One-Step Covalent Immobilization of β -Cyclodextrin on sp^2 Carbon Surfaces for Selective Trace Amount Probing of Guests

Zhi Li, Joachim F. R. Van Guyse, Victor Retamero de la Rosa, Hans Van Gorp, Peter Walke, Miriam C. Rodríguez González, Hiroshi Uji-i, Richard Hoogenboom,* Steven De Feyter,* and Stijn F. L. Mertens*

The modification of solid surfaces with supramolecular hosts is a powerful method to tailor interfacial properties and confer chemical selectivity, but often involves multistep protocols that hinder facile upscaling. Here, the one-step covalent modification of highly oriented pyrolytic graphite (HOPG) with a β -cyclodextrin (β -CD) derivative, which efficiently forms inclusion complexes with hydrophobic guests of suitable size is demonstrated. The grafted β -CD-HOPG surface is investigated toward electrochemical detection of ferrocene and dopamine. The enrichment of the analytes at the electrode surface, through complex formation with the β -CD units, leads to an enhanced electrochemical response and an improved detection limit. Furthermore, the modified β -CD-HOPG electrode discriminates analytes that form host–guest complexes with β -CD against a 100-fold higher background of electroactive substances that do not. Characterization of the surface using atomic force microscopy, scanning tunneling microscopy, and Raman spectroscopy confirmed the covalent nature of the modification and revealed high stability toward solvent rinsing, ultrasonication, and temperatures up to 140 °C. The one-step covalent modification therefore holds substantial promise for the routine production of inexpensive, yet robust and highly performant electrochemical sensors. Beyond electrochemical sensor development, our strategy is valuable to prepare materials where accurate spatial positioning of functional units and efficient current collection are crucial, e.g. in photoelectrodes or electrocatalysts.

1. Introduction

Cyclodextrins (CDs) are a class of cyclic oligosaccharides with repeating D-glucose units and consist of a hydrophobic cavity and a hydrophilic shell. They are classified as α -, β -, and γ -cyclodextrins depending on the number of glucopyranoside units, which determines the cavity size.^[1] Due to their geometric shape and hydrophobic cavity, CDs selectively form inclusion complexes with various hydrophobic guest molecules in aqueous environment, which has led to applications in molecular recognition,^[2] drug delivery,^[3] explosives detection,^[4] water purification,^[5] and chiral separation.^[6] Electroactive guests are of particular interest toward the development of CD-based sensors,^[2,7] but require the reliable immobilization of the host molecule.^[8] To this end, many procedures to immobilize CDs on diverse electrode materials (e.g., graphene,^[9] carbon nanotubes,^[10] silicon carbide^[11] through noncovalent^[12] and covalent^[13] modification have been developed. However, most immobilization protocols are time consuming and involve multiple steps.

In this paper, we propose a simple and fast method for covalent modifica-

tion of HOPG as a representative sp^2 carbon surface with β -CD (Scheme 1). An aniline-modified β -CD is converted to its diazonium salt, and, subsequently, electrochemically grafted on HOPG through the formation of aryl radicals that attack the sp^2 carbon surface and form covalent C–C bonds.^[14] The resulting modified β -CD-HOPG surface is characterized using scanning tunneling microscopy (STM), atomic force microscopy (AFM), and Raman spectroscopy. Cyclic voltammetry (CV) is used to study the electrochemical behavior of the modified surface toward ferrocene (Fc), hexacyanoferrate [$Fe(CN)_6^{3-/4-}$], and the neurotransmitter dopamine.

