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Transition Metal-catalyzed Coupling of [1-(Arylimino)alkyl]zinc with Aromatic Iodide

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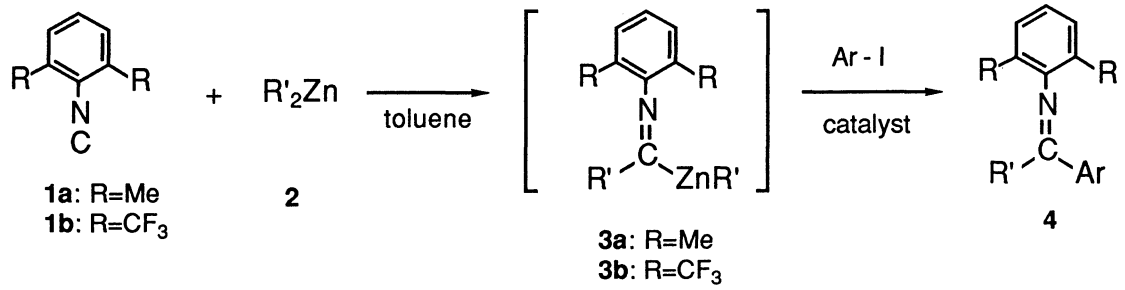
[1-(Arylimino)alkyl]zinc, prepared by α-addition of organozinc to aryl isocyanide, was coupled with aromatic iodide in the presence of palladium or nickel catalyst to give the corresponding N-aryl aromatic imine.

Much attention has been focused on chemistry of acylmetals in terms of synthetic reagents for nucleophilic introduction of acyl group as well as important intermediates in transition metal-catalyzed reaction with carbon monoxide. N-Substituted (α-iminoalkyl)metal compounds, nitrogen analog of acylmetals, are also expected to act as acyl anion equivalents. In the previous paper,[1] we have reported that organozinc underwent α-addition to aryl isocyanide to afford [1-(arylimino)alkyl]zinc. Herein, we wish to report transition metal-catalyzed coupling reaction of [1-(arylimino)alkyl]zinc with aromatic iodides giving the corresponding N-aryl aromatic imines **4** with chemoselectivity.

[1-(Arylimino)alkyl]zinc **3**, prepared by reaction of 2,6-disubstituted phenyl isocyanide[2] [**1a**:R=Me, **1b**:R=CF_3[3]] with organozinc **2** in toluene, was treated with aromatic iodide in the presence of a catalytic amount of transition metal catalyst (1-2 mol%) to produce the corresponding N-aryl aromatic imine **4** in moderate to good yield (Table 1). The coupling of [1-(arylimino)alkyl]zinc **3a**, prepared from 2,6-xylyl isocyanide (**1a**), was efficiently catalyzed by palladium catalysts (entries 1-7), whereas dichloro[1,3-bis(diphenylphosphino)propane]nickel [$NiCl_2$(dppp)] did not

give the coupling product under the similar conditions. The reaction of 1-iodo-4-methoxybenzene was rather slow compared with those of *p*-iodoacetophenone and ethyl *p*-iodobenzoate, which may suggest that the oxidative addition of carbon-iodine bond onto palladium(0) compound generated in situ is involved in the rate determining step (entries 2-4).[4] On the other hand, $NiCl_2$(dppp) was the catalyst of choice for



1a: R=Me
1b: R=CF_3

2

3a: R=Me
3b: R=CF_3

4

Table 1. Transition Metal-catalyzed Coupling of **3** with Aromatic Iodides[a]

