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Bite angle effects in diphosphine metal catalysts: steric or electronic? †

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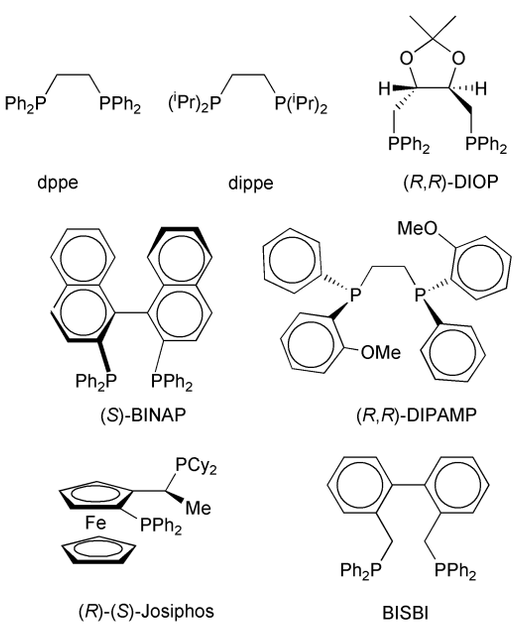
Received 9th January 2003, Accepted 6th February 2003
First published as an Advance Article on the web 23rd April 2003

The effects of wide bite angles of bidentate phosphine ligands on three catalytic reactions are reviewed: rhodium catalysed hydroformylation, nickel catalysed hydrocyanation, and palladium catalysed reactions of ethene, carbon monoxide and methanol leading to polyketone or methyl propanoate. The P–M–P bite angle plays a crucial role in determining the selectivity and rate in all three reactions. In this review an attempt is made to separate the mode of action into a steric and an electronic one. The regioselectivity of hydroformylation seems to be governed by steric factors, while the rate of reaction is determined by the electronic influence of the bite angle. The rates in hydrocyanation and polyketone formation were previously thought to be determined by orbital effects, but that should be questioned. Selectivity in the palladium carbonylation reaction is mainly due to steric factors.

Introduction

The development of new diphosphine ligands for specific catalytic applications has been the subject of research for several decades. The influence of the stereo-electronic properties of the ligands in the catalyst activity and selectivity is evident, but the specific effects are often difficult to rationalize. The main reason for this is still, in many cases, lack of knowledge of the reaction mechanism, the rate, or selectivity limiting steps in the catalytic cycle. For a long time this limitation made the discovery of new ligands a matter of trial and error. Nevertheless several breakthroughs are due to the design of new ligands, although the catalytic results are mostly serendipitous. Especially important for the progress in this field were, and still are, those ligands designed to have unusual properties compared to the ones already known; *e.g.* the introduction of more basic alkyl groups in tricyclohexylphosphine compared to the traditional triphenylphosphine ligand or dippe compared to dppe, the introduction of bidentates with a wide bite angle such as BISBI, or the use of binaphthyl backbones as in BINAP to introduce "unusual" chirality in the ligands, the use of chiral phosphorus centres in bidentates as in DIPAMP, or the use of chiral backbones as in DIOP, the additional use of planar chirality as in Josiphos are only some examples of them. In general, the huge number of phosphine and diphosphine ligands in the literature were generated by variations or combinations of the properties of those "unprecedented" ligands, which, by their unusual nature, also showed new and attractive catalytic properties.



† Based on the presentation given at Dalton Discussion No. 5, 10–12th April 2003, Noordwijkerhout, The Netherlands.

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DOI: 10.1039/b300322c

A deeper insight into the catalytic systems and the relationship between ligand properties and catalytic performance will give us access to more catalysts *via* rational design of the ligands. To facilitate this, many experimental and theoretical studies have been devoted to define easily quantifiable parameters that describe ligand properties. The final goal is to relate these ligand parameters to the catalyst performance in order to understand the crucial steps in more detail.

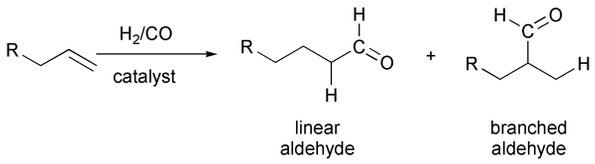
Some of the ligand parameters, described in detail and used in many publications are the Tolman parameters θ and χ, which proved to be very useful to quantify steric and electronic properties in monophosphine ligands.[1] The solid angle (Ω),[2] pocket angle,[3] repulsive energy,[4] and the accessible molecular surface[5] have been defined for bidentate phosphine ligands. These closely related parameters refer to the steric properties of the ligand and extensive studies by molecular mechanics are needed to evaluate them. The natural bite angle, introduced by Casey and Whiteker,[6] can be easily obtained by using simple molecular mechanics calculations and it is the most extensively applied parameter for diphosphines. The bite angle effect on the activity or selectivity has been studied and reviewed for many catalytic reactions.[7–10] However, in spite of the large amount of data the origin of this effect is often not clear and naturally, its mode of operation is not necessarily the same for all reactions.

With the aim to rationalize the effect of (wide) bite angle diphosphines in catalytic reactions a distinction can be made between two different effects, both related to the bite angle of diphosphine ligands: The first one, which we will call *steric bite angle effect* is related to the steric interactions (ligand–ligand or ligand–substrate) generated when the bite angle is modified by changing the backbone and keeping the substituents at the phosphorus donor atom the same. The resulting steric interactions can change the energies of the transition states and the catalyst resting states, thus modifying the activity or selectivity of the catalytic system. The second one, the *electronic bite angle effect* is associated with electronic changes in the catalytic centre when changing the bite angle.[10] It can be described as an orbital effect, because the bite angle determines metal hybridisation and as a consequence metal orbital energies and reactivity. This effect can also manifest itself as a stabilisation or destabilisation of the initial, final or transition state of a reaction. When the substituents at the phosphorus donor atom are kept the same while the bite angle is changed, the steric properties also change, unfortunately.

These two effects, different in nature but with the same origin, are concomitant when diphosphines with variable bite angles are used. Even though it is not always feasible to analyse them separately, they can obviously affect to the catalytic system in distinct manners. Sometimes the changes in activity or selectivity can be attributed to mainly one of them. The knowledge of which effect (electronic or steric) is governing the catalyst performance will contribute to the knowledge of the catalytic reactions and the future design of ligands. In this contribution we will try to separate the contributions of the *steric bite angle effect* and the *electronic bite angle effect* to the selectivities and rates for several catalytic reactions.

Hydroformylation

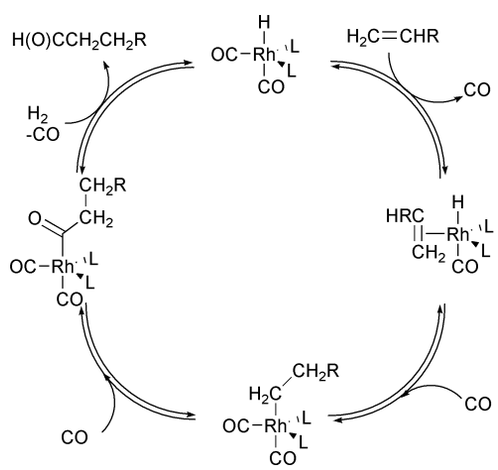
Hydroformylation of alkenes is one of the most extensively applied homogeneous catalytic processes in industry (Scheme 1). More than six million tons of aldehydes and alcohols are produced annually.[11] Many efforts have been devoted in the last few years to the development of systems with improved regioselectivity toward the formation of the industrially more important linear aldehyde. Both phosphine and phosphite based systems giving high regioselectivities to linear aldehyde for the hydroformylation of terminal and internal alkenes have been reported.[12–15]



Scheme 1 The hydroformylation reaction.

