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[19] CD spectrum of enantiomerically pure C_{76} ($c = 3.8 \times 10^{-5}$ M) in toluene:[14a] λ[nm] ($\Delta\varepsilon$ [$\mathrm{M^{-1}cm^{-1}}$]: 315 (−11.7), 330 (+8.9), 354 (−4.2), 394 (+29.4), 405 (+31.6), 460 (+12.6), 541 (−11.1), 573 (−18.2), 639 (+2.5).

[20] Preparative HPLC on a Regis Buckyclutcher I Trident-Tri-DNP (10 mm) 500 mm × 21.1 mm column with an n-hexane/toluene (60/40) mobile phase at 8 mL min^{-1}.

[21] The chiroptical properties of both functionalized inherently chiral fullerene derivatives and derivatives with an inherently chiral addition pattern are largely determined by the chirality of the carbon sphere and not by the chirality of the addends.[17a, 18]

[22] We determined the concentrations of the enantiomeric solutions based on their known UV/Vis absorptions (see reference [13] and A. Herrmann, doctoral dissertation, ETH Zürich, **1997**).

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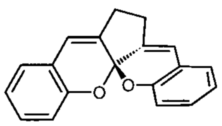
Enantiomeric Enrichment of Stereolabile Chiral Spiro Compounds by Dynamic HPLC on Chiral Stationary Phases[**]

Klaus Lorenz, Eiji Yashima, and Yoshio Okamoto[*]

Chromatographic enantioseparation on chiral stationary phases (CSPs)[1–5] has become a very useful method for the analysis of chiral compounds and the preparative separation of enantiomers because of recent progress in the development of CSPs with high chiral recognition ability. In addition, the newly developed dynamic high-performance liquid chromatography (DHPLC) has received considerable attention as a powerful tool for investigating dynamic processes of interconverting enantiomers;[6–11] kinetic data and enantiomerization barriers for stereolabile compounds can be obtained from a series of temperature-dependent plateaus and peak shapes by chiral DHPLC. Here, we focus on the influence of CSPs on the equilibrium of interconverting enantiomers which will result in nonracemic mixtures. In the case of interconverting enantiomers, the use of CSPs opens the possibility for combining separation techniques and equilibrium shift in one step. By employing quite simple new chromatographic procedures we may, in principle, obtain one enantiomerically pure enantiomer in 100% yield from a racemate with standard HPLC equipment.

We investigated the racemic spiro compounds **1** and **2** as model compounds. Both enantiomerize thermally and photochemically through an electrocyclic [1,6]-ring opening of the C–O bond next to the spiro center and consecutive ring closure.[12]



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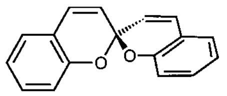

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Figure 1a shows a standard HPLC chromatogram for the resolution of **1** on Chiralcel OD.[13] Compound **1** can be completely resolved at 20 °C without any enantiomerization. However, at higher temperatures (ca. 50 °C), the enantiomerization processes described in Scheme 1 (DHPLC on CSPs)[14,15] lead to plateaulike elution profiles[16] (Figure 1b). In the heterogeneous system (CSP/mobile phase) the adsorbed enantiomer showing a longer retention time (B) should be enriched, whereas the eluent may contain a racemic mixture under equilibrium conditions.

According to the kinetic differential equations describing the enantiomerization processes during DHPLC, only race-

