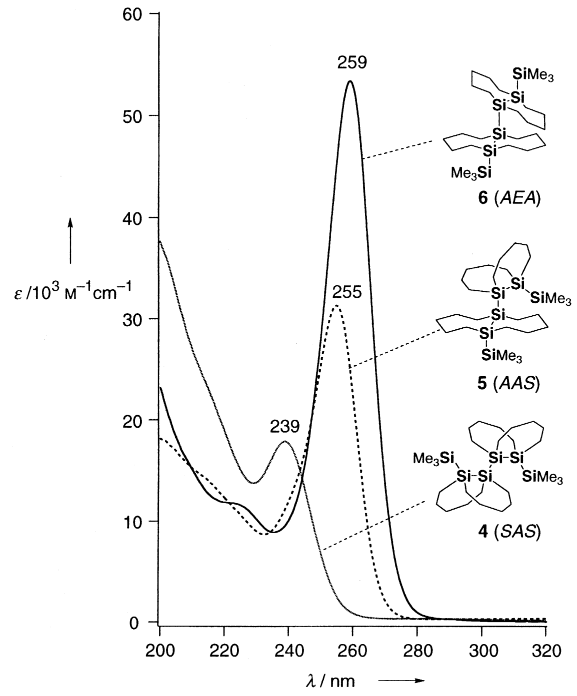


Figure 2. UV absorption spectra of the hexasilane compounds **4**–**6**.

AEA-hexasilane compound **6** indicates that the connection of two constrained *A* conformations with one *E* conformation is the main contribution to the enhancement in the intensity.[12]

Received: March 21, 2000 [Z14878]

---

[1] a) R. D. Miller, J. Michl, *Chem. Rev.* **1989**, *89*, 1359; b) R. West in *The Chemistry of Organic Silicon Compounds* (Eds.: S. Patai, Z. Rappoport), Wiley, Chichester, **1989**, pp. 1207–1240; c) H. S. Plitt, J. W. Downing, M. K. Raymond, V. Balaji, J. Michl, *J. Chem. Soc. Faraday Trans.* **1994**, *90*, 1653.

[2] a) B. Albinsson, H. Teramae, J. W. Downing, J. Michl, *Chem. Eur. J.* **1996**, *2*, 529; b) F. Neumann, H. Teramae, J. W. Downing, J. Michl, *J. Am. Chem. Soc.* **1998**, *120*, 573; c) R. Crespo, H. Teramae, D. Antic, J. Michl, *Chem. Phys.* **1999**, *244*, 203.

[3] Oligo- and/or polysilanes having alkyl and chiral alkyl side chains: a) M. Fujiki, *J. Am. Chem. Soc.* **1994**, *116*, 6017; b) K. Obata, C. Kabuto, M. Kira, *J. Am. Chem. Soc.* **1997**, *119*, 11345; c) R. Tanaka, M. Unno, H. Matsumoto, *Chem. Lett.* **1999**, 595.

[4] Introduction of the hexasilane chain into a unique macrocyclic framework: S. Mazières, M. K. Raymond, G. Raabe, A. Prodi, J. Michl, *J. Am. Chem. Soc.* **1997**, *119*, 6682.

[5] R. Imhof, H. Teramae, J. Michl, *Chem. Phys. Lett.* **1997**, *270*, 500.

[6] The primary *eclipsed* conformer corresponds to *syn* ($\omega = 0°$). The conformer with a dihedral angle of $\approx 120°$ in the Si-Si-Si-Si framework is also eclipsed but has a different eclipsed geometry. Thus we suggest calling this conformation "*second-eclipsed*".

[7] M. Kumada, K. Tamao, T. Takubo, M. Ishikawa, *J. Organomet. Chem.* **1967**, *9*, 43.

[8] Experimental details for the preparation of all the compounds can be found in the Supporting Information.

[9] a) R. J. P. Corriu, C. Guerin, J. J. E. Moreau in *The Chemistry of Organic Silicon Compounds* (Eds.: S. Patai, Z. Rappoport), Wiley, Chichester, **1989**, pp. 305–370; b) R. R. Holmes, *Chem. Rev.* **1990**, *90*, 17.

[10] Stereospecific substitution with retention of configuration (Ret) is also part of the preparation of **1**.

