Useful and Easily Prepared Chiral Stationary Phases for the Direct Chromatographic Separation of the Enantiomers of a Variety of Derivatized Amines, Amino Acids, Alcohols, and Related Compounds

William H. Pirkle,* Thomas C. Pochapsky, George S. Mahler, Debbi E. Corey, Daniel S. Reno, and Donna M. Alessi

School of Chemical Sciences, University of Illinois at Urbana-Champaign, Roger Adams Laboratory, Urbana, Illinois 61801

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Chiral stationary phases (CSPs) derived from 10-undecenyl esters of *N*-(2-naphthyl)-α-amino acids may be prepared from readily available enantiomerically pure α-amino acids. Such CSPs are useful for the chromatographic separation of the enantiomers of a variety of functionalized chiral molecules including many amines, alcohols, α- and β-amino acids, and related compounds, all as their 3,5-dinitrobenzamides, (3,5-dinitrophenyl)ureas, or (3,5-dinitrophenyl)carbamates. Separability factors exceeding 18 at room temperature have been observed in some instances. A simple chiral recognition model is proposed to account for the remarkably regular order of elution of enantiomers from these CSPs.

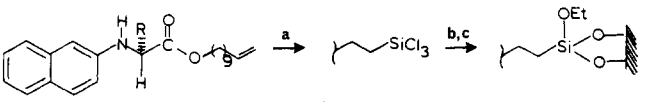
The enantiomers of esters or amides of *N*-aryl-α-amino acids, especially those of the *N*-(2-naphthyl)-α-amino acids, exhibit a high degree of "chiral recognition" toward chiral stationary phases (CSPs) derived from *N*-(3,5-dinitrobenzoyl)-α-amino acids. Chromatographic separability factors for some of these enantiomers exceed ten.[1] Because of the reciprocal nature of chiral recognition (that is, if a CSP derived from compound A resolves the enantiomers of B, a CSP derived from B should, in turn, resolve the enantiomers of A), these compounds seemed promising as precursors for CSPs in their own right. We have reported a simple method for preparing *N*-(2-naphthyl)-α-amino acids of high enantiomeric purity.[2] This reaction, a slight variation on the classical Bucherer reaction, can be carried out with enantiomerically pure α-amino acids and proceeds with little or no racemization. Thus, the CSP precursor is readily available in high enantiomeric purity. Alternatively, such enantiomers can be easily separated on a multigram scale by chromatography on a large column packed with a CSP derived from *N*-(3,5-dinitrobenzoyl)-phenylglycine, thereby making both enantiomers of the *N*-(2-naphthyl)-α-amino acids available.

This paper reports the preparation of CSPs derived from *N*-(2-naphthyl)alanine and *N*-(2-naphthyl)valine, the latter CSP having been recently reported.[3]

The resulting CSPs separate the enantiomers of a wide range of derivatized racemates such as primary amines, α- and β-amino acids, amino alcohols, and alcohols. The chromatographic efficiency and mobile-phase tolerance of these CSPs is similar to that of other microparticulate silica-based HPLC adsorbents. Generally, the peak broadening and asymmetry often seen with chiral polymeric adsorbents are not observed. Readily prepared, these CSPs are now commercially available in prepacked HPLC columns.[4]

Separation of enantiomers on these CSPs occurs in a remarkably regular fashion and the elution orders of enantiomers can be related to absolute configuration for a wide range of racemates by one simple chiral recognition model. Though not yet generally accepted as rigorously relating elution order to absolute configuration, chiral recognition models can, within definable limits, lead to correct assignment of absolute configuration. Like all models, they can be misused, especially if applied without a clear understanding of the intermolecular interactions involved in chiral recognition. Properly used, chiral recognition models allow one to establish absolute configurations of a great many molecules of moderate structural complexity.

Scheme I



[a] (a) $HSiCl_3$, H_2PtCl_6, (catalytic amt), 5-h reflux; (b) Et_3N, EtOH followed by flash chromatography on silica a using CH_2Cl_2/hexane mobile phase; (c) 5 μm silica gel, in vacuum at 110 °C for 12 h in Kugelrohr apparatus.

For mechanistic reasons, the enantiomers of most alcohols, thiols, and amines must be derivatized prior to separation on the present CSPs. This may be accomplished by using 3,5-dinitrophenyl isocyanate (prepared in situ by thermolysis of 3,5-dinitrobenzoyl azide[5-7]) or 3,5-dinitrobenzoyl chloride.[8] Such derivatization is quickly accomplished, is amenable to small-scale work, and enhances the detectability of the analytes.

Owing to the scope, selectivity, predictability, and durability shown by these easily prepared CSPs, we anticipate their use for preparative as well as analytical separations. Since alcohols and thiols will often be resolved as the 3,5-dinitrophenyl carbamates, it is worth noting that carbamates may be cleaved under mild nonracemizing conditions.[9] This approach affords both enantiomers in high and easily determinable enantiomeric purity and, in many instances, of known absolute configuration.

Results and Discussion

Two of the CSPs derived from *N*-aryl-α-amino esters, (*S*)-(−)-11-siloxyundecanyl *N*-(2-naphthyl)alaninate, **1d**, and (*S*)-(−)-11-siloxyundecanyl *N*-(2-naphthyl)valinate, **2d**, show excellent selectivity toward appropriately derivatized enantiomers. Both phases are easily prepared by the reaction of the appropriate 11-(triethoxysilyl)undecanyl *N*-(2-naphthyl-2-amino ester with microparticulate silica.

(1) Pirkle, W. H.; Pochapsky, T. C.; Mahler, G. S.; Field, R. E., *J. Chromatogr.* **1985**, *348*, 89.
(2) Pirkle, W. H.; Pochapsky, T. C. *J. Org. Chem.* **1986**, *51*, 102.
(3) Pirkle, W. H.; Pochapsky, T. C. *J. Am. Chem. Soc.* **1986**, *108*, 352.
(4) Regis Chemical Co., 8210 Austin Avenue, Morton Grove, IL 60053.
(5) Oi, N.; Kitahara, H. *J. Chromatogr.* **1983**, *265*, 117.
(6) Oi, N.; Nagase, M.; Doi, T. *J. Chromatogr.* **1983**, *257*, 111.
(7) Pirkle, W. H.; Mahler, G. S.; Hyun, M. H., *J. Liq. Chromatogr.* **1986**, *9*, 443–453.
(8) Pirkle, W. H.; Hyun, M. H. *J. Org. Chem.* **1984**, *49*, 3034.
(9) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 278.

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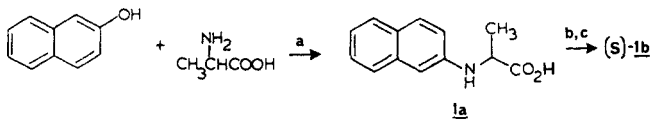
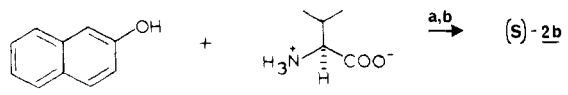
Scheme II



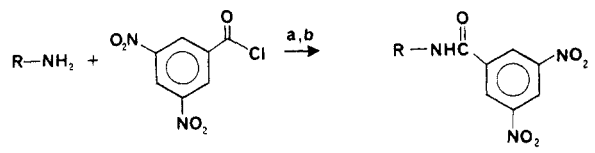
[a] (a) 1 equiv of α-amino acid, 1 equiv of 2-naphthol, 1 equiv of anhydrous Na_2SO_3, 5 vol saturated aqueous NaHSO solution, pressure vessel, 110 °C, 3 days; (b) 1.1 equiv of undec-10-en-1-ol, catalytic amount of HSO_3CH_3, toluene at reflux, azeotropic removal of H_2O, 14 h; (c) preparative chromatography on (*S*)-(−)-*N*-(3,5-dinitrobenzoyl)leucine- or (*R*)-(−)-*N*-(3,5-dinitrobenzoyl)-phenylglycine-derived CSP.

