Pergamon

Tetrahedron Letters, Vol. 35, No. 43, pp. 7977-7980, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01693-3

Acetal-Induced Cleavage of Carbon-Carbon Bond of MEM Ethers of (*E*)-4-Alkyl-1-trimethylsilyl-1-alken-4-ols Providing Ketones

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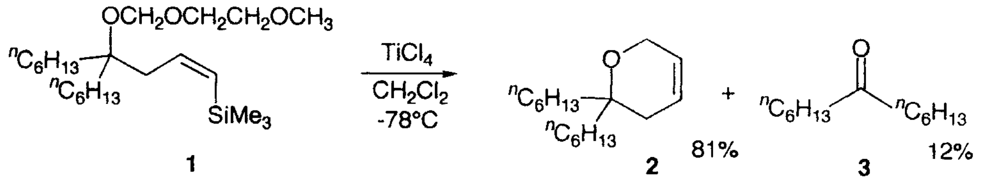
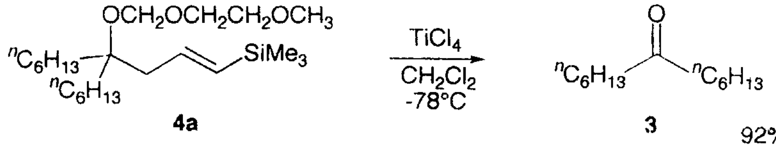
***Abstract*:** Treatment of methoxyethoxymethyl (MEM) ether of (*E*)-4-hexyl-1-trimethylsilyl-1-decen-4-ol with titanium(IV) chloride at –78 °C afforded 7-tridecanone in 92% yield under cleavage of carbon-carbon bond. The new method was applied to the conversion of epoxides into ketones.

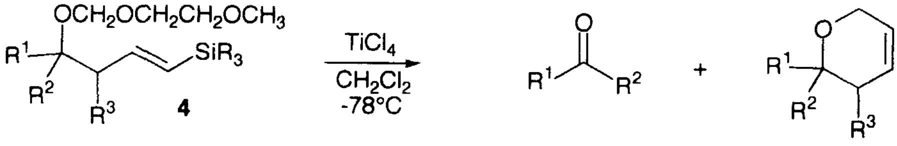
Vinylsilanes react readily with a wide range of electrophiles to give products of substitution.[1] Intramolecular reaction of MEM ether with alkenylsilanes in the presence of Lewis acid such as tin(IV) chloride provides a method for the synthesis of allylically unsaturated oxacycles.[2] Here we wish to report that the product distribution of such intramolecular reaction heavily depends on the stereochemistry of the alkene terminus. Whereas MEM ether of (*Z*)-4,4-dialkyl-1-trimethylsilyl-1-alken-4-ol provided dihydropyran derivative by acetal-induced cyclization with titanium(IV) chloride, MEM ether of (*E*)-isomer afforded ketone under carbon-carbon bond cleavage.

An addition of $TiCl_4$ to a solution of MEM ether of (*Z*)-4-hexyl-1-trimethylsilyl-1-decen-4-ol (**1**) in dichloromethane at –78 °C under argon atmosphere gave 6,6-dihexyl-5,6-dihydro-2*H*-pyran (**2**, 81%) along with 7-tridecanone (**3**, 12 %). In marked contrast to the generation of oxacycle **2**, reaction of MEM ether of (*E*)-4-hexyl-1-trimethylsilyl-1-decen-4-ol (**4a**) with $TiCl_4$ afforded 7-tridecanone in 92% yield without contamination by dihydropyran derivative **2** (<1%).

