Ring-Opening Iodo- and Bromosilation of Lactones for the Formation of Silyl Haloalkanoates

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Received December 19, 2001

Abstract: Ring-opening halosilation of lactones with two types of reagents, $Et_3SiH/MeI(PdCl_2)$ (**1a**) and $Et_3SiH/AllylBr(PdCl_2)$ (**1b**), was studied. Cyclic esters such as γ-butyrolactones, δ-valerolactone, and 6-hexanolide reacted with 1 equiv of **1a**,**b** to give triethylsilyl ω-iodo- and ω-bromoalkanoates in good yields. Reaction of an acyclic ester, methyl benzoate, with **1a** afforded triethylsilyl benzoate. *O*-Silyl-protected amino acids could be obtained by amination of the halosilation products, triethylsilyl ω-bromoalkanoates.

Iodo- and bromosilanes play an important role in synthetic organic chemistry.[1] However, iodo- and bromosilanes have a strong tendency to undergo hydrolytic cleavage of silicon−halogen bonds even with atmospheric moisture giving silanols, unless the silicon center is protected with sterically bulky substituent(s),[2] and therefore, iodo- and bromosilanes must be handled with special care, compared with chloro- and fluorosilanes.

Recently, we found two types of reagents that can be used conveniently as the synthetic equivalents of iodo- and bromosilanes. One involves a 1:2 mixture of diethylaminotrimethylsilane and methyl iodide or allyl bromide (Me_3SiNEt_2/2RX, RX = MeI, AllylBr),[3−5] while the other comprises 1:1 mixtures of hydrosilanes with methyl iodide or allyl bromide and a catalytic amount of palladium dichloride ($R'_3SiH/RX(PdCl_2)$, R'_3 = Et_3, $PhMe_2$, Ph_2Me, RX = MeI, AllylBr).[6] Both types of the reagents react readily with cyclic ethers, such as tetrahydrofuran and tetrahydropyran, giving ring-opening halosilation products, α-halo-ω-siloxyalkanes.[7] With the reagent Me_3SiNEt_2/RI, the dioxolane rings of cycloalkanone ethylene acetals also undergo the ring-opening halosilation affording siloxyethyl enol ethers,[8] while the reaction of acyclic esters produces trimethylsilyl alkanoates with the liberation of iodoalkanes.[4]

To extend more the utility of these reagents, we examined the reactions of cyclic esters. In this paper, we describe the ring-opening halosilation of five- to seven-membered lactones with the reagent R'_3SiH/RX ($PdCl_2$), which produces triethylsilyl ω-haloalkanoates in good yields. The products thus obtained may be potentially useful starting material for *O*-silyl-protected amino acids.

Table 1 summarizes the results of ring-opening iodo- and bromosilation of lactones with the use of reagents $Et_3SiH/MeI(PdCl_2)$ (**1a**) and $Et_3SiH/AllylBr(PdCl_2)$ (**1b**). Thus, when γ-butyrolactone was treated with 1 equiv of Et_3SiH and 1.7 equiv of MeI in the presence of a catalytic amount of $PdCl_2$ (reagent **1a**), triethylsilyl 4-iodobutanoate (**2a**) was obtained in 68% isolated yield. In this reaction, a small amount of a hydrosilation product, triethylsilyl butanoate, was detected by GC/MS analysis, although γ-butyrolactone did not react with Et_3SiH alone, in the presence of the $PdCl_2$ catalyst. When AllylBr was used (reagent **1b**) instead of MeI in **1a**, bromosilation of γ-butyrolactone occurred to give triethylsilyl 4-bromobutanoate (**2b**) in 74% yield. No hydrosilation product was found to be formed in this reaction. Previously, we reported that the reagent consisting of a mixture of Me_3SiNEt_2/2RX (RX = MeI, AllylBr) reacts readily with cyclic ethers to give halosilation products. However, interaction of γ-butyrolactone with this reagent, Me_3SiNEt_2/2RX, gave no ring-opened product, but the starting lactone was recovered unchanged.

The present method could be applied also to ring-opening iodo- and bromosilation of six- and seven-membered lactones as shown in Table 1. Heating a mixture of δ-valerolactone and **1a** at 80−90 °C for 5 h gave triethylsilyl 5-iodopentanoate (**3a**) in 88% yield as the sole volatile product. Bromosilation of δ-valerolactone with **1b** gave triethylsilyl 5-bromopentanoate (**3b**) in 79% yield. 6-Hexanolide also underwent halosilation with **1a** and **1b** to give triethylsilyl 6-iodohexanoate (**4a**) and triethylsilyl 6-bromohexanoate (**4b**), respectively, in good yields.

