to split dimers with efficiencies comparable to those found in systems with short, covalent linkers. If the behavior of methoxyindole is typical of electron-donating sensitizers (e.g., the reduced flavin[13] cofactor employed by photolyases), hydrogen bonding may be a viable dimer recognition motif available to photolyases.

Acknowledgment. We thank the National Institutes of Health (CA49729) and the Del E. Webb Foundation for financial support.

Supplementary Material Available: Experimental procedures, characterization data, and UV absorption spectra (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

---

[13] (a) Okamura, T.; Sancar, A.; Heelis, P. F.; Begley, T. P.; Hirata, Y.; Mataga, N. *J. Am. Chem. Soc.* **1991**, *113*, 3143–3145. (b) Jorns, M. S. *J. Am. Chem. Soc.* **1987**, *109*, 3133–3136. (c) Kim, S. T.; Heelis, P. F.; Okamura, T.; Sancar, A. *Photochem. Photobiol.* **1991**, *53S*, 17S. (d) Hartman, R. F.; Rose, S. D. *J. Am. Chem. Soc.*, in press.

1,4-Silyl Migration Reactions. Applicability to Alkyl-, Vinyl-, and Cyclopropylsilanes[†]

Mark Lautens,*[,1a] Patrick H. M. Delanghe,[1b] Jane Betty Goh, and C. H. Zhang

Department of Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A1

Received March 18, 1992

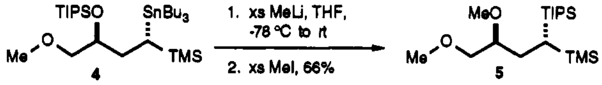
Summary: A series of silyl protected alcohols containing a tin substituent were found to undergo transmetalation followed by silyl migration from oxygen to carbon in the presence of methyllithium.

The utility of 1,1-dimetallo compounds as building blocks in organic synthesis has become increasingly apparent in the past few years.[2] Several papers have appeared describing the synthesis and reactivity of these compounds. Our interest in this area has focused on the preparation of dimetallo compounds of silicon and tin via hydrometalation reactions.[3]

We recently described a hydrometalation–stannylation sequence catalyzed by titanium for the stereoselective synthesis of γ-hydroxyvinylstannanes A–C, R, R′ = alkyl (Figure 1). These substrates were shown to undergo highly diasteroselective hydroxyl-directed hydrogenation and cyclopropanation reactions leading to novel heterobimetallic derivatives 2 and 3 (Figure 2).[4,5] Claisen rearrangement of a derivative of 1 was also explored leading to allylic dimetallo compounds.[6]

In order to evaluate the reactivity of the stereoisomeric silyl and stannyl compounds (i.e., M′ = Si, M = Sn) toward the abovementioned reactions, synthetic routes to these compounds were required. We report a particularly facile entry into silicon-containing compounds by taking advantage of a stereoselective 1,4-oxygen to carbon migration of a silyl group. Several different silyl groups were shown to migrate in high yield. We also report the first example of migration of a silicon to a cyclopropyl anion.

We first encountered a silyl migration during a study of the transmetalation of 4. Our objective was to transmetalate the C–Sn bond then alkylate the resulting carbanion and determine if the remote methoxy group controlled the stereochemistry at the carbanionic center. A TBDMS group was chosen to minimize complexation to the oxygen at C-2. Instead, upon treatment of 4 with MeLi in THF followed by addition of methyl iodide, we isolated 5 in 66% yield as a 3:1 mixture of isomers. The major product arose from a 1,4-migration of the TIPS with retention of stereochemistry as determined by comparison of a related compound of known configuration.



(1)

Migration of silicon is a ubiquitous process.[7] The best studied of these reactions are the Brook- and retro-Brook-type 1,2-rearrangements.[8a,b] Higher order reactions are also known, although they are generally considered to be less facile. One study reports the relative ease of migration to be 1,2 > 1,3 ≫ 1,4 or 1,5.[8c,d] We considered that 1,4-rearrangement of silicon could represent a useful route for preparation of stereoisomeric silanes (Figure 3).[9]

The first example of a 1,4-rearrangement appears to be that reported by Speier.[10] Later, during a study of homoenolate equivalents, Evans established that the steric

---

[†] Dedicated to our colleague, and a seminal contributor to silicon migration chemistry, Professor Adrian Brook.

