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Carbon Dots as Nano-Organocatalysts for Synthetic Applications

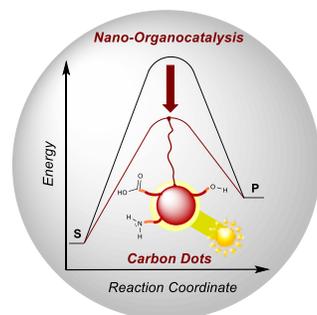
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ABSTRACT: Over the last decades, organic chemistry has taken a resolute step towards green catalytic synthesis. This tries to ensure efficient and sustainable base chemical production, while also safeguarding human health and environment. To this end, the development of novel, non-toxic and effective catalytic systems, capable of driving value-added chemical transformations in environmentally benign solvents (e. g. water) is highly desirable. Moreover, these new catalysts need to be metal-free, easy to prepare and potentially recyclable. Carbon dots, that are relatively new carbon-based nanoparticles, fulfil all these requirements owing to their outstanding physico-chemical features, thus emerging as promising nano-catalytic platforms. This Perspective highlights the recent advances in carbon dots synthesis and their applications in organic catalysis and photocatalysis, with particular attention to green non-metal-doped systems. Finally, forward-looking opportunities within this field are mentioned here.

1. INTRODUCTION

Carbon dots (CDs) are a new class of fluorescent carbon-based nanomaterials consisting of quasi-spherical nanoparticles, with dimensions smaller than 10 nm.^{1,2} Since the CDs family is fairly broad, it may be relevant to recall the classification and the nomenclature of these nanoparticles. Specifically, CDs can be divided into different subgroups depending on the nature of the nanostructures obtained during the synthesis. Namely, graphene quantum dots (GQDs), carbon quantum dots (CQDs), carbon nanodots (CNDs) and polymer-like dots (PDs).¹⁻⁵

GQDs are two-dimensional nanoparticles of one or few-layer graphene sheets, that are formed during the exfoliation processes of graphitic materials.⁶ Alternatively, quasi-spherical nanoparticles with a crystalline graphitic core, obtained by high-temperature thermal treatment ($T > 300^\circ\text{C}$) of suitable precursors, are called CQDs. The word “quantum” refers to nanostructures possessing delocalized band structures and sizes in the quantum-confined regime.⁷ Conversely, amor-

phous nanoparticles (obtained at lower temperatures) that do not show quantum confinement effects, but reveal excited states arising from molecular-like species, are called CNDs.^{2,3} Notwithstanding, discerning between CQDs and CNDs is often challenging since the relative contributions from the structure and the excitation states can be difficult to unravel. To this aim, it has been recommended to use the general term carbon dots (CDs) to describe all of the quasi-spherical carbon nanoparticles, including those with molecular-like behavior and delocalized electronic structure, as well as all the nanoparticles that span between CNDs and CQDs.^{2,3} Finally, polymer-like dots (PDs) are aggregated or cross-linked polymers prepared from linear polymers or monomeric precursors. Their carbon core and the connected polymer chains can self-assemble to form the final PDs.⁸

Generally, CDs consist of carbon cores that can be surrounded by shells containing numerous polar groups such as carboxylic acids, alcohols and amines.¹ The nature of these heteroatom functionalities arises from the precursors and the operative conditions employed in the CD synthesis. Important-

ly, these surface groups play a pivotal role in determining the overall chemical behavior of the whole nanoparticles.^{1,4,5} In fact, the surface features control the interaction of the CDs with the surrounding environment in terms of reactivity, recognition/binding, solvation, redox properties and material processability.^{9,10} Moreover, CDs have been found to have excellent optical and luminescence properties, considerable solubility in polar solvents (including water), high chemical and photo-stability, as well as low toxicity and excellent biocompatibility.^{1,4}

These characteristics have generated a broad, interdisciplinary research interest, spanning over chemistry, materials science, biology and medicine.¹¹ Consequently, since their discovery in 2004,¹² CDs have found numerous applications in optoelectronic devices, functional materials, catalysis, agriculture, bioimaging, sensors and drug delivery.^{1,4,5,11,13–15} The ever-growing popularity of these nanoparticles is also substantiated by their fast and facile preparation from economic raw materials (including natural renewable sources or waste), their scalability for large-scale productions and their tailorable surfaces.^{1,16} Furthermore, specific precursors/additives, including heteroatom-containing species or metal complexes, can be used to fine tune the properties of CDs to make them ideal for a wide range of applications.^{4,5,17} Indeed, the luminescence, redox properties and chirality of CDs can be controlled at least to some extent with a proper choice of the molecular precursors.²

Among the above mentioned areas of application of CDs, catalysis and photocatalysis are extremely appealing fields for chemists. Indeed, catalysis is a well-established tool broadly employed for designing and developing novel chemical processes, including organic transformations and artificial photosynthesis.^{18–22} Specifically, the presence of reactive surface groups on light-absorbing CDs have paved the way to new catalytic possibilities, enabling the preparation of valuable organic compounds under mild operating conditions by means of classical polar or (light-driven) radical reactivities.^{5,18,23–26} Similarly, these superficial groups on photoactive CDs have also facilitated applications related to energy, such as the generation of solar fuels through water-splitting, CO₂ or oxygen reduction.^{27–32} CDs are therefore emerging as promising nanocatalytic platforms that fulfil the sustainability requirements of non-toxic, water-compatible, readily available and potentially recyclable catalysts for green chemical production.^{16,33} This has resulted in an ascending interest, both academic and industrial, in CD-catalyzed synthetic routes. This is reinforced by the ever-increasing pressure on the chemical industry for a rapid swing to new sustainable synthetic routes to access chemicals of widespread use.^{33–36}

However, recent review articles solely report the use of metal-doped CDs or composite nanohybrids in organic synthesis (especially photo-oxidation and reduction of simple substrates), or for solar fuel production.^{1,4,5,14–16,25,30–32} On the other hand, the utilization of green non-metal-doped CDs in catalysis has not been reviewed until now. This Perspective is primarily geared towards critically highlighting the advances in the preparation of CDs and their application in organo- and photocatalysis, namely acid-base catalysis, hydrogen bond catalysis, aminocatalysis and photoredox catalysis for synthetic purposes (Figure 1). Additionally, future prospects offered by

this thriving research field will be proposed in order to help address the current dilemmas in organic synthesis.

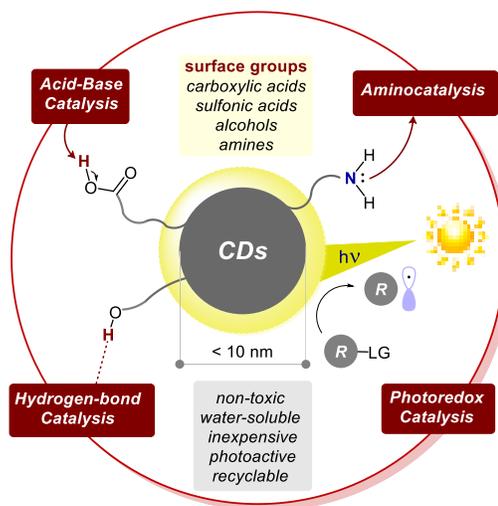


Figure 1. CD application in nano-organocatalysis and photocatalysis. LG = leaving group.

