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Convenient synthesis of phosphinecarboxamide and phosphinecarbothioamide by hydrophosphination of isocyanates and isothiocyanates†

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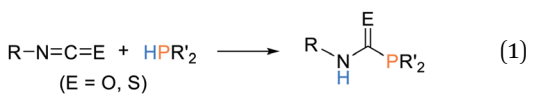
Reactions of isocyanates with primary and secondary phosphines without solvent at room temperature afforded the corresponding phosphinecarboxamide ($RN(H)COPR'_2$) in excellent yields. This reaction system is applicable for isothiocyanates. The compounds newly obtained were fully characterized using multielement NMR spectroscopy. In addition, the molecular structure of $Cl(CH_2)_2N(H)COPPh_2$ 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 bonds.[2] Although the hydrophosphination of olefins and alkynes has been well-established in the last decade,[3] that of heterocumulenes has been less explored. Therefore, the development of synthetic routes for functionalized phosphine compounds containing hetero atoms (such as O, N, and S) is desired.

Phosphinecarboxamide ($RN(H)COPR'_2$) and phosphinecarbothioamide ($RN(H)CSPR'_2$) are heavier analogues of urea and thiourea and molecules of appreciable interest, particularly due to their role as supporting ligands in a transition-metal complex[4] 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 (eqn (1)).



(1)

In 1959, Buckler reported the first example of hydrophosphination of isocyanates RNCO with phosphine PH_3 in the presence of triethylamine NEt_3 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 the first catalytic hydrophosphination using a homoleptic α-metalated *N*,*N*-dimethylbenzylamine (DMBA) lanthanide 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 $HPPh_2$ or phenylphosphine H_2PPh in the presence of a catalytic amount of $(2,6\text{-}Mes_2C_6H_3)_2Fe$ (Mes = 2,4,6-$Me_3C_6H_2$) or $(2,6\text{-}Tmp_2C_6H_3)_2Fe(THF)$ (Tmp = 2,4,5-$Me_3C_6H_2$) 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 chemoselectivity, the reaction was adaptable to only $HPPh_2$ as a phosphine compound. However, examples of hydrophosphination of isocyanates and isothiocyanates have been limited to date: two examples of Th,[9,10] two examples of U,[9,10] one example of rare-earth-metal (Y, Eu, Er, and Yb),[11] and one example of Zr (for isocyanates).[12]

Previously, we achieved the regioselective hydrophosphination of unsaturated C–C bonds of alkynes and vinylphosphines with secondary phosphines catalyzed by iron complexes Cp*Fe(CO)(py)(Me) (Cp* = η^5-C_5Me_5) and $CpFe(CO)_2(Me)$ (Cp = η^5-C_5H_5) (Scheme 1).[13] Therefore, we tried to perform the hydrophosphination of isocyanates and isothiocyanates.

We firstly examined the hydrophosphination of phenylisocyanates under the same reaction conditions for hydrophosphination of terminal arylalkynes.[13,14] The reaction of phenylisocyanates with diphenylphosphine $HPPh_2$ in a 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).

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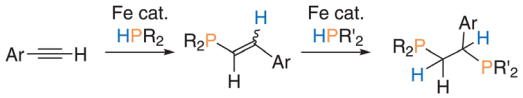
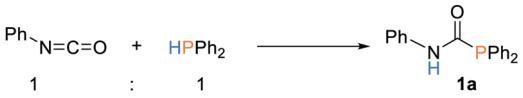


Scheme 1 Regioselective hydrophosphination of terminal arylalkynes and vinylphosphine catalyzed by iron complexes.

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



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

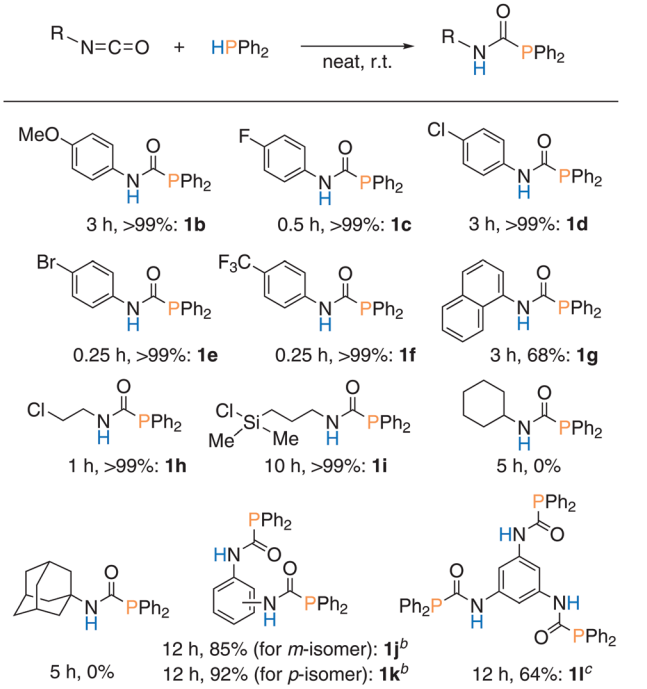
[a] 5 mol% $CpFe(CO)_2(Me)$ was used as a catalyst. [b] Determined by ^1H NMR. [c] Isolated yield.

