Click preparation of multiple-thioether bridged cyclodextrin chiral materials for efficient enantioseparation in high performance liquid chromatography

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1. Experimental Section

1.1 The synthesis of alkene silica

Alkene silica were prepared using our previous approaches. Specifically, activated silica gel (3.0 g, dried overnight at 120 ℃ in vacuum) was uniformly dispersed in anhydrous toluene (30 mL), the vinyl triethoxy silane (1.3 mL) was added to the reaction solution. The solution was heated to 120 °C and reacted for 24 h under argon atmosphere. Then filtered and extracted the crude product with acetone soxhlet for 24 h, and dried in vacuum to afford the product 3.42g.

1.2 The synthesis of heptakis(6-iodo-6-deoxy)-*β*-CD (7ICD)

7ICD was synthesized according to the methods reported in the previous literature. Briefly, triphenylphosphine (28 g, 0.107 mol) was reacted with iodine (26.93 g, 0.106 mol) in freshly distilled DMF (80 mL) in a 250 mL round bottom flask with a magnetic stirrer bar. After reacting for 2 h at ice temperature, *β*-CD (4.32 g, 3.806 mmol) was charged. The solution was heated to 80 °C and reacted for 15 h. Then, the solution was concentrated to half volume in vacuum. The residue solution was added with sodium methoxide in methanol (3M, 30 mL) with simultaneous cooling. After reacting for 30 min, the solution was poured into 1.2 L water in ice bath. The precipitate was filtered on a sintered glass funnel and washed by MeOH. After a night of natural drying, the product was extracted with MeOH and acetone soxhlet until colorless, and dried in vacuum to afford the beige color product 5.75g, yield 79.3%. ^{1}H NMR (400 HMz, ppm, DMSO-d6): 6.06-5.90 (m, 14H), 4.99 (s, 7H), 3.82-3.35 (m, 42H).

