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Derivatized Cyclodextrins For Normal-Phase Liquid Chromatographic Separation Of Enantiorners

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(9), it is clear that the performance of the dual-channel FIRE detector is comparable to that of a typical TCD. Examination of Figure 9 also shows that the response of the dual-channel FIRE detector probably becomes greater than that of the TCD detector when the number of carbon atoms in the analyte increases (i.e., for hexane and heptane). This increase in response for the FIRE detector undoubtedly reflects an increase in the number of CO_2 molecules produced by combustion of these higher molecular weight analytes in the hydrogen-air flame.

CONCLUSIONS

This paper describes a new dual-channel FIRE detector for gas chromatography that reduces the adverse effects of additive background noise in the detector output by subtracting both the dc component of the background and the common-mode background fluctuations from the analytical channel. Because the dc component of the flame background is removed by the dual-channel instrument, the lock-in amplifier can be used at higher gain settings than were possible in the single-channel (unsubtracted) mode. Using the dual-channel configuration, detection limits for Freon-113 are improved by a factor of about 3-5 compared with a single-channel FIRE detector. At its present stage of development, the flame infrared emission GC detector is about as sensitive as a TCD detector.

Registry No. HOH, 7732-18-5.

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Derivatized Cyclodextrins for Normal-Phase Liquid Chromatographic Separation of Enantiomers

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Several different derivatized β-cyclodextrins were synthesized and used as chiral stationary phases in normal-phase liquid chromatography. The multiply substituted derivatives were made with acetic anhydride, (*R*)- and (*S*)-1-(1-naphthyl)ethyl isocyanate, 2,6-dimethylphenyl isocyanate, and *p*-toluoyl chloride. The first successful cyclodextrin-based, normal-phase separation of enantiomers was accomplished on these derivative phases. In contrast to chiral separations on the native β-cyclodextrin stationary phase, the enantiomeric separation mechanism on these new phases is not thought to be dependent on inclusion complexation. The similarities and differences between the derivatized cyclodextrin stationary phases and the cellulosic stationary phases are discussed.

INTRODUCTION

Cyclodextrin bonded phases have been used for the reversed-phase separation of a variety of enantiomers (*1*), diastereoisomers (*2*), structural isomers (*2*), enzymes (*3*), and routine compounds (*4*). Of these, the enantiomeric separations probably have received the greatest attention. In order to evaluate the mechanism of enantioselective chromatography, a number of empirical and theoretical studies have been done (*5-9*). In specific cases involving cyclodextrins, the formation of an inclusion complex seems to be a fundamental part of the chiral recognition and separation process (*1*, *2*, *4*, *9*). As yet, there have been no reports of normal-phase, enantiomeric separations on cyclodextrin bonded phase columns. Indeed, the fact that facile enantiomeric resolution obtained in the reversed-phase mode could not be duplicated in the normal-phase mode has been used as indirect evidence to support the premise that inclusion complexation is necessary for enantioselectivity (*9*). However, cyclodextrin bonded phases have been used successfully in normal-phase liquid chromatography (LC) for a number of achiral separations (*10-12*). The retention behavior was somewhat like that of a diol column. It is believed that the nonpolar portion of the mobile phase (e.g., hexane, heptane, etc.) occupies the cavity of cyclodextrin and that solute retention was due mainly to interaction with the external hydroxyl groups that line the top and bottom of the cyclodextrin torous (*10-13*).

While it is interesting that native cyclodextrins (i.e., cyclic α-1,4-linked glucose) do not seem to effectively resolve enantiomers under normal phase conditions, there are analogous examples for other naturally occurring chiral molecules. For instance, cellulose (linear β-1,4 linked glucose) seems to be much more effective as a chiral stationary phase when extensively derivatized. Triacetyl cellulose was one of the first derivatives to be used in this way (*13*). Subsequently, a large number of aromatic cellulose derivatives were shown to be even more widely useful (*14*). Typically, all of the derivatized cellulose columns are used in the normal-phase mode.

