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Asymmetric palladium(0)-catalyzed synthesis of allylic ethers

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Abstract

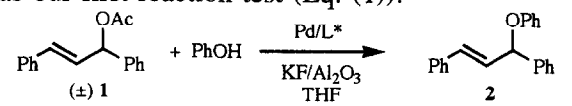
Palladium-catalyzed reaction of phenol with allylic carbonates and acetates in the presence of various chiral ligands afforded the corresponding allyl phenyl ethers with moderate to good enantioselectivities (up to 83%). © 1997 Elsevier Science B.V.

Keywords: Allylic substitution; Palladium; Phenol; Chiral allylic ether

Obtention of enantiomerically pure compounds using homogeneous organometallic catalysis has grown in importance during the last years [1]. Very high enantioselectivities have been achieved in hydrogenation [2], epoxydation [3], dihydroxylation [4] and cyclopropanation [5]. In allylic alkylation, the progress has been more sporadic; nevertheless high enantioselectivities have also been obtained in the formation of carbon–carbon and carbon–nitrogen bond [6]. However to our knowledge only one example of asymmetric catalytic formation of carbon–oxygen bond appeared in the literature [7].

In a program directed towards the use of organometallic catalysis in the formation of carbon–heteroatom bond, we shown recently that alcohols and phenols reacted with allylic carbonates in the presence of a palladium(0)-complex to give regioselectivity and stereospecifically the corresponding allylic ether in quite good yields under very mild conditions [8]. Herein we report our preliminary results concerning the asymmetric *O*-alkylation of allylic carbonates and acetates by phenols and alcohols catalyzed by palladium complexes associated to chiral diphosphines (Scheme 1).

Early work established that excellent enantioselectivity was obtained in the alkylation of racemic 1,3-diphenylallyl acetate **1** with various carbon as well nitrogen nucleophiles [6]. We employed the reaction of racemic **1** with phenol as our first reaction test (Eq. (1)).



(1)

The reaction was performed in the presence of a catalyst prepared from $Pd_2(dba)_3$ and the chiral ligand and of potassium fluoride supported on alumina as previously described [9] and at 40°C;

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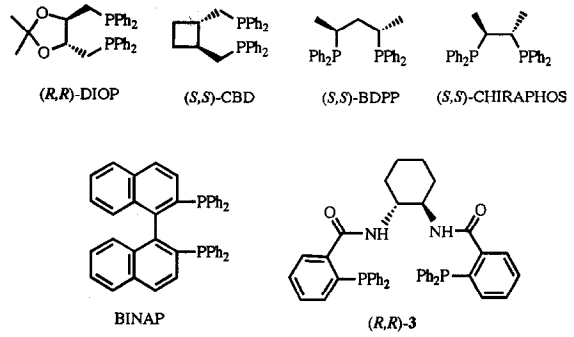
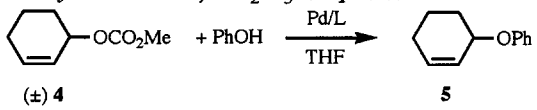


Scheme 1.

it was effectively shown that heating is required to form π-allylpalladium complexes from allyl phenyl ethers, the phenoxy group being not a good leaving group at room temperature [10]. The results summarized in Table 1 show that the chemical yields are good and that the highest enantioselectivity was obtained using BINAP as the chiral ligand (entries 5 and 6); the other ligands such as DIOP, CBD, BDPP and CHIRAPHOS gave lower enantioselectivities (entries 1–4). It is to be noticed that when a sample of (*R*)-cyclohexenyl phenyl ether ($[\alpha]_D^{20} = +38.2$, 22.5% ee) was stirred for 24 h in THF in the presence of $Pd_2(dba)_3$ and BDPP, no racemization was observed, the resulting isolated product having $[\alpha]_D^{20} = +38$. Unfortunately the catalytic system obtained by mixing $Pd_2(dba)_3$ and the chiral diphosphine **3** developed by Trost et al. [12] and which is known to give very high enantioselectivities in this kind of reaction was completely inactive under these conditions.

We then turned out our attention to the *O*-alkylation of the methyl carbonate of cyclohexen-3-ol **4** leading to the ether **5**, the better leaving-group ability of the methyl carbonate allowing the reaction to occur at room temperature without any added KF/Al_2O_3 (Eq. (2)).