[1] (a) Fellow of the Alfred P. Sloan Foundation, 1991–1993, NSERC (Canada) University Research Fellow, 1987–1992. BioMega Young Investigator Awardee, 1990–1992. (b) Simcoe Scholar 1991–1993.

[2] (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611. (b) Tanaka, K.; Uneme, H.; Matsui, K. S.; Tanikaga, R.; Kaji, A. *Chem. Lett.* **1980**, 287. (c) Halazy, S.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1981**, 4737. (d) Krief, A.; Evrard, G.; Badaoui, E.; De Beys, V.; Dieden, R. *Tetrahedron Lett.* **1989**, *30*, 5635. (e) Eisch, J. J.; Piotrowski, A. *Tetrahedron Lett.* **1983**, *24*, 2043. (f) Mitchell, T. N.; Reimann, W. *J. Organomet. Chem.* **1985**, *281*, 163. (g) Mitchell, T. N.; Reimann, W. *J. Organomet. Chem.* **1987**, *322*, 141. (h) Barrett, A. G. M.; Hill, J. M. *Tetrahedron Lett.* **1991**, *32*, 3285. (i) Magriotis, P. A.; Doyle, T. J.; Kim, K. D. *Tetrahedron Lett.* **1990**, *31*, 2541. (j) Magriotis, P. A.; Brown, J. T.; Scott, M. E. *Tetrahedron Lett.* **1991**, *32*, 5047. (k) Barrett, A. G. M.; Hill, J. M.; Wallace, E. M.; Flygare, J. A. *Synlett.* **1991**, 764. (l) Pine, S. H.; Shen, G. S.; Hoang, H. *Synthesis* **1991**, 165 and references therein. (m) Marek, I.; Lefrançois, J.-M.; Normant, J. F. *Tetrahedron Lett.* **1991**, *32*, 5969. (n) Marek, I.; Normant, J. F. *Tetrahedron Lett.* **1991**, *32*, 5973. (o) A significant amount of work has been carried out by Knochel and co-workers. For a leading reference see: Tucker, C. E.; Knochel, P. *J. Am. Chem. Soc.* **1991**, *113*, 9888.

[3] Lautens, M.; Huboux, A. H. *Tetrahedron Lett.* **1990**, *31*, 3105.

[4] Lautens, M.; Zhang, C. H.; Crudden, C. M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 232.

[5] Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1992**, *57*, 798.

[6] Lautens, M.; Huboux, A. H.; Chin, B.; Downer, J. *Tetrahedron Lett.* **1990**, *31*, 5829.

[7] (a) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77. (b) Brook, A. G.; Bassendale, A. R. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 149–227.

[8] (a) Brook, A. G.; Pascoe, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 6224. (b) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392 and references cited therein. (c) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London; 1981. (d) Eisch, J. J.; Tsai, M.-R. *J. Organomet. Chem.* **1982**, *225*, 5 and references cited therein.

[9] For a related approach, see: Kim, K. D.; Magriotis, P. A. *Tetrahedron Lett.* **1990**, *43*, 6137.

[10] Speier, J. L. *J. Am. Chem. Soc.* **1952**, *74*, 1003.

0022-3263/92/1957-3270$03.00/0

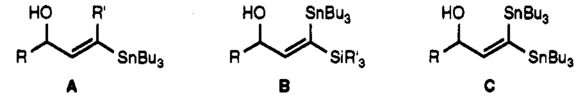


Figure 1.

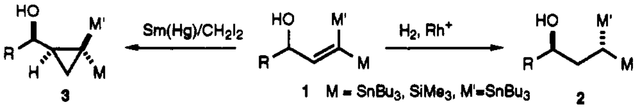


Figure 2.

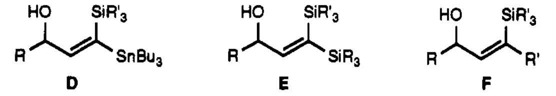
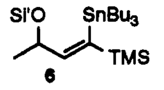
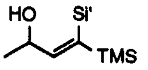
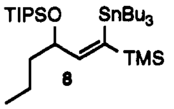
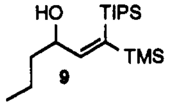
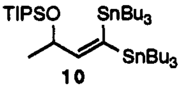
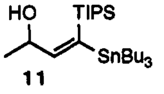
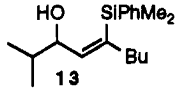
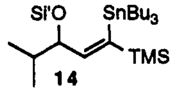
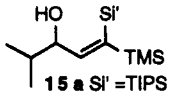
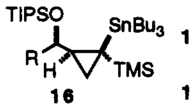
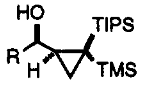
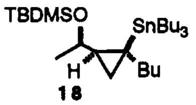
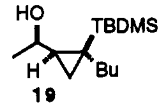


