HOKKAIDO UNIVERSITY

Title	Construction of Seven-Membered Carbocycles via 8π Electrocyclic Reactions
Author(s)	斎藤, 優輝
Degree Grantor	北海道大学
Degree Name	博士(理学)
Dissertation Number	甲第14901号
Issue Date	2022-03-24
DOI	https://doi.org/10.14943/doctoral.k14901
Doc URL	https://hdl.handle.net/2115/85594
Type	doctoral thesis
File Information	SAITO_Hiroki.pdf

DISSERTATION

Construction of Seven-Membered Carbocycles via 8π Electrocyclic Reactions

(8π 系電子環状反応による炭素 7 員環の構築法)

Hiroki Saito

Hokkaido University

2022

CONTENTS

GENERAL INTRODUCTION

1.1 Cationic Cyclization Reactions in Biosynthesis

Carbocycles with various ring sizes are widely contained in naturally occurring organic compounds. As one of the most important pathways to form these rings, nature has utilized cationic cyclization reactions of olefinic compounds. After an intramolecular addition reaction, the newly formed cationic center on the cyclized product can contribute to sequential reactions such as cyclization, Wagner-Meerwein rearrangement, or elimination to form an alkene moiety, that enriches the structural diversity of natural products. For example, even in biosynthesis of monoterpenes, a wide variety of compounds are synthesized from a single starting material (Scheme 1). Under the influence of (+)-limonene synthase, geranyl diphosphate (GPP) cationically cyclizes to afford six-membered cationic intermediate **1**, which is converted to (+)-limonene via simple deprotonation. Pinene synthase also transforms GPP into the same cationic species **1**, but what happens next is an intramolecular addition with an alkene moiety, resulting in formation of the four-membered ring of (α)-pinene. Other monoterpenes having different carbon frameworks such as camphor, thujone, 3-carene are also synthesized through common intermediate **1**.
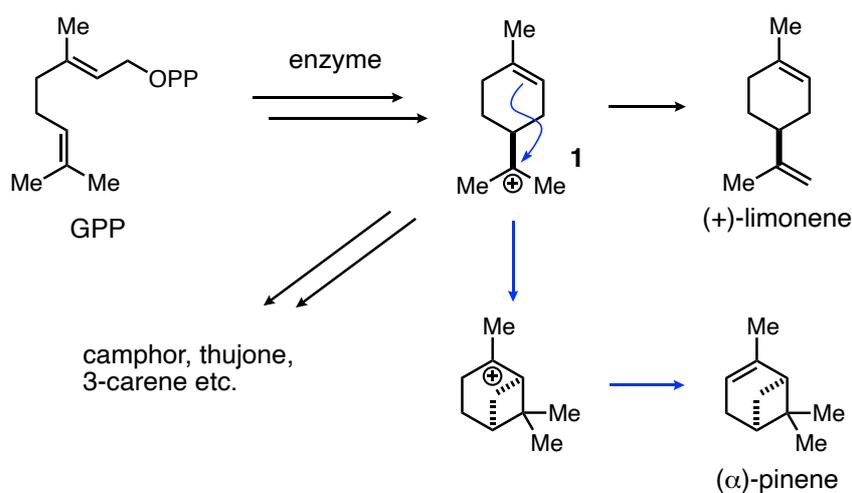

Scheme 1. Structural diversity arising from cationic monoterpenes biosynthesis.

More complex molecules such as lanosterol and cycloartenol, which are precursors of various steroids, are biosynthesized from a single open-chain compound via cationic cyclization and rearrangement cascade reactions (Scheme 2). Squalene oxide, which comes from three equivalents of GPP and an oxidant, undergoes sequential cyclization and subsequent rearrangement upon cleavage of the epoxide ring under the influence of an enzyme. Simple deprotonation of the resulting C8 tertiary cation **2** gives lanosterol, while alternative pathway through 1,2-hydride shift and subsequent cyclopropanation gives cycloartenol.[1]
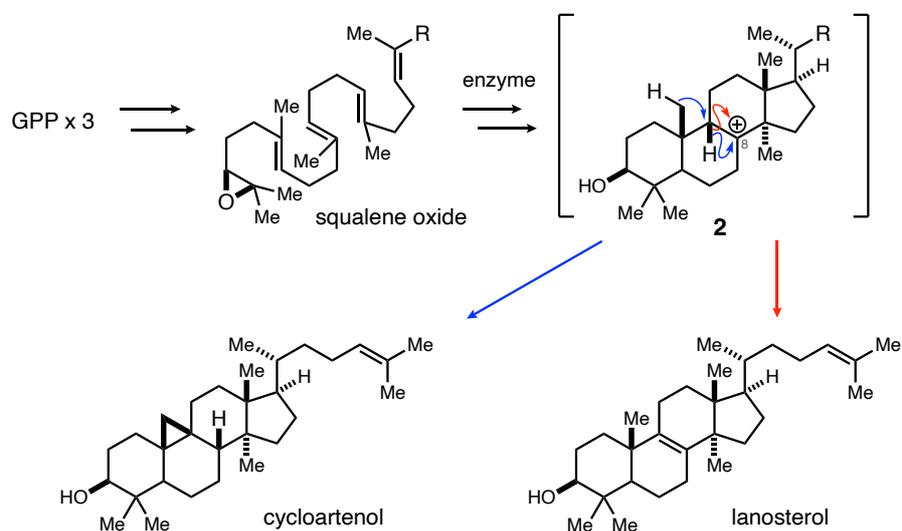
Scheme 2. Carbon framework construction via cation species in biosynthesis of lanosterol and cycloartenol.

Also, cationic electrocyclic reactions have been utilized for the formation of carbocycles in biosynthesis. In a proposed biosynthetic pathway of (3*R*,7*S*)-jasmonic acid (**3**),[2] the five-membered ring is formed via electrocyclization of intermediate **5** which is enzymatically generated from allenepoxide **4** (Scheme 3). The electrocyclization reaction of a pentadienyl cation species is well known as Nazarov cyclization, which has also widely been utilized in organic synthesis including total synthesis of natural products (*vide infra*).
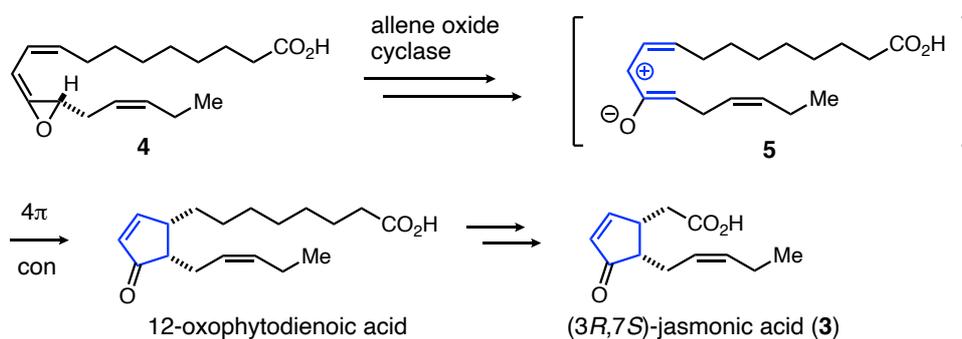
Scheme 3. Cationic electrocyclic reaction (Nazarov cyclization) in biosynthesis.

1.2 Electrocyclic Reactions

1.2.1 Stereochemistry

The electrocyclic reaction is intramolecular cyclization of a conjugated polyene to form a new sigma bond across the ends of the conjugated system, and the reverse process by cleavage of the carbocycle is also called an electrocyclic reaction. The electrocyclic reaction is classified as a pericyclic reaction, and the stereochemistry of the reaction is predictable according to the Woodward-Hoffmann rules (Figure 1).[3] The stereochemistries of the alkenes at the cyclization termini are transcribed to the newly formed two stereogenic sp^3 carbon atoms on the cyclization product. This stereospecificity is explained based on the symmetry of frontier orbitals; thermal 4nπ cyclization proceeds in a conrotatory manner, and *trans*-products are obtained from the substrate bearing R groups at the outer positions. (4n+2)π cyclization proceeds in a disrotatory manner, and *cis*-products are obtained from the same-type substrate. The stereospecificity in

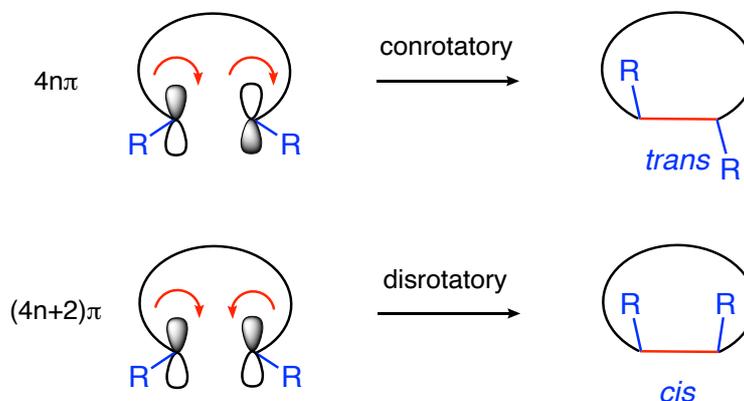thermal reaction become opposite under the photo-irradiated conditions.

Figure 1. Stereochemistry in electrocyclization reactions

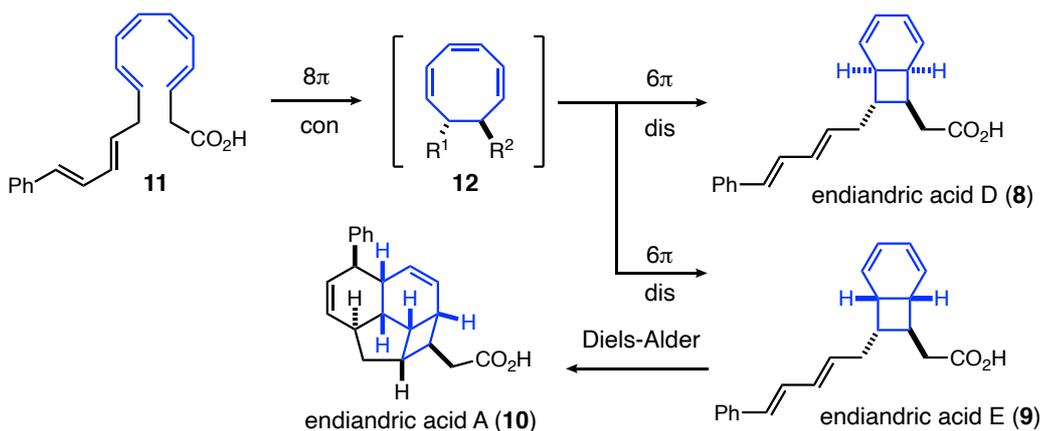## 1.3 Neutral Electrocyclic Reactions in Biosynthesis

Electrocyclic reactions of a neutral molecule are also important in biosynthesis. A 6π electrocyclic reaction is involved in the pathway of eudesmane-type sesquiterpene biosynthesis (Scheme 4).[4] Farnesyl pyrophosphate enzymatically cyclizes to generate ten-membered compound hedycaryol, which is oxidatively transformed into conjugated triene **7**. Finally, thermal 6π electrocyclization of triene **7** in a disrotatory manner affords (+)-occidentalol (**6**) having a *cis*-decalin skeleton.
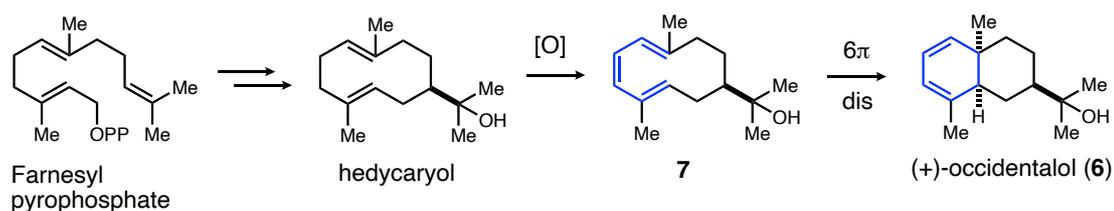
Scheme 4. Proposed biosynthetic pathway of (+)-occidentalol (**6**)

A biosynthetic pathway of endiandric acids is proposed to proceed via an 8π-6π cascade electrocyclization from a polyene compound having an (*E,Z,Z,E*)-1,3,5,7-octatetraene unit (Scheme 5).[5] The precursor of endiandric acids (**8**–**10**), fatty acid (**11**), having a polyene unit, undergoes 8π electrocyclization to give cyclooctatriene **12**, from which 6π electrocyclization

proceeds in a disrotatory manner but non-diastereoselectively, giving rise to both endiandric acid D (**8**) and its diastereomer, endiandric acid E (**9**). Furthermore, endiandric acid A (**10**) is expected to be biosynthesized from endiandric acid E (**9**) by an intramolecular Diels-Alder reaction between a diene side chain and an alkene moiety of a cyclohexadiene moiety.

Scheme 5. Proposed biosynthetic pathway of endiandric acids

Ring-opening electrocyclic reactions also play important roles in the biosynthesis. Vitamin D_3, an essential nutrient for human body is synthesized via a 6π electrocyclic reaction fueled by the sun light (Scheme 6). 7-Dehydrochlesterol undergoes conrotatory 6π electrocyclic ring opening upon irradiation with sun light to generate pre-vitamin D_3, from which vitamin D_3 is produced via 1,7-hydrogen shift.
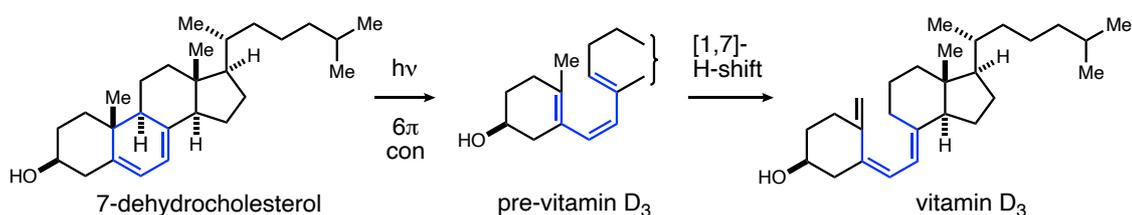

Scheme 6. Biosynthetic pathway of vitamin D_3

Based on the biosynthetic pathway or hypothesis, considerable numbers of biomimetic total synthesis of natural products were accomplished,[6] which proved the efficiency and rationality of the synthetic strategy the nature chose, and the correctness of the hypotheses.

5

1.4 Electrocyclizations in non-Biomimetic Total Synthesis

Electrocyclic reactions have been utilized by organic chemists not only by nature, and this type of reactions cultivated the areas including natural product synthesis. Smith and coworkers constructed the five-membered ring of (–)-calyciphylline N by Nazarov cyclization (Scheme 7).[7a,b] Starting from ketone **13**, preparation of an enol triflate followed by Stille coupling under carbon monoxide atmosphere afforded divinyl ketone **14**. Upon treatment with HBF$_4$·Et$_2$O, **14** underwent Nazarov cyclization via pentadienyl cation **15** to form a cyclopentene moiety of tetracyclic compound **16**.
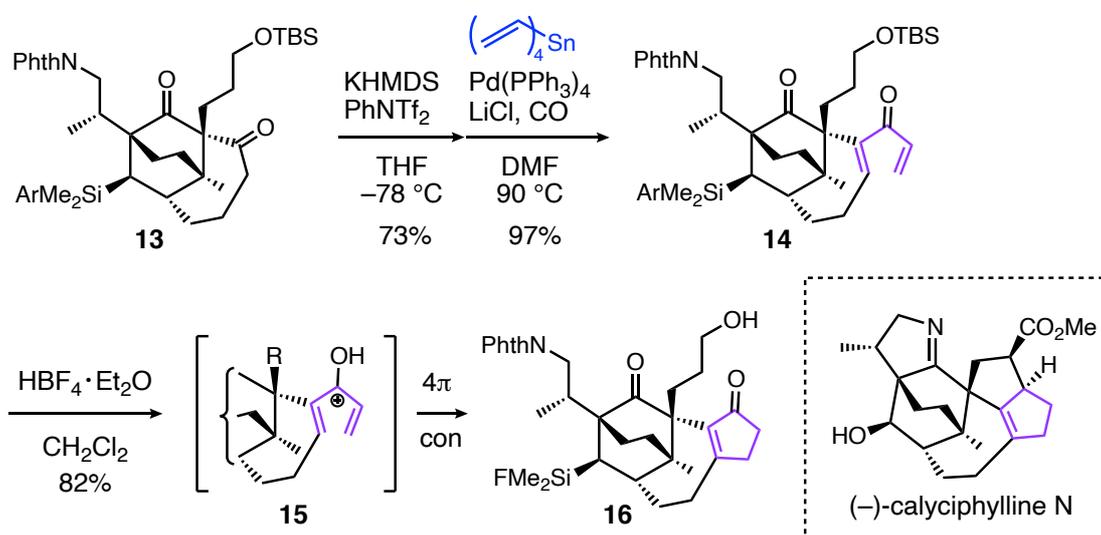
Scheme 7. Total synthesis of (–)-calyciphylline N by Smith and coworkers

In the total synthesis of (–)-oridonin by Liu and coworkers, two contiguous stereogenic centers at the C9 and C10 positions were constructed via conrotatory interrupted Nazarov cyclization (Scheme 8).[8] The cyclization precursor **19** was prepared from two enantioenriched fragments **17** and **18** via a coupling using *tert*-butyllithium (*t*-BuLi). Under the influence of ethylalminum dichloride, 4π electrocyclization of pentadienyl cation **20** occurred to form cyclopentenyl cation **21** which underwent an intramolecular addition reaction with the allyl silane moiety, giving rise to **22** in 64% yield.
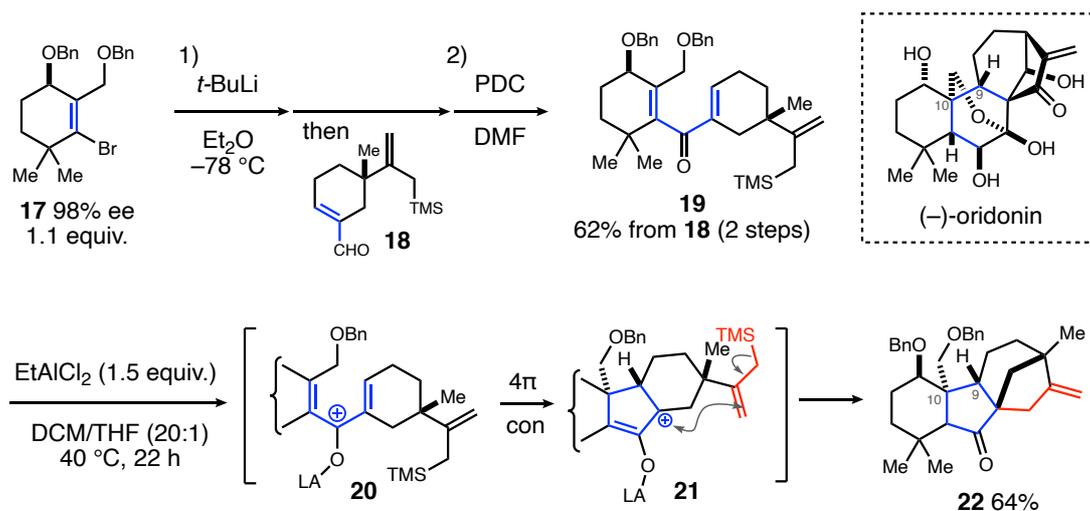
Scheme 8. Total synthesis of (–)-oridonin by Liu and coworkers

The 6π electrocyclization reactions can be utilized for constructing a benzene ring from a 1,3,5-hexatriene moiety[9a–d] as shown in the racemic synthesis of daphenylline by Li and coworkers (Scheme 9).[10] Hexatriene **25**, which was prepared from ketone **23** and vinyl boronate ester **24** via Suzuki-Miyaura coupling, was irradiated with a Hg lump to promote 6π electrocyclization through *E,Z*-isomerization of the alkene moiety. The resulting cyclohexadiene derivative **27** was subjected to aerobic oxidation promoted by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give aromatic compound **28**.
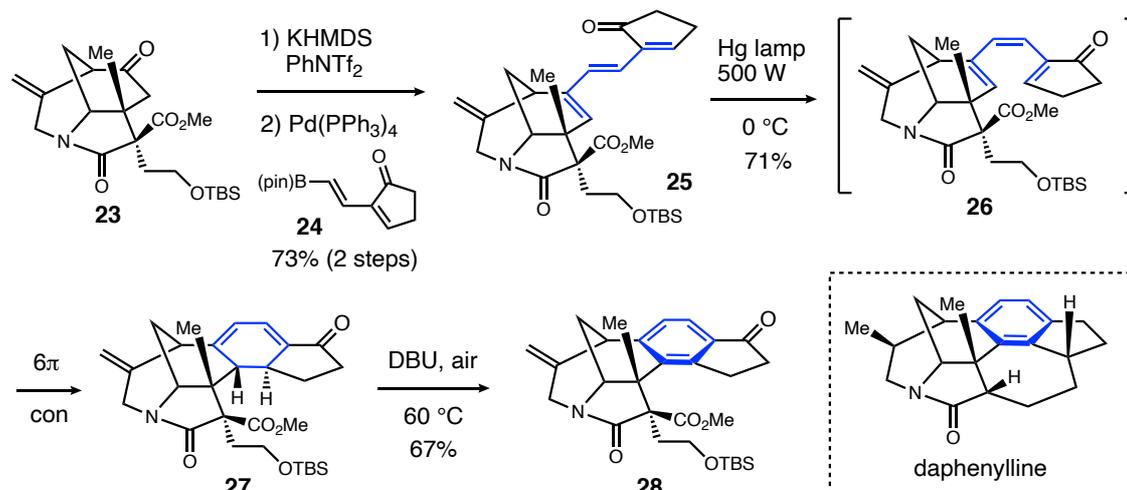
Scheme 9. Total synthesis of daphenylline by Li and coworkers

Talking regard to 8π electrocyclizations in total synthesis, all the successful examples are based on biomimetic pathways, which was shown in Scheme 5.

