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PLATINUM COMPLEXES IN REVERSED- AND NORMAL-PHASE CHROMATOGRAPHY

ANALYTICAL- AND PREPARATIVE-SCALE SEPARATIONS OF ENANTIOMERIC OLEFINS

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SUMMARY

The separation of different enantiomeric olefins, even of those containing other polar functional groups, was achieved via their diastereomeric platinum complexes olefin–PtCl–OOCCH(NR_1R_2)C_6H_5 (I: $R_1 = R_2 = CH_3$; II: $R_{1,2} = H$, $R_{2,1} = (CH_2)_3CH_3$; III: $R_{1,2} = H$, $R_{2,1} = (CH_2)_6CH_3$) by normal- or reversed-phase liquid chromatography.

The influence of the molecular structure of the olefins on the resolution of the complexes was investigated. Epimerization reactions of those diastereomeric species that are formed through the presence of prochiral C atoms at the double bonds are interpreted in terms of a dissociation–association process. The validity of this mechanism was confirmed by kinetic measurements.

A method for the determination of the enantiomeric composition of olefins and certain derivatives is described. This method can also be applied to mixtures containing olefins and requires only small amounts of sample. Its precision and accuracy is generally superior to that of previous methods.

Pure (+)- and (−)-enantiomers could be isolated from their corresponding platinum complexes by on-line displacement in a column which was coupled with a separation column.

INTRODUCTION

The analysis of olefins by chromatography presents a number of difficulties caused by

(i) a great number of structurally similar isomers,

(ii) weak and not very selective intermolecular interaction in the common gas and liquid chromatographic systems,

(iii) low solubility of the olefins in polar mobile phases of LC systems,

(iv) insufficient sensitivity with LC detectors.

Further problems arise with the separation of enantiomeric olefins. On optically active organic stationary phases, such separations cannot be realized on the

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basis of the "three-point-attachment concept" of Dalgliesh[1] because the olefinic molecules do not contain any functional groups, able to form the necessary hydrogen-bondings for a specific attachment of the enantiomer to the stationary phase molecules. Charge-transfer interactions with optically active acceptor molecules as parts of a stationary phase can be assumed to be too weak to separate olefins into their enantiomers.

To enhance the selectivity of chromatographic olefin analysis, metal complexation seems to be the method of choice. In this case, LC is superior to GC because at the high temperatures required for the volatilization of high-molecular-weight compounds in GC, the metal complexes are not stable enough in most cases and may be isomerized or decomposed. Moreover, the high chromatographic selectivity necessary with diastereomer separations is considerably decreased at elevated temperatures.

In a previous paper[2] we described how platinum-complexes could be used to increase selectivity for the separation of various types of olefins, amines and heterocyclic compounds, by analogy to "argentation chromatography"[3–5], the metal salt or complex being a component of the mobile phase. Besides those investigations involving metals such as Ag(I)[6–8] or Rh(II)[8] as additives to stationary phases, few attempts at "external" olefin complex formation and subsequent LC separation have been made[2,9]. "External" here means that the olefin species are complexed outside and not inside the chromatographic system.

Using C_2H_4–PtCl–$OOCCH[N(CH_3)_2]C_6H_5$ (I), introduced by Gil-Av and coworkers[9], for complexation of optically active olefins outside the chromatographic system, several pure enantiomers could be separated via their diastereomers[2]. Because all platinum–olefin complexes of the described type are very stable they could readily be prepared outside the chromatographic system[2], thus avoiding the difficulties with metal compounds in the mobile or stationary phase (see Table I).

Fig. 1 gives the ligand exchange reaction between platinum complexes and olefins, showing that

TABLE I

DIFFICULTIES ARISING WITH METAL SALTS OR COMPLEXES CONTAINED IN MOBILE OR STATIONARY CHROMATOGRAPHIC PHASES

Mobile phase	*Stationary phase*
Corrosion of equipment	Column bleeding
High background (UV detection often not applicable)	Baseline drift
High costs (large amounts of metal salts or complexes required)	No defined amount of metal salt or complex present
	Decomposition of compounds on the phase
Poor separations due to column overloading arising from metal compounds in stationary or mobile phases	
Incomplete complexation as a consequence of slow reactions or production of volatile reaction components	

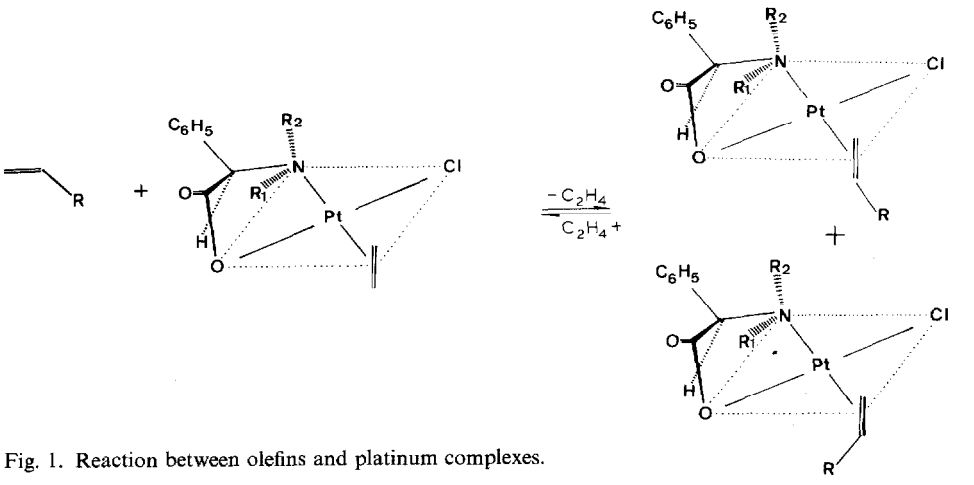


Fig. 1. Reaction between olefins and platinum complexes.

the equilibrium can be shifted to the right-hand side by removal of the volatile ethylene from a solution of the components,

that even non-chiral olefins produce two diastereomers because of the prochirality of the second C atom of a non-symmetrically substituted double bond (Fig. 2),

that chiral olefins with one double bond in the molecule can form up to four diastereomers depending on the steric properties of the olefin structure[2].

The described platinum complexes meet very well the requirements of olefin complexation and of application for chromatographic separations. The complexes

can easily be synthesized[2,9], even with structural modifications,

are not sensitive to oxygen,

are not hydrolyzed by water or commonly used reversed- and normal-phase eluents,

allow fast and complete reactions with olefins, as one reaction product can be removed from the mixture,

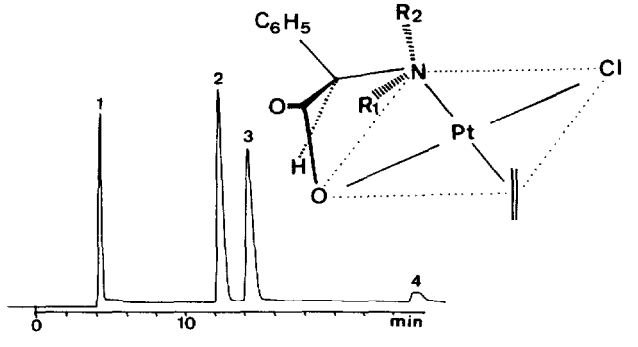


Fig. 2. Separation of the diastereomers formed by the reaction of non-chiral octene-1 with complex I introduced by Goldman *et al.*[9]. Insert: complex I, $R_1 = R_2 = CH_3$. Column, 300 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:38:2); flow-rate, 0.80 ml/min; pressure, 38 bar; detection, UV, 254 nm. Peaks: 1 = impurity; 2 and 3 = two diastereomers; 4 = complex I.

improve the detectability of the olefins by introducing a UV-absorbing chromophore,

exhibit higher chromstographic polarity than the olefins.

The separation of two diastereomers formed from one enantiomer requires such a high separation efficiency that it cannot be easily achieved, not even with modern high-performance liquid chromatography (HPLC).

In this paper we present results of further investigations on olefin isomer and enantiomer analysis on the basis of external derivatization of the olefins via platinum complexation.

EXPERIMENTAL

The chromatography was carried out using a Kipp and Zonen LC 771 instrument or a Varian 5060 liquid chromatograph, thermostatted Knauer RI detectors, a Varian fixed-wavelength UV-detector operating at 254 nm or a Perkin-Elmer LC 55 spectrophotometer. Different columns for reversed-phase and normal-phase chromatography were packed with 5-μm particles (Macherey, Nagel & Co. or E. Merck) by a "viscosity-slurry" method.

All solvents were of GC tested reagent grade. No trace of olefin should contaminate the solvents used as components of the mobile phases. All complexes were prepared according to procedures described previously[2].

RESULTS AND DISCUSSION

Separation and peak correlation of the diastereomeric complexes

It is very important in this method to separate all of the possible diastereomers and to be able to correlate these with the enantiomeric olefins. The correlation can be done in different ways.

