COUPLING REACTION OF ORGANOMERCURY COMPOUNDS WITH ARYL HALIDES CATALYZED BY PALLADIUM COMPLEXES

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Organometallic compounds of aluminum [1], zinc [2], zirconium [3], and, especially, of tin [4, 5] permit the introduction of organic halides containing various functional groups into coupling reactions. Significant interest lies in the application of readily available organomercury compounds (OMC) in coupling reactions. Organomercury compounds, similar to organotin compounds, are resistant to the action of oxygen and atmospheric moisture, thermally stable, and inert relative to virtually all functional groups. However, OMC have almost never been introduced in coupling reactions with organic halides in the presence of transition metal complexes. Only two such reactions have been reported: 1) the acyldemetallation of R_2Hg in the presence of $Pd(PPh_3)$ (I) [6] and 2) the coupling reaction of CH_3I in the presence of $CH_3RhI_2(PPh_3)_2$ (II) [7].

In the present work, we studied the feasibility of using R_2Hg and RHgX in coupling reactions with aryl iodides. The reaction of R_2Hg with ArI in the presence of $PhPdI(PPh_3)_2$ (III) gives the product of oxidative demercuration R_2 in addition to the cross-coupling product RAr. Thus, the reaction of 1 eq. Ph_2Hg (IV) with 2 eq. p-$NO_2C_6H_4I$ (V) in HMPTA in an argon atmosphere catalyzed by (III) (1 mole %) at 80°C for 3 h gives 35% p-nitrodiphenyl (VI), 10% diphenyl (VII), and 60% unreacted (V). The formation of demercuration products R_2 is seen also in the reaction of R_2Hg and RHgX with CH_3I catalyzed by (II) [7]. Thus, the major difficulty in using OMC in cross-coupling reaction lies in their facile demercuration in the presence of transition metal complexes [8, 9].

We have found that the formation of the homocoupling products R_2 may almost be completely avoided by running the reaction of R_2Hg with ArI in the presence of added iodide ion [10]. The reaction is performed under mild conditions and the yields of the cross-coupling products are close to quantitative. It is very important that both the organic groups in R_2Hg participate in the reaction. Only one R group is affected in the acyldemetallation of R_2Hg catalyzed by (I) while organomercury salts do not react at all [6]. Not only symmetric R_2Hg but also organomercury salts RHgX may be introduced into the reaction in the presence of iodide ion. The results obtained are given in Table 1.

Merthylmercuric iodide reacts with (V) in HMPTA at 70°C in the presence of 1 eq. (VIII) and 1 mole % (III) over 1.5 h to give 91% p-nitrotoluene

$$CH_3HgI + p\text{-}NO_2C_6H_4I \xrightarrow[\text{HMPTA } 70^\circ]{\text{(III), I}^-} p\text{-}CH_3C_6H_4NO_2 + HgI_2 \tag{1}$$

The coupling reaction of aryl OMC with aryl iodides proceeds, as a rule, under significantly milder conditions. Ph_2Mg (IV), di-p-tolylmercury, di-p-chlorophenylmercury, and di-2-thienylmercury react with aryl iodides containing substituents in the para and meta positions in HMPTA at room temperature with the formation of the corresponding diaryls

$$Ar_2Hg + 2Ar'I \xrightarrow[\text{HMPTA, } 20^\circ]{\text{(III), I}^-} \underset{86-98\%}{2ArA'r} + HgI_2 \tag{2}$$

An exception is found for dimesitylmercury which reacts with aryl iodides at 70°C. This is apparently a result, on the one hand, of its low solubility in organic solvents and, on the other, the steric hindrance created by the two methyl groups in the ortho position:

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TABLE 1.[a] Coupling Reactions of Organomercury Compounds R_2Hg and RHgX with Aryl Halides in the Presence of 1-3 eq. Iodide Ion and 1 mole % $PhPdI(PPh_3)_2$, C_0 = 0.25 M, 20°C

