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A Comparison of (*R*,*R*)-Me-DUPHOS and (*R*,*R*)-DUPHOS-*i*Pr Ligands in the Pd^0-Catalysed Asymmetric Allylic Alkylation Reaction: Stereochemical and Kinetic Considerations

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A relatively unexploited commercial ligand, (*R*,*R*)-DUPHOS-*i*Pr (**1b**) was tested in the Pd^0-catalysed asymmetric allylic alkyation reaction using *rac*-1,3-diphenylpropenyl acetate as substrate, malonate as nucleophile and a variety of Pd pre-catalysts under standard conditions. Excellent *ee* values (up to ≥ 98%) could be obtained with **1b**, but the conversions were generally inferior to those obtained using (*R*,*R*)-Me-DUPHOS (**1a**) under similar conditions. It was also observed that there was a switch in the absolute configuration of the malonate product to (R) on using **1b** to form the catalyst. This was an indication of the complementary nature of these two ligands. In order to explain this, a rigorous detailed semi-emperical computational study was undertaken. DFT calculations of the Fukui Function (FF) were also conducted to confirm the most likely site (electrophilic) for nucleophilic attack on the active Pd-allyl complex. In the case of the Pd catalyst formed with **1b**. This result indicated that stereochemical factors were more important than electronic factors in this reaction with **1b**. Kinetic studies were also conducted to compare the activities of the catalysts **2a** and **2b** formed with (*R*,*R*)-Me-DUPHOS (**1a**) and (*R*,*R*)-DUPHOS-*i*Pr (**1b**).

Introduction

At the present time asymmetric synthesis finds considerable application in providing useful enantiomerically pure compounds. Since 1977 the asymmetric allylic alkylation (AAA) reaction has become a standard approach for the creation of both C–C and C–X bonds.[1,2] Many chiral ligands have been screened for this particular reaction, these generally contain P or N, possess C_2 or C_1 symmetry and can be of a homobidentate type (e.g., diphosphanes, bisoxazolines, etc.) or of a heterobidentate nature (e.g. phosphanyloxazolines etc).[1] Several useful chiral diphosphane ligands are known for catalytic asymmetric hydrogenations, like, chiraphos,[3] DIPAMP,[3] DIOP[4] and many more. Unfortunately these "borrowed" ligands are less successful in other catalytic reactions. For this reason we have established a research program to screen key phosphane and other ligands (with a proven track record) for effectiveness in other key asymmetric catalytic processes. For example, we have recently demonstrated that Berens' ligand[4,5] and WalPhos[6] – which has been so successful in catalytic asymmetric hydrogenation[7,8] – shows potential in other catalytic asymmetric reactions like, the AAA reaction, ketone hydrosilylation and vinylarene hydroboration.

We became interested in accessing (*R*,*R*)-DUPHOS-*i*Pr (**1b**)[9] in the AAA reaction of both *rac*-1,3-diphenylpropenyl acetate and *rac*-1-acetoxycyclohexene with malonate nucleophile (Figure 1). Our rationale was based on the supposition that the presence of bulky groups around the P atoms should give high enantioselectivities. It must be noted that, Drago and Pregosin[10] have already demonstrated (as a one-off study) an *ee* as high as 98% for the alkylation of *rac*-1,3-diphenylpropenyl acetate with dinuclear [PdCl-(PhCHCHCHPh)]$_2$, malonate as nucleophile and (*R*,*R*)-Me-DUPHOS and Malaisé et al.[11] showed a similar result, but only when the sodium salt of dimethyl maloante was used [as they claimed that BSA was not an appropriate base for reactions involving (*R*,*R*)-Me-DUPHOS]. In the case of (*R*)-Josiphos it was shown by Togni and Spindler that *ee* values of up to 93% could be achieved for this reaction.[12]

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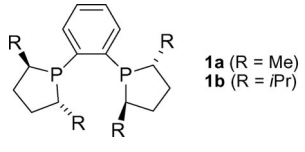


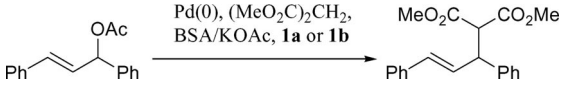
Figure 1. (*R*,*R*)-Me-DUPHOS (**1a**) and (*R*,*R*)-DUPHOS-*i*Pr (**1b**).

DUPHOS-*i*Pr (**1b**) has previously been screened in the AAA reaction of ethyl 2-oxocyclohexanecarboxylate with cinnamyl acetate, but the authors claimed unsatisfactory results for the reaction.[13]

In this paper we disclose our results on the use of ligand **1b** in the AAA reaction, comparative kinetics between the catalysts bearing **1a** and **1b** and computational studies to explain the switch in configuration using **1b**.

