First highly enantioselective allylic alkylations catalysed by platinum complexes

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Received (in Liverpool, UK) 25th February 1999, Accepted 7th April 1999

Platinum complexes derived from phosphino-oxazolines are highly enantioselective catalysts for allylic alkylation reactions, but show different behaviour from related palladium complexes.

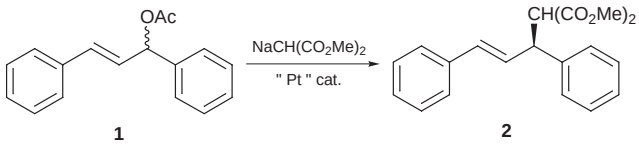
Transition metal catalysed allylic substitution reactions are classically carried out with palladium catalysts.[1] Although palladium often gives excellent results, the use of alternative metal catalysts has expanded the scope of the reaction considerably. Consequently, the study of different transition metals in this type of reaction is currently attracting considerable attention,[1,2] and there are recent reports on enantioselective allylic substitutions catalysed by iridium, [3] tungsten,[4] molybdenum[5] and nickel.[6] Reports on platinum catalysed allylic substitution reactions are extremely rare,[7] so we elected to study whether the different properties of platinum could expand the scope of this reaction still further.

Our initial studies have focused on the alkylation of diphenylpropenyl acetate with dimethyl sodiomalonate (Scheme 1). The chiral ligand **3** was chosen as it has been shown to be particularly suited to the palladium catalysed reaction.[8] As a starting point, we tested some readily available precursors in the presence of the chiral ligand. For example, 5 mol% of $(Ph_3P)_2Pt–(C_2H_4)$ in the presence of 10% of ligand **3** gave complete conversion to product at room temperature, but with low enantioselectivity (90% yield; 28% ee, 16 h, CH_2Cl_2, 20 °C).

We thought it likely that the PPh_3 present was competing with ligand **3**, and hence reducing the ee. We therefore felt that we needed to prepare a catalyst which would contain a single P,N ligand as the only phosphine present.

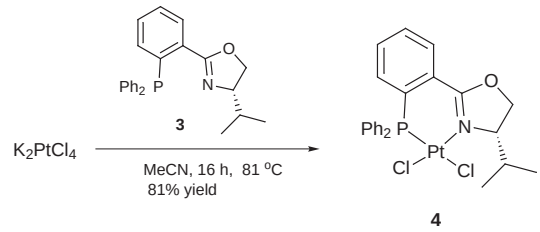
We had previously found that a combination of $(Ph_3P)_2PtCl_2$ and the reducing agent $NaBH(OMe)_3$ generates a Pt^0 complex which is an active catalyst (100% conversion: 16 h, 20 °C). We therefore chose to prepare the related complex **4**. This is readily accomplished by stirring the ligand and K_2PtCl_4 in refluxing MeCN (Scheme 2).

In contrast to the $(Ph_3P)_2PtCl_2/NaBH(OMe)_3$ system, a combination of complex **4** and $NaBH(OMe)_3$ does not catalyse the allylic alkylation of **1** at room temperature (Table 1, entry 1). However, after 30–50 h in refluxing THF, complete conversion into product is observed. It seems that complexes containing a bidentate P,N ligand make much less reactive catalysts when compared with complexes containing two phosphines. The ee of the products was high, but not as high as can be obtained with palladium.[8,9] If **4** is used in conjunction with 5% of ligand **3**, a small increase in ee was observed, whereas 10% added ligand



1 **2**

Scheme 1



Scheme 2

gives significantly lower ee as shown in Table 1 (entries 4 and 5). If 5% PPh_3 is added, a highly reactive (but unselective) catalyst is generated (Table 1, entry 6). These results suggest that the P–Pt–N chelate ring is not stable in the presence of other ligands.

Despite early failures using the readily available tetrameric compound $[(C_3H_5)PtCl]_4$, **5**,[10] it was found that 1.25 mol% of **5** in combination with 5 mol% of ligand **3** catalysed the reaction. This system also requires reflux temperatures to obtain high yields of product. The highest ee (90%) was obtained at room temperature (Table 2, entry 1) and is reduced somewhat (entry 2) when the reaction is carried out at 65 °C. It should be noted that at high conversions, the ee of the starting acetate **1** had

Table 1 Enantioselective allylic alkylation of acetate **1** with complex **4** in the presence of 10% $NaBH(OMe)_3$[a]

