

Article

Not peer-reviewed version

Optimized Synthesis of Dinitrochalcones via Ultrasonic Bath in a Cyclohexane-Methanol Solvent System

[Alam Yair Hidalgo](#)*, [Quirino Torres-Sauret](#), [Carlos Ernesto Lobato-García](#), Erika Madeyne Ramos-Rivera, [Luis Fernando Roa de la Fuente](#), [Abraham Gómez-Rivera](#), [Miguel Ángel Vilchis-Reyes](#), Erika Alarcón-Matus, [Oswaldo Hernández-Abreu](#), [Nancy Romero-Ceronio](#)*

Posted Date: 30 October 2024

doi: 10.20944/preprints202410.2259.v1

Keywords: Dinitrochalcones; Ultrasound; Claisen-Schmidt Condensation



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Article

Optimized Synthesis of Dinitrochalcones via Ultrasonic Bath in a Cyclohexane-Methanol Solvent System

Alam Yair Hidalgo ^{1,2,*}, Quirino Torres-Sauret ¹, Carlos Ernesto Lobato-García ¹, Erika Madeyne Ramos-Rivera¹, Luis Fernando Roa de la Fuente ¹, Abraham Gómez-Rivera ¹, Miguel Ángel Vilchis-Reyes ¹, Erika Alarcón-Matus ¹, Oswaldo Hernández-Abreu ¹ and Nancy Romero-Ceronio ^{1,*}

¹ División Académica de Ciencias Básicas, Universidad Juárez Autónoma de Tabasco, Carretera Cunduacán-Jalpa km 1, Col. La Esperanza, Cunduacán 86690, Tabasco, Mexico

² Tecnológico Nacional de México-Instituto Tecnológico Superior de Comalcalco, Carretera Vecinal, Comalcalco-Paraiso Km 2, R/a Occidente 3ra Sección, Comalcalco 86650, Tabasco, Mexico

* Correspondence: nancy.romero@ujat.mx, alam.yair.hidalgo@gmail.com

Abstract: This study describes the efficient synthesis of five dinitrochalcones (DNCH) using an ultrasonic bath as an unconventional method to improve reaction yields and reduce reaction times. The Claisen-Schmidt condensation of nitroacetophenones and nitrobenzaldehydes was carried out in a cyclohexane-methanol solvent system under ultrasonic irradiation, achieving yields between 56% and 92%. The application of ultrasound not only accelerated the reaction but also improved the overall efficiency compared to conventional methods such as magnetic stirring. Characterization of the synthesized compounds was performed by NMR spectroscopy, confirming the consistency of their structures. Thus, it is confirmed that obtaining DNCH with a nitro group in ortho provide by ultrasonic irradiation is an energetically efficient and environmentally friendly alternative.

Keywords: dinitrochalcones; ultrasound; claisen-schmidt condensation

1. Introduction

The synthesis of organic compounds with relevant biological and pharmacological properties is an area of great interest in synthetic chemistry [1]. Chalcones, a type of α,β -unsaturated compounds, have been shown to have a wide range of biological activities, including anti-inflammatory, antioxidant, and antitumor properties, among others [2–5]. These biological activities are determined by the type of substituent these molecules possess [6].

Among the substituents is the nitro group (NO_2), which is a functional group that attracts electrons due to the positive charge of nitrogen. In aromatic rings, resonance with the nitro group deactivates certain positions and alters the polarity of the molecules, which can favor interaction with nucleophilic sites of enzymes, inhibiting their activity [7]. In this context, the synthesis of chalcones containing the nitro group in the rings of the structure is of particular interest, since these compounds may exhibit improved biological properties compared to their analogs that do not possess substituents [8]. However, the synthesis of these compounds often requires drastic reaction conditions, such as the use of strong acids or bases, which can limit their applicability [9]. This has led researchers to try alternative routes of synthesis, among which are methods that apply green chemistry paradigms, an example of which is ultrasound [10,11].

