# NEW REACTIONS OF PHOSGENE WITH TERTIARY AMINES[†]

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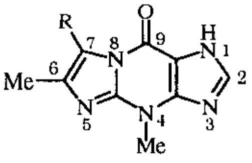
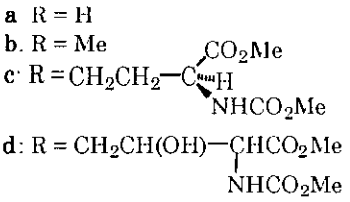
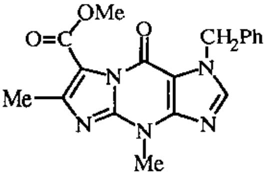
*Abstract* — 1-Benzylwye (**3**) underwent substitution at the 7-position in the presence of $COCl_2$ and pyridine in THF to afford various products depending upon the post-treatment through 1,4-dihydropyridine (**7**) and carboxylic acid derivative (**8**). When $Et_3N$ was used instead of pyridine, it reacted with $COCl_2$ to provide two enamines (**18** and **19**), together with diethylcarbamyl chloride (**20**), after treatment of the reaction mixture with MeOH.

In the course of our studies on the hypermodified bases (**1**)[1] of phenylalanine transfer ribonucleic acids, we required **2** in order to check the stability of the ring system.[2] Thus, we treated 1-benzylwye (**3**) with excesses of $COCl_2$ and pyridine in THF at room temperature for 9 h and then with MeOH overnight to give **2** (mp 176—177 °C)[3] in 65% yield, together with 32% recovery of **3**.



**1 a—d**





**2**

The recovery of **3** deserved further investigation because MeOH was added to the reaction mixture after **3** had been consumed. TLC analysis of the reaction mixture suggested that **2** was rapidly formed after addition of MeOH while **3** generated slowly. We obtained dihydropyridine derivatives (**6**, **12**, and **13**),[4] besides **2**, **11**, **14**, and **10**,[5] after short treatment of the reaction mixture with MeOH followed by aqueous treatment. Aromatic substitution leading to dihydropyridines has been reported for *N*-acylpyridinium and *N*-(alkoxycarbonyl)pyridinium ions.[6] Furthermore, it has been reported that $COCl_2$ reacts

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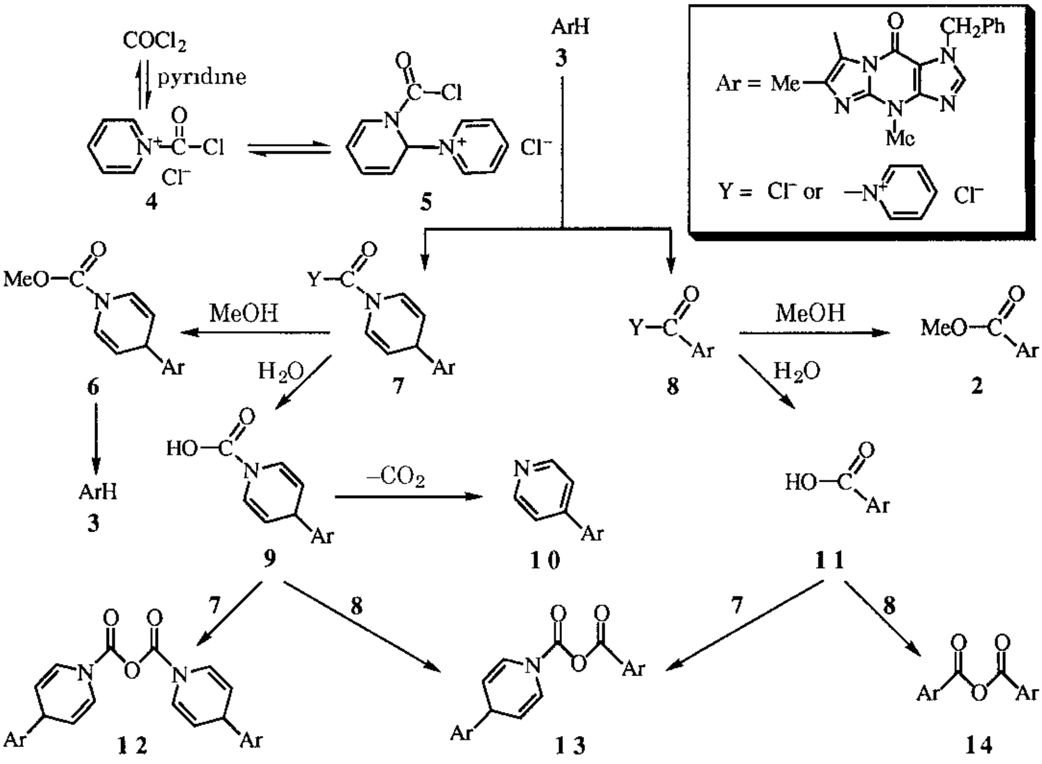
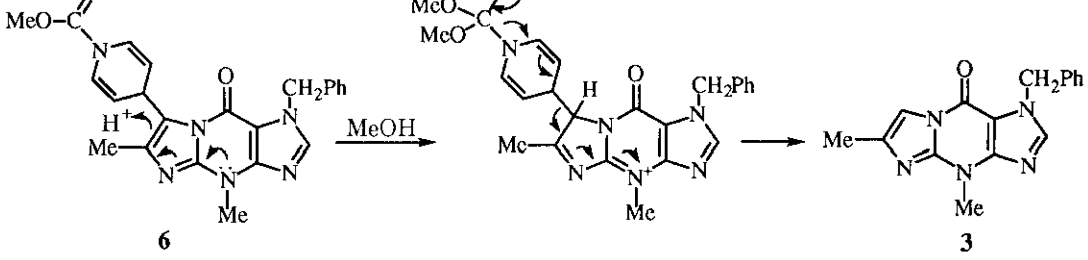
[†] This article is dedicated to the memory of Emeritus Professor Dr. Shun-ichi Yamada (University of Tokyo).