2. SYNTHESIS AND PROPERTIES

2.1. Synthesis of CDs and Doped-CDs. The two main preparation methods of CDs consist of “top-down” and “bottom-up” approaches, starting respectively from bulk materials or molecular precursors.^{37,38} In the “top-down” approach, CDs are typically obtained by breaking down larger carbon-based structures (graphite, nanotubes, etc.) through chemical or electrochemical oxidation, arc discharge, laser ablation, acidic exfoliation or ultrasonic procedures.³⁸ Despite the possible large-scale production, this methodology presents several drawbacks due to harsh conditions, long reaction times and high cost of the required starting materials.^{4,39}

On the other hand, the “bottom-up” approach refers to the carbonization, pyrolysis or hydrothermal/microwave treatment of small organic molecules or natural biomasses to afford CDs. These approaches are generally greener, simpler and cheaper when compared to “top-down” methods. In addition, “bottom-up” synthetic routes typically lead to the production of CDs with well-defined sizes and shapes. This level of control, combined with the possibility of easily introducing doping with different heteroatoms, allows the production of tailored doped-carbon nanoparticles.^{4,5,15}

Specifically, heteroatoms such as oxygen, nitrogen, sulphur, phosphorous, boron, etc., can be easily incorporated into the CD structures by using suitable heteroatom-rich precursors (e.g. amino acids, amines, thiols, phosphonates, borates, etc.).¹⁷ The resulting doped-CDs, which may bear numerous reactive functionalities on their surfaces, typically display enhanced solubility in polar solvents and can be prone to catalytically activate a variety of specific substrates for synthetic purposes. For all these reasons, the “bottom-up” approach is usually the preferred route for preparing catalytically active carbon nanoparticles.^{25,26,40–42} Besides, it has been shown that hetero-doping may enhance the photophysical and electronic

features of CDs, by generating new energy levels and promoting radiative combination, therefore facilitating the process of designing and customizing of effective nanostructured photocatalysts.^{1,4,5}

One of the most important examples of doping is the widely investigated nitrogen incorporation, leading to the preparation of *N*-doped-CDs. These nanoparticles possess longer wavelength absorption and emission, higher fluorescence quantum yield (QY) and more tailorable electronic features than the non-doped CDs.⁵ These improvements can be attained by simply combining nitrogen-rich compounds (e.g. alkyl amines, amino acids or urea) to the carbonaceous source during the synthetic process.¹⁷ In addition, the use of either transition metal salts (e.g. Au, Ag, Co, Cu, Zn, etc.) or metal nanoparticles can be usefully employed as doping agents.^{1,4,5} The use of these dopants leads to production of nanoparticles with excellent physicochemical properties, that are caused by the intrinsic traits of the employed metal.⁵ However, the presence of precious or potentially toxic metals in CDs may undermine the sustainability and safety of their end-use.⁴³⁻⁴⁵ This Perspective is therefore primarily oriented to non-metal-doped nanocatalytic systems.

Another noteworthy modification of CDs is the encapsulation into host materials in order to form composite nanohybrids. To this aim, metal-organic frameworks (MOFs) and mesoporous silica have been used to embed CDs into a porous structure to capitalize on the properties of both host and guest materials for detecting analytes.⁵ Following an alternative approach, the covalent or non-covalent post-synthetic modification of CD surface with suitable chemical systems may open up new opportunities.² As an example, the use of either electron donor or acceptor motifs in combination with CDs has allowed the design of novel charge-transfer systems.^{2,46-51} Nevertheless, the formulation of nanohybrid-based CDs may be challenging, and their concrete application remains fairly rare.⁵

In all preparative procedures of CDs, the crude reaction is typically contaminated with unreacted substrates, by-products and side-products, which could span from small molecules to large carbon particles. In order to reach the purity levels required for many applications, including catalysis, purification is crucial to remove the undesired species through methods such as filtration, dialysis, gel filtration, high-performance liquid chromatography, gel electrophoresis, etc.^{1,46,52,53}

2.2. Properties and Characterization. The characterization of the purified CDs is a matter of paramount importance. Indeed, both the mapping of the surface groups and the assessment of chemical and optical properties of the materials can allow for specific applications. It is noteworthy to recall that the exact chemical structure of most, if not all, CDs remains unclear because of the unknown nature of their formation mechanisms and their difficult structural analysis.¹

Nonetheless, some basic information can be derived from specific techniques routinely carried out in all laboratories. For instance, the crystalline structure of graphitic CDs may be distinguished from amorphous CDs by using transmission electron microscopy (TEM) or Raman spectroscopy.^{1,4} The dimensions of the carbon nanoparticles can be determined by atomic force microscopy (AFM), dynamic light scattering (DLS) or

by TEM.^{2,54} In addition, optical spectroscopy is normally employed to study the electronic properties of CDs, via their UV-Vis absorption or photoluminescence (PL). Indeed, most CDs show a strong absorption centered in the UV region with a tail extending into the visible region (π - π^* or n - π^* transitions) which varies depending on the CD nature and preparation.⁵⁵⁻⁵⁷

More importantly, the vast majority of the CDs have a peculiar PL which involves a strong blue emission, that rapidly declines in the red region, generally characterized by dependence from excitation wavelength.^{2,17,58} This PL can consist of piezochromic fluorescence, phosphorescence and up-conversion.^{1,57} Usually, PL properties rely on the intrinsic nature of the CDs and their surface state, the presence of conjugated motifs in the core, quantum confinement effects, emissive traps and other factors. Nevertheless, the currently PL mechanism remains unclear.⁵⁹ However, the resulting fluorescence quantum yield (QY) of CDs depends on the precursors and the doping agents used in their fabrication, ranging up to more than 90% in solution.^{1,59,60} The PL of CDs can be effectively quenched by either electron donor or acceptor species through the formation of charge-transfer systems, paving the way for photocatalytic applications in organic synthesis and solar fuel production.^{25,26,30,31,61,62} Precisely, upon light absorption, the photoexcited CDs are able to undergo single electron transfer processes with a variety of organic or inorganic substrates, thus allowing photocatalysis.^{13,32,62-65}

Aiming at a systematic development of all of these chemical processes, it is imperative to identify the typology and the amount of catalytically active functionalities on the CD surface. Therefore, as an example, amino groups can be detected by X-ray photoelectron spectroscopy (XPS) and quantified by Kaiser test (KT) or by nuclear magnetic resonance (NMR) upon the formation of covalent adducts (e.g. imines).^{2,46,66} Conversely, the carboxyl and hydroxyl groups can be recognized by infrared spectroscopy (FT-IR) and quantified by acid-base or conductometric titrations.^{40,67-69} Furthermore, the surface group density and the pyrolytic behavior of CDs at high temperatures may be roughly valued by thermogravimetric analysis (TGA), correlating the mass loss at a certain temperature to the uniformity of functionalities on the CDs surface.^{70,71} With all of these pieces of information in hand, it becomes feasible to figure out the range of catalytic use of the considered CDs, and ultimately to estimate the catalytic loading with respect to the referred functional groups.

Finally, as previously anticipated, a further remarkable feature of CDs is the high dispersibility in polar solvents, including water, due to the presence of hydrophilic groups on their surface. This is of practical importance for most of the biologically and environmentally benign applications of CDs,^{41,72} thank also to the existence of degradation and removal pathways from the organism.^{73,74} Despite this, it should be cautioned that measurable toxicity might be reported for certain CDs at high concentrations or in the presence of light, through the generation of reactive oxygen species.^{4,73,74}

3. APPLICATIONS IN NANO-CATALYSIS

The physicochemical features of CDs make them promising platforms for green and sustainable synthetic catalysis. The following sections will explore the recent advances within the

fields of both polar and light-driven radical organic transformations, promoted by non-metal-doped CDs catalysts.

3.1. CDs as Nano-Organocatalysts. Over the last decades, organocatalysis has attained an extraordinary usefulness in synthetic chemistry.^{18,75–77} Among the many branches within this field, this Perspective will focus on those cases where CDs can exert an effect owing to their surface functional groups. In particular, acid-base catalysis, hydrogen bond catalysis and aminocatalysis will be considered.

