CHEMISTRY LETTERS, pp. 1775-1778, 1992. 

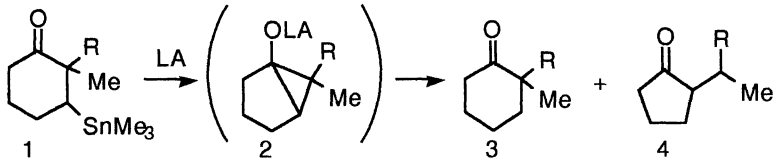
# Dependence of the Lewis Acid-induced Reaction of β-Stannyl Ketones upon Substitution Pattern. 1,2-Alkyl Migration *versus* Cyclopropanation

Jun FUJIWARA, Taro YAMAMOTO, and Tadashi SATO*
Department of Applied Chemistry, Faculty of Science and Engineering, Waseda University, Ookubo 3, Shinjuku-ku, Tokyo 169

3-Stannylcyclohexanones fully substituted at 2 and 3 positions undergo a 1,2-alkyl migration and cyclopropanation. The balance of the reaction pattern depends upon the steric environment and migratory aptitude of the alkyl groups.

Due to the latent carbanionic character of the carbon-tin bond, tin compounds containing cationic centers within the same molecule undergo various types of reactions.[1] Typical types of the reactions are cyclizations and hydride shifts, and the reaction types depend upon the relative positions of the cationic center and the carbon-tin bond, the number of the substituents at the tin-bearing carbon, and the activation methods. In case of β-stannyl ketones, the reaction usually proceeds with cyclopropanation.[2] In the present study, we found that a 1,2-alkyl migration competed with the cyclopropanation under specific conditions.

So far, we have investigated the Lewis acid-induced reaction of β-stannyl ketones having at least one hydrogen atom at α-position in **1** (R = H). In every case, the reaction proceeded *via* cyclopropanol intermediates **2**, which afforded saturated ketones **3** or **4**, according to the position of the bond cleavage of the cyclopropane




1 2 3 Type A 4 Type B

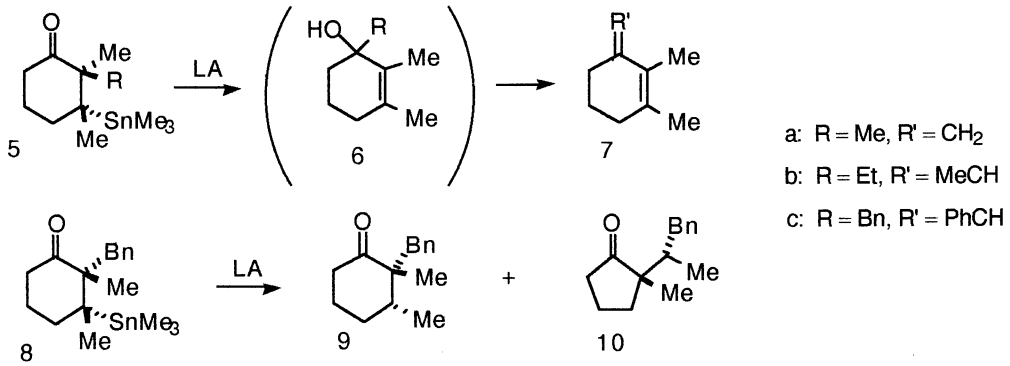
a: R = Me, b: R = Bn

ring of **2** (Type A and Type B reactions, respectively). The general trend is that, (1) the ring cleavage of the cyclopropanol intermediates **2** occurs at the bond leading to the less substituted carbon, (2) in cases where both α and β-carbons have the same number of substituents, trimethylsilyl trifluoromethanesulfonate (TMSOTf) facilitated the Type B reaction, while $TiCl_4$ induced both reactions unselectively, and (3) the introduction of a hydroxyl group into the α-substituent induces the Type B reaction, irrespective of the substitution pattern or the nature of Lewis acid.[2]

