UNIVERSITY OF BUCHAREST
FACULTY OF CHEMISTRY
DOCTORAL SCHOOL IN CHEMISTRY

DOCTORAL THESYS SUMMARY

NEW ORGANIC MOLECULES OBTAINED BY COMBINING ISOMERIZABLE UNITS WITH STABLE FREE RADICALS

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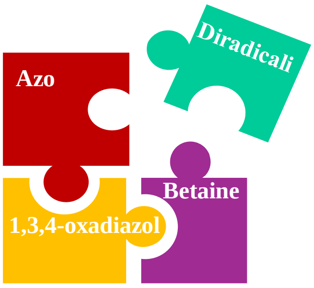
Introduction

The doctoral thesis entitled *"New organic molecules obtained by combining isomerizable units with stable free radicals"* presents the results obtained for the synthesis of novel series of compounds containing the three structural motifs: azobenzene, 1,3,4-oxadiazole and the DPPH radical. Azobenzenes are known for their applications as molecular photoswitches, participating in the dynamic equilibrium between the two molecular states (isomers), activated by light. 1,3,4-oxadiazoles are attractive structural units, recognized for their emission properties and ability to transport electrons. The DPPH hydrazil radical has various properties: from acid-base and electrochemical properties to paramagnetic properties. The integration of two DPPH units offers new properties, influenced by the diradicaloid structure, such compounds being studied for molecular magnetism. The study focused on synthesis of novel derivatives with absorption and emission properties, photoswitching properties induced by the equilibrium between the two isomers upon light irradiation, or the paramagnetism provided by the radical units. The possibility of influencing the properties provided by the units when they were combined was also explored.

The thesis is divided into four chapters. The first chapter covers theoretical concepts from the literature on molecular photoswitches and diradicals. The second chapter presents the synthesis of azobenzenes decorated with 1,3,4-oxadiazole units, exploring the emission and photoswitchable properties offered by the two units. Chapter three presents the synthesis of DPPH-derived betaines functionalized with 1,3,4-oxadiazole heterocycle and other structural units. This chapter also presents synthesis of the first dimer derived from DPPH and the corresponding diradical. Chapter four contains a detailed description of the experimental procedures and structural characterization of obtained compounds.

Experimental results fit the data in the literature and are appropriately integrated, standing out through original data and conclusions. The development of the fields of study show interest in these types of molecules, which impress with their ability to switch between properties.



CHAPTER 1. Azobenzenes and diradicals

Azobenzenes and the 1,3,4-oxadiazole heterocycle

Azobenzenes are the most intensively studied and applied molecular photoswitches[1], compounds that can interconvert between several states (isomers) under the action of light. The process is dictated by the isomerization of the N=N [2] double bond: the *E* state (thermodynamically stable) and *Z* state (metastable) presenting different properties (polarity, geometry, absorption parameters - $\lambda_{(max)}$,ε , π-π* and n-π* absorption bands, ^{1} H NMR spectra). The dynamic process offers applicability in the development of smart materials[3] sensitive to light or in photopharmacology[4] (photoswitchable pharmacophores that activate in the presence of light).

The parent compound, azobenzene, presents disadvantages in development of applications, mainly due to the limitations imposed by its structure[5]. The overlap of the n-π* bands in the UV-Vis spectra of *trans* and *cis* isomers (**Error! Reference source not found.**) leads to incomplete isomerization. The half-life of the metastable form (*cis*-azobenzene) is 2 days[5] (in solution, acetonitrile) and the wavelengths for initiating the isomerization process belong to the UV range for most molecules, limiting its applicability.

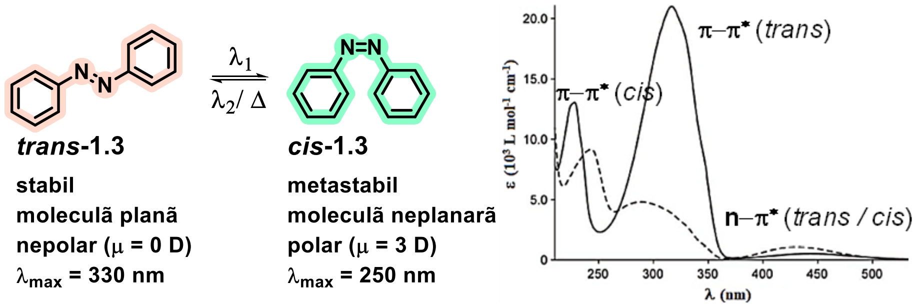


Figure 1 Isomerization of azobenzene and the different properties of the two isomers.

The disadvantages of azobenzenes[6] lead to derivatization strategies in order to increase performance of molecular photoswitches by improving the following parameters: addressability (separation of n-π* bands, irradiation wavelengths in the Vis range), efficiency (photostationary state of specific isomer), thermal stability (high values of $t_{1/2}$ of metastable) and fatigue resistance to repeated irradiation cycles. Main strategies[7] (Figure 1) consisted in extending π conjugation systems, substitution with acceptor-acceptor or donor-acceptor substituents, ethylene-bridged azobenzes or complexation of azo group to BF_2 units. The most efficient derivatization strategy involves tetra*ortho*substitution of azobenzene, especially with *fluoro* units[8]. Results demonstrated impressive improvements: shifting n-π* bands for both isomers (high photostationary states), addressability in Vis/NIR range and metastable forms with half-lives on the order of years.

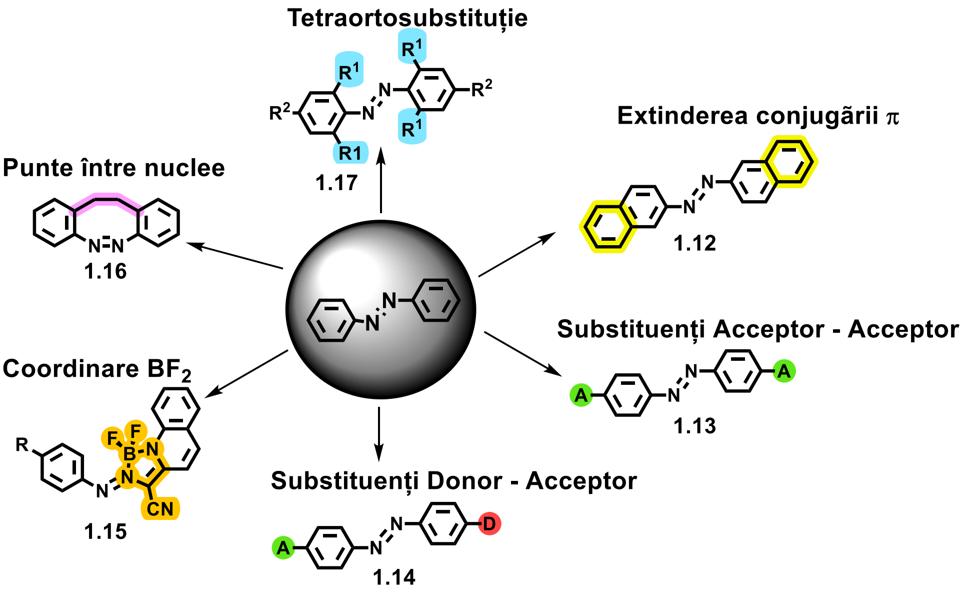


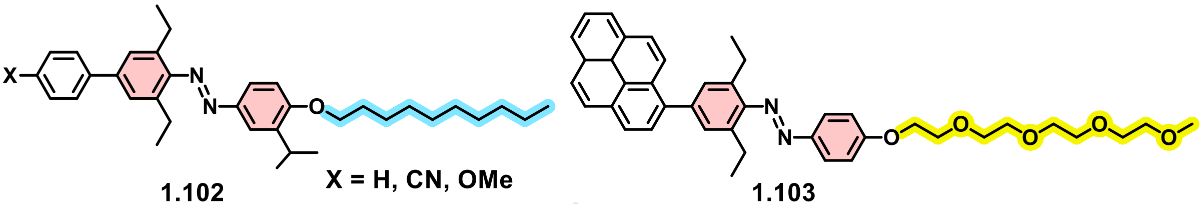
Figure 1 Derivatization strategies for azobenzene.

Azobenzenes can be obtained from various starting materials (primary aromatic amines – oxidation, nitroderivatives – reduction, hydrazoderivatives – oxidation or azoxiazobenzenes – Wallach reaction), but the most commonly used methods are *diazo coupling* and *Mills reaction*.

Diazotization and coupling reaction of primary aromatic amines is the main synthesis method used to obtain symmetrical and non-symmetrical azobenzene derivatives, due to its simplicity and high value yields. The method involves generation of diazonium salts as electrophilic partners, followed by coupling with nucleophilic agents (phenols or amines), under controlled pH conditions. The reaction mechanism is based on aromatic electrophilic substitution, which is simple and efficient. *The Mills reaction* is an excellent alternative, using nitroso and aniline derivatives in acidic medium (acetic acid). The method allows azobenzenes to be obtained with good yields and is applicable to a variety of substrates.

Photochromic fluorescent molecules are a class of compounds that combine two properties: the ability to switch between states under the influence of light and the emission of electromagnetic radiation in response to irradiation. The introduction of azobenzenes alongside the structure of a fluorophore leads to quenching of emission[9]. Derivatization strategies[10] have been developed to block the isomerization process, which subsequently allows the emission properties to be restored. Introduction of bulky substituents[10] in *ortho/ para* positions (**Error!**

Reference source not found.) or attachment of fluorophores[10] (pyrene or 1,3,4-oxadiazole) generated emission properties.



