ELSEVIER

Journal of Chromatography A, 749 (1996) 25–32

JOURNAL OF CHROMATOGRAPHY A

Enantioseparation in the synthesis of *myo*-inositol phosphates by high-performance liquid chromatography using a β-cyclodextrin-bonded column

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Received 30 January 1996; revised 9 April 1996; accepted 12 April 1996

Abstract

A study of chromatographic enantioseparation in the synthesis of DL-*myo*-inositol derivatives by HPLC is presented. All intermediates in the synthesis of fully protected DL-*myo*-inositol 1,4,5-trisphosphate and some isomers thereof could be separated using a commercially available analytical β-cyclodextrin-bonded column. The retention behaviour of the inositol derivatives under reversed-phase conditions using methanol and acetonitrile as organic modifiers was investigated. In contrast to fully protected *myo*-inositol derivatives, the fully protected *myo*-inositol phosphates could be separated. Although enantiomeric separations were successful in the majority of cases, anticipation of chiral recognition for the derivatives is complicated. In knowledge of our results successful separation requires a benzyl ether and/or a cyclohexylidene ketal.

Keywords: Enantiomer separation; β-Cyclodextrin; *Myo*-inositol phosphate

1. Introduction

Commercially available β-cyclodextrin-bonded stationary phases for HPLC have been successfully used for the separation of a variety of racemates, e.g., metallocene enantiomers [1], alkaloids and resembling molecules [2], barbiturates [3], dansyl amino acids [4], and also α-hexachlorocyclohexane [5]. Cyclodextrin columns can be used in both the reversed and the normal-phase mode and are therefore widely applicable [6].

Most enantioseparations are usually obtained in the reversed-phase mode based on hydrophobic interactions and hydrogen bonding [7]. Nevertheless, the exact mechanism of chiral recognition remains unclear. Therefore, predictions on the chromatographic behaviour of new substance classes are difficult.

With respect to the significance of stereoisomerism in biological systems, investigations with enantiomerically pure derivatives are preferred to studies with racemic mixtures. This also holds for the *myo*-inositol phosphates because some of these compounds occur in both the D- and the L-form [8].

Optically active *myo*-inositol phosphates play an important role in signal transduction across cell membranes and are generated from the receptor-controlled hydrolysis of inositol phospholipids [9,10].

Synthetic *myo*-inositol phosphate derivatives are

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0021-9673/96/$15.00
PII S0021-9673(96)00367-6

used to study the biological functions of the naturally occurring compounds which are generally enantiomerically pure (for example D-*myo*-inositol 1,4,5-trisphosphate, Fig. 1.). Therefore the synthesis of *myo*-inositol phosphates from commercially available *myo*-inositol (a *meso* compound, Fig. 1) requires the resolution of racemates. In general, this involves additional synthetic steps to generate and separate the diastereomers and is inevitably related with losses in product yield.

A valuable alternative to chemical separation would be direct chromatography of the enantiomers, but in the field of inositol chemistry this technique has not yet been investigated systematically. Only a few examples for the separation of racemates using chiral HPLC (on a cellulose-derived stationary phase) have been reported [11–13]. It has been previously shown by ^{1}H NMR spectroscopy that *myo*-inositol ethers form diastereomeric complexes with β-cyclodextrin in aqueous solutions [14], suggesting this type of chiral phase to be appropriate for enantioseparation of inositol derivatives.

In this study the application of a β-cyclodextrin HPLC column in reversed-phase mode for common *myo*-inositol derivatives mainly protected by cyclic ketals and benzyl ethers was investigated. Special interest has been focused on the enantiomeric separation after each distinct step in the total synthesis of the fully protected *myo*-inositol phosphate, since the final deprotection step will generate the charged inositol phosphate, which is unlikely to be a candidate for the chromatographic enantioseparation.

2. Experimental

2.1. Chemicals

All chemicals (analytical grade) were used without further purification. NMR spectra were recorded on a Bruker AM 360 NMR spectrometer.

