

# First General Synthesis of Monosilyl Acetals. Trimethylsilyl Trapping of the Intermediate in DIBALH Reduction of Carboxylic Acid Esters using Trimethylsilyl Trifluoromethanesulfonate<sup>1</sup>

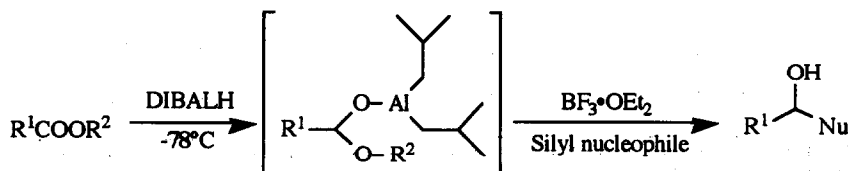
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*Key Words:* Monosilyl acetal; DIBALH reduction intermediate

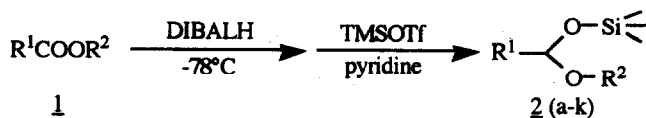
*Abstract:* The intermediate generated by the DIBALH reduction of carboxylic acid esters reacts with trimethylsilyl trifluoromethanesulfonate (TMSOTf) in the presence of pyridine to afford the corresponding monosilyl acetals in good yields.

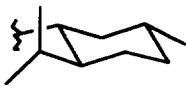
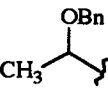
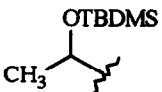
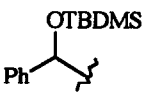
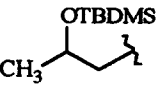
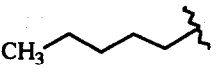
The low-temperature DIBALH reduction of carboxylic acid esters is well known to have versatile synthetic value by permitting direct conversion of such esters to aldehydes.<sup>2</sup> Although an intermediate in the reaction seems to be the aluminoxy acetal because of the considerable strength of the Al-O bond, it has not been isolated as of yet. If the intermediate can be converted to another more stable species, the DIBALH reduction mechanism will become clear and then such species are expected to play a novel role in organic synthesis. We have recently reported a boron trifluoride-promoted aldol reaction of silyl ketene acetals with the supposed intermediates in a one-pot procedure.<sup>3</sup> The anticipated success of this sequential reaction persuaded us to confirm the actual



intermediate; monosilyl acetals<sup>4</sup> may usually be the desired species by metal-exchanging transformation from the intermediate. We report herein that the intermediate in the DIBALH reduction is trapped with TMSOTf in the presence of pyridine to afford monosilyl acetals in good yields.

Table I. Trimethylsilyl Trapping of the Intermediate Generated in the DIBALH Reduction of Carboxylic Acid Esters