1.102 X = H, CN, OMe 1.103

Figure 3 Fluorescent azobenzenes – examples of derivatization.

Stable free radicals of the hydrazil type and diradicals

Free radicals[11] are chemical species that have an unpaired electron and stable ones can be manipulated under normal conditions of temperature, humidity, and light without losing their properties. Classification of radicals is presented inFigure 2. Their stability[12] (stable, persistent, unstable radicals) depends on factors like steric hindrance and system conjugation, which stabilize the unpaired free electron. Applications of such compounds can be found in materials chemistry (spintronics[13]) or design of molecules with interesting photophysical and optoelectronic properties (fluorescence and paramagnetism[14]).

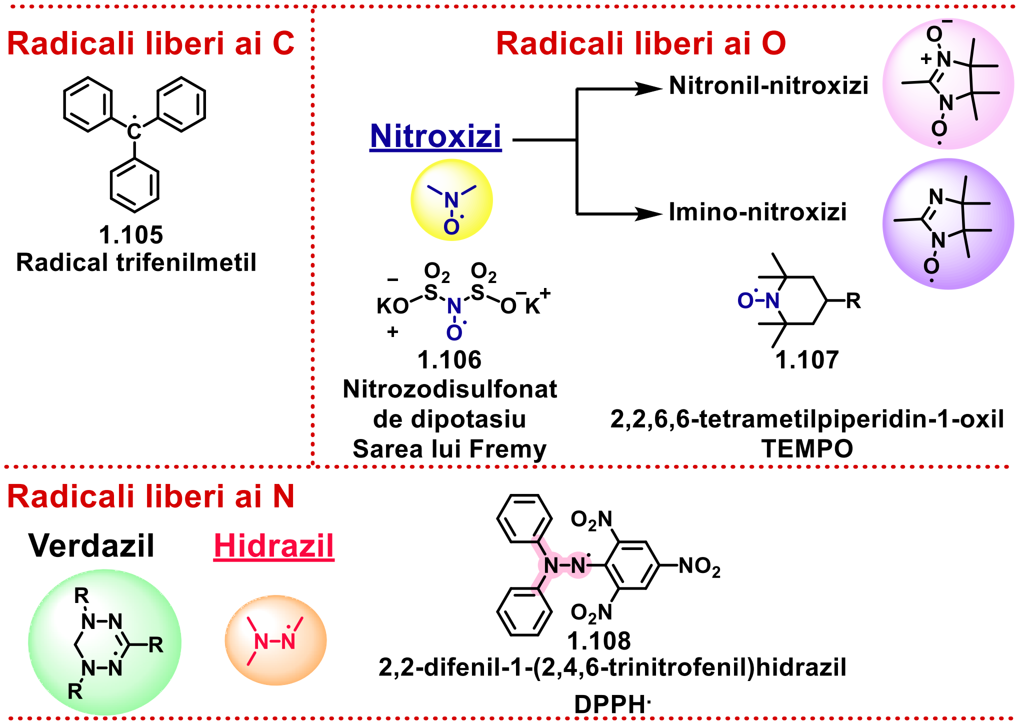


Figure 2 Classification of free radicals.

Hydrazil radicals[11], especially the DPPH molecule (2,2-diphenyl-1-(2,4,6-trinitrophenyl)hydrazil), are notable for their high stability (in solid or solution form), electrochemical, acid-base, and paramagnetic properties. The DPPH radical is used in the antioxidant assay test or as standard[15] in electron spin resonance spectroscopy (ESR). Stability[11] is provided by the steric hindrance generated by the bulky groups and the conjugation effect. The presence of donor (diphenylamino) and acceptor (picryl group) substituents contributes to this aspect. The resonance structures[11] of DPPH free radical (Figure 3) indicate the distribution of the free electron, which is found in a majority percentage on the hydrazine nitrogen atom bound to the picryl unit.

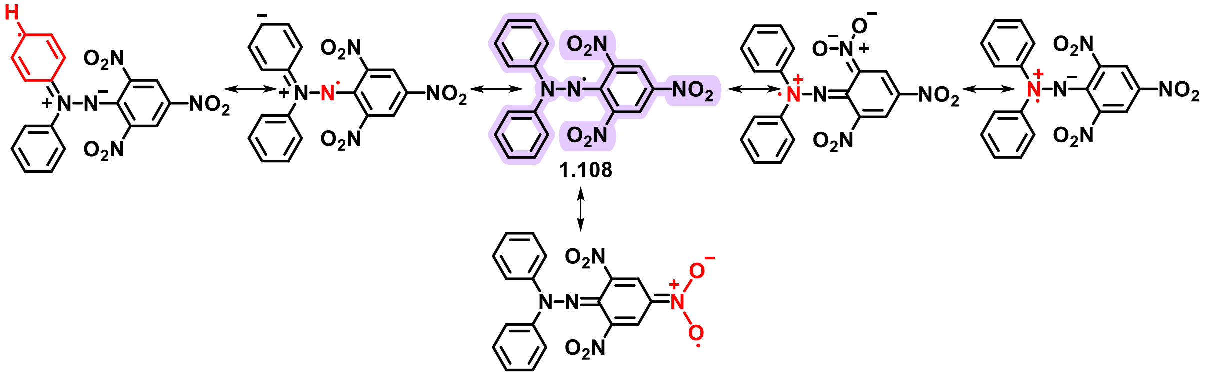


Figure 3 Resonance structures for the DPPH radical.

The DPPH radical[11] can be obtained in several steps (Figure 4): substitution reaction between picryl chloride and *N,N*-diphenylhydrazine, forming the reduced form DPPH-H, which subsequently, through the oxidation reaction in the presence of PbO_2, generates the DPPH radical.

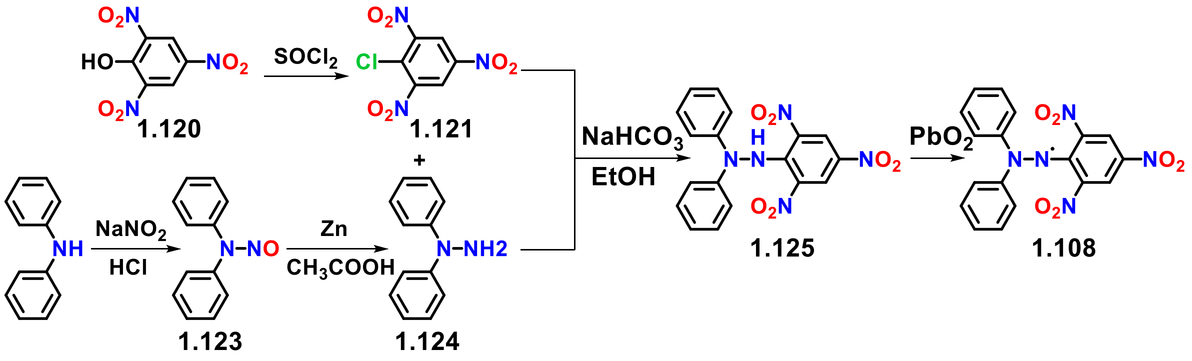


Figure 4 Synthesis of the DPPH radical.

Monoradicals[16] are defined as chemical species with single unpaired electron, characterized by the spin quantum number *S* = ½. When an external magnetic field (H*)* is applied in a certain direction, the magnetic moment of the electron (m_S) aligns parallel (m_S = -½) or antiparallel (m_S = +½) to it. The two orientations come from spin multiplicity value (2·*S* + 1 = 2·½ + 1 = 2 orientations), so that monoradicals are doublet species[16] . Diradicals[16] contain two unpaired electrons with parallel or antiparallel spins. These molecules can exist in singlet form (antiparallel spins, $S = 0$, multiplicity = 1) or triplet form (parallel spins, $S = 1$, multiplicity = 3). Diradicals in the singlet form cannot be detected by ESR (no Zeeman effect), but the triplet state can be characterized by ESR, having three energy levels. This spectroscopic method is an excellent way to differentiate between state of diradical system[16].

Kekulé delocalized diradicals (Figure 5) are notable for their ability to exist in two different molecular states: *closed-shell* (chinoid) and *open-shell* (*diradialoid*), based on the presence of a chemical equilibrium between them. Physical and chemical properties of such compounds are influenced by external stimuli (pH, reducing/ oxidizing agents, presence of oxygen, light), having interesting optical, magnetic, redox and acid-base properties. They can be classified [16] (Figure 5) into *homodiradialoids* quinodimethane (C,C*)*, quinone (O,O*)* and quinodiimine (*N*,*N*). The tri-*p*-quinodimethane derivative[16] **1.143** functionalized with four -CN functional groups is notable for its high stability in the diradical form, compared to the quinone form. It has been studied for possible applications in the field of organic batteries.

