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A New Entry to the Ethynylation of Azaaromatics Using Bis(tributylstannyl)acetylene in the Presence of Alkyl chloroformate

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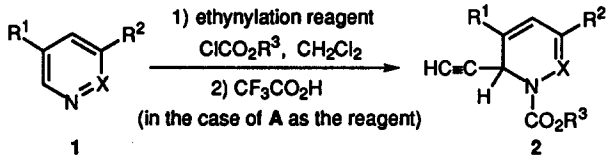
Abstract: Unstable *N*-alkoxycarbonyl quaternary salts of azaaromatics were trapped *in situ* by bis(tributylstannyl)acetylene followed by the treatment with trifluoroacetic acid to give 2-ethynyl adducts in good yields. The same compounds were obtained only in low yields when ethynyltributyltin was used as a nucleophile. The reaction was revealed to be available for various aromatics including pyridine, pyridazine, imidazole, thiazole, oxazole, and benzodiazines.

Recently we have been investigating the application of *N*-alkoxycarbonyl quaternary salts of azaaromatics for the introduction of nucleophiles.[2] Although they are unstable and unisolable except the salts of pyridines, the *in situ* trapping of them was successful when the reagent used was unreactive to alkoxycarbonyl groups. Using the methods, the introduction of allyl group with allyltributyltin[3] was performed for various kind of azaaromatics.[4] The results prompted us to search for the other nucleophiles which are suitable for this system.

Ethynylation of azaaromatics has been one of the most important methods for substituents introduction.[5] It was reported that the reaction of pyridines with alkynyl Grignard reagents in the presence of an alkyl chloroformate afforded alkynyl adducts in good yields, including ethynyl derivative.[6] In this reaction, rapid formation of *N*-alkoxycarbonyl pyridinium salts was crucial for the product formation in order to prevent the side reaction, in which the Grignard reagents underwent the nucleophilic attack to carbonyl group of alkyl chloroformate. Therefore, this reaction system cannot be applied to other azaaromatics because of the instability or the low concentration of their alkoxycarbonyl quaternary salts in solution.

At first, we tried the ethynylation using ethynyltributyltin, expecting that the reaction would progress in the same manner as in the cases of allyltributyltin[2,4] and alkynyltin.[7] However, the yields were very low because of the insufficient nucleophilicity of the reagent. Hence the other reagents were investigated and bis(tributylstannyl)acetylene was revealed to afford good results, which are described in this paper.[8]

When pyridine **1a** was allowed to react with ethynyltributyltin (reagent **B**) in the presence of 1-chloroethyl chloroformate, 2-ethynyl adduct was obtained in only 11% yield (Table 1, entry 3). Replacement of **B** with bis(tributylstannyl)acetylene (reagent **A**) and succeeding treatment with trifluoroacetic acid (TFA) afforded ethynyl adduct **2** in 62% yield, although it was necessary to use 1-chloroethyl chloroformate (Table 1, entries 1 and 2).



1 2

Scheme 1

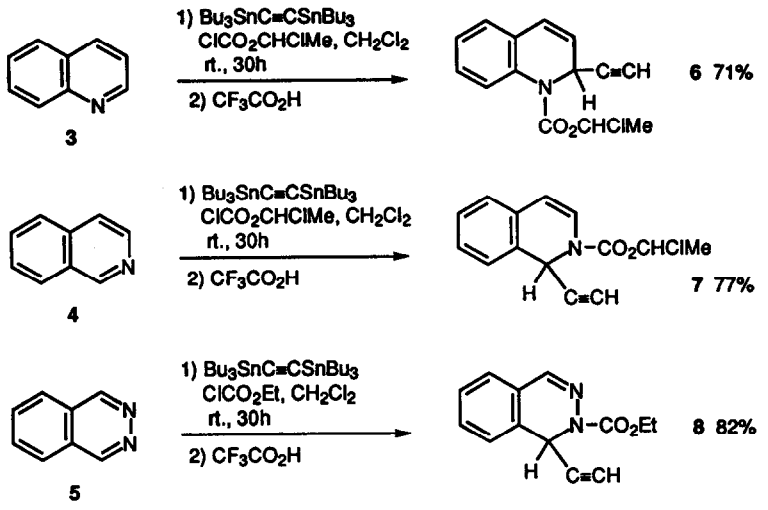
Table 1. The Reaction of Pyridines and Pyridazine with Ethynyltin **A** or **B** in the Presence of Alkyl Chloroformate

Entry	X	R^1	R^2	R^3	Reagent [a]	Conditions	Products	Yield (%)
1	CH	H	H	CHClMe	A	rt. 30h	2a	62
2	CH	H	H	Et	A	rt. 24h	2b	0
3	CH	H	H	CHClMe	B	rt. 30h	2a	11
4	CH	CO_2Me	CO_2Me	Et	A	rt. 3 days	2c	72
5	CH	CO_2Me	CO_2Me	Et	B	rt. 3 days	2c	3
6	CH	CO_2Et	H	CHClMe	A	rt. 24h	2d	84[b]
7	CH	CO_2Et	H	Et	A	rt. 2 days	2e	65[c]
8	CH	Cl	H	Et	A	rt. 3 days	2f	67[d]
9	N	H	H	Et	A	rt. 2 days	2g	71
10	N	H	H	Et	B	rt. 2 days	2g	6

a) Reagent A: Bis(tributylstannyl)acetylene. Reagent B: Ethynyltributyltin
b) The corresponding 1,6-isomer 2d' was obtained in 12% yield.
c) The 1,6-adduct 2e' was obtained in 10% yield.
d) The 1,6-adduct 2f' was obtained in 7% yield.