1.3 The characterization comparison chart of products

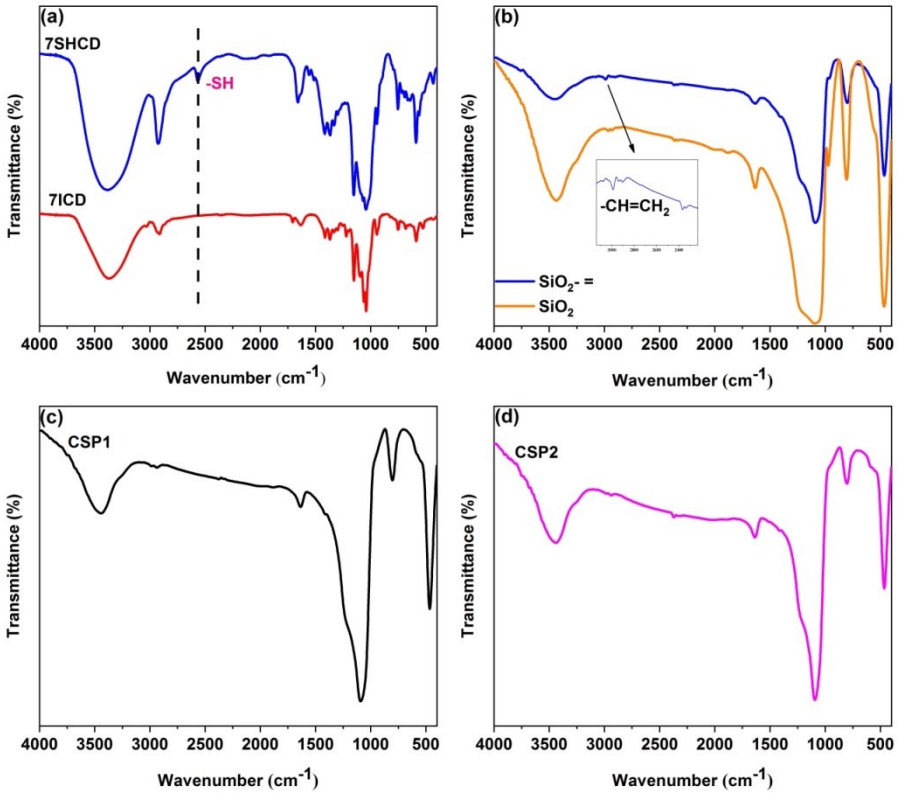

Fig.S1 The FTIR of products

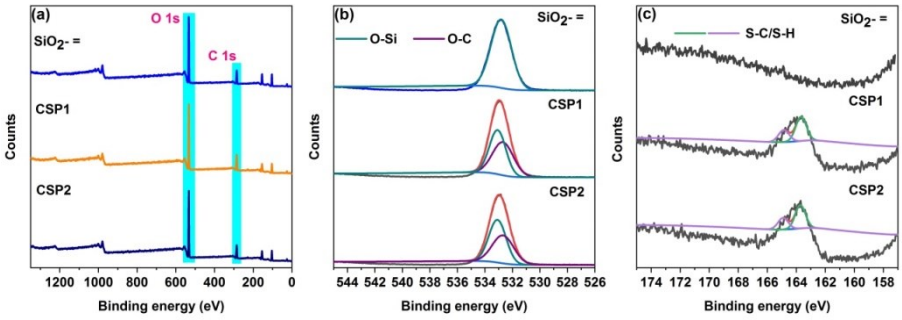

Fig.S2 The XPS of products (a. XPS; b. O 1s; c. S 2p).

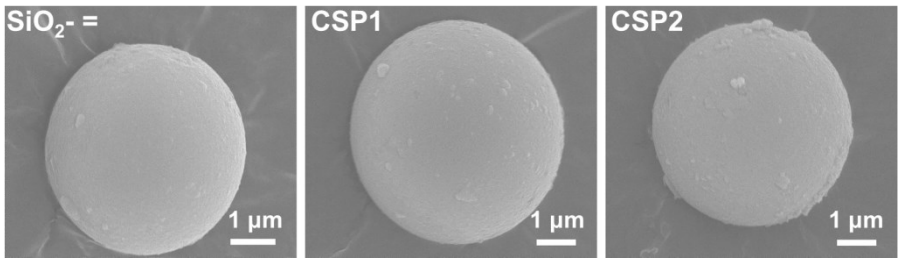

Fig.S3 The SEM of products.

1.4 Comparison of enantioseparation ability on CSP1 and CSP2

Table S1 Comparison of enantioseparation ability on CSP1 and CSP2

	CSP1				CSP2				
Analyte	k_1	k_2	R_s	α	k_1	k_2	R_s	α	Trailing
Ph-Ph	2.50	3.38	0.81	1.35	8.11	11.07	1.16	1.36	✔
4MOPh-OPr	0.98	1.22	1.51	1.24	2.61	3.32	2.16	1.27	
MDOPh-Py	3.00	3.78	0.84	1.26	8.75	11.07	1.29	1.26	✔
4ClPh-Ph	4.32	7.16	2.04	1.66	12.33	19.83	2.45	1.61	✔
4NPh-OPr	0.89	1.20	1.77	1.35	2.36	3.31	2.77	1.4	
4NPh-Py	2.45	3.59	1.41	1.47	7.10	10.37	2.65	1.46	✔
3ClPh-OPr	0.88	1.07	1.60	1.22	2.15	2.74	2.38	1.27	
4MetPh-OPr	1.11	1.39	1.42	1.25	3.00	3.88	2.16	1.29	
4MetPh-Py	2.27	2.82	0.79	1.24	6.70	8.60	1.19	1.28	✔
4MetPh-2Py	1.63	1.84	＜0.5	1.13	4.79	5.61	0.78	1.17	✔
L-1	1.34	1.53	0.71	1.14	3.56	4.14	0.99	1.17	
L-2	2.50	2.85	0.82	1.14	7.3	8.42	1.09	1.15	
L-9	1.45	1.69	0.81	1.16	3.95	4.73	1.08	1.2	
L-11	1.36	1.63	1.21	1.19	3.68	4.47	1.49	1.21	
L-12	1.17	1.40	0.75	1.19	2.83	3.46	0.95	1.22	
D-1	0.97	1.07	＜0.5	1.11	2.03	2.33	1.02	1.15	
D-2	0.80	0.93	0.81	1.16	1.71	2.14	1.41	1.25	
D-3	1.59	1.81	0.95	1.14	3.59	4.29	1.39	1.20	
D-5	0.49	0.69	1.47	1.43	0.93	1.58	2.47	1.71	
Dns-Aca	3.00	3.24	＜0.5	1.08	13.73	15.27	＜0.5	1.11	
Dns-Nle	1.24	1.38	＜0.5	1.11	3.93	4.40	0.71	1.15	
Dns-Nva	1.07	1.27	1.14	1.19	3.45	4.41	1.70	1.28	
Dns-Aba	0.98	1.23	1.57	1.25	2.83	3.83	2.69	1.35	
Dns-Leu	1.38	1.53	＜0.5	1.10	5.11	5.77	＜0.5	1.13	
Dns-Val	1.21	1.53	1.50	1.27	3.97	5.49	2.31	1.38	
Dns-Thr	1.03	1.49	2.86	1.45	3.26	5.14	4.38	1.58	
Dns-Ser	0.95	1.27	2.13	1.34	2.85	4.04	3.30	1.42	
Dns-Glu	0.76	0.97	1.53	1.29	2.53	3.43	2.28	1.36	
Dns-Apa	0.78	0.99	1.25	1.27	2.64	3.62	1.56	1.37	
Dns-Phe	1.84	2.13	0.73	1.16	6.48	7.77	0.87	1.20	
Ac-1	1.17	1.25	＜0.5	1.07	3.30	3.68	0.97	1.11	
Ac-2	0.68	0.79	0.92	1.12	1.82	2.23	1.93	1.23	
Ac-3	6.11	6.58	＜0.5	1.08	4.14	7.77	2.32	1.88	✔