Scheme III



[a] (a) 1 equiv of α-amino acid, 1 equiv of 2-naphthol, 1 equiv of anhydrous Na_2SO_3, 5 vol saturated aqueous NaHSO solution, pressure vessel, 110 °C, 3 days; (b) 1.1 equiv of undec-10-en-1-ol, catalytic amount, HSO_3CH_3, toluene at reflux, azeotropic H_2O removal, 18 h.

Scheme IV



[a] (a) CH_2Cl_2, aqueous $NaHCO_3$, 1.1 equiv of 3,5-dinitrobenzoyl chloride, 10 min; (b) 1 N HCl wash, H_2O wash, saturated NaCl wash, filter through anhydrous Na_2SO_4.

These silanes are derived from the corresponding 10-undecenyl esters (**1b** and **2b**, respectively) (Scheme I) which are, in turn, prepared by acid-catalyzed esterification of the free acids. These acids may be synthesized either enantiomerically pure or as racemates. More than 100 g of the racemic esters have been resolved per pass on a large column filled with 13 kg of the CSP derived from (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine (Scheme II). Alternatively, the enantiomerically pure acids may be prepared by a variation on the classical Bucherer reaction using enantiomerically pure commercial amino acids (Scheme III). Scheme III is particularly attractive as it avoids the necessity of alkylating 2-naphthylamine, a potent carcinogen.[10]

Enantiomer Separations Afforded by CSPs 1d and 2d. Table I lists representative types of compounds the enantiomers of which separate on CSP **1d**. Table II gives similar results for CSP **2d**. In all cases, the mobile phase used is a 2-propanol–hexane mixture and the compounds listed have been converted to either their 3,5-dinitrobenzoyl or 3,5-dinitrophenyl derivatives (Schemes IV and V).

As Tables I and II reveal, there is relatively little difference between CSP **1d** and CSP **2d** in terms of separability factors observed. This is interesting since CSP **2d** is sterically much more hindered at the chiral center. Such similar behavior implies that chiral recognition does not depend heavily upon direct steric interactions between the analytes and the CSP. Rather, the function of the CSP's

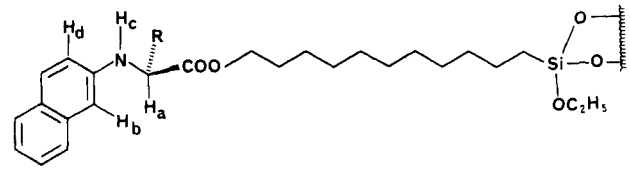
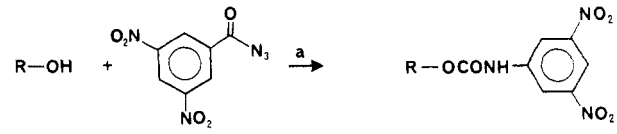


Figure 1. Conformation of CSPs **1d** (R = CH_3) and **2d** (R = i-propyl) during interaction with derivatives of (*S*)-*N*-(3,5-dinitrobenzoyl)-α-amino acid derivatives as determined by $^1H\{^1H\}$ nuclear Overhauser effects (NOE) seen for mixtures of (*S*)-**1e** (methyl ester of (*S*)-**1a**) and (*S*)-*N*-(3,5-dinitrobenzoyl)leucine *n*-propylamide in $CDCl_3$ solution. Labeled protons refer to NOE enhancements reported in the text.

Scheme V



[a] (a) Toluene, 112 °C, 1.1 equiv of 3,5-dinitrobenzoyl azide, 10 min.

alkyl substituent is to exert conformational control, thus making one face of the CSP more accessible than the other. The conformation around the chiral center of the CSP is controlled by several additional factors. For example, delocalization of the nitrogen lone pair into the naphthyl system, evidenced by the relatively low basicity of these compounds, results in the naphthyl ring populating conformations which maximize π–p overlap. Because of dipolar interactions and/or intramolecular hydrogen bonding, one might expect preferential population of the rotamer that places that carbonyl oxygen near the amino proton in uncomplexed **1d**.[11] Preferential population of such a rotamer is in accord with MM2 calculations.

Evidence for population of the conformation shown in Figure 1 *during complexation* is provided by study of the $^1H\{^1H\}$ nuclear Overhauser effects observed for the *S* enantiomer of the methyl ester of *N*-(2-naphthyl)alanine, (*S*)-**1e**, while it interacts in $CDCl_3$ solution with (*S*)-(−)-*N*-(3,5-dinitrobenzoyl)leucine *n*-propylamide (the analyte enantiomer most retained on (*S*)-CSP **1d**). Irradiation of the resonance arising from the proton on the chiral center of **1e** (corresponding to proton a in Figure 1) gives a large (10%) enhancement of the resonance arising from the proton at position 1 of the naphthyl ring (corresponding to proton b in Figure 1). Similar irradiation of amino proton c of **1e** greatly enhances the resonance assigned to proton d at position 3 of the naphthyl ring.[12] These observations indicate the preferential population, while complexed, of a conformation which positions H_a near H_b and H_c near H_d (i.e., that shown in Figure 1). A more complete account of these studies will be published elsewhere.

The molecular "face" presented to the viewer in Figure 1 by CSPs **1d** and **2d** is the one important to chiral recognition. The π-donor (naphthyl ring), acidic (amino proton), and basic (carbonyl oxygen) sites are those at

(10) It should be noted that although compounds derived from *N*-(2-naphthyl)-α-amino acids are very different in physical properties and water solubility from 2-naphthylamine, their physiological properties are uninvestigated and due care should be exercised in their handling and preparation.

(11) The ^1H NMR amino proton chemical shift (δN–*H* = 4.2 ppm) for methyl *N*-(2-naphthyl)alaninate in CCl_4 is 1 ppm downfield of the corresponding resonance in *N*-(2-naphthyl)-2-amino-3-methylpentane (δN–H = 3.2 ppm) and exhibits no concentration dependence, indicating the downfield shift is an intramolecular effect. Comparison of IR spectra for **1e** and *N*-(2-naphthyl)aminomethane in CCl_4 reveals that the N–H stretch for **1e** is 39 cm^{-1} lower in energy (3400 cm^{-1} vs. 3439 cm^{-1}) than the N–H stretch of *N*-(2-naphthyl)aminomethane independent of concentration over a 0.1 M to 0.005 M range.

(12) Pirkle, W. H.; Pochapsky, T. C. *J. Am. Chem. Soc.* **1986**, *108*, 5627.

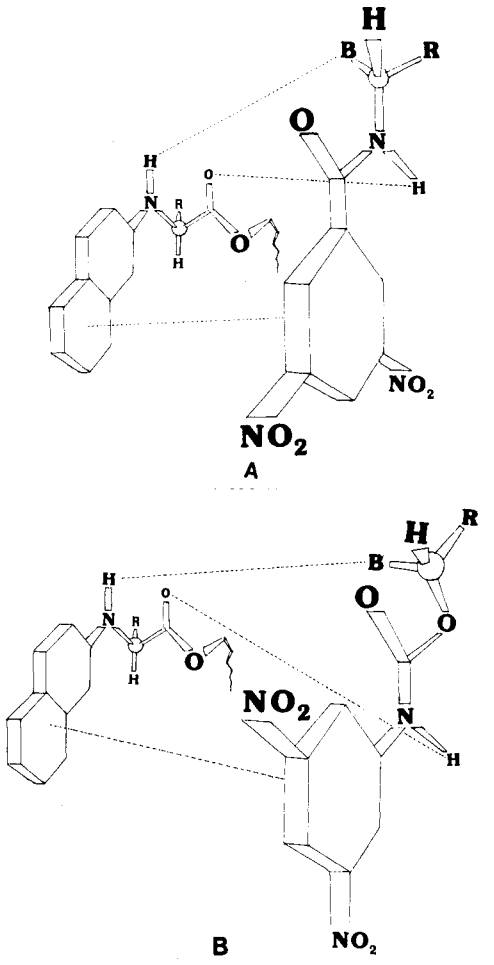


Figure 2. Generalized chiral recognition model between CSPs **1d** (or **2d**) and the most retained enantiomer of (A) a chiral dinitrobenzamide, (B) a chiral (dinitrophenyl)carbamate. "B" indicates a basic site on the analyte molecule which is capable of hydrogen bonding to the CSP N–*H*. Other interactions indicated include a π–π complex between the aryl rings of the CSP and analyte and a hydrogen bond between the acidic N–H proton of the analyte and the ester carbonyl of the CSP.