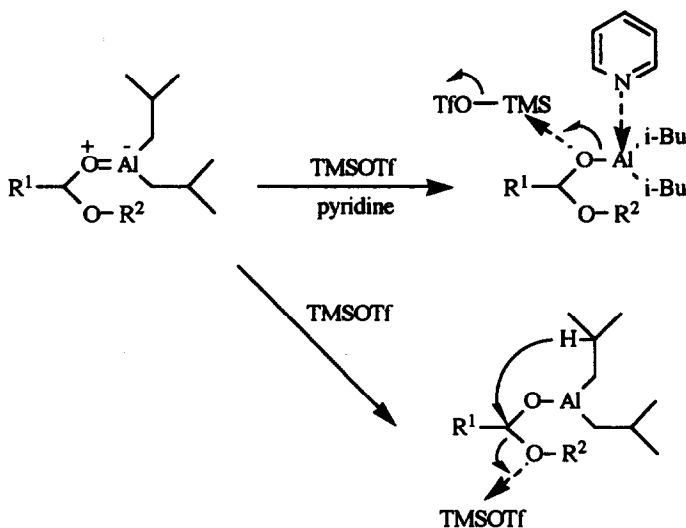


entry	R <sup>1</sup> COOR <sup>2</sup>		Isolated yield (%) <sup>a</sup> of product 2	
	R <sup>1</sup>	R <sup>2</sup>	(Diastereomeric ratio) <sup>b</sup>	
1	PhCH <sub>2</sub>	Me	<u>2a</u>	91
2	Ph <sub>2</sub> CH	Me	<u>2b</u>	78
3	PhCH <sub>2</sub> CH <sub>2</sub>		<u>2c</u>	73 (2.4 : 1)
4	PhCH <sub>2</sub> CH <sub>2</sub>	t-Bu	<u>2d</u>	71
5		Me	<u>2e</u>	87 (3.5 : 1)
6		Me	<u>2f</u>	69 (1.6 : 1)
7		Me	<u>2g</u>	72 (3.0 : 1)
8		Me	<u>2h</u>	85 (3.7 : 1)
9		Me	<u>2i</u>	91
10	Ph	Me	<u>2j</u>	50
11	CH <sub>3</sub> CH=CH	Et	<u>2k</u>	14

<sup>a</sup> Reaction with carboxylic acid esters (entries 1-9) did not give byproducts like a overreduced primary alcohol, whereas reactions with methyl benzoate (entry 10) and ethyl crotonate (entry 11) gave the corresponding primary alcohols in 31% and 55% yields, respectively. <sup>b</sup> The ratios of diastereomers were determined from their <sup>1</sup>H-NMR data, but the stereochemistry was not assigned.

**Typical Procedure :** To a stirred solution of the carboxylic acid ester (2mmol) and anhyd.  $\text{CH}_2\text{Cl}_2$  (10mL) at  $-78^\circ\text{C}$  under Ar, DIBALH (2.2mmol; 2.2mL of 1.0M solution in toluene) was dropwise added. After 2h at  $-78^\circ\text{C}$ , pyridine (6mmol) and trimethylsilyl trifluoromethanesulfonate (2.2mmol) were added. The resulting solution was stirred at  $-78^\circ\text{C}$  for 3h. The mixture was then extracted with pentane (20mL). After the usual workup, the pure product was isolated by flash column chromatography.

The results are summarized in Table I. The reaction is very clean without byproducts and the procedure is very simple. The monosilyl acetals (entries 1-9) were obtained in good yields<sup>5</sup>; this is the first example of the synthesis of monosilyl acetals. The reactions with  $\gamma$ -butyrolactone and  $\delta$ -valerolactone also gave the silyl-trapped products of the corresponding lactols.<sup>6</sup> However, TBDMSOTf did not work well under similar conditions. The reaction without pyridine almost led to the corresponding alcohols which were brought by hydride transfer enhanced with the Lewis acid character of TMSOTf from the aluminum moiety. Pyridine presumably facilitates the metal exchange reaction by significantly affecting the stable Al-O bond as illustrated in Scheme 1. The



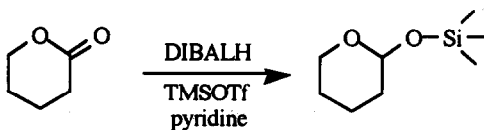
reaction with esters from benzoic acid and  $\alpha,\beta$ -unsaturated acid resulted in low yields of the desired products along with a large amount of the corresponding alcohols by overreduction (entries 10 and 11), because of the inherent high reactivity of their intermediates.

Further studies concerning the reactivity of monosilyl acetals towards a variety of reagents are in progress.

### References and Notes

1. This work was presented in part at the 63rd Annual Meeting of the Chemical Society of Japan, Osaka, March, 1992; Abstract p 1574.
2. Winterfeldt, E. *Synthesis* **1975**, 617. Maruoka, K.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 5001.