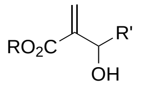
[11] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-141477 (**4**), -141479 (**11**), -141478 (**13**), -141475 (**15**), and -141476 (**19**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[12] The λ_{max} of **6** in the solid state was confirmed to be the same as that in solution, and suggests that the dihedral angle ω_2 around the "non-constrained" Si–Si bond is comparable in both the solution and the solid state.

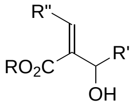
Asymmetric Synthesis of Baylis–Hillman-Type Allyl Alcohols via a Chiral Acetylenic Ester Titanium Alkoxide Complex**

Daisuke Suzuki, Hirokazu Urabe, and Fumie Sato*

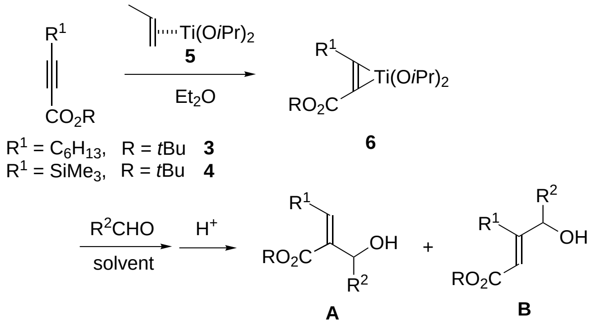
Functionalized allyl alcohols such as **1** and **2** are useful intermediates in organic synthesis.[1, 2] Several recent reports have revealed that the asymmetric Baylis–Hillman reaction afforded alcohols **1** in a highly optically active form.[1, 3] However, asymmetric synthesis of the homologues **2**, which contain a substituent β to the acrylate group, has not been successful by this method.[4] We recently reported the first generation of the acetylenic ester Group 4 transition metal complexes such as **6**[5] from esters **3** or **4** and a low-valent titanium complex, [(η^2-propene)Ti(O*i*Pr)$_2$] (**5**)[6] (Scheme 1).



1



2



Scheme 1. Reaction of acetylene complex **6** with aldehydes.

---

[*] Prof. Dr. F. Sato, D. Suzuki, Dr. H. Urabe
Department of Biomolecular Engineering
Tokyo Institute of Technology
4259 Nagatsuta-cho, Midori-ku, Yokohama
Kanagawa 226-8501 (Japan)
Fax: (+81) 45-924-5826
E-mail: fsato@bio.titech.ac.jp

[**] We thank the Ministry of Education, Science, Sports and Culture (Japan) for financial support.

As the coupling reaction between **6**, generated from chiral acetylenic esters, and aldehydes[7] may serve for the asymmetric and stereoselective preparation of **2** (see **A** in Scheme 1) in one step like the Baylis–Hillman reaction, we pursued this possibility and disclose herein the preliminary results.

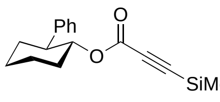
At the outset, we were rather discouraged by the fact that the regioselectivity of the aldehyde addition was not very high under our standard reaction conditions; the addition was carried out in diethyl ether (Table 1; **A**:**B** in the right column).[7a] However, gratifyingly, the selectivity was considerably improved by simply switching the solvent from diethyl ether to a 1:1 mixture of diethyl ether and THF (Table 1; **A**:**B** in the left column); this favored the production of **A** (corresponding to **2**). The regio- and stereochemistry of **A** was established by ^{1}H NMR analysis (NOE study). In general, the silylated substrate **4** showed very high regioselectivity to give adducts **9**–**11**.

Table 1. Regioselectivity on the addition of acetylenic ester titanium complexes to aldehydes (Scheme 1).

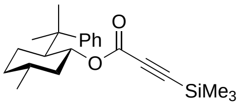
Entry	Ynoate	Aldehyde R^2		Product solvent: Et_2O/THF **A**:**B**[a]	yield [%][b]	Et_2O **A**:**B**[a]
1	**3**	Et	**7**	90:10	84	75:25
2	**3**	cC_6H_{11}	**8**	87:13	64	87:13
3	**4**	Et	**9**	97:3	72	89:11
4	**4**	cC_6H_{11}	**10**	97:3	71	93:7
5	**4**	Ph	**11**	98:2	84	96:4

[a] Determined for crude samples. [b] Yield of isolated products with the virtually same **A**:**B** ratio.