Acid-base catalysis and, specifically, Brønsted acid catalysis employs a protic acid to enhance the electrophilicity of a substrate towards a nucleophilic reagent.⁷⁸ CDs bearing carboxylic acids on their surface can act as Brønsted acid catalysts in various organic transformations. Indeed, Sarma and co-workers reported the synthesis of biologically relevant aza-Michael adducts **3** and dihydro/spyro/glycol quinazolinones **6** by exploiting the surface acidity of CDs-**1** catalysts displaying carboxyl functionalities (Figure 2).⁴⁰ These carbon nanoparticles were obtained from β -carotene through a hydrothermal treatment in water at 180°C over 3 h under air, followed by filtration, affording spherical carbon nanoparticles with size in the range of 3.5–5.5 nm (determined by TEM and AFM). Despite the nanomaterial precursor did not contain any oxygen atom, the superficial -COOH groups were generated during the carbonization process in the presence of water and air (concentration of carboxylic groups calculated to be 145 $\mu\text{mol/L}$, determined by acid-base titration of 2.5 mg of CDs-**1**, Figure 2a).

The described CDs-**1** were able to drive aza-Michael reactions between amines **1** and electron-deficient α,β -unsaturated compounds **2** in water at room temperature. The condensations proceeded in the order of minutes in good yields (up to 94% yield of **3**) and with low catalyst loading (0.5 mg/mL CDs-**1**), while the background reactions in absence of CDs-**1** required almost an hour (Figure 2b).

Moreover, the authors found the inherent acidity of CDs-**1** surface capable of promoting condensation reactions between carbonyl compounds **4** and 2-aminobenzamides **5** in a mixture of water/acetonitrile as solvent at 40°C to afford the corresponding quinazolinones **6** (up to 97% yield, Figure 2c), using the same catalyst loading (0.5 mg/mL CDs-**1**). In a plausible mechanism, the authors proposed the initial protonation of the carbonyl substrates **4** by the action of -COOH functionalities on CDs-**1** surface, followed by the nucleophilic attack of the amino reagents **5** and subsequent intramolecular cyclization to give the desired products **6** (Figure 2d). Lastly, the reusability of the catalyst was demonstrated for both the model transformations for at least three cycles, without any significant detriment on the yield of the products. The CDs-**1** recycling procedure involves the simple reusing of the aqueous layer after an extractive work-up, confirming the green approach of the system.

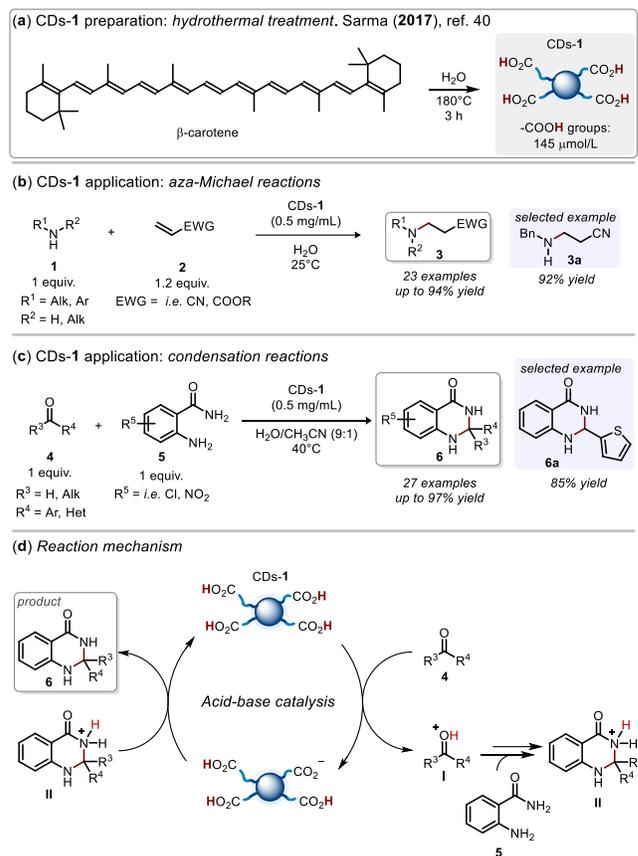


Figure 2. (a) CDs-**1** preparation from β -carotene through a hydrothermal treatment in water. (b) CDs-**1** application in aza-Michael reactions. (c) CDs-**1** application in condensation reactions. (d) Simplified reaction mechanism via acid-base catalysis, described in ref. 40.

Hydrogen bond catalysis is an alternative route to activate electrophiles by the formation of a hydrogen bond network between the proton donor and the acceptor, represented by the organocatalyst and the electrophilic reaction substrate, respectively.⁷⁹ CDs bearing hydroxyl groups on their surface can act as hydrogen bond catalysts in nucleophilic addition reactions towards the appropriate electrophiles.⁸⁰ In fact, Sing, Jang and co-workers described the synthesis of pharmaceutically relevant *4H*-chromene derivatives **10** employing CDs-**2** in micelles, as proton donor species in water (Figure 3).⁷⁰ These carbon nanoparticles were prepared by autoclave pyrolysis of an aqueous solution of citric acid at 160°C over 6 h under air and purified through centrifugation followed by dialysis against water. The obtained CDs-**2** were classified as CQDs, showing an average size range of 7.5 nm (determined by DLS) and a high density of hydroxyl and carboxyl functionalities on the surface of the nanomaterial (evaluated by TGA). CDs-**2** were then incorporated into micelles formed by imidazolium-based ionic liquids (**L**) in water. The resulting hybrid systems CDs-**2-L**, having dimensions of 27–32 nm by DLS, were able to trap organic reactants in their interior cavity where the reactions take place (Figure 3a). In this way, mixing naphthols **7**, benzaldehydes **8**, malononitrile **9** in the presence of a stoichiometric amount of CDs-**2-L** in water, the corresponding *4H*-

chromene derivatives **10** were obtained under sonication at room temperature (up to 99% yield in 15 min, Figure 3b). A series of control experiments confirmed the crucial role of both micelles and proton donor catalyst CDs-2. Indeed, the exclusion of the ionic liquids **L** or CDs-2 from the reaction mixture provided lower yields of **10** (below 47%).

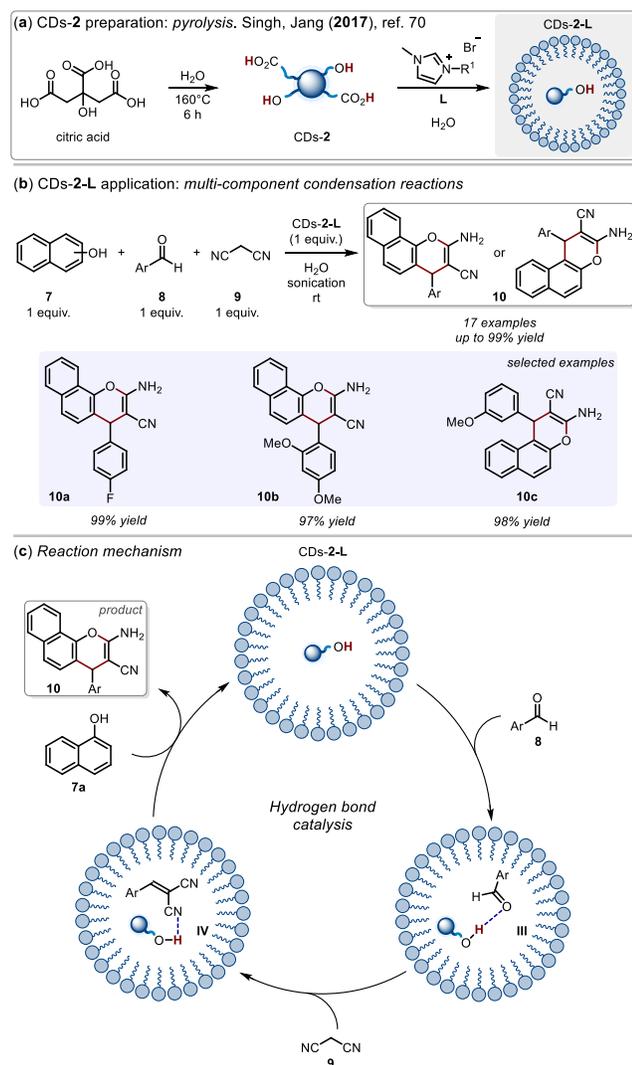


Figure 3. (a) CDs-2 preparation from citric acid through pyrolysis in water followed by incorporation into micelles to afford the hybrid catalysts CDs-2-L. (b) CDs-2-L application in multi-component condensation reactions. (c) Simplified reaction mechanism via hydrogen bond catalysis for the substrate **7a**, described in ref. 70.

