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1,5-Remote stereocontrol using allylgermanes

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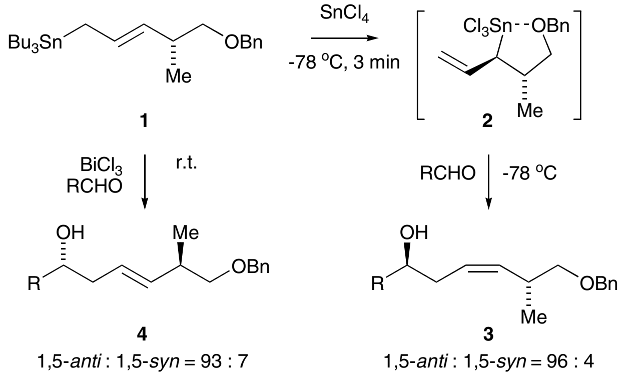
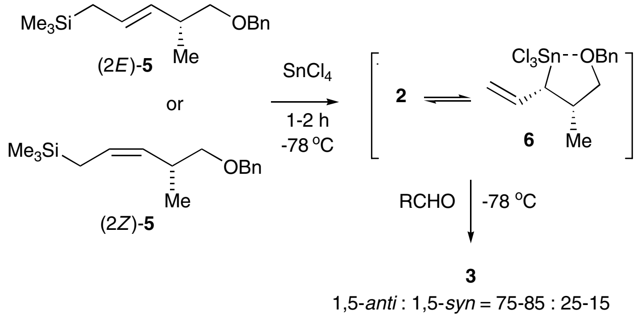
Abstract—Transmetallation of 5- and 4-alkoxypent-2-enylgermanes **8**, **10** and **13** using tin(IV) chloride is stereoselective and generates allyltin trichlorides which react with aldehydes with useful levels of 1,5-stereocontrol.

Allylstannanes with heteroatom functionality at the 4-, 5- and 6-positions can be transmetallated to give more reactive allylmetal reagents which react with aldehydes with useful levels of remote stereocontrol.[1] For example, 5-benzyloxy-4-methylpent-2-enyl(tributyl)stannane **1** gives 1-substituted (3*Z*)-1,5-*anti*-hex-3-enols **3** with aldehydes after transmetallation to the allyltin trichloride **2** using tin(IV) chloride[2] and diastereoisomeric (3*E*)-1,5-*anti*-hex-3-enols **4** on reaction with bismuth(III) iodide and an aldehyde.[3] Although these reactions are useful in synthesis,[4–6] it is of interest to develop analogous reactions which avoid the use of *organo*-tin starting materials because of the toxicity of *organo*-tin compounds.



Allylsilanes are transmetallated by tin(IV) halides, but transmetallation of allylsilanes **5** at −78 °C is relatively slow, so allowing the intermediate *anti*-allyltin trichloride **2** time to begin to equilibrate with its *syn*-diastereoisomer **6** leading to a reduced overall stereoselectivity in the reactions with aldehydes, although slightly better stereoselectivity was observed for the (2*Z*)-isomer rather than for the (2*E*)-isomer of silane **5**.[7,8]



Organogermanium compounds are intermediate between *organo*-silicon and -tin compounds in reactivity and reactions of allylgermanium compounds with aldehydes promoted by Lewis acids are known although cycloaddition reactions predominate with 1-substituted allylgermanes.[9] Therefore it was of interest to investigate the reactivity of allylgermanium compounds towards transmetallation and the use of these compounds for remote stereochemical control. We now report preliminary results in this area.

The racemic 5-benzyloxy-4-methylpent-2-enyl(triphenyl)germane **8** was prepared as a mixture of (*E*)- and (*Z*)-isomers, from chloride **7**, triphenylgermanium bromide and magnesium, using the Barbier procedure.[10] The (2*E*)- and (2*Z*)-triphenyl- and -triethylgermanes (2*E*)- and (2*Z*)-**8** and (2*E*)- and (2*Z*)-**10** were prepared with retention of the double-bond geometry from allylic acetates (2*E*)- and (2*Z*)-**9**[11] using the cuprate prepared

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Keywords: Remote stereocontrol; Allylmetal; Organogermanium; Diastereoselectivity.

