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Regio- and enantioselective synthesis of allenic esters by samarium(II)-mediated reduction of propargylic compounds through dynamic kinetic protonation

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Dedicated to Professor Jean François Normant on the occasion of his 65th birthday on January 29th

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Abstract—Regioselective synthesis of allenic esters was attained by SmI_2-mediated reduction of propargylic phosphates and ethers bearing alkoxycarbonyl groups at the acetylene terminus. Using suitable chiral proton source in this system, highly enantio-enriched allenic ester was obtained through dynamic kinetic resolution by Lewis acidic Sm(III)-mediated enantioselective protonation, even if starting with racemic propargylic phosphates.

1. Introduction

Allenic esters are valuable synthetic targets, since they constitute an important class of natural products and the key intermediates thereof.[1] As allenic compounds in the case that A is not B and X is not Y are chiral, synthesis of enantio-enriched allenic esters is a challenging subject (Fig. 1). Since van't Hoff predicted the existence of chiral allenic compounds in 1875,[2] much attention has been paid on asymmetric synthesis of the allenic compounds, particularly allenic esters. The first asymmetric synthesis of allenic compounds was reported by Maitland and Mills in 1935.[3] They carried out dehydration of racemic allylic alcohol in the presence of optically pure 10-camphorsulfonic acid. Enantio-enriched allenic compound was obtained via kinetic resolution of racemic allylic alcohol, though in quite a low enantiomeric excess (Scheme 1).

Since then, there have been a number of reports on the asymmetric synthesis of allenes, however, almost all of them are based on the chirality transfer process starting from enantio-enriched propargylic compounds. The chirality transfer reactions include transmission of chirality from

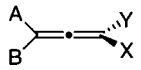
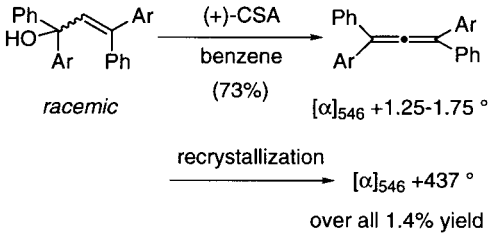
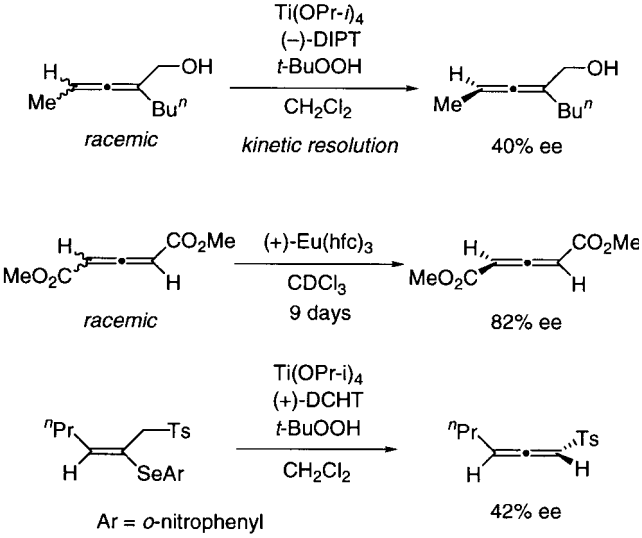


Figure 1.



Scheme 1.



Scheme 2.

Keywords: samarium(II) iodide; allenic ester; regioselectivity; enantioselectivity; dynamic kinetic resolution; asymmetric protonation.

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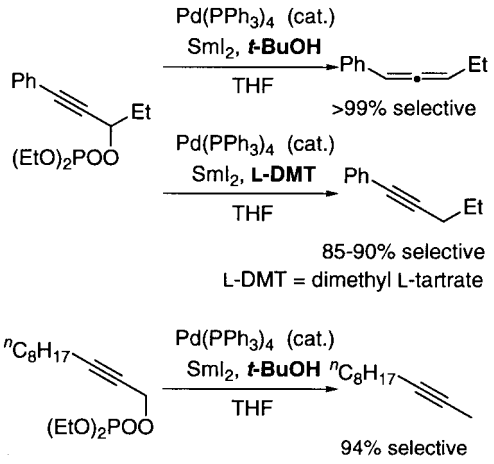
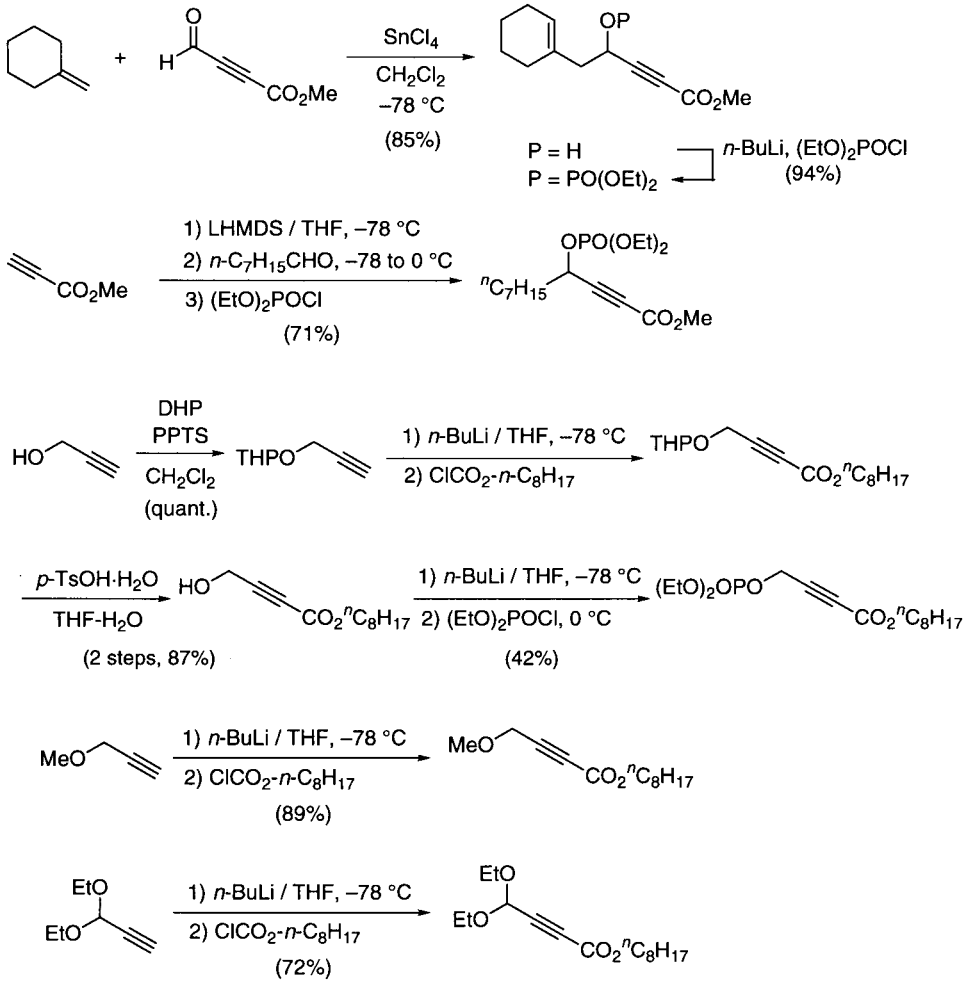


