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# Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: [www.elsevier.com/locate/saa](http://www.elsevier.com/locate/saa)

## The use of new metallophthalocyanines carrying peripherally 4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide moieties for the sensitive fluorimetric determination of banned food dye Sudan II in red chili peppers



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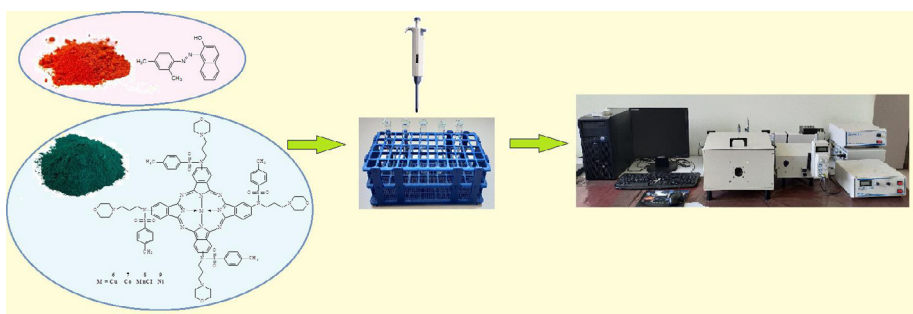
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### HIGHLIGHTS

- The synthetic procedures and spectrofluorimetric studies of new MPcs described.
- The new procedure suggests detecting the banned food colorant Sudan II dye.
- The new simpler, cheaper, and faster fluorimetric method was described instead of HPLC.
- MPcs were used for the first time as spectrofluorimetric agents to detect Sudan II dye.

### GRAPHICAL ABSTRACT



### ARTICLE INFO

#### Article history:

Received 17 July 2020

Received in revised form 7 November 2020

Accepted 10 November 2020

Available online 16 November 2020

#### Keywords:

Morpholine

Phthalonitrile

Cobalt phthalocyanine

Sudan II

Fluorimetric definition procedure

Food colorant

### ABSTRACT

The structural elucidation and syntheses methods of new peripherally tetra-substituted MPcs [Cu<sup>II</sup> (**6**), Co<sup>II</sup> (**7**), MnCl<sup>III</sup> (**8**), and Ni<sup>II</sup> (**9**) phthalocyanines] carrying 4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide moieties were reported in the present study. The corroboration of the prepared compounds (**3**, **5**, and **6** to **9**) was made by LC-TOF/MS, UV-Vis, Fourier Infrared, <sup>1</sup>H NMR, <sup>13</sup>C NMR, and MALDI-TOF mass spectral data. Herein, we submit a new procedure that uses metallophthalocyanine complexes for the first time as spectrofluorimetric agents to detect and determine health-threatening food additive, Sudan II dye, with a new simpler, cheaper, and faster spectrofluorimetric method instead of time-consuming and expensive HPLC processes. Furthermore, the sensitivities of the proposed methods are good enough to determine the amount of dye at a concentration of 0.1 mg/L. The methods have LOD values between 0.035 and 0.050 mg/L. The linear ranges are found to be between 0 and 8.3 mg/L. The precision of the methods is determined to be between 1.1 and 2.4 % RSD. Therefore, this study would make a good contribution to the food industry and phthalocyanine chemistry by detecting and determining the hazardous food colorant Sudan II with metal phthalocyanines.

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## 1. Introduction

Phthalocyanines (Pcs) and their metal inserted congeners, metallophthalocyanines (MPcs), are one of the most important classes of chromophores and aromatic macrocycles. From their discovery by Braun and Tcherniac in 1907 [1,2] up to now, miscellaneous researches and studies have been conducted to make use of varied advantages of phthalocyanine compounds in science and technology. There is a large volume of published studies describing their spectacular photochemical, optical, redox, electronic and color features [3–8] together with their high thermal and chemical stability [9], both Pcs and MPcs have been using widely as electronic materials [10,11], dyes [12], optical materials [13], photosensitizer agents [14–16], liquid crystal displays (LCDs) [17], semiconductors [18], solar cells [19], in photodynamic therapy applications [14–16,20], fluorescence “off-on-off” sensors [21] as well as catalysts [22,23] and nonlinear optics [24]. To play a remarkable role and obtain targeted molecules or materials for the above-mentioned applications of phthalocyanines, their adjustable properties are tuned by the incorporation of many sorts of substituents at different binding positions of Pc ring (i.e., peripheral, non-peripheral or axial) and changing the central metal ions and as well as designing different types of Pc molecules such as ball-type, double-decker and so on.

As being a marvelous pharmacophore [25,26] and important building blocks in medicinal chemistry, morpholine nucleus, and its assorted derivatives has been of tremendous significance and made use of as capping component and primary skeleton to develop new drugs [27–29] owing to their diverse biological and pharmacological activities with the inclusion of local anesthetic, selective inhibitor of protein kinase C, neuroprotective, anti-malarial, antidepressant, appetite suppressant, antitumor, analgesic, antifungal, anti-tuberculosis, anticancer, antiplatelet, anti-parasitic, HIV-protease inhibitors, anti-inflammatory, hypocholesterolemic and hypolipidemic activities as well [30–34]. Nowadays, so many drugs containing morpholine backbone or its various derivatives have been approved by the FDA (U.S. Food & Drug Administration) and they are in use for the treatment of aforesaid diseases [35]. In addition to pharmaceutical and medicinal applications, morpholine derivatives are also utilized including in air conditioners, in water boiling systems as an anticorrosive agent, in the textile industry, in the production of waxes, in catalysts as a chemical intermediate and as well as in book paper preservation applications [36,37]. Of the great significance and potential, morpholine units bearing compounds have been of particular attention, numerous studies have been carried out and published comprising morpholine scaffold fused phthalocyanines [38–41].