2.2. HPLC

All chromatographic experiments were performed at ambient temperature. Chiral column: LiChroCART Chiradex, 250×4 mm I.D., 5 μm was from Merck, Darmstadt, Germany. The flow-rate was 1 ml/min.

Analytical HPLC system: HPLC pump 64 was from Knauer, an injection valve (Rheodyne) with a 175-μl loop was used, peaks were detected by a fixed wavelength detector at 254 nm (Milton Roy).

Preparative column: Prepbar LiChrospher RP-18, 250×50 mm I.D., 10 μm was from Merck, Darmstadt, Germany.

Preparative HPLC system: LC A8 (Shimadzu), injection valve with 10-ml loop (Rheodyne), peaks were detected using a fixed-wavelength LDC UV III monitor (Milton Roy) at 254 nm.

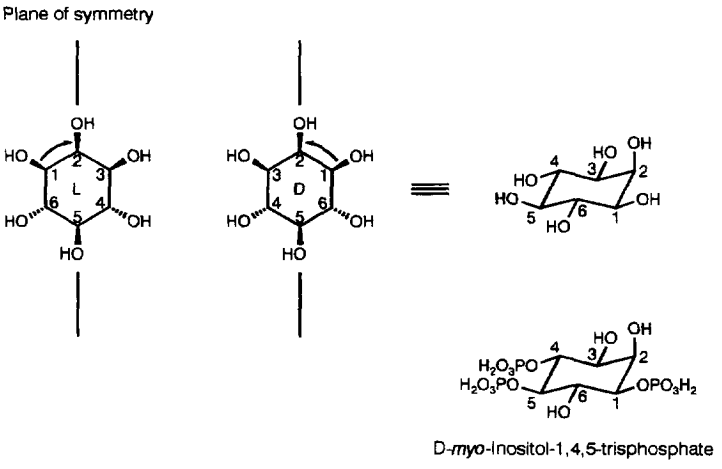


Fig. 1. Structure, symmetry and nomenclature of *myo*-inositol.

2.3. Synthesis of myo-inositol derivatives

DL-6-*O*-Benzyl-1,3,5-*ortho*-formyl *myo*-inositol (**1**): Treatment of 1,3,5-*ortho*-formyl *myo*-inositol [15] with 1 equivalent NaH and benzylchloride in *N,N*-dimethylformamide. Purity was confirmed by HPLC analysis. ^{1}H NMR (($C^2H_3)_2SO$, 360 MHz), δ 7.3 (m, 5H, H-aromatic), δ 5.5 (d, J=1.25 Hz, 1H, H-formyl), δ 5.3 (d, J=6 Hz, 1H, OH-2), δ 5.21 (d, J=5 Hz, 1H, OH-4), δ 4.6 (AB, J=10 Hz, 2H, CH_2-benzyl), δ 4.33 (dq, J=2, 5 Hz, 1H, H-5), δ 4.29 (dt, J=2, 5 Hz, 1H, H-4), δ 4.2 (dt, J=2, 5 Hz, 1H, H-6), δ 4.04 (dt, J=2, 5 Hz, 1H, H-1), δ 4.02 (dq, J=2, 6 Hz, 1H, H-2), δ 3.95 (dt, J=2, 5 Hz, 1H, H-3).

DL-6-*O*-Benzyl *myo*-inositol (**2**): Treatment of **1** with trifluoroacetic acid–water 4:1 (vol) [16]. ^{1}H NMR (($C^2H_3)_2SO$, 360 MHz) δ 7.3 (m, 10H, H-aromatic), δ 4.7 (m, 3H, OH and CH_2-benzyl), δ 4.65 (d, J=5 Hz, 1H, OH), δ 4.6 (d, J=5 Hz, 1H, OH), δ 4.57 (d, J=5 Hz, 1H, OH), δ 4.3 (d, J=5 Hz, 1H, OH), δ 3.7 (dt, J=4, 5 Hz, 1H, H-2), δ 3.4–3.3 (m, 3H, H-1/3/4), δ 3.2–3.1 (m, 2H, H-5/6).

