3,5-Dinitrobenzoylphenylglycine Analogues Bearing the 1,1′-Binaphthalene Moiety − Synthesis, Conformational Study, and Application as Chiral Solvating Agents

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The two new diastereoisomeric chiral auxiliaries (*aR*,*R*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(3,5-dinitrobenzoyl)amino](phenyl)acetate and (*aR*,*S*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(3,5-dinitrobenzoyl)amino](phenyl)acetate have been synthesised and their efficiency as chiral solvating agents for the determination of the enantiomeric composition of amides and amines has been demonstrated. A conformational study of the two chiral solvating agents (CSAs) by means of NMR and CD spectroscopy is also presented.

Introduction

Chiral solvating agents (CSAs) are widely employed in determining the enantiomeric composition of chiral compounds,[1] both natural and synthetic. Their success lies mainly in the simplicity of their use (the CSA is added to a solution of the chiral substrate in a deuterated solvent and a NMR spectrum is recorded), which allows one to easily perform a quick and accurate measurement.[1] For this reason, many research groups have been prompted to develop new CSAs with different structures, such as amines,[2] alcohols,[3] carboxylic acids,[4] and others,[5] aimed at solving the problem of the enantiomeric purity determination of various chiral compounds. Most of these chiral auxiliaries, however, are useful only with a single class of chiral substrates (for example carboxylic acids are used in the assessment of the enantiomeric purity of amines[4]), and therefore the bench chemist needs more than one CSA for determining the enantiomeric composition of different chiral products. A broadly applicable CSA would therefore be very useful in this field.

In addressing this problem, we turned our attention to the design of a new chiral auxiliary (Figure 1) in which the methyl group of the 3,5-dinitrobenzoylphenylglycine methyl ester has been replaced by the chiral 2′-hydroxy-1,1′-binaphthalene moiety, bound at its 2 position. In this way, we hoped to generate a hybrid material with wider chiral recognition properties.[6]

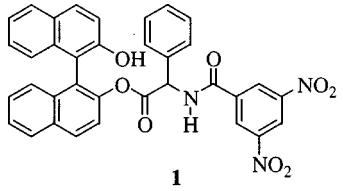

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Figure 1. Structure of the chiral auxiliary

In fact this compound possesses the characteristics of a well-known Pirkle's CSA[7] coupled with those of BINOL, a very popular chiral ligand for asymmetric synthesis[8] as well as a versatile scaffold in molecular recognition.[9] The hybrid system **1** should exhibit a broader applicability as a CSA, because of the new electronic and structural characteristics introduced by the binaphthyl moiety. This could enable the chiral auxiliary to enantiodiscriminate other classes of chiral substrates besides those recognised by the Pirkle's CSA. In addition, compound **1** is very attractive as a CSA because its proton signals are found in a relatively restricted region of the NMR spectrum, allowing the signals of sample, whose enantiomeric composition you wish to determine, to be easily recognised. Finally, since compound **1** possesses two stereogenic sources (the axial chirality of BINOL and the stereogenic centre of the amino acid moiety), and the two possible diastereoisomers can behave differently in an enantiodiscrimination process,[10] we wanted to determine which of the diastereomers is the more efficient CSA. In the present paper, we report the preparation of both the diastereoisomers of **1**, their use as CSAs for the determination of the enantiomeric composition of chiral compounds, and a conformational study by NMR techniques and CD spectroscopy.

Results and Discussion

Synthesis of the Diastereoisomer 1a and 1b

Although the simplest way to obtain the two diastereoisomers of **1** would appear to be the direct esterification of the 3,5-dinitrobenzoylphenylglycine by means of BINOL, this reaction did not give the expected product. In fact, when (*R*)-BINOL was reacted in dichloromethane using

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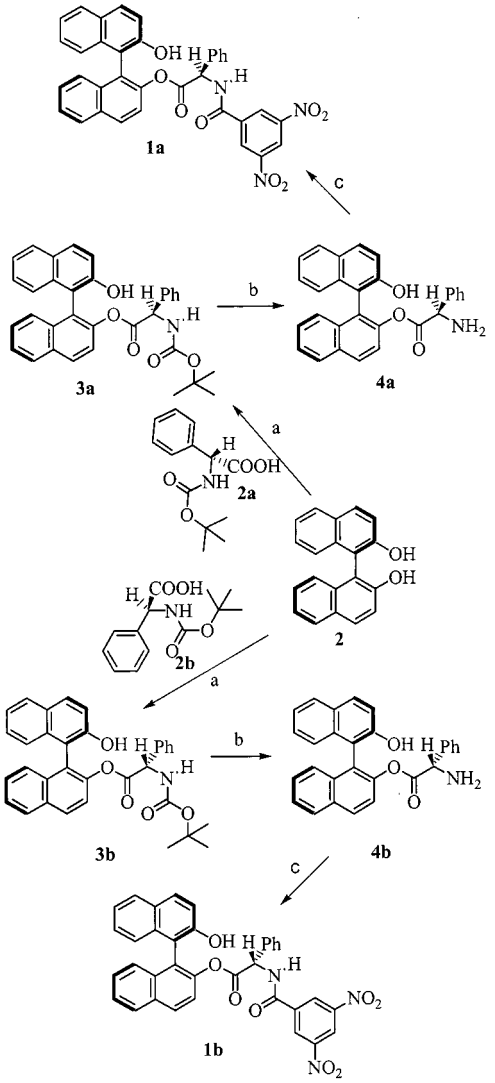
DCC and a catalytic amount of DMAP as coupling reagent,[11] an immediate darkening of the solution was observed, and no conversion of the reagents took place even after a prolonged reaction time. In order to avoid this problem, we decided to react BINOL with the *N*-Boc-protected phenylglycine under the above described reaction conditions, and to introduce the 3,5-dinitrobenzoyl group in a second step. Scheme 1 illustrates the synthetic route followed to obtain the two diastereoisomers of **1**.



