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PALLADIUM-CATALYZED COUPLING OF N-SUBSTITUTED ISOCYANIDE DICHLORIDES WITH ALKYNYLTIN COMPOUNDS: NEW SYNTHESIS OF DIALKYNYLKETONES

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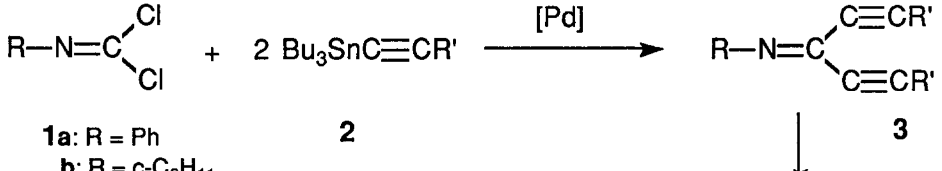
Abstract : N-Substituted isocyanide dichlorides were coupled with alkynyltin compounds in the presence of palladium catalyst to produce N-substituted dialkynylimines, of which hydrolysis provides a convenient preparative method of dialkynylketones.

Synthetic utility of N-substituted isocyanide dichloride (**1**), which may be regarded to be a synthetic equivalent to phosgene, has been limited due to its relatively low reactivity.1) Nucleophilic substitutions of **1** with alcohols and amines have afforded N-substituted imino carbonate2) and urea3) derivatives, respectively. However, useful synthetic reactions of **1** with carbon nucleophiles have scarcely been reported. Herein, we wish to describe palladium-catalyzed coupling reactions of isocyanide dichloride (**1**) with alkynyltin (**2**) to produce N-substituted dialkynylimines (**3**), of which hydrolysis provides a convenient preparative method of dialkynylketones (**4**).4)

equation 1



1a: R = Ph
b: R = c-C_6H_{11}

2

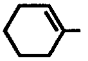
3

4

Alkyltin and alkenyltin compounds were both inert toward phenyl isocyanide dichloride (**1a**) in benzene at reflux in the presence of palladium catalyst. However, the reaction of **1a** with alkynyltin compounds (**2**)5) was catalyzed by bis(triphenylphosphine)palladium(II) dichloride to afford the corresponding (N-phenyl)dialkynylimines (**3**) in moderate yields. The preparation of **3** was exemplified by a palladium-catalyzed reaction of tributyl(trimethylsilylethynyl)tin (**2d**) with phenyl isocyanide dichloride (**1a**). A solution of **1a** (0.20 mmol), **2d** (0.45 mmol), and bis(triphenylphosphine)palladium(II) dichloride (0.002 mmol) in benzene (1 mL) was stirred at 70 °C for 5 h. The reaction mixture was diluted with ether, treated with aqueous KF at room temperature for 15 min, and filtered to remove white precipitate of tributyltin fluoride. Extractive workup of the filtrate followed by preparative TLC on silica gel [R_f = 0.4 (hexane : ether = 15:1)] afforded (N-phenyl)bis(trimethylsilylethynyl)imine (**3d**) in 60 % yield. **3d**: IR (neat) $\nu_{C=N}$ 1550 cm^{-1}; ^1H NMR ($CDCl_3$ with c-C_6H_{12} as an internal standard) δ 0.12 (s, 9 H), 0.30 (s, 9 H), 6.86 ~ 7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ -0.96, -0.55, 96.57, 97.77, 102.31, 102.77, 121.07, 126.04, 128.34, 133.45, 149.68; MS (24 eV) m/e 297 (M^+, 100 %), 282 (M - CH_3, 40 %), 97 ($Me_3SiC{\equiv}C$, 45 %).

Preparation of a variety of **3** was summarized in Table 1.

Table 1. Synthesis of N-Substituted Dialkynylimines (**3**).

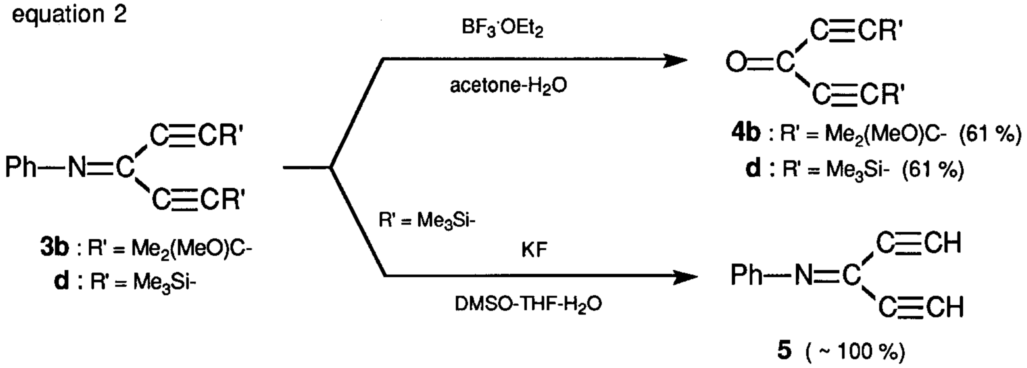
entry	**1**	R' of **2**	**3**	yield / %[a]
1	**1a** (R = Ph)	n-Bu- (**2a**)	**3a**	70
2	**1a**	$Me_2(MeO)C$- (**2b**)	**3b**	64
3	**1a**	Ph- (**2c**)	**3c**	65[b]
4	**1a**	Me_3Si- (**2d**)	**3d**	60
5	**1a**	 (**2e**)	**3e**	74
6	**1a**	EtC≡C- (**2 f**)	**3f**	31[c]
7	**1b** (R = c-C_6H_{11})	Me_3Si- (**2d**)	**3g**	35