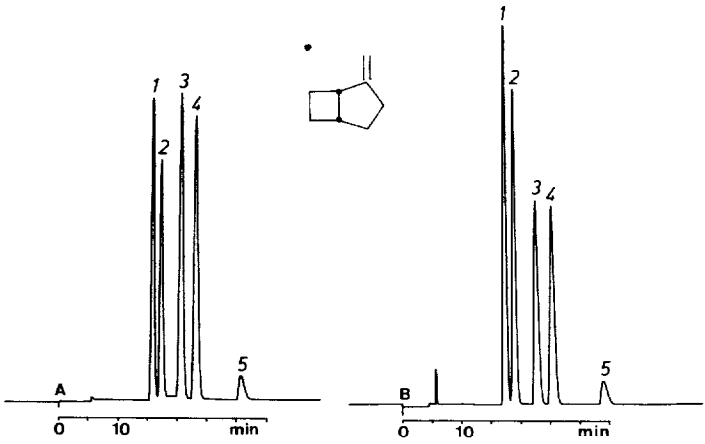


Fig. 3. Separation of the four diastereomers formed by the reaction of chiral 2-methylidenebicyclo[3.2.0]-heptane (structure: see insert) with complex I. A and B: two samples of different enantiomer composition. Conditions as in Fig. 2 except pressure 50 bar. Peaks: 1 and 2 = diastereomers belonging to one enantiomer; 3 and 4 = diastereomers belonging to the other enantiomer; 5 = complex I. The area ratio of peaks 1 and 2 stays constant, as well as the area ratio of peaks 3 and 4.

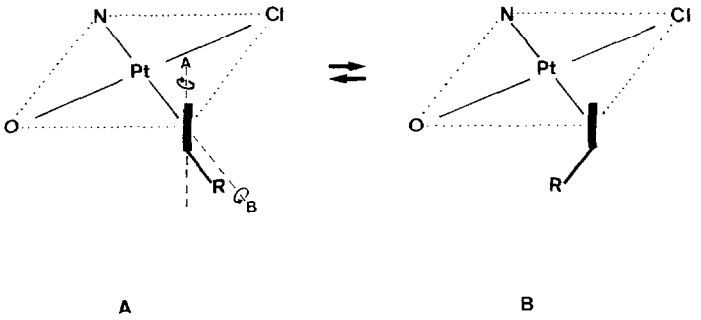


Fig. 4. Epimerization between A and B does not occur by rotation around the two axes indicated, but by dissociation–association equilibria.

(a) Complexation and separation of two pure olefinic samples with different enantiomer ratios is carried out. In the case of four separable diastereomers formed from two enantiomers, the peak area ratios of those peaks corresponding to a certain enantiomer have the same value in both samples (Fig. 3).

(b) Those diastereomers that have been formed because of the prochirality of the second C atom of the double bond can be interconverted[9]. Since it is dependent on the structure of the bonded olefin, this epimerization sometimes occurs at room temperature and is accelerated at higher temperatures. By kinetic measurements (see below) it could be shown that the epimerization reaction proceeds via dissociation–association equilibria. Rotation around the platinum–π-bond axis (B) or the axis through the double bond (A) cannot be assumed to be responsible for this interconversion (Fig. 4).

Thus, all four diastereomers appearing in the chromatogram were individually isolated and then heated in the eluent. Subsequent chromatographic separations showed that each diastereomer produced only one further member of the separated four, both being derivatives of the same enantiomer.

(c) The olefin is displaced from each of the isolated diastereomers. In each case, from two of the four diastereomer fractions the same enantiomer of the olefin is obtained. Repeated complexation and chromatographic separation of each of the fractions only leads to two peaks in each chromatogram.

(d) With racemic mixtures of mono-olefins four diastereomers can be formed and resolved in most cases. The areas of the two peaks corresponding to each enantiomer add up to 50% of the total peak area. For quantitative measurements, an excess of initial complex (reagent) should be present to avoid distortions of the enantiomeric ratios due to kinetic effects (*i.e.*, asymmetric induction).

Influence of the molecular structure of olefins on the retention and resolution of their complex diastereomers

The four diastereomers formed by the reaction of α-akyl-substituted alkenes with complex I can easily be resolved in normal-phase liquid chromatography as has been demonstrated for instance with 3-methylpentene-1[9] or 3,7-dimethyloctene-1[2]. Nevertheless, it is obvious that there should be an influence of the distance of the chiral centre from the double bond on the retention and resolution of the diastereomers. To investigate this effect all chiral monomethyl-substituted octenes-1 (3-,

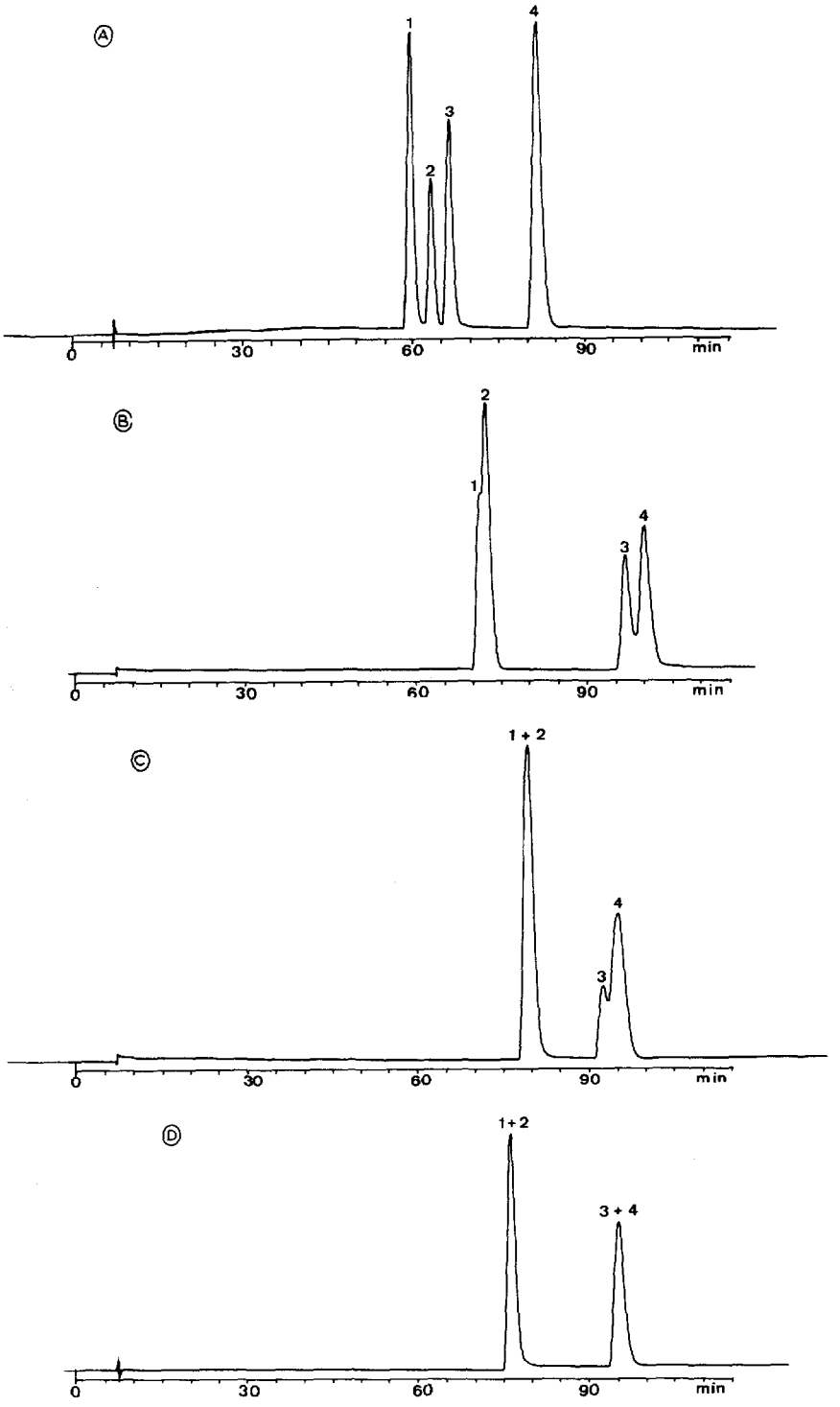


Fig. 5. Separation of the diastereomers formed by the reaction of isomeric methyloctenes with complex I. (a), ´-Methyloctene-1; (b) 4-methyloctene-1; (c) 5-methyloctene-1–5-ethylheptene-1 (3:1); (d) 6-methyloctene- . Column: two 250 × 4.4 mm I.D. LiChrosorb Si 60 (5 μm) columns; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:39:1); flow-rate, 0.80 ml/min; pressure, 82 bar; detection, UV, 254 nm. Peaks: 1 and 3 = diastereomers of one enantiomer; 2 and 4 = diastereomers of the other enantiomer.

