Silica columns covalently bonded with chiral poly (2-oxazoline) derivatives as chiral stationary phases for high-performance liquid chromatography

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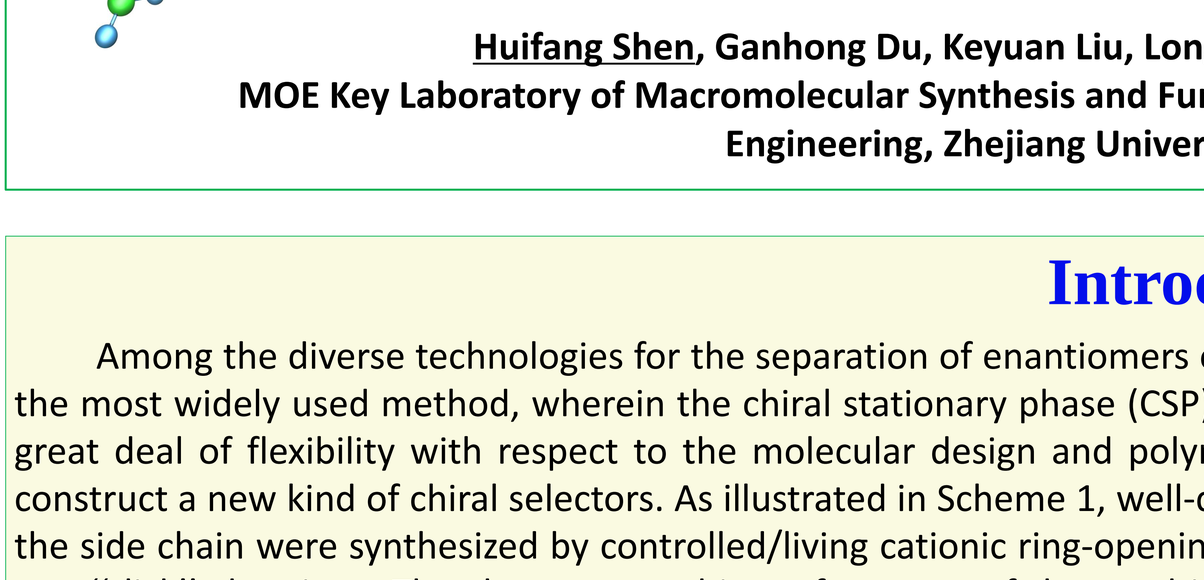
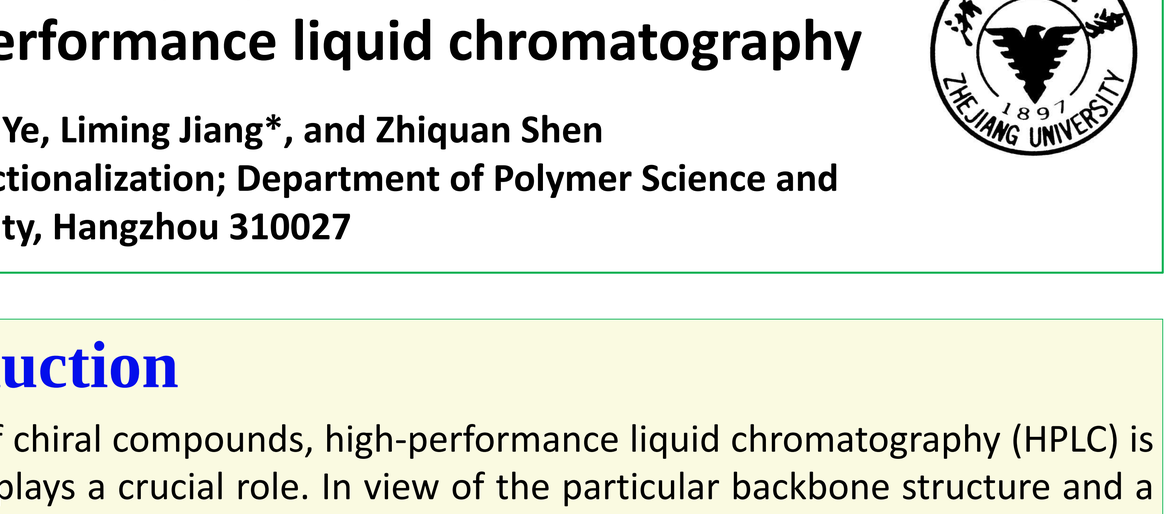
Introduction

