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Convenient Synthesis of Phosphinecarboxamide and Phosphinecarbothioamide by Hydrophosphination of Isocyanate and Isothiocyanate†

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Reactions of isocyanates with primary and secondary phosphines without solvent at room temperature afforded the corresponding phosphinecarboxamide (RN(H)COPR'₂) in excellent yields. This reaction system is applicable for isothiocyanate. The compounds newly obtained were fully characterized using multielement NMR spectroscopy. In addition, the molecular structure of Cl(CH₂)₂N(H)COPPh₂ was studied by single-crystal X-ray diffraction.

Organophosphorus compounds are widely used in commercial applications.¹ One of the most efficient methods for the synthesis of functionalized phosphorus products is hydrophosphination of C–C/X (X = O, N, S) multiple bond.² Although the hydrophosphination of olefins and alkynes are well-established in the last decade,³ that of heterocumulenes has been less explored. Therefore, it is desired the development of synthetic routes for functionalized phosphine compounds containing hetero atoms (such as O, N, S).

Phosphinecarboxamides (RN(H)COPR'₂) and phosphinecarbothioamide (RN(H)CSPR'₂) are a heavier analogue of urea and thiourea and molecules of appreciable interest, particularly due to their role as supporting ligands in a transition-metal complex⁴ and as facile precursors for zinc phosphide thin films.⁵ It was known that phosphinecarboxamide and phosphinecarbothioamide were obtained by hydrophosphination of isocyanates and isothiocyanates, respectively (Eq. 1).

In 1959, Buckler reported the first example of hydrophosphination of isocyanates RNCO with phosphine PH₃ in the

presence of triethylamine NEt₃ at room temperature in benzene. However, drawbacks of the reaction are the low yield (13%) and long reaction time (4 days) when phenyl isocyanate was used.⁶ Recently, metal-mediated catalytic hydrophosphination reactions have attracted considerable attention. Behrle and Schmidt reported that the first catalytic hydrophosphination using a homoleptic α -metalated *N,N*-dimethylbenzylamine (DMBA) lanthane complex α -La(DMBA)₃ in 2013. The reaction of isocyanates and isothiocyanates with secondary diarylphosphines afforded the corresponding phosphinecarboxamides and phosphinecarbothioamide in moderate to high yields.⁷ Kays and co-workers found the first transition metal complex-catalyzed hydrophosphination of isocyanates.⁸ The reaction of isocyanates with diphenylphosphine HPPH₂ or phenylphosphine H₂PPh in the presence of catalytic amount of (2,6-Mes₂C₆H₃)₂Fe (Mes = 2,4,6-Me₃C₆H₂) or (2,6-Tmp₂C₆H₃)₂Fe(THF) (Tmp = 2,4,5-Me₃C₆H₂) afforded the corresponding phosphinecarboxamides and/or phosphinodicarboxamides as a result of single and double insertion of isocyanates into the P–H bond of the phosphine. Although this reaction shows good reactivity and chemo-selectivity, the reaction was adaptable to only HPPH₂ as a phosphine compound. However, examples of hydrophosphination of isocyanates and isothiocyanates are limited to date: two examples of Th,^{9,10} two examples of U,^{9,10} one example of rare-earth-metal (Y, Eu, Er, Yb),¹¹ and one example of Zr (for isocyanates).¹²

Previously, we achieved that the regioselective hydrophosphination of unsaturated C–C bonds of alkynes and vinylphosphines with secondary phosphines catalysed by iron complexes Cp*Fe(CO)(py)(Me) (Cp* = η^5 -C₅Me₅) and CpFe(CO)₂(Me) (Cp = η^5 -C₅H₅) (Scheme 1).¹³ Therefore, we tried to the hydrophosphination of isocyanate and isothiocyanate.

Scheme 1 Regioselective hydrophosphination of terminal arylalkynes and vinylphosphine catalyzed by iron complexes.

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Table 1 Reaction condition screening for the hydrophosphination of arylisocyanates and alkylisocyanates.

$\text{Ph-N=C=O} + \text{HPPH}_2 \longrightarrow \text{Ph-NH-C(=O)-PPh}_2$					
Entry	Temp.	Catalyst	Time/h	Solvent	Yield/%
1	110 °C	CpFe(CO) ₂ (Me) ^a	0.5	–	>99% ^b
2	r.t.	CpFe(CO) ₂ (Me) ^a	0.5	–	>99% ^b
3	r.t.	–	0.25	–	>99% ^c
4	r.t.	–	5	toluene	8% ^c

^a5 mol% CpFe(CO)₂(Me) was used as a catalyst. ^bDetermined by ¹H NMR.^cIsolated yield.

We firstly examined the hydrophosphination of phenylisocyanate under the same reaction conditions for hydrophosphination of terminal arylalkynes.^{13,14} The reaction of phenylisocyanate with diphenylphosphine HPPH₂ in 1:1 molar ratio at 110 °C for 0.5 h without solvent in the presence of 5 mol% of the iron complex CpFe(CO)₂(Me) produced the desired hydrophosphination product **1a** in >99% yield (Table 1, Entry 1). Although high reaction temperature was required for the hydrophosphination of terminal arylalkynes, room temperature was enough for that of isocyanate (Table 1, Entry 2). Therefore, we thought that the iron complex might not be necessary for this hydrophosphination, and we found out that this reaction proceeds without iron (Entry 3): the reaction of phenylisocyanate with diphenylphosphine at room temperature for 0.25 h without solvent. After 5 hours, the yield drastically decreased when toluene was used as a solvent (Table 1, Entry 4). This tendency is similar to the previously reported.³ These results shows that neat (no solvent) is the most important condition for this hydrophosphination.

