„Babeș-Bolyai“ University of Cluj-Napoca

Faculty of Chemistry and Chemical Engineering

PhD Thesis Abstract

Synthesis and characterization of novel electron-rich phenothiazines

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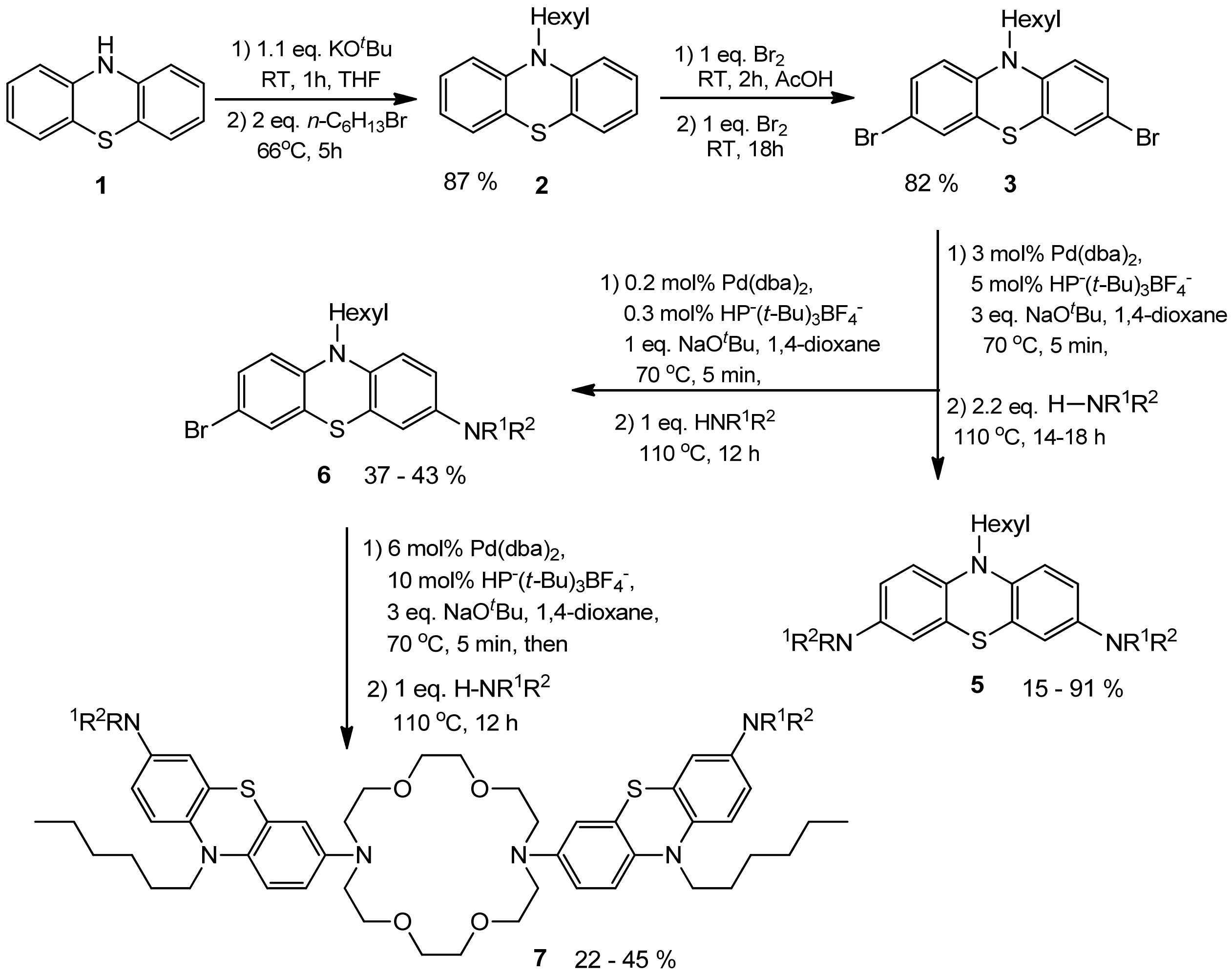
Key words: electron-rich phenothiazine, polyaniline, amino-phenothiazine, *Buchwald-Hartwig* coupling, diazacrown ethers, cyclic voltammetrie, DFT computations, hole-transport materials, chemosensors.

