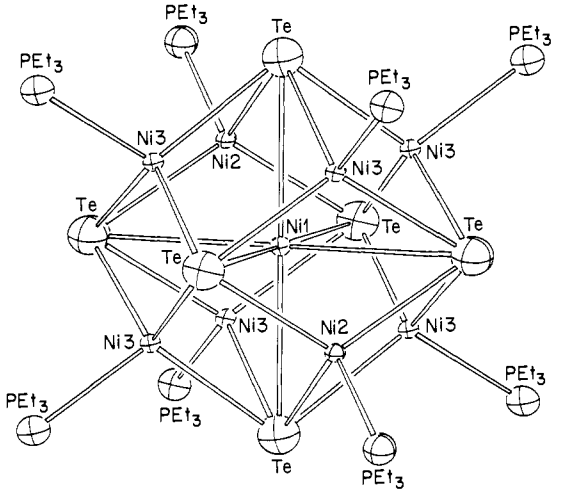

Figure 2. Structure of $Ni_9Te_6(PEt_3)_8$. Significant distances: Ni_1-Ni_2, 2.486 (4) Å; Ni_1-Ni_3, 2.4671 (23) Å; Ni_1-Te, 2.981 (2) Å; Ni_2-Ni_3(av), 2.87 Å; Ni_3-Ni_3(av), 2.84 Å; Ni_2-Te, 2.5489 (16) Å; Ni_3-Te(av), 2.55 Å. For related structures, see ref 6 and 10.

Ni_a has a square-pyramidal coordination environment. Inside the Ni_a layer are the other eight Ni centers (each of which, curiously, bonds to the central Te atom). Six of these (Ni_b in Figure 1) are tetrahedrally coordinated by four Te atoms. The remaining two Ni atoms (Ni_c) are each bonded to five Te atoms in a distorted trigonal bipyramid. This analysis shows that although the combination of the Ni-centered coordination polyhedra seems almost random, there are only three types of Ni coordination and each of these is regular.

It is important to note that although reaction 3 leads to NiTe in refluxing toluene, the structure of this Ni–Te cluster apparently has no features in common with that of the bulk solid-state compound. From this it is clear that the activation energy for atomic movement within the cluster (the molecular equivalent of solid-state diffusion in the bulk material) is low. In contrast, nanometer-sized clusters of CdSe prepared at room temperature are crystalline and mimic the structure of the bulk solid.[7]

A distinctly different cluster results when $Ni(COD)_2$, Et_3PTe, and Et_3P are combined in heptane in the ratio of 2:1:22. Rhombohedral crystals form directly from the optically dense brown reaction mixture in several hours (yield: 45%). We have also characterized this compound crystallographically, and a representation of this cluster, whose stoichiometry is $Ni_9Te_6(PEt_3)_8$, is shown in Figure 2.

The structure of this smaller cluster is much more symmetrical than that of **1**. A single, central Ni atom is surrounded by an octahedron of six Te atoms and a cube of eight Ni atoms, with each exterior Ni atom being capped with a single phosphine. There are a number of interesting features in this structure. First, if each Te is considered Te^{2-}, then there are six Ni(II) and three Ni(0) centers. This assignment is consistent with the fact that the cube of external Ni atoms is slightly elongated along one of the body diagonals. This suggests that the three "Ni(0)" sites are the central Ni and two antipodal Ni vertices. A second noteworthy aspect in the central Ni which is surrounded by an octahedron of Te^{2-} centers. This is the same as the Ni environment in bulk NiTe. In this sense, this structure mimics that of the related solid-state compound.[8] Finally, the concentric cube of metal atoms and octahedron of chalcogens is reminiscent of the well-known Chevrel[9] solid-state phases. In these materials, each cluster is a combination of a cube of chalcogens and an octahedron of metals. The present case is an example of an anti-Chevrel cluster.

In this communication we have shown that organometallic complexes of Ni(0) and Te(0) can be combined to yield the solid-state material NiTe and that this process can be interrupted and large molecular clusters isolated by the appropriate choices of stoichiometry, solvent, and reaction temperature. It is hoped that the isolation and characterization of a larger number of such intermediates in molecule-to-solid reactions will help elucidate the pathways by which these complicated reactions occur.

