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# Synthesis of γ-methylene oxacycles and α- and β-alkylidene lactones *via* silicon-assisted ring opening of cyclopropyl carbinols†

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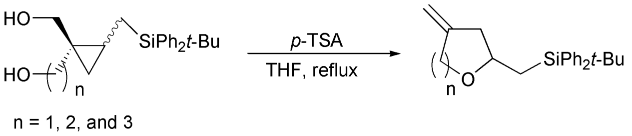
**Cyclopropyl carbinols bearing a (*tert*-butyldiphenylsilyl)methyl substituent undergo silicon-assisted regioselective ring cleavage and the resulting β-silyl carbocation is intramolecularly trapped with hydroxy and ester functions to generate γ-methylene oxacycles and α- and β-alkylidene lactones without the cleavage of the silicon function.**

Cyclopropanes constitute versatile intermediates for the synthesis of a wide range of molecular skeletons including carbocycles and heterocycles.[1] Amongst the known cleavages of cyclopropanes, acid-promoted cleavage of cyclopropyl carbinols has been extensively studied from both theoretical and synthetic viewpoints.[2] The initially formed cyclopropyl carbinyl cation can undergo either ring expansion to give a cyclobutyl cation[3] or ring cleavage to result in a homo allyl cation[4] in order to relieve ring strain. The resulting carbocation could also be trapped by nucleophiles for further synthetic manipulations. The former pathway has been studied in great detail.

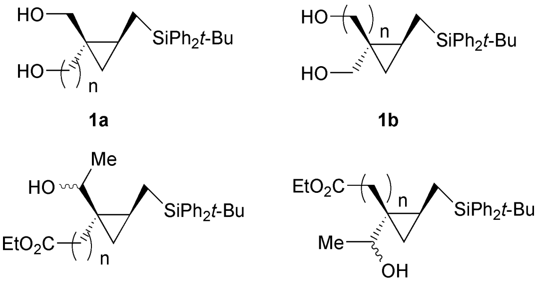
We have recently disclosed the importance of a bulky silyl substituent in the transformation of donor–acceptor substituted cyclopropanes into substituted dihydrofurans without the extrusion of the silicon function.[5] These results prompted us to study the silicon-assisted ring opening of the cyclopropyl carbinols **1** and **2** (Fig. 1) and intramolecular trapping of the resultant ring-opened β-silyl carbocations with heteroatoms.[6] Our results are summarized in Table 1.

In an exploratory experiment, we studied the ring cleavage of **1a** ($n$ = 1) that was prepared by the LiAlH$_4$ reduction of the corresponding diester. Compound **1a** ($n$ = 1) underwent, on treatment with *p*-TSA in THF at reflux, smooth and regioselective ring cleavage to furnish **3** in 86% yield (Scheme 1). Encouraged from this result, we set out to study the scope of the reaction and prepared the other diols **1a** and **1b** by increasing the length of one of the hydroxymethyl side chains. We aimed to synthesize γ-methylenetetrahydropyran and γ-methyleneoxepan as these skeletons are found in many natural products.[7,8] When $n$ = 2, γ-methylenetetrahydropyran **4** was obtained in good yield (entries 2 and 3). Both the isomers **1a** and **1b**, when $n$ = 3, gave a mixture of **5** and **6**; the latter being formed by isomerization of the former under the reaction conditions. To exploit the present methodology further, we reacted the substrates **2a** and **2b** that bear one hydroxy and one ester function to prepare lactones.

These substrates were prepared in excellent yields by selective reduction of the methyl ketone function in the corresponding keto ester precursors with NaBH$_4$ or NaCNBH$_3$. The substrates **2a** and **2b** ($n$ = 0) gave, on treatment with *p*-TSA in THF at reflux, a mixture of the α-ethylidene-γ-lactones[9] **7a** and **7b**. The geometry of the olefin was discerned from the downfield $^1$H shifts of the vinylic methyl and the vinylic hydrogen in compounds **7a** and **7b**, respectively, due to the anisotropic effect of the carbonyl function. The isomers **2a** and **2b** ($n$ = 1) furnished the corresponding spirocyclic γ-lactones **9a** and **9b** on reflux with *p*-TSA in THF for 2 and 1 h,



