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Preparation of silyl polyenol ethers by carbonyl olefination of silyl esters

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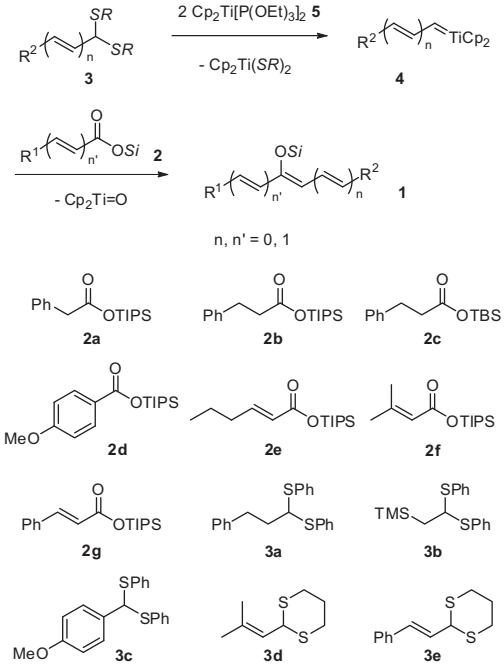
ABSTRACT

Silyl enol ethers were produced by the carbonyl olefination of silyl esters with titanium carbene complexes generated by the desulfurizative titanation of thioacetals. The regioselective preparation of silyl dienol and trienol ethers has been achieved by using unsaturated silyl esters and thioacetals.

Silyl enol ethers are useful synthetic intermediates as enolate equivalents and electron-rich olefins.[1] Their vinylogues, silyl dienol and trienol ethers, are versatile building blocks[2] and have been employed for various cyclization reactions,[3] which include the Diels–Alder[4] and hetero Diels–Alder[5] reactions. The use of silyl dienol ethers in the Mukaiyama aldol type reaction as dienolate equivalents has also been investigated.[6] Several methods for the preparation of silyl polyenol ethers,[2] such as transformation of enones through the Wittig-type carbonyl olefination,[7] the reaction of allyllithiums generated from 3-trialkylsiloxy-1,4-pentadienes with electrophiles,[8] isomerization of 1-(siloxylmethyl)butadienes,[9] and the tandem epoxysilane rearrangement/Wittig reaction of phosphorus-containing epoxy silanes,[10] have been investigated. Despite these extensive studies, base-induced deprotonation of unsaturated carbonyl compounds followed by exposure to a silylating agent is still the major approach to silyl polyenol ethers.[8,11] The preparation of silyl enol ethers by silylation of enolates, however, suffers a serious drawback in that it generally lacks regioselectivity. In contrast, no ambiguity as to the location of the double bond exists in their preparation by the carbonyl olefination of silyl esters. Although the organometallic species generated by the treatment of *gem*-dibromides with $TiCl_4$–Zn–TMEDA[12] and α-elimination of dimethyltitanocene[13] are employed for the transformation of silyl esters into silyl enol ethers, their application to the preparation of silyl polyenol ethers is largely restricted due to unavailability of appropriate starting materials.

We have studied the carbonyl olefination using titanium carbene complexes generated by the desulfurizative titanation of



Scheme 1. Preparation of silyl polyenol ethers **1** by carbonyl olefination of silyl esters **2**.

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thioacetals and related compounds.[14] Since our carbonyl olefination works well for carboxylic acid derivatives such as esters,[14a] thioesters,[14d] and amides,[14i] we envisioned the preparation of silyl enol ethers by the carbonyl olefination of silyl esters. Here we describe a versatile method for the preparation of silyl polyenol ethers **1** using saturated as well as unsaturated silyl esters **2** and thioacetals **3** as starting materials (Scheme 1).