DL-6-*O*-Benzyl-2,3;4,5-di-*O*-cyclohexylidene *myo*-inositol (**3**) and DL-6-*O*-Benzyl-1,2;4,5-di-*O*-cyclohexylidene *myo*-inositol (**7**): Treatment of **2** with cyclohexanone and *p*-toluene sulfonic acid in toluene [17]. Products were isolated from the reaction mixture by HPLC (LiChrosorb RP-18, 10 μm, 5×25 cm, 85% methanol–water, 20 ml/min, t_R=46′45 min (**3**) and t_R=32′40 min (**7**)), ^{1}H NMR (($C^2H_3)_2SO$, 360 MHz) **3**, δ 7.3 (m, 5H, H-aromatic), δ 5.1 (d, J=5 Hz, 1H, OH), δ 4.6 (AB, J=12 Hz, 2H, CH_2-benzyl), δ 4.3 (m, 2H, H-2/3), δ 3.95 (dd, J=7,10 Hz, 1H, H-5), δ 3.84 (dq, J=2, 5 Hz, 1H, H-1), δ 3.65 (dd, J=3, 8 Hz, 1H, H-6), δ 3.5 (dd, J=8, 10 Hz, 1H, H-4), δ 1.7–1.3 (m, 20H, H-cyclohexylidene).

^{1}H NMR (C^2HCl_3) **7**: δ 7.3 (m, 5H, H-aromatic), δ 5.35 (d, J=6 Hz, 1H, OH), δ 4.74 (AB, J=12 Hz, 2H, CH_2-benzyl), δ 4.24 (dd, J=4, 5 Hz, 1H, H-2), δ 4.07 (dd, J=5, 6 Hz, 1H, H-1), δ 3.9 (ddd, J=4, 6, 10 Hz, 1H, H-3), δ 3.67 (dd, J=9, 10 Hz, 1H, H-4), δ 3.53 (dd, J=6, 10 Hz, 1H, H-6), δ 3.4 (dd, J=9, 10 Hz, 1H, H-5), δ 1.7–1.2 (m, 20H, H-cyclohexylidene).

DL-6-*O*-Benzyl-2,3-*O*-cyclohexylidene *myo*-inositol (**4**): **3** was stirred with ethylene glycol and *p*-toluene sulfonic acid in acetonitrile [18]. ^{1}H NMR (($C^2H_3)_2SO$, 360 MHz) δ 7.3 (m, 5H, H-aromatic), δ 4.97 (s, 2H, 2×OH), δ 4.85 (s, 1H, OH), δ 4.76 (AB, J=10 Hz, 2H, CH_2-benzyl), δ 4.7 (dd, J=4, 6 Hz, 1H, H-2), δ 4.2 (dd, J=6, 7 Hz, 1H, H-3), δ 3.8 (dd, J=4, 8 Hz, 1H, H-1), δ 3.45 (t, J=7 Hz, 1H, H-4), δ 3.4 (t, J=7 Hz, 1H, H-6), δ 3.1 (t, J=9 Hz, 1H, H-5), δ 1.7–1.3 (m, 10H, H-cyclohexylidene).

