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Silver Technology for Stabilization of Simple (*Z*)-Enethiols: Stereoselective Synthesis and Reaction of Silver (*Z*)-Enethiolates

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We report herein the first example of the stereoselective synthesis and reaction of simple silver (*Z*)-β-alkylenethiolates **1** (M = Ag), which serve as stabilized (*Z*)-enethiol storage. Enethiols **1** (M = H) are tautomerically stable isomers of thioaldehydes with a high kinetic barrier for their interconversion,[1,2] but in general, they are thermally labile because of their pronounced tendency to dimerize to dithiohemiacetals or divinyl sulfides or to polymerize on standing at room temperature.[3,4] These properties make it very difficult to synthesize simple enethiols **1** with defined stereochemistry in a pure form.[5] Furthermore, in contrast to the substituted enethiolates, some alkali metal salts of simple enethiolates are configurationally labile;[6] for instance, the *E*-isomer of lithium enethiolate **1** (R = Bu, M = Li), prepared by $LiAlH_4$ reduction of 1-alkenesulfenate anion, isomerizes to an equilibrium mixture of *Z*:*E* = 55:45 above −40 °C in THF.[7] It occurred to us that the use of silver(I), instead of an alkali metal, with formation of silver enethiolates **1** (M = Ag), would stabilize the enethiols through the preferable soft−soft combination.[8,9]

The chemistry of simple silver enethiolates remains unknown, mostly due to the lack of an efficient method for their syntheses.[10] Deprotonation chemistry is not viable for simple thioaldehydes as they are not sufficiently stable under the conditions.[7] Our method for the stereoselective synthesis of enethiolates involves an unusual vinylic S_N2 reaction of (*E*)-vinyl-λ^3-iodanes **3**:[11] bimolecular substitution of (*E*)-λ^3-iodane **3** with *N*,*N*-dimethylthiobenzamides in dichloromethane at room temperature afforded the inverted (*Z*)-*S*-vinylthioimidonium salts **2** in high yields.[12] Silver salts undergo a regioselective C−S bond cleavage of **2**: exposure of **2a** (Ar = *p*-ClC_6H_4) to silver acetate (1.2 equiv) in THF:water (4:1) at room temperature in the dark gave silver (*Z*)-1-decenylthiolate (**1a**) stereoselectively in 77% yield, along with the formation of *N*,*N*-dimethyl-*p*-chlorobenzamide (82%) and (*Z*)-*S*-1-decenyl-*p*-chlorothiobenzoate (18%). Isolation and purification of the silver thiolate **1a** are simple, and a repeated washing of a crude mixture with methanol and ethyl acetate successively, which removes the byproducts amide and thiocarboxylate, afforded the pure enethiolate **1a** as a yellow powder. Silver (*Z*)-1-hexenylthiolate (**1b**) was also prepared from **2b** (Ar = Ph) in 80% yield. These silver vinylthiolates **1** are sparingly soluble in water, methanol, acetonitrile, and ethyl acetate, but soluble in hexane, dichloromethane, chloroform, and pyridine.

In a marked contrast to (*Z*)-enethiols, silver (*Z*)-enethiolates **1** are thermally and stereochemically stable, and neither decomposition nor isomerization of stereochemistry was observed when they were left standing over 3 months in a refrigerator in the dark. In solution, however, silver (*Z*)-1-decenylthiolate (**1a**) gradually decomposes at 25 °C with a half-life time ($t_{1/2}$) of 6 h in $CDCl_3$ under argon (Figure 1a). On the other hand, in the air (Figure 1b), silver thiolate **1a** is highly stable and no isomerization as well as decomposition was detected on standing for more than 3 days in the dark. Furthermore, we found that the addition of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO, 1 equiv) completely inhibits the decomposition of **1a** in $CDCl_3$ solution under argon. These results probably suggest the intervention of some radical species during the decomposition of **1a** under argon.

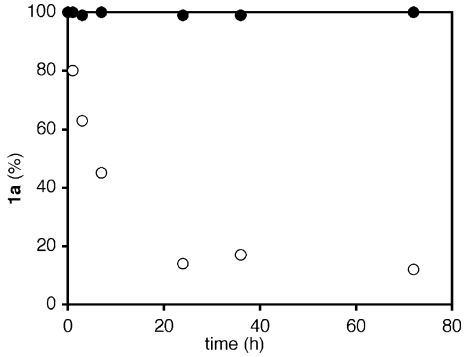

Figure 1. Decomposition of silver enethiolate **1a** in $CDCl_3$ at 25 °C in the dark (determined by ^1H NMR analyses). (a) (○) 0.029 M in argon and (b) (●) 0.022 M in the air.

