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Bite angle effect of bidentate P–N ligands in palladium catalysed allylic alkylation †

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Two series of new bidentate P–N ligands have been synthesized. Application of these ligands in the palladium catalysed allylic alkylation of crotyl chloride and cinnamyl chloride leads to the preferential formation of the branched product. A larger bite angle of the ligand leads to higher regioselectivity. Stoichiometric alkylation of the complex $[Pd(C_4H_7)\{p\text{-}MeOC_6H_4C{=}N(CH_2)_4OPPh_2\}][O_3SCF_3]$ proceeds with 88% regioselectivity to the branched product.

Introduction

A tremendous research effort has been devoted to the enantioselective alkylation of symmetrically disubstituted allylic substrates, such as 3-acetoxy-1,3-diphenyl-1-propene and cyclohex-2-enyl acetate[1–3] using malonate nucleophiles. In the case of non-symmetrically *mono*substituted substrates, *e.g.* crotyl acetate (but-2-enyl acetate) or cinnamyl acetate (3-phenylprop-2-enyl acetate), regiocontrol is a prerequisite for enantiocontrol.[4] Palladium complexes have a preference for the formation of the linear, achiral product.[5] Excellent regio- and enantio-selectivities[6] have been obtained using metals other than palladium such as iridium,[6a] rhodium,[6b] iron[6c] and tungsten.[4a,6d]

Recently it was shown that, by careful ligand design, palladium can also show a preference for the branched, chiral product. Up to 96% regioselectivity to the formation of the branched, chiral product was obtained for cinnamyl acetate.[4b] Very high enantioselectivities have been found using phosphinooxazoline ligands (Pfaltz,[4a,b] Williams[4e,f]) and the MAP ligand (*R*(−)-2-(dimethylamino)-2′-(diphenylphosphino)-1,1′-binaphthyl, Kocovsky[4c,g]). The phosphinooxazoline ligands contain a soft phosphorus donor atom and a relatively hard nitrogen donor atom. It has been established that in the corresponding (allyl)palladium complex the nucleophilic attack takes place at the allylic carbon atom *trans* to phosphorus.[1,4,7] In the case of monosubstituted substrates it is therefore essential that the substituted allylic carbon atom is bound *trans* to phosphorus. In the above mentioned phosphinooxazoline ligands the steric bulk of the nitrogen donor is much smaller than that of the phosphorus donor. A substituent on the allyl moiety will therefore encounter less steric hindrance when it is positioned *cis* to the nitrogen donor ligand.

Apart from these steric reasons, the electronic difference between phosphorus and nitrogen also plays a role.[1,4,7] Although the allyl moiety remains bonded *via* all three carbon atoms in a covalent manner,[8] the presence of a substituent on one of the terminal positions distorts its symmetry.[9b] The allylic carbon–carbon bond next to the substituent (C3–C2) will show more double bond character than the other allylic carbon–carbon bond (C1–C2). As a consequence, the bonding between palladium and the substituted allyl will be distorted to a π(to C2–C3)–σ(to C1–C2) type complex. Since phosphorus exerts a stronger *trans* influence than nitrogen, the Pd–allyl bond *trans* to phosphorus is weakened. As a result, the allylic C–C bond *trans* to phosphorus has more double bond character. Thus σ(C1–C2) will be found *cis* to phosphorus and π(C2–C3) *trans* to phosphorus. The preference for nucleophilic attack on the allylic carbon atom *trans* to phosphorus is therefore caused both by steric and electronic effects (see Fig. 1).

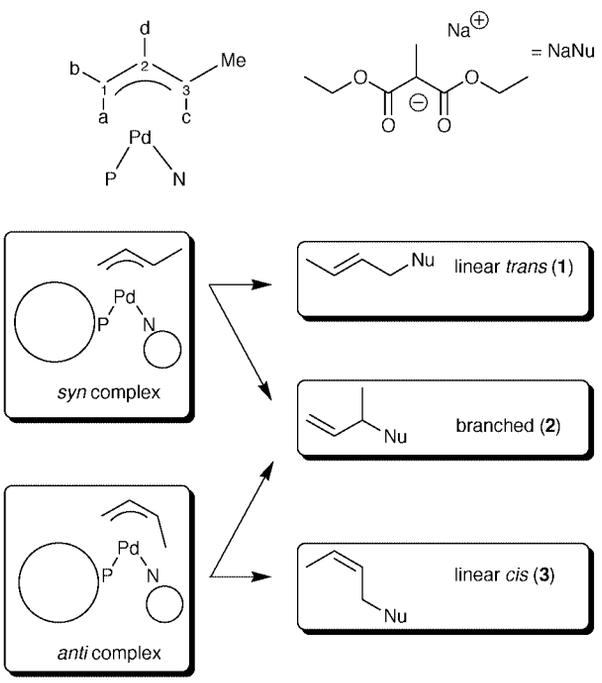

Fig. 1 Regioselectivity in the palladium catalysed allylic alkylation.

