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The Development of a New Water-Soluble Zinc Porphyrin, ZnTPP-2MP, as a Photodynamic Therapy Agent

Emily Payne

Ouachita Baptist University

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Abstract

Photodynamic therapy is a new technique used in cancer treatment involving the use of a photosensitizer and light exposure to kill malignant cells. This research tested the use of ZnTPP-2MP as a photosensitizer using white light as a source of possible treatment of the A549 cancer cell line, with preliminary testing on MYC-22 and other G-quadruplex DNA samples. ZnTPP-2MP was synthesized by the reaction of the porphyrin, ZnTPPC, with 2-amino-2-methyl-1-propanol. Following synthesis, the new porphyrin was purified by column chromatography using Sephadex LH-20 and G-50. To confirm the identity and structure of the product, ZnTPP-2MP was analyzed through nuclear magnetic resonance (NMR), infrared (IR), ultraviolet-visible (UV-vis) and fluorescence spectroscopies. Purity of the final compound was determined using HPLC. Additionally, ROS (reactive oxygen species) production using the novel porphyrin, is currently being tested.

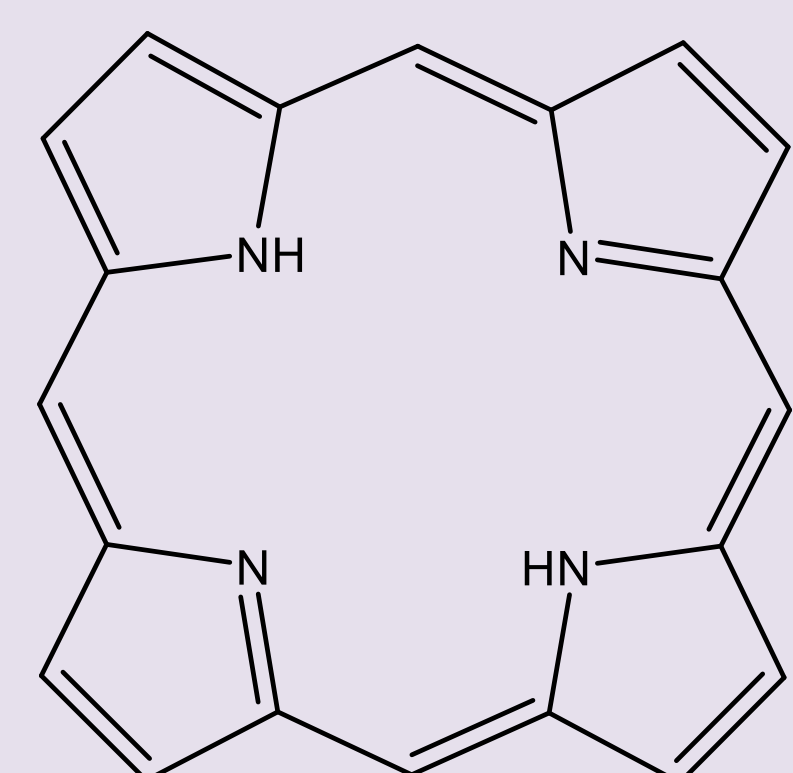


Figure 1: Standard Porphyrin Core Structure, Unsubstituted

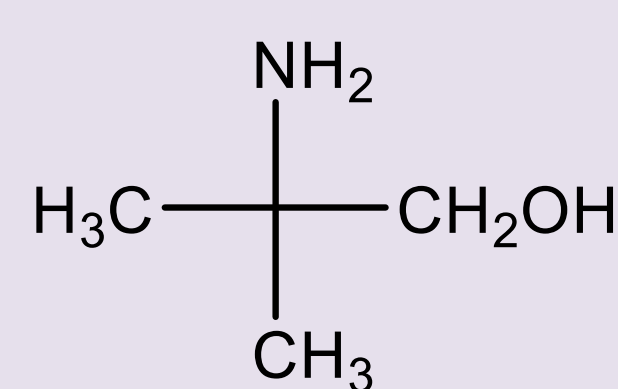
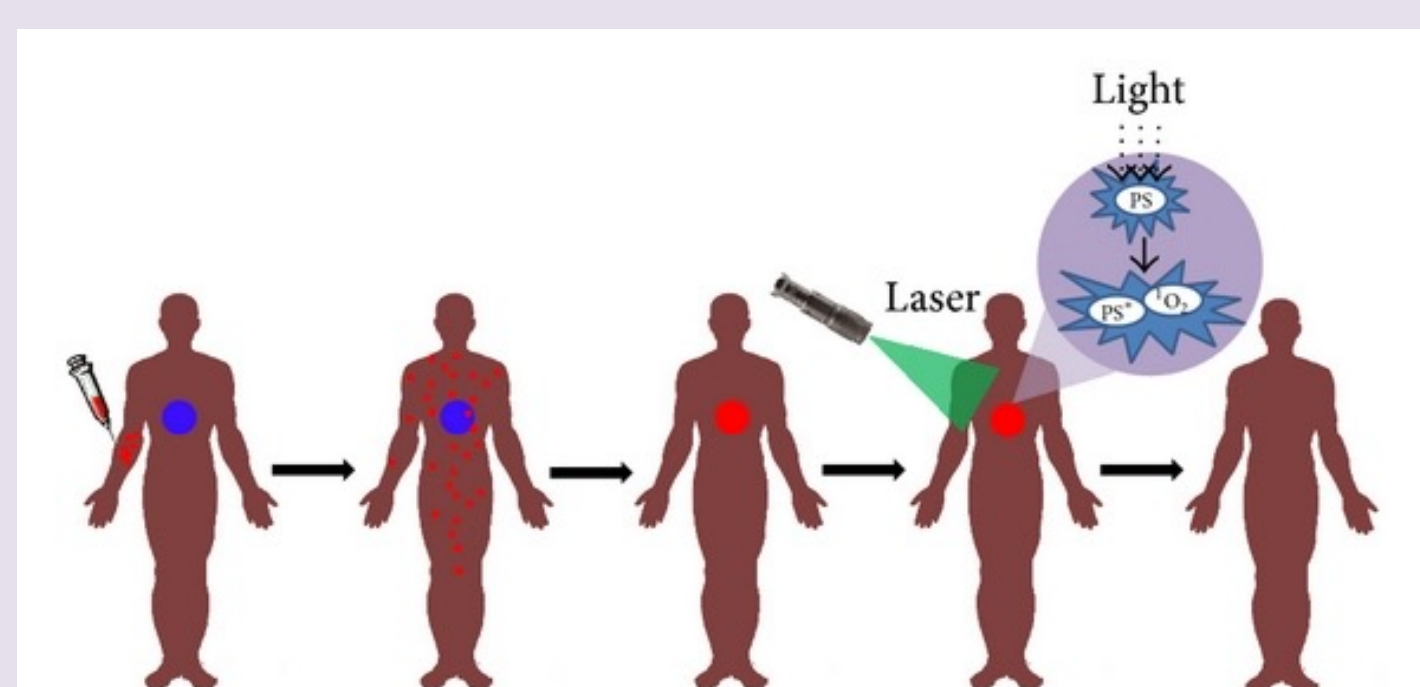