Rhodium catalysed hydroformylation

The generally accepted mechanism for the rhodium triphenylphosphine catalysed hydroformylation reaction originally proposed by Heck and Breslow[16] is shown in Scheme 2. The catalytically active species is a trigonal bipyramidal hydrido rhodium complex, which usually contains two phosphorus donor ligands. In early mechanistic studies[17] it was already demonstrated that this catalyst exists as two isomeric structures, depending on the coordination of the triphenylphosphine ligands, namely equatorial–equatorial (ee) and equatorial–apical (ea) in a 85 : 15 ratio.‡ It was tentatively suggested that the ee isomer leads selectively to the linear product. Since this first rhodium–phosphine system a lot of research has been devoted to the development of more active and selective systems. In 1987, Devon *et al*. at Texas Eastman,[18] patented the BISBI–rhodium catalyst, which gave excellent selectivity toward the linear aldehyde compared with other diphosphine ligands previously studied.[19] In order to rationalize this result Casey and Whiteker[13] studied the relationship between selectivity and bite angle for different diphosphine ligands. They found a very good correlation between the bite angle of the diphosphines and the regioselectivity. The high regioselectivity observed with BISBI was attributed to the preferential coordination mode, ee, in the catalytically active [RhH(diphosphine)$(CO)_2$] species, due to BISBI's natural bite angle close to 120°.



Scheme 2 Simplified catalytic cycle for the hydroformylation reaction.

In recent years, van Leeuwen *et al*. synthesized a series of Xantphos type diphosphines possessing closely related backbones, and natural bite angles ranging from 102 to 123°.[8,14] These ligands, designed to ensure that the bite angle is the only factor that has a significant variation within the series (the differences in electronic or steric properties are minimal) have been applied to study the bite angle effect on the coordination mode, selectivity, and activity in the hydroformylation reaction. Although the conclusions presented in the various publications do not fit into one simple picture, in the present review of this work we speculate that the bite angle has two distinct effects

‡ A similar dynamic equilibrium between ee and ea species, observed for monophosphines, is demonstrated to exist also when diphosphine ligands are used. Nevertheless, the position of the equilibrium is dependent on the ring size (and finally bite angle) and the basicity of the phosphines.[20,21,23]

Table 1 1-Octene hydroformylation using xantphos ligands **1**–**10** [a]

Ligand	β_n [b]/°	l : b ratio [c]	% linear aldehyde [c]	% Isomer [c]	TOF [c,d]	Ratio ee : ea
1	102.0	8.5	88.2	1.4	37	3 : 7
2	107.9	14.6	89.7	4.2	74	7 : 3
3	108.5	34.6	94.3	3.0	81	6 : 4
4d	109.6	50.0	93.2	4.9	110	7 : 3
5	111.4	52.2	94.5	3.6	187	7 : 3
6	113.2	49.8	94.3	3.8	162	8 : 2
7	114.1	50.6	94.3	3.9	154	7 : 3
8	114.2	69.4	94.9	3.7	160	8 : 2
9	120.6	50.2	96.5	1.6	343	6 : 4
10	123.1	66.9	88.7	10.0	1560	>10 : 1

[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 taken from ref. 14. [c] Linear over branched ratio and turnover frequency were determined at 20% alkene conversion. [d] Turnover frequency = (mol of aldehyde) (mol of Rh)$^{-1}$ h^{-1}.

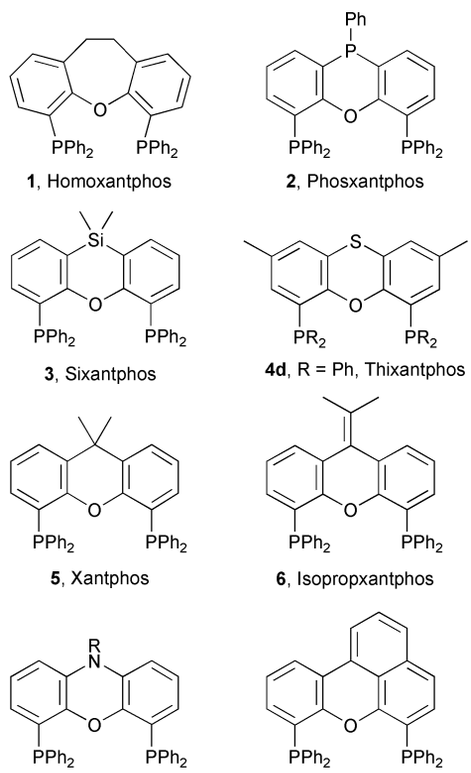
(electronic and steric) on the activity and selectivity in the hydroformylation reaction.

Steric bite angle effect and regioselectivity

In the first publication on the Xantphos series[14] a regular increase of the selectivity to linear product in 1-octene hydroformylation when increasing the bite angle was reported. The importance of the backbone rigidity compared with BISBI was also assessed. The suggestion of a shift in the ee/ea equilibrium in the rhodium hydride resting state toward the ee isomer, which is considered to be the more selective one, was the tentative explanation. However, later work[15,20,21] (Table 1) showed that in a series of very similar ligands the ee and ea species are present in equilibrium (ranging from 3 : 7 to >10 : 1), but small variations in calculated bite angles do not translate into the equilibrium constants observed, while in catalysis good selectivities are obtained with all of them. These results indicate unambiguously that, even though there is a clear bite angle-selectivity correlation when a wide range of angles is considered, the ee/ea equilibrium in the hydride precursor is not the factor governing the regioselectivity in the hydroformylation reaction when a smaller range of bite angles is considered.

The $RhH(diphosphine)(CO)_2$ species itself, however, is not involved in the step that determines the selectivity, but the latter is determined in the alkene coordination to RhH(diphosphine)(CO) or in the hydride migration step, which is virtually irreversible when linear aldehyde is formed with the use of phosphine ligands. A plausible explanation of the bite angle effect is that in these steps, an increase in the steric congestion around the metal centre is produced when enlarging the bite angle. This favours the less sterically demanding transition state of the possible ones, driving the reaction toward the linear product. In a recent publication[22] this fact has been quantified by means of an integrated molecular orbital/molecular mechanics method, demonstrating that the regioselectivity is controlled by steric interactions between the diphenylphosphino substituents and the substrate. In order to "maximize" the effects, the two limiting examples in the bite angle in the Xantphos series, homoxantphos **1** and benzoxantphos **9**, were investigated.

The ee-isomer HRh(CO)(alkene)(diphosphine) stemming from ee-$RhH(diphosphine)(CO)_2$ was considered to be the key intermediate in determining the regioselectivity, and thus the energies of the TS of the possible pathways in the alkene insertion were evaluated for both ligands. From the results obtained it was concluded that for both ligands linear product will be obtained predominantly and moreover the trend in differences between the two ligands was reproduced. In order to evaluate the importance of the steric ligand–substrate interactions in these results, the phenyl groups in the phosphorus atoms were replaced by hydrogen atoms. When using these "PH_2" model systems the difference in the calculated selectivity



is proportionally small compared to the one observed in the diphenylphosphine system, thus demonstrating the steric origin of the regioselectivity. Furthermore, larger bite angles were observed in the PH_2 model system compared to the diphenylphosphine system, but this orbital (electronic) effect showed not to be crucial in determining regioselectivity.

