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Synthesis of Covalent Organic Polymers and Their Applications in Separation and Analysis

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Abstract: *Covalent organic polymers (COPs) are porous organic materials assembled from symmetric and rigid organic building blocks via strong covalent bonds. Compared with traditional organic polymers, COPs feature tunable porosity, ordered channels, topological structures, stable physicochemical properties, and easy functionalization. These advantages have attracted increasing attention in analytical chemistry. This review summarizes the synthesis methods of COPs and their applications in separation and analysis, including solid-phase extraction, solid-phase microextraction, seawater purification, and chromatographic separation. Current challenges and future trends in their practical applications are also discussed.*

Keywords: *Covalent organic polymers; Synthetic methods; Solid-phase extraction; Solid-phase microextraction; Separation*

1. Introduction

Covalent organic polymers (COPs) are network-structured materials formed by light elements (C, B, O, Si, N, etc.) through strong covalent crosslinking. Their core feature is the formation of porous materials with stable properties and designable structures via irreversible or reversible covalent polymerization. Unlike traditional linear polymers, the three-dimensional networks of COPs endow them with rigid or semi-rigid backbones while retaining the flexibility and functional tunability of organic materials. Thanks to their adjustable porosity and ease of modification, COPs have been applied in gas adsorption, optoelectronics, biosensing, catalysis, and chemistry.

Covalent organic frameworks (COFs), a subclass of COPs, are crystalline porous polymers constructed by reversibly connecting organic monomers via covalent bonds. They share similar characteristics such as highly tunable porosity, predictable structural control, and easy functionalization [1]. In 2005, Omar M. Yaghi’s team first reported COF-1 and COF-5 via boric acid self-polymerization, introducing the concept of COFs [2]. Since then, rapid progress has been made in developing new COFs with unique applications in gas transportation [3], adsorption separation [4,5], heterogeneous catalysis [6], and optics [7]. This review focuses on the synthesis of COPs and their applications in separation and analysis.

2. Synthetic Methods for COPs

The design flexibility of COPs, derived from their diverse sizes, shapes, and tunable open pores, enables various synthesis strategies to achieve different structures and functions. However, synthesizing highly crystalline COFs remains challenging. Common methods include one-pot synthesis, solvothermal synthesis, microwave-assisted synthesis, and room-temperature solution methods.

2.1 One-Pot Synthesis

This method combines irreversible and reversible reactions (e.g., Suzuki coupling, Schiff base reaction) to construct highly crystalline and stable microporous COFs. Post-synthesis modification introduces functional groups into COF pore surfaces via electrophilic/nucleophilic substitution or click chemistry. NA Babujohn et al. synthesized crown ether-bound COP-TPC6 and COP-TPC8 via oxidative trimerization of dibenzo-crown ether monomers. The flexible crown ether structure and triphenylene π-π stacking created multi-level adsorption sites, enabling efficient removal of thiazine, triarylmethane, and azo dyes [8]. Li et al. prepared mesoporous silica/nanocopper nanocapsules via one-step sol-gel hydrolysis in nanocolloidal solutions, enhancing the photocatalytic reductive dehalogenation of α-bromoacetophenone [9].

2.2 Solvothermal Synthesis

Conducted in closed systems with organic solvents under controlled temperature and pressure, this is the most common method for COF synthesis. Adjusting parameters like temperature, reaction time, and reactant ratios tunes COF structures and functions. Xu et al. constructed two highly ordered COFs via Zincke reaction, achieving morphology and crystallinity control by optimizing conditions and precursor structures. These COFs selectively recovered rhenium from wastewater with competitive anions, providing a method for recycling this scarce metal [10]. Sun et al. used supercritical solvothermal synthesis to prepare olefin-linked COFs (TMT-PA), reducing synthesis time from days to hours and enabling high-stability, high-crystallinity olefin-linked COFs [11].

2.3 Microwave-Assisted Synthesis

Microwave heating accelerates reactions and shortens synthesis time by providing uniform temperature and precise condition control [12]. Alsudairy et al. combined linker methods with microwave assistance, rapidly preparing COFs using benzidine and BD-OMe in different ratios. COFs with 50% BD-OMe showed ultra-high adsorption (8.2 g/g) for radioactive iodine vapor and maintained performance after 7 cycles [13].

2.4 Room-Temperature Solution Synthesis

This method typically uses highly soluble solvents to increase reaction rates and yields, enabling COF formation at room temperature, which is extremely convenient. Lu et al. prepared hydrophilic polydopamine solutions and COFs separately, then mixed and stirred them at room temperature to obtain COFs with good water-dispersible extraction ability, providing advantages for detecting phthalates (PAEs). Conventional channels allowed small molecules to enter while excluding large-sized interferents, greatly improving selectivity and specificity for PAEs. Additionally, π-π conjugation and strong magnetic response provided affinity sites for PAEs and facilitated rapid and convenient separation, resulting in superior analytical performance for PAEs [14].

