Electronic Supplementary Information

Preparation of chiral metal-organic framework L-his-MIL-53-NH_2@SiO_2 composite by *in situ* growth and chiral post-modification strategies for HPLC enantiomeric separation

An-Xu Ma, Cai-Fang Liu, Yu-Lan Zhu, Zong-Hong Luo, Hong-Mei Zhou, Yue Zhang, Bang-Jin Wang*, Jun-Hui Zhang, Sheng-Ming Xie*, Li-Ming Yuan
Department of Chemistry, Yunnan Normal University, Kunming 650500, P.R. China.
Corresponding authors: Bang-Jin Wang, wangbangjin711@163.com; Sheng-Ming Xie, xieshengming_2006@163.com.
Tel: +86 871 65941088; Fax: +86 871 65941088.

1. Synthesis of MIL-53-NH_2

MIL-53-NH_2 was synthesized with reference to the method of Sun et al:[1] aluminum chloride hexahydrate (0.76 g, 3.1 mmol) and 2-aminoterephthalic acid (0.56 g, 3.1 mmol) were added to 30 mL of DMF and sonicated for 30 min. Next, the mixture was transferred to a 100 mL PTFE-lined steel autoclave and reacted at 150 °C for 24 hours. Cooled to room temperature, the solid product was collected, activated in DMF for 24 h, and then washed three times with excess methanol to exchange the DMF inside the MOF pores. Finally, the resulting yellow powder was dried under vacuum at 120 °C for 12 h.

2. Synthesis of L-his-MIL-53-NH_2

L-his-MIL-53-NH_2 was synthesized by referring to the method of Sun et al:[1] EDC (0.192 g, 1 mmol), NHSS (0.043 g, 0.2 mmol), MIL-53-NH_2 (120 mg), and L-histidine (0.155 g, 1 mmol) were dissolved in 20 mL of phosphate-buffered solution (pH 5.0) and stirred at room temperature for 5 days. The L-histidine-functionalized MOF nanocrystals were collected by centrifugation and washed three times with deionized water. Finally, the product was vacuum dried at room temperature for 2 days.

3. Calculation formulas of the thermodynamic and chromatographic parameters

$$k_1 = \frac{t_1 - t_0}{t_0} \quad (1)$$

$$k_2 = \frac{t_2 - t_0}{t_0} \quad (2)$$

$$\alpha = \frac{t_2 - t_0}{t_1 - t_0} \quad (3)$$

$$R_S = \frac{t_2 - t_1}{W_{1/2(1)} + W_{1/2(2)}} \quad (4)$$

$$\ln k' = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} + \ln \Phi \quad (5)$$

