Pergamon

Tetrahedron Letters, Vol. 38, No. 3, pp. 403-406, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(96)02310-6

Triflate Ion-Promoted Addition Reactions of Allylsilane to Quinolines and Isoquinolines Acylated by Chloroformate Esters

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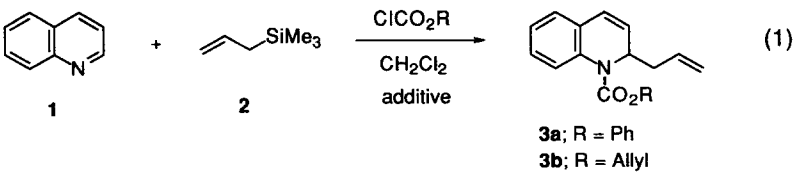
Abstract: Reaction of allyltrimethylsilane with a variety of quinolines acylated by chloroformate esters can be promoted by a catalytic amount of a triflate ion to afford 2-allyl-1,2-dihydroquinolines in good to high yields. A similar reaction with isoquinolines afforded benzoisoquinuclidine derivatives by consumption of 2 eq of allyltrimethylsilane. Copyright © 1996 Elsevier Science Ltd

Addition reactions of organometallic reagents with aza-aromatics acylated by acyl chlorides have been of great importance for synthesizing a variety of physiologically active nitrogen compounds, including alkaloids.[1] Recently, allylation reactions have been extensively studied[2] and we have reported that allylic tin reagents readily react with aza-aromatics activated by acyl chlorides in a chemo- and/or regioselective manner, providing a simple and effective method for introducing allylic substituents into nitrogen heterocycles.[3] However, it has been proven that allylic silicon reagents are not sufficiently nucleophilic to react with pyridine acylated by methyl chloroformate.[3a] Considering that the organosilicon reagents are generally less toxic and more easily handled than organotin reagents,[4] participation of such organosilicon reagents in the above reactions would be highly advantageous. We now wish to report that the reactions of allylsilane with quinolines and isoquinolines acylated by acyl chlorides can be promoted by a catalytic amount of a triflate ion to afford allylated heterocyclic products in good yields.

When quinoline (**1**) acylated by phenyl chloroformate was allowed to react with allyltrimethylsilane (**2**) in dry dichloromethane at rt for 24 h, the addition reaction was hardly observed in contrast to the reported result that a similar reaction of allyltributyltin gives the 2-allyl-1,2-dihydroquinoline derivative in high yield.[3a] It is apparent that allylsilane is less reactive than allyltin. Since it can be anticipated that the silver ion pulls off the chloride ion and, eventually, the electrophilicity of the *N*-acylquinolinium ion would be enhanced, we added silver salts to the reaction mixture. When silver triflate (1.5 eq) was added to the reaction mixture, the addition proceeded rapidly at rt (2 h) to give *N*-phenoxycarbonyl-2-allyl-1,2-dihydroquinoline (**3a**) in 98% yield (Eq. 1). The results are summarized in Table 1.



1 + **2** → (1)

3a; R = Ph
3b; R = Allyl

Table 1. Reactions of **2** with **1** Acylated by Phenyl Chloroformate in the Presence of Silver Salt

Run	Additive	Time (h)	Yield of **3a** (%)[a]
1	none	24	—
2	AgOTf	2	98
3	$AgBF_4$	3	47
4	$AgClO_4$(2,6-lu)$_2$	3	93

[a] Isolated yield.

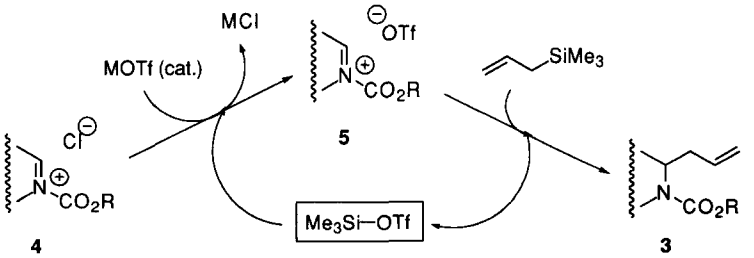
The above results clearly indicate that replacement of the chloride ion with the less nucleophilic counter anion enhances the electrophilicity of the *N*-acylquinolinium ion. Among the silver salts employed, silver triflate gave the best result, as indicated in Table 1. Thus, we next pursued the possibility of the addition reaction promoted by *a catalytic amount* of silver triflate and other triflates. The results are summarized in Table 2.