Ultrasound is a technique that has gained popularity in organic synthesis due to its ability to accelerate and improve the efficiency of chemical reactions [12]. Ultrasound is a form of energy produced when a pressure wave propagates through a medium, such as a liquid or gas. When

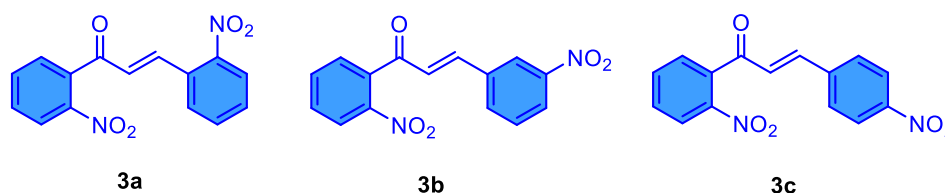
ultrasound energy is applied to a chemical system, physical and chemical phenomena are generated that can influence the reaction. These phenomena include the formation of gas bubbles, the generation of free radicals, and the creation of more favorable reaction conditions, such as the dissolution of insoluble substances and the reduction of the reaction temperature [13,14]. In this context, ultrasound-induced chemistry can be accurately defined as cavitation chemistry. Cavitation involves the formation of micrometer-sized voids or bubbles in a liquid when a sufficient pressure drop occurs that alters its cohesive forces. The violent collapse of these bubbles to re-establish intermolecular interactions releases a large amount of energy, which explains the effects mentioned above. Although there are several methods for generating cavitation, acoustic cavitation is the most widely recognized [15–21].

The application of ultrasound in organic synthesis has proven to be effective in improving the efficiency and selectivity of reactions, as well as reducing reaction times and eliminating toxic residues. In addition, ultrasound can be used for the synthesis of compounds that cannot be obtained by conventional methods, such as the synthesis of compounds that require extreme reaction conditions or the synthesis of compounds that are unstable under normal conditions [22–24].

In previous work, we reported the synthesis of three chalcone isomers using conventional mechanical stirring conditions, as well as the use of a strong base such as sodium hydroxide in methanol at 0 °C (Figure 1) [25].

The objective of this work was to perform the synthesis of five dinitrosubstituted chalcones in rings A and B (compounds 3a-e) (Figure 2) through Claisen-Schmidt condensation between o, m and p-nitroacetophenones (1a-c) and the corresponding o, m and p-nitrobenzaldehydes (2a-c) using a nonconventional method by irradiation with an ultrasound bath. This approach seeks to decrease the drastic reaction conditions and to be aligned with the green chemistry paradigm.

Previous work, synthesis of DNCH by a conventional method.



In this work, synthesis of DNCH by a nonconventional method (Ultrasound).

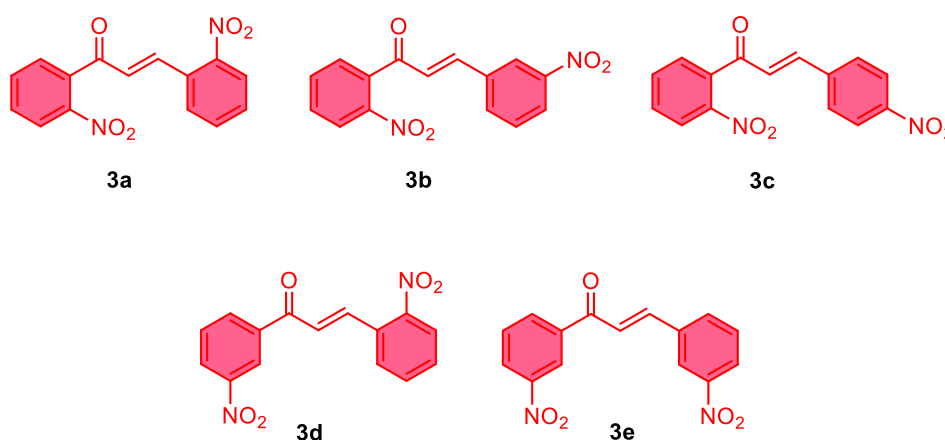


Figure 1. Dinitrochalcones (DNCH).

2. Materials and Methods

2.1. General

All the reagents used in the synthesis and spectroscopic characterization of DNCH were of analytical and spectroscopic grade respectively (Sigma Aldrich) and were used without prior purification. Thin layer chromatography (TLC) was used to monitor the reactions, which were performed on a Merck silica gel 60 chromatofold with fluorescent indicator 254 nm, with a thickness of 0.2 mm. The melting points were determined in SMP 10 equipment, of the STUART brand, using the capillary technique and are not corrected. The NMR spectra were performed on a Bruker Ascend™ 600 MHz NMR spectrometer. Chemical shifts are expressed in parts per million (ppm) and are referenced to TMS as an internal standard, coupling constants (J) are expressed in Hertz. The ultrasonic irradiation generator with a power of 100 W was a Cole Parmer ultrasonic cleaner model 08891-21.

