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Palladium-catalyzed reactions of 1-phenylphospholene-1-oxides with aryl iodides and aryldiazonium salts.

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Abstract

1-Phenylphosphol-2-en-1-oxide **1a** reacts with aryl iodides in the presence of ammonium formate and a catalytic amount of $Pd(OAc)_2$ to give 3-aryl-1-phenylphospholane-1-oxides **3**, whereas 4-aryl-1-phenylphosphol-2-en-1-oxides **4** are obtained from 1-phenylphosphol-3-en-1-oxide **2a** under modified Heck reaction conditions (aryldiazonium salt, catalytic $Pd(OAc)_2$).

Keywords: Heck reaction; phospholenes; phospholanes.

Palladium-catalyzed Heck reaction [1-4] of dihydrofuran **1b** and dihydropyrrole **1c** with aryl iodides and triflates is well documented [5-12], especially in the context of asymmetric synthesis [13-18]. Similar behavior of compounds **2b** [19] **2c** [20, 21] and **2d** [22] is also described.

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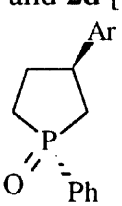

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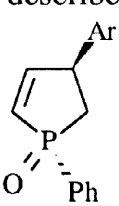

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a: X = P(O)Ph; **b**: X = O; **c**: X = NR; **d**: $X = SO_2$

1-Phenylphospholene-1-oxides **1a** and **2a** are easily prepared by Mc Cormack cycloaddition of butadiene with dichloro- and dibromophenylphosphine, respectively [23].[2] These substrates are potential precursors of new monophosphine ligands based on a phospholane skeleton [25-27].

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[2] 1-Phenylphosphol-3-ene (**2**, X =PPh) was recently prepared by ring closure metathesis of diallylphenylphosphine [24].

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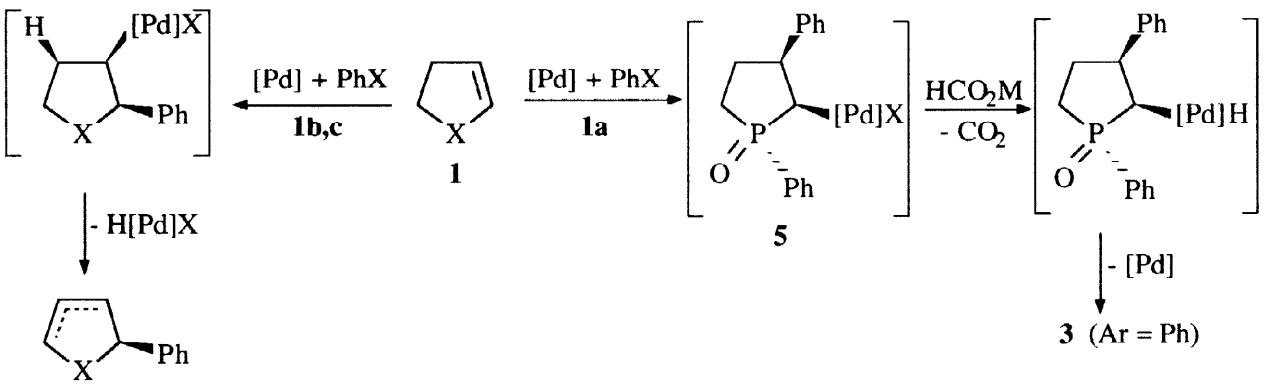
We report in this letter our prelimilary results on palladium-catalyzed reactions of **1a** and **2a** to give substituted phospholane and phospholene oxides **3** and **4** respectively.

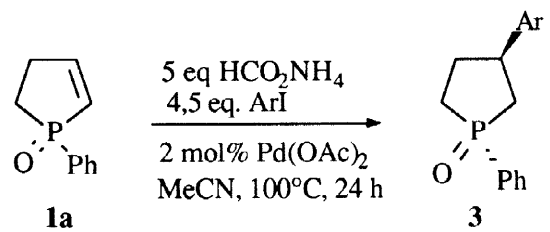
The reaction of iodobenzene with compound **1a** under various Heck reaction conditions led to recovery of starting material. This lack of reactivity is the result of the insertion of the double bond of compound **1a** into the aryl-palladium bond of $PhPdXL_2$ (resulting from oxidative addition of PhI onto a Pd(0) species) gives Pd-complex **5** (see Scheme 1). This intermediate can not undergo syn β-hydride elimination, the following step of the Heck reaction. The regioselectivity of this process is hence opposite to the one observed on dihydrofuran **1b** and dihydropyrrole **1c**, but is in good agreement with the well-documented Heck reaction on olefins substituted by an electron-withdrawing group, in particular with the results of Pietrusiewicz concerning the regioselectivity of the arylation of vinylphosphine oxides [28, 29].

To confirm this hypothesis, we have examined the reactivity of **1a** under hydrophenylation conditions [4, 30]. In the presence of a formate salt, **5** would undergo ligand exchange, decarboxylation and finally reductive elimination to give **3** (Ar = Ph).



