



Review article

Advances in covalent organic frameworks in separation science[☆]

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ABSTRACT

Covalent organic frameworks (COFs) are a new class of multifunctional crystalline organic polymer constructed with organic monomers via robust covalent bonds. The unique properties such as convenient modification, low densities, large specific surface areas, good stability and permanent porosity make COFs great potential in separation science. This review shows the state-of-the-art for the application of COFs and their composites in analytical separation science. COFs and their composites have been explored as promising sorbents for solid phase extraction, potential coatings for solid phase microextraction, and novel stationary phases for gas chromatography, high-performance liquid chromatography and capillary electrochromatography. The prospects of COFs for separation science are also presented, which can offer an outlook and reference for further study on the applications of COFs.

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1. Introduction

Covalent organic frameworks (COFs) are a new class of ordered crystalline organic polymer constructed with organic monomers

via covalent bonds [1–5]. As one of the typical representative of novel porous materials, COFs own low density, large specific surface area, great stability and permanent porosity with predictable design at the atomic level, including geometry, structure and functional properties [6–8]. COFs are synthesized on the basis of dynamic covalent chemistry, enabling “error checking” and “proof-reading” of the reaction systems, the key process in formation of crystalline and ordered structures [9,10]. Finding a proper synthetic method involving the reaction media, temperature, time and catalyst plays the key role in the formation of the crystalline structure. In addition to typical solvothermal methods,

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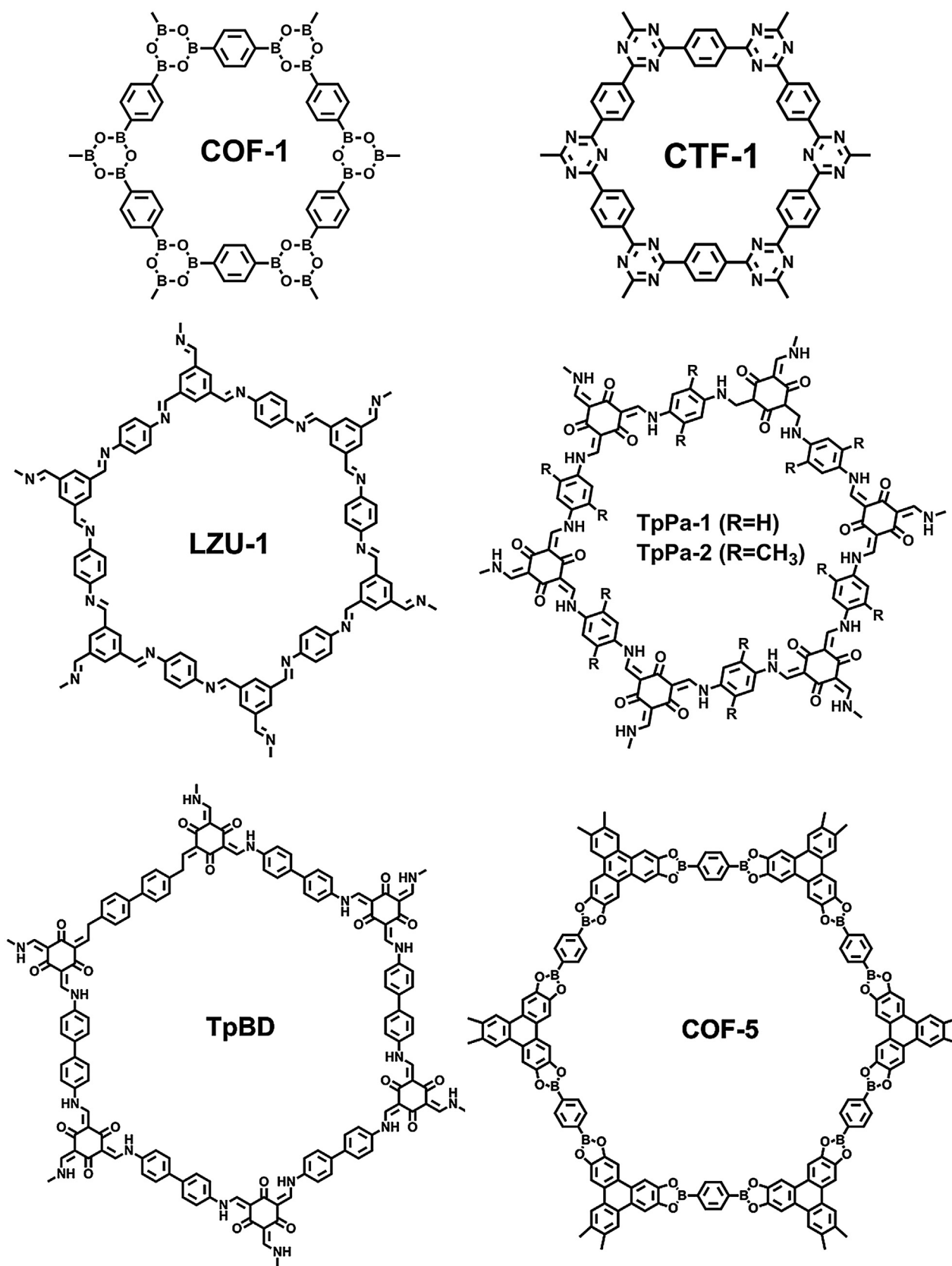


Fig. 1. Schematic representation of typical COFs used in separation science.

various approaches to the synthesis of COFs including microwave synthesis, mechanochemical synthesis, ionothermal synthesis and room-temperature synthesis have been developed [11–13].

COFs can mainly be divided into three classes: the boronate ester linked COFs such as COF-1, COF-5 and COF-66 [1,14,15], the cyano-containing covalent triazine-based frameworks (CTFs) [16,17], and

Table 1
Properties, preparation and application of typical COFs in separation science.

COFs	Properties		Building blocks		Synthetic method	Applications	Refs
	BET surface area (m ² g ⁻¹)	Pore size (Å)	Thermal stability (°C)	Chemical stability			
CTF-1	791	12	420	strong	lonothermal synthesis	SPE/HPLC	[29,30,37,47]
CTpBD	114	20	-	strong	Refluxed synthesis	SPE	[31]
TpPa-1	535	12.5	350	strong	Solvothetmal synthesis	SPE/HPLC	[32,30,41,49]
TpPa-2	339	13.5	350	strong	Solvothetmal synthesis	SPE	[33]
TpBD	537	24	350	strong	Solvothetmal/room temperature synthesis	SPE/HPLC/GC	[34,44,46]
LZU-1	410	18	310	strong	Solvothetmal synthesis	SPE/CEC	[35,50,52]
COF-1	711	7	-	weak	Solvothetmal synthesis	SPE	[36]
TAPB-PDA	1250	34	400	strong	Room temperature synthesis	SPE	[38]
TbBd	196	28	350	strong	Room temperature synthesis	SPE	[39]
CTpPa-1	146	13	300	strong	Refluxed synthesis	GC	[45]
COF-5	1590	27	-	weak	Solvothetmal synthesis	CEC	[51]
Hydrazone COF	723	16	330	strong	Solvothetmal synthesis	HPLC	[48]

the imine and hydrazone linked COFs [18–20]. These COFs with unique structure properties show great potential in gas storage [5,21], sensing [22–24], catalysis [25,26] and drug delivery [27,28]. The diverse structures of COFs with various functionalities also make COFs attractive in separation science. Recently, COFs and their composites such as COFs coatings, COFs@SiO₂ and COFs@Fe₃O₄ have been fabricated to make them more competent as potential sorbents for sample pretreatment as well as novel stationary phases for chromatography [29–52].

In this review article, we show recent advances in COFs in analytical separation science. COFs have been used or engineered as promising sorbents for sample pretreatment such as solid-phase extraction (SPE) [29–41] and solid-phase microextraction (SPME) [42,43], and as novel stationary phases for chromatography including gas chromatography (GC) [44,45], high-performance liquid chromatography (HPLC) [46–49] and capillary electrochromatography (CEC) [50–52]. We also give prospects of COFs in separation science.

2. COFs applied in analytical separation science

The properties, preparation and applications of typical COFs in separation science are summarized in Table 1. The COFs used in separation science exhibit various properties. The Brunauer-Emmett-Teller (BET) surface area and pore size range from 114 to 1590 m² g⁻¹ and 7 to 34 Å, respectively. Imine linked COFs have gained a dominant position in separation science due to their high stability and good crystallinity. Currently, all COFs used in separation science are two-dimensional COFs, in which the building monomers link to form extended networks with hexagonal topologies (Fig. 1). Some of these COFs, such as CTF-1, CTpBD, TpPa-2 and COF-1, can be directly applied as sorbents for SPE. However, most of the COFs need to be engineered to make them more acceptable for different analytical technologies. Magnetic COFs@Fe₃O₄ composites such as TpBD@Fe₃O₄, TbBd@Fe₃O₄ and TpPa-1@Fe₃O₄ have been prepared for magnetic solid phase extraction (M-SPE). COFs@SiO₂ composites such as CTF-1@SiO₂, TpBD@SiO₂ and hydrazone COF@SiO₂ have been synthesized as stationary phases for HPLC. In addition, COFs have been fabricated as coatings for applications in SPME, GC and CEC. These COFs and their composites show high promise in sample pretreatment and chromatography.

3. COFs for sample pretreatment

3.1. COFs for SPE

The unique properties of COFs make them good candidates as sorbents in SPE. As early as 2012, Liu et al. [29] reported CTF-1 as adsorbent for aromatic compounds (Fig. 2). Their results revealed that CTF-1 was a superior adsorbent for the extraction of eight monocyclic aromatic compounds in aqueous solution with fast adsorption/desorption kinetics and complete adsorption reversibility. Several specific, non-hydrophobic mechanisms including hydrogen bonding, electrostatic attraction, and π - π electron-donor-acceptor interaction were considered as the reasons for its excellent extraction performance. Comparison of CTF-1 with the most efficient commercial polymeric resin, Amberlite XAD-4, indicates that CTF-1 sorbent exhibited stronger adsorption to polar and/or ionic compounds. All the results show the high potential of COFs as adsorbent in SPE.

