Acc. Chem. Res. **2001,** *34,* 895−904

Wide Bite Angle Diphosphines: Xantphos Ligands in Transition Metal Complexes and Catalysis

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Received December 21, 2000

ABSTRACT

The reactivity of organotransition metal complexes is dependent on the ligand environment of the metal. This Account describes the development and application of new diphosphine ligands, designed to induce large P−M−P angles in transition metal complexes. Aided by computational chemistry, a homologous range of diphosphines based on rigid heterocyclic aromatic backbones of the xanthene-type with natural bite angles of ∼100−134° have been developed. The special structure of the ligands has an enormous impact on stability and reactivity of various transition metal complexes. Highly active and selective catalysts have been obtained by influencing this reactivity.

Introduction

The effects of ligands on structure and reactivity of transition metal complexes are important topics of research in coordination and organometallic chemistry as well as in homogeneous catalysis. The large impact of phosphine ligands became evident by the important discovery of the Wilkinson hydrogenation catalyst, $RhCl(PPh_3)_3$.[1] Substitution at the aromatic ring of the ligand revealed an electronic effect on the reaction rate, illustrating the distinct ligand effect on the reactivity of a transition metal complex. Since then, an impressive number of phosphine ligands has been applied in many catalytic reactions, and it became obvious that the steric and electronic properties of the ligands have an enormous effect on the reactivity of metal complexes.

Strohmeier showed that the IR carbonyl frequencies of metal complexes were a measure of the electronic properties of ligands.[2] Tolman introduced a systematic approach to describe steric and electronic ligand effects.[3] For phosphorus ligands the cone angle θ (Figure 1) is defined as the apex angle of a cylindrical cone, centered 2.28 Å from the center of the P atom, which touches the outermost atoms of the model. The electronic parameter χ is based on the difference in the IR frequencies of $Ni(CO)_3L$ and the reference compound $Ni(CO)_3$(P-*tert*-Bu_3).

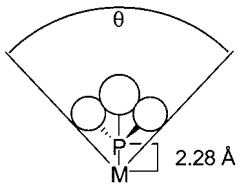

FIGURE 1. Tolman cone angle θ.

A means to predict chelational preferences of bidentate ligands was recently developed by Casey and Whiteker.[4] They introduced the concepts of the *natural bite angle* and the *flexibility range* for diphosphine ligands, which can be calculated by molecular mechanics. The natural bite angle (β_n) is defined as the preferred chelation angle determined by ligand backbone only and not by metal valence angles. The flexibility range is defined as the accessible range of bite angles within less than 3 kcal mol^{-1} excess strain energy from the calculated natural bite angle.

Diphosphines have a marked influence on the reactivity and selectivity of a catalyst. The effect of geometrical constraints on the reactivity of metal complexes was already underlined by the theoretical work of Thorn and Hoffmann.[5] They calculated that during migration a phosphine ligand would have a tendency to widen the P−M−P angle in the process to "pursue" the migrating group. It was anticipated that ligands enforcing an enlarged P−M−P angle, i.e., resembling the transition state, would accelerate migration reactions. Experimental support was provided by Dekker et al., who found increasing migration rates with larger bite angles of palladium diphosphine complexes.[6] Rigid backbones that can actually *enforce* a constrained geometry and, thereby, a certain coordination mode can influence a reaction step of a catalytic cycle in several ways: i.e., stabilization or destabilization of the initial, transition, or final state.

One of the first successful examples of a rationally designed bidentate ligand, intended to enforce a certain conformation, is Venanzi's transphos (**1**).[7a] This ligand contains a rigid polyaromatic backbone, forcing the formation of trans chelates. The flexibility of the ligand, however, was larger than expected; bite angles as low as 104° were also observed.[7b]

Ligand Design

We started a search for organic backbones for diphosphine ligands that would enforce coordination modes between cis and trans coordination,[8] applying the modeling meth-

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10.1021/ar000060+ CCC: $20.00
Published on Web 09/28/2001

