CHEMISTRY LETTERS, pp. 1375-1378, 1994.

Reaction of 2-(Ethoxycarbonyl)pentadienylsilane under Ritter Condition. Formation of α-Methylene-γ-lactone by Self-cyclization

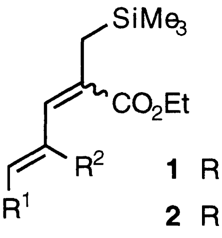
Chiaki KURODA* and Naoko MITSUMATA
Department of Chemistry, Rikkyo University, Nishi-Ikebukuro, Toshima-ku, Tokyo 171

An acylative C(3)-C(4)-bond cleavage of 4,5-disubstituted-2-trimethylsilylmethyl-penta-2,4-dienoate occurred by treatment with trifluoromethanesulfonic acid in nitriles, while a self-cyclization giving an α-methylene-γ-lactone also occurred when the reactions were carried out in bulky nitriles.

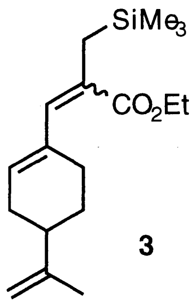
The synthetic utility of organosilicon compounds is increasing in these years.[1] 2-(Ethoxycarbonyl)-allylsilane is an interesting bifunctional unit which can react with both nucleophile and electrophile. We described intramolecular reaction of this unit with aldehyde or α,β-unsaturated ketone producing α-methylene-γ-lactone[2,3] or carbocycle,[4] respectively, including its application to terpenoid synthesis.[5]

2-(Ethoxycarbonyl)pentadienylsilane has an extra reaction site, compared with corresponding allylsilane, as well as the possibility of self-cyclization. Even the synthesis of this unit is reported,[6] its nature is not known so far. On the course of our continuous study on the chemistry of 2-(ethoxycarbonyl)allylsilane, we examined an acid treatment of 2-(ethoxycarbonyl)pentadienylsilane and here report that an acylative C-C single bond cleavage and a self-cyclization reaction occur under Ritter condition.[7]

Substrates used in this study are **1**, **2**, and **3**, which were prepared from corresponding aldehyde via Hoffmann's Wittig reaction.[2,4] Thus, **1**, **2**, and **3** were obtained from tiglic aldehyde, 1-cyclohexene-carbaldehyde, and perillaldehyde, respectively. The mixture of geometrical isomers (*Z* : *E* = 5 : 1 to 18 : 1) were used in the following acid treatment without separation.



1 R^1=R^2=CH$_3$
2 R^1,R^2=(CH$_2$)$_4$



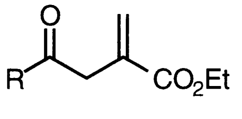
3

A typical procedure of an acid treatment under Ritter condition is as follows. To a stirred solution of substrate (0.1 mmol) in nitrile (2 cm^3) was added TfOH (3 eq.; 0.23 mol cm^{-3} solution in the same nitrile) at room temperature. After being stirred for appropriate time, aqueous NaHCO$_3$ was added, and the mixture was

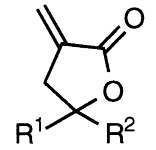
Table 1. Reduction of 2-(Ethoxycarbonyl)pentadienylsilane under Ritter Condition[a]

