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Communications

Palladium-Catalyzed Asymmetric Allylic Alkylations Using Diphenylphosphino(oxazolinyl)ferrocene Ligands: Effects of Planar Chirality on the Reactivity and Selectivity

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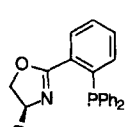
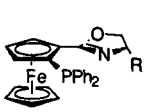
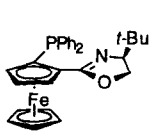
Asymmetric allylic substitutions catalyzed by transition metals have been the subject of extensive research in the area of catalytic asymmetric reactions.[1] A variety of chiral ligands for allylic substitution has been studied in the hope of obtaining high enantioselectivity and a better understanding of the reaction mechanism.[2] Although much effort has been made to understand the reaction mechanism of the Pd-catalyzed allylic substitution, little is known about the facts influencing the reactivity of the catalysts.[3] Recently, (phosphinoaryl)oxazoline ligands **1** have been introduced by several authors.[2f-2h] These *N,P*-chelates are demonstrated to be efficient, particularly in the Pd-catalyzed allylic substitution of acyclic allylic acetates. We were interested in utilizing ferrocene-based *N,P*-chelates, diphenylphosphino(oxazolinyl) ferrocenes (DPOF **2-3**), as chiral ligands in the Pd-catalyzed allylic substitution. Several ferrocene-based chiral *P,P*-chelates have been successfully utilized in transition metal-catalyzed asymmetric reactions such as Grignard coupling reactions, aldol reactions, and allylic substitution reactions.[4] However, the application of ferrocene-based *N,P*-chelates to catalytic asymmetric reactions has appeared only recently.[5] The DPOF ligands have both planar and central chirality. Since DPOF **2b** and **3** have opposite planar chiralities, it would be of interest to know the effect of planar chirality in asymmetric induction.



1: R = *i*-Pr, *t*-Bu, Ph



2a: R = *i*-Pr
2b: R = *t*-Bu



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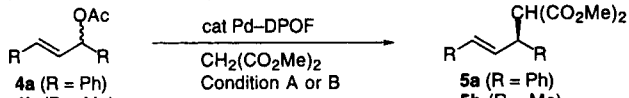
The DPOF **2** and DPOF **3** are synthesized from the corresponding oxazolinylferrocenes according to the diastereoselective lithiation protocol.[6] The Pd-catalyzed allylic alkylation was carried out using racemic (*E*)-1,3-diphenylprop-2-enyl-1-acetate (**4a**) and (*E*)-1,3-dimethylprop-2-enyl-1-acetate (**4b**) as standard substrates, and dimethyl malonate as a nucleophile. The results are summarized in Table 1.[7]

Under condition A, in which NaH was used as base, the enantioselectivity with ligand **2a** was moderate (44-48% ee). However, a dramatic increase in the enantioselectivity was observed under condition B, where the base system *N,O*-bis (trimethylsilyl)acetamide (BSA)-OAc was used.[2o,2t] A nearly complete enantioselection was obtained for acetate **4a** using the DPOF **2b**-Pd catalyst (entry 4). In addition, the reaction was complete within 30 min at 25 °C, resulting in a near-quantitative yield. In the case of acetate **4b**, which is known to be a less reactive and inferior substrate in enantioselection than **4a**,[2f] the reaction took 5 h at room temperature to give a yield of 82%. Only moderate enantioselectivity was obtained with the DPOF **2b**-Pd catalyst (entry 7). The reaction time was shortened to 1 h with an increased amount of the catalyst (entry 8). These results show that in the allylic alkylations, our ferrocene-based *N,P*-chelates generate Pd-catalysts of much greater reactivity than most other known ligands,[2c-2e,2i-2l,2o-2q] which produce Pd-catalysts that usually require a reaction time of one to three days at room temperature to produce good yields, even for the reactive acetate **4a**. In addition, DPOF ligands seem to produce more reactive catalysts than *N,P*-chelates **1**, which

Table 1. Eantioselective allylic substitution of *rac*-**4** catalyzed by the Pd-DPOF complexes