The possibility that derivatized cyclodextrin bonded phases could be used for enantiomeric LC separations in the normal-phase mode has not been considered previously. If derivatized cyclodextrins have good enantioselectivity under

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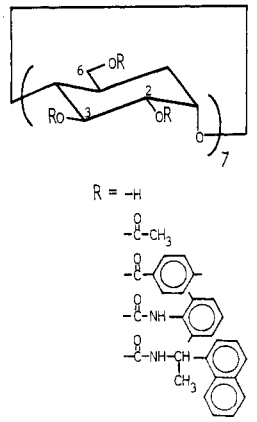


Figure 1. Schematic showing the sites available for derivatizing on β-cyclodextrin and the pendant groups used in the study.

normal-phase conditions, it would be highly advantageous and interesting from a mechanistic point-of-view. Unlike cellulosic LC stationary phases that are adsorbed, derivatized cyclodextrins are covalently bonded to the silica gel support. Consequently, there are few solvent and temperature limitations. Also, as discrete molecular entities, rather than a distribution of polymers, cyclodextrins are more amenable to theoretical, mechanistic, and modeling studies.

In this study, several different derivatized β-cyclodextrin bonded phases were evaluated for their ability to resolve enantiomeric solutes (Figure 1). In all cases, they were utilized in the normal-phase liquid chromatographic mode.

EXPERIMENTAL SECTION

Chemicals. The structures of the solutes, which were obtained from various sources, are presented in the tables. Dinitrobenzoyl chloride, 2,6-dimethylphenyl isocyanate, (*R*)- and (*S*)-1-(naphthyl)ethyl isocyanate and *p*-toluoyl chloride were obtained from Aldrich Chemical Co. (Milwaukee, WI). Hexane and 2-propanol were obtained from Fisher Scientific (St. Louis, MO). The acetylated β-CD column was a 250 × 4.6 mm column obtained from Advanced Separation Technologies, Inc. (Whippany, NJ).

Preparation of Bonded Sorbents. β-Cyclodextrin was attached to 5-μm spherical silica as previously reported (*15*). Four grams of the β-CD bonded phase was dried overnight under vacuum in a drying gun using MeOH and P_2O_5. The dried sorbent was placed in a three-necked round-bottom flask. Anhydrous solvent (Aldrich) (100 mL) was added. Pyridine was used as the solvent for the isocyanate derivatized phases and toluene (+3 mL of pyridine) was used for the acid chloride derivatized phase. The mixture was refluxed until all the water was removed (as an azeotrope into a Dean-Stark trap). The derivatizing agent was added (neat) and the mixture was refluxed for about 4 h (3 h for the acid chloride derivatized phase). The isocyanate-derivatized β-CD bonded phases were collected on a fritted glass filter and washed with approximately 100 mL of pyridine followed by 200 mL of MeOH and then air-dried. The acid chloride derivatized β-CD phase was also collected on a fritted glass filter and washed with approximately 100 mL each of pyridine and MeOH, about 10 mL of H_2O followed by MeOH and then air dried.

The bonded sorbents were submitted for carbon analysis. The surface concentration was calculated according to the equation (*16*)

$$(\mu\text{mol/m}^2) = \frac{\%\text{C} \times 10^6}{S[1200N_C - \%\text{C}(M-1)}$$

where N_C is the number of carbons in the ligand, M is the molecular weight of the ligand, and S is the surface area of the substrate, which, according to the manufacturer, is 170 m^2/g. For β-CD (N_C = 42, M = 1135), the coverage was calculated to be 0.20 $\mu mol/m^2$. To determine the degree of substitution on the β-CD of the derivatized β-CD phases, the %C from the CD + linkage chain was subtracted from the total %C and M − 1 was substituted by M in the denominator. The degrees of substitution for each of the phases were calculated and are reported in Table I. The sorbents were all packed into 250 × 4.6 mm stainless steel columns.

