Symmetrically Substituted Zinc Phthalocyanine Derivatives Bearing *N*-heterocycle Moieties

Synthesis and structural analysis investigations

TAMER E. YOUSSEF[1,2]*, HAMAD AL-TURAIF[1], DUMITRU BALEANU[1,3,4]

[1]Chemical and Materials Engineering Department, Faculty of Engineering, King Abdulaziz University, P. O. Box 80204, Jeddah, 21589, Saudi Arabia

[2]Applied Organic Chemistry Department, National Research Center, Dokki, Cairo, 12622, Egypt

[3]Department of Mathematics and Computer Sciences, Faculty of Arts and Sciences, Cankaya University, TR-06530 Ankara, Turkey

[4]Institute of Space Sciences, Magurele, 077125, Bucharest, Romania

*Zinc(II)phthalocyanines bearing N-heterocycle moieties units were synthesized and characterized. Their Fourier transform infrared spectroscopic data were compared in order to characterize the investigated spectra. Fuzzy C-Means clustering technique was applied to extract some new information about these data. Hay synthesis of a novel series of symmetrically substituted zinc phthalocyanine derivatives, [(heteroxy)$_8$ZnPcs] **4(a-e)** bearing N-heterocycle moieties, i.e. Imidazol, Thiazol, Piperazine and Tetrazol rings, was reported. Their novel heterocycle-oxyphthalonitrile precursors **3(a-e)** were synthesized by the aromatic nucleophilic substitution reaction of 4,5-dichlorophthalonitrile with hetero-substituted phenols **2(a-e)**. The structure of the compounds was revealed by the spectroscopic analysis tools, in addition some hidden similarities of the raw spectra were revealed within the Fuzzy C-Means clustering technique.*

Keywords: zinc(II)phthalocyanines, hetero-substituted phthalocyanines, Fourier transform infrared spectroscopy, fuzzy C-means clustering

Zinc phthalocyanines (ZnPcs) have planar or nearly planar structures with an extended network of π-electrons. They are known to exhibit a higher photodynamic effect and special photosensitizing properties.They are used as phototoxic drugs for photodynamic therapy (PDT) [1].

Previous reports showed introduction of heterocycle subunits onto the peripheral positions of Pcs, resulted in increased solubility and semiconducting properties [2]. According to literature survey, some of them, bearing 6-membered *N*- heterocycles, pyridine and pyrazine rings, were synthesized [3,4]. They have been designed to establish themselves in many applied fields.

In previous studies, we have investigated several approaches to obtain such symmetrically and asymmetrically metallophthalocyanines (MPcs) with different peripheral or non-peripheral substitutents on the Pc ring in addition to, different central metal ion and axial ligands [5-8].

In order to get more information about the analyzed spectra of complex systems in the last few decades several new signal processing methods were developed and applied successfully to various types of data [9-12] .

Taking into account these considerations and in connection with a previous work we have current interest in the synthesis of zinc phthalocyanines (ZnPcs) bearing heterocyclic moieties for biological evaluations in pharmaceutical application [13] .

In this work we report, the synthesis of novel symmetrically substituted Zinc phthalocyanine derivatives bearing *N*-heterocycle moieties, i.e. Imidazol, Thiazol, Piperazine and Tetrazol rings. A novel heterocycle-oxy phthalonitriles **2(a-e**) and phthalocyanines **3(a-e**) have also been reported for the first time. Besides of this novelty we studied the clusters of the Fourier transform infrared spectroscopy (FTIR) spectra.

In this manuscript we also presented the similarities of the analyzed spectra with the help of the fuzzy C-Means (FCM) clustering technique.

We organized the structure of the manuscript as follows:

Section 1 deals with the preparation and characterization of zinc phthalocyanine derivatives. After that we discuss the application of the new procedure of optimal smoothing for five ZnPcs **4(**a-e) spectra. In the next section, the Fourier transform of the second type was applied in order to characterize the investigated spectra. Finally, we present our conclusions.

Experimental part

Materials and methods

All reagents and solvents were commercial reagent grade and used without further purification. The following chemicals were purchased commercially from Aldrich and used as received: 4,5-dichloro-phthalonitrile, 4-(2-Pyridinyloxy)phenol, 4-(Imidazol-1-yl)phenol, 4-(4-Methyl-1,3-Thiazol-2-yl)phenol, 4-(1-Piperazinyl)phenol, 4-(2H-Tetrazol-2-yl)phenol. Solvents (GR grade) from Merck (Germany) were distilled. Silica gel thin-layer chromatography (TLC) plates 250 microns from Analtech (USA) were used.