Figure 2: 2-amino-2-methyl-1-propanol

Introduction

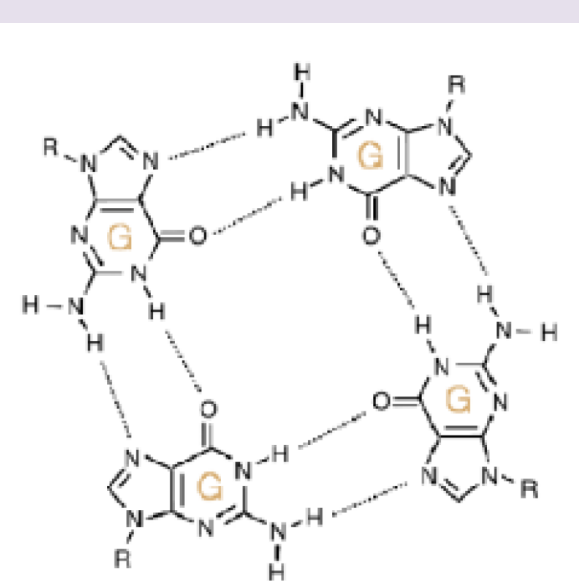
Photodynamic Therapy

The photosensitizing agent is injected into the patient. The compound accumulates at the site of the tumor, and the site is exposed to light. The porphyrin is then activated, killing the malignant cells.



G-quadruplex DNA

- C-MYC is persistently expressed in cancer, and specifically upregulated in carcinoma of the cervix, colon, breast, lung, and stomach.
- MYC-22 Sequence:
TGAGGGTGGGTAGGGTGGGTAA

