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Design of Novel Phthalocyanines as Potential Antimicrobial Agents Starting with Synthesized Phthalonitrile Derivatives:Complexation, Extraction and Antimicrobial Studies

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Abstract

New phthalonitrile derivatives 1-4 were considered as the key intermediates for the synthesis of new phthalocyanines. Their capacity to bind various transition metal and heavy metal cations was studied in methanol. The absorbance and conductivity were measured using UV spectrophotometry. Spectral and elemental investigations revealed the structures of the newly synthesized phthalocyanines. The complexes formed were analyzed, and their stability constants were determined through digital data processing. The ability of water to extract these compounds in dichloromethane was also examined. It was discovered that compound 1 had a lower affinity for metal picrates compared to compound 2-4, especially Fe(III). The stoichiometry of the complex was confirmed by conducting conductivity studies. The antimicrobial properties of the novel compounds were investigated, and it has been established that have compounds 9, 12 and 13 potent inhibitory activities against both Gram-positive and Gram negative bacteria and fungi.

Keywords: Catalysis, Catalysts, Structure analysis, Stoichiometry, Complexation, Phthalonitriles, metallophthalocyanine derivatives.

1. Introduction

The importance of phthalonitriles extends beyond their role as intermediates or precursors in synthetic chemistry; they also hold great potential for industrial material design. These compounds have garnered considerable attention due to their wide range of applications in various fields, including electronics, machinery, automobile, aerospace, and shipping, both in military and civilian contexts. The demand for cutting-edge equipment in these industries makes phthalonitriles particularly valuable [1,2]. Additionally, phthalonitrile derivatives have shown exceptional promise in the development of liquid crystal displays (LCDs) because of their negative dielectric anisotropy values in their liquid crystalline forms [3], [4], [5-6]. It is worth noting that phthalonitriles play a crucial role as precursors for the synthesis of phtalocyanines, which are essential for creating macrocyclic organic materials with functional properties. These materials exhibit similarities to the porphyrin ring structure and possess remarkable symmetry. The substitution of phthalonitriles allows for functionalization, serving specific purposes [7,8]. This versatility opens up

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possibilities for synthesizing novel phthalocyanine compounds with varying electrical, optical, or magnetic properties. Phthalocyanines (Pcs) are highly conjugated and essentially planar aromatic macrocycles, consisting of four iminoisoindoline units, containing 18 delocalized π-electrons and widely praised for their thermal and chemical stability. Such electronic delocalization permits Pcs to display intense absorption bands in the near infrared region of the electronic spectrum, reaching very high extinction coefficients (~10^5 M^{-1} cm^{-1}), accompanied by high fluorescence quantum yields, concomitantly with favorable redox activity and rich electrochemistry [9-13]. These findings have implications in various applications. Recent research has demonstrated that phthalocyanine derivatives containing carboxylic acid (-COOH) as an electron-withdrawing group exhibit charge transfer capabilities in a π-conjugated bridge structure, making them highly suitable for the advancement of DSSCs [14], [15], [16]. Conductivity measurements play a vital role in the identification of organic compounds that can be utilized as electronic materials. Crystalline materials possess high mobility and are highly suitable for electronic device applications, as well as organic thin film devices due to their ability to form regular thin film structures [17]. A major problem in the development of novel phthalocyanine compounds containing peripherally functionalized fused heterocyclic systems is low solubility, which prevents their use in medical applications. Our main objective is to synthesize new phthalocyanines in high yields with different substituents, which enhance their use in a broad spectrum of medical applications.In this paper, the focus is directed to the synthesis of phthalocyanine molecules and to study their complexation, extraction and antimicrobial studies**.**

2. Experimental

All reagents were obtained from Fluka and Aldrich. The purity of the products was tested in each step by TLC (SiO_2, $CHCl_3$/MeOH and THF/MeOH). Melting points were determined using an Electrothermal apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were determined on a Varian Gemini 300 (300 MHz) spectrometer using TMS as internal standard (δ = 0 ppm). IR spectra were recorded on a Perkin-Elmer 398 spectrophotometer. MS were recorded on a LC-MS-MS 8030 Shimadzu spectrometer. Elemental analyses were performed on Perkin-Elmer 2400 elemental analyser, and the values found were within ±0.3% of the theoretical values. The UV-Vis spectra were recorded on a Perkin Elmer Lambda 11 spectrophotometer.

2.1 Synthesis of 4-(2,4,6-trimethylphenylamino)phthalonitrile (1)

4-nitrophthalonitrile (0.38 g, 1.92 mmol), 2,4,6-trimethylphenylamine (0.55 g, 1.92 mmol) and anhydrous DMF (15 mL) were added to a round bottom flask under a nitrogen atmosphere. A fine powder of anhydrous potassium carbonate (0.8 g, 5.76 mmol) was added to this mixture. The resulting mixture was stirred at room temperature for 24 h. The crude product was collected by filtration, washed with distilled water, then recrystallised from THF-petroleum ether to afford a white powder. Yield: 0.77 g (98%); m.p. = 400 °C; IR (KBr pellet) vmax cm–1: 1305 (C–N), 1568 (C=C), 2235 (C≡N), 3049 (C–H, aromatic); ^{1}H NMR (DMSO-d_6 , 300 MHz): d 2.02 [s, 3H, CH_3 (a)], 2.08 (s, 3H, CH_3), 2.09 [s, 6H, CH_3 (b,c)], 4.21 (s, 1H, NH), 6.57 (s, 2H, $H_{3',5'}$), 8.38 (s, 1H, H_3), 8.63 (s, 1H, H_5), 8.98 (s, 1H, H6); ^{13}C NMR (DMSO-d_6 , 75 MHz): d 17.5 [C(a,b)], 19.9 (Cb), 114.5 (CN), 114.8 (CN), 116.4 (C_2), 120.0 ($C_{2'}$), 120.5 ($C_{6'}$), 123.9 (C4'), 128.2 (C3',5'), 128.3 (C3), 128.6 (C_5), 135.4 (C_6), 141.3 (C11), 149.5 (C_4); MS (LCMSMS) m/z: Calcd. 261.3; found: 261.3. Anal. calcd for $C_{17}H_{15}N_3$: C, 78.14; H, 5.79; N, 16.08; found: C, 78.1; H, 5.6; N, 16.0%.