which the complimentary sites present in the analyte enantiomers may interact strongly. Figure 2A represents a generalized chiral recognition model for the most retained enantiomer of a 3,5-dinitrobenzamide derivative of a chiral amine, while Figure 2B represents essentially the same model for a (3,5-dinitrophenyl)carbamate derivative of a chiral alcohol. In all cases, the enantiomer most retained by the CSP is that which, while maintaining the π–π and stronger hydrogen bonding interactions, holds the *basic* group "B" in close proximity to the amino proton of the CSP *while maintaining a low energy conformation.* B is defined as a basic hydrogen bonding site and, in most instances, is easily identified. For α- and β-amino acid derivatives, for example, B is the C-terminal carbonyl oxygen. Since amide carbonyls are more basic than ester carbonyls, it is not surprising that larger separability factors are observed for C-terminal amide derivatives of amino acids than for C-terminal ester derivatives (**4** vs. **6f**, Table I). For α-arylalkylamine and arylalkylcarbinol derivatives, the aryl group serves as B.[13]

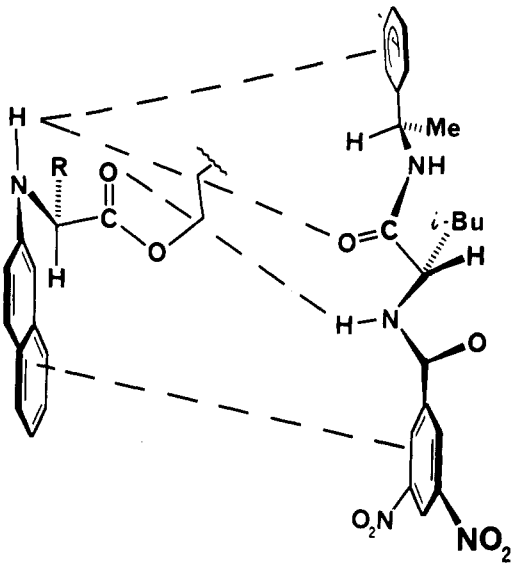


Figure 3. Tentative explanation of diastereomeric recognition between CSP **2d** and **30a**. The most retained diastereomer is shown.

In some instances, more than one basic site may be present. Note that the separability factors for derivatives of α-aryl-α-amino acids (e.g., phenylglycine, **4**, **6a–h**) are reduced relative to those of most other α-amino acid derivatives. Here, the ability of the aryl group to function as B in the R enantiomer enhances the retention of the least retained enantiomer. In terms of chiral recognition, this partially compensates for the ability of the C-terminal carboxyl to function as B in the *S* enantiomer.[13] The presence of electron-withdrawing or -donating phenyl substituents affects the magnitudes of the separability factors of phenylglycines **6a–h** in the expected way. They either diminish or enhance the ability of the phenyl to contribute to the retention of the less retained *R* enantiomer.

Whether the *R* or *S* enantiomer of an analyte is most retained depends upon the configuration of the CSP, the structure of the analyte, and the priority sequence of the substituents about the chiral center(s). In the absence of unusual priority sequences, the (*S*)-CSPs described here will more strongly retain the *S* enantiomers of the derivatized α-amino acids, α-arylalkylamines, and arylalkylcarbinols.

Of particular interest is the separation of the stereoisomeric derivatives of *N*-(3,5-dinitrobenzoyl)leucine prepared from chiral amines or α-amino esters (**3a–f**, Table II). Here, separation of diastereomers as well as separation of enantiomers is observed. Enantiomer separation is facile whereas diastereomer separation is relatively more difficult. Clearly, the effect of a chiral center remote from the major interaction sites is of minor importance. While it is premature to do more than speculate on the origin of diastereoselectivity on these CSPs, we do note for **3b** that the most retained diastereomer is the one in which (in the

(13) See, for example: Basila, M. R.; Saier, E. L.; Cousins, L. R. *J. Am. Chem. Soc.* **1965**, *87*, 1665.

(14) The separability factor, α, is the ratio of retention times measured from the time of elution of a nonretained solute. This ratio is related to the difference in energy of the diastereomeric adsorbates formed when the enantiomers interact with the CSP.

(15) The resolution, R_s, of the two enantiomers is a measure of the chromatographic efficiency of the separation. An $R_s \gtrsim 1$ indicates effectively complete band separation. R_s is defined by the equation

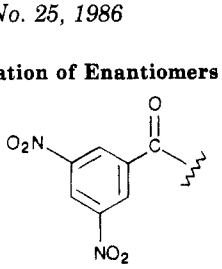
$$R_s = 2(t_2' - t_1')/(w_2 + w_1)$$

where the t_i are the corrected retention times of the enantiomers and the w_i are the widths of the peaks at their bases.

(16) The capacity ratio, k_1', is the number of void volumes of mobile phase beyond the initial void volume needed to elute the first enantiomer.

(17) The absolute configuration of the most-retained enantiomer is determined from chromatography of samples enriched in one enantiomer of known configuration.

Table I. Separation of Enantiomers on CSP 1d. Mobile Phase is % v/v 2-Propanol in Hexane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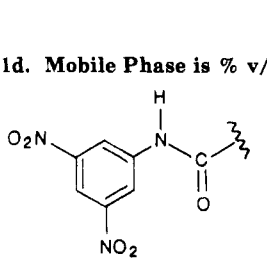
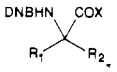
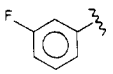
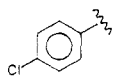
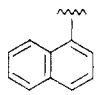
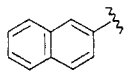
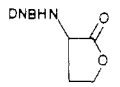
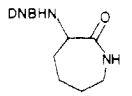
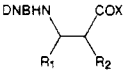

= DNAn

compd	R_1	R_2	X	α[14]	R_s[15]	k_1'[16]	mobile phase	enantiomer most retained[17]
			A. Derivatives of α-Amino Acids					
								
3a	H	$-CH_2CH(CH_3)_2$	$NH(CH_2)_4H$	15.40	14.3	2.0	10%	L, (*S*)
4	H			5.54	14.5	4.4	10%	L, (*S*)
5f	H	$-(CH_2)_6H$	OCH_2CH_3	5.52	16.9	3.7	10%	
6a	H		OCH_2CH_3	2.60	9.5	4.0	20%	
6b	H		OCH_2CH_3	2.68	9.9	4.0	20%	
6c	H		OCH_2CH_3	2.46	10.8	4.7	20%	
6d	H		OCH_2CH_3	2.45	11.9	5.3	20%	
6e	H		OCH_2CH_3	2.30	7.7	3.8	20%	
6f	H		OCH_3	2.08	9.1	5.2	20%	L, (*S*)
6g	H		OCH_2CH_3	2.13	7.7	5.9	20%	
6h	H		OCH_2CH_3	2.28	9.4	6.8	20%	
7	CH_3	$-CH_2CH(CH_3)_2$	$NH(CH_2)_4H$	1.41	4.2	9.8	5%	
8				1.74	7.2	32.7	5%	
9				2.63	11.3	6.5	5%	L, (*S*)
			B. Derivatives of β-Amino Acids					
								
10a	$-CH_3$	H	$O(CH_2)_8H$	1.58	3.7	2.6	10%	
10b	$-CH_2CH_3$	H	$O(CH_2)_8H$	1.81	5.1	3.2	10%	
10c	$-(CH_2)_3H$	H	$O(CH_2)_8H$	1.64	3.5	3.3	10%	L, *S*
10d	$-CH(CH_3)_2$	H	OCH_3	2.03	7.0	4.9	10%	L, *R*
10e	$-(CH_2)_6H$	H	$O(CH_2)_8H$	1.88	4.7	2.7	10%	
			C. Derivatives of Amines and Amino Alcohols					
								

