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HIGHLY DIASTEREOSELECTIVE HYDROSILATION REACTIONS. SPIROCYCLIC SILOXANES: SOURCES of Si-BASED LEWIS ACIDS

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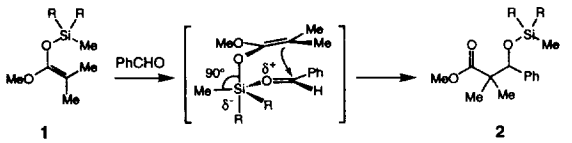
Abstract. Cyclohexylsiloxy hydrides (*e.g.*, **6**) undergo intramolecular hydrosilation with significantly higher levels of stereochemical control (versus their dimethylsilyl counterparts such as **3**). The resulting spirocyclic silanes may serve as effective Lewis acids; association with a Lewis basic site allows these entities to exist in the trigonal bipyramidal geometry wherein ring strain is released.

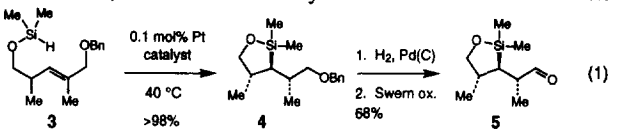
One of the most versatile attributes of silicon, which renders Si-containing molecules attractive candidates for reaction design, is its ability to adopt pentacoordinate geometry. As far as new reaction development is concerned, this important property has received relatively sparse - but notable - attention in the past. A recent advance, wherein a pentavalent silyl intermediate is believed to be involved, is the uncatalyzed aldol process (*e.g.*, **1**→**2**) reported by Myers and Denmark.[1] In these transformations, the resident Si atom associates with the C=O group of the reacting aldehyde, which in turn leads to enhanced reactivity. Ring strain in the starting silacycle is partially relieved by Si achieving penta-coordinate geometry: In the original tetrahedral system, angles of ~90°, favored by cyclic silanes, engender significant strain; in the trigonal bipyramidal arrangement, on the other hand, the five-membered ring can exist such that one C-Si bond is axial and the other equatorial (the requisite 90° C-Si-C bond angle can be accommodated).



Herein we report our observations with regard to intramolecular hydrosilation reactions that occur with excellent diastereocontrol and the effectiveness of resulting spirocyclic siloxanes to serve as a mild and efficient source of Lewis acidic silicon. The noteworthy feature of these studies is that hydrosilations with non-cyclic silyl (dimethylsilyl) hydrides are less selective and the chemistry of the resulting siloxanes represents no unusual chemical reactivity. Intramolecular hydrosilation of cyclohexylsilyl hydrides, however, are appreciably more diastereoselective. Furthermore, the presence of the second ring system lends the heterocyclic structure sharply different chemical properties.

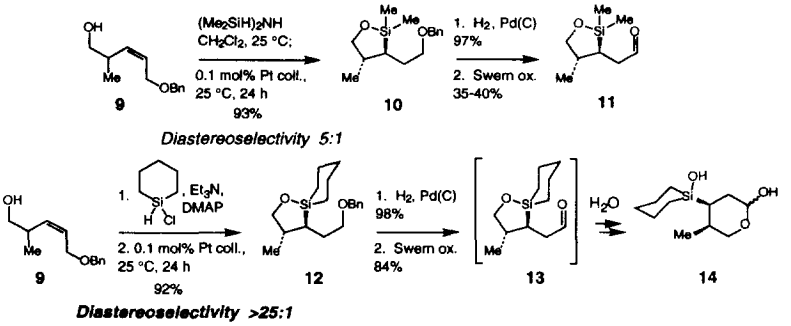
Our observations were made within the context of our studies in connection to the utility of cyclic siloxanes to relay acyclic stereochemistry.[2] As shown in Scheme 1, as reported by Tamao,[3] the intramolecular hydrosilation of the trisubstituted alkene **3** in the presence of 0.1 mol% Pt-divinylsiloxane and air can be carried out in excellent yield but modest stereoselectivity (→**4**; 4:1 diastereoselection). Deprotection of the benzyl unit and subsequent oxidation proceeds uneventfully to provide aldehyde **5** in good yield. Since chromatographic separation of **4** and its diastereomers proved somewhat tedious, we searched for a similar process that would yield

significantly higher levels of stereoselectivity. As shown in eq 2, *the simple expedience of using a cyclohexyl siloxy hydride*[4] *affords the desired siloxane* **7** *in >25:1 diastereocontrol* (judged by 300 MHz ^{1}H NMR).[5] As before, conversion to aldehyde **8** was carried out uneventfully.



