SYNTHESIS AND OPTICAL PROPERTIES OF NOVEL STRONTIUM TETRANITROPHTHALOCYANINE

Silviu GROZA[a], Bianca STOEAN[a], Adriana GROZAV[b,*], Ana-Maria CRACIUN[c], Castelia CRISTEA[a], Luminita SILAGHI-DUMITRESCU[a], Dan PORUMB[a]

ABSTRACT. Two convenient alternatives for the synthesis of metal(II) 2,9,16,23-tetranitrophthalocyanines (TNPc) were applied in the synthesis of the novel Strontium(II)TNPc and its Zinc(II)TNPc, Copper(II)TNPc and Cobalt(II)TNPc analogues. The thermal activation required for the tetramerization of the phthalic acid derivatives used as substrates (4-nitro-phthalimide or 4-nitrophthalodinitrile) was provided by convective heating in solution or solvent free conditions. The optical properties of the synthesized metal(II)TNPc were compared by means of UV-vis spectroscopy. In solution, the novel Sr(II)TNPc was characterized by absorption bands with maxima situated around 690 nm (similar to Cu(II)TNPc), while its fluorescence emission maxima lays close to Zn(II)TNPc (710 nm), with a three times longer fluorescence emission life time in solid state (3.04 ns).

Keywords: phthalocyanine; strontium-complex; UV-vis spectroscopy; fluorescence emission life time

[a] *Faculty of Chemistry and Chemical Engineering, Babeş-Bolyai University, 11 Arany Janos str., RO-400028, Cluj-Napoca, Romania*
[b] *Department of Organic Chemistry, "Iuliu Hatieganu" University of Medicine and Pharmacy, 41 Victor Babes, Street, 400012 Cluj-Napoca, Romania*
[c] *Nanobiophotonics and Laser Microspectroscopy Center, Interdisciplinary Research Institute in Bio-Nano-Sciences, Babes-Bolyai University, 42 Treboniu Laurian Street, 400271 Cluj-Napoca, Romania*
* *Corresponding author: adriana.ignat@umfcluj.ro*

SILVIU GROZA, BIANCA STOEAN, ADRIANA GROZAV, ANA-MARIA CRACIUN,
CASTELIA CRISTEA, LUMINITA SILAGHI-DUMITRESCU, DAN PORUMB

INTRODUCTION

Phthalocyanine (**Pc**) is a macrocyclic compound belonging to the class of aza[18]anulenes which was discovered at the beginning of the 20th century. The macrocyclic structure of **Pc** embodies four isoindole ([3,4]benzopyrrole) moieties connected by imine bridges (-N=) enabling a continuous conjugated system of 18 π-electrons complying with the aromaticity Huckel's rule [1]. Functionalization of **Pc** imply peripheral substitution, core metalation and axial substitution. Various metallophthalocyanines (**MPc**) containing a metal ion coordinated in the central cavity of the macrocyclic dianion ligand were reported with the aim of tuning the **Pc**s' chemical and dyeing properties. The properties of **Pc** derivatives were subsequently investigated leading to their use as pigments and dyes in various inks, paints and varnishes formulations due to their exceptional thermal stability and resilience to the action of acids and bases [2]. **Pc** derivatives exhibit high values of molar extinction coefficients for the main absorption bands situated in visible and near-infrared spectra.

