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Mercuri-desilylation of Chiral Cyclopropylmethylsilanes.

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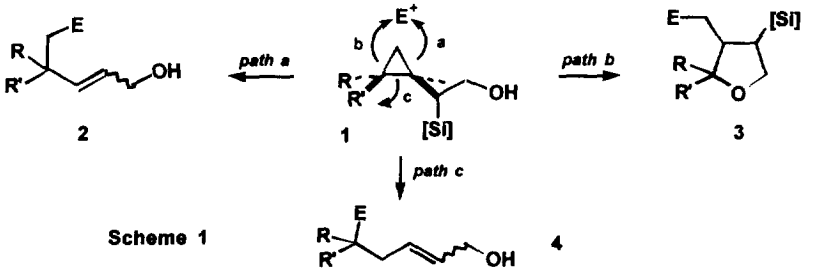
Abstract: Mercuri-desilylation of cyclopropylmethylsilanes such as **1** has been shown to occur with high regioselectivity. The cyclopropane ring-opening followed by desilylation proceeds *stereospecifically* to afford the corresponding olefins in good yields. The mercuri-mediated opening of cyclopropylmethyl alcohol analogues gives the opposite regioselectivity and affords only the tetrahydrofuran through a *5-endo-trig* cyclization.

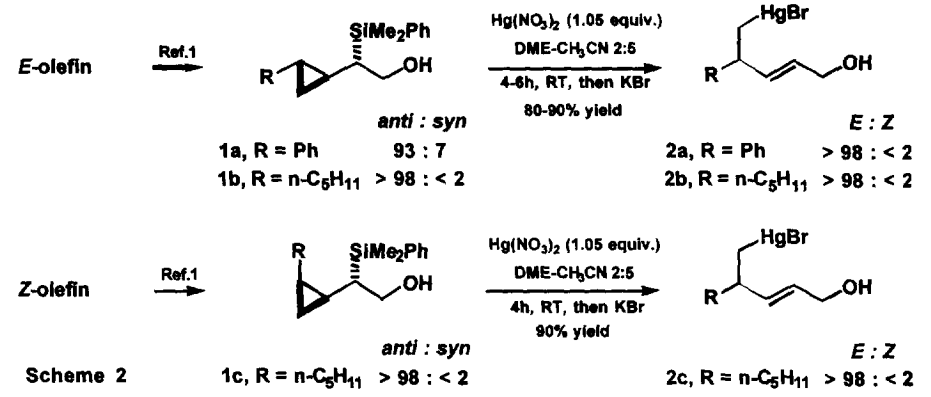
During the course of our studies on the epoxidation of 2-silyl-3-alkenols we showed that the relative stereochemistry of our epoxides could be unambiguously determined using the *anti* stereospecific acid-catalyzed Peterson elimination.[1] In the meantime, the determination of the relative configuration of cyclopropane analogues **1** proved to be much more problematic. Our unsuccessful attempts to produce suitable crystals for X-ray structure determination prompted us to investigate the electrophilic cyclopropane ring opening of **1** to give products which would be more amenable to structure determination. The opening of small rings such as cyclopropanes is relatively easy due to the release of a significant angle strain energy (~30 kcal/mole).[2] However, the regioselectivity of this reaction is often difficult to predict with certainty.[3,4] In our case, the presence of a β-hydroxysilyl moiety, prone to Peterson elimination, also add to the complexity of the problem. Three different routes could be envisaged : (*path a*): a ring-opening followed by elimination of the silicon group; (*path b*): a ring-opening, followed by a *5-endo-trig* cyclization to form the corresponding tetrahydrofuran **3**; (*path c*): a ring-opening, followed by desilylation to give the homologated olefin **4**. We report herein that using mercury(II) salts in polar media, it is possible to open cleanly the cyclopropane to afford in excellent yields, either the corresponding olefin **2** (*path a*) or a mixture of the olefin **2** and the tetrahydrofuran **3** (*path b*) depending on the substitution pattern on the olefin (Scheme 1). In contrast, the extension of this electrophilic process to cyclopropylmethyl alcohol analogues led only to ring-opening following *path b*.



