Mechanochemical *in situ* generated gas reactant for the solvent-free hydrogenation of porphyrins

Marta Pineiro, Carla Gomes & Mariana Peixoto

Published online: 04 May 2021.

Submit your article to this journal ⬩

Article views: 1027

View related articles ⬩

View Crossmark data ⬩

Taylor & Francis
Taylor & Francis Group

LETTER

🔓 OPEN ACCESS ✓ Check for updates

Mechanochemical *in situ* generated gas reactant for the solvent-free hydrogenation of porphyrins

Marta Pineiro 🔟, Carla Gomes and Mariana Peixoto

University of Coimbra, Department of Chemistry and CQC, Coimbra, Portugal

ABSTRACT
The synthesis of chlorins was performed by hydrogenation of porphyrins using diimide generated and consumed under mechanical activation. The reaction conditions achievable under ball milling, absence of solvent and use of hydrazine hydrate as diimide source, allowed the hydrogenation of porphyrins with high conversion, high selectivity, and nearly ideal sustainability scores (atom economy of 97% and E-factor of 0.96).
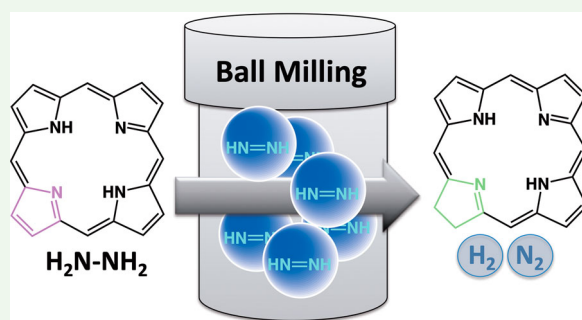
Introduction

Mechanochemistry has emerged as a tool for organic synthesis (*1–7*) that allows reactions in neat conditions using solid reactants or through liquid assisted mechanochemistry (*8*). The use of neat conditions led to an improvement of the sustainability, avoiding the reaction solvent, the major source of waste in the chemical industry, and led to new reaction outcomes, that make this technique an important tool for the development of new sustainable reactions (*9–14*). More scarce and recent are the examples of mechanochemistry involving gas reactants (*15–17*). The *in situ* generation and consumption of gaseous reagents by ball milling techniques, on one hand, reduce direct handling of, and exposure to toxic or highly reactive substances and on the other hand increase stoichiometric control reducing the accumulation of large amounts of solvent waste contaminated with unreacted toxic reagents, is only in the beginning. There are only a few examples of hydrogenation of organic compounds under mechanical conditions using gas reactants (*18*), generation of hydrogen

from dimethylamine borane for hydrogenation of olefins catalysed by Wilkinson's catalyst (*19*), the use of polymethylhydrosiloxane as a hydrogen source for the reduction of carbonyl groups (*20*) and the used of heterogenous Ru catalyst, water and hydrogen for the hydrolytic hydrogenation of cellulose to sorbitol (*21*).

Chlorins are the tetrapyrrolic macrocycle core of chlorophylls, one of the most abundant pigments of life. The function of chlorins in nature is undoubtedly related to their unique photophysical properties, which are also the basis for many of their applications (*22–26*).

The synthesis of *meso*-substituted chlorins recently reviewed by Taniguchi and Lindsey (*27*), can be achieved using diverse strategies through controlled porphyrinogen oxidation (*28*), exploring the reactivity of pyrrole as a synthetic unit in cyclization reactions (*29*) or via hydrogenation of *meso*-substituted porphyrins (Scheme 1).

