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Microwave Solventless Synthesis of Meso-Tetrakis (Pentafluorophenyl)Poprphyrin (TPPF20) and Tris(Pentafluorophenyl))Corrole [Chemistry]

Sunaina Singh
CUNY La Guardia Community College

Dr. Sunaina Singh
Organic Chemistry I-SCC 251
Biology/Environmental Science
Natural Sciences Department, LaGuardia Community College, CUNY

Assignment Title:
Microwave Solventless Synthesis of Meso-Tetrakis (Pentafluorophenyl)Poprphyrin ($TPPF_{20}$) and Tris(Pentafluorophenyl))Corrole

Organic chemistry is a two-semester course (Organic Chemistry I, SCC 251 and Organic Chemistry II, SCC 252) required for majors in Biology. The SCC 251 course has been designated for the Integrative Learning Core Competency as well the Digital Communication Ability. This course emphasizes the synthesis, structure, reactivity, and mechanisms of reaction of organic compounds. Laboratory stresses various organic synthetic and analytic techniques (distillation, extraction, chromatography and spectroscopy).

This lab provided an opportunity for students to go deeper with the chemistry content by correlating to the concepts they learned in General Chemistry courses such as Valence shell electron pair repulsion theory (VSEPR), resonance, polarity, dipole moment, acid-base reactions, mole concept, thermochemistry and chemical kinetics. In addition, for the experimental part, applying the techniques such as qualitative analysis of ions, filtration, melting point, optical spectroscopy, and molecular modelling. This lab was performed at the end of the semester when students are familiar with basic organic techniques such as distillation, crystallization, thin layer chromatography (TLC) and column chromatography--techniques they learned previously in this lab. Overall, this lab was designed to develop critical thinking and integrative learning skills while introducing students to the porphyrin and green chemistry concepts. This experiment illustrates the several principles of green chemistry and is easily extendable to introduce topics in other chemistry courses such as NMR spectroscopy (^{1}H, ^{13}C and ^{19}F NMR), material chemistry, click chemistry coordination chemistry, and environmental chemistry.

Learning outcomes that can be assessed using this lab include an understanding of laboratory procedures (methods and techniques), safety hazards, and instrumentation, understanding of concepts and theories gained by performing the experiment, collecting data through observation and/or experimentation (TLC and column chromatography), interpretation of the data (percent yield, UV-vis spectra), drawing conclusions and perspective of the experiment. The knowledge students gain during this process will be useful to connect with future chemistry courses and can also be utilized to do research.

The digital aspect of the assignment will entail students using chemistry software (Chem Draw) to draw out the chemical reaction from the lab. This software is available free via CUNY website using this link:

http://sitelicense.cambridgesoft.com/sitelicense.cfm?sid=1680

Students need LaGuardia email address to download this software on their computer.

Students will be able to predict properties, generate spectra, write the IUPAC names, and calculate reaction stoichiometry. This software helps to find compounds (structures) of interest much faster. To be successful in organic chemistry courses, it is important that students are able to draw structures, mechanisms, and synthesis. To prepare high quality chemical structures ChemDraw program is used.

This assignment is part of the Research in the Classroom Idea Grant (CUNY). The assignment was scaffolded over about 2 weeks and was worth about 5% of the final grade.

List the Program Goals that this assignment targets:

1**.** To provide training to the students in various organic lab techniques and utilize them to conduct research.

List the Student Learning Objective (s) that this assignment targets:

1. Students will have an enhanced conceptual understanding of the theory–practical relationship and will achieve higher level reasoning skills.

2. Students will be able to develop their practical competence in laboratory work.

3. Students will be able to collect data through observation and/or experimentation, purification by column chromatography, characterize the compounds by UV-vis spectra, check the purity of the porphyrin and corrole synthesized by melting point and TLC and draw conclusions and perspective of the experiment.