Sudan dyes, which are azo dyes, are known to have the potential for toxic properties. For example, Li et al. showed by spectroscopic methods that Sudan II and Sudan IV bind effectively with the catalase enzyme, which is effective in protecting the cell from oxidative stress [42]. It has been reported in another study that these dyes affect the physiological activity of bovine hemoglobin [43].

Sudan dyes generally have been detected and determined by chromatographic methods [44]. These methods are often time-consuming and require the use of expensive devices such as HPLC-MS-MS [45,46]. For the determination of these dyes, some electrochemical methods, and enzyme-linked immunosorbent assay (ELISA) have also been proposed [47–49]. The intrinsic selection and high sensitivity of fluorescence methods provide generally an overall advantage in analytical assays. However, the number of recommended fluorescence methods for the determination of Sudan dyes is also very few [50–53], and there are only several recommended fluorescence methods for determining Sudan II among

these methods [52,53]. These methods applied to determine Sudan II in chili powder samples are based on the fluorescence properties of the polyethyleneimine-capped silver [53] and copper [52] nanoclusters. Previous studies have shown the use of MPc complexes with suitable functional groups as fluorescent reagents for the determination of metal ions in food samples [54]. In the present study, the usability of MPc complexes showing fluorescent property in the determination of Sudan II dyes from the banned food dyes was investigated.

As can be seen from the research in the literature, there are many published papers associated with medicinal and pharmaceutical applications of morpholine-based heterocycles. However, to the best of our knowledge, no report has been found so far concerning the morpholine-based phthalocyanine agent that is eligible, simple, and economical for the detection and determination of Sudan II dye. In line with this purpose, we designed and synthesized the new metallic phthalocyanines [Cu<sup>II</sup> (6), Co<sup>II</sup> (7), MnCl<sup>III</sup> (8), and Ni<sup>II</sup> (9)]. After the confirmation of the structures of these newly synthesized metallated Pc complexes, we studied banned food dye Sudan II in red chili peppers for the sensitive fluorimetric determination procedure to determine a new simpler, cheaper, and faster spectrofluorimetric strategy as compared to time-consuming and expensive HPLC methods. By looking at analytical data of the spectrofluorimetric measurements, it is elicited that the new copper(II) phthalocyanine (6), cobalt(II) phthalocyanine (7), manganese(III) chloride phthalocyanine (8), and nickel(II) phthalocyanine (9) compounds are the new simpler, cheaper, and faster spectrofluorimetric agents for detection and determination of a banned azo-dye Sudan II in red pepper samples. In our time, specifically during of Covid-19 pandemic, people pay much more attention more than ever regarding the health, healthy life and healthy food and nutrition. To that end, the present study attempts to contribute as a simpler, cheaper, and faster detection and determination of banned or health-threatening food additives such as azo-dye Sudan II by using metallic phthalocyanine complexes for the first time.

## 2. Experimental

### 2.1. Materials, instrumentation, and method

The materials, instrumentation, Sudan II determination method, and some of the figures were given as [Supplementary information](#).

### 2.2. Syntheses

#### 2.2.1. 4-Methyl-N-(3-morpholinopropyl)benzenesulfonamide (3)

Under a dry nitrogen atmosphere, a two-necked round-bottomed 100 mL flask was charged with 3-morpholinopropan-1-amine (1) (2.50 g, 17.34 mmol, 1 eq.) and dry pyridine (2 mL) and then degassed several times on a vacuum line. At -5 °C, a solution of *p*-toluenesulfonyl chloride (2) (3.34 g, 17.51 mmol, 1.01 eq. in 4 mL dry pyridine) was added dropwise in 1 h to the reaction mixture. As the addition of *p*-toluenesulfonyl chloride solution was over, it was stirred at -5 °C for 4 h and the stirring was then continued at room temperature overnight. During the addition of *p*-toluenesulfonyl chloride solution, the color change was observed at the beginning from pale yellow to dark orange and finally to reddish-brownish color. Later, the reaction mixture was poured into 300 g of crushed ice and stirred at room temperature for 3 h. The pH of the aqueous media was monitored and adjusted approximately to pH = 7.00. Thereafter, aqueous media was extracted with 4x30 mL of chloroform and the collected organic phase was dried over anhydrous MgSO<sub>4</sub>. By the evaporation of

chloroform from the collected extract, the compound (**3**) obtained, and the ultimate purification of the product was performed on a microcolumn charged with silica gel with chloroform:ethanol (50 mL:5 mL) solvent mixture to give as the yellow oily product. Yield: 3.38 g (65.4%). FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3272 (N-H), 3068 (C-H aromatic), 2962–2914–2850 ( $\text{CH}_3$ ), 1596 (C = C), 1494, 1445, 1318 (Tosyl group, S = O asymmetric), 1275, 1155 (Tosyl group, S = O symmetric), 1116, 1092 (N-H), 988, 922, 862, 817, 747, 706 and 659 (C-S).  $^1\text{H}$  NMR (ppm,  $\text{CDCl}_3$ ):  $\delta$  = 7.75–7.73 (d, 2H, Tosyl, Ar-H), 7.32–7.30 (d, 2H, Tosyl, Ar-H), 7.00 (broad, 1H, N-H), 3.73–3.71 (t, 4H,  $\text{H}_2\text{C-O-CH}_2$ ), 3.08–3.05 (t, 2H,  $-\text{CH}_2-\text{CH}_2-\text{N-H}$ ), 2.43–2.40 (m, 7H,  $\text{H}_2\text{C-N-CH}_2$  and Tosyl,  $-\text{CH}_3$ ), 1.68–1.62 (m, 4H,  $-\text{N-CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{N-H}$ ).  $^{13}\text{C}$  NMR (ppm,  $\text{CDCl}_3$ ):  $\delta$  = 143.19, 137.12, 135.98, 129.65, 126.99, 126.42, 124.82, 66.88–61.46 ( $\text{H}_2\text{C-O-CH}_2$ ), 58.44–58.22–53.53 ( $\text{H}_2\text{C-N-CH}_2$ ), 43.86–42.94 ( $-\text{CH}_2-\text{CH}_2-\text{N-H}$ ), 30.58–30.31–23.90 ( $-\text{N-CH}_2-\text{CH}_2-\text{CH}_2-\text{N-H}$ ), 21.53 (Tosyl,  $-\text{CH}_3$ ). LC-TOF/MS  $m/z$ : Calculated: 298.40, Found: 299.147 [ $\text{M} + \text{H}$ ] $^+$ .