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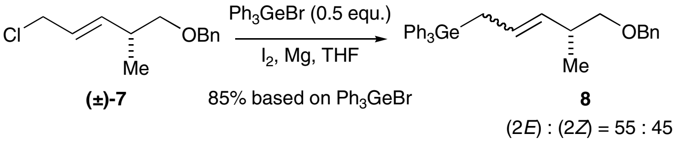
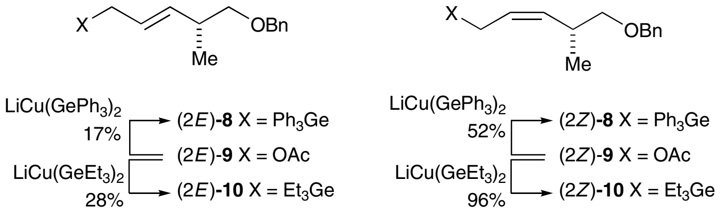
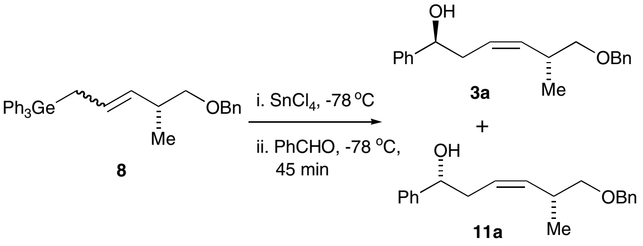




in situ from the appropriate lithiated germane and copper(I) iodide.[12] This displacement, in our hands, was more efficient for the preparation of triethylgermanes than for triphenylgermanes.

The tin(IV) chloride promoted reaction between the (2*E*)/(2*Z*)-mixture of pent-2-enyl(triphenyl)germanes **8** with benzaldehyde gave mixtures of 1,5-*anti*- and *syn*-products **3a** and **11a**, the ratio depending on the time allowed for the transmetallation. If, following the addition of the tin(IV) chloride to a solution of the pent-2-enylgermane **8** in dichloromethane at −78 °C, the reaction mixture was stirred at −78 °C for 45 min before the addition of the benzaldehyde, a mixture of (3*Z*)-1,5-*anti*- and (3*Z*)-1,5-*syn*-products **3a** and **11a** was obtained, 1,5-*anti*-**3a**:1,5-*syn*-**11a** = 82:18. If, however, the time allowed for the transmetallation was reduced, the 1,5-stereoselectivity improved, the ratio of the 1,5-*anti*:1,5-*syn* products **3a** and **11a** being 88:12 in favour of the 1,5-*anti*-product **3a** if 30 min was allowed for transmetallation before addition of the aldehyde, and 94:6 if only 15 min was allowed for the transmetallation (see Table 1).[13,14]

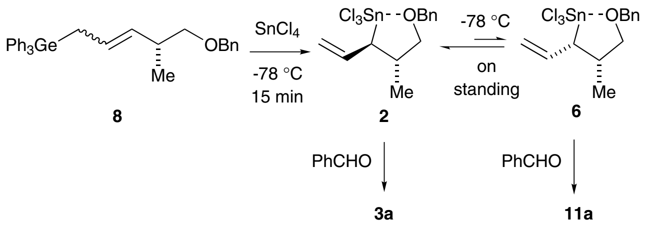


These observations are consistent with initial transmetallation of allylgermane **8** giving allyltin trichloride **2** as the kinetically formed intermediate which can begin to equilibrate with its diastereoisomer **6** at −78 °C this equilibration being more evident after a period of 30–45 min.[8] Allyltin trichloride **2** then reacts with benzaldehyde to give (3*Z*)-1,5-*anti*-product **3a** via a six-membered chair-like transition structure,[1,2] whereas isomeric tin trichloride **6** gives (3*Z*)-*syn*-product **11a**.[1]