Chart 1

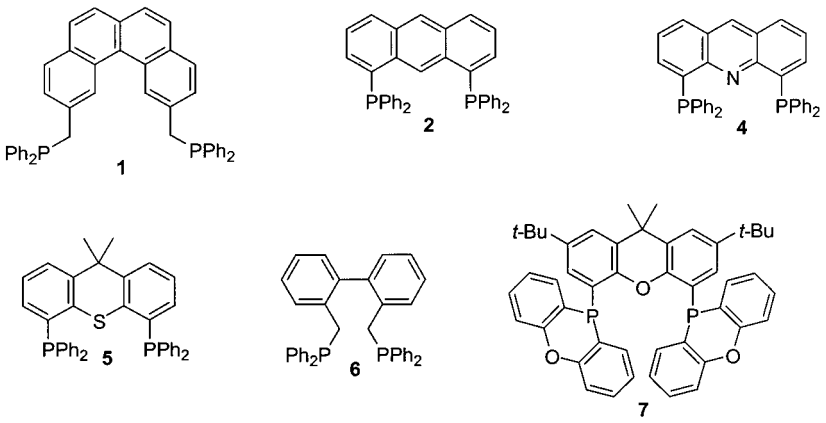
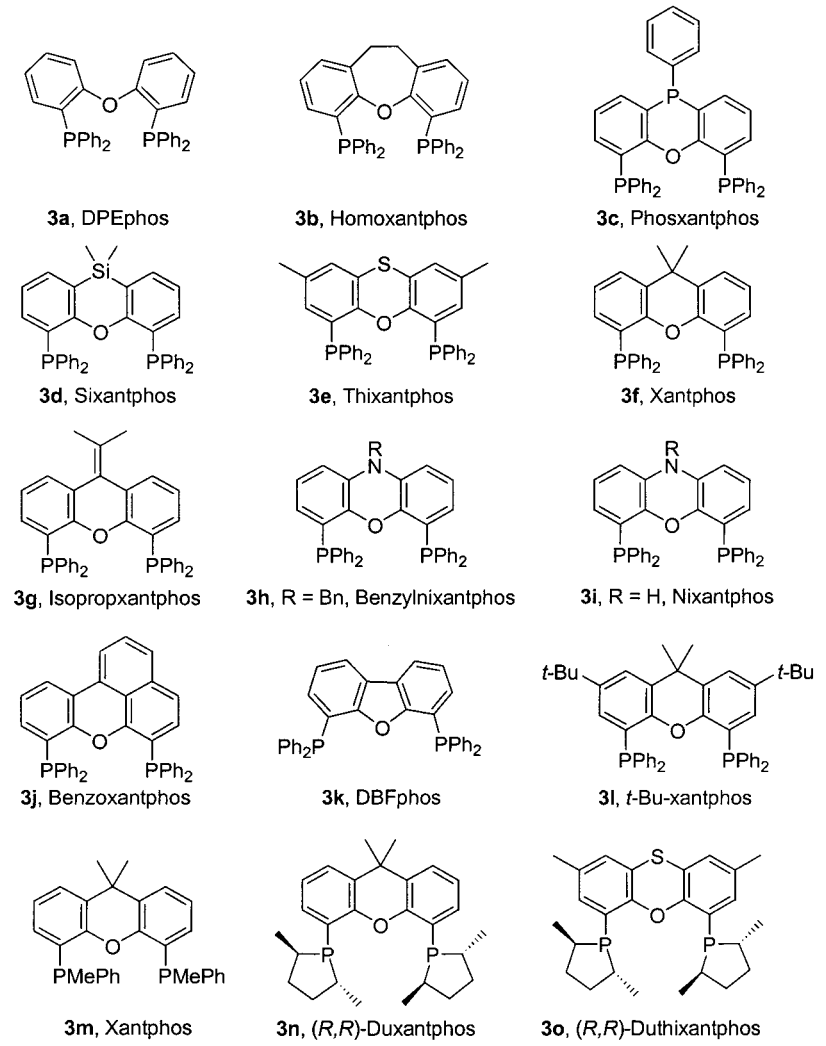


Chart 2



odology developed by Casey and Whiteker.[4] Most ligands studied by molecular modeling were too flexible and could easily adopt a small bite angle. The fact that even Transphos (**1**, Chart 1) can form complexes close to cis coordination illustrates this clearly. An additional problem was anticipated upon using hydrocarbon bridges. When a C−H bond is brought in close proximity to the metal, metalation may occur as observed for 1,8-bis(diphenylphosphine)anthracene (**2**).[9] Candidates with promising structural characteristics were found in a series of new bidentate ligands based on rigid heterocyclic xanthene-like aromatics.[8] These rigid heteroaromatics can be converted easily to diphosphine ligands (**3**, Chart 2), and the central oxygen atom prevents metalation.[8] The first example of this series, DPEphos (**3a**), was reported by Taube et al. in 1984,[10] but this promising ligand was not used in

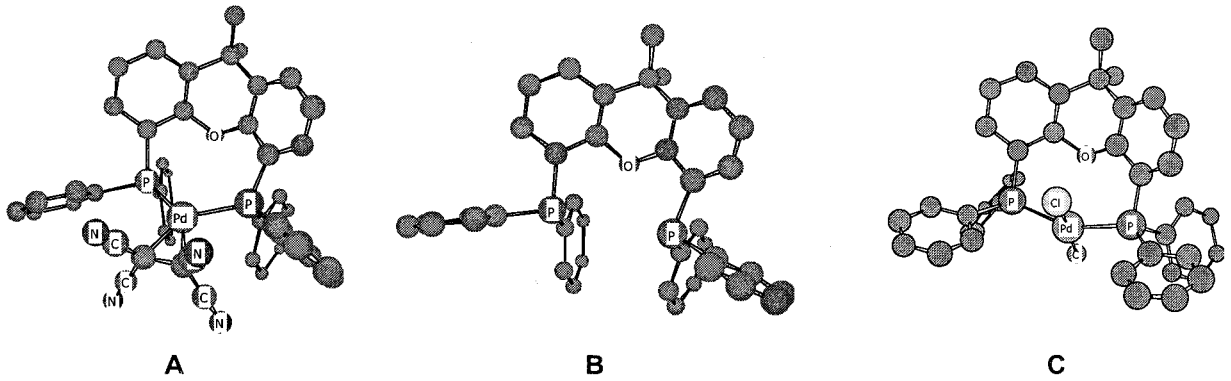


FIGURE 2. Crystal structure of (Xantphos)Pd(TCNE), Xantphos (**3f**), and (Xantphos)PdMeCl.