Supplementary Material Available: Tables listing positional and thermal parameters, significant distances and angles, and calculated and observed X-ray diffraction powder patterns for $Ni_9Te_6(PEt_3)_8$ and $Ni_{20}Te_{18}(PEt_3)_{12}$ and experimental details (synthesis of NiTe, **1**, and **2** and crystallography of **1** and **2**) (28 pages); tables of calculated and observed structure factors (133 pages). Ordering information is given on any current masthead page.

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Enzymatic Asymmetric Hydroxylation of Pentadienols Using Soybean Lipoxygenase

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Despite the high regio- and stereoselectivity of lipoxygenase-catalyzed oxidations of unsaturated fatty acids,[1] the potential utility of these enzymes for synthesizing chiral alcohols has attracted little attention. Previous studies of modified substrates with soybean lipoxygenase (SBLO) suggest that the essential structural requirements are a single ω-6 (*Z*,*Z*)-1,4-pentadienyl moiety and an appropriately spaced proximal[2] carboxyl group as characterized by the natural substrate linoleic acid.[3] On the basis of this premise, we envisaged an enzymatic method for the asymmetric hydroxylation of unsaturated alcohols **1** via their adipate monoesters **2** (Scheme I) where the adipoyl prosthesis provides the additional lipophilic scaffold required for SBLO recognition. We now report our results for the asymmetric oxidation of these surrogate substrates to afford, after reduction and hydrolysis, the chiral diols **3**.

Substrates were prepared by the condensation of (*Z*)-$THPOCH_2CH_2CH{=}CHCH_2CH{=}PPh_3$[4] with the appropriate aldehyde (RCHO; cf. Table I), followed by deprotection (*p*-TsOH, MeOH, 23 °C) to afford the (*Z*,*Z*)-dienols[5] **1** containing small amounts (5–10%) of the *Z*,*E* isomers.[6] The alcohols were transformed to their adipate monoesters **2** by using adipic anhydride monomer[7] and pyridine/DMAP (cat.) in CH_2Cl_2.

As shown in Table I, all substrates were enzymatically oxidized when treated with SBLO (Sigma Co., type I) and O_2 (0.2 L min^{-1}) at 0 °C in 0.20 M borate buffer, pH 8.5. Control experiments

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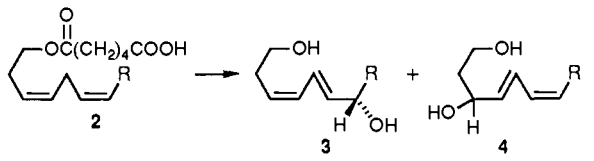
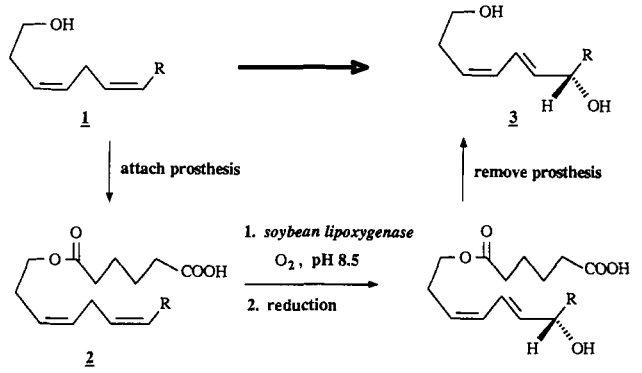
Table I. Soybean Lipoxygenase Catalyzed Oxidation of **2**[a]



	R	2:SBLO (w/w)[b]/ incubatn time (h)	3:4[c]	yield of 3 (%)	% ee of 3[d]	α_D of 3[e] (deg), confign
a	$(CH_2)_4CH_3$	0.06/1.5	97:3	92	98	+56, *S*
b	$CH_2CH(CH_3)_2$	2.5/14	82:18	72	96	+24, *S*
c	$CH(CH_3)_2$	3/12	87:13	53	>99	+83, *S*
d	$(CH_2)C_6H_5$	1/3	89:11	83	98	+30, *S*
e	$(CH_2)_3C_6H_5$	1/3	77:23	71	98	+24, *S*
f	$CH_2OCH_2C_6H_5$	2/10	85:15	52	97	+43, *R*
g	$(CH_2)_3C(O)CH_3$	0.25/24	99:1	83	97	+75, *S*
h	$(CH_2)_3C(CH_3)_2OH$	1/1	99:1	68	99	+33, *S*

