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The First Example for Reactivity Umpolung of Diaryliodonium Salts: Chromium(II)-Mediated Arylation of Aldehydes

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Abstract: Reported is the reactivity umpolung of diaryliodonium salts mediated by anhydrous chromium dichloride in the presence of a $NiCl_2$ catalyst, which involves generation of an arylchromium(III) species, followed by the nucleophilic addition to aldehydes yielding benzyl alcohols.
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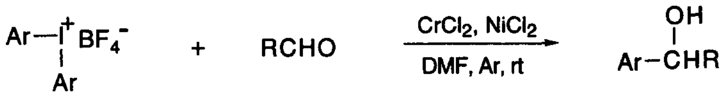
Diaryliodonium salts, as precursors of aryl cation equivalents, have been shown to be useful in organic synthesis.[1] Because of their highly electron deficient nature, they undergo arylation of a variety of organic substrates including carbon, nitrogen, phosphorus and group 16 element-centred nucleophiles under mild conditions.[1] No strategy, however, is available for the use of diaryliodonium salts as an aryl anion equivalent species that can react with carbonyl compounds, and an efficient method for this purpose remains to be established. We report herein, for the first time, chromium(II)-mediated reactivity umpolung of the diaryliodonium salts **1**, which involves intermediacy of arylchromium(III), followed by the nucleophilic addition to aldehydes **2** yielding benzyl alcohols **3**.



1 **2** **3**

Because of the moderate reducing power as a single-electron transfer agent[2] and the potential synthetic utility of organochromium(III),[3] commercially available anhydrous chromium dichloride was used for reduction of the diaryliodonium tetrafluoroborates **1**.[4] The results of reactions of the iodonium salts **1** with $CrCl_2$ in the presence of an aldehyde in DMF are summarized in Table 1.

It has been well established that chromium(II)-mediated coupling of aryl halides (I and Br) with aldehydes requires a catalytic amount of nickel salts for efficient generation of nucleophilic arylchromium(III) intermediates, which probably involves oxidative addition of an aryl halide to Ni(0) generated by reduction of Ni(II) with 2 equiv. of $CrCl_2$, followed by transmetallation reaction with Cr(III).[5] In marked contrast to this reaction of aryl halides, the phenylchromium(III) species seems to be generated directly from diphenyliodonium salt **1a** under action of $CrCl_2$ without using a Ni catalyst; thus, reaction of **1a** (1 equiv.) with benzaldehyde **2a** using $CrCl_2$ (4 equiv.) at room temperature afforded benzhydrol **3a** in 69% yield (Table 1, entry 3). By-products of this reaction were found to be benzene and a large amount (84%) of iodobenzene, which will not be able to generate phenylchromium(III) without a Ni catalyst under the conditions. Use of a catalytic amount of $NiCl_2$ as an additive makes the utilization of both moieties of the phenyl group in **1a** possible, which resulted in a much improved yield of **3a** (87%) and a decreased amount of iodobenzene (Table 1, entry 4). Use of **1a** (1.5 equiv.)/$CrCl_2$ (6 equiv.)/$NiCl_2$ (0.03 equiv.) afforded a 92% yield of **3a**, but with formation of a large amount of benzene. The original reactions between aryl halides and aldehydes require 2 equiv. of the halides for

Table 1 Chromium-Mediated Arylation of Aldehydes **2** with Diaryliodonium Salts **1**[a]

	Iodonium Salt					$CrCl_2$	$NiCl_2$	Product (10^2 mol)[b]		
Entry	1	Ar	mol[b]	2	R	mol[b]	mol[b]	3[c]	ArI[d]	ArH[d]
1	**1a**	Ph	0.5	**2a**	Ph	4	0.02	**3a** (57)	2	33
2	**1a**		0.5	**2a**		4	0.02[e]	**3a** (48)	5	39
3	**1a**		1	**2a**		4	0	**3a** (69)	84	34
4	**1a**		1	**2a**		4	0.02	**3a** (87)	35	44
5	**1a**		1.5	**2a**		6	0.03	**3a** (92)	24	153
6	**1a**		1	**2b**	*p*-ClC_6H_4	4	0.02	**3b** (82)	49	42
7	**1a**		1	**2c**	*p*-MeC_6H_4	4	0.02	**3c** (78)	66	34
8	**1a**		1	**2d**	*p*-$MeOC_6H_4$	4	0.02	**3d** (72)	-	-
9	**1a**		1	**2e**	*o*-MeC_6H_4	4	0.02	**3e** (79)	-	-
10	**1a**		1.5	**2f**	*n*-$C_{10}H_{21}$	6	0.03	**3f** (82)	64	30
11	**1a**		1	**2g**	Me_2CH	4	0.02	**3g** (74)	-	-
12	**1a**		1	**2h**	*t*-Bu	4	0.02	**3h** (0)	47	-
13	**1a**		1.5	**2i**	*E*-MeCH=CH	6	0.03	**3i** (71)	-	-
14	**1a**		2	**2j**	*E*-PhCH=CH	4	0	**3j** (56)	-	-
15	**1b**	*p*-ClC_6H_4	1.5	**2a**		6	0.03	**3b** (79)	36	-
16	**1c**	*p*-MeC_6H_4	1	**2a**		4	0.02	**3c** (72)	73	41