### 2.2.2. *N*-(3,4-dicyanophenyl)-4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide (**5**)

A two-necked round-bottomed 100 mL flask was charged with 4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide (**3**) (1.00 g, 3.35 mmol, 1 eq.), 4-nitroptalonitrile (**4**) (0.58 g, 3.35 mmol, 1 eq.) and dry acetonitrile (15 mL). Following the vigorously stirring at reflux temperature (approximately at 85 °C), anhydrous  $\text{K}_2\text{CO}_3$  (1.84 g, 13.40 mmol, 4 eq.) was added to the solution by portion-wise over 1 h and the reaction mixture was degassed under the nitrogen stream on a vacuum line. Under the  $\text{N}_2(\text{g})$  blanket, the reaction mixture was continued to reflux for 6 days and monitored by Thin Layer Chromatography technique (TLC) with chloroform as a mobile phase on silica gel plates with UV indicator. The residue was dissolved in 125 mL of chloroform and extracted with (4x25 mL) distilled water, after cooling to room temperature. The organic phase was then dried over  $\text{MgSO}_4$ , filtered off and chloroform was removed by evaporation. The crude product was purified by chromatographic separation from unreacted reagents and byproducts on a silica gel charged column with chloroform:ethanol (50 mL:7.5 mL) to give the phthalonitrile derivative (**5**) as a light brown viscous oily product. Yield: 0.79 g (55.6%). FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3075–3042 (C-H aromatic), 2921–2851 ( $\text{CH}_3$ ), 2234 ( $\text{C}\equiv\text{N}$ ), 1596 (C = C), 1569, 1488, 1457, 1349 (Tosyl group, S = O asymmetric), 1291, 1252, 1162 (Tosyl group, S = O symmetric), 1115, 940, 850, 815, 750, 706, 674 and 660 (C-S).  $^1\text{H}$  NMR (ppm,  $\text{CDCl}_3$ ):  $\delta$  = 7.78–7.72 (m, 1H, Ar-H), 7.58–7.55 (m, 1H, Tosyl, Ar-H), 7.44–7.42 (m, 1H, Ar-H), 7.32–7.29 (m, 4H, Ar-H and Tosyl, Ar-H), 3.73–3.61 (m, 6H,  $\text{H}_2\text{C-O-CH}_2$  and  $-\text{CH}_2-\text{N-}$ ), 2.45–2.32 (m, 9H,  $\text{H}_2\text{C-N-CH}_2$  and Tosyl,  $-\text{CH}_3$ ), 1.67–1.60 (m, 2H,  $-\text{N-CH}_2-\text{CH}_2-\text{CH}_2-\text{N-}$ ).  $^{13}\text{C}$  NMR (ppm,  $\text{CDCl}_3$ ):  $\delta$  = 144.93, 144.41, 143.24, 137.10, 134.26, 133.91, 132.01, 131.56, 130.09, 129.68, 127.41, 127.19, 127.00, 124.84, 116.77–114.90–114.70 ( $\text{C}\equiv\text{N}$ ), 113.73, 66.90–66.88–66.04–65.18–63.34 ( $\text{H}_2\text{C-O-CH}_2$ ), 58.47–58.26–55.22–54.27–53.62–53.55 ( $\text{H}_2\text{C-N-CH}_2$ ), 47.81–43.92–42.99 ( $-\text{CH}_2-\text{CH}_2-\text{N-}$ ), 25.43–24.93–23.88–23.20–22.72 ( $-\text{N-CH}_2-\text{CH}_2-\text{CH}_2-\text{N-}$ ), 21.66–21.55 (Tosyl,  $-\text{CH}_3$ ). LC-TOF/MS  $m/z$ : Calculated: 424.52, Found: 425.17 [ $\text{M} + \text{H}$ ] $^+$ .

### 2.2.3. The syntheses of $\text{Cu}^{\text{II}}$ (**6**), $\text{Co}^{\text{II}}$ (**7**), $\text{MnCl}^{\text{III}}$ (**8**) and $\text{Ni}^{\text{II}}$ (**9**) phthalocyanines

*N*-(3,4-dicyanophenyl)-4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide (**5**) (0.212 g, 0.5 mmol, 2 eq.) was dissolved in 6 mL of dry pentan-1-ol under a stream of  $\text{N}_2(\text{g})$  in a Schlenk tube. Later, anhydrous metal salts [ $\text{CuCl}_2$ , 33.9 mg, 0.25 mmol, 1 eq. for **6**;  $\text{CoCl}_2$ , 32.5 mg, 0.25 mmol, 1 eq. for **7**;  $\text{MnCl}_2$ , 31.5 mg, 0.25 mmol, 1 eq. for **8** and  $\text{NiCl}_2$ , 32.4 mg, 0.25 mmol, 1 eq. for **9**] along with 6 drops of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)

were subsequently added into the solution and the sealed tube was purged with dry nitrogen gas for several times to remove dissolved oxygen. At 160 °C, the reaction mixture was then refluxed for 18 h. After cooling to room temperature, the reaction mixture was precipitated by the addition of 10 mL ethanol. The resulting precipitate was filtered off, washed with distilled water and ethyl alcohol separately, and following that, the crude product was dried *in vacuo*. The crude products were purified by column chromatography on neutral alumina with chloroform:ethanol (50 mL:1.5 mL) for **6** and **7**; chloroform:ethanol (50 mL:3 mL) for **8** and **9**. The collected organic phase was evaporated to dryness and finally dried under vacuum to give the corresponding metallic phthalocyanines (**6–9**). Figure S1 illustrates the synthetic pathway for compounds **3**, **5**, and **6** to **9**.