Physical characterization

Melting points were determined by the open capillary method and were uncorrected. Infrared spectra were recorded on a Nicolet Magna 560 spectrophotometer in the spectral range 4000–400 cm^{-1} using KBr pellets. ^{1}H NMR spectra were recorded using a BVT 3000 Bruker Spectro

* email: tamezzat@yahoo.com

spin instrument operating at 300.13 MHz. Spectra were referenced internally to residual solvent (DMSO). UV-Vis spectra were recorded using an Agilent 8453 UV-vis spectrophotometer with Dimethyl sulfoxide (DMSO) used as solvent. Field depolarization mass spectroscopy technique (FDMS) mass spectra were recorded using a Varian MAT 711A spectrometer, operated at 70 eV for using the electron ionization technique (EIMS) and reported in mass/charge (m/z). Elementary analyses were performed on Carlo Erba Elemental Analyzer 1106. Purity of all synthesized compounds were checked by TLC on precoated silica gel plates utilizing chloroform/methanol in different ratios (8:2 / 7:3 v/v) as developing solvent system and spots were detected on exposure to UV lamp.

Synthesis

Typical procedure for synthesis of 4,5-Bis-hetercycle-oxyphthalonitriles **3(a-e**)

4,5-dichloro-phthalonitrile (**1**) (2.84 g, 14.4 mmol) was dissolved in DMF (50 mL) under nitrogen and hetero-substituted-phenols **2**(**a-e**) were added, then stirred for 30 min at room temperature, an anhydrous potassium carbonate finally podwered (5 g, 36.24 mmol) was added in portions during 3 h with efficient stirring. Followed by stirring again at 70°C for 24 h. The mixture was poured into 200 mL ice water. Then the precipitate was filtered off, washed with water and methanol and then dried. The crude products was recrystallized from methanol to give **3(a-e)** as a white or a pale yellow crystalline solids.

3a

Prepared from 4-(2-Pyridinyloxy)phenol (**2a**) as a white crystalline solid (1.92 g, 80.5%). Mp 170- 173°C. IR (KBr): ν = 3082 (w), 3050 (s) (Ar–CH), 2957 (s), 2932 (w), 2850 (m), 2233 (CN), 1598 (C-N; C-C), 1540 (s), 1470 (s), 1436 (m), 1323 (m), 1211-1234 (C-O-C), 1178 (s), 1130 (s), 1072 (s), 941 (s), 890 (m), 775 (m), 540 (m) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ= 7.0-7.2 (4H, m, Hb-py), 7.2-7.4 (2H, m, Hc-py), 8.4 (2H, dd, Ha-py), 8.5 (2H, m, H-arom), 8.6-8.7 (8H, m, ph) ppm. MS (EI): m/z (%) 498.49 (90) (M^+). Anal. Calcd. (%) for $C_{30}H_{18}N_4O_4$: C 72.28, H 3.63, N 11.23 (Found C 70.92, H 3.00, N 10.19).

3b

Prepared from 4-(Imidazol-1-yl)phenol (**2b**) as a white crystalline solid (1.35 g, 74.8%). Mp 179- 182°C. IR (KBr): ν = 3082 (w), 3051 (s) (Ar–CH), 2959 (s), 2930 (w), 2857 (m), 2232(CN), 1602 (C-N; C-C), 1551 (s), 1468 (s), 1433 (m), 1328 (m), 1212-1220 (C-O-C), 1177 (s), 1130 (s), 1073(s), 943 (s), 890(m), 776(m), 540 (m) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ =6.76-6.79 m (2H, H-imidazole-4), 7.35 s (2H, H-imidazole-5), 7.90 s (2H, H-imidazole-2), 8.3 (2H, m, H-arom), 8.6-8.9 (8H, m, ph) ppm. MS (EI): *m/z* (%) 444.44 (90) (M^+). Anal. Calcd. (%) for $C_{26}H_{16}N_6O_2$: C 70.26, H 3.62, N 18.90 (Found C 69.92, H 2.93, N 17.19).

