Electronic Ligand Effects on the Regioselectivity of the Rhodium−Diphosphine-Catalyzed Hydroformylation of Propene

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Received October 24, 2006

Electronic effects induced by diphosphine bidentate ligands on the regioselectivity of the rhodium-catalyzed hydroformylation of propene were investigated using density functional theory based calculations (B3LYP). To this end, the key hydride migration step was evaluated for HRh(propene)(CO)L_2 (L_2 = PF_3, PF_3; PH_3, PH_3; PMe_3, PMe_3; PH_3, PF_3; PH_3, PMe_3) incorporating either two identical or two electronically distinct phosphorus moieties. The phosphorus moieties span a wide range of ligand basicities. While the electronic properties of the ligands do not influence the regioselectivity of the hydride migration reaction directly, they do govern the amount of back-donation from the metal to the alkene substrate. As a result, important differences in transition-state geometries are obtained for different ligand systems. For electron-withdrawing ligands low activation energies and trigonal-bipyramidal transition-state geometries are observed. Increasing the basicity of the diphosphine ligand leads to higher activation energies and distortion of the transition-state structures toward square-pyramidal geometries. In systems containing two electronically distinct phosphorus ligands, this geometric distortion leads to a preference for the formation of the new rhodium−alkyl σ-bond trans to the least donating phosphorus moiety, generating the most stable rhodium−alkyl isomer. In all cases, bis-equatorial coordination of the two phosphorus ligands yields considerably lower transition-state energies than equatorial−axial coordination of the same ligands. The resulting rhodium−alkyl products are stabilized relative to the reactant by electron-donating ligands. On the basis of these observations it is argued that, for electron-withdrawing and/or wide-bite-angle ligands, β-hydride elimination plays an important role in determining the overall regioselectivity of the hydroformylation reaction, while for equatorial−axial coordinating ligands, the regioselectivity is determined exclusively by the relative energies of the hydride migration transition states.

1. Introduction

The hydroformylation reaction is one of the most important reactions catalyzed by homogeneous transition-metal complexes in the industrial production of bulk chemicals. In order to elucidate the mechanism of the rhodium-catalyzed hydroformylation (Figure 1) and ascertain the role of spectator ligands in determining the activity of the catalyst system, the reaction has been studied extensively using computational techniques. Both Morokuma and co-workers and Decker and co-workers studied the hydroformylation of ethene catalyzed by Rh(H)-$(CO)_2(PH_3)_2$, calculating different reaction pathways where the catalyst is ligated by either one or two phosphine moieties.[1−4] For catalysts containing a single phosphine moiety, the highest barriers were obtained for the oxidative addition of hydrogen to the catalyst, while for catalysts containing two phosphorus moieties, the highest barriers were obtained for the CO-insertion step of the catalytic cycle. More recently, Gleich et al. investigated electronic effects induced by phosphine ligands in the complete catalytic cycle of the hydroformylation of ethene, catalyzed by $HRhL_3$ (L = CO, PH_3, PF_3, PMe_3).[5] These calculations suggest that the rate-determining step in the hydroformylation reaction for both the unmodified rhodium−carbonyl catalyst and catalysts modified by electron-withdrawing ligands is either the coordination of ethene to the catalyst or the insertion of ethene into the rhodium−hydride bond. This contradicts experimental studies that clearly show, for these catalyst systems, oxidative addition of hydrogen to the catalyst is rate-determining.

In the hydroformylation of substituted alkenes, regioselectivity has proven to be an important parameter in the development of new catalyst systems. Experimental studies have shown that the regioselectivity of the catalyst is influenced by both the steric[6−8] and electronic[9−12] properties of the ligands surrounding the catalytically active metal center. Casey and co-workers showed that, for catalysts containing bidentate ligands, the regioselec-

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10.1021/om060981+ CCC: $37.00
Publication on Web 03/28/2007

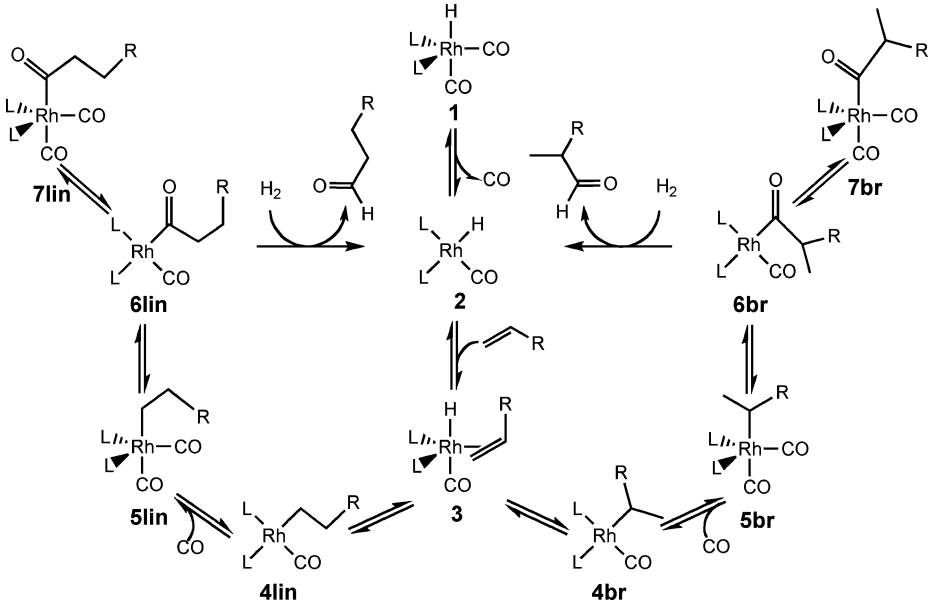

Figure 1. Dissociative mechanism for the hydroformylation of substituted alkenes as proposed by Wilkinson et al.

tivity is often determined by an essentially irreversible hydride migration from the metal center to the coordinated alkene ligand (reaction **3** → **4** in Figure 1).[13] For wide-bite-angle ligands, however, studies have shown that the formation of the branched alkyl intermediate **4br** is reversible under the reaction conditions.[13,14] For strongly electron-withdrawing ligands, even the formation of the linear alkyl intermediate **4lin** can be reversible.[15]

Computational studies have been employed in order to elucidate the origin of the regioselectivity in the hydroformylation reaction. Rocha and co-workers have argued that the hydride migration reaction involving $Rh(C_3H_7)(PH_3)_2(CO)$ is reversible and that the experimentally observed regioselectivity of PPh_3-modified rhodium catalysts must be explained by the relative stabilities of the linear and branched alkyl complexes **4**. Alagona et al. reported a similar study on the hydroformylation of several different alkenes, catalyzed by $Rh(H)(CO)_3$.[16] They suggest that, for this catalyst system, the regioselectivity is controlled exclusively by the relative stabilities of the hydride migration transition states, in line with experimental results obtained for this catalyst system.

