Tetrahedron Letters, Vol. 34, No. 31, pp. 4985-4988, 1993
Printed in Great Britain

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

Rearrangement of β-*tert*-Butyldimethylsiloxy Carbenoids. Regio- and Stereoselective Synthesis of (Z)-1-Halo-2-*tert*-butyldimethylsiloxy-1-alkenes

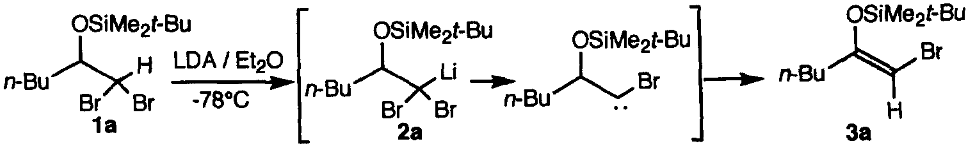
Hiroshi Shinokubo, Koichiro Oshima,* and Kiitiro Utimoto*

Department of Material Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

Abstract: Treatment of an ether solution of 1,1-dihalo-2-*tert*-butyldimethylsiloxyalkane **1** with lithium diisopropylamide at -78 °C gave lithium carbenoid **2** which provided (Z)-1-halo-2-*tert*-butyldimethylsiloxy-1-alkene regio- and stereoselectively upon warming to room temperature.

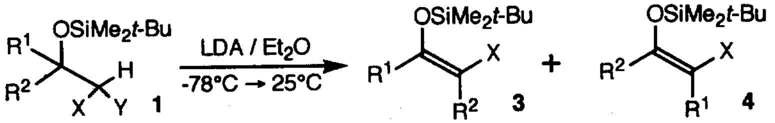
The utility of silyl enol ethers as versatile intermediates in organic synthesis is well recognized and numerous studies have been devoted to the development of methods for the preparation of such compounds.[1] We recently reported[2] that an addition of *tert*-butyldimethylsilyldihalomethyllithium to carbonyl compound provided silyl ether **1** through 1,3-migration of silyl group from carbon to oxide. Here we wish to describe that deprotonation of **1** with lithium diisopropylamide in ether at low temperature forms β-*tert*-butyldimethylsiloxy lithium carbenoid **2** which loses LiBr (or LiCl) on warming, and rearranges through a carbene intermediate to (Z)-1-halo-2-*tert*-butyldimethylsiloxy-1-alkene **3**[3] stereoselectively.

A solution of *tert*-butyldimethylsilyl ether **1a** (0.37 g, 1.0 mmol) in ether (2 ml) was added to a solution of lithium diisopropylamide (1.2 mmol) in ether (3 ml) at -78 °C. After stirring for 1 h at -78 °C,[4] the cold bath was removed and the reaction mixture was warmed to room temperature. The resulting mixture was stirred for another 1 h. Extractive workup (hexane, 1 *M* HCl) followed by purification by short silica-gel column gave silyl enol ether **3a**[5] (0.27 g) in 93% yield.



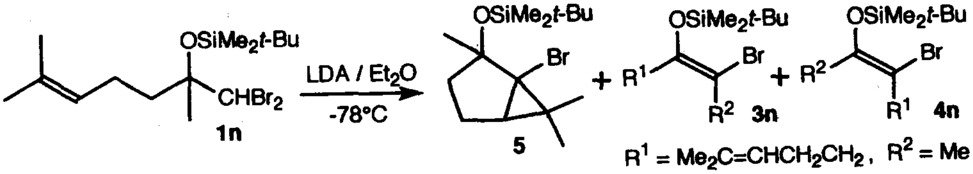
The representative results are shown in Table 1. Several comments are worth noting. (1) In the case of *tert*-butyldimethylsilyl ethers **1a**-**1i**, generated from aldehydes, hydrogen migrated selectively to give 1-halo-2-*tert*-butyldimethylsiloxy-1-alkenes regioselectively with exceptional examples of **1d** and **1e**. Treatment of **1d** (or **1e**) with lithium diisopropylamide provided a mixture of **3d** and **4d** (or **3e** and **4e**). Phenyl group migration or styryl group migration competed with hydrogen migration and phenyl or styryl group migrated preferentially. (2) Whereas dichloride **1g** and bromofluoro compound **1h** were equally reactive as dibromides

