Ynolate Chemistry. Reaction of a Silylynolate with Aziridines Leading to γ-Lactams

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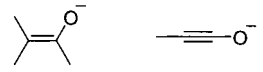
A silylynolate, generated via the carbonylation of lithium silyldiazomethane, was reacted with *N*-tosyl aziridines to produce various five-membered lactams in good yields. The key step of this reaction involves the ring-opening ketenylation of aziridines by the silylynolate. The reaction proceeded in a highly stereoselective manner, and ketenylation took place at the less hindered carbon. When treated with aldehydes prior to protonation, the α-silylated lactam enolates gave α-vinylidene γ-lactams. These reactions represent a unique path to the generation of and for controlling the reactivity of a rare class of reactive intermediates, namely, acyllithium derivatives and ynolates.

Introduction

The use of enolates as synthetic intermediates represents a powerful method for the construction of C−C bonds in synthetic organic chemistry.[1] On the other hand, ynolates, which are triple bond analogues of enolates, have received little attention by chemists, because they cannot be conveniently generated and few examples of their reactions have been reported.[2]



In 1975, the first generation of an ynolate species was reported by Schöllkopf, who generated a phenylynolate through the elimination reaction of benzonitrile from 5-lithio-3,4-diphenylisoxazole.[3] Kowalski also reported the preparation of ynolates via rearrangement of the dianions of α-bromo ketones.[4] The formation of ynolate species from alkynyl tosylates and 2 equiv of methyllithium was reported by Stang.[5] Julia showed that the oxidation of acetylides constituted an effective path to ynolates.[6] Recently, Shindo obtained alkylynolates via the cleavage of ester dianions.[7] Silylynolate species represent a potentially more useful synthetic intermediate since a silyl group can be converted to other function groups in a variety of ways.[8] In 1978, Rathke reported on the preparation of a silylynolate via the deprotonation of monosilylketene with butyllithium.[9] This species reacted with a silylating agent to afford a bis(silyl)ketene, but attempts to trap the species with carbon electrophiles were not successful. Later, Kita further examined Rathke's method in detail.[10] Recently, the generation of other silylynolates was developed by Ito, who obtained lithium silylynolate via the oxidation of lithium silylacetylide by nitrous oxide (N_2O).[11]

We previously demonstrated a new method of the generation of silylynolate **3** from the reaction of lithium silyldiazomethane **1** with carbon monoxide.[12] The reaction of **1** with carbon monoxide gave **2** which underwent the extrusion of dinitrogen to generate **3**. It is known that the silylynolate species **3** is unreactive toward carbon electrophiles,[9] but we found that, on the addition of Me_3-Al, the silylynolate **3** smoothly reacted with a variety of carbon electrophiles such as epoxides (Scheme 1) and α,β-unsaturated carbonyl compounds.[12] This was the first example to show that the silylynolate species **3** could be used for organic synthesis.[13] In the case of reactions with aziridines and imines, the addition of Me_3Al was not required. The reaction of aziridines gives γ-lactams, which, as a group, possess a variety of biological and pharmaceutical activities.[14] This transformation represents a new method for the preparation of 2-pyrrolidi-

(1) *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, pp 99−319.
(2) For a recent review, see: Shindo, M. *Chem. Soc. Rev.* **1998**, *27*, 367.
(3) Schöllkopf, U.; Hoppe, I. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 765. Hoppe, I.; Schöllkopf, U. *Liebigs. Ann. Chem.* **1979**, 219. Adlington, R. M.; Barrett, A. G. M.; Quayle, P.; Walker, A.; Bettz, M. J. *J. Chem. Soc., Chem. Commun.* **1981**, 404.
(4) Kowalski, C. J.; Fields, K. W. *J. Am. Chem. Soc.* **1982**, *104*, 323. Kowalski, C. J.; Reddy, R. E. *J. Org. Chem.* **1992**, *57*, 7194. Reddy, R. E.; Kowalski, C. J. *Org. Synth.* **1993**, *71*, 146 and references therein.
(5) Stang, P. J.; Roberts, K. A. *J. Am. Chem. Soc.* **1986**, *108*, 7125.
(6) Julia, M.; Saint-Jalmes, V. P.; Verpeaux, J.-N. *Synlett* **1993**, 233.
(7) Shindo, M. *Tetrahedron Lett.* **1997**, *38*, 4433. Shindo, M.; Sato, Y.; Shishido, K. *Tetrahedron* **1998**, *54*, 2411. Shindo, M.; Sato, Y.; Shishido, K. *Tetrahedron Lett.* **1998**, *39*, 4857. Shindo, M.; Oya, S.; Sato, Y.; Shishido, K. *Heterocycles* **1998**, *49*, 113. Shindo, M.; Sato, Y.; Shishido, K. *J. Am. Chem. Soc.* **1999**, *121*, 6507. Shindo, M.; Oya, S.; Murakami, R.; Sato, Y.; Shishido, K. *Tetrahedron Lett.* **2000**, *41*, 5943. Shindo, M.; Oya, S.; Murakami, R.; Sato, Y.; Shishido, K. *Tetrahedron Lett.* **2000**, *41*, 5947.
(8) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. Colvin, E. W. *Silicon in Organic Synthesis*; R. E. Krieger Press: Malabar, FL, 1985.
(9) Woodbury, R. P.; Long, N. R.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 376.
(10) Akai, S.; Kitagaki, S.; Naka, T.; Yamamoto, K.; Tsuzuki, Y.; Matsumoto, K.; Kita, Y. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1705.
(11) Ito, M.; Fujita, Y.; Ikariya, T. Presented at the 76th Annual Meeting of the Chemical Society of Japan, Yokohama, 1999, Abstr, 1B506.
(12) Kai, H.; Iwamoto, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 7634.
(13) Kita also independently found that a silylynolate was trapped with cyclohexanone leading to a β-lactam; see ref 10.