Scheme 1 (additional ligands are omitted for clarity)

The results are presented in Scheme 2. In the presence of an excess of formate anion and aryl iodide, the hydroarylation product was obtained in moderate to good yield (67-91%). Aryl bromides (phenyl, p-methoxyphenyl and 2-pyridyl), phenyl triflate and p-nitrophenyl iodide were unreactive under the same conditions. With the latter substrate, substrate **1a** was recovered together with nitrobenzene resulting from reduction prior to double bond insertion.



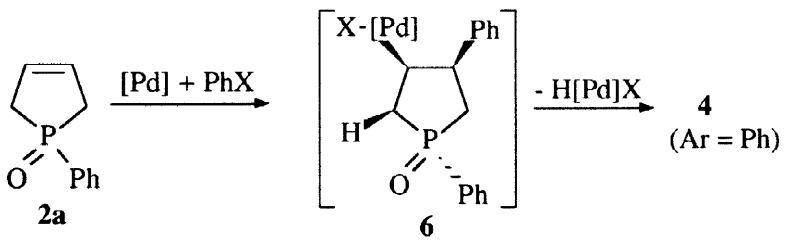
Ar	Isolated yield (%)
Ph	67
$pMeC_6H_4$	69
$pMeOC_6H_4$	91

Scheme 2

In every case, only one stereoisomer of **3** was detected by TLC and ^{31}P NMR analysis (a single peak in the range 58.5-59.4 ppm was observed on the spectrum). The stereochemistry of

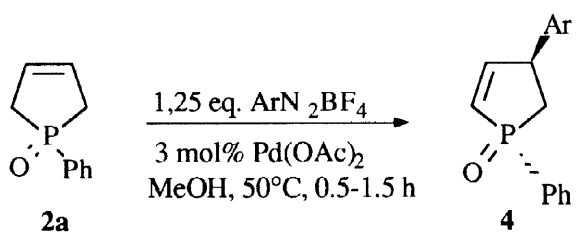
the compound **3** (Ar = $pMeOC_6H_4$) was established by a NOESY experiment: a spatial interaction was detected between the benzylic proton on the phospholane ring and the ortho protons of the phenyl group on phosphorus. The reaction is stereoselective to give only the *(R*R*)* stereoisomer of **3**, with the two aryl groups in a trans relationship, resulting from approach of the palladium(II) complex by the less hindered face of **1a**.

Next, we have studied the Heck reaction of **2a**, since β-hydride elimination is not inhibed by stereochemical constraint on intermediate **6** (Scheme 3). Preliminary experiments showed a moderate reactivity of **2a** toward aryl iodides, since yields of 24-40% (not optimized) of product **4** (Ar = Ph, $pMeOC_6H_4$) were obtained after 48 hours of reaction at 80-100°C in acetonitrile (catalyst = $Pd(OAc)_2$ + PPh_3).



Scheme 3

Our best results, collected in Scheme 4, were obtained with aryldiazonium salts [31], which are now frequently used in palladium-catalyzed Heck reactions [19, 22, 32-35]. On heating at 50°C a methanol solution of **2a** and ArN_2BF_4 in slight excess in the presence of a catalytic amount (3 mol%) of palladium acetate, compound **4** was isolated in good yield. The less satisfactory result with the p-bromo derivative can be attributed to the one pot-procedure adopted in this case: $pBrC_6H_4N_2BF_4$ was prepared in aqueous solution and a solution of **2a**, $Pd(OAc)_2$ in MeOH was then added and the mixture heated to 50°C for 1.5 h.



Ar	t (h)	Isolated yield (%)
Ph	0.5	79
$pMeC_6H_4$	1	80
$pMeOC_6H_4$	1	83
1-Naphthyl	0.5	89
$pBrC_6H_4$	1.5	64

Scheme 4

Here again, in every case, only one stereoisomer of **4** was detected by TLC and ^{31}P NMR analysis (a single peak in the range 59.9-60.7 ppm was observed on the spectrum). The stereochemistry of compound **4** (Ar = $pMeOC_6H_4$) was also determined by a NOESY experiment. The reaction is totally stereoselective to give *(R*S*)* **4**, resulting from approach of the palladium(II) complex by the less hindered face of **2a**.

Finally, we attempted to prepare 1,3,5-triphenylphospholane oxide by hydrophenylation of compound **4** (Ar = Ph). Unfortunately, under the conditions of hydroarylation of **1a**, no reaction was observed and **4** was recovered almost quantitatively. This failure is probably due to the steric hindrance of both faces of the double bond of **4** by the two phenyl groups.

In summary, hydroarylation of **1a** and Heck arylation of **2a** gave regio- and stereoselectively phospholane and phospholene oxide derivatives **3** and **4**. Since **1a** has been already resolved [36], the first reaction constitutes an access to new enantiomerically pure monophosphines after reduction. Moreover, the Heck reaction of prochiral **2a** in the presence of a chiral palladium complex could give the same product by asymmetric catalysis. This work is presently in progress in our laboratory.

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