Currently, **Pc** derivatives are utilized in industrial sectors, such as dyes industry, molecular electronics, and solar cells, due to their distinctive characteristics [3]. Recently, there has been a significant interest in the study of **Pc** and **MPc** derivatives containing core substitution with transition metals. This is due to their exceptional features, which make them very promising for modern growing sectors including liquid crystals, catalysts, and photochromic materials [4]. **Pc** derivatives have also found application in medicinal preclinical investigations due to their biological activity, potential usage as photosensitizers in photodynamic therapy and ability to provide fluorescence imaging of tumour tissues [5-7]. Nanomedicine has come a long way in the past few years, especially when it comes to synthesize multifunctional theragnostic drugs that can be used for specific cancer imaging and treatment. Two new ways to obtain protein-based (anti-folate receptor anti-body) nanoparticles that encapsulate (Zn(II)-2,9,16,23-tetranitrophthalocyanine for specific fluorescence imaging and dual treatment of ovarian cancer have been reported [8]. Further, nanoparticles made of bovine serum albumin that are loaded with (Zn(II)-2,9,16,23-tetraaminphthalocyanine showed great biocompatibility and efficient photothermal conversion, suggesting a potential for biomedical applications [9]. **MPc** derivatives are redox active compounds which were exploited in the preparation of modified gold electrodes for electrocatalytic oxidation and detection of different analytes. Unlike redox active phenothiazine derivatives mediators which strongly adsorb directly on gold electrodes (based on the the presence of the sulphur atom in the structure of the heterocycle) [10], self-assembled monolayer films of Fe(II)Pc were axially ligated to mercaptopyridine modified gold electrodes [11].

Pc derivatives can be synthesized by the cyclization of precursors based on an array of phthalic acid derivatives (anhydride, imide, diamide, dinitrile) [12,13] and metal salts containing the metal ion as template for the cyclotetramerization which proceeds in a melt or in a high boiling solvent (Scheme 1).
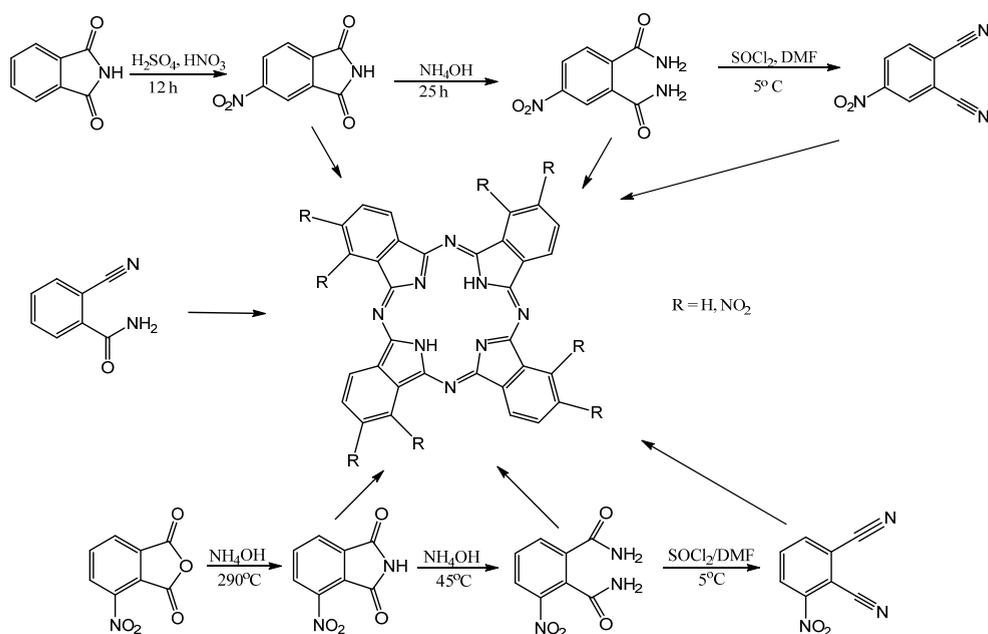
Scheme 1. Synthesis of **Pc**s from phthalic acid derivatives
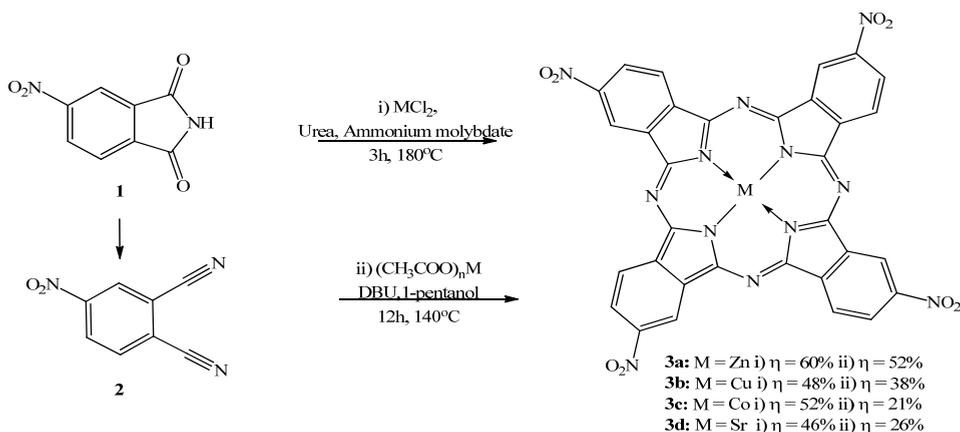
Many **MPc** derivatives were synthesized using a wide array of metal salts. Free phthalocyanines (**H$_2$-Pc**) can be obtained directly by the macrocyclization of the above mentioned precursors or by reducing a **MPc** in pyridine and hydrochloric acid [14]. The majority of **Pc** exhibit limited solubility in various solvents, such as water, bases, and acids. However, they do exhibit solubility in dimethylsulfoxide (DMSO) and concentrated sulfuric acid (H$_2$SO$_4$). In order to enhance their applicability in photodynamic therapy and other bio-medical fields, there are currently explored new analogues of phthalocyanines that contain hydroxyl, carboxyl, amino or sulfonyl groups, which significantly enhance their solubility in water [15].