Table 1. Results of the Hydroformylation of 1-Octene at 80 °C Using Xantphos Ligands (3)[a]

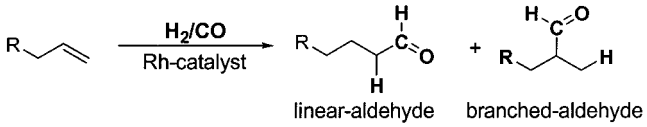
ligand	β_n (°)[b]	l:b ratio[c]	% linear aldehyde[c]	% isomer.[c]	tof[c,d]	ratio ee:ae
3a[e]	102	6.7	87.0	0	250	
3b	102	8.5	88.2	1.4	36.9	3:7
3c	108	14.6	89.7	4.2	74.2	7:3
3d	108	34.6	94.3	3.0	81.0	6:4
3e	110	50.0	93.2	4.9	110	7:3
3f	111	52.2	94.5	3.6	187	7:3
3g	113	49.8	94.3	3.8	162	8:2
3h	114	50.6	94.3	3.9	154	7:3
3i	114	69.4	94.9	3.7	160	8:2
3j	120.6	50.2	96.5	1.6	343	6:4

[a] Conditions: $CO/H_2 = 1$, $P(CO/H_2) = 20$ bar, ligand/Rh = 5, substrate/Rh = 637, [Rh] = 1.00 mM, number of experiments = 3. In none of the experiments was hydrogenation observed. [b] Natural bite angles β_n are taken from ref 14. [c] Linear over branched ratio, percent linear aldehyde, percent isomerization to 2-octene, and turnover frequency were determined at 20% alkene conversion. [d] Turnover frequency = (mol of aldehyde) (mol of Rh)$^{-1}$ h^{-1}. [e] $P(CO/H_2) = 10$ bar, ligand/Rh = 2.2, substrate/Rh = 674, [Rh] = 1.78 mM.

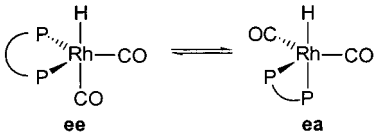
catalysis until the study of van Leeuwen et al.[8a,b] The ligand derived from dibenzofuran, **3k**, was first reported by Haenel et al.[11] Other heteroatoms such as nitrogen in acridine-type ligands (**4**)[12] or sulfur in thioxanthene (**5**)[13] coordinate too strongly and form terdentate complexes. Because of their butterfly-type structure, the donor atoms of the xanthene-type ligands are well oriented to form complexes with many transition metals, having bite angles much larger than 90°. By varying the bridge at the 10-position (see also Table 1), we induced small variations in the bite angle and thereby the desired bonding mode.[8,14] In this way a series of ligands was obtained that showed remarkable coordination behavior in several transition metal complexes. Furthermore, this has resulted in exceptional reactivity and selectivity in many organometallic and catalytic reactions.

The molecular structures of Xantphos (**3f**),[8b,c] its palladium TCNE complex,[15] and its palladium(II) methyl chloride complex[16] showed that the ligand structure hardly changes upon coordination (Figure 2). The observed P−P distance in the free ligand is 4.059(2) Å, while the P−P distance in the TCNE complex is 3.726 Å. The P−P distance in *trans*-L_2PdMeCl is 4.46 Å. The P atoms are brought together by means of a slight decrease of the angle between the two phenyl planes in the backbone of the ligand. As a consequence, Xantphos-type ligands do not

Scheme 1



Scheme 2



form bimetallic species, whereas the oxygen in the backbone prevents metalation of the ligand. When the bite angle becomes too large, as in DBFphos (**3k**), stable mononuclear complexes are not formed.[8b,11] Remarkably, the P−Pd−P angle in the zerovalent palladium TCNE complex was restricted to 104°, whereas palladium−phosphorus distances were slightly enlarged. Apparently, the palladium centers prefer to adapt to the ligand structure by enlarging the bond length rather than adjusting the bite angle. XantphosPdMeCl showed a P−Pd−P bite angle of 153° for the trans complex, which is significantly smaller than the ideal trans coordination angle.[16] Furthermore, in solution the cis complex was in equilibrium with the trans complex. The calculated flexibility range[4] of Xantphos (**3f**) was between 97 and 133°,[14] which explains the relatively small angle of 153° of the trans complex.

Hydroformylation

The first catalytic reaction that was studied applying this new set of ligands was the rhodium-catalyzed hydroformylation of alkenes. This reaction provides a mild and clean method for the functionalization of hydrocarbons (Scheme 1).[17] Brown and Kent suggested that the highest selectivity for the linear aldehyde was obtained when two phosphine ligands were coordinated in the equatorial plane of the trigonal bipyramidal rhodium complex (Scheme 2).[18] Therefore, bidentate ligands that would enforce a coordination angle of 100−120°, stabilizing bisequatorial coordination, were expected to have a positive effect on the selectivity of the hydroformylation reaction.

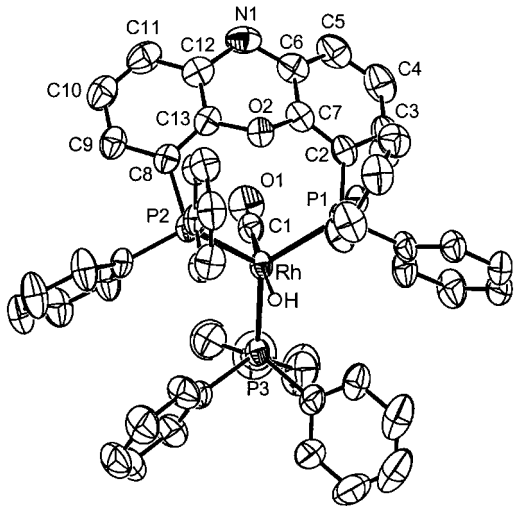


FIGURE 3. Crystal structure of HRh(**3i**)PPh_3.

