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The Hydroxyphenylation of Methylstyrenes with Phenylpalladium Chloride

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The reaction of α- or β-methylstyrene with phenylpalladium chloride in aqueous acetone were studied. From *cis*- or *trans*-β-methylstyrene, a mixture of *erythro* and *threo* isomers of hydroxyphenylation products PhMeCHCHOHPh (VIa, VIb) and chlorophenylation products PhMeCHCHClPh (IVa, IVb) were obtained accompanying the phenylated olefins (I, II, and III). The main reaction product was the tertiary alcohol $PhCH_2C(OH)MePh$ (V). The reaction of α-methylstyrene with phenylpalladium chloride gave V exclusively. Phenylpalladium acetate and phenylpalladium bromide were used as phenylating agents. The yields of hydroxyphenylation products are in decreasing order: chloride > bromide > acetate.

Recently, Heck reported a new arylation of olefins with the reactive organopalladium compounds prepared *in situ* from organomercurials and palladium salts to give the arylated olefins.[1]

When the Heck reaction was applied to some conjugated benzocycloalkenes with phenylpalladium chloride in protic solvents, the phenyl group and an anion part of the protic solvent were found to add to the olefins simultaneously (Oxyphenylation)[2a,b] The formation of the oxyphenylation products was illustrated by solvolysis of the organopalladium intermediate in which *cis*-elimination of hydridopalladium moiety is prevented by the *cis* configuration between a vicinal phenyl group and the palladium atom.[2b]

In order to study the general applicability of the oxyphenylation reaction and clarify the reason why the *trans* isomer is obtained exclusively in the reaction of conjugated benzocycloalkenes, we extended our studies to acyclic olefins conjugated to a benzene ring.

In this paper, we describe the reaction of styrene, α- and β-methylstyrene with phenylpalladium chloride in an aqueous acetone.

Results and Discussion

The reaction of *cis*-β-methylstyrene with an equivalent amount of phenylpalladium chloride gave a complicated mixture of products which produced seven peaks in its gas chromatogram. Identification of these compounds was carried out by gas chromatographic analyses (glc) and also isolation by elution column chromatography. They are numbered I, II, III, IV, V and VI in the order of their appearance in the gas chromatogram. (Table 1). Although compounds I and II were unable to be isolated due to their poor yield, they were determined by glc analysis to be *cis*-1,2-diphenyl-1-propene[3] and 2,3-diphenyl-1-propene,[3] respectively.

Column chromatography succeeded in isolating the other products. Three crystalline products III (mp 79 °C), IVa (mp 138 °C) and IVb (mp 44 °C) were obtained upon elution with *n*-hexane. Compound III was identified as *trans*-1,2-diphenyl-1-propene.[3] Further elution with a mixture of benzene and *n*-hexane (1 : 1) produced crystals with a mp of 50 °C (V), whose IR spectrum showed the presence of a carbinol moiety at 3600—3500 cm^{-1} and 1100 cm^{-1}. The structure of V was determined to be 1,2-diphenylpropan-2-ol by comparison with an authentic sample.[5]

Elution with benzene gave an oily substance VI having absorption bands at 3500—3300 cm^{-1} and 1030—1000 cm^{-1} (carbinol). However, the comparison of the NMR spectrum of VI with those of authentic samples[3] indicate that VI is a mixture of *erythro*- and

Table 1. Hydroxyphenylation of methylstyrene with phenylpalladium complexes[a]