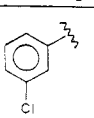
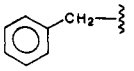
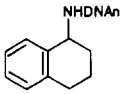
compd	R_1	R_2	R_3	derivative	α[14]	R_s[15]	k_1'[16]	mobile phase	enantiomer most retained[17]
11	H			DNAn	1.30	3.7	13.5	10%	

Table I (Continued)

compd	R_1	R_2	R_3	derivative	α^{14}	R_s^{15}	$k_1'^{16}$	mobile phase	enantiomer most retained[17]
12	H		CH_3	DNAn	1.25	2.2	5.3	10%	
13a	H	$H(CH_2)_2-$	CH_3	DNB	1.16	1.2	1.7	20%	(*R*)
13a	H	$H(CH_2)_2-$	CH_3	DNAn	1.15	1.2	4.2	10%	(*R*)
13b	H	$H(CH_2)_5-$	CH_3	DNAn	1.21	1.4	3.3	10%	(*R*)
13c	H	$H(CH_2)_8-$	CH_3	DNAn	1.21	1.4	2.8	10%	
14a	H		CH_3	DNB	1.40	2.9	7.3	10%	(*S*)
14h	H		$-(CH_2)_{17}H$	DNAn	1.43	4.0	3.9	10%	
15a		$-CH_2OH$	CH_3	DNAn	3.79	8.6	1.5	20%	L, (*S*)
16		$-CH_2CH(C_6H_5)_2$	CH_3	DNAn	1.26	2.6	6.2	10%	
17					2.58	9.4	6.6	10%	

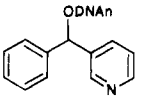
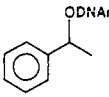
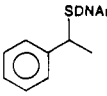
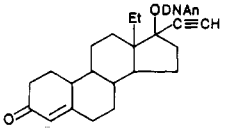
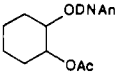
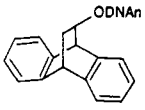
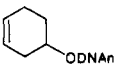
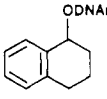
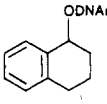
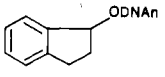
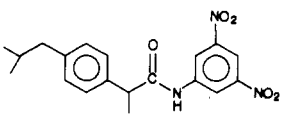
compd	R_1	derivative	α^{14}	R_s^{15}	$k_1'^{16}$	mobile phase	enantiomer most retained[17]
		D. Derivatives of Alcohols and Thiols					
18			1.87	6.1	7.7	10%	
19a			1.15	1.2	3.2	10%	
20			1.20	1.5	3.7	10%	
21			1.38	3.6	27.0	10%	L
22			1.19	1.4	2.7	10%	
23			1.05	0.7	4.9	10%	
24			1.08	0.7	2.4	10%	
25			1.18	1.2	3.4	10%	(*S*)
25			1.46	4.8	22.9	1%	(*S*)
26			1.15	1.2	3.4	10%	
		E. Carboxylic Acid Dinitroanilide					
27			1.33	1.1	1.5	10%	

Table II. Separation of Enantiomers on CSP 2d. Mobile Phase is % v/v 2-Propanol-Hexane

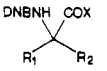
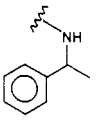
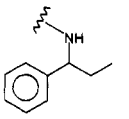
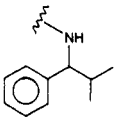
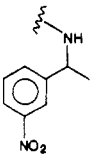
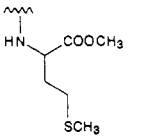
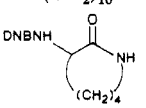
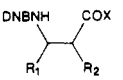
compd	R_1	R_2	X	α	R_s	k_1'	mobile phase	enantiomer most retained
			A. Derivatives of α-Amino Acids					
								
3a	H	$-CH_2CH(CH_3)_2$	$-NH(CH_2)_4H$	17.66	10.5	0.4	5%	L, (*S*)
3b	H	$-CH_2CH(CH_3)_2$						
			(*RR*)-(*SS*)	11.86	11.7	1.7	20%	(*SS*)
			(*RS*)-(*SR*)	18.00	12.8	1.7	20%	(*SR*)
3c	H	$-CH_2CH(CH_3)_2$						
			(*RR*)-(*SS*)	12.14	11.8	1.7	20%	(*SS*)
			(*RS*)-(*SR*)	17.85	12.9	1.7	20%	(*SR*)
3d	H	$-CH_2CH(CH_3)_2$						
			(*RR*)-(*SS*)	12.57	11.3	1.7	20%	(*SS*)
			(*RS*)-(*SR*)	18.71	12.9	1.7	20%	(*SR*)
3e	H	$-CH_2CH(CH_3)_2$						
			(*RR,RS*) (*SR,SS*)	17.00	13.6	3.0	20%	(*SR*, *SS*)
3f	H	$-CH_2CH(CH_3)_2$						
			(*RS*)-(*SR*)	11.78	20.4	2.7	20%	(*SR*)
			(*RR*)-(*SS*)	18.66	21.1	1.9	20%	(*SS*)
5a	H	$-CH_3$	$-OCH_2CH_3$	4.71	13.9	2.6	20%	L, (*S*)
5b	H	$-(CH_2)_2H$	$-OCH_2CH_3$	5.49	15.5	2.4	20%	
5c	H	$-(CH_2)_3H$	$-OCH_2CH_3$	5.40	12.9	2.3	20%	
5d	H	$-(CH_2)_4H$	$-OCH_2CH_3$	5.92	12.8	2.2	20%	L, (*S*)
5e	H	$-(CH_2)_5H$	$-OCH_2CH_3$	5.80	13.3	2.2	20%	
5f	H	$-(CH_2)_6H$	$-OCH_2CH_3$	5.73	12.6	2.1	20%	
5g	H	$-(CH_2)_8H$	$-OCH_2CH_3$	5.52	12.9	2.1	20%	
5h	H	$-(CH_2)_9H$	$-OCH_2CH_3$	5.32	12.8	1.9	20%	
5i	H	$-(CH_2)_{10}H$	$-OCH_2CH_3$	5.45	12.1	1.7	20%	
5j	H	$-(CH_2)_{11}H$	$-OCH_2CH_3$	5.33	10.7	1.7	20%	
5k	H	$-(CH_2)_{12}H$	$-OCH_2CH_3$	5.19	8.5	1.6	20%	
5l	H	$-(CH_2)_{14}H$	$-OCH_2CH_3$	5.06	9.9	1.5	20%	
5m	H	$-(CH_2)_{15}H$	$-OCH_2CH_3$	4.96	10.0	1.5	20%	
	H	$-(CH_2)_{16}H$	$-OCH_2CH_3$	5.11	10.0	1.4	20%	
9				2.58	4.4	2.4	5%	L, (*S*)
			B. Derivatives of β-Amino Acids					
								
28	$-CH_2COO(CH_2)_4H$	H	$-O(CH_2)_4H$	1.37	3.9	11.7	5%	
29	H	$-CH_3$	$-OCH_3$	1.12	1.5	14.0	5%	
30	$-COOCH_3$	H	$-OCH_3$	1.11	1.4	14.0	5%	
31	H	$-(CH_2)_4H$	$-O(CH_2)_4H$	1.12	1.6	10.0	5%	

Table II (Continued)

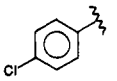
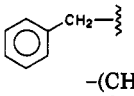
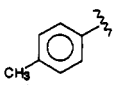
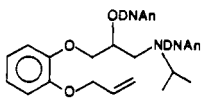
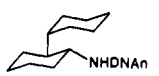
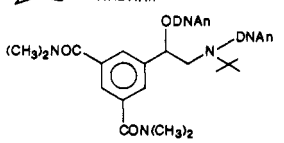
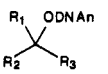
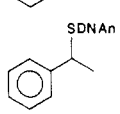
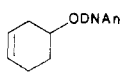
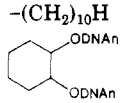
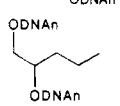
compd	R_1	R_2	R_3	derivative	α	R_s	k_1'	mobile phase	enantiomer most retained
		C. Derivatives of Amines and Amino Alcohols							
									