2. Results and Discussion

Covalent grafting of HOPG with β -CD-aniline, which was prepared by reaction of monotosylate β -CD with aminothiophenol

Dr. Z. Li, H. Van Gorp, P. Walke, Dr. M. C. Rodríguez González, Prof. H. Uji-i, Prof. S. De Feyter, Dr. S. F. L. Mertens
Department of Chemistry
KU Leuven

Celestijnenlaan 200F, 3001 Leuven, Belgium
E-mail: steven.defeyter@kuleuven.be

Dr. J. F. R. Van Guyse, Dr. V. Retamero de la Rosa, Prof. R. Hoogenboom
Department of Organic and Macromolecular Chemistry
Ghent University
9000 Gent, Belgium
E-mail: richard.hoogenboom@ugent.be

Dr. S. F. L. Mertens
Department of Chemistry and Energy Lancaster
Lancaster University
Lancaster LA1 4YB, UK
E-mail: s.mertens@lancaster.ac.uk

The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/adfm.201901488>.

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Scheme 1. a) Chemical structure of mono-6-dehydroxy-6-aniline-beta-cyclodextrin (β-CD-aniline); b) reaction scheme showing in situ conversion of β-CD-aniline to its diazonium salt, electrochemical radical formation, and surface grafting.

(for details see Supporting Information), is based on the concept that one-electron electrochemical reduction of diazonium salts generates radicals that subsequently attack the sp² carbon surface, leading to covalent attachment of the β-CD.^[15]

Figure 1 shows cyclic voltammograms (CVs) of freshly exfoliated HOPG in 2 × 10^{−3} M β-CD-aniline in the presence of excess diazotization reagents NaNO₂ and HCl. The first cycle shows a small irreversible peak around *E* = −400 mV versus Ag/AgCl, corresponding to the reduction of the generated diazonium compound and the generation of the corresponding aryl radicals.^[16] The following cycles are featureless and the reduction current decreases due to self-inhibition, i.e., blocking of the surface by the products formed during the preceding cycles.^[16]

The formation of covalent carbon–carbon bonds between sp² carbon surfaces and generated radicals alters the hybridization of the graphitic atoms from sp² to sp³, creating lattice defects in sp² materials. The resulting modification of the conjugation length of the delocalized carbon lattice can be used to tune the electronic and surface properties of carbonaceous materials, including graphene.^[17,18] Raman spectroscopy has been proposed as a rapid and nondestructive spectroscopic method to quantify lattice defects in sp² carbon surfaces, as a specific D-band is only activated when sp³ sites are present.^[19] Pristine graphitic surfaces without defects show zero D-band intensity.^[18,20] Therefore, the integrated intensity ratio between

D- and G-band (*I_D/I_G*) can be used as a measure of the extent of covalent surface functionalization.

The Raman spectra in Figure 2a were recorded for β-CD-phenyldiazonium grafted on HOPG from solutions with varying concentrations. To achieve better statistics, all Raman spectra were averaged over 5–8 sample spots. The intense peaks at 1579 and 2680 cm^{−1} correspond to the G-band and 2D-band, respectively. The small band at 1338 cm^{−1} is assigned to the D-band, which only appears when a structural defect is present in the sp² carbon lattice.^[21] Figure 2b shows the enlarged D-band region of Figure 2a. The D-band intensity after grafting from a 0.1 × 10^{−3} M solution of β-CD-aniline is fairly low (*I_D/I_G* = 0.0263), suggesting that a low number of sp³ defects is created in the HOPG sp² lattice due to covalent grafting. If the solution concentration is varied, see Figure 2c, a maximum in D-band intensity is found for grafting from 2 × 10^{−3} M solutions, with higher concentrations again leading to lower grafting density. The low grafting density from 5 × 10^{−3} M solutions may originate from blocking of the HOPG surface by physisorbed β-CD-aniline molecules, preventing the efficient attack of the substrate by electrochemically generated radicals. Importantly, the Raman spectrum for bare HOPG showed no D-band (see Figure S3, Supporting Information), indicating the high quality of the HOPG substrate without significant defects. Therefore, any D-band intensity measured on grafted HOPG samples can be ascribed to conversion of original sp² carbons to sp³. In a control experiment, physisorbed β-CD-aniline on HOPG was shown not to cause any D-band intensity (Figure S3, Supporting Information).

