Efficient Synthesis of 6-Trimethylsiloxy- and 6-(Trimethylsilyl)-methyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazines by Cycloaddition of α-Nitrosostyrene to Silyl Enol Ethers and Allyltrimethylsilane

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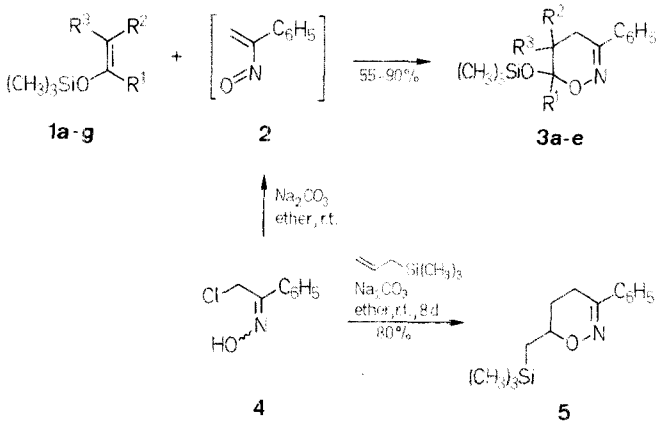
The title compounds **3** are prepared in good yield from silyl enol ethers **1** and α-nitrosostyrene **2**, generated *in situ* from α-chloroacetophenone oxime **4**. Allyltrimethylsilane smoothly affords cycloadduct **5** which could be opened to the unsaturated ketone **6** or amino olefin **7**.

5,6-Dihydro-4*H*-1,2-oxazines are heterocycles of considerable synthetic potential. Prepared by Diels-Alder reaction of olefins and nitrososoalkenes – generated from α-halogen oximes – some of these heterocycles have been converted to amino alcohols, amino acids and γ-butyrolactones.[2] However, only relatively few olefins give satisfying yields in the crucial cycloaddition. In consideration of the electronic demand of this step, silyl enol ethers **1** should be alkenes of sufficient reactivity[3,4] and provide products **3**, which can be regarded as masked 1,4-dicarbonyl compounds and should therefore be of preparative value. In addition, the facile synthesis of **1** from carbonyl compounds by chemo-, regio- and stereoselective methods[5] would be a further advantage of the desired sequence. A recent communication[6] on the additions of ethyl α-nitrosoacrylates to the related allylsilanes prompts us to report our results with silyl enol ethers.



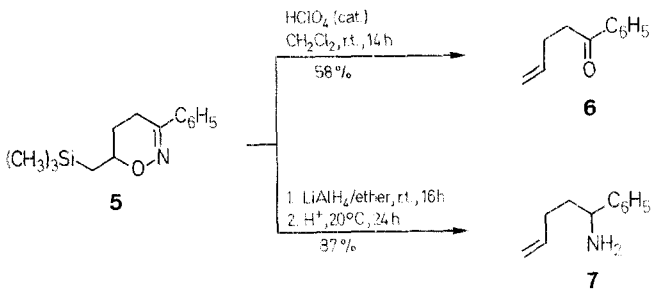
Scheme A

1/3	R^1	R^2	R^3	Yield (%)
a	H	CH_3	CH_3	90
b	H	H	CH_3	55
c	$-(CH_2)_4-$		H	62
d	CH_3	H	H	72
e	$CH=CH_2$	H	H	65
f	C_6H_5	H	H	–
g	t-C_4H_9	H	H	–

We found that silyl enol ethers **1** can indeed serve as potent dienophiles, when reacted with α-chloroacetophenone oxime **4**, as precursor for **2**, in the presence of sodium carbonate (Scheme A). Best yields were obtained running the cycload-

dition in ether, with freshly ground sodium carbonate (electric coffee-mill) as base and using five equivalents of olefin **1**. Since most of the excess can be recovered by careful distillation, even valuable silyl enol ethers **1** should be convertible to 6-siloxy-5,6-dihydro-4*H*-1,2-oxazines **3** without waste of material. Use of less olefin **1**, other bases and solvents, or α-bromoacetophenonoxime as precursor for **2** gave lower yields and higher amounts of undefined polymers formed from α-nitrosostyrene. As illustrated in Scheme **A** adducts **3a–e** have been synthesized in good to excellent yields, showing that the substitution pattern can be widely varied. Regiochemistry is governed by the trimethylsiloxy function, giving only products with this group in 6-position as determined by ^{1}H-NMR spectroscopy. Oxazine derivative **3e** results from the periselective reaction of 2-trimethylsiloxy-1,3-butadiene **1e**, which enters the cycloaddition as dienophile only, and not as diene.

