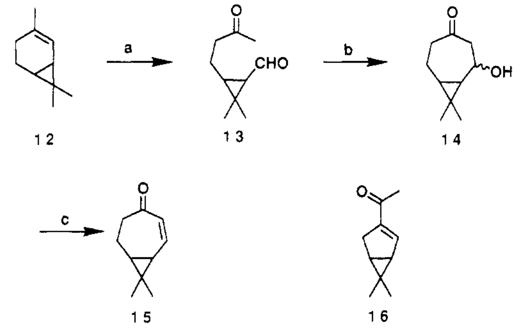
Scheme IV[a]



[a] (a) Reference 17; (b) $Zr(O\text{-}t\text{-}Bu)_4$ (2.0 molar equiv), THF, −30 °C to room temperature, 6 h; (c) AcONa, Ac_2O, AcOH, 90 °C, 4 h.

construct the α-bromo enone **9** from the α-bromo ketone **6** and the aldehyde **7** using LDA, $Sn(OTf)_2$[13] or n-Bu_2BOTf[14] were unsatisfactory.[15] Thus, we have accomplished a cross aldol reaction using the α-bromo ketone **6** for the first time. Furthermore, the α-bromo enone **11** was also obtained, from bromoacetone. That is, treatment of a mixture of benzaldehyde (2.0 mmol) and $Zr(O\text{-}t\text{-}Bu)_4$ (1.2 mmol) in THF (−30 °C) with bromoacetone (1.0 mmol) gave a mixture of the α-bromo β-hydroxy ketones **10**,[15,16] which was transformed to **11** in 56% overall yield from bromoacetone (Scheme III).

A further excellent example that shows the utility of $Zr(O\text{-}t\text{-}Bu)_4$ is a synthesis of (−)-8,8-dimethylbicyclo[5.1.0]oct-2-en-4-one (**15**),[17] which is a useful intermediate for many natural products syntheses.[18] The enone **15** has previously been synthesized from (−)-2-carene (**12**) by the Mukaiyama reaction in order to avoid the formation of the thermodynamically favorable five-membered-ring product **16**.[17] We found that **15**[19] could be readily prepared from **13**[17] via the intramolecular aldol adduct **14**, which was produced in 78% yield by treatment of **13** with 2 molar equiv of $Zr(O\text{-}t\text{-}Bu)_4$ in THF.[20] Dehydration of **14** was carried out using NaOAc and Ac_2O in AcOH at 90 °C to give the desired enone **15** in 79% yield. Other metal enolates (Li, Cp_2ZrCl,[21] ZnCl[22]) generated by LDA or metal exchange from the corresponding lithium enolate gave **14** in less than 10% yield together with a mixture of the intermolecular aldol products and the starting material **13**. Another approach using $Sn(OTf)_2$[13] and n-Bu_2BOTf[14] gave **14** in trace and 13% yields, respectively (Scheme IV). The facile formation of **14** is attributed to the following features. Owing to the bulkiness of both the tri-*tert*-butoxyzirconium cation and the counter *tert*-butoxy anion, the sterically favorable kinetic enolate should be generated. Also the aldol reaction appears to proceed via an acyclic transition state, thus avoiding the retro-aldol reaction.

In conclusion, we have succeeded in demonstrating the mild basic nature of $Zr(O\text{-}t\text{-}Bu)_4$ and its utility in organic synthesis. We expect $Zr(O\text{-}t\text{-}Bu)_4$ will serve as a new reagent for the synthesis of complex molecules. Utilization of its basicity in other types of reactions and the introduction of chirality to zirconium alkoxides are now in progress.

Acknowledgment. This study was financially supported by Grant-in-Aid for Scientific Research on Priority Areas (Multiplex Organic Systems) from the Ministry of Education, Science and Culture, Japan.

Supplementary Material Available: Experimental procedures and spectral data for **9**, **14**, and **15** (3 pages). Ordering information is given on any current masthead page.

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(13) (a) Mukaiyama, T.; Iwasawa, N.; Stevens, R. W.; Haga, T. *Tetrahedron* **1984**, *40*, 1381. (b) Abdel-Magid, A.; Pridgen, L. N.; Eggleston, D. S.; Lantos, I. *J. Am. Chem. Soc.* **1986**, *108*, 4595.

(14) (a) Mukaiyama, T.; Inoue, T. *Chem. Lett.* **1976**, 559. (b) Inoue, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 174. See also ref 13b and the references cited therein.