Apart from these two studies, computational studies on the origin of the regioselectivity of the hydroformylation reaction have focused mainly on steric effects caused by phosphorus-based spectator ligands coordinated to the rhodium center. Casey et al. investigated the hydride migration reaction as the regioselectivity-determining step of the hydroformylation using molecular mechanics calculations.[13] They were unable to reproduce the experimentally observed difference in the regioselectivities between the BISBI and DIPHOS ligands in the hydroformylation of 1-hexene using these models. Using a similar approach, Paciello et al. were able to reproduce the experimentally observed ligand trends within a set of electronically similar diphosphite ligands.[17] Herrmann and co-workers used density functional theory based calculations to obtain structures for the transition states of hydride migration in $HRh(propene)(PH_3)_2CO$. From these structures suitable molecular force field parameters for rhodium-based hydroformylation catalysts were obtained,[18] which were subsequently used to predict regioselectivities and enantioselectivities of full diphosphine-modified catalyst systems in the hydroformylation of propene[19] and styrene.[18,20]

More recently, ONIOM calculations[21] have been applied to investigate steric effects in the hydroformylation reaction. Cundari and co-workers investigated the hydride migration step in the hydroformylation of ethene[22] and propene[4] for several monodentate ligands. They suggest that the regioselectivity of the reaction is determined not only by the relative energies of the transition states but also by the preferential orientation of the alkene moiety in the alkene intermediate **3**. Some of us have studied the role of the ligand bite angle and steric properties of wide-bite-angle diphosphine ligands in the hydroformylation of propene.[23] The origin of the regioselectivity of the catalyst system was mainly attributed to nonbonding interactions between the diphenylphosphine groups of the ligand and the methyl group of the propene moiety. The entire catalytic cycle of the hydroformylation of propene, catalyzed by the rhodium−Xantphos catalyst system, was studied by Landis and co-workers.[24] While the ONIOM calculations reproduced the high regioselectivity of the Xantphos ligand system in the hydro-

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formylation of propene, they failed to reproduce the overall activity of the rhodium−Xantphos catalyst system.

While experimental studies have clearly demonstrated that the regioselectivity of the hydroformylation reaction is also influenced by the electronic properties of the spectator ligands surrounding the rhodium center, theoretical studies on the origin of this electronic effect are lacking. Here we present a computational study into electronic effects in the hydroformylation of propene, catalyzed by diphosphine-modified rhodium catalysts. This study focuses on the hydride migration reaction step, the key step determining the overall regioselectivity of the hydroformylation reaction. Both ligand systems incorporating two identical donor moieties and ligand systems containing two electronically distinct donor moieties are considered, and the effect of isomerization and coordination mode of the diphosphine ligand on the regioselectivity of the catalyst is discussed.

2. Computational Details

Structures and energies were obtained using the Gaussian 98 (rev. A7) program.[25] All structures were fully optimized using density functional theory based calculations, with Becke's three-parameter exchange functional (B3)[26] and Lee, Yang, and Parr (LYP) correlation energies.[27] For rhodium and phosphorus, basis sets and effective core potentials from the Stuttgart group were employed.[28−30] The effective core potentials replaced 28 electrons for rhodium and 10 electrons for phosphorus. For phosphorus, one d function with an exponent of 0.386 was added to the valance basis set. The hydride, carbon monoxide, and alkene ligands were described using a 6-311G** basis set, while the substituents at the phosphorus atoms were treated using a 6-31G* basis set. Reactants were characterized by the absence of imaginary frequencies, while the transition states exhibited only one imaginary frequency, corresponding to the migration of the hydride moiety from the metal center to the alkene ligand.

3. Results

3.1. Bis(phosphine) Complexes. In order to assess the electronic effects of bidentate ligands containing two identical donating phosphorus moieties on the activity and selectivity of the rhodium catalyst in the hydride migration step of the hydroformylation of propene, three model systems were investigated. In these systems, the bidentate ligand is represented by two PF_3 ligands, two PH_3 ligands, or two PMe_3 ligands. These model ligands were chosen to span a wide range of ligand basicities while minimizing the steric repulsion normally induced by bidentate ligands used in the hydroformylation reaction.

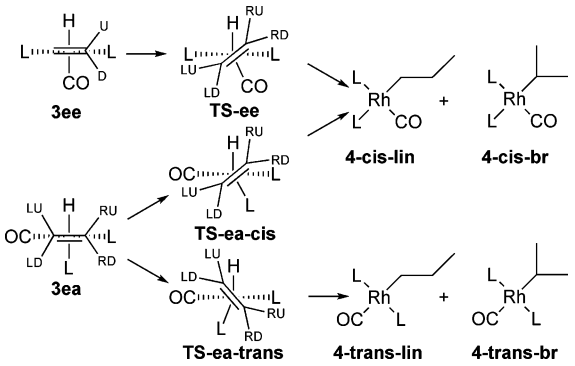

Figure 2. Reaction pathways for complexes incorporating two identical phosphorus ligands. For the two isomers of structure **3ee**, the possible orientations of the propene moiety are designated U (up) and D (down). For the different isomers of reactant **3ea** and transition state **TS**, the possible orientations of the propene moiety are designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). L = PF_3, PH_3, PMe_3.

As the starting point of our investigations, we chose the rhodium alkene complex **3**, which is generated in the catalytic cycle from the rhodium dicarbonyl hydride resting state of the catalyst **1** by loss of one carbon monoxide ligand followed by addition of propene. For the reactant **3**, several different geometries were investigated. In all structures, the propene adopts an equatorial side-on coordination, which yields four different possible orientations of the CH_3 moiety, designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). Since it is known that, depending on the bite angle of the diphosphine ligand, the ligand can adopt either a bis-equatorial (ee) or an equatorial−axial coordination mode (ea) in trigonal-bipyramidal rhodium complexes, both coordination modes were considered. The two different coordination modes of the diphosphine ligand and the different orientations of the CH_3 moiety of the propene substrate yield a total of eight possible isomers of complex **3** (Figure 2). Due to the symmetry of the $HRh(L)_2CO$ fragment in reactants **3ee**, the number of unique isomers for complex **3** considered in this study is reduced to 6.

