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Enantioseparation of anionic analytes by non-aqueous capillary electrophoresis using quinine and quinidine derivatives as chiral counter-ions

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Abstract

A non-aqueous capillary electrophoretic method developed for the enantioseparation of N-protected amino acids has been applied to the investigation of five new quinine and quinidine derivatives as chiral selectors: 1-adamantyl carbamoylated quinine, 3,4-dichlorophenyl carbamoylated quinidine, allyl carbamoylated dihydroquinine, allyl carbamoylated dihydroquinidine and 1-methyl quininium iodide. The composition of the background electrolyte was 12.5 m*M* ammonia, 100 m*M* octanoic acid in an ethanol–methanol (60:40 v/v) mixture containing a 10 m*M* concentration of the chiral selector. Under these conditions, the enantioseparation of a series of various benzoyl, 3,5-dinitrobenzoyl and 3,5-dinitrobenzyloxycarbonyl amino acid derivatives was studied with respect to selectand–selector relationship and enantioselectivity.

Keywords: Non-aqueous capillary electrophoresis; Enantiomeric separation; Derivatization electrophoresis, Chiral selectors; Amino acids

1. Introduction

Among chiral selectors, quinine has been used for enantioseparation in HPLC as a chiral ion-pairing agent in the mobile phase [1,2] and as a chiral stationary phase ligand [3,4] but with moderate enantioselectivity. Further developments revealed that carbamoylated quinine (QN) and quinidine (QD) based chiral stationary phases (CSPs) expose also high stereoselectivity for the direct resolution of chiral acids at hydroorganic or organic conditions using mixtures of aqueous buffers and methanol or acetonitrile as mobile phases [5–10]. Between the negatively charged anionic analytes (selectands, SAs^-) and this kind of positively charged chiral selectors (SOs^+), the primary, at this point, non-stereoselective ionic interaction is significantly accompanied by additional SO–SA intermolecular interactions related to hydrogen bonding, dipole–dipole, $\pi-\pi$ and hydrophobic interactions, leading to enantioselective molecule recognition if steric aspects come into play. These simultaneously acting multiple and complementary interactions can be seen as the basis for the high stereoselectivity of these SOs for given SA analytes. In this context the introduction of a bulky alkyl substituent at the carbamate function of O9 carbamoylated QN turned out to be advantageous to stereoselectivity [5,6].

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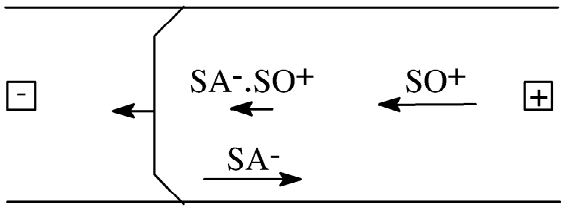

Fig. 1. Enantioseparation of anionic substances (SA^-) in NACE by formation of diastereoisomeric ion pairs with a chiral counter-ion (SO^+).

The objective of this study is to set up a screening protocol for a fast evaluation of the chiral discrimination potential of a larger set of newly developed QN and QD derivatives.

In previous work, a non-aqueous capillary electrophoretic (NACE) system using QN and *tert*.-butyl carbamoylated quinine (*t*Bu-CQN) in the background electrolyte was investigated for evaluating the chiral discrimination ability of cinchona alkaloids and different kinds of carbamoylated derivatives of QN- and QD-type chiral selectors towards acidic analytes and selectands, in particular N-protected amino acids [11]. The effect of a series of parameters on the enantioseparation of these compounds was studied: the composition and concentration of the background electrolyte, the concentration of the chiral counter-ion, the nature and relative proportions of the organic solvents, the capillary temperature and the applied voltage. Optimum selectivity and resolution were obtained with a background electrolyte made of 12.5 m*M* ammonia and 100 m*M* octanoic acid, containing the chiral selector at 10 m*M* concentration in an ethanol–methanol (60:40, v/v) mixture, at 15°C and −25 kV [11].

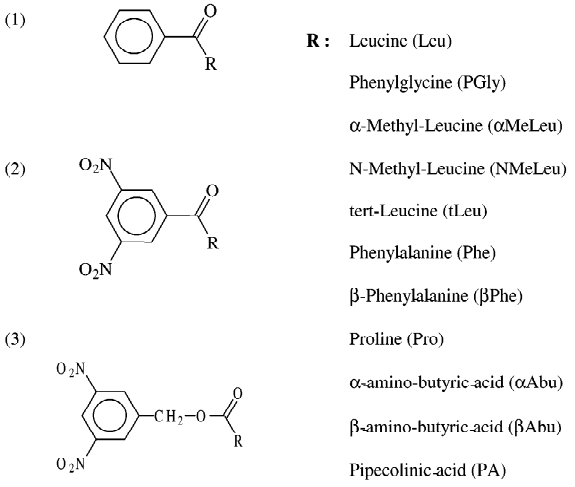

Fig. 2. N-protected amino acid derivatives: (1) Bz (benzoyl), (2) DNB (3,5-dinitrobenzoyl), (3) DNZ (3,5-dinitrobenzyloxycarbonyl).

