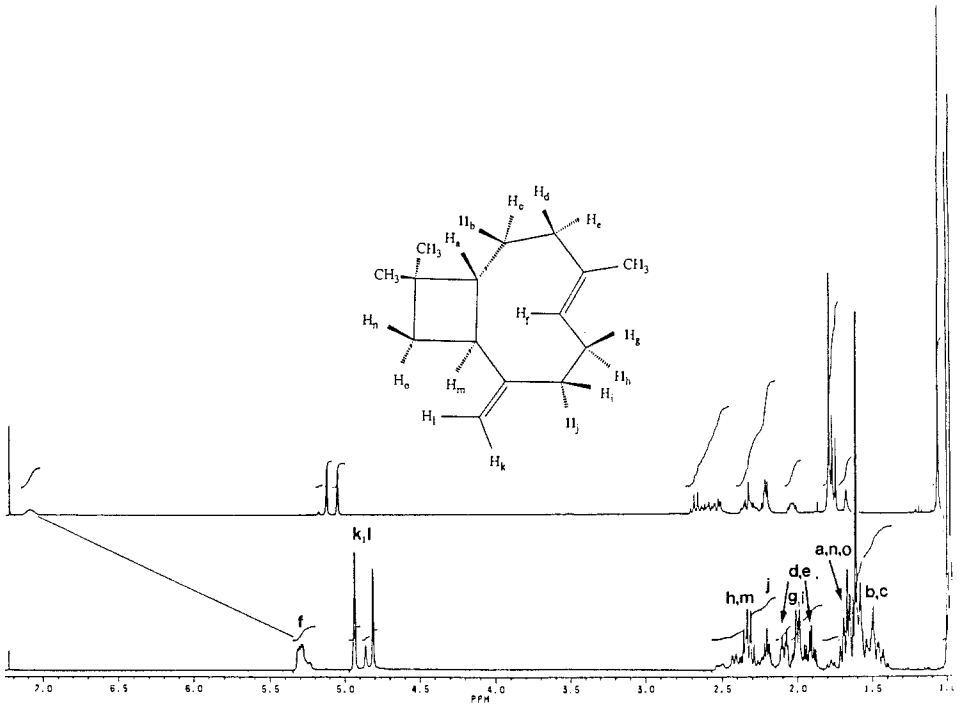

Figure 2. ^{1}H NMR spectra of $Rh_2(O_2CCF_3)_4$((−)-*trans*-caryophyllene)$_2$ (top) and of pure ligand (bottom) in $CDCl_3$. The assignments of hydrogen atoms were made by different COSY experiments.

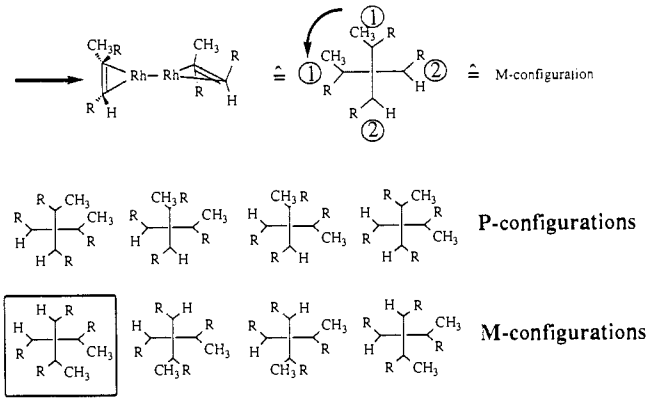

Figure 3. The eight possible isomers of dimetallic clusters with two chiral olefins of given absolute configuration. The two olefins are axially bound perpendicular to each other as in allenes. The framed isomer corresponds to the structure given in Figure 1.

