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Notes

Preparation of Silyl Enol Ethers by the Reaction of Ketones with Silylamines and Methyl Iodide

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Summary: Transformation of ketones to silyl enol ethers using (trimethylsilyl)diethylamine and methyl iodide is described. Both cyclic and acyclic ketones gave silyl enol ethers in high yield, whose stereochemistry showed that the formation of thermodynamically stable isomers was favored. A cyclic diketone, 1,4-cyclohexanedione, gave a 1:1 mixture of 1,4-bis((trimethylsilyl)oxy)-1,3-cyclohexadiene and 1,4-bis((trimethylsilyl)oxy)-1,4-cyclohexadiene, while 1,3-cyclohexanedione gave 3-((trimethylsilyl)oxy)-2-cyclohexenone alone. The tert-butyldimethylsilyl enol ethers of ketones also were obtained in high yield when (tert-butyldimethylsilyl)diethylamine, combined with methyl iodide, was used. A combination of allyl bromide and (trimethylsilyl)diethylamine was also effective for the transformation of ketones to silyl enol ethers.

Introduction

It is well-known that silyl enol ethers are useful intermediates in organic synthesis, and many methods for their preparation have been developed.[2] Those reported thus far involve the silylation of ketones and aldehydes by trimethylsilyl trifluoromethanesulfonate,[3] allyltrimethylsilane assisted by trifluoromethanesulfonic acid,[4] iodotrimethylsilane,[5] chlorotrimethylsilane combined with a tertiary amine,[6] lithium amide[6a] or alkali-metal hydride,[7] *N*,*O*-bis(trimethylsilyl)acetamide,[8] and hydrosilane catalyzed by cobalt carbonyl.[9] In this paper, we report a convenient preparation of silyl enol ethers by use of (trimethylsilyl)diethylamine in the presence of stoichiometric methyl iodide. We previously reported that (trialkylsilyl)dialkylamines combined with methyl iodide show a reactivity similar to that of iodotrialkylsilane in the dealkylation of esters,[10a] the double silylation of primary amines,[10b] and the ring opening of oxiranes.[10c] During the course of this study we have found that the above combination is useful for the preparation of silyl enol ethers.

Results and Discussion

A representative general procedure for the transformation of ketone to silyl enol ether with silylamine and halide is as follows. A solution of silylamine **2** (1.2 equiv) and halide **3** (1.3 equiv) dissolved in benzene was heated at 50−60 °C for 1 h. Ketone **1** (1 equiv) was added gradually, keeping the temperature at 50−60 °C. The mixture was stirred at 70−80 °C. After the ammonium salt was filtered from the reaction mixture, the silyl enol ether **4** was isolated by evaporation of solvent, followed by distillation at the reduced pressure. The examples of cyclic monoketones are shown in Table 1.

$$\mathrm{R{-}CH_2\underset{\overset{\|}{O}}{C}{-}R^1 + R^2Me_2SiNR^3{}_2 + R^4X \longrightarrow R{-}CH{=}\underset{\overset{|}{OSiMe_2R^2}}{C}{-}R^1 + R^3{}_2R^4HN^+X^-}$$

1 **2** **3** **4**

The isolation of products is comparatively easy, as the readily removable hydrocarbon solvent such as benzene or toluene can be recycled and the ammonium salts formed during the reaction can be separated readily by filtration. *tert*-Butyldimethylsilyl enol ethers are obtained in high yield, although somewhat longer reaction times are necessary, compared to those for trimethylsilyl derivatives. The silyl enol ethers derived from 2-me-