2.2.3.1. *Copper(II) phthalocyanine (6)*. Color: Blue. Yield: 50.00 mg (22.0%), m.p. > 300 °C. FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3062 (C-H aromatic), 2918–2850 ( $\text{CH}_3$ ), 1597 (C=C), 1495, 1448, 1326 (Tosyl group, S=O asymmetric), 1157 (Tosyl group, S=O symmetric), 1116, 918, 862, 815, 749, 708 and 660 (C-S). UV-Vis (chloroform),  $\lambda_{max}$ , nm ( $\log\epsilon$ ): 681 (5.01), 614 (4.35) and 343 (4.75). MALDI-TOF-MS  $m/z$ : Calculated: 1761.61, Found: 1761.69 [ $\text{M}$ ] $^+$ .

2.2.3.2. *Cobalt(II) phthalocyanine (7)*. Color: Blue. Yield: 85.00 mg (38.8%), m.p. > 300 °C. FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3059 (C-H aromatic), 2953–2927–2854 ( $\text{CH}_3$ ), 1598 (C=C), 1494, 1448, 1324 (Tosyl group, S=O asymmetric), 1288, 1155 (Tosyl group, S=O symmetric), 1116, 970, 918, 862, 815, 707 and 660 (C-S). UV-Vis (chloroform),  $\lambda_{max}$ , nm ( $\log\epsilon$ ): 672 (4.99), 607 (4.44) and 329 (4.91). MALDI-TOF-MS  $m/z$ : Calculated: 1757.01, Found: 1758.49 [ $\text{M} + \text{H}$ ] $^+$ .

2.2.3.3. *Manganese(III) chloride phthalocyanine (8)*. Color: Green. Yield: 100.00 mg (44.9%), m.p. > 300 °C. FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3033 (C-H aromatic), 2951–2919–2850 ( $\text{CH}_3$ ), 1599 (C=C), 1494, 1447, 1326 (Tosyl group, S=O asymmetric), 1156 (Tosyl group, S=O symmetric), 1116, 973, 862, 815, 707 and 659 (C-S). UV-Vis (chloroform),  $\lambda_{max}$ , nm ( $\log\epsilon$ ): 732 (5.08), 670 (4.68), 521 (4.55) and 315 (5.57). MALDI-TOF-MS  $m/z$ : Calculated: 1788.45, Found: 1754.84 [ $\text{M-Cl} + \text{H}$ ] $^+$ .

2.2.3.4. *Nickel(II) phthalocyanine (9)*. Color: Dark green. Yield: 40.00 mg (18.3%), m.p. > 300 °C. FT-IR:  $\nu_{max}$  ( $\text{cm}^{-1}$ ) = 3064 (C-H aromatic), 2924–2852 ( $\text{CH}_3$ ), 1611 (C=C), 1532, 1487, 1445, 1346 (Tosyl group, S=O asymmetric), 1261, 1159 (Tosyl group, S=O symmetric), 976, 862, 814, 750, 709 and 661 (C-S).  $^1\text{H}$  NMR (ppm,  $\text{CDCl}_3$ ):  $\delta$  = 8.00–7.85 (br, 4H, Ar-H), 7.68–7.66 (br, 4H, Ar-H), 7.59–7.39 (m, 20H, Ar-H), 3.71 (br, 24H,  $\text{H}_2\text{C-O-CH}_2$  and  $-\text{CH}_2-\text{N-}$ ), 2.42–2.19 (br, 36H,  $\text{H}_2\text{C-N-CH}_2$  and Tosyl,  $-\text{CH}_3$ ), 1.64–1.52 (br, 8H,  $-\text{N-CH}_2-\text{CH}_2-\text{CH}_2-\text{N-}$ ). UV-Vis (chloroform),  $\lambda_{max}$ , nm ( $\log\epsilon$ ): 701 (5.08), 638 (4.60) and 314 (5.00). MALDI-TOF-MS  $m/z$ : Calculated: 1756.75, Found: 1744.26 [ $\text{M-12H}$ ] $^+$ .

## 3. Results and discussion

### 3.1. Synthesis and characterization

The synthetic procedures including the purification methods, the verification of the chemical structures of new peripherally 4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide components fused copper(II) phthalocyanine (**6**), cobalt(II) phthalocyanine (**7**), manganese(III) chloride phthalocyanine (**8**), and nickel (II) phthalocyanine (**9**) complexes and the detection and fluorimetric determination of a health-threatening food colorant Sudan II dye was explained in this work. We outlined a cheaper, faster, simpler, and sensitive spectrofluorimetric method for the



detection and determination of Sudan II dye to overcome the time consuming, tiring, and expensive HPLC methods. To put it another way, the copper(II) phthalocyanine (**6**), cobalt(II) phthalocyanine (**7**), manganese(III) chloride phthalocyanine (**8**), and nickel(II) phthalocyanine (**9**) compounds were utilized for the first time for the detection and determination of banned food dye Sudan II in red chili peppers. The FT-IR, LC-TOF/MS (for the new compounds **3** and **5**),  $^1\text{H}$  NMR (for the new compounds **3**, **5** and **9**),  $^{13}\text{C}$  NMR (for the new compounds **3** and **5**), UV-Vis (for the new MPcs **6** to **9**), and MALDI-TOF (for the new MPcs **6** to **9**) spectral methods were utilized to confirm the chemical structures of newly synthesized compounds (**3**, **5**, **6** to **9**). Based on the above-mentioned spectroscopic results, the new compounds (**3**, **5**, **6** to **9**) were agreeing well with the suggested structures in Figure S1.

