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The *s*-triazine moiety as a scaffold for connecting different chiral auxiliaries: synthesis of new biselector CSPs for enantioselective chromatography

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Abstract—An *s*-triazine scaffold bearing a free and a protected amino group was synthesised and used for connecting two different and differently derivatised aminoacids. Two diastereoisomeric chiral systems were obtained and, once linked to silica gel, they were used in the chromatographic resolution of structurally and electronically different racemic analytes, chosen among the racemates resolved by the isolated aminoacid derivatives. The collected results demonstrate the biselector behaviour of the CSPs in terms of enantiodiscriminating capability towards the class of racemic compounds resolved by both the isolated selectors as well as in terms of the independent action of the two chiral moieties of the system.

1. Introduction

The use of independent chiral stationary phases in enantioselective chromatography, although introduced by Pirkle more than 20 years ago,[1] is still topical.[2] Indeed, because the phenomena which govern the chiral recognition process upon an independent CSP are fairly well understood,[3] it is possible to know in advance if a racemate will be separated or not using these CSPs, on the basis of the structure of the chiral selector linked to silica gel. Most of the independent CSPs, and among them Pirkle's CSPs,[4] are obtained starting from derivatized aminoacids:[5] as a consequence, the choice of a Pirkle-like CSP depends on the type of racemate because the molecular recognition between the enantiomers and the selector linked to silica gel depends on the type of modification (introduction of a π-acceptor or π-donor moiety) of the parent aminoacid. To overcome this problem we have recently addressed our attention toward the synthesis of biselector CSPs, i.e. CSPs whose chiral selector possesses the structural characteristics of two dissimilar chiral auxiliaries, which are known to act as selectors for HPLC toward different classes of racemic compounds.[6] Since Lin et al. have used the s-triazine unit for linking two different moieties and thus preparing CSPs, able to separate the enantiomers of 3,5-dinitrophenyl derivatives of various racemic compounds,[7] in order to connect the two dissimilar chiral auxiliaries to each other we used the 1,3,5-triazine moiety to which optically active 1-(1-naphthyl)ethylamine and, by means of a C2 tether, a 3,5-dinitrobenzoyl aminoacid were bonded.[6] However, the enantiodiscriminating capability of the 1-(1-naphthyl)ethylamine-*s*-triazine moiety (the π-basic selector) depended both on the nature and the absolute configuration of the stereogenic centre of the other chiral moiety, as well as the enantioselectivity of the derivatised aminoacid (π-acid selector) depended on the absolute configuration of the 1-(1-naphthyl)ethylamine.[6] This fact led to the necessity of synthesising a group of biselector systems (at least the two diastereoisomeric forms) by combining different chiral auxiliaries in order to find the matched combination. Therefore, a biselector system whose chiral moieties act independently would be attractive. Since the dependence of the enantiodiscrimination of one moiety on the nature and absolute configuration of the other one is probably due to their proximity allowing them to interact with each other, a way to obtain a biselector system whose moieties act independently could be to distance the two fragments far enough apart to prevent their interaction. In order to build up a system having these characteristics we decided to use the *s*-triazine merely as a connection unit to which two different and differently derivatised aminoacids are linked by means of a tether. To verify this hypothesis we chose, as derivatised

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aminoacids, the *N*-3,5-dinitrobenzoylleucine, one of the most popular selectors of the Pirkle's CSPs, and the *N*-1-naphthoylphenylglycine. We present herein the synthesis of the two diastereoisomeric biselector CSPs **1a**–**b** (Figure 1) and their use in enantioselective chromatography, aimed to demonstrate their behaviour as biselector CSPs.

2. Results and discussion

2.1. Synthesis of CSPs 1a–b

The synthetic route to the CSPs **1a** and **1b** is summarised in Scheme 1. In order to obtain a suitable scaffold to which two different aminoacid derivatives

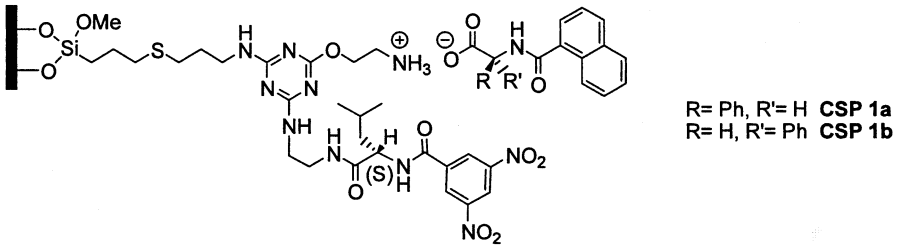
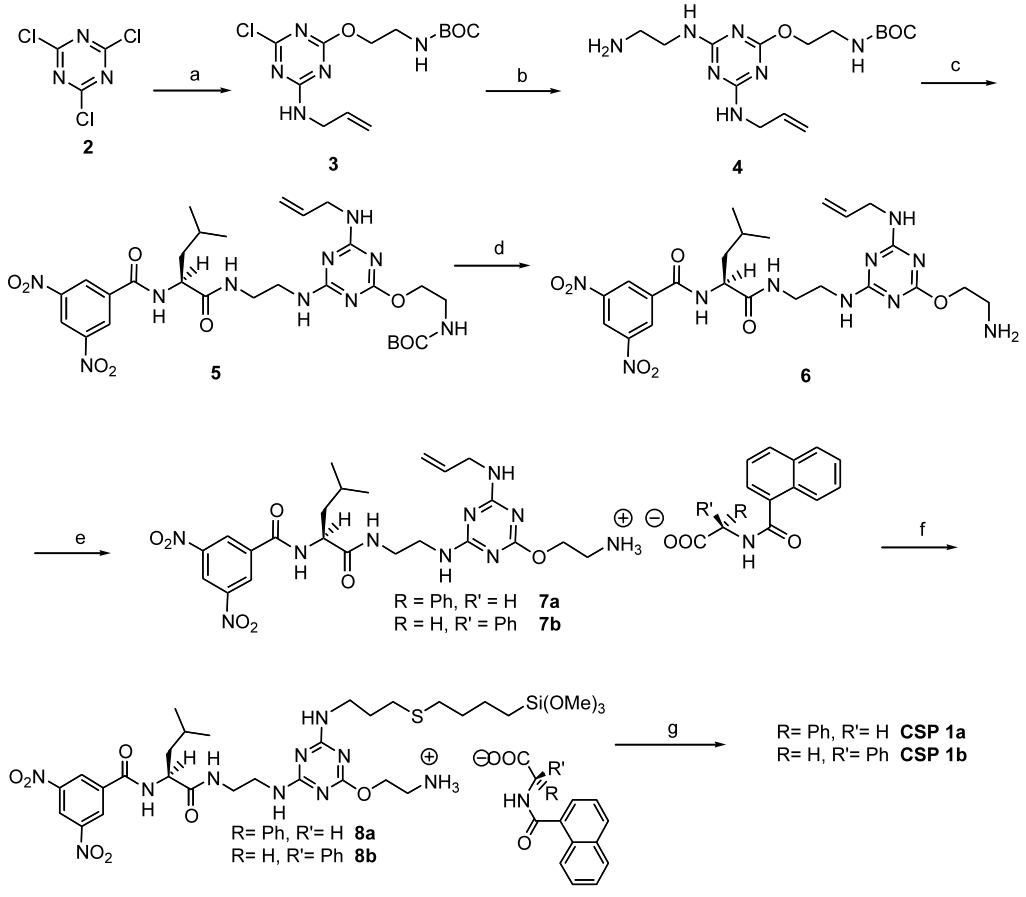
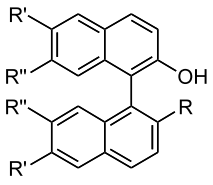


Figure 1. Structure of the CSPs **1a** and **1b**.