Subsequently, in the context of a related synthetic objective, we required siloxane-aldehyde **11**, which, as shown in Scheme 1, was readily prepared through intramolecular hydrosilation of the cis disubstituted olefin, as described above with only 5:1 diastereochemical control (GLC analysis). Moreover, aldehyde **11** proved difficult to manipulate, particularly in large scale, as a result of its unexpected volatility, an issue that is reflected in the low yield observed in the oxidation procedure that leads to this compound (50-55%). To remedy both the selectivity and volatility problems, we turned our attention to the cyclohexyl siloxane derivative **13**. As before, with cyclohexylsilyl hydride the intramolecular hydrosilation proceeds with excellent diastereochemical control (**9**→**12**, >25:1, judged by 300 MHz ^{1}H NMR).

Scheme 1

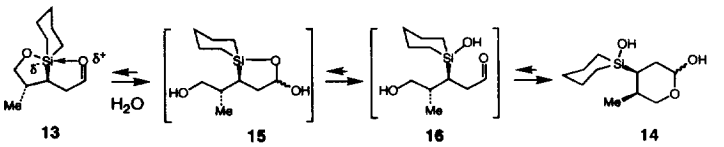


However, as shown in Scheme 1, similar treatment of **12** (Scheme 1), derived from the stereoselective intramolecular hydrosilation of **9**, does *not* afford the expected β-siloxy aldehyde **13** as the major product. When the primary alcohol derived from **12** is subjected to Parikh-Doering or Swern oxidation conditions, the ^{1}H NMR spectrum of the unpurified reaction mixture indicates that the majority of the product mixture consists of two isomeric acetals **14** (2:1 ratio);[6] there is only ~10-20% of the expected aldehyde **13**. When **13** is allowed to stand exposed to air at 22 °C, complete conversion to **14** is observed within 1-2 hrs. After silica gel chromatography, **14** is obtained as the only isolable product in 84% yield. When **14** is dissolved in freshly dried $CDCl_3$, slow reversion to aldehyde **13** is observed, as indicated by analysis of the ^{1}H NMR

spectra. A sample that is initially exclusively **14**, after 20 h, consists of **13** and **14** in a 40:60 ratio; after three days, the ^{1}H NMR spectrum reveals a sample that contains nearly 80% of **13**. The identity of cyclic acetal **14** was established, based on extensive spectroscopic data. For example, the signal in the ^{29}Si NMR spectrum of this compound (δ 9.72 (major) and 10.53 (minor), in $CDCl_3$ with Me_4Si as reference) is characteristic of a silylhydroxide, but not a typical cyclic siloxane (the acetate derived from **14** exhibits a peak at δ 9.82 (major) and 10.34 (minor) in the ^{29}Si NMR spectrum).[7]

A plausible mechanism for the generation of **14** via **13** is shown in Scheme 2. Rapid hydration of the aldehyde function in **13** leads to the formation of **15**, wherein the released primary carbinol adds to the unmasked hemiacetal (aldehyde) to yield **14**. *Thus, a key feature of the proposed mechanism is the high reactivity of the carbonyl group in 13 towards even a mild nucleophile such as water.*

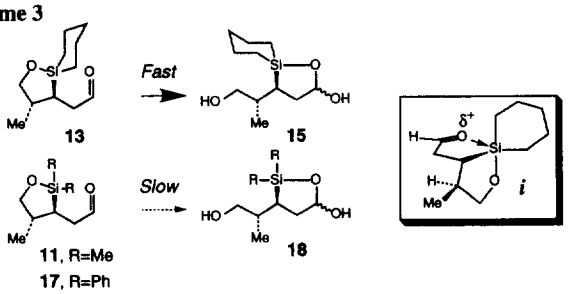
Scheme 2



13 15 16 14

The unusual tendency of **13** to undergo hydration is particularly striking, when its reactivity is compared to other related monocyclic siloxane systems: Whereas **13** is readily converted to **14**, related aldehydes **11** and the dimethylsilyl derivative **17**[8] are indefinitely stable and can be easily purified by silica gel chromatography (illustrated in Scheme 3). To account for the difference in reactivity between spirocyclic silane **13** and **11** or **17**, as before,[1] analogy to phosphorous-containing heterocycles can be made,[9] where a near 90° bond angle at phosphorous is favored. In these complexes, there is a preference for trigonal bipyramidal structures so that the P-C bonds may occupy an apical and an equatorial position (diequatorial would require ~120° angle). A cyclic pentavalent siloxane[10] (*e.g.*, **13**) may, for similar reasons, have a tendency to exist as a trigonal bipyramidal complex. (Within the trigonal bipyramidal complex (*i*) the bond angle at Si can readily be the expected (and favored) 90°.) That is, formation of a hypervalent siloxane is favored in the case of **13**, but not with **11** or **17**, since relief of the *additional* ring strain[11] serves as an effective driving force for the silicon complex to accept a fifth ligand.[12]

