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DOI: 10.1002/asia.200900452

Regioselective Silylzincation of Phenylallene Derivatives

Mitsuhiro Yonehara,^[a, b] Shinji Nakamura,^[b] Atsuya Muranaka,^[a] and Masanobu Uchiyama^{*[a, b]}

Dedicated to the 150th anniversary of Japan–UK diplomatic relations

Allyl- and vinylsilanes are important organometallics in synthetic organic chemistry, because of their unique stability, reactivity, and functional group tolerance, which make them synthetically attractive.^[1] Intermolecular silylmetalation of alkynes, dienes, allenes, and alkenes^[1d,2] constitutes an excellent method for construction of the above compounds. However, controlling the regioselectivity in the silylmetalation of unsaturated C-C bonds remains an important challenge. Unsymmetrically substituted allenes are regarded as among the most challenging, because the intermolecular silvlmetalation reaction can generate four isomers (exo/endo-vinyl/allylsilane) (Figure 1). Herein, we describe our new approach for the preparation of regio-controlled exo/endo-vinylsilanes through silylzincation as a key reaction, using newly developed silvlzinc reagents. We also describe the dramatic effects of the number and the nature of the ligands on Zn upon the direction of the silylzincation reaction.



Figure 1. Reaction patterns in silylmetalation of unsymmetrical allenes.

[a]	M. Yonehara, Dr. A. Muranaka, Prof. Dr. M. Uchiyama					
	Advanced Elements Chemistry Laboratory					
	Advanced Science Institute, RIKEN					
	2-1 Hirosawa, Wako-shi, Saitama 351-0198 (Japan)					
	Fax: (+81)48-467-2879					
	E-mail: uchi_yama@riken.jp					
[b]	M. Yonehara, Dr. S. Nakamura, Prof. Dr. M. Uchiyama					
	Graduate School of Pharmaceutical Sciences					

- The University of Tokyo 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033 (Japan)
- Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.200900452.

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The silvlcupration of allenes by using higher/lower-order cuprates has been extensively investigated,^[3] whereas silylzincation remains relatively unexplored.^[4] We have recently reported that a bulky zincate having one dimethylphenylsilyl (DMPS) group (DMPS) $ZntBu(OR)_2(MM')$ (1) ((OR)₂= 2,2'-biphenoxo, M=Li or MgCl, M'=MgCl, abbreviated as SiBNOL-Zn-ate) can promote chemo- and regioselective silylzincation of terminal alkynes to give branched vinylsilanes regioselectively.^[5] However, simple application of this protocol to allenes using 1 proved unsuccessful because of the low regioselectivity. Our initial studies using phenylallene (2a) as a model substrate, aimed at identifying more favorable reaction conditions, revealed that a dimethylphenylsilvl (DMPS) group as the silvl moiety and THF as the solvent were suitable starting points for optimization of the silylzincation reaction conditions. The silylzincation reactions of 2a with the use of DMPS-Li or DMPS-Zn-Cl were unsatisfactory in terms of reactivity (yield) and selectivity; instead, undesired reactions occurred (Table 1, Entry 8 and Supporting Information). However, when a mixture of

Table 1. Screening of zinc reagents for highly regio-selective silylzincation of phenylallene $(2\,a).^{\rm [a]}$

	1.1 eq Si–Zn Reagent THF, 1 h, RT	SiMe ₂ Ph +	SiMe ₂ Ph
2a		3a (<i>exo-</i>)	4a (<i>endo-</i>)
Entry	Si-Zn Reagent	Yield ^[b] [%]	Selectivity 3a/4a
1	(PhMe ₂ Si)ZnMe	83	90:10
2	(PhMe ₂ Si)ZnMe	84 ^[c]	88:12
3	(PhMe ₂ Si)ZntBu	76	89:11
4	(PhMe ₂ Si) ₂ Zn	85 ^[c]	41:59
5	(PhMe ₂ Si) ₃ ZnLi	90	30:70
6	(PhMe ₂ Si) ₃ ZnLi	93 ^[c]	8:92
7	(PhMe ₂ Si) ₄ ZnLi ₂	50	31:69
8	(PhMe ₂ Si)Li	trace	-