Figure 3.

bulk of the migrating group was extremely important.[11] The migration could be suppressed by substituting a triethylsilyl for a trimethylsilyl group. Others showed that the basicity of the carbanion also played a significant role and that triethylsilyl, triisopropylsilyl, and *tert*-butyldimethylsilyl groups also can undergo migration if the anion is very basic.[12,13] Our strategy was to take advantage of this process for the synthesis of those vinylsilanes which are difficult to prepare by existing methodology. Our result was particularly interesting since Negishi had shown that 1,4-migration of a *tert*-butyldimethylsilyl group *did not compete* with alkylation if the electrophile was part of the same molecule, i.e., an intramolecular cyclization.[14] We decided to investigate the generality of this reaction, focusing on vinyl- and cyclopropylsilanes.

The data in Table I show that migration is general and facile for transfer to vinyl and cyclopropyl carbanions and that silicon groups of varying size react equally well. Isolated yields of the vinylsilanes were high, and no contamination by the protonated allylic alcohols was observed. Migration of a phenyldimethylsilyl group, entry 4, was particularly important in light of the synthetic utility of this group as a precursor to a hydroxyl moiety with retention of stereochemistry.[4,15] Retention of configuration at the carbon-bearing tin was observed for the vinyl and cyclopropyl substrates examined. Transmetalation of a distannyl alkene and migration of the silicon provides a novel route to (*E*)-stannyl-(*Z*)-silyl olefins, entry 3, which are unavailable by other routes including our modification of the Sato reaction. While either tin moiety might have been cleaved in the initial transmetalation step,[2f,g] isomerization to the (*Z*)-lithio species must precede migration.

Table I. 1,4 Silyl Migration via Transmetalation

entry	substrate	condns[a] equiv MeLi, temp	adduct[b]	yield[c]
1		**6a** 1.2 eq., THF -40 °C, 2 h **6b** 1.2 eq., THF -40 °C, 30 min	 **7 a** Si' = TIPS **b** Si' = TBDMS	88% 92%
2		5 eq., THF, 0 °C, 1 h		94%
3		3.4 eq., THF, 0 °C, 2.5 h, rt, 1 h		40%[d]
4		1.5 eq., THF, -40 °C, 1.5 h		79%
5		**14a** 1.5 eq., THF, -78 °C, 2 h, -78 to 0 °C, 10 min **14b** 5 eq., THF, -78 °C, 1.5 h 0 °C, 1 h	 **15 a** Si' = TIPS **b** Si' = TBDMS	86% 91%
6		**16a** 10 eq., THF, 0 °C, 1 h **16b** 5 eq., THF, 0 °C, 1 h	 **17 a** R = Me **b** R = n-Pr	75% 91%
7		5 eq., THF, 0 °C to rt, 20 h		90%

[a] Reactions were often complete after 15–30 min, based on TLC. [b] Only one diastereomer was observed. [c] Isolated yields of analytically pure material. [d] Some destannylated product was also observed by TLC.

A crossover experiment was conducted to demonstrate the intramolecularity of the migration process. Upon treatment of a mixture of **6a** and **14b** with 1.5 equiv of MeLi in THF at 0 °C for 45 min, only two products were isolated. Examination of the ^{13}C NMR spectrum (100 MHz) of the mixture and comparison to authentic samples of all four possible products showed that only **7a** and **15b** were formed. No crossover products could be observed.

The synthetic utility of this reaction becomes apparent in considering routes to (*Z*)-silylalkenes. A general strategy which is effective for R groups of differing steric bulk is currently unavailable. The most often used approaches involve hydrometalation or silylmetalation[16] of an acetylene. For example, hydromagnesiation,[17] hydroboration,[18] and hydroalumination[19] of silyl alkynes have been successfully applied for simple acetylenes but few of these reactions have been shown to be applicable to propargyl alcohols. Furthermore, the regioselectivity of the hydrometalation is influenced by the steric bulk of the silyl group and reversal of regioselectivity has been noted for TIPS substituted acetylenes and a bulky hydroborating

---

[11] (a) Evans, D. A.; Takacs, J. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371. (b) For an N to N 1,4 silyl migration: West, R.; Ishikawa, M. *J. Am. Chem. Soc.* **1967**, *89*, 5049.