To see the scope and limitation of this hydrophosphination, we examined reactions with several isocyanate derivatives other than phenylisocyanate. Table 2 summarizes the results showing good functional group tolerance. Several isocyanates RNCO could be employed in the reaction, in which R is phenyl ring with electron-donating or -withdrawing groups such as OMe, F, Cl, Br, and CF₃ at the *para* position, a naphthyl group, and alkyl groups. The hydrophosphination products were not obtained when sterically-bulky cyclohexylisocyanate and adamantylisocyanate were used. Reaction of 1,3- and 1,4-diisocyanatobenzene with diphenylphosphine HPPH₂ in 1:2 molar ratio yielded the double hydrophosphination product **1j** and **1k** in 85% and 92% yield, respectively. In addition, 1,3,5-triisocyanatobenzene could be converted into triple hydrophosphination product **1l**.

The structures of **1h** was determined by X-ray crystallography.¹⁵ Two independent molecules of **1h** crystallized in the unit cell. As these are basically the same, only one P1 molecule is shown in Fig. 1. The P1–C3, C3–O1, and C3–N1 bond distances are 1.870(2) Å, 1.231(2) Å, and 1.328(3) Å, respectively. In addition, the phosphinecarboxamide moiety displays a pyramidalized

Table 2 Reaction condition screening for the hydrophosphination of isocyanates.^a

$\text{R-N=C=O} + \text{HPPH}_2 \xrightarrow{\text{neat, r.t.}} \text{R-NH-C(=O)-PPh}_2$
3 h, >99%: 1b		0.5 h, >99%: 1c
3 h, >99%: 1d		0.25 h, >99%: 1e
0.25 h, >99%: 1f		3 h, 68%: 1g
1 h, >99%: 1h		10 h, >99%: 1i
5 h, 0%		12 h, 85% (for <i>m</i> -isomer): 1j ^b 12 h, 92% (for <i>p</i> -isomer): 1k ^b
12 h, 64%: 1l ^c		

^aReaction conditions: HPPH₂ : isocyanate = 1:1 molar ratio. ^bReaction conditions:80 °C, 2 equiv. of HPPH₂ was used (vs isocyanate). ^cReaction conditions: 80 °C, 3equiv. of HPPH₂ was used (vs isocyanate). **Fig. 1** ORTEP drawing of Cl(CH₂)₂N(H)COPPh₂ (P1 molecule) **1h** with 50% thermal ellipsoidal plots. All hydrogen atoms except for the amine proton are omitted for clarity. Selected bond lengths (Å) and angles (°): P1–C3 1.870(2), N1–C2 1.452(3), N1–C3 1.328(3), C3–O1 1.231(2), N1–H1 0.81(3), C3–P1–C4 98.62(9), C3–P1–C10 103.32(9), C4–P1–C10 101.86(9), C2–N1–C3 123.30(19), C2–N1–H1 121.1(19), C3–N1–H1 115.4(19) for P1 molecule.

geometry at the P atom (sum of angle around P1 = 330.8°) with a planar carboxamide moiety (sum of angle around N1 = 359.89°). This result shows delocalization of π electron density between the carbonyl and amide groups. These are consistent with the phosphinecarboxamide reported previously.¹⁶

Next, we investigated the substrate scope for phosphine, and found that the desired hydrophosphination reaction took place (Table 3).

Table 3 Hydrophosphination of phenylisocyanate with secondary phosphines HPR₂.

Diarylphosphines with electron-donating or -withdrawing groups such as Me, OMe, and F at the para position of the aryl rings, dialkylphosphines such as HP^tPr₂ and HP^tBu₂ could be employed. Furthermore, primary phosphine H₂PPh instead of secondary phosphine HPPH₂ was also adaptable to this reaction. This is the first example of hydrophosphination of primary phosphine with isocyanate. Single hydrophosphination product **7** was obtained in 71% yield but this reaction required significantly longer reaction times (Eq. 2). We thought that it was due to a small amount of hexane existing in commercially available H₂PPh (see ESI). Compound **7** was a major product even when H₂PPh was treated with 2 equiv of PhNCO.

Finally, we demonstrated the hydrophosphination of isothiocyanate in our system because the La catalyzed hydrophosphination have also been reported by Behrle and Schmidt.⁴ Reaction of phenylisothiocyanate with diphenylphosphine HPPH₂ in 1:1 molar ratio afforded the corresponding phosphinecarbothioamide **8** in >99% yield (Eq. 3).

It has been reported that a secondary phosphine reacts with aldehyde at room temperature using neat reagents to afford α-hydroxyphosphine via nucleophilic attack of phosphine phosphorus to the carbonyl carbon.¹⁷ In our cases, it can be similarly considered that the phosphine phosphorus nucleophilically attacks the carbon in isocyanate, and then the hydrogen on the phosphorus migrates to the amine nitrogen to give phosphinecarboxamide.

In summary, we found the convenient synthesis of phosphinecarboxamide by hydrophosphination of isocyanate. This system shows shorter reaction time, high yield, and good functional group tolerance, and is applicable not only for isocyanates but also

for isothiocyanate. We thought the key condition of this reaction is neat (no solvent).

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Conflicts of interest

There are no conflicts to declare.

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