[a] Unless otherwise noted, the silylzincation reaction was carried out using silylzinc reagent (1.1 equiv) and phenylallene (**2a**) (1.0 equiv) in THF at room temperature for 1 h. [b] Yield of isolated vinylsilanes. [c] The reaction was carried out for 24 h.



newly designed heteroleptic silylzinc reagent, DMPS-Zn-R (R = Me or tBu), prepared in situ from ZnCl₂, RMgCl and DMPS-Li, and 2a (1.1:1.0 molar ratio) in THF, was stirred at room temperature for 1 h, the silylzincation proceeded smoothly without any catalyst to give predominantly exo-vinylsilane (3a), and formation of allylsilane was undetectable (Entries 1 and 3). Extension of the reaction time to 24 h gave almost the same results (e.g., Entries 1 and 2). Attempts to use homoleptic-type disilylzinc reagents, such as (DMPS)₂Zn, proved unsuccessful in terms of the selectivity (Entry 4). On the hand, trisilylzincate, other (DMPS)₃ZnLi turned out to promote the silvlzincation reaction of 2a in good yield at room temperature for 1 hour, and endo-vinylsilane (4a) was obtained as the major product, in contrast with the case of heteroleptic-type DMPS-Zn-R reagent. The endo selectivity increased with the prolongation of the reaction time when (DMPS)₃ZnLi was used. Several attempts to use dianion-type silylzincates, including

Table 2. Silylation	of	various	phenylallene	derivatives	with	$(PhMe_2Si)ZnMe$	and	(PhMe ₂ Si) ₃ ZnLi. ^[4]
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				1e ₂ Ph	SiMe ₂ Ph	
	т	HF, Time, Temp.	''	+ "	````	
	2		3		4	
Entry	Substrate	Si-Zn Reagent	<i>t</i> [h]	<i>T</i> [°C]	Yield ^[b] [%]	Selectivity 3:4
1	•	(PhMe ₂ Si)ZnMe	1	RT	69	83:17
2	Me 2b	(PhMe ₂ Si) ₃ ZnLi	24	RT	89	1:99
3	•	(PhMe ₂ Si)ZnMe	1	RT	57	94:6
4	tBu 2c	(PhMe ₂ Si) ₃ ZnLi	24	RT	89	12:88
5		(PhMe ₂ Si)ZnMe	24	-78	44	98:2
6	F 2d	(PhMe ₂ Si) ₃ ZnLi	24	RT	72	16:84
7	~~~•~	(PhMe ₂ Si)ZnMe	24	-78	71	94:6
8	CI 2e	(PhMe ₂ Si) ₃ ZnLi	24	RT	90	16:84
9	~~~•~	(PhMe ₂ Si)ZnMe	24	-78	57	97:3
10	Br 2f	(PhMe ₂ Si) ₃ ZnLi	24	RT	<26 ^[c]	12:88
11	•	(PhMe ₂ Si)ZnMe	1	-100	55	64:36
12	EtO ₂ C ² 2g	(PhMe ₂ Si) ₃ ZnLi	24	-78	72	15:85
13	<i>I</i> Pr	(PhMe ₂ Si)ZnMe	1	-78	44	89:11
14	<i>i</i> ₽r ^N II O 2h	(PhMe ₂ Si) ₃ ZnLi	24	-40	75	28:72
15	~~~•×	(PhMe ₂ Si)ZnMe	1	RT	58	90:10
16	MeO 2i	(PhMe ₂ Si) ₃ ZnLi	24	RT	100	1:99
17	•	(PhMe ₂ Si)ZnMe	1	RT	76	95:5
18	2j	(PhMe ₂ Si) ₃ ZnLi	24	RT	92	10:90
19	•	(PhMe ₂ Si)ZnMe	6	-78	46	93:7
20	2k	(PhMe ₂ Si) ₃ ZnLi	24	RT	78	19:81

[a] Unless otherwise noted, the silvlzincation reaction was carried out using silvlzinc reagent (1.1 equiv) and substrate (1.0 equiv) in THF under the given conditions. [b] Yield of isolated vinylsilanes. [c] Several minor products that were difficult to separate were observed, resulting from halogen-metal exchange reaction.