These hydrogenation reactions, which mostly use diimide as reducing agent and *p*-toluenesulfonylhydrazine as diimide source- based on the original method described by Whitlock (*30*) – suffer from several
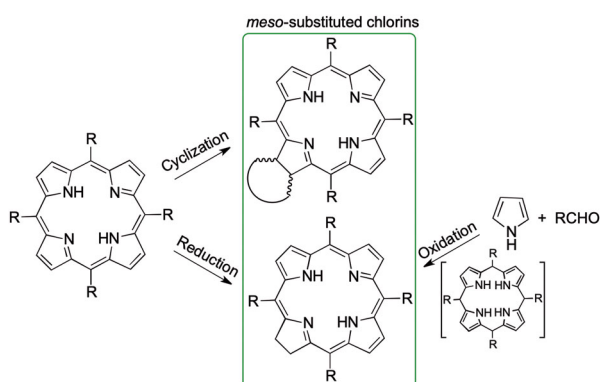
Scheme 1. Synthetic routes to *meso*-substituted chlorins.

drawbacks: large excess of diimide source, large amounts of solvents and base, long reaction times or high temperature, reaction waste with large amounts of *p*-toluenesulfinic acid and the selectivity to chlorin is not easy to control. The most critical aspect is the control of the reaction conditions to obtain chlorin selectively, avoiding the synthesis of the related bacteriochlorin (tetrahydroporphyrin) through double hydrogenation at opposite pyrrole rings. Nevertheless, the selectivity can be improved by re-oxidation using MnO$_2$ or hydrogen peroxide and iron trichloride as oxidant (*31*, *32*).

Herein, we describe the synthesis of chlorins through the hydrogenation of the porphyrin macrocycle under mechanochemical action in solvent-free conditions using hydrazine hydrate for the *in situ* generation and consumption of diimide (gas, melting point −80°C), which acts as a reducing agent.

Results and discussion

Looking for alternatives for the reduction of *meso*-tetraarylporphyrins with increased sustainability, we looked into the mechanochemical reduction of porphyrins with hydrazines to selectively synthesized chlorins (Scheme 2).
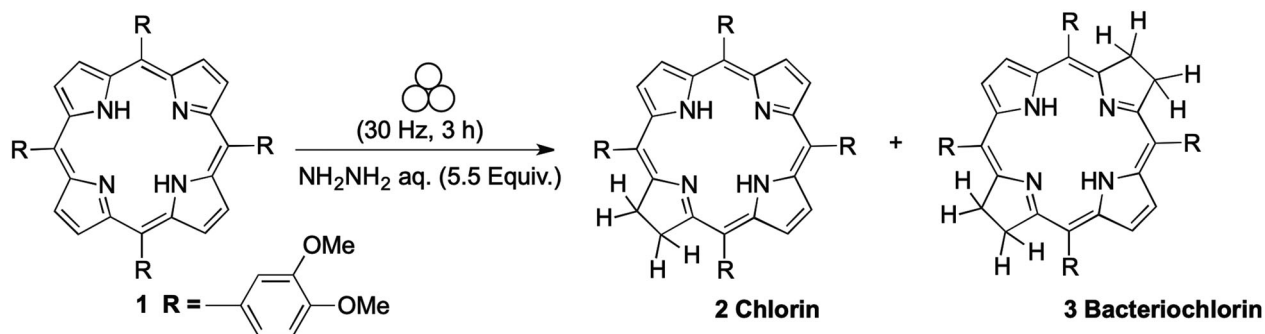
Initially, we performed the reaction between 5,10,15,20-*tetrakis*(3,4-dimethoxyphenyl)porphyrin (*33*), chosen as a model compound, and *p*-toluenesulfonylhydrazine, under mechanical action. Using 10 equivalents of *p*-toluenesulfonylhydrazine and a ball milling system with 10 mL jars and two steel balls with 7 mm of diameter during 3 h at 25 Hz, no reduction products were identified by UV–Vis or ^{1}H NMR analysis. The increase of the number of equivalents of *p*-toluenesulfonylhydrazine (12.5 and 25 equiv), the addition of a base (K$_2$CO$_3$, DBU or KOH) in 1:1 ratio to *p*-toluenesulfonylhydrazine to promote the decomposition in basic media, the increase of the ball milling frequency to 30 Hz or the increase of the reaction time to 7 h did not result in the promotion of any reaction, recovering in all cases the initial porphyrin.

