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Short communication

Simple stationary phases derived from gluconolactone for chiral high-performance liquid chromatography

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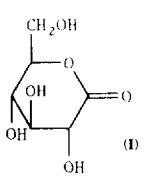
Abstract

A new family of chiral stationary phases (CSPs) have been prepared by chemical modification of D-δ-gluconolactone with ring opening. They were chemically bonded to 5-μm microporous silica and evaluated as column packing materials for chiral analysis by HPLC. The best was the CSP in which the hydroxyl groups derived from the ring-opened gluconolactone were converted to carbamate residues using a naphthylethyl isocyanate.

1. Introduction

Lactones have been used in the preparation of chiral stationary phases (CSPs) [1] for HPLC and as chiral analytes [2] in GC. These applications demonstrate their ability to take part in chiral recognition processes with either an open chain or a closed ring system. With the earlier work of Lourenco [3] in mind, a number of novel CSPs for HPLC were synthesised from a cheap and readily available carbohydrate, D-δ-gluconolactone (**I**).



(I)

2. Experimental

2.1. Instrumentation

The HPLC system consisted of a Shimadzu LC-5A single-head pump, Rheodyne 7125 manual injector valve and Cecil Instruments CE 212 variable-wavelength UV monitor (254 nm).

2.2. Materials

HPLC-grade solvents were obtained from Rathburn. N-3,5-Dinitrobenzoyl (DNB) derivatives of various amino acids (Aldrich and Janssen) were synthesised at UMIST using established methods [4]. Hypersil silica (5 μm) was supplied by Shandon HPLC.

2.3. Preparation of CSPs

CSPs 1–5 were prepared according to Fig. 1. The synthesis involved nucleophilic ring opening of the lactone (**I**) with allylamine, followed by acetylation and conversion to an active silane

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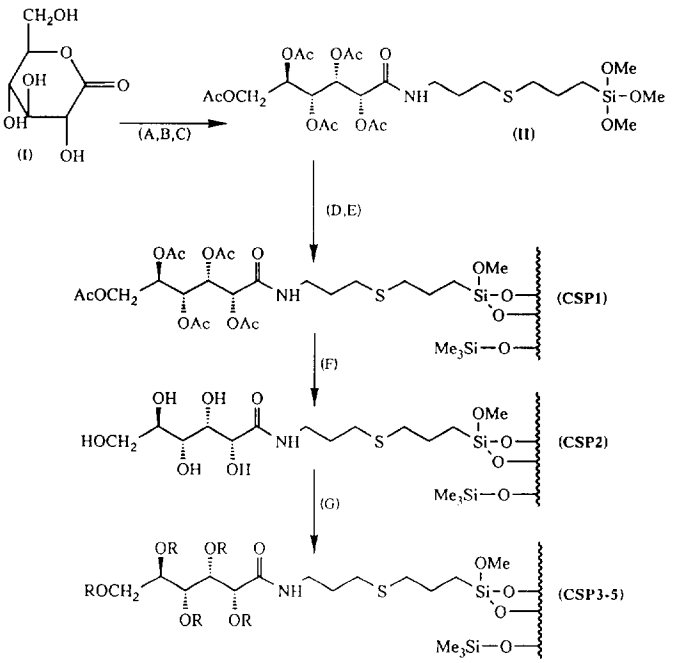
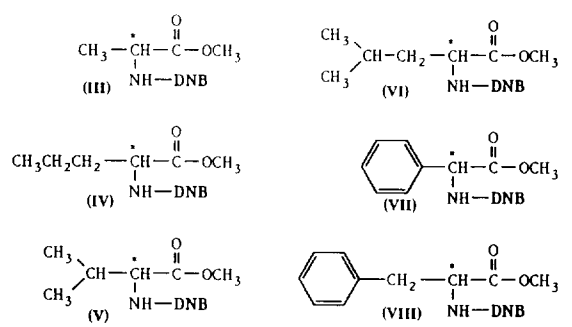


Fig. 1. Synthesis of novel CSP from gluconolactone. RO = Aryl–NH–(CO)–O and HO, according to Table 1. Reagents: A = allylamine; B = Ac_2O; C = $(MeO)_3Si(CH_2)_3SH$; D = silica; E = Me_3SiCl; F = NH_3–MeOH; G = aryl isocyanate.

derivative. The acetylated silane (**II**) was bonded to 5-μm Hypersil silica. Residual silanols on the silica surface were then end-capped with trimethylsilyl (TMS) chloride. This was followed by deacetylation and carbamate formation. The CSPs were then packed into standard steel HPLC columns (15 cm × 4.5 mm I.D.) by Shandon HPLC.



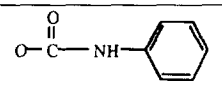
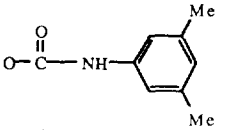
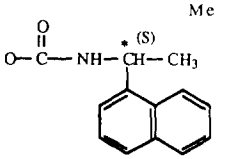
3. Results and discussion

The surface coverages of the phases were estimated from their % carbon contents. CSP 1 contained 237 μmol of chiral selector and 422 μmol of TMS groups per gram of silica. The corresponding values for CSP 2 were 274 and 174 μmol g^{-1}. The chiral selector strands on CSPs 3–5 were not fully carbamated: the ratios of carbamate to hydroxyl groups on these phases are shown in Table 1.

