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Silicon-Assisted Ring Opening of Donor–Acceptor Substituted Cyclopropanes. An Expedient Entry to Substituted Dihydrofurans

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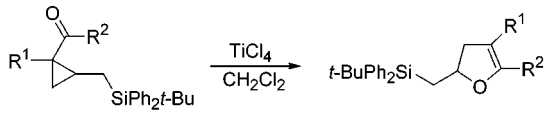
ABSTRACT



(*tert*-Butyldiphenylsilyl)methylcyclopropanes undergo ring opening to furnish substituted dihydrofurans in good to excellent yields on treatment with $TiCl_4$ in dichoromethane. The silicon that assists the regioselective ring opening is retained in the product to allow further functional group manipulations.

Cyclopropanes are useful synthetic intermediates because of their ready accessibility and good reactivity. The silicon-assisted ring opening of cyclopropane derivatives has been utilized in the synthesis of substituted olefins.[1] Vicinal substitution of a donor and an acceptor on the cyclopropane ring gives a sort of double activation and makes the ring cleavage possible under mild conditions.[2] The fluoride ion and BF_3−acetic acid systems have been used to cleave cyclopropanes having a trimethylsilylmethyl group as the donor substituent.[3] The cleavage of the carbon−silicon bond restricts the scope of this reaction, because an important functionality is lost to allow further synthetic manipulations. Hence, methods are required to effect ring opening without the extrusion of the silicon. In doing so, the resulting ring-opened species will have the features of a homo Michael system and those of an enolate equivalent (Figure 1).

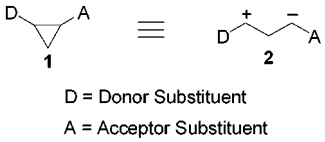


Figure 1.

The best way to achieve the above objective could be the placement of bulky substituents on silicon, as these would prevent the silicon from being attacked by nucleophiles, which is the exclusive pathway in the allylsilane chemistry.[4] In this report, we describe the $TiCl_4$-assisted transformation of such cyclopropylmethylsilanes having electron-attracting groups into substituted dihydrofurans (Scheme 1).[5] The overall results are collected in Table 1.

tert-Butyldiphenylsilylmethyl-substituted cyclopropanes[6] carrying different electron-attracting groups were treated with $TiCl_4$ under mild conditions.[7] Cyclopropanes bearing two

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(2) Reissig, H.-U. In *Topics in Current Chemistry*; de Meijere, A., Ed.; Springer-Verlag: Berlin, Heidelberg, Germany, 1991; Vol. 144, pp 73−135.

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(4) Organ, M. G.; Dragan, V.; Miller, M.; Froese, R. D. J.; Goddard, J. D. *J. Org. Chem.* **2000**, *65*, 3666 and references therein. For an excellent review on the subject, see: Knolker, H.-J. *J. Prakt. Chem.* **1997**, *339*, 304.

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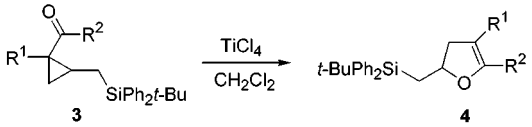
Scheme 1



a $R^1 = CO_2Me$, $R^2 = OMe$
b $R^1 = COMe$, $R^2 = Me$
c $R^1 = CO_2Et$, $R^2 = Me$
d $R^1 = SO_2Ph$, $R^2 = OEt$

electron-attracting groups (entries 1−4) underwent facile regioselective ring opening to furnish substituted dihydrofurans[8] in good to excellent yields. A ketone enolate cyclized in preference to an ester enolate (entry 3). This is in accordance with the results observed in the copper-catalyzed 1,3-dipolar addition of diazomethylacetoacetate to electron-rich olefins.[9] No ring cleavage was observed, even at room temperature, when the cyclopropane ring had a single ester function (entry 5). This may be due to the insufficient activation of the ring. In contrast, a single phenyl ketone (2.4:1 mixture of isomers) brought about the ring cleavage smoothly to furnish 3-hydroxy-4-*tert*-butyldiphenylsilylbutyl phenyl ketone. It is significant to note that the enolate did not cyclize on the incipient carbocation to give the desired dihydrofuran.

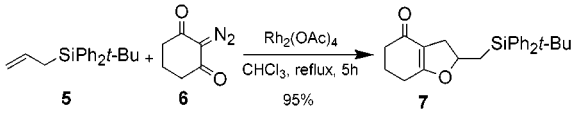
Table 1. Transformation of the (*tert*-butyldiphenylsilyl)methylcyclopropanes **3** into the Dihydrofurans **4**

entry	silane	temp (°C)	time	product	yield (%)[a]
1	**3a**	−30	3 h	**4a**	96
2	**3b**	0 to room temp	3 h	**4b**	81
3	**3c**	−30	10 min	**4c**	70
4	**3d**	−30 to room temp	8 h	**4d**	75
5	**3e**[b]	0 to room temp	21 h	no reaction	

[a] Isolated overall yield. [b] $R^1 = H$, $R^2 = OEt$.