[a] Reactions were carried out using 0.3 mmol of an aldehyde in DMF at room temperature under Ar for 5 h. [b] Molar ratios per mol of an aldehyde. [c] Isolated yields. [d] GC yields. -: not determined. [e] Reactions were carried out in the presence of excess amounts of 1,1-diphenylethylene.

efficient coupling.[5] Therefore, this is probably due to occurrence of a competing side reaction, *i.e.*, reductive dehalogenation of aryl halides leading to arenes.

As shown in Table 1, the phenylchromium(III) generated from **1a** readily undergoes additions to aromatic aldehydes **2b-e** with electron-withdrawing and -donating substituents as well as aliphatic aldehydes **2f,g** to give the alcohols **3** in good yields. With α,β-unsaturated aldehydes, selective 1,2-addition to the carbonyl groups was observed (Table 1, entries 13 and 14).[5] Sterically demanding pivalaldehyde did not react under our conditions. Substituted phenylchromium species with *p*-chloro and *p*-methyl groups could also be generated from the diaryliodonium salts **1b,c** and react with **2a** affording addition products in good yields (Table 1, entries 15 and 16).

As illustrated in Scheme 1, the reaction mechanism for the Cr-mediated coupling of diaryliodonium salts **1** with aldehyde **2** might be assumed to involve reduction to [9-I-2][6] iodanyl radical **4**,[7] which will decompose to aryl radical **5** and aryl iodide **6**. Arylchromium(III) **7** generated both by further reduction of aryl radical **5**

Scheme 1

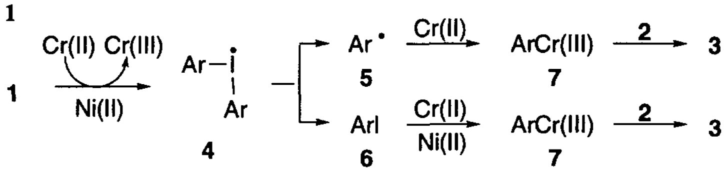
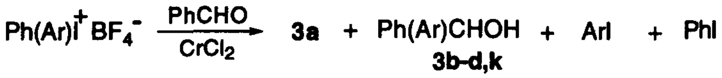


Table 2 Product Distribution in Arylation of **2a** with Unsymmetrical Iodonium Salts **8**[a]



$$\mathrm{Ph(Ar)\overset{+}{I}\,BF_4^-} \xrightarrow[\mathrm{CrCl_2}]{\mathrm{PhCHO}} \mathbf{3a} + \underset{\mathbf{3b\text{-}d,k}}{\mathrm{Ph(Ar)CHOH}} + \mathrm{ArI} + \mathrm{PhI}$$

8a: Ar = p-$MeOC_6H_4$ **8c**: Ar = p-MeC_6H_4
8b: Ar = 2,4,6-$Me_3C_6H_2$ **8d**: Ar = p-ClC_6H_4

Entry	8	Product (Yield, %)			
		3a[b]	3[b]	ArI[c]	PhI[c]
1	**8a**	**3a** (60)	**3d** (20)	69	16
2	**8b**	**3a** (56)	**3k** (0)	81	19
3	**8c**	**3a** (42)	**3c** (24)	58	23
4	**8d**	**3a** (26)	**3b** (31)	26	44

[a] Reaction conditions: **2a**/**8** (1 equiv.)/$CrCl_2$(4 equiv.)/DMF/25 °C/5 h/Ar. [b] Isolated yields. [c] GC yields.