Entry	R	Ar-I	R'_2Zn	Catalyst	Product	Yield / %[b]
1	Me	Ph-I	Et_2Zn	$PdCl_2(PPh_3)_2$	**4a**[c]	55
2	Me	*p*-EtO_2C-C_6H_4-I	Et_2Zn	$PdCl_2(PPh_3)_2$	**4b**[c]	70
3	Me	*p*-MeCO-C_6H_4-I	Et_2Zn	$PdCl_2(PPh_3)_2$	**4c**[c]	62
4	Me	*p*-MeO-C_6H_4-I	Et_2Zn	$PdCl_2$(dppf)	**4d**[c]	37
5	Me	α-naphthyl-I	Et_2Zn	$PdCl_2$(dppf)	**4e**[c]	50[d]
6	Me	*p*-EtO_2C-C_6H_4-I	Ph_2Zn	$PdCl_2(PPh_3)_2$	**4f**[c]	52
7	Me	*p*-MeCOC-C_6H_4-I	Ph_2Zn	$PdCl_2(PPh_3)_2$	**4g**[c]	61
8	CF_3	*p*-MeCO-C_6H_4-I	Et_2Zn	$NiCl_2$(dppp)	**4h**	81
9	CF_3	*p*-EtO_2C-C_6H_4-I	Et_2Zn	$NiCl_2$(dppp)	**4i**	72
10	CF_3	Ph-I	Et_2Zn	$NiCl_2$(dppp)	**4j**	60
11	CF_3	*p*-Br-C_6H_4-I	Et_2Zn	$NiCl_2$(dppp)	**4k**	66

a) All reactions were carried out by a similar procedure as described in the text, unless otherwise noted.

b) All products gave satisfactory ^1H NMR and IR spectra.

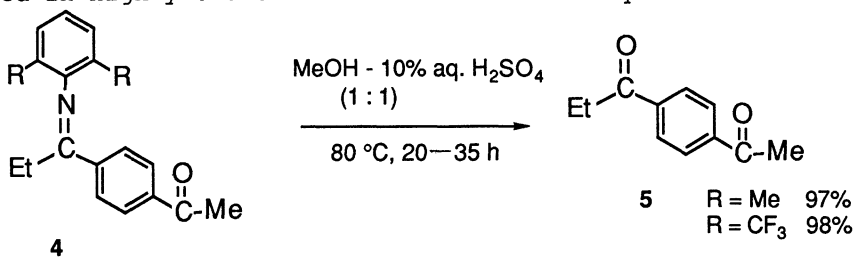
c) [1-(Arylimino)alkyl]zincs (**3a**, R=Me) were generated under the following conditions: R'=Et 90 °C, 8 h; R'=Ph 80 °C, 4 h.

d) 1-Ethylnaphthalene was formed in 68% yield along with **4e**.

[1-(arylimino)alkyl]zinc **3b** prepared from 2,6-bis(trifluoromethyl)phenyl isocyanide (**1b**) (entries 8-11). Use of other catalysts, including $PdCl_2(PPh_3)_2$, $PdCl_2$(dppf), $Pd(PPh_3)_4$, $Pd(PEt_3)_4$, and $NiCl_2(PPh_3)_2$, required a longer reaction time and yielded **4** in lower yield. Alkenyl iodide,[5] aromatic chloride or bromide did not react with **3** under the present reaction conditions. It should be remarked that [1-(arylimino)-alkyl]zinc **3** was chemoselectively coupled with aromatic iodides bearing other functionalities; 1-bromo-4-iodobenzene reacted with **3b** selectively at the carbon bound to iodine giving the corresponding bromo derivative **4k** (entry 11). Further, *p*-iodoacetophenone and ethyl *p*-iodobenzoate afforded **4** without affecting acetyl and ethoxycarbonyl groups on the aromatic ring (entries 2,3, and 6-9).

The preparation of **4** was exemplified by a nickel-catalyzed coupling reaction of [1-(arylimino)alkyl]zinc **3b**, prepared from **1b** and diethylzinc, with *p*-iodo-acetophenone; to a solution of 2,6-bis(trifluolomethyl)phenyl isocyanide (**1b**, 0.20 mmol) and diethylzinc (0.22 mmol) in toluene (0.4 mL), which was stirred at 30 °C for 5 h, were added *p*-iodoacetophenone (0.42 mmol) and dichloro[1,3-bis(diphenyl-phosphino)propane]nickel (0.004 mmol) in toluene (0.4 mL) and the mixture was stirred at 60 °C for 3 h. The reaction mixture was diluted with ether and then treated with aqueous ammonium hydroxide. Extractive workup followed by preparative TLC on silica gel (hexane:ether = 5:1) afforded 1-[2,6-bis(trifluoromethyl)-phenylimino]-1-(4-acetylphenyl)propane (**4h**) in 81% yield. **4h**: IR (neat) 1692, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (t, J=7 Hz, 3H), 2.59 (q, J=7 Hz, 2H), 2.65 (s, 3H), 7.25 (t, J=8 Hz, 1H), 7.84 (d, J=8 Hz, 2H), 7.88 (d, J=8 Hz, 2H), 8.05 (d, J=8 Hz, 2H).

