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New Reagents for Radical Allylations

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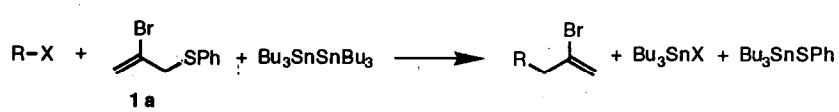
Summary: *Three reagents are introduced for radical allylations: 3-phenylthio-2-bromopropene, 2,3-bis(trimethylstannyl)propene, and 3-tris(trimethylsilyl)silylthiopropene.*

Introducing allyl groups into organic molecules is an important transformation because allyl groups are quite stable yet provide convenient handles for introduction of many other functional groups. Radical allylations provide some of the mildest, most general methods to introduce allyl groups into functionalized molecules. Early reagents used for the allylations of halides and phenyl selenides were based on the chemistry of the trialkyltin radical (allyl stannanes,[2] allyl phenyl sulfides/$Bu_3SnSnBu_3$[3]), and they transferred allyl groups or 2-carbon substituted allyl groups.[4] Recently, 2-heteroatom substituted (Cl,[5a] Si,[5b] NO_2,[5c] SO_2[5d]) radical allylating reagents have been introduced often with the goal of controlling the oxidation level at C2. 2-Heteroatom substituted allylating reagents should be especially valuable because the residual heteroatoms can later be used to promote ionic or radical carbon-carbon bond formation.[5d] We now describe the application of two simple reagents, 3-phenylthio-2-bromopropene (**1a**, 2-bromoallyl phenyl sulfide) and 2,3-bis(trimethylstannyl)propene (**1b**),[5e] for the preparation of vinyl bromides and vinyl stannanes through radical allylations. We also introduce a new reagent, 3-tris(trimethylsilyl)silylthiopropene (**1c**, allyl tris(trimethylsilyl)silyl sulfide), for standard radical allylations.

The basic transformations of the three reagents are summarized in equations 1a-c. 2-Bromoallyl phenyl sulfide (**1a**) was prepared by the reaction of sodium thiophenoxide (PhSH, CH_3ONa, CH_3OH) with 2,3-dibromopropene, and was isolated in 81% yield after distillation (bp 89-90°C, 0.7 mm Hg). 2,3-Bis(trimethylstannyl)propene (**1b**)[6] was prepared by mesylation of 2-bromopropen-3-ol and subsequent reaction with $Me_3Sn(Me)(CuCN)Li_2$.[6a] Allyl tris(trimethylsilyl)silylsulfide (**1c**) was prepared in one flask by addition of tris(trimethylsilyl)silicon hydride to carbon tetrachloride (which forms tris(trimethylsilyl)silicon chloride), followed by addition of allyl thiol and triethylamine.[7] Reagent **1c** is a new compound that was isolated in 60% yield after vacuum distillation (bp 98-100°C, 0.4 mm Hg).

eq 1a

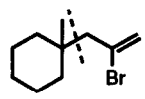


eq 1b

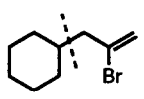
eq 1c

Reactions with **1a** were conducted by the method of Keck and Byers.[3] Sunlamp irradiation of a benzene solution of an alkyl iodide or bromide (1 equiv, 0.5M), **1a** (2 equiv), and hexabutylditin (1.0 equiv) for 30 min to 12 h provided the products shown in Figure 1. The yield and reaction time are indicated for the appropriate precursor. The selectivity of these reactions is noteworthy because each reaction mixture contains three potential radical precursors: the substrate RX, the allyl sulfide, and the vinyl bromide. Provided that the substrate RX is sufficiently reactive (iodides preferred), the selectivity is excellent.[8] The isolation of pure products was complicated by the large quantities of tin- and sulfur-containing products, and we suspect that the modest yields in some cases reflect this complication (crude ^{1}H NMRs and TLC were often very clean). To facilitate separation, we treated the crude reaction mixtures first with I_2/DBU[9] and then with aqueous oxone™ to oxidize the non-polar sulfide products to more polar materials. Subsequent purification by MPLC provided the yields recorded in Figure 1.

