

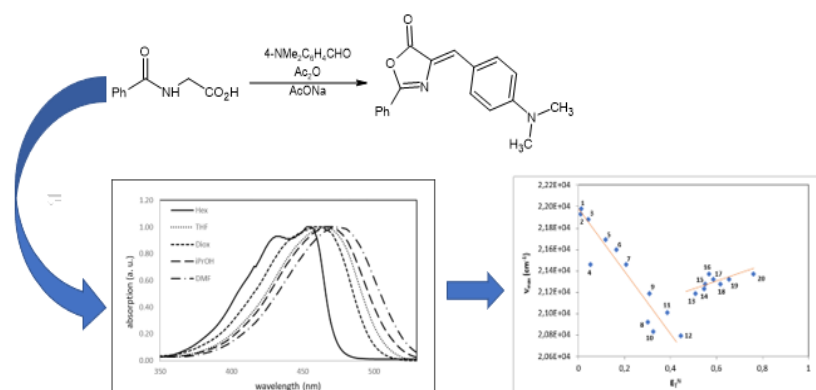
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# Synthesis and Solvatochromism of Oxazolone Derivative: Combining Organic Synthesis and Physical Organic Chemistry in a Single Experiment

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This work presents a proposal of experimental activity involving organic synthesis and solvatochromism of an organic molecule, correlating the content of organic chemistry and physical organic chemistry. This experiment presents a good opportunity to work with the classroom some of the content related to the mechanisms of organic reactions and the relationship between energy, electronic states, solute-solvent interactions, spectroscopy, among others in the area of physical chemistry, thus integrating knowledge. Experimentally, we synthesized through the Plöchl-Erlenmeyer method the oxazolonic derivative 4-[(p-N,N-dimethylamino)benzylidene]-2-phenyloxazole-5-one (AZA2) with good yield (78%), while the solvatochromic study showed that this derivative presented reverse solvatochromism; since in non-hydroxyl solvents it presented positive solvatochromism, but in protic solvents it presented negative solvatochromism. These different behaviors can be justified by the different solute-solvent interactions existing in each medium, which favors the prevalence of different mesomeric structures.

## Graphical abstract



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## 1. Introduction

Compounds which are able to induce a change in the color of the solution with the change in the polarity of the solvent, are called solvatochromic compounds (or solvatochromic dyes), and this phenomenon is called solvatochromism. This behavior can be used to probe one of the properties of the solvent, namely, its polarity. Seminal contributions were done by Kosower [1a-c] and Dimroth [2], but the greatest contributions to the study of this phenomenon were given by Reichardt [3-4].

Kosower [3a-c] was the first to propose a solvent polarity scale, the Z-scale, from spectroscopic properties based on the dye 4-methoxycarbonylpyridinium iodide as an indicator. On the other hand, Dimroth et al. [4] proposed the use of the dye pyridinium N-phenoxide betaine, which according to the authors circumvented some practical limitations found with the dye proposed by Kosower, as a spectroscopic indicator of the solvent polarity. From the data obtained with this dye, the authors constructed the uniparametric scale called  $E_T(30)$ .

The unit of the  $E_T$  scale (30) is  $\text{kcal mol}^{-1}$  which represents the electronic transition energy between the two states. This parameter was calculated for different solvents from the wavelengths of absorption maxima ( $\lambda_{\text{max}}$ ) using Equation (1), shown below, in which  $h$  is the Planck constant,  $c$  the speed of

light,  $N_A$  the Avogadro constant,  $\nu_{\text{max}}$  is the wavenumber and  $\lambda_{\text{max}}$  the wavelength (nm) of the maximum absorption band of the betaine dye.

$$E_T(30) (\text{kcal mol}^{-1}) = hc\nu_{\text{max}}N_A = (2.8591 \times 10^{-3}) \nu_{\text{max}} = 28591 / \lambda_{\text{max}} (\text{nm}) \quad (1)$$