Results and Discussion

(*R*,*R*)-DUPHOS-*i*Pr (**1b**) was tested in the AAA reaction with 1,3-diphenylpropenyl acetate using dimethyl malonate with a variety of Pd pre-catalysts (Scheme 1) (the active chiral catalyst was thus prepared in situ) giving the following results (Table 1).



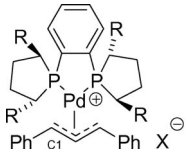
Scheme 1. Palladium-catalysed asymmetric allylic alkylation of *rac*-1,3-diphenylpropenyl acetate with dimethyl malonate.

Table 1. Asymmetric allylic alkylation of *rac*-1,3-diphenylpropenyl acetate using ligand **1b**.[a]

Entry	Pre-catalyst	Solvent	Conv.[b] (%)	*ee*[c] (%)
1	$[Pd(allyl)Cl]_2$	CH_2Cl_2	25	94 (*R*)
2[d]	$[Pd(allyl)Cl]_2$	CH_2Cl_2	6	53(*R*)
3[d,e]	$[Pd(allyl)Cl]_2$	THF	60	≥ 98% (*R*)
4	$Pd(dba)_2$	CH_2Cl_2	12	≥ 98% (*R*)
5	$Pd(dba)_2$	$ClCH_2CH_2Cl$	21	≥ 98% (*R*)
6	$Pd_2(dba)_3{\cdot}CHCl_3$	CH_2Cl_2	11	81 (*R*)
7[d]	$Pd_2(dba)_3{\cdot}CHCl_3$	CH_2Cl_2	23	82 (*R*)
8[f]	$Pd_2(dba)_3{\cdot}CHCl_3$	CH_2Cl_2	58	≥ 98% (*R*)

[a] Reaction conditions: 2.5 mol-% of ligand and pre-catalyst 1 mol-% were used, complexation conducted at reflux temperature for 2 h and then room temp. for 20 h (base: BSA/KOAc, 3 equiv. BSA and 1 mol-% KOAc was used). [b] Pertains to the ratio of substrate to product as determined by HPLC. [c] Determined by HPLC using a Chiralcel OD-H column. [d] Conducted at reflux temperature. [e] 1.2 mol-% of ligand and pre-catalyst 0.5 mol-% were used, complexation conducted at reflux temperature for 2 h and then room temp. for 20 h, base: NaH. [f] 2.5 mol-% of ligand and pre-catalyst 10 mol-% were used, complexation conducted at reflux temperature for 2 h and then room temp. for 1 h.

Despite the generally very good enantioselectivities (with a maximum of ≥ 98%) obtained, in all cases the substrate conversions were moderate (with a maximum of 60%, see Table 1). We assume that this may be linked to the considerable steric hindrance inherent in the active allylpalladium complex **2b** derived from *rac*-1,3-diphenylpropenyl acetate, or in forming the intermediate π-allyl palladium complex that is attacked by malonate (see Figure 2).



2a (R = Me, X = Cl)
2b (R = *i*Pr, X = Cl)
2c (R = *i*Pr, X = OTf)

Figure 2. Pd-allyl complexes **2**.

Support for this conjecture comes from the observation that when the reaction was performed according to the conditions of Malaisé et al.[11] (Table 1, entry 3) a poorer conversion of 60% was obtained as opposed to the quantitative yield reported by these workers using Me-DUPHOS.

Some interesting temperature effects were observed. In the case of the reactions using $[Pd(allyl)Cl]_2$ when the temperature was increased to 40 °C there was a substantial reduction in the reaction conversion and *ee* (Table 1, entry 2) and we assume that this is due to chiral catalyst degradation at the higher temperature. The same was observed on using $Pd(dba)_2$ as the conversion dropped to 2% and the *ee* to 62% as opposed to a conversion of 12% and an *ee* of ≥ 98% (Table 1, entry 4). However, in the case of $Pd_2(dba)_3{\cdot}CHCl_3$ when the temperature was raised, the conversion doubled although the *ee* remained constant (Table 1 entries 6 and 7). In terms of the effect exerted by the solvents in the reactions using $[Pd(allyl)Cl]_2$ and $Pd_2(dba)_2$ pre-catalysts, it would appear that when BSA/KOAc are used, it was the polar non-coordinating solvents CH_2Cl_2 and $ClCH_2CH_2Cl$ which gave the highest *ee* values (Table 1, entries 1, 4 and 5) when compared to the polar coordinating solvent, THF and acetonitrile which gave low conversions and *ee* values. However, in one case when THF was used with NaH as base an *ee* of ≥ 98% was obtained (Table 1, entry 3).