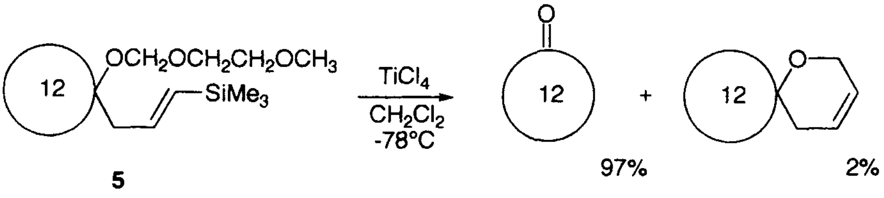




Other Lewis acids such as $SnCl_4$ and $BF_3 \cdot OEt_2$ were also effective for the cleavage reaction of **4a** and gave ketone **3** in 94% and 80% yields, respectively. The representative examples are shown below.[3,4] Not only acyclic ketones but also cyclic ketones were produced readily starting from the corresponding MEM ethers. Treatment of MOM ether of (*E*)-4-hexyl-1-trimethylsilyl-1-decen-4-ol instead of MEM ether **4a** with $TiCl_4$ gave 7-tridecanone **3** in 92% yield. The cleavage reaction proceeded well with 4,4-dialkyl-substituted substrate to provide ketones. In contrast, treatment of 4-monoalkyl substituted alkenylsilane with $TiCl_4$ gave the corresponding aldehyde in poor yield. For instance, MEM ether of (*E*)-1-trimethylsilyl-1-tridecen-4-ol afforded decanal in only <2% yield along with 6-nonyl-5,6-dihydro-2*H*-pyran (95%) upon treatment with $TiCl_4$.[5]

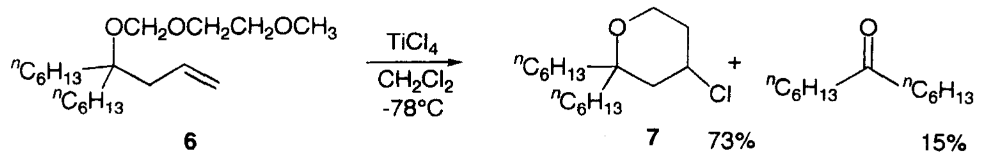


4b :	$R^1 = {}^nC_{10}H_{21}$ $R^2 = Me$ $R^3 = H$ $R = Me$	95%	5%
4c :	$R^1 = Ph$ $R^2 = Et$ $R^3 = H$ $R = Me$	54%	3%
4d :	$R^1 = R^2 = {}^nC_6H_{13}$ $R^3 = {}^nC_9H_{19}$ $R = Et$	74%	<1%