Part of our own work in the field of allylic alkylation[5] has been concerned with the effect of the bite angle of achiral, symmetric bidentate phosphine ligands on the regioselectivity.[5a,b] It was found that a larger bite angle of the ligand results in 100% formation of the linear, non-chiral product for *trans*-hex-2-enyl acetate. We now report on the remarkable, opposite effect of the bite angle of bidentate P–N ligands on the regioselectivity of the alkylation of non-symmetrically substituted

† Electronic supplementary information (ESI) available: characterisation data. See http://www.rsc.org/suppdata/dt/b0/b001355m/

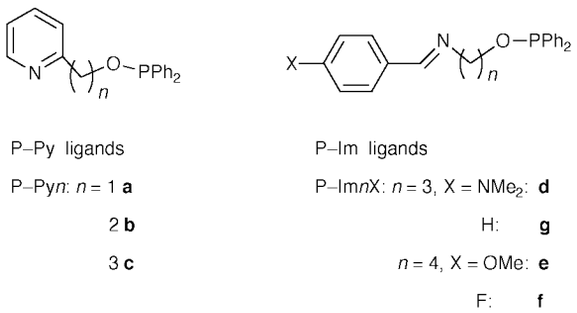

Fig. 2 Generic structures of two new classes of P–N ligands.

allyl moieties. In this study the (allyl)palladium complexes bearing new P–N ligands are synthesized and characterized. The exact orientation of the substituent on the allyl group is established by means of NMR spectroscopy. Use of the complexes in the stoichiometric and the catalytic alkylation shows a pronounced effect of the counter ion of the cationic (allyl)-(ligand)palladium complex.

Results

Ligand synthesis

We have prepared two series of mixed phosphorus–nitrogen ligands. One series of ligands consists of a Ph_2PO unit that is connected to an *ortho* substituted pyridine moiety *via* an alkyl chain of variable length (P–Py ligands (**a**–**c**); the generic structure is given in Fig. 2). By changing the length of the alkyl chain the bite angle of the ligand can be tuned. Another class of ligands (**d**–**g**) is based on the same phosphorus unit, with an alkyl group of variable length linked to an imine moiety (see Fig. 2). At the *para* position of the imine moiety a substituent was introduced. By changing this substituent the electronic properties of the ligand can be tuned. The P–Py type ligands (**a**–**c**) were conveniently prepared by coupling Ph_2PCl to *o*-$NC_5H_4(CH_2)_nOH$ in the presence of NEt_3. The P–Im class of ligands (**d**–**g**) were synthesized in two steps. The imine was synthesized according to a literature procedure[10] by condensation of the *para*-substituted aldehyde with $H_2N(CH_2)_nOH$ ($n = 3$ or 4), followed by coupling to Ph_2PCl.

Synthesis and structures of Pd(allyl)(P–N)X complexes

We have prepared cationic crotyl and cinnamyl palladium complexes of these new ligands by reaction of the appropriate ligand with the $[(C_4H_7$ or $C_9H_9)PdCl]_2$ dimer,[11] followed by chloride abstraction with silver triflate. Using these P–N ligands, four isomeric complexes can be formed: the substituent can be oriented either *syn* or *anti* with respect to Hd and *cis* or *trans* to the phosphorus atom (see Fig. 3). The value of the coupling constant ($^4J_{(P–CH3)}$) is diagnostic for the orientation of the substituent, enabling elucidation of the structure of the complexes.[5b] The value of the coupling constant of the *syn* oriented CH_3 groups with a *trans* phosphorus atom is around 10–12 Hz ($^4J_{(P–CH3)}$). Both a *cis* orientation with respect to phosphorus and an *anti* orientation with respect to Hd would result in a lower value of $^4J_{(P–CH3)}$ (around 6 Hz). When ligand **a** is used all four isomers of the $(C_4H_7)Pd$(**a**) complex are formed. The *syn-trans*-P isomer predominates over the other isomers (>90%). When the substituent is a phenyl rather than a methyl group the amount of *syn-trans*-P isomer exceeds 97%. The minor isomer (<3%) could not be identified by NMR. Based on the results of allylic alkylation (see below) we assign the minor signal to the *anti-trans*-P isomer.