Electronic bite angle effect and activity

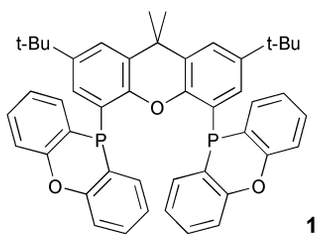
While the effect of the bite angle on selectivity in 1-octene hydroformylation (and styrene as well)[14] seems to be steric, the existence of a relationship between activity and bite angle in the hydroformylation reaction, which can be easily deduced from the experiments done within the Xantphos ligands family, might well have electronic origins. An increase in rate was found with increasing bite angle (**1**–**9**), but ligand **10**, having the widest bite angle, showed a sharp increase in rate of reaction (see Table 1).

The rate of dissociation of CO was studied separately *via* ^{13}CO exchange in a rapid scan IR spectroscopy study under pressure.[15] In this study no influence of the natural bite angle on the rate of formation of the (diphosphine)Rh(CO)H complexes

Table 2 1-Octene hydroformylation using ligands **4a**–**g**[a]

Ligand	R	ee : ea ratio	l : b ratio[b]	% linear aldehyde[b]	% isomer[b]	TOF[b,c]
4a	$N(CH_3)_2$	47 : 53	44.6	93.1	4.8	28
4b	OCH_3	59 : 41	36.9	92.1	5.3	45
4c	CH_3	66 : 34	44.4	93.2	4.7	78
4d	H	72 : 28	50.0	93.2	4.9	110
4e	F	79 : 21	51.5	92.5	5.7	75
4f	Cl	85 : 15	67.5	91.7	6.9	66
4g	CF_3	92 : 8	86.5	92.1	6.8	158

[a] Data taken from ref. 20. 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] Linear over branched ratio and turnover frequency were determined at 20% alkene conversion. [c] Turnover frequency = (mol of aldehyde) (mol of Rh)$^{-1}$ h^{-1}.



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was found for ligands **2**, **4**, and **6**, implying that the activation energy for the formation of these complexes is not affected significantly. Therefore, the increase in hydroformylation rate with increasing bite angle must originate from an increase in the concentration of these four-coordinate complexes, or from a decrease in the activation energy for alkene coordination (if this step were rate-determining), or a lower energy of the alkene complex, or a faster migratory insertion (*i.e.* either the resting state has a higher energy or the TS is lower). Ligand **10** shows a sharp increase in CO dissociation rate (the rate is seven times that of the other ligands). As steric effects on CO coordination are supposed to be small, this was explained by assuming a larger stabilisation of the four-coordinate intermediate for ligand **10** having the wider bite angle. This is what one might expect, but it does not explain fully the higher rate of hydroformylation.

In a series of electronically distinct but sterically equal ligands **4** it was found that the overall selectivity for linear aldehyde increased, while the linear branched ratio and the rate increased concomitantly with the ee/ea ratio in the hydrido isomers (Table 2).[20] The higher l : b ratio was due to an increase in 2-octene, the "escape" route for the formed branched alkylrhodium intermediate.

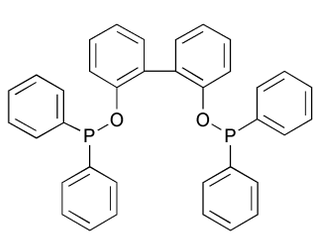
It is likely that increasing the bite angle will increase the activation energy for alkene coordination. Increasing the bite angle results in increased steric congestion around the rhodium centre and consequently in more steric hindrance for the alkene entering the coordination sphere. What kind of electronic effect the widening of the bite angle has on the activation energy for alkene coordination is unclear, since it depends on the dominant type of bonding of the alkene. Rhodium to alkene back-donation is promoted by narrow bite angles, while alkene to rhodium donation is enhanced by wide bite angles.

Widening the bite angle of a *cis* bidentate in a square planar complex would certainly accelerate a migration reaction, and the same mechanism might be operative in a trigonal bipyramid having the diphosphine as a bis-equatorial ligand.[12e] Summarising, a wider bite angle will increase the concentration of unsaturated (diphosphine)Rh(CO)H and other effects being absent or cancelling one another (alkene coordination and insertion) the overall effect will be an acceleration of the hydroformylation reaction.

When the backbone of a ligand allows both ee and ea coordination, the basicity of the phosphine has a pronounced effect on the chelation mode.[23–25] One of the first systematic studies using diphosphines is from Unruh who used substituted dppf.[26] Both rate and selectivity increase when the χ-value of the ligands increase. There are two possible explanations: electronic preference for linear alkyl complex formation when the π-back-donation to the phosphine increases, or alternatively, EWD ligands enhance formation of the ee isomer as was observed later in the Xantphos complexes.[14] This can be explained by the general preference of electron withdrawing ligands for the equatorial positions in trigonal bipyramidal complexes. Loss of CO is faster for complexes containing ligands with higher χ-values. As mentioned above, a stronger complexation of the alkene donor ligand may be expected for more electron deficient rhodium complexes. Thus, higher rates can be explained because in most phosphine based systems the step involving replacement of CO by alkene contributes to the overall rate. The reaction rate is 1st order in alkene concentration and minus one in CO in many catalyst systems.

The introduction of electron withdrawing substituents on the aryl rings of the bis-equatorial chelate of (BISBI)RhH$(CO)_2$ leads to an *increase* in linear aldehyde selectivity as well as the rate. This must be an electronic effect on the l : b ratio since BISBI containing phenyl substituents coordinates already purely in the bis-equatorial fashion.[13]

A similar electronic effect has been observed for ligands **11** and **12**. Both coordinate exclusively in the ee mode in rhodium hydrido dicarbonyl, but for the electron withdrawing ligand **11** a moderate l : b ratio of 6 was found while that for the electron poor ligand **12** was as high as 100. Increased l : b ratios at higher χ-values are relatively general for ligand effects in hydroformylation, but in the last cases they cannot be assigned to an electronic *bite angle* effect and they must represent an electronic effect *per se*, which is not fully understood yet.[27]



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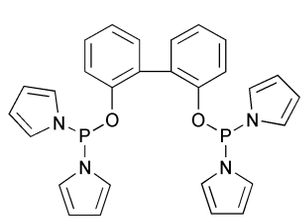

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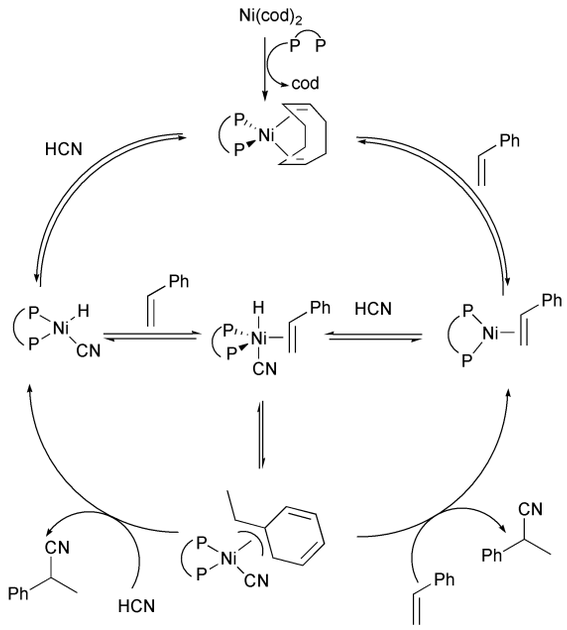
Hydrocyanation