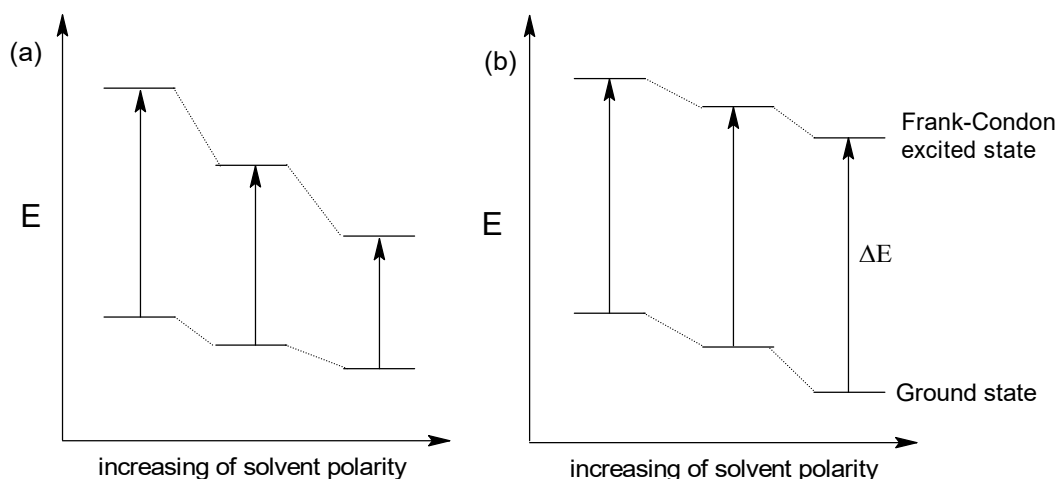
Then the normalized scale of  $E_T^N$  was introduced, which is dimensionless and defined by Equation (2), in which TMS

(tetramethylsilane) and water represent the extremes of apolarity and polarity of solvents, respectively.

$$E_T^N = (E_T(\text{solvent}) - E_T(\text{TMS})) / (E_T(\text{water}) - E_T(\text{TMS})) = (E_T(\text{solvent}) - 30.7) / 32.4 \quad (2)$$

The phenomenon of solvatochromism is directly related to the change of the dipole moment of the solute, the speed of the electronic transition and the reorientation of the solvation shell. The electronic transition occurs much faster than the reorientation of the solvent (Franck-Condon excited state), so the solvent does not have enough time to reorient its dipoles to better stabilize the molecule in the excited state. In this way, the displacement of the  $\lambda_{\text{max}}$  can occur in both directions, red shift or blue shift, depending on the greater or lesser

stabilization of the ground and excited states of the indicator. Thus, a shift of  $\lambda_{\text{max}}$  in the direction of lower energies (bathochromic shift or red shift) as a function of increasing the polarity of the solvent is called positive solvatochromism, while the shift in the direction of higher energies (hypsochromic shift or blue shift) as a function of increasing the polarity of the solvent is called negative solvatochromism. This behavior can be schematically represented in Fig. 1.

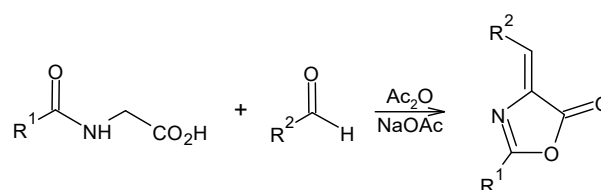


**Fig. 1.** Qualitative schematic representation of the effect of the solvent on the electronic transition energy of dipole solutes in polar solvents. (a) positive solvatochromism, the Franck-Condon excited state is more stabilized than the ground state; (b) negative solvatochromism, the ground state is more stabilized than the Franck-Condon excited state.

In case (a) is represented the situation in which the indicator is more polar in the excited state than in the ground state ( $\mu_e > \mu_g$ ). As such the excited state will be more stabilized than the ground state, and the energy difference between both states decreases with increasing solvent polarity, a typical case of positive solvatochromism. On the other hand, in negative solvatochromism, the excited state is less polar than the ground state ( $\mu_g > \mu_e$ ), and as such the opposite occurs, that is, there is greater stabilization of the ground state relative to the excited state with the increase in the polarity of the solvent.