List the Course Objective (s) that this assignment targets:

1. Based on the principles and methods of green chemistry concept, students will be able to develop the ability to analyze and evaluate organic chemical reactions and processes.
2. Gather, analyze, and interpret experimental data and graph the UV visible spectra using Microsoft excel.
3. The ChemDraw program is used to increase classroom experiences in the preparation of high quality chemical drawings. This software is used to draw and submit chemical compound. ChemDraw Professional can also be used to predict properties, generate spectra, construct correct IUPAC names, and calculate reaction stoichiometry.

The pedagogy involved in executing this assignment

This assignment demonstrates the concepts and techniques of green synthesis on a practical level in organic chemistry laboratory. This assignment provides a platform for the discussion of environmental issues in the classroom. Experiments are selected so that they reduce laboratory waste and hazards, use inexpensive solvents and reagents. The simple, solvent-free and solid-supported microwave porphyrin and corrole synthesis of two of these biologically relevant

macromolecules can be performed and the discussion of bioorganic and coordination chemistries reinforced in the lecture class. The students will be able to purify the compounds synthesized by doing TLC and column chromatography and characterize them by doing melting point and UV-visible spectra.

Rubric for Abstract, Data and Discussion of the Experiment:

Name		Excellent	Good	Fair	Poor	Score
Abstract **(5 pts)**	An abstract contains five basic essentials (briefly describe): 1) The statement of the experiment, what was the objective of the experiment. 2) What method was used to examine the problem 3) Results including data in tables or graphs or pictures 4) Conclusions 5) Significance of the results					
Purpose of Experiment **(5 pts)**	What is the objective of experiment? (2 pts)					
	Which methods or techniques were used to examine the problem? (3 pts)					
Data **(8 pts)**	Label your UV-visible spectrum, including the wavelength and absorbance of each peak (3 pts)					

	Show the TLC plate and calculate the R_f Value (3 pts)					
	3. Report the theoretical and experimental yield for the reaction (2 pts)					
Discussion (10 pts)	Understating of instrumentation, concepts and theories gained by performing the experiment, collecting data through observation and/or experimentation (TLC and column chromatography), Melting point, interpretation of the data (percent yield, UV-vis spectra), drawing conclusions and perspective of the experiment.					
References (2pts)	ACS reference style					

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Prelab questions:

1. What is porphyrin? Give one example of porphyrin besides meso-tetrakis(pentafluorophenyl) porphyrin ($TPPF_{20}$).
2. List two reasons, why the method used for this lab is a greener method for the preparation of porphyrin and corrole?
3. Differentiate between porphyrin and corrole based upon their structure.
4. What are heterocyclic compounds?
5. Name the bridging group that joins the four pyrrole units to make a porphyrin macrocycle.

Introduction

Pophyrins: Porphyrins aretetrapyrrolic macrocycle, where the four pyrrole subunits are interconnected at their α-carbon atoms via methine bridges (=CH−). The basic structure of a free base porphyrin macrocycle is shown in figure 1. The Porphyrin macrocycles are aromatic in nature with conjugated 11 π bonds. The entirety of the macrocycle is aromatic in step with Hückel's (4n +2) π electron rule for aromaticity. The high degree of conjugation makes these compounds to absorb strongly in the visible region of the electromagnetic spectrum and therefore exhibit deep colors. The name "porphyrin" comes from the Greek word *porphyros*, meaning *purple* (1,2). Many porphyrins are naturally occurring; one of the best-known porphyrins is heme (iron containing porphyrin), the pigment in red blood cells and a cofactor of the protein hemoglobin. Other biologically important porphyrins include a magnesium porphyrin responsible for green pigment of plants (chlorophyll), a cobalt porphyrin, which are a common vitamin of Vitamin B_{12} family (cyanocobalamin) and many more (3).