Olefin[b]	PhHgX	PdX_2	Yield[c] (%)	Product ratio[c] (%) I	II	III	IV	V	VI
c-MS	PhHgCl	Li_2PdCl_4	83.9	0.8	1.3	33.6	5.4[d]	40.4	22.8[f]
t-MS	PhHgCl	Li_2PdCl_4	92.9	1.0	0.2	12.8	27.2[e]	30.1	15.2[g]
α-MS	PhHgCl	Li_2PdCl_4	83.8	3.6		4.5		91.9	
c-MS	PhHgBr	Li_2PdBr_4	69.8	9.0	22.5	33.1			11.3
t-MS	PhHgBr	Li_2PdBr_4	37.6	19.1	21.0	45.8		2.1	12.0
α-MS	PhHgBr	Li_2PdBr_4	57.6	1.2	21.0	12.8		64.9	
c-MS	PhHgOAc	$Pd(OAc)_2$	43.0	28.8	32.0	34.2			
t-MS	PhHgOAc	$Pd(OAc)_2$	57.0	9.1	13.5	65.1			
α-MS	PhHgOAc	$Pd(OAc)_2$	37.6	2.6	60.1	37.2			
Styrene	PhHgCl	Li_2PdCl_4	57.1	*t*-Stilbene (88.4)			1,2-Diphenylethanol (6.1)		

a) In a mixture of acetone and water (1 : 1) at 30 °C for 2 hr. b) *c*-MS; *cis*-β-methylstyrene. *t*-MS; *trans*-β-methylstyrene. α-MS; α-methylstyrene. c) Determined by glc analysis (PEG 20M, 180 °C) using α-methylstilbene as the external standard. d) As the decomposition of IVb occurred during glc analyses, the net yield of IV (17%) and the ratio of *erythro* to *threo* IVa/IVb (30/70) was determined independently by column chromatography. e) Only the *erythro* isomer IVa was detected. f) The ratio of *erythro* to *threo* isomer VIa/VIb (47/53) (NMR). g) VIa/VIb (34/66) (NMR).

threo-1,2-diphenylpropan-1-ol (VIa and VIb). The doublet peaks centered at 1.07 and 1.35 ppm were assigned to the methyl protons of VIa and VIb, respectively. The NMR spectrum shows that VI consists of VIa and VIb in a ratio of 47 : 53.

Both IVa and IVb showed the same gas chromatographic peak. The patterns of the NMR spectra of IVa and IVb were very similar to those of VIa and VIb, respectively, and their elemental analyses correspond to $C_{15}H_{15}Cl$. The treatment of VIb with thionyl chloride produced two chlorides which were found to be identical with IVa and IVb. Since the chemical shift of the methyl protons of the *erythro* isomer VIa is located at higher magnetic field than that of the *threo* isomer VIb, the doublet peak centered at 1.17 ppm for IVa and that of 1.54 ppm for IVb were assigned to the methyl protons of *erythro* and *threo*-1,2-diphenylpropyl chloride, respectively. This is the first example of chloride formation in the Heck reaction without cupric chloride. Attention should be called to the glc analysis (PEG 20 M, 180 °C) in which the *threo* chloride IVb decomposed to give olefines I (5.6%), II (4.4%) and III (76%). On the other hand, the *erythro* isomer IVa decomposed to III only in a 12% conversion with the recovery of IVa.

The product distribution in the reactions of *trans*-*β*-methylstyrene under the same conditions was different from that of *cis*-*β*-methylstyrene in the following points: 1) the amount of chloride IV from the *trans* olefin was considerably greater than that from the *cis* olefin, 2) only the *erythro* chloride IVa was isolated in the reaction with the *trans* olefin, and 3) the ratio of *erythro* alcohol VIa to the *threo* isomer VIb was determined to be 34 : 66, whereas the *cis* olefin gave a ratio of 47 : 53.

The reaction of *α*-methylstyrene with phenylpalladium chloride under the same conditions gave the tertiary alcohol V (91.9%) accompanying a small amount of olefins I and III. Styrene reacted with phenylpalladium chloride under the same conditions to give a mixture of *trans*-stilbene (88%) and 1,2-diphenylethanol[6] (6%).

