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Preparation of silyl enol ethers from acyloin derivatives using silyllithium reagents

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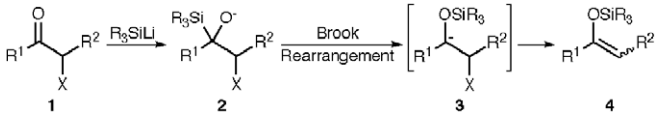
Abstract

A new method for the regioselective preparation of silyl enol ethers from acyloin derivatives using silyllithium reagents has been developed. Both dimethylphenyl- and methyldiphenylsilyllithium were found to be effective, the latter providing greater stereocontrol. The reaction is believed to proceed via Brook rearrangement assisted by expulsion of the adjacent leaving group. A number of acyclic acyloin derivatives were reacted to form the corresponding silyl enol ethers in good to excellent yield.

1. Introduction

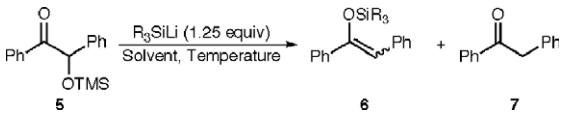
Silyl enol ethers are prominent and versatile intermediates in organic synthesis.[1] They are particularly useful in carbon–carbon bond forming reactions such as the Mukaiyama aldol addition.[2] Limitations on the traditional preparation of silyl enol ethers via the reaction of carbonyl compounds with base and chlorosilane have given rise to several routes that do not involve direct enolization, such as the isomerization of allyl silyl ethers,[3] and the rearrangements of α-silylcarbonyls,[4] silylepoxides,[5] and *S*-α-silylbenzyl thioesters.[6]

Additionally, a number of methods for the preparation of silyl enol ethers have been developed that utilize the Brook rearrangement as a key step.[7–9] Many of these methods involve the reaction of acylsilanes with functionalized carbon nucleophiles.[8] Comparatively, the reaction of α-substituted ketones with silicon nucleophiles (Scheme 1) has remained largely unexplored. Reich reported one example of an α-phenylthioketone reacting with dimethylphenylsilyllithium to give the silyl enol ether.[8h] Fleming demonstrated that the reaction of acyloin derivatives with dimethylphenylsilyllithium proceeds to give the α-reduced ketones, evidently formed via the cleavage of initially formed silyl enol ethers.[9] The silyl enol ethers were observed only in a few cases and in low yield. Silyl enol ether intermediates have also been observed in the reaction of an α,β-epoxyketone with dimethylphenylsilyllithium.[10]



Scheme 1.

We envisioned that the suppression of the silicon–oxygen bond cleavage would provide a new general method for the regioselective preparation of silyl enol ethers from acyloin derivatives. A series of reactions using benzoin derivative **5** was performed to determine the effect of temperature, solvent, and silyllithium reagent on the relative amounts of silyl enol ether **6** and ketone **7** formed (Scheme 2). The results are summarized in Table 1.



Scheme 2.

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Table 1
Reaction of **5** with silyllithium reagents (1.25 equiv)

Entry	Silyllithium	Solvent	Temperature (°C)	**6**[a] (%)	**7**[a] (%)	*E*/*Z*
1	$Me_2PhSiLi$	THF	−40	0	>99	—
2	$Me_2PhSiLi$	Ether	−40	76	22	84/16
3	$Me_2PhSilLi$	Toluene	−40	74	11	81/19
4	$Me_2PhSiLi$	Ether	−78	91	9	83/17
5	$Me_2PhSiLi$	Toluene	−78	80	8	74/26
6	$MePh_2SiLi$	THF	−40	Trace	>99	—
7	$MePh_2SiLi$	Ether	−40	71	28	100/0
8	$MePh_2SiLi$	Toluene	−40	84	8	100/0
9	$MePh_2SiLi$	Ether	−78	85	12	100/0
10	$MePh_2SiLi$	Toluene	−78	77	17	100/0

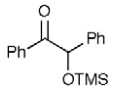
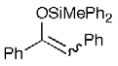
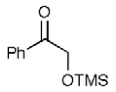
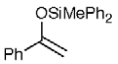
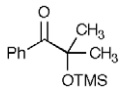
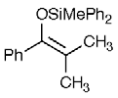
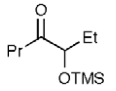
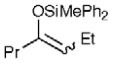
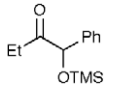
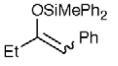
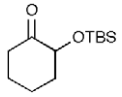
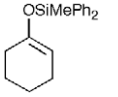
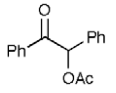
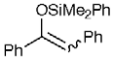
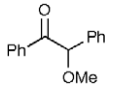
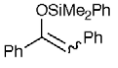
Effects of temperature, silyl group, and solvent.
[a] Yields determined by ^1H NMR using hexamethylbenzene as an internal standard.

