ELSEVIER

Journal of Chromatography A, 715 (1995) 219–226

JOURNAL OF CHROMATOGRAPHY A

High-performance liquid chromatographic method for the separation of isomers of *cis*- and *trans*-2-amino-cyclopentane-1-carboxylic acid

Antal Péter[a,*], Ferenc Fülöp[b]

[a]*Department of Inorganic and Analytical Chemistry, Attila József University, P.O. Box 440, H-6701 Szeged, Hungary*
[b]*Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University, P.O. Box 121, H-6701 Szeged, Hungary*

First received 28 February 1995; revised manuscript received 23 May 1995; accepted 23 May 1995

Abstract

A method was developed for the separation of *cis*-(1*S*,2*R*)-, *cis*-(1*R*,2*S*)-, *trans*-(1*S*,2*S*)- and *trans*-(1*R*,2*R*)-2-amino-cyclopentane-1-carboxylic acids by using pre-column derivatization with the chiral derivatizing reagents 1-fluoro-2,4-dinitrophenyl-5-L-alanine amide and 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate. The method is suitable for the separation of both diastereomeric and enantiomeric pairs. The high-performance liquid chromatographic conditions (pH, eluent composition and different buffers) were varied to obtain optimal separation.

1. Introduction

In recent years, a number of investigations have been performed [1–5] to introduce alicyclic β-amino acids such as *cis*- and *trans*-2-amino-cyclopentane-1-carboxylic acids (*cis*- and *trans*-ACPC, Fig. 1) into peptides in order to increase their stability and to modify their biological activity. Also, *cis*- and *trans*-ACPC have been used in the syntheses of biologically active heterocycles [6–9].

Although the syntheses [10–12] and trans-formations of racemic *cis*- and *trans*-ACPC have long been known, interest in this field was

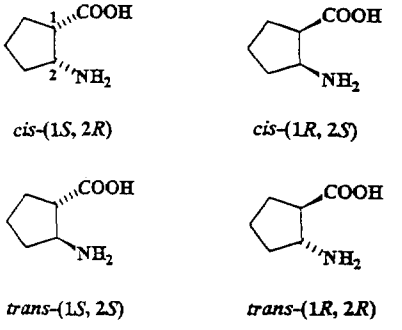

Fig. 1. Structures of four stereoisomers of *cis*-(1*S*,2*R*, 1*R*,2*S*)- and *trans*-(1*S*,2*S*, 1*R*,2*R*)-2-amino-cyclopentane-1-carboxylic acid.

* Corresponding author. Address for correspondence until December 1995: Vrije Universiteit Brussel, ORGC-VUB, c/o Dr. D. Tourwe, Pleinlaan 2, B-1050 Brussels, Belgium.

0021-9673/95/$09.50
SSDI 0021-9673(95)00615-X

enhanced when *cis*-(1*R*,2*S*)-ACPC (cispentacin) was found in nature [13–16].

Cispentacin [(−)-*cis*-(1*R*,2*S*)-ACPC] was isolated [13–16] by two independent laboratories from *Bacillus cereus* L450-B2 and *Streptomyces setonii* 7562. (−)-*cis*-ACPC exerts a marked protective effect against *Candida albicans* and *Cryptococcus neoformans* in mice [13–18]. Because of their biological importance, a number of methods have been developed [19–22] and patented [23–30] for the preparation of cispentacin. These methods mainly involve enzymatic separation techniques [31].

The difficulty to obtain many uncommon amino acids in a homochiral form underline the importance of having at hand effective chromatographic methods for the characterization and identification of enantiomers.

Several papers and reviews have been published on the development of enantioselective separations by means of liquid chromatographic techniques. Enantioselective separations involving high-performance liquid chromatographic (HPLC) methods can be divided into three main groups: direct separation on chiral stationary phases [32–34], separation on achiral columns with chiral eluents [34–36], and separation of the diastereoisomers formed by pre-column derivatization with chiral reagents [34,37–48].

