THE REACTION OF DIAZINES WITH ALLYLTRIBUTYLTIN *via N*-ALKOXYCARBONYLDIAZINIUM SALTS#

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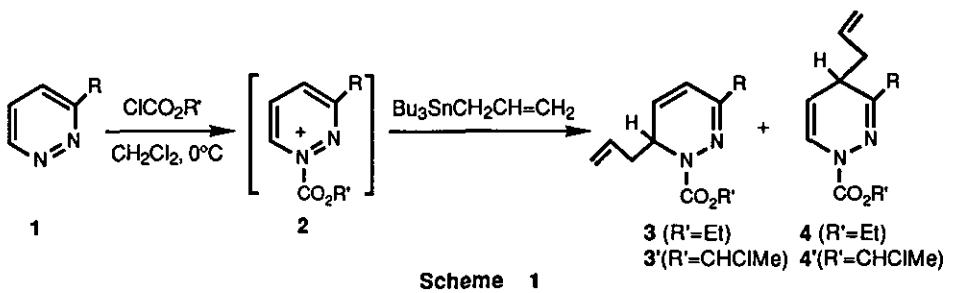
Abstract-Pyridazines were allowed to react with allyltributyltin in the presence of chloroformate to give 1-alkoxycarbonyl-6-allyl- and 1-alkoxycarbonyl-4-allyl-dihydro-pyridazines as major and minor products, respectively. The reaction was applied to other diazines, and tetrahydro-adducts were obtained in the case of pyrimidine and pyrazine. Benzo-fused diazines also reacted in the same manner to afford the allyl-adducts in good yields.

Introduction of substituents to pyridazine derivatives (**1**) has been widely investigated.[2] The π-electron deficiency of the ring causes nucleophilic reagents rather available.[3] The reactions have been performed mainly using chloropyridazines or pyridazine *N*-oxides as substrates,[4] and only few reports exhibited the direct nucleophilic addition followed by the oxidation.[5] While, the ring activation through the quaternary salts ordinarily resulted in the ring opening,[6] and there are few papers that reported the reaction of *N*-alkoxycarbonyl salts of pyridazines (**2**).[7] In fact, the compound (**2**) couldn't be readily isolated, which is quite different from the case of pyridines. And, the attempts of *in situ* trapping of **2** using some nucleophiles were unsuccessful because chloroformates were reactive to them.

This paper is dedicated to Professor A. R. Katritzky on the occasion of his 65th birthday.

Therefore, tin reagents are thought to be appropriate for this system because they are nucleophiles which don't react with carbonyl groups.[8] Thus we investigated the use of tin reagent and it was revealed that the one-pot reaction of **1** with allyltributyltin in the presence of chloroformate proceeded to afford 1,4- and 1,6-dihydroadducts, which are entirely new compounds, in good yields.[9] Moreover, this reaction system was applied to other diazines. This paper describes these results.

At first, pyridazines (**1**) and allyltributyltin were allowed to react in the presence of ethyl chloroformate, 6-allyl-1-ethoxycarbonyl-1,6-dihydropyridazine (**3**) and 4-allyl-1-ethoxycarbonyl-1,4-dihydropyridazine (**4**) in 63% and 14% yields, respectively (Scheme 1).[10] In the typical experiment, pyridazine (10 mmol) and allyltributyltin (12 mmol) were dissolved in CH_2Cl_2 (40 ml) at 0°C, and chloroformate (12 mmol) was added dropwise. The mixture was allowed to stand at 0°C for 1h, then treated with 1M KF solution of H_2O (30 ml) and ether (100 ml), and the precipitate thus formed was removed by filtration. The filtrate was dried over anhydrous $MgSO_4$ and evaporated to leave the residue, which was chromatographed on silica gel to afford the products. Other 3-substituted pyridazines were also adopted as substrates and the results are summarized in Table I. 1,6-Dihydroderivatives (**3**) were dominant products in all cases.

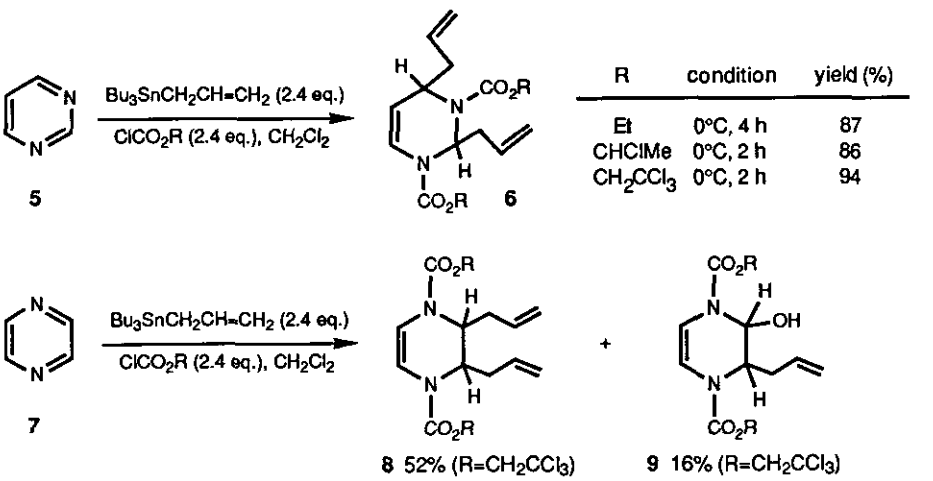


Scheme 1

Table I Reaction of Pyridazines (1) with Allyltributyltin in the Presence of Chloroformate

substrate	R	R'	yield of 3(%)	yield of 4(%)	ratio of 3/4
1a	H	Et	63	14	4.50
		CHClMe	77	12	6.42
1b	Me	Et	67	18	3.72
		CHClMe	59	13	4.54
1c	Ph	Et	65	8	8.13
		CHClMe	80	8	10.00
1d	CO_2Me	Et	79	7	11.29
		CHClMe	80	4	20.00

