

Phthalocyanines Synthesis: A State-of-The-Art Review of Sustainable Approaches Through Green Chemistry Metrics

Gloria Zanotti,^{*[a]} Federica Palmeri,^[a, b] and Venanzio Raglione^[a]



Driven by escalating environmental concerns, synthetic chemistry faces an urgent need for a green revolution. Green chemistry, with its focus on low environmental impacting chemicals and minimized waste production, emerges as a powerful tool in addressing this challenge. Metrics such as the E-factor guide the design of environmentally friendly strategies for chemical processes by quantifying the waste generated in obtaining target products, thus enabling interventions to minimize it. Phthalocyanines (Pcs), versatile molecules with exceptional physical and chemical properties, hold immense

potential for technological applications. This review aims to bridge the gap between green chemistry and phthalocyanine synthesis by collecting the main examples of environmentally sustainable syntheses documented in the literature. The calculation of the E-factor of a selection of them provides insights on how crucial it is to evaluate a synthetic process in its entirety. This approach allows for a better evaluation of the actual sustainability of the phthalocyanine synthetic process and indicates possible strategies to improve it.

1. Introduction

The complex and urgent issue of climate change demands action on multiple fronts. Mitigating its effects in the coming years will require a fundamental reevaluation of how many technologies are developed and utilized. This encompasses the acquisition and preparation of materials necessary for their advancement, procedures which must prioritize environmental sustainability. Over the past three decades, green chemistry^[1] has emerged as a powerful discipline in this regard. Its proposed paradigm shift embodies a holistic approach to environmental issues, focusing on the development of increasingly efficient methods to minimize waste throughout the production, processing, and utilization of materials and associated devices. Multiple strategies can be employed to satisfy this premise, such as opting for safer and less polluting reagents, solvents and reaction conditions, as well as designing synthetic pathways that retain the majority of the atoms of the reactants in the products. Additionally, identifying low-impact techniques to process target materials in the technology for which it was designed is crucial. To assess the environmental impact of chemical processes, a set of metrics is utilized. Among these, the E-factor is widely recognized. It is defined as the ratio of the mass of waste generated per mass of product obtained and quantifies various components including byproducts, unreacted substrates, non-recyclable solvents, catalysts, and any irrecoverable chemicals, offering valuable insights into the overall environmental footprint of a process. Phthalocyanines (Pcs) are versatile planar, aromatic molecules that have been of great interest to the scientific community due to their outstanding chemical, electronic and optical properties. In fact, in the last decades the interest in phthalocyanines, in addition to fundamental research, has been extended to technology applications such as chemical sensing,^[2,3] organic electronics

(organic thin film transistors (OTFTs), Organic Field-Effect Transistors (OFETs))^[4–7] photodynamic therapy,^[8–10] CO₂ conversion in valuable chemicals^[11–13] and hybrid photovoltaic technologies such as dye-sensitized solar cells (DSSCs),^[14–16] organic solar cells^[17–19] and perovskite solar cells (PSCs)^[20–24] Their structure consists in an isoindolic 18- π aromatic electron ring system having an oxidation state of -2 . Therefore, its central cavity is capable of hosting a variety of metal ions mostly in the $+2$ oxidation state. Derivatives bearing two monovalent cations, such as lithium, sodium, and potassium, can be synthesized and isolated; however, they are not very stable in acidic conditions and in the presence of humidity, which can lead to demetallation (Figure 1c). Ions in the $+3$ state, such as aluminum and indium, can be coordinated too, in the presence of an anionic ligand such as a halide (Figure 1d). Larger trivalent cations, such as those from lanthanides and actinides, cannot be fully accommodated within the phthalocyanine ring. Instead, two phthalocyanine ligands may surround the same ion, forming a so-called “sandwich” type double-decker complex (Figure 1e).

The carbon atoms in the α - and β - positions of the macrocycle (Figure 1) can be widely functionalized to finely tune the optoelectrochemical properties according to specific needs. Given their wide aromatic delocalization, phthalocyanines in solution show typical absorption spectra composed by two main contributions: a Q band typically ranging in the 600–700 nm and a B (Soret) band between 300 and 400 nm. The sharpness of the bands depends on the degree of aggregation of the macrocycles, frequently affected by the donating or non-donating nature of the chosen solvent. The phthalocyanine ring is typically synthesized via a cyclocondensation reaction involving several starting materials summarized in Scheme 1. Phthalimides, phthalic anhydrides, and phthalic acid can all serve as useful precursors for synthesizing both metal-free and metal-containing phthalocyanines, as summarized in Scheme 1. Most commercial processes utilize these compounds, particularly phthalic anhydride, due to its lower cost with respect to other precursors. Along with the appropriate metal salt, if needed, urea is required as a nitrogen source, and ammonium molybdate ((NH₄)₂MoO₄) as a catalyst.

These reactions typically require heating and are conducted in the melt,^[25,26] although solvents such as nitrobenzene have also been employed.^[27,28] Even though the reaction mechanism is not fully understood, some key steps appear to be sufficiently clear: phthalic anhydride initially reacts with urea or its

[a] G. Zanotti, F. Palmeri, V. Raglione
Istituto di Struttura della Materia (ISM), Consiglio Nazionale delle Ricerche (CNR), Via Salaria km 29.300, Monterotondo 00015, Italy
E-mail: gloria.zanotti@ism.cnr.it

[b] F. Palmeri
Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro, 5, Rome 00185, Italy

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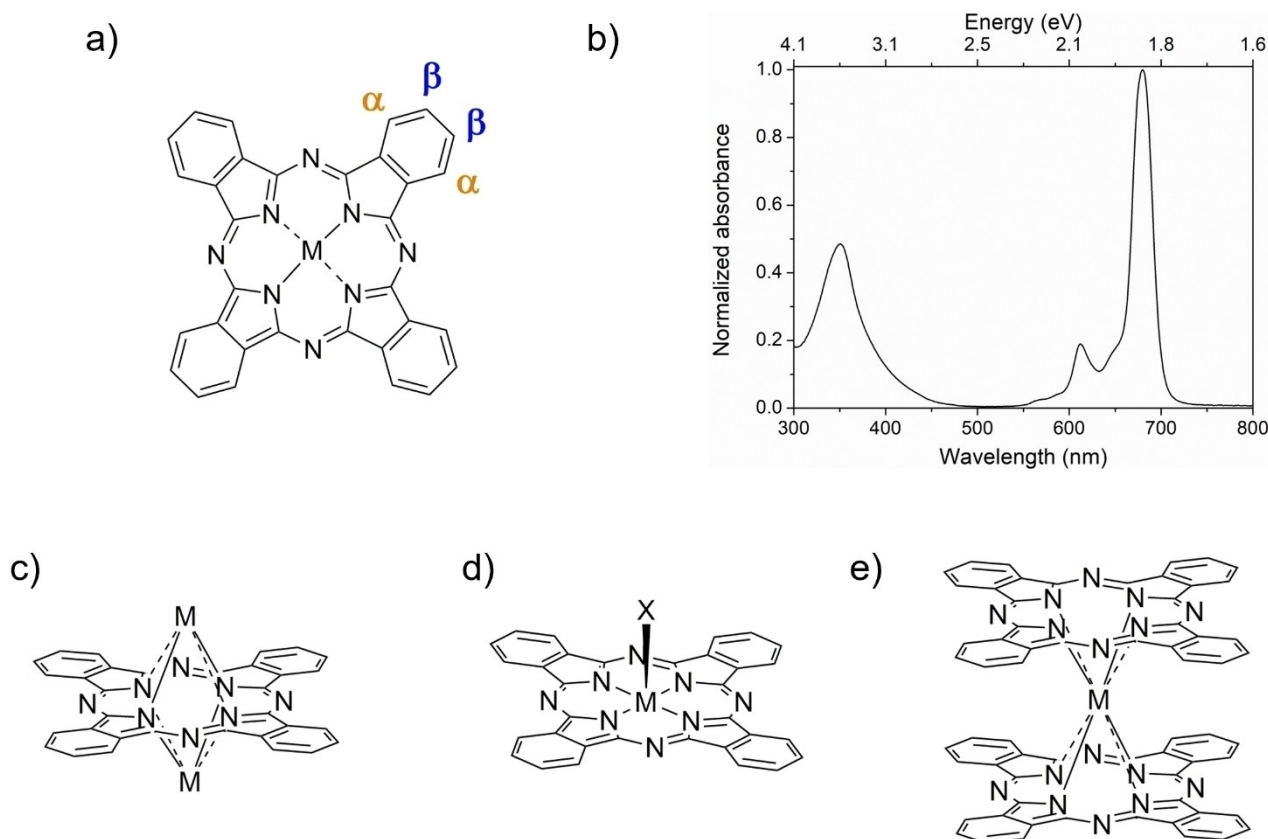


Figure 1. a) Structure of a metal phthalocyanine in which the α and β positions are marked. b) Typical phthalocyanine spectrum in tetrahydrofuran (THF). c) Phthalocyanine complex with monovalent cations d) Phthalocyanine complex with trivalent cations. e) double-decker phthalocyanine. The torsion angle between neighboring Pc depends on the nature of the metal ion.



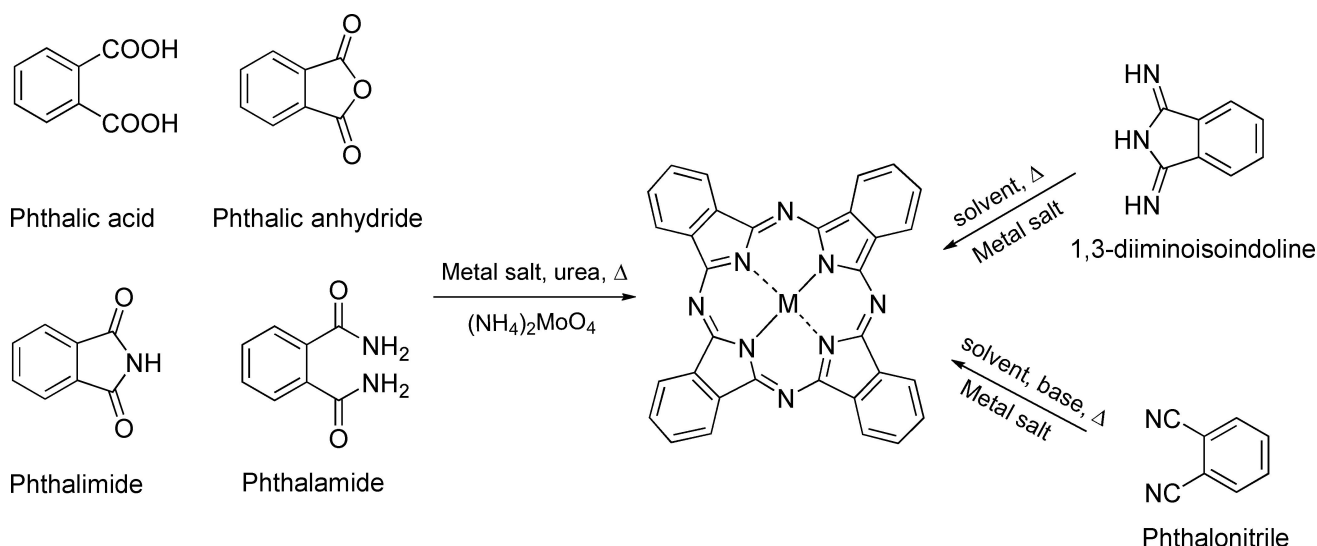
Gloria Zanotti is a researcher at the Italian National Research Council (CNR). Her primary scientific interests are focused on identifying new synthetic methodologies for obtaining organic functional materials with applications in clean energy generation technologies.



Federica Palmeri got her Master's degree in Chemistry, discussing a thesis on the role of bile acids derivatives as organocatalysts in chemical reactions performed in water, and is currently a PhD student in Chemical Sciences at Sapienza University of Rome. Her scientific research has always been driven by her interest in sustainable synthetic approaches of functional materials for different applications, with an emphasis on environment-friendly sensors and biosensors development.



Dr. Venanzio Raglione graduated from Sapienza University of Rome in 2018 and received his Ph.D. in Chemical Sciences from the same University in 2022. He is currently a postdoctoral researcher at the National Research Council (CNR). His main scientific interests concern the development of environmentally friendly methods for the synthesis of molecular luminophores and hole-transporting materials (HTMs) for organic electronics and photovoltaics. He is also exploring innovative approaches for recovering and reusing the materials utilized in photovoltaic devices with the main goal of contributing to the development of more sustainable and efficient solar energy technologies.