Zhong et al. [30] reported a sol-gel procedure to fabricate polydimethylsiloxane (PDMS)/CTFs coated stir bar for on-line SPE of phenols in water samples prior to HPLC determination. The obtained PDMS/CTF stir bar showed good reproducibility, low detection limits (0.08–0.30 μ g L⁻¹), good linear range

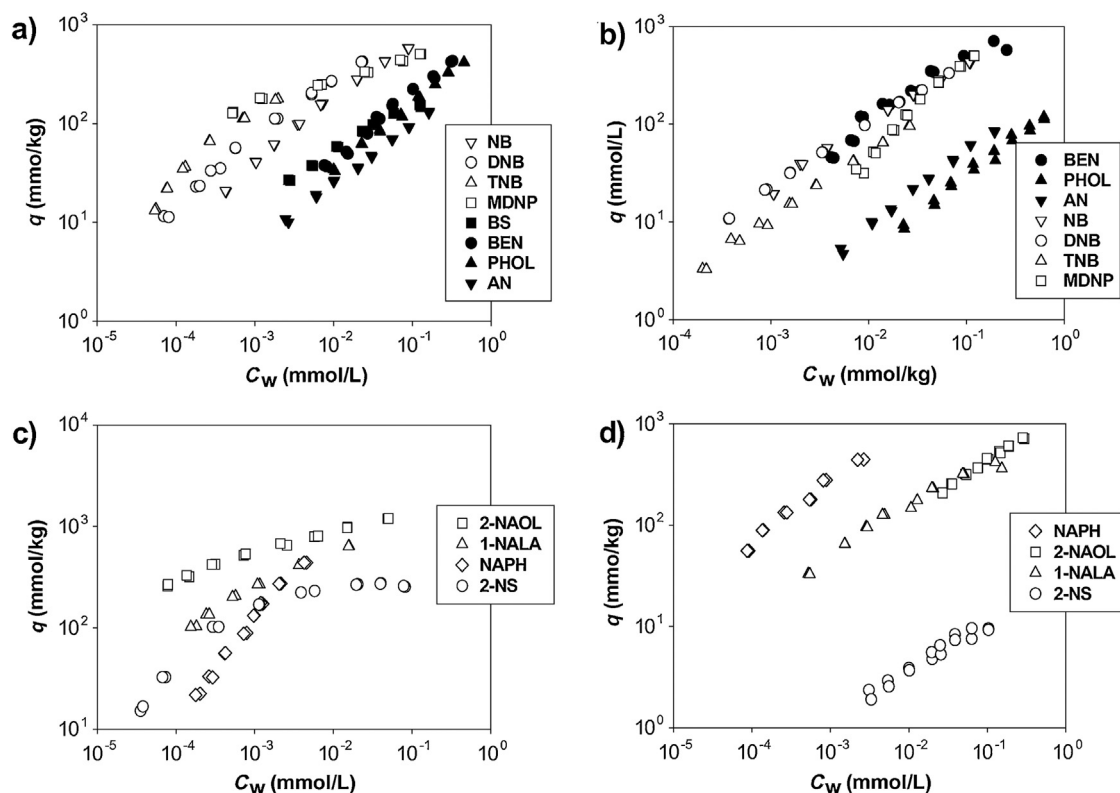


Fig. 2. Adsorption isotherms for the monocyclic aromatic compounds on CTF-1 (a, c) and Amberlite XAD-4 (b, d). Analytes: benzene (BEN), phenol (PHOL), aniline (AN), benzenesulfonate (BS), nitrobenzene (NB), 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), 4-ethyl-2,6-dinitrophenol (MDNP), naphthalene (NAPH), 2-naphthol (2-NAOL), 1-naphthalenamine (1-NALA), and 2-naphthalenesulfonate (2-NS). Note: sorption of benzenesulfonate to XAD-4 is negligible and is not presented. Adapted with permission from Ref. [29]. Copyright 2012 Elsevier.

(0.5–500 $\mu\text{g L}^{-1}$) and enrichment factors (64.9–145.6), which are comparable or better than those for commercial PEG and PDMS coated stir bars (Fig. 3). The proposed method was successfully applied to the determination of phenols in environmental water samples with good recovery.

In addition to the above COFs-based SPE of organic molecules, Liu et al. [31] recently reported the fabrication of CTpBD as sorbents for the on-line preconcentration of trace inorganic ions via flow injection followed by inductively coupled plasma mass spectrometry (ICP-MS) detection (Fig. 4). They achieved the SPE of Cr(III), Mn(II), Co(II), Ni(II), Cd(II), V(V), Cu(II), As(III), Se(IV) and Mo(VI) in water samples on CTpBD for ICP-MS determination with low detection limits (2.1–21.6 ng L^{-1}), good anti-interference ability, stability and reusability.

Although on-line SPE has the merits of reducing analysis time and procedural steps, improving the sample throughput and reproducibility, only very few COFs can be used for on-line SPE. COFs with sub-micrometer particle size and irregular shape may cause high backpressure, limiting the application of COFs in on-line SPE. Matrix solid-phase dispersion extraction is an effective method to solve the above problems. Ma et al. [32] utilized TpPa-1 as a hydrophilic porous material for matrix solid-phase dispersion extraction of N-linked glycopeptides in complex biological samples (Fig. 5). TpPa-1 had good selectivity and sensitivity for glycopeptides, allowing selective extraction of glycopeptides at femtomole levels in tryptic digests of human IgG. In addition, the good stability, low density, and abundant binding sites on frameworks afford TpPa-1 good reusability and high binding capacity (178 mg g^{-1} , IgG/TpPa-1), demonstrating the potential of COFs in pretreatment of complex biological samples.

Recently, Wang et al. [33] reported the chelation of Ti (IV) ion into TpPa-2 to synthesize Titanium (IV) ion-modified COFs for

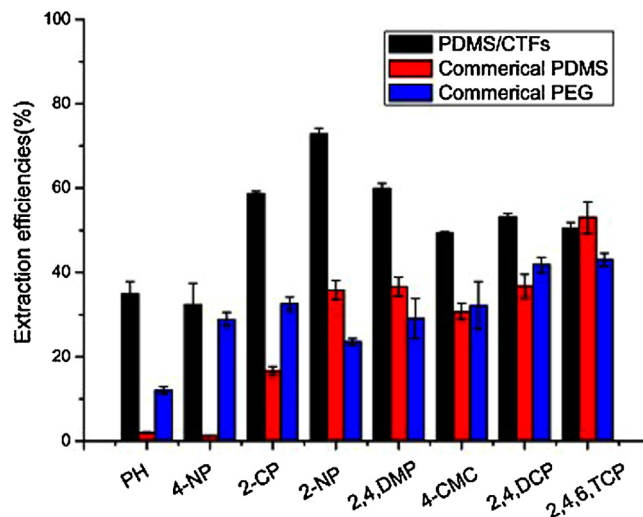


Fig. 3. Comparison of the extraction efficiencies of PDMS/CTFs coated stir bar with those of commercial PDMS (Gerstel) and PEG (Gerstel) stir bars for the target phenols. Analytes: phenol (PH), 2-chlorophenol (2-CP), 2-nitrophenol (2-NP), 4-nitrophenol (4-NP), p-chloro-m-cresol (4-CMC), 2,4-dimethylphenol (2,4-DMP), 2,4-dichlorophenol (2,4-DCP) and 2,4,6-trichlorophenol (2,4,6-TCP). Reprinted with permission from Ref. [30]. Copyright 2016 Elsevier.

matrix solid-phase dispersion extraction of phosphopeptides. The prepared TpPa-2-Ti (IV) exhibited a high capacity (100 $\mu\text{g mg}^{-1}$), excellent sensitivity (0.02 $\text{fmol } \mu\text{L}^{-1}$), good selectivity and reusability for phosphopeptide enrichment. In addition, TpPa-2-Ti (IV) displayed high enrichment efficiency for phosphopeptide in more complex samples including α -casein digestion, non-fat milk and

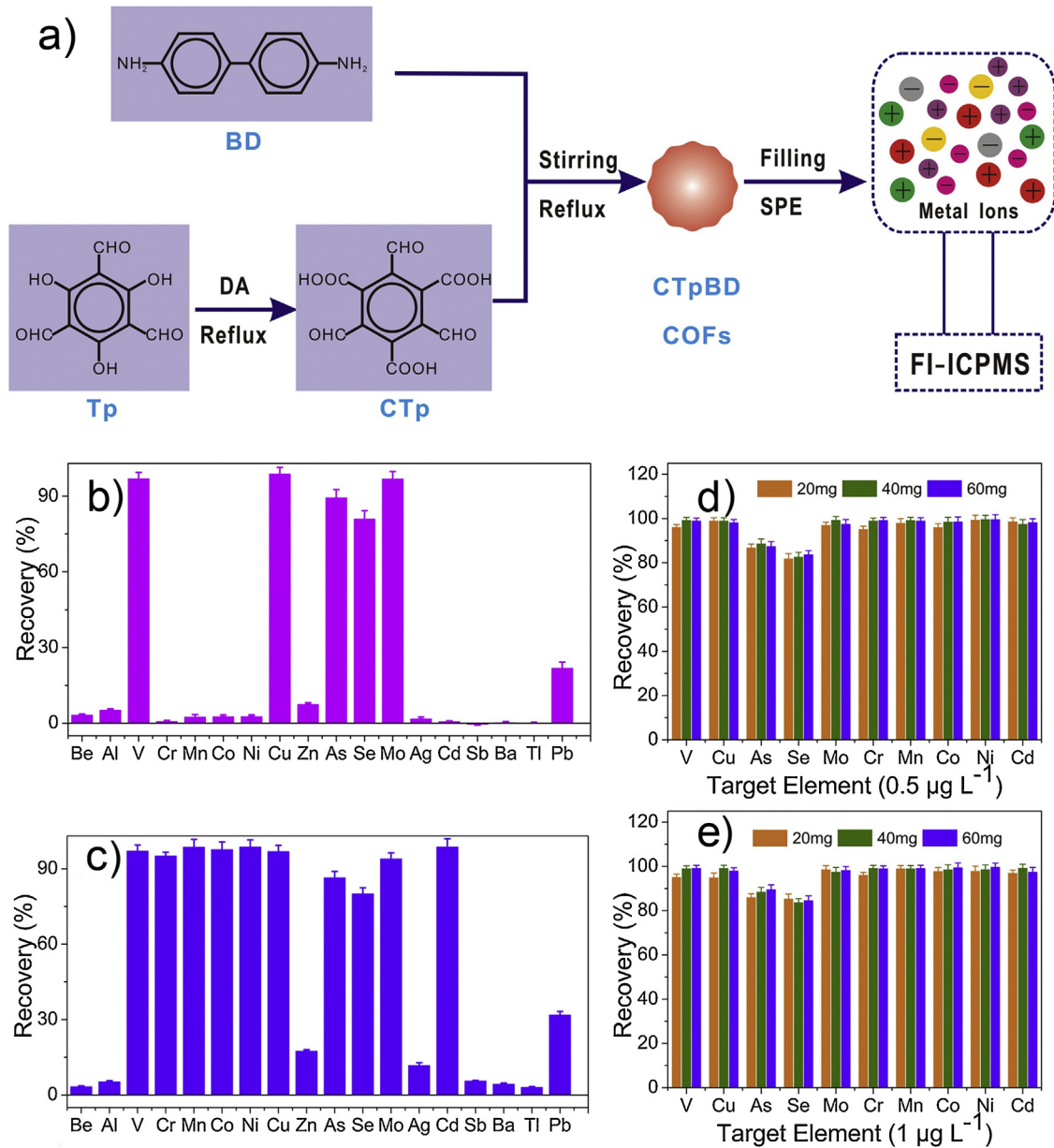


Fig. 4. (a) Fabrication of CTpBD as sorbent for the SPE of heavy metals for ICP-MS detection. Adsorption selectivity of TpBD (b) and CTpBD (c) for various metal elements. (c, d) Effect of the packed adsorbent amount on the adsorption efficiency of CTpBD. Adapted with permission from Ref. [31]. Copyright 2018 Elsevier.

