Tetrahedron Letters No. 47, pp 4591 - 4594.
0040-4039/79/1115-4591$02.00/0

ADDITION OF BENZENE TO α,β-UNSATURATED KETONES IN A TWO PHASE SYSTEM IN THE PRESENCE OF THE TBA$^+$PdCl$_3^-$ CATALYST

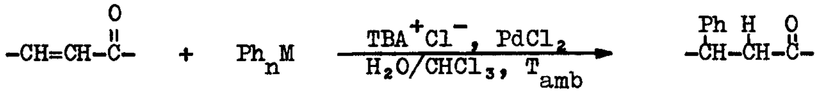
S. Cacchi[a], F. La Torre[b], D. Misiti[a]

a) Cattedra di Chimica Organica, Via Castro Laurenziano 9, 00161 Roma, Italy
b) Istituto Superiore di Sanita', Laboratorio Chimica del Farmaco, 00161 Roma, Italy

Summary - β-Phenyl derivatives of saturated ketones were obtained from the reaction of α,β-unsaturated ketones and PhHgCl or Ph_4Sn in the presence of catalytic amount of TBA$^+$Cl$^-$ and $PdCl_2$ in a two phase system.

In the last few years, the phase-transfer catalysis has growth to the most versatile, useful and relatively inexpensive method in organic synthesis. In spite of the rather limited utilization of the phase-transfer conditions to organo-metallic reactions, this methodology has been successfully applied to a number of metallic systems to attain oxidation[1], reduction[2], reductive dehalogenation[3], carbonylation[4] and vinylic nucleophilic substitution[5].

Now we wish to report on the application of the phase-transfer technique to the palladium catalyzed carbon-carbon bond formation. It is well known that arylpalladium compounds prepared in situ from a proper arylmercurial and a Pd(II) salt, react with olefinic double bonds to give vinylic substitution[6]. Almost surprisingly, we found that when this reaction is carried out with α,β-unsaturated ketones[7], using an excess of PhHgCl or Ph_4Sn[8] as phenyl-donors, $PdCl_2$ (5 mol %) and tetrabutylammonium chloride (TBA$^+$Cl$^-$, 10 mol %) in an acidic (HCl 3N) CH_2Cl_2/H_2O two phase system, the addition of benzene to olefinic double bond occurs in good yield according to the following scheme:



$$\text{-CH=CH-}\overset{O}{\overset{\|}{C}}\text{-} + Ph_nM \xrightarrow[H_2O/CHCl_3,\ T_{amb}]{TBA^+Cl^-,\ PdCl_2} \text{-}\overset{Ph}{CH}\text{-}\overset{H}{CH}\text{-}\overset{O}{\overset{\|}{C}}\text{-}$$

(1) (2)

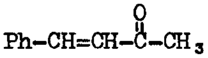
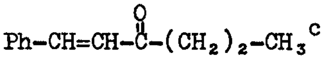
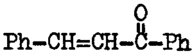
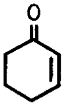
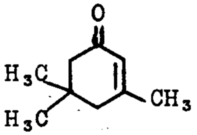
M = Sn, n = 4
M = HgCl, n = 1

Scheme 1

The results are summarized in the table.

Presumably, under the reported conditions, the active palladium species is the dichlorometane soluble TBA$^+$PdCl$_3^-$ salt derived from the in situ reaction of TBA$^+$Cl$^-$ and $PdCl_2$[9]. Control experiment with benzalacetone as starting material revealed that the ammonium salt greatly enhances the reaction yield; 4,4-di

Table - Addition of benzene to α,β-unsaturated ketones.

