Applications of Consecutive Radical Addition–Elimination Reactions in Synthesis

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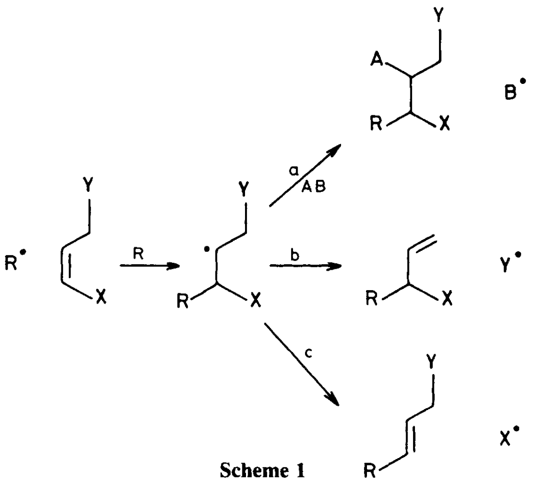
Alkyl radicals add to the tri-n-butylstannyl substituted terminus of several alkenes; elimination of the stannyl radical results in a preparatively useful, carbon–carbon bond forming reaction, under mild and neutral conditions.

When a carbon radical attacks an alkene there are two possible pathways from the radical adduct to a diamagnetic product: reaction with a radical donor[1] (*e.g.* tri-n-butyltin hydride, pathway a, Scheme 1) or elimination of a radical moiety of the adduct. Elimination may occur in two ways; distal to the attacking radical (the S_H' reaction, pathway b)[2,3] or proximal (pathway c). We have developed a new suite of reactions based on the proximal elimination of the tri-n-butylstannyl group,[4] from radical adducts.

In the course of a total synthesis of a naturally occurring dienyl isonitrile[5] we discovered that the oxazolo-cyclopentyl bromide (**10**) reacted with a β-stannyl acrylate (**1**) to give overall addition–elimination. We have now examined a range of primary, secondary, and tertiary bromides and have found the reaction to be general (Table 1). Thus the bromides (**3a**)—(**10a**) were heated (86 °C, toluene, 1 ml/mmol of bromide) with the β-stannyl acrylate (**1**) (2 equiv.) initiated with azoisobutyronitrile (AIBN) (16 mol % every 12 h) for



Scheme 1

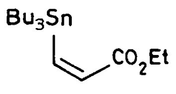
Table 1. Radical additions of the bromides (**3a**)—(**10a**) to the vinylstannanes (**1**) and (**2**).

Radical precursor	Product, % yield[d]	
	Reaction with (**1**)	Reaction with (**2**)
(**3a**)	(**3b**), 52	(**3c**), 52
(**4a**)	(**4b**), 63	(**4c**), 22
(**5a**)	—	(**5c**), 32
(**6a**)[a]	(**6b**), 43	(**6c**), 41
(**7a**)	(**7b**), 74	(**7c**), 82
(**8a**)[b]	*trans*-(**8b**), 44 *cis*-(**8b**), 13	(**8c**), 51
(**9a**)	(**9b**), 49	(**9c**), 42
(**10a**)[c]	(**11**), 79	(**12**), 70

[a] For rearrangement of α-acyloxyl radicals see L. R. C. Barclay, J. Lusztyk, and K. U. Ingold, *J. Am. Chem. Soc.*, 1984, **106**, 1793. [b] G. Zweifel and R. A. Lynd, *Synthesis*, 1976, 625. [c] The initial adducts (**10b**) and (**10c**) of the dihydro-oxazole (**10a**) were hydrolysed with tetrahydrofuran (THF; 15 ml), water (2 ml), and glacial acetic acid (80 μl) to facilitate isolation. [d] Yields of the non-polar adducts are appreciably lower than those of the polar adducts because of difficulties in separating the products from the non-polar tin residues. When the reactions were performed in deuteriated solvents, and small aliquots taken for examination by 300 MHz ^{1}H n.m.r. spectroscopy, no other olefinic products were detected except for small amounts (<20%) of the *cis*-isomers [except for the adduct (**8b**)] and the *trans*-isomer of the stannane (**1**).