The reaction solvent had the greatest influence on product distribution. Reactions in THF greatly favored the undesired ketone **7**. The use of the less polar solvents, toluene and ether, provided significantly improved yields of **6**. The effect of temperature was less significant, although colder conditions generally also enhanced the yield. The choice of silyllithium reagent had a minimal effect on the product distribution but showed a significant effect on the stereoselectivity of the reaction. While the use of dimethylphenylsilyllithium showed a preference for the formation of the *E* stereoisomer, use of methyldiphenylsilyllithium showed complete selectivity for the *E* stereoisomer in each case. An excellent balance of yield and stereoselectivity was achieved using 1.25 equiv of methyldiphenylsilyllithium in ether at −78 °C.

A number of protected acyloins underwent reaction with dimethylphenyl- or methyldiphenylsilyllithium in ether at −78 °C to form the corresponding silyl enol ethers. These results are summarized in Table 2. Both silyloxide (entries 1–5) and carboxylate (entry 7) leaving groups were found to be effective; however, alkoxide (entry 8) gave poor results. We were pleased to find that both aromatic and aliphatic ketones reacted to give the silyl enol ether. The Brook rearrangement of α-silylalkoxides under kinetic conditions (complete and irreversible formation of the alkoxide) is usually disfavored unless an anionic stabilizing group (phenyl, vinyl, silyl) is present on the α-carbon.[11] In this case, the rearrangement of **2** is promoted by expulsion of the adjacent leaving group, transferring the developing negative charge from carbon to oxygen. It is unclear whether carbanion **3** is an intermediate in the overall reaction or if the migration of silicon and leaving group expulsion are concerted. The cyclic substrate (entry 6) gave only a trace of the desired silyl enol ether. It is likely that the anti-periplanar arrangement of silyl group and leaving group necessary for fast rearrangement–elimination is inaccessible in this rigid cyclic system.[9]

While the yields were often excellent, attempts to purify the silyl enol ethers by chromatography or distillation resulted in poor separation from the primary contaminant (1,3-dimethyl-1,1,3,3-tetraphenyldisiloxane) or significant decomposition. The identities of the new silyl enol ethers (entries 1 and 3–5) were confirmed by comparison to authentic samples prepared by the treatment of the corresponding ketone with LDA followed by chloromethyldiphenylsilane.

Table 2
Reaction of acyloin derivatives with 1.25 equiv of silyllithium reagent in ether at −78 °C

Entry	Substrate	Silyllithium	Product	Yield[a] (%)	*E*/*Z*
1		$MePh_2SiLi$		82	100/0
2		$MePh_2SiLi$		86	—
3		$MePh_2SiLi$		>99	—
4		$MePh_2SiLi$		90	43/57
5		$MePh_2SiLi$		66	93/7
6		$MePh_2SiLi$		Trace	—
7		$Me_2PhSiLi$		>99[b]	89/11
8		$Me_2PhSiLi$		47	96/4

[a] Yields determined by ^1H NMR using hexamethylbenzene as an internal standard.
[b] Yield determined using 1,4-di-*tert*-butylbenzene as an internal standard.

In conclusion, a new method for the regioselective preparation of silyl enol ethers from acyloin derivatives using silyllithium reagents has been developed. Both aryl and alkyl ketones reacted efficiently; however, the method was ineffective for a cyclic substrate.

2. Typical procedure

1-Trimethylsilyloxy-1,2-diphenyl-1-ethanone (0.160 g, 0.563 mmol) and hexamethylbenzene (0.016 g) were dissolved in 6.8 mL ether and cooled to −78 °C under argon. A 0.46 M solution of methyldiphenylsilyllithium in THF (1.6 mL, 1.25 equiv) was added dropwise via syringe

with stirring. The reaction was immediately quenched[12] at −78 °C with an equal volume of saturated NH_4Cl and warmed to room temperature. The mixture was extracted twice with an equal volume of CH_2Cl_2 and the combined organic layers dried over Na_2SO_4. The dried solution was concentrated in vacuo to give the crude *E*-1-methyldiphenylsilyloxy-1,2-diphenylethene.

Acknowledgments

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Supplementary data

Spectroscopic data for the new silyl enol ethers (entries 1 and 3–5). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.01.133.

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12. Reaction times longer than 15 min often resulted in significant formation of the α-reduced ketone.