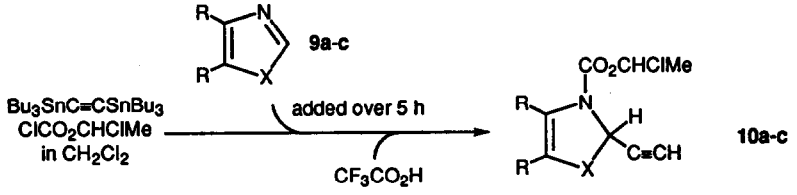
The presence of electron-withdrawing substituents increased the reaction yields even when ethyl chloroformate was used as an activator, although the use of **B** resulted in low yield (entries 4 and 5). 3-Monosubstituted pyridines afforded 2-ethynyl adducts dominantly accompanied by small amount of 6-isomers (entries 6,7, and 8). Yamaguchi et al. reported the reaction of alkynyltin with 3-acylpyridines to form 2-alkynyl adducts dominantly.[7] They suggested the C-2 selectivity to be rationalized by the coordination of tin[9] to acyl groups. Our results showed that 3-chloro substituent also directed C-2 selectivity,[10] hence there might also be the coordination between halo group and tin reagent. Pyridazine gave 6-ethynyl-1,6-dihydro adduct in the same manner (entries 9 and 10), and 4-ethynyl isomer was not obtained.

The reaction was applied to benzo-fused azines **3** - **5** to give the 1,2-dihydro adducts in good yields (Scheme 2). In the cases of quinoline **3** and isoquinoline **4**, more than half amount of the starting material was recovered by the use of ethyl chloroformate even after 3 days' reaction. When quinazoline or quinoxaline was adopted as a substrate, complicated mixture of products was obtained probably because the second quaternization and addition were proceeded.



Scheme 2

Next, heteroazoles **9** were adopted as substrates. In these cases, the consumption of starting material was slower than those of azines. It was reported[11] that imidazoles were dimerized in the presence of alkyl chloroformate to give the compounds such as **11a**, and the existence of these side-products was confirmed in our reaction system. In order to prevent this side reaction, substrate **9a** was slowly added at constant rate to the solution of reagent A and alkyl chloroformate over 5 h, and ethynyl adduct **10a** was obtained in good yield (Scheme 3 and Table 2).



Scheme 3

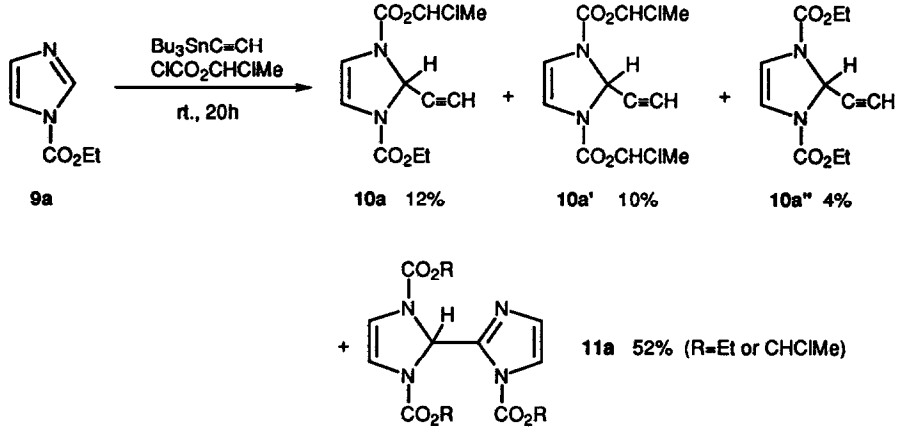
The same reaction conditions was applied to thiazole **9b** and oxazole **9c** to afford **10b** and **10c**, respectively (Table 2,entries 2 and 3). In the cases of benzo-fused azoles **9d-9f**, dimerization process was slower than the reaction with the tin reagent, therefore the ethynyl adducts **10d-10f** were obtained under the same conditions as those of azines (Table 2, entries 4,5, and 6).

The reaction of 1-ethoxycarbonylimidazole with reagent **B** gave a mixture of the products shown in Scheme 4. The formation of **11a** suggested that the attack of ethynyltin to the quaternary salt was slower than dimeric process. Moreover, formations of the formate-exchanged products **10a'**, **10a''**, and **11a** suggested that there was an equilibrium between **9a** and corresponding *N*-alkoxycarbonyl quaternary salt, and that a chloroformate was exchanged to other one when consumption of the quaternary salt was slow.

Table 2. The Reaction of Heteroazoles with Bis(tributylstannyl)acetylene in the presence of 1-Chloroethyl Chloroformate

Entry	Substrate	X	R	Conditions	Products	Yield (%)
1	9a	N-CO_2Et	H	rt., 5 h[a)]	10a	79
2	9b	S	H	rt., 5 h[a)]	10b	51
3	9c	O	H	rt., 5 h[a)]	10c	45
4	9d	N-CO_2Et	-CH=CH-	0°C, 1 h[b)]	10d	83
5	9e	S	-CH=CH-	rt., 16 h[b)]	10e	75
6	9f	O	-CH=CH-	rt., 20 h[b)]	10f	84

a) The substrate was added over 5 h to the mixture of reagent **A** and 1-chloroethyl chloroformate.
b) The substrate was added at one time, and the mixture was reacted for 1 to 20 h.