It was concluded from ^{31}P and ^1H NMR spectroscopy that the bite angle of the ligand has an effect on the isomer distribution. Use of the ligand **b** or **c**, having a large bite angle, results in almost exclusive formation (>97%) of the *syn-trans*-P isomer of

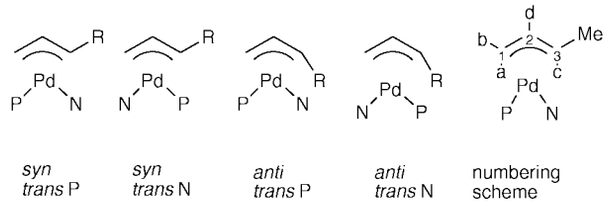

Fig. 3 Possible isomeric structures of cationic $(C_4H_7)Pd$(P–N) complexes.

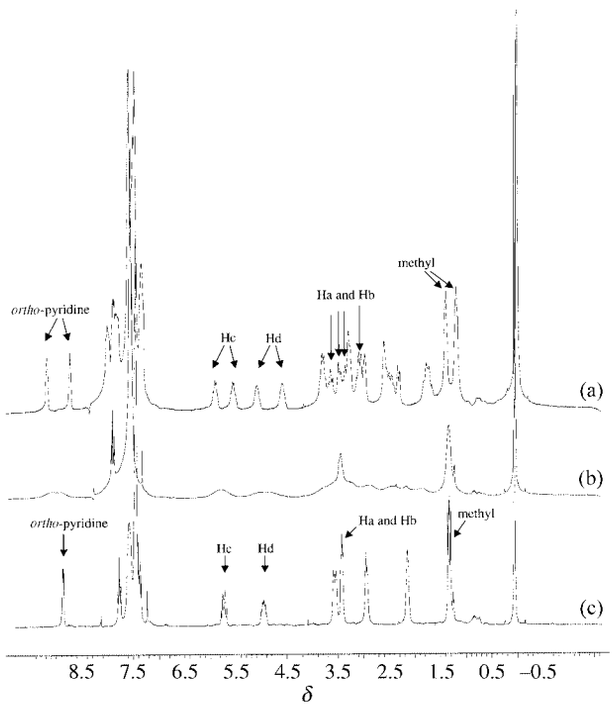

Fig. 4 Variable temperature NMR spectra of cationic $(C_4H_7)Pd$(**c**) at 218 (a), 273 (b) and 328 K (c), recorded in $CDCl_3$.

the crotyl and cinnamyl complexes. When the ligand with the smallest bite angle is used (**a**), only 81% of the *syn-trans*-P isomer is formed, with the *anti-trans*-P complex (14%) as the other main isomer. The remaining signals (4 and 1%) are ascribed to the *syn-trans*-N and the *anti-trans*-N isomer.

In general, the signals in the ^1H NMR spectra (at 298 K) are relatively broad, which is indicative of a dynamic exchange process. As it is crucial to determine the orientation of the substituent on the allyl moiety, we conducted variable temperature NMR experiments with the cationic $(C_4H_7)Pd$(**c**) complex (Fig. 4). The fast exchange limit is reached at +55 (c) and at −55 °C (a) the slow exchange limit is almost reached.[12] All signals in the fast exchange spectrum decoalesce into two signals when going to lower temperatures. At −55 °C the value of $^4J_{(P–CH3)}$ could not be determined exactly, but was approximately the same as in the fast exchange limit.

In order to gain more insight we have prepared the imine based ligand **g**, that differs from ligand **c** only in the nature of the nitrogen donor group. The crotyl complex of ligand **g** shows the same type of fluxional behaviour as the analogous complex of ligand **c**. A low temperature (−25 °C) spectrum recorded for the complex of ligand **g** shows that in the slow exchange regime the methyl groups of both isomers have the same coupling constant ($^4J_{(P–CH3)}$). This indicates that both isomers have the methyl group in a *syn* orientation. The spectra of all complexes ligated with the imine type ligands show the presence of two structures. All are identified as *syn-trans*-P complexes.

