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CARBONYLATION OF AMINES WITH CARBON DIOXIDE UNDER ATMOSPHERIC CONDITIONS

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In the previous reports of this series on the reactions of the N-phosphonium salts of pyridines, carboxylic acids have shown to be activated via the acyloxy N-phosphonium salts of pyridine given by the dephenoxylation of diphenyl and triphenyl phosphites in pyridines, producing the corresponding amides in excellent yields followed by aminolysis at ambient temperature for a short period.[1,2)]

Considering similar reactions of carbonic acid to those of carboxylic acids, such as amide formation, we have introduced gaseous carbon dioxide in the place of carboxylic acids in the coupling reaction with amines in the presence of tertiary amines like pyridine. Actually, we found that N,N'-diphenylurea was produced in a nearly quantitative yield together with phenol by bubbling carbon dioxide into a pyridine solution of diphenyl phosphite and aniline. It was also found that N,N'-diphenylthiourea was obtained in an excellent yield from carbon disulfide and aniline under mild conditions.

This paper presents a new and simple method for the preparation of ureas and thioureas from carbon dioxide and disulfide by means of diphenyl and triaryl phosphites in the presence of tertiary amines.

The reactions producing ureas and thioureas were summarized in the following equations:

$$CO_2 + 2\ R\text{-}NH_2 + H\text{-}\overset{O}{\overset{\|}{P}}(OPh)_2\ (\text{ or } 1/2\ P(OPh)_3) \xrightarrow[t\text{-Amines}]{\sim 40^\circ C} R\text{-}NHC(=O)NH\text{-}R + PhOH + H\text{-}\overset{O}{\overset{\|}{P}}(OPh)(OH)\ (\text{ or } 1/2\ H\text{-}\overset{O}{\overset{\|}{P}}(OPh)(OH)) \quad \ldots \text{ eq. 1.}$$

$$CS_2 + 2\ R\text{-}NH_2 + H\text{-}\overset{\overset{O}{\|}}{P}(OPh)_2\ (\text{ or } 1/2\ P(OPh)_3) \xrightarrow[t\text{-Amines}]{40^\circ C} R\text{-}NH\overset{\overset{S}{\|}}{C}NH\text{-}R$$

$$PhOH + H\text{-}\overset{\overset{O}{\|}}{P}(OPh)(SH)\ (\text{ or } 1/2\ H\text{-}\overset{\overset{O}{\|}}{P}(OPh)(SH)) \quad \ldots \text{ eq. 2.}$$

In a typical experiment, carbon dioxide was passed through a mixture of diphenyl phosphite (47 mmol) and aniline (47 mmol) in 40 ml of pyridine at 40°C for 4 hr. The resulting mixture was concentrated to a syrup under reduced pressure. The syrup was treated with 20 ml of 50% aqueous ethanol and then the precipitate was collected by filtration. Recrystallization of the product from ethanol gave 85% (4.3 g) of N,N'-diphenylurea, mp. 238°. The urea was also obtained in 93% yield in a similar manner in the presence of imidazole in N,N-dimethylformamide (DMF).

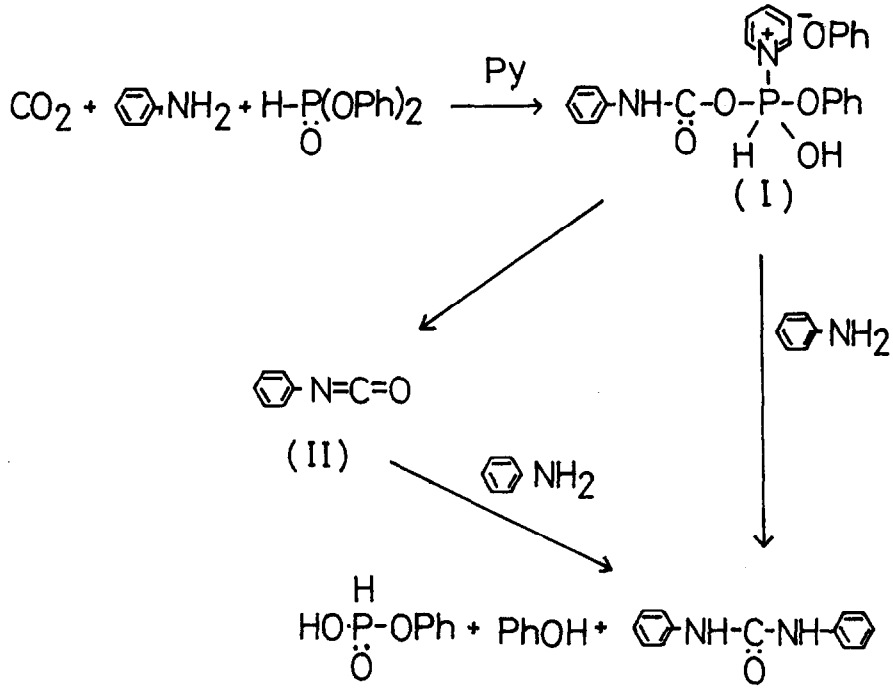
Similarly, N,N'-dicyclohexylurea was prepared in 40% yield by the reaction with cyclohexylamine at 60°C for 4 hr.

The yield of the urea increased with an increase in the reaction temperature and time. No reaction took place in the absence of the phsophite. Among the phosphites examined, diphenyl and triaryl phosphite were effective for the reaction with carbon dioxide, whereas alkyl phosphites gave no urea under identical conditions. The increased amount of diphenyl phosphite improved the yield of the urea, showing a limiting value when the molar ratio of the phosphite over aniline was about 1.0. This led us to consider that the phosphite was involved stoichiometrically in the reaction.

Tertiary amines also played an important role in the reaction. The yield of the urea was negligibly small (4%) in the absence of tertiary amines, even when diphenyl phosphite was present. Imidazole gave N,N'-diphenylurea in 78% yield in the reaction using triphenyl phosphite, whereas pyridine yielded no urea.

In a similar manner to the reaction of carboxylic acids with diphenyl phosphite in pyridine, the reaction of carbon dioxide with the phosphite in the presence of aniline may proceed via such a carbamyl N-phosphonium salt of

pyridine (I) as carbamyl phosphate in volving in urea cycle in living cells (Scheme 1). I reacts with another aniline to produce the urea. Another possible pathway for forming the urea can be considered through phenyl isocyanate (II) derived from I. However, it is difficult to state which pathway is more plausible in the reaction. Further study is in progress and will be reported in the near future.



SCHEME 1

Similarly, N,N'-diphenylthiourea was obtained in theoretical yield, when a mixture of carbon disulfide (94 mmol), equimolar amounts of diphenyl phosphite (47 mmol) and aniline in 40 ml of pyridine was kept at 40°C for 4 hr.

In conclusion, this procedure provides a simple method for the preparation of ureas by passing carbon dioxide through a pyridine solution of diphenyl and triaryl phosphites at ordinary pressure, and also a convenient method for the

synthesis of thioureas from carbon disulfide.

REFERENCES

1) N. Yamazaki and F. Higashi, Tetrahedron Lett., 5047(1972).

2) N. Yamazaki and F. Higashi, Tetrahedron, in press.