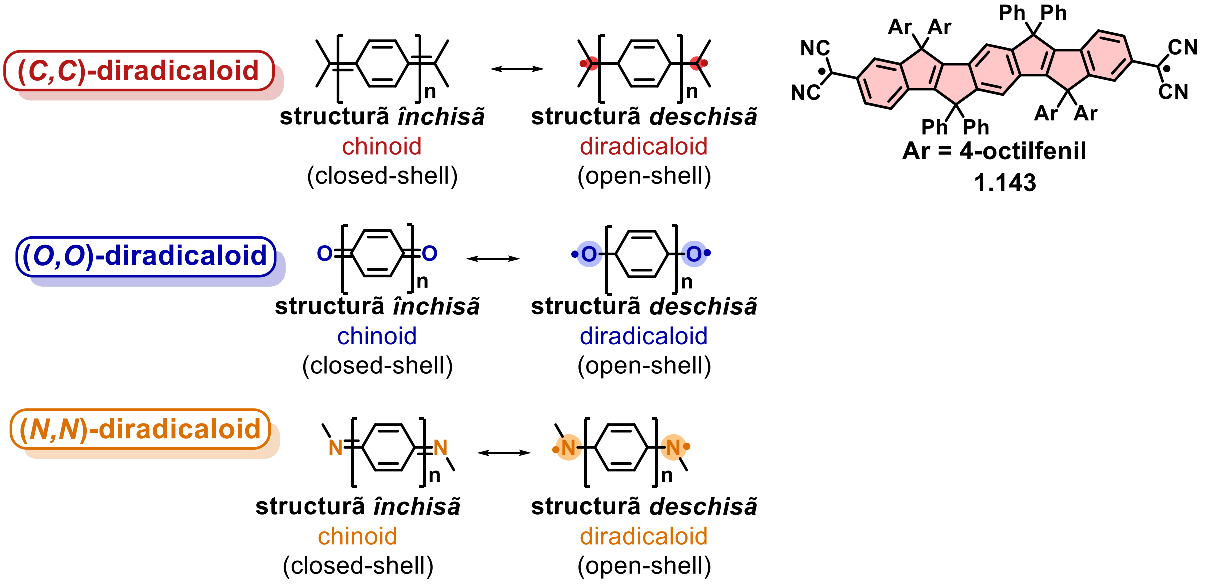


Figure 5 Classification of diradicals.

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CHAPTER 2. Azobenzenes and diradicals

In this chapter we designed new series of azobenzenes **2.1a-h** (Figure 6), decorated with 1,3,4-oxadiazole units, presenting structural functionalization. Derivative **2.1a** has a donor-acceptor structure (*methoxy* - electron donor effect and *1,3,4-oxadiazole heterocycle* – behaves as electron acceptor substituent). Derivatives **2.1b** and **2.1g,h** present stabilizing substituents in *ortho, ortho'* positions, with a steric (*dimethyl*, for **2.1b)** or electronic (*difluoro*, for **2.1g** and *pentafluoro* **2.1h)** role. The naphthalene derivative **2.1c** was designed to extend the π conjugation of the system and finally long hydrocarbon units of the alkoxy type (hexyloxy – **2.1d** and **2.1e;** dodecyloxy – **2.1f)** or pyrenyl groups (**2.1e** and **2.1f)** were introduced to generate emission properties.

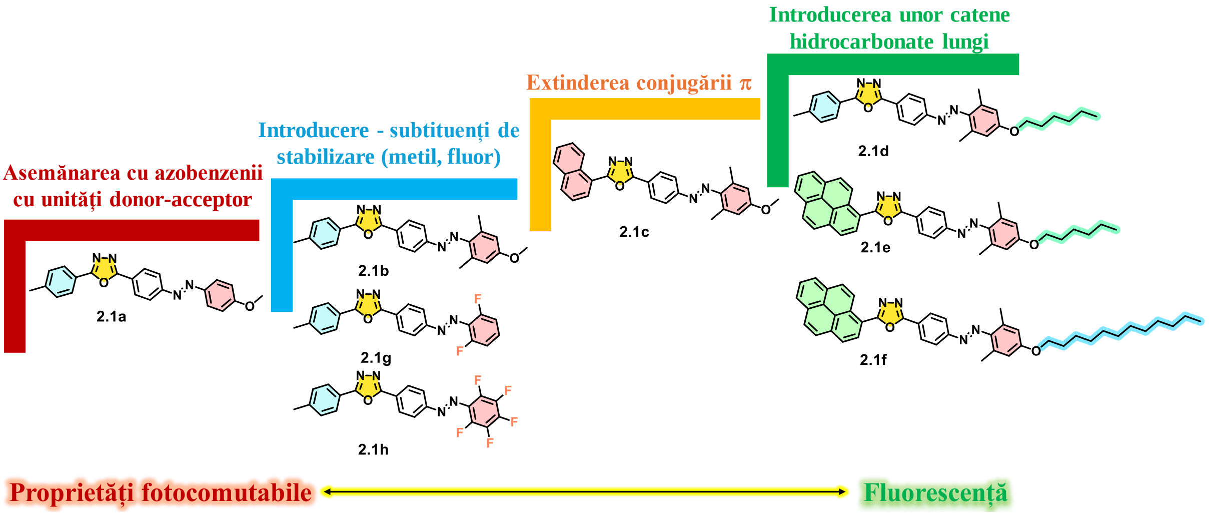
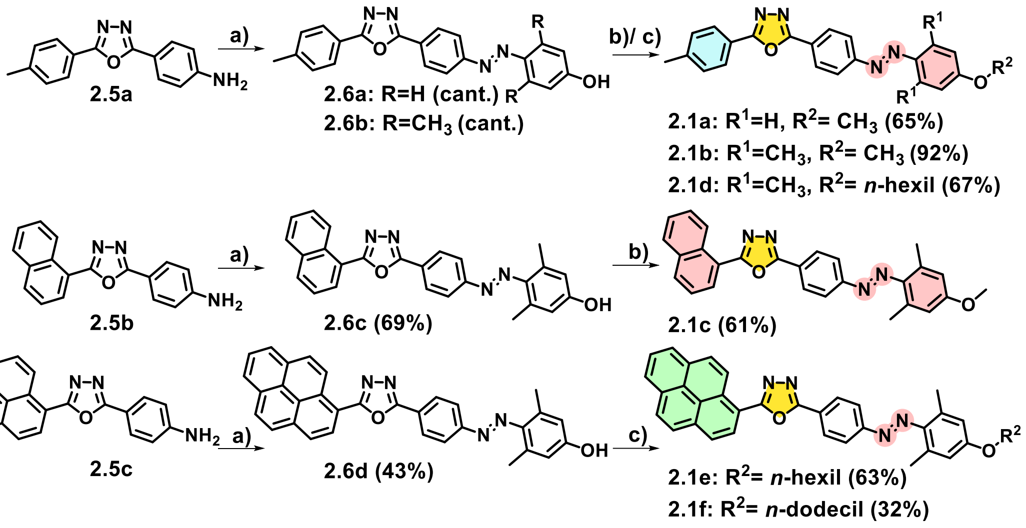
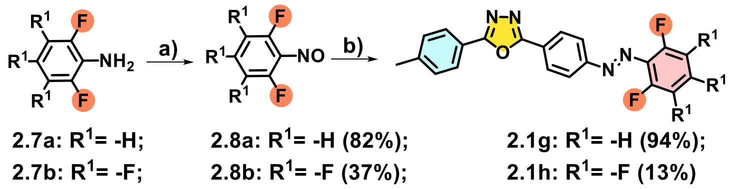


Figure 6 Structures of azobenzenes decorated with 1,3,4-oxadiazole units – justification of substituents.

Primary aromatic amines functionalized with different aryl groups (*p*-tolyl, 1-naphthyl, 1-pyrenyl) **2.5a-d** were used as starting materials in diazotation and coupling reactions with phenol and 3,5-dimethylphenol (Figure 7). The resulting hydroxyazobenzenes further participated in alkoxylation reactions in the presence of halogenated agents (methyl iodide, hexyl bromide or dodecyl bromide) to generate target azobenzenes **2.1a-e.** The polyfluorinated azobenzene derivatives **2.1g,h** were obtained by Mills reaction, starting from the corresponding halogenated anilines, which were initially converted into the nitroso derivatives **2.8a,b.** Last stept consists in reaction with 1,3,4-oxadiazole amine **2.5a** in the presence of acetic acid to form fluorinated azobenzenes **2.1g** and **2.1h.**



a) *i)* $NaNO_2$, HCl, 0-5°C; *ii)* NaOH, fenol pentru **2.6a**/3,5-dimetilfenol pentru **2.6b,c**, 8h, rt;
b) CH_3I, K_2CO_3, acetonă/DMSO, rt (**2.1a-c**);
c) $Br(CH_2)_5CH_3$ (**2.1d,e**) / $Br(CH_2)_{11}CH_3$ (**2.1f**), K_2CO_3, KI, acetona/DMSO, rt.



a) Oxonă, H_2O/DCM, rt, 2h; b) **2.5a**, AcOH, reflux, 24h.

Figure 7 Synthesis of intermediates (hydroxyazobenzene) and azobenzenes 2.1a-h.