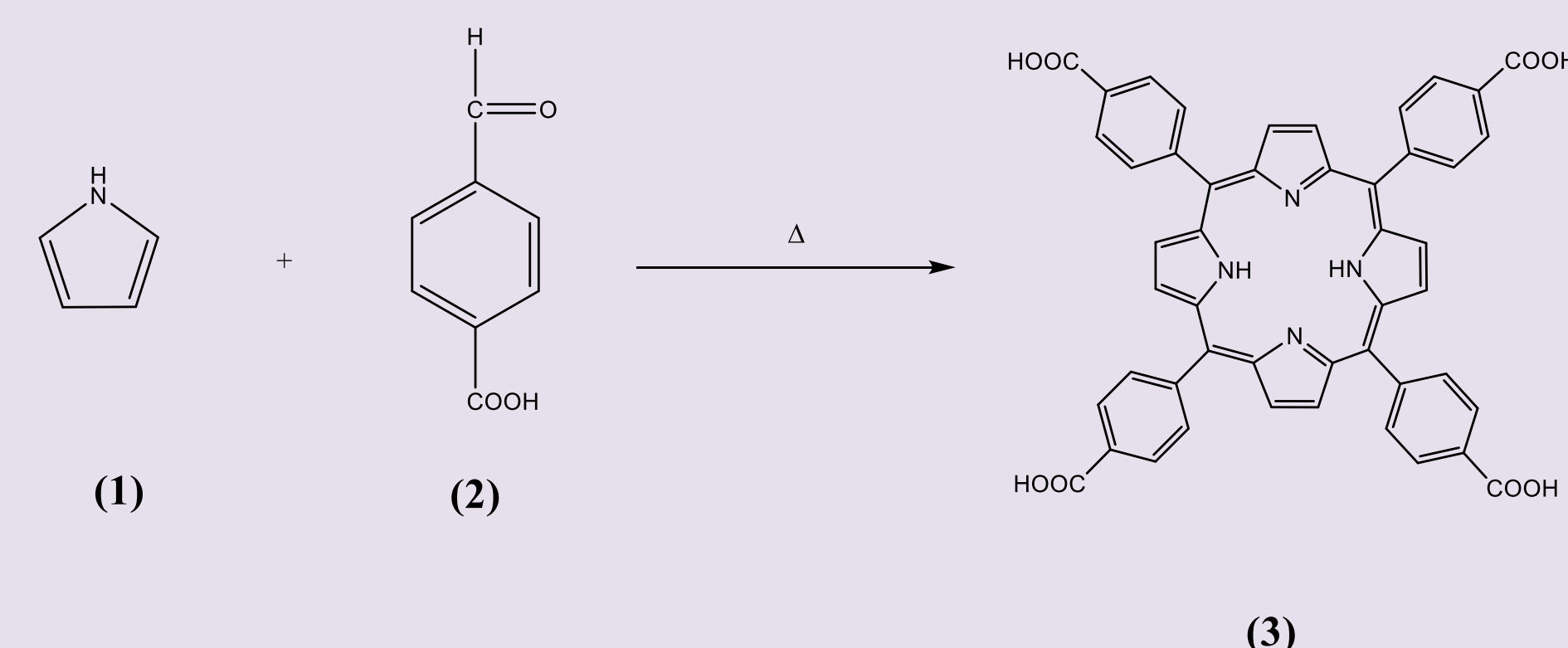


Porphyrins

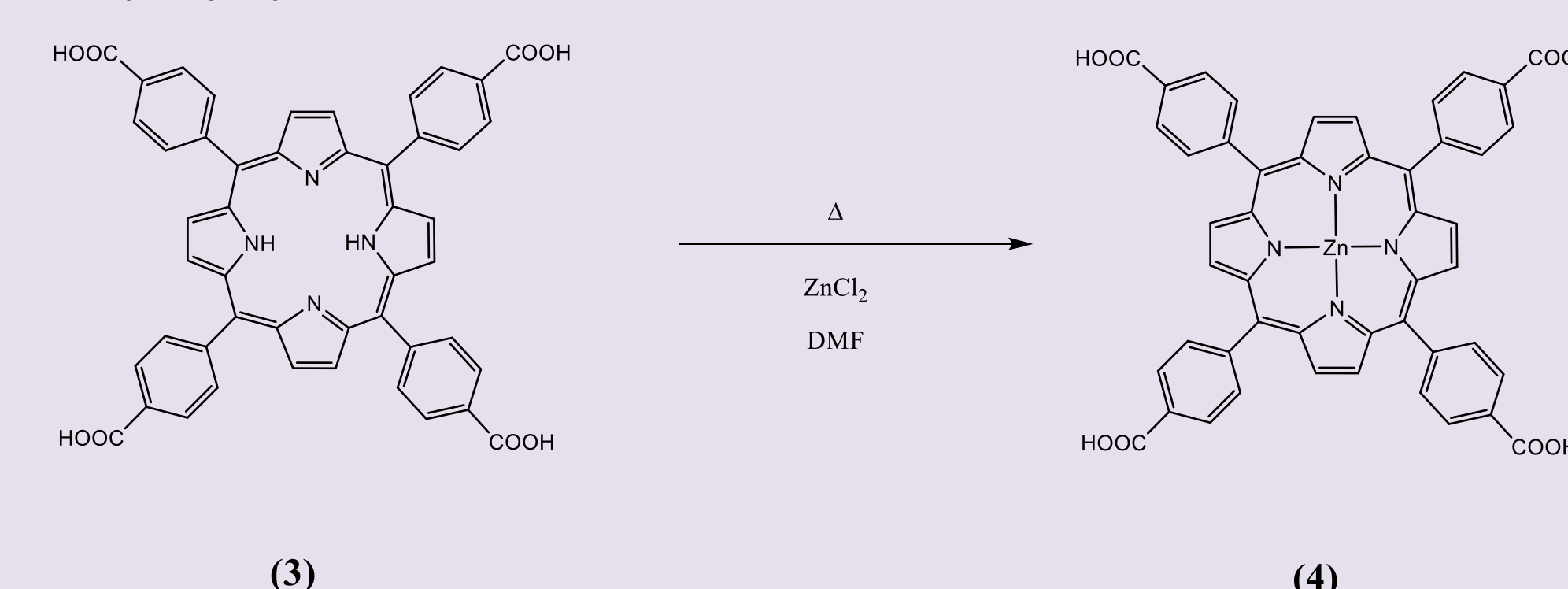
- Porphyrins are proven to be a successful photosensitizing agent, as their conjugated structure enables them to absorb high wavelengths of light.
- Porphyrins play a key role in numerous biological functions, such as electron transport, gene regulation, iron metabolism, and hormone synthesis.
- This research explores the properties of the porphyrin ZnTPP-2MP, and its efficacy in the fragmentation of G-quadruplex using MYC-22 DNA.