Solvatochromism enables different theoretical and experimental applications. Solvatochromism can be used, for example, to determine the dipole moment of a molecule in the excited state ( $\mu_e$ ) [5-6], characterization of polymers [7-8], in the biological field [9], in the detection and quantification of metal ions [10-11], among others.

Oxazolones, also known as azlactones, are 5-membered heterocyclic compounds easily obtained by the Plöchl-Erlenmeyer methodology, presented in the reaction scheme of Fig. 2.



R<sup>1</sup> = Alkyl, Aryl

R<sup>2</sup> = Aryl

**Fig. 2.** General scheme of oxazolone synthesis by the Plöchl-Erlenmeyer route.

The synthesis of oxazolone derivatives by this method is a simple process, but it is somewhat time-consuming since it requires a cooling period at low temperature for the formation of the product. Laboratory operations for isolation and purification are routine and can be carried out by filtration and recrystallization.

The solvatochromic properties of oxazolones have already been reported in the literature [12], and the use of these properties have been reported in the detection of  $\text{Fe}^{3+}$  ions [11], pH indicators [13], chemo [14-15] and biosensors [16], among other properties [17-18].

Our work proposes the application of synthetic methods of obtaining oxazolone derivatives and the solvatochromic study of the obtained derivatives, in order to combine the contents of organic synthesis and physical organic chemistry, presenting a more interdisciplinary character.

## 2. Results and Discussion

The AZA2 derivative (Fig. 3), isolated as crystals in the form of dark-red-colored needles, was obtained with 78% yield and characterized by the melting point (uncorrected) of 210-212 °C (lit. 214-215 °C [19]) and by the FTIR bands ( $1762\text{ cm}^{-1}$  (C=O stretching),  $1647\text{ cm}^{-1}$  (C=N stretching),  $1595\text{ cm}^{-1}$  (C=C stretching) (Fig. 4).

The Plöchl-Erlenmeyer reaction is a variation of the Perkin reaction and the proposed mechanism for this reaction is shown in Fig. 5. [20] As such, this is a good opportunity to discuss the mechanism involved in the reaction of obtaining oxazolones. Recently Marra et al. [21] published a review on synthetic methods and the chemistry of oxazolones.

Fig. 6 shows the absorption spectra of AZA2 for five different solvents (Hex, Diox, THF, DMF and iPrOH). We can clearly see that for the solvent iPrOH ( $E_T^N = 0.546$ ) the  $\lambda_{\text{max}}$  undergoes a hypsochromic shift of 5 nm relative to the  $\lambda_{\text{max}}$  in DMF ( $E_T^N = 0.386$ ).

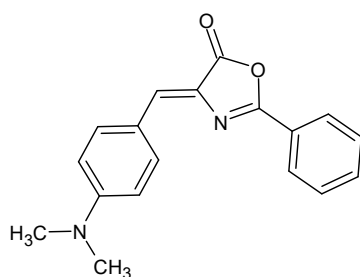


Fig. 3. Chemical structure of the AZA2 synthesized in this work.

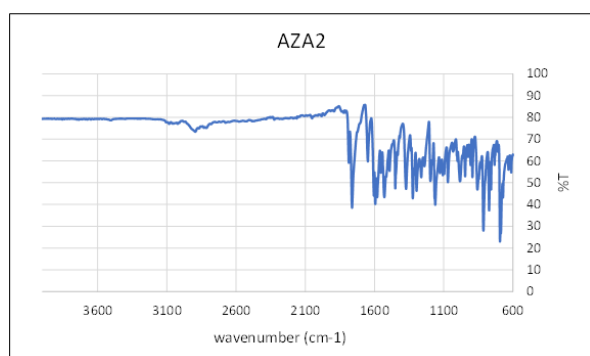


Fig. 4. FTIR spectrum of AZA2 obtained using ATR technique.