The photochromic properties of derivatives **2.1a-h** are found in

Compound	λ_{max} (nm) ($\varepsilon \times 10^4$ M^{-1} cm^{-1})						**PSS (%)**		$t_{1/2}$ **(h)**
	π–π*			**n–π***			***Z***	***E***	
	E	***Z***	**Δλ**	***E***	***Z***	**Δλ**			
2.1a	376 (2.35)	324	-52	460 (0.33)	443	-17	93	66	11.72 (DMSO)
2.1b	377 (2.24)	311	-66	466 (0.19)	467	1	81	76	105.02 (DMSO)
2.1c	373 (2.16)	311	-62	467 (0.23)	454	-13	63	75	115.52 (DMSO)
2.1d	376 (3.81)	306	-70	470 (3.33)	451	-25	81	74	82.5 (DMSO)

2.1e	382 (4.29) 395 (4.17)	-	-	470 (0.44)	-	-	48	66	103.4 (DMSO)
2.1f	378 (4.87) 396 (4.61)	-	-	486 (0.53)	-	-	40	70	154.03 (DCM)
2.1g	355 (3.44)	307	-48	454 (0.3)	426	-28	81	73	1732.86 (DMSO)
2.1h	354 (2.66)	321	-33	465 (0.13)	429	-36	74	54	866.4 (DMSO)
azobenzene[2,3,4]	320	280	40	440	440	0	70	70	48 (ACN)

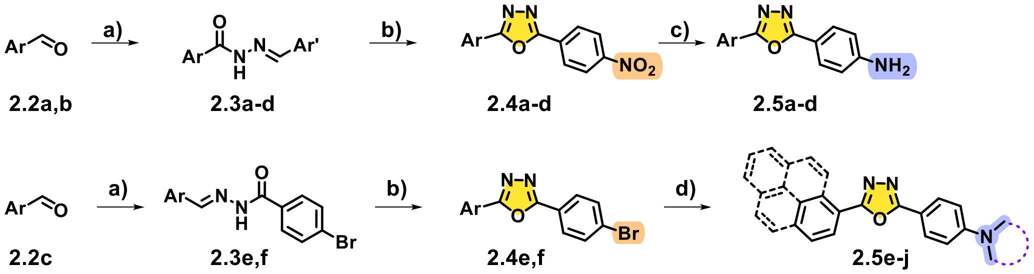
Table *1*. The absorption wavelengths corresponding to the π-π* bands of the synthesized azobenzenes are red-shifted (λ_{max}= 370 nm for **2.1a-f** and λ_{max}= 350 nm for **2.1g,h)**, compared to unsubstituted azobenzene (λ_{max}= 320 nm). The n-π* bands showed smaller differences, with the highest values found for fluorinated azobenzenes ($\Delta\lambda$= -48 nm for **2.1g** and $\Delta\lambda$= -33 nm for **2.1h**). Influence of the 1,3,4-oxadiazole heterocycle is observed both for the positions of the absorption bands relative to the unsubstituted azobenzene and for the high values of the molar absorption coefficients for the *E* isomers. Efficiency of photochemical process shows high values, generally being PSS (%*E*) > 63% and PSS (%*Z*) > 54% for azobenzenes **2.1a-c** and **2.1g,h.** Compounds **2.1e,f** showed lower efficiency values, but are notable for their emission properties in solution. All compounds were stable under repeated irradiation cycles. The half-life times for metastable forms vary with substituents, the best value being obtained for the difluorinated derivative **2.1g**: $t_{1/2}$= 1732 h. The compound stands out from the series of synthesized azobenzenes, the two substituents in the *ortho* and *ortho'* positions being sufficient to ensure the performance of the system, along with the attachment of the heterocycle 1,3,4-oxadiazolic, comparable to results obtained in the literature[1]. Addressability and reliability were evaluated by UV-Vis spectroscopy and the efficiency and half-life of the metastable form were investigated using ^{1}H NMR spectroscopy.

Compound	**λ_{max} (nm) ($\varepsilon \times 10^4$ M^{-1} cm^{-1})**						**PSS (%)**		**t$_{1/2}$ (h)**
	π–π*			**n–π***			***Z***	***E***	
	E	***Z***	**Δλ**	***E***	***Z***	**Δλ**			
2.1a	376 (2.35)	324	-52	460 (0.33)	443	-17	93	66	11.72 (DMSO)
2.1b	377 (2.24)	311	-66	466 (0.19)	467	1	81	76	105.02 (DMSO)
2.1c	373 (2.16)	311	-62	467 (0.23)	454	-13	63	75	115.52 (DMSO)
2.1d	376 (3.81)	306	-70	470 (3.33)	451	-25	81	74	82.5 (DMSO)
2.1e	382 (4.29) 395 (4.17)	-	-	470 (0.44)	-	-	48	66	103.4 (DMSO)
2.1f	378 (4.87) 396 (4.61)	-	-	486 (0.53)	-	-	40	70	154.03 (DCM)
2.1g	355 (3.44)	307	-48	454 (0.3)	426	-28	81	73	1732.86 (DMSO)
2.1h	354 (2.66)	321	-33	465 (0.13)	429	-36	74	54	866.4 (DMSO)
azobenzene[2,3,4]	320	280	40	440	440	0	70	70	48 (ACN)

Table 1 Photochromic properties of synthesized azobenzenes.

The integration of 1,3,4-oxadiazole moiety into azobenzene molecules **2.1a-d** and **2.1f,g** quenches light emission. The phenomenon is attributed to the photoisomerization process, being similar to data found in the literature[5]. Replacing aryl units with condensed structures (1-pyrenyl) and attaching long hydrocarbon chains (azobenzenes **2.1e,f)** leads to recovery of the emission properties. Azobenzenes that exhibit emission in solution, while maintaining their photoswitchable properties represent promising aspects for new applications in development of fluorescent photochromic materials.

Study and synthesis of azobenzenes required obtaining the primary aromatic amines **2.5a-d**. Synthetic methodology (Figure 8) begins with **condensation** of aldehydes with corresponding hydrazides, followed by **cyclization** of *N*-acylhydrazones, forming 1,3,4-oxadiazoles substituted with nitro (**2.4a-d**) or bromo (**2.4e,f**) units, followed by **reduction** of nitro group to the corresponding amines. Derivatization of primary amines was achieved by C-N coupling reaction[6] of synthesized bromoderivatives **2.4e,f** with secondary commercial amines. Thus, the series of compounds **2.5e-j** was obtained, presenting donor (diethylamino, diphenylamino, carbazole) and acceptor (9-anthracenyl, 1-pyrenyl) substituents.



a) 4-metilbenzohidrazida, 1-naftilaldehida, 9-antracenilcarbaldehida, 1-pirencarboxaldehida, **TFA**, **DMSO/ $CHCl_3$,** 90°C, 12h;

b) **I_2, K_2CO_3, DMSO,** 90°C, 5h (**2.4a,b**, **2.4e,f**) / **PIFA, DCM,** DMF, r.t., 3 zile **(2.4c,d);**

c) **NH_2-NH_2 H_2O, Pd/C**, EtOH, DMF, reflux, 24h.

d) Carbazol/ dietilamina/ difenilamina, Pd_2dba_3, Xantphos, toluen anhidru, argon, reflux, 24 (2.5e-j).

Figure 8 Synthesis of primary aromatic amines 2.5a-d and tertiary amines 2.5e-j.

The absorption properties of **2.5a-j** were studied in different polarity solvents: toluene, DCM, THF, ACN, DMSO and MeOH. A weak positive solvatochromism was observed (Figure 9) with shifting wavelengths towards the red region as the polarity of the solvents increases. These characteristics are attributed to intramolecular charge transfer ICT[7] between the donor and acceptor units.

For primary aromatic amines with condensed aromatic cores, solvatofluorochromism has been observed - different emission wavelengths depending on polarity of the solvent. For example, anthracene substituted amine **2.5e** (Figure 9) exhibits emission wavelengths in green range (λ_{em}= 500 nm, toluene), yellow range (λ_{em}= 560 nm, THF and λ_{em} = 564 nm, DCM), shifting to orange (λ_{em}= 625 nm, MeOH) and red (λ_{em}= 660 nm, ACN and λ_{em}= 678 nm, DMSO) as the polarity increases. Synthesized novel compounds generally exhibit emissions over broad wavelength ranges, covering the entire UV-Vis spectrum[8].

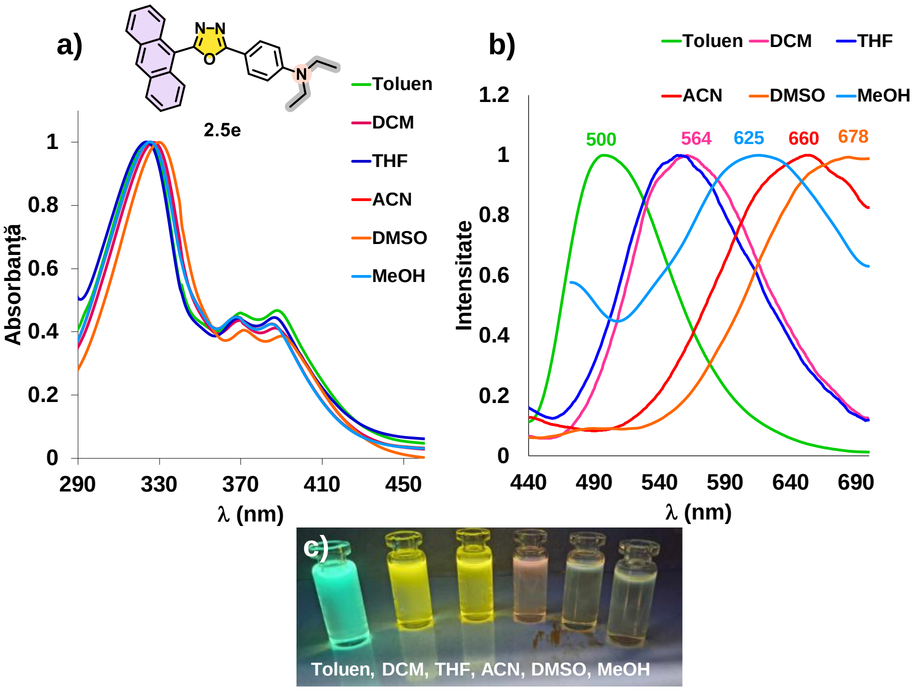


Figure 9 a) Normalized absorption spectra for 2.5e (2 x 10^{-5} M) in solvents with different polarities. b) Normalized emission spectra in all solvents (10^{-6} M), except ACN and MeOH (10^{-5} M) and DMSO (10^{-4} M). c) Photographs of solutions for 2.5e in different solvents, under a UV lamp.

