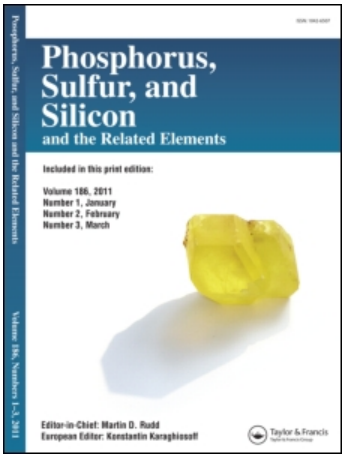

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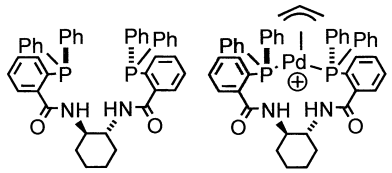
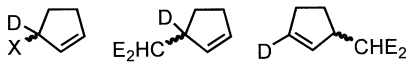
NMR studies on isotopically desymmetrized ligands and substrates have been used to demonstrate and investigate an apparent "memory effect" in palladium-catalysed nucleophilic substitution at allylic centres. The explanation for this "memory effect" is shown to be the participation of both monomeric and oligomeric complexes, with different reaction rates.

Keywords: Diphosphine ligands; isotopically desymmetrized ligands; NMR

The chiral diphosphine ligand (**1**), developed by Trost,[1] is an extremely effective catalyst for asymmetric nucleophilic substitution at allylic centres. In suitable cases enantiomeric excesses close to 100% can be achieved, but the reaction is markedly sensitive to solvent, concentration, and counter-ions. The active species has been postulated as a cyclic palladium complex (**2**), which forms a new ally1 complex with the substrate, but no such mononuclear complex has ever been isolated.



R,R-**1** [*R,R*-**2**]$^+$



rac-**3** *rac*-**4a** *rac*-**4b**

The fact that the catalytic system reacts quantitatively with both enantiomers of many substrates confirms that enantioselectivity occurs at the second stage of the reaction, where the palladium is replaced

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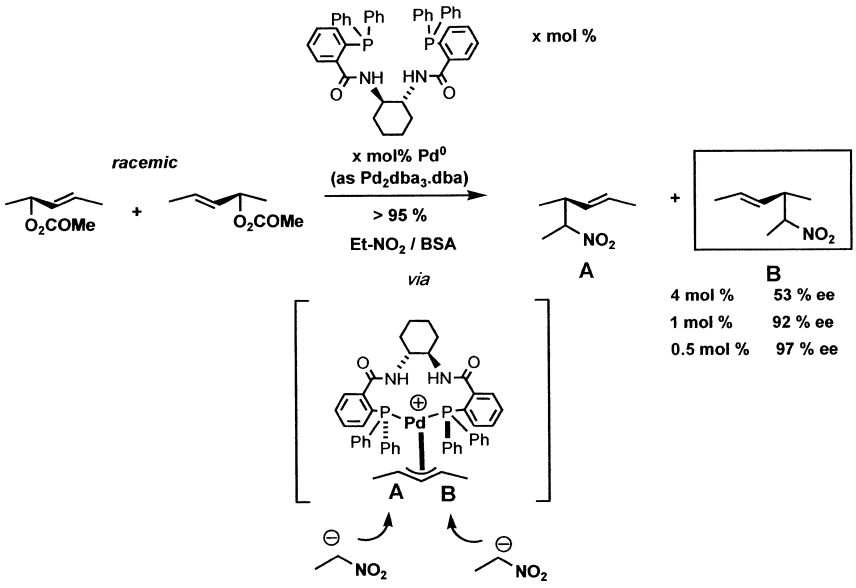

SCHEME 1

by the incoming nucleophile (Scheme 1). However, whether both enantiomers of the substrate react via the same catalytic intermediate is not evident. In other words, the enantioselectivity in the reaction of the enantiomers may be different—in contrast to what is predicted by the classical mechanism. Among issues that need explaining is the fact that the enantioselectivity in Scheme 1 increases with decreasing concentration of the catalyst.

In an attempt to gain a better understanding of the mechanistic processes involved, we have employed deuterated substrates, e.g., (**3**), which can produce enantiomers of both (**4a**) and (**4b**). The enantiomers of (**4**) thus produced were distinguished by ^{13}C NMR using a chiral lanthanide shift reagent, and the diastereomers ((**4a**) and (**4b**)) by the differential deuterium isotope shifts of the signal of C-2. Surprisingly, the products derived from the (*S*)-enantiomer of (**3**) had a high enantiomeric excess, reaching 80% when CH_2Cl_2 was used as solvent, whereas the products from the (*R*)-enantiomer were racemic, and were not formed if chloride ion was absent.

The fact that one enantiomer of (**3**) produces a different ee from the other enantiomer is an apparent "memory effect," which suggests that the proposed mechanism cannot be always valid. We therefore used ^{31}P NMR to study the species present in solutions containing the ligand and palladium allyl sources. The spectra were initially inconclusive,

the principal signal being a broad line suggestive of oligomeric or polymeric species.[2] Two weak AB systems, consistent with an asymmetric complex of the ligand with a palladium-allyl center, were observed, and these became stronger at lower concentrations. By using racemic ligand we isolated and characterized a tetrameric species containing a 52-membered ring (4 Pd, 8 P, 8 N, and 32 C).

We have further established that the oligomerization-deoligomerization is catalyzed by the anion, which possibly acts as a weak H-bond donor, interacting with the amide —NH protons and allowing the carbonyl oxygens to interact with the palladium, releasing a phosphine. Even with the weakly nucleophilic triflate anion an equilibrium between monomeric and oligomeric species is established within a few seconds. Replacement of the triflate anion by the much less interactive BArF anion (tetrakis(3,5-bis(trifluoromethyl)phenyl)borate) reduces the rate and extent of oligomerization such that almost pure monomeric species can be observed. Two monomers are observed, each with chemically nonequivalent phosphoruses; the two monomers must arise from an asymmetric conformation of the formally C_2-symmetric ligand.

We have proved that the monomers really are monomers by replacing the two phenyl groups on one of the phosphoruses by C_6D_5 groups, creating an asymmetric ligand.[3] P-P COSY experimens then showed that the two phosphoruses bonded to the palladium in each monomer are always of different types, ($P(C_6H_5)_2$ and $P(C_6D_5)_2$), so the possibility of two separate ligand molecules being bound to the same palladium atom is excluded.

The two monomers undergo a slow exchange, as was proved by a P-P NOESY (EXSY) experiment. Using a ^{13}C-labelled (positions 1 or 3) allyl group, it could be further shown that each phosphorus site in each isomer only exchanges with one of the phosphorus sites in the other isomer, and the *trans* PC coupling is retained during the exchange process.[4] This observation rules out the possibility of allyl rearrangement being responsible for the interconversion of the two monomeric isomers.

The equilibrium between monomeric and oligomeric species allows us to explain the apparent "memory effect," in that one enantiomer of substrate (e.g., (**3**)) reacts rapidly with the monomeric allyl complex, giving high enantioselectivity of (**4**), whereas the other enantiomer of (**3**) reacts more slowly, via one or more of the oligomeric complexes, to give a racemic mixture. This explains the sensitivity of the system to solvent, concentration, and anion, since all these affect the relative concentrations of the monomeric and oligomeric species.

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