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# The Reaction of (Trialkylsilyl)vinylketenes with Carbenoid Reagents: A New [4+1] Annulation Route to Cyclopentenones

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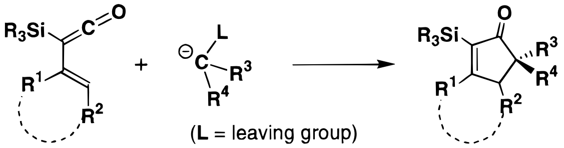
The invention of new methods for the construction of five-membered rings continues to be a problem of considerable importance in organic synthesis.[1] Only a few [4+1] annulation strategies have been reported to date, one example being the methodology based on oxyanion and carbanion-accelerated vinylcyclopropane rearrangements developed in our laboratory.[2,3] In this paper, we now report a stereoselective [4+1] annulation strategy for the synthesis of substituted cyclopentenones based on the reaction of (trialkylsilyl)vinylketenes ("TAS-vinylketenes") with nucleophilic "carbenoid" reagents such as sulfur ylides and diazo compounds (eq 1).

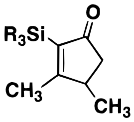
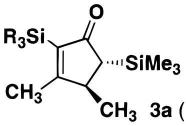
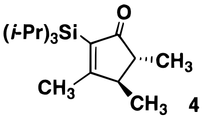
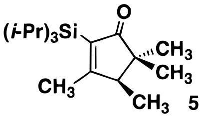
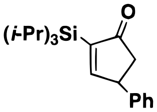
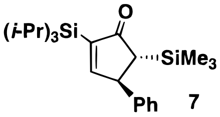
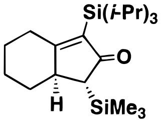


(1)

**1a** R = *i*-Pr, $R^1 = R^2 = CH_3$ **1c** R = *i*-Pr, $R^1 = H$, $R^2 = Ph$
**1b** R = Et, $R^1 = R^2 = CH_3$ **1d** R = *i*-Pr, $R^1,R^2 = (CH_2)_4$

Vinylketenes[4] function as versatile four-carbon building blocks in a variety of useful annulation strategies leading to four-,[5a] six-,[5a,b] and eight-membered carbocycles.[5c] Our plan for the application of vinylketenes to the synthesis of five-membered rings called for their reaction with nucleophilic carbenoid reagents to generate dienolate species that would then cyclize to the desired cyclopentenones. Like most ketenes, however, vinylketenes are rarely isolable species and usually must be generated as transient intermediates for in situ trapping by ketenophilic $\pi$ bonds. For the proposed [4+1] annulation, we therefore focused our attention on reactions of *TAS-vinylketenes*. The remarkable ability of silyl substituents to stabilize ketenes and suppress their tendency to undergo dimerization and [2+2] cycloaddition is well documented[4] and has been exploited, for example, by Tidwell for the synthesis of stable silylated bisketenes[6] and in our laboratory for the generation and isolation of (trimethylsilyl)vinylketene.[7] Several classes of carbanionic nucleophiles are known to add smoothly to simple silylketenes (including (trimethylsilyl)ketene itself),[8] and we therefore anticipated that TAS-vinylketenes would participate in the proposed [4+1] annulation provided that carbenoid reagents of suitable reactivity could be identified.

**Table 1.** [4+1] Cyclopentenone Annulation[a]

| entry | ketene | carbenoid reagent[b] | product | yield (%)[c] |
|---|---|---|---|---|
| 1 | **1a** | $Me_2\overset{+}{S}-\overset{-}{C}H_2$ |  **2a** (R=*i*-Pr) | 75 |
| 2 | **1a** | $Me_2\overset{\overset{O}{\parallel}}{\overset{+}{S}}-\overset{-}{C}H_2$ | **2a** | 43 |
| 3 | **1a** | $CH_2N_2$ | **2a** | 96 |
| 4 | **1a** | $Me_3SiCHN_2$ |  **3a** (R=*i*-Pr) | 84-92 |
| 5 | **1a** | $Ph_2\overset{+}{S}-\overset{-}{C}HCH_3$ |  **4** | 68 |
| 6 | **1a** | $Ph_2\overset{+}{S}-\overset{-}{C}Me_2$ |  **5** | 57 |
| 7 | **1b** | $Me_2\overset{+}{S}-\overset{-}{C}H_2$ | **2b** (R=Et) | 75 |
| 8 | **1b** | $Me_3SiCHN_2$ | **3b** (R=Et) | 95 |
| 9 | **1c** | $Me_2\overset{+}{S}-\overset{-}{C}H_2$ |  **6** | 65 |
| 10 | **1c** | $Me_3SiCHN_2$ |  **7** | 81 |
| 11 | **1d** | $Me_3SiCHN_2$ |  **8** | 83 |

[a] See Supporting Information for detailed procedures. [b] Reaction conditions: for $Me_2SCH_2$, THF−DMSO (entries 1 and 7) or DME (entry 9), 0−25 °C; for $Me_2SOCH_2$, DMSO−THF, 0−25 °C; for $Ph_2SCHCH_3$, DME, −50 to −20 °C; for $Ph_2SCMe_2$, THF, −20 to 25 °C; for $CH_2N_2$, $CH_2Cl_2$, −120 to 25 °C, 3 h; for $Me_3SiCHN_2$, $CH_2Cl_2$, 25 °C, 21−32 h. [c] Isolated yield.

