Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 6353–6356

N-Acyliminium ion cyclizations of trimethylsilylmethylallenes

Sang Hee Kim,[a,b] Hyung Gyu Kim,[a,b] Hyunah Choo,[a] Joo Hwan Cha,[a] Ae Nim Pae,[a] Hun Yeong Koh,[c,*] Bong Young Chung[b] and Yong Seo Cho[a,*]

[a]*Biochemicals Research Center, Korea Institute of Science and Technology, Cheongryang, Seoul 130-650, South Korea*
[b]*Department of Chemistry, Korea University, Seongbuk-gu, Seoul 136-704, South Korea*
[c]*Department of Chemistry, Inha University 253 Younghyun-dong, Nam-gu, Incheon 402-751, South Korea*

Received 3 June 2005; revised 28 February 2006; accepted 6 July 2006

Abstract—*N*-Acyliminium ion cyclizations were studied with allenylmethylsilanes to synthesize nitrogen heterocycles. *N*-Acyliminium ion cyclizations were carried out by exposure of precursors **6** and **7** to Lewis acid. The precursors **6** were converted to pyrrolizidinone derivatives **9** with an exo-allene moiety, while the precursors **7** to indolizidinone derivatives **10** with an exo-1,3-diene moiety.
© 2006 Elsevier Ltd. All rights reserved.

N-Acyliminium ion cyclizations have attracted considerable interest because they are very useful in syntheses of nitrogen-containing heterocycles.[1] Various nucleophiles are available for C–C bond formation via *N*-acyliminium ion cyclizations such as alkenes, alkynes, aryl groups, and silicon-containing π-nucleophiles.[1] Especially, silicon-containing π-nucleophiles such as allylsilanes, propargylsilanes, allenylsilanes, and vinylsilanes have been used for *N*-acyliminium ion cyclizations.[1,2] However, allenylmethylsilanes have not been used as π-nucleophiles, even though they are very useful in reactions with aldehydes and acetals like Prins type cyclizations.[3] There is only one example where allenylmethylsilanes are used in intermolecular reactions with *N*-acyliminium ions.[4] Herein, we report the use of trimethylsilylmethylallenes for intramolecular *N*-acyliminium ion cyclizations to afford nitrogen-containing heterocycles bearing an exo-allene and an exo-1,3-diene unit.

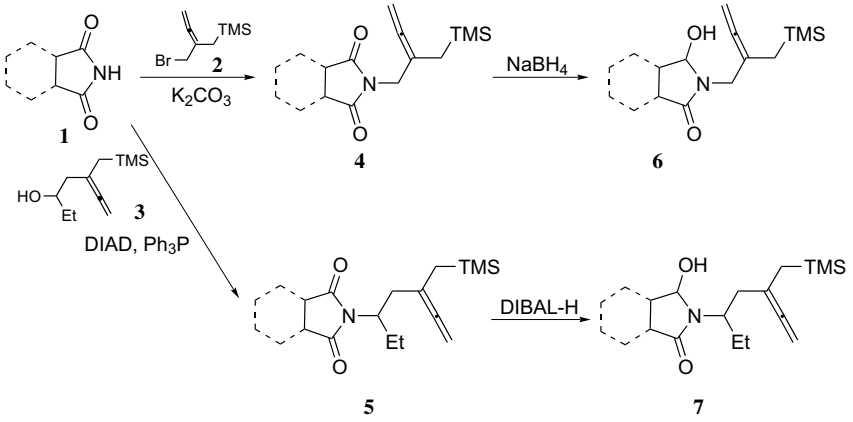
N-Acyliminium ion precursors **6** and **7** were synthesized to examine intramolecular reactions of *N*-acyliminium ions bearing allenylmethylsilanes (Scheme 1). *N*-Acyliminium ion precursors **6** and **7** were obtained from several imides **1** such as succinimides and phthalimides. The imides **1** were coupled with trimethylsilylmethylallenes **2** and **3**[5] by S_N2 reaction and Mitsunobu reaction to give N-alkylated imides **4** and **5**, respectively, in 46–87% yields. The N-alkylated imides **4** and **5** were reduced by $NaBH_4$ or DIBAL-H to give the corresponding *N*-acyliminium ion precursors **6** and **7** in 24–88% yields. The precursors **6** were designed for pyrrolizidinone derivatives, while the precursors **7** were designed for indolizidinone derivatives.

