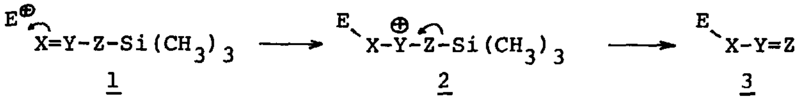
Tetrahedron Letters No. 49, pp 4925 - 4928.
© Pergamon Press Ltd. 1978. Printed in Great Britain.
0040-4039/78/1201-4925$02.00/0

SYNTHESIS OF BRIDGEHEAD SUBSTITUTED ADAMANTANE DERIVATIVES USING A REAGENT HAVING TRIMETHYLSILYL GROUP [1]

Tadashi Sasaki,* Arimitsu Usuki, and Masatomi Ohno
Institute of Applied Organic Chemistry, Faculty of Engineering,
Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464, Japan

In the past decade, the use of organosilicon compounds as reagents and as intermediates in organic synthesis has become a field of considerable interest.[2] Their wide applications are based on the characteristic properties of silicon element. Cationic site-stabilizing ability of silicon due to σ(C-Si)-π conjugation increases nucleophilicity of the double bond containing a silyl moiety at its allylic position.[2] A wide variety of electrophiles have been documented to react with such a double bond, although a few are known about an alkyl cation arising from haloalkane and Lewis acid.[3] [eq. 1]



$$\underset{\underline{1}}{\overset{E^{\oplus}}{X}{=}Y{-}Z{-}Si(CH_3)_3} \longrightarrow \underset{\underline{2}}{E{-}X{-}\overset{\oplus}{Y}{-}Z{-}Si(CH_3)_3} \longrightarrow \underset{\underline{3}}{E{-}X{-}Y{=}Z} \qquad [eq.\ 1]$$

In this paper we wish to report the reaction of 1-chloroadamantane 4 as a precursor of adamantyl cation and also as a representative of tertiary cations with some organosilicon compounds shown in eq. 1 in the presence of Lewis acid. This substitution method at the bridgehead seems to be useful means for preparing the adamantane derivatives.

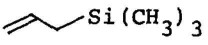
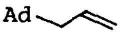
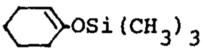
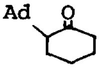
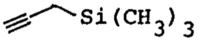
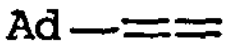
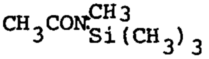
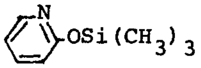
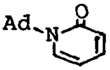
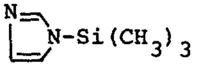
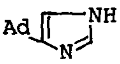
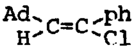
Allyltrimethylsilane 5 was at first selected as a typical reagent: To a solution of 1-chloroadamantane 4 (1 mM) and $TiCl_4$ (1 mM) in CH_2Cl_2 (3 ml) was added 5 (1 mM) in CH_2Cl_2 (1 ml) dropwise at room temperature. The reaction proceeded very smoothly and the usual work up (1. washing with water 2. drying the solution with Na_2SO_4 3. purification on silica gel chromatography) afforded 1-allyladamantane 6 in 85% yield. This result indicates that allyltrimethylsilane 5 is also reactive with adamantyl cation in addition to known electrophilic species like $RCO^{\oplus}$, $R_2(RO)C^{\oplus}$, $RS^{\oplus}$, and $Br^{\oplus}$.[3a-f] Under the same conditions, silyl enol ether of cyclohexanone 7 underwent facile addition-elimination with 4 to give 2-(1-adamantyl)cyclohexanone 8 in 61% yield. Similar observations were communicated very recently.[4] Benzyltrimethylsilane 9 was treated in the same manner. If the cyclic transition state is participated, the preferencial formation of o-adamantyltoluene might be anticipated. However, p-adamantylbenzyltrimethylsilane 10 was obtained as a sole product in this reaction. In acetylenic analogy, propargyltrimethylsilane 11 was expected to lead to allene 12 and examined; however, no reactions took place.

Next, we attempted the reaction of heteroanalogues of allylsilane such as N-trimethylsilyl-N-methylacetamide 13, trimethylsiloxypyridine 15, and N-trimethylsilylimidazole 17. In these experiments, use of any kinds and amounts of catalysts are necessary; $TiCl_4$ was not so effective but 2 eq. of aluminum chloride accomplished the reactions. In the experiment using 17, $CHCl_3$ is recommended as a solvent to avoid side products. In addition, the reaction mixture, after being poured onto ice water, should be neutralized with Na_2CO_3 or NaOH prior to extraction. Structural determination of these products was performed by spectral and elemental analyses and independent synthesis if required. It is to be noted that substitution on 17 occurred at C_4-carbon, different from the usual position at nitrogen, observed in acylation of 17 to N-acylimidazole or ethoxycarbonylmethylation of 17 to N-ethoxycarbonylmethylimidazole.[5]