Using these experimental conditions, the ion-pairing type interaction of SO^+, and SAs^- remains in action as a basis for chiral recognition, however under those conditions also the electrophoretic (μ_e) and the electroosmotic (μ_{EOF}) mobilities of all ionic and non-ionic species must be taken into consideration to judge the overall process. Free SO^+ and SA^- species exhibit countercurrent-like electrophoretic migration and their overall velocity is also influenced by the cathodic electroosmotic flow derived from the negative charge of the capillary wall (cf. Fig. 1). Differences in the ion-pair formation constants for (*R*) and (*S*)-enantiomers of the SAs, based on enantioselective intermolecular interactions with the chiral SO, are the principal contributions to the enantioseparation.

The amino acid derivatives could be detected with good sensitivity at 214 nm, in spite of the use of highly absorbing cationic compounds as chiral counter-ions, because the reservoir at the detector side of the capillary (anodic side) was devoid of this absorbing counter-ion. Before sample injection, the capillary was filled with the background electrolyte containing the counter-ion. When the voltage was applied and the separation started, the counter-ion migrated towards the injection side of the capillary (cathodic side) so that the high absorbance background left the detection window after about 10 min i.e. usually before the analytes reached this window [12].

Under the conditions selected, good results with respect to the repeatability of migration and resolution were obtained, as illustrated by the RSD values obtained for 3,5-dinitrobenzyloxycarbonyl-phenylalanine (DNZ-Phe) with *tert*.-butyl carbamoylated quinine (*t*Bu-CQN) as selector (0.56, 0.92 and 1.59% for the migration times of the first and the second migrating enantiomer and resolution, respectively) [12].

