Synthesis and antimicrobial activity of new phthalocyanine complexes and electrochemical and spectroelectrochemical behaviour of cobaltphthalocyanine

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A novel phthalocyanine bearing oxygen donor atoms on the peripheral positions has been synthesised by cyclotetramerisation of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile and its nickel, zinc, cobalt, copper and lead derivatives prepared. The thermal stabilities of the phthalocyanine compounds have been determined and their possible biological activities (antibacterial, anticandidal and antifungal) studied. The effects of substituent on the electrochemical and *in situ* spectroelectrochemical behaviour of cobaltphthalocyanine have been investigated and an *in situ* electrocolorimetric method was applied to investigate the colour of the electrogenerated anionic and cationic forms of the complex.

Keywords: phthalocyanine, metal complexes, antimicrobial activity, spectroelectrochemistry, chromaticity diagram.

For many years, phthalocyanine (Pc) compounds have been widely used as organic pigments and dyestuffs. Besides their application in such traditional areas, phthalocyanines (Pcs) have been extensively studied due to their spectroscopic electrochemical, electrical and photoelectric properties. The solubility of Pcs is very important for the investigation of their chemical and physical characteristics and can be increased by introducing different kinds of solubility-enhancing substituents such as alkyl, alkoxy, phenoxy and macrocyclic groups at the peripheral and axial position of the Pc ring.[1–3] Metallophthalocyanines can be obtained by the classial template reactions of diverse precursors such as phthalonitrile, cyano-benzamide, phthalamide and phthalic acid with metal salts in high-boiling nonaqueous solvents at elevated temperatures.[4,5] Pcs are generally blue-green in colour due to the $\pi \rightarrow \pi^*$ bands associated with the planar heteroaromatic π- conjugation system. Pcs and their metal complexes have been widely used as dyes and pigments. In particular, they have drawn much attention in recent years by their functional properties and potential application to chemical sensors, electrophotography, photovoltaics, optical discs, solar cells, photodynamic therapy, catalysis, *etc*.[6–12] Pcs and their analogues (*e.g.* naphthalocyanines) show great potential as phototherapeutic agents for the treatment of a variety of oncological and non-oncological diseases.[13,14] Previous investigations showed that some Zn(II)-phthalocyanines (ZnPcs) can efficiently photosensitise the inactivation of various microbial pathogens.[15–17] The importance of this class of compounds as antimicrobial photosensitisers was further enhanced by the observation that the presence of positively charged functional groups allows an extensive photoinduced killing of Gram-negative bacterial cells, [18] which are usually resistant to the action of non-cationic porphyrinoid photosensitisers.[19] In recent years, growing interest has focused on the application of microwave irradiation in organic synthesis. Microwave processing has attracted potential interest as an alternative to classical thermal processing because of the inherent advantages of microwave heating, which is selective, direct, rapid, internal and controllable.[20–24] The use of microwave irradiation for synthesis of phthalocyanines reduces reaction time and enhances yield in comparison with classical methods.[25,26] We now describe the synthesis and characterisation of metal-free- and metallo-phthalocyanines bearing oxygen donor atoms on the peripheral positions. In addition, we investigated the antimicrobial activities of these novel metallophthalocyanine complexes. Furthermore, we report the voltammetric, *in situ* spectroelectrochemical, and *in situ* electrocolorimetric responses of newly synthesised CoPc **7**.

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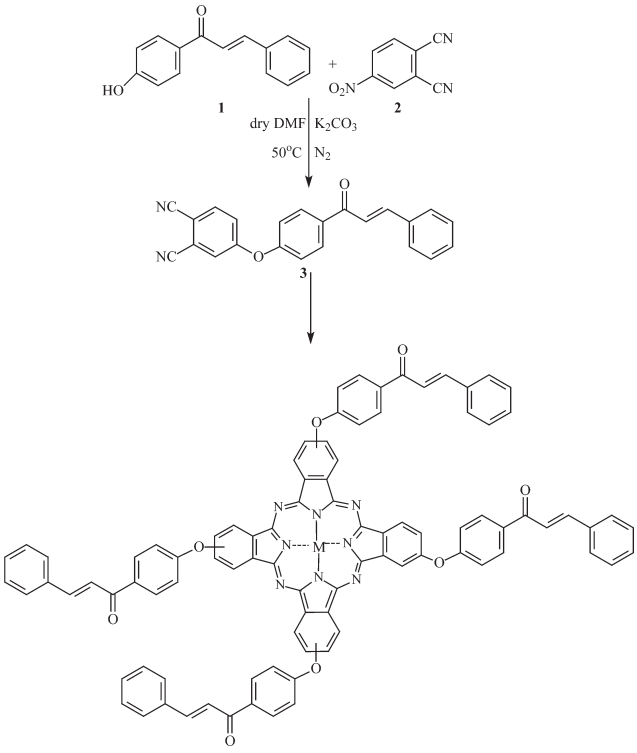
Results and discussion

Synthesis and characterisations

The general route for the synthesis of the new phthalocyanines is shown in Fig. 1. As the first step, (*E*)-1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one was used to prepare (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile through base-catalysed, nucleophilic aromatic nitro displacement of 4-nitrophthalonitrile. The reaction was catalysed by K_2CO_3 in dimethylformamide (DMF). The IR spectrum of **3** clearly indicates the presence of C≡N groups by the intense stretching band at 2232 cm^{-1}. In the ^1H NMR spectrum of **3** in deuterated chloroform, the aromatic protons and olefinic protons appear as a multiplet at 8.16–7.17 ppm. The ^{13}C NMR spectrum of **3** indicated the presence of nitrile carbon atoms in **3** at 115.44, 115.01 (C≡N) ppm. The mass spectrum of this compound at (*m/z)*: 350 $[M]^+$ supports the proposed formula for this compound and elemental analysis confirms the desired compound **3**.