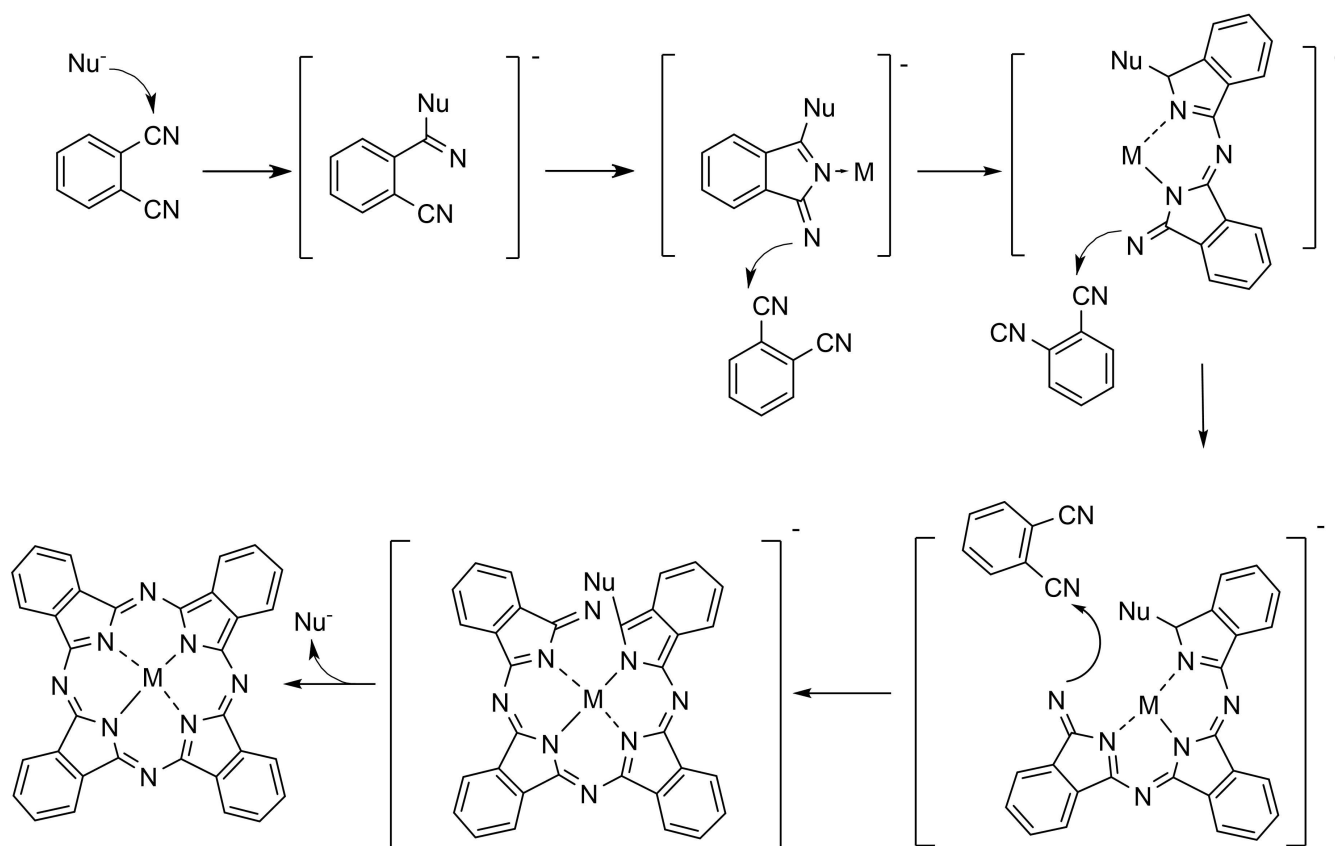


Scheme 1. General reaction conditions scheme for the synthesis of phthalocyanines starting from phthalic acid, phthalic anhydride, phthalimide, phthalamide, 1,3-diiminoisoindoline or phthalonitrile. No metal salt is required for the synthesis of metal-free derivatives ($M = 2H$).

decomposition products, progressively replacing oxygen atoms with nitrogen to ultimately form the key intermediate 1,3-diiminoisoindoline. The presence of ammonium molybdate is essential to catalyze this part of the sequence. Subsequently, this intermediate undergoes tetramerization with cyclization, possibly aided by the presence of a metal ion, to form the desired phthalocyanine.

When employed as starting materials, 1,3-diiminoisoindolines undergo self-condensation at high temperatures. A typical procedure for obtaining the phthalocyanine macrocycle therefore consists of dissolving them in an appropriate solvent, for example *N,N*-dimethylaminoethanol (DMAE), *N,N*-dimethylformamide (DMF) or quinoline, and allowing them to react under reflux.^[29,30] For syntheses conducted on a laboratory scale, however, phthalonitrile and its derivatives are by far the most versatile and used precursors. The reaction is conducted at temperatures ranging from 130 to 250 °C in solvents such as alkyl alcohols, DMF, DMAE, quinoline, or α -chloronaphthalene, in an alkaline environment. An organic non nucleophilic base such as 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) or an in-situ generated lithium alcoholate are frequently used to assist the formation of the macrocycle. The most plausible mechanism for the formation of the phthalocyanine ring starting from phthalonitrile is shown in Scheme 2 and involves the interaction between a CN and a nucleophile, followed by intramolecular nucleophilic attack on the carbon of the *ortho* cyano group and further cascade steps that ultimately lead to the formation of the final product. The presence of a templating metal significantly aids the tetramerization, instead of promoting side oligomerizations or polymerizations. Typically, the nucleophilic function is carried out by the deprotonated form of a protic polar solvent or by the counterion of the selected salt. In recent years, alongside conventional procedures, alternative methodologies have emerged with the goal of conducting reactions under milder and less environmentally impactful conditions.

These approaches often involve the utilization of alternative energy sources or innovative reaction protocols and reactants. Despite the attention given to this issue by many research groups, as evidenced by the specific literature on the topic, there are relatively few and outdated reviews on synthetic methodologies with low environmental impact published thus far.^[31,32] Furthermore, to the best of our knowledge the discussion about the environmental impact itself is limited to the proposed synthetic approaches without discussing their environmental footprint more in detail. Evidence of this can be seen in the limited inclusion of green metrics in these discussions. Only very recently, some evaluations on the Environmental Factor (E-factor) related to the synthesis of unsubstituted and tetra-*tert*-butyl substituted phthalocyanines have been made.^[33,34] In contrast, examples of E-factor calculations in porphyrin synthesis have been available for some time.^[35–38] This important metric is defined as the ratio between the mass of waste generated and the mass of product obtained. It does not differentiate between various types of waste, thus it should be complemented with other metrics to assess toxicity. However, even when used alone, it can offer valuable insights into the studied synthetic process. Its simple calculation procedure, based on objective data, makes it a useful tool for a quick evaluation of the environmental impact of a synthetic process. This review describes the main advances in the field of research into synthetic protocols with reduced environmental impact to produce phthalocyanines over the last 25 years. Our goal is to provide an updated state-of-the-art understanding of the topic and offer an exhaustive overview of the progress made in this field. Furthermore, as a first step towards the evaluation of synthetic processes for obtaining phthalocyanines through ex post evaluations, we will present the calculation of the E-factor of a selection of procedures taken from the articles under examination. These reference values will serve as useful benchmarks for an initial assessment of the “greenness” of a



Scheme 2. Proposed mechanism for the synthesis of phthalocyanines starting from phthalonitriles.

synthesis based on the generated waste materials. Far from being exhaustive, this approach can indeed facilitate the development of more sustainable synthetic methodologies for phthalocyanine ring synthesis.

2. Discussion

We have categorized the various synthetic methodologies into three primary groups: the utilization of alternative energy sources for heating, the selection of reaction environments with a low environmental footprint, and synthetic strategies aimed at reducing reaction temperatures using specific reagents. In cases where an article encompasses more than one of these types—for instance, microwave reactions conducted in an environmentally compatible solvent—it will be categorized under the most relevant classification for discussion.

2.1. Alternative Energy Inputs

In this section, we will discuss examples of phthalocyanine synthesis conducted with alternative energy inputs such as microwave (MW) radiation, ultraviolet (UV) radiation, and ultrasound. One advantage of these approaches is the localized generation of hot spots within the reaction environment, where very high temperatures are rapidly attained and dissipated. This

enables a significant amount of energy to be delivered to the system while minimizing the risk of thermal degradation of reactants or products. However, it is crucial to ensure that the energy is uniformly distributed throughout the system, particularly when considering process scaling-up. In the case of UV irradiation, it is especially important to carefully design the synthesis process, as the interaction between photons and matter often results in the formation of highly reactive radical species that may induce unwanted side reactions.

2.1.1. Microwave Irradiation

Microwave irradiation has emerged as a powerful technique for promoting chemical reactions. Microwaves are electromagnetic radiation ranging from 0.3 to 300 GHz, absorbed by materials that exhibit dipolar polarization or ionic conduction. The impact of microwave irradiation on chemical reactions arises from a combination of thermal and non-thermal effects. The former effects primarily stem from dipolar and interfacial polarization, although conduction losses can also become significant at elevated temperatures. When a molecule is exposed to microwaves, it rotates to align with the applied field, resulting in continuous attempts to realign with changing fields, leading to energy absorption. The latter effects may primarily arise from an increased probability of molecular collisions, a reduction in activation energy, and the occurrence of localized hot spots.

Microwaves improve synthetic processes by accelerating reaction rates, thereby reducing reaction times. Additionally, they enable working with reduced quantities of solvent or even in solvent-free conditions. Furthermore, microwaves can enhance the selectivity of a synthetic process by favoring desired reactions over potential collateral processes.^[39,40] This approach is by far the most represented green synthetic method in literature for the synthesis of phthalocyanines. Microwave-assisted synthesis has successfully provided macrocycles functionalized with halides,^[41–44] terminal alkynes,^[45] crown ethers,^[46] substituted phenoxy^[47–49] and 1-naphthoxy^[50] groups, tetraaza,^[51] tetraoxamonoaza,^[52] tetrathiacyclohexadecane,^[53] dithiadiazadioxo,^[54] diazadithio^[55] and tetrathiadiaz rings,^[56,57] thiazoles,^[58] functionalized triazoles,^[59–62] phenylthioethanol,^[63] monoterpenes like (1R)-(–) myrtenol and (1R,2S,5R)-(–)-menthol,^[64] benzenesulfonamide,^[65] pyridine^[66] and azo compounds.^[67] Microwaves have been also employed to synthesize silicon^[68] lanthanide(III),^[69] lead,^[49,70] and platinum^[71] derivatives, and phthalocyanine-based polymers.^[72–74] Kantar et al. used the microwave-assisted approach for the tetramerization of phthalonitriles bearing different substituents at positions 4- and 5-. They successfully synthesized tetra- and octa-substituted metal-free, zinc, and copper phthalocyanines and compared the alternative procedure with the standard solution-based method.^[75] By exploiting the different reactivity of the two chlorine atoms of 4,5 dichlorophthalonitrile when one of them is subjected to nucleophilic aromatic substitution (S_NAr), they synthesized two asymmetric precursors: 4-chloro-5-(3,5-dimethoxyphenoxy)phthalonitrile and 4-octanethio-5-(3,5-dimethoxyphenoxy)phthalonitrile. Subsequently, these precursors reacted in DBU or DMAE for 8 minutes at a power of 350 W using microwave irradiation to provide **MW1** and **MW2** derivatives. In all cases investigated, the yields were at least 75%, surpassing those of the corresponding standard procedures conducted for comparison. DMAE was chosen as the reaction solvent for the synthesis of the polyfluorinated zinc phthalocyanine **MW3**,^[44] which was subsequently grafted onto a suitably functionalized silica. The resulting inorganic–organic hybrid material was used as a catalyst for the solvent-free synthesis of biologically important 1,5-benzodiazepines, and proved to be recoverable and reutilized. The use of the **MW3**-based catalyst in solvent-free reaction conditions at room temperature, led to an improvement in conversions with respect to control experiments. The environmentally friendly synthesis of its precursor adds significant value, further advancing the target application towards greater sustainability.

Acetyl-substituted zinc phthalocyanines have been synthesized by Koyun et al. in a similar way.^[45] By irradiating the precursors in *n*-pentanol at 360 W, yields up to 86% for **MW4** and 81% for **MW5** were obtained. The MW-based approach outperformed the conventional one (79% and 74% yields for **MW4** and **MW5** respectively) and reduced the reaction time from 6 hours to 15 minutes. Remarkably, the synthetic approach was efficient in providing the target products without needing to protect the terminal acetyl functional group. Chiral monoterpene derivatives (**MW6** and **MW7**) have been recently synthesized by Gonzalez et al.^[64] yielded the desired phthalocyanines with comparable yields to the conventional procedure.

The copper derivatives exhibited slightly higher yields than the zinc derivatives. Notably, a significant reduction in reaction time from seven hours to one hour was observed. Taking advantage of the local generation of large amounts of energy, microwaves can be exploited to obtain products that would not be synthesized using conventional methods. Makhseed et al. succeeded in obtaining hexadeca(2,6-dimethylphenoxy)phthalocyanines^[76] (**MW8**) in a 9% yield by reacting 3,4,5,6-tetrakis(2,6-dimethylphenoxy)phthalonitrile in the presence of hydroquinone in hexanol at 350 W for 10 minutes. Microwaves irradiation mitigated the decrease in reactivity of the cyano groups due to the steric hinderance and electron-donating nature of the bulky 2,6-dimethylphenoxy substituents. The related metallated derivatives were obtained in 18%–24% yields by adding the desired salt to the mixture. On the contrary, attempts using the lithium pentoxide/pentanol system to obtain the free-base or metal ion-template reactions in hexanol led to inseparable mixtures of byproducts with an overall very low yield. Several solvent-free procedures have also been reported. Sharma et al. straightforwardly synthesized 2,9,16,23-tetrachlorophthalocyanines **MW9** starting from the cheap sodium 2-carboxy-4-chlorobenzoate and a suitable anhydrous metal salt ($CoCl_2$, $CuCl_2$, $NiCl_2$, $ZnCl_2$) in presence of urea as the source of nitrogen.^[42] The reported yields are generally high (75–92%). The absence of a proper solvent enhanced the interaction between microwaves and reactants and drove the chemical reaction toward completion. Moiseeva et al. succeeded in synthesizing 1.9 grams of 2(3),9(10),16(17),23(24)-tetraiodophthalocyanine **MW10** in a single batch by irradiating a mixture of 4-iodophthalonitrile and $Zn(quinoline)_2Cl_2$ salt in a microwave reactor at 150 W for 7 minutes.^[43] The authors achieved a high 83% yield at analytical grade ($\geq 98\%$) purity. This result is promising as this molecule is a versatile intermediate, whose iodide atoms can be widely substituted by exploiting the rich palladium-catalyzed chemistry to provide functionalized derivatives with high complexity. Furthermore, it is interesting to report here the synthesis of the **MW11** cobalt derivative starting from 1,2,4-benzene tricarboxylic anhydride, urea, cobalt chloride and $(NH_4)_2MoO_4$, carried out on a total of approximately 100 grams of reagents. The authors report a very high yield, equal to 90%, validating the use of microwaves even on large quantities, although still on a laboratory scale.^[77] Solventless microwave-assisted syntheses have been reported also for unsubstituted Cu(II), Mn(II), Al(III), Co(II) and Zn(II) Pcs,^[78] and for nitro- and polychlorinated-derivatives.^[79,80] Lead phthalocyanine and lead 2(3),9(10),16(17),23(24)-tetra-nitrophthalocyanine were obtained in 90–92% yields by reacting phthalonitriles and lead oxide in a domestic microwave oven for 13–15 minutes with a range of power irradiation.^[70] The method was applied to batches of reagents up to approximately six grams. Comparison reactions carried out in molten phthalonitrile at 140–180 °C for 1–4 hours consistently resulted in lower overall yields. On the contrary, more complex lead derivatives (**MW12**, **MW13**) synthesized in pentanol using DBU as base provided lower yields, ranging between 19 and 46%.^[49] Although a direct comparison of such

different synthetic procedures is inappropriate, it is possible that the absence of solvent may be particularly advantageous for the synthesis of this family of metallophthalocyanines. Alternatively, pentanol may not be the most suitable choice as a reaction medium in this particular case. The chemical structures of the phthalocyanines discussed in this paragraph are gathered in Figure 2.

