

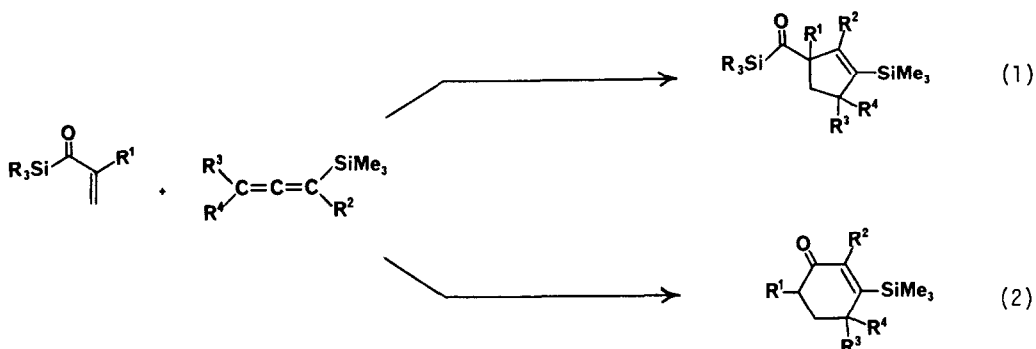
THE REACTION OF ALLENYLSILANES WITH α,β -UNSATURATED ACYLSILANES:
NEW ANNULATION APPROACHES TO FIVE AND SIX-MEMBERED
CARBOCYCLIC COMPOUNDS

Rick L. Danheiser*¹ and David M. Fink

Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Summary: The reaction of α,β -unsaturated acylsilanes with allenylsilanes can be directed to produce either five or six-membered carbocyclic compounds.

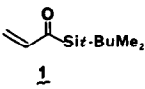
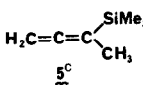
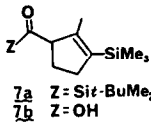
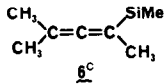
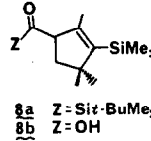
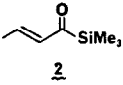
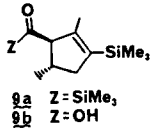
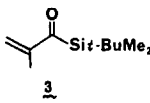
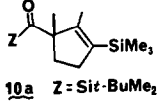
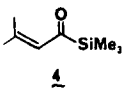
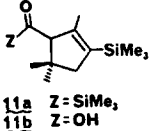
α,β -Unsaturated acylsilanes are versatile synthetic intermediates, readily participating in Brook reactions,² Diels-Alder additions,² and TiCl_4 mediated conjugate allylations.³ In this Letter we report that α,β -unsaturated acylsilanes combine with allenylsilanes in new [3+2] and [3+3] annulation routes to five and six-membered carbocycles (eqns 1 and 2).



By manipulating the nature of the acylsilane trialkylsilyl group, the course of these reactions can be controlled to produce either five or six-membered rings.

The α,β -unsaturated acylsilanes required for these studies were synthesized employing several alternative routes. The propenoylsilane 1 was prepared as previously reported by Reich,² and the crotonyl derivative 2 was synthesized using the general method of Zweifel⁴ as described in the accompanying Letter.³ The Zweifel route was also used for the preparation of the tigloyl derivative 16 (57% yield from $\text{Me}_3\text{SiCH}_2\text{CO}_2\text{SiMe}_3$). A modification of the Corey-Brook acylsilane synthesis furnished the mesityloylsilane 4³; however, this approach could not be successfully applied for the preparation of the methacryloyl derivatives 3 and 12.⁵ The following α -methylenation strategy was developed to provide access to these sensitive α,β -unsaturated acylsilanes. Treatment of propionyltrimethylsilane with 1.1 equiv of NaHMDS in

Table I. 3+2 Annulations Employing α,β -Unsaturated Acylsilanes

Acylsilane	Allenylsilane	Product	% Yield ^a	
			annulation step ^b	oxidation step
		 7a Z = Si <i>t</i> -BuMe ₂ 7b Z = OH	72	81
<u>1</u>		 8a Z = Si <i>t</i> -BuMe ₂ 8b Z = OH	55	88
	<u>5</u>	 9a Z = SiMe ₃ 9b Z = OH	66	62
	<u>5</u>	 10a Z = Si <i>t</i> -BuMe ₂	78	
	<u>5</u>	 11a Z = SiMe ₃ 11b Z = OH	74	85