Table 2. Reactions of **2** with **1** Acylated by Chloroformate Esters in the Presence of a Triflate Ion (0.1 eq)

Run	R	MOTf	Product	Yield (%)[a,b]
1	Ph	AgOTf	**3a**	84
2	Ph	LiOTf	**3a**	87
3	Ph	NaOTf	**3a**	76
4	Ph	Me_3SiOTf	**3a**	85
5	Allyl	AgOTf	**3b**	81
6	Allyl	LiOTf	**3b**	43

[a] Isolated yield. [b] Reaction time is 24 h in all cases.

As shown in Table 2, silver triflate as well as other triflates can work well even in a catalytic amount, although a longer reaction time is required. Thus, it is evident that the triflate ion promotes the present reaction. A plausible reaction pathway for the catalytic reaction is depicted in Scheme 1. Exchange of the chloride ion of *N*-acylquinolinium chloride **4** with the triflate ion should generates the more electrophilic *N*-acylquinolinium triflate **5**,[5] which would react with allyltrimethylsilane to give the adduct **3** as well as trimethylsilyl triflate. Then, trimethylsilyl triflate should replace the chloride ion of **4** with the triflate ion to regenerate **5**. Indeed, trimethylsilyl triflate can promote the reaction (run 4).[6]



Scheme 1

Other quinoline derivatives with substituents have been also subjected to the present catalytic reaction (Eq. 2). The results are summarized in Table 3.[7] As shown in Table 3, a variety of functional groups, including the nitro group, can be tolerated in the present reaction.

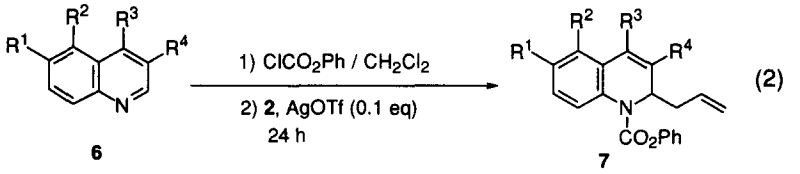


Table 3. Reactions of **2** with Substituted Quinolines Acylated by Phenyl Chloroformate in the Presence of Triflate Ion (0.1 eq)

Run	R^1	R^2	R^3	R^4	Product	Yield(%)[a]
1	H	H	H	Br	**7a**	86
2	H	H	H	Me	**7b**	73
3	H	H	H	CN	**7c**	79[b]
4	H	H	H	CO_2Me	**7d**[c]	53
5	H	H	CHO	H	**7e**	59
6	NO_2	H	H	H	**7f**	91
7	H	NO_2	H	H	**7g**	92

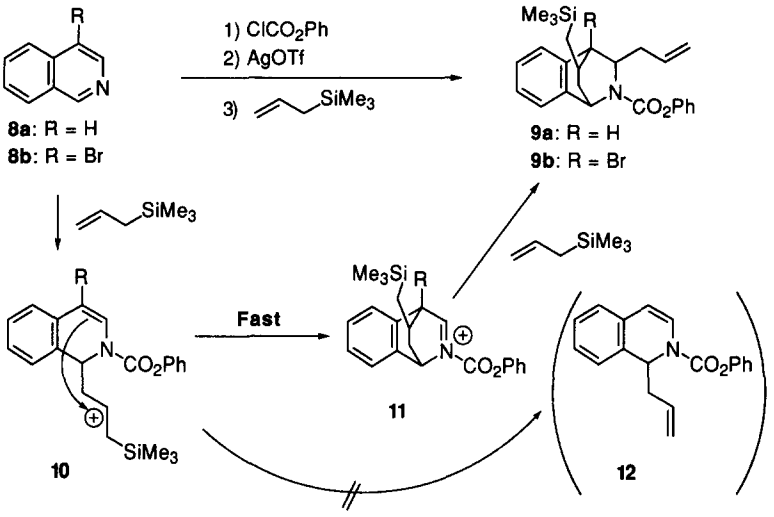
[a] Isolated yield. [b] The reaction was carried out at 70 °C in $ClCH_2CH_2Cl$.
[c] A small amount of the 4-allyl adduct was produced.