4-Methyl-*N*-(3-morpholinopropyl)benzenesulfonamide (**3**) was obtained by the synthesis reaction of 3-morpholinopropan-1-amine (**1**) and *p*-toluenesulfonyl chloride (**2**) at  $-5^\circ\text{C}$  in dry pyridine by the customizing of the published work [55]. The purification process of the phthalonitrile derivative (**5**) was carried out by chromatographic separation on a silica gel charged column with chloroform:ethanol (50 mL:5 mL). The  $^1\text{H}$  NMR signal corresponding to the  $\text{NH}_2$  group in (**1**) evanesced and a new broad signal belonging to the N-H proton at  $\delta = 7.00$  ppm was observed in the  $^1\text{H}$  NMR spectrum of tosylated compound (**3**). The aromatic ring protons were resonated at  $\delta = 7.75\text{--}7.73$  (d, 2H, Tosyl, Ar-H) and 7.32–7.30 ppm (d, 2H, Tosyl, Ar-H) (Figure S2). Other  $^1\text{H}$  NMR signals were detected at  $\delta = 3.73\text{--}3.71$  (t, 4H,  $\text{H}_2\text{C}\text{--}\text{O}\text{--}\text{CH}_2$ ), 3.08–3.05 (t, 2H,  $\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{N}\text{--}\text{H}$ ), 2.43–2.40 (m, 7H,  $\text{H}_2\text{C}\text{--}\text{N}\text{--}\text{CH}_2$  and Tosyl,  $\text{--}\text{CH}_3$ ) and 1.68–1.62 ppm (m, 4H,  $\text{--}\text{N}\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{N}\text{--}\text{H}$ ). The characteristic aromatic carbon atoms signals in  $^{13}\text{C}$  NMR of (**3**) were observed at  $\delta = 143.19$ , 137.12, 135.98, 129.65, 126.99, 126.42, 124.82 ppm. The other resonances in  $^{13}\text{C}$  NMR of (**3**) were resonated at  $\delta = 66.88\text{--}61.46$  ( $\text{H}_2\text{C}\text{--}\text{O}\text{--}\text{CH}_2$ ), 58.44–58.22–53.53 ( $\text{H}_2\text{C}\text{--}\text{N}\text{--}\text{CH}_2$ ), 43.86–42.94 ( $\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{N}\text{--}\text{H}$ ), 30.58–30.31–23.90 ( $\text{--}\text{N}\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{N}\text{--}\text{H}$ ), 21.53 (Tosyl,  $\text{--}\text{CH}_3$ ) (Figure S3). The evanesce of the  $\text{NH}_2$  group of (**1**) and the arising new stretching vibrations associated with the N-H (stretching and bending) and the tosyl groups (asymmetric and symmetric) of compound (**3**) at  $\nu_{\text{max}} = 3272\text{--}1092\text{ cm}^{-1}$  and  $1318\text{--}1155\text{ cm}^{-1}$  respectively in the FT-IR spectrum of (**3**) was one of the best indications that the tosylation reaction was succeeded. Mass spectral data for compound (**3**) was measured by the LC-TOF/MS device and the molecular ion peak was observed at  $m/z = 299.147$ .

The dicyano compound (**5**), *N*-(3,4-dicyanophenyl)-4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide, was prepared as a light brown viscous oily product by the substitution reaction of compound (**3**) with 4-nitroptalonitrile (**4**), anhydrous  $\text{K}_2\text{CO}_3$  and dry  $\text{CH}_3\text{CN}$  at  $85^\circ\text{C}$  for 6 days under the nitrogen. The purification process of the phthalonitrile derivative (**5**) was carried out by chromatographic separation on a silica gel charged column with chloroform:ethanol (50 mL:7.5 mL). In the  $^1\text{H}$  NMR spectrum of precursor compound (**3**), the N-H proton signal at  $\delta = 7.00$  ppm vanished in the case of compound (**5**) (Figure S4). The  $\text{C}\equiv\text{N}$  signals in the  $^{13}\text{C}$  NMR spectrum of phthalonitrile derivative (**5**) were resonated at  $\delta = 116.77\text{--}114.90\text{--}114.70$  ppm (Figure S5). The other proton and  $^{13}\text{C}$  NMR resonance peaks were nearly the same with precursor tosylated compound (**3**) except some little chemical shifts. In the case of compound (**5**), a new vibration of the  $\text{C}\equiv\text{N}$  functional group was seen at  $\nu_{\text{max}} = 2234\text{ cm}^{-1}$  while the vibration of the N-H group (stretching and bending) at  $\nu_{\text{max}} = 3272\text{--}1092\text{ cm}^{-1}$  was evanesced as expected. Molecular ion peak was observed at  $m/z = 425.17$  in the mass spectrum of compound (**5**) (Figure S6). All obtained spectral data were agreeing well with the dicyano compound (**5**).