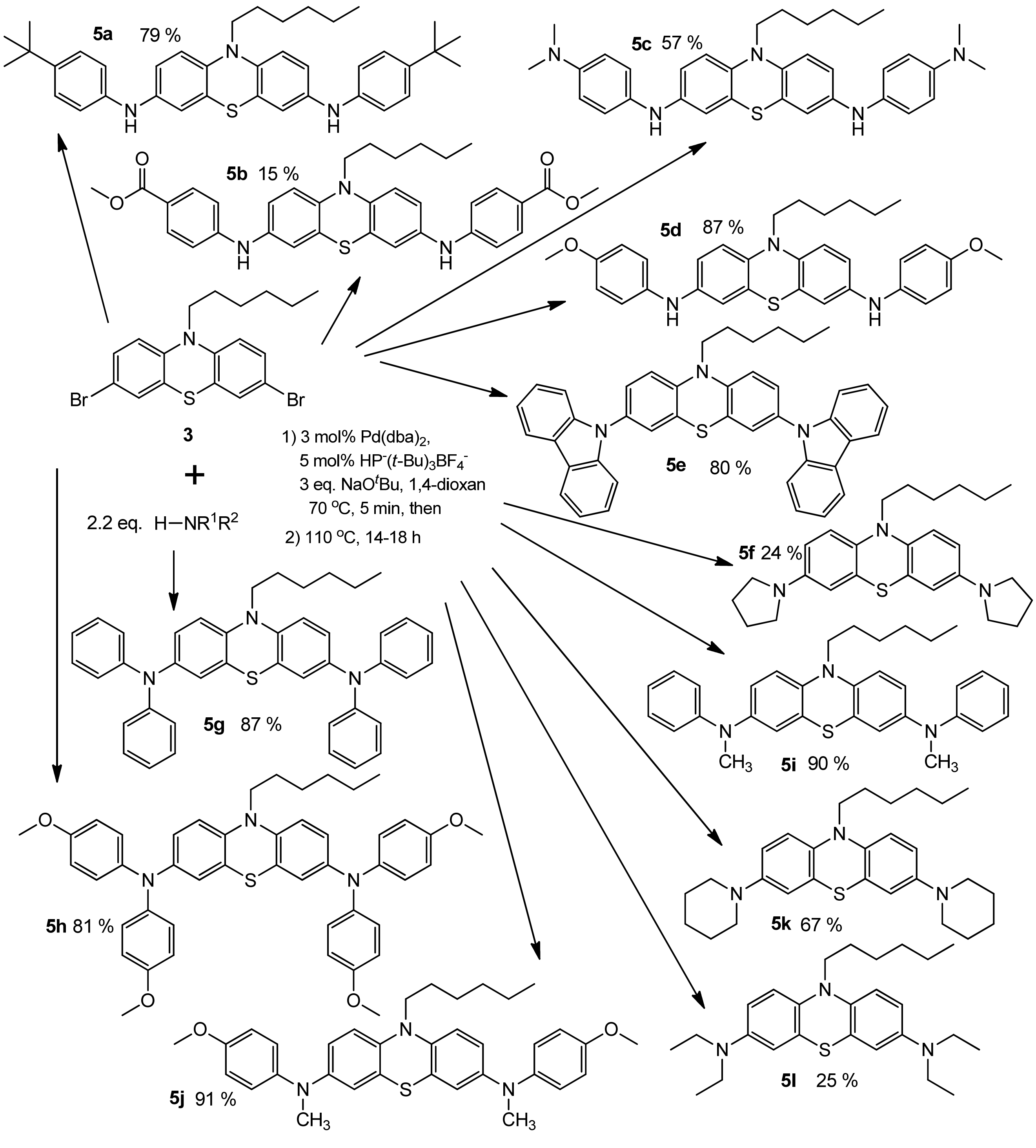
Abstract

Phenothiazine[1] derivatives have been widely used in the dyestuff industry,[2] pharmacology[3],[4],[5],[6],[7],[8],[9],[10],[11],[12] and most recent studies focus mainly on their applications in material science.[13],[14],[15] This is due to their redox activity and propensity to form stable radical cations.[16]

Starting from 10*H*-phenothiazine **1**,**[17]** a whole toolbox of *N*-amino-phenothiazine compounds[18] can be created in a few straightforward synthetic steps (**Scheme 1**). For the sake of solubility, *n*-hexyl substituents are introduced onto the deprotonated phenothiazine nitrogen atoms by nucleophilic substitution. Upon bromination, **2** is readily converted into the 3,7-dibromo derivative **3** by electrophilic aromatic substitution.