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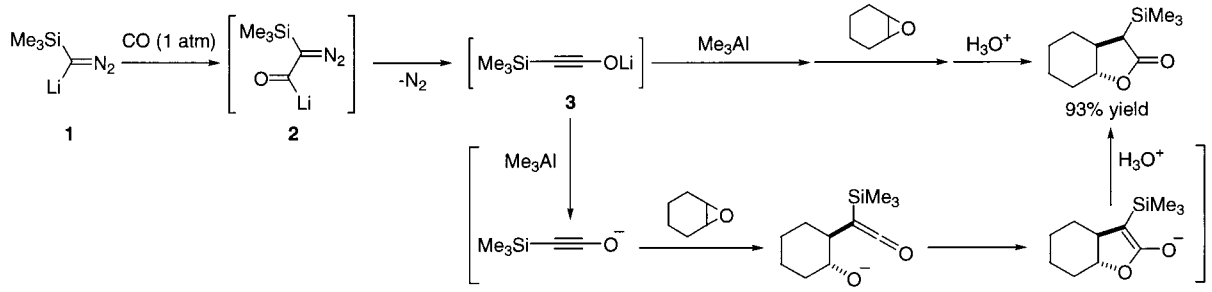
Scheme 1

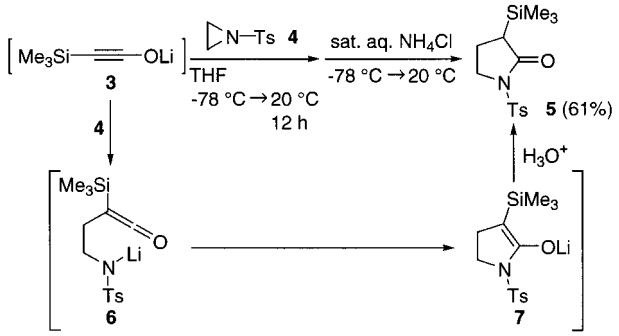


nones. We now report on a detailed study of the reaction of a silylynolate with aziridines.[15]

Results and Discussion

The reaction of silylynolate **3** with aziridines was carried out as follows. To a THF-hexane solution of the lithium silylynolate **3** was added a THF solution of *N*-tosyl aziridine **4** at −78 °C. The reaction mixture was stirred at 20 °C for 12 h and then quenched with a saturated aqueous solution of NH_4Cl to afford the five-membered lactam **5** in 61% yield (SiO_2 column).

Scheme 2



The reaction sequence leading to lactam formation is shown in Scheme 2. Ring-opening ketenylation of *N*-tosyl aziridine **4** by the silylynolate **3** would be expected to give the ketene intermediate **6**, which would then cyclize to the lactam enolate **7** via the intramolecular nucleophilic addition of lithium amide. In contrast to the reaction with an epoxide,[12] activation of the silylynolate **3** by Me_3Al was not required. This result suggests that the nitrogen atom in the aziridine is able to coordinate to the lithium cation of the silylynolate and, as a result, a more reactive ynolate anion is formed by dissociation of ynolate−metal ion pairs, which, thereby, leads to the smooth ring opening ketenylation. The addition of Me_3Al resulted in a somewhat complicated mixture of products containing a slightly lower yield (43% yield) of **5**.

The result of the trapping of silylynolate **3** with various aziridines is shown in Table 1. Ring-opening ketenylation of the monosubstituted aziridines **8**, **10**, and **12** proceeded regioselectively to give the γ-lactams **9**, **11**, and **13** (entries 1−3). Ketenylation by the silylynolate **3** occurred at the less hindered carbon site of the aziridine. The silylynolate **3** could be trapped with aziridine **12**, which is derived from (−)-valinol to afford the corresponding lactams **13** (entry 3). In these cases, γ-lactams which contain a substituent at the 5-position were produced. In the reaction with an aziridine derived from styrene, a mixture of two regioisomeric products and the desilylated products were obtained. The trapping with the 2,2-disubstituted aziridine **14** was also successful (entry 4).

Table 1. Reactions of the Silylnolate 3 with Aziridines

3 → aziridine, -78 °C → 20 °C, 12 h → sat. aq. NH_4Cl, -78 °C → 20 °C → product

entry	aziridine	product	yield (%)[a,b]
1	N—Ts **8**	SiMe3, Ts **9**	65% (68:32)[c]
2	N—Ts **10**	SiMe3, Ts **11**	67% (58:42)
3	*i*-Pr, N—Ts **12**	*i*-Pr, SiMe3, Ts **13**	72% (60:40)
4	N—Ts **14**	SiMe3, Ts **15**	76% (59:41)
5	N—Ts **16**	SiMe3, Ts **17**	77% (77:23)
6	Et, Et, N—Ts **18**	Et, Et, SiMe3, Ts **19**	39% (52:48)
7	Et, Et, N—Ts **20**	Et, Et, SiMe3, Ts **21**	36% (100[d]:0)

[a] Isolated yields (based on trimethylsilyldiazomethane, the starting material for lithium trimethylsilyldiazomethane **1**). [b] The ratios in parentheses are the diastereomeric ratio at the α position to the carbonyl group. [c] Reaction with the aziridine was carried out for 6 h. [d] The stereochemistry of the diastereomer has not yet been established.