with pyridine to form **5** through **4**.[7] However, the formation of **6**, **10**, **12**, or **13** is the first example of aromatic substitution with **4** or **5**. Compounds (**6**) was quantitatively transformed into **3** upon treatment with pyridine hydrochloride in MeOH at room temperature for 24 h, probably by the mechanism depicted in Scheme 2. These results permit us to propose that the reaction follows the sequence as shown in Scheme 1. Compound (**10**) was most likely formed from **7** through subsequent hydrolysis, decarboxylation, and oxidation.



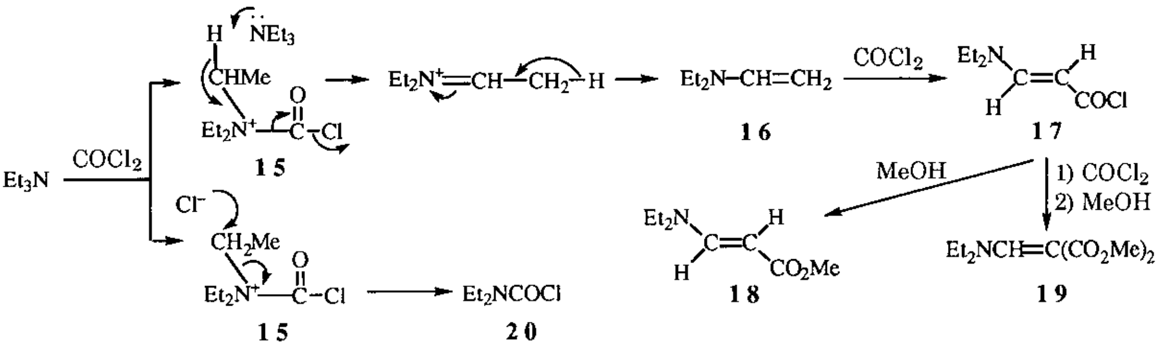
Scheme 1



Scheme 2

We next attempted to improve the yield of **2** by controlling the formation of the dihydropyridine derivatives. $Et_3N$ might be a good substitute for pyridine for this purpose.

Somewhat surprisingly, **3** was recovered unchanged on treatment with $COCl_2$ in THF in the presence of $Et_3N$ at room temperature for 9 h. Instead methyl (*E*)-3-diethylaminopropenoate (**18**),[8] dimethyl 2-(diethylaminomethylene)propanedioate (**19**),[9] and diethylcarbamyl chloride (**20**) were obtained in 4%, 4%, and 18% yields, respectively, after treatment of the reaction mixture with MeOH. Although the formation of **20** has already been reported for the reaction of $COCl_2$ and $Et_3N$,[10] that of a vinylamine derivative such as **17** from $Et_3N$ has not been reported except for the reactions with perhalogenated acetyl chlorides[10b] including trichloroacetyl chloride,[11] trichloroacetic anhydride,[12] or hexachloroacetone.[13] The reaction sequences similar to that delineated in Scheme 3 have already been proposed[11a,12,13] for these reactions.



Scheme 3

In conclusion, we have revealed that $COCl_2$ activates tertiary amines such as pyridine and $Et_3N$ to produce a variety of compounds, demonstrating that the choice of the base to be employed may be of prime importance for the reactions with $COCl_2$ or its equivalents.

## ACKNOWLEDGMENT

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2. Compound (**2**) underwent rearrangement to provide the isomeric 6-carboxylic acid ester. Details will be reported elsewhere.
3. Satisfactory analytical and/or spectroscopic data were obtained for all new compounds described.

4. $^{1}$H NMR (CDCl$_3$) $\delta$ for **6**: 2.29, 3.84, and 3.89 (3H each, s), 5.02 (2H, m), 5.59 (2H, s), 5.84 (1H, m), 6.79 and 6.93 (1H each, m), 7.36 (5H, m), 7.64 (1H, s); for **12**: 2.30 and 3.90 (6H each, s), 5.16 and 5.29 (2H each, m), 5.59 (4H, s), 5.90 (2H, m), 6.72 and 6.96 (2H each, m), 7.34 (10H, m), 7.66 (2H, s); for **13**: 2.30, 2.60, 3.89, and 3.97 (3H each, s), 5.06 and 5.25 (1H each, m), 5.59 (4H, s), 5.89 (1H, m), 6.99 (2H, m), 7.34 (10H, s), 7.65 and 7.71 (1H each, s).
5. $^{1}$H NMR (CDCl$_3$) $\delta$ for **11**: 2.74 and 4.03 (3H each, s), 5.61 (2H, s), 7.38 (5H, m), 7.87 (1H, s), 14.48 (1H, br s); for **14**: 2.65 and 3.96 (6H each, s), 5.50 (4H, s), 7.26 (10H, s), 7.65 (2H, s); for **10**: 2.32 and 3.99 (3H each, s), 5.57 (2H, s), 7.24—7.40 (7H, m), 7.65 (1H, s), 8.64 (2H, m).
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