Synthesis

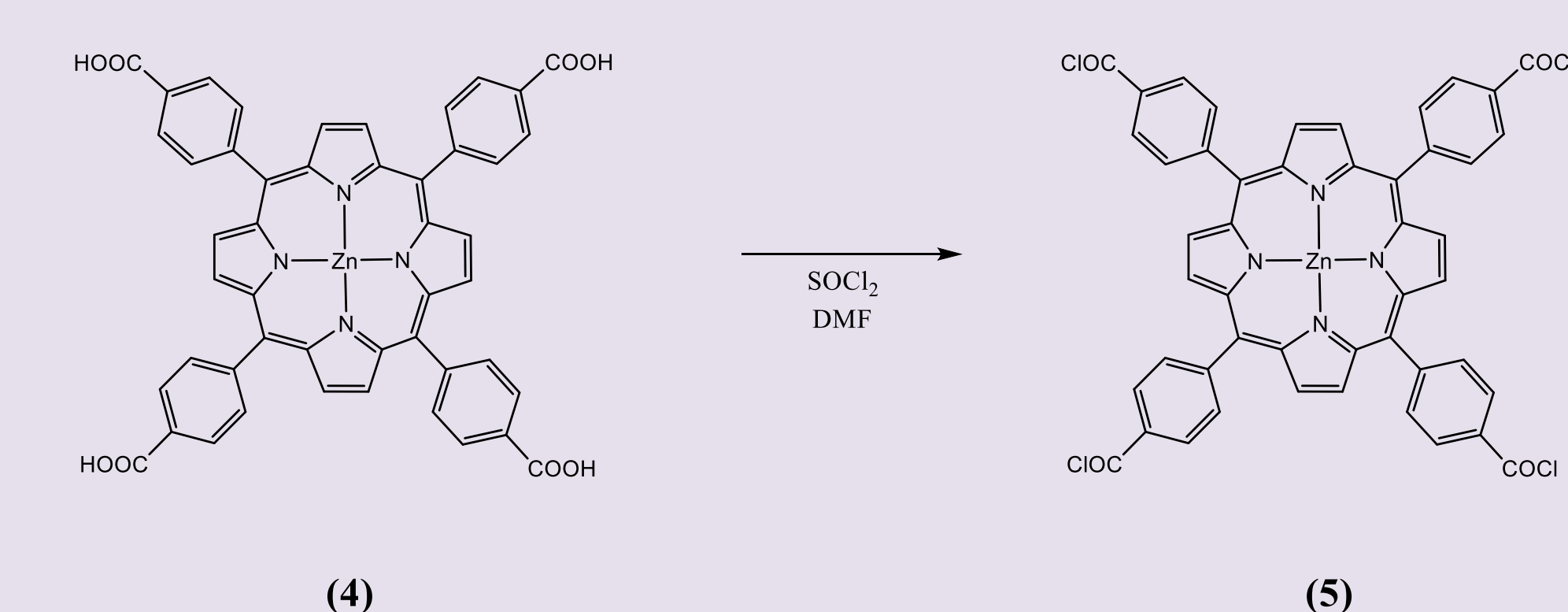
Reaction 1: formation of H₂TPPC (3) by the reaction of 4-formylbenzoic acid (2) with pyrrole (1) in a propionic acid solution.



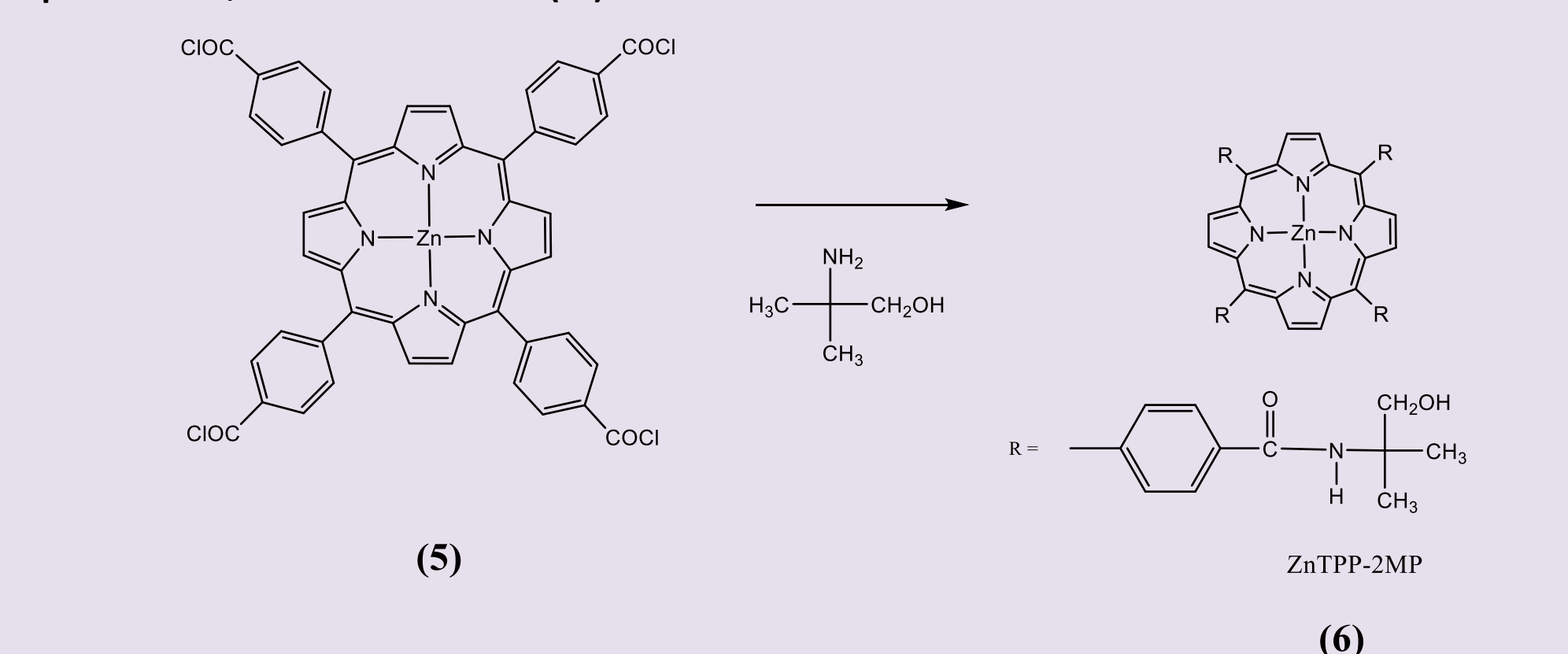
Reaction 2: H₂TPPC (3) is reacted with ZnCl₂ in DMF, forming ZnTPPC – a porphyrin with a metallated core (4).