N-Acyliminium ion precursor **6a** was exposed to several Lewis acids for *N*-acyliminium ion cyclization. Surprisingly, the reaction product was not a pyrrolizidinone derivative **8** with an exo-1,3-diene moiety as expected, but a pyrrolizidinone derivative **9a** with an exo-allene moiety (Scheme 2). It is very interesting that the precursor **6a** was cyclized via direct substitution at the α-carbon of TMS group, resulting in an exo-allene product **9a**.[6] There are some examples that allenylmethylsilanes act as π-nucleophiles.[3] However, there has been no example where an allenylmethylsilane is used as α-nucleophile up to now. A similar example was reported where an alkylsilane was employed as α-nucleophile in transfer of an alkyl group to an acylium ion.[7]

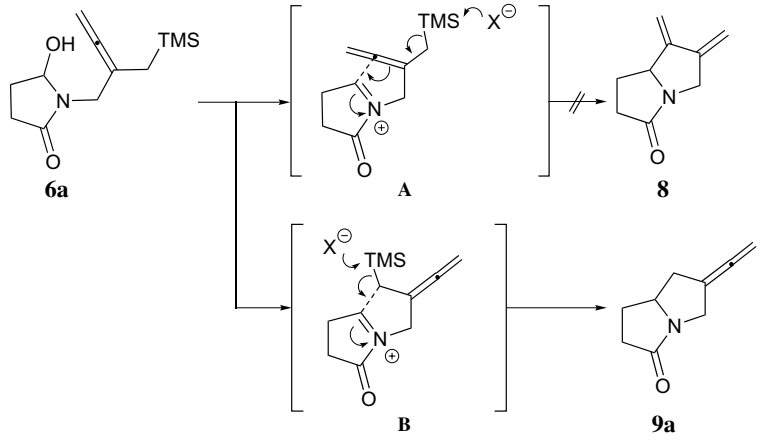
In order to optimize the reaction conditions, several Lewis acids were tried in CH_2Cl_2 as shown in Table 1. No product was obtained with trifluoroacetic acid, and BF_3OEt_2 gave a pyrrolizidinone derivative **9a** in a very poor yield, while indium(III) halides such as $InBr_3$ and $InCl_3$, and TMSOTf were effective for the cyclization.

Keywords: Acyliminium ion.
* Corresponding authors. Tel.: +82 2 958 5156; fax: +82 2 958 5189 (Y.S.C.); e-mail: ys4049@kist.re.kr

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.07.013



Scheme 1.

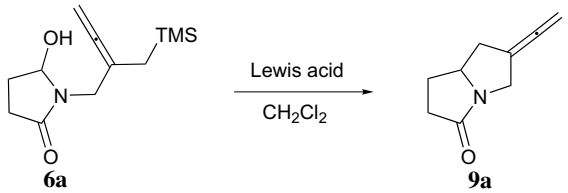


Scheme 2.

TMSOTf was chosen as Lewis acid for the *N*-acyliminium ion cyclization.

