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Palladium-Catalyzed Asymmetric Synthesis of Axially Chiral (Allenylmethyl)silanes and Chirality Transfer to Stereogenic Carbon Centers in S_E' Reactions

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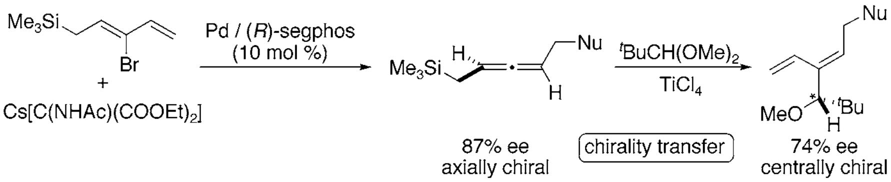
ABSTRACT



Novel stereoselective reactions of 4-substituted-1-trimethylsilyl-2,3-butadienes ((allenylmethyl)silanes) were developed. The axially chiral (allenylmethyl)silanes were prepared from (3-bromopenta-2,4-dienyl)trimethylsilane by a Pd-catalyzed asymmetric reaction with soft nucleophiles with up to 88% enantioselectivity. The (allenylmethyl)silanes reacted with acetals in the presence of a $TiCl_4$ promoter to give 1,3-diene derivatives via an S_E' pathway. The 1,3-dienyl products have (*E*)-geometry exclusively and up to 88% chirality transfer from the axially chiral allenes to the centrally chiral 1,3-dienes was observed in the S_E' reaction.

Allylsilanes and allenylsilanes are useful synthetic intermediates reacting with electrophiles in an S_E' fashion to give the corresponding allylated and propargylated products, respectively (eq 1 and 2),[1] and chirality transfer to stereogenic carbon centers has been studied by use of enantiomerically enriched allyl-[1a,c−e,2] and allenylsilanes.[1b−e,3] On the other hand, the chirality transfer from their homologous (allenylmethyl)silanes in the S_E' reactions (eq 3) has not been reported except for one recent report by Hiemstra and coworkers.[4] Probably, the lack of efficient routes to enantiomerically enriched axially chiral (allenylmethyl)silanes[4,5] has restricted their use as chiral reagents, while the S_E' reaction of (allenylmethyl)silanes has been conveniently used for the

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(1) (a) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200. (b) Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p 81. (c) Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I. Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p 563. (d) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (e) Fleming, I.; Barbero, A. Walter, D. *Chem. Rev.* **1997**, *97*, 2063.

(2) (a) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (b) Hayashi, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4963. (c) Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281.

(3) For recent examples, see: (a) Suginome, M.; Matsumoto, A.; Ito, Y. *J. Org. Chem.* **1996**, *61*, 4884. (b) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1997**, *62*, 8976. (c) Marshall, J. A.; Maxson, K. *J. Org. Chem.* **2000**, *65*, 630. (d) Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915.

(4) Mentink, G.; van Maarseveen, J. H.; Hiemstra, H. *Org. Lett.* **2002**, *4*, 3497.

(5) There is a report on partial optical resolution of an axially chiral (allenylmethyl)silane by chiral HPLC; see: Colvin, E. W.; König, W. A.; Loreto, M. A.; Rowden, J. Y. Tommasini, I. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2405.