The authors suggested a mechanism where the organic reagents are gathered into the hydrophobic cavity of CDs-2-L (Figure 3c). Thus, CDs-2 activate benzaldehydes **8** through hydrogen bonding by means of the polar groups on their surface (III), accelerating the nucleophilic attack of malononitrile **9**. The same proton donor catalysts further trigger the reaction of the corresponding condensation intermediate IV with naphthols **7** to give the products **10** (Figure 3c, referred to 1-naphthol).

Finally, the recyclability of the hybrid catalytic system CDs-2-L has been verified over ten cycles without important loss in

reactivity. The recovery procedure envisaged the separation of products **10** from the reaction mixture followed by concentration of the liquid fraction containing CDs-2-L to the initial critical micellar concentration. According to the authors, the described methodology is green, since it leads to high yields in non-toxic solvent and it involves a recyclable hybrid catalyst and an easy work-up.

Aminocatalysis is one of the most important branches of organocatalysis. It employs primary and secondary amines to activate the functionalization of carbonyl compounds.⁷⁵ CDs carrying amino groups on their surface are capable of driving catalytic aldol-type reactions on suitable carbonyl substrates.

For instance, Wang and co-workers reported the use of amine-terminated CDs-3 to catalyze Knoevenagel condensation reactions in a biphasic mixture of water and 1-octanol (Figure 4).⁴¹ These carbon nanoparticles were prepared by pyrolysis of a mixture of citric acid and suitable diamines in 1-octanol at 180°C (over 6 h) under argon and purified by washing with water (to remove the unreacted precursors). These CDs-3 possess aliphatic primary, secondary or tertiary amines on their surface, according to the nitrogen-rich precursor added, and they display an average particle diameter of 5.5 nm (determined by TEM). The density of surface amino groups on CD-3 ranged between 2.79 to 4.06 μmol/g, calculated by TGA and XPS (Figure 4a). CD-3 were able to carry out Knoevenagel condensations between benzaldehydes **11** and malononitrile **9** in a mixture of 1-octanol and water at 45°C to afford the related benzyldene malononitriles **12** (up to 95% yield in 4 h) in low catalytic loadings (0.14 g/L, Figure 4b). The authors demonstrated that carbon nanoparticles bearing primary amines are more efficient in promoting condensation reactions than those holding secondary or tertiary amines (95%, 81% and 75% yield of **12**, respectively).

A key peculiarity of the described catalytic system has implicated the presence of a phase transfer mechanism enabled by a biphasic medium made of 1-octanol and water and the rational use of CO₂. Initially, reagents **11** and **9** and the catalysts CDs-3 were solubilized in the organic phase, while the products **12**, formed over the reaction time, remained suspended. Then, CDs-3 could be transferred into the aqueous phase upon bubbling CO₂, due to the formation of ammonium carbamate and bicarbonate on their surface. Subsequently, products **12** were collected by filtration, while the presence of CDs-3 in 1-octanol was restored by removing CO₂, through N₂ bubbling. Once new reactants were added to the system, the same reaction occurred again, thereby achieving a bright methodology to recycle the organocatalysts.

Following this procedure, the authors proved the reusability of CDs-3 for at least six runs without significant impact in terms of yield of **12**. This, together with a green reaction system and a simple work-up, make the overall process attractive from the point of view of sustainability. Although not discussed in the original article, the mechanism of the Knoevenagel condensation likely proceeds via the generation of the anion V by deprotonation of malononitrile **9** by CDs-3. The condensation of benzaldehydes **11** gives the electrophilic intermediates VI, which undergo nucleophilic addition from anion V. Lastly, the intermediates VII decompose to afford the products **12** and the regenerated catalyst CDs-3 (Figure 4c).⁸¹

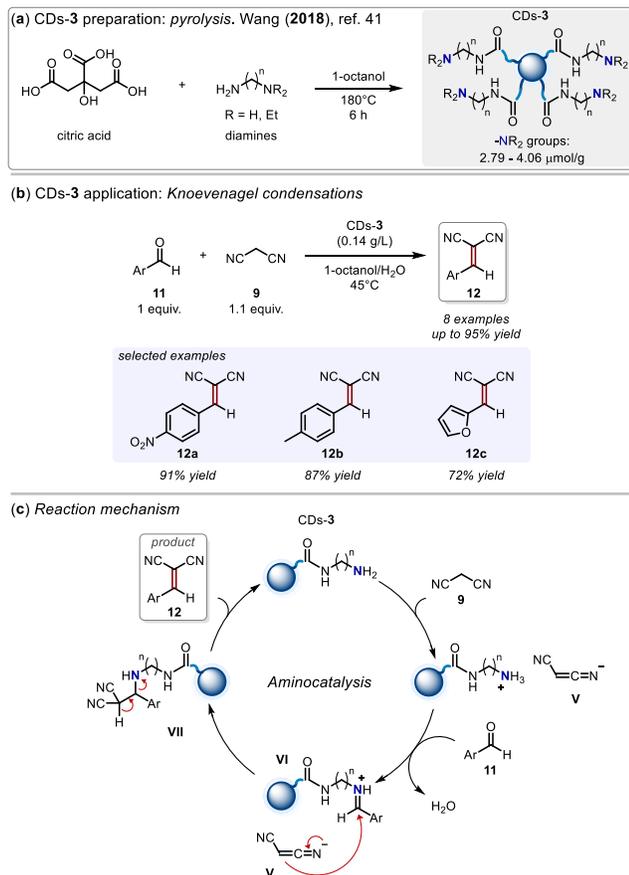


Figure 4. (a) CDs-3 preparation from citric acid and diamines through pyrolysis in 1-octanol. (b) CDs-3 application in Knoevenagel condensation reactions. (c) Proposed reaction mechanism for ref. 41, via aminocatalysis for CDs-3 bearing primary amino groups.

As a further development, the primary amine functionalities present on the surface of the CDs could also serve as catalysts for the functionalization of a variety of sterically hindered carbonyl compounds through enamine or iminium ion activations, respectively.⁸² Enamine activation (HOMO-raising, highest occupied molecular orbital) accounts for the direct α -functionalization of saturated carbonyl compounds in the presence of a suitable electrophile.⁸³ Conversely, iminium ion catalysis (LUMO-lowering, lower unoccupied molecular orbital) represents a reliable way for the catalytic introduction of a nucleophile at the β position of α,β -unsaturated enals and enones.^{84,85} These unprecedented activation modes for CDs can pave the way for the implementation of a wide diversity of synthetically relevant nano-organocatalyzed transformations. In this regard, an investigation to establish both the nature and the reactivity of the main amine structural motifs on CDs is critically important. Studies in this direction are currently undergoing in our laboratories.