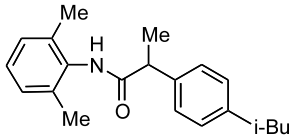


Scheme 1. *Reagents and conditions*: (a) 1. DIPEA, acetonitrile, Boc-ethanolamine, rt 2. DIPEA, allylamine 0°C to rt; (b) acetonitrile, ethylenediamine, rt; (c) EEDQ, THF, (*S*)-*N*-3,5-dinitrobenzoylleucine, rt; (d) TFA, CH_2Cl_2, rt; (e) (*R*)- or (*S*)-*N*-(1-naphthoyl)phenylglycine, $CHCl_3$, rt; (f) 3-mercaptopropyltrimethoxysilane, AIBN, $CHCl_3$, reflux; (g) SiO_2, dioxane, reflux.



9a R= OH, R'= H, R''=H
9b R= OH, R'=Br, R''= H
9c R= OH, R'= H, R''= Br
9d R= SO_2Et, R'= H, R''= H
9e R= OH, R'= H, R''= allyl

10a Ar= 1-naphthyl, R= i-Pr, R'= H
10b Ar= 9-anthryl, R= $-CF_3$, R'= H
10c Ar= 4-$MeOC_6H_4$, R=Ph, R'= H
10d Ar= 4-$Me_2NC_6H_4$, R= cyclohexyl, R'=H



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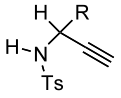
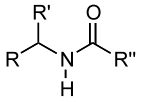
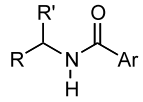


14a R= CH_3
14b R= t-Bu



11a R= 1-naphthyl R'= cyclohexyl, R''= methyl
11b R= 1-naphthyl, R'= cyclohexyl, R''= phenyl
11c R= 2-hydroxy-1-naphthyl, R'= Etile, R''= methyl
11d R= 2-hydroxy-1-naphthyl, R'= i-Pr, R''= methyl
11e R= 1-naphthyl, R'= methyl, R''= R''= 3,5-dimethylphenyl
11f R= phenyl, R'= n-Esile, R''= phenyl
11g R= 2-hydroxy-7-methoxy-1-naphthyl, R'= i-Pr,R''= methyl
12 R= i-Pr, R'= -COOMe, R''= phenyl



15a R= 1-naphthyl, R'= methyl, Ar= 4-nitrophenyl
15b R= methyl, R'= -COOMe, Ar= 3,5-dinitrophenyl
15c R= phenyl, R'= -COOMe, Ar= 3,5-dinitrophenyl
15d R= t-Butile, R'= -COOMe, Ar= 3,5-dinitrophenyl
15e R=sec-Butile, R'= -COOMe, Ar= 3,5-dinitrophenyl
15f R= i-Pr, R'= -COOMe, Ar= 3,5-dinitrophenyl
15g R= i-Pr, R'= $-COO^iPr$, Ar= 3,5-dinitrophenyl
15h R= hydroxymethyl, R'= -COOMe, Ar= 3,5-dinitrophenyl
15i R= i-Bu, R'= -COOMe, Ar= 3,5-dinitrophenyl
15l R= i-Pr, R'= -COOMe, Ar= 4-nitrophenyl
15m R= benzyl, R'= $-COO^nBu$, Ar= 3,5-dinitrophenyl
15n R= i-Bu, R'= $-CONH^nBu$, Ar= 3,5-dinitrophenyl
15o R= phenyl, R'= hydroxymethyl, Ar= 3,5-dinitrophenyl

Chart 1.

can be linked a tether having a terminal free amino group and another one possessing a protected amino function were introduced on the *s*-triazine ring. Allylamine was introduced as third substituent in order to have a terminal double bond which can be used for linking the chiral auxiliary to silica gel.[6] The order of introduction of the three substituents was chosen on the basis of the reactivity of chloro-*s*-triazine derivatives toward nucleophilic substitution. Since *s*-trichlorotri-azine, **2**, is very reactive, the poorest nucleophile, i.e. Boc-ethanolamine, was introduced at the first step.

The reaction was carried out in acetonitrile as a solvent at room temperature, using diisopropylethylamine (DIPEA) as a base.[8] The monosubstituted *s*-triazine derivative was not isolated but when the conversion of the *s*-trichlorotriazine was judged complete by TLC analysis, the second nucleophile, i.e. allylamine, and an equimolar amount of DIPEA were added in the same reaction *flask* at 0°C. The disubstituted product was obtained in 70% yield from trichlorotriazine after purification of the crude product by flash chromatography. The introduction of the third substituent was performed by slow addition of a dilute solution of **3** to a dilute solution of a fourfold excess of ethylenediamine. These reaction conditions prevent the formation of dimeric species, which can originate from the attack of the new formed trisubstituted product, *bearing* a terminal amino group, on the still unreacted disubstituted derivative, and afforded pure **4** in 96% yield. The trisubstituted *s*-triazine scaffold was reacted with (*S*)-*N*-3,5-dinitrobenzoylleucine in the presence of EEDQ[9] affording chemically pure **5** in 73% yield after chromatographic purification. Removal of the BOC protecting group by means of standard procedures followed by treatment with an equimolar amount of (*R*)- or (*S*)-*N*-naphthoylphenylglicine afforded the biselector systems in quantitative yield. The second aminoacid derivative was linked to the system by means of an ionic bond because every attempt to link the naphthoylphenylglycine covalently was unsuccessful, affording only in one case the desired product in 10% yield. The ionic systems were bonded to silica gel exploiting the presence of the terminal double bond: Thus, they were reacted with a fivefold excess of 3-mercaptopropyltrimethoxysilane in the presence of AIBN in $CHCl_3$ at the reflux for 48 h.[6,10] The silane derivatives were washed with pentane to remove the excess 3-mercaptopropyltrimethoxysilane and reacted with silica gel in refluxing dioxane. The derivatised silica materials were filtered, washed and then packed in stainless steel columns using conventional techniques.

2.2. Use of CSPs 1a and 1b in the HPLC resolution of racemic compounds

The enantiodiscriminating capabilities of CSPs **1a** and **1b** were examined in the chromatographic resolution of

racemic compounds having different structural features. In particular, taking into account the different electronic character of the aromatic groups of the selectors of the systems, the separation of the enantiomers of π-donor and π-acceptor analytes (Chart 1) was checked in order to verify if both the chiral moieties of the biselector system exhibit enantiorecognition. Furthermore, the resolution of the racemic compounds was checked against the two diastereomeric CSPs, under the same chromatographic conditions, in order to verify if the two portions of the biselector system act independently, or whether differences in the enantiodiscriminating capability could be found in passing from **1a** to **1b**.