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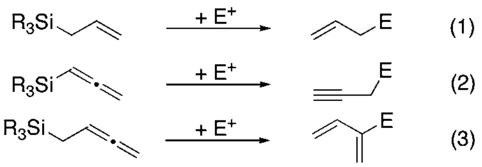
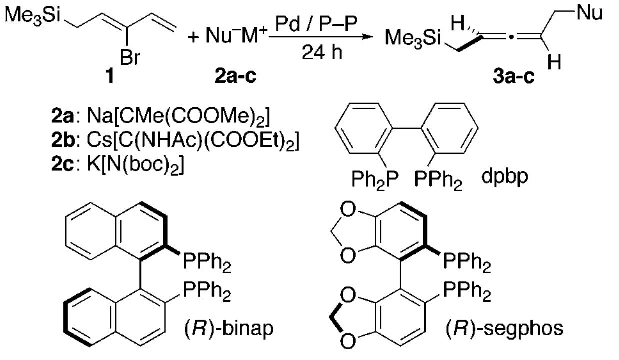
introduction of 1,3-dien-2-yl groups onto electrophiles.[6−8] Here we wish to report the first example of catalytic asymmetric synthesis of axially chiral (allenylmethyl)silane derivatives. We also demonstrate the chirality transfer with high selectivity from the (allenylmethyl)silanes onto stereogenic carbon centers in the S_E' reaction.[4]



Easily accessible (3-bromopenta-2,4-dienyl)trimethylsilane (**1**), which was reported by Parrain and Santelli,[9] is an excellent precursor to (allenylmethyl)silane derivatives (Table 1). A series of 4-substituted-1-trimethylsilyl-2,3-butadienes **3a**−**c** were prepared from **1** and soft nucleophiles **2a**−**c** in THF in the presence of 2 mol % of Pd catalyst generated in situ from $[PdCl(\pi\text{-allyl})]_2$ and dpbp.[10a] With **2a** and **2b**, the reaction proceeded cleanly and the (allenylmethyl)silanes **3a** and **3b** were isolated in excellent yield (entries 1 and 2). With more basic nucleophile **2c**, dehydrobromination from **1** giving an enyne $Me_3SiCH_2C{\equiv}C{-}CH{=}CH_2$ was competing with the allene formation, and thus isolated yield of **3c** was moderate (64%, entry 3). Under reaction conditions similar to those in our previous report on asymmetric synthesis of axially chiral allenes,[10b] i.e., with a palladium catalyst (10 mol %) generated from $Pd(dba)_2$ and (*R*)-binap at 20 °C, (*R*)-**3a** and (*R*)-**3b** were obtained in lower yield with unsatisfactory enantioselectivity (entries 4 and 7). It was found that a Pd/(*R*)-segphos[11] system was much better in terms of enantioselectivity, although its catalytic activity was not high enough (entries 5 and 8). At higher temperature with (*R*)-segphos, yield of the chiral allenes (*R*)-**3a** and (*R*)-**3b** was dramatically improved at very little sacrifice of the enantioselectivity (entries 6 and 9).

Table 1. Palladium-Catalyzed Synthesis of (Allenylmethyl)silanes **3**[a]



2a: $Na[CMe(COOMe)_2]$
2b: $Cs[C(NHAc)(COOEt)_2]$
2c: $K[N(boc)_2]$

entry	Nu-H⁺ 2	P−P	solvent	*T* (°C)	yield[b] (%)	% ee[c] (config)[d]	$[\alpha]^{20}_D$ (*c* $CHCl_3$)
1	**2a**	dpbp	THF	23	91 (**3a**)		
2	**2b**	dpbp	THF	50	90 (**3b**)		
3	**2c**	dpbp	THF	50	64 (**3c**)		
4	**2a**	(*R*)-binap	THF	20	32 (**3a**)	41 (*R*)	
5	**2a**	(*R*)-segphos	THF	20	10 (**3a**)	83 (*R*)	
6	**2a**	(*R*)-segphos	THF	40	57 (**3a**)	79 (*R*)	−60 (0.99)
7	**2b**	(*R*)-binap	CH_2Cl_2	20	8 (**3b**)	62 (*R*)	
8	**2b**	(*R*)-segphos	CH_2Cl_2	20	12 (**3b**)	88 (*R*)	
9	**2b**	(*R*)-segphos	THF	50	63 (**3b**)	87 (*R*)	−60 (1.01)

[a] The reaction was carried out with **1** (0.50 mmol) and **2** (0.55 mmol) in a given solvent (5.0 mL) for 24 h. For entries 1−3, the palladium catalyst (2 mol %) was generated from $[PdCl(\pi\text{-allyl})]_2$ and dpbp; for entries 4−9, the chiral catalyst (10 mol %) was generated from $Pd(dba)_2$ and a given chiral phosphine. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (**3a**, Chiralpak AD; **3b**, Chiralcel OG). [d] The absolute configurations were deduced by the Lowe-Brewster rule (ref 12).