DL-6-*O*-Benzyl-2,3-*O*-cyclohexylidene *myo*-inositol-1,4,5-tris-(dibenzyl)phosphate (**5**): **3** was stirred with *N,N*-diethyl dibenzyl phosphoramidite [19] in presence of tetrazole in acetonitrile. Then *t*-butylhydroperoxide was added. The product was isolated by HPLC (LiChrosorb RP-18, 5×25 cm, 90% methanol–water, 30 ml/min, t_R=36′50 min). ^{1}H NMR (C^2HCl_3, 360 MHz) δ 7.3 (m, 35H, H-aromatic), δ 5.1–4.8 (m, 14H, 7×CH_2-benzyl), δ 4.93 (ddd, J=7, 9, 12 Hz, 1H, H-4), δ 4.77 (ddd, J=4, 8, 8 Hz, 1H, H-1), δ 4.64 (ddd, J=4, 6, 9 Hz, 1H, H-5), δ 4.63 (dd, J=4, 6 Hz, 1H, H-2), δ 4.23 (dd, J=6, 7 Hz, 1H, H-3,), δ 4.17 (dd, J=6, 8 Hz, 1H, H-6), δ 1.7–1.25 (m, 10H, H-cyclohexylidene). ^{31}P NMR (C^2HCl_3, 360 MHz, ^{1}H decoupled) δ -1.2, -1.4, -1.6.

DL-3-*O*-Benzyl-*myo*-inositol (**6**) was prepared following a published procedure [20].

DL-3-*O*-Benzyl-1,2;4,5-di-*O*-cyclohexylidene *myo*-inositol (**8**) was prepared as described by [21].

DL-3-*O*-Benzyl-1,2;5,6-di-*O*-cyclohexylidene *myo*-inositol (**9**) was prepared as described for the enantiomerically pure material by [22].

DL-6-*O*-Benzyl-1,2;4,5-di-*O*-isopropylidene *myo*-inositol (**10**): treatment of **2** with 2,2-dimethoxypropane and *p*-toluene sulfonic acid [23] . The product was isolated from the reaction mixture by preparative HPLC (LiChrosorb RP-18, 250×50 mm, 75% methanol–water, 25 ml/min, t_R=29′10 min). ^{1}H NMR (C^2HCl_3, 360 MHz) δ 7.3 (m, 5H, H-aromatic), δ 4.7 (AB, J=10 Hz, 2H, CH_2-benzyl), δ 4.25 (dd, J=4, 5 Hz, 1H, H-2), δ 4.1 (dd, J=5, 6 Hz, 1H, H-1), δ 3.85 (dd, J=4, 10 Hz, 1H, H-3), δ 3.7 (dd, J=9, 10 Hz, 1H, H-4), δ 3.5 (dd, J=6, 10 Hz, 1H, H-6), δ 3.4 (dd, J=9, 10 Hz, 1H, H-5), δ 2.7 (s, 1H, OH), δ 1.55 (s, 3H, CH_3-isopropylidene), δ 1.5 (s, 3H, CH_3-isopropylidene), δ 1.48 (s, 3H, CH_3-isopropylidene), δ 1.4 (s, 3H, CH_3-isopropylidene).

DL-6-*O*-Benzyl-2,3;4,5-di-*O*-cyclohexylidene *myo*-inositol 1-dibenzylphosphate (**11**): **3** was phosphorylated as described above for the synthesis of **5**. The product was isolated by HPLC (LiChrosorb RP-18, 5×25 cm, 93% methanol–water, 30 ml/min, t_R=10′18 min). ^{1}H NMR (C^2HCl_3, 360 MHz) δ 7.3 (m, 15H, H-aromatic), δ 5.1–4.6 (m, 6H, CH_2-benzyl), δ 4.68 (ddd, J=4, 6, 10 Hz, 1H, H-1), δ 4.5 (dd, J=3, 6 Hz, 1H, H-2), δ 4.35 (t, J=7 Hz, 1H, H-5), δ 4.04 (dd, J=3, 8 Hz, 1H, H-3), δ 4.02 (t, J=7 Hz, 1H, H-4), δ 3.52 (dd, J=7, 10 Hz, 1H, H-6), δ 1.8-1.3 (m, 20H, *H*-cyclohexylidene).

^{31}P NMR (C^2HCl_3, 360 MHz, ^{1}H decoupled) δ -1.2.