Isolation of the chlorides IVa and IVb is based on the assumption that the hydroxyphenylated product, *e.g.*, the alcohols VIa and VIb, may be derived from IVa and IVb. With the view of confirming this possibility, the chlorides IVa and IVb were treated with a mixture of lithium chloropalladite and mercuric chloride in 50% aqueous acetone at 30 °C for 2 hr. The *threo* isomer IVb gave a mixture of VIa and VIb (34 : 66) with a conversion of 76.3%. On the other hand, the *erythro* isomer VIa was unchanged under the same conditions. This fact indicates that a part of the secondary alcohols VIa and VIb was formed *via* *threo*-1,2-diphenylpropyl chloride IVb.

Heck[1b] proposed step by step and stereospecific reaction mechanisms consisting of the *cis* addition of the phenylpalladium compound to the olefins and subsequent *cis* elimination of the hydridopalladium species. The phenylated olefins I, II and III were obtained in the reaction of *cis*-*β*-methylstyrene with phenylpalladium acetate. (PhPdOAc in place of PhPdCl in Fig. 1). However, II and III cannot arise from the direct *cis* elimination of hydridopalladium acetate (HPdOAc) from the initially formed intermediate (A). To explain the formation of II and III, he proposed the formation of a rearranged intermediate (C) which is able to produce the olefins by the *cis* elimination of HPdOAc. The complex C was also used to illustrate the formation of the unexpected olefins I and II from *trans*-methylstyrene.

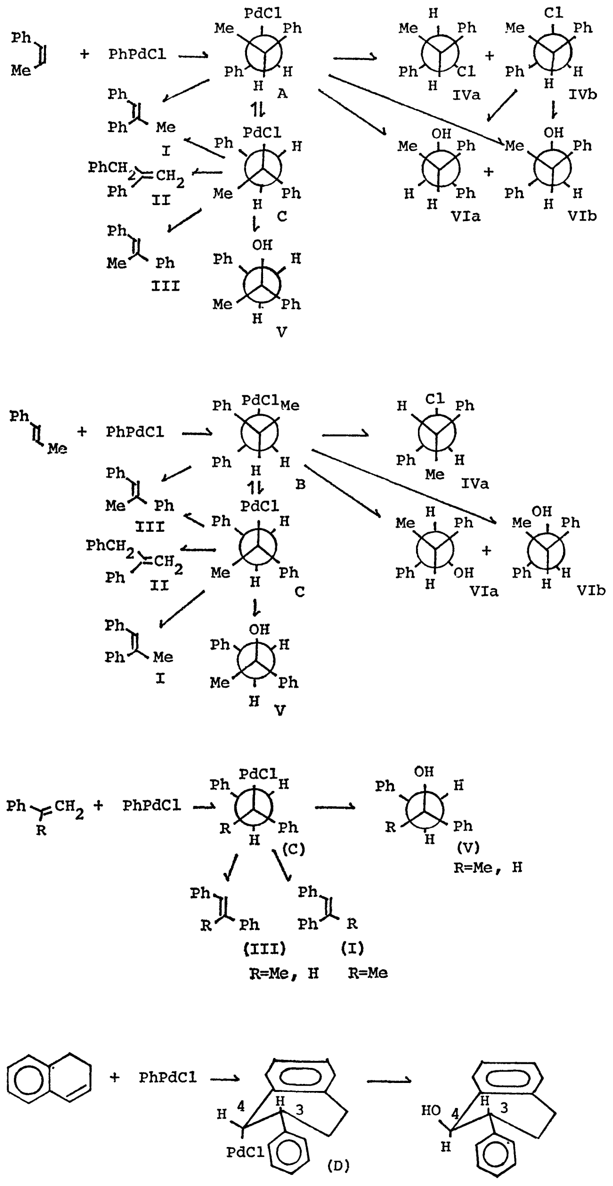

Fig. 1

Henry[7] has studied the stereochemistry of the acetoxypalladation of cyclohexene. He suggested that the reaction intermediate, the *trans* acetoxypalladium compound, was decomposed by the chloride ion *via* the S_N1 mechanism to give the *trans* chloroacetate (with retention of configuration), while *cis* diacetate was produced by reaction with the acetate ion in S_N2 fashion (with inversion of configuration).[8]