This NACE system was applied to the rapid

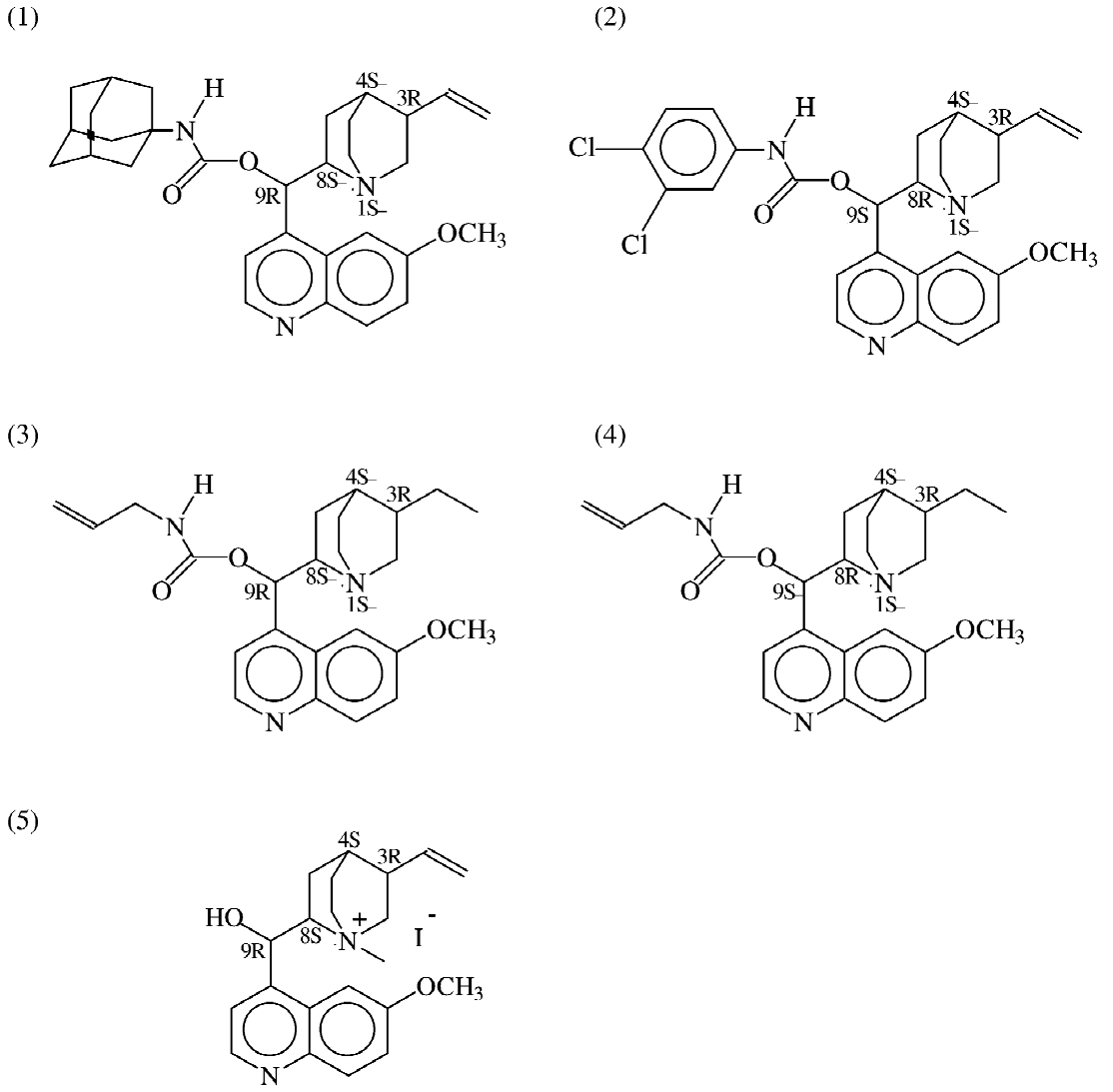

Fig. 3. Chiral selectors: (1) 1-adamantyl carbamoylated quinine, (2) 3,4-dichlorophenyl carbamoylated quinidine, (3) allyl carbamoylated dihydroquinine, (4) allyl carbamoylated dihydroquinidine and (5) 1-methyl quininium iodide.

screening of different cinchona alkaloids and derivatives as chiral selectors with regards to their enantioselectivity towards various acid analytes [12,13]. The following series of SOs was studied: quinine (QN), quinidine (QD), cinchonine (CN), cinchonidine (CD), *tert*.-butyl carbamoylated quinine (*t*Bu-CQN), *tert*.-butyl carbamoylated quinidine (*t*Bu-CQD), dinitrophenyl carbamoylated quinine (DNP-CQN) and cyclohexyl carbamoylated quinine (cHex-CQN). Various Bz-(benzoyl), DNB-(3,5-dinitrobenzoyl) and DNZ-(3,5-dinitrobenzyloxycarbonyl) N-protected amino acids served as chiral selectands.

In this study, the electrophoretic behaviour of the same series of selectands (cf. Fig. 2) has been systematically investigated with five new cinchona alkaloid derivatives as selectors: 1-adamantyl carbamoylated quinine (Ad-CQN), 3,4-dichlorophenyl carbamoylated quinidine (DCP-CQD), allyl car-

Table 1
Enantioresolution of amino acid derivatives with Ad-CQN as selector[a]

Analyte	t_1(min)	t_2(min)	α	R_s
DNB-Leu	14.60	52.85	2.445	53.5
DNB-PGly	12.57	28.58	1.884	46.4
DNB-tLeu	11.91	26.38	1.864	65.4
DNB-αMeLeu	11.76	12.62	1.061	6.6
DNB-NMeLeu	12.08	12.22	1.009	<0.7
DNB-Phe	11.59	29.10	2.044	55.3
DNB-Pro	12.55	[b]–	–	–
DNB-αAbu	11.42	25.36	1.877	65.0
DNB-βAbu	21.60	44.33	1.625	42.3
DNZ-Leu	17.50	25.57	1.331	27.9
DNZ-αMeLeu	12.69	12.89	1.013	1.5
DNZ-NMeLeu	16.51	16.91	1.019	1.9
DNZ-Phe	15.39	19.84	1.221	20.4
DNZ-βPhe	21.20	24.93	1.127	12.5
DNZ-Pro	15.55	16.03	1.025	1.5
DNZ-αAbu	14.28	18.15	1.212	20.9
DNZ-βAbu	25.48	29.36	1.105	10.1
DNZ-PA	18.66	18.91	1.011	1.2
Bz-Leu	15.20	17.84	1.136	12.9
Bz-Phe	13.22	15.03	1.111	11.1
Bz-βPhe	18.33	19.78	1.061	6.0
Bz-αAbu	12.53	13.71	1.078	5.1
Bz-βAbu	19.25	20.09	1.033	2.7
Bz-PA	13.98	–	–	–

[a] Conditions as described in Section 2.
[b] –: no enantiomeric separation observed (R_s<0.5).

bamoylated dihydroquinine (All-CDHQN), allyl carbamoylated dihydroquinidine (All-CDHQD) and 1-methyl quininium iodide (1-Me-QN^+I^-) (cf. Fig. 3). The enantioselectivity and resolution values have been collected in order to set up a screening protocol for the evaluation of the chiral discrimination potential of newly developed quinine and quinidine derivatives as SOs.

2. Experimental

2.1. Apparatus and chemicals

All experiments were performed on a Spectraphoresis 1000 CE instrument (SpectraPhysics, San Jose, CA, USA) equipped with an automatic injector, an autosampler, an UV–visible detector (190–800 nm) and a temperature control system (15–60°C). An IBM PS/2 Model 90 486 computer was used for instrument control and data handling. Electropherograms were printed on a HP DeskJet 500 printer. A column cartridge was obtained from SpectraPhysics.