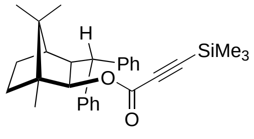
In the next stage, we examined the diastereoselectivity of the reaction starting with optically active silylpropiolates **12**-**14**,[8] which are readily prepared in good yields from the corresponding chiral alcohols.[5] The results of the diastereoselective addition starting from these substrates are summarized in Table 2.



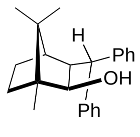
12



13



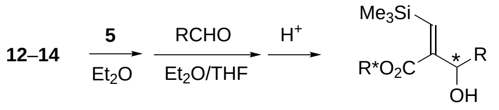
14



15

In all cases, the regioselectivities were excellent as expected from Table 1. The esters **12** and **13** derived from the most commonly used *trans*-2-phenylcyclohexanol and 8-phenylmenthol showed selectivities not necessarily very high (up to 89:11, Table 2; entries 1–4). However, the ester **14** derived from alcohol **15**,[9] which was very conveniently prepared from D-camphor but has not yet been widely utilized as a chiral auxiliary,[10] was found to give marginally the best results (Table 2, entries 5–7). The diastereoselectivity as well as the regioselectivity lies in a range between 97:3 and 99:1 with various aldehydes to give **20**–**22**, which are versatile compounds densely functionalized with ester, allyl alcohol, and vinylsilane moieties.

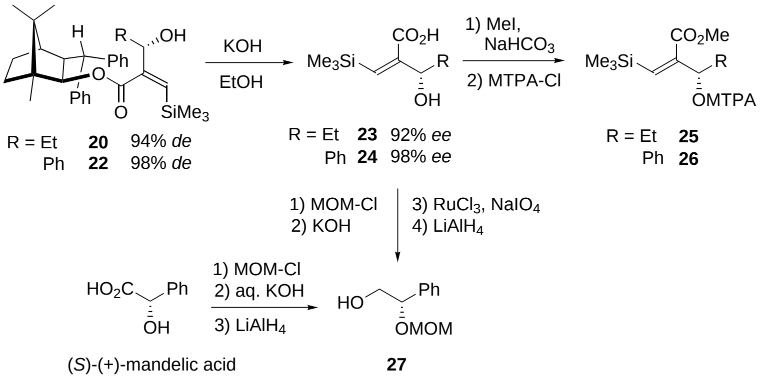
Table 2. Asymmetric addition to aldehydes.



Entry	Ynoate	Aldehyde R		Product selectivity[a] regio-	diastereo-[b]	config.[c]	Yield [%][d]
1	**12**	Et	**16**	95:5	64:36		80
2	**12**	cC_6H_{11}	**17**	97:3	72:28		63
3	**12**	Ph	**18**	97:3	89:11		85
4	**13**	Ph	**19**	98:2	80:20		[e]
5	**14**	Et	**20**	97:3	97:3	*S*	95
6	**14**	cC_6H_{11}	**21**	98:2	98:2		77
7	**14**	Ph	**22**	99:1	99:1	*S*	97

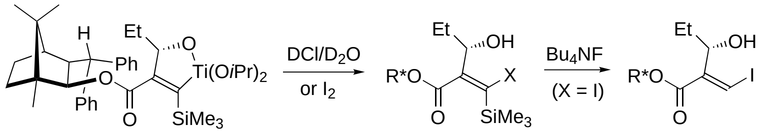
[a] For crude samples. [b] Diastereoselectivity of the major regioisomer. [c] Configuration with respect to the alcohol carbon of the major isomer. [d] Yield of product isolated with essentially the same isomeric composition shown for crude samples. [e] Not determined.

The cleavage of the ester bond of **20** and **22** with KOH in boiling ethanol afforded optically active, pure hydroxycarboxylic acids **23** and **24**, respectively (Scheme 2).[11] The carboxylic acids were transformed to the methyl esters and, then, to methoxy(trifluoromethyl)phenylacetic acid (MTPA) esters **25** and **26**, the analysis of which by ^{1}H NMR spectroscopy disclosed **23** and **24** to be of 92 and 98 % *ee*, respectively, in good agreement with the diastereoselectivities shown in Table 2. The absolute structure of **22** was unambiguously determined by the derivatization to alcohol **27** prepared from (*S*)-mandelic acid (Scheme 2). Alternatively, the absolute configurations of **25** and **26** were assigned by using the empirical Mosher method (^{1}H NMR spectroscopy),[12] which determined the allyl alcohol carbon of **20** and **22** to be *S*.