3.2. CDs as Nano-Photocatalysts. Nowadays, photochemistry is an established field in synthetic organic chemistry, particularly by means of photoredox catalysis.^{20,86-92} Indeed, chemical and pharmaceutical industries have shown a growing interest in photocatalysis for their production, confirming that

it is no longer strictly an academic field of research.⁹²⁻⁹⁴ Furthermore, photoredox catalysis provides green opportunities for both fundamental and applied investigations, through improved energy efficiency, atom economy and sustainability.³⁶ As illustrated in the previous sections, this is an important social need. To this end, CDs can serve as prominent green photocatalytic platforms for light-driven transformations in organic chemistry. In this section we will explore a variety of photo-reactions driven by the photochemical activity of non-metal-doped CDs. In particular, since photo-oxidations and reductions of simple organic substrates have already been extensively reviewed,^{4,5,25} C-C and C-X bond forming -or cleavage- reactions will be considered, due to their synthetic convenience.

One of the first examples was reported by Liu, Kang and co-workers.⁸⁰ These authors described photoenhanced aldol condensation reactions triggered by CDs-4 as photocatalysts under light irradiation (Figure 5). These carbon nanoparticles were prepared by electrochemical ablation of graphite in water (30 V for 120 h) and purified by filtration and centrifugation (Figure 5a). The so-obtained water-soluble CDs-4 were classified as CQDs, possessing a uniform-dispersed diameter centered at 5 nm (determined by TEM). Despite the pure carbon composition of the precursor, CDs-4 show the presence of hydroxyl and carboxyl groups on their surface (detected by FT-IR), formed during the synthesis in water. The quantification of these functionalities has been obtained through acid-base titration, resulting in a total concentration of 10.1 $\mu\text{mol/g}$. Moreover, the relative content of -OH and -COOH groups was ascertained by conductometric titration and estimated to be 10:1, respectively.

The consequent optical properties of CDs-4 were characterized by a broad absorption from the UV to the visible region. A bright wavelength-dependent PL centered at 500 nm was observed, which can be quenched by electron-donors such as anilines, demonstrating the electron-acceptor features of these nanoparticles. Therefore, CDs-4 were able to carry out photo-enhanced aldol condensations between α -enolizable ketones **13** and aromatic aldehydes **14** under visible light irradiation (Xe lamp, $\lambda > 420$ nm, 300 W). The corresponding α,β -unsaturated compounds **15** were obtained in good yield (up to 89% in 24 h), even if a relatively high loading of CDs-4 was required (30 mg/mL) as well as the superstoichiometric use of ketone substrates **13** (used as solvent, Figure 5b).

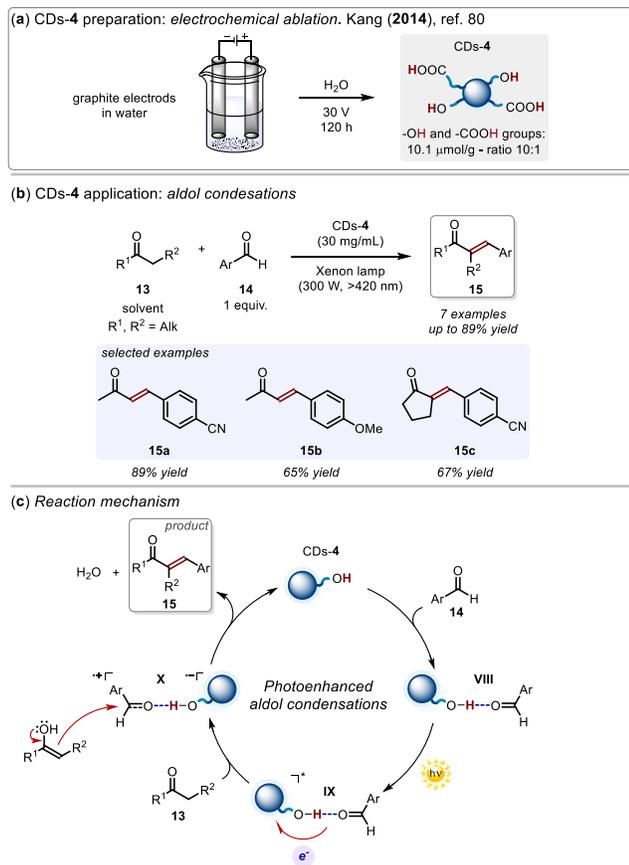


Figure 5. (a) CDs-4 preparation from graphite electrodes through electrochemical ablation in water. (b) CDs-4 application in photoenhanced aldol condensations. (c) Simplified reaction mechanism for CDs-4 bearing hydroxyl and carboxylic groups, described in ref. 80.

On the contrary, the utilization of hydroxyl group-free CDs cannot drive the aldol reaction, consequently verifying the catalytic activity of these functionalities. In all the experiments performed with CDs-4, visible light irradiation drastically enhanced the reactivity, producing better yields of **15** than in the dark. The authors attributed this improvement to a more efficient hydrogen bond catalysis operated by light-excited CDs-4 with respect to the related ground state nanoparticles. In fact, the effective electron-accepting properties of CDs-4 allow the reinforcement of the O–H bonds upon photoinduced electron transfer from the O–H···O region to the CDs-4 core. As a consequence, the carbonyl bond of aldehydes **14** was further activated, thus accelerating the aldol condensation.^{95,96} Hence, the proposed reaction mechanism may involve the formation of the hydrogen-bonded complex **VIII** between CDs-4 and aldehydes **14**. Then, upon light absorption (**IX**) and photoinduced electron transfer, the activated species **X** can undergo attack by ketones **13** (in their enol form) to yield the corresponding products **15** (Figure 5c). Finally, the recyclability of CDs-4 was assessed over five catalytic cycles without any loss of reactivity, recovering the nanostructured photocatalysts by centrifugation.

In a similar case study, MacFarlane and coll. reported the use of sulfonated CDs-5 as a photo-switchable acid catalyst for ring-opening reactions (Figure 6).⁹⁷ Similar to the previous example, the physicochemical properties of the CDs can be

altered upon light irradiation, in this case their acidity. The carbonaceous core of CDs-5 was prepared by electrochemical ablation of graphite rods in water (15–60 V for 6 days), then purified by filtration and centrifugation. The sulfur decoration was then introduced using sulfuric acid in water (1:1 v/v, 60°C for 24 h) to afford CDs-5, which bear hydrosulfate groups on their surface (Figure 6a). The obtained nanoparticles were classified as water-dispersible CQDs, having a spherical shape and size in the range of 2–9 nm (determined by TEM). The presence of –SO₃H groups on CDs-5 surface was demonstrated by FT-IR and energy-dispersive X-ray (EDX) spectroscopy. The sulfur content was quantified by elemental analysis (1.97 wt%), albeit no further information regarding the surface concentration of these functionalities was provided by the authors.

CDs-5 showed intense PL centred at 560 nm (upon excitation at 485 nm), which can be efficiently quenched by electron-donors in solution (e.g. anilines), demonstrating the electron-acceptor nature of these sulfonated carbon nanoparticles. Thus, CDs-5 were employed to drive ring-opening reactions of styrene oxide **16** in methanol under visible light irradiation (Xe lamp, $\lambda > 400$ nm, 450 W). The corresponding product **17** was obtained in high conversion and selectivity in the order of minutes (up to 98% conversion, up to 98:2 ratio of product **17** to side-product **18**), employing a low catalytic loading of CDs-5 (0.5 mg/mL, Figure 6b). Conversely, non-doped CDs or molecular carboxylic acids were not able to carry out the reaction, even in presence of light, confirming the catalytic role of the hydrosulfate groups.