Table 1. Preparation of (*Z*)-1-halo-2-*tert*-butyldimethylsiloxy-1-alkenes

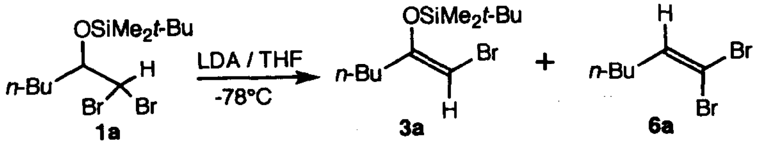


Entry		Substrate R^1	R^2	X	Y	Yield (%) 3	4
1	**1a**	*n*-Bu	H	Br	Br	93	0
2	**1b**	*t*-Bu	H	Br	Br	97	0
3	**1c**	Me	H	Br	Br	85	0
4	**1d**	Ph	H	Br	Br	21	72
5	**1e**	PhCH=CH	H	Br	Br	19	77
6	**1f**	$MeCH{=}CHCH_2CH_2$	H	Br	Br	95	0
7	**1g**	*n*-Hex	H	Cl	Cl	95	0
8	**1h**	n-C_9H_{19}	H	F	Br	82	0
9	**1i**	*n*-Hex	H	Cl	Br	97	0
10	**1j**	Me	Me	Br	Br	45	0
11	**1k**	Me	Ph	Br	Br	95	0
12	**1l**	-(CH2)4-		Br	Br	99	0
13	**1m**	Me	Et	Br	Br	42	21

and gave the corresponding 1-chloro- and 1-fluoro-2-*tert*-butyldimethylsiloxy-1-alkene (**3g** and **3h**), diiodide n-$C_6H_{13}CH(OSiMe_2{}^tBu)CHI_2$ did not provide 1-iodo-2-*tert*-butyldimethylsiloxy-1-octene and afforded n-$C_6H_{13}CH{=}CI_2$ (30%) along with recovered starting material. (3) Silyl ether **1i** (1 : 1 diastereoisomeric mixture), prepared from heptanal by an addition of bromochloromethyllithium followed by silylation, provided (*Z*)-1-chloro-2-*tert*-butyldimethylsiloxy-1-octene as a single product. No trace of (*Z*)-1-bromo-2-*tert*-butyldimethylsiloxy-1-octene was observed in the reaction mixture (Entry 9).[6] (4) Silyl ethers **1j**-**1m**, generated from ketones and *tert*-butyldimethylsilyldibromomethyllithium,[7] also gave (*Z*)-silyl enol ethers stereoselectively upon treatment with lithium diisopropylamide, although the rearrangement proceeded slowly compared to the reaction of **1a**-**1l**. 1,1-Dibromo-2-*tert*-butyldimethylsiloxy-2-methylbutane **1m** provided a mixture of (*Z*)-3-bromo-2-*tert*-butyldimethylsiloxy-2-pentene and (*Z*)-2-bromo-3-*tert*-butyldimethylsiloxy-2-pentene (66 : 34). In contrast, 1,1-dibromo-2-*tert*-butyldimethylsiloxy-2-phenylpropane **1k** gave 3-bromo-3-phenyl-2-*tert*-butyldimethyl-siloxy-2-propene **3k** exclusively (Entry 11). Thus, the migratory aptitudes were in the order phenyl ~ hydrogen >> alkyl. Ring-enlargement product was obtained from **1l**.[8] (5) (*Z*)-1-Halo-2-*tert*-butyldimethylsiloxy-1-alkenes were produced with high stereoselectivity (*Z*/*E* = >99/1)[9] for all of the substrates examined with an exceptional case of **1j**, whose selectivity was somewhat low (*Z*/*E* = 96/4). (6) An attempt to trap an intermediary carbene with olefins intramolecularly failed in the reaction of **1f** with lithium diisopropylamide (Entry 6).[10] Thus, 1,2-hydrogen shift was much faster than intramolecular cyclopropane formation.[11] However, an intermediary carbene could be trapped in the case of **1n** to give bicyclo[3.1.0]hexane **5** in 50% yield in addition to the rearranged products (**3n** and **4n**, 40%).

