Chemo-enzymatic routes to enantiopure haloalcohols and epoxides
Haak, Robert M.

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Chapter 6
Enantiopure alcohols as amplifiers of 2D chirality

In this chapter, the preparation of enantiomerically pure (R)- and (S)-1-phenyl-1-octanol by enzymatic kinetic resolution of the corresponding racemic acetate is described. Using lipase from Pseudomonas cepacia, both enantiomers were obtained in >98% ee. Subsequently, the products were used as chiral solvents to control the enantiopreference of the chiral self-assembly of achiral molecules on an achiral surface. These results demonstrate for the first time that enantiopure solvents may be used to control chiral self-assembly on a surface, providing an elegant and low-cost method to form large enantiomerically pure organic surfaces.a,1

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Chapter 6

6.1 Introduction

Asymmetric transformations using enzymes are very efficient means of obtaining enantiopure compounds, because of their generally high activity and selectivity (see, for instance, Chapters 3 and 4 of this thesis). A popular class of enzymes for organic reactions are lipases (EC 3.1.1.3), owing to the mild reaction conditions they allow, their availability at low cost, their stability in various media, in particular organic solvents, their broad substrate range and high stereoselectivity. Also called “the workhorses of biocatalysis”, they have been used for years in the enantioselective hydrolysis or formation of esters. The first reaction is performed in aqueous media, while the latter often proceeds in organic solvents.

In this chapter, lipase-catalyzed preparation of enantiopure alcohols (R)- and (S)-6.1 (Figure 6.1) is combined with nanoscale investigations on the control of two-dimensional (2D) chirality. The study of chiral surfaces has become an important scientific field in recent years, initial interest coming from the area of heterogeneous catalysis. A recent example is the single-molecule imaging of a manganese-porphyrin catalyst at work during an oxidation reaction, reported by Elemans and coworkers. Furthermore, asymmetric catalysis on solid supports has great potential as an efficient, sustainable methodology in the synthesis of optically active chemicals.

The importance of surface chemistry, especially to catalytic processes, is emphasized by the awarding of the 2007 Nobel Prize in Chemistry to Gerhard Ertl. However, the study and selective functionalization of chiral surfaces is also relevant for purposes such as chiral recognition, new thin film devices for optical and electronic applications, and nanotechnology. The critical influence of surface/molecule interactions on expression of chirality at the fluid/solid interface, which is a relevant topic for the development of material sciences, has also been recently reviewed.

Self-assembly, i.e. the spontaneous formation of highly organized structures from molecular components by noncovalent interactions, is an elegant way to achieve surface functionalization. The supramolecular assemblies formed by self-assembly can be studied using a variety of techniques, but for the observation of surface patterns the most prominent techniques are high-resolution microscopy techniques such as atomic force microscopy (AFM) and scanning tunneling microscopy (STM). STM, originating in the early 1980’s, is a convenient technique to study chirality in 2D supramolecular self-assemblies, since it allows for the resolution of structures on a surface at submolecular or even atomic level. Hembury et al. have recently given an overview of various supramolecular systems for chirality-sensing purposes, including some examples of direct chirality observation on surfaces. Besides pointing out some advances that
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have been made in this area, these authors emphasize that the exact nature of the mechanisms of chirality transfer from the molecular to the supramolecular level in these systems is often poorly understood. Moreover, the 2D supramolecular structures described so far are mostly only locally chiral. This means that, even when chiral domains are spontaneously formed on a surface, both enantiomorphous domains are statistically formed in equal amounts, so overall, the samples are racemic. For future applications, it is essential to control the formation of homochiral domains in order to obtain an excess of a single enantiomorph on a surface. An example of such an amplification of chirality was recently reported for heptahelicene monolayers on Cu(111) in ultra-high vacuum, showing a strongly positive non-linear dependence of lattice chirality on the enantiomeric excess of the heptahelicene.\textsuperscript{13}

Another possibility to create macroscopically chiral monolayers, in contrast to locally chiral but globally racemic monolayers, could be the use of chiral solvents. So far, optically active solvents have been used in areas unrelated to the research described here, such as double stereodifferentiation in enantioselective reactions\textsuperscript{14} or chromatographic separation of \textalpha-amino acid enantiomers using a chiral eluent.\textsuperscript{15} The use of chiral solvents to achieve control over supramolecular stereochemistry on surfaces has not been reported.

