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DESIGN, PREPARATION AND PERFORMANCE OF A PHTHALIDE-BASED CHIRAL STATIONARY PHASE

WILLIAM H. PIRKLE* and THOMAS J. SOWIN
Roger Adams Laboratory, School of Chemical Sciences, University of Illinois, Urbana, IL 61801 (U.S.A.)
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SUMMARY

A phthalide structurally optimized to maximize the chromatographic separability of its enantiomers on chiral stationary phases (CSPs) derived from the N-3,5-dinitrobenzamides of (*S*)-leucine and (*R*)-phenylglycine was prepared, preparatively resolved, and incorporated into a reciprocal phthalide-based CSP. This CSP, derived from 3-(4′,7′-dimethyl-1′-naphthyl)-3-(undec-10′-enyl) phthalide, has proven to be efficient for the separation of the enantiomers of numerous amino ester, amino amide, amino phosphonate, amino alcohol, amine, and alcohol 3,5-dinitrobenzoyl derivatives. Although not exhibiting the remarkably high degree of enantiomeric separation for some of the aforementioned analytes as some other reciprocal CSPs, the phthalide-based CSP is the most effective CSP to date for the separation of the enantiomers of secondary alcohols as their 3,5-dinitrobenzoates. Specific representative resolutions are presented for each of the aforementioned analyte classes. A study of the resolution of homologous series of α-phenylalkylamine and α-phenylalkanol derivatives is included.

INTRODUCTION

In recent years, the chromatographic separation of enantiomers by high-performance liquid chromatography (HPLC) upon chiral stationary phases (CSPs) has become increasingly useful[1–4]. For example, it has been demonstrated that literally thousands of racemates may be resolved on CSPs derived from the N-3,5-dinitrobenzamides of (*R*)-phenylglycine and (*S*)-leucine[5]. However, as useful as the α-amino acid-derived CSPs have proven to be, they do have limitations on the types of analytes which they can resolve. In an effort to increase the clientele of racemates which are resolvable on CSPs, we have focused on the production of several so-called "reciprocal" CSPs.

In the chiral recognition of an analyte enantiomer by a CSP there must be at least three simultaneous interactions, at least one of which is stereochemically dependent, between the CSP and the recognized analyte enantiomer. Inherent in this process is a certain amount of reciprocity. For example, the interactions that allow a CSP derived from (+)-A to separate the enantiomers (+)-B and (−)-B should

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also be operative in a reciprocal sense. Thus, a CSP derived from (+)-B or (−)-B should be able to separate the enantiomers (+)-A and (−)-A assuming that the method of attachment of (+)-B or (−)-B to silica does not alter the interactions necessary for chiral recognition[6]. Therefore, analyte enantiomers which separate well on CSPs derived from the N-3,5-dinitrobenzamides of (*S*)-leucine or (*R*)-phenylglycine are obvious candidates for incorporation into reciprocal CSPs which should effectively separate the enantiomers of α-amino acids, and other analyte classes, as their 3,5-dinitrobenzoyl derivatives.

Intrinsic in the design of a reciprocal-type CSP is the structural optimization of the CSP candidate to maximize its enantiomeric separation on existing CSPs. Maximizing the enantiomeric separation of the candidate is, in effect, maximizing the interactions between the solute enantiomer and the CSP that are important for chiral recognition. Because the method of attaching the candidate to the underlying support may somewhat alter the chiral recognition processes, exact reciprocity is not expected. However, the concept is an extremely useful guide. On this premise, a number of useful reciprocal-type CSPs derived from 5-arylhydantoins[7], α-arylalkylamines[8–10], and N-(2-naphthyl)-α-amino acids[11,12] have been synthesized and reported from these laboratories.