Scheme 1: General synthesis of amino-phenothiazine derivatives



Scheme 2: Synthesis of di-coupled amino phenothiazines **5 a - l**

3,7-dibromo-10-hexyl-10*H*-phenothiazine **3** is a quite unique and versatile starting compound that can be coupled via a *Buchwald-Hartwig* amination methodology to a vast series of amines (**Scheme 1 and Scheme 2**).

Compounds **5 a – l** absorb in UV/Vis in the area 316 nm and 348 nm and emission from 444 nm to 496 nm with Stokes shifts of 7000 to 11000 cm^{-1} (**Figure 1**). Quantum yields range from 0.1 to 19 %.

The most spectacular results come from cyclic voltammetrie where the first oxidation potential ranges from 0 mV (for compounds **5f** and **5l**) to 770 mV and second oxidation potential from 360 mV to 1060 mV (**Figure 1**). Compounds **5e** and **5h** show also a third quasi-reversible oxidation at 1250 mV and 1210 mV respectively.

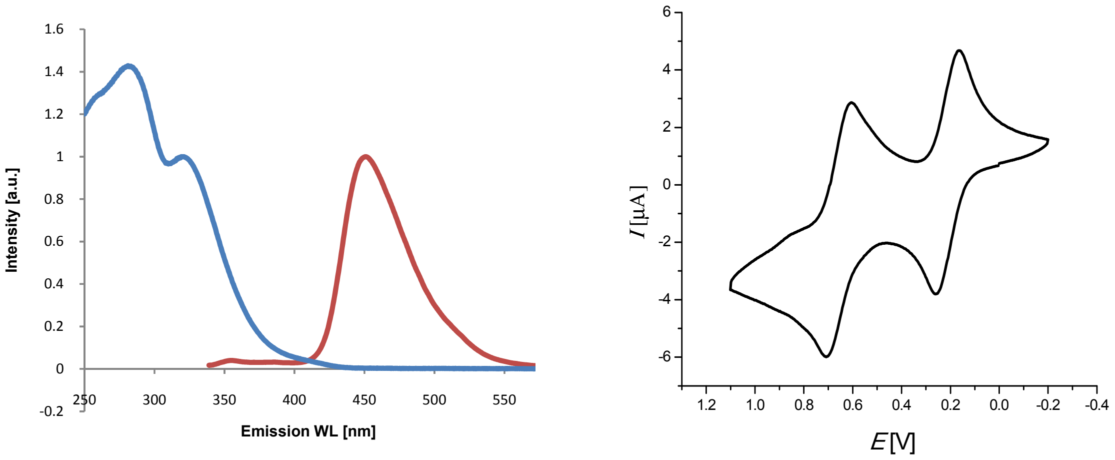
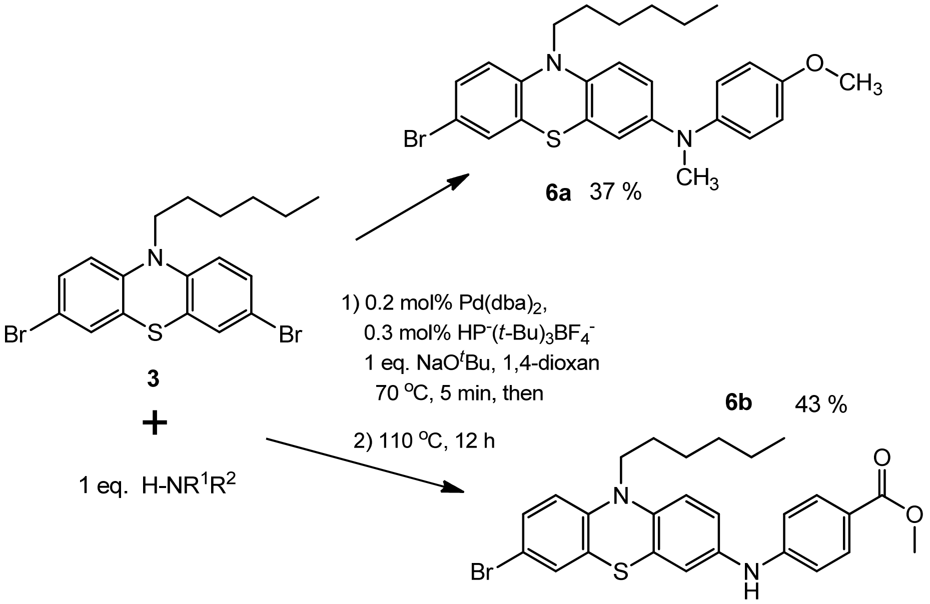