Reaction 3: ZnTPPC (4) reacts with SOCl₂ in DMF to form an acid chloride porphyrin intermediate (5).

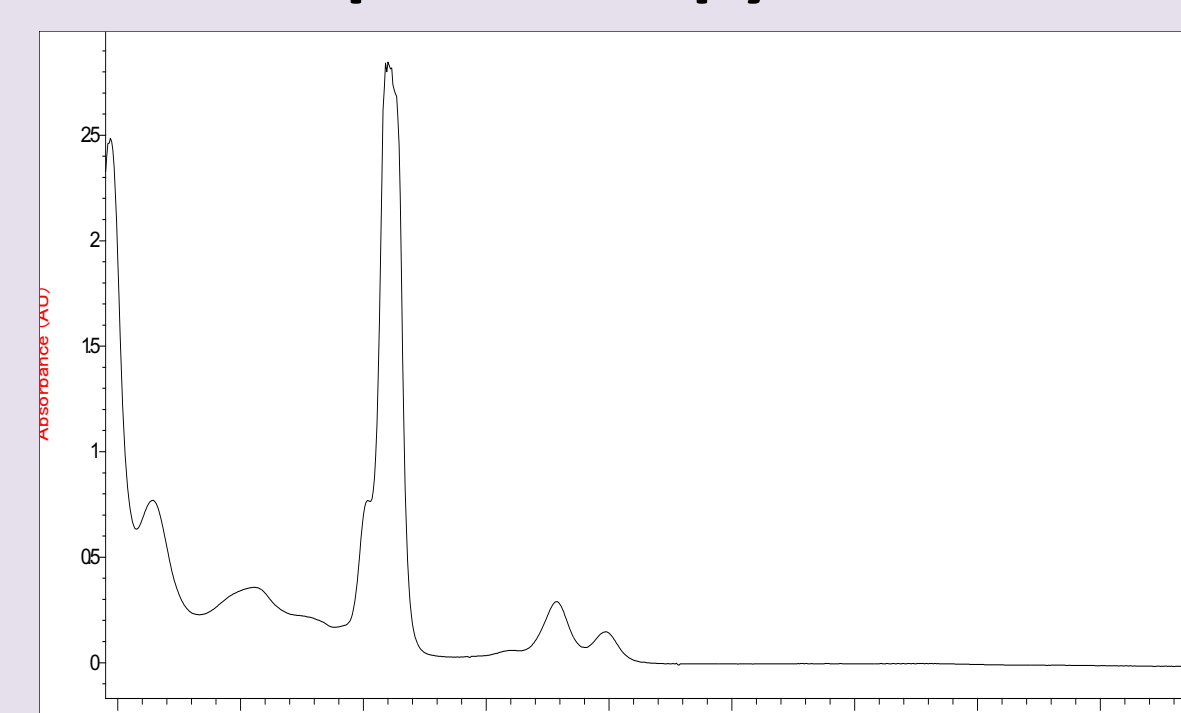


Reaction 4: the acid chloride porphyrin intermediate (5) is reacted with 2-amino-2-methyl-1-propanol in methanol to form the final product, ZnTPP-2MP (6).