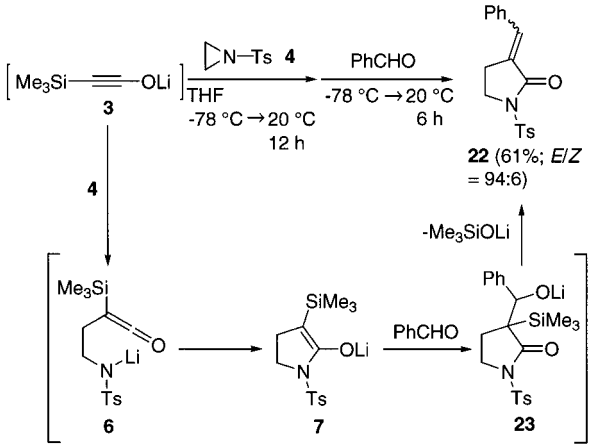
(14) Lin, N.-H.; Carrera, G. M., Jr.; Anderson, D. J. *J. Med. Chem.* **1994**, *37*, 3542. Shih, N. Y.; Lupo, A. T., Jr.; Aslanian, R.; Orlando, S.; Piwinski, J. J.; Green, M. J.; Ganguly, A. K.; Clark, M. A.; Tozzi, S.; Kreutner, W.; Hey, J. A. *J. Med. Chem.* **1995**, *38*, 1593. Elliott, R. L.; Kopecka, H.; Lin, N.-H.; He, Y.; Garvey, D. S. *Synthesis* **1995**, 772. Katritzky, A. R.; Mehta, S.; He, H.-Y.; Cui, X. *J. Org. Chem.* **2000**, *65*, 4364.

(15) One example in ref 12.

The reaction with 2,3-disubstituted aziridines is deserving of special comment. The bicyclic lactam **17** was obtained from the reaction with aziridine **16** (entry 5). The product possessed a *trans*-ring junction, which was confirmed by ^{1}H NMR spectroscopy.[15] The result shows that apparently the reaction proceeds in an anti manner. The results in entries 6 and 7 indicate that the reaction is highly stereospecific.[16] In both cases, an approximately 40% yield of the aziridine was recovered from the crude mixture. The silylynolate **3** failed to react with *N*-benzyl or *N*-benzoyl aziridines.

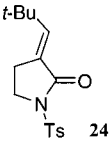
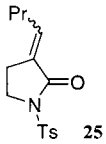
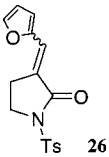
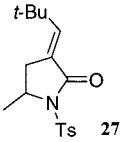
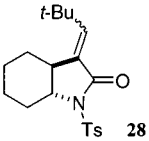
In the reaction of the silylynolate **3** with aziridines, lactam enolates that contain a silyl group at the α position are formed. Since various methods for the conversion of silyl groups into other functional groups have been reported,[8] the existence of the silyl group in the products is interesting from the point of view of synthetic chemistry. The Peterson olefination of the lactam enolate **7** with 3 equiv of benzaldehyde was examined (Scheme 3). The expected product **22** was obtained as a mixture of *E*- and *Z*-isomers in a total yield of 61%. The α-benzylidene lactam **22** would have been produced by the elimination of siloxy anion from the primary adduct **23**. It should be noted that the enolate **7** is a precursor of the parent carbonyl compounds. In the conventional methods, carbonyl compounds are the precursors of enolates. The reactions in Scheme 3 demonstrate the shorter, direct access to the enolates such as **7**.

Scheme 3



An excess of various aldehydes (3 equiv) could be utilized in the Peterson olefination (Table 2). The reaction with pivalaldehyde gave, exclusively, the thermodynamically stable *E*-product **24** in 71% yield (entry 1). By the present transformation, a variety of vinylidene groups can be introduced at the α position of the γ-lactams. Butyraldehyde (entry 2) and furfural (entry 3) could also be trapped with the lactam enolate **7**. Various lactam enolates can be generated via the reaction of the silylynolate **3** with the other aziridines. The lactam enolates derived from aziridines **8** and **16** were also used for this olefination (entries 4 and 5). The use of the bicyclic lactam enolate resulted in the low selectivity of the products because of the steric hindrance between the cyclohexyl ring and *tert*-butyl group of the aldehyde (entry 5).

Table 2. Peterson Olefination of Lactam Enolates with Aldehydes

entry	aziridine	aldehyde	product	yield %[a] (E/Z)
1	 **4**	*t*-BuCHO	 **24**	71% (100:0)
2	**4**	PrCHO	 **25**	49% (96:4)
3	**4**		 **26**	64% (96:4)
4	 **8**	*t*-BuCHO	 **27**	80% (100:0)
5	 **16**	*t*-BuCHO	 **28**	70% (60:40)

[a] Isolated yields (based on trimethylsilyldiazomethane, the starting material for lithium trimethylsilyldiazomethane **1**).

In conclusion, we report that a silylynolate, developed by our group,[12] reacts with various aziridines to give γ-lactams in good yields. The key step in this reaction is the ring opening ketenylation of an aziridine ring, which proceeds in a highly stereoselective manner. The generated lactam enolates were treated with aldehydes, prior to protonation, to afford α-vinylidene γ-lactams. This study shows that the silylynolate serves as a useful synthetic intermediate as a ketenylation reagent and further advances in the use of silylynolates are expected to extend the potential of ynolate chemistry. We are presently studying further applications of this ketenylation protocol.