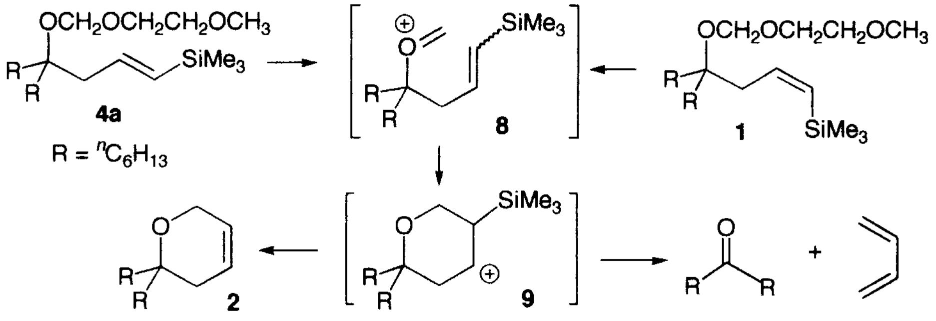
5

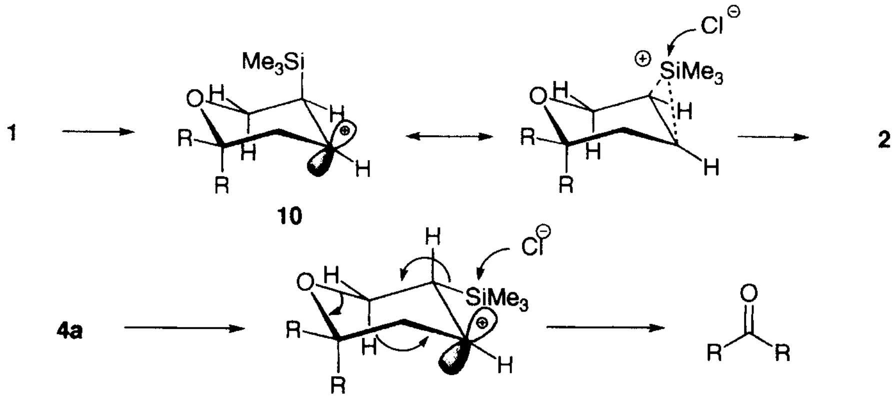
Treatment of MEM ether of 4-hexyl-1-decen-4-ol **6** with $TiCl_4$ provided 4-chlorotetrahydropyran **7** in 73% yield along with 7-tridecanone (15%). Thus, trimethylsilyl group plays a critical role for the successful formation of ketones.



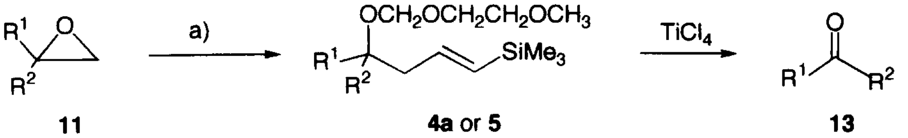
6 **7**

We assume following reaction mechanism based on these facts. Treatment of **1** or **4a** with $TiCl_4$ produces oxonium ion **8** which cyclizes to form six-membered cationic intermediate **9**. The carbonium ion **9** collapses to dihydropyran **2** or ketone under C-C bond cleavage by an attack of chloride ion on silicon. Dihydropyran formation would be favored with (*Z*)-vinylsilane since trimethylsilyl group would occupy an axial position and significant (σ-p)π overlap between the bonding σ-level of the C-Si bond with the adjacent empty *p*-orbital of the carbonium ion would be possible in a chairlike intermediate **10**, while similar mode of dihydropyran formation with (*E*)-vinylsilane **4a** is disfavored since trimethylsilyl group would adopt an equatorial orientation.





The reaction was applied to a transformation of epoxides into ketones. Treatment of epoxide **11a** or **11b** with *trans*-β-trimethylsilylvinyllithium,[6] derived from (*E*)-1-tributylstannyl-2-trimethylsilylethene and butyllithium, in the presence of trimethylgallium[7] provided homoallylic alcohol which was converted into MEM ether **4a** or **5**. An addition of $TiCl_4$ to **4a** or **5** afforded the corresponding ketones as shown above.



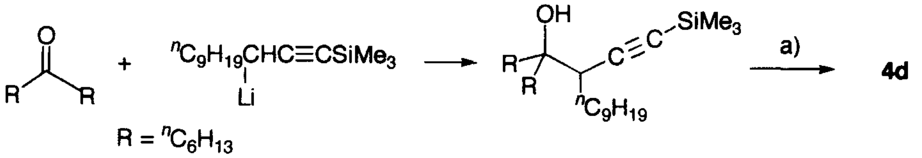
11a $R^1 = R^2 = {}^nC_6H_{13}$ **4a** 55% **11b** $R^1 = R^2 = (CH_2)_{11}$ **5** 52%

a) : i) $LiCH{=}CHSiMe_3$, Me_3Ga in THF ii) MEMCl, $^iPr_2NEt$

Typical procedure is as follows. Conversion of **4b** into 2-dodecanone is representative. A dichloromethane solution of $TiCl_4$ (1.0 *M*, 2.0 ml, 2.0 mmol) was added to a solution of MEM ether of 4-methyl-1-trimethylsilyl-1-tetradecen-4-ol (**4b**, 0.39 g, 1.0 mmol) in dichloromethane (5.0 ml) at –78 °C under argon atmosphere. The mixture was stirred for 30 min at –78 °C. Extractive workup (EtOAc, 1*M* HCl) followed by purification by silica-gel column chromatography gave 2-dodecanone (175 mg) in 95% yield along with 6-decyl-6-methyl-5,6-dihydro-2H-pyran (11 mg, 5% yield).[8]

