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# REACTION OF IMIDAZOLES WITH ALLYLTRIBUTYLTIN IN THE PRESENCE OF CHLOROFORMATE

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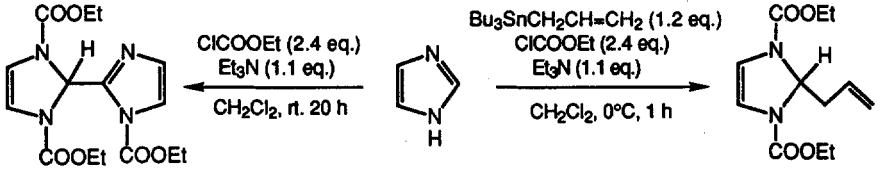
**Abstract**: The reaction of imidazoles with allyltributyltin in the presence of chloroformate gave 2-allyl-1,3-dialkoxycarbonyl-4-imidazolines in good yields. The addition products were aromatized with potassium ferricyanide under basic condition to afford corresponding 2-allylimidazoles.

In the field of heteroaromatic chemistry, substitution reactions are performed mainly with nucleophilic reagents because of electron deficiency of rings.[2] However, five membered heterocycles such as imidazoles do not have enough reactivity to nucleophiles.[3] Several groups reported the attempts to activate imidazole ring toward nucleophile via quaternization.[4] The activation by acyl halide or chloroformate with base resulted in ring opening,[5] 1,2-diacylation,[6] and dimerization[7] according to reaction conditions. Recently, Reissert type reaction of benzimidazole was reported,[8] which introduced cyano group to C-2 position. However, the attempt to aromatize failed because the retro-Reissert reaction proceeded to afford starting material.[9]

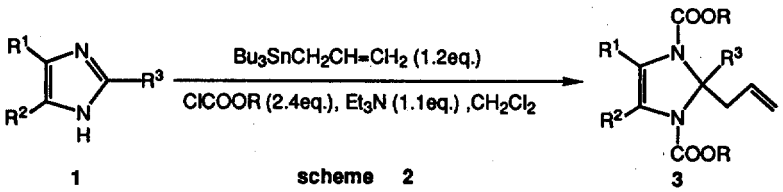
In the course of our study of heteroaromatic quaternary salts,[10] we focused on the lability of 1,3-bis(alkoxycarbonyl)imidazolium salts. Since organotin reagents[11] are known to be mild nucleophiles which do not react with carbonyl groups,[12] we tried one-pot synthesis of 2-allylimidazoline derivatives using allyltributyltin with chloroformate, which we wish to report in this paper.

Imidazole **1a** is dimerized to triethyl-[2,2'-bi-1H-imidazole]-1,1',3(2H)-tricarboxylate **2a** in the presence of ethyl chloroformate and triethylamine. The addition of allyltributyltin in the above reaction changed the product to 2-allyl-1,3-diethoxycarbonyl-4-imidazoline **3a** in 96% yield (scheme 1).




**2a** 70% **1a** **3a** 96%

**scheme 1**




1 scheme 2 3

**Table I** Reactions of Allyltributyltin with Imidazoles in the Presence of Chloroformate.

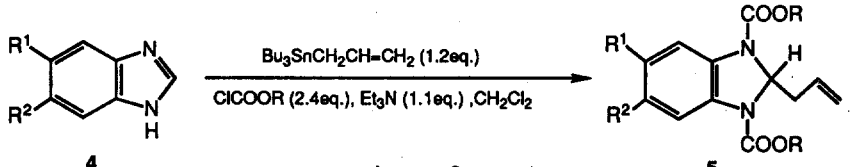
| entry | substrate | $R^1$ | $R^2$ | $R^3$ | R of formate | conditions | yield of 3 (%) |
|---|---|---|---|---|---|---|---|
| 1 | 1a | H | H | H | Et | 0°C, 1.0hr | 96 |
| 2 | 1b | Me | H | H | Et | 0°C, 1.5hr | 90 |
| 3 | 1c | Me | Me | H | Et | 0°C, 2.0hr | 69 |
| 4 | 1d | H | H | Me | Et | rt , 3.0hr | 42 |
| 5 | 1a | H | H | H | Me | 0°C, 1.5hr | 63 |
| 6 | 1a | H | H | H | $CHClCH_3$ | 0°C, 2.0hr | 80 |
| 7 | 1a | H | H | H | $CH_2CCl_3$ | 0°C, 1.0hr | 78 |

In the typical experiment, 10 mmol of imidazole, 12 mmol of allyltributyltin, and 11 mmol of triethylamine were dissolved in 40 ml of $CH_2Cl_2$, and the mixture was cooled in ice bath. Ethyl chloroformate (24 mmol) was added dropwise to the mixture, and the solution was allowed to stand at 0°C under stirring for 1 h. Then the solvent was treated with aq. KF solution and the precipitate thus formed was removed by filtration. The filtrate was dried over $MgSO_4$ and evaporated to leave the residue, which was chromatographed on silica gel to afford **3a** as colorless oil. Table I shows the yields of monocyclic 2-allylimidazolines **3**. Even in the case of 2-methylimidazole, addition of allyl group occurred at C-2 position (entry 4). Variation of chloroformates didn't give significant effect on the yields (entries 1, 5, 6, and 7).

