Formation, characterization and electrochemical properties of novel tetrasubstituted cobalt phthalocyanines bearing tetrahydropyran, furan and coumarin moieties

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ABSTRACT

Cobalt phthalocyanines (CoPcs) bearing peripherally tetrasubstituted tetrahydropyran (thp) or furan (fur) moieties were formed and spectroscopically characterized. Structural elucidations of 4-(tetrahydropyran-2-methoxy)phthalonitrile (1) and 4-(furan-2-methylthio)phthalonitrile (2) were confirmed *via* single crystal X-ray analysis. The redox properties of CoPc-thp (3) and CoPc-fur (4) were investigated *via* cyclic and squarewave voltammetry as well as UV–Vis spectroelectrochemistry. Glassy carbon electrodes (GCEs) modified with 3, 4 and a previously reported coumarin (cou) substituted CoPc (CoPc-cou, 5), were tested for their electrocatalytic activities toward L-cysteine. While the bare GCE and 4-GCE showed no peaks for L-cysteine oxidation in the 0.0–0.70 V potential window; 3-GCE and 5-GCE showed peaks at 0.42 V and 0.52 V, respectively. Kinetic parameters were determined by chronoamperometry studies. L-Cysteine oxidation using 3-GCE was found to proceed at a faster rate than 5-GCE.

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1. Introduction

L-Cysteine is an amino acid that plays a crucial role in biological systems for the functioning of various proteins [1]. It has several applications in the pharmaceutical and food industries for the formulation of drugs and the production of antibiotics and antioxidants [2]. A deficiency in L-cysteine is associated with many health issues such as liver damage, skin lesions, hair depigmentation and muscle loss; hence, its detection is of great importance for physiological and clinical diagnosis [3,4]. Electrochemical methods have proved to be the preferred choice for this purpose above other techniques like chromatographic separation and spectrometric methods [5,6] due to their simplicity, enhanced selectivity and high sensitivity [7]. The detection of L-cysteine on bare electrodes requires high overpotentials which results in sluggish responses, surface fouling and interference from other analytes [3,7,8]. To overcome these shortcomings, researchers are focusing on the development of chemically modified electrodes (CMEs) to electrocatalytically enhance the detection of L-cysteine [9,10].

Metallophthalocyanines (MPcs) are versatile materials that are particularly useful in the preparation of biosensors [11–13]. The high chemical, thermal and mechanical stability of these metal complexes makes them an attractive choice for such application [14,15]. In many instances, electrodes modified with MPcs have shown excellent electrocatalytic behavior towards various biologically important analytes [16,17]. MPc modified electrodes can be prepared in various ways such as the drop-dry method, formation of Langmuir–Blodgett films, self-assembled monolayers, electropolymerization and electrodeposition [18–21].

Optimization of the electrochemical properties of MPcs can be achieved by modification of the substituents and/or metal centres [22,23]. Redox active metal centres like Co, Fe and Mn promote electron mediation [24] while biosensors prepared with MPcs containing biologically active substituents have been reported to show improved selectivity and sensitivity towards biological analytes [25,26]. Furan derivatives are known to possess anti-bacterial, anti-tumor and analgesic properties [27,28] while pyrans have been discovered to have antimicrobial and antioxidant activities [29,30]. In this study, we report on the synthesis and characterization of CoPcs substituted with biologically relevant tetrahydropyran (thp) and furan (fur) moieties. In addition, we explore the comparative electrocatalytic capabilities of glassy carbon electrodes (GCEs) modified with MPcs containing thp and coumarin (cou) moieties, towards L-cysteine.

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2. Experimental

2.1. Materials

4-Nitrophthalonitrile, tetrahydropyran-2-methanol, 2-furan-methanethiol, potassium carbonate, cobalt(II) chloride, 1,8-diaz-abicyclo[5.4.0]undec-7-ene (DBU) and electrochemical analysis grade tetrabutylammoniumtetrafluoroborate (TBABF$_4$) were purchased from Sigma–Aldrich and used without further purification. Organic solvents, phosphorus pentoxide (P$_2$O$_5$), molecular sieves (4 Å), aluminum oxide (alumina), silicon dioxide (silica) for column chromatography and silica plates for thin layer chromatography were purchased from Merck SA. Dimethylformamide (DMF) used in ligand syntheses, UV–Vis spectroscopy and electrochemical experiments was dried and stored over molecular sieves. All metal complexes and ligands were stored over P$_2$O$_5$. Ultrapure water was obtained from an ElgaPurelab Ultra system.