$$\Delta G = \Delta H - T\Delta S \quad (6)$$

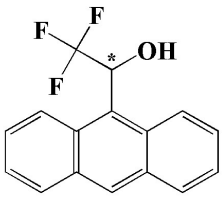
$$\Phi = \frac{V_S}{V_0} \quad (7)$$

$$V_S = V_{col} - V_0 \quad (8)$$

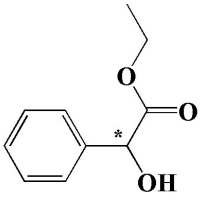
$$V_0 = t_0 \times F \tag{9}$$

$$N = 5.54(\frac{t_R}{2\Delta t_{1/2}})^2 \tag{10}$$

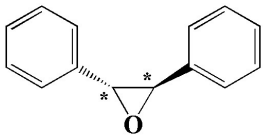
4. Structures of racemates



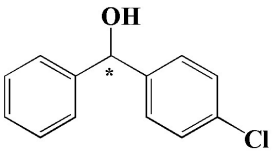
2,2,2-Trifluoro-1-(9-anthryl)ethanol



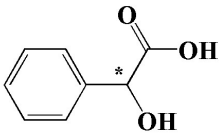
Ethyl mandelate



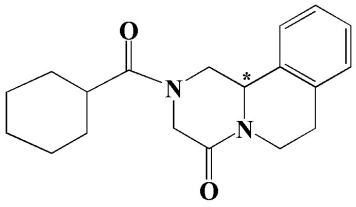
Trans-stilbene oxide



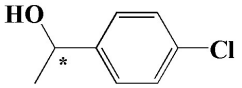
4-Chlorobenzhydrol



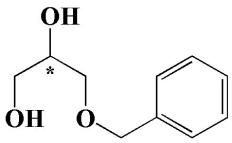
Mandelic acid



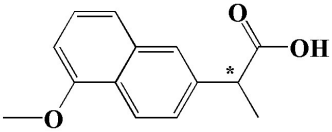
Praziquantel



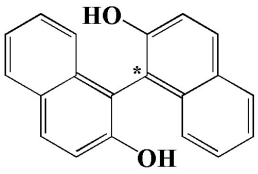
1-(4-Chlorophenyl)ethanol



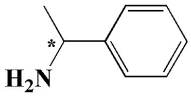
3-Benzyloxy-1,2-propanediol



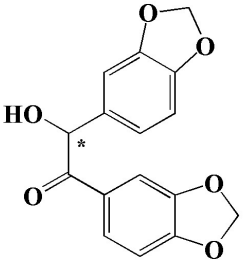
Naproxen



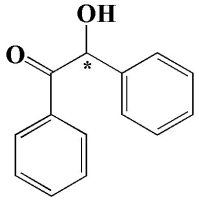
1,1'-Bi-2-naphthol



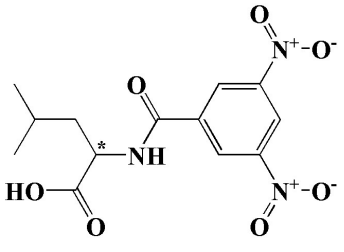
1-Phenylethylamine



Piperoin



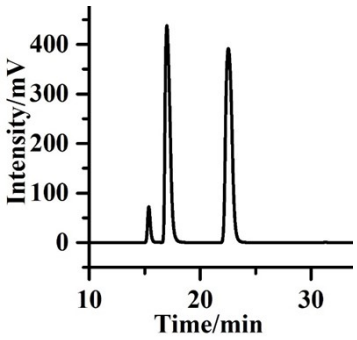
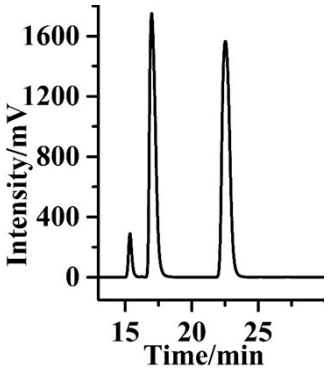
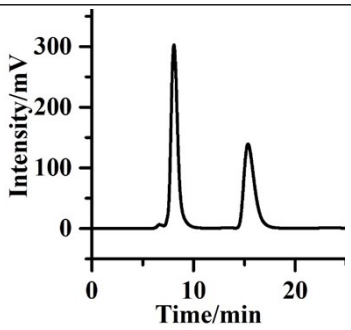
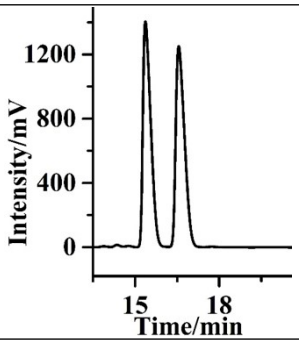
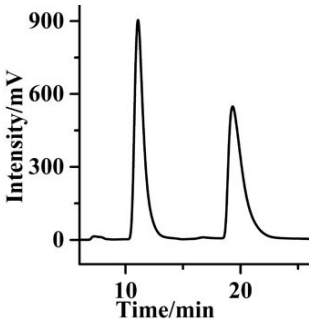
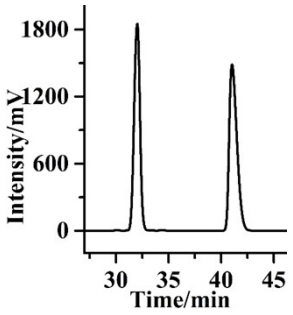
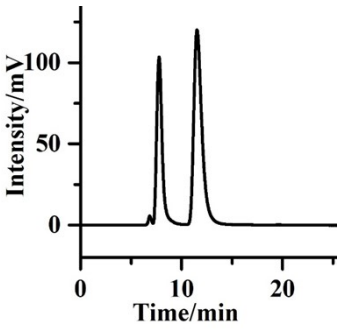
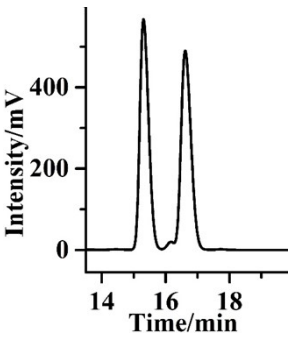
Benzoin