The substrates **6** were converted to the corresponding pyrrolizidinone derivatives **9** in CH_2Cl_2 at 0 °C to room temperature in the presence of TMSOTf in 39–70% yields (Table 2). All the products have characteristic chemical shifts in all ^1H NMRs and ^{13}C NMRs, where the chemical shift of the two protons in the allene moiety was about δ 4.8 ppm in multiplet and that of the sp-hybridized allene carbon was about δ 200 ppm in ^{13}C NMR.[6]

Table 1. Optimazation of *N*-acyliminium ion cyclizations[a]



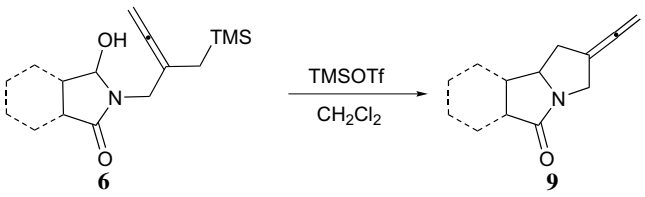
Entry	Lewis acid[b]	Time (h)	Yield[c] (%)
1	TFA	2	NR[d]
2	BF_3OEt_2	24	18
3	$InBr_3$	24	45
4	$InCl_3$	1	65
5	TMSOTf	24	70

[a] All reactions were carried out on a 0.15–0.2 mmol scale at 0 °C–rt.
[b] 1.0 equiv was used.
[c] Isolated yields.
[d] No reaction.

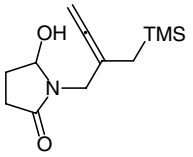
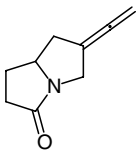
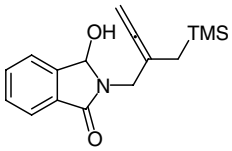
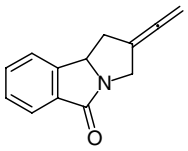
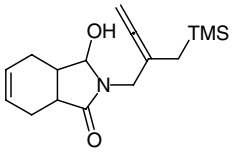
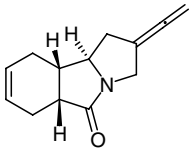
We extended the *N*-acyliminium ion cyclization to one-carbon-elongated substrates **7** compared to substrates **6**. Cyclization reactions of substrates **7** proceeded well in the presence of TMSOTf to give the indolizidinone derivatives **10** with a exo-1,3-diene in high yields (Table 3). *N*-Acyliminium ions were attacked by π-nucleophiles of the allenylmethylsilanes to give the products with a exo-1,3-diene from 6-endo cyclization as expected (Scheme 3). When the substrates **7** were exposed to TMSOTf, *N*-acyliminium ions were generated as intermediates, which underwent cyclization via transition states **C** or **D**. In the transition state **D**, there would be steric hindrance between the carbonyl group of the *N*-acyliminium moiety and the ethyl group.[9] The transition state **C** would be more favorable, resulting in *cis*-**10** obtained as majors, which was proved by difference NOE experiment where there was a very weak NOE between H_a and H_b in *trans*-**10**, while there was no NOE between H_a and H_b in *cis*-**10** (Scheme 3).

We also studied *N*-acyliminium ion cyclization starting with a glutarimide, which was converted to a compound

Table 2. The five-membered ring cyclizations[a]

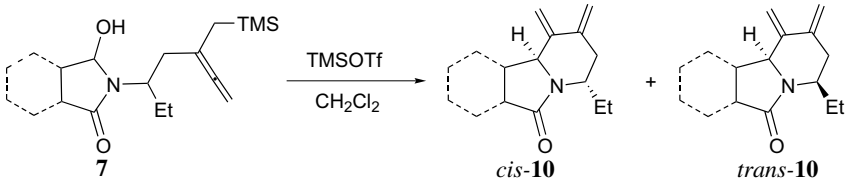


6 **9**

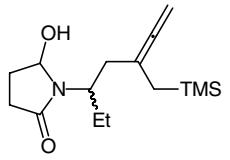
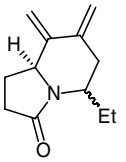
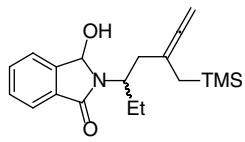
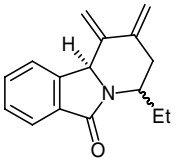
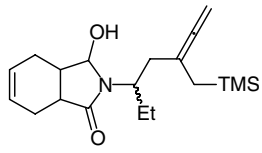
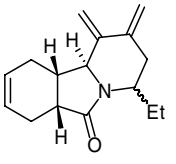
Entry	Reactants		Products		Yield[b] (%)
1		**6a**		**9a**	70
2		**6b**		**9b**	40
3		**6c**		**9c**[8]	39

[a] All reactions were carried out on a 0.15-0.5 mmol scale by treatment with 1.0 equiv of TMSOTf.
[b] Isolated yields.

