Extending the Scope of Enantiomer Resolution by Complexation Gas Chromatography

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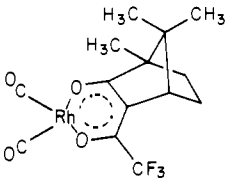
Abstract: Nickel(II) bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (**3b**) is an efficient optically active stationary phase for the quantitative gas chromatographic resolution of racemic alkyl-substituted cyclic ethers containing rings of up to six members (**6–16**), the cyclic ketone *trans*-2,5-dimethylcyclopentanone (**19**), and the aliphatic alcohol *tert*-butylmethylcarbinol (**20**). Thermodynamic parameters of enantiomer discrimination, i.e., $-\Delta_{S,R}(\Delta G°)$, between ten cyclic ethers (**6–15**) and **3b** are reported and discussed. The molecular configurations of the invertomers of 1-chloro-2,2-dimethylaziridine (**21**) eluting on **3b** are assigned by indirect evidence, and for the first time, "enantiomerization" of **21** and 1,6-dioxaspiro[4.4]nonane (**17**) on the metal chelates **3a** and **3b**, respectively, is chromatographically detected. The racemic alkyl-substituted thiiranes and thietanes **23–26** are quantitatively resolved on **3b**. A quadrant rule, which correlates molecular configuration and chromatographic elution order on **3b**, derived from (+)-(1*R*)-camphor, is valid for alkyl-substituted oxiranes; however, a notable exception is found for *trans*-2,3-dimethylthiirane (**25**). The absence of racemization in the preparation of *trans*-(1*S*,2*S*)-1-chloro-2-methylaziridine (**22**) from (*S*)-alanine and in the conversion of *trans*-(2*S*,3*S*)-2,3-dimethyloxirane (**11**) to *trans*-(2*R*,3*R*)-2,3-dimethylthiirane (**25**) with inversion of configuration is proved by complexation gas chromatography. Neither substrate derivatization nor isolation and purification are necessary for the chromatographic determination of enantiomeric compositions (ee), and 10 ng of sample is required for the assignment of molecular configurations.

Following the classical resolution experiments on Troeger's base by Prelog and Wieland in 1944,[1] many examples of "chiral recognition" have been described in chromatographic systems resulting from various types of enantiospecific solute–solvent interactions, e.g., hydrogen bonding,[2] charge transfer,[3] dipole–dipole,[4] inclusion,[5] and combinations thereof.[6] It is obvious that many racemic mixtures while lacking appropriate chemical functionalities are not prone to resolution by the above-mentioned criteria of chemical interaction. Enantiospecific complex formation of chiral solutes with optically active organometallic compounds offers an important complementary approach to chiral recognition in chromatography due to the marked sensitivity of the coordination bond to steric, strain, and electronic effects,[7] and because of the great variety of selective substrate–metal interactions. In addition, coordination to metal ions generally requires no solute derivatization, which greatly facilitates potential analytical applications of complexation gas chromatography.[8]

In liquid chromatography, copper(II)-containing optically active supports have been successfully selected for preparative enantiomer resolutions,[9] and, more recently, racemic amino acid derivatives have been analytically resolved by addition of an optically active metal chelate to the mobile phase.[10] In gas chromatography, solutions of the (chiral) metal β-diketonates **1**, **2a**, **3a**, **4a**, and **5a** in squalane have been used as highly selective stationary phases for the study of association equilibria with σ-donor solutes.[7,11-13]

Chart I. Chromatographic Parameters of Enantiomer Resolution

(a) *peak retention*: a thermodynamic measure for the selective coordination between solute and metal chelate (R', K, $-\Delta G°$).
(b) *peak separation*: a thermodynamic measure for chiral recognition between racemic solute and optically active metal chelate ($-\Delta_{S,R}(\Delta G°)$).
(c) *peak assignment*: a correlation of solute retention and molecular configuration (assignment of absolute configurations).
(d) *peak ratio*: a precise quantitative measure for the enantiomeric composition of the solute (enantiomeric excess, ee).
(e) *peak coalescence* (2nd kind): a kinetic measure for solute enantiomerization occurring during the resolution event ($\Delta G^{\ddagger}$).



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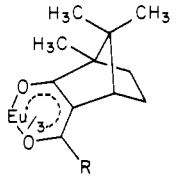
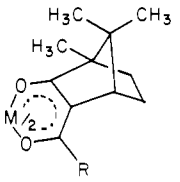


2a, R = CF_3
2b, R = $CF_2CF_2CF_3$



3a, M = Ni; R = CF_3
3b, M = Ni; R = $CF_2CF_2CF_3$
4a, M = Co; R = CF_3
4b, M = Co; R = $CF_2CF_2CF_3$
5a, M = Mn; R = CF_3
5b, M = Mn; R = $CF_2CF_2CF_3$

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Although enantiomer resolution was not the prime object of that work, the great potential of complexation gas chromatography[8] for chiral recognition through coordination has been recognized.[11-13] In 1977, one of us demonstrated for the first time that gas chromatography may exhibit the necessary *kinetic* (i.e., a fast and reversible coordination interaction along the column) and *thermodynamic* (i.e., chiral recognition due to the requirement $\Delta_{S,R}(\Delta G°) \neq 0$) parameters for enantiomer discrimination via π complexation by the separation of a chiral alkene (3-methylcyclopentene) on the optically active rhodium(I) chelate (**1**).[14] This method has consequently been extended to the resolution of racemic oxygen-containing solutes, e.g., to methyloxirane **6** on **2a** (semiquantitatively on a packed column)[15] and on **3a** (quantitatively on a capillary column).[16,17] The approach is highlighted by the recent quantitative resolution of pheromone acetals (e.g., chalcogran and related spiroketals, *endo*- and *exo*-brevicomin, frontalin, and lineatin).[18]

Scope

Chiral molecules lacking suitable chemical functionalities for conventional diastereomeric derivatization (ethers, esters, acetals, unsaturated hydrocarbons) were not, or only with difficulty, resolved in the past, and, as a consequence, the knowledge of the chiral properties of these compounds is still limited. Our first results on enantiomer resolution by complexation gas chromatography[14,16-18] are encouraging since valuable informations can be obtained from the complexation chromatogram (cf. Chart I).

In this report we present results on the resolution of new types of racemic mixtures on nickel(II) bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (**3b**), and we describe applications obtained via the analysis of the peak parameters mentioned in Chart I. Unless stated otherwise, only *quantitative* enantiomer resolutions are reported.

Resolution of Oxygen-Containing Racemates

The first *quantitative* analytical resolution of racemic alkyl-substituted oxiranes has been detected on nickel(II) bis[(1*R*)-3-(trifluoroacetyl)camphorate] (**3a**) in squalane.[16] Improved resolutions have been achieved with the bis[(1*R*)-3-(heptafluorobutyryl)camphorates] of nickel(II) (**3b**),[19] cobalt(II) (**4b**),[20] and manganese(II) (**5b**).[21] A similar influence of the perfluoroacyl group on resolution has been observed by the apparent improvement of chemical shift nonequivalence of enantiotopic nuclei in the chiral environment of the NMR lanthanide shift reagent **2b** vs. **2a**.[22]

The *racemic* nickel chelate **3b** has been tested as a stationary phase to prove that, indeed, true enantiomer resolutions have been achieved on optically active **3b**, and, as expected, racemic oxiranes elute as only one peak. This observation is referred to as *peak coalescence of the first kind* (vide infra).

