Addition of Organostannanes to Isocyanate Catalyzed by a Rhodium Complex

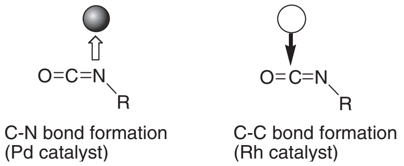
Tooru Koike, Masabumi Takahashi, Nobumichi Arai, and Atsunori Mori*
Chemical Resources Laboratory, Tokyo Institute of Technology, R1-4, 4259 Nagatsuta, Yokohama 226-8503

(Received August 11, 2004; CL-040955)

Arylstannanes add to isocyanate in the presence of a rhodium catalyst to afford amides in good to excellent yields. Use of a phenol derivative as an additive is found to play an essential role for the successful reaction.

A transition metal-catalyzed incorporation of an unsaturated compound into organic molecules is of considerable interest in organic and organometallic chemistry directed for the synthesis of a wide range of biologically and non-biologically important materials.[1] Isocyanate, which is a heterocumulene composed of C=N and C=O bonds, has been employed as an unsaturated organic compound with a palladium catalyst using organic electrophiles.[2] In these reactions, palladium mainly serves as a catalyst to induce the carbon–nitrogen bond formation. Meanwhile, formation of a carbon–carbon bond onto the central carbon atom of isocyanate with a transition metal catalyst has not been studied extensively.[3] Although Grignard reagents have shown to react with isocyanate,[4] available reagents and substrates are limited.

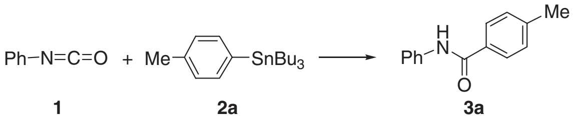
On the other hand, the reaction of main group organometallic compounds such as silicon, boron, and tin with various unsaturated organic electrophiles using a rhodium catalyst have been studied recently.[5,6] Subsequently, a wide range of carbon–carbon bond-forming reactions were achieved with unsaturated organic compounds. Nevertheless, isocyanate despite being a reactive unsaturated organic molecule has long been an unexploited frontier in this area.[7] The difficulties to achieve the reaction with rhodium would be caused by the hydrolysis of isocyanates leading to the corresponding primary amines whereas the reactions of such main group reagents favors protic reaction conditions. Herein, we report that first catalytic nucleophilic arylation and alkenylation of isocyanate with organostannanes[8] are achieved by using phenol derivatives as an additive.



When PhNCO (**1**) was treated with 4-$CH_3C_6H_4SnBu_3$ (**2a**) in the presence of a rhodium complex $[Rh(OH)(cod)]_2$ (5 mol %), 33% of the addition product **3a** was obtained after stirring in THF at 70 °C for 24 h. These results suggest that the catalytic reaction of isocyanate appears to be difficult probably because catalytically active rhodium species is hardly regenerated in the addition reaction. The reaction in the presence of water also resulted in no reaction and only induced hydrolysis of **1** to afford aniline by contrast to the remarkable effect of water in the rhodium-catalyzed conjugate addition and several other reactions.[5,6]

Worthy of note, however, is remarkable improvement of the yield by the addition of phenol to the reaction mixture of **2**.[9] The yield of **3a** was high when the reaction was carried out with 1:2:1 of **2a**, **1**, and phenol, while increasing the ratio of phenol toward isocyanate resulted in lower yields. Several neutral rhodium catalysts, $[RhCl(cod)]_2$ and $[Rh(OPh)(cod)]_2$ similarly effected the reaction in good to excellent yields. The reaction proceeded in THF, 1,4-dioxane, cyclopentyl methyl ether,[10] toluene, 1,2-dichloroethane, and acetonitrile in good to excellent yields. These results are summarized in Table 1.

Table 1. The reaction of PhNCO (**1**) with aryltributyltin **2a** catalyzed by a rhodium complex[a]



Rh Cat	Solvent	Additive /equiv.[b]	Yield /%
$[Rh(OH)(cod)]_2$	THF	none	33
	THF	PhOH	93
	THF	PhOH (1)	68
	THF	PhOH (2)	59
	THF	PhOH (3)	28
none	THF	PhOH	0
$[RhCl(cod)]_2$	THF	PhOH	99
$[Rh(OPh)(cod)]_2$	THF	PhOH	92
$[Rh(OH)(cod)]_2$	toluene	PhOH	88
	CH_3CN	PhOH	55
	c-C_5H_9OMe	PhOH	59
	$Cl(CH_2)_2Cl$	PhOH	93

[a] Unless noted, the reaction was carried out with (4-methylphenyl)tributyltin (0.3 mmol) and the rhodium catalyst (0.015 mmol) in THF at 70 °C for 24 h. [b] The ratio of isocyanate **1** (0.6 mmol) and the additive is 2:1 unless specified. Otherwise, the ratio of additive/**1** (0.3 mmol) was shown in the parenthesis.