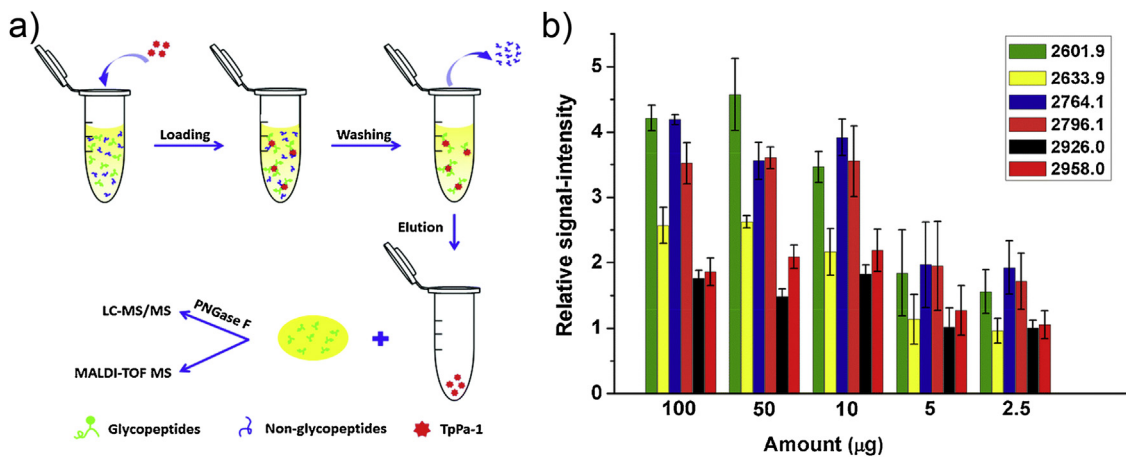


Fig. 5. (a) Illustration of enrichment and detection of glycopeptides based on TpPa-1. (b) Signal intensity ratios of six most intense glycopeptides to internal standard hepcidin with different amounts of TpPa-1.

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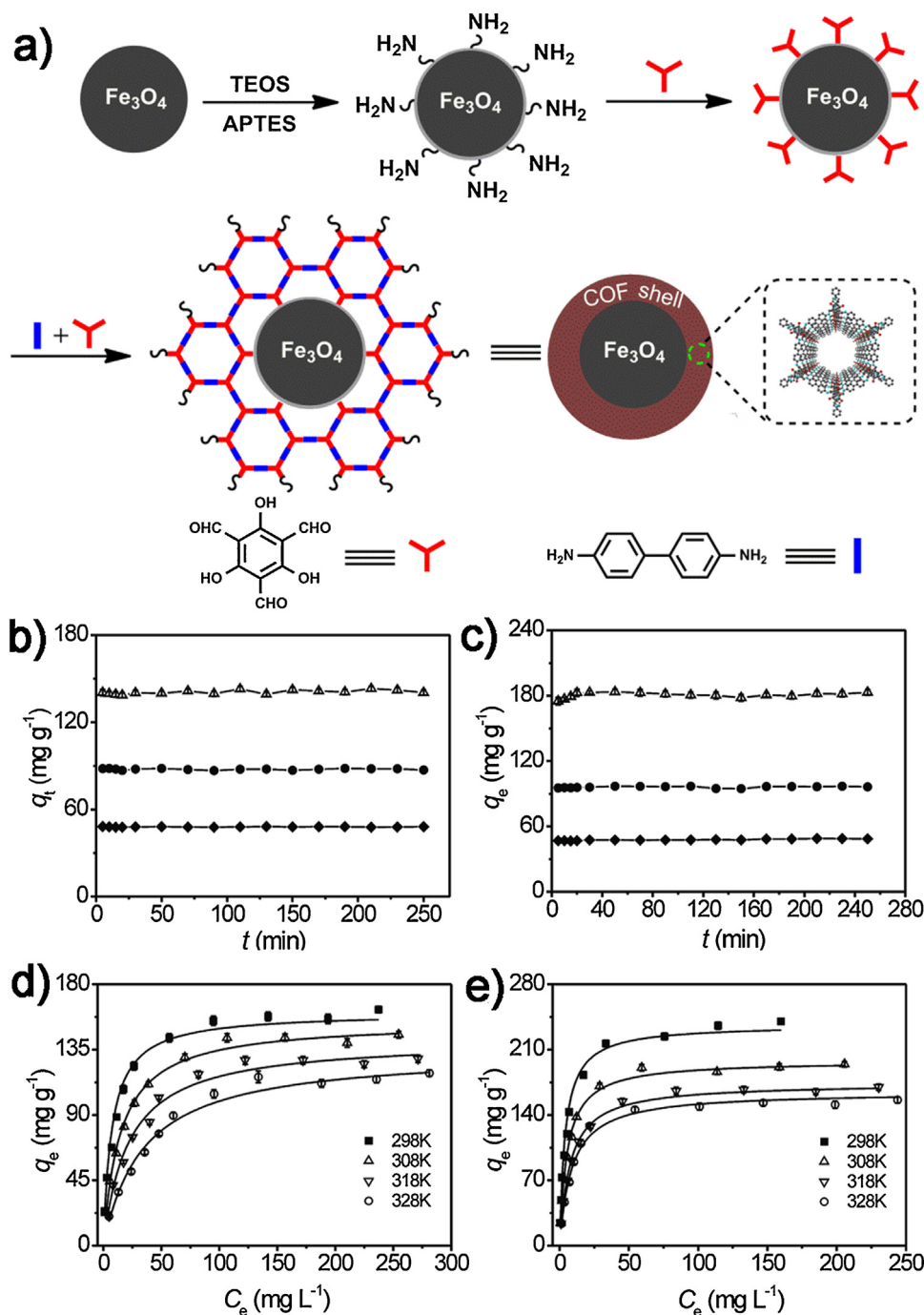


Fig. 6. (a) Synthesis of core-shell Fe₃O₄@TpBD nanospheres via monomer-mediated in situ growth strategy. Time-dependent adsorption of bisphenol A (b) and bisphenol AF (c) on Fe₃O₄@TpBD (♦, 50 mg L⁻¹; ●, 100 mg L⁻¹; Δ, 200 mg L⁻¹). Adsorption isotherms of bisphenol A (d) and bisphenol AF (e) on Fe₃O₄@TpBD. The solid lines were obtained by the Langmuir model simulations.

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HeLa cells, indicating the feasibility of the COF-based materials in phosphoproteomics research.

Magnetic solid-phase extraction (M-SPE) as an important sample pretreatment technique is always of great concern for its convenience, high mass transfer efficiency and good environmental friendliness. Integrating the merits of magnetic separation and the good extraction performance of COFs to fabricate magnetic COFs composites in SPE has received considerable attention recently. Our group [34] developed a monomer-mediated in situ growth method to fabricate core-shell Fe₃O₄@TpBD nanospheres for M-SPE of bisphenols from aqueous solution (Fig. 6). The uniform COFs

shell thickness of Fe₃O₄@TpBD was easily controlled by tuning the concentration of COFs monomers. The π - π and hydrogen bonding interactions provided by the TpBD shell allowed Fe₃O₄@TpBD to be used for bisphenols extraction with fast adsorption, large adsorption capacity, easy desorption and good reusability. Such a strategy provides a rational design for core-shell composites with magnetic platforms and tunable porous COF shells for wide range of applications. Meanwhile, Wang and Chen et al. [35,36] reported the fabrication of magnetic Fe₃O₄@LZU1 and M-COF-1 nanoparticles for M-SPE of polycyclic aromatic hydrocarbons (PAHs) and paclitaxel in environmental and biological samples.