In this chapter, the enantioselective formation of chiral monolayers of achiral molecules on achiral surfaces is investigated by means of STM at the liquid/solid interface. In the next paragraphs, it will be shown that chiral surface patterns can be formed from achiral molecules on an achiral surface, by using enantiomerically pure 1-phenyl-1-octanol (6.1, Figure 6.1) as chiral solvent.

The choice for 6.1 was motivated by the fact that it is the logical hybrid form between 1-phenyloctane and 1-octanol, typical solvents for scanning tunneling microscopy (STM) imaging at the liquid – solid interface.\textsuperscript{4,8,9,16} Since we used 1-phenyloctyl acetate (6.2, Figure 6.1) as a precursor for enantiomerically pure 6.1 (see paragraph 6.2), this solvent was also employed as solvent in STM imaging (\textit{vide infra}).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure6.1.png}
\caption{The chiral solvents used in this study, (R)- and (S)-1-phenyl-1-octanol ((R)-6.1 and (S)-6.1) and (R)- and (S)-1-phenyloctyl acetate ((R)-6.2 and (S)-6.2).}
\end{figure}

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The compound used as adsorbate was a hydrogen-bonding achiral diamino triazine oligo-(p-phenylenevinylene) oligomer (A-OPV4T, Figure 6.2). It had already been shown that its chiral analogue, (S)-OPV4T\textsuperscript{17} (Figure 6.2) assembles exclusively in a counterclockwise rosette motif at the liquid-solid interface, using graphite as substrate and 1-phenyloctane as solvent.\textsuperscript{18,19} Such transfer of molecular chirality to a surface, creating enantiomorphous patterns, has been observed more often.\textsuperscript{11} Furthermore, amplification of chirality in dynamic supramolecular aggregates has been observed in solution, as recently reviewed by Meijer \textit{et al.}\textsuperscript{20} In most cases, the self-assembly of achiral molecules on an atomically flat surface also involves the breaking of symmetry leading to the formation of locally chiral, enantiomorphic structures.\textsuperscript{8,9,21} Although it has been demonstrated that the structure of the surface has a dramatic influence on the chiral properties of the monolayers,\textsuperscript{9} solvents had not yet been demonstrated to be a symmetry breaking agent with respect to surface organisation.

More specifically, it was not known whether an achiral oligo-(p-phenylenevinylene) such as A-OPV4T (Figure 6.2), would adsorb from a chiral solvent onto graphite by forming a chiral pattern similar to (S)-OPV4T, and if so, whether the configuration of the resulting chiral surface structures could be influenced by choosing an appropriate chiral solvent.

\textbf{Figure 6.2} a) A-OPV4T, the compound used in this study; b) (S)-OPV4T, the chiral counterpart of A-OPV4T.
6.2 Synthesis of chiral solvents

The synthesis and kinetic resolution of 1-aryl-1-alkanols with long alkyl chains was described in 1990 by Mori and Bernotas, with the objective of applying these compounds in liquid crystal technology. First, racemic 6.1 was prepared by Grignard addition of n-heptyl magnesium bromide to benzaldehyde, as depicted in Scheme 6.1.

![Scheme 6.1 Synthesis of rac-1-phenyl-1-octanol.](image)

Subsequent esterification using acetic anhydride in pyridine yielded 6.2 in quantitative yield (Scheme 6.2).