Starting from the dicyano derivatives, many chemical routes may be used to form the corresponding metal-free phthalocyanines. Metal-free phthalocyanine **4** was synthesised from the corresponding dicyano compound **3** in dry *n*-pentanol under dinitrogen in the presence of 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU). The IR spectrum of metal-free phthalocyanine **4** shows (NH) vibrations at 3430 cm^{-1}. The disappearance of the C≡N stretching vibration in the IR spectrum of **3** indicates the formation of compound **4**. In the ^1H NMR spectra of this compound, the inner core protons of Pc-2H could not be observed due to strong aggregation of molecules.[27] The mass spectrum of this compound at (*m/z)*: 1403 $[M]^+$ supports the proposed formula for this compound and elemental analysis confirms the desired compound **4**.

The metallophthalocyanines **5**, **6**, **7**, **8** and **9** were obtained from dicyano derivative **3** and corresponding anhydrous metal salts $NiCl_2$, $Zn(CH_3COO)_2$, $CoCl_2$, $CuCl_2$ and $PbCl_2$ respectively, by microwave irradiation in 2-(dimethyl-amino)ethanol at 175 °C, 350 W.



Compound	4	5	6	7	8	9
M	2H	Ni (II)	Zn(II)	Co(II)	Cu(II)	Pb(II)

Fig. 1 The synthesis of the metal-free phthalocyanine and metallophthalocyanines.

In the IR spectra of metallophthalocyanines **5**, **6**, **7**, **8** and **9** the disappearance of the strong C≡N stretching vibration of **3** was evidence for the IR spectra of metallophthalocyanines, and the IR spectra of **5**, **6**, **7**, **8** and **9** are very similar to those of the metal-free phthalocyanine **4**. The NMR characteristics of these compounds were similar to those of the precursor dicyano compound **3** and the metal-free phthalocyanine **4**. In the mass spectrum of Ni, Zn, Co, Cu and Pb phtahlocyanines, the presence of molecular ion peaks at (*m/z)*: 1460 $[M]^+$, 1467 $[M+1]^+$, 1460 $[M]^+$, 1465 $[M]^+$, 1608 $[M]^+$ respectively, and their elemental analyses, confirm the proposed structures of **5**, **6**, **7**, **8** and **9**.

Phthalocyanines **4**–**9** show typical electronic spectra with two different strong absorption regions. The first, in the UV region at around 340 nm and called the Soret (or B) band, [28] arising from the deeper π levels→LUMO transition between an a_{2u} and the same eg orbitals and extending to the blue of the visible spectrum, is generally much less intense. The second, in the visible region at 600–700 nm and called the Q band, is attributed to the π–π* transition from the HOMO to the LUMO of the Pc^{2-} ring.[29,30] The electronic absorption spectrum of the metal-free Pc **4** in chloroform at room temperature is shown in Fig. 2. The split Q bands in **4**, which are characteristic of metal-free phthalocyanines, were observed at λ_{max} 698(2.58) and 660(2.50) nm. These Q band absorptions indicate a monomeric species with D_{2h} symmetry due to the phthalocyanine ring being involved in a fully conjugated 18 π electron system.[31–33] Phthalocyanine **4**, in chloroform, an intense peak at λ_{max} = 292(3.18) (B-band region).

The UV-Vis absorption spectra of the metallophthalocyanines **5**–**9** show intense Q band absorptions at λ_{max} = 672(2.87), 678(2.80), 668(2.88), 676(2.83), 668 (2, 73) nm, respectively (Figs 2 and 3). The single Q band in metallo-derivatives and

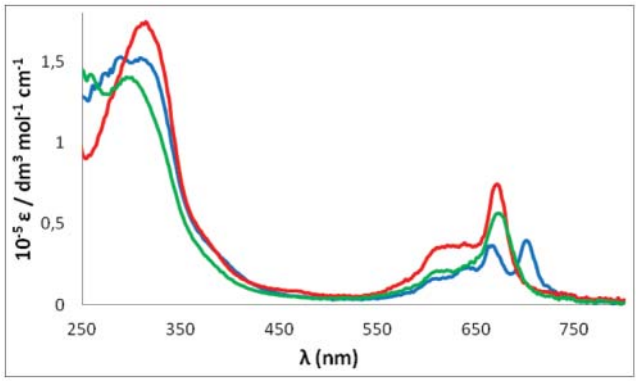


Fig. 2 UV-Vis spectra of H_2Pc (——), NiPc (——) and ZnPc (——) complexes.

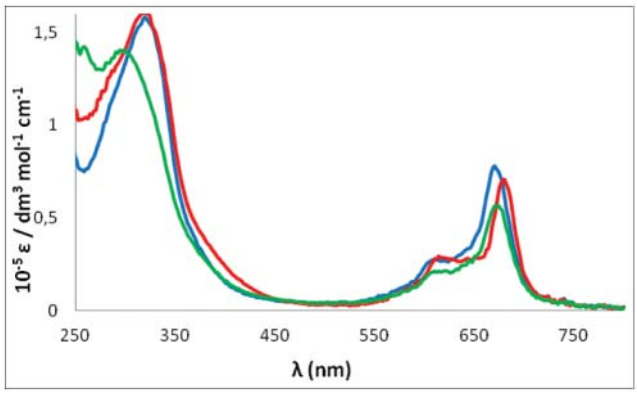


Fig. 3 UV-Vis spectra of CoPc (——), CuPc (——) and PbPc (——) complexes.

the split form in their metal-free derivatives are their basic characteristic.[34]

The thermal behaviour of the metallophthalocyanines were investigated by TG/DTA. Although the thermal stabilities of phthalocyanines are well known, the phthalocyanine compounds are not stable above 364.9 °C. The initial and main decomposition temperatures are given in Table 1. The initial decomposition temperature decreased in the order: **8** > **6** > **7**> **9** > **5** > **4**.