11	H			DNAn	1.16	2.2	8.8	10%	
12	H		$-CH_3$	DNAn	1.19	2.1	6.4	5%	
13a	H	$-(CH_2)_2H$	$-CH_3$	DNAn	1.19	1.5	5.9	5%	(*R*)
13c	H	$-(CH_2)_8H$	$-CH_3$	DNAn	1.10	1.3	6.7	5%	
14a	H		$-CH_3$	DNB	1.30	3.1	5.2	10%	(*S*)-(−)
14a	H			DNAn	1.30	2.8	5.0	10%	(*S*)-(−)
14b	H		$(CH_2)_2H$	DNAn	1.34	3.5	4.6	10%	(−)
14c	H		$(CH_2)_3H$	DNAn	1.34	3.4	4.3	10%	(−)
14d	H		$(CH_2)_4H$	DNAn	1.33	3.5	3.9	10%	(−)
14e	H		$(CH_2)_5H$	DNAn	1.34	3.4	3.8	10%	(−)
14f	H		$(CH_2)_7H$	DNAn	1.33	3.4	3.5	10%	(−)
14g	H		$(CH_2)_{11}H$	DNAn	1.30	3.0	3.2	10%	L, (*S*)
15a	H	$-CH_2OH$	$-CH_3$	DNAn	4.09	11.8	2.4	10%	L, (*S*)
15b	H	$-CH_2OH$	$-(CH_2)_3H$	DNAn	4.52	9.0	1.4	10%	
32	H		$-CH_3$	DNAn	1.40	3.7	4.8	10%	(−)
33	H			DNAn	3.21	7.2	3.3	10%	
34				DNAn	1.41	3.6	13.2	5%	
35				DNAn	1.24	2.2	2.6	10%	
36					1.10	1.2	42.2	10%	
		D. Derivatives of Alcohols, Diols, Hydroxy Esters and Thiols							
									
18	H				2.51	10.6	10.8	5%	
19a	H		$-CH_3$		1.18	1.8	6.4	5%	*S*-(−)
19b	H		$-(CH_2)_2H$		1.23	2.1	5.6	5%	(−)
19c	H		$-(CH_2)_3H$		1.27	2.3	5.4	5%	(−)

Table II (Continued)

compd	R_1	R_2	R_3	α	R_s	k_1'	mobile phase	enantiomer most retained
19d	H		$-(CH_2)_4H$	1.24	2.0	3.2	10%	(-)
19e	H		$-(CH_2)_5H$	1.24	2.1	3.0	10%	(-)
19f	H		$-(CH_2)_6H$	1.24	1.4	3.6	5%	(-)
19g	H		$-(CH_2)_7H$	1.24	1.2	3.5	5%	(-)
19h	H		$-(CH_2)_8H$	1.24	1.2	3.5	5%	(-)
19i	H		$-(CH_2)_{11}H$	1.24	1.6	3.1	5%	(-)
20				1.40	3.5	9.4	5%	
24				1.09	0.6	5.4	5%	
37	$-CF_3$		$-C\equiv CH$	1.47	3.2	4.9	5%	
38	H	$-(CH_2)_{10}H$	$-COOCH_3$	3.31	8.8	1.0	20%	
39				1.12	1.3	5.7	5%	
40				1.15	1.3	5.6	5%	

conformation expected to be most stable) the basic groups of *both* chiral moieties project in the direction of the amino proton of the stationary phase (Figure 3). When the aromatic ring of the (1-phenylethyl)amino moiety bears a nitro substituent (**3e**), diastereomeric recognition is lost. This may indicate that even less than optimally located secondary basic sites interact with the CSP to a degree adequate to product modest diastereoselectivity. This hypothesis is being examined more thoroughly.

In some instances, enantiomers not conforming totally to the requirements of the model in Figure 2 have been separated on CSPs **1d** and **2d**. For example, the *R* enantiomers of *N*-(3,5-dinitrophenyl)urea and 3,5-dinitrobenzamide derivatives of 2-aminobutane and homologues (**13a–c**, Table I) are more strongly retained than their antipodes. However, the separability factors are quite small. The chiral recognition shown here presumably stems from the size difference between the methyl and alkyl substituents (ethyl for **13a**) rather than from differences in their basicity. The usual π–π and hydrogen-bonding interactions shown in Figure 4 are invoked. During these, the ethyl group of (*S*)-**13a** is held in proximity to the CSP. The resulting steric interaction is more severe than it is in the alternate diastereomeric adsorbate where it would be the smaller methyl group which is held in the proximate position. Hence, the *R* enantiomer is the last to be eluted. The magnitudes of the separability factors increase for the derivatives of other 2-aminoalkanes as the size of the alkyl substituent increases. However, these separability factors never become very large. It is observed that differential steric repulsions are generally less effective in generating stability differences between diastereomeric adsorbates than is the presence (as opposed to the absence) of a stereochemically dependent third bonding interaction. Studies to further our understanding of the mechanism(s) of chiral recognition employed by these CSPs is underway.

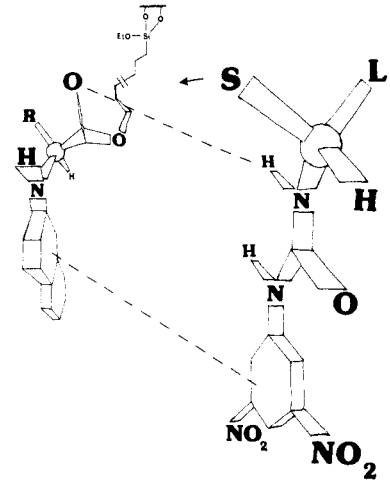


Figure 4. Chiral recognition between CSP **2d** and the most retained enantiomer (*R*) of chiral alkylamine (3,5-dinitrophenyl)ureas **13a–c**. The more retained enantiomer is that which places the smaller alkyl group near to the CSP while maintaining a π–π interaction and the N–*H*···O=C hydrogen bond with the CSP.

Experimental Section

All reagents were of reagent or pharmaceutical grade and were used without further purification. All HPLC experiments were performed on an Altex 100A pump and either a Beckmann 165 multiwavelength detector operating at 254 and 280 nm or an Altex 152 UV detector operating at 254 nm in series with a Rudolph Autopol III digital polarimeter operating at 589 nm (sodium D line) and equipped with a 20-cm flow cell. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Varian XL 200-MHz FT NMR spectrophotometer equipped with a switchable probe unless otherwise noted. All ^{1}H and ^{13}C NMR resonances are recorded in parts per million relative to tetramethylsilane. Infrared spectra were obtained on an IBM IR32 FT IR or Nicolet 7000 FT IR spectrophotometer. Low resolution mass spectra were obtained on a Varian MAT CH-5 with electron-impact ionization. High resolution mass spectra were obtained on a Varian 731 mass spectrometer using electron-impact ionization. Optical rotations were recorded on a Rudolph Autopol III digital polarimeter equipped with a 1 dm flow cell operating at 589 nm (sodium D line). Elemental analyses were performed by J. Nemeth and Associates of the University of Illinois microanalytical service. Melting points were obtained on a Buchi melting point apparatus and are uncorrected.

Enantiomeric purities of CSP precursors were established by chromatography on commercial analytical columns (J. T. Baker or Regis Chemical) containing covalent CSPs derived from (*S*)-*N*-(3,5-dinitrobenzoyl)leucine or (*R*)-*N*-(3,5-dinitrobenzoyl)-phenylglycine. It should be noted that the elution orders of CSP precursors **1b** and **2b** differ on L-DNBLeu and D-DNBPG CSPs, allowing either enantiomer to be distinguished easily from front-running impurities.