2.2 Synthesis of 4-(pyridine-2-ylsulfanyl) phthalonitrile (2)

The synthesis of 2 was similar to 1 but the mixture was stirred for 72 h; pyridine-2-thiol (0.55 g, 1.92 mmol) was employed instead of 2,4,6-trimethylphenylamine. The amounts of the other reagents were 4-nitrophthalonitrile, 1 g (5.55 mmol) and anhydrous potassium carbonate, 2 g (13.88 mmol). Yield: 0.77 g (85%); m.p. = 370 °C; IR vmax cm–1: 3077 (Ar–CH), 3049 (Ar–CH), 2233 (C–N), 1601 (C–C), 1568 (C=C), 1263 (C–S–C); 1 H NMR (DMSO-d_6 , 300 MHz): δ 7.33–8.52 (m, ArH, 7H). ^{13}C NMR (DMSO-d_6 , 75 MHz): d 113.5 (C_2), 115.9 (CN), 116.2 (C_1), 123.2 ($C_{2'}$), 125.3 ($C_{4'}$), 134.7 (C_6), 136.3 (C_4), 138.7 ($C_{3'}$), 141.3 (C_5), 150.8 ($C_{5'}$), 154.8 ($C_{1'}$); MS (LCMS-MS) m/z: Calc. 237.2; found: 237.2. Anal. calcd for $C_{13}H_7N_3S$: C, 65.80; H, 2.97; N, 17.71; found: C, 65.8; H, 2.9; N, 17.7%.

2.3 Synthesis of metal-free phthalocyanines (5 and 6)

A solution of 4-(2,4,6-trimethylphenylamino)phthaloni-trile 1 or 4-(pyridine-2-ylsulfanyl) phthalonitrile 2 (0.20 g, 0.79 mmol) in N,N-dimethylaminoethanol (DMAE, 4 mL) was heated to 90 °C in a glass tube and DBU (0.44 mL, 0.80 mmol) was added to this solution at this temperature. The mixture was heated to 150 °C for 24 h. Then it was cooled to room temperature and diluted with n-hexane (ca. 30 mL)and stirred for 12 h.

The precipitated product was filtered and thenwashed with methanol, hot ethanol, and diethyl ether and dried ina vacuum over P_2O_5. The solid product was purified with column chromatography on alumina with chloroform/methanol (100:4) solvent system as eluent to give a dark green product.

2.4 Metal-free phthalocyanine 3

Yield: 83 mg (33%); m.p. > 200 °C; FTIR(KBr) nmax cm^{-1}: 3442 (N–H), 1612 (C=N), 1403 (C=C), 1093 (C–N), 794(C–C); ^{1}H NMR. (DMSO-d_6, 300 MHz): δ 2.85 (s, 36H, CH_3), 6.30 (m,4H, NH), 7.29–7.03 (m, 12H, ArH); UV-Vis (DMSO): lmax, nm (log ε):643 (4.90), 693 (1.21), 344 (4.81); Anal. calcd for $C_{68}H_{62}N_{12}$: C, 77.98; H,5.96; N, 16.05; found: C, 77.70; H, 5.80; N, 16.29%.

2.5 Metal-free phthalocyanine 6

Yield: 150 mg (66%); m.p. > 200°C; FTIR (KBr) nmax cm^{-1}: 3443 (N–H), 1416 (C=N), 1091 (C–N),796 (C–C). ^{1}H NMR (DMSO-d_6 , 300 MHz): d 6.70 (m, 16H, ArH),7.29–7.03 (m, 12H, ArH); UV-Vis (DMSO): lmax , nm (log ε): 617(4.56), 678 (5.08), 313 (4.43), 405 (4.53). Anal. calcd for $C_{68}H_{62}N_{12}$: C,65.66; H, 3.18; N, 17.67; found: C, 65.40; H, 3.30; N, 17.20%.

2.6 General procedure for synthesis of metallophthalocyanines (7-10) and (11–14).

Compound 1 (0.24 mmol) or compound 2 (0.24 mmol), DMAE(4 mL), DBU (3 drops) and (0.06 mmol) of corresponding metalsalts $Zn(ClO_4)_2 .6H_2O$, $CuCl_2 .2H_2O$, $CoCl_2 .6H_2O$ and $NiCl_2 .6H_2O$)were added to a Schlenk tube. The mixture was heated at reflux temperature of 170 °C for 24 h under an N_2 atmosphere. The mixture was left to cool to room temperature then treated with ethyl acetate to precipitate the product which was filtered off and quickly washed with water. The green solid product was washed with hot ethanol and hot acetic acid and dried in a vacuum. The raw product was purified by chromatography on a silica gel column.

Compound 7: Elution solvent system: chloroform/methanol (100:2).Yield: 132 mg (49%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1633(C=N), 1478 (C=C), 1090 (C–N), 792 (C–C); ^{1}H NMR (DMSO-d6 ,300 MHz): δ 2.94–4.41(s, 36H, CH_3), 6.50 (m, 4H, NH), 7.29–7.56 (m,12H, ArH). UV-Vis (DMSO): lmax , nm (log ε): 640 (5.31), 690 (2.54),341 (5.37). Anal. calcd for $C_{68}H_{60}N_{12}Zn$: C, 73.53; H, 5.45; N, 15.13;found: C, 73.2; H, 5.1; N, 15.3%.

Compound 8: Elution solvent system: chloroform/methanol (100:3).Yield: 156 mg (59%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1610(C=N), 1488 (C=C), 1092 (C–N), 789 (C–C); ^{1}H NMR (DMSO-d_6 ,300 MHz): δ 3.10–4.20 (s, 36H, CH_3), 6.30 (m, 4H, NH) 7.37–8.85 (m,12H, ArH); UV-Vis (DMSO): lmax , nm (log ε): 643 (5.25), 687 (2.24),341 (5.20); Anal. calcd for $C_{68}H_{60}N_{12}Ni$: C, 73.98; H, 5.47; N, 15.22;found: C, 73.4; H, 5.2; N, 15.1%.

Compound 9: Elution solvent system: chloroform/methanol (100:3).Yield: 145 mg (55%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1620(C=N), 1408 (C=C), 1093 (C–N), 793 (C–C); UV-Vis (DMSO):lmax , nm (log ε): 645 (5.15), 694 (2.01), 342 (5.14); Anal. calcd for $C_{68}H_{60}N_{12}Co$: C, 73.96; H, 5.48; N, 15.22; found: C, 73.8; H, 5.4; N,15.1%.

Compound 10: Elution solvent system: chloroform/methanol (100:3).Yield: 184 mg (69%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1611(C=N), 1407 (C=C), 1093 (C–N), 796 (C–C); UV-Vis (DMSO):lmax , nm (log ε): 644 (5.09), 693 (1.49), 341 (5.06); Anal. calcd for $C_{68}H_{60}N_{12}Cu$: C, 73.66; H, 5.45; N, 15.16; found: C, 73.5; H, 5.3; N,15.1%.

Compound 11: Elution solvent system: chloroform/methanol (100:3).Yield: 107 mg (44%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1635(C=N), 1418 (C=C), 1382 (C–N), 1093 (C–C); 1H NMR (DMSO-d_6 ,300 MHz): δ 2.92–3.41(s, 36H, CH 3), 6.20 (m, 4H, NH) 7.27–8.76 (m,12H, ArH); UV-Vis (DMSO): lmax , nm (log ε): 623 (4.91), 679 (5.21),305 (4.74), 384 (5.08); Anal. calcd for C 52 H 28 N12 S 4 Zn: C, 61.56; H,2.78; N, 16.57; found: C, 61.3; H, 2.6; N, 16.4%.