Experimental Section

Materials. THF was distilled from sodium benzophenone ketyl immediately prior to use. A hexane solution of BuLi was purchased from Nakalai Tesque, Inc. A 2.0 M hexane solution of trimethylsilyldiazomethane and a 2.0 M hexane solution of Me_3Al were purchased from Aldrich Chemical Co. and Kanto Chemical Co., Inc., respectively. Aziridines were prepared according to literature procedures.[17] All reagents were used after distillation or recrystallization.

General Procedure for the Generation of the Silylynolate 3. A 30 mL round-bottomed flask equipped with a

(16) The assignment was based on the ^{1}H NMR vicinal coupling constant of the two bridgehead protons. In a *trans*-lactam this coupling constant is 10−11 Hz, whereas a *cis*-lactam gives a coupling constant of 6−7 Hz: Martin, S. F.; Tu, C.-Y.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634. Ikeda, M.; Ohtani, S.; Okada, M.; Minakuchi, E.; Sato, T.; Ishibashi, H. *Heterocycles* **1998**, *47*, 181.

magnetic stirring bar, a three-way stopcock, and a nitrogen line was flame-dried under a stream of nitrogen. In the reaction flask was placed 10 mL of dry THF and 1.0 mL of a hexane solution of trimethylsilyldiazomethane (2.0 M, 2.0 mmol), and the solution was then cooled to −78 °C. To the stirred solution was added 1.6 mL of a hexane solution of BuLi (1.5 M, 2.4 mmol) via a syringe. After stirring for 1 h, the reaction mixture was stirred under an atmospheric pressure of carbon monoxide for 2 h.

General Procedure for the Reaction of the Silylynolate 3 with Aziridines. To a THF−hexane solution of the silylynolate **3** was added 3 mL of a THF solution of aziridine (2.2 mmol) at −78 °C. The reaction mixture was then warmed to 20 °C and stirred for 12 h at that temperature (20 °C or reflux temperature). The mixture was quenched with 2 mL of saturated aqueous NH_4Cl at −78 °C, and the resulting mixture was then allowed to warm to room temperature. After aqueous workup, the solvents were removed under reduced pressure to give a brown solid, which was subjected to column chromatography on silica gel to give an analytically pure sample of the corresponding γ-lactam.

1-[(4-Methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (5): 61% yield; R_f = 0.37 (hexane/EtOAc = 2/1); colorless solid; mp 106−108 °C; ^{1}H NMR ($CDCl_3$) δ 0.013 (s, 9H), 1.91−2.07 (c, 2H), 2.19−2.33 (m, 1H), 2.41 (s, 3H), 3.76 (ddd, J = 7.9 Hz, J = 7.9 Hz, J = 9.6 Hz, 1H), 3.87 (ddd, J = 4.0 Hz, J = 9.6 Hz, J = 9.6 Hz, 1H), 7.32 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −3.07, 19.93, 21.42, 34.41, 46.65, 127.78, 129.33, 135.23, 144.67, 175.58; IR (cm^{-1}) (KBr) 1716 s; MS *m*/*z* (relative intensity) 311 (M^+, 2.8), 73 (100). Anal. Calcd for $C_{14}H_{21}NO_3SSi$: C, 53.99; H, 6.80; N, 4.50; S, 10.29. Found: C, 53.97; H, 6.80; N, 4.50; S, 10.30.

5-Methyl-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (9): 65% yield (68:32); colorless solid; mp 116−120 °C; R_f = 0.23 (hexane/EtOAc = 5/1). The spectral data were obtained as a mixture of diastereomers: ^{1}H NMR ($CDCl_3$) major δ 0.04 (s, 9H), 1.44 (d, J = 6.3 Hz, 3H), 1.70−1.90 (c, 1H), 2.05−2.20 (c, 3H), 2.42 (s, 3H), 4.30−4.50 (m, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H); minor δ 0.81 (s, 9H), 1.55 (d, J = 6.2 Hz, 3H), 1.50−1.57 (c, 1H), 2.42 (s, 3H), 2.40−2.55 (c, 1H), 4.30−4.50 (m, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) major δ −3.16, 21.57, 22.05, 28.66, 32.19, 55.83, 128.16, 129.31, 136.59, 144.47, 175.74; minor δ −2.53, 22.05, 23.72, 28.70, 32.99, 55.56, 128.09, 129.31, 136.30, 144.47, 176.46; IR (cm^{-1}) (KBr) 1714 s; MS *m*/*z* (relative intensity) 270 (M^+ − 55, 13), 84 (100). Anal. Calcd for $C_{15}H_{23}NO_3SSi$: C, 55.35; H, 7.12; N, 4.30; S, 9.85. Found: C, 55.25; H, 7.17; N, 4.45; S, 9.80.

5-Ethyl-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (11): 67% yield (58:42); colorless solid; mp 90−92 °C; R_f = 0.29 (hexane/EtOAc = 5/1). The spectra data was obtained as a mixture of diastereomers: ^{1}H NMR ($CDCl_3$) major δ 0.029 (s, 9H), 0.88 (t, J = 7.3 Hz, 3H), 1.48−2.12 (c, 4H), 2.25−2.39 (m, 1H), 2.42 (s, 3H), 4.25−4.33 (m, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H); minor δ 0.088 (s, 9H), 0.97 (t, J = 7.3 Hz, 3H), 1.48−2.12 (m, 5H), 2.42 (s, 3H), 4.12−4.22 (m, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.91 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) major δ −3.12, 8.99, 21.64, 25.11, 28.01, 32.42, 60.83, 128.05, 129.16, 136.39, 144.33, 175.82; minor δ −2.32, 9.48, 21.66, 25.22, 29.16, 32.42, 61.01, 127.98, 129.20, 136.17, 144.31, 176.48; IR (cm^{-1}) (KBr) 1712 s; MS *m*/*z* (relative intensity) 339 (M^+, 2.2), 246 (100). Anal. Calcd for $C_{16}H_{25}NO_3SSi$: C, 56.60; H, 7.42; N, 4.12; S, 9.44. Found: C, 56.56; H, 7.25; N, 4.08; S, 9.52.