For **2.5e**, aggregate formation in solution (Figure10) was observed upon successive addition of 0-98% H_2O to DMSO solution (10^{-5} M). A decrease in band intensity of emission (λ_{em}= 678 nm) was observed, upon addition of H_2O, from 0-25%, reaching an almost completely quenched emission at 50% H_2O (Aggregation Caused Quenching[9]) and the appearance of a new emission band at λ_{em}= 531 nm (75% H_2O), which increases in intensity upon the addition of 90-98% H_2O (Aggregation Induced Emission[9]).

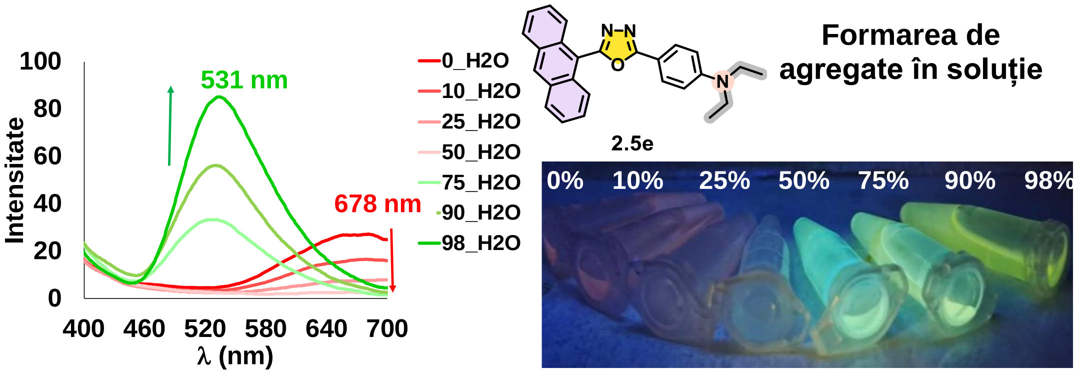


Figure10 Addition of H_2O (0-98%) over DMSO solution (2.5e), solutions irradiated under UV lamp (365 nm).

To evaluate the influence of emission upon acidic medium on amines, we investigated solution of pyrene derivative **2.5h**, recorded in DMSO, at 10^{-5} M. The same concentration was achieved by adding 100 μL of 0.1 M HCl. Recordings indicate changes in emission wavelengths, with hypochromic shifts in the blue range, from λ_{em}= 608 nm to λ_{em}= 429 nm. At the same time, an increase in the intensity of emission in acidic medium was observed, as a result of protonation of the nitrogen.

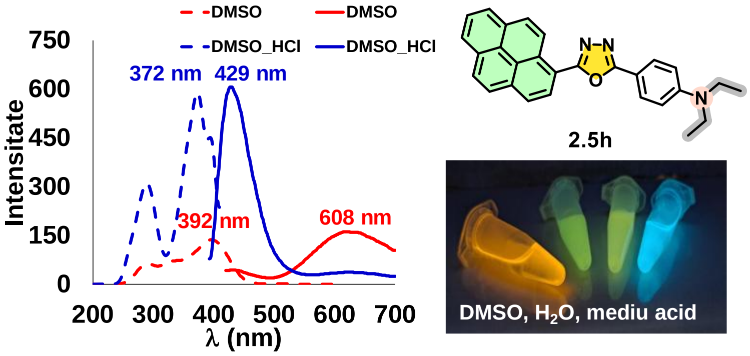
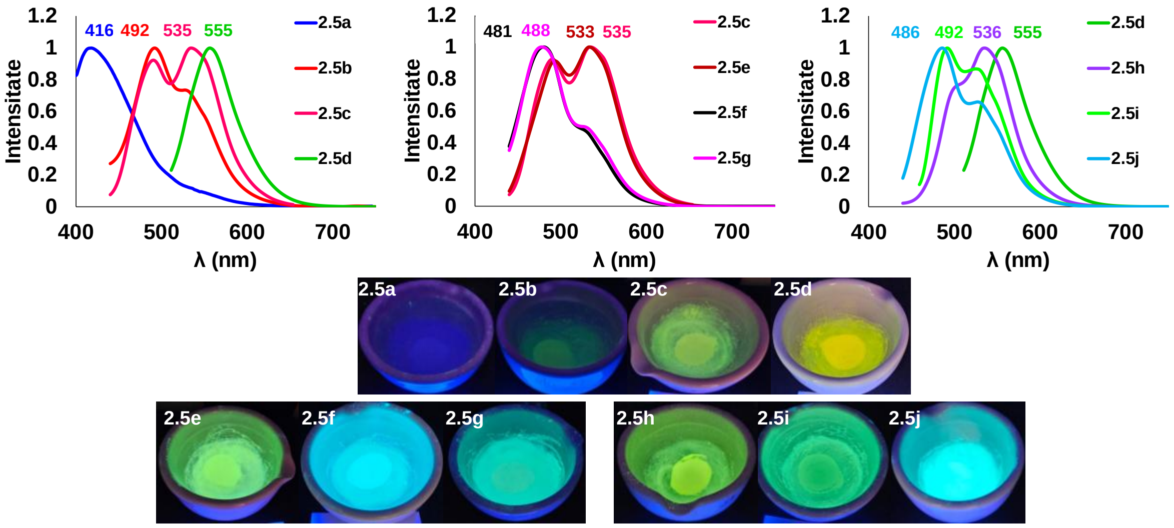


Figure11 Excitation and emission spectra in DMSO (2.5h, 10^{-5}M) and in acidic medium (100 µL HCl 0.1 M).

Solid-state emission is observed for all amines **2.5a-j** (12). The reported wavelengths vary in several ranges: blue (λ_{em}= 416–492 nm), green (λ_{em}= 533–536 nm), or yellow (λ_{em}= 555 nm). The Stokes shift values are high, especially for amines functionalized with 9-anthracenyl units: **2.5c** (8631 cm^{-1}/ 169 nm), **2.5e** (8265 cm^{-1}/ 163 nm), with pyrene amine exhibiting the highest value: **2.5h** (8666 cm^{-1}/ 170 nm). The fluorescence quantum yields vary, but do not exceed 0.1.



12 Figure. Solid-state emission spectra. Images of synthesized amines, under UV lamp.

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CHAPTER 3. Functionalized betaines derived from stable DPPH radical and their diradicaloid behavior

The most well-known hydrazil radical, 2,2-diphenyl-1-(2,4,6-trinitrophenyl)hydrazil (DPPH)[1] is valued for its acid-base, electrochemical and paramagnetic properties. The thesis involved synthesis and characterization of novel compounds derived from DPPH (Figure 13). Combination of the free radical unit with 1,3,4-oxadiazole heterocycle (known for the optical properties[2]) can influence the behavior of multifunctional molecules[3]. In this chapter, the diradicaloid character[4] of some betaines derived from DPPH was investigated. Finally, the first dimer of the DPPH radical was synthesized, obtaining the corresponding diradical, whose properties were analyzed by CV, ESR or SQUID. The results presented in this chapter are surprising and encourage further exploration of the field of DPPH-type diradicals.

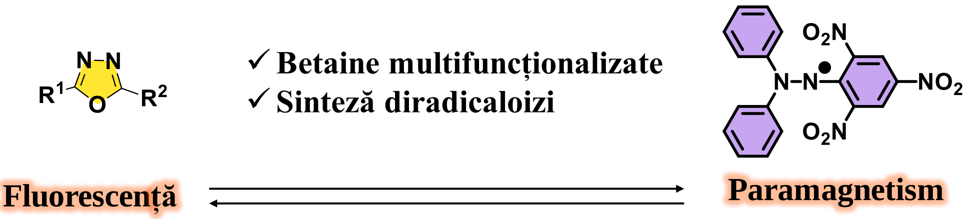
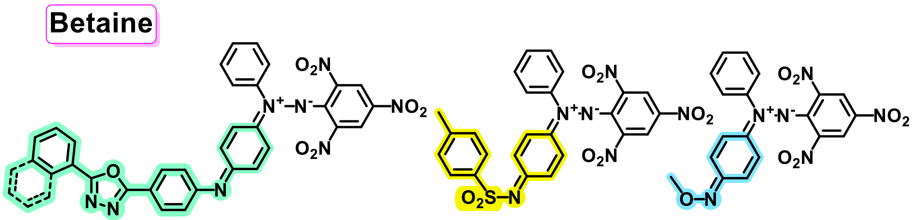


Figure 13 The relationship between the 1,3,4-oxadiazole heterocycle and the DPPH structural motif.

Based on data from the literature[6], functionalized betaines with various aryl units (tosyl – **3.3a**, aminomethyl – **3.4**) and with 1,3,4-oxadiazole heterocycle (**3.1a** and **3.2a**) were synthesized. The structures can be found in Figure Figure **14** .



3.1a Ar = *p*-tolil
3.2a Ar = 1-naftil

3.3a

3.4

Figure 14 Betaine derivatives of DPPH with different aryl units.

The betaines were synthesized by reacting the reduced form of DPPH radical (DPPH-H) with aromatic amines, functionalized with different aryl units, in the presence of the oxidizing agent PbO_2 (Figure 15 – 1,3,4-oxadiazole betaines and hydrazines). Through a radical mechanism, the corresponding betaines (**3.1a-3.4)** are synthesized and their reduction leads to the corresponding hydrazines (**3.1b-3.5)** (Figure 15), in the presence of sodium ascorbate.