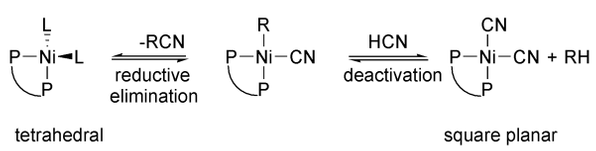
The most important application of the hydrocyanation reaction on an industrial scale is the nickel-catalysed addition of HCN to butadiene, known as the Dupont ADN process.[28] A simplified catalytic cycle for the hydrocyanation of styrene when using chelating diphosphines is depicted in Scheme 3. The intermediates are stabilized by P–Ni–P angles of 120° (in trigonal compounds), 109° (in the tetrahedral Ni(0) species), or 90° for the allyl, alkyl or hydrido cyano Ni(II) complexes,



Scheme 3 Simplified catalytic cycle for the styrene hydrocyanation.

eventually though these can also adopt distorted square planar or tetrahedral structures depending on the bulk of the ligands.[29]

The rate-determining step of this reaction is the reductive elimination of the alkyl-cyanide (or allyl-cyanide when considering vinylarenes as substrates). When using electron-withdrawing ligands the rate of this step increases, because of the release of some electronic density from the Ni by back donation into non-occupied orbitals.[29,30] Therefore, for a long time it was thought that only phosphites and phosphinites were suitable ligands. In fact, it has been reported that bidentate diphosphites[31] and diphosphinites[30] generate very active catalysts, which are also quite resistant to deactivation. On the other hand, the more basic phosphine ligands showed no activity in the hydrocyanation reaction. The main drawback of this reaction, even when using electron-withdrawing ligands, is the deactivation of the catalyst. When an excess of HCN is used, the formation of inactive square-planar Ni(diphosphine)$(CN)_2$ complexes occurs. This detrimental process is competing with the productive reductive elimination (Scheme 4).



Scheme 4 Competitive reductive elimination and deactivation reactions.

In order to suppress this side-reaction, the concentration of HCN has to be kept low during the catalytic process, and a high excess of ligand has to be used.[28,29]

The use of chelating diphosphines as ligands in the hydrocyanation reacion can be considered the main progress in this reaction. Although nickel complexes of monophosphines showed no activity in this reaction, probably due to their electronic properties, some chelating diphosphines generate very active catalysts. Moreover, there is a very strong dependence of the activity on the natural bite angle. In fact, it is possible, by tuning the bite angle of the diphosphine ligand, to generate catalysts very active and resistant to deactivation pathways.

Bite angle effects

In order to study the origin of the bite angle effect of diphosphines, some ligands with natural bite angles between 79 and 110° were tested in styrene hydrocyanation and compared with triphenylphosphine (Table 3).[32] The results obtained clearly indicate that diphosphines with natural bite angles close to 105° show very good activities. In contrast, when "classical" diphosphine ligands ($79 < \beta < 96°$) were used, hardly any activity was detected, and formation of Ni(diphosphine)$(CN)_2$ was observed. The same trend has been reported for other substrates.[33]

Table 3 Nickel-catalysed hydrocyanation of styrene, using diphosphine ligands[a]

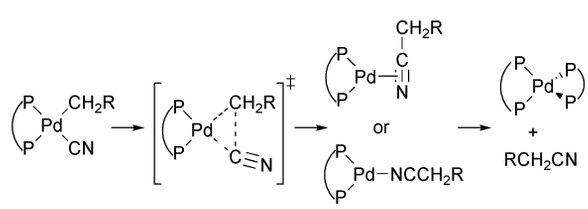
Ligand	β/°	% yield[b]	% branched
DPEphos	101	35–41	88–91
3	105	94–95	97–98
4	106	69–92	96–98
5	109	27–75	96–99
PPh_3	—	0	—
dppe	79	<1	*ca.* 40
dppp	87	4–11	*ca.* 90
dppb	99	3–8	92–95
BINAP	85	4	29

[a] Data from ref. 32. Reaction conditions: styrene/Ni = 28.5, HCN/Ni = 17.5, [Ni] = 73.3 mM, T = 60 °C, t = 18 h. [b] Yields are based on HCN. Maximum yields based on styrene are 61%.

The beneficial effect of the diphosphines with wider bite angles were described as an *electronic bite angle effect*. These diphosphines destabilize square planar geometries, and stabilize the tetrahedral Ni(0) compounds. These facts are reflected in two cooperative effects: the formation of Ni(II) species more resistant to deactivation and a rate increase of the reductive elimination step.

Higher resistance to deactivation. When "common" diphosphines were used (*e.g.* dppe, dppp), the natural bite angles of these ligands (around 90°) stabilize square planar geometries, accelerating the deactivation pathway as was corroborated by the formation of Ni(diphosphine)$(CN)_2$. It can be considered as a negative *electronic (narrow) bite angle effect.* On the other hand, diphosphine ligands showing wider bite angles destabilize square planar geometries. So, dicyano Ni(II) complexes are disfavoured and catalysts more resistant to deactivation are formed.

Enhanced rate of reductive elimination. The use of diphosphines stabilising wider bite angles also produces a clear enhancement in the rate of the reductive elimination (reflected in the overall TOF). A similar increase was previously reported for (diphosphine)Ni$(Me)_2$ where elimination of ethane occurs 50 times faster for dppp than for dppe.[34] Also the reductive elimination of Pd(diphosphine)(Ar)(Me) (diphosphine = dppp or dppf) corroborates this trend,[35] the larger the angle, the easier the elimination. Several studies deal with the elucidation of the origin of this effect and with the mechanism of the reductive elimination step for the hydrocyanation reaction (Scheme 5). In 1998, Moloy[36] studied the rate of reductive elimination of complexes Pd(diphosphine)(R)(CN), (diphosphine = dppe, dppp, DIOP). A 10^4-fold enhancement in the reductive elimination rate with increasing the diphosphine bite angle from dppe (85°) to DIOP (~100°) was observed. The kinetic data obtained pointed to an intramolecular mechanism (zero



Scheme 5 Proposed mechanism for the reductive elimination.

Table 4 Palladium catalysed CO/C_2H_4 copolymerisation. The effect of variation of the chain length, *m*, of bidentate phosphines $Ph_2P(CH_2)_mPPh_2$ [a]

Ligand $Ph_2P(CH_2)_mPPh_2$		Product [c] $H(CH_2CH_2CO)_nOCH_3$	
m	β_n [b]/°	$\bar{n}$	Reaction rate [d]/g (g Pd)$^{-1}$ h^{-1}
1	72	2	1
2	85	100	1000
3	91	180	6000
4	98	45	2300
5		6	1800
6		2	5

[a] Data taken form ref. 48. The reaction was carried out in 150 ml of MeOH with $Pd(MeCN)_2(OTs)_2$, (0.1 mmol), and diphosphine (0.1 mmol); C_2H_4/CO = 1; the temperature was maintained at 84 °C; the pressure was maintained constant at 45 bar. [b] Natural bite angles taken from ref. 10. [c] The averaged degree of polymerisation ($\bar{n}$) determined by end-group analysis from ^{13}C-NMR spectra, except for the low molecular weight products, where a combination of GC and NMR was used. [d] Reaction time was between 1 and 5 h; the rate was the highest measured during the reaction period.

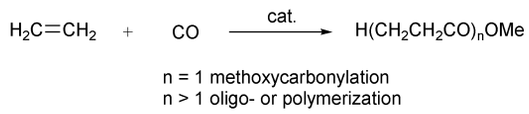
order in diphosphine excess, and first order in Pd(II) complex). This is in contrast with the associative mechanism found by McKinney for monophosphite ligands.[37] A mechanism very similar to migratory insertion of CO into M–C to generate acyl compounds, where the elimination of the coupled product occurs after the transition state is suggested. This is reasonable considering that CO and CN^- are isoelectronic.