[12] O to C 1,4 silyl migrations: (a) Mora, J.; Costa, A. *Tetrahedron Lett.* **1984**, *25*, 3493. (b) Rucker, C. *Tetrahedron Lett.* **1984**, *25*, 4349. (c) Bures, E. J.; Keay, B. A. *Tetrahedron Lett.* **1987**, *28*, 5965.

[13] C to O 1,4 silyl migrations: (a) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 1947. (b) Matsuda, I.; Murata, S.; Ishii, Y. *J. Chem. Soc., Perkin Trans. 1* **1979**, 26. (c) Fleming, I.; Floyd, C. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 969. (d) Takeda, T.; Naito, S.; Ando, K.; Fujiwara, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 967. (e) Brook, A. G.; Chrusciel, J. J. *Organometallics* **1984**, *3*, 1317. (f) Isobe, M.; Ichikawa, Y.; Funabashi, Y.; Mio; S. Goto, T. *Tetrahedron* **1986**, *42*, 2863. (g) Spinazzé, P. G.; Keay, B. A. *Tetrahedron Lett.* **1989**, *30*, 1765.

[14] Negishi, E.; Zhang, Y.; Bagheri, V. *Tetrahedron Lett.* **1987**, *28*, 5793.

[15] Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.*, **1987**, *28*, 4229.

[16] Fugami, K.; Hibino, J.; Nakatsukasa, S.; Matsubara, S.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1988**, *44*, 4277.

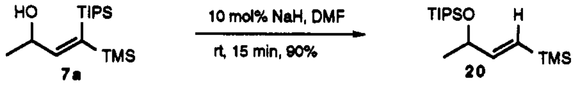
[17] (a) See ref 3. (b) Sato, F.; Kobayashi, Y. *Org. Synth.* **1990**, *69*, 106 and references cited therein.

[18] (a) Uchida, K.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1976**, *41*, 2941. (b) Uchida, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1977**, *33*, 2987. (c) Zweifel, G.; Backlund, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 3184.

[19] (a) Baba, S.; Van Horn, D. E.; Negishi, E. *Tetrahedron Lett.* **1976**, 1927. (b) Eisch, J. J.; Damasevitz, G. A. *J. Org. Chem.* **1976**, *41*, 2214. (c) Uchida, K.; Utimoto, K.; Nozaki H. *J. Org. Chem.* **1976**, *41*, 2215. (d) Marshall, J. C.; Shearer, B. G. Crooks, S. L. *J. Org. Chem.* **1987**, *52*, 1236. (e) Ziegler, F. E. Mikami, K. *Tetrahedron Lett.* **1984**, *25*, 131.

agent.[20] Another challenge in preparing (*Z*)-trisubstituted vinylsilanes is the sluggishness of the hydrometalated intermediate toward alkylation with electrophiles which are less reactive than methyl or allyl halides. A significant amount of the protonated product often accompanies the desired products and separation of these products can be difficult. Utilization of a silyl migration on a (*Z*)-vinylstannane, prepared via the Piers palladium-catalyzed conjugate addition of a tin group to an ynone, provides a simple solution to these problems.[21] Transmetalation and migration occurs to give **13** in 79% yield, entry 4.

Although these migrations are formally reversible, no starting material was recovered after workup. Under these conditions the equilibrium clearly lies completely on the side of the lithium alkoxide. The driving force for this reaction may be the formation of a covalent O–Li bond (hard–hard) rather than a C–Li bond (soft–hard).[9] Replacement of lithium by sodium should cause reversal of the migration and that process is well documented.[13] We found that treatment of **7a** with 10 mol % NaH in DMF caused a carbon–oxygen migration providing **20** in 90% yield.



(2)

In conclusion, we have shown that 1,4-silyl migrations of stereochemically defined vinylstannanes can be utilized in the synthesis of a variety of (*Z*)-vinylsilanes and hetero- and homobimetallic compounds. This sequence provides additional substrates for hydrogenation and cyclopropanation reactions, the results of which will be reported shortly.

Acknowledgment. This research was supported by the Alfred P. Sloan Foundation, the Natural Science and Engineering Research Council (NSERC) of Canada, the Merck Frosst Centre for Therapeutic Research, and BioMega (Canada). We thank a reviewer for bringing refs 9 and 10 to our attention.