Some reasonable separations were obtained on the acetylated phase, CSP 1. The chromatograms of a series of racemic N-3,5-DNB-amino acid methyl esters (**III–VIII**) on this phase are presented in Fig. 2. The hydroxyl-containing phase, CSP 2, showed very poor enantioselectivity.

The carbamate phases (CSPs 3–5) all afforded better enantioresolutions than CSP 1. Fig. 3 compares the α values for the same amino acid derivatives on the carbamate CSPs. As the carbamate is made more electron-rich from phenyl (CSP 3) to dimethylphenyl (CSP 4) to naphthylethyl (CSP 5), the separation of these electron-deficient analytes improves. This suggests that a π–π interaction is important in the chiral recognition process on these CSPs. Fig. 4 shows the resolution of the racemic samples (**III–VIII**) on the best performing phase, CSP 5.

Table 1
Structures of carbamate CSPs

Phase	OR group on strands of chiral selector	Concentration of strands	Concentration of TMS	OR:OH ratio on chiral strand
CSP 3		270	170	3.1:1.9
CSP 4		270	170	2.3:2.7
CSP 5		180	70	1.0:4.0

Concentrations are reported as μmol per gram of silica gel. Average ratios of OR:OH groups on the chiral strands are also quoted.

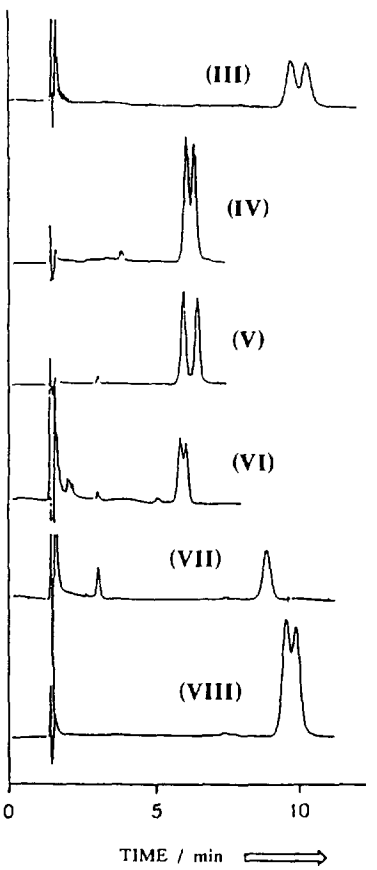


Fig. 2. Chromatograms of racemic N-3,5-DNB-amino acid methyl esters on CSP 1. Mobile phase: tetrahydrofuran (THF)–*n*-hexane (15:85) at 1.0 ml min^{-1}.

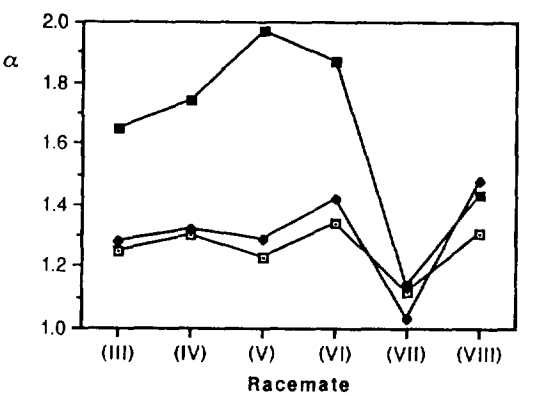


Fig. 3. Comparison of the α values for the racemic N-3,5-DNB-amino acid methyl esters on the carbamate phases CSP 3 (□), CSP 4 (◆) and CSP 5 (■). Mobile phase: THF–*n*-hexane (25:75) at 1.0 ml min^{-1}.

4. Conclusions

A family of simple CSPs for HPLC were prepared from a cheap and readily available starting material, D-δ-gluconolactone. These chiral stationary phases were used to separate the enantiomers of amino acid derivatives that contained the electron-deficient 3,5-DNB group. The phase that shows the most commercial promise (CSP 5) contains the naphthylethyl carbamate functionality.

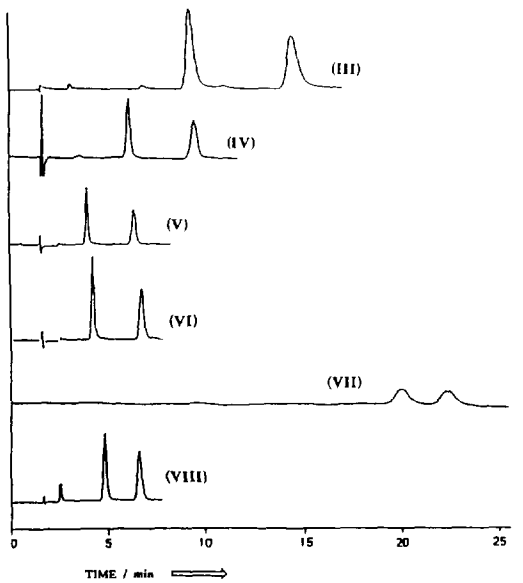


Fig. 4. Chromatograms of racemic N-3,5-DNB-amino acid methyl esters on CSP 5. Mobile phase as in Fig. 3.

Acknowledgements

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