Stereospecific Cyclopropanation Reactions of Stannyl-Substituted Acetals with Alkenes via γ-Elimination of Tin.

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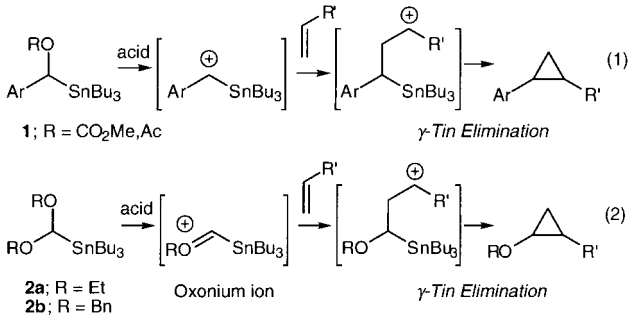
Abstract: The reactions of stannyl substituted acetals with olefins resulted in the elimination of both the triorganostannyl group and the alkoxy group on the same carbon, and the production of the corresponding alkoxycyclopropanes in good yields. The stereospecificity of the present reaction suggests that γ-elimination of tin is very fast.

The γ-elimination of tin has been recognized as a useful method for the construction of cyclopropane rings.[1] This type of reaction is normally achieved using organostannanes having an appropriate leaving group at γ position, such as halo,[1b] hydroxyl,[1c] carbonyl,[1d] and epoxy[1e] groups. Recently we have developed a new acid promoted cyclopropanation of α-oxybenzylstannanes (**1**) with alkenes. This reaction proceeds by the addition of the initially generated stannyl-substituted benzyl cation to alkenes followed by the γ-elimination of tin to produce the cyclopropanes (eq. 1).[2] Therefore, α-oxybenzylstannanes serve as formal carbenoids.

In order to expand the synthetic utility of this type of cyclopropanation,[3] we searched for other types of organostannanes which act as formal carbenoids, and envisioned that stannyl substituted acetals **2**[4] serve as effective reagents for cyclopropanation (eq. 2). The acid catalyzed reaction of acetals **2** is expected to give the stannyl-substituted oxonium ions which would add to alkenes to give the γ-stannyl-substituted carbocations. The concept works. The acid promoted reaction of **2** with alkenes gave the corresponding alkoxy-substituted cyclopropanes[5] and here we report preliminary results of this study.

The reactions of **2** with alkenes (1.1 eq) were carried out in the presence

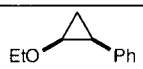
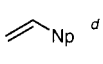
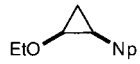
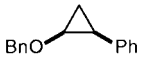
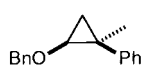
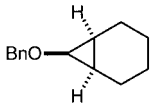
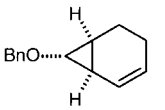


Scheme 1

of BF_3•OEt_2 (1.1 eq) in dichloromethane at room temperature, and the corresponding alkoxycyclopropanes were obtained in good yields as shown in Table 1. The dibenzyloxyacetal **2b**[6] gave better yields than the diethoxyacetal **2a**. Stereochemistry of the present reaction is interesting. In most cases, the *cis* isomers of cyclopropanes were produced predominantly from mono-substituted alkenes, although the reason for this stereoselectivity has not been clarified as yet.[7] The *endo* isomer was obtained predominantly from cyclohexene. It is also worth noting that the present reaction is stereospecific as far as the geometry of the alkene is concerned (*vide infra*).

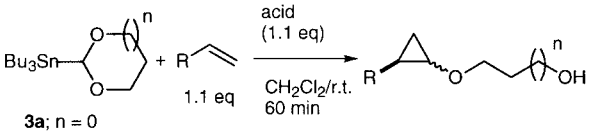
Stannyl substituted cyclic acetals were also effective as formal tin carbenoids (Table 2). Although the reaction of 2-stannyl-1,3-dioxolane

Table 1. Cyclopropanation Reactions of **2** and Olefins[a]

acetal	olefin	product	yield[b] (%)	*cis/trans*[c] *endo/exo*
2a			58	74/26
	 [d]		75	69/31
2b			89	74/26
			86	89/11
			74	65/35
			31	33/67

[a] Reactions were usually carried out with 0.2 mmol of **2** and 0.22 mmol of an olefin in the presence of 0.22 mmol of BF_3•OEt_2 in CH_2Cl_2 at room temperature. [b] Isolated yield. [c] The isomer ratio was determined by ^1H NMR. [d] Np: 2-naphthyl