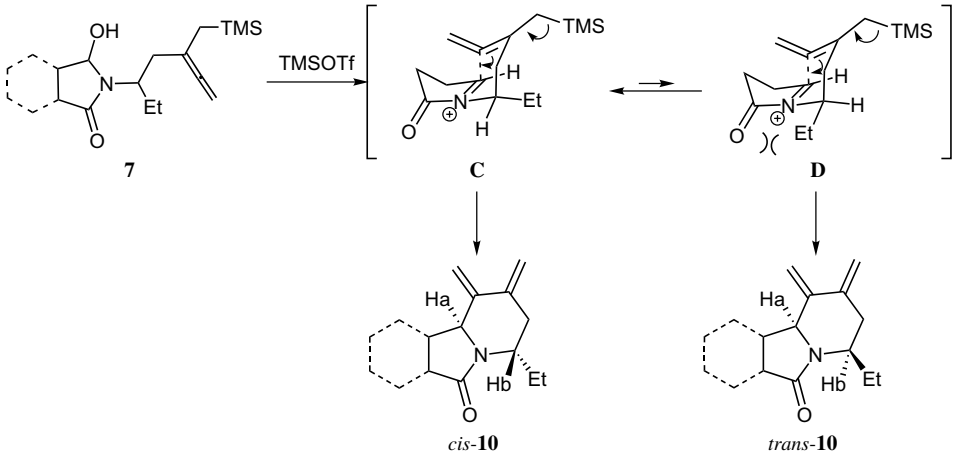
Table 3. The six-membered ring cyclizations[a]



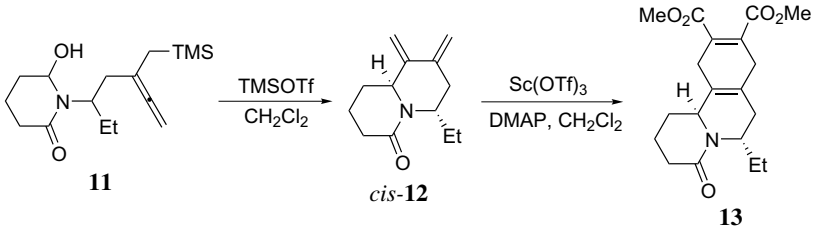
7 *cis*-**10** *trans*-**10**

Entry	Reactant		**10**		Yield[b] (%)	dr[c]
1		**7a**		**10a**	87	2:1
2		**7b**		**10b**	87	6:1
3		**7c**		**10c**[8]	88	1:1

[a] All reactions were carried out on a 0.15–0.5 mmol scale.
[b] Isolated yields.
[c] Diasteromeric ratio between *cis*-**10** and *trans*-**10**.



Scheme 3.



Scheme 4.

11 with a similar procedure as before (Scheme 1). The substrate **11** gave the exo-1,3-diene product *cis*- and *trans*-**12** with 2.5/1 diastereomeric ratio in 90% yield. The exo-1,3-diene *cis*-**12** underwent Diels–Alder reaction with dimethyl acetylenedicarboxylate by treatment with $Sc(OTf)_3$ and DMAP to give a tricyclic compound **13** in 32% yield, which proved the existence of the exo-1,3-diene moiety in the compound **12** (Scheme 4).