I. Preparation of CSP 1d (Scheme II). A. (*RS*)-*N*-(2-Naphthyl)alanine (1a) was prepared by the method reported earlier:[2] mp 170 °C; ^{1}H NMR (acetone-d_6) δ 1.5 (d, J = 7.5 Hz, 3 H), 4.23 (q, J = 7.5 Hz, 1 H), 6.85 (d, J = 3 Hz, 1 H), 7.05–7.12 (dd, J = 9 Hz, J = 3 Hz, 1 H), 7.35–7.50 (dt, J = 7 Hz, 2 H), 7.58–7.68 (m, 3 H); ^{13}C NMR (Me_2SO-d_6) δ 18.0, 50.9, 104.9, 119.4, 122.7, 126.9, 127.1, 128.3, 128.4, 129.5, 136.2, 146.8, 175.7; MS (10 eV), m/e (relative intensity) 216 (M + 1, 20.5), 215 (M^+, 100), 171 (92), 170 (100), 156 (62), 128 (42.8), 127 (48.5). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.61. Found: C, 72.56; H, 6.14; N, 6.42.

B. (*S*)-(−)-1-Undec-10-enyl *N*-(2-Naphthyl)alaninate (1b). To 30 g (0.14 mol) of dried (*RS*)-**1a** in a 500-mL, one-necked round-bottomed flask were added 26.2 g (0.154 mol) of undec-10-en-1-ol (Aldrich) and 200 mL of toluene along with 0.5 mL of methanesulfonic acid. The flask was equipped with a Dean–Stark water trap and heated under reflux until no more water was collected (about 16 h). The reddish solution was cooled, washed twice with 50 mL portions of 5% aqueous $NaHCO_3$ and once with 50 mL of saturated NaCl solution, filtered through Celite, and concentrated under vacuum. The crude ester was purified by flash chromatography on silica gel using 30% CH_2Cl_2 in hexane as eluent. Fractions were monitored for purity by TLC on silica gel using CH_2Cl_2 as the mobile phase. Ethanolic 1% phosphomolybdic acid was used as a visualizing agent (**1b**, R_f 0.39). After concentration of the product fractions, 50 g (97%) of purified racemic **1b** was obtained. Separation of the enantiomers of **1b** was accomplished for 100 g of racemate in one pass on 13 kg of commercial (*R*)-DNBPG (Baker) silica-bonded CSP in a 4 ft × 6 in. stainless steel column (10% 2-propanol/hexane mobile phase) using an automated MPLC system. The first eluted enantiomer (ee > 98% by HPLC on (*R*)-DNBPG) was (*S*)-(−)-**1b**: 25 g (100%) of yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.10–1.45 (m, 14 H), 1.56 (d, J = 3.4 Hz, 3 H), 1.58 (m, 2 H), 4.12 (t, J = 3.2 Hz, 2 H), 4.26 (q, J = 3.4 Hz, 1 H), 4.28 (b, 1 H), 4.93 (m, 1 H), 4.95 (dm, J = 13 Hz, 1 H), 6.81 (d, J = 1.2 Hz, 1 H), 6.92 (dd, J = 1.2 Hz, J = 4.4 Hz, 1 H), 7.18 (t, J = 4 Hz, 1 H), 7.33 (t, J = 4 Hz, 1 H), 7.56–7.68 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 18.7, 21.3, 26.3, 28.8, 29.0, 29.4, 29.5 (m), 34.0, 52.0, 64.7, 105.4, 114.2, 114.3, 118.0, 122.3, 126.1, 126.2, 127.7, 127.9, 129.0, 136.8, 139.0, 144.3, 174.8; IR (neat) 742, 806, 827, 1188, 1225, 1263, 1392, 1468, 1522, 1603, 1632, 1730, 2855, 2926, 3055, 3397 cm^{-1}; MS (70 eV), m/e (relative intensity) 366 (M^+, 4.6), 170 (100), 132 (46.0), 77 (14.9). Anal. Calcd for $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.35; H, 8.98; N, 3.81. $[\alpha]^{20}_D$ −94.0° (c 1.8, CCl_4).

C. (*S*)-(−)-11-(Triethoxysilyl)-1-undecanyl *N*-(2-Naphthyl)alaninate (1c). Two grams (2.72 mmol) of dried ester (*S*)-**1b** were dissolved in 20 mL of $HSiCl_3$ (Aldrich) and 5 mL of CH_2Cl_2 in a dry 100-mL one-necked round-bottomed flask equipped with a magnetic stirrer. A solution of 0.01 g of H_2PtCl_6 (Mallinkrodt) in 0.5 mL of 2-propanol was added dropwise with stirring to the $HSiCl_3$ solution. A precipitate formed immediately. The flask was fitted with a reflux condenser and blanketed with N_2, and the reaction mixture was warmed to reflux (40 °C) for 5 h. After the reflux condenser was then replaced with a distillation head, excess $HSiCl_3$ was removed at aspirator pressure. Twenty milliliters of dry CH_2Cl_2 was added as a chaser before the solution was concentrated on a rotary evaporator. To the remaining clear yellow oil was added dropwise 15 mL of a 1:1 mixture of absolute ethanol and dry triethylamine. After concentrating the solution on a rotary evaporator, the residue was dissolved in 50 mL of dry diethyl ether. This solution was filtered through Celite to remove triethylammonium chloride. The filter cake was washed with an additional 50 mL of diethyl ether, and the filtrates were concentrated. The resulting oil was purified by flash chromatography on silica gel (**1c**, R_f 0.12, CH_2Cl_2), yielding 1.74 g (60% of theoretical) of (*S*)-**1c** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.62 (m, 2 H), 1.10–1.50 (m, 31 H), 1.53 (t, J = 3.4 Hz, 3 H), 3.84 (q, J = 3.5 Hz, 6 H), 4.12 (t, J = 3.2 Hz, 2 H), 4.26 (q, J = 3.4 Hz, 1 H), 4.28 (b, 1 H), 6.81 (d, J = 1.2 Hz, 1 H), 6.92 (dd, J = 1.2 Hz, 4.4 Hz, 1 H), 7.18 (t, J = 4 Hz, 1 H), 7.33 (t, J = 4 Hz, 1 H), 7.53–7.65 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 11.4, 18.2, 18.8, 22.8, 26.0, 28.7, 29.2, 29.7, 30.0, 33.5, 52.1, 58.6, 65.3, 105.5, 118.2, 122.3, 124.2, 124.4, 125.8, 126.0, 127.1, 132.8, 145.3, 174.3; IR (neat) 740, 802, 826, 1220, 1400, 1460, 1462, 1520, 1600, 1625, 1730, 2860, 2920, 2959, 3380 cm^{-1}; HRESMS, calcd for $C_{30}H_{49}NO_5Si$ 531.3373, found 531.3376.

D. (*S*)-11-Siloxy-1-undecanyl *N*-(2-Naphthyl)alaninate CSP 1d. To 5 g of 5-μm silica gel (Shperisorb) suspended in CH_2Cl_2 (50 mL) was added 1.5 g (1.88 mmol) of the triethoxysilane **1d**. After thorough mixing, the solvent was evaporated, and the silica gel–silane mixture was placed in a 100-mL round-bottomed flask and heated to 110 °C under a vacuum (0.5 torr) for 15 h while being rocked in a Kugelrohr apparatus. Afterward, the silica gel was washed with methanol, suspended in CCl_4, and allowed to settle. Fines were removed by decantation and the settled material was slurry-packed (methanol) into a 4.6 mm × 25 cm stainless steel HPLC column. The column was washed thoroughly with CH_2Cl_2 to remove the methanol, and a solution of 1 g of hexamethyldisilazane (Petrarch) in 10 mL of CH_2Cl_2 was pumped through it and followed by an additional CH_2Cl_2 wash. Elemental analysis of the derivatized but non-end-capped silica gel showed a loading of 0.19 mmol of silane/g of silica gel by N, 0.23 mmol/g by C.