According to this mechanism an increase of the P–Pd–P angle produces a complex closer to the transition state compared to the square planar starting compound. It also compresses the C–Pd–C angle forcing the two C atoms closer together, which makes the coupling more favourable. This can be indirectly observed in the structures of the (diphosphine)-$PdCl_2$ (dppe,[38] dppp,[38] diop[39]) where the Cl ··· Cl distances decrease from 3.397 and 3.341 to 3.280 Å. Also, extended Hückel calculations carried out in the model complex $(PH_3)_2$-$Pd(CH_3)(CH{=}CH_2)$ indicated that as the reaction proceeds, the P–Pd–P angle increases so reductive elimination proceeds faster when P–Pd–P is allowed to increase along the reaction coordinate.[40] All these results accord nicely with the hypothesis that the transition state for the reductive elimination has an enhanced P–Pd–P angle. Consequently, the use of diphosphine ligands with wide bite angles increases the reductive elimination rate. Because it is the rate-determining step, this enhance is reflected in the overall activity.

This reaction represents an example in which the *electronic bite angle effect* is the key parameter directing a catalytic reaction. However, one might argue that the crucial experiments in which β_n is kept the same and the steric bulk is varied have not been carried out yet. The similarity of the reductive elimination and the migratory insertion reaction may well point to a steric interpretation of both reactions, even though the electronic bite angle concept prompted us to have a look at hydrocyanation initially. Future experimental and theoretical studies may provide an answer to this.

CO/Ethene copolymerisation

One of the most astonishing manifestations of the dependence of a catalytic reaction on the bite angle of chelating diphosphines is the subtle balance between CO/alkene copolymerisation and alkoxycarbonylation of alkenes (Scheme 6).[7,41] In fact, methyl propanoate (product of the methoxycarbonylation of ethene) is the smallest possible product of the CO/ethene copolymerisation. It is produced when chain transfer occurs immediately after the insertion of just two monomers. Consequently, the selectivity control between copolymerisation and alkoxycarbonylation implies a tuning between chain



Scheme 6 Alkoxycarbonylation and CO/ethene copolymerisation.

propagation and chain transfer rates, which can be directed by modifications in the ligands.

In the late 1940s, Reppe[42] discovered the metal catalysed copolymerisation of ethene/CO. He observed that, in water, $K_2Ni(CN)_4$ produces CO/ethene oligomers together with diethyl ketone and propionic acid.

In 1967, Gough (ICI)[43] reported the first active Pd-phosphine catalyst for CO/ethene copolymerisation. Although the rates were promising, (300 g (g Pd)$^{-1}$ h^{-1}) the harsh conditions required (250 °C, 2000 bar) made it inadequate for commercial applications. In the following years, some related palladium compounds were explored: palladium chlorides, cyanides and zero-valent palladium compounds with a variety of solvents.[44] These new catalysts operate under milder conditions (typically 120 °C, 70 bar), but still low activities and a high quantity of residual palladium in the product were obtained.

A decisive breakthrough took place in the early 1980s. Sen reported that certain Pd(II)–PPh_3 cationic complexes containing weakly coordinating anions (*i.e.* $[Pd(CH_3CN)_4][BF_4]_2{\cdot}nPPh_3$, $n = 1$–3) produce polymers in $CHCl_3$ or CH_2Cl_2 under very mild conditions (25 °C, 4–1.5 bar).[45,46] These new systems evidenced that the use of weakly coordinating anions improve the productivity probably because they create easily accessible coordination sites, which also explains the lower activity obtained when a large excess of PPh_3 was used.

In the same year, Drent (Shell), when studying the alkoxycarbonylation reaction in methanol by using palladium complexes similar to those used by Sen, discovered that replacing the excess of PPh_3 by a stoichiometric amount of diphosphine generates catalysts for the polymerisation reaction that are orders of magnitude faster.[47] Using these complexes, $PdX_2(L–L)$ (L–L being a bidentate phosphorus or nitrogen ligand chelating in a *cis* fashion, X a weakly coordinating anion, and methanol as solvent), perfectly alternating CO/ethene copolymer was produced with only ppm quantities of residual catalyst. Suitable ligands are coordinating diphosphines (*i.e.* dppe, dppp, dppb). The number of carbon atoms in the backbone was shown to have a dramatic influence on the activity and selectivity (see Table 4).[48]

The change of selectivity from alkoxycarbonylation to oligomerisation or polymerisation when changing from monophosphines to chelating diphosphines was first rationalized in terms of what we might call a bite angle effect.[48] With monophosphines, a *trans* orientation of the phosphine ligands is more stable for steric reasons when considering the acyl or alkyl species. Therefore, immediately after an insertion, a fast *cis*–*trans* isomerisation occurs. The new species formed opposes further insertions and chain growth. Thus, the acyl palladium will eventually terminate by alcoholysis of the Pd–acyl bond.[49,50] When *cis* and *trans* isomers occur in equilibrium this is reflected in a tendency to form oligomers.

On the other hand, when diphosphines are used, in which the phosphorus donors are always *cis* to one another (all the

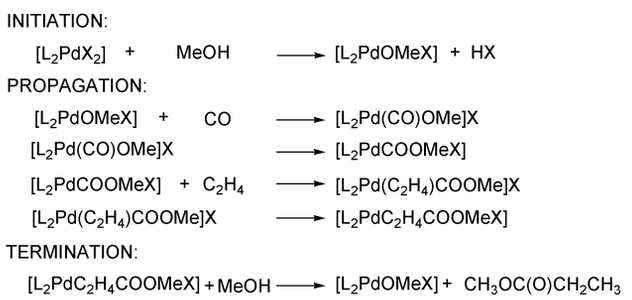
ligands assayed were *cis* coordinating) the growing chain and monomer are in *cis* positions as well, which is the most favourable position for insertion reactions. As a result, diphosphines with natural bite angles close to 90° (dppp) stabilize the transition state for insertion reactions (chain growth), explaining also the higher activity and polymer selectivity of dppp when compared to monophosphines. The trend for the bidentates in Table 4 together with those of other series of diphosphine ligands[51] will be discussed below. The lower activity observed when using bidentates containing four or more atoms in the backbone may in part be due to the higher tendency to form bimetallic complexes having the phosphines in a *trans* disposition.[52]

Nowadays this explanation for the difference between mono- and di-phosphines has to be reconsidered. The recent emergence of new catalytic systems in which other effects can either cooperate or rule against the *bite angle effect* (*vide infra*) evidences that this is not the only parameter controlling the productivity and selectivity in the copolymerisation reaction.

"For a complete understanding all mechanistic aspects need to be taken into consideration: initiation modes; propagation; the perfect alternation; chain transfer, or rather the combined result of initiation and termination as a process of chain transfer; resting states of the catalyst; or dormant states of the catalyst."[7]

Chain transfer mechanisms (initiation–termination)

In the earliest publications[48] it was proposed that the initiation step in both the hydroxycarbonylation and polymerisation reaction involved the reaction of the alcohol with the palladium complex to give the catalytically active palladium methoxy complexes. After chain growing reactions, the termination mechanism was supposed to proceed *via* protonolysis of the alkyl-palladium complex to give the keto-ester product (methyl propanoate or polymer) and regenerate the active catalyst (Scheme 7). In addition hydrido palladium species are smoothly formed from palladium(II) salts in methanol (not shown).[44]

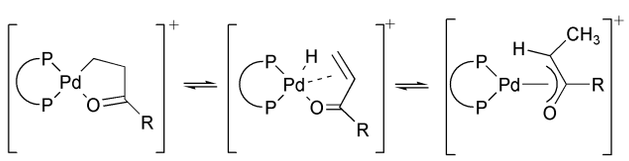


Scheme 7 Mechanism initially proposed for ethene hydroxycarbonylation.