Antimicrobial activity

The antimicrobial activities of metallophthalocyanines **5**, **6**, **7**, **8** and **9** were assayed against the microorganisms considered in the present study and were qualitatively and quantitatively assessed, evaluating the presence of inhibition zones, zone diameter, and MIC values. As shown in Table 2 *Acinetobacter haemolyticus* bacterium and *Enterobacter cloacea* are sensitive to all the complexes. The maximal inhibition zones and MIC values for microorganisms, which were sensitive to **5**, **6**,

Table 1 Thermal properties of the metallo-phthalocyanines

Compound	M	İnitial decomposition temperature/°C	Main decomposition temperature/°C
4	H_2	364.9	482.3
5	Ni	380.0	460.0
6	Zn	405.0	472.1
7	Co	395.9	464.2
8	Cu	410.3	495.4
9	Pb	395.4	434.8

Table 2 Antimicrobial activity of the metallo phthalocyanines

Sample	9		8		7		6		5		K*	
	DD*	MIC*	DD	MIC	DD	MIC	DD	MIC	DD	MIC	DD	MIC
A. haemolyticus	12	1000	12	1000	12	2000	11	2000	12	2000	18(NET)	31–25
B. subtilis	–	–	–	–	–	–	–	–	–	–	20(NET)	7–8
E. cloacae	13	500	13	1000	13	500	12	2000	12	2000	14(NET)	31–25
E. faecalis	–	–	–	–	–	–	–	–	–	–	12(NET)	31–25
E. coli	–	–	–	–	–	–	–	–	–	–	18(NET)	62–5
P. vulgaris	–	–	–	–	–	–	–	–	–	–	20(NET)	125
Ps. aeruginosa	–	–	–	–	–	–	–	–	–	–	22(NET)	31–25
St. aureus	–	–	–	–	–	–	–	–	–	–	16(NET)	31–25
C. albicans	–	–	–	–	–	–	–	–	–	–	–(NET)	31–25
Rhyzopus sp.	–	–	–	–	–	–	–	–	–	–	–(NET)	–
Fusarium sp.	–	–	–	–	–	–	–	–	–	–	–(NET)	62–5
Aspergillus sp.	–	–	–	–	–	–	–	–	–	–	–(NET)	15–62

DD, Maximal inhibition zone; MIC, minimal inhibitor concentration; K, control; NET, Netilmicin. –, No activity

7, **8** and **9**, were in the range of 11–13 mm and 500–2000 μL mL^{-1}, respectively (Table 2). As a result, **5**, **6**, **7**, **8** and **9** exerted slight antibacterial activity against *A. haemolyticus* and *E. cloacae*. However, the rest of the test microorganisms, including fungi and the yeast, showed resistance. Lead (II) phthalocyanine **9** and cobalt (II) phthalocyanine **7** were found to be more effective compared to the other samples by exhibiting inhibition zones in the disk diffusion assay (MIC: 500nμL mL^{-1}).

Electrochemical measurements

Solution redox properties of the complexes were studied using CV and SWV measurements in DCM containing TBAP as supporting electrolyte on a Pt electrode. Table 3 lists the assignments of the redox couples and the electrochemical parameters, which included the half-wave peak potentials ($E_{1/2}$), anodic to cathodic peak potential separation (ΔE_p), ratio of the anodic to cathodic peak currents (I_{pa}/I_{pc}), and difference between the first oxidation and reduction processes ($\Delta E_{1/2}$). Peak to peak separations as well as the $E_{1/2}$ and $\Delta E_{1/2}$ values were in agreement with the reported data for redox processes in metallophthalocyanine complexes in the literature.[35–42]

Within the potential window of the DCM/TBAP electrolyte system, two reductions and two oxidation processes are recorded with CoPc **7** (Fig. 4). The couples at –0.30 V (ΔE_p = 74 mV and $I_{p,a}/I_{p,c}$ = 0.98), at –1.39 V(ΔE_p = 64 mV and $I_{p,a}/I_{p,c}$ = 0.85), at 0.56 V (ΔE_p = 90 mV and $I_{p,a}/I_{p,c}$ = 0.87 at 0.100 Vs^{-1}), and at 1.05 V are well resolved. For the first reduction couple, ΔE_p values change from 60 to 140 mV with increasing scan rate; suggesting electrochemical reversibility of the electron transfer process.[43] Theoretically, for a system that is both electrochemically and chemically reversible, ΔE_p should be 0.059/n and independent of scan rate. In practical applications, ΔE_p of a couple is compared with that of universal indicator ferrocene/ferrocenium couple. In our system, ΔE_ps were changed from 60 to 110 mV for ferrocene with increasing scan rates from 0.010 to 1.00 V s^{-1}. With respect to ΔE_p values, the redox couples of the complex are electrochemically reversible at all scan rates. SWVs clearly show the reversibility of the redox processes (Fig. 4b).[43] The effect of coupled chemical reactions to the electron transfer reactions is illustrated with the $I_{p,a}/I_{p,c}$ ratio change as a function of the scan rate and I_p changes as a function of the square root of the scan rate ((I_{pc}–$v^{1/2}$). While the first reduction and oxidation processes are purely diffusion controlled with respect to unit $I_{p,a}/I_{p,c}$ ratio at all scan rates and linear variation of I_{pc}–$v^{1/2}$, deviation of the $I_{p,a}/I_{p,c}$ ratio from unity with decreasing scan rate indicates the kinetic complication of the second electrochemically reversible reduction and oxidation processes. First-row transition metals-Pc differ from those of the main-group metals-Pc because the energy of the metal d-orbitals may be positioned between the energies of HOMO and LUMO of the phthalocyanine (Pc^{2-}) ligand. The first oxidation and first reduction processes occur on the metal centre in the MPc complexes only for Mn, Fe and Co derivatives in polar solvents such as DMF and DMSO, while the first reduction and second oxidation processes are metal-based in nonpolar solvents such as DCM. Thus, the first reduction and second oxidation processes of CoPc **7** recorded at –0.30 V and 1.05 V could be assigned easily to the Co^{II}/Co^{I} and Co^{II}/Co^{III} redox couples respectively and the remaining processes to the phthalocyanine ring.[39] Assignments of the redox couples are performed by the *in situ* spectroelectrochemical measurements given below.