The hydride migration reaction proceeds through rotation of the alkene moiety out of the equatorial plane of the trigonal-bipyramidal reactant complex **3**, followed by the transfer of the hydride moiety to generate the linear and branched alkyl species **4-cis** and **4-trans**. Since this rotation can occur in both a clockwise and a counterclockwise fashion, two transition-state isomers **TS** are obtained for every reactant.[23] One transition-state isomer leads to one of the two linear products **4-cis-lin** and **4-trans-lin**, while the other transition-state isomer leads to the branched product **4-cis-br** or **4-trans-br**. For the reactant complexes exhibiting bis-equatorial coordination of the diphosphine ligand, all transition-state isomers **TS-ee** lead to square-planar products **4-cis** in which the two phosphine moieties are coordinated in a cis fashion. Numerous attempts to find transition-state structures that lead directly from reactants **3ee** to trans-alkyl species **4-trans** failed. Landis et al. reported that these transition states do exist for the rhodium−Xantphos system,[24] but our unconstrained systems tend to rearrange to the ea transition-state structure **TS-ea-trans** during optimization. For the reactant isomers with equatorial−axial coordination of the diphosphine ligand, we did find four transition-state isomers **TS-ea-trans** that lead to trans products **4-trans** as well as four transition-state isomers **TS-ea-cis** that lead to cis products **4-cis**. In total, 12 reaction pathways were found. The activation and reaction energies of these pathways are shown in Table 1. It

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Table 1. Activation and Reaction Energies for the Hydride Migration Reaction Involving Complexes Containing Two Identical Phosphine Moieties[a]

			$\Delta E^{\ddagger}$			ΔE_r		
reactant	TS	product	PF_3	PH_3	PMe_3	PF_3	PH_3	PMe_3
ee-U	ee-RU	cis-lin	12.3	15.3	17.0	3.0	−4.0	−5.1
ee-U	ee-LU	cis-br	12.8	14.9	17.4	3.1	−3.9	−4.4
ee-D	ee-RD	cis-lin	12.5	14.9	17.4	3.1	−3.9	−4.4
ee-D	ee-LD	cis-br	14.9	16.7	19.0	4.0	−2.0	−1.9
ea-RU	ea-cis-RU	cis-lin	16.7	19.3	20.5	−0.1	−5.0	−5.3
ea-RD	ea-cis-RD	cis-lin	14.1	18.6	19.0	0.1	−5.1	−6.6
ea-LU	ea-cis-LU	cis-br	13.7	19.9	20.0	0.8	−2.7	−2.2
ea-LD	ea-cis-LD	cis-br	16.6	20.0	22.6	1.0	−2.6	−3.8
ea-RU	ea-trans-RU	trans-br	10.5	14.1	17.3	−0.7	−4.0	−5.2
ea-RD	ea-trans-RD	trans-br	13.0	15.8	18.9	−0.5	−4.1	−6.5
ea-LU	ea-trans-LU	trans-lin	10.9	14.4	17.5	−0.6	−7.2	−9.7
ea-LD	ea-trans-LD	trans-lin	10.3	13.8	15.5	−0.4	−7.1	−11.3

[a] Structures are labeled as in Figure 2. Energies are calculated relative to the corresponding isomer of reactant **3**. Energy values are reported in kcal mol^{-1}.

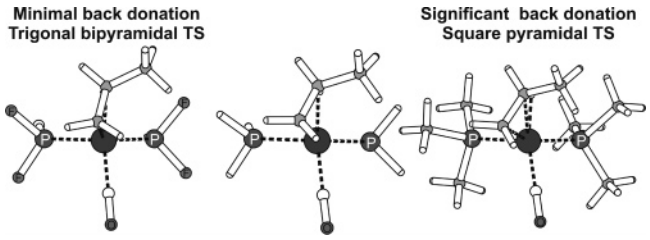

Figure 3. Calculated structures for **TS-ee-RD** for (left) the PF_3-ligated system, (middle) the PH_3-ligated system, and (right) the PMe_3-ligated system. Atom labels for rhodium (dark gray), carbon (light gray), and hydrogen (white) are omitted for clarity.

should be noted that both the activation and reaction energies are reported relative to the corresponding isomer of alkene intermediate **3** and not to the rhodium hydride dicarbonyl resting state of the catalyst **1**. Clearly, the energy of the different isomers of alkene complex **3** relative to the resting state of the catalyst **1** will be influenced by the electronic properties of the ligands employed in the reaction. As such, the values reported here cannot be taken as a measure for the *overall* activity and regioselectivity of the catalyst system in the hydroformylation reaction. They do allow comparison of the activity and selectivity of the different catalyst systems in the hydride migration step of the hydroformylation reaction and the propensity of the resulting alkyl complexes to undergo the reverse reaction (i.e., β-hydride elimination).

As was previously observed by Gleich and Hutter for the hydroformylation of ethene catalyzed by rhodium catalysts incorporating a single monodentate phosphine ligand, the activation energy of this step in the catalytic cycle increases with increasing basicity of the phosphine ligand.[5] Representative transition-state structures for the three ligand systems are shown in Figure 3. Clearly, the increase in activation energy is accompanied by an increased geometric distortion of the transition-state structure. For the PF_3-ligated system, the alkene moiety is rotated almost 90° in the transition state relative to the orientation in the reactant, while the geometry at the metal center does not significantly change from the trigonal-bipyramidal structure of complex **3**. The rotation of the alkene moiety in the PMe_3-ligated transition states is much less than 90° and the geometry around the metal center distorted toward a square-pyramidal type structure.

For the electron-withdrawing PF_3-substituted catalyst system, the lowest activation energies for this step in the hydroformylation of propene are obtained for the pathways originating from the equatorial−axial reactant **3ea** to the trans product **4-trans**. For the other two catalyst systems, the energy differences between the activation energies for **TS-ee** and **TS-ea-trans** are small. The activation energies for transition-state isomers **TS-ea-cis** are consistently higher than those for the other transition-state isomers for all three ligand systems. This means that for the reactant isomers **3ea**, the hydride migration step in the catalytic cycle will preferentially proceed via transition-state isomers **TS-ea-trans**, yielding the thermodynamically more stable trans products **4-trans**. It should be noted that these reaction pathways are only accessible for flexible bidentate ligands that can adopt both the small 90° bite angle of the reactant **3ea** and the large 180° of the product **4-trans**. Rigid small-bite-angle bidentate ligands will actually prevent the formation of the trans product **4-trans**, favoring the smaller bite angle of the cis transition-state structures **TS-ea-cis**. Large rigid bite angle bidentate ligands will prefer bis-equatorial coordination of the bidentate ligand in the trigonal-bipyramidal reactant complexes **3ee** and therefore react preferentially through transition-state isomers **TS-ee-cis**, which exhibit bis-equatorial coordination of the bidentate ligand.

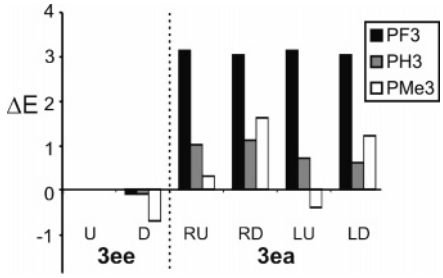

Figure 4. Relative stabilities of the different isomers of reactant **3** containing two identical phosphorus moieties. Values were obtained by subtracting the calculated absolute energy of isomer **3ee-U** from the calculated absolute energies of the other isomers of **3**. The possible orientations of the propene moiety are designated U (up) and D (down) for structures **3ee** and RU (right-up), RD (right-down), LU (left-up), and LD (left-down) for structures **3ea**. Energy values are reported in kcal mol^{-1}.