2 1 3 4

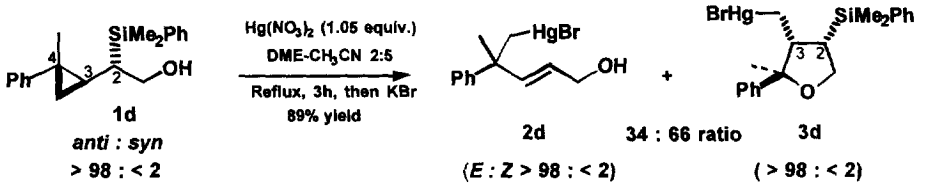
Scheme 1

With the cyclopropanes **1a-d** in hand, we first started to investigate what electrophile would be able to cleanly open the cyclopropane ring. Whereas thallium salts,[5] Br_2,[6] and Lewis acids[7] were found to be unsuitable for our purposes, $Hg(NO_3)_2$ in a mixture of DME-CH_3CN[8] was found to be the most efficient reagent, affording the expected olefins in good yields.[9] Thus, the ring-opening of cyclopropanes **1a-b** obtained from the *E*-olefins produced only the *E* olefins **2a-b** (>98:<2). Similarly, the cyclopropane **1c** obtained from a *Z* olefin produced also a *E*-olefin **2c** with selectivity as high as >98:<2 (Scheme 2).



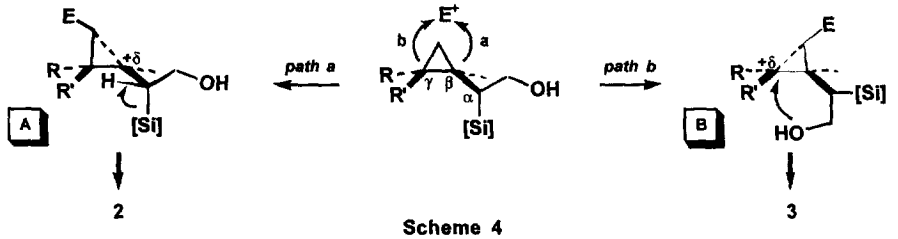
Scheme 2

Interestingly, cyclopropane **1d** having both substituents on C-4 produced, when treated with $Hg(NO_3)_2$ under reflux, a mixture of the *E* olefin **2d** along with the tetrahydrofuran **3d**, obtained as a single diastereoisomer with the stereochemistry depicted below, determined using difference NOE experiments (Scheme 3). The stereochemistry of the tetrahydrofuran being well secured, we can conclude that the stereochemistry of **1d** is *anti*, since the stereochemistry at C-2 and C-3 centres is left unchanged during the *5-endo-trig* process. Following this, it is likely that, according to the transition state proposed for the cyclopropanation reactions,[1] *Z*-olefins will produce *anti* cyclopropanes as the major isomer (*i.e.* **1c**).



Scheme 3

The results of the mercuri-desilylation of **1a-d** show that only *path a*, and to a lesser extent *path b* are operative. Attack following *path a* is directed by the disposition of the silicon moiety to stabilize a developing positive charge by hyperconjugation (*silicon-β-effect*).[10] Elimination of the silicon group then occurs in a similar

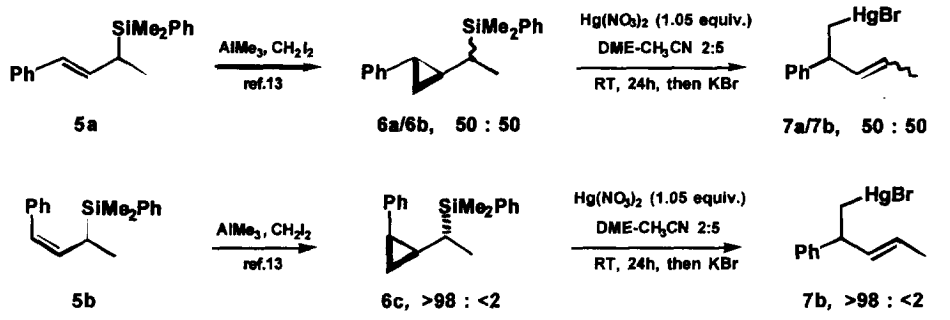


Scheme 4

fashion to what is observed for the acid-catalyzed Peterson elimination of epoxides (Scheme 4).[1,11] The positive charge could also develop in the γ position relative to the carbon attached to the silicon group, in the presence of substituents which are able to stabilize this positive charge.[10a] This is the case with **1d** where the development of a positive charge on a centre which is both benzylic and tertiary drives the reaction towards the cyclization (*i.e.* **3a**).[12]