DL-1,2-Di-*O*-butyryl-*myo*-inositol 3,4,5,6-tetrakis-(dibenzyl)phosphate (**12**) and DL-2-*O*-butyryl-1-*O*-methyl-*myo*-inositol 3,4,5,6-tetrakis-(dibenzyl)phosphate (**13**) were gifts of Marco Rudolf and Stefan Roemer; for synthesis see: [24].

3. Results

The structures of the inositol derivatives and selected chromatographic data are depicted in Table 1. For each compound only one enantiomer is shown. An example of the behaviour of k' values, selectivity, and resolution in dependence of the mobile phase used is given in Fig. 2 for compound **7**. Although the curves obtained for the k' values can be generalized for all inositol derivatives bearing unprotected hydroxylgroups (**1–4**, **6–10**), the data for separation did not exhibit an uniform feature.

For compound **4** similar results were obtained as for its diketal analogue **7**. The isomer of the latter, monohydroxy compound **8** was not separated at middle range acetonitrile percentages. Compound **2** and its diketal isomer **3** were only separated at high, the isomer of the former (**6**) as well as the diol **1** only at low acetonitrile percentages, but none of them with methanol as organic modifier. The monohydroxy compounds **9** and **10** were not separated at all.

The fully protected inositol phosphates (**5**, **11–13**) could only be separated with pure acetonitrile. Retention and chiral recognition broke down when as little as 1% water was added. With pure methanol or organic modifier–water compositions only low retention was observed, in the latter case down to 50% organic modifier. Higher amounts of water led to a dramatic increase of retention, so that the analytes were not eluted from the column.

4. Discussion

4.1. Mobile phases

The results observed with methanol as organic modifier are significantly different from those with acetonitrile. The analytes showed with methanol as organic component the same retention behaviour as on a classical reversed-phase: high k' values at high water percentages. This is combined with an increase in resolution while selectivity seems not to be affected. Similar relations are known by literature for amino acid derivatives [24]. In contrast, the chromatographic behaviour with acetonitrile as eluent could be divided into two characteristic sections: (a) high percentages of acetonitrile where retention behaviour was similar to a normal-phase (increasing polarity of the mobile phase decreases k' values), and (b) middle range and low acetonitrile contents with classical reversed-phase retention behaviour. The former phenomenon is known for unprotected carbohydrates [25], and less extensive for aniline derivatives [26]. The more free hydroxylgroups present in the inositol derivative, the higher were the k' values at high acetonitrile concentrations combined with a drop in the retention when water was added [27]. Obviously, hydrophobic interactions are of secondary importance at high contents of acetonitrile [28].

For very polar inositol derivatives (e.g., **1**, **2**, **6**) and fully protected inositol phosphates (**5**, **11–13**), it seems to be likely that retention and separation at high acetonitrile concentrations was primarily based on hydrogen bonding. This appears to be especially true for the fully protected inositol phosphates (**5**, **11–13**) for which a total breakdown of retention and separation is already observed when 1% water was added to the eluent.

Normal-phase conditions using isopropanol–hexane (data not shown) led to no separation even of racemates which showed good separations with pure

Table 1
Structures and chromatographic data of the inositol derivatives investigated