Organomercury compound	Aryl halide	Solvent	Time, h	ArR, %	R_2, %
CH_3HgI[b]	p-$NO_2C_6H_4I$	HMPTA (1)	1,5	91	
	p-NCC_6H_4I	Acetone (2)	4	85	15
Same	p-$CH_3COC_6H_4I$	HMPTA (2)	1,5	86	14
	p-$NO_2C_6H_4I$	Acetone (3)	0,5	98	
Same	p-NCC_6H_4I	Same	1	85	15
»	p-$CH_3O_2C_6H_4I$	»	2	71	29
	p-$NO_2C_6H_4I$	HMPTA (1)	4	92	
Same[b]	p-NCC_6H_4I	Same	2	85	
»[b]	p-$CH_3O_2C_6H_4I$	»	10	91	
»[b]	p-$CH_3COC_6H_4I$	»	10	90	
$(p$-$CH_3OC_6H_4)_2Hg$	p-$NO_2C_6H_4I$	»	1	97	
$(o$-$CH_3OC_6H_4)_2Hg$[b]	Same	»	1	96	
$(p$-$CH_3C_6H_4)_2Hg$	»	»	1	98	
Ph_2Hg	»	»	1,5	98	2
Same[b]	2,4-$(NO_2)_2C_6H_4Br$	HMPTA (2)	0,5	99	
»[d]	Picryl iodide	THF (1)	3	57	
»	m-$NO_2C_6H_4I$	HMPTA (2)	0,3	92	8
»	o-$NO_2C_6H_4I$	The same	2,5	63	37
»	p-$NO_2C_6H_4Br$	»	1	69	25
PhHgI	p-$NO_2C_6H_4I$	HMPTA (1)	1,5	85	15
Same	Same	THF (2)	0,25	98	2
»	»	Acetone (2)	0,3	91	9
PhHgCl	»	HMPTA (1)	47	50	26
$(p$-$ClC_6H_4)_2Hg$	»	HMPTA (1)	3	98	

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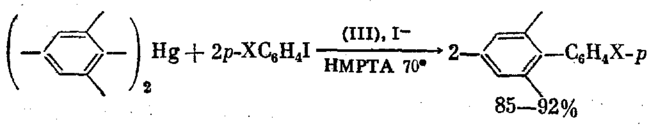
[a] Tables 1-4 give the yields found by thin layer chromatography using UV spectroscopy and standard compounds.

[b] The reaction was carried out at 70°C.

[c] The number of iodide ion equivalents is given after the solvent in parentheses.

[d] The reaction was carried out at 64°C.



(3)

X = NO_2, CN, CH_3O_2C, and CH_3CO.

The later hypothesis was supported by the finding that while di-p-anisylmercury reacts with (V) at about 20°C, di-o-anisylmercury (IX) reacts only at 70°C

$$p\text{-}NO_2C_6H_4I + \begin{cases} (p\text{-}CH_3OC_6H_4)_2Hg \xrightarrow[\text{HMPTA } 20^\circ]{(III),\ I^-} p\text{-}CH_3OC_6H_4C_6H_4NO_2\text{-}p \quad 97\% \\ (o\text{-}CH_3OC_6H_4)_2Hg \xrightarrow[\text{HMPTA } 70^\circ]{(III),\ I^-} o\text{-}CH_3OC_6H_4C_6H_4NO_2\text{-}p \quad 96\% \end{cases} \qquad (4)$$

Aryl iodides with a substituent in the ortho position, similar to the analogous OMC, have reduced reactivity. Thus, o-nitrobenzene reacts with (IV) at 20°C over 2.5 h in the presence of 2 eq. (VIII) and 37% demercuration product (VII) is formed in addition to the cross-coupling product, o-nitrodiphenyl (63%).

The reaction of picryl iodide with (IV) requires heating at 64°C in THF; after 3 h, a 57% yield of 2,4,6-trinitrodiphenyl is obtained

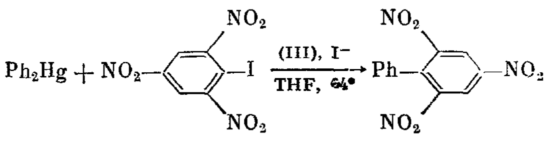


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TABLE 2. Effect of the Nature of the Solvent on the Coupling Reactions of Ph_2Hg with p-$NO_2C_6H_4I$ in the Presence of Iodide Ion in 1 mole % $PhPdI(PPh_3)_2$, C_0 = 0.25 M, 20°C

Solvent	Reaction time, h	p-$NO_2C_6H_4Ph$, %	Unreacted p-$NO_2C_6H_4I$, %	Ph_2, %
HMPTA (1)*	1,5	98	–	2
DMSO (1)	2,5	63	33	8
DMF (1)	4	71	29	16
THF (1)	2,5	82	13	10
Acetone (1)	2,5	72	26	24
CH_3CN (1)	2,5	54	42	12
Benzene (1)	3	54	42	17
CH_2Cl_2 (1)	3	37	58	5
Acetone (1) †	1,5	72	24	21
DMSO (2)	2,5	91	5	8
DMF(2)	0,75	98	2	2
THF (2)	0,25	98	–	2
Acetone (2) †	0,3	96	3	4
CH_3CN (2)	2,5	94	6	6

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*The number of equivalents of iodide ion is given after the solvent in parentheses.

†The iodide ion was introduced as NaI.