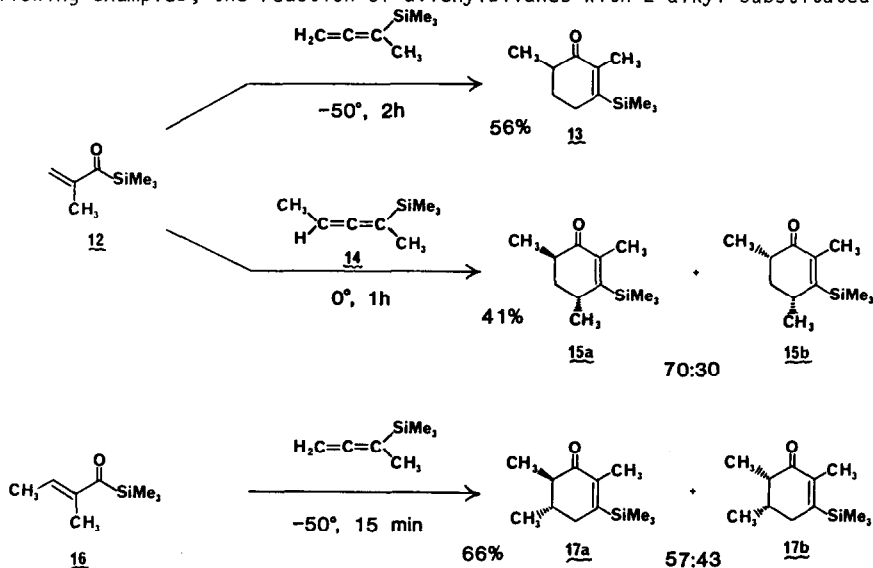
^aIsolated yields of products purified by chromatography. Infrared, ¹H NMR, ¹³C NMR, and high resolution mass spectra were fully consistent with the assigned structures. ^bAnnulations were carried out using 1.0-1.5 equiv of allene and 1.5 equiv of TiCl₄ in CH₂Cl₂ at -78°C for 0.5-1.0 h (30 sec in the case of 9a and 2 min for 10a). Reactions were quenched by transferring the resulting mixtures via cannula into a rapidly stirred mixture of 1:1 ether-water. ^cFor preparation, see ref. 7b.

THF (-78°C, 1 h) generated the corresponding enolate, which was transferred via cannula to a well-stirred cold (-78°C) suspension of N,N-dimethyl(methylene)ammonium iodide (Eschenmoser's salt)⁶ in THF. After 1 h the reaction was quenched by addition of excess methyl iodide. Upon exposure to 1.1 equiv of DBU in CH₂Cl₂ (25°C, 5 min), the resulting quaternary ammonium salt underwent smooth elimination to provide the desired acylsilane 12 in 63-70% overall yield. The analogous *t*-butyldimethylsilyl derivative 3 was prepared in 65-75% yield in a similar fashion.

The α,β -unsaturated acylsilanes **1-4** combine with allenylsilanes at -78°C in the presence of TiCl_4 to afford TMS-cyclopentene annulation products⁷ in good yield (Table I). A noteworthy feature of these [3+2] annulations is that they proceed significantly faster than the analogous reactions using α,β -unsaturated ketones. Thus, the β,β -disubstituted derivative **4** combines with allenylsilane **5** at -78°C within 45 min, whereas the analogous reaction of mesityl oxide required 1 h at 25°C .^{7b}

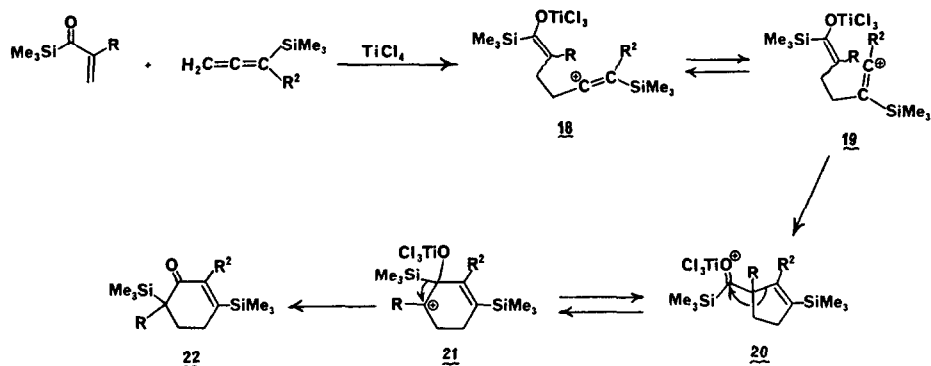
Exposure of the acylsilane annulation products to the action of 10% aqueous NaOH and 30% aqueous H_2O_2 in THF at 40°C for 30 min⁴ effects their smooth conversion to the corresponding carboxylic acids **7b-11b**. α,β -Unsaturated acylsilanes can thus be regarded as allenophilic carboxylic acid equivalents for our [3+2] annulation. Note that although methyl acrylate does participate in this reaction,^{7b} more highly substituted esters have proved to be unreactive.⁸