The present paper deals with the separation of enantiomers of *cis*- and *trans*-ACPC by using pre-column derivatization with 1-fluoro-2,4-dinitrophenyl-5-L-alanine amide (FDAA, Marfey's reagent) or 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (GITC). The separations were carried out in different buffer systems, acetonitrile or methanol being used as organic modifier. The effects of pH, mobile phase composition and organic modifier content on the separation were also investigated.

2. Experimental

2.1. Chemicals and reagents

(±)-*cis*-ACPC was prepared from cyclopentene via chlorosulphonyl isocyanate addition, followed by aqueous hydrochloric acid treatment and ion-exchange chromatography [12]. (±)-*trans*-ACPC was synthesized by Michael addition of ammonia to 1-cyclopentenecarboxylic acid in a steel autoclave at 170°C for 80 h, followed by ion-exchange chromatography [10]. (−)-*cis*-(1*R*,2*S*)-ACPC and (+)-*trans*-(1*S*,2*S*)-ACPC were prepared from the corresponding esters by lipase acylation, followed by hydrolysis [49].

GITC was purchased from Aldrich (Steinheim, Germany), FDAA from Pierce Chemical (Rockford, IL, USA), and potassium dihydrogenphosphate, trifluoroacetic acid, sodium acetate, phosphoric acid, acetic acid of analytical reagent grade, acetonitrile and methanol of HPLC grade from Merck (Darmstadt, Germany). Buffers were prepared with doubly distilled water and further purified by filtration on a 0.45-μm filter, type HV, Millipore (Molsheim, France). The pH was adjusted with phosphoric acid, acetic acid and sodium hydroxide.

2.2. Apparatus

HPLC analyses were performed on an M-600 low-pressure-gradient pump equipped with an M-996 photodiode-array detector and a Millennium 2010 Chromatography Manager data system (Waters Chromatography, Division of Millipore, Milford, MA, USA) and on an L-6000 liquid chromatographic pump (Merck Hitachi, Tokyo, Japan) equipped with a UV 308 detector (Labor MIM, Budapest, Hungary) and an HP 3395 integrator (Hewlett-Packard, Waldbronn, Germany).

The columns used were Lichrospher 100 RP18 (125 × 4 mm I.D.), 5 μm particle size (Merck, Darmstadt, Germany).

2.3. Derivatization of amino acids for chromatographic analysis

An amount of 0.5–1 mg of *cis*- or *trans*-ACPC was derivatized with FDAA by the method of Marfey [43] and with GITC by the method of Nimura et al. [40].

3. Results and discussion

Control of the carboxylate group ionization requires the control of pH, i.e. buffering of the mixed aqueous–organic modifier phase system, in order to maintain equilibrium constancy within the column. The pK values of ACPC are not known; for 1-amino-cyclopentane-1-carboxylic acid, $pK_1 = 10.31$ and $pK_2 = 2.40$ [50]. The effect of pH on the separation was investigated in the 0.01 M potassium dihydrogenphosphate (pH 2–6)–acetonitrile system; the results can be found in Fig. 2. It is clear from Fig. 2 that the k' values are higher at lower pH, while at pH < 3 and at pH > 5 k' varies slightly with a change in pH. These results led to the choice of three systems to keep the ionization at a constant level: a 0.1% aqueous solution of trifluoroacetic acid, which is often used in the separation of derivatized amino acids and peptides, 0.01 M potassium dihydrogenphosphate at pH 3, and 0.01 M sodium acetate at pH 3.

3.1. Separation of ACPC–GITC derivatives

Separations were carried out in the three systems, with methanol or acetonitrile as organic modifier; the results are given in Tables 1 and 2. Table 1 demonstrates that decrease of the methanol content results in an increase in k' for all four enantiomers, while the α and R_s values also improve.