On the other hand, the ring-opening reaction was significantly improved by shining light, versus those performed in the dark, when CDs-5 were used as catalysts. The authors assigned this enhancement to a more efficient acid catalysis operated by light-excited CDs-5 than the related ground state nanoparticles. Indeed, the authors inferred that a photoinduced electron transfer process from the hydrosulfate groups to the electron-acceptor CDs-5 core, ensures charge delocalization across the carbon atom lattice, which finally translates into an increased acidity of these functionalities. Essentially, the pH of an aqueous solution of CDs-5 (0.5 mg/mL) decreases in response to light exposure and is restored to the original value when the light is turned off. Therefore, the suggested reaction mechanism may involve the photo-assisted protonation of epoxide **16** by CDs-5, followed by the ring-opening reaction upon methanol addition. The ultimate deprotonation of the resultant intermediates **XII–XIII** provides the compounds **17–18** (Figure 6c). Finally, the recyclability of CDs-5 was evaluated over three consecutive runs, giving almost identical catalytic results. The photocatalysts recovery was carried out by filtration and centrifugation.

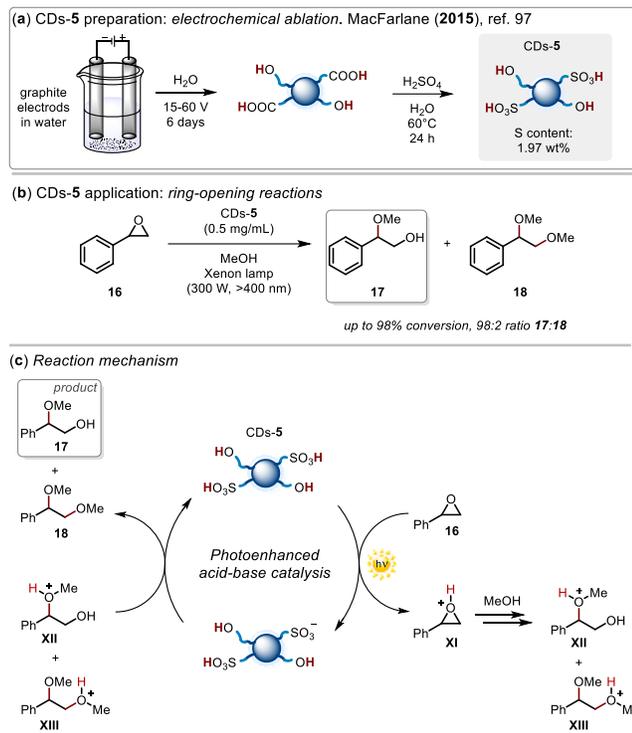


Figure 6. (a) CDs-5 preparation from graphite electrodes through electrochemical ablation in water. (b) CDs-5 application in photo-enhanced acid-base catalysis. (c) Proposed reaction mechanism for ref. 97 for CDs-5 bearing hydrogensulfate groups.

Another example of using S-doped-CDs was reported by Sarma and co-workers. They described photoinduced cross-dehydrogenative coupling reactions taking advantage of the surface acidity and the photochemical properties of sulfonated CDs-6 (Figure 7).⁹⁸ The core of these carbon nanoparticles was prepared by microwave-assisted carbonization of glucose in oleic acid at 180°C for 7 min and purified by extraction and dialysis against water. Then, the sulfate functionalities were introduced by treating the material with fuming sulfuric acid (at room temperature for 72 h, under nitrogen atmosphere). The final CDs-6 was isolated by centrifugation and purified by washing with water and ethanol (Figure 7a).

The resulting nanoparticles had an average diameter in the range of 3.2 ± 1.5 nm (determined by TEM). The presence of -OSO₃H groups on CDs-6 surface was demonstrated by FT-IR and quantified by acid-base titration (on 5 mg of CDs-6), confirming their surface acidity. These functionalities turned out to be present at concentration of 400 $\mu\text{mol/L}$ on the surface, while the amount of -OH and -COOH groups was found to be 3.5 and 1.25 times higher, respectively. Furthermore, CDs-6 showed excitation-dependent emission properties centred at 424 nm (upon excitation at 300 nm), which can be quenched in the presence of either electron acceptor or electron donor molecules in solution (e.g. 2,4-dinitrotoluene or *N,N*-diethylaniline). In addition, an optical band gap of 2.55 eV was evaluated by Kubelka–Munk-transformed reflectance spectrum, corresponding to a LUMO at -0.68 V and a HOMO at +1.87 V vs. saturated calomel electrode (SCE). These data show the dual photo-oxidizing and reducing nature of CDs-6.

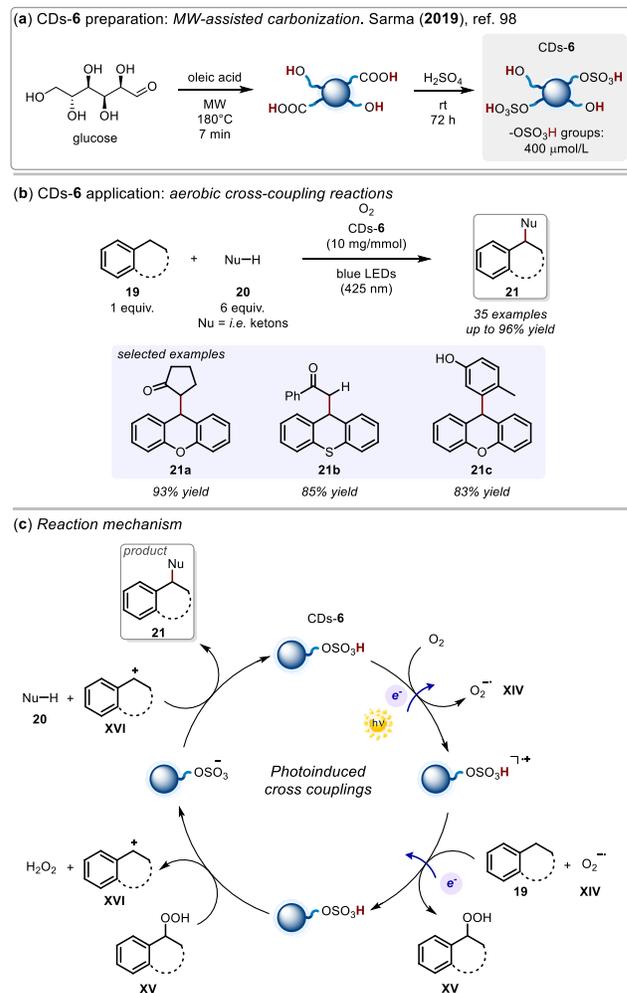


Figure 7. (a) CDs-6 preparation from glucose through MW-assisted carbonization in oleic acid. (b) CDs-6 application in photoinduced cross coupling reactions. (c) Simplified reaction mechanism for CDs-6 bearing sulfate groups, described in ref. 98.

Thus, CDs-6 were employed to carry out aerobic cross-coupling reactions between benzyl hydrocarbons **19** and nucleophiles **20** (including ketones and arenes) under blue light irradiation (425 nm, 34 W). The corresponding coupling products **21** were afforded in high yield (up to 96% in 12 h) under solventless conditions and oxygen environment, using a low catalytic loading of CDs-6 (10 mg/mmol with respect to **19**, Figure 7b). Performing the reactions in the dark as well as in the absence of the catalyst or oxygen provided the products **21** in very low yield (below 31%), even upon heating at 70°C, confirming the photocatalytic role of CDs-6. In addition, the use of molecular acids or other carbon-based nanomaterials (e.g. graphene oxides) gave comparably poor results, endorsing the involvement of the sulfate groups on CDs-6 surface in the reactivity.

