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Radical-chain isomerisation of allyl silyl ethers to silyl enol ethers in the presence of thiols as polarity reversal catalysts

Alistair J. Fielding and Brian P. Roberts*

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK

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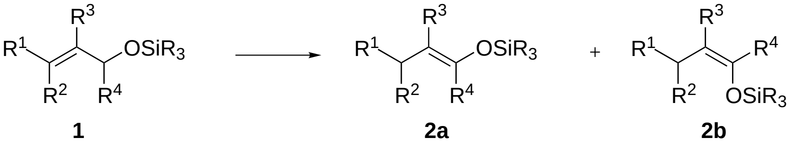
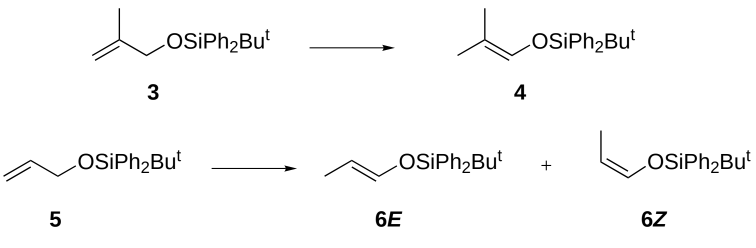
Abstract—The radical-chain isomerisation of allyl silyl ethers to silyl enol ethers takes place on heating in the presence of an initiator and an arenethiol as a protic polarity reversal catalyst; pentafluorothiophenol is particularly effective in this role. The reaction complements the transition-metal-catalysed isomerisation and could be useful for the preparation of silyl enol ethers from readily available allylic alcohols. © 2001 Elsevier Science Ltd. All rights reserved.

Silyl enol ethers are important reagents for organic synthesis, when they provide a source of nucleophilic carbon for C–C bond formation,[1] for example in their reactions with carbonyl electrophiles in the presence of Lewis acid catalysts.[2] The most common preparative methods for silyl enol ethers involve *O*-silylation of an enolate ion or hydrosilylation of an α,β-unsaturated carbonyl compound in the presence of a transition metal catalyst. A third route involves the rearrangement of an allyl silyl ether **1**, generalised in Scheme 1, again under the influence of a transition metal catalyst (usually Ru or Ir based),[3] and a degree of stereoselectivity (**2a** versus **2b**) has been obtained recently under conditions of kinetic control.[4] We reasoned that allyl silyl ethers should also undergo this type of rearrangement by a radical-chain mechanism, in the presence of an appropriate thiol which would act as a protic polarity reversal catalyst[5] to promote the overall abstraction of hydrogen from the electron-rich allylic H–CO bond in **1** by the chain-carrying nucleophilic allylic radical. In this paper we report that such rearrangements do indeed take place under relatively mild, metal-free conditions and could provide a useful route to silyl enol ethers **2** when the starting allylic alcohol is readily available.



Scheme 1.



Scheme 2.

Keywords: radicals and radical reactions; catalysis; thiols; isomerisation; silicon and compounds.

* Corresponding author.

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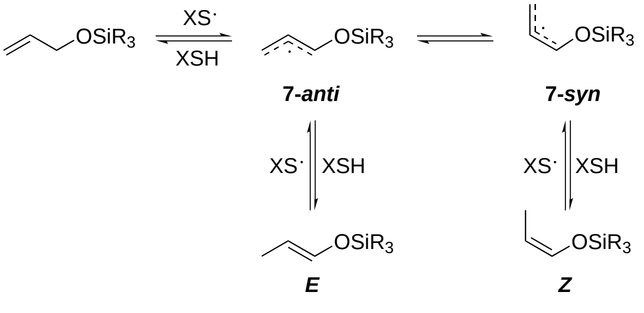
Initial experiments were carried out with the 2-methylallyloxysilane **3**[6] and conversion to the silyl enol ether **4** (Scheme 2) was monitored by ^{1}H NMR spectroscopy. When a solution of **3** (1 mol) and azobis(isobutyronitrile) (AIBN, 10 mol%) in dry benzene (1.5 cm^3) was heated under reflux under nitrogen for 2.5 h, the allyl silyl ether was unchanged and no silyl enol ether was detectable. However, when the experiment was repeated in the additional presence of pentafluorothiophenol (PFTP, 10 mol%), clean and complete conversion of **3** to **4** took place. The same result was obtained when the AIBN was replaced by dilauroyl peroxide (DLP, 10 mol%), whereas without any initiator but in the presence of thiol, no conversion to silyl enol ether was observed. Choice of the thiol catalyst proved to be critical since, under otherwise identical conditions, thiophenol, *tert*-dodecanethiol and tri-*tert*-butoxysilanethiol gave conversions to **4** of 21, 5 and 17%, respectively.[7]