Synthetic transformation of N-aryl aromatic imines **4** thus prepared was presented by hydrolysis of imino functionality. The corresponding aromatic ketone **5** was obtained in high yield on treatment of **4** with aqueous acid.



4 **5** R = Me 97%
R = CF_3 98%

It should be noted that the present transition metal-catalyzed coupling reaction demonstrates utility of [1-(arylimino)alkyl]zinc **3** as an acyl anion equivalent.

References

1) M. Murakami, H. Ito, and Y. Ito, J. Org. Chem., 53, 4158 (1988).

2) The substituents of aromatic isocyanide had a remarkable effect on α-addition of organozinc (Table 2); ortho-substituted aromatic isocyanide afforded the α-addition product **7** selectively and further reaction of **7** with another isocyanide molecule was hampered (entries 1-3). Especially, α-addition was so accelerated by electron-withdrawing trifluoromethyl group on ortho-position as to proceed even at 30 °C (entries 2 and 3). Aliphatic isocyanides, including 1-(dimethylamino)prop-2-yl isocyanide whose α-addition product **7** might be stabilized by chelating amino group (entry 4), did not react at all.

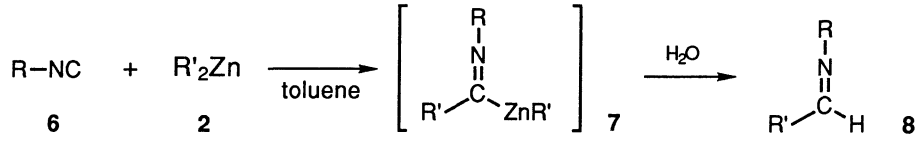
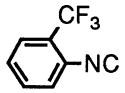
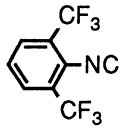
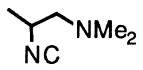
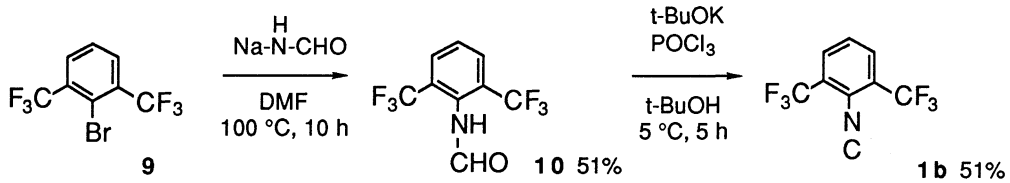


Table 2. The Effect of the Substituent of Isocyanide on α-Addition of Organozinc

Entry	R-NC	R'$_2$Zn	Temperature / °C	Time / h	Yield / %
1	*p*-tolyl-NC	*i*-Pr$_2$Zn	60	3	32
2		Et$_2$Zn	30	12	67
3		Et$_2$Zn	30	5	82
4		*i*-Pr$_2$Zn	40	12	0

3) 2,6-Bis(trifluoromethyl)phenyl isocyanide (**1b**) was prepared from 1-bromo-2,6-bis(trifluoromethyl)benzene (**9**) via 2,6-bis(trifluoromethyl)-N-formylaniline (**10**) as shown below. **1b**: mp 57-58 °C; IR (KBr disk) 2128 (-NC) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.69 (t, J=8 Hz, 1H), 7.96 (d, J=8 Hz, 2H); exact mass calcd for $C_9H_3F_6N$: 239.0170, found: 239.0163.



4) P. Fitton and E. A. Rick, J. Organomet. Chem., 28, 287 (1971).

5) The reaction of **3** with 1-hexenyl iodide gave many products including homo-coupling dimer of 1-(arylimino)alkyl group.

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