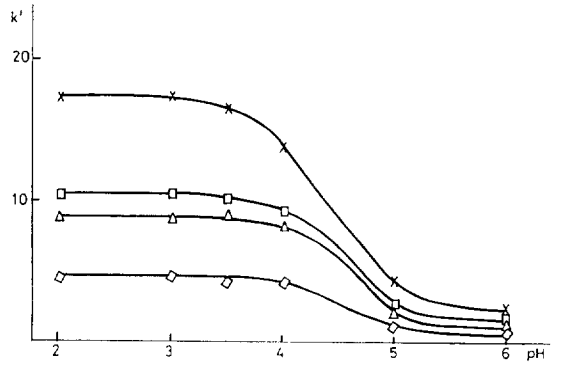

Fig. 2. Dependence of retention factor (k') of four diastereoisomers of ACPC–FDAA derivatives on pH of buffer. Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, 340 nm; mobile phase, 0.01 M potassium dihydrogenphosphate (pH 2–6)–acetonitrile (70:30). (◇) *cis*-(1*R*,2*S*) derivative; (△) *cis*-(1*S*,2*R*) derivative; (□) *trans*-(1*S*,2*S*) derivative; (×) *trans*-(1*R*,2*R*) derivative.

The optimal mobile-phase composition contains 42.5% or less methanol. In this case, the four enantiomers can be separated with R_s higher than 1.5. Comparison of the three buffer systems reveals only slight differences. Better resolutions were generally obtained in phosphate buffer, but at the same time the k' value of the last peak, i.e. the total time of analysis, was the largest in this system. The elution order of the peaks was identified by comparing the individual k' values with standards prepared by enzymatic resolution. These experiments showed that the first peak corresponds to the *trans*-(1*S*,2*S*), the second to the *trans*-(1*R*,2*R*), the third to the *cis*-(1*R*,2*S*) and the fourth to the *cis*-(1*S*,2*R*) isomer (Fig. 3).

When acetonitrile was applied as organic modifier, decrease of the acetonitrile content of the mobile phase resulted in behaviour similar to that observed in the methanol-containing system. Resolutions similar to those observed in the methanol-containing mobile phase could be achieved with much larger k' values (Table 2). This corresponds with our earlier findings [51,52]: in acetonitrile-containing systems, a similar resolution of diastereoisomers of some unusual aromatic amino acids with GITC can be attained at higher k' values as compared with the methanol-containing systems. With regard to the buffer systems, phosphate seems favourable with respect to resolution and peak shape. The elution order of the four enantiomers is the same as that observed in methanol.

The described method is suitable for the determination of less than 0.1% minor isomer content in excess of the major isomer.

3.2. Separation of ACPC–FDAA derivatives

The results of separations with methanol as organic modifier are given in Table 3. The elution order, determined by comparison with standards, was *cis*-(1*R*,2*S*), *cis*-(1*S*,2*R*), *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) isomer (Fig. 3). This

Table 1
Dependence of retention factor (k'), separation factor (α) and resolution (R_s) of ACPC–GITC derivatives on eluent composition

Eluent composition	k'				$\alpha_{t,t}$	$\alpha_{t,c}$	$\alpha_{c,c}$	$R_{s;t,t}$	$R_{s;t,c}$	$R_{s;c,c}$
	trans		*cis*							
	(1*S*,2*S*)	(1*R*,2*R*)	(1*R*,2*S*)	(1*S*,2*R*)						
TFA–CH_3OH										
55:45	5.38	5.93	6.53	7.25	1.10	1.10	1.11	0.75	0.80	0.65
57.5:42.5	6.55	8.34	11.41	13.36	1.27	1.36	1.17	2.04	2.50	1.53
60:40	8.69	11.50	15.88	18.97	1.32	1.38	1.19	2.67	3.50	1.91
KH_2PO_4–CH_3OH										
55:45	4.17	5.55	8.14	9.70	1.33	1.47	1.19	1.26	2.14	0.90
57.5:42.5	5.83	8.00	11.80	14.40	1.37	1.48	1.22	1.96	3.35	2.03
60:40	8.50	12.11	17.90	22.17	1.42	1.48	1.24	3.63	4.40	2.40
NaOAc–CH_3OH										
55:45	4.67	5.69	7.60	9.72	1.22	1.34	1.27	1.45	2.04	1.16
57.5:42.5	5.86	7.37	10.02	11.71	1.26	1.36	1.17	2.04	2.84	2.01
60:40	8.29	10.56	14.70	17.13	1.28	1.39	1.17	2.13	3.38	2.30

Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, 250 nm; TFA, 0.1% aqueous solution of trifluoroacetic acid; KH_2PO_4, 0.01 *M* aqueous solution of potassium dihydrogenphosphate (pH 3); NaOAC, 0.01 *M* aqueous solution of sodium acetate (pH 3); $\alpha_{t,t}$ and $R_{s;t,t}$ represent separation of *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) derivatives; $\alpha_{t,c}$ and $R_{s;t,c}$ represent separation of *trans*-(1*R*,2*R*) and *cis*-(1*R*,2*S*) derivatives; $\alpha_{c,c}$ and $R_{s;c,c}$ represent separation of *cis*-(1*R*,2*S*) and *cis*-(1*S*,2*R*) derivatives.

Table 2
Dependence of retention factor (k'), separation factor (α) and resolution (R_s) of ACPC–GITC derivatives on eluent composition

Eluent composition	k'				$\alpha_{t,t}$	$\alpha_{t,c}$	$\alpha_{c,c}$	$R_{s;t,t}$	$R_{s;t,c}$	$R_{s;c,c}$
	trans		*cis*							
	(1*S*,2*S*)	(1*R*,2*R*)	(1*R*,2*S*)	(1*S*,2*R*)						
TFA–CH_3CN										
77.5:22.5	20.98	24.80	32.48	36.46	1.18	1.31	1.12	1.75	2.96	1.35
KH_2PO_4–CH_3CN										
77.5:22.5	17.58	21.36	30.14	34.41	1.22	1.41	1.14	2.31	4.26	1.71
NaOAc–CH_3CN										
77.5:22.5	16.06	20.09	28.70	33.54	1.25	1.43	1.17	1.84	3.10	1.42

Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, 250 nm; TFA, 0.1% aqueous solution of trifluoroacetic acid; KH_2PO_4, 0.01 *M* aqueous solution of potassium dihydrogenphosphate (pH 3); NaOAC, 0.01 *M* aqueous solution of sodium acetate (pH 3); $\alpha_{t,t}$ and $R_{s;t,t}$ represent separation of *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) derivatives; $\alpha_{t,c}$ and $R_{s;t,c}$ represent separation of *trans*-(1*R*,2*R*) and *cis*-(1*R*,2*S*) derivatives; $\alpha_{c,c}$ and $R_{s;c,c}$ represent separation of *cis*-(1*R*,2*S*) and *cis*-(1*S*,2*R*) derivatives.