[a] All incubations were conducted with 1 mmol of substrate in 60 mL of buffer at 0 °C for the specified time. [b] This weight ratio corresponds to the commercial enzyme, whose activity was ~190 000 units/mg of total protein as determined by the standard assay procedure. [c] Values were determined by normal-phase HPLC at 234 nm. [d] *S*:*R* ratios were determined by normal-phase HPLC of the bis MTPA esters according to the method of Funk; see ref 11. These values are corrected for the small amount of *R* enantiomer produced by the oxidation of the small amount of trans isomer in **2**. Pure *Z*,*E* substrate was found to undergo enzymatic oxidation, albeit at a somewhat slower rate than the *Z*,*Z* substrate. [e] All rotations were measured as solutions in ethanol, $c = 3$ at 23 °C.

Scheme I



showed no measurable oxidation in the absence of enzyme. Although it was possible to isolate the intermediate hydroperoxides from the incubation mixture, reactions were terminated by a reduction/hydrolysis sequence involving the addition of excess (40 equiv) 2-(methylthio)ethanol (7 h, 23 °C; ROOH → ROH) and then addition of KOH (180 equiv, 12 h, 23 °C) followed by extractive workup and chromatography, to afford diols **3**. Hence, the overall sequence of enzymatic oxidation, reduction, and hydrolysis can be performed as a simple "one-pot" operation.

The results in Table I show that SBLO displays a broad range of substrate flexibility. However, increasing the steric encumbrance of the distal group decreases both the rate and efficiency of enzymatic oxidation. For example, the complete oxidation of **2b–e** required longer incubation times and/or larger amounts of enzyme than substrate **2a**, which possesses the favored ω-6 structural element. Also, in keeping with previous findings, the enzymatic oxidation is not completely regioselective.[8] The major product in all cases was diol **3** accompanied by small amounts of regioisomer **4**. To ascertain whether **4** was produced by congeneric lipoxygenases in the type I enzyme, we conducted experiments using purified enzyme (DEAE-Sephadex chromatography)[9] but found no improvement in the ratio **3**:**4**. Also, variations in buffer, pH, or temperature served only to diminish both the regioselectivity and the rate of oxidation.[10]

In contrast to the variable regioselectivity, the enzymatic reaction consistently afforded products of high enantiomeric purity. The enantiomeric excess for each product was established by the method of Funk et al.,[11] which required conversion of diols **3** to their corresponding bis MTPA esters followed by HPLC analysis and comparison with the diastereomeric esters derived from the racemic counterparts. The absolute configurations for **3a–f** were determined by degrading each dienediol to a known chiral glycol or α-hydroxy acid, which involved ozonolysis of the dienic moiety followed by either $NaBH_4$/MeOH reduction or H_2O_2/AcOH[12] oxidation. Stereochemical assignments for **3** were based on the sign of optical rotation of these latter products, and the absolute configurations correspond to that as drawn for **3**. Interestingly, the sense of asymmetric induction for the surrogate substrates **2a–f** parallels the stereoselectivity observed for linoleic[13] and arachidonic acids,[14] affording predominantly, but not exclusively, the *S* enantiomer regardless of the structure of either the proximal or terminal substituent. Consequently, the absolute configurations for **3g,h**, though not known with certainty, were assigned by analogy to the consistent pattern for **3a–f**.

The results disclosed herein demonstrate a synthetically useful enzymatic method for the overall asymmetric hydroxylation of pentadienic alcohols and illustrate a remarkable substrate flexibility profile for the type I lipoxygenase. However, SBLO-mediated oxidations appear less regioselective for substrates possessing terminal substituents more lipophilic than the *n*-C_5H_{11} terminus of **2a** (e.g., **2d** and **2e**). Hence, while the primary purpose of the prosthetic modifier is to supply the missing structural features needed for enzymatic recognition, its influence on the regiochemistry of the reaction by effecting the head-to-tail vs tail-to-head mode of binding to the presumed lipophilic binding domain[15] of lipoxygenase remains unclear. This issue, as well as extension of the method to other modified substrates, is currently under investigation.

Acknowledgment. This work was assisted financially by grants from the National Science Foundation (CHE 8906497) and the American Heart Association.

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