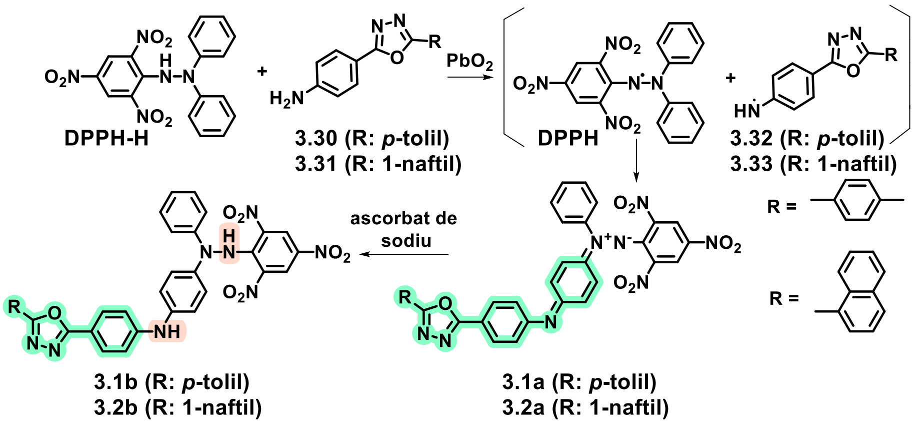


Figure 15 Reaction for obtaining betaines functionalized with 1,3,4-oxadiazole aryl units.

An interesting aspect of the chemical behavior corresponding to functionalized betaine with aminomethyl unit (derivative **3.4**) is the reduction step in the presence of sodium ascorbate (Figure 16). This step does not exhibit classic behavior, yielding amino-DPPH (derivative **3.5)**, which leads to the formation of a homocoupling product, azo-DPPH.

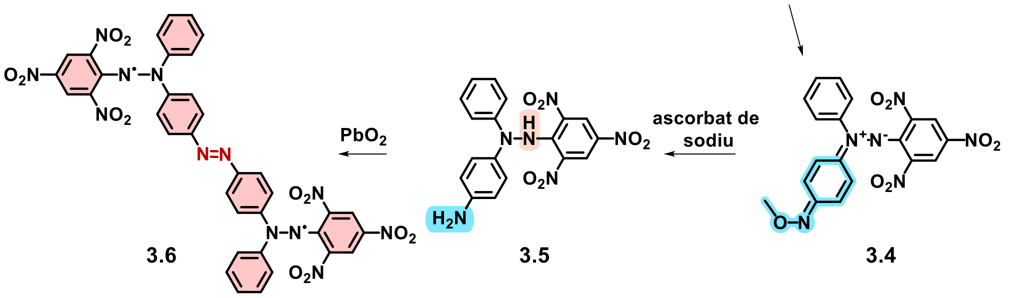


Figure 16 Obtaining amino-DPPH.

Being paramagnetic species, the structure of azo-DPPH derivative was confirmed by its slow crystallization from a solution in DCM, its crystals being subsequently analyzed by single crystal X-ray diffraction. The structure can be seen inFigure 17. It can be mentioned that azodiradical **3.6** crystallizes together with the DCM solvent, in a 2:1 ratio.

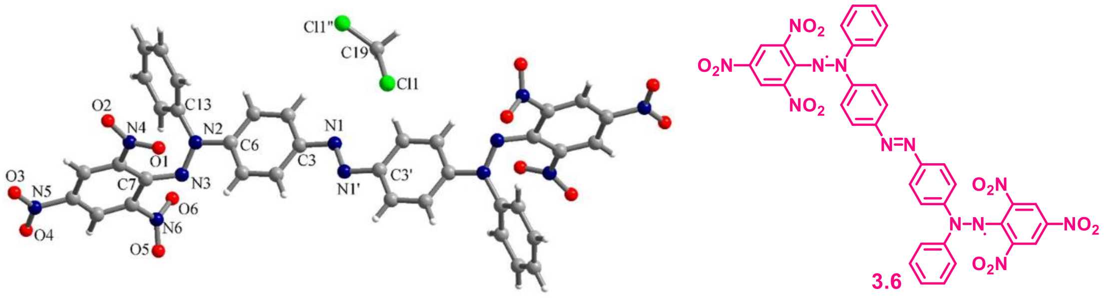


Figure 17 X-ray structure obtained for the DPPH azodiradical 3.6.

Betaine derivatives of DPPH[1] are compounds that exhibit complex equilibria resulting from resonance structures and free electron mobility. They are found in amphionic (zwitterionic/aromatic) or diradicaloid (Figure 18) forms, which behave different in terms of absorption spectra, RES signal, acid-base or redox behavior.

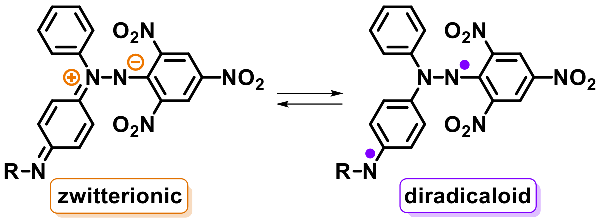


Figure 18 The equilibrium between the zwitterionic (aromatic) and diradicaloid forms of the synthesized betaines.

The diradicaloid character of betaines **3.1** - **3.3a** and **3.4**, respectively of azo-DPPH **3.6**, was investigated by electron spin resonance spectroscopy (ESR). No signals were observed for solution of betaines, regardless of the attached aryl group. Solid-state studies indicate an ESR signal only for the betaine functionalized with tosyl unit (**3.3a)**, with weak intensity. The spectrum (Figure 19) shows quintet multiplicity of 1:2:3:2:1, with intense central line. Appearance of RES signal, even in the solid state, suggests the presence and interaction of free electrons in betaines, and therefore the possibility of presence for diradicaloid state.

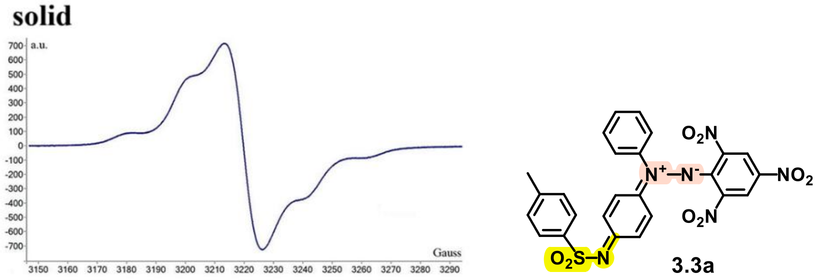


Figure 19 ESR spectrum for betaine 3.3a in the solid state (left).

Other DPPH derivatives with diradical properties are presented in Figure 20. Structure **3.9**, which has two radical centers, may be one such example. The synthesis was approached based on the reaction between the bromoderivative derived from DPPH **3.7** and amino-DPPH **3.8**. To obtain the amino derivative **3.8**, the synthetic strategy started from diphenylamine **3.34** as starting material and leads to protected amino compounds (DPPH derivatives **3.11** and **3.12**), which were investigated in terms of structure and reactivity.

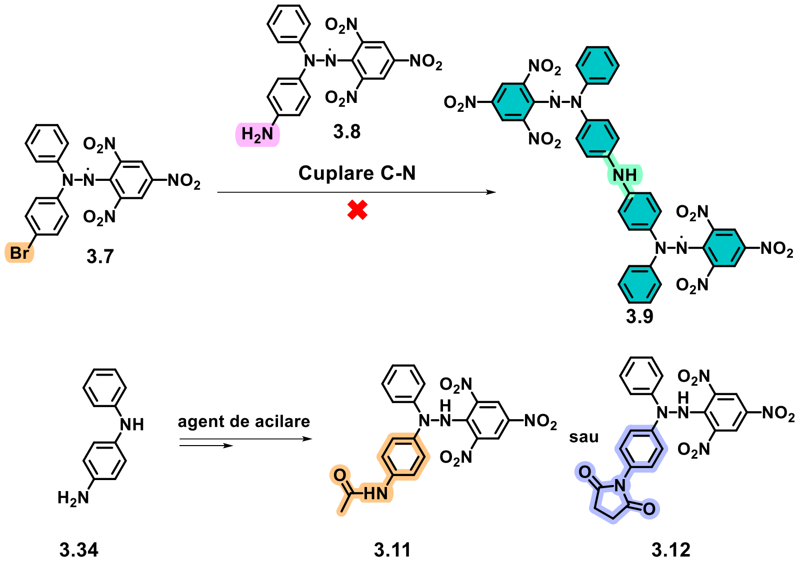


Figure 20 Structures of compounds of interest by methods that generated DPPH derivatives.

The synthesis fromFigure 20 presented limitations in obtaining the amino derivative **3.8**, so the focus shifted to obtaining the dimer derived from DPPH **3.10a** (Figure 21). The symmetrical derivative was not synthesized by this synthesis route (formation of degradation products). During the process of obtaining derivative **3.7** by bromination of DPPH, brominated derivatives of DPPH with several halide units (**3.14**, **3.15**, and **3.16)** were synthesized and investigated. Figure 21 shows the oxidation reaction of DPPH, yielding oxo-betaine **3.17**[7]. We obtained novel brominated DPPH derivatives, betaines **3.18** and **3.19**.

