CHEMISTRY LETTERS, pp. 1519-1522, 1987.

Reactions of Allenylic Tin Reagents to N-Alkoxycarbonyl-isoquinolinium and -quinolinium Salts. Effective Introduction of 2-Alkynylic Groups to Isoquinoline and Quinoline Systems

Ryohei YAMAGUCHI,* Masataka MORIYASU, Ichiro TAKASE, Mituyosi KAWANISI, and Sinpei KOZIMA+

Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto 606

+Department of Chemistry, College of Liberal Arts and Science, Kyoto University, Yoshida, Kyoto 606

Reactions of allenylic tin reagents with isoquinoline in the presence of chloroformate esters as acylating agents give 2-alkoxycarbonyl-1-(2-alkynyl)-1,2-dihydroisoquinolines in good to excellent yields. Similarly, the reactions with quinoline give 1-alkoxycarbonyl-2-(2-alkynyl)-1,2-dihydroquinolines exclusively.

Development of methods for effective introduction of a variety of carbon substituents into nitrogen heterocycles has been one of the very important subjects of synthetic organic chemistry. Nucleophilic addition of organometallic reagents to nitrogen heteroaromatics activated by chloroformate esters or acyl halides has proven to be a valuable means and is now studied extensively.[1-5] We have recently reported the highly selective allylation[4] and benzylation[5] of nitrogen heteroaromatics by means of organotin reagents. We wish to report here that 2-alkynylic groups can be effectively introduced to isoquinoline and quinoline by utilizing allenylic tin reagents.

Since allenylic tin reagents do not react with chloroformate esters or nitrogen heteroaromatics, quaternized salts are not necessarily prepared in advance. Thus, chloroformate ester can be conveniently added to a mixture of nitrogen heteroaromatic and allenylic tin reagent. First, we examined reactions

of isoquinoline with allenyltributyltin.[6] When methyl chloroformate was added to a solution of isoquinoline and allenyltributyltin in dry dichloromethane, the reaction proceeded very smoothly to give 1-(2-propynyl)-2-methoxycarbonyl-1,2-dihydroisoquinoline (**2a**) in 94% yield after flash chromatography. Then, reactions of a couple of substituted isoquinolines with a few allenylic tin reagents[7] were studied. The results are summarized in Table 1.

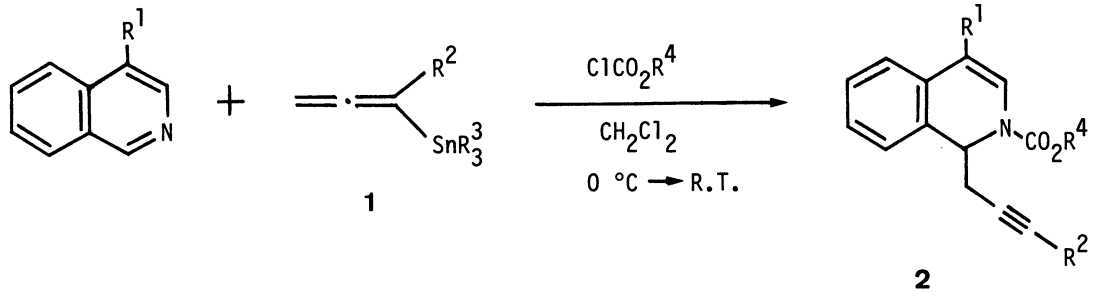


Table 1. Reactions of Allenylic Tin Reagents with Isoquinolines in the Presence of Chloroformate Esters

Entry	Product	R^1	R^2	R^3	R^4	Yield/%[a]
a	**2a**	H	H	n-Bu	Me	94
b	**2b**	Br	H	n-Bu	Me	82
c	**2c**	CHO	H	n-Bu	Me	81
d	**2d**	H	n-Bu	Ph	CH_2CCl_3	73
e	**2e**	H	Et	Ph	CH_2CCl_3	84
f	**2f**	H	i-Pr	Ph	CH_2CCl_3	95
g	**2g**	Br	Et	Ph	CH_2CCl_3	77
h	**2h**	Br	i-Pr	Ph	CH_2CCl_3	75

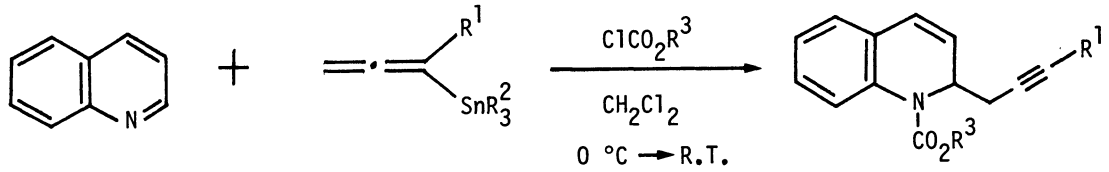
a) Isolated yield.