Table 2 shows the rhodium-catalyzed addition reaction of several organostannanes and isocyanates in the presence of several phenol derivatives. The reaction was found to occur with several arylstannanes to afford the corresponding amide derivatives. The reaction proceeded at 70 °C for 3–24 h. Phenol derivatives equally effected the reaction irrespective of the electronic effect by the substituent of the aromatic ring. Among those use of 4-*t*-butylphenol was found to result in a slightly higher yield when the reaction was terminated within a shorter reaction period. In addition to arylstannanes, alkenylstannanes, which were easily prepared by the reaction of $HSnBu_3$ with alkynes, similarly reacted with isocyanate affording α,β-unsaturated amides **3e** and **3f**, which allowed further conjugate addition of boronic acid in situ without isolation of **3**.[11] The reaction of an isocyanate bearing a nitro group, with which Grignard reagents would not be tolerable, at the 2- or 3-position of the aromatic ring occurred

Table 2. The rhodium-catalyzed reaction of isocyanate **1** (R^1NCO) with **2** in the presence of Aryl–OH[a]

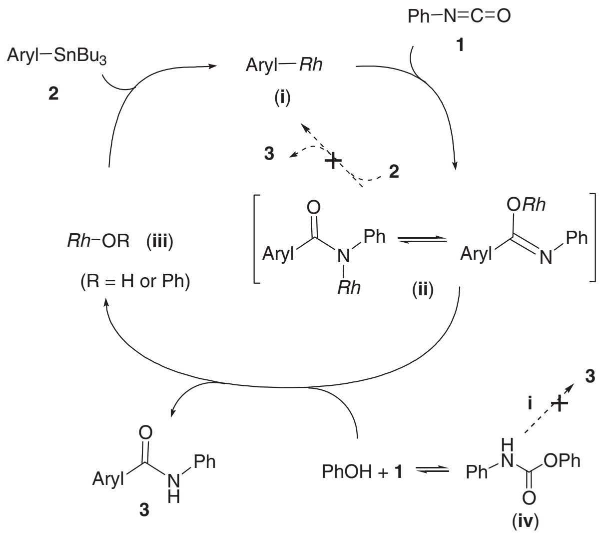
R^1	Reagent	ArylOH (Aryl)	Time /h	Yield /%
Ph	$4\text{-}MeC_6H_4SnBu_3$ (**2a**)	Ph	3	64
	$PhSnBu_3$ (**2b**)	Ph	24	81
	$2\text{-}MeC_6H_4SnBu_3$ (**2c**)	Ph	24	56[b]
	$4\text{-}MeOC_6H_4SnBu_3$ (**2d**)	Ph	24	99
	2d	Ph	3	76
	2d	[c]	3	92
	2d	[d]	3	69
	$H_2C{=}C(Ph)SnBu_3$ (**2e**)	Ph	24	76[b]
	$PhCH{=}CHSnBu_3$ (**2f**)	Ph	24	64[e]
$4\text{-}EtC_6H_4$	**2a**	Ph	24	85
$2\text{-}O_2NC_6H_4$	**2a**	Ph	24	99
$3\text{-}O_2NC_6H_4$	**2a**	Ph	24	86
$n\text{-}C_6H_{13}$	**2a**	Ph	24	52

[a] Unless otherwise specified, the reaction was carried out with **2** (0.3 mmol), isocyanate (0.6 mmol), and a phenol derivative (0.3 mmol) in the presence of 5 mol % of $[Rh(OH)(cod)]_2$ in THF at 70 °C. [b] The reaction was performed at 120 °C in toluene. [c] $4\text{-}t\text{-}BuC_6H_4$ [d] $4\text{-}F_3CC_6H_4$ [e] The reaction was carried out in toluene.

to afford the corresponding amide in a reasonable yield. Hexylisocyanate was also found to effect the reaction efficiently.

We consider that the reaction proceeds as depicted in Scheme 1. Arylrhodium **i** is formed by migration of the aryl group of the tin reagent **2** to rhodium via transmetalation. The intermediate **i** of thus formed allows the addition to isocyanate forming N- or O-bound rhodium species **ii**. Since these species hardly reacted with the tin reagent to regenerate **i**, the catalytic reaction did not take place efficiently in the absence of phenol. By contrast, protonation of **ii** takes place with phenol to give amide **3** accompanied by phenoxyrhodium species **iii**, which is the active species for the transmetalation to allow the further catalytic reaction smoothly.