2.2. Procedure for the Synthesis of Dinitrochalcones (DNCH)

The procedure for synthesis of DNCH was carried out by Claisen-Schmidt condensation between the respective o-nitroacetophenone (1a), m-nitroacetophenone (1b), p-nitroacetophenone (1c) and the respective o-nitrobenzaldehyde (2a), m-nitrobenzaldehyde (2b), p-nitrobenzaldehyde (2c). All nitroacetophenones and nitrobenzaldehydes were added equimolar in all reactions.

The technique employed consisted of adding 10 mmol of the corresponding nitroacetophenones together with their carbonate equivalents. The mixture was then solubilized with 10 mL of methanol in a 50 mL flask until the nitroacetophenones were completely dissolved. Next, 10 mmol of the corresponding benzaldehyde was added. Subsequently, 1 mL of cyclohexane was added and subjected to ultrasound irradiation for the time and at the temperature specified in the results table. Once the reaction was finished, the solid obtained was filtered and washed with cold water. Finally, the product was purified.

3a (*E*)-1,3-bis(2-nitrophenyl)prop-2-en-1-one. (56%) was obtained as a white solid; mp: 140–142 °C [lit. 136–137 °C][26]; ¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.25 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.95 (t, J = 7.5 Hz, 1H), 7.83 (m, 2H), 7.76 (d, J = 7.5 Hz, 1H), 7.69 (t, J = 7.9 Hz, 1H), 7.66 (d, J = 16.1 Hz, 1H), 7.24 (d, J = 16.1 Hz, 1H); DEPTQ NMR (150 MHz, DMSO-*d*₆) δ = 193.3, 149.3, 147.4, 142.1, 135.8, 135.5, 134.9, 132.7, 132.4, 130.5, 130.1, 125.8, 125.5, 124.3, 124.1.

3b (*E*)-1-(2-nitrophenyl)-3-(3-nitrophenyl)prop-2-en-1-one. (92%) was obtained as a white solid; mp: 145–147 °C [lit. 143–145 °C][26]; ¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.64 (s, 1H), 8.29 (m, 3H), 7.97 (t, J = 7.5 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 16.3 Hz, 1H), 7.56 (d, J = 16.3 Hz, 1H); DEPTQ NMR (150 MHz, DMSO-*d*₆) δ = 193.1, 149.3, 147.5, 144.1, 136.9, 136.1, 135.4, 132.5, 131.3, 130.0, 129.1, 125.9, 125.5, 124.5, 123.9.

3c (*E*)-1-(2-nitrophenyl)-3-(4-nitrophenyl)prop-2-en-1-one. (86%) was obtained as a yellow solid; mp: 175–177 °C [lit. 168–169 °C][26]; ¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.23 (m, 3H), 8.03 (d, J = 8.8 Hz, 2H), 7.93 (t, J = 7.5 Hz, 1H), 7.84 (t, J = 7.7 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 16.2 Hz, 1H), 7.48 (d, J = 16.2 Hz, 1H); DEPTQ NMR (150 MHz, DMSO-*d*₆) δ = 193.0, 149.3, 147.5, 143.6, 141.3, 135.9, 135.5, 132.6, 130.8, 130.2, 130.0, 125.6, 124.9.

3d (*E*)-3-(2-nitrophenyl)-1-(3-nitrophenyl)prop-2-en-1-one. (65%) was obtained as a white solid; mp: 160 – 162 °C [lit. 159–161 °C] [26]; ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.35 (t, J = 1.9 Hz, 1H), 9.09 (m, 1H), 9.02 (m, 1H), 8.73 (dd, J = 7.9, 1.3 Hz, 1H), 8.62 (dd, J = 8.2, 1.1 Hz, 1H), 8.57 (d, J = 15.5 Hz, 1H), 8.46 (d, J = 15.5 Hz, 1H), 8.38 (m, 2H), 8.24 (m, 1H); RMN DEPTQ (150 MHz, DMSO-*d*₆) δ = 188.6, 149.7, 149.2, 140.9, 139.2, 135.8, 134.7, 132.2, 131.6, 130.6, 130.4, 128.6, 126.8, 125.7, 124.6.