Casey and co-workers were the first to report that by influencing the chelate angle of bidentate diphosphines, the regioselectivity of the rhodium-catalyzed hydroformylation of 1-alkenes was affected dramatically.[19] They studied a ligand introduced by Eastman, 2,2′-bis-((diphenylphosphino)methyl)-1,1′-biphenyl (BISBI, **6**), and found that the preferential mode of coordination is bis-equatorial. For BISBI, a linear to branched aldehyde ratio (l:b) as high as 66:1 was reported, while equatorially apically coordinating dppe (1,2-bis(diphenylphosphino)-ethane) gave a l:b of only 2.1.

The X-ray crystal structure of (**3i**)Rh(CO)H(PPh_3) shows that Xantphos-type ligands induce bis-equatorial coordination (Figure 3). We tested the selectivity of our ligands in the rhodium-catalyzed hydroformylation of 1-octene (Table 1).[8,14] DPEphos (**3a**), with a calculated natural bite angle of 102.2°, induced an enhanced, though moderate selectivity for the linear aldehyde (compared to most diphosphines). The ligands **3c**−**j** have calculated natural bite angles near 110° and showed a high regioselectivity and a low rate of isomerization to internal alkenes. Compound **3k**[11] proved not to be selective, probably because the bite angle was too large to form a chelating complex. The ultimate test for a catalyst to check its selectivity toward the linear aldehyde is the hydroformylation of styrene, since this is a substrate with a distinct preference for the formation of the branched aldehyde. The hydroformylation of styrene with (**3f**)Rh resulted in high selectivity for the linear aldehyde (a l:b of up to 2.35 was obtained).

Ligands having even wider bite angles are obtained when rigid, cyclic substituents are used, as in **7**.[20] The wide bite angle now leads to a high propensity to isomerization, whereas the high selectivity to linear product is retained. As a result, internal alkenes can be hydroformylated to linear aldehydes.[20] For octene-2 the l:b is 9 and for octene-4 this value is 4. At higher pressures of CO less linear aldehyde is formed, because the rate of isomerization decreases. This is the first rhodium−phosphine catalyst giving such high selectivity for linear aldehydes from internal alkenes.

The structures of the (diphosphine)Rh(CO)H(PPh_3) complexes and the (diphosphine)$RH(CO)_2H$ complexes of all Xantphos ligands were studied in detail.[8,14] Recent in situ high-pressure NMR and IR experiments[20,21] showed that (diphosphine)$RH(CO)_2H$ complexes of ligands **3e** form mixtures of bis-equatorial and equatorial-apical isomers, which rapidly equilibrate. By introduction of substituents at the 4-position of the phenyls of **3e**, the electronic ligand properties were altered. For the HRh**3e**$(CO)_2$ complexes decreasing phosphine basicity gives decreasing rhodium−proton (^1J(Rh,H)) and phosphorus−proton (^2J(P,H)) coupling constants, but increasing rhodium−phosphorus (^1J(Rh,P)) coupling constants.[20,21] The ratio of the two isomers can be calculated from the average observed coupling constant if the values for the pure isomers are known.[22] The equilibrium between the **ee** and **ea** isomers is greatly influenced by phosphine basicity. For the strongly electron-donating $N(CH_3)_2$ substituent the **ea** isomer is slightly favored, while for the strongly electron-withdrawing CF_3 substituent the equilibrium is shifted almost completely to the **ee** isomer.

Unambiguous evidence for the existence of a dynamic equilibrium between **ee** and **ea** complex isomers was supplied by HP-IR spectroscopy. The spectra of the (diphosphine)$Rh(CO)_2H$ complexes all showed four absorption bands in the carbonyl region (Figure 4). The shift in isomer composition that was found in the NMR spectra was confirmed and clearly visualized when comparing the IR spectra of the series of complexes.

From these results it was concluded that the coordination mode in the five-coordinated hydrido complexes by itself is not crucial in the determination of the regioselectivity of the reaction. Regioselectivity correlates only roughly with the (predominant) chelation mode of the electronically modified ligands **3e** in the (diphosphine)-$Rh(CO)_2H$ complexes, since the ratio of **ee** and **ea** isomers varies from almost 1 for X = NMe_2 to more than 9 for X = CF_3, while the selectivity for linear aldehyde remains the same for all ligands. Instead, the calculated bite angle seems to display a higher correlation with the regioselectivity!

The regioselectivity is controlled by the hydride migration, provided that this is largely irreversible.[19b] The rigid xanthene backbones induce an increased stability of four-coordinated trans complexes as already evidenced for related nickel and palladium complexes.[16,23] A larger bite angle of the diphosphine stabilizes trans intermediate **A** and results in increased embracing of the rhodium center by the ligand (Scheme 3).[21] Furthermore, after alkene addition, the complex encounters large steric hindrance in the equatorial plane of conformers **B** and **B′**. Presumably, the backbone constrains the orientation of the phenyl substituents of the diphosphines in such a way that the substituent R is forced in the direction of the hydride, resulting in preferential formation of linear **C** over branched **C′**.