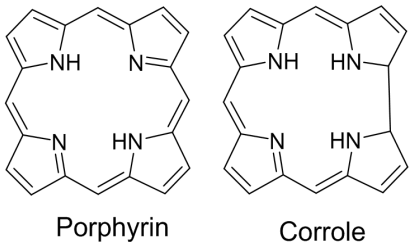


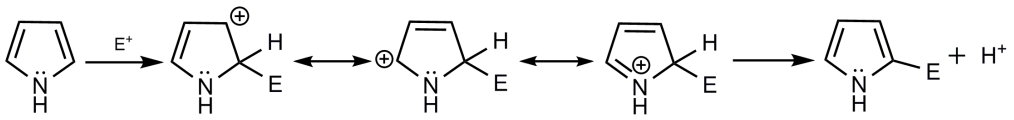
Figure 1: Skeletal structures of a free base porphyrin (left) and a free base corrole (right)

Corroles: Corroles are one example of a porphyrin analogue. Corroles are tetrapyrrolic macrocycle with 18-π conjugated electrons where one meso position has been eliminated resulting in a direct pyrrole-pyrrole bond and possessing the aromaticity of porphyrins. The skeletal structure of a free base corrole is shown in figure 1. Corroles have ability to bind a wide range of transition metal ions and stabilize them in higher oxidation states. This macrocycle can be used as potential platform for diverse applications, such as in cancer diagnosis and treatment, solar cell research due to its unique optoelectronic and physicochemical properties (4).

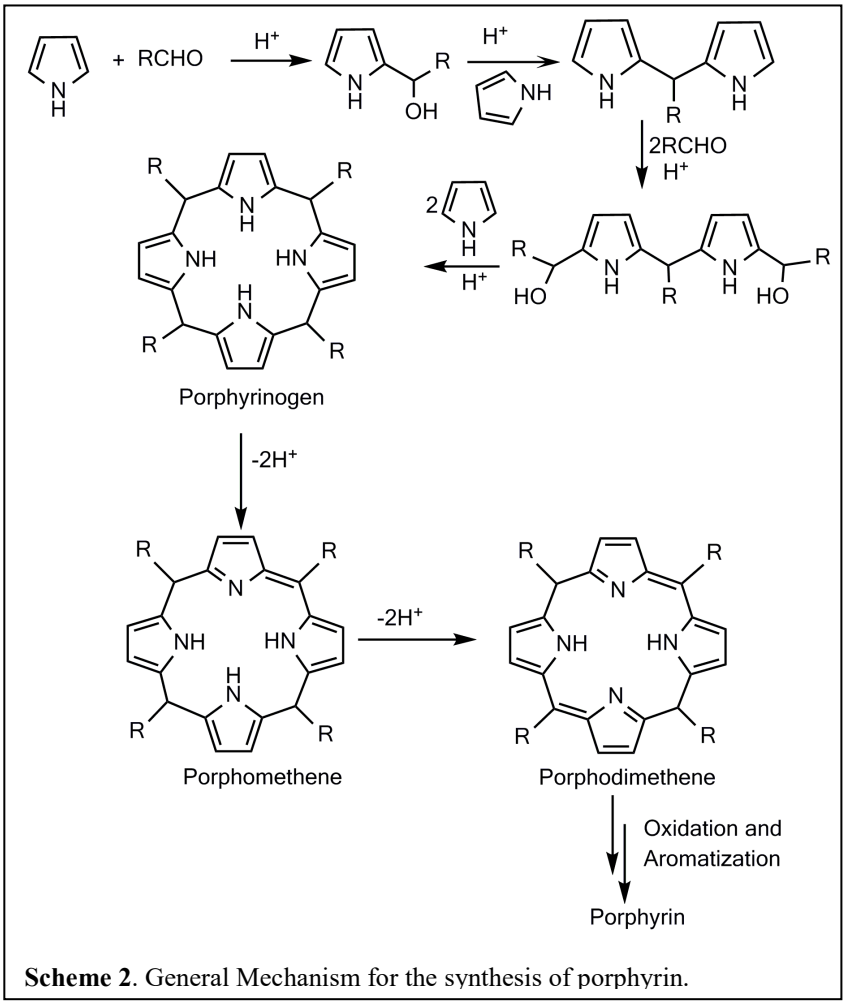
The other porphyrin related macrocycles known as porphyrinoids include porphyrazines, phthalocyanines, naphthalocyanines etc are also known and found to have diverse roles in

biological systems. The optoelectronic properties and conformational flexibility of the porphyrin macrocycle can be easily modified (3).