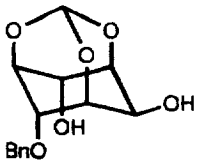
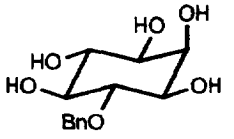
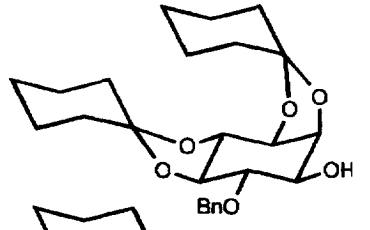
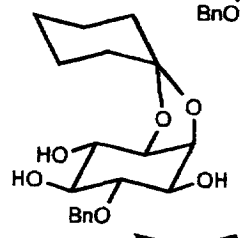
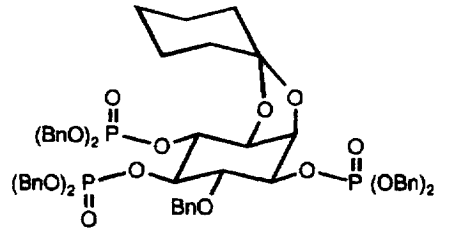
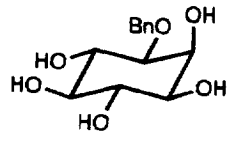
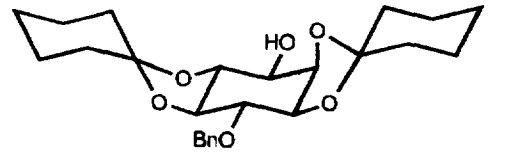
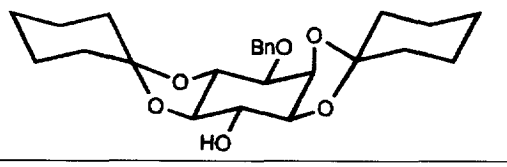
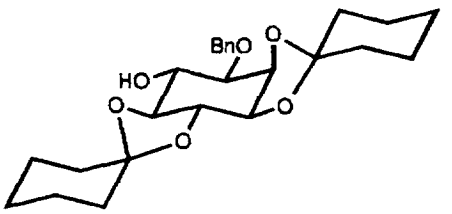
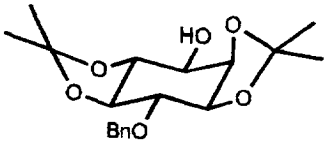
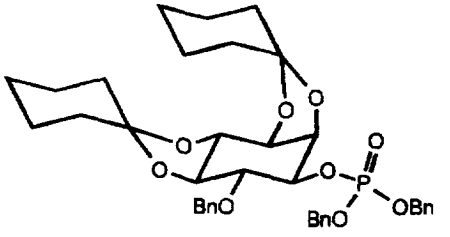
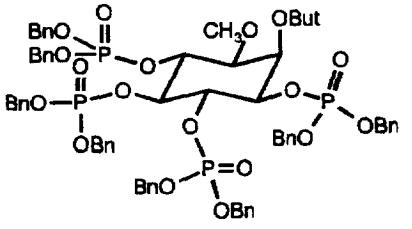
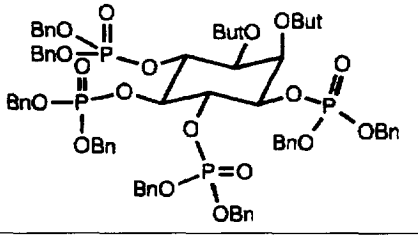
	Structure	Mobile phase	k'_1	α	R
1		20% acetonitrile	2.2	1.1	0.5
2		90% acetonitrile	3.3	1.1	0.7
3		100% acetonitrile	0.3	1.6	0.8
4		30% acetonitrile 50% methanol	2.4 4.3	1.2 1.2	0.6 0.5
5		100% acetonitrile	2.2	1.2	0.9
6		2% acetonitrile	1.7	1.1	0.7
7		50% acetonitrile 60% methanol	0.9 7.2	1.9 2.0	1.2 2.8
8		40% acetonitrile 50% methanol	1.5 5.6	1.4 1.4	1.0 1.5

Table 1 (*Continued*)

	Structure	Mobile phase	k'_1	α	R
9		no separation			
10		no separation			
11		100% acetonitrile	2.2	1.8	0.7
12		100% acetonitrile	5.4	1.1	0.8
13		100% acetonitrile	1.7	2.0	0.8

acetonitrile. The use of *tert.*-butyl-methyl ether–acetonitrile gave moderate separations in the case of the fully protected phosphates without reaching the separation factors of pure acetonitrile (data not shown). These findings indicate that with both mixtures only hydrogen bonding factors were decisive. In the presence of a H-bonding competitor like isopropanol the interactions between the analytes and the stationary phase were prevented and no separation was observed.