We described here *N*-acyliminum ion cyclizations with allenylmethylsilanes. Five-membered exo-allene products **9** were generated by cyclization via direct substitution at the α-carbon of TMS group. On the other hand, the six-membered exo-1,3-diene products **10** were obtained from 6-endo cyclization.

Acknowledgment

This work was supported by INHA University Research grant.

References and notes

1. For reviews: (a) Maryanoff, B. E.; Zhang, H.-C.; Cohen, J. H.; Turch, I. J.; Maryanoff, C. A. *Chem. Rev.* **2004**, *104*, 1431; (b) Speckamp, W. N.; Moolenaar, M. J. *Tetrahedron* **2000**, *56*, 3817; (c) Thebtaranonth, C.; Thebtaranonth, Y. *Cyclization Reactions*; CRC Press: Boca Raton, 1994; p 5.
2. (a) Gelas-Mialhe, Y.; Gramain, J.-J.; Louvet, A.; Remuson, R. *Tetrahedron Lett.* **1992**, *33*, 73; (b) Daub, G. W.; Heerding, D. A.; Overman, L. E. *Tetrahedron* **1988**, *44*, 3919; (c) Gardette, D.; Gelas-Mialhe, Y.; Gramain, J.-C.; Perrin, B.; Remuson, R. *Tetrahedron: Asymmetry* **1998**, *9*, 1823; (d) Sun, P.; Sun, C.; Weinreb, S. M. *J. Org. Chem.* **2002**, *67*, 4337; (e) Sun, P.; Sun, C.; Weinreb, S. M. *Org. Lett.* **2001**, *22*, 3507.
3. (a) Cho, Y. S.; Karupaiyan, K.; Kang, H. J.; Cha, J. H.; Pae, A. N.; Koh, H. Y.; Chang, M. H. *Chem. Commun.* **2003**, 2346–2347; (b) Cho, Y. S.; Chang, M. H.; Koh, H. Y.; Pae, A. N.; Kang, H. J. US 2005059832, 2005; (c) Trost, B. M.; Urabe, H. *J. Am. Chem. Soc.* **1990**, *112*, 4982.
4. Mentinkm, G.; van Maarseveen, J. H.; Hiemstra, H. *Org. Lett.* **2002**, *4*, 3497.
5. Lee, P. H.; Bang, K.; Lee, K.; Lee, C.-H.; Chang, S. *Tetrahedron Lett.* **2000**, *41*, 7521.
6. General Procedure: To a solution of **6a** (0.18 mmol) was added TMSOTf (0.18 mmol) under N_2 at 0 °C. After stirring the mixture for 30 min at 0 °C, the reaction mixture was allowed to slowly warm to rt. The mixture was quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2, dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash chromatography to afford the desired product **9a**; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.89$–4.78 (m, 2H), 4.31 (td, 1H, $J = 14.8$ Hz, $J = 4.40$ Hz), 4.03 (dq, 1H, $J = 9.83$ Hz, $J = 6.80$ Hz), 3.64 (br d, 1H, $J = 14.8$ Hz), 2.71–2.65 (m, 2H), 2.48–2.41 (m, 1H), 2.38–2.31 (m, 1H), 2.28–2.18 (m, 1H), 1.83–1.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.0, 174.4, 99.7, 78.4, 61.3, 43.8, 37.6, 34.1, 26.5; EIMS *m*/*z* 150 (2.7), 149 (M^+, 26), 148 (100).
7. Urabe, H.; Kuwajima, I. *J. Org. Chem.* **1984**, *49*, 1140.
8. Huang, H.-L.; Sung, W.-H.; Liu, R.-S. *J. Org. Chem.* **2001**, *66*, 6193.
9. (a) Gardette, D.; Gelas-Mialhe, Y.; Gramain, J.-C.; Perrin, B.; Remuson, R. *Tetrahedron: Asymmetry* **1998**, *9*, 1823; (b) Gelas-Mialhe, Y.; Gramain, J.-C.; Louvet, A.; Remuson, R. *Tetrahedron Lett.* **1992**, *33*, 73.