

An Efficient Chiral Stationary Phase for High Performance Liquid Chromatographic
Separation of Enantiomeric Aliphatic Alcohols

Shuichi ÔI, Masayuki SHIJO, Junzo YAMASHITA,[†] and Sotaro MIYANO*
Department of Biochemistry and Engineering, Faculty of Engineering,
Tohoku University, Aramaki-Aoba, Sendai 980

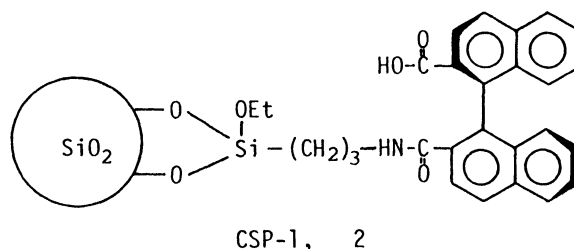
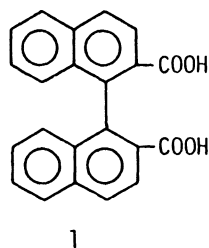
[†]Chemical Research Laboratory, Tokyo Medical College,
1-1, 6-chome, Shinjuku, Tokyo 160

(S)-1,1'-Binaphthyl-2,2'-dicarboxylic acid was chemically bonded to an aminopropylsilanized silica through amido linkage to give a chiral stationary phase for HPLC, which efficiently differentiated enantiomeric aliphatic alcohols as 3,5-dinitrophenylcarbamates.

Although a variety of chiral stationary phases (CSPs) have recently been developed for the separation of enantiomers by HPLC,¹⁾ those widely applicable to enantiomeric aliphatic alcohols are still awaited.²⁾ As a part of our continuing efforts to exploit highly selective asymmetric reactions by use of axially chiral biaryls,³⁾ we have reported a preparation of CSPs having atropisomeric 1,1'-binaphthyl residue as the chiral element.^{4,5)} Quite recently, Suda and his coworkers have shown that (R)-1,1'-binaphthyl-2,2'-dicarboxylic acid ((R)-1) serves as a chiral host molecule to resolve alkyl aryl carbinols.⁶⁾

Their report prompted us to disclose our results that normal phase HPLC performed on a readily accessible aminopropylsilanized silica modified with (S)-1 (CSP-1, 2) efficiently discriminates not only alkyl aryl carbinols but also simple aliphatic alcohols higher than pentanol (Table 1 and Fig. 1).

The CSP-1 was simply prepared by the reaction of an aminopropylsilanized silica gel⁷⁾ with ca. 1.3 equiv. of optically pure (S)-1 in the presence of N-ethoxycarbonyl-2-ethoxy-1,3-dihydroquinoline (EEDQ) in DMF under ultrasound irradiation (70-80 °C, 8 h; uptake of the binaphthyl residue, 0.41 mmol equiv./g gel).⁴⁾ After rinsing and drying, the chirally modified gel was slurry packed to a stainless-steel column (250 mm x 4.6 mm i.d.) using a conventional technique. Samples of racemic alcohols (10-20 mg) were treated with an excess amount of 3,5-dinitrophenylisocyanate and triethylamine in THF to form the corresponding carbamates, which



were separated by TLC and then subjected to the HPLC analysis. It seems that the presence of the amide and free -COOH functionalities attached to the axially twisted binaphthyl residue is essential for the discrimination.

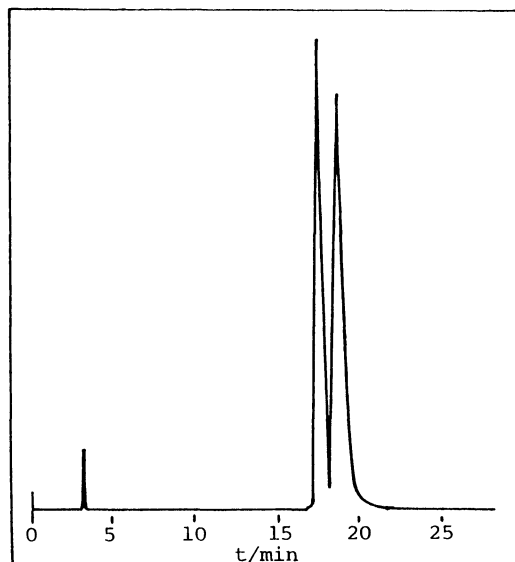


Fig. 1. Resolution of (RS)-2-pentanol as the carbamate.

Table 1. Separation of Enantiomeric Alcohols as 3,5-Dinitrophenylcarbamates on CSP-1^a)

$\begin{array}{c} R^1-CH-R^2 \\ \\ OH \end{array}$		i-PrOH (%)	k'_1	α
R ¹	R ²			
CH ₃	C ₂ H ₅	10	5.36	1.00
CH ₃	n-C ₃ H ₇	10	4.78	1.08
CH ₃	n-C ₄ H ₉	10	4.38	1.15
CH ₃	n-C ₅ H ₁₁	10	4.11	1.19
CH ₃	n-C ₆ H ₁₃	10	3.93	1.21
CH ₃	n-C ₇ H ₁₅	10	3.76	1.22
CH ₃	n-C ₈ H ₁₇	10	3.68	1.24
CH ₃	CH=CH ₂	10	5.90	1.08
CH ₃	C≡CH	10	9.77	1.18
CH ₃	Ph	15	3.86	1.54
C ₂ H ₅	Ph	15	3.44	1.53
n-C ₃ H ₇	Ph	15	3.33	1.43

a) The column was operated at room temperature with UV detection at 254 nm. Mobile phase, hexane-i-PrOH; flow rate, 1 cm³/min; k'_1 , capacity factor for the fast eluting enantiomer; α , separation factor.

This work was partly supported by a Grant-in-Aid for Scientific Research No. 61550609 from the Ministry of Education, Science and Culture. We thank Messrs. Hiroo Sasaki and Katuo Komiya of Toso Co., Ltd. for a gift of the spherical silica.

References

- 1) For example, Y. Okamoto, CHEMTECH, 1987, 176; W. H. Pirkle, T. C. Pochapsky, G. S. Mahler, D. E. Corey, D. S. Reno, and D. M. Alessi, J. Org. Chem., 51, 4991 (1986).
- 2) Cf., N. Ôi and H. Kitahara, J. Chromatogr., 265, 117 (1983).
- 3) S. Miyano and H. Hashimoto, Yuki Gosei Kagaku Kyokai Shi, 44, 713 (1986).
- 4) J. Yamashita, T. Numakura, H. Kita, T. Suzuki, S. Ôi, S. Miyano, H. Hashimoto, and N. Takai, J. Chromatogr., 403, 275 (1987).
- 5) See also, L. R. Sousa, G. D. Y. Sogah, D. H. Hoffman, and D. J. Cram, J. Am. Chem. Soc., 100, 4569 (1978); F. Mikes and G. Boshart, J. Chem. Soc., Chem. Commun., 1978, 173.
- 6) S. Kanoh, Y. Hongoh, S. Katoh, M. Motoi, and H. Suda, J. Chem. Soc., Chem. Commun., 1988, 405.
- 7) Prepared by the treatment of a Toso silica gel (spherical 5- μ m particles with micropores of 100-Å diameter) with aminopropyltriethoxysilane in boiling toluene (-NH₂ contents, 1.01 mmol equiv./g gel).

(Received June 23, 1988)