Synthesis of porphyrins involves electrophilic aromatic substitution, where a hydrogen atom on an aromatic ring is substituted by an electrophile (scheme 1). The detailed mechanism of the synthesis of porphyrins using an aldehyde and a pyrrole is shown in scheme 2. The product of these substitution reactions is called a porphyrinogen. Oxidation of the porphyrinogen yields a porphyrin.



Scheme1. Electrophilic aromatic substitution on pyrrole



Scheme 2. General Mechanism for the synthesis of porphyrin.

In this experiment, you will prepare a porphyrin, meso-tetrakis(pentafluorophenyl) porphyrin ($TPPF_{20}$) and a corrole, tris(pentafluorophenyl) corrole, from pyrrole and pentafluorobenzaldehyde. Porphyrin synthesis is usually done in corrosive, high boiling solvents such as acetic acid, propionic acid or in large amounts of halogenated solvents containing a corrosive Lewis acid catalyst. Here, a solventless reaction conditions are used to prepare porphyrin and corrole (Figure 2). The reaction between Pentafluorobenzaldehyde and pyrrole takes place while they are adsorbed on a solid support (silica gel). Microwave irradiations are used instead of conventional heating. The temperature of the reaction mixture increases very rapidly when microwave radiations are used as a heat source making the entire sample heat simultaneously. When compared with the conventional heating method, microwave-assisted reactions are very fast, cleaner and more economical. Since these reactions are conducted in the absence of solvent, the reactions become greener and offer an environmentally friendly way of practicing chemistry (5,6).

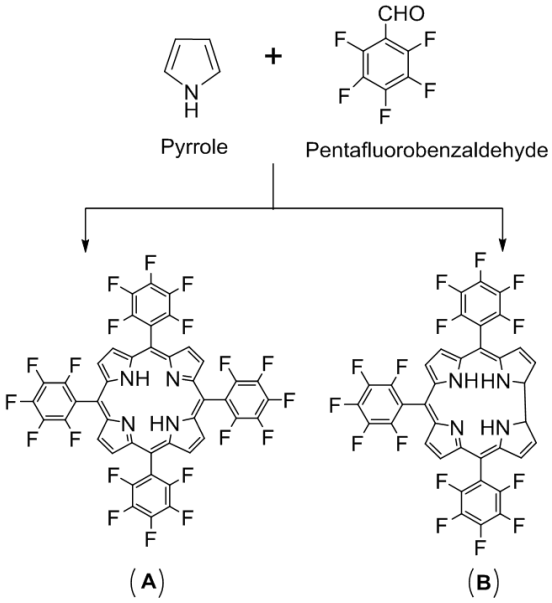


Figure. 2 Synthesis of porphyrin and corrole at high temperature in microwave by varying the ratio of pyrrole and aldehyde. A mixture of 4:4 (pyrrole to aldehyde) leads to the formation of porphyrin and a ratio of 4:3 leads to formation of corrole.

The porphyrin and the corrole synthesized here have the advantages that both of these molecules can serve as a core platform for a host of materials and biochemical applications because the para fluoro group can easily be substituted with a variety of nucleophiles to form bioconjugates and biocompatible compounds; click-type chemistry (7).