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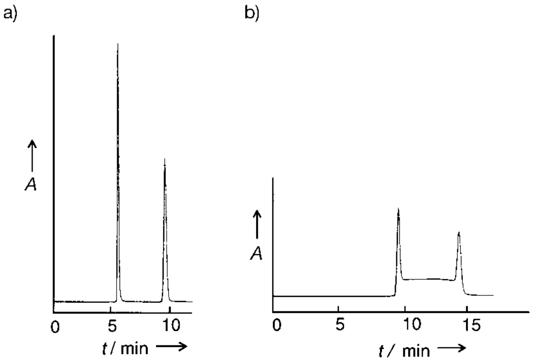
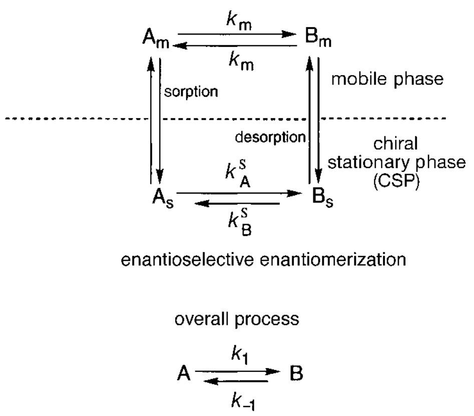


Figure 1. Chromatograms in the resolution of spiro compound **1** on Chiralcel OD with hexane/2-propanol (9/1) as eluent at 20 °C (a) and 50 °C (b). The flow rate was 1.0 mL min^{-1} (a) and 0.25 mL min^{-1} (b).



Scheme 1. Processes occurring during DHPLC: vertical sorption/desorption of enantiomers A (first eluted) and B (second eluted), horizontal enantiomerization in the mobile phase and enantioselective enantiomerization[15] of adsorbed species with respective kinetic rate constants. The indices m and s indicate the enantiomer in the mobile phase and a sorbed enantiomer; the rate constants for the "overall process" k_1 and k_{-1} describe the sum of enantiomerization in the mobile phase and enantioselective enantiomerization, respectively.

mic samples are to be expected on elution under usual conditions (constant temperature and constant flow). Nevertheless, an enantiomeric surplus of the second eluted compound is built up during the time that both enantiomers are on the column; removal of the first eluted enantiomer by elution disturbs the equilibrium and a rather fast back-reaction towards the first eluted enantiomer will take place. Finally, the racemic compound is obtained.

To suppress the back-reaction, the time interval after elution of the first peak until elution of the second ($t_B - t_A$) should be kept as small as possible with respect to t_A. Therefore, experiments were carried out as follows:[17–19] After injection of the racemic solution into the HPLC apparatus the chromatographic flow (1.5 mL min^{-1}) was stopped after 2 min for equilibration on the CSP. After an appropriate time (1–6 h) the chromatographic flow was restarted, which delivered chromatograms showing an excess of the second eluted enantiomer. The chromatograms usually contained two peaks for the optical antipodes, but in the case of high α values four peaks appeared (Figure 2; $\alpha = \frac{t_B - t_0}{t_A - t_0} = 2.29$). The peaks A and A′ as well as B and B′ were derived from enantiomers already separated during the initial separation. Experimental chromatograms before complete equilibrium (Figure 2 a,b) and at equilibrium (Figure 2 c) indicate that the third peak (B) is derived from the first (A) and the second peak (A′) from the last (B′) during the time interval of enantiomerization. Equilibrium rate constants k_1 and k_{-1} can be calculated from these data (see below).

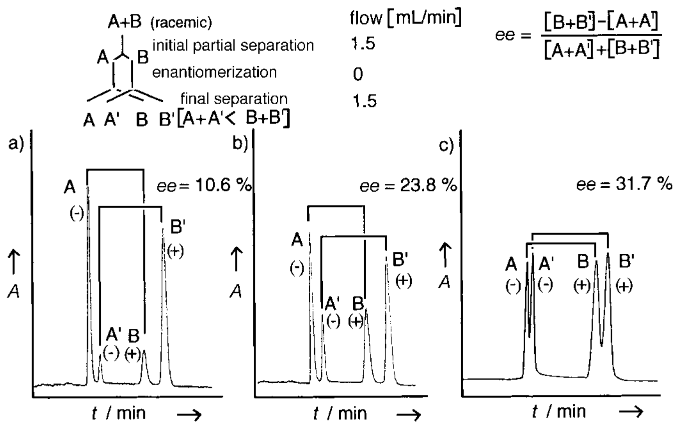


Figure 2. Chromatograms of compound **1** on Chiralcel OD with hexane/2-propanol (99/1) as eluent at 40 °C. After 2 min the flow was stopped for equilibration on the CSP. Equilibration time was 16 min (a), 57 min (b), and 6 h (c). Then flow was then restarted, and the chromatograms were monitored.