II. Preparation of CSP 2d (Scheme III). A. (*S*)-(−)-*N*-(2-Naphthyl)valine (2a) was prepared by a modified Bucherer reaction. Ten grams (85 mmol) of L-valine (Sigma), 12.3 g (85 mmol) of 2-naphthol (Aldrich), and 10.8 g (85 mmol) of anhydrous Na_2SO_3 were placed in a pressure vessel equipped with a magnetic stirrer along with 60 mL of saturated aqueous $NaHSO_3$ solution. The vessel was heated with stirring to 115 °C. A second liquid layer began to form after 1 day. After 3 days, the mixture was cooled and poured into a 1000-mL beaker. The reaction vessel was washed alternately with acetone and 2 N Na_2CO_3 (10-mL portions). The washings were added to the reaction mixture which was then diluted to 500 mL with water and the pH adjusted to 8.8–9.0 with saturated aqueous Na_2CO_3. The mixture was extracted with two 50-mL portions of CH_2Cl_2 to remove unreacted β-naphthol. The CH_2Cl_2 phase was back-washed twice with 20-mL portions of 5% $NaHCO_3$ and these washes were combined with the original aqueous layer. The pH was adjusted to 3–3.5 using 6 N HCl (CO_2 and SO_2 are evolved!). The resultant white precipitate was collected by filtration, and the aqueous filtrate was extracted twice with ethyl acetate. The combined ethyl acetate extracts were concentrated under vacuum, the residue added to the collected solid, and the mixture was recrystallized from 95% ethanol to give, after two crops, 5.1 g (21.3 mmol, 25%) of (*S*)-(−)-**2a**: mp 125 °C; ^{1}H NMR (acetone-d_6) δ 1.05–1.15 (dd, J = 3 Hz, 6 H), 2.13–2.32 (m, J = 3 Hz, J = 3 Hz, 1 H), 4.0 (d, J = 3 Hz, 1 H), 6.85 (d, J = 3 Hz, 1 H), 7.05–7.12 (dd, J = 9 Hz,

J = 3 Hz, 1 H), 7.05–7.35 (dt, J = 7 Hz, 1 H), 7.58–7.68 (m, 3 H); ^{13}C NMR (acetone-d_6) δ 19.2, 19.5, 31.7, 62.8, 104.9, 119.4, 122.7, 126.9, 127.1, 128.3, 128.4, 129.5, 136.2, 146.8, 174.9; MS (70 eV), m/e (relative intensity) 244 (M + 1$^+$, 7.2), 243 (M$^+$, 43.7), 200 (35.8), 198 (95.9), 154 (100), 143 (34.3), 127 (85.0); HRESMS, calcd for $C_{15}H_{17}NO_2$ 243.1255, found 243.1255. Anal. Calcd for the ethyl ester of **2a**, $C_{17}H_{21}NO_2$: C, 75.35; H, 7.80; N, 5.16: Found: C, 75.33; H, 8.05; N, 4.90. The enantiomeric purity of the ethyl ester was determined to be greater than 98% by HPLC on a Baker L-DNBLeu column. $[\alpha]^{20}_D$ −168.7° (c 1.0, THF) for free acid **2a**.

B. (*S*)-(−)-1-Undec-10-enyl *N*-(2-Naphthyl)valinate (2b). This compound was prepared by the same procedure as reported for the preparation of **1b**. However, no optical resolution was necessary in this case. From 2.0 g of **2** was obtained 3.0 g (92%) of (*S*)-(−)-**2** as a yellow oil: R_f 0.56 (CH_2Cl_2, silica gel); ^{1}H NMR ($CDCl_3$) δ 1.07 (dd, J = 3.6 Hz, 6 H), 1.13–1.40 (m, 16 H), 1.58 (m, J = 3.8 Hz, 2 H), 2.04 (q, J = 3.4 Hz, 1 H), 2.18 (sept, J = 3.6 Hz, J = 3.4 Hz, 1 H), 3.90 (b, 1 H), 3.98 (d, J = 3.4 Hz, 1 H), 4.08 (t, J = 3.8 Hz, 2 H), 4.94 (m, 1 H), 4.96 (d, J = 13 Hz, 1 H), 5.80 (dm, J = 13 Hz, 1 H), 6.83 (d, J = 1 Hz, 1 H), 6.93 (dd, J = 13 Hz, 1 H), 6.83 (d, J = 1 Hz, 1 H), 6.93 (dd,J = 1 Hz, J = 4 Hz, 1H), 7.18 (td, J = 1 Hz, J = 3.4 Hz, 1 H), 7.33 (td, J = 1 Hz, J = 3.4 Hz, 1 H), 7.55–7.68 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 19.3, 19.6, 26.2, 28.8, 29.0, 29.2, 29.5, 29.7, 31.7, 34.3, 62.5, 65.1, 105.5, 114.3, 118.2, 122.2, 126.1, 126.3, 127.7, 127.9, 129.0, 135.8, 139.5, 175.9; IR (neat) 742, 806, 827, 1055, 1188, 1147, 1163, 1392, 1460, 1522, 1603, 1630, 2855, 2926, 3404 cm^{-1}. Anal. Calcd for $C_{26}H_{37}NO_2$: C, 78.94; H, 9.43; N, 3.54. Found: C, 78.79; H, 9.50; N, 3.48. The enantiomeric purity of this material was found to be greater than 98% by HPLC on a Baker L-DNBLeu column. $[\alpha]^{20}_D$ −65.8° (c 3.8, CCl_4).

C. (*S*)-(−)-11-(Triethoxysilyl)-1-undecanyl *N*-(2-naphthyl)valinate (2c) was prepared from **2b** by the procedure used to prepare **1c**. From 2 g of **2b** was obtained 1.7 g (3 mmol, 60% yield) of **2c** as a yellow oil: R_f 0.16 (CH_2Cl_2 on silica gel); ^{1}H NMR ($CDCl_3$) δ 0.65 (m, 2 H), 1.07 (dd, J = 3.6 Hz, 6 H), 1.14–1.38 (m, 25 H), 1.58 (m, 2 H), 2.18 (sept, J = 3.6 Hz, J = 3.4 Hz, 1 H), 3.82 (q, J = 3 Hz, 6 H), 3.86 (b, 1 H), 3.98 (d, J = 3.4 Hz, 1 H), 4.09 (t, J = 3.8 Hz, 2 H), 6.83 (d, J = 1 Hz, 1 H), 6.93 (dd, J = 1 Hz, J = 4 Hz, 1 H), 7.18 (td, J = 1 Hz, J = 3.4 Hz, 1 H), 7.33 (td, J = 1 Hz, J = 3.4 Hz, 1 H), 7.55–7.68 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 10.2, 18.8–19.5, 26.0, 28.4–30.5, 31.4, 33.8, 58.3, 62.8, 65.9, 118.3, 122.4, 126.1, 126.3, 127.7, 127.9, 129.2, 135.8, 139.5, 173.8; IR (neat) 739, 802, 826, 1010, 1070, 1141, 1188, 1220, 1260, 1365, 1389, 1462, 1519, 1600, 1625, 1728, 2860, 2920, 2959, 3380 cm^{-1}; MS (70 eV), m/e (relative intensity) 559 (M$^+$, 0.9), 395 (16.7), 199 (15.0), 198 (100), 154 (13.7), 55 (15.0), 41 (14.1); HRESMS, calcd for $C_{32}H_{53}NO_5Si$ 559.3694, found 559.3694.

D. (*S*)-11-Siloxy-1-undecanyl *N*-(2-Naphthyl)valinate CSP 2d. This material was prepared in the same manner as CSP **1d** from 1.7 g of silane **2c**. Loading was calculated from the elemental analysis to be 0.3 mmol/g of silica gel based on N, 0.3 mmol/g based on C.