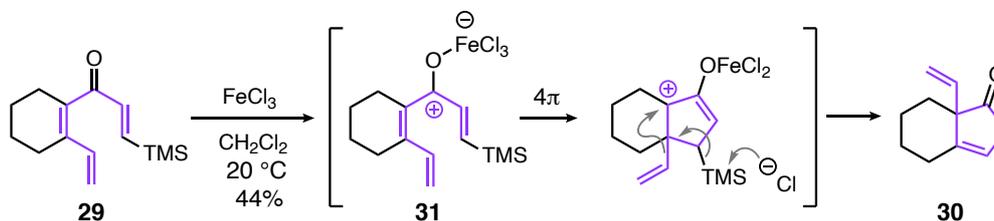## 1.5 Construction of Seven-Membered Carbocycles by Electrocyclization

While cycloheptane rings are found as a substructure of various natural products,[11] the literature search on chemical reactions for the construction of seven-membered carbocycles by electrocyclization resulted in finding a few examples. Moreover, no works on natural product synthesis including this type of transformation has been reported so far.

As possible precursors for carbon seven-membered ring construction by an electrocyclization reaction, heptatrienyl cation or heptatrienyl anion would be presumed (Figure 2).

Figure 2. Possible modes of electrocyclization for a carbon seven-membered construction.

However, the 6π electrocyclization of heptatrienyl cation might suffer from an alternative pathway, namely, Nazarov cyclization. Denmark and coworkers reported that ketone **29** was transformed into five-membered ketone **30** under the influence of FeCl$_3$ at 20 °C (Scheme 10).[12] The result clearly indicated that heptatrienyl cation **31** preferred Nazarov cyclization rather than 6π electrocyclization.

Scheme 10. An example of Nazarov cyclization of heptatrienyl cation

On the other hand, a heptatrienyl anion can undergo 8π electrocyclization to give a seven-membered carbocycle, as was reported by Kleinschmidt and coworkers (Scheme 11).[13] In the report, cycloheptadienes **33** were obtained in high yield from a mixture of trienes **32a** and **32b** via deprotonation and 8π electrocyclization upon treatment with a base. However, some drawbacks remained in this reaction; (i) the reaction conditions using a strong amide base in refluxing cyclohexane are harsh, (ii) the products are obtained as a mixture regarding double bonds due to the non-selective protonation of the anionic intermediate upon quenching the reaction.
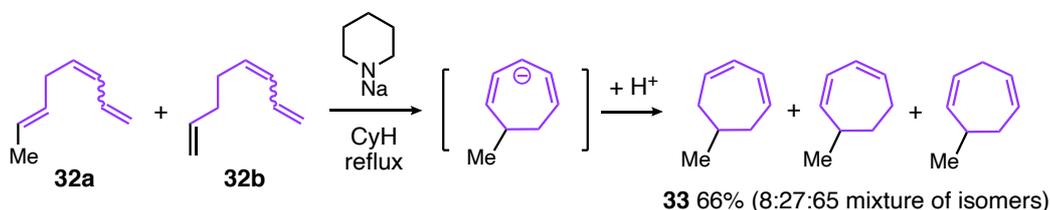
Scheme 11. An example of a seven-membered ring construction by 8π electrocyclization

As explained in Figure 1, electrocyclization enables to establish the relative stereochemistry of sequential two carbon centers on a newly formed ring, which makes this reaction advantageous against other cyclization methods. From these backgrounds, the author decided to develop new reactions for the seven-membered ring formation via 8π electrocyclization reactions of heptatrienyl anion, which would solve the drawbacks described above.

1.6 References

(1)   Kushiro, T.; Ebizuka, Y. *Comprehensive Natural Products II Chemistry and Biology;* Elsevier, Netherlands, 2010.

(2)   (a) Vick, B. A.; Feng, P.; Zimmerman, D. C. *Lipids* **1980**, *15*, 468. (b) Brash, A. R.; Baertschi, S. W.; Ingram, C. D.; Harris, T. M. *J. Biol. Chem.* **1987**, *262*, 15829. (c) Brash, A. R.; Baertschi, S. W.; Harris, T. M. *J. Biol. Chem.* **1990**, *265*, 6705. (d) Hess, B. A.; Smentek, L.; Brash, A. R.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 5603. (e) Grechkin, A. N.; Chechetkin, I. R.; Mukhtarova, L. S.; Hamberg, M. *Chem. Phys. Lipids* **2002**, *120*, 87.

(3)   (a) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395-397. (b) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, Germany, **1970**.

(4)   Hortmann, A. G. *Tetrahedron Lett.* **1968**, *9*, 5785.

(5)   Bandaranayake, W. M.; Banfield, J. E.; Black, D. St. C. *J. Chem. Soc., Chem. Commun.* **1980**, 902.

(6)   For the examples of biomimetic total syntheses including electrocyclic reactions, see: [4π electrocyclization]: Fu, C. C.; Zhang, Y. B.; Xuan, J.; Zhu, C. L.; Wang, B. N.; Ding, H. F. *Org. Lett.* **2014**, *16*, 3376. [6π electrocyclization]: (a) Hortmann, A. G.; Daniel, D. S.; Martinelli, J. E. *J. Org. Chem.* **1973**, *38*, 728. (b) Moses, J. E.; Adlington, R. M.; Rodriguez, R.; Eade, S. J.; Baldwin, J. E. *Chem. Commun.* **2005**, 1687. (c) Miller, A. K.; Trauner, D. *Angew. Chem., Int. Ed.* **2005**,*44*, 4602. [8π/6π cascade electrocyclization]: (e) Nicolaou, K. C.; Petasis, N. A.; Zipkin, R. E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555–5557. (f) Nicolaou, K. C.; Petasis, N. A.; Uenishi, J.; Zipkin, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 5557–5558. (g) Nicolaou, K. C.; Zipkin, R. E.; Petasis, N. A. *J. Am. Chem. Soc.* **1982**, *104*, 5558–5560. (h) Nicolaou, K. C.; Petasis, N. A.; Zipkin, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 5560–5562. (i) Drew, S. L.; Lawrence, A. L.; Sherburn, M. S. *Angew. Chem. Int. Ed.* **2013**, *52*, 4221. (j) Drew, S. L.; Lawrence, A. L.; Sherburn, M. S. *Chem. Sci.* **2015**, *6*, 3886.

(7)   (a) Shvartsbart, A.; Smith, A. B. *J. Am. Chem. Soc.* **2014**, 136, 870–873. (b) Shvartsbart, A.; Smith, A. B. *J. Am. Chem. Soc.* **2015**, *137*, 3510–3519.

(8)   Kong, L.; Su, F.; Yu, H.; Jiang, Z.; Lu, Y.; Luo, T. *J. Am. Chem. Soc.* **2019**, *141*, 20048–20052.

(9)   (a) Li, J.; Yang, P.; Yao, M.; Deng, J.; Li, A. *J. Am. Chem. Soc.* **2014**, *136*, 16477. (b) Yang, P.; Yao, M.; Li, J.; Li, Y.; Li, A. *Angew. Chem., Int. Ed.* **2016**, *55*, 6964. (c) Abe, T.; Ikeda, T.; Yanada, R.; Ishikura, M. *Org. Lett.* **2011**, *13*, 3356. (d) Bian, M.; Wang, Z.; Xiong, X. C.; Sun, Y.; Matera, C.; Nicolaou, K. C.; Li, A. *J. Am. Chem. Soc.* **2012**, *134*, 8078.

(10)   Lu, Z. Y.; Li, Y.; Deng, J.; Li, A. *Nat. Chem.* **2013**, *5*, 679.

(11)   Various bioactive terpenoids and alkaloids bearing seven-membered carbocycles are listed in: (a) Ma, X.; Gang, D. R. *Nat. Prod. Rep.* **2004**, *21*, 752–772. (b) Kobayashi, J.; Kubota, T. *Nat. Prod. Rep.* **2009**, *26*, 936–962. (c) Wang, F.-P.; Chena, Q.-H.; Liu, X.-Y. *Nat. Prod. Rep.* **2010**, *27*, 529–570. (d) Fraga, B. M. *Nat. Prod. Rep.* **2013**, *30*, 1226–1264. (e) Kohnen-Johannsen, K. L.; Kayser, O. *Molecules* **2019**, *24*, 796. (f) Hanson, J. R.; Nichols, T.; Mukhrish, Y.; Bagley, M. C. *Nat. Prod. Rep.* **2019**, *36*, 1499–1512. (g) Hill, R. A.; Connolly, J. D. *Nat. Prod. Rep.* **2020**, *37*, 962–998.

(12)   Denmark, S. E.; Hite, G. A. *Helv. Chim. Acta* **1988**, *71*, 195–208.

(13)   Zuech, E. A.; Crain, D. L.; Kleinschmidt, R. F. *J. Org. Chem.* **1968**, *33*, 771–775；Also, for examples of anionic 8π electrocyclizations, see: (a) Bates, R. B.; Deines, W. H.; McCombs, D. A.; Potter, D. E. *J. Am. Chem. Soc.* **1969**, *91*, 4608. (b) Staley, S. W.; Heyn, A. S. *J. Am. Chem. Soc.* **1975**, *97*, 3852–3854. (c) Gridnev, I. D.; Gurskii, M. E.; Geiderikh, A. V.; Bubnov, Y. N. *Mendeleev Commun.* **1996**, *6*, 185–187. (d) Saitoh, H.; Ijuin, H. K.; Watanabe, N.; Matsumoto, M. *Helv. Chim. Acta* **2013**, *96*, 1704–1713.

CHAPTER 1

Electrocyclization of Heptatrienyl Anion
# with a Leaving Group

2.1 Introduction

In connection with the background described in General Introduction, Ms. Uda, a graduate student of the author's laboratory, found a novel 8π electrocyclization reaction of nitrile **P1** (Scheme 1). Upon treatment with a base, the nitrile having an ammonium salt moiety was converted to 3-methylene-1,4-cycloheptadiene derivative **P5**.[1] The reaction was supposed to occur through deprotonation at an allylic position followed by β-elimination of a cyano group, affording triene **P2** which is a substrate of the one-pot cyclization reaction. Thus, deprotonation of **P2** at the doubly allylic position generates conjugated heptatrienyl anion **P3** which undergoes 8π electrocyclization. Finally, the ammonium ion moiety of the resulting seven-membered anion **P4** is eliminated to afford **P5**. The cyclic triene product was obtained as a single diastereomer possessing two phenyl groups in *trans*-relationship, indicating that the cyclization proceeded in conrotatory fashion. Although this unique cyclization reaction was successfully adapted to a middle range of substrates, formation of undesired cyclopropane **P7** by an intramolecular S$_N$2 reaction of intermediate **P6** led to low yield of the desired product.
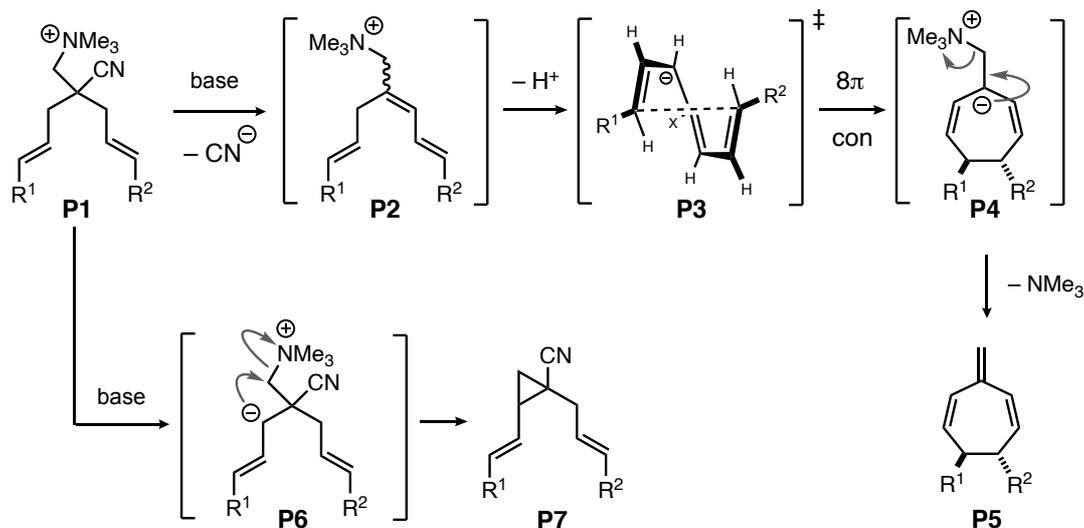
**Scheme 1.** Preceded work described in master's thesis by Uda

Consequently, the author newly designed a substrate having a 1,3,6-heptatriene moiety and a suitable leaving group (X), with a view to avoiding formation of cyclopropane-type side product (Scheme 2).
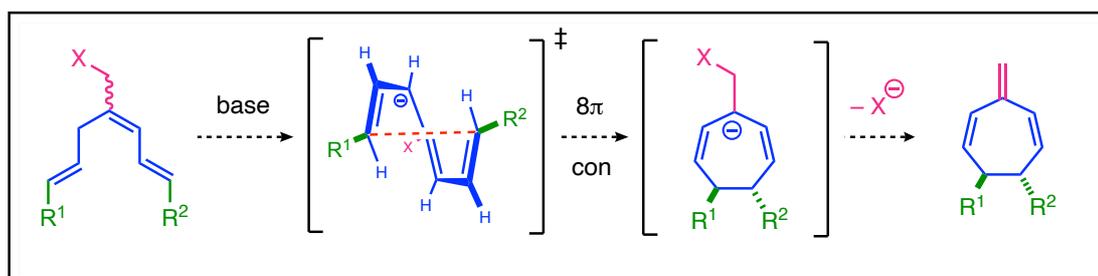
**Scheme 2.** A reaction of a newly designed substrate

2.2 Results and Discussion

The triene substrates were synthesized from a common intermediate (Scheme 3). Thus, the successive treatment of unsaturated ester **1** with lithium diisopropylamide (LDA) and unsaturated aldehyde **2a** afforded the corresponding aldol adduct **3a** in a quantitative yield. The dehydration reaction through mesylation of the hydroxy group of **3a** afforded ester **4a** whose E/Z ratio was assigned by comparing the ^{1}H NMR chemical shift of β−vinyl proton of **4a** with those of ethyl (*E*)- and (*Z*)-2-methyldodecadienoate reported by Radha and coworkers.[2] The E/Z ratio of other related compounds are assigned in the same manner. After reduction of ester **4a** to alcohol **5a** using diisobutylaluminium hydride (DIBAL), the hydroxy group of **5a** was converted to various leaving groups. Unfortunately, **5a** could not be successfully converted to the corresponding chloride or sulfonates owing to the labile nature of the desired products; consequently, alternative derivatives of **5a**, namely, phosphate **6a** and carbamate **7a** were prepared in good yields.
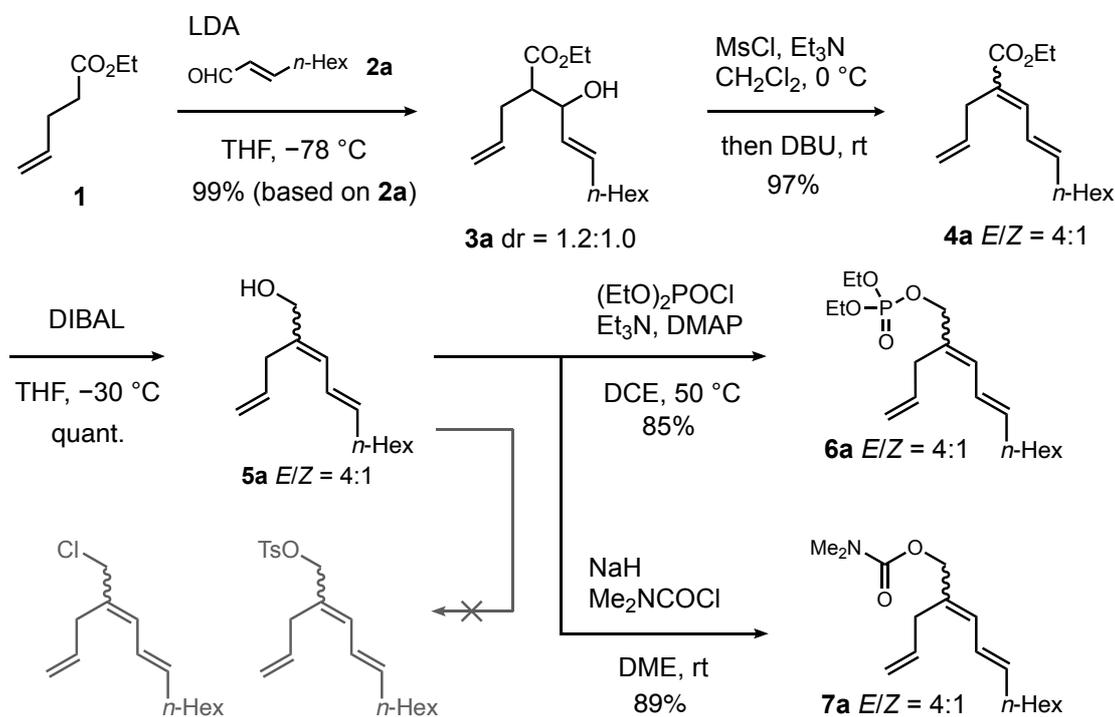

Scheme 3. Preparation of cyclization precursors

14

Extensive investigations revealed that the choice of a suitable base and a substrate with an appropriate leaving group is essential for initiating the desired cyclization reaction (Table 1). Upon treatment with 2.0 equiv of LDA at room temperature, phosphate **6a** did not give the desired compound **8a** (entry 1), and aldehyde **9** was obtained in 53% NMR yield (Scheme 4). Whereas the use of lithium 2,2,6,6-tetramethypyperidide (LTMP) also failed to give the desired compound (entry 2), the reaction with lithium bis(trimethylsilyl)amide (LHMDS) afforded **8a** in 35% NMR yield without the formation of aldehyde **9** (entry 3). The origin of the different behavior of **6a** dependent on bases is not clear, but LDA or LTMP preferentially abstracts the α-proton of the phosphate moiety (Scheme 3). The resulting anion **10** undergoes the retro-phospha-Brook rearrangement to give anion **11**, a precursor of aldehyde **9**.[3] In contrast, LHMDS effects selective deprotonation at the doubly allylic position, resulting in the formation of **8a** through 8π electrocyclization. When sodium bis(trimethylsilyl)amide (NaHMDS) or potassium bis(trimethylsilyl)amide (KHMDS) was used, the NMR yield of **8a** increased to 69% (entry 4) and 64% (entry 6), respectively. The NMR yield of **8a** decreased when lower amount of the base (1.1 equiv.) was used (entries 5 and 7). A similar behavior was observed for the reaction of carbamate **7a** in the presence of LDA, which gave a complex mixture without the formation of **8a** (entry 8). Although the sluggish reaction with LHMDS (entry 9) indicated a lower reactivity of carbamate **7a** compared with that of phosphate **6a** (entry 3), the use of NaHMDS (entry 10) or KHMDS (entry 11) resulted in the formation of **8a** in good yield. The use of lower amount of the base (1.1 equiv.) decreased the NMR yield of **8a** from carbamate **7a** (entry 12).
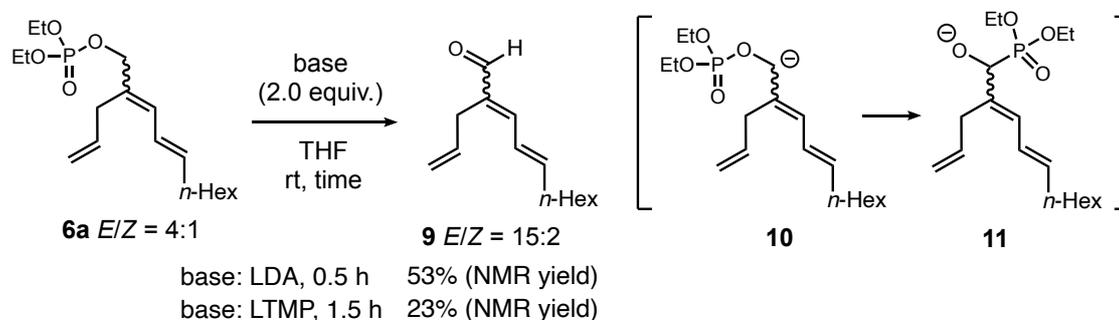
**Scheme 4.** Unexpected reactions of phosphate **6a**