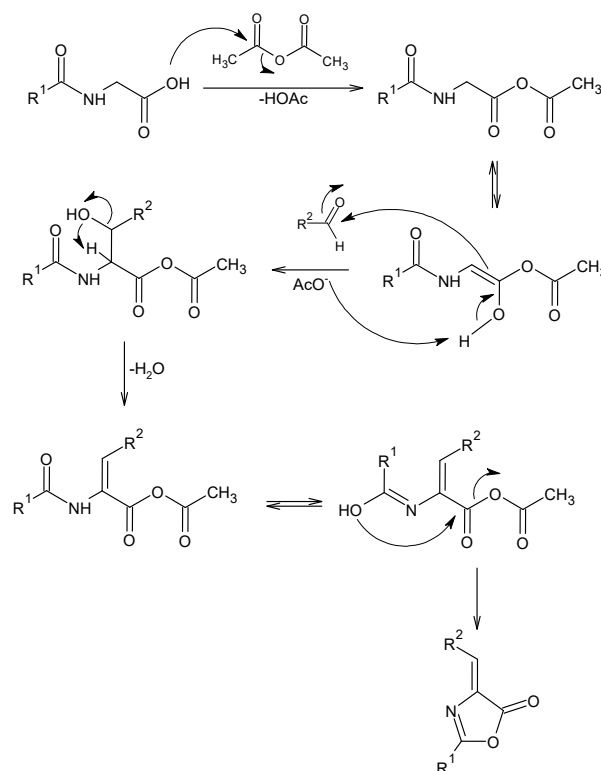


Fig. 5. Mechanism of formation of the oxazolone nucleus. Source: adapted from [18].

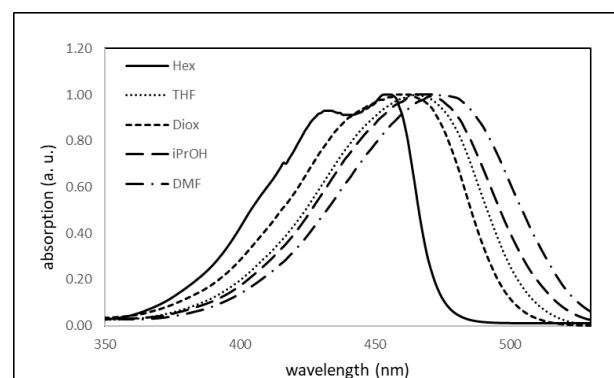
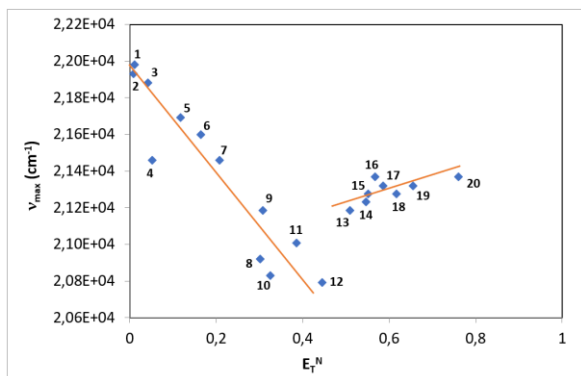


Fig. 6. Absorption spectra of AZA2 ( $1 \times 10^{-5}\text{ mol L}^{-1}$ ) in Hex (—), Diox (---), THF (···), DMF (---) and iPrOH (— · —).