Although high reaction temperature was required for the hydrophosphination of terminal arylalkynes, room temperature was enough for that of isocyanates (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 the iron catalyst (entry 3): the reaction of phenylisocyanates 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 that reported previously.[3] These results show 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 phenylisocyanates. Table 2 summarizes the results showing good functional group tolerance. Several isocyanates RNCO could be employed in the reaction, in which R is the phenyl ring with electron-donating or -withdrawing groups such as OMe, F, Cl, Br, and CF_3 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 $HPPh_2$ in a 1 : 2 molar ratio yielded the double hydrophosphination products **1j** and **1k** in 85% and 92% yield, respectively. In addition, 1,3,5-triisocyanatobenzene could be converted into triple hydrophosphination product **1l**.

The structure 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 pyramidal geometry at the P atom (sum of angles around P1 = 330.8°) with a planar carboxamide moiety (sum of angles 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]

Table 2 Reaction condition screening for the hydrophosphination of isocyanates[a]



[a] Reaction conditions: $HPPh_2$: isocyanate = 1 : 1 molar ratio. [b] Reaction conditions: 80 °C, 2 equiv. of $HPPh_2$ was used (*vs.* isocyanate). [c] Reaction conditions: 80 °C, 3 equiv. of $HPPh_2$ was used (*vs.* isocyanate).

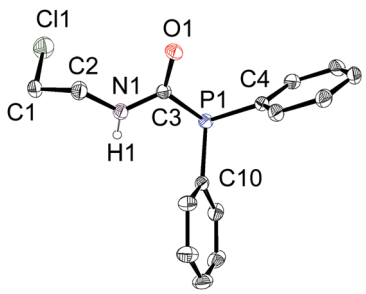
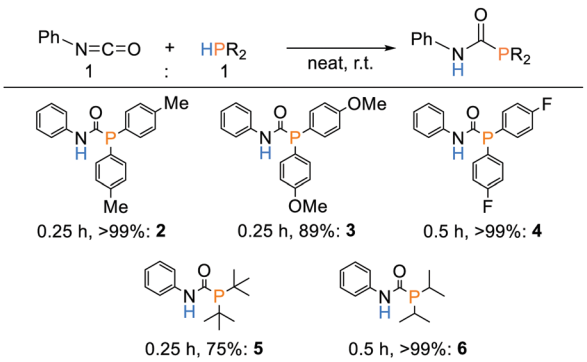


Fig. 1 ORTEP drawing of $Cl(CH_2)_2N(H)COPPh_2$ (P1 molecule) **1h** with 50% thermal ellipsoidal plots. All hydrogen atoms except for the amine proton are omitted for clarity. Selected bond lengths (Å) and angles (°): P1–C3 1.870(2), N1–C2 1.452(3), N1–C3 1.328(3), C3–O1 1.231(2), N1–H1 0.81(3), C3–P1–C4 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 the P1 molecule.

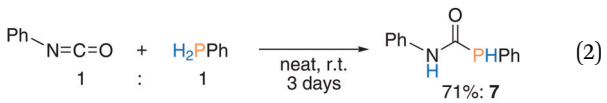
Next, we investigated the substrate scope for phosphine, and found that the desired hydrophosphination reaction took place (Table 3).

Diarylphosphines with electron-donating or -withdrawing groups such as Me, OMe, and F at the *para* position of the aryl rings, and dialkylphosphines such as HP^iPr_2 and HP^tBu_2 could be employed. Furthermore, primary phosphine H_2PPh instead of secondary phosphine $HPPh_2$ was also adaptable to this reaction. This is the first example of hydrophosphination of

Table 3 Hydrophosphination of phenylisocyanates with secondary phosphines HPR_2

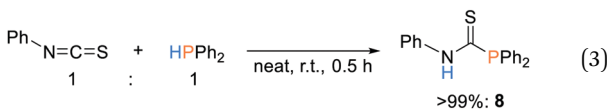


primary phosphine with isocyanates. Single hydrophosphination product **7** was obtained in 71% yield but this reaction required significantly longer reaction times (eqn (2)). We thought that it was due to a small amount of hexane existing in commercially available H_2PPh (see the ESI†). Compound **7** was a major product even when H_2PPh was treated with 2 equiv. of PhNCO.



(2)

Finally, we demonstrated the hydrophosphination of isothiocyanate in our system because the La catalyzed hydrophosphination has also been reported by Behrle and Schmidt.[4] Reaction of phenylisothiocyanate with diphenylphosphine $HPPh_2$ in a 1:1 molar ratio afforded the corresponding phosphinecarbothioamide **8** in >99% yield (eqn (3)).



(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 carbonyl carbon.[17] In our cases, it can be similarly considered that the phosphine phosphorus nucleophilically attacks the carbon in isocyanates, and then the hydrogen on the phosphorus migrates to the amine nitrogen to give phosphinecarboxamide.

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