Table 1. Effect of transmetallation time on the ratio of **3a**:**11a**

Transmetallation time (min)	Isolated yield[a] (%)	Ratio **3a**:**11a**
45	80	82:18
30	83	88:12
15	77	94:6

[a] Benzaldehyde (3 equiv) was used relative to the mixture of allylgermanes (2*E*)- and (2*Z*)-**8**. The yields are based on the allylgermane.



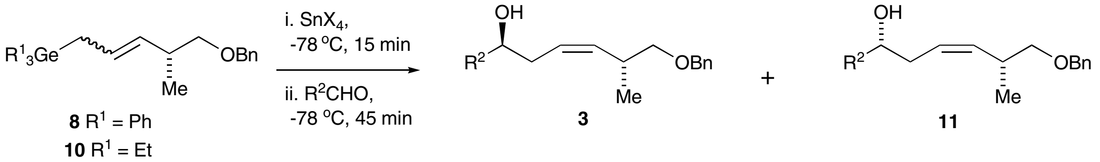
The tin(IV) halide promoted reactions of pent-2-enyl(triphenyl)germanes **8** with a range of aldehydes allowing 15 min for transmetallation were then investigated and the results obtained are shown in Table 2.[15]

Benzaldehyde reacted with (2*Z*)-pent-2-enylgermanes (2*Z*)-**8** and (2*Z*)-**10** to give (3*Z*)-1,5-*anti*-product **3a** more stereoselectively than with the (2*E*)-isomers (2*E*)-**8** and (2*E*)-**10** (Table 2, entries 2–5). This may be due to a more stereoselective transmetallation of the (2*Z*)-pent-2-enylgermanes.[16] However, in practice, the useful levels of stereoselectivity in favour of (3*Z*)-1,5-*anti*-products **3** were obtained using the (*E*,*Z*)-mixture of the pent-2-enyl(triphenyl)germanes **8** with a range of aldehydes (Table 2, entries 6–13), albeit slightly better stereoselectivities were observed using (2*Z*)-pent-2-enyl(triethyl)germane (2*Z*)-**10** (Table 2, entries 14–17).[17]

Transmetallations using tin(IV) bromide were also briefly investigated. The (2*E*)- and (2*Z*)-(triphenyl)germanes were recovered unchanged from reactions with benzaldehyde carried out under usual conditions (15 min for transmetallation and 45 min reaction time at −78 °C). However, (2*Z*)-(triethyl)pent-2-enylgermane (2*Z*)-**10** reacted with an excellent stereocontrol under these conditions to give 1,5-(3*Z*)-*anti*-1-phenylhex-3-en-1-ol **3a**.

Finally, 4-benzyloxypent-2-enyl(triethyl)germane **13** was prepared by treatment of the corresponding acetate **12**[18] with the cuprate prepared from lithiated triethylgermane and copper(I) iodide. With this germane, the tin(IV) chloride promoted reaction with benzaldehyde was stereoselective, but gave only a modest yield, 53%, of (3*Z*)-1,5-*syn*-hex-3-enol **14**[19] and lower yields were obtained