From the sustainability point of view, hydrazine hydrate oxidation, a known source of diimide either by catalytic or thermal decomposition, is more interesting than sulfonylhydrazines because it only generates N$_2$ and H$_2$ after complete decomposition avoiding the formation of *p*-toluenesulfinic acid reducing to the minimum the generation of waste. Hydrazine hydrate was successfully used, in fairly sustainable conditions, for the catalyst-free reduction of alkenes in the presence of oxygen at 35 °C in ethanol (*34*). Under those reaction conditions, only traces of the desired chlorin were obtained, 26% after 7 days at 35 °C. Therefore, we performed the reduction of 5,10,15,20-*tetrakis*(3,4-dimethoxyphenyl)porphyrin using hydrazine hydrate (20 μL, 5.5 equiv) under ball milling at 30 Hz frequency. After 2 h a conversion of 63% was obtained with 90% selectivity for the desired chlorin (entry 1, Table 1). Increasing the reaction time to 3 h, increases conversion to 85% of chlorin (entry 2, Table 1) while selectivity remained unchanged. The increase of the reaction time to 4 h (entry 3, Table 1) or increase of hydrazine hydrate equivalents and reaction time (entry 4, Table 1) do not significantly change conversion or selectivity to chlorin. Considering the mechanism for the catalytic decomposition of hydrazine hydrate to form diimide

Scheme 2. Reduction of 5,10,15,20-*tetrakis*(3,4-dimethoxyphenyl)porphyrin to the corresponding chlorin and bacteriochlorin.

Table 1. Optimization of the reaction conditions for the reduction of 50 mg (0.06 mmol) of 5,10,15,20-*tetrakis*(3,4-dimethoxyphenyl)porphyrin.

Entry	Hydrazine hydrate (equiv)	Time (h)	Reaction product according with Scheme 2				
			1 (%)[a]	2 (%)[a]	3 (%)[a]	Conversion (%)	Selectivity[b] (%)
1	5.5	2	37	57	6	63	90
2	5.5	3	15	72	13	85	85
3	5.5	4	17	75	8	83	90
4	10	6	15	76	9	85	89
5	2.5	3	27	65	8	73	89

[a]Determined by ^{1}H NMR from the reaction crude in accordance with the data previously described (38).
[b]Selectivity to chlorin **2**, the other reaction product is bacteriochlorin **3**.

jointly with the mechanism of the macrocycle reduction, in which it is established that only the syn diimide is capable of transferring the hydrogen atoms (31) at least two equivalents of hydrazine hydrate will be necessary to reduce one porphyrin. Using 2.5 equiv of hydrazine hydrate (entry 5, Table 1) a significant decrease of conversion was observed. Therefore, the best results were obtained milling the porphyrin with 5.5 equivalents of hydrazine hydrate at 30 Hz during 3 h.

Hydrazine could be transformed into diimide by catalytic decomposition mediated by metals or through thermal decomposition, forming *syn* and *anti* diimide (35,36) or ammonia and *syn* diimide (37), respectively. Under mechanical action using the optimize reaction conditions described we observed gas pressure build-up in the jars, when they were opened after the milling, and also the reduction of the porphyrin. Therefore, it is possible conclude that *syn* diimide was formed (the only form of diimide capable of performing the reduction because it is assumed to be a synchronous transport of hydrogen through a cyclic transition state) (31, 35). To clarify the role of mechanical activation in the decomposition of hydrazine hydrate and to exclude the possibility of the metal from the container being the catalyst of the reaction, the reaction was performed in Teflon jars with Teflon spheres, under these conditions the same amount of chlorin was obtained. The reaction mixture was placed into the ball milling container and instead of milling, mechanical stirring was applied, after 3 h the reactants remained unchanged. These results imply that mechanical action is necessary to decompose hydrazine hydrate and produce diimide.

The absence of solvent and waste from the source of the reducing agent make the isolation of the final product very easy, since it is a solid containing only the original porphyrin, chlorin and traces of bacterio-chlorin (for NMR analysis of the reaction crude see supplementary materials, Figure S1), without other organic compounds or inorganic salts, Figure 1.

The optimize reaction conditions were used for the synthesis of several chlorins (Table 2).

Regarding the substituent at the *meso* position all compounds were obtained with high yields and selectivity for the chlorin. Bulky substituents at the *ortho* position of the phenyl ring gave good yields as expected because this substitution favors the stability of reduced macrocycles (28, 39).