Table I. List of Bonded Sorbents

derivatizing agent	amt of reagent, g	% C	units/CD
dimethylphenyl isocyanate	5	7.87	10
p-toluoyl chloride	5	8.33	13
(*R*)-(−)-1-(1-naphthyl)ethyl isocyanate[a]	3	7.58	6.6
(*S*)-(+)-1-(1-naphthyl)ethyl isocyanate[a]	3	8.89	6.3

[a] The (*R*)- and (*S*)-naphthyl derivatized phases were prepared from different lots of CD bonded sorbent. The difference in % C between the two phases may reflect the lot to lot substrate variation in surface area, etc. However, the degree of substitution is calculated from degree of substitution = ($\mu mol/m^2$ of naphthyl)/($\mu mol/m^2$ of CD), which eliminates the variation due to surface area.

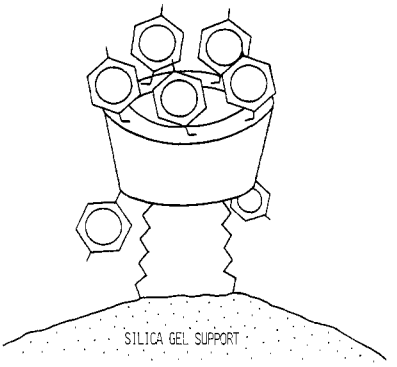


Figure 2. Simplified model of toluoyl-derivatized β-cyclodextrin attached to a silica gel support.

RESULTS AND DISCUSSION

β-Cyclodextrin has 21 hydroxyl groups available for modification. The seven primary 6-hydroxyls are at the "base" or narrow end of the CD torous while the 14 secondary 2- and 3-hydroxyl groups are at the "mouth" or wide end of the CD torous. Also, the CD is attached to silica gel via its hydroxl groups through an average of two linkage chains. In order to obtain the maximum degree of substitution per cyclodextrin, a large molar excess of derivatizing agent was used under vigorous conditions. The average degree of substitution for naphthylethyl isocyanate was ~6, for 2,6-dimethylphenyl isocyanate, 10, and for *p*-toluoyl chloride, 13. Acetyl-modified β-CD is thought to be about 90% substituted. Figure 2 is an idealized model of toluoyl-derivatized β-CD. Except in the case of the acetyl-modified cyclodextrins, an appreciable number of residual hydroxyl groups remain available for hydrogen bonding. It appears that cyclodextrins modified with the larger, bulkier substituents consistently had a lower degree of substitution. Presumably, this is because of steric reasons. Lower degrees of substitution could be obtained by using less derivatizing agent and shorter reaction times. An (*S*)-naphthylethyl isocyanate derivatized β-CD stationary phase, with degree of substitution of 3 (DS-3), was made in this manner. On comparison of the DS-3 and DS-6 (*S*)-naphthylethyl isocyanate derivatized β-CD phases, it was noted that under identical conditions a solute's retention time increased as the degree of substitution increased. However, the selectivity (α) did not change appreciably for most compounds as long as low levels of analyte were used.

In the presence of nonpolar solvents (such as hexane–2-propanol mixtures) it may be difficult for trace organic solutes to form traditional inclusion complexes with cyclodextrins.

Table II. Normal-Phase LC Separation Data for a Variety of Enantiomeric Solutes on Bonded Derivatized β-Cyclodextrin Columns