In all cases the (*R*)-enantiomer of the alkylated malonate product was the major isomer. A surprising result and contrary to the results obtained using **1a**[10,11] where the (*S*)-malonate product was the major enantiomer. Drago and Pregosin[10] have previously shown on the basis of extensive ^1H NMR studies on the isolated Pd-allyl complex with an *exo*-conformation that the malonate nucleophile attacks preferentially C-1 as this is the most electrophilic of the two terminal allyl carbons. This was postulated to be due to the steric hindrance imparted by the ligand methyl group. Due to facial selectivity in this case the (*S*)-malonate enantiomer is preferred. We prepared the triflate salt of the Pd complex **2c** (Figure 1) by a method similar to that described by Pregosin and Drago[10] (in fact we had problems making it by their method), but despite our best efforts we have been unable to grow suitable crystals of **2c** for single-crystal X-ray crystallographic analysis. However, we did indeed obtain a ^{31}P NMR spectrum of **2c** which had much the same characteristics as the triflate complex of **2a** reported by Pregosin and Drago[10] (one doublet at δ = 64.35 ppm with J = 31 Hz for P1 and another doublet at 62.55 ppm with J = 31 Hz for P2). This thus prompted us to carry out a very detailed computational study to understand the nature of the configurational switch of the malonate product on going from **1a** to **1b**.

In our hands the results using *rac*-1-acetoxycyclohexene as substrate in this reaction were very poor, in fact, moderate conversions and no enantioselectivity was obtained.

Theoretical Studies

Considering the number and the size of these systems, a semi-empirical method proved to be the best choice for

geometry optimization. The PM6 Hamiltonian[14] included in the recent version of MOPAC 2007[15] was employed. The geometries were fully optimized in Cartesian coordinates and the stationary points were further characterised by frequency calculations as minima. Following the initial geometry optimization with the PM6 method, Density Functional Theory (DFT) calculations were carried out on all complexes. Calculations carried out at the DFT level were performed using the hybrid Becke exchange functional[16] and the correlation functional B3LYP[17] as contained in the Gamess package.[18] The Lanl2DZ effective core basis set was employed for the metal and the P atom while the 6-31G* basis set was used for all the other atoms.

There was a significant degree of approximation between the calculated values for the Pd–C1 and Pd–C3 bond lengths (2.253 and 2.204 Å), with those measured in the X-ray crystal structure obtained by Pregosin and Drago,[10] which were 2.238 and 2.221 Å, respectively. The good agreement seen here supports the suitability of the PM6 method to determine molecular geometries for this family of complexes.

After completing this step, the next step was the calculation of the Fukui Function (FF) on the Pd-allyl complexes of **2a** and **2b** (without the chloride ion) to establish the most likely site of nucleophilic attack. The Fukui function is one of the more common descriptors widely used to predict relative site reactivities[19] and in fact has been used to provide a more solid theoretical base for the local HSAB principle.[20] The Fukui function has been defined as the electron density derivative with respect to the electron number, at constant external potential $v(\mathbf{r})$ generated by the nuclei acting on the electrons,

$$f(\mathbf{r}) = [\partial\rho(\mathbf{r})/\partial N]_{v(\mathbf{r})} \quad (1)$$

where, $\rho(\mathbf{r})$ is the ground state electronic density of the system at point $\mathbf{r}$, and N is the total electron number.

Yang and Mortier[21] proposed the condensed Fukui function indices,

$$f_k^+ \approx q_k(N+1) - q_k(N)$$

$$f_k^- \approx q_k(N) - q_k(N-1) \quad (2)$$

$$f_k^0 \approx q_k(N+1) - q_k(N-1)$$

where, the Fukui function is condensed in the individual atoms. Here $q_k(N+1)$, $q_k(N-1)$ and $q_k(N)$ are the atomic populations of atom k in the $N+1$, N and $N-1$ electron systems. The indice f_k^+ reflects the capacity of atom k to accommodate an extra electron and is the indice most suited for studies of nucleophilic attack, f_k^- describes the ability of the atom to donate an electron and is appropriate for studies of electrophilic attack and f_k^0 is an indicator for radical reactivity. Parr and Yang proposed that the higher Fukui function values are related with increased reactivity on that site. So, a larger condensed Fukui function on an atom indicates an increased reactivity at that particular atom.

Another approach is the method proposed by Contreras et al.[22] in the framework of frontier orbital theory. This approach involves a single calculation with the FF at an atom k being given by

$$f_k^a = \sum_{\mu \in k} f_\mu^a \quad (3)$$

having

$$f_\mu^a = |c_{\mu a}|^2 + c_{\mu a} \sum_{\nu \neq \mu} c_{\nu a} S_{\mu\nu} \quad (4)$$

where $c_{\mu\nu}$is the frontier molecular orbital coefficients and $S_{\mu\nu}$ is the overlap integral between the atomic basis functions $\chi_\mu(\mathbf{r})$ and $\chi_\nu(\mathbf{r})$. Equation (3) gives the condensed Fukui functions for electrophylic ($a = -$) and for nucleophilic ($a = +$) attacks, whilst an average is considered for radical attacks.