The Raman D-band intensity was also used to quantify the stability of the surface modification toward various solvents and thermal treatment (Figure S3, Supporting Information). The D-band intensity did not decrease after rinsing and sonication in hot milli-Q water, hot *N,N*-dimethyl sulfoxide (DMSO) nor hot toluene, indicating strong bonding of the grafted layer as expected for covalent modification. The thermal stability of the grafted layer was tested by heating the sample to a fixed temperature for 30 min in air, cooling down, and measuring the Raman spectrum. The D-band intensity remained similar for temperatures up to 140 °C, beyond which it decreased dramatically up to 200 °C and disappeared completely at 220 °C. This indicates that the covalently attached molecules were thermally stable up to 140 °C, after which gradual breakdown of covalent bonds occurred.

STM is a technique for imaging at the atomic level, allowing direct visualization of defect sites and determination of defect density on carbon surfaces, Figure 3a–f.^[22,23] Each bright

Figure 1. CVs of HOPG in 2 × 10^{−3} M β-CD-phenyldiazonium, starting at 0.2 V versus Ag/AgCl. Supporting electrolyte 50 × 10^{−3} M HCl. Scan rate, 100 mV s^{−1}.

Figure 2. a) Raman spectra of HOPG after grafting from solutions with varying β -CD-phenyldiazonium concentrations. b) Zoom-in of D bands for the spectra in panel (a). c) Plot of D/G-band intensity ratio versus solution concentration used for grafting. The spectra were averaged over 5 to 8 sample spots. Integration time, 100 s.

feature represents a single grafting site or a cluster thereof, with an apparent height of around 0.6 nm. This value is much smaller than the expected length (1.4 nm) of the grafted β -CD-phenyldiazonium molecule. The likely explanation is that the tunneling mechanism mainly visualizes the grafting site in the substrate.^[23] The grafting density analysis based on the STM results, see Figure 3h, is in good agreement with the Raman measurement shown in Figure 2. Figure 3g shows

a high-resolution image of a single defect site and its surrounding area. The defect induces a relatively large distorted area around the actual defect. The observed standing-wave patterns around the defect site indicate a local modification of the carbon lattice and the corresponding fast Fourier transform (FFT) image taken near the modification region (Figure 3g, upper white dashed square) shows spots in addition to the hexagonal pattern of the HOPG lattice, confirming the lattice

Figure 3. STM images of HOPG grafted with β -CD-phenyldiazonium from a) 0.1×10^{-3} M; b) 0.3×10^{-3} M; c) 0.6×10^{-3} M; d) 1×10^{-3} M; e) 2×10^{-3} M, and f) 5×10^{-3} M solutions. Insets show line profiles as indicated in the STM images. g) High-resolution STM image of covalent β -CD-HOPG graft. Insets show fast Fourier transforms of undistorted (lower) and distorted graphite lattice region (upper) following covalent grafting. Tunneling parameters: a–f) $I_{\text{set}} = 0.05$ nA, $V_{\text{bias}} = -0.9$ V; g) $I_{\text{set}} = 0.12$ nA, $V_{\text{bias}} = -1$ mV. h) Plot of grafting density versus β -CD-phenyldiazonium concentration. The grafting sites were averaged over 10 to 20 sample spots of 200×200 nm² each.

distortion. By contrast, in more remote regions (Figure 3g, lower white dashed square), the FFT only shows the hexagonal pattern of the HOPG lattice.

The grafting density from experiment to experiment showed some variation, estimated at 20%, which we ascribe to the chemically irreversible and far-from-equilibrium nature of the radical generation and grafting process, in line with previous work.^[23] The reproducibility of the grafting process may be further improved by titrating, using coulometry, the charge that is consumed in the electroreduction of the diazonium salt, instead of performing cyclic voltammetry for a fixed number of cycles.

