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1,6-Remote stereocontrol using allylgermanes

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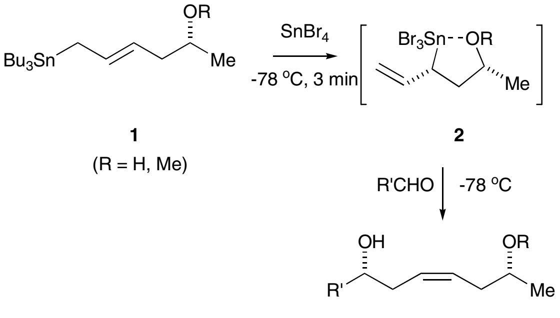
Abstract—Transmetallation of 5-hydroxy- and 5-methoxyhex-2-enyl(triethyl)germanes **8** and **9** with tin(IV) bromide is stereoselective and generates allyltin tribromides, which react with aldehydes to give (3*Z*)-homoallylic alcohols **3** with useful levels of 1,6-*syn*-stereocontrol.

In the accompanying paper, it is reported that transmetallation of 4- and 5-alkoxypent-2-enylgermanes by tin(IV) halides is stereoselective leading to effective 1,5-stereocontrol in reactions with aldehydes[1] providing an alternative to the use of allylstannanes for these conversions.[2] Transmetallation of 5-hydroxy- and 5-methoxyhex-2-enyl(tributyl)stannanes **1** by tin(IV) bromide has been shown to be stereoselective in favour of allyltin tribromides **2**, which react with aldehydes to give (3*Z*)-*syn*-products **3** with an useful overall 1,6-stereocontrol.[3] In view of the continuing interest in remote stereocontrol[4] and 1,6-stereocontrol in particular,[5] we now report preliminary observations on the use of 5-substituted hex-2-enylgermanes as alternatives to allylstannanes for 1,6-stereocontrol.



1
(R = H, Me)

2

3
1,6-*syn*:1,6-*anti* = 90:10

The (2*E*)- and (2*Z*)-5-*tert*-butyldimethylsilyloxyhex-2-enyl(triphenyl)- and -(triethyl)germanes (2*E*)- and (2*Z*)-**5** and (2*E*)- and (2*Z*)-**7** were prepared from allylic acetates (2*E*)-**4** and (2*Z*)-**4**[6] using the cuprates prepared from lithiated triphenyl- and triethylgermane and copper(I) iodide.[7] Desilylation gave the corresponding hydroxyalkenyl germanes (2*E*)- and (2*Z*)-**6** and (2*E*)- and (2*Z*)-**8**. *O*-Methylation of the (2*E*)- and (2*Z*)-5-hydroxyhex-2-enyl(triethyl)germanes (2*E*)- and (2*Z*)-**8** using sodium hydride and methyl iodide gave the corresponding methoxyhex-2-enylgermanes (2*E*)- and (2*Z*)-**9**.

During the studies of 1,6-stereocontrol using allylstannanes, better 1,6-stereoselectivity had been obtained using tin(IV) bromide rather than tin(IV) chloride to transmetallate 5-hydroxyhex-2-enyl(tributyl)stannane **1** (R = H).[3] However, tin(IV) bromide had been found to be unreactive towards 5-benzyloxypent-2-enyl(triphenyl)germanes under the usual reaction conditions at −78 °C for 1,5-stereocontrol, although successful transmetallation had been achieved with tin(IV) bromide for the analogous (triethyl)germanium compounds.[1]

In the event, unreliable results were obtained when tin(IV) chloride was used to transmetallate 5-hydroxyhex-2-enyl(triphenyl)- and -(triethyl)germanes (2*E*)- and (2*Z*)-**6** and (2*E*)- and (2*Z*)-**8**, reactions with benzaldehyde giving rise to complex mixtures of products consisting mainly of branched homoallylic alcohols formed by the reaction of benzaldehyde at the 3-position of the allylgermane. As with the 5-benzyloxypent-2-enyl(triphenyl)germanes, no reaction was observed when attempts were made to transmetallate (2*E*)-5-hydroxyhex-2-enyl(triphenyl)germane (2*E*)-**6** under the usual reaction conditions using tin(IV) bromide.