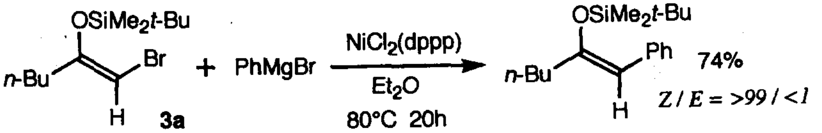


An appropriate choice of the reaction solvent was essential for successful formation of silyl enol ether **3**. Whereas silyl enol ethers were obtained as a single product in diethyl ether, in tetrahydrofuran β-elimination of $LiOSiMe_2{}^tBu$ competed with α-elimination of LiBr and alkylidene dibromides **6** were produced as major products. For instance, treatment of **1a** with lithium diisopropylamide in THF provided a mixture of **6a** (41%) and **3a** (31%).



Replacement of *tert*-butyldimethylsiloxyl group by a trimethylsiloxyl or an ethoxyl group also resulted in a formation of β-elimination product along with α-bromoenol ether. Treatment of *n*-$BuCH(OSiMe_3)CHBr_2$ with lithium diisopropylamide in ether gave 1,1-dibromo-1-hexene **6a** (25%) and (Z)-1-bromo-2-trimethylsiloxy-1-hexene (66%). Moreover, 1,1-dibromo-2-ethoxyhexane afforded 1,1-dibromo-1-hexene **6a** (29%) in addition to 1-bromo-2-ethoxy-1-hexene (55%). Thus, the bulkiness of *tert*-butyldimethylsilyl group plays a critical rôle to lead to α-elimination product selectively.[12]

(Z)-1-Bromo-2-siloxy-1-alkene coupled with Grignard reagents in the presence of Ni catalyst to produce alkylated and arylated silyl enol ethers stereoselectively.[13,14]



References and Notes

1. Colvin, E. W. ***Silicon in Organic Synthesis***, Butterworths and Co Ltd.: London, 1981; pp. 198-287; Colvin, E. W. ***Silicon Reagents in Organic Synthesis***, Academic Press: London, 1988; pp. 99-117.
2. Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1993**, *34*, 1951.
3. Treatment of α-chloroalkanones with hexamethyldisilazane (or triethylamine) and trimethylsilyl iodide has been reported to give regioisomeric mixture of chlorotrimethylsilyl enol ether. For instance, 1-chloro-2-octanone provided 1-chloro-2-trimethylsiloxy-2-octene and 1-chloro-2-trimethylsiloxy-1-octene (75 : 25). Poirier, J.-M.; Hennequin, L. *Syn. Commun.* **1985**, *15*, 217; Miller, R. D.; McKean, D. R. *ibid.* **1982**, *12*, 319. Alternative preparative method for 1-halo-2-trimethylsiloxy-1-alkenes from silyl enol ethers has been reported. Zembayashi, M.; Tamao, K.; Kumada, M. *Synthesis*, **1977**, 422.
4. The carbenoid **2** was not so stable in ether at -78°C. For instance, $PhCH(OSiMe_2\text{-}t\text{-}Bu)CBr_2Li$ **2d**, derived from **1d**, afforded a mixture of **3d** and **4d** in 65% combined yield along with recovered **1d** (27%)

upon treatment with MeOH after stirring for 30 min at -78 °C. On the other hand, the carbenoid **2d** was stable in THF at -78°C and **1d** was recovered almost quantitatively (97%) under the same reaction conditions.