Ad-CQN, DCP-CQD, All-CDHQN, All-CDHQD, 1-Me-QN^+I^- were synthesized according to a standard procedure described elsewhere [14]. The organic solvents were of HPLC grade: ethanol absolute from Merck (Darmstadt, Germany) and methanol from Fisher Scientific, (Leicestershire, UK). Octanoic acid was from Sigma and ammonia solution 25% from Carlo Erba (Rodano, Italy). The racemic and enantiomerically pure amino acids were purchased from Sigma. Bz- and DNB-derivatives were synthesized according to standard derivatization procedures [9] except DNB-Leu and DNB-PGly obtained by Sigma. To synthesize the DNZ-compounds, aqueous solutions of amino acids were derivatized with 3,5-dinitrobenzyl chloroformate [10]. The sample solutions were prepared by dissolving each amino acid derivative at a concentration of 50 μg/ml in methanol. Benzyl alcohol from Sigma (0.01% methanolic solution) was used as neutral marker to visualize the electroosmotic flow breakthrough. Buffers and samples were filtered through a Polypure polypropylene membrane filter (0.2 μm) from Alltech (Laarne, Belgium) before use.

2.2. Electrophoretic technique

Electrophoretic separations were carried out with uncoated fused-silica capillaries, 44 cm (37 cm to the detector) 50 μm I.D. provided by Supelco (Bellefonte, PA, USA). The background electrolyte (BGE) was made of 100 m*M* octanoic acid and 12.5 m*M* ammonia in a mixture of ethanol–methanol (60:40) containing the chiral selector at 10 m*M* concentration. At the beginning of each working day, the capillary was washed with ethanol–methanol (60:40) for 10 min and with the BGE for 10 min, while after each injection the capillary was washed with the solvent mixture for 1 min and was equilibrated with the BGE for 10 min. The injections were made at the cathodic side and the applied voltage was −25 kV (reversed polarity mode). The normal polarity mode (+25 kV) was used to measure the cathodic electroosmotic mobility μ_{EOF}: (i~6.5 μA). The UV detection (at the anodic side) was performed at 214 nm.

Injections were made in the hydrodynamic mode for a period of 5 s (corresponding to 13.3 nl) and the capillary was thermostated at 15°C. The resolution (R_s) was calculated according to the standard expressions based on peak width at half-height [15]. The selectivity (α) was calculated according to $\alpha = \mu_{e1}/\mu_{e2}$ where $\mu_e = \mu_a - \mu_{EOF}$ (μ_e is the effective mobility, μ_a is the apparent mobility and μ_{EOF} is the electroosmotic mobility).

3. Results and discussion

The enantiomeric selectivity and resolution for all amino acid derivatives examined were studied with the five new quinine and quinidine derivatives as chiral counter-ions under the selected NACE operating conditions.

Using Ad-CQN, DCP-CQD and 1-Me-QN$^+$I$^-$, the migration times (t), enantioselectivity (α) and resolution (R_s) for the two SAs enantiomers are presented, in Table 1, 2 and 3 respectively.

Particularly high selectivity and resolution values were obtained using Ad-CQN as counter-ion with the DNB derivatives as SAs, resulting in high migration times for the second amino acid derivative enantiomer. For example: $R_s = 65.4$ and $\alpha = 1.864$ for DNB-tLeu; $R_s = 65.0$ and $\alpha = 1.877$ for DNB-αAbu; $R_s = 55.3$ and $\alpha = 2.044$ for DNB-Phe.

With Ad-CQN, the (*R*)-DNB-Leu enantiomer migrated first ($R_s = 53.5$ and $\alpha = 2.445$) but with DCP-CQD ($R_s = 32.4$ and $\alpha = 1.326$) or 1-Me-QN$^+$I$^-$ ($R_s = 0.79$ and $\alpha = 1.008$), the (*S*)-DNB-Leu enantiomer migrated first. This confirms the reversed migration order previously observed with carbamoylated quinine derivatives compared to the quinine [12,13]. With the carbamoylated SOs (Ad-CQN and DCP-CQD), enantiomeric separations could be achieved

Table 2
Enantioresolution of amino acid derivatives with DCP-CQD as selector[a]