Table 1. Methylation of Silver Thiolate **1a** with Methyl Iodide[a]

entry	solvent	ϵ_r[b]	conditions	**4a** yield (%)[c]	ratio[d]
1	hexane	1.88		77	80:20
2	hexane		O_2	76	89:11
3	Et_2O	4.20		74	82:18
4	CH_2Cl_2	8.93		65	92:8
5	CH_2Cl_2		O_2	60	98:2
6	CH_2Cl_2		TEMPO[e]	91	>99:1
7	acetone	20.56		42	69:31
8	MeOH	32.66		65	43:57
9	MeOH		air	64	83:17
10	MeOH		O_2	72	89:11
11	MeCN	35.94		48	47:53

[a] Unless otherwise noted, reaction was carried out using 10 equiv of MeI at room temperature for 7 h under nitrogen in the dark. [b] Dielectric constants. [c] Isolated yields. [d] *Z*:*E* ratios of **4a** determined by ^1H NMR. [e] TEMPO (1 equiv) was used as an additive under argon.

Direct methylation of silver enethiolate **1a** with excess methyl iodide under nitrogen affords a mixture of (*E*)- and (*Z*)-1-decenyl methyl sulfides (**4a**) (Table 1). The stereochemistry of **4a** seems to depend on the solvent polarity,[13] and a high degree of stereoisomerization was observed in polar solvents with a large dielectric constant. It is noted that the *Z*-selectivity with retention of stereochemistry of **1a** was considerably improved in the presence of a molecular dioxygen or by the addition of TEMPO. These radical scavengers probably slow down the rate of the isomerization and/or decomposition of silver thiolate **1a** under the conditions.[14]

Silver thiolates AgSR generally adopt a cyclic oligomer structure $(AgSR)_n$ (n = 3, 4, 8, and 12) through the intermolecular Ag···S interactions or a nonmolecular layered structure.[15] The degree of aggregation of the silver thiolates mostly depends on the steric demanding of the thiolate ligands. In solutions, electrospray (ESI)

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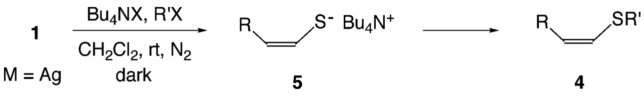
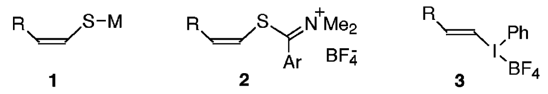
Table 2. Alkylation of **1** in the Presence of Bu_4NX[a]



entry	1	Bu_4NX (X)	R′X (equiv)	time (h)	4 yield (%)[b]	4 ratio[c]
1	**1a**	F	MeI (3)	2	44	94:6
2	**1a**	Cl	MeI (3)	2	89	96:4
3	**1a**	Br	MeI (3)	2	90	96:4
4	**1a**	I	MeI (3)	2	77	97:3
5	**1b**	I	MeI (3)	3	87	99:1[d]
6	**1a**	I	EtI (3)	16	73	95:5
7	**1b**	I	EtI (3)	16	70	98:2[d]
8	**1a**	I	*i*-PrI (3)	35	18[e]	97:3
9	**1a**	I	*i*-PrI (3)	35[f]	55	65:35
10	**1a**	I	$PhCH_2Br$ (3)	2	76	96:4
11	**1b**	I	$PhCH_2Br$ (3)	2	98	98:2[d]
12	**1a**	I	$CH_2{=}CHCH_2Br$ (3)	3	98	97:3
13	**1a**	I	*E*-$PhCH{=}CHCH_2Br$ (1)	2	87	>96:4
14	**1a**	I	$PhCOCH_2Br$ (1)	1	77	96:4

[a] Reaction was carried out in CH_2Cl_2 in the presence of Bu_4NX (1−1.2 equiv) at room temperature under nitrogen in the dark. [b] Isolated yield. [c] *Z*:*E* ratios determined by ^1H NMR. [d] Determined by GC. [e] Dithioacetal **6** (22%) was obtained. [f] CCl_4 was used as a solvent.