Ac-4	1.68	1.76	＜0.5	1.05	6.01	6.52	0.81	1.09
Ac-5	0.04	0.46	＜0.5	1.16	1.09	1.35	1.53	1.24
Al-1	0.890	0.960	＜0.5	1.07	2.94	3.23	0.79	1.10
Al-2	3.140	3.550	1.07	1.13	10.61	12.07	1.34	1.14
Al-3	0.800	0.840	＜0.5	1.05	2.64	2.85	＜0.5	1.08
Al-4	4.25	5.13	1.74	1.21	15.20	18.72	2.34	1.23
Fla-1	5.91	6.27	0.99	1.06	19.90	21.32	1.59	1.07
Fla-2	6.44	6.80	＜0.5	1.06	24.91	26.59	1.24	1.07
Fla-3	5.13	5.37	＜0.5	1.05	18.08	19.12	＜0.5	1.06
Fla-4	2.48	2.67	0.73	1.07	8.20	8.93	1.07	1.09
Benzoin	1.39	1.51	0.77	1.09	4.04	4.45	1.05	1.10

Conditions: Same as Table 1.

1.5 Comparison of enantioseparation ability on CSP1 and CSP3

Table S2 Comparison of enantioseparation ability on CSP1 and CSP3

	CSP1				CSP3				
Analyte	k_1	k_2	R_s	α	k_1	k_2	R_s	α	Condition
Ph-Ph	22.33	30.36	1.05	1.36	1.56	1.76	1.14	1.13	
Ph-OPr	3.68	4.39	1.39	1.19	0.64	0.72	＜0.5	1.12	
4MOPh-OPr	4.45	5.56	1.59	1.25	0.77	0.89	0.98	1.16	
MDOPh-Py	17.24	20.55	0.7	1.19	2.21	-	0.00	1.00	
4ClPh-Ph	29.74	42.01	2.58	1.41	2.91	3.47	2.04	1.19	
4NPh-OPr	4.02	4.98	1.87	1.24	1.04	1.24	1.36	1.19	
4NPh-Py	13.73	17.78	1.59	1.29	1.79	1.88	＜0.5	1.05	
4MetPh-OPr	6.27	7.69	1.4	1.23	1.57	1.86	1.46	1.19	
4MetPh-Py	15.57	18.18	＜0.5	1.17	3.09	3.25	＜0.5	1.05	
4MetPh-2Py	11.32	12.28	＜0.5	1.09	0.77	-	0.00	1.00	I
L-1	15.31	17.24	1.29	1.13	6.79	7.29	＜0.5	1.07	
L-2	35.21	39.9	1.6	1.13	10.81	11.87	0.96	1.10	
L-6	41.45	46.05	1.81	1.11	8.85	9.38	＜0.5	1.06	
L-9	17.34	20.02	1.49	1.15	8.02	8.79	＜0.5	1.10	
L-11	14.91	17.34	1.53	1.16	8.56	9.37	＜0.5	1.09	
L-12	17.82	20.67	1.02	1.16	6.78	7.29	＜0.5	1.08	
D-1	5.59	6.16	0.53	1.1	5.07	-	0.00	1.00	
D-2	5.86	6.74	0.87	1.15	7.68	-	0.00	1.00	
D-3	10.79	12.47	1.03	1.16	6.73	-	0.00	1.00	