Table 1. Optimization of cyclization reaction
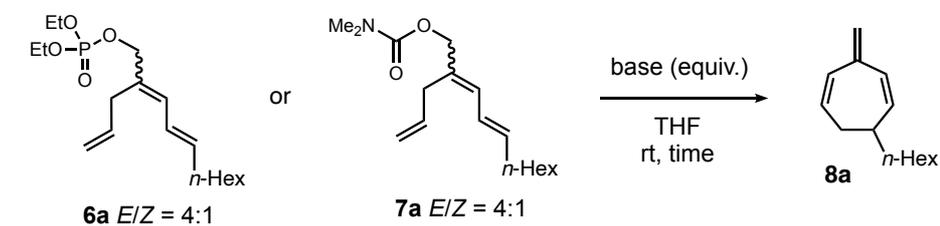
entry	substrate	base (equiv.)	time (h)	8a (NMR yield)
1	6a	LDA (2.0)	0.5	0%[b]
2	6a	LTMP (2.0)	1.5	0%[b]
3	6a	LHMDS (2.0)	1.5	35%
4	6a	NaHMDS (2.0)	1.5	69%
5	6a	NaHMDS (1.1)	1.5	59%
6	6a	KHMDS (2.0)	0.5	64%
7	6a	KHMDS (1.1)	0.5	36%
8	7a	LDA (2.0)	0.5	0%
9	7a	LHMDS (2.0)	2	trace[c]
10	7a	NaHMDS (2.0)	2	72%
11	7a	KHMDS (2.0)	2	64%
12	7a	KHMDS(1.1)	2	55%

[a] Reactions were conducted on a 0.10 mmol scale under an Ar atmosphere using anhydrous THF.
[b] See Scheme 4. [c] NMR yield of **8a** increased to 30% when the reaction was conducted at 50 °C for 3 h

16

With the optimized conditions in hand, the reactivities of separated *E/Z* isomers of **7a** was investigated (Scheme 5). Each *E/Z* isomers of carbamate **7a**, which were partially separated by using silica gel flash column chromatography, was treated with 2.0 equiv of NaHMDS at 50 °C, respectively. These experiments revealed (*E*)-**7a** is more reactive in the cyclization reaction, which afforded **8a** in 84% yield, while the reaction of (*Z*)-**7a** failed to give **8a** in satisfying yield and purity.
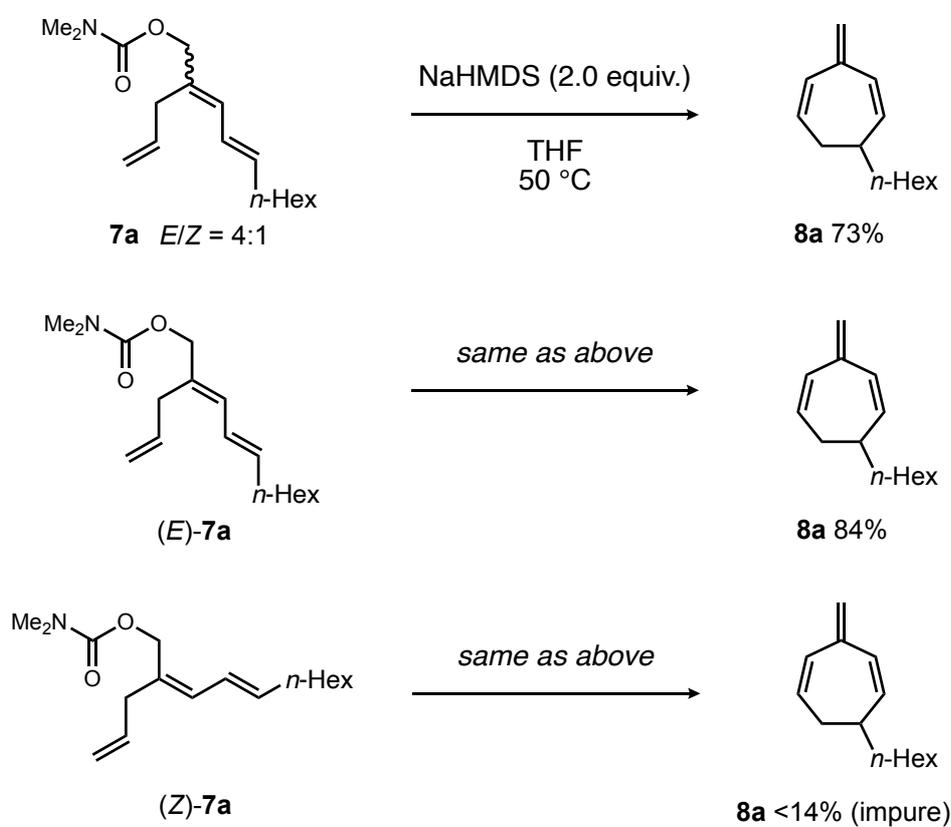

Scheme 5. Comparison of the reactivities of *E/Z* isomers of **7a**

The reaction of (*Z*)-**7a** afforded linear conjugated triene **B** as a major product (Scheme A), suggesting that a side reaction occurred through proton exchange between anionic species **A** and the substrate. While the stereochemistry at the C3-C4 bond in a resonance form (**A'**) should be rotated prior to the cyclization step, the side reaction caused by proton exchange seems to occur faster than the rotation. On the other hand, (*E*)-**7a** directly provides anion **C** having a suitable conformation for the cyclization reaction, giving rise to **8a** in high yield along with a small amount of corresponding conjugated triene.
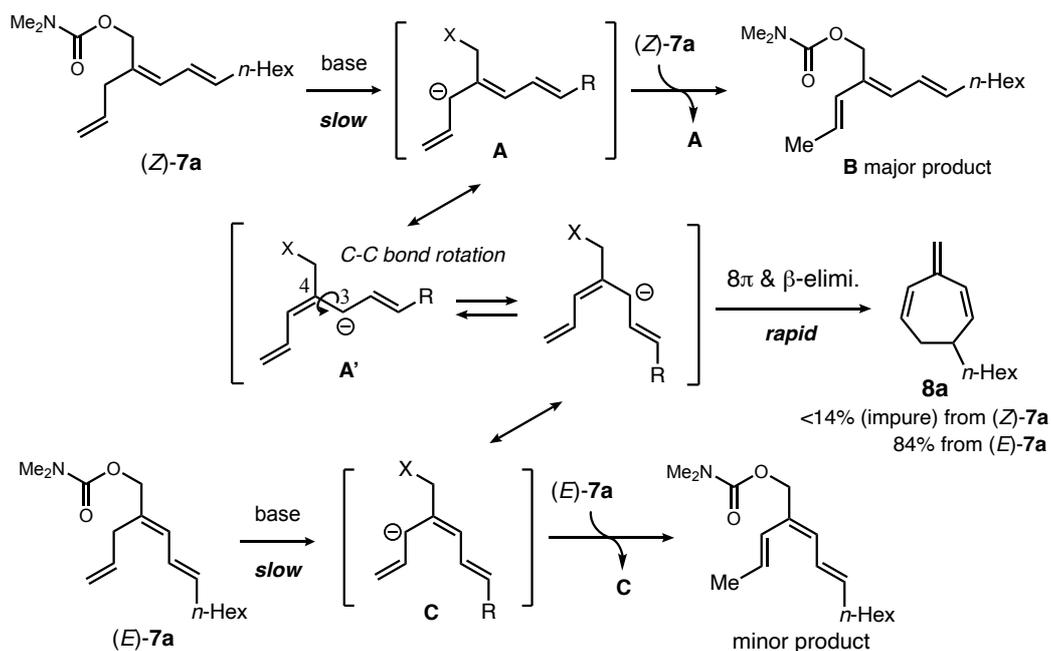

Scheme A. The origin of different reactions between the *E* and *Z* isomers

Next, the scope of the cyclization reaction was explored using several substrates having a carbamate moiety. Owing to the low reactivity of these substrates, the reactions were performed at 50 °C. The reactions of the corresponding phosphates generally proceeded under milder conditions, but the resulting mixture contained inseparable side products, thus hindering the isolation of the desired triene. The 6-alkylated-3-methylene-1,4-cycloheptadienes **8b**, **8c** and **8d** were obtained in moderate to good yields from carbamates **7b**, **7c** and **7d**, respectively (Scheme 6). From **8b** to **8d**, the decrease in the yield were observed. The low yield of **8c** and **8d** would come from the higher ratio of (*Z*)-isomer, which leads to low yield of the cyclization product (see Scheme 5), in **7c** (*E*/*Z*=4:1) and **7d** (*E*/*Z* = 2.6:1.0) rather than sterically hindered C-1 substituents (Cy or *t*-Bu).
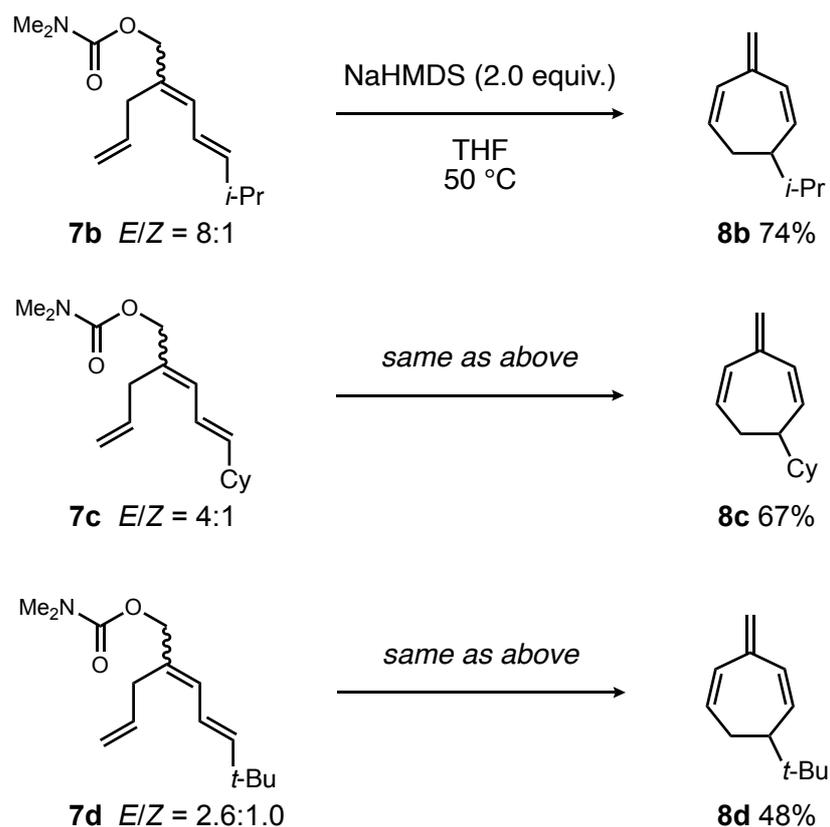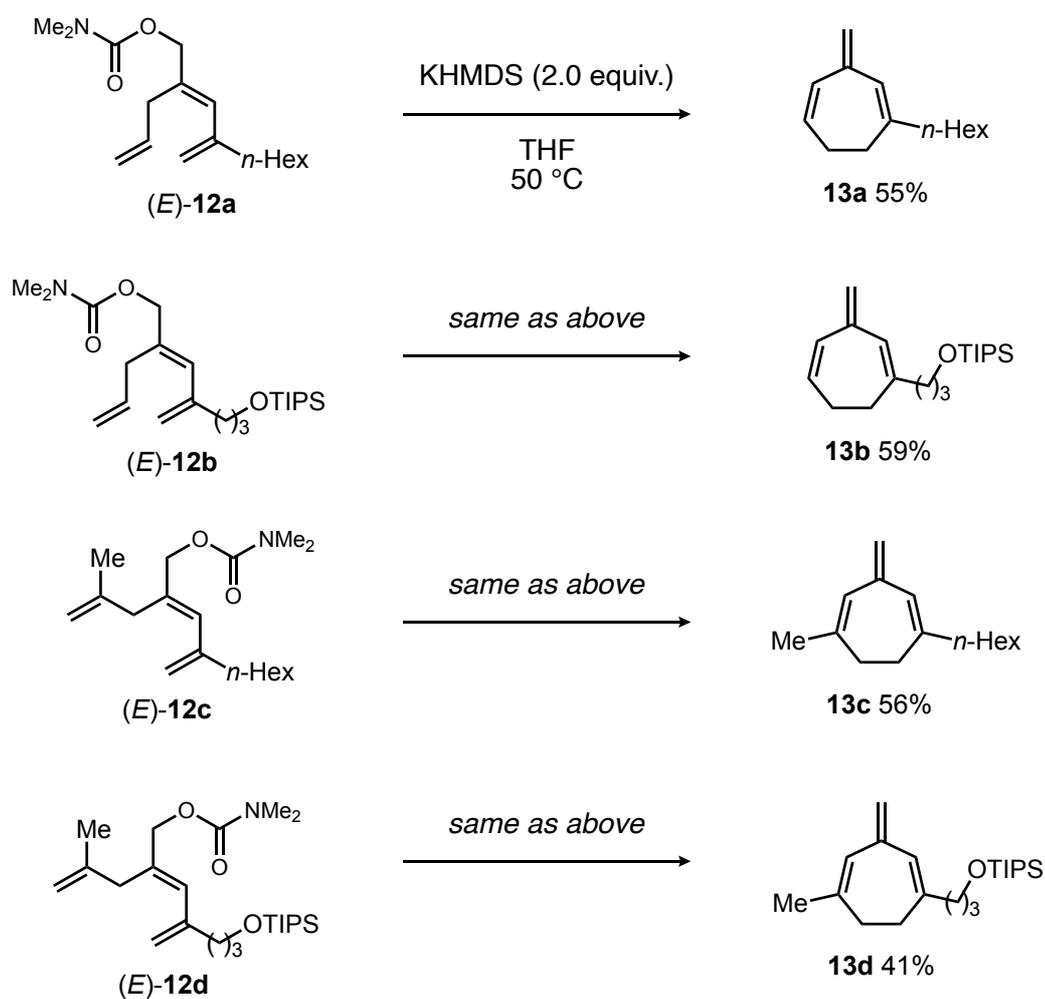

Scheme 6. Synthesis of 6-alkylated-3-methylene-1,4-cycloheptadienes

The alkyl group at the termini of the substrates can be replaced by an aryl group (Scheme 7). The desired product **8e** bearing a phenyl group and **8f** bearing a *p*-methoxyphenyl (*p*-MeO-Ph) group were obtained in good yields from carbamates **7e** and **7f**, respectively. On the other hand, the cyclization reaction of carbamate **7g** having a *p*-bromophenyl (*p*-Br-Ph) group was accompanied with a partial isomerization of double bonds, giving rise to **8g** containing isomeric product *iso*-**8g**. The different behavior of **7g** would be attributable to inductive effect of the bromo group which facilitates deprotonation at the benzylic position under basic conditions. These results indicated that a branched alkyl group or an aryl group at the termini of the substrates does not prevent the cyclization reaction.
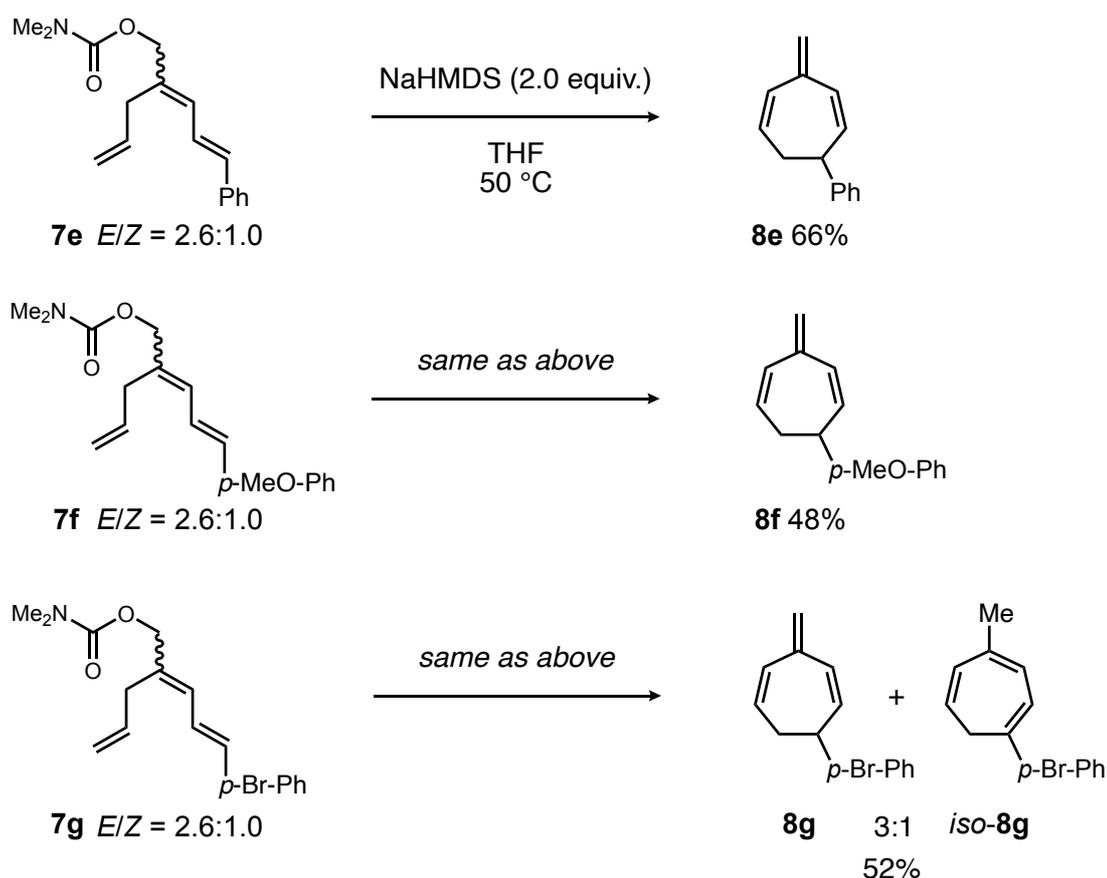

Scheme 7. Synthesis of 6-arylated-3-methylene-1,4-cycloheptadienes

1-Substituted- and 1,5-disubstituted-3-methylene-1,4-cycloheptadienes **13a**, **13b**, **13c**, and **13d** were synthesized by the treatment of carbamates (*E*)-**12a**, (*E*)-**12b**, (*E*)-**12c**, and (*E*)-**12d** with KHMDS (Scheme 8). Notably, each substrate **12a–d** was obtained as a (*E*)-isomer by the preparative method described in Scheme 3, while the yields of the cyclized products were moderate. The silyloxy groups of (*E*)-**12b** and (*E*)-**12d** were not affected under basic conditions.

