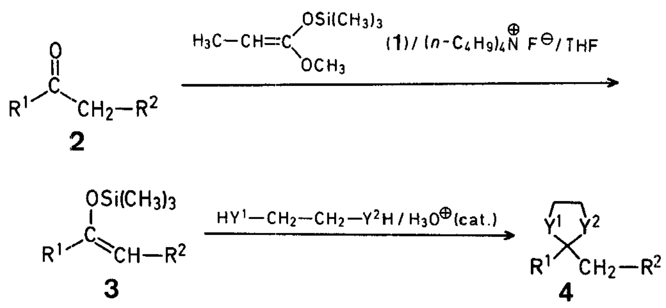
The Chemistry of *O*-Silylated Ketene Acetals[1]; A Mild and Facile Preparation of Trimethylsilyl Enol Ethers and of Cyclic *O,O*-, *O,S*-, and *S,S*-Acetals from Enolizable Carbonyl Compounds

Yasuyuki KITA, Hitoshi YASUDA, Jun-ichi HARUTA, Jun SEGAWA, Yasumitsu TAMURA*

Faculty of Pharmaceutical Sciences, Osaka University, 1-6, Yamada-oka, Suita, Osaka, Japan

There are numerous reports on the *O*-silylation of carbonyl compounds[2]. However, most of the methods described have some drawbacks such as requirement of strongly basic or other forcing conditions and the separation of moisture-sensitive products from a large amount of inorganic or amine salt. Improved methods which were recently reported[3,4] involve the reaction of carbonyl compounds with ethyl trimethylsilylacetate in the presence of a catalytic amount of tetrabutylammonium fluoride (TBAF) or chlorotrimethylsilane in the presence of lithium sulfide, respectively. We now report an alternative improved method for the conversion of enolizable ketones (**2**) into their enol trimethylsilyl ethers (**3**) using methylketene methyl trimethylsilyl acetal[5] (**1**) in the presence of a catalytic amount of TBAF and the application of this silylation method to the synthesis of cyclic acetals (**4**; including thioacetals) via the trimethylsilyl enol ethers **3** by a one-pot procedure under mild conditions.



The *O*-silylation of ketones **2** to give the silyl enol ethers **3** is generally carried out under weakly basic conditions employing equivalent amounts of reagent **1** and substrate **2** in tetrahydrofuran containing a catalytic amount of TBAF. The silylation proceeds to completion within 1-2 h at 20 °C (**2a-e**) or even within 2 h at −78 °C (**2f**). The yields of silyl enol ethers **3** thus obtained are generally high and comparable to or better than those reported[2] for the silylation of **2** by other methods.

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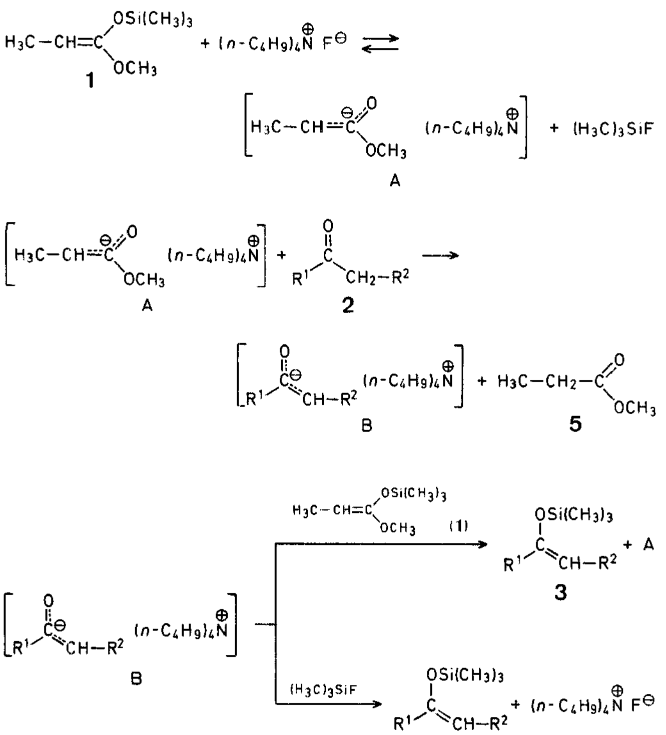
The formation of compounds **3** may be rationalized by the following catalytic cycle which involves the initial reversible formation of the ammonium enolate A. This enolate A undergoes anion exchange with the ketone **2** to give the ammonium enolate B which is then *O*-silylated by reagent **1**[6] and/or fluorotrimethylsilane[3].



The *O*-silylation **2**→**3** using reagent **1** may be utilized for a facile one-pot acetalization of ketones **2** since silyl enol ethers (**3**) are known to be versatile intermediates for acetal formation under mild conditions[7] and methyl propanoate (**5**), the only by-product, may be separated from the product acetals **4** by distillation. Thus, the cyclic *O,O*-, *O,S*-, and *S,S*-acetals **4a, d** ($Y^1 = Y^2 = O$), **4b** ($Y^1 = O$, $Y^2 = S$), and **4c** ($Y^1 = Y^2 = S$) were obtained from ketones **2** and ethylene glycol, 2-mercaptoethanol, or 1,2-ethanedithiol, respectively, in the presence of a catalytic amount of concentrated hydrochloric acid.

The acetalization method described here is advantageous over the known methods[8] in terms of mild reaction conditions and short reaction times. A one-pot procedure for the introduction of various electrophiles into the α-position of enolizable carbonyl compounds by utilizing the present silylation method is currently under investigation[9].