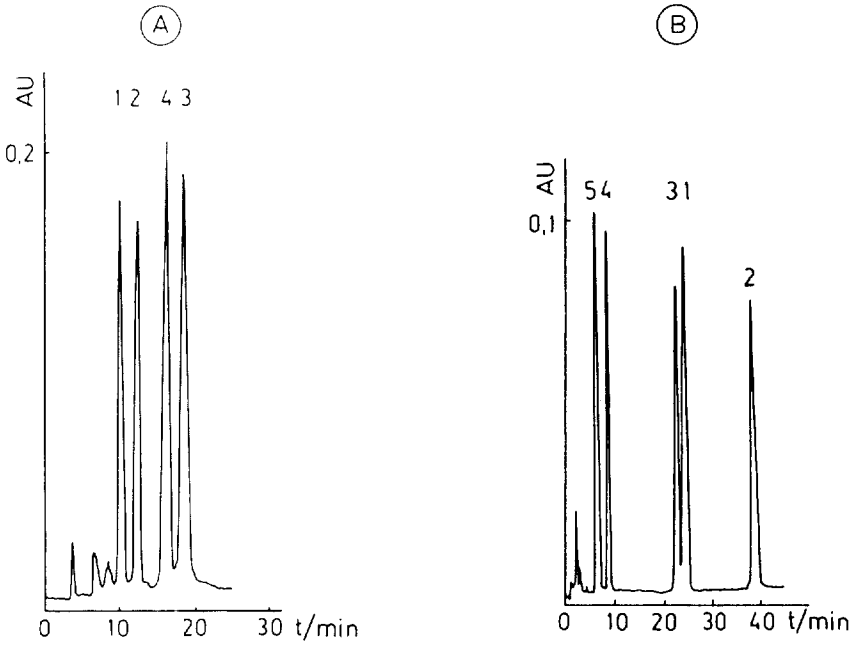

Fig. 3. Representative chromatograms of separation of four diastereoisomers of ACPC derivatives. (A) GITC derivatives, (B) FDAA derivatives. Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, (A) 250 nm, (B) 340 nm; mobile phase, (A) 0.01 *M* sodium acetate (pH 3)–methanol (57.5:42.5), (B) 0.01 *M* sodium acetate–methanol (77.5:22.5). Peaks: 1 = *trans*-(1*S*,2*S*) derivative; 2 = *trans*-(1*R*,2*R*) derivative; 3 = *cis*-(1*S*,2*R*) derivative; 4 = *cis*-(1*R*,2*S*) derivative; 5 = unreacted FDAA.

cis/*trans* sequence is the reverse of that observed for the GITC derivatives.

At a given eluent composition, the k' values of the diastereoisomers in the trifluoroacetic acid system are the highest, and the resolutions are also the best here. As can be seen in Fig. 3, the *cis*-(1*R*,2*S*) and *cis*-(1*S*,2*R*) isomers and the *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) isomers separate very well. The peaks of the *cis*-(1*S*,2*R*) and *trans*-(1*S*,2*S*) isomers are close, and good separation requires optimization of the conditions. Peak number 5, which elutes first, corresponds to unreacted reagent.

The results of separations in the acetonitrile-containing system are shown in Table 4. The elution order of the four enantiomers is the same as that observed in methanol. In the eluent system with a buffer–acetonitrile ratio of 70:30, the unreacted FDAA elutes after, and very close to, the *cis*-(1*R*,2*S*) isomer. Complete separation of these two peaks can be achieved at 25% acetonitrile content. Comparison of the three buffer systems at a given eluent composition reveals that the k' values are the lowest in sodium acetate, while the resolutions are better in the trifluoroacetic acid and phosphate buffer systems. There is no significant difference in separation capability between the two organic modifiers, methanol and acetonitrile.

The chiral purity of ACPC isomers can also be determined by derivatization with FDAA. The detection limit is less than 0.1% for the minor isomer in the presence of the major isomer.

4. Conclusions

The described procedure can be applied for the separation and identification of four enantiomers: *cis*-(1*S*,2*R*)-, *cis*-(1*R*,2*S*)-, *trans*-(1*S*,2*S*)- and *trans*-(1*R*,2*R*)-2-aminocyclopentane-1-carboxylic acid. The method permits a check on the configuration of the amino acid after synthesis, and hence optimization of the conditions of synthesis. In general, the GITC derivatives give better resolution than the FDAA derivatives for

Table 3
Dependence of retention factor (k'), separation factor (α) and resolution (R_s) of ACPC–FDAA derivatives on eluent composition

Eluent composition	k'				$\alpha_{c,c}$	$\alpha_{c,t}$	$\alpha_{t,t}$	$R_{s;c,c}$	$R_{s;c,t}$	$R_{s;t,t}$
	cis		*trans*							
	(1*R*,2*S*)	(1*S*,2*R*)	(1*S*,2*S*)	(1*R*,2*R*)						
$TFA–CH_3OH$										
50:50	3.75	10.92	13.26	21.36	2.91	1.21	1.61	8.90	2.36	5.41
52.5:47.5	4.95	14.89	16.67	27.51	3.01	1.12	1.65	10.25	2.37	6.41
55:45	6.80	21.26	23.14	38.97	3.12	1.09	1.68	14.72	2.40	8.67
$KH_2PO_4–CH_3OH$										
50:50	3.50	10.81	11.43	18.58	3.08	1.05	1.62	8.70	1.05	6.20
52.5:47.5	4.51	14.14	15.25	25.13	3.13	1.08	1.65	9.34	1.08	6.62
55:45	6.36	20.59	22.41	37.52	3.23	1.09	1.67	15.01	1.52	8.61
$NaOAc–CH_3OH$										
50:50	2.77	7.95	8.70	13.79	2.87	1.09	1.59	6.36	0.91	4.10
52.5:47.5	3.56	10.04	11.32	18.97	2.82	1.12	1.67	6.97	1.25	4.77
55:45	4.96	15.00	16.12	20.64	3.02	1.08	1.28	11.40	1.36	8.14

Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, 340 nm; TFA, 0.1% aqueous solution of trifluoroacetic acid; KH_2PO_4, 0.01 *M* aqueous solution of potassium dihydrogenphosphate (pH 3); NaOAC, 0.01 *M* aqueous solution of sodium acetate (pH 3); $\alpha_{c,c}$ and $R_{s;c,c}$ represent separation of *cis*-(1*R*,2*S*) and *cis*-(1*S*,2*R*) derivatives; $\alpha_{c,t}$ and $R_{s;c,t}$ represent separation of *cis*-(1*S*,2*R*) and *trans*-(1*S*,2*S*) derivatives; $\alpha_{t,t}$ and $R_{s;t,t}$ represent separation of *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) derivatives.

Table 4
Dependence of retention factor (k'), separation factor (α) and resolution (R_s) of ACPC–FDAA derivatives on eluent composition

Eluent composition	k'				$\alpha_{c,c}$	$\alpha_{c,t}$	$\alpha_{t,t}$	$R_{s;c,c}$	$R_{s;c,t}$	$R_{s;t,t}$
	cis		*trans*							
	(1*R*,2*S*)	(1*S*,2*R*)	(1*S*,2*S*)	(1*R*,2*R*)						
$TFA–CH_3CN$										
70:30	5.32	10.49	11.90	19.20	1.97	1.14	1.61	6.89	1.58	5.85
72.5:27.5	6.89[a]	16.26	18.68	32.70	–	1.14	1.75	–	2.19	8.77
$KH_2PO_4–CH_3CN$										
70:30	5.01	8.97	10.24	16.70	1.79	1.14	1.63	5.78	1.27	4.67
72.5:27.5	6.46[a]	14.03	16.24	27.86	–	1.16	1.72	–	2.60	9.18
$NaOAc–CH_3CN$										
70:30	3.78	7.85	8.70	14.23	2.07	1.11	1.64	5.60	1.16	4.53
72.5:27.5	5.34	12.09	13.29	22.98	2.26	1.10	1.73	10.03	1.38	6.83

Column, Lichrospher 100 RP18; flow-rate, 0.8 ml/min; detection, 340 nm; TFA, 0.1% aqueous solution of trifluoroacetic acid; KH_2PO_4, 0.01 *M* aqueous solution of potassium dihydrogenphosphate (pH 3); NaOAC, 0.01 *M* aqueous solution of sodium acetate (pH 3); $\alpha_{c,c}$ and $R_{s;c,c}$ represent separation of *cis*-(1*R*,2*S*) and *cis*-(1*S*,2*R*) derivatives; $\alpha_{c,t}$ and $R_{s;c,t}$ represent separation of *cis*-(1*S*,2*R*) and *trans*-(1*S*,2*S*) derivatives; $\alpha_{t,t}$ and $R_{s;t,t}$ represent separation of *trans*-(1*S*,2*S*) and *trans*-(1*R*,2*R*) derivatives.
[a] The peak of the *cis*-(1*R*,2*S*) derivative coincides with that of unreacted FDAA.

all four enantiomers. Of the three buffer systems applied in the case of the GITC derivatives, the phosphate buffer seems best; in the case of the FDAA derivatives, trifluoroacetic acid seems most efficient. With respect to the two organic modifiers, the methanol-containing mobile phase system seems to be more efficient than the acetonitrile-containing one. The elution order of the diastereomers of the *cis* and *trans* isomer derivatives with GITC was opposite to that of the FDAA derivatives.

The detection limit for the minor isomer is less than 0.1% in excess of the major isomer.

Acknowledgements

This work was supported in part by a grant from the Hungarian Research Foundation (OTKA T 14898). The authors express their thanks to Prof. Liisa Kanerva and Péter Csomós (Department of Chemistry, University of Turku, Finland) for the enzymatic resolutions of *cis*- and *trans*-ACPC.