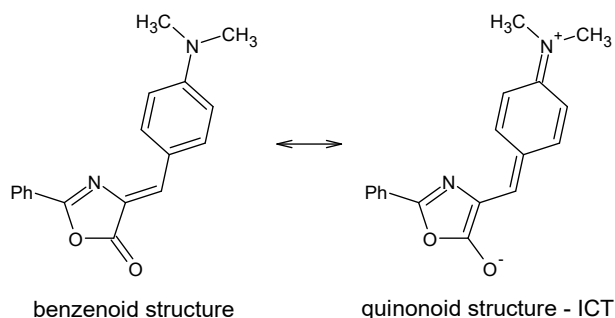
The  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) vs  $E_T^N$  graph clearly shows two different trends (Fig. 7). Hydroxylic solvents (13 to 20) do not fall in the same line where non-hydroxylic solvents (1 to 12) fit. In the latter group there is a clear tendency to decrease the  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ), ( $\Delta\nu_{\text{max}} = 1139.6\text{ cm}^{-1}$  or  $\Delta\lambda_{\text{max}} = 25\text{ nm}$ ), as the  $E_T^N$  value increases which is a characteristic of positive solvatochromism. On the other hand, in the presence of hydroxylic solvents the opposite is observed, that is, an increase in  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) as  $E_T^N$  also increases, which is a characteristic of a negative solvatochromism. It should be noted that the lines shown on the plot do not represent an adjustment of the points, but only to show the trend of the values.

This behavior was observed by Asiri et al. [12] for the same derivative, which justified the positive solvatochromic behavior due to the increased polarity of the AZA2 in the excited state, whose variation of the dipole moment ( $\Delta\mu$ ) was estimated by the authors at 5.52 Debye. This increase is resulting from the formation of a structure with

intramolecular charge transfer (ICT-quinonoid) due to the presence of a charge donor group (NMe<sub>2</sub>) and a charge acceptor group (C=O) in its structure, as shown in Fig. 8.



**Fig. 7.** Plot of  $v_{\max}$  (cm<sup>-1</sup>) vs  $E_T^N$  for AZA2 (1x10<sup>-5</sup> mol L<sup>-1</sup>) for the 20 used solvents. The line shown does not represent a linear fit, but only shows the trend of the experimental points.

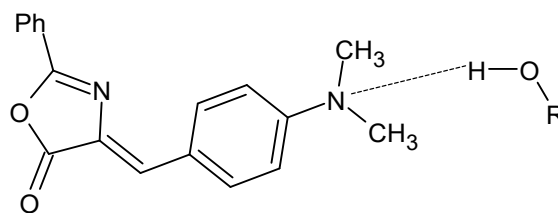


**Fig. 8.** Mesomeric structures (ICT) of the AZA2 derivative.

Thus, with the increase in the polarity of the solvent, a greater stabilization of the quinonoid structure (ICT) occurs, decreasing the energy difference between the ground and excited states.

In the presence of hydroxylic solvents, however, the electron pair of the dimethylamino group interacts with the proton of the solvent by means of a hydrogen bond (Fig. 9). This interaction prevents the formation of the quinonoid structure, indicating that the nature of the species that is

absorbing the energy is different in this case.



**Fig. 9.** Schematic representation of the hydrogen bond between the protic solvent and the solute (AZA2).

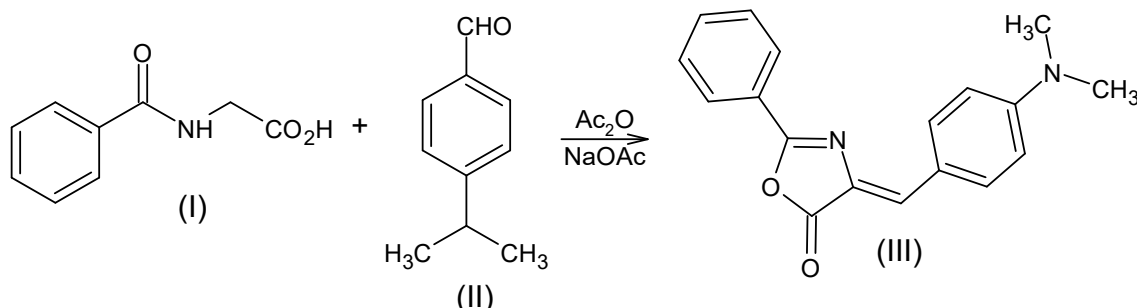
According to Asiri et al. (2012) this strong band shift in aprotic solvents shows that the specie responsible for the absorption is a strongly photoinduced intramolecular charge transfer (ICT), while in protic solvents the absorbing specie is a strong hydrogen-bonded complex. From the didactic point of view this behavior can be emphasized by showing the importance of hydrogen bonds in the spectral behavior of some molecules.