Table 3 Voltammetric data of **CoPc** (**7**) with the related metallophthalocyanines for comparison

Complex		Ring oxidations		M^{III}/M^{II}	M^{II}/M^{I}	Ring reductions			$\Delta E_{1/2}$[d]	Ref
..CoPc	[a]$E_{1/2}$ *vs* SCE		0.56	1.05[e]	–0.30	–1.39			0.98	
(**7**)	[b]ΔE_p (mV) *vs* SCE	–	90	–	74	64				Tw
	[c]I_{pa}/I_{pc}	–	0.87	–	0.98	0.85				
CoPc	[f]$E_{1/2}$ (in DMSO)		0.91	0.48	–0.47	–0.81	–1.30	–1.62	0.95	35
CoPc	$E_{1/2}$ (in THF)		0.75	1.13	–0.21 (–0.55)	–1.29			0.90	40
CoPc	[f]$E_{1/2}$ (in DMSO)			0.43	–0.43	–0.83	–1.39		0.87	41
CoPc	[a]$E_{1/2}$ (in DCM)		0.85 (0.70)	1.55	–0.28 (–0.70)	–1.42			0.98	52
CoPc	[a]$E_{1/2}$ (in DCM)		0.76 (0.59)	–	–0.21 (–0.62)	–1.40			0.81	52
CoPc	[a]$E_{1/2}$ (in DCM)		0.65 (0.45)		–0.39 (–0.72)	–1.45			1.04	52

[a] $E_{1/2}$=(E_{pa}+E_{pc})/2 at 0.100 V s^{-1}. [b] ΔE_p= |E_{pa} – E_{pc}| at 0.100 V s^{-1}. [c] I_{pa}/I_{pc} for reduction, I_{pc}/I_{pa} for oxidation processes at 0.100Vs^{-1} scan rate. [d] $\Delta E_{1/2}$ = $E_{1/2}$ (first oxidation)–$E_{1/2}$ (first reduction) = HOMO–LUMO gap for metallophthalocyanines having electro-inactive metal centre (metal to ring (MLCT) or ring to metal (LMCT) charge transfer transition gap for MPc having redox active metal centre.). [e] The process is recorded with SWV. Tw, This work.

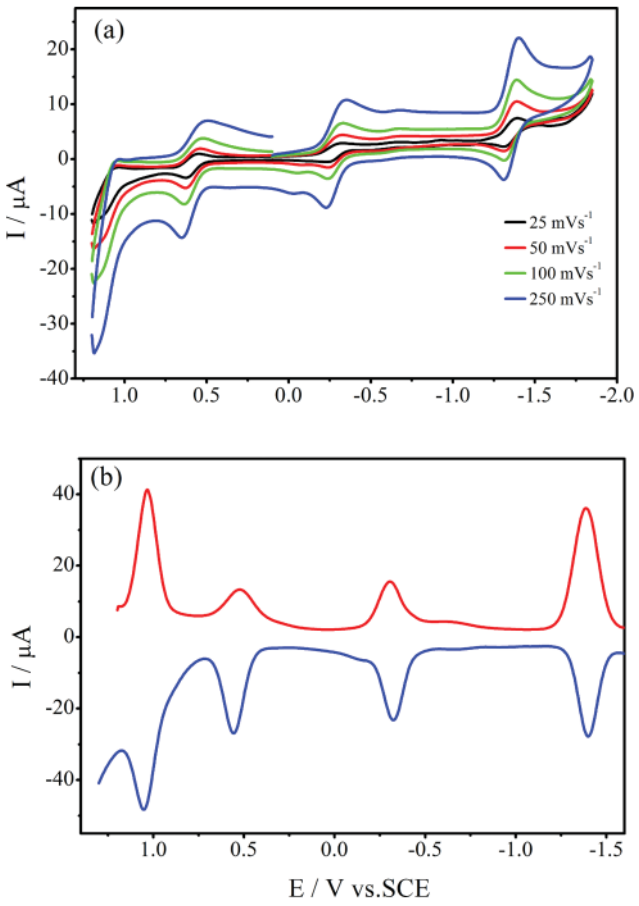


Fig. 4 (a) CVs of CoPc (7) (5.0 10^{-4} mol dm^{-3}) at various scan rates on a Pt working electrode in DCM/TBAP. (b) SWV of CoPc (**7**) with SWV parameters: step size = 5 mV; pulse size = 100 mV; Frequency = 25 Hz.