![Scheme 6.2 Synthesis of rac-1-phenyloctyl acetate.](image)

Mori and Bernotas reported that lipase-catalyzed transesterification of 1-phenyloctanol with vinyl and 2-propenyl acetate in organic solvents such as benzene and n-heptane proceeded slowly and with low enantioselectivity. However, lipase-catalyzed hydrolysis of the acetate in aqueous phosphate buffer – i.e. the reverse reaction – gave excellent results. We adopted their system and obtained (R)-6.1 and (S)-6.2 in good yield and excellent enantioselectivity (>98% ee for both compounds, determined using chiral HPLC), after an initial screening of a number of Pseudomonas lipases, of which *Pseudomonas cepacia* gave the best results (Scheme 6.3). As an extension of this approach, we successfully scaled up this protocol from 1 to 20 mmol.

The enantiomers (S)-6.1 and (R)-6.2 were obtained by acetylation of (R)-6.1 and base-assisted deprotection of (S)-6.2, respectively.
Thus, four solvents were prepared in high (enantiop)urity for use in STM studies, namely \((R)\)- and \((S)\)-1-phenyl-1-octanol and \((R)\)- and \((S)\)-1-phenyl-1-octanoic acid.

### 6.3 Control of enantioselective 2D self-assembly using chiral solvents

Nanoscale investigation on 2D self-assembly of OPVs has been carried out by STM at the interface between highly oriented pyrolytic graphite (HOPG) and a solution of A-OPV4T in enantiomerically pure \(6.1\). STM images demonstrate the formation of monolayers of A-OPV4T (Figure 6.3). Within the monolayer, A-OPV4T self-assembles into star-shaped features with six bright arms, hereafter called "rosettes" (Figure 6.3). These bright arms correspond to the conjugated OPV backbone (Figure 6.2) with the molecular axis lying parallel to the surface. The alkyl chains are adsorbed in the low-contrast areas, but in high-resolution STM images they are visible (e.g. Figure 6.3b and c).

Since the OPV units at opposite sides of the rosettes are not in line, but show a clear non-radial orientation (Figure 6.3a, b, and c), they can be classified as clockwise (CW) or counterclockwise (CCW), which are mirror images of each other. In other words, the rosettes show 2D chirality.

Using \((S)\)-6.1 as solvent, a clear bias towards the formation of CW rosettes is observed, whereas using \((R)\)-6.1 primarily CCW rosettes are formed. This bias demonstrates the control which the chiral solvent exerts on supramolecular surface chirality. Furthermore, not only the chirality of the rosettes themselves is dependent on the solvent, but also the –chiral – orientation of the rosettes with respect to each other. This next level of hierarchical self-assembly is illustrated in Figure 6.3b and c, where the dashed marker lines are longer than the solid ones, representing a non-superimposable 2D-chiral arrangement of the rosettes.

In both \((R)\)- and \((S)\)-6.1, many ordered domains of variable size have been observed. Within a given domain, the rosettes are ordered in rows and form a homochiral crystalline lattice characterized by the following unit cell parameters: \(a = 6.11 \pm 0.06\)
nm, \( b = 6.13 \pm 0.04 \text{ nm}, \gamma = 60 \pm 1^\circ \) in (\( S \))-6.1 (Figure 6.3c) and \( a = 6.09 \pm 0.06 \text{ nm}, \ b = 6.04 \pm 0.05 \text{ nm}, \gamma = 62 \pm 2^\circ \) in (\( R \))-6.1 (Figure 6.3b). These values are identical – within experimental error – to those of enantiopure (\( S \))-OPV4T at the interface of 1-phenyloctane and HOPG.\(^{18}\) A-OPV4T self-assembles into a chiral pattern in accordance with the plane group \( \rho 6 \), one of the five possible chiral space groups on surfaces.\(^{23,24}\)

**Figure 6.3** Enantioselective formation of rosettes on a surface using chiral solvents as visualized by STM. a) and b) are STM images of an A-OPV4T monolayer at the (\( R \))-6.1 – HOPG interface. A) In addition to several domains of CCW rosettes, one CW domain is observed as marked. Scale bar is 10 nm. B) High-resolution image of the CCW rosette. Individual OPV units are indicated to emphasize the non-radial orientation (top right corner). The rotation direction is highlighted by the white arrow. Scale bar is 3 nm. c) Molecular resolution STM image of an A-OPV4T monolayer at the (\( S \))-6.1 – HOPG interface. The CW rotation direction is highlighted by the white arrow. Scale bar is 3 nm. d) Proposed hydrogen bonding motif of the CCW rotating rosette, involving six A-OPV4T molecules. Arrows indicate the nitrogen atoms which remain free to interact by hydrogen bonding with the solvent molecules.

