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REGIO- AND STEREODEFINED SYNTHESIS OF TRIMETHYLSILYL ENOL ETHERS RESULTED FROM THE ISOMERIZATION OF α-TRIMETHYLSILYL KETONES

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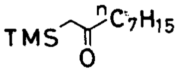
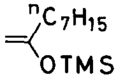
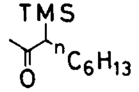
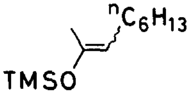
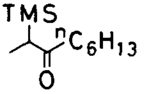
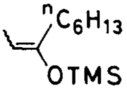
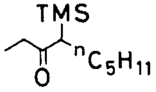
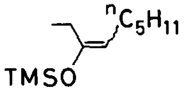
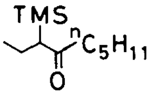
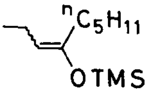
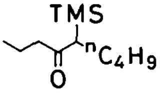
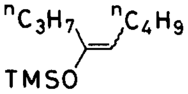
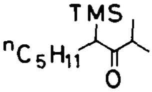
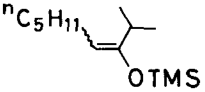
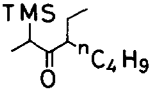
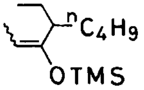
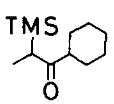
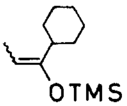
Summary: The isomerization of an α-trimethylsilyl ketone is lead to the corresponding trimethylsilyl enol ether with the enhanced regioselectivity by heating or by the assist of trimethylsilyl trifluoromethanesulfonate.
The thermal reaction discloses a new regiodefined (E)-selective route to silyl enol ethers.

Silyl enol ethers have been employed as one of the most promising nucleophilic substrates resulting carbon carbon bond formation or functionalization onto α-carbons of carbonyl compounds in organic synthesis.[1] Since the conventional method for their preparation includes the silylation of preformed enolate anion, it is difficult to differentiate two α-positions of an unsymmetrically substituted ketone except the case of which the appreciable energy difference is present between two enolate forms.[2] Stereochemical control forming enolate anion is also pursued related to stereoselective aldol reactions.[3] Few methods have succeeded to control the stereochemistry of enolate anions, (Z)- or (E)-selectively in the case of freed from regiochemistry[4].

Recently, the reliable regioselection of an unsymmetrical ketone have been attained by two indirect methods depending on the isomerization of α-trimethylsilyl-[5] or β-trimethylsilylallyl alcohols.[6] The former method gave **2** (Z)-selectively as the result of the intermediacy of equilibrated homoenolate anion. On the contrary, the latter one suggested (E)-selective formation of **2** as the result of consecutive isomerization of isolable α-trimethylsilyl ketone. Therefore, the isolated α-trimethylsilyl ketone would promise the regio- and stereocontrol in the formation of trimethylsilyl enol ethers. We describe herein a successful method to control the regio- and stereochemistry of trimethylsilyl enol ethers in unsymmertrically substituted ketones.

Since the regiodefined synthesis of aliphatic α-trimethylsilyl ketones was attained by the rhodium catalyzed methods under the nonaqueous

Table 1. Results of the isomerization of α-trimethylsilyl ketones.

Entry	α-Silyl ketone (1)		Silyl enol ether (2)	Method[i]	Yield[ii] (%)	E/Z[iv]
1		a		A	56[iii]	-
2				C	92(1)	-
3		b		A	100(1)	93/7
4				C	86(1)	11/89
5		c		A	96(0.5)	93/7
6				B	97(2)	75/25
7				C	95(0.5)	14/86
8				D	90(1)	25/75
9		d		A	98	96/4[v]
10				B	90	78/22[v]
11				C	95(2)	28/72[v]
12				D	96	18/82[v]
13		e		A	97(0.5)	93/7
14				C	89	19/81
15		f		A	98	95/5[v]
16				C	86	21/79[v]
17		g		A	97	98/2
18		h		A	94	94/6
19		i		A	96	94/6

i, A; neat/175°C/15 min. B; 5 mol% $HRh(CO)(PPh_3)_3/C_6H_6/105°C/12h$.
C; 10 mol% $Me_3SiOTf/(Me_3Si)_2NH/CH_2Cl_2/0°C/5$ min.
D; 5 mol% $Me_3SiI/HgI_2/(Me_3Si)_2NH/CH_2Cl_2$/r.t./15 h.

ii, Distilled yield. The content of the regioisomers is shown in parentheses.

iii, 35% of 1a was recovered.

iv, The ratio was determined by GLC analyses (OV 101, 50m column).

v, The ratio was determined by GLC analyses (PEG-HT Bonded, 25m column).

conditions[6b, 7] a series of silylated nonanones (1a - 1f) was designed and isolated in order to evaluate the regio- and stereoselectivity of the resultant silyl enol ethers 2. Results are summarized in Table 1.

First of all 3-nonanone derivatives 1c and 1d were checked under the following conditions; heat (method A), $HRh(CO)(PPh_3)_3$ catalysis (method B), Me_3SiOTf catalysis (method C),[8, 9] and Me_3SiI catalysis (method D).[8] The reaction of 1c and 1d proceeded smoothly to give 2c and 2d, respectively under all conditions. The π-bond location of the resultant 2c and 2d is strictly (more than 98% selectivity[10]) directed to the original position of trimethylsilyl group in 1. Different from the regiochemistry, the stereoselectivity depends on the reaction conditions. (E)-Form of 2c and 2d was obtained selectively in method A or B (entry 5, 6, 9, and 10), whereas (Z)-form was given predominantly in method C or D (entry 7, 8, 11, and 12). Based on the above results, methods A and C were applied to the other α-silyl ketones as the standard conditions.

An excellent (E)-selective formation of 2 is observed in the thermal isomerization of 1 except 1a. It is noteworthy that such a high (E)-selectivity can be attained even in the formation of 2g, 2h, and 2i where the selection of (E)-form is relatively difficult in the conventional method. The present method is sharply contrasted with Kuwajima's work[5] which brought about 2, (Z)-selectively and discloses a novel route to the (E)-selective formation of 2. The high (E)-selectivity can be rationalized by the concerted intramolecular migration of the trimethylsilyl group via the four membered transition state which was proposed in the thermal isomerization of silylmethyl ketones.[12]

On the other hand, Me_3SiOTf catalyzed isomerization of 1 gives predominantly (Z)-2. The reverse selectivity in method C is pertinent to the intermolecular migration of the trimethylsilyl group mediated by the catalyst.[13] Thus, the regio- and stereoselection can be attained uniformly by this approach in the formation of trimethylsilyl enol ethers derived from unsymmetrically substituted ketones. Although (Z)-selectivity in 2 is rather moderate in the present time, it is important to make possible the choice of the stereochemical course from the identical starting materials.

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