Spectroelectrochemical studies

All CoPc complexes give very similar *in situ* recorded UV-Vis spectral changes and chromaticity diagrams. The differences between them are only the wave length of the absorption bands recorded. Figure 5 presents *in situ* UV-Vis spectral changes and chromaticity diagrams of CoPc **7** as a representative of the CoPcs complexes under applied potentials. As shown in Fig. 5a during the first reduction process, the Q band shifts from 667 to 700 nm with descending intensity with a new band increasing at 471 nm. These spectroscopic changes indicate a metal-based reduction and are assigned to the $[Co^{II}Pc^{-2}]/[Co^{I}Pc^{-2}]^{1-}$ process.[44–48] During the electrochemical reduction at –0.50 V, well-defined isosbestic points were recorded at 395, 562, and 685 nm. These isosbestic points demonstrate that the reduction proceeds cleanly in deoxygenated DCM to give a single, reduced species. Further reduction of $[Co^{I}Pc^{-2}]^{1-}$ at –1.50 V expresses the ring-based redox process. During this process, the Q band decreases in intensity without shift, while a new broad band is recorded at around 540 nm (Fig. 5b). Well-defined isosbestic points demonstrate that the second reduction proceeds to give single, reduced $[Co^{I}Pc^{-3}]^{2-}$ species. Figure 5c represents the spectral changes during the oxidation processes of the complex. Decreasing of the Q band without a shift and observation of new bands at around 530 and 750 nm indicate the ring-based $[Co^{II}Pc^{-2}]$ / $[Co^{II}Pc^{-1}]^{1+}$ oxidation process during the controlled potential application at 0.70 V.[44–48] Further oxidation of the species showed the oxidation of the metal centre. There are deep colour differences between the electro-generated species of CoPc's (Figure 5d). Without any potential application, the solution of CoPc **7** is green (x = 0.3581 and y = 0.4336). As the potential is stepped from 0 to –0.50 V and then –1.50 V, the colour of the neutral $[Co^{II}Pc^{-2}]$ starts to change to yellow (x = 0.4378 and y = 0.4403) and then orange (x = 0.4522 and y = 0.4221), these colours were observed for the anionic forms of the complex respectively during the reduction processes. Similarly the colour of the solution changes from green to yellow (x = 0.4143 and y = 0.4169) during the first oxidation process of CoPc **7**. Deep colour differences between the electrogenerated anionic and cationic species of CoPc's indicate possible electrochromic applications of this complex.

Experimental

All reactions were carried out under dry N_2 using standard Schlenk techniques. The IR spectra were recorded on a Perkin Elmer 1600 FTIR spectrophotometer, using potassium bromide pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 200 MHz spectrometer in $CDCl_3$, and chemical shifts are reported (δ) relative to Me_4Si as internal Standard. Mass spectra were measured on a Varian 711 and VG Zapspec spectrometer. UV-Vis absorpion spectra were measured by a Unicam UV-Vis spectrometer. Melting points were measured on an Electrothermal apparatus. A domestic oven (Arçelik MD 823, 350 W) was used for all the syntheses of metallophthalocyanines. A Seiko II Exstar 6000 thermal analyser was used to record the DTA curves under N_2, with a heating rate of 20 °C min^{-1} in the temperature range of 30–900 °C, using platinum crucibles.

(*E*)*-4-(4-cinnamoylphenoxy) phthalonitrile* (**3**): (*E*)-1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one **1**[49] (1 g, 4.46 mmol) was dissolved in dry DMF (15 mL) under N_2 and 4-nitrophthalonitrile **2** (0.773 g, 4, 46 mmol) was added to the solution. After stirring for 10 min finely ground anhydrous K_2CO_3 (3.07 g, 22.3 mmol) was added portionwise within 2 h with efficient stirring. The reaction mixture was stirred under N_2 at 50 °C for 72 h. Then the solution was poured into ice-water (100 mL) and was stirred for one day. The solid product was filtered, washed in water and dried *in vacuo* over P_2O_5. The product was crystallised from ethanol. Yield: 1.35 g (86%). M.p. 128 °C. Anal. Calcd for $C_{23}H_{14}N_2O_2$: C, 78.84; H, 4.03; N; 8.00. Found: C, 78.87; H, 4.09; N, 8.02%. IR (KBr pellets), υ_{max} (cm^{-1}): 3077 (ArH), 2917–2851 (Aliphatic. C–H), 2232 (C≡N), 1603(C=O), 1589, 1486, 1338, 1277, 1211, 1155, 844, 773, 693. ^{1}H NMR ($CDCl_3$), (δ: ppm): 8.16–7.17(m, ArH, olefinic C–H). ^{13}C NMR ($CDCl_3$), (δ: ppm): 189.00 (C=O), 160.80, 157.65 (ArC), 145.79 (ArCH), 136.08 (ArC), 135.88 (ArCH), 134.82 (ArC), 131.56, 131.13, 129.30, 128.81, 122.67, 122.50, 121.53, 120.41 ArCH, olefinic C–H), 118.13 (ArC), 115.44, 115.01 (C≡N), 110.14 (ArC). MS (ES^+), (*m/z*): 350 $[M]^+$.

Metal-free phthalocyanine (**4**): (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (300 mg, 0, 86 mmol), DBU (five drop) and dry *n*-pentanol (4 mL) were added to a Schlenk tube and then heated and stirred at 160 °C for 24 h under N_2, then the reaction mixture was cooled at 30 °C and precipitated by adding ethanol. The solid product was filtered and washed with ethanol. The green solid product was chromatographed on silica gel with chloroform/methanol (7:1) as eluent. Yield: 63 mg (21%). Anal. Calcd for $C_{92}H_{58}N_8O_8$: C, 78.76; H, 4.13; N, 7.98. Found: C, 78.71; H, 4.19; N, 7.96%. IR (KBr tablets), υ_{max} (cm^{-1}): 3430 (N–H), 3054 (ArH), 2924–2853 (Aliphatic. C–H), 1660, 1594, 1497, 1360, 1232, 1164, 1026, 824, 764, 697. ^{1}H NMR ($CDCl_3$), (δ: ppm): 8.23–7.21(m, ArH, olefinic C–H). ^{13}C NMR. ($CDCl_3$), (δ: ppm): 183.12 (C=O), 178.22, 172.74, 165.31, 160.82, 153.61, 154.76, 146.11, 134.13, 131.12, 130.86, 129.18, 128.65, 123.24, 120.32, 119.42, 119.28, 116.31, 110.28. UV-Vis[in chloroform) λ_{max} /nm10^{-5} ε($mol^{-1}cm^{-1}$)]: 698(2.58), 660(2.50), 632(2.33), 596(2.09), 292(3.18). MS (ES^+), (*m/z*): 1403 $[M]^+$.