Reagents and conditions: (a) DCC, DMAP, CH_2Cl_2, 0 °C to r.t.; (b): TFA, CH_2Cl_2, r.t.; (c) 3,5-dinitrobenzoyl chloride, triethylamine, THF, 0 °C to r.t.

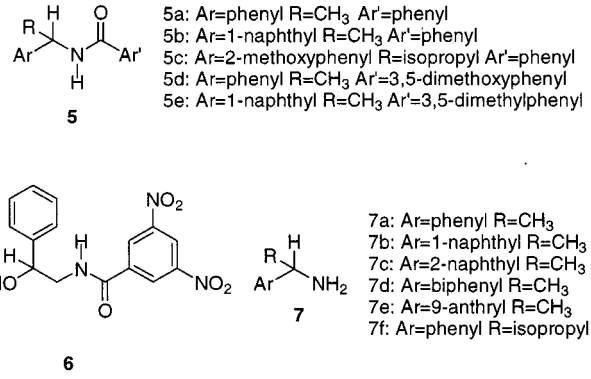
Scheme 1

By treating (*R*)-BINOL with an equimolar amount of (*R*) or (*S*)-Boc-phenylglycine, **2a** and **2b**, using DCC and a catalytic amount of DMAP as coupling reagent[11] in dichloromethane as a solvent at room temperature, **3a** and **3b** were obtained in good yields (78−80%) after chromatographic purification. The reaction requires only one hour for completion and, owing to the bulkiness of the amino acid derivative, only one of the two hydroxy groups of BINOL is esterified. The proton on the stereogenic centre of **3a** resonates at δ = 5.39, whereas the signal of the corresponding proton of **3b** is found at δ = 5.25. This difference in the position of the two proton signals allowed us to use NMR to determine if any racemisation had occurred. Since any signal at δ = 5.25 is present in the NMR spectrum of **3a** and no absorption is detectable at δ = 5.39 in the spectrum of **3b**, we can conclude that no appreciable racemisation occurs in the formation of **3a** and **3b**.

Deprotection of the amino group by means of trifluoroacetic acid,[12] followed by usual workup (see Exp. section) afforded the amino derivatives **4a** and **4b** together with 15% of BINOL,[13] as a result of acid-promoted hydrolysis of the ester function. Although BINOL can be separated from the amino derivatives, we preferred to use crude **4a** and **4b** in the next reaction and to purify the final products. The amino derivatives were therefore reacted with 3,5-dinitrobenzoyl chloride in the presence of triethylamine in THF as a solvent, and, after usual workup and purification by flash chromatography, pure **1a** and **1b** were obtained in 77% and 75% yield, respectively.

Using 1a and 1b as CSAs

Chiral auxiliaries **1a** and **1b** were tested as CSAs towards several chiral substrates, whose structure is reported in Scheme 2.



Scheme 2

At first, we were interested in assaying the efficiency of **1a** and **1b** as CSAs towards benzamides and substituted benzamides of alkylarylamines, a class of chiral compounds enantiodiscriminated by Pirkle's CSA,[7] in order to check if the structural modification due to the introduction of the binaphthyl moiety had not been detrimental for the chiral recognition capability of the amino acid moiety. As Table 1 shows, appreciable nonequivalences were measured for the enantiotopic protons of amides **5a**−**e**, when equimolar mixtures **1a**/amide and **1b**/amide, at concentration 20 mM, were examined.

The methine protons of the two enantiomers of **5a**−**e** become asynchronous in the presence of **1a**, producing two distinguishable signals with nonequivalences (ΔΔδ) dependent on the amide structure. The highest value (ΔΔδ = 0.134 ppm) is measured for **5b** and, as Figure 2 shows, corresponds to a baseline separation of the two double

Table 1. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) nonequivalences (ΔΔδ, ppm, difference between the chemical shifts of corresponding protons of the two enantiomers) for protons of **5a**−**e** and **6** in the presence of CSAs **1a** and **1b** (molar ratio 1:1; 20 mM)

		ΔΔδ							
		1a				1b			
		R[a]	**R**[a]	CH_3	*R*[a]	R[a]	**R**[a]	CH_3	*R*[a]
5a	$CH_3-CH-Ph-NHCOPh$	0.030	0.008			0.015	-		
5b	$1-Naphth-CH(CH_3)NHCOPh$	0.134	0.052	0.023		0.047	-	0.020	
5c	$PhCONHCHPh(o\text{-}\mathbf{OCH_3})CH(CH_3)_2$	0.021	0.005	0.006	0.007	0.014	0.003	0.002	-
5d	$CH_3-CHPh-NHCOAr$	0.024		0.007		0.013		-	
5e	$1\text{-naphthCH}(CH_3)NHCOPh(3,5\text{-}CH_3)$	0.089	0.044	0.017		0.036	-	0.023	0.008
6	HO−CH (Ph)−CH*H*−NH−DNB	0.017 0.030[b]	8.2 0.045[b]		0.005 0.011[b]	0.028	-		-