References

[1] D.F. Mierke, G. Nössner, P.W. Schiller and M. Goodman, Int. J. Peptide Protein Res., 35 (1990) 35.
[2] T. Yamazaki, A. Pröbstl, P.W. Schiller and M. Goodman, Int. J. Peptide Protein Res., 37 (1991) 364.
[3] T. Yamazaki, Y.F. Zhu, A. Pröbstl, R.K. Chadha and M. Goodman, J. Org. Chem., 56 (1991) 6644.
[4] T. Yamazaki and M. Goodman, Chirality, 3 (1991) 268.
[5] Z. Huang, A. Pröbstl, J.R. Spencer, T. Yamazaki and M. Goodman, Int. J. Peptide Protein Res., 42 (1993) 352.
[6] G. Bernáth, Acta Chim. Hung. Mod. Chem., 129 (1992) 107.
[7] G. Bernáth, L. Gera, G. Göndös, Z. Ecsery, M. Hermann, M. Szentiványi and E. Janváry, Hung. Patent 172460 (Chem. Abstr., 94 (1981) 175144).
[8] F. Fülöp, G. Csirinyi and G. Bernáth, Acta Chim. Hung., 125 (1988) 193.
[9] F. Fülöp, K. Pihlaja, J. Mattinen and G. Bernáth, Tetrahedron, 43 (1987) 1863.
[10] H. Pleiniger and K. Schneider, Chem. Ber., 92 (1959) 1594.
[11] G. Bernáth, K.L. Láng, G. Göndös, P. Márai and K. Kovács, Acta Chim. Acad. Sci. Hung., 74 (1972) 479.
[12] E. Nativ and P. Rona, Isr. J. Chem., 10 (1972) 55.
[13] M. Konishi, M. Nishio, K. Saitoh, T. Miyaki, T. Oki and H. Kawaguchi, J. Antibiot., 42 (1989) 1749.
[14] T. Oki, M. Hirano, K. Tomatsu, K. Numata and H. Kamei, J. Antibiot., 42 (1989) 1756.
[15] T. Iwamoto, E. Tsujii, M. Ezaki, A. Fujie, S. Hashimoto, M. Okuhara, M. Koshaka, H. Imanaka, K. Kawabata, Y. Inamoto and K. Sakane, J. Antibiot., 43 (1990) 1.
[16] K. Kawabata, Y. Inamoto, K. Sakane, T. Iwamoto and S. Hashimoto, J. Antibiot., 43 (1990) 513.
[17] J.O. Capobianco, D. Zakula, M.L. Coen and R.C. Goldman, Biochem. Biophys. Res. Commun., 190 (1993) 1037.
[18] N. Naruse, S. Yamamoto, H. Yamamoto, S. Kondo, S. Masuyoshi, K. Numata, Y. Fukagawa and T. Oki, J. Antibiot., 46 (1993) 685.
[19] C. Evans, R. McCague, S.M. Roberts, A.G. Sutherland and R. Wisdom, J. Chem. Soc. Perkin Trans. 1, (1991) 2276.
[20] T. Konosu and S. Oida, Chem. Pharm. Bull., 41 (1993) 1012.
[21] S.G. Davies, O. Ichihara and I.A.S. Walters, Synlett, (1993) 461.
[22] H. Nakano, Y. Okuyama, K. Iwasa and H. Hongo, Tetrahedron Asymmetry, 5 (1994) 1155.
[23] N. Oishi, S. Maeno, M. Kobayashi, H. Sugiyama and K. Toyaka, Jpn. Kokai Tokkyo Koho JP 63 83,040 (Chem. Abstr., 109 (1988) 165710).
[24] K. Sakane, K. Kawabata and Y. Inamoto, Jpn. Kokai Tokkyo Koho JP 02 49,758 (Chem. Abstr., 113 (1990) 40012).
[25] K. Sakane, K. Kawabata and Y. Inamoto, Jpn. Kokai Tokkyo Koho JP 02 174,753 (Chem. Abstr., 114 (1991) 24607).
[26] M. Miyauchi, E. Tsujii, M. Ezaki, H. Hashimoto and M. Okuhara, Eur. Pat. Appl. EP 298,640 (Chem. Abstr., 114 (1991) 24607).
[27] S. Oida and T. Konosu, Jpn Kokai Tokkyo Koho JP 04 243,870 (Chem. Abstr., 118 (1993) 80923).
[28] C.T. Evans, S.M. Roberts and A.G. Sutherland, PCT Int. Appl. WO 92 18,477 (Chem. Abstr., 118 (1993) 168892).
[29] Y. Mikami, G.M. Scalarone, N. Kurita, Y.K. Nobuyuki, K. Yazawa and M. Miyaji, Nippon Ishinkin Gakkai Zasshi, 33 (1992) 355 (Chem. Abstr., 118 (1993) 76906).
[30] P.J. Crowley, D. Youle and S.P. Heaney, PCT Int. Appl WO 94 03,061 (Chem. Abstr., 120 (1994) 263835).
[31] S.M. Roberts, Pure Appl. Chem., 64 (1992) 1933.
[32] W.H. Pirkle and J. Finn, in J. Morrison (Editor), Asymmetric Sythesis, Vol. I, Analytical Methods, Academic Press, New York, 1983, Ch. 6.
[33] W.F. Lindner and C. Petterson, in I. Wainer (Editor), Liquid Chromatography in Pharmaceutical Development: an Introduction, Aster, Springfield, VA, 1985, Part 1.