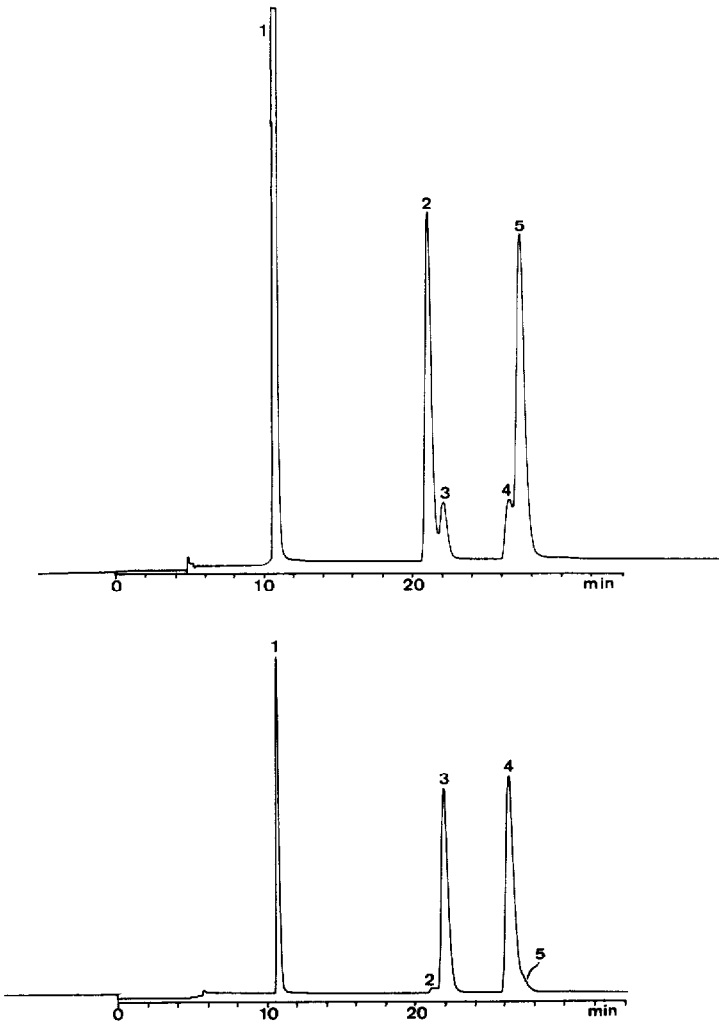


Fig. 6. Separation of the diastereomers formed by the reaction of (+)- and (−)-β-citronellol with complex I (two samples of different enantiomer composition). Column, temperature and detection as in Fig. 5; mobile phase, *n*-heptane-dichloromethane–*n*-propanol (60:34:6); flow-rate, 1.2 ml/min; pressure, 108 bar. Peaks: 1 = complex I; 2 and 5 = diastereomers belonging to (+)-β-citronellol; 3 and 4 = diastereomers belonging to (−)-β-citronellol.

4-, 5- and 6-methyloctene-1) were synthesized by Grignard reactions. (5-Methyloctene-1 contains an impurity of 5-ethylheptene-1).

After reaction of the olefins with equimolar amounts of complex I, LC separation was performed with two 250 × 4.4 mm silica columns and *n*-heptane–dichloromethane–*n*-propanol (60:39:1) as eluent. Fig. 5 shows that the resolution of the diastereomers, 1 and 3, and 2 and 4, decreases with increasing distance of the chiral centre from the double bond. (Peak correlation was performed by methods b and d.) The resolution of 4-methyloctene-1 is no longer easy.

With ring systems different results could be obtained. 4-Ethylcyclohexene-1

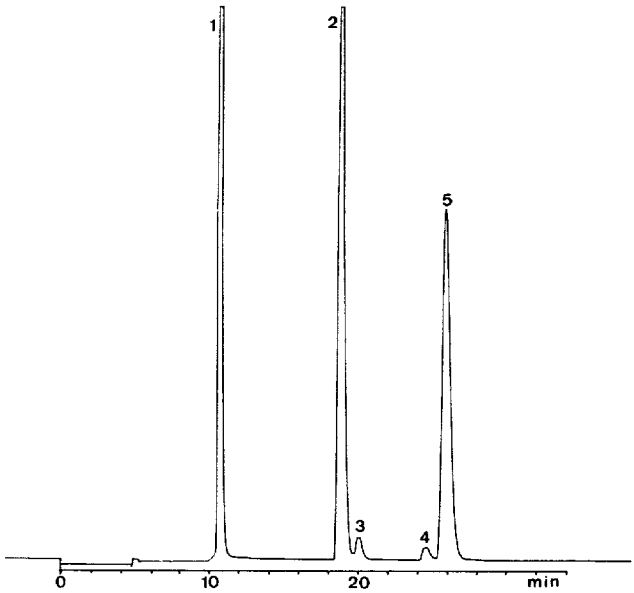


Fig. 7. Separation of the diastereomers formed by the reaction of (+)- and (−)-α-citronellol. Conditions as in Fig. 6. Peaks: 1 = complex I; 2 and 5 = diastereomers belonging to (−)-α-citronellol; 3 and 4 = diastereomers belonging to (+)-α-citronellol.

forms four diastereomers with complex I. Two of these (1 and 4), originating from different enantiomers, can be isolated 100% pure. Peak 1 is converted into 3, which is overlapped by peak 2, generated by the epimerization of 4. The resolution of the diastereomers depends on the steric properties of the ring molecule. The distance between the double bond and the chiral centre along the C atom chain is not the decisive criterion, rather the actual amount of space between them.

Investigations of the enantiomer ratios of (+)- and (−)-β-citronellols (3,7-dimethyl-6-octen-1-ol), the chiral centre being at the 5-position with respect to the double bond, showed similar effects concerning the diastereomer resolution (Fig. 6). In spite of the great distance between the chiral centre and the double bond, the four diastereomers of complex I are resolved. Even better resolution was obtained of the diastereomers, formed by reaction of complex I with (−)-α-citronellol (3,7-dimethyl-7-octen-1-ol), the chiral centre being at the 6-position with respect to the double bond (Fig. 7). Hydrogen-bonding between the OH group of the olefin and other polar parts of the platinum complex, leading to "ring-formation", thus diminishing the amount of space between the chiral centre and the double bond, may explain these results.

It is remarkable that the diastereomers of the unsaturated alcohols are eluted later than complex I due to their high chromatographic polarity. All diastereomers of pure olefins exhibit shorter retention times than complex I. With polar eluents (4–10% *n*-propanol) it is not difficult to resolve diastereomers of olefinic solutes containing polar groups such as ketones and alcohols.

Complexation of diolefins

With an excess of reagent, α,ω-diolefins containing isolated double bonds of

identical reactivity form several complexes in which one or both double bonds may be involved. Each diene can react with one or two equivalents of complex I to give mono- (1:1) or dicomplexes (1:2). The dicomplexes exhibit much higher chromatographic polarity than the monocomplexes and are eluted after unreacted complex I in a normal-phase system. Non-chiral α,ω-dienes with carbon numbers of 4, 5 and greater than 9 form the usual two diastereomeric monocomplexes (two peaks). Those with a chainlength of 6, 7 and 8 atoms form only one diastereomeric monocomplex (one peak). The exclusive formation of one species of monocomplex may be explained by an optimal chain length of the olefin for chelation of the Pt atom by both double bonds.

Fig. 8–10 show the separations of the diastereomers formed by the reaction of pentadiene-1,4, hexadiene-1,5 and decadiene-1,9 with complex I.

Long-chained α,ω-dienes are not able to chelate the Pt atom with both double bonds as a consequence of entropic effects and special strains, and short dienes cannot undergo chelation because of steric reasons. Dienes with too short chains do not form dicomplexes (Fig. 11). For example 2,3-dimethylbutadiene-1,3 generates two species of monocomplexes but no dicomplexes with reagent I.

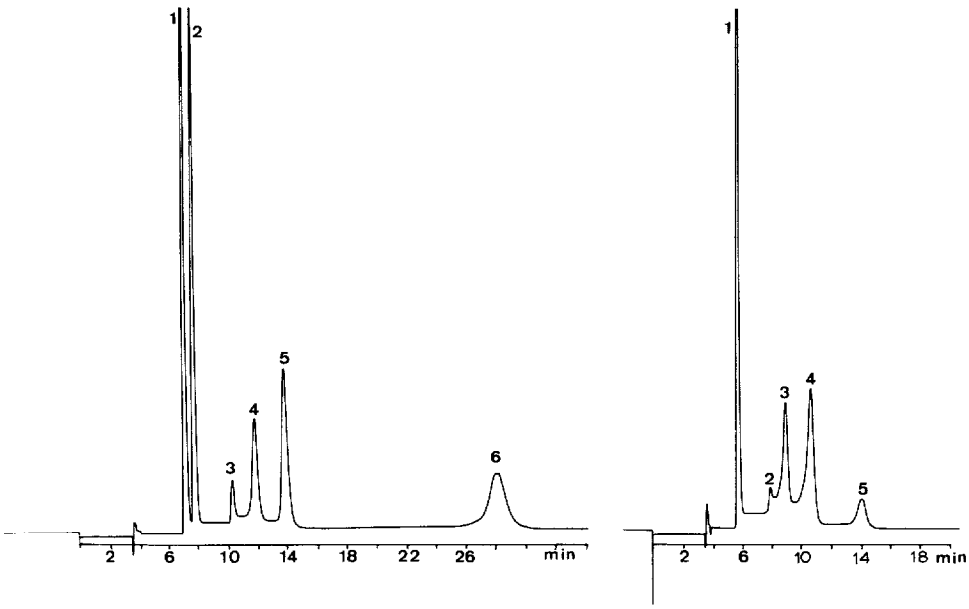


Fig. 8. Separation of diastereomers formed by the reaction of pentadiene-1,4 with complex I. Two monocomplexes and several dicomplexes appear. Column, 250 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:36:4); flow-rate, 0.80 ml/min; pressure, 38 bar; detection, UV, 254 nm. Peaks: 1 and 2 = diastereomers formed by the reaction of only one double bond with complex I; 3 = complex I; 4–6 = diastereomers formed by the reaction of both double bonds with complex I.

Fig. 9. Separation of diastereomers formed by the reaction of hexadiene-1,5 with complex I. Only one monocomplex appears. Conditions as in Fig. 8, except mobile phase *n*-heptane–dichloromethane–*n*-propanol (60:34:6). Peaks: 1 = monocomplex; 2 = complex I; 3–5 = dicomplexes.