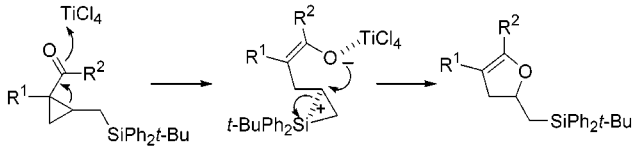
The above methodology was extended to prepare bicyclic ethers. The cyclopropane derived from 2-diazocyclohexane-1,3-dione was so reactive that it furnished the desired product under the conditions of its formation itself (Scheme 2). The use of a Lewis acid was not necessary. This high reactivity may be attributed to the ring strain present in the spirobicycle.

Scheme 2



The formation of the dihydrofuran proceeds presumably through the 5-exo-trig cyclization of titanium enolate on the silicon-stabilized carbocation[10] that is formed from ring opening (Scheme 3). The products of intermolecular additions were not observed.

Scheme 3 Mechanism of Dihydrofuran Formation



In conclusion, cyclopropanes bearing electron-attracting groups as the acceptor and the (*tert*-butyldiphenylsilyl)methyl group as the donor are easily cleaved with $TiCl_4$ to furnish substituted dihydrofurans. The carbon−silicon bond is not cleaved, and it is preserved in the product for its further manipulation into useful functional groups, including OH.[11] The reaction of the above enolate with electrophiles such as aldehydes and ketones in an intermolecular process followed by an intramolecular cyclization on the silicon-stabilized carbocation to form substituted tetrahydrofuran rings is currently under investigation. The 1,4-addition of the in situ generated enolate to enones, followed by cyclization of the newly generated enolate onto the silicon-stabilized carbocation, is likely to culminate in the synthesis of substituted cyclopentanes. This aspect is also being investigated concurrently. The results of these and other studies will be reported in due course.

(5) For alternate syntheses of dihydrofurans, see: Antonioletti, R.; Righi, G.; Oliveri, L.; Bovicelli, P. *Tetrahedron Lett.* **2000**, *41*, 10127. Hwu, J. R.; Chen, C. N.; Shiao, S.-S. *J. Org. Chem.* **1995**, *60*, 856. Abdallah, H.; Gree, R.; Carrie, R. *Tetrahedron* **1985**, *41*, 4339. Also, see ref 9 of this paper.

(6) The substituted cyclopropylmethylsilanes were prepared conveniently by a rhodium-catalyzed carbene insertion reaction of the corresponding diazo compound with allyl-*tert*-butyldiphenylsilane. **3c**, **3d**, and **3e** were respectively 1.3:1, 1.4:1, and 1.7:1 mixtures of isomers.

(7) *Typical Procedure:* To a solution of the cyclopropylmethylsilane **3a** (102 mg, 0.25 mmol) in dry CH_2Cl_2 (1.5 mL) was added a solution of $TiCl_4$ (57 mg, 0.3 mmol) in dry CH_2Cl_2 (1.5 mL) at −30 °C. The reaction mixture was stirred for 3 h and then quenched with saturated aqueous NH_4Cl solution. Et_2O (10 mL) was added to it, and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 5 mL). The combined organic extracts were washed with water and brine and dried over anhydrous Na_2SO_4. Removal of the solvents under reduced pressure furnished the crude product, which was purified by column chromatography (EtOAc/hexanes) to isolate **4a**; yield 98 mg, 96%.

(8) The structures of **4b** and **4c** were confirmed by comparing the spectral data available for similar known compounds reported in ref 5. The structures of **4a** and **4d** were confirmed by transforming them into 5-((*tert*-butyldiphenylsilyl)methyl)-γ-lactone by acid hydrolysis followed by dealkylation-decarboxylation and desulfonation, respectively.

(9) Alonso, M. E.; Morales, A.; Chitty, A. W. *J. Org. Chem.* **1982**, *47*, 3747. Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L. *J. Am. Chem. Soc.* **1983**, *105*, 2021.

(10) For discussions on silyl-stabilized β-carbocations, see: Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976; p 81. Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496. Lambert, J. B.; Wang, G.-T.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838. Lambert, J. B. *Tetrahedron* **1990**, *46*, 2677. Lambert, J. B.; Chelius, E. C. *J. Am. Chem. Soc.* **1990**, *112*, 8120. Green, A. J.; Kuan, Y.-L.; White, J. M. *J. Org. Chem.* **1995**, *60*, 2734. Gabelica, V.; Kresge, A. J. *J. Am. Chem. Soc.* **1996**, *118*, 3838. Chan, V. Y.; Clark, C. I.; Giordano, J.; Green, A. J.; Karalis, A.; White, J. M. *J. Org. Chem.* **1996**, *61*, 5227.

(11) Knolker, H.-J.; Jones, P. G.; Wanzl, G. *Synlett* **1998**, 613.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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