Studies on Reactions of the *N*-Phosphonium Salts of Pyridines. XIX. Carbonylation of Amines with Carbon Dioxide by Means of Phosphorus Chlorides in Tertiary Amines

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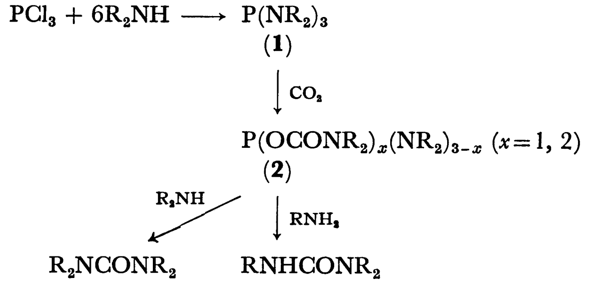
Reactions of carbon dioxide and disulfide with primary amines in the presence of phosphorus chlorides gave the corresponding symmetrically disubstituted ureas and thioureas in high yields under atmospheric conditions. Phosphorus trichloride and di- and mono-chlorophosphites were remarkably effective for the reactions, whereas phosphorus pentachloride and phosphoryl chloride were ineffective. The presence of tertiary amines such as pyridine satisfactorily favored the reactions. The reaction seems to proceed *via* the *N*-phosphonium salts of pyridines as those obtained from diphenyl and triaryl phosphites, on the basis of their IR spectroscopic analyses, stoichiometric relationship between reactants and the steric effect of tertiary amines.

Phosphorous acid hexaalkyltriamide (**1**) prepared from phosphorus trichloride and secondary amines afforded the corresponding carbamoyloxy compounds (**2**) by inserting carbon dioxide.[1] **2** was aminolysed with primary amines into ureas, but not with secondary amines.[2]



$$PCl_3 + 6R_2NH \longrightarrow P(NR_2)_3\ (\mathbf{1})$$

$$P(NR_2)_3 \xrightarrow{CO_2} P(OCONR_2)_x(NR_2)_{3-x}\ (x=1,2)\ (\mathbf{2})$$

$$R_2NCONR_2 \xleftarrow{R_2NH} (\mathbf{2}) \xrightarrow{RNH_2} RNHCONR_2$$

Some primary amines also reacted with phosphorus trichloride to give the phosphorus–nitrogen compounds such as phosphenimidous amide derivatives (RNH–P=NR) from the aromatic amines,[3] and the amides ($P(NHR)_3$) from the alkylamines.[4] However, these phosphorus–nitrogen compounds have not been fully investigated, nor has the insertion reaction of carbon dioxide been reported.

The phosphorus–nitrogen bonds in these phosphorous amides and imides were expected to bring about the reaction with carbon dioxide, yielding ureas by aminolysis with amines as those in **1**. Ureas were, in fact, obtained in high yields using PCl_3 and chlorophosphites ($RO\text{–}PCl_2$, $(RO)_2\text{–}PCl$) in pyridine,[5] and the reaction was successfully applied to the preparation of polyureas under mild conditions.[6]

This paper gives detailed results of the reactions of phosphorus chloride and primary amines with carbon dioxide and disulfide in the presence of tertiary amines.

$$CX_2 + 2RNH_2 + \left\{\begin{array}{l} PCl_3 \\ RO\text{–}PCl_2 \\ (RO)_2\text{–}PCl \end{array}\right. \longrightarrow \begin{array}{c} RNHC(X)NHR \\ (X=O,\ S) \end{array}$$

Results and Discussion

When carbon dioxide was passed at 60 °C for 6 h into a cylindrical flask[7] containing phosphorus trichloride and aniline (4 equiv.) in pyridine, *N,N'*-diphenylurea was obtained in 93% yield based on aniline. The yield was lowered to 21%, when the reaction was carried out in the absence of pyridine by using 7 equivalents of aniline (3 equivalent excess as HCl scavenger) in toluene, suggesting that pyridine significantly facilitates the reaction.

TABLE 1. *N,N'*-DIPHENYLUREA FROM CARBON DIOXIDE AND ANILINE BY USE OF PHOSPHORUS TRICHLORIDE IN VARIOUS TERTIARY AMINES AT 60 °C FOR 6 h

Tertiary amine	pK_a	Yield, %[a]
None	—	21[b]
Pyridine	5.19	93
γ-Picoline	6.08	88
β-Picoline	5.52	85
α-Picoline	6.20	73
2,4-Lutidine	6.99	77
2,6-Lutidine	6.99	28
Triethylamine	10.87	50[c]

a) Based on aniline used. b) In toluene.
c) In an autoclave at 20 atm of CO_2.