Scheme 3.

chiral center to allenyl axis. For example, Alexakis and Normant reported the nucleophilic substitution reaction of enantio-enriched propargylic acetate by cuprate reagent.[4] Marshall reported [2,3] Wittig rearrangement of propargyl α-stannylalkyl ether via transmetallation from Sn to Li.[5] Vermeer reported the cross coupling reaction between organozinc reagent and allenylpalladium(II) obtained starting from propargylic mesylate.[6] However, there are a few reports for enantioselective synthesis of allenes without chirality transfer.

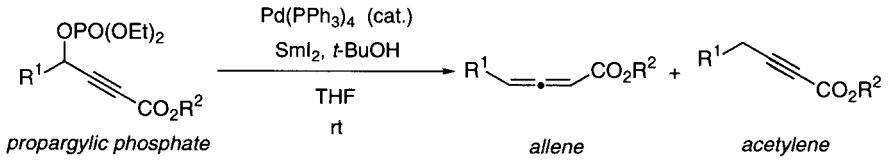
There are three examples for enantioselective synthesis of allenic compounds without chirality transfer. Marshall attempted kinetic resolution of racemic allenylcarbinol by Sharpless asymmetric epoxidation.[7] Naruse reported destruction of allenedicarboxylate using chiral NMR shift reagent, $Eu(hfc)_3$ as a chiral Lewis acid.[8] Uemura reported asymmetric oxidation of vinylic selenide followed by elimination to give an enantio-enriched allenic sulfone.[9] This is, however, a chirality transfer reaction of non-racemic selenium oxide intermediate (Scheme 2).

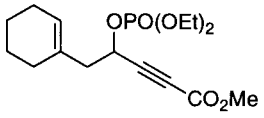
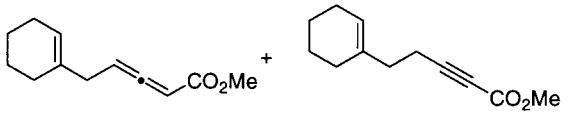
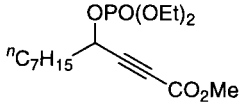
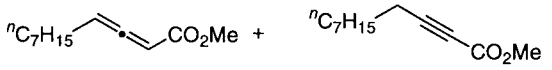
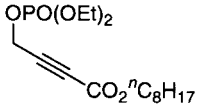
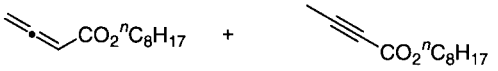
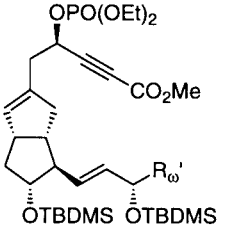
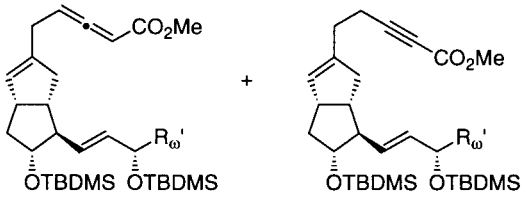
On the other hand, Professor Inanaga's group and we have already reported that the reductions of secondary propargylic phosphates provide allenes with higher regioselectivity than the propargylic acetates through samarium(II) iodide[10]-mediated reduction followed by protonation in the presence of palladium(0) catalyst.[11] In contrast, the reduction of primary propargylic phosphates gave acetylene derivatives interestingly. Furthermore, we attained the regiodivergent synthesis of allenes/acetylenes from secondary propargylic phosphates by tuning proton sources[12] (Scheme 3).



Scheme 4.

Table 1. Regioselective reduction–protonation of propargylic phosphates in the presence of Pd(0) catalyst



substrate[a]	product (ratio)[a,b]	% yield
	 (>99 : <1)	53
	 (>99 : <1)	100
	 (>99 : <1)	83
	 (>99 : <1)	86[c]

[a] $R_\omega'=(2R)$–$CH_2CH(CH_3)(CH_2)_2CH{=}C(CH_3)_2$.
[b] Determined by ^1H NMR analysis.
[c] See Ref. 13.

We describe herein samarium(II) iodide-mediated reduction of secondary and primary propargylic phosphates and ethers to obtain allenic esters regio- and enantioselectively through dynamic kinetic protonation without chirality transfer process.

2. Results and discussion

2.1. Regioselective SmI_2-mediated reduction–protonation

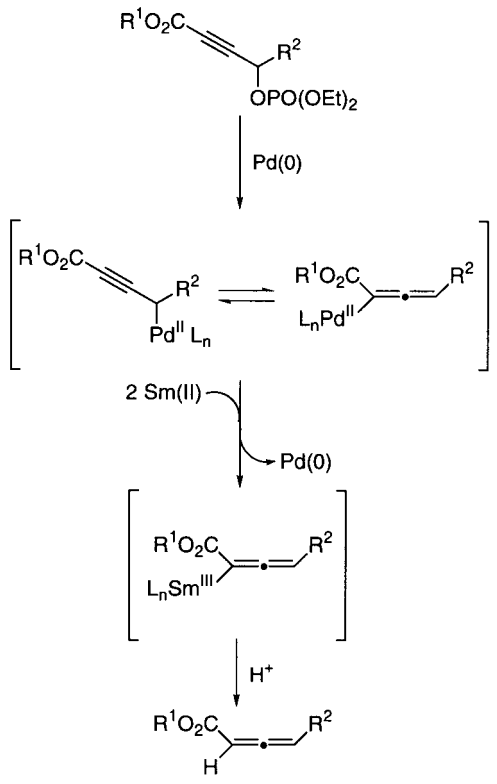
In order to synthesize allenic esters, propargylic compounds bearing alkoxycarbonyl groups at acetylene terminus were prepared as follows (Scheme 4).