Equations (1)–(3) have been developed in order to find a quantitative relation between retention factors k' and equilibrium concentrations c_A^{eq} and c_B^{eq} on the CSP.; c_A^{eq} and c_B^{eq} are

$$\frac{k_1}{k_{-1}} = \frac{c_B^{eq}}{c_A^{eq}} \qquad (1)$$

$$\frac{k_1}{k_{-1}} = \frac{1 + k'_B}{1 + k'_A} \qquad (2)$$

$$\frac{c_B^{eq}}{c_A^{eq}} = \frac{1 + k'_B}{1 + k'_A} \qquad (3)$$

defined as overall equilibrium concentrations of A (A + A′) and B (B + B′) on the CSP. To prove Equation (3) as a combination of Equations (1) and (2)[20] experimentally, racemic spiro compounds **1** and **2** were equilibrated on various CSPs under the conditions described above. The results are summarized in Table 1. To determine the retention factors, one additional experiment at constant chromatographic flow was necessary. The plot in Figure 3 according to Equation (3) gave a straight line in good agreement with the calculated one. Deviations from the calculated values may be due to errors in retention factors and experimental equilibrium concentrations.

To increase the enantiomeric excess of spiro compounds obtained after DHPLC, only one enantiomer was equilibrated selectively. Two CSPs were employed, as represented in Scheme 2. The basic idea is that enantiomerization occurs on the second CSP at relatively high temperature, whereas thermal interconversion can be suppressed on the first CSP at relatively low temperature.

After the first eluted enantiomer A had left the first column (0 °C) and had been transported to the second column (40 °C), the chromatographic flow was stopped and enantioselective

Table 1. DHPLC of spiro compounds **1** and **2**.[a]

Entry	Compd	CSP	Eluent	T [°C]	t [min]	k'_A	k'_B	$\frac{1+k'_B}{1+k'_A}$	$\frac{C^{eq}_B}{C^{eq}_A}$
1	**1**	A	hexane/*i*PrOH (99/1)	40	360	2.55	5.85	1.93	1.93
2	**1**	A	hexane/EtOH (99/1)	32	210	1.36	3.09	1.73	1.80
3	**2**	B	hexane/*i*PrOH (99/1)	45	165	1.66	3.38	1.65	1.62
4	**1**	A	hexane/*i*PrOH (9/1)	40	200	0.78	1.61	1.47	1.50
5	**2**	A	hexane/*i*PrOH (99/1)	45	167	3.08	4.31	1.30	1.30
6	**2**	C	hexane/*i*PrOH (99/1)	45	155	1.00	1.55	1.29	1.22
7	**1**	B	hexane/*i*PrOH (99/1)	32	150	3.13	4.25	1.27	1.22
8	**2**	A	hexane/EtOH (99/1)	40	170	1.55	2.09	1.20	1.15
9	**2**	A	hexane/*i*PrOH (9/1)	50	67	0.75	1.05	1.17	1.14

[a] t is the time for equilibration on the CSPs; the flow rate after equilibration was 1.5 mL min^{-1}; A, B, and C stand for the following CSPs: A: cellulose tris(3,5-dimethylphenylcarbamate) (Chiralcel OD), B: xylan bis(3,5-dimethylphenylcarbamate),[21] C: cellulose tris(3-fluoro-5-methylphenylcarbamate).[22]