3c

Prepared from 4-(4-Methyl-1,3-Thiazol-2-yl)phenol (**2c**) as a pale yellow crystalline solid (1.12 g, 71.2%). Mp 180-183°C. IR (KBr): ν = 3092 (w), 3057 (s) (Ar–CH), 2962 (s), 2937 (w), 2859 (m), 2231(CN), 1612 (C-N; C-C), 1553 (s), 1469 (s), 1430 (m), 1320 (m), 1218-1227 (C-O-C), 1179 (s), 1129 (s), 1070(s), 940 (s), 894(m), 777(m), 542 (m) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ= 1.2-1.4 (6H, m, $2CH_3$-Thiazol), 3.23-3.53 (m, 4H; 2SCH2), 8.2 (2H, m, H-arom), 8.5-8.7 (8H, m, ph) ppm. MS (EI): *m/z* (%) 506.60 (90) (M^+). Anal. Calcd. (%) for $C_{28}H_{18}N_4O_2S_2$: C 66.38, H 3.58, N 11.05 (Found C 65.92, H 2.86, N 10.19).

3d

Prepared from 4-(1-Piperazinyl)phenol (**2d**) as a white crystalline solid (1.2 g, 67.5%). Mp 171- 173°C. IR (KBr): ν= 3091 (NH), 3087 (w), 3055 (s) (Ar–CH), 2960 (s), 2931(w), 2863(m), 2233(CN), 1615 (C-N; C-C), 1558 (s), 1472 (s), 1445 (m), 1331 (m), 1213-1218 (C-O-C), 1183 (s), 1135 (s), 1075(s), 943 (s), 892(m), 779(m), 544 (m) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ = 2.1-2.3 (m, 4H, $2CH_2$, Pip-H), 2.5-2.9 (m, 4H, $2CH_2$, Pip-H), 8.0 (2H, m, H-arom), 8.3-8.5 (8H, m, ph), 8.7 (s, 1H, NH, exchangeable with D_2O) ppm. MS (EI): *m/z* (%) 480.56 (90) (M^+). Anal. Calcd. (%) for $C_{28}H_{28}N_6O_2$: C 69.98, H 5.87, N 17.48 (Found C 68.92, H 4.98, N 16.19).

3e

Prepared from 4-(2H-Tetrazol-2-yl)phenol (**2e**) as a pale yellow crystalline solid (0.93 g, 62.2%). Mp 152- 158°C. IR (KBr): ν = 3090 (w), 3055 (s) (Ar–CH), 2966 (s), 2928(w), 2860 (m), 2229 (CN), 1617 (C-N; C-C), 1560 (s), 1478 (s), 1455 (m), 1339 (m), 1215-1220 (C-O-C), 1190 (s), 1144 (s), 10703(s), 940 (s), 898(m), 781(m), 540 (m) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ=7.1 (2H, m, H-arom), 7.3-7.6 (8H, m, ph) 8.4 (s, 2H, Tetrazol-CH) ppm. MS (EI): *m/z* (%) 392.37 (90) (M^+). Anal. Calcd. (%) for $C_{22}H_{12}N_6O_2$ C 67.34, H 3.08, N 21.41 (Found C 66.92, H 2.94, N 20.83).

Typical procedure for synthesis of octa[4,5-Bis-heteroxy-substituted]phthalocyaninatozinc(II)[(heteroxy)$_8$ ZnPcs] **4(a-e**)

A solution of 4,5-Bis-heterocycle-oxy phthalonitrile derivative **3(a-e);** (1.9 mg, 4.00 mmol) **3a**, (1.7 mg, 4.00 mmol) **3b**, (2.0 mg, 4.00 mmol) **3c,** (1.9 mg, 4.00 mmol) **3d,** (1.5 mg, 4.00 mmol) **3e** and zinc(II) acetate dihydrate (0.1 g, 0.05 mmol) in 10 mL of *n*-pentanol was stirred for 10 min under argon atmosphere. Then, DBU (5 mL, 0.05 mmol) was added. The mixture was refluxed for 20 h at 130-135 °C. Followed by cooling at room temperature and precipitated with methanol (25 mL). Then the solid was filtered off, washed with water and dried under vacuum. The crude products were purified by column chromatography (silica gel, ethyl acetate/ *n*-hexane) in different ratios (7:3 / 8:2 v/v) yielding **4(a-e)** as a green or blue green solids.