Samarium(II) iodide-mediated reductions of these propargylic compounds in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0) were examined and the results were summarized in Table 1.

Not only secondary but also primary propargylic substrates gave allenic esters, and no propiolate derivatives could be obtained. In contrast, primary substrates without alkoxycarbonyl groups at acetylene terminus give acetylenic compounds regioselectively.[11] We have already reported the regiodivergent synthesis of allenes/acetylenes from secondary propargylic phosphates as described above.[12] Now, we also attained the regiodivergent synthesis of allenes/acetylenes from primary one by tuning substrates including alkoxycarbonyl moiety or not. In order to synthesize α-allenyl side chain of prostacyclin analogue, this method is particularly useful because of exclusively high allene selectivity.[13]

We propose two possible reaction mechanisms. One contains Umpolung process from σ-allenyl/propargylpalladium(II) to allenylsamarium(III) species (Scheme 5). The other involves the reduction of alkoxycarbonyl group followed by formation of allenylsamarium(III) species through unstable cumulenic trienolate (Scheme 6). Finally, kinetic protonation of allenylsamarium(III) takes place in both mechanisms. It is remarkable that the latter mechanism includes no palladium(0) catalyst. Therefore, the reductions without palladium(0) catalyst were performed (Table 2).

Propargylic phosphate bearing alkoxycarbonyl group at the acetylene terminus was reduced to allenic ester as a sole



Scheme 5.

product even without palladium(0) catalyst. Surprisingly, primary propargyl ether, methoxy group of which possessed a lower level of the leaving ability, also gave allenic esters. However, propargylic acetal was not reduced at all and the starting acetal was recovered. Thus, it is reasonable that the reactions proceed through latter mechanism as shown in Scheme 6, when no use of palladium(0) catalyst.

2.2. Enantioselective SmI_2-mediated reduction–protonation

Next, we attempted the asymmetric synthesis of allenic ester through chirality transfer reduction of enantio-enriched phosphates. In order to synthesize allenic ester with high enantiopurity, we attempted chirality transfer reaction from propargylic phosphate of 91% ee, which was prepared by asymmetric carbonyl-ene reaction with alkynylogous analogue of glyoxylate catalyzed by binaphthol–titanium complex[13] followed by phosphorylation.

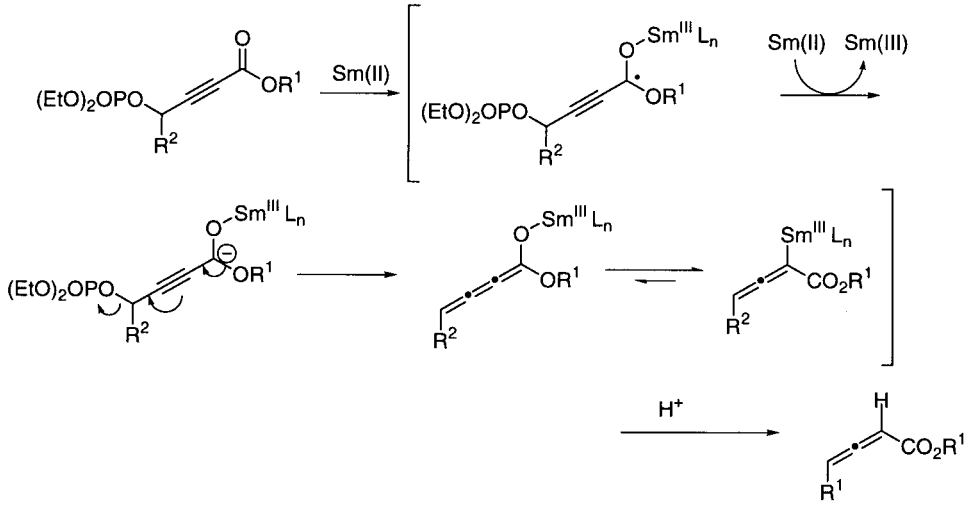
The chirality transfer reaction was carried out under usual conditions to give, surprisingly however, essentially racemic allenic ester (Scheme 7).

The stereochemical course for racemization can be explained as follows. First, oxidative addition to propargylic phosphate gives allenylpalladium(II) through back side attack of palladium(0). Thus, enantio-enriched allenylpalladium(II) is stereospecifically formed starting from enantio-enriched propargylic phosphate without loss of enantiopurity. The cationic allenylpalladium(II) species are converted to anionic organosamarium(III) species by double one-electron reductions of samarium(II). This carbanionic samarium(III) species is readily racemized. Thus, racemic allenic compound is obtained after protonation with achiral proton source such as *tert*-butyl alcohol (Scheme 8).

This result, in turn, suggests the possibility for dynamic kinetic resolution[14] using chiral proton sources[15] even when starting from racemic phosphates, namely deracemization process of racemic allenylsamarium(III) species (Fig. 2). In addition, organosamarium(III), which is formed by reduction of phosphates with samarium(II), possesses strong Lewis acidity and oxophilicity.[10] Thus, chiral diols and hydroxycarbonyl compounds can be effective proton sources, since the chelation of such chiral alcohols with samarium(III) can construct a favorable asymmetric environment.