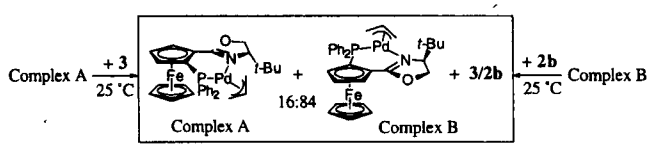


Entry	Substrate	DPOF[a]	Condition[b]	Molar equiv of the Pd-cat[c]	Reaction time (h)	%Ee[e]	5 %Yield[g]	
1	*rac*-**4a**	**2a**	A	0.02	1.0	48	93	(*S*)[h]
2	*rac*-**4a**	**2a**	A	0.01	1.0[d]	44	-	
3	*rac*-**4a**	**2a**	B	0.02	1.5	90	95	(*S*)
4	*rac*-**4a**	**2b**	B	0.02	0.5	≥99	99	(*S*)
5	*rac*-**4a**	**3**	B	0.02	0.5	73	14	(*S*)
6	*rac*-**4a**	**3**	B	0.02	5.0	67	73	(*S*)
7	*rac*-**4b**	**2b**	B	0.02	5.0	34[f]	82	(*S*)
8	*rac*-**4b**	**2b**	B	0.10	1.0	35[f]	98	(*S*)

[a] Ligand Purity: **2a**, 98% de; **2b** and **3**, ≥99% de. [b] Condition A: 1.2 equiv of NaH, 1.5 equiv of $CH_2(CO_2Me)_2$, THF, r.t.; Condition B: 3.0 equiv of BSA, 3.0 equiv of $CH_2(CO_2Me)_2$, 2 mol% of KOAc, CH_2Cl_2, r.t. [c] $[Pd(allyl)Cl]_2$ was used as Pd source and Pd/DPFO=1.0/1.2. [d] Under reflux. [e] Determined by HPLC (Chiralcel OD®) and ^1H NMR analysis with $Eu(hfc)_3$. [f] Determined from $[\alpha]_D$ values.[2f] [g] Purified yield by column chromatography on SiO_2. [h] Absolute configuration.

are also known to generate reactive catalysts. The different π-electron-accepting properties of the *P*-ligand and the *N*-ligand may play an important role in the pronounced reactivity of the *N,P*-chelates compared to the *N,N*- and *P,P*-chelates. The lower enantioselectivity of our DPOF-Pd catalysts for acetate **4b**, compared to those of the benzene-based *N,P*-chelates **1**, may be ascribed to the diminished steric interaction between the substituents of the ligand and the acetate. The (π-allyl)Pd complex from DPOF is expected to have less steric strain due to the difference in the inner angles of the Cp (cyclopentadienyl) and the benzene ring. As Trost has pointed out,[2m] a decrease in the steric interaction between the substituents of the allylic acetate and the ligand would result in lower selectivity.

With DPOF **3**, which has opposite planar chirality to DPOF **2b**, a modest enantioselectivity was observed in the Pd catalyzed allylic alkylation of **4a** (entry 5 and 6).[8] The absolute configuration of the major product was identical to that in the case of **2b**. It is of particular interest that the Pd-catalyst from DPOF **3** was much less reactive than that generated from DPOF **2b** (entry 5 *vs* 4). These results suggest that the ferrocene moiety does not affect the stereochemical course of the reaction but affects the reaction rate and enantioselectivity. The steric strain of the (π-allyl)Pd complexes is among various possible factors that may explain the large difference in the reactivity observed between DPOF **2b** and DPOF **3**. Compared to the corresponding Pd-complex from DPOF **3**, a sterically less stable (π-allyl)Pd complex may be generated from DPOF **2b** and, to relieve its steric strain, it may undergo the substitution more readily. The relative stability of DPOF-(π-allyl)Pd complexes has been determined by ^1H NMR study (Scheme 1). It was found that the (π-allyl)Pd complexes A and B are interconvertable by a fast ligand exchange process at room temperature. The corresponding (π-allyl)Pd complexes generated from acetate **4a**



Scheme 1.

also exhibited a similar process but with much slower interconversion.[9] The difference in the stability of complex A and complex B may result from the steric strain imposed by the Fe-Cp moiety. This "back strain" of the Fe-Cp moiety toward *tert*-butyl and a phenyl group of the ligand may exert steric strain between these groups and the substituents of acetate **4**, rendering the rate-limiting nucleophilic substitution by the malonate more feasible.