4a

Prepared from **3a** as a green solid (8.37 mg, 65.5%). IR (KBr): ν= 3070-3065 (Ar-H_{str}), 2977, 2871 (C-H_{str}, CH_3), 1670 (C-O-C_{str}, qz ring), 1658 (C-C); 1587, 1575, 1473 (C–CH); 1413 mPh, 1411, 858, 745, 747,640, 521 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ= 7.0-7.1 (16H, m, Hb-py), 7.3-7.6 (8H, m, Hc-py), 8.25 (8H, dd, Ha-py), 8.2 (8H, m, H-arom), 8.4 - 8.7 (32H, m, ph) ppm. UV-vis (DMSO): λ_{max} (nm): 685,620, 350 sh, 252 nm. MS (FD): m/z = 2067.40 (M^+). Elemental analysis: $C_{120}H_{80}N_{16}O_{16}Zn$, found C 68.17, H 3.66, N 9.01, Calcd. C 69.71, H 3.90, N 10.84.

4b

Prepared from **3b** as a green solid (7.24 mg, 58.4%). IR (KBr): ν= 3069-3060 (Ar-H_{str}), 2977, 2879(C-H_{str}, CH_3), 1654 (C-C); 1577, 1572, 1473 (C–CH); 1443 mPh, 1409, 859, 743, 747 d(C–C), 640, 524 cm^{-1}. ^{1}H-NMR (DMSO-d_6):δ =6.71-6.78 m (8H, H-imidazole-4), 7.24 s (8H, H-imidazole-5), 7.83 s (8H, H-imidazole-2), 8.32 (8H, m, H-arom), 8.4-8.7 (32H, m, ph) ppm. UV-vis (DMSO): λ_{max} (nm): 684,627, 359 sh, 255 nm. MS (FD): m/z = 1851.23 (M^+). Elemental analysis: $C_{104}H_{72}N_{24}O_8Zn$, found C 66.90, H 3.17, N 17.01, Calcd. C 67.47, H 3.92, N 18.15.

4c

Prepared from **3c** as a blue green solid (7.90 mg, 60.2%). IR (KBr): ν= 3070-3062 (Ar-H_{str}), 2970, 2872 (C-H_{str}, CH_3), 1654 (C-C); 1576, 1570, 1475 (C–CH); 1442 mPh, 1409, 860, 744, 747 d(C–C), 645, 520 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ= 1.30-1.6 (24H, m, CH_3-Thiazol), 3.20-3.63 (m, 2H; SCH2), 8.4 (8H, m, H-arom), 8.7 -8.9 (32H, m, ph) ppm.

UV-vis (DMSO): λ_{max} (nm): 688, 630, 360 sh, 258 nm. MS (FD): m/z = 2099.85 (M^+). Elemental analysis: $C_{112}H_{80}N_{16}O_8S_8Zn$, found C 64.90, H 2.97, N 9.31, Calcd. C 64.06, H 3.84, N 10.67.

4d

Prepared from **3d** as a green solid (6.87 mg, 70.2%). IR (KBr): ν= 3093 (NH), 3072-3060 (Ar-H_{str}), 2979, 2873 (C-H_{str}, CH_3), 1660 (C-C); 1588, 1573, 1470 (C–CH); 1415 mPh, 1413, 851, 740, 749,643, 525 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ= 2.3-2.8 (m, 16H, 8CH_2, Pip-H), 2.9-3.2 (m, 16H, 8CH_2, Pip-H), 7.7 (8H, m, H-arom), 8.1-8.3 (32H, m, ph), 8.5 (s, 1H, NH, exchangeable with D_2O) ppm. UV-vis (DMSO): λ_{max} (nm): 683, 635, 361 sh, 254 nm. MS (FD): m/z = 1995.69 (M^+). Elemental analysis: $C_{112}H_{120}N_{24}O_8Zn$, found C 66.95, H 5.17, N 15.11, Calcd. C 67.40, H 6.06, N 16.84.

4e

Prepared from **3e** as a blue green solid (7.65 mg, 79.2%). IR (KBr): ν= 3070-3064 (Ar-H_{str}), 1657(C-C); 1575, 1571, 1470 (C–CH); 1441 mPh,1409, 859, 744, 740 d(C–C), 645, 522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ=7.3 (8H, m, H-arom), 7.5-7.8 (32H, m, ph) 8.2 (s, 8H, Tetrazol-CH) ppm. UV-vis (DMSO): λ_{max} (nm): 688, 641, 360 sh, 258 nm. MS (FD): m/z = 1867.03 (M^+). Elemental analysis: $C_{88}H_{56}N_{40}O_8Zn$, found C 55.90, H 2.67, N 29.01, Calcd. C 56.61, H 3.02, N 30.00.