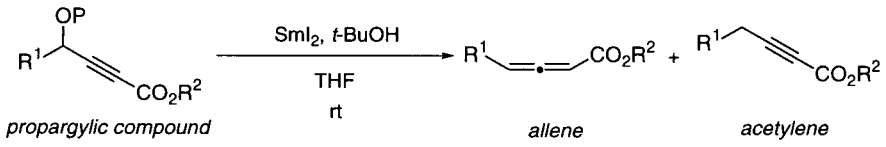
So, we attempted dynamic kinetic resolution by asymmetric protonation, namely dynamic kinetic protonation, using racemic propargylic phosphate with various chiral proton sources (Table 3).[16]

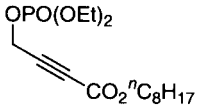
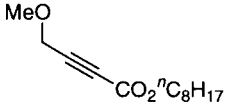
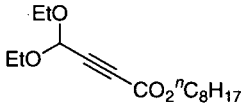
First, we examined the C_2-symmetrical diols such as



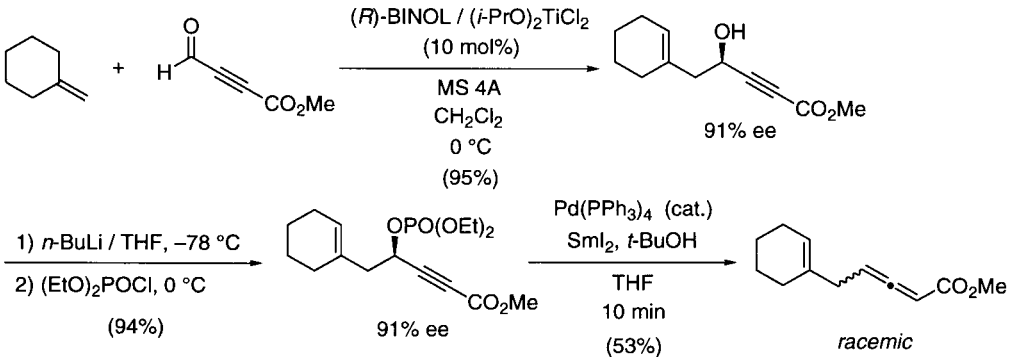
Scheme 6.

Table 2. Regioselective reduction–protonation of propargylic compounds in the absence of Pd(0) catalyst

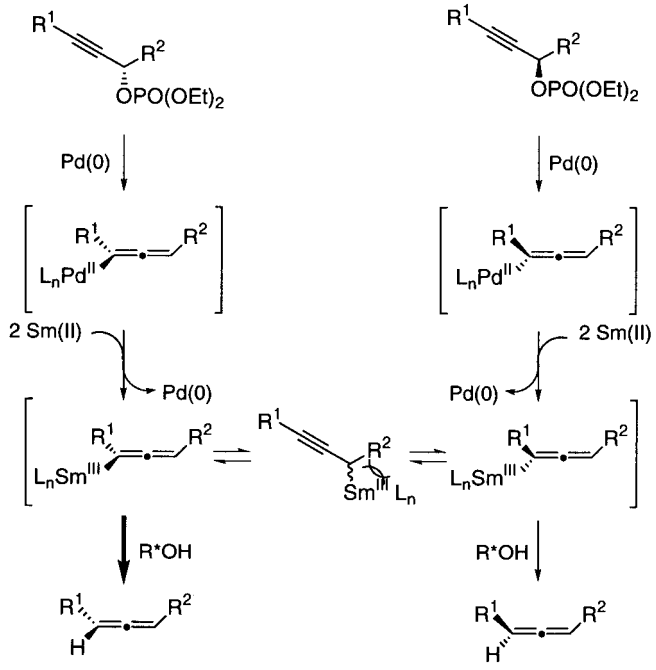


substrate	product (ratio)[a]	% yield
	 (>99 : <1)	79
	 (>99 : <1)	84
	no reaction	—

[a]Determined by ^{1}H NMR analysis.



Scheme 7.



Scheme 8.

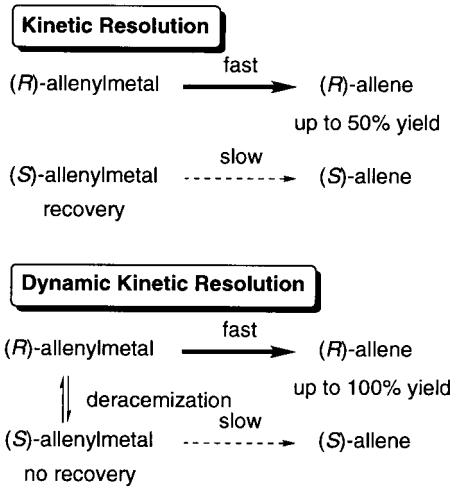
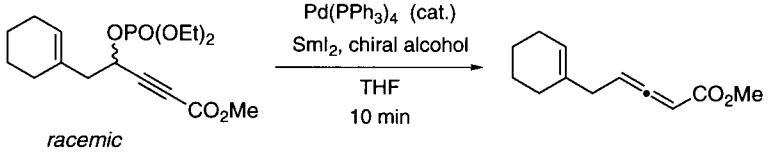


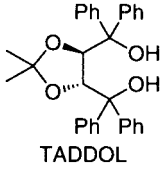
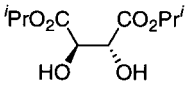
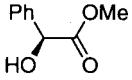
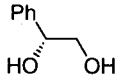
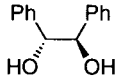
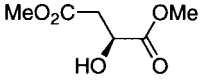
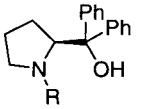
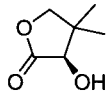
Figure 2.

TADDOL and diisopropyl tartrate, which were often used as chiral ligands for asymmetric metal complex catalysts (entries 1–2). The reaction was carried out as follows. To a THF solution of racemic phosphate was added a chiral proton source, palladium(0) catalyst, and a THF solution of samarium(II) iodide at room temperature, and the mixture was stirred for ten minutes. The enantiomeric excess of the allenic esters thus obtained was determined by lanthanide induced shift-NMR (LIS-NMR) method using $Eu(hfc)_3$.[17] Medium level of enantioselectivity was observed. The absolute configuration was determined by Lowe–Brewster's rule.[18] Only when diisopropyl tartrate was used, propiolate derivative was also obtained as a by-product (entry 2).[12]

Next, we used α-hydroxycarbonyl compounds and 1,2-diols, which could form 5-membered chelate because of high Lewis acidity of trivalent samarium (entries 3–6). All chiral proton sources gave enantio-enriched allenic ester and no propiolate derivative was obtained. In

Table 3. Regio- and enantioselective reduction–protonation of propargylic phosphate



entry	chiral alcohol	% yield	% ee[a]	config.[b]
1	 TADDOL	52	41	*R*
2[c]		70	24	*S*
3		71	67	*S*
4		86	13	*R*
5		71	86	*R*
6		46	24	*S*
7	 R = H	25	45	*R*
8	R = Me	24	80	*R*
9		68	95	*R*

[a] Determined by LIS-NMR analysis using $Eu(hfc)_3$.
[b] Determined by Lowe–Brewster's rule.
[c] Acetylene-type product was also obtained in 9% yield.