a) All compounds gave satisfactory spectroscopic data (IR, ^1H NMR, MS) and elemental analyses. b) By-products: PhC≡C-C≡CPh and PhNC. c) 5 Mol% of $(PPh_3)_2PdCl_2$ was used.

As seen in Table 1, not only alkynyltin compounds **2a** ~ **2d**, but also alkenynyltin (**2e**) and alkadiynyltin (**2f**) compounds reacted with **1a** to give the corresponding imines (**3**). It may be remarked that a homocoupling dimer, 1,4-diphenylbutadiyne (21%) and phenyl isocyanide were produced together with the desirable **3c** in the palladium-catalyzed reaction of **1a** with **2c**.

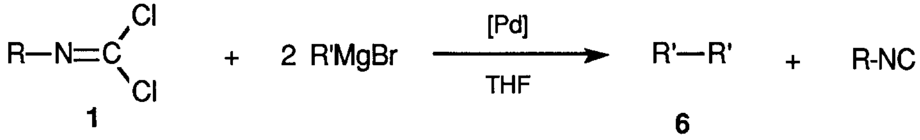
Synthetic transformations of (N-phenyl)dialkynylimines (**3**) thus prepared were presented by hydrolysis of **3b** and **3d**[6] to dialkynylketones (**4b**, **4d**[4c]), and protodesilylation of **3d**[7] to **5** [IR (KBr disk) 3270, 2116, 2080, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (s, 2 H), 7.10 ~ 7.56 (m, 5 H); MS (24 eV) m/e 153 (M^+)] (equation 2).

Finally, it is to be noted that the use of the corresponding Grignard reagents in place of tin compounds in the present palladium-catalyzed coupling reaction gave oxidative coupling dimers (**6**) of the Grignard reagents in high equation 2



yields with the comparable amount of isocyanides (Table 2).[8] The palladium-catalyzed dimerization of the Grignard reagent is suggesting that N-substituted isocyanide dichloride has served as a reoxidant[9] of palladium catalyst in a catalytic cycle.

Table 2. Oxidative Coupling Reaction of Grignard Reagents.



entry	**1**	R'	[Pd]	temperature	yield of **6** / %
1	**1a** (R = Ph)	PhCH=CH-	$Pd(PPh_3)_4$	rt	80
2	**1a**	PhC≡C-	$PdCl_2(dppf)$[a]	rt	91
3	**1a**	$Me_2(MeO)CC≡C$-	$PdCl_2(dppf)$	rt	75
4	**1b** (R = c-C_6H_{11})	PhC≡C-	$Pd(PPh_3)_4$	50 °C	95

a) dppf = 1,1'-bis(diphenylphosphino)ferrocene.

Mechanistic study and synthetic applications of the palladium-catalyzed coupling reaction of N-substituted isocyanide dichlorides and organometallic compounds are now in progress in our laboratory.

References and Notes.

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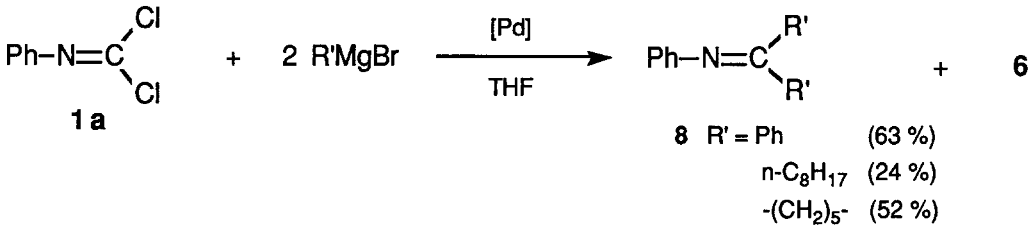
6) Imine (**3d**, 0.09 mmol) in acetone (1 mL) was treated with H_2O (50 mL) and $BF_3 \cdot OEt_2$ (0.12 mmol) for 2 h at room temperature. Extractive workup followed by column chromatography on silica gel gave **4b** (61 %): cf. C. E. Sacks and P. L. Fuchs, Synthesis, 1976, 456.

7) Imine (**3d**, 0.10 mmol) in DMSO-THF (1:1, 2 mL) was treated with sat. aqueous KF (0.4 mL) for 10 min at 0 °C. Extractive workup with Et_2O gave **5** (~100 %).

8) Imines (**8**) were obtained as a major product along with oxidative coupling dimers (**6**) by the reaction of **1a** (R = Ph) with the following Grignard reagents (R'= Ph, n-C_8H_{17}, -$(CH_2)_5$-).



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