It has been suggested that the sterically induced activation of a (π-allyl)Pd bond and the release of the strain associated with the bond-breaking process are responsible for the enantioselection of bis(oxazoline)-Pd complexes.[3c] Our results suggest that the steric interaction between the ligand and allylic substituents in the (π-allyl)Pd complex may also influences on the substitution rate, and on enantioselectivity. Thus, a less stable and sterically more congested (π-allyl)Pd complex may undergo the substitution faster, and *vice versa*. This steric strain-reactivity argument may also provide a plausible explanation of why DPOF **2b** produces a more reactive catalyst than DPOF **2a** (entry 3 *vs* 4).

Although the rationalization that the reactivity and selectivity changes depend on the ligand structure needs further scrutiny, our results again highlight the important aspect of steric interaction between ligands and substrates in the Pd-catalyzed allylic substitution. Detailed spectroscopic and X-ray crystallographic analysis data for the (π-allyl)Pd complexes will be reported in due course.

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7. These results were presented at the 74th Annual Meeting of the Korean Chemical Society, Chungju, Chungbuk, Korea, October 1994; paper ORGN C17.

8. The difference in the observed %ee between entry 5 and 6 is due to the slow decomposition of the catalyst.

9. It took 2 days to reach at the equilibrium state [(π-allyl) Pd complex from **2b**/(π-allyl)Pd complex from **3**=6 : 94)] from the initially formed (π-allyl)Pd complexes (~3 : 7).

Crystal Structure and Rutile-Mimetic Framework in Cyanocadmate Clathrate $[Cd\{Cd(CN)_3(imH)\}_2]\cdot p\text{-}C_6H_4Me_2$ Involving Unidentate Imidazole ($imH=C_3H_4N_2$) Ligand

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The structural similarity between $Cd_x(CN)_y$ and Si_xO_y in coordination and linking structures may exhibit inclusion ability for guest molecules and/or ions, and can be utilized in developing mineral-like multi-dimensional inclusion or supramolecular structures such as 1D-chains, 2D-layers and 3D-lattices. We have demonstrated such inclusion host structures as silica-mimetic 3D-lattices,[1] clay-mimetic 2D-layers[2] and zeolite-mimetic 3D-lattices[3] materialized using cyanometallates.

In contrast to the topological similarity, the Cd-CN-Cd span length of *ca.* 5.5 Å is longer by *ca.* 2.5 Å than the span length of Si-O-Si and O-H···O in silica and ice, at *ca.* 3 Å. Therefore, the $Cd_x(CN)_y$ host structures are less complicated in topography than the structures of clathrate hydrates and clathrasils upon accommodating guests. This is the remarkable feature of the $Cd_x(CN)_y$ which gives structures similar in some ways but dissimilar in others to the Si_xO_y structures occurring in nature. In addition to that the presence or absence of complementary ligand in cyanometallate systems is one of the important factors for the inclusion host structures to provide cavities appropriate in size and shape for accommodating guest molecules.[4]

One of our recent attempts is to develope mineralomimetic structures using cyanocadmate and imidazole (imH), a five-membered aromatic amine, as the complementary ligand. We reports here on the structural results that we have obtained mineral-like inclusion clathrate of $3Cd(CN)_2\cdot 2imH\cdot p\text{-}C_6H_4Me_2$.

Into an aqueous solution containing an equimolar mixture of $CdCl_2$ and $K_2[Cd(CN)_4]$ (10 mmol each in 100 cm^3 H_2O), 10 mmol of imH was added in stirring. After filtration through a plastic membrane (Millipore, pore size of 0.45