Table 2. Intermolecular Cyclopropanation of Cyclic Acetals **3** with Olefins



3a; n = 0
3b; n = 1

acetal	R	acid	yield[a]	*cis/trans*[b]
3a	Ph	BF_3•OEt_2	28	50/50
3b	Ph	BF_3•OEt_2	57	47/53
3b	Ph	$TiCl_4$	60	57/43
3b	CH_2SiMe_3	BF_3•OEt_2	67	67/33
3b [c]	CH_2SiMe_3	$TiCl_4$	67	50/50

[a] Isolated yields. [b] Determined by capillary GLC analyses. [c] At -72 °C, 3 h

with styrene afforded the cyclopropanation product in only 28% yield, the reaction of 2-stannyl-1,3-dioxane with alkenes gave the corresponding cyclopropanes in good yields.[8] However, the *cis*/*trans* ratios of the products were much lower than those of non-cyclic stannyl acetals, although the reason is not clear at present. It is noteworthy that allyltrimethylsilane mainly gave the cyclopropanation product together with a small amount of allylated product (5%), indicating that the γ-elimination of tin is more favorable than the β-elimination of silicon.[2]

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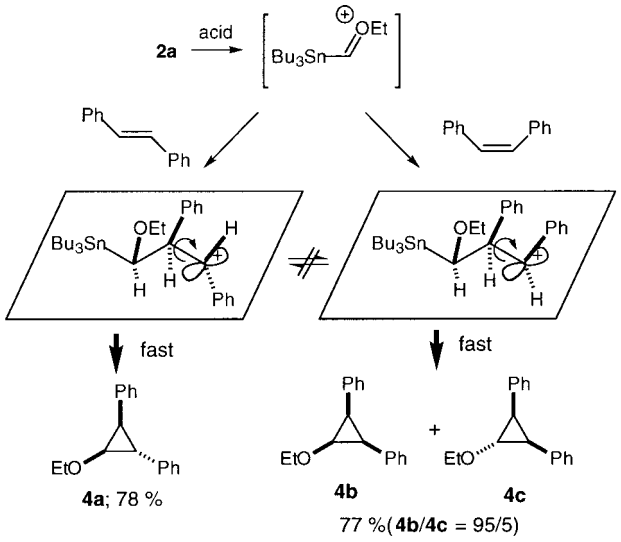
The cyclopropanes thus obtained would be able to be transformed into the corresponding cyclopropanol by oxidation of the side chain according to the literature procedure.[9]



Scheme 2

The stereospecificity of the present reaction seems to be important for the elucidation of the reaction mechanism (Scheme 1). The reaction of **2a** with *trans*-stilbene gave rise to the formation of the ethoxycyclopropane **4a** in 78% yield as a single isomer (Scheme 2).[10,11] In **4a** two phenyl groups are trans to each other. On the other hand, the reaction with *cis*-stilbene afforded the cyclopropane **4b** preferentially together with a small amount of the epimer **4c**. In **4b** and **4c** two phenyl groups are cis to each other. The formation of **4a** was not detected. Therefore, the stereochemistry of the starting alkene was retained. The observed stereospecificity indicates that the γ-elimination of tin is too fast to allow the rotation about the carbon-carbon bond of the original alkene. The stereospecificity can also be explained in terms of synchronous formation of two carbon-carbon bonds of the cyclopropane. Anyway the present stereospecificity suggests that γ-elimination of tin is a very fast process. Although more data should be accumulated before elucidation of the detailed mechanism, its complete stereospecificity opens possibilities of various synthetic applications of this reaction.

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References and Notes:

(1) (a) Pereyre, M.; Quintard, J-B.; Rahm, A. *Tin in Organic Synthesis*; Butterworth & Co.: London, 1987; p 235 and references cited therein. Selected examples (b) Peterson, D. J.; Robbins, M. D.; Hansen, J. R. *J. Organometal. Chem.* **1974**, *73*, 237. (c) Fleming, I.; Urch, C. *Tetrahedron Lett.* **1983**, *24*, 4591. (d) Sato, T.; Watanabe, M.; Watanabe, T.; Onoda, Y.; Murayama, E. *J. Org. Chem.* **1988**, *53*, 1894. (e) Plamondon, L.; Wuest, J. D. *J. Org. Chem*. **1991**, *56*, 2066.

(2) Sugawara, M.; Yoshida, J. *J. Am. Chem. Soc.* **1997**, *119*, 11986.