N-3-5-Dinitrobenzoyl-L-Leucine

Fig. S1 Structures of 14 racemates separated on the L-his-MIL-53-NH_2@SiO_2 packed column.

5. Comparison of resolution performance between L-his-MIL-53-NH_2@SiO_2-packed column and Chiralpak AD-H column.

Racemates	L-his-MIL-53-NH_2@SiO_2 column	Chiralpak AD-H column
2,2,2-Trifluoro-1-(9-anthryl)ethanol		
Ethyl mandelate		
Benzoin		
4-Chlorobenzhydrol		

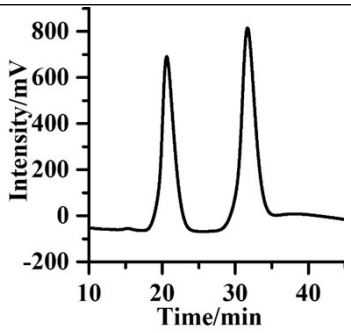
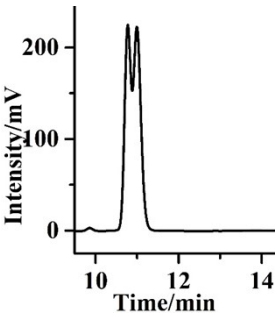
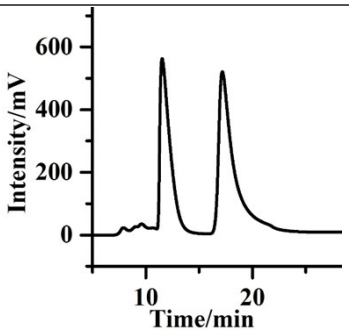
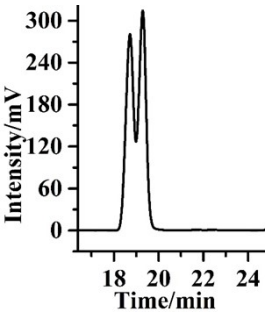
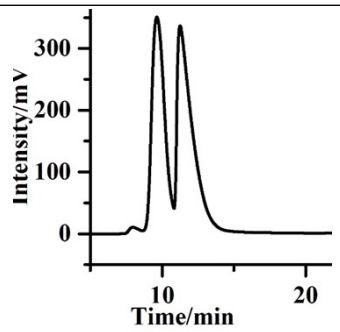
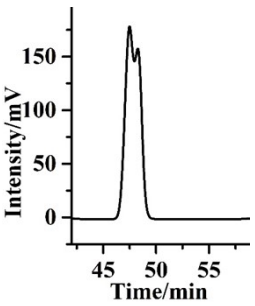
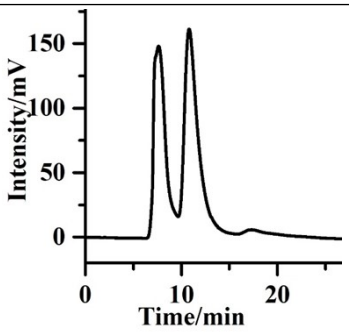
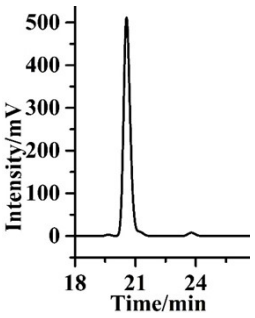
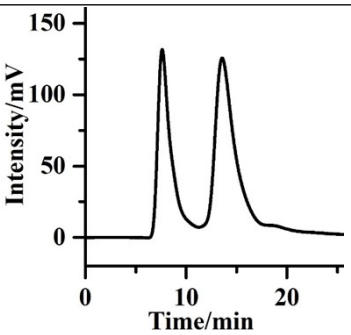
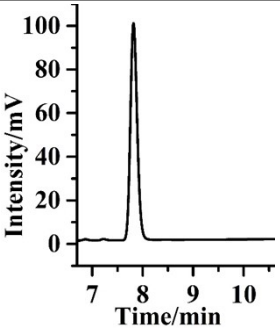
1-(4-Chlorophenyl)ethanol		
3-Benzyloxy-1,2-propanediol		
1,1'-Bi-2-naphthol		
Naproxen		
Praziquantel		