In Table I, the separation factor (α) of enantiomer resolution for racemic cyclic ethers of rings of up to six members on **3b**, **4b**, and **5b** are compared. It has been pointed out[21] that the separation factor (α) of enantiomer resolution is merely a useful practical expression for chromatographic separability. Thus, it follows from Table I that **5b** is preferred as a resolving stationary phase for quantitative enantiomer separations of racemic oxiranes and oxetanes[21] while **3b** is the optically active metal chelate of choice for cyclic ethers of larger ring size, i.e., for tetrahydrofurans and tetrahydropyrans (cf. Figures 1 and 2). The inspection of α, however, must fail when aspects of the mechanism of chiral recognition are considered.

In complexation gas chromatography,[8,17] the observed overall retention of a solute B is the result of two independent contri-

Table I. Separation Factor α[a] of Quantitative Enantiomer Resolution for Racemic Cyclic Ethers on Bis[(1*R*)-3-(heptafluorobutyryl)camphorates] of Nickel(II) (3b), Cobalt(II) (4b), and Manganese(II) (5b) in Squalane at 60 °C

substrate	no.	Ni[b]	Co[c]	Mn[d]
methyloxirane	6	1.19	1.18	1.08[f]
ethyloxirane	7	1.08	1.17	1.15
isopropyloxirane	8	0[e]	1.13	1.17
tert-butyloxirane	9	1.11	1.11	1.15
2-ethyl-2-methyloxirane	10	1.05	0[e]	1.02[f]
trans-2,3-dimethyloxirane	11	1.32	1.24	1.30
trimethyloxirane	12	1.30	1.12	1.20
2-methyloxetane	13	*g*	1.11	1.11
2-methyltetrahydrofuran	14	1.06	1.01[f]	1.04
trans-2,5-dimethyltetrahydrofuran	15	1.18	0[e]	1.02
2-methyltetrahydropyran	16	1.05	0[e]	0[e]

[a] For dead-volume (methane peak) adjusted retention time t' of the second eluting enantiomer over that of the first eluting enantiomer. [b] 0.1 *m* in squalane, 100 m × 0.5 mm nickel capillary. [c] 0.1 *m* in squalane, 26.6 m × 0.25 mm stainless steel capillary.[20] [d] 0.5 *m* in squalane, 160 m × 0.4 mm stainless steel capillary.[21] [e] Not resolved. [f] Partially resolved. [g] Exceedingly long retention time.

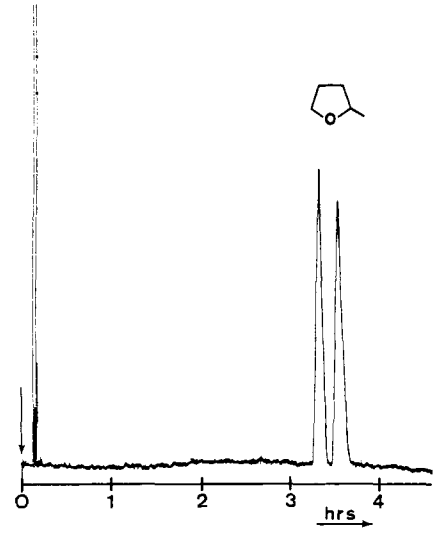

Figure 1. Enantiomer resolution of 2-methyltetrahydrofuran (**14**) on (1*R*)-**3b** (0.156 *m* in squalane) at 70 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 3.1 mL/min N_2; split ratio 1:50.

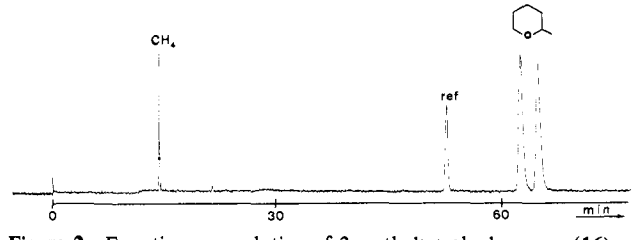

Figure 2. Enantiomer resolution of 2-methyltetrahydropyran (**16**) on (1*R*)-**3b** (0.1 *m* in squalane) at 60 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 1.4 mL/min N_2; split ratio 1.50 (reference solute, *n*-octane).

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(21) V. Schurig and R. Weber, *J. Chromatogr.*, **217**, 51 (1981).
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Table II. Comparison of Thermodynamic Parameters of Enantiomer Discrimination between Cyclic Ethers and Bis[(1*R*)-3-(heptafluorobutyryl)camphorates] of Nickel(II) (3b), Cobalt(II) (4b), and Manganese(II) (5b) in Squalane at 60 °C[23]

substrate	no.	Ni[a]		Co[b]		Mn[c]	
		R'	$-\Delta(\Delta G^\circ)$[d]	R'	$-\Delta(\Delta G^\circ)$[d]	R'	$-\Delta(\Delta G^\circ)$[d]
methyloxirane	6	58.5	0.11	1.97	0.16	0.97	0.13
		69.3		2.50		1.18	
ethyloxirane	7	58.9	0.05	2.09	0.14	0.89	0.18
		63.3		2.60		1.16	
isopropyloxirane	8	55.4	0	1.96	0.12	0.84	0.20
				2.35		1.14	
tert-butyloxirane	9	39.0	0.07	1.23	0.13	0.58	0.23
		43.5		1.49		0.82	
2-ethyl-2-methyloxirane	10	35.5	0.03	1.71[e]	0	1.01	0.03
		37.3				1.06	
trans 2,3-dimethyloxirane	11	24.4	0.19	1.34	0.23	1.19	0.29
		32.4		1.90		1.85	
trimethyloxirane	12	24.6	0.20	1.26	0.13	1.46	0.18
		33.1		1.54		1.93	
2-methyloxetane	13	*f*		37.1	0.07	12.5	0.08
				41.3		14.2	
2-methyltetrahydrofuran	14	58.4	0.04	3.27	0.01	2.40	0.04
		62.2		3.31		2.54	
trans-2,5-dimethyltetrahydrofuran	15	2.3	0.15	0.36[e]	0	0.76	0.03
		2.9				0.80	

[a] 0.1 *m* in squalane, 100 m × 0.5 mm nickel capillary. [b] 0.1 *m* in squalane, 26.6 m × 0.25 mm stainless steel capillary.[20] [c] 0.05 *m* in squalane, 160 m × 0.4 mm stainless steel capillary.[21] [d] kcal/mol. [e] Not resolved. [f] Exceedingly long retention time.

butions: (i) the *physical* partition of B between the gaseous and the liquid phase and (ii) the *chemical* equilibrium of molecular association (eq 1) between the solute B and the metal chelate A

$$A + B \rightleftharpoons AB; \qquad K_{(m)} \sim R' \tag{1}$$

in the liquid phase. The latter contribution introduces chemical selectivity into chromatography by causing a retention increase R', which can easily be determined from relative retention data (r and r_0). According to the simplified equation 2, the retention increase R' is proportional to the stability constant $K_{(m)}$ and the metal chelate concentration m_A in the solvent S (preferably related to the molality concentration scale):[13]

$$K_{(m)}m_A = (r - r_0)/r_0 = R' \tag{2}$$

where r = relative dead-volume adjusted retention of the solute B with respect to an inert reference standard (not interacting with the metal chelate A) on a column containing the molal concentration m_A of the metal chelate A in a nonvolatile solvent S (e.g., squalane) and r_0 = relative adjusted retention of the solute B with respect to the inert reference standard on a reference column containing the pure solvent S. Thus, the comparison of the retention increase R'[23] for different solutes B is a direct measure for their coordination ability with the metal chelate A (cf. Chart I, a). From the difference of the retention increase R' for a pair of enantiomers,[24] the following thermodynamic expression for enantiomer discrimination in complexation gas chromatography can be derived:[21]