Reported herein we describe the preparation and performance of a similarly designed phthalide-based CSP. Systematic study of the separation of a series of 3-aryl-3-alkylphthalide enantiomers on CSPs derived from the N-3,5-dinitrobenzamides of (*S*)-leucine and (*R*)-phenylglycine revealed that phthalides in which the aryl group is dimethyl-1′-naphthyl and the alkyl substituent is either long or sterically large (*i.e.*, undecenyl) afford high degrees of enantiomeric separation[13]. Therefore, 3-(4′-7′-dimethyl-1′-naphthyl)-3-(undec-10′-enyl)phthalide (2) was selected as a candidate for incorporation into a reciprocal-type phthalide-based CSP owing both to its relatively facile preparation and its high degree of enantiomeric separation on the aforementioned CSPs. Furthermore, the terminal double bond of the alkyl substituent, remote from the stereogenic center of 2 provides, after hydrosilyation, a mode of attachment to silica that we hoped would have little effect on the chiral recognition process.

EXPERIMENTAL

General

Melting points were obtained using a Büchi apparatus and are uncorrected. Mass spectra were recorded using a Varian MAT CH-5 spectrometer (low-resolution electron impact) and a Varian Model 731 (high-resolution electron impact) mass spectrometer. Proton NMR spectra were recorded on either a Varian XL-200 (200 MHz) or a GE-QE 300 (300 MHz) spectrometer using tetramethylsilane as an internal reference. IR spectra were obtained on either a IBM IR-32 FT-IR or a Nicolet 7000 FT-IR spectrometer. Optical rotations were observed at 589 nm at room temperature using a Rudolph Autopol III polarimeter and a 10 cm polarimeter cell.

The phthalide-based CSP was packed into a 250 × 4.6 mm I.D. stainless-steel column as a methanol slurry. Analytical chromatography was performed using an Altex 100A pump, Altex 210 injector, and an Altex Model 152 dual-wavelength (254 and 280 nm) detector. Either Kipp and Zonen BD 41 or Altex Model C-R1A integrating recorders were used. A Rudolph Autopol III digital polarimeter containing a 20 cm flow cell was used in series with the UV detector to monitor simultaneously the sign of $[\alpha]_D$ as the enantiomers eluted. Flash chromatography was performed using Grace grade 951 silica gel (58 μm). Preparative resolutions of phthalides[4] similar to the one used in this study, as well as the preparation of analytes as their 3,5-dinitrobenzoyl[8] or 3,5-dinitroanilido[12] derivatives, have been previously reported.

3-(4′,7′-Dimethyl-1′-naphthyl)phthalide (1)

To 150 ml of aqueous sodium hydroxide (pH 11–12) in a 250-ml round-bottom flask was dissolved 5 g (0.016 mol) of 2-(4′,7′-dimethyl-1′-naphthyl)benzoic acid[15]. To this stirred solution at room temperature was added 2.5 g (0.066 mol) sodium borohydride. The solution was allowed to reflux overnight, cooled to room temperature and acidified by slow addition of concentrated aqueous hydrochloric acid (caution! Heat and gas evolution) to pH 1 producing a white precipitate which was collected by filtration. The white precipitate was dissolved in 200 ml dichloromethane and extracted two times with 100 ml cold 1 *M* aqueous sodium hydroxide. Unreacted starting material was recovered by acidification of combined base extracts. The organic layer was isolated, dried over anhydrous magnesium sulfate and concentrated to afford 4.1 g (88%) of phthalide 1 as a white solid. Recrystallization from ethanol gave 1 as fine white needles. m.p. 135–137°C; Analysis calculated for $C_{20}H_{16}O_2$: C, 83.30; H, 5.59; found: C, 83.11; H, 5.33. ^1H NMR (C^2HCl_3) δ 2.55 (s, 3H), 2.60 (s, 3H), 7.00–7.95 (m, 10H). IR (KBr) 3100–2900, 1772 (C=O), 1599, 1464, 1282, 1213, 955 cm^{-1}.