Table 2. 1,5-Stereocontrol using pent-2-enylgermanes **8** and **10**



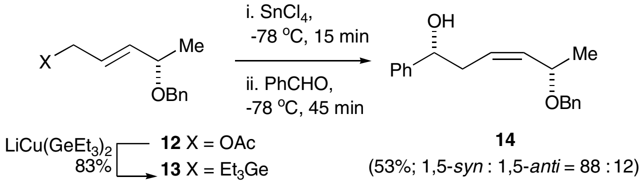
Entry	Pent-2-enyl-germane	SnX_4	Aldehyde R^2	Isolated yield[a] (%)	Products[b]	Ratio 1,5-*anti*:1,5-*syn*
1	(2*E*,*Z*)-**8**	X = Cl	Ph	58 (77)	**3a**, **11a**	94:6
2	(2*E*)-**8**	X = Cl	Ph	(86)[c]	**3a**, **11a**	72:28
3	(2*E*)-**10**	X = Cl	Ph	(63)	**3a**, **11a**	87:13
4	(2*Z*)-**8**	X = Cl	Ph	(73)	**3a**, **11a**	97:3
5	(2*Z*)-**10**	X = Cl	Ph	(98)	**3a**, **11a**	95:5
6	(2*E*,*Z*)-**8**	X = Cl	4-$O_2NC_6H_4$	88	**3b**, **11b**	94:6
7	(2*E*,*Z*)-**8**	X = Cl	4-ClC_6H_4	56	**3c**, **11c**	98:2
8	(2*E*,*Z*)-**8**	X = Cl	3-ClC_6H_4	(34)	**3d**, **11d**	98:2
9	(2*E*,*Z*)-**8**	X = Cl	4-$MeOC_6H_4$	42	**3e**, **11e**	93:7
10	(2*E*,*Z*)-**8**	X = Cl	$(CH_3)_2CH$	66 (78)	**3f**, **11f**	98:2
11	(2*E*,*Z*)-**8**	X = Cl	$CH_3(CH_2)_2$	(67)	**3g**, **11g**	94:6
12	(2*E*,*Z*)-**8**	X = Cl	(*E*)-$CH_3CH{=}CH$	(86)	**3h**, **11h**	93:7
13	(2*E*,*Z*)-**8**	X = Cl	$BnOCH_2$	69	**3i**, **11i**	96:4
14	(2*Z*)-**10**	X = Cl	4-$O_2NC_6H_4$	(85)	**3b**, **11b**	97:3
15	(2*Z*)-**10**	X = Cl	4-ClC_6H_4	(84)	**3c**, **11c**	98:2
16	(2*Z*)-**10**	X = Cl	4-$MeOC_6H_4$	81	**3e**, **11e**	96:4
17	(2*Z*)-**10**	X = Cl	$(CH_3)_2CH$	(57)	**3f**, **11f**	99:1
18	(2*Z*)-**10**	X = Cl	$CH_3(CH_2)_2$	(74)	**3g**, **11g**	96:4
19	(2*E*)-**8**	X = Br	Ph	NR	—	—
20	(2*Z*)-**8**	X = Br	Ph	NR	—	—
21	(2*Z*)-**10**	X = Br	Ph	(67)	**3a**, **11a**	99:1

[a] For the reactions in parentheses, 3 equiv of aldehyde were used relative to the germane. For all other reactions, the mole ratio of germane to aldehyde was 1:1.

[b] The structures of the products were assigned by comparison with earlier work (see Ref. 15).

[c] The transmetallation time in this case was 7 min (see Ref. 14).

for aliphatic aldehydes. Although these reactions were not optimised, it may be that in these cases, Lewis acid promoted 1,4-elimination reactions of the allylgermanes were competing with the required transmetallation.



(53%; 1,5-*syn* : 1,5-*anti* = 88 : 12)

To summarise, (2*E*)- and (2*Z*)-5-benzyloxy-4-methylpent-2-enylgermanes **8** and **10** can be transmetallated at −78 °C by tin(IV) chloride in less than 15 min with useful stereoselectivity to generate the reactive allyltin trichloride **2**, which reacts with aldehydes to give (3*Z*)-1,5-*anti*-hex-3-enols **3** with efficient 1,5-stereocontrol.[20] Overall, the reactions of (2*Z*)-pent-2-enylgermanes were slightly more stereoselective. Analogous reactions of 4-benzyloxypent-2-enylgermane **13** gave lower yields. This work confirms the influence of the transmetallation time on the overall stereoselectivity of these reactions and suggest a secondary influence of the geometry of the double bond of the allylmetal reagent. Finally, although the inorganic tin reagent, tin(IV) chloride, is used in these transmetallations, the use of allylgermanes provides an alternative to the use of *organo*-stannanes for a remote stereocontrol, in particular for the synthesis of (3*Z*)-1,5-*anti*-hex-3-enols **3**. Further work in this area is in progress.