Scheme 2. Derivatization and structural determination of the products.

In the above transformations, the reaction intermediates were simply hydrolyzed. However, the remaining carbon–metal bond could be used for further synthesis. In fact, deuterolysis or iodinolysis of the intermediate oxatitanacycle **28** afforded the corresponding deuterated product [D$_1$]**20** or vinylic iodide **29** (Scheme 3), the latter of which may be useful for further transformation as such or after fluoride-mediated desilylation.[13]



28

X = D [D$_1$]**20** 94% deuterated 77%
I **29** 93% from **14**

Scheme 3. Preparation of functionalized Baylis–Hillman-type products.

In conclusion, a new chiral dimetallic species, the acetylenic ester titanium alkoxide complex with a camphor-derived auxiliary, enabled the preparation of highly optically active, stereodefined hydroxyacrylates. The scope and limitations of this reaction will be reported in due course.

Experimental Section

Typical procedure for the asymmetric addition to aldehydes (entry 7, Table 2): *i*PrMgCl (1.45 M in Et$_2$O, 0.323 mL, 0.468 mmol) at −78 °C under argon was added to a stirred solution of acetylenic ester **14** (52 mg, 0.117 mmol) and [Ti(O*i*Pr)$_4$] (0.069 mL, 0.234 mmol) in Et$_2$O (3 mL) to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period it turned red. After the mixture had been stirred at −50 °C for an additional 5 h, THF (3 mL) was introduced to the reaction mixture at −50 °C, followed 10 minutes later by benzaldehyde (1.0 M in Et$_2$O, 0.94 mL, 0.94 mmol). After the solution had been stirred at −50 °C for 3 h, the reaction was terminated by the addition of 1 N HCl, and the organic products were extracted with diethyl ether. The combined organic layers were washed with an aqueous solution of NaHCO$_3$, dried over Na$_2$SO$_4$, and concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane/diethyl ether) to give (1*R*,2*R*,3*S*,3′*S*)-(*Z*)-3-(diphenylmethyl)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl 3′-hydroxy-3′-phenyl-2′-[(trimethylsilyl)methylene]propanoate (**22**) (50.5 mg, 97 %) as a colorless oil, which was fully characterized by IR, ^{1}H, and ^{13}C NMR spectroscopy, and elemental analysis. The following NOE study of **22** by ^{1}H NMR spectroscopy confirmed the assigned regio- and stereochemistry. Irradiation of the proton at $\delta = 0.02$ (Me$_3$Si) and that at $\delta = 5.47$ (C*H*OH) showed 11 % and 6 % NOE enhancements to the peak at $\delta = 6.09$ (Me$_3$Si–C*H*=C), respectively. Optical rotations of products (for the isomeric purities or *ee* values, see Table 2 and Scheme 2): **20**: $[\alpha]_D^{25} = -132.70$ ($c = 1.00$ in CHCl$_3$); **21**: $[\alpha]_D^{25} = -108.60$ ($c = 1.00$ in CHCl$_3$); **22**: $[\alpha]_D^{25} = -103.6$ ($c = 1.00$ in CHCl$_3$); **23**: $[\alpha]_D^{25} = -18.00$ ($c = 1.20$ in CHCl$_3$); **24**: $[\alpha]_D^{25} = +6.67$ ($c = 0.60$ in CHCl$_3$).

Received: April 10, 2000 [Z 14967]

---

[1] D. Basavaiah, P. D. Rao, R. S. Hyma, *Tetrahedron* **1996**, *52*, 8001–8062; E. Ciganek in *Organic Reactions*, *Vol. 51* (Ed.: L. A. Paquette), Wiley, New York, **1997**, pp. 201–350.

[2] J. M. Brown, P. L. Evans, A. P. James in *Organic Synthesis*, *Vol. 68* (Ed.: J. D. White), Wiley, New York, **1990**, pp. 64–75.

