Could Salts Be the Answer to Combatting Alzheimer's?

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Introduction

Alzheimer's and Parkinson's Disease are widely known health issues that affect over 50 million people worldwide.[1,2]

From previous research, we know that both diseases cause damage to a cell's mitochondria.[3] The mitochondria produce the cell's energy, making itself negatively charged. If this part of the cell is damaged, then the negative charge is minimized or lost.

This means that a salt (a compound with positively and negatively charged components) can be manipulated to have a visible compound attached to the positive ion.

If there is damage to the mitochondria, the positive ion will not congregate as normal and this will be visible to medical imaging techniques. Therefore, this compound has potential as an early detection method for these devastating diseases.

Theory

A **BODIPY** (BOron-DIPYrromethene) **core** is known to have fluorescent properties[4], this means the compound absorbs radiation that we cannot see (such as UV light) and re-emits it at a longer wavelength which may be visible, or noticeable for medical imaging.

Due to the compound being a **halogen salt** (containing a fluoride, chloride, bromide or iodide ion) there is a good method to exchange the bromide, in this case, for a radioactive $^{19}F^-$ ion. This can then be used as a radiolabel in Positron Emission Tomography (PET) scans, for which scanners are available in most larger hospitals.

The **alkyne group** (C≡C) is within the molecule to allow it to be used in 'click chemistry' to easily attach a biomolecule at this position. This will allow a better uptake in the body, enabling the compound to enter the bloodstream and reach its targeted organelles (the mitochondria).

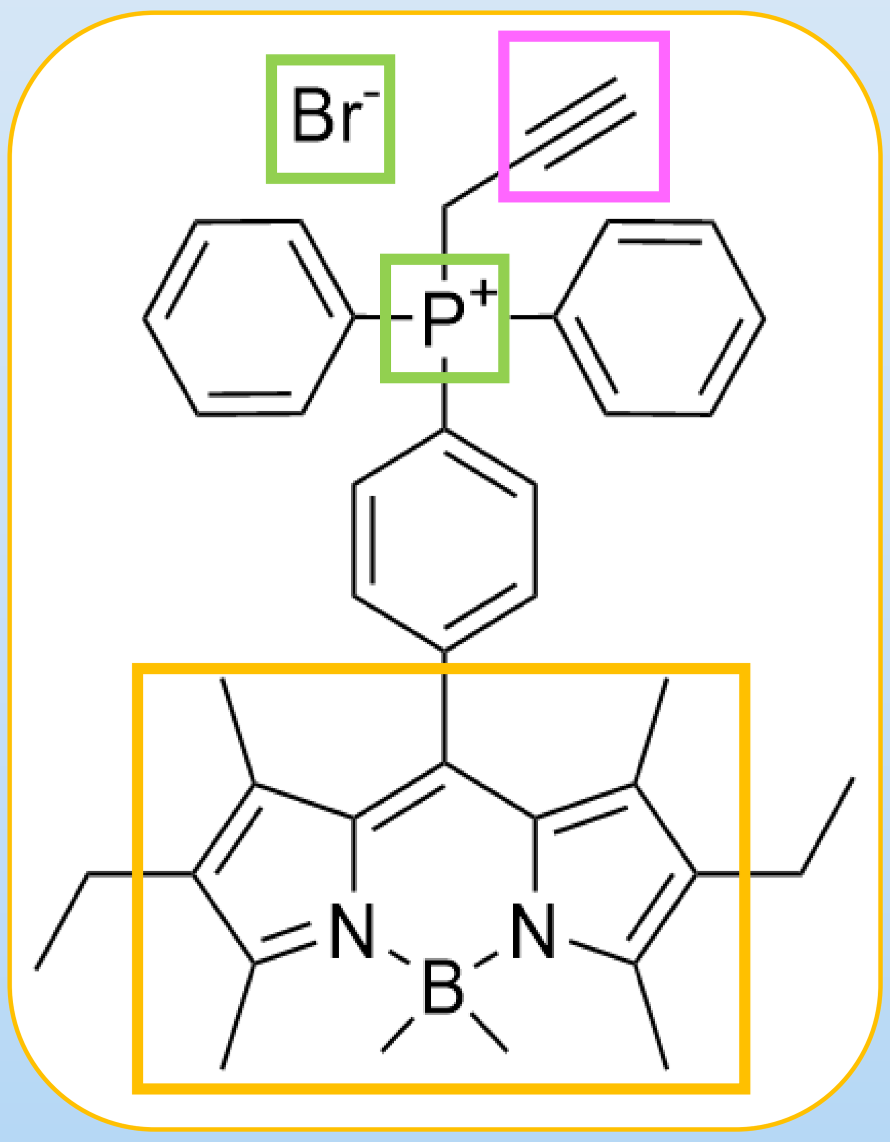


Figure 1: The final product (phosphonium salt of BODIPY), labelled with colour for clarity.