The peripherally 4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide substituents fused CuPc (**6**), CoPc (**7**), MnClPc (**8**), and NiPc (**9**) was synthesized from *N*-(3,4-dicyanophenyl)-4-methyl-*N*-(3-morpholinopropyl)benzenesulfonamide (**5**) and the related anhydrous metal salts in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene and dry pentan-1-ol under nitrogen gas stream. The purification procedures were made by chromatographic separation on neutral alumina with chloroform:ethanol (50 mL:1.5 mL) for **6** and **7**; chloroform:ethanol (50 mL:3 mL) for **8** and **9**. After successful syntheses of the above-mentioned complexes [ $\text{Cu}^{\text{II}}$  (**6**),  $\text{Co}^{\text{II}}$  (**7**),  $\text{MnCl}^{\text{III}}$  (**8**), and  $\text{Ni}^{\text{II}}$  (**9**) phthalocyanines], two important spectroscopic alterations were recognized in the  $^{13}\text{C}$  NMR and infrared spectra of the complexes as expected. These two spectral changes were the evanescence of the  $\text{C}\equiv\text{N}$  functionalities of the dicyano compound (**5**) both in the  $^{13}\text{C}$  NMR ( $\delta = 116.77\text{--}114.90\text{--}114.70$  ppm) and infrared ( $\nu_{\text{max}} = 2234\text{ cm}^{-1}$ ) spectra. The mass spectral data were acquired by MALDI-TOF technique by using the 2,5-dihydroxybenzoic acid (DHB) as the MALDI matrix for all complexes (**6**–**9**). The parent molecular ion peaks of the new MPcs [ $\text{Cu}^{\text{II}}$  (**6**) (Figure S7),  $\text{Co}^{\text{II}}$  (**7**) (Figure S8),  $\text{MnCl}^{\text{III}}$  (**8**) and  $\text{Ni}^{\text{II}}$  (**9**)] were measured at  $m/z = 1761.69$ , 1758.49, 1754.84, and 1744.26, respectively.

Coupled with the above-mentioned spectral data, one of the best substantial proofs regarding the successful preparation of the  $\text{Cu}^{\text{II}}$  (**6**),  $\text{Co}^{\text{II}}$  (**7**),  $\text{MnCl}^{\text{III}}$  (**8**), and  $\text{Ni}^{\text{II}}$  (**9**) phthalocyanine compounds was obtained from the ground state electronic absorption spectra. The distinctive Soret (B-) and Q- bands were seen in chloroform at room temperature at  $1.0 \times 10^{-5}$  M concentration. The significant Q- and Soret bands appeared at  $\lambda_{\text{max}} = 681$  ( $\log \epsilon = 5.01$ ), 614 (4.35) and 343 nm ( $\log \epsilon = 4.75$ ) for (**6**); 672 (4.99), 607 (4.44) and 329 nm (4.91) for (**7**); 732 (5.08), 670 (4.68), 521 (4.55) and 315 nm (5.57) for (**8**); 701 (5.08), 638 (4.60) and 314 nm (5.00) for (**9**), respectively (Fig. 1). Based on the absorption spectra in the ultraviolet-visible spectrum of the MPc compounds (**6**–**9**), all new complexes exhibited a specific absorption spectrum related to non-aggregated substituted and unsubstituted MPc species with  $D_{4h}$  symmetry that is consistent with other phthalocyanine metal complexes reported in the literature [14,16,22].

### 3.2. Spectrofluorimetric determination studies

The toxic properties of Sudan dyes [42,43] make their determination by cheap, fast, and simple determination methods important. In this study, primarily the fluorescence properties of MPc complexes prepared for the development of new determination methods having mentioned properties based on fluorescence measurement were determined. Consequently, it has been shown that the new MPc complexes can be used as fluorescent reagents for the sensitive determination of Sudan II (Fig. 2) in red pepper.

Fig. 3 shows the fluorescence spectra of the MPc complexes in ethanol. As seen from Fig. 3, the fluorescence characteristics of CoPc (**7**) and CuPc (**6**) complexes with emission maximums at approximately 360 and 415 nm are similar. MnClPc (**8**) complex spectrum is similar to those of the CoPc (**7**) and CuPc (**6**) complexes. However, while the fluorescence intensity increased at all wavelengths, the emission peak at 360 nm shifted to a blue of about 10 nm. The NiPc (**9**) complex showed a small emission peak at 360 nm while showing a flat emission band between 375 and 495 nm.

The effect of Sudan II on the emission spectrum of the CuPc (**6**), CoPc (**7**), MnClPc (**8**), and CuPc (**6**) complexes was examined. The results show that Sudan II caused an increase in fluorescence intensity of the metal complexes at all wavelengths. The fluorescence enhancement results from the hiding of the intramolecular photoinduced electron transfer (PET) from morpholine donors to MPc moiety providing a moderate fluorescence intensity by the

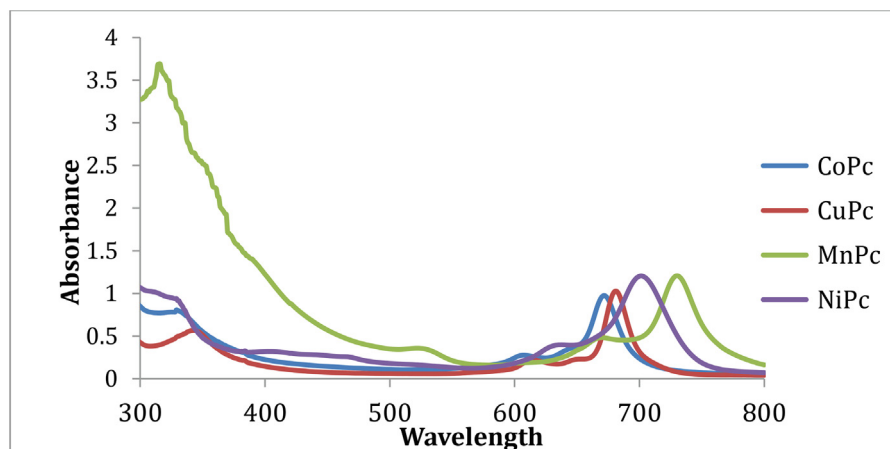


Fig. 1. The UV-Vis spectrum of new metallophthalocyanine compounds (6–9) in chloroform at room temperature (Concentration:  $1.0 \times 10^{-5}$  M).