Similar iodosilation of γ-valerolactone with **1a** proceeded again smoothly to afford triethylsilyl 4-iodopentanoate (**5a**) in 87% yield. In contrast, the reaction of γ-valerolactone with **1b** gave a mixture of the starting lactone and bromotriethylsilane, without any formation of bromosilation products. The reaction of γ-ethyl-γ-butyrolactone with **1a** produced a 1:1 isomeric mixture of triethylsilyl 4-iodohexanoate (**6a**) and triethylsilyl 5-iodohexanoate (**6a′**) in 60% combined yield, while similar reaction of δ-methyl-δ-valerolactone gave **6a′** as the sole product. A likely mechanism for the formation of **6a′** from γ-ethyl-γ-butyrolactone is given in Scheme 1. Interaction of the starting γ-lactone with $PdCl_2$ leads to isomerization to δ-lactone via a Pd(II)-coordinated unsaturated intermediate, and thus, **6a′** is formed competitively.[9] Similar ring-opening isomerization of lactones

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(2) Walsh, R. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; Part 1, Chapter 5.

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(4) Yamamoto, Y.; Shimizu, H.; Hamada, Y. *J. Organomet. Chem.* **1996**, *509*, 119.

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(6) Kunai, A.; Sakurai, T.; Toyoda, E.; Ishikawa, M. *Organometallics* **1994**, *13*, 3233.

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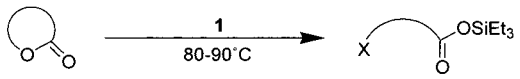
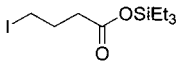
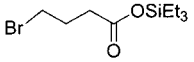
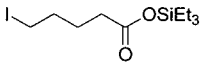
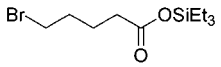
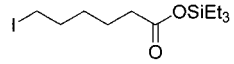
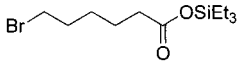
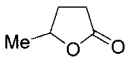
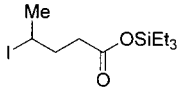
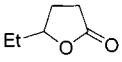
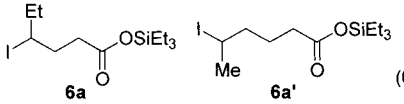
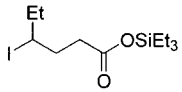
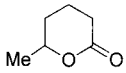
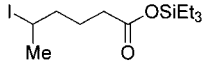
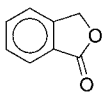
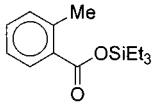
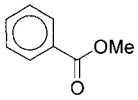
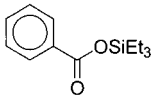
(8) Ohshita, J.; Iwata, A.; Tang, H.-q.; Yamamoto, Y.; Matui, C.; Kunai, A. C. *Chem. Lett.* **2001**, 740.

10.1021/jo011153n CCC: $22.00
Published on Web 04/26/2002

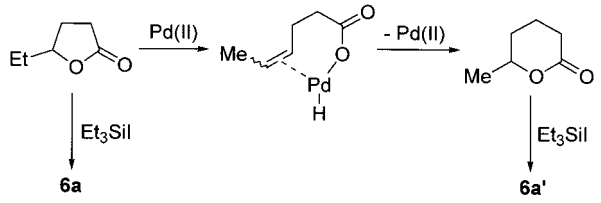
Table 1. Ring-Opening Halosilation of Lactone with Reagent 1 at 80−90 °C[a]



lactone	reagent	reaction time	product		yield
	**1a**	5 h[b]		**2a**	68%
	1b	12 h		**2b**	74%
	**1a**	5 h		**3a**	88%
	1b	12 h		**3b**	79%
	**1a**	4 h		**4a**	68%
	1b	12 h		**4b**	75%
	**1a**	12 h		**5a**	87%
	**1a**	12 h	 **6a** **6a'**		60% (**6a**/**6a'** = 50/50)
	1a'	12 h		**6a**	82%
	**1a**	5 h		**6a'**	60%
	**1a**	12 h		**7a'**	85%[c]
	**1a**	18 h		**8a**	76%

[a] Reactions were carried out without solvent, using **1a** (Et_3SiH/MeI($PdCl_2$)), **1a′** (Et_3SiH/MeI($Pd(acac)_2$/dppe)), and **1b** (Et_3SiH/AllylBr($PdCl_2$)). [b] At room temperature. [c] The reaction mixture was further treated with 1 equiv of Et_3SiH for 5 h.