Synthesis

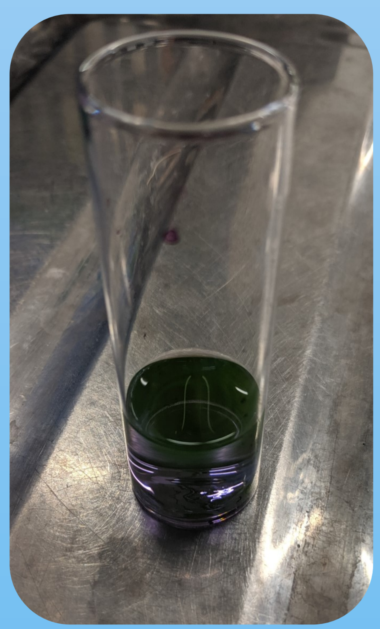
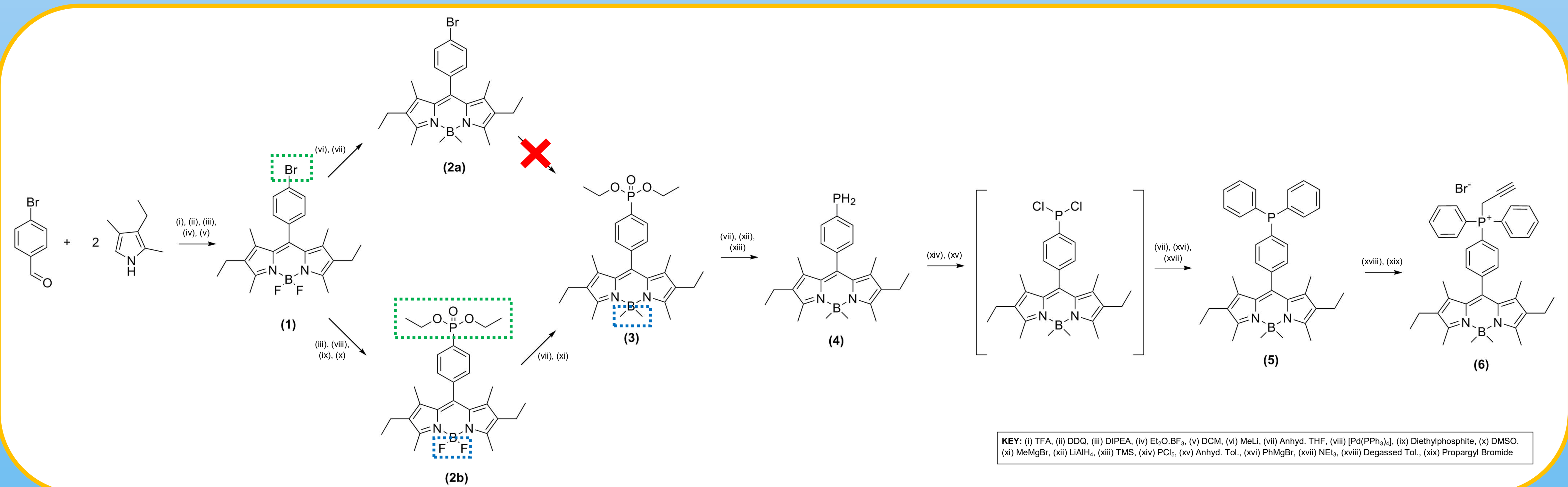


Figure 2: The dichromatic (two-coloured) nature of the dyes synthesised.



The full 7-step reaction scheme to achieve the final product from available starting materials. The route via compound **2a** was attempted first but this did not produce the target (**3**) so the route via **2b** was successfully used instead. Most steps also included purification by column chromatography to achieve a more purified sample.

Figure 3: A typical column chromatography, used for purification of each compound.

Analysis

NMR (Nuclear Magnetic Resonance) is a vital analytical technique used in chemistry. It can help identify and characterise many different classes of compounds. It is also able to give some assessment of purity and to identify changes to a compound's structure or composition.