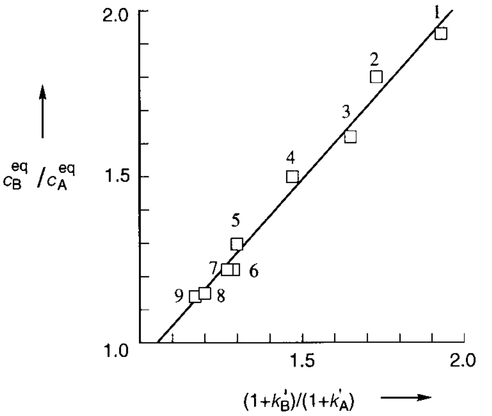
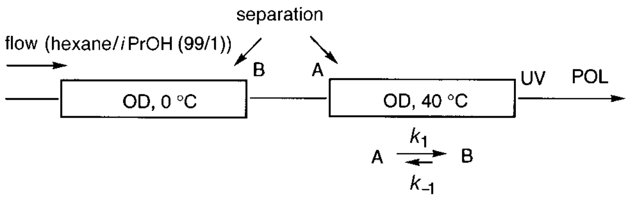


Figure 3. Plot of $(1+k'_B/(1+k'_A)$ versus the ratio of equilibrium concentrations c^{eq}_B/c^{eq}_A [Eq. (3)], as obtained by DHPLC on various CSPs (Table 1). The numbers represent entry numbers in Table 1.



Scheme 2. Two-column system for selective enantiomerization of one enantiomer. Left: B does not equilibrate at 0 °C. Right: equilibration of the first eluted A (40 °C).

enantiomerization[15] of A was allowed to proceed for 2 h. On elution three peaks appeared in the chromatogram as expected (Figure 4). The first and second peaks can be assigned to A (ca. 20 mol %) and B (ca. 30 mol %), respectively. Peak B was derived from A on the second CSP by enantiomerization. The equilibrium between A and B was not completely reached after 2 h. The last peak is noninterconverted B (50 mol %). As a result, the enantiomeric excess increased from 31 % (normal equilibrium) to about 60 % in the case of selective enantiomerization of A. If the equilibrium between A and B would have been completely reached, the enantiomeric excess would be even higher (68 %). More cycles of enantioselective equilibration of one enantiomer—for example, by recycling the undesired enantiomer in a chromatographic recycling system (reinjection) and collecting the desired enantiomer—would lead to an enantiomerically pure compound.

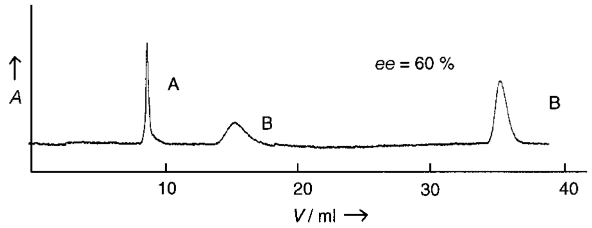


Figure 4. Chromatogram of spiro compound **1** in selective enantiomerization on the CSPs. For details, see Scheme 2.

The kinetics of enantiomerization on a CSP can be experimentally estimated in the same way as for the thermodynamic equilibrium (Figure 2). The only difference is that the time interval allowed for enantiomerization was shorter and variable. Plots according to Equations (4) and (5)

$$-\ln\left(1-\frac{B_{(t)}(2+k'_A+k'_B)}{(A_{(t)}+B_{(t)})(1+k'_B)}\right)=(k_1+k_{-1})(t-t_0) \quad (A \rightarrow B) \tag{4}$$

$$-\ln\left(1-\frac{A'_{(t)}(2+k'_A+k'_B)}{(A'_{(t)}+B'_{(t)})(1+k'_A)}\right)=(k_1+k_{-1})(t-t_0) \quad (B' \rightarrow A') \tag{5}$$

gave straight lines, and the sum of kinetic rate constants k_1 and k_{-1} was determined for both plots to be 3.4×10^{-4} s^{-1} for **1** on Chiralcel OD as a CSP, with hexane/2-propanol (99/1) as eluent at 40 °C. With Equation (6) k_1 and k_{-1} were finally calculated to be 2.2×10^{-4} and 1.2×10^{-4} s^{-1}, respectively.

$$k_1/k_{-1}=(1+k'_B)/(1+k'_A) \tag{6}$$

The compounds presented in this work readily undergo thermal interconversions and are thus of interest as model compounds. It would be an interesting perspective to replace the CSP at higher temperature by acid or basic catalysts such as ion exchangers, as many other classes of stereolabile compounds—for example, carbonyl compounds bearing a hydrogen-substituted, asymmetric carbon center in the α-position—could be investigated.