In order to elucidate the favorable effect of tertiary amines on the reaction, the reaction of carbon dioxide with aniline was investigated in several tertiary amines (Table 1). The presence of tertiary amines favored the reaction; of the tested amines, pyridine and β- and γ-picolines with smaller steric hindrance around the nitrogen atom gave satisfactory yields, whereas the yield was lowered in sterically hindered amines such as α-picoline and 2,4-lutidine, and strikingly low in 2,6-lutidine with the largest hindrance in pyridine derivatives. The unsatisfactory result in highly basic triethylamine even under severe reaction conditions indicated that the steric hindrance was more influential than the basicity.

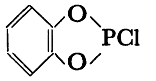
Various ureas were prepared using phosphorus trichloride in pyridine (Table 2). In the reactions of amines more basic than pyridine, 7 equivalents of the amines were used, since 3 equivalents were consumed as HCl scavenger. Primary amines afforded the corresponding *N,N'*-disubstituted ureas, whereas secondary amines gave no ureas.

Table 2. N,N'-Disubstituted ureas from amines and carbon dioxide by use of phosphorus trichloride in pyridine at 60 °C for 6 h

Amine (mol)		Yield mol	Yield %[a]
Aniline	(4.0)	1.86	93
Cyclohexylamine	(7.0)[b]	1.64	82
Benzylamine	(7.0)[b]	1.40	70
Isopropylamine	(7.0)[b]	0.92	46
Piperidine	(7.0)[b]	0	—
Diphenylamine	(4.0)	0	—
N-Methylaniline	(4.0)	0	—

a) Based on amines (4 mol). b) Three equivalents were used as HCl scavenger.

Table 3. N,N'-Diphenylurea from aniline and carbon dioxide by use of various phosphorus chlorides in pyridine at 60 °C for 6 h

Phosphorus chloride (mol)		Aniline (mol)	Yield mol	Yield %[a]
PhO-PCl$_2$	(0.01)	0.02 0.04	0.009 0.0173	90.0 86.5
EtO-PCl$_2$	(0.01)	0.02 0.04	0.0087 0.0123	87.0 61.5
Ph-PCl$_2$	(0.01)	0.04	0.0050	25.0
(PhO)$_2$-PCl	(0.01)	0.02	0.0020	20.0
(EtO)$_2$-PCl	(0.01)	0.02 0.04	0.0028 0.0047	28.0 23.5
	(0.01)	0.02	0.0030	30.0
O=PCl$_3$	(0.01)	0.05	0	—
Ph-P(O)Cl$_2$	(0.01)	0.05	0	—
PCl$_5$	(0.01)	0.05	0	—

a) Yield (%) based on aniline used.

Other phosphorus chlorides were tested in the reaction of carbon dioxide with aniline in pyridine (Table 3). Phenyl dichlorophosphite gave the best results, giving a nearly quantitative yield of N,N'-diphenylurea from both 2 and 4 equivalents of aniline. Monochlorophosphites gave moderate results. On the other hand, phosphorus(V) chlorides afforded no urea, but the corresponding phosphorus amides; phosphoryl chloride and phenylphosphinylidene dichloride yielded phosphoric trianilide and phenylphosphinic dianilide in 69 and 60% yields, respectively. These anilides unreactive to carbon dioxide gave no urea.

Similar to the reaction of carbon dioxide, carbon disulfide reacted with aniline in pyridine with use of phosphorus trichloride and phenyl dichlorophosphite, yielding thioureas in high yields (Table 4).

The reaction of carbon dioxide with aniline was carried out by varying the molar ratios of aniline to phosphorus chlorides, in order to examine how many mols of aniline can be converted into urea by one mol of phosphorus chloride. Figure 1 shows the variation of the produced amount of N,N'-diphenylurea with the ratio, indicating an increase of amount until a limiting value of *ca.* 4. Above this value, no substantial increase was found by additional aniline.

The results are represented in another way in terms of the yields based on phosphorus chloride (Fig. 2). Nearly quantitative yields were obtained at the ratio of 4 for phosphorus trichloride, and at both ratios of 2 and 4 for phenyl dichlorophosphite.

The results in Figs. 1 and 2 indicate that the trichloride can transform 4 mol of aniline into 2 mol of N,N'-diphenylurea, whereas the dichlorophosphite can react with 2 mol of aniline into 1 mol of the urea, and also with 4 mol of aniline into 2 mol of the urea.