2.1.2. UV Irradiation

Photochemical substrate activation with UV irradiation frequently occurs without the need for additional reagents, leading to reduced formation of byproducts. This feature makes photochemical reactions particularly attracting within the framework of green chemistry. Moreover, certain reactions can be carried out using visible light or sunlight as a renewable energy source, further enhancing their environmental appeal. The study of UV light to assist the synthesis of phthalocyanines dates to 1976, when Tomoda et al. observed that room light could positively affect the formation of phthalocyanines, and that UV irradiation could promote it even at room temperature.^[81] Kharisov et al.^[31,82] then studied the effect of solvent on the synthesis of metal-free phthalocyanine (PCH₂) in the temperature range 0–60 °C choosing different linear, branched, and cyclic alcohols, as well as in ethylene glycol and dimethylaminoethanol (DMAE) as reaction media. Under the best experimental conditions, using the Ethanol/CH₃ONa and Methanol/CH₃ONa systems could produce quantitative yields in the 30–60 °C temperature range. The rationalization of this evidence involves the formation of free RO[•] radicals upon irradiation with UV light, which increases the effectiveness of nucleophilic attacks on the cyano group of phthalonitrile.

Experimental evidence suggests that the presence of more than one hydroxy group in solvents, such as in ethylene glycol and glycerol, can enhance yields and enable reaction temperatures to be lowered, even to near-zero degrees. However, it is important to note that the authors report difficulties in precisely calculating these effects due to the high viscosity of these solvents, that made the isolation of the product from the reaction mixture challenging. Therefore, while this evidence is promising, it should be considered probable rather than fully verified. In 2010, Youssef reported the UV-assisted synthesis of metal-free 2,3,9,10,16,17,23,24-octamethoxyphthalocyanine (UV1, Figure 3) in DMAE, as a precursor for more complex alkynyl substituted derivatives.^[60] The yield obtained was 60% starting from 3.5 g of phthalonitrile, a quantity still on a lab-scale, but significant in phthalocyanine synthesis, often carried out in quantities much lower than one gram. Instead, any attempt to synthesize the corresponding metallophthalocyanines in the same reaction conditions failed. Saito et al. reported the first direct synthesis of Cu and Zn phthalocyanines in nanosized micelles irradiated with UV light.^[83] The size of the micelles, that was found to be averagely 24.7 nm, allowed to control the morphology of target products, obtaining CuPc in α -form. The order in which the reagents are added was found to be crucial for the success of the reaction: adding CuCl₂ before

the surfactants resulted in large aggregates caused by the formation of complexes between Cu²⁺ and isoindoline intermediates outside the micelles. This approach was subsequently applied to the synthesis of unsubstituted crystalline naphthalocyanines and tetrapyrroldiporphyradine, thus demonstrating its potential versatility.^[84]

2.1.3. Ultrasounds

For over 80 years, sonochemistry, or ultrasound-driven chemical reactions, has captivated researchers as a powerful tool. The effectiveness of ultrasound stems from cavitation, where bubbles form, expand, and violently collapse within a liquid. These collapsing bubbles generate intense, localized bursts of high pressure (up to 1,000 bar) and temperatures up to 5,000 K, initiating high-energy radical reactions. However, sonochemistry is more than just brute force; it also facilitates micro-mixing, ensuring thorough interaction between reaction components, and enhances mass transport, allowing materials to move more freely within the system. Additionally, it can reduce particle size, resulting in a larger surface area and faster reaction rates. Studies have shown that sonochemistry can significantly enhance reaction efficiency by accelerating rates, increasing yields, and influencing product selectivity in specific cases. This influence may even lead to the discovery of entirely new reaction pathways. Several ultrasounds-assisted organic reactions have been reported, such as the synthesis of esters,^[85] hydrolysis of nitriles,^[86] nucleophilic aromatic substitutions^[64] and preparation of metal-organic frameworks (MOFs).^[87,88] The literature concerning this approach for the synthesis of phthalocyanines is scarce and notably dated. There is evidence of ultrasound-assisted synthesis of PCH₂ at low temperature (0–40 °C) using zeolites of the clinoptilolite type as solid support.^[89,90] Ultrasound accelerates the reaction by 2–3 times compared to control experiments conducted without it. The authors hypothesize that this acceleration is attributable to the improved generation of radical species and the continuous exposure of new active catalytic surfaces of the zeolites themselves. Differences in reaction yields observed depending on the zeolite used were attributed to calcite impurities present in the composition of one of them, which are inert with respect to the phthalonitrile cyclization reaction. As a side note, ultrasonic treatments were reported to obtain lithium phthalocyanine nanotubes from micrometer-sized particles in water.^[91] Combinations of high frequency ultrasound and a surfactant like sodium dodecyl sulfate (SDS) reduced their size to diameters of tens of nanometers. Lastly, ultrasounds have found application in processes aimed at destroying the phthalocyanine aromatic ring in decolorization processes of industrial waste.^[92,93]

2.2. Alternative Reaction Media

Solvents represent a significant fraction of the whole material involved in a chemical process and play many roles in the

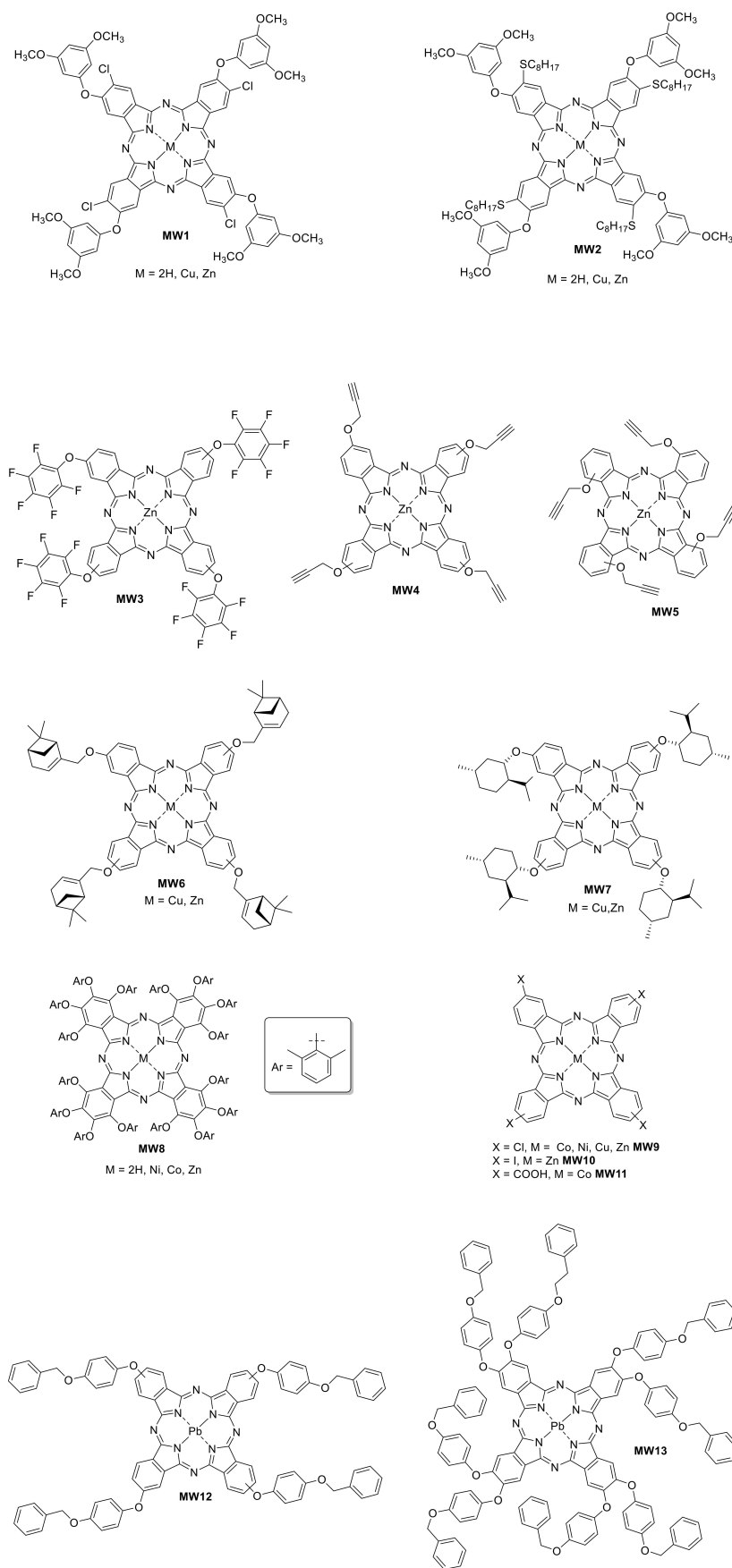


Figure 2. Phthalocyanines synthesized using MW-assisted methods.

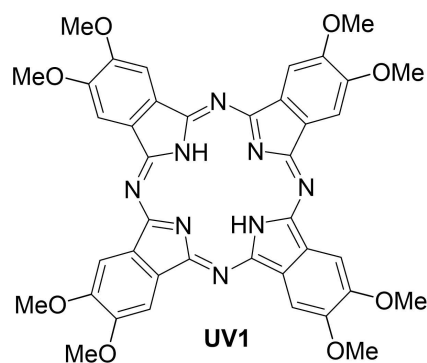


Figure 3. Chemical structure of 2,3,9,10,16,17,23,24-octamethoxyphthalocyanine.

success of a synthesis. They can homogenize the concentration of reactants in the reaction medium and its temperature, improve its efficiency through favorable interactions with the reagents, induce the activation of specific molecular positions among others, suppress the formation of byproducts, and promote a straightforward purification of the resulting crude mixture. All this leads to an increase in the reaction yields and indirectly contributes to reducing the production of waste, as well as the economic cost, of a synthetic process. The investigation of low-impact reaction media alternative to those conventionally used can therefore translate in many advantages in addition to the reduction of environmental criticalities of a synthesis.^[94–96] Water is the solvent of choice for green chemistry given its abundance and lack of toxicity. However, the alkaline environment required for generating nucleophilic species that promote ring cyclization leads to the production of OH[−] ions, which undergo unwanted reactions with the precursors, particularly phthalonitriles.^[97,98] Consequently, water not only becomes unsuitable as a solvent but also an unwanted impurity, even in small quantities, in the reaction environment. The development of micellar approaches, building on the extensive research already conducted for numerous organic synthesis reactions,^[99] could overcome the issue. However, to date, the synthesis of phthalocyanines in micelles is limited to a few examples in polar organic solvents,^[83] rendering it a relatively underexplored area with significant potential.

2.2.1. Benign Solvents

Zanotti et al.^[100] tested anisole, glycerol, and their mixtures as solvents for the ring formation of unsubstituted and tetra-*tert*-butyl substituted cobalt, copper, and zinc phthalocyanines. Anisole was chosen because of its low toxicity and biodegradability,^[96,101] and because it can be obtained by renewable feedstocks like lignin and guaiacol.^[102–104] Glycerol is a low-impact solvent that is already utilized in organic synthesis,^[105] is available on a large scale from the vegetable oil industry and can solubilize both inorganic salts and a large variety of organic species.^[106,107] (Figure 4). The formation of

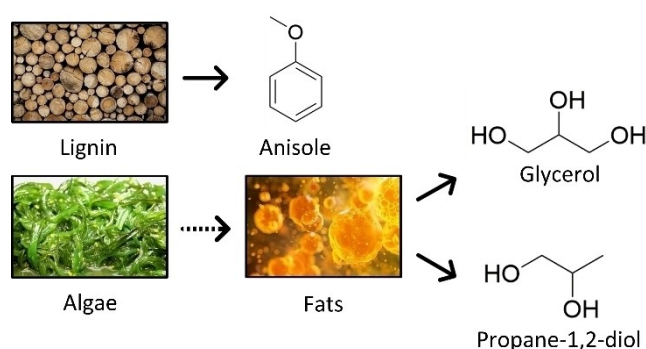


Figure 4. A selection of benign solvents explored as reaction media for the synthesis of metallophthalocyanines in solution, along with renewable feedstocks from which they can currently be obtained.

phthalocyanines in the various solvents and mixtures was found to be dependent on the nature of the templating metal.

