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Synthesis of *o*-(diphenylphosphinoyloxy)anilines by the rhodium-catalyzed reaction of nitroarenes and diphenylphosphine oxide

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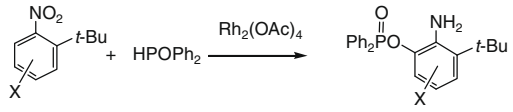
ABSTRACT

A rhodium complex $Rh_2(OAc)_4$ catalyzed the reaction of nitrobenzenes and diphenylphosphine oxide $HP(=O)Ph_2$ giving *o*-(diphenylphosphinoyloxy)anilines predominantly, which were accompanied by small amounts of the *p*-isomers. Nitorobenzenes possessing a bulky *o*-substituent, particularly *o*-(*t*-butyl)nitrobenzenes, underwent the reaction in high yields. The reaction is considered to involve the reductive formation of *O*-phosphinoyl-*N*-arylhydroxyamines from nitrobenzenes, and *o*-phosphinoyloxylation by the rearrangement.

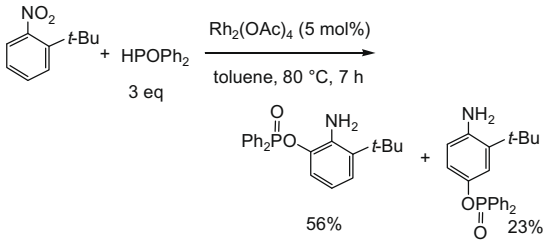
The Bamberger reaction is the rearrangement of *N*-arylhydroxyamines under strong acid conditions giving *p*-aminophenols, and is considered to proceed via nitrenium cations.[1] This method introduces an oxygen functional group directly to the aromatic nuclei. Modified methods using carboxylate[2] and sulfonate[3] derivatives of hydroxyamines were reported, which often gave the *o*-substituted products. Nitrobenzenes, which are readily available compared to *N*-arylhydroxyamines, could be converted to *p*-aminophenols under acidic conditions in the presence of reducing agents.[4] Electrochemical method or metal-catalyzed hydrogenation was generally employed for the reduction,[4,5] and the use of phosphinic acid in the presence of palladium catalyst was reported.[6] The reaction using nitrobenzenes is considered to proceed via in situ formed *N*-arylhydroxyamines.

Previously, we reported rhodium-catalyzed phosphinoylation and phosphination reaction of 1-alkynes with tetraphenyldiphosphine in the presence of 2,4-dimethylnitrobenzene.[7,8] The diphosphine was converted to tetraphenyldiphosphine monooxide or *N*-phosphinyl-*N*-phosphinoylaniline without catalyst. The former was the phosphinoylation reagent of 1-alkynes and the latter phosphination reagent. During the examination on the rhodium-catalyzed reaction of nitrobenzenes and organophosphorus compounds, reductive phosphinoyloxylation reaction of nitrobenzene was developed, which gave *o*-(phosphinoyloxy)anilines predominantly (Scheme 1). This method introduces a diphenylphosphinoyloxy group at the *o*-position of nitrobenzenes without using strong acid. Such aromatic phosphinoyloxylation was not known before, and *O*-phosphinoyl-*N*-arylhydroxyamines were reported not to give the phosphorous compounds.[9]

When *o*-(*t*-butyl)nitrobenzene and diphenylphosphine oxide $HPOPh_2$ (3 equiv) were reacted in the presence of $Rh_2(OAc)_4$ (5 mol %) at 80 °C in toluene for 7 h, 2-(diphenylphosphinoyloxy)-6-(*t*-butyl)aniline was obtained in 56% yield along with the 4-isomer in 23% yield (Scheme 2). No reaction occurred in the absence of the rhodium complex. Rh_2L_4 complexes with L = acetate, trifluoroacetate, and pivalate exhibited similar catalytic activities, while those with L = benzoate and *o*-methylbenzoate gave very small amounts of the product. Among other rhodium complexes examined, $Rh(acac)(CH_2{=}CH_2)_2$ showed a similar activity with $Rh_2(OAc)_4$, whereas the yields lowered to 10–20% using phosphine complexes, $RhH(PPh_3)_4$, $RhCl(PPh_3)_3$, and $[Rh(cod)(PPh_3)_2]PF_6$.



Scheme 1.



Scheme 2.