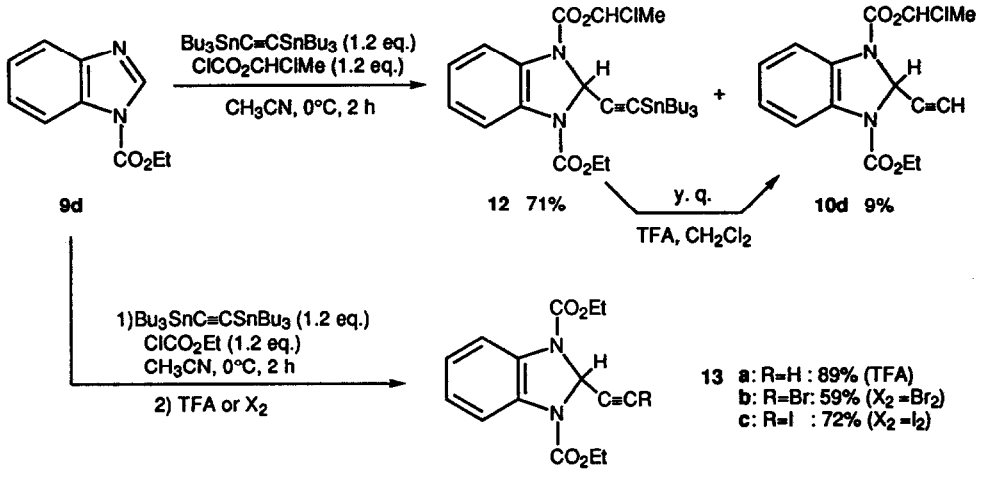
Scheme 4

The reacions mentioned above must involve tributylstannylethynyl adducts as intermediates. In fact, the existence of an another product was indicated on TLC plate, but the spot changed to the one of ethynyl adduct in the work-up procedure. A stable tributylstannylethynyl adduct **12** was obtained as shown in Scheme 5 in the absence of TFA when 1-ethoxycarbonylbenzimidazole was used as a substrate. The result prompted us to the chemical modification of mono-stannyl adducts using reagents other than TFA. Instead of adding TFA, slightly excess amount of bromine or iodine was added to form bromoethynyl- or iodoethynyl adduct **13** in 59% or 72% yield, respectively.

There is other possiblity that a mono-stannyl adduct attacks the second quaternary salt to form a dimeric compound, bis(azacyclic)acetylene. However, there was no such a product in this reaction system except in the case of thiazole **9b**, which afforded a corresponding dimer **14** in 17% yield other than **10b**.

In this paper, we described the ethynylation of *N*-alkoxycarbonyl quaternary azaaromatics with bis(tributylstannyl)acetylene **A**. This is the first reaction that reagent **A** was used for ionic nucleophile, rather

than electron-rich dienophile. It was revealed that A was more reactive than ethynyltributyltin B, and that the treatment of dihydro-adducts with TFA readily removed a remaining stannyl group to give ethynyl adducts. The reaction system was generally available for azaaromatic *N*-alkoxycarbonyl quaternary salts, and might be useful for the selective ethynylation of the substrates which have multi-reactive sites.



Scheme 5

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.

Experimental

All melting points were taken on a Büchi 535 micro melting point apparatus and are uncorrected. The mass spectra were recorded on JEOL JMS-D300 and JMS-SX102A instruments. The nuclear magnetic resonance spectra (NMR) were measured with JEOL JNM-FX100 and GX400 spectrometers using tetramethylsilane as an internal standard. The abbreviations used are as follows: s, singlet; d, doublet; dd, double doublet; dt, double triplet; t, triplet; q, quartet; m, multiplet. A most of new products were obtained as mixtures of conformational and/or diastereomeric isomers except in the cases of **2c**, **2g**, and **8**. When ethyl chloroformate was used, NMR spectra were measured at 80°C in dimethyl sulfoxide-d_6 (DMSO-d_6) to

simplify the signals derived from the conformational isomerism except for **2c**, **2g**, and **8**. However, the products which have 1-chloroethoxycarbonyl group was decomposed on heating, therefore the NMR spectra were recorded at 25°C in $CDCl_3$ except **2d'**. It should be noted that the ^1H signals of ethynyl-H were shifted drastically to low field when DMSO-d6 was used as solvent.

The Reactions of Azines 1 with Bis(tributylstannyl)acetylene in the Presence of Alkyl Chloroformate: General Procedure An azine **1** (1 mmol) and bis(tributylstannyl)acetylene (1.2 mmol) were dissolved in CH_2Cl_2 (3 ml), and the mixture was cooled to 0°C. Alkyl chloroformate (1.2 mmol) was added dropwise and the mixture was allowed to stand at room temperature for 24h to 3 days. Thereafter, 2 mmol of TFA was added and the mixture was allowed to stir for another 30 min. Then the mixture was diluted with diethyl ether (15 ml) and treated with 1 M aq.KF solution (3 ml) to make tributyltin fluoride precipitate. The solid was filtered, and the filtrate was dried over $MgSO_4$ and evaporated off to leave a residue, which was chromatographed on silica gel to give the product.

1-(1-Chloroethoxycarbonyl)-2-ethynyl-1,2-dihydropyridine (2a) Colorless oil. ^1H-NMR ($CDCl_3$) δ: 1.87 (3H, d, *J*=5.4 Hz), 2.38 (1H, d, *J*=2.0 Hz), 5.16-5.73 (3H, m), 5.95-6.08 (1H, m), 6.55-6.80 (2H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.09, 25.76, 25.35 (CH_3), 43.42, 43.49, 43.71 (CH), 71.58, 71.85, 71.95 (CH), 80.30, 80.49, 80.67 (C), 83.17, 83.27 (CH), 106.45, 106.62 (CH), 118.47, 118.93 (CH), 122.20, 122.57 (CH), 123.57, 123.83, 124.60 (CH), 150.49 (CO). HRMS *m/z* (M^+); Calcd for $C_{10}H_{10}{}^{35}ClNO_2$: 211.0400. Found: 211.0415.