Silyl enol ethers **1f** and **1g** could not be converted to the corresponding heterocycles **3f** or **3g**. Only polymer formation has been observed with these olefins. Apparently two groups of moderate to large size on the olefin ($(CH_3)_3SiO$ and C_6H_5 or *t*-C_4H_9, respectively) are not tolerated in the cycloaddition step, thus leading to self-addition of **2**; electronic effects of these substituents, however, cannot be excluded. Borderline cases have not yet been investigated.



Scheme **B**

On the other hand, smooth reaction of **2** has been observed with allyltrimethylsilane (two equivalents). The high yield of 80% for **5** is surprising, since competition experiments established that allyltrimethylsilane is by far less reactive than the enol ethers.

Preliminary experiments with **5** take advantage of two cleavage modes (Scheme **B**) which generate either the unsaturated ketone **6** or the amino olefin **7**. In both cases an acid induced trimethylsilanol elimination (Peterson reaction) forms the olefinic unit. Similar transformations should be applicable to compounds **3** and will be reported in due time.

^{1}H-NMR spectra were recorded on a Varian T 60 (60 MHz) or a Bruker WM 400 (400 MHz) spectrometer; IR spectra were recorded on a Perkin-Elmer 1420 spectrophotometer. Melting points are corrected.

5,5-Dimethyl-3-phenyl-6-trimethylsiloxy-5,6-dihydro-4*H*-1,2-oxazin (3a); Typical Procedure:

A solution of α-chloroacetophenone oxime **4**[7] (0.86 g, 4.00 mmol) and silyl enol ether **1a** (2.94 g, 20.0 mmol) in dry ether (50 ml) is stirred with freshly ground anhydrous sodium carbonate (2.40 g, 22.0 mmol) at room temperature for 12 h (TLC control). The suspension is filtered through a pad of celite; the filtrate is concentrated, and chromatographed on a column of aluminum oxide (neutral, activity III, petroleum ether/ethyl acetate, 8:2, as eluant); concentration (0.02 torr) provides **3a** as a colorless oil; yield: 1.00 g (90%).

$C_{15}H_{23}NO_2Si$ (277.5) calc. C 64.95 H 8.35 N 5.05
found 64.64 8.66 4.64

IR (CCl_4): ν = 3100–2800 (C–H), 1600 cm^{-1} (C=N).

^{1}H-NMR ($CDCl_3$): δ = 0.25 (s, 9H, $OSi(CH_3)_3$); 0.92, 1.08 (2 s, 6H, 5-CH_3); 2.12, 2.55 (AB-signal, 2H, J = 17 Hz, 4-H); 4.83 (s, 1H, 6-H); 7.3–7.5, 7.5–7.7 ppm (2 m, 5H, C_6H_5).

For **3b–e** and **5** see the Table.

1-Phenyl-4-penten-1-one (6):

A solution of 6-(trimethylsilyl)methyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazine (**5**; 0.99 g, 4.00 mmol) in dichloromethane (20 ml) is treated with five drops of perchloric acid (70%).[6] After 14 h at room temperature, water (10 ml) is added and the aqueous phase is extracted with dichloromethane (2 × 10 ml). The combined organic phase is dried with magnesium sulfate and concentrated. Kugelrohr distillation (100 °C/0.02 torr) affords **6** as colorless oil;[8] yield: 370 mg (58%).

Table. 3-Phenyl-6-trimethylsiloxy-5,6-dihydro-4*H*-1,2-oxazines **3b–e** and 6-(Trimethylsilyl)methyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazine (**5**) Prepared