Scheme 3



13 15 11, R=Me 17, R=Ph 18

Observations disclosed in this Letter indicate that: (1) Intramolecular hydrosilation can be made significantly more diastereoselective when cyclic silyl hydrides are used. (2) Our data imply that an appropriately designed chiral *spirocyclic* silane, one that has a strong tendency to bind to Lewis basic sites, may represent an effective class of chiral catalysts. Rather than using electron

withdrawing groups to modulate Lewis acidity (in addition to a Si-containing ring),[1b] spirocyclic silanes offer two ring systems that can be manipulated in order to fine-tune catalyst reactivity (the more strained ring systems can carry higher Lewis acidic properties). Studies in relation to the design and synthesis of chiral spirocyclic Si-base Lewis acids are in progress.

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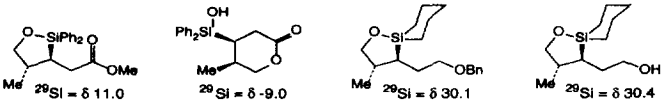
(5) The reason for this enhancement in stereoselectivity is not clear at present and must await the outcome of ongoing mechanistic studies.

(6) Representative spectral data for **14**: IR (KBr): 3374, 2914, 2858 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): (major isomer) δ 4.92 (dd, 1H, J=5.4, 3.0 Hz, **CH**(OH)), 3.78 (dd, 1H, J=11.1, 5.4 Hz, $\mathbf{CH_2}$OSi), 3.57 (dd, 1H, J=11.1, 3.0 Hz, $\mathbf{CH_2}$OSi), 2.0-1.5 (m, 6H, $SiCH_2(\mathbf{CH_2})_3CH_2$), 1.09 (dd, 3H, J=7.2 Hz, $\mathbf{CHCH_3}$), 0.85-0.60 (m, 5H, **CH**Si and $\mathbf{CH_2}$Si). The 300 MHz ^1H NMR of minor the isomer of **14** exhibits a broad singlet at δ 5.20 (2:1, with δ 4.92 for the major isomer). ^{13}C NMR: (both acetal isomers) δ 94.9, 90.8, 70.8, 66.7, 30.2, 29.7, 29.4, 25.9, 25.5, 24.2, 24.1, 20.4, 16.0, 14.2, 13.9, 13.8. The ^{13}C NMR of a sample containing ~20% **13** shows a peak at 204.0 for the C=O group. MS, *m/z* (rel. intensity): 230 (M, 0.8), 229 (2.4), 213 (3.6). The corresponding acetate was subjected to rigorous analysis: IR (KBr): 2919, 2855, 1741 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ (major isomer) 5.68 (dd, 1H, 9.4, 3.8 Hz, **CH**OAc), 3.71 (m, 2H, $\mathbf{CH_2}$OSi), 2.00 (s, 3H, $OCOCH_3$), 1.90 (m, 1H, $\mathbf{CHCH_3}$), 1.75-1.50 (m, 9H, $\mathbf{CH_2}CH_2$, **CH**Si), 1.11 (d, 3H, J=7.7 Hz, $\mathbf{CHCH_3}$), 0.68 (m, 4H, $SiCH_2$). ^{13}C NMR: (major isomer) δ 170.3, 95.8, 92.1, 73.9, 69.4, 29.7, 29.1, 26.4, 25.5, 21.2, 15.6, 13.7, 13.5. Anal. Cacd for $C_{13}H_{29}O_4Si$: C, 57.32; H, 8.88. Found: C, 57.47; H, 8.82.

(7) Several ^{29}Si chemical shifts are provided below for comparison ($CDCl_3$, Me_4Si reference). These data clearly indicate that the silanol Si appears ~20 ppm upfield of its derived siloxane. For a compilation of relevant ^{29}Si NMR data, see: Brey, S. W. In *Petrarch Systems Catalogue* **1987**, pp 60-68.



(8) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1994**, *59*, 4370-4374.

(9) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70-78 and references cited therein.

(10) For X-ray structures of spirocyclic disiloxanes and their derived hypervalent derivatives, see: Stevenson, W. H.; Wilson, S.; Martin, J. C.; Farnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340-6352. In the tetravalent and hypervalent (trigonal bipyramidal systems) the bond angle at the Si is 94° and 85°, respectively.

(11) Ring strain may be due to longer C-Si bond lengths. If Si were to adopt the expected 109° angle, the two carbon sites (C-Si) would have to be stretched apart, causing torsional strain. To avoid strain, the bond angle at Si is smaller than expected for a tetrahedral structure.

(12) Both **11** and **17** also contain a siloxy ring; these compounds have less of a tendency to adopt a trigonal bipyramidal structure probably because **13** possesses an additional ring system which enhances ring strain. Formation of the derived hydrate is not favored with **8**, probably because of an α-Me substituent.

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