Tetrahedron Letters, Vol. 34, No. 16, pp. 2613-2616, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Intramolecular Cyclization of β-(Alkoxycarbonyl)allylsilane with Conjugated Ketone. A New Entry to Bicyclo[4.3.0]nonane

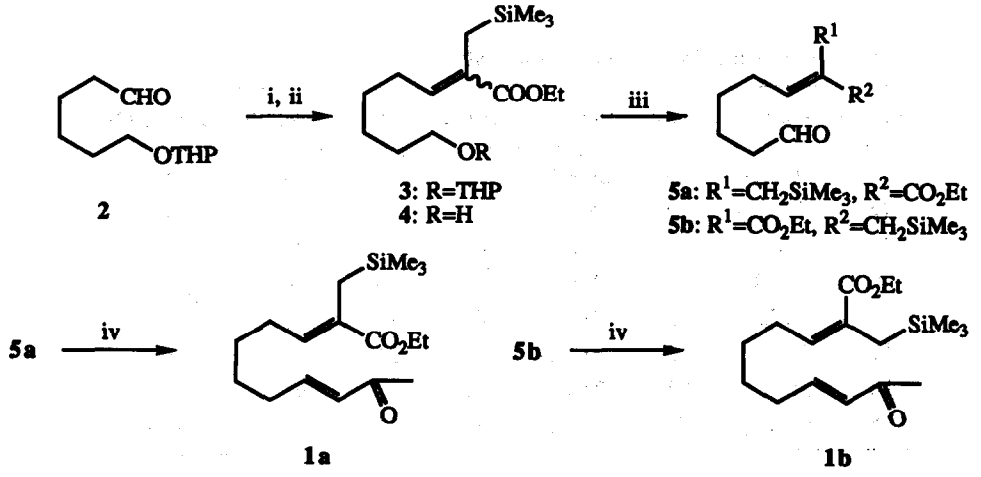
Chiaki Kuroda,* Yuki Ohnishi, and James Y. Satoh

Department of Chemistry, Rikkyo University, Nishi-Ikebukuro, Toshima-ku, Tokyo 171, Japan

Abstract: Bicyclo[4.3.0]nonane ring systems with exo-methylene group on five membered ring were synthesized by using intramolecular cyclization between β-(alkoxycarbonyl)allylsilane and α,β-unsaturated ketone. The stereochemistry of cyclization is also described.

Recently we reported that intramolecular cyclization of ω-formyl-α-trimethylsilylmethyl-α,β-unsaturated carboxylic esters produces a carbocyclic ring and an α-methylene-γ-lactone moiety at once.[1,2] Since α-trimethylsilylmethyl-α,β-unsaturated carboxylic ester group can react as both nucleophile (allylsilane) and electrophile (Michael accepter), the reaction of this moiety with appropriate C-C bond is expected to form five memberd carbocyclic ring. While β-(functionalized-methyl)allylsilanes are studied as useful building block to form five or seven membered carbocycles.[3] We now report an intramolecular reaction of β-(ethoxycarbonyl)allylsilane with α,β-conjugated ketone[4] in the presence of Lewis acid or fluoride to form bicyclo[4.3.0]nonane with exo-methylene group on five membered ring.

Cyclization precursors (**1a** and **1b**) were synthesized as shown in Scheme 1. Hoffmann's Wittig reaction[5] of 6-(tetrahydropyranyloxy)hexanal (**2**), prepared from 1,6-hexanediol[2], produced (*Z*)- and (*E*)-mixture of β-

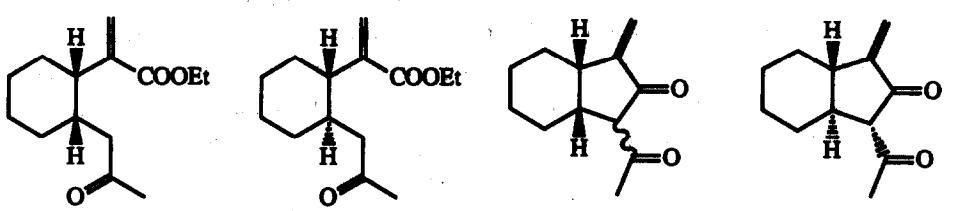


Scheme 1. Reagents and conditions. i. $(EtO)_2POCH(CH_2SiMe_3)COOEt$, NaH, DME, r.t. ii. 5%HCl/THF (1:4), reflux. iii. DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, -60°C. iv. $(MeO)_2POCH_2COCH_3$, NaH, DME, r.t.