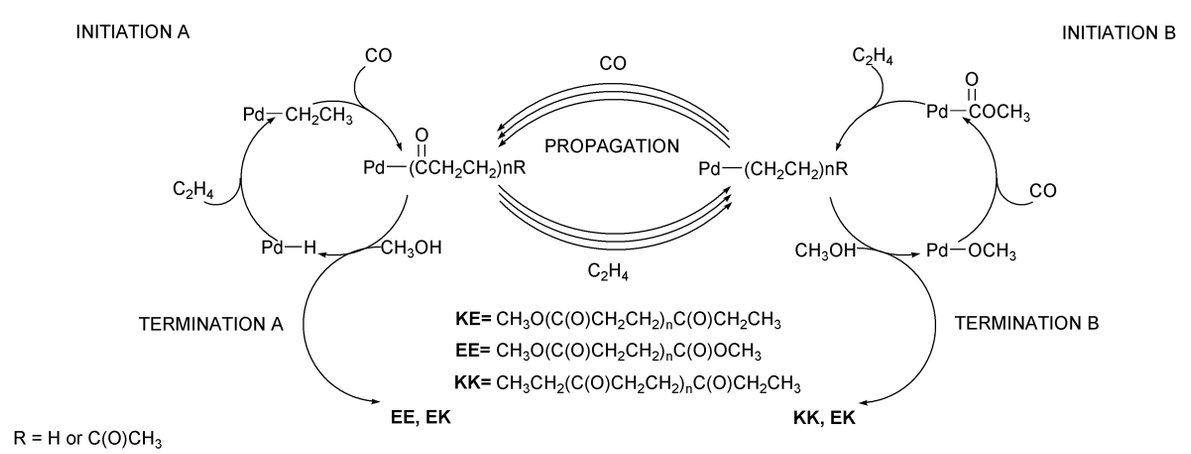
However, an analysis of the oligomeric fractions obtained when using dppb (1,4-diphenylphosphinobutane) showed that although the ratio of ketone/ester ends was close to one, together with the keto-ester (KE) polyketone, products containing diketo (KK) or diester (EE) end groups were also obtained. The appearance of these palindrome products cannot be explained *via* the catalytic cycle mentioned before. If only one chain transfer mechanism is active (one termination releasing the polymer and regenerating the initiation active species) *via* methanol reaction with the palladium-chain compound, in the absence of oxidants or reductants it is not possible to obtain KK or EE products. In order to explain the formation of these products, at least two chain transfer mechanisms must occur simultaneously, one leading to the end group that is obtained as a head group *via* the other mechanism. In fact, two different chain transfer mechanisms A and B (corresponding to Pd-hydride and the Pd-methoxy initiation species) have been proposed (Scheme 8).[48]

In the simplest case (the termination occurs *via* the same mechanism as the initiation) each route leads to KE polymers. The almost complete absence of KK or EE products at lower temperatures indicates that under these conditions one initiation and one termination mechanism dominate, but product analysis is not indicative of which is the head and which the end group. Therefore, without further evidence, it is not possible to determine which is the active chain transfer mechanism.

When both chain transfer mechanisms (A and B) occur at comparable rates, which actually is the case in several catalyst systems, a statistical distribution of chain ends within one molecule is obtained (EE : KE : KK = 1 : 2 : 1). This is so because the growing polymer chain does not "remember" whether it started from a hydride or a methoxy group.[48,53] Studies on the copolymerisation reaction performed using CH_3OD as a solvent showed that the two mechanisms occur simultaneously in the dppp-based catalyst.[54] Both mechanisms lead to $–COCH_2CH_2D$ end groups (either initiation with Pd–D or termination *via* deuteration of Pd-alkyl). However, the high ratio of $–COCHDCH_3$/$–COCH_2CH_2D$ end groups obtained (46/26) cannot be explained by a fast and reversible ethene insertion *via* mechanism A only, and an enolate isomerisation (Scheme 9) of the acyl compound in mechanism B must be invoked as well (β-elimination and reinsertion into the palladium hydride). Consequently, it can be concluded that the two chain transfer mechanisms are competing in the copolymerisation reaction.



Scheme 9 Enolate isomerisation of the ketoalkyl compound.



Scheme 8 Proposed catalytic cycle for CO/ethene polymerisation.

A recent study demonstrated that in fact the termination–initiation mechanism is also dependent on the phase where the catalytic reaction happens. When the growing polymer reaches a length of 13–20 insertions, the polymer with the catalyst attached to it precipitates, and a transition between homogeneous and heterogeneous phase occurs. It was observed that termination in the homogeneous phase takes place predominantly *via* protonolysis, whereas termination in the heterogeneous phase occurs *via* both protonolysis and alcoholysis.[53]

The effect of the bite angle on the termination reaction has been the topic of recent studies in our laboratory. Mechanism B involving the enolate formation is only slightly sensitive to changes in the bidentate ligand (dppe, dppp, dppf) and the reaction is slightly faster for ligands having a wider bite angle.[54]

The effect of the bite angle on termination reaction A has also been studied recently on model acyl-palladium compounds containing a variety of bidentate phosphine ligands.[55] The reaction turned out to be extremely sensitive to the steric properties of the ligand (and therefore also to the bite angle, if ligands with different backbones but equal substituent are considered). The rate of reaction increased several orders of magnitude when the steric bulk of the ligand increased.

Propagation mechanisms

The active species for the propagation mechanism is a palladium complex containing the chelating ligand and the growing polymer. An anion, a solvent, the carbonyl group of the growing chain, or the next monomer to be incorporated can occupy the fourth vacant site. The rate of the insertion reaction is reduced when a strongly coordinating ligand is in this position (*vide supra*).[56,57]

There are two alternating propagation steps, migratory insertion of CO and ethene. Migratory insertion of CO into palladium–alkyl is thought to be rapid and reversible, and insertion of an alkene into an acyl-palladium species represents the thermodynamic driving force of the polymerisation, usually irreversible. It is likely that alkene insertion is the rate-determining step, preceded by competitive coordination with other ligands present, such as CO and methanol.

CO insertion into the Pd–alkyl bond (refs. 52 and 58). This mechanistic step, better described as a nucleophilic attack of the alkyl migrating group to the carbon atom of the co-ordinated carbonyl substrate has been extensively studied. When comparing palladium-methyl complexes of several diphosphines, the calculated rates of CO insertion into the methyl–palladium bond showed that the cationic complexes were one order of magnitude faster than the neutral ones. The reactivity was in both cases dependent on the bite angle, being higher when using dppb or dppp ligands than with dppe. The initial mechanistic explanations were all based on the extended Hückel calculation carried out for the migration reaction by Hoffmann and co-workers.[59] They found that during the migration of the methyl group to the CO or ethene ligand, the ligand residing next to the methyl group will follow the movement of the methyl group, thereby enlarging the bite angle of the diphosphine, in case the remaining sites are occupied by a diphosphine. Actually their statement was that dppe, rigid as it is, would be a poor ligand for complexes undergoing migratory insertions! Sakaki found the same type of stabilisation for related complexes. *Ab initio* calculations on the carbonylation of the Pt–methyl bond in $Pt(CH_3)$-$F(CO)(PH_3)$ with the CO and methyl ligands in relative *cis* positions also showed that the migration of the methyl group was energetically favoured by simultaneous enlargement of the F–Pt–P bond.[60] As mentioned before for the related reductive elimination reaction in the hydrocyanation reaction, this reaction step is favoured when ligands containing large bite angles are used. A larger, flexible P–Pd–P angle will allow one phosphorus ligand to "follow" the migrating methyl moiety on its way to the CO group thus lowering the energy of the transition state. So, flexible bidentate ligands with larger bite angles stabilize the transition state relative to the ground state, which can be considered as an *electronic bite angle effect*.

