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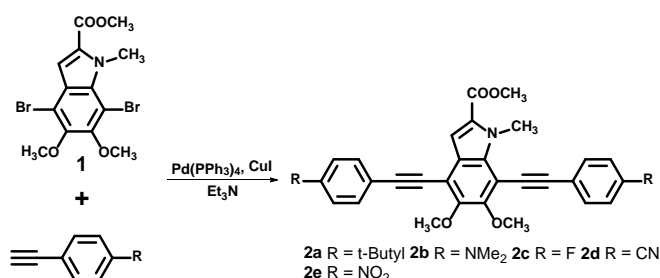
Effects of Structural Variations on the Optical and Electronic Properties of Eumelanin-Inspired Small Molecules

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In this work, five new eumelanin-inspired indole small molecules have been synthesized which differ by the substituents attached to the para positions of the phenylene ring. The effects of structural variations on the optoelectronic properties of these molecules have been studied by combining both synthetic and computational techniques. It has been found that Density Functional Theory (DFT) is well suited to predict energetic values for HOMOs, with maximum difference between experiment and theory error of 6.2% while time-dependent density functional theory (TD-DFT) predictions for LUMO energies differ at most by 5.2%. The results suggest that the frontier orbitals, and hence the bandgap of the molecules can be manipulated by putting different electron donating and electron withdrawing groups at the para position of the phenylene ring. DFT can be useful in the prediction of the eigenvalues of molecular orbitals of eumelanin-inspired conjugated molecules. Furthermore, the effect of protonation on dimethylamino functionalized small molecule showed potential application as acidochromic sensor.

Introduction

Melanins are naturally occurring pigmentary macromolecules found throughout nature.¹ In mammals, it occurs in the hair, eyes, skin and brain.¹⁻³ Two major types of melanin are pheomelanin and eumelanin. It is well-known that eumelanin, the black-brown variety of melanin, results from the oxidative polymerization of two building blocks, 5,6-dihydroxyindole (DHI) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA).⁴ Since the groundbreaking discovery that natural and synthetic eumelanin have semiconducting properties, eumelanin-based materials have gained much attention for use in various applications.⁵⁻¹³ Recently, Meredith and coworkers reported that melanin is an electronic-ionic hybrid conductor, rather than the amorphous organic semiconductor, which opens new opportunities in bioelectronics given its biocompatibility.¹⁴⁻¹⁷ Although the overall composition of the eumelanin is reasonably understood, the exact structure remains ambiguous.¹⁸ Others have synthesized the undefined eumelanin materials via oxidative polymerization of the DHI and DHICA or dopamine.¹ In contrast, we have employed a



Scheme 1: Synthesis of Eumelanin-Inspired Small Molecules 2a-e.

new approach to elucidate and enhance the optical and electronic properties of natural eumelanin by methodically modifying the structure of a eumelanin-inspired indole core. The work demonstrated that a eumelanin-inspired core, 4,7-dibromo-5,6-dimethoxy-N-methyl-1H-indole-2-carboxylate (DBI), could be utilized as a bioinspired building block for organic semiconductors.¹⁹ Our previous data also suggested that with proper substitution on the phenylene ring system, the optoelectronic properties could be tuned.¹⁹ To conduct investigations of the effect of substituents (or structural variations) on the optoelectronic properties of the eumelanin-inspired indole core, five new eumelanin-inspired small molecules were synthesized and differ by substituents attached to the para positions of the phenylene ring. Herein,

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we demonstrate that different electron withdrawing groups (EWGs) and electron donating groups (EDGs) are effective in manipulating the highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO), and hence bandgap. Using a combination of synthetic and computational methods, we studied the tunability of the absorption and emission properties of functional eumelanin-inspired compounds **2a-e** based on the substitution on the phenyl ring. We also present the effect of protonation on optical properties of the dimethylamino compound **2b**.