Scheme 1



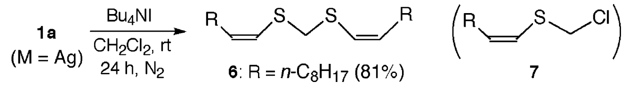
a: R = *n*-C_8H_{17}, **b**: R = Bu

MS spectra (negative) for both **1a** and **1b** clearly indicated the selective formation of unusual hexamers (Figure S1). This aggregation will be partly responsible for the moderate reactivity of silver thiolate **1a** toward the direct methylation, shown in Table 1. It should be noted that the addition of tetrabutylammonium halides (Cl, Br, and I) increases the rate of methylation of silver enethiolates **1**, probably because of the in situ generation of the ionic tetrabutylammonium enethiolates **5**, which will show an increased nucleophilicity toward methyl iodide. Thus, use of an equivalent amount of Bu_4NX (X = Cl, Br, and I) afforded a high yield of (*Z*)-vinyl methyl sulfide **4a** within 2 h at room temperature with >96% stereoselectivity (Table 2, entries 2−4). On the other hand, use of Bu_4NF was found to be fruitless, yielding a low yield of **4a**.

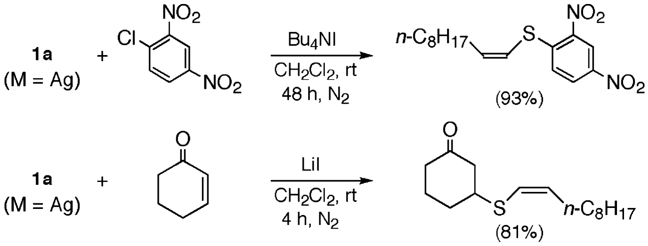
Addition of Bu_4NI to a $CDCl_3$ solution of **1a** caused a dramatic change in ^1H NMR (Scheme S1, Figure S2): α vinylic proton signals of **1a** are considerably deshielded (0.13 ppm), while the β vinylic proton exhibits an upfield shift of 0.2 ppm. A similar chemical shift change in vinylic protons but to a lesser extent was observed by the use of Bu_4NBr and Bu_4NCl. These results suggest the formation of a common species, ammonium (*Z*)-1-decenylthiolate **5a**, probably with a various degree of association with the silver halides produced in situ. In contrast, such a countercation exchange with Bu_4NF will not be important due to the soft (Ag)−hard (F) combination.

Table 2 shows the results for alkylation with a variety of alkyl halides in the presence of Bu_4NI,[16] yielding (*Z*)-vinyl sulfides **4** stereoselectively (>96% selectivity) in good to excellent yields.

Scheme 2



Scheme 3



Interestingly, the solvent dichloromethane itself reacts with silver enethiolate **1a** in the presence of excess Bu_4NI (Scheme 2) and affords a 94:6 mixture of *Z*,*Z*- and *E*,*Z*-isomers of dithioacetal **6** in a high yield. In this reaction, no formation of chloromethyl vinyl sulfide **7** was detected, which indicates that the rate of the reaction of enethiolate **5a** with the sulfide **7** is faster than that with dichloromethane. Silver iodide formed during the reaction probably activates the sulfide **7** more effectively than dichloromethane, by the simultaneous coordination of Ag(I) to the sulfur and chlorine atoms of **7**.

Scheme 3 shows that arylation as well as Michael addition of (*Z*)-silver thiolate **1a** also proceeds smoothly in high yields.

In conclusion, we have developed an efficient method for the stereoselective synthesis of simple silver (*Z*)-enethiolates, which serve as stabilized (*Z*)-enethiols and efficient agents for the synthesis of a variety of (*Z*)-vinyl sulfides.

Supporting Information Available: Experimental details, Schemes S1−S3, Figure S1 and S2. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) No isomerization of (*Z*)-vinyl sulfides under our conditions was observed (Scheme S2). For a possible mechanism of the isomerization of silver enethiolates **1** and of inhibition of the isomerization by TEMPO, see Scheme S3.
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(16) Bu_4NI is easy to handle because of the nonhygroscopic nature, while the other salts Bu_4NBr and Bu_4NCl are highly hygroscopic.

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