Another important observation is concerned to the type of transition which are involved in each situation for AZA2. In aprotic solvents the electronic transition  $\pi-\pi^*$  is clearly favored, on the other side, in protic solvents the electronic transition  $n-\pi^*$  is favored.

### 3. Material and Methods

In this work was synthesized the derivative 4-[(p-N,N-dimethylamino)benzylidene]-2-phenyloxazole-5-one (AZA2 - III) obtained by the Plöchl-Erlenmeyer methodology as shown in Fig. 10.

In brief, the procedure consisted of the reaction of 1.2 g of hippuric acid (I) (6.7 mmol) with 1.00 g of N,N-dimethylamino benzaldehyde (II) (6.7 mmol) in the presence of 10 mL of acetic anhydride (211 mmol) and 0.55 g of anhydrous sodium acetate (6.7 mmol) and the mixture was left under heating (80°C) and stirring for 2 hours. After heating, the mixture was left to reach room temperature and then placed under refrigeration for 12 hours. The obtained solid was then filtered, washed with cold ethanol and recrystallized in ethanol. The product characterization was made by melting point and FTIR (Fourier-transform infrared spectroscopy).



**Fig. 10.** Synthetic route for obtaining the oxazolone derivative AZA2 (III).

For the solvatochromic study, 20 different organic solvents were used, which had no additional purification treatment. A stock solution of AZA2 was prepared by solubilizing 37.3 mg of AZA2 in 50 mL of diethyl ether ([AZA2] = 5 × 10<sup>-3</sup> mol L<sup>-1</sup>). Then 20 aliquots of 10 mL were removed and transferred to volumetric flasks of 5 mL, which had their

volumes completed with the solvents used in the study. The final concentration of AZA2 in each flask was within the magnitude of 10<sup>-5</sup> mol L<sup>-1</sup>.

The solvents used, their abbreviations and their respective  $E_T^N$  values, obtained from Reichardt [1] are shown in Table 1.

**Table 1.** Solvents used in this study, abbreviations and  $E_T^N$  values.

No.	Solvent	Abbreviation	$E_T^N$
1	hexane	Hex	0.0092
2	heptane	Hept	0.012
3	triethylamine	Et <sub>3</sub> N	0.043
4	carbon tetrachloride	CCl <sub>4</sub>	0.052
5	diethyl ether	Et <sub>2</sub> O	0.117
6	1,4-dioxane	Diox	0.164
7	tetrahydrofuran	THF	0.207
8	pyridine	Pyr	0.302
9	dichloromethane	DCM	0.309
10	nitrobenzene	DNB	0.324
11	dimethylformamide	DMF	0.386
12	dimethylsulfoxide	DMSO	0.444
13	cyclohexanol	CHxOH	0.509
14	isopropanol	iPrOH	0.546
15	isobutanol	iBuOH	0.552
16	n-pentanol	PentOH	0.568
17	n-butanol	nBuOH	0.586
18	n-propanol	nPrOH	0.617
19	ethanol	EtOH	0.654
20	methanol	MeOH	0.762

The absorption spectra were obtained in a Shimadzu 1800 PC UV-vis spectrophotometer using a quartz cell of 10 mm optical path. Excel® spreadsheet was used to construct the  $\nu_{\max}$  (cm<sup>-1</sup>) ×  $E_T^N$  plot.

## 4. Conclusions

The oxazolone derivative AZA2 was synthesized by the Plöchl-Erlenmeyer method with good yields. The study of the solvatochromism of this derivative in 20 solvents of different polarities showed positive solvatochromism for non-hydroxylic solvents, due to greater stabilization of the structure with charge transfer (ICT) in the excited state. The presence of proton-donor solvents prevents the formation of this structure (ICT) due to the formation of hydrogen bonds with the electron pair of the nitrogen of the dimethylamine group. Thus, for protic solvents, a negative solvatochromism for this derivative is observed.