Among the diverse technologies for the separation of enantiomers of chiral compounds, high-performance liquid chromatography (HPLC) is the most widely used method, wherein the chiral stationary phase (CSP) plays a crucial role. In view of the particular backbone structure and a great deal of flexibility with respect to the molecular design and polymer synthesis, in this study we used poly (2-oxazoline) as scaffolds to construct a new kind of chiral selectors. As illustrated in Scheme 1, well-defined poly(2-oxazoline) derivatives bearing different capping groups at the side chain were synthesized by controlled/living cationic ring-opening polymerization and grafted on silica bead matrices by means of thiol-ene ‘‘click’’ chemistry. The chromatographic performance of the resulting columns was evaluated with nine racemic analytes. The preliminary results suggested that the dimethylbenzoyl-group (DMB) containing CSP shows better enantio-separating ability than the corresponding 3, 5-dinitrobenzoyl (DNB) and *t*-butyloxycarbonyl (BOC) counterparts.

Synthesis and characterization



Scheme 1 Synthesis route of the three chiral stationary phases.

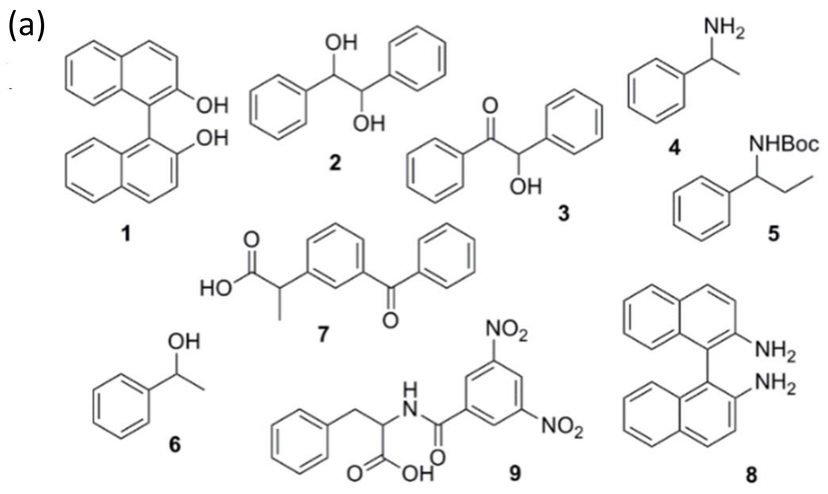


(c)

CSP	N[%]	C[%]	H[%]	[M](mmol/g)
CSP-1	1.90	13.63	2.288	0.45
CSP-2	4.365	17.24	2.439	0.62
CSP-3	1.66	10.69	1.816	0.39

Figure 1 The structure and the reaction efficiency of target product were characterized by (a)^{1}H-NMR, (b)FTIR and (c)elemental analysis.

