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Eugenol and Its *azo* Derivatives: An Auspicious Tool for Potential Detecting Metal Cations †

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Abstract: Natural products exhibit an exceptional level of versatility. For example, eugenol, the major phenylpropanoid in the essential oil of cloves (*Syzygium aromaticum*), is known to be a reasonable siderophore. On this basis, it was possible to evaluate eugenol's ability to complex with various metal cations, by UV-vis spectroscopy, and to construct a series of *azo* dyes through the coupling reaction with diazonium salts of different aromatic amines. The new eugenol-based *azo* dyes as potential coloured chelating agents were full characterized by the usual analytical techniques. The UV-vis properties with emphasis in solvent effects were studied and will be discussed.

Keywords: eugenol; essential oils; *azo* dyes

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1. Introduction

Natural products are an essential source for obtaining versatile building blocks for various purposes. Many of these molecules are present in plant extracts and essential oils, which give them interesting physicochemical properties and relevant biological activities. From a chemical point of view, essential oils are synergistic volatile mixtures based essentially on phenolic compounds, terpenes and phenylpropanoids [1–3]. Phenylpropanoids are an extremely promising class of lead compounds, into which eugenol, the major constituent of clove essential oil, fits perfectly.

Harnessing the potential of secondary metabolites provides an encouraging avenue for diverse research areas. For example, eugenol is a reasonable siderophore, capable of forming complexes with ferrous ions [4,5]. From this perspective, it is possible to implement structural alterations to the respective molecules through synthetic processes, to enhance their ability to form complexes with other metal cations, namely by incorporating functional groups that have donor atoms that facilitate the formation of complexes [6–8].

In this way, based on eugenol's ability to complex with various metal cations, a series of *azo* dyes through the coupling reaction with diazonium salts of different aromatic amines was synthesised. These new eugenol-based *azo* dyes as potential coloured chelating agents were full characterized by the usual analytical techniques. The UV-vis properties with emphasis in solvent effects were studied and will be discussed.

2. Results and Discussion

2.1. Preliminary Chemosensing Studies of Eugenol

One of the potential uses for phenolic compounds is their ability to establish complexes with metal cations. Eugenol is known to be a good siderophore, where it tends to form blue complex in the presence of $FeCl_2$ [9,10]. In addition, eugenol can form

complexes with the Cu^{2+} cation, with applications that include to voltammetric characterisation, as well as its antioxidant and fungitoxic activity [11,12].

To observe the behaviour of eugenol in the presence of various metal cations and confirm a possible colorimetric change, a preliminary evaluation of eugenol (EUG) **2** was performed in acetonitrile solution in the presence of some metallic cations. The study was carried out by addition of 30 equivalents of each cation to the compound's solution (Figure 1). The chromogenic response of the compound **2** was remarkably visible to the naked eye, with a colour change from light yellow in the presence of Al^{3+} and dark brown for Fe^{3+} and Cu^{2+}. About the Ni^{2+} cation, the colorimetric response is considered negative, despite the colour displayed, as it is due to the ionic salt used (nickel(II) nitrate hexahydrate).

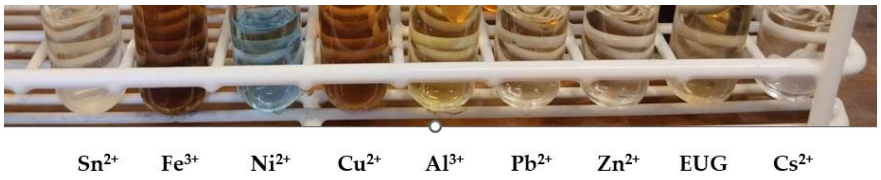
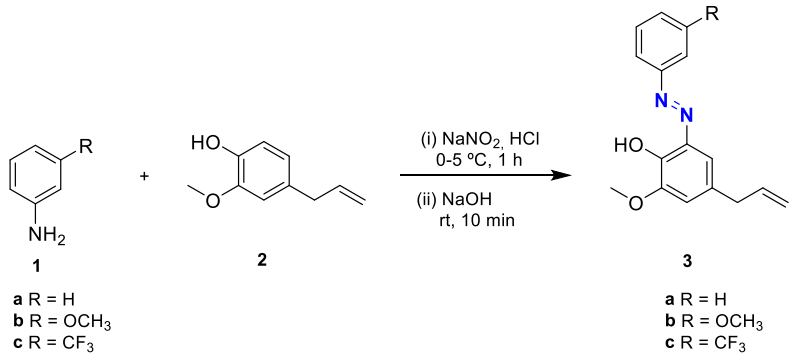


Figure 1. Colour changes observed for eugenol (EUG) **2** in acetonitrile solution after addition of 30 equivalents of each cation.