In order to find the limitation of the trend, we extended our investigation to the reaction of 3-stannylcyclohexanones having substituents at the 2 and/or 3-positions. First we chose stannyl ketones fully substituted at 2-position by alkyl groups. The starting materials **1a** and **1b** were prepared from 2-methyl-2-cyclohexen-1-one by conjugate addition of $Me_3SnLi$, followed by quenching the enolate with methyl iodide or benzyl bromide, respectively.[3] When **1a** and **1b** were treated with $TiCl_4$ or TMSOTf, the Type A products **3a**

and **3b** were obtained in 98% and 79% yields, respectively, although **3b** contained a trace amount of impurity which could be assigned as **4b** in view of the small doublet at δ 0.80 in the NMR spectrum. The preferential formation of the Type A products is consistent with the general trend that the ring cleavage of the cyclopropanol intermediate **2** occurs at the bond leading to the less substituted carbon.

In contrast with the exclusive cyclopropanation of **1a** and **1b**, 1,2-alkyl migration competes with the cyclization, when both the 2 and 3-positions are fully substituted by alkyl groups. The starting materials **5a** – **5c** were prepared from 2,3-dimethyl-2-cyclohexen-1-one in the same way as mentioned above, by conjugate addition



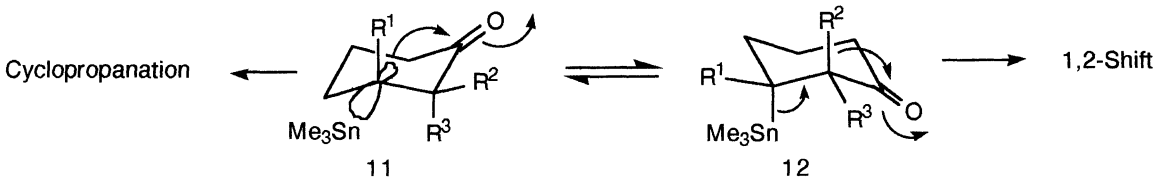

of $Me_3SnLi$, followed by quenching the enolate with methyl iodide, ethyl iodide, and benzyl bromide, respectively. It has been established that the introduction of the alkyl groups takes place at a position *trans* to the stannyl group.[4] When **5b** and **5c** were treated with $TiCl_4/BnEt_3NBr$, the major products were dienes **7b** and **7c** in 78 and 73% yields, respectively. In case of **5a**, however, the reaction afforded diene **7a** in only 16% yield, and major products were the corresponding Type A (17%) and Type B (46%) products. The reactions were not clean with $TiCl_4$ or TMSOTf treatment. Evidently the dienes are the products resulting from a 1,2-alkyl migration to afford **6**, followed by dehydration. Although the dehydration of 1,3,5-trimethyl-2-cyclohexen-1-ol is known to produce a mixture of *exo* and *endo* dienes in 3 : 2 ratio, respectively,[5] no *endo* diene was identified in the present reaction. Probably the presence of three consecutive substituents would destabilize the planar ring structure required for the endocyclic diene.

In the 1,2-alkyl migration reactions, the migrating group was always R, which had been introduced after the stannylation, and occupied a position *trans* to the stannyl group. No products involving the methyl migration were identified in the reactions of **5b** and **5c**. The emergence of the competing cyclopropanation of **5a** is an indication of the lower migratory aptitude of methyl group as compared with benzyl and ethyl groups.[6] In order to verify whether the absence of the methyl migration products in the reactions of **5b** and **5c** is due to the low migratory aptitude of the methyl group, or to the steric requirement imposed by the *cis*-relation of the methyl *versus* stannyl group, we examined the reaction of **8**, which is a stereoisomer of **5c**. The starting material was prepared from 2-benzyl-3-methyl-2-cyclohexen-1-one by the addition of $Me_3SnLi$ followed by quenching the enolate with methyl iodide. In contrast to the exclusive 1,2-alkyl migration observed with **5c**, **8** gave only the Type A and Type B products, **9** and **10**, in 33% and 34% yields, respectively, under the same conditions. Neither the other possible stereoisomers nor alkyl migration products were identified. Evidently **9** and **10** are the products resulting from the protonative opening of the cyclopropane ring of the intermediate cyclopropanols with inversion.[7] The results indicate that even a benzyl group, which has an ample migrating ability, can not migrate when it occupies a position *cis* to the stannyl group.