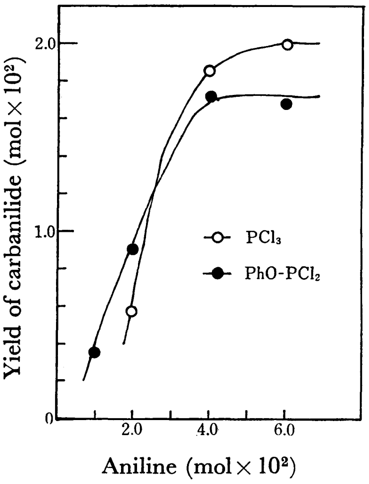


Fig. 1. Variation of urea yield with the amount of aniline employed: PCl$_3$=PhO–PCl$_2$=0.01 mol; temperature=60 °C; time=6 h.

Table 4. Thioureas from carbon disulfide and amines by use of phosphorus chlorides in pyridine at 40 °C for 6 h

Phosphorus chloride (mol)		Amide (mol)		Yield mol	Yield %[a]
PCl$_3$	(0.01)	Aniline	(0.04)	0.0175	87.5
PCl$_3$	(0.01)	Benzylamine	(0.07)[b]	0.0113	56.5
PCl$_3$	(0.01)	Cyclohexylamine	(0.07)[b]	0.0158	79.0
PhO-PCl$_2$	(0.01)	Aniline	(0.02)	0.0066	66.0
PhO-PCl$_2$	(0.01)	Aniline	(0.04)	0.0169	84.5

a) Yield (%) based on amines used. b) Three equivalents of amines were used as HCl scavenger.

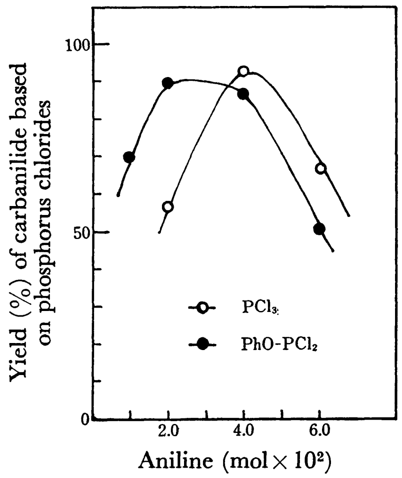
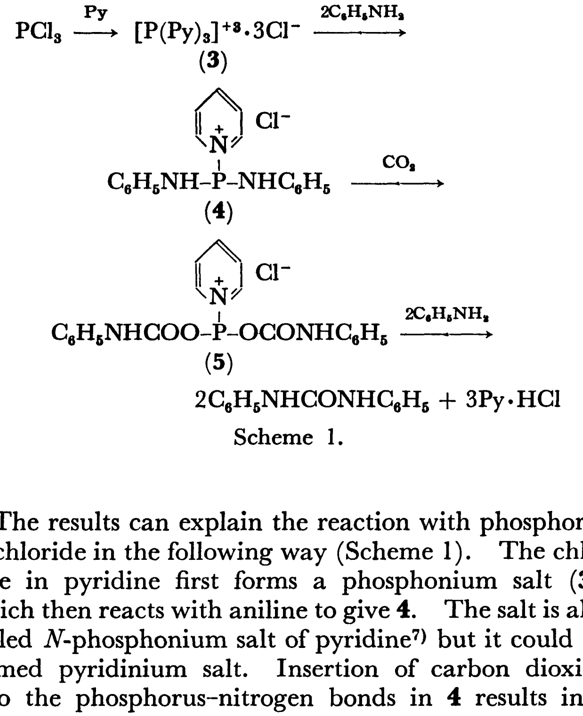


Fig. 2. Variation of urea yield with the amount of aniline employed: $PCl_3 = PhO\text{-}PCl_2 = 0.01$ mol; temperature = 60 °C; time = 6 h.



Scheme 1.

The results can explain the reaction with phosphorus trichloride in the following way (Scheme 1). The chloride in pyridine first forms a phosphonium salt (**3**), which then reacts with aniline to give **4**. The salt is also called *N*-phosphonium salt of pyridine⁷⁾ but it could be named pyridinium salt. Insertion of carbon dioxide into the phosphorus-nitrogen bonds in **4** results in a carbamoyloxy *N*-phosphonium salt (**5**) which is similar to that obtained from diphenyl phosphite.⁸⁾ Aminolysis of **5** with additional aniline gives urea.