While STM is helpful in investigating the grafting density on the surface, AFM is a reliable technique not only for obtaining the 2D surface morphology of the covalently grafted substrate, but also for determining the thickness of the grafted layer.^[23,24] The morphology of the bare HOPG surface is shown in Figure 4a, revealing the smooth basal planes and several step edges. After grafting from 2×10^{-3} M β -CD-phenyldiazonium and sonication in hot milli-Q water, hot DMSO and hot toluene, the surface shows high coverage by a roughly 1.7 nm thick layer, Figure 4b, suggesting monolayer thickness.

A more accurate thickness determination is possible by scratching through the layer with the AFM tip, yielding a height

of 1.9 ± 0.3 nm (see Figure S3, Supporting Information). The formation of multilayers was experimentally never observed and is also not expected for theoretical reasons. If we consider the structure of the cyclodextrin precursor (Scheme 1a), multilayer formation would require any of the following options: i) radical attack on the phenyl ring of an already-grafted β -CD; ii) hydrogen abstraction from an OH group, or iii) a CH group in one of the D-glucose units in β -CD, followed by dimerization of this radical with a nearby β -CD radical in solution. Option i) is excluded for steric reasons: once a β -CD is grafted to the HOPG surface, the phenyl linker is shielded from radical attack by the much larger β -CD suspended above it. For options ii) and iii), hydrogen abstraction in both cases would yield an extremely short-lived oxygen or aliphatic carbon radical. The second molecule to dimerize with the first radical needs to reach the short-lived radical by diffusion, which therefore becomes extremely unlikely.

Besides the AFM investigation on the grafted surface, we also studied various forms of ungrafted β -CD-aniline on HOPG. Figure 4c shows HOPG covered by a dropcast thick film of β -CD-aniline. Full coverage of the surface by a layer of at least 12 nm thick is observed, which can be partially removed after moderate rinsing with milli-Q water (Figure 4d). In

Figure 4. AFM images of a) bare HOPG; b) β -CD-HOPG grafted from 2×10^{-3} M solution after sonication in hot (100 °C) water, hot DMSO, and hot toluene (inset top right: zoom-in); c) drop-cast film of β -CD-aniline on HOPG before (inset top right: optical photograph) and d) after washing with milli-Q water; e) thin film of physisorbed β -CD-aniline on HOPG before and f) after ultrasonication in hot water, hot DMSO, and hot toluene. Insets show line profiles as indicated in AFM images.

Figure 4e, a thin physisorbed layer of β -CD-aniline on HOPG is visualized, with 1.7 nm thickness corresponding to monolayer height. Figure 4f shows that this physisorbed layer can be largely removed by sequential sonication in hot milli-Q water, hot DMSO, and hot toluene, leaving only very few residual clusters on the surface. This observation also underlines the high stability of grafted molecules compared to the physisorbed layer.

Following physical characterization of the grafted β -CD-HOPG, we now turn our attention to the electrochemical properties of this covalently modified surface. Ferrocene (Fc) is a redox compound with very low solubility in water that undergoes a one-electron oxidation reaction at moderate potentials, and is often employed as an internal standard and redox mediator in electrochemical measurements. Stable inclusion complexes can be formed between Fc and various CDs, including α -CD, β -CD, and γ -CD; the complex with β -CD is the most stable and has an association constant $K = 3.54 \times 10^4 \text{ M}^{-1}$.^[25,26] The oxidized form of Fc, the water-soluble ferrocenium cation Fc^+ , forms far less stable inclusion complexes with CDs than the neutral form due to loss of the hydrophobic driving force.^[26]

Figure 5a shows how electron transfer occurs in a coupled chemical–electrochemical process where the complex first dissociates (chemical process), followed by the redox reaction of free Fc or Fc^+ .^[26,27] The electrochemical behavior of Fc and its derivatives in the presence of β -CD in solution has been investigated extensively, and has shown that on addition of β -CD, the Fc redox behavior remains reversible while peaks shift to more positive potentials and peak currents substantially decrease due to the low diffusion coefficient of the inclusion complexes in solution.^[28] For β -CD immobilized on the electrode surface, such as in the present case, host–guest chemistry between Fc

and β -CD leads to an increase of the analyte's concentration in the vicinity of the electrode and to a concomitant increase of the redox signal.^[29,30]