Table 1 shows the chromatographic results relating to the use of **1a** and **1b** in the separation of the enantiomers of π-basic racemic compounds, i.e. binaphthyl derivatives and alkylaryl carbinols, analytes resolved by the 3,5-dinitrobenzoylleucine based CSP,[4a,11] which is reproduced in the π-acidic moiety of the biselector system, and the resolution of π-basic amides **11**–**14**. Perusal of Table 1 shows that both **1a** and **1b** are able to resolve binaphthyl derivatives as well as alkylaryl carbinols with enantioselectivity factors which, in most cases, allow a baseline separation of the chromatographic peaks (Figure 2). Furthermore, the two CSPs show no differences as far as their enantiodiscriminating capability is concerned, since they resolve all the π-basic analytes with the same enantioselectivity factors. Some differences can be found in the retention times of the racemic compounds when they are eluted upon the two different CSPs, however, these differences can be attributed to a slightly different packing of the two CSPs.

These results show that the presence of the 1-naphthoylphenylglicine moiety does not affect the enantiodiscriminating properties of the π-acidic moiety of CSPs **1a**–**b**, which is most likely to be responsible for the enantioresolution of this class of racemates.[12] The change of the absolute configuration of the stereogenic center of the phenylglycine does not result in a change of the enantiodiscriminating properties of CSPs **1a**–**b** towards π-basic racemic compounds. The enantioresolution does depend on the nature of the racemic compound in the same way as has been observed for the 3,5-dinitrobenzoylphenylglicine based Pirkle's CSP.

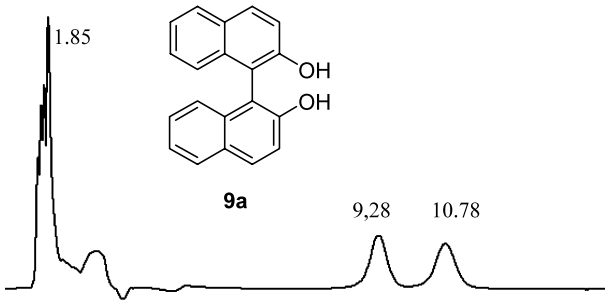


Figure 2. Chromatographic resolution of **9a** upon CSP **1b**.

Table 1. Chromatographic resolution[a] of π-basic compounds upon CSPs **1a** and **1b**

Entry	Compound	CSP **1a**			CSP **1b**			
		k'[b]	α[c]	e.o.[d]	k'[b]	α[c]	e.o.[d]	Eluent[e]
1	**9a**	4.29	1.20	(−)-(*R*)	4.01	1.20	(−)-(*R*)	A
2	**9b**	7.63	1.18	(−)-(*R*)	8.80	1.18	(−)-(*R*)	A
3	**9c**	8.55	1.18	(−)-(*R*)	9.28	1.18	(−)-(*R*)	A
4	**9d**	1.90[f]	1.27	(−)-(*R*)	8.42	1.27	(−)-(*R*)	A
5	**9e**	3.81	1.16	(−)-(*R*)	3.94	1.16	(−)-(*R*)	A
6	**10a**	2.77	1.07	(−)	2.72	1.07	(−)	B
7	**10b**	2.81	1.20	(+)	2.63	1.20	(+)	A
8	**10c**	4.43	1.05		4.24	1.05		B
9	**10d**	3.95	1.05	(−)	3.91	1.05	(−)	B
10	**11a**	10.40	1.29	(−)	9.55	1.29	(−)	A
11	**11b**	2.22	1.15	(+)	2.05	1.15	(+)	A
12	**11c**	7.57	1.19	(−)	7.67	1.19	(−)	C
13	**11d**	6.70	1.23	(+)	6.75	1.23	(+)	C
14	**11e**	2.24	1.16	(−)	2.07	1.16	(−)	A
15	**11f**	1.25	1.28		1.19	1.28		A
16	**11g**	6.67	1.23		6.45	1.23		C
17	**12**	1.15	1.29		1.10	1.29		A
18	**13**	2.16	1.21	(+)	2.36	1.21	(+)	A
19	**14a**	8.87	1.04		8.78	1.04		B
20	**14b**	4.01	1.20	(+)	4.02	1.20	(+)	B

[a] Chromatographic conditions: UV detection (λ = 254 nm), T = 25°C, flow 1 ml/min.
[b] Retention factor of the first eluted enantiomer.
[c] Enantioselectivity factor.
[d] Sign of the circular dichroism at 254 nm (at 240 for binaphthyl compounds) and absolute configuration of the first eluted enantiomer.
[e] A: hexane/dichloromethane/propan-2-ol 70/30/1; B: hexane/dichloromethane/propan-2-ol 90/10/1; C: hexane/dichloromethane/propan-2-ol 70/30/5.
[f] Eluent C.

Even using CSPs **1a**–**b**, the best resolved alkylarylcarbinol results the trifluoromethyl-(9-anthryl)carbinol **10b** (entry 7).[11c] In addition, as far as the chromatographic resolution of binaphthyl derivatives (entries 1–5) is concerned, we observe for CSPs **1a**–**b** the same elution order found for the Pirkle's CSP.[11d] Both these results suggest that the enantiorecognition mechanism exhibited by **1a** and **1b** towards binaphthyl derivatives and alkylaryl carbinols must be the same as that of Pirkle's CSP and, hence, it means that the enantiodiscriminating capability of the 3,5-dinitrobenzoylleucine does not undergo appreciable changes when this moiety is part of the **1a**–**b** chiral system.

The good results obtained in the chromatographic resolution of racemic compounds enantiodiscriminated by the Pirkle's CSP, prompted us to use CSPs **1a**–**b** in the separation of the enantiomers of other kinds of π-basic substrates such as amides having different structures (Table 1). The two diastereomeric CSPs behave in the same way even towards these racemic compounds, since they are able to separate the enantiomers of the analytes with the same enantioselectivity factors. The enantiodiscriminating capability of these CSPs towards this class of racemates is good and independent of the chemical structure of the substrates: good enantioselectivity factors are observed for benzamides **11b** and **11f** (entries 11 and 15), acetamides **11a**, **11c**, **11d** and **11g** (entries 10, 12,13 and 16) and the anilide **13** (entry 18). Baseline separation of the peaks is obtained very often (Figure 3) allowing an easy determination of the enantiomeric composition of enriched samples. The separation of the enantiomers of the *p*-toluensulphonamides **14a** and **14b** (entries 19 and 20) are quite interesting results, since these derivatives are precursors of β-lactames,[13] used for synthesizing antibiotics and anticancer drugs.[14]

Having established that the enantiodiscriminating capability of the π-acid moiety of the biselector system is not influenced by the presence of the other moiety, the second step was to ascertain if the same independence of action is found for the π-basic fragment. The *N*-(1-naphthoyl)-phenylglycine has *never* been used as selector for enantioselective chromatography, to the best of our knowledge: however this aminoacid derivative possesses structural and electronic characteristics similar to other kinds of π-donor chromatographic selectors:[4b] hence, in order to verify the enantiodiscriminating capabilities of this fragment of the biselector system, the chromatographic resolution of π-acid racemic compounds was checked. Furthermore, to exclude the possibility that the 3,5-dinitrobenzoylleucine moiety of the biselector system is involved in the enantiodiscrimination of this class of racemic compounds, the chromatographic resolutions of compounds **15** were checked with commercial 3,5-dinitrobenzoylleucine CSP under the same chromatographic conditions used with CSPs **1a** and **1b**: a slight separation ($\alpha = 1.04$) is observed only in the case of **15m**.

