CONJUGATE ADDITION OF ALLYLSILANES TO α,β-UNSATURATED ACYLSILANES

Rick L. Danheiser[*1] and David M. Fink

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

Summary: *α,β-Unsaturated acylsilanes serve as highly reactive carboxylic acid equivalents in conjugate allylation reactions with allylsilane derivatives.*

A recent objective in the development of our regio- and stereocontrolled [3+2] annulation[2] has been the application of this methodology to the synthesis of cyclopentene *carboxylic acid* derivatives (eqn 1, W=COOH). Unfortunately, α,β-unsaturated carboxylic acids and esters have

$$(1)$$

$$(2)$$
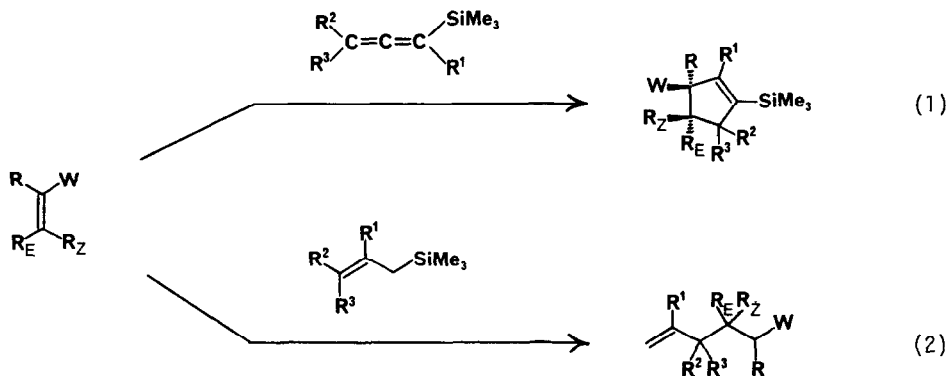
generally proven to be unreactive allenophiles in our reaction,[2b] as expected in view of their well-documented failure to participate in mechanistically related conjugate allylations (eqn 2).[3] Apparently the cation-stabilizing capacity of an additional terminal alkoxy group significantly reduces the electrophilicity of the intermediate alkoxy allylic carbocations involved in these reactions. Although Jellal and Santelli have previously demonstrated the reactivity of α,β-unsaturated acyl nitriles in conjugate allylations,[4] these compounds have not proved to be satisfactory allenophiles for our [3+2] annulation.

In this and the accompanying Letter we report that *α,β-unsaturated acylsilanes* serve as reactive electrophiles in the transformations outlined in eqns 1 and 2. As predicted (vide

infra), the reactivity of acylsilanes in these electrophilic substitution reactions exceeds that of analogous α,β-unsaturated ketones. Since the oxidation of acylsilanes to carboxylic acids is a well-established process, acylsilanes can be viewed as carboxylate equivalents for each of these transformations.
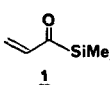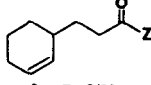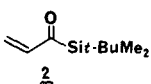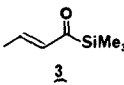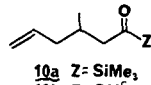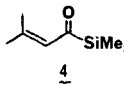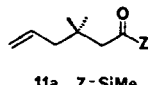
Table I delineates the scope of the conjugate allylation of α,β-unsaturated acylsilanes. Several standard routes to acylsilanes were employed for the synthesis of the α,β-unsaturated derivatives (1-5) required in this study. The known acylsilanes 1 and 2 were prepared as previously reported by Reich,[5] and the crotonyl derivative 3[6] was obtained via the Peterson reaction of $Me_3SiCH_2COSiMe_3$ and acetaldehyde according to the general method of Zweifel and Miller[7] (31% yield, not optimized). A modification of the classic Corey-Brook dithiane app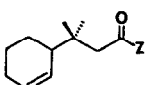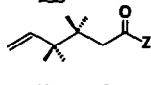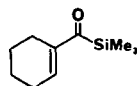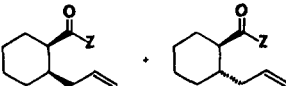roach[8] provided access to the more highly substituted derivatives 4 and 5. Thus, a THF solution of the dithiane derivative[9] of 3-methyl-2-butenal was treated with 1.1 equiv of n-BuLi (-25°C, 2.5 h) and 4.0 equiv of Me_3SiCl (-78° → 25°C, 2.5 h), and the resulting dithiane was then hydrolyzed by exposure to 2.2 equiv of $HgCl_2$ in the presence of $CaCO_3$ (aqueous acetone, reflux, 12 h) to furnish the acylsilane 4[5,6] in 46% overall yield from 3-methyl-2-butenal. The α,β-unsaturated acylsilane 5 was prepared from 2-cyclohexylidene-1,3-dithiane[10] in a similar manner. In this case this ketene thioacetal was first silylated in 61% yield by sequential treatment with 4 equiv of $LiNiPr_2$ (25°C, 2 h) and 8 equiv of Me_3SiCl (0°C, 20 min) in THF containing 4 equiv of HMPT.[11] Hydrolysis of the resulting dithiane with 2 equiv of HgO in 35% HBr_4-THF[12] at 25°C for 5 min then furnished the acylsilane 5 in 59% yield after distillation.