(ethoxycarbonyl)allylsilane **3** in 84% yield. The ratio of two products was determined to be 2:1 from the ^{1}H-NMR spectrum of the reaction mixture [δ 6.54 (t, J=7.3Hz) for *Z*-isomer and 5.64 (t, J=7.7Hz) for *E*-isomer]. Deprotection of **3** by HCl aq. in refluxing THF afforded alcohol **4** (95% yield), which was converted to aldehyde **5** by Swern oxidation (64%). Two geometrical isomers **5a** and **5b** were separated by silica gel chromatography at this stage. The cyclization precursors **1a** and **1b** were obtained by Wittig-Horner reaction of **5a** and **5b**, respectively, with $(MeO)_2POCH_2COCH_3$/NaH (78% from **5a** and 61% from **5b**). The *E*-configuration of the enone moiety was established from NOE between olefinic protons and acetyl protons.

Cyclization reaction was then examined by using some Lewis acids. The results are summarized in Table. The stereochemistries of the products **6a** and **6b** were determined by J-values, after separation by silica gel column chromatography[6]. Although the ratio of two products **6a** and **6b** was dependent on cyclizing reagent, *cis*-product **6a** was predominant from *Z*-precursor **1a**, and *trans*-product **6b** was predominant from *E*-precursor **1b**. This stereochemical feature of cyclization can be rationalized as follows. From the assumption that the six-membered carbocyclic ring takes chair conformation, **6a** and **6b** are considered to be formed from **1a** via **i**-**iii** (Scheme 2). The results indicate that conformation **i**, in which two side chains are both equatorial, is disfavored because of the interaction between two oxygen functionalities[1]. While such interaction is not expected for both **ii** and **iii**, and therefore, **6a** was obtained as the major isomer. The favorable formation of **6b** from **1b** is simply rationalized by intermediate **iv**, which has two equatorial side chains with no oxygen repulsion.

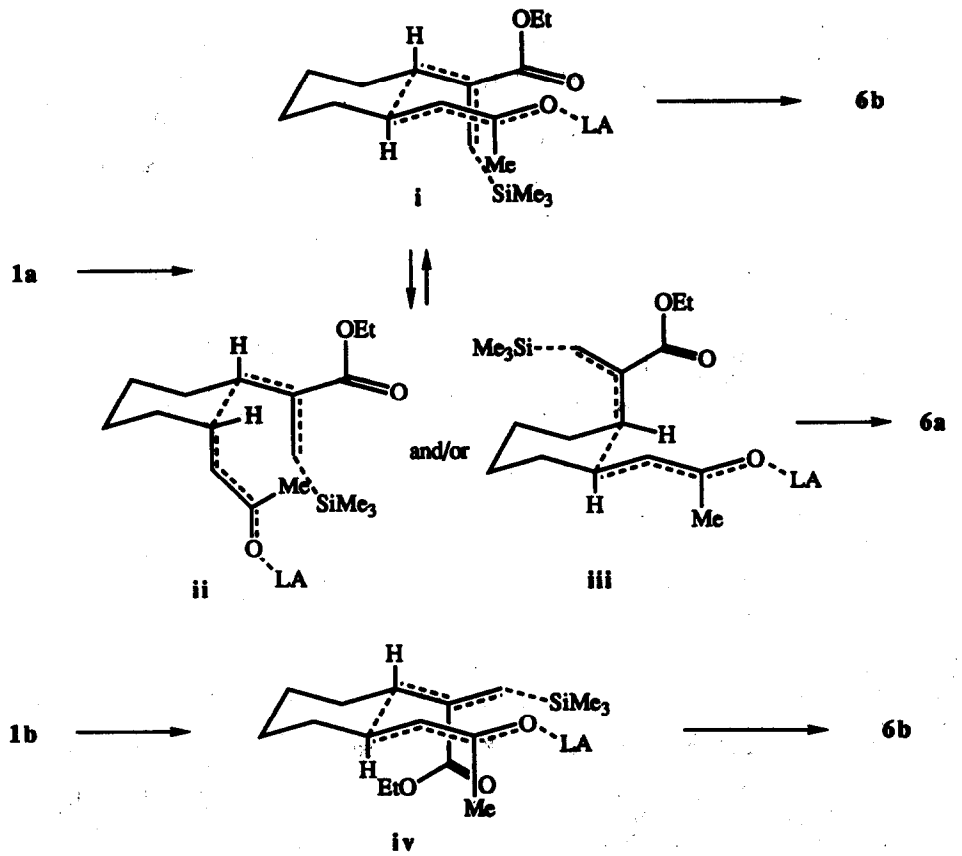
The second cyclization reactions of both **6a** and **6b** were carried out by two ways as follows. First, treatment with NaH in THF at room temperature afforded bicyclic compounds **7a** and **7b** in 60% and 77% yields,