The annulation products derived from 2-alkyl substituted α,β -unsaturated acylsilanes undergo a novel rearrangement to β -silylcyclohexenone derivatives upon exposure to TiCl_4 at temperatures above -78°C . If desired, this further transformation can be prevented simply by employing *t*-butyldimethylsilyl acylsilane derivatives (e.g. **3**), minimizing the reaction time (≤ 2 min), and not permitting the reaction temperature to exceed -78°C . However, as illustrated with the following examples, the reaction of allenylsilanes with 2-alkyl substituted

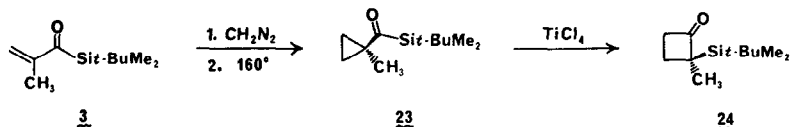


trimethylsilyl acylsilane derivatives provides the basis for a new [3+3] annulation approach to six-membered carbocycles. A possible mechanism for this unusual reaction is outlined in the following scheme. Regiospecific electrophilic substitution at C_3 of the allenylsilane provides a vinyl cation (**18**) which undergoes a 1,2-cationic TMS shift⁷ to afford an isomeric vinyl cation (**19**). Cyclization then provides the cyclopentene **20**.⁷ Ring expansion of this [3+2] annulation product next generates the tertiary carbocation **21**, which undergoes a second 1,2-cationic TMS shift⁹ to produce the cyclohexenone **22**. Desilylation finally furnishes the [3+3] annulation product.

The rearrangement step **20** \rightarrow **21** in these reactions proceeds regiospecifically via migration



of the vinylic carbon atom, as expected in view of the greater intrinsic migratory aptitude of the vinyl group,¹⁰ and the directing effect of the β trimethylsilyl substituent.¹¹ Also noteworthy is the fact that these *acylsilane* ring expansion reactions proceed with much greater facility than the analogous rearrangements of cycloalkyl *ketone* derivatives.¹² The following example demonstrates the potential utility of this process in the synthesis of other alicyclic systems. 1,3-Dipolar cycloaddition of CH_2N_2 to the acylsilane 3 (25°C, 2.5 h) afforded a



pyrazoline derivative (64% yield), which was subjected to vapor phase pyrolysis to produce the first recorded cyclopropyl acylsilane, 23, in 44% yield. Exposure of 23 to 1.0 equiv of TiCl_4 in CH_2Cl_2 ($-78^\circ\text{C} + 0^\circ\text{C}$, 1 h) then provided the cyclobutanone 24 in 75% yield.

Acknowledgments. We thank the National Science Foundation, Firmenich AG, and Eli Lilly and Co. for generous financial support.

References and Notes

- Alfred P. Sloan Research Fellow, 1981-1985.
- Reich, H.J.; Kelly, M.J.; Olson, R.E.; Holtan, R.C. *Tetrahedron* 1983, **39**, 949 and references cited therein.
- Danheiser, R.L.; Fink, D.M. *Tetrahedron Lett.* accompanying paper.
- Miller, J.A.; Zweifel, G. *J. Am. Chem. Soc.* 1981, **103**, 6217.
- In the case of 3 and 12 we were unable to hydrolyze the corresponding dithianes without inducing partial decomposition of the product acylsilanes.
- Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem., Int. Ed.* 1971, **10**, 330.
- (a) Danheiser, R.L.; Carini, D.J.; Basak, A. *J. Am. Chem. Soc.* 1981, **103**, 1604. (b) Danheiser, R.L.; Carini, D.J.; Fink, D.M.; Basak, A. *Tetrahedron* 1983, **39**, 935. (c) Danheiser, R.L.; Fink, D.M.; Tsai, Y.-M. *Organic Synth.*, submitted.
- We have found that β -substitution blocks the reaction of α,β -unsaturated anhydrides, and that annulations employing substituted α,β -unsaturated acyl nitriles proceed in poor yield.
- For related 1,2-cationic TMS shifts, see: Sato, T.; Matsumoto, K.; Abe, T.; Kuwajima, I. *Bull. Chem. Soc. Jpn.* 1984, **57**, 2167.
- See Hanack, M.; Schneider, H.-J. *Tetrahedron* 1964, **20**, 1863.
- The β -trimethylsilyl group has the capacity to stabilize the cationic character which develops at the migrating carbon atom. For a related example, see: Hudrlík, P.F.; Hudrlík, A.M.; Nagendrappa, G.; Yimenu, T.; Zellers, E.T.; Chin, E. *J. Am. Chem. Soc.* 1980, **102**, 6894.
- For reviews of ring expansions involving cycloalkyl ketones, see (a) Gutsche, C.D.; Redmore, D. "Carbocyclic Ring Expansion Reactions"; Academic Press: New York, 1968; pp.3-80. (b) Fry, A. In "Mechanisms of Molecular Migrations"; Thyagarajan, B.S., Ed.; Wiley-Interscience: New York, 1971; Vol. 4, pp. 113-195.

(Received in USA 6 March 1985)