Scheme 8. Synthesis of 1-substituted- and 1,5-disubstituted-3-methylene-1,4-cycloheptadienes

Seven-membered trienes **15** and **17**, which possess a quaternary carbon center, were obtained in moderate yields from carbamates **14** and **16**, respectively (Scheme 9). The reaction of **14** with 2.0 equiv of KHMDS resulted in the formation of an inseparable mixture of **15** and its isomer of double bonds, but pure **15** could be obtained by using a smaller amount of the base (1.1 equiv.).
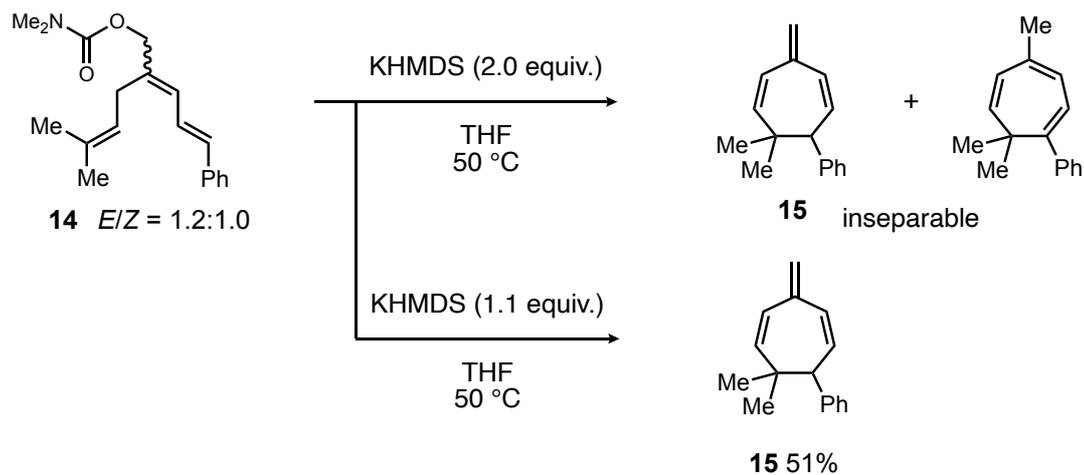
Scheme 9. Construction of a quaternary carbon center

The present cyclization reaction can also be employed for the construction of bicyclic or tricyclic skeletons (Scheme 10). Carbamates (*E*)-**18a** and (*E*)-**18b** afforded the corresponding hydroazulene derivatives **19a** and **19b** in good yields, respectively. Substrates (*E*)-**20a** and **20b**, which have two cycloalkene moieties at the termini, also underwent cyclization reactions, giving tricyclic products **21a** and **21b** in moderate yields, respectively.
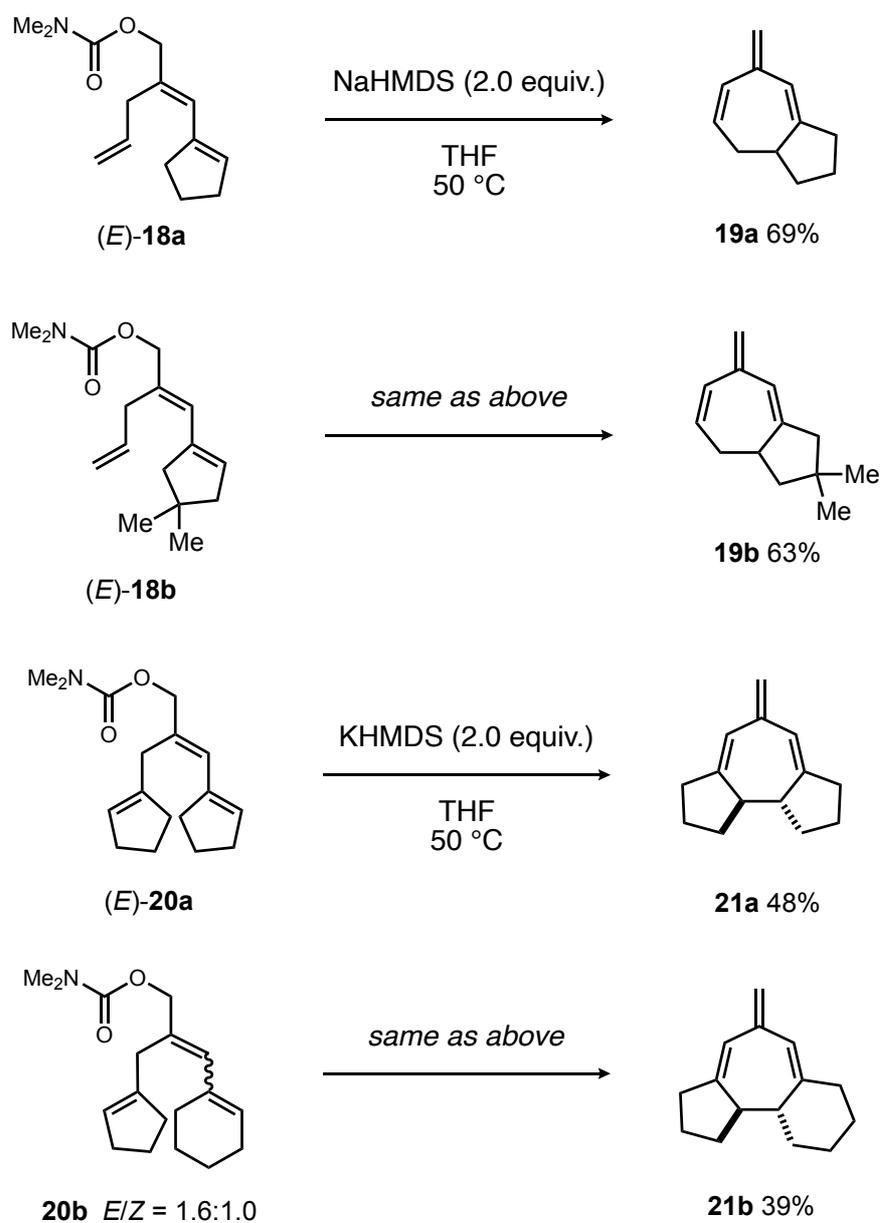
Scheme 10. Synthesis of bicyclic and tricyclic compounds

It should be noted that **21a** and **21b** were obtained as a single diastereomer, and the configuration of these compounds is consistent with a conrotatory 8π electrocyclization reaction. The configuration of **21a** was determined after cyclopropanation of the methylene group through Simmons-Smith reaction (Scheme 11). The C2 molecular symmetry of the product was confirmed by observing the ^{13}C NMR spectra, which showed 8 peaks including a pair of equivalent methylene carbon atoms of the cyclopropane moiety. The configuration of **21b** was assumed by analogy based on that of **21a**.
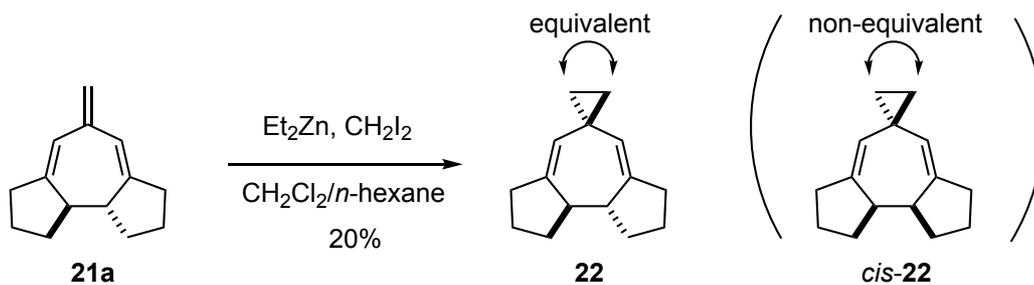
Scheme 11. Determination of the *trans*-configuration of **21a** after cyclopropanation

There are a few examples of the transformation of 3-methylene-1,4-cycloheptadiene derivatives.[4] Therefore, the author focused on the highly unsaturated nature of the triene, which renders it a useful precursor of a tropylium ion, a non-benzenoid aromatic species. The chemistry of the tropylium ion has attracted significant attention, especially in the field of organocatalysis.[5–7] First, cross-conjugated triene **8a** was subjected to double-bond isomerization in the presence of potassium *t*-butoxide (*t*-BuOK) in dimethyl sulfoxide (DMSO) to afford a more stable linearly conjugated triene **23** along with its regioisomers (Scheme 12). Upon treatment with tritylium tetrafluoroborate,[8] the mixture was converted to the desired tropylium salt **24** in good yield.
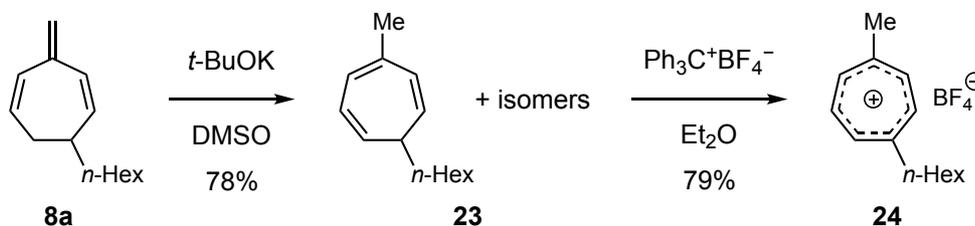
Scheme 12. Transformation of cross-conjugated cyclic triene into tropylium salt

2.3 Conclusion

In conclusion, the author developed a new method for the synthesis of 3-methylene-1,4-cycloheptadiene derivatives via an 8π electrocyclization reaction (Scheme 13). In the presence of NaHMDS or KHMDS, a heptatrienyl anion intermediate **c-4** was generated from triene substrate **c-3**, which was readily prepared from γ,δ-unsaturated esters **c-1** and α,β-unsaturated aldehydes **c-2** in four steps. By using substrates bearing a phosphate or a carbamate moiety, the resulting cycloheptadienyl anions were smoothly converted to cross-conjugated cyclic trienes through β-elimination. These leaving groups are important for facilitating the generation of heptatrienyl anions, which led the author to conduct the reaction under milder conditions than those required for conventional methods. Various 3-methylene-1,4-cycloheptadene derivatives were prepared including bicyclic and tricyclic compounds, which shows significant potential of this reaction as a key step in the total synthesis of terpenoids.
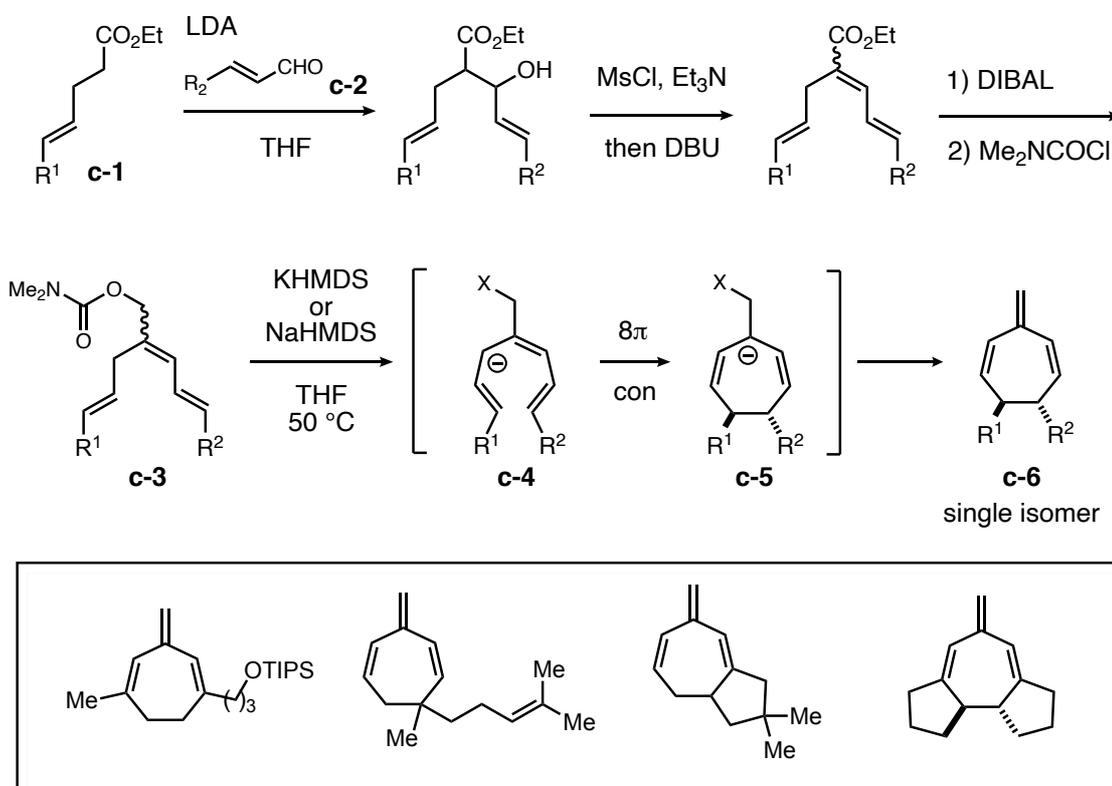
Scheme 13. 8π electrocyclization of heptatrienyl anion with a leaving group

2.4 References

(1)   Uda, S. Master's thesis, Hokkaido University, 2019.

(2)   (a) Falck, J. R.; He, A.; Fukui, H.; Tsutsui, H.; Radha, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4527–4529. (b) Wadsworth, D. H.; Schupp, O. E., III; Seus, E. J.; Ford, J. A., Jr. *J. Org. Chem.* **1965**, *30*, 680–685. (c) Kinstle, T. H.; Mandanas, B. Y. *Chem. Commun.* **1968**, 1699–1700.

(3)   (a) Hamerschmidt, F.; Hanninger, A. *Chem. Ber.* **1995**, *128*, 823–830. (b) Hammerschmidt, F.; Schmidt, S. *Chem. Ber.* **1996**, *129*, 1503–1508.

(4)   An example of the transformation of 3-methylen-1,4-cycloheptadiene: Williams, D. R.; Reeves, J. T. *J. Am. Chem. Soc.* **2004**, *126*, 3434–3435.

(5)   (a) Lyons, D. J. M.; Crocker, R. D.; Enders, D.; Nguyen, T. V. *Green Chem.* **2017**, *19*, 3993–3996. (b) Oss, G.; Ho, J.; Nguyen, T. V. *Eur. J. Org. Chem.* **2018**, *2018*, 3974–3981. (c) Tran, U. P. N.; Oss, G.; Pace, D. P.; Ho, J.; Nguyen, T. V. *Chem. Sci.* **2018**, *9*, 5145–5151. (d) Hussein, M. A.; Huynh, V. T.; Hommelsheim, R.; Koenigs, R. M.; Nguyen, T. V. *Chem. Commun.* **2018**, *54*, 12970–12973. (e) Omoregbee, K.; Luc, K. N. H.; Dinh, A. H.; Nguyen, T. V. *J. Flow Chem.* **2020**, *10*, 161–166. (f) Empel, C.; Nguyen, T. V.; Koenigs, R. M. *Org. Lett.* **2021**, *23*, 548–553. (g) Ton, N. N. H.; Mai, B. K.; Nguyen, T. V. *J. Org. Chem.* **2021**, *86*, 9117–9133.

(6)   (a) Allen, J. M.; Lambert, T. H. *J. Am. Chem. Soc.* **2011**, *133*, 1260–1262. (b) Oss, G.; de Vos, S. D.; Luc, K. N. H.; Harper, J. B.; Nguyen, T. V. *J. Org. Chem.* **2018**, *83*, 1000–1010.

(7)   Ferrer, S.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2016**, *55*, 11178–11182. (b) Herlé, B.; Holstein, P. M.; Echavarren, A. M. *ACS Catal.* **2017**, *7*, 3668–3675. (c) Mato, M.; Herlé, B.; Echavarren, A. M. *Org. Lett.* **2018**, *20*, 4341–4345. (d) Mato, M.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2019**, *58*, 2088–2092. (e) García-Morales, C.; Pei, X.-L.; Sarria Toro, J. M.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2019**, *58*, 3957–3961. (f) Yin, X.; Zuccarello, G.; García-Morales, C.; Echavarren, A. M. *Chem. Eur. J.* **2019**, *25*, 9485–9490. (g) Mato, M.; García-Morales, C.; Echavarren, A. M. *ACS Catal.* **2020**, *10*, 3564–3570. (h) Armengol-Relats, H.; Mato, M.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2021**, *60*, 1916–1922. (i) Mato, M.; Montesinos-Magraner, M.; Sugranyes, A. R.; Echavarren, A. M. *J. Am. Chem. Soc.* **2021**, *143*, 10760–10769.

(8)   Dauben, H. J., Jr.; Honnen, L. R.; Harmon, K. M. *J. Org. Chem.* **1960**, *25*, 1442–1445.

2.5 Experimental Section

General Information

The reactions were performed using flame-dried glasswares under a positive pressure of argon. Oil bath was used when reactions required heating. Tetrahydrofuran (THF) and Et_2O were distilled from sodium benzophenone ketyl. Anhydrous dichloromethane and toluene were purchased from Kanto Chemical Co. Other anhydrous solvents were purchased from chemical companies. Diisopropylamine, diethylamine, and triethylamine were distilled from CaH_2 under argon and stored in the presence of NaOH (pellets). (*E*)-3-cyclohexylpropenal[1] was prepared by the known procedures. All other reagents were used as received from commercial sources without further purification.
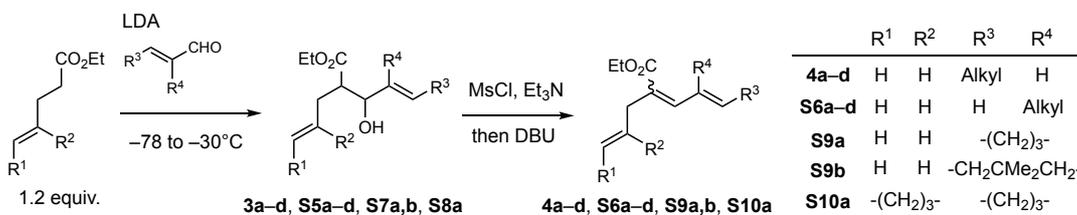
Analytical thin layer chromatography (TLC) was performed using 0.25 mm Silica gel (60F-254) plates purchased from Merck Millipore or Chromatorex NH-TLC Plates from Fuji Silysia Chemical Ltd. Reaction components were visualized by illumination with ultraviolet light (254 nm) and by staining with 8% ethanolic phosphomolybdic acid, ceric ammonium molybdate in 10% sulfuric acid, or basic potassium permanganate solution. Flash column chromatography was performed with Silica Gel 60N (neutral, particle size 40–50 μm) purchased from Kanto Chemical Co., Inc. or Chromatorex NH-DM1020 from Fuji Silysia Chemical Ltd. Preparative thin layer chromatography (PTLC) was performed using PLC Silica Gel 60 F254 purchased from Merck Millipore.

The melting points were determined using an AS ONE ATM-02 apparatus and uncorrected. ^{1}H (500 MHz) and ^{13}C (126 Hz) NMR spectra were measured using a JEOL ECA-500. Chemical shifts are reported in parts per million (ppm) with internal $CDCl_3$ (^{1}H NMR, δ_H 7.26. ^{13}C NMR, δ_C 77.0). Signals are expressed as broad (br), singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), septet (sept), and multiplet (m). Coupling constants are reported in Hz. IR spectra were recorded on JASCO FT/IR-4100 and the major absorbance bands are all reported in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-T100GCV (GC-TOFMS).
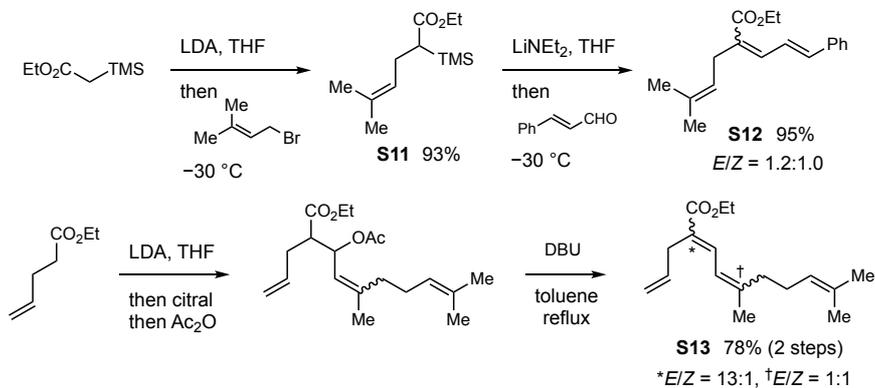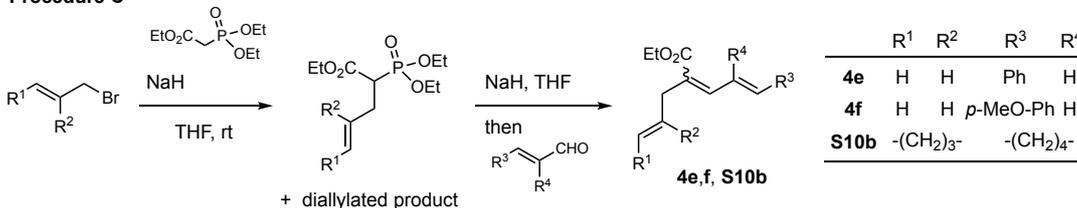
Experimental and Characterization Details

Outline for Preparation of Cyclization Precursors

Procedures A and B

	R^1	R^2	R^3	R^4
4a–d	H	H	Alkyl	H
S6a–d	H	H	H	Alkyl
S9a	H	H	-(CH$_2$)$_3$-	
S9b	H	H	-CH$_2$CMe$_2$CH$_2$-	
S10a	-(CH$_2$)$_3$-		-(CH$_2$)$_3$-	

Procedure C

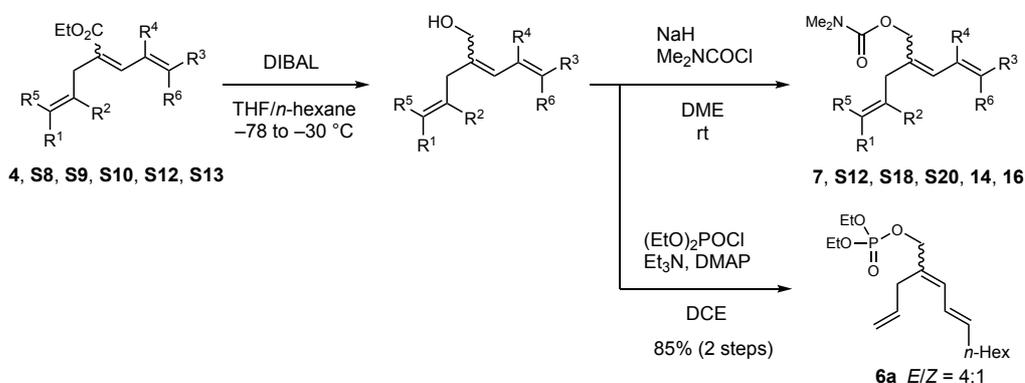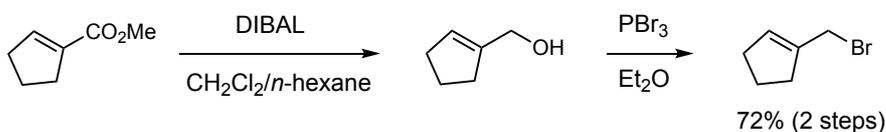|	R^1	R^2	R^3	R^4
4e	H	H	Ph	H
4f	H	H	p-MeO-Ph	H
S10b	-(CH$_2$)$_3$-		-(CH$_2$)$_4$-	

Procedure D

Synthesis of 1-(Bromomethyl)cyclopent-1-ene

To a solution of methyl 1-cyclopentene-1-carboxylate (612 μL, 5.00 mmol) in CH_2Cl_2 (25 mL) was added a 1.03 M solution of DIBAL in n-hexane (10.7 mL, 11.0 mmol) at –78 °C. After stirring for 15 min, the reaction was quenched with saturated aqueous Rochelle salt (30 mL), and the biphasic mixture was stirred vigorously overnight. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a crude material.