[a] R, **R**, *R* correspond to the underlined, bold or italic protons in the second column. − [b] Molar ratio CSA:amide = 2:1

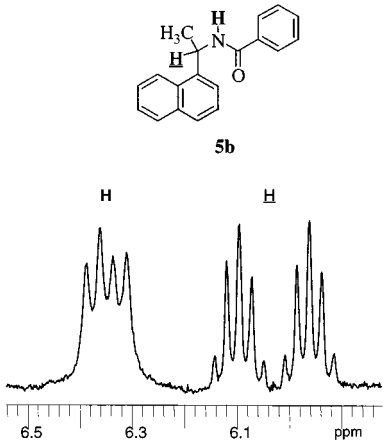


Figure 2. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, δ values referred to TMS as external standard) spectral regions corresponding to the amide and methine proton absorptions of racemic **5b** (20 mM) in the presence of an equimolar amount of **1a**.

quadruplets, which allows for an accurate determination of the enantiomeric composition of an enriched sample.

Diastereoisomer **1b** induces lower nonequivalences on the same protons (Table 1). The trend observed in the case of **1b** is unchanged, the substrate that is best discriminated is again **5b**. However, due to the lower efficiency exhibited by **1b**, several proton signals of **5a**−**e**, which underwent doubling in the presence of **1a**, remain unsplit under the same experimental conditions. Therefore, although the structural modification of Pirkle's CSA has not destroyed the chiral recognition ability of the amino acid moiety, the introduction of another stereogenic source has afforded two diastereoisomers that behave differently towards the same chiral substrate. On the basis of the experimental data we could say that the *aR*,*R* diastereoisomer **1a** represents the "matched couple"[10] of the CSA towards amides **5a**−**d**, whereas the *aR*,*S* diastereoisomer is the "mismatched couple".[10]

Both **1a** and **1b** are able to induce nonequivalences in the enantiotopic protons of the 3,5-dinitrobenzoyl derivative of phenylethanolamine **6**, a chiral substrate not enantiodiscriminated by Pirkle's CSA. Also in this case, **1a** works better than **1b** and, although the nonequivalences are not very high, a remarkable improvement can be obtained simply by increasing the molar ratio CSA:substrate to 2:1 (Table 1).

Chiral auxiliaries **1a** and **1b** also behave as CSAs towards alkylarylamines, an interesting class of chiral substrates due to their use as resolving agents[14] and chiral building blocks.[15]

Splitting of the resonance of the proton on the stereogenic centre of alkylarylamines **7a**−**e** is observed in the presence of an equimolar amount of **1a** (Table 2), which affords two partially superimposed quadruplets. Conversely, no doubling of this proton signal of **7f** is detected, probably because the steric hindrance exerted by the isopropyl group prevents an efficient CSA−substrate interaction.

The nonequivalences induced on the methine protons depend on the nature of the aromatic moiety: in fact, when

Table 2. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) nonequivalences (ΔΔδ, ppm, difference between the chemical shifts of corresponding protons of the two enantiomers) for protons of **7a**−**g** in the presence of CSAs **1a** and **1b** (molar ratio 1:1; 20 mM)

		ΔΔδ	
CSA	Substrate	*CH*	CH_3
1a	**7a**	0.019	0.006
1a	**7b**	0.007	0.005
1a	**7c**	0.006	0.007
1a	**7d**	0.022	0.006
1a	**7e**	n.d.	0.018
1a	**7f**	−	0.004[a]
1b	**7a**	0.023	0.006
1b	**7a**[b]	0.053	0.015
1b	**7a**[c]	0.051	0.014
1b	**7b**	0.022	0.013
1b	**7b**[b]	0.060	0.030
1b	**7b**[c]	0.051	0.028
1b	**7b**[d]	0.078	0.039
1b	**7c**	0.015	0.010
1b	**7d**	0.022	0.006
1b	**7e**	0.056	0.018
1b	**7f**	0.017	0.004[e]

[a] CH_3 of the isopropyl group that resonates at the lowest frequency. − [b] CSA:amine = 1:1, 50 mM. − [c] CSA:amine = 2:1, 20 mM. − [d] CSA:amine = 3:1, 20 mM. − [e] CH_3 of the isopropyl group that resonates at the highest frequency

the β-alkyl group is methyl, the lowest values are measured for the amines bearing a naphthyl moiety (**7b**, **7c**). In contrast, the nonequivalences detected for the protons of the β-alkyl groups are less dependent on the alkylarylamine structure, their values ranging from 0.043 to 0.018 ppm.

The diastereoisomer **1b** affords better enantiodiscrimination of the same substrates than **1a**. In fact, higher nonequivalences are measured for the methine protons of all the compounds: splitting of the signal is also detected in the case of **7f** ($\Delta\Delta\delta$ = 0.017 ppm) and a baseline separation of the two quadruplets generated by the splitting of the proton signal of **7e** is observed. Also, the signals of the β-alkyl protons undergo doubling, and the nonequivalences induced on these protons by **1b** are equal, or even higher than those measured for the mixture of **1a** and amine. Although the nonequivalences induced by **1b** on the protons of **7a**−**d** and **7f** are small enough for a baseline separation of the signals to be observed, a remarkable improvement in the enantiodiscrimination can be obtained simply by increasing either the total concentration of both substrate and CSA or the molar ratio CSA:substrate (Table 2). As Figure 3 shows, when this ratio is increased from 1:1 to 3:1, the two partially superimposed quadruplets, originated by the splitting of the methine proton signal, undergo a nearly baseline separation, allowing an accurate determination of the enantiomeric composition of an enriched sample.

