Lewis Acid-Promoted [2+2] Azetidine Annulation of *N*-Acylaldimines with Allyltriisopropylsilane

Tadao Uyehara,* Mizue Yuuki, Hiroaki Masaki, Moriji Matsumoto, Masako Ueno,† and Toshio Sato†
Department of Applied Chemistry, Faculty of Engineering, Utsunomiya University, Utsunomiya 321
†*Instrumental Analytical Center for Chemistry, Faculty of Science, Tohoku University, Sendai 980*

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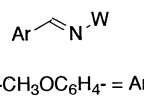
Lewis acid-catalyzed reactions of an *N*-acylaldimine with allyltriisopropylsilane gave [2+2] azetidine annulation products, while those of an *N*-ethoxycarbonylaldimine gave an allylated product.

Titanium tetrachloride-catalyzed reactions of α,β-unsaturated carbonyl compounds with trialkylallylsilanes are classified into three categories. A reaction with allyltrimethylsilane gives generally an β-allylated carbonyl compound.[1] Reactions with allyltriisopropylsilane instead of allyltrimethylsilane give [3+2] cyclopentane annulation products[2] and/or [2+2] cyclobutane annulation products.[3]

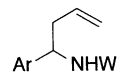
Recently a nitrogen analog version of the [3+2] annulation that gives pyrrolidines has been reported using in situ generated *N*-alkoxycarbonylaldimine and a crotylsilane derivative.[4] In the course of our studies on reactions of isolable *N*-acyl- and *N*-alkoxycarbonylaldimines,[5] we noticed that Lewis acid-mediated ones with trialkylallylsilanes gave the allylated products and/or the [2+2] azetidine annulation products instead of [3+2] pyrrolidine annulation products.

The representative results are listed in Table 1. Reactions of an *N*-ethoxycarbonylaldimine **1** with trialkylallylsilanes **5** and **6** using titanium tetrachloride as the catalyst gave only the allylated product (**7**).[6] Allyltrimethylsilane—$TiCl_4$ is a suitable combination for the allylation of *N*-acyl- and *N*-alkoxycarbonylaldimines.

Similar reactions of an *N*-pivaloylaldimine **2** with trialkylallylsilanes **5** and **6** gave [2+2] annulation products (vide infra). A reaction of **2** with allyltrimethylsilane (**5**) formed an allylated product **8** mainly and small amounts of azetidines **12** and **17**.[7]



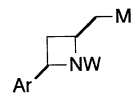
p-$CH_3OC_6H_4$- = Ar

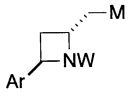


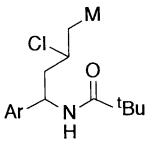
1 W = $COOC_2H_5$
2 W = $COC(CH_3)_3$
3 W = COC_6H_5
4 W = COC_6H_5, Ar = C_6H_5

5 M = $Si(CH_3)_3$
6 M = $Si(^iPr)_3$

7 W = $COOC_2H_5$
8 W = $COC(CH_3)_3$
9 W = COC_6H_5
10 W = COC_6H_5, Ar = C_6H_5







11 M = $Si(^iPr)_3$, W = $COOC_2H_5$
12 M = $Si(CH_3)_3$, W = $COC(CH_3)_3$
13 M = $Si(^iPr)_3$, W = $COC(CH_3)_3$
14 M = $Si(^iPr)_3$, W = COC_6H_5
15 M = $Si(^iPr)_3$, W = COC_6H_5, Ar = C_6H_5

16 M = $Si(^iPr)_3$, W = $COOC_2H_5$
17 M = $Si(CH_3)_3$, W = $COC(CH_3)_3$
18 M = $Si(^iPr)_3$, W = $COC(CH_3)_3$
19 M = $Si(^iPr)_3$, W = COC_6H_5
20 M = $Si(^iPr)_3$, W = COC_6H_5, Ar = C_6H_5

21 M = $Si(^iPr)_3$

Table 1. Lewis acid-mediated reactions of activated aldimines with trialkylallylsilanes [a]

imine	silane	conditions (time/h)	products (yield/ %)[b]
1	**5**	-78°C (4.5) then rt (18)	**7** (88)
1	**6**	-78°C (4) then rt (14)	**7** (35)
2	**5**	-78°C (1) then -40°C (3)	**8** (38), **12** (5), **17** (3)
2	**5**	-78°C (3)	**8** (38), **12** (5), **17** (3)
2	**6**	-78°C (1) then rt (17)	**13** (40), **18** (11)
2	**6**	-78°C (3)	**21** (28), **13** (12), **18** (8)
3	**6**	-78°C (1) then rt (24)	**9** (18), **14** (23), **19** (29)
4	**6**	-78°C (1) then rt (48)	**10** (32), **20** (8)
1[c]	**5**	-78°C (4.5) then rt (12)	**7** (86)
1[c]	**6**	-78°C (4) then rt (14)	**7** (19), **11** (<1), **16** (19)
2[c]	**5**	-78°C (1) then rt (20)	**8** (62), **12** (7), **16** (15)
2[c]	**6**	-78°C (1) then rt (39)	**13** (49), **18** (32)
2[c]	**6**	-78°C (3)	**13** (22), **18** (9)
3[c]	**6**	-78°C (1) then rt (24)	**14** (45), **19** (23)
4[c]	**6**	-78°C (1) then rt (24)	**15** (30), **20** (36)