The value for $^4J_{(P–CH3)}$ in the fast exchange spectrum of the complex of ligand **c** is the same as in the slow exchange spectrum of the complex of ligand **g**. Apart from the value for

Table 1 Stoichiometric alkylation of $(C_4H_7)Pd(P–N)OTf$ complexes (OTf = O_3SCF_3)

Entry	Ligand	% Branched	% *trans*	% *cis*
1	**a**	37.2	56.1	6.7
2	**b**	65.6	31.0	3.4
3	**c**	79.0	18.2	2.8
4	**d**	84.1	14.2	1.7
5	**e**	88.0	10.9	1.1
6	**f**	79.8	17.9	2.3

Table 2 Stoichiometric alkylation of $(C_9H_9)Pd(P–N)OTf$ complexes

Entry	Ligand	% Branched	% *trans*
1	**a**	43.7	56.3
2	**b**	67.5	32.5
3	**c**	77.8	22.2
4	**d**	75.3	24.7
5	**e**	78.4	21.6
6	**f**	81.8	18.2

$^4J_{(P–CH3)}$, the chemical shift of the CH_3 group for all complexes > 1.3 ppm, is also indicative of a *trans*-P orientation. A *trans*-N orientation of the methyl group would result in a signal at higher field (<0.6 ppm).[13e,f]

Apart from the splitting of all signals, it can be seen that at +55 °C the allylic protons Ha and Hb are in a fast exchange. At low temperature (−55 °C), the one, averaged signal of these two protons is not split into only two, but into four signals, two for each proton. The signals of the *ortho*-pyridine proton are separated from the rest of the signals and were used to obtain rate data by simulation of the spectra.[14] The Eyring plot shows that the rate of exchange is linearly dependent on the reciprocal temperature: $-\ln (k/T) = -33 + 7 \times 10^3\ T^{-1}$. From this it follows that $\Delta H^{\ddagger} = 60$ kJ mol^{-1} and $\Delta S^{\ddagger} = 34$ J K^{-1} mol^{-1}.

Stoichiometric alkylation

The results of the stoichiometric alkylation of these complexes with sodium diethyl 2-methylmalonate are presented in Tables 1 and 2 (see also Fig. 1). Reaction of the crotyl complex provided mainly the linear *trans* and the branched product. The linear *cis* product is formed in only minor amounts (up to 7%). When the bridge length and consequently the bite angle of the ligand are larger, the regioselectivity to the branched product of the stoichiometric alkylation increases, up to 79% for ligand **c**.

If the substituent on the allyl moiety is a bulkier phenyl rather than a methyl group only two products are observed: the linear *trans* and the branched product. Again the ligands with a larger bite angle direct the regioselectivity towards the preferential formation of the branched product up to 78% (ligand **c**). There is no significant change in regioselectivity when neutral instead of cationic complexes are used (entry 4).

Tables 1 and 2 show that the regioselectivity of stoichiometric alkylation of the complexes ligated with imine based ligands (**d**–**f**) is similar to that obtained using the pyridine based ligands (**a**–**c**). For the crotyl complexes, the highest regioselectivity is found for methoxy substituted ligand **e**, which gives 88% of the branched product, whereas for cinnamyl complexes the highest regioselectivity (82%) is found using the fluoro substituted ligand **f**.

Catalytic alkylation and kinetics

We have studied the catalytic alkylation of crotyl chloride (*trans*-but-2-enyl chloride) and cinnamyl chloride (*trans*-3-phenylprop-2-enyl chloride) using the corresponding (allylpalladium) complex as the catalyst. Also in the catalytic reactions, the regioselectivity for the branched product increases when the bite angle of the pyridine based ligands is larger (entries 1–3, Tables 3 and 4). The branched : linear ratio obtained in the catalytic reactions, however, is lower than that found for the stoichiometric reactions.

Table 3 Catalytic alkylation of crotyl chloride

Entry	Ligand	TOF after 5 min/mol mol^{-1} h^{-1}	% Branched	% *trans*	% *cis*
1	**a**	1000	33.3	58.6	8.1
2	**b**	200	41.7	49.6	8.7
3	**c**	1000	55.1	37.8	7.1
4	**d**	900	52.3	39.0	8.7
5	**e**	300	50	41	9
6	**f**	200	33	57	10

Table 4 Catalytic alkylation of cinnamyl chloride

Entry	Ligand	TOF after 5 min mol mol^{-1} h^{-1}	% Branched	% *trans*
1	**a**	2700	29.4	70.6
2	**b**	1700	26.7	73.3
3	**c**	2800	56.9	43.1
4	**d**	7300	22.5	77.5
5	**e**	3000	31.5	68.5
6	**f**	3500	13	87

Table 5 Regioselectivity in the catalytic alkylation of crotyl acetate[a]

Entry	Complex (ligand/Pd)[b]	% Branched	% *trans*	% *cis*
1	**a** (1)	29.6	62.3	8.0
2[b]	**a** (3)	29.2	63.1	7.7
3[b]	**a** (4)	24.5	68.3	7.2
4	**b** (1)	24.5	64.6	10.9
5	**b** (1) 20 equivalents LiBr/Pd	50.4	44.0	5.6
6[b]	**b** (1.5)	19.3	77.5	3.2
7[b]	**b** (2)	13.9	84.1	2.0
8	**c** (1)	29.1	59.6	11.3

[a] After 24 hours quantitative conversion was reached. Initial reaction rates were not determined. [b] Extra ligand was added from a stock solution to the isolated complex.