We were particularly interested in clarifying where the preferential site of attack would occur in this alkylation reaction and thus have calculated the FF values for this molecule knowing that nucleophilic addition will preferentially occur at the carbon atom with the highest f_k^+ value.

Both the Pd-allyl complex **2a** (Figure 3) and **2b** (Figure 4) were studied in the gas phase using this technique. In both cases, it was calculated that the C-1 site had the largest f_k^+ value and thus the greatest susceptibility for nucleophilic attack. This was fine in the case of **2a** where it has been experimentally shown that the preferential site of attack is at C-1,[10] however in the case of **2b** this can not be the case and warranted a series of further studies to understand this result.

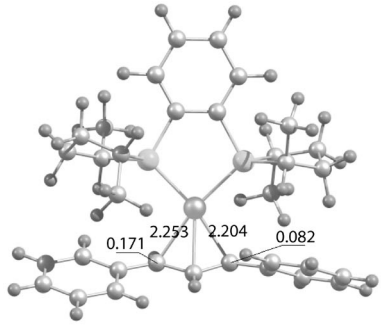


Figure 3. Calculated structure of (*R*,*R*)-Me-DUPHOS-Pd-(PhCHCHCHPh) (**2a**) (without chloride ion), with f_k^+ values for C1 and C3 and Pd–C1 and Pd–C3 distances [Å].

We considered the possibility of the formation of two other active catalysts – *trans*-**2b** and *trans*-**2b′** which are both diastereomers of *cis*-**2b** (Scheme 2) – via the well known π-σ-π (η^3-η^1-η^3) isomerisation mechanism, which allows for *syn-anti* interconversions to occur[1] (Scheme 2). In the case of *trans*-**2b** (Figure 5), once again it was shown that C1 was the more susceptible site for nucleophilic attack, thus ruling out the possibility of this complex to be the active catalyst.

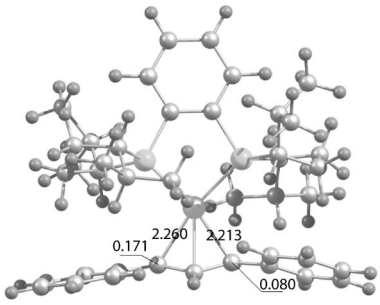


Figure 4. Calculated structure of (*R*,*R*)-DUPHOS-*i*Pr-Pd-(PhCHCHCHPh) (*cis*-**2b**) (without chloride ion), with f_k^+ values for C1 and C3 and Pd–C1 and Pd–C3 distances [Å].

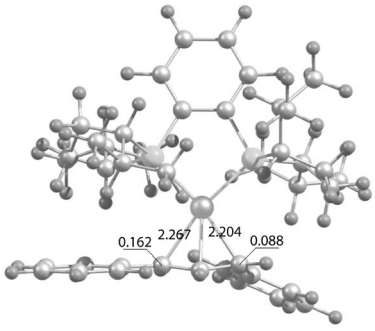


Figure 5. Calculated structure of (*R*,*R*)-DUPHOS-*i*Pr-Pd-(PhCHCHCHPh) (*trans*-**2b**) (without chloride ion), with f_k^+ values for C1 and C3 and Pd–C1 and Pd–C3 distances [Å].

In the case of the *trans*-**2b′** (Figure 6) it was C-3 that had the greater f_k^+ value for the first time. We then calculated the energies for each of the three complexes, *cis*-**2b**, *trans*-**2b** and *trans*-**2b′** (Table 2) in the gas phase.

It was observed that *cis*-**2b** was calculated to be the most stable, followed closely by *trans*-**2b**, with *trans*-**2b′** the most unstable. This has led us to postulate that due to stereochemical hindrance the maloante attacks preferentially C-3 despite the fact that electronically it is C-1 that is favoured.

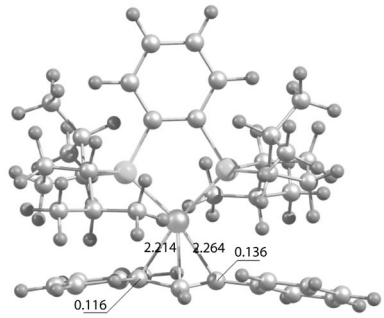


Figure 6. Calculated structure of (*R*,*R*)-DUPHOS-*i*Pr-Pd-(PhCHCHCHPh) (*trans*-**2b′**), with f_k^+ values for C1 and C3 and Pd–C1 and Pd–C3 distances [Å].