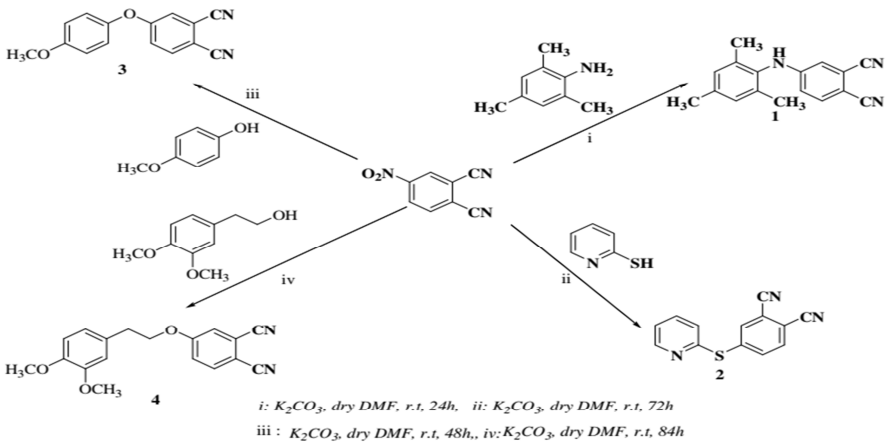
Compound 12: Elution solvent system: chloroform/methanol (100:3).Yield: 187 mg (77%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1603(C=N), 1415 (C=C), 1310 (C–N), 1085 (C–C); ^{1}H NMR (DMSO-d_6 ,300 MHz): δ 2.94–4.30 (s, 36H, CH 3), 6.30 (m, 4H, NH), 7.05–9.10 (m,12H, ArH); UV-vis (DMSO): lmax , nm (log ε): 625 (4.82), 679 (5.17),309 (4.69), 383 (4.96); Anal. calcd for $C_{52}H_{28}N_{12}S_4Ni$: C, 61.97; H, 2.80;N, 5.82; found: C, 61.8; H, 2.6; N 5.7%.

Compound 13: Elution solvent system: chloroform/methanol (100:3).Yield: 158 mg (65%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1568(C=N), 1446 (C=C), 1316 (C–N), 1098 (C–C); UV-Vis (DMSO): lmax ,nm (log ε): 629 (4.70), 690 (5.05), 316 (4.61), 388 (4.91); Anal. calcd for $C_{52}H_{28}N_{12}S_4Co$: C, 61.96; H, 2.80; N, 16.67; found: C, 61.8; H, 2.6; N,16.5%.

Compound 14: Elution solvent system: chloroform/methanol (100:3).Yield: 122 mg (50%); m.p. > 200 °C; FTIR (KBr) nmax cm^{-1}: 1573(C=N), 1417 (C=C), 1096 (C–N), 917 (C–C); UV-Vis (DMSO): lmax ,nm (log ε): 637 (4.71), 697 (4.92), 322 (4.50), 395 (4.86); Anal. Calcd for $C_{52}H_{28}N_{12}S_4Cu$: C, 61.68; H, 2.79; N, 16.60; found: C, 61.5; H, 2.6;N, 16.5%.

3. Results and Discussions

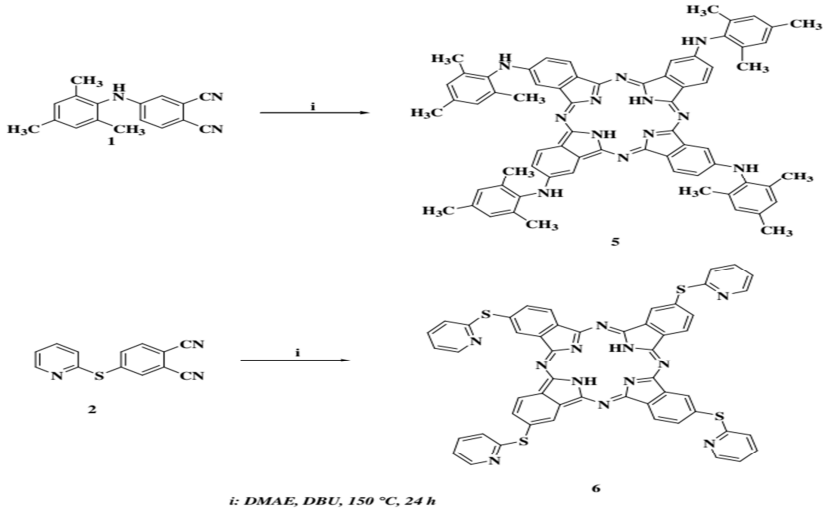
To synthesize compounds **1-4**, anhydrous DMF was used to dissolve 4-Nitrophthalonitrile, after which 2,4,6-Trimethyl-phenylamine or 4-Methoxy-phenol or 2-(3,4-Dimethoxy-phenyl)-ethanol or Pyridine-2-thiol was introduced. The resulting mixture was stirred for 15 minutes, and then finely ground anhydrous K_2CO_3 was added gradually over a span of 2 hours while maintaining continuous stirring. The reaction mixture was kept under magnetic stirring at 50°C for 72 hours. Upon completion of the reaction, as indicated by TLC analysis, the mixture was poured into 200 mL of an ice and water mixture. The precipitate formed was filtered, rinsed with water until the filtrate reached neutrality, and subsequently dried under vacuum. Finally, the precipitate was crystallized using ethanol to yield the target compounds **1-4**. **Scheme 1**.



Scheme 1: Synthesis of the phthalonitriles **1-4**.