**Scheme 1**

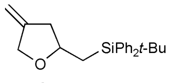
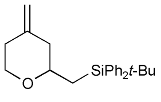
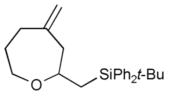
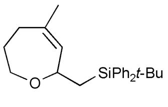
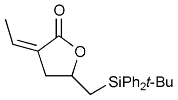
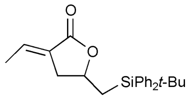
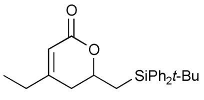


**1a** **1b**

**2a** **2b**

**Fig. 1** Structures of different cyclopropyl carbinols studied.

**Table 1** Conversion of cyclopropyl carbinols **1** and **2** into different γ-methylene oxacycles and lactones[a]

| Entry | Silane | Product(s) and yield (%) | |
|---|---|---|---|
| | | <br>**3** | |
| 1 | **1a** ($n$ = 1) | 86 (3 h) | |
| | | <br>**4** | |
| 2 | **1a** ($n$ = 2) | 72 (7 h) | |
| 3 | **1b** ($n$ = 2) | 74 (6 h) | |
| | | <br>**5** | <br>**6** |
| 4 | **1a** ($n$ = 3) | 31 | 58 (3 h) |
| 5 | **1b** ($n$ = 3) | 16 | 64 (8 h) |
| | | <br>**7a** | <br>**7b** |
| 6 | **2a** ($n$ = 0) | 33 | 46 (35 h) |
| 7 | **2b** ($n$ = 0) | 18 | 69 (15 h) |
| | | <br>**8** | |
| 8 | **2a** ($n$ = 1) | 81 (26 h) | |
| 9 | **2b** ($n$ = 1) | 92 (13 h) | |

[a] In all the experiments, 1.2 equivalents of *p*-TSA was used.

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† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b1/b111332c/

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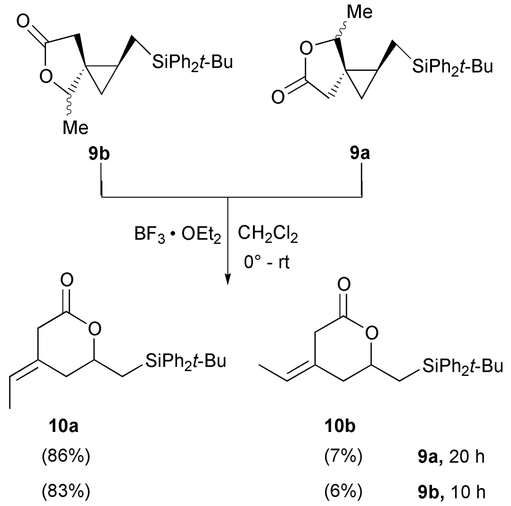

**Scheme 2** Conversion of spirocyclic lactones **9a** and **9b** into β-ethylidene-δ-lactones **10a** and **10b**.

respectively, in >95% yield. On further reflux, the spirocyclic γ-lactones were transformed into the α,β-unsaturated-δ-lactone **8** (entries 8 and 9) *via* isomerization of the primary products β-ethylidene-δ-lactones **10a** and **10b**. In order to obtain the desired β-ethylidene-δ-lactones **10a** and **10b**, we treated separately the spirocyclic γ-lactones with $BF_3{\cdot}OEt_2$ in anhydrous $CH_2Cl_2$ to effect ring opening. Indeed, the expected products were obtained in excellent yields (Scheme 2).[10] Cyclobutane formation was not observed from any of the reactions.

In conclusion, we have demonstrated a simple and efficient method to prepare synthetically important 5-, 6-, and 7-membered γ-methylene cyclic ethers, α-ethylidene-γ-lactones and β-ethylidene-δ-lactones in good to excellent yields. The preserved silicon function could be easily converted into a hydroxy function using a literature protocol.[11] Studies focused on the intramolecular trapping of the β-silyl carbocations resulting from the cleavage of cyclopropyl carbinols with olefins to synthesize carbocycles are under way.

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