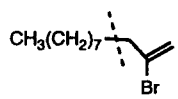
Figure 1



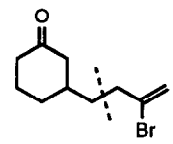
from iodide, 84% (30 min)
from bromide, 44% (12 h)



from iodide, 75% (2 h)
from bromide, 41% (12 h)
from phenylselenide, <20% (12 h)



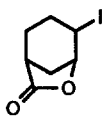
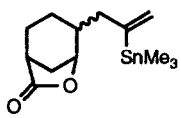
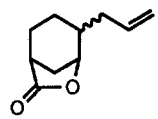
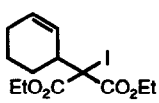
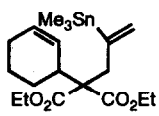
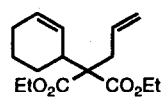
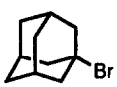
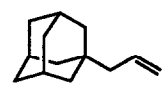
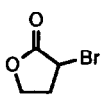
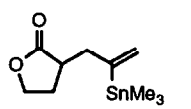
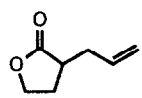
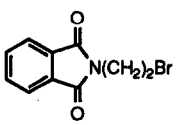
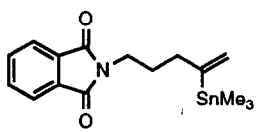
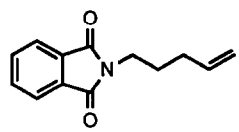
from iodide, 59% (3 h)
from bromide, 36% (12 h)



from iodide, 52% (3 h)

Reactions of **1b** were conducted by the standard photolytic procedure of Keck and coworkers,[2a] and precursors, products, and isolated yields (after purification by flash chromatography) are recorded in Table 1. As expected,[2] a variety of functional groups are tolerated. Isolation of the products of these reactions is easier because trimethyltin iodide and bromide are relatively volatile; however, *appropriate precautions*

Table 1

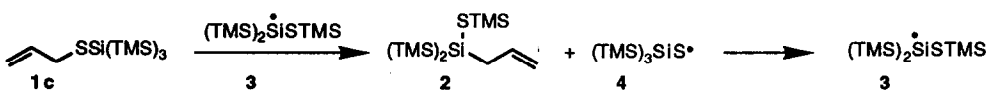
R–X	Product from **1b**	Time	Yield	Product from **1c**	Time	Yield
$CH_3CO_2(CH_2)_4I$	$CH_3CO_2(CH_2)_5C(SnMe_3)=CH_2$	12 h	51%	$CH_3CO_2(CH_2)_5CH=CH_2$	18 h	41%
		12 h	53%		12 h	42%
		8 h	62%		12 h	61%
	not conducted				12 h	48%
		18 h	72%		18 h	54%
		18 h	41%		18 h	43%

must be taken because volatile tin compounds are potentially toxic. Since vinyl stannanes are readily converted to vinyl bromides and iodides, reagent **1b** provides a two-step alternative to reagent **1a**.

With the advent of tris(trimethylsilyl)silicon hydride as an ecologically acceptable alternative to tributyltin hydride,[10] replacement of allyltributylstannane with allyl tris(trimethylsilyl)silane[11] is also attractive. However, an important difference between trialkyltin and tris(trimethylsilyl)silicon radicals is the higher affinity of the latter for double bonds.[10] Said another way, the β-elimination of tris(trimethylsilyl)silicon radicals may not always be easy.[12] To address this problem, we prepared **1c** guided by Chatgilialoglu's introduction of tris(trimethylsilyl)silicon thiol as a new radical reducing agent.[13] We found it very difficult to initiate and maintain chains with **1c** under Keck's standard thermal or photolytic conditions for allyl stannanes.[2a] However, irradiation of **1c** with alkyl halides in the presence of 10% hexabutylditin did result in the slow conversion to the expected allylation products in modest yields.[14] Table 1 lists the results of several reactions. Isolated yields were obtained after I_2/DBU workup and flash chromatography.