The reaction energies for this step in the hydroformylation cycle are also shown in Table 1. The hydride migration reaction becomes thermodynamically more favorable with increasing basicity of the diphosphine ligand. Electron-donating ligand systems stabilize the 16-electron species **4** relative to the 18-electron reactants **3**. Since the barrier for hydride migration reaction also increases with increasing basicity of the ligand, the barrier for the reverse reaction (β-hydride elimination) increases considerably with increasing basicity of the ligand. Furthermore, the next step in the hydroformylation catalytic cycle, coordination of carbon monoxide to alkyl complexes **4**, is facilitated by electron-donating ligands coordinated to the metal center. Therefore, the rate of β-hydride elimination, associated with isomerization of the alkene substrate during the hydroformylation process, should be low for electron-donating catalyst systems. Indeed, all effective hydroformylation catalysts for the hydroformylation of internal alkenes to linear aldehydes (which requires isomerization of the alkene prior to hydroformylation) are based on electron-withdrawing phosphine or phosphite ligand systems.

In order to analyze the differences in activation energy between the different reaction pathways in more detail and assess the overall regioselectivities of the three catalyst systems in the hydroformylation reaction, the relative stabilities of the different isomers of reactant **3** (Figure 4) and transition state **TS** (Figure

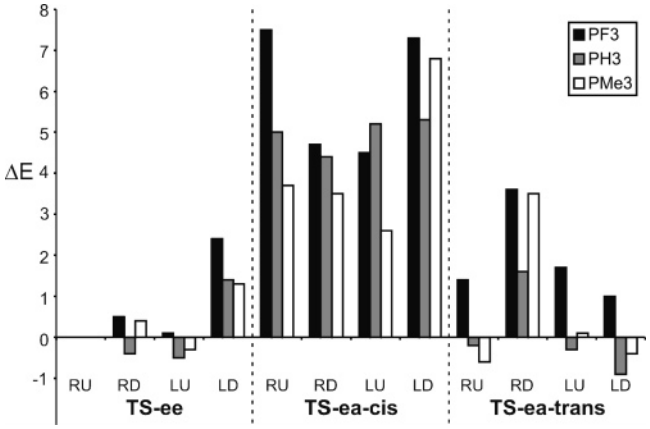

Figure 5. Relative stabilties of the different isomers of transition state **TS** containing two identical phosphorus moieties. Values were obtained by subtracting the calculated absolute energy of transition state isomer **TS-ee-RU** from the calculated absolute energies of the other transition-state isomers. The possible orientations of the propene moiety are designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). Energy values are reported in kcal mol^{-1}.

5) were compared. For the PH_3 and PMe_3 systems the energy differences between the different isomers of reactant **3** are small. For the more bulky PMe_3, reactant isomers **3ea-RD** and **3ea-LD**, in which the CH_3 group points toward the axial PMe_3 ligand, are slightly higher in energy than the other isomers due to steric repulsion between the two moieties. For the electron-withdrawing PF_3 ligand system, structures **3ea** are significantly higher in energy than bis-equatorial isomers **3ee**. Experimental studies have previously shown that, for the trigonal-bipyramidal resting state of catalysts $HRh(L_2)(CO)_2$, bis-equatorial coordination of the diphosphine ligand L_2 can be favored over equatorial−axial coordination by the addition of electron-withdrawing groups to the ligand.[10] Probably, a decrease in the electron-donating ability of the axial phosphine moiety destabilizes the rhodium−hydride bond.

The relative stabilities of the isomers of the transition state are shown in Figure 5. For all three ligand systems, the energy differences between transition-state isomers **TS-ee** and the **TS-ea-trans** are small. The lower activation energies for transition-state isomers **TS-ea-trans** of the electron-withdrawing PF_3-substituted system (Table 1) can completely be ascribed to the destabilization of the alkene reactants **3ea** (Figure 4). The transition-state isomers **TS-ea-cis**, which lead to cis products **4-cis**, are significantly higher in energy for all three ligand systems. Small-bite-angle ligands, for which the other pathways are inaccessible, will therefore be intrinsically less active in this step of the hydroformylation catalytic cycle than their large-bite-angle counterparts. Since the products obtained from transition-state isomers **TS-ee-cis** and **TS-ea-cis** are identical, this also implies that the reverse reaction, β-hydride elimination, is less facile for small-bite-angle ligands. Both the lower activity and decreased reversibility of the hydride migration reaction for catalysts incorporating small-bite-angle ligands, relative to complexes containing electronically similar large-bite-angle ligands, have indeed been observed experimentally.[13]

Within each type of transition-state structure, there is little electronic preference for the orientation of the methyl moiety of the alkene ligand, but for all three ligand systems we do observe an interesting steric effect. For each of the three types of transition-state structures, one transition-state isomer is consistently higher in energy than the other three. These three structures, **TS-ee-LD**, **TS-ea-cis-LD**, and **TS-ea-trans-RD**, all correspond to geometries where the CH_3 moiety of the alkene ligand is pointing toward the axial phosphine or carbon monoxide ligand. The steric repulsion is more pronounced in the transition state than in the corresponding reactant complex since the distance between the CH_3 group of the propene substrate and axial ligand decreases during the reaction. This can be attributed to the rotation of the alkene moiety, which occurs in such a way that the alkyl group is pointing directly toward the axial ligand. Furthermore, the axial ligand moves toward the equatorial plane during the reaction, increasing the steric repulsion between the propene moiety and the axial ligand. Importantly, all of these transition states lead to the branched-alkyl products **4-cis-br** and **4-trans-br**, making all three phosphine-modified catalyst systems studied here biased toward the formation of linear alkyl products **4-cis-lin** and **4-cis-lin**.

3.2. Ligands Containing Two Electronically Distinct Phosphine Moieties. In an attempt to reproduce experimentally observed ligand effects induced by bidentate ligands incorporating two electronically different phosphine moieties[11,12] and mixtures of monodentate ligands[31] on the regioselectivity of the hydroformylation reaction, the hydride migration reaction was investigated for catalyst systems that contain one PH_3 and either one PF_3 or one PMe_3 ligand. In addition to the different geometries of the reactant, transition state, and product of the reaction involving complexes incorporating two identical phosphine moieties studied in the previous section, the two distinct orientations of these nonsymmetrical ligand combinations were considered. This doubles the number of structures and reaction pathways. The possible pathways are shown in Figure 6, and the corresponding computed energy values are given in Table 2.

For the electron-withdrawing PH_3-PF_3 ligand system, the activation energies obtained for the hydride migration starting from alkene complexes containing two equatorially coordinated phosphine ligands are between values previously obtained for the PH_3-PH_3 and PF_3-PF_3 ligand systems studied in the previous section. Furthermore, differences in activation energies between the eight different pathways are small. There is little or no preference for the formation of the new rhodium−carbon bond either cis or trans relative to the PF_3 ligand. As was observed for the PF_3-PF_3 ligand combination, the transition states for this electron-withdrawing ligand combination do not deviate significantly from the trigonal-bipyramidal structure of the reactant. The propene moiety is rotated almost 90° relative to the reactant. Therefore, the geometrical differences between all eight transition states exhibiting a bis-equatorial coordination mode of the two phosphine moieties are extremely small. This results in minor differences in the activation energies of the different pathways. Consequently, no kinetic preference is observed for the formation of either **4-cis-lin-t** and **4-cis-br-t** or **4-cis-lin-c** and **4-cis-br-c** alkyl isomers via bis-equatorial pathways for this ligand combination.