Accordingly, the authors proposed a reaction mechanism involving the initial photo-reduction of molecular oxygen to superoxide radical anion **XIV** by CDs-6. Then, upon addition to the substrates **19** at the benzylic position, the resulting hydroperoxide intermediates **XV** were generated. The following release of hydrogen peroxide, facilitated by the surface acidity of CDs-6, gave the stabilized carbocation **XVI**. Finally, the

nucleophilic addition of **20** yielded the coupling products **21** (Figure 7c). Lastly, CDs-6 were found to be recyclable for at least four cycles by simple extraction and centrifugation, without any significant impact on the yield of the **21**, demonstrating the greenness of the described mild process.

Amadio, Perosa and co-workers reported the reductive photocleavage reaction of picolinium esters driven by *N*-doped CDs, namely CDs-7 (Figure 8).⁹⁹ The reaction chosen is particularly relevant in organic synthesis, since it may be used as a deprotection methodology for these photolabile protecting groups.¹⁰⁰ CDs-7 were prepared from an aqueous solution of citric acid and diethylenetriamine through a hydrothermal treatment in an autoclave at 180°C for 6 h (Figure 8a). Then, the resulting solid was collected by evaporation and utilized without further purification, obtaining amorphous nanoparticles along with luminescent molecular fluorophores. The presence of amino and amido groups on CDs-7 surface was confirmed by FT-IR, but no additional information regarding their quantification was provided by the authors.

In terms of optical properties, CDs-7 showed two absorption bands in the UV region at 240 and 350 nm as well as excitation-independent luminescence at 450 nm due to the presence of the aforementioned molecular fluorophores.¹⁰¹ The redox features of CDs-7 were evaluated by cyclic voltammetry, displaying a high reduction potential of -1.94 V vs. Ag/AgCl reference electrode. Indeed, these carbon nanoparticles were able to carry out the reductive photocleavage of picolinium esters **22** to give *N*-methyl-4-methylpyridinium **23** and the corresponding carboxylic acids **24** under UV light irradiation (365 nm).

In these transformation, ethylenediaminetetraacetic acid (EDTA) was used as sacrificial electron donor at lower catalytic loading of CDs-7 (20 mg/mL), although it was not necessary at higher loadings (100 mg/mL). The cleavage products **24** were obtained with high conversion and selectivity against the competitive ester hydrolysis (up to 99% conversion and 99% selectivity in 48 h) under nitrogen atmosphere (Figure 8b), in a mixture of deuterated acetonitrile and water as solvent. A series of control experiments conducted in the absence of either CDs-7 or light exhibited negligible reactivity therefore indicating that the combination of both components was required for the reaction to take place.

Other kinds of amorphous or graphitic CDs were able to drive the photodeprotection transformation but in lower yield, in line with their lower reduction potential. Hence, the authors proposed a reaction mechanism that involves photoinduced electron transfer from CDs-7 to the esters **22**, leading to a reactive pyridinium radical **XVII**. This process may be favored by the presence of EDTA, which acts as a reductive quencher. The radical intermediate **XVII** quickly undergoes reductive C-O bond cleavage to release the resulting pyridinium open-shell species **XVIII** along with the carboxylate **XIX**. Finally, hydrogen and proton abstraction from either the deuterated solvent or EDTA decomposition products yields *N*-methyl-4-methylpyridinium **23** and the carboxylic acids **24** (Figure 8c). The potential recyclability of CDs-7 has not been mentioned by the authors.

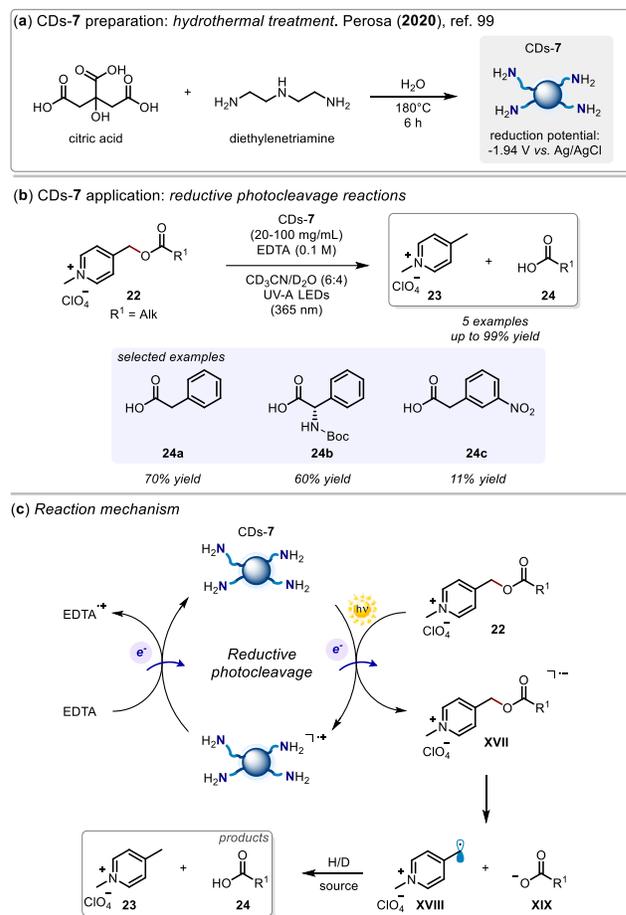


Figure 8. (a) CDs-7 preparation from citric acid and diethylenetriamine through hydrothermal treatment in water. (b) CDs-7 application in reductive photocleavage reactions. (c) Simplified reaction mechanism for CDs-7 bearing amino groups, described in ref. 99.

Recently, we reported the application of *N*-doped CDs, in particular CDs-8, for the photochemical perfluoroalkylation of organic compounds (Figure 9).¹⁰² This type of transformation is of practical importance because fluorinated compounds play a pivotal role in medicinal chemistry, agrochemistry and materials science.^{103–105} CDs-8 were prepared from arginine and ethylenediamine by microwave-assisted (MW) hydrothermal treatment at 240°C for 3 min, followed by filtration and dialysis purification against water (Figure 9a).⁴⁶ The resulting carbon nanoparticles show a narrow size distribution of 2.47 ± 0.84 nm (determined by AFM) and an amino-rich surface, confirmed by a positive Kaiser test (KT) of 1350 $\mu\text{mol/g}$ performed at 120°C.⁵³ In this case, the optical properties of CDs-8 have been exploited for the photochemical reactivity. In particular, these carbon nanoparticles display an intense absorption in the UV region and a tail in the visible, up to 500 nm. In addition, CDs-8 exhibit a wavelength-dependent emission in the blue region that is effectively quenched by radical sources such as perfluoroalkyl iodides **25** (Stern–Volmer constant, $K_{\text{sv}}=2.14 \text{ M}^{-1}$).

In fact, CDs-8 can act as a strong reductant in the excited state, with an estimated potential of about -2.2 V vs. SCE. This evidence strongly suggests that a photoinduced single

electron transfer from the excited nanoparticles to the radical sources **25** is feasible, thus prompting the formation of reactive fluorinated open-shell species. Therefore, CDs-**8** were utilized to trigger photochemical fluoroalkylation reactions between perfluoroalkyl iodides **25** and electron-rich organic compounds **26** in *N,N*-dimethylformamide (DMF) under visible light irradiation (395 nm). The corresponding products **27** were obtained in high yield (up to 93% yield in 24 h) under argon, in presence of potassium carbonate as base (Figure 9b).