Fig. S2 HPLC chromatograms of racemates obtained on the L-his-MIL-53-NH_2@SiO_2-packed column and the Chiralpak AD-H column.

6. N_2 adsorption-desorption isotherms and pore size distributions.

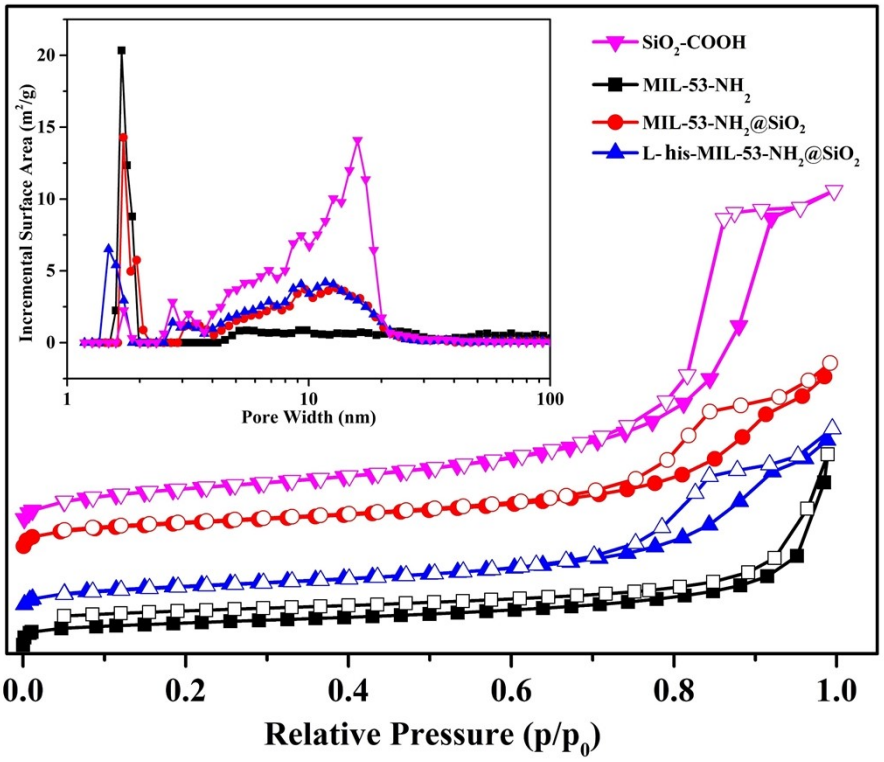
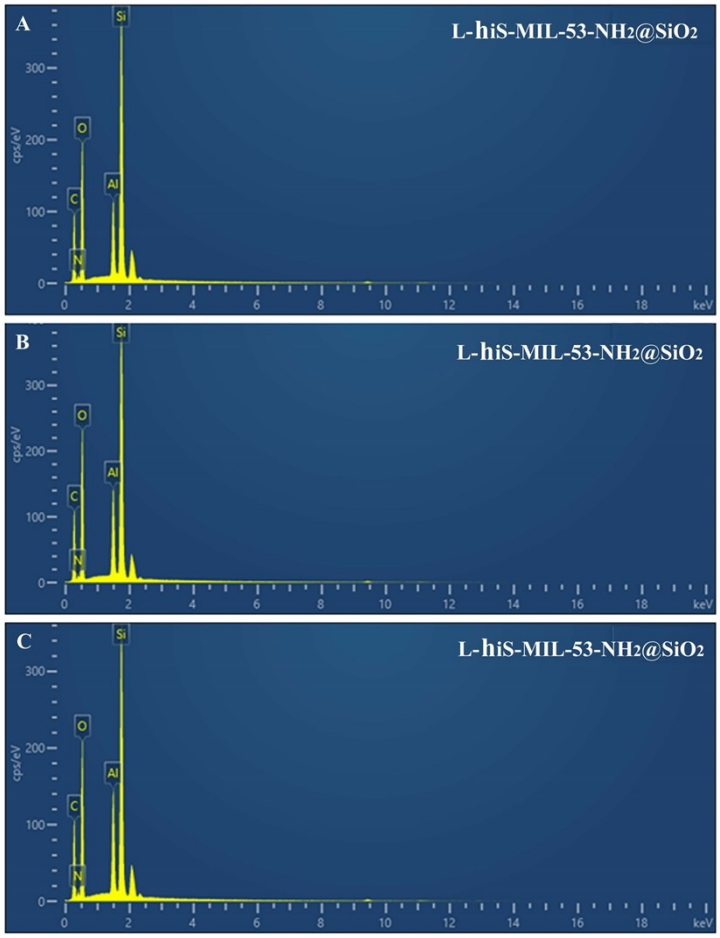