Analyte	t_1(min)	t_2(min)	α	R_s
DNB-Leu	17.74	26.16	1.326	32.4
DNB-PGly	14.25	19.00	1.250	26.3
DNB-tLeu	17.46	26.46	1.353	35.0
DNB-αMeLeu	14.10	15.44	1.075	8.5
DNB-NMeLeu	16.23	16.57	1.016	1.7
DNB-Phe	16.41	24.20	1.334	33.8
DNB-Pro	15.62	–[b]	–	–
DNB-αAbu	15.28	20.37	1.245	25.1
DNB-βAbu	36.10	52.29	1.234	25.9
DNZ-Leu	24.02	27.34	1.094	9.4
DNZ-αMeLeu	20.13	21.29	1.042	5.0
DNZ-NMeLeu	25.60	–	–	–
DNZ-Phe	22.15	29.55	1.220	20.6
DNZ-βPhe	40.93	48.78	1.103	11.3
DNZ-Pro	25.47	26.80	1.036	2.2
DNZ-αAbu	22.58	25.68	1.095	10.2
DNZ-βAbu	53.00	59.16	1.057	6.3
DNZ-PA	25.25	25.50	1.007	<0.7
Bz-Leu	24.97	27.13	1.059	6.6
Bz-Phe	20.29	22.43	1.076	9.0
Bz-βPhe	27.45	28.67	1.030	2.9
Bz-αAbu	19.79	21.03	1.046	5.3
Bz-βAbu	34.69	35.62	1.017	1.6
Bz-PA	19.13	19.28	1.006	<0.7

[a] Conditions as described in Section 2.
[b] –: no enantiomeric separation observed ($R_s < 0.5$).

Table 3
Enantioresolution of amino acid derivatives with 1-Me-QN$^+$I$^-$ as selector[a]

Analyte	t_1(min)	t_2(min)	α	R_s
DNB-Leu	16.58	16.74	1.008	0.79
DNB-PGly	13.26	13.37	1.007	0.72
DNB-tLeu	14.16	14.62	1.026	3.1
DNB-αMeLeu	11.95	–[b]	–	–
DNB-NMeLeu	12.41	–	–	–
DNB-Phe	14.05	14.44	1.023	2.6
DNB-Pro	14.35	15.05	1.039	<0.7
DNB-αAbu	15.24	15.37	1.007	<0.7
DNB-βAbu	26.48	37.83	1.263	17.0
DNZ-Leu	21.19	–	–	–
DNZ-αMeLeu	13.81	–	–	–
DNZ-NMeLeu	19.97	–	–	–
DNZ-Phe	17.39	–	–	–
DNZ-βPhe	32.92	–	–	–
DNZ-Pro	18.85	–	–	–
DNZ-αAbu	16.32	–	–	–
DNZ-βAbu	41.89	–	–	–
DNZ-PA	22.36	–	–	–
Bz-Leu	17.67	–	–	–
Bz-Phe	14.32	–	–	–
Bz-βPhe	27.06	–	–	–
Bz-αAbu	15.43	–	–	–
Bz-βAbu	32.51	–	–	–
Bz-PA	17.40	–	–	–

[a] Conditions as described in Section 2.
[b] –: no enantiomeric separation observed ($R_s < 0.5$).

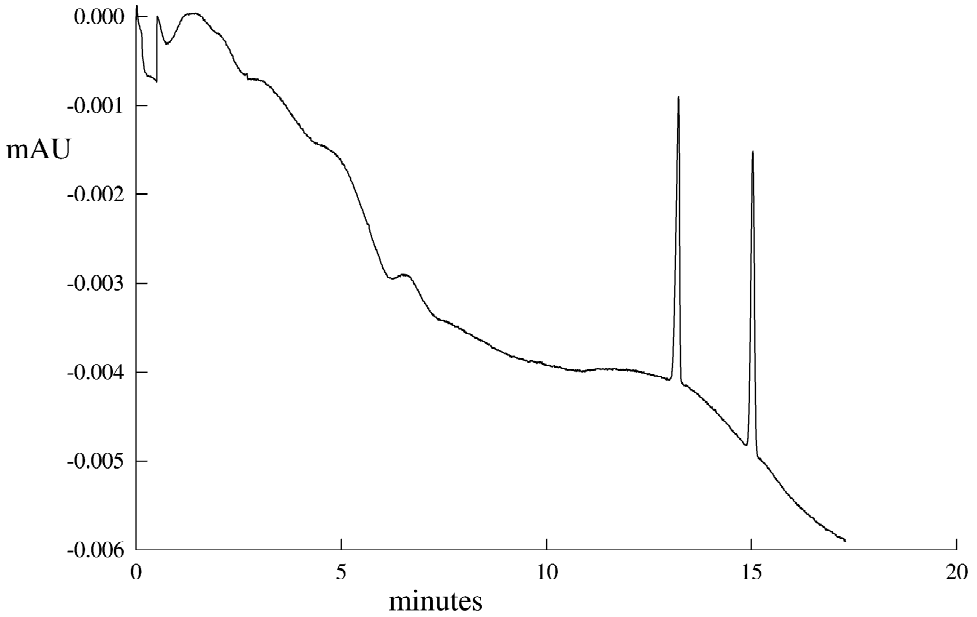

Fig. 4. Enantioseparation of Bz-Phe. Background electrolyte: 100 m*M* octanoic acid and 12.5 m*M* ammonia in methanol–ethanol (40:60) containing 10 m*M* Ad-CQN. Other conditions as described in Section 2.

