A New Synthetic Route to Alkenyl-substituted Tetrahydrofurans *via* Successive Intra- and Inter-molecular Radical Reactions

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Tetrahydrofurans with alkenyl substituents were obtained by the radical cyclization of β-bromoethers using allyltri-n-butylstannane in a one-pot reaction.

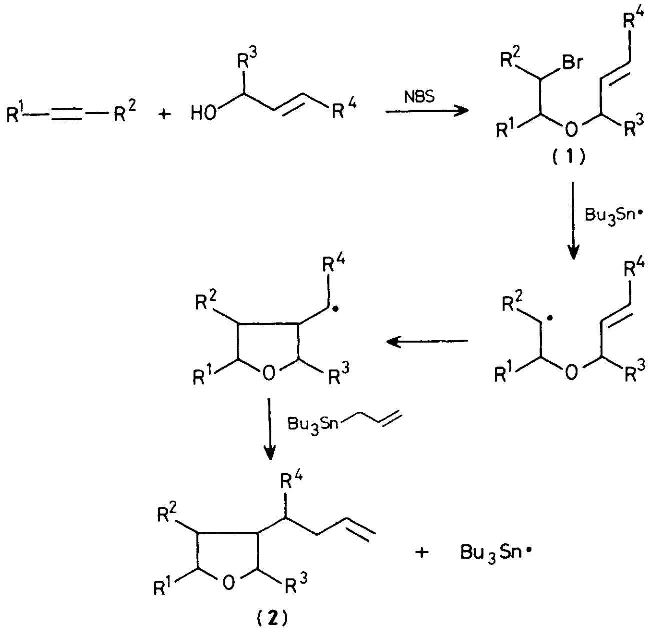
Allyltri-n-butylstannane is known to be a useful allylating reagent;[1] the effective conversion of alkyl halides into allylic compounds by S_H2' substitution has recently been reported.[2] We have been studying the synthetic applications of radical cyclization using tri-n-butylstannane (Bu_3SnH).[3] In such reactions, the last step of intramolecular cyclizations is hydrogen abstraction by a resulting carbon-centred radical from Bu_3SnH, *i.e.*, the reaction proceeds under reductive conditions. Modification of this step to C–C bond formation without loss of a free radical chain process appears to be an attractive possibility. However, this type of reaction has not been adequately investigated except for the work of Stork.[4] We now report a new approach for such reaction sequences using allyltri-n-butylstannane, in which radical cyclization takes place coupled with an S_H2' process.

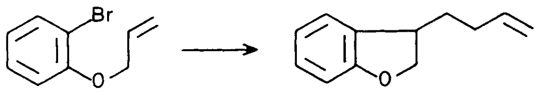
The reaction of the β-bromoethers (**1**) with allyltri-n-butylstannane proceeded *via* a free radical process such that the formation of a five-membered ring and addition of an allylated substituent led to the alkenyl-substituted tetrahydrofurans (**2**) in a one-pot reaction. The starting materials (**1**) were prepared by the alkoxy-bromination of alkenes with allylic alcohols in the presence of N-bromosuccinimide (NBS).[5] For cyclization of (**1**), a solution of (**1**), allyltri-n-butylstannane (3 mol. equiv.), and a catalytic amount of azoisobutyronitrile (AIBN) in degassed benzene (1 ml/mmol of substrate) was stirred at 80 °C for 20—24 h under nitrogen. After chromatography (SiO_2, n-hexane–$CHCl_3$), the product was isolated by distillation (Table 1).

This method was applied to the syntheses of various tetrahydrofurans, including monocyclic and bicyclic, from easily available alkenes and allylic alcohols. Its potential

Table 1. Preparation of β-bromoethers (**1**) and tetrahydrofurans (**2**).

	Starting alkene		Allylic alcohol		% Yield	
	R^1	R^2	R^3	R^4	(**1**)	(**2**)
a	$-[CH_2]_4-$		H	H	70	49
b	$-[CH_2]_4-$		Me	H	70	48
c	$-[CH_2]_4-$		H	Me	53	43
d	Ph	H	H	H	50	35
e	Ph	H	Me	H	40	25
f	Me_2	CH_2OH	H	H	48	37





(3) (4)

utility for straightforward synthesis of multifunctional tetrahydrofurans is illustrated by the preparation of (**2f**), in which no protection of the hydroxy group is necessary. In addition, the use of the allyloxylated bromobenzene (**3**) as starting bromoether enabled the dihydrobenzofuran (**4**) with a butenyl substituent to be prepared.

The two-dimensional ^{1}H n.m.r. spectrum (300 MHz, $CDCl_3$) of the 2,3-disubstituted octahydrobenzofuran (**2b**) was measured to estimate the stereoselectivity. Two signals for the C-2 methine (δ 3.56 and 3.81) and methyl protons (δ 1.35 and 1.25) were observed. The isomeric ratio was estimated from the intensity of one of these signals and that of the C-7 *O*-methine proton, which appeared in a similar region (δ 3.82) and indicated the existence of two stereoisomers in approximately equal proportions. The configuration of the isomers was not assigned, but radical cyclizations in this case did not show a preference for the *trans*-isomer.[6]

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