Olefin (Equiv.)	Reaction Time (days)	Product (% yield)	m.p.[a] (°C)	Molecular Formula[b]	IR (CCl_4) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[c] δ (ppm)
1b (5)	3	**3b** (55)	26–32	$C_{14}H_{21}NO_2Si$ (263.5)	1590	0.18 (s, 9H, $OSiMe_3$); 1.05 (d, 3H, J = 6 Hz, 5-CH_3); 2.04 (mc, 1H, 5-H); 2.31 (dd, 1H, J = 12 Hz, 17 Hz, 4-H); 2.49 (dd, 1H, J = 6 Hz, 17 Hz, 4-H); 5.28 (d, 1H, J = 2.5 Hz, 6-H)[d]
1c (2)	5	**3c** (62)	90	$C_{17}H_{25}NO_2Si$ (287.5)	1600	0.24 (s, 9H, $OSiMe_3$); 1.1–2.6 (m, 10H); 3.07 (dd, 1H, J = 9 Hz, 17 Hz, 4-H)
1d (10)	3	**3d** (72)	72–73	$C_{14}H_{21}NO_2Si$ (263.5)	1600	0.24 (s, 9H, $OSiMe_3$); 1.60 (s, 3H, 6-CH_3); 1.7–2.2 (m, 2H, 5-H); 2.4–2.8 (m, 2H, 4-H)
1e (5)	4	**3e** (65)	69	$C_{15}H_{21}NO_2Si$ (275.4)	1590	0.24 (s, 9H, $OSiMe_3$); 1.8–2.2 (m, 2H, 5-H); 2.4–2.8 (m, 2H, 4-H); 5.26, 5.5, 6.09 (ABM-signal, 3H, J_{AB} = 2 Hz, J_{AM} = 10 Hz, J_{BM} = 17 Hz, $CH=CH_2$)
Allyltrimethylsilane (2)	8	**5** (80)	58–59	$C_{14}H_{21}NOSi$ (247.4)	1590	0.02 (s, 9H, $SiMe_3$); 0.94, 1.15 (2dd, 2H, J = 7 Hz, 14 Hz, CH_2Si); 1.75 (dddd, 1H, J = 7 Hz, 10 Hz, 11 Hz, 13.5 Hz, 5-H); 2.06 (tdd, 1H, J = 2 Hz, 7 Hz, 13.5 Hz, 5-H); 2.5–2.7 (m, 2H, 4-H); 3.88 (dtd, 1H, J = 2 Hz, 7 Hz, 11 Hz, 6-H)

[a] Recrystallized from petroleum ether.
[b] Satisfactory microanalyses obtained: C ±0.23, H ±0.22, N ±0.41.
[c] All compounds: δ = 7.3–7.5, 7.5–7.7 ppm (2m, 3H, 2H, C_6H_5).
[d] Signals for the *cis*-isomer (90%); signals for the corresponding *trans*-isomer (10%): δ = 0.20 (s, 9H, $OSiMe_3$); 1.03 (d, 3H, J = 8 Hz, 5-CH_3) 2.11 (m, 1H, 5-H); 2.33 (dd, 1H, J = 3 Hz, 17 Hz, 4-H); 2.83 (dd, 1H, J = 7 Hz, 17 Hz, 4-H); 5.10 (d, 1H, J = 3.5 Hz, 6-H).[9]

^{1}H-NMR ($CDCl_3$): δ = 2.0–3.2 (m, 4H, 2-H, 3-H); 4.8–5.2, 5.4–6.2 (2 m, 2H, 1H, 5-H, 4-H); 7.3–7.6, 7.6–8.1 ppm (2 m, 3H, 2H, C_6H_5).

1-Amino-1-phenyl-4-pentene (7):
A solution of **5** (0.74 g, 3.00 mmol) and lithium aluminum hydride (0.40 g, 10.4 mmol) are stirred in dry ether (30 ml) at room temperature for 16 h. Slow addition of concentrated hydrochloric acid (10 ml) was followed by stirring at 20°C for 24 h, dilution with water (40 ml), extractions with ether (5 × 10 ml), stirring of the combined organic layers with sodium hydroxide pellets (10 g), filtration, and concentration to afford crude **7** (0.401 g). Kugelrohr distillation (80°C/0.02 torr) provides **7** as a colorless liquid; yield: 0.387 g (87%).

$C_{10}H_{15}N$	calc.	C 80.48	H 10.13	N 9.39
(149.2)	found	80.52	10.31	9.41

IR (film): ν = 3700–3100 (NH_2), 3100–2800 (C–H), 1635 (C=C), 1600, 1490 cm^{-1} (C_6H_5).

^{1}H-NMR ($CDCl_3$): δ = 1.8–2.2 (m, 6H, 2-H, 3-H, NH_2); 3.9 (t, 1H, J = 7 Hz, 1-H); 4.9–5.1, 5.6–6.0 (2 m, 3H, 4-H, 5-H); 7.3 ppm (s, 5H, C_6H_5).

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(9) Starting with *Z*-**1b** (*Z*:*E* = 99.5:0.5) one obtains **3b** as a *cis*/*trans*-mixture (90:10). The stereospecificity of the cycloaddition is currently being investigated in more detail.