2.5 Other Methods

Ionothermal synthesis occurs in molten salts (e.g., molten zinc chloride as the reaction medium), suitable for synthesizing triazine-based COFs. Kuhn et al. synthesized triazine-based materials with high porosity and large surface area via high-temperature reaction in molten zinc chloride [15]. Heat reflux synthesis involves heating reactants in solvents under reflux, operable at lower temperatures but usually requiring longer reaction times. Dynamic covalent chemistry uses reversible covalent bond reactions (e.g., imine formation and exchange) to synthesize highly crystalline and stable COFs.

3. Applications of COPs

Due to their adjustable pore size, large specific surface area, and easy modifiability, COPs exhibit excellent application potential in sample pretreatment, liquid-phase separation, removal of organic pollutants in seawater, seawater desalination, and chromatographic separation [16].

3.1 Sample Pretreatment

3.1.1 Solid-Phase Extraction (SPE)

SPE is a sample preparation technique using solid adsorbents to separate analytes from other components based on differences in interaction forces between the mobile phase and stationary phase. Compared with liquid-liquid extraction (LLE), it offers advantages such as simple operation, low solvent consumption, high extraction efficiency, and flexibility in adsorbent use [17]. However, SPE has drawbacks including high cost, long time consumption, poor selectivity, low sensitivity, and susceptibility to matrix interference in complex sample systems, leading to co-extraction.

Li et al. developed a simple method for preparing nanocomposites with strong hydrophobic surfaces at room temperature, using COFs for affinity adsorption of various hydrophobic biotoxins and further surface imprinting for selective enrichment of specific biotoxins (COF@MIP). COF@MIP achieved highly specific and sensitive selective identification of sterigmatocystin, showing good reusability with 81% initial activity after 6 cycles. Coupled with SPE and HPLC, it was successfully applied to 5 common grains, with recoveries ranging from 70.3% to 100.7% [18]. Cheng et al. prepared a nitrogen-rich COP containing phenyl, triazine, and amine groups via solvent-free copolymerization as an SPE adsorbent. Combined with HPLC-diode array detection, they established an SPE-HPLC technique for non-steroidal anti-inflammatory drugs in environmental water samples, featuring a wide linear range (0.2–100 μg/L) and low detection limits (0.06–0.2 μg/L) [19].

3.1.2 Magnetic Solid-Phase Extraction (MSPE)

MSPE offers advantages over SPE such as simple operation, fast extraction, easy extract recovery, and good reproducibility [20]. It uses magnetic nanoparticles as adsorbents, with the advantage of easy recovery via external magnets and combination with other materials [21]. Magnetic nanoparticles typically consist of a magnetic core and an outer modified layer. Due to toxicity concerns, iron and its oxides—low-toxic, stable, inexpensive, and with abundant hydroxyl groups on the surface—are preferred as magnetic carriers for MSPE [22]. Materials like molecularly imprinted polymers (MIPs) [23], covalent organic frameworks [24], and metal-organic frameworks [25] can be used as outer modifiers for magnetic nanoparticles, improving adsorption performance and avoiding particle aggregation [26]. The combination of COFs and MSPE has attracted significant attention due to COFs’ large specific surface area and stable properties. Magnetic composites prepared by modifying magnetic nanoparticles with COFs possess both good magnetism and stability, enabling selective and efficient adsorption and separation of analytes, with significant advantages in actual sample processing.

Chen et al. coated Fe_3O_4 with COFs via one-pot synthesis, then modified COFs with amino acid ionic liquid (AAIL) through covalent radical polymerization using abundant unsaturated vinyl groups. The resulting Fe_3O_4@COF-AAIL had a stable structure, and the strong hydrogen bonding and π-π interactions between AAIL and benzimidazoles (BZDs) established a rapid and sensitive method for analyzing trace BZDs in plasma [27].

3.1.3 Solid phase microextraction (SPME)

Solid-phase microextraction is a green and efficient technique that integrates sampling, separation, and preconcentration into a single step. It offers advantages such as simplicity, high efficiency, low sample volume requirement, high detection sensitivity, and easy compatibility with various analytical devices [28,29], enabling high-throughput sample testing and miniaturization of detection equipment. Due to these merits, SPME has been widely applied for enriching and detecting trace analytes in diverse complex sample systems [17].