The trend Cu(II) > Co(II) > Zn(II) is in agreement with the greater templating power of copper compared to the other two ions. Conversely, zinc was found to be the least reactive metal, due to its 3d¹⁰ shell. Some exceptions were rationalized by analyzing the reaction environment and the interactions of the solvent with the reacting species. For example, the synthesis of CuPc in anisole using DMAE as the base had the lowest yield among all, probably because of the polar aprotic nature of the solvent that may have favored competitive copper-catalyzed reactions rather than templating the tetramerization of phthalonitrile. Instead, the formation of CuPc in the same solvent when using potassium hydroxide as the base provided a yield as high as 76%. It is possible that the greater nucleophilicity of KOH compared to DBU in a relatively non-polar environment allowed an effective attack on the cyano groups of phthalonitrile, aided by the extreme coordinating capacity of copper, promoting the Pc ring formation among other processes. KOH has generally provided much lower yields for the other metal ions because of a side-reaction involving the hydration of nitrile groups in polar environments and subsequent formation of phthalimides. Copper has been the best performing ion also in the synthesis of tetra-*tert*-butylphthalocyanines, yielding the desired product in all the screened conditions although in smaller amounts than the standard protocols. This evidence highlights how the choice of an alternative reaction environment can depend on parameters such as the nature of one or more reagents, in a manner that is not always easily predictable. Consequently, it can be challenging to develop a general procedure with a broad spectrum of applicability. As a follow up of this work, Podapangi, Mancini et al.^[34] investigated a propane-1,2-diol/anisole mixture with DBU as the base for the synthesis of the same derivatives, obtaining yields close to those of standard conditions at least for the copper and zinc tetra-*tert*-butylphthalocyanines. In the literature, propane-1,2-diol has been utilized as a solvent or co-solvent in reactions involving ionic liquids.^[108] An intriguing extension of this study, aimed at broadening the range of alternative reaction media, could involve solvents like polyethylene glycols (PEGs), which have

already demonstrated success in the synthesis of organic materials with high added value.^[109,110]

2.2.2. Solvothermal Synthesis

Solvothermal synthesis is a method used to produce chemical compounds that involves placing a solvent containing reagents into an autoclave and subjecting it to high pressure and temperature. Under these conditions, many substances dissolve more readily in the solvent compared to standard conditions. This increased solubility enables reactions that might not occur under normal circumstances otherwise. This approach is mostly applied to synthesize inorganic materials, while for the synthesis of phthalocyanines there have been limited successful attempts starting from several organic precursors, the first of which dates to 2008 and involves the use of harmful solvents like quinoline at temperatures $> 200\text{ }^{\circ}\text{C}$.^[111] Over the past fifteen years, research efforts in solvothermal synthesis have mainly focused on identifying solvents with fewer environmental concerns. This focus has resulted in the synthesis of phthalocyanines with diverse central metals and a restricted range of ring substituents. Notably, the products are often obtained as single crystals, rendering the solvothermal approach a valuable strategy for synthesizing highly organized materials. These materials offer a platform for investigating fundamental and structural properties that would otherwise be inaccessible. In 2015, Li et al. reported the synthesis of manganese phthalocyanine in ethanol at $190\text{ }^{\circ}\text{C}$ for 3 hours.^[112] Interestingly, both the synthesis and the purification steps do not require obnoxious solvents, since water is the only other chemical required to accomplish the task. The size of the crystals obtained is considerable, and in some cases exceeds 10 mm. The resulting crystals were characterized by SEM measurements, which showed a well-defined quadrangular shape and different morphologies on the top/bottom planes. X-ray diffraction disclosed a monoclinic phase. The same author successfully synthesized ZnPc and CoPc with a similar procedure, screening three different alcohols to individuate the best experimental conditions to maximize the length of the resulting crystals.^[113] Benzyl alcohol gave the best performances among the choices, providing ZnPc crystals up to 8 mm and CoPc up to 1 mm. TEM images of ZnPc crystals obtained in different solvents provide interesting information, as their morphology significantly changes with the reaction media: benzyl alcohol gave quadrangular prisms with smooth surfaces along with some multi-layer plates. 1-pentanol provided rougher surfaces with nano-sheet arrays intersecting on the exterior surface. Ethanol-derived crystals displayed a quadrangular contour with additional secondary structures observed on their surface. Conversely, the smoothest surface for CoPc was obtained with ethanol. This evidence suggests that the reaction media interactions with the reactants and the induced reactivity on the OH and cyano group, perhaps as well as the reaction temperature, play a crucial role in defining the morphology of the resulting products. The synthesis of a ZnPc hierarchical nanostructure with hollow interior space using ethylene glycol

as a solvent has also been reported.^[114] More recently, the solvothermal synthesis of a metal-free Pc in non-harmful solvents was achieved.^[115] Since the reaction cannot take advantage of the templating effect of metal ions, DBU or 1,5-diazabicyclo-[4.3.0]-non-5-ene (DBN) were necessary to obtain the final product. Additionally, ethanol emerged as the better solvent option. The presence of a protic functional group on the solvent was found to be fundamental for the reaction to happen, attempts in pyridine, tetrahydrofuran, and acetonitrile failed in giving the phthalocyanine. Solvothermal synthesis has also been exploited to obtain rod-like iron phthalocyanine^[116,117] and hierarchical tetranitrophthalocyanines with potential application in photocatalysis and for capacitive energy storage^[118,119] The solvothermal synthesis of copper phthalocyanine nanotubes and nanostructures in ethylene glycol has been recently reported for the electrosynthesis of urea^[120] and ammonia^[121] respectively.

2.2.3. Ionic Liquids

Ionic liquids have gained momentum as appealing reaction media for organic synthesis because of their low vapor pressure, high thermal stability, high ionic conductivity, and ease of recovery. Due to their ionic nature, ionic liquids are particularly advantageous for reactions involving charged reactive species. Their high chemical stability and low volatility guarantee that emissions from ionic liquids pose minimal environmental concerns. However, this same characteristic renders them persistent substances in natural environments, thus potentially leading to pollution. The debate regarding the classification of ionic liquids as sustainable reaction media persists in the literature. We include them in this review because, based on our analysis of the articles, they have demonstrated recyclability for a certain number of cycles under the specified conditions and are typically used in modest quantities on a lab-scale. Their use in the formation of the phthalocyanine ring can be advantageous, as ionic liquids can generally enhance the reactivity of nucleophiles, thereby reducing the yield of side products formed.^[122,123] In addition to their use as reaction media, ionic liquids have been employed in the removal of the central metal of the macrocycle.^[124] Some ionic liquids successfully used in the synthesis of phthalocyanines are shown in Figure 5. In 2005, Lo et al. explored the potential of tetrabutylammonium bromide (TBAB) as a solvent for obtaining alkylthio, alkoxy, and phenoxy-substituted phthalonitriles by S_NAr and for subsequent cyclization to obtain the corresponding phthalocyanines (IL1-IL6).^[125] It is interesting to note that the S_NAr step did not require the presence of a base, as is normally necessary in this type of reaction, probably because the ionic nature of the solvent increases the nucleophilicity of the thiol and alcohol groups. The phthalocyanines were then synthesized in the same ionic liquid using varying amounts of DBU, in yields comparable to reactions carried out with conventional procedures. As a collateral reaction, the authors report the formation of significant amounts of metal-free tetrakis(alkylthio) phthalocyanine

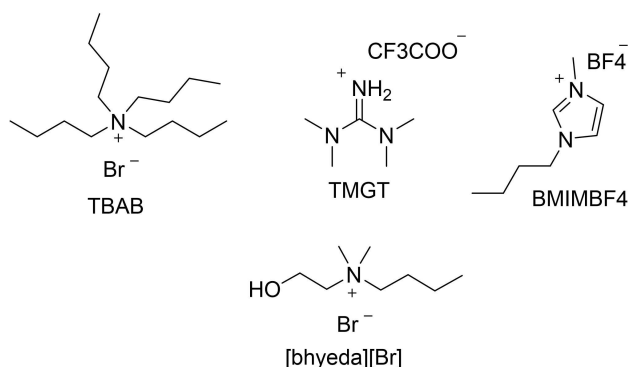


Figure 5. Structure of ionic liquids mentioned in this review. From left to right, Tetrabutylammonium bromide (TBAB), 1,1,3,3-Tetramethylguanidinium trifluoroacetate (TMGT), 1-butyl-3-methylimidazolium tetrafluoroborate (BMIMBF4) and butyl(2-hydroxyethyl)-dimethylammonium bromide ([bhyeda][Br]).

cyanines when four equivalents of thiols were used in the nucleophilic aromatic substitution of 4-nitrophthalonitrile.

It would have been interesting to investigate this occurrence further, as the possibility of pushing this side reaction would have led to the final product reducing both reaction time and required chemicals. TBAB has been employed also in the synthesis of unsubstituted, chlorinated and nitro phthalocyanines bearing several metal ions.^[126] Phthalonitriles, phthalimides and phthalic anhydrides have been used as reactants, in the classic reaction system involving urea and ammonium heptamolybdate. Overall, the reactions were found to proceed at least an order of magnitude faster than their standard counterparts. Tests have indicated a general tendency for phthalonitriles to necessitate shorter reaction times and achieve higher yields than other precursors. Furthermore, phthalonitriles required lower amounts of urea, aligning with the reduced need for a nitrogen source compared to phthalimides and phthalic anhydrides. The ionic liquid was found to be recyclable up to 4 times, although with a progressive decrease in yield from 95% to 70%. Nickel phthalocyanine has been synthesized in 1-butyl-3-methylimidazolium tetrafluoroborate giving a high yield of one-dimensional structures without using a template or stabilizing agent.^[127] This occurrence was rationalized with the unique π - π stacking of the imidazole ring that induces a specific directed growth of the phthalocyanine product. 1,1,3,3-Tetramethylguanidinium trifluoroacetate (TMGT) and TBAB have been investigated as ionic liquid and as phase transfer reagent, respectively, for the synthesis of PcH_2 .^[108] These studies were conducted under both conventional heating conditions or microwave irradiation using hexamethyldisilylazane, sodium sulfide or urea as co-reactants. In all the examined cases, microwaves promoted the efficient formation of target product in 3–5 minutes depending on the reaction system, with high yields (up to 80%) comparable to those of conventional heating. All in all, the best performances were obtained with TMGT regardless of the experimental procedure. The authors rationalize this evidence with the formation of 1,1,3,3-tetramethylguanidine (TMG) and trifluoroacetic acid (TFA) due to thermal dissociation of TMGT. The nucleophilicity of the nitro-

gen atom of TMG is strong enough to react with one cyano group, assisted by its activation with a strong protic acid such as TFA or the conjugated acid of TMG itself, and initiate the tetramerization of phthalonitrile. Chauchan et al. investigated the effect of ionic liquid composition on the synthesis of phthalocyanines **IL1**, **IL7**, **IL8**, and **IL9**.^[128] A selection of functional ammonium-, pyridinium- and imidazolium ILs in the presence of DBU were examined, resulting in a pyridinium > imidazolium > ammonium general reactivity scale. Pyridinium-based materials degraded quickly due to the presence of the organic base. The imidazolium-IL effectiveness was explained with the deprotonation of the ring with generation of a negatively charged nucleophilic ion reacting with CN groups of phthalonitrile. All in all, hydroxylated ionic liquids gave the best result due to the formation of alkoxy anions, that similarly attack cyano groups. A dependence on the nature of the ionic liquid anion was also reported. Once that N-(2-hydroxyethyl)-N,N-dimethylbutan-1-ammonium bromide ([bhyeda][Br]) was identified as the best-performing reaction medium, it was used to synthesize methyl-, methoxy-, alkoxy- and nitro-substituted phthalocyanines with several metal ions. Target products were synthesized in generally high yields, up to 74%. The structures of the phthalocyanines discussed in this paragraph are illustrated in Figure 6.

2.2.4. Deep Eutectic Solvents

Deep eutectic solvents (DESs) have garnered widespread attention as efficient and innovative media in the past decade. The environmentally friendly nature of deep eutectic solvents (DESs) stems from several key properties, including low vapor pressure, non-flammability, recyclability, biodegradability, and non-toxicity. DESs typically consist of two components: a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA) the nature of which influences their physical properties. By mixing the HBA and HBD components (quaternary ammonium salt or metal salt and species like alcohols, amides, amines, acids, urea, sugars, carboxylic acids, and glycerol, among others, respectively) in a specific molar ratio, a homogeneous solvent is commonly formed with a melting point lower than that of its pure constituents.^[129] DESs share similar features with ionic liquids but offer considerable advantages, including being derived from biodegradable and non-toxic starting materials, having a cheaper production process, lower cost of raw materials, and importantly, being obtainable from renewable feedstocks and rapidly degradable in the environment.^[130] Nowadays, DESs have been applied in fields such as inorganic^[131] and organic synthesis^[131–133] and biocatalysis.^[134] To the best of our knowledge, only a few papers discuss the synthesis of phthalocyanines in DESs. Shaabani et al.^[135] report the use of several deep eutectic systems based on choline chloride (ChCl) and several hydrogen donors. After optimizing the system and identifying urea as the best choice, ChCl-urea mixtures in a 2:1 molar ratio were used for the synthesis of a wide range of unsubstituted and tetra-nitro-substituted metallophthalocyanines with variable yields in times