III. Preparation of Analytes. A. General Procedure for Preparation of (3,5-Dinitrophenyl)carbamates and -ureas. To 2 mL of toluene was added 100 mg (0.42 mmol) of 3,5-dinitrobenzoyl azide.[6] The solution was heated to 110 °C for 6 min, and 0.4 mmol of amine or alcohol was then added. Heating was continued for 2 min. In general, the sample may be analyzed without any workup other than cooling and dilution. For actual analysis of the enantiomeric purity of an unknown, these reactions may be conducted on a much smaller scale. Impurities typically elute prior to the derivatives. If further purification of a racemic analyte is desired, recrystallization of most of these carbamates may be achieved from hexane, while the more polar ureas may be recrystallized from acetone. *Sample for enantiomeric purity determinations should not be recrystallized.* Some typical analytes are **1-phenylethanol (3,5-dinitrophenyl)carbamate (19a)** [mp 127–128 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.7–8.5 (m, 3 H), 7.4–7.2 (m, 5 H), 5.9 (q, 1 H), 1.7 (d, 3 H) and **1-phenylethylamine (3,5-dinitrophenyl)urea (14a)** [mp 156–158 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.7–8.4 (m, 3 H), 7.4–7.2 (m, 5 H), 6.3 (b, 1 H), 5.9 (q, 1 H), 1.8 (d, 3 H)].

B. Preparation of the 3,5-Dinitrobenzamides of Amines and Amino Acid Derivatives. The preparation of these derivatives has been described elsewhere.[8]

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Registry No. (±)-**1a**, 99631-78-4; (±)-**1b**, 104336-51-8; (*S*)-**1b**, 104336-50-7; (*S*)-**1c**, 104336-53-0; (*S*)-**1c** (trichlorosilyl deriv.), 104336-52-9; (*S*)-**1e**, 103794-11-2; (*S*)-**1f**, 99631-85-3; (*S*)-**2b**, 99727-11-4; (*S*)-**2c**, 99727-12-5; (±)-**3a**, 74928-27-1; (*S*)-**3a**, 95588-91-3; (±)-**3b** (isomer 1), 104350-51-8; (±)-**3b** (isomer 2), 104336-89-2; (*SS*)-**3b**, 104419-12-7; (*SR*)-**3b**, 104419-13-8; (±)-**3c** (isomer 1), 104336-90-5; (±)-**3c** (isomer 2), 104350-52-9; (*SS*)-**3c**, 104419-14-9; (*SR*)-**3c**, 104419-15-0; (±)-**3d** (isomer 1), 104336-91-6; (±)-**3d** (isomer 2), 104336-92-7; (*SS*)-**3d**, 104419-16-1; (*SR*)-**3d**, 104419-17-2; (±)-**3e** (isomer 1), 104351-06-6; (±)-**3e** (isomer 2), 104336-93-8; (*SR*)-**3e**, 104419-64-9; (*SS*)-**3e**, 104419-65-0; (±)-**3f** (isomer 1), 104336-94-9; (±)-**3f** (isomer 2), 104419-04-7; (*SR*)-**3f**, 104419-18-3; (*SS*)-**3f**, 104419-19-4; (±)-**4**, 74928-29-3; (*S*)-**4**, 69632-59-3; (±)-**5a**, 104336-95-0; (*S*)-**5a**, 98160-46-4; (±)-**5b**, 104336-96-1; (±)-**5c**, 104336-97-2; (±)-**5d**, 104336-98-3; (*S*)-**5d**, 104337-28-2; (±)-**5e**, 104336-99-4; (±)-**5f**, 104336-56-3; (±)-**5g**, 104337-00-0; (±)-**5h**, 104337-01-1; (±)-**5i**, 104337-02-2; (±)-**5j**, 104337-03-3; (±)-**5k**, 104337-04-4; (±)-**5l**, 104337-05-5; (±)-**5m**, 104337-06-6; (±)-**5n**, 104337-07-7; (±)-**6a**, 104336-57-4; (±)-**6b**, 104336-58-5; (±)-**6c**, 104336-59-6; (±)-**6d**, 104336-60-9; (±)-**6e**, 104336-61-0; (±)-**6f**, 74928-23-7; (*S*)-**6f**, 69632-49-1; (±)-**6g**, 104336-62-1; (±)-**6h**, 104336-63-2; (±)-**7**, 104336-64-3; (±)-**8**, 104336-65-4; (±)-**9**, 104336-66-5; (*S*)-**9**, 104419-05-8; (±)-**10**, 104336-67-6; (±)-**10b**, 104336-68-7; (±)-**10c**, 104336-69-8; (*S*)-**10c**, 104419-06-9; (±)-**10d**, 104336-70-1; (*R*)-**10d**, 104419-07-0; (±)-**10e**, 104336-71-2; (±)-**11**, 104336-72-3; (±)-**12**, 104336-73-4; (±)-**13a** (DNB), 85873-86-5; (*R*)-**13a** (DNB), 85922-26-5; (±)-**13a** (DNAn), 104336-74-5; (*R*)-**13a** (DNAn), 104419-08-1; (±)-**13b**, 104336-75-6; (*R*)-**13b**, 104419-09-2; (±)-**13c**, 104336-76-7; (*R*)-**13c**, 104419-20-7; (±)-**14a** (DNB), 14402-00-7; (*S*)-**14a** (DNB), 69632-31-1; (±)-**14a** (DNAn), 104419-21-8; (±)-**14b**, 104337-46-4; (*S*)-**14b**, 104337-29-3; (±)-**14c**, 104337-47-5; (−)-**14c**, 104337-30-6; (±)-**14d**, 104337-48-6; (−)-**14d**, 104337-31-7; (±)-**14e**, 104337-08-8; (−)-**14e**, 104337-32-8; (±)-**14f**, 104337-09-9; (−)-**14f**, 104373-40-2; (±)-**14g**, 104337-10-2; (−)-**14g**, 104337-33-9; (±)-**14h**, 104336-77-8; (±)-**15a**, 104336-78-9; (*S*)-**15a**, 104419-10-5; (±)-**15b**, 104337-11-3; (±)-**16**, 104336-79-0; (±)-**17**, 104336-80-3; (±)-**18**, 104336-81-4; (±)-**19a**, 92943-03-8; (*S*)-**19a**, 92898-89-0; (±)-**19b**, 104337-17-9; (−)-**19b**, 104337-35-1; (±)-**19c**, 104337-18-0; (−)-**19c**, 104337-36-2; (±)-**19d**, 104337-19-1; (−)-**19d**, 104337-37-3; (±)-**19e**, 104337-20-4; (−)-**19e**, 104337-38-4; (±)-**19f**, 104337-21-5; (−)-**19f**, 104337-39-5; (±)-**19g**, 104421-40-1; (−)-**19g**, 104337-40-8; (±)-**19h**, 104337-22-6; (−)-**19h**, 104337-41-9; (±)-**19i**, 104337-23-7; (−)-**19i**, 104337-42-0; (±)-**20**, 104336-82-5; **22**, 104336-83-6; (±)-**23**, 104336-84-7; (±)-**24**, 104336-85-8; (±)-**25**, 104336-86-9; (*S*)-**25**, 104419-11-6; (±)-**26**, 104336-87-0; (±)-**27**, 104336-88-1; (±)-**28**, 104337-43-1; (±)-**29**, 104337-44-2; (±)-**30**, 92915-44-1; (±)-**31**, 104337-45-3; (±)-**32**, 104337-12-4; (−)-**32**, 104337-34-0; (±)-**33**, 104337-13-5; (±)-**34**, 104337-14-6; (±)-**35**, 104337-15-7; (±)-**36**, 104337-16-8; (±)-**37**, 104337-24-8; (±)-**38**, 104337-25-9; (±)-**39**, 104337-26-0; (±)-**40**, 104337-27-1; 2-naphthol, 135-19-3; *N*-(2-naphthyl)-2-amino-3-methylpentane, 104336-55-2; *N*-(2-naphthyl)aminomethane, 2216-67-3; undec-10-en-1-ol, 112-43-6; L-valine, 72-18-4; L-alanine, 56-41-7; 1-phenylethanol, 98-85-1; 1-phenylethylamine, 98-84-0; 3,5-dinitrobenzoyl azide, 42444-51-9; 3,5-dinitrobenzyl chloride, 99-33-2.