Later studies carried out at a higher level of theory gave little evidence for such movements of the phosphine ligands during the migration which would lend support to a steric explanation;[61] more steric bulk from the ligand manifold increases the energy of the CO adduct of palladium-methyl and since the TS is less affected, the barrier of insertion becomes effectively lower. This explanation has been brought forward for the increasing rate of insertion of ethene in palladium–alkyl bonds for diimine complexes.[62,63]

Even though these studies show that the bite angle of the ligand strongly influences the rate of CO insertion (or methyl migration) in methyl-Pd complexes, it remains unclear whether this will affect the catalytic process in the same manner as CO insertion is not the rate-limiting step.

Alkene insertion into Pd–acyl and Pd–carbomethoxy (refs. 56 and 58). By comparing the insertion of alkenes into $(L–L)Pd(C(O)CH_3)Cl$ and $[(L–L)Pd(C(O)CH_3)L][CF_3SO_3]$ (L = CH_3CN or PPh_3, L–L = dppp, dppe and dppb) it was demonstrated that whereas the ionic complex reacted with a long variety of alkenes, the neutral acetyl complex underwent insertion only with norbornadiene and norbornene. The cationic carbomethoxy compound $[(L–L)Pd(C(O)OCH_3)(PPh_3)]$-$[CF_3SO_3]$ was also investigated, but it was shown to be less reactive towards alkenes than the analogous acyl derivative. In both cases, after insertion, an intermediate containing intramolecular coordination of the ketone oxygen atom to the palladium centre is formed. This insertion product underwent β-hydrogen elimination to give unsaturated ketones and Pd-hydrides. The rate of this elimination was higher when using small bite angle diphosphines. This is in contrast with our findings on termination reaction B (Scheme 8) referring to the ethene-inserted product, which undergoes a slightly slower β-hydride elimination when the bite angle decreases.[54c]

Especially, when comparing the alkene insertion rates of the complexes containing diphosphines with different bite angles, dppp derivatives showed to be also faster than dppe complexes. The data obtained by Dekker[56] give only a rough indication, because decarbonylation occurred as a side reaction, and when this was prevented by adding CO, clearly a competition between coordination of CO and the alkene plays a role.

Kinetic data for all insertion steps were obtained by Brookhart and co-workers for the (dppp)Pd(II)-based catalyst.[58] Even the acetyl ethene complex has been observed at −135 °C and the rate of insertion was studied at −101 °C. The barrier for ethene insertion into the acetyl group was even lower than that for CO insertion in palladium ethyl carbonyl and palladium methyl carbonyl species. Ethene insertions in palladium alkyl ethene species were the slowest reaction. Insertion reactions are slow compared to substrate-palladium exchange reactions. The preference for alternating insertions is mainly due to the preferred coordination of CO over ethene (10^4), further enhanced by the faster insertion of ethene into acyl palladium species than in alkyl palladium species (10^2), and partly offset by the higher solubility of ethene compared with CO in the medium (~10).

Highly accurate data concerning ligand effects were obtained for the insertion of ethene in methyl-palladium complexes containing a range of diphosphines (*vide infra*).[58] The *electronic bite angle effect*, previously explained in more detail for the CO insertion step was also proposed here to explain the dependence of the rate of ethene insertion into Me–Pd *versus* the diphosphine bite angle. Therefore, the bite angle of

chelating diphosphines might affect both propagation reactions in the same manner.

Steric bite angle effect

Polyketone formation. The remarkable effect that the chain length of the backbone in the chelating ligand exerts on the activity and selectivity in the CO/ethene copolymerisation reaction, already manifested in the early studies,[48] has been the focus of several studies concerning the relationship between bite angle and ligand flexibility and the activity/selectivity of the reaction. More recently, several groups have been concerned about steric modifications of the ligands, and their influence in this reaction.[51,64–67] The striking results obtained evidenced the fact that, although *electronic bite angle effects* play an important role in determining the activity and selectivity in polyketone chemistry, steric effects are also important and they can even overrule electronic effects.

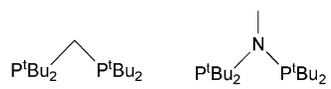
From the results mentioned before, it could be concluded that the dppp backbone (bite angle close to 90°) is decisive in obtaining high molecular weight polymers in CO/ethene copolymerisation due to *electronic bite angle effects*. The use of bdompp (bdompp = 1,3-bis(di(*o*-methoxyphenyl)phosphino)propane) gave a polymer of higher molecular weight than that obtained with dppp.[47,68] This is not easily explained as on the one hand the ligand is somewhat more bulky than dppp, but on the other the hemilabile methoxy groups may participate in the coordination sphere of palladium, the effect of which we do not know. At that point in time it seemed fair to conclude that:[68]

"Nowadays the catalyst selected for the manufacture of Carilon Polymer at commercial scale is Pd(bdompp)X_2. This catalyst is not only more active than the most prominent member of the first generation of CO–ethene copolymerisation catalysts (dppp), but also produces co- and terpolymers with a considerably higher molecular weight."

In conclusion, the ligand chosen by the industry in the early 90s showed a synergism between the *electronic* and *steric bite angle effect*.

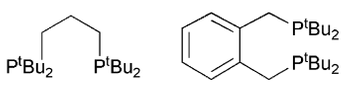
Not only the use of substituents at the phenyl groups at phosphorus, but also the introduction of groups attached to the backbone has been exploited. A study on dppp modified ligands showed that the introduction of alkyl substituents on the 2 position of the propane chain did not improve catalyst performance. In contrast, the productivity increased remarkably when methyl groups were introduced in 1 and 3 positions of the diphosphine ligand, the effect being dependent on the configuration of the stereogenic centres generated.[66] The same effect has been observed for 2,3-substituted dppb derivatives.[64] Thus a slight increase of the steric constraints leads to a faster catalyst, while the length of the backbone and the bite angle remain the same. Some mechanistic studies have also been developed to determine the origin of these steric effects.[64] Although a conclusive explanation is still lacking, it seems clear that β-chelates (with the oxygen of the acyl group occupying a coordination site) are resting states in the catalytic cycle.[69] This observation is in agreement with previous studies (*vide supra*). A possible explanation could involve the opening of the β-chelates *via* a five coordinate transition state constituting the rate-limiting step or a step close to it. This step could be strongly influenced by the steric environment of the metal centre.

For a long time it had been generally accepted that diphosphine ligands containing only one carbon atom in the backbone (dppm derivatives) do not generate active catalysts for CO/ethene oligomerisation or polymerisation (Table 4). An important observation is that ligands **13** and **14** having still larger substituents at phosphorus but a backbone that consists of just one atom gave highly active catalysts producing polymer! Recently it has been reported that several dppm derivatives with various types of bulky groups on the phosphorus atoms form active catalysts for polyketone synthesis, whereas the dppm ligand under the same reaction conditions shows lower productivities.[64] Thus, neither the bite angle nor the flexibility of the backbone is a prerequisite for making a polymer, but instead it would seem that a certain steric bulk around the palladium site is required that tunes the reactivity for insertion and termination reactions, and also reduces the amount of catalyst residing in one of the inactive resting states. The latter is usually neglected, but it surely is of great importance in palladium catalysis.