6a **6b** **7a** **7b**

Table: Cyclization of **1a** and **1b** by Lewis acids.

precursor	reagent	equiv.	solvent	temp.	time(h)	yield(%)	ratio(**6a**:**6b**)
1a	$TiCl_4$	1.5	CH_2Cl_2	r.t.	18	89	8:1
1a	BF_3OEt_2	1.5	CH_2Cl_2	r.t.	18	89	20:1
1a	$SnCl_4$	1.5	CH_2Cl_2	r.t.	1	96	16:1
1a	$EtAlCl_2$	3	CH_2Cl_2	r.t.	46	89	6:1
1b	$TiCl_4$	1.5	CH_2Cl_2	r.t.	20	91	1:9
1b	BF_3OEt_2	1.5	CH_2Cl_2	r.t.	24	91	1:6
1b	$SnCl_4$	1.5	CH_2Cl_2	r.t.	1	98	1:3
1b	$EtAlCl_2$	3	CH_2Cl_2	r.t.	45	91	1:2.5



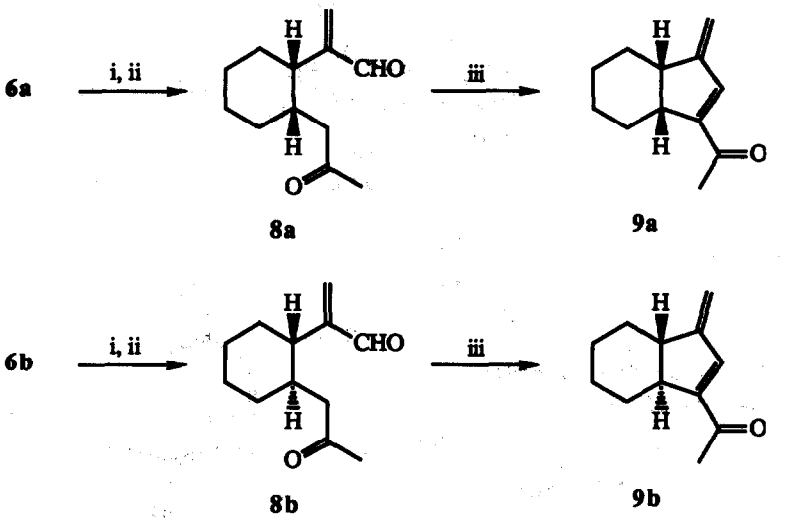
Scheme 2.

respectively. Compound **7a** was found to be a mixture of isomers (ratio 4:1), while **7b** was obtained as a single isomer[7]. We suppose that the configurations of acetyl groups are the result of equilibration under basic condition.

Since **7a** and **7b** were unstable on silica gel, another route to bicyclo[4.3.0]nonane skeleton was examined (Scheme 3). Thus reduction of **6a** with $LiAlH_4$ followed by PDC oxidation afforded keto aldehyde **8a**. Then bicyclic compound **9a** was obtained by intramolecular aldol condensation of **8a** using KOH-EtOH. Similarly, **6b** was converted to **9b** by the same route.