Nickel (II) phthalocyanine (**5**): A mixture of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (200 mg, 0.57 mmol), anhydrous $NiCl_2$ (18.5 mg, 0.14 mmol), and 2-(dimethylamino)ethanol (3 mL) was irradiated in a microwave oven at 175 °C, 350 W for 8 min. After cooling to room temperature the reaction mixture was refluxed with ethanol to precipitate the product which was filtered off and dried *in vacuo* over P_2O_5. The obtained green solid product was purified by column chromatography on silica gel with chloroform–methanol (5:1) as eluent. Yield: 67mg (32%). Anal. Calcd for $C_{92}H_{56}N_8O_8Ni$: C, 75.68; H, 3.83; N, 7.67. Found: C, 75.62; H, 3.89; N, 7.64%. IR (KBr

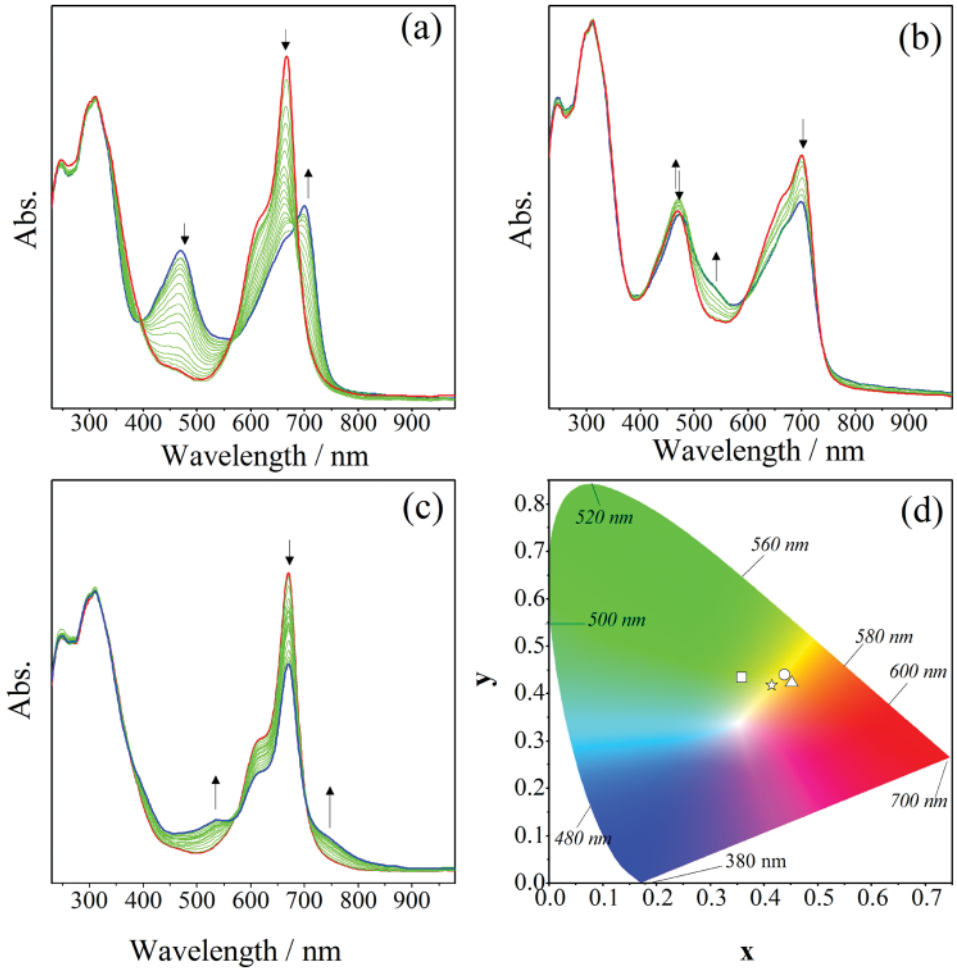


Fig. 5 *In situ* UV-Vis spectral changes of CoPc (**7**). (a) (inset: initial part of the spectral changes at E_{app} = -0.50 V) final part of the spectral changes at E_{app} = –0.50 V. (b) E_{app} = –1.50 V. (c) E_{app} = 1.00 V (Inset: E_{app} = 1.60 V). (d) Chromaticity diagram of CoPc (**7**). (each symbol represents the colour of electro-generated species; □: $[Co^{II}Pc^{-2}]$, ○:$[Co^{I}Pc^{-2}]^{-1}$ (initial part of the first reduction), △: $[Co^{I}Pc^{-2}]^{-}$ (final part of the first reduction), ▽: $[Co^{I}Pc^{-3}]^{-2}$, ◇: $[Co^{II}Pc^{-1}]^{+1}$ ☆:$[Co^{III}Pc^{-1}]^{+2}$.

pellets), υ_{max}/cm^{-1}: 3054 (ArH), 2917–2846 (Aliphatic. C–H), 1657, 1597, 1472, 1412, 1333, 1238, 1163, 1093, 1031, 834, 765. ^{1}H NMR. ($CDCl_3$), (δ: ppm): 8.49–6.34 (m, ArH, olefinic C–H). ^{13}C NMR. ($CDCl_3$), (δ: ppm): 189.06 (C=O), 175.25, 170.71, 162.01, 161.91, 157.81, 153.41, 143.51, 135.03, 133.12, 130.96, 129.19, 128.79, 122.49, 121.42, 119.86, 119.18, 117.51, 107.88. UV-Vis (chloroform): λ_{max}/nm: [(10^{-5} ε dm^3 mol^{-1} cm^{-1})]: 672(2.87), 608(2.53), 318(3.23). MS (ES^+), (*m/z*): 1460 $[M]^+$.