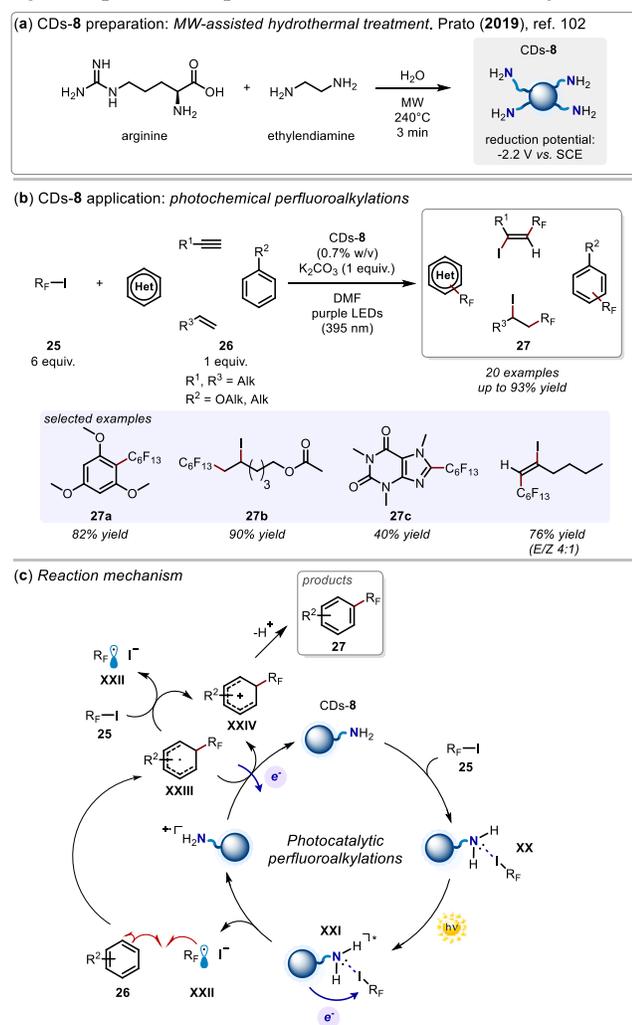


Figure 9. (a) CDs-**8** preparation from arginine and ethylenediamine through MW-assisted hydrothermal treatment in water. (b) CDs-**8** application in photocatalytic fluoroalkylation reactions. (c) Simplified reaction mechanism for CDs-**8** bearing amino groups, described in ref. 102.

Remarkably, the transformations were carried out using low catalytic loading of CDs-**8** (0.7% w/v) and the suitable substrates **26** ranged from arene to olefin derivatives. Control experiments substantiated the photocatalytic role of CDs-**8** since no reaction occurred either in the absence of the catalysts or using a wavelength that could not be absorbed by the nanoparticles. Our previous studies suggested that simple alkyl amines can photoactivate perfluoroalkyl iodides **25** through halogen bond formation.^{105,106} On the basis of this, the amine functionalities on CDs-**8** surface can provide halogen-bonded adducts with compounds **25**, placing them in close proximity and

therefore weakening the C-I bond. This hypothesis was supported by ¹⁹F-NMR analysis.

Consequently, we proposed a reaction mechanism that starts with the halogen bond association of the radical source **25** with CDs-**8** (**XX**), followed by photoinduced electron transfer from the excited nanoparticles to **25** (**XXI**). Afterwards, the addition of the resulting electrophilic radicals **XXII** to the electron-rich compounds **26** affords the cyclohexadienyl open-shell species **XXIII**. Their subsequent oxidation to **XXIV** allows the regeneration of CDs-**8**. Alternatively, the reactive intermediates **XXIII** may initiate a radical chain process by reducing **25**, thereby renewing **XXII**. Lastly, deprotonation of cationic **XXIV** yields the perfluoroalkylated arenes **27** (Figure 9c). The potential recyclability of CDs-**8** has not been attempted.

4. CONCLUSIONS AND PERSPECTIVES

Traditionally, most reported nano-catalytic transformations have been driven by metal nanoparticles. Only in recent times, has the growing attention in the direction of green and sustainable processes prompted the development of metal-free nano-catalytic systems. CDs represent excellent candidates, thanks to their outstanding physicochemical properties along with their tailorable surface. This translates into good biocompatibility, excellent optoelectronic characteristics, rapid availability from economic precursors and potential recyclability. Therefore, CDs have been exploited as effective nano-organocatalytic and nano-photocatalytic platforms for a wide range of reactions. In particular, the examples discussed in this Perspective highlight the current progress towards the preparation and application of non-metal-doped CDs in both polar and light-driven radical transformations of synthetical importance.

Although promising results have been obtained so far, a number of unsolved challenges and opportunities remain to be addressed. One of the fundamental controversies concerns the determination of the exact formation processes of CDs and, specifically, the origin of their superficial groups. Besides, the deep understanding of CD structure in terms of nature, reactivity and availability of their functionalities often remains unclear, despite the efforts. Notably, with this information in hands, an easier design of advanced nano-catalytic systems would be feasible, thus allowing their implementation to explore new reactivities. In this regard, we believe that a plethora of relevant organic reactions may be further developed in the near future.

Particularly, green enantioselective catalysis in environmentally benign solvents, or even in biological media, may be carried out by using chiral CDs that mimic the enzymes. This general concept is known as nanozymes and, in principle, might result in in vivo clinical applications, including diagnostics, therapeutics and drug synthesis.^{19,107} To this aim, careful control of the chiral CDs surface is pivotal to capitalize on the reactive properties of its functionalities.¹⁰⁸ It is worth mentioning that, although the preparation of CDs which exhibit an intrinsic chirality is known in literature, their use for asymmetric catalytic purposes, without post-synthetic modifications, is unprecedented.

Moreover, further stereocontrolled transformations could be achieved by merging the organocatalytic and photocatalytic aptitudes of chiral CDs. This implies the exploitation of the

photochemical activity of carbon nanoparticles to produce open-shell species from suitable radical sources. Then, these reactive fragments may be trapped by the chiral organocatalytic intermediates, such as enamines or iminium ions, generated on the CDs surface, possibly in an enantioselective fashion. If this occurs without the involvement of any external photocatalyst, it is called single catalyst approach.⁸⁸ This methodology may lead to the development of simple, safe and reusable stereoselective nano-catalytic systems. The described system would differ from a classical chiral supported molecular catalyst, having improved sustainability, affordability and applicability even in biological environments. We therefore foresee that forthcoming investigations on such CDs materials will resolve the related present-day challenges in green organic synthesis for both academia and industry.

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The authors declare no competing financial interest.

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ABBREVIATIONS

CDs, carbon dots; GQDs, graphene quantum dots; CQDs, carbon quantum dots; CNDs, carbon nanodots; PDs, polymer-like dots; QY, quantum yield; MOFs, metal-organic frameworks; TEM, transmission electron microscopy; AFM, atomic force microscopy; DLS, dynamic light scattering; UV-Vis, ultraviolet-visible; PL, photoluminescence; XPS, X-ray photoelectron spectroscopy; KT, Kaiser test; NMR, nuclear magnetic resonance; FT-IR, Fourier transform infrared spectroscopy; TGA, thermogravimetric analysis; HOMO, highest occupied molecular orbital; LUMO, lower unoccupied molecular orbital; MW, microwave; EDX, energy-dispersive X-ray; SCE, saturated calomel electrode; EDTA, ethylenediaminetetraacetic acid; K_{sv}, Stern–Volmer constant; DMF, *N,N*-dimethylformamide.

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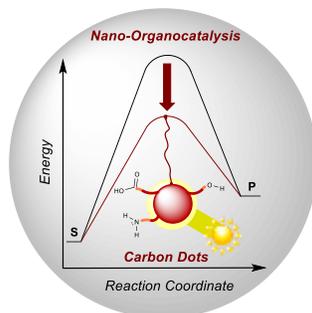
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Carbon dots (CDs), quasi-spherical carbon-based nanoparticles, hold great promises as sustainable nano-catalytic platforms. This Perspective summarizes recent examples in CDs preparation and application in synthetic organic catalysis and photocatalysis. The peculiarities of the different nanostructured systems along with their mode of catalysis are discussed, including the future challenges within this field of research.



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