In this work are presented two alternative synthetic routes validated in the preparation of four **MPc** derivatives branded by the macrocycle peripheral substitution with nitro auxochromic groups and core metalation with the divalent

cations: strontium(II), copper(II), cobalt(II) and zinc(II) respectively. The electronic properties of the novel Sr(II)**MPc** are compared with the Cu(II), Co(II) and Zn(II) **MPc** analogues based on the recorded UV-vis spectroscopic data.

RESULTS AND DISCUSSION

The target metallocomplexes of 2,9,16,23–tetranitro-phthalocyanine (**TNPc***)* were successfully obtained by two synthetic pathways as presented in Scheme 2.

3a: M = Zn i) η = 60% ii) η = 52%
3b: M = Cu i) η = 48% ii) η = 38%
3c: M = Co i) η = 52% ii) η = 21%
3d: M = Sr i) η = 46% ii) η = 26%

Scheme 2. Alternative syntheses of metal(II)**TNPc**

The first approach for the synthesis of Zn(II)TNPc **3a,** Cu(II)TNPc **3b,** Co(II)TNPc **3c** and Sr(II)TNPc **3d** respectively, involves a solvent-free method utilizing 4-nitro-phthalimide **1** as the starting material, urea as a source of nitrogen, ammonium molybdate catalyst and the metal chloride template.

The second method employs 4-nitro-phthalodinitrile **2** substrate dissolved in a high boiling point solvent, specifically 1-pentanol, along with the non-nucleophilic hindered base1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) and the metal acetate template. Given that 4-nitro-phthalodinitrile **2** is the starting material in this process, the presence of an additional nitrogen source was no longer necessary.

As it may be seen from Scheme 1, 4-nitro-phthalodinitrile **2** can be obtained from 4-nitro-phthalimide **1** in two additional reaction steps (ammonolysis followed by dehydration of the 4-nitro-phthalamide intermediate) and thus, overall reaction yields of metal(II)**TNPc** are not higher. While the solvent-free approach offers benefits such as increased yields and reduced expenses,

there is a potential issue related to the convective heating ensuring an uneven distribution of the temperature within the reaction mixture. Consequently, when temperature rise above 180°C, a potential risk of partial carbonization of the reaction mixture may occur.