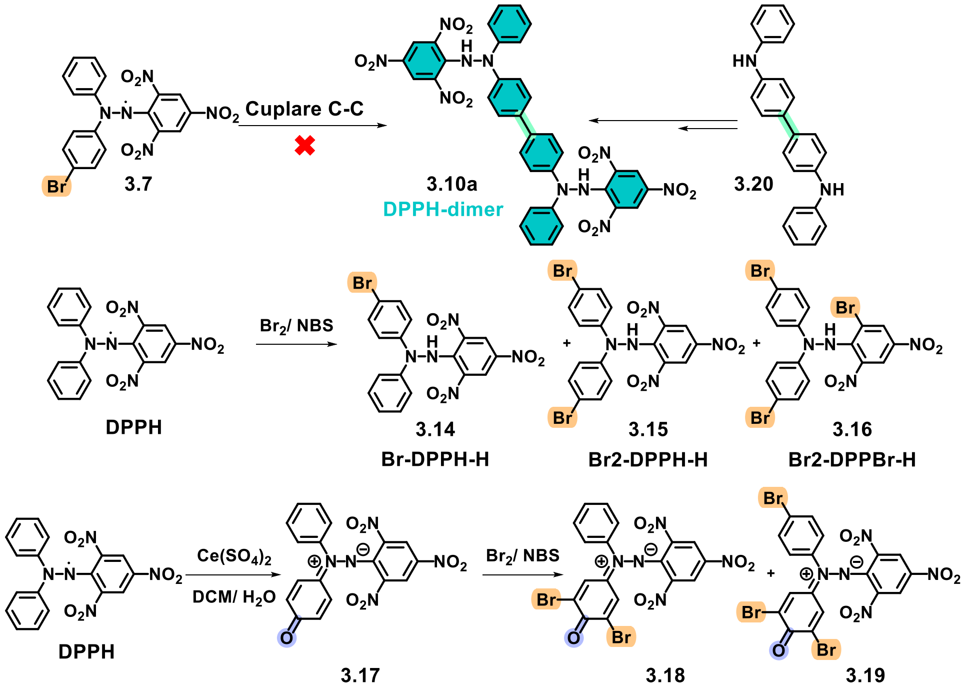


Figure 21 Structure of the dimer and brominated derivatives obtained by stepwise synthetic strategies.

Derivatives **3.17-3.19** were investigated for their diradicaloid character (Figure 22), observing absence of ESR signals (in solution/solid state) for brominated derivatives **3.18** and **3.19**. Derivative **3.17** shows an ESR signal in the solid state, indicating the zwitterionic form of brominated betaines **3.18** and **3.19,** with the oxo derivative being in equilibrium with the diradicaloid form. The data encourages the study of betaines for the development of diradicaloid properties.

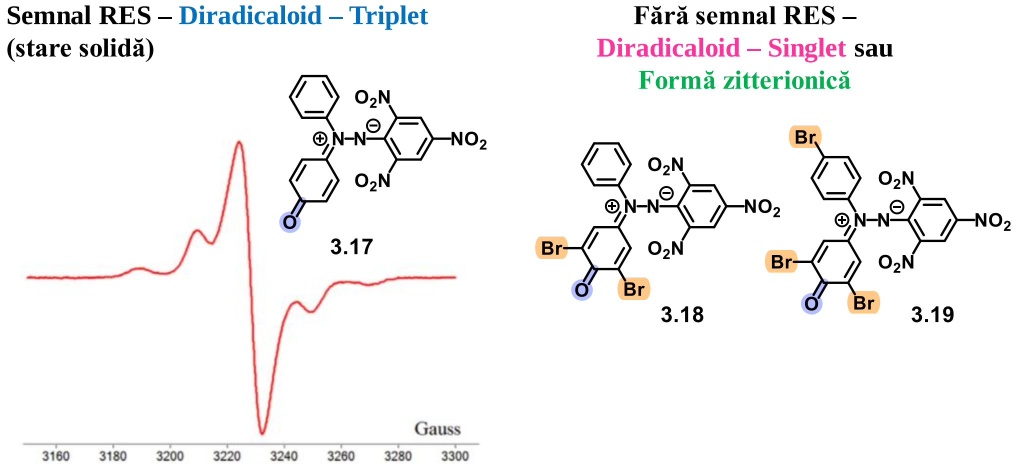


Figure 22 Solid-state RES spectrum for 3.17.

The cyclic voltammograms of betaines **3.17-3.19** are shown inFigure 23. Dibrominated derivative **3.18** shows two pairs of peaks corresponding to the generation of cation and dication radicals, obtained only for this betaine, as shown in the presented voltammograms.

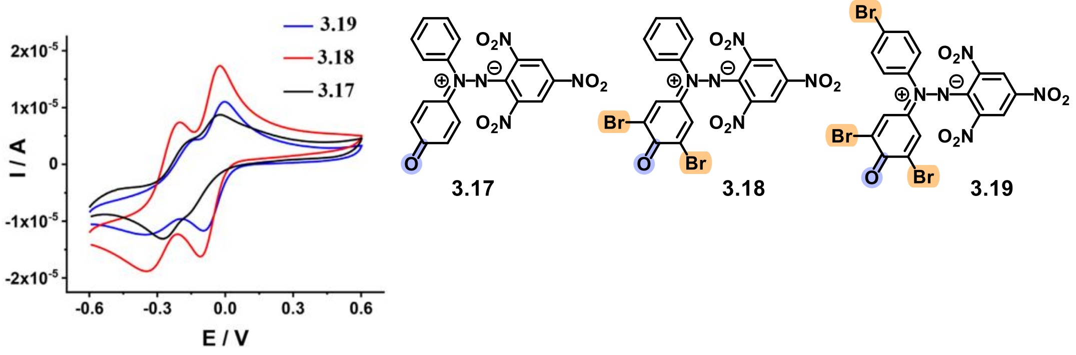


Figure 23 Cyclic voltammograms for 3.17-3.19.

Figure 24. The starting material was symmetrical molecule *N*,*N*-diphenylbenzidine **3.41**, every unit being attached step by step, as in classic synthesis routes of the DPPH[1] free radical. We obtained diradical **3.10b** by oxidizing the DPPH dimer **3.**10a, in the presence of PbO_2.

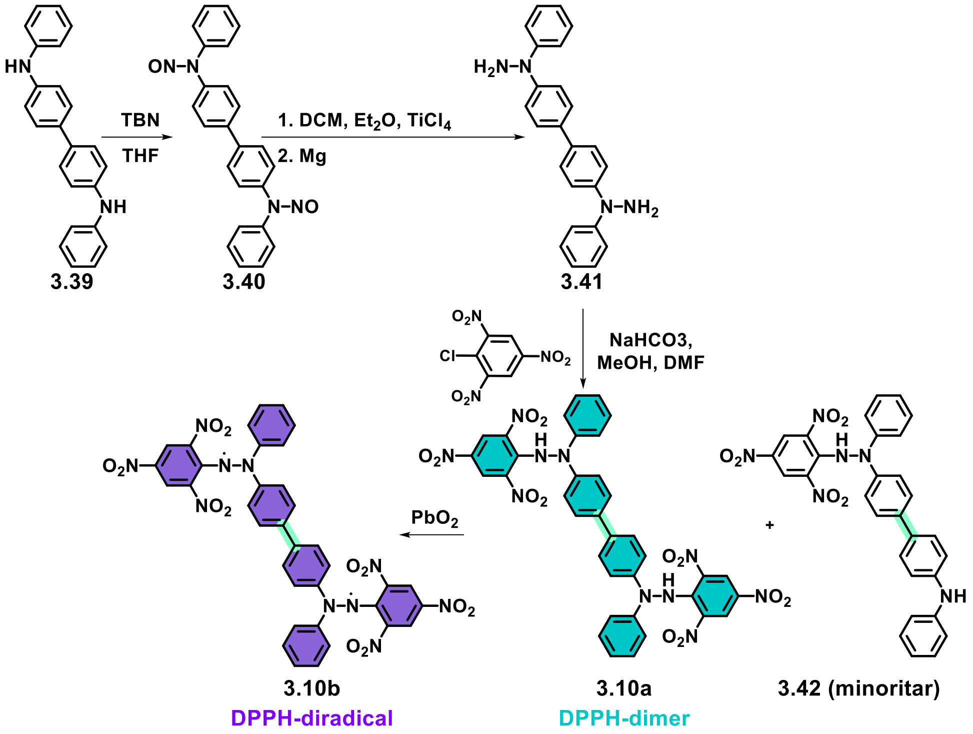
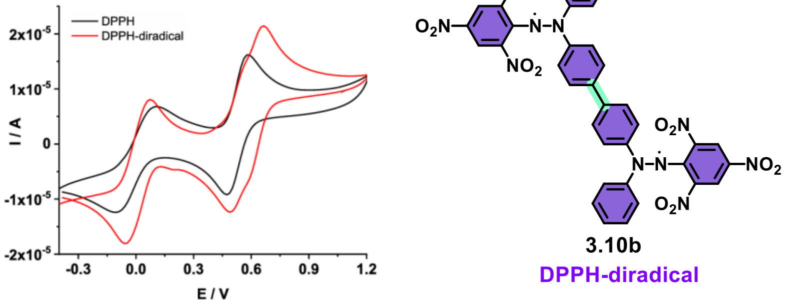


Figure 24 Synthesis of DPPH dimer and DPPH diradical.

Electrochemical properties of DPPH radical and DPPH diradical (**3.10b**) were investigated by cyclic voltammetry. InFigure 25, we observe similarity between voltamograms of the two derivatives, especially with regard to the shape of the voltamograms and the values for the oxidation and reduction peaks.

a) VC



b) RES în soluție (DCM) **c) RES în solid**

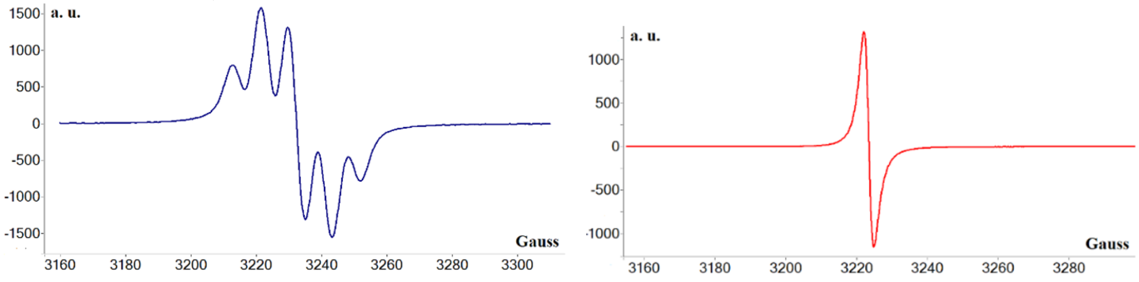


Figure 25 a) Cyclic voltamograms of the DPPH radical (black) and the DPPH diradical (red). ESR spectra of the 3.10b diradical in solution (a) and in the solid state (b).