1-Ethoxycarbonyl-2-ethynyl-3,5-di(methoxycarbonyl)-1,2-dihydropyridine (2c) Pale yellow needles from ethyl acetate; mp 135.5-136°C. *Anal.* Calcd for $C_{14}H_{15}NO_6$: C, 57.34; H, 5.16; N, 4.78. Found: C, 57.43; H, 5.13; N, 4.67. ^1H-NMR ($CDCl_3$) δ: 1.40 (3H, t, *J*=6.8 Hz), 2.35 (1H, d, *J*=2.4 Hz), 3.83 (3H, s), 3.84 (3H, s), 4.41 (2H, q, *J*=6.8 Hz), 6.07 (1H, bs), 7.60 (1H, s), 8.14 (1H, bs). ^{13}C-NMR ($CDCl_3$) δ: 14.34 (CH_3), 43.29 (CH), 51.94 (CH_3), 52.21 (CH_3), 64.48 (CH_2), 72.37 (CH), 79.99 (C), 108.54 (C), 118.23 (C), 130.70 (CH), 138.68 (CH), 152.06 (CO), 164.46 (CO), 164.87 (CO).

1-(1-Chloroethoxycarbonyl)-3-ethoxycarbonyl-2-ethynyl-1,2-dihydropyridine (2d) Colorless oil. ^1H-NMR ($CDCl_3$) δ: 1.33 (3H, t, *J*=7.3 Hz), 1.84-1.94 (3H, m), 2.32 (1H, bs), 4.28 (2H, q, *J*=7.3 Hz), 5.58-5.67 (1H, m), 5.98-6.14 (1H, m), 6.61-6.67 (1H, m), 6.97-7.11 (2H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 14.27, 14.32 (CH_3), 25.18, 25.31 (CH_3), 42.68, 42.92 (CH), 61.10 (CH_2), 71.52, 71.74, 71.82 (CH), 79.70, 79.85, 79.97 (C), 83.38, 83.50 (CH), 105.92 (CH), 119.97, 120.37, 120.87 (C), 128.66, 128.95, 129.96 (CH), 131.36, 131.86 (CH), 150.00, 150.80 (CO), 163.93, 163.97, 164.15 (CO). HRMS *m/z* (M^+); Calcd for $C_{13}H_{14}{}^{35}ClNO_4$: 283.0611. Found: 283.0594. The 1,6-adduct **2d'** was obtained as a minor compound. It was impossible to purify it thoroughly from the 1,2-adduct, and the NMR spectra were measured as those of a mixture of both adducts. ^1H-NMR (DMSO-d_6, 60°C) δ: 1.26 (3H, t, *J*=6.8 Hz), 1.84 (3H, t, *J*=6.4 Hz), 3.41 (1H, bs), 4.22 (2H, q, *J*=6.8 Hz), 5.64 (1H, d, *J*=4.9 Hz), 5.78 (1H, dd, *J*=9.8 Hz, 4.9 Hz), 6.38 (1H, d, *J*=9.8 Hz), 6.67 (1H, q, *J*=6.4 Hz), 7.63 (1H, bs). ^{13}C-NMR spectrum was obtained as that of a

mixture of at least two isomers. ^{13}C-NMR (DMSO-d_6, 60°C) δ: 14.03 (CH_3), 25.02, 25.06 (CH_3), 43.84, 43.89 (CH), 60.31 (CH_2), 75.29, 75.37 (CH), 80.38 (C), 84.66 (CH), 110.04 (C), 119.31, 119.35 (CH), 119.57 (CH), 131.86, 132.00 (CH), 149.76 (CO), 163.99 (CO).

1,3-Di(ethoxycarbonyl)-2-ethynyl-1,2-dihydropyridine (2e) Colorless oil. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.25 (3H, t, *J*=6.8 Hz), 1.28 (3H, t, *J*=6.8 Hz), 3.14 (1H, d, *J*=2.0 Hz), 4.21 (2H, q, *J*=6.8 Hz), 4.27 (2H, q, *J*=6.8 Hz), 5.62-5.65 (1H, m), 5.89-5.90 (1H, m), 7.06 (1H, d, *J*=5.9 Hz), 7.09 (1H, d, *J*=7.3 Hz). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.06 (CH_3), 14.10 (CH_3), 42.19 (CH), 60.48 (CH_2), 63.11 (CH_2), 73.61 (CH), 80.69 (C), 104.81 (CH), 118.82 (C), 130.41 (CH), 131.84 (CH), 152.19 (CO), 163.66 (CO). HRMS *m/z* (M^+); Calcd for $C_{13}H_{15}NO_4$: 249.1001. Found: 249.0980. The 1,6 adduct **2e'** was obtained as a minor compound. It was impossible to purify it thoroughly from the 1,2-adduct, and the NMR spectra were measured as those of a mixture of both adducts. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.25 (3H, t, *J*=6.8 Hz), 1.28 (3H, t, *J*=6.8 Hz), 3.26 (1H, d, *J*=2.0 Hz), 4.21 (2H, q, *J*=6.8 Hz), 4.27 (2H, q, *J*=6.8 Hz), 5.58-5.61 (1H, m), 5.70 (1H, dd, *J*=9.3 Hz, 6.4 Hz), 6.36 (1H, d, *J*=9.3 Hz), 7.70 (1H, s). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.06 (CH_3), 14.10 (CH_3), 43.76 (CH), 60.06 (CH_2), 63.57 (CH_2), 74.69 (CH), 81.13 (C), 108.56 (C), 118.51 (CH), 119.84 (CH), 133.27 (CH), 152.19 (CO), 164.30 (CO).