The conjugate allylation of α,β-unsaturated acylsilanes proceeds extremely rapidly even at -78°C. In a typical reaction, 1.2-1.5 equiv of $TiCl_4$ is added to a cold solution of acylsilane and 1.1-1.5 equiv of allylsilane derivative in CH_2Cl_2, and the resulting red solution is stirred at -78°C for 1-15 min.[13] Even highly sterically congested products such as 13a are produced in good yield under these mild conditions. The conjugate adducts are then easily transformed into the corresponding carboxylic acids employing the general method of Zweifel.[7,14] Exposure of the acylsilanes 9a-15a to 1.2 equiv of 10% aqueous NaOH and 2.2 equiv of 30% aqueous H_2O_2 in THF at 40°C for 30 min generates the expected carboxylic acids in 77-89% yield. Interestingly, we have also found that the more hindered t-butyldimethylacylsilanes (e.g. 9c) undergo efficient oxidation under identical conditions.

In recent years acylsilanes have emerged as valuable synthetic intermediates,[15] and the conjugate adducts 9a-15a should be subject to a variety of other useful transformations. For example, the conversion of 12a to the corresponding aldehyde 16 was achieved in 60% yield by treating this acylsilane with 1.3 equiv of $nBu_4NF \cdot 3H_2O$ in DMSO[16] at 25°C, and then quenching the reaction mixture after 1.5 min with formic acid.[17]

A noteworthy feature of our conjugate allylation reactions is the remarkable reactivity displayed by the α,β-unsaturated acylsilanes. The reactivity of the intermediates (e.g. 17) involved in these reactions can be attributed to the net destabilizing effect of trialkylsilyl groups on α carbocationic centers.[18,19] Apparently carbocations such as 17 receive little stabilization through hyperconjugative interaction with the trialkylsilyl group, and in

Table I. Conjugate Addition of Allylsilanes to α,β-Unsaturated Acylsilanes

Acylsilane	Allylsilane	Product(s)	% Yield[a]	
			conjugate allylation	oxidation step
1	2-cyclohexenyl-trimethylsilane **6**	**9a** Z = SiMe₃ **9b** Z = OH[b]	61	80
2	**6**	**9c** Z = Sit-BuMe₂ **9b** Z = OH[b]	73	66
3	allyltrimethylsilane **7**	**10a** Z = SiMe₃ **10b** Z = OH[c]	74	83
4	**7**	**11a** Z = SiMe₃ **11b** Z = OH[c]	82	86
4	**6**	**12a** Z = SiMe₃ **12b** Z = OH	75	89
4	3-methyl-2-butenyl-trimethylsilane **8**	**13a** Z = SiMe₃ **13b** Z = OH	59	77
5	**7**	**14a** Z = SiMe₃ **14b** Z = OH + **15a** Z = SiMe₃ **15b** Z = OH 6:1	65	80

[a] Isolated yields of products purified by chromatography. Infrared, ¹H and ¹³C NMR, and high resolution mass spectra were fully consistent with the assigned structures. [b] House, H.O.; Carlson, R.G.; Babad, H. J. Org. Chem. 1963, 28, 3359. [c] Jellal, A.; Santelli, M. Tetrahedron Lett. 1980, 21, 4487.

addition, the stabilizing σ inductive effect of the TMS substituent is overwhelmed by the
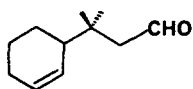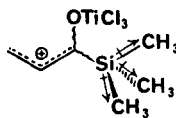
16   **17**

destabilizing field effect created by the polarization of the Si-CH$_3$ bonds.