The different distances between the metal and the two carbon atoms of the double bond (e.g., Rh(1)–C(9), C(10)) are also reflected in the ^{13}C NMR spectrum of $CDCl_3$ solutions of the caryophyllene complex. The signals of these two carbon atoms were shifted in different directions and with different magnitudes. The signal of C(10) was deshielded by 10 ppm from 135.37 (free ligand) to 145.31 ppm (in the complex); that of C(9) was shielded ~5 ppm from 124.30 to 119.07 ppm. The same effects were observed for the complexes with l-menthene and 3-carene. The ^{1}H NMR spectrum of the caryophyllene complex is given in Figure 2 and shows an enormous low-field shift for the signal of the olefin proton H_f, which is connected to C(9) or C(24), respectively.

Even knowing the absolute configuration of (−)-*trans*-caryophyllene,[11] we must still consider eight possible isomers of the complex because of the axis of chirality (allene type). They are summarized in Figure 3. Our complex has the configuration marked by a frame in Figure 3.

Previous spectroscopic studies[7-9] of the binding of olefins to $Rh_2(O_2CCF_3)_4$ and $Rh_2(O_2CC_3F_7)_4$ in solution or the gas phase have either not indicated the stoichiometry or have explicitly favored 1:1 stoichiometry. The present characterization of a 1:2 complex suggests that more needs to be learned about these systems both in solution and in the crystalline state.

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Supplementary Material Available: Tables of crystal data, atomic coordinates, anisotropic displacement parameters, and full listings of bond distances and angles (13 pages). Ordering information is given on any current masthead page.

Application of the Orbital Mixing Rule to Heteroatom-Dependent π-Facial Stereoselectivity in the Diels–Alder Reaction of 5-Substituted 1,3-Cyclopentadienes[1]

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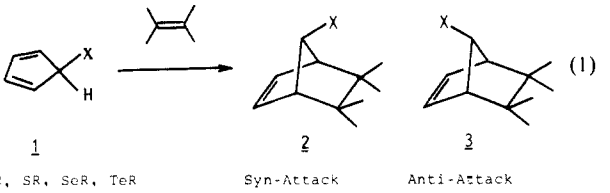
The orbital mixing rule[2] gave an unprecedented insight into the π-facial stereoselectivity in the Diels–Alder reactions of 5-substituted cyclopentadienes (eq 1), while some other theories were



developed.[3-6] These theories are in agreement with the selec-

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Table I. π-Facial Selectivities of 1,3-Cyclopentadienes Having 5-Heteroatom Substituents (X)

		MO calcn[b]			selectivity		
				coeff	pred		
X	IP,[a] eV		energies, eV	$C_{p\pi}$	C_n	IP (class)	MO (class)	obsd
OR	10.04	ψ_1	-7.374	0.523	0.137	syn (A)	syn (A)	syn (R = Ac,[7f] H[7g])
		ψ_2	-9.578	0.081	0.829			
SR	8.71	ψ_1	-6.857	0.368	0.730	syn/anti (B)	syn/anti (B)	syn/anti = 4:6 (R = Ph)[9]
		ψ_2	-7.619	0.384	0.693			
SeR	8.40	ψ_1	-6.857	0.319	0.804	anti (C)	anti (C)	anti (R = Ph)[9]
		ψ_2	-7.700	0.426	0.606			
TeR	7.89					anti (C)		anti (R = Ph)[c]
	8.566	(cyclopentadiene)						

[a] Ionization potentials of the corresponding methyl derivatives $(CH_3)_2Y$ (Y = O, S, Se, Te).[11] [b] The coefficient $C_{p\pi}$ is that of p-atomic orbital at the reaction center, C_1. [c] Beniya, Y.; Ishida, M.; Yamamoto, M.; Kato, S.; Inagaki, S. The 59th Annual Meeting of Chemical Society of Japan, Yokohama, April 1990.

tivities[7] observed so far. Recently the selectivities were found to be dependent on the 5-substituent heteroatoms, i.e., O, S, and Se.[8,9] Fallis[8] tried to explain the dependence on the basis of the Cieplak concept.[10]

In this communication, we show that the orbital mixing rule[2] is applicable to the heteroatom-dependent selectivities when the relative energies of the π HOMO of the diene and the n orbital on the heteroatom are taken into account.