To a solution of the crude alcohol in Et_2O (25 mL) was added PBr_3 (237 μL, 2.50 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was warmed to room temperature and stirred for 21 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL), the two layers were separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, n-hexane/EtOAc = 20:1) afforded the title compound (579 mg, 3.60 mmol, 72% for 2 steps). ^{1}H NMR spectral property in $CDCl_3$ was identical to that reported.[2]

Preparation of γ,δ-Unsaturated Esters

Ethyl 4-methyl-4-pentenoate
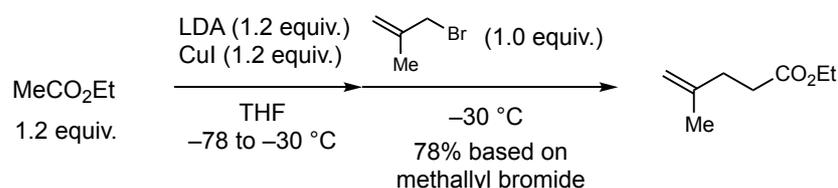
To a solution of i-Pr_2NH (1.69 mL, 12.0 mmol) in THF (50 mL) was added a 2.69 M solution of n-BuLi in n-hexane (4.46 mL, 12.0 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was cooled to –78 °C and $MeCO_2Et$ (1.17 mL, 12.0 mmol) and CuI (2.29 g, 12.0 mmol) were added successively. The reaction mixture was then warmed to –30 °C and stirred for 30 min at the temperature. To this mixture was added methallyl bromide (1.02 mL, 10.0 mmol) and the reaction mixture was stirred for 10 min at the same temperature. The reaction was quenched with

29

saturated aqueous NH$_4$Cl (30 mL). The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 20 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-pentane/Et$_2$O = 20:1) afforded the title compound (1.11 g, 7.81 mmol, 78%). ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[3]

Ethyl 3-(cyclopenten-1-yl)propanoate
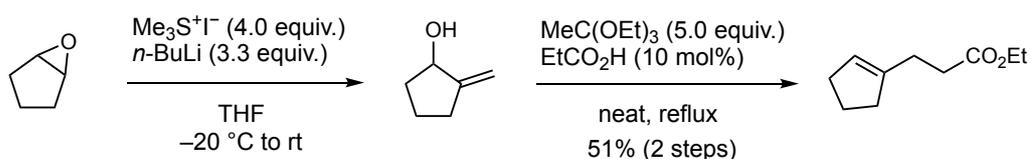
To a solution of trimethylsulfonium iodide (8.16 g, 40.0 mmol) in THF (50 mL) was added a 2.64 M solution of *n*-BuLi in *n*-hexane (12.5 mL, 33.0 mmol) at –20 °C. After stirring for 30 min, cyclopentene oxide (867 µL, 10.0 mmol) was added to the reaction mixture. The reaction mixture was then warmed to room temperature over 30 min and stirred for 1.5 h at the temperature. Then, the reaction was quenched with H$_2$O (30 mL). The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 30 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure to give a crude allyl alcohol.

To a solution of crude allyl alcohol in triethyl orthoacetate (9.11 mL, 50.0 mmol) was added propionic acid (74.1 µL, 1.00 mmol), and the reaction mixture was refluxed at 145 °C for 4 h. The reaction mixture was then cooled to room temperature. Et$_2$O (10 mL) and 1 M aqueous HCl (10 mL) were added to the reaction mixture, and the mixture was stirred for 1.5 h. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 10 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 20:1) afforded the title compound (859 mg, 5.11 mmol, 51% for 2 steps). ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[4]

Synthesis of 4,4-Dimethylcyclopentene-1-carbaldehyde (S4)

Nitrile aldol reaction the author developed before current work was used (**S2**→**S3**) for the construction of a five-membered ring contained in **S4**.[5]
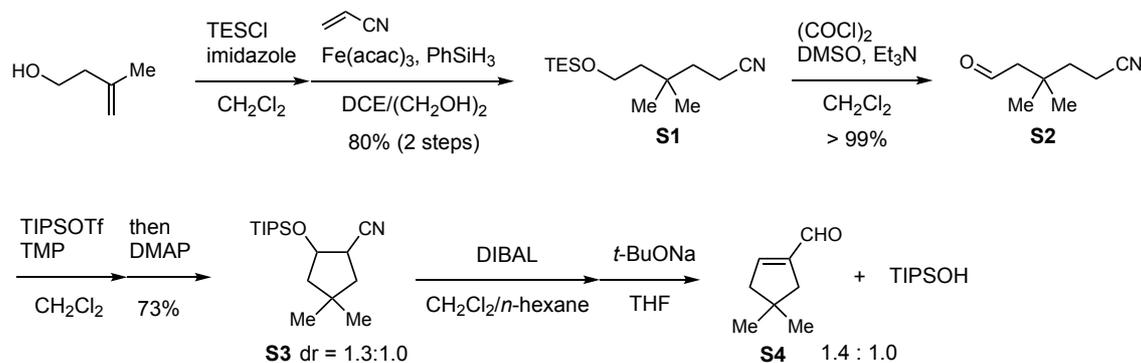

4,4-Dimethyl-6-((triethylsilyl)oxy)hexanenitrile (S1)
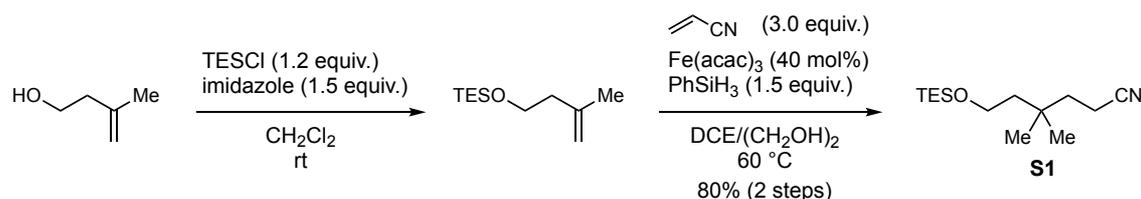
To a solution of imidazole (1.02 g, 15.0 mmol) and 3-methyl-3-buten-1-ol (1.01 mL, 10.0 mmol) in CH_2Cl_2 (20 mL) was added TESCl (2.01 mL, 12.0 mmol) at 0 °C. The reaction mixture was then warmed up to room temperature and stirred for 1 h. Then, the reaction mixture was cooled to 0 °C and added MeOH (1 mL). After stirring at room temperature for several minutes, the solvent was removed under reduced pressure. The resulting mixture was filtered through a pad of Celite® and the residue was washed with *n*-hexane. The resulting filtrate was concentrated to give a crude material.

The transformation of the silylated product to **S1** was conducted referred to the Baran's procedures.[6] To a solution of the crude material in DCE and ethylene glycol (100 mL, 5:1) were added Fe(acac)₃ (1.41 g, 4.00 mmol), acrylonitrile (1.97 mL, 30.0 mmol), and PhSiH₃ (1.84 mL, 15.0 mmol) successively at room temperature. The reaction mixture was then warmed to 60 °C and stirred for 1 h. The reaction was cooled to room temperature and quenched with brine (50 mL). The two layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layer was washed with brine (100 mL), dried over $MgSO_4$, filtered, and

concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 20:1) afforded **S1** (2.04 g, 7.98 mmol, 80% for 2 steps).

S1: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.66 (t, *J* = 6.9 Hz, 2H), 2.31 (t, *J* = 8.2 Hz, 2H), 1.67 (t, *J* = 8.2 Hz, 2H), 1.47 (t, *J* = 6.9 Hz, 2H), 0.96 (t, *J* = 7.8 Hz, 9H), 0.93 (s, 6H), 0.60 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 120.5, 59.1, 43.1, 37.6, 32.2, 26.9 (2C), 12.4, 6.8 (3C), 4.3 (3C). IR (ATR) ν 2955, 2875, 2247, 1459, 1092, 1001, 726 cm^{-1}. HRMS (FD) *m/z* [M + H]$^+$ calcd for C$_{14}$H$_{30}$NOSi 256.2097; found: 256.2085.

4,4-Dimethyl-6-oxohexanenitrile (S2)
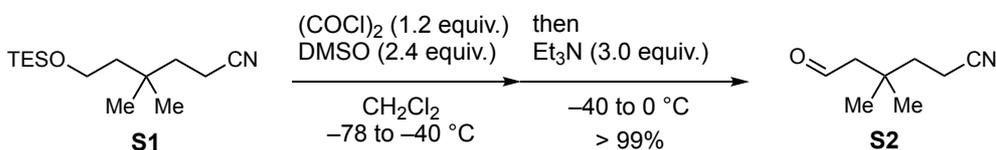
To a solution of oxalyl chloride (822 μL, 9.58 mmol) in CH$_2$Cl$_2$ (30 mL) was added DMSO (1.36 mL, 19.2 mmol) in CH$_2$Cl$_2$ (5.0 mL) at –78 °C, and the reaction mixture was stirred for 15 min. To this mixture was added alcohol **S1** (2.04 g, 7.98 mmol) in CH$_2$Cl$_2$ (3.0 mL) and the reaction mixture was warmed to –40 °C over 30 min. The resulting mixture was stirred for 20 min at the same temperature before Et$_3$N (3.28 mL, 23.5 mmol) was added. The reaction mixture was then warmed to 0 °C and stirred for 20 min. The reaction was quenched with saturated aqueous NH$_4$Cl. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 20 mL). The combined organic layer was washed with brine (50 mL), dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1 to 2:1) afforded aldehyde **S2** (1.11 g, 7.97 mmol, >99%).

S2: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.83 (t, *J* = 2.9 Hz, 1H), 2.35–2.31 (m, 4H), 1.78 (t, *J* = 8.0 Hz, 2H), 1.11 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 201.8, 119.8, 53.9, 37.3, 33.1, 26.7 (2C), 12.3. IR (ATR) ν 2964, 2875, 2738, 2247, 1716, 1472 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_8$H$_{13}$NO 139.0997; found: 139.1004.

## 4,4-Dimethyl-2-((triisopropylsilyl)oxy)cyclopentane-1-carbonitrile (S3)
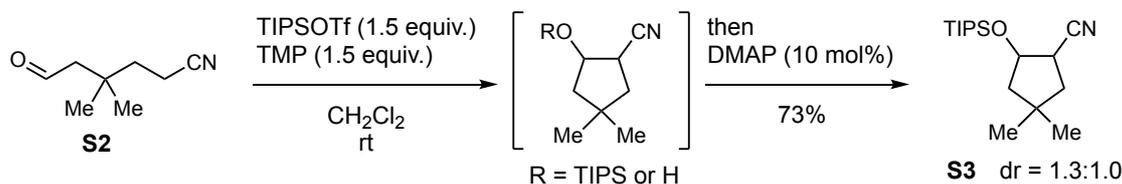
To a solution of cyanoaldehyde **S2** (1.12 g, 8.02 mmol) in CH_2Cl_2 (40.0 mL) were added 2,2,6,6-tetramethylpiperidine (TMP) (2.05 mL, 12.0 mmol) and TIPSOTf (3.23 mL, 12.0 mmol) successively at room temperature. After stirring for 45 min, 4-dimethylaminopyridine (DMAP) (95.1 mg, 0.778 mmol) was added and the reaction mixture was stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, n-hexane/EtOAc = 50:1 to 20:1) afforded **S3** (1.74 g, 5.89 mmol, 73%) as a 1.3:1.0 mixture of diastereomers.

S3 (dr = 1.3:1.0): yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 4.61 (q, J = 6.9 Hz, 0.37H), 4.52 (q, J = 5.5 Hz, 0.63H), 2.97–2.93 (m, 0.63H), 2.85–2.80 (m, 0.37H), 2.05–1.68 (m, 4H), 1.20 (s, 0.63 × 3H), 1.11–1.05 (m, 0.73 × 21H + 0.37 × 27H), 0.98 (s, 0.63 × 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 122.4, 120.3, 77.8, 74.1, 50.1, 49.9, 43.3, 43.1, 38.1, 38.0, 36.9, 36.8, 30.9, 30.3, 30.1, 29.7, 18.0, 17.9, 12.1, 12.0 (Only the detected signals were recorded). IR (ATR) ν 2944, 2867, 2240, 1463, 881, 681 cm^{-1}. HRMS (FI) m/z $[M]^+$ calcd for $C_{17}H_{33}NOSi$ 295.2331; found: 295.2320.

NOTE: DMAP was added to promote silylation of concomitant β-hydroxynitrile, but the reproducibility of this step was low.

4,4-Dimethylcyclopentene-1-carbaldehyde (S4)
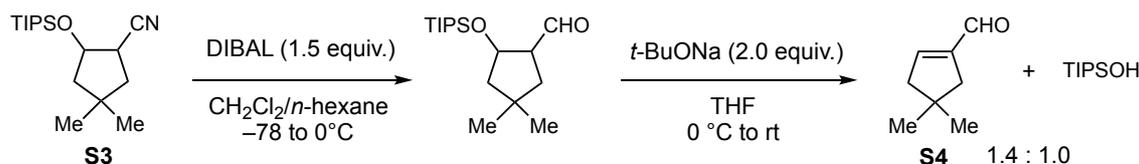
To a solution of **S3** (887 mg, 3.00 mmol) in CH_2Cl_2 (15 mL) was added a 1.03 M solution of DIBAL in n-hexane (4.37 mL, 4.50 mmol) at –78 °C. The reaction mixture was then warmed to

0 °C and stirred for 1.5 h. The reaction was quenched with 10% aqueous tartaric acid (10 mL), and the biphasic mixture was vigorously stirred overnight. The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a crude material.

To a solution of the crude aldehyde in THF (15 mL) was added t-BuONa (577 mg, 6.00 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 40 min. The reaction was quenched with saturated aqueous NH_4Cl (15 mL). The two layers were separated, and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, n-pentane/Et_2O = 30:1, 20:1 to 5:1) afforded **S4** as a 1.4:1.0 mixture with TIPSOH (480 mg). The obtained mixture was directly used for the next step without further purification.

Preparation of Other α,β-Unsaturated Aldehydes

2-Methyleneoctanal
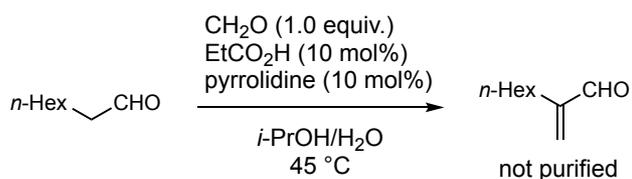
To a solution of n-octanal (469 µL, 3.00 mmol) in i-PrOH (300 µL) were added 37% aqueous solution of CH_2O (221 µL, 3.00 mmol), propionic acid (22.2 µL, 0.300 mmol), and pyrrolidine (24.8 µL, 0.300 mmol) successively. The reaction mixture was then warmed to 45 °C and stirred for 4 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL). The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (5 × 1 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the title compound in a crude form. The crude product was directly used for next steps without further purification. ^{1}H NMR spectral property in $CDCl_3$ was identical to that reported.[7]

## 2-Methylene-5-((triisopropylsilyl)oxy)pentanal
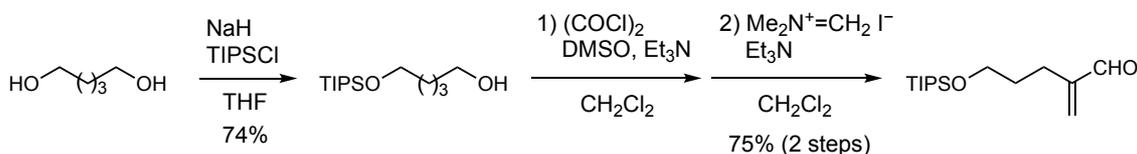
55% NaH in paraffin (873 mg, 20.0 mmol) was washed with *n*-hexane and then THF was added (40 mL). To this mixture was added 1,5-pentanediol (2.10 mL, 20.0 mmol) at 0 °C and the reaction mixture was then warmed to room temperature. After stirring for 1 h, the reaction mixture was cooled to 0 °C and TIPSCl (4.28 mL, 20.0 mmol) was added. The reaction mixture was then warmed to room temperature and stirred for 3 h. The reaction was quenched with H_2O (20 mL). The two layers were separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 5:1) afforded 5-((triisopropylsilyl)oxy)pentan-1-ol (3.83 g, 14.7 mmol, 74%). ^1H NMR spectral property in $CDCl_3$ was identical to that reported.[8]

To a solution of oxalyl chloride (515 µL, 6.00 mmol) in CH_2Cl_2 (21 mL) was added a solution of DMSO (852 µL, 12.0 mmol) in CH_2Cl_2 (2.0 mL) at –78 °C. After stirring for 25 min, 5-((triisopropylsilyl)oxy)pentan-1-ol (1.30 g, 5.00 mmol) in CH_2Cl_2 (2.0 mL) was added, and the reaction mixture was stirred for 15 min at the same temperature before Et_3N (3.48 mL, 25.0 mmol) was added. The reaction mixture was then warmed to room temperature and stirred for 15 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL). The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford 5-((triisopropylsilyl)oxy)pentanal in a crude form.

To a solution of the crude aldehyde in CH_2Cl_2 (25 mL) were added *N,N*-dimethylmethylene ammonium iodide (Eschenmoser's salt) (1.85 g, 10.0 mmol) and Et_3N (1.95 mL, 14.0 mmol) successively at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 15 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL). The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 20:1) afforded 2-methylene-5-((triisopropylsilyl)oxy)pentanal (1.02 g, 3.76 mmol, 75% for 2 steps).

2-methylene-5-((triisopropylsilyl)oxy)pentanal: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.55 (s, 1H), 6.28 (s, 1H), 6.01 (s, 1H), 3.70 (t, J = 6.3 Hz, 2H), 2.34 (t, J = 7.4 Hz, 2H), 1.72–1.67 (m, 2H), 1.08–1.05 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 194.7, 150.0, 134.1, 62.5, 30.9, 24.3, 18.0 (6C), 12.0 (3C). IR (ATR) ν 2942, 2865, 2341, 1697, 1463, 1105, 881, 679 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{15}$H$_{30}$O$_2$Si 270.2015; found: 270.2005.

1-Cyclopentenecarbaldehyde
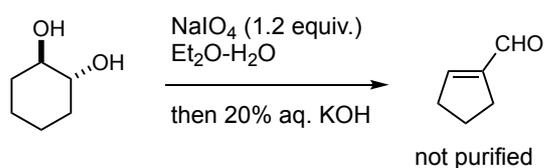
To a suspension of NaIO$_4$ (512 mg, 2.39 mmol) in Et$_2$O (3.0 mL) was added *trans*-1,2-cyclohexanediol (233 mg, 2.00 mmol) in H$_2$O (5.0 mL) at room temperature. After stirring vigorously for 30 min, 20% aqueous KOH (550 µL) was added, and the reaction mixture was stirred for 1 h at the same temperature. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 8 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure to afford the title compound (133 mg, 1.38 mmol, ca. 69%) in a crude form. The resulting crude product was directly used for next steps without further purification.