The observed solvent-induced asymmetry at the liquid-solid interface has been quantitatively confirmed by statistical analysis, wherein a large number of individual rosettes (>1000 per experiment) were indexed as CW or CCW. This analysis has been
carried out using several batches of solvent and substrate in order to ensure reproducibility of the results. As is shown in Table 6.1, monolayer formation in enantiopure 6.1 is characterized by solvent-controlled asymmetric induction. However, complete induction of asymmetry is never observed, possibly because of the slow kinetics of the ordering process. The measured enantiomeric ratios (CCW : CW) range from 17 : 83 in (S)-6.1 (entry 2) to 91 : 9 in (R)-6.1 (entry 1), comparable values within the experimental error.

### Table 6.1 Asymmetric induction in monolayers of A-OPV4T on HOPG using various solvents.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Rosettes analyzed (#)</th>
<th>Distinctly rotating rosettes (%)b</th>
<th>CCW:CW (Std. dev.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(R)-6.1</td>
<td>2209</td>
<td>86</td>
<td>91 : 9 (9)</td>
</tr>
<tr>
<td>2</td>
<td>(S)-6.1</td>
<td>1948</td>
<td>71</td>
<td>17 : 83 (14)</td>
</tr>
<tr>
<td>3</td>
<td>rac-6.1</td>
<td>4190</td>
<td>78</td>
<td>54 : 46 (14)</td>
</tr>
<tr>
<td>4</td>
<td>(R)-6.2</td>
<td>1019</td>
<td>44</td>
<td>55 : 45 (15)</td>
</tr>
<tr>
<td>5</td>
<td>(S)-6.2</td>
<td>1194</td>
<td>42</td>
<td>48 : 52 (12)</td>
</tr>
</tbody>
</table>

a) All STM images were registered at least one hour after deposition on the surface, to allow the monolayers to organize in view of the dynamics taking place. Typically, the waiting time was longer for rac-6.1 than for the corresponding enantiomerically pure solvent. A significant number of areas per solvent was probed: (R)-6.1: 16, (S)-6.1: 17, rac-6.1: 52, (R)-6.2: 13, (S)-6.2: 15. The standard deviation of the weighted mean of the enantiomeric ratio (that is, corrected for the number of chiral rosettes per area) is given in parentheses. Note that the standard deviation for a constant number of probed rosettes should become smaller by scanning larger areas, which is limited though by the need for high spatial resolution; b) CCW and CW combined.

Three other solvents have been investigated, racemic 1-phenyl-1-octanol (rac-6.1) and both enantiomers of 1-phenyloctyl acetate ((R)- and (S)-6.2). Using rac-6.1, a comparable percentage of distinctly ordered rosettes is observed, however, as expected, without enantiomeric bias (Table 6.1, entry 3). Also when (R)- and (S)-6.2 are employed, there is no preference for any one of the rosette enantiomers. Moreover, the number of distinctly rotating rosettes compared to other surface structures is noticeably lower (entries 4 and 5). These results suggest that hydrogen bonding interactions between enantiomerically pure 6.1 and A-OPV4T are of key importance in inducing the preferred surface chirality, probably through H-bonding of the hydroxyl moiety of the solvent with the unbound nitrogen atoms in triazine hydrogen-bonded rosettes, as illustrated in Figure 6.3d.