Fig. S3 N_2 adsorption-desorption isotherms and pore size distributions.

7. Surface elemental composition of L-his-MIL-53-NH_2@SiO_2.



	A		B		C	
	Weight (%)	**Weight (%) Sigma**	**Weight (%)**	**Weight (%) Sigma**	**Weight (%)**	**Weight (%) Sigma**
C	40.22	0.30	40.29	0.28	40.32	0.36
N	4.66	0.33	4.39	0.31	4.89	0.41
O	32.65	0.23	32.38	0.22	32.67	0.28
Al	5.02	0.05	5.19	0.05	5.33	0.07
Si	17.45	0.12	17.75	0.11	16.79	0.14

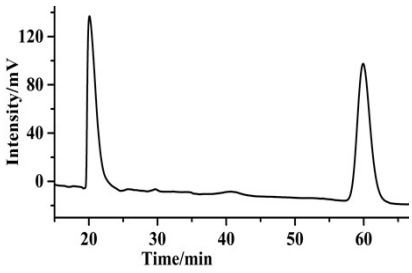
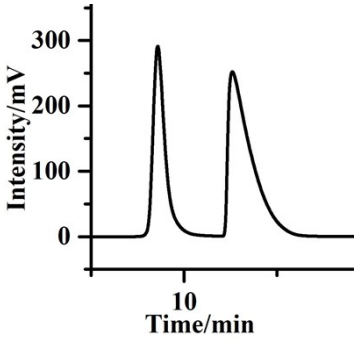
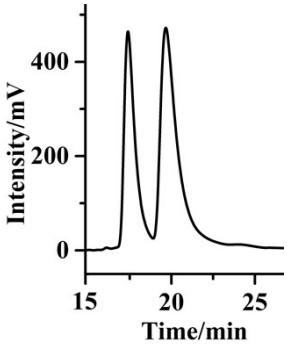
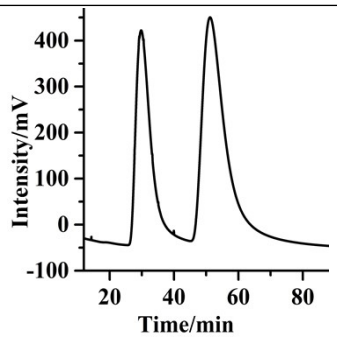
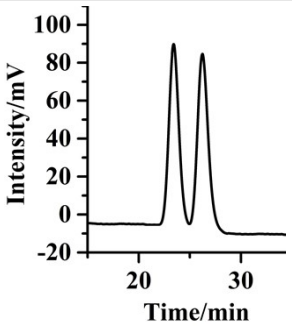
Fig. S4 SEM-energy dispersive X-ray spectroscopy results of three batches of L-his-MIL-53-NH_2@SiO_2 composite.