The obtained axially chiral (allenylmethyl)silanes (*R*)-**3a** and (*R*)-**3b** were applied to the Lewis acid promoted S_E' reaction, and the results are summarized in Table 2. The (allenylmethyl)silane **3** was treated with dimethylacetal or aldehyde **4** in the presence of $TiCl_4$ in CH_2Cl_2 at −78 °C, and the conjugated diene **5** was isolated in high yield. All of the dienes **5** have (*E*)-configuration exclusively, and no (*Z*)-isomers were detected in the reaction mixtures (NMR analysis).[13] The (*E*)-geometry in **5** indicates that the electrophile approaches the central carbon of the allene from the

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(6) (a) Montury, M.; Psaume, B.; Goré, J. *Tetrahedron Lett.* **1980**, *21*, 163. (b) Psaume, B.; Montury, M.; Goré, J. *Synth. Commun.* **1982**, *12*, 409. (c) Imai, T.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4849. (d) Hatakeyama, S.; Sugawara, K.; Kawamura, M.; Takano, S. *Tetrahedron Lett.* **1991**, *32*, 4509. (e) Hatakeyama, S.; Sugawara, K.; Takano, S. *Tetrahedron Lett.* **1991**, *32*, 4513. (f) Hatakeyama, S.; Sugawara, K.; Takano, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1533. (g) Hatakeyama, S.; Kawamura, M.; Takano, S. *J. Am. Chem. Soc.* **1994**, *116*, 4081. (h) Hatakeyama, S.; Yoshida, M.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Kawamoto, T.; Yamada, H.; Nishizawa, M. *Tetrahedron Lett.* **1997**, *38*, 7887. (i) Yu, C.-M.; Yoon, S.-K. Lee, S.-J.; Lee, J.-Y.; Kim, S. S. *Chem. Commun.* **1998**, 2749. (j) Luo, M.; Matsui, A.; Esumi, T.; Iwabuchi, Y.; Hatakeyama, S. *Tetrahedron Lett.* **2000**, *41*, 4401. (k) Parsons, P. J.; Gold, H.; Semple, G.; Montagnon, T. *Synlett* **2000**, 1184.

(7) For preparation of (allenylmethyl)silanes, see: (a) Pornet, J.; Kolani, N. *Tetrahedron Lett.* **1981**, *22*, 3609. (b) Nativi, C.; Ricci, A.; Taddei, M. *Tetrahedron Lett.* **1987**, *28*, 2751. (c) Harada, T.; Osada, A.; Oku, A. *Tetrahedron Lett.* **1995**, *36*, 723. (d) Creary, X.; Jiang, Z.; Butchko, M.; McLean, K. *Tetrahedron Lett.* **1996**, *37*, 579. (e) Harada, T.; Katsuhira, T.; Osada, A.; Iwazaki, K.; Maejima, K.; Oku, A. *J. Am. Chem. Soc.* **1996**, *118*, 8, 11377. (f) Lahrech, M.; Hacini, S.; Parrain, J.-L.; Santelli, M. *Tetrahedron Lett.* **1997**, *38*, 3395. (g) Maruyama, Y.; Yoshiuchi, K.; Ozawa, F. *J. Organomet. Chem.* **1999**, *64*, 8582. (h) Prabharasuth, R.; Van Vranken, D. L. *J. Org. Chem.* **2001**, *66*, 5256. See also ref 6a.