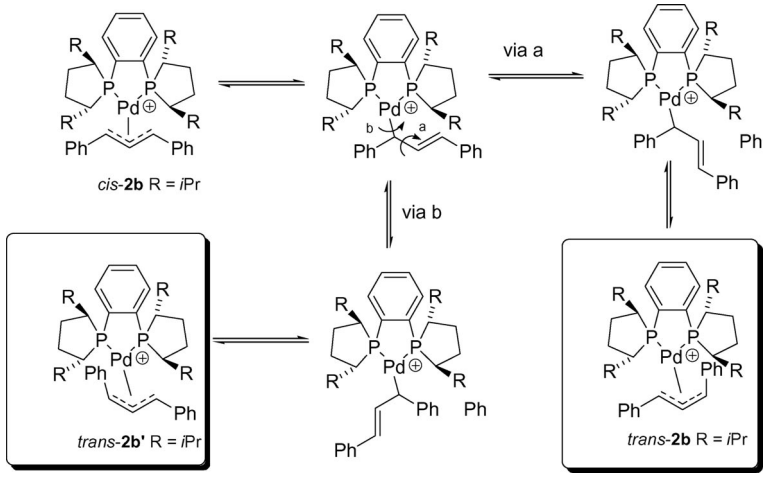
Table 2. Calculated energies for complexes *cis*-**2b**, *trans*-**2b** and *trans*-**2b′** at the B3LYP/G-31G*//PM6 level.

Complex	*cis*-**2b**	*trans*-**2b**	*trans*-**2b′**
Energy	–1735.04774	–1735.04287	–1735.03395

In those reactions where the *ee* values were lower (Table 1, entries 1, 2, 6 and 7) it is likely that there was nucleophilic attack at C-1.

Kinetic Studies

It was of interest to compare quantitatively the reactivities of complex **2a** with **2b** in the early stages of the reaction. Thus the asymmetric allylic alkylation using *rac*-1,3-diphenylpropenyl acetate as substrate and $[Pd(allyl)Cl]_2$ as pre-catalyst was conducted under standard conditions (see Table 1) using ligands **1a** and **1b**. During the first 4.5 hours of the reaction a sample was removed at 30 min intervals and analysed by HPLC. The results are shown in Figure 7. The *ee* values at each stage of the reaction were also determined.



Scheme 2. Possible interconversions of the **2b** complex.

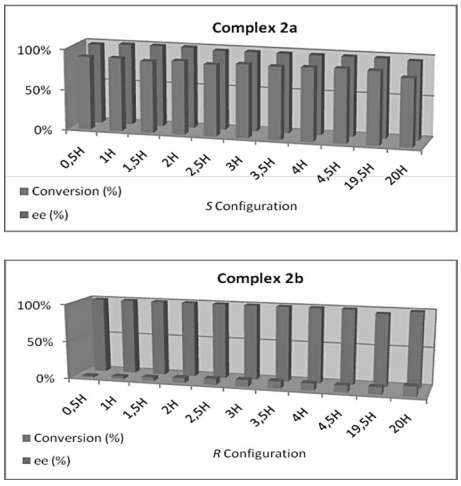
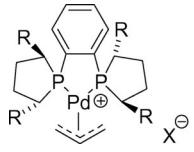


Figure 7. Kinetic studies using complexes **2a** and **2b** formed in situ.

This study showed that the reaction which involved in situ formation of complex **2a** went to completion within the first hour whereas that involving complex **2b** was very sluggish throughout the reaction course. This observation supports the conjecture that either, (1) there is stereochemical hindrance during the malonate nucleophilic addition step which is perhaps the reason for the configurational switch in the product configuration on going from **2a** to **2b** or (2) the rates of ionization and formation of complexes **2a** and **2b** are different, with **2a** manifesting more rapid reaction kinetics. The fact, that the *ee* values remained constant throughout was an indication that one principle catalyst was catalysing the reaction and it was stable. In order to determine the most likely reason for these differential reaction rates, we decided to conduct two key kinetic experiments. Due to the difficulty in preparing the triflate salts of both **2a** and **2b** in accordance with the procedure of Pregosin and Drago,[10] we opted for a study to compare the relative reactivities of the pre-complexes of both **2a** and **2b** but used the trifluoroborate salts **3a** and **3b** (Figure 8).



3a (R = Me, X = BF_4)
3b (R = *i*Pr, X = BF_4)
4a (R = Me, X = Cl)
4b (R = *i*Pr, X = Cl)

Figure 8. Isolated Pd-allyl complexes **3a** and **3b** formed using $AgBF_4$ and in situ formed complexes **4a** and **4b**.