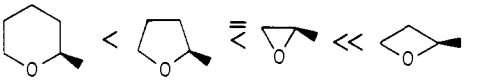
$$-\Delta_{S,R}(\Delta G^\circ) = RT \ln (R'_S/R'_R) = RT \ln [(r_S - r_0)/(r_R - r_0)] \tag{3}$$

Thus, the ratio of the retention increase R' of one enantiomer over that of the other is a highly accurate measure for enantiomer discrimination (cf. Chart I, b). It should be noted that only for $r \gg r_0$, eq 3 approaches eq 4, which is frequently used in gas chromatography as a measure for chiral recognition.[25]

$$-\Delta_{S,R}(\Delta G^\circ) = RT \ln \alpha \tag{4}$$

In Table II, thermodynamic data of enantiomer discrimination for racemic cyclic ethers on the optically active bis[(1*R*)-3-(heptafluorobutyryl)camphorates] of nickel(II) (**3b**), cobalt(II) (**4b**), and manganese(II) (**5b**) are compared. For the following discussion, it is relevant to separate (i) the ability of the solute B to coordinate with the metal chelate A (as expressed by the retention increase R'[23]) and (ii) the extend to which the coordination equilibrium (eq 1) differs for the antipodes (as expressed by $-\Delta_{S,R}(\Delta G^\circ)$). It will be revealed that the intuitive presumption of a strong coordination interaction being the prerequisite to efficient enantiomer discrimination is unfounded.

In close agreement with previous results obtained for the association equilibria of (achiral) solutes and **3a**, **4a**, and **5a**,[13] the interaction of cyclic ethers with **3b**, **4b**, and **5b** increases remarkably in the order Mn(II) < Co(II) ≪ Ni(II). For a given metal chelate, the coordination ability of methyl-substituted cyclic ethers increases in the order



Noteworthy, though not well understood, is the exceedingly strong coordination interaction of oxetanes with the metal chelates. Although Mn(II) is only a weak acceptor for cyclic ethers, chiral recognition for alkyl-substituted oxiranes is more pronounced as compared to the strong acceptor Ni(II). However, the failure of **5b** to resolve 2-methyltetrahydropyran (**16**) is due to the total absence of molecular association (i.e., $R' = 0$). Hence, the strongly coordinating nickel chelate **3b** is recommended for enantiomer resolutions of weak racemic donor molecules (cf. Figures 1 and 2). Increasing alkyl substitution at the oxirane carbon atoms (i.e., **6**, **11**, **12**) leads to a decrease of interaction with nickel(II) (**3b**), but, concomitantly, the efficiency toward chiral recognition is improved. A peculiar trend of enantiospecificity vs. steric bulk of the alkyl group of the oxiranes **6**–**9** is observed on **3b**: an increase of branching in the alkyl group causes first a decrease of resolution, which approaches zero for **8** but subsequently increases again for **9**, although, simultaneously, a steady decrease of coordination interaction is observed. Thus, the comparison of the thermodynamic data mentioned in Chart I (a and b) reveals some unexpected features in coordination selectivity and enantiospecificity. A full understanding of the parameters, however, requires information on the true configurational structure and the associative behavior of the metal chelates **3b**, **4b**, and **5b** in squalane solution as well as the knowledge of the coordination geometries of the donor–acceptor adducts formed. Such infor-

(23) R' remained constant during the measurements recorded in Table II. After prolonged use of the columns, some fluctuations of R' (<10%) occurred. Because of a possible error in m_A, no absolute values for $K_{(m)}$ and $-\Delta G^\circ$ are reported in Table II.

(24) The first eluting enantiomer is arbitrarily denoted R and the second one S, respectively.

(25) C. H. Lochmüller, J. M. Harris, and R. W. Souter, *J. Chromatogr.*, **71**, 405 (1972); U. Beitler and B. Feibush, *ibid.*, **123**, 149 (1976).

Figure 3. Peak coalescence (2nd kind) for 1,6-dioxaspiro[4.4]nonane (**17**) resolved on (1*R*)-**3b** (0.1 *m* in squalane) at 70 °C. Column, 100 m × 0.5 mm nickel capillary, carrier gas 1.0 mL/min N_2; split ratio 1:50 (reference solute, *n*-decane).

mation is not at hand, at present. A similar situation still prevails in the domain of the chiral lanthanide shift reagents **2a** and **2b**.[26]

In a previous report from this laboratory,[19] a *quadrant rule* has been formulated that aims to correlate the molecular configuration of alkyl-substituted oxiranes with the order of chromatographic elution from the optically active stationary phase **3b** derived from (+)-(1*R*)-camphor (cf. Chart I, c). When the oxirane molecule is viewed from the oxygen atom in the direction of the horizontal C–C bond, the molecular configuration of the enantiomer eluting later on (1*R*)-**3b** is that in which the bulkiest substituent is residing in the position to the upper left or lower right that corresponds to the absolute configuration *S* for alkyl groups. This rule has been confirmed for **3b**, **4b**, **5b**, and the oxiranes listed in Table II, and, furthermore, for **5b** and the two enantiomeric pairs of *sec*-butyloxirane[27] as well as 2-methyloxetane.[28] As will be shown below, the rule is also valid for 1-chloro-2-methylaziridine and methylthiirane, but a remarkable exception is found for *trans*-2,3-dimethylthiirane (vide infra).

Highly beneficial for analytical purposes is the fact that, unlike other methods of gas chromatographic enantiomer resolution,[2,4] no substrate derivatization is required in complexation gas chromatography. Thus, the enantiomeric composition (enantiomeric purity, enantiomeric excess (ee)) (cf. Chart I, d) of racemic compounds can directly be determined from relative peak areas with approximately 10^{-8} g of sample, without chemical manipulations, isolation, and purification. A typical analytical applications for chiral oxiranes has recently been described in a study of the stoichiometric asymmetric epoxidation of prochiral olefins with an optically active molybdenum(VI) peroxo reagent where chemical and enantiomeric yields as well as the molecular configuration of the predominant enantiomer have been simultaneously determined during the entire reaction period by complexation gas chromatography on **3b** or **5b**.[29]

A precondition for the precise determination of enantiomeric compositions is the configurational integrity of the respective antipodes during the entire chromatographic resolution event. We define "enantiomerization" as a process in which both antipodes of a racemic (or nonracemic) mixture of enantiomers invert their respective configuration during resolution, e.g., in the presence of an optically active stationary phase in chromatography or in the presence of an optically active solvent in NMR spectroscopy. Such a transition phenomenon has been observed for the first time

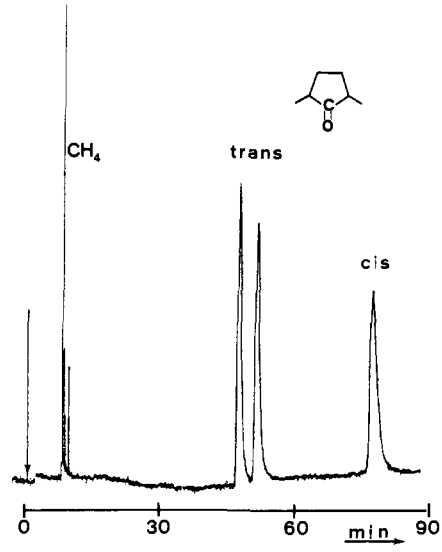


Figure 4. Enantiomer resolution of *trans*-2,5-dimethylcyclopentanone (**19**) on (1*R*)-**3b** (0.132 *m* in squalane) at 70 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 2.6 mL/min N_2; split ratio 1:50.