The alkylation of allylic acetates compared to chlorides resulted in a significant decrease of the regioselectivity towards the branched product: from 56.9% for crotyl chloride to 24.5% for crotyl acetate (see Table 5). Addition of extra halide (LiBr) to the reaction mixture containing crotyl acetate restored the regioselectivity to a value of 50.4%.

When extra ligand was added to the isolated complexes a sharp decrease in regioselectivity was observed (Tables 5 and 6). The addition of two extra equivalents of ligand **b** resulted in the formation of only 6% of the branched product (entry 7, Table 6). The effect is more pronounced for the ligand having the longer bridge length (ligand **b** *versus* **a**). This product distribution is similar to that obtained with the bidentate phosphine ligand dppe (entry 9, Table 6).[15]

Kinetic experiments on the catalytic alkylation of cinnamyl chloride using the ligand **c** were performed by variation of the concentrations of palladium, diethyl 2-methylmalonate and cinnamyl chloride. The reactions were monitored with GC. The alkylation reaction proceeds with a zeroth order dependency on the concentration of cinnamyl chloride, and a first order dependency on both the malonate anion and the palladium complex.

Table 6 Regioselectivity in the catalytic alkylation of cinnamyl acetate[a]

Entry	Complex (ligand/Pd)[b]	% Branched	% *trans*
1	**a** (1)	33.0	67.0
2[b]	**a** (2)	22.4	77.6
3[b]	**a** (3)	22.3	77.7
4[b]	**a** (4)	5.9	94.1
5	**b** (1)	21.5	78.5
6[b]	**b** (2)	7.7	92.3
7[b]	**b** (3)	5.9	94.4
8	**c** (1)	39.1	60.9
9	dppe[c]	4.7	95.3

[a] After 24 hours quantitative conversion was reached. Initial reaction rates were not determined. [b] Extra ligand was added from a stock solution to the isolated complex. [c] 1,2-Bis(diphenylphosphino)ethane.

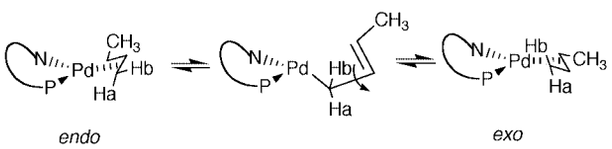

Fig. 5 Dynamic exchange of *endo* and *exo* isomers in cationic (C_4H_7)Pd(P–N) complexes *via* π–σ–π rearrangement.

Discussion

Structures of the complexes

The ^{1}H NMR spectra showed that all complexes exhibit dynamic behaviour at room temperature. Variable temperature NMR spectroscopy of the complex bearing ligand **c** showed that the observed exchange process does not involve the *syn-trans*-P and one of the other isomers of the types *syn-trans*-N, *anti-trans*-P or *anti-trans*-N. Surprisingly, the two different isomers that were observed under the slow exchange conditions are both identified as a *syn-trans*-P isomer. The two isomers are proposed to be conformers differing in the orientation of the ligand backbone, which can be either up (*endo*) or down (*exo*) with respect to the orientation of the allyl moiety.

The protons Ha and Hb (see Fig. 1) are in fast exchange at +55 °C, *via* the π–σ–π rearrangement[13] of the allyl moiety, one averaged signal being observed. This one signal is split into two signals for each proton at −55 °C. The fluxional behaviour is thus caused by a selective π–σ–π isomerization, during which the Pd–allyl bond *trans* to phosphorus is broken. The *syn-trans*-P structure is retained during this rearrangement, but the orientation has changed from *endo* to *exo* or *vice versa* (see Fig. 5). Thus, the dynamic exchange between the *endo* and the *exo* form of the complex is a result of the π–σ–π rearrangement of the allyl moiety and not of other processes such as flipping of the backbone.