References and Notes

1. Alfred P. Sloan Research Fellow, 1981-1985.
2. (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.
3. (a) Hosomi, A.; Sakurai, H. J. Am. Chem. Soc. 1977, 99, 1673. (b) Pornet, J.; Kolani, N.; Mesnard, D.; Miginiac, L.; Jaworski, K. J. Organomet. Chem. 1982, 236, 177.
4. Jellal, A.; Santelli, M. Tetrahedron Lett. 1980, 21, 4487.
5. Reich, H.J.; Kelly, M.J.; Olson, R.E.; Holtan, R.C. Tetrahedron 1983, 39, 949 and references cited therein.
6. First prepared using an alternative route: Soderquist, J.A.; Hassner, A. J. Am. Chem. Soc. 1980, 102, 1577.
7. Miller, J.A.; Zweifel, G. J. Am. Chem. Soc. 1981, 103, 6217.
8. (a) Brook, A.G.; Duff, J.M.; Jones, P.F.; Davis, N.R. J. Am. Chem. Soc. 1967, 89, 431.
   (b) Corey, E.J.; Seebach, D.; Freedman, R. J. Am. Chem. Soc. 1967, 89, 434.
9. Poulter, C.D.; Hughes, J.M. J. Am. Chem. Soc. 1977, 99, 3830.
10. Seebach, D.; Kolb, M.; Grobel, B.-T. Chem. Ber. 1973, 106, 2277.
11. Seebach, D.; Kolb, M. Justus Liebigs Ann. Chem. 1977, 811.
12. Degani, I.; Fochi, R.; Regondi, V. Synthesis 1981, 51.
13. In the case of conjugate allylations involving 1, decomposition of this relatively unstable acylsilane can be minimized by adding it to a cold (-78°C) solution of the allylsilane and TiCl$_4$.
14. Zweifel, G.; Backlund, S.J. J. Am. Chem. Soc. 1977, 99, 3184.
15. For recent reviews, see: (a) Fleming, I. In "Comprehensive Organic Chemistry", Barton, D.H.R. and Ollis, W.D. Eds.; Pergamon Press: Oxford, 1979; Vol. 3, pp. 647-653. (b) (b) Magnus, P.D.; Sarkar, T.; Djuric, S. In "Comprehensive Organometallic Chemistry", Wilkinson, G.; Stone, F.G.A.; Abel, E.W. Eds.; Pergamon Press: Oxford, 1982; Vol. 7, pp. 631-639.
16. For other examples of the fluoride-promoted conversion of acylsilanes to aldehydes, see ref. 7 and: (a) Schinzer, D.; Heathcock, C.H. Tetrahedron Lett. 1981, 22, 1881. (b) Degl'Innocenti, A.; Pike, S.; Walton, D.R.M.; Seconi, G.; Ricci, A.; Fiorenza, M. J. Chem. Soc., Chem. Commun. 1980, 1201. (c) Sato, T.; Arai, M.; Kuwajima, I. J. Am. Chem. Soc. 1977, 99, 5827.
17. This procedure fails in the case of less substituted acylsilanes (e.g. 9a) due to the propensity of the aldehyde products to decompose via aldol reactions.
18. For experimental data pertaining to the reactivity of α-trialkylsilyl carbocations, see: (a) Cartledge, F.A.; Jones, J.P. Tetrahedron Lett. 1971, 2193. (b) Cook, M.A.; Eaborn, C.; Walton, D.R.M. J. Organomet. Chem. 1971, 29, 389. (c) Stang, P.J.; Ladika, M.; Apeloig, Y.; Stanger, A.; Schiavelli, M.D.; Hughey, M.R. J. Am. Chem. Soc. 1982, 104, 6852; and references cited therein.
19. For theoretical discussions, see ref. 18c and: (a) Eaborn, C.; Feichtmayer, F.; Horn, M.; Murrel, J.N. J. Organomet. Chem. 1974, 77, 39. (b) Apeloig, Y.; Schleyer, P.V.R.; Pople, J.A. J. Am. Chem. Soc. 1977, 99, 1291. (c) Adcock, W.; Aldous, G.L.; Kitching, W. Tetrahedron Lett. 1978, 3387. (d) Olah, G.A.; Berrier, A.L.; Field, L.D.; Surya Prakash, G.K. J. Am. Chem. Soc. 1982, 104, 1349.