Applying the mechanism proposed by Heck and Henry, our experimental results can be explained by the reaction scheme shown in Fig. 1. A *cis* addition of phenylpalladium chloride to *cis* and *trans*-*β*-methylstyrenes produced the organopalladium intermediates

A and B, respectively. Phenylated olefins I and III are formed by the *cis* elimination of HPdCl from A and B, respectively, while C explains the formation of II and III from *cis*-methylstyrene, or the production of I and II from the *trans* olefin. The secondary chlorides (IVa and IVb) and the secondary alcohols (VIa and VIb) are produced by S_N1-type substitution with the chloride ion and S_N1-type hydrolysis of A and B.

The ratio of *erythro* to *threo* IVa/IVb (30/70) from *cis*-methylstyrene shows that IVb is the main product in S_N1-type substitution of A with the chloride species. However, the failure to isolate IVb from *trans* methylstyrene may be attributed not only to the sensitivity of IVb to hydrolysis under the reaction conditions but also to the small quantity of IVb in this S_N1-type substitution of B. The retention of configuration tendency in the chloride formation is consistent with Henry's conclusion mentioned above. Also, unsuccessful isolation of the expected tertiary chloride from C may be due to its higher reactivity, even if it is produced.

The formation of the tertiary alcohol V from either A or B is unimaginable. The rearrangement of A and B to the tertiary intermediate C is necessary to explain the formation of V. In a protic solvent, the carbon-palladium bond of A, B and C may be somewhat ionic, since the carbon atom bearing the palladium atom is located at a benzylic position liable to solvolysis. On the assumption that the stability of A, B and C is based only on the structure of the benzylic carbon, the tertiary intermediate C is more favorable to the secondary A and B. If an equilibrium between A or B and C exists,[1b)] the higher reactivity of C increases the amount of V at the expense of IV and VI. This is supported by the exclusive formation of V from α-methylstyrene. The yield of V is higher than VIa and VIb in the reaction of both *cis* and *trans* β-methylstyrenes.

In previous papers,[2)] the authors reported that the oxyphenylation of conjugated benzocycloalkenes gave large quantities of the *trans* alcohols. The elimination of hydridopalladium species between C_3 and C_4 from D (Fig. 1) is difficult because of its *trans* configuration. The exclusive formation of the *trans* alcohol was interpreted on the basis of the prevention of *cis* S_N1-type attack at C_4 by *cis* phenyl group at C_3. However, the corresponding hydroxyphenylation products from methylstyrenes were a mixture of *erythro* and *threo* isomers (VIa and VIb). In the case of acyclic A or B, it is possible to rotate around the carbon-carbon bond of A or B to give the most favorable conformation for S_N1-type solvolysis. Therefore, S_N1-type substitution is rather general for the palladium intermediate in hydroxy- or oxyphenylation.

In order to examine the effect of a chloride ion, the reactions of methylstyrene with phenylpalladium acetate were carried out in the same conditions as in the case of phenylpalladium chloride. The glc and IR analyses of the reaction products indicate the absence of alcohols, but the phenylated olefins I, II and III were obtained in good yields (Table 1).

The reaction of methylstyrenes with phenylpalladium bromide in aqueous acetone gave predominantly phenylated olefins (I, II and III). A trace of the tertiary alcohol V in the reaction of β-methylstyrene suggests the characteristic distinction between bromide and chloride ions (Table 1). However, α-methylstyrene reacted with phenylpalladium bromide producing predominantly V. It is not clear why the ligands of the palladium complexes and the position of the methyl groups on the substrate play a significant role in controlling the direction and extent of the hydroxyphenylation.