(15) The LDA–Cp_2ZrCl_2-assisted reaction afforded none of the desired products.

(16) The $Sn(OTf)_2$-mediated reaction also afforded **10**, which was converted into the α,β-epoxy ketone derivative in 72% overall yield. Mukaiyama, T.; Haga, T.; Iwasawa, N. *Chem. Lett.* **1982**, 1601.

(17) Taylor, M. D.; Minaskanian, G.; Winzenberg, K. N.; Santone, P.; Smith, A. B., III *J. Org. Chem.* **1982**, *47*, 3960.

(18) (a) Smith, A. B., III; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. *J. Am. Chem. Soc.* **1986**, *108*, 3040. (b) Smith, A. B., III; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. *J. Org. Chem.* **1985**, *50*, 3239. (c) Taylor, M. D.; Smith, A. B., III *Tetrahedron Lett.* **1983**, *24*, 1867.

(19) For convenience, commercially available (+)-2-carene was used.

(20) A coordinating solvent like THF is essential. When this reaction was carried out in dichloromethane, toluene, or hexane, a complex mixture was produced.

(21) (a) Panek, J. S.; Bula, O. A. *Tetrahedron Lett.* **1988**, *29*, 1661. (b) Evans, D. A.; McGee, L. R. *J. Am. Chem. Soc.* **1981**, *103*, 2876. (c) *Tetrahedron Lett.* **1980**, *21*, 3975.

(22) (a) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310. See also ref 13b.

N-(Silylmethyl)-Substituted Ketene *N*,*S*-Acetals as a Synthetic Equivalent of Novel 1,3-Dipolar Reagent, Alkylideneazomethine Ylids: Synthesis and [3 + 2] Cycloadditions[1]

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Summary: A variety of *N*-(silylmethyl)-substituted ketene *N*,*S*-acetals, readily prepared by the reaction of ketene dithioacetals with ((trimethylsilyl)methyl)amine, followed by N-alkylation, react smoothly with activated alkenes, carbonyl compounds, and thioketones, to afford α-alkylidenepyrrolidines, oxazolidines, and thiazolidines, via a 1,3-elimination of (methylthio)trimethylsilane. These reagents are synthetic equivalents of alkylideneazomethine ylids.

Azomethine ylids and related 1,3-dipolar reagents are important and interesting chemical species from both synthetic and theoretical points of view. These species are generally unstable and inaccessible if the dipolar centers are not stabilized by electron-withdrawing or conjugating groups.[2] Previously we reported a new method for pre-

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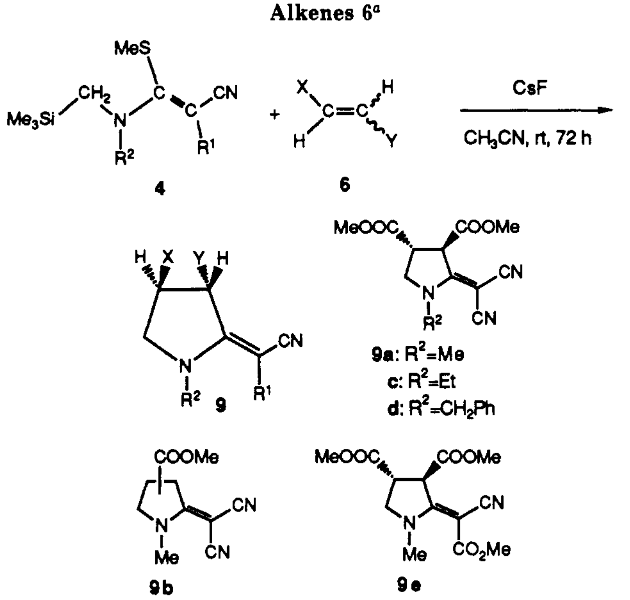
† Nagasaki University.

(1) Studies on organosilicon chemistry. 107.

(2) (a) Kellogg, R. M. *Tetrahedron* **1976**, *32*, 2165. (b) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565. (c) *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley & Sons: New York, 1984; Vols. 1 and 2.