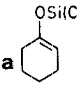
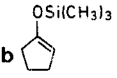
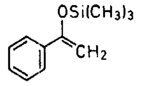
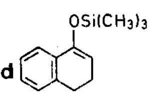
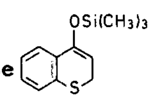
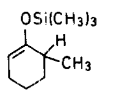
Trimethylsilyl Enol Ethers (3a-f); General Procedure:

To a stirred mixture of the enolizable ketone **2** (3 mmol), TBAF (7.8 mg, 0.03 mmol), and dry tetrahydrofuran (3 ml), reagent **1** (481 mg, 3 mmol) is added dropwise at room temperature under argon. The mixture is stirred for 1 h under the same conditions and is then diluted with pentane (10 ml). A small quantity of unsoluble material is filtered off and the filtrate is concentrated under reduced pressure to give the silyl enol ether **3**. Pure samples are obtained by distillation under the conditions listed in Table 1.

One-Pot Conversion of Enolizable Ketones (2) into *O,O*-, *O,S*-, and *S,S*-(1,2-Ethanediyl) Acetals (4) via Silyl Enol Ethers (3); General Procedure:

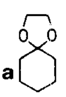
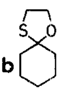
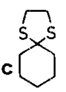
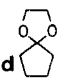
To a stirred mixture of the enolizable ketone **2** (4 mmol), TBAF (10.5 mg, 0.04 mmol), and dry tetrahydrofuran (4 ml), reagent **1** (641 mg, 4 mmol) is added dropwise at room temperature under argon. Stirring is continued for 1 h and then, 1,2-ethanediol (248 mg, 4 mmol), 2-mercaptoethanol (313 mg, 4 mmol), or 1,2-ethanedithiol (337 mg, 4 mmol) is added followed by the addition of conc. hydrochloric acid (~0.2 ml or 2 drops). Stirring is continued at room temperature for 30 min. The mixture is diluted with ether (50 ml), washed with saturated sodium hydrogen carbonate solution (10 ml) and with water (10 ml), and concentrated under reduced pressure. The pure acetal **4** is obtained by distillation of the residue under the conditions given in Table 2.

Table 1. Trimethylsilyl Enol Ethers (3) prepared

Product[a]	Reaction conditions [h], [°C]	Yield [%]		b.p./torr[d] [°C]	
		crude product[b]	distilled product[c]	found	reported
3a 	1, 20°	90	70	78-80°/22	74-75°/20[10]
3b 	1, 20°	92	73	78-80°/50	158-159°/76[10]
3c 	2, 20°	95	81	97-98°/16	93-94°/14[11]
3d 	2, 20°	93	87	120-123°/16	95-98°/0.8[12]
3e 	1, 20°	95	79	160-162°/3	115-118°/0.75[12]
3f 	2, −78°	80	68	50-55°/5	59-61°/7[10]

[a] All products were identified by comparison with authentic samples.
[b] Purity >90% as determined by G.L.C. and ¹H-N.M.R. analysis.
[c] Preparation of a 3-4 mmol scale.
[d] Uncorrected.

Table 2. Cyclic *O,O*-, *O,S*-, and *S,S*-Acetals (4) prepared[a]

Product	Yield[b] [%]	b.p./torr[c] [°C]	
		found	reported
4a 	66	78-80°/18	88-90°/28[7]
4b 	61	102-104°/16	119°/25[7]
4c 	63	120-123°/8	107°/5[13]
4d 	43	65-67°/41	57°/18[14]

[a] Conditions are given in the general procedure.
[b] Yield of distilled product which was identified by comparison with an authentic sample.
[c] Uncorrected.

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* Address for correspondence.

[1] A conjugated addition of ketene silyl acetals to α,β-unsaturated carbonyl compounds leading to methyl jasmonates and related compounds has been reported: Y. Kita, J. Segawa, J. Haruta, H. Yasuda, Y. Tamura, *J. Chem. Soc. Perkin Trans. 1* **1982**, 1099.

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E. Nakamura, T. Murofushi, M. Shimizu, I. Kuwajima, *J. Am. Chem. Soc.* **98**, 2346 (1976).

[4] G. A. Olah, B. G. B. Gupta, S. C. Narang, R. Malhotra, *J. Org. Chem.* **44**, 4272 (1979).

[5] Reagent **1** and related reagents have been shown to be useful for silylation of *H*-acidic materials and for conjugate addition of α,β-unsaturated carbonyl compounds.
Silylation:
Y. Kita, J. Haruta, J. Segawa, Y. Tamura, *Tetrahedron Lett.* **1979**, 4311.
Y. Kita, J. Haruta, T. Fujii, J. Segawa, Y. Tamura, *Synthesis* **1981**, 451.
Y. Guindon, R. N. Young, R. Frenette, *Synth. Commun.* **11**, 391 (1981).
Conjugate addition[1]:
Y. Kita, J. Segawa, J. Haruta, T. Fujii, Y. Tamura, *Tetrahedron Lett.* **21**, 3779 (1980).

[6] Cyclohexanone lithium enolate generated from cyclohexanone *O*-silyl enol ether and butyllithium was found to react with **1** to give **3a** under the same conditions.

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D. R. Morton, S. J. Hobbs, *J. Org. Chem.* **44**, 656 (1979).
B. S. Ong, T. H. Chan, *Synth. Commun.* **7**, 283 (1979).
B. S. Ong, *Tetrahedron Lett.* **21**, 4225 (1980).
T. Tsunoda, M. Suzuki, R. Noyori, *Tetrahedron Lett.* **21**, 1357 (1980).
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[9] We have now succeeded in the one-pot preparation of 2-bromocyclohexanone by addition of *N*-bromosuccinimide to the crude mixture resulting from the reaction of ketone **2a** with reagent **1** [73% yield, based on **2a**; b.p. 73-75 °C/0.6 torr (Ref.[15], b.p. 40-42 °C/0.01 torr)].

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