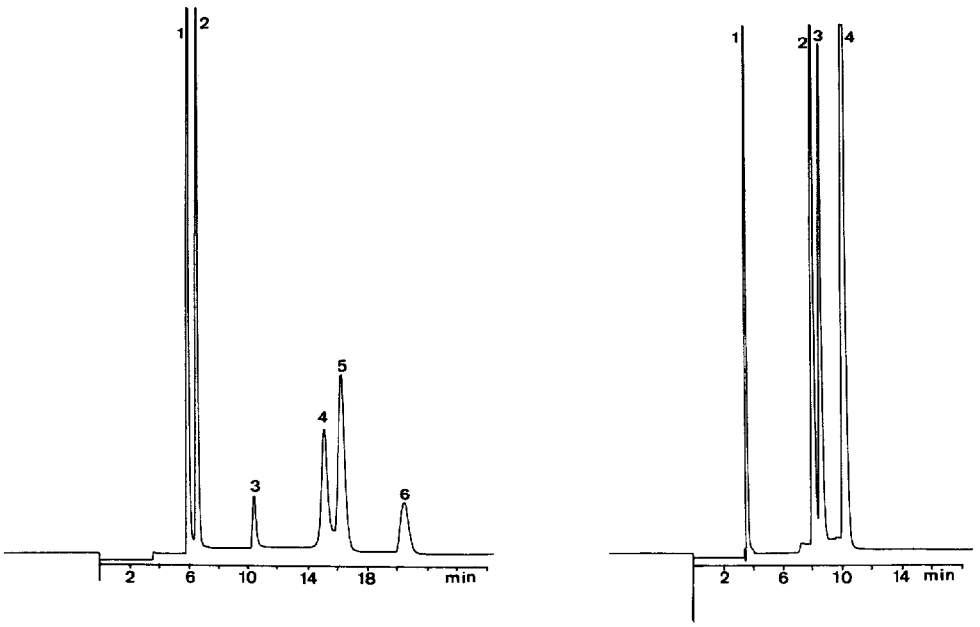


Fig. 10. Separation of diastereomers formed by the reaction of decadiene-1,9 with complex I. Two monocomplexes and several dicomplexes appear. Conditions as in Fig. 8. Peaks: 1 and 2 = diastereomers formed by the reaction of only one double bond with complex I; 3 = complex I; 4–6 = diastereomers formed by the reaction of both double bonds of the olefin.

Fig. 11. Separation of diastereomers formed by the reaction of 2,3-dimethylbutadiene-1,3 with complex I. No dicomplexes appear. Conditions as in Fig. 8. Peaks: 1 = impurity; 2 and 3 = two monocomplex diastereomers; 4 = complex I.

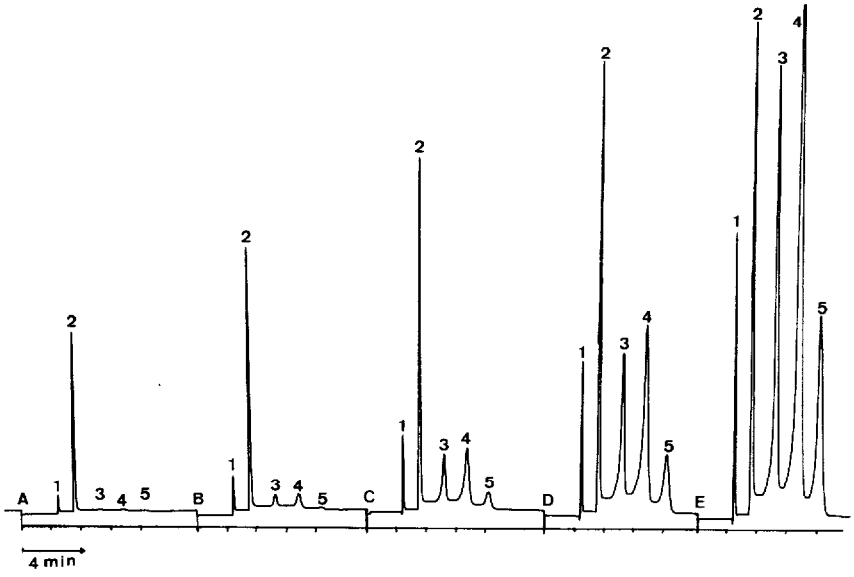


Fig. 12. Separation of diastereomers formed by the reaction of octadiene-1,7 with complex I; disproportionation of mono- into dicomplexes during chromatographic separation dependent on the entire amount of sample present in the chromatographic system. Injection of 0.5 (A), 1 (B), 2 (C), 4 (D) and 8 (E) μl of the diastereomer mixture in dichloromethane. Conditions as in Fig. 9, except flow-rate: 1.2 ml/min. Peaks: 1 = impurity; 2 = monocomplex; 3–5 = dicomplexes.

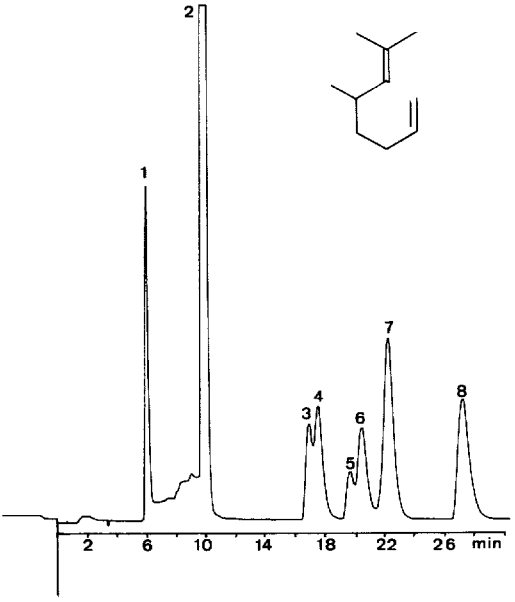
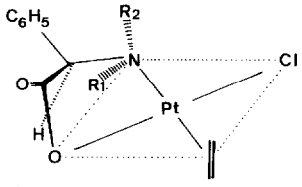


Fig. 13. Separation of diastereomers formed by the reaction of (+)-isocitronellene (structure: see insert) with complex I. One monocomplex and several dicomplexes appear. Conditions as in Fig. 8. Peaks: 1 = monocomplex; 2 = complex I (in excess) (increase of baseline between peaks 1 and 2 is caused by traces of olefins in the *n*-heptane component of the mobile phase); 3–8 = dicomplexes.

At higher concentrations in the mobile phase, monocomplexes disproportionate, forming dicomplexes and diolefins. This also results in a raised baseline in the chromatograms (Fig. 12). Diolefins with double bonds of different substitution can form many dicomplex species, so that separation and complexation becomes increasingly difficult, as can be seen from Fig. 13 which shows the separation of the diastereomers of pure (+)-isocitronellene (5,7-dimethyloctadiene-1,6). (The poorly resolved area between peaks 1 and 2 originates from traces of olefins contained in the *n*-heptane component of the mobile phase.)

The formation of dicomplexes is not desirable in the quantitative analyses of enantiomeric excesses (ee) (commonly used for the characterization of enantiomeric purity). Diolefins having double bonds of different reactivities offer the possibility of producing only monocomplexes by avoiding an excess of the platinum reagent. Thus, the determination of the enantiomer ratios of β-citronellene (3,7-dimethyloctadiene-1,6) can easily be performed by reacting one equivalent of diene with one equivalent



I $R_1 = R_2 = CH_3$
II $R_{1,2} = H$ $R_{2,1} = (CH_2)_3CH_3$
III $R_{1,2} = H$ $R_{2,1} = (CH_2)_6CH_3$

Fig. 14. Different types of platinum complexes. II and III form two diastereomers (ratio 70:30; ^{13}C NMR) which cannot be separated.

of complex I. Approximately racemic β-citronellene yielded two diastereomers only, one belonging to the (+)- and the other to the (−)-enantiomer. The use of an excess of the diolefin revealed no evidence for strong distortion of the enantiomer ratios by asymmetric induction.

Influence of alkyl substitution at the N atom of the platinum complex on retention and selectivity

The complexes II and III of Fig. 14 were prepared analogously to I[2]. For steric reasons, only one alkyl chain could be fixed to the N atom, thus producing two diastereomers of each of the two complexes in the ratio 70:30 (^{13}CNMR). Separation of these diastereomers by LC could not be achieved. The lipophilicity of the complex increases with increasing number of C atoms in the alkyl group. The retentions of the complexes therefore decrease in normal-phase and increase in reversed-phase

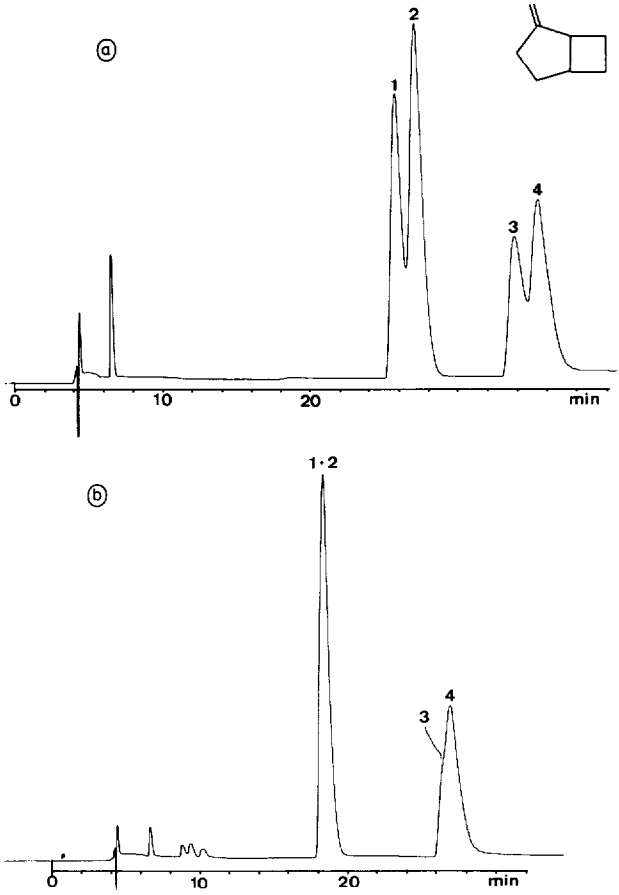


Fig. 15. Separation of the two diastereomeric pairs formed by the reaction of 2-methylidenebicyclo[3.2.0]-heptane (structure: see insert in Fig. 3) (20% ee) with complex II (a) or complex III (b). Column, 300 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:39:1); flow-rate, 0.80 ml/min; pressure, 40 bar; detection, UV, 254 nm. Peaks: 1 and 2 = diastereomers of one enantiomer; 3 and 4 = diastereomers of the other enantiomer.