Figure 5c shows the electrochemical behavior of $1 \times 10^{-3} \text{ M}$ Fc dissolved in a 1:1 (vol:vol) mixture of ethanol and 0.5 M H_2SO_4 on unmodified HOPG and β -CD-HOPG electrodes. On bare HOPG (black curve), Fc undergoes a reversible one-electron transfer process with a pair of peaks located at 198 and 279 mV, respectively, while on β -CD-HOPG (red curve), there is only a negligible enhancement of the peak current and a small positive shift of both redox peaks. However, in aqueous 0.1 M sulfuric acid solution, where the solubility of Fc was determined spectroscopically as $(4.25 \pm 0.02) \times 10^{-5} \text{ M}$,^[31] the β -CD-HOPG electrode yields a considerably enhanced response compared to bare HOPG (Figure 5d). Furthermore, the sensor displays an accumulation effect, in which the redox current of Fc increases over time (see Figure S5, Supporting Information), and excellent linearity over the entire concentration range up to saturation (Figure S6, Supporting Information).

Hexacyanoferrate(II/III) ($[\text{Fe}(\text{CN})_6]^{4-/3-}$) is a widely used water-soluble outer-sphere redox couple with reversible kinetics on many common electrode materials. Often, grafted layers display a barrier effect toward electron transfer of hexacyanoferrate,^[32] caused by the increased tunneling distance between electrode and redox species and the modification of the tunneling barrier.^[33] Figure 6a shows reversible redox behavior of $[\text{Fe}(\text{CN})_6]^{4-}$ on bare HOPG (black trace) and no blocking effect from a thin physisorbed film of β -CD-phenyldiazonium (blue trace). On the other hand, a high-density grafted layer shows strong blocking (red trace), as does a drop-cast film (12 nm) of β -CD-phenyldiazonium (purple trace). Simple washing with

Figure 5. a) Scheme explaining the chemical–electrochemical mechanism involved in the redox chemistry of the inclusion complex between Fc and β -CD. b) Structural formula of grafted β -CD-HOPG after inclusion of Fc. CV of bare HOPG (black traces) and β -CD-HOPG (red traces) in c) $1 \times 10^{-3} \text{ M}$ Fc in ethanol/0.5 M H_2SO_4 (v:v = 1:1), and d) saturated Fc in 0.1 M H_2SO_4 (aq). Scan rate for all curves, 100 mV s⁻¹.

Figure 6. a) CV in 1×10^{-3} M $K_4[Fe(CN)_6]$ of bare HOPG (black trace), HOPG modified with a thin film of physisorbed β -CD-aniline (blue trace), HOPG grafted from 2×10^{-3} M (repeatedly grafted 3 times) β -CD-phenyldiazonium (red trace), and 0.1×10^{-3} M β -CD-phenyldiazonium (dashed trace), HOPG modified with a drop-cast film of physisorbed β -CD-aniline before (purple trace) and after washing with milli-Q water (green trace). b) CV of bare HOPG (black trace) and of β -CD-HOPG (grafted three times from 2×10^{-3} M β -CD-phenyldiazonium) (red trace) in 1×10^{-3} M $K_4[Fe(CN)_6]$ saturated with Fc; CV of β -CD-HOPG in 1×10^{-3} M $K_4[Fe(CN)_6]$ only (purple trace). Supporting electrolyte in all measurements: 0.2 M Na_2SO_4 (aq). Scan rate, 100 mV s^{-1} .

water, however, partially removes the drop-cast layer and largely restores facile electron transfer (green trace). Low-density grafted films (from 0.1×10^{-3} M diazonium solution) partially block the electron transfer process (dashed curve), as reflected in a widened peak separation and reduced peak current density.