2.2.5. Solid-State Synthesis

Solid state syntheses take the minimization of the quantities of solvent used to extreme consequences, avoiding its use altogether or reducing it by orders of magnitude compared to conventional procedures. Energy input can be provided by heating or mechanochemistry, thus employing mechanical forces to enable chemical reactivity. When heating, reaction temperatures equal to or higher than the melting temperature of one or more reagents are frequently chosen, to increase contact between them and improve yields. We point out that, for simplicity, we will refer to this specific type of procedure as “solid state” even though it technically occurs in a liquid phase due to the reaction conditions. The main drawback of syntheses in molten mixtures is the high temperatures required, often equal to or higher than those of corresponding solution-based methods. Additionally, the thermal energy involved, combined with the high concentration of reagents and reaction intermediates, can promote degradation processes or the formation of by-products, potentially catalyzed or influenced by impurities such as oxygen or humidity if the reaction setup is not meticulously controlled. Nonetheless, we believe it is worthwhile to describe some methodologies where temperatures are kept within 150–170 °C, such as those reported for solvents like glycerol and anisole in this review. Molten urea is typically employed both as a solvent and a source of nitrogen when phthalic precursors are used,^[137] though there are also reports of its use with phthalonitriles.^[138] In 2013, Lokesh et al. reported on the synthesis of functionalized palladium phthalocyanines, achieving some derivatives by simply mixing phthalonitriles with a desired salt and heating to 140–160 °C.^[139] While the yields are promising, the authors suggest possible contaminations by impurities, likely due to the formation of phthalocyanine oligomers as suggested by evidence in the Q-band absorption region of the UV-Vis spectra and small discrepancies between theoretical and experimental elemental analysis values. Reducing the environmental impact of synthesizing

palladium derivatives is a pertinent topic, given their potential catalytic activity in palladium-mediated C–C couplings. This has recently been demonstrated to be feasible for Sonogashira coupling of triple bonds with aryl halides at room temperature without the need for phosphine ligands.^[140] Remaining within the topic of catalysis and transitioning to the equally broad and relevant subject of producing biofuels and carbon-based chemicals through CO₂ reduction, we highlight the solventless synthesis of tetra-nitro cobalt phthalocyanine in molten urea starting from 4-nitrophthalonitrile, cobalt chloride hexahydrate, and a catalytic amount of ammonium heptamolybdate tetrahydrate ((NH₄)₆Mo₇O₂₄·4H₂O), reported in 2019 by Wu et al.^[11] This compound, obtained in a 44 % yield, serves as a direct precursor to tetra-amino cobalt phthalocyanine, which is among the first transition-metal-based molecular electrocatalysts capable of performing the six-electron reduction of CO₂ to methanol with an appreciable activity and selectivity when immobilized on carbon nanotubes. In 2022, Langterreiter et al. investigated the solid-state synthesis of tetra-*tert*-butylphthalocyanines.^[141] They developed a synthetic procedure based on a combination of mechanochemical liquid-assisted grinding and aging at a certain temperature, optimizing it by systematically varying a series of variables. In particular, the use or not of the ball mill as the initial step, the quantity of DMAE and DBU and the temperature and aging time were systematically varied obtaining conversions of up to 99%. The procedure was then successfully applied to a series of metal ions to verify their tolerability. Regarding scalability, the reaction was tested up to 2 grams of reagent without substantial changes in conversion, a remarkable result in the context of the synthesis of phthalocyanines on a laboratory scale. Mechanochemical synthesis is so far generally underexplored in the literature regarding phthalocyanines. Recently, Fan et al. reported the synthesis of a series of phthalocyanine polymeric materials with hierarchical porosity by exploiting a mechanochemical approach (Figure 7).^[142] The possibility of working with reagents that are poorly soluble and have a high melting temperature by exploiting the mechanical

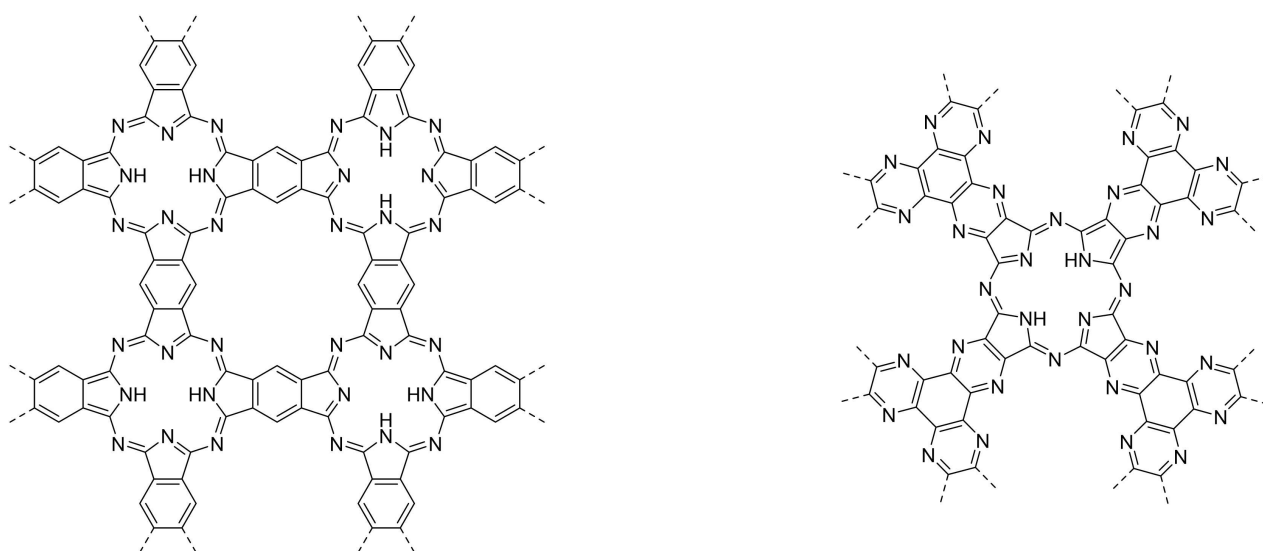


Figure 7. Two examples of polymeric phthalocyanines synthesized with ball-milling methods.

energy of the ball mill allows for easy access to classes of materials that would otherwise be difficult to obtain.

2.3. Alternative Experimental Conditions Aimed at Lowering the Reaction Temperature

Since the 1990s, literature has featured articles discussing the synthesis of phthalocyanines at low temperatures. The advantage of reducing the temperature for phthalocyanine ring formation lies in its capacity to minimize both the energy input required for the process and the formation of undesirable byproducts during synthesis. Achieving lower temperatures comes at the price of significantly longer reaction times, with the increase theoretically scaling proportionally with the desired temperature decrease. In 1996, Leznoff et al. reported the synthesis of several tetra-substituted zinc derivatives using lithium octan-1-olate in octan-1-ol at 20 °C or lithium-dimethylaminoethanolate in DMAE at 3, 20 and 50 °C.^[143]

Specifically, they tested their experimental procedures on phthalonitrile and several of its 3- and 4- derivatives like 4-neopentoxypthalonitrile, 4-nitrophthalonitrile, 3-neopentoxypthalonitrile, 3-*p*-butylbenzyloxypthalonitrile and 3-methoxypthalonitrile to obtain the derivatives **RT1**, **2**, **3** and **4** respectively. As expected, the reaction time was inversely proportional to the temperature. The highest yield achieved was 56% for PCH₂ synthesized at 50 °C for 24 hours. In contrast, condensation of 4-nitrophthalonitrile in Li-DMAE at a temperature as low as 3–5 °C resulted in obtaining 2(3),9(10),16(17),23(24)-tetranitrophthalocyanine with a 45% yield over a period of 3–5 weeks. This remarkable result is likely due to the activation of the CN group by the strongly electron accepting nitro group, along with the presence of THF in solution. Notably, the yields of other derivatives at that temperature did not exceed 10%. While 2(3),9(10),16(17),23(24)-tetrasubstituted phthalocyanines were synthesized as mixtures of regioisomers, only one isomer was obtained for the 1,8,15,22-tetra-substituted phthalocyanines. The authors suggest that the observed phenomenon may be attributed to a combination of steric and electronic effects. This is evidenced by the fact that the formation of a single isomer occurs even for phthalonitriles with less bulky functional groups, such as methoxy groups. Various metals in their elemental state have been investigated in different alcohols to determine the most effective combination for achieving room-temperature access to tetra-substituted phthalocyanines.^[144] Metal-free and metal 2(3),9(10),16(17),23(24)-tetrasubstituted phthalocyanines were prepared at room temperature from phthalonitrile, 4-neopentoxypthalonitrile (**RT1**), 4-bis(4-methoxyphenyl)methoxypthalonitrile (**RT5**), and 4-[1-(4-ethoxy-3-methoxyphenyl)-1-phenyl]-methoxypthalonitrile (**RT6**). The authors reported higher yields and quicker rates of Pc formation at room temperature when lithium metal and long-chain alcohols were used. They rationalize these results by postulating the formation of inverse micelles in which phthalonitriles may intercalate singularly, enhancing the formation of monomeric alkoxyisindole intermediates,^[145] or in groups of

four or more, favoring a template effect that would be responsible for higher reaction rates and yields. Interestingly, the resulting tetrasubstituted Pcs showed a non-statistical distribution of regioisomers, suggesting that electronic effects could play a crucial role in room-temperature phthalonitriles cyclotetramerization to form phthalocyanines. Uchida et al. investigated the metal-templated synthesis of unsubstituted phthalocyanines in DMF, employing hexamethyldisilazane (HMDS) as the base. They explored reaction temperatures ranging from 80 to 125 °C and tested various molar equivalents of HMDS.^[146] The procedure proved to be compatible with a variety of metal salts. Once the optimal reaction conditions were identified, they were applied to several 4-substituted phthalonitriles and to naphthalonitrile, yielding the related phthalocyanines and naphthalocyanine between 46 and 68%. Although the temperature is higher than what would be expected for a synthesis process defined as “low temperature”, the experimental conditions are milder than several others published in the literature. Yields in the range 20–58% were obtained for the synthesis of metal-free derivatives and 10–72% for metalated phthalocyanines when using phthalimides and phthalic anhydrides in similar reaction conditions.^[147,148] In the literature there are also examples of synthesis of phthalocyanine rings with Rieke metals, highly reactive metal powders generated by reduction of a metal salt with an alkali metal, in short alkyl chain alcohols at temperatures between 20 and 50 °C.^[82,149] In 2015, Zheng et al. published a paper in which the tetramerization of unsubstituted and 4-alkyl (**RT7**) and thioalkyl (**RT8**, **RT9**) substituted phthalonitriles was performed at room temperature by using lithium diisopropylamide (LDA) as nucleophile in THF solution.^[150] By carefully studying the relationships between yields to reactant molar ratio, reaction temperature, and time, several interesting observations have been made. The ideal molar ratio between phthalonitrile and LDA is 1:1, since increasing the quantity of the base does not provide significant improvements in the yield of the reaction. The best results have been obtained at 25 °C, with some phthalocyanine formation even at temperatures as low as –20 °C. Also, after 10 minutes the reaction at 25 °C in the optimized experimental conditions afforded the phthalocyanine with a yield of 37.1%, with no significant improvements if prolonging the reaction. The formation of diisopropylamine anions from LDA, which act as nucleophiles on the cyano group of the phthalonitrile, is suggested as the key step of the reaction mechanism, which is similar to that of alkoxy nucleophiles. The proposed mechanism of the reaction, involving nucleophilic attacks, cyclization, reduction and acidification steps, was further verified with DFT calculations, from which an activation energy as low as 13.16 kcal/mol was estimated. Typically, a reaction with an activation energy of less than approximately 20 kcal/mol is considered accessible at room temperature. Therefore, the formation of phthalocyanine at ambient or even lower temperatures is reasonable due to the low activation energy involved. Figure 8 displays the structures of the phthalocyanines whose synthesis is described in this paragraph.

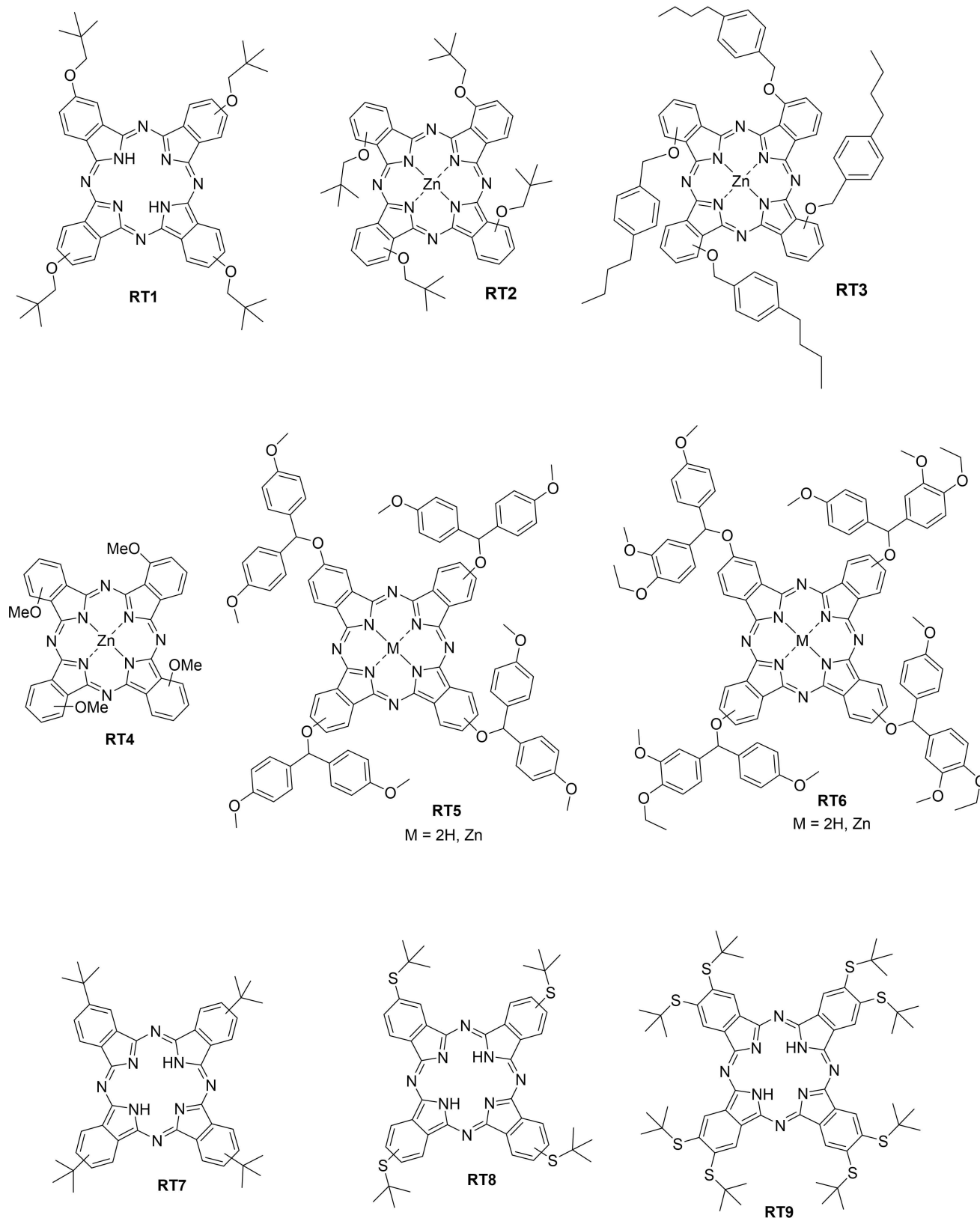


Figure 8. Phthalocyanines synthesized with solution-based room temperature methods.