Since electrophilic substitution on alkynylsilanes are also known,[6] reaction using phenylethynyltrimethylsilane 19 was carried out with a large excess of $ZnCl_2$ as a milder catalyst. Prolonged reaction time (more than 2 days) was required to expense the whole reagents. The reaction mixture was then poured onto water and the products from organic layer were recrystallized from methanol to give white crystals. The structure was primarily assigned as α-chloro-β-adamantylstyrene 20 by positive Beilstein test, spectral inspections, and elemental analysis. Furthermore, an independent synthesis confirmed its configuration: Wittig reaction of adamantanecarboxaldehyde 21 and benzylidenetriphenylphosphorane 22 afforded β-adamantylstyrene 23 in 42% yield, and each stereoisomer (trans and cis) was separated by silica gel chromatography. Their nmr spectra showed an AB quartet at 3.78τ and 4.10τ (J=16.5 Hz) for trans, and 3.70τ and 4.77τ (J=12.7 Hz) for cis, respectively. The latter was consistent with the reduced product of 20 with Zn metal in refluxing ethanol. The mechanism for the formation of 20 may be elucidated by the following process; 1) addition of 1-chloroadamantane 4, and 2) subsequent electrophilic substitution with water. The above experimental results are summarized in Table 1.

Finally it is pointed out that haloadamantanes are known to react hardly with anionic reagents,[7] however, once anionic reagents are silylated, reaction conditions can be altered from anionic to cationic one which is more advantageous for adamantane system.

TABLE 1

$X{=}Y{-}Z{-}Si(CH_3)_3$[1]		$\xrightarrow[\text{reaction time, solvent}]{\text{Ad-Cl } 4\text{, Lewis acid}}$	Ad-R[2]		Yield	m.p.
	5	$TiCl_4$ 12 hr, CH_2Cl_2		6[3]	85%	oil
	7	$TiCl_4$ 12 hr, CH_2Cl_2		8[4]	61%	87-88°
$phCH_2Si(CH_3)_3$	9	$TiCl_4$ 12 hr, CH_2Cl_2	p-$AdphCH_2Si(CH_3)_3$	10	45%	129-131°
	11	$TiCl_4$ ($ZnCl_2$) 12 hr, CH_2Cl_2		12	0%	
 $CH_3CON(CH_3)Si(CH_3)_3$	13	$AlCl_3$ 12 hr, CH_2Cl_2	 $AdN(CH_3)COCH_3$	14[5]	56% (lit.	122-123° 122-123°)
	15	$AlCl_3$ 12 hr, CH_2Cl_2		16	52%	180-182°
	17	$AlCl_3$ ($TiCl_4$) 12 hr, $CHCl_3$		18[6]	52% (lit.	227-230° 222-225°)
$phC{\equiv}CSi(CH_3)_3$	19	$ZnCl_2$ 2 days, CH_2Cl_2	 $Ad(H)C{=}C(ph)Cl$	20	49%	74-75°

1) All the organosilicon reagents were synthesized according to the reported procedures

2) Ad = 1-Adamantyl

3) E. C. Capaldi and A. E. Borchert, *Chem. Abst.*, 71 81931v (1969).

4) We reported 8 as an oil in the preceding paper (T. Sasaki, S. Eguchi, I. H. Ryu, and Y. Hirako, *Tetrahedron Letters*, 2011 (1974)). Therefore, the compound obtained from 1-adamantylmethyl carbene should be revised.

5) E. I. du Pont de Nemours & Co., *Chem. Abst.*, 63 9838a (1965).

6) F. N. Stepanov and S. D. Isaev, *Zh. Org. Khim.*, 6 1195 (1970).

REFERENCES

1. Synthesis of Adamantane Derivatives. 45. Part 44: T. Sasaki, S. Eguchi, and S. Hattori, *Heterocycles*, in press.
2. P. F. Hudrlick,"*New Application of Organometallic Reagents in Organic Synthesis*" edited by D. Seyferth, p 127, Elsevier, New York, N. Y., 1976.
3. For silyl enol ether, see p 133 in ref. 2, and for allylsilane, a) A. Hosomi and H. Sakurai, *Tetrahedron Letters*, 1295 (1976). b) A. Hosomi, M. Endo, and H. Sakurai, *Chem. Letters*, 941 (1976). c) A. Hosomi and H. Sakurai, *J. Amer. Chem. Soc.*, 99 1673 (1977). d) I. Ojima, M. Kumagai, and Y. Miyazawa, *Tetrahedron Letters*, 1385 (1977). e) B. W. Au-Yeung and I. Fleming, *Chem. Comm.*, 79 (1977). f) K. Itoh, M. Fukui, and Y. Kurachi, *Chem. Comm.*, 500 (1977).
4. a) M. T. Reetz and W. F. Maier, *Angew. Chem. Int. Ed.*, 17 48 (1978).
   b) M. T. Reetz and K. Schwellnus, *Tetrahedron Letters*, 1455 (1978).
   c) T. H. Chan, I. Paterson, and J. Pinsonnault, *Tetrahedron Letters*, 4183 (1977).
5. L. Birkofer, P. Richter, and A. Ritter, *Chem. Ber.*, 93 8204 (1960).
6. Footnote 100 in ref. 2.
7. Cf. R. C. Fort Jr., and P. R. Schleyer, *Advan. Alicyc. Chem.*, 1 283 (1966).

(Received in Japan 31 August 1978)