# General Procedures for Preparation of Trienyl Esters via Aldol Reaction
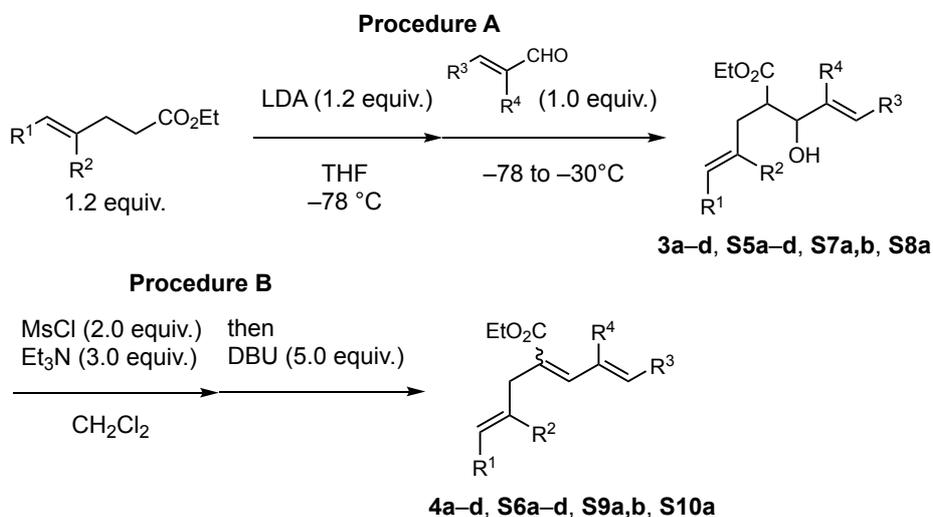
Procedure A: To a 0.24 M solution of *i*-Pr₂NH (1.2 equiv.) in THF was added a solution of *n*-BuLi (1.2 equiv.) in *n*-hexane at 0 °C. After stirring for 30 min, the mixture was cooled to –78 °C and a solution of ester (1.2 equiv.) in THF was added. After stirring for 30 min at –78 °C, a solution of aldehyde in THF was added and the resulting mixture was stirred at appropriate temperature (–78 ~ –30 °C) until no further changes in TLC spots were observed (10 ~ 30 min). The reaction was quenched with saturated aqueous NH₄Cl. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, *n*-hexane/EtOAc = 10:1 to 3:1) afforded the desired aldol product.

NOTE: For small-scale reactions (smaller than 0.5 mmol), a 1.0 M solution of LDA (1.2 equiv.) prepared in another flask was added to a 0.24 M solution of ester (1.2 equiv.) in THF via a syringe at –78 °C. The 1.0 M solution of LDA was prepared at 0 °C from *i*-Pr₂NH (281 μL, 2.00 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (743 μL, 2.00 mmol), and THF (1.26 mL). The procedure after this is same as the standard procedure described above.

Procedure B: To a 0.2 M solution of β-hydroxyester in CH₂Cl₂ were added Et₃N (3.0 equiv.) and MsCl (2.0 equiv.) successively at 0 °C. After stirring for 30 min, DBU (5.0 equiv.) was added. The reaction mixture was warmed to room temperature and stirred overnight. (For some substrates, the reactions were performed at 50 °C in DCE) The reaction was quenched with saturated aqueous NaHCO₃. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO₄, filtered, and concentrated under

reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 20:1) afforded trienyl ester.

Synthesis of β-Hydroxyesters and the Corresponding Trienyl Esters according to Procedure A and B
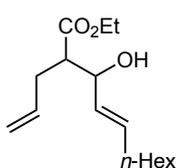
According to Procedure A (reaction conditions: –78 °C, 10 min), *trans*-2-nonenal (825 µL, 5.00 mmol) was converted to β-hydroxyester **3a** (dr = 1.0:1.2, 1.33 g, 4.96 mmol, 99%) by using *i*-Pr$_2$NH (843 µL, 6.00 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (2.23 mL, 6.00 mmol), and ethyl 4-pentenoate (854 µL, 6.00 mmol).

3a (dr = 1.0:1.2): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.83–5.69 (m, 2H), 5.49–5.41 (m, 1H), 5.09–5.01 (m, 2H), 4.27 (t, *J* = 6.3 Hz, 0.55H), 4.21–4.11 (m, 2H + 0.45H), 2.61 (dt, *J* = 10.3, 4.6 Hz, 0.55H), 2.53 (q, *J* = 7.1 Hz, 0.45H), 2.47–2.34 (m, 2H), 2.06–2.01 (m, 2H), 1.36–1.24 (m, 11H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.4, 173.8, 135.5, 134.7, 134.2, 134.1, 129.9, 128.9, 117.1, 116.7, 73.1, 72.9, 60.5, 60.5, 51.14, 51.08, 33.5, 32.20, 32.18, 32.0, 31.6, 29.00, 28.98, 28.8, 22.6, 14.2, 14.0 (Only the detected signals were recorded). IR (ATR) ν 3449 (br), 3079, 2957, 2925, 2855, 1732, 1715, 1178 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{16}$H$_{28}$O$_3$ 268.2038; found: 268.2045.
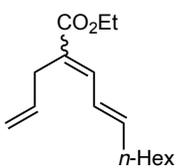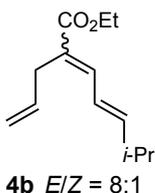
According to Procedure B (reaction conditions: rt, 14 h), β-hydroxyester **3a** (dr = 1.0:1.2, 1.33 g, 4.96 mmol) was converted to trienyl ester **4a** (*E/Z* = 4:1, 1.21 g, 4.82 mmol, 97%) by using Et$_3$N (2.08 mL, 14.9 mmol), MsCl (772 µL, 9.92 mmol), and DBU (3.70 mL, 24.8 mmol).

4a (*E/Z* = 4:1): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.23 (d, *J* = 10.9 Hz, 0.80H), 7.10–7.05 (m, 0.20H), 6.39–6.29 (m, 1H), 6.11 (dt, *J* = 14.7, 7.3 Hz, 0.80H), 5.95 (dt, *J* = 15.0, 7.4 Hz, 0.20H), 5.87–5.79 (m, 1H), 5.08–4.98 (m, 2H), 4.25–4.18 (m, 2H), 3.16 (d, *J* = 5.7 Hz, 0.80 × 2H), 3.04 (d, *J* = 6.3 Hz, 0.20 × 2H), 2.20–2.14 (m, 2H), 1.45–1.39 (m, 2H), 1.33–1.28 (m, 9H), 0.90–0.87 (m, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.0, 167.3, 144.3, 142.9, 140.8, 139.8, 136.1, 135.6, 127.4, 126.9, 126.6, 125.6, 116.1, 115.1, 60.4, 60.2, 38.2, 33.3, 33.0, 31.7, 31.6, 30.8, 28.9, 28.80, 28.78, 22.6, 14.3, 14.2, 14.0 (Only the detected signals were recorded). IR (ATR) ν 2956, 2926, 2856, 1703, 1638, 1205 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{16}$H$_{26}$O$_2$ 250.1933; found: 250.1943.

CO₂Et / OH structure
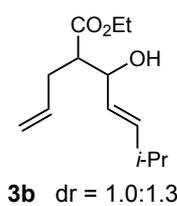
3b dr = 1.0:1.3

According to Procedure A (reaction conditions: –78 °C, 15 min), (*E*)-4-methyl-2-pentenal (581 µL, 5.00 mmol) was converted to β-hydroxyester **3b** (dr = 1.0:1.3, 1.10 g, 4.86 mmol, 97%) by using *i*-Pr$_2$NH (843 µL, 6.00 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (2.23 mL, 6.00 mmol), and ethyl 4-pentenoate (854 µL, 6.00 mmol).

3b (dr = 1.0:1.3): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.83–5.66 (m, 2H), 5.45–5.36 (m, 1H), 5.09–5.01 (m, 2H), 4.27 (t, *J* = 6.3 Hz, 0.57H), 4.21–4.11 (m, 2H + 0.43H), 2.63–2.59 (m, 0.57H), 2.54 (q, *J* = 6.9 Hz, 0.43H), 2.47–2.26 (m, 3H), 1.28–1.24 (m, 3H), 1.00–0.98 (m, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.4, 173.8, 140.8, 135.5, 134.7, 127.0, 126.0, 117.1, 116.7, 73.1, 73.0, 60.51, 60.47, 51.2, 51.1, 33.5, 32.0, 30.7, 22.18, 22.15, 14.3, 14.2 (Only the detected signals were recorded). IR (ATR) ν 3448 (br), 3079, 2959, 2870, 1732, 1715, 1178, 971 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{13}$H$_{22}$O$_3$ 226.1569, found: 226.1573.

CO₂Et structure

4b *E/Z* = 8:1

According to Procedure B (reaction conditions: rt, 18 h), β-hydroxyester **3b** (dr = 1.0:1.3, 1.04 g, 4.58 mmol) was converted to trienyl ester **4b** (*E/Z* = 8:1, 925 mg, 4.44 mmol, 97%) by using Et$_3$N (1.91 mL, 13.7 mmol), MsCl (714 µL, 9.16 mmol), and DBU (3.42 mL, 22.9 mmol).

4b (*E/Z* = 8:1): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.23 (d, *J* = 11.6 Hz, 0.89H), 7.06 (dd, *J* = 15.5, 11.2 Hz, 0.11H), 6.38 (d, *J* = 11.2 Hz, 0.11H), 6.29 (dd, *J* = 14.6, 11.6 Hz, 0.89H), 6.08 (q, *J* = 7.3 Hz, 0.89H), 5.92 (dd, *J* = 15.2, 6.5 Hz, 0.11H), 5.87–5.79 (m, 1H), 5.08–4.98 (m, 2H), 4.25–4.18 (m, 2H), 3.16 (d, *J* = 6.3 Hz, 0.89×2H), 3.04 (d, *J* = 6.5 Hz, 0.11×2H), 2.47–2.40 (m, 1H), 1.33–1.28 (m, 3H), 1.04 (t, *J* = 6.0 Hz, 6H). ^{13}C NMR for (*E*)-**4b** (126 MHz, CDCl$_3$) δ 167.9, 150.8, 139.9, 135.6, 127.1, 122.7, 115.1, 60.4, 31.8, 30.9, 21.9 (2C), 14.3. IR (ATR) ν 3080, 2961, 2871, 1703, 1638, 1267, 1206 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{13}$H$_{20}$O$_2$ 208.1463; found: 208.1470.

CO₂Et / OH structure
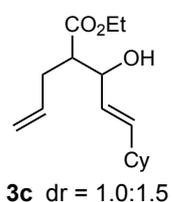
3c dr = 1.0:1.5

According to Procedure A (reaction conditions: –78 °C, 15 min), (*E*)-3-cyclohexylpropenal (138 mg, 1.00 mmol) was converted to β-hydroxyester **3c** (dr = 1.0 :1.5, 211 mg, 0.791 mmol, 80%) by using *i*-Pr$_2$NH (169 µL, 1.20 mmol), a 2.64 M solution of *n*-BuLi in *n*-hexane (455 µL, 1.20 mmol), and ethyl 4-pentenoate (171 µL, 1.20 mmol).

3c (dr = 1.0:1.5): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.82–5.70 (m, 1H), 5.68 (dd, *J* = 6.3, 2.3 Hz, 0.40H), 5.65 (dd, *J* = 6.5, 2.0 Hz, 0.60H), 5.45–5.36 (m, 1H), 5.09–5.05 (m, 1H), 5.03–

5.01 (m, 1H), 4.26 (br, 0.60H), 4.21–4.09 (m, 2H + 0.40H), 2.61 (dt, J = 9.2, 5.4 Hz, 0.60H), 2.53 (q, J = 7.1 Hz, 0.4H), 2.48–2.34 (m, 3H), 1.96 (br, 1H), 1.72–1.63 (m, 5H), 1.30–1.22 (m, 5H), 1.18–1.02 (m, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.4, 173.8, 139.70, 139.66, 135.5, 134.7, 127.4, 126.5, 117.1, 116.7, 73.2, 73.1, 60.51, 60.47, 51.3, 51.1, 40.3, 33.5, 32.73, 32.71, 32.68, 32.0, 26.1, 25.9, 14.3 (Only the detected peaks were recorded). IR (ATR) ν 3457 (br), 1731, 1715, 1177 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{16}$H$_{26}$O$_3$ 266.1882; found: 266.1869.
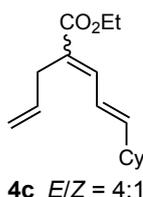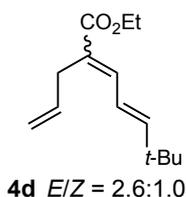
According to Procedure B (reaction conditions: rt, 15 h), β-hydroxyester **3c** (dr = 1.0:1.5, 88.0 mg, 0.330 mmol) was converted to trienyl ester **4c** (E/Z = 4:1, 70.8 mg, 0.285 mmol, 86%) by using Et$_3$N (140 μL, 0.990 mmol), MsCl (51.3 μL, 0.660 mmol), and DBU (247 μL, 1.65 mmol).

4c (E/Z = 4:1): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.23 (d, J = 11.4 Hz, 0.80H), 7.06 (dd, J = 15.2, 11.4 Hz, 0.20H), 6.37 (d, J = 11.4 Hz, 0.20H), 6.29 (dd, J = 15.0, 11.4 Hz, 0.8H), 6.06 (dd, J = 15.0, 6.8 Hz, 0.80H), 5.92–5.79 (m, 1H + 0.20H), 5.08–4.98 (m, 2H), 4.24–4.17 (m, 2H), 3.15 (d, J = 5.7 Hz, 0.80 × 2H), 3.04 (d, J = 6.9 Hz, 0.20 × 2H), 2.14–2.07 (m, 1H), 1.76–1.65 (m, 5H), 1.33–1.08 (m, 8H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.0, 167.4, 149.7, 148.3, 141.1, 140.1, 136.1, 135.7, 127.1, 126.8, 125.0, 123.1, 116.1, 115.1, 60.4, 60.2, 41.4, 41.1, 38.3, 32.5, 32.4, 30.9, 26.1, 26.0, 25.9, 25.8, 14.3 (Only the detected peaks were recorded). IR (ATR) ν 2924, 1702, 1637, 1203 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{16}$H$_{24}$O$_2$ 248.1776; found: 248.1774.
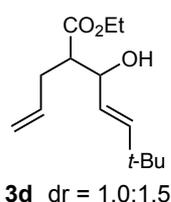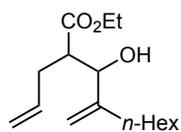
According to Procedure A (reaction conditions: –78 °C, 15 min), (E)-4,4-dimethyl-2-pentenal (376 mg, 3.35 mmol) was converted to β-hydroxyester **3d** (dr = 1.0:1.5, 618 mg, 2.57 mmol, 77%) by using i-Pr$_2$NH (707 μL, 5.03 mmol), a 2.64 M solution of n-BuLi in n-hexane (1.91 mL, 5.03 mmol), and ethyl 4-pentenoate (716 μL, 5.03 mmol)

3d (dr = 1.0:1.5): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.83–5.70 (m, 2H), 5.40–5.32 (m, 1H), 5.09–5.01 (m, 2H), 4.27 (dd, J = 11.3, 6.1 Hz, 0.60H), 4.23–4.09 (m, 0.60 × 2H + 0.40 × 3H), 2.61 (dt, J = 9.0, 6.1 Hz, 0.60H), 2.55 (q, J = 7.1 Hz, 0.40H), 2.50–2.32 (m, 3H), 1.28–1.24 (m, 3H), 1.01 (s, 0.4 × 9H), 1.01 (s, 0.6 × 9H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.4, 173.8, 144.6, 135.6, 134.7, 124.8, 124.0, 117.1, 116.7, 73.21, 73.16, 60.5, 60.4, 51.4, 51.2, 33.5, 32.9, 32.0, 29.38, 29.36, 14.2 (Only the detected peaks were recorded). IR (ATR) ν 3462 (br), 2959, 1732, 1176 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{14}$H$_{24}$O$_3$ 240.1725, found: 240.1718.
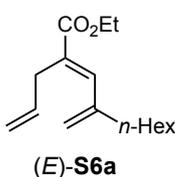
4d *E/Z* = 2.6:1.0

According to Procedure B (reaction conditions: rt, 11 h), β-hydroxyester **3d** (dr = 1.0:1.5, 242 mg, 1.01 mmol) was converted to trienyl ester **4d** (*E/Z* = 2.6:1.0, 210 mg, 0.945 mmol, 94%) by using Et$_3$N (418 μL, 3.00 mmol), MsCl (156 μL, 2.00 mmol), and DBU (746 μL, 5.00 mmol).

4d (*E/Z* = 2.6:1.0): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.24 (d, *J* = 11.1 Hz, 0.72H), 7.05 (dd, *J* = 15.5, 11.2 Hz, 0.28H), 6.40 (d, *J* = 11.2 Hz, 0.28H), 6.26 (dd, *J* = 15.4, 11.1 Hz, 0.72H), 6.13 (d, *J* = 15.4 Hz, 0.72H), 5.96 (d, *J* = 15.5 Hz, 0.28H), 5.88–5.79 (m, 1H), 5.09–4.98 (m, 2H), 4.25–4.18 (m, 2H), 3.17 (d, *J* = 5.7 Hz, 0.72×2H), 3.05 (d, *J* = 6.3 Hz, 0.28×2H), 1.34–1.28 (m, 3H), 1.07 (s, 0.72×9H), 1.07 (s, 0.28×9H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.9, 167.4, 154.6, 153.2, 141.2, 140.2, 136.1, 135.6, 127.2, 126.9, 122.5, 120.4, 116.1, 115.1, 60.4, 60.2, 38.3, 34.0, 33.8, 30.9, 29.2, 29.1, 14.3, 14.2. IR (ATR) ν 2960, 1703, 1637, 1194 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{14}$H$_{22}$O$_2$ 222.1620; found: 222.1616.

S5a dr = 1.0:1.3

According to Procedure A (reaction conditions: –78 °C, 25 min), crude 2-methyleneoctanal (prepared from 1.00 mmol of *n*-octanal) was converted to β-hydroxyester **S5a** (dr = 1.0:1.3, 192 mg, 0.715 mmol, 72% for 2 steps from *n*-octanal) by using *i*-Pr$_2$NH (169 μL, 1.20 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (446 μL, 1.20 mmol), and ethyl 4-pentenoate (171 μL, 1.20 mmol).

S5a (dr = 1.0:1.3): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.84–5.71 (m, 1H), 5.14–4.93 (m, 4H), 4.35 (d, *J* = 5.2 Hz, 0.43H), 4.19–4.11 (m, 2H + 0.57H), 2.74–2.65 (m, 1H), 2.42–2.30 (m, 2H), 2.14–1.92 (m, 2H), 1.50–1.44 (m, 2H), 1.32–1.23 (m, 9H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.6, 174.5, 149.2, 148.3, 135.8, 134.6, 117.3, 116.6, 111.3, 111.2, 75.4, 74.6, 60.6, 48.7, 48.6, 34.0, 31.9, 31.7, 31.3, 31.0, 29.2, 29.1, 27.8, 27.7, 22.6, 14.3, 14.2, 14.1 (Only the detected peaks were recorded). IR (ATR) ν 3471 (br), 3080, 2956, 2927, 2858, 1733, 1715, 1177, 1030, 909 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{16}$H$_{28}$O$_3$ 268.2038, found: 268.2035.

(*E*)-**S6a**

According to Procedure B (reaction conditions: rt, 17 h), β-hydroxyester **S5a** (dr = 1.0:1.3, 192 mg, 0.716 mmol) was converted to trienyl ester (*E*)-**S6a** (167 mg, 0.667 mmol, 93%) by using Et$_3$N (299 μL, 2.15 mmol), MsCl (112 μL, 1.43 mmol), and DBU (534 μL, 3.58 mmol).

(*E*)-**S6a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.15 (s, 1H), 5.92–5.84 (m, 1H), 5.12 (d, *J* = 1.7 Hz, 1H), 5.07 (s, 1H), 5.03–4.98 (m, 2H), 4.22 (q, *J* = 7.0 Hz, 2H), 3.20 (d, *J* = 6.3 Hz, 2H), 2.15 (t, *J* = 7.7 Hz, 2H), 1.42–1.37 (m, 2H), 1.32–1.26 (m, 9H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR

(126 MHz, CDCl$_3$) δ 167.9, 144.7, 141.4, 136.4, 130.5, 116.0, 115.2, 60.7, 36.7, 31.9, 31.6, 28.8, 28.2, 22.6, 14.2, 14.0. IR (ATR) ν 3081, 2956, 2928, 2857, 1712, 1204, 907 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{16}$H$_{26}$O$_2$ 250.1933; found: 250.1943.
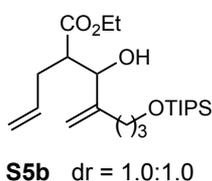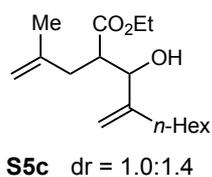
According to Procedure A (reaction conditions: –78 °C, 20 min; –30 °C, 10 min), 2-methylene-5-((triisopropylsilyl)oxy)pentanal (123 mg, 0.453 mmol) was converted to β-hydroxyester **S5b** (dr = 1.0:1.0, 126 mg, 0.315 mmol, 70%) by using a 1.0 M solution of LDA in THF/*n*-hexane (543 µL, 0.543 mmol), and ethyl 4-pentenoate (77.3 µL, 0.543 mmol).