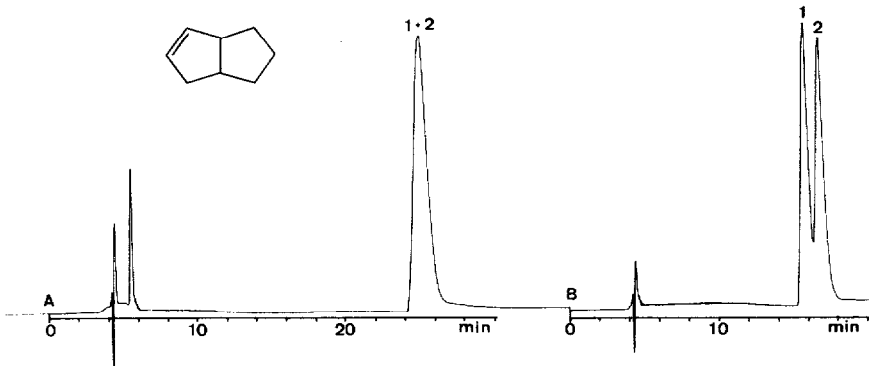


Fig. 16. Separation of the diastereomeric pairs formed by the reaction of racemic bicyclo[3.3.0]octene-2 (structure: see insert) with complex II (A) or complex III (B). Conditions as in Fig. 15. Peaks: 1 = diastereomers of one enantiomer; 2 = diastereomers of the other enantiomer.

chromatography. Moreover, a strong influence of substitution at the N atom on the selectivity of diastereomer separation is observed. The selectivity is also affected by the nature of the olefin. Figs. 15 and 16 show the separations of the diastereomers of two olefins formed with the complexes II and III. In both cases not all diastereomers but those originating from the different enantiomers can be separated.

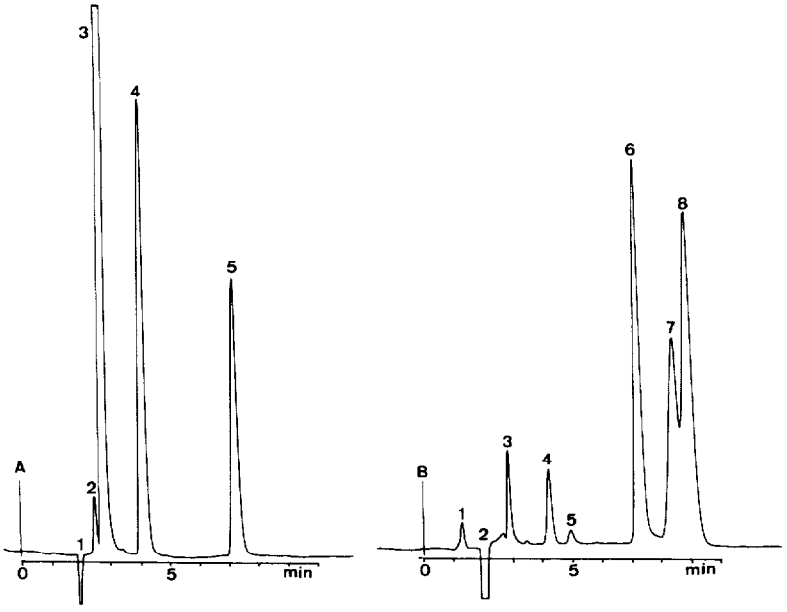


Fig. 17. Separation of diastereomers formed by the reaction of 2-methylidenebicyclo[3.2.0]heptane (structure: see Fig. 15) (20% ee) with complex I (A) or complex III (B). Column, 150 × 4.4 mm I.D. Nucleosil 5 C_{18}; temperature, 22°C; mobile phase, methanol–water (5:1); flow-rate, 0.80 ml/min; pressure, 97 bar; detection, refractive index. Peaks: A: 1 = solvent; 2 = impurity; 3 = complex I; 4 = all diastereomers of the heptane–platinum compound; 5 = 2-methylidenebicyclo[3.2.0]heptane; B: 1, 3 and 5 = impurities; 2 = solvent; 4 = complex III; 6 = 2-methylidenebicyclo[3.2.0]heptane; 7 = diastereomers of one enantiomer; 8 = diastereomers of the other enantiomer.

The different behaviours of complexes I and III in reversed-phase chromatography can be seen from Fig. 17. Because the retention time of complex I and its olefin derivatives is so short, no resolution of the diastereomers is achieved (Fig. 17A), whereas with complex III a separation of the diastereomers belonging to different enantiomers is possible (Fig. 17B).

Fig. 18 shows the separation of the diastereomers formed by the reaction of partly racemic bicyclo[3.3.0]octene-2 with complex III. The two peaks belong to the (+)- and (−)-olefin.

A versatile micromethod for evaluation of the enantiomeric olefin composition of complex mixtures

The determination of enantiomer ratios is difficult even when chemically pure samples are available. Generally, polarimetry or NMR spectroscopy of diastereomeric systems, with optically active shift-reagents or solvents, is used.

Polarimetric measurements cannot be applied without the knowledge of the specific rotation of the olefins (most values given in literature suffer from uncertainty about the optical purities of the enantiomers). The second method requires specific reagents, sufficient resolution between the signals and the absence of kinetic effects leading to wrong enantiomer ratios. If the compound of interest is contained in complex matrices of other molecules the solution of this analytical problem becomes even more difficult. The optical rotations depend on the type of solvents, the measured polarimetric rotation values may be too small and the presence of impurities of other enantiomers may lead to unreliable results. NMR measurements

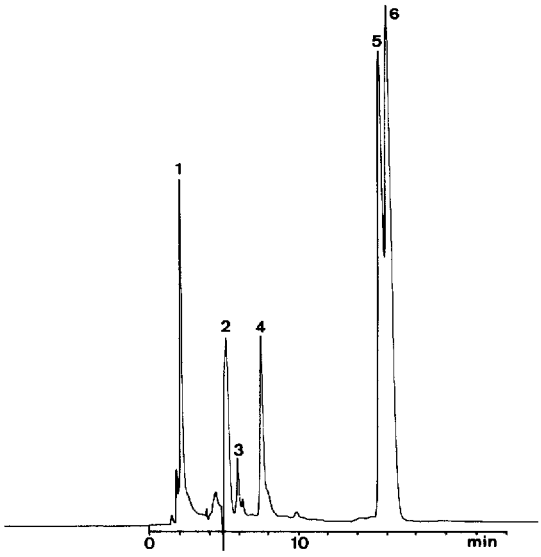


Fig. 18. Separation of the two diastereomeric pairs formed by the reaction of (non-racemic) bicyclo[3.3.0]octene-2 (structure: see Fig. 16) with complex III by reversed-phase chromatography. Column, 300 × 4.4 mm I.D. Nucleosil 5 C_{18}; temperature, 22°C; mobile phase, methanol–water (5:1); flow-rate, 0.80 ml/min; pressure, 126 bar; detection, UV, 254 nm. Peaks: 1 and 3 = impurities; 2 = solvent; 4 = complex III; 5 = two diastereomers of one enantiomer; 6 = two diastereomers of the other enantiomer.

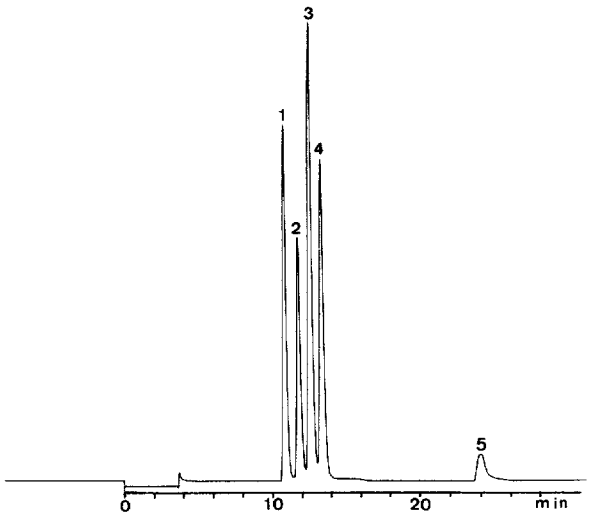


Fig. 19. Determination of the enantiomer composition of 4-vinylcyclohexene-1 contained in mixtures originating from asymmetric catalysis: separation of the diastereomers formed by the reaction of racemic 4-vinylcyclohexene-1 with complex I. Column, 250 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-hexane–dichloromethane–*n*-propanol (60:38:2); flow-rate, 0.80 ml/min; pressure, 38 bar; detection, UV, 254 nm. Peaks: 1 and 4 = diastereomers of one enantiomer (−); 2 and 3 = diastereomers of the other enantiomer (+); 5 = complex I.