In order to confirm the proposed mechanism, **4** was obtained as a syrup contaminated with pyridine hydrochloride, after the reaction mixture of phosphorus trichloride and aniline in pyridine had been extracted with ether until no detectable amounts of pyridine and aniline were found in the ether layer.

In the IR spectrum of the syrup, a peak at 1630 cm^{-1} is due to ν $C{=}N^+$ of the *N*-phosphonium salt of pyridine, and is in good agreement with that of the phosphonium salts⁷⁾ given by the oxidation of phosphites in pyridine followed by aminolysis. Although the band is overlapped with that of pyridine hydrochloride, the latter intensity contained in the band is less than half, judging from the medium intensity of a couple of other peaks due to hydrochloride.

The syrup was decomposed in 1 M-sodium hydroxide, and the liberated pyridine and aniline were extracted with ether. The results of GLC analyses of the extract indicate that 3 mol of pyridine and 2 mol of aniline are present in the syrup. According to Scheme 1, **4** was contaminated with 2 mol of pyridine hydrochloride. Thus 1 mol of pyridine and 2 mol of aniline are involved in **4**.

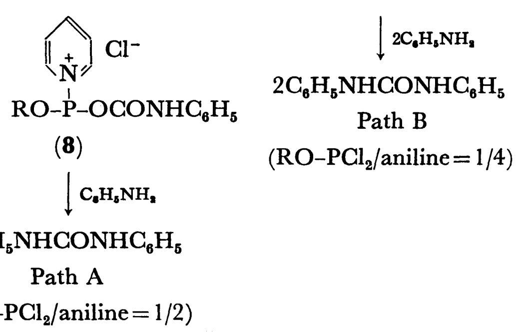
In the reaction with amines more basic than pyridine such as cyclohexylamine, 3 mol of pyridine of **3** may be replaced by the amines to form triamide, and the amine hydrochloride, and 7 mol of the amine added can theoretically produce only 1 mol of the urea. However, better yield (1.64 mol) of the urea excluded the involvement of the triamide intermediate, although it is not clear why **3** did not react with 3 mol of the amine.

Another possible intermediate is a phosphenimidous derivative (**6**), which was proposed in amidation of carboxylic acids as shown before:⁹⁾

$$PCl_3 + 2R^1NH_2 \xrightarrow{\text{toluene}} \underset{(\mathbf{6})}{R^1N{=}P\text{-}NHR^1}$$

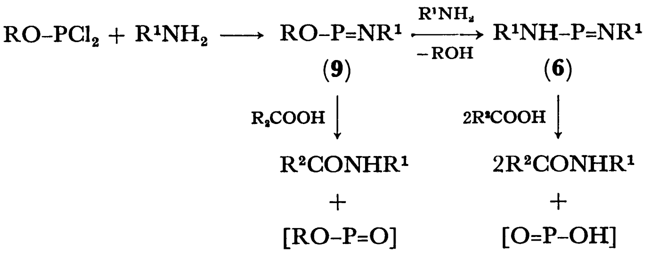
$$\xrightarrow{2R^2COOH} 2R^2CONHR^1 + [O{=}P\text{-}OH]$$

However, it can not be a dominant one in the reaction of carbon dioxide, since only a small amount (12% yield based on aniline) of **6** was obtained from the reaction mixture of phosphorus trichloride and aniline in pyridine. A separate reaction of **6** with carbon dioxide and aniline gave *N*,*N*′-diphenylurea in 38% yield as compared to 93% in the standard procedure in this study.



Scheme 2.

Similarly, dichlorophosphites might bring about two different reactions involving 2 and 4 equivalents of aniline (Scheme 2). In Path A phosphites react initially with 1 equivalent of aniline to give the *N*-phosphonium salt (**7**) like **4**, which is converted into *N,N'*-diphenylurea by treating with carbon dioxide and then with aniline ($RO-PCl_2$/aniline=1/2). In Path B ($RO-PCl_2$/aniline=1/4), **7** reacts further with additional aniline to afford **4** by releasing phenol or alcohols. Insertion of carbon dioxide into the P–N bonds of **4** followed by aminolysis yields *N,N'*-diphenylurea. Actually, phenol ($R=C_6H_5-$) was obtained in 42% yield in the reaction by Path B. Better results with phenyl dichlorophosphite than with ethyl dichlorophosphite in Path B (Table 3) may be due to easier dephenoxylation than deethylation which promotes the formation of **4**.