S5b (dr = 1.0:1.0): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.83–5.69 (m, 1H), 5.15–4.96 (m, 4H), 4.35 (d, *J* = 5.2 Hz, 0.50H), 4.21–4.11 (m, 0.50×5H), 3.74–3.70 (m, 2H), 2.75–2.55 (m, 1H), 2.43–2.29 (m, 2H), 2.23–2.04 (m, 2H), 1.79–1.68 (m, 2H), 1.28–1.23 (m, 3H), 1.11–1.05 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.6, 174.4, 148.8, 147.9, 135.8, 134.6, 117.3, 116.5, 111.8, 111.6, 75.6, 74.9, 62.85, 62.82, 60.6, 60.5, 48.9, 48.7, 34.0, 31.4, 31.3, 31.2, 28.0, 27.6, 18.0, 14.3, 14.2, 11.9 (Only the detected peaks were recorded). IR (ATR) ν 3491 (br), 3080, 2942, 2866, 1734, 1716, 1103 cm^{-1}. HRMS (FD) *m/z* [M + H]$^+$ calcd for C$_{22}$H$_{43}$O$_4$Si 399.2931; found: 399.2924.
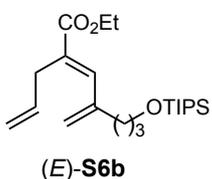
According to Procedure B (reaction conditions: rt, 45 min; 50 °C, 3 h, in DCE, eluent for column chromatography: *n*-hexane/EtOAc = 50:1), β-hydroxyester **S5b** (dr = 1.0:1.0, 117 mg, 0.292 mmol) was converted to trienyl ester (*E*)-**S6b** (88.0 mg, 0.231 mmol, 79%) by using Et$_3$N (122 µL, 0.877 mmol), MsCl (45.5 µL, 0.584 mmol), and DBU (218 µL, 1.46 mmol).

(*E*)-**S6b**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.16 (s, 1H), 5.91–5.86 (m, 1H), 5.16 (s, 1H), 5.10 (s, 1H), 5.02–4.98 (m, 2H), 4.21 (q, *J* = 7.3 Hz, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 3.21 (d, *J* = 5.2 Hz, 2H), 2.26 (t, *J* = 7.7 Hz, 2H), 1.68–1.62 (m, 2H), 1.30 (t, *J* = 7.3 Hz, 3H), 1.10–1.03 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.9, 144.3, 141.3, 136.3, 130.6, 116.4, 115.3, 62.5, 60.7, 32.9, 31.9, 31.6, 18.0 (6C), 14.2, 11.9 (3C). IR (ATR) ν 3080, 2942, 2866, 1712, 1206, 1102 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{22}$H$_{40}$O$_3$Si 380.2747; found: 380.2749.

According to Procedure A (reaction conditions: –78 °C, 15 min), crude 2-methyleneoctanal (271 mg, ca. 1.93 mmol) was converted to β-hydroxyester **S5c** (dr = 1.0:1.4, 269 mg, 0.952 mmol, 59%) by using *i*-Pr$_2$NH (271 µL, 1.93 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (717 µL, 1.93 mmol),

and ethyl 4-methyl-4-pentenoate (229 mg, 1.61 mmol).

S5c (dr = 1.0:1.4): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.14 (s, 0.42H), 5.05 (s, 0.58H), 4.96 (s, 0.42H), 4.93 (s, 0.58H), 4.77–4.71 (m, 2H), 4.33 (d, J = 5.2 Hz, 0.42H), 4.16–4.08 (m, 2H + 0.58H), 2.88–2.78 (m, 1H), 2.44–2.39 (m, 1H), 2.31 (dd, *J* = 15.1, 3.2 Hz, 0.42H), 2.22 (dd, *J* = 14.3, 5.2 Hz, 0.58H), 2.15–1.92 (m, 2H), 1.77–1.72 (m, 3H), 1.51–1.41 (m, 2H), 1.35–1.22 (m, 9H), 0.89 (t, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.7, 149.4, 148.2, 143.2, 142.2, 112.6, 111.8, 111.3, 111.2, 75.8, 74.8, 60.6, 60.5, 47.4, 47.2, 38.1, 34.8, 31.8, 31.7, 31.3, 29.1, 27.8, 22.6, 22.3, 22.1, 14.23, 14.17, 14.1 (Only the detected peaks were recorded). IR (ATR) ν 3478 (br), 3078, 2956, 2927, 2857, 1734, 1716, 1161, 1028, 896 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{17}$H$_{30}$O$_3$ 282.2195; found: 282.2207.
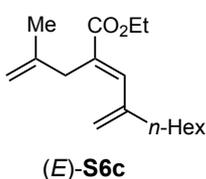
According to Procedure B (reaction conditions: rt, 2 days, eluent for column chromatography: *n*-hexane/EtOAc = 50:1), β-hydroxyester **S5c** (dr = 1.0:1.4, 248 mg, 0.878 mmol) was converted to trienyl ester (*E*)-**S6c** (166 mg, 0.628 mmol, 71%) Et$_3$N (367 μL, 2.63 mmol), MsCl (137 μL, 1.76 mmol), and DBU (655 μL, 4.39 mmol).

(*E*)-**S6c**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.18 (s, 1H), 5.09 (s, 2H), 4.74 (s, 1H), 4.53 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.10 (s, 2H), 2.14 (t, J = 7.7 Hz, 2H), 1.77 (s, 3H), 1.42–1.37 (m, 2H), 1.32–1.24 (m, 9H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.3, 144.7, 144.2, 141.5, 130.6, 115.9, 109.8, 60.6, 36.8, 35.4, 31.6, 28.8, 28.3, 23.5, 22.6, 14.2, 14.1. IR (ATR) ν 3080, 2928, 2856, 1712, 1201, 1096 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{17}$H$_{28}$O$_2$ 264.2089; found: 264.2089.
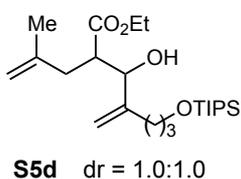
According to Procedure A (reaction conditions: –78 °C, 20 min; –30 °C, 10 min), 2-methylene-5-((triisopropylsilyl)oxy)pentanal (123 mg, 0.455 mmol) was converted to β-hydroxyester **S5d** (dr = 1.0:1.0, 119 mg, 0.287 mmol, 63%) by using a 1.0 M solution of LDA in THF/hexane (547 μL, 0.547 mmol), and ethyl 4-methyl-4-pentenoate (77.8 mg, 0.547 mmol).

S5d (dr = 1.0:1.0): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.15 (s, 0.5H), 5.08 (s, 0.5H), 4.97 (d, *J* = 8.6 Hz, 1H), 4.77–4.70 (m, 2H), 4.32 (d, *J* = 5.7 Hz, 0.5H), 4.19–4.07 (m, 2H + 0.5H), 3.74–3.70 (m, 2H), 2.89–2.79 (m, 1H), 2.44–2.33 (m, 1H + 0.5H), 2.23–2.04 (m, 2H + 0.5H), 1.77–1.70 (m, 5H), 1.26–1.21 (m, 3H), 1.11–1.05 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.73, 174.66, 149.0, 147.8, 143.3, 142.2, 112.6, 111.9, 111.8, 111.5, 75.9, 75.2, 62.9, 62.8, 60.51,

60.49, 47.7, 47.2, 38.1, 35.0, 31.4, 31.3, 27.9, 27.7, 22.3, 22.1, 18.0, 14.24, 14.17, 11.9 (Only the detected peaks were recorded). IR (ATR) ν 3482 (br), 3078, 3942, 2866, 1735, 1716, 1103, 882 cm^{-1}. HRMS (FD) *m/z* [M + H]$^+$ calcd for C$_{23}$H$_{45}$O$_4$Si 413.3087; found: 413.3088.
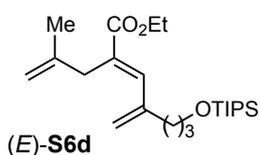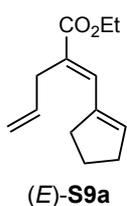
According to Procedure B (reaction conditions: rt, 45 min; 50 °C, 3 h, solvent: DCE, eluent for column chromatography: *n*-hexane/EtOAc = 50:1), β-hydroxyester **S5d** (dr = 1.0:1.0, 110 mg, 0.266 mmol) was converted to trienyl ester (*E*)-**S6d** (66.8 mg, 0.169 mmol, 64%) by using Et$_3$N (111 µL, 0.797 mmol), MsCl (83.0 µL, 1.06 mmol), and DBU (199 µL, 1.33 mmol).

(*E*)-**S6d**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.19 (s, 1H), 5.12 (d, *J* = 8.6 Hz, 2H), 4.74 (s, 1H), 4.53 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 3.11 (s, 2H), 2.25 (t, *J* = 7.7 Hz, 2H), 1.77 (s, 3H), 1.68–1.62 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.10–1.03 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.2, 144.2, 144.1, 141.3, 130.8, 116.2, 109.8, 62.5, 60.7, 35.5, 33.0, 31.6, 23.5, 18.0 (6C), 14.2, 12.0 (3C). IR (ATR) ν 3080, 2941, 2866, 1713, 1203, 1098, 882 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{23}$H$_{42}$O$_3$Si 394.2903; found: 394.2916.
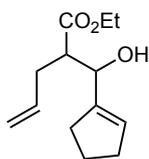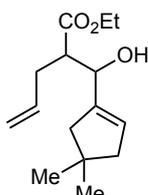
According to Procedure A (reaction conditions: –78 °C, 15 min), crude cyclopentene-1-carboxaldehyde (133 mg, ca. 1.38 mmol) was converted to β-hydroxyester **S7a** (dr = 1.0:1.2, 215 mg, 959 µmol, 48% for 2 steps from *trans*-1,2-cyclohexanediol) by using *i*-Pr$_2$NH (233 µL, 1.66 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (617 µL, 1.66 mmol), and ethyl 4-pentenoate (236 µL, 1.66 mmol).

S7a (dr = 1.0:1.2): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.84–5.66 (m, 2H), 5.10–5.00 (m, 2H), 4.52 (d, *J* = 5.2 Hz, 0.45H), 4.38 (d, *J* = 6.9 Hz, 0.55H), 4.18–4.12 (m, 2H), 2.71–2.65 (m, 1H), 2.47–2.20 (m, 6H), 1.93–1.86 (m, 2H), 1.26–1.23 (m, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.7, 174.3, 144.5, 143.7, 135.8, 134.7, 127.6, 127.3, 117.1, 116.5, 71.6, 71.5, 60.5, 49.4, 49.1, 33.8, 32.2, 32.1, 31.5, 31.4, 31.1, 23.35, 23.33, 14.25, 14.21 (Only the detected peaks were recorded). IR (ATR) ν 3462 (br), 3078, 2951, 2847, 1731, 1715, 1176, 1029 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{13}$H$_{20}$O$_3$ 224.1412; found: 224.1416.
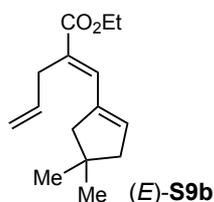
According to Procedure B (reaction conditions: rt, 20 h), β-hydroxyester **S6a** (dr = 1.0:1.2, 215 mg, 0.957 mmol) was converted to trienyl ester (*E*)-**S9a** (193 mg, 0.936 mmol, 98%) by using Et$_3$N (400 μL, 2.87 mmol), MsCl (149 μL, 1.91 mmol), and DBU (713 μL, 4.78 mmol)

(*E*)-**S9a**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41 (s, 1H), 6.12 (s, 1H), 5.91–5.83 (m, 1H), 5.02 (d, *J* = 1.1 Hz, 1H), 5.00–4.98 (m, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.25 (d, *J* = 5.7 Hz, 2H), 2.65–2.62 (m, 2H), 2.42 (td, *J* = 7.4, 2.3 Hz, 2H), 1.99–1.92 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.5, 140.7, 140.3, 136.5, 127.3, 115.0, 60.6, 33.7, 32.5, 31.3, 24.0, 14.3 (One signal could not be judged due to overlap to the signals among 140.7–127.3 ppm.). IR (ATR) ν 3080, 2956, 2843, 1703, 1274, 1199 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{13}$H$_{18}$O$_2$ 206.1307; found: 206.1302.

According to Procedure A (reaction conditions: –78 °C, 15 min), unsaturated aldehyde **S4** (mixture with TIPSOH, **S4**:TIPSOH = 1.0:1.4, 480 mg) was converted to β-hydroxyester **S7b** (dr = 1.0:1.4, 394 mg, 1.56 mmol, 52% for 3 steps from **S3**) by using *i*-Pr$_2$NH (843 μL, 6.00 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (2.23 mL, 6.00 mmol), and ethyl 4-pentenoate (854 μL, 6.00 mmol).

S7b (dr = 1.0:1.4): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.85–5.71 (m, 1H), 5.57 (s, 0.42H), 5.54 (s, 0.58H), 5.11–5.00 (m, 2H), 4.46 (d, *J* = 5.2 Hz, 0.42H), 4.30 (d, *J* = 6.3 Hz, 0.58H), 4.18–4.11 (m, 2H), 2.68–2.61 (m, 1H), 2.47–2.30 (m, 2H), 2.22–2.03 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H) 1.07 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.7, 174.3, 143.0, 142.2, 135.7, 134.7, 126.1, 125.9, 117.2, 116.6, 71.6, 71.4, 60.5, 49.3, 49.0, 47.3, 47.2, 46.6, 46.2, 38.52, 38.48, 33.8, 31.5, 29.8, 29.75, 29.66, 14.24, 14.21 (Only the detected peaks were recorded). IR (ATR) ν 3470 (br), 3078, 2952, 2866, 2840, 1732, 1715, 1176 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{15}$H$_{24}$O$_3$ 252.1725; found: 252.1729.

According to Procedure B (reaction conditions: rt, 21 h), β-hydroxyester **S6b** (dr = 1.0:1.4, 341 mg, 1.35 mmol) was converted to trienyl ester (*E*)-**S9b** (300 mg, 1.28 mmol, 95%) by using Et$_3$N (564 μL, 4.05 mmol), MsCl (210 μL, 2.70 mmol), and DBU (1.01 mL, 6.75 mmol).

(*E*)-**S9b**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (s, 1H), 6.01 (s, 1H), 5.91–5.83 (m, 1H), 5.02–4.98 (m, 2H), 4.20 (q, *J* = 7.0 Hz, 2H), 3.23 (d, *J* = 5.2 Hz, 2H), 2.45 (s, 2H), 2.23 (s,

2H), 1.29 (t, J = 7.0 Hz, 3H), 1.10 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.5, 139.5, 139.1, 136.9, 136.5, 127.2, 115.1, 60.6, 48.8, 47.4, 39.3, 31.3, 29.6 (2C), 14.3. IR (ATR) ν 2953, 2867, 2836, 1704, 1273, 1203, 1193 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{15}$H$_{22}$O$_2$ 234.1620; found: 234.1623.
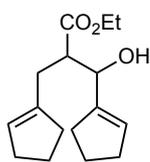
According to Procedure A (reaction conditions: –78 °C, 20 min), cyclopentene-1-carboxaldehyde (270 mg, ca. 2.81 mmol) was converted to β-hydroxyester **S8a** (dr = 1.0:1.0, 472 mg, 1.79 mmol, 76%) by using i-Pr$_2$NH (395 μL, 2.81 mmol), a 2.64 M solution of n-BuLi in n-hexane (1.06 mL, 2.81 mmol), and ethyl 3-(cyclopenten-1-yl)propanoate (394 mg, 2.34 mmol).

S8a (dr = 1.0:1.0): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.69 (s, 0.48H), 5.65 (s, 0.52H), 5.42 (s, 0.52H), 5.37 (s, 0.48H), 4.49 (d, J = 5.2 Hz, 0.48H), 4.33 (d, J = 5.7 Hz, 0.52H), 4.16–4.08 (m, 2H), 2.84–2.78 (m, 1H), 2.54–2.46 (m, 1H), 2.40–2.17 (m, 9H), 1.92–1.81 (m, 4H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 175.1, 174.7, 144.7, 143.7, 141.9, 141.0, 127.4, 127.3, 126.0, 125.3, 72.1, 71.8, 60.4, 48.4, 48.0, 34.9, 34.8, 32.43, 32.41, 32.2, 32.1, 31.5, 31.3, 31.1, 28.7, 23.4, 23.42, 23.39, 23.3, 14.20, 14.15 (Only the detected peaks were recorded). IR (ATR) ν 3448 (br), 3044, 2950, 2845, 1732, 1715, 1157, 1026 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{16}$H$_{24}$O$_3$ 264.1725; found: 264.1726.
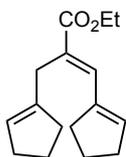
According to Procedure B (reaction conditions: rt, 13 h), β-hydroxyester **S7a** (472 mg, 1.79 mmol) was converted to trienyl ester (*E*)-**S10a** (dr = 1.0:1.0, 398 mg, 1.62 mmol, 91%) by using Et$_3$N (747 μL, 5.36 mmol), MsCl (278 μL, 3.57 mmol), and DBU (1.33 mL, 8.93 mmol).

(*E*)-**S23a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39 (s, 1H), 6.08 (s, 1H), 5.20 (s, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.21 (s, 2H), 2.61–2.58 (m, 2H), 2.43–2.39 (m, 2H), 2.26 (t, J = 7.4 Hz, 4H), 1.97–1.91 (m, 2H), 1.89–1.83 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.9, 142.9, 140.9, 139.9, 135.8, 128.1, 124.0, 60.5, 35.6, 33.5, 32.5, 32.3, 29.2, 24.0, 23.3, 14.3. IR (ATR) ν 3043, 2951, 2843, 1703, 1275, 1211, 1188 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{16}$H$_{22}$O$_2$ 246.1620; found: 246.1630.

General Procedure for Preparation of Trienyl Ester by Horner-Wadsworth-Emmons Reaction
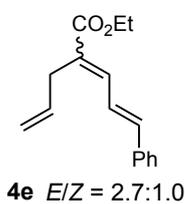
Procedure C
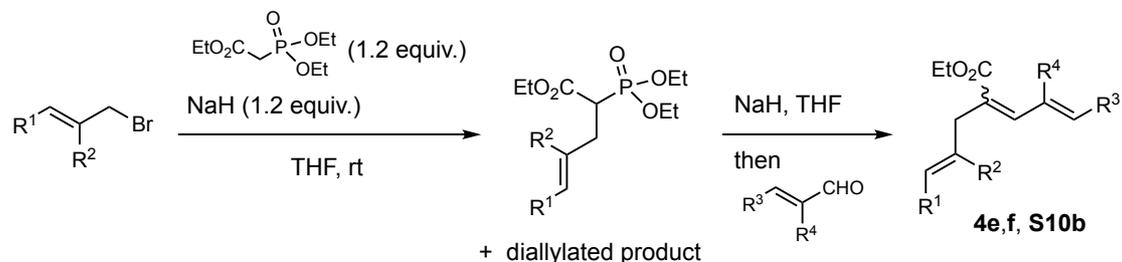
55% NaH in paraffin (1.2 equiv.) placed in a flask was washed with THF under argon atmosphere, and then THF (0.2 M to allyl bromide) was added. To this mixture was added triethyl phosphonoacetate (1.2 equiv.) at 0 °C. After stirring for 30 min, allyl bromide was added. The reaction mixture was then warmed up to room temperature and stirred for 19–23 h (t_1). The reaction was quenched with saturated aqueous NH$_4$Cl. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by silica gel flash column chromatography afforded the desired monoallylated product as an inseparable mixture with diallylated product.

55% NaH in paraffin (1.2 equiv to the amount of monoallylated product) placed in a flask was washed with THF under argon atmosphere, and then THF was added. To the mixture was added the mixture of mono and diallylated product in THF at 0 °C. After stirring for 30 min, aldehyde (1.2 equiv to the amount of monoallylated product) was added. The reaction mixture was then warmed to room temperature and stirred for 30 min–3.5 h (t_2). The reaction was quenched with saturated aqueous NH$_4$Cl. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 50:1) afforded trienyl ester.

Synthesis of Trienyl Esters according to Procedure C

4e *E/Z* = 2.7:1.0

According to Procedure C, allyl bromide (423 µL, 5.00 mmol) was converted to the desired monoallylated product as a 3.6:1.0 inseparable mixture with diallylated product (1.17 g) by using 55% NaH in paraffin (266 mg, 6.10 mmol) and triethyl phosphonoacetate (1.20 mL, 6.00 mmol) (t_1: 20 h, eluent for column chromatography: *n*-hexane/EtOAc = 1:2). The obtained mixture was converted to trienyl ester **4e** (*E/Z* = 2.7:1.0, 738 mg, 3.05 mmol, 61% for 2 steps) by using 55% NaH in paraffin (165 mg, 3.78 mmol) and *trans*-cinnamaldehyde (475 µL, 3.78 mmol) (t_2: 30 min, eluent for column chromatography: *n*-hexane/EtOAc = 50:1).