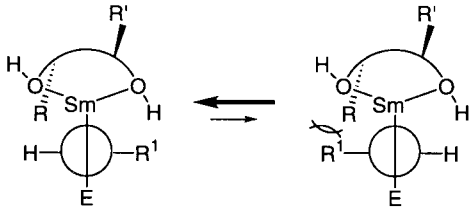


Figure 3.

particular, hydrobenzoin gave allenic ester with high chemical and high optical yield (entry 5).

Finally, we employed the cyclic chiral proton sources, which could form bicyclo[3.3.0]octane system such as pyrrolidinemethanols and pantolactone in order to construct a more rigid transition state (entries 7–9). As we would have expected, enantio-enriched allenic ester was obtained with exclusively high regioselectivity. In particular, pantolactone gave allenic ester in much more than 50% yield, the maximum yield through ordinary kinetic resolution, with extremely high enantiomeric excess (entry 9).

The sense of asymmetric protonation to provide (*R*)-allenic ester using (*R*,*R*)-hydrobenzoin (or pantolactone) correlates well to this transition state model, wherein the severe steric repulsion between alkyl groups is operative in the right diastereomer. Thus, protonation proceeds through the favorable diastereomer in left-hand side to give highly enantio-enriched allenic ester (Fig. 3).

In summary, we report here efficient regiospecific synthesis of allenic esters and the first example of the asymmetric synthesis of allenic compounds through dynamic kinetic protonation of anionic allenylsamarium(III) species without involvement of chirality transfer or destruction of one enantiomer. The present protonation using chiral proton sources such as hydrobenzoin and pantolactone will provide a powerful strategy using racemic allenyl carbanion species for the asymmetric synthesis of allenic compounds. This efficient asymmetric protonation could be attained due to the chelation of chiral alcohol with samarium(III) possessing strong Lewis acidity and oxophilicity. Thus, we now investigate the development of asymmetric reactions promoted by samarium(III) species obtained after the reduction of various organic compounds with samarium(II).

3. Experimental

3.1. General

Boiling points were uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Varian GEMINI 300 (300 MHz), a JEOL GSX-500 (500 MHz) and a JEOL EX-270 (270 MHz) spectrometers. Chemical shifts of ^{1}H NMR were expressed in parts per million relative to chloroform (δ 7.26) or tetramethylsilane (δ 0.00) as an internal standard in chloroform-*d*. Chemical shifts of ^{13}C NMR were expressed in parts per million relative to chloroform-*d* (*d* 77.0) as an internal standard. IR spectra were measured on a JASCO FT/IR-5000 spectrometer. Optical rotations were measured on a JASCO DIP-140. High-performance liquid chromatography were performed with a Shimadzu LC-6A instrument equipped with a Shimadzu SPD-6A spectrometer as an ultra violet (UV) light detector. Peak area was calculated by a Shimadzu C-R6A as an automatic integrator.

Tetrahydrofuran was distilled from sodium benzophenone ketyl immediately prior to use. Dichloromethane was freshly distilled from calcium hydride.

3.2. Preparation of propargylic phosphates

3.2.1. Methyl (±)-5-(cyclohex-1-en-1-yl)-4-hydroxypent-2-ynoate. To a solution of methyl 3-formylpropiolate (102 mg, 0.91 mmol) in dry dichloromethane (3 mL) were added methylidenecyclohexane (0.13 mL, 1.1 mmol) and then a 1.0 M solution of tin(IV) chloride in dichloromethane (0.91 mL, 0.91 mmol) at −78°C under an argon atmosphere. After stirring for 3 h, the reaction mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate, filtered through a pad of Celite and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=4:1) afforded methyl 5-(cyclohex-1-en-1-yl)-4-hydroxypent-2-ynoate in 85% yield (162 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5–1.7 (m, 4H), 1.9–2.1 (m, 5H), 2.41 (d, J=6.8 Hz, 2H), 3.77 (s, 3H), 4.55 (t, J=6.8 Hz, 1H), 5.61 (br.s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 22.6, 25.2, 28.3, 43.4, 52.7, 60.1, 76.1, 88.1, 127.0, 132.3, 153.9. IR (neat)3436, 2932, 2862, 2240, 1717, 1644, 1437, 1377, 1257, 1199, 1178, 1104, 1050, 915, 859, 803, 733 cm^{-1}.

3.2.2. Methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-hydroxypent-2-ynoate. To a suspension of powdered molecular sieves 4A (MS 4A; 100 mg) in dry dichloromethane (3 mL) were added (*R*)-binaphthol–titanium dichloride catalyst (50 mg, 0.125 mmol, 10 mol%), methylidenecyclohexane (0.18 mL, 1.5 mmol) and then freshly-distilled methyl 3-formylpropiolate (140 mg, 1.25 mmol) at 0°C under an argon atmosphere. After stirring overnight at that temperature, the reaction mixture was diluted with diethyl ether and poured into a saturated aqueous solution of sodium hydrogencarbonate. MS 4A was filtered off through a pad of Celite and the filtrate was extracted twice with diethyl ether and once with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=4:1) afforded methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-hydroxypent-2-ynoate in 95% yield (248 mg). $[\alpha]_D^{26}$=+46.6° (*c* 1.20, $CHCl_3$), 91% ee. HPLC (DAICEL CHIRALCEL OD, eluent, hexane/2-propanol=20:1, flow rate 0.6 mL/min, detection 230-nm light) t_R of (*R*)-isomer 15.2 min and (*S*)-isomer 17.4 min. ^{1}H NMR, ^{13}C NMR, IR: See corresponding racemic product.