Table 2 reports on the chromatographic results related to the separation of the enantiomers of π-acid racemates (Chart 1) upon CSPs **1a** and **1b**.

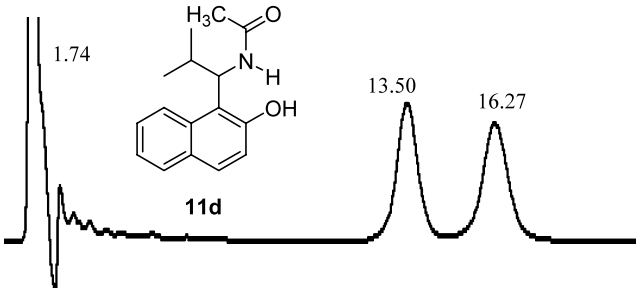


Figure 3. Chromatographic resolution of **11d** upon CSP **1b**.

Table 2. Chromatographic resolution[a] of π-acid racemic compounds upon CSPs **1a** and **1b**

Entry	Compound	CSP **1a**		CSP **1b**		
		k'^{b}	α^{c}	k'^{b}	α^{c}	Eluent[d]
1	**15a**	2.25	1.18	1.90	1.18	A
2	**15b**	9.79	1.18	9.71	1.18	B
3	**15c**	4.73	1.14	4.36	1.14	B
4	**15d**	1.04	1.14	2.14	1.14	B
5	**15e**	2.90	1.31	2.92	1.31	B
6	**15f**	3.65	1.29	3.35	1.29	B
7	**15g**	2.11	1.42	1.88	1.42	B
8	**15h**	4.81	1.13	4.75	1.13	A
9	**15i**	3.24	1.43	3.43	1.43	B
10	**15l**	15.20	1.16	15.65	1.16	C
11	**15m**	2.90	1.31	2.71	1.31	B
12	**15n**	10.11	1.17	9.99	1.17	B
13	**15o**	4.61	1.22	4.80	1.22	D

[a] Chromatographic conditions: UV detection ($\lambda = 254$ nm), $T = 25$°C, flow 1 ml/min.
[b] Retention factor of the first eluted enantiomer.
[c] Enantioselectivity factor.
[d] A: hexane/dichloromethane/propan-2-ol 70/30/3; B: hexane/dichloromethane/propan-2-ol 70/30/1; C: hexane/dichloromethane/propan-2-ol 90/5/0.5; D: hexane/dichloromethane/propan-2-ol 70/30/5.

Perusal of Table 2 shows that CSPs **1a** and **1b** behave in the same way as in the case of the resolution of π-acid racemic compounds, affording the same enantioselectivity factors in all the examined cases; slight differences in the retention factors are observed also in these enantioseparations in passing from CSP **1a** to CSP **1b**. These results suggest that the enantiodiscriminating capability of the π-basic portion of the biselector system is not affected by the change of stereochemistry of the system: in fact the enantioselectivity of the two diastereoisomeric chiral auxiliaries towards this class of racemic compounds, which most likely interact with the π-basic moiety of the biselector systems, is the same (Table 2).

The two CSPs are able to resolve not only 3,5-dinitrobenzoyl derivatives of aminoacid alkylesters, but also other classes of π-acid racemic compounds such as 4-nitrobenzamide derivatives **15a** and **15l** (entries 1 and 10), the *N*-3,5-dinitrobenzamide of phenylglycinol **15o** (entry 13) and *N*-3,5-dinitrobenzoyl derivatives of aminoacid alkylamides (entry 12). All the enantioselectivity factors are high enough to observe baseline separation of the chromatographic peaks (Figure 4). A structural feature which affords better resolutions of the aminoacid derivatives is the presence of a branched substituent or a benzyl group on the stereogenic centre of the aminoacid (entries 4, 5, 6, 7, 9 and 11). The enantioselectivity factor obtained in the resolution of **15g** (entry 7) bearing an isopropyl ester group is higher than that observed in the resolution of the analogous methylester derivative **15f** (entry 6), suggesting that the structure of the ester group also influences the enantioselectivity. The π–π donor–acceptor interaction plays an important role in the enantiodiscrimination process: when the 3,5-dinitrophenyl group is replaced by the less π-acid 4-nitrophenyl moiety, as in the case of **15l**, the enantiodiscrimination capability of the CSPs decreases (compare entry 6 with entry 10). Even the presence of an alkylamide moiety instead of an ester group represents a less favourable feature for the enantiodiscrimination, a lower enantioselectivity factor being obtained in the resolution of the *n*-butylamide derivative of valine **15n** (entry 12) with respect the corresponding methylester **15f** (entry 6).

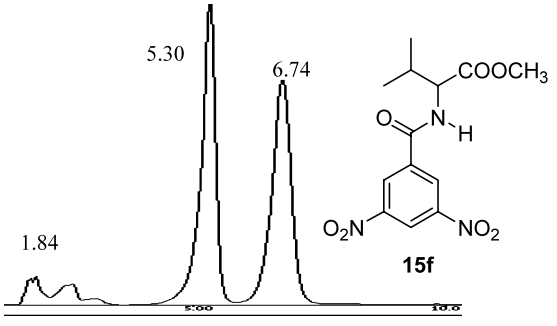


Figure 4. Chromatographic resolution of **15f** upon CSP **1a**.

3. Conclusions

The results obtained in the chromatographic resolution of both π-acid and π-basic racemic compounds upon CSPs **1a** and **1b** demonstrate that the two diastereoisomeric chiral auxiliaries linked to the silica gel behave as true biselector systems, being able to resolve π-basic racemic compounds as well as π-acid racemates. In addition, since there is no difference in the enantiodiscriminating capability exhibited by the two CSPs in the resolution of all the classes of examined racemic compounds, a complete independence of action of the two moieties of the biselector system can be inferred. This represents an advantage in the design of a biselector system, since the synthesis of both the diastereoisomeric forms of the chiral auxiliary can be avoided. Therefore, the *s*-triazine derivative **4** emerges as a useful scaffold to which different kind of chiral selectors can be linked, to obtain various class of biselector systems.

4. Experimental

^{1}H and ^{13}C NMR spectra were recorded on a NMR Varian Gemini 200 or on a Varian VXR-300 in $CDCl_3$, DMSO-d_6 or acetone-d_6, as specified in each case and using TMS as internal standard. The following abbreviations were used: s = singlet; br s = broad signal; d = doublet; dd = double doublet; t = triplet; m = multiplet.

TLC analyses were performed on a silica gel plates Macherey–Nagel 60 F_{254}. Chromatographic purification were performed using silica gel Macherey–Nagel, 70–230 or 230–400 for flash chromatography. Optical rotations were measured at the sodium D-line on a digital polarimeter JASCO-DIP 360: concentration, solvent and temperature are those specified. Melting points were taken using a Kofler Reichert–Jung apparatus (heating rate = 4°C/min) and are uncorrected. IR (KBr) spectra were recorded on a Perkin–Elmer 1710 spectrophotometer. HPLC analyses were performed on a JASCO PU-980 chromatograph, equipped with a JASCO UV-975 detector and a circular dichroism JASCO J-600 detector. Elemental analyses were carried out at Laboratorio di Microanalisi, Dipartimento di Farmacia, Università di Pisa.