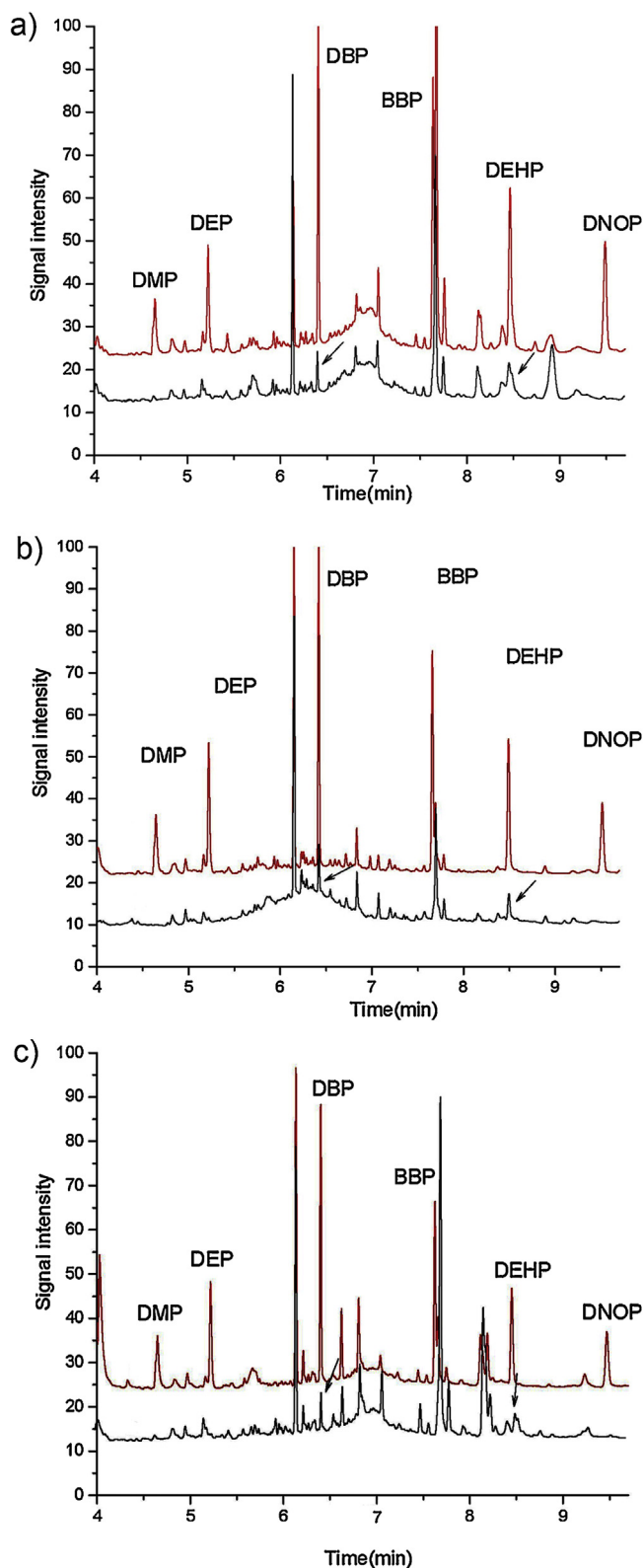


Fig. 7. Chromatograms of target PAEs in the mineral water bottle Brand A (a), Brand B (b) and plastic bottle Brand C (c). Red curve: M-SPE of the spiked water bottle ($8 \mu\text{g g}^{-1}$); black curve: MSPE of the unspiked water bottle. Analytes: dimethyl phthalate (DMP), diethyl phthalate (DEP), di-n-butylphthalate (DBP), benzyl butyl phthalate (BBP), di-2-ethylhexylphthalate (DEHP), and di-n-octyl phthalate (DNOP). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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Recently, Yan et al. [37] demonstrated an *in situ* solvothermal reduction of nickel ions on CTFs matrix to synthesize magnetic CTFs/Ni composite for rapid extraction of phthalate esters in plastic

packaging materials (Fig. 7). The strong π - π and hydrophobic interaction between CTF/Ni composite and phthalate esters resulted in the good extraction efficiency of phthalate esters on CTF/Ni

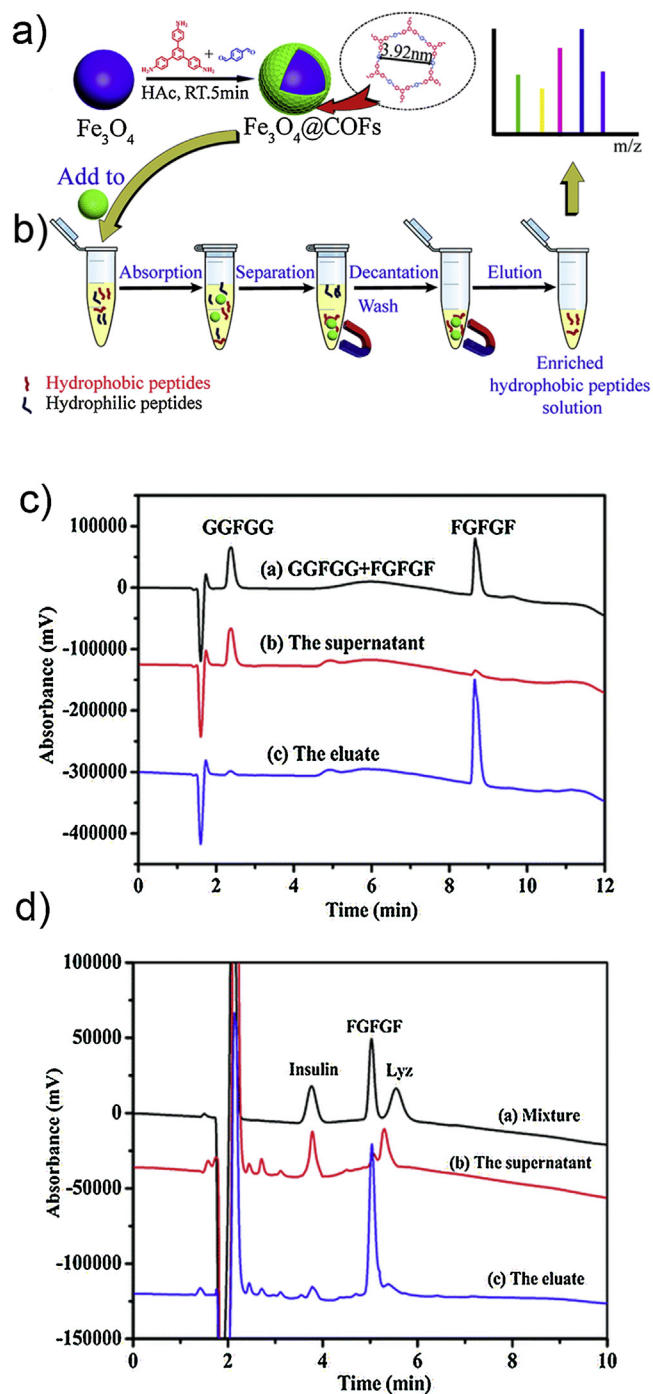


Fig. 8. (a) Fabrication of Fe_3O_4 @COFs. (b) Schematic illustration for M-SPE of peptides. (c) Chromatogram of FGFGF and GGFGG before and after treatment with Fe_3O_4 @COFs. (d) Chromatogram of FGFGF, insulin and Lyz before and after treatment with Fe_3O_4 @COFs.

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composite. In addition, the magnetic nature of CTF/Ni composite enabled the fast transfer of target phthalate esters from aqueous solution to the adsorbents, reducing the matrix interference for the extraction. The merits of short analysis time, good selectivity and high sensitivity indicate the potential of CTF/Ni composite for the analysis of other trace aromatic compounds.

As the above synthesis of magnetic COF composites was performed at high temperature with a long time, Lin's group [38] reported a facile room temperature approach to synthesize core-shell structured magnetic Fe_3O_4 @COFs composites for efficient enrichment of peptides with simultaneous exclusion of proteins

(Fig. 8). The COF shell was formed within 5 min. The prepared Fe_3O_4 @COFs exhibited good selectivity, high adsorption capacity, fast adsorption kinetics, high recovery, and excellent recyclability for magnetic SPE of hydrophobic peptides. In addition, the Fe_3O_4 @COFs composites gave good size-exclusion effect for selectively capturing peptides and repelling proteins, expanding the application of COFs in proteomic analysis. The rapid room-temperature synthesis of core-shell structured magnetic Fe_3O_4 @TbBd for selective enrichment of peptides with simultaneous exclusion of proteins was also reported by Lin's group recently [39]. He et al. [40] developed a facile strategy to synthe-

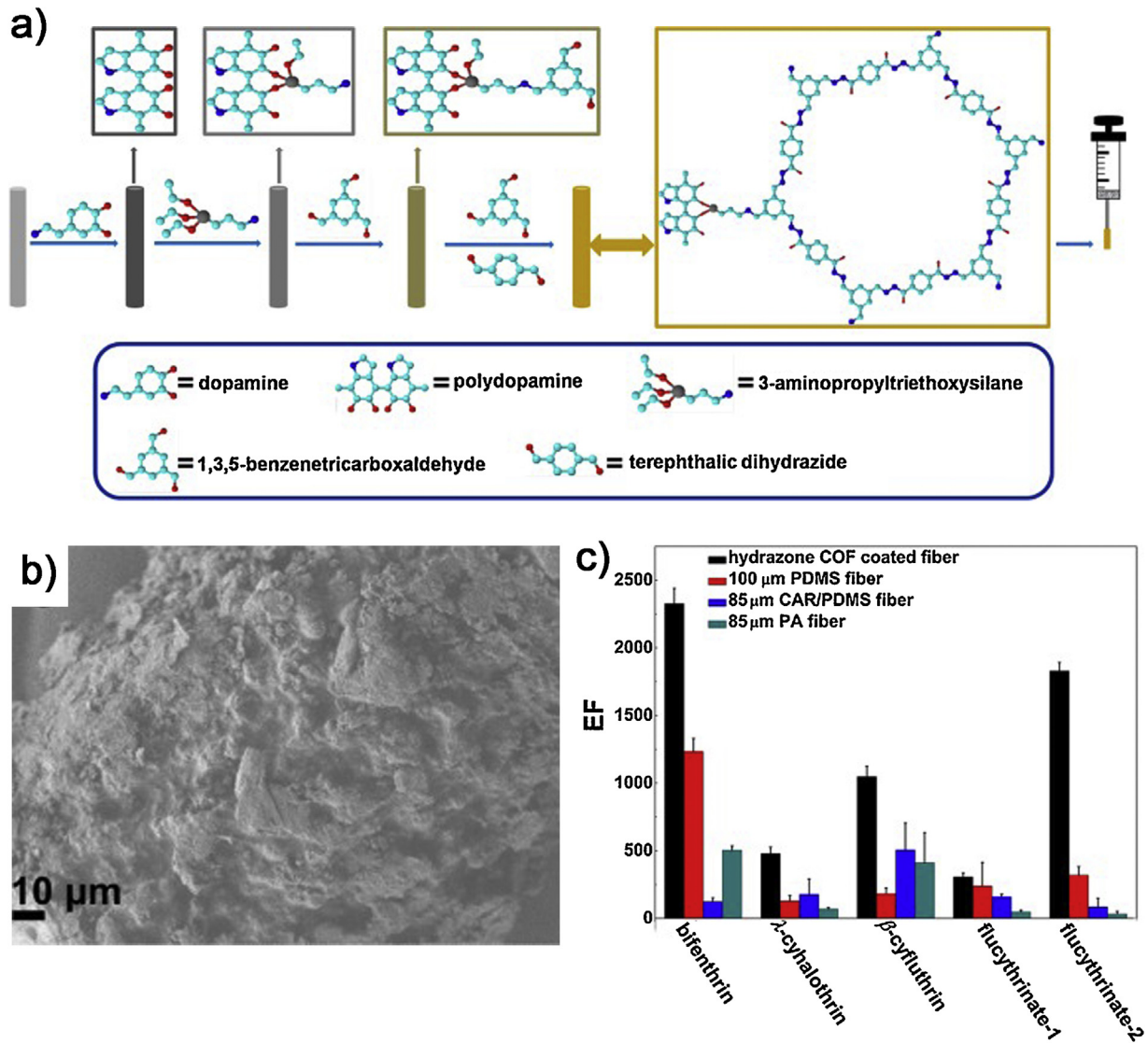


Fig. 9. (a) Synthesis of hydrazone COF-based SPME fiber. (b) SEM image of hydrazone COF-based SPME fiber. (c) Comparison of enhancement factors for pyrethroids hydrazone on COF coated fiber and commercial fibers.