Dns-Aca	4.77	5.39	＜0.5	1.13	2.32	3.36	2.02	1.45	
Dns-Nle	1.71	2.02	0.89	1.18	0.79	1.13	1.3	1.43	
Dns-Nva	1.49	1.92	1.79	1.29	0.68	0.69	0.81	1.31	
Dns-Aba	1.37	1.85	2.43	1.35	0.66	0.84	＜0.5	1.26	
Dns-Leu	2.13	2.52	0.67	1.18	1.47	2.36	2.23	1.61	
Dns-Val	1.9	2.64	2.17	1.39	0.89	1.23	1.19	1.38	
Dns-Thr	1.5	2.34	3.95	1.56	0.55	0.85	1.37	1.56	
Dns-Ser	1.26	1.78	2.85	1.41	0.61	0.8	0.77	1.3	
Dns-Glu	1.24	1.7	2.11	1.37	0.93	-	0.00	1.00	
Dns-Apa	1.59	2.26	1.42	1.42	1.72	2.34	3.21	1.36	
Dns-Phe	3.01	3.62	0.99	1.2	1.71	2.32	1.42	1.36	
Ac-1	1.36	1.49	＜0.5	1.1	0.7	-	0.00	1.00	
Ac-2	0.77	0.93	1.19	1.21	0.38	-	0.00	1.00	II
Ac-3	5.73	6.66	0.75	1.16	1.92	-	0.00	1.00	
Ac-4	2.39	2.58	＜0.5	1.08	1.58	-	0.00	1.00	
Ac-5	0.44	0.56	0.93	1.26	0.45	-	0.00	1.00	
Al-1	1.36	1.48	＜0.5	1.08	1.02	-	0.00	1.00	
Al-2	4.85	5.41	0.91	1.12	3.33	3.54	＜0.5	1.06	
Al-3	1.17	1.24	＜0.5	1.06	0.97	-	0.00	1.00	
Al-4	5.61	6.78	1.7	1.21	3.36	4.06	1.14	1.21	
Fla-1	8.01	8.55	0.86	1.07	5.3	5.79	0.95	1.09	
Fla-2	8.79	9.28	＜0.5	1.06	5.75	6.53	1.11	1.14	
Fla-3	6.91	7.21	＜0.5	1.04	3.49	3.7	＜0.5	1.06	
Fla-4	3.34	3.59	0.73	1.08	2.17	2.35	＜0.5	1.08	
Benzoin	1.75	1.91	0.81	1.09	1.17	-	0.00	1.00	

Conditions: CSP1: 1.0 mL/min, CSP3: 0.5 mL/min I. mobile phase, MeOH/H_2O, (50:50, v/v); 30 ℃; II. mobile phase, MeOH/TEAA (pH = 5.30) , (50:50, v/v); 30 ℃.

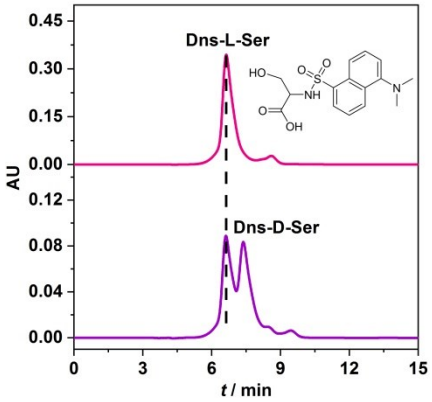

Fig.S4 Chromatograms of Dns-Ser separated on CSP3 (Conditions: see Table S2).