First, the preparation of dienol ether **1d** bearing a siloxy group at the terminus of diene system by the reaction of silyl ester **2b** with unsaturated thioacetal **3d** was examined under various conditions (Table 1). The treatment of **2b** with the carbene complex **4d**, generated by the desulfurizative titanation of unsaturated thioacetal **3d** with titanocene(II) **5**, in THF at 25 °C for 2 h produced **1d** in moderate yield (entry 1). The reaction carried out at reflux gave **1d** in better yield (entry 2). The use of several mixed solvent systems was examined, and cyclopentyl methyl ether (CPME) was found to be an efficient co-solvent (entry 5). The best result was obtained when the reaction was performed at 50 °C using a prolonged reaction time (entry 6). Satisfactory results were also obtained under similar reaction conditions in the preparation of silyl dienol ether **1i** using the unsaturated silyl ester **2g** (entries 7 and 8).

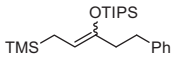
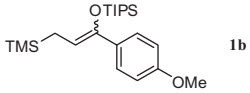
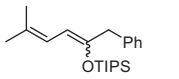
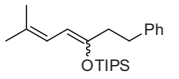
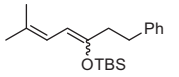
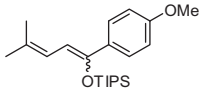
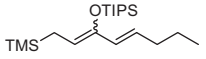
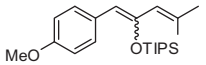
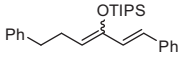
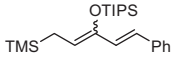
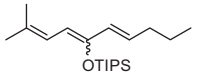
Table 1
Formation of the silyl dienol ethers **1d** and **i**[a]

Entry	2	3	Temp/°C, time/h	Solvent	1 (Yield/%)[b]
1	**2b**	**3d**	25, 2	THF	**1d** (19)
2	**2b**	**3d**	Reflux, 4	THF	**1d** (46)
3	**2b**	**3d**	Reflux, 4	THF/toluene = 1:3	**1d** (49)
4	**2b**	**3d**	Reflux, 4	THF/diglyme = 1:3	**1d** (50)
5	**2b**	**3d**	Reflux, 4	THF/CPME = 1:3	**1d** (59)
6	**2b**	**3d**	50, 14	THF/CPME = 1:3	**1d** (64)
7	**2g**	**3a**	Reflux, 1	THF/CPME = 1:3	**1i** (64)
8	**2g**	**3a**	50, 14	THF/CPME = 1:3	**1i** (64)

[a] $Cp_2Ti[P(OEt)_3]_2$ **5** (5 equiv) and **3** (2 equiv) were used.
[b] Isolated yield based on **2** used.

With optimized reaction conditions in hand, we next examined the reactions of various types of carbene complexes **4** with silyl esters **2** (Table 2). The silyl enol ethers **1a** and **b** were obtained by the reaction of alkylidene complex generated from **3b** with the silyl esters **2b** and **d** (entries 1 and 2). The reaction of unsaturated carbene complex derived from **3d** with saturated and aromatic silyl esters **2a–d** resulted in the regioselective formation of dienol ethers **1c–f** with a siloxy group at the terminal sp^2 carbon (entries 3–6). The silyl dienol ethers **1g–j** bearing a siloxy group at the inner sp^2 carbon in the conjugated system were also regioselectively obtained by the reaction of saturated carbene complexes generated from **3a–c** with α,β-unsaturated silyl esters **2e–g** (entries 7–10). Likewise, the carbonyl olefination of unsaturated ester **2e** with unsaturated thioacetal **3d** produced the trienol ether **1k** (entry 11). In these reactions, the stereochemistry of the silyl esters was completely retained. As for the geometry of the double bond formed by the carbonyl olefination, the *Z*-isomers generally predominated, and higher *Z*-stereoselectivity was observed in the reactions using unsaturated thioacetals. It is noteworthy that the carbonyl olefination of **2** carried out in a larger scale produced the silyl dienol ethers **1** in better yields (see entries 3 and 4).