3-(4′,7′-Dimethyl-1′-naphthyl)-3-(undec-10′-enyl)phthalide (2)

Phthalide 1 (3.00g, 0.010 mol) was dissolved in 100 ml anhydrous tetrahydrofuran contained in a 200-ml round-bottom flask equipped with nitrogen atmosphere and magnetic stirrer. To this solution cooled to −78°C was added (via cannula) 1.1 equivalents of lithium diisopropylamide in 20 ml anhydrous tetrahydrofuran, also cooled to −78°C, affording a dark red solution. To this solution at −78°C was added 5.6 g (0.020 mol) of undec-10-enyl iodide (obtained from undec-10-enyl bromide[16,17] by Finkelstein reaction[18]) via syringe. The solution was allowed to slowly warm to room temperature over a 4-h period and the reaction was quenched as soon as the red color no longer persisted by addition to 100 ml saturated aqueous ammonium chloride. This mixture was extracted two times with 100 ml dichloromethane, the combined organic extracts were washed two times with 100 ml water, dried over anhydrous magnesium sulfate and concentrated to give a pale yellow oil. The residue was purified by flash chromatography on silica (60% dichloromethane in hexane as mobile phase) to afford 3.3 g (75%) of phthalide 2 as a colorless oil. High resolution mass spectrum: calculated for $C_{31}H_{36}O_2$: 440.2715; found: 440.2715. ^1H NMR (C^2HCl_3) δ 1.15–1.48 (m, 14H), 2.02 (m, 1H), 2.60 (s, 3H), 2.64 (s, 3H), 3.04 (m, 1H), 4.96 (m, 2H), 5.78 (m, 1H), 7.04–8.00 (m, 8H), 8.49 (s, 1H). IR (neat) 3050–2900, 1765 (C=O), 1599 (C=C), 1464, 1260, 1111, 928 cm^{-1}.

Preparative resolution of phthalide 2

Phthalide 2 was resolved by medium-pressure liquid chromatography (MPLC) using a 2 in. × 30 in. column packed with 1.2 kg of (*R*)-N-3,5-dinitrobenzoylphenylglycine CSP (2% 2-propanol in hexane as mobile phase; flow-rate, 30 ml/min) using apparatus as previously described[14]. High-R_F enantiomer, (*S*)-2, was obtained in greater than 98% enantiomeric excess (e.e.) as a colorless oil. $[\alpha]_D^{25}$ − 342.5 (c 1.06, $CHCl_3$). Low R_F enantiomer, (*R*)-2, was obtained in 90% e.e. as a colorless oil.

(S)-3-(4′-,7′-Dimethyl-1′-triethoxysilylundecyl)phthalide (3)

To a 50-ml round-bottom flask equipped with reflux condensor, nitrogen atmosphere and magnetic stirrer was added 1.41 g (3.2 mmol) of enantiomerically pure (*S*)-2 dissolved in 25 ml triethoxysilane. The solution was warmed to 60°C and 0.5 ml of 0.1 *M* freshly prepared chloroplatinic acid [freshly prepared catalyst minimizes production of the major side product resulting from saturation of the terminal double bond of (*S*)-2] in 2-propanol was added. The solution was heated at 100°C for 4 h, and the reaction was monitored by thin-layer chromatography (TLC). Since unreacted starting material remained, 0.5 ml of chloroplatinic acid in 2-propanol was added and the reaction was allowed to proceed 1 h longer. The excess triethoxysilane was removed *in vacuo* and the orange colored residue was purified by flash chromatography on silica (70% dichloromethane) in hexane as mobile phase) to afford 0.96 g (50%) of (*S*)-3 as a colorless oil. High-resolution mass spectrum: calculated for $C_{37}H_{52}O_5$: 604.3584; found: 604.3588. ^{1}H NMR (C^2HCl_3) δ 0.64 (m, 2H), 1.06–1.48 (m, 27H), 2.25 (m, 1H), 2.61 (s, 3H), 2.64 (s, 3H), 3.02 (m, 1H), 3.82 (m, 6H), 7.04–8.00 (m, 8H), 8.49 (s, 1H). IR (neat) 3050–2900, 1764 (C=O), 1467, 1259, 1114, 1054 cm^{-1}. $[\alpha]_D^{25}$ − 265.8 (c 0.89, $CHCl_3$).