Determining the environmental standpoint of our methodology compared with those previously described in the literature and the resulting

Figure 1. Picture of the reaction crude after 3 h of ball milling.

Table 2. Substrate scope of the mechanochemical reduction of porphyrins.

R	Yield (%)[a]
phenyl	48
2-chlorophenyl	78
2,6-dichlorophenyl	68
4-bromophenyl	63
4-*tert*-butylphenyl	25
4-methoxyphenyl	68
3-methoxyphenyl	73
3-hydroxyphenyl	55

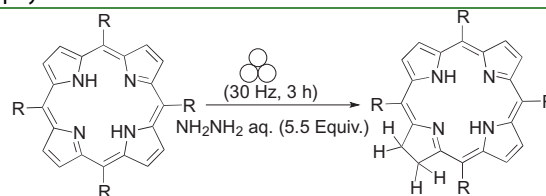[a]Yield determined by ^{1}H NMR. Characterization in accordance with the data previously described (32, 38, 40).

Table 3. Calculated green metrics of previous reports and this process.

Method	Atom Economy	E-Factor	EcoScale
Withlock *et al.* Diimide generation with base in solution (*30*).	72.2	132.1	25
Pereira *et al.* Diimide thermal generation (*31*).	82.3	3.95	54.4
This work. Diimide mechanical generation	96.6	0.96	63

improvement obtained introducing mechanochemistry requires assessment of the metrics.

Mechanochemistry enables the solvent-free reduction of porphyrins to chlorins with hydrazine hydrate, which is a precursor for CO-free H_2 production, therefore the reaction waste is only formed by diatomic gases and the reaction is performed with 100% of carbon efficiency and a very high atom economy of 97% (Table 3). The elimination of the solvent and the reduction of the mass of waste allows to decrease the E-factor (41) value to decimal proximity to the ideal value (0.96). To complete this mass-based metric EcoScale was determined. EcoScale is a post-synthetic metric that takes into consideration price, safety, reaction operation conditions as well as isolation and purification steps (42, 43). For our method, a EcoScale value of 63 was obtained, the highest of the known methods. The deviation of the ideal value reflects the safety issues of the use of reactants capable of generating inflammable gases, inherent to this reaction. Table 3 (for details see supplementary materials, section S2).

Conclusion

In conclusion, mechanochemistry reveals to be an efficient way to decompose hydrazine hydrate to generate diimide gas opening the way to metal free, carbon-free hydrogenations. Under mechanical action it was possible to promote diimide reaction with porphyrins to yield the desired chlorins in high yield. The methodology developed using mechanochemistry, hydrazine hydrate and solvent-free conditions have very high atom economy, high conversion, high selectivity and minimum waste generation, thus approaching to the Green Chemistry ideals.

Material and methods

Aldehydes (3,4-dimethoxybenzaldehyde (120-14-9; Aldrich, 99%); 3-methoxybenzaldehyd (591-31-1; Aldrich, 97%); 2,6-dichlorobenzaldehyde (83-38-5; Aldrich, 99%); pyrrole (109-97-7; Alfa Aesar, 98+), deuterated chloroform or dimethyl sulfoxide-d6 (865-49-6; VWR Chemicals, +0,03%TMS)).

Porphyrins were obtained by MW assisted methods (25, 26).

Ball milling reactions were performed in a Retsch MM 400 with constant frequency and time monitoring. Steel jars (10 mL) and balls (7 mm diameter, 1.40 g), were used as well as Teflon jars (10 mL) and balls (10 mm diameter, 1.75 g). ^{1}H NMR spectra were registered at room temperature in a Bruker Avance III or Bruker-AMX spectrometer, operating at 400 MHz and 300 MHz, respectively. TMS was the internal standard used. Chemical shifts (δ) and coupling constants (J) are indicated in ppm and Hz, respectively.

Typical procedure

About 50 mg of porphyrin 20 μL of hydrazine hydrate 50–60% (5.5 equiv) and two steel spheres were placed in a steel jar and submitted to mechanical action in a ball milling system (Retsch 400 MM) at 30 Hz during 3 h. The solid reaction crude was dissolved in deuterated chloroform and analyzed by ^{1}H NMR.

