Ring-Opening Iodo- and Bromosilation of Cyclic Ethers by Treatment with Iodo- and Bromotrialkylsilane Equivalents

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Introduction

Iodo- and bromosilanes play a vital role in organic synthetic chemistry, and their synthetic utilities have been demonstrated.[1] Interaction of cyclic ethers with iodo- or bromotrimethylsilane affords the respective ring-opened iodo- or bromosilation products in good yields.[2] Iodo- and bromosilanes, however, exhibit a high tendency to undergo hydrolytic cleavage of the Si−halogen bond with atmospheric moisture, leading to the formation of the respective silanols, unless the silicon atom is substituted by protecting substituent(s) with appropriate steric bulkiness,[3] and therefore, iodo- and bromosilanes are usually difficult to handle as compared with the other halosilanes, chloro- and fluorosilanes.

Recently, we have reported that 1:1 mixtures of diethylaminotrimethylsilane with methyl iodide (Et_2NSiMe_3/MeI) and allyl bromide (Et_2NSiMe_3/AllylBr) behave as synthetic equivalents of iodo- and bromotrimethylsilane, respectively, and the reactions with epoxides afford the corresponding ring-opened 1,2-halosilation products.[4] The reagent of Et_2NSiMe_3/MeI reacts also with alkyl esters to give high yields of trimethylsilyl esters with liberation of iodoalkanes.[5] More recently, we have demonstrated that silyl enol ethers are obtained from the reactions of the respective aliphatic ketones with Et_2NSiMe_3/MeI.[6] We also found that treatment of 1:1 mixtures of hydrosilanes and alkyl iodides with a catalytic amount of $PdCl_2$, $R_3SiH/R'I(PdCl_2)$, produces high yields of iodosilanes by hydride−iodide exchange.[7]

To explore further the scope of synthetic utilities of these reaction systems, we studied ring-opening halosilation of five- and six-membered cyclic ethers, which are less strained than epoxides, with the reagents of Et_2NSiMe_3/R^1X and $Et_3SiH/R^1X(PdCl_2)$ (R^1X = MeI, EtI,

EtBr, AllylBr). The reactions led to the one-step synthesis of bifunctional halo(siloxy)alkanes, including a halogenated silyl enol ether. They may be potentially useful in organic synthesis as silyl-protected hydroxyalkyl halides.[8]

Results and Discussion

Table 1 summarizes the ring-opening halosilation of cyclic ethers with the use of iodosilane or bromosilane equivalents **1a,b**. When a mixture of tetrahydrofuran (THF) and 0.99 equiv of the reagent composed of Et_2NSiMe_3 and MeI (**1a**) was heated at 80−90 °C for 5 h in toluene, 1-iodo-4-trimethylsiloxybutane (**3a**) was obtained in 81% isolated yield as shown in Table 1. No other volatile products were detected by either ^{1}H NMR spectrometry and GLC analysis of the reaction mixture. With 2.4 equiv of **1a**, THF was converted into 1,4-diiodobutane (**3c**) in 53% yield, although several unidentified products were also found to be formed in low yields by GC−MS analysis of the reaction mixture. Similarly, tetrahydropyran (THP) underwent smooth iodosilation with reagent **1a** under the same conditions to afford 1-iodo-5-(trimethylsiloxy)pentane (**4a**) in 74% yield. Diiodopentane (**4c**) was obtained in 33% yield from the reaction of THP with 2.8 equiv of **1a**.