13 **14**

Methyl propanoate formation. By introducing steric modifications on the ligand maintaining the propane backbone it is possible to radically change the selectivity. It has been established that the use of dtbpp, **15**, a bidentate in which tertiary butyl groups replace the phenyl groups in dppp changes the selectivity of the catalyst completely from polyketone to methyl propanoate.[67] Both the selectivity and the rate were further improved by slightly enlarging the backbone of the catalyst with the use of a xylene moiety, **16**.[70]

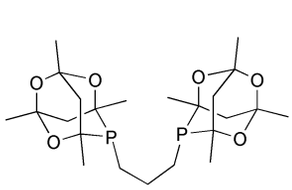


dtbpp dtbpx

15 **16**

From all these results, it can be concluded that the catalyst sensitivity to the chelate ring can be rationalized in terms of *electronic bite angle effect*, but it can be dramatically modified by the presence of bulky substituents on the phosphorus or in the α-positions of the backbone.

In recent years a whole range of bulky bidentate phosphine ligands have been added to the initial two examples all giving methyl propanoate, or mixtures with oligomers, with moderate to high rates (**17**,[71] **18**,[72] **19**,[73] **20**[55]).



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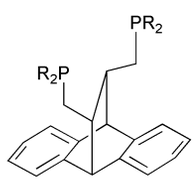
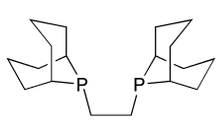


18 PR$_2$ = PPh$_2$, Me$_4$-phospholyl



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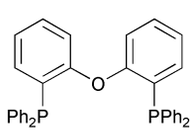

DPEphos

20

Another example in which backbone substitution affords the effect of increasing steric bulk is provided by octamethyl-dppf, carrying eight methyl substituents at the ferrocene rings.[74] While dppf gives oligomers in the methoxycarbonylation/

polyketone reaction (rate 5000 mol mol^{-1} h^{-1}, at 85 °C), octamethyl-dppf gave methyl propanoate. Octamethyl-dppf is sterically more crowded albeit not via substitution directly at the phosphorus atoms, as appears from the P–Pd–P angle, which is 101° as compared to 96° for dppf in the dicationic palladium diaqua adducts. Indeed, octamethyl-dppf gives methyl propanoate in the palladium-catalysed reaction with ethene, CO, and MeOH, albeit at a modest rate (600 mol mol^{-1} h^{-1}, at 85 °C).

DPEphos, **20**, gave methyl propanoate at a rate of 2000 mol mol^{-1} h^{-1}, at 80 °C and 20 bar and an additional 10% of the lowest oligomer.[55] Surprisingly, Xantphos, **5**, gave hardly any activity in this reaction. Xantphos is capable of forming *trans* complexes and these are inactive in this type of catalytic reactions.[8,75,76] Not unexpectedly, since insertion reactions require a *cis* disposition of the migrating group and the unsaturated fragment.

Oligomer formation. When the *tert*-butyl groups are replaced by the smaller *iso*-propyl groups in **15**[67] or **16**[70] both systems gave oligomers as the product instead of methyl propanoate at high rates. When the 1,3-propanediyl bridge in $(t\text{-Bu})_2P(CH_2)_3P(t\text{-Bu})_2$ was replaced by a 1,2-ethanediyl bridge the accessiblity of the catalyst for ethene increases such that in the reaction of ethene, CO, MeOH, and H_2 pentan-3-one was formed at extremely high rates instead of methyl propanoate, the product of the more bulky ligand.[67]

The effect of steric bulk. From the data of the last decade a new picture appears concerning the effect of steric bulk. Clearly, starting from dppe, continuing with dppp and then on with still larger ligands the overall rate of polymer production increases, which can be assigned to a destabilisation of resting states preceding the insertion of ethene, the rate-determining step. However, at a certain point this relationship is broken, perhaps by hampering coordination of ethene altogether to the intermediate palladium-acyl species. Simultaneously the rate of reaction of the acyl species with methanol to form ester increases, as we have observed in stoichiometric reactions of palladium-acetyl complexes.[55] The rate of the alcoholysis reaction increases by orders of magnitude with increasing steric bulk of the ligand. The first insertion of ethene in the methyl propanoate forming reaction is much less sensitive to changes in the ligand bulk, because this takes place at a palladium-hydrido species, as has been proven for a few bidentate ligands[77] and for a few monodentate phosphine catalysts.[49,50,78] This concerns a one-step sequence of mechanism A in Scheme 8.

Previously the formation of methyl propanoate has been associated with *trans* complexes generated by monodentate ligands. Indeed, *trans* acyl complexes are the resting states of these catalytic systems.[41,49,50]

> "In monophosphine systems (compared to *cis* diphosphine systems) the group *trans* to acyl is a solvent molecule and in this case the insertion reactions are slower and the acyl group is more susceptible to nucleophilic attack due to the smaller *trans* influence."[49]

Following this explanation, an "arm-off" mechanism for the strained bidentates such as **15**–**20** could be imagined replacing the phosphine *trans* to acyl also with a solvent molecule. Recent measurements have shown that this is not the case and that the alcoholysis reaction requires *cis* orientation for the acyl group and the alcohol, and thus a *cis* diphosphine.[55] The decisive factor is the steric hindrance exerted by the ligand: the larger the steric bulk, the faster the ester formation. Presumably, for monodentate ligands such as PPh_3 the *trans* complexes undergo an isomerisation to a *cis* complex, which behaves effectively as a complex containing a bulky bidentate, and then the sequence of reactions is terminated by alcoholysis. Thus, we arrive at the conclusion that in both the polymerisation as well as the methoxycarbonylation reaction, all data point to merely steric causes.

Concluding remarks

When we started our work on the Xantphos ligands about a decade ago, our plan was to prepare a series of ligands with a bite angle around 120°, similar to BISBI, but having a backbone that could be easily tuned. The aim was to stabilise trigonal coordination geometries in the isolable complexes at the end or beginning of the catalytic reaction, or as a transition state only. The initial focus was on electronic or orbital effects rather than on steric effects, certainly for the hydroformylation reaction and the hydrocyanation reaction discussed above. The present understanding tells us that *steric effects* or non-bonding interactions between ligand and substrates play a definite role in determining selectivity of rhodium catalysed hydroformylation. On the other hand, the rate in both hydroformylation and in hydrocyanation seems to be affected by *an electronic bite angle effect* within the range of ligands studied.

Many palladium-catalysed reactions have been studied by us and others using also Xantphos type ligands,[7,10] but above we have only reviewed the methoxycarbonylation reaction. In palladium chemistry it turned out that Xantphos can also act as a *trans* ligand, with or without the participation of the oxygen atom in the coordination of the metal.[8,75,76] Recently we have extended the range of ligands with one that coordinates in a *trans* fashion only (so far!), which extends our mechanistic tools.[79]

Initially, in the polyketone catalysis, the prevailing concept was that of a flexible, wide bite-angle backbone accelerating migration reactions. Many recent findings have taught us that the key parameter is the total steric bulk provided by the *cis* diphosphine.[64] Alcoholysis of an intermediate palladium acyl species is greatly accelerated when even larger steric bulk is applied, notably in *cis* complexes.

We realise that in practice palladium carbonylation catalysis is even more complicated than the picture we have sketched above. Drent[41,80] has demonstrated the effect of many more ligands, anions, hydrogen, oxidising agents, *etc*. on the course and rate of these catalytic systems. For other substrates such as styrene, higher alkenes, and butadiene, the rules of the game may be very different; understanding them a little bit makes the discoveries even more exciting.

Acknowledgements

The authors 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. Z. F. is also grateful to the Netherlands' Research School Combination—Catalysis for financial support.

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