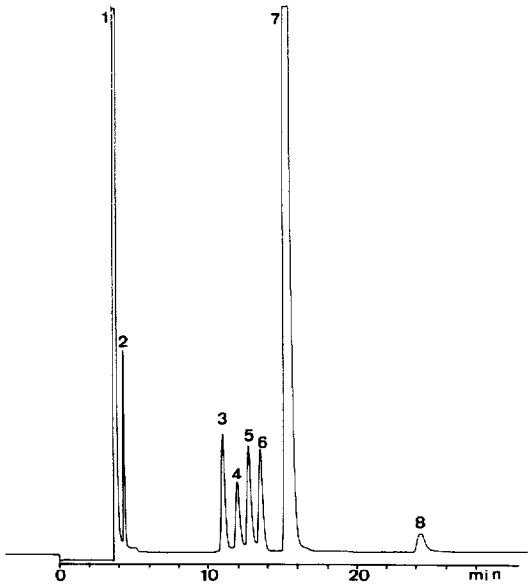


Fig. 20. Determination of the enantiomer composition of 4-vinylcyclohexene-1 contained in mixtures originating from asymmetric catalysis: complexation of olefins in a mixture containing only 4% 4-vinylcyclohexene-1 (complex I). Conditions as in Fig. 19. Peaks: 1 = toluene; 2 = unknown impurity; 3 and 6 = diastereomers of (−)-4-vinylcyclohexene-1 (excess); 4 and 5 = diastereomers of (+)-4-vinylcyclohexene-1; 7 = diastereomeric complex of cyclooctadiene-1,5; 8 = complex I.

are time-consuming, and the signals to be used for determination may be overlapped by the signals of the matrix.

The chromatographic method described here offers a chance to solve these problems in many cases, especially if preseparations by GC or LC are carried out before complexation. Complexation of olefins leads to compounds that can easily be detected, even at low concentrations, by UV absorption. Nevertheless high chromatographic resolution is necessary because each olefinic component forms at least two diastereomers. In the case of mixtures that are too complex, micropreparative GC or LC can be successfully applied for preisolation of selected peak groups before complexation. Sample volumes lower than 1 μl of the pure olefins can be employed, even for repeated chromatographic separations. If all diastereomers of the two optical antipodes can be baseline-resolved, the peak areas and the enantiomeric ratios can be reproduced with a relative standard deviation (R.S.D.) of less than 1 %.

Figs. 19–22 show the determination of the optical purity of 4-vinylcyclohexene-1 (VCH) originating from asymmetric catalysis[10]. After complexation of racemic VCH (Fig. 19), a laevorotatory (Fig. 20) and a dextrorotatory (Fig. 21) complex catalysis mixture containing VCH only in low concentrations was analyzed. In the last case, direct determination of the enantiomer ratios from the original mixture is impossible because of peak overlapping. After preparative scale GC separation the enantiomeric excess of (+)-VCH could be determined with a R.S.D. of 0.7 % (Fig. 22). With only a small excess of reagent I, no dicomplex formation could be observed.

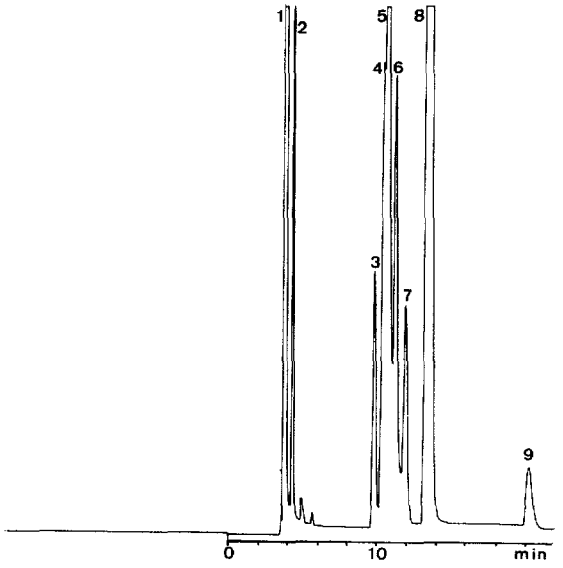


Fig. 21. Determination of the enantiomer composition of 4-vinylcyclohexene-1 contained in mixtures originating from asymmetric catalysis: complexation of olefins in a dextrorotatory mixture containing only small amounts of 4-vinylcyclohexene-1 (complex I). Overlapping of the 4-vinylcyclohexene-1 diastereomers by cyclododecatriene-1,5,9 complexes. Conditions as in Fig. 19, except mobile phase *n*-heptane–dichloromethane–*n*-propanol (60:38:2). Peaks: 1 = toluene; 2 = unknown impurity; 3 and 7 = diastereomers of (−)-4-vinylcyclohexene-1; 4 and 6 = diastereomers of (+)-4-vinylcyclohexene-1 (excess); 5 = diastereomer of cyclododecatriene-1,5,9; 8 = diastereomer of cyclooctadiene-1,5; 9 = complex I.

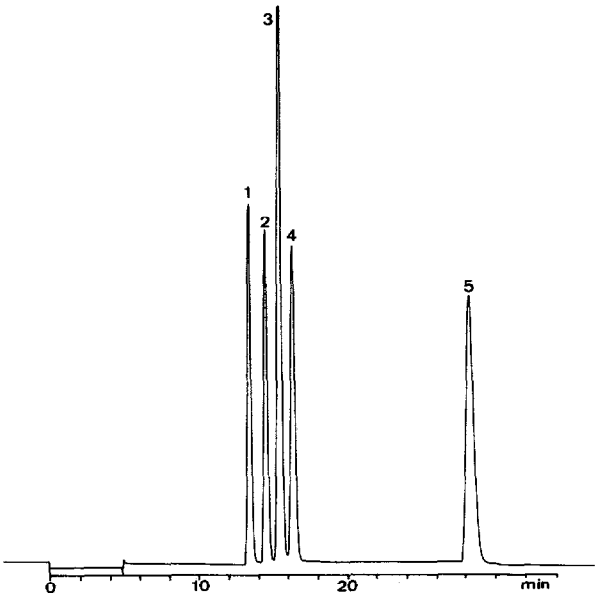


Fig. 22. Determination of the enantiomer composition of 4-vinylcyclohexene-1 contained in mixtures originating from asymmetric catalysis: complexation of dextrorotatory 4-vinylcyclohexene-1 after preparative gas chromatographic isolation (complex I). Column, two 250 × 4.4 mm I.D. LiChrosorb Si 60 (5 μm) columns; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:38:2); flow-rate, 1.2 ml/min; pressure, 108 bar; detection, UV, 254 nm. Peaks: 1 and 4 = diastereomers of (−)-4-vinylcyclohexene-1; 2 and 3 = diastereomers of (+)-4-vinylcyclohexene-1 (16.4% ee); 5 = complex I.

This behaviour can be explained by the much higher reactivity of the vinyl bond in comparison to the double bond within the ring.

On-line displacement of the olefin substrate from the separated platinum complex

For various practical reasons the free optically pure olefins are of interest; mainly of course for the determination of their specific rotations. After the separation of the diastereomers the olefins can be liberated from the complexes, *e.g.*, by reaction with KCN[9]. The displacement can also be performed continuously within the second column of a system of coupled columns. After the usual separation of the diastereomers the olefins can be liberated from their platinum complexes within the coupled column containing silica impregnated with diallylamine. Diallylamine is much more strongly complexed by the platinum and displaces the olefins; the resulting complex cannot be eluted under normal separation conditions.

The overall retention time of the displaced olefins is precisely the sum of the retentions of the diastereomeric complexes on the first column and the dead-time of the second column. Depending on the injected amounts and the capacity of the diallylamine column, the capability of the system for displacement decreases after several injections (ten to twenty injections of 4 μl of solution containing 10–20 mg complex I–olefin derivative in 1000 μl dichloromethane on a 300 × 3.8 mm displacement column); this leads to poor peak shapes. The column can easily be regenerated by elution with a 10% diallylamine–dichloromethane solution.