The chromatographic procedures summarized under the title "enantiomeric enrichment by HPLC" are a new method to convert an interconvertible racemic mixture into an excess of one enantiomer and to separate the enantiomers at the same time. Especially in cases where only one enantiomer is of interest, this may be a new approach to obtain enantiomerically pure compounds.

Experimental Section

Compounds **1** and **2** were prepared according to literature procedures.[23,24] For the chromatographic experiments the following equipment was used: pump: JASCO PU 986, degasser: JASCO DC-980-50, UV detector JASCO MD-910 multiwavelength detector and JASCO 875-UV, polarimetric detector: JASCO OR990 and JASCO Shodex OR1.

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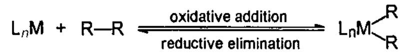
The First Metathesis of C–C Single Bonds in Homogeneous Solution: Titanocene-Mediated and Photocatalyzed Cleavage and Recombination of Disubstituted Butadiynes[**]

Siegmar Pulst, Frank G. Kirchbauer, Barbara Heller, Wolfgang Baumann, and Uwe Rosenthal[*]

Dedicated to Dr. Erhard Kurras
on the occasion of his 70th birthday

The cleavage (oxidative addition) and coupling (reductive elimination) of carbon–carbon bonds (Scheme 1) are elemental steps in many transition metal catalyzed reactions and are strongly influenced by the nature of the ligands L, metal centers M, and organic groups R. The copper-catalyzed Glaser coupling reaction (R = alkynyl) has long been known and is a well-established method for preparing 1,4-disubstituted 1,3-butadiynes.[1] In contrast, examples of the reverse reaction, the activation and cleavage of the central C–C single bond, are rare.[2]



Scheme 1.

The cleavage of the C–C single bonds of butadiynes with "Cp_2Ti" and "Cp_2Zr" (Cp = cyclopentadienyl) is influenced by the metal,[2c] the substituents,[3] and by the stoichiometry.[4] So far, all attempts to combine the cleavage reaction with a subsequent coupling reaction of the resulting alkynyl groups have failed, both with homobimetallic Ti and Zr systems and early/late heterobimetallic systems such as Ti/Ni and Zr/Ni.[2e] The high thermal stability of the intermediate metal complexes and side reactions such as diyne coupling[4, 5] and ligand cleavage[6] have until now prevented the controlled metathesis of diynes.[2c, 4] Recently, we found that the coupling reaction of the alkynyl groups in $[\mathrm{Cp_2Ti(C{\equiv}C}t\mathrm{Bu)_2}]$[7] is photo-accelerated.[8] Basset et al.[9] described the first heterogeneous "metathesis of alkanes" with silica-supported transition metal hydrides as catalysts. Here we report the first metathesis of the C–C single bonds of disubstituted butadiynes in homogeneous solution; the reaction is mediated by titanocene and photocatalyzed.

An equimolar mixture of the symmetrically substituted butadiynes **1** and **2** was irradiated with light of wavelength 390–450 nm in the presence of an excess of the titanocene ("Cp_2Ti") source $[\mathrm{Cp_2Ti}(\eta^2\text{-}\mathrm{Me_3SiC{\equiv}CSiMe_3})]$[10] at 100 °C in toluene. After oxidative workup with $AgSO_3CF_3$, the diyne starting materials and the unsymmetrically substituted butadiyne **3** were detected by gas chromatography (Scheme 2,

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