Synthesis

Efforts were directed to synthesize eumelanin-inspired small molecules whose properties can be tuned based on the certain substitution. The 4,7-positions of the DBI were functionalized with phenyleneethynylene rings with EWGs and EDGs. Previously, the synthesis of two eumelanin-inspired small molecules were reported from our laboratory.¹⁹ The syntheses of the derivatives of **1** were achieved by using a similar approach and are shown in the Scheme 1. The reaction yields ranged from 42 % to 99 %.

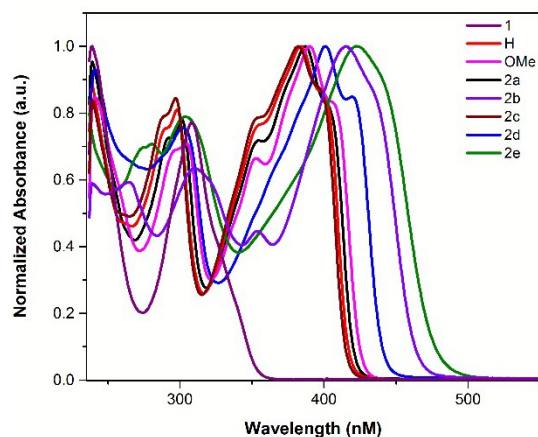


Fig. 1: UV-vis absorption spectra of compound **1** (DBI)*, R= H*, OMe* and compounds **2a-e**. *Note: These compounds have been previously reported.¹⁶

Results and Discussion

The absorption spectra are shown in Fig. 1. The UV-vis absorption and the emission data of the compounds **2a-e** are summarized in Table 1. All compounds, except for the unsubstituted DBI core, exhibited two major absorption peaks. The high energy absorption was observed in the range of 250-350 nm, while the low energy absorptions were in the range of 380-425 nm. The maximum absorption (λ_{max}) increased as the electron-donating strength of the substituent on the phenyl ring increased. The alkyl substituent had the lowest λ_{max} (387 nm), followed by the alkoxy (390 nm) and dimethylamino substituent (415 nm).¹⁹ The same increasing trend was observed in the case of electron-withdrawing groups, that is, as the strength of the substituent on the phenyl increased, an increase in the λ_{max} was observed. The photoluminescence study (Fig. 2) displayed a similar trend as the UV-vis spectra in that the stronger EDGs and EWGs exhibited the most red shifted emission versus the weaker EDGs and EWGs.

Table 1: Optical Data of Eumelanin-Inspired Small Molecules

Compound	λ_{abs}^a (nm)	ϵ^a ($\text{M}^{-1}\text{cm}^{-1}$)	Φ_{re}^b	λ_{ems} (nm)	E_g^c (eV)
2a	387*, 301, 239	39500	0.77	441	2.92
2b	415*, 310, 239	56600	0.87	476	2.62
2c	382*, 297, 239	4500	0.67	432	2.95
2d	401*, 302, 241	50200	0.65	458	2.77
2e	423*, 304, 280	48200	---	---	2.55

* λ_{max} , ^aMeasured in dilute chloroform, ^bquantum yields measured in dilute chloroform solutions relative to quinine sulfate, and ^cmeasured from the tangent drawn at the onset of absorption.

The NMe₂ had the most redshifted emission in the series while NO₂ show no emissive property. This is not surprising because it is known that NO₂ can quench emission.^{20, 21} The Φ_{PL} values for compounds **2a-d** are listed in Table 1.

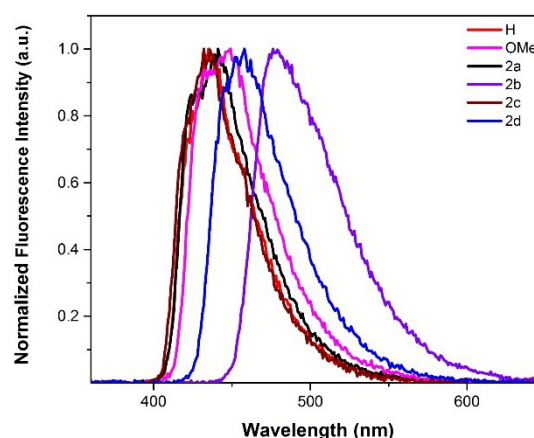


Fig. 2: Emission spectra of compounds H*, MeO*, and **2a-d**. *Note: These compounds have been previously reported.¹⁶