5-(1-Methylethyl)-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (13): 72% yield (60:40); colorless solid; mp 103−105 °C; R_f = 0.43 and 0.39 (hexane/EtOAc = 4/1). The spectra data was obtained as a mixture of diastereomers: ^{1}H NMR ($CDCl_3$) major δ 0.024 (s, 9H), 0.68 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 1.82−2.10 (m, 3H), 2.42 (s, 3H), 2.48 (dqq, J = 3.6 Hz, J = 6.9 Hz, J = 6.9 Hz, 1H), 4.31 (d, J = 3.6 Hz, J = 8.2 Hz, 1H), 7.30 (d, J = 8.3 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H); minor δ 0.096 (s, 9H), 0.79 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 2.42 (s, 3H), 2.80 (dqq, J = 4.6 Hz, J = 6.9 Hz, J = 6.9 Hz, 1H), 4.23 (dt, J = 4.6 Hz, J = 8.2 Hz, 1H), 7.30 (d, J = 8.6 Hz, 2H), 7.90 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) major δ −3.42, 14.39, 18.42, 20.01, 21.43, 31.15, 33.17, 63.98, 127.89, 128.93, 136.04, 144.15, 176.03; minor δ −2.68, 14.25, 18.07, 19.79, 21.46, 29.74, 31.92, 64.61, 127.72, 129.03, 135.80, 144.12, 177.18; IR (cm^{-1}) (KBr) 1712 s; MS *m*/*z* (relative intensity) 353 (M^+, 3.1), 73 (100). Anal. Calcd for $C_{17}H_{27}NO_3SSi$: C, 57.75; H, 7.70; N, 3.96. Found: C, 57.68; H, 7.59; N, 3.98.

5-Ethyl-5-methyl-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (15): 76% yield (59:41); colorless solid; mp 120−124 °C; R_f = 0.19 (hexane/EtOAc = 7/1). The spectra data was obtained as a mixture of diastereomers: ^{1}H NMR ($CDCl_3$) major δ 0.073 (s, 9H), 0.92 (t, J = 7.3 Hz, 3H), 1.70 (s, 3H), 1.62−2.21 (m, 5H), 2.42 (s, 3H), 7.29 (d, J = 8.2 Hz, 2H), 7.93 (d, J = 8.2 Hz, 2H); minor δ 0.0066 (s, 9H), 1.02 (t, J = 7.3 Hz, 3H), 1.58 (s, 3H), 1.62−2.21 (m, 5H), 2.42 (s, 3H), 7.29 (d, J = 8.2 Hz, 2H), 7.93 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) major δ −2.96, 8.91, 21.67, 28.84, 31.61, 33.56, 33.75, 69.46, 128.47, 128.95, 136.77, 140.30, 176.61; minor δ −2.73, 8.80, 21.66, 26.13, 30.52, 33.52, 34.18, 69.97, 128.62, 128.91, 136.80, 144.03, 176.59; IR (cm^{-1}) (KBr) 1712 s; MS *m*/*z* (relative intensity) 338 (M^+ − Me, 2.3), 73 (100). Anal. Calcd for $C_{17}H_{27}NO_3SSi$: C, 57.75; H, 7.70; N, 3.96; S, 9.07. Found: C, 57.87; H, 7.61; N, 3.96; S, 9.06.

(3a*R,7a*R**)-Octahydro-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2*H*-indol-2-one (17):** 77% yield (77:23). The major isomer: colorless solid; mp 128−130 °C; R_f = 0.31 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.097 (s, 9H), 1.11−1.90 (c, 9H), 2.43 (s, 3H), 2.83 (dd, J = 3.3 Hz, J = 12.4 Hz, 1H), 3.21 (dt, J = 3.3 Hz, J = 10.9 Hz, 1H), 7.31 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −2.29, 21.53, 24.54, 25.63, 29.72, 34.74, 38.96, 44.15, 68.03, 127.82, 129.43, 135.69, 144.35, 177.21; IR (cm^{-1}) (KBr) 1726 s; MS *m*/*z* (relative intensity) 365 (M^+, 2.7), 73 (100). Anal. Calcd for $C_{18}H_{27}NO_3SSi$: C, 59.14; H, 7.44; N, 3.83; S, 8.77. Found: C, 59.01; H, 7.46; N, 3.80; S, 8.74. The minor isomer was obtained by HPLC as a single isomer: colorless solid; mp 123−124 °C; R_f = 0.26 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.046 (s, 9H), 1.20−1.50 (c, 4H), 1.75−1.97 (c, 3H), 2.05 (d, J = 8.2 Hz, 1H), 2.10−2.27 (m, 1H), 2.42 (s, 3H), 2.80−2.91 (m, 1H), 3.53 (dt, J = 3.3 Hz, J = 10.6 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.91 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −0.58, 21.58, 24.51, 25.99, 28.94, 32.34, 41.10, 45.13, 65.13, 127.86, 129.16, 136.43, 144.24, 176.45; IR (cm^{-1}) (KBr) 1714 s; MS *m*/*z* (relative intensity) 365 (M^+, 2.0), 73 (100). Anal. Calcd for $C_{18}H_{27}NO_3SSi$: C, 59.14; H, 7.44; N, 3.83; S, 8.77. Found: C, 59.08; H, 7.44; N, 3.80; S, 8.74.