Although a 1,2-alkyl or hydride shift is observed along with the cyclopropanation in the stannyl and silyl compounds having a cationic carbon at γ-position, the stannyl compounds generally undergo the cyclopropanation

in preference to the 1,2-shift, while the silyl compounds favor the 1,2-shift over the cyclization, when respective compounds having the same carbon skeleton were compared under the same conditions.[8] The 1,2-alkyl shift driven by a stannyl group has been observed in norbornane system by Hartman and Traylor.[9] They speculated from kinetic data that the reaction proceeded through a transition state in which the Sn–C–C–R bonds are coplanar, although their system lacked the requirement for the stereochemical discussions. A definite stereochemical environment for the 1,2-shift, albeit hydride shift, was provided by Wuest, who carried out a Lewis acid-induced reaction of stereochemically defined spirocyclic (3,4-epoxybutyl)stannanes.[10] They found that the reaction types were dependent critically upon the relative orientations of tin, oxygen and the three connecting carbon atoms, and that 1,2-shift of the axial C2-hydrogen was driven by the antiperiplanar carbon-tin bond.

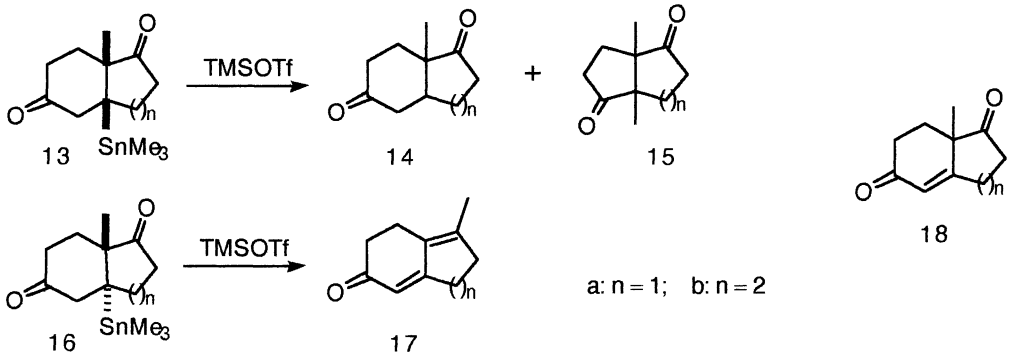
Referring to our findings that the cyclopropanation proceeds with inversion of the configuration of the tin-bearing carbon,[11] while the *anti* configuration of the stannyl and the migrating group is requisite for the alkyl




Scheme 1.

migration, we assume that the cyclopropanation proceeds *via* the conformer **11**, while the alkyl migration proceeds *via* the conformer **12** (Scheme 1). The reaction types could be balanced by the relative stability of the conformers and migratory aptitude of the alkyl groups. The 1,2-alkyl migration proceeds only with compounds in which $R^1$ and $R^3$ are alkyl groups and $R^2$ has sufficient migratory aptitude. Presumably the bulkiness of $R^1$ and $R^3$ would make the conformation **12** not so unstable compared to **11**, thus inducing the alkyl migration.

In order to verify the stereochemical requirement as shown in Scheme 1, we investigated the reaction with bicyclic compounds having more rigid conformations. The starting materials having *cis* ring junction, **13a** and **13b**, were prepared from the corresponding enones **18** by conjugate addition of [$Me_3SnCuSPh$]Li,[12] while the *trans*-isomers, **16a** and **16b**, were prepared by the addition of $Me_3SnLi$. The stereochemistry of the products was deduced in view of the documented results.[10] When *cis*-compounds **13a** and **13b** were treated with TMSOTf, the Type B reaction proceeded predominantly, affording **15a** and **15b** in 38% and 26% isolated yields, respectively, although the Type A product **14b** was also identified in 12% yield in the reaction of **13b**. The reactions were quite clean; almost pure **15a**, contaminated by a trace amount of **18a**, was obtained in 62% yield from **13a** prior to the purification by column chromatography. In case of the *trans*-isomer **16a**, however, the 1,2-methyl migration was the sole reaction pattern, affording **17a** in 56% yield. The TMSOTf treatment of **16b**



also proceeded in the same pattern, affording **17b** in 37% yield, but the reaction was slower and accompanied by a β-elimination affording **18b** in 25% yield. No products *via* the Type A or Type B reaction were identified in the reactions from **16a** and **16b**.