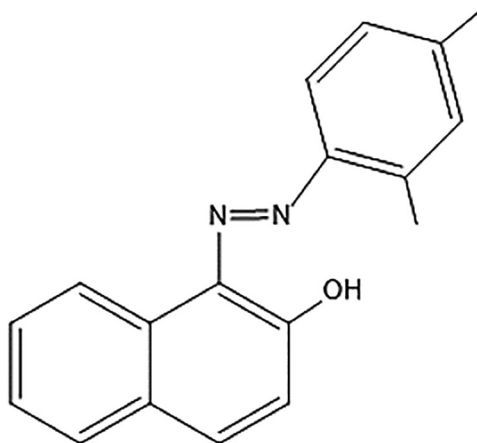


Fig. 2. The structure of Sudan II azo-dye.

effect of Sudan II [56]. This increase was highly effective at approximately 360 nm and it was determined that there was a regular relationship between the increasing Sudan II concentration and the fluorescence intensity of the  $\text{Cu}^{\text{II}}$  (6),  $\text{Co}^{\text{II}}$  (7),  $\text{MnCl}^{\text{III}}$  (8) and  $\text{Ni}^{\text{II}}$

(9) phthalocyanine compounds. As a representative result related to the change of the fluorescence spectra was given for the CoPc (7) complex in Fig. 4. The 356 nm band observed in the fluorescence spectrum of the CoPc (7) complex can be explained by the emission  $\pi^* \rightarrow \pi$ , which is related to the Soret (B) band in PCs [57]. The band around 425 nm is related to the bridging nitrogen of the Pc ring and is caused by the  $\pi^* \rightarrow n$  transitions that contribute to the Soret band [58,59]. With the increasing Sudan II concentration in the fluorescence spectrum of the CoPc (7) complex, the increase in emission intensity around 425 nm is very small compared to the increase at 356 nm (Fig. 4). That the band at 425 nm gradually disappears can be explained by the decrease in the  $n^* \rightarrow n$  transition due to the interaction of the Sudan II molecule with the donor groups at the peripheral positions in the CoPc (7) complex. On the other hand, a significant increase in the fluorescence spectrum of the CoPc (7) complex at 356 nm was observed with increasing the Sudan II dye concentration. Moreover, this increase has been found to be linearly related to the Sudan II concentration (Fig. 4, inset). Thus, analytical method development studies were carried out at 356 nm. Nearly similar changes were obtained with the other metal complexes. Suitable calibration graphs were formed from the fluorescence increase about

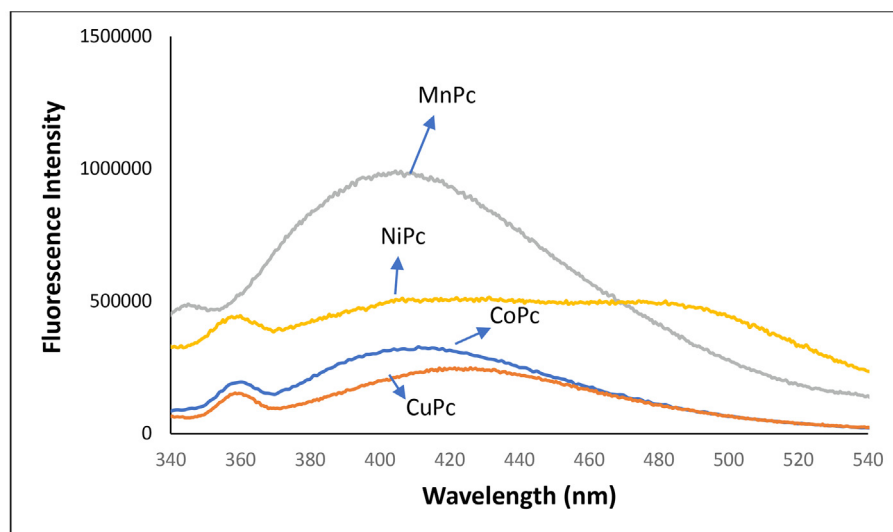
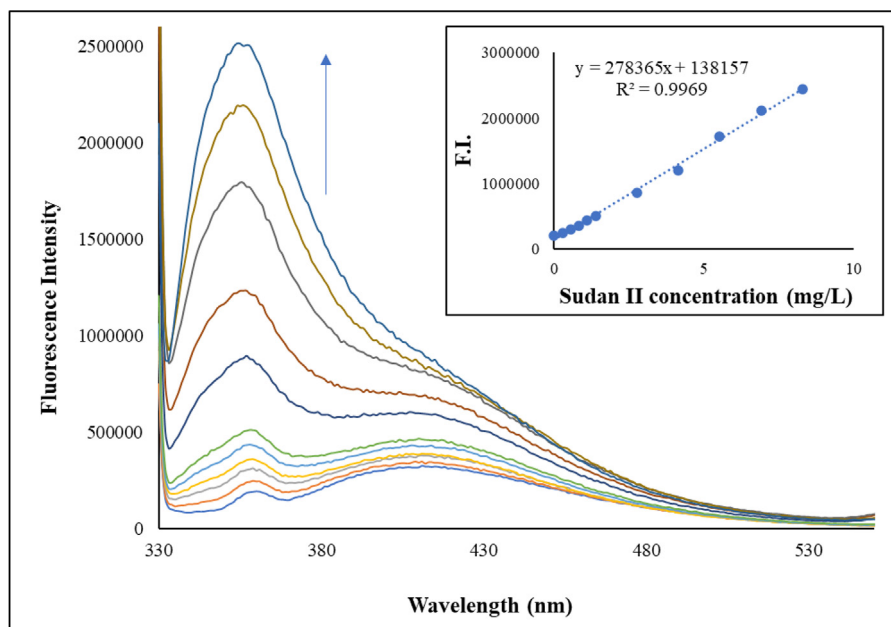


Fig. 3. The fluorescence spectra of the MPc complexes (6–9) in ethanol. The excitation wavelength is 320 nm. Concentration:  $1.0 \times 10^{-5}$  M.