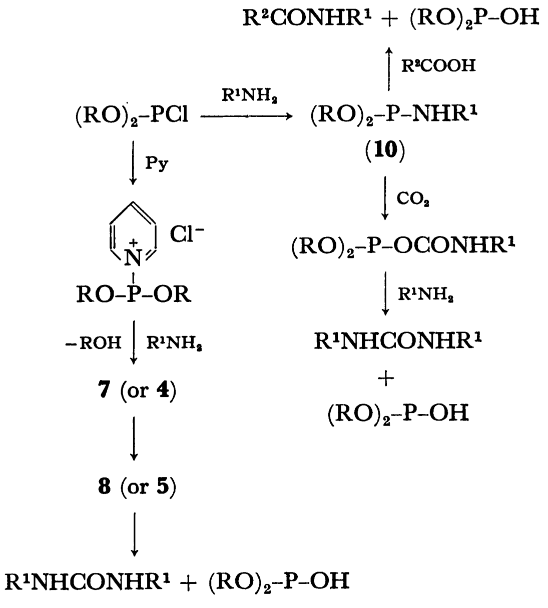
Scheme 3.

An alternative mechanism[11] *via* a phosphinimidite **6** and **9** proposed for amidation of carboxylic acids may not be reasonable, because of the lower reactivity of **6** to carbon dioxide (Scheme 3).

Similarly, the reaction with monochlorophosphites may proceed *via* the *N*-phosphonium salts of pyridine (**7** and **8**, or **4** and **5**) by releasing alcohols and phenol. Phenol was found in 47% yield (about a half of two phenoxy groups in the phosphite) in the reaction mixture with diphenyl monochlorophosphite.

An amidophosphite[11] also can be considered as an intermediate. In a separate experiment, diethyl anilidophosphite (**10**) gave the urea in 25% yield which is comparable to 29% obtained by the reaction with diethyl chlorophosphite.

Thus the reaction with monochlorophosphites may involve two paths as above (Scheme 4).



Scheme 4.

Experimental

N,N'-Diphenylurea from Carbon Dioxide and Aniline by Use of Phosphorus Trichloride in Various Tertiary Amines. Gaseous carbon dioxide was introduced at 60 °C for 6 h into a cylindrical flask containing a mixture of phosphorus trichloride (0.01 mol) and aniline (0.04 mol) in 30 ml of tertiary amines. In volatile triethylamine, the reaction was carried out in an autoclave at the pressure (20 atm) of carbon dioxide. The reaction was also carried out in 40 ml of toluene by using phosphorus trichloride (0.01 mol) and aniline (0.04 mol). The reaction mixture was condensed to a syrup under reduced pressure, and then treated with 20 ml of 50% aqueous ethanol, yielding *N,N'*-diphenylurea in high yields (Table 1).

Separation and Decomposition of ***4***. A mixture of phosphorus trichloride (0.01 mol) and aniline (0.04 mol) in 30 ml of pyridine was heated at 40 °C for 1 h, and the mixture was extracted with dry ether until no pyridine and aniline were detected in the ether solution. **4** was separated as an ether-insoluble syrup, and was decomposed in 20 ml of 1 M-sodium hydroxide at ambient temperature for 1 h. The aqueous solution was extracted well with ether, and the combined ether solution was subjected to gas-liquid chromatographic analyses.

N,N'-Disubstituted Ureas from Carbon Dioxide and Various Amines by Use of Phosphorus Trichloride in Pyridine. Similarly, carbonylation of amines (0.04 mol) or amines (0.07 mol) more basic than pyridine was carried out at 60 °C for 6 h by adding the amines in pyridine to a mixture of phosphorus trichloride (0.01 mol) and pyridine (30 ml). Ureas were obtained by working up as above.

N,N'-Diphenylurea from Aniline and Carbon Dioxide by Use of Various Phosphorus Chlorides in Pyridine. The urea was obtained by the reaction at 60 °C for 6 h in 30 ml of pyridine with use of phosphorus chlorides (0.01 mol) and aniline (0.02—0.05 mol).

Thioureas from Carbon Disulfide and Amines by Use of Phosphorus Chlorides in Pyridine. A mixture of amines (0.02—0.07 mol) and phosphorus chlorides (0.01 mol) in 30 ml of pyridine was heated at 40 °C for 6 h. The resulting mixture was evaporated to a syrup under reduced pressure. Thioureas were obtained by treating the syrup with 20 ml of 50% aqueous ethanol.

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