The partial deco-ordination of the allylic moiety during this process accounts for the observed positive $\Delta S^{\ddagger}$ value. The values of the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ correspond to literature values for the π–σ–π rearrangement.[13e]

Stoichiometric alkylation

As expected, the *syn-trans*-P isomeric form of the cationic $(C_4H_7$ or $C_9H_9)$Pd(P–N) complexes is the main isomer present in solution. The NMR spectra show that for a small methyl substituent there is 3% of the *anti-trans*-P isomer present. The study of the dynamic behaviour shows that there is no isomerization from the *syn* to the *anti* isomer on the NMR timescale. The 3% linear *cis* product that is found (Table 1) corresponds with the 3% *anti-trans*-P isomer that is present. When the substituent is a larger phenyl group only the *syn-trans*-P isomer is observed. This is also reflected in the absence of the linear *cis* product in the alkylation reactions (Table 2). VT-NMR experiments show that the cationic complexes do not interconvert between the different isomers.

The regioselectivities found for the stoichiometric reactions therefore indicate that the nucleophilic attack takes place *trans* to the phosphorus atom, having a larger *trans* influence. This observation is in agreement with a model, recently presented in the literature, in which it is predicted that the regioselectivity for the branched product is higher when the non-symmetry of the allyl moiety is enhanced.[9] Substitution of the imine at the *para* position with an electron donating group, such as a methoxy (**e**) or a dimethylamino (**d**) group, will increase the non-symmetry of the allyl. The results in Tables 1 and 2 show that this is indeed the case, both for bridge length 3 and 4. The regioselectivity towards the branched product can be increased to a value of 88% for the methoxy substituted ligand (**e**).

The regioselectivity for the branched product increases when going from a small bite angle (ligand **a**) to a larger bite angle (ligand **c**). This is observed both for the crotyl and the cinnamyl complexes. The regioselectivities obtained using P–N type ligands may therefore be related to the non-symmetry of the allyl moiety. The substituted allylic carbon atom C3 is more electrophilic than C1 and becomes even more electrophilic when the bite angle is larger.

For cinnamyl complexes, the difference between the regioselectivity obtained with the fluoro substituted ligand **f** and the methoxy substituted ligand **e** is smaller than for the corresponding crotyl complexes. The regioselectivity obtained using ligand **f** is slightly higher than that obtained using ligand **e**. Since these observations cannot be explained in terms of electronic non-symmetry of the allyl moiety only, it is concluded that in this case either steric or other secondary interactions, such as π–π stacking, can play a role.[16]

Catalytic alkylation, kinetics

The regioselectivity found for the catalytic reactions is lower than that found for the stoichiometric reactions. This can be explained as follows. After oxidative addition of the substrate two types of isomeric palladium complexes can be formed: one type having the substituent oriented *trans* to the phosphorus atom and one type having the substituent oriented *trans* to the nitrogen atom. The *syn-trans*-P isomer is thermodynamically favoured and the *syn-trans*-N will isomerize to the more stable *syn-trans*-P isomer. This isomerization is facilitated by strongly co-ordinating counter ions, such as chloride, which is the leaving group in the catalytic reactions (Tables 3 and 4).[13]

If the subsequent alkylation step is slow relative to isomerization (*trans*-N to *trans*-P), the product distribution will be determined by the *syn-trans*-P isomer only and therefore will be equal to the regioselectivity in the stoichiometric alkylation. If the alkylation, however, occurs at a rate similar to or faster than the rate of isomerization, the observed regioselectivity is determined by the isomer ratio formed, their rate of isomerization and their respective rates of alkylation. Since nucleophilic attack will primarily take place at the carbon atom *trans* to phosphorus, alkylation of the *syn-trans*-N isomer will yield relatively large amounts of the linear *trans* product. This explanation in terms of competition between isomerization and alkylation is supported by the results of the catalytic alkylation of both crotyl and cinnamyl acetate. The acetate anion co-ordinates not as strongly to the palladium centre as the chloride anion. It was shown that a co-ordinating anion facilitates dynamic behaviour of the allyl moiety.[13d,e] It has indeed been found that the regioselectivity is lower when acetate is the leaving group (and therefore also the counter ion (Table 6)). The influence of a co-ordinating anion is further shown by addition of LiBr to the crotyl acetate reaction mixture (Br^- replaces OAc^-: entry 5, Table 5). In this case the regioselectivity is similar to that obtained using crotyl chloride.

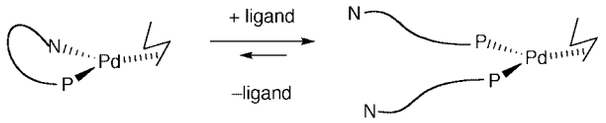

Fig. 6 Proposed formation of bis-phosphine co-ordinated complexes by addition of extra ligand to cationic (C_4H_7 or C_9H_9)Pd(P–N) complexes.