ESR spectrum in solution (DCM) of diradical **3.10b** (Figure 25) indicates similarity to DPPH derivative, with quintet multiplicity and intensities 1:2:3:2:1. The solid-state signal (Figure 25) is represented by a single line with 2.78 Gauss width. The presence of signals indicates diradical state in both solution and solid state, with the triplet stated probably also present in equilibrium with the singlet.

SQUID[8] is the technique used to study magnetism of molecules at different temperatures. Recordings for **3.10b** can be found inFigure 26 . To investigate the equilibrium between the triplet and singlet states, saturation magnetization parameter (emu/mol/Oe) was calculated for several temperatures (300 K, 200 K, and 2 K). Saturation magnetization appears at a value of 632 emu/mol, while converting this value to magnetic moment represents 0.11 μB. A triplet state can have a magnetic moment of 2 μB, so 0.11/2 = 5.5% of the species exhibit triplet-type characteristics. Most of the **3.10b** diradical molecules are found in singlet form (which does not exhibit paramagnetism), and 5.5% of them belong to the triplet state, which indicates weak magnetism.

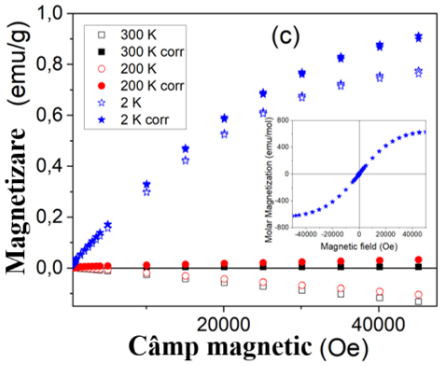


Figure 26 SQUID measurements recorded for the DPPH 3.10b diradical.

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General conclusions

The doctoral thesis entitled *"New organic molecules obtained by combining isomerizable units with stable free radicals"* presents synthesis and characterization of novel organic derivatives containing the following structural units: azobenzene, 1,3,4-oxadiazole heterocycle and the stable DPPH free radical. Azobenzenes are known for their photoswitching properties and the dynamic equilibrium between the two isomers, when irradiated with light. The synthesized derivatives alternate between this property and the light emission generated by the presence of the 1,3,4-oxadiazole heterocycle. DPPH derivatives exhibit properties offered by their radical nature (acid-base, electrochemical, and paramagnetic). Synthesis of DPPH betaines led to characterization of diradicaloid nature. Designing compounds with two radical centers was concluded by the synthesis of the first DPPH dimer and the corresponding diradical, which was characterized for molecular magnetism.

The paper was structured in four chapters. The first was based on a literature review, the next two chapters focused on describing the synthesis and properties of the molecules using various spectroscopic methods, and the last chapter was based on detailing the experimental part. The synthesized compounds were analyzed by physical and spectral methods (nuclear magnetic resonance spectroscopy, IR spectroscopy, mass spectroscopy, single crystal X-ray diffraction, absorption and emission spectroscopy, cyclic voltammetry, DFT and SQUID calculations) to confirm their structural identity, purity and to explore their properties.

The first chapter, *"Azobenzenes and diradicals,"* contains data from the literature on the development of azobenzenes in the field of molecular photoswitching (derivatization strategies, system performance, synthesis, functionalization for accessing light emission properties) and the synthesis and applications of the stable DPPH free radical in the context of the development of diradicals.

The second chapter, *"Azobenzenes functionalized with 1,3,4-oxadiazole units,"* presents the synthesis of azobenzenes functionalized with aryl units (*p*-tolyl, 1-naphthyl, 1-pyrenyl) and various substituents (*methyl, fluoro, alkoxy)* with the aim of improving photoswitching performance and accessing emission properties. The experimental results indicate an improvement in photoswitching parameters, particularly in terms of addressability and thermal stability. All compounds were stable under repeated irradiation cycles, and the difluorinated derivative stands out from the azobenzene series with the best properties: the difference in n-π* absorption band separation between *E/ Z* isomers $\Delta\lambda$ = -28 nm, the high efficiency of obtaining a certain form by irradiation (PSS (%*Z)* = 81% and PSS (%*E)* = 73%), but also the highest half-life value for the *Z* form in solution ($t_{1/2}$ = 1732 h / 72 days). The results are promising and demonstrate the benefits offered by the presence of the 1,3,4-oxadiazole heterocycle, which behaves like electron-withdrawing substituent, the structure of the compounds being associated with donor-acceptor azobenzenes. Furthermore, the two *fluoro* substituents are sufficient to achieve good photoswitching performance, determining interest in such molecules in the context of molecular photoswitch applications. Derivatives functionalized with alkoxy units show weak emission in solution while, which is encouraging from this perspective.

The primary aromatic 1,3,4-oxadiazole amines used as starting materials in the synthesis of azobenzenes, as well as the series of synthesized tertiary amine derivatives (functionalized with diethylamino, diphenylamino, or carbazole residues) and various aryl rings (*p*-tolyl, 1-naphthyl, 9-anthracenyl, and 1-pyrenyl) are notable for their exceptional absorption and emission properties. The experiments were carried out in solvents with different degrees of polarity (toluene, CH_2Cl_2, THF, ACN, DMSO, MeOH). Small differences in absorption properties were observed, indicating weak solvatochromism, with the maximum absorption wavelength shifting bathochromically as the polarity of the solvent increased. These aspects were encountered for derivatives with a donor-π-acceptor structure, and the explanation was based on the presence of intramolecular charge transfer between the two units – ICT (*Intramolecular Charge-Transfer)*. This phenomenon substantially influences the emission properties, resulting in solvatofluorocromism with large shifts in emission wavelengths recorded in polar solvents, especially for amines substituted with the 9-anthracenyl/1-pyrenyl and diethylamino units. Emissions covering the entire Vis spectrum of light (blue, green, yellow, orange, red) were observed for the synthesized amines. The ability to form aggregates in solution was demonstrated by adding increasing amounts of H_2O (0-98%) to the DMSO solution, observing the change in emission. The influence of nitrogen atom protonation regarding emission was observed, both in solution and in the solid state. The series of 1,3,4-oxadiazole amines exhibit emission in the solid state, with different behavior depending on the structure: blue, green, or yellow emission.

The third chapter, *"Betaine derivatives of the stable DPPH free radical and diradicaloid behavior"* describes the synthesis of betaines functionalized with various units, acting as diradicaloids and the synthesis of the first dimer/diradical derived from DPPH.

Betaine and hydrazine derivatives of DPPH with various aryl groups (1,3,4-oxadiazoles, tosyl, aminomethy) were synthesized and investigated for their optical, electrochemical, acid-basic, and paramagnetic properties, exploring their diradicaloid behavior. The surprising results consisted in obtaining the corresponding azo-diradical, whose structure was confirmed by single-crystal X-ray diffraction and mass spectrometry. During the synthesis of the first dimer derived from DPPH, new DPPH derivatives were obtained: amino- and bromo-substituted, which were characterized structurally and in terms of reactivity. Bromo-derived oxo-betaine derivatives from DPPH were synthesized and characterized, and investigated for the equilibrium between the aromatic and diradicaloid forms.

The methodology for synthesizing the DPPH dimer consisted of a series of steps, ultimately yielding the designed compound and, through its oxidation, the corresponding DPPH diradical. The compound was analyzed for its electrochemical, optical, and paramagnetic properties, exploring diradicaloid character. The presence of signals in ESR spectroscopy in both solution and solid state indicated diradicaloid state. DFT calculations and SQUID measurements were performed to determine percentage of singlet/triplet states of molecules, observing the presence of 5% of the species in the triplet diradicaloid form, the rest being of the singlet type. The results obtained complete part of the behavior of DPPH diradicals, being an important fingerprint in the presented data in the literature.

In conclusion, the dynamics of azobenzenes, the emission of 1,3,4-oxadiazole units, and the stability of diradicals were explored, outlining a molecular space in which chemical structures and their properties meet in a complex equilibrium.

Publications in which the experimental data obtained can be found:

1. **Dobre, A. F.**; Mădălan, A. M.; Ionescu, S.; Hanganu, A.; Lete, C.; Popescu, C. C.; Păun, A.; Matache, M.; Ioniță, P. Zwitterion or Diradicaloid? The Case of Diazenium Betaines Derived from DPPH. *J. Mol. Struct.* **2023**, *1275*. https://doi.org/10.1016/j.molstruc.2022.134703. **Impact factor: 4.7**
2. **Dobre, A. F.**; Hanganu, A.; Nicolau, I.; Popescu, C. C.; Păun, A.; Mădălan, A. M.; Tăbleț, C.; Mirea, A. G.; Matache, M. A Synthetic Approach for Oxadiazole-Decorated Azobenzene Photoswitches. *ChemPlusChem* **2024**, *89* (2), e202300504. https://doi.org/10.1002/cplu.202300504. **Impact factor: 2.8**
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