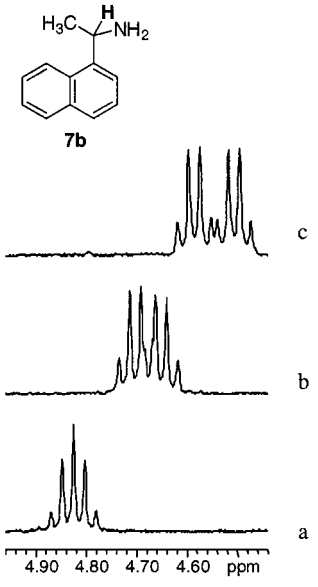


Figure 3. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, δ values referred to TMS as external standard) spectral regions corresponding to the proton on the stereogenic centre absorptions of racemic **7b** (20 mM) in the presence of: a) an equimolar amount of **1b**; b) two equivalents of **1b**; and c) three equivalents of **1b**.

A comparison of the nonequivalences induced on the protons of the same amines by **1a** and **1b** demonstrates that the two diastereoisomers behave quite differently towards this class of chiral compounds. However, in this case the "matched couple"[10] is represented by the *aR*,*S* diastereoisomer **1b**, whereas **1a** is the "mismatched couple".[10]

To complete the study of the enantiorecognition of amines, equimolar mixtures of **1b** with a tertiary alkylarylamine, i.e. the *N*,*N*-dimethyl-1-phenylethylamine, and an aliphatic amine, 1-methylpropargylamine, were analysed. No doubling of the proton signals was observed in either case, indicating that the contemporary presence of an aromatic moiety and a protic amino group is mandatory in order for enantiorecognition of an amine to take place.

Conformational Analysis of 1a and 1b

In order to gain some insight into the differences of the enantiorecognition capabilities exhibited by **1a** and **1b**, in particular towards amines, the conformation that they assume in solution must be known. The study of the conformation of **1a** and **1b** was approached using both CD and NMR spectroscopies. Indeed, the first technique allowed us to establish the conformation of the binaphthylic moiety in terms of dihedral angle between the two naphthalene rings, while the NMR gave us the conformation of the amino acidic moiety as well as the relative disposition of the two moieties.

The UV spectrum of **1a** (Figure 4a) shows an intense absorption band at 225 nm (ε = 115000) attributable to the ^1B_b transition of the naphthalene chromophores,[16] and a long tail extending to 340 nm, on which a less intense absorption band at 285 nm (ε = 10000) is visible as a shoulder. The CD spectrum (Figure 4a) presents, besides two weak positive Cotton effects at 320 nm (Δε = 14) and 280 nm (Δε = 23) and another positive band at 200 nm (Δε = 44), two intense Cotton effects having opposite sign at 230 nm (Δε = −95) and at 216 nm (Δε = 74), which are the two components of the exciton couplet of the ^1B_b transitions of the naphthalene chromophores.[17]

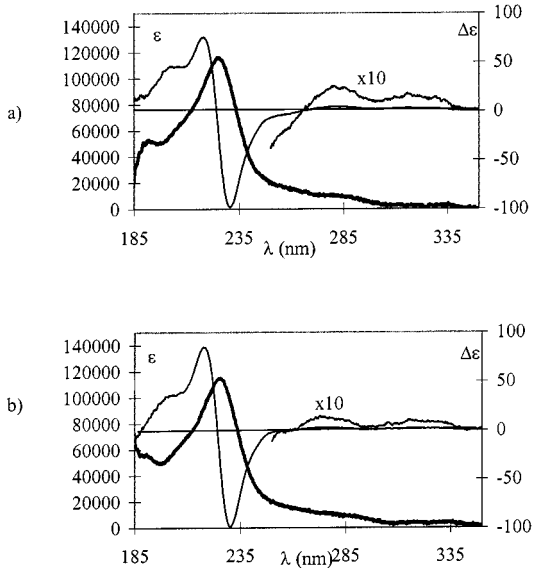


Figure 4. UV (bold line) and CD spectra in acetonitrile solutions of a) *aR*,*R* diastereoisomer, **1a**; b) *aR*,*S* diastereoisomer, **1b**.

Given that the amplitude of the split-type Cotton effects in a biaryl system can be related to the dihedral angle between the aromatic rings,[18] it is possible to obtain the conformation assumed by the binaphthyl moiety of **1a** simply on the basis of its CD spectrum. Using the Mason's rela-

tionship for the 1,1′-binaphthyl systems,[18] a dihedral angle between the naphthalene rings having a mean value of 80−85° is attributable to the binaphthyl moiety of **1a**. The UV spectrum of **1b** (Figure 4b) is in practice superimposable with that of **1a**, the same absorption bands with the same intensity at the same wavelength being detectable. The CD spectrum of **1b** (Figure 4b) is very similar to the CD spectrum of **1a** (Figure 4a), as far as number, position and sign of the Cotton effects are concerned; the only difference between the two spectra is the lower intensity of the two weak positive Cotton effects at 320 nm ($\Delta\varepsilon$ = 8) and at 280 nm ($\Delta\varepsilon$ = 13) and of the positive Cotton effect at 200 nm ($\Delta\varepsilon$ = 35). In contrast, the intensity of the binaphthyl exciton-couplet is the same as in the CD spectrum of **1a**. This means that the conformation of the binaphthyl moiety of **1b** is the same of its diastereoisomer and hence the mean value of the dihedral angle between the two naphthalene rings is about 80−85°.