3.2.3. Methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-[(diethoxyphosphoryl)oxy]pent-2-ynoate. To a solution of methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-hydroxypent-2-ynoate (48 mg, 0.23 mmol) in dry tetrahydrofuran (4 mL) was added a 1.6 M solution of butyllithium in hexane (0.14 mL,

0.23 mmol) at −78°C under a nitrogen atmosphere. After stirring for 1 h, to the resultant solution was added triethylamine (0.038 mL, 0.28 mmol) and then diethyl chlorophosphate (0.040 mL, 0.28 mmol), then the mixture was warmed to 0°C. After stirring for 1 h at that temperature, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=3:1) afforded methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-[(diethoxyphosphoryl)oxy]pent-2-ynoate in 94% yield (75 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (dq, J=1.1, 7.0 Hz, 6H), 1.5–1.7 (m, 4H), 1.8–2.1 (m, 4H), 2.44 (dd, J=6.2, 13.9 Hz, 1H), 2.53 (dd, J=7.8, 13.9 Hz, 1H), 3.77 (s, 3H), 4.0–4.2 (m, 4H), 5.13 (dt, J=6.2, 7.8 Hz, 1H), 5.59 (br.s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9 (d, $^3J_{CCOP}$=5.3 Hz), 21.9, 22.6, 25.2, 28.1, 44.2 (d, $^3J_{CCOP}$=6.3 Hz), 52.8, 64.1 (d, $^2J_{COP}$=5.9 Hz), 64.3 (d, $^2J_{COP}$=5.9 Hz), 65.7 (d, $^2J_{COP}$=5.9 Hz), 77.7, 84.4 (d, $^3J_{CCOP}$=3.0 Hz), 126.9, 131.2, 153.5. IR (neat) 3430, 3248, 2988, 2934, 2862, 2246, 1721, 1437, 1373, 1251, 1168, 980, 806, 750 cm^{-1}. $[\alpha]_D^{26}$=34.7° (*c* 1.50, $CHCl_3$), 91% ee.

3.2.4. Methyl 4-[(diethoxyphosphoryl)oxy]undec-2-ynoate. To a solution of methyl propiolate (0.44 mL, 5.0 mmol) in dry tetrahydrofuran (8 mL) was added a 1.0 M solution of lithium hexamethyldisilazide in tetrahydrofuran (5.0 mL, 5.0 mmol) dropwise at −78°C under a nitrogen atmosphere. After stirring for 15 min at that temperature, octanal (0.86 mL, 5.5 mmol) was added to the resultant solution, then the mixture was stirred for 1 h at that temperature, and for 1 h at 0°C. After adding diethyl chlorophosphate (2.60 mL, 18 mmol) to the reaction mixture, the mixture was stirred for 1 h at that temperature. The resultant mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=2:1) afforded methyl 4-[(diethoxyphosphoryl)oxy]undec-2-ynoate in 71% yield (1.241 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, J=6.9 Hz, 3H), 1.2–1.3 (m, 8H), 1.31 (dq, J=1.1, 7.1 Hz, 3H), 1.33 (dq, J=1.1, 7.1 Hz, 3H), 1.4–1.5 (m, 2H), 1.8–1.9 (m, 2H), 3.75 (s, 3H), 4.0–4.2 (m, 4H), 5.03 (q, J=6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 15.9 (d, $^3J_{CCOP}$=7.3 Hz), 22.5, 24.4, 28.8, 28.9, 31.6, 35.6 (d, $^3J_{CCOP}$=6.1 Hz), 52.7, 64.0 (d, $^2J_{COP}$=7.3 Hz), 64.1 (d, $^2J_{COP}$=6.1 Hz), 67.0 (d, $^2J_{COP}$=6.1 Hz), 77.4, 84.2 (d, $^3J_{CCOP}$=4.8 Hz), 153.3. IR (neat) 2958, 2932, 2862, 2246, 1723, 1636, 1437, 1371, 1261, 1166, 1033, 750 cm^{-1}.

3.2.5. 2-[(Prop-2-yn-1-yl)oxy]tetrahydropyran. Octyl 4-[(diethoxyphosphoryl)oxy]but-2-ynoate was prepared from prop-2-yn-1-ol described as follows. To a solution of prop-2-yn-1-ol (propargyl alcohol; 0.87 mL, 18 mmol) in dry dichloromethane (15 mL) were added 2*H*-3,4-dihydropyran (1.37 mL, 15 mmol) and then pyridinium *p*-toluenesulfonate (377 mg, 1.5 mmol) at room temperature under a nitrogen atmosphere. After stirring for 15 h, the reaction mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate, and extracted three times with dichloromethane. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and distilled under reduced pressure to afford pure 2-[(prop-2-yn-1-yl)oxy]tetrahydropyran in 95% yield (2.001 g). bp 63–65°C/9 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.4–1.9 (m, 6H), 2.41 (t, J=2.4 Hz, 1H), 3.5–3.6 (m, 1H), 3.8–3.9 (m, 1H), 4.24 (dd, J=2.4, 15.7 Hz, 1H), 4.28 (dd, J=2.4, 15.7 Hz, 1H), 4.82 (t, J=3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 25.2, 30.1, 54.0, 62.0, 73.9, 76.6, 96.9.

3.2.6. Octyl 4-[(tetrahydropyran-2-yl)oxy]but-2-ynoate. To a solution of 2-[(prop-2-yn-1-yl)oxy]tetrahydropyran (0.84 mL, 6.0 mmol) in dry tetrahydrofuran (6 mL) was added a 1.6 M solution of butyllithium in hexane (4.1 mL, 6.6 mmol) at −78°C under a nitrogen atmosphere. After stirring for 1 h at that temperature, octyl chloroformate (1.3 mL, 6.6 mmol) was added to the resultant solution. After stirring for 2 h at that temperature, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford octyl 4-[(tetrahydropyran-2-yl)oxy]but-2-ynoate (2.083 g), the crude product, which would be used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J=6.9 Hz, 3H), 1.2–1.4 (m, 10H), 1.5–1.9 (m, 8H), 3.5–3.6 (m, 1H), 3.8–3.9 (m, 1H), 4.17 (t, J=6.7 Hz, 2H), 4.38 (s, 2H), 4.81 (t, J=3.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 18.9, 22.7, 25.3, 25.9, 28.4, 29.2, 29.2, 30.1, 31.8, 53.7, 62.0, 66.3, 77.6, 83.4, 97.1, 153.2. IR (neat) 2932, 2860, 2242, 1717, 1458, 1390, 1346, 1251, 1203, 1125, 1029, 944, 903, 872, 750 cm^{-1}.