2.2. Synthesis of Eugenol Azo Derivatives

The synthesis of *azo* dyes based on eugenol was carried out by means of an *azo* coupling. The process described is one of the most widely used for obtaining dyes and pigments [13,14]. Aromatic diazonium ions acts as electrophiles in coupling reactions with activated aromatics such as anilines or phenols. The substitution normally occurs at the *para* position, except when this position is already occupied, in which case *ortho* position is favoured, such as eugenol **2**. *Azo* coupling includes diazotisation, which consists of converting aromatic amines into diazonium salts, generated in situ using sodium nitrite and strong acidic conditions.

The *azo* derivatives **3a–c** were synthesised by diazotisation of aromatic amines, namely aniline **1a**, *m*-anisidine **1b** and 3-(trifluoromethyl)aniline **1c**, whose respective diazonium salts reacted with eugenol **2**, under alkaline conditions, to generate 4-allyl-2-methoxy-6-(phenyldiazenyl)phenol **3a**, 4-allyl-2-methoxy-6-((3-methoxyphenyl)diazenyl)phenol **3b** and 4-allyl-2-methoxy-6-((3-(trifluoromethyl)phenyl)diazenyl)phenol **3c**, respectively (Scheme 1).



Scheme 1. Synthesis of *azo* dyes **3a–c**.

Compounds **3a–c** were isolated as solids in 14 to 36% yields and were fully characterized by IR, ^{1}H, and ^{13}C NMR spectroscopy.

The ^{1}H NMR spectra of compounds **3a–c** showed the different characteristic signals for the aliphatic protons of CH_2 groups as doublets (δ = 3.41–3.43 ppm), as well as OCH_3 groups as singlets (δ = 3.87–3.96 ppm), in addition to the expected protons of the eugenol's

double bond as multiplets CH_2 (δ = 5.12–5.20 ppm) and CH (δ = 5.98–6.08 ppm). The protons of the aromatic rings from eugenol (δ = 6.80–7.47 ppm) and the amines were also visible (δ = 7.01–7.98 ppm).

The ^{13}C NMR spectra of all compounds showed signals of the aliphatic carbons from the CH_2 groups (δ = 39.40–39.43 ppm), as well as OCH_3 groups (δ = 55.32–55.33 ppm), in addition to carbons of the eugenol's double bond CH_2 (δ = 116.05–116.23 ppm) and CH (δ 137.00–137.87 ppm). The carbons of the aromatic rings were also shown (δ = 104.62–148.71 ppm). For dye **3c**, there is a signal alluding to a quaternary carbon associated with the CF_3 group (δ = 130.89 ppm).

The FTIR spectra of the dyes **3a–c** revealed the presence of the *azo* group at 1453 cm^{-1}, which shows the asymmetric stretching of the respective double bond. For dye **3c**, the presence of CF_3 group is confirmed by to the presence of bands in the region between 1440–1200 cm^{-1}.

The UV-visible absorption spectra of dyes **3a–c** in solvents of different polarities revealed wavelengths of maximum absorption (λ_{max}) in the range 340–347 nm, with molar extinction coefficient (ε), showed as log ε, between 4.15 and 4.59 (Table 1). The presence of trifluoromethyl group influences the λ_{max}, since it causes a slight bathochromic shift in dye **3c**, compared to **3a** and **3b**, in polar solvents (Figure 2).

Table 1. The absorption data of compounds **3a-c** from 2.6 × 10^{-5} to 4.9 × 10^{-5} M in different solvents.

Solvent	Dye					
	3a		3b		3c	
	λ_{max}	log ε	λ_{max}	log ε	λ_{max}	log ε
EtOH	340	4.41	340	4.27	345	4.34
MeOH	340	4.15	339	4.34	345	4.39
DMF	343	4.59	341	4.36	347	4.30
Acetone	341	4.41	340	4.38	345	4.26
AcOEt	341	4.31	340	4.44	345	4.30

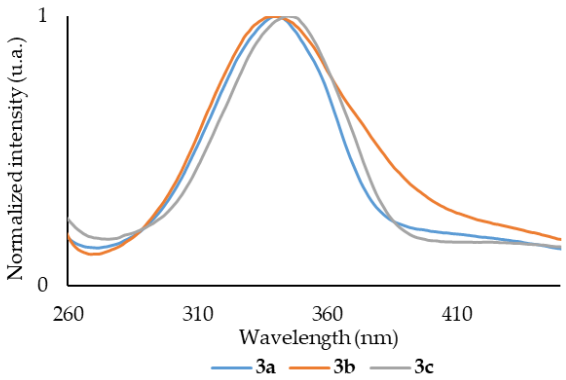


Figure 2. Absorption spectra of dyes **3a–c** in absolute ethanol (4.6 × 10^{-5} to 4.9 × 10^{-5} M).