Although these results point strongly to a radical-chain mechanism for the isomerisation of **3** to **4**, in principle, some form of acid-catalysed process might be involved, the acid being generated in situ during the reaction.[8] In order to exclude this possibility, two identical reactions **A** and **B** (10 mol% each of PFTP and AIBN) were run side by side and samples were withdrawn from both for NMR analysis after 15 min. At the same time, the isolable aryloxyl radical galvinoxyl (10 mol%) was added to flask **B**.[9] After 15 min heating, conversion of **3** to **4** was 48% in reaction **A** and 45% in reaction **B**, while after 2.5 h heating conversion was complete in reaction **A** but still only 45% in the inhibited reaction **B**. These results strongly support a radical-chain mechanism for the isomerisation process.

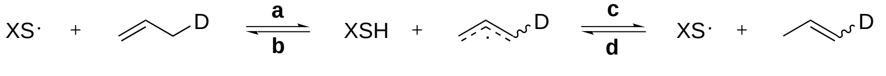
After 2.5 h in refluxing benzene under the usual conditions, using PFTP as catalyst and DLP as initiator, 90% of the allyl silyl ether **5** was converted to silyl enol ether **6** with an *E*:*Z* ratio of 1:3.0.[10] However, isomerisation was complete in refluxing toluene with 1,1-di-*tert*-butylperoxycyclohexane (DBPC, 10 mol%) as initiator or in refluxing octane with 2,2-di-*tert*-butylperoxybutane (DBPB, 10 mol%) as initiator; the *E*:*Z* ratio was 1:2.8 in both cases. Simple distillation afforded **6** in 85% isolated yield and chromatography on silica gel yielded pure **6*Z***, a sample of which was then heated under reflux in octane for 2.5 h in the presence of PFTP and DBPB (10 mol% of each). Isomerisation of the silyl enol ether took place to give a final *E*:*Z* ratio of 1:2.8, indicating that thermodynamic equilibrium between **6*E*** and **6*Z*** is established under the conditions used to convert **5** to **6**. The radical-chain mechanism for the isomerisation of allyl silyl ethers to silyl enol ethers is illustrated in Scheme 3 and the function of the thiol is to act as a protic polarity reversal catalyst to promote the *overall* abstraction of allylic hydrogen from the allyloxysilane by the allylic radical **7**, a reaction that is slow in the absence of thiol because of the lack of favourable charge-transfer stabilisation of the transition state.[5] The allylic radical **7** exists in *syn* and *anti* forms, that can be detected separately by EPR spectroscopy at low temperature,[11] and trapping of **7-*anti*** by the thiol presumably gives the *E*-isomer of the silyl enol ether, while trapping of **7-*syn*** will give the *Z*-isomer.



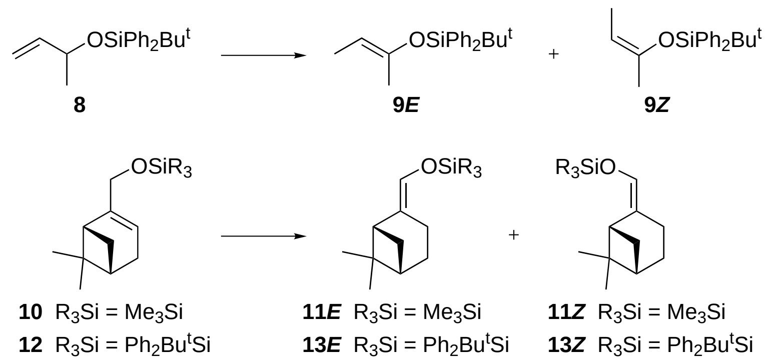
Scheme 3.