References and Notes

1. Colvin, E. W. *Silicon in Organic Synthesis*, Butterworths, London, 1981, pp. 44-82; Weber, W. P. *Silicon Reagents for Organic Synthesis*, Springer-Verlag, Berlin, 1983, pp. 79-113.
2. Overman, L. E.; Castañeda, A.; Blumenkopf, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 1303; Overman, L. E.; Blumenkopf, T. A.; Castañeda, A.; Thompson, A. S. *ibid.* **1986**, *108*, 3516.
3. Alkenylsilane **1**, **4**, and **5** were prepared as follows. An addition of lithium trimethylsilylacetylide to 2-hexyl-1,2-epoxyoctane in the presence of catalytic amount of Me_3Ga gave homopropargylic alcohol which was converted into **1** by hydrogenation(H_2/Pd on $BaSO_4$) and successive etherification with MEM chloride. *E*-Isomer **4a**, **4b**, **4c**, and **5** were prepared by an addition of (trimethylsilyl)allyllithium (Corriu, R. J. P.; Masse, J.; Samate, D. *J. Organomet. Chem.* **1975**, *93*, 71; Yamamoto, K.; Ohta, M.; Tsuji, J. *Chem. Lett.* **1979**, 713; Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 5004) to the corresponding ketones followed by etherification. The acetal **4d** was generated by an addition of trimethylsilylpropargyllithium, derived from 1-trimethylsilyl-1-dodecyne and *t*-BuLi (Colvin, E. W. *Silicon reagents in Organic Synthesis*, Academic Press, London, 1988, p. 47), and successive desilylation and platinum catalyzed hydrosilylation with Et_3SiH as depicted below. The ^1H NMR ($CDCl_3$) data for olefinic protons of these alkenylsilanes are as follows. **1**: δ 5.56 (d, J = 14.0 Hz), 6.33 (dt, J = 14.0, 7.0 Hz); **4a**: δ 5.67 (d, J = 18.6 Hz), 5.99 (dt, J = 18.6, 6.8 Hz); **4b**: δ 5.68 (d, J = 18.6 Hz), 6.01 (dt, J = 18.6, 6.7 Hz); **4c**: δ 5.60 (d, J = 18.7 Hz), 5.83 (dt, J = 18.7, 6.6 Hz); **4d**: δ 5.51 (d, J = 19.0 Hz), 5.87 (dd, J = 19.0, 9.0 Hz); **5**: δ 5.64 (d, J = 18.7 Hz), 6.06 (dt, J = 18.7, 6.5 Hz).



a) : i) KF / DMF 80 % , ii) Et_3SiH, cat. H_2PtCl_6 , rt 1day 52% , iii) MEMCl, $^iPr_2NEt$ 64%

4. The reaction of **4d** with $TiCl_4$ would produce 1,3-dodecadiene in addition to 7-tridecanone, but 1,3-dodecadiene could not be isolated because of its instability under C-C bond cleavage reaction conditions. In fact, 1,3-dodecadiene, which was prepared independently, gave a complex mixture upon treatment with $TiCl_4$ in dichloromethane at –78 °C.
5. Treatment of the same MEM ether with $SnCl_4$ in place of $TiCl_4$ provided decanal in 23% yield in addition to pyran derivative (45%) and recovered starting material (25%). Moreover, the use of MEM ether of (*E*)-1-dipropylmethylgermyl-1-tridecen-4-ol instead of silylalkene improved the yield of decanal and provided decanal (45%) and 6-nonyl-5,6-dihydro-2*H*-pyran (12%) upon treatment with $TiCl_4$.
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8. Financial supports by the Ministry of Education, Science and Culture of Japan (Grant-in-Aid for Scientific Research No. 05235106 and 00041191) are acknowledged.

(*Received in Japan* 2 *June* 1994)