3. Materials and Methods

3.1. Preliminary Chemosensing Studies

The evaluation of eugenol **2** as a ligand was performed in the presence of some cations (Sn^{2+}, Pb^{2+}, Zn^{2+}, Cu^{2+}, Cs^{2+}, Fe^{3+}, Ni^{2+} and Al^{3+}). Solutions of compound **2** and solutions of respective cations were prepared in UV-grade acetonitrile. A preliminary study was carried out by addition of 30 equivalents of each cation (3 mL, 1 × 10^{-3} M) to the solution (1 mL, 1 × 10^{-4} M) of eugenol **2** and the assessment of the colour was evaluated by naked eye.

3.2. General Procedure for the Preparation of Compounds **3a**–**c** *(Illustrated for* **3a***)*

A mixture of 3-(trifluoromethyl)aniline **1c** (0.589 g, 3.65×10^{-3} mol, 2 equiv), 1 M HCl (7.5 mL) and 6 M HCl (0.42 mL) was cooled to 0–5 °C. Aqueous sodium nitrite (0.251 g, 1.83×10^{-3} mol, 1 equiv, in 1 mL of water) was added and the reaction mixture was stirred for 45 min. The diazonium salt solution previously prepared was added dropwise to a solution of eugenol, 4-allyl-2-methoxyphenol **2** (0.300 g, 1.83×10^{-3} mol, 1 equiv) in NaOH pellets (0.120 g, 3.00×10^{-3} mol, 1.6 equiv) and H_2O (1 mL). The precipitated dye was filtered, washed with cold water and diethyl ether, and dried. The crude product was subjected to flash column chromatography on silica gel, with dichloromethane/light petroleum, mixtures of increasing polarity, as eluent giving 4-allyl-2-methoxy-6-((3-(trifluoromethyl)phenyl)diazenyl)phenol **3c** as an orange solid (0.097 g, 16% yield). R_f = 0.23 (silica; dichloromethane/light petroleum 1:1), m.p. = 86.1–88.0 °C. IR ($\upsilon_{max.}$): 3080, 3000, 2840, 2158, 1585, 1495, 1453, 1412, 1372, 1268, 1124, 1054, 1034, 990, 910, 881 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 3.44 (2H, d, *J* = 6.4 Hz, CH_2Ph), 3.96 (3H, s, OCH_3), 5.15–5.20 (2H, m, $CH=CH_2$), 6.00–6.07 (1H, m, $CH=CH_2$), 6.87 (1H, d, *J* = 2.0 Hz, H-3), 7.46 (1H, d, *J* = 2.0 Hz, H-5), 7.55 (1H, t, *J* = 7.6 Hz, H-5 Ph-CF_3), 7.67 (1H, t, *J* = 7.2 Hz, H-4 Ph-CF_3), 7.81 (1H, d, *J* = 7.6 Hz, H-6 Ph-CF_3), 7.98 (1H, d, *J* = 8.0 Hz, H-2 Ph-CF_3), 12.58 (1H, s, OH) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ_C 39.40 (CH_2Ph), 56.30 (OCH_3), 115.57 (C-3), 116.23 ($CH=CH_2$), 116.54 (C-2 Ph-CF_3), 124.61 (C-5), 125.20 (C-6), 126.82 (C-6 Ph-CF_3), 130.41 (C-5 Ph-CF_3), 130.89 (CF_3) 132.75 (C-4 Ph-CF_3), 136.87 ($CH=CH_2$), 137.44 (C-3 Ph-CF_3), 137.50 (C-4), 140.99 (C-1), 147.43 (C-2), 148.71 (C-1 Ph-C CF_3) ppm.

4. Conclusions

Through *azo* coupling, it was possible synthesised three dyes. It is worth highlighting the semi-synthetic nature of these dyes, which showed maximum absorption 340–347 nm (in different solvents). To understand the potential of the respective dyes in terms of their ability to complex with metals, due to the incorporation of the eugenol nucleus into the respective dye structures, a preliminary colorimetric study of eugenol was carried out in relation to a set of metal cations. The promising results obtained in relation to the Al^{3+}, Fe^{3+} and Cu^{2+} cations, could be the starting point for understanding the application of the dyes described as cation colorimetric sensors.

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