As we showed in the previous section, electron-donating ligands yield more distorted pseudo square pyramidal type transition states for the hydride migration reaction. Because of this, differences between the different pathways involving bis-equatorial coordination of two phosphine moieties are more pronounced for the PH_3-PMe_3 ligand combination than for the PH_3-PF_3 ligand combination. For pathways where the new rhodium−carbon σ-bond is formed trans relative to the PH_3 ligand via transition state isomers **TS-ea-c**, the calculated activation energies resemble those of the PH_3-PH_3 ligand

(31) Reetz, M. T.; Li, X. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 2962.

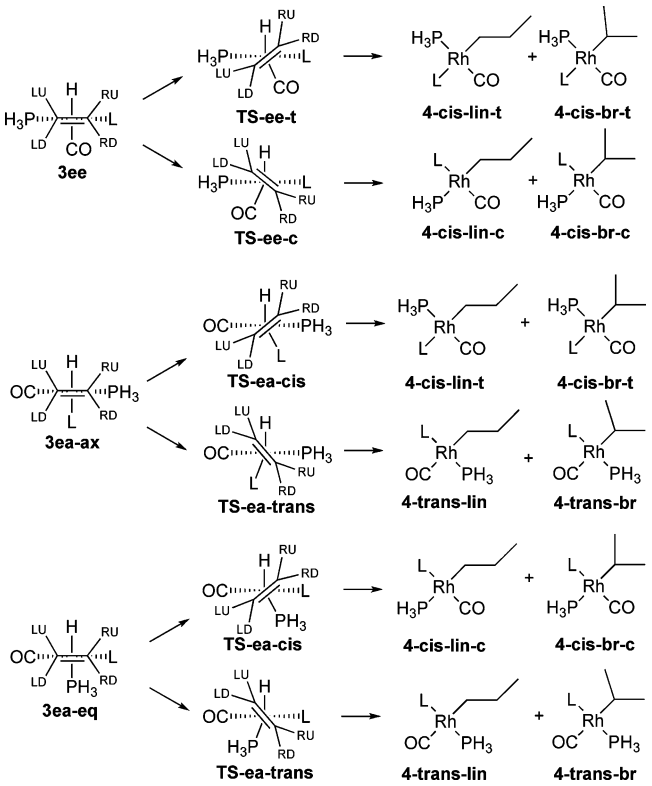

Figure 6. Reaction pathways for complexes containing two electronically distinct phosphine ligands. For the different isomers of reactant **3** and transition state **TS**, the possible orientations of the propene moiety are designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). For the reactant isomers **3ea** and transition-state isomers **TS-ea**, **eq** and **ax** denote the position of L in the complex (equatorial or axial). L = PF_3, PMe_3. For product **4**, **c** and **t** denote the position of L relative to the alkyl moiety (cis or trans).

system studied in the previous section (Table 1). On the other hand, pathways leading to formation of the new rhodium−carbon bond trans to the PMe_3 ligand give rise to higher activation energies, comparable to those obtained for the PMe_3−PMe_3 ligand combination. This results in an effective kinetic preference for the formation of alkyl complexes **4-cis-lin-c** and **4-cis-br-c** over alkyl intermediates **4-cis-lin-t** and **4-cis-br-t** for this ligand system via bis-equatorial pathways.

In contrast to reactions originating from alkene complexes **3ee**, not all isomers of the alkyl complex **4-cis** can be formed directly from each isomer of the alkene complex **3ea**. While complexes **4-trans-lin** and **4-trans-br** are both accessible from each isomer of the reactant **3ea** via transition states **TS-ea-trans**, not all isomers of alkyl complex **4** can be formed directly from each reactant via the transition-state structures **TS-ea-cis**. For isomers of complex **3ea** incorporating an axial PX_3 moiety, all pathways lead to alkyl complexes **4-cis-lin-c** and **4-cis-br-c**, in which the PX_3 ligand is coordinated cis relative to the alkyl moiety. For alkene complexes **3ea** containing equatorial PX_3 ligands, only the alkyl complexes **4-cis-lin-t** and **4-cis-br-t**, in which the PX_3 moiety is coordinated trans relative to the alkyl moiety, are directly accessible. Therefore, the geometry of the reactant **3ea** directly influences the product distribution of the hydride migration reaction.

Due to the destabilizing effect of an axial PF_3 moiety in alkene complexes **3ea-ax** (vide supra), the formation of the thermodynamically unfavorable alkyl complexes **4-cis-lin-c** and **4-cis-br-c** appears kinetically favored over the formation of thermodynamically more stable alkyl complexes **4-cis-lin-t** and **4-cis-br-t** for the electron-withdrawing PH_3−PF_3 ligand combination. For pathways leading to trans diphosphine complexes **4-trans**, we also observe this destabilizing effect of an axial PF_3 ligand in reactant complexes **3ea-ax**. Since there is only a single coordination mode of the mixed ligand combination in the alkyl complex **4-trans**, this does not affect the product distribution.

Table 2. Activation and Reaction Energies for Reaction Pathways Involving Complexes Incorporating One PH_3 Ligand and One PX_3 (X = F, Me) Ligand[a]

structure			$\Delta E^{\ddagger}$		ΔE_r	
reactant	TS	product	PF_3	PMe_3	PF_3	PMe_3
ee-RU	ee-t-RU	cis-lin-t	13.8	14.3	−2.1	−5.0
ee-RD	ee-t-RD	cis-lin-t	13.7	17.6	−2.0	−4.4
ee-LU	ee-t-LU	cis-br-t	13.9	17.0	−0.3	−2.2
ee-LD	ee-t-LD	cis-br-t	15.3	19.8	−0.4	−1.1
ee-RU	ee-c-RU	cis-br-c	13.5	14.4	1.0	−2.2
ee-RD	ee-c-RD	cis-br-c	15.8	16.1	0.9	−1.3
ee-LU	ee-c-LU	cis-lin-c	13.8	14.1	0.3	−5.0
ee-LD	ee-c-LD	cis-lin-c	13.6	15.0	0.2	−3.9
ea-RUax	ea-cis-RUax	cis-lin-c	16.6		−2.4	−4.4
ea-RDax	ea-cis-RDax	cis-lin-c	15.3		−2.8	−5.9
ea-LUax	ea-cis-LUax	cis-br-c	15.1	20.1	−1.4	−1.3
ea-LDax	ea-cis-LDax	cis-br-c	17.8	23.1	−1.6	−2.6
ea-RUeq	ea-cis-RUeq	cis-lin-t	17.8	18.4	−2.9	−5.6
ea-RDeq	ea-cis-RDeq	cis-lin-t	17.2	17.5	−3.6	−6.0
ea-LUeq	ea-cis-LUeq	cis-br-t	16.7	17.9	−0.9	−2.0
ea-LDeq	ea-cis-LDeq	cis-br-t	20.1	18.8	−1.6	−2.7
ea-RUax	ea-trans-RUax	trans-br	12.3	15.0	−1.3	−4.7
ea-RDax	ea-trans-RDax	trans-br	13.8	15.8	−1.8	−6.2
ea-LUax	ea-trans-LUax	trans-lin	12.4	15.1	−4.4	−7.8
ea-LDax	ea-trans-LDax	trans-lin	11.4	16.5	−4.6	−9.0
ea-RUeq	ea-trans-RUeq	trans-br	13.2	17.1	0.6	−5.7
ea-RDeq	ea-trans-RDeq	trans-br	14.4	17.7	−0.1	−6.1
ea-LUeq	ea-trans-LUeq	trans-lin	13.4	16.7	−2.7	−8.5
ea-LDeq	ea-trans-LDeq	trans-lin	12.3	16.7	−3.4	−9.2