***trans*-4,5-Diethyl-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (19):** 39% yield (52:48). The major isomer was obtained by HPLC as a single isomer colorless oil: R_f = 0.34 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 0.85 (t, J = 7.6 Hz, 3H), 0.99 (t, J = 7.6 Hz, 3H), 1.22−1.61 (c, 3H), 1.79 (d, J = 2.3 Hz, 1H), 1.89 (t, J = 6.9 Hz, 1H), 2.17−2.30 (m, 1H), 2.42 (s, 3H), 3.79 (d, J = 9.9 Hz, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.89 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −1.78, 9.93, 10.86, 21.64, 29.12, 30.93, 39.62, 40.83, 66.60, 127.96, 129.16, 136.07, 144.38, 175.53; IR (cm^{-1}) (neat) 1716 s; MS *m*/*z* (relative intensity) 338 (M^+ − Et, 49), 91 (100). Anal. Calcd for $C_{18}H_{29}NO_3SSi$: C, 58.82; H, 7.95; N, 3.81; S, 8.72. Found: C, 58.68; H, 7.89; N, 3.83; S, 8.53. The minor isomer was obtained as a colorless solid: mp 107−109 °C; R_f = 0.43 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.068 (s, 9H), 0.91−0.98 (c, 3H), 1.41−1.48 (m, 1H), 1.53−1.72 (m, 1H), 1.87−1.99 (c, 2H), 2.29 (d, J = 7.3 Hz, 1H), 2.42 (s, 3H), 3.96 (dd, J = 3.6 Hz, J = 9.9 Hz, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −0.95, 10.35, 12.08, 21.69, 25.14, 26.33, 37.69, 40.94, 65.33, 127.91, 129.19,

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136.17, 144.36, 175.02; IR (cm^{-1}) (KBr) 1724 s; MS *m/z* (relative intensity) 338 ($M^+ - Et$, 70), 91 (100), 73 (100). Anal. Calcd for $C_{18}H_{29}NO_3SSi$: C, 58.82; H, 7.95; N, 3.81; S, 8.72. Found: C, 58.73; H, 7.96; N, 3.82; S, 8.73.

***cis*-4,5-Diethyl-1-[(4-methylphenyl)sulfonyl]-3-trimethylsilyl-2-pyrrolidinone (21):** 36% yield (100:0); colorless solid; mp 80−82 °C; $R_f = 0.37$ (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 0.011 (s, 9H), 0.83 (t, $J = 7.3$ Hz, 3H), 0.93 (t, $J = 7.3$ Hz, 3H), 1.38−1.50 (m, 2H), 1.76−1.89 (m, 2H), 1.79 (d, $J = 9.6$ Hz, 1H), 2.16−2.27 (m, 1H), 2.42 (s, 3H), 4.41 (dt, $J = 7.3$ Hz, $J = 4.9$ Hz, 1H), 7.30 (d, $J = 8.6$ Hz, 2H), 7.95 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −2.43, 9.76, 12.55, 21.68, 22.16, 22.66, 39.77, 40.44, 62.94, 128.22, 129.16, 136.37, 144.29, 176.02; IR (cm^{-1}) (KBr) 1712 s; MS *m/z* (relative intensity) 338 ($M^+ - Et$, 39), 73 (100). Anal. Calcd for $C_{18}H_{29}NO_3SSi$: C, 58.82; H, 7.95; N, 3.81; S, 8.72. Found: C, 58.60; H, 7.82; N, 3.75; S, 8.78.

The Reaction of the Lactam Enolate with Aldehydes. Preparation of α-Vinylidene γ-Lactams. To a solution of the lactam enolate, prepared from the silylynolate **3** with *N*-tosyl aziridine, *vide supra*, was added the aldehyde (6.0 mmol) at −78 °C. The reaction mixture was warmed to 20 °C for 6 h. After aqueous workup, the solvents were removed under reduced pressure to give a brown slurry, which was subjected to column chromatography on silica gel to give the corresponding α-vinylidene γ-lactams.

1-[(4-Methylphenyl)sulfonyl]-3-(phenylmethylene)-2-pyrrolidinone (22): 61% yield (*E*/*Z* = 94:6). The *E*-isomer was separated by column chromatography on silica gel (hexane/EtOAc = 2/1). *E*-Isomer: colorless solid; mp 163−164 °C; $R_f = 0.34$ (hexane/EtOAc = 2/1); ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.10 (dt, $J = 3.0$ Hz, $J = 7.3$ Hz, 2H), 3.98 (t, $J = 7.3$ Hz, 2H), 7.25−7.45 (c, 8H), 8.00 (dd, $J = 6.6$ Hz, $J = 1.7$ Hz, 2H); (DMSO-d_6) δ 2.41 (s, 3H), 3.13 (dt, $J = 6.9$ Hz, $J = 2.6$ Hz, 2H), 3.96 (t, $J = 6.9$ Hz, 2H), 7.26 (t, $J = 6.9$ Hz, 1H), 7.30−7.60 (m, 7H), 7.91 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.46, 23.97, 43.87, 128.00, 128.66, 129.43, 129.49, 129.85, 134.32, 134.72, 134.84, 145.03, 167.04; IR (cm^{-1}) (KBr) 1714 s; MS *m/z* (relative intensity) 327 (M^+, 7.5), 116 (100). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28; S, 9.79. Found: C, 65.82; H, 5.19; N, 4.27; S, 9.75. Spectral data of the *Z*-isomer were obtained from the mixture of *E*- and *Z*-isomers. In the ^{13}C NMR spectrum of the mixture of *E*- and *Z*-isomers, the resonances arising from the *Z*-isomer could not be observed. *Z*-Isomer: colorless oil; $R_f = 0.39$ (hexane/EtOAc = 2/1): ^1H NMR ($CDCl_3$) δ 2.42 (s, 3H), 2.95 (dt, $J = 2.3$ Hz, $J = 6.9$ Hz, 2H), 3.94 (t, $J = 6.9$ Hz, 2H), 6.81 (t, $J = 2.3$ Hz, 1H), 7.30−7.42 (c, 5H), 7.73−7.77 (m, 2H), 7.96 (d, $J = 8.2$ Hz, 2H); IR (cm^{-1}) (neat) 1713 s; MS *m/z* (relative intensity) 327 (M^+, 6.3), 263 (100); HRMS $C_{18}H_{17}NO_3S$ calcd for 327.0929, found 327.0924.