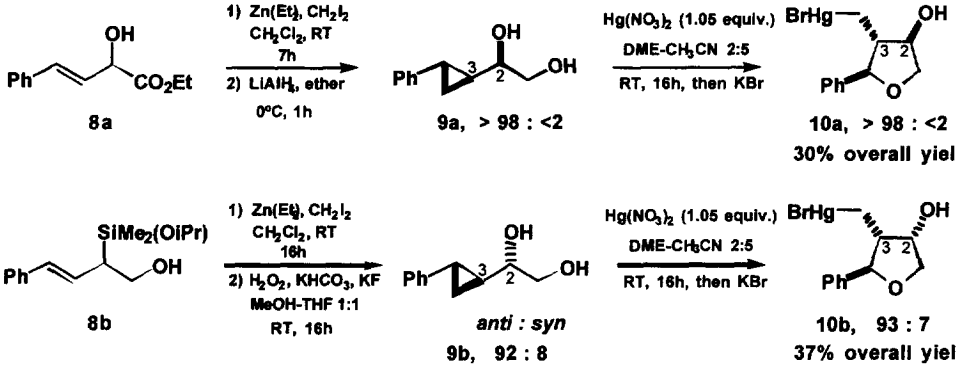
Another question which is raised by these preliminary results is the stereospecificity of the mercuri-desilylation. In order to have further insight into this problem which has never so far been addressed, we investigated the mercuri-desilylation of simple cyclopropylmethylsilanes prepared from the corresponding *E* and *Z*-allylsilanes **5a-b**[13] (Scheme 5). We observed that the treatment of an equimolar amount of *syn* cyclopropylmethylsilanes **6a** and *anti* **6b** with $Hg(NO_3)_2$ as above gave the *Z* and *E*-olefins **7a** and **7b** with the same ratio. Similarly, treatment of the pure *anti* **6c** under the same conditions gave only the *E*-olefin **7b** (^1H and ^{13}C NMR). This strongly suggests that similar to the protodesilylation of epoxides, *the mercuri-desilylation of*

cyclopropylmethylsilanes is stereospecific. Moreover, it is likely that other electrophile-mediated desilylations[3b] of cyclopropylmethylsilanes will also be *anti stereospecific*, the reaction proceeding through a conformation such as **A**. Therefore, we can assume that cyclopropanes **1a-d** all possess the *anti* stereochemistry (Scheme 2 and 3).



Scheme 5

Nevertheless, we decided to establish unambiguously the relative stereochemistry of **1a-b** using a series of independent experiments starting from allylic alcohol **8a** and allylsilane **8b** (Scheme 6). These were both submitted to Simmons-Smith type cyclopropanation[14] to produce, after the reduction of the ester function for the former and oxidation of the C-Si bond[15] for the latter, the stereochemically differentiated cyclopropane diols **9a** and **9b** (Scheme 6). Cyclopropane ring opening then gave rise to diastereoisomeric tetrahydrofurans **10a** and **10b** as the sole products. The difference NOE experiments (and NOESY) carried out on **10a** and **10b** allowed us to determine the relative stereochemistry of both the tetrahydrofurans and their precursors **9a** and **9b**, since the C-2 and C-3 centres are left unchanged during the cyclizations. These experiments thus demonstrate that cyclopropylmethylsilane **1a** (and consequently **1b**) possess a configuration which is *anti*. It is also worth mentioning that cyclopropylmethyl alcohols such as **9a-b**, give exclusively cyclopropane ring-opening according to *path b*, in contrast with the regioselectivity observed for their silyl counterparts **1a-d**.



Scheme 6

Using this methodology with the appropriate precursor, *syn* and *anti* cyclopropane diols such as **9a** and **9b** are available in reasonable yields and excellent diastereoselectivities, leading after *5-endo-trig* cyclization to tetrahydrofurans **10a-b** with excellent stereoselectivity and opposite stereochemistry at C-2.

In summary, we have demonstrated here that cyclopropylmethylsilanes react with $Hg(NO_3)_2$ in a very regioselective manner, affording the corresponding olefins after loss of the silicon group. We have also shown for the first time that mercuri-desilylation and related electrophilic reactions are, like the acid-catalyzed-Peterson elimination, *anti stereospecific*. This allowed us to assign confidently the stereochemistry of cyclopropanes **1a-d**. At the same time, this transformation can be regarded as a stereoselective methylation or alkylation of allylsilanes since the mercuri-olefins **2a-d** and **7a-b** can be further functionalized using radical or organometallic processes.[3b] Interestingly, we observed for the first time that cyclopropylmethanol analogues (having a styryl

system) react exclusively according to route *b* producing the corresponding tetrahydrofurans with excellent stereocontrol.

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