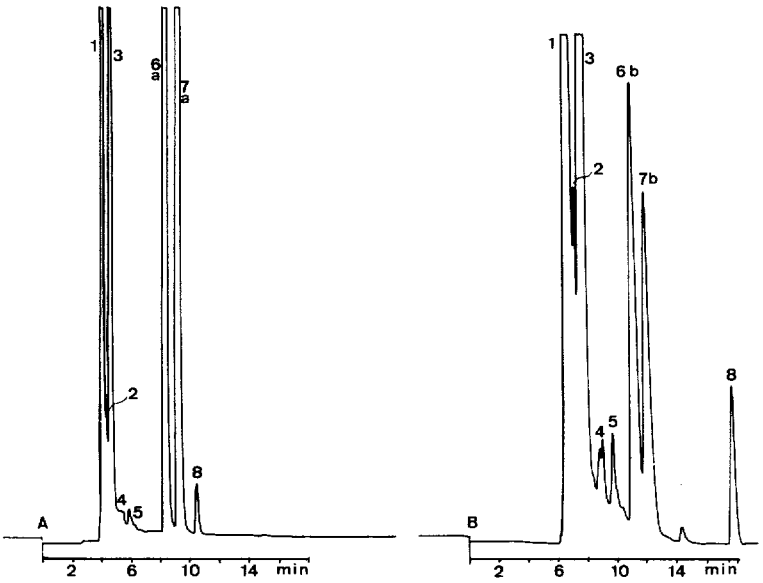


Fig. 23. Displacement column. A, Separation of two diastereomers formed by the reaction of 4-phenylbutene-1 with complex I. Column, 250 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:37:3); flow-rate, 0.80 ml/min; pressure, 38 bar; detection, UV, 254 nm. Peaks: 1 = 4-phenylbutene-1; 2–5 and 8 = impurities; 6a and 7a = two diastereomers. B, Separation of the diastereomers formed by the reaction of 4-phenylbutene-1 with complex I on the first column (see A) and displacement of the olefin on a second column. Columns, 250 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm, and 300 × 3.8 mm I.D. LiChrosorb Si 60, 5 μm, impregnated with 10% diallylamine in dichloromethane; pressure, 80 bar; other conditions as in A. Peaks: 1 = 4-phenylbutene-1; 2–5 and 8 = impurities; 6b and 7b = two peaks of 4-phenylbutene-1.

Instead of direct coupling of the separation and displacement columns, a UV detector with a pressure-stable flow-cell (Perkin-Elmer LC 55) can be inserted between the columns. This version allows the chromatographic separation of the diastereomers to be followed.

As most olefins do not contain chromophores absorbing above 220 nm, a UV signal cannot be observed at the end of the displacement column. Low concentrations of the olefins in the eluent sometimes complicate the use of a refractive index detector. The purity of the olefin enantiomers after displacement was tested by repeated complexation of the fractions and subsequent chromatography of the diastereomers (method c above). (+)- and (−)-bicyclo[4.4.0]decene-1 as well as (+)-bicyclo[3.3.0]octene-2 with optical purities higher than 99% could be obtained by this method, starting from the racemates.

Some olefins that are easily isomerized, such as 3-phenylbutene-1, could not be liberated from their diastereomers without decomposition. Fig. 23 shows the separation of the two diastereomers (6a, 7a) formed by the reaction of 4-phenylbutene-1 with complex I (A), and the two peaks of pure olefin (6b, 7b) after displacement (B).

Another elegant approach for the preparative scale liberation of the olefins from their Pt complexes is to react the suspension of the separated diastereomers in *n*-pentane in an autoclave applying an excess of ethylene (40 bars). After 2 h the

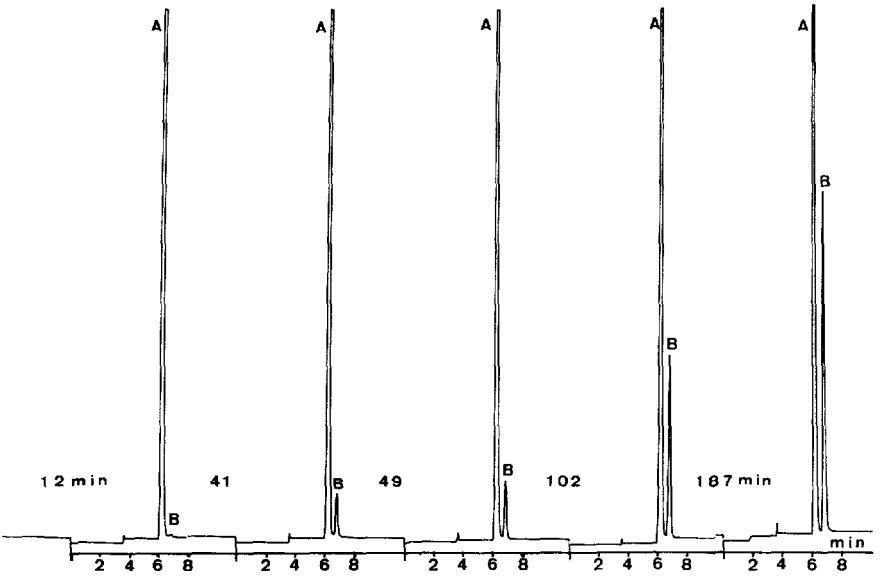


Fig. 24. Liquid chromatographic analysis of an epimerization process, A → B; interconversion of diastereomers formed by the reaction of octene-1 with complex I after preparative isolation of substance A in the eluent. Column, 250 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:36:4); flow-rate, 0.80 ml/min; pressure, 36 bar; detection, UV, 254 nm.

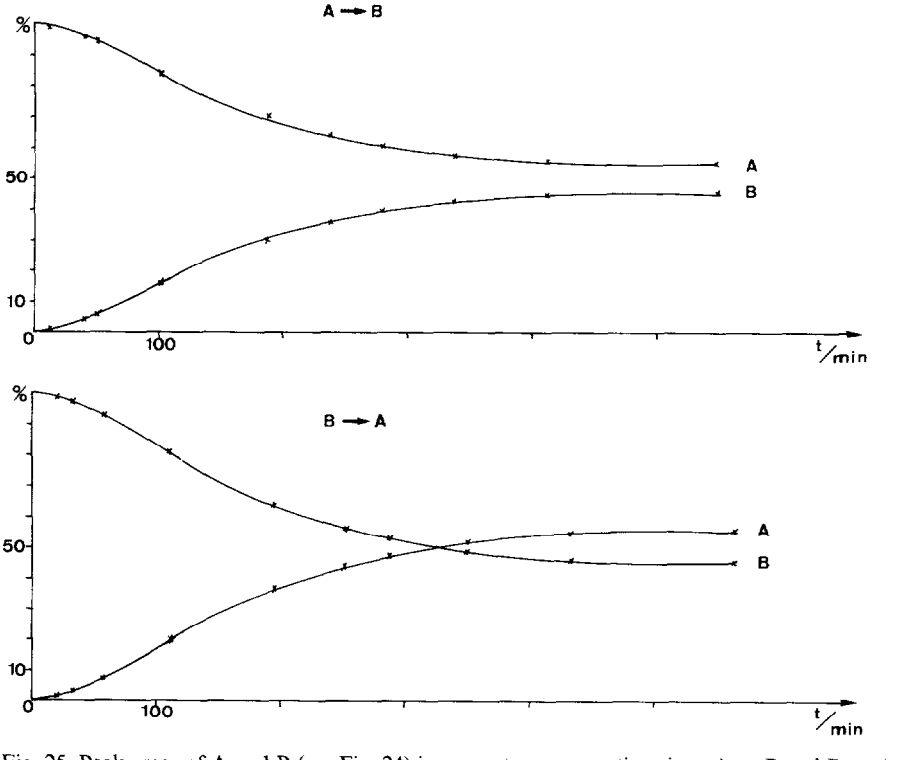


Fig. 25. Peak areas of A and B (see Fig. 24) in percent *versus* reaction time, A → B and B → A.

insoluble reagent-complex can be filtered from the pentane which contains the enantiomeric olefin. In that way, the recovery of the Pt complex and the "mild" liberation of the olefin is possible.

Kinetic measurements on the epimerization of the two diastereomers (A and B) formed by reaction of octene-1 with complex I

The interconversion of diastereomers that are formed because of the prochirality of double-bonded C atoms may be disadvantageous for the versatility and reliability of this method of enantiomer analysis. According to our investigations, epimerizations are so slow at normal temperatures that undisturbed resolution can be achieved. Nevertheless, the LC separations, necessary for kinetic measurements, had