Cyclic voltammetry measurements were carried out in dry degassed acetonitrile under an inert atmosphere using 0.1 M tetrabutylammonium hexafluorophosphate as the supporting electrolyte. The Ag/AgCl reference electrode was calibrated against a ferrocene/ferrocenium (Fc/Fc⁺) redox couple. The HOMO and LUMO energy values were calculated from the onset of the first oxidation and reduction potentials from the equations E_{HOMO} (eV) = - [E_{ox}^{onset} - E_{1/2} (Fc/Fc⁺) + 4.8] and E_{LUMO} (eV) = - [E_{red}^{onset} - E_{1/2} (Fc/Fc⁺) + 4.8], where E_{1/2} (Fc/Fc⁺) was the cell correction. The lowest bandgap was observed for compounds **2b** (-NMe₂) and **2e** (-NO₂). In both cases the bandgap values were 2.15 eV. The same was observed in the case of the optical bandgap where both **2b** and **2e** had lower optical bandgaps in the series. It was noted that **2e** had the strongest EWG substituent; and **2b** has the strongest EDG in the series. As expected, it was observed that in the case of **2b**, the HOMO was higher as in contrast to **2e** deeper LUMO level and both resulted in smaller bandgaps. Other substituents, like *t*-butyl (**2a**) and F (**2c**), exhibited similar data as H. Compound **2d** showed a reduction in bandgap but not as significant as in **2b** and **2e**. The HOMO and LUMO values calculated for DBI, H, OMe, and **2a-e** from the CV experiments are shown in the Fig. 2, along with H and OMe previously reported.¹⁹

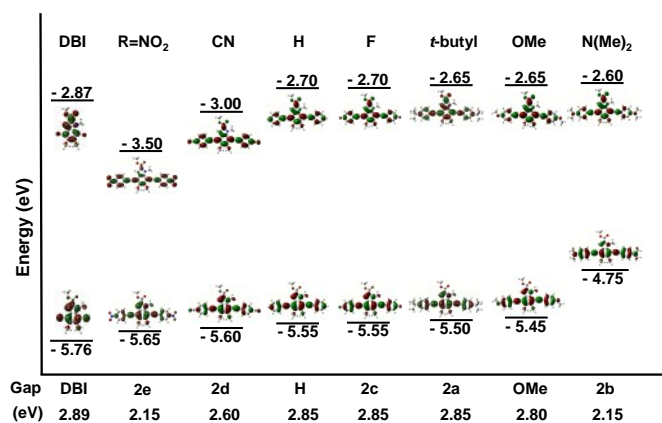


Fig. 3: HOMO and LUMO levels obtained from CV measurements and frontier molecular orbitals for Eumelanin-Inspired Small Molecules.

Optimized equilibrium structures were obtained using Density Functional Theory (DFT).²² In all cases, we employed the B3LYP exchange-correlation functional^{23, 24} and the 6-311G(d) basis set as implemented in the Gaussian 09 package.^{25, 26} The optimized geometries were also verified through the vibration frequency studies. Second, the molecular orbital densities of HOMOs and LUMOs were calculated with the same functional and the more accurate 6-311G(2d) basis set.²⁷ The frontier orbitals for all compounds are presented in Fig. 3, while compounds **2b** and **2e** are shown in Fig. 4

Table 2: Experimental and theoretical comparison of the electronic level of Eumelanin-Inspired Small Molecules.