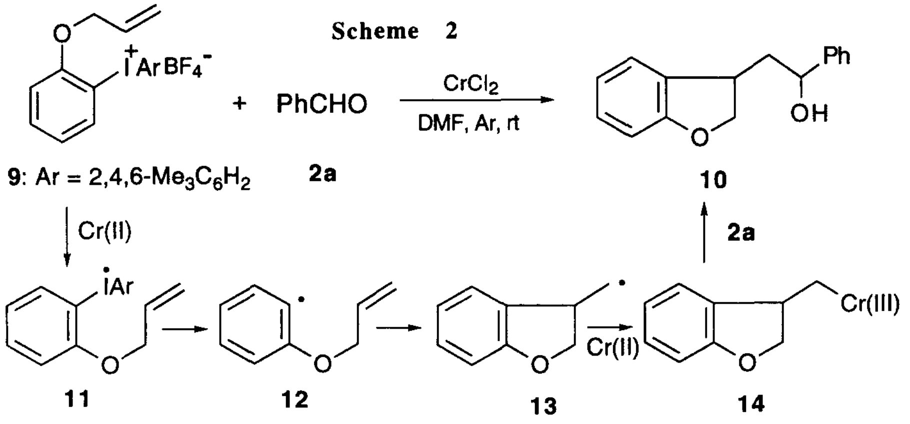
with Cr(II) and by the known Ni-catalyzed reduction[5] of aryl iodide **6** produces the alcohol **3** by the reaction with aldehydes **2**.

Several experimental evidences are in line with this mechanism. It has been well established that unsymmetrically substituted [9-I-2] diaryliodanyl radicals ($Ar\text{–}\dot{I}\text{–}Ar'$) may decompose by two paths, one leading to Ar• and Ar'I and the other to Ar'• and ArI, and the decomposition of the radicals favors cleavage of the C–I bond attached to the aryl groups with electron-withdrawing substituents.[7] Product compositions for the Cr-mediated coupling of unsymmetrical aryl(phenyl)iodonium salts **8** with **2a** in the absence of Ni catalyst are listed in Table 2.

In iodonium salts **8a-c** with electron-donating methoxy or methyl groups, the amounts of benzhydrol **3a** and aryl iodide were greater than those of substituted benzhydrols **3d,k,c** and iodobenzene. On the other hand, introduction of an electron-withdrawing p-chloro group reversed the major reaction course, with the substituted benzhydrol **3b** and iodobenzene predominating. These substituent effects on the product ratios are in good agreement with the reported mode of decomposition of unsymmetrical diaryliodanyl radicals[7] and, thereby, suggest the involvement of the [9-I-2] iodanyl radical **4** in this Cr-mediated coupling of **1**.

Both the formyl C–H bond and the methyl group of DMF act as a good hydrogen atom donor toward carbon- and oxygen-centred radicals.[8] Formation of a considerable amount of arenes as by-products (Table 1)

Scheme 2



might partly involve the intervention of aryl radicals which will abstract hydrogen from the solvent DMF; when Cr-mediated coupling of **1a** with **2a** was performed in DMF-d_7, GC-MS analysis showed a 20% deuterium incorporation in the by-product benzene. This hydrogen abstraction from DMF by aryl radicals **5** might compete with the reduction by Cr(II), yielding the arylchromium(III) **7**. Although use of a radical inhibitor 1,1-diphenylethylene, being an efficient phenyl radical trap,[9] showed negligible effects on the product compositions for the coupling of **1a** (compare Table 1, entries 1 and 2), intervention of aryl radicals **5** was firmly established by an intramolecular radical trapping method;[10] thus, exposure of (*o*-allyloxyphenyl)-mesityliodonium salt **9** to $CrCl_2$ (3 equiv.) in the presence of **2a** (5 equiv.) afforded a diastereomeric mixture of dihydrobenzofuran **10** (47%), which was presumably produced via intramolecular 5-exo cyclization of the aryl radical **12** followed by association of the resulting alkyl radical **13** with Cr(II).[11] The aryl radical **12** undergoes 5-exo cyclization with the first order rate constant of 5.3×10^9 s^{-1} at 25 °C.[12] The fact that there is no formation of the uncyclized products derived from the radical **12** clearly indicates that the association of the radical **12** with Cr(II) yielding the corresponding arylchromium(III) species will not be able to compete with this rapid 5-exo cyclization.[13]

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