[3] L. J. Brzezinski, S. Rafel, J. W. Leahy, *J. Am. Chem. Soc.* **1997**, *119*, 4317–4318; Y. Iwabuchi, M. Nakatani, N. Yokoyama, S. Hatakeyama, *J. Am. Chem. Soc.* **1999**, *121*, 10219–10220; T. Iwama, S. Tsujiyama, H. Kinoshita, K. Kanematsu, Y. Tsurukami, T. Iwamura, S. Watanabe, T. Kataoka, *Chem. Pharm. Bull.* **1999**, *47*, 956–961.

[4] Baylis–Hillman reaction under high pressure could be applied to the preparation of **2**, but so far only for its racemic synthesis lacking control of the olefinic geometry (see ref. [1]). For stepwise synthesis of optically active **2** (achieving 50 % *ee*) relevant to Baylis–Hillman reaction, see: M. Brand, S. E. Drewes, N. D. Emslie, A. A. Khan, *Synth. Commun.* **1991**, *21*, 727–732.

[5] T. Hamada, D. Suzuki, H. Urabe, F. Sato, *J. Am. Chem. Soc.* **1999**, *121*, 7342–7344.

[6] F. Sato, H. Urabe, S. Okamoto, *Pure Appl. Chem.* **1999**, *71*, 1511–1519.

[7] For the aldehyde addition of nonfunctionalized, achiral acetylene Group 4 transition metal complexes, see: a) K. Harada, H. Urabe, F. Sato, *Tetrahedron Lett.* **1995**, *36*, 3203–3206; b) S. L. Buchwald, R. B. Nielsen, *Chem. Rev.* **1988**, *88*, 1047–1058; c) E. Negishi, T. Takahashi, *Acc. Chem. Res.* **1994**, *27*, 124–130; d) A. Ohff, S. Pulst, C. Lefeber, N. Peulecke, P. Arndt, V. V. Burkalov, U. Rosenthal, *Synlett* **1996**, 111–118; e) E. Negishi, T. Takahashi, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 755–769. For the aldehyde addition of achiral acetylenic ester tantalum complexes, see: f) Y. Kataoka, J. Miyai, M. Tezuka, K. Takai, K. Utimoto, *J. Org. Chem.* **1992**, *57*, 6796–6802.

[8] For a review on chiral auxiliaries of this type, see: W. Oppolzer, *Tetrahedron* **1987**, *43*, 1969–2004; J. K. Whitesell, *Chem. Rev.* **1992**, *92*, 953–964; G. B. Jones, B. J. Chapman, *Synthesis* **1995**, 475–497; J. Seyden-Penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley, New York, **1995**, pp. 513–592.

[9] K. Hakam, M. Thielmann, T. Thielmann, E. Winterfeldt, *Tetrahedron* **1987**, *43*, 2035–2044; W. Oppolzer, M. Kurth, D. Reichlin, C. Chapuis, M. Mohanhaupt, F. Moffatt, *Helv. Chim. Acta* **1981**, *64*, 2802–2807. The *cis*, *exo*-structure of **15** was characterized by a ^{1}H NMR NOE study and comparison of its m.p. (125–126 °C) with a reported one (126 °C, P. Binger, A. Brinkmann, P. Roefke, B. Schäfer, *Liebigs Ann. Chem.* **1989**, 739–750). The antipode of auxiliary **15** is readily prepared from commercially available L-camphor.

[10] G. Helmchen, A. Selim, D. Dorsch, I. Taufer, *Tetrahedron Lett.* **1983**, *24*, 3213–3216; B. Mucha, H. M. R. Hoffmann, *Tetrahedron Lett.* **1989**, *30*, 4489–4492. See also ref. [9].

[11] Hydroxy acids **23** and **24** were isolated in 60 % (at 75 % conversion) and 80 % (at 50 % conversion) yields, respectively. The esters that were recovered unchanged exhibited exactly the same diastereomeric purities as those of the original samples, confirming that no kinetic resolution occurred during this hydrolysis.

[12] I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc.* **1991**, *113*, 4092–4096; for recent applications, see: F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 7026–7033, and references therein.

[13] W. P. Weber, *Silicon Reagents for Organic Synthesis*, Springer, Berlin, **1983**; E. W. Colvin, *Silicon in Organic Synthesis*, Butterworth, London, **1981**; Z. P. Mincheva, Y. Gao, F. Sato, *Tetrahedron Lett.* **1998**, *39*, 7947–7950.