Chiral stationary phase (S)-4

A 4.6-g amount of 5-μm Spherisorb silica gel was slurried in 90 ml of toluene contained in a 200 ml round-bottom flash equipped with a Dean-Stark trap, magnetic stirrer and nitrogen atmosphere. This mixture was azeotropically dried and hydrosilylated phthalide (*S*)-3 (0.66g, 1.1 mmol) was added and the mixture heated at reflux for 43 h with intermittent gentle agitation to keep the silica from settling. The modified silica was isolated by filtration and washed successively with 100 ml protions of methanol, ethyl acetate, methylene chloride and hexane. Microanalysis found: C, 5.09; H, 0.69; Si, 43.59; calculated: 0.128 mmol/g of CSP (based on C).

RESULTS AND DISCUSSION

The phthalide-based CSP 4 chemically bonded to 5-μm Spherisorb silica gel particles, was prepared from phthalide 1 (Fig. 1). Phthalide 1 is easily prepared, in 88% yield, by sodium borohydride reduction of 2-(4′,7′-dimethyl-1′-naphthyl)benzoic acid in aqueous base followed by acidification with concentrated hydrochloric acid. Phthalide 1 was alkylated by treatment with lithium diisopropylamide in tetrahydrofuran followed by addition of undec-10-enyl iodide affording phthalide 2 in 75% yield. Preparative MPLC resolution of phthalide 2 on (*R*)-N-3,5-dinitrobenzoylphenylglycine CSP gave the least retained enantiomer, (*S*)-2, in greater than 98% e.e. The absolute configuration of phthalide 2 had been determined from our previous study[19]. Hydrosilylation of (*S*)-2 with excess triethoxysilane and chloroplatinic acid catalyst provided hydrosilylated phthalide (*S*)-3 (50% yield) which was chemically

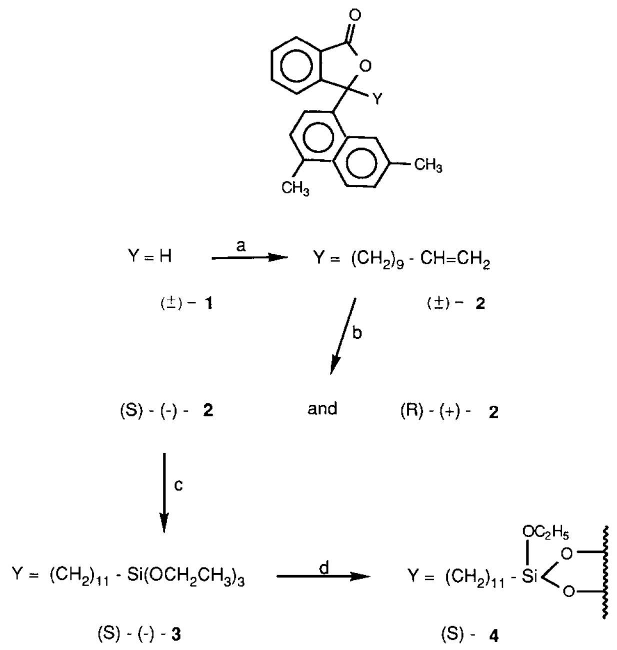


Fig. 1. Preparation of phthalide-based CSP 4. (a) lithium diisopropylamide, tetrahydrofuran (−78°C), undec-10-enyl iodide. (b) Resolution upon preparative (*R*)-N-3,5-dinitrobenzoylphenylglycine CSP. (c) Triethoxysilane, chloroplatinic acid, 110–130°C. (d) 5-μm silica gel, toluene, 110°C.

bonded to 5-μm Spherisorb silica gel by heating the two in toluene for 43 h. The resulting modified silica gel was slurry packed in methanol into a 250 × 4.6 mm I.D. stainless-steel column using conventional packing techniques.