Chemicals and equipment

Pentafluorobenzaldehyde

Pyrrole

Ethyl acetate

Dichloromethane

Hexanes

Silica gel

Vials

Pyrex watch glass

Thin-layer chromatography plate

Glass wool

Sand

Microwave oven

Experimental Procedure

SAFETY PRECAUTIONS

Avoid inhalation of Silica gel and pentafluorobenzaldehyde. Ethyl acetate, hexanes, and dichloromethane are flammable, so avoid exposing them to flames or heat sources.

Mix the starting reagents 0.975 g of pentafluorobenzaldehyde and 0.335 g of pyrrole (4:4 ratio) for porphyrin and 0.731 g of pentafluorobenzaldehyde and 0.335 g of pyrrole (3:4 ratio) for corrole in two separate vials, one each for a porphyrin and a corrole. Once the reagents are thoroughly mixed, add 6-8 g of silica gel in both the vials, which acts as the solid support medium. Stopper the vials, and mix well until the silica gel is evenly and completely covered with the reaction mixture. Place the vial in the microwave oven (a standard 1000-W model works well), one at a time and heat it for 10 min in five 2-min intervals. Using several shorter heating intervals reduces overheating of the microwave oven. Once the reaction is complete, allow the mixture to cool to room temperature and then the reaction vial is rinsed with dichloromethane (DCM, CH_2Cl_2) which removes most of the porphyrin or corrole in ca. 80% purity as measured by UV-vis spectroscopy, while the remaining insoluble material contains trace amount of porphyrin or corrole.

Thin-Layer Chromatography (TLC)

TLC of the product mixture is performed on silica TLC plates using a 6:1 hexanes:ethyl acetate mixture as a mobile phase or eluent. Perfluorophenyl porphyrin ($TPPF_{20}$) and a terfluoropheny lcorrole will appear as the leading spot on the silica plate. The remaining impurities appear as a broad band.

Column Chromatography

Prepare a silica gel column in a glass column fitted with a Teflon stopcock. Use a layer of glass wool covered with a layer of sand to provide a flat base, then add silica gel so that the total column height results about 40 cm. Then place a 2 cm layer of sand on the top of the settled silica gel to protect the top surface of the column. Elute the column with hexane: ethyl acetate

(5:1) mixture. Carefully load the entire 1 mL solution of the product mixture in dichloromethane on the top of the column, and elute until the solvent level has reached the top of the sand. Elute the column with hexane:ethyl acetate (5:1) mixture at a rate of ~30 drops/min until the leading purple porphyrin or corrole band elutes. Collect the entire sample in a test tube.

UV-visible Spectroscopy

Take the UV-visible spectra of the porphyrin and corrole solution collected during column chromatography by diluting 2-3 drops of the samples with 4 mL of 5:1 hexanes: ethyl acetate mixture solution in a cuvette. A typical UV-visible absorption spectra of a porphyrin and a corrole is shown here (Figure. 3). The UV-visible absorption spectra of a porphyrin shows a strong absorbance near 420 nm (the Soret band) along with four weaker absorbances in the range of 500-650 nm (the Q bands). The absorption spectra of corroles is similar to porphyrins with a Soret band around 420 nm and Q absorption bands which are much stronger than that of porphyrins between 450 nm and 650 nm.

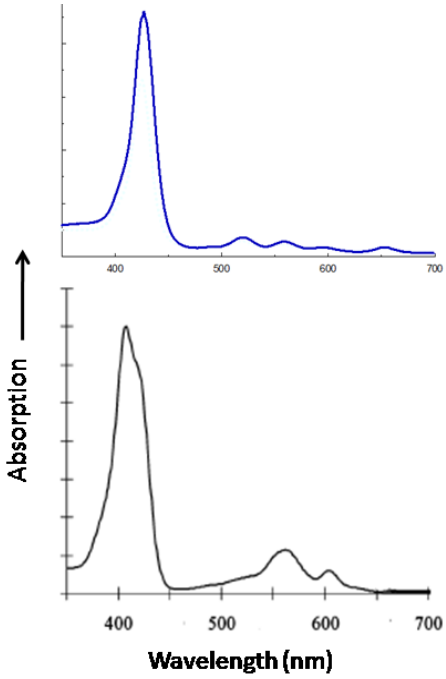


Figure 3. A typical UV-vsible absorption spectra of porphyrin (top) and corrole (bottom).