Acknowledgement

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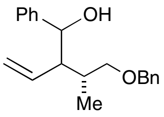
References and notes

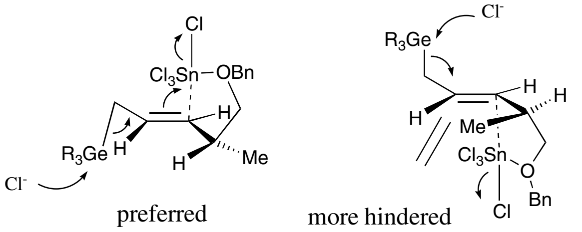
1. Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1997**, 411.
2. Carey, J. S.; Thomas, E. J. *Synlett* **1992**, 585.
3. Donnelly, S.; Thomas, E. J.; Arnott, E. A. *J. Chem. Soc., Chem. Commun.* **2003**, 1460.
4. Dorling, E. K.; Thomas, E. J. *Tetrahedron Lett.* **1999**, *40*, 471.
5. Martin, N.; Thomas, E. J. *Tetrahedron Lett.* **2001**, *42*, 8373.
6. Germay, O.; Kumar, N.; Thomas, E. J. *Tetrahedron Lett.* **2001**, *42*, 4969.
7. Brain, C. T.; Thomas, E. J. *Tetrahedron Lett.* **1997**, *38*, 2387.
8. Beddoes, R.; Hobson, L. A.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1997**, 1929.
9. Akiyama, T.; Suzuki, M. *Chem. Commun.* **1997**, 2357.

10. Spivey, A. C.; Diaper, D. H. In *Science of Synthesis: Houben Weyl Methods of Molecular Transformations*; Molony, M. G., Ed.; Thieme: Stuttgart, 2002; Vol. 5, p 181; Hagen, G.; Mayr, H. *J. Am. Chem. Soc.* **1991**, *113*, 4954.
11. The (2*E*)- and (2*Z*)-acetates **9** were prepared from the corresponding alcohols (see Ref. 2). Details will be included in a full paper.
12. Yamaguchi, J.; Tamada, Y.; Takeda, T. *Bull. Chem. Soc., Jpn.* **1993**, *66*, 607.
13. Products **3a** and **11a** were identified as a mixture by comparison with authentic samples prepared using pent-2-enylstannane **1** (see Refs. 1 and 2). The **3a**:**11a** ratio was estimated from ^{1}H NMR by the integration of benzylic and methyl protons.
14. If the aldehyde was added to the reaction mixture before transmetallation was complete, complex mixtures of products were obtained which appeared to include branched product **i**, as a mixture of stereoisomers, possibly formed by the reaction of allylgermane with the Lewis acid co-ordinated aldehyde. Transmetallation times of less than 15 min were possible with increased concentrations of reactants (cf. Table 2, entry 2), but allowing 15 min for this process proved reliable, convenient and maintained useful levels of stereoselectivity.



i

15. The ratios of the products from the aromatic aldehydes were estimated from their ^{1}H NMR spectra by integration of the benzylic and methyl protons, which were distinct for 1,5-*anti*- and -*syn*-diastereoisomers. These ratios were also confirmed for products **3b/11b** and **3c/11c**, by comparison of their 4-nitrobenzoates prepared by a direct esterification, and by esterification with inversion of configuration using a Mitsunobu reaction. Comparison of 4-nitrobenzoates also provided the product ratios for products **3f/11f**, **3g/11g** and **3i/11i**.
16. These transmetallations are believed to take place via antarafacial SE′ processes with the trichlorotin group delivered by the oxygen of the benzyloxy substituent, the diastereofacial selectivity being controlled by the preference of the 4-methyl substituent to adopt the less hindered 'outside' rather than the more hindered 'inside' position (see Ref. 1). These steric interactions may be larger for (2*Z*)-pent-2-enyl isomers so leading to the slightly better overall stereoselectivity observed for (2*Z*)-pent-2-enylgermanes.
17. The overall stereoselectivities observed using the 55:45 mixture of the (2*E*)- and (2*Z*)-pentenyl(triphenyl)germanes appeared to be slightly higher than would have been predicted from the results using the separate (2*E*)- and (2*Z*)-isomers (cf. Table 2, entries 1–5). The reason for this has not been elucidated.



