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CARBON-CARBON BOND FORMATION *VIA* TRANSITION METALS: ADDITION-ELIMINATION OF ARYL AND ALKENYL HALIDES TO METHYLTRIS(TRIPHENYLPHOSPHINE)RHODIUM(I)

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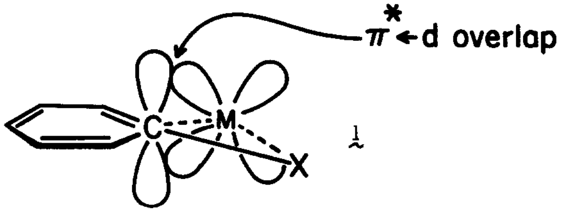
Direct oxidative-addition of organic halides to low-valent metals is potentially a selective method for activating a carbon atom toward carbon-carbon bond formation.[1] Two general mechanisms have been put forward for such reactions: (1) S_N2-like attack by the electron-rich metal atom on the carbon of the organic halide,[6] and (2) three-center (more or less symmetrical) interaction of the carbon-halogen bond with the metal atom.[7,8] The second possibility has found support from observation of net retention of configuration at carbon,[7a,9] and from comparison of kinetic parameters for oxidative-addition with similar parameters for simple addition of a donor ligand to the coordination sphere.[7b] Most mechanistic studies have involved alkyl, allyl, and benzyl halides which can react smoothly by either mechanism. The S_N2 mechanism implies low reactivity of aryl and alkenyl halides in oxidative-addition, whereas the three-center mechanism provides no such restriction. In fact, halides attached to sp^2-hybridized carbon might be particularly reactive by the latter mechanism due to stabilization of the three-center transition state (*i.e.*, **1**) *via* back-bonding from the metal into the π^* orbital of the carbon unit.[10]



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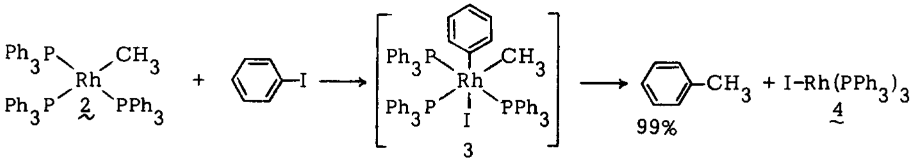
As part of a general investigation of the direct addition of aryl[11] and alkenyl halides[12] to low-valent transition metals, we have found that methyltris(triphenylphosphine)rhodium(I) (**2**) readily adds such halides under mild conditions in a coordinating solvent. The expected rhodium(III) complexes (*e.g.*, **3**) are not isolated, but undergo reductive-elimination under the reaction conditions to form a new carbon-carbon bond (*e.g.*, toluene, according to eq.1). The reactivity of aryl and alkenyl halides is similar to that for alkyl halides, a fact inconsistent with an S_N2-like transition state for the oxidative-addition, for at least this particular case.



eq. 1

The results of reactions of **2** with a representive series of organic halides are displayed in the Table; the experimental procedure is exemplified as follows. To a suspension of **2** (0.681 g, 0.754 mmol)[13] in 4 ml of dimethylformamide under argon at -78° was added all at once 4-bromobiphenyl (0.174 g, 0.746 mmol). The orange suspension was stirred at 63° for 48 hr; then the system was cooled to 25°, opened to the air, and 50 ml of ether was added. The red-orange suspension was stirred for 15 min and then filtered to remove **4**. From the filtrate was isolated (aqueous wash, preparative layer chromatography) 4-methylbiphenyl (81 mg, 65% yield), identical with an authentic sample (Aldrich Chemical Company).

Chlorobenzene gave no toluene and was detected unreacted (90%) after 18 hr at 65°; aryl iodides react faster than the corresponding bromides and give significantly higher yields. *Ortho* substituents seem to interfere with carbon-carbon bond formation. For example, *o*-methylbromobenzene reacts completely over 18 hr at 65°, but o-xylene is formed in less than 2% yield. In one example, with *p*-bromoanisole, a *para* substituent completely inhibits coupling with **2**. This bromide shows the usual reactivity (complete conversion after 24 hr at 58°) but the coupling product, *p*-methylanisole, was not detected (< 2% yield) even after 18 hr at 93°.