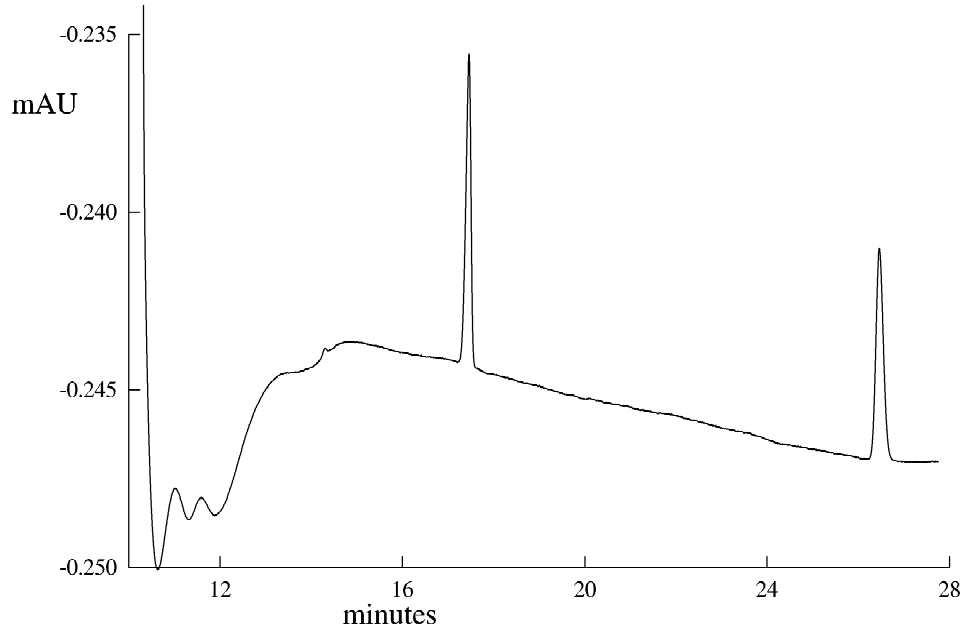

Fig. 5. Enantioseparation of DNB-tLeu background electrolyte: 100 m*M* octanoic acid and 12.5 m*M* ammonia in methanol–ethanol (40:60) containing 10 m*M* DCP-CQD. Other conditions as described in Section 2.

for all the amino acid derivatives except DNB-Pro. The presence of an alkyl substituent is favourable for the enantioselectivity, as observed previously [12,13].

The enantioseparation of Bz-PA was only observed using DCP-CQD. This counter-ion has a structure like the dinitrophenyl carbamoylated quinine (DNP-CQN) that has already permitted the separation of the Bz-PA enantiomers (data from Ref [12]).

With 1-Me-QN^+I^-, devoid of carbamate function, no enantioseparations were observed for DNZ- and Bz-derivatives and only poor selectivity values were observed for DNB-amino acid derivatives except DNB-αMeLeu and DNB-NMeLeu (for example, $R_s = 17.0$ and $\alpha = 1.263$ for DNB-βAbu). However, it is worth noting that, including data from Ref [12], DNB-Pro was only enantioseparated with precisely this selector ($R_s < 0.7$ and $\alpha = 1.039$).

Typical electropherograms are presented in Fig. 4 which shows the enantioseparation obtained for Bz-Phe with Ad-CQN as counter-ion and in Fig. 5 which illustrates the separation of DNB-tLeu enantiomers with DCP-CQD as counter-ion.

Using All-CDHQN and All-CDHQD as chiral SOs, the corresponding t, α and R_s values for the two SAs enantiomers are presented in Tables 4 and 5.

With these SOs generally, the enantioselectivity was lower than with Ad-CQN but higher than with DCP-CQD or 1-Me-QN^+I^-.

With All-CDHQN, the (*R*)-DNB-Leu enantiomer migrated before the (*S*)-DNB-Leu ($R_s = 39.8$ and $\alpha = 1.670$) while with All-CDHQD, the migration order

Table 4
Enantioresolution of amino acid derivatives with All-CDHQN as selector[a]