In order for effective thiol-catalysed conversion of an allylic molecule to a more stable vinylic isomer (Scheme 4, D = electron-donating substituent), *both* reactions **a** and **c** must be rapid. Furthermore, removal of thiol by radical addition to the double bonds in the reactant or product must be minimised, by making addition of $XS^{\bullet}$ to the C=C bonds highly reversible and/or retarded by the steric bulk of the thiyl radical. Both reactions **a** and **c** will be favoured for more electrophilic thiyl radicals but, since the activation energy for a reaction cannot be less than its endothermicity, the strength of the S–H bond should be such that neither reaction is significantly endothermic. Although reaction **a** will be very rapid with alkane- or silane-thiols as catalysts, reaction **c** (and reaction **b**) is likely to be appreciably endothermic and relatively slow, with the equilibrium favouring the allylic radical. Because of the weaker S–H bond in thiophenol, reaction **c** will be faster and this thiol is a more efficient catalyst. The S–H bond in PFTP is likely to be stronger than that in thiophenol,[12] leading to a still more favourable balance between reactions **a** and **c**, and the presence of the ring-fluorine atoms in PFTP will also maximise favourable polar effects for the abstraction of hydrogen by the especially electrophilic thiyl radical $C_6F_5S^{\bullet}$, to give the nucleophilic siloxyallyl radical (reaction **a**), as well as for abstraction of hydrogen from the thiol by the latter radical (reaction **c**).

The secondary allyl silyl ether **8** underwent isomerisation somewhat less readily than the primary analogue **5**. Thus, in refluxing benzene with AIBN and PFTP (both 10 mol%), conversion was 77% after 2.5 h (**9*E***:**9*Z*** = 1:1.9),[13] although the conversion was increased to 86% when the AIBN was replaced by DLP (Scheme 5). In refluxing toluene (DBPC initiator) or refluxing octane



Scheme 4.

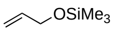
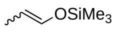
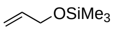
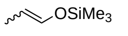
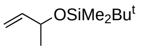
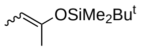
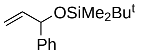
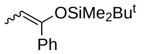
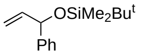
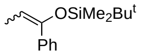
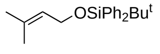
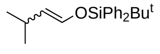
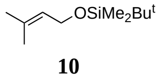
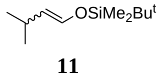


Scheme 5.

(DBPB initiator) conversion was >98% (**9***E*:**9***Z* = 1:1.6 in both cases). The lower reactivity of secondary allyloxysilanes seems likely to be mainly a stereoelectronic effect, arising from the fact that the single allylic CH bond is positioned close to the nodal plane of the double bond in the preferred conformation of the starting material, such that the allylic hydrogen atom is abstracted relatively slowly by a thiyl radical; steric effects may also play a role. A number of other allyl silyl ethers were isomerised to silyl enol ethers under similar conditions and the results are summarised in Table 1.

Isomerisation of the prototypical allyloxytrimethylsilane took place readily either in refluxing toluene or in the neat silane as solvent (entries 2 and 3). In the latter case, the silyl enol ether could be isolated easily by simple distillation of the reaction mixture. Density functional calculations at the (U)B3LYP/6-31G(d,p) level of theory predict that the *E*- and *Z*-isomers of $Me_3SiOCH{=}CHMe$ are lower in energy than the most stable conformation of allyloxytrimethylsilane[14] by 29.7 and 33.0 kJ mol^{-1} (ΔG at 25°C), respectively, while the *syn*-isomer of the allylic radical **7** (R = Me) is more stable than the *anti*-isomer by 1.4 kJ mol^{-1} (compare Ref. 11). The appreciably greater stability of the silyl enol ether compared with the allyl silyl ether accords with the effectively complete isomerisation of the latter observed experimentally and the predicted equilibrium *E*:*Z* ratio is ca. 1:2.8 at 115°C, in excellent agreement with the result obtained in refluxing toluene (1:2.2).

Table 1. Isomerisation of allyl silyl ethers to silyl enol ethers catalysed by pentafluorothiophenol[a]

Entry	Allyl silyl ether	Silyl enol ether	Solvent	Initiator	Conversion (%)[b]	*E*:*Z* ratio[c]
1			Toluene	DBPC	95	1:2.6
2			Toluene	DBPC	>98	1:2.2
3			Neat[d]	DBPC	>98 (82)	1:2.2
4			Octane	DBPB	>98	1:2.0
5			Toluene	DBPC	96[e]	1:13.0
6			Octane	DBPB	>98	1:14.0
7			Octane	DBPB	87	1:1.3
8			Octane	DBPB	91	1:1.3
9	**10**	**11**	Benzene	AIBN	96	4.2:1
10	**10**	**11**	Neat[d]	DBPC	95 (78)	4.4:1
11	**12**	**13**	Benzene	AIBN	96[f] (81)	4.6:1

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[a] Unless stated otherwise, reactions were carried out on the 1 mmol scale in 1.5 cm^3 of solvent under reflux for 2.5 h, in the presence of PFTP and initiator (both 10 mol%). [b] Determined by ^{1}H NMR spectroscopy; isolated yields of *E*/*Z* mixtures in parentheses. [c] Isomers identified on the basis of the magnitudes of the vicinal vinylic-proton coupling constants or of NOE experiments. [d] Large scale (10-20 mmol); bath temperature 120°C. [e] Conversions using *tert*-dodecanethiol or 4-fluorothiophenol (both 10 mol%) as catalysts were 2% and 11%, respectively. [f] In refluxing octane with DBPB as initiator, the conversion was >98% (*E*:*Z* = 4.8:1).