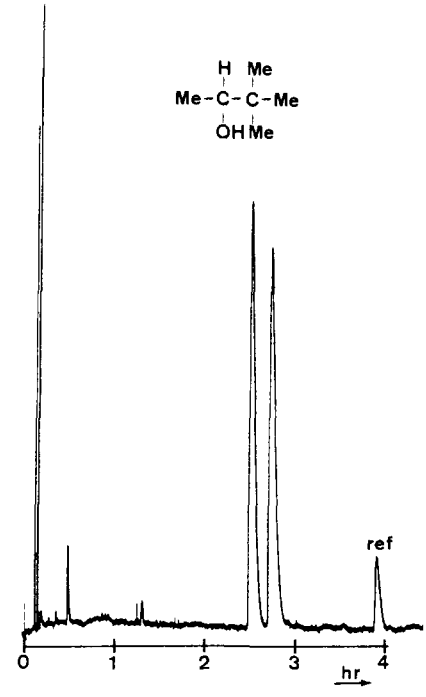
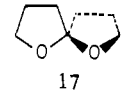


Figure 5. Enantiomer resolution of *tert*-butylmethylcarbinol (3,3-dimethylbutan-2-ol) (**20**) on (1*R*)-**3b** (0.156 *m* in squalane) at 70 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 3.0 mL/min N_2; split ratio 1:50.

in chromatography: in the enantiomer resolution of the spiroketal 2,6-dioxaspiro[4.4]nonane (**17**) on **3b**, the chromatographic elution



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between the terminal peaks does not approach the zero base line but forms a *plateau* obviously caused by molecules that have inverted their configuration during resolution and that travel now with the speed of the antipode (cf. Figure 3). This dynamic chromatographic elution pattern is referred to as *peak coalescence of the second kind* (cf. Chart I, e). It is evident that the shape of the plateau depends on the rate of configurational change, and, in principle, kinetic parameters of enantiomerization should be

(26) M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974); J. A. Cunningham and R. E. Sievers, *ibid.*, **97**, 1586 (1975); H. G. Brittain, *ibid.*, **101**, 1733 (1979); G. R. Sullivan, *Top. Stereochem.*, **10**, 287 (1978).
(27) B. Koppenhoefer, R. Weber, and V. Schurig, *Synthesis*, 316 (1982).
(28) K. Hintzer, B. Koppenhoefer, and V. Schurig, *J. Org. Chem.*, **47**, 3850 (1982).
(29) H. B. Kagan, H. Mimoun, C. Mark, and V. Schurig, *Angew. Chem., Int. Ed. Engl.*, **18**, 485 (1979).

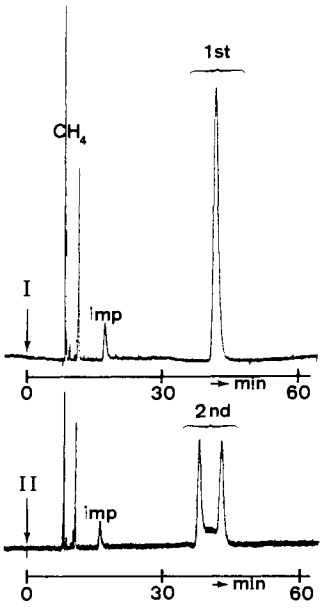
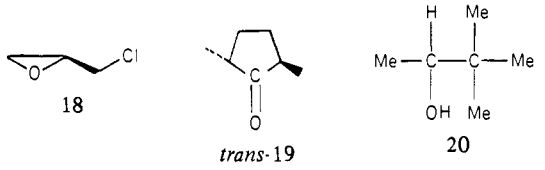


Figure 6. Coalescence phenomena for 1-chloro-2,2-dimethylaziridine (**21**) on **3a** (0.13 *m* in squalane) at 60 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 2.4 mL/min N_2; split ratio 1:50. (top) Peak coalescence (1st kind) of **21** on racemic **3a**; (bottom) peak coalescence (2nd kind) during resolution of **21** on optically active (1*R*)-**3a** with a plateau between the terminal peaks.

accessible by peak-form analysis.[30]

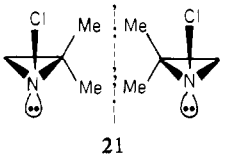
Enantiomer resolution by complexation gas chromatography is not only limited to simple cyclic ethers. Thus, a chlorinated oxirane (i.e., epichlorohydrin (**18**)), an underivatized cyclic ketone



(i.e., *trans*-2,5-dimethylcyclopentanone (**19**)) (cf. Figure 4), and an underivatized aliphatic alcohol (i.e., *tert*-butylmethylcarbinol (**20**)) (cf. Figure 5) have been quantitatively resolved for the first time on **3b**. The latter example vividly demonstrates that resolution by complexation gas chromatography is not restricted to cyclic compounds.[31]

Resolution of Nitrogen-Containing Racemates

The enantiomer resolution of the invertomers of 1-chloro-2,2-dimethylaziridine (**21**) has recently been described by complexation



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gas chromatography on **3b**.[32] The successful resolution of **21** is of special interest as the nitrogen atom constitutes the sole chiral center in the molecule, which, in this particular constrained-ring structure, is stable to inversion.[33] We have predicted[32] that

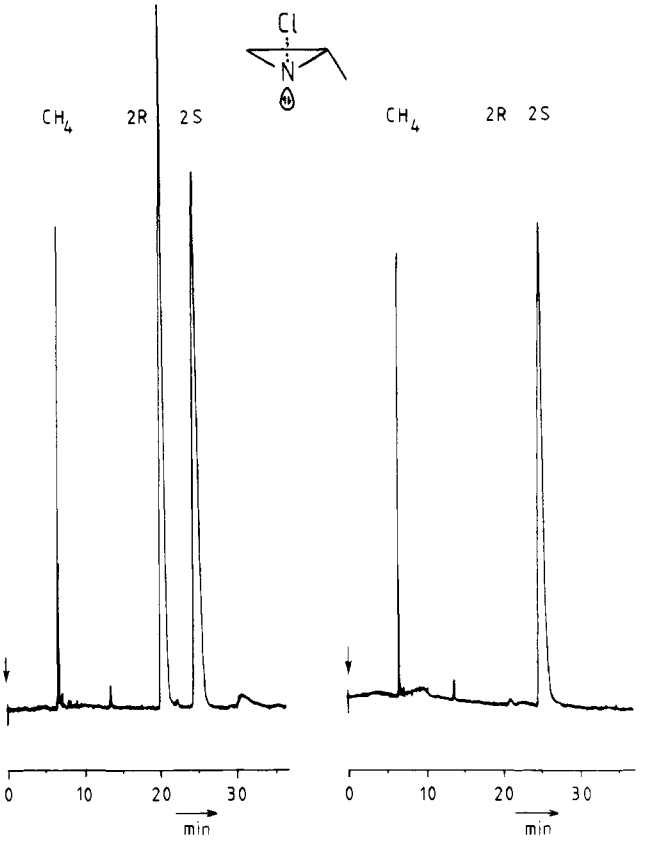


Figure 7. Invertomer resolution of *trans*-1-chloro-2-methylaziridine (**22**) on (1*R*)-**3b** (0.156 *m* in squalane) at 63 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 2.9 mL/min N_2; split ratio 1:50. (left) racemic *trans*-**22**; (right) (1*S*,2*S*)-*trans*-**22** (ee 99%).

complexation gas chromatography may be a useful tool for the detection of slow processes of enantiomerization (vide supra) or specifically, of inversion of **21**. This has now been borne out by the experiment. In Figure 6, two kinds of coalescence phenomena (vide supra), which may be encountered in the chromatography of racemic molecules on optically active stationary phases, are demonstrated. In the first (trivial) case (cf. Figure 6, top), the two enantiomeric fractions coalesce to one peak when the optically active stationary phase is replaced by the racemic one. This strategy is the method of choice to distinguish a true enantiomer resolution from the separation of diastereomers with an accidental peak ratio of 1:1. In the second (nontrivial) case (cf. Figure 6, bottom), a plateau is built up between the two enantiomeric fractions caused by molecules inverting configuration during resolution on the optically active stationary phase. It is important to note that the transition phenomenon shown in Figure 6 (bottom) was pronounced only when **3a** was used instead of **3b** as resolving stationary phase. Thus, the metal chelate may participate in decreasing the activation barrier of nitrogen inversion in compound **21**. It should be mentioned that the mass spectra of the chromatographic eluate were identical for the entire peak area (terminal peaks and peak plateau).[30]