 $(DMPS)_4ZnLi_2$ and **1**, proved unsuccessful at this early stage. The steric bulkiness of the silyl group in the zinc reagent had little effect on the exo/endo selectivity (Supporting Information).

With optimized conditions for the regio-controlled synthesis of exo/endo-vinylsilane in hand, we studied the scope of this new protocol,^[6] and representative results are summarized in Table 2. A variety of functional groups, including alkyl, halogen, carbonyl, and alkoxy on a benzene ring, and various aryl groups could be utilized in the reaction. In this system, by choosing appropriate zinc reagents and reaction conditions for the silylzincation, either exo-vinylsilane or endo-vinylsilane could be obtained with good regioselectivity, using the same phenylallene substrate. To our knowledge, the reaction with the use of heteroleptic-type DMPS-Zn-R reagent is the first example of an efficient exo-selective silylmetalation with wide substrate generality. On the other hand, endo-selective silylmetalations of unsymmetrical allenes under thermodynamic conditions have been reported in some cases with silvlcuprates.^[2c]

The potential to generate functionalized exo/endo-vinylsilanes was next examined.^[5c,7] We verified that the resultant vinylsilane **3a** generated by the silylmetalation of **2a** with DMPS-Zn-R could be transformed into cross-coupling and ketone products (Scheme 1).

Finally, a theoretical/computational study was performed to understand the present silylzincation.^[8] The experimental results strongly indicate that exo-selective silvlmetalation with DMPS-Zn-R is controlled kinetically, whereas endo-selective silvlmetalation is subject to thermodynamic control. DFT/MP2 calculations (MP2/6311SVP//B3LYP/ 631SVPs)^[9,10] were carried out to investigate the reaction pathway of the silylzincation of 2a with DMPS-Zn-R. We



Scheme 1. Transformation of the resultant vinylsilane 3a.

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Figure 2. Reactants, TSs, and complexes in the silylmetalation reaction of $(Me_3Si)ZnMe$ with **2a**. Bond lengths, angles, and energy changes at the MP2/6311SVP//B3LYP/631SVPs level are shown in Å, deg, and kcalmol⁻¹, respectively.

and we could identify \mathbf{CP}_{exo} and \mathbf{CP}_{endo} as the global minima for *exo-* and *endo-*adducts, respectively (Figure 4). While it is difficult to provide hard theoretical evidence in support of an energy difference of only several kcalmol⁻¹ between the CPs, \mathbf{CP}_{endo} is more stable by 2.6 kcal mol⁻¹ than \mathbf{CP}_{exo} , which is in good agreement with the experimental observations.

employed (Me₃Si)ZnMe as a chemical model for DMPS-Zn-R. Although it is important to keep in mind the possibility that the simplification of the silyl moiety of this model may lead to underestimation of the steric interactions, this structure provides a valuable starting point for consideration of the reactivity of DMPS-Zn-R. The reaction pathway of the silylzincation of **2a** using (Me₃Si)ZnMe is shown in Figure 2. In both routes, we could not find any energetically plausible initial complex, and it appears that the silylmetalation takes place directly from the reactants (**SM**) via the distorted "triangular transition state (**TS**)" with relatively low activation energy. The TS for the *exo*-silylzincation is more stable by approximately 3 kcalmol⁻¹ than that for *endo*-one, which is in good agreement with the experimental selectivity.