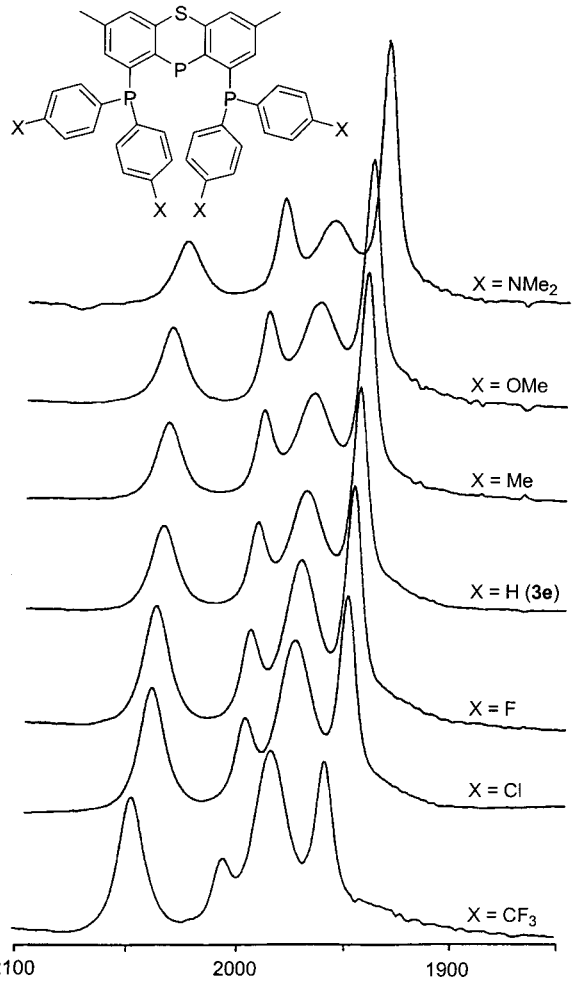


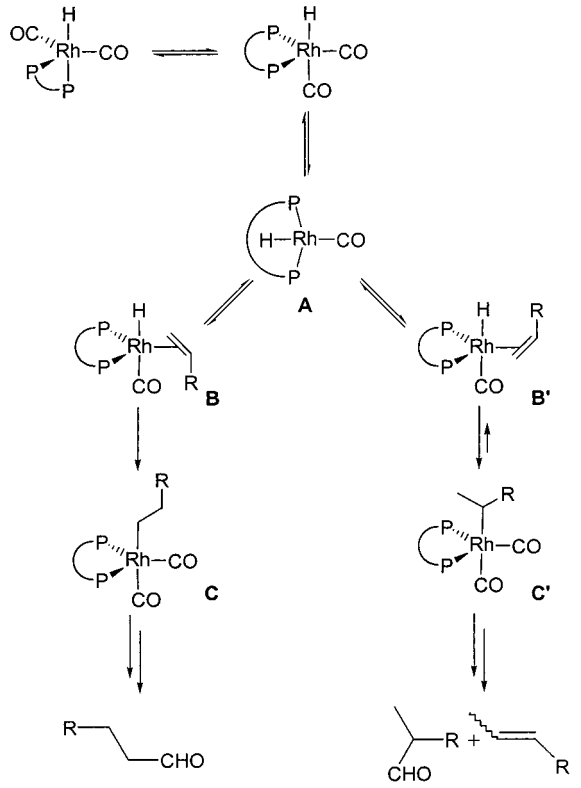
FIGURE 4. IR spectra of electron-donating and -withdrawing derivatives of HRh(**3e**)$(CO)_2$.

Platinum-Catalyzed Hydroformylation

Alkenes can be hydroformylated selectively by employing platinum−diphosphine complexes with or without tin chloride as cocatalyst.[24] Despite the high l:b ratios induced by the platinum−diphosphine catalysts, these systems have mainly been applied to asymmetric hydroformylation so far. Major drawbacks of these catalyst systems are extensive isomerization and hydrogenation of the substrate alkenes.[24,25]

A remarkably selective platinum catalyst for the hydroformylation of methyl 3-pentenoate applying Xantphos ligands was reported by Vogt and co-workers.[26] For obtaining the desired linear aldehyde, a nylon-6 precursor, selective isomerization to methyl 4-pentenoate prior to regioselective hydroformylation is required. The highest selectivity was obtained using **3d**, which was ascribed to the large bite angle enforced by this ligand. Ligands that induced even larger bite angles such as **3e** and **3f** resulted in a decrease of selectivity. This could be due to the fact that all active platinum-Xantphos catalysts still have a cis coordination mode as was shown in an NMR spectroscopy study by van Leeuwen et al.[27] The selectivity for the linear aldehyde in the hydroformylation of 1-octene was moderate. Remarkably, the selectivity and reaction rate increased

Scheme 3



enormously if one of the phosphorus donor atoms was replaced by arsenic.[27]

In line with the work of Vogt et al., the best results for the hydroformylation of methyl 3-pentenoate were obtained using **3b**, although the high selectivity achieved using **3d** was not reached.

Palladium Allyl Complexes and Allylic Substitution

Palladium-catalyzed allylic alkylation was originally discovered by Tsuji,[28] and especially the asymmetric version has been pioneered by Trost and others.[29] Relatively little research effort has been put into understanding the regioselectivity of the reaction.[30,31] Åkermark[30] has shown that the cone angle of substituted phenanthrolines has a large influence on both the isomer distribution of 1-methylallyl-Pd complexes and the regioselectivity of stoichiometric alkylation (Scheme 4). Stoichiometric alkylation of the syn complex resulted in almost exclusive formation of the linear trans product (**I**). The anti complex reacted to form the branched (**II**) and the linear cis product (**III**) in an approximately 1:1 ratio.