(8) For application of (allenylmethyl)silanes to other organic transformations, see, (a) Trost, B. M.; Urabe, H. *J. Am. Chem. Soc.* **1990**, *112*, 4982. (b) Colvin, E. W.; Monteith, M. *J. Chem. Soc., Chem. Commun.* **1990**, 1230. (c) Hatakeyama, S.; Sugawara, K.; Takano, S. *J. Chem. Soc., Chem. Commun.* **1993**, 125. (d) Hojo, M.; Tomita, K.; Hirohara, Y.; Hosomi, A. *Tetrahedron Lett.* **1993**, *34*, 8123. (e) Hojo, M.; Murakami, C.; Aihara, H.; Tomita, K.; Miura, K.; Hosomi, A. *J. Organomet. Chem.* **1995**, *499*, 155. (f) Nishiyama, T.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1998**, *39*, 43. (g) Hojo, M.; Murakami, C.; Nakamura, S.; Hosomi, A. *Chem. Lett.* **1998**, 331.

(9) Roux, M.; Santelli, M.; Parrain, J.-L. *Org. Lett.* **2000**, *2*, 1701.

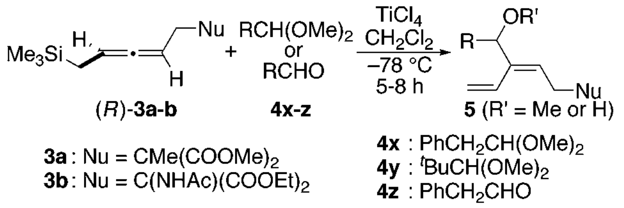
(10) (a) Ogasawara, M.; Ikeda, H.; Hayashi, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1042. (b) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 2089.

(11) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264.

(12) (a) Lowe, G. *Chem. Commun.* **1965**, 411. (b) Brewster, J. H. *Top. Stereochem.* **1967**, *2*, 1.

(13) The (*E*)-configuration of the internal double bond in **5ax** was assigned on the basis of ^1H NMR NOE experiments. The NOE was detected between MeOC*H*− and $NuCH_2CH{=}C{-}$, while no nOe was observed between $NuCH_2CH{=}C{-}$ and $CH_2{=}CH{-}$. The other conjugated dienes **5** showed similar ^1H NMR behavior as well.

Table 2. Lewis Acid Promoted $S_{E'}$ Reactions of (Allenylmethyl)silanes **3** with Electrophiles **4**[a]

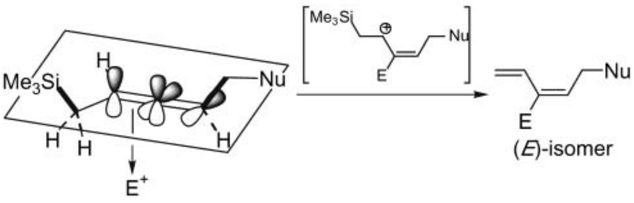


entry	allene **3** (% ee)	**4** (eq)	yield[b] (%)	% ee **5**[c] (config)	$[\alpha]^{20}_D$ (*c* $CHCl_3$)	chirality transfer[d]
1	(*R*)-**3a** (79)	**4x** (1.5)	89 (**5ax**)	21	−10.4 (0.99)	26%
2	(*R*)-**3a** (79)	**4y** (2.0)	87 (**5ay**)	70 (*S*)	−1.0 (1.02)	88%
3	(*R*)-**3a** (79)	**4z** (2.0)	52 (**5az**)	8	−3.8 (0.98)	10%
4	(*R*)-**3b** (87)	**4x** (2.5)	95 (**5bx**)	30	−13.8 (1.03)	35%
5	(*R*)-**3b** (87)	**4y** (1.5)	90 (**5by**)	74 (S)	−1.3 (1.00)	85%

[a] The reaction was carried out with **3** (0.35 mmol) and a given amount of **4**/$TiCl_4$ (1/1 molar ratio) in CH_2Cl_2 (3.0 mL). [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Chiralcel OD-H). [d] (ee of **5**) × 100/(ee of **3**).