A comparative study of the optical properties displayed by the synthesized metal(II)**TNPc 3a-d** was performed. Table 1 provide the typical visible absorption and fluorescence emission data recorded by UV-vis spectroscopy in dimethylsulfoxide (DMSO) solution. As it may be seen in Figure 1a showing the overlaid visible absorption spectra of metal(II)**TNPc 3a-d,** a slight bathochrome shift was recorded for the novel Sr(II)TNPc **3d**, while Co(II)TNPc **3c** exhibited an apparent hyperchromic effect. While the absorption characteristics of Sr(II)TNPc **3d** are similar to that of Cu(II)TNPc **3a**, its fluorescence emission maxima is situated in the near-infrared region similar to Zn(II)TNPc **3a** (Figure 1b). Co(II)TNPc **3c** was characterized by the greatest Stokes shift value (645 cm^{-1}).
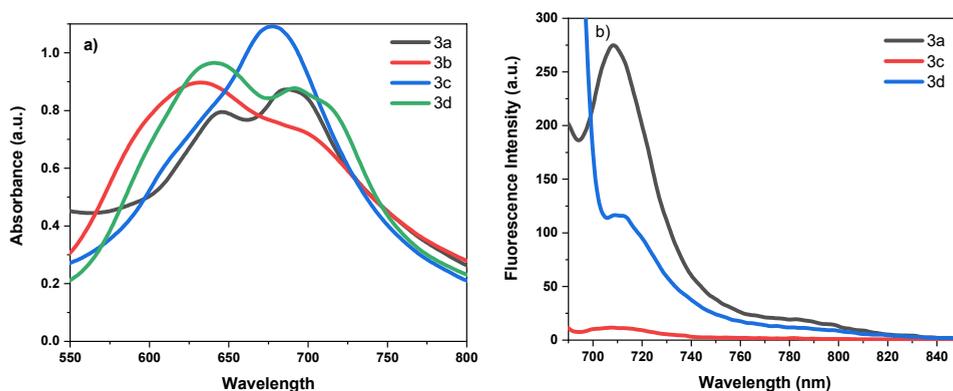

Figure 1. UV-vis spectra of metal(II)TNPc **3a-d** in DMSO solution: a) absorption spectra (C_M=4x10^{-5}M), b) fluorescence emission spectra (C_M=4x10^{-8}M).

Table 1. UV-vis absorption/emission wavelength maxima, molar extinction coefficients, Stokes shifts and fluorescence lifetime of metal(II)**TNPc 3a-d** in DMSO solutions.

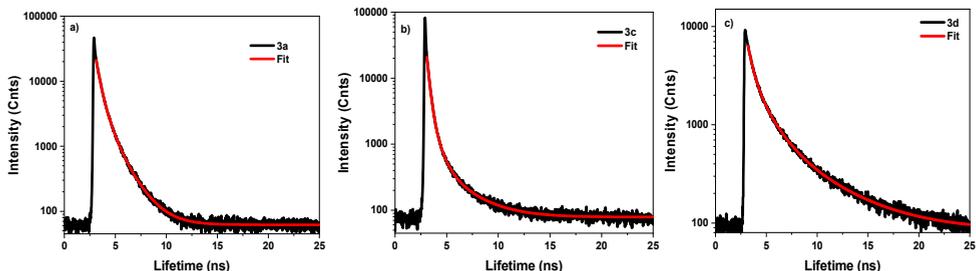| Cpd.	λ_{abs} (nm)	ε (cm^{-1}M^{-1})	λ_{em} (nm)	Stokes Shift (cm^{-1})	Fluorescence lifetime (ns)
3a	687	16578	708	432	0.9
3b	690	18500	-	-	-
3c	678	27288	709	645	0.8
3d	691	21935	710	387	3.04

Figure 2. Fluorescent lifetime histograms for metal(II)TNPc **3a** – a), **3c** – b), **3d** – c).

Additionally, when comparing the fluorescence lifetimes determined by time-resolved confocal fluorescence microscopy for **3a**, **3c**, **3d** in solid state, Sr(II)TNPc **3d** exhibited a fluorescence lifetime that is three times longer than its Zn(II)TNPc **3a** and Co(II)TNPc **3c** analogues. The variations in fluorescence lifetimes are most likely due to the modifications in electronic structure, non-radiative decay pathways, and energy transfer processes induced by the metal ions.