Xantphos ligands (**3**) were found to direct the regioselectivity to the linear trans product **I**, resulting in smaller amounts of the branched product **II** in the alkylation of *trans*-2-hexenyl acetate with sodium diethyl 2-methylmalonate.[32] This was explained by the large bite angle induced by these ligands in the palladium allyl complexes. The increasing embracement of the palladium using large bite angle ligands dictates the regioselectivity to the linear product. NMR studies (^1H and ^{31}P) of isolated Pd(1-

Scheme 4

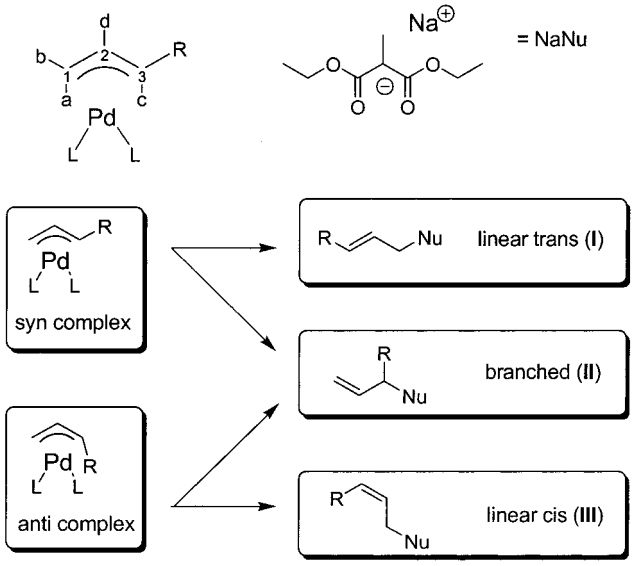


Table 2. Relationship between the Bite Angle and (1) Δ*E* (Syn/Anti) Calculated by Molecular Modeling (PM3(tm) Level) and Obtained from Experimental Data (NMR) and (2) the Regioselectivity in Stoichiometric Alkylation of the Equilibrium Mixtures of (1-Me-allyl)Pd(diphosphine)OTf Complexes

complex (ligand)	β^a (Y)	% syn	% anti	ΔE (NMR) (kJ mol^{-1})	ΔE^b (PM3(tm)) (kJ mol^{-1})	% **I**	% **II**	% **III**
dppe	85	90	10	−5.4	−23.7	70.0	8.9	21.1
dppp	95	92	8	−6.1	−21.9	79.2	4.6	16.2
dppb	99	86	14	−4.5	−20.0	71.7	8.0	20.3
dppf	106	78	22	−3.1	−18.9	68.9	8.9	22.2
3a	108	72	28	−2.3	−15.4	66.4	9.6	24.0
3d	110	57	43	−0.7	−12.5	54.5	12.4	33.1

[a] β obtained from the calculated (1-Me-allyl)Pd(diphosphine) complexes. [b] The relative large energy difference in the calculations is most likely the result of the absence of solvent and anion.

methylallyl)(diphosphine)OTf complexes of several diphosphine ligands show that they exist as an equilibrium mixture of the syn and anti isomers.[33] The syn/anti ratio is significantly lower in complexes of ligands inducing larger bite angles (Table 2), again caused by increasing embracement of the palladium allyl moiety.

The syn/anti ratio governs the regioselectivity of the stoichiometric alkylation (Table 2, Figure 5). In (1-methylallyl)Pd(diphosphine)OTf complexes of ligands inducing a *small* bite angle, the syn isomer prevails, and the relative amount of the linear trans product **1** is high. Going to a larger bite angle (from dppp to **3d**), the percentage of syn isomer as well as the selectivity to **I** drops, whereas the selectivity to the branched product **II** increases.

The situation becomes more complicated in the catalytic alkylation. Since the substrate consists mainly of the *E*-isomer, the syn product is formed initially. The selectivity for the product is now also dependent on the relative rate of the syn/anti isomerization compared to the alkylation reaction. Ligands showing a large embracing effect such as **3d** result in a fast alkylation rate compared to syn/anti isomerization. Therefore, the selectivity for the linear

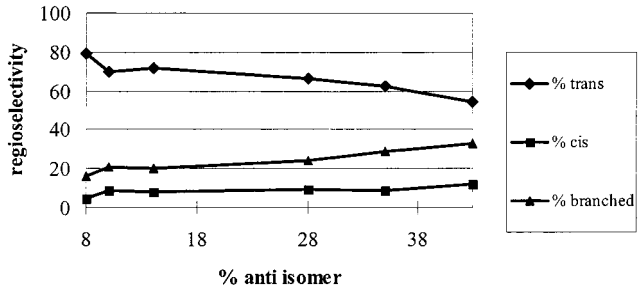


FIGURE 5. Relationship between isomer distribution in cationic (1-methylallyl)Pd(diphosphine)OTf complexes and the regioselectivity of stoichiometric alkylation.

E-product is much larger than in the stoichiometric reaction.

Both the size of the substituent and the double bond geometry of the allylic substrate have a pronounced influence on the product selectivity. The alkylation of substrates with an *E*-conformation of the double bond results in the preferential formation of the linear *E*-product. The larger embracing effect of the **3d** ligand results in an increase of the regioselectivity to >98% for *E*-pent-2-enyl acetate as substrate. Analogously, the alkylation of *Z*-substrates results in the formation of the linear *Z*-product. Remarkably, for *Z*-substrates, a larger bite angle of the ligand leads to an increased regioselectivity for the formation of the branched product instead of the linear product, up to 47.5% for **3d**.

Oxidative addition of the *Z*-substrate will result in formation of mainly the anti-allyl complex. The substituent in the anti position will encounter steric interaction with the phosphine ligand, especially when the ligand (**3d**) induces a large bite angle. This results in a longer palladium−carbon distance for the substituted carbon atom. As a consequence, this carbon atom gains in electrophilicity resulting in formation of the branched product. Ligands enforcing a small bite angle such as dppe give lower reaction rates allowing syn/anti isomerization. Therefore, the more stable syn complex will be formed predominantly, which gives largely the linear *E*-product.