As shown in Table 1, the products were obtained in good to excellent yields. The fact that bromo and formyl groups are intact (entries b and c) demonstrates the high chemoselectivity of the reaction. It should be noted that 2,2,2-trichloroethyl chloroformate is preferred as the acylating agent in the cases of 1-

alkylallenyltin reagents (entries d-h), because these tin reagents are less reactive.

Typical experimental procedures are as follows: To a solution of isoquinoline (268 mg, 2.1 mmol) and allenyltributyltin (661 mg, 2.0 mmol) in dry dichloromethane (8 mL) was added methyl chloroformate (0.20 mL, 2.6 mmol) dropwise under ice-cooling. After 2 h, an ice-bath was removed and the reaction mixture was allowed to stand at room temperature for 3 h. After the solvent was evaporated, the residue was rapidly chromatographed on silica gel to give **2a** (428 mg, 94%)[8]: MS m/e (relative intensity) 227 (M^+, 6), 188 (100); IR (neat) 3300, 1720 cm^{-1}; ^{1}H-NMR δ ($CDCl_3$) 7.00-7.24 (m, 4H), 6.76-6.94 (m, 1H), 5.96-6.78 (m, 1H), 5.62-5.51 (m, 1H), 3.81 (s, 3H), 2.49 (d.d, 2H, J=2 and 4 Hz), 1.91-1.96 (br s, 1H); ^{13}C NMR δ ($CDCl_3$) 153.7 and 153.1 (s), 130.7 (s), 129.9 (s), 128.1 (d), 127.0 (d), 126.6 (d), 124.6 (d), 124.0 (d), 108.6 (d), 80.3 (s), 71.2 (d), 54.6 and 54.1 (d), 53.6 and 53.2 (q), 24.7 and 24.4 (t).

We next examined the reaction of allenylic tin reagents with quinoline system, in which the regioselectivity (α- or γ-addition) is crucial.[9] When the reaction of allenyltributyltin with quinoline in the presence of methyl chloroformate was conducted in a similar manner to the above, the α-addition product, i.e. 1-methoxycarbonyl-2-(2-propynyl)-1,2-dihydroquinoline (**3a**) was obtained almost exclusively in 59% yield after chromatography. The use of trichloroethyl chloroformate as the acylating agent increased the yield up to 98%. The results are summarized in Table 2, along with those of the reaction with 1-substituted allenyltin reagents. No γ-addition product was detected in NMR analyses. Thus, 2-alkynylic groups can be introduced into the α-position of quinoline system effectively.



3

In summary, we have demonstrated the highly effective method for introduction of 2-alkynylic groups into the α-positions of isoquinoline and quinoline systems

by means of organotin reagents. Further studies on organotin methods for selective introduction of functionalized carbon substituents into nitrogen heterocycles are under way.

Table 2. Reactions of Allenylic Tin Reagents with Quinoline in the Presence of Chloroformate Esters

Entry	Product	R^1	R^2	R^3	Yield/%[a)]
a	**3a**	H	Bu	Me	59
b	**3b**	H	Me	CH_2CCl_3	98
c	**3c**	Bu	Ph	CH_2CCl_3	77
d	**3d**	Et	Ph	CH_2CCl_3	86
e	**3e**	i-Pr	Ph	CH_2CCl_3	82

a) Isolated yield.

References

1) R. Yamaguchi, Y. Nakazono, T. Matsuki, E. Hata, and M. Kawanisi, Bull. Chem. Soc. Jpn., 60, 215 (1987), and references cited therein.

2) K. Akiba, M. Nakatani, M. Wada, and Y. Yamamoto, J. Org. Chem., 50, 63 (1985), and references cited therein.

3) D. L. Comins and J. D. Brown, Tetrahedron Lett., 27, 4549 (1986), and references cited therein.

4) R. Yamaguchi, M. Moriyasu, M. Yoshioka, and M. Kawanisi, J. Org. Chem., 50, 287 (1985).

5) R. Yamaguchi, M. Moriyasu, and M. Kawanisi, Tetrahedron Lett., 27, 211 (1986).

6) Y. Ueno and M. Okawara, J. Am. Chem. Soc., 101, 1893 (1979).

7) K. Ruitenbery and P. Vermeer, Tetrahedron Lett., 25, 3019 (1984).

8) All new compounds gave consistent spectral data with the proposed structures.

9) K. Akiba, T. Kasai, and M. Wada, Tetrahedron Lett., 23, 1709 (1982); K. Akiba, T. Kobayashi, and Y. Yamamoto, Heterocycles, 22, 1519 (1984), and references cited therein.

(Received May 6, 1987)