The catalytic intermediates used as precursors in the catalytic experiments contain only one ligand per palladium atom. In Tables 5 and 6 it is shown that the addition of extra ligand to the isolated complex causes a significant change in regioselectivity. The resulting regioselectivity is similar to that obtained when bidentate phosphine ligands are used (entry 9, Table 6). When extra ligand is present it is plausible that two ligands are co-ordinated to palladium, both *via* the phosphorus atom (Fig. 6). The system then behaves as a bidentate phosphine ligand.

Kinetic experiments on the alkylation of cinnamyl chloride, using (C_9H_9)Pd(**c**)OTf as the catalyst, show that the rate of reaction is independent of the cinnamyl chloride concentration and that it is linearly dependent on the concentration of both the malonate anion and the palladium complex. This indicates that the nucleophilic attack is the rate determining step of the reaction.

Although palladium allyl complexes have been studied in great detail, little is known about the influence of the properties of ion pairs, which seem to be important for this chemistry. It has been reported that solvent polarity can have an effect on the outcome of enantioselective alkylation reactions.[2h] Currently, we are studying the effect of polarity effects on the *regio*-selectivity of the alkylation reaction.[5d]

Conclusion

In conclusion, we have shown that mixed bidentate P–N ligands with a large bite angle direct the regioselectivity to the formation of the branched product. Since the nitrogen donor atom is incorporated in a small pyridine group the effect is electronic in nature. This is in contrast with our previous results concerning the effect of the bite angle of bidentate phosphine ligands, which could be explained in terms of steric hindrance.[5a,b] Thus, the effect of a larger bite angle on the regioselectivity has a steric component (leading to more linear product) and an electronic component (leading to more branched product).

Therefore we conclude that for a rational design of ligands that favour the formation of the branched product the following parameters are of importance: (1) relative donor–acceptor strength of the ligand donor atoms; (2) steric hindrance in the transition state; (3) bite angle of the ligand.

Experimental

^{1}H (300 MHz, TMS, $CDCl_3$), ^{31}P-{^{1}H} (121.5 MHz external 85% H_3PO_4, $CDCl_3$) and ^{13}C NMR (75.4 MHz, TMS, $CDCl_3$) were recorded on a Bruker AMX-300 spectrometer. Elemental analyses were performed on an Elementar Vario EL apparatus (Foss Electric). The product distribution of the alkylation experiments was measured on an Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 μm, and a flame ionization detector.

All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use. Crotyl chloride, cinnamyl chloride, benzaldehyde, 4-fluorobenzaldehyde, 4-dimethylaminobenzaldehyde, 4-methoxybenzaldehyde, 3-aminopropanol, 4-aminobutanol, diethyl 2-methylmalonate, NaH, AgOTf and $PdCl_2$ were obtained from Aldrich. Crotyl chloride and the aldehydes were distilled prior to use.

General synthetic procedures

Sodium diethyl 2-methylmalonate (0.5 M in THF) was prepared from diethyl 2-methylmalonate and NaH in THF at 273 K. The dimers [Pd(C_4H_7)(μ-Cl)]$_2$ and [Pd(C_9H_9)(μ-Cl)]$_2$ were prepared following a literature procedure.[11] The synthesis and characterization of [Pd(dppe)(C_4H_7)]OTf,[5b] crotyl acetate[5b] and the alkylation products of the coupling of crotyl acetate to sodium diethyl 2-methylmalonate are described elsewhere.[13e]

The P–Py type ligands (**a**–**c**) were prepared *via* condensation of 2-pyridine-methanol (P–Py1 (**a**)), -ethanol (P–Py2 (**b**)) and -propanol (P–Py3 (**c**)) with Ph_2PCl in the presence of an excess of NEt_3. The alcohol and NEt_3 were dissolved in diethyl ether and cooled to 0 °C, after which a solution of Ph_2PCl in diethyl ether was added dropwise. A white precipitate was formed (NEt_3·HCl). After filtration the reaction volume was concentrated under reduced pressure. Flash chromatography (silica) of this residue yielded the ligand as a colourless oil, in a yield of around 70%, based on Ph_2PCl.

The P–Im type ligands (**d**–**g**) were synthesized using a similar procedure, but required as an extra step the synthesis of the imine alcohol.[10] In a typical procedure, the aldehyde was dissolved in toluene and the α- to ω-aminoalcohol was added in one portion. The equilibrium of this condensation reaction was directed towards the imine alcohol by removing the water formed with dehydrated K_2CO_3. After stirring for 12 hours the reaction was complete and after filtration the solvent was removed by evaporation. The alcohol was then coupled to Ph_2PCl using the same procedure as for the P–Py type ligands. As a side reaction, cyclization of the imine took place.[10] This could only be prevented by the presence of an excess of the aldehyde. It should be noted that especially aldehydes bearing electron withdrawing substituents required this excess. The aminoalcohol could be quantitatively converted into the corresponding imine. The mixture of imine and aldehyde (colourless oil) was used as such in the coupling to Ph_2PCl. The aldehyde–ligand mixture (colourless oil) was then used in the synthesis of the corresponding (allyl)palladium complexes.

