NMR Characterization of Tetra-*meso*-substituted Porphyrins Synthesized by Mechanochemistry

T.D. Hamilton (Barry University, Physical Sciences), D. Gharbharan, H. Shy (BU), James R. Rocca (AMRIS)

Introduction

Solvent-free carbon-carbon bond forming reactions are becoming more sought-after, due to lower waste generation and potential access to products unattainable through solution synthesis. Porphyrins are usually synthesized under high dilution conditions in order to avoid linear byproducts, necessitating the use of large volumes of propionic acid or chlorinated organic solvent.[1] Yields from these synthetic protocols are low, ranging from 20-30%, depending on the substituents present on the aldehyde starting material. The reaction mechanism is a four-fold acid-catalyzed condensation between pyrrole and an aldehyde, followed by oxidation to produce the porphyrin. We are investigating a two-step solvent-free approach involving automated grinding of reactants with an acid catalyst using a Retsch MM200 ball-mill grinder followed by a second grinding step in the presence of an oxidizing agent, to produce a porphyrin. The method has proven effective using benzaldehyde as a reactant to produce tetraphenyl porphyrin (TPP) in significant yields. TPP has been characterized using UV-Vis spectroscopy, ^{1}H Nuclear Magnetic Resonance, and Mass Spectrometry. To investigate the general applicability of the approach, a series of substituted benzaldehydes were ground in the presence of pyrrole and toluene sulfonic acid as a catalyst. Various oxidizing agents are also being tested for their efficacy.

Experimental

Equimolar amounts of pyrrole and substituted benzaldehyde, and a catalytic amount (10%) of toluenesulfonic acid were added to a stainless steel grinding jar along with two stainless steel grinding balls. The capsule was placed in a Retsch MM200 ball-mill grinder and the mixture was shaken for 30 minutes at 25 Hz to yield a pink powder. The powder was then oxidized using one of two methods: 1) adding 3 eq. 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in 30 mL chloroform, and stirring for 30 minutes, followed by passing the mixture through a one-centimeter plug of alumina to remove DDQ; or 2) addition of a solid state oxidizing agent, followed by a second grinding step. Analysis by TLC, UV-Vis Spectroscopy and ^{1}H NMR confirm the presence of a porphyrin in the mixture.

Results and Discussion

Various halogen and alkyl-substituted benzaldehydes as well as polycyclic aromatic aldehydes were used as starting material to produce the corresponding tetra-*meso*-substuted porphyrins, as evidenced by the presence of Soret Bands (around 420 nm) in their UV-Vis spectra. Further characterization (*i.e.* ^{1}H and ^{13}C NMR) of the purified components of the mixture is needed to confirm this result.

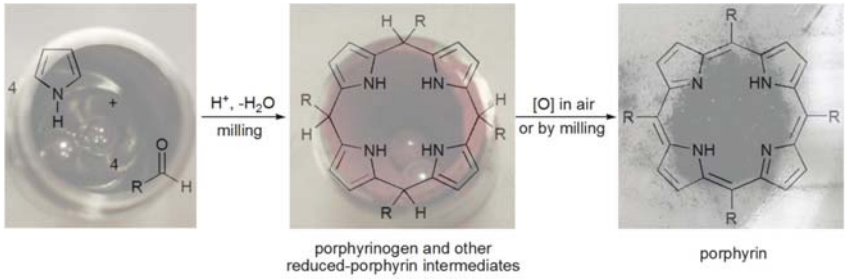

Figure 1: Two-step mechanochemical synthesis of porphyrins.

Conclusions/Future Work

Solvent-free grinding holds promise for the synthesis of porphyrins and substituted porphyrins without the need for large amounts of chlorinated or caustic solvents. UV-Vis spectra confirm the presence porphyrins in the reaction mixture, but the whole series of products need to be purified and confirmed with NMR spectroscopy. Once so confirmed, this study will help to establish solvent-free grinding as a viable synthetic method for porphyrins and related compounds.

Acknowledgements

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References

[1] Lindsey, J. S. *et al.,* J. Org. Chem., **52**, 827-836 (1987).