3-Chloro-1-ethoxycarbonyl-2-ethynyl-1,2-dihydropyridine (2f) Colorless oil. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.27 (3H, t, *J*=6.8 Hz), 3.32 (1H, d, *J*=2.0 Hz), 4.24 (2H, q, *J*=6.8 Hz), 5.41 (1H, dd, *J*=7.3 Hz, 6.4 Hz), 5.49 (1H, d, *J*=2.0 Hz), 6.24 (1H, d, *J*=6.4 Hz), 6.75 (1H, d, *J*=7.3 Hz). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.12 (CH_3), 48.85 (CH), 62.87 (CH_2), 74.98 (CH), 78.99 (C), 104.41 (CH), 120.79 (C), 121.07 (CH), 123.59 (CH), 152.17 (CO). HRMS *m/z* (M^+); Calcd for $C_{10}H_{10}{}^{35}ClNO_2$: 211.0400. Found: 211.0394. The 1,6 adduct **2f'** was obtained as a minor compound. It was impossible to purify it thoroughly from the 1,2-adduct, and the NMR spectra were measured as those of a mixture of both adducts. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.26 (3H, t, *J*=6.8 Hz), 3.24 (1H, d, *J*=2.4 Hz), 4.24 (2H, q, *J*=6.8 Hz), 5.54-5.56 (1H, m), 5.80 (1H, dd, *J*=9.3 Hz, 6.4 Hz), 6.03 (1H, dt, *J*=9.3 Hz, 1.5 Hz), 6.86 (1H, d, *J*=1.5 Hz). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.12 (CH_3), 42.57 (CH), 62.87 (CH_2), 74.47 (CH), 80.60 (C), 81.90 (C), 121.21 (CH), 121.93 (CH), 124.10 (CH), 151.97 (CO).

1-Ethoxycarbonyl-6-ethynyl-1,6-dihydropyridazine (2g) Colorless needles from isopropyl ether; mp 75-75.5°C. *Anal.* Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.73; H, 5.67; N, 15.62. ^{1}H-NMR ($CDCl_3$) δ: 1.39 (3H, t, *J*=7.3 Hz), 2.41 (1H, d, *J*=2.4 Hz), 4.38 (2H, q, *J*=7.3 Hz), 5.68-5.69 (1H, m), 5.97-6.00 (1H, m), 6.19-6.23 (1H, m), 7.21-7.23 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.56 (CH_3), 41.35 (CH), 63.35 (CH_2), 73.17 (CH), 79.57 (C), 117.48 (CH), 127.69 (CH), 139.81 (CH), 154.11 (CO).

1-(1-Chloroethoxycarbonyl)-2-ethynyl-1,2,-dihydroquinoline (6) Colorless needles from isopropyl ether; mp 82-83°C. *Anal.* Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.11; H, 4.57; N, 5.35. ^{1}H-NMR ($CDCl_3$) δ: 1.82-1.89 (3H, m), 2.24 (1H, d, *J*=2.4 Hz), 5.83-5.87 (1H, m), 6.06 (1H, dd, *J*=9.3 Hz, 6.4 Hz), 6.57 (1H, d, *J*=9.3 Hz), 6.66-6.72 (1H, m), 7.13-7.18 (2H, m), 7.27-7.32 (1H, m), 7.64 (1H, bs). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers.

^{13}C-NMR ($CDCl_3$) δ: 25.22, 25.38 (CH_3), 44.00, 44.07 (CH), 72.16 (CH), 79.55 (C), 83.32, 83.54 (CH), 124.25, 124.38 (CH), 124.56, 124.69, 124.98 (CH), 125.33 (CH), 126.22, 126.30 (CH), 126.52 (C), 126.74, 126.83 (CH), 128.11, 128.16 (CH), 133.17 (C), 151.00 (CO).

2-(1-Chloroethoxycarbonyl)-1-ethynyl-1,2,-dihydroisoquinoline (7) Colorless needles from isopropyl ether; mp 83-84°C. *Anal.* Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.07; H, 4.57; N, 5.36. ^{1}H-NMR ($CDCl_3$) δ: 1.84-1.96 (3H, m), 2.36 (1H, d, *J*=2.0 Hz), 5.99-6.21 (2H, m), 6.67 (1H, q, *J*=5.4 Hz), 6.80-6.90 (1H, m), 7.12 (1H, d, *J*=7.3 Hz), 7.21-7.30 (3H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.35, 25.38 (CH_3), 46.65, 46.98 (CH), 72.20, 72.33, 72.44 (CH), 80.87, 81.05 (C), 83.23, 83.34 (CH), 109.93, 109.98, 110.04 (CH), 122.91, 123.23 (CH), 123.96, 124.10 (C), 125.47, 125.57 (CH), 126.11 (CH), 127.72, 127.94 (CH), 128.78, 128.84 (CH), 129.17, 129.24, 129.41 (C), 150.07, 150.42 (CO).

1-Ethoxycarbonyl-2-ethynyl-1,2-dihydrophthalazine (8) Colorless granules from isopropyl ether; mp 97.5-98°C. *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.39; H, 5.25; N, 12.37. ^{1}H-NMR ($CDCl_3$) δ: 1.41 (3H, t, *J*=7.3 Hz), 2.38 (1H, d, *J*=2.4 Hz), 4.42 (2H, q, *J*=7.3 Hz), 6.25 (1H, d, *J*=2.4 Hz), 7.29-7.52 (4H, m), 7.78 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.57 (CH_3), 44.25 (CH), 63.38 (CH_2), 73.43 (CH), 80.28 (C), 123.17 (C), 125.91 (CH), 126.24 (CH), 129.15 (CH), 130.44 (C), 132.10 (CH), 142.53 (CH), 154.05 (CO).