These results are generally consistent with the scheme shown above, but the following questions remain unanswered: why methyl migration occurs from **5a** (albeit in lower extent), but not from its epimer **8**, and why the reactivities differ remarkably between **16a** and **16b**. The absence of the methyl migration from **8** is particularly embarrassing, considering that the presence of the bulkier benzyl group as $R^3$ would shift the conformation in favor of **12**, which induces the 1,2-shift. Although we have no satisfactory explanation for the observation, we assume at present that the dihedral angle of $R^2$–C–C=O might be critical for the migration of a group with less migratory aptitude such as methyl group. Eclipsing effect between benzyl and carbonyl group in **8**, and angle distortion imposed by the ring size in B-ring of **16** might be responsible for the difference.

Financial supports from The Asahi Glass Foundation and The Grant-in-Aid for Scientific Research No. 03453033 from the Ministry of Education, Science and Culture are greatly acknowledged. We also would like to thank Shin-Etsu Chemical Co., Ltd. and Toray Silicone Co., Ltd. for generous gift of silyl reagents.

References

1) T. Sato, *Synthesis*, **1990**, 259.
2) T. Sato, T. Watanabe, T. Hayata, and T. Tsukui, *Tetrahedron*, **45**, 6401 (1989).
3) All the new compounds were isolated in pure states, which showed consistent spectroscopic data. The following compounds have appeared in the respective literatures. **3a**: M. Nanzyo, T. Oritani, and K. Yamashita, *Agric. Biol. Chem.*, **41**, 1711 (1977); **3b**: H. O. House, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **36**, 2361 (1971); M. Gall and H. O. House, *Org. Synth.*, Coll Vol. 6, 121; **14b**: G. Bauduin and Y. Pietrasanta, *Tetrahedron*, **29**, 4225 (1973); **15a**: H. Quast and J. Christ, *Liebigs Ann. Chem.*, **1984**, 1180; **15b**: W. Reusch, K. Grimm, J. E. Karoglan, J. Martin, K. P. Subrahamanian, P. S. Venkataramani, and J. D. Yordy, *J. Am. Chem. Soc.*, **99**, 1958 (1977). The products **7a**, **9**, and **10** were confirmed by the independent syntheses.
4) W. C. Still, *J. Am. Chem. Soc.*, **99**, 4836 (1977); M. Ochiai, T. Ukita, Y. Nagao, and E. Fujita, *J. Chem. Soc., Chem. Commun.*, **1985**, 637.
5) P. Eilbracht, C. Huttinger, and K. Kufferath, *Chem. Ber.*, **123**, 1071 (1990).
6) M. Saunders, J. Chandrasekhar, and P. v. R. Schleyer, "Rearrangements of Carbocations," in "Rearrangements in Ground and Excited States I," ed by P. deMayo, Academic Press, New York (1980), p. 1.
7) C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Am. Chem. Soc.*, **88**, 3347 (1966).
8) I. Fleming and C. J. Urch, *J. Organomet. Chem.*, **285**, 173 (1985).
9) G. D. Hartman and T. G. Traylor, *J. Am. Chem. Soc.*, **97**, 6147 (1975).
10) L. Plamondon and J. D. Wuest, *J. Org. Chem.*, **56**, 2066 (1991).
11) The inversion has been confirmed by NOE experiment,[2] and by the (+)-β-cuparenone synthesis from a stereochemically defined β-silyl-β'-stannyl ketone: T. Sato, M. Hayashi, and T. Hayata, *Tetrahedron*, in press.
12) E. Piers, H. E. Morton, and J. M. Chong, *Can. J. Chem.*, **65**, 78 (1987).

(Received June 5, 1992)