Chromatographic enantioseparation



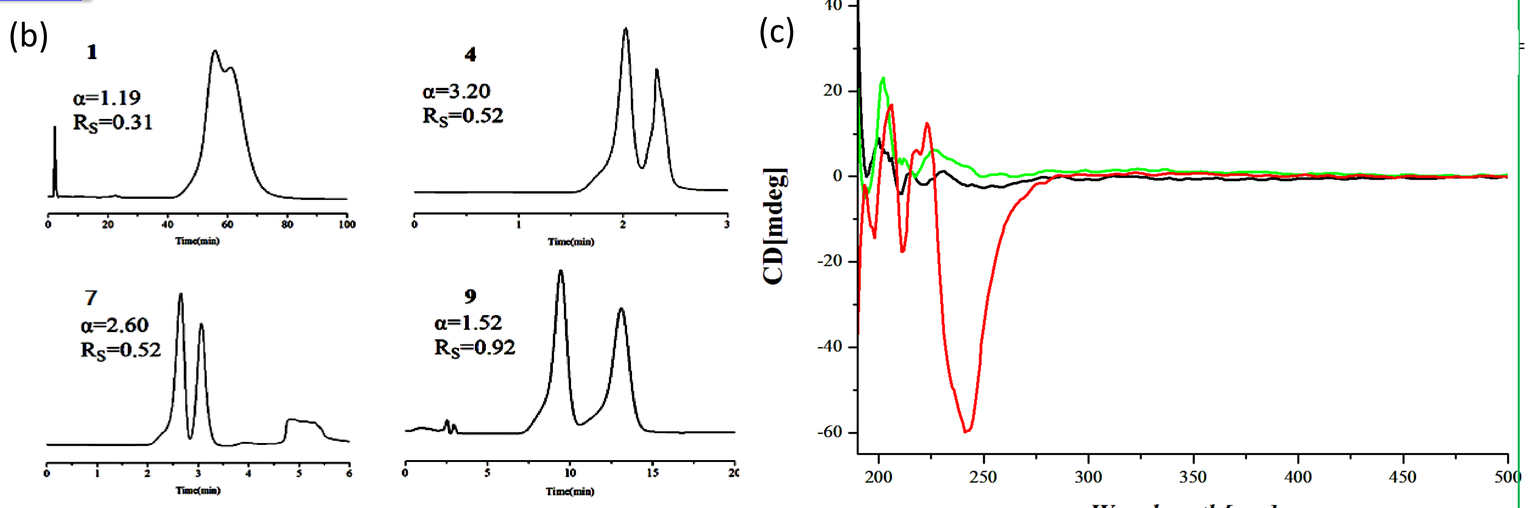


Figure 2 (a) Structures of analytes tested, (b) representative chromatograms on CSP-1, mobile phase: hexane/CH_2Cl_2 (20:80), flow rate: 1.0mL/min and (c) different Cotton effect of the CSP1 copolymer detected by circular dichroism spectroscopy (CD) which indicated different optical rotations were found in 80%DCM in Hexane.

Racemic analytes	CSP-1[a]		CSP-2[b]		CSP-3[b]	
	α	Rs	α	Rs	α	Rs
1	1.19	0.31	1.00	/	1.15	0.70
2	1.00	/	1.00	/	1.00	/
3	1.00	/	1.00	/	4.57	0.51
4	2.60	0.52	9.80	0.8	11.57	0.48
5	1.00	/	1.00	/	1.00	/
6	1.0	/	1.00	/	1.00	/
7	3.20	0.66	1.00	/	1.00	/
8	2.17	0.51	1.00	/	1.00	/
9	1.52	0.92	/	/	/	/

Table 1 Separating ability of the three chiral stationary phases towards different analytes. Mixtures (a) hexane:2-propanol (90 : 10) and (b) Hexane:DCM(80:20) were used as the eluent at a flow rate of 1 mL/ min.

Conclusion

Novel poly(2-oxazoline)s with dependent diprolinamide moieties bonded chiral stationary phases were prepared. The CSP1 evaluated by HPLC resolved five of the nine enantiomeric compounds with an average separation factor 0.58. Similarly, we also prepared CSP2 and CSP3 by replacing 3,5-dimethylbenzoyl group(DMB) with 3,5-dinitrobenzoyl(DNB) and t-butyloxycarbonyl group(Boc) respectively, in order to investigate the role of DMB end-capping group. In a result, the CSP1 shows better enatioselectivity.

References

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