Catalytic Hydrophosphination of Alkenylalkyl Ethers

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Received 4 August 2003

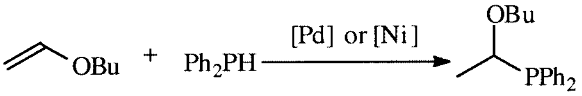
Abstract: Hydrophosphination of alkenylalkyl ethers catalyzed by Pd- and Ni-complexes is described. The reaction is regioselective giving only Markovnikov product isolated as α-alkoxyalkyldiphenyl oxide after oxidation by H_2O_2.

Key words: nickel, palladium, alkenes, hydrophosphination, alkenylalkyl ethers

The reaction of diphenylphosphine with alkenes is a simple and convenient way to alkyldiphenylphosphines and particularly to functionalized phosphines of this type.[1] Hydrophosphination of alkenes is usually carried out using radical initiators,[2] or in the presence of strong bases[3] or Brønsted acids.[4] In all these reactions R_2P-group is usually directed in β-position of terminal alkenes. Inter- or inrtamolecular hydrophosphination of alkenes under the action of PH_3 or R_2PH can be catalyzed by platinum and palladium complexes,[5] as well as by complexes of lanthanides.[6] However Pt- and Pd-complexes catalyze only the reaction with the activated alkenes, having electron withdrawing groups (EWG) and R_2P-group is always added to the terminal carbon atom as in the case of radical reactions.

Recently we have performed hydrophosphination of styrenes and heteroanalogs of styrene catalyzed by Pd- and Ni-complexes and have shown that Ni-complexes are more active than Pd-complexes.[7] In all reaction only anti-Markovnikov products – β-isomers were formed. Apparently aryl groups activate the double bond because alkylalkenes failed to react with Ph_2PH under these conditions. We suppose that this reaction can be considered as a catalytic analog of Michael addition.

In this report we have shown that hydrophosphination catalyzed by nickel and palladium complexes proceeds easily with alkenes having an electron-donating group – alkenylalkyl ethers (Equation 1). However in contrast to hydrophosphination of alkenes with EWG-groups this reaction is not catalyzed by Pd(0)-and Ni(0)-complexes but proceeds in the presence of Pd^{2+} or Ni^{2+} complexes. The regioselectivity of the reaction is also different, the reaction leads to Markovnikov products – α-alkoxyalkylphosphines.



1a **2a**

Equation 1

The results of the model reaction of vinylbutyl ether with Ph_2PH [conversion (%) of Ph_2PH measured by ^{31}P NMR] are given in Table 1. It was shown that the yield of the product was equal to conversion.

As can be seen from Table 1 Pd(0)- or Ni(0)-complexes are inefficient (entries 1, 2, 11, 12). The $PdCl_2(PPh_3)_2$ complex is more active than $PdCl_2(CH_3CN)_2$ (entries 5 and 7). But Ni^{2+}-complexes $NiBr_2(PPh_3)_2$ (entries 14, 15) and 'ligandless' $NiBr_2$ (entry 17) are the most active. The activity of $NiBr_2$ can be apparently concerned with the formation of $NiBr_2(Ph_2PH)_2$. The efficiency of Pd-complexes having secondary phosphine as a ligand has been recently demonstrated.[8]

The high activity of Ni^{2+}-complexes allowed us to use lower concentration of the catalyst and to reduce the reaction temperature and reaction time compared to Pd^{2+}-complexes. The reaction can be carried out even at room temperature but needs 7 days for completion (entry 14). The anion in Ni^{2+}-complexes plays an important role because $Ni(acac)_2$ does not catalyze the reaction (entry 13).

We did not observe any significant influence of solvents. The reaction proceeds equally well in benzene, THF or MeCN (entry 3, 9, 10).

The fact that this reaction is not catalyzed by zerovalent nickel complexes, as the reaction of styrenes and alkenes with EWG, suggests that they have different mechanisms. Earlier we have shown that the mechanism and regioselectivity of hydrophosphination of alkynes changes in the presence of acids.[9] It is obvious that acids can be formed by the reduction of $PdCl_2$ and $NiBr_2$[10] and in such way can catalyze the addition to nucleophilic alkenes. However we have shown that in the presence of acids (HCl or CF_3COOH) (entries 19, 20) reaction proceeds very slowly and the result is the same as for Ni(0)–HCl (entry 21). A different situation is observed when HCl is added to $Ni(acac)_2$ (entry 22), probably because of $NiCl_2$ formation.