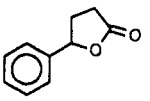
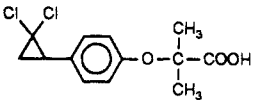
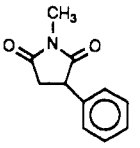
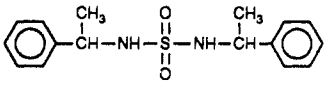
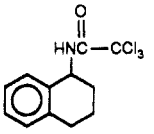
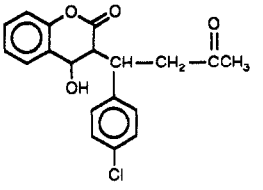
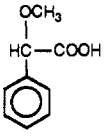
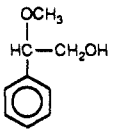
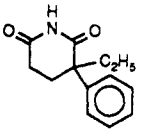
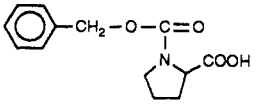
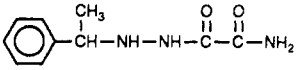
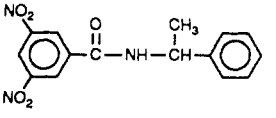
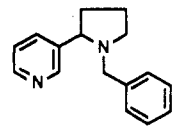
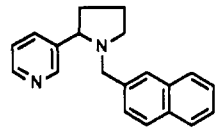
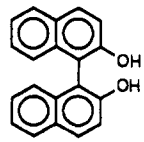
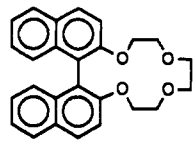
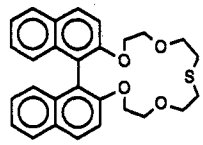
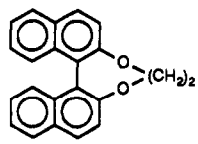
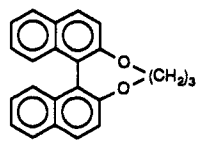
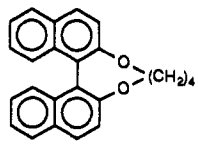
no.	compound	structure	k'_1	α^a	mobile phase[b]	stationary phase
1	(±)-γ-phenyl-γ-butyrolactone		14.5	1.10	98:2, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
2	(*R*,*S*)-ciprofibrate		2.36	1.20	80:20:0.2, AcN:EtOH:HOAc	*S*-naphthylethyl isocyanate derivatized β-CD
3	(±)-phensuximide		11.20	1.30	90:10, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
			3.38	1.07	90:10, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
4	(*R*,*R*)-(*S*,*S*)-(±)-*N*,*N*′-bis(α-methylbenzyl)sulfamide		4.33	1.21	90:10, hex:ipa	peracetyl derivatized β-CD
5	(*R*,*S*)-*N*-trichloroacetyl-1,2,3,4-tetrahydro-1-naphthylamine		7.70	1.3	95:5, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
			1.28	1.06	90:10, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
6	D,L-3-(α-acetonyl-4-chlorobenzyl)-4-hydroxycoumarin		23.6	1.12	70:30, AcN:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
			21.5	1.13	60:40, hex:ipa	peracetyl derivatived-β-CD
7	(*R*,*S*)-α-methoxyphenylacetic acid		2.55	1.27	99.5:0.5, EtOH:HoAC	toluoyl derivatized-β-CD
8	(*R*,*S*)-2-methoxy-2-phenylethanol		4.5	1.10	95:5, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
9	(±)-glutethimide		14.3	1.10	90:10, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
10	*N*-CBZ-DL-proline		3.1	1.08	90:10, hex:ipa	toluoyl derivatized β-CD
			13.3	1.16	99.9:0.1, EtOH:HOAc	(*R*)-naphthylethyl isocyanate derivatized β-CD
11	(±)-5-(α-phenethyl)semioxamazide		3.31	1.03	90:10, hex:ipa	peracetyl derivatized β-CD
12	(*R*,*S*)-*N*-(3,5-di-nitrobenzoyl-α-methylbenzylamine		6.2	1.61	70:30, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD

Table II (Continued)

no.	compound	structure	k'_1	α^a	mobile phase[b]	stationary phase
13	*N'*-benzylnor-nicotine		2.61	1.18	98:2, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
14	*N'*-(2-naphthyl-methyl)nor-nicotine		4.4	1.13	98:2, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
15	(*R,S*)-2,2'-bi-2-naphthol		23.4	1.10	98:2, hex:ipa	2,6-dimethylphenyl isocyanate derivatized β-CD
16	(*R,S*)-2,2'-bi-naphthyldiyl-crown-4		2.6	1.23	95:5, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
17	(*R,S*)-2,2'-bi-naphthyldiyl-17-thia-crown-5		5.2	1.08	95:5, hex:ipa	toluoyl derivatized β-CD
18			2.9	1.06	98:2, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
19			4.20	1.07	98:2, hex:ipa	(*R*)-naphthylethyl isocyanate derivatized β-CD
20			3.14	1.07	98:2, hex:ipa	(*R*)-naphthylethyl isocyanate derivatived β-CD

[a] The resolutions (R_s) for all compounds are ≥1.5 except for compounds 18–20 which had R_s values between 1.0 and 1.3. [b] hex is the abbreviation for hexane and ipa is the abbreviation for 2-propanol, AcN is the abbreviation for acetonitrile.