By combining the behavior of high-density grafted β -CD-HOPG toward Fc (enhancement) and hexacyanoferrate (blocking), we propose to use this modified electrode for electroanalysis of hydrophobic redox species in the presence of high backgrounds of interfering hydrophilic redox compounds, even with very similar redox potentials. Figure 6b shows the response of the bare and modified electrodes in saturated Fc ($\approx 10^{-5}$ M) in the presence of 1×10^{-5} M $[Fe(CN)_6]^{4-}$. On bare HOPG (black trace), the response is entirely dominated by the more abundant hexacyanoferrate, making the determination of Fc impossible. The grafted β -CD-HOPG (red trace), however, effectively suppresses the hexacyanoferrate redox

signal yet allows quantitative analysis of the Fc trace amount. To minimize the occurrence of graft-free areas (as grafting is a stochastic process) and achieve maximal selectivity against hydrophilic analytes, repeated grafting of the surface was sometimes necessary. The degree of blocking can conveniently be monitored from the residual current in hexacyanoferrate solution alone (Figure 6a).

Finally, we demonstrate the usefulness of the β -CD-HOPG electrode in the analysis of dopamine, an important neurotransmitter that has attracted intense efforts regarding sensor development.^[34] Figure 7b shows that bare HOPG in 100×10^{-5} M dopamine (black trace) yields a CV signal that disappears in the capacitive background. However, on β -CD-HOPG (red trace), the host-guest interaction between dopamine and β -CD (association constant $K = 95.06$ M $^{-1}$)^[35] leads to a substantial enhancement of the redox signal, with an oxidation peak current density of 5.4 μA cm^{-2} . The excellent sensitivity of 54 mA mm^{-1} cm^{-2} is

Figure 7. a) Dopamine inclusion and blocking with 1-AdCA of β -CD-HOPG. b) CV in 100×10^{-5} M dopamine on bare HOPG (black trace), β -CD-HOPG (red trace), and β -CD-HOPG after incubation in 1-AdCA (blue trace). Supporting electrolyte: 10×10^{-3} M PBS buffer (pH = 7.4). Scan rate, 100 mV s^{-1} .

an order of magnitude higher than the value recently reported for a 3D nitrogen-doped graphene/ β -CD electrode,^[30] and comparable to the highest sensitivity currently reported for any electrochemical dopamine sensor.^[36]

If desired, the redox enhancement functionality of β -CD-HOPG can be switched off by occupying the cavities of the β -CD moiety by a redox-inactive guest molecule with a higher association constant. On the β -CD-HOPG electrode, when the cavities of β -CD moiety are occupied by 1-adamantanecarboxylic acid (1-AdCA, blue trace) with an association constant of $K = 3 \times 10^4 \text{ M}^{-1}$,^[37] electrochemical signal enhancement of dopamine is switched off due to the formation of the more stable inclusion complex between β -CD and 1-AdCA. This further confirms that the redox enhancement effect is caused by the host–guest interaction between the grafted host and the solution-based electroactive guest. The decrease in double layer capacitance is caused by the insulating nature of the grafted layer.

3. Conclusions and Outlook

We have presented a simple and fast single-step method for grafting HOPG with β -CD by electrochemical reduction of its corresponding phenyldiazonium salt. The grafted layer simultaneously shields the electrode from high concentrations of analytes that cannot form complexes with the surface-immobilized hosts while boosting the redox signal from low concentrations of analytes that do form inclusion complexes, enabling the reliable determination of hydrophobic guest species against much higher interfering backgrounds of hydrophilic analytes, even with similar redox potentials. The sensor design also shows excellent sensitivity for the detection of dopamine at the nanomolar level, an order of magnitude higher than the state-of-the-art for a CD-based electrochemical sensor. The enhancement effect can be switched off by occupying the cavities of the host layer with electroinactive guest molecules.