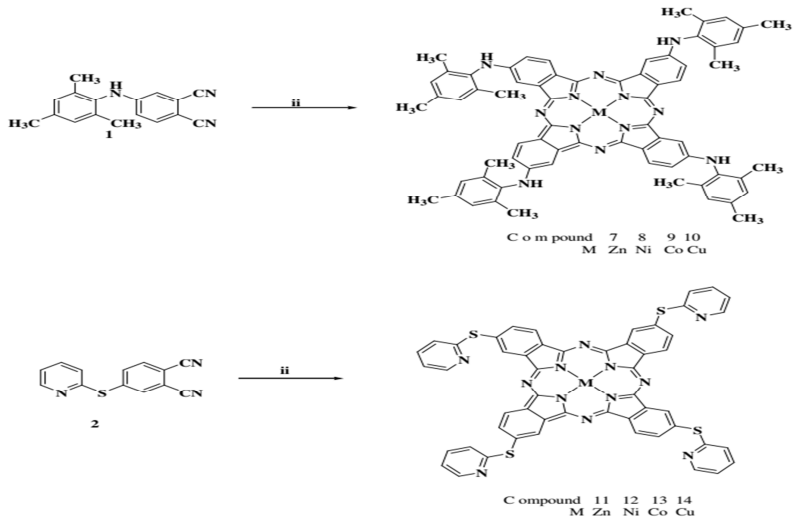
The characterization of the products **1–3** involved a combination of methods including, ^{1}H NMR, ^{13}C NMR, and NMR 2D, FT-IR, UV–vis, elemental analysis and LC–MS spectroscopy. In the IR spectrum of compound **1**, stretching vibrations of CN groups at 2227 cm^{-1} and aromatic groups (ArCH) at 3079 cm^{-1}appeared at expected frequencies. The ^{1}H NMR spectrum of **1** in DMSO-d_6 showed signals with ranging from 7.43 to 8.11 ppm belonging to aromatic protons and $H_{2,3}$. The methyl protons appeared at 2.42 ppm. In the ^{13}C NMR spectra of **1**, the aromatic, and CH_3 carbon atoms of 1 appeared between 116.2 and 161.7 ppm and at18.5 ppm, respectively, whereas carbon atom C_2 was observed at 159.8 ppm. The structures of the compounds **3-4** were confirmed using IR, ^{1}H NMR, ^{13}C NMR, MS spectroscopic data, elemental analysis and NMR 2D. In the IR spectra of **3** and **4**, the characteristic CN stretching vibrations were observed at 2235 and 2233 cm^{-1}, respectively. The ^{1} H NMR spectra of **4** and **3** were in excellent agreement with the proposed structures. Characteristic nitrile carbon atoms were observed at 114.5 and 114.8 ppm for 4 and at 115.9 and 116.2 ppm for 5. ^{1}H NMR spectral assignments are also supported *via* ^{1}H–^{13}C HMBC experiments. As can be seen from the ^{1}H–^{13}C HMBC spectrum, the H_5 aromatic proton at 8.63 ppm correlates with C_4 at 149.5 ppm and $C_{1'}$ at 141.3 ppm. $H_{3',5'}$ at 6.57 ppm correlates to $C_{4',6'}$ at 17.5 pm. The mass spectra of phthalonitrile derivatives **3-4** gave the characteristic molecular ion peaks at m/z = 261 and 237, respectively. Phthalocyanine, commonly referred to as Pcs, is a planar aromatic ring that consists of four isoindole units. These units create aromatic clouds that distribute 18 π-electrons across alternating carbon and nitrogen atoms. [18] Ever since its initial synthesis in the early 1900s, [19] Pc has found extensive use as dyes and pigments. However, ongoing research has expanded the scope of these compounds beyond their traditional [20] applications. This includes their use in catalysis, [21] chemical sensing, electrochromism, [22-23] photodynamic therapy (PDT), nonlinear optical (NLO) materials, [24] and liquid crystals. [25] Of particular interest is the exploration of new compounds through the incorporation of different substituents and central metal ions into the macrocyclic structure of Pcs. The synthesis of phthalocyanines and metal phthalocyanines follows the following procedure. (**Schemes 2-3**).The self-condensation of **1** and **2** in high-boiling solvent N,N-dimethylaminoethanol (DMAE) in the presence of a few drops of DBU (1,8-

diazobicylo[4.3.0]non-5-ene) at reflux temperature under N_2 afforded the metal-free phthalocyanines **5** and **6** as green solids after purification by column chromatography (aluminium oxide) using $CHCl_3$:CH_3OH (100:4) as the solvent system (**Scheme 2**). The IR spectrum of metal-free phthalocyanine 6 shows the classical NH band (inner NH) at 3442 cm^{-1} The rest of the spectrum of **6** was similar to that of 4 except for the CN group in **4**. In the ^1H NMR spectrum of **6**, the typical shielding of inner core protons could not be observed due to the probable strong aggregation of the molecules. The signals related to aromatic and aliphatic protons in the macrocyclic moieties and phthalocyanine skeleton gave a significant absorbance characteristic of the proposed structure.



Scheme 2. Synthesis of the metal-free phthalocyanines **5** and **6**.

Substituted phthalonitriles or 1,3-diimino-1H-isoindoles are generally used as starting materials for synthesis of Pcs.[26-29] Furthemore, phthalonitrile compounds **1** and **2** were also used as starting compounds for synthesis of the metallo-Pcs (Zn, Cu, Co, Ni) since only relatively mild reaction conditions were necessary. The synthesis of the metallophthalocyanines **7-14** was achieved by metal ion mediated cyclotetramerisation reactions of the corresponding precursors **1-2** in high boiling DMAE under an N_2 atmosphere. Four metal salts, $Zn(ClO_4)_2$.$6H_2O$, $CuCl_2$.$2H_2$ O, $CoCl_2$.$6H_2O$ and $NiCl_2$.$6H_2O$ salts, were used as templates for the formation of metallophthalocyanines, particularly since it is known that phthalocyanines containing cobalt and copper templates can be used as effective catalysts in oxygenation[30] and oxyhalogenation processes. [31] In a typical experiment, the reactions were carried out by simply mixing and grinding substituted nitriles **1** or **2** with one of the metal salts (Scheme 3). Characterisation of new Pc compounds was performed using IR, ^1H NMR, elemental analysis and UV-Vis. The IR spectra of all Pcs 7-14 are in good agreement with the proposed structures. The sharp peak for the (C≡N) vibrations of phthalonitrile 4 at 2235 cm^{-1}disappeared after its conversion into metal-free, nickel(II), cobalt(II), copper(II) and zinc(II) phthalocyanines **7-10**, indicative of metallophthalocyanine formation. Phthalocyanines **11-14** also have very similar IR absorptions. The IR spectra of metallophthalocyanines **11-14** are very similar, except the NH vibrations of the inner phthalocyanine core in the metal-free molecules show an NH stretching band peak at 3443 cm^{-1}. The NH proton of compound 8 could not be observed owing to the probable strong aggregation of the molecule. [32-33] The ^1H NMR spectrum of zinc phthalocyanine 8 showed the aromatic protons between 7.29 and 7.56 ppm and methylic protons at 2.94–4.41 ppm.36,37 The tetra-substituted metallo-phthalocyanine complexes (**7–11**) showed the phthalocyanine ring protons as unresolved multiplets (most likely due to the presence of isomers). The phthalocyanine ring and aromatic protons for peripherally substituted complexes were observed in the range 7.37 to 8.85 ppm for metallophthalocyanine 5, 7.27 to 8.76 for metallophthalocyanine 9 and 7.05 to 9.10 ppm for metallophthalocyanine 10. Although the presence of isomers as well as phthalocyanine aggregation at the concentrations used for the NMR measurements may lead to broadening of the aromatic signals, the observed spectra of all the complexes were relatively well resolved.



ii: $Zn(ClO_4)2.6H_2O$, $NiCl_2.6H_2O$, $CoCl_2.6H_2O$, $CuC_{l2}.2H_2O$, DMAE, 170 °C, 24 h

Scheme 3: Synthesis of the metallophthalocyanines **7–14**.