The Reaction of Monocyclic Azoles with Bis(tributylstannyl)acetylene: A Typical Procedure To the CH_2Cl_2 solution (5 ml) of bis(tributylstannyl)acetylene (1.2 mmol) and 1-chloroethyl chloroformate (1.2 mmol), CH_2Cl_2 solution (5 ml) of azole (1.0 mmol) was added at constant rate over 5 h using a motor drive syringe under stirring at room temperature. Then 2 mmol of TFA was added and the same work-up was performed as that of azines to give 2-ethynyl adducts. In the cases of benzo-fused azoles, the procedure was as same as that of azines.

1-(1-Chloroethoxycarbonyl)-3-ethoxycarbonyl-2-ethynyl-4,5-imidazoline (10a) Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, t, *J*=7.0 Hz), 1.85 (3H, d, *J*=5.7 Hz), 2.50-2.58 (1H, m), 4.26 (2H, q, *J*=7.0 Hz), 6.21-6.38 (3H, m), 6.60 (1H, q, *J*=5.7 Hz). ^{13}C-NMR spectrum was obtained as that of a mixture of at least four isomers. ^{13}C-NMR ($CDCl_3$) δ: 14.21, 14.50 (CH3), 25.15, 25.33, 25.40 (CH3), 62.60, 62.66 (CH2), 62.82, 63.15, 63.51 (CH), 73.28, 73.34, 73.52, 73.77 (CH), 76.90 (C), 82.92, 83.03 (CH), 110.77, 110.83, 111.43, 111.56 (CH), 112.97, 113.22, 113.61, 113.75 (CH), 147.26 (CO), 150.00, 150.05 (CO). HRMS *m/z* (M^+); Calcd for $C_{11}H_{13}{}^{35}ClN_2O_4$: 272.0564. Found: 272.0562.

3-(1-Chloroethoxycarbonyl)-2-ethynyl-4,5-thiazoline (10b) Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.86 (3H, d, *J*=5.7 Hz), 2.72 (1H, d, *J*=2.2 Hz), 5.67-5.76 (1H, m), 6.04-6.21 (1H, m), 6.37-6.45 (1H, m), 6.60 (1H, q, *J*=5.7 Hz). ^{13}C-NMR spectrum was obtained as that of a mixture of at least four isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.18, 25.35, 25.40 (CH_3), 51.88, 52.91, 52.98 (CH), 74.34, 74.74, 74.85 (CH), 79.96, 80.05, 80.36 (C), 83.01, 83.16 (CH), 104.61, 104.96, 104.99 (CH), 119.29, 119.46, 120.59,

120.72 (CH), 149.30, 149.45 (CO). HRMS *m/z* (M^+); Calcd for $C_8H_8{}^{35}ClNO_2S$: 216.9964. Found: 216.9977.

3-(1-Chloroethoxycarbonyl)-2-ethynyl-4,5-oxazoline (10c) Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.84 (3H, d, *J*=5.9 Hz), 2.66 (1H, d, *J*=1.5 Hz), 6.24-6.42 (3H, m), 6.59 (1H, q, *J*=5.9 Hz). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.16, 25.35 (CH3), 74.49, 74.93, 75.05 (CH), 77.25, 77.67 (C), 79.75, 80.38 (CH), 82.83 (CH), 107.33, 107.77 (CH), 133.01, 133.32 (CH), 147.35, 147.49 (CO). HRMS *m/z* (M^+); Calcd for $C_8H_8{}^{35}ClNO_3$: 201.0192. Found: 201.0187.

1-(1-Chloroethoxycarbonyl)-3-ethoxycarbonyl-2-ethynylbenzimidazoline (10d) Colorless needles from hexane-isopropyl ether; mp. 96-97°C. *Anal.* Calcd for $C_{15}H_{15}ClN_2O_4$: C, 55.82; H, 4.68; N, 8.68. Found: C, 55.54; H, 4.68; N, 8.55. ^{1}H-NMR ($CDCl_3$) δ: 1.41 (3H, t, *J*=6.8 Hz), 1.93 (3H, d, *J*=5.9 Hz), 2.49-2.55 (1H, m), 4.39 (2H, q, *J*=6.8 Hz), 6.50-6.72 (2H, m), 7.02-7.11 (2H, m), 7.41-7.78 (2H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 14.52 (CH_3), 25.16, 25.35 (CH_3), 62.64, 63.15 (CH_2), 64.98, 65.33, 65.47 (CH), 73.12, 73.21, 73.61 (CH), 77.71, 77.94 (C), 82.77, 82.88, 83.21 (CH), 114.41, 114.63, 114.90 (2CH), 123.63, 123.87, 124.58 (2CH), 129.19, 130.28, 130.81, 131.24, 131.77 (2C), 147.60, 148.81 (CO), 150.31, 151.37 (CO).