THF and 1,4-dioxane were refluxed over sodium-benzophenone and distilled before use. Acetonitrile, dichloromethane, triethylamine, allylamine and *N*-ethyldiisopropylamine were distilled over CaH_2. Ethylenediamine was distilled over KOH dust. Ethanolamine was distilled under reduced pressure. Methanol was refluxed on Mg and distilled before use. Chloroform was distilled under nitrogen atmosphere just before use. 3-Mercaptopropyltrimethoxysilane was distilled under reduced pressure before use. 3,5-Dinitrobenzoylchloride was recrystallised from light petroleum. 2,4,6-Trichloro-1,3,5-triazine was recrystallised from CCl_4 and stored under a nitrogen atmosphere. Trifluoroacetic acid was distilled over P_2O_5. 1-Naphthoyl chloride was distilled under reduced pres-

sure and stored under nitrogen atmosphere. Unless otherwise specified, commercial reagents were used without further purifications.

4.1. Tertbutyloxy-2-[4-allylamino-6-*c*hloro-1,3,5-triazin-2-yl]ethylcarbamate, 3

N-*t*-Butyloxycarbonilethanolamine (6.75 g, 42.00 mmol) was added at room temperature to a stirred solution of 2,4,6-trichloro-1,3,5-triazine (7.74 g, 42.00 mmol) and *N*-ethyldiisopropylamine (7.3 ml, 42.00 mmol) in 125 ml of dry acetonitrile. After stirring the mixture at room temperature for 2 h, it was cooled to 0°C and *N*-ethyldiisopropylamine (7.3 ml, 42.00 ml) was added; allylamine (3.15 ml, 42.00 mmol) was then added dropwise at the same temperature. The mixture was stirred at 0°C for 1 h and at room temperature for 2 h. The solvent was removed under reduced pressure and the crude product was dissolved in dichlorometane; the solution was washed with 10%HCl, water, 10% $NaHCO_3$ and water, in that order, then dried over anhydrous Na_2SO_4. After removing the solvent at reduced pressure, the crude product was purified by flash chromatography (SiO_2, CH_2Cl_2 first and then CH_2Cl_2/acetone = 90/10), affording **3** (9.3 g, 28.22 mmol) in 67% yield: mp = 105–107°C. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, δ/ppm): 1.42 (s, 9H, -C(C$\underline{H}_3$)$_3$); 3.46 (dd, 2H, -O-CH$_2$-C$\underline{H}_2$-NH); 4.04 (m, 2H, -C$\underline{H}_2$-CH=CH$_2$); 4.38 (t, 2H, -O-C$\underline{H}_2$-CH$_2$-NH-); 5.00 (br s, 1H, -CH$_2$-N$\underline{H}$-CO-); 5.16 (m, 2H, -CH=C$\underline{H}_2$); 5.84 (m, 1H, -C$\underline{H}$=CH$_2$); 6.68 (t, 1H, Ar-N$\underline{H}$-CH$_2$-); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C, δ/ppm): 28.4 (-C(C$\underline{H}_3$)$_3$); 29.6; 39.8; 40.8 (-NH-C$\underline{H}_2$-CH=CH$_2$); 42.2; 43.2 (-O-CH$_2$-C$\underline{H}_2$-NH-); 65.8; 77.4 (-C(CH$_3$)$_3$); 79.2; 115.9 (-CH=C$\underline{H}_2$); 134.6 (-C$\underline{H}$=CH$_2$); 135.2; 156.1; 166.8; 169.9; 170.5; IR (KBr, cm^{-1}): 3369; 3262; 3122; 2984; 1682; 1638; 1526; 1430; 1344; 1302; 1222; 1164; 1080; 993; 924; 858; 805; 664; 587.

4.2. Tertbutyloxy-2-[4-allylamino-6-(2-amino)-ethylamino-1,3,5-triazin-2-yl]ethylcarbamate, 4

A solution of **3** (5.9 g, 17.9 mmol) in 180 ml of acetonitrile was added dropwise at room temperature to a stirred solution of dry ethylenediamine (7.2 ml, 0.107 mol) in 160 ml of acetonitrile. The resulting mixture was stirred at room temperature for 2 h and the solvent was removed at reduced pressure; 10% $NaHCO_3$ was added to the residue and the aqueous solution was extracted with dichloromethane. The combined organic extracts were washed with water and dried over anhydrous Na_2SO_4. After removing the solvent at reduced pressure, pure **4** (6.1 g, 17.27 mmol) was obtained in 96%: mp = 35–40°C. ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 1.42 (s, 9H, -C(C$\underline{H}_3$)$_3$); 2.69 (t, 2H, -NH-CH$_2$-C$\underline{H}_2$-NH$_2$, J = 6.4 Hz); 3.25 (m, 4H, -C$\underline{H}_2$-NH-CO- superimposed to -NH-C$\underline{H}_2$-CH$_2$-NH$_2$, J = 6.4 Hz, J = 5.96 Hz); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH=CH$_2$); 4.19 (t, 2H, -O-C$\underline{H}_2$-CH$_2$-NH-, J = 5.96 Hz); 5.00–5.20 (m, 2H, -CH=C$\underline{H}_2$); 5.87 (m, 1H, -C$\underline{H}$=CH$_2$); 6.40–6.90 (br. s, 3H, Ar-N$\underline{H}$-CH$_2$-CH=CH$_2$, Ar-N$\underline{H}$-CH$_2$-CH$_2$-NH$_2$ and -CH$_2$-N$\underline{H}$-CO-); ^{13}C NMR (50 MHz, DMSO-d_6, 100°C, δ/ppm): 27.9 (-C(C$\underline{H}_3$)$_3$); 39.40; 41.0 (-NH-C$\underline{H}_2$-CH=CH$_2$); 42.3 (-NH-CH$_2$-C$\underline{H}_2$-NH$_2$); 43.5 (-O-CH$_2$-C$\underline{H}_2$-NH-); 64.2; 77.5 (-C(CH$_3$)$_3$); 114.5 (-CH=C$\underline{H}_2$); 135.5 (-CH$_2$-C$\underline{H}$=CH$_2$); 166.7; 166.9; IR (KBr, cm^{-1}): 3360; 2977; 2362; 1700; 1585; 1430; 1335; 1252; 1166; 918; 864; 814.

4.3. (*S*)-*N*-(1-Naphthoyl)phenylglycine

To a solution of (*S*)-(*N*)-phenylglycine (2.0 g, 13.2 mmol) and propylene oxide (2.78 ml, 39.7 mmol) in 40 ml of dry THF, 1-naphthoylchloride (2 ml, 13.2 mmol) was added. The resulting mixture was stirred at room temperature overnight and the solvent was evaporated under reduced pressure. The crude was recrystallised from CH_2Cl_2, affording the pure product (9.9 mmol, 75%): mp = 90–95°C, $[\alpha]_D^{25}$ = +91.8 (*c* 1.4, CH_2Cl_2).