The nonequivalent extension of the π HOMO of the plane asymmetric dienes (**1**) is caused by mixing of the σ orbitals of the carbon framework through the interaction with orbitals (n) on the 5-substituents.[2] The direction of the extension is controlled by the orbital phase relation, which is determined by the relative energies of the π HOMO (ϵ_π) and the n orbitals (ϵ_n). So, we classify the dienes into the three groups: (A) $\epsilon_\pi > \epsilon_n$; (B) $\epsilon_\pi \simeq \epsilon_n$; (C) $\epsilon_\pi < \epsilon_n$.

The orbital mixing rule was previously applied only to case A.[2] The π HOMO of the diene is combined with the low-lying n orbital out of phase and mixes the σ orbitals in such a way that σ and n are out of phase ($\psi_1 = C_\pi\pi - C_n n + C_\sigma\sigma$; $C_\pi > C_n$ in Figure 1). The mixing of the p-orbital component (p_σ) of the σ orbitals rotates the p-orbital axis at the reaction centers, favoring the interaction with dienophiles on the syn side. The syn attack is similarly favored by the s orbital mixing leading to the syn extension. In case C, the π HOMO is modified by an in-phase mixing with n and an out-of-phase σ–n mixing ($\psi_2 = C_\pi\pi + C_n n - C_\sigma\sigma$; $C_\pi > C_n$). This orbital (NHOMO) is distorted in a manner opposite to the HOMO (ψ_1:$C_\pi < C_n$). The anti selectivity is expected. In case B, the π HOMO and the n orbital appreciably contribute to ψ_1 and ψ_2. Both HOMO and NHOMO can play significant roles. The loss of selectivity is expected (Figure 1). In general, the higher row heteroatom substituents are predicted to favor the anti attack.

The ionization potentials[11] of cyclopentadiene and the compounds $(CH_3)_2Y$ (Y = O, S, Se, and Te) suggest that the orbital energy increases in the order of $\epsilon_n(O) < \epsilon_n(S) \simeq \epsilon_\pi$(cyclopentadiene) $< \epsilon_n(Se) < \epsilon_n(Te)$. The O-, S-, Se-, and Te-substituted dienes are then classified into A, B, C, and C groups, and the π-facial selectivities are predicted to be syn, syn/anti, anti, and anti, respectively.

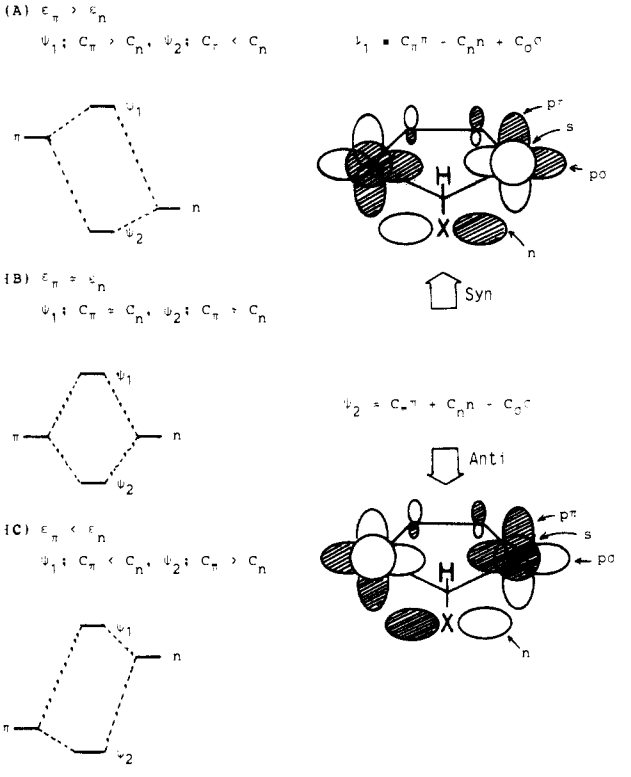

Figure 1. Directions of nonequivalent HOMO ψ_1 and NHOMO ψ_2 extensions of 5-heteroatom-substituted cyclopentadienes.