On performing kinetic studies with both **3a** and **3b** in the same way as previously, but only over a 2 h period we noticed that although the enantioselectivities were comparable to those obtained using in situ formed **2a** and **2b** the conversions were much lower over the same period as for the in situ kinetic study described above (Figure 9). This we attribute to the presence of the tetrafluoroborate ion and the fact that the complexes had to be isolated in air and light, and thus some decomposition was inevitable. However, it was indeed the reaction that involved complex **3a** that was quicker. The reaction involving **3b** was very sluggish over this time period. Although this result indicated that kinetics for formation of complexes **4a** and **4b** did not intefere with the overall kinetics of the reaction, it still did not indicate if steric hindrance or a slower rate of formation of **2b** from the pre-allyl palladium complex **4b** was the reason for the slower overall reaction kinetics with **1b**. Thus a second kinetic study was conducted using ligands **1a** and **1b**. Both ligands were refluxed with $[Pd(allyl)Cl]_2$ to form the respective allyl chloride complexes **4a** and **4b** (Figure 8) in situ with subsequent addition of *rac*-1,3-diphenylpropenyl acetate to form complexes **2a** and **2b** (Figure 2). It was observed that in fact (see Figure 10) the consumption of *rac*-1,3-diphenylpropenyl acetate with **1a** was faster than with **1b** (after 1 h 37% of the substrate was consumed with **1a** whereas only 27% was consumed with **1b**). This strongly indicated that the reaction rate for formation of complex **2a** was faster. Overall these results were an indication that the faster overall kinetics for the reaction involving **2a** was probably a consequence of both the rapid formation of the 1,3-diphenylallyl palladium complex **2a** coupled with a reduced level of stereochemical hindrance on attack by malonate nucleophile. The fact that the consumption of *rac*-1,3-diphenylpropenyl acetate only reached ca. 37% and 35% for both **1b** and **1a**, after 20 h, strongly indicated the presence of an equilibrium process and the requirement of the malonate nucleophile to push the equilibrium towards product formation and *rac*-1,3-diphenylpropenyl acetate consumption, this is particularly the case with **1a**. In the case of **1b**, it seems that the overall reaction conversion mirrors the substrate consumption value over the 20 h period.

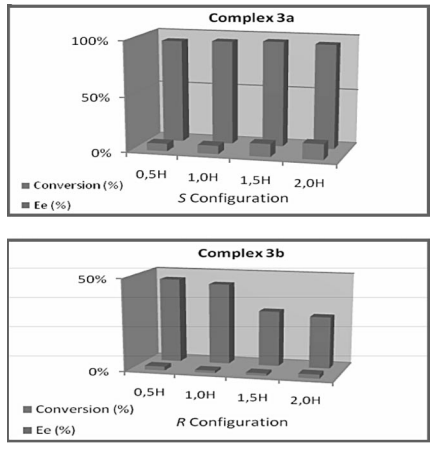


Figure 9. Kinetic studies using pre-formed complexes **3a** and **3b**.

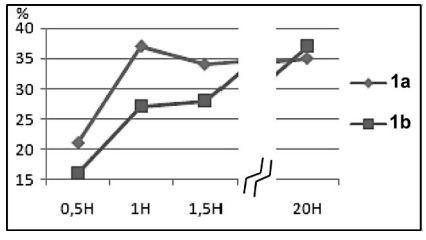


Figure 10. Kinetic studies using ligands **1a** and **1b**.

Conclusions

The commercial ligand, (*R*,*R*)-DUPHOS-*i*Pr **1b** was tested in the asymmetric allylic alkylation using *rac*-1,3-diphenylpropenyl acetate as substrate, malonate as nucleophile and a variety of Pd pre-catalysts under standard conditions. Excellent *ee* values could be achieved with **1b** but the conversions were moderate (except when NaH was used as base and the reaction heated – entry 3, Table 1 and when we increased the loading of palladium pre-catalyst by one order of magnitude – entry 8, Table 1) and inferior to those reported with (*R*,*R*)-Me-DUPHOS **1a** under similar conditions. This was attributed to both slower reaction kinetics in the formation of the 1,3-diphenylallyl palladium complex **2b** which affords the alkylated malonate product after attack by the malonate nucleophile and to increased stereochemical hindrance during the attack of the malonate nucleophile on **2b**. The surprising change of configuration in the malonate product on going from **2a** to **2b** was rationalised on the basis of a significant stereochemical hindrance event at C-1 of **2b** which resulted in preferential attack at C-3. Further theoretical studies will be undertaken to substantiate this postulate.