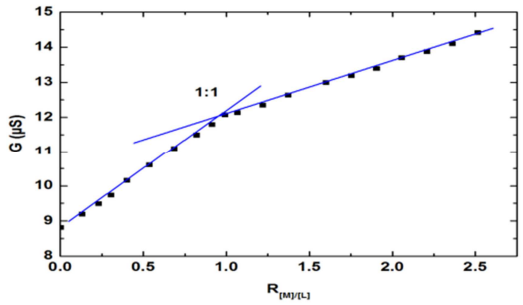
3.1 Complexation of metal cations in methanol

An examination of the relationship between compounds **1-4** and cations from alkali and alkaline earth metals revealed no notable affinity for these cations. Conversely, it was noted that transition metal cations can form mononuclear complexes in a 1:1 ratio. The logarithm of the stability constant, log βxy, for different complexes involving particular transition metals, along with the ligand's stoichiometry in methanol, is displayed in Table 1. The stability constants log βxy of compounds **1-4** with certain transition metal cations in methanol at 25 °C, I = 10^{-2} M, where the range of σn^{-1} is 0.01 to 0.14, are provided in Table 1.

Table 1: The stability constants log βxy of compounds 1-4 with certain transition metal cations in methanol

Ligands	M:L	Co(II)	Ni(II)	Cu(II)	Zn(II)	Cr(II)	Mn(II)	Fe(III)	Pb(II)	Sn(II)
1	1:1	-	3.42	3.03	3.09	4.10	4.40	4.07	4.01	3.04
2	1:1	4.10	3.30	3.19	-	-	-	3.20	-	-
3	1:1	2.90	3.12	3.03	3.09	-	-	3.16	-	-
4	1:1	2.10	3.85	3.19	3.65	-	3.01	3.50	-	4.05

The primary focus of this study is the examination of transition metal cations and their propensity to form complexes with ligands **1-4**. Interestingly, these cations do not interact with basic or alkaline earth metals, which are classified as monovalent and divalent cations. The observed behavior may be attributed to differences in the hardness levels of the cations being studied. In terms of selectivity, ligand **1** exhibits a preference for iron and chromium complexation in methanol, while ligand **2** displays a shift towards cobalt within the same solvent. However, the complex formed by ligand **3** lacks stability to a similar degree, indicating that the size of the transition metal cations does not have a significant impact on this type of complexation. Regarding the complexation stability with Ni(II), ligand 4 showed higher stability in methanol and reduced complexation with Cu(II). Notably, complexation with Co(II) is significantly reduced by a factor of 100 when comparing ligand 2 and ligand **4**. Ligand **1**, in its fundamental form, demonstrates a strong attraction to transition metal cations such as chromium and lead, resulting in the formation of singular complexes. Conversely, cyanopyranopyridothiazole **2** forms 1:1 complexes with Ni(II), Cu(II), Co(II), and Fe(III), but fails to exhibit any affinity towards Zn(II) and Mn(II). However, compound **4** displays a distinct affinity for Sn(II) and Mn(II), potentially due to the absence of phenyl groups, which allows for a more flexible ligand geometry. Notably, the nitrile functionality of ligand **2** transforms into the amide functionality of ligand **3**, thereby enhancing the affinity for complexation with Zn(II) cations.



Scheme 4: Conductometric titration in the case of **4** with Cu(II)

The stoichiometries obtained from the conductometric analysis of **1-4** with the Ni(II) and Cu(II) cations have effectively validated the findings derived from the UV spectrophotometry study.

3.2 Extraction of metal picrates

In order to assess the conjugation efficiency of pyranopyridothiazole derivatives, dichloromethane was used to extract metal picrates under neutral conditions at a temperature of 20 °C. Table 2 displays the extraction percentages (%E) of specific transition metal picrates from samples **1, 2, 3**, and **4** in aqueous dichloromethane. The %E values for the metal cations analyzed are notably low, remaining below 10%. In contrast, the %E values for metal cations **2-4** varied between 18% and 53%.

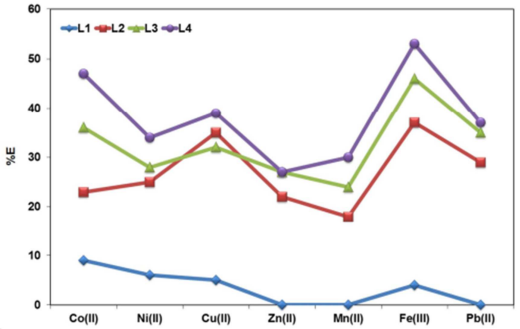
Table 2 also contains the percent extraction (%E) of various transition metal picrates 1, 2, 3 and 4 from water in dichloromethane at 25 °C concentration CL = CM = 2.5×10^{-4} mol/L.

Table 2 : The extraction percentages (%E) of specific transition metal picrates from samples 1, 2, 3, and 4 in aqueous dichloromethane

ligands	Co(II)	Ni(II)	Cu(II)	Zn(II)	Mn(II)	Fe(III)	Pb(II)
1	9	6	5	≤1	≤1	4	≤1
2	23	25	35	22	18	37	29
3	36	28	32	27	24	46	35
4	47	34	39	27	30	53	37

Research on ligands reveals that compound **4** serves as a more efficient extractant than both **2** and **3.** Likewise, an analysis of the cation series shows that Fe(III) outperforms the assessed M(II) cations as an extractant. Consequently, it can be inferred that the studied pyranopyridothiazole derivatives lack notable selectivity, as illustrated in **scheme 5.**

UV absorption spectra were recorded in the wavelength range from 220 to 360 nm. The absorption spectra of free phthalonitriles **1–3** showed single absorption peaks at 285, 308, and 310 nm, respectively, and in addition, a second peak at 255 nm for **1, 2,** and **3** was observed at 280 nm. Interactions between metal cations and these ligands are evident in the observed spectral changes. In particular, titration resulted in a decrease in absorption and a slight shift of the absorption peak to shorter wavelengths (subtractive shift) in all metal/ligand systems ($\Delta\lambda \approx 3$ nm). The completion of the interaction between phthalonitrile and cations is indicated by the spectral overlap (R (R=CM/CL) of 8). Isoabsorbance points are clearly observed at Ag^{+}/1, Hg^{2+}/**2** and **3**. The results for transition metal cations are summarized in Table 3 and for heavy metal cations in Table 4. The complex formed was ML in all cases. However, in the case of Cu^{2+} and Zn^{2+}, two complexes ML and ML_2 were found with ligand **3**. For Pb^{2+}/**2**-**3** and Mn^{2+}/**1**-**3** the variations of spectra are very small to not enable their treatments by the program Letagrop.



Scheme 5: Trends of the extraction percentages (%E) for some transition metal and heavy metal picrates from water into dichloromethane with **1-4**

Table 3: Complexation of transition metal cations by **1**-**3** in methanol, at 25°C, I=10^{-2} mol.L^{-1}.