Table I. Reaction of Ketene *S*,*N*-Acetals 4 with Activated Alkenes 6[a]



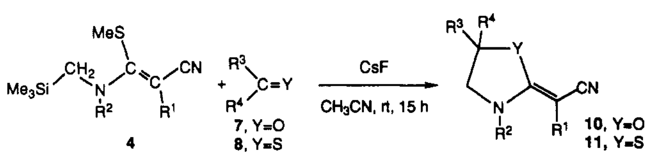
entry	*S*,*N*-acetal (4)	alkene (6)	product (9)	(% yield)[b]
1	**4a**: R^1 = CN; R^2 = Me	**6a**: X = Y = CO_2Me (*E*)	**9a** (trans)	(68)
2	**4a**	**6b**: X = Y = CO_2Me (*Z*)[c]	**9a** (trans)	(70)
3	**4a**	**6c**: X = H; Y = CO_2Me	**9b**[d]	(48)
4	**4b**: R^1 = CN; R^2 = Et	**6a**	**9c** (trans)	(47)
5	**4c**: R^1 = CN; R^2 = CH_2Ph	**6a**	**9d** (trans)	(36)
6	**4d**: R^1 = CO_2Me; R^2 = Me	**6a**	**9e** (trans)	(55)
7	**4d**	**6b**[c]	**9e** (trans)	(47)

[a] *S*,*N*-Acetal (**4**):Alkene (**6**):CsF = 1:3:1. [b] Yield after isolation by TLC. [c] For 10 days. [d] Although a regioisomer was obtained, its structure is not yet known.

paring pyrrolidine and tetrahydrothiophene derivatives from silicon-based 1,3-dipolar synthons by a 1,3-elimination reaction.[3] Now we report a facile preparation of alkylideneazomethine ylid equivalents[4] (i.e., *N*-((trimethylsilyl)methyl)-substituted ketene *N*,*S*-acetals **3** and their N-alkylated derivatives **4**) and their [3 + 2] cycloaddition to a variety of dipolarophiles, giving N-containing α-alkylideneheterocycles (Scheme I).

Ketene dithioacetals **2**,[5] readily available from the reaction of carbon disulfide and active methylene compounds in the presence of potassium carbonate, were treated with ((trimethylsilyl)methyl)amine (**1**) in MeOH at reflux for 10 min to afford the corresponding *N*,*S*-acetals **3** as single stereoisomers in high yield. N-Alkylation of **3** with alkyl halides was readily achieved in the presence of potassium carbonate in acetone at room temperature, giving the corresponding N-alkylated derivatives **4** in high yield (Scheme II).

Table II. Reaction of Ketene *S*,*N*-Acetals 4 with Carbonyl Compounds 7 and Thioketones 8[a]



entry	*S*,*N*-acetal (3 or 4)	carbonyl compound (7 or 8)	product (10 or 11) (% yield)[b]
1	**3a**: R^1 = CN; R^2 = H	**7a**: R^3 = 2,6-$Cl_2C_6H_3$; R^4 = H	**10a** (68)
2	**3a**	**7b**: R^3 = 4-CNC_6H_4; R^4 = H	**10b** (27)[c]
3	**3a**	**7c**: R^3 = 4-$C_6H_4C_6H_4$; R^4 = H	**10c** (48)
4	**3b**: R^1 = CO_2Me; R^2 = H	**7a**	**10d** (74)
5	**3b**	**7c**	**10e** (66)
6	**3b**	**7d**: R^3 = C_6H_5; R^4 = H	**10f** (24)[c]
7	**3b**	**7e**: R^3 = 4-ClC_6H_4; R^4 = H	**10g** (27)[c]
8	**3b**	**7f**: R^3 = 4-$NO_2C_6H_4$; R^4 = H	**10h** (30)[c]
9	**3b**	**7g**: R^3 = (*E*)-$C_6H_5CH{=}CH$; R^4 = H	**10i** (41)[c]
10	**3c**: R^1 = CO_2Et; R^2 = H	**7a**	**10j** (61)
11	**3d**: R^1 = $CONH_2$; R^2 = H	**7a**	**10k** (37)
12	**3e**: R^1 = $SO_2C_6H_5$; R^2 = H	**7a**	**10l** (57)
13	**4a**: R^1 = CN; R^2 = Me	**7a**	**10m** (54)
14	**4a**	**7d**	**10n** (42)
15	**4a**	**7e**	**10o** (60)
16	**4a**	**7h**: R^3 = 2-$MeOC_6H_4$; R^4 = H	**10p** (53)
17	**4b**: R^1 = CN; R^2 = Et	**7d**	**10q** (54)
18	**4c**: R^1 = CN; R^2 = CH_2Ph	**7d**	**10r** (32)[c]
19	**4d**: R^1 = CO_2Me; R^2 = Me	**7d**	**10s** (18)[c]
20	**4d**	**7i**: R^3 = 2-furyl; R^4 = H	**10t** (21)[c]
21	**3b**	**7j**: R^3 = Me, R^4 = 4-$NO_2C_6H_4$	**10u** (36)
22	**3b**	**7k**: R^3 = R^4 = CO_2Et	**10v** (55)
23	**3b**	**7l**: R^3 = C_6H_5; R^4 = C_6H_5CO	**10w** (38)
24	**4d**	**7m**: R^3 = R^4 = C_6H_5	**10x** (24)[c]
25	**4d**	**7n**: R^3 = 4-ClC_6H_4; R^4 = Me	**10y** (20)[c]
26	**3b**	**8a**: R^3 = R^4 = C_6H_5	**11a** (61)
27	**3b**	**8b**: R^3 = C_6H_5; R^4 = 2-benzo[*b*]thienyl	**11b** (77)