The two diastereoisomers **1a** and **1b** have been characterised in $CDCl_3$ solutions by analyses of the DQF-COSY and NOESY maps (see Exp. section).

Information on their stereochemical features was obtained on the basis of the proximity constraints imposed by the dipolar interactions detected in the 1D and 2D−NOE spectra.

In fact, for both species the binaphthyl hydroxyl group (Figure 5a) produces relevant NOE on the 3,5-dinitrobenzoyl protons in addition to a less remarkable effect on the *ortho* protons of the phenyl group. The same proton does not give any dipolar interaction with the methine and NH protons of the aminoacid fragment. The methine proton (Figure 5b) induces NOE on the phenyl and NH protons, on the *peri*-proton 8′ of the naphthalene ring bearing the OH group, as well as on proton 3 of the other naphthalene ring to which the derivatized amino acid is bound. This is true for both diastereoisomers and the only detectable difference is that the same proton produces NOE on the 3,5-dinitrobenzoyl protons in **1b**, but not in **1a**. Finally, it must be noted that dipolar interactions among protons of the 3,5-dinitrophenyl and phenyl groups are detected.

Therefore, the two species give rise to a "close" structure in solution, having the three aromatic moieties, i.e. the naphthalene bearing the OH group, the phenyl, and 3,5-dinitrophenyl groups in spatial proximity, creating a kind of cavity. The methine proton of the tetrahedral chiral carbon atom and the NH proton are external to the cavity, *cisoid* to each other, with the first in proximity of the binaphthol moiety and the latter far away from any other group. Therefore, the sole significant difference for the two diastereoisomers must concern the relative positions of the phenyl and 3,5-dinitrophenyl rings with respect to the naphthalene moiety: in **1b** the phenyl group should face it, and in **1a** the 3,5-dinitrophenyl moiety does face the naphthalene ring. The above interchange of the two aromatic mononuclear groups also justifies the fact that in **1b** the methine proton can experience a dipolar interaction with the 3,5-dinitrophenyl protons, but not in **1a**.

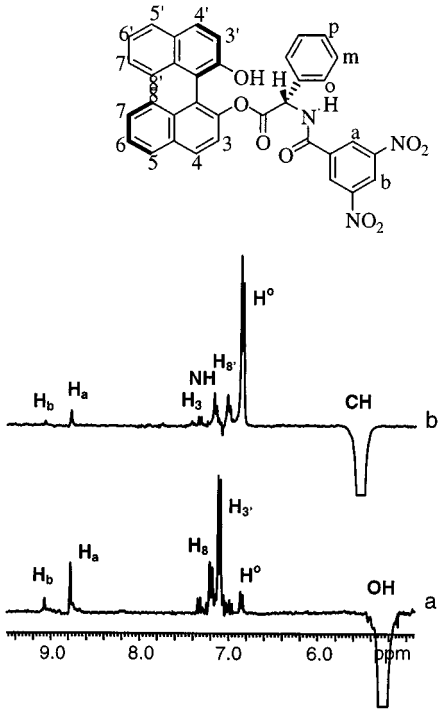


Figure 5. ^1H-^1H dipolar interactions produced by the proton (a) OH and (b) CH of **1b** detected by difference spectroscopy (300 MHz, $CDCl_3$, 25 °C).

In Figure 6 are depicted the conformations of **1a** and **1b**, obtained on the basis of the stereochemical information from the NMR and CD analysis, where the cavity formed by the naphthalene ring bearing the OH group, the phenyl group, and the 3,5-dinitrobenzoyl moiety is clearly visible. It should also be noted that the 3,5-dinitrophenyl ring is found close to the OH group, and faces the naphthalene moiety in the *aR*,*R* diastereoisomer **1a**, whereas the same group is found far away from the OH and is directed almost perpendicular to the naphthalene ring in the *aR*,S diastereoisomer **1b**.

On the basis of the conformations depicted in Figure 6, one could think that some differences must be present in the CD spectra of **1a** and **1b**, due to the different disposition of the aromatic chromophores of the amino acid moiety with respect to the binaphthyl one: this could generate, in principle, a naphthalene-phenyl or a naphthalene-3,5-dinitrobenzoyl or a phenyl-3,5-dinitrobenzoyl coupling, depending on the different arrangement of the three moieties in **1a** and **1b**. However, it should be noted that the 3,5-dinitrobenzamide chromophore possesses two weak transitions, at 230 nm (ε = 20000) and 207 nm (ε = 24000), and the allowed transition of the benzene chromophore (ε = 60000) absorbs at 190 nm. Furthermore, the ^1B_b transitions of the naphthalene chromophores are more intense and the distance between the two transition dipole moments is lower than the distance between each naphthalene moiety and the transition dipole moments of the aromatic chromophores of the amino acid moiety. Therefore, the CD spectra of the binaphthyl derivatives **1a** and **1b** are dominated by the exciton couplet of the ^1B_b transitions of the naph-