The TAS-vinylketenes (**1a**−**1d**) required for this study were prepared via the photochemical Wolff rearrangement of α′-silyl-

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[1] For reviews, see: (a) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (b) Ramaiah, M. *Synthesis* **1984**, 529. (c) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467.

[2] Reviewed in: Bronson, J. J.; Danheiser, R. L. Charge-Accelerated Small Ring Rearrangements. In *Comprehensive Organic Synthesis*; Paquette, L. A., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 5, pp 999−1035. A related intramolecular [4+1] annulation based on thermal vinylcyclopropane rearrangements has been developed by Hudlicky; see: Hudlicky, T.; Reed, J. W. Rearrangements of Vinylcyclopropanes and Related Systems. In *Comprehensive Organic Synthesis*; Paquette, L. A., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 5, pp 899−970.

[3] For a recent [4+1] heteroannulation based on the addition of dimethoxycarbene to vinyl isocyanates, see: Rigby, J. H.; Cavezza, A.; Ahmed, G. *J. Am. Chem. Soc.* **1996**, *118*, 12848.

[4] Reviewed in: Tidwell, T. T. *Ketenes*; Wiley: New York, 1991.

[5] (a) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943. (b) Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093. (c) Danheiser, R. L.; Gee, S. K.; Sard, H. *J. Am. Chem. Soc.* **1982**, *104*, 7670.

[6] (a) Egle, I.; Lai, W.-Y.; Moore, P. A.; Renton, P.; Tidwell, T. T.; Zhao, D. *J. Org. Chem.* **1997**, *62*, 18. (b) Colomvakos, J. D.; Egle, I.; Ma, J.; Pole, D. L.; Tidwell, T. T.; Warkentin, J. *J. Org. Chem.* **1996**, *61*, 9522 and references therein.

[7] Danheiser, R. L.; Sard, H. *J. Org. Chem.* **1980**, *45*, 4810.

[8] For examples, see: (a) Ruden, R. A. *J. Org. Chem.* **1974**, *39*, 3607. (b) Baigrie, L. M.; Seiklay, H. R.; Tidwell, T. T. *J. Am. Chem. Soc.* **1985**, *107*, 5391. (c) Kita, Y.; Matsuda, S.; Kitagaki, S.; Tsuzuki, Y.; Akai, S. *Synlett* **1991**, 401.

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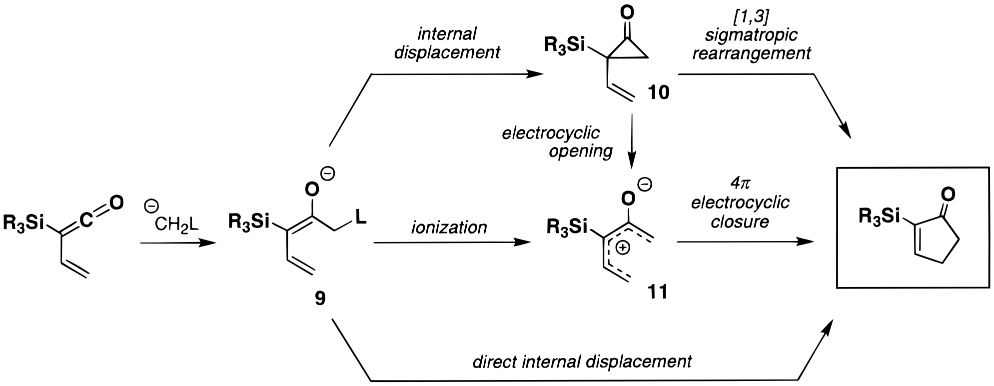
**Scheme 1**



α′-diazo-α,*β*-unsaturated ketones,[9] which are themselves readily available by silylation of the corresponding diazoketones.[10] Among the several classes of carbenoid reagents we have examined, sulfur ylides[11] and diazo compounds have thus far proved most effective for the desired [4+1] annulation.[12] Table 1 delineates the scope of this new route to substituted cyclopentenones. In a typical reaction, addition of 1.05 equiv of dimethylsulfonium methylide to **1a** in 1:1 THF−DMSO at 0−25 °C for 1.5 h gave the desired cyclopentenone **2a** in 75% yield after chromatographic purification. Dimethyloxosulfonium methylide also combines with **1a** to produce this cyclopentenone, though in lower yield (entry 2). Protodesilylation of annulation product **2a** was readily achieved by exposure to methanesulfonic acid in methanol at 25 °C for 3 h to afford 3,4-dimethylcyclopentenone in 95% yield.

