Supporting Information

Tuning the physicochemical properties of reticular covalent organic frameworks (COFs) for biomedical applications

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Table S1. The synthetic strategies of COFs.

Synthetic method	Procedure	Advantage	Limitation	Ref.
Bottom-up strategy				
Solvothermal method	Disperse monomers in solvents. Seal the vessel and react under a certain temperature (80-120 ˚C) for several days.	The most commonly used synthetic method for COFs; simple and straightforward.	Request strict synthetic condition and long reaction time; need a large amount of organic solvent, which may cause environmental pollution; produce COF product as powder, which is hard for incorporating into devices.	[1,2]
Ionothermal method	Use ionic liquid (e.g. $ZnCl_2$) as solvent, which is a relatively complex solvothermal strategy.	Mild and green; able to obtain crystalline structure.	Difficult to control crystallinity; require high reaction temperature thus narrow the scope of building units.	[3,4]
Microwave-assisted synthesis	Dissolve monomers in solvent and sealed with nitrogen. Heat the system by microwave irradiation and kept at certain temperature for several minutes.	Fast and clean, providing new possibility for further applications in large scale.	Obtain COFs as powder.	[5,6]
Mechanochemical method	Place the monomers in a mortar and ground by using a pestle at room temperature; catalyst solution is needed in some cases added to enhance the reaction rate and improve crystallinity.	Easy to operate; eco-friendly and timesaving, which is promising to produce COFs in large-scale.	The suitable monomers and reaction are limited.	[7,8]
Interfacial synthesis	A widely used approach for the fabrication of thin films. Solid-vapor interface synthesis: under ultrahigh vacuum, halogenate monomers will be turned into vapor at first and	Efficient method for fabricating COF thin films with simultaneous control of their thickness.	The production capacity is rather low.	[9,10]

	deposited on the surface of clean metal surface; Liquid-liquid interface synthesis: dissolve monomers and catalysts in two immiscible solvents. Monomers are polymerized and transformed into thin film at the interface.			
Top-down strategy				
Solvent-assisted exfoliation	Weaken the π−π interaction between the COF layers with the help of a suitable solvent (CH_2Cl_2, $CHCl_3$, MeOH, and Tetrahydrofuran, etc.)	The most used method for COF exfoliation; enable the high-yield and large-scale production of ultrathin nanosheets in solution at low cost.	The crystallinity of COF may decrease; monolayered nanosheet is difficult to obtain; the aggregation of monolayers exists due to the stacking interaction; the yield of COF thin film is relatively low.	[11,12]
Mechanical delamination	Break the strong π−π interactions between the COF layers through mechanical grinding.	Effective and solvent-free		[13,14]
Chemical exfoliation	Intercalate groups into the COF backbone through chemical reaction. Weaken the planarity of each layer and the π−π stacking between layers.	Improved aqueous dispersibility; easier to control the thickness of COFs; able to introduce functional groups.		[15,16]
Self-exfoliation method	Choose well-designed building blocks to induce peeling-off by an internal force. Introduce certain groups to enlarge the distance between neighboring layers and reduce the π−π interaction.	Simple; avoid restacking; the ionic building units can not only initiate the self-exfoliation process but also introduce targeted functional groups.		[17,18]

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