3-(2,2-Dimethylpropylidene)-1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinone (24): 71% yield; colorless solid; mp 195−196 °C; $R_f = 0.46$ (hexane/EtOAc = 2/1); ^1H NMR ($CDCl_3$) δ 0.073 (s, 9H), 0.92 (t, $J = 7.3$ Hz, 3H), 1.70 (s, 3H), 1.62−2.21 (m, 5H), 2.42 (s, 3H), 7.29 (d, $J = 8.2$ Hz, 2H), 7.93 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −2.96, 8.91, 21.67, 28.84, 31.61, 33.56, 33.75, 69.46, 128.47, 128.95, 136.77, 140.30, 176.61; IR (cm^{-1}) (KBr) 1713 s; MS *m/z* (relative intensity) 307 (M^+, 3.7), 91 (100). Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.38; H, 6.85; N, 4.58; S, 10.46.

3-Butylidene-1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinone (25): 61% yield (*E*/*Z* = 94:6). The *E*-isomer was separated by column chromatography on silica gel (hexane/EtOAc = 3/1). *E*-Isomer: colorless solid; $R_f = 0.29$ (hexane/EtOAc = 3/1); mp 78−80 °C; ^1H NMR ($CDCl_3$) δ 0.90 (t, $J = 7.6$ Hz, 3H), 1.45 (qt, $J = 7.6$ Hz, $J = 7.6$ Hz, 2H), 2.08 (dtt, $J = 7.6$ Hz, $J = 7.6$ Hz, $J = 1.6$ Hz, 2H), 2.43 (s, 3H), 2.65−2.75 (c, 2H), 3.89 (t, $J = 7.6$ Hz, 2H), 6.60 (tt, $J = 7.6$ Hz, $J = 3.0$ Hz, 1H), 7.33 (d, $J = 8.2$ Hz, 2H), 7.96 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.56, 21.19, 21.37, 21.43, 31.08, 43.70, 129.10, 129.20, 134.67, 138.72, 144.64, 165.80; IR (cm^{-1}) (KBr) 1721 s; MS *m/z* (relative intensity) 293 (M^+, 0.90), 91 (100). Anal. Calcd for $C_{15}H_{19}NO_3S$: C, 61.41; H, 6.53; N, 4.77; S, 10.93. Found: C, 61.32; H, 6.52; N, 4.74; S, 10.88. Spectra data of the *Z*-isomer were obtained from the mixture of *E*- and *Z*-isomers. In the ^{13}C NMR spectrum of the mixture of *E*- and *Z*-isomers, the resonances arising from the *Z*-isomer could not be observed. *Z*-Isomer: colorless oil; $R_f = 0.34$ (hexane/EtOAc = 3/1); ^1H NMR ($CDCl_3$) δ 0.88 (t, $J = 7.6$ Hz, 3H), 1.38 (qt, $J = 7.6$ Hz, $J = 7.6$ Hz, 2H), 2.44 (s, 3H), 2.61 (dtt, $J = 7.6$ Hz, $J = 7.6$ Hz, $J = 2.0$ Hz, 2H), 2.69−2.76 (c, 2H), 3.85 (t, $J = 7.6$ Hz, 2H), 6.04 (tt, $J = 7.6$ Hz, $J = 2.0$ Hz, 1H), 7.34 (d, $J = 8.2$ Hz, 2H), 7.96 (d, $J = 8.2$ Hz, 2H); IR (cm^{-1}) (neat) 1723 s; MS *m/z* (relative intensity) 293 (M^+, 29), 138 (100); HRMS $C_{15}H_{20}NO_3S$ (M + H) calcd for 294.1164, found 294.1162.