Scheme 1



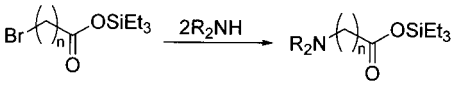
in the presence of a $PdCl_2$ catalyst has been reported previously.[10] In contrast to this, when $Pd(acac)_2$/dppe was used (reagent **1a′**) as the catalyst, iodosilation of γ-ethyl-γ-butyrolactone occurred selectively to give **6a** as the sole volatile product in a higher yield (82%). In a separate experiment, Et_3SiI reacted with γ-ethyl-γ-butyrolactone to give **6a** in 68% yield, without the formation of **6a′**. These facts seem to indicate that Et_3SiI is concerned as the active species in the present reaction with reagent **1a′**. However, it is uncertain whether the increased yield (82%) of **6a** with the used of **1a′**, compared to the use of Et_3SiI alone (68%), arises partially from the formation of a homogeneous complex of $Pd(L_2)$ and iodosilane, as suggested previously.[7] γ-Phenyl-γ-butyrolactone did not react with **1a** nor **1b** at 80−90 °C, although iodo- and bromotriethylsilane were found to be formed. Carrying out the reactions at higher temperature (100−110 °C) led to the formation of complex mixtures, from which no major products were isolated.

Attempted iodosilation of unsaturated lactones, such as α-angelicalactone and 2-furanone with **1a** was unsuc-

(9) However, the fact that no isomerization products would be observed in the reactions of γ-valerolactone and δ-methyl-δ-valerolactone with reagent **1a** indicates that such isomerization seems unfavorable when the lactones have a methyl group as the substituent, probably because a less stable terminal double bond is involved in the intermediate.

(10) Noels, A. F.; Herman, J. J.; Teyssie, P. *J. Org. Chem.* **1976**, *15*, 2527.

Scheme 2



2b: n = 3 **2c**: n = 3, R = Et, 78% **2d**: n = 3, R = Bu, 72%
3b: n = 4 **3c**: n = 4, R = Et, 71% **3d**: n = 4, R = Bu, 84%
4b: n = 5 **4c**: n = 5, R = Et, 73% **4d**: n = 5, R = Bu, 74%

cessful and gave complex mixtures. The reaction of phthalide with **1a** gave a 26/74 mixture of triethylsilyl *o*-(iodomethyl)benzoate (**7a**) and triethylsilyl *o*-methylbenzoate (**7a′**). Presumably, the reduction of an iodomethyl unit in the initial product **7a** took place under the reaction conditions to give **7a′**. In fact, when the reaction mixture was further treated with 1 equiv of triethylsilane for 5 h, **7a′** was obtained as the sole product in 85% yield. Treating methyl benzoate with **1a** for 18 h at 80−90 °C, followed by distillation of the primary reaction mixture under reduced pressure, afforded triethylsilyl benzoate (**8a**) in 76% yield. Dealkylation of methyl benzoate with iodotrimethylsilane or a mixture of Me_3SiNEt_2/2MeI has been previously reported.[4,11]

To demonstrate the synthetic utility of the halosilation products, we examined conversion of C-halogen bonds to C−N bonds (Scheme 2). Thus, treatment of **3b** with 2 equiv of diethylamine or dibutylamine led to triethylsilyl 5-diethylamimopentanoate (**3c**) and triethylsilyl 5-dibutylamimopentanoate (**3d**) as *O*-silyl-protected *δ*-amino acids, in 71% and 84% yield, respectively. Similar treatment of **2b** and **4b** with these amines afforded the respective O-silylated amino acids **2c**,**d** and **4c**,**d** in 78%, 72%, 73%, and 74% yields.

In conclusion, we investigated ring-opening iodo- and bromosilation of lactones with reagents **1a**,**b**. *γ*-Butyrolactone, *δ*-valerolactone, and 6-hexanolide reacted with 1 equiv of **1a**,**b** to give triethylsilyl *ω*-haloalkanoates in good yields. The reactions of methyl-substituted *γ*- and *δ*-lactones with **1a** also produced iodosilation products. The reaction of *γ*-ethyl-*γ*-butyrolactone with **1a** produced iodosilation products as a mixture of the structural isomers, arising from initial isomerization, while treatment with **1a′** produced the expected product. Treatment of methyl benzoate with **1a** afforded triethylsilyl benzoate. It was demonstrated that halosilation products can be converted to *O*-silyl-protected amino acids by the reaction with secondary amines.