The same experimental procedure was used to obtain (*R*)-*N*-(1-naphthoyl)phenylglycine (10.3 mmol, 78%): mp = 95–100°C, $[\alpha]_D^{25}$ = −91.7 (*c* 1.1, CH_2Cl_2), ^{1}H NMR (200 MHz, $CDCl_3$, 25°C, δ/ppm): 3.50 (br s, 1H, -COO$\underline{H}$); 5.85 (d, 1H, -C*$\underline{H}$-); 6.95 (d, 1H, -N$\underline{H}$-CO-); 7.30–7.60 (m, 9H, aromatics); 7.65 (d, 1H, aromatic); 7.80–8.00 (m, 2H, aromatics); 8.40 (m, 1H, aromatic); ^{13}C NMR (50 MHz, DMSO-d_6, 100°C, δ/ppm): 57.1 (-C*H-); 125.0; 125.5; 125.7; 126.3; 126.8; 128.1; 128.2; 128.6; 130.0; 133.2; 134.1; 137.0; 168.7 (-CO- amidic); 172.1 (-COOH); IR (KBr, cm^{-1}): 3287; 3047; 2924; 2344; 1715; 1640; 1527; 1412; 1317; 1223; 1028; 784; 695.

4.4. Tertbutyloxy-2-{4-allylamino-6-[2-(*S*)-*N*-3,5-dinitrobenzoylaminoisobutylacetyl]-ethylamino-1,3,5-triazin-2-yl}ethylcarbamate, 5

A solution of (*S*)-*N*-(3,5-dinitrobenzoyl)leucine (0.920 g, 2.83 mmol) and EEDQ (0.70 g, 2.83 mmol) in 60 ml of dry THF was stirred at room temperature for 3 h, then **4** (1.0 g, 2.83 mmol) was added and the resulting mixture was stirred for 20 h at room temperature. The solvent was evaporated under reduced pressure and the crude product was dissolved in CH_2Cl_2; the solution was washed with 10% HCl, H_2O, 10% $NaHCO_3$ and H_2O, in that order, then dried over anhydrous Na_2SO_4. After removing the solvent at reduced pressure, the crude product was purified by flash chromatography (SiO_2, AcOEt/hexane = 90/10), affording pure **5** (1.36 g, yield 73%); mp = 185–190°C, $[\alpha]_D^{29}$ = −7.17 (*c* 0.99, CH_2Cl_2). ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.94 (t, 6H, -CH(C$\underline{H}_3$)$_2$, J = 5.2 Hz); 1.42 (s, 9H, -C(C$\underline{H}_3$)$_3$); 1.68 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$(CH$_3$)$_2$, J = 5.2 Hz); 3.20–3.40 (m, 6H, -C$\underline{H}_2$-NH-Boc, J = 6.0 Hz, Ar-NH-C$\underline{H}_2$-CH$_2$-NH-CO- superimposed to Ar-NH-CH$_2$-C$\underline{H}_2$-NH-CO-); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH=CH$_2$); 4.19 (t, 2H, -O-C$\underline{H}_2$-CH$_2$-NH-, J = 6.0 Hz); 4.54 (m, 1H, -C*$\underline{H}$-, J = 7.38 Hz); 5.00–5.20 (m, 2H, -CH=C$\underline{H}_2$); 5.87 (m, 1H, -C$\underline{H}$=CH$_2$); 6.40–6.90 (br s, 3H, Ar-N$\underline{H}$-CH$_2$-CH=CH$_2$, Ar-N$\underline{H}$-CH$_2$-CH$_2$-NH- e Ar-O-CH$_2$-CH$_2$-N$\underline{H}$-CO-); 7.75 (br s, 1H, -N$\underline{H}$-CO-C*H-); 8.95 (t, 1H, aromatic, J = 2.4 Hz); 8.99 (d, 1H, -C*H-N$\underline{H}$-CO-, J = 7.38 Hz); 9.08 (d, 2H, aromatics, J = 2.4 Hz). ^{13}C NMR (75 MHz, DMSO-d_6, 25°C, δ/ppm): 21.5; 23.1; 24.5 (-CH(C$\underline{H}_3$)$_2$); 28.3 (-C(C$\underline{H}_3$)$_3$); 40.3 (-NH-C$\underline{H}_2$-CH=CH$_2$); 42.4; 42.8; 52.6 (-C*H); 64.5; 78.0; 115.0 (-CH=C$\underline{H}_2$); 121.1; 128.0; 135.8 (-C$\underline{H}$=CH$_2$); 136.7; 148.2; 155.8; 162.5; 166.7; 167.0; 170.1; 172.0; IR (KBr, cm^{-1}): 3436; 3343; 3082; 2959; 1704; 1651; 1538; 1464; 1429; 1343; 1251; 1162; 1074; 994; 919; 865; 809; 730.

4.5. 2-{4-Allylamino-6-[2-(*S*)-*N*-3,5-dinitrobenzoyl-aminoisobutylacetyl]-ethylamino-1,3,5-triazin-2-yloxy}ethylamine, 6

Trifluoroacetic acid (6.6 ml, 0.086 mol) was added at room temperature to a solution of **5** (1.67 mmol) in 13 ml of CH_2Cl_2. This mixture was stirred for 15 min at room temperature, then 10% $NaHCO_3$ was added slowly; the crude product was extracted with AcOEt, washed with water and dried over anhydrous Na_2SO_4. After removing the solvent at reduced pressure, pure **6** was obtained in quantitative yield: mp = 105–115°C, $[\alpha]_D^{29} = +8.93$ (*c* 1.1, THF); ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.94 (t, 6H, -CH(C$\underline{H}_3$)$_2$); 1.68 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$(CH$_3$)$_2$); 3.15 (t, 2H, -O-CH$_2$-C$\underline{H}_2$-NH$_2$); 3.20–3.40 (m, 4H, Ar-NH-C$\underline{H}_2$-C$\underline{H}_2$-NH-CO- superimposed); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH=CH$_2$); 4.40 (t, 2H, -O-C$\underline{H}_2$-CH$_2$-NH$_2$); 4.54 (m, 1H, -C*H-); 5.00–5.25 (m, 2H, -CH=C$\underline{H}_2$); 5.87 (m, 1H, -C$\underline{H}$=CH$_2$); 6.70–7.00 (br s, 2H, Ar-N$\underline{H}$-CH$_2$-CH=CH$_2$ and Ar-N$\underline{H}$-CH$_2$-CH$_2$-NH-); 7.50–8.10 (br s, 3H, -N$\underline{H}_2$ superimposed to -CH$_2$-N$\underline{H}$-CO-C*H-); 8.95 (t, 1H, aromatic); 8.99 (d, 1H, -C*H-N$\underline{H}$-CO-); 9.08 (d, 2H, aromatics). ^{13}C NMR (50 MHz, DMSO-d_6, 100°C, δ/ppm): 21.3–22.4 (-CH(C$\underline{H}_3$)$_2$); 24.2 (-C*H-C$\underline{H}_2$-); 38.5; 40.2 (-C$\underline{H}$(CH$_3$)$_2$); 42.1–42.6 (-C$\underline{H}_2$-NH$_2$); 52.4 (-C$\underline{*}$H-); 60.3; 114.2; 114.5 (-CH=C$\underline{H}_2$); 120.2; 127.3; 135.3; 135.6 (-C$\underline{H}$=CH$_2$); 148.0; IR (KBr, cm^{-1}): 3310; 3090; 2959; 1654; 1542; 1430; 1344; 1203; 1175; 1136; 1076; 991; 919; 813; 721.