Experimental Section

General Remarks: Both (*R*,*R*)-Me-DUPHOS **1a** and (*R*,*R*)-DUPHOS-*i*Pr **1b** were obtained from Strem chemicals. All other reagents were obtained from Aldrich, Fluka, Alfa Aesar or Acros. Solvents were dried using common laboratory methods.[23]

High Performance Liquid Chromatography (HPLC) analysis was performed on an Agilent 1100 series instrument. The following conditions were used: p_{max} = 50 bar, flux = 1 mL/min, detector = DAD (λ = 210.10 nm), eluent: *n*-hexane/2-propanol (98:2). To calculate the reaction conversion (ratio substrate to product), given that both the substrate and malonate product have different molar extinction coefficients a correction factor of 0.65 was introduced in order to correct the product peak area.

The column used was a Chiralcel OD-H (0.46 cm × 25 cm) fitted with a guard column composed of the same stationary phase. In all cases, the reaction conversions were calculated by simply determining the ratio of the peak areas for the substrate and the alkylated product.

In the case of the kinetic studies the reactions were monitored by collecting 1 mL samples at 30 min intervals for the first 1.5–4.5 h and for the last hour. The samples were analyzed using HPLC. For the kinetic studies involving complexes **3a** and **3b** the conversions were determined as described above. In the case of the kinetic study that involved determining the rate of consumption of the *rac*-1,3-diphenylpropenyl acetate substrate this was calculated using a calibration curve for *rac*-1,3-diphenylpropenyl acetate between $4.2 \cdot 10^{-3}$ to $40.0 \cdot 10^{-3}$ M ($y = 1227.7x + 36.677$; $R^2 = 0.9495$).

General Procedure for the Catalytic Asymmetric Allylic Alkylation Reactions Using Ligands 1a and 1b: The Pd pre-catalyst (0.5 or 1 mol-%) and the chiral ligand (1.2 or 2.5 mol-%) were placed in a flask with dry solvent (2 mL) under a nitrogen atmosphere and refluxed for 2 h. The temperature was then reduced to room temp. after which the substrate (100 mg, 0.39 mmol) dissolved in a dry solvent (2 mL) was added. Dimethyl malonate (0.15 mL, 3 equiv.), BSA (0.3 mL, 3 equiv.) and KOAc (0.4 mg, 1 mol-%) were added (In the case of the reaction with NaH the procedure given in ref.[11] was followed). The mixture was maintained at room temp. (or, in some cases, refluxed) for 20 h, after which it was filtered using a pad of celite and silica gel and washed with a mixture of hexane/EtOAc (2:1). The solvent was evaporated under vacuum and the resulting mixture analysed by HPLC.

Preparation of the [AllylPd-1b]CF_3SO_3 Complex 2c: Ligand **1b** (2.1 mg, 2.5 mol-%) and $[Pd(C_3H_5)Cl]_2$ (0.7 mg, 1 mol-%) were dissolved in dry CH_2Cl_2 (5 mL) and stirred at room temp., under a nitrogen atmosphere. After 30 min $AgCF_3SO_3$ (0.5 mg, 1 equiv. to Pd) was added. The reaction mixture was stirred for 45 min and then *rac*-1,3-diphenylpropenyl acetate (50 mg, 100 mol-%) was added. After 20 h stirring at room temp., the mixture was filtered over a pad of celite and silica. The filtrate was concentrated in vacuo giving a green oil. MS (MaldiTOF, *m*/*z*): 527.22 (Pd-**1b** + 3, cleavage). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ = 64.35 (d, J = 31 Hz, P1) and 62.55 (d, J = 31 Hz, P2) ppm. ^{1}H NMR ($CDCl_3$, 300 MHz, substrate signals were detected, but are ignored here): δ = 0.45–0.47 (d, J = 6.5 Hz, 3 H, CH_3 isopropyl), 0.54–0.56 (d, J = 6.5 Hz, 3 H, CH_3 isopropyl), 0.72–0.84 (m, 12 H, 4 CH_3, 2 isopropyl), 0.95–0.98 (d, J = 6.7 Hz, 3 H, CH_3 isopropyl), 1.0–1.1 (d, J = 6.6 Hz, 3 H, CH_3 isopropyl), 1.2–1.3 (m, 8 H, cyclopentane), 3.5 (d, J = 6.3 Hz, 1 H, –C*H*Pd), 6.3–6.4 (m, 2 H, –C*H*=C*H*) and 7.2–7.6 (m, 14 H, H^{ar}) ppm.