On the other hand, when **1a** and **1b** were treated with tetra-*N*-butylammonium fluoride (TBAF), both hydroxy esters **6a,b** and bicyclic compounds **7a,b** were obtained. The ratio was found to be **6a:6b:7a:7b**=57:16:21:6 from **1a** (totally 79%) and 25:65:2:8 from **1b** (83%), both of which were determined from the ^{1}H-NMR spectra of the reaction mixtures. In respect to the substitution pattern of six membered ring, combined *cis*/*trans* ratio was roughly same as the case of Lewis acid promoted cyclizations for both **1a** and **1b**[8].

We thank Dr. M. M. Ito and Dr. T. Niitsu, Soka University, for the measurements of mass spectra. This work was partly supported from Rikkyo University Grant for the Promotion of Research.



Scheme 3. Reagents and conditions. i. $LiAlH_4$, THF, r.t. ii. PDC, CH_2Cl_2, r.t. iii. KOH, EtOH-H_2O, r.t.

References and Notes

1. Kuroda, C.; Shimizu, S.; Satoh, J. Y. *J. Chem. Soc., Chem. Commun.*, **1987**, 286; *J. Chem. Soc., Perkin Trans. 1*, **1990**, 519.
2. A similar procedure was developed by Nishitani, K. and Yamakawa, K.: *Tetrahedron Lett.*, **1987**, *28*, 655.
3. a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.*, **1983**, *105*, 2315. b) Giguere, R. G.; Duncan, S. M.; Bean, J. M.; Purvis, L. *Tetrahedron Lett.*, **1988**, *29*, 6071. c) Lee, T. V.; Boucher, R. J.; Porter, J. R.; Taylor, D. A. *Tetrahedron*, **1988**, *44*, 4233. d) Knapp, S.; O'Connor, U.; Mobilio, D. *Tetrahedron Lett.*, **1980**, *21*, 4557.
4. For reviews regarding intramolecular addition of allylsilanes to conjugated ketones: a) Majetich, G.; Hull, K.;Lowery, D.; Ringold, C.; Defauw, J. in *Selectivities in Lewis Acid Promoted Reactions*; ed. by Schinzer, D.; Kluwer Academic Publishers: Dordrecht, 1989; pp 169-188. b) Schinzer, D. *Synthesis*, **1988**, 263.
5. Henning, R.; Hoffmann, H. M. R. *Tetrahedron Lett.*, **1982**, *23*, 2305.
6. **6a**: IR 1725, 1715 cm^{-1}, ^1H-NMR ($CDCl_3$) δ 6.81 (1H, t, J=1 Hz), 5.35 (1H, t, J=1.5 Hz), 2.79 (1H, br dt, J=11, 4 Hz), 2.58 (1H, d quint, J=8, 4 Hz), 2.31 (1H, dd, J=16, 8 Hz), 2.24 (1H, dd, J=16, 5 Hz), 2.05 (3H, s); **6b**: IR 1720 cm^{-1}, ^1H-NMR ($CDCl_3$) δ 6.21 (1H, d, J=1 Hz), 5.56 (1H, brs), 2.43 (1H, dd, J=16, 3 Hz), 2.29 (1H, dt, J=3.5, 12 Hz), 2.12 (1H, dd, J=16, 10 Hz), 2.07 (3H, s), 2.02 (1H, tq, J=3, 10 Hz).
7. **7a**: IR 1730, 1710 cm^{-1}, ^1H-NMR ($CDCl_3$) δ 5.88 and 5.23 (each 1H, d, J=3 Hz, for major isomer), 6.11 and 5.29 (each 1H, d, J=3 Hz, for minor isomer); **7b**: IR 1730, 1710 cm^{-1}, ^1H-NMR ($CDCl_3$) δ 5.94 and 5.18 (each 1H, dd, J=3, 1 Hz).
8. Fluoride promoted cyclization involves kinetically controlled process: see Majetich, G.; Defauw, J.; Ringold, C. *J. Org. Chem.*, **1988**, *53*, 50.

(Received in Japan 23 January 1993)