A reaction of 2-methyltetrahydrofuran (2-MeTHF) with 1.2 equiv of reagent **1a** gave a 82:18 mixture of iodosilation products **5a** and **6a** in 75% yield. No diiodation products were detected in the reaction mixture, in contrast to the fact that the independent reaction of 2-MeTHF with 1 equiv of Me_3SiI gave 1,4-diiodopentane (**5c**) in 34% yield without any detectable formation of **5a** and **6a**. To obtain better regioselectivity of the iodosilation of 2-MeTHF, we carried out the reactions of 2-MeTHF using bulkier aminosilanes instead of Et_2NSiMe_3. However, attempted iodosilation of 2-MeTHF with $Et_2NSiEtMe_2$/MeI, Et_2NSiEt_3/MeI, and $Et_2NSiPhMe_2$/MeI was unsuccessful, and 2-MeTHF was recovered unchanged from these reactions. No reactions took place when i-PrI or OctylI was used instead of MeI in **1a**. However, with Et_2NSiMe_3/EtI (**1a′**) the reaction proceeded with higher regioselectivity to give a 89:11 mixture of **5a** and **6a** in 73% yield. Similar to THF and THP, 2-MeTHF was transformed into diiodide **5c** in 51% yield by treating it with 2.2 equiv of **1a**. In contrast to the reaction of 2-MeTHF with **1a**, tetrahydrofurfuryl alcohol reacted with 2.0 equiv of **1a** to produce product **7a** exclusively, by the cleavage of the C4−O bond. No products arising from C1−O cleavage were obtained. In this reaction, silation of the hydroxyl group of tetrahydrofurfuryl alcohol would occur prior to the C−O bond cleavage, which gives rise to a bulkier trimethylsiloxy group relative to the methyl group to lead to better regioselectivity.

Heating 2,5-dihydrofuran and **1a** at 80−90 °C for 7 h gave a mixture of stereoisomers, **9a** and **10a**, in a ratio of 96:4 in 67% yield. Monitoring the reaction progress by ^{1}H NMR spectrometry indicated that **9a** was produced as the initial product and was then gradually converted into an equilibrium mixture of **9a** and **10a** (Table 2). The similar reaction of 2,3-dihydrofuran at 50−60 °C led to

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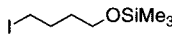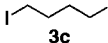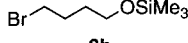(4) Yamamoto, Y.; Shimizu, H.; Matui, C.; Chinda, M. *Main Group Chem.* **1996**, *1*, 409.
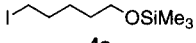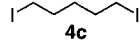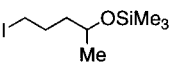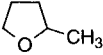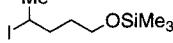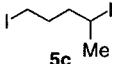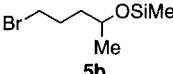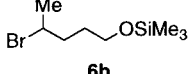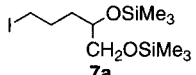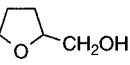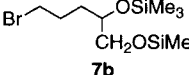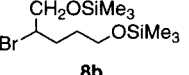
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Table 1. Ring-Opening Halosilation of Cyclic Ethers with Reagent 1 at 80–90 °C[a]

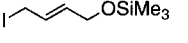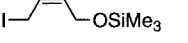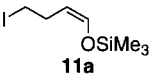| ether	reagent	reagent/ether	time/h	product	yield/% (ratio)
(THF)	1a	0.99	5	I~~OSiMe₃ **3a**	81
	1a	2.4	46	I~~I **3c**	53
	1b	1.1	17	Br~~OSiMe₃ **3b**	76
	1b'	1.0	94[b]		53
(THP)	1a	1.0	16	I~~OSiMe₃ **4a**	74
	1a	2.8	48	I~~I **4c**	33
(2-MeTHF)	1a	1.2	6	I~~OSiMe₃ (Me) **5a** / Me~I~OSiMe₃ **6a**	75 (82/18)
	1a'	1.1	40		73 (89/11)
	1a	2.2	103	I~~I (Me) **5c**	51
	1b	1.1	16	Br~~OSiMe₃ (Me) **5b** / Me~Br~OSiMe₃ **6b**	40 (60/40)
(THFfuryl-CH₂OH)	1a	2.0	6	I~~OSiMe₃, CH₂OSiMe₃ **7a**	75
	1b	2.2	42	Br~~OSiMe₃, CH₂OSiMe₃ **7b** / CH₂OSiMe₃, Br~~OSiMe₃ **8b**	50 (69/31)[d]
	1b	2.5	46[c]		57 (81/19)[e]
(2,5-dihydrofuran)	1a	1.1	7	I~~OSiMe₃ **9a** / I~~OSiMe₃ **10a**	67 (96/4)
(2,3-dihydrofuran)	1a	1.0	12[b]	I~~OSiMe₃ **11a**	60

[a] Reactions were carried out in toluene, using **1a** (Et₂NSiMe₃/2MeI), **1a'** (Et₂NSiMe₃/2EtI), **1b** (Et₂NSiMe₃/2AllylBr), **1b'** (Et₂NSiMe₃/2EtBr). [b] At 50–60 °C. [c] At 110 °C. [d] Trimethylsilyl tetrahydrofurfuryl ether was obtained in 11% yield. [e] Trimethylsilyl tetrahydrofurfuryl ether was obtained in 7% yield.