**Fig. 4.** The fluorescence enhancement of the CoPc (7) complex with increasing Sudan II concentration. The concentration range: 0–8.3 mg/L. Inset: The increase of fluorescence intensity at 356 nm with increasing Sudan II concentration.

360 nm for the fluorimetric determination of Sudan II. A representative calibration graph is given in Fig. 4 inset.

It was determined that all MPC complexes (6–9) can be used in the fluorimetric determination of Sudan II. The proposed methods base on the use of a simple external calibration graph. Measurement conditions and calibration data of the proposed methods are given in Table 1. It can be seen from Table 1 that high determination coefficients ( $R^2$ ) are obtained for copper(II) phthalocyanine (6), cobalt(II) phthalocyanine (7), manganese(III) chloride phthalocyanine (8), and nickel(II) (9) phthalocyanine complexes.

Table 2 gives the analytical performance data of the method under the optimized conditions for all MPC complexes (6–9). For these methods, the LOD and LOQ are defined as  $3S_b/m$  and  $10S_b/m$ , respectively. Therefore, LOQ is about 3.3 times of LOD. The standard deviation of fluorescence intensity of 11 blank solutions and slope of calibration equation have been indicated as  $s$  and  $m$ , respectively. As can be seen from Table 2, the high recovery percentages (R%) were obtained for the Sudan II spiked samples (1.0 mg/L). The precision of the results is given for intra-day and inter-day measurements as percent relative standard deviation (RSD %). The number of repeated measurements in these studies is 3. Table 2 shows that the uncertainty in the measurement results

as RSD % is between 2.4 and 1.1. The LOD values and linear ranges of the proposed methods are comparable to those of the fluorimetric methods recommended for the determination of Sudan II in the literature [53,54]. So, the analytical studies showed that the proposed methods can be applied for the determination of banned dye Sudan II in red pepper samples.

The proposed methods do not require laborious pre-treatment or extractions steps before the determination. It is sufficient to use only an external calibration graph to determine Sudan II. Therefore, the proposed methods are rapid and not complicated.

#### 4. Conclusion

In this paper, we declared the synthesis and structural verification of new peripherally tetra-substituted phthalocyanine derivatives fused 4-methyl-*N*-(3-morpholinopropyl) benzenesulfonamide moieties. The confirmation of the chemical structures of studied compounds was made via Fourier Infrared,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, LC-TOF/MS, UV-Vis, and MALDI-TOF mass spectral data. Simple and economical detection and determination of a banned azo-dye Sudan II using especially to increase red color

**Table 1**

Measurement conditions and calibration data of the proposed fluorimetric methods for Sudan II determination.

MPC	Excitation wavelength (nm)	Measurement wavelength (nm)	Calibration equation	The determination coefficient ( $R^2$ )
CuPc (6)	320	356	$y = 216596x + 53693$	0.9981
CoPc (7)	320	356	$y = 278365x + 138157$	0.9969
MnClPc (8)	320	356	$y = 271201x + 594419$	0.9891
NiPc (9)	320	356	$y = 270323x + 499260$	0.9927

**Table 2**

Analytical performance data of the proposed methods for Sudan II determination with the MPC complexes.

MPC	Linear range (mg/L)	LOD (mg/L)	LOQ (mg/L)	Added (mg/L)	R % ± RSD % (Intra-day precision, N = 3)	R % ± RSD % (Inter-day precision, N = 3)
CuPc (6)	0–2.9	0.050	0.149	1.0	101.7 ± 2.1	100.7 ± 1.1
CoPc (7)	0–8.3	0.035	0.106	1.0	102.3 ± 2.4	101.1 ± 1.6
MnClPc (8)	0–6.0	0.050	0.149	1.0	100.4 ± 2.4	101.0 ± 2.1
NiPc (9)	0–5.5	0.045	0.136	1.0	103.0 ± 2.0	100.8 ± 1.4

in spices is still a critical problem in many countries of the world. Time-consuming and expensive HPLC methods are generally recommended for the determination of Sudan II for this purpose. In the present study, it is suggested that new MPC complexes can be used for the determination by simpler, cheaper, and faster spectrofluorimetric methods. Moreover, the sensitivity of the proposed method is good enough to determine the amount of dye at a concentration of 0.1 mg/L. That is to say, we offer a new procedure for those who are interested in food chemistry and industry to detect and determine the hazardous food colorant Sudan II dye.

### CRedit authorship contribution statement

**Halit Kantekin:** Supervision, Funding acquisition, Methodology, Resources. **Beytullah Ertem:** Writing - original draft. **Nurten Aslan:** Investigation. **Halise Yalazan:** Investigation. **Ümmühan Ocak:** Methodology, Investigation. **Ender Çekirge:** . **Abidin Gümrukçüoğlu:** . **Volkan Çakır:** Methodology. **Miraç Ocak:** Methodology, Investigation.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Acknowledgments

The authors thank Karadeniz Technical University Scientific Research Projects Coordination Unit (Project Number: FHD-2018-7866) for the financial support for this work.

### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.saa.2020.119222>.

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