5. **3a**: IR (neat) 2954, 2928, 2856, 1635, 1465, 1255, 1005, 958, 838, 780, 724, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.20 (s, 6H), 0.89 (t, *J* =7.1 Hz, 3H), 0.98 (s, 9H), 1.20-1.55 (m, 4H), 2.09 (t, *J* = 7.6 Hz, 2H), 5.19 (s, 1H); ^{13}C NMR (C_6D_6) δ -3.23, 14.42, 19.08, 22.73, 26.43, 29.49, 36.55, 85.05, 155.31. Found: C, 49.32; H, 8.36%. Calcd for $C_{12}H_{25}BrOSi$: C, 49.14; H, 8.59%. The (*Z*)-stereochemistry was assigned by NOE experiment. The compound **3a** showed NOE (16%) between the olefinic proton and allylic methylene protons.
6. This result might suggest that the rearrangement did not proceed directly from lithium carbenoid and proceeded through a carbene intermediate.
7. Reaction of *tert*-butyldimethylsilyldibromomethyllithium and ketone gave the desired silyl ethers in fair to good yield. However, some of silyl ethers were prepared more conveniently by the silylation (*t*-$BuMe_2SiOTf$ and 2,6-lutidine) of dibromohydrins $R^1R^2C(OH)CHBr_2$, produced by the addition of dibromomethyllithium to ketones following to the reported procedure. Taguchi, H.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* **1972**, 4661; Köbrich, G.; Grosser, J. *ibid.* **1972**, 4117; Villieras, J.; Bacquet, C.; Normant, J. F. *J. Organomet. Chem.* **1972**, *40*, C1.
8. Ring enlargement reaction via β-oxido carbenoid has been reported (Taguchi, H.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1592; *idem*, *Tetrahedron Lett.* **1976**, 2617). Treatment of dibromohydrins ($R^1R^2C(OH)CHBr_2$, $R^1 = R^2 = -(CH_2)_n-$) with two equivalents of base affords the *monobromo dianion* by lithium-bromine exchange. On warming, this β-oxido carbenoid loses LiBr to give a carbene, which rearranges with migration of a substituent to form the enolate of the expanded ketones. In contrast, when silyl ether **11** were exposed to lithium diisopropylamide, deprotonation occurs to produce the *dibromo anion* which produce 1-bromo-2-siloxy-1-cycloalkene.
9. Theoretical studies of the reactions of carbene systems have shown that the planar double bond geometry of the product is already achieved in the hydrogen 1,2-shift transition structure (Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 9148). Thus, selective formation of (*Z*)-isomer might be attributed to a steric repulsion between bromine and alkyl group which is larger than that between bromine and siloxy group. Indeed, the calculation on MacroModel (kindly provided by Still, W. C. at Columbia University) indicates that (*Z*)-$MeC(OSiMe_3)=CHBr$ is about 1.5 Kcal/mol more stable than (*E*)-isomer.
10. In addition, intermolecular trap with large excess of 2,3-dimethyl-2-butene in the reaction of **1c** with lithium diisopropylamide also failed and the reaction gave **3c** exclusively.
11. Kirmse has reported that β-alkoxyl substituent enhances the migration of hydrogen to carbene center substantially. Kirmse, W.; Buschoff, M. *Chem. Ber.* **1967**, *100*, 1491; Taylor, K. G. *Tetrahedron*, **1982**, *38*, 2751.
12. Villieras *et al.* have reported the competition of α- and β-elimination of β-alkoxy and β-siloxy α,α-dichlorocarbenoids. Villieras, J.; Bacquet, C.; Normant, J. F. *J. Organomet. Chem.* **1975**, *97*, 355.
13. Tamao, K.; Zembayashi, M.; Kumada, M. *Chem. Lett.* **1976**, 1239.
14. Financial supports by the Ministry of Education, Science and Culture of Japan (Grant-in-Aid for Scientific Research No. 04453098) and Asahi Glass Foundation for Industrial Technology are acknowledged.

(Received in Japan 24 April 1993)