3. E-factor Calculations

In this section, we will present the E-factor values of several syntheses discussed in this review. This calculation depends on what is defined as “waste” in a synthetic process, and water is probably the most discussed material in this sense. Given its abundance and non-toxicity, there is no uniformity of opinion on whether to consider it in the calculation or not. However, to evaluate the total quantity of waste produced by a synthesis, we will always include it, also giving the E-factor value without it. This will provide the upper limit value for the procedure considered, allowing to evaluate the relative impact of water on it and decide whether to include it in an optimization process aimed at reducing the overall waste produced during a synthesis. To carry out comparisons based on experimental parameters such as yield, reaction time and quantities of reagents involved, we report only the E-factor of the cyclization step of the macrocycle, even if the precursor is not commercial and must therefore be synthesized in turn. Focusing solely on experimental procedures with complete data would have resulted in a very limited table, as quantities required for workup and purification are often omitted. To expand the number of cases examined, we have thus opted to apply arbitrary quantities of chemicals to partially incomplete procedures, drawing upon our experience in the field. The approximations we have settled on are as follows: (i) We assume that 2x20 mL of water or water-solvent mixtures and 2x15 mL of organic solvents are required to wash crudes derived from 1.0 g of precursor.^[100] The quantities can be linearly scaled up. Since scaling down is more complex as linearity is not guaranteed, assumptions will be made on a case-by-case basis and highlighted in footnotes. (iii) We assume that the crystallization of 1 g of product requires 100 mL of solvent, and that the procedure is performed only once. As reported in the introduction, the E-factor represents the ratio between the mass of the total waste of a synthesis (considered as the mass of all materials used minus the mass of the product obtained) and the mass of the product obtained and is therefore a dimensionless number. The equation for the E-factor calculation is reported below

$$E^- \text{ factor} = \frac{\text{Mass of total waste (g)}}{\text{Mass of product (g)}}$$

The conversion of any chemical volume to mass is essential, derived from its density. For clarity, we report in full an example of E-factor calculation for the synthesis of copper phthalocyanine reported in^[100] (entry 8 in Table 1). In accordance with the experimental procedure described, the quantities of chemical products expressed in grams are the following: 1.000 g of phthalonitrile, 0.467 g of copper acetate monohydrate, 4.975 g of anisole (density 0.995 g/cm³), 0.131 g of KOH, 15.000 g of 1 N hydrochloric acid (density approximated to 1.000 g/cm³), 23.760 g of methanol (density 0.792 g/cm³), and 40.000 g of water. The quantity of product obtained was equal to 0.854 g. Therefore, the value of E-factor amounts to:

$$E^- \text{ factor} = \frac{[(1.000 + 0.467 + 4.975 + 0.131 + 15.000 + 23.760 + 40.000) - 0.854] \text{ g}}{0.854 \text{ g}} = 98.921 \sim 98.9$$

The methanol used for the Soxhlet extraction is not considered in the calculation, as the same batch can be reused many times.

The first observation upon examining the table is the magnitude of the numbers presented. In many cases, E-factors exceed 1000. These values, pertaining to single synthetic steps, are notably high when compared to other reference values on a laboratory scale. Syntheses considered environmentally sustainable typically score values up to a few hundreds, depending on the number of steps involved.^[151,152] According to data reported in the table, there is not a methodology that stands out among the others. Microwave-assisted syntheses on average show the best results. E-factors look quite consistent, with only a few exceptions above 300 including water. Instead, for syntheses based on ionic liquids and deep eutectic solvents, E-factors above 1000 are frequently achieved, which is surprisingly high considering that the reaction media are reusable. A comparison between the values with and without water, the latter lower even by an order of magnitude, reveals that the biggest issue lies in its use in the workup and purification steps. Although we have already pointed out that water may not present critical environmental issues, such significant discrepancies deserve to be highlighted. E-factor values for benign solvents suffer great fluctuations, ranging from 98.9 to 1124.0, mostly depending on reaction yields and isolation of some target products using chromatography. Generally speaking, workup and purification steps appear to be materials-demanding in phthalocyanine synthesis and it is likely that their optimization has not yet been addressed as much as the synthetic procedures. For instance, the two reported syntheses of (NO₂)₄-CoPc (entries 20 and 21 in Table 1) exhibit very different E-factors despite having the same yields. We highlight that working with small reaction batches, as in the case of entry 20, can significantly amplify the E-factor compared to larger reaction batches. However, as a general criterion, meticulously attending to details in purification processes can help in reducing waste production and improve the environmental (and economic) quality of a synthesis. Lastly, the reaction time is indeed a significant parameter that is worth highlighting in a dedicated column. While not considered in the calculation of the E-factor, the energy consumption of a synthesis conducted on a hot plate for several hours is inherently more impactful than one performed in a microwave reactor for just a few minutes. When comparing different synthetic procedures, this information should therefore be considered.

Table 1. E-factors of a selection of phthalocyanine syntheses.

Entry	Phthalocyanine	Quantity of reactant (g)	Methodology	Reaction time	Yield (%)	E factor [without water]	Ref
1	PcH ₂ ^[a]	0.128	IL/MW	5 min	80	TMGT 2870.9 [249,5] TBAB 2871.8 [250,4]	[108]
2	PcH ₂ ^[a]	0.128	IL/MW	3 min	88	TMGT 2612.3 [223.0] TBAB 2612.6 [223.2]	[108]
3	PcH ₂ ^[a]	0.128	IL/MW	5 min	70	TMGT 3287.3 [287.3] TBAB 3288.3 [288.3]	[108]
4	PcH ₂	0.128	DES	60 min	32	4796.9 [424.2]	[135]
5	CoPc	0.25	IL	5 min	63	1633.2 [225.5]	[128]
6	CoPc	0.256	DES	25 min	72	958.4 [83.5]	[135]
7	CoPc	1.0 g	benign solvent (Anisole, DBU)	3 h	72	105.3 [55.5]	[100]
8	CuPc	1.0 g	benign solvent (Anisole, KOH)	3 h	76	98.9 [52.1]	[100]
9	CuPc	1.0 g	benign solvent (Glycerol/anisole, DBU)	3 h	73	103.6 [54.9]	[100]
10	CuPc	0.25	IL	5 min	76	1358.1 [187.5]	[128]
11	CuPc	0.256	DES	15 min	83	824.6 [71.7]	[135]
12	ZnPc	1.0 g	benign solvent (Anisole, DBU)	3 h	56	133.2 [69.9]	[100]
13	ZnPc	0.25	IL	10 min	59	1799.2 [296.1]	[128]
14	ZnPc	0.25	IL	10 min	59	1799.2 [296.1]	[128]
15	FePc	0.25	IL	5 min	58	1803.9 [249.2]	[128]
16	FePc	0.256	DES	40 min	60	1157.0 [101.3]	[135]
17	PdPc	5.0	solid state	2 h	93	78.3 [42.6]	[139]
18	PtPc	1.0	MW	5 min	93	95.6 [64.4]	[71]
19	(NO ₂) ₄ -PcH ₂ ^[a]	0.173	IL	25 min	74	TMGT 2301.5 [200.2]	[108]
20	(NO ₂) ₄ -CoPc	0.25	IL	10 min	43	1213.4 [344.7]	[128]
21	(NO ₂) ₄ -CoPc ^[b]	1.73	solid state	5 h	44	585.2 [500.9]	[11]
22	(NO ₂) ₄ -ZnPc	0.25	IL	10 min	40	1293.4 [366.7]	[128]
23	(NO ₂) ₄ -PdPc	6.5	solid state	3 h	81	94.3 [51.3]	[139]
24	(NO ₂) ₄ -PtPc	1.0	MW	5 min	90	106.0 [71.4]	[71]
25	(<i>t</i> -bu) ₄ -CoPc	0.203	benign solvent (1,2-propane diol/anisole, DBU)	6 h	33	1124.0 [1008.0]	[34]
26	(<i>t</i> -bu) ₄ -CuPc	0.200	benign solvent (1,2-propane diol, DBU)	3 h	55	316.5 [233.1]	[34]
27	(<i>t</i> -bu) ₄ -ZnPc	0.200	benign solvent (1,2-propane diol, DBU)	3 h	51	696.7 [624.7]	[34]
28	MW1	1.0	MW	8 min	75	290.0 [160.1]	[75]
29	MW2	0.8	MW	8 min	80	276.3 [151.3]	[75]
30	MW3 ^[c]	0.31	MW	10 min	75	156.9 [116.0]	[44]
31	MW4	1.0	MW	8 min	85	245.8 [134.7]	[75]
32	MW5	0.7	MW	8 min	75	329.0 [179.7]	[75]
33	MW6	0.7	MW	8 min	75	434.0 [248.8]	[75]
34	MW7	0.8	MW	8 min	80	455.6 [288.9]	[75]
35	MW8 ^[d]	2.1	MW	7 min	83	61.0 [57.2]	[43]
36	MW11	34.58	MW	5 min	90	158.0 [69.3]	[77]

[a] 10 mL of water were estimated to be used to wash the phthalocyanine after precipitation from sulfuric acid/water. [b] The catalytic amount of (NH₄)₆Mo₇O₂₄·4H₂O required to perform the reaction was estimated to be 0.035 g (2% by weight). [c] The amount of water:methanol 1:3 mixture employed in the workup was estimated to be 20 mL for each step. [d] 10 mL of methanol were estimated to be used to precipitate the phthalocyanine during the workup.

4. Summary and Outlook

Green chemistry is a powerful tool to advance research in the synthesis of phthalocyanines towards improved economic and environmental sustainability. Given their widespread use in cutting-edge technologies such as clean energy production, rethinking their synthesis with sustainability in mind is of significant interest. Given the general requirements for their synthesis, such as high temperatures (>100 °C), alkaline reaction environment, absence of water, and the common use of problematic solvents, developing general protocols that are truly sustainable proves challenging. Therefore, we believe it is crucial to identify the strengths of each synthetic strategy that we have analyzed and synergistically combine them with one another. This body of work serves as a starting point for identifying new strategies that integrate various aspects discussed here, ultimately aiming to increase yields and purity of products while minimizing waste generation. Microwave radiation-assisted syntheses have been extensively explored and have demonstrated the highest tolerance towards substituents present on the precursor molecule. Undoubtedly, the possibility of working with minimal quantities of solvent entails a great advantage in terms of material consumption and simplicity of workup of the reaction crude. Scaling up optimized synthetic protocols could present challenges due to the need for considerably larger reactors capable of providing adequate homogeneity of irradiation. However, the results achieved on a laboratory scale are already notable. To reduce the E-factor values, which are less sensitive to the quantities of reaction materials compared to other procedures due to the modest or absent presence of solvents, the focus should be on improving the workup and purification processes where possible. As regards benign reaction media, we believe it is interesting to extend the study of low-impact solvents such as glycerol, propylene glycol and anisole also to other substrates, taking into consideration the favorable and unfavorable interactions with the metal ions used and the possible collateral reactions with functional-reactive groups present on the precursors. For example, nitro- and fluoride/chloride precursors may not efficiently react in OH-containing solvents, as the alkaline environment may favor concomitant aromatic nucleophilic substitution. Redesigning the synthesis of functionalized derivatives by leveraging micellar processes in aqueous or other environmentally benign media could open a field of investigation that is currently underexplored. The enormous number of studies on the topic to date allows to outline a plausible action plan, for example envisaging the synthesis of designer surfactants optimized for the synthesis of the phthalocyanine macrocycle. This would open up an entirely unexplored research field concerning the synthesis of phthalocyanines. Furthermore, their general poor solubility in water makes the reaction medium potentially recoverable and recyclable. In addition, it would be worth increasing the solvent portfolio to include significant materials such as poly-ethylene glycols (PEGs) and other benign reaction media. With the aim of synergistically combining two synthetic strategies, and based on what is reported in the literature, it could be extremely

interesting to exploit UV irradiation in the first phases of reactions carried out in non-toxic hydroxy-based solvents to increase the number of reactive species capable of nucleophilically attacking the reactants and increasing the quantity of products obtained. The solvothermal approach is extremely useful for the synthesis of three-dimensional architectures with specific properties and large crystals. This latter option would pave the way both to the detailed study of the structural properties of a specific phthalocyanine and to the obtaining of highly ordered materials for technological applications. While interest in the use of ionic liquids for the synthesis of phthalocyanines appears to be on a downward trend, as deduced from the years of publication of the articles we have reviewed, deep eutectic solvents deserve more attention. Their sustainability and recyclability combined with their chemical characteristics make them excellent candidates as low-impact and very effective reaction media. Calculating the E-factor of a selection of phthalocyanine ring syntheses and establishing a database, however limited, of comparable data is a fundamental first step towards applying green chemistry metrics to these processes. While not exhaustive, it provides valuable insights into where strategies should be developed to minimize waste production during synthesis. The high values of the E-factors, along with the significant variability of values obtained for overall similar procedures, underscore the importance of evaluating this metric to swiftly assess whether a process demands improvements, and at which step. In this particular case, we believe that a significant effort should be directed towards minimizing the environmental impact of the purification processes. We are confident that such analysis, combined with the consideration of other parameters such as energy inputs, costs, and intrinsic toxicity of materials used, will contribute to making the synthesis of phthalocyanines significantly less impactful than it currently is.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Porphyrinoids · Synthetic methods · E-factor · Sustainable chemistry · Waste prevention