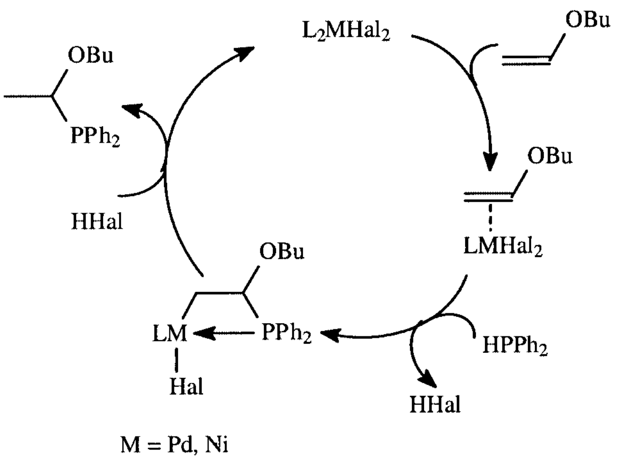
SYNLETT 2003, No. 14, pp 2155–2158
Advanced online publication: 15.10.2003
DOI: 10.1055/s-2003-42092; Art ID: G19803ST

Table 1 The Influence of the Catalyst Nature and Temperature on the Reaction of Ph_2PH with Vinylbutyl in Benzene

Entry	Catalyst	Mol% catalyst	Temp °C [time (h)]	Conversion[a]
1	$Pd(PPh_3)_4$	2	100 (8)	0
2	$Pd(PPh_3)_4$	5	120 (8)	<1
3	$PdCl_2(CH_3CN)_2$	5	100 (8)	100
4	$PdCl_2(CH_3CN)_2$	5	80 (15)	>90
5	$PdCl_2(CH_3CN)_2$	2	100 (8)	<50
6[b]	$PdCl_2(PPh_3)_2$	2	100 (8)	100
7	$PdCl_2(PPh_3)_2$	2	100 (8)	90
8	$PdCl_2(PPh_3)_2$	5	100 (8)	95
9[c]	$PdCl_2(CH_3CN)_2$	5	100 (8)	100
10[d]	$PdCl_2(CH_3CN)_2$	5	100 (8)	100
11	$Ni(cod)_2$	5	120 (8)	0
12	$Ni[P(OEt)_3]_4$	5	80 (8)	0
13	$Ni(acac)_2$	5	120 (8)	0
14	$NiBr_2(PPh_3)_2$	5	80 (2)	100
15	$NiBr_2(PPh_3)_2$	2	80 (2)	100
16	$NiBr_2(PPh_3)_2$	2	r.t. (7 d)	100
17	$NiBr_2$	2	80 (2)	100
18	$NiBr_2(PPh_3)_2/Et_3N$	5/10	80 (2)	0
19	CF_3COOH	10	80 (2)	<10
20	HCl	10	80 (2)	25
21	$Ni(cod)_2$/HCl	5/10	80 (2)	25
22	$Ni(acac)_2$/HCl	5/10	80 (2)	100

[a] Determined by NMR ^{31}P.
[b] 1.5 Molar excess of vinyl ether.
[c] Reaction in THF.
[d] Reaction in CH_3CN.

We can assume that the mechanism of this reaction involves activation of double bond by M^{2+} with subsequent nucleophilic attack (as at the first step of Wacker process). But at the next step the protonolysis (the acid may be complexed by Ph_2PH) of carbon-metal bond takes place instead of β-hydrogen elimination. Probably this reaction pathway is due to the stabilization of organometallic intermediate by intramolecular M-P bond.[11] The necessity of protonolysis allows to explain the absence of the reaction in the presence of $Ni(acac)_2$. Another proof of this assumption is the absence of reaction catalyzed by $NiBr_2(PPh_3)_2$ in the presence of Et_3N (entry 18). The following catalytic cycle can be suggested (Scheme 1).



Scheme 1

Notice that besides $MHal_2$, $HalMPPh_2$ or $M(PPh_2)_2$ formed by the exchange reaction between $MHal_2$ and Ph_2PH, may also participate in the catalytic cycle. The mechanism explains the formation of Markovnikov product in the reaction. Proving of this mechanism means that Wacker-type activation of alkenes can be performed by Ni^{2+}.