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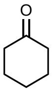
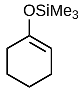
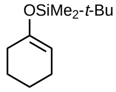
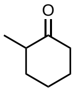
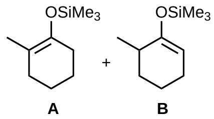
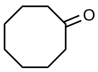
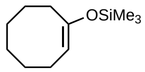
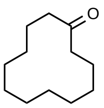
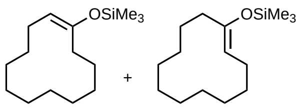
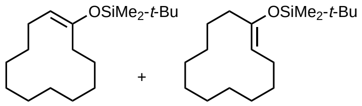
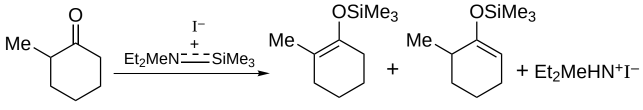
Table 1. Preparation of Silyl Enol Ethers from Cyclic Ketones

ketone **1**	silyl enol ether **4**	silylamine **2**/halide **3**	reacn[a] time (h)	reacn temp (°C)	yield (%)[b]
		Et_2NSiMe_3/MeI	1.5	50−70	89
		Me_2NSiMe_3/MeI	1	60−80	93
		$Et_2NSiMe_3/CH_2{=}CHCH_2Br$	3	60−80	92
		Et_2NSiMe_2-*t*-Bu/MeI	5	75−80	94
		Et_2NSiMe_3/MeI	3.5	58−60	89 (**A**:**B** = 84:16)[c]
		Et_2NSiMe_3/MeI	1.5	75−78	90 (**A**:**B** = 81:19)[c]
		Et_2NSiMe_3/MeI	2	60−75	91
		Et_2NSiMe_3/MeI[d]	3	60−80	95 (*E*:*Z* = 35:65)[c]
		Et_2NSiMe_2-*t*-Bu/MeI[d]	13	60−80	91 (*E*:*Z* = 38:62)[c]

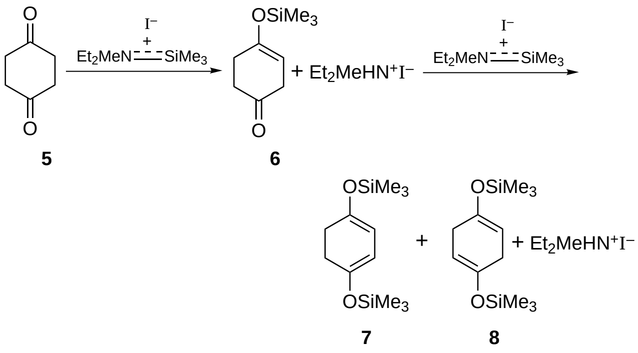
[a] Reaction time includes the addition time of ketones to the mixture of silyl amine and halide. [b] Isolated yield. [c] The ratio is a GC peak ratio of isomers included in the crude reaction mixture. [d] Toluene was used as a solvent instead of benzene.

thylcyclohexanone and cyclododecanone predominantly contained the thermodynamically more stable isomers.



isomer ratio 84:16

The silylation of 1,4-cyclohexanedione at 70−80 °C for 1.5 h gave a 1:1 mixture of 1,4-bis((trimethylsilyl)oxy)-1,3-cyclohexadiene and 1,4-bis((trimethylsilyl)oxy)-1,4-cyclohexadiene in 88% total yield.[11a] The monosilylated ketone **6** was observed as the initial product by gas chromatography. The isomer ratio of the cyclohexadiene products **7** and **8** did not change on prolonged stirring after the complete consumption of starting diketone **5** and monosilylated ketone **6**.



isomer ratio 50:50

On the other hand, the reaction of 1,3-cyclohexanedione with 1.5 equiv each of (trimethylsilyl)diethylamine and methyl iodide at room temperature for 0.5 h gave only the monosilylated product 3-((trimethylsilyl)oxy)-2-cyclohexenone in 60% yield.[11b] Furthermore, even with a prolonged reaction time at higher temperature with more than 2 equiv of silylamine and methyl iodide, the production of 1,3-bis((trimethylsilyl)oxy)-1,3-cyclohexadiene was not observed.