TABLE 3. Effect of Other Additives in the Coupling Reaction of Ph_2Hg with p-$NO_2C_6H_4I$ in the Presence of 1 mole % $PhPdI(PPh_3)_2$, C_0 = 0.25 M, 1 h, 20°C

Solvent	Additive, eq.	p-$NO_2C_6H_4Ph$, %	Unreacted p-$NO_2C_6H_4I$, %	Ph_2, %
HMPTA*	Bu_4NBr (1)	90	9	10
Acetone	Bu_4NBr (2)	96	4	4
Same	LiBr (2)	48	50	10
» †	Bu_4NCl (2)	48	52	8
»	KSCN (2)	3	94	5
»	NEt_3 (2)	10	85	6

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*2.5-h reaction time.

†2-h reaction time.

As noted above, not only symmetrical compounds may be brought into the coupling reaction with aryl iodides in the presence of the iodide ion but also organomercury salts. However, these salts react with less selectivity than the corresponding R_2Hg. The reactions of PhHgI (X) and PhHgCl (XI) with (V) in the presence of 1 eq. (VIII) in HMPTA at 20°C give (VI) (85 and 50%, respectively) and (VII) (15 and 26%, respectively). Thus (X) is more reactive: Its reaction with (V) is complete in 1.5 h, while 47 h are required for (XI). In order to increase the selectivity, the reaction with (X) was conducted in the presence of 2 eq. iodide ion. A yield of 98% (VI) was obtained after 15 min in THF

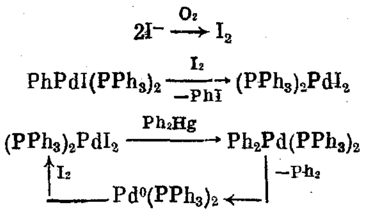
$$PhHgI + p\text{-}NO_2C_6H_4I \xrightarrow[THF,\ 20^\circ]{(III),\ I^-} p\text{-}NO_2C_6H_4Ph \qquad (6)$$

The effect of the nature of the solvent on the product yield and rate of the cross-coupling reaction was examined for the reaction of (IV) with (V) in the presence of 1 eq. (VIII) and 1 mole % (III) (Table 2). The highest reaction rate under these conditions was found for HMPTA. The reaction is complete in this solvent in 1.5 h and (VI) is formed in 98% yield. The reaction time is greater in the other solvents used and the selectivity is less. However, there is no clear relationship between the solvent properties such as DN_{SbCl_5} and ε and the reaction rate. The reaction also proceeds with rather high selectivity in THF: The yield of (VI) was 82% and that of (VII) was 10% after 2.5-h reaction. The reaction selectivity may be increased significantly by using 2 eq. iodide ion. For example, the reaction requires only 15 min in THF in the presence of 2 eq. (VIII) and (VI) is formed in 98% yield.

The cross-coupling reaction of OMC with aryl iodides may be carried out not only in the presence of iodide ion but also in the presence of other additives (Table 3). Bromide ion added as Bu_4NBr is highly effective. LiBr, Bu_4NCl, KSCN, and Et_3N were markedly less efficient. While the yield of (VI) was 96% in the reaction of (IV) with (V) catalyzed by (III) in the presence of 2 eq. Bu_4NBr, the corresponding yields were only 48 and 3% in the presence of LiBr and KSCN, respectively.

The effect of the nature of the catalyst on the reaction rate and the cross-coupling product yield was studied for the reaction of (IV) with (V) in HMPTA in the presence of 1 eq. (VIII) (Table 4). The reaction proceeds significantly more rapidly in the presence of $(Ph_3As)_2PdCl_2$ and $(Ph_3Sb)_2PdCl_2$, i.e., palladium complexes containing ligands less basic than Ph_3P but less selectively is found in these cases than when using (III). The use of palladium complexes containing bidentate ligands 1,1'-bis(diphenylphosphino)ferrocene and 1,2-bis(diphenylphosphino)ethane gives reduced reaction rates and selectivity. The yields of (VI) and (VII) are comparable in the presence of these catalysts and also in the presence of $LiPdCl_3$. $Pd(acac)_2$ does not catalyze the reaction at 20°C but the reaction proceeds at 60°C to give 73% (VI) and 24% (VII). Thus, all the catalysts studied were less effective than (III).