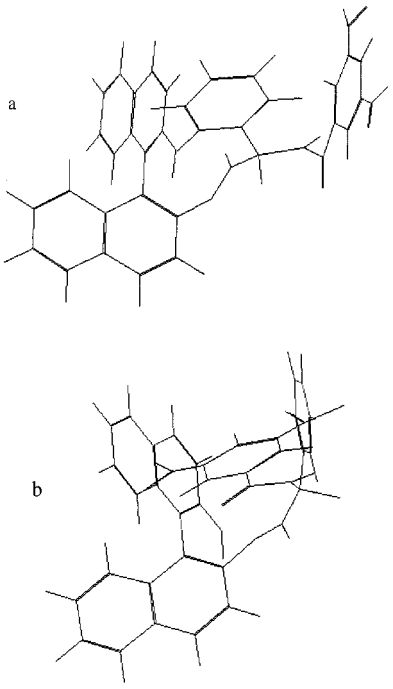


Figure 6. Conformation obtained on the basis of the spectroscopic data: a) *aR,R* diastereoisomer, **1a**; b) *aR,S* diastereoisomer, **1b**.

thalene chromophores, regardless of the conformation of the amino acid moieties.

These conformations should afford an explanation to the different behaviour of **1a** and **1b** in the enantiodiscrimination of alkylarylamines. The chiral cleft created in **1b** by the perpendicular disposition of the naphthalene and 3,5-dinitrobenzoyl moieties should give rise to face to face and face to edge π stacking[19] with the aromatic moiety of the alkylarylamine. The same kind of interaction is prevented with the *aR,R* diastereoisomer, where the 3,5-dinitrobenzoyl group faces the naphthalene ring. This should engender a stronger binding of the alkylarylamine to the *aR,S* diastereoisomer than to the *aR,R* one, which results in higher nonequivalences of its protons in the presence of **1b**.

In summary, the esterification of BINOL at its 2 position with the 3,5-dinitrobenzoylphenylglycine has afforded a new CSA having enhanced enantiorecognition capability with respect to the two isolated moieties; in particular, it has allowed enantiodiscrimination of alkylarylamines, an interesting class of substrates for which few CSAs are available.[1,23]

The study of the conformation of the two diastereoisomeric CSAs has allowed us to obtain a possible explanation to the difference of the enantiorecognition of alkylarylamines.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded on spectrometers, equipped with a temperature control unit (±0.1 °C), operating at 200 and 300 MHz for ^{1}H, and at 50 and 75 MHz for ^{13}C. Spectra were run in $CDCl_3$ using TMS as external standard. The following abbreviations are used: s = singlet, d = doublet, t = triplet, br. s = broad signal. The 2D NMR spectra were obtained using standard sequences. The double quantum filtered DQF-COSY experiments were recorded with a spectral width of 3300 Hz; 512 increments of 8 scans and 2 K data points were acquired. The relaxation delay was 5 s. The data were zero-filled to 2 K × 1 K, and a Gaussian function was applied for processing in both dimensions. The NOESY spectra were recorded in the phase-sensitive mode, by employing a mixing time of 0.6 s. A spectral width of 3300 Hz was used in both ω_1 and ω_2 dimensions. The pulse delay was maintained at 6 s; 512 hypercomplex increments of 8 scans and 2 K data points each were collected. The data matrix was zero-filled at 2 K × 1 K and a Gaussian function was applied for processing in both dimensions. The ^{1}H{^{1}H}-NOE experiments were performed in the difference mode. The decoupler power used was the minimum required to saturate the spin of interest. A waiting time of 5−10 s was used to allow the system to reach the equilibrium. Each NOE experiment was repeated at least four times. All the solutions were accurately degassed by freeze-pump-thaw cycles for 1D and 2D NOE experiments. Circular dichroic spectra were obtained on a spectropolarimeter using a 0.1-mm path length cell and spectropolarimetric grade acetonitrile as a solvent. Sample concentration for CD analysis were typically (6−9) × 10^{-4} M. − Ultraviolet-visible absorption spectra were obtained on spectrophotometer using a 0.1-mm path length cell and spectrophotometric grade acetonitrile as a solvent. Sample concentrations of UV/Vis analysis were typically (6−9) × 10^{-4} M. − TLC analysis were performed on silica gel 60 sheets; flash chromatographic separation were carried out on adequate dimension columns using silica gel 60 (230−400 mesh). Optical rotations were measured on a digital polarimeter using a 1-dm path length cell. − Melting points are uncorrected. Dichloromethane (CH_2Cl_2) was distilled over CaH_2. Tetrahydrofuran (THF) was refluxed over sodium/benzophenone and distilled before the use. Dicyclohexylcarbodiimide (DCC) was distilled under vacuum. 3,5-Dinitrobenzoyl chloride was recrystallised from light petroleum before the use. Unless otherwise specified the reagents were used without any purification.

Standard procedures were used for preparing racemic amides,[5d] the DNB derivative of the 1-phenylethanol[5d] and racemic amines[20] **7c−d** and **7f**. Racemic amine **7e** was prepared according a literature method and matched the reported characteristics.[21] Optically pure (*R*)-2,2′-dihydroxy-1,1′-binaphthyl was obtained by resolution of the racemic compound according the method of Cai and co-workers[22] and matched the reported characteristics: $[\alpha]_D^{21}$ = 34.6 (*c* = 1, THF), ref.[22] $[\alpha]_D^{21}$ = 34.3 (*c* = 1, THF).