3e (*E*)-1,3-bis(3-nitrophenyl)prop-2-en-1-one. (88%) was obtained as a yellow solid; p.f. 214 – 216 °C [lit. 210 – 211 °C] [27]; ¹H NMR (600 MHz, DMSO-*d*₆) δ 8.87 (s, 1H), 8.81 (s, 1H), 8.64 (d, J = 7.7 Hz, 1H), 8.52 (m, 1H), 8.38 (d, J = 7.7 Hz, 1H), 8.30 (m, 1H), 8.22 (d, J = 15.7 Hz, 1H), 7.94 (d, J = 15.7 Hz, 1H), 7.90 (d, J = 6 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H); RMN DEPTQ (150 MHz, DMSO-*d*₆) δ = 188.6, 149.4, 149.2, 143.8, 139.4, 137.3, 136.2, 135.8, 131.6, 131.3, 128.5, 125.9, 125.2, 124.2, 123.9.

3. Results

Initially, we proceeded to optimize the reaction conditions avoiding drastic conditions taking as a starting point the reaction of m-nitroacetophenone (**1b**) and m-nitrobenzaldehyde (**2b**) to obtain m,m-dinitrochalcone (**3e**) reported by [27], for the optimization of the reaction several variations in the reaction conditions were tested, which are summarized in Table 1.

By way of comparison, a protocol was established where conventional conditions were established, using reflux (experiments 2 and 3). On the other hand, the effect of the base was tested by comparing the effectiveness of the reaction in the presence of NaOH, K₂CO₃, Na₂CO₃, Li₂CO₃, Ce₂CO₃, and Ca₂CO₃.

Table 1. This is a table. Tables should be placed in the main text near to the first time they are cited.

Entry*	Activation method	Base	Solvent	Time	Yield*
1**	Magnetic stirring	NaOH (2 Eq.)	Methanol	120	----
2	Reflux	NaOH (2 Eq.)	Methanol	240	25
3	Reflux	K ₂ CO ₃ (0.3 Eq.)	Methanol	240	29
4	Ultrasound	K ₂ CO ₃ (0.3 Eq.)	Methanol	60	22
5	Ultrasound	K ₂ CO ₃ (0.6 Eq.)	Methanol/ cyclohexane	60	49
6	Ultrasound	K ₂ CO ₃ (0.9 Eq.)	Methanol/ cyclohexane	60	44
7	Ultrasound	Na ₂ CO ₃ (0.4 Eq.)	Methanol/ cyclohexane	30	88
8	Ultrasound	Li ₂ CO ₃ (0.4 Eq.)	Methanol/ cyclohexane	30	48
9	Ultrasound	Cs ₂ CO ₃ (0.4 Eq.)	Methanol/ cyclohexane	15	80
10	Ultrasound	Ca ₂ CO ₃ (0.4 Eq.)	Methanol/ cyclohexane	60	----

* The experiment was conducted at a temperature of 60 °C. ** The experiment was conducted at room temperature.

The same methanol/cyclohexane mixture was employed as the reaction medium for the synthesis of the remaining isomeric DNCH. However, experimental modifications in temperature were necessary to optimize the yield of the reactions. The optimum conditions for obtaining each product are summarized in Figure 2 and Table 2.

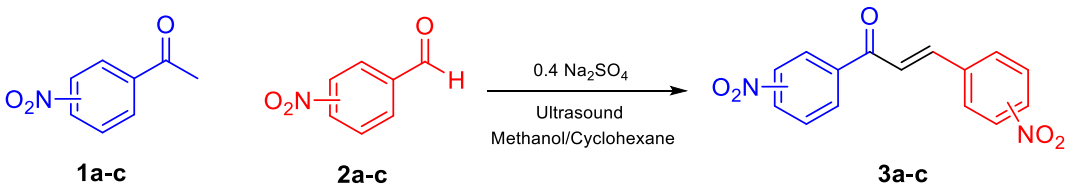


Figure 2. General reaction scheme for obtaining the 3a-e compounds.

Table 2. DNCH synthesized by ultrasonication.