4.6. General procedure for the preparation of ionic derivatives

A solution of **6** (1.43 mmol) in 50 ml of chloroform was mixed at room temperature with a solution of aminoacidic derivative (1.43 mmol) in 40 ml of chloroform. The mixture was stirred at room temperature overnight and then the solvent was evaporated under reduced pressure, affording 1.43 mmol of pure ionic derivative.

4.7. 2-{4-Allylamino-6-[2-(*S*)-*N*-3,5-dinitrobenzoyl-aminoisobutylacetyl]-ethylamino-1,3,5-triazin-2-yloxy}-ethylamonium (*S*)-*N*-(1-naphthoyl)aminophenylacetate, 7a

Mp = 80–85°C, $[\alpha]_D^{24} = +38.4$ (*c* 1, THF), ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.94 (t, 6H, -CH(C$\underline{H}_3$)$_2$); 1.68 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$(CH$_3$)$_2$ superimposed); 3.18 (t, 1H, -O-CH$_2$-C$\underline{H}_2$-NH$_3^+$, J = 5.5 Hz); 3.36 (m, 5H, Ar-NH-C$\underline{H}_2$-CH$_2$-NH-, Ar-NH-CH$_2$-C$\underline{H}_2$-NH- and one proton -O-CH$_2$-C$\underline{H}_2$-NH$_3^+$ (J = 5.5 Hz) superimposed); 3.55 (t, 1H, -O-C$\underline{H}_2$-CH$_2$-NH$_3^+$, J = 5.5 Hz); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH=CH$_2$); 4.41 (t, 1H, -O-C$\underline{H}_2$-CH$_2$-NH$_3^+$, J = 5.5 Hz); 4.54 (m, 1H, -C*H- leucine); 5.00–5.25 (m, 2H, -CH=C$\underline{H}_2$); 5.75 (d, 1H, -C*H- phenylglycine); 5.87 (m, 1H, -C$\underline{H}$=CH$_2$); 6.75–7.00 (br s, 2H, Ar-N$\underline{H}$-CH$_2$-CH=CH$_2$ and Ar-N$\underline{H}$-CH$_2$-CH$_2$-NH-); 7.30–8.25 (3 m, 16H, 12 aromatics, -N$\underline{H}_3^+$ superimposed to Ar-NH-CH$_2$-CH$_2$-N$\underline{H}$-CO-); 8.81 (d, 1H, -C*H(Ph)-N$\underline{H}$-CO-); 8.96 (t, 1H, aromatic); 9.03 (ds, 1H, -C*H(^{i}Bu)-N$\underline{H}$-CO-); 9.09 (d, 2H, aromatics). ^{13}C NMR (75 MHz, DMSO-d_6, 25°C, δ/ppm): 21.4–23.0 (-CH(C$\underline{H}_3$)$_2$); 24.4 (-C*H-C$\underline{H}_2$-leucine); 38.3; 40.3 (-C$\underline{H}$(CH$_3$)$_2$); 42.3–42.7 (-C$\underline{H}_2$-NH$_3^+$); 52.4 (-C$\underline{*}$H-leucine); 56.9; 59.3; 62.6; 79.2 (-C$\underline{*}$H- phenylglycine); 121.0; 124.9; 125.4; 125.6; 126.2; 126.6; 127.9; 128.0; 128.1; 128.5; 130.0; 133.1; 134.1; 136.6; 136.9; 148.1; 162.3; 168.6; 171.9; IR (KBr, cm^{-1}): 3295; 3090; 2959; 2363; 1654; 1541; 1436; 1344; 1258; 1202; 1139; 1076; 920; 785; 722.

4.8. 2-{4-Allylamino-6-[2-(*S*)-*N*-3,5-dinitrobenzoyl-aminoisobutylacetyl]-ethylamino-1,3,5-triazin-2-yloxy}-ethylamonium (*R*)-*N*-(1-naphthoyl)aminophenyl-acetate, 7b

Mp = 95–100°C, $[\alpha]_D^{21} = -13.6$ (*c* 1.14, THF), ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.94 (t, 6H, -CH(C$\underline{H}_3$)$_2$); 1.68 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$(CH$_3$)$_2$ superimposed); 3.18 (t, 1H, -O-CH$_2$-C$\underline{H}_2$-NH$_3^+$, J = 5.5 Hz); 3.36 (m, 5H, Ar-NH-C$\underline{H}_2$-CH$_2$-NH-, Ar-NH-CH$_2$-C$\underline{H}_2$-NH- and one proton -O-CH$_2$-C$\underline{H}_2$-NH$_3^+$ (J = 5.5 Hz) superimposed); 3.55 (t, 1H, -O-C$\underline{H}_2$-CH$_2$-NH$_3^+$, J = 5.5 Hz); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH=CH$_2$); 4.41 (t, 1H, -O-C$\underline{H}_2$-CH$_2$-NH$_3^+$, J = 5.5 Hz); 4.54 (m, 1H, -C*H-leucine); 5.00–5.25 (m, 2H, -CH=C$\underline{H}_2$); 5.75 (d, 1H, -C*H- phenylglycine); 5.87 (m, 1H, -C$\underline{H}$=CH$_2$); 6.75–7.00 (br s, 2H, Ar-N$\underline{H}$-CH$_2$-CH=CH$_2$ and Ar-N$\underline{H}$-CH$_2$-CH$_2$-NH-); 7.30–8.25 (3 m, 16H, 12 aromatics, -N$\underline{H}_3^+$ superimposed to Ar-NH-CH$_2$-CH$_2$-N$\underline{H}$-CO-); 8.81 (d, 1H, -C*H(Ph)-N$\underline{H}$-CO-); 8.96 (t, 1H, aromatic); 9.03 (d, 1H, -C*H(^{i}Bu)-N$\underline{H}$-CO-); 9.09 (d, 2H, aromatics); ^{13}C NMR (75 MHz, DMSO-d_6, 25°C, δ/ppm): 21.4–23.0 (-CH(C$\underline{H}_3$)$_2$); 24.4 (-C*H-C$\underline{H}_2$-leucine); 38.2; 40.3 (-C$\underline{H}$(CH$_3$)$_2$); 42.3–42.7 (-C$\underline{H}_2$-NH$_3^+$); 52.4 (-C$\underline{*}$H- leucine); 56.9; 59.3; 62.6; 79.2 (-C$\underline{*}$H-phenylglycine); 121.0; 124.9; 125.4; 125.6; 126.2; 126.6; 127.9; 128.0; 128.1; 128.4; 130.0; 133.1; 134.1; 136.6; 136.9; 148.1; 162.3; 168.6; 172.0; IR (KBr, cm^{-1}): 3295; 3089; 2958; 2363; 1654; 1541; 1436; 1343; 1258; 1201; 1139; 1076; 920; 785; 722.