Next, benzimidazoles **4** were adopted as substrates, and the results are summarized in scheme 3 and Table II. The reaction proceeded slowly, but the yields were good for the substrates which have no, or electron-donating substituents (entries 1 to 4). Introduction of electron-withdrawing substituent decreased the yield of **5** in the case of ethyl chloroformate as activating group (entries 5, 6, and 7).[13] In order to improve the reaction yields, more electron-deficient chloroformates were investigated and it was revealed that 1-chloroethyl chloroformate gave good yields even in the presence of electron-withdrawing group in the substrate (entries 9, 10, and 11).

Facile synthesis of 2-allyl-1,3-dialkoxycarbonyl-4-imidazolines **3** and **5** prompted us to synthesize substituted 2-allylimidazoles, and the first attempt was carried out to aromatize **3** and **5**. The results are shown in scheme 4. Monocyclic dialkoxycarbonyl-allylimidazoline **3** was readily aromatized to 2-allylimidazole by potassium ferricyanide with KOH under reflux. The reaction might proceed by the hydrolysis of carbamate and succeeding oxidation of unstable imidazoline. Under the same reaction, however, benzimidazoline derivative **5** afforded a vinylimidazole **8** in 90% yield probably through allylbenzimidazole **7**. The derivation to **7** from **5** was achieved by the use of excess

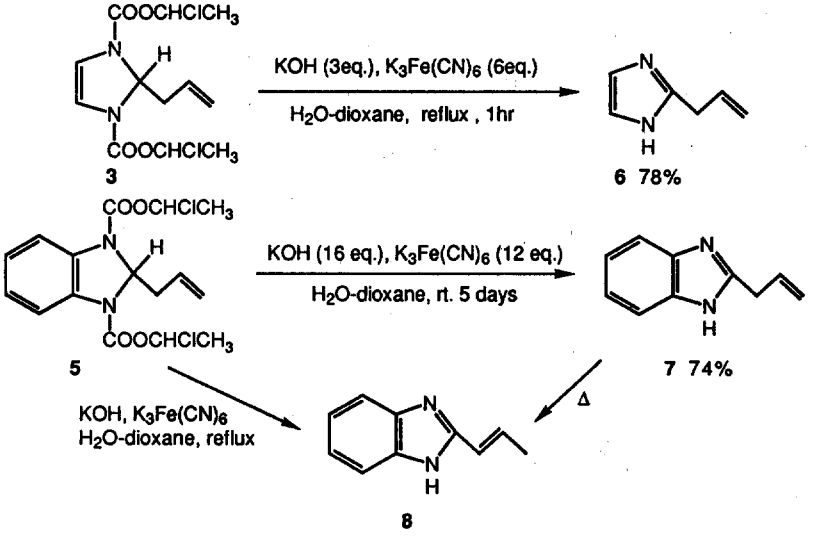
amounts of the reagents at room temperature in 74% yield. The compound **7** thus obtained was easily isomerized to **8** on heat. There is only one paper[14] reporting the synthesis of 2-allylimidazole. Since the method involves the thermal rearrangement of 1-allylimidazole at 530°C to give 2-and 4-allylimidazoles, allylbenzimidazoles described here won't be able to be obtained. Hence our reaction system is the first general synthetic method for 2-allylimidazole derivatives.




**4** **scheme 3** **5**

**Table II** Reactions of Allyltributyltin with Benzimidazoles in the Presence of Chloroformate.

| entry | substrate | $R^1$ | $R^2$ | R of formate | conditions | yield of 5 (%) |
|---|---|---|---|---|---|---|
| 1 | 4a | H | H | Et | rt. 3 h | 70 |
| 2 | 4b | Me | H | Et | rt. 3 h | 83 |
| 3 | 4c | Me | Me | Et | rt. 15 h | 84 |
| 4 | 4d | OMe | H | Et | rt. 15 h | 81 |
| 5 | 4e | Cl | H | Et | rt. 3 days | 39 |
| 6 | 4f | COOMe | H | Et | rt. 3 days | 0 |
| 7 | 4g | $NO_2$ | H | Et | rt. 3 days | 0 |
| 8 | 4a | H | H | $CHClCH_3$ | 0°C- rt. 2 h | 69 |
| 9 | 4e | Cl | H | $CHClCH_3$ | 0°C- rt. 2 h | 94 |
| 10 | 4f | COOMe | H | $CHClCH_3$ | 0°C- rt. 5 h | 73 |
| 11 | 4g | $NO_2$ | H | $CHClCH_3$ | 0°C- rt. 7 h | 87 |




**3** **6** 78%

**5** **7** 74%

**8**

**scheme 4**

In this paper, we reported the one-pot synthesis of 2-allyl-1,3-dialkoxycarbonyl-4-imidazoline using allyltributyltin in the presence of chloroformate, and succeeding aromatization to give 2-allylimidazoles, which are rarely synthesized. Introduction of other substituents using tin reagents, and the application of the products are now in progress.

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