Characterization

5,10,15,20-*tetrakis*(3,4-dimethoxyphenyl)chlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.64 (2H, d, J = 5 Hz), 8.48 (2H, s), 8.24 (2H, d, J = 5 Hz), 7.67 (4H, d, J = 5 Hz), 7.39 (4H, d, J = 5 Hz), 7.16 (4H, t, J = 15 Hz), 4.2 (4H, s), 4.14 (6H, s), 4.11 (6H, s), 3.95 (12H, s), −1.44 (2H, s). Characterization is in accordance with that previously described (38, 40).

5,10,15,20-*tetra*-phenylchlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.56 (2H, d, J = 4.9 Hz), 8.42 (2H, s), 8.17 (2H, d, J = 4.9 Hz), 8.10 (4H, dd, J1 = 7.7 Hz, J2 = 1.6 Hz), 7.87 (4H, m), 7.68 (12H, m), 4.16 (4H, s), −1.45 (2H, bs). Characterization is in accordance with that previously described (32).

5,10,15,20-*tetrakis*(2-chlorophenyl)chlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.45 (2H, d, J = 4.9 Hz), 8.28 (2H, s), 8.09 (2H, d, J = 4.9 Hz), 7.98–7.95 (4H, m), 7.80–7.56 (12H, m), 4.12 (s, 4H), −1.40 (2H, s). Characterization is in accordance with that previously described (40).

5,10,15,20-*tetrakis*(2,6-dichlorophenyl)chlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.46 (2H, d, J = 4.8 Hz), 8.27 (2H, s), 8.09 (2H, d, J = 4.8 Hz), 7.67 (12, m), 4.09 (4H, s), −1.31 (2H, bs). Characterization is in accordance with that previously described (32).

5,10,15,20-*tetrakis*(4-bromophenyl)chlorin ^{1}H NMR δ, ppm (400 MHz, CDCl$_3$, Me$_4$Si): 8.55 (2H, d, J = 4.8 Hz), 8.39 (2H, s), 8.18 (2H, d, J = 4.8 Hz), 7.94 (4H, d, J = 8 Hz), 7.81 (8H, d, J = 8 Hz), 7.72 (4H, d, J = 8 Hz),

4.14 (4H, s), −1.53 (2H, bs). Characterization is in accordance with that previously described (*27*).

5,10,15,20-*tetrakis*(4-*tert*-butylphenyl)chlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.59 (2H, d, J = 4.8 Hz), 8.43 (2H, s), 8.17 (2H, d, J = 4.8 Hz), 7.77 (8H, d, J = 8.4 Hz), 7.67 (8H, d, J = 8.4 Hz), 4.15 (4H, s), 1.56 (18H, s), 1.54 (18H, s), −1.41 (2H, bs). Characterization is in accordance with that previously described (*32*).

5,10,15,20-*tetrakis*(4-methoxyphenyl)chlorin ^{1}H NMR δ, ppm (300 MHz, CDCl$_3$, Me$_4$Si): 8.58 (2H, d, J = 4.8 Hz), 8.44 (2H, s), 8.19 (2H, d, J = 4.8 Hz), 8.01 (4H, d, J = 8.5 Hz), 7.76 (4H, d, J = 8.5 Hz) 7.21 (4H, d, J = 8.3 Hz), 7.19 (4H, d, J = 8.3 Hz), 4.143 (4H, s), 4.05 (12H, s), −1.43 (2H, bs). Characterization is in accordance with that previously described (*32*).

5,10,15,20-*tetrakis*(3-methoxyphenyl)chlorin ^{1}H NMR δ, ppm (400 MHz, CDCl$_3$, Me$_4$Si): 8.62 (2H, d, J = 4.6 Hz), 8.46 (2H, s), 8.23 (2H, d, J = 4.6 Hz), 7.70 (4H, m), 7.59 (4H, m), 7.44 (4H, m), 7.24 (4H, m), 4.19 (4H, s), 3.94 (12H, s), −1.49 (2H, bs). Characterization is in accordance with that previously described (*32*).