1.6 Comparison of enantioseparation ability on CSP1 and the commercial column

Table S3 Comparison of enantioseparation ability on CSP1 and commercial column

	CSP1				Commercial column			
Analyte	k_1	k_2	R_s	α	k_1	k_2	R_s	α
Ph-Ph	2.50	3.38	0.81	1.35	0.15	-	0.00	1.00
MDOPh-Ph	5.63	9.42	2.90	1.67	0.21	-	0.00	1.00
3ClPh-Ph	4.10	5.71	2.70	1.39	0.13	-	0.00	1.00
Ph-Py	2.02	2.58	2.28	1.28	0.16	-	0.00	1.00
4NPh-Py	2.45	3.59	1.41	1.47	0.15	-	0.00	1.00
4MOPh-OPr	0.98	1.22	1.51	1.24	0.10	-	0.00	1.00
4NPh-OPr	0.89	1.20	1.77	1.35	0.09	-	0.00	1.00
4MetPh-OPr	1.11	1.39	1.42	1.25	0.11	-	0.00	1.00
Dns-Aba	0.98	1.23	1.57	1.25	1.36	-	0.00	1.00
Dns-Thr	1.03	1.49	2.86	1.45	1.36	1.48	0.80	1.09
Dns-Ser	0.95	1.27	2.13	1.34	1.39	1.45	＜0.5	1.05
Ac-2	0.68	0.79	0.92	1.12	1.21	-	0.00	1.00
Al-4	4.25	5.13	1.74	1.21	0.56	-	0.00	1.00
Fla-1	5.91	6.27	0.99	1.06	0.39	-	0.00	1.00
Fla-4	2.48	2.67	0.73	1.07	0.33	-	0.00	1.00

Conditions: Same as Table 1.

In order to examine the separation performance of CSP1, a commercial column (CYCLOBOND I 2000) and CSP1 were further compared (Table S3). Compared with the commercial column, CSP1 has a clear structure, and its separation ability is significantly better than the commercial column with unclear structures.

1.7 The synthesis and characterization of novel multifunctional CD-CSPs

CSP1 (2.5 g) was dissolved in anhydrous pyridine (30 mL), and excess p-tolyl isocyanate (3.85 mL) was added. The mixture was reacted at 85 ℃ under argon atmosphere for 18 h, then filtered and extracted with acetone soxhlet for 8 h, and dried in vacuum to get the product. The characterization of the CSP will be published elsewhere.

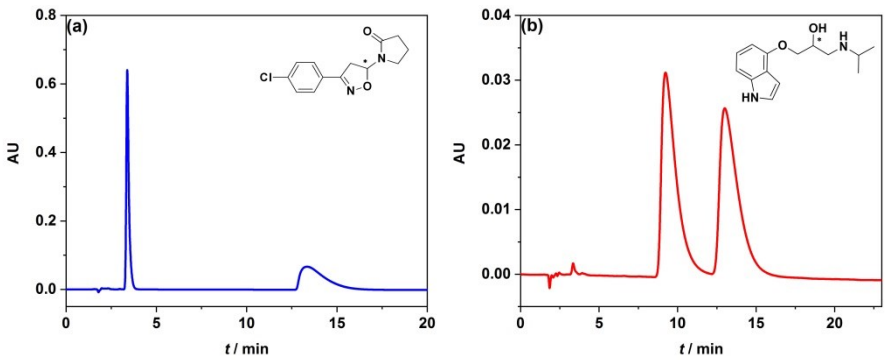

Fig.S5 Typical chromatograms of analytes separated on novel multifunctional CD-CSPs (Conditions: (a) mobile phase, MeOH/H_2O, (70:30, v/v); 1.0 mL/min; 30 ℃; (b) mobile phase, MeOH/TEAA (pH = 4.50) (50:50, v/v); 1.0 mL/min; 30 ℃).