side opposite to the sterically demanding $NuCH_2$ substituent (Scheme 1). The same stereochemical outcome has been reported in the protodesilylation of (allenylmethyl)silanes.[6b]

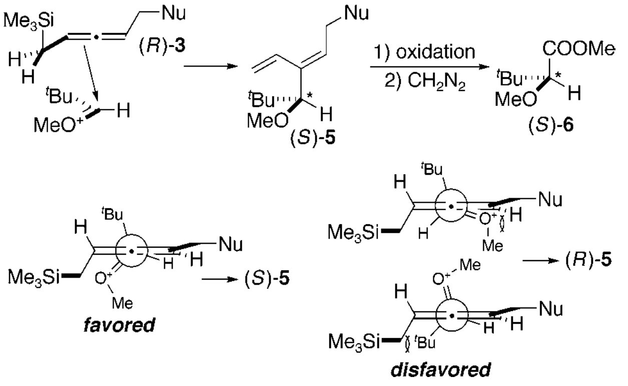
Scheme 1



The reaction of the enantiomerically enriched (allenylmethyl)silane (*R*)-**3a** (79% ee) with an electrophile generated from pivalaldehyde dimethyl acetal **4y** and titanium tetrachloride gave 87% yield of **5ay**, which is an (*S*)-isomer of 70% ee (88% chirality transfer, entry 2). Similarly, (*R*)-**3b** (87% ee) was converted into the S_E' product (*S*)-**5by** of 74% ee in 90% yield (85% chirality transfer, entry 5). The 1,3-dienes **5ay** and **5by** were converted into ^{t}BuCH(OMe)-COOMe (**6**) by successive oxidation and a diazomethane treatment (Scheme 2), and the absolute configuration of both **5ay** and **5by** was determined to be (*S*) by correlation with the authentic sample (*S*)-**6**, which was prepared from (*S*)-^{t}BuCH(OH)COOH.

On the basis of the *anti* stereochemistry observed for the S_E' reactions of allylsilanes where electrophiles approach the carbon−carbon double bond from the side opposite to the trimethylsilyl group,[2,14] we propose the stereochemical pathway for the reaction of (*R*)-**3** with **4y** giving **5y** of (S) configuration as shown in Schemes 1 and 2. When the electrophile ^{t}BuCH═O$^+$Me reacts with (*R*)-**3**, the nucleophilic attack takes place onto the *re* face of the electrophile. The steric interactions between the electrophile and (*R*)-**3** are minimized in the relative orientation of the two reactants, which is illustrated in Scheme 2 (bottom left). At this synclinal-like transition state,[14] the bulkiest substituent in the electrophile (^{t}Bu group) occupies the sterically least congested position, while the smallest one (methine hydrogen) possesses a position adjacent to the ═C*H*CH_2Nu hydrogen in (*R*)-**3**, which sticks out toward the electrophile. Antiperiplanar-like and another synclinal-like transition states (Scheme 2, bottom right), which would lead to (*R*)-**5y**, are unfavorable as a result of steric repulsions between ═C*H*CH_2Nu and the OMe group or ═CHCH_2SiMe_3 and the ^{t}Bu substitutent.

Scheme 2



The bulky ^{t}Bu substituent in **4y** is important for the effective chirality transfer in the S_E' reaction. With sterically more compact acetal **4x** and aldehyde **4z**, the chirality transfer efficiency in **5x** and **5z** was considerably diminished as a result of ineffective descrimination between the two enantiotopic faces in the electrophiles (entries 1, 3, and 4).

In summary, we have shown the first example of preparation of axially chiral (allenylmethyl)silanes by asymmetric catalysis. The enantiomerically enriched (allenylmethyl)-silanes obtained were applied to the Lewis acid promoted S_E' reaction, where unique chirality transfer from allenic axial to stereogenic carbon was observed.

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Supporting Information Available: Detailed experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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[14] Denmark, S. E.; Weber, E. J. *Helv. Chim. Acta* **1983**, *66*, 1655.