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Triazine-based covalent organic frameworks for photodynamic inactivation of bacteria as type-II photosensitizers

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ABSTRACT

With the increase of antibiotic resistances in microorganisms, photodynamic inactivation (PDI) as a clinically proven antibacterial therapy is gaining increasing attention in recent years due to its high efficacy. Herein, we reported two covalent organic frameworks (COFs) materials, namely COFs-Trif-Benz and COF-SDU1, as effective type-II photosensitizers for photodynamic inactivation of bacteria. COFs-Trif-Benz and COF-SDU1 are synthesized through a facile solvothermal reaction between tri-(4-formacylphenoxy)-1,3,5-triazine (trif) and benzidine or *p*-phenylenediamine with high yield. Their highly ordered and porous structures were confirmed by Fourier transform infrared (FT-IR) spectra, solid state ^{13}C CP/MAS NMR spectrum, powder X-ray diffraction (PXRD) and Brunauer–Emmett–Teller (BET) analyses. The electronic absorption spectra and electrochemical experiments revealed that the extensive π-conjugation over COFs-Trif-Benz and COF-SDU1 greatly enhance their absorbance capability for visible light and make them have a lower band gap. The photocatalytic antibacterial assay was studied against both Gram-positive *Staphylococcus aureus* (*S. aureus*) and Gram-negative *Escherichia coli O86:B7* (*E. coli O86*) bacteria. Two materials can kill more than 90% bacteria at concentrations of 100 μg mL^{-1} after 60–90 min of illumination. Thus, both COFs are effective photosensitizers. Mechanism investigation revealed the antibacterial characteristics of the COFs-Trif-Benz and COF-SDU1 can generate reactive oxygen species (ROS) by energy transfer to molecular oxygen ($^3O_2$) to produce a highly reactive singlet oxygen ($^1O_2$). Hence, the two materials during the photodynamic were mainly via mechanism type II.

1. Introduction

Antibacterial resistance has become one of the global serious threats to human health [1]. In addition to the very swift replication and the high mutation rate of bacteria, the excessive utilization of existing antibiotics to treat illnesses, using them as growth promoters in livestock production and the inappropriate release in the environment further reinforced the emergence and dissemination of antibiotic-resistant pathogenic bacteria. To address this serious issue, it requires not only an adequate and rationalized use of antimicrobials, but also exploration of innovative therapeutic approaches [2]. Among them, photodynamic inactivation (PDI) as a clinically proven antibacterial therapy is gaining increasing attention in recent years due to its high efficacy [3]. This approach bases on the interaction of a non-toxic photosensitizer (PS), oxygen and light of appropriate wavelength to yield highly reactive oxygen species (ROS), which react immediately with the surrounding biomolecules and damage their bioactive components, such as cytoplasmic membranes, intracellular proteins and DNA and lead to the irreversible cell inactivation [4]. To date, a large number of photosensitizers have been used as antimicrobial materials in the killing or growth inhibition of bacteria, such as TiO_2 [5], fullerenes [6], phenalenones [7], methylene blue [8–10], and porphyrins [11–13]. However, due to the difference of PSs in the structure and physicochemical properties, together with the diversity of the various bacteria membrane structures, PSs often exhibit activity against certain types or strains of bacteria. Therefore, it is still a big challenge to design and explore new PSs to realize the higher efficiency for most bacteria.

Over the past decade, organic porous materials have attracted much interest in gas adsorption, energy storage and sensing because of their high porosity, robust thermal stability, and low densities [13–15]. However, these materials have found relatively limited applications in photocatalysis owing to their poor chemical stability as in the case of

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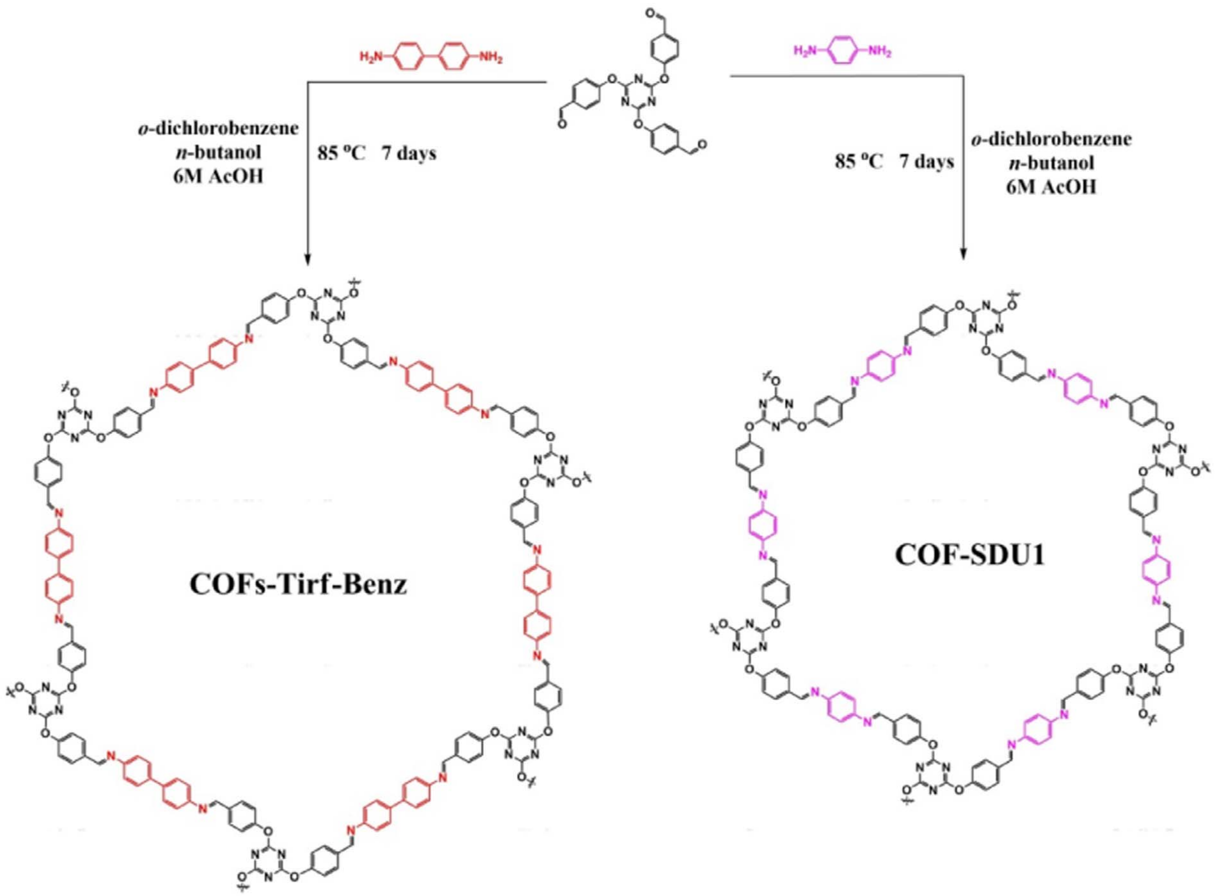