Another point of interest is the assignment of absolute configuration to the resolved invertomers of **21**. Since any synthesis of optically active **21**[33d] will be extremely difficult because of the low barrier of inversion for potential precursors, we considered an assignment via comparison of the chromatographic behavior of a structurally related compound in which an additional chiral center of known molecular configuration is related to the asym-

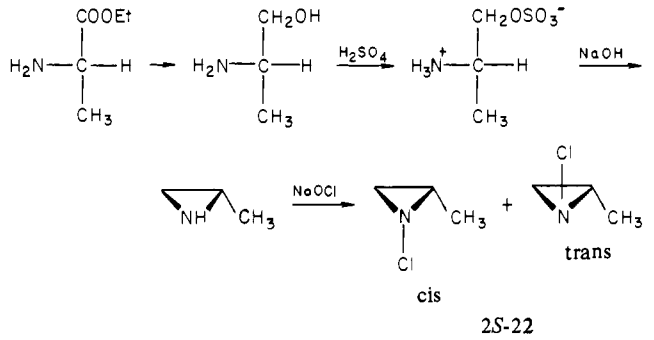
(30) The mathematical simulation aided by data processing of chromatograms featuring "enantiomerization" is forthcoming (W. Bürkle, H. Karfunkel, and V. Schurig, to be published).

(31) Recently, racemic amino alcohols and amines have been resolved on a optically active copper(II) Schiff base complex: N. Ôi, K. Shiba, T. Tani, H. Kitahara, and T. Doi, *J. Chromatogr.*, **211**, 274 (1981).

(32) V. Schurig, W. Bürkle, A. Zlatkis, and C. F. Poole, *Naturwissenschaften*, **66**, 423 (1979).

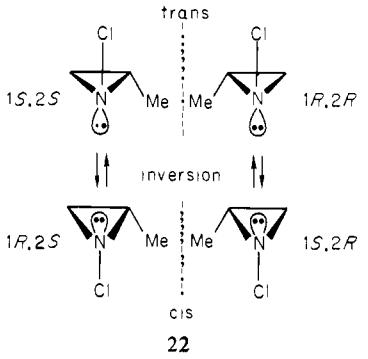
(33) (a) S. J. Brois, *J. Am. Chem. Soc.*, **90**, 506, 508 (1968). (b) J. M. Lehn and J. Wagner, *J. Chem. Soc. Chem. Commun.*, 148 (1968). (c) R. G. Kostyanovsky, Z. E. Samojlova, and I. I. *Tchervin, Tetrahedron Lett.*, 719 (1969). (d) R. G. Kostyanovsky and G. K. Kadorkina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1686 (1977).

Scheme I. Synthesis of 2S-22 from (S)-Alanine



2S-22

metric nitrogen atom through the ring structure. We have selected 1-chloro-2-methylaziridine (**22**), which occurs as two enantiomeric



22

pairs of cis and trans diastereomers,[33] for this purpose. Chlorination[34] of 2-methylaziridine led to cis- and trans-**22**, which were identified by GCMS. On standing at elevated temperature, one diastereomer disappeared. In the complexation chromatogram of racemic **22** on **3b**, only one resolved enantiomeric pair, which we refer to as the thermodynamically stable trans isomer,[33c] has been observed (cf. Figure 7). In this isomer the methyl group is located cis to the coordinating lone pair at nitrogen, which may, incidentally, explain the greater enantiomer discrimination (α = 1.33) of the aziridine as compared to that of methyloxirane (**6**) (α = 1.18). In the next step, **22** with configuration *S* at the chiral carbon atom was prepared from (*S*)-alanine by a synthesis of well-defined stereochemical course[35] (Scheme I).

In the complexation gas chromatogram of 2*S*-labeled trans-**22** resolved on **3b** derived from (+)-(1*R*)-camphor, the first peak was reduced to 0.5% as compared to racemic **22** (cf. Figure 7). This result allows the following conclusions: (a) The separation shown in Figure 7 is a true enantiomer resolution. (b) The enantiomeric excess (ee 99%) for (2*S*)-**22** shows that the synthesis (Scheme I) proceeds essentially without racemization[36] (cf. Figure 7, right). (c) The second peak in Figure 7 arises from the enantiomer with configuration *S* at the carbon atom. Since this isomer is assigned trans geometry, the configuration at nitrogen is *S*. (d) The order of peak emergence of **22** on (1*R*)-**3b** is the same as that for methyloxirane (**6**); i.e., the *S* enantiomer is eluted after the *R* antipode, in agreement with the quadrant rule.

We may now proceed to assign the absolute configuration of the invertomers of **21** resolved on **3b**. Since the coordination geometry of **21** and trans-**22** (the latter being devoid of a methyl group *opposite* to the coordinating lone pair at nitrogen) are closely related and since trans-**22** with *S* configuration at nitrogen is eluted after the *R* antipode, it is concluded that also for **21** the invertomer

(34) A. F. Graefe and R. E. Meyer, *J. Am. Chem. Soc.*, **80**, 3939 (1958).
(35) Y. Minora, M. Takebayashi, and C. C. Price, *J. Am. Chem. Soc.*, **81**, 4689 (1959).
(36) This results clarifies the incertitude of the origin of 40% racemization noted in the formation of (*R*)-2-amino-3-methylbutane from (*S*)-valinol via 2-isopropylaziridine (H. Rubinstein, B. Feibush, and E. Gil-Av, *J. Chem. Soc., Perkin Trans. 2*, 2094 (1973)). Racemization must have occurred during hydrogenolysis of the aziridine with Raney nickel.

Table III. Comparison of Stability Constants *K* of δ-Donor Molecules with Bis[3-(trifluoroacetyl)camphorates] of Nickel(II) (3a), Cobalt(II) (4a), and Manganese(II) (5a) at 75 °C[13]

substrate	no.	*K*, L/mol Ni	Co	Mn
methyloxirane	6	53	16	7
methylthiirane	23	51	7	1
diethyl ether	27	21	6	3
diethyl sulfide	28	127	17	1.5

Table IV. Comparison of the Separation Factor α^a of Quantitative Enantiomer Resolution for Racemic Oxiranes vs. Thiiranes on Nickel(II) Bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (3b) in Squalane (0.1 *m*) at 60 °C

substrate	no.	α^a
methyloxirane	6	1.19
methylthiirane	23	1.05
ethyloxirane	7	1.08
ethylthiirane	24	1.08
trans-2,3-dimethyloxirane	11	1.23[b]
trans-2,3-dimethylthiirane	25	1.08[b]

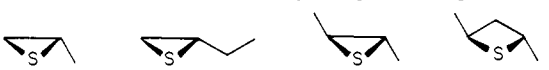
[a] For dead-volume (methane peak) adjusted retention time *t'* of the second eluting enantiomer over that of the first eluting enantiomer. [b] At 70 °C.

with configuration *S* is eluted after the *R* antipode on **3b** derived from (+)-(1*R*)-camphor.