3.2.7. Octyl 4-hydroxybut-2-ynoate. To a solution of octyl 4-[(tetrahydropyran-2-yl)oxy]but-2-ynoate (2.083 g), the crude material obtained as above, in tetrahydrofuran (10 mL) and water (2 mL) was added *p*-toluenesulfonic acid monohydrate (456 mg, 2.4 mmol) at room temperature. After stirring for 1 day at that temperature, the reaction mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate and extracted three times with diethyl ether. The combined organic layer was washed with a saturated aqueous solution of sodium hydrogencarbonate and brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=8:1) afforded octyl 4-hydroxybut-2-ynoate in 87% yield (2 steps, 1.022 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J=6.9 Hz, 3H), 1.2–1.4 (m, 10H), 1.6–1.7 (m, 2H), 2.21 (t, J=6.3 Hz, 1H), 4.17 (t, J=6.7 Hz, 2H), 4.39 (d, J=6.3 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 25.6, 28.2, 29.0, 29.0, 31.6, 50.6, 66.4, 77.3, 85.1, 153.6. IR (neat) 3420, 2932, 2860, 2242, 1715, 1444, 1386, 1253, 1079, 1025, 752 cm^{-1}.

3.2.8. Octyl 4-[(diethoxyphosphoryl)oxy]but-2-ynoate. To a solution of octyl 4-hydroxybut-2-ynoate (738 mg, 3.76 mmol) in dry tetrahydrofuran (4 mL) was added a 1.56 M solution of butyllithium in hexane (2.4 mL, 3.76 mmol) at −78°C under a nitrogen atmosphere. After stirring for 30 min at that temperature, diethyl chlorophosphate

(0.65 mL, 4.50 mmol) was added to the resultant solution, then the mixture was warmed to 0°C. After stirring for 2 h at that temperature, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=3:1) afforded octyl 4-[(diethoxyphosphoryl)oxy]but-2-ynoate in 42% yield (552 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J=7.0 Hz, 3H), 1.2–1.4 (m, 10H), 1.33 (dt, J=1.1, 7.1 Hz, 3H), 1.35 (dt, J=1.1, 7.1 Hz, 3H), 1.6–1.7 (m, 2H), 4.0–4.2 (m, 2H), 4.77 (d, J=10.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 15.9 (d, $^3J_{CCOP}$=6.7 Hz), 16.0 (d, $^3J_{CCOP}$=7.1 Hz), 22.5, 25.6, 28.2, 29.0, 29.0, 31.6, 54.3 (d, $^2J_{COP}$=4.7 Hz), 64.3 (d, $^2J_{COP}$=5.8 Hz), 66.4, 78.8, 80.6 (d, $^3J_{CCOP}$=7.4 Hz), 153.0. IR (neat) 2924, 2862, 2250, 1717, 1460, 1394, 1373, 1251, 1168, 1029, 832, 750 cm^{-1}.

3.3. Preparation of propargylic ether and acetal

3.3.1. Octyl 4-methoxybut-2-ynoate. To a solution of methyl prop-2-yn-1-yl ether (0.46 mL, 5.5 mmol) in dry tetrahydrofuran (5 mL) was added a 1.65 M solution of butyllithium in hexane (3.33 mL, 5.5 mmol) dropwise at −78°C under a nitrogen atmosphere. After stirring for 1 h at that temperature, octyl chloroformate (0.98 mL, 5.0 mmol) was added to the reaction mixture. After stirring for 2.5 h at that temperature, the resultant mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=15:1) afforded octyl 4-methoxybut-2-ynoate in 89% yield (1.002 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J=6.6 Hz, 3H), 1.2–1.4 (m, 10H), 1.6–1.7 (m, 2H), 3.41 (s, 3H), 4.17 (t, J=6.8 Hz, 2H), 4.22 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 25.7, 28.3, 29.0, 29.0, 31.6, 58.0, 59.4, 66.3, 78.3, 83.0, 153.4. IR (neat) 2930, 2862, 2238, 1781, 1717, 1466, 1379, 1359, 1249, 1189, 1162, 1110, 1065, 944, 909, 750 cm^{-1}.

3.3.2. Octyl 4,4-diethoxybut-2-ynoate. To a solution of propiolaldehyde diethyl acetal (0.79 mL, 5.5 mmol) in dry tetrahydrofuran (5 mL) was added a 1.58 M solution of butyllithium in hexane (3.50 mL, 5.5 mmol) dropwise at −78°C under a nitrogen atmosphere. After stirring for 1 h at that temperature, octyl chloroformate (0.70 mL, 3.6 mmol) was added to the reaction mixture. After stirring for 2.5 h at that temperature, the resultant mixture was poured into a saturated aqueous solution of ammonium chloride and extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (hexane/ethyl acetate=20:1) afforded octyl 4,4-diethoxybut-2-ynoate in 72% yield (728 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J=6.8 Hz, 3H), 1.24 (t, J=7.1 Hz, 6H), 1.2–1.4 (m, 10H), 1.6–1.7 (m, 2H), 3.62 (dq, J=9.4, 7.1 Hz, 2H), 3.75 (dq, J=9.4, 7.1 Hz, 2H), 4.17 (t, J=6.8 Hz, 2H), 5.36 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.8, 22.5, 25.6, 28.2, 29.0, 29.0, 31.6, 61.5, 66.4, 76.2, 81.0, 90.9, 153.4.

3.4. Typical procedure for palladium(0)-catalyzed reduction of propargylic compounds with samarium(II) iodide

3.4.1. Methyl (*R*)-(−)-5-(cyclohex-1-en-1-yl)penta-2,3-dienoate. To a solution of methyl (*R*)-(+)-5-(cyclohex-1-en-1-yl)-4-[(diethoxyphosphoryl)oxy]pent-2-ynoate (75 mg, 0.22 mmol), tetrakis(triphenylphosphine)palladium(0) (13 mg, 0.011 mmol; 5 mol%) and (*R*)-styrene glycol (33 mg, 0.24 mmol; as a proton source) in dry tetrahydrofuran (2 mL) was added a 0.1 M solution of samarium(II) iodide in tetrahydrofuran (5.5 mL, 0.55 mmol) at room temperature under an argon atmosphere. After stirring for 10 min, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride, filtered through pads of Celite–Florisil and extracted three times with diethyl ether. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure. Purification by silica-gel column chromatography (pentane) afforded methyl (*R*)-(−)-5-(cyclohex-1-en-1-yl)penta-2,3-dienoate. in 86% yield (36 mg). The regioselectivity was >99% *allene*, determined by ^{1}H NMR analysis. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5–1.7 (m, 4H), 1.9–2.1 (m, 4H), 2.6–2.9 (m, 2H), 3.73 (s, 3H), 5.4–5.7 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 22.9, 25.1, 28.0, 36.2, 51.9, 87.6, 93.8, 123.2, 135.1, 166.8, 213.0. IR (neat) 2928, 1961, 1723, 1439, 1408, 1375, 1261, 1195, 1162, 1035, 803 cm^{-1}. $[\alpha]_D^{25}$=−0.41° (*c* 0.90, $CHCl_3$), 13% ee.