Most research in palladium-catalyzed allylic alkylation has been focused on the asymmetric version. Effective diphosphine ligands have been developed by Trost et al.[29a] Detailed studies revealed that these ligands formed palladium complexes with a large P−Pd−P angle of 104°.[34] Therefore, chiral derivatives of Xantphos-type ligands were expected to perform well in asymmetric allylic substitution reactions. A straightforward method to obtain chiral Xantphos ligands is the introduction of stereogenic phosphorus atoms. Hamada et al. synthesized enantiomerically pure 2,7-di-*tert*-butyl-9,9-dimethyl-4,5-bis(methylphenylphosphino)xanthene (**3m**).[35] Both the *R,R*- and the *S,S*-forms were applied in the allylic substitution of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. The obtained enantiomeric excess was good (up to 85%).

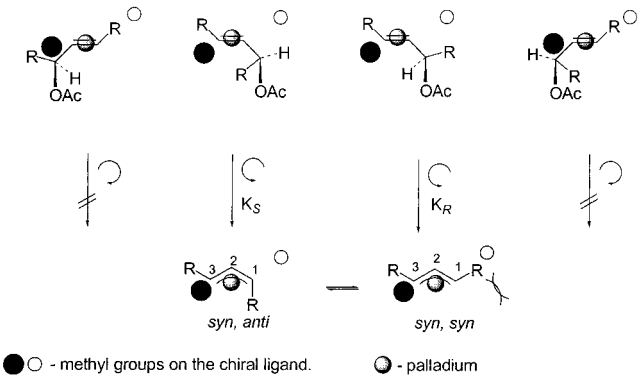
Osborn and van Leeuwen et al.[29b,c] applied chiral phospholane substituents previously described by Burk.[36] Two derivatives **3n** and **3o** were prepared and studied in allylic substitution reactions. Next to 1,3-diphenyl-2-

Table 3. Asymmetric Allylic Alkylation Using Duxantphos Ligands[a]

ligand	substrate	solvent	T (°C)	t (h)	ee (%)
3o	cyclohex-2-en-1-yl acetate	THF	−20	4	93 (*S*)
3n	pent-3-en-2-yl acetate	THF	0	3	82 (*S*)
3o	1,3-diphenyl-2-propenyl acetate	CH_2Cl_2	0	24	97 (*R*)

[a] Conditions: 1 mol % Pd, Ligand: Pd = 2.2 *N*,*O*-bis(trimethylsilyl)acetamide as base, 0.18 M substrate, 0.36 M dimethyl malonate.

Scheme 5



propenyl acetate, the sterically less demanding pent-3-en-2-yl acetate and cyclohex-2-en-1-yl acetate as substrates also gave high ee's (Table 3). The crystal structure of the intermediate palladium complex derived from cyclohex-2-en-1-yl acetate did not show much difference in steric hindrance for nucleophilic attack on C1 or C3. Therefore, it was concluded that an early transition state in this system was unlikely. Molecular modeling studies showed that the most stable, analogous cyclohexene complex has the double bond in the P−Pd−P plane. Formation of the intermediate palladium olefin complex by attack of the nucleophile on the η^3-allyl complex must be accompanied by rotation. The high enantioselectivity was explained by selective hampering of one rotational direction (Scheme 5). One of the substrate enantiomers reacted much faster than the other, resulting in kinetic resolution. (k_s/k_r up to 8 was observed). Remarkably, similar product enantioselectivities were observed at 50 and 100% conversion. It was proposed that both the *R*- and *S*-substrates led to the same allylic intermediate, which had the syn/anti configuration. This diastereomer showed the least steric interaction with the chiral ligand. Fast equilibration to this isomer, followed by selective nucleophilic attack at one allylic carbon by preferential rotational movement, results in high product enantioselectivity.

Amination of Aryl Halides

Aromatic and aliphatic amines such as aniline and piperidine derivatives are an important class of fine chemicals. A mild and clean preparation of these compounds is the palladium-catalyzed carbon−heteroatom bond formation discovered by Hartwig and Buchwald.[37] Recent improvements involve the use of bidentate phosphine[38] and aminophosphine[39] ligands. It was suggested that

Table 4. Catalytic Amination of Bromobenzene at 25 °C Using Pd Xantphos Complexes[a]

entry	ligand	TOF_{ini}[b] (mol mol^{-1} h^{-1})	conversion[c] (%)	natural bite angle[d]
1	**3a**	22	3	102
2	**3b**	27	11	102
3	**3d**	80	40	109
4	**3e**	86	47	110
5	**3f**	140	96	111
6	dppf	0	1	96
7	dppe	0	0	85

[a] Conditions: see Experimental Section. [b] TOF_{ini} is the amount of product formed per mole of Pd per hour after 6 min. [c] Based on bromobenzene (*o*-anisidine and product yield gives similar results) after 1 h. [d] Values taken from reference ref 13.

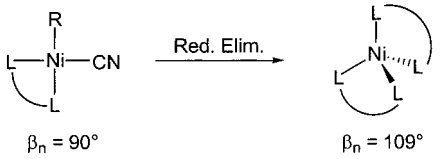
bidentate ligands caused reduced β-hydride elimination as a consequence of the higher coordination number of the palladium complexes. This effect becomes more distinct with increasing bite angle of the ligand.[6,40] Furthermore, reductive elimination, the product-forming step, is promoted by chelating ligands with larger bite angles.[41,42]

We anticipated that Xantphos complexes were promising catalysts for the palladium-catalyzed amination. Buchwald et al. successfully used DPEphos as ligand in the coupling reaction of anilines with aryl bromides.[38b] Subsequent studies by van Leeuwen[43] and Buchwald[44] showed that for many systems palladium−Xantphos proved to be a superior catalyst. Buchwald suggested that facile dissociation of one of the phosphorus donor atoms of Xantphos was caused by the increased bite angle of this ligand. Van Leeuwen et al. performed a detailed kinetic and structural study of palladium−Xantphos catalysts.[13,16] The catalytically active complexes (diphosphine)Pd(4-CNC_6H_4)Br were prepared, and some have a common cis coordination mode, whereas others coordinate in a trans fashion. It is assumed that the oxygen is forced into proximity of the Pd center by the trans coordination mode of the phosphine groups, leading to a weak Pd−O interaction. In solution, the compounds show cis/trans isomerization. Cationic complexes [(diphosphine)Pd(*p*-C_6H_4CN)]$^+$ adopt an almost square-planar geometry around the metal center with the ligand acting as a "pincer" with the phosphines in trans orientation and the oxygen coordinated to the metal.