3. Lewis acid mediated reaction: Kiyooka, S. -i.; Shirouchi, M. *J. Org. Chem.* **1992**, *57*, 1.  
Grignard reaction: Kano, S.; Yuasa, Y.; Yokomatsu, T.; Shibuya, S. *Chem. Pharm. Bull.* **1989**, *37*, 2867. Ibuka, T.; Habashita, H.; Otaka, A.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1991**, *56*, 4370. The following Lewis acid-assisted aldol reaction after DIBALH reduction proceeded completely at the same temperature ( $-78^{\circ}\text{C}$ ), but similar Grignard reactions with such intermediates needed a higher temperature so that the actual intermediates might be considered to be different species between the two reactions.
4. The general preparation of monosilyl acetals, to our knowledge, is not known except those from monosilyl acetals having some functional groups: Ojima, I.; Kumagai, M.; Nagai, Y. *J. Organomet. Chem.* **1976**, *111*, 43. Cooke, M. P. *J. Org. Chem.* **1986**, *51*, 951. Kiyooka, S. -i.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *56*, 2276.  
With the same purpose as ours, the trapping of DIBAL-TRIBAL reduction intermediate of Schiff base esters with (trimethylsilyl)imidazole was quite recently reported by Polt : Polt, R.; Peterson, M. A.; Young, L. D. *J. Org. Chem.* **1992**, *57*, 5469.
5. All new compounds were characterized by the spectroscopic data and elemental analysis. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR data of the representative acetals 2a, 2e, 2i are as follows : 1-Methoxy-1-trimethylsiloxy-2-phenylethane (2a) ;  $^1\text{H}$ -NMR(90MHz,  $\text{CDCl}_3$ )  $\delta$  0.00(s, 9H), 2.82(d,  $J=5.4$ , 1H), 2.88(d,  $J=5.4$ , 1H), 3.28(s, 3H), 4.76(t,  $J=5.4$ , 1H), 7.20(s, 5H).  $^{13}\text{C}$ -NMR(22.6MHz,  $\text{CDCl}_3$ )  $\delta$  0.29, 44.3, 54.3, 100.0, 126.3, 128.1, 129.8, 137.1. : 1-Methoxy-1-trimethylsiloxy-2-benzyloxypropane (2e) ;  $^1\text{H}$ -NMR (90MHz,  $\text{CDCl}_3$ )  $\delta$  0.13, 0.19\*(s, 9H), 1.15\*, 1.17(d,  $J=6.4$ , 3H), 3.36(s, 3H), 3.50-3.90(m, 1H), 4.60(s, 2H), 4.45-4.79(m, 1H), 7.32(s, 5H). Asterisks indicate the minor isomer.  $^{13}\text{C}$ -NMR(22.6MHz,  $\text{CDCl}_3$ ) Major isomer  $\delta$  0.29, 14.0, 54.9, 71.3, 77.3, 100.5, 127.2, 127.4, 128.0, 138.6. Minor isomer  $\delta$  0.44, 14.4, 54.6, 71.3, 76.8, 100.2, 127.2, 127.4, 128.0, 138.6. : 1-Methoxy-1-trimethylsiloxyhexane (2i) ;  $^1\text{H}$ -NMR(90MHz,  $\text{CDCl}_3$ )  $\delta$  0.16(s, 9H), 0.80-1.00 (m, 5H), 1.10-1.70(m, 6H), 3.31(s, 3H), 4.64(t,  $J=5.0$ , 1H) .  $^{13}\text{C}$ -NMR(22.6MHz,  $\text{CDCl}_3$ )  $\delta$  0.41, 13.9, 22.6, 24.1, 31.7, 37.2, 53.7, 99.4.
6. The reaction of  $\delta$ -valerolactone under the conditions described in the text yielded the corresponding silyl product (70%) as a major product.  $^{13}\text{C}$ -NMR(22.6MHz,  $\text{CDCl}_3$ )  $\delta$ -0.05, 19.8, 25.3, 33.2, 62.9, 94.2.



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