Methyl *trans*-3-bromoacrylate (Table, entry 11) couples with moderate efficiency and complete retention of geometry at the double bond; the corresponding *cis* isomer (entry 12) produces 48% of the expected product (methyl *cis*-crotonate) with no methyl *trans*-crotonate detectable by glpc (< 1% yield). Simple alkenyl iodides (entries 13 and 14) give mixtures of the two coupling products, and in low yield.

The requirement for a coordinating, but not necessarily highly polar, solvent is shown by the smooth reaction of **2** with iodobenzene at reflux in tetrahydrofuran containing an equimolar amount of triphenylphosphine (80% yield of toluene). With no triphenylphosphine or with two molar-equivalents, the yield of toluene is substantially decreased (35-55% yield).

Preliminary tests suggest that functional groups which are sensitive to polar reagents are inert to **2**; even α, β-unsaturated ketones and esters are unreactive toward **2** in contrast to their reactivity toward lithium dimethylcuprate.[14] For example, 1-acetylcyclohexene was recovered (67%) after 32 hr at 52° with an equimolar quantity of **2** in dimethylformamide. In a parallel experiment, an equimolar mixture of **2**, 1-acetylcyclohexene, and iodobenzene produced toluene in 93% yield. Variations in the organic ligand in the rhodium(I) complex have met with limited success. Phenyltris-(triphenylphosphine)rhodium(I) reacts with methyl iodide to give toluene (96% yield; 18 hr at 56° in dimethylformamide), but produces biphenyl from iodobenzene in only 12% yield.

The general reaction described here is the second method[15] of carbon-carbon bond formation *via* addition-elimination to rhodium(I) complexes, and the first demonstration of high reactivity toward aryl and alkenyl halides for this metal. These particular examples serve to delineate the functional group selectivity possible for such reactions. Although stoichiometric amounts of rhodium are required, the product(**4**) can be easily recycled to **2** with methyl magnesium iodide.[16]

TABLE

	Halide	Conditions[a]	Product (yield, %)[b]
1	iodobenzene	60°/24 hr	toluene (99)[c]
2	bromobenzene	44°/16 hr; 65°/ 6 hr	toluene (60)[c]
3	*o*-iodotoluene	65°/18 hr	*o*-xylene (< 2)
4	*p*-iodotoluene	62°/19 hr	*p*-xylene (80)[c]
5	*p*-bromobenzonitrile	75°/28 hr	*p*-methylbenzonitrile (59)[c]
6	*p*-bromonitrobenzene	70°/24 hr	*p*-nitrotoluene (44)[c]
7	*p*-bromoacetophenone	56°/25 hr	*p*-tolylmethyl ketone (76)[c]
8	*p*-bromoanisole	93°/18 hr	*p*-methylanisole (< 2)
9	*p*-bromobiphenyl	63°/48 hr	*p*-methylbiphenyl (65)[e]
10	methyl *o*-bromobenzoate	65°/24 hr	methyl *o*-toluate (26)[c]
11	methyl *trans*-3-bromoacrylate	55°/18 hr	methyl *trans*-crotonate (50)[c]
12	methyl *cis*-3-bromoacrylate	63°/18 hr	methyl *cis*-crotonate (48)[c]
13	*trans*-1-iodohexene	66°/18 hr	2-heptene (*cis*, 12; *trans*, 23)[e]
14	*cis*-1-iodohexene	63°/18 hr	2-heptene (*cis*, 10; *trans*, 13)[e]

(a) Equimolar quantities of **2** and the organic halide were stirred in dimethylformamide, then flash distilled at 25-50°/.001 Torr. To recover nonvolatile products, the residue was partitioned between ether and water, and the ether solution was analyzed. (b) The distillates and ether-soluble residual material were analyzed by quantitative glpc analysis. (c) The product was identified by comparison with an authentic sample. (d) Isolated material. (e) The isomers were identified by comparison with commerical samples on three different glpc columns.

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