Further insight into the mechanism of induction of preferred surface chirality was provided by circular dichroism (CD) measurements of A-OPV4T in either (R)- or (S)-6.1, using a typical concentration for STM (c = 3 x 10^{-5} M). No CD effects were observed.
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in solution, revealing that neither potential pre-formation of the rosettes nor formation of other chiral assemblies are involved. The fact that rosettes are formed exclusively at the liquid-solid interface is also demonstrated by STM images recorded a few minutes after deposition on the surface, showing disordered monolayers typically observed when achiral solvents are used. Crucially, large areas of the ordered structure formed by the rosettes only develop with time, indicating that the chiral solvent is not directly incorporated in the rosettes, but is in dynamic interaction with the surface.

The emergence of chiral OPV4T monolayers could also be explained by the formation of a solvent monolayer acting as a chiral template for the rosettes to form on. However, this hypothesis is unlikely, since deposition of pure (R)- or (S)-6.1 on HOPG has never resulted in the observation of any ordered layer. In addition, the unit cell parameters of ordered rosette domains are identical in all different solvents used. Therefore, we attribute the emergence of enantiopreference to dynamic interactions of the enantiopure solvent on top of the rosettes. Interestingly, the 2D stereochemistry of enantiopure (S)-OPV4T is not affected by the chiral nature of the solvent when experiments are performed in (R)- or (S)-6.1. This means that the effect of molecular chirality overrules the effect of solvent chirality.

Figure 6.4 Time-dependent emergence of preferred chirality. Evolution of the enantiomeric ratio (CCW/(CCW+CW)) and the number of rosettes of a given orientation (CCW, CW, or NO orientation) as a function of time.
STM has also been used to observe in real time how enantiomeric excess emerges, by recording a series of STM images at the (R)-6.1 – HOPG interface over a period of 50 min. The evolution in time of the number of rosettes (CW and CCW) and ill-defined cyclic hexamers without identifiable orientation (NO) is depicted in Figure 6.4. The emergence of order, i.e. the decrease of NO-labeled hexamers, and the increase in enantioselectivity, i.e. the increase of the CCW / CW ratio, are clearly correlated. In this time-dependent sequence, the enantiomeric ratio (CCW : CW) increases from about 50 : 50 in the beginning to 80 : 20 after 50 min.\(^b\)

In all experiments, this evolution from non-ordered rosettes to CCW or CW rosettes has been observed. Also other changes, such as the evolution of CW into CCW rosettes (or vice versa, depending on the chirality of the solvent) or the transition of e.g. dimers of molecules into rosette-type objects have been identified.

The detailed mechanism for the emergence of 2D enantiomorphic selectivity remains unknown. When an isolated rosette is considered, the energy difference between the two possible orientations is likely to be small. However, in the 2D lattice, the addition of small energy differences at the supramolecular level will lead to the preference of a conglomerate 2D lattice over the racemic lattice.

### 6.4 Conclusions and outlook

It has been demonstrated that chirality on a supramolecular level can emerge by self-assembly of achiral molecules on an achiral surface, through the use of an enantiopure solvent. More specifically, \(p\)-phenylenevinylene oligomer A-OPV4T (Figure 6.2) self-assembles on a HOPG surface in the form of chiral rosettes, which can be clockwise (CW) or counterclockwise (CCW). Using (R)-1-phenyl-1-octanol ((R)-6.1), there is a preference for CCW rosettes, whereas the use of (S)-6.1 leads to an excess of CW rosettes.

The mechanism of chirality transfer from the solvent to the supramolecular structure likely involves hydrogen bonding, since the corresponding enantiopure acetates 6.2 did not lead to any enantiopreference in the supramolecular surface structure. However, the role of \(\pi-\pi\) interactions cannot be ruled out. Experiments using an analogous aliphatic chiral solvent, for instance 1-cyclohexyl-1-octanol, could provide additional evidence to understand the mechanism of emergence of enantiopreference.

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\(^b\) When a different area of the same sample was scanned three hours later, the enantiomeric ratio was already at a high level and no longer changed significantly with time.
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There are reports in the literature about the hydrogenation of chiral 1-phenyl-1-alkanols to the corresponding 1-cyclohexyl-1-alkanols, where the stereochemical integrity remained intact. An example is the PtO$_2$-catalyzed hydrogenation in glacial acetic acid described by Levene et al.,$^{25}$ later employed by Cram and Tadanier.$^{26}$ Both groups use this reaction in stereochemical studies. However, in our hands, attempts to hydrogenate 6.1 to 6.3 using PtO$_2$ as the catalyst have repeatedly led to hydrogenolysis of the hydroxy moiety, furnishing 1-phenyloctane 6.4 (Scheme 6.4).