Preparation of the [AllylPd-1a]BF_4 Complex 3a: Ligand **1a** (30 mg, 9.8×10^{-2} mmol) and $[Pd(C_3H_5)Cl]_2$ (17.9 mg, 0.5 equiv.) were dissolved in dry CH_2Cl_2 (5 mL) and stirred at room temp., under a nitrogen atmosphere. After 30 min $AgBF_4$ (19.1 mg, 1 equiv.) was added. The reaction mixture was stirred for 45 min. $AgCl_2$ was removed and the solvent was reduced in vacuo. The isolated complex **3a** was obtained as a white solid (32 mg, 60%). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ = 74.15–74.45 (d, J = 36 Hz, P1) and 75.00–75.29 (d, J = 35 Hz, P2) ppm. ^{1}H NMR ($CDCl_3$, 300 MHz, substrate signals were detected, but are ignored here): δ = 0.87–0.93 (m, 3 H, CH_3), 1.13–1.30 (m, 6 H, 2 CH_3), 1.33–1.39 (m, 3 H, CH_3), 1.79–1.93 (m, 8 H, cyclopentane), 4.7 (m, 1 H, C*H*Pd), 5.50–5.65 (m, 2 H, C*H*=C*H*) and 7.8–7.9 (m, 14 H, H^{ar}) ppm.

Preparation of the [AllylPd-1b]BF_4 Complex 3b: As described above for **3a** but using ligand **1b** (40 mg, 9.8×10^{-2} mmol). The isolated complex **3b** was obtained as a white solid (43 mg, 68%). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ = 61.84–62.09 (d, J = 31 Hz, P1) and 63.63–63.89 (d, J = 31 Hz, P2) ppm. ^{1}H NMR ($CDCl_3$, 300 MHz, substrate signals were detected, but are ignored here): δ = 0.46–0.48 (d, J = 6.5 Hz, 3 H, CH_3 isopropyl), 0.55–0.57 (d, J = 6.5 Hz, 3 H, -CH_3 isopropyl), 0.73–0.85 (m, 12 H, 4 CH_3, 2 isopropyl), 0.97–0.99 (d, J = 6.6 Hz, 3 H, -CH_3 isopropyl), 1.05–1.07 (d, J = 6.5 Hz, 3 H, CH_3 isopropyl), 1.69–1.87 (m, 8 H, cyclopentane), 4.7 (m, 1 H, –C*H*Pd), 5.46–5.60 (m, 2 H, –C*H*=C*H*) and 7.8–7.9 (m, 14 H, H^{ar}) ppm.

General Procedure for Kinetic Studies with Ligands 1a and 1b in the Presence of Dimethyl Malonate and Base: $[Pd(allyl)Cl]_2$ (7.2 mg, 1 mol-%) and the chiral ligand **1a** (15.2 mg, 2.5 mol-%) or **1b** (20.7 mg, 2.5 mol-%) were placed in a flask with dry CH_2Cl_2 (5 mL) under a nitrogen atmosphere and refluxed for 2 h. The temperature was then reduced to room temp. after which *rac*-1,3-diphenylpropenyl acetate (500 mg, 1.9 mmol) dissolved in dry CH_2Cl_2 (2 mL) was added. Dimethyl malonate (0.7 mL, 3 equiv.), BSA (1.5 mL, 3 equiv.) and KOAc (2 mg, 1 mol-%) were added. The mixture was maintained at room temp. During the first 4.5 h and the last hour of the reaction a sample was removed at intervals of 30 min and analysed by HPLC.

General Procedure for Kinetic Studies with Complexes 3a and 3b: Complexes **3a** (5.4 mg, 10^{-3} mmol) or **3b** (6.5 mg, 9.9×10^{-3} mmol) were placed in a flask with dry CH_2Cl_2 (2 mL) under a nitrogen atmosphere. *rac*-1,3-Diphenylpropenyl acetate (100 mg, 0.39 mmol) dissolved in dry CH_2Cl_2 (2 mL), dimethyl malonate (0.15 mL, 3 equiv.), BSA (0.3 mL, 3 equiv.) and KOAc (0.4 mg, 1 mol-%) were added. The mixture was maintained at room temp. for 20 h. During the first 3 h and the last hour of the reaction a sample was removed at intervals of 30 min and analysed by HPLC.

General Procedure for Kinetic Studies with Ligands 1a and 1b in the Absence of Dimethyl Malonate and Base: $[Pd(allyl)Cl]_2$ (22 mg, 0.06 mmol) and the chiral ligand **1a** (36 mg, 2 equivs) or **1b** (49 mg, 0.12 mmol) were placed in a flask with dry CH_2Cl_2 (5 mL) under a nitrogen atmosphere and refluxed for 2 h. The temperature was then reduced to room temp. after which *rac*-1,3-diphenylpropenyl acetate (30 mg, 0.12 mmol) dissolved in dry CH_2Cl_2 (2 mL) was added. The mixture was maintained at room temp. for 20 h. During the first 1.5 h of the reaction a 1 mL aliquot was removed at intervals of 30 min and analysed by HPLC.

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