Starting material (1)	Reaction time (h)	PhHgCl/(1) molar ratio (yield % of (2))^{a,b}		Reaction time (h)	Ph_4Sn/(1) molar ratio (yield % of (2))^{a,b}	
 $Ph-CH=CH-\overset{O}{\overset{\|}{C}}-CH_3$	5	1.5	(85)	4.5	1.5	(88)
 $Ph-CH=CH-\overset{O}{\overset{\|}{C}}-(CH_2)_2-CH_3$ [c]	7	1.5	(78)	24	1.5	(73)
 $Ph-CH=CH-\overset{O}{\overset{\|}{C}}-Ph$	8	1.5	(54)	24	1.5	(23)
	14	3.0	(78)	24	3.0	(75)
	24	1.5	(80)	24	1.5	(60)
	24	1.5	(0)	24	1.5	(0)
Cholest-4-en-3-one	14	1.5	(0)	14	1.5	(0)

a) Yields are not optimized, are calculated on the starting α,β-unsaturated ketone and are given on the pure, isolated product.

b) Products were identified by comparison of the spectral data (ir, ^{1}H-nmr, ms) with those for authentic specimens.

c) Prepared from benzaldehyde and butan-2-one according to standard methods

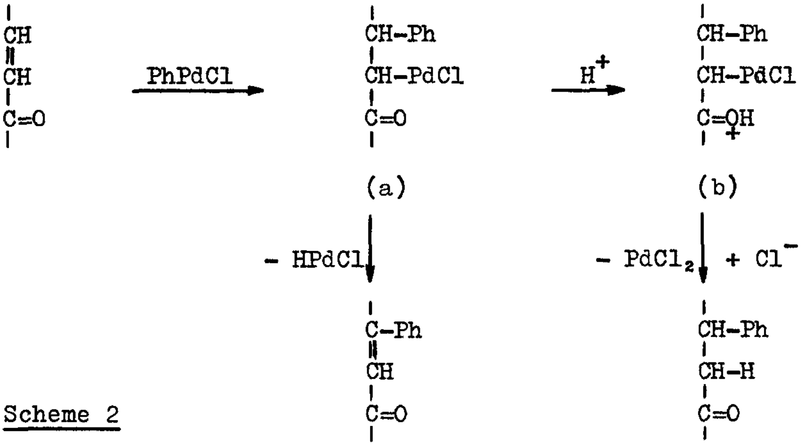
---

phenyl-butan-2-one was isolated in only 11% yield[10] after 11 h if the ammonium salt is omitted.

Even the acidic medium is critical because if the same reaction is carried out under initially neutral conditions[11] no 4,4-diphenyl-butan-2-one and only traces (2-3%) of the vinylic substituted product[6] were recovered, the main product being the unreacted starting material. As expected, owing to the absence of any Pd(O) reoxydative system, the percentage of the vinylic substituted product roughly corresponds to the amount of the added palladium.

If the palladium catalyst/substrate molar ratio was rised to 1:1 without the addition of the acid, the vinylic substituted product was isolated in 55% yield together with 12% of 4,4-diphenyl-butan-2-one. The formation of this last compound was ascribed to the presence of hydrogen chloride derived from the decomposition of hydridopalladium chloride. In a sufficiently acidic medium, the reaction occurs mainly according to the scheme 1 with catalytic amounts of the Pd(II) salt. Thus, the Pd(II) must participate in the reaction mechanism without modificating its oxidation state. The above reported experimental results seem to be consistent with the proposed scheme 2.

The initially formed intermediate (a) may give a cis-elimination of HPdCl[6] or, under acidic conditions, may react with H^+ to give the protonated inter-



Scheme 2

mediate (b) that undergoes the eterolytic fission of the palladium-carbon bond faster than any conformational change required for cis-elimination. Assistance of the chloride atom may be involved in this step through nucleophilic attack to the rising palladium chloride cation. However, it must be emphasized that no benzene adduct was isolated in the absence of an acidic medium even with an excess of $Na^{+}Cl^{-}$ or $TBA^{+}Cl^{-}$[12].

The only example we have found in the literature[13] of this palladium catalyzed reaction, reported the benzene addition to α-substituted chalcone derivatives to occur in a benzene/acetic acid refluxing mixture as a result of two simultaneous effects: restriction in the rotation necessary to attain the nevertheless steric hyndered conformation required for cis-elimination of hydridopalladium acetate and mesomeric stabilization of the carbanion leaving the palladium acetate cation. Chalcone itself and α-phenyl chalcone were reported to give β-vinylic substitution and chalcones α-substituted with electron withdrawing groups to give benzene addition.