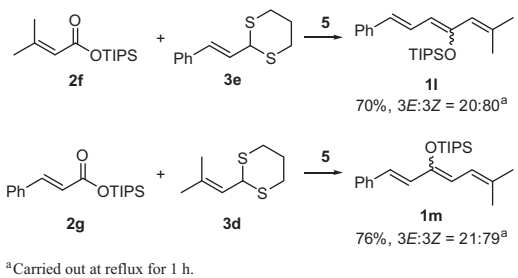
Table 2
Preparation of silyl enol ethers **1**[a]

Entry	2	3	1	Yield/%[b] (*E*:*Z* ratio)[c]
1	**2b**	**3b**	 **1a**	42 (56:44)
2	**2d**	**3b**	 **1b**	63 (40:60)
3	**2a**	**3d**	 **1c**	65, 72[d] (28:72)
4	**2b**	**3d**	 **1d**	64, 75[e] (17:83)
5	**2c**	**3d**	 **1e**	66 (22:78)
6	**2d**	**3d**	 **1f**	83[d] (22:78)
7[f]	**2e**	**3b**	 **1g**	76[d] (40:60)
8[f]	**2f**	**3c**	 **1h**	83 (66:34)
9[f]	**2g**	**3a**	 **1i**	64 (45:55)
10[f]	**2g**	**3b**	 **1j**	78 (38:62)
11[f]	**2e**	**3d**	 **1k**	74 (25:75)

[a] All reactions were performed at 50 °C for 14 h using 0.3 mmol of **2**, unless otherwise noted.
[b] Isolated yields based on **2** used.
[c] Determined by NMR spectroscopies. The stereochemistry of products was confirmed by NOE or NOESY experiment.
[d] Carried out in 0.5 mmol scale.
[e] Carried out in 1 mmol scale.
[f] Carried out at reflux for 1 h.

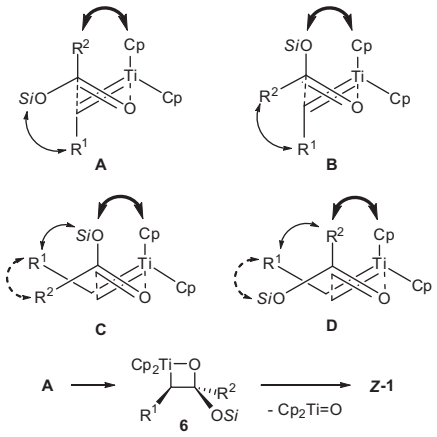
The synthetic utility of the present method is further demonstrated in Scheme 2. The selective formation of silyl trienol ethers, 6-methyl-1-phenyl-1,3,5-heptatrienes **1l** and **m** bearing a siloxy group at a different position, was achieved by selection of appropriate silyl esters and thioacetals.

The preferential formation of (*Z*)-silyl enol ethers **1** is rationalized by the transition states for the formation of oxatitanacyclobutane intermediates depicted in Scheme 3. The transition states **A** and **B** would be relatively stable because the transition states **C** and **D** suffer an additional gauche-like steric interaction between the substituents of carbene complex **4** and silyl ester **3** indicated by a hashed double headed arrow. The reaction preferentially proceeds via the transition state **A** to produce the titanacyclobutane **6** because the transition state **B** is rather destabilized by steric interaction between the quasi-axial Cp group and trialkylsiloxy group which is more bulky than R^2. The titanacycle **6** affords (*Z*)-silyl enol ether **Z-1** through the extrusion of titanocene oxide with retention of configuration. The better *Z* selectivity observed in the reaction of



[a]Carried out at reflux for 1 h.

Scheme 2. Preparation of 6-methyl-1-phenyl-1,3,5-heptatrienes **1l** and **m** bearing a siloxy group at a different position.



Scheme 3. Transition states for the formation of oxatitanacyclobutanes.

alkenylcarbene complexes is rationalized by a planar transoid conformation of alkenylcarbene complex, which partially alleviates steric repulsion between R^1 and the trialkylsiloxy group in the transition state **A**.

In conclusion, we have developed a new and efficient method for the preparation of silyl di- and trienol ethers, which are multipurpose synthetic intermediates. Further study on the synthetic application of these siloxy group substituted polyenes is now under investigation.

Supplementary data

Supplementary data (experimental procedures and full characterization of all products) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01.040.

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