The silylation of the symmetric acyclic ketones 3-pentanone at 70−75 °C for 2 h and 4-heptanone at 70−75 °C for 3.5 h also gave the corresponding silyl enol ethers 3-((trimethylsilyl)oxy)-2-pentene and 4-((trimethylsilyl)oxy)-3-heptene in 87% and 83% total yield whose ratios of *E* and *Z* isomers were 22:78 and 40:60, respectively. Unsymmetrical 2-heptanone gave an isomer mixture of 2-((trimethylsilyl)oxy)-1-heptene and (*E*)- and (*Z*)-2-((trimethylsilyl)oxy)-2-heptene in 82% total yield whose isomer ratio was 21:21:58, respectively.

As mentioned above, the results indicate that (a) the formation of thermodynamically more stable silyl enol ethers is favored, which is analogous to the previously reported results obtained using a combination of amine and halosilane,[3a,5a,6a,11b] and (b) the isomer balance of silyl enol ethers produced did not change under the present reaction conditions. Accordingly, it is presumed that the reaction proceeds by capturing the enol isomer effectively from the mixture of keto and enol tautomers, because the adduct, obtained from silylamine and organic halide, is a very active silylating reagent as shown previously.[10b]

In summary, the combination of silylamine and methyl iodide is a useful silylating reagent for ketones and provides a convenient method for the preparation of silyl enol ethers.

Experimental Section

General Remarks. Commercially available ketones, toluene, benzene, methyl iodide, and allyl bromide were used without purification. (Trimethylsilyl)diethylamine, (trimethylsilyl)dimethylamine, and (*tert*-butyldimethylsilyl)diethylamine were prepared by reaction of diethylamine and di-

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(11) (a) Torkelson, S.; Ainsworth, C. *Synthesis* **1977**, 431. (b) Torkelson, S.; Ainsworth, C. *Synthesis* **1976**, 722.

methylamine with chlorotrimethylsilane and *tert*-butylchlorodimethylsilane, respectively. Gas chromatography was carried out with a Hewlett-Packard Model HP6890 instrument equipped with a Hewlett-Packard Model HP-5 capillary column. IR spectra were recorded on a JASCO IR-810 spectrometer. ^{1}H NMR spectra were obtained using a JEOL JNM-PMX60si spectrometer, and ^{13}C and ^{29}Si NMR were obtained using a JEOL FT-NMR EX-90 and a Lambda-300WB spectrometer. GC−MS spectra were measured by a Hewlett-Packard GCD system.

Illustrative Procedure for the Preparation of the Trimethylsilyl Enol Ether. In a four-necked flask, equipped with a mechanical stirrer, a condenser, a thermometer, and a dropping funnel, was placed 87.0 g (0.60 mol) of (trimethylsilyl)diethylamine, 93.7 g (0.66 mol) of methyl iodide, and 100 mL of benzene. The mixture was heated at 50−60 °C for 1 h. To this solution was added 49.0 g (0.50 mol) of cyclohexanone over a period of 0.5 h. The mixture was stirred at 70−80 °C for 1 h, until the ketone was consumed as shown by gas chromatography. After the formed ammonium salt was separated by filtration, the solvent and volatile materials were evaporated and the residue was fractionally distilled under reduced pressure to give 76.0 g of 1-((trimethylsilyl)oxy)cyclohexene, bp 65 °C/16 Torr.

All silyl enol ethers were identified by comparison of their spectral data with those of authentic samples or with those described in the literature.[5,6,11−16] Furthermore, *E* and *Z* isomers of silyl enol ether were assigned on the basis of NOE between protons on the carbons adjacent to the double bond, an olefinic proton, and protons of the (trimethylsilyl)oxy group in addition to the data described in the literature.[6a,12] The assignment of isomers of 1-((trimethylsilyl)oxy)cyclododecene was carried out using each isomer fraction enriched to 80% purity by fractional distillation.

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