	M:L	Mn^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
1	1:1	a	3.45	4.12	4.76	3.42
2	1:1	a	2.80	3.60	4.05	3.56
3	1:1	a	3.34	3.44	3.87	3.73
	1:2		-	-	7.32	6.98

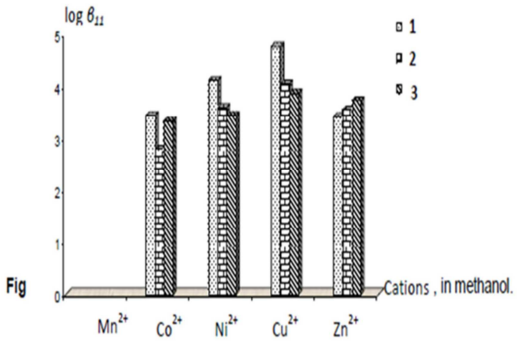
a: Absorbance changes too small to enable satisfactory fitting. 0.01 $<\sigma_{N-1}<$ 0.2

Table 4: Complexation of heavy metal cations by **1**-**3** in methanol, at 25◦C, I=10^{-2} mol.L^{-1}.

	M:L	Hg^{2+}	Pb^{2+}	Ag^{+}
1	1:1	4.78	4.09	3.12
2	1:1	4.00	a	3.41
3	1:1	3.89	a	3.09

a: Absorbance changes too small to enable satisfactory fitting. 0.01 $<\sigma_{N-1}<$ 0.06

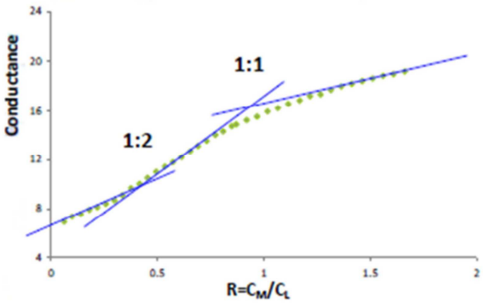
The stability constants for complex MLs in transition metal cations in the first row vary between 2.80 and 4.76 log units. Among them, the highest value was observed for Cu^{2+} bound to ligand **1**, indicating that this ligand is superior to Cu^{2+} (SCu^{2+}/Co^{2+} = 26). Ligand **2** also showed selectivity for Cu^{2+}, with an SCu^{2+} /Co^{2+} selectivity of approximately 18. The stability curve of the ML complex (shown in Scheme 6) shows a similar stability sequence - the Williams rule - to that observed for octahedral high-spin Owen metal complexes. It is characterized by an increase in complex stability from Mn^{2+} to Cu^{2+} and then decrease to Zn^{2+}. Furthermore, the ML2 complexes formed by Cu^{2+} and Zn^{2+} with ligand **3.** The corresponding ML complexes were discovered to possess lower stability compared to their counterparts, with stability constants measuring at 3.45 and 3.25 log units, respectively. A comparison of the three phthalonitriles reveals that ligand 1 exhibits a stronger attraction towards transition metal and heavy metal cations. In both series of metal cations, the ML complex formed by ligand 1 demonstrates greater stability than those formed by ligands 2 and 3, and even surpasses the stability of ML_2. The inclusion of nitrile functionality and nitrogen in the bridge connecting the two aromatic moieties seems to heighten the affinity of ligand **1**. The presence of a triple bond between the N and C atoms enhances aromaticity, resulting in more robust interactions between ligand **1** and the cation. Additionally, as Lewis suggests, the soft nature of nitrogen atoms and aromatic moieties could account for the heightened interactions with soft acids such as transition acids and heavy metal cations.



Scheme 6: The profiles of stability of ligands **1-3**

3.3 Complexation by conductometry

The approach suggested in this research offers a simple, precise, and economical method for conductometric detection in complexometric titrations that use metal cation chlorides as titrants. It operates by leveraging the chemical interactions between phthalonitriles and cations derived from chlorides. This technique is applicable to metal/ligand systems that posed challenges in earlier UV-Vis absorption analyses. The results obtained from this method were consistent with those obtained from the first technique, with the Cu^{2+}/3 system being the only one presented in this study (Scheme 7). The conductivity value altered during the titration of $CuCl_2$ solution with phthalonitrile **3** solution.



Scheme 7: Conductometric titration of **3** by Cu^{2+} in methanol, CL = 3.88 x 10-5 mol.L^{-1}.

3.4 Extraction studies

The percentage of extracted material, %E, was generally low for all of the cation scenarios, and it only improved marginally for Ligand **1**, where %E fluctuated between 4 and 36. This improvement could be attributed to Ligand **1** containing more N atoms than Ligands **2** and **3**. The highest values of %E were observed for Cu^{2+} (36%) and Ag^{+} (27%). These results reinforce the high affinity of Ligand 1 for Cu^{2+}. The soft characteristics of base N alongside the acidic properties of Ag^{+} can account for the preference for Ag^{+}. Nevertheless, this inclination was not evident in the complexation studies [29-37]. Phthalonitrile derivatives can be synthesized via nucleophilic aromatic substitution reactions, which entail the reaction between 4-nitrophthalonitrile and nucleophilic compounds in the presence of potassium carbonate. Typically, this reaction takes place in dipolar aprotic solvents like DMF and DMSO. The general methodology for creating new phthalocyanines and their quaternized derivatives, beginning with pyridine-2-thiol, 2,4,6-trimethylaniline, and 4-nitrophthalonitrile, is depicted in **Schemes 3** and **4**. To create the original phthalonitrile derivative 4, 4-nitrophthalonitrile and 2,4,6-trimethylaniline were reacted in DMF under a nitrogen atmosphere at room temperature for a period of 24 hours.

3.5 Antimicrobial activity of compounds 7-14

The synthesized compounds (**7-14**) were evaluated for *in vitro* antimicrobial activity by using agar well diffusion techniques against one strain of gram-positive bacteria *(Staphylococcus)* and four strains of gram-negative bacteria *Escherichia coli, Pseudomonas aeruginosa, salmonella* and *Klebsiella aerogenes.* Significant antimicrobial activities listed in Table 5.

Table 5: Antimicrobial activity spectrum of the synthesized compound

	Microrganism indicator						
	Micrococcus luteus LB 14110	*Staphylococcus aureus* ATCC 6538	*Listeria monocytogenes* ATCC 19117	*Agrobacterium tumefaciens*	*Salmonella typhimurium* ATCC 14028	*Pseudomonas aeruginosa* ATCC 49189	*Candida albicans*
Compounds no.	Inhibition zone (mm)						
7	26	21	23	21	14	20	-
8	26	25	16	14	13	22	10
9	22	23	20	16	12	18	12
10	14	14	13	18	12	16	13
11	16	18	20	20	12	14	16
12	18	14	19	15	14	22	14
13	13	12	20	19	12	12	16
14	14	13	18	17	19	19	17
Ampicillin	12						-
Fluconazole	-	-	-	-	--	-	9

The results show a difference between all tested compounds in bioactivity on pathogenic bacterial growth. We could say that compounds **7**, **8** showed the same activity against *Micrococcus luteus.* LB 14110 bacteria. Compounds **10** and **13** showed the least activity against *Staphylococcus aureus.* ATCC 6538 bacteria. Likewise, all other compounds were less active than ampicillin against *Staphylococcus aureus* (ATCC 6538). Promising results can be said to have been obtained when the antibacterial activity of all silver-NHC complexes was evaluated compared with standard drugs such as ampicillin and flucarbazole. The minimum inhibition concentration (MIC), which is the lowest concentration of test sample that completely inhibits the growth of microorganisms, was determined for the antibacterial study by the broth dilution method and the disc diffusion method, respectively [49]. The MIC values of compounds **7-14** against all bacterial strains are tabulated in Table 6. These results show that the most synthesized compounds have potent inhibitory activities against both Gram-positive and Gramnegative bacteria and fungi. Thus, they have an effective antimicrobial potential against food- borne pathogens and clinical microorganisms.