The quantitative conversion of $Bu^tMe_2SiOCHPh$-$CH=CH_2$ to the corresponding silyl enol ether (entry 5) was reduced to almost zero when the PFTP was replaced by *tert*-dodecanethiol, again emphasising the importance of the choice of thiol catalyst. The low efficiency of the alkanethiol is presumably a consequence of the low rate of reaction **c** (Scheme 4), because of the effective stabilisation of the phenyl-substituted allylic radical intermediate involved in this isomerisation.

The PFTP-catalysed isomerisation of primary allyl silyl ethers could provide a very convenient source of silyl enol ethers that might be less accessible from the appropriate aldehydes by *O*-silylation of their enolates. Thus, the terpenoid (1*R*)-(−)-myrtenol, a primary allylic alcohol that is readily available from the chiral pool, can be silylated under standard conditions to give the silyl ethers **10** and **12** (Scheme 5). Isomerisation of both compounds took place readily in refluxing benzene (or in the neat state for ease of product isolation), to give the silyl enol ethers **11** and **13** as predominantly the *E*-isomers, presumably because of steric destabilisation of the *Z*-isomers (entries 9–11).

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7. *Typical procedure*: A solution of the allyl silyl ether **3**[6] (0.31 g, 1.0 mmol), PFTP (13.3 μL, 0.1 mmol) and 2,2-di-*tert*-butylperoxybutane (DBPB: 54 μL of a 50% w/w solution in mineral oil, 0.1 mmol) in dry octane (1.5 cm^3) was stirred and heated under reflux under nitrogen for 2.5 h. The solvent was removed under reduced pressure and the silyl enol ether **4** (0.27 g, 87%) was isolated by chromatography on silica gel (petroleum, bp 40–60°C, eluent) as a colourless oil that solidified on standing (mp ca. 30°C). (Found: C, 77.3; H, 8.2. $C_{20}H_{26}OSi$ requires C, 77.4; H, 8.4%). NMR data for compound **4** (400 MHz for ^1H, 100 MHz for ^{13}C, $CDCl_3$ solvent, *J* in Hz). δ_H 1.09 (9H, s, Bu^t), 1.35 (3H, s, Me), 1.66 (3H, s, Me), 6.07 (1H, apparent septet, *J* ca.1.4, vinyl-H), 7.24–7.43 (6H, m, aryl-H), 7.68–7.72 (4H, m, aryl-H); δ_C 15.0, 19.2, 26.6, 29.7, 113.0, 127.7, 129.9, 133.3, 133.7 and 135.4. Satisfactory spectroscopic data and elemental analyses were obtained for all other new compounds.
8. Pentafluorothiophenol is itself a relatively strong acid (pK_a ca. 2.7) because of the presence of the electronegative ring-fluorine atoms, see: Jencks, W. P.; Salvesen, K. *J. Am. Chem. Soc.* **1971**, *93*, 4433.
9. As evidenced by the rapid colour change of the solution from dark brown to pale yellow, galvinoxyl reacts immediately with PFTP, presumably by abstraction of hydrogen to give the phenol monohydrogalvinoxyl that must also act as a radical scavenger to inhibit the radical-chain process. 2-6-Di-*tert*-butyl-4-methylphenol also inhibited the isomerisation, although less effectively.
10. The *E*- and *Z*-isomers were readily distinguished on the basis of the coupling constants between the vinylic protons.
11. Elford, P. E.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2247.
12. The presence of electronegative substituents on the ring would be expected to strengthen the SH bond, compared with that in thiophenol, see: Nau, W. M. *J. Org. Chem.* **1996**, *61*, 8312; *J. Phys. Org. Chem.* **1997**, *10*, 445.
13. Geometrical isomers were identified on the basis of NOE wexperiments.
14. The Si–O bond eclipses the C=C bond in the preferred conformation; the conformation in which an allylic C–H bond eclipses the C=C bond is less stable by 3.1 kJ mol^{-1}.