Cleanup

Place the chromatography fractions in the halogenated waste container and silica gel in the solid waste container

Post Lab Questions

1. Could this experiment have been completed without taking any SCC courses? Explain.
2. How are porphyrins used in medicine and how are they environmentally friendly?
3. Give an example where porphyrins are relevant in biological systems and determine the NMR or UV peaks?
4. Choose a compound in your SCB biology classes and conducting a literature search identify any relevant UV or NMR peaks?
5. Label your UV-visible spectrum of the porphyrin and corrole synthesized in this lab, including the wavelength and absorbance of each peak.
6. Report the theoretical and experimental yield for the reactions performed.
7. Compare the microwave synthesis of the porphyrin with that of the conventional method for the preparation of porphyrin.
8. How can you predict the ^{1}H NMR peaks for the reactant (pyrrole and pentafluorobenzaldehyde) from the chem draw Software?
9. Assign the peaks in the ^{1}H NMR spectrum of the $TPPF_{20}$ in Figure 4. Explain why the peak at -2.9 ppm occurs at that chemical shift.

10. Draw the structure of Foscan, photosensitizer used in photodynamic therapy (PDT), on the chemdraw. Predict the molecular formula, molecular weight and specify the ^{1}H NMR peaks as aromatic or aliphatic.

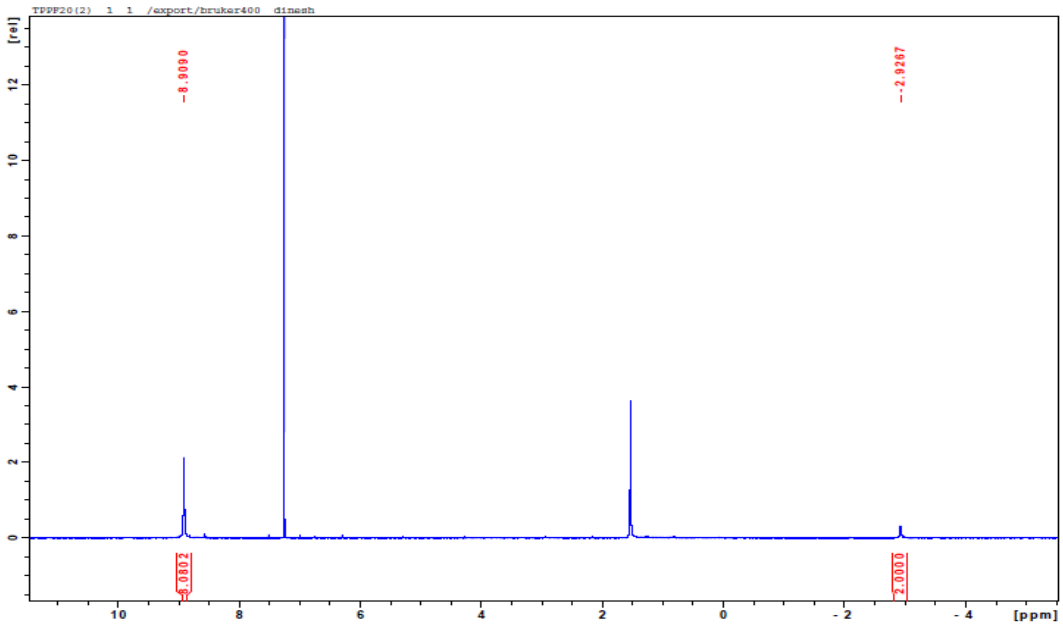


Figure 4:^{1}H NMR of $TPPF_{20}$.

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