

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]

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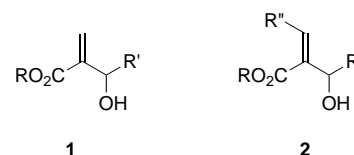
Crystallographic Data Centre as supplementary publication nos. CCDC-141477 (**4**), -141479 (**11**), -141478 (**13**), -141475 (**15**), and -141476 (**19**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: 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.

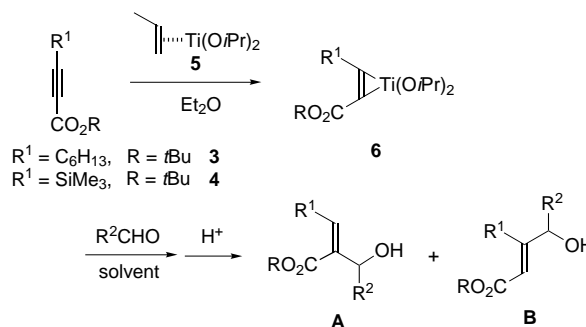
Asymmetric Synthesis of Baylis–Hillman-Type Allyl Alcohols via a Chiral Acetylenic Ester Titanium Alkoxide Complex**

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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, $[(\eta^2\text{-propene})\text{Ti}(\text{O}i\text{Pr})_2]$ (**5**)^[6] (Scheme 1).



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

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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

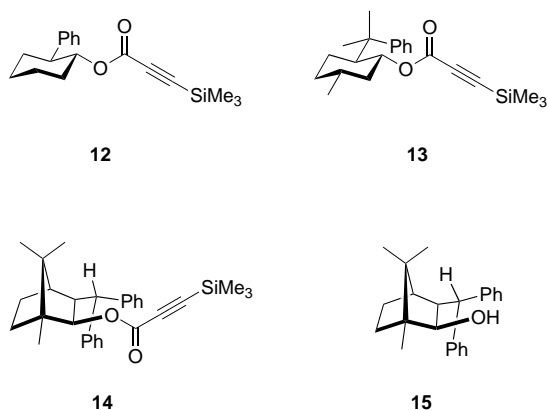
Table 1. Regioselectivity on the addition of acetylenic ester titanium complexes to aldehydes (Scheme 1).

Entry	Ynoate	Aldehyde R ²	Product		
			solvent: Et ₂ O/THF A:B ^[a]	yield [%] ^[b]	Et ₂ O A:B ^[a]
1	3	Et	7 90:10	84	75:25
2	3	<i>c</i> C ₆ H ₁₁	8 87:13	64	87:13
3	4	Et	9 97:3	72	89:11
4	4	<i>c</i> C ₆ H 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.

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 ¹H NMR analysis (NOE study). In general, the silylated substrate **4** showed very high regioselectivity to give adducts **9–11**.

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.

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

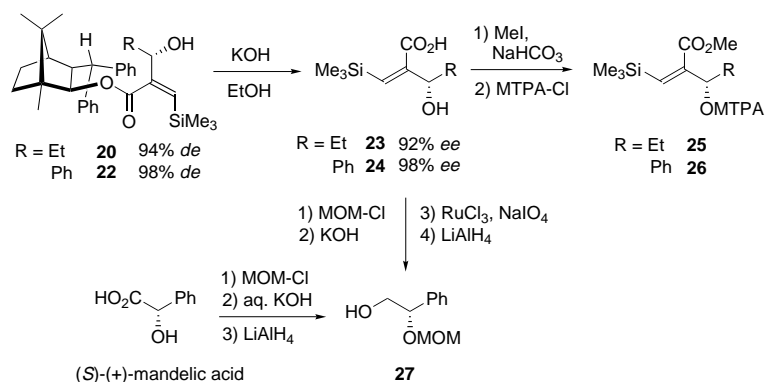
Table 2. Asymmetric addition to aldehydes.

Entry	Ynoate	Aldehyde R	selectivity ^[a]			Yield [%] ^[d]
			regio-	diastereo- ^[b]	config. ^[c]	
1	12	Et	16 95:5	64:36		80
2	12	<i>c</i> C ₆ H 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	<i>S</i>	95
6	14	<i>c</i> C ₆ H ₁₁	21 98:2	98:2		77
7	14	Ph	22 99:1	99:1	<i>S</i>	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.

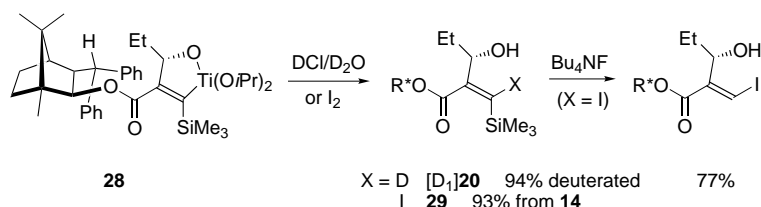
necessarily very high (up to 89:11, Table 2; entries 1–4). However, the ester **14** derived from alcohol **15**,^[9] which was very conveniently prepared from D-camphor but has not yet been widely utilized as a chiral auxiliary,^[10] was found to give marginally the best results (Table 2, entries 5–7). 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.

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 ¹H 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 (¹H 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 iodolysis of the intermediate oxatitanacycle **28** afforded the corresponding deuterated product $[D_1]\mathbf{20}$ or vinylic iodide **29** (Scheme 3), the latter of which may be useful for further transformation as such or after fluoride-mediated desilylation.^[13]



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 Et₂O, 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 Et₂O (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 Et₂O, 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 NaHCO₃, dried over Na₂SO₄, 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, ¹H, and ¹³C NMR spectroscopy, and elemental analysis. The following NOE study of **22** by ¹H NMR spectroscopy confirmed the assigned regio- and stereochemistry. Irradiation of the proton at $\delta = 0.02$ (Me₃Si) and that at $\delta = 5.47$ (CHOH) showed 11 % and 6 % NOE enhancements to the peak at $\delta = 6.09$ (Me₃Si–CH=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 CHCl₃); **21**: $[\alpha]_D^{25} = -108.60$ (*c* = 1.00 in CHCl₃); **22**: $[\alpha]_D^{25} = -103.6$ (*c* = 1.00 in CHCl₃); **23**: $[\alpha]_D^{25} = -18.00$ (*c* = 1.20 in CHCl₃); **24**: $[\alpha]_D^{25} = +6.67$ (*c* = 0.60 in CHCl₃).

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