Resolution of Sulfur-Containing Racemates

The thermodynamic association constants of σ-donor solutes with bis[(1*R*)-3-(trifluoroacetyl)camphorates] of nickel(II) (**3a**), cobalt(II) (**4a**), and manganese(II) (**5a**) have previously been determined by complexation gas chromatography.[13] Relevant to the present work is the comparison of the coordination ability of substrates containing oxygen (undergoing prevalent electrostatic interaction) and sulfur (undergoing prevalent covalent interaction) with **3a**–**5a**. The results (Table III) show that the nickel chelate exhibits the best acceptor properties for solutes containing sulfur.

While no enantiomer separation for methylthiirane (**23**) was observed on **3a** under the design of the previous experiment,[13] quantitative resolutions of the racemic thiiranes and thietanes (**23**–**26**) have now been achieved by complexation gas chroma-



23 24 *trans*-25 *trans*-26

tography on optically active nickel(II) bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (**3b**) in squalane coated on a 100-m capillary column. In Table IV, separation factors (α) of enantiomer resolution between oxiranes and thiiranes are compared. The first successful enantiomer resolution of thiiranes offers the opportunity to study the chiral properties of this class of compounds. The absolute configuration of thiiranes has in the past been assigned by indirect chemical evidence through transformations of well-defined stereochemical course from precursors of known chirality. Thus, the conversion of oxiranes to thiiranes with thiocyanate anion[37] or with triphenylphosphine sulfide[38] is known to proceed with inversion of configuration at the chiral carbon atom.

We applied this reaction for the comparison of the correlation of molecular configuration and order of peak elution for chiral oxiranes vs. thiiranes on optically active **3b** derived from (+)-(1*R*)-camphor (cf. Chart I, c). The purpose of this study was to investigate whether the empirical quadrant rule formulated for alkyl-substituted oxiranes ("hard" donor solutes) is valid also for thiiranes ("soft" donor solutes). Surprisingly, no agreement could be established. In a preceding experiment, racemic *trans*-2,3-

(37) E. E. van Tamelen, *J. Am. Chem. Soc.*, **73**, 3444 (1951).
(38) T. H. Chan and J. R. Finkenbine, *J. Am. Chem. Soc.*, **94**, 2880 (1972).

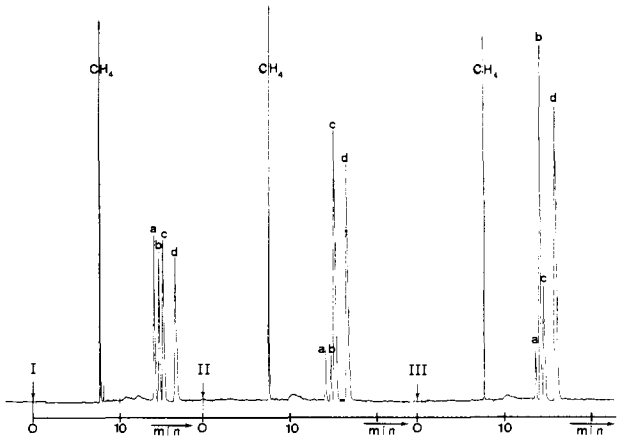
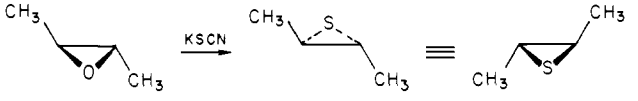


Figure 8. Enantiomer resolution of *trans*-2,3-dimethylthiirane (**25**) and *trans*-2,3-dimethyloxirane (**11**) on (1*R*)-**3b** (0.156 *m* in squalane) at 90 °C. Column, 100 m × 0.5 mm nickel capillary; carrier gas 2.6 mL/min N_2; split ratio 1:50. (left) Racemic thiirane and racemic oxirane (~1:1); (middle) racemic thiirane and racemic oxirane (~1:5); (right) *trans*-(2*R*,3*R*)-dimethylthiirane (**25**) and *trans*-(2*S*,3*S*)-dimethyloxirane (**11**) with a deficient admixture of racemate to aid peak assignment. Assignment: a = *trans*-(2*S*,3*S*)-dimethylthiirane, b = *trans*-(2*R*,3*R*)-dimethylthiirane, c = *trans*-(2*R*,3*R*)-dimethyloxirane, d = *trans*-(2*S*,3*S*)-dimethyloxirane.

dimethyloxirane (**11**) was converted with KSCN to *trans*-2,3-dimethylthiirane (**25**). An 1:1 mixture of both substrates could simultaneously been resolved on **3b** (cf. Figure 8, left). A mixture enriched in the oxirane resulted in a deficiency of peaks a and b (cf. Figure 8, middle), which are consequently assigned to the thiirane enantiomers. In another experiment, enantiomerically pure (>99%) *trans*-(2*S*,3*S*)-dimethyloxirane (**11**) obtained from (2*R*,3*R*)-tartaric acid[39] was converted with KSCN to *trans*-(2*R*,3*R*)-dimethylthiirane (**25**) accompanied with inversion of configuration at both carbon atoms.[37] In the chromatogram of



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the 1:1 mixture of both solutes, only two single peaks were observed, which were assigned b and d through admixture of racemic samples (cf. Figure 8, right). Thus, upon chromatography on **3b** derived from (+)-(1*R*)-camphor, both *trans*-(2*S*,3*S*)-**11** and *trans*-(2*R*,3*R*)-**25** are eluted as the second peak of each respective enantiomeric pair (ab, cd), although their absolute configurations are *opposite* to each other. The same order of elution was obtained when triphenylphosphine sulfide was used as conversion agent, which is also known to induce inversion of configuration at both carbon atoms.[38]

In a further experiment, additional evidence for the elution order of *trans*-(2*R*,3*R*)-dimethylthiirane (**25**) was obtained. (+)-**25** is preferentially enclathrated in (−)-tri-*o*-thymotide (TOT) crystals,[40] and its absolute configuration (2*R*,3*R*) has been determined by crystal structural analysis of the clathrate (−)-tri-*o*-thymotide–(+)-*trans*-2,3-dimethylthiirane.[41] The thiirane, expelled from (−)-TOT, was chromatographed on (1*R*)-**3b**, and coincidence with peak b, previously assigned 2*R*,3*R* by indirect chemical evidence, was observed. The results allow the following conclusions: (a) Enantiomers of *trans*-2,3-dimethyloxirane (**11**) and of *trans*-2,3-dimethylthiirane (**25**) of opposite absolute configuration are eluted in the same relative order on (1*R*)-**3b** in violation of the quadrant rule. (b) The conversion of *trans*-2,3-dimethyloxirane (**11**) to *trans*-2,3-dimethylthiirane (**25**) with KSCN proceeds with complete (>99%) inversion of configuration at both carbon atoms. Neither racemization nor partial retention, which would lead to the cis epimer, was observed.

We have also determined the order of elution vs. molecular configuration for (*R*)-methylthiirane (**23**). This enantiomer was independently obtained by synthesis from (*S*)-methyloxirane (**6**)[19] with KSCN and by kinetic resolution of racemic methylthiirane (**23**) via stereoelective polymerization of the *S* antipode.[42] Chromatography of (*R*)-methylthiirane (**23**) on (1*R*)-**3b** disclosed an elution order consistent with that previously found for (*R*)-methyloxirane (**6**);[19] i.e., the first peak was more abundant.

The inconsistency of the empirical quadrant rule for thiiranes themselves and between thiiranes and oxiranes illuminates the difficulties and shortcomings in attempts to rationalize mechanisms of chiral recognition in chromatographic systems. Therefore, caution has to be exercised when predictions of enantiospecificities are advanced, even in cases of apparent simplicity such as those described here: the smallest dissymmetric (C_2) molecules coordinate in a one-point interaction with metal chelates of simple structure. Infact, Drago et al. have already discussed different bonding characteristics between (hard) oxygen and (soft) sulfur donor molecules with vanadium(IV) and copper (II) β-diketonate acceptors.[43]

It should again be noted that the investigations that led to the above results can be performed with great ease. Thus, for the determination of the enantiomeric composition of (−)-TOT-enclathrated guests[40] or for the monitoring of asymmetric inductions during stereoelective polymerizations of racemic monomers,[44] only minute amounts of chiral sample (10^{-8} g), usually drawn from the head space, is required. The conversion of oxiranes to thiiranes can be equally carried out by smallest scale operations, and the enantiomeric composition and the absolute configuration can be determined directly without chemical manipulations, isolation, and purification.