Zinc (*II*) *phthalocyanine* (**6**): A mixture of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (200 mg, 0.57 mmol), anhydrous $Zn(CH_3COO)_2$ (29 mg, 0.14 mmol), and 2-(dimethylamino)ethanol (3 mL) was irradiated in a microwave oven at 175 °C, 350 W for 6 min. After cooling to room temperature the reaction mixture was refluxed with ethanol to precipitate the product which was filtered off and dried *in vacuo* over P_2O_5. The obtained green solid product was purified by column chromatography on silica gel with chloroform–methanol (6:1) as eluent. Yield: 75 mg (36%). Anal. Calcd for $C_{92}H_{56}N_8O_8Zn$: C, 75.37; H, 3.82; N, 7.64. Found: C, 75.43; H, 3.79; N, 7.68%. IR (KBr pellets), υ_{max}/cm^{-1}: 3049 (ArH), 2926–2846 (Aliphatic. C–H), 1659, 1596, 1487, 1393, 1334, 1235, 1163, 1088, 944, 835, 765. ^{1}H NMR. ($CDCl_3$), (δ: ppm): 8.11–6.68 (m, ArH, olefinic C–H). ^{13}C NMR. ($CDCl_3$), (δ: ppm): 187.56 (C=O), 172.14, 172.01, 162.98, 162.54, 158.54, 152.51, 144.97, 144.85, 135.82, 134.91, 134.53, 129.21, 128.70, 122.51, 121.72, 120.81, 118.35, 118.01, 110.01. UV-Vis (chloroform): λ_{max}/nm: [(10^{-5} ε dm^3 mol^{-1} cm^{-1})]: 678(2.80), 608(2.36), 278(3.19). MS (ES^+), (*m/z*): 1467 $[M+1]^+$.

Cobalt (*II*) *phthalocyanine* (**7**): A mixture of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (200 mg, 0.57 mmol), anhydrous $CoCl_2$ (18.5 mg, 0.14 mmol) and 2-(dimethylamino)ethanol (3 mL) was irradiated in a microwave oven at 175 °C, 350 W for 8 min. After cooling to room temperature the reaction mixture was refluxed with ethanol to precipitate the product which was filtered off and dried *in vacuo* over P_2O_5. The obtained green solid product was purified by column chromatography on silica gel with chloroform–methanol (5:1) as eluent. Yield: 79 mg (38%). Anal. Calcd for $C_{92}H_{56}N_8O_8Co$): C, 75.68; H, 3.83; N, 7.67. Found: C, 75.65; H, 3.87; N, 7.69%. IR (KBr pellets), υ_{max}/cm^{-1}: 3054 (ArH), 2923–2857 (Aliphatic. C–H), 1662, 1597, 1471, 1333, 1238, 1162, 1095, 833, 765. UV-Vis (chloroform): λ_{max}/nm: [(10^{-5} ε dm^3 mol^{-1} cm^{-1})]: 668(2.88), 598(2.34), 312(3.18). MS (ES^+), (*m/z*): 1460 $[M]^+$.

Copper (*II*) *phthalocyanine* (**8**): A mixture of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (200 mg, 0.57 mmol), anhydrous $CuCl_2$ (19.1 mg, 0.14 mmol) and 2-(dimethylamino)ethanol (3 mL) was irradiated in a microwave oven at 175 °C, 350 W for 5 min. After cooling to room temperature the reaction mixture was refluxed with ethanol to precipitate the product which was filtered off and dried *in vacuo* over P_2O_5. The obtained green solid product was purified column chromatography on silica gel with chloroform–methanol (6:1) as eluent. Yield: 73 mg (35%). Anal. Calcd for $C_{92}H_{56}N_8O_8Cu$: C, 75.45; H, 3.82; N, 7.65. Found: C, 75.41; H, 3.87; N, 7.63%. IR (KBr pellets), υ_{max}/cm^{-1}: 3049 (ArH), 2928–2857 (Aliphatic. C–H), 1659, 1596, 1473, 1404, 1333, 1237, 1163, 1093, 946, 834, 765. UV-Vis (chloroform):λ_{max}/nm: [(10^{-5} ε dm^3 mol^{-1} cm^{-1})]: 676(2.83), 604(2.35), 308(3.18). MS (ES^+), (*m/z*): 1465 $[M]^+$.

Lead (*II*) *phthalocyanine* (**9**): A mixture of (*E*)-4-(4-cinnamoylphenoxy) phthalonitrile **3** (200 mg, 0.57 mmol), anhydrous $PbCl_2$ (39.6 mg, 0.14 mmol) and 2-(dimethylamino)ethanol (3 mL) was irradiated in a microwave oven at 175 °C, 350 W for 6 min. After cooling to room temperature the reaction mixture was refluxed with ethanol to precipitate the product which was filtered off and dried *in vacuo* over

P_2O_5. The obtained green solid product was purified from the column chromatography on silica gel with chloroform–methanol (7:1) as eluents. Yield: 64 mg (28%). Anal. Calcd for $C_{92}H_{56}N_8O_8Pb$: C, 68.72; H, 3.48; N, 6.96. Found: C, 68.76; H, 3.42; N, 6.94%. IR (KBr pellets), υ_{max}/cm^{-1}: 3057 (ArH), 2921–2846 (Aliphatic. C–H), 1661, 1594, 1474, 1333, 1231, 1163, 1091, 939, 835, 765. ^{1}H NMR. ($CDCl_3$), (δ: ppm): 8.03–6.72 (m, ArH, olefinic C–H). ^{13}C NMR. ($CDCl_3$), (δ: ppm): 188.52 (C=O), 173.26, 171.06, 164.72, 163.56, 160.44, 154.72, 146.86, 145.32, 136.42, 135.18, 134.43, 128.52, 128.26, 122.14, 121.46, 120.83, 118.38, 118.33, 112.27. UV-Vis (chloroform): λ_{max}/nm: [(10^{-5} ε dm^3 mol^{-1} cm^{-1})]: 668(2.73), 604(2.28), 286(3.13). MS (ES^+), (*m/z*): 1608 $[M]^+$.

