Erlenmeyer flask, and stir the solution magnetically. In a small test tube, dissolve the sodium borohydride 84 mg (2.2 mmol) in 1.5 mL cold water, and add this solution one drop at a time to the stirred ethanolic solution of benzophenone at room temperature. After all the sodium borohydride has been added, continue to stir the mixture for a further 40 min. Slowly pour the mixture into a 50 mL beaker containing a mixture of 10 mL ice-water and 1 mL concentrated hydrochloric acid. After a few minutes collect the precipitated product by suction filtration, and wash it with 2X5 mL portions of water. Dry the crude product by suction at the filter pump for l0 min, and then recrystallize it from petroleum. Record the yield and mp of the product. Finally record an IR spectrum of your diphenylmethanol, and one of benzophenone for comparison.

To check the purity of the recrystallized diphenylmethanol by TLC, dissolve *ca.* 10 mg of the product in few drops of dichloromethane, and spot this solution onto a 77 silica gel TLC plate. Similarly spot a reference solution of the starting ketone, benzophenone onto the same plate. Develop the plate in a mixture of petroleum and ethyl acetate (9:1). Visualize the developed plate under UV light and work out the Rf values for the two compounds.

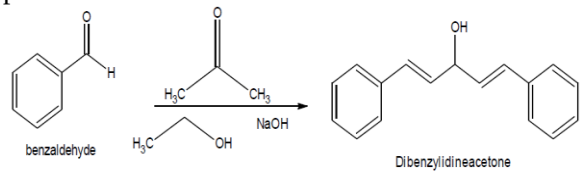


Synthesis of Dibenzylidineacetone:

A cooled solution of 10 gm of sodium hydroxide in 100 ml of water and 80 cc. of alcohol is placed in a 2-l. wide-mouthed glass jar which is surrounded with water and fitted with a mechanical stirrer. The solution is kept at about 20–25° and stirred vigorously while one-half of a mixture of 10.6 gm of benzaldehyde and 2.9 gm of acetone is added. In about two or three minutes a yellow cloud forms which soon becomes a flocculent precipitate. After fifteen minutes the rest of the mixed reagents is added, and the container is rinsed with a little alcohol which is added to the mixture. Vigorous stirring

is continued for one-half hour longer, and the mush is then filtered with suction on a large Büchner funnel. The product is thoroughly washed with distilled water and then dried at room temperature to constant weight. The yield is 10.5–11.0 gm (90–94 per cent of the theoretical amount) of a product which melts at 104–107°.

The crude dibenzalacetone may be recrystallized from hot ethyl acetate, using 10 cc. of solvent for each 4 gm of material. The recovery in this purification is about 80 per cent; the purified product melts at 110–111°.



RESULTS AND DISCUSSIONS:

The various products synthesized by using ultrasonicator were compared with the conventional methods are as follows:

Sr.No.	Product	Conventional methods		Ultrasonicator mediated methods	
		% age yield	Time	% age yield	Time
1.	Benzylidine acetophenone	66.66	3 hrs.	92	90 min
2.	1,2,3,4-Tetrahydrocarbazole	55	2 hrs.	86	65 min.
3.	Benzhydrol	95	3 hrs.	98	95 min.
4.	Dibenzylidineacetone	75	2 hrs.	89	55 min.

These examples conclude that the organic synthesis by ultrasonic methods gives excellent results as compared to the conventional methods of organic syntheses.

CONCLUSION:

Sonochemistry is gaining significance based on laboratory results and the availability of scale-up systems. Sonochemical applications can be envisaged in all types of systems, including homogenous reactions. Wide acceptance has been gained at a practical/empirical level, however, the theoretical understanding still lags significantly behind. The usefulness of sonochemistry continues to expand into the arena of electrochemistry, photochemistry and biotechnology.

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REFERENCES

1. T. J. Mason, *Chem. Soc. Rev*. 1997, *26*, 443. DOI: 10.1039/CS9972600443.
2. Price, G.J. (ed.)., Current Trends in Sonochemistry, Royal Society of Chemistry, Oxford, 1993.
3. Mason, T.J. (ed.), Chemistry With Ultrasound, Elsevier Applied Science, London, New York, 1990.
4. van Eldik, R.; Hubbard, C.D. (eds.), Chemistry Under Extreme or Non-Classical Conditions, Spektrum/Wiley, 1997.
5. Abdulla, R.F. Adrichimica Acta 21, 1988, 31 – 42.