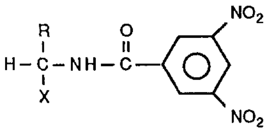
Table I provides pertinent chromatographic data for the resolution of representative examples of various analytes, all as their 3,5-dinitrobenzamide derivatives, on the phthalide-based CSP. In general, the phthalide-based CSP provides useful enantiomer separations for the 3,5-dinitrobenzamides of α-amino acid esters and amides, amines, amino alcohols and amino phosphonates. In comparison to the enantiomeric separation factors afforded by the other reciprocal-type CSPs; the phthalide-based CSP is generally inferior for α-amino acid esters and amides, approximately equivalent for amines, and, except for the hydantoin-based CSP superior for amino alcohols. All of the proceeding are chromatographed as their 3,5-dinitrobenzamides. Fig. 2 shows the resolution of the 3,5-dinitrobenzamide of 1-amino-1-phenylheptane on CSP 4, illustrating the good band shapes and the quality of enantiomer separations which may be obtained on this CSP.

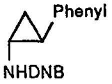
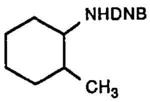
Although providing useful separations for the aforementioned analytes, the phthalide-based CSP is of special interest owing to the relative facility with which it resolves secondary alcohols as their 3,5-dinitrobenzoates. Table II provides the relevant chromatographic data for such separations. In this respect, the phthalide-based CSP is superior to other reciprocal-type CSPs we have prepared. As shown, CSP 4 readily separates the enantiomers of aryl-alkyl, as well as alkyl-alkyl secondary al-

TABLE I

RESOLUTION OF ENANTIOMERIC 3,5-DINITROBENZAMIDES ON PHTHALIDE-BASED CHIRAL STATIONARY PHASE (*S*)-4

α = Chromatographic separation factor; NHDNB = 3,5-dinitrobenzamides.



R	*X*	α	k'_1*	*First eluted***
Isopropyl	$\mathrm{COOCH_3}$	1.11	3.93	*S*
Isobutyl	$\mathrm{COOCH_3}$	1.38	3.00	*S*
Methyl	$\mathrm{COOCH_2CH_3}$	1.32	5.60	*S*
Methyl	COO-Isopropyl	1.50	5.00	*S*
Phenyl	$\mathrm{COOCH_3}$	1.04	13.14	*S*
Benzyl	$\mathrm{COOCH_3}$	1.42	12.29	*S*
1-Naphthyl	$\mathrm{COOCH_2CH_3}$	1.10	10.36	
2-Naphthyl	$\mathrm{COOCH_2CH_3}$	1.55	6.71	
Isopropyl	COO-*n*-Butyl	1.22	1.29	*R*
Isobutyl	COO-*n*-Butyl	1.21	1.35	*R*
Methyl	COO-*n*-Butyl	1.19	4.36	*R*
Phenyl	COO-*n*-Butyl	1.32	2.43	*R*
Methyl	$\mathrm{CH_2CH_3}$	1.14	9.21	
Methyl	*n*-Pentyl	1.19	7.28	
Methyl	Isopropyl	1.17	5.86	
Methyl	Isobutyl	1.15	4.86	
Phenyl	Methyl	1.65	20.62	*S*
Phenyl	Isopropyl	1.38	24.71	*S*
Benzyl	Methyl	1.07	9.86	*R*
	(*trans*)	1.06	11.14	
	(*trans*)	1.19	11.86	
	(*cis*)	1.18	16.43	
Isopropyl	$\mathrm{CH_2OH}$	1.29	2.29	*R*
Benzyl	$\mathrm{CH_2OH}$	1.12	3.57	*R*
2-Butyl	$\mathrm{CH_2OH}$	1.22	6.21	*R*
1-Naphthyl	$\mathrm{CH_2OH}$	1.29	4.00	
4-Biphenyl	$\mathrm{CH_2OH}$	2.18	5.43	
Phenyl	$\mathrm{C(CH_3)_2OH}$	1.53	8.29	
Ethyl	$\mathrm{CH_2OH}$	1.51	2.64	*R*
$\mathrm{CH_3SCH_2CH_2}$	$\mathrm{CH_2OH}$	1.59	3.86	*R*
Ethyl	$\mathrm{CH_2OCH_3}$	1.13	6.86	*R*
Phenyl	$\mathrm{PO(OCH_3)_2}$	1.74	16.93	*R*
4-Methoxyphenyl	$\mathrm{PO(OCH_2CH_3)_2}$	1.61	6.57	*R*
4-Cl-Phenyl	$\mathrm{PO(OCH_2CH_3)_2}$	1.83	4.79	*R*