Experimental

All melting points and boiling points are uncorrected. Glc analyses were performed using a Shimadzu GC 5A on a 2 m column packed with 5% PEG 20 M. IR and NMR spectra were measured with a Hitachi 215 grating infrared spectrometer by the KBr method, and with a Hitachi R22 in carbon tetrachloride or deuteriochloroform using TMS as the internal standard.

Materials. *cis*-β-Methylstyrene[9)] and *trans*-β-methylstyrene[9)] were synthesized by decarboxylation of α-methylcinnamic acid and by reduction with cinnamic chloride with lithium aluminum hydride. Styrene and α-methylstyrene of commercial grade were used for distillation before use. Phenylmercuric chloride was prepared by treating commercial phenylmercuric acetate with lithium chloride.

Standard Samples. According to the appropriate references, the following standard samples were synthesized, with which the reaction products were compared by glc analyses, mixed-melting-point tests and spectroscopic techniques.

cis-1,2-diphenyl-1-propene I, mp 46—48 °C (lit,[3)] mp 47—48 °C; Found: C, 92.71; H, 7.32%); *trans*-1,2-diphenyl-1-propene III, mp 81—82 °C (lit, [3,5)] mp 81—82 °C; Found: C, 92.85; H. 7.41%); 2,3-diphenyl-1-propene II, bp 113—114 °C/4 Torr (lit,[4)] 140—143 °C under reduced pressure; Found: C, 92.62; H, 7.38%); *erythro*-1,2-diphenylpropan-1-ol VIa, mp 49—51 °C (lit,[3)] mp 50—51 °C; Found: C, 84.20; H, 7.56%); *threo*-1,2-diphenylpropan-1-ol VIb, mp 27 °C (bp 136—137 °C/1—2 Torr. Reported as an oily substance[3)]; Found: C, 84.88; H, 7.70%); *p*-nitrobenzoate of VIb, mp 142—143 °C (lit,[3)] mp 143—144 °C; Found: C, 73.20; H, 5.42; N, 3.78%); 1,2-diphenylpropan-2-ol V, mp 50 °C (lit,[5)] mp 50—51 °C; Found: C, 84.88; H. 7.65%).

erythro- *and* threo-*1,2-Diphenylpropyl Chloride IVa and IVb.* Thionyl chloride (0.72 g, 6 mmol) was added to a cooled solution of VIb (1.06 g, 5 mmol) in dry ether (20 ml) with stirring. The solution became turbid when pyridine (0.2 ml) was introduced. The reaction mixture was stirred for 30 min, and then refluxed for 2 hr. After evaporation of the solvent by suction, the residue was recrystallized from *n*-hexane to give 25 mg of VIa, mp 132—133 °C. Concentration of the mother liquor yielded 955 mg of IVb, mp 48—50 °C. Recrystallization of IVa and IVb was carried out from *n*-hexane and *n*-pentane, respectively. IVa, mp 138 °C. Found: C, 78.09; H, 6.53%. Calcd for $C_{15}H_{15}Cl$: C, 78.09; H, 6.55%. IVb, mp 55 °C. Found: C, 78.29; H, 6.75%. Calcd for $C_{15}H_{15}Cl$: C, 78.09; H, 6.55%.