Antimicrobial activity assays

The metallophthalocyanines **5**, **6**, **7**, **8** and **9** were individually tested against 12 microorganisms, among which there are eight bacteria and four fungi and yeast species. The list of microorganisms used is given in Table 4.

The metallophthalocyanines **5**, **6**, **7**, **8** and **9** were dissolved in dimethyl sulfoxide to a final concentration of 30 mg mL^{-1}. Antimicrobial tests were then carried out by the disk diffusion method.[50] The disks (6 mm in diameter), impregnated with samples (300 μg/disk), were placed on the inoculated agar. Negative controls were prepared with the same solvents used to dissolve the samples. Netilmicin (30 μg/disk) was used as positive reference standard to determine the sensitivity of one strain/isolate in each microbial species tested. The inoculated plates were incubated at 37 °C for 24 h for clinical bacterial strains, 48 h for the yeast, and 72 h for fungi isolates. Plant-associated microorganisms were incubated at 27 °C. Antimicrobial activity was evaluated by measuring the zone of inhibition against test organisms. Each assay was repeated twice.

MIC values were determined for the bacterial strains that were sensitive to the complexes in the disk diffusion assay. The inocula of the bacterial strains were prepared from 12 h broth cultures, and suspensions were adjusted to 0.5 McFarland standard turbidity. MIC values of the complexes against bacterial strains and *Candida albicans* isolates were determined on the basis of a microwell dilution method[51] with some modifications.

96-Well plates were prepared by dispensing 95 μL of nutrient broth and 5 μL of the inoculum into each well; 100 μL from the stock solutions of the samples prepared at the 500 μg mL^{-1} concentration was added into the first wells. Then, 100 μL from the serial dilutions was transferred into the six consecutive wells. The last well containing 195 μL of nutrient broth without compound and 5 μL of the inoculum on each strip was used as a negative control. The final volume in each well was 200 μL. The plate was covered with a sterile plate sealer. The complexes tested in this study were screened twice against each organism.

Electrochemical analysis

Electrochemical and spectroelectrochemical measurements were carried out with a Gamry Reference 600 potentiostat/galvanostat utilising a three-electrode configuration at 25 °C. The working electrode was a Pt disc with a surface area of 0.071 cm^2. The surface of the working electrode was polished with a diamond suspension before each run. A Pt wire served as the counter electrode. Saturated calomel electrode (SCE) was employed as the reference electrode and separated from the bulk of the solution by a double bridge. Ferrocene was used as an internal reference. Tetrabuthylammonium perchlorate (TBAP) in dichloromethane (DCM) was employed as the supporting electrolyte at a concentration of 0.10 mol dm^{-3}. High purity N_2 was used to remove dissolved O_2 at least for 15 minutes prior to each run and to maintain a dinitrogen blanket during the measurements. IR compensation was applied to the CV and SWV scans to minimise the potential control error.[52]

UV-Vis absorption spectra and chromaticity diagrams were measured by an OceanOptics QE65000 diode array spectrophotometer. *In situ* spectroelectrochemical measurements were carried out by utilising a three-electrode configuration, thin-layer quartz spectroelectrochemical cell at 25 °C. The working electrode was a Pt gauze. A Pt wire counter electrode and a SCE reference electrode, separated from the bulk of the solution by a double bridge, were used. *In situ* electrocolorimetric measurements under potentiostatic control were obtained by using an OceanOptics QE65000 diode array spectrophotometer in colour measurement mode by utilising a three-electrode configuration, thin-layer quartz spectroelectrochemical cell. The standard illuminant A with 2 degree observer at constant temperature in a light booth designed to exclude external light was used. Prior to each set of measurements, background colour coordinates (*x*, *y*, and *z* values) were taken at open-circuit, using the electrolyte solution without the MPc under study. During the measurements, readings were taken as a function of time under kinetic control.

Table 4 The list of microorganisms used in antimicrobial tests

	Microorganisms
Bacteria	*Escherichia coli* ATCC 25922
	Staphylococcus aureus ATCC 25923
	Pseudomonas aeruginosa ATCC 27853
	Acinetobacter haemolyticus ATCC 19002
	Bacillus subtilis ATCC 6633
	Proteus vulgaris ATCC 13315
	Enterobacter cloacea ATCC 13047
	Enterococcus faecalis ATCC 29212
Fung and yeast	*Candida albicans* ATCC 60193
	Aspergillus sp.
	Fusarium sp.
	Rhizopus sp.

Conclusion

In this work, we describe the synthetic procedure and characterisation of new metal-free and metallophthalocyanines bearing oxygen donor atoms on the peripheral positions. In addition, thermal properties of the phthalocyanines were examined by thermogravimetric analysis. The biological activities (antibacterial, anticandidal and antifungal) of the new metallo-phtalocyanines were also investigated. All of the new metallo phtalocyanines exerted slight antibacterial activity against *A. Haemolyticus* and *E. cloacae.* However, the rest of the test microorganisms, including fungi and the yeast, showed resistance. Voltammetric and spectroelectrochemical studies show that cobalt phthalocyanine complex (**7**) give both metal and ring-based, diffusion controlled, multi-electrons and reversible/quasi-reversible reduction processes. Definite determination of the colours of the electrogenerated anionic and cationic forms of the complexes is important to decide about their possible electrochromic application. Diffusion-controlled, multi-electron and reversible redox processes of the complexes indicate possible electrocatalytic activity for different target species.

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