* Capacity ratio for the first eluted enantiomer. The mobile phase was 2-propanol–hexane (10:90).

** Absolute configuration for first eluted enantiomer.

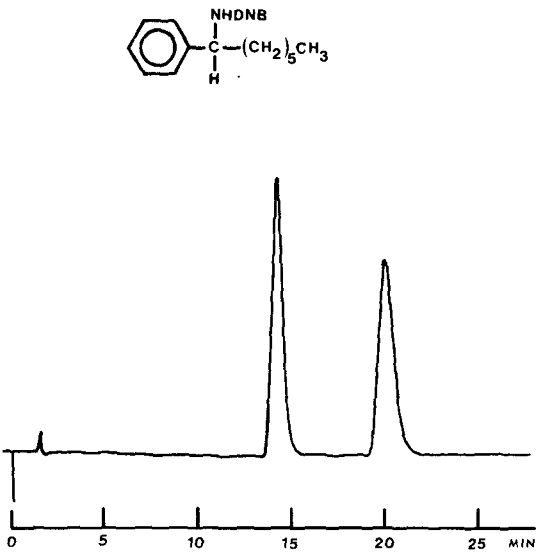
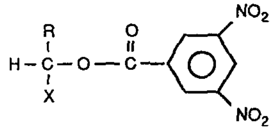


Fig. 2. The resolution on CSP (*S*)-4 of the N-3,5-dinitrobenzoyl derivative of 1-amino-1-phenylheptane. The mobile phase was 2-propanol–hexane (10:90) and the flow-rate was 2 ml/min.

TABLE II

SEPARATION OF ENANTIOMERIC SECONDARY ALCOHOLS AS THEIR 3,5-DINITROBENZAMIDES

α = Chromatographic separation factor.



R	*X*	α	k'_1[*]	*First eluted*[**]
Phenyl	Benzyl	1.43	3.00	(−)
Phenyl	Methyl	1.19	2.29	(+)
Phenyl	CF_3	1.18	2.43	(+)
Phenyl	Propyl	1.18	1.57	(+)
4-Methoxyphenyl	Propyl	1.19	2.71	(+)
Phenyl	*n*-Butyl	1.25	1.50	(+)
Phenyl	Cyclopropyl	1.23	2.14	(+)
Phenyl	Cyclobutyl	1.19	1.93	(+)
Phenyl	Cyclopentyl	1.17	1.90	(+)
Phenyl	Isobutyl	1.27	1.57	(+)-S
Phenyl	*tert.*-Butyl	1.42	1.35	(+)
Phenyl	$COOCH_2CH_3$	1.09	3.00	(−)
1-Naphthyl	Methyl	1.06	3.71	(+)
Ethyl	C≡C–H	1.18	1.57	(+)
n-Propyl	C≡C–H	1.08	1.71	(+)
Methyl	CH(Phenyl)$_2$	1.08	1.78	(−)

[*] Capacity ratio for the first eluted enantiomer. The mobile phase was 2-propanol–hexane (10:90)

[**] Sign of rotation measured at 589 nm for first eluted enantiomer.

cohol 3,5-dinitrobenzoates, thus providing a convenient method for the resolution and accurate determination of enantiomeric purities for these alcohols.