The two unique features we have demonstrated for the covalently grafted β -CD-HOPG electrode (selective sensing of hydrophobic analytes and ultrasensitive dopamine detection) do not come at the expense of ease of preparation: the one-step covalent modification can be completed in minutes, using standard electrochemical cells and equipment. Also, the procedure uses robust, commercially available HOPG substrates that can be reused by mechanical exfoliation many times, lowering the operational cost and further increasing wide accessibility and attractiveness of our approach.

The fundamental reasons for the high performance of the sensor may be related to its simple and well-defined structure, in which all the sensing units (covalently attached β -CD moieties) are positioned uniformly and close to the collector surface (HOPG). This is achieved by the chemical characteristics of both reagent (a highly reactive, but sterically hindered diazonium compound, yielding monolayer modification exclusively) and substrate (low-reactive sp^2 carbon surface, requiring highly reactive radical reagents for its modification), resulting in negligible side reactions despite the simplicity of the approach. These principles, and the resulting sensor, can be taken as a proof of concept for entirely different sensors, e.g. using other

van der Waals solids as substrates, but based on analogous chemistries, or utilizing other supramolecular hosts (e.g., cucurbituril).^[38]

We anticipate that additional layers of selectivity, apart from the hydrophilic/hydrophobic discrimination demonstrated here, can be engineered into the sensing units in various ways:

By varying the size of the cavity (α -, β -, γ -CD),^[39] altering the physicochemical interactions between guest and host through synthetic modification of CD,^[40] or by pretreating the sensor with an agent with a chosen association constant, selectively blocking the sensor for analytes with lower association constants (as we demonstrated with adamantanecarboxylic acid).

Finally, the list of analytes that can be successfully detected by our sensor may be much longer than the few compounds tested here, and may include many toxins,^[41] metabolites,^[42] and drug molecules, for which cyclodextrin is currently used as an excipient (classified GRAS by the Federal Drug Administration).^[43] This property could potentially make for an excellent sensor to detect drugs in biological samples.

4. Experimental Section

All STM experiments were performed using an Agilent SPM system in constant-current mode. The ambient STM tips were produced by mechanically cutting Pt/Ir wire (80%/20%, diameter 0.25 mm). The bias voltage refers to the substrate. AFM measurements were performed in air with a Multimode AFM with a Nanoscope IV controller (Veeco/Digital Instruments) in tapping mode. HOPG substrates (grade ZYB) were obtained from Advanced Ceramics Inc., Cleveland, USA. STM and AFM data analysis was performed using Scanning Probe Image Processor (SPIP) software (Image Metrology ApS). Sample heat treatment was performed in a petri dish on a hotplate for 30 min, followed by cooling down before Raman measurements.

Raman measurements were performed with an OmegaScope 1000 (AIST-NT) with 632.8 nm He–Ne laser. The laser light was reflected by a long pass dichroic beam splitter (Chroma Technology Corporation, Z633RDC) and then was focused onto the sample surface through an objective (MITUTOYO, BD Plan Apo 100 $\times$, N.A. 0.7) with 500 kW cm^{-2} optical density at the sample surface. Raman scattering was collected and directed to a Raman spectrograph (HoribaJY, iHR-320) equipped with a cooled-charge coupled device (CCD) camera operated at -100°C (Andor Technology, DU920P) through the dichroic mirror, a pinhole and long pass filter (Chroma Technology Corporation, HQ645LP). All of the measurements were performed under ambient conditions.

Electrochemical measurements were performed using an Autolab PGSTAT101 potentiostat (Metrohm-Autolab BV, the Netherlands). The HOPG surface was freshly cleaved using scotch tape prior to each experiment. Voltammetry and grafting were performed in a lab-built single-compartment three-electrode cell, with HOPG as working electrode (geometric area 38.5 mm^2), Pt wire counter, and Ag/AgCl/3 M NaCl reference electrodes.