		H	OCH ₃	2a	2b	2c	2d	2e
HOMO (eV)	Expt.	-5.55	-5.45	-5.50	-4.75	-5.55	-5.60	-5.65
	Theory	-5.44	-5.27	-5.37	-5.05	-5.47	-5.73	-5.77
	Dev. (%)	2.00	3.36	2.39	6.12	1.45	2.29	2.10
LUMO (eV)	Expt.	-2.70	-2.65	-2.65	-2.60	-2.70	-3.00	-3.50
	Theory	-2.74	-2.62	-2.69	-2.49	-2.78	-3.16	-3.33
	Dev. (%)	1.47	1.14	1.50	4.32	2.92	5.19	4.98
GAP (eV)	Expt.	2.85	2.80	2.85	2.15	2.85	2.60	2.15
	Theory	2.70	2.65	2.68	2.56	2.69	2.57	2.44
	Dev. (%)	5.41	5.50	6.15	17.41	5.78	1.16	12.64

Compounds **2b** and **2e** were chosen as they exhibited the strongest EDG and EWG capacities in the series. It can be seen that in the HOMO of **2b**, the electron density is mostly distributed along the phenyleneethynylene conjugated system, and in the LUMO they are more localized along the indolyne ring. However, in the case of **2e**, the electron density is more localized along the indolyne axis in the HOMO, while in the LUMO, it is delocalized along the phenyleneethynylene axis bearing the NO₂ substituent. The LUMO and optical bandgaps were obtained from time-dependent density functional theory (TDDFT)²⁸ utilizing the first 20 excited states of each compound. We also carried out a linear correlation between the calculated and experimental values to correct the theoretical values found.²⁹ A comparison of the HOMO and LUMO values for **2a-e**, MeO and H from cyclic voltammetry

experiments and computational studies appear, in Table 2. We found that DFT is well suited to predict energetic values for HOMOs, with the biggest deviation being 6.2%. As expected, the LUMO and optical gap values obtained from DFT are inaccurate for the compounds studied. However, TD-DFT calculations for the energetics of the LUMO correlated well with experimental measurements. Here, the largest difference was below 5.2%. Errors in HOMO-LUMO gaps range from 0.15 to 0.41 eV. Although the accuracy of *ab initio* calculations depends on the level of theory employed, the small deviation between theory and experiment demonstrates that these methods (DFT + TDDFT) can be useful in the prediction of the eigenvalues of molecular orbitals of eumelanin-inspired conjugated molecules.

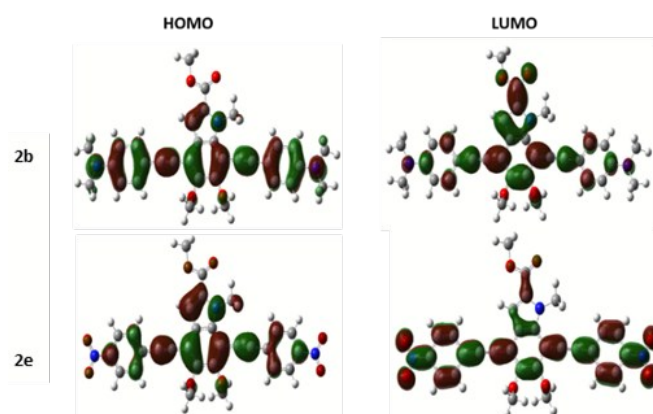


Fig. 4: Frontier molecular orbitals of compounds **2b** and **2e**.

Among the different small molecules, compound **2b** was chosen in order to study the optical response to protonation with trifluoroacetic acid (TFA) in view of the presence of the basic N,N-dimethylamino group directly connected to the conjugated system. Furthermore, protonation of dimethylamino group changes from an EDG to an EWG which completely alters the optical and electronic properties. Such studies could be vital in establishing this molecule as an ideal chemosensor. All experiments for optical responses to protonation with the addition of TFA were performed in dilute CHCl₃ solution, and the results are displayed in Fig 5. The absorption spectra exhibit blue shifted absorbance at 415 nm with the addition of TFA. These changes are attributed to the stabilization of the HOMO level due to the protonation of N,N-dimethylamino group. Similarly, the emission spectra were also blue-shifted at high TFA concentrations (-log[TFA] = 2.05). Fluorescence quenching was also observed in the emission spectra with the addition of TFA.