Despite its remarkable strengths in sample pretreatment, SPME still faces challenges including low reusability, fragile fibers, and poor stability and reproducibility [30]. Additionally, the limited choices of fiber coatings for SPME have led to increasing attention on COP-based coatings [31].

Yu et al. first synthesized imine-based magnetic COPs via a simple one-step Schiff base reaction using 1,3,5-tris(p-formylphenyl)benzene and tetrakis(4-aminophenyl)methane. The established MSPE-HPLC method exhibited excellent adsorption capacity for flavonoids in citrus, honey, soybeans, and Dioscorea bulbifera [32].

3.1.4 Stir Bar Sorptive Extraction (SBSE)

Similar to SPME, SBSE uses a magnetic stir bar coated with adsorbent instead of a silica fiber, offering a larger specific surface area, higher reusability, and better extraction efficiency and reproducibility than SPME [33,34]. Commercial SBSE coatings include PDMS and EG-silicone, but these lack sufficient adsorption capacity and selectivity, especially for trace target compounds in complex matrices. PDMS coatings are only suitable for non-polar compounds with poor specificity, leading to co-extraction, while EG-silicone has significant enrichment for non-polar substances but low stability and short lifespan. The good stability and reusability of COFs can address these issues.

Zang et al. synthesized a fluorine-containing COF via room-temperature synthesis and physically adhered it to a stir bar, establishing an analytical method for 5 trace fluorine-containing compounds in pear juice and pear beverages by combining SBSE with HPLC. Compared with commercial stir bars, this coated stir bar showed higher extraction recovery for target analytes in a shorter time [35].

3.2 Liquid-Phase Separation

3.2.1 Water Treatment

Under the dual pressures of global environmental crises and rapid population growth, the challenges faced by human society regarding freshwater resources have become increasingly evident, manifested in severe issues such as simultaneous water scarcity and aggravated water quality pollution. Against this backdrop, providing freshwater through the purification of seawater and contaminated water sources has emerged as a green and viable approach, leading to the extensive development and application of various advanced separation technologies [36,37]. COPs, owing to their unique properties, have been confirmed as core functional materials in the field of water treatment, with their applications spanning the selective removal of various pollutants in water bodies.

Loh's research group successfully constructed a salicylanilide-based COF (SA-COF) with reversible proton tautomerism. SA-COF exhibited excellent chemical selectivity, repelling and adsorbing positively charged molecules under acidic and basic conditions, respectively, and preferentially binding to aromatic hydroxyl groups over aromatic amines, showing high selectivity for dye molecule separation. This study demonstrated COFs as potential candidates for molecular separation [38].

Reverse osmosis is a highly feasible and highly concerned seawater desalination solution widely used for its high energy efficiency [16,39-41]. COPs have now been prepared into desalination membranes. Jiang's group computationally designed a series of two-dimensional COFs composed of triformylphloroglucinol and p-phenylenediamine with different functional groups [42]. Simulation data for seawater desalination showed that the water flux of various COF membranes was enhanced by three orders of magnitude compared with traditional reverse osmosis membranes. Molecular dynamics simulations further revealed that adjusting the pore size of COFs could induce exponential growth in water transport flux.

3.2.2 Chromatographic Separation

Chromatography demonstrates excellent separation efficiency in fields such as pesticide monitoring [43], drug development, and traditional Chinese medicine fingerprinting [44]. The core of this technology lies in the selection of stationary phases [45], which directly affect separation efficiency and selectivity through molecular interactions (including hydrophobic interactions, π-π conjugation, hydrogen bonding networks, and electrostatic forces) with analytes. COPs, with their adjustable pore size and surface chemical modifiability, exhibit excellent physical and chemical stability and high separation efficiency, providing a promising material basis for developing new chromatographic stationary phases.

Dowlatshah's team increased the polar functional groups of 1,5-diaminonaphthalene-covalent organic polymer (DAN-COP) and prepared a new DAN-COP film based on cellulose nanocrystals for thin-film microextraction, coupled with gas chromatography to extract and separate imipramine from biological fluids.

Wei et al. synthesized PAA/COF@SiO_2 composites using deep eutectic solvents, improving separation selectivity and column efficiency by addressing COF rigidity issues. The hydrophilic flexible polymer enhanced hydrophilic-lipophilic balance for better chromatographic performance [46].

4. Conclusion

Significant progress has been made in COP synthesis and separation applications, but challenges remain. Harsh reaction conditions hinder large-scale, low-cost production of highly crystalline COFs, while selective adsorption in complex matrices requires functional group modification or composite engineering. Future efforts should focus on optimizing synthesis methods and enhancing material selectivity, driving COPs toward practical environmental and biomedical applications.

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