Chemicals and Solutions Preparation: Ultrapure water (milli-Q, Millipore, 18.2 $\text{M}\Omega \text{ cm}$, total organic carbon < 3 ppb) was used throughout. Sodium nitrite (99%, Sigma-Aldrich) was dissolved in ultrapure water to prepare a $0.1 \times 10^{-3} \text{ M}$ solution. Potassium hexacyanoferrate(II) trihydrate (99%, Sigma-Aldrich) was dissolved in aqueous 0.2 M sodium sulfate (99%, Sigma-Aldrich), ferrocene (98%, Sigma-Aldrich) was dissolved in 1:1 (by volume) of a mixture of ethanol (99.9%, Merck)/aqueous 0.5 M sulfuric acid (96%, Merck) to prepare $1 \times 10^{-3} \text{ M}$ solution or equilibrated with aqueous 0.2 M sodium sulfate or aqueous 0.1 M sulfuric acid to prepare saturated solutions. The saturated solution was filtered with filter paper (grade MN615 for qualitative analysis, Macherey–Nagel, Germany) before electrochemical measurements. Dopamine hydrochloride (98%, Sigma-Aldrich)

was dissolved in 10×10^{-3} M phosphate buffered saline (pH 7.4, Sigma-Aldrich). 1-Adamantanecarboxylic acid (99%, Acros Organics) was dissolved in ethanol. Electrolyte solutions were deoxygenated with argon (grade 5.0, Praxair) before use. β -CD was kindly donated by Wacker Chemie. Sodium hydroxide (98%) and bicarbonate (99%+) were purchased from Acros Organics, aminothiophenol (97%), *N,N*-Dimethylformamide (DMF), and acetone (both HPLC grade) from Sigma-Aldrich and hydrochloric acid (37%, reagent grade) from Fischer Scientific. The synthesis of β -CD-phenyldiazonium is described in full detail in the Supporting Information.

Electrode Preparation: Covalently grafted β -CD-HOPG: β -CD-phenyldiazonium solutions were prepared ex tempore by dissolving the desired amount in aqueous HCl (4.9 mL , 50×10^{-3} M) except for the cases of 2×10^{-3} M and 5×10^{-3} M (4.8 mL and 4.5 mL 50×10^{-3} M HCl, respectively) and adding aqueous NaNO_2 (0.1 mL 0.1 M solution, except for the cases of 2 and 5×10^{-3} M where respectively 0.2 and 0.5 mL 0.1 M NaNO_2 were added). The mixture was shaken for 30 s prior to injection into the electrochemical cell. After modification, the HOPG samples were rinsed with milli-Q water to remove the electrolyte and sonicated in hot (100°C) water, hot DMSO (99.5%, Sigma-Aldrich), and hot toluene (99.9%, Sigma-Aldrich), then rinsed with 10 mL of each of these three solvents to remove physisorbed material from the surface, and dried in an Ar atmosphere. For maximum coverage and minimal leakage current in the experiments with hexacyanoferrate, the grafting and rinsing/sonication sequence detailed above was repeated three times for each HOPG sample, using a 2×10^{-3} M β -CD-aniline solution. Drop-cast β -CD-aniline on HOPG: $100 \mu\text{L}$ of 1×10^{-3} M β -CD-aniline water solution was placed on freshly cleaved HOPG ($12 \text{ mm} \times 12 \text{ mm}$), covered by a petri dish and left to dry overnight in a fume hood. For rinsing experiments, 10 mL of milli-Q water was used, followed by drying of the sample in an Ar atmosphere. Physisorbed β -CD-aniline thin film on HOPG: Freshly cleaved HOPG was dipped into aqueous 1×10^{-3} M β -CD-aniline for 5 min , emersed and dried in an Ar atmosphere. 1-AdCA blocking of β -CD-HOPG: the HOPG electrode, after grafting from 2×10^{-3} M β -CD-phenyldiazonium solution, was immersed in ethanolic 1×10^{-3} M 1-AdCA for 30 min , emersed and rinsed with milli-Q water.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

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