Entry	Substrate	Acid	Solvent	Time	Product(s)	Yield / %
1	**1**	TfOH	MeCN	17 h	**4a**	57
2	**1**	TfOH	EtCN	20 h	**4b**	67
3	**1**	TfOH	*i*-PrCN	20 h	**4c**	93
4	**1**	TfOH	*t*-BuCN	20 h	**4d+5**	74 (**4d**:**5**=1:1.2)[b]
5	**2**	TfOH	MeCN	21 h	**4a**	43
6	**2**	TfOH	EtCN	18 h	**4b**	91
7	**2**	TfOH	*i*-PrCN	22 h	**4c+6**	52 (**4c**:**6**=1:1.4)[c]
8	**2**	TfOH	*t*-BuCN	22 h	**4d+6**	55 (**4d**:**6**=1:1.8)[c]
9	**3**	TfOH	MeCN	1 h	**7a**	88 (*E*:*Z*=2.4:1)[b,c]
10	**3**	TfOH	EtCN	1 h	**7b**	78 (*E*:*Z*=2.3:1)[c]
11	**3**	TfOH	*i*-PrCN	1 h	**7c**	89 (*E*:*Z*=2.2:1)[c]
12	**3**	TsOH	MeCN	20 h	**7a**	61 (*E*:*Z*=1.8:1)[c]

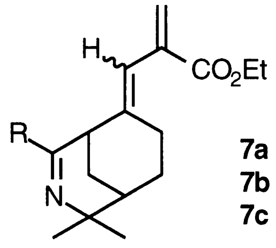
a) The reactions were carried out at room temperature with 3 equiv. of acid.
b) Separated by column chromatography.
c) The ratio was determined from ^{1}H NMR spectrum of the product mixture.



4a R=Me
4b R=Et
4c R=*i*-Pr
4d R=*t*-Bu



5 $R^1=C_2H_5$, $R^2=CH_3$
6 R^1, $R^2=(CH_2)_5$

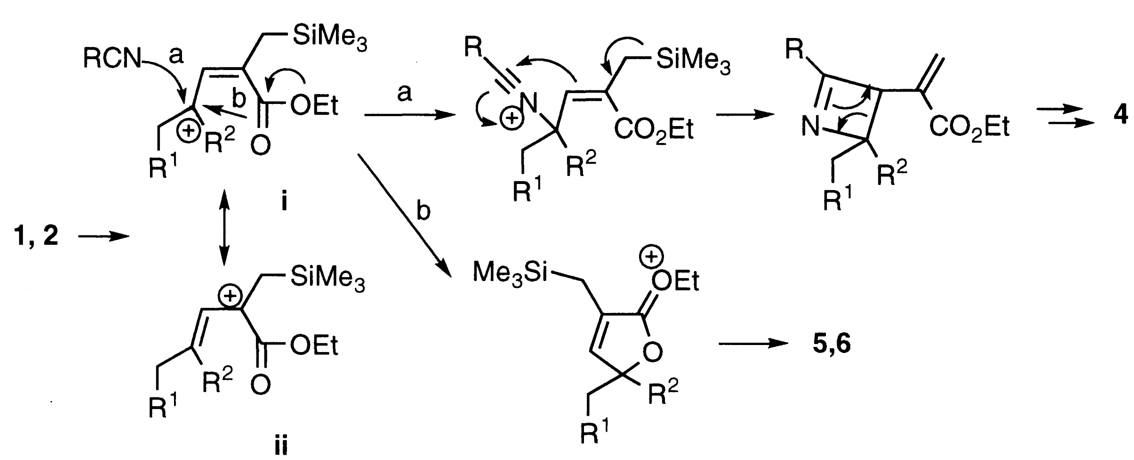


7a R=Me
7b R=Et
7c R=*i*-Pr

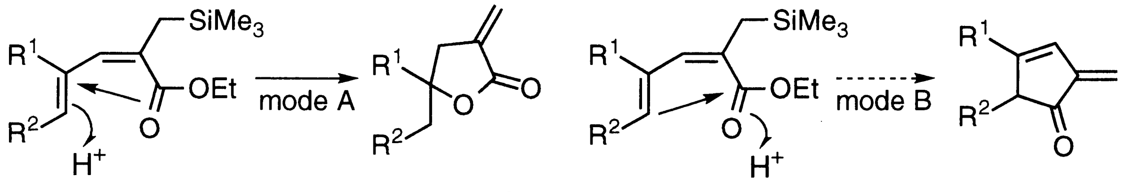
extracted with Et_2O and dried over $MgSO_4$. The product(s) was purified by silica-gel column chromatography using hexane-AcOEt as eluent.