![Scheme 6.4](image)

Scheme 6.4 Attempted hydrogenation of 6.1 to 6.3, leading to 6.4.

Given these disappointing results in the PtO$_2$-catalyzed hydrogenation of 6.1, other catalysts should be considered. A possible candidate is rhodium on carbon, which was used by Minnaard et al. to catalyze the hydrogenation of (S)-phenylglycine to (S)-cyclohexylglycine.$^{27}$ A related reaction described in the literature is the hydrogenation of acetophenone to 1-cyclohexylethanol using a rhodium catalyst$^{28}$ or nanoparticles of ruthenium or rhodium on carbon nanofibers.$^{29}$ Furthermore, alternative routes to 6.3 should be taken into consideration, such as enantioselective reduction of ketone 6.5. This could be done in a variety of ways, for example biocatalytically,$^{30}$ using asymmetric (transfer) hydrogenation,$^{31}$ or other chiral reduction methods.$^{32}$

6.5 Experimental part

6.5.1 General remarks
For general information, see Chapters 2 and 3.
6.5.2 Synthesis of chiral solvents

rac-1-Phenyl-1-octanol (6.1)

Racemic 1-phenyl-1-octanol (6.1) was prepared by Grignard addition of \textit{in situ} prepared heptyl magnesium bromide to benzaldehyde in Et₂O using standard techniques. Purification was achieved by column chromatography over SiO₂ (gradient \(n\)-heptane – \(n\)-heptane/EtOAc 9:1). To obtain samples for use in STM measurements, the compound was further purified by Kugelrohr distillation. \( ^1\text{H} \text{NMR (CDCl}_3 \text{)}\ \delta 7.38-7.20 \text{ (m, 5H), 4.63 (dd, } J = 7.3, 5.9 \text{ Hz), 1.90 (s, 1H), 1.83-1.62 \text{ (m, 2H), 1.44-1.16 \text{ (m, 10H), 0.86 (t, } J = 6.6 \text{ Hz, 3H); } ^{13}\text{C NMR (CDCl}_3 \text{)}\ \delta 144.9 \text{ (s), 128.4 (d), 127.4 (d), 125.9 (d), 74.7 (d), 39.1 (t), 31.8 (t), 29.5 (t), 29.2 (t), 25.8 (t), 22.6 (t), 14.0 (q); MS (EI+): m/z = 206 \text{ (M+), 188, 117, 104, 82, 79, 77; HRMS (EI+): calc. for C}_{14}\text{H}_{22}\text{O: 206.1671, found: 206.1681; Chiral HPLC: Chiralcel OD, 40°C, } n\text{-heptane/IPA 99:1, 1.0 mL/min, } T_r = 14.5 \text{ min ((R)-6.1), 16.6 min ((S)-6.1).}

rac-1-phenyloctyl acetate (6.2)