The optimum conditions for the hydrophosphination of vinylbuthyl ether are 2 mol% of $NiBr_2(PPh_3)_2$ in benzene at 80 °C. Under these conditions the hydrophosphination of several alkenylalkyl ethers having alkyl substituents at α- or β-carbon was carried out (Table 2). As can be seen from Table 2 the introduction of alkyl group in both positions has little influence on the yield, which remains moderately high (entries 2–5). The only exception is the cyclic ether dihydro-2*H*-pyrane, the reaction of which requires more rigid conditions (100 °C) and gives the product in a lower yield (entry 6).

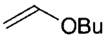
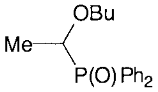
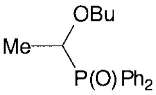
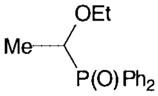
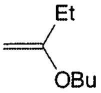
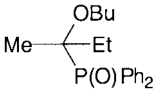
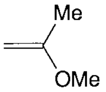
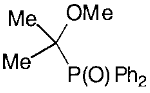
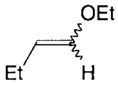
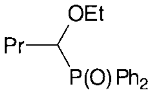
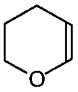
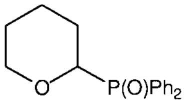
The synthesized phosphines are readily oxidized upon isolation and for obtaining good NMR spectra and analytical data all phosphines (**2a**–**f**) were oxidized by 30% H_2O_2 to corresponding phosphine oxides (**3a**–**f**).

It should be noted that conventional syntheses of α-alkoxyalkylphosphines are multi step or require reagents easily hydrolyzed with formation of HCl.[12]

The synthesized phosphines (**3a**–**f**) and their oxides (**4a**–**f**) are not well-studied compounds. However, their application in Horner–Wittig reaction for stereoselective synthesis of functionalized alkenes[13] or as complexing agents for extraction of uranium and thorium salts from acidic solutions is known.[14] Apart from this, these phosphines having chiral carbon atom can be considered as potentially interesting ligands for transition metal catalysis.

Conclusion: we proposed a simple and efficient method for the synthesis of α-alkoxyalkyldiphenylphosphines by hydrophosphination of alkylvinyl ethers in the presence of Ni-salts.[15]

Table 2 Hydrophosphination of Vinylethers with Ph_2PH[a]

Entry	Ether	Phosphine oxide	Yield (%)[b]
1	 **1a**	 **3a**	83
2	 **1b**	 **3b**	85
3	 **1c**	 **3c**	80
4	 **1d**	 **3d**	76
5	 **1e**	 **3e**	70
6[c]	 **1f**	 **3f**	40

[a] Conditions: vinyl ether(1.65 mmol), Ph_2PH (1.5 mmmol) and $Ni(PPh_3)_2Br_2$ (2% mol) in benzene (3 mL), 2 hours, 80 °C.

[b] Isolated yield.

[c] 8 Hours, 100 °C

Acknowledgment

We thank Trostyanskaya I.G. and Kirichenko E. for the preparation of starting compounds and The Grant of Russian Federation President supporting Leading Scientific Schools – 1611.2003.3 for financial support.

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(15) **Experimental Conditions:** In a 8 mm tube filled with argon were placed $Ni(PPh_3)_2Br_2$ (55 mg, 5 mol%), Ph_2PH (279 mg, 1,5 mmol), alkenyl ether (1.65 mmol) and dry benzene (3 mL). The tube was sealed and placed in a hot bath. Reaction time and temperature are given in Table 2. After cooling the tube was opened and the solvent was evaporated. The residue was dissolved in 15 mL of Et_2O and 2 ml 30% H_2O_2 was added. The mixture was stirred until the organic phase discoloured. The organic phase was separated, washed with water, dried under $MgSO_4$ and evaporated in vacuum. The target compound was recrystallized from hexane or purified by column chromatography (Al_2O_3, Et_2O). 1-Butoxyethyl(diphenyl)phosphine oxide (**3a**) was recrystallized from hexane (cooling up to –18 °C), colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.85 (t, 3 H), 1.22–1.26 (m, 2 H), 1.45–1.51 (m, 5 H), 3.19–3.25 (m, 1 H), 3.58–3.64 (m, 1 H), 4.19–4.23 (m, 1 H), 7.45–7.58 (m, 6 H), 7.88–7.92 (m, 2 H), 8.05–8.09 (m, 2 H). $^{31}P\{^1H\}$ NMR (162.6 MHz, $CDCl_3$): δ = 30.0. Anal. Calcd: C, 71.52; H, 7.61. Found: C, 71.35; H, 7.45.