Supplementary Material Available: General experimental procedures, details for specific representative reactions, and compound characterization data (17 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

---

[20] (a) Soderquist, J. A.; Colberg, J. C.; Del Valle, L. *J. Am. Chem. Soc.* **1989**, *111*, 4873. (b) Soderquist, J. A.; Colberg, J. C. *Synlett.* **1989**, 25.

[21] Piers, E.; Tillyer, R. D. *J. Chem. Soc., Perkin Trans 1* **1989**, 2124 and references cited therein.

A Microscale NMR Method of Determining Absolute Stereochemistries in β-Amino Alcohols by Enantioselective Complexation and the Mode of Action of Their Oxidative Resolution

Pierre G. Potvin

Department of Chemistry, York University, 4700 Keele Street, North York, Ontario, Canada M3J 1P3

Received July 23, 1991 (Revised Manuscript Received April 9, 1992)

Summary: By reactions of six examples of the title compounds with the Katsuki–Sharpless catalyst, enantioselective complexation was found to be at the origin of the oxidative resolution of the *N*,*N*,α-trisubstituted β-amino alcohols and provides a means of assigning absolute stereochemistries to the title compounds.

In 1983, the Sharpless group[1] described a kinetic resolution of *N*,*N*-dialkyl β-amino alcohols (Scheme I) based on the preferred oxidation of one enantiomer (that related to (*S*)-1-amino-2-propanol) by ^{t}BuOOH, promoted by 2 equiv of $Ti(O^iPr)_4$ in the presence of 1.2–1.5 equiv[2] of (*R*,*R*)-diisopropyl tartrate (H_2DIPT), with isolation of the unreacted antipode in high ee. These reactions were not catalytic, as is the Katsuki–Sharpless asymmetric epoxidation,[3] but were nonetheless a useful alternative to classical resolutions that depend on diastereomers possessing different physical properties, especially because the absolute stereochemistries of the products were consistently the same, as is true of the epoxidation system. For quite unrelated purposes, I had occasion to examine the reactions of such amino alcohols with the parent Katsuki–Sharpless catalyst, $Ti_2DIPT_2(O^iPr)_4$. This has led to an explanation of the mode of action of this remarkable resolution and to a microscale method of assigning absolute stereochemistries to such amino alcohols.

Scheme I

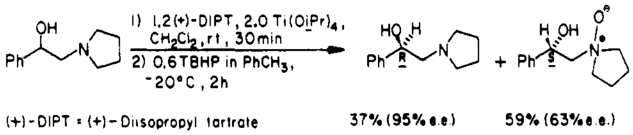


Table I. Spreads in Chemical Shifts in ppm (Δδ) and H–H Coupling Constants in Hz (*J*) for Tartrate Signals in the NMR Spectra of $Ti_2DIPT_2A(O^iPr)_3$

	first type			second type		
HA	$\Delta\delta_H$	$\Delta\delta_C$	*J*	$\Delta\delta_H$	$\Delta\delta_C$	*J*
HDMAE	0.13	1.73	9.3	0.55	0.51	7.2
HEPY	0.10	1.40	9.1	0.64	0.94	8.0
HDMAP	0.06	1.42	9.15	0.52	0.37	7.3
HDMAC	0.082	1.52	9.25	0.51	0.25	7.33
l-ephedrine	0.27	1.58	9.4	0.72	0.75	8.6

N,*N*-Dimethyl-2-aminoethanol (HDMAE) and *N*,*N*-dimethyl-1-amino-2-propanol (HDMAP) were known to form the monomeric, pentacoordinate complexes $TiDMAE(O^iPr)_3$ and $TiDMAP(O^iPr)_3$.[4] These and analogous complexes of other amino alcohols (generically represented by HA) are reactive toward alkoxide substitutions, as 1:1

---

[1] Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3608.

[2] Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 4350.

[3] Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. Reviews: Sharpless, K. B.; Woodard, S. S.; Finn, M. G. *Pure Appl. Chem.* **1983**, *55*, 1823. Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, p 247. Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 7, Chapter 3.2.

[4] Alyea, E.; Merrell, P. H. *Inorg. Nucl. Chem. Lett.* **1973**, *9*, 69.

0022-3263/92/1957-3272$03.00/0 © 1992 American Chemical Society