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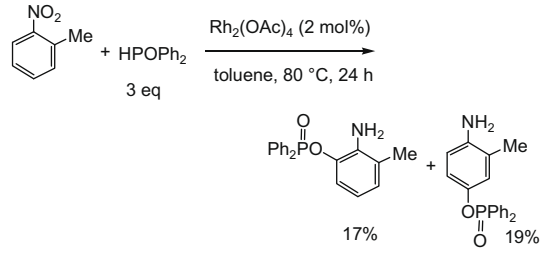
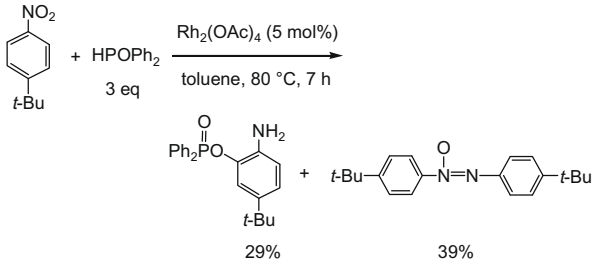
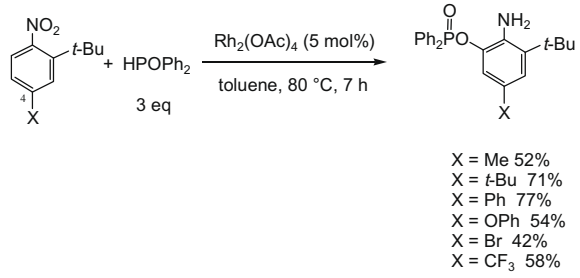


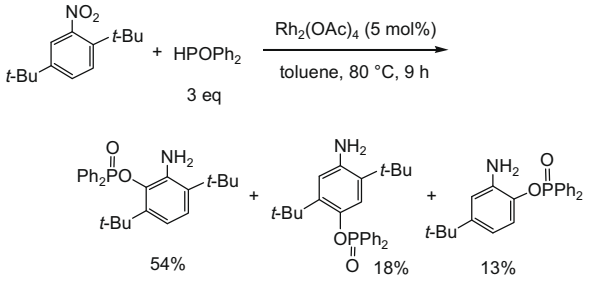
Scheme 3.



Scheme 4.



Scheme 5.



Scheme 6.

When *o*-nitrotoluene was subjected to the reaction, 2- and 4-(phosphinoyloxy)aniline were obtained in 17% and 19% yields, respectively (Scheme 3). The reaction of 4-(*t*-butyl)nitrobenzene gave 4-(*t*-butyl)-2-(phosphinoyloxy)aniline in 29% yield, which was accompanied by a considerable amount of azoxybenzene (39%) (Scheme 4). Thus, the presence of a bulky *o*-substituent increased the yield, which was ascribed to the suppression of the nitrogen coupling reaction during the reduction of nitro group. Formation of azoxy compounds was observed in the conventional Bamberger reaction.[1]

Several 2-(*t*-butyl)nitrobenzenes with different 4-substituents, alkyl, phenyl, phenoxy, halogen, and trifluoromethyl groups were reacted, and the corresponding *o*-(phosphinoyloxy)anilines were obtained in good yields (Scheme 5). The electronic effect of the *p*-substituent was small. The reaction of 2,5-di(*t*-butyl)nitrobenzene gave the *o*-phospinoyloxylated product in 54% yield along with the *p*-product in 18% yield (Scheme 6). A small amount of a product derived from the *ipso*-substitution at the 2-(*t*-butyl) group was also formed in 13% yield.

A model mechanism is as follows: the formation of *O*-phosphinoyl-*N*-arylhydroxyamines; the rearrangement to the products (Scheme 7). Since no reaction occurred in the absence of the rhodium complex, the catalyst should be involved in the reduction of the nitro group to form the O-phosphinoylated intermediate. The second step, the rearrangement of phosphinoyloxy group to the aromatic nuclei is presumed also to be the rhodium-catalyzed process. The lack of electronic effect on the nitrobenzene may not be consistent with the generation of nitrenium cation.

Typical experimental procedures: In a two-necked flask equipped with a reflux condenser were placed $Rh_2(OAc)_4$ (5.0 mol %, 5.5 mg), 2-(*t*-butyl)nitrobenzene (0.25 mmol, 44.8 mg), and diphenylphosphine oxide (0.75 mmol, 151.6 mg) under an argon atmosphere. Degassed dry toluene (2 mL) was added, and the solution was heated at 80 °C for 7 h. Then, satd $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel giving 6-(*t*-butyl)-2-(diphenylphosphinoyloxy)aniline (51.4 mg, 56%) and 2-(*t*-butyl)-4-(diphenylphosphinoyloxy)aniline (20.6 mg, 23%). Diphenylphosphinic acid (74.3 mg) was also obtained.

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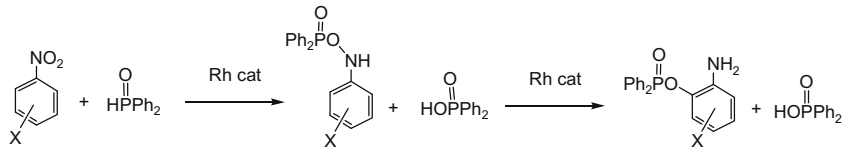

Scheme 7.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.029.

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