24—36 h (Table 1).† Since xanthate esters have been shown to be an effective source of alkyl radicals[6] we subjected the methyl xanthate of diacetone glucose (**13a**) to these conditions. At 86 °C the reaction was very slow but at 105—110 °C the desired adduct (**13b**) (30%) was obtained accompanied by the reduced product (**13c**) (30%).‡

It is known that the electronic nature of the vinyl substituents strongly influences the rate of attack of the radical on the alkene[7] and so we examined a less electron-withdrawing substituent, the phenyl group. Reaction of β-tri-n-butylstannylstyrene (**2**)[8] as before gave products of the addition–elimination reaction (**3c**)—(**10c**) along with varying amounts of the adduct (**14**) of the isobutyronitrile radical.[9] In a competitive reaction monitored by 500 MHz ^{1}H n.m.r. spectroscopy, it was shown that the β-stannyl acrylate (**1**) reacted *ca.* 1.5 times more quickly with α-bromoacetaldehyde diethyl acetal (**3a**) than did the β-stannyl styrene (**2**)§ in agreement with previous results.[10] The dienyl stannane (**15**)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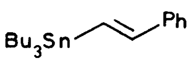
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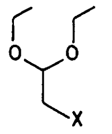
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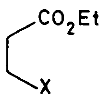
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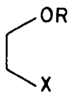
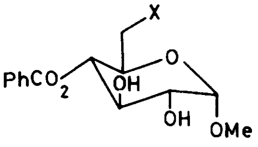

(5), R = H
(6), R = Ac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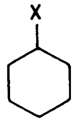
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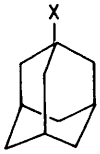
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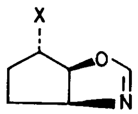
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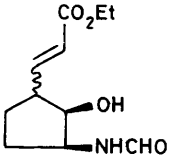
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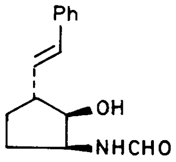
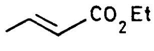
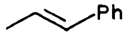
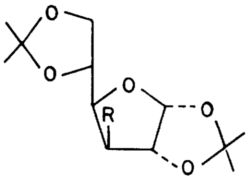
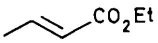

(12)

a; X = Br

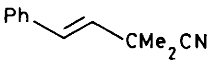
b; X = 

c; X = 


(13) a; R = $\mathrm{O{-}\overset{\overset{\large S}{\|}}{C}{-}SMe}$

b; R = 

c; R = H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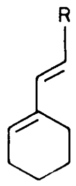
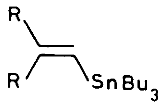
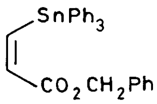

(15) R = SnBu$_3$
(16) R = CMe$_2$CN


(17) R = H
(18) R = Me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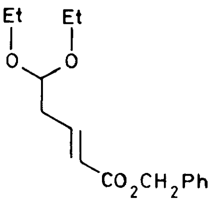
(20)

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† All yields are of isolated materials, purified by flash column chromatography and/or Kugelrohr distillation, which have been characterised by ^{1}H n.m.r., ^{13}C n.m.r., i.r., u.v., mass spectroscopy, and combustion analysis or high-resolution mass spectrometry.

‡ This probably arises by retro-hydrostannylation of the β-stannyl-acrylate to yield tri-n-butyltin hydride, which reduces the xanthate ester directly. Control experiments indicated that the solvent, AIBN, and hexabutylditin were not the sources of the reductant hydrogen.

§ This measurement was made using a larger excess of the stannanes (5 equiv. of each) and less AIBN (2 mol%) than usual in [^{2}H$_8$]toluene. The rate ratio was determined by measuring the relative amounts of the acrylate-derived product (**3b**) and the styryl-derived product (**3c**) from the integral at 20 and 40% conversion of α-bromoacetaldehyde diethyl acetal (**3a**). At higher conversions appreciable amounts of the isobutyronitrile adduct (**14**) were observed.

prepared by hydrostannylation[11] of the corresponding enyne[12] did not react with the bromide (**3a**), merely producing the initiator adduct (**16**), even after prolonged reaction times (10 days); no adducts were obtained with the vinyl stannanes and (**18**).[13] In a preliminary experiment the triphenylstannyl acrylate (**19**)[14] with the bromide (**3a**) gave comparable results to the tributyl analogue (**1**) and gave the adduct (**20**) in 34% yield.

Thus it seems clear that for radical addition–elimination to be usefully applied to simple alkyl radicals an electron-withdrawing group must be present in the vinyl stannane. This is consistent with the 'nucleophilic' nature of simple alkyl radicals. In contrast the isobutyronitrile radical which bears an electron-withdrawing group expresses 'electrophilic' reactivity and so reacts more readily with the stannyl styrene (**2**) and dienyl stannane (**15**), than with the stannyl acrylate (**19**).[7]

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