Synthesis of 1-phenyloctyl acetate (6.2) was achieved by subjecting 1-phenyl-1-octanol (6.1) to acetic anhydride in pyridine at 0 °C overnight. The crude acetate thus obtained was purified using column chromatography over silica gel (eluent: \(n\)-pentane/Et₂O 50:1). \( ^1\text{H} \text{NMR (CDCl}_3 \text{)}\ \delta 7.35 – 7.25 \text{ (m, 5H), 5.72 (ddd, } J = 7.7, 6.2, 1.5 \text{ Hz, 1H), 2.05 (d, } J = 1.8 \text{ Hz, 3H), 1.97 – 1.85 \text{ (m, 1H), 1.80 – 1.70 \text{ (m, 1H), 1.38 – 1.15 \text{ (m, 10H), 0.86 (t, } J = 6.6 \text{ Hz, 3H); } ^{13}\text{C NMR (CDCl}_3 \text{)}\ \delta 170.3 \text{ (s), 140.9 (s), 128.3 (d), 127.8 (d), 126.5 (d), 76.14 (d), 36.3 (t), 31.7 (t), 29.3 (t), 29.1 (t), 25.5 (t), 22.6 (t), 21.2 (q), 14.0 (q); MS (EI+): m/z = 248 \text{ (M+), 206, 188, 149, 117, 107, 105, 104, 91; HRMS (EI+): calculated for C}_{16}\text{H}_{24}\text{O}_{2: 248.1776, found: 206.1782; Chiral HPLC: Chiralcel OB-H, 40°C, } n\text{-heptane/IPA 99:1, 1.0 mL/min, } T_r = 10.6 \text{ min ((R)-6.2), 16.9 min ((S)-6.2).}

(R)-1-phenyl-1-octanol ((R)-6.1) and (S)-1-phenyloctyl acetate ((S)-6.2)

Kinetic resolution was performed using the procedure of Mori and Bernotas\textsuperscript{22} on a larger scale. Thus, 20.5 mmol of rac-1-phenyloctyl acetate (rac-6.2) was dissolved in 100 mL of acetone and added to 900 mL of phosphate buffer (100 mM, pH 6.9). Furthermore, 40 drops of Triton-X100 were added. Finally, 1.94 g of \textit{Pseudomonas cepacia} lipase was added. After 16 d, the mixture was extracted with EtO (3x), the combined organic layers were washed with a saturated solution of NaHCO₃ sat. and brine, respectively, dried over MgSO₄, filtered and the solvent evaporated. Purification
was achieved by column chromatography over silica gel using a gradient of \( n \)-pentane/Et\(_2\)O 19:1 – 1:1. (\(R\))-6.1 and (\(S\))-6.2 were both obtained in >98% ee and further purified using kugelrohr distillation.

(\(S\))-1-phenyl-1-octanol ((\(S\))-6.1) and (\(R\))-1-phenylbutyl acetate ((\(R\))-6.2)

Enantiomerically pure (\(S\))-1-phenyl-1-octanol ((\(S\))-6.1) and (\(R\))-1-phenylbutyl acetate ((\(R\))-6.2) were obtained by deprotection of (\(S\))-6.2 (K\(_2\)CO\(_3\) in MeOH at rt) and acetylation of (\(R\))-6.1 (Ac\(_2\)O in pyridine at 0 °C → rt), respectively. Spectral data were in accordance with those obtained for (\(R\))-6.1 and (\(S\))-6.2 and both (\(S\))-6.1 and (\(R\))-6.2 were obtained with >98% ee.

6.5.3 Scanning tunneling microscopy (STM)

STM measurements were performed by N. Katsonis and T. Kudernac (University of Groningen) and H. Xu (University KU Leuven). All experiments were performed at room temperature. Pt/Ir STM tips were prepared by mechanical cutting from Pt/Ir wire (80:20, diameter 0.25 mm). Prior to imaging, A-OPV4T or (\(S\))-OPV4T molecules were dissolved in the solvents by sonication (few min) and heating at 40 °C (15 min). The solutions obtained had a concentration ranging between 10\(^{-4}\) to 10\(^{-5}\) M.

Subsequently, a drop of the solution was applied to a freshly cleaved surface of highly oriented pyrolytic graphite (HOPG, from Goodfellow), and then the STM tip was immersed into the drop. The system was then allowed to cool down for at least 30 min before measuring, after which STM imaging was performed at the solution – HOPG interface on two PicoSPM machines (Molecular Imaging, Scientec), using constant current mode. Images shown are subjected to a first-order plane-fitting procedure to compensate for sample tilt.

6.6 Notes and references

1. The STM measurements described in this chapter were performed by N. Katsonis and T. Kudernac (University of Groningen) and H. Xu (University KU Leuven). A-OPV4T was provided by the group of Prof. E. W. Meijer (Eindhoven University of Technology).


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