Entry	Additive	*T*/°C	*t*/h	Conversion (%)[b] (% yield)	Ee (%) (config.)
1	—	20	20	—	—
2 [c]	—	65	90	48	77 (*S*)
3	—	65	44	65 (—)	77 (*S*)
4	**3** (5%)	65	35	100 (93)	83 (*S*)
5	**3** (10%)	65	44	100 (—)	61 (*S*)
6	PPh_3 (5%)	20	16	100 (91)	2 (*S*)

[a] All reactions carried out in THF, using 1.7 equiv. $NaCH(CO_2Me)_2$ as nucleophile. [b] Determined by HPLC using Daicel Chiralcel® OD column (hexane–Pr^{i}OH, 99 : 1) Configuration by comparison with known Pd catalysed products (ref. 8). [c] Reaction carried out in MeCN.

Table 2 Enantioselective allylic alkylation of acetate **1** using $[(C_3H_5)PtCl]_4$ in the presence of ligand **3**

Entry	**3** (%)	*T*/°C	*t*/h	Conversion (%) (% yield)	Ee (%) (config.)
1	5	20	72	25 (—)	90 (*S*)
2	5	65	48	81 (74)	84 (S)
3	10	20	24	32 (—)	86 (*S*)
4	10	65	44	100 (90)	57 (*S*)

[a] All reactions carried out in THF, using 1.7 equiv. $NaCH(CO_2Me)_2$ as nucleophile. [b] Determined by HPLC using Daicel Chiralcel® OD column (hexane/Pr^{i}OH 99 : 1). Configuration by comparison with known Pd catalysed products (ref. 8).

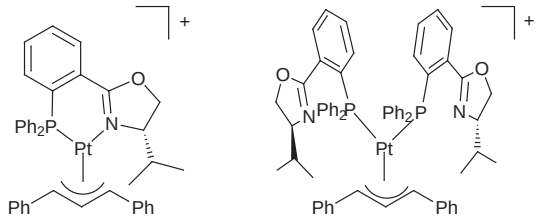
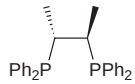


Fig. 1 Possible competing pathways in Pt catalysed allylic alkylation.

reached significant levels (73% ee). With this catalytic system, the presence of an increased amount of ligand is again detrimental to the enantioselectivity.

It seems clear that enantioselectivity and reactivity in the platinum catalysed reaction are much more sensitive to reaction conditions when compared with palladium. A possible explanation for this is that ligand **3** can be hemilabile when complexed to platinum. If this were the case, even to a small extent, it would be possible for the reaction to go *via* two competing pathways (Fig. 1). It is assumed that intermediate B would fail to give any significant level of enantiocontrol.

The platinum catalysed reaction had one more surprise in store for us, we tested the ligand (*R*,*R*)-chiraphos **6** in the catalytic reactions using tetramer **5** as our platinum source.



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Bosnich and co-workers had previously found that, in the Pd catalysed reaction, this ligand does not give high enantioselectivity for substrate **1** (100% yield, 22% ee).[11] It was therefore interesting to find that at moderate conversion the product obtained had 95% ee. If the reaction was carried out at higher temperatures, moderate yields and somewhat lower enantioselectivity were obtained (Table 3, entry 2). The reaction was then tested using the palladium catalyst $[(C_3H_5)PdCl]_2$. In this instance we observed substantially higher enantioselectivity than was previously obtained (entry 3).

In conclusion, we have shown that several Pt complexes catalyse allylic alkylation with good enantioselectivity. Carefully controlled conditions are required in order to prevent loss of enantioselectivity by less selective pathways. This suggests that ligand **3** shows different coordination chemistry for platinum (compared with palladium). We are now trying to exploit the different properties of platinum to develop new asymmetric allylation reactions.

Table 3 Enantioselective allylic alkylation of acetate **1** in the presence of (*R*,*R*)-chiraphos[a]

Entry	Catalyst	*T*/°C	*t*/h	Conversion (%)[b]	Ee (%)[b] (config.)
1	5% $[(C_3H_5)PtCl]_4$	20	72	39	95 (S)
2	5% $[(C_3H_5)PtCl]_4$	56	67	57	74 (S)
3	5% $[(C_3H_5)PdCl]_2$	20	16	100	85 (S)

[a] All reactions carried out in THF, using 1.7 equiv. $NaCH(CO_2Me)_2$ as nucleophile. [b] Determined by HPLC using Daicel Chiralcel® OD column (hexane/Pr^{i}OH 99 : 1). Configuration by comparison with known Pd catalysed products (ref. 8).

We are grateful to the LINK asymmetric synthesis programme, Glaxo-Wellcome and Zeneca for financial support.

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Communication 9/01555H