4.9. Preparation of silane derivatives: representative procedure

3-Mercaptopropyltrimethoxysilane (1.7 ml, 9 mmol) and AIBN (0.05 g, 0.3 mmol) were added to a solution of **7** (1.40 mmol) in 20 ml of $CHCl_3$, and the resulting mixture was heated under reflux for 48 h. After cooling, the solvent was evaporated under reduced pressure, and the remaining oil was dispersed in pentane (30 ml); the precipitate was filtered and washed again with pentane (5×30 ml) to afford the pure product.

4.9.1. Compound 8b. 1.17 mmol (83.5%) of product **8b** were obtained: mp = 50–60°C, $[\alpha]_D^{24} = -13.8$ (*c* 1.035, THF), ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.75 (m, 8H, -C$\underline{H}_2$-Si(OMe)$_3$ and -CH(C$\underline{H}_3$)$_2$ superimposed); 1.10–1.30 (m, 2H, -C$\underline{H}_2$- aliphatics); 1.68 (m, 7H, -S-C$\underline{H}_2$-C$\underline{H}_2$-CH$_2$-Si- and -C$\underline{H}_2$-C$\underline{H}$(CH$_3$)$_2$ superimposed); 2.65–2.85 (m, 1H, aliphatic); 3.20–3.60 (m, 19H, Ar-NH-C$\underline{H}_2$-C$\underline{H}_2$-NH-, Ar-O-C$\underline{H}_2$-C$\underline{H}_2$-NH$_3^+$,

-NH-CH_2-C$\underline{H}_2$-C$\underline{H}_2$-S- superimposed to -Si(OC$\underline{H}_3$)$_3$ and to aliphatics protons); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH_2-CH_2-S-); 4.54 (m, 1H, -C*$\underline{H}$- leucine); 5.75 (d, 1H, -C*$\underline{H}$- phenylglycine); 7.30–8.30 (3 m, 19H, 13 aromatics, -N$\underline{H}_3^+$, Ar-NH-CH_2-CH_2-N$\underline{H}$-CO-, Ar-N$\underline{H}$-CH_2-CH_2-CH_2-S- and Ar-N$\underline{H}$-CH_2-CH_2-NH- superimposed); 8.81 (d, 1H, -C*H(Ph)-N$\underline{H}$-CO-); 8.96 (t, 1H, aromatic); 9.03 (d, 1H, -C*H(^{i}Bu)-N$\underline{H}$-CO-); 9.09 (d, 2H, aromatics); ^{13}C NMR (75 MHz, DMSO-d_6, 25°C, δ/ppm): 12.7; 21.4; 22.1; 23.0; 24.4; 27.2; 28.6; 29.0; 34.6; 40.4; 42.9 (-$\underline{C}H_2$-NH_3^+); 52.5 (-$\underline{C}$*H- leucine); 57.0; 59.5; 121.0; 125.0; 125.5; 125.7; 126.3; 126.7; 127.7; 127.9; 128.1; 128.2; 128.2; 128.6; 128.7; 130.0; 133.2; 134.1; 136.7; 136.9; 148.2; 162.4; 168.7; 172.0; IR (KBr, cm^{-1}): 3295; 3090; 2932; 2344; 1636; 1541; 1437; 1343; 1258; 1186; 1077; 919; 784; 721; 698.

4.9.2. Compound 8a. 1.13 mmol (81%) of product **8a** were obtained: mp = 55–60°C, $[\alpha]_D^{24} = +14.7$ (c 0.99, THF), ^{1}H NMR (200 MHz, DMSO-d_6, 100°C, δ/ppm): 0.75 (m, 8H, -C$\underline{H}_2$-Si(OMe)$_3$ and -CH(C$\underline{H}_3$)$_2$ superimposed); 1.10–1.30 (m, 2H, -C$\underline{H}_2$- aliphatics); 1.68 (m, 7H, -S-C$\underline{H}_2$-C$\underline{H}_2$-CH_2-Si- and -C$\underline{H}_2$-C$\underline{H}$(C$\underline{H}_3$)$_2$ superimposed); 2.65–2.85 (m, 1H, aliphatic); 3.20–3.60 (m, 19H, Ar-NH-C$\underline{H}_2$-C$\underline{H}_2$-NH-, Ar-O-C$\underline{H}_2$-C$\underline{H}_2$-N$\underline{H}_3^+$, -NH-CH_2-C$\underline{H}_2$-C$\underline{H}_2$-S- superimposed to -Si(OC$\underline{H}_3$)$_3$ and to aliphatics protons); 3.88 (m, 2H, -NH-C$\underline{H}_2$-CH_2-CH_2-S-); 4.54 (m, 1H, -C*$\underline{H}$- leucine); 5.75 (d, 1H, -C*$\underline{H}$- phenylglycine); 7.30–8.30 (3 m, 19H, 13 aromatics, -N$\underline{H}_3^+$, Ar-NH-CH_2-CH_2-N$\underline{H}$-CO-, Ar-N$\underline{H}$-CH_2-CH_2-CH_2-S- and Ar-N$\underline{H}$-CH_2-CH_2-NH- superimposed); 8.81 (d, 1H, -C*H(Ph)-N$\underline{H}$-CO-); 8.96 (t, 1H, aromatic); 9.03 (d, 1H, -C*H(^{i}Bu)-N$\underline{H}$-CO-); 9.09 (d, 2H, aromatics); ^{13}C NMR (75 MHz, DMSO-d_6, 25°C, δ/ppm): 12.7; 21.4; 22.1; 23.0; 24.4; 27.2; 28.6; 29.0; 34.6; 40.4; 42.9 (-$\underline{C}H_2$-NH_3^+); 52.5 (-$\underline{C}$*H- leucine); 57.0; 59.5; 121.0; 125.0; 125.5; 125.7; 126.3; 126.7; 127.7; 127.9; 128.1; 128.2; 128.2; 128.6; 128.7; 130.0; 133.2; 134.1; 136.6; 136.9; 148.2; 162.4; 168.7; 172.0; IR (KBr, cm^{-1}): 3295; 3090; 2932; 2344; 1636; 1541; 1437; 1343; 1258; 1186; 1077; 919; 784; 721; 698.

4.10. General procedure for the preparation of the CSPs

A solution of the 3-mercaptopropyltrimethoxysilanic derivative in dry dioxane (15 ml) was added dropwise to a suspension of spherical silica gel (2.5 g) [previously dried under reduced pressure ($p = 0.01$ mmHg) at 180°C overnight] in dry dioxane under nitrogen atmosphere. The resulting mixture was heated under reflux, with gentle stirring, for 24 h. After cooling, the silica was filtered and washed with dry dioxane (3×30 ml), chloroform (3×30 ml), diethyl ether (3×30 ml) and pentane (3×30 ml) in that order, then dried under reduced pressure ($p = 0.01$ mmHg) at 45°C for 8 h. The amount of selector linked to silica gel was then determined by elemental analysis. CSP **1a**: C, 7.21; H, 1.35; N, 2.60% corresponding to 0.179 mmol/g. CSP **1b**: C, 7.64; H, 1.41; N, 2.78% corresponding to 0.189 mmol/g. Two 15 cm stainless steel columns were slurry packed with each of these materials, using conventional high pressure packing techniques.

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