(3) (a) Clark, H. C.; Willis, C. J. *J. Am. Chem. Soc*. **1960**, *82*, 1888. (b) Seyferth, D.; Dertouzos, H.; Suzuki, R.; Mui, J. Y. P. *J. Org. Chem*. **1967**, *32*, 2980. (c) Seyferth, D.; Armbrecht, F. M.; Prokai, B.; Cross, R. J. *J. Organometal. Chem*. **1966**, *6*, 573. (d) Seyferth, D.; Armbrecht, F. M. *J. Am. Chem. Soc*. **1969**, *91*, 2616. (e) Seyferth, D.; Lambert, R. L. *J. Organometal. Chem*. **1975**, *91*, 31.

(4) Stannyl substituted acetal **2a** was prepared according to the literature procedure: (a) Shiner, C. S.; Tsunoda, T.; Goodman, B. A.; Ingham, S.; Lee, S-h.; Vorndam, P. E. *J. Am. Chem. Soc.* **1989**, *111*, 1381. The other method: (b) Quintard, J. P.; Elissondo, B.; Mpegna, D. M. *J. Ornamet. Chem.* **1983**, *251*, 175.

(5) Wong, H. N. C.; Hon, M.; Tse, C.; Yip, Y. *Chem. Rev.* **1989**, *89*, 165.

(6) Acetals **2b**, **3a**, and **3b** were prepared by TsOH catalyzed transacetalization of **2a** in the excess amount of the corresponding alcohols.

(7) Doyle, M. P. *Acc. Chem. Res*. **1986**, *19*, 348.

(8) Recently, it was reported that the reactions of α-stannyl cyclic acetals with allyl stannanes and enol silyl ethers afforded the corresponding products. Cintrat, J. C.; Blart, E.; Parrain, J. L.; Quintard, J. P. *Tetrahedron* **1997**, *53*, 7615.

(9) Sugimura, T.; Futagawa, T.; Tai. A. *Tetrahedron Lett.* **1988**, *29*, 5775

(10) The stereochemistry of **4a** was determined by NOE experiment. The stereochemistry of **4b** and that of **4c** were also determined by NOE experiments.

(11) Typical experimental procedure for the cyclopropanation. Synthesis of **4a**. To a solution of (diethoxy)(tributylstannyl)-methane **2a** (74.8 mg, 0.190 mmol) and *trans*-stilbene (36.3 mg, 0.201 mmol) in toluene (0.50 mL) was added BF_3•OEt_2 (25.0 μl, 0.197 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 1 h. After **2a** was consumed, sat *aq* $NaHCO_3$ (1.0 mL) was added to the reaction mixture, and the organic phase was separated. The aqueous phase was extracted with ether (x3), and the combined organic phase was washed with sat. *aq* NaCl, and dried over $MgSO_4$. After removal of the solvent, the residue was purified *via* flash chromatography to obtain 35.2 mg (78%) of the 2,3-diphenylethoxycyclopropane.
4a: TLC Rf 0.29 (hexane:AcOEt = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.2 Hz, 3 H), 2.38 (t, *J* = 6.9 Hz, 1 H), 2.59 (dd, *J* = 6.6, 3.6 Hz, 1 H), 3.35 (dq, *J* = 9.3, 7.2 Hz, 1 H), 3.53 (dq, *J* = 9.3, 7.2 Hz, 1 H), 3.78 (dd, *J* = 6.9, 3.6 Hz, 1 H), 7.1-7.4 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.72, 31.79, 33.55, 65.98, 66.19, 125.87, 126.07, 126.30, 127.95, 128.04, 128.50, 137.53, 140.70; MS (EI) m/e (%) 238 (M^+, 100), 209 (32), 178 (48), 105 (88); HRMS calcd for $C_{17}H_{18}O$ 238.1358, found 238.1365.
4b: TLC Rf 0.31 (hexane:AcOEt = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.2 Hz, 3 H), 2.43 (d, *J* = 6.6 Hz, 2 H), 3.31 (q, *J* = 7.2 Hz, 2 H), 3.89 (t, *J* = 6.6 Hz, 1 H), 7.0-7.2 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.62, 26.49, 60.85, 66.30, 125.49, 127.45, 130.62, 135.48; MS (EI) m/e (%) 238 (M^+, 100), 209 (25), 178 (41), 105 (80); HRMS calcd for $C_{17}H_{18}O$ 238.1358, found 238.1367.

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