[a] Structures are labeled as in Figure 6. Energies are calculated relative to the corresponding isomer of reactant **3**. Energy values are reported in kcal mol^{-1}.

For the more electron-donating PH_3−PMe_3 ligand combination, we were unable to locate the transition-state isomers **TS-ea-cis-RUax** and **TS-ea-cis-RDax**. For these two transition-state structures, optimization led to the transition-state isomers **TS-ea-trans-LDax** and **TS-ea-trans-LUax** through rotation of the alkene moiety. The equatorial PH_3 and carbon monoxide ligands yield low barriers of rotation for the alkene moiety. Furthermore, movement of the axial PMe_3 moiety toward the alkene moiety during the reaction leads to highly congested transition-state structures **TS-ea-cis**. Therefore, it is not surprising that transition-state isomers **TS-ea-cis-RUax** and **TS-ea-cis-RDax** do not exist for this ligand combination. For transition-state structures **TS-ea-cis-LUax** and **TS-ea-cis-LDax**, further rotation of the alkene moiety is actually hindered by the axial PMe_3 ligands. Despite the electronic preference for formation of the new rhodium−carbon σ-bond trans to a PH_3 moiety over a PMe_3 moiety, the activation energies observed for these transition-state isomers are higher than for the corresponding transition states containing an equatorially coordinated PMe_3 ligand. The electronic preference for the formation of alkyl complexes **4-cis-lin-c** and **4-cis-br-c** is completely negated in favor of the formation of the sterically less congested complexes **4-cis-lin-t** and **4-cis-br-t**. In contrast, for pathways leading to the trans diphosphine products **4-trans**, the transition-state isomers **TS-ea-trans** are much less sterically congested. As expected on the basis of the different electronic properties of the PH_3 and PMe_3 moieties, the lowest activation energies are observed for alkene complexes incorporating an equatorial PH_3 ligand.

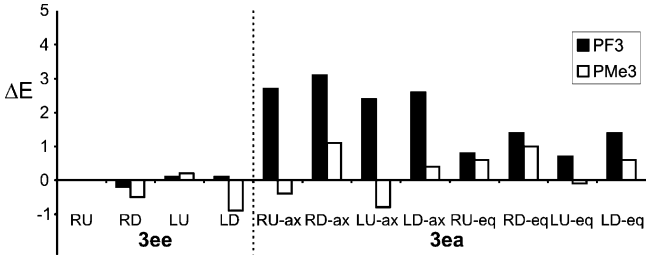

Figure 7. Relative stabilities of the different isomers of reactant **3** containing two electronically distinct phosphorus moieties. Values were obtained by subtracting the calculated absolute energy of complex **3ee-RU** from the calculated absolute energies of the other reactant complexes. The possible orientations of the propene moiety are designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). For reactants **3ea**, eq and ax denote the position of ligand L in the complex (equatorial or axial). Energy values are reported in kcal mol^{-1}.

Figures 7 and 8 show the relative stabilities of the different isomers of the reactant **3** and transition state **TS** containing two electronically distinct phosphine moieties. From a comparison of the relative stabilities of the different isomers of reactant **3** for the electron-withdrawing PF_3-PH_3 combination, it is clear that axial coordination of the electron-withdrawing PF_3 moiety is unfavorable. Interestingly, this electronic destabilization is absent in the transition states involving this ligand system (Figure 8). Placement of the electron-withdrawing PF_3 ligand in either the equatorial or axial position does not affect the energy of the transition state. Similar to the case for the ligand combinations studied in the previous section, the calculated energies of transition-state structures **TS-ee** and **TS-ea-trans** are virtually the same, except for structures in which the methyl group of the propene substrate points toward the axial phosphine or carbon monoxide ligand. These structures are higher in energy, as are transition state isomers **TS-ea-cis**.

In contrast to the observations for the PH_3-PF_3 ligand combination, there is no preferential orientation of the model diphosphine ligand in reactant structures **3ea** for the PH_3-PMe_3 ligand system. On the basis of the χ parameter introduced by Tolman,[32] PMe_3 is electronically more similar to PH_3 than PF_3 is to PH_3. Therefore, the electronic preference for coordination of the best σ-donating moiety of the "diphosphine" ligand in the axial position of reactant **3ea** will be smaller for the PH_3-PMe_3 ligand system than for the PH_3-PF_3 ligand combination. Steric repulsion caused by the relatively more bulky PMe_3 is minimal in the reactant **3ea**. The orientation of the methyl group of propene in structures incorporating either an axial or equatorial PMe_3 ligand does not affect the relative stabilities of the different reactant isomers **3ea** (Figure 7).

For the transition-state isomers **TS-ee**, we do observe the expected electronic destabilization of transition-state structures leading to the formation of alkyl complexes **4-cis-lin-t** and **4-cis-br-t**. Interestingly, for the transition-state isomers connecting reactants **3ea** to trans products **4-trans**, an electronic effect is also observed. Structures containing an equatorially coordinated PMe_3 ligand are consistently higher in energy than structures containing an axial PMe_3 ligand. For the transition states connecting **3ea** to cis products **4-cis**, steric effects play an important role. While it is clear that coordination of the PMe_3 ligand in the axial position of the transition-state structure is electronically favored, this is cancelled by the large steric hindrance caused by placing the PMe_3 ligand in this position.

(32) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2953.

4. Discussion

Previous computational studies have demonstrated that nonbonding effects induced by spectator ligands play an important role in determining the regioselectivity in the hydride migration reaction of the hydroformylation of 1-alkenes. Also in this study we have identified several steric effects, despite our choice for relatively nonbulky ligand models. More importantly, our calculations clearly show that electronic properties of the spectator ligands affect the behavior of the hydroformylation catalyst in various ways.