The results are summarized in Table 1. When **1** was treated with TfOH in acetonitrile, propionitrile, or isobutyronitrile, α-methylene-γ-keto ester **4a**,[8,9] **4b**, or **4c** were obtained respectively (Entries 1 to 3). Moreover, when the reaction was carried out in pivalonitrile, formation of α-methylene-γ-lactone **5**[9,10] was also observed as the major products in addition to the corresponding γ-keto ester (Entry 4). The reaction of **2** showed almost parallel results (Entries 5 to 8), except spiro-lactone **6**[10,11] was also produced in isobutyronitrile as solvent. On the other hand, when **3** was treated with TfOH in nitriles, bicyclic compounds **7**[9] were obtained depending on the solvent, as mixtures of geometrical isomers (Entries 9 to 11). The same reaction also proceeded slowly by treatment with TsOH (Entry 12).

A possible reaction mechanism of the formation of α-methylene-γ-keto ester or α-methylene-γ-lactone is illustrated in Scheme 1. Thus, protonation occurred at olefinic terminal position giving a stable tertiary cation,



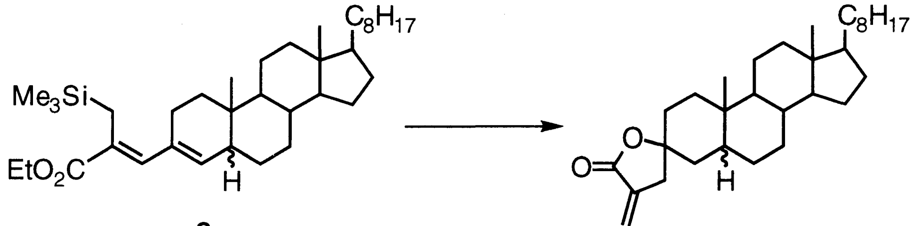
Scheme 1.



Scheme 2.

which also can be stabilized by silicon atom (**i** and **ii**).[12] Attack of nitrile followed by cyclization of allylsilane and subsequent C-C bond cleavage gives α-methylene-γ-keto esters (route a), while intramolecular attack of ester oxygen followed by protiodesilylation giving α-methylene-γ-lactones takes place when R group is bulky (route b). It is interesting that the self-cyclization occurred via "mode A" rather than "mode B" (Scheme 2), where the role of two double bonds, terminal C=C and carbonyl C=O, are opposite in these two modes. While the formation of imines **7** from **3** can be easily explained. Thus the Ritter reaction occurred at isopropenyl group followed by intramolecular cyclization of pentadienylsilane. This indicates that ester-conjugated pentadienylsilane is less reactive than isopropenyl group against protonic acid.

Since the α-methylene-γ-lactone moiety is often found in natural terpenoids as a part of biologically important structural unit,[13] spiro-α-methylene-γ-lactone annulation was further examined using **8**, obtained from cholest-4-en-3-one, as substrate. Thus treatment of **8** with TfOH in pivalonitrile yielded spirolactone **9**[14] in 39% yield. This new entry to α-methylene-γ-lactone includes construction of lactone moiety from single oxygen function.



8 **9**

We thank Dr. M. M. Ito and Dr. T. Niitsu, Soka University, for the measurements of mass spectra.

References

1) G. Majetich, "Organic Synthesis: Theory and Application," ed by T. Hudlicky, JAI Press, Greenwich (1989), Vol. 1, p 173; B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, **25**, 1 (1986); G. L. Larson, "The Chemistry of Organic Silicon Compounds," ed by S. Patai and Z. Rappoport, Wiley, Chichester (1989), p 763.