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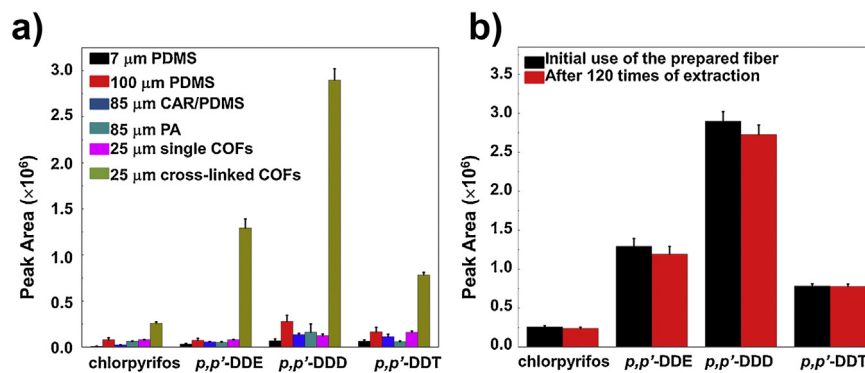


Fig. 10. (a) Comparison of cross-linked COFs coated fiber with commercial fibers for SPME of the pesticides. (b) Comparison of peak areas of the pesticides before and after 120 cycles of SPME with the cross-linked COFs coated fiber. Analytes: 1,1-dichloro-2,2-bis(4-chlorophenyl)ethylene (p,p'-DDE), 1,1-dichloro-2,2-bis(4-chlorophenyl)ethane (p,p'-DDD), and 2,2-bis(4-chlorophenyl)-1,1,1-tri-chloroethane (p,p'-DDT).

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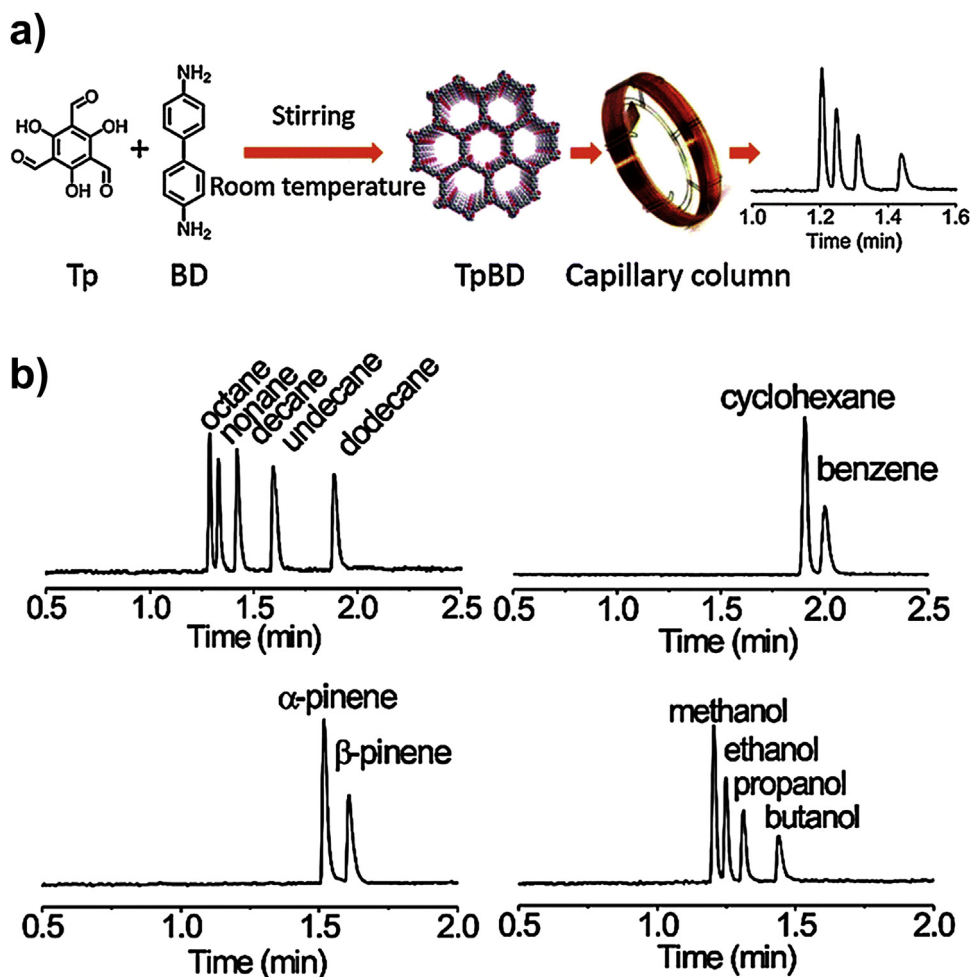


Fig. 11. (a) Room-temperature solution-phase synthesis of TpBD. (b) Chromatograms for GC separation of alkanes, cyclohexane and benzene, α -pinene and β -pinene, and alcohols on TpBD coated column (20 m long \times 0.25 mm i.d.).

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size bouquet-shaped magnetic COF composites via grafting TpPa-1 onto surface-modified Fe_3O_4 nanoparticles for M-SPE of PAHs from environmental samples with low limits of detection, excellent extraction performance, satisfactory precision and accuracy.

Protein glycosylations play significant roles in many biological processes. The development of selective adsorbents and efficient sample pretreatment strategies is quite essential for glycoproteins analysis. Wang et al. [41] reported a two-step solvothermal reaction to synthesize sea urchin-type magnetic Fe_3O_4 @TpPa-1 composites for hydrophilic enrichment of glycopeptides. The developed M-SPE method gave ultralow detection limits (28 fmol), satisfactory selectivity and high recovery for glycopeptides. A total of 37 and 22 glycopeptides were easily detected from IgG and HRP digests, respectively. In addition, 228 glycopeptides corresponding to 114 glycoproteins in human serum digests were detected. Their results show that COFs are better than commercial HILIC materials in glycoproteomic studies.

3.2. COFs for SPME

SPME is one of the most promising sample pretreatment techniques integrating sampling, extraction, and sample introduction into one step with less solvent consumption. Exploring novel SPME coatings remains an interesting topic in separation science. The application of COFs in SPME has received increasing attention recently. Jia's group reported the polydopamine supported cova-

lent immobilization of a hydrazone COF on stainless steel fiber for headspace SPME of pyrethroids in fruit and vegetable samples (Fig. 9) [42]. The abundant phenyl rings and C=N groups on hydrazone COFs provide possibilities for π - π stacking, hydrophobic, and hydrogen bonding interaction, and van der Waals forces, making them highly selective for pyrethroids. The developed fiber was utilized for the extraction of pyrethroids in fruit and vegetable samples with high enhancement factors (307–2327), good selectivity, low detection limits (0.11–0.23 $\mu\text{g kg}^{-1}$) and good precision (3.6–12.1% RSD).

Recently, Wu et al. [43] utilized thiol-ene click chemistry to synthesize a cross-linked hydrazone COFs coated fiber for SPME of pesticides in vegetables (Fig. 10). The robust covalent bonds and the multilayered COFs ensure the large adsorption capacity and good lifetime of the prepared SPME fiber. The fiber also exhibited large enrichment factors (2190–10998), low detection limits (0.0003–0.0023 ng kg^{-1}) and good precisions for pesticides. The π - π , hydrogen bonding and van der Waals interactions between the analytes and COFs played significant roles in extraction.

4. COFs as stationary phases for chromatography

4.1. COFs for GC

The large surface area, good thermal and chemical stability make COFs ideal candidates as the stationary phase for GC. Our group

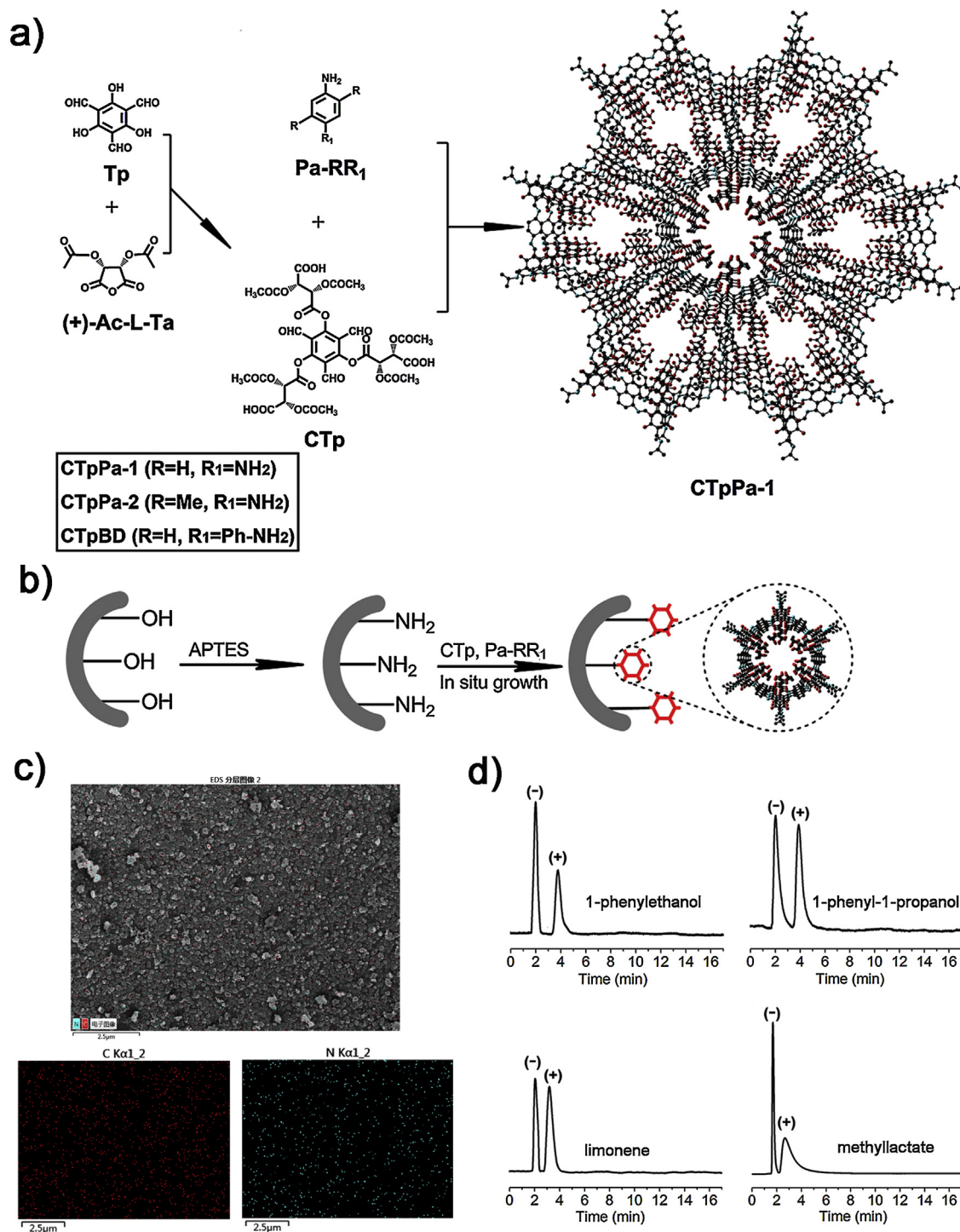


Fig. 12. Synthesis of (a) chiral COFs and (b) chiral COFs-bound capillary columns. (c) Energy dispersive X-ray spectroscopy (EDS) element mapping images of the inner wall of CTPa-1-bound capillary column. (d) Gas chromatograms of 1-phenylethanol, 1-phenyl-1-propanol, limonene, and methyl lactate on CTPa-1 column.