3.4.2. Methyl undeca-2,3-dienoate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J=6.9 Hz, 3H), 1.2–1.4 (m, 8H), 1.4–1.5 (m, 2H), 2.12 (dq, J=3.3, 6.9 Hz, 2H), 3.73 (s, 3H), 5.58 (dt, J=3.3, 6.9 Hz, 1H), 5.60 (q, J=6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 27.6, 28.8, 29.0, 29.1, 31.9, 52.0, 88.0, 95.5, 166.8, 212.5. IR (neat) 2930, 2862, 1963, 1725, 1663, 1537, 1439, 1412, 1346, 1325, 1259, 1230, 1195, 1162, 1035, 872, 801 cm^{-1}.

3.4.3. Octyl allenecarboxylate. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J=6.9 Hz, 3H), 1.2–1.4 (m, 10H), 1.64 (tt, J=6.8, 7.4 Hz, 2H), 4.12 (t, J=6.8 Hz, 2H), 5.20 (d, J=6.5 Hz, 2H), 5.63 (t, J=6.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 25.7, 28.5, 29.1, 29.1, 31.7, 65.1, 79.2, 88.1, 166.0, 216.0. IR (neat) 2930, 2860, 1974, 1943, 1719, 1468, 1427, 1383, 1342, 1299, 1261, 1166, 1085, 1021, 859 cm^{-1}.

References

1. Reviews: (a) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; Wiley-Interscience: New York, 1984. (b) Pasto, D. J. *Tetrahedron* **1984**, *40*, 2805–2827. (c) Smadja, W. *Chem. Rev.* **1983**, *83*, 263–320. (d) Rossi, R.; Diversi, P. *Synthesis* **1973**, 25–36.
2. van't Hoff, J. H. In *La Chimie dans l'Espace*, Bazendijk: Rotterdam, 1875; pp 29.
3. (a) Maitland, P.; Mills, W. H. *Nature* **1935**, *135*, 994–994. (b) Maitland, P.; Mills, W. H. *J. Chem. Soc.* **1936**, 987–998.

4. (a) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *J. Am. Chem. Soc.* **1990**, *112*, 8042–8047. (b) Alexakis, A. *Pure Appl. Chem.* **1992**, *64*, 387–392.
5. (a) Marshall, J. A.; Robinson, E. D.; Zapata, A. *J. Org. Chem.* **1989**, *54*, 5854–5855. (b) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991**, *56*, 4913–4918.
6. Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716–720.
7. (a) Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589–604. (b) See Ref. 5a. (c) Noguchi, Y.; Takiyama, H.; Katsuki, T. *Synlett* **1998**, 543–545.
8. (a) Naruse, Y.; Watanabe, H.; Inagaki, S. *Tetrahedron: Asymmetry* **1992**, *3*, 603–606. (b) Naruse, Y.; Watanabe, H.; Ishiyama, Y.; Yoshida, T. *J. Org. Chem.* **1997**, *62*, 3862–3866.
9. Komatsu, S.; Murakami, T.; Nishibayashi, Y.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 3697–3702.
10. Reviews on samarium(II) iodide: (a) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573–6614. (b) Inanaga *J. Synth. Org. Chem., Jpn.* **1989**, *47*, 200–211. (c) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453–460. (d) Molander, G. A. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, pp 251–282. (e) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943–961. (f) Brandukova, N. E.; Vygodskii, Y. S.; Vinogradova, S. V. *Russ. Chem. Rev.* **1994**, *63*, 345–355. (g) Imamoto, T. In *Lanthanides in Organic Synthesis*, Academic: London, 1994; pp 21–65. (h) Kamochi, Y.; Kudo, T. *J. Synth. Org. Chem., Jpn.* **1994**, *52*, 285–294. (i) Molander, G. A. *Org. React.* **1994**, *46*, 211–367. (j) Matsuda, F. *J. Synth. Org. Chem., Jpn.* **1995**, *53*, 987–998. (k) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338. (l) Utimoto, K.; Matsubara, S. *J. Synth. Org. Chem., Jpn.* **1998**, *56*, 908–918. (m) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321–3354. (n) Mikami, K. *Rare Earths* **2000**, *11*, 47–64.
11. Mikami, K.; Yoshida, A.; Matsumoto, S.; Feng, F.; Matsumoto, Y.; Sugino, A.; Hanamoto, T.; Inanaga, J. *Tetrahedron Lett.* **1995**, *36*, 907–908.
12. Yoshida, A.; Mikami, K. *Synlett* **1997**, 1375–1376.
13. Mikami, K.; Yoshida, A.; Matsumoto, Y. *Tetrahedron Lett.* **1996**, *37*, 8515–8518.
14. (a) Ward, S. R. *Tetrahedron: Asymmetry* **1995**, *6*, 1475–1490. (b) Noyori, R.; Tokunaga, M.; Kitamura, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36–56.
15. Reviews on asymmetric protonation using chiral proton sources: (a) Fehr, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2566–2587. (b) Waldmann, H. *Nachr. Chem., Tech. Lab.* **1991**, *39*, 413–418. (c) Fehr, C. *Chimia* **1991**, *45*, 253–261. (d) Duhamel, L.; Duhamel, P.; Launay, J.-C.; Plaquevent, J.-C. *Bull. Soc. Chim. Fr.* **1984**, *2*, 421–430.
16. Mikami, K.; Yoshida, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 858–860.
17. (a) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949–3954. (b) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940–1941.
18. (a) Lowe, G. *Chem. Commun.* **1965**, 411–413. (b) See also Ref. 1d.