Figure 1: Absorption, emission and cyclo-voltammogram of compound **5d**

Compound **5l** has the largest *semiquinone* formation constant of 14.2×10^{8}, which is a measure of how much of the semiquinone (the intermediate radical cation) is formed before the apparition of the fully oxidized species.[19]

DFT computations[20] were also performed and showed a good correlation between the HOMO energy and the oxidation potentials and between the HOMO-LUMO gap and absorption energy.



Scheme 3: Synthesis of mono-brominated-mono-amino phenothiazines **6 a, b**

Also starting from the dibrominated phenothiazine **3**, and using a modified method for the *Buchwald-Hartwig* coupling, the mono-brominated-mono-amino coupled phenothiazines **6**, can be obtained (**Scheme 3**). These compounds are extremely valuable building-blocks in the synthesis of un-symmetric compounds.

With the mono-brominated compounds **6**, another *Buchwald-Hartwig* coupling procedure was performed in order to couple them to diaza-18-crown-6 ether **4b**. Thus a new class of compounds, electron-rich phenothiazines coupled to diaza-crown ethers **7**, was obtained (**Scheme 4**) and investigated.

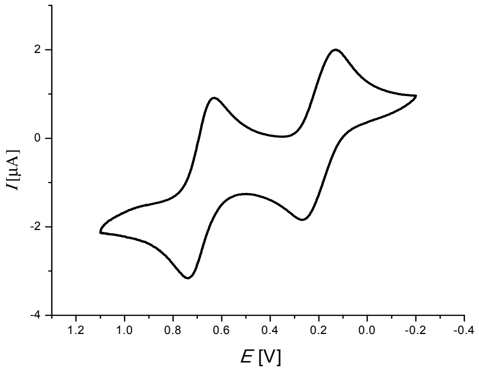
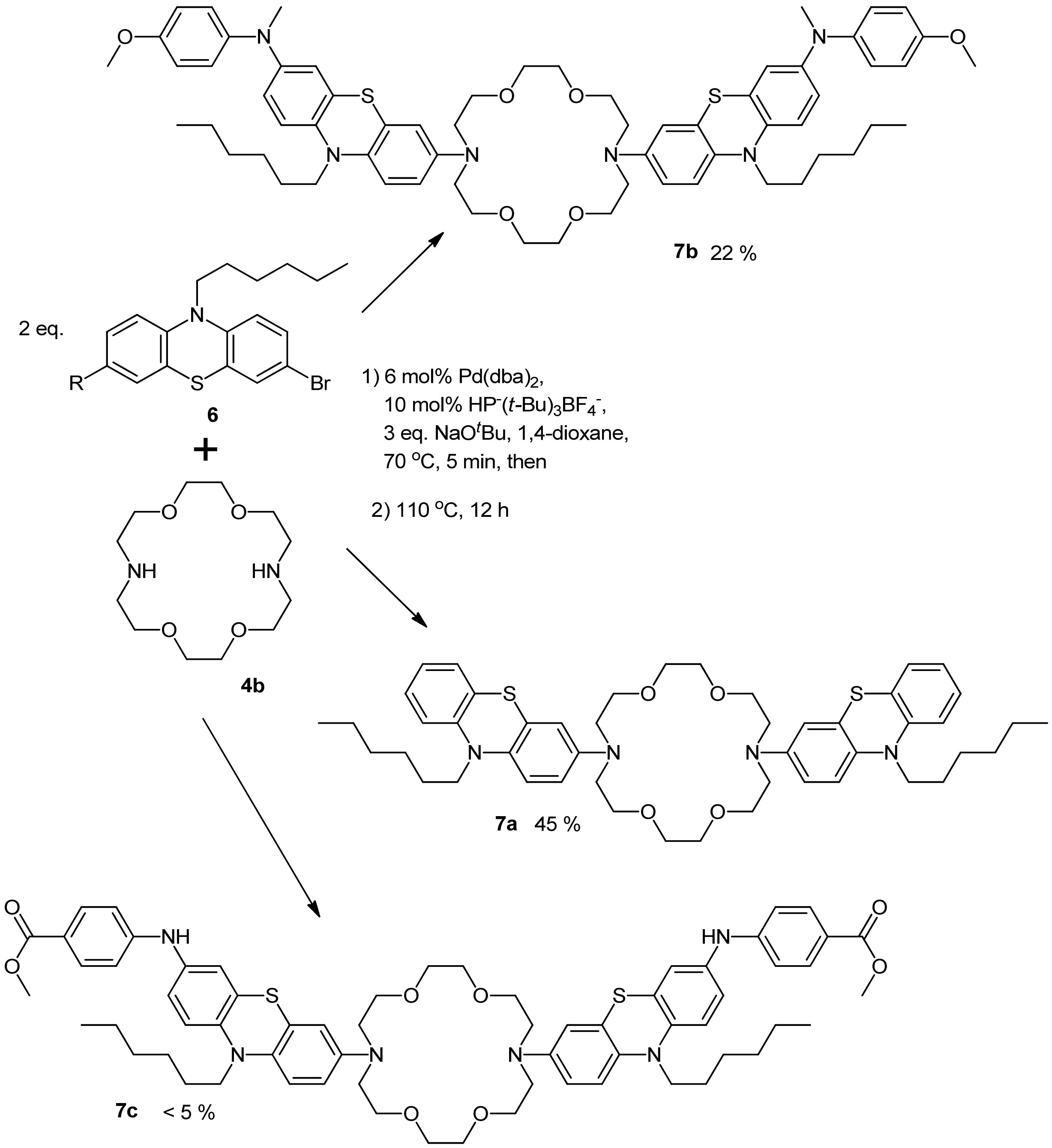