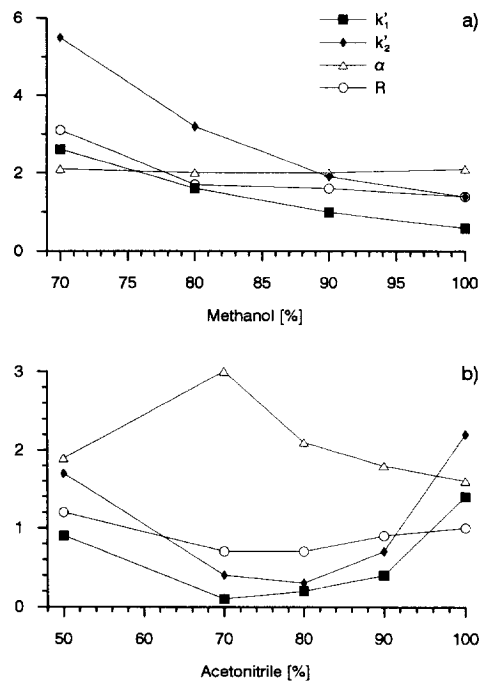


Fig. 2. Capacity factors, selectivity and resolution of **7** versus percent of organic modifier: (a) methanol–water and (b) acetonitrile–water. Abbreviations: k'_1=capacity factor of the first eluting enantiomer; k'_2=capacity factor of the second eluting enantiomer; α=selectivity; R=resolution.

4.2. Structural parameters

The two monobenzyl ethers of *myo*-inositol (**1** and **6**) could be separated with acetonitrile but not with methanol as organic modifier. It is noteworthy, that **1** was separated at high and **6** at low acetonitrile percentages which suggests that different separation mechanisms were involved [27]. The derivatives bearing both benzyl ethers and ketals, showed different separation behaviour. While **9** and **10** were not separated at all, the enantioseparation of **3**, **4**, **7** and **8** showed good results. Comparison of **7** and its isopropylidene analogue **10** implies, that one of the lipophilic cyclohexylidene ketals was responsible for the separation, although even one single lipophilic benzyl ether was sufficient in other cases (see above).

The phosphorylation of **4** leading to **5**, and **3** leading to **11**, respectively, did not decrease the chiral recognition. Obviously, the hydroxylgroups in **4** and **3** (acceptors and donors of hydrogen bonding) could be displaced by phosphoric acid triesters (only acceptors) without loosing diastereomeric interaction. Taking into account the chromatographic behaviour of the fully protected inositol phosphates, the large number of lipophilic groups in these molecules makes it improbable that lipophilic interactions are relevant for chiral recognition by β-cyclodextrin. Once more hydrogen bonding seems to be decisive for the preservation of the chiral interaction.

5. Conclusions

A commercially available β-cyclodextrin-bonded column was proven to be successful in the enantioseparation of different *myo*-inositol derivatives. For chiral recognition, different factors seem to be responsible depending on the eluent. Generally, fully protected *myo*-inositol phosphates were separated with pure acetonitrile. In contrast, fully protected *myo*-inositols were not separated at all. Derivatives bearing free hydroxylgroups and common protecting groups as benzyl ethers and cyclohexylidene ketals were separated using reversed-phase conditions. Furthermore, our results show that during and even on the very last step of inositol phosphate syntheses before the phosphates are liberated, chromatographic enantioseparation using a β-cyclodextrin-bonded column could be successfully carried out.

Acknowledgments

We thank the Deutsche Forschungsgemeinschaft for financial support.