The aggregation of **Pc** chromophore system may impede its efficacy in various applications by influencing its photophysical properties (such as fluorescence quenching) or photochemical properties (such as singlet oxygen generation or loss of catalytic activity). A first attempt to detect the aggregation tendency of metal(II)TNPc **3a-d** is presented below.
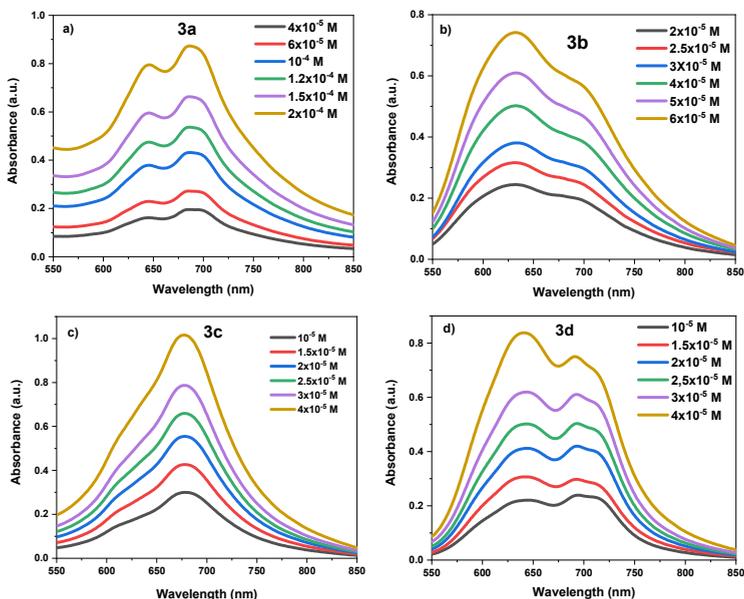

Figure 3. UV-vis spectra of metal(II)TNPc **3a-d** in DMSO at different concentration ranges.

Absorption spectra of metal(II)TNPc **3a-d** were recorded in DMSO solution at various concentrations ranging between 10^{-4} and 10^{-6}M. As it may be seen from the overlaid absorption spectra presented in Figure 3 for each metal(II)TNPc **3a-d** the Lambert-Beer law is followed, with absorbance increasing in proportion to the concentration of the compound in solution, suggesting that the aggregation does not occur in the aprotic dipolar DMSO solvent at concentrations ranging between 10^{-4} and 10^{-5}M.

CONCLUSIONS

This work described two convenient approaches for the synthesis of metal(II)TNPc validated in the synthesis of Zn(II)TNPc **3a**, Cu(II)TNPc **3b** and Co(II)TNPc **3c** and the novel Sr(II)TNPc **3d**. The thermal activation required for the tetramerization of the phthalic acid derivatives used as substrate (4-nitro-phthalimide / 4-nitrophthalodinitrile) was provided by convective heating in solvent-free / in solution conditions. Although the solvent-free strategy may provide issues in temperature distribution, the study highlights its advantages in terms of increased yield, reduced costs and the possibility of avoiding the hazards induced by the use of volatile organic compounds (VOC).

In terms of optical properties, the novel Sr(II)TNPc **3d** displayed the strong visible absorption maxima and fluorescence emission maxima in both solution and solid state, with fluorescence lifetime of 3.04 ns, having the potential to become a valuable candidate as fluorophore in tissue bioimaging using fluorescence microscopy, as well as photosensitizer in photodynamic therapy.

EXPERIMENTAL SECTION

Unless otherwise specified, all experimental materials, reagents, and solvents were procured from commercial suppliers and utilized without additional purification. Mass spectra were recorded using Bruker Rapiflex MALDI-TOF apparatus from Bruker Daltonics (Bremen, Germany), equipped with a Smartbeam 3D laser. The UV-Vis absorption and fluorescence emission spectra were recorded using the Perkin Elmer Lambda 35 and Perkin Elmer LS55 spectrophotometers.