Table 6: Determination of the Minimum Inhibitory Concentrations (MICs) expressed in mg/ml

	Microrganism indicator					
	Micrococcus luteus LB 14110	*Staphylococcus aureus* ATCC 6538	*Listeria monocytogenes* ATCC 19117	*Salmonella typhimurium* ATCC 14028	*Pseudomonas aeruginosa* ATCC 49189	*Candida albicans*
Compounds no.	(MICs) expressed in mg/ml.					
7	4	10	2.5	2.5	2.5	5
8	5	-	5	5	5	10
9	5	2.5	1.32	1.25	1.25	5
10	-	5	5	1.2	1.2	-
11	5	-	10	1.1	1.1	-
12	2.5	5	-	5	5	2.3
13	-	0.625	10	5	5	-
14	5	-	5	10	10	2.1

4. Conclusion

In this article, the synthesis of novel phthalonitrile derivatives **1–3** and their binding properties toward certain transition metal and heavy metal cations are discussed. These compounds are used to prepare novel unsubstituted metallophthalocyanines and metallophthalocyanines. Its aggregation behavior in different solvents (DMSO, DMF, and THF) and different DMSO concentrations was studied.UV spectrophotometric and conductometric studies show that in the case of Cu^{2+} and Zn^{2+} with ligand 3, in addition to ML, complexes ML and ML_2 are also formed. In addition, the stability curve of complex ML follows the Owen-Williams rule, which indicates that it has high stability towards Cu^{2+} complexes. The selectivity $S(Cu^{2+}/Co^{2+})$ of **1** is 26 and the selectivity $S(Cu^{2+}/Co^{2+})$ of **2** is 26. In terms of stability, the presence of nitrogen atoms in the bridge between the two moieties in ligand 1 seems to increase the stability compared to ligands **2** and **3**, whose structures contain oxygen (hard atoms).

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6. **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.

7. **Data availability** Data will be made available on request.

8. REFERENCES

[1] E. G. Paronikyan, Sh. F. Akopyan, A. S. Noravyan, S. S. Mamyan, R. G. Paronikyan & I. A. Dzhagatspanyan, "Synthesis and anticonvulsant activity of condensed thieno [2, 3-e] pyrrolo [1, 2-a] pyrimidin-8, 12-diones," Pharm. Chem. J., vol. 47, pp. 92-95, 2013, doi: 10.1007/s11094-013-0902-9.

[2] E. M. Grivsky, S. Lee, C. W. Sigel, D. S. Duch, C. A. Nichol, "Synthesis and antitumor activity of 2, 4-diamino-6-(2, 5-dimethoxybenzyl)-5-methylpyrido [2, 3-d] pyrimidine," J. Med. Chem., vol. 23, no. 3, pp. 327-329, 1980, doi:10.1021/jm00177a025.

[3] M. A. Matulenko, C. H. Lee, M. Jiang, R. R. Frey, M. D. Cowart, E. K. Bayburt, S. S. Bhagwat, "5-(3-Bromophenyl)-7-(6-morpholin-4-ylpyridin-3-yl) pyrido [2, 3-d] pyrimidin-4-ylamine: structure–activity relationships of 7-substituted heteroaryl analogs as non-nucleoside adenosine kinase inhibitors," Bioorg. Med. Chem., vol. 13, no. 11, pp. 3705-3720, 2005, doi:10.1016/j.bmc.2005.03.023.

[4] G. Z. Zheng, C. H. Lee, J. K. Pratt, R. J. Perner, M. Q. Jiang, A. Gomtsyan,... and A. O. Stewart, "Pyridopyrimidine analogues as novel adenosine kinase inhibitors," Bioorg. Med. Chem. Let., vol. 11, no. 16, pp. 2071-2074, 2001, doi:10.1016/S0960-894X(01)00375-4.

[5] G. A. Gfesser, E. K.. Bayburt, M. Cowart, S. DiDomenico, A. Gomtsyan, C. H. Lee,… and S. S. Bhagwat, "Synthesis and structure-activity relationships of 5-heteroatom-substituted pyridopyrimidines as adenosine kinase inhibitors," Eur. J. Med. Chem., vol. 38, no. 3, pp. 245-252, 2003, doi:10.1016/S0223-5234(03)00019-9.

[6] H. A. Soleiman, A. K. Khalafallah, H. M. Abdelzaher, "Synthesis of Some New Fu Sed/Spiro of Benzoindole Derivatives and Their Biological Activity," J. Chin. Chem. Soc., vol. 47, no. 6, pp. 1267-1272, 2000, doi:10.1002/jccs.200000175.

[7] H. A. Soleiman, A. I. M. Koraiem,& N. Y. Mahmoud, "Synthesis of New Fused Hetecrocyclic Compounds of Benzpyrid-4-One Derivatives and Their Some Biological Activity," J. Chin. Chem. Soc, vol. 51, no. 3, pp. 553-560, 2004, doi:10.1002/jccs.200400083.

[8] G. A. Gfesser, E. K. Bayburt, M. Cowart, S. DiDomenico, A. Gomtsyan, C. H. Lee,... and S. S. Bhagwat, "Synthesis and structure-activity relationships of 5-heteroatom-substituted pyridopyrimidines as adenosine kinase inhibitors," Eur. J. Med. Chem., vol. 38, no. 3, pp. 245-252, 2003, doi:10.1016/S0223-5234(03)00019-9.

[9] D. Dini, and M. Hanack, "Physical Properties of 107," The Porphyrin Handbook: Phthalocyanines: Properties and Materials, vol. 17, p. 1, 2000.

[10] K. M. Kadish, K. M. Smith, R. Guilard, "Phthalocyanines: spectroscopic and electrochemical characterization," Academic Press: San Diego, CA, USA, vol. 16, pp. 117–170, 2003.

[11] T. Nyokong, E. Antunes, "Photochemical and photophysical properties of metallophthalocyanines. In : Handbook of Porphyrin Science with Applications to Chemistry, Physics, Materials Science, Engineering, Biology and Medicine," ScienceHandbook of Porphyrin Science, vol. 7 pp. 247-357, 2010. doi:10.1142/9789814307246_0006.