Formation of carbamate **iv** by the reaction of isocyanate with phenol and following substitution of **iv** with **i** might be an alternative pathway, which would also be an unprecedented reaction of the organorhodium reagent **i**. Nevertheless, we consider that such a substitution pathway is unlikely. The reaction of isocyanate with phenol proceeded at room temperature to give **iv** without catalyst[12] and **iv** would be under the equilibrium with isocyanate and phenol at the higher temperature. Thereby, considering the result to afford a good yield in the reaction with 1:2 of phenol and isocyanate, under which conditions isocyanate would exist along with **iv** in the reaction system, insertion of isocyanate to arylrhodium **i** is plausible. Indeed, the yield of amide **3** gradually lowered with increasing the amount of phenol, by which isocyanate would be completely converted into **iv**.



Scheme 1. Plausible mechanism of the reaction of isocyanate.

In summary, the rhodium-catalyzed reaction of isocyanate with organostannanes provides a facile synthesis of amides under mild conditions. A variety of secondary amides were synthesized by the combination of isocyanates and tin reagents.

References and Notes

1 “Metal-catalyzed Cross-coupling Reactions,” ed. by F. Diederich and P. J. Stang, Wiley-VCH, Weinheim, Germany (1999).

2 a) S. Kamijo and Y. Yamamoto, *J. Org. Chem.*, **68**, 4764 (2003). b) C. Larksarp and H. Alper, *J. Org. Chem.*, **65**, 2773 (2000).

3 T. Muraoka, I. Matsuda, and K. Ito, *Organometallics*, **20**, 4676 (2000).

4 Addition of Grignard reagents to isocyanate: a) Y. Zhang, J. Jiang, and Y. Chen, *Tetrahedron Lett.*, **28**, 3815 (1987). b) H. M. Singleton and W. R. Edwards, Jr., *J. Am. Chem. Soc.*, **60**, 540 (1938). c) H. Gilman and M. Furry, *J. Am. Chem. Soc.*, **50**, 1214 (1928).

5 a) Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, and N. Miyaura, *J. Am. Chem. Soc.*, **120**, 5579 (1998). b) S. Oi, M. Moro, S. Ono, and Y. Inoue, *Chem. Lett.*, **1998**, 83. c) A. Mori, Y. Danda, T. Fujii, K. Hirabayashi, and K. Osakada, *J. Am. Chem. Soc.*, **123**, 10774 (2001). d) T. Koike, X. Du, T. Sanada, Y. Danda, and A. Mori, *Angew. Chem., Int. Ed.*, **42**, 89 (2003). e) T.-S. Huang and C.-J. Li, *Chem. Commun.*, **2002**, 2348. f) M. Yamane, K. Uera, and K. Narasaka, *Chem. Lett.*, **33**, 424 (2004) and references cited therein.

6 For reviews: a) K. Fagnou and M. Lautens, *Chem. Rev.*, **103**, 169 (2003). b) A. Mori, in “Latest Frontiers of Organic Synthesis,” ed. by Y. Kobayashi, Research Signpost, India (2002), pp 83–102.

7 Friedel–Crafts reaction of isocyanates with arylstannanes in the presence of stoichiometric Lewis acid: a) M. Arnswald and W. P. Neumann, *J. Org. Chem.*, **58**, 7022 (1993). See also: b) J. W. McFarland, and L. C. Yao, *J. Org. Chem.*, **35**, 123 (1970).

8 a) M. Kosugi, K. Sasazawa, Y. Shimizu, and T. Migita, *Chem. Lett.*, **1977**, 301. b) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, **25**, 508 (1986).

9 Similar effect of a phenol derivative as an additive was also observed in the rhodium-catalyzed reactions: a) L. Navarre, S. Darses, and J.-P. Genet, *Angew. Chem., Int. Ed.*, **43**, 719 (2004). b) T. Fujii, T. Koike, A. Mori, and K. Osakada, *Synlett*, **2002**, 295.

10 Cyclopentyl methyl ether was kindly donated by Nippon Zeon Co. Ltd.

11 For example, **3e** that was formed in situ further reacted with $PhB(OH)_2$ and $4\text{-}CF_3C_6H_4B(OH)_2$ at 120 °C for 24 h to afford the conjugate addition products in 52 and 67% yields, respectively.

12 The reaction of **1** with phenol at room temperature for 2 h afforded the corresponding carbamate in a quantitative yield.

Published on the web (Advance View) September 18, 2004; DOI 10.1246/cl.2004.1364