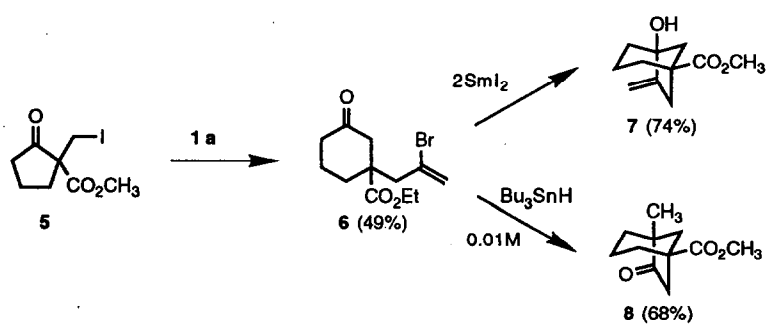
The yields with **1c** are respectable, but do not match Keck's yields with allyltributyl stannane.[2a] Further, since some distannane is still required, we have not yet reached the goal of a "tin free" allylation reagent.[11] To help identify the problems in chain propagation, we heated **1c** with a 10% AIBN, and we observed smooth formation of the rearranged allyl silane **2** over only 2 h (eq 2).[15] This implies that elimination of the thio radical **4** and 1,2-silicon shift (**4** → **3**) occur as expected.[13] Reactions of **1c** in the presence of halides are much slower, yet **2** is not formed. This implies that the halogen abstraction reaction of silyl radical **3** is faster than addition to **1c**. Thus, the problem with **1c** seems to be in chain propagation,[16] and the evidence that the elimination, silyl transfer, and halogen transfer steps are reasonable implies that the radical addition step is the culprit. Perhaps **1c** is not a very good acceptor for alkyl radicals? Further experiments to improve this reagent are planned.

eq 2



The residual vinyl bromide or vinyl stannane obtained from allylation with **1a** or **1b** will permit many further transformations with more functionalized substrates. A single example is illustrated in eq 3. During the reaction of **5** and **1a**, ring expansion (à la Dowd and Beckwith[17]) preceeds allylation to form **6**. Reduction of **6** with SmI_2[18] (THF/HMPA) forms the directly coupled product **7** while reduction of **6** with Bu_3SnH forms **8**, probably by a sequence of radical cyclization to the carbonyl, fragmentation, and recyclization to the newly formed alkene.[19] We plan to publish a full paper describing all the radical sequences that we have developed with the reagent.

eq 3



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References and Notes

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7. A solution of tris(trimethylsilyl)silane in CCl_4 was allowed to stand for 3 d at 25°C. Evaporation of solvent gave $(TMS)_3SiCl$; ^1H NMR ($CDCl_3$) δ 0.22 (27H, s). To a solution of allyl mercaptan (2.68 g, 9.46 mmol) and Et_3N (97.5 mg, 0.96 mmol) in ether (33 mL) was slowly added $(TMS)_3SiCl$ (200 mg, 0.71 mmol) at 0°C. The mixture was then treated with 1N HCl, extracted with ether (3x30 mL), dried over $MgSO_4$. The residue was purified by vacuum distillation to yield **1c** (1.82 g, 60%) as a colorless oil: bp = 98-100°C/0.4 mm; ^1H NMR ($CDCl_3$) δ 5.96-5.83 (1H, m), 5.19 (1H, d, J = 16.8 Hz), 5.02 (1H, d, J = 9.9 Hz), 3.16 (2H, d Hg, J = 6.7 Hz), 0.21 (27H, s); ^{13}C NMR ($CDCl_3$) δ 136.8, 116.0, 33.4, 0.84; MS 191, 173, 142, 131, 73; HRMS *m/e* calculated for $C_9H_{14}SSi_4$ ($M^+ - C_3H_5$): 279.0911; found: 279.0911.
8. Small amounts of allene were detected in ^1H NMR experiments with less reactive precursors. This is diagnostic of **1a** functioning as a radical precursor.
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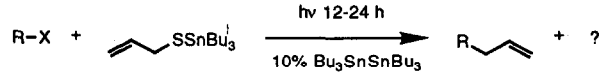
14. **6-Heptenylacetate, General Procedure.** A solution of 4-iodobutyl acetate (59.0 mg, 0.24 mmol), **1c** (154 mg, 0.48 mmol), and hexabutylditin (10 µl, 0.02 mmol) in C_6D_6 (0.5 mL) was placed in ^1H NMR tube and degassed with nitrogen for 20 min. The tube was sealed and irradiated with a 275-W GE sunlamp at 25°C for 18 h. The crude mixture was treated with DBU/I_2, filtered through a pad of silical gel, and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc = 5:1) afforded allylation product (15.0 mg, 41%) as a colorless oil.
15. A new doublet at δ 2.10 (allylic CH_2) is diagnostic of the formation of **2**.
16. It is not even certain that chains are propagating with **1c**. Similar yields in the allylations in Table 1 are obtained by using allylthio(tributyl)stannane. With this reagent, no obvious chain mechanism is available because a good halogen abstraction step is apparently lacking.



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