References

[1] D.W. Armstrong, W. DeMond and B.P. Czech, Anal. Chem., 57 (1985) 481.
[2] D.W. Armstrong, T.J. Ward, R.D. Armstrong and T.E. Beesley, Science, 232 (1986) 1132.
[3] N. Thuaud and B. Sebille, J. Chromatogr. A, 685 (1994) 15.
[4] W.L. Hinze, T.E. Riehl, D.W. Armstrong, W. DeMond, A. Alak and T. Ward, Anal. Chem., 57 (1985) 237.
[5] K. Möller, C. Bretzke, H. Hühnerfuss, R. Kallenborn, J.N. Kinkel, J. Kopf and G. Rimkus, Angew. Chemie Int. Ed. Eng., 33 (1994) 862.

[6] H.J. Isaaq, J. Liq. Chromatogr., 11 (1988) 2131.
[7] S.M. Han and D.W. Armstrong, in A.M. Krstulovic (Editor), Chiral Separations by HPLC, Ellis Horwood, Wiley, Glasgow and London, 1989, p. 209.
[8] B.V.L. Potter and D. Lampe, Angew. Chem. Int. Ed. Eng., 34 (1995) 1933.
[9] B.W. Agranoff and S.K. Fisher, Am. Chem. Soc. Symp. Ser., 463 (1991) 20.
[10] C.P. Downes and C.H. McPhee, Eur. J. Biochem., 193 (1990) 1.
[11] Y. Watanabe, T. Ogasawara, H. Nakahira, T. Masuki and S. Ozaki, Tetr. Lett., 29 (1988) 5259.
[12] Y. Watanabe, A. Oka, Y. Shimizu and S. Ozaki, Tetr. Lett., 31 (1990) 2613.
[13] L. Ling and S. Ozaki, Carb. Res., 256 (1994) 49.
[14] M. Bernabé, Jiménez-Barbero, M. Martin-Lomas and S.V. Penadés, Carb. Res., 208 (1990) 255.
[15] H.W. Lee and Y. Kishi, J. Org. Chem., 50 (1985) 4402.
[16] D.C. Billington, R. Baker, J.J. Kulagowski, I.M. Mawer, J.P. Vacca, S.J. de Solms and J.R. Huff, J. Chem. Soc. Perkin Trans. I, (1989) 1423.
[17] S.J. Angyal, G.C. Irving, D. Rutherford and M.E. Tate, J. Chem. Soc., (1965) 6662.
[18] C.E. Dreef, R.J. Tuinman, A.W.M. Lefeber, C.J.J. Elie, G.A. van der Marel and J.H. van Boom, Tetrahedron, 447 (1991) 4709.
[19] L.I. Smirnova, M.A. Malenkovslaya, D.A. Predvoditelev and E.E. Nifant'ev, J. Org. Chem. UdSSR, 16 (1980) 1011.
[20] S.J. Angyal, M.H. Randall and M.E. Tate, J. Chem. Soc. C, (1967) 919.
[21] D.C. Billington, R. Baker, J.J. Kulagowski and I.M. Mawer, J. Chem. Soc. Chem. Commun., (1987) 314.
[22] A.P. Kaplun, V.N. Krylova, G.Y. Soloveichik, B.A. Klyatshchitskii and V.I. Shvets, J. Org. Chem. UdSSR, 14 (1978) 1730.
[23] S.-K. Chung and Y. Ryu, Carb. Res., 258 (1994) 145.
[24] S. Roemer, M.T. Rudolf, C. Stadler and C. Schultz, J. Chem. Soc. Chem. Commun., (1995) 411.
[25] D.W. Armstrong and H.L. Jin, J.Chromatogr., 462 (1989) 219.
[26] C.A. Chang, Q. Wu and M.P. Eastman, J. Chromatogr., 371 (1986) 269.
[27] S.C. Chang, G.L. Reid III, S. Cheng, C.D. Chang and D.W. Armstrong, Trends Anal. Chem., 12 (1993) 144.
[28] A.J. Alpert, J. Chromatogr., 499 (1990) 177.