DNCH	Time (min)	Temperature (°C)	Yield (%)	m.p (°C)
3a	60	0	56	140-142
3b	60	0	92	145-147
3c	60	0	86	175-177

3d	60	0	65	160-162
3e	30	60	88	214-216

4. Discussion

The synthesis of DNCH using ultrasound, presented in this work, stands out for avoiding drastic reaction conditions, aligning with principle 6 of green chemistry (energy efficiency) [28]. The optimization of experimental conditions, detailed in Tables 1 and 2, showed several observations regarding reaction efficiency and factors influencing yields. Although experiments initially included both magnetic stirring and refluxing (Table 1), conventional synthesis methods, to establish a point of comparison with ultrasonic activation. Magnetic stirring, performed at room temperature, and refluxing at elevated temperatures, are widely used in organic synthesis due to their ability to efficiently promote chemical reactions under controlled conditions. However, these methods often require long reaction times and can result in low yields, confirmed in this work. For example, magnetic stirring with NaOH did not produce any quantifiable yields, while refluxing, although slightly increasing yields, kept them at low values (25% and 29% with NaOH and K₂CO₃, respectively, in 240 min). These results reflect the limitations of conventional methods.

In contrast, ultrasound irradiation allowed a significant reduction of the reaction time to 60 min or less, increasing the yields in most of the experiments carried out by this non-conventional technique. Ultrasonic cavitation and the generation of free radicals may explain this improvement in efficiency [29]. These effects facilitate the cleavage and formation of bonds, promoting Claisen-Schmidt condensation between nitroacetophenones and nitrobenzaldehydes.

The use of different bases also had a crucial impact on the reaction yields. Optimization showed that the most effective base was Na₂CO₃, with a yield of 88% (experiment 7), while other bases such as K₂CO₃ and Li₂CO₃ resulted less efficient, with yields of 49% and 48%, respectively. This behavior may be related to the strength and solubility of the bases in the reaction system. Thus, Na₂CO₃ appears to provide an optimal balance between the catalysis of the reaction and the formation of undesired side products, a critical aspect to ensure the selectivity of the synthesis.

The solvent played a crucial role in optimizing the yields. The combination of methanol and cyclohexane markedly increased the yields compared to using methanol alone, as observed when comparing experiments 4 and 5 (22% *vs* 49%). Cyclohexane probably acted as a co-solvent, enhancing the solubilization of carbonates and facilitating better interaction between the reagents and the base. Something similar has been reported previously, where cyclohexane, in solvent mixtures, is used as a surfactant to improve the efficiency of reactions by increasing the accessibility of the substrate to the catalysts [30,31]. This surface effect is a concrete example of how solvents not only dilute the reactants but also directly influence the reaction dynamics.

On the other hand, Table 2 presents the yields of DNCH synthesized under optimal ultrasound conditions. An analysis of these data reveals a remarkable influence of the position of the nitro groups in the aromatic rings on the yields and reaction conditions. Chalcones with at least one nitro group in ortho position (3a-3d) show yields between 56% and 92%, while chalcone (3e), with nitro groups in meta position on both rings, reached a yield of 88%, although it required a higher temperature (60 °C) to optimize the reaction in only 30 min. This behavior can be attributed to the inductive effect of the nitro group, which increases the electrophilic character of the carbonyl carbon, favoring condensation, while the higher temperature required for (3e) could be related to a lower reactivity of the target positions.

In particular, compound (3b), with a nitro group in the ortho position on one ring and meta on the other, presented the highest yield (92%). This structural configuration may generate a favorable combination of inductive and steric effects that optimize the reactivity of the reagents. The reactivity also seems to be influenced by the possibility that the nitro groups in the ortho position facilitate the formation of intramolecular interactions, reducing the energetic barriers of the reaction.

5. Conclusions

The synthesis of five isomers of DNCH (**3a-e**) was achieved, decreasing the drastic reaction conditions, using ultrasound and with the addition of a co-solvent that optimizes the interaction of the organic phase with the basic catalyst. The spectroscopic characterization of the obtained products agrees with the expected structures. Differences were found in the reaction conditions necessary to optimize the synthesis of each of the compounds, which is attributed, in principle, to the electroattracting effect exerted by the nitro group on the electronic cloud of the aromatic systems and which depends on the relative position of the nitro group concerning the corresponding carbonyl.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Figure S1: title; Table S1: title; Video S1: title.