Fuzzy C-means clustering technique

We recall that the clustering of a given data is the basis of several classifications and the system modeling algorithms. As it is known, the goal in clustering is to identify how much closer points in the cluster are to one another compared to points outside the cluster.. We have used Fuzzy C-Means (FCM) clustering technique to find clusters in our dataset. FCM is a data clustering technique such that each data point belongs to a cluster up to some degree quantified by a membership grade. The original technique was proposed by Bezdek in [14] to improve the earlier clustering methods. We have implemented our FCM code using MATALB Fuzzy Logic Toolbox. It gives a methodology that shows how to group data points that exist in a multidimensional space into a given number of different clusters. It has been popularly used in many past [15,16] and recent [17,18] studies.

Results and discussions

*Characterization of Zn(II)phthalocyanines **4(a-e)***

An nucleophilic aromatic substitution reaction occured between the commercially obtained 4,5-dichloro-phthalonitrile (**1**) and the heterosubstituted-phenols **2**(**a-e**) at 70-80?C in DMF in the presence of K_2CO_3, to yield the corresponding phtalonitriles, 4,5-bis-hetercycle-oxy phthalonitrile derivatives **3(a-e**) in 62-80 %. Improved synthetic procedure for the newly Zn(II)phthalocyanines [(heteroxy)$_8$ZnPcs] **4(a-e)** substituted by hetercycle-oxy units has been described. They were synthesized from their phthalonitrile derivatives **3a-e** by the cyclotetramerization reaction of **3a-e** with Zn(II)acetate in the presence of organic base DBU in *n*-pentanol for 20-24 hrs at 130-135 °C, afforded the corresponding [(heteroxy)$_8$ZnPcs] **4(a-e**) with 65-79% yield. The desired phthalocyanines were separated chromatographically (scheme 1). The analyses of FTIR, ^{1}H NMR and mass spectroscopy spectra are consistent with the predicted structures as shown in the experimental section.

The FTIR spectra of 4,5-bis-hetercycle-oxyphthalonitrile precursors **3(a-e)** showed the appearance of absorption bands at ν = 2235-2229 cm^{-1} (CN). Cyclotetramerization of the 4,5-*bis*-hetercycle-oxyphthalonitrile precursors **3(a-e)** to the zinc(II)phthalocyanines, [(heteroxy)$_8$ZnPcs] **4(a-e**) lead to the disappearance of (CN) vibration in their IR spectra.

The ^{1}H NMR spectra of **4(a-e)** were obtained as expected (see experimental part).

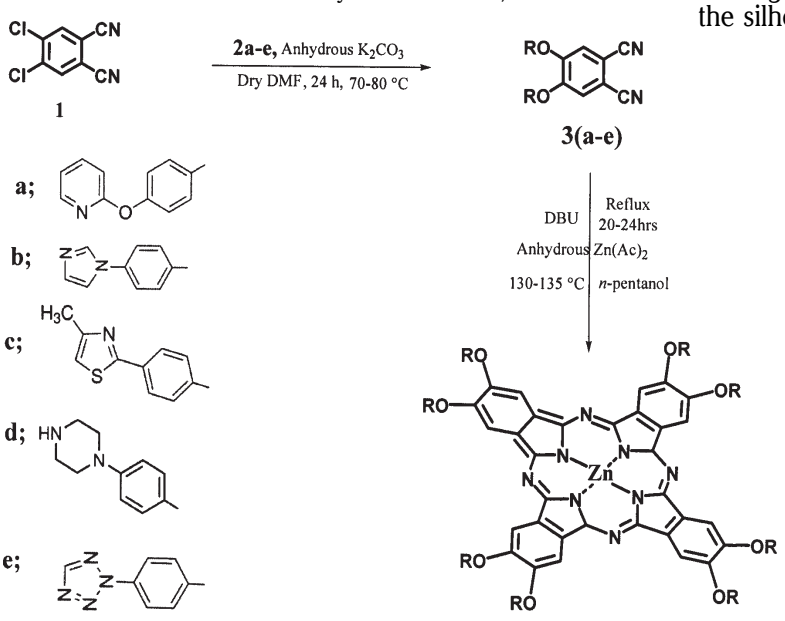
The UV-Vis spectra of **4(a-e**) showed the Q band region at around 683-688 nm in DMSO. and the B-bands at around 350-360 nm, respectively.

Computational model to cluster data

The results of our FCM clustering are depicted in figure 1 and the objective function plot is presented in figure 3. From figure 1, it is clear that the centers of **4a, 4c** and **4e** are very close indicating close similarity among them and also the centers of **4b** and **4d** is very similar as evident from FCM plot. In other words our dataset is fuzzy in nature because every data point in the given dataset belonging to every cluster to a certain degree.