The synthesis of the starting 4-nitrophthalimide **1** was achieved according to literature data by subjecting phthalimide to nitration using a concentrated solution of sulfuric acid and nitric acid at room temperature [13].

The synthesis of the starting 4-nitrophthalodinitrile **2** was performed according to literature data by ammonolysis of 4-nitrophthalimide to 4-nitrophthalamide using ammonium hydroxide solution, followed by dehydration using thionyl chloride at low temperature [13].

Fluorescence emission life time was recorded from solid-state samples deposited on glass slides with a time-resolved confocal fluorescence microscopy system (MicroTime 200, PicoQuant, Germany) equipped with an Olympus IX71 microscope. Samples were excited with a pulsed laser diode at 640 nm (LDH-D 640 nm, 40 MHz). The signal was collected using a UPLSAPO 60×/NA=1.2 water immersion objective, and a BLP01-647R emission filter (Semrock) was used to filter the signal. The mean values of the fluorescence lifetimes of the samples were obtained by fitting operations on the experimental curves with exponential equations.

Experimental procedures for the synthesis of zinc(II), copper(II), cobalt(II) and strontium(II) 2,9,16,23–tetranitro-phthalocyanines

a) Solvent-free procedure

A mixture containing 4 mmol of metal chloride (copper(II) chloride, zinc(II) chloride, cobalt(II) chloride and respectively strontium(II) chloride), 12.5 g (0.208 mol) of urea, 2.33 g (12 mmol) of 4-nitrophthalimide, and 0.015 g (0.013 mmol) of ammonium molybdate was thoroughly grounded in an agate mortar. The mixture was then transferred into a 100 mL round bottom flask equipped with an air condenser. The mixture was occasionally stirred with a glass rod while being heated on a sand bath at 180°C for 3 hours. After the completion of the reaction, the crude black product was refluxed for 30 minutes in 50 mL of 1M hydrochloric acid solution. Subsequently, the black product was filtered and rinsed with distilled water until reaching a neutral pH. Further, the precipitate was refluxed with a 1M NaOH solution, followed by filtration and thorough washing with ample amounts of distilled water. The acid-base treatment was reiterated thrice. The precipitate was further purified by refluxing in a 1:1 (v/v) mixture of acetone and acetonitrile for one hour. After that, the mixture was filtered and the resulting solid was washed with distilled water. The product was subjected to a final purification step by refluxing it in a mixture of tetrahydrofuran and chloroform 1:6 (v/v) for one hour. After hot filtration, it resulted the formation of a blue or green-metallic precipitate (1.36g, 60% yield for $C_{32}H_{12}N_{12}O_8Zn$ (**3a**), 1.09g, 48% yield for $C_{32}H_{12}N_{12}O_8Cu$ (**3b**), 1.17g, 52% yield for $C_{32}H_{12}N_{12}O_8Co$ (**3c**), 1.08g, 46% yield for $C_{32}H_{12}N_{12}O_8Sr$ (**3d**)).

b) Procedure in 1-pentanol

In a 100 mL round flask with three necks, fitted with a reflux condenser, a thermometer, and an argon source to maintain the reaction in an inert atmosphere, 0.95 g (5.5 mmol) of 4-nitrophthalodinitrile, 20 mL of 1-pentanol, and 1.4 mmol of metal acetate (copper(II)acetate, zinc(II) acetate, strontium(II)

acetate, cobalt(II) acetate) and 0.5 mL (3.34 mmol) of DBU were added. The reaction mixture was heated at 140°C for 24 hours in an oil bath upon stirring under an inert atmosphere. After the completion of the reaction, the solvent was distilled, and the crude product underwent the identical purification steps outlined above in the solvent-free synthesis (0.54g, 52% yield for $C_{32}H_{12}N_{12}O_8Zn$ (**3a**), 0.40g, 38% yield for $C_{32}H_{12}N_{12}O_8Cu$ (**3b**), 0.22g, 21% yield for $C_{32}H_{12}N_{12}O_8Co$ (**3c**), 0.28g, 26% yield for $C_{32}H_{12}N_{12}O_8Sr$ (**3d**)).