Shown (*right*) are some spectra obtained from compounds **1, 2b** & **3** above with the key differences highlighted. The data points from these were also cross-referenced to previously reported data[5,6,7] to ensure the desired compounds were correctly synthesised.

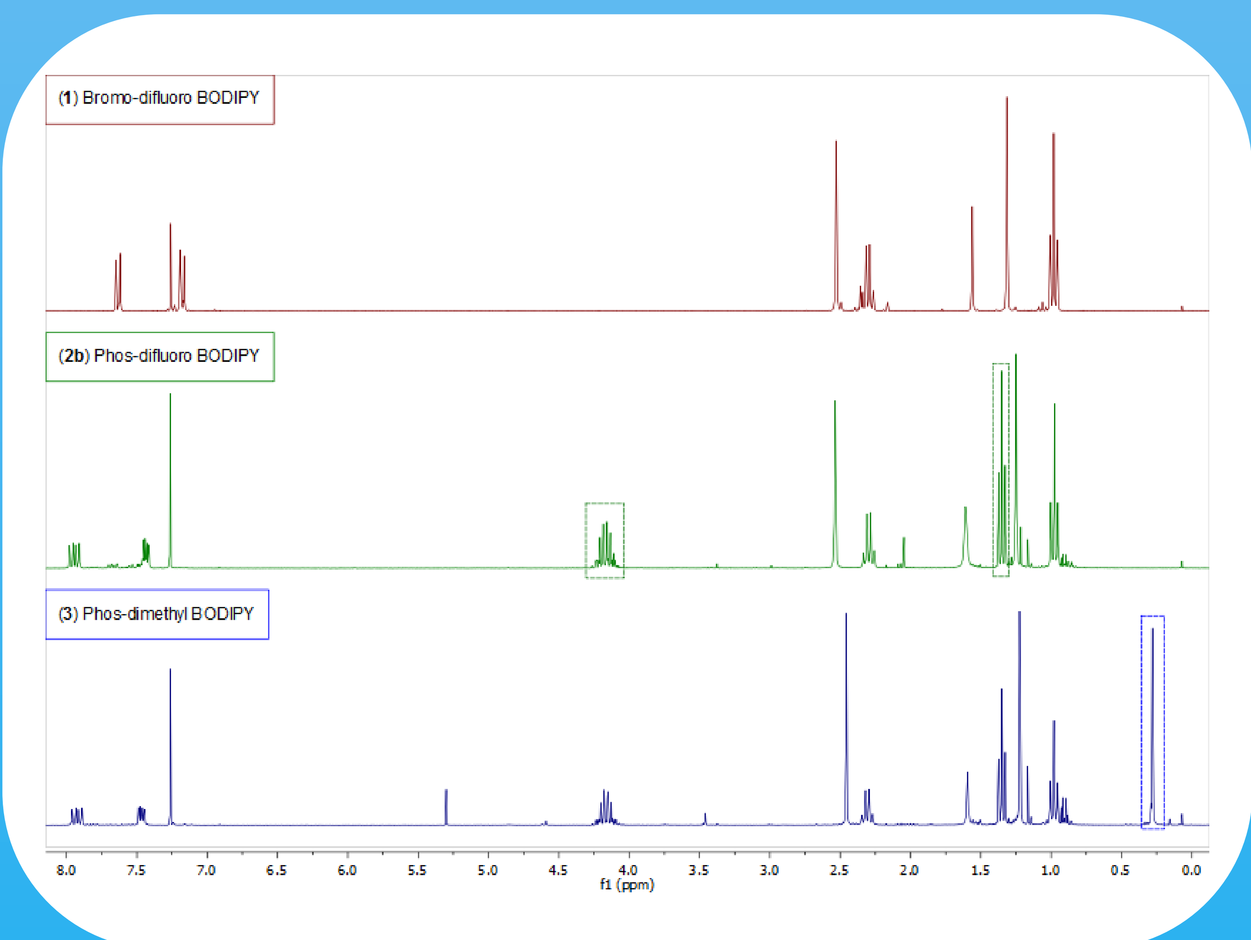


Figure 4: Three ^{1}H NMR spectra for three different compounds, as labelled. The differences in the spectra are emphasised and demonstrated in the *Synthesis* section above.

Acknowledgements

I would like to thank Newcastle University and Dr Lee Higham for their funding. I would also like to thank the LJH Research group for their support, expertise and use of equipment.

References

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