Orbital analysis lends some support to this regioselectivity. The localized Kohn–Sham (HOMO) orbital of **2a** is localized on the double bond adjacent to the benzene moiety because of their conjugation (Figure 3), and hence the



Figure 3. The Kohn–Sham MO of **2a**.

double bond reacts with the vacant orbital of the zinc of **2a** preferentially over the other outside one. Among several possible TSs for the silylzincation of **2a** using (Me₃Si)ZnMe to afford *exo/endo*-allysilanes, we could identify one of each, which are much less stable than the TSs for vinylsilane formation by more than 10 kcalmol⁻¹ (Supporting Information).

It is experimentally observed that the regioselectivity in the silylzincation of phenylallenes with $(DMPS)_3ZnLi$ is thermodynamically controlled, giving predominantly *endo*vinylsilanes as the reaction time is extended. To examine the regioselectivity in question, we examined each plausible intermediate generated by the silylzincation of **2a** with a silylzincate. $(Me_3Si)_3ZnLi$ was used as a model of $(DMPS)_3ZnLi$. Several local minimum structures of each were optimized



Figure 4. Comparison of thermal stability of the possible vinylsilane intermediates. Bond lengths, angles, and energy changes at the MP2/ 6311SVP/B3LYP/631SVPs level are shown in Å, deg, and kcalmol⁻¹, respectively. (*S*=Me₂O).

In conclusion, regioselective silylzincation of functionalized phenylallenes and versatile generation of vinylsilanes could be achieved by utilizing the drastic ligand effects found in zinc reagents. The present work underlines the utility of adjusting the nature and number of ligands of zinc reagents as a means of tuning functionality in the development of new reactions. Efforts to expand the reaction scope and to elucidate the reaction pathway with the help of theoretical and spectroscopic studies are in progress in our laboratory.

Experimental Section

Typical procedure for the silylzincation reaction of **2a** (Table 1, Entry 1): To a stirred solution of (PhMe₂Si)ZnMe (1.1 mmol) in THF, 1-phenylallene (116 mg, 1.0 mmol) was added with a syringe at -78 °C. The mixture was stirred at room temperature for 1 h, then was quenched with a saturated aqueous solution of NH₄Cl at 0 °C, and was extracted with Et₂O (2×30 mL). The organic solution was washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo. Purification of the residue by silica gel column chromatography (*n*-hexane), furnished a mixture of 2-(dimethylphenylsilyl)-3-phenyl-1-propene (**3a**) and 2-(dimethylphenylsilyl)-3-phenyl-2-propene (**4a**) as a colorless oil (209 mg, 83%). The ratio of products was determined from the ¹H NMR (**3a/4a**=90:10). ¹H NMR (300 MHz, CDCl₃, TMS) (**3a**): δ =7.49–7.44 (2H, m), 7.38–7.29 (3H, m), 7.24–7.12 (3H, m), 7.05 (2H, d, *J*=7.5 Hz), 5.55 (1H, s), 5.49 (1H, s), 3.42 (2H, s), 0.25 ppm (6H, s); ¹H NMR (**4a**): δ =7.58–7.54 (2H, m), 7.43–7.15 (8H, m), 6.80 (1H, s), 1.94 (3H, s), 0.44 ppm (6H, s); HRMS (EI): *m/z* (%) calcd for C₁₇H₂₀Si: 252.1334 [*M*⁺]; found: 252.1324. For preparative procedures and spectroscopic data, see the Supporting Information.

Acknowledgements

We gratefully acknowledge financial support from Hoansha, the Naito foundation, Mochida memorial foundation, and KAKENHI (Young Scientist (A), Houga, and Priority Area No. 459) (to M.U.). This work was also supported by the Junior Research Associate Program in RIKEN (The Institute of Physical and Chemical Research), Japan (to M.Y.). The calculations were partially performed on the RIKEN Super Combined Cluster (RSCC).

Keywords: allenes \cdot metalation \cdot regioselectivity \cdot silanes \cdot zinc

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Received: September 13, 2009 Published online: January 21, 2010