Figure 2: Cyclo-voltammogram of compound **7b**



Scheme 4: Synthesis of the phenothiazine coupled diaza-crown ethers **7 a - c**

Compounds **7a** and **7b** showed two reversible oxidations at 330 mV and 915 mV, respectively 120 mV and 610 mV (**Figure 2**).

UV/Vis absorption maxima is located at 321 nm for both compounds and emissions at 464 nm and 461 nm with quantum yields of 0.9 and 0.6 %.

Metal binding tests (Ca, Zn, Mg, K and Na triflates) were also performed and determined by UV/Vis absorption and emission (**Figure 3**). Metal complexes of compound **7a** showed a slight hypsochromic shift of up to 8 nm for the absorption and up to 21 nm in the emission with increase in the quantum yields up to 2.3 %.

Complexes of **7b** also showed a slight hypsochromic shift of up to 9 nm in the absorption and bathochromic shift of up to 8 nm in the emission with quantum yields increase to 1 %.

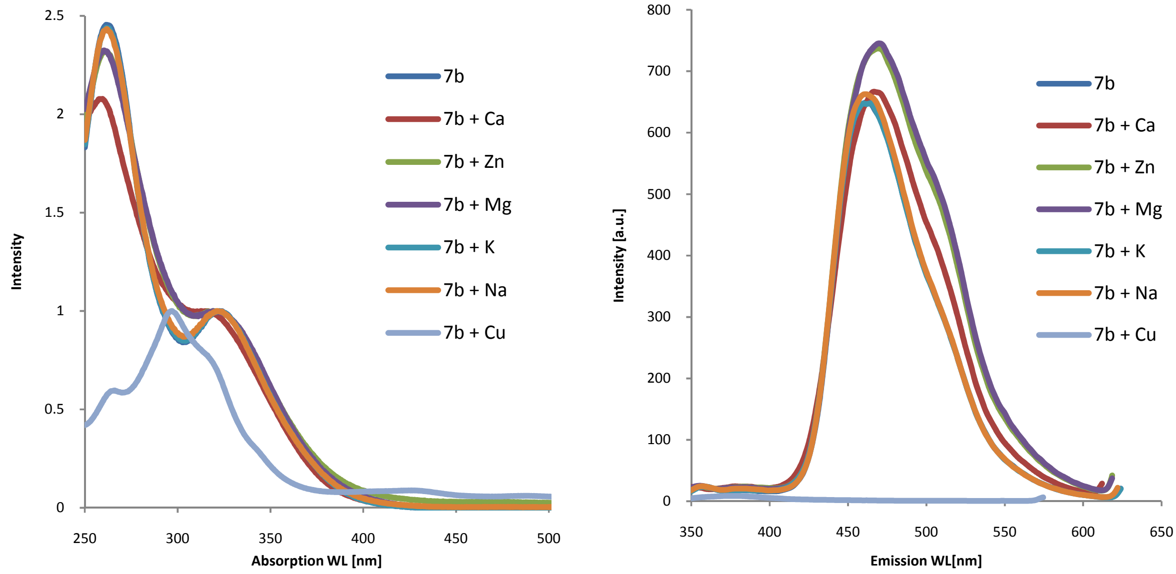


Figure 3: Absorption and emission spectra of compound **7b** with various metal salts

In the case of the complex with Cu triflate wide peaks in the 400 to 550 nm area in the absorption spectra and a quenching of fluorescence appeared, due to the reduction of Cu^{II}.[21]

Conclusions

A method for the *Buchwald-Hartwig* **di**-coupling of dibromo-phenothiazine with various primary, secondary, aromatic, cyclo-alifatic or mixed amines was developed and 12 new compounds were synthesized with yields from 15 % to 91 %; the structures of these compounds were established by mass, NMR, elemental analysis and IR measurements.

Spectroscopical characterization was performed, leading to Stokes-shifts between 7000 and 11000 cm^{-1} and quantum yields of up to 19 %. Electrochemical measurements were also very satisfactory with low first (from 0 mV to 390 mV) and second oxidation potentials (from 524 mV to 813 mV) for 11 out of 12 compounds. Molecular modelling on a DFT level was peformed and all practical measurements were correlated to and supported by these models.

Summing up, the newly synthesized compounds make good candidates for hole-transport and material science applications.