[a] To a solution of an aldimine (1 mmol) in dry dichloromethane (10 cm^3) was added a solution of $TiCl_4$ (1M) in dichloromethane (1 cm^3) at -78°C. The mixture was stirred for 5 min. To the resulting mixture was added an trialkylallylsilane (1.3 mmol) over a period of 10 min. The reaction was conducted under the conditions listed and terminated by treatment with a saturated aqueous sodium hydrogen carbonate solution. [b] Products were isolated by silica-gel column chromatography. [c] BF_3-etherate was used as the catalyst instead of $TiCl_4$.

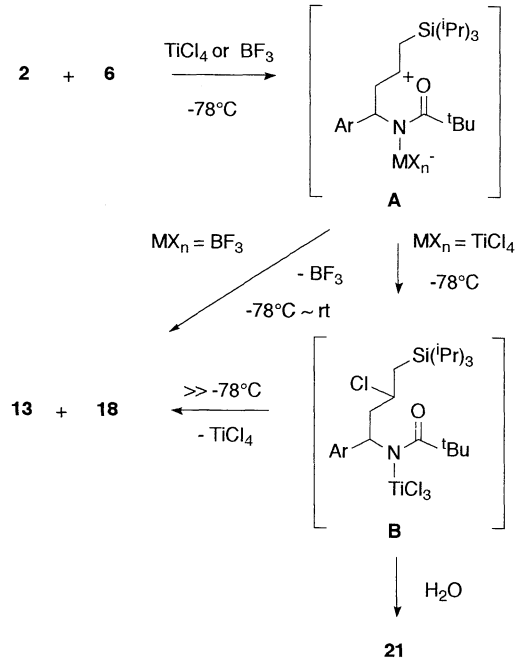
This reaction seems to complete at -78 °C, since the effect of the reaction temperature is very small. In contrast to this, a reaction of an *N*-pivaloylaldimine **2** with allyltriisopropylsilane (**6**) gave azetidines **13** and **18**. When this reaction was terminated at -78 °C, chlorides **21**[8] were obtained along with small amounts of azetidines **13** and **18**.

When *N*-benzoylaldimines **3** and **4** were employed instead of the *N*-pivaloylaldimine **2**, the allylation and the [2+2] annulation were competitive and none of the chlorides like **21** was isolated.

A treatment of the purified chloride **21** with equimolar amounts of $TiCl_4$ in dichloromethane at -78 °C and then at room temperature for 3 h gave the allylated product **8** in 80% yield. The feature of the Lewis acid-mediated reactions seems to form a β-silyl cation such as **A** at -78 °C. Chlorides **21** seem to be the secondary products derived during aqueous work up at low temperature from a reaction intermediate such as **B** that would change to azetidines **13** and **18** in the medium upon warming to room temperature.

This consideration prompted us to examine the reaction catalyzed by boron trifluoride etherate that does not form a strong nucleophile like a chloride ion in media. As expected, a reaction with allyltriisopropylsilane **6** gave the azetidines in better yields.

In conclusion, novel [2+2] azetidine annulation products were derived by a Lewis acid-mediated reaction of a trialkylallylsilane with an *N*-acylaldimine.



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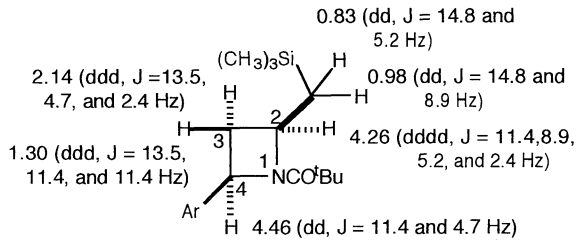
5 Isolable *N*-acyl- and *N*-alkoxycarbonylaldimines are limited; aldimines derived from enolizable aldehydes are oligomeryzed during concentration at room temperature. Such labile aldimines may be generated in situ and be used for synthesis, while they are less suitable to discuss the reaction paths than isolable ones. For preparation of isolable *N*-acyl- and *N*-alkoxycarbonylaldimines see; P. Kupfer, S. Meier, and E.-U. Würthwein, *Synthesis*, **1984**, 688.

6 All new compounds reported here exhibit satisfactory spectral and analytical and/or HRMS characteristics.

7 In contrast with the case of carbocyclic annulation products, the structure of the azetidine-annulation product was determined easily by ^{1}H-NMR studies. For an example, those of an azetidine **12** revealed the presence of NOE (8%) between the signals due to H-2 and H-4.



8 Compounds **21** were obtained as a mixture of the diastereoisomers. The major isomer was purified by recrystallization from hexane as colorless fine needles, mp 144 °C. When this isomer was treated with NaH in THF, an azetidine **18** was derived exclusively.