[a] *S*,*N*-Acetal **4**:carbonyl compound **7** or **8**:CsF = 1:3:1. [b] Yield after isolation by TLC. [c] *S*,*N*-Acetal **4**:carbonyl compound **7** or **8**:CsF = 1:1:1.

The *N*,*S*-acetals **4** react smoothly with dimethyl fumarate (**6a**) in the presence of cesium fluoride to give the corresponding α-alkylidene-substituted [3 + 2] cycloadducts **9a** with trans stereochemistry in a stereocontrolled mode (Table I).[6-9] With dimethyl maleate, however, the

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[3] (a) Hosomi, A.; Sakata, Y.; Sakurai, H. *Chem. Lett.* **1984**, 1117. (b) Hosomi, A.; Matsuyama, Y.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1073. (c) Hosomi, A.; Hayashi, S.; Kohra, S.; Tominaga, Y. *Ibid.* **1987**, 1442. (d) Hosomi, A.; Hayashi, S.; Hoashi, K.; Kohra, S.; Tominaga, Y. *J. Org. Chem.* **1987**, *52*, 4423. (e) For a leading review on related work using silicon-based azomethine ylid and related species, see: Vedjs, E.; West, F. G. *Chem. Rev.* **1986**, *86*, 941 and references cited therein.

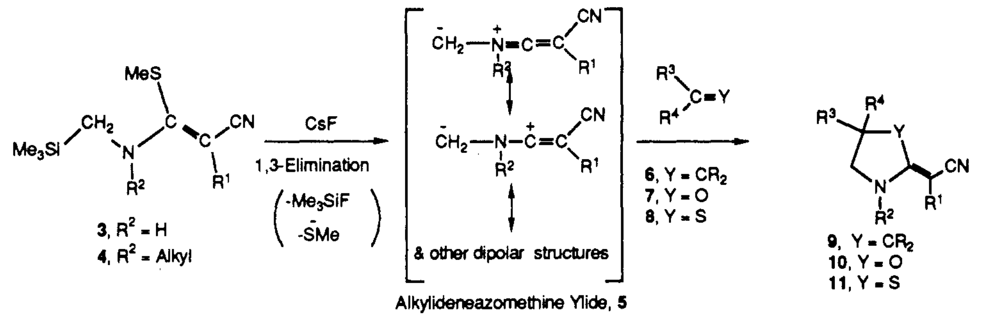
[4] Deyrup and Kuta have observed the formation of an α-alkylideneazomethine ylid which resulted from the deprotonation of a hindered ketenimimium salt in the presence of norbornene. See: Deyrup, J. A.; Kuta, G. S. *J. Org. Chem.* **1978**, *43*, 501.

[5] For recent work on ketene dithioacetals, see: Tominaga, Y.; Matsuoka, Y.; Kamio, C.; Hosomi, A. *Chem. Pharm. Bull.* **1989**, *37*, 3168 and references cited therein.

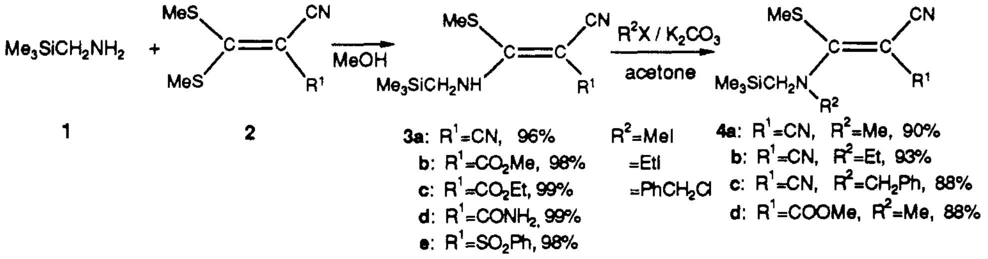
[6] General procedure: a solution of a dipolarophile (1.5 mmol), *N*,*S*-acetal (0.5 mmol), and cesium fluoride (0.5 mmol) was stirred in dry acetonitrile (10 mL) at room temperature for 15 h under an argon atmosphere. After the solvent was evaporated, and water and ether were added. The organic layer was dried over Na_2SO_4 and evaporated to yield a crude product which was purified by preparative TLC.