2.2. Equipment

FTIR spectra were recorded using a Bruker Alpha FTIR spectrometer equipped with an ATR platinum Diamond 1 reflectance accessory. NMR experiments were conducted in d^6-DMSO using a 400 MHz Bruker NMR spectrometer. UV–Vis spectroscopy was carried out using a Perkin-Elmer Spectrum 25 containing quartz cuvettes having a path length of 1 cm. All UV–Vis spectra were recorded in N,N'-dimethylformamide. Melting points were recorded using a Stuart SMP3 melting point apparatus. Elemental analysis was carried out using a CHNS-O Flash 2000 Organic Elemental Analyser. Mass spectrometry (MS) was conducted in both the positive and negative modes via direct injection of the samples into a Waters Micromass LCT Premier MS instrument equipped with an electrospray ionization (ESI) source and a time-of-flight (TOF) mass analyzer. Single crystal X-ray diffraction (XRD) studies were conducted using a Bruker Apex Duo equipped with an Oxford Instruments Cryojet operating at 120(±2) or 100(±2) K and an Incoatec microsource operating at 30 W. The XRD experimental parameters, refinement details of the solid-state structures as well as their descriptions can be found in the online supporting information documents. Voltammetric studies were conducted using an Autolab Potentiostat equipped with a three-electrode system: a Pt or glassy carbon working electrode, a pseudo Ag|AgCl reference electrode and a Pt counter electrode. The Autolab Nova 1.7 software was used for operation of the potentiostat and data analysis. A GCE was used for all electrocatalytic experiments. Spectro-electrochemical experiments were undertaken using a Specac optically transparent thin-layer electrochemical (OTTLE) cell.

2.3. Electrochemical methods

All electrochemical studies on the metal complexes were conducted in deoxygenated DMF solutions containing 0.1 M equivalents of tetrabutylammoniumtetrafluoroborate (TBABF$_4$) as a supporting electrolyte. The Pt electrode surface was regenerated between voltammetric scans by polishing over a slurry of alumina and ultra-pure water on a diamond polishing pad followed by rinsing with ultra-pure water and anhydrous DMF. The GCE was polished over alumina on Buehler and diamond polishing pads, rinsed in Millipore water and ultrasonicated in methanol (MeOH) for 2 min prior to use. Square wave voltammetry (SWV) was conducted by setting the step potential at 4 mV, the amplitude at 20 mV and the frequency at 25 Hz.

Adsorption of the MPcs onto a GCE was achieved via the drop-dry method. Concentrated solutions of the metal complexes were prepared in dichloromethane (DCM) and a drop of each metal complex was transferred onto the electrode surfaces which were then dried for 1 h at 100 °C. The CMEs were rinsed with DCM, ethanol (EtOH) and ultrapure water prior to use. A 1 mM solution of L-cysteine was prepared in pH 4 buffer for electrocatalysis. Tetra-4-(7-oxy-4-trifluoromethylcoumarin phthalocyaninato)Co (II) (CoPc-cou, **5**) used in the preparation of CMEs was synthesized as previously reported [31].