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[44] developed a facile room-temperature solution-phase method to synthesize TpBD for high resolution GC separation of diverse important industrial analytes (Fig. 11). The spherical TpBD with large surface area, good thermostability and solvent stability was prepared in ethanol at room-temperature within 30 min. A TpBD coated capillary column was then fabricated via a dynamic coating method. The fabricated TpBD coated column was shown to have high polarity and provided high resolution for the separation of various industrial analytes such as alcohols, alkanes, cyclohexane

and benzene, pinene isomers owing to the combination of the interactions of van der Waals, π - π and hydrogen bonding between the analytes and the TpBD frameworks. The results reveal the great potential of COFs in chromatographic separation.

The separation of enantiomers is constantly challenging and significant in chemistry, pharmacology and biology [53–55]. The application of COFs in chiral separation is still in its infancy because of the limited number of chiral COFs available and their challenging synthesis. Recently, our group [45] proposed a bottom-up strategy

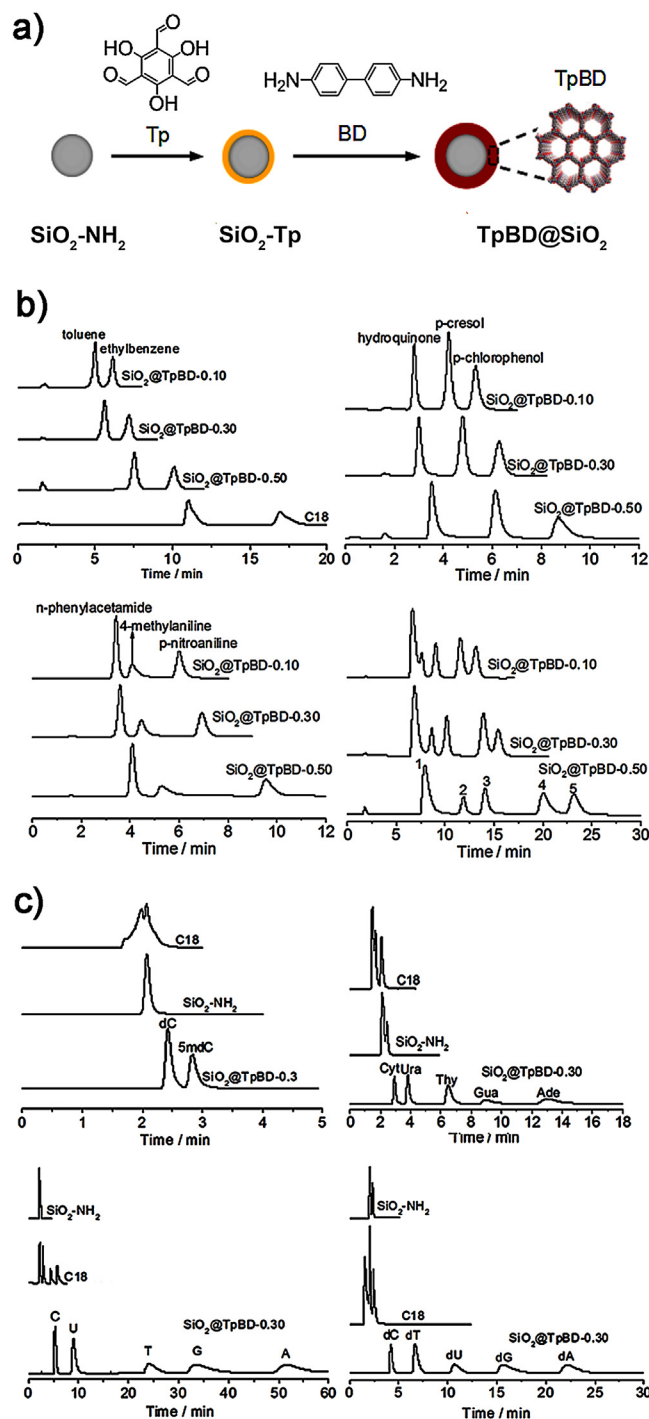


Fig. 13. (a) Fabrication of core-shell TpBD@SiO₂ microspheres for HPLC. (b) HPLC separation of toluene, ethylbenzene, acidic compounds, basic compounds and PAHs on TpBD@SiO₂ packed column. (c) HPLC separation of dC and 5mdC, nucleobases, nucleosides, and deoxynucleosides on the TpBD@SiO₂ packed column. Adapted with permission from Ref. [46]. Copyright 2017 Wiley-VCH.

to synthesize chiral COFs and *in situ* growth approach to prepare chiral COFs capillary columns for chiral GC (Fig. 12). An enantiomer of (+)-diacetyl-L-tartaric anhydride was utilized to react with 1,3,5-triformylphloroglucinol (Tp) to form chiral monomer CTP. The obtained CTP was then condensed with the corresponding diamine to construct chiral COFs. The chiral COF-bound capillary columns were then synthesized via an *in situ* growth approach. The McReynolds constants show that the chiral COF-bound capillary columns are of moderate polarity. Baseline separation of (±)-methyl lactate, (±)-1-phenylethanol, (±)-limonene and (±)-

1-phenyl-1-propanol was achieved on the chiral COFs-bound capillary columns within 5 min. The chiral COFs-bound capillary columns also gave better resolution and larger separation factors than commercial chiral capillary columns Cyclosil B and β-DEX 225. The chiral microenvironment, π-π interaction, hydrogen-bonding and van der Waals interaction played significant roles in chiral GC. The developed strategy offers a promising platform for the construction of chiral COFs for further applications in separation science.

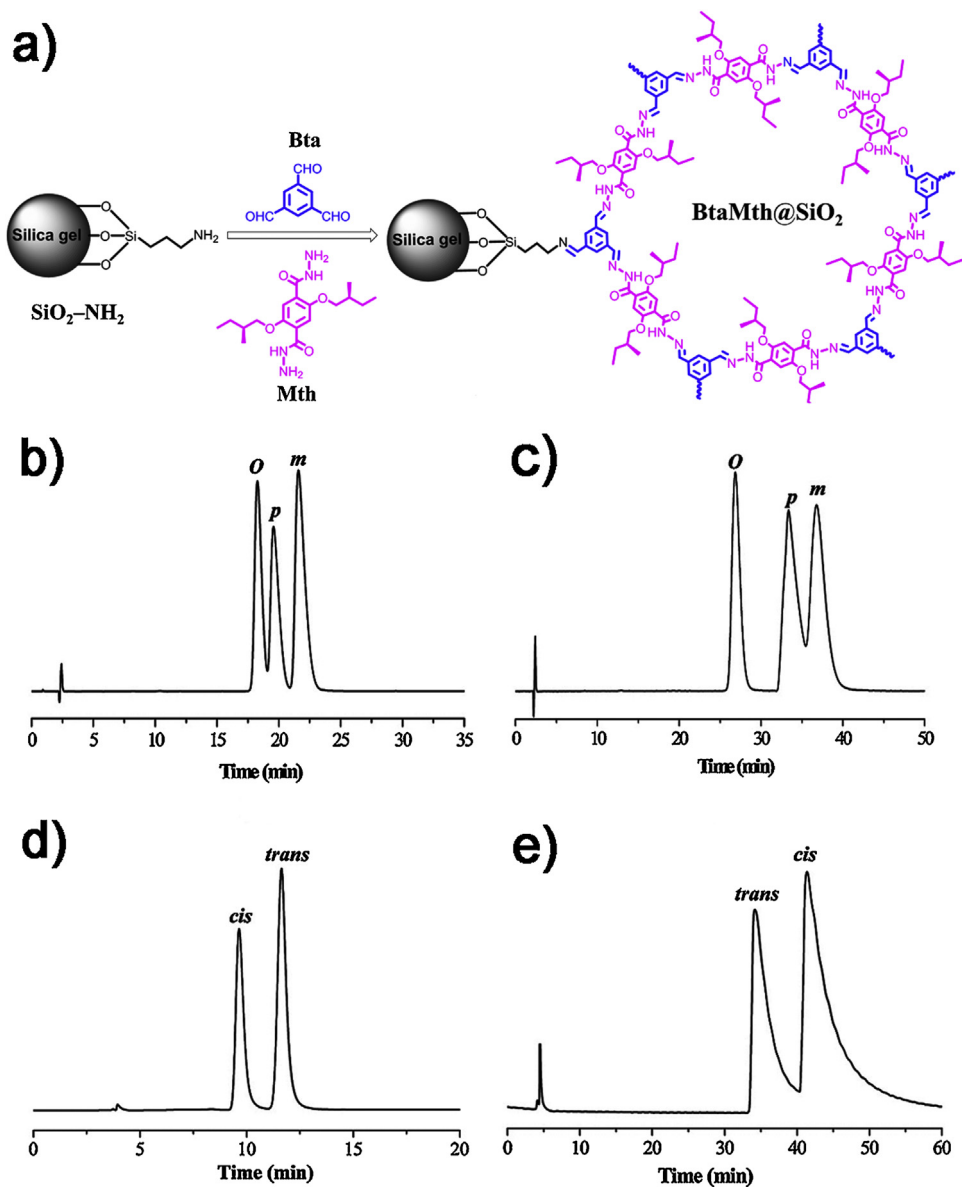


Fig. 14. (a) Schematic for the fabrication of BtaMth@SiO₂ composite. HPLC chromatograms of BtaMth@SiO₂ packed column for the separation of isomers: nitrotoluene (b), nitrochlorobenzene (c), beta-cypermethrin (d), metconazole (e). Adapted with permission from Ref. [48]. Copyright 2017 Elsevier.