General Procedure for the Reaction of Methylstyrenes with Phenylpalladium Chloride. To a solution of palladium chloride (1.78 g, 10 mmol) and lithium chloride (0.85 g, 20 mmol) in aqueous acetone (50%, 200 ml), the olefin (12 mmol) and then phenylmercuric chloride (3.13 g, 10 mmol) were added. The mixture was stirred for 2 hr at 30 °C, and then poured into a saturated solution of sodium chloride. The resulting oil was extracted with benzene, dried over sodium sulfate, and then evaporated under reduced pressure. The residue was diluted with ether to provide a sample solution for glc analysis. After the solvent was replaced with *n*-hexane, the solution was chromatographed on a silica gel column (Wako gel C 200, 60 g). Each volume of these eluted fractions was maintained below 60 ml, some of which were analysed by glc and also checked by IR spectra. Elution with *n*-hexane gave crystals of III, IVb and IVa successively in the order of separation. No depression was observed in the mixed-melting-point tests of III, IVa and IVb with *trans*-1,2-diphenyl-1-propene, *erythro*- and *threo*-1,2-diphenylpropyl chloride, respectively. Evaporation of the benzene-*n*-hexane (1 : 1) eluent produced an oily substance, a part of which was distilled under reduced pressure to give crystals of V. This was identified to be 1,2-diphenylpropan-2-ol from a comparison of the mixed-melting-point test and IR spectrum with those of the authentic sample.[5] Elution with benzene produced another oily substance which, although it possessed a single peak in its gas chromatogram, was found to be a mixture of VIa and VIb from its NMR spectrum. Their structure was determined by comparison of their glc and NMR spectra with those of the standard samples. The ratio was confirmed by comparison of the area of the methyl protons in the NMR spectrum.

Reaction of Methylstyrenes with Phenylpalladium Bromide or Phenylpalladium Acetate. These experiments were carried out in a manner similar to that described above, except for the use of a bromide or an acetate for all anions in the reactions.

Reaction of Styrene with Phenylpalladium Chloride. To a solution of lithium chloropalladite (3 mmol) in a mixture of acetone and water (1 : 1), styrene (345 mg, 3.3 mmol) and phenylmercuric chloride (940 mg, 3 mmol) were added successively. The reaction mixture was treated in the same way as in the reaction of methyl-styrenes. By column chromatography on silica gel, *trans*-stilbene (225 mg) and 1,2-diphenylethanol (20 mg)[6] were eluted with *n*-hexane and benzene, respectively. They were identified by the mixed-melting-point test and the comparison of IR spectra with authentic samples.

Solvolysis of IVa and IVb. A solution of lithium chloropalladite (1 mmol) and mercuric chloride (270 mg, 1 mmol) in aqueous acetone (50%, 20 ml) was added to IVa or IVb (230 mg, 1 mmol), and stirred for 2 hr at 30 °C. The reaction mixture was diluted with an aqueous solution of sodium chloride and extracted with ether. The extract was analyzed by the glc method and then chromatographed on a silica gel column. A mixture of VIa and VIb (42 mg) was prepared and the recovery of IVb (166 mg) were performed, however, no alcohol formation was observed with the quantitative recovery of IVa from the glc and IR analyses of the solvolysis of IVa.

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References

1) a) R. F. Heck, *J. Amer. Chem. Soc.*, **90**, 5518 (1968). b) R. F. Heck, *ibid.*, **91**, 6707 (1969).

2) a) H. Horino and N. Inoue, This Bulletin, **44**, 3200 (1971). b) H. Horino, M. Arai, and N. Inoue, *ibid.*, **47**, 1683 (1974). c) M. Arai, K. Kabuto, H. Horino, and N. Inoue, *Chem. Lett.*, **1972**, 889.

3) D. J. Cram and F. A. A. Elhalez, *J. Amer. Chem. Soc.*, **74**, 5829 (1952). b) F. A. A. Elhalez and D. J. Cram, *ibid.*, **74**, 5846 (1952).

4) J. von Braun, J. Seeman, and A. Schutheiss, *Ber.*, **55**, 3808 (1922).

5) C. Hell, *Ber.*, **37**, 457 (1904).

6) W. Gerrad and J. Kenyon, *J. Chem. Soc.*, **1928**, 2564.

7) P. M. Henry and G. A. Ward, *J. Amer. Chem. Soc.*, **93**, 1494 (1971).

8) In the paper of Henry, a chloroacetate of the same configuration as the chloropalladium group of the reaction intermediate was explained to result from the S_N1 substitution by a chloride complexed to palladium.

9) W. R. R. Park and G. F. Wright, *J. Org. Chem.*, **19**, 1435 (1959).