[12] T. Fukuda, N. Kobayashi, "UV-Visible absorption spectroscopic properties of phthalocyanines and related macrocycles. In : Handbook of Porphyrin Science With Applications to Chemistry, Physics, Materials Science, Engineering, Biology and Medicine," Handbook of Porphyrin Science., vol. 9, pp. 1-644, 2010, doi:10.1142/9789814307246_0014.

[13] M. J. F. Calvete, "Future Trends for Top Materials," Bentham Science Publishers, 2016.
[14] S. R. Kanth, G. V. Reddy, K. H. Kishore, P. S. Rao, B. Narsaiah, U. S. N. Murthy, "Convenient synthesis of novel 4-substitutedamino-5-trifluoromethyl–2, 7-disubstituted pyrido [2, 3-d] pyrimidines and their antibacterial activity," Eur. J. Med. Chem., vol. 41, no. 8, pp. 1011-1016, 2006, doi:10.1016/j.ejmech.2006.03.028.
[15] H. A. Soleiman, "Synthesis and studies absorption spectra behaviour on some selected monomethine cyanine dye-, apocyanine dye-, and aza cyanine dye derivatives," Can. J. Chem. Eng. Tech., vol. 1, no. 4, pp. 33-42, 2010.
[16] G. G. Dgdyusha, V. M. Zybarovskii, V. M. Moreiko, O. V. Parhonskaya, E. D. Sych, E. A. Tikhonov, G. P. Khodot, USSR Patent 568318; Appln (1975) 2157563;(1979) Chem.
[17] Y. Inagaki, K. Adachi, M. Yabe, 1988,GerOffen. DE 3819688 (C1G. 11B7124) Appl. 87 143 46809; Chemical Abstract, 1988, *111*, 68030a.
[18] T. Ikeat, H. Takei, H. Yamashita, Eur Pat. Appl. Ep. 144091 (1C031128); Chemical Abstract, vol. *104*, pp.12987, 1985.
[19] S. Sun, P. Chen, D. Zheng, (Proc. SPIE-Int. Soc. Opt. Eng. 1998, 3562 (Optical Storage Technology), 11, 16 (Eng.), SPIE. Chemical Abstract, vol. 130, pp. 175194w, 1999.
[20] A. Onodera, H. Ninomia, H. Ghya, D. Ishibashi, T. Komamura, K.Katoh, T. Tanaka, R. Morimoto, (Konica Corporation, Japan). Eur. Pat.Appl. Ep 7C9, 53j (C1CO9B 55100), 23 Apr. **1997**. Jp Appl. 96172, 257, 27 Mar **1996,** 55 pp. (Eng). Chemical Abstract, 1997, 126, 344433t.
[21] J. Fabian, H. Hatmann, "Light Absorption of Organic Colorants," Springer., pp. 162-197, 1980, doi:10.1007/978-3-642-67587-4.
[22] J. Rochlitz, "ENERGY CONVERTING DYES. Chimia," vol. 34, no. 3, pp. 131-144, 1980, doi:10.2533/chimia.2013.155.
[23] A. S. Alayed, Can. J. Chem. Eng. Vol. 2, pp.87-105, 2011.
[24] A. S. Alayed, H. A. Soleiman, *Int. J. Basic App. Sci.* vol. 11, pp.1-8, 2 011.
[25] T. M. Keller, T. R. Price, J. Macromol. Sci. Chem., vol. A18, pp. 931-917, 1982.
[26] I. Degirmencioglu, R. Bayrak, M. Er and K. Serbest, "The microwave-assisted synthesis and structural characterization of novel, dithia-bridged polymeric phthalocyanines containing a substituted thiophenylamine Schiff base," *Dyes Pigm*., vol. 83, no. 1, pp. 51-58, 2009, doi:10.1016/j.dyepig.2009.03.011.
[27] O. E. Sielcken, L. A. Van de Kuil, W. Drenth, J. Schoonman and R.J.M. Nolte, "Phthalocyaninato polysiloxanes substituted with crown ether moieties," J. Amer. Chem. Soc., vol. 112, no. 8, pp. 3086-3093, 1990, doi:10.1021/ja00164a032.
[28] M. Kandaz, A. T. Bilgicli, A. Altındal, "Metal ion sensing functional mono and double-decker lanthanide phthalocyanines: Synthesis, characterization and electrical properties," Synth. Met., vol. 160, no. 1-2, pp. 52-60, 2010, doi:10.1016/j.synthmet.2009.09.039.
[29] A. Sorokin and B. Meunier, "Oxidation of polycyclic aromatic hydrocarbons catalyzed by iron tetrasulfophthalocyanine FePcS: inverse isotope effects and oxygen labeling studies," Eur. J. inorg. Chem.., vol. 1998, no. 9, pp. 1269-1281, 1998,doi:10.1002/(SICI)1099-0682(199809)1998:9%3C12 69::AID-EJIC1269%3E3.0.CO;2-G.
[30] R. Raja and P.J. Ratnasamy, "Oxyhalogenation of aromatics over copper phthalocyanines encapsulated in zeolites," J. Catal., vol. 170, no. 2, pp. 244-253, 1997, doi:10.1006/jcat.1997.1749.
[31] I. Acar, Z. Bıyıklıoğlu, A. Koca and H. Kantekin, "Synthesis, electrochemical, in situ spectroelectrochemical and in situ electrocolorimetric characterization of new metal-free and metallophthalocyanines substituted with 4-{2-[2-(1-naphthyloxy) ethoxy] ethoxy} groups," Polyhedron, vol. 29, no. 5, pp. 1475-1484, 2010, doi:10.1016/j.poly.2010.01.032**.**
[32] I. Acar, H. Kantekin and Z. Bıyıklıoğlu, "The synthesis, using microwave irradiation and characterization of novel, metal-free and metallophthalocyanines," J. Org. Chem., vol. 695, no. 2, pp. 151-155, 2010, doi:10.1016/j.jorganchem.2009.10.021.
[33] W. Wu, S. Ji, H. Guo, X. Wang and J. Zhao, "The synthesis of 5, 10, 15, 20-tetraarylporphyrins and their platinum (II) complexes as luminescent oxygen sensing materials," Dyes pigm, vol. 89, no. 3, pp. 199-211, 2011, doi:10.1016/j.dyepig.2010.01.020.
[34] T. M. Keller, "Phthalonitrile-based high temperature resin," J. Polym. Sci., Part A: Polym. Chem., vol. 26, no. 12, pp. 3199-3212, 1988, doi:10.1002/pola.1988.080261207.
[35] T. M. Keller, "Fluorinated high temperature phthalonitrile resin. Polymer communications (Guildford)," vol. 28, no. 12, pp. 337-339, 1987.
[36] T. M. Keller, Imide-containing phthalonitrile resin. Polymer, vol. 34, no. 5, pp. 952-955, 1993, doi:10.1016/0032-3861(93)90213-T.
[37] T. M. Keller, "Imide-containing phthalonitrile resin," Polymer, vol. 34, no. 5, pp. 952-955, 1993, doi:10.1016/0032-3861(93)90213-