Author Contributions: Conceptualization, A.Y.H. and N.R.C.; methodology, C.E.L.G.; software, Q.T.S.; validation, M.A.V.R., C.E.L.G., and N.R.C.; formal analysis, A.G.R.; investigation, A.Y.H.; resources, O.H.A; data curation, E.M.R.R.; writing—original draft preparation, A.Y.H; writing—review and editing, L.F.R.F.; visualization, E.A.M.; supervision, N.R.C; project administration, A.G.R; funding acquisition, C.E.L.G.

Funding: This research received no external funding.

Data Availability Statement: The data presented in the study is available in the article.

Acknowledgments: We thank CONAHCyT for a postdoctoral fellowship for AYH.

Conflicts of Interest: The authors state that they have no financial interests or personal relationships that could have influenced the research presented in this paper.

References

- Campos, K. R.; Coleman, P. J.; Alvarez, J. C.; Dreher, S. D.; Garbaccio, R. M.; Terrett, N. K.; Tillyer, R. D.; Truppo, M. D.; Parmee, E. R. The Importance of Synthetic Chemistry in the Pharmaceutical Industry. *Science* (80-.). **2019**, 363 (6424), eaat0805.
- Rajendran, G.; Bhanu, D.; Aruchamy, B.; Ramani, P.; Pandurangan, N.; Bobba, K. N.; Oh, E. J.; Chung, H. Y.; Gangadaran, P.; Ahn, B.-C. Chalcone: A Promising Bioactive Scaffold in Medicinal Chemistry. *Pharmaceuticals* **2022**, 15 (10), 1250.
- Narwal, S.; Devi, B.; Dhanda, T.; Kumar, S.; Tahlan, S. Exploring Chalcone Derivatives: Synthesis and Their Therapeutic Potential. *J. Mol. Struct.* **2024**, 137554.
- Salehi, B.; Quispe, C.; Chamkhi, I.; El Omari, N.; Balahbib, A.; Sharifi-Rad, J.; Bouyahya, A.; Akram, M.; Iqbal, M.; Docea, A. O. Pharmacological Properties of Chalcones: A Review of Preclinical Including Molecular Mechanisms and Clinical Evidence. *Front. Pharmacol.* **2021**, 11, 592654.
- Michalkova, R.; Mirossay, L.; Kello, M.; Mojzisova, G.; Baloghova, J.; Podracka, A.; Mojzis, J. Anticancer Potential of Natural Chalcones: In Vitro and in Vivo Evidence. *Int. J. Mol. Sci.* **2023**, 24 (12), 10354.
- Salem, M. S.; Hussein, R. A.; El-Sayed, W. M. Substitution at Phenyl Rings of Chalcone and Schiff Base Moieties Accounts for Their Antiproliferative Activity. *Anti-Cancer Agents Med. Chem. (Formerly Curr. Med. Chem. Agents)* **2019**, 19 (5), 620–626.
- Noriega, S.; Cardoso-Ortiz, J.; López-Luna, A.; Cuevas-Flores, M. D. R.; Flores De La Torre, J. A. The Diverse Biological Activity of Recently Synthesized Nitro Compounds. *Pharmaceuticals* **2022**, 15 (6), 717.
- Gómez-Rivera, A.; Aguilar-Mariscal, H.; Romero-Ceronio, N.; Roa-de la Fuente, L. F.; Lobato-García, C. E. Synthesis and Anti-Inflammatory Activity of Three Nitro Chalcones. *Bioorg. Med. Chem. Lett.* **2013**, 23 (20), 5519–5522.
- Leitão, E. Chalcones: Retrospective Synthetic Approaches and Mechanistic Aspects of a Privileged Scaffold. *Curr. Pharm. Des.* **2020**, 26 (24), 2843–2858.
- Marotta, L.; Rossi, S.; Ibba, R.; Brogi, S.; Calderone, V.; Butini, S.; Campiani, G.; Gemma, S. The Green Chemistry of Chalcones: Valuable Sources of Privileged Core Structures for Drug Discovery. *Front. Chem.* **2022**, 10, 988376.
- Rosa, G. P.; Seca, A. M. L.; Barreto, M. do C.; Pinto, D. C. G. A. Chalcone: A Valuable Scaffold Upgrading by Green Methods. *ACS Sustain. Chem. Eng.* **2017**, 5 (9), 7467–7480.