3-[(2-Furanyl)methylene]-1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinone (26): 64% yield (*E*/*Z* = 96:4). The *E*-isomer was separated by column chromatography on silica gel (hexane/EtOAc = 2/1). *E*-Isomer: brown solid; $R_f = 0.29$ (hexane/EtOAc = 2/1); mp 150−153 °C; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.12 (dt, $J = 3.0$ Hz, $J = 7.3$ Hz, 2H), 3.97 (t, $J = 7.3$ Hz, 2H), 6.49 (dd, $J = 1.6$ Hz, $J = 3.3$ Hz, 1H), 6.59 (d, $J = 3.3$ Hz, 1H), 7.17 (t, $J = 3.0$ Hz, 1H), 7.33 (d, $J = 8.2$ Hz, 2H), 7.53 (s, 1H), 7.98 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.57, 23.73, 44.04, 112.24, 115.65, 121.12, 125.38, 127.86, 129.39, 134.77, 144.87, 144.91, 150.98, 166.71; IR (cm^{-1}) (KBr) 1710 s; MS *m/z* (relative intensity) 317 (M^+, 3.5), 106 (100); Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.55; H, 4.76; N, 4.41; S, 10.10. Found: C, 60.43; H, 4.78; N, 4.37; S, 10.10. Spectral data of the *Z*-isomer were obtained from the mixture of *E*- and *Z*-isomers. In the ^{13}C NMR spectrum of the mixture of *E*- and *Z*-isomers, the resonances arising from the *Z*-isomer could not be observed. *Z*-Isomer: colorless oil; $R_f = 0.34$ (hexane/EtOAc = 2/1); ^1H NMR ($CDCl_3$) δ 0.88 (t, $J = 7.6$ Hz, 3H), 1.38 (qt, $J = 7.6$ Hz, $J = 7.6$ Hz, 2H), 2.44 (s, 3H), 2.61 (dtt, $J = 7.6$ Hz, $J = 2.0$ Hz, 2H), 2.69−2.76 (c, 2H), 3.85 (t, $J = 7.6$ Hz, 2H), 6.04 (tt, $J = 7.6$ Hz, $J = 2.0$ Hz, 1H), 7.34 (d, $J = 8.2$ Hz, 2H), 7.96 (d, $J = 8.2$ Hz, 2H); IR (cm^{-1}) (neat) 1710 s; MS *m/z* (relative intensity) 317 (M^+, 58), 253 (100); HRMS $C_{16}H_{15}NO_4S$ calcd for 317.0722, found 317.0718.

3-(2,2-Dimethylpropylidene)-5-methyl-1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinone (27): 80% yield; colorless solid; mp 165−167 °C; $R_f = 0.20$ (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 1.10 (s, 9H), 1.44 (s, $J = 6.3$ Hz, 3H), 2.42 (s, 3H), 2.54 (ddd, $J = 16.5$ Hz, $J = 2.3$ Hz, $J = 2.3$ Hz, 1H), 3.03 (ddd, $J = 16.5$ Hz, $J = 8.9$ Hz, $J = 3.3$ Hz, 1H), 4.50 (ddq, $J = 2.3$ Hz, $J = 8.9$ Hz, $J = 6.3$ Hz, 1H), 6.61 (dd, $J = 2.3$ Hz, $J = 3.3$ Hz, 1H), 7.31 (d, $J = 8.5$ Hz, 2H), 7.98 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.72, 23.32, 29.36, 31.96, 33.73, 53.07, 125.07, 128.35, 129.29, 135.99, 144.66, 148.95, 167.23; IR (cm^{-1}) (KBr) 1722 s; MS *m/z* (relative intensity) 321 (M^+, 11), 91 (100). Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 63.72; H, 6.92; N, 4.37; S, 10.00. Found: C, 63.36; H, 7.24; N, 4.31; S, 9.87.

(3a*R,7a*R**)-Octahydro-3-(2,2-dimethylpropylidene)-1-[(4-methylphenyl)sulfonyl]-2*H*-indol-2-one (28):** 70% yield (60:40). The major isomer (*E*-isomer); colorless solid; mp 207−210 °C; $R_f = 0.24$ (hexane/EtOAc = 9/1); ^1H NMR ($CDCl_3$) δ 1.13 (s, 9H), 1.40−1.76 (c, 4H), 1.76−2.00 (m, 2H), 2.35−2.60 (m, 2H), 2.43 (s, 3H), 2.95−3.08 (m, 1H), 3.32 (dt, $J = 2.6$ Hz, $J = 9.9$ Hz, 1H), 6.76 (d, $J = 3.3$ Hz, 1H), 7.32 (d, $J = 8.2$ Hz, 2H), 7.92 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.68, 24.57, 26.15, 30.60, 30.88, 31.90, 32.11, 45.90, 64.65, 128.09, 129.31, 129.41, 135.37, 144.47, 149.83, 169.49; IR (cm^{-1}) (KBr) 1722 s; MS *m/z* (relative intensity) 361 (M^+, 5.9), 91 (100). Anal. Calcd for $C_{20}H_{27}NO_3S$: C, 66.45; H, 7.53; N, 3.87; S, 8.87. Found: C, 66.29; H, 7.51; N, 3.94; S, 8.91. The minor isomer (*Z*-isomer): colorless solid; mp 132−134 °C; $R_f = 0.16$ (hexane/EtOAc = 9/1); ^1H NMR ($CDCl_3$) δ 1.05−1.70 (c, 4H), 1.10 (s, 9H), 1.80−2.00 (c, 3H), 2.20−2.35 (m, 1H), 2.42 (s, 3H), 2.86 (dd, $J = 3.0$ Hz, $J = 11.5$ Hz, 1H), 3.27 (dt, $J = 3.0$ Hz, $J = 10.6$ Hz, 1H), 5.69 (d, $J = 3.0$ Hz, 1H), 7.31 (d, $J = 8.2$ Hz, 2H), 7.90 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.55, 24.52, 24.83, 26.11, 29.81, 31.83, 32.68, 47.90, 64.94, 127.67, 129.18, 130.57, 135.69, 144.25, 147.93, 167.07; IR (cm^{-1}) (KBr) 1726 s; MS *m/z* (relative intensity) 361 (M^+, 5.2), 91 (100). Anal. Calcd for $C_{20}H_{27}NO_3S$: C, 66.45; H, 7.53; N, 3.87; S, 8.87. Found: C, 66.10; H, 7.31; N, 3.88; S, 8.92.

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Supporting Information Available: Characterization data for the new compounds **5**, **9**, **11**, **13**−**15**, **17**, **19**, **21**, **22**, and **24**−**28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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