3-(1-Chloroethoxycarbonyl)-2-ethynylbenzothiazoline (10e) Colorless needles from isopropyl ether; mp 111-112°C. *Anal.* Calcd for $C_{12}H_{10}ClNO_2S$: C, 53.83; H, 3.76; N, 5.23. Found: C, 53.75; H, 3.65; N, 5.12. ^{1}H-NMR ($CDCl_3$) δ: 1.90-1.94 (3H, m), 2.61-2.64 (1H, m), 6.34 (1H, bs), 6.69 (1H, q, *J*=5.9 Hz), 7.05-7.09 (1H, m), 7.14-7.18 (1H, m), 7.20 (1H, d, *J*=7.3 Hz), 7.50-7.88 (1H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.31 (CH_3), 53.60, 53.79, 54.02 (CH), 73.96, 74.16 (CH), 80.32, 80.49 (C), 83.05 (CH), 117.61, 117.81 (CH), 122.57, 122.66 (CH), 125.18 (CH), 125.95 (CH), 127.18 (C), 136.06, 136.17 (C), 149.10 (CO).

3-(1-Chloroethoxycarbonyl)-2-ethynylbenzoxazoline (10f) Colorless needles from isopropyl ether; mp 104-105°C. *Anal.* Calcd for $C_{12}H_{10}ClNO_3$: C, 57.27; H, 4.01; N, 5.57. Found: C, 57.21; H, 3.90; N, 5.49. ^{1}H-NMR ($CDCl_3$) δ: 1.89-1.98 (3H, m), 2.66-2.70 (1H, m), 6.59-6.68 (2H, m), 6.87-7.03 (3H, m), 7.28-7.63 (1H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.13, 25.31, 25.48 (CH_3), 75.04, 75.31, 75.44 (C), 77.25, 77.51 (CH), 81.69, 82.26 (CH), 82.72, 82.81, 83.05 (CH), 109.45, 110.00 (CH), 114.41, 114.48, 114.85 (CH), 122.13, 122.26 (CH), 124.58, 124.69 (CH), 126.30, 127.58 (C), 147.38, 148.40 (C), 149.49, 149.80 (CO).

The Reaction of 1-Ethoxycarbonylimidazole (9a) with Ethynyltributyltin in the Presence of 1-Chloroethyl Chloroformate To the CH_2Cl_2 solution (5 ml) of ethynyltributyltin(1.2 mmol) and 1-chloroethyl chloroformate (1.2 mmol), CH_2Cl_2 solution (5 ml) of 1-ethoxycarbonylimidazole (1.0 mmol) was added at constant rate over 5 h using a motor drive syringe under stirring at room temperature. The mixture was allowed to stir for anther 15 h at room temperature, then 2 mmol of TFA was added and the same work-up was performed as that of azines to give a mixture of **10a**, **10a'**, **10a''**, and **11a**.

1,3-Bi(1-Chloroethoxycarbonyl)-2-ethynyl-4,5-imidazoline (10a') Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.86 (6H, d, *J*=5.7 Hz), 2.57-2.61 (1H, m), 6.25-6.45 (3H, m), 6.60 (2H, q, *J*=5.7 Hz). ^{13}C-NMR spectrum was obtained as that of a mixture of at least four isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.13, 25.31, 25.40 ($2CH_3$), 62.80, 63.26, 63.59 (CH), 73.88, 74.05, 74.36, 74.52 (CH), 77.27 (C), 82.97, 83.01, 83.10 (2CH), 111.97, 112.23, 112.73, 112.87 (2CH), 147.13, 147.24 (2CO). HRMS *m/z* (M^+); Calcd for $C_{11}H_{12}{}^{35}Cl_2N_2O_4$: 306.0174. Found: 306.0167.

1,3-Di(ethoxycarbonyl)-2-ethynyl-4,5-imidazoline (10a'') Colorless needles from isopropyl ether; mp 72-72.5°C. *Anal.* Calcd for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.76. Found: C, 55.21; H, 5.89; N, 11.63. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.24 (6H, t, *J*=6.8 Hz), 3.45 (1H, d, *J*=1.5 Hz), 4.17 (4H, q, *J*=6.8 Hz), 6.25 (1H, d, *J*=1.5 Hz), 6.31 (2H, s). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.25 ($2CH_3$), 61.89 ($2CH_2$), 63.06 (CH), 75.18 (CH), 78.47 (C), 112.22 (2CH), 149.71 (2CO).

Compounds **11a** were obtained as a mixture of formate-exchanged products. They exhibited only one spot on TLC, whose Rf value was exactly as same as that of triethyl-[2,2'-bi-1H-imidazole]-1,1',3(2H)-tricarboxylate,[11] although the NMR spectra showed those of the complicated mixture. The yield was estimated by supposing that the whole weight was derived from 1-(1-chloroethyl)-1',3-diethyl-[2,2'-bi-1H-imidazole]-1,1',3(2H)-tricarboxylate.

The Reaction of 1-Ethoxycarbonylbenzimidazole (9d) with Bis(tributylstannyl)acetylene in the Presence of 1-Chloroethyl Chloroformate in acetonitrile To the CH_3CN solution (3 ml) of 1-ethoxycarbonylbenzimidazole (1.0 mmol) and bis(tributylstannyl)acetylene (1.2 mmol), 1-chloroethyl chloroformate (1.2 mmol) in 1 ml of CH_3CN was added at 0°C, and the mixture was allowed to stir for 2 h. Thereafter, the mixture was treated with diethyl ether (20 ml) and 1M aq.KF (3 ml) for 1 h to form the precipitate, which was removed by filtration. The filtrate was dried over $MgSO_4$ and evaporated off to leave a residue, which was chromatographed on silica gel to give the products.