Keywords: Remote stereocontrol; Allylmetal; Organogermanium; Diastereoselectivity.

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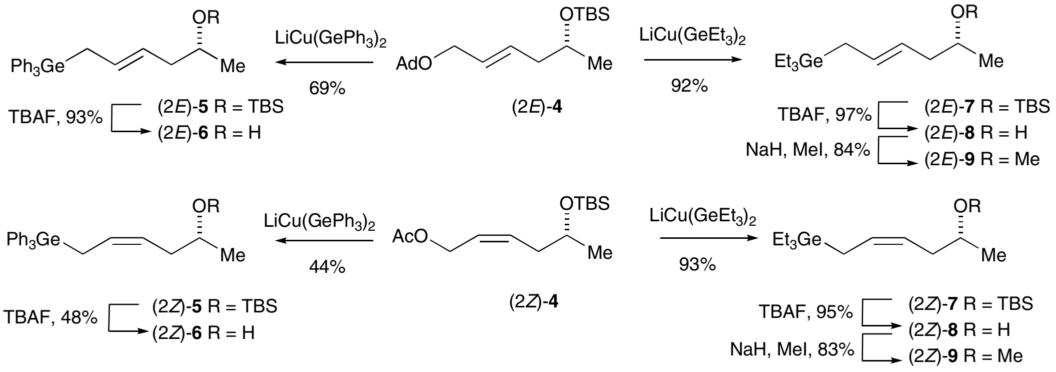
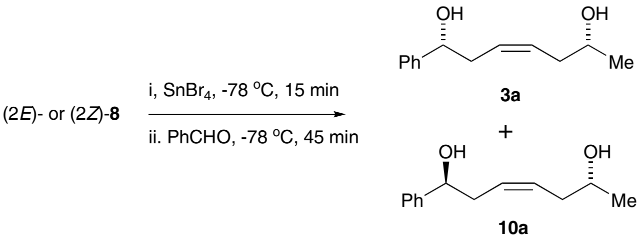


However, more promising results were obtained with triethylgermanes (2*E*)- and (2*Z*)-**8**. Allowing 15 min for transmetallation of (2*E*)-hex-2-enyl(triethyl)germane (2*E*)-**8** using tin(IV) bromide, the reaction with benzaldehyde was stereoselective in favour of (3*Z*)-1,6-*syn*-hept-3-ene-1,6-diol **3a**, 1,6-*syn*-**3a**:1,6-*anti*-**10a** = 89:11. With the (2*Z*)-hex-2-enyl(triethyl)germane (2*Z*)-**8**, a slightly better stereoselectivity in favour of the (3*Z*)-1,6-*syn*-product was observed,1,6-*syn*-**3a**:1,6-*anti*-**10a** = 94:6.[8]



1,6- *syn*-**3a**:1,6-*anti*-**10a** = 89:11 from (2*E*)-**8** and 94:6 from (2*Z*)-**8**

Similar stereoselectivities were observed for tin(IV) bromide promoted reactions of hex-2-enyl(triethyl)germanes (2*E*)- and (2*Z*)-**8** with several aromatic and aliphatic aldehydes, see Table 1. Useful 1,6-stereocontrol, typically ⩾91:9 in favour of (3*Z*)-1,6-*syn*-stereoisomer **3** was obtained in all cases.[9] Analogous results were obtained using (2*E*)- and (2*Z*)-5-methoxyhex-2-enyl(triethyl)germanes (2*E*)- and (2*Z*)-**9**, see Table 1, entries 9–12.[9] In fact, tin(IV) chloride was also effective for transmetallation of (2*E*)- and (2*Z*)-5-methoxyhex-2-enyl(triethyl)germanes, but variable stereoselectivities were observed in reactions with benzaldehyde, in some cases in favour of 1,6-*anti*-product **10g**, so the use of tin(IV) bromide is preferred for 1,6-*syn*-stereocontrol using allylgermanes, as had been observed for allylstannanes.