Cluster Validation

We evaluated our clustering results through Silhouette widths, which was first described in [19]. We used MATLAB Statistics Toolbox for our work. Ideally observations with large and positive silhouette value (~1) are well clustered, those with silhouette value around 0 lie between clusters, and those with negative silhouette value are placed in the "wrong" cluster. We started with 5 clusters as shown by the silhouette plot in figure 2(a) and from the figure we



Scheme 1. The synthetic pathway for the preparation of **4(a-e)**

notice that, 1st, 3rd and 4th clusters contain some negative silhouette value meaning that they are not well separated from neighboring clusters. However most data points in 2nd and 5th clusters have high silhouette value and hence are well separated. We then reduced the number of clusters and invoked silhouette procedure for 4 clusters and the silhouette plot is shown in figure 2(b). In figure 2(b) we can still notice that 4 clusters are not well separated from neighboring clusters. Then we repeated the experiment again for 3 clusters and the results is shown in figure 2(c) and we found that in 2nd cluster only very tiny instance of data points has negative silhouette values in. Therefore, we run the silhouette clustering once more for 2 cluster and this time it resulted in 2 clearly separated clusters with most data points in both the clusters having high silhouette widths and result is shown in figure 2(d).

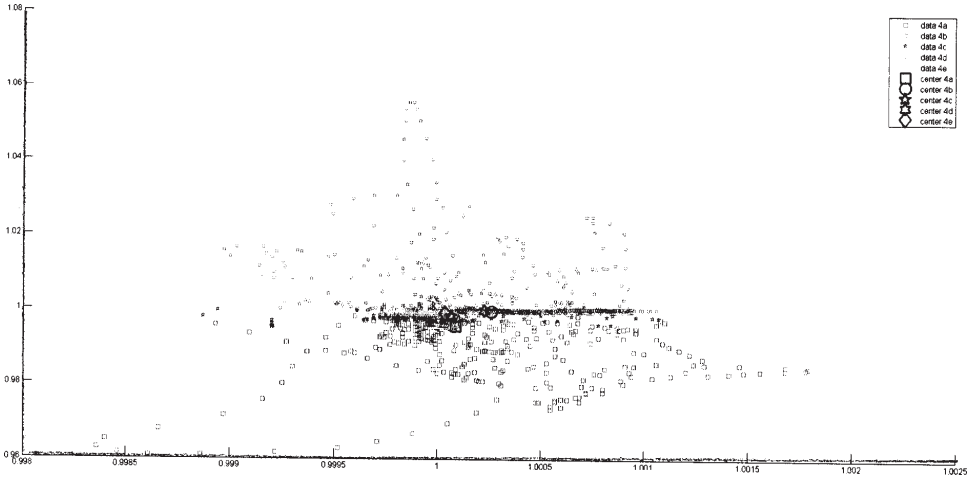


Fig. 1. Fuzzy C-Means clustering

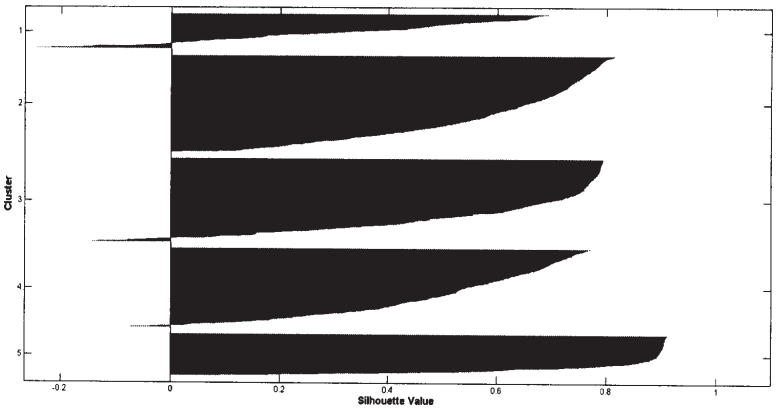


Fig 2(a). Silhouette plot assuming 5 clusters.