5,10,15,20-*tetrakis*(3-hydroxyphenyl)chlorin ^{1}H NMR δ, ppm (400 MHz, DMSO-d6, Me$_4$Si): 8.63 (2H, d, J = 4.8 Hz), 8.37 (2H, s), 8.24 (2H, d, J = 4.8 Hz), 7.51 (6H, m), 7.26 (10H, m), 4.16 (4H, s), −1.65 (2H, bs). Characterization is in accordance with that previously described (*32*).

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Marta Pineiro http://orcid.org/0000-0002-7460-3758

References

[1] Do, J.-L.; Friščić, T. *ACS Cent. Sci.* **2017,** *3*, 13–19.

[2] Howard, J.L.; Cao, Q.; Browne, D.L. *Chem. Sci.* **2018**, *9*, 3080–3094.

[3] Achar, T.K.; Bose, A.; Mal, P. *Beilstein J. Org. Chem.* **2017**, *13*, 1907–1931.

[4] Leonardi, M.; Villacampa, M.; Menéndez, J.C. *Chem. Sci.* **2018**, *9*, 2042–2064.

[5] Margetić, D.; Štrukil, V. *Mechanochemical Organic Synthesis*. 1st ed.; Elsevier: Amsterdam, 2016.

[6] Andersen, J.; Mack, J. *Green Chem.* **2018,** *20*, 1435–1443.

[7] Tan, D.; Friščić, T. *J. Org. Chem.* **2018**, *2018*, 18–33.

[8] Bowmaker, G.A. *Chem. Commun.* **2013,** *49*, 334–348.

[9] Pineiro, M.; Calvete, M. J. F. Sustainable Synthesis of Pharmaceuticals Using Alternative Techniques: Microwave, Sonochemistry and Mechanochemistry. In *Sustainable Synthesis of Pharmaceuticals: Using Transition Metal Complexes as Catalysts*; G. C. Series, Ed.; RSC, 2018; pp 8–39.

[10] Hernández, J.G.; Bolm, C. *J. Org. Chem.* **2017,** *82*, 4007–4019.

[11] Pineiro, M. Microwave and Mechanochemistry: Tools for the Sustainable Synthesis of Pyrroles, Porphyrins and Related Macrocycles. In *Targets in Heterocyclic Systems*; Attanasi, O. A.; Merino, P., Spinelli, D., Eds. Società Chimica Italiana: Roma, 2016; Vol. 20, pp 197–221.

[12] Friščić, T.; Motillo, C.; Titi, H.M. *Angew. Chem. Int. Ed.* **2020,** *59*, 1018–1029.

[13] Tan, D.; García, F. *Chem. Soc. Rev.* **2019**, *48*, 2274–2292.

[14] Charnay, C.; Porchedu, A.; Delogu, F.; Colacino, E. New and Up-and-Coming Perspectives for Unconventional Chemistry: From Molecular Synthesis to Hybrid Materials by Mechanochemistry. In *Green Synthetic Processes and Procedures*; G. C. Series, Ed.; RSC, 2019; pp 192–215.

[15] Bolm, C.; Hernández, J.G. *Angew. Chem. Int. Ed.* **2019**, *58*, 3285–3299.

[16] Al-Terkawi, A.-A.; Lamaty, F.; Métro, T.-X. *ACS Sus. Chem. Eng.* **2020**, *8*, 13159–13166.

[17] Felderhoff, M. *Joule* **2021**, *5*, 297–299.

[18] Fiss, B.G.; Richard, A.J.; Friščić, T.; Moores, A. *Canad. J. Chem* **2021**, *99*, 87–92.

[19] Schumacher, C.; Crawford, D.E.; Raguž, B.; Glaum, R.; James, S.L.; Bolm, C.; Hernández, J.G. *Chem. Commun.* **2018,** *54*, 8355–8358.

[20] Li, A.Y.; Segalla, A.; Li, C.-J.; Moores, A. *ACS Sustainable Chem. Eng.* **2017,** *5*, 11752–11760.

[21] Ribeiro, L.S.; Órfão, J.J.M.; Pereira, M.F.R. *Green Chem.* **2015**, *17*, 2973–2980.

[22] de Oliveira, K.T.; Momoa, P.B.; de Assisa, F.F.; Ferreira, M.A.B.; Brocksoma, T.J. *Curr. Org. Syn.* **2014,** *11*, 42–58.