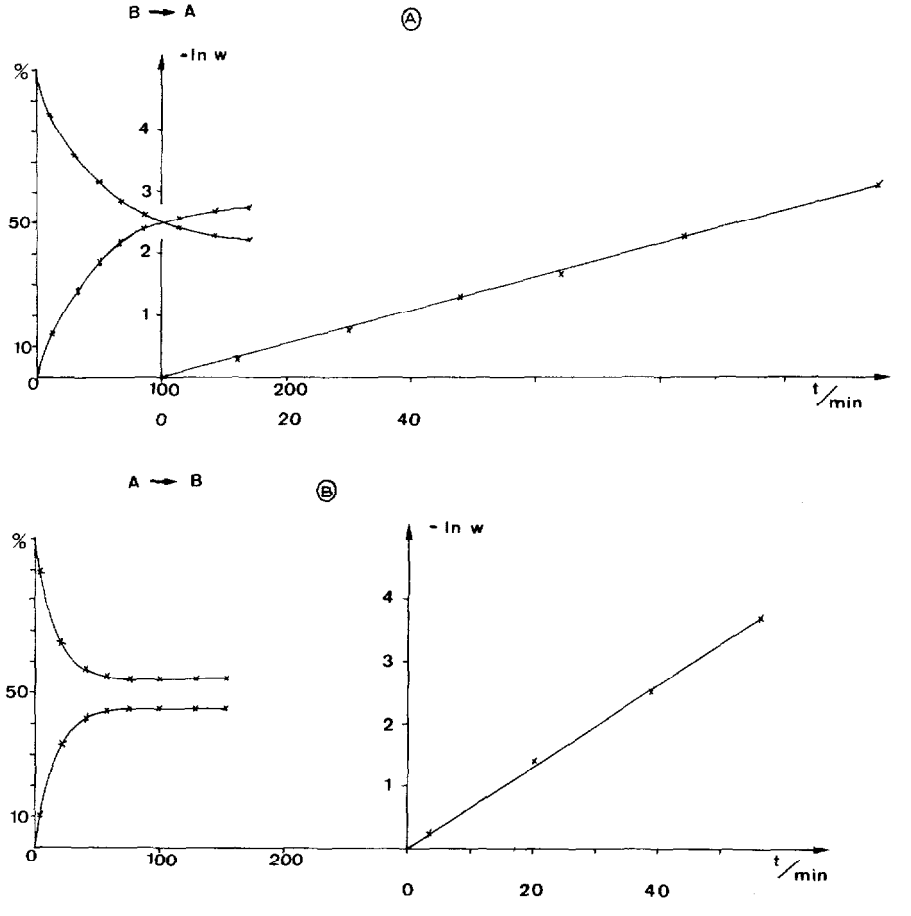


Fig. 26. Time dependence of B/A and A/B (see Fig. 24) equilibria: addition of octene-1 to the reaction mixture. (A) B/A equilibrium; octene-1: 1/10 stoichiometric with respect to the complex concentration; solvent, *n*-heptane–dichloromethane–*n*-propanol (60:36:4). $\ln w = -c_0(k_1 + k_2)t$, where $w = (Kc_B - c_A)/K(c_A + c_B)$, K = equilibrium constant = $c_{AE}/c_{BE} = k_2/k_1$, k_1 and k_2 = rate constants of the reversible reaction, c_A and c_B = concentrations of A and B, c_{AE} and c_{BE} = equilibrium concentrations of A and B, c_0 = olefin concentration = constant, and t = time. (B) A/B equilibrium; octene-1: 1/4 stoichiometric with respect to the complex concentration; solvent as in (A). $\ln w = -c_0(k_1 + k_2)t$, where $w = (Kc_A - c_B)/K(c_A + c_B)$; other symbols as in (A).

to be optimized for resolution and retention time; the latter has to be short in comparison with the conversion rate.

The kinetic measurements were executed in the following steps. Each of diastereomers A and B are isolated by preparative liquid chromatography. Reagents are added to the solution of the diastereomers in the eluting solvent to study their influence on the conversion rate. Species A is converted into species B and *vice versa* until equilibrium concentrations are reached. The equilibration process is followed by LC analysis (Fig. 24).

The following results were obtained. A slow epimerization reaction occurs in the eluting solvent after an induction period. No simple kinetic model is applicable (Fig. 25). Experiments with different concentrations of octene-1 in the diastereomer mixture show that the reaction can be greatly accelerated by adding olefins and also indicate that the epimerization does not occur by rotation of the olefin within the complex but is controlled by a dissociation–association of the olefin induced by another molecule, which can be olefin or solvent (bimolecular mechanism). [Paiaro and Panunzi[11] observed a similar influence of olefins on the epimerization of *trans*-dichloro(olefin)(amine)platinum(II) complexes.] The reaction can be described mathematically by a reversible first-order kinetics as the concentration of the free olefin is constant (see Fig. 26A, B). The slope of the straight line obtained by plotting $(-)\ln w$ *versus* t is directly proportional to the concentration of free olefin in the mixture. A similar acceleration effect can be achieved by the use of strongly solvating solvents such as tetrahydrofuran.

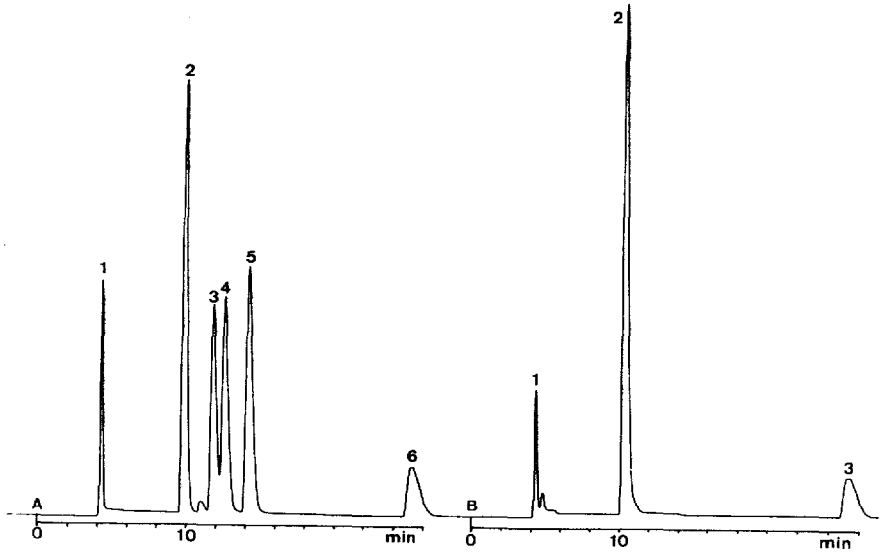


Fig. 27. A, Separation of the four diastereomers formed by the reaction of *cis*- and *trans*-decene-2 with complex I. Column, 300 × 4.4 mm I.D. LiChrosorb Si 60, 5 μm; temperature, 22°C; mobile phase, *n*-heptane–dichloromethane–*n*-propanol (60:38:2); flow-rate, 0.80 ml/min; pressure, 38 bar; detection, UV, 254 nm. Peaks: 1 = impurity; 2 and 5 = diastereomers of *trans*-decene-2; 3 and 4 = diastereomers of *cis*-decene-2; 6 = complex I. B, No separation of the diastereomers formed by the reaction of *trans*-decene-4 with complex I. Conditions as in A. Peaks: 1 = impurity; 2 = two diastereomers of trans-decene-4; 3 = complex I.

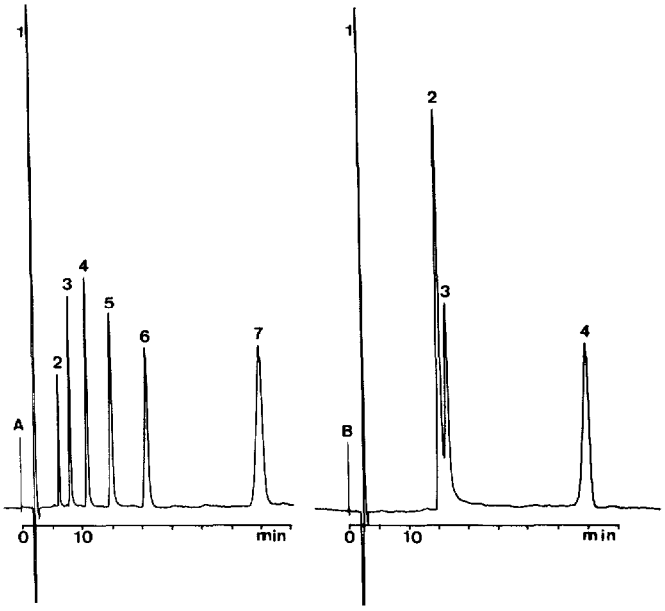


Fig. 28. Use of complex I for group separations of olefins in a reversed-phase system. Column, 150 × 4.4 mm I.D. Nucleosil 5 C_{18}; temperature, 22°C; mobile phase, methanol–water (5:1); flow-rate, 0.80 ml/min; pressure, 100 bar; detection, refractive index. A, Dodecene-1 and *n*-alkane standards. Peaks: 1 = solvent; 2 = *n*-pentane; 3 = *n*-hexane; 4 = *n*-heptane; 5 = *n*-octane; 6 = *n*-nonane; 7 = dodecene-1. B, Dodecene-1 and its diastereomers formed by the reaction with complex I. Peaks: 1 = solvent; 2 and 3 = diastereomers; 4 = dodecene-1.

As association–dissociation disturbs the separation and quantification of the diastereomers, the continuous contact of strongly solvating solvents and free olefins with the diastereomers must be avoided. Separations without rapid interconversion of the diastereomers can only be achieved because olefins, frequently present in the reaction mixture, elute early within the dead-time of the normal-phase column. Thus, these olefins are soon separated from the complexes and do not travel together with the diastereomers for a long period.

The use of platinum complexes for analytical separations of non-chiral olefins

The described platinum complexes can also be applied to certain analytical problems which require the separation of various types of non-chiral olefins. Fig. 27A shows the normal-phase separation of the diastereomers formed by the reaction of *cis*- and *trans*-decene-2 with complex I. The two diastereomers of *trans*-decene-4 cannot be resolved because the double bond is almost symmetrically substituted and the selectivity of the chromatographic separation is not sufficient (Fig. 27B).

External derivatization of olefins mixed with solutes which do not complex offers the possibility to execute group separations in reversed-phase LC systems. Complex I is very polar compared to olefins and diminishes their retentions remarkably (Fig. 28). ΔI values of 200–300 for alkenes-1 are observed.

CONCLUSIONS

Platinum complexation, as described in this paper, presents new possibilities for the analyses of olefinic compounds. The determination of enantiomer ratios of solutes present only at small concentrations in mixtures, by a precise and accurate micromethod, may be of interest in the field of asymmetric catalysis. Analytical chromatography of this kind cannot replace the requirement for the isolation of pure enantiomer species, but in many cases can help to determine whether a time-consuming work-up of a mixture will be promising or not.

ACKNOWLEDGEMENTS

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