However, the presence of aromatic and carbonyl groups in modified CDs provide opportunities for π–π interactions that do not exist with native cyclodextrins. This, combined with the hydrogen bonding sites of the residual hydroxyl groups, provides the type of interactions commonly associated with Pirkle-type chiral stationary phases (*17*). Furthermore, the nonpolar solvents do not compete with the solute for the residual hydrogen bonding sites on the cyclodextrin.

Table II lists 20 different enantiomeric compounds that were resolved on one or more of the derivatized cyclodextrin stationary phases. Figure 3 shows the normal-phase separation of two pairs of enantiomers. Seven of these racemic compounds (nos. 13, 14, and 16–20) also could be resolved on native β-cyclodextrin columns in the reversed-phase mode (*18*, *19*), but the rest of the compounds could not. For the compounds that were resolved on both types of columns, the selectivity (α) obtained on the derivatized β-cyclodextrin columns was comparable or better (and with smaller k' values) than that obtained on the native β-cyclodextrin columns. Also, it should be noted that for compounds 18, 19, and 20, two conventional β-cyclodextrin columns (a 25 cm and 15 cm column) used in series were required to obtain similar selectivity.

Occasionally, two different modified CD columns could resolve the same racemate (see nos. 3–6; Table II). However, the retention and resolution characteristics were significantly different. All racemates were tested under a variety of conditions on all of the modified CD columns. Each derivatized CD seemed to have a distinct enantioselectivity. Several of the compounds were highly selective for one particular stationary phase (Table III). The seemingly random selectivities, column efficiencies, and mobile phase requirements of the derivatized CD column are analogous to those reported for the modified cellulosic chiral stationary phases (*14*). In general, the isocyanate-derivatized phases seemed to have the best selectivity. The resultant carbamate linkage of the isocyanate-derivatized phases may provide additional sites for hydrogen bonding and/or stronger dipole–dipole interactions relative to the ester linkage of the acid chloride derivatized phases. The naphthylethyl isocyanate derivatized β-CD

Table III. Comparison of Derivatized Cyclodextrin and Derivatized Cellulosic Chiral Stationary Phases for Normal-Phase LC Separation

derivatized cyclodextrin	derivatized cellulose
1. individual molecules covalently bonded to silica gel	1. distribution of polymers adsorbed on silica gel
2. no solvent restrictions except for strong acids and bases	2. must avoid halogenated solvent or any other mobile phases that will dissolve and remove the substituted cellulose (as well as strong acids and bases)
3. can be stored at room temperature indefinitely in typical normal-phase solvents; no irreversible conformational changes that affect chiral recognition are possible	3. storage recommended hexane at ~4 °C; upon standing at room temperature, polar organic modifiers (2-propanol, etc.) sometimes can cause an alteration in the secondary structure of adsorbed cellulose polymers resulting in a loss of chiral recognition
4. enantioselectivity can be different for some compounds compared to cellulosic phases	4. enantioselectivity can be different for some compounds (compared to cyclodextrin phases)
5. can be bonded to a variety of different pore-size silica gels (60–300 Å)	5. must be adsorbed on a large enough pore size silica gel (≥300 Å) that the polymer can enter the pore
6. highly purified derivatives can be crystallized thereby allowing computer modeling and theoretical evaluation of enantioselective properties	6. cannot be crystallized at the present time; secondary structure that contributes to enantioselectivity is unknown