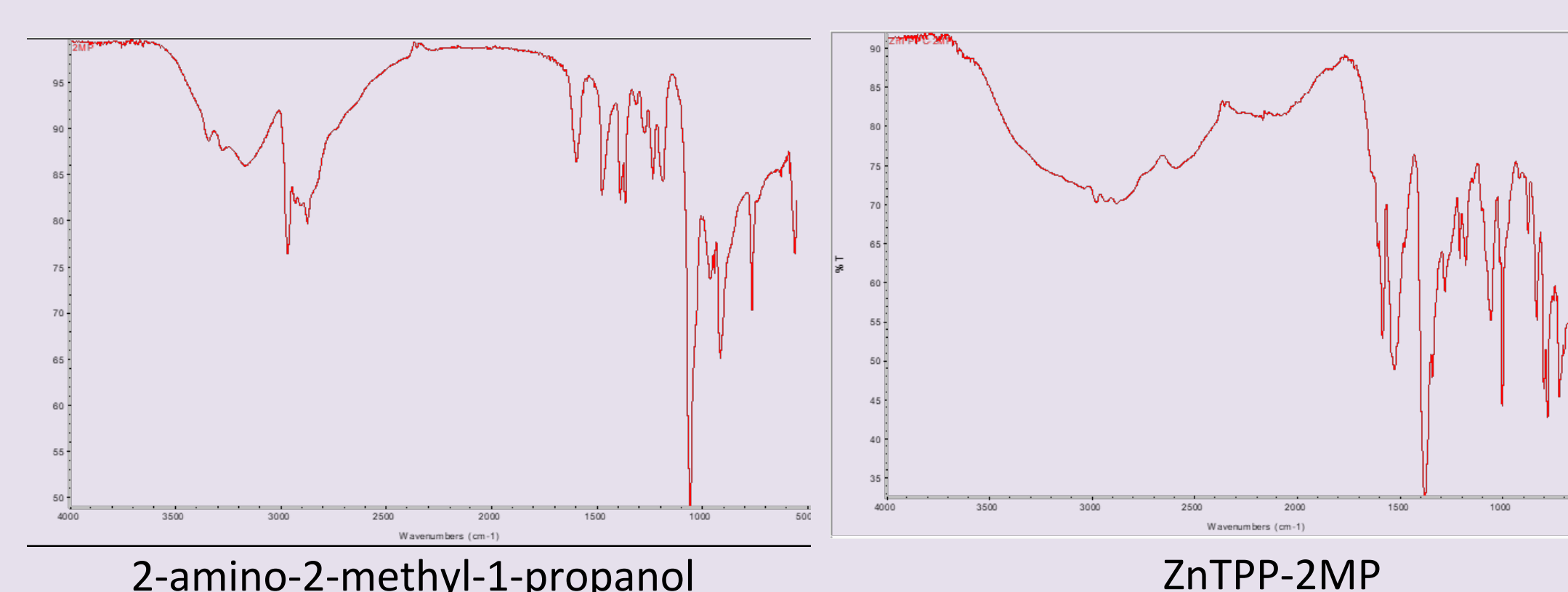
Characterization

UV-vis Spectroscopy

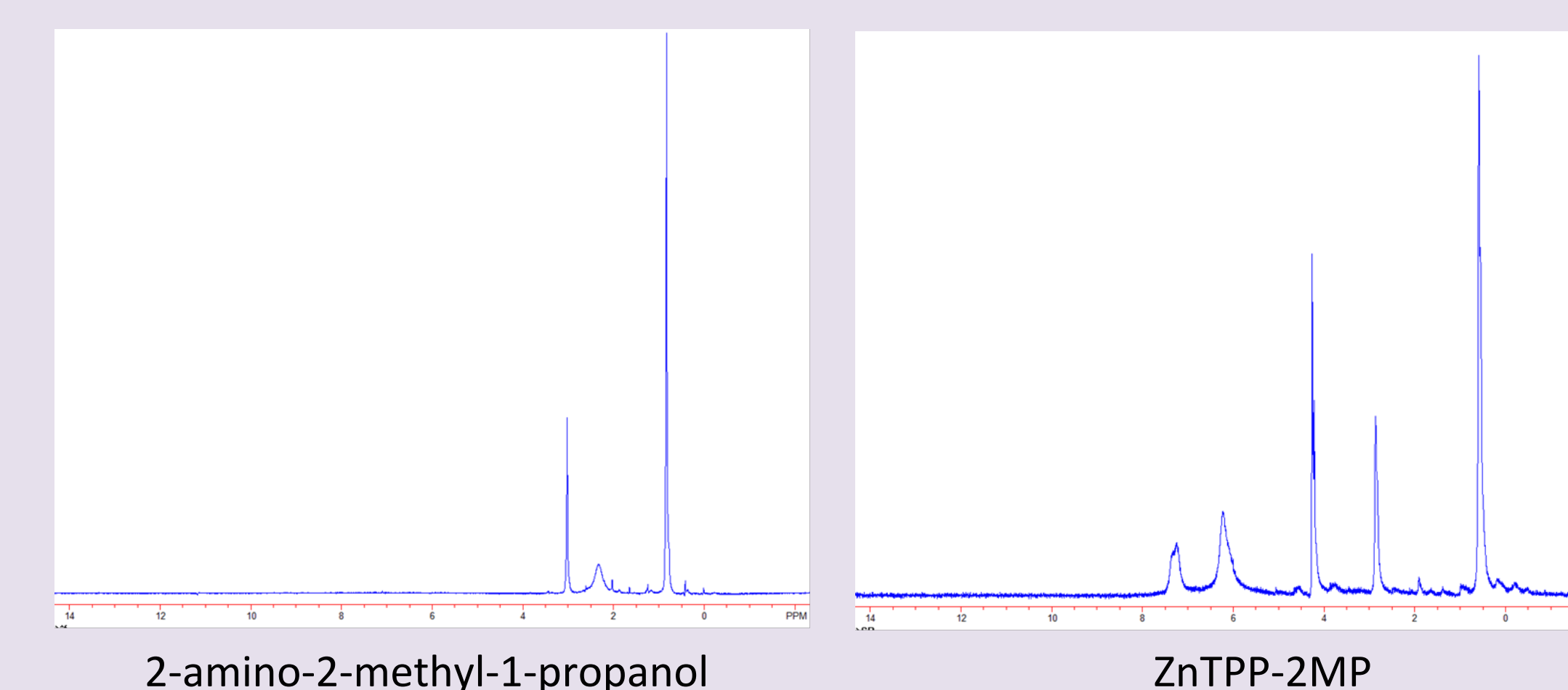


Peaks (nm)	Molar Absorptivity Coefficient (mM ⁻¹ cm ⁻¹)
423	531
557	19.2
597	9.27