A method for the *Buchwald-Hartwig* **mono**-coupling of dibromo-phenothiazine with various amines was developed and 2 new compounds were synthesized with yields from 37 % to 43 %. Using the method for the previous project these mono-brominated-mono-aminated phenothiazines were successfully coupled to diaza-crown ethers leading to 2 new compounds with yields from 22 % to 45 %. All structures for the compounds were established by mass, NMR and IR measurements.

Spectroscopical characterization was performed, leading to Stokes-shifts of 9400 and 9600 cm^{-1} and quantum yields of 0.9 and 0.6 %. Electrochemical measurements were performed (cyclic voltammetrie) giving first oxidation potentials of 330 mV and 120 mV, while second oxidation potentials were of 915 mV and 610 mV.

For the newly synthesized crown ethers the complexes of 6 metals were investigated by UV/Vis absorption and emission. The absorption maxima showed a red-shift of up to 9 nm for the complexes of both compounds while the emission maxima showed a red-shift of up to 20 nm for one compound and a blue-shift of up to 8 nm for the other. Quantum yields increased from 0.9 up to 2.3 and from 0.6 up to 1 respectively.

The newly synthesized crowns clearly showed the capacity to bind metals and have the possibility to be further investigated as chemosensors for metals.

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Poster presentations

1. "Novel electronrich amino substituted phenothiazine derivatives with tunable electronic properties", Iani S. Pereteanu, Thomas J. J. Müller, poster presented at the ICPOC 21: 21st IUPAC Conference on Physical Organic Chemistry, 9 – 13 September 2012, Durham University, UK.

2. "Synthesis and DFT calculations of Alkynylated Phenothiazines", Iani Pereteanu, Luiza Gaina, Luminita Silaghi-Dumitrescu, poster presented at the International Conference MOLMOD – Molecular Modelling in Chemistry and Biochemistry, 28 May 2010, Cluj – Napoca, Romania.

Publications

1. L. Gaina, T. Dallos, C. Cristea, T. Lovasz, I. Pereteanu, M. Surducan, L. Silaghi-Dumitrescu, "Microwaves assisted *N*-alkylation of phenothiazine", *Studia Universitatis Babes-Bolyai,Chemia,* **2010**, 2, 97 – 102.

- 2 other manuscripts still in progress.