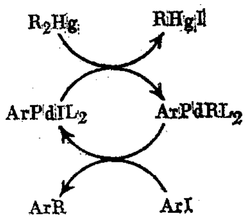
The coupling reaction of R_2Hg with aryl iodides should be carried out in an inert atmosphere. The reaction proceeds significantly more slowly in the presence of O_2 and a greater yield of the homocoupling product R_2 was obtained. We should note that the rate of coupling of organotin compounds with aryl iodides increases sharply in the presence of oxygen [4]. The different effect of added oxygen on the rate of the coupling reactions for organotin and organomercury compounds is apparently due to the presence of iodide ion in the case of the reactions of the mercury compounds. These ions may be oxidized by O_2 to iodine which converts Pd complexes to L_2PdI_2. Product (VII) is formed in the reaction of L_2PdI_2 with (IV)



(7)

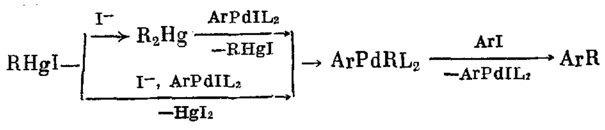
For example, 30% (VI) and 35% (VII) are formed in an oxygen atmosphere in the reaction of (IV) with (V) in HMPTA with 1 eq. (VIII) over 2 h, while the yield of (VI) is quantitative in an argon atmosphere over this time period.

The mechanism for the cross coupling of OMC with aryl halides is apparently analogous to the mechanism for the reaction for other organometallic compounds [5, 11] and involves steps featuring transmetallation and oxidative elimination



(8)

The salt RHgI which is formed as a result of transmetallation either symmetrizes by the action of iodide ion and reacts as R_2Hg or directly enters the transmetallation reaction



(9)

The transmetallation reaction is an electrophilic substitution and is facilitated in the presence of iodide ion which acts as a nucleophilic catalyst [12]. The effect of the nucleophilic catalyst is so great that OMC approach magnesium and zinc organic derivatives in their

TABLE 4. Effect of the Nature of the Catalyst on the Coupling Reaction of Ph_2Hg with p-$NO_2C_6H_4I$ in the Presence of 1 eq. Bu_4NI and 1 mole% Palladium in HMPTA, C_0 = 0.25 M, 20°C

Catalyst	Reaction time, h	p-$NO_2C_6H_4Ph$, %	Unreacted p-$NO_2C_6H_4I$, %	Ph_2, %
$(Ph_3Sb)_2PdCl_2$	0,1	83	17	17
$(Ph_3As)_2PdCl_2$	0,2	81	18	19
$LiPdCl_3$	1	59	37	40
(dppf)$PdCl_2$	2,5	59	38	31
(dppe)$PdCl_2$	2,5	64	33	26
Pd(acac)$_2$*	2	73	22	24

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*Reaction carried out at 60°C.

activity in cross coupling reactions [2, 13]. Since bromide and chloride ions have much less affinity for mercury than the iodide ion [14], their catalytic effect is much weaker (see Table 3).

EXPERIMENTAL

2-Methoxy-4'-nitrodiphenyl (XII). A sample of 104 mg (0.25 mmole) (IX), 124.5 mg (0.5 mmole) (V), 93 mg (0.25 mmole) (VIII), 2 ml HMPTA, and 4.2 mg (0.005 mmole) (III) were placed in a flask equipped with a magnetic stirrer in an argon stream. The reaction mixture was heated for 1 h at 70°C. Thin layer chromatography and UV spectroscopy using a standard component were employed to establish that the reaction mixture contained 96% (XII). A sample of 20 ml water was added to the reaction mixture which was then extracted with four 10-ml portions of ether. The combined extract was washed with three 20-ml portions of water and dried over $MgSO_4$. Thin layer chromatography on silica gel using 2:1 hexane–chloroform as eluant was used to isolate 101 mg (88%) (XII), mp 63-65°C [15]. The other coupling reactions of OMC with aryl halides were carried out analogously. The results are given in Tables 1-4.

CONCLUSIONS

1. Organomercury compounds R_2Hg and RHgX [R = CH_3, C_4H_3S (2-thienyl), 2,4,6-$(CH_3)_3C_6H_2$, p-$CH_3OC_6H_4$, o-$CH_3OC_6H_4$, p-$CH_3C_6H_4$, Ph, p-ClC_6H_4; X = I, Br, Cl] enter coupling reactions with aryl halides ArY [Ar = p-$NO_2C_6H_4$, m-$NO_2C_6H_4$, o-$NO_2C_6H_4$, p-NCC_6H_4, p-$CH_3COC_6H_4$, p-$CH_3O_2C_6H_4$, 2,4-$(NO_2)_2C_6H_3$, 2,4,6-$(NO_2)_3C_6H_2$; Y = I, Br] in the presence of 1-3 eq. iodide or bromide ion and 1 mole % palladium complex to give the corresponding RAr in high yield.

2. A study was carried out on the effect of the nature of the solvent, various additives, oxygen, and the ligand in the palladium complex on this reaction.

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