1-(1-Chloroethoxycarbonyl)-3-ethoxycarbonyl-2-(tributylstannylethynyl)benzimidazoline (12) Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (9H, t, *J*=7.3 Hz), 0.97 (6H, q, *J*=7.8 Hz), 1.24-1.33 (6H, m), 1.40 (3H, t, *J*=6.8 Hz), 1.46-1.53 (6H, m), 1.91 (3H, d, *J*=5.9 Hz), 4.36 (2H, q, *J*=6.8 Hz), 6.43-6.71 (2H, m), 7.01-7.06 (2H, m), 7.37-7.78 (2H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least three isomers. ^{13}C-NMR ($CDCl_3$) δ: 11.08 ($3CH_2$), 13.59 ($3CH_3$), 14.61 (CH_3), 25.24, 25.42 (CH_3), 26.87 ($3CH_2$), 28.75 ($3CH_2$), 62.31, 62.80 (CH_2), 65.43, 65.87 (CH), 82.66, 82.79, 82.88 (CH), 89.68 (C), 103.13 (C), 114.37, 114.56, 114.83 (2CH), 123.32, 123.57, 124.36 (2CH), 129.60, 130.47, 130.58, 131.58, 132.05 (2C), 147.82 (CO), 150.57, 151.40 (CO). HRMS *m/z* (M^+); Calcd for $C_{27}H_{41}{}^{35}ClN_2O_4{}^{120}Sn$: 612.1777. Found: 612.1756.

The Conversion of Compound 12 to 10d Compound **12** (0.20 mmol) in CH_2Cl_2 (1 ml) was allowed to react with TFA (0.26 mmol) for 30 min at room temperature. The same work up procedure as that of azines gave **10d** in a quantative yield.

The Synthesis of 13 with 9d and Bis(tributylstannyl)acetylene To the CH_3CN solution (3 ml) of **9d** (1 mmol) and bis(tributylstannyl)acetylene (1.2 mmol), ethyl chloroformate (1.2 mmol) in CH_3CN (1 ml) was added dropwise at 0°C, and the mixture was allowed to stir for 1 h at 0°C, then for another 3.5 h at room temperature. a) In the case of the synthesis of **13a**, 2 mmol of TFA was added at this point, and the mixture was allowed to react at room temperature for 30 min. The work up procedure thereafter was as same as that of azines. b) In the cases of **13b** or **13c**, Br_2 (1.2 mmol) or I_2 (1.4 mmol) was added at this point, and the mixture was reacted for 30 min at room temperature. Then the mixture was cooled to 0°C, and the precipitate thus formed was filtrated, washed with a little amount of CH_3CN, and recrystallized with CH_3CN to give **13b** or **13c**.

1,3-Di(ethoxycarbonyl)-2-ethynylbenzimidazoline (13a) Colorless needles from ethanol; mp 128-128.5°C. *Anal.* Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.43; H, 5.49; N, 9.73. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.32 (6H, t, *J*=7.3 Hz), 3.51 (1H, d, *J*=1.5 Hz), 4.31 (4H, q, *J*=7.3 Hz), 6.53 (1H, d, *J*=1.5 Hz), 7.01-7.05 (2H, m), 7.53-7.56 (2H, m). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.21 ($2CH_3$), 62.31 ($2CH_2$), 65.25 (CH), 75.29 (CH), 78.84 (C), 114.04 (2CH), 123.44 (2CH), 130.91 (2C), 150.31 (2CO).

1,3-Di(ethoxycarbonyl)-2-bromoethynylbenzimidazoline (13b) Colorless needles from acetonitrile; mp 203.5-204°C. *Anal.* Calcd for $C_{15}H_{15}BrN_2O_4$: C, 49.06; H, 4.12; N, 7.63. Found: C, 49.18; H, 4.01; N, 7.53. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.32 (6H, t, *J*=7.3 Hz), 4.23-4.37 (4H, m), 6.58 (1H, s), 7.01-7.06 (2H, m), 7.53-7.55 (2H, m). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 14.21 ($2CH_3$), 48.23 (CBr), 62.34 ($2CH_2$), 66.13 (CH), 75.55 (C), 114.04 (2CH), 123.50 (2CH), 130.78 (2C), 150.27 (2CO).

1,3-Di(ethoxycarbonyl)-2-iodoethynylbenzimidazoline (13c) Colorless needles from acetonitrile; mp 228-228.5°C. *Anal.* Calcd for $C_{15}H_{15}IN_2O_4$: C, 43.50; H, 3.65; N, 6.76. Found: C, 43.27; H, 3.48; N, 6.66. ^{1}H-NMR (DMSO-d_6, 80°C) δ: 1.31 (6H, t, *J*=7.3 Hz), 4.26-4.36 (4H, m), 6.57 (1H, s), 7.01-7.05 (2H, m), 7.52-7.54 (2H, m). ^{13}C-NMR (DMSO-d_6, 80°C) δ: 13.60 (CI), 14.26 ($2CH_3$), 62.27 ($2CH_2$), 66.45 (CH), 88.49 (C), 114.04 (2CH), 123.46 (2CH), 130.83 (2C), 150.29 (2CO).

Bis-2-[3-(1-chloroethoxycarbonyl)thazolyl]acetylene (14) Colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.82-1.90 (6H, m), 5.67-5.70 (2H, m), 6.17-6.62 (6H, m). ^{13}C-NMR spectrum was obtained as that of a mixture of at least two isomers. ^{13}C-NMR ($CDCl_3$) δ: 25.07, 25.16, 25.22, 25.31 ($2CH_3$), 52.16, 53.11, 53.20, 53.46 (2CH), 82.17, 82.33, 82.61 (2C), 83.14, 83.45 (2CH), 104.46, 105.08, 105.16 (2CH), 119.38, 120.48, 120.59, 121.16 (2CH), 149.18, 149.54 (2CO). HRMS *m/z* (M^+); Calcd for $C_{14}H_{14}{}^{35}Cl_2N_2O_4$: 407.9772. Found: 407.9781.

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