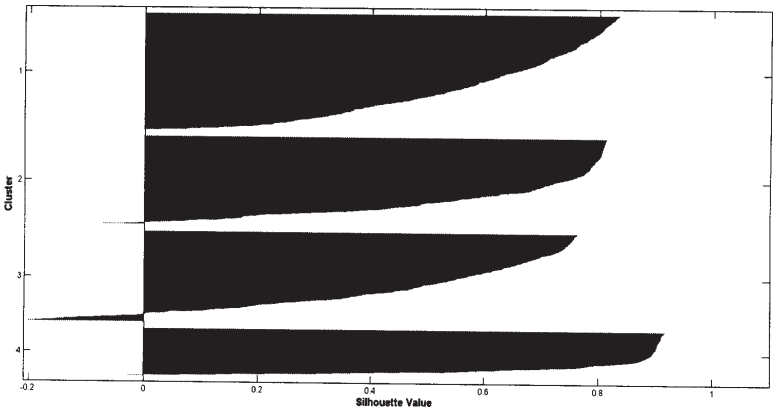


Fig 2(b). Silhouette plot assuming 4 clusters.

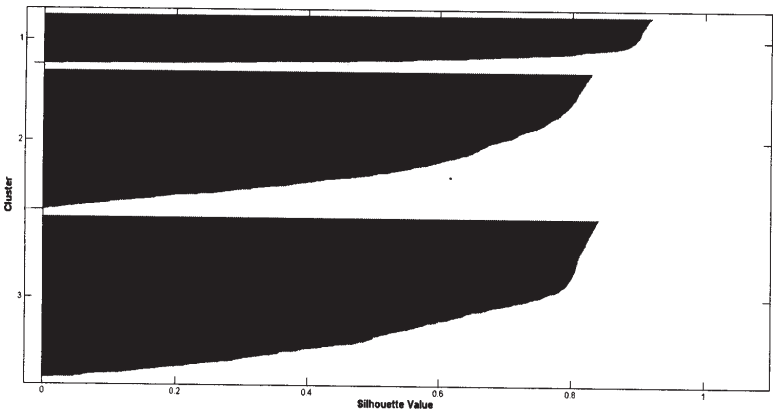


Fig. 2(c). Silhouette plot assuming 3 clusters

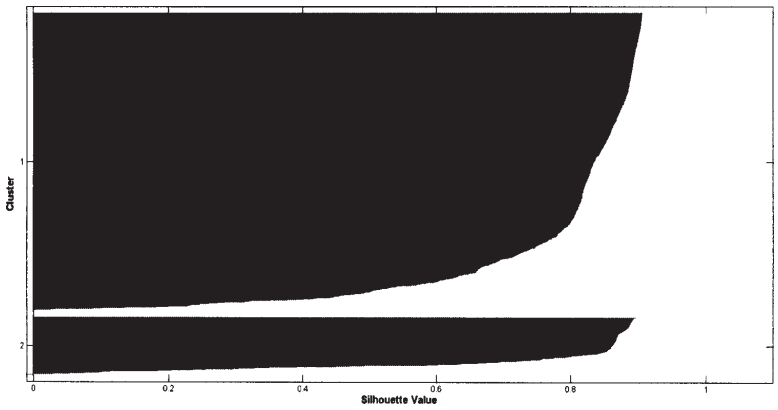


Fig. 2(d). Silhouette plot assuming 2 clusters

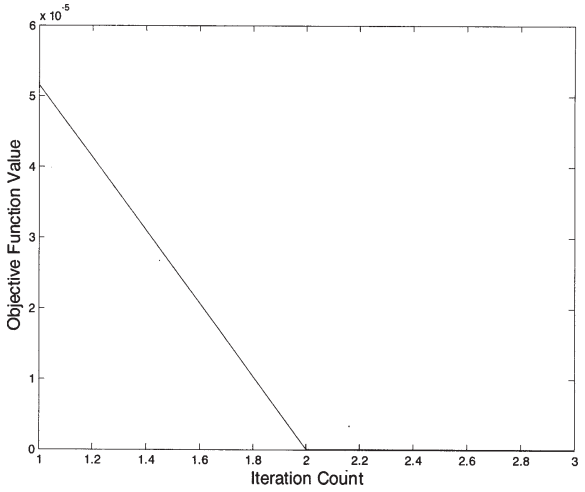


Fig. 3. Objective function of FCM clustering

After correlating the results obtained from FCM and Silhouette clustering we conclude that our dataset can be clustered into 2 main clusters namely clusters for **4a, 4c** and **4e** in one cluster and data **4b** and **4d** in another cluster.

Conclusions

We have prepared and characterized a series of octasubstituted zinc(II)phthalocyanines, [(heteroxy)$_8$ Zn Pcs] **4(a-e**) bearing *N*-heterocycle moieties.