Table 2. Iodosilation of 1,4-Dihydrofuran with Reagent 1a

temp/°C	time/h	conversion/%	yield/% (**9a/10a**)
25	1	3	3 (0/100)
80–90	1	20	20 (18/82)
80–90	5	84	67 (90/10)
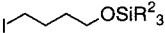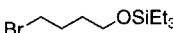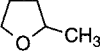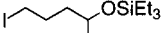
the stereoselective formation of an iodosilation product, **11a**. The reactions of 2,5- and 2,3-dihydrofuran with an excess of reagent **1a** resulted in the formation of complex mixtures and no diiodination products were separated from the reaction mixtures.

When AllylBr was used (reagent **1b**) instead of MeI in **1a**, bromosilation of THF occurred to give product **3b** in 76% yield (Table 1). Using EtBr as the halogen source (**1b'**) also gave the bromosilation product, although the yield was a little lower (53%). In the reaction of 2-tetrahydrofurfuryl alcohol with **1b**, a mixture of regioisomers of bromobis(trimethylsiloxy)pentanes (**7b** and **8b**) was obtained in 50% yield, together with the 11% yield

of a monosilation product, 2-tetrahydrofurfuryl trimethylsilyl ether, in contrast to the iodosilation of 2-tetrahydrofurfuryl alcohol with **1a**, which gave **7a** as the single isomer. Carrying out the reaction of tetrahydrofurfuryl alcohol at higher temperature (110 °C) led to better regioselectivity (81:19) and a slightly hig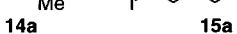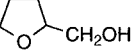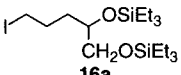her yield (57%). Bromosilation of 2-MeTHF with **1b** proceeded with less regioselectivity, as compared with that with **1a**, to give a 60:40 mixture of products **5b** and **6b**. Reagent **1b** did not react with 2,5- and 2,3-dihydrofuran and THP.

Similar halosilation of cyclic ethers was performed with the use of reagent Et₃SiH/MeI(PdCl₂) (**2a**) and Et₃SiH/AllylBr(PdCl₂) (**2b**). The results are summarized in Table 3. Thus, when THF was treated with 1 equiv of Et₃SiH and MeI in the presence of a catalytic amount of PdCl₂, product **12a** was obtained in 70% yield. Other hydrosilanes, PhMe₂SiH (reagent **2a'**) and Ph₂MeSiH (reagent **2a''**), can also be used as the silyl source to give **12a'** and **12a''**, respectively, although the reactions proceeded

**Table 3. Ring-Opening Halosilation of Cyclic Ethers with Reagent 2 at 80–90 °C[a]**

ether	reagent	reagent/ether	time/h	product		yield/% (ratio)
	2a	1.0	5[b]	I〜〜〜OSiR²₃	**12a** : R² = Et	70
	2a'	0.33	24		**12a'** : R²₃ = PhMe₂	62[d]
	2a''	0.27	92		**12a''** : R²₃ = Ph₂Me	40[d]
	2b	0.65	10	Br〜〜〜OSiEt₃ **12b**		82[d]
	2a	0.99	16[c]	I〜〜〜〜OSiEt₃ **13a**		74
	2a	0.94	6	I〜〜OSiEt₃ / Me OSiEt₃		67[d] (45/55)
	2c	1.0	6	Me / I〜〜		90 (88/12)
	2d	0.70	48	**14a** **15a**		59[d] (86/14)
	2a	2.0	42[c]	I〜〜OSiEt₃ / CH₂OSiEt₃ **16a**		53

[a] Reactions were carried out without solvent, using **2a** (Et₂SiH/MeI(PdCl₂)), **2a'** (PhMe₂SiH/MeI(PdCl₂)), **2a''** (Ph₂MeSiH/MeI(PdCl₂)), **2b** (Et₃SiH/AllylBr(PdCl₂)), **2c** (Et₃SiH/MeI(PdCl₂(PPh₃)₂)), **2d** (Et₃SiH/MeI(Pd(PPh₃)₄)). [b] At room temperature. [c] At 100 °C. [d] Yield based on the silane used.