2′-Hydroxy-1,1′-binaphthyl-2-yl [(*tert*-Butoxycarbonyl)amino](phenyl)acetate. − General Procedure: To a solution of **2** (2 g, 7 mmol) in dry CH_2Cl_2 (30 mL), (*tert*-butoxycarbonyl)phenylglycine (1.76 g, 7 mmol) and 4-(dimethylamino)pyridine (0.15 g, 1.26 mmol) were added. The resulting solution was kept at 0 °C and dicyclohexylcarbodiimide (1.58 g, 7.6 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min then at room temperature for 1 h. The precipitated dicyclohexylurea was filtered off, the solvent evaporated under vacuum, and the crude product was purified by flash chromatography (SiO_2, CH_2Cl_2/ethyl acetate, 96:4).

(a*R,R*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(*tert*-Butoxycarbonyl)amino](phenyl)acetate (3a): Yield 2.83 g, 78%. M.p. 75−77 °C. $[\alpha]_D^{21}$ = 25.2 (*c* = 1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.15−6.60 (17 H, aromatic protons), 5.25 (s, 1 H, C*H*), 5.20 (br s, 2 H, NH and OH), 1.35 (s, 9 H, *tert*-butyl). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.6 (ester C=O), 151.4 (carbamate C=O), 132.4,

131.3, 130.9, 130.4, 129.8, 128.9, 128.8, 128.4, 128.2, 127.9, 127.5, 127.1, 126.7, 126.5, 126.4, 126.3, 125.8, 125.7, 124.6, 124.1, 123.3, 121.4, 118.0, 57.6, 28.2. − $C_{33}H_{29}NO_5$: calcd. C 76.28, H 5.63, N 2.70; found C 76.35, H 5.62, N 2.69.

(a*R*,*S*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(*tert*-Butoxycarbonyl)-amino](phenyl)acetate (3b): Yield 2.90 g, 80%. M.p. 79−82 °C. $[\alpha]_D^{21}$ = 10.6 (*c* = 1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.15−6.65 (17 H, aromatic protons), 5.39 (s, 1 H, C*H*), 5.15 (br. s, 2 H, NH and OH), 1.38 (s, 9 H, *tert*-butyl). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.3 (ester C=O), 151.8 (carbamate C=O), 132.3, 130.7, 130.4, 129.7, 129.0, 128.8, 128.6, 128.6, 128.5, 128.3, 128.0, 127.3, 126.8, 126.5, 126.3, 125.8, 124.4, 121.4, 118.2, 58.1, 26.2. − $C_{33}H_{29}NO_5$: calcd. C 76.28, H 5.63, N 2.70; found C 76.33, H 5.64, N 2.70.

2′-Hydroxy-1,1′-binaphthyl-2-yl (Amino)(phenyl)acetate. − General Procedure: To a solution of **3** (2.83 g, 5.46 mmol) in CH_2Cl_2 (20 mL) trifluoroacetic acid (27 mL) was added and the mixture was stirred at room temperature for 15 min. A 10% solution of $NaHCO_3$ was added until alkaline pH, then the mixture was extracted with CH_2Cl_2 (3 × 60 mL). The collected organic extracts were washed with brine, then dried (Na_2SO_4). The solvent was evaporated under reduced pressure and a sample was purified by flash chromatography for characterisation.

(a*R*,*R*)-2′-Hydroxy-1,1′-binaphthyl-2-yl (Amino)(phenyl)acetate (4a): M.p. 94−96 °C. $[\alpha]_D^{21}$ = 10.9 (*c* = 0.97, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.10−6.67 (17 H, aromatic protons), 4.40 (s, 1 H, C*H*), 3.15 (br. s, 3 H, NH_2 and OH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.3 (ester C=O), 131.3, 130.6, 130.5.128.7, 128.4, 128.2, 128.0, 127.6, 127.4, 127.2, 127.9, 126.7, 126.5, 126.4, 126.4, 126.0, 125.6, 124.3, 124.1, 123.9, 123.5, 123.4, 121.3, 117.6, 58.5. − $C_{28}H_{21}NO_3$: calcd. C 80.17, H 5.05, N 3.34; found C 80.25, H 5.07, N 3.33.

(a*R*,*S*)-2′-Hydroxy-1,1′-binaphthyl-2-yl (Amino)(phenyl)acetate (4b): M.p. 98−100 °C. $[\alpha]_D^{21}$ = 53.7 (*c* = 1, $CHCl_3$). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.05−6.85 (17 H, aromatic protons), 4.25 (s, 1 H, C*H*), 2.95 (br s, 3 H, NH_2 and OH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 172.9 (ester C=O), 133.4, 132.1, 131.1, 130.6, 130.4, 128.7, 128.6, 128.3, 128.0, 127.8, 127.3, 127.0, 126.8, 126.7, 126.4, 126.3, 125.7, 124.5, 124.2, 123.6, 123.4, 121.3, 116.1, 58.4. − $C_{28}H_{21}NO_3$: calcd. C 80.17, H 5.05, N 3.34; found C 80.23, H 5.04, N 3.34.