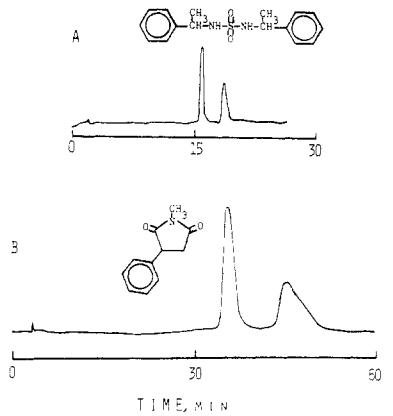


Figure 3. Normal-phase chromatograms showing enantiomeric separation on derivatized cyclodextrin bonded phases: (A) separation of (*R*,*R*)- and (*S*,*S*)-*N*,*N*′-bis(α-methylbenzyl)sulfamide on a 25 cm peracetyl-β-CD column; mobile phase, 90:10 (v/v) hexane–2-propanol; flow rate, 1.0 mL/min; (B) separation of (±)-phensuximide on a 25 cm 2,6-dimethylphenyl isocyanate derivatized β-CD column; mobile phase, 90:10 (v/v) hexane–2-propanol; flow rate, 1.0 mL/min.

columns had a definite logic for the separation of at least one group of compounds. Solutes that contain an aromatic π-acidic group and an amide, urethane, or urea group usually were resolved. Indeed, a number of chiral amines, alcohols, carboxylic acids, and so on were derivatized to contain a 3,5-dinitrobenzyl group and subsequently resolved. These particular separations will be discussed in a subsequent monograph. In this respect, the naphthylethyl isocyanate derivatized CD phase is somewhat analogous to the naphthylvaline reciprocal CSPs developed by Pirkle and Pochapsky (*20*).

As has been noted, there are a number of analogies that can be drawn between the derivatized cyclodextrin bonded phases and modified cellulosic phases. For example, both are modified carbohydrates containing glucose monomer units. Many of the substituents attached to the 2-, 3-, and 6-hydroxyl groups of cellulose and cyclodextrins are identical (i.e., acetyl and toluoyl) or analogous (i.e., the aromatic isocyanates). However, there are a number of important differences in these two classes of chiral stationary phases which can significantly affect the chromatographic approach and results. A comparison of these two classes of CSP is given in Table III. One of the obvious differences is that the derivatized cyclodextrins are discrete molecules covalently bonded to silica gel while the cellulosic CSPs consist of a distribution of polymers that are adsorbed onto silica gel. As a result, the cellulosic phases are limited to fairly large pore-size silica gels (e.g., ≥300 Å), so that the cellulose polymer can go into the pores and coat the internal surface) while the derivatized-CD CSPs are not. At least two precautions must be observed with the coated chiral stationary phases that are unnecessary with bonded varieties. For example, mobile phase solvents that dissolve the polymer (such as halocarbons, THF, etc.) must be strictly avoided for the cellulosic CSPs as they quickly strip the derivatized cellulose from the silica gel. Also, there seems to be a definite secondary structure to the adsorbed cellulose polymer which leads to chiral recognition. If this secondary structure is altered or changed, enantioselectivity can be lost even though the chiral polymer remains on the silica gel. Storing these columns in mobile phases containing a more polar solvent (such as 2-propanol) at room temperature is sometimes sufficient to cause a change in the secondary structure of the polymer.

Despite the empirical similarities between the derivatized cyclodextrin and derivatized cellulosic stationary phases, they do not have identical enantioselectivities. There are racemates that have been resolved on the derivatized-CD columns that have not been resolved on the analogous cellulosic phases (e.g., compounds **5** and **19** of Table II) and vice versa. Other racemates can be resolved on both phases thereby giving one a choice. Having such a choice frequently is useful since the efficiency, selectivity, loading capacity, retention time, optimal solvent composition, cost, etc. usually are different for different CSPs.

As the number of available chiral stationary phases increase, there is bound to be overlap in the types of compounds separated. Clearly, more studies need to be done comparing many of the existing columns. This is likely to occur in the near future.