The results show that these compounds have a well-defined structure. Besides, the numerical computation proves that we have two main clusters. A detailed analysis with the help of powerful FCM clustering technique followed by a validation results through Silhouette widths. We have started by assumptions of having 5 clusters and with the help of the objective function of FCM clustering we finally conclude that we have two main clusters. What is important to remark for this type of data and the used computational algorithm is that for three clusters, as can be seen in figure 2(c),we have one negative value which can be interpreted as the cluster error produced by the classifier.

Acknowledgment : This work was funded by the Deanship of Scientific Research (DSR), King Abdulaziz University, Jeddah, under grant No. (135-138-D1435). The authors, therefore, acknowledge with thanks DSR technical and financial support.

References

1. T. C. TEMPESTI, M. GABRIELA ALVAREZ, E. N. DURANTINI, Dyes and Pigments, 91(1), (2011), p. 6–12.
2. HARISH M.N.K., KESHAVAYYA J., VENUGOPALA REDDY K.R, J. Coor. Chem., 63, 4050 (2010).
3. CHEN S., LIU Y., XU Y., SUN Y., QIU W., SUN X., ZHU D., Synthetic Mat., 156, 1236 (2006) .
4. HARISH M.N.K., KESHAVAYYA J., VENUGOPALA REDDY K.R., MALLIKARJUNA H.R, J. Coor Chem., 64, 2075-2087 (2011).
5. T.E. YOUSSEF, M. HANACK, J. Porphyrn. Phthalocyan. 6 (2002) 571.
6. T.E. YOUSSEF, S. O'FLAHERTY, B. WERNER, M. HANACK, Eur. J. Org. Chem. 1(2004) 101.
7. T.E. YOUSSEF, Polyhedron 29 (2010) 1776.
8. T.E. YOUSSEF, H.H. MOHAMED, Polyhedron, 30 (2011) 2045.
9. W. AFTAB, A. MEMIC, D. BALEANU, ON CLASSIFICATION OF PDZ DOMAINs: A Computational Study, Mathematical Problems in Engineering, Article Number: 419485 (2013)
10. R.R. NIGMATULLIN, D. BALEANU, D. POVAROVA, N. SALAH, S.S. HABIB, A. MEMIC, Mathematical Problems in Engineering, Raman Spectra of Nanodiamonds: New Treatment Procedure Directed for Improved Raman Signal Marker Detection,Article Number: 847076 (2013)
11. R.R. NIGMATULLIN, C. IONESCU, D. BALEANU, Nimrad: novel technique for respiratory data treatment, Signal, Image and Video Processing, 1-16 (2012)
12. R.R. NIGMATULLIN, D. BALEANU,A.A. ALZAHRANI, Y.A. ALHAMED, A.H. ZAHID, T.E.YOUSSEF, Rev. Chim. (Bucharest), **64,** no. 9, 2013, p. 987.
13. T.E. YOUSSEF, M. HANACK, J. Porphyrn. Phthalocyan. 9 (2005) 28.
14. BEZDEC, J.C., Pattern Recognition with Fuzzy Objective Function Algorithms, Plenum Press, New York, 1981.
15. DOULAYE DEMBÉLÉ , PHILIPPE KASTNER, "Fuzzy C-means method for clustering microarray data". Bioinformatics, Vol. 19 no. 8, p. 973–980, 2003.
16. DAO-QIANG ZHANG, SONG-CAN CHEN, "A novel kernelized fuzzy C-means algorithm with application in medical image segmentation", Artificial Intelligence in Medicine, Vol. 32, Issue 1, p. 37–50, 2004.
17.T. V. CLENDENEN, A. ZELENIUCH-JACQUOTTE,L. MOY, M. C. PIKE, H. RUSINEK , S. KIM, "Comparison of 3-point dixon imaging and fuzzy C-means clustering methods for breast density measurement", J. Magnetic Resonance Imag.,Vol. 38, Issue 2, p. 474–481, 2013.
18. H. CAO, H.W DENG AND Y.P. WANG, Segmentation of M-FISH Images for Improved Classification of Chromosomes With an Adaptive Fuzzy C-means Clustering Algorithm, Fuzzy Systems, IEEE Transactions on, Vol. 20, Issue 1, p. 1-8, 2012.
19. P. J. ROUSSEEUW, SILHOUETTES: a Graphical Aid to the Interpretation and Validation of Cluster Analysis. Computational and Applied Mathematics Vol. 20, 1987, p. 53–65

Manuscript received: 9.09.2014