The oily ligand (1.0 equivalent) was weighed in a Schlenk Vessel and dissolved in 10 mL of CH_2Cl_2. To this mixture a solution of exactly 0.5 equivalent of the [Pd(C_4H_7)(μ-Cl)]$_2$ or [Pd(C_9H_9)(μ-Cl)]$_2$ dimer was added (dissolved in 10 mL of CH_2Cl_2). The solution changed from colourless to bright yellow instantaneously. After stirring for 15 minutes, exactly 1.0 equivalent of AgOTf was added. Immediately, a white precipitate was formed and the solution changed to light yellow. After filtration over Celite, the solvent was removed *in vacuo*. After this step, the excess of aldehyde could be removed by repetitive washing with either pentane or benzene. All palladium complexes were isolated as a white microcrystalline powder in *ca.* 90% yield based on palladium and were used in the alkylation reaction.

Alkylation reactions

The stoichiometric alkylation reactions were performed at room temperature (292 K) by adding an excess of sodium diethyl 2-methylmalonate (0.1 ml of a 0.5 M solution in THF) to a solution of 10 mg of the palladium complex in 1 ml of THF. Reaction was instantaneous and after one minute the mixture was worked up with water, filtered over silica and analysed by GC.

The catalytic reactions were performed at room temperature (292 K) in THF (5 mL), using 0.05 mol% of catalyst (0.25 μmol), 0.5 mmol of substrate and 1.0 mmol of sodium diethyl 2-methylmalonate. The reaction was monitored by taking samples from the reaction mixture which, after aqueous work-up, were analysed by GC using decane as the internal standard.

The kinetic experiments were performed using stock solutions of all reaction components. The amount of each reagent was, one at a time, varied by changing the amount of stock

solution added. The amount of catalyst was varied from 0.000625 to 0.0200 mmol, the amount of cinnamyl chloride from 0.125 to 1.000 mmol and the amount of malonate from 0.200 to 2.000 mmol.

NMR data were obtained in $CDCl_3$ (δ in ppm), IR recorded in CH_2Cl_2. Complete analytical data of the compounds presented in this paper are available as supporting information.†

Pd(P–Py1 (**a**))(C_4H_7)[SO_3CF_3]: δ_H (*syn-trans*-P isomer) 1.83 (d, $J1 = 6.2$, $J2 = 10.6$, 3 H (Me)); 3.21 (hump, 2 H (Ha and Hb)); 5.05 (m, 1 H (Hc)); 5.16 (d, $J = 21.9$ Hz, 2 H ($POCH_2$)); 5.75 (dt, $J1 = J2 = 9.4$, $J = 13.2$, 1 H (Hd)); 7.5 (m, 10 H (Ar)); 7.63 (t, $J = 7.4$, 1 H (*m*-H of pyridine) (NCHC*H*)); 7.65 (d, $J = 7.4$, 1 H (*m*-H of pyridine) (NCC*H*)); 7.95 (t, $J = 7.4$, 1 H (*p*-H of pyridine); and 8.81 (d, $J = 5.3$ Hz, *o*-H of pyridine); δ_C 17.7, 50.6, 73.1, 103.7, 119.0, 121.7, 123.3, 126.8, 127.1, 129.3, 129.5, 131.8, 132.6, 134.3, 140.7, 154.5 and 155.0; δ_P {^{1}H} (*syn-trans*-P isomer) 128.3 (s, 1P); other isomers appear at 132.7 (s, 0.04P), 130.1 (s, 0.03P) and 129.7 (s, 0.14P); IR ($\tilde{\nu}_{max}$/cm^{-1}) 3058, 2991, 2923, 1607 and 1438; FAB-MS $m/z = 454.0550$ ($C_{22}H_{23}NOPPd^+$ requires 454.0552); Found C, 45.35; H, 3.84; Calc. for $C_{22}H_{23}NOPPd^+CF_3SO_3 + 0.1CH_2Cl_2$ C, 45.31; H, 3.82%.

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15 The alkylation of cinnamylpalladium complexes bearing other bidentate ligands resulted in similar regioselectivities.

16 Molecular modelling (Spartan PM3(tm) method) shows that the phenyl substituent on the allyl moiety is oriented parallel to the imine functionality.