2.4. Synthesis of 4-(tetrahydropyran-2-methoxy)phthalonitrile (**1**)

A mixture of 4-tetrahydropyran-2-methanol (0.653 cm³, 5.78 mmol) and potassium carbonate (2.30 g, 16.64 mmol) was stirred in anhydrous dimethylformamide (DMF) (30.0 cm³) at room temperature under N$_2$ for 1 h. Thereafter, to the resultant reaction mixture, 4-nitrophthalonitrile (1.00 g, 5.78 mmol) was added. The reaction mixture was removed after 48 h and poured into 300 cm³ of a water–ice slurry. The resulting precipitate was filtered and purified via column chromatography using a 1:1 (v:v) ethyl acetate:hexane solvent system to produce a white compound. Yield: 20%; m.p (°C): 62.3–62.9; FT-IR (ν_{max}/cm⁻¹): ν (C≡N) 2240, ν(C—O—C) 1252, 1090, 1027; UV–Vis (DMF, λ_{max} (ε, M⁻¹cm⁻¹)): 306 nm (13081), 299 (12647); ¹H NMR (ppm): 8.04 (d, 1H, H14), 7.78 (d, 1H, H13), 7.47 (d, 1H, H12), 4.06–4.14 (m, 2H, H10, H11), 3.85–3.92 (m, 1H, H8), 3.62–3.70 (m, 1H, H9), 3.35–3.42 (m, 1H, H7), 1.78–1.87 (m, 1H, H4), 1.59–1.67 (m, 1H, H2), 1.42–1.59 (m, 3H, H3, H5, H6), 1.26–1.38 (m, 1H, H1); ¹³C NMR (ppm): 22.92, 25.87, 27.67, 67.74, 72.57, 75.41, 106.38, 116.20, 116.69, 116.74, 120.57, 120.83, 136.20, 162.48. Molecular mass (m/z): Calc.: 242.27. Found: 265.10 [M+Na]⁺. Anal. Calc. for C$_{14}$H$_{14}$N$_2$O$_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 64.32; H, 4.91; N, 10.73%.

2.5. Synthesis of 4-(furan-2-methylthio)phthalonitrile (**2**)

A mixture of 4-nitrophthalonitrile (1.00 g, 5.78 mmol), 2-furan-methanethiol (0.583 cm³, 5.78 mmol) and potassium carbonate (2.30 g, 16.64 mmol) was added to anhydrous DMF (30.0 cm³). The reaction mixture was stirred at 90 °C under N$_2$ for 48 h after which it was cooled to room temperature and poured into 300 cm³ of a water–ice slurry. The resulting white precipitate was filtered and recrystallized from hot methanol (MeOH). Yield: 80%; m.p (°C): 127.8–128.5; FT-IR (ν_{max}/cm⁻¹): ν(C≡N) 2228, ν (C—O—C) 1249, 1061; UV–Vis (DMF, λ_{max} (ε, M⁻¹cm⁻¹)): 323 nm (76752), 295 (137469); ¹H NMR (ppm): 8.15 (d, 1H, H7), 8.01 (d, 1H, H8), 7.85 (d, 1H, H6), 7.62–7.59 (m, 1H, H3), 6.42–6.38 (m, 2H, H1, H2), 4.56 (s, 2H, H4, H5); ¹³C NMR (ppm): 28.10, 109.37, 110.73, 111.23, 115.52, 116.07, 116.49, 131.40, 131.47, 131.19, 143.58, 145.85, 149.77. Molecular mass (m/z): Calc.: 240.28. Found: 263.03 [M+Na]⁺. Anal. Calc. for C$_{13}$H$_8$N$_2$OS: C, 64.98; H, 3.36; N, 11.66; S, 13.34. Found: C, 65.10; H, 3.36; N, 11.64; S, 13.05%.

2.6. Synthesis of tetra-4-(tetrahydropyran-2-methoxyphthalocyaninato) Co(II) (CoPc-thp, **3**)

A mixture of **1** (0.125 g, 0.516 mmol), CoCl$_2$ (0.0167 g, 0.129 mmol) and DBU was heated with stirring in n-pentanol (20.0 cm³) at 160 °C under nitrogen for 16 h. The reaction mixture was then cooled to room temperature and n-hexane was added drop-wise to induce precipitation. The precipitate was filtered off using a millipore filtration setup and then washed with water, MeOH, EtOH, hexane and acetonitrile. The desired product was thereafter recovered via column chromatography using a 1:10 (v: v) tetrahydrofuran (THF):CHCl$_3$ solvent system. Yield: 15%; IR (ν_{max}/cm⁻¹): ν(C=N) 1601, ν(C—O—C) 1232, 1123, 1088; UV–Vis (DMF, λ_{max} (ε, M⁻¹cm⁻¹)): 667 nm (285321), 330 nm (189512),