From Table 1, it can be seen that useful stereoselectivities in favour of (3*Z*)-1,6-*syn*-products **3** were obtained in all cases. As observed for the reactions of allgermanes proceeding with 1,5-stereocontrol, slightly better stereo-

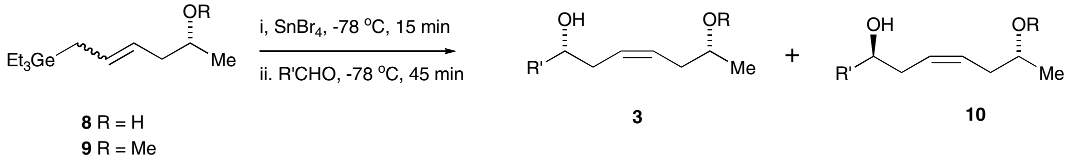


Table 1. 1,6-Stereocontrol using 5-hydroxy- and -5-methoxyhex-2-enyl(triethyl)germanes

Entry	Germane	*R*	Aldehyde[a] *R′*	Products[b]	Isolated yield (%)	Ratio 1,6-*syn*:1,6-*anti*
1	(2*E*)-**8**	H	Ph	**3a**, **10a**	63	89:11
2	(2*E*)-**8**	H	$(CH_3)_2CH$	**3b**, **10b**	51	90:10
3	(2*Z*)-**8**	H	Ph	**3a**, **10a**	80(80)[c]	94:6
4	(2*Z*)-**8**	H	$(CH_3)_2CH$	**3b**, **10b**	82	93:7
5	(2*Z*)-**8**	H	$CH_3(CH_2)_2$	**3c**, **10c**	75	93:7
6	(2*Z*)-**8**	H	4-ClC_6H_4	**3d**, **10d**	81	92:8
7	(2*Z*)-**8**	H	3-ClC_6H_4	**3e**, **10e**	83	93:7
8	(2*Z*)-**8**	H	4-$NO_2C_6H_4$	**3f**, **10f**	81	91:9
9	(2*E*)-**9**	Me	Ph	**3g**, **10g**	83	86:4
10	(2*Z*)-**9**	Me	Ph	**3g**, **10g**	94	94:6
11	(2*E*)-**9**	Me	4-ClC_6H_4	**3h**, **10h**	86	95:5
12	(2*E*)-**9**	Me	$CH_3(CH_2)_2$	**3i**, **10i**	61	90:10

[a] Three equivalents of the aldehydes were used.

[b] The products were identified by comparison with authentic samples (see Refs. 6 and 7).

[c] One equivalent of aldehyde in this case.

selectivities were obtained using (2*Z*)-hexenylgermanes (2*Z*)-**8** and (2*Z*)-**9** than for the analogous (2*E*)-hexenylgermanes, perhaps due to more stereoselective transmetallation for the (2*Z*)-isomers. Notwithstanding this detail, it would appear that 5-substituted hex-2-enyl-(triethyl)germanes can be used for 1,6-stereocontrol in tin(IV) bromide promoted reactions with aldehydes so alleviating the need for allylstannanes.

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References and notes

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8. 1,6-*syn*- and 1,6-*anti*-diols **3a** and **10a** were identified by comparison with samples prepared earlier (see Ref. 3). The ratio **3a**:**10a** was best estimated by integration of the benzylic C–H peaks in ^{1}H NMR spectra: δ_H 4.68 (1H, dd, *J* 5, 11 Hz) for **3a** and 4.75 (1H, t, *J* 5) for **10a**.
9. Diols **3** and **10** were identified by comparison with samples prepared using the hexenylstannane **1**. For the products derived from aromatic aldehydes, the *syn*:*anti* ratios were estimated from the integration of the benzylic protons. For products **3b**,**c**,**i** and **10b**,**c**,**i** prepared using aliphatic aldehydes, the *syn*:*anti* ratios were estimated from ^{13}C spectra.