Experimental Section

Instrumentation. Carlo Erba gas chromatographs, Fractovap 2101 and 2350, equipped with FID detectors and suitable for operations with capillary columns, were used. The carrier gas was high-purity-grade nitrogen.

Columns. Nickel capillary columns (100 m × 0.5 mm and 67 m × 0.5 mm), 200 seamless, 99.53%, Ni, 0.24% Mn) furnished from Handy & Harmon Tube Co., Norristown, PA, were used. Prior to use the columns were washed with *n*-hexane, chloroform (purified over basic alumina), acetone, and water. The cleaning procedure was repeated in the reverse order.

Coating of columns was performed by the dynamic plug method as described earlier.[17,21] A homemade coating device prepared from Teflon was used. In a typical coating procedure, 15.1 mg of (1*R*)-**3b** and 200 mg of squalane (Applied Science) (0.1 *m*) were dissolved in 3.5 mL of acid-free and high-purity-grade chloroform with warming. A 100 m × 0.5 mm capillary column was coated with this solution at 0.6 atm of N_2 (over pressure) and at 22 °C. The N_2 pressure was maintained for 5 h after the coating solution had passed through the capillary. The column was connected to the gas chromatograph and conditioned at 0.3 atm (overpressure) N_2 at a temperature that was raised from 22 to 100 °C within 12 h with the exit end left open. Before the detector was connected to the end of the column, the column end was heated with a free flame in order to remove volatiles. Dead volumes in the flow system were avoided as the column was connected to the injector and detector. The separation of racemic solutes was carried out isothermically between 60 and 90 °C. The overpressure of the carrier gas was 0.3–0.5 atm, the split ratio was 1:50.

Reference Solutes. Methane was coinjected to measure the dead volume (gas holdup) of the capillary column. *n*-Octane was coinjected

(39) V. Schurig, B. Koppenhöfer, and W. Bürkle, *J. Org. Chem.*, **45**, 538 (1980).
(40) R. Arad-Yellin, B. S. Green, and M. Knossow, *J. Am. Chem. Soc.*, **102**, 1157 (1980).
(41) R. Arad-Yellin, B. S. Green, M. Knossow, and G. Tsoucaris, *Tetrahedron Lett.*, 387 (1980).
(42) N. Spassky and P. Sigwalt, *Tetrahedron Lett.*, 3541 (1968); *Macromolecules*, **5**, 92 (1971).
(43) D. R. McMillin, R. S. Drago, and J. A. Nusz, *J. Am. Chem. Soc.*, **98**, 3120 (1976); R. S. Drago, T. C. Küchler, and M. Kroeger, *Inorg. Chem.*, **18**, 2337 (1979).
(44) M. Sepulchre, K. Hintzer, V. Schurig, and N. Spassky, Comptes Rendus Acad. Sci., **291**, C 267 (1980); M. Sepulchre, N. Spassky, C. Mark, and V. Schurig. *Makromol. Chem., Rapid Commun.*, **2**, 261 (1981).

as noncoordinating reference standard. The retention times t' of all solutes were related to that of *n*-octane (relative retention *r*).

Calculation of the Retention Increase R' and of the Free Enthalpy Difference of Enantiomer Discrimination ($-\Delta_{S,R}(\Delta G°)$). Adjusted retention times (t'_{sol}) were measured as the distance between the maximum peak heights of the solute and the methane peak. t'_{sol} was then related to t'_{ref} of the inert reference standard *n*-octane to give *r*. The relative retention of a solute obtained from a column containing the metal chelate dissolved in squalane (r) and that of the same solute obtained from a column containing pure squalane (r_0) were used to calculate R' according to eq 2, i.e., $(r - r_0)/r_0 = R'$. From the retention increase R' for the respective enantiomers, $-\Delta_{S,R}(\Delta G°)$ is calculated according to eq 3.

Solutes. Substrates with suspected alkylating properties (aziridines, epoxides) were handled with great care. Most of the substrates were commercially available. Oxiranes were prepared from alkenes by epoxidation with *m*-chloroperbenzoic acid. In a typical experiment, 100 mg of *m*-chloroperbenzoic acid was dissolved in 2 mL of diethyl ether, 150 μL of alkene was added, and the reaction mixture was stored at 5 °C for 24 h. The vapor of the reaction mixture containing the oxirane was injected into the gas chromatograph without isolation by the "head-space technique". Oxiranes, enriched in the *R* enantiomer, were obtained in a similar fashion from prochiral alkenes and $MoO(O_2)_2$-(*S*)-MeCH(OH)CONMe$_2$ in nitrobenzene.[29] 2-Methyloxetane was obtained according to ref 28. (*S*)-Methyloxirane (**6**) was prepared according to ref 19 and *trans*-(2*S*,3*S*)-dimethyloxirane (**11**) according to ref 39. (2*S*)-2-Methylaziridine was obtained from (*S*)-alanine via (*S*)-alaninol, according to ref 35.

N-Chlorination of Aziridines.[34] Eight grams (0.11 mol) chlorine gas was introduced into a solution of 40 mL of water and 9.25 g (0.22 mol) of sodium hydroxide at −10 °C. In this solution, 0.1 mol of chilled aziridine was introduced with vigorous stirring. The crude 1-chloroaziridine separated as a colorless liquid, which was separated, washed five times with water, and dried over sodium sulfate. The vapor of the 1-chloroaziridine was injected into the gas chromatograph without further purification. In the synthesis of (2*S*)-1-chloro-2-methylaziridine (**22**) from (2*S*)-2-methylaziridine, two epimers (cis and trans) were initially formed as shown by GC–MS. On standing at elevated temperature, one epimer (cis) disappeared. Epimerization of cis-**22** to *trans*-**22** has been quantitatively measured by Kostyanovsky et al.[33c]

Transformation of Oxiranes to Thiiranes.[45] Ten millimoles of oxirane, 1.25 g (12.9 mmol) of potassium thiocyanate, and 1.5 mL of water were sealed into an ampule, which was slowly shaken for 2 days at 22 °C. After the ampule was opened, the organic layer containing the thiirane was separated and dried over magnesium sulfate. The vapor of the thiirane was injected into the gas chromatograph without further purification. Conversion to methylthiirane (**23**) and ethylthiirane (**24**) was quantitative and that to *trans*-2,3-dimethylthiirane (**25**) 55%, by GC. (*R*)-Methylthiirane (**23**) and *trans*-2,4-dimethylthietane (**26**) were obtained from the authors of ref 42. Crystals of (−)-TOT-(+)-**25** were supplied from the authors of ref 41.