Analyte	t_1(min)	t_2(min)	α	R_s
DNB-Leu	14.86	31.60	1.670	39.8
DNB-PGly	13.30	24.14	1.536	41.1
DNB-tLeu	15.71	34.30	1.681	33.2
DNB-αMeLeu	12.64	13.09	1.028	2.4
DNB-NMeLeu	13.82	14.00	1.010	<0.7
DNB-Phe	15.29	35.68	1.754	41.5
DNB-Pro	15.42	–[b]	–	–
DNB-αAbu	12.88	27.96	1.731	62.7
DNB-βAbu	24.47	45.68	1.437	42.1
DNZ-Leu	20.94	27.44	1.195	19.3
DNZ-αMeLeu	16.85	17.23	1.017	1.9
DNZ-NMeLeu	21.60	22.12	1.016	1.9
DNZ-Phe	15.18	20.40	1.239	22.1
DNZ-βPhe	24.57	27.84	1.083	9.3
DNZ-Pro	16.59	17.21	1.027	1.9
DNZ-αAbu	16.22	20.40	1.179	17.7
DNZ-βAbu	29.61	34.07	1.087	10.2
DNZ-PA	19.63	19.80	1.006	<0.7
Bz-Leu	18.36	20.64	1.086	7.9
Bz-Phe	15.47	17.27	1.085	7.9
Bz-βPhe	22.63	23.93	1.038	3.9
Bz-αAbu	15.61	17.10	1.070	4.1
Bz-βAbu	25.43	26.63	1.030	2.2
Bz-PA	16.82	–	–	–

[a] Conditions as described in Section 2.
[b] –: no enantiomeric separation observed ($R_s < 0$ 5).

Table 5
Enantioresolution of amino acid derivatives with All-CDHQD as selector[a]

Analyte	t_1(min)	t_2(min)	α	R_s
DNB-Leu	16.17	34.95	1.620	32.2
DNB-PGly	14.67	27.47	1.518	33.7
DNB-tLeu	12.22	32.05	1.901	52.5
DNB-αMeLeu	14.17	15.06	1.046	5.1
DNB-NMeLeu	15.14	–[b]	–	–
DNB-Phe	14.95	30.93	1.603	25.3
DNB-Pro	15.39	–	–	–
DNB-αAbu	13.23	32.12	1.792	71.3
DNB-βAbu	24.40	55.24	1.531	56.8
DNZ-Leu	18.46	22.81	1.150	8.7
DNZ-αMeLeu	16.01	16.34	1.015	1.4
DNZ-NMeLeu	16.72	16.93	1.009	1.2
DNZ-Phe	21.62	29.98	1.221	24.8
DNZ-βPhe	32.02	42.78	1.162	21.7
DNZ-Pro	16.55	17.18	1.027	2.3
DNZ-αAbu	14.85	19.81	1.223	23.5
DNZ-βAbu	41.62	50.72	1.096	12.9
DNZ-PA	33.12	33.56	1.007	1.0
Bz-Leu	16.37	18.88	1.104	11.0
Bz-Phe	14.51	16.13	1.080	6.8
Bz-βPhe	18.84	20.90	1.072	8.7
Bz-αAbu	14.85	16.03	1.056	3.3
Bz-βAbu	25.32	26.49	1.028	2.5
Bz-PA	15.98	–	–	–

[a] Conditions as described in Section 2.
[b] –: no enantiomeric separation observed ($R_s < 0.5$).

was reversed, the (*S*)-DNB-Leu enantiomer migrating first ($R_s = 32.2$ and $\alpha = 1.620$). The best resolution values were obtained for DNB-αAbu enantiomers ($R_s = 62.7$ with All-CDHQN and $R_s = 71.3$ with All-CDHQD).

Fig. 6 shows the electropherogram obtained for DNB-αMeLeu with All-CDHQD as counter-ion while Fig. 7 presents the electropherogram of DNB-PGly with All-CDHQN as SO.

For the five tested chiral SOs, the following order in α values was observed for the enantiomers of DNB-Leu: α Ad-CQN > α All-CDHQN > α All-CDHQD > α DCP-CQD > α 1-Me-QN^+I^-. The difference between the ion-pair formation constants for (*R*)- and (*S*)-enantiomers of the SAs, based on the enantioselective intermolecular interactions mentioned in Section 1, represents the major contribution to selectivity. Additionally the SO structure including different substitution influences the chiral recognition mechanism.

Among all the counter-ions studied till now (including data from Ref [12] and [13]), the highest enantioselectivity values were obtained with Ad-CQN for DNB-Leu (α 2.445). This fact clearly confirms that the presence of a bulky substituent on the quinine or quinidine derivative used as chiral SO has a favourable effect on enantioselectivity.

As observed above, the enantiomers of DNB-Pro were never separated except partly with 1-Me-QN^+I^-. On the contrary, the enantiomers of DNZ-Pro were separated with all the carbamoylated SOs (including data from Ref [12]) except 1-Me-QN^+I^-. This seems to indicate that the presence of the DNZ group improves particularly the chiral discrimination of the proline derivative by additional interactions with the carbamate function of the counter-ion.