- [1] P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 1998.
- [2] D. Mukherjee, R. Manjunatha, S. Sampath, A. K. Ray, in *Materials for Chemical Sensing*, Springer International Publishing, Cham, Switzerland, 2016, pp. 165–226.
- [3] D. Gounden, N. Nombona, W. E. van Zyl, *Coord. Chem. Rev.* **2020**, *420*, 213359.
- [4] W. Zhou, N. J. Yutronkie, B. H. Lessard, J. L. Brusso, *Mater. Adv.* **2021**, *2*, 165–185.
- [5] O. A. Melville, B. H. Lessard, T. P. Bender, *ACS Appl. Mater. Interfaces* **2015**, *7*, 13105–13118.
- [6] N. T. Boileau, R. Cranston, B. Mirka, O. A. Melville, B. H. Lessard, *RSC Adv.* **2019**, *9*, 21478–21485.
- [7] T. M. Grant, N. A. Rice, L. Muccioli, F. Castet, B. H. Lessard, *ACS ACS Appl. Electron. Mater.* **2019**, *1*, 494–504.
- [8] P. C. Lo, M. S. Rodríguez-Morgade, R. K. Pandey, D. K. P. Ng, T. Torres, F. Dumoulin, *Chem. Soc. Rev.* **2020**, *49*, 1041–1056.
- [9] X. Li, B. De Zheng, X. H. Peng, S. Z. Li, J. W. Ying, Y. Zhao, J. D. Huang, J. Yoon, *Coord. Chem. Rev.* **2019**, *379*, 147–160.
- [10] A. Galstyan, *Chem. - Eur. J.* **2021**, *27*, 1903–1920.
- [11] Y. Wu, Z. Jiang, X. Lu, Y. Liang, H. Wang, *Nature* **2019**, *575*, 639–642.
- [12] M. Wang, K. Torbensen, D. Salvatore, S. Ren, D. Joulié, F. Dumoulin, D. Mendoza, B. Lassalle-Kaiser, U. İşci, C. P. Berlinguette, M. Robert, *Nat. Commun.* **2019**, *10*, 3602.
- [13] Y. Liu, C. C. L. McCrory, *Nat. Commun.* **2019**, *10*, 1683.
- [14] G. Zanotti, N. Angelini, A. M. Paoletti, G. Pennesi, G. Rossi, A. A. Bonapasta, G. Mattioli, A. Di Carlo, T. M. Brown, A. Lembo, A. Reale, *Dalton Trans.* **2011**, *40*, 38–40.
- [15] M. Ragoussi, M. Ince, *Eur. J. Org. Chem.* **2013**, *2013*(29), 6475–6489.
- [16] M. Urbani, M. E. Ragoussi, M. K. Nazeeruddin, T. Torres, *Coord. Chem. Rev.* **2019**, *381*, 1–64.
- [17] D. Molina, A. Guerrero, G. Garcia-Belmonte, F. Fernández-Lázaro, Á. Sastre-Santos, *Eur. J. Org. Chem.* **2014**, *2014*, 4585–4591.
- [18] J. Meiss, A. Merten, M. Hein, C. Schuenemann, S. Schäfer, M. Tietze, C. Uhrich, M. Pfeiffer, K. Leo, M. Riede, *Adv. Funct. Mater.* **2012**, *22*, 405–414.
- [19] G. de la Torre, G. Bottari, T. Torres, *Adv. Energy Mater.* **2017**, *7*, 1601700.
- [20] D. Molina, J. Follana-Berná, Á. Sastre-Santos, *J. Mater. Chem. C* **2023**, *11*, 7885–7919.
- [21] Y. C. Kim, T. Y. Yang, N. J. Jeon, J. Im, S. Jang, T. J. Shin, H. W. Shin, S. Kim, E. Lee, S. Kim, J. H. Noh, S. I. Seok, J. Seo, *Energy Environ. Sci.* **2017**, *10*, 2109–2116.
- [22] M. Urbani, G. De La Torre, M. K. Nazeeruddin, T. Torres, *Chem. Soc. Rev.* **2019**, *48*, 2738–2766.
- [23] K. T. Cho, O. Trukhina, C. Roldán-Carmona, M. Ince, P. Gratia, G. Grancini, P. Gao, T. Marszalek, W. Pisula, P. Y. Reddy, T. Torres, M. K. Nazeeruddin, *Adv. Energy Mater.* **2017**, *7*, 1601733.
- [24] Y. Feng, Q. Hu, E. Rezaee, M. Li, Z. X. Xu, A. Lorenzoni, F. Mercuri, M. Muccini, *Adv. Energy Mater.* **2019**, *9*, 1901019.
- [25] X. Sun, L. Wang, Z. Tan, *Catal Letters* **2015**, *145*, 1094–1102.
- [26] X. Bai, Y. Xin, T. Jia, L. Guo, W. Song, D. Hao, *New J. Chem.* **2024**, *48*, 7213–7224.
- [27] K. R. V. Reddy, M. N. K. Harish, Fassiulla, M. H. Moinuddin Khan, J. Keshavayya, *J. Fluor. Chem.* **2007**, *128*, 1019–1025.
- [28] J. Metz, O. Schneider, M. Hanack, *Inorg. Chem* **1984**, *23*, 1065–1071.
- [29] N. Kobayashi, F. Furuya, G. C. Yug, H. Wakita, M. Yokomizo, N. Ishikawa, *Chem. - Eur. J.* **2002**, *8*, 1474–1484.
- [30] E. W. Y. Wong, A. Miura, M. D. Wright, Q. He, C. J. Walsby, S. Shimizu, N. Kobayashi, D. B. Leznoff, *Chem. - Eur. J.* **2012**, *18*, 12404–12410.
- [31] B. I. Kharisov, U. Ortiz Méndez, J. L. Almaraz Garza, J. R. Almaguer Rodríguez, *New J. Chem.* **2005**, *29*, 686–692.
- [32] L. Jean-Gérard, N. Kardos, M. Draye, B. Andrioletti, in *Handbook of Porphyrin Science* (Eds: K. M. Kadish, K. M. Smith, R. Guilard), World Scientific Publishing Co. Pte. Ltd., Singapore, 2016, pp. 1–87.
- [33] G. Zanotti, L. Mancini, A. M. Paoletti, G. Pennesi, V. Raglione, *J. Porphyrins Phthalocyanines* **2023**, *27*, 398–401.
- [34] S. K. Podapangi, L. Mancini, J. Xu, S. H. Reddy, A. Di Carlo, T. M. Brown, G. Zanotti, *Energies* **2023**, *16*, 3643.
- [35] M. J. F. Calvete, L. D. Dias, C. A. Henriques, S. M. A. Pinto, R. M. B. Carrilho, M. M. Pereira, *Molecules* **2017**, *22*, 741.
- [36] C. Gomes, M. Peixoto, M. Pineiro, *J. Porphyrins Phthalocyanines* **2019**, *23*, 889–897.
- [37] C. A. Henriques, S. M. A. Pinto, G. L. B. Aquino, M. Pineiro, M. J. F. Calvete, M. M. Pereira, *ChemSusChem* **2014**, *7*, 2821–2824.
- [38] S. M. A. Pinto, C. A. Henriques, V. A. Tomé, C. S. Vinagreiro, M. J. F. Calvete, J. M. Dąbrowski, M. Piñeiro, L. G. Arnaut, M. M. Pereira, *J. Porphyrins Phthalocyanines* **2016**, *20*, 45–60.
- [39] A. de la Hoza, Á. Díaz-Ortiz, A. Moreno, *Chem. Soc. Rev.* **2005**, *34*, 164–178.
- [40] J. Jacob, L. H. L. Chia, F. Y. C. Boey, *J. Mater. Sci.* **1995**, *30*, 5321–5327.
- [41] D. Villemin, M. Hammadi, M. Hachemi, N. Bar, *Molecules* **2001**, *6*, 831–844.
- [42] R. K. Sharma, S. Gulati, S. Sachdeva, *Green Chem. Lett. Rev* **2012**, *5*, 83–87.
- [43] E. O. Moiseeva, A. D. Kosov, N. E. Borisova, B. N. Tarasevich, T. V. Dubinina, L. G. Tomilova, *Inorg. Chim. Acta* **2022**, *535*, 120855.
- [44] R. K. Sharma, S. Gulati, A. Pandey, *Inorg. Chim. Acta* **2013**, *397*, 21–31.
- [45] Ö. Koyun, S. Gördük, B. I. Keskin, A. Çetinkaya, A. I. Koca, U. Avcıata, *Polyhedron* **2016**, *113*, 35–49.
- [46] Z. Biyiklioğlu, H. Kantekin, *Dyes and Pigments* **2009**, *80*, 17–21.
- [47] W. Qian, W. Wei, M. Hong, C. Jianfeng, C. Guangwen, Z. Haikui, *Colloids Surf., A* **2014**, *443*, 52–59.
- [48] M. B. Kılıçaslan, F. Aşın, H. Kantekin, *J. Coord. Chem.* **2010**, *63*, 861–867.
- [49] D. K. Modibane, T. Nyokong, *Polyhedron* **2009**, *28*, 1475–1480.
- [50] I. Acar, H. Kantekin, Z. Biyiklioğlu, *J. Organomet. Chem.* **2010**, *695*, 151–155.
- [51] Z. Biyiklioğlu, H. Kantekin, M. Özil, *J. Organomet. Chem.* **2007**, *692*, 2436–2440.
- [52] H. Kantekin, Z. Biyiklioğlu, E. Çelenk, *Inorg. Chem. Commun.* **2008**, *11*, 633–635.
- [53] Z. Biyiklioğlu, I. Acar, H. Kantekin, *Inorg. Chem. Commun.* **2008**, *11*, 630–632.
- [54] Z. Biyiklioğlu, H. Kantekin, *J. Organomet. Chem.* **2008**, *693*, 505–509.
- [55] E. Çelenk, H. Kantekin, *Dyes and Pigments* **2009**, *80*, 93–97.
- [56] H. Kantekin, G. Dilber, A. Nas, *J. Organomet. Chem.* **2010**, *695*, 1210–1214.
- [57] A. Nas, E. Ç. Kaya, H. Kantekin, A. Sökmen, V. Çakır, *J. Organomet. Chem.* **2011**, *696*, 1659–1663.
- [58] E. G. Duruk, H. Y. Yenilmez, A. Altındal, Z. Altuntaş Bayır, *Dalton Trans.* **2015**, *44*, 10060–10068.
- [59] M. Özil, M. Canpolat, *Polyhedron* **2013**, *51*, 82–89.
- [60] T. E. Youssef, *Polyhedron* **2010**, *29*, 1776–1783.
- [61] K. Serbest, I. Değirmencioğlu, Y. Ünver, M. Er, C. Kantar, K. Sancak, *J. Organomet. Chem.* **2007**, *692*, 5646–5654.
- [62] G. K. Kantar, N. Baltaş, E. Menteşe, S. Şaşmaz, *J. Organomet. Chem.* **2015**, *787*, 8–13.
- [63] I. Acar, E. T. Saka, S. Topçu, Z. Biyiklioğlu, H. Kantekin, A. Aktaş, *J. Coord. Chem.* **2015**, *68*, 1847–1858.
- [64] A. C. S. Gonzalez, L. Damas, R. T. Aroso, V. A. Tomé, L. D. Dias, J. Pina, R. M. B. Carrilho, M. M. Pereira, *J. Porphyrins Phthalocyanines* **2020**, *24*, 947–958.
- [65] Z. Biyiklioğlu, H. Kantekin, I. Acar, *Inorg. Chem. Commun.* **2008**, *11*, 1448–1451.
- [66] Z. Biyiklioğlu, H. Kantekin, *Transition Met. Chem.* **2007**, *32*, 851–856.
- [67] C. Kantar, F. Mert, S. Şaşmaz, *J. Organomet. Chem.* **2011**, *696*, 3006–3010.
- [68] D. A. Davies, C. Schnick, J. Silver, J. L. Sosa-Sanchez, P. G. Riby, *J. Porphyrins Phthalocyanines* **2001**, *5*, 376–380.
- [69] E. A. Kuzmina, T. V. Dubinina, N. E. Borisova, L. G. Tomilova, *Macrocyclic Heterocycles* **2017**, *10*, 520–525.
- [70] B. Narayana Achar, T. Manjappa, M. Kumar, K. S. Lokesh, *J. Porphyrins Phthalocyanines* **2005**, *9*, 872–879.
- [71] K. S. Lokesh, N. Uma, B. N. Achar, *Polyhedron* **2009**, *28*, 1022–1028.
- [72] H. Kantekin, G. Dilber, Z. Biyiklioğlu, *J. Organomet. Chem.* **2008**, *693*, 1038–1042.
- [73] Z. Biyiklioğlu, H. Kantekin, *Polyhedron* **2008**, *27*, 1650–1654.
- [74] E. Ç. Kaya, H. Karadeniz, H. Kantekin, *Dyes Pigm.* **2010**, *85*, 177–182.
- [75] C. Kantar, N. Akdemir, E. Açar, N. Ocak, S. Şaşmaz, *Dyes Pigm* **2008**, *76*, 7–12.
- [76] S. Makhseed, M. Al-Sawah, J. Samuel, H. Manaa, *Tetrahedron Lett.* **2009**, *50*, 165–168.
- [77] A. Kumar, P. K. Prajapati, M. S. Aathira, A. Bansiwali, R. Boukherroub, S. L. Jain, *J. Colloid Interface Sci.* **2019**, *543*, 201–213.