2′-Hydroxy-1,1′-binaphthyl-2-yl [(3,5-Dinitrobenzoyl)amino](phenyl)acetate. − General Procedure: To a solution of **4** (2.17 g, 5.19 mmol) in dry THF (30 mL), triethylamine (0.78 mL, 5.69 mmol) was added. The solution was kept at 0 °C and 3,5-dinitrobenzoyl chloride (1.29 g, 5.69 mmol) dissolved in dry THF (15 mL) was added dropwise at the same temperature. The reaction mixture was stirred at room temperature for 2 h, then the solvent was evaporated under vacuum, and the residue dissolved in CH_2Cl_2. The organic phase was washed with a 10% HCl solution, a 10% $NaHCO_3$ solution, and water in that order then dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (SiO_2, $CHCl_3$/ethyl acetate 98:2).

(a*R*,*R*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(3,5-Dinitrobenzoyl)-amino](phenyl)acetate (1a): Yield 2.44 g, 77%. M.p. 113−115 °C. $[\alpha]_D^{21}$ = 64.7 (*c* = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.09 (t, *J* = 2.0 Hz, 1 H, Hb), 8.77 (d, *J* = 2.0 Hz, 2 H, Ha), 8.06 (d, *J* = 8.9 Hz, 1 H, H_4), 7.94 (d, *J* = 7.7 Hz, 1 H, H_5), 7.71 (d, *J* = 8.9 Hz, 1 H, $H_{4'}$), 7.62 (d, *J* = 7.3 Hz, 1 H, $H_{5'}$), 7.48 (dd, *J* = 7.7 and 7.0 Hz, 1 H, H_6), 7.44 (d, *J* = 8.9 Hz, 1 H, H_3), 7.29 (dd, *J* = 8.6 and 7.0 Hz, 1 H, H_7), 7.13 (dd, *J* = 7.3 and 7.1 Hz, 1 H, $H_{6'}$), 7.15 (d, *J* = 8.6 Hz, 1 H, H_8), 7.15 (d, *J* = 8.9 Hz, 1 H, $H_{3'}$), 7.08 (dd, *J* = 8.4 and 7.1 Hz, 1 H, $H_{7'}$), 7.07 (d, *J* = 6.9 Hz, 1 H, NH), 7.07 (t, *J* = 7.7 Hz, 1 H, H_p), 6.94 (t, *J* = 7.7 Hz, 2 H, H_m), 6.84 (d, *J* = 8.4 Hz, 1 H, $H_{8'}$), 6.81 (d, *J* = 7.7 Hz, 2 H, H_o), 5.67 (d, *J* = 6.9 Hz, 1 H, CH), 5.13 (s, 1 H, OH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 (ester C=O), 148.4 (amide C=O), 136.5, 133.5, 133.3, 133.1, 132.4, 131.0, 130.5, 128.8, 128.6, 128.2, 127.8, 127.6, 127.4, 127.3, 127.1, 126.6, 126.6, 125.6, 124.0, 123.3, 123.0, 121.2, 121.1, 120.8, 117.8, 57.3. − $C_{35}H_{23}N_3O_8$: calcd. C 68.51, H 3.78, N 6.85; found C 68.52, H 3.77, N 6.84.

(a*R*,*S*)-2′-Hydroxy-1,1′-binaphthyl-2-yl [(3,5-Dinitrobenzoyl)-amino](phenyl)acetate] (1b): Yield 2.44 g, 77%. M.p. 116−120 °C. $[\alpha]_D^{21}$ = 25.8 (*c* = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.05 (t, *J* = 2.0 Hz, 1 H, Hb), 8.76 (d, *J* = 2.0 Hz, 2 H, Ha), 7.99 (d, *J* = 8.9 Hz, 1 H, H_4), 7.91 (d, *J* = 8.1 Hz, 1 H, H_5), 7.76 (d, *J* = 7.3 Hz, 1 H, $H_{5'}$), 7.75 (d, *J* = 7.3 Hz, 1 H, $H_{4'}$), 7.46 (dd, *J* = 8.1 and 6.9 Hz, 1 H, H_6), 7.31 (d, *J* = 8.9 Hz, 1 H, H_3), 7.27 (dd, *J* = 8.5 and 6.9 Hz, 1 H, H_7), 7.25 (dd, *J* = 7.3 and 6.9 Hz, 1 H, $H_{6'}$), 7.19 (d, *J* = 8.5 Hz, 1 H, H_8), 7.16 (dd, *J* = 8.1 and 6.9 Hz, 1 H, $H_{7'}$), 7.14 (d, *J* = 6.6 Hz, 1 H, NH), 7.09 (d, *J* = 8.9 Hz, 1 H, $H_{3'}$),. 7.03 (t, *J* = 7.7 Hz, 1 H, H_p), 7.03 (t, *J* = 7.7 Hz, 2 H, H_m), 6.96 (d, *J* = 8.1 Hz, 1 H, $H_{8'}$), 6.83 (d, *J* = 7.7 Hz, 2 H, H_o), 5.50 (d, *J* = 6.6 Hz, 1 H, CH), 5.25 (s, 1 H, OH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 (ester C=O), 151.4 (amide C=O), 136.4, 133.8, 133.3, 130.7, 130.5, 129.9, 129.0, 128.9, 128.8, 128.2, 128.0, 127.3, 127.1, 126.6, 126.5, 126.3, 125.7, 124.4, 123.5, 122.9, 121.3, 120.9, 120.4, 117.9, 57.5. − $C_{35}H_{23}N_3O_8$: calcd. C 68.51, H 3.78, N 6.85; found C 68.49, H 3.77, N 6.83.

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