[23] Kataoka, H.; Nishie, H.; Hayashi, N.; Tanaka, M.; Nomoto, A.; Yano, S.; Joh, T. *Ann. Transl. Med.* **2017,** *5* (8), 183–183.

[24] Yaghini, E.; Dondi, R.; Tewari, K.M.; Loizidou, M.; Eggleston, I.M.; MacRobert, A.J. *Nature Sci. Rep.* **2017,** *7*, 6059–6070.

[25] Hopper, C.; Niziol, C.; Sidhu, M. *Oral Oncol.* **2004,** *40*, 372–382.

[26] Senge, M.O. *Photodiagn. Photodyn. Ther.* **2012,** *9*, 170–179.

[27] Taniguchi, M.; Lindsey, J.S. *Chem. Rev.* **2017,** *117* (2), 344–535.

[28] Serra, A.C.; Rocha Gonsalves, A.M.d.A. *Tet. Lett.* **2010**, *51*, 4192–4194.

[29] Pereira, N.A.M.; Laranjo, M.; Pina, J.; Oliveira, A.S.R.; Ferreira, J.D.; Sánchez-Sánchez, C.; Casalta-Lopes, J.; Gonçalves, A.C.; Sarmento-Ribeiro, A.; Piñeiro, M.; Seixas de Melo, J.S.; Botelho, M.F.; Pinho e Melo, T.M.D.V. *Eur. J. Med. Chem* **2018**, *146*, 395–408.

[30] Whitlock Jr, H.W.; Hanauer, R.; Oester, M.Y.; Bower, B.K. *J. Am. Chem. Soc* **1969,** *91* (26), 7485–7489.

[31] Pereira, M.M.; Abreu, A.R.; Goncalves, N.P.F.; Calvete, M.J.F.; Simões, A.V.C.; Monteiro, C.J.P.; Arnaut, L.G.; Eusébio, M.E.; Canotilho, J. *Green Chem.* **2012,** *14*, 1666–1672.

[32] Nascimento, B.F.O.; Rocha Gonsalves, A.M.d.A.; Pineiro, M. *Inorg. Chem. Commun.* **2010**, *13*, 395–398.

[33] Nascimento, B.F.O.; Pineiro, M.; Gonsalves, R.; d, A.M.; Silva, A.; Beja, M.R.; Paixão, A.M.; A, J. *J. Porphyr. Phthalocyanines* **2007,** *11*, 77–84.

[34] Menges, N.; Balci, M. *Synlett.* **2014,** *25*, 671–676.

[35] Miller, C.E. *J. Chem. Educ.* **1965,** *42*, 254–259.

[36] Furst, A.; Berlo, R.C.; Hooton, S. *Chem. Rev.* **1965,** *65*, 51–68.

[37] Pakdehi, S.G.; Salimi, M.; Rasoolzadeh, M. *Res. Appl. Mechan. Eng.* **2014**, *3*, 21–25.

[38] Marydasan, B.; Madhuri, B.; Cherukommu, S.; Jose, J.; Viji, M.; Karunakaran, S.C.; Chandrashekar, T.K.; Rao, K.S.; Rao, C.M.; Ramaiah, D. *J. Med. Chem.* **2018,** *61*, 5009–5019.

[39] Pineiro, M.; Gonsalves, R.; d, A.M.; Pereira, A.; Formosinho, M.M.; Arnaut, S.J.; G, L. *J. Phys. Chem. A* **2002,** *106*, 3787–3795.

[40] Pineiro, M.; Pereira, M.M.; Gonsalves, R.; d, A.M.; Arnaut, A.; Formosinho, L.G.; J, S. *J. Photochem. Photobiol. A: Chem* **2001,** *138*, 147–157.

[41] Sheldon, R.A. *Green Chem.* **2017,** *19*, 18–43.

[42] Van Aken, K.; Strekowski, L.; Patiny, L. *Beilstein J. Org. Chem.* **2006,** *2* (3), 1–7.

[43] Sheldon, R. *ACS Sustain. Chem. Eng.* **2018,** *6* (1), 32–48.