much slower than that with **2a**. Iodosilation of THP, 2-MeTHF, and 2-tetrahydrofurfuryl alcohol, with **2a** proceeded smoothly to give the expected ring-opened products (**13a**–**16a**). The reaction of 2-MeTHF proceeded less selectively relative to that with **1a**, and a 45:55 mixture of **14a** and **15a** was obtained. In contrast to the reactions with **1a**, those of 2,5- and 2,3-dihydrofuran with reagent **2a** gave complex mixtures and no products analogous to **9a**–**11a** were separated from the mixtures. Palladium complexes, PdCl₂(PPh₃)₄ and Pd(PPh₃)₄ (reagents **2c** and **2d**), can also catalyze the iodosilation of 2-MeTHF with Et₃SiH/MeI, leading to better regioselectivities than **2a**. Bromosilation of THF proceeded with the use of **2b** to give **12b**. However, no reactions of 2,3- and 2,5-dihydrofuran, and THP, took place with reagent **2b**.

In conclusion, we have demonstrated that reagents of Et₂NSiMe₃/R¹X (**1**, R¹X = MeI, EtI, EtBr, AllylBr) and R²₃SiH/R¹X(PdCl₂) (**2**, R¹X = MeI, AllylBr; R²₃ = Et₃, PhMe₂, Ph₂Me) can be used as synthetic equivalents of iodo- and bromosilanes. These reagents reacted with cyclic ethers, leading to the clean formation of halosilation products.

Remarkable changes in regioselectivity observed for iodosilation of 2-MeTHF may provide information on the reactive species. From dominant formation of **5a** with aminosilane reagents **1a** (R¹X = MeI) and **1a'** (R¹X = EtI), actual species in **1a** and **1a'** are postulated to be bulky ammonium salts that are in equilibrium with Me₃SiI, as presented below. This hypothesis is also supported by the fact that the reaction did not occur when bulkier Et₂NSiEtMe₂ and Et₂NSiEt₃ were employed in place of Et₂NSiMe₃.

$$Et_2N-SiMe_3 + R^1I \rightarrow [Et_2R^1N^+-$$
$$SiMe_3]I^- \rightleftarrows Et_2R^1N + Me_3SiI$$
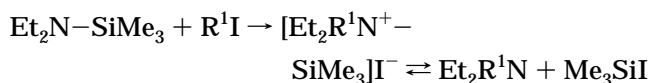
In contrast, the active species in the reaction with hydrosilane reagent **2a** (PdCl₂ catalyst) is undoubtedly free Et₃SiI,[7] resulting in a nearly 1:1 mixture of **14a** and **15a**. Fine black precipitates probably due to metallic Pd were observed in the reaction mixture in this case. On the other hand, a much higher selectivity for **14a** attained with reagent **2c** (PdCl₂(PPh₃)₂ catalyst) and **2d** (Pd-(PPh₃)₄ catalyst) is explained by the formation of homogeneous complexes such as Et₃Si–Pd(L₂)–I as the active species, since clear solutions resulted from these reagent systems.

Experimental Section

Reactions were carried out under an atmosphere of dry argon. Illustrative procedures for halosilation reactions of cyclic ethers with reagents **1** and **2** are as follows.

Reaction of THF with 1a. A mixture of diethylaminotrimethylsilane (7.78 g, 53.7 mmol), THF (3.89 g, 54.0 mmol), methyl iodide (20.3 g, 143 mmol), and toluene (20 mL) was stirred at 80–90 °C for 5 h. After the resulting ammonium salts were filtered, the solvent was evaporated and the residue was distilled under reduced pressure to give 1-iodo-4-trimethylsiloxybutane (**3a**, 11.9 g; 81%).

Reaction of THF with 2a. A mixture of triethylsilane (3.87 g, 33.4 mmol), THF (2.36 g, 32.7 mmol), methyl iodide (6.74 g, 47.5 mmol), and palladium dichloride (70 mg, 0.40 mmol) was stirred at room temperature for 5 h. After evaporation of the excess methyl iodide, the residue was distilled under reduced pressure to give 1-iodo-4-triethylsiloxybutane (**12a**, 7.22 g; 70%).

Supporting Information Available: Detailed experimental procedures and spectral and analytical data for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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