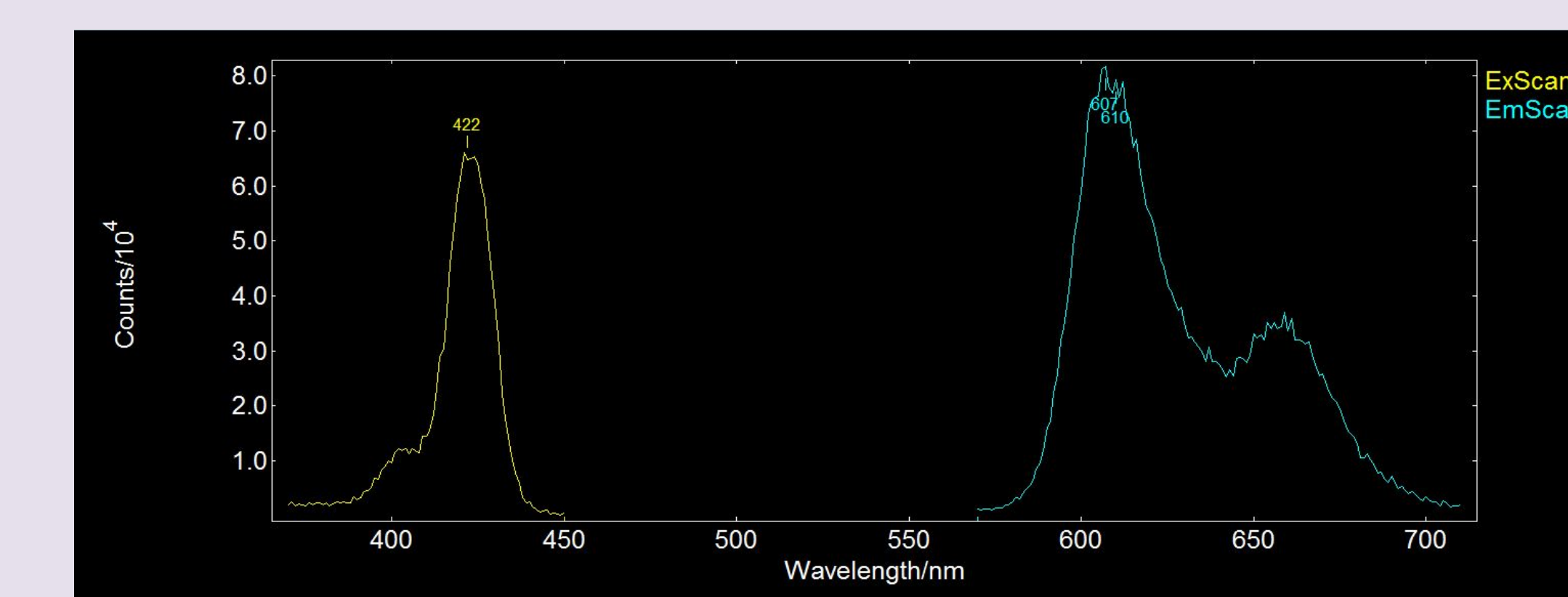
Infrared Spectroscopy



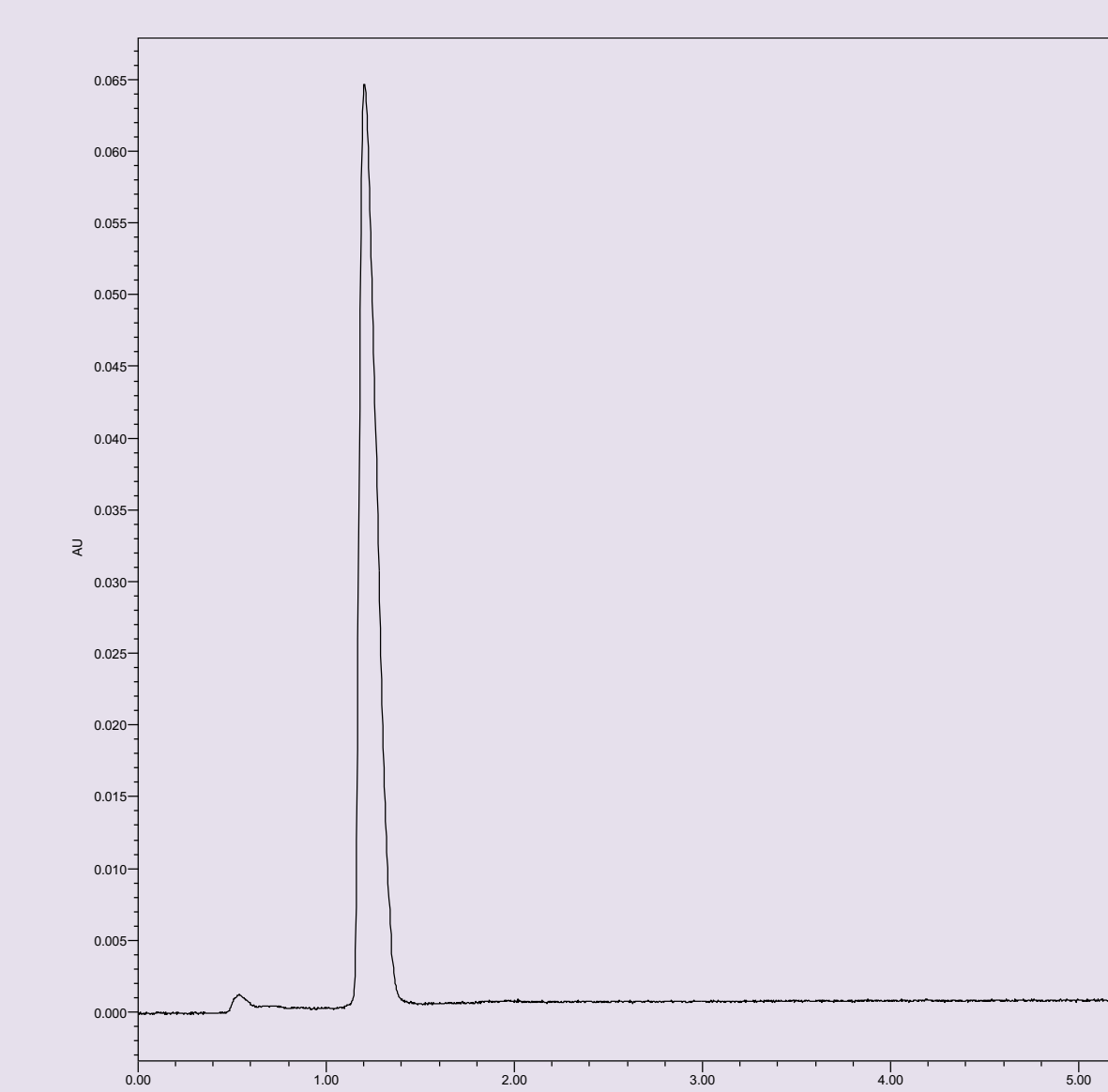
Nuclear Magnetic Resonance Spectroscopy



Fluorescence



HPLC

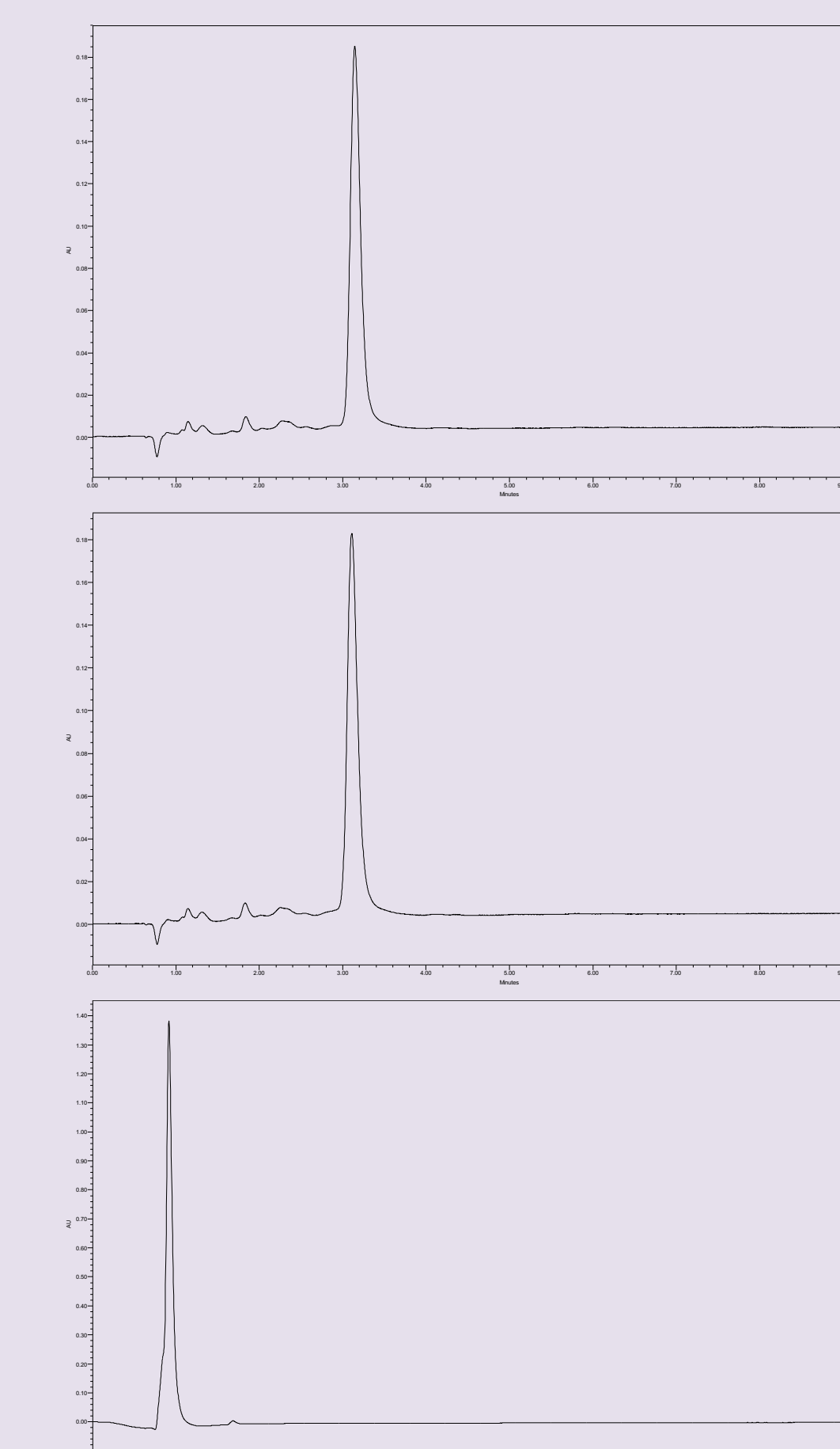


Solvent: 100% acetonitrile
Flow rate: 1.00 mL per minute
Column: Hamilton PRP-1 5 μm 4 x 150 mm
Sample dissolved in H₂O
98.5% purity

Results

Reaction of ZnTPP-2MP with MYC-22 DNA

- HPLC analysis of MYC-22 DNA treated with ZnTPP-2MP indicated fragmentation after exposure to white light for 22 minutes, while DNA kept in the dark showed no fragmentation.



No fragmentation at initial reaction conditions.

No fragmentation after 10 minutes of white light exposure.

Cleavage of MYC-22 DNA sample after 22 minutes of white light exposure.

Conclusions

- A novel water-soluble porphyrin, ZnTPP-2MP, was successfully synthesized.
- The formation of the porphyrin was confirmed through multiple methods of characterization: UV-vis, IR, and NMR spectroscopy, fluorescence, and HPLC.
- When treated with ZnTPP-2MP, MYC-22 DNA samples were cleaved after exposure to white light, making the compound an excellent candidate for photodynamic therapy.

Future Direction

- Perform ROS assays using ZnTPP-2MP.
- Test the cytotoxicity of ZnTPP-2MP using MTT assay with the A549 lung cancer cell line.
- Perform *in vivo* testing using ZnTPP-2MP.

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