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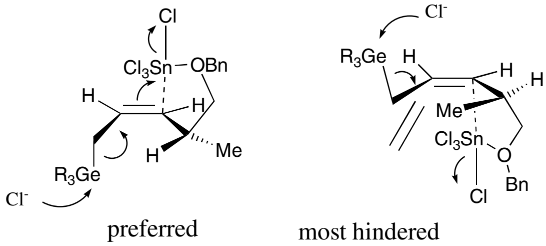
Transition structures for the antarafacial transmetallation of (2*E*)-**8** and **-10.**



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Transition structures for the antarafacial transmetallation of (2*Z*)-**8** and **-10.**

18. Acetate **12** was prepared from the corresponding alcohol (see Ref. 19).
19. MacNeill, A. H.; Thomas, E. J. *Synthesis* **1994**, 322.
20. *Representative experimental*: A cooled solution of tin(IV) chloride (1 M in CH_2Cl_2; 0.22 cm^3) was added to a solution of (2*E*,2*Z*)-pent-2-enyl(triphenyl)germane **8** (100 mg, 0.203 mmol) in CH_2Cl_2 (0.8 cm^3) at −78 °C, and the solution stirred at −78 °C for 15 min. (*E*)-Crotonaldehyde (0.06 cm^3; 0.61 mmol) was added and the solution stirred at −78 °C for 45 min. Saturated methanolic ammonium chloride (7 cm^3) and water (30 cm^3) were added and the mixture extracted with diethyl ether. Flash chromatography using light petroleum and diethyl ether as the eluent (5:1) gave (4*RS*,8*SR*,2*E*,6*Z*)-9-benzyloxy-8-methylnona-2,6-dien-4-ol **3h** together with its (4*RS*,8*RS*)-diastereoisomer **11h** (46 mg, 86%, **3h**:**11h** = 93:7) (Found: $M^+ + NH_4$, 278.2116. $C_{17}H_{28}O_2N$ requires *M*, 278.2115.) υ_{max}/cm^{-1} 3426, 1453, 1434, 1094, 966 and 737; δ_H ($CDCl_3$, 300 MHz) **3h**: 0.97 (3H, d, *J* 6.5 Hz, 8-CH_3), 1.75 (3H, m, 1-H_3), 2.27 (1H, dt, *J* 14, 5.5 Hz, 5-H), 2.42 (1H, dt, *J* 14, 9 Hz, 5-H′), 2.92 (2H, m, OH and 8-H), 3.23 (1H, t, *J* 9, 9-H), 3.37 (1H, dd, *J* 9, 5.5 Hz, 9-H′), 4.09 (1H, m, 4-H), 4.57 (2H, s, $PhCH_2O$), 5.38 (1H, t, *J* 11, 7-H), 5.54 (2H, m, 3-H and 6-H), 5.74 (1H, dq, *J* 15, 6.5 Hz, 2-H) and 7.38 (5H, m, ArH); δ_C ($CDCl_3$, 75 MHz) 17.6, 18.0, 32.6, 36.5, 72.1, 73.3, 75.0, 126.2, 126.5, 127.9, 128.1, 128.3, 134.2, 136.6 and 138.4; *m*/*z* (CI) 278 (M^++18, 7%) and 243 (M^+−17, 90%).