Scheme 1. Synthesis of COFs-Trif-Benz and COF-SDU1.

metal organic frameworks (MOFs) and the intermolecular irregular arrangement as in the case of polymers, which seriously affects their photocatalytic activity. Benefiting from the conveniently chemical regulation, highly ordered structures and helpful π-induced stacking behavior, the emerging of covalent organic frameworks (COFs) are believed to be the brilliant candidates to break through this key scientific problem [16,17]. The high specific surface area provides ample interface for the electrostatic charge separation. The π-stacked layers within these COFs enable the formation of conductive paths. Furthermore, the inherent optimized pore structure provides adequate space for the infiltration and sufficient contact with reaction species [18,19]. Based on these advantages, COFs are obviously quite suitable to be used as photocatalytic materials. To date, investigation about the semiconducting properties of the COFs materials have attracted increasing interests, however, their potential as photocatalysts [20,21], in particular as PSs for PDI, remains hardly explored.

With these considerations in mind, in the present study we contributed a strategy for the design and construction of two cost-effective conjugated porous COFs materials, namely COF-SDU1 and COFs-Trif-Benz, Scheme 1. The PDI activity of COF-SDU1 and COFs-Trif-Benz were systematically studied. Both materials exhibited excellent performances in photodynamic inactivation toward Gram-positive *Staphylococcus aureus* (*S. aureus*) and Gram-negative *Escherichia coli O86:B7* (*E. coli O86*) bacteria. Particularly, the latter bacteria as an enteropathogenic strain can cause a broad spectrum of disease in human [22]. Compared with COF-SDU1, COFs-Trif-Benz possesses a higher efficiency due to its more extensive π-conjugated structure and lower bad gap. Further exploration about the antibacterial mechanism of COF-SDU1 and COFs-Trif-Benz implied singlet oxygen ($^1O_2$) generated on COF-SDU1 and COFs-Trif-Benz by visible light irradiation was the main reason for strong bactericidal effects.

2. Material and Methods

2.1. General

Column chromatography was carried out on silica gel (Merck, Kieselgel 60, 200–300 mesh) with the indicated eluents. Benzidine was purchased from Beijing Ouhe Science and Technology Co., Ltd. *p*-Hydroxybenzaldehyde was obtained from Sinopharm Chemical Reagent Limited Company. Tri-(4-formacylphenoxy)-1,3,5-triazine (trif) was prepared according to the published procedure [23]. COF-SDU1 was synthesized according to our previously report [24]. All other reagents and solvents were of analytical grade and used as received without further purification.

2.2. Measurements

Solid-state ^{13}C CP/MAS NMR experiments were performed on Bruker AVANCE III 600 spectrometer at a resonance frequency of 150.9 MHz. ^{13}C CP/MAS NMR spectra were recorded using a 3.2 mm MAS probe and a spinning rate of 14 kHz. A contact time of 2 ms, a recycle delay of 5 s, and 4000 accumulations were used for the ^1H–^{13}C CP/MAS measurement. The chemical shifts of ^{13}C were externally referenced to TMS. Fourier transform infrared (FT-IR) were recorded in KBr pellets with 2 cm^{-1} resolution using an ALPHA-T spectrometer. Elemental analyses were performed on an Elementar Vavio El III elemental analyzer. Powder X-ray diffraction (PXRD) measurements were carried out on a Rigaku D/mas-γB X-ray diffractometer with a Cu-Kα sealed tube (λ = 1.5406 Å) at 293 K. The scanning electron microscopy (SEM) images were obtained using a JEOL JSM-6700F field-emission scanning electron microscopy. For SEM imaging, C (1–2 nm) was sputtered onto the grids to prevent charging effects and to improve the