CONCLUSIONS

While native cyclodextrin bonded LC stationary phases have shown little enantioselectivity in the normal-phase mode, derivatized CD stationary phases show a definite enantioselectivity for a variety of compounds. Retention seems to be due to π–π interactions as well as hydrogen bonding and dipolar interactions as has been reported for other normal-phase CSPs. There are a number of compositional similarities between the derivatized cyclodextrin bonded phases and the derivatized cellulosic CSPs. However, each column has distinct characteristics that will make it more or less useful for any given enantiomeric separation.

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Transferability of Relative Sensitivity Factors in Secondary Ion Mass Spectrometry: An Evaluation of the Potential for Semiquantitative Ultratrace Analysis of Metals

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Secondary ion mass spectrometry (SIMS) has turned out to be a powerful tool for multielemental ultratrace characterization of metals. In many cases, a limiting factor for the evaluation of quantitative results is the availability of reference materials. For that reason, it would be desirable to perform quantitative or at least semiquantitative analysis by means of a transfer of relative sensitivity factors (RSFs) from one matrix to another and to calculate RSFs through interpolation using an experimental regression function. The results shown in this paper suggest that a transfer of RSFs for semiquantitative multielemental ultratrace analysis with SIMS referring to the matrices W, Mo, Ta, Nb, WTi10%, $TaSi_2$, and Si is possible whenever an error factor of 2 can be accepted.

INTRODUCTION

According to the great number of different analytical questions arising from the technology of materials, it would be desirable to be able to perform quantitative trace analysis of any analyte–target combination under multielemental conditions. Secondary ion mass spectrometry (SIMS) in principle exhibits this capability. Due to the large variation of ionization probabilities for various elements and the dependence of these on sample composition (matrix effects), the use of matrix matched reference materials forms the most successful basis for quantitative analysis (*1*, *2*). The availability of reference materials is limited and their preparation rather tedious. A method for the preparation of multielement reference materials by homogeneous doping of a metal—here W and Mo—with trace elements has been described elsewhere (*3*, *4*). The value of ion implantation for the preparation of reference materials for refractory metals is demonstrated in ref 5. In order to reduce the elaborate efforts for the preparation and the characterization of reference materials, it would be very useful to quantify SIMS data without matrix matched reference materials for a wide range of matrices and trace elements. For many cases, an accuracy within a factor of 2 would be sufficient.

Table I. Experimental Parameters

instrument:	Cameca ims 3f ion microanalyzer
primary ions:	O_2^+
primary ion energy:	5.5 keV
primary ion beam size:	about 100-μm diameter
primary ion raster size:	250 × 250 μm² for implantation standards 500 × 500 μm² for powder standards
primary ion current density:	10^{-3} A/cm²
mass resolution:	300
secondary ion polarity:	positive
secondary ion energy range:	0–70 eV for masses < 48 45–145 eV for masses ≥ 48
imaged field:	10-μm diameter for implantation standards 150-μm diameter for powder standards
field aperture:	750 μm for implantation standards 1800 μm for powder standards
contrast diaphragm aperture:	60 μm for implantation standards 400 μm for powder standards
entrance slit:	700 μm
exit slit:	700 μm
detection system:	electron multiplier
residual sample pressure:	approx 10^{-5} Pa

The aim of this paper will be to show the practical value of empirical relations between relative sensitivity factor (RSF) data and the physical properties of elements for the transfer of RSFs. It is not intended to incorporate the theoretical approach in detail into the considerations, since, on the one hand, in most cases this is not possible for lack of known parameters and, on the other hand, it is not meaningful for many practical applications, because no significant improvement of accuracy can be achieved. Moreover, only relative ionization probabilities are used for evaluation. For that reason, theoretical approaches will only be involved as far as they provide plausible explanations for the patterns found.

EXPERIMENTAL SECTION

Instrumentation. All RSF data presented in this paper have been obtained with a Cameca ims 3f ion microanalyzer interfaced to a Hewlett-Packard 9825 A microcomputer. Instrumental parameters are listed in Table I.

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