While an in-depth discussion of chiral recognition mechanisms for the separation of various analyte enantiomers on CSP 4 is premature, some general observations can be made. One notes that the relative order of elution for the α-amino acid amide and α-amino acid ester derivatives are opposite. As expected, owing to the reciprocal nature of chiral recognition, the (*S*)-enantiomers of the α-amino amides were the most retained on the (*S*)-phthalide-based CSP since the (*S*)-phthalide enantiomers are more strongly retained on CSPs derived from the 3,5-dinitrobenzamides of α-amino acids[13]. We had expected the chiral recognition mechanisms for the α-amino acid amide and ester derivatives to be similar, thus affording the same elution order for the two. However, an as yet unrecognized chiral recognition process must be accessible to the α-amino ester derivatives and this process selectively retains the (*R*)-enantiomers. This process contributes to a lesser extent during the resolution of the α-amino amides. Noting that the general performance level of the phthalide-based CSP is not as high as initially expected for the separation of the enantiomers of α-amino acid amide and ester derivatives, a possible rationalization entails the competition of the second process. In other words, attachment of the phthalide to a solid support may have produced subtle changes (possibly conformational) that have significantly altered the interactions involved in chiral recognition. As previously reported, the conformation of the naphthyl-substituent with respect to the rest of the molecule, is critical in the chiral recognition of phthalides on the α-amino acid-derived

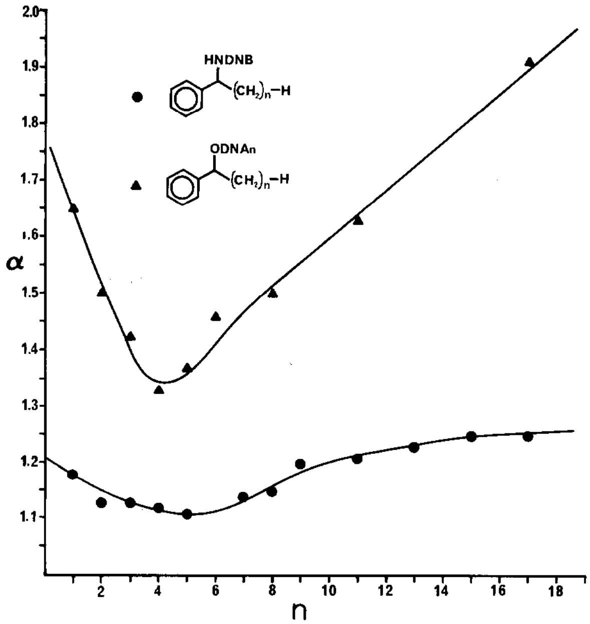


Fig. 3. Chromatographic resolution of a series of 3,5-dinitrobenzoyl and 3,5-dinitroanilido derivatives on the phthalide-based CSP using 2-propanol–hexane (10:90) as mobile phase. The (*S*)-enantiomers are least retained.

CSPs[13]. Hence, the unexpectedly mediocre separation of the enantiomers of α-amino acid ester and amide 3,5-dinitrobenzamide derivatives is suspected to arise from conformation altering intermolecular interactions between neighboring silica-bound phthalide molecules.