Using these palladium catalysts, the coupling of 2-methoxyaniline with bromobenzene was studied. Compounds with the ligands enforcing cis coordination gave low conversions (Table 4, entries 1, 2, and 6), whereas the complexes possessing wide P−Pd−P angles showed an excellent conversion. The observed reaction rates for these ligands increased with wider bite angles. The reaction between 2-methoxyaniline and phenyl triflate catalyzed by the cationic palladium complexes gave a reversed trend: smaller ligand bite angles led to higher reaction rates.

Kinetic studies showed a first-order rate dependency in palladium, aniline, and base concentration for cationic complexes.[13] The reaction rate was independent of the aryl triflate concentration. Using neutral palladium bromide complexes, the reaction rate showed a broken order in

Scheme 6



palladium, first order in base, and zeroth order in both substrates. At high halide concentrations the first-order rate dependency in palladium was restored. Due to the wide ligand bite angle the oxygen is in close proximity to the palladium center and assists the bromide dissociation by formation of a relatively stable trans complex. Since this cationic species is the active catalyst, the reaction rate increases with larger ligand bite angles. Replacement of the oxygen by the stronger donor atom sulfur results in a stable cationic complex that shows no catalytic activity, illustrating the delicate effect of ligand structure on catalytic activity.

Nickel-Catalyzed Hydrocyanation

The addition of HCN to alkenes is a useful reaction for the functionalization of organic substrates. Industrially it has tremendous impact mainly because of the adiponitrile production by Du Pont via hydrocyanation of butadiene using nickel-tris-*o*-tolyl phosphite catalysts.[45]

Kinetic studies by McKinney[46] showed that rate-determining reductive elimination of RCN from square-planar Ni(II) assisted by phosphite addition yields the product and the formation of a tetrahedral Ni(0) (Scheme 6). This reaction is facilitated by electron-withdrawing ligands. Therefore, phosphites have proven to be versatile ligands in the hydrocyanation reaction, whereas phosphine ligands lead to catalysts with hardly any activity.[47,48]

Recently Moloy showed that reductive elimination of nitriles from nickel−diphosphine complexes was strongly enhanced by ligands that induce large bite angles.[41] Bidentate phosphine ligands favoring bite angles of ca. 110° destabilize the square-planar Ni(II) species and stabilize the tetrahedral Ni(0) complexes.

The hydrocyanation of styrene using nickel catalysts containing Xantphos ligands (**3**) resulted indeed in remarkable yields and selectivity (Table 5).[49] Ligand **3a** gave yields (based on HCN) of 35−41%, which are modest but still significantly higher compared to those of PPh_3 or $Ph_2P(CH_2)_nPPh_2$ (n = 2−4). Optimal yields up to 95% were obtained when the bite angle was increased further to 105−106°, using **3d** or **3e**. When **3f** was applied the yield was slightly lower, 75%. For comparison several well-known diphosphines were tested as catalyst components under identical conditions. Yields of nitriles were 0−11% (based on HCN), and the formation of nickel dicyanides was observed.

These results show that effective nickel−phosphine-catalyzed hydrocyanation can be achieved when bidentate ligands enhance the reductive elimination step by stabilizing a tetrahedral geometry. The optimal natural bite angle is 105−106°, while either a slight increase to 109° or a decrease to 101° already results in a significant drop in activity.

Table 5. Nickel-Catalyzed Hydrocyanation of Styrene, Using Diphosphine Ligands[a]

ligand	β_n (°)[b]	% yield[c]	% branched
3a	101	35−41	88−91
3d	105	94−95	97−98
3e	106	69−92	96−98
3f	109	27−75	96−99
3k	138	0.7	83
PPh_3		0	
dppe	79	<1	ca. 40
dppp	87	4−11	ca. 90
dppb	99	3−8	92−95
BINAP	85	4	29

[a] Reaction conditions: styrene/Ni = 28.5, HCN/Ni = 17.5, [Ni] = 73.3 mM, T = 60 °C, t = 18 h. [b] Natural bite angles for nickel complexes are taken from ref 49. [c] Yields are based on HCN. Maximum yields based on styrene are 61%.

Conclusions

The diphosphine ligands based on a xanthene backbone (**3**) can enforce constrained coordination geometries in their transition metal complexes. The rigid heteroaromatic backbone has a pronounced preference for intermediate bite angles of approximately 110°, between cis and trans coordination modes. Both cis and trans complexes have been prepared, which show significant deviation from their ideal coordination angles of 90 and 180°, respectively. As a result, these ligands have a pronounced effect on the rate and selectivity of several metal-catalyzed reactions.

We are indebted to the postdoctoral researchers, graduate and undergraduate students, as well as the research groups we collaborate with, who are mentioned in the references, for their valuable contributions to this research.

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AR000060+