(±) **4** **5** (2)

As shown in the table, although the chemical yields were good, very low enantioselectivities were again obtained using DIOP (entry 7), CHIRAPHOS (entry 10) and even BINAP (entry 11) as the chiral ligand; it is to be noticed that with BINAP the reaction has to be performed at 50°C, no reaction occurring at 30°C. The use of BDPP as the ligand at 30°C in THF gave a moderate level of 32% enantioselectivity (entry 8); in this case, performing the reaction at 0°C gave a similar chemical yield, but lowered the

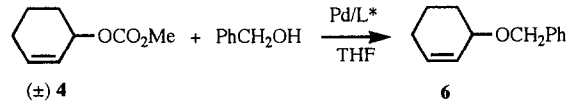
Table 1
Alkylation of 1,3-diphenylallyl acetate **1** and methyl cyclohex-2-enyl carbonate **4** with phenol [a]

Entry	Substrate	Ligand	*T* (°C)	Time (h)	Compound (Yield %) [b]	ee (%) [c] (config.)
1	**1**	(*R,R*)-DIOP	40	24	**2** (48)	7
2	**1**	(*S,S*)-CBD	40	24	**2** (72)	7
3	**1**	(*S,S*)-BDPP	40	24	**2** (48)	12
4	**1**	(*S,S*)-CHIRAPHOS	40	24	**2** (61)	3
5	**1**	(*S*)-BINAP	40	24	**2** (79)	46 [d]
6	**1**	(*R*)-BINAP	40	24	**2** (75)	46
7	**4**	(*R,R*)-DIOP	30	19	**5** (51)	7 (*R*)
8	**4**	(*S,S*)-BDPP	30	17	**5** (60)	32 (*R*)
9	**4**	(*S,S*)-BDPP	0	80	**5** (70)	15 (*R*)
10	**4**	(*S,S*)-CHIRAPHOS	30	3	**5** (40)	9 (*R*)
11	**4**	(*R*)-BINAP	50	60	**5** (89)	16 (*S*)
12	**4**	(*R,R*)-**3**	30	30	**5** (95)	83 (*S*) [e]

[a] Reaction conditions: [**1**]:[phenol]:[palladium]:[ligand] = 25:50:1:1, solvent THF; KF/Al_2O_3 500 mg/mmol of **1** for entries 1–6.
[b] Isolated yields after purification by column chromatography and not optimized.
[c] Enantiomeric excess was determined by chiral HPLC: Chiralpak AD (0.46 cm × 25 cm) using hexane/*i*-PrOH (95/5) as the eluent and a flow of 0.05 mL/min. Absolute stereochemistry for **5** was assigned according to Ref. [11].
[d] $[\alpha]_D^{25} = -15$ (*c* 1, CH_2Cl_2).
[e] $[\alpha]_D^{25} = -141$ (*c* 1, CH_2Cl_2).

enantioselectivity in the formation of the allylic ether (entry 9). As expected the highest enantioselectivity (up to 83%, entry 12) was obtained using the chiral ligand recently developed by Trost et al. [12]; it is also to be noticed that the chemical yield in this case is very high, up to 95% and that the observed configuration for **5** followed Trost's mnemonic for determination of the sense of chirality.

Finally we used also benzyl alcohol as the nucleophile, methyl cyclohexenyl carbonate **4** as the π-allyl precursor and the catalyst prepared from $Pd_2(dba)_3$ and DIOP, BDPP or ligand **3** (Eq. (3)).



(±) **4** **6**

(3)

Although the chemical yields in pure product were low after purification (respectively 23, 13 and 5%) and needed to be optimized, the benzyl ether **6** was obtained respectively in 7%, 36% and 98% ee [1].

In conclusion this palladium(0)-catalyzed methodology should prove a useful approach for the asymmetric synthesis of arylic allylic ethers from racemic allylic alcohols, which could be deprotected to yield the corresponding non-racemic allylic alcohols in the case of *p*-anisyl ether [13] or benzyl ether [14] of allylic carbinol. Further studies in this area are currently in progress in this laboratory and will be reported later.

Acknowledgements

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[1] $[\alpha]_D^{25} = -104$ (c 0.5, CH_2Cl_2) for the *S* isomer for alkylation with ligand **3**; enantiomeric excess was determined by chiral HPLC: Chiralpak AD (0.46 cm×25 cm) using hexane as the eluent and a flow of 0.07 mL/min.

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