4.2. COFs for HPLC

The unique structures, good solvent stability and large surface area also make COFs potentially useful in HPLC. However, COFs synthesized via traditional methods often show irregular shape, sub-micrometer size, or broad size distribution, which is the greatest challenge for the application of COFs in HPLC. Fabrication of COFs@SiO₂ core-shell microspheres is one of promising and feasible strategies to overcome the above-mentioned limitations of bare COFs for HPLC. Recently, our group [46] developed an *in situ* growth approach to synthesize spherical core-shell TpBD@SiO₂ composites as the stationary phase for HPLC (Fig. 13). The uniform TpBD shell thickness was controlled by tuning the concentration of COFs monomers. The TpBD@SiO₂ columns were evaluated with diverse probe molecules including toluene and ethylbenzene, PAHs, acidic and basic compounds, and RP 5 (theophylline, anisole, methyl benzoate, p-nitro-aniline, and o-xylene). All probe molecules were baseline separated due to the hydrophobic, hydrogen-bonding and

π - π interactions between the TpBD@SiO₂ and the analytes. In addition, baseline separation of five nucleobases (Cyt, Ura, Thy, Gua, and Ade), five nucleosides (C, U, T, G, and A), five deoxynucleosides (dC, dU, dT, dG, and dA), 5mdC, and dC on the TpBD@SiO₂ packed column was achieved by isocratic elution without addition of buffers in the mobile phase, an improvement on commercial C18 and NH₂-SiO₂ columns. The good column packing properties of the uniform silica microspheres combined with the good separation ability of COFs make COFs@SiO₂ composites promising in HPLC.

Recently, Zhao et al. [47] reported the synthesis of sheet-like CTFs decorated silica gel microspheres CTF@SiO₂ to improve HPLC separation and selectivity. The CTFs were decorated on the surface of cyano-terminated silica sphere (CN-SiO₂) via cyclical trimerization of terephthalonitrile. Mono-substituted benzenes, PAHs, phenols, anilines and bases were used to evaluate the HPLC performance of the prepared CTF@SiO₂ in the reversed phase mode. The synergism of triazine and aromatic moieties on CTF@SiO₂ led to better selectivity and resolution on the CTF@SiO₂ column in HPLC

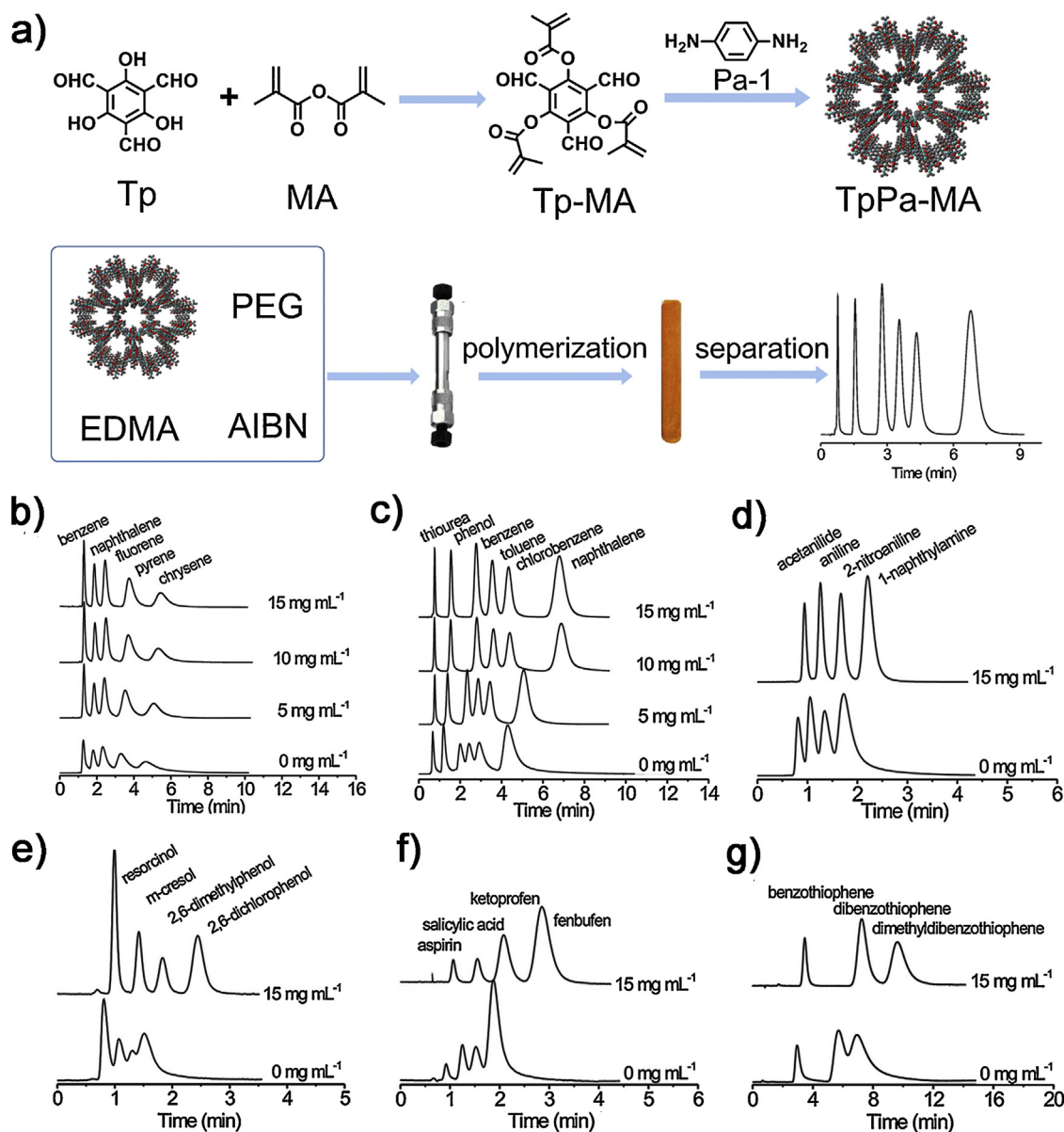


Fig. 15. (a) Illustration for the preparation of poly (TpPa-MA-co-EDMA) monolith for HPLC. Effect of TpPa-MA concentration on HPLC separation of different analytes: PAHs (b); thiourea, phenol, benzene, toluene, chlorobenzene and naphthalene (c); basic compounds (d); acidic compounds (e); nonsteroidal anti-inflammatory drugs (f); benzothiohenes (g). Adapted with permission from Ref. [49]. Copyright 2017 Elsevier.

than CN-SiO₂ and C18 columns, proving the potential of CTF@SiO₂ composite in HPLC.

Chiral COFs can also be utilized to fabricate chiral COFs@SiO₂ composite. Zhang et al. [48] constructed a new hydrazone-linked chiral COF BtaMth to fabricate BtaMth@SiO₂ composite for HPLC (Fig. 14). The BtaMth was synthesized via the bottom-up concept and subsequently grew on the SiO₂-NH₂ via a one-pot synthesis method. The BtaMth@SiO₂ packed column allowed working in both normal-phase and reverse-phase modes. The HPLC separation of positional isomers including nitrotoluene and nitrochlorobenzene, as well as *cis-trans* isomers including β -cypermethrin and metconazole were realized on the BtaMth@SiO₂ packed column, revealing the dominant contribution of BtaMth in HPLC.

Monolithic columns are known for their simple synthesis, great stability, outstanding permeability and rapid mass transfer, but poor efficiency in isocratic separations of small molecules [56,57]. The combination of the distinctive architecture of monolithic column and the specific merits of COFs to fabricate COFs mono-

lithic columns is another strategy to overcome the limitations of bare COFs for HPLC application. However, the homogeneous dispersion of COFs in the polymerization precursor solution is difficult to obtain, resulting in inhomogeneous COFs monolithic columns. For the above reasons, our group [49] reported the fabrication of methacrylate-bonded COF monolithic columns to improve the HPLC separation of small organic molecules (Fig. 15). The homogeneous poly(TpPa-methacrylic anhydride co-ethylene dimethacrylate) (poly(TpPa-MA-co-EDMA)) monolithic column was successfully synthesized via the condensation of a polymerization precursor with methacrylate-bonded TpPa-1. Baseline separation of PAHs, phenols, nonsteroidal anti-inflammatory drugs and benzothiohenes was achieved on a poly(TpPa-MA-co-EDMA) monolithic column with high column efficiency, good resolution and precision. The COFs bonded monolithic column also shows enhanced hydrophobic, π - π and hydrogen bond interactions compared with the bare polymer monolithic column without COFs, and improved separation per-

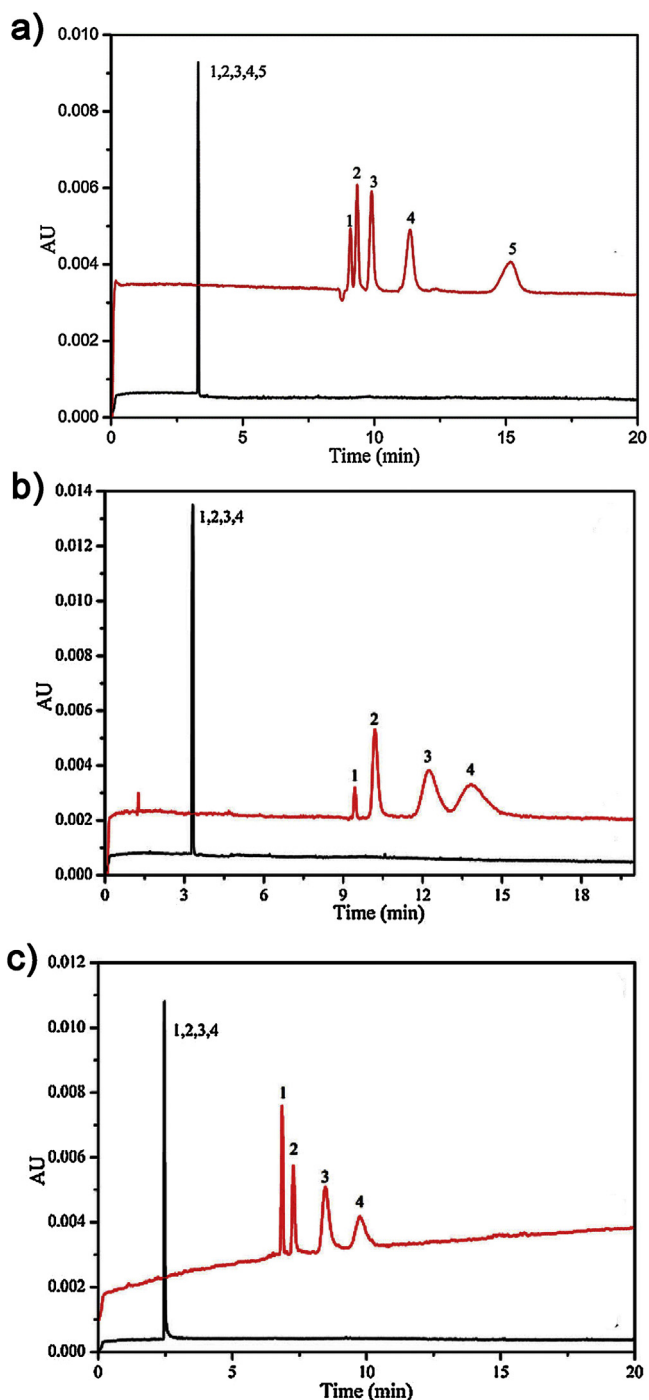


Fig. 16. Typical electropherograms of alkylbenzenes (a), PAHs (b), and anilines (c) on bare (black curve) and COF-LZU1-coated capillaries (red curve). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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formance for small molecules. These results reveal the feasibility and potential of COFs based monoliths in HPLC.