Ab initio molecular orbital calculation with the minimum basis set (STO-3G)[12] on the cyclopentadienes with OH, SH, and SeH confirmed the qualitative theory and the prediction of the selectivities.[13] For X = OH, the main component of the HOMO is the π HOMO (syn selectivity). For X = SH, the coefficients of the p orbital at C_1 are very similar in ψ_1 and ψ_2. Since the energy gap ($\Delta\epsilon$) between ψ_1 and ψ_2 is smaller than that for X = OH, both orbitals can be expected to contribute (syn/anti selectivity). For X = SeH, the p-orbital coefficient in ψ_2 is larger than that in ψ_1 (anti selectivity).

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In summary, π-facial stereoselectivities in the Diels–Alder reactions of the 5-heteroatom-substituted 1,3-cyclopentadienes can be predicted by the orbital mixing rule. In the HOMO and the NHOMO of the whole molecules, the orbitals at the reaction sites are distorted to favor the syn and anti attack, respectively. As the n-orbital energy of the heteroatoms rises, the π HOMO of the diene part contributes more to the NHOMO and less to the HOMO. The selectivities change from syn (X = OR) to syn/anti (X = SR) to anti (X = SeR, TeR). The effect of the V, VII heteroatom substituents will be described in the forthcoming full paper.

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Chemical Model for the Pyridoxal 5′-Phosphate Dependent Lysine Aminomutases

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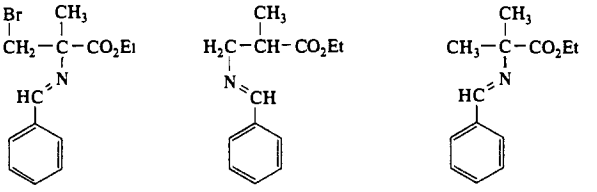
The reaction of *N*-benzylidene-(2-bromomethyl)-DL-alanine ethyl ester **1** with tributyltin hydride under free radical initiation conditions leads to *N*-benzylidene-2-methyl-β-alanine ethyl ester **2** and *N*-benzylidene-2-methyl-DL-alanine ethyl ester **3**. 1,2-Migration of the benzaldimino group through radical intermediates may be a chemical model for the pyridoxal 5′-phosphate (PLP) dependent lysine 2,3-aminomutase and β-lysine 5,6-aminomutase reactions.

Two enzymes of lysine metabolism catalyze 1,2 amino group migrations in the first and second steps of lysine catabolism in *Clostridia*.[1-3] Lysine 2,3-aminomutase catalyzes the interconversion of L-α-lysine and L-β-lysine, and β-lysine 5,6-aminomutase catalyzes the interconversion of L-β-lysine and L-3,5-diaminohexanoic acid. Both enzymes are PLP-dependent, and both have been postulated to involve radicals as intermediates.[4-7] β-lysine 5,6-aminomutase is also adenosylcobalamin-dependent, and the latter coenzyme is thought to initiate rearrangements by generating a substrate radical.[8,9] Lysine 2,3-aminomutase, on the other hand, is an iron- and *S*-adenosylmethionine-dependent enzyme;[2,3] and the putative radical rearrangement is thought to be initiated by a cofactor generated by the interaction of *S*-adenosylmethionine with a metal.[7]

No precedent for PLP catalysis of 1,2 amino migrations has been described in the literature, and no attractive mechanism can be written based on the known propensity of PLP to stabilize carbanions at the α- and β-carbons of amino acids. The hypothesis that PLP could facilitate 1,2 imino rearrangements in amino acid–PLP aldimine radicals has been advanced as a chemically attractive mechanism.[4-7] However, there appears to be no specific literature precedent for these rearrangements. We have, therefore, undertaken to determine whether a rearrangement of this type can be observed in a nonenzymatic reaction.