8. Comparison of separation performance on the L-his-MIL-53-NH_2@SiO_2 packed column and the $[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ packed column.[2]

Table S1 Separations of racemates on the L-his-MIL-53-NH_2@SiO_2 and $[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ packed column.

Chiral compounds	L-his-MIL-53-NH_2@SiO_2 column			$[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ column		
	k	**α**	**Rs**	***k***	**α**	**Rs**
2,2,2-Trifluoro-1-(9-anthryl)ethanol [a]	3.26	1.48	4.86	2.49	3.84	11.22
Ethyl mandelate [a]	1.92	3.52	4.07			—[e]
Trans-stilbene oxide [a]	1.38	2.25	2.38	1.90	1.21	1.42
4-Chlorobenzhydrol [a]	1.19	2.59	2.37			—[e]
Mandelic acid [b]	1.67	2.11	2.59			—[e]
Praziquantel [a,d]	1.56	3.62	2.22	4.50	1.67	2.05
1-(4-Chlorophenyl)ethanol [a]	4.98	1.72	3.04	3.07	1.26	1.62
3-Benzyloxy-1,2-propanediol [a]	2.23	1.89	2.72	4.02	1.77	2.16
Naproxen [a]	1.07	2.32	1.39			—[e]
1,1'-Bi-2-naphthol [c]	1.11	1.37	0.89			—[e]
1-Phenylethylamine [c]	1.96	1.29	1.28			—[e]
Piperoin [a]	2.61	1.33	1.59			—[e]
Benzoin [a,d]	1.12	2.41	4.65	4.03	1.16	1.36
N-3-5-Dinitrobenzoyl-L-Leucine [a]	0.80	1.99	0.96			—[e]

Mobile phase of L-his-MIL-53-NH_2@SiO_2 packed column: [a] n-hexane/isopropanol (9/1, v/v); [b] n-hexane/isopropanol (8/2, v/v); [c] n-hexane/isopropanol (95/5, v/v). Mobile phase of $[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ packed column: [d] n-hexane/isopropanol (99/1, v/v). All chromatographic separations were performed at 25°C using n-hexane/isopropanol as mobile phase at flow rate of 0.1 $mL \cdot min^{-1}$. The UV detection wavelength was 254 nm. —[e] Cannot be separated.

Racemates	L-his-MIL-53-NH_2@SiO_2 column	$[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ column
2,2,2-Trifluoro-1-(9-anthryl)ethanol		
Trans-stilbene oxide		
Praziquantel		
1-(4-Chlorophenyl)ethanol		

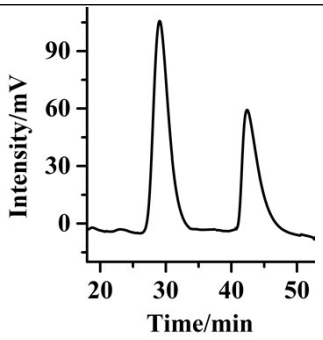
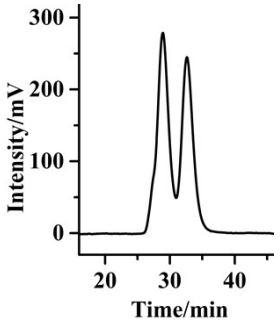
3-Benzyloxy-1,2-propanediol		
Benzoin		

Fig. S5 HPLC chromatograms of some racemates obtained on the L-his-MIL-53-NH_2@SiO_2 column and the $[Cu_2(D\text{-}Cam)_2(4,4'\text{-}bpy)]_n$@$SiO_2$ column.

References

1 X. D. Sun, B. Niu, Q. Zhang and Q. Chen, *J. Pharm. Anal.*, 2022, **12**, 509-516.

2 J. K. Chen, N. Y. Xu, P. Guo, B. J. Wang, J. H. Zhang, S. M. Xie and L. M. Yuan, *J. Sep. Sci.*, 2021, **44**, 3976-3985.