MS (MALDI-TOF/TOF) m/z: 757.900 calcd. for $C_{32}H_{12}N_{12}O_8Zn$, found: 757.918; 756.060 calcd. for $C_{32}H_{12}N_{12}O_8Cu$ found: 755.540; 751.450 calcd. for $C_{32}H_{12}N_{12}O_8Co$ found: 751.421; 779.996 calcd. for $C_{32}H_{12}N_{12}O_8Sr$ found: 778.196.

ACKNOWLEDGMENTS

REFERENCES

1 A. Gök, E. B. Orman, Ü. Salan, A. R. Özkaya and M. Bulut, *Dye. Pigment.*, **2016**, *133*, 311–323.

2 R. A. S. Ali, J. Keshavayya, A. S. Jagadisha, S. D. Umesha, K. N. Gujjar, S. A. Narasimha, D. G. Prasanna and E. Nagaraja, *Mater. Today Proc.*, **2021**, *49*, 644–649.

3 M. Pişkin, *J. Photochem. Photobiol. A Chem.*, **2023**, *435*, 114325.

4 Y. Baygu, N. Kabay, B. Kabay, B. Yıldız, İ. Ömeroğlu, M. Durmuş, E. Rıza Karagür, H. Akça, Ç. Ergin and Y. Gök, *J. Mol. Struct.*, **2023**, *1271*, 134010.

5 H. M. Almuzafar, H. M. Ahmed, N. N. AlDuhaisan, A. M. Elsharif, H. Aldossary, S. Rehman, S. Akhtar and F. A. Khan, *J. Saudi Chem. Soc.*, **2022**, *26*, 101436.

6 R. A. Barmin, E. A. Maksimova, P. G. Rudakovskaya, A. V. Gayer, E. A. Shirshin, K. S. Petrov, D. A. Terentyeva, O. I. Gusliakova, O. A. Sindeeva, O. A. Klimenko, R. N. Chuprov-Netochin, A. A. Solovev, G. Huang, A. V. Ryabova, V. B. Loschenov and D. A. Gorin, *Colloids Surf. B.*, **2022**, *219*, 112856.

7 G. Gümrükçü Köse and G. Keser Karaoğlan, *Chem. Phys.*, **2023**, *565*, 111737.

8 R. Borlan, M. Focsan, M. Perde-Schrepler, O. Soritau, A. Campu, L. Gaina, E. Pall, B. Pop, O. Baldasici, C. Gherman, D. Stoia, D. Maniu and S. Astilean, *Biomater. Sci.*, **2021**, *9*, 6183–6202.

9 R. Borlan, D. Stoia, L. Gaina, A. Campu, G. Marc, M. Perde-Schrepler, M. Silion, D. Maniu, M. Focsan and S. Astilean, *Molecules*, **2021**, *26*, 1–21.

10 V. Rosca, L. Muresan, I. C. Popescu, C. Cristea and I. A. Silberg, *Electrochem. commun.*, **2001**, *3*, 439–445.

11 K. I. Ozoemena and T. Nyokong, *Talanta*, **2005**, *67*, 162–168.

12 J. T. Engle, A. N. Allison, J. M. Standard, I. S. Tamgho and C. J. Ziegler, *J. Porphyr. Phthalocyanines*, **2013**, *17*, 712–721.

13 B. I. Kharisov, U. Ortiz Mendez, J. L. Almaraz Garza and J. R. Almaguer Rodriguez, *New J. Chem.*, **2005**, *29*, 686–692.

14 J. Alzeer, P. J. C. Roth and N. W. Luedtke, *Chem. Commun.*, **2009**, 1970–1971.

15 C. G. Claessens, U. Hahn and T. Torres, *Chem. Rec.*, **2008**, *8*, 75–97.