From our studies on ligand systems incorporating two identical donating moieties, it is clear that, in the absence of steric interactions, electronic ligand effects do not influence the regioselectivity of the hydroformylation reaction directly. On the basis of the relative stabilities of the different isomers of the transition state (Figure 5), one would expect similar regioselectivities for all three ligand systems. The electronic properties and the coordination mode of the two phosphine moieties do affect the overall rate of the hydride migration reaction and, more importantly, the geometries of the transition-state structures. While electron-withdrawing ligand systems yield low activation barriers and trigonal-bipyramidal type transition-state structures, electron-donating ligands yield high barriers and distorted pseudo square pyramidal transition-state geometries. Clearly, in real ligand systems, this change in geometry of the transition state would result in a change in the nonbonding interactions between the substrate and the spectator ligand(s) and ultimately the regioselectivity of the catalyst system.

The changes in transition-state geometry as a function of the electronic properties of spectator ligands observed in our calculations can be explained by the Chatt−Dewar−Duncanson model of metal−alkene binding.[33−35] The donating contribution to the metal−alkene bond is indifferent to rotation around the metal−alkene bond. The orbitals involved in back-donation, however, are highly sensitive to the orientation of the alkene moiety. As a result, the rotational barrier of the alkene is largely determined by the amount of back-donation from the metal center to the alkene moiety. For our electron-withdrawing PF_3-ligated catalyst system, the contribution of back-donation to the metal−alkene bond is small, leading to facile rotation of the alkene moiety and therefore a low activation barrier for the hydride migration reaction. In contrast, the back-donation is pronounced for the electron-donating PMe_3-substituted catalyst system, which prevents the rotation of the alkene moiety. In order to form the new carbon−hydrogen bond, the hydride ligand moves out of the axial position of the trigonal-bipyramidal structure, resulting in more distorted geometries of the transition states for this ligand system. Indeed, the equatorial−axial transition-state geometries **TS-ea** are slightly less distorted than the bis-equatorial structures **TS-ee**. It is interesting to note that the carbon monoxide ligand in the equatorial plane of reactant isomers **3ea**, while facilitating rotation of the alkene moiety, does not yield activation energies significantly lower than those for reactants **3ee**.

The lower activation barriers in the hydride migration reaction for less basic ligand systems are accompanied by a lower stability of 16-electron alkyl products **4** relative to 18-electron species **3**. As a result, the reverse reaction, β-hydride elimination, becomes increasingly facile for electron-withdrawing ligands. Furthermore, coordination of carbon monoxide to alkyl

(33) Dewar, M. J. S. *Bull. Soc. Chim. Fr.* **1951**, C71.
(34) Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939.
(35) Frenking, G.; Frolich, N. *Chem. Rev.* **2000**, *100*, 717.

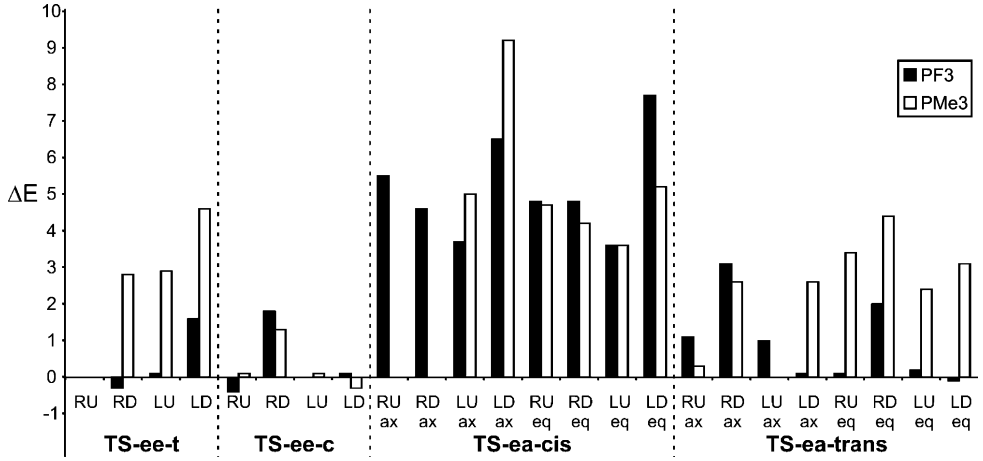

Figure 8. Relative stabilities of the different isomers of transition state **TS** containing two electronically distinct phosphorus moieties. Values were obtained by subtracting the calculated absolute energy of isomer **TS-ee-t-RU** from the calculated absolute energies of the other transition-state isomers. The possible orientations of the propene moiety are designated RU (right-up), RD (right-down), LU (left-up), and LD (left-down). For transition-state isomers **TS-ea**, eq and ax denote the position of ligand L in the complex (equatorial or axial). Energy values are reported in kcal mol^{-1}.

complex **4** is expected to be unfavorable for complexes containing electron-withdrawing ligands, due to the low electron density at the metal center induced by these ligands. Therefore, electron-withdrawing ligands strongly favor alkene isomerization over carbon monoxide coordination and subsequent steps in the hydroformylation cycle. These observations are in line with experimental studies which show that decreasing the ligand basicity of the diphosphine ligand leads to an increased rate of alkene isomerization.

Because of the relatively high energies of the branched alkyl intermediates **4-cis-br** and **4-trans-br** relative to those of the linear isomers **4-cis-lin** and **4-trans-lin**, the barrier for β-hydride elimination is lower for these branched intermediates than for their linear counterparts. Bidentate ligands that preferably adopt natural bite angles close to 120° further enhance the destabilization of alkyl intermediates **4** relative to alkene complex **3ee**, because of the constraints imposed by the backbone of the ligand. Furthermore, the steric bulk in these ligands enhances the preference of the system for the formation of the less sterically demanding linear alkyl complexes **4-cis-lin** and **4-trans-lin**. Casey and co-workers have shown using deuterioformylation experiments that, in the (highly regioselective) hydroformylation of hexene using the rhodium−BISBI catalyst system, the formation of linear alkyl complexes is essentially irreversible, but the formation of branched alkyl intermediates can be reversible under the reaction conditions.[13] Furthermore, van Leeuwen and co-workers have shown that the regioselectivity of a catalyst system modified by a Xantphos-type wide-bite-angle diphosphine ligand is dependent on the carbon monoxide pressure. Coordination of carbon monoxide stabilizes the high-energy complexes **4**, trapping the branched alkyl intermediates. Higher carbon monoxide pressures therefore favor formation of branched aldehyde products over isomerization via β-hydride elimination (Figure 9). van der Slot et al. demonstrated that, for strongly electron-withdrawing ligands, even the formation of linear alkyl intermediates can become reversible.[15] These studies show that, for wide-bite-angle diphosphine ligands, regioselectivity is not determined solely by the relative energies of the transition states in the hydride migration reaction. For these ligands, the relative stabilities of linear and branched alkyl complexes **4**, as well as the barriers of reaction steps later in the catalytic cycle, play an important role in determining the overall regioselectivity of the catalyst system in the hydroformylation reaction.