Preparation of Nickel(II) Bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (3b). 1. (1*R*)-3-(Heptafluorobutyryl)camphor.[46] This ligand was prepared according to the general procedure of Whitesides et al.[26] To a flame-dried, nitrogen-purged, 250-mL flask equipped with mechanical stirrer, nitrogen inlet, and low-temperature thermometer was added 42.5 mL (67.5 mmol) of a 5% solution of methyllithium in ether (Merck), and it was cooled to −20 °C in a cryostat. After the careful addition of 9.5 mL (67.2 mmol) of diisopropylamine (Fluka), stirring was continued for 30 min at −20 °C. A 10.2-g (67.0 mmol) sample of (+)-(1*R*)-camphor (Merck) was dissolved in dry ether, the solution cooled to −20 °C under nitrogen, and then added rapidly to the reaction flask. The reaction mixture was stirred for 30 min at −20 °C and afterward cooled to −60 °C. A 10-mL (66.5 mol) sample of heptafluorobutyryl chloride (Riedel-de Haen) was dissolved in 20 mL of dry ether and added to the solution via dropping funnel with vigorous stirring at a rate sufficient to maintain the temperature at −60 °C. The reaction mixture was stirred for 60 min at −60 °C, then allowed to gradually warm up to −20 °C over a period of 30 min, and afterward transferred into a well-stirred mixture of 150 mL of 1 M hydrochloric acid and ice. The organic phase was separated, and the aqueous phase was extracted four times with 120 mL of ether. The combined organic phases were washed twice with 50 mL of sodium chloride solution, dried over sodium sulfate, and then concentrated in vacuo. Unreacted camphor was removed by sublimation at 40 °C (15 mmHg). Distillation of the remaining red-brown oil at 70–80 °C (1 mmHg) yielded 7.5 g (32.1%) of a colorless liquid: $[\alpha]^{22}_D$ +121.8° (*c* 2.58, CCl_4); ^{13}C NMR δ 8.30, 17.98, 20.13, 26.63, 30.07, 47.56, 48.99, 57.96, 120.61, 213.95; MS, *m/e* (rel int) 349 (15), 348 (M^+, 100), 333 ($M^+ - CH_3$, 29), 320 ($M^+ - CO$, 42). Further purification of the ligand was carried out via its sodium salt.[47]

2. Sodium (1*R*)-3-(Heptafluorobutyryl)camphorate.[46] A 0.3-g sample of 80% sodium hydride suspension in paraffin (10 mmol of NaH) (Fluka) was washed under nitrogen with dry benzene until the paraffin was completely removed. The residue was suspended in benzene and transferred into the reaction flask. 2.5 g (7.2 mmol) of (1*R*)-3-(heptafluorobutyryl) camphor was dissolved in 80 mL of dry benzene and added to the suspension of sodium hydride in benzene. The mixture was stirred for 3 h under nitrogen, then carefully concentrated (foaming!) in vacuo, the residue was dissolved in warm chloroform, and the solution was filtered. The filtrate was diluted (1:1) with dry ether with vigorous mixing. The mixture was allowed to cool to 5 °C whereby a gelatinous precipitate was gradually formed. The solid was isolated by suction and repeatedly reprecipitated from chloroform/ether. The final product was dried at 20 °C (0.01 mmHg) to yield 2.45 g (92%) of a white product: mp 236–237 °C; $[\alpha]^{20}_D$ +209.9° (*c* 2.6, CCl_4); ^1H NMR δ 0.67 (s, 3, CH_3), 0.78 (s, 6, CMe_2), 2.54–2.75 (br 1 H, bridgehead H); IR (KBr) 1660, 1550, 1225 cm^{-1}.

3. Nickel(II) Bis[(1*R*)-3-(heptafluorobutyryl)camphorate] (3b).[46] A 2-g (5.4 mmol) sample of sodium (1*R*)-3-(heptafluorobutyryl)camphorate was dissolved in 50 mL of dry ethanol. Then 0.37 g (2.85 mmol) of anhydrous powdered nickel(II) chloride was added, and the mixture was refluxed for 12 h. The green solution was filtered from the sodium chloride formed, then carefully concentrated (foaming!), and the residue sublimed at 140–160 °C (0.02 mmHg). Yield: 1.3 g (32%) of a pale green glassy powder, which softens at 100–115 °C. Higher yields are obtained if the residue is extracted with *n*-pentane and the solvent allowed to evaporate: $[\alpha]^{20}_D$ +123.9° (*c* 0.7, $CHCl_3$), $[\alpha]^{20}_D$, +115.0° (*c* 0.8, *n*-pentane).

Anal. Calcd for $NiC_{28}H_{28}F_{14}O_4$ (753.2 for monomer, 1506.4 for dimer): C, 44.65; H, 3.75; F, 35.31; Ni, 7.79. Found: C, 44.86; H, 3.92; F, 35.21; Ni, 7.13.

Molecular weight (by osmometry of the vapor phase in anhydrous *n*-heptane at 45 °C): 815 (*c* 4.986 mg/mL), 794 (*c* 3.760 mg/mL). These data are 8.2% and 5.4%, respectively, above the calculated molecular weight of the monomer, which may indicate minor oligomerization. MS, *m/e* 755 (12), 754 (46), 753 (35), 752 (100), 727 (12), 726 (37), 725 (26), 724 (79), 709 (16), 698 (11), 696 (24), 683 (5) for ^{60}Ni and ^{58}Ni. *m/e* for dimer are less than 1%: 1504 (trace), 1160 (1), 1158 (1). In the field-desorption mass spectrum, only peaks due to the dimer occur: *m/e* 1506 and 1504.

Electronic spectra: three d–d absorptions were observed: λ_{max} 1115 (log ε 1.16), 646 (0.75), and 339 nm (3.93 sh), ν 8980, 15 475, and 29 500 cm^{-1}, respectively.

IR (KBr) 1620, 1490, 1330, 1230 cm^{-1}.

Magnetic measurements:[48] **3b** is paramagnetic; 3.04 μ_B (72 K), 3.12 μ_B (300 K). $1/\chi_{mol}$ as a function of *T* fulfills Curie's law.

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Registry No. 3b, 68457-34-1; **4b**, 83664-34-0; **5b**, 76059-35-3; (±)-**6**, 16033-71-9; (±)-**7**, 55555-96-9; (±)-**8**, 83708-80-9; (±)-**9**, 62137-90-0; (±)-**10**, 83708-81-0; (±)-**11**, 6189-41-9; (±)-**12**, 83708-82-1; (±)-**13**, 75492-27-2; (±)-**14**, 74069-67-3; (±)-**15**, 38484-59-2; (±)-**16**, 83664-35-1; (±)-**17**, 83664-36-2; (±)-**18**, 13403-37-7; (±)-**19**, 83664-37-3; (±)-**20**, 20281-91-8; (±)-**21**, 83708-83-2; (*s*)-**21**, 83664-41-9; (*R*)-**21**, 28112-60-9; (±)-*trans*-**22**, 83664-38-4; (±)-*cis*-**22**, 83664-40-8; (2*s*)-*trans*-**22**, 83708-85-4; (±)-**23**, 15423-00-4; (±)-**24**, 83708-84-3; (±)-*trans*-**25**, 70492-83-0; (±)-*trans*-**26**, 83664-39-5; (1*R*)-3-(heptafluorobutyryl)camphor, 51800-99-8; (+)-(1*R*)-camphor, 464-49-3; heptafluorobutyryl chloride, 375-16-6; sodium (1*R*)-3-(heptafluorobutyryl)-camphorate, 83664-42-0.

(45) C. C. Price and P. F. Kirk, *J. Am. Chem. Soc.*, **75**, 2396 (1953).

(46) The reaction was carried out under high-purity-grade nitrogen. The solvent was dried with benzophenone–sodium.

(47) **Note Added in Proof**: Column chromatography (silica, benzene/*n*-hexane (1:1)) yielded pure (1*R*)-3-(heptafluorobutyryl)camphor: bp 55–57 °C (0.05 mmHg); $[\alpha]^{22}_D$ +126.5° (*c* 2.7, CCl_4); α^{20}_D +170.8° (neat).

(48) The magnetic measurements were performed in the laboratory of Professor O. Kahn, Laboratoire de Spectrochimie des Elēments de Transition, Universitē de Paris-Sud, Orsay, France.