4. Conclusions

A NACE system using a background electrolyte made of 100 m*M* octanoic acid and 12.5 m*M* ammonia in an ethanol–methanol (60:40) mixture was applied to the investigation of the potential of five new quinine and quinidine derivatives for the enantioseparation of N-protected amino acids. The highest enantiomeric selectivity and resolution values were obtained using DNB-derivatives as SAs and adamantyl carbamoylated quinine (Ad-CQN) as SO. In further work, dimeric forms of quinine or quini-

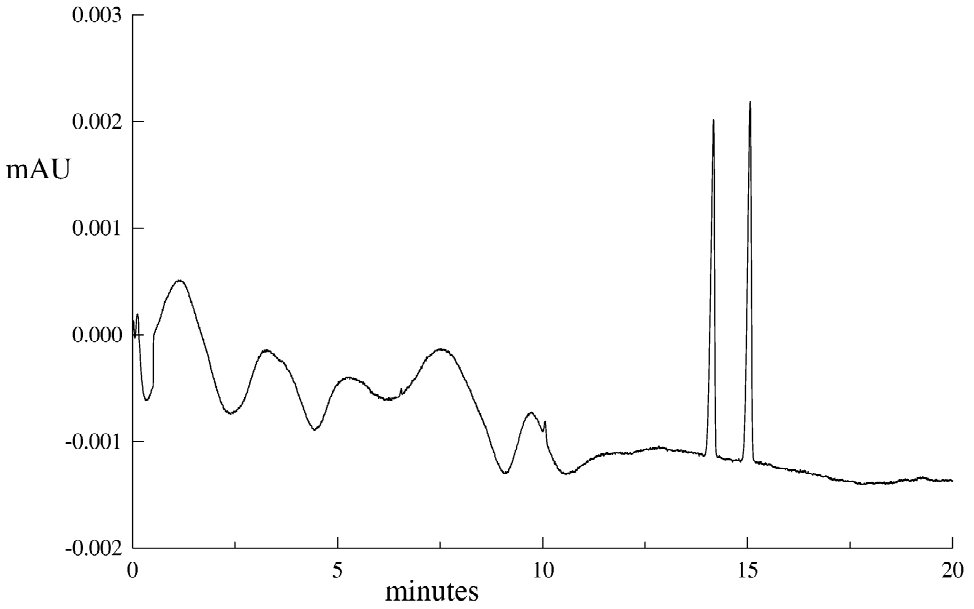

Fig. 6. Enantioseparation of DNB-αMeLeu. Background electrolyte: 100 m*M* octanoic acid and 12.5 m*M* ammonia in methanol–ethanol (40:60) containing 10 m*M* All-CDHQD. Other conditions as described in Section 2.

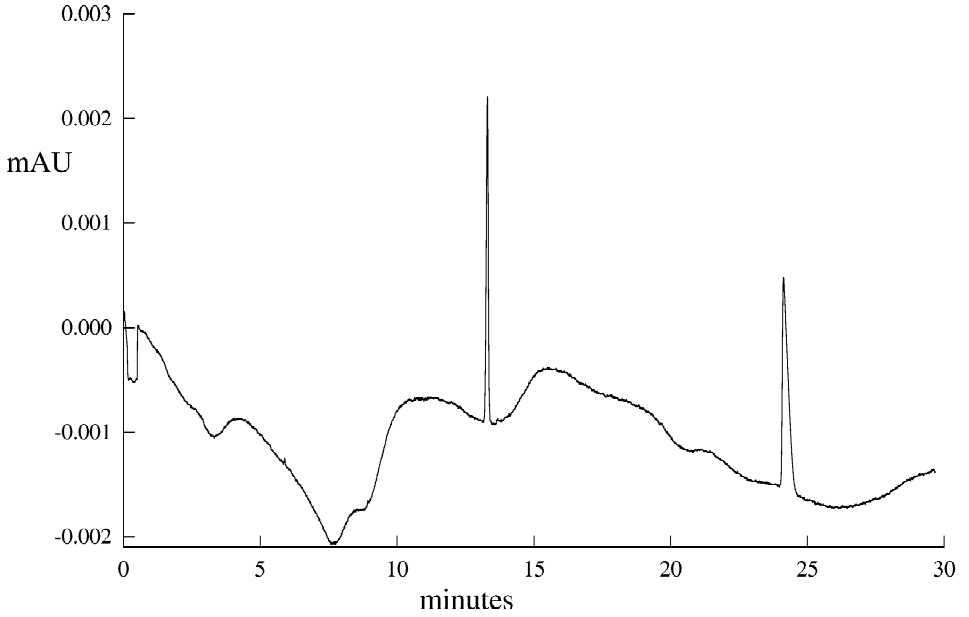

Fig. 7. Enantioseparation of DNB-PGly. Background electrolyte: 100 m*M* octanoic acid and 12.5 m*M* ammonia in methanol–ethanol (40:60) containing 10 m*M* All-CDHQN. Other conditions as described in Section 2.

dine derivatives will be investigated as counter-ions. The enantioselectivity values obtained with the different SOs will be correlated with those found in HPLC using the same SOs immobilized onto silica as chiral stationary phases. In this manner, this NACE method will be apply as a screening tool for the rapid evaluation of the chiral discrimination potential of a large set of newly developed chiral SOs derived from quinine and related alkaloids.

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