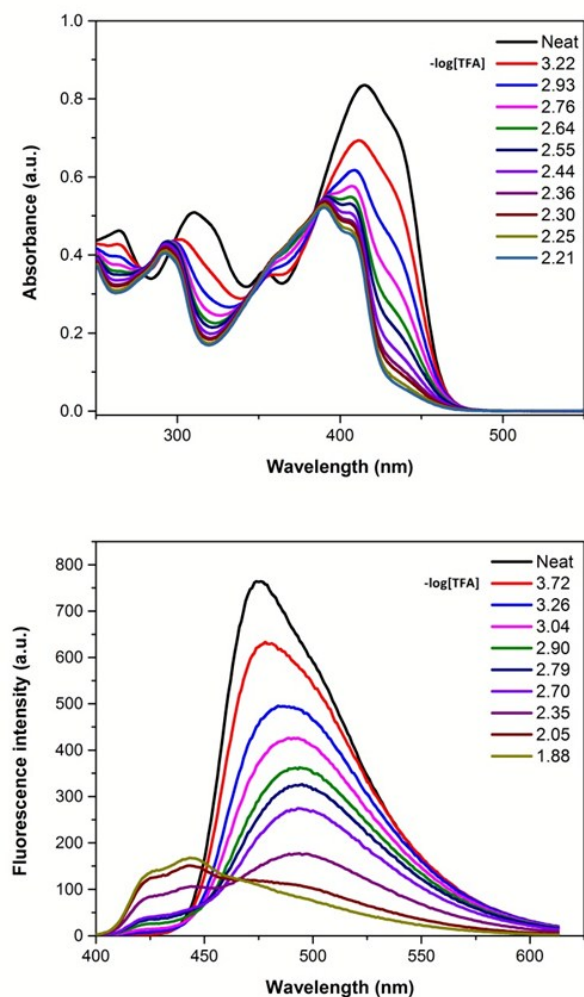


Fig. 5: Optical responses towards protonation of **2b** in the presence of TFA a) absorption spectra and b) emission spectra.

The optical changes at high concentration of TFA were visible to the naked eye and found to be reversible upon addition of ammonia as displayed in Fig. 6. At the low concentration of TFA (0.18 mM to 2.16 mM), the fluorescence quenching data correlated well in terms of the standard Stern-Volmer relationship with the Stern-Volmer constant of 0.086 LMol^{-1} . Such phenomenon marks this system as a potential acidochromic sensor.

Conclusion

In summary, five new eumelanin-inspired conjugated molecules were synthesized differing by the functional group at the para position of the phenyleneethynylene ring. These five molecules were compared to two previous synthesized conjugated structures in an effort to explore the effect of structural variations (electron withdrawing and donating groups) on the optoelectronic properties of the eumelanin inspired indole core. We demonstrated that the substituents can alter the electronic characteristics of these molecules, hence changing their optoelectronic properties. Furthermore, the optical

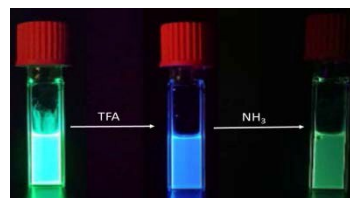


Fig. 6: Emission of **2b** in chloroform (left cuvette, green emission), upon addition of a large excess of TFA (center cuvette, blue emission), and upon addition of a large excess of NH_3 (right cuvette, green emission)

response of compound **2b** to acid was studied and the data suggests that it could act as an acidochromic sensor due to its unique chromic response when exposed to TFA. This work demonstrates the utility of the eumelanin-inspired indole core and opens the possibility of designing materials with interesting properties for specific applications by decorating this core with various functionalities. Moreover, this work brings the field one step closer to elucidating and enhancing the properties of the naturally occurring eumelanin.

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