We next examined a similar reaction of isoquinoline (**8a**) to the above. When allyltrimethylsilane (**2**) was allowed to react with **8a** acylated by phenyl chloroformate in the presence of silver triflate (1.5 eq), the addition of 2 eq of **2** to **8a** took place, affording a benzoisoquinuclidine derivative **9a** as a 1 : 1 mixture of stereoisomers in 83% yield (Scheme 2). The reaction was able to proceed in the presence of 0.1 eq of silver triflate to give **9a** in 77% yield. The same catalytic reaction of 4-bromoquinoline (**8b**) also afforded a benzoisoquinuclidine derivative **9b** in 55% yield.

The above results are in marked contrast to the reaction of allyltin in which 1-ally-1,2-dihydroisoquinoline derivative **12** is obtained in high yield.[3a] A possible reaction pathway is depicted in Scheme 2. The first addition of allyltrimethylsilane (**2**) would produce the cationic intermediate **10**, which should undergo the intramolecular electrophilic addition to the enamide moiety to produce the cyclized iminium ion **11**. The second addition of **2** to **11** would afford benzoisoquinuclidine derivative **9**. It should be noted that the sterically hindered 4-substituted quinoline **8b** can produce the cyclized product **9b**.

A typical experimental procedure is as follows: To a solution of quinoline (129 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) was added phenyl chloroformate (236 mg, 1.5 mmol) at rt. Then the reaction mixture was stirred for 1 h. To the reaction mixture was added allyltrimethylsilane (228 mg, 2.0 mmol) and silver trifluoromethanesulfonate (26 mg, 0.1 mmol) at rt. Then the reaction mixture was stirred for 24 h. Ether (5 mL) and saturated aqueous $NaHCO_3$ (3 mL) were added, and the organic layer was separated. The aqueous layer was extracted with ether (5 mL X 5). The combined organic layer was dried (Na_2SO_4) and the solvent was evaporated. The residue was purified on silica gel to give 2-allyl-1-phenoxycarbonyl-1,2-dihydroquinoline (**3a**) (245 mg, 84%)

In summary, we have found that a triflate ion can effectively promote the addition reaction of allylsilanes to a variety of quinolines acylated by chloroformate esters, providing a useful new method for allylation of quinoline derivatives. In addition, the reactions with isoquinolines afforded benzoisoquinuclidine derivatives by consumption of 2 eq of allylsilane.



Scheme 2

Acknowledgment: This research is partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture (No. 08455415) to R. Y.

References and Notes

1. For a review, see (a) Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223-243. For recent examples, see (b) Comins, D. L.; Dehgani, A. *J. Org. Chem.* **1995**, *60*, 794-795, and references cited therein; (c) Nishikawa, T.; Yoshikai, M.; Obi, K.; Kawai, T.; Unno, R.; Jomori, T.; Isobe, M. *Tetrahedron* **1995**, *51*, 9339-9352, and references cited therein; (d) Magnus, P.; Rodríguez-Lopez, J.; Mulholland, K.; Matthews, I. *J. Am. Chem. Soc.* **1992**, *114*, 382-383; (e) Braña, M. F.; Morán, M.; Pérez de Vega, M. J.; Pita-Romero, I. *J. Org. Chem.* **1996**, *61*, 1369-1374.

2. For a recent review, see Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207-2293.

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4. For use of a silyl radical instead of a tin radical, see (a) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188-194; (b) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229-1251; (c) Chatgilialoglu, C.; Ferreri, C.; Ballestri, M. *Tetrahedron Lett.* **1996**, *37*, 6387-6390.

5. We have traced the reaction by NMR. When AgOTf was added to a solution of **1** and phenyl chloroformate in $CDCl_3$, ^1H NMR showed new signals at 10.02, 9.34, and 8.75 ppm, probably due to the assumed **5**, which disappeared by addition of allyltrimethylsilane to the mixture giving the adduct **3a**. This preliminary result should support the plausible reaction pathway shown in Scheme 1.

6. It has been reported that trimethylsilyl triflate promotes the reactions of allyltrimethylsilane with α-alkoxyamides. For example, see Bernardi, A.; Micheli, F.; Potenza, D.; Scolastico, C.; Villa, R. *Tetrahedron Lett.* **1990**, *31*, 4949-4952.

7. All new compounds gave satisfactory spectral and analytical data.

(*Received in Japan* 11 *October* 1996; *revised* 18 *November* 1996; *accepted* 22 *November* 1996)