- [78] K. Suck Jung, J. H. Kwon, S. M. Shon, J. K. Phil, J. Sik Shin, S. Soo Park, *J. Mater. Sci.* **2004**, *39*, 723–726.
- [79] S. M. S. Chauhan, K. A. Srinivas, P. K. Srivastava, B. Sahoo, *J. Porphyrins Phthalocyanines* **2003**, *7*, 548–550.
- [80] N. Safari, P. R. Jamaat, M. Pirouzmand, A. Shaabani, *J. Porphyrins Phthalocyanines* **2004**, *8*, 1209–1213.
- [81] H. Tomoda, E. Hibiya, T. Nakamura, H. Ito, S. Saito, *Chem. Lett.* **1976**, 1003–1006.
- [82] B. I. Kharisov, U. Ortiz Mendez, J. Rivera De La Rosa, *Russ. J. Coord. Chem.* **2006**, *32*, 617–631.
- [83] Y. Saito, T. Higuchi, H. Sugimori, H. Yabu, *ChemNanoMat* **2015**, *1*, 92–95.
- [84] Y. Hirai, B. Sawano, T. Takaki, Y. Matsuo, H. Yabu, *Chem. Lett.* **2017**, *46*, 695–698.
- [85] S. Ge, Y. Zhang, B. Huang, S. Huang, W. Tie, Y. Lei, Q. He, G. Tu, Q. Qin, S. Niu, M. Li, D. Li, Z. Zheng, *Mater. Lett.* **2016**, *163*, 61–64.
- [86] P. Lignier, J. Estager, N. Kardos, L. Gravouil, J. Gazza, E. Naffrechoux, M. Draye, *Ultrason. Sonochem.* **2011**, *18*, 28–31.
- [87] C. Vaitis, G. Sourkouni, C. Argiris, *Ultrason. Sonochem.* **2019**, *52*, 106–119.
- [88] N. A. Khan, S. H. Jung, *Coord. Chem. Rev.* **2015**, *285*, 11–23.
- [89] J. Rivera-De La Rosa, B. I. Kharisov, A. M. Medina, U. Ortiz-Méndez, A. K. Ibarra-Arvizu, *Mater. Manuf. Processes* **2007**, *22*, 314–317.
- [90] B. I. Kharisov, A. M. Medina, J. Rivera De La Rosa, U. Ortiz Méndez, *J. Chem. Res.* **2005**, *2005*, 404–406.
- [91] J. Z. Sostaric, R. P. Pandian, L. K. Weavers, P. Kuppasamy, *Chem. Mater.* **2006**, *18*, 4183–4189.
- [92] S. P. Tu, D. Kim, T. F. Yen, *J. Environ. Eng. Sci.* **2002**, *1*, 237–246.
- [93] C. E. Banks, A. H. Wylie, R. G. Compton, *Ultrason. Sonochem.* **2004**, *11*, 327–331.
- [94] C. J. Clarke, W. C. Tu, O. Levers, A. Bröhl, J. P. Hallett, *Chem. Rev.* **2018**, *118*, 747–800.
- [95] F. P. Byrne, S. Jin, G. Paggiola, T. H. M. Petchey, J. H. Clark, T. J. Farmer, A. J. Hunt, C. Robert McElroy, J. Sherwood, *Sustainable Chem. Processes* **2016**, *4*, 1–24.
- [96] C. M. Alder, J. D. Hayler, R. K. Henderson, A. M. Redman, L. Shukla, L. E. Shuster, H. F. Sneddon, *Green Chem.* **2016**, *18*, 3879–3890.
- [97] P. K. Verma, U. Sharma, M. Bala, N. Kumar, B. Singh, *RSC Adv.* **2013**, *3*, 895–899.
- [98] T. Tu, Z. Wang, Z. Liu, X. Feng, Q. Wang, *Green Chem.* **2012**, *14*, 921–924.
- [99] B. H. Lipshutz, S. Ghorai, M. Cortes-Clerget, *Chem. - Eur. J.* **2018**, *24*, 6672–6695.
- [100] G. Zanotti, P. Imperatori, A. M. Paoletti, G. Pennesi, *Molecules* **2021**, *26*, 1760.
- [101] D. Prat, A. Wells, J. Hayler, H. Sneddon, C. R. McElroy, S. Abou-Shehadeh, P. J. Dunn, *Green Chem.* **2015**, *18*, 288–296.
- [102] S. Gillet, M. Aguedo, L. Petitjean, A. R. C. Morais, A. M. Da Costa Lopes, R. M. Łukasik, P. T. Anastas, *Green Chem.* **2017**, *19*, 4200–4233.
- [103] C. M. Bernat, G. Bottari, J. A. Barrett, S. L. Scott, K. Barta, P. C. Ford, *Catal. Sci. Technol.* **2016**, *6*, 2984–2994.
- [104] K. Leiva, R. Garcia, C. Sepulveda, D. Laurenti, C. Geantet, M. Vrinat, J. L. Garcia-Fierro, N. Escalona, *Catal. Today* **2017**, *296*, 228–238.
- [105] M. J. Rodríguez-Álvarez, J. García-Álvarez, M. Uzelac, M. Fairley, C. T. O'Hara, E. Hevia, *Chem. - Eur. J.* **2018**, *24*, 1720–1725.
- [106] Y. Gu, F. Jérôme, *Green Chem.* **2010**, *12*, 1127–1138.
- [107] A. Wolfson, C. Dlugy, Y. Shotland, *Environ. Chem. Lett.* **2007**, *5*, 67–71.
- [108] A. Shaabani, A. Maleki, *J. Porphyrins Phthalocyanines* **2006**, *10*, 1253–1258.
- [109] A. Hasaninejad, M. Beyrati, *RSC Adv.* **2018**, *8*, 1934–1939.
- [110] M. M. Hoffmann, *Curr. Opin. Colloid Interface Sci.* **2022**, *57*, 101537.
- [111] D. Xia, S. Yu, R. Shen, C. Ma, C. Cheng, D. Ji, Z. Fan, X. Wang, G. Du, *Dyes Pigment.* **2008**, *78*, 84–88.
- [112] D. Li, S. Ge, G. Sun, Q. He, B. Huang, G. Tian, W. Lu, G. Li, Y. Chen, S. An, Z. Zheng, *Dyes Pigment.* **2015**, *113*, 200–204.
- [113] D. Li, S. Ge, T. Yuan, J. Gong, B. Huang, W. Tie, W. He, *CrystEngComm* **2018**, *20*, 2749–2758.
- [114] Z. Guo, B. Chen, M. Zhang, J. Mu, C. Shao, Y. Liu, *J. Colloid Interface Sci.* **2010**, *348*, 37–42.
- [115] D. Li, P. Zhang, S. Ge, G. Sun, Q. He, W. Fa, Y. Li, J. Ma, *RSC Adv.* **2021**, *11*, 31226–31234.
- [116] X. Wang, X. Wang, J. Gao, B. Xu, *Micro Nano Lett.* **2016**, *11*, 348–350.
- [117] T. Liu, F. Zhang, L. Ruan, J. Tong, G. Qin, X. Zhang, *Mater. Lett.* **2019**, *237*, 319–322.
- [118] M. Zhang, C. Shao, Z. Guo, Z. Zhang, J. Mu, P. Zhang, T. Cao, Y. Liu, *ACS Appl. Mater. Interfaces* **2011**, *3*, 2573–2578.
- [119] J. Mu, C. Shao, Z. Guo, M. Zhang, Z. Zhang, P. Zhang, B. Chen, Y. Liu, *Nanoscale* **2011**, *3*, 5126–5131.
- [120] J. Mukherjee, S. Paul, A. Adalder, S. Kapse, R. Thapa, S. Mandal, B. Ghorai, S. Sarkar, U. K. Ghorai, *Adv. Funct. Mater.* **2022**, *32*, 2200882.
- [121] J. Mukherjee, A. Adalder, N. Mukherjee, U. K. Ghorai, *Catal. Today* **2023**, *423*, 113905.
- [122] D. W. Kim, C. E. Song, D. Y. Chi, *J. Org. Chem.* **2003**, *68*, 4281–4285.
- [123] Z. Liu, Z. C. Chen, Q. G. Zheng, *Synthesis* **2004**, 33–36.
- [124] J. Alzeer, P. J. C. Roth, N. W. Luedtke, *Chem. Commun.* **2009**, 1970–1971.
- [125] P. C. Lo, D. Y. Y. Cheng, D. K. P. Ng, *Synthesis* **2005**, 1141–1147.
- [126] N. Safari, P. R. Jamaat, S. A. Shirvan, S. Shoghpour, A. Ebadi, M. Darvishi, A. Shaabani, *J. Porphyrins Phthalocyanines* **2005**, *9*, 256–261.
- [127] D. S. Jacob, S. Mallenahalli, A. Gedanken, L. A. Solovoyov, E. Xenogian-nopoulou, K. Iliopoulos, S. Couris, *J. Porphyrins Phthalocyanines* **2007**, *11*, 713–718.
- [128] S. M. S. Chauhan, P. Kumari, S. Agarwal, *Synthesis* **2007**, 3713–3721.
- [129] E. L. Smith, A. P. Abbott, K. S. Ryder, *Chem. Rev.* **2014**, *114*, 11060–11082.
- [130] A. Paiva, R. Craveiro, I. Aroso, M. Martins, R. L. Reis, A. R. C. Duarte, *ACS Sustainable Chem. Eng* **2014**, *2*, 1063–1071.
- [131] T. Zhang, T. Doert, H. Wang, S. Zhang, M. Ruck, *Angew. Chem. int ed* **2021**, *60*, 22148–22165.
- [132] D. Arnodo, C. Meazzo, S. Baldino, M. Blangetti, C. Prandi, *Chem. - Eur. J.* **2023**, *29*, e202300820.
- [133] S. Perrone, F. Messa, L. Troisi, A. Salomone, *Molecules* **2023**, *28*, 3459.
- [134] R. A. Sheldon, *Chem. - Eur. J.* **2016**, *22*, 12984–12999.
- [135] A. Shaabani, S. E. Hooshmand, R. Afshari, S. Shaabani, V. Ghasemi, M. Atharnezhad, M. Akbari, *J. Solid State Chem.* **2018**, *258*, 536–542.
- [136] A. Joglekar-Athavale, G. S. Shankarling, *Pigm. Resin Technol.* **2020**, *49*, 325–330.
- [137] L. Zhu, X. Jing, L. Song, B. Liu, Y. Zhou, Y. Xiang, D. Xia, *New J. Chem.* **2014**, *38*, 663–668.
- [138] M. Mayukh, C. M. Sema, J. M. Roberts, D. V. McGrath, *J. Org. Chem.* **2010**, *75*, 7893–7896.
- [139] K. S. Lokesh, A. Adriaens, *Dyes Pigment.* **2013**, *96*, 269–277.
- [140] Y. B. Platonova, A. N. Volov, L. G. Tomilova, *J. Catal.* **2020**, *391*, 224–228.
- [141] D. Langerreiter, M. A. Kostianinen, S. Kaabel, E. Anaya-Plaza, *Angew. Chem. Int. Ed.* **2022**, *61*, e202209033.
- [142] J. Fan, T. Wang, B. P. Thapaliya, L. Qiu, M. Li, Z. Wang, T. Kobayashi, I. Popovs, Z. Yang, S. Dai, *Angew. Chem. Int. Ed.* **2022**, *61*, e202207607.
- [143] C. C. Leznoff, M. Hu, K. J. M. Nolan, *Chem. Commun.* **1996**, 1245–1246.
- [144] C. C. Leznoff, A. M. D'Ascanio, S. Z. Yildiz, *J. Porphyrins Phthalocyanines* **2000**, *4*, 103–111.
- [145] S. W. Oliver, T. D. Smith, *J. Chem. Soc. Perkin Trans. II* **1987**, *11*, 1579–1582.
- [146] H. Uchida, H. Tanaka, H. Yoshizawa, Y. Reddy, S. Nakamura, T. Toru, *Synlett* **2002**, 1649–1652.
- [147] H. Uchida, P. Y. Reddy, S. Nakamura, T. Toru, *J. Org. Chem.* **2003**, *68*, 8736–8738.
- [148] H. Uchida, H. Yoshizawa, P. Y. Reddy, S. Nakamura, T. Toru, *Synlett* **2003**, 2083–2085.
- [149] B. I. Kharisov, L. A. Garza-Rodríguez, H. M. Leija Gutiérrez, U. Ortiz Méndez, R. García Caballero, A. Y. Tsvadze, *Synth. React. Inorg., Met.-Org., Nano-Met. Chem.* **2005**, *35*, 755–760.
- [150] W. Zheng, C. Z. Wan, J. X. Zhang, C. H. Li, X. Z. You, *Tetrahedron Lett.* **2015**, *56*, 4459–4462.
- [151] S. Mattiello, A. Sanzone, F. Bruni, M. Gandini, V. Pinchetti, A. Monguzzi, I. Facchinetti, R. Ruffo, F. Meinardi, G. Mattioli, M. Sassi, S. Brovelli, L. Beverina, *Joule* **2020**, *4*, 1988–2003.
- [152] S. Mattiello, G. Lucarelli, A. Calascibetta, L. Polastri, E. Ghiglietti, S. K. Podapangi, T. M. Brown, M. Sassi, L. Beverina, *ACS Sustainable Chem. Eng* **2022**, *10*, 4750–4757.

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