- Mason, T. J. Ultrasound in Synthetic Organic Chemistry. *Chem. Soc. Rev.* **1997**, 26 (6), 443–451.
- Suslick, K. S.; Price, G. J. Applications of Ultrasound to Materials Chemistry. *Annu. Rev. Mater. Sci.* **1999**, 29 (1), 295–326.
- Yao, Y.; Pan, Y.; Liu, S. Power Ultrasound and Its Applications: A State-of-the-Art Review. *Ultrason. Sonochem.* **2020**, 62, 104722.
- Cravotto, G.; Cintas, P. Power Ultrasound in Organic Synthesis: Moving Cavitation Chemistry from Academia to Innovative and Large-Scale Applications. *Chem. Soc. Rev.* **2006**, 35 (2), 180–196.
- Luche, J.-L. Sonochemistry: From Experiment to Theoretical Considerations. *Adv. sonochemistry* **1993**, 3, 85–124.
- Cravotto, G.; Cintas, P. Introduction to Sonochemistry: A Historical and Conceptual Overview. *Handb. Appl. Ultrasound* **2011**, 23–40.
- Chen, C.; Anchecta, K.; Lee, Y.-D.; Dahlgaard, J. J. A Stepwise ISO-Based TQM Implementation Approach Using ISO 9001: 2015. *Manag. Prod. Eng. Rev.* **2016**, No. 4.
- McNamara III, W. B.; Didenko, Y. T.; Suslick, K. S. Sonoluminescence Temperatures during Multi-Bubble Cavitation. *Nature* **1999**, 401 (6755), 772–775.
- Flannigan, D. J.; Suslick, K. S. Inertially Confined Plasma in an Imploding Bubble. *Nat. Phys.* **2010**, 6 (8), 598–601.
- Martínez, R. F.; Cravotto, G.; Cintas, P. Organic Sonochemistry: A Chemist's Timely Perspective on Mechanisms and Reactivity. *J. Org. Chem.* **2021**, 86 (20), 13833–13856.
- Brahmachari, G.; Nayek, N.; Mandal, M.; Bhowmick, A.; Karmakar, I. Ultrasound-Promoted Organic Synthesis-A Recent Update. *Curr. Org. Chem.* **2021**, 25 (13), 1539–1565.
- Gharat, N. N.; Rathod, V. K. Ultrasound-Assisted Organic Synthesis. In *Green sustainable process for chemical and environmental engineering and science*; Elsevier, 2020; pp 1–41.
- Draye, M.; Chatel, G.; Duwald, R. Ultrasound for Drug Synthesis: A Green Approach. *Pharmaceuticals* **2020**, 13 (2), 23.
- Hidalgo, A. Y.; Velasco, M.; Sánchez-Lara, E.; Gómez-Rivera, A.; Vilchis-Reyes, M. A.; Alvarado, C.; Herrera-Ruiz, M.; López-Rodríguez, R.; Romero-Ceronio, N.; Lobato-García, C. E. Synthesis, Crystal Structures, and Molecular Properties of Three Nitro-Substituted Chalcones. *Crystals* **2021**, 11 (12), 1589.
- Kinkle, P.; Gibian, H. Uber Chalkone. *Chem. Ber* **1961**, 94, 26–38.
- Wei, W.; Qunrong, W.; Liqin, D.; Aiqing, Z.; Duoyuan, W. Synthesis of Dinitrochalcones by Using Ultrasonic Irradiation in the Presence of Potassium Carbonate. *Ultrason. Sonochem.* **2005**, 12 (6), 411–414.
- Anastas, P.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev.* **2010**, 39 (1), 301–312.

29. Merouani, S.; Hamdaoui, O.; Rezgui, Y.; Guemini, M. Modeling of Ultrasonic Cavitation as an Advanced Technique for Water Treatment. *Desalin. Water Treat.* **2015**, *56* (6), 1465–1475.
30. Andrade, S. M.; Costa, S. M. B.; Pansu, R. Structural Changes in W/O Triton X-100/Cyclohexane-Hexanol/Water Microemulsions Probed by a Fluorescent Drug Piroxicam. *J. Colloid Interface Sci.* **2000**, *226* (2), 260–268.
31. Cheng, S.; Han, F.; Wang, Y.; Yan, J. Effect of Cosurfactant on Ionic Liquid Solubilization Capacity in Cyclohexane/TX-100/1-Butyl-3-Methylimidazolium Tetrafluoroborate Microemulsions. *Colloids Surfaces A Physicochem. Eng. Asp.* **2008**, *317* (1–3), 457–461.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.