[7] Fluoride ion promoted protodesilylation of **4** occurred in all cases to give 3-(*N*-alkyl-*N*-methylamino)-3-(methylthio)acrylonitrile derivative **12** as a byproduct, although the amount of **12** formed decreased as the ratio of the acceptor to **4** was increased.

Scheme I



Scheme II



cycloaddition was slow and the trans cycloadduct **9a** was obtained selectively with inversion of the stereochemistry, in sharp contrast to the results with the parent azomethine ylid synthon promoted by acid.[3a] N-Unsubstituted *N*,*S*-acetals **3** did not give cycloadduct **9**[10] under similar reaction conditions. Although the mechanism of these cycloadditions has not been clarified, the results may be rationalized by assuming faster *Z*-*E* isomerization of the maleate to the fumarate than cycloaddition under the present conditions.[11] Acids such as trimethylsilyl triflate, trimethylsilyl iodide, or trichloroacetic acid did not promote the reaction.

The synthetic utility of the reaction was further demonstrated with representative heterodipolarophiles, affording the corresponding N-containing α-alkylideneheterocycles. The results are listed in Table II.

Not only N-unsubstituted ketene *N*,*S*-acetals **3** but also N-alkylated acetals **4** react effectively with various aldehydes and ketones **7**. Substituted aromatic and heteroaromatic aldehydes, including those bearing electron-donating and electron-withdrawing groups, α,β-unsaturated aldehydes, aromatic ketones, and ketomalonate react with **4** to give the corresponding alkylideneoxazolidines **10** in modest yields. Furthermore, thioketones **8**[12] are also good acceptors for this [3 + 2] cycloaddition, giving the corresponding alkylidenethiazolidines **11**.

This work demonstrates that *N*-(silylmethyl)-substituted ketene *N*,*S*-dithioacetals **3** and **4** are storable and easy to handle synthetic equivalents of alkylideneazomethine ylids **5**. The reaction displays complete regiospecificity in the cycloaddition with heterodipolarophiles.

Acknowledgment. Financial support for our work is provided by Grants-in-Aid for Scientific Research and Grants-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture, the Naito Foundation, the CIBA-GEIGY Foundation for the promotion of Science, Japan. We thank Dow Corning Toray Silicone Co. Ltd. for a gift of organosilicon compounds.

Supplementary Material Available: Spectra and analytical data for 3, 4, 9, 10, and 11 (4 pages). Ordering information is given on any current masthead page.

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(8) For the synthesis of α-alkylidenepyrrolidines, see: Meerwein, H.; Borner, P.; Fuchs, O.; Sasse, H. J.; Schrodt, H.; Spille, J. *Chem. Ber.* **1956**, *89*, 2060.

(9) The regiochemical outcome with methyl acrylate (unsymmetrical dipolarophile) is important for elucidating the reaction mechanism, but the structure **9b** is not yet known.

(10) A complex mixture, presumably including a 1:2 adduct of 3 to alkenes was obtained in these reactions.

(11) It was found that methylthiolate, generated in situ, catalyzed this *Z*-*E* isomerization and cycloaddition to the fumarate was faster than to the maleate.

(12) (a) Padwa, A.; Dent, W. *J. Org. Chem.* **1987**, *52*, 235. (b) Aono, M.; Terao, Y.; Achiwa, K. *Chem. Lett.* **1987**, 1851.

Regioselective Synthesis of Highly Substituted Furans via Tantalum-Alkyne Complexes

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Summary: A variety of 2,3,4-trisubstituted furans are prepared by treatment of tantalum-alkyne complexes with aldehydes, followed by addition of an isocyanide in DME-PhH-THF (1:1:1).

Transition metals exhibit a variety of interesting reactivities, thereby suggesting new methods in organic synthesis. We disclose here a regioselective preparation of highly substituted furans[1] from three components, i.e.