[34] D.W. Armstrong and S.M. Han, CRC Crit. Rev. Anal. Chem., 19 (1988) 175.
[35] V.A. Davankow, A.A. Kurganov and A.S. Bochkov, Adv. Chromatogr., 22 (1983) 71.
[36] C. Petterson, Trends Anal. Chem., 7 (1988) 209.
[37] W.F. Lindner, in L. Crane and B. Zief (Editors), Chromatographic Chiral Separations, Marcel Dekker, New York, 1987, p. 91.
[38] W.F. Lindner, in J.F. Lawrence and R.W. Frei (Editors), Chemical Derivatization in Analytical Chemistry, Vol. 2, Plenum Press, New York, 1982, p. 145.
[39] T. Nambara, in W.S. Hancock (Editor), CRC Handbook of HPLC for the Separation of Amino Acids, Peptides and Proteins, Vol. I, CRC Press, Boca Raton, FL, 1984, p. 383.
[40] N. Nimura, H. Ogura and T. Kinoshita, J. Chromatogr., 202 (1980) 375.
[41] T. Kinoshita, Y. Kasahara and N. Nimura, J. Chromatogr., 210 (1981) 77.
[42] N. Nimura, A. Toyama and T. Kinoshita, J. Chromatogr., 316 (1984) 547.
[43] P. Marfey, Carlsberg Res. Commun., 49 (1984) 591.
[44] S. Einarsson, B. Josefsson, P. Möller and D. Sanchez, Anal. Chem., 59 (1987) 1191.
[45] H. Brückner and C. Gah, J. Chromatogr., 555 (1991) 81.
[46] H. Brückner, R. Wittner and H. Godel, Chromatographia, 32 (1991) 383.
[47] H. Brückner and B. Strecker, Chromatographia, 33 (1992) 586.
[48] S. Einarsson and G. Hansson, in C.T. Mant and R.S. Hodges (Editors), High Performance Liquid Chromatography of Peptides and Proteins, CRC Press, Boca Raton, FL, 1991, p. 369.
[49] L. Kanerva, P. Csomós, F. Fülöp and G. Bernáth, Tetrahedron, submitted for publication.
[50] A.E. Martell and R.M. Smith (Editors), Critical Stability Constants, Vol. 1, Plenum, Press, 1974.
[51] A. Péter, G. Tóth and D. Tourwé, J. Chromatogr. A, 668 (1994) 331.
[52] A. Péter, G. Tóth, E. Olajos, F. Fülöp and D. Tourwé, J. Chromatogr. A, 705 (1995) 257.