Under our conditions, unhyndered α,β-unsaturated ketones give palladium--catalyzed benzene addition independently from conformational crowdings and/or from the presence of strongly electron withdrawing groups.

In a typical case, to a stirred solution of benzalacetone (0.5 g, 3.42 mmol) in dichloromethane (6.5 ml) are added a 3N aqueous solution of HCl (4.0 ml), $TBA^{+}Cl^{-}$ (0.095 g, 0.34 mmol), $PdCl_2$ (0.030 g, 0.17 mmol) and PhHgCl (1.61 g, 5.14 mmol). The resultant mixture is stirred for 5 h at room temperature, the organic layer is separated, washed with a 10% sodium thiosulfate solution and water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue is chromatographed on Silica Gel. Elution with a 80/20 n-hexane/ ethyl acetate mixture gives 4,4-diphenyl-butan-2-one (0.651 g, 85%).

Aknowledgment - We are thankful to dr. Antonio Arcadi for collaboration in the experimental part.

References and Footnotes

1) W.P. Weber, G.W. Gokel, Phase-Transfer Catalysis in Organic Synthesis, Springer-Verlag 1977, sect. 11.2, 11.3 and 11.5
2) H. des Abbayes, H. Alper, J. Am. Chem. Soc. 99, 98 (1977); D.L. Reger, M.M. Habib and D.J. Fauth, Tetrahedron Lett., 115 (1979)

3) H. Alper, K.D. Logbo and H. des Abbayes, Tetrahedron Lett., 2861 (1977)
4) L. Cassar, M. Foa' and A. Gardano, J. Organomet. Chem. 121, C55 (1976)
5) K. Yamamura, Shun-Ichi Murahashi, Tetrahedron Lett., 4429 (1977)
6) R.F. Heck, J. Am. Chem. Soc. 90. 5518 (1968); R.F. Heck, J. Am. Chem. Soc. 91, 6707 (1969)
7) Cinnamaldehyde, cinnamonitrile and methyl cinnamate were also tested under our conditions. However, only methyl cinnamate gave the corresponding benzene adduct (42% yield, 24 h) in the presence of Ph_4Sn. No reaction was observed in the other cases. It is of interest to note that in a competition experiment, addition of PhHgCl, $PdCl_2$ and TBA^+Cl^- to a 1:1 mixture of benzalacetone and cinnamaldehyde yielded product only resulting from reaction of benzalacetone (4,4-diphenyl-butan-2-one, 72% yield). The aldehyde was recovered unchanged.
8) Benzalacetone was almost quantitatively recovered when the reaction was carried out (24 h) with MeHgCl or Me_4Sn.
9) The $TBA^+PdCl_3^-$ salt, presumably in a dimeric form, may be easily prepared in 60% yield (calculated on the crystallized product, CH_2Cl_2/n-hexane) from the reaction (overnight) of $PdCl_2$ and aqueous TBA^+Cl^- (1:1.5 molar ratio) at room temperature. The red-brown solid can be stored for extended periods at room temperature without change.
Anal.: Calcd. for $C_{16}H_{36}NPdCl_3$: C, 42.21; H, 7.97; N, 3.08; Pd, 23.37; Cl, 23.36. Found: C, 41.66; H, 7.94; N, 3.05; Pd, 23.74; Cl, 23.56. Microanalysis was performed by F. Pascher, E. Pascher, Mikroanalytisches Laboratorium, Bonn.
10) The starting material was recovered in 85% yield.
11) If the vinylic substitution pathway is followed, as Pd(0) and HCl are formed from the reaction of an olefinic double bond with PhPdCl, the pH of the medium goes down as the reaction proceeds.
12) Even under the high chloride ion concentrations utilized (1:7, substrate/chloride ion molar ratio) no chlorobenzene addition to olefinic system was observed (See: R.F. Heck, J. Am. Chem. Soc. 90, 5538 (1968)).
13) K. Yamamura, J. Org. Chem. 43, 724 (1978)

(Received in UK 25 September 1979)