A model for the first radical intermediate for the lysine 2,3-aminomutase reaction is the radical produced by abstraction of Br• from the β-carbon of compound **1**, which has been synthesized

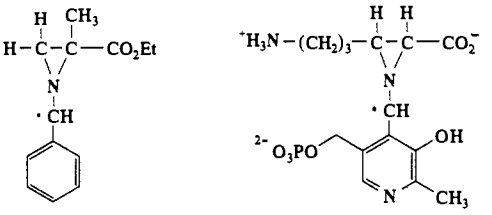


1 **2** **3**

as the precursor for this radical.[10] Reaction of **1** (1.22 mmol) and a catalytic amount (0.05 mmol) of 2,2′-azobis(2-methylpropionitrile) in refluxing benzene with tributyltin hydride (0.9 mmol), added gradually over 2 h, led to **2** (62%) and **3** (4.7%), which were identified by referencing their proton NMR spectra to those of authentic samples.[11] Rapid addition of tributyltin hydride led exclusively to **3**, the product of radical quenching, rather than to **2**, the rearrangement product. Compound **2** was the favored product under rearrangement conditions, presumably owing to the stability of the α radical.

The rearrangement of **1** to **2** under radical-generating reaction conditions may be a chemical model for the PLP-dependent reactions catalyzed by lysine 2,3-aminomutase and β-lysine 5,6-aminomutase. This rearrangement joins other radical rearrangements recently reported by Halpern and Dowd and their co-workers, who have modeled carbon skeletal rearrangements catalyzed by adenosylcobalamin-dependent enzymes.[12-14] To the best of our knowledge, this is the first explicit example of a 1,2 imino rearrangement through a radical mechanism, although the mechanism has been discussed as a reasonable hypothesis.[4-7,15]

The rearrangement here described may be a precedent for PLP-dependent imino rearrangements to the extent that the benzyl radical **4** is valid as a model for the corresponding pyridoxyl radical



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(10) **1** was synthesized by reaction of benzaldehyde with DL-alanine ethyl ester hydrochloride in CH_2Cl_2 in the presence of crushed, activated 4-Å molecular sieves to form *N*-benzylidene-DL-alanine ethyl ester in 85% yield: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 7.3 Hz, 3 H), 1.53 (d, 7.0 Hz, 3 H), 4.14 (q, 7.0 Hz, 1 H), 4.21 (m, 2 H), 7.4-7.7 (m, aromatic, 5 H), 8.32 (s, 1 H). *N*-benzylidene-DL-alanine ethyl ester was converted to **1** by initial reaction with potassium *tert*-butoxide in the presence of 18-crown-6 in dry benzene to generate the α anion, followed by alkylation to **1** by reaction with CH_2Br_2. After removal of solvent, purified **1** was obtained in 80% yield by chromatography through Et_3N-washed silica gel, with ethyl acetate–hexane–Hunig's base (4:1:0.25) as the mobile phase. ^{1}H NMR ($CDCl_3$) δ 1.30 (t, 7.5 Hz, 3 H), 1.63 (s, 3 H), 3.75 and 3.87 (AB q, 9.9 Hz, 2 H), 4.26 (m, 2 H), 7.4-7.7 (m, 5 H), 8.28 (s, 1 H). Mass spectrum, FAB showed two parent ions ([^{79}Br]:[^{81}Br] = 1:1) *m/e* 298 and 300 (1:1) for protonated **1**.

(11) **2** and **3** were synthesized by reaction of the corresponding amino acid ethyl esters with benzaldehyde as described for *N*-benzylidene-DL-alanine ethyl ester. For **2**: ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 7.3 Hz, 3 H), 1.27 (d, 7.0 Hz, 3 H), 2.89 (sextet, 7.0 Hz, 1 H), 3.87 and 3.68 (ABXY, 11.7, 7.0, 1.3 Hz, 2 H), 4.14 (q, 7.3 Hz, 2 H), 7.4-7.9 (m, aromatic, 5 H), 8.28 (s, 1 H). For **3**: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, 7.3 Hz, 3 H), 1.55 (s, 6 H), 4.18 (q, 7.3 Hz, 2 H), 7.4-7.8 (m, aromatic, 5 H), 8.28 (s, 1 H).
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