4.3. COFs for CEC

Capillary electrochromatography (CEC) is a highly selective separation technique combining the merits of HPLC and capillary electrophoresis [58,59]. Open-tube CEC (OT-CEC), as one of the most common CEC modes, suffers from low column capacity and

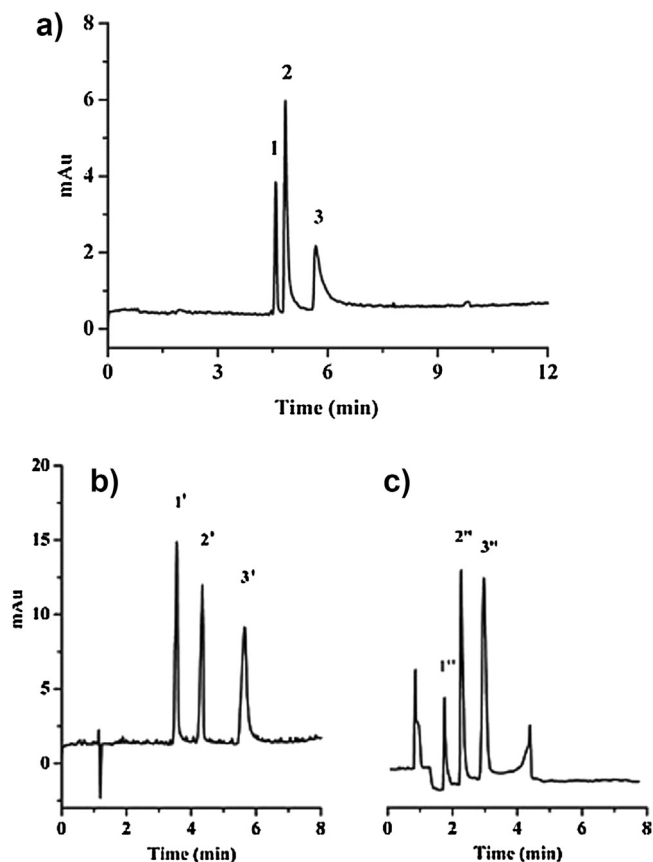


Fig. 17. Typical electropherograms for CEC separation of neutral compounds (a), acidic compounds (b), basic compounds (c) on COF-5 coated capillary column. Peak identities: 1, methylbenzene; 2, naphthalene; 3, 4-methylbiphenyl; 1', 3,5-dimethylbenzoic acid; 2', 4-aminobenzoic acid; 3', benzoic acid; 1'', 2-phenylethylamine; 2'', *N,N*-dimethylbenzenamine; 3'', phenylamine.

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an inadequate phase ratio [60]. However, the property of accessible modification with porous materials of OT-CEC column gives COFs high feasibility to make up the mentioned deficiencies due to the high surface area and abundant organofunctional groups of COFs. Chen and co-workers [50] reported the first example of COFs coated open-tube capillary column for CEC (Fig. 16). The COF LZU1 dispersion was filled into 3-glycidoxypropyltrimethoxysilane modified capillary to prepare the LZU1 coated capillary. The good size selectivity and hydrophobic interaction of LZU1 resulted in high resolution separation of the alkylbenzenes, PAHs, and anilines. In addition, the LZU1 coated capillary had a large load capacity, good stability and precision. This study shows the promising future of COFs in CEC.

Bao et al. [51] developed a polydopamine-supported immobilization approach along with a layer-by-layer approach to fabricate COF-5 coated capillary columns for CEC (Fig. 17). The noncovalent and covalent interaction between polydopamine, capillary and COF-5 played key roles for the fabrication of the multilayer COF-5 coated capillary. The COF-5 coated capillary gave high column efficiency ($154060 \text{ plates m}^{-1}$ for toluene), good stability and reproducibility for CEC separation of neutral, acidic and basic compounds. Such polydopamine-supported method paves the way for the application of boron COFs in analytical separations.

Recently, Kong et al. [52] reported the epitaxial growth to *in situ* fabricate COF LZU1 coated capillary column for CEC (Fig. 18). Baseline separation of the neutral analytes, amino acids and nonsteroidal anti-inflammatory drugs (NSAIDs) was achieved with good

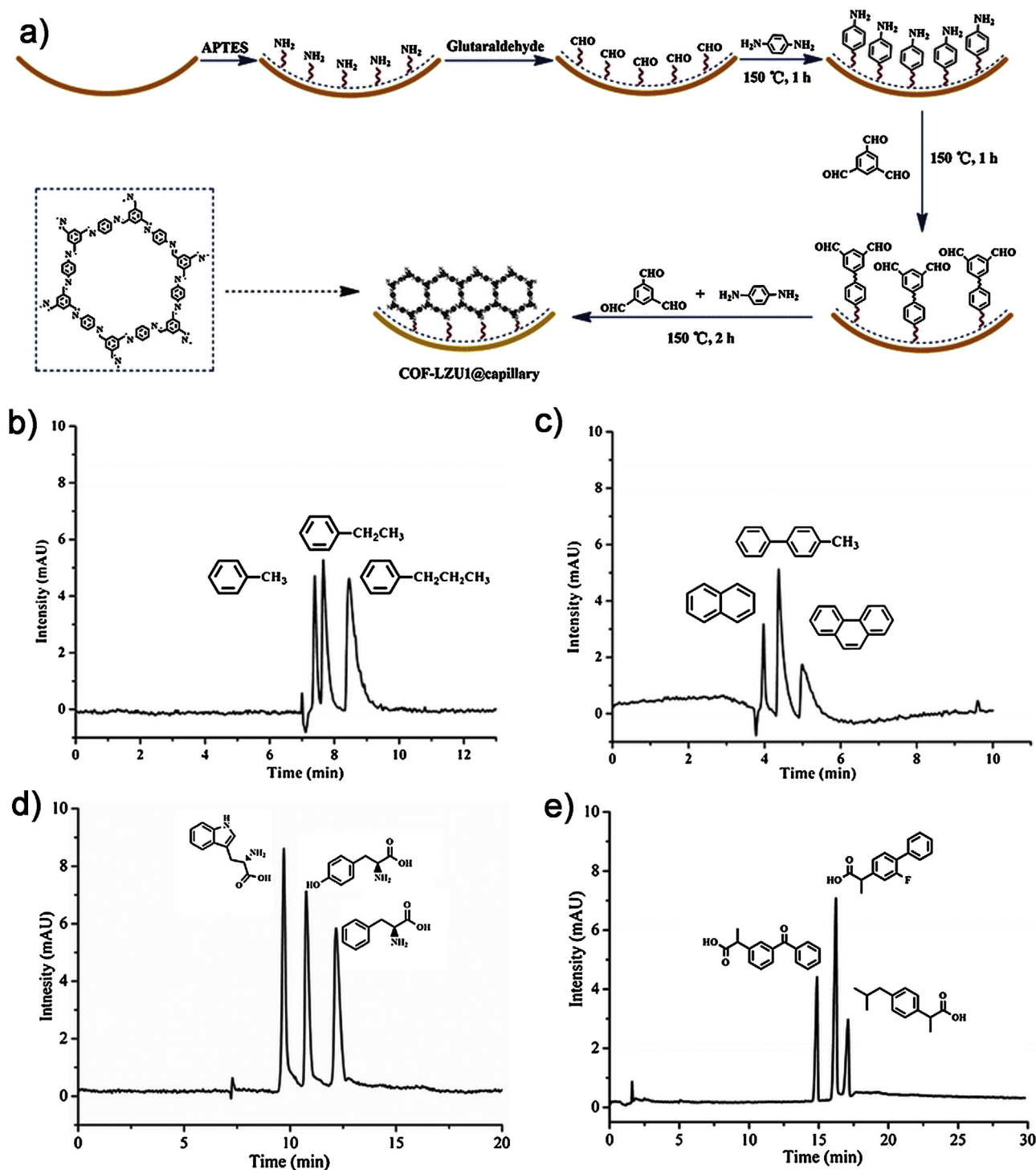


Fig. 18. (a) Scheme for the growth of COF-LZU1 on the inner wall of aldehyde group-functionalized capillary. Typical electropherograms for CEC separation of neutral compounds (b, c), amino acids (d), NSAIDs (e) on the COF-LZU1 coated open-tubular column.

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stability and reproducibility. The hydrophobic, π - π and hydrogen bond interaction played key roles in the separation.

5. Conclusions and perspectives

In summary, COFs have been shown to be promising in separation science from sample pretreatment (SPE and SPME) to chromatography (GC, HPLC, CEC) for diverse targets. Not only the

bulk COFs partials but also COFs composites have been prepared to meet the demands of different separation technologies and to improve sensitivity and selectivity. Even so, the development of the COFs in separation science is still in its infancy. Further effort is needed to improve the serviceability of COFs in separation science. The increasing number of new COFs with superb properties provides vast possibility for separation applications. Specific design and functionalization of COFs are necessary to enhance the per-

formance of COFs in separation science. The combination of COFs with other functional materials is still the potent way to expand the application COFs in separation science.

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