REDOX FORMATION OF PYRIMIDINYL METHYLENEPHOSPHORANES BY REACTION OF TRICHLOROMETHYL PYRIMIDINES WITH TRIPHENYLPHOSPHINE

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Abstract — The reaction of trichloromethylpyrimidines (1) with ca. 5 equivalent amounts of TPP gave pyrimidinylmethylenephosphoranes (9), whereas in the presence of 2 equivalent amounts of TPP, 1 was converted into the corresponding pyrimidinylchloromethylenephosphoranes (2). Condensation of 2 and 9 with aldehydes gave smoothly pyrimidine derivatives having an olefinic side chain. The pathway of the reduction to form the phosphoranes was discussed with experimental evidence.

It was previously reported that the reaction of 4-trichloromethylpyrimidines (1) with triphenylphosphine (TPP) forms chloromethylenephosphoranes (2). The condensation of 2 with propionaldehyde (or benzaldehyde) gave a mixture of the corresponding chloroalkenyl- (3) and alkenylpyrimidines (4). The mechanism of the formation of 4 was not clear, because in some cases compound of type 3 was isolated as a sole product.

\[
\begin{align*}
\text{PhN,PPh₃} & \text{PhN} \\
\text{Cl-C=PPh₃} & \text{Cl-C=CHR} \\
\text{PhN,Ph} & \text{PhN,CHR} \\
\text{Cl-C=CHR} & \text{Cl-C=CHR} \\
\end{align*}
\]

Scheme 1
On the other hand, when this reaction was applied to the synthesis of 1,2,4-triazine derivatives, 5,6-diphenyl-3-trichloromethyl-1,2,4-triazine (5) was found to react with excess TPP to give the methylene phosphorane (7), instead of the expected chloromethylene phosphorane (6). Accordingly, in the case of 5,6-diphenyl-3-trichloromethyl-1,2,4-triazine (5), the reaction can be utilized conveniently for the introduction of an olefinic side chain into the 3-position. ²

In order to clarify the difference in the reactivity between the pyrimidine and the triazine, we re-investigated the reaction of 4-trichloromethylpyrimidines (1), focusing our attention upon reductive dechlorination process. In the present paper, we describe the probable reaction course which is sensitively affected by amounts of TPP.

When 4-chloro-2-methyl-6-trichloromethylpyrimidine (1a) was allowed to stand with 2 eq. amounts of TPP in benzene for 3 h, 6-chloro-2-methyl-4-pyrimidinylchlorophosphorane (2a), mp 200–201°C (dec.), was obtained in 76 % yield. The condensation of 2a with propionaldehyde at room temperature for 5 days afforded 4-chloro-6-(1-chloro-1-butenyl)-2-methylpyrimidine (3a) in 91 % yield. In this reaction, (E)-4-(1-butenyl)-6-chloro-2-methylpyrimidine (4a) was not detected. On the contrary, the reaction of 1a with 5 eq. amounts of TPP in benzene under reflux for 8 h resulted in the exclusive formation of 6-chloro-2-methyl-4-pyrimidinylmethylene phosphorane (9a), mp 163–164.5°C ³, in 77 % yield. When 2a was heated with 3 eq. amounts of TPP in benzene under reflux, the same phosphorane (9a) was obtained in 90 % yield. The condensation of 9a with propionaldehyde gave 4a in 77 % yield.

![Scheme 2](image-url)

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On the basis of these experiments, the following interpretation was reasonably concluded.

i) When 1a was treated with excess TPP, 2a formed initially was reduced to give 9a by the action of remaining TPP.

ii) The chlorophosphorane (2a) was not reduced with the aldehyde, and the condensation of 2a with aldehyde gave 3a as a sole product.

Further investigation was made to confirm the reaction pathway described above. Namely, after 4-phenyl-6-trichloromethylpyrimidine (1b) had been heated with an appropriate amount of TPP in toluene, the resulting crude phosphorane was treated with benzaldehyde to give a mixture of 4-(2-chlorostyryl)-6-phenylpyrimidine (3b) and 4-phenyl-6-styrylpyrimidine (4b). As shown in Scheme 3, the ratio of 3b to 4b was remarkably affected by amounts of TPP employed. Although the separation of the chlorophosphorane (2b) and the phosphorane (9b) failed, these results are not contradicted with those obtained on the reaction of 1a. In addition, when the reaction mixture of 1b with 2 eq. amounts of TPP was treated with ethanolic sodium hydroxide, 4-ethoxymethyl-6-phenylpyrimidine (10), bp 160°C (5mmHg), was obtained, while the same treatment of the mixture obtained on the reaction with 5 eq. amounts of TPP afforded mainly 4-methyl-6-phenylpyrimidine (12). It is acceptable that 4-chloromethyl-6-phenylpyrimidine (11) derived from the hydrolysis of 2b reacted immediately with ethoxide ion to give 10.

\[ \text{Scheme 3} \]
Similar phenomenon was commonly observed on the reaction of such compounds as 4-trichloromethyl-, 2-phenyl-4-trichloromethyl-, and 4-phenyl-2-trichloromethylpyrimidines. Particularly, 4-dichloromethyl-2-phenylpyrimidine (E) was isolated from the reaction mixture, when the trichloromethylpyrimidine was heated with 2 eq. amounts of triphenylphosphine in toluene.

Accordingly, the reaction of trichloromethyl pyrimidines and the triazine (A) with triphenylphosphine proceeds stepwise to give B, C, and D, as illustrated in Scheme 4. The isolation of E, F, and G is evidence of the presence for B, C, and D, respectively. The ease of the reductive phosphorane formation may depend on the electron deficiency of the heteroaromatics.

REFERENCES AND NOTES

4. Pure 4-(2-chlorostyryl)-6-phenylpyrimidine (3b), mp 106-107°C, and 6-phenyl-4-styrylpyrimidine (4b), mp 127-128°C, were isolated by column chromatography (SiO₂-benzene) from the mixture.
5. All new compounds gave IR, ¹H-NMR spectra and elemental analyses consistent with the proposed structures.

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