(11) Jung, M. E.; Lyster, M. A. *J. Am. Chem. Soc.* **1977**, *99*, 968.

Experimental Section

Reactions were carried out under an atmosphere of dry argon. Representative procedures for the reactions of lactones and methyl benzoate with reagent **1a** and amination of the halosilation products are as follows.

Reaction of *γ*-Butyrolactone with 1a. A mixture of triethylsilane (1.85 g, 15.9 mmol), *γ*-butyrolactone (1.35 g, 15.7 mmol), methyl iodide (3.86 g, 27.2 mmol), and palladium chloride (25 mg, 0.14 mmol) was stirred at room temperature for 5 h. After evaporation of excess methyl iodide, the reaction mixture was fractionally distilled under reduced pressure to give triethylsilyl 4-iodobutanoate (**2a**, 3.48 g, 10.6 mmol, 68%).

Data for **2a**: bp 75−76 °C (1 mmHg); IR (neat) 1716 cm^{-1}; ^1H NMR (*δ* in $CDCl_3$) 3.23 (t, *J* = 6.8 Hz, 2H), 2.46 (t, *J* = 7.1 Hz, 2H), 2.15−2.06 (m, 2H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.76 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (*δ* in $CDCl_3$) 172.72, 36.24, 28.64, 6.46, 5.59, 4.47; MS *m*/*z* 299 (M^+ − Et), 201 (M^+ − I). Anal. Calcd for $C_{10}H_{21}IO_2Si$: C, 36.59; H, 6.45. Found: C, 36.35; H, 6.45.

Reaction of Methyl Benzoate with 1a. A mixture of triethylsilane (3.01 g, 25.9 mmol), methyl benzoate (3.40 g, 25.0 mmol), methyl iodide (5.40 g, 38.0 mmol), and palladium chloride (18 mg, 0.10 mmol) was stirred at 80−90 °C for 18 h. After evaporation of excess methyl iodide, the reaction mixture was fractionally distilled under reduced pressure to give triethylsilyl benzoate (**8a**, 4.51 g, 19.1 mmol, 76%).

Data for **8a**: bp 64−65 °C (1 mmHg); IR (neat) 1703 cm^{-1}; ^1H NMR (*δ* in $CDCl_3$) 8.05 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 1.04 (t, *J* = 7.7 Hz, 9H), 0.88 (q, *J* = 7.7 Hz, 6H); ^{13}C NMR (*δ* in $CDCl_3$) 166.56, 132.85, 131.38, 130.12, 128.26, 6.55, 4.63; MS *m*/*z* 221 (M^+ − Me), 207 (M^+ − Et). Anal. Calcd for $C_{13}H_{20}O_2Si$: C, 66.05; H, 8.53. Found: C, 66.15; H, 8.55.

Reaction of 3b with Et_2NH. A mixture of triethylsilyl 5-bromopentanoate (**3b**, 1.83 g, 6.20 mmol) and diethylamine (1.11 g, 14.8 mmol) was stirred at 60 °C for 5 h. The reaction mixture was fractionally distilled by a Kugelrohr distillation apparatus to give triethylsilyl 5-diethylaminopentanoate (**3c**, 1.27 g, 4.43 mmol, 71%).

Data for **3c**: bp 120−125 °C (1 mmHg, oven temp); IR (neat) 1715 cm^{-1}; ^1H NMR (*δ* in $CDCl_3$) 2.50 (q, *J* = 7.0 Hz, 4H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.62−1.55 (m, 2H), 1.50−1.45 (m, 2H), 0.99 (t, *J* = 7.0 Hz, 6H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.74 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (*δ* in $CDCl_3$) 174.12, 52.43, 46.83, 35.72, 26.41, 23.22, 11.62, 6.46, 4.47; MS *m*/*z* 287 (M^+), 258 (M^+ − Et), 215 (M^+ − NEt_2), 156 (M^+ − $OSiEt_3$). Anal. Calcd for $C_{15}H_{33}NO_2Si$: C, 62.66; H, 11.57; N, 4.87. Found: C, 62.33; H, 11.96; N, 4.77.

Acknowledgment. We thank Sankyo Kasei Co. Ltd., Tokuyama Corp., and Sumitomo Electric Industry for financial support.

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.

JO011153N