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Synthesis of Novel Fluorescent Probes for the Early Diagnosis of Alzheimer's Disease

UNLV

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Introduction

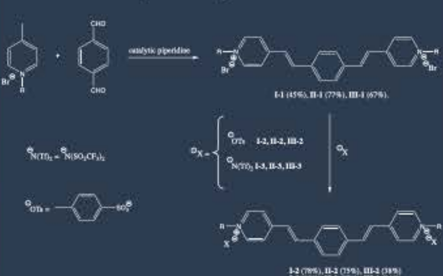
- Alzheimer's Disease (AD) is a neurodegenerative disease that manifests itself through a progressive decline in motor function, memory, and cognition.
- AD is closely associated with the accumulation of amyloid- β (Aβ) proteins that form insoluble plaques.
- The formation of Aβ is a hallmark of AD and can serve as a means for diagnosis.

Objectives

- To synthesize a series of potential candidates for a practical and safe means to detect AD in its early stages via Aβ binding.
- To confirm the identity of the products by ^{1}H & ^{13}C nuclear magnetic resonance (NMR) and elemental analysis (EA).
- To determine melting point, thermal stability, and fluorescent properties of the products by Differential Scanning Calorimetry (DSC), Thermogravimetric Analysis (TGA), and Fluorescence Spectroscopy, respectively.

Methodology

Scheme 1. Synthesis of γ-picolinium bromide salts



Scheme 2. Synthesis of *p*-styryl pyridinium salts

Results

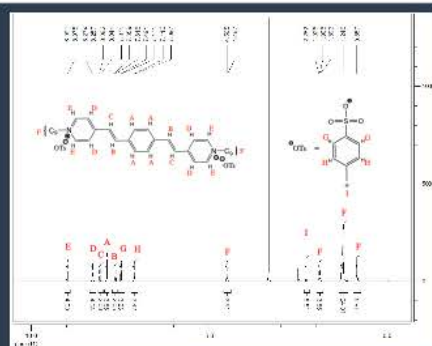


Figure 1. ^{1}H NMR spectrum of *p*- C_9-styryl pyridinium OTs in d_6-DMSO.

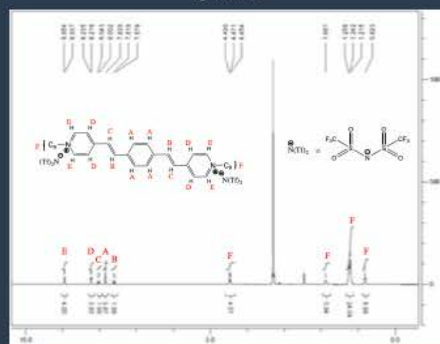


Figure 2. ^{1}H NMR spectrum of *p*- C_9-styryl pyridinium $N(Tf)_2$ in d_6-DMSO.

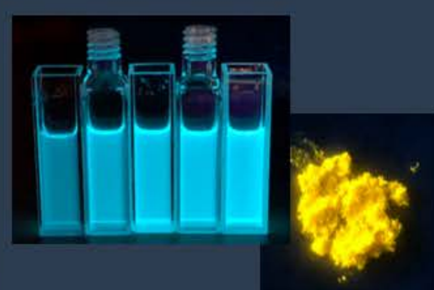


Figure 3. Serial dilutions in methanol (10^{-5} M) and solid state of *p*- C_9-styryl pyridinium OTs showing fluorescence under UV-light.

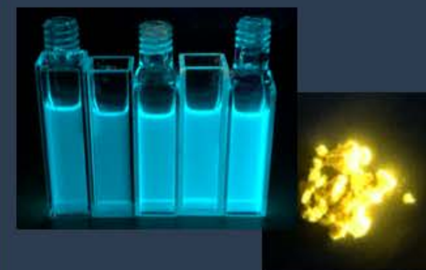


Figure 4. Serial dilutions in methanol (10^{-5} M) and solid state of *p*- C_9-styryl pyridinium $N(Tf)_2$ showing fluorescence under UV-light.

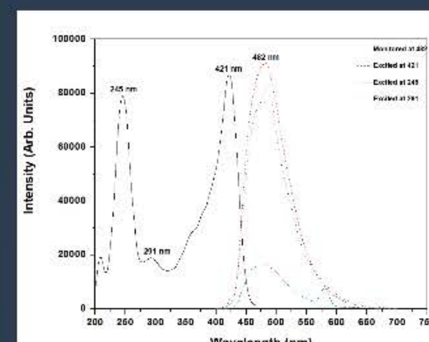


Figure 5. Emission/Excitation spectra of *p*- C_9-styryl pyridinium OTs in methanol.

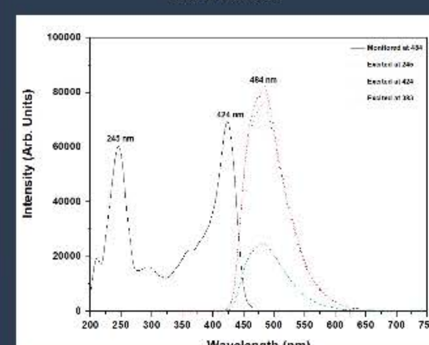


Figure 6. Emission/Excitation spectra of *p*- C_9-styryl pyridinium $N(Tf)_2$ in methanol.

Conclusions

- The C_6, C_9, and C_{12} *p*-styryl pyridinium salts containing bromide, tosylate, and triflimide counterions were synthesized.
- The identities of the *p*-styryl pyridinium salts were confirmed by ^{1}H NMR, ^{13}C NMR, and elemental analysis.
- The UV-Vis spectra of *p*-C_9 styryl pyridinium OTs and $N(Tf)_2$ showed λ_{max} peaks at 383 nm and 384 nm in methanol, respectively.
- The emission spectra of *p*-C_9 styryl pyridinium OTs and $N(Tf)_2$ displayed λ_{em} peaks at 482 nm and 484 nm in methanol, respectively.
- Solubility test shows C_6, C_9, and C_{12} *p*-styryl pyridinium salts are soluble in DMSO, making it suitable for *in vivo* applications.

Future Work

- Further fluorescence measurements in different solvents
- Further counter ion exchanges
- Carbon chain length extensions
- Structural modifications of meta- and ortho- salts
- Biological testing *in vivo* for fluorescent probes binding to Aβ insoluble plaques

Acknowledgements

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