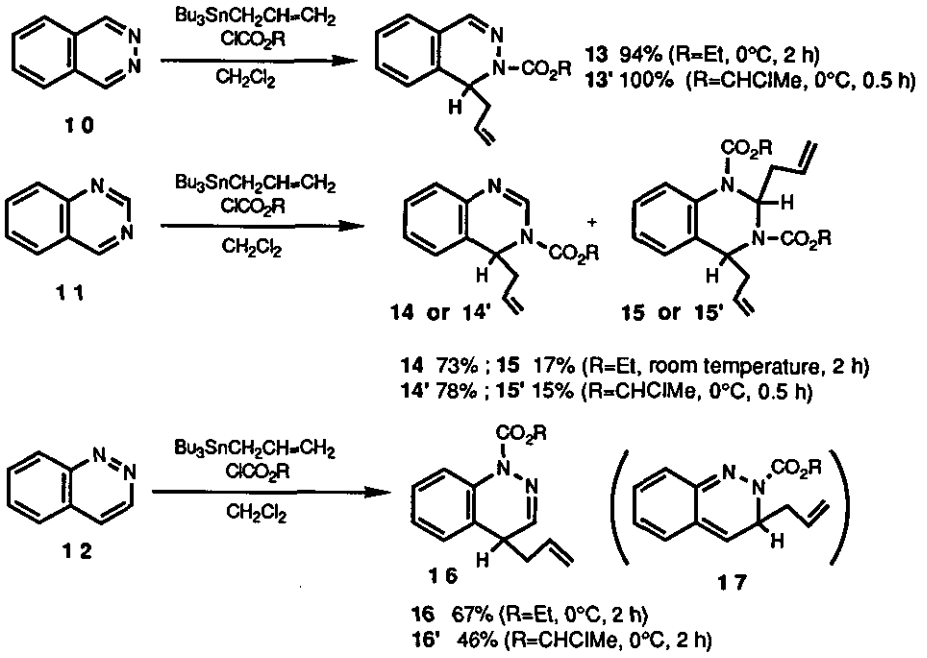
Next, other diazines were adopted as the substrates. Pyrimidine (**5**) was readily reacted with allyltributyltin in the presence of chloroformate to give 1,3-dialkoxycarbonyl-2,4-diallyl-1,2,3,4-tetrahydropyrimidine (**6**) in good yields regardless of chloroformates (Scheme 2). In these cases, mono-allyl adducts analogous to (**3**) or (**4**) in pyridazines were not obtained even when 0.5 eq. of allyltributyltin and chloroformate were used. The fact suggests that the second addition was much faster than the first one. Thus the first reaction site of the tin reagent was remained unclear, although the results of quinazoline (**11**) suggested 4-position shown below. Pyrazine (**7**) was also allowed to react under the same conditions to afford **8**, and no monoallyladduct was obtained. A by-product **9** was obtained probably because the steric hindrance interfered the second attack of allyltributyltin, and H_2O derived from moisture might add instead to intermediary iminium salt.



Scheme 2

Then the above reaction system was applied to the benzodiazines, and the results are summarized in Scheme 3. Phthalazine (**10**) and quinazoline (**11**) were easily attacked under the same condition to afford 1,2-dihydro-adducts (**13**) and (**14**), respectively, accompanied by the tetrahydro-adduct (**15**) from **11**. When cinnoline (**12**) was used, the progress of the reaction was slow and the obtained product was 1,4-adduct (**16**), which had different regioselectivity from those of pyridazines and phthalazine.

It was because the expected product (**17**) was thought to be less stable than **16** by the rupture of aromatic nature of the fused benzene ring.



Scheme 3

In this paper, we reported the allylation of diazines with allyltributyltin. Pyridazines afforded 1,6-dihydroadducts (**3**) dominantly, since allyltributyltin is known to be a hard nucleophile,[8] and 6-position of pyridazinium salts is thought to be harder site than 4-position. The substrates other than 1,2-diazines underwent the second addition reaction to give diallyladducts. The results suggested the second quaternarization and addition of tin reagent were faster than the first one. Thus, it was supposed that the difficulty of second quaternarization resulted in the monoallyl addition of diazines. The introduction of other substituents using this method, and the application of the obtained allyl-adducts, are now in progress.

ACKNOWLEDGMENT

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

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10. The adducts mentioned in this paper were obtained as a mixture of two to four conformational isomers. The details will be reported in following papers.

Received, 29th September, 1993