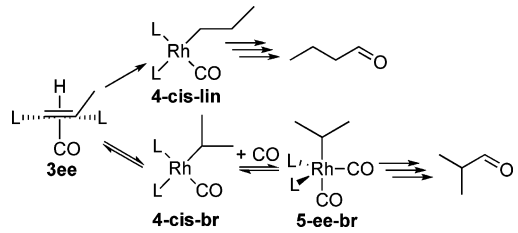

Figure 9. Proposed mechanism for the highly regioselective hydroformylation of linear alkenes to linear aldehydes involving wide-bite-angle diphosphine ligands.

In contrast, for small-bite-angle ligands isomerization of terminal alkenes to internal alkenes is usually negligible under hydroformylation conditions. This is reproduced by our calculations. For the formation of alkyl complexes **4-cis**, pathways originating from alkene complexes **3ea** show considerably higher transition-state energies than pathways originating from **3ee** for all three ligand systems (Figure 5). This indicates that ligands exhibiting a preferential equatorial−axial coordination mode in trigonal-bipyramidal rhodium complexes are intrinsically less active and yield less isomerization than wide-bite-angle ligands. While for wide-bite-angle ligands isomerization seems to play an important role in determining the overall regioselectivity of the catalyst system, it is less important for electronically similar small-bite-angle ligands. For these ligands, both the linear and branched alkyl complexes formed in the hydride migration reaction step are probably committed to the formation of the final linear and branched aldehyde products.

Hydride migration reactions involving ligand systems having two electronically distinct donating moieties are considerably more complex. Our model predicts several interesting electronic ligand effects. From the relative transition-state energies of pathways involving two equatorially coordinated phosphine moieties (Figure 8), it is clear that the new rhodium−carbon σ-bond preferably forms trans to the least basic phosphorus moiety, yielding the thermodynamically most stable isomer of the alkyl complex **4-cis** in which the carbon monoxide ligand is coordinated trans to the most donating phosphine moiety. This preference increases as the geometry of the transition state changes from a reactant-like trigonal-bipyramidal structure for

electron-withdrawing catalyst systems to a more product-like square-pyramidal structure for electron-donating catalyst systems.

For ligand systems which preferentially adopt an equatorial−axial coordination mode in trigonal-bipyramidal structures, the preferred orientation of propene and the two distinct phosphine moieties in reactant **3ea** also affects the overall product distribution, since not all isomers of the product **4-cis** can be formed from all isomers of reactant **3ea**. In the absence of steric bulk, the orientation of the methyl moiety of the propene substrate does not affect the stability of complex **3ea** (Figure 7). As was observed experimentally for the resting state of the catalyst, there is a preference for coordination of strongly electron-withdrawing ligands in the equatorial plane of complex **3ea**. One clear exception to this rule is the BINAPHOS ligand system, developed by Nozaki and co-workers.[36,37] For this ligand, the electron-donating phosphine moiety occupies an equatorial site, while the π-accepting phosphite occupies the axial position in the resting state of the catalyst. This unusual coordination mode adopted by this rigid ligand might be attributed to steric effects, as more flexible phosphine−phosphite ligands do not exhibit this unusual coordination mode.[38]

For the electron-donating PH_3−PMe_3 ligand combination the energy difference between the two possible orientations of the diphosphine ligand in reactant isomers **3ea** is small. We do observe a preferential coordination mode of the model diphosphine ligand in transition-state structures **TS-ea**. Because of the increased importance of back-donation from the metal to the alkene ligand for this electron-donating ligand system, hydride migration proceeds preferentially through transition-state structures **TS-ea-trans** involving equatorial coordination of the PH_3 moiety and axial coordination of the more electron-donating PMe_3 ligand.

Unfortunately, it is unclear whether high kinetic barriers exist for the formation of one or more isomers of alkene complex **3ea**. When overly high barriers exist, the resulting alkene complexes will not be formed and, as a result, the transition-state isomers originating from these alkene complexes will not be accessible either. Clearly, in this case the regioselectivity is not determined exclusively by the relative energies of the different isomers of the transition state for hydride migration but also by the barriers for the formation of the different alkene isomers **3ea**.

5. Conclusions

We have investigated electronic effects in the hydride migration step of the hydroformylation of propene, catalyzed by rhodium catalysts containing model bidentate ligands. Changing the electronic properties of the ligand in the absence of steric effects does not alter the relative barriers for the formation of linear and branched alkyl species directly. Instead, we have shown that the electronic properties of the spectator ligands control the geometry of the transition state. They determine the amount of back-donation from the metal center to the coordinated alkene moiety, thereby determining the rotational barrier of the alkene moiety during the reaction. As a result, the transition-state geometries vary from trigonal bipyramidal for electron-withdrawing ligands to distorted-square-pyramidal structures for electron-donating ligands (Figure 3). When steric interactions in catalyst systems are taken into account, these significant differences in the geometry of the transition state will result in differences in the observed regioselectivity of the hydroformylation reaction catalyzed by metal complexes containing isosteric but electronically distinct ligand systems.

For bidentate ligands exhibiting bis-equatorial coordination, significantly lower transition-state energies were obtained in comparison to those for ligands exhibiting equatorial−axial coordination, in line with experimental observations. The low barriers obtained for these wide-bite-angle ligands increases the propensity of the catalyst system toward isomerization via β-hydride elimination. Since the branched alkyl complex **4-cis-br** is thermodynamically less stable than the linear alkyl product **4-cis-lin**, the rate of β-hydride elimination is considerably higher for the branched alkyl intermediate **4-cis-br**. This greatly enhances the regioselectivity in the hydroformylation reaction catalyzed by rhodium complexes containing wide-bite-angle ligands. Due to the higher activation barriers for complexes containing ligands with equatorial−axial coordination, β-hydride elimination is significantly slower for small-bite-angle ligands than for their wide-bite-angle counterparts. Consequently, for these ligands the overall regioselectivity of the hydroformylation reaction is mainly determined by the relative energies of the different transition states of the hydride migration step.

For ligands containing two electronically different phosphorus moieties, we observe a distinct electronic preference for the formation of the new rhodium−alkyl σ-bond trans to the least basic phosphorus moiety. This generates the thermodynamically most stable rhodium−alkyl isomer, in which the carbon monoxide ligand is coordinated trans to the most donating phosphine moiety (trans effect). This preference increases with increasing basicity of the bidentate ligand, due to the more product-like square-pyramidal transition-state geometry observed for these ligands. Since not all alkyl isomers are accessible from all alkene isomers containing equatorial−axial ligands, the coordination modes of the alkene and diphosphine ligands in alkene complex **3** also affect the observed regioselectivity of catalyst systems modified by bidentate ligands containing two electronically dissimilar donating moieties.

Acknowledgment. This work was supported by The Netherlands Organization for Scientific Research (NWO/CW), the Ministry of Science and Education of Spain (Project CTQ2005-0609-c02-02/BQU), the ICIQ foundation, and Consolider Ingenio 2010 (Grant CSD2006-0003). The SARA center for high-performance computing is acknowledged for use of their computational facilities.

Supporting Information Available: Tables giving calculated structures and energies of all the reactants, transition states, and products and the imaginary frequencies of the transition states. This material is available free of charge via the Internet at http://pubs.acs.org.

OM060981+

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