2) C. Kuroda, S. Shimizu, and J. Y. Satoh, *J. Chem. Soc., Chem. Commun.*, **1987**, 286; *J. Chem. Soc., Perkin Trans. 1*, **1990**, 519; C. Kuroda, S. Inoue, S. Kato, and J. Y. Satoh, *J. Chem. Res. (S)*, **1993**, 62; C. Kuroda, S. Inoue, R. Takemura, and J. Y. Satoh, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 521.

3) K. Nishitani and K. Yamakawa have developed similar reaction independently: *Tetrahedron Lett.*, **28**, 655 (1987).

4) C. Kuroda, Y. Ohnishi, and J. Y. Satoh, *Tetrahedron Lett.*, **34**, 2613 (1993).

5) C. Kuroda, S. Shimizu, T. Haishima, and J. Y. Satoh, *Bull. Chem. Soc. Jpn.*, **66**, 2298 (1993).

6) J. Pornet, B. Khouz, and L. Miginiac, *Tetrahedron Lett.*, **26**, 1861 (1985); J. Pornet, A. Rayadh, and L. Miginiac, *ibid.*, **27**, 5479 (1986).

7) For Ritter reaction, see: R. Bishop, "Comprehensive Organic Synthesis," ed by B. M. Trost, Pergamon Press, Oxford (1991), Vol. 6, p 261.

8) T. Fujisawa, K. Morita, and T. Takeda, *Bull. Chem. Soc. Jpn.*, **62**, 1524 (1989); W. M. Best and D. A. Widdowson, *Tetrahedron*, **45**, 5943 (1989).

9) **4a**: IR (neat) 1725, 1720, 1640, and 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.29 (3H, t, J=7 Hz), 2.21 (3H, s), 3.41 (2H, br s), 4.20 (2H, q, J=7 Hz), 5.64 (1H, q, J=1 Hz), and 6.34 (1H, d, J=1 Hz). **5**: IR (neat) 1760 and 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.95 (3H, t, J=7 Hz), 1.39 (3H, s), 1.71 (2H, q, J=7 Hz), 2.67 (1H, dt, J=17, 2.5 Hz), 2.79 (1H, dt, J=17, 3 Hz), 5.60 (1H, t, J=2.5 Hz), and 6.22 (1H, t, J=3 Hz). *Z*-isomer of **7a**: IR (neat) 1725, 1655, and 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.18 (3H, s), 1.29 (3H, t, J=7 Hz), 1.29 (3H, s), 1.79 (3H, s), 2.15 (1H, ddt, J=2, 5, 13 Hz), 3.29 (1H, br s), 4.21 (2H, q, J=7 Hz), 5.58 (1H, t, J=1.5 Hz), 5.96 (1H, br s), and 6.32 (1H, d, J=2 Hz). *E*-isomer of **7a**: ^1H NMR ($CDCl_3$) δ=1.18 (3H, s), 1.28 (3H, t, J=7 Hz), 1.29 (3H, s), 1.88 (3H, s), 2.46 (1H, dd, J=5, 14 Hz), 2.79 (1H, br s), 4.20 (2H, q, J=7 Hz), 5.48 (1H, t, J=1.5 Hz), 6.03 (1H, br s), and 6.27 (1H, d, J=2 Hz).

10) R. M. Adlington and A. G. M. Barrett, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2848.

11) G. P. Boldrini, D. Savoia, E. Tagliavini, C. Trombini, and A. Umani-Ronchi, *J. Org. Chem.*, **48**, 4108 (1983).

12) M. A. Brook, C. Henry, R. Jueschke, and P. Modi, *Synlett*, **1993**, 97.

13) J. M. Cassady and M. Suffness, "Anticancer Agents Based on Natural Product Models," ed by J. M. Cassady and J. D. Douros, Academic Press, New York (1980), p 201.

14) L. S. Hegedus, S. D. Wagner, E. L. Waterman, and K. Siirala-Hansen, *J. Org. Chem.*, **40**, 593 (1975).

(Received April 7, 1994)