As indicated in Table 1, diazomethane reacts with TAS-vinylketenes in a similar fashion, as does commercially available (trimethylsilyl)diazomethane.[13] However, all attempts to employ higher diazoalkanes and substituted TMS-diazomethanes in the [4+1] annulation have been unsuccessful; in each case no significant reaction occurred and the TAS-vinylketene was recovered unchanged. Fortunately, substituted sulfur ylides[11,14] are more nucleophilic and do react with TAS-vinylketenes in the desired fashion, providing access to highly substituted cyclopentenones in good yield (entries 5 and 6). A notable feature of annulations involving substituted carbenoid reagents is the exclusive formation of trans-4,5-substituted cyclopentenones (entries 4, 5, 8, 10, and 11).

Scheme 1 outlines several alternative pathways to account for the mechanistic course of the [4+1] annulation. Addition of a carbenoid reagent to the vinylketene should be highly stereoselective due to the shielding effect of the bulky trialkylsilyl group and should result in the formation of the (*Z*)-enolate **9**.[8b] Cyclization of this intermediate could produce the five-membered ring product directly, although the planar structure of the dienolate system in **9** may not allow it to achieve an arrangement in which the $\pi$ electrons are suitably situated for direct backside displacement of the leaving group. An alternative pathway involves ionization to produce the 2-oxidopentadienylic cation **11**, which can then undergo conrotatory 4$\pi$ electrocyclic closure[15,16] to generate the cyclopentenone product. A third pathway, proceeding via the cyclopropanone intermediate **10**, cannot be excluded, particularly in view of the finding that diazomethane adds to (trimethylsilyl)ketene to generate (trimethylsilyl)cyclopropanone in good yield.[17]

The stereochemical outcome of the reactions of substituted sulfur ylides and diazo compounds (entries 4, 5, 10, and 11) is consistent with a mechanism involving stereospecific conrotatory electrocyclic ring closure if one assumes that ionization of the initial dienolate intermediate occurs to generate a 2-oxidopentadienylic cation **11** with the C-1 substituent cis to the oxygen atom to minimize nonbonded interactions. If a mechanism involving concerted electrocyclization is indeed operative, then [4+1] annulations beginning with TAS-vinylketenes with *Z*-substituted alkenyl groups should afford cis-4,5-substituted cyclopentenones. Studies are underway in our laboratory to test this hypothesis and to demonstrate the utility of the [4+1] annulation strategy in the total synthesis of cyclopentanoid natural products.

**Acknowledgment.** Dedicated to Professor Satoru Masamune on the occasion of his 70th birthday. We thank the National Institutes of Health (Grant GM 28273) for generous financial support. J.L.L. and D.M.B. were supported in part as National Science Foundation Predoctoral Fellows.

**Supporting Information Available:** Experimental procedures and characterization data for all annulation products (10 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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[9] Details will be provided in a forthcoming paper. We have previously described the generation of vinylketenes by photochemical Wolff rearrangement,[5b] and Maas has reported the preparation of alkyl- and aryl-(TAS)ketenes using this reaction.[10a,b]

[10] (a) Maas, G.; Brückmann, R. *J. Org. Chem.* **1985**, *50*, 2802. (b) Brückmann, R.; Schneider, K.; Maas, G. *Tetrahedron* **1989**, *45*, 5517. (c) Brückmann, R.; Maas, G.; *Chem. Ber.* **1987**, *120*, 635.

[11] Reviewed in: Trost, B. M.; Melvin, L. S. *Sulfur Ylides*; Academic Press: New York, 1975.

[12] Concurrently with our studies, Tidwell has found that diazo compounds add to silylated bisketenes in a related process to produce cyclopentene-1,3-diones and 5-methylene-2(5*H*)-furanones.[6b]

[13] (a) Seyferth, D.; Dow, A. W.; Menzel, H.; Flood, T. C. *J. Am. Chem. Soc.* **1968**, *90*, 1080. (b) Shioiri, T.; Aoyama, T.; Mori, S. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. 8, pp 612−615.

[14] Diphenylsulfonium ethylide: Corey, E. J.; Jautelat, M.; Oppolzer, W. *Tetrahedron Lett.* **1967**, 2325. Diphenylsulfonium isopropylide: Nadeau, R. G.; Hanzlik, R. P. *Methods Enzymol.* **1969**, *15*, 347.

[15] Pentadienyl cation electrocyclic ring closures are involved in the mechanism of the Nazarov cyclization. For a review, see: Habermas, K. L.; Denmark, S. E. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1994; Vol. 45, pp 1−158.

[16] Epoxidation of vinylallenes produces cyclopentenones via electrocyclization of 2-oxidopentadienylic cations analogous to **11**. See: Kim, S. J.; Cha, J. K. *Tetrahedron Lett.* **1988**, *29*, 5613 and references therein.

[17] Zaitseva, G. S.; Bogdanova, G. S.; Baukov, Y. I.; Lutsenko, I. F. *J. Organomet. Chem.* **1976**, *121*, C1−C22. Zaitseva, G. S.; Bogdanova, G. S.; Baukov, Y. I.; Lutsenko, I. F. *Zh. Obshch. Khim.* **1978**, *48*, 131.