Homologous series of α-arylamines, derivatized as their 3,5-dinitrobenzamide, and α-arylalcohols, as their 3,5-dinitroanilido derivatives, were chromatographed on CSP 4 with 2-propanol–hexane (10:90) as the mobile phase. As shown in Fig. 3, the length of the analyte's alkyl chain influences the magnitude of the enantiomeric separation factor, α. Plots such as these have previously been used by us as a vehicle for assignment of absolute configuration for an entire homologous series (based on the known configuration of one member of the series) as well as to provide evidence for the operation of multiple chiral recognition processes[9,10]. Previous studies of the resolution of these homologous series of compounds on the α-arylakylamine reciprocal-type CSPs have shown that with increasing alkyl chain length, a maximum of α is obtained followed by a steady decrease and eventual elution order inversion. This provided strong evidence for the competition of two "opposite sense" mechanisms, the outcome of the competition being influenced by the length of the alkyl group. However, on CSP 4, an increase in alkyl chain length produces an α minimum followed by a steady increase in α-value. No elution order inversion is noted. This is the first time we have observed such a minimum for a homologous series of analytes on any of the aforementioned reciprocal type CSP. The observed curve shape in Fig. 2 is perhaps indicative of two competing "same sense" chiral recognition mechanisms each selectively retaining the (*R*)-enantiomers of the investigated homologous series. In view of its mechanistic interest, the behavior of CSP 4 and analogues is being further studied.

CONCLUSION

A readily prepared phthalide-derived CSP shows a performance level adequate for both analytical and small scale preparative separations of the enantiomers of the 3,5-dinitrobenzoyl derivatives of a great many amines, amino alcohols and alcohols.

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REFERENCES

1 W. H. Pirkle and J. Finn, J. D. Morrison (Editor), *Asymmetric Synthesis*, Vol. 1, Academic Press, New York, 1983, pp. 87–124.
2 V. A. Davankov, A. A. Kurganov and A. S. Bochkov, *Adv. Chromatogr. (N.Y.)*, 21 (1984) 1–116.
3 A. Mannschreck, H. Koiler and R. Wernicke, *Kontakte*, 1 (1985) 40–48.
4 R. W. Souter, *Chromatographic Separations of Stereoisomers*, CRC Press, Boca Raton, FL, 1985, Ch. 3, pp. 87–183.
5 W. H. Pirkle, J. M. Finn, B. C. Hamper, J. Schreiner and J. R. Pribish, in E. L. Eliel and S. Otsuka

(Editors), *Asymmetric Reactions and Processess in Chemistry*, ACS Symp. Ser. No. 185, American Chemical Society, Washington, DC, 1982, Ch. 18 and references cited therein.
6 W. H. Pirkle, M. H. Hyun, A. Tsipouras, B. C. Hamper and B. Bank, *J. Pharm. Biomed. Anal.*, 2 (1984) 173–181.
7 W. H. Pirkle and M. H. Hyun, *J. Chromatogr.*, 322 (1985) 309–320.
8 W. H. Pirkle and M. H. Hyun, *J. Org. Chem.*, 49 (1984) 3043–3046.
9 W. H. Pirkle, M. H. Hyun and B. Bank, *J. Chromatogr.*, 316 (1984) 585–604.
10 W. H. Pirkle and M. H. Hyun, *J. Chromatogr.*, 322 (1985) 295–307.
11 W. H. Pirkle and T. C. Pochapsky, *J. Am. Chem. Soc.*, 108 (1986) 352–354.
12 W. H. Pirkle, T. C. Pochapsky, G. S. Mahler, D. E. Corey, D. S. Reno and D. M. Alessi, *J. Org. Chem.*, 51 (1986) 4991.
13 W. H. Pirkle and T. J. Sowin, *J. Chromatogr.*, 387 (1987) 313.
14 W. H. Pirkle and J. M. Finn, *J. Org. Chem.*, 47 (1982) 4037.
15 L. F. Fieser and M. Fieser, *J. Am. Chem. Soc.*, 55 (1933) 3342.
16 M. S. R. Nair, B. B. Ghatge and S. C. Bhattacharyya, *Indian J. Chem.*, 2 (1964) 355–357.
17 D. G. M. Diaper, *Canadian J. Chem.*, 39 (1961) 1723–1726.
18 F. Brody and M. T. Bogert, *J. Am. Chem. Soc.*, 65 (1943) 1081–1083.
19 W. H. Pirkle and T. J. Sowin, *J. Org. Chem.*, in press.