The proposed experiment can be a great opportunity to merge organic chemistry contents, especially those related to synthesis, mechanisms and resonance structures, and physical organic chemistry (spectroscopy and energy levels).

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## Author Contributions

MFR – Conceptualization, formal analysis, original draft, writing, review & editing, visualization, supervision; TDK – Methodology, formal analysis, validation, investigation; LHFMC – Methodology, formal analysis, validation, investigation.

## References and Notes

[1] a) Kosower, E. M. *J. Am. Chem. Soc.* **1958**, *80*, 3253.

- [2] Dimroth, K.; Reichardt, C.; Siepmann, T.; Bohlmann, F. *Liebigs Ann. Chem.* **1963**, *661*, 1. [Crossref]
- [3] Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319. [Crossref]
- [4] Reichardt, C. *Solvents and solvents effects in organic chemistry*, 3rd ed. Weinheim: Wiley-VCH, 2003.
- [5] Rani, S. A., Sobhanadri, J., Rao, T. A. P. *Spectrochim. Acta A.* **1995**, *51*, 2473. [Crossref]
- [6] Abdullah, A-S.; Pannipara, M.; Abul, K. *Spectrochim. Acta A.* **2017**, *171*, 97. [Crossref]
- [7] Paley, M. S.; McGill, R. A.; Howard, S. C.; Wallace, S. E.; Harris, J. M. *Macromolecules* **1990**, *23*, 4557. [Crossref]
- [8] Borger, D. P.; Frens, G. *Colloids Surfaces* **2000**, *161*, 75. [Crossref]
- [9] Marsh, D. *Biophys. J.* **2009**, *96*, 2549. [Crossref]
- [10] Homocianu, M.; Airinei, A.; Hamciuc, C.; Ipate, A. M. *J. Mol. Liquids* **2019**, *281*, 141. [Crossref]
- [11] Ozturk, G.; Alp, S.; Ertekin, K. *Dyes Pigm.* **2007**, *72*, 150. [Crossref]
- [12] Asiri, A. M.; El-Daly, S. A.; Khan, S. *Spectrochim. Acta A.* **2012**, *95*, 679. [Crossref]
- [13] Ertekin, K.; Karapire, C.; Alp, S.; Yenigül, B.; Içli, S. *Dyes Pigm.* **2003**, *56*, 125. [Crossref]
- [14] Ertekin, K.; Alp, S. *Sensors Actuators B.* **2006**, *115*, 672. [Crossref]
- [15] Ertekin, K.; Cinar, S.; Aydemir, T.; Alp, S. *Dyes Pigm.* **2005**, *67*, 133. [Crossref]
- [16] Ozturk, G.; Alp, S.; Timur, S. *Dyes Pigm.* **2008**, *76*, 792. [Crossref]
- [17] Song, H-C.; Wen, H.; Li, W.-M. *Spectrochim. Acta A* **2004**, *60*, 1587. [Crossref]
- [18] Rodrigues, C. A. B.; Mariz, I. F. A.; Maçõas, E. M. S.; Afonso, C. A. M.; Martinho, J. M. G. *Dyes Pigm.* **2013**, *99*, 642. [Crossref]
- [19] Içli, S.; Içil, H.; Alp, S.; Koc, H.; Mckillop, A. *Spectrosc. Lett.* **1994**, *27*, 1115. [Crossref]
- [20] Wang, Z. *Comprehensive organic name reactions and reagents*. Wiley, 2009.
- [21] Marra, I. F. S.; Castro, P. P.; Amarante, G. W. *Eur. J. Org. Chem.* **2019**, *34*, 5830. [Crossref]
- [22] El-Daly, S. A.; Abdel-Kader, M. H.; Issa, R. M.; El-Sherbini, E.-S. A. *Spectrochim. Acta A.* **2003**, *59*, 405. [Crossref]

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