4c (*E/Z* = 2.7:1.0): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (dd, *J* = 15.5, 11.2 Hz, 0.27H), 7.48–7.26 (m, 5H + 0.73H), 7.05 (dd, *J* = 15.2, 11.2 Hz, 0.73H), 6.90 (d, *J* = 15.5 Hz, 0.73H), 6.73 (d, *J* = 15.5 Hz, 0.27H), 6.58 (d, *J* = 11.2 Hz, 0.27H), 5.93–5.84 (m, 1H), 5.12–5.02 (m, 2H), 4.30–4.22 (m, 2H), 3.28 (d, *J* = 5.7 Hz, 0.73 × 2H), 3.13 (d, *J* = 6.3 Hz, 0.27 × 2H), 1.36 (t, *J* = 7.2 Hz, 0.27 × 3H), 1.33 (t, *J* = 6.9 Hz, 0.73 × 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.7, 167.1, 140.3, 139.8, 139.3, 138.7, 136.8, 136.4, 135.8, 135.6, 129.2, 129.0, 128.8, 128.7, 128.6, 128.4, 127.1, 125.8, 123.6, 116.4, 115.4, 60.6, 60.3, 38.4, 31.1, 14.29, 14.26 (Only the detected peaks were recorded). IR (ATR) ν 2979, 1698, 1620, 1201, 747, 689 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{16}$H$_{18}$O$_2$ 242.1307; found: 242.1297.
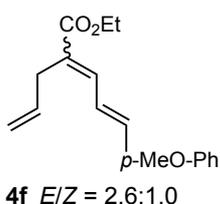
4f *E/Z* = 2.6:1.0

According to Procedure C, allyl bromide (423 µL, 5.00 mmol) was converted to the desired monoallylated product as a 2.6:1.0 inseparable mixture with diallylated product (1.02 g) by using 55% NaH in paraffin (265 mg, 6.08 mmol) and triethyl phosphonoacetate (1.20 mL, 6.00 mmol) (t_1: 19 h, eluent for column chromatography: *n*-hexane/EtOAc = 1:2). The obtained mixture was converted to trienyl ester **4f** (*E/Z* = 2.6:1.0, 688 mg, 2.52 mmol, 50% for 2 steps) by using 55% NaH in paraffin (141 mg, 3.22 mmol) and *p*-methoxycinnamaldehyde (475 µL, 3.78 mmol) (t_2: 30 min, eluent for column chromatography: *n*-hexane/EtOAc = 50:1 to 20:1).

4f (*E/Z* = 2.6:1.0): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.80 (dd, *J* = 15.7, 11.6 Hz, 0.28H), 7.44–7.41 (m, 2H + 0.72H), 6.95–6.83 (m, 3H + 0.72 × 2H), 6.68 (d, *J* = 15.7 Hz, 0.28H), 6.57 (d, *J* = 11.6 Hz, 0.28H), 5.93–5.84 (m, 1H), 5.12–5.02 (m, 2H), 4.29–4.21 (m, 2H), 3.82 (s, 0.72 × 3H), 3.81 (s, 0.28 × 3H), 3.27 (d, *J* = 6.3 Hz, 0.72 × 2H), 3.11 (d, *J* = 6.3 Hz, 0.28 × 2H), 1.36 (t, *J* = 7.2 Hz, 0.28 × 3H), 1.32 (t, *J* = 7.2 Hz, 0.72 × 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.8, 167.3, 160.2, 159.9, 141.0, 139.8, 139.5, 138.5, 136.1, 135.7, 129.6, 129.3, 128.52, 128.47, 127.9, 127.6, 123.9,

121.6, 116.2, 115.3, 114.2, 114.1, 60.5, 60.2, 55.3, 38.4, 31.0, 14.3 (Only the detected peaks were recorded). IR (ATR) ν 2979, 1695, 1595, 1509, 1251 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{17}$H$_{20}$O$_3$ 272.1412, found: 272.1411.
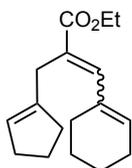
According to Procedure C, 1-(bromomethyl)cyclopent-1-ene (242 mg, 1.50 mmol) was converted to the desired monoallylated product as a 7.7:1.0 inseparable mixture with diallylated product (385 mg) by using 55% NaH in paraffin (77.8 mg, 1.78 mmol) and triethyl phosphonoacetate (360 µL, 1.80 mmol) (t$_1$: 20 h, eluent for column chromatography: n-hexane/EtOAc = 1:1).

S10b $E/Z = 1.4:1.0$

The obtained mixture was converted to trienyl ester **S10b** (E/Z = 1.4:1.0, 82.8 mg, 0.318 mmol, 46% for 2 steps) by using 55% NaH in paraffin (26.2 mg, 0.600 mmol) and 1-cyclohexene-1-carboxaldehyde (68.4 µL, 0.600 mmol) (t$_2$: 3.5 h, eluent for column chromatography: n-hexane/EtOAc = 50:1).

S10b (E/Z = 1.4:1.0): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.11 (s, 0.58H), 6.00 (s, 0.42H), 5.96 (s, 0.58H), 5.75 (s, 0.42H), 5.41 (s, 0.42H), 5.20 (s, 0.58H), 4.21–4.15 (m, 2H), 3.19 (s, 0.58 × 2H), 3.04 (s, 0.42 × 2H), 2.30–2.09 (m, 8H), 1.89–1.82 (m, 2H), 1.66–1.48 (m, 4H), 1.29−1.25 (m, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.3, 169.0, 143.1, 142.4, 141.4, 136.0, 134.8, 134.7, 133.5, 131.0, 128.6, 127.5, 126.3, 123.8, 60.4, 60.3, 37.6, 35.6, 34.6, 32.5, 32.4, 29.5, 27.8, 26.5, 26.1, 25.9, 23.5, 23.3, 22.6, 22.6, 21.9, 21.7, 14.2, 14.1. IR (ATR) ν 2978, 2930, 2844, 1706, 1213, 1183 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{17}$H$_{24}$O$_2$ 260.1776; found: 260.1773.

Synthesis of Trienyl Esters S12 and S13
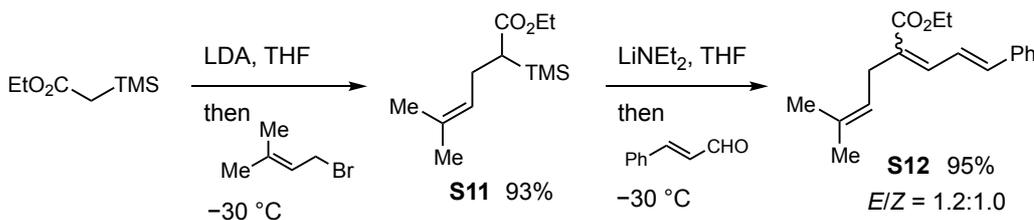
To a solution of i-Pr$_2$NH (843 µL, 6.00 mmol) in THF (25 mL) was added a 2.67 M solution n-BuLi in n-hexane (2.25 mL, 6.00 mmol) at 0 °C and the reaction mixture was stirred for 30 min. The reaction mixture was then cooled to –78 °C and ethyl (trimethylsilyl)acetate (911 µL, 5.00 mmol) was added. After stirring for 30 min, 1-bromo-3-methyl-2-butene (693 µL, 6.00 mmol) was added. The reaction mixture was then warmed to –30 °C and stirred for 30 min. The reaction was quenched with saturated aqueous NH$_4$Cl. The two layers were separated, and the aqueous

layer was extracted with EtOAc (3 times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 50:1) afforded **S11** (1.07 g, 4.68 mmol, 93%).

To a solution of Et_2NH (373 μL, 3.60 mmol) in THF (15 mL) was added a 2.67 M solution of *n*-BuLi in *n*-hexane (1.35 mL, 3.60 mmol) at 0 °C and the reaction mixture was stirred for 30 min. The reaction mixture was then cooled down to –78 °C and **S11** (686 mg, 3.00 mmol) in THF (1.0 mL) was added. After stirring for 30 min, *trans*-cinnamaldehyde (566 μL, 3.60 mmol) was added. The reaction mixture was then warmed up to –30 °C and stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 50:1) afforded **S12** (*E*/*Z* = 1.2:1.0, 773 mg, 2.86 mmol, 95%).

S11: colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.08 (t, *J* = 6.6 Hz, 1H), 4.13–4.06 (m, 2H), 2.47–2.41 (m, 1H), 2.13–2.08 (m, 1H), 1.96 (dd, *J* = 11.2, 3.7 Hz, 1H), 1.66 (s, 3H), 1.61 (s, 3H), 1.23 (t, *J* = 6.9 Hz, 3H), 0.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 132.0, 124.1, 59.6, 38.3, 25.7, 25.2, 17.7, 14.5, –2.6 (3C). IR (ATR) ν 2963, 2914, 1716, 1250, 1140, 840 cm^{-1}. HRMS (FI) *m/z* $[M]^+$ calcd for $C_{12}H_{24}O_2Si$ 228.1546; found: 228.1543.

S12 (*E*/*Z* = 1.2:1.0): yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 15.7, 11.1 Hz, 0.45H), 7.48–7.45 (m, 2H), 7.37–7.24 (m, 0.45×3H + 0.55H×4), 7.09 (dd, J = 15.5, 11.5 Hz, 0.55H), 6.88 (d, *J* = 15.5 Hz, 0.55H), 6.71 (d, *J* = 15.7 Hz, 0.45H), 6.54 (d, *J* = 11.1 Hz, 0.45H), 5.18 (t, *J* = 7.2 Hz, 0.45H), 5.08 (t, *J* = 6.9 Hz, 0.55H), 4.30–4.21 (m, 2H), 3.22 (d, *J* = 6.9 Hz, 0.55×2H), 3.06 (d, *J* = 7.2 Hz, 0.45×2H), 1.78 (s, 0.55×3H), 1.75 (s, 0.45×3H), 1.70 (s, 0.55×3H), 1.67 (s, 0.45 × 3H), 1.37 (t, *J* = 7.2 Hz, 0.45×3H), 1.33 (t, *J* = 7.2 Hz, 0.55×3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 167.6, 139.2, 139.0, 138.1, 138.0, 136.9, 136.6, 133.8, 132.3, 131.3, 130.3, 128.75, 128.67, 128.6, 128.2, 127.0, 126.0, 123.8, 121.9, 121.1, 60.6, 60.3, 32.8, 26.3, 25.8, 25.7, 17.9, 17.8, 14.32, 14.29 (Only the detected peaks were recorded). IR (ATR) ν 2979, 2911, 1699, 1220, 1173, 746, 689 cm^{-1}. HRMS (FD) *m/z* $[M]^+$ calcd for $C_{18}H_{22}O_2$ 270.1620, found: 270.1612.
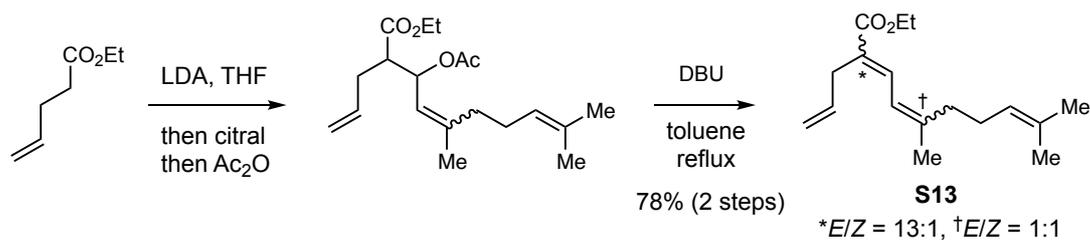
To a solution of i-Pr$_2$NH (169 μL, 1.20 mmol) in THF (5.0 mL) was added a 2.69 M solution of n-BuLi in n-hexane (449 μL, 1.20 mmol) at 0 °C, and the reaction mixture was stirred for 30 min. The resulting mixture was then cooled to –78 °C and ethyl 4-pentenoate (142 μL, 1.00 mmol) was added. After stirring for 30 min, citral (*cis* and *trans* mixture, 205 μL, 1.20 mmol) was added and the reaction mixture was stirred for 15 min at the same temperature before Ac$_2$O (189 μL, 2.00 mmol) was added. After stirring for additional 15 min, the reaction was quenched with saturated aqueous NH$_4$Cl solution (5 mL). Two layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure to afford a crude material.

β-elimination reaction was conducted referred to the literature procedure reported by Ozeki *et al*.[9] To a solution of the crude β-acetoxyester in toluene (5.0 mL) was added DBU (746 μL, 5.00 mmol) at room temperature. The reaction mixture was then refluxed at 130 °C for 2.5 h. The reaction was quenched with saturated aqueous NaHCO$_3$ (5 mL). The two layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 50:1) afforded **S13** ($^*E/Z$ = 13:1, $^†E/Z$ = 1:1, 205 mg, 0.781 mmol, 78% for 2 steps).[8]

S13 ($^*E/Z$ = 13:1, $^†E/Z$ = 1:1): yellow oil. ^{1}H NMR for **S13** ($^*E$ only, $^†E/Z$ = 1:1) (500 MHz, CDCl$_3$) δ 7.56–7.52 (m, 1H), 6.13 (s, 0.50H), 6.11 (s, 0.50H), 5.87–5.79 (m, 1H), 5.14–4.97 (m, 3H), 4.24–4.20 (m, 2H), 3.16 (d, J = 6.3 Hz, 2H), 2.32–2.10 (m, 4H), 1.90 (s, 3H), 1.68 (s, 3H), 1.62 (s, 0.50×3H) 1.61 (s, 0.50×3H), 1.31–1.28 (m, 3H). ^{13}C NMR for **S13** ($^*E$ only, $^†E/Z$ = 1:1) (126 MHz, CDCl$_3$) δ 168.3, 149.1, 148.9, 135.8, 135.7, 135.4, 135.1, 132.5, 132.1, 126.5, 126.2, 123.43, 123.37, 121.1, 120.4, 114.99, 114.95, 60.41, 60.36, 40.6, 32.8, 30.7, 30.6, 26.9, 26.3, 25.7, 24.9, 17.7, 17.6, 17.4, 14.3 (Only the detected peaks were recorded). IR (ATR) ν 2977, 2915, 2856, 1702, 1633, 1263, 1199 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{17}$H$_{26}$O$_2$ 262.1933, found: 262.1941.

Synthesis of Phosphate 6a
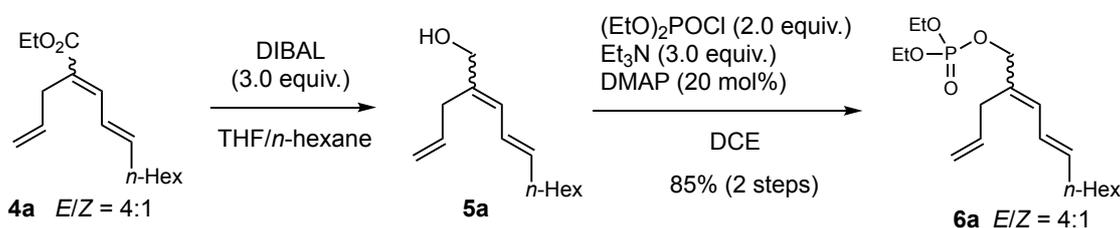
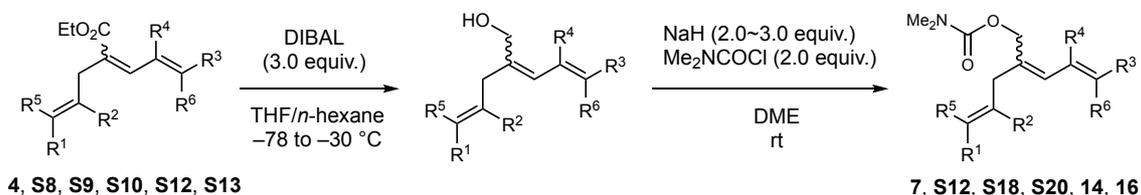To a solution of **4a** (E/Z = 4:1, 1.21 g, 4.82 mmol) in THF (24 mL) was added a 1.03 M solution of DIBAL in n-hexane (14.0 mL, 14.4 mmol) at –78 °C. The reaction mixture was then warmed to –30 °C and stirred for 30 min. The reaction was quenched with saturated aqueous Rochelle salt (40 mL), and the biphasic mixture was stirred vigorously overnight. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure to afford a crude alcohol **5a** (1.02 g, ca. 99%).

To a solution of a part of the crude **5a** (208 mg, ca. 1.00 mmol) in DCE (5.0 mL) were added 4-dimethylaminopyridine (DMAP) (24.7 mg, 0.202 mmol), Et₃N (418 μL, 3.00 mmol), and (EtO)₂POCl (288 μL, 2.00 mmol) successively at room temperature. The reaction mixture was then warmed up to 50 °C and stirred for 2.5 h. The reaction was quenched with saturated aqueous NaHCO₃ (5 mL). The two layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, n-hexane/EtOAc/Et₃N = 15:5:1) afforded **6a** (287 mg, 0.834 mmol, ca. 85%).

6a (E/Z = 4:1): yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 6.34–6.29 (m, 0.20H), 6.25–6.20 (m, 0.80H), 6.15 (d, J = 11.5 Hz, 0.80H), 6.01 (d, J = 10.9 Hz, 0.20H), 5.83–5.71 (m, 2H), 5.10–5.02 (m, 2H), 4.64 (d, J = 6.9 Hz, 0.20 × 2H), 4.46 (d, J = 6.9 Hz, 0.80 × 2H), 4.13–4.07 (m, 4H), 2.97 (d, J = 6.3 Hz, 0.8 × 2H), 2.91 (d, J = 6.3 Hz, 0.20 × 2H), 2.13–2.09 (m, 2H), 1.40–1.27 (m, 14H), 0.88 (t, J = 6.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 137.8, 137.3, 135.5, 134.8, 131.3, 131.2, 131.1, 131.02, 130.96, 129.9, 125.0, 124.9, 116.8, 116.0, 70.83, 70.78, 64.34, 64.30, 63.7, 63.64, 63.62, 63.59, 38.9, 32.9, 32.8, 32.3, 31.65, 31.62, 29.2, 29.1, 28.82, 28.77, 22.5, 16.1, 16.0, 14.0 (Only the detected peaks were recorded). IR (ATR) ν 2926, 1263, 1028, 965 cm⁻¹. HRMS (FD) m/z [M]⁺ calcd for C₁₈H₃₃O₄P 344.2116; found: 344.2124.

General Procedure for Preparation of Carbamates

Procedure D

4, **S8**, **S9**, **S10**, **S12**, **S13**   7, **S12**, **S18**, **S20**, **14**, **16**

To a 0.2 M solution of α,β-unsaturated ester in THF was added a 1.03 M solution of DIBAL in *n*-hexane (3.0 equiv.) at –78 °C. The reaction mixture was then warmed to –30 °C and stirred until the full consumption of the substrate was observed (**t₁**, 30–45 min). The reaction was quenched with saturated aqueous Rochelle salt, and the biphasic mixture was stirred vigorously for more than 3 h. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure to afford a crude product.

60% NaH in mineral oil (2.0 or 3.0 equiv.) was washed with hexane and suspended in DME (0.4 M) at 0 °C. To this mixture was added the crude alcohol in DME and Me₂NCOCl (2.0 equiv.) successively at the same temperature. The reaction mixture was then warmed up to room temperature and stirred overnight (**t₂**). The reaction was quenched with saturated aqueous NH₄Cl, and the mixture was extracted with EtOAc (5 times). The combined organic layer was dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (amino-functionalized SiO₂, *n*-hexane/EtOAc = 50:1) afforded carbamate.
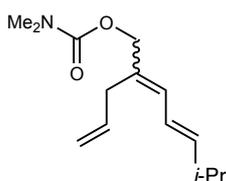
Synthesis of Carbamates
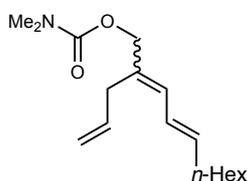
7a *E/Z* = 4:1

According to Procedure D (**t₁**: 30 min, **t₂**: 19 h), trienyl ester **4a** (*E/Z* = 4:1, 720 mg, 2.87 mmol) was converted to crude alcohol **5a** by using a 1.02 M solution of DIBAL in *n*-hexane (8.45 mL, 8.62 mmol). The obtained crude **5a** was converted to carbamate **7a** (*E/Z* = 4:1, 707 mg, 2.53 mmol, 88% for 2 steps) by using 60% NaH in mineral oil (346 mg, 8.64 mmol) and Me₂NCOCl (528 µL, 5.74 mmol).

(*E*)-**7a** and (*Z*)-**7a** were partially separated by silica gel flash column chromatography to give analytically pure samples.

(*E*)-**7a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.23 (dd, *J* = 14.9, 10.9 Hz, 1H), 6.10 (d, *J* = 10.9 Hz, 1H), 5.82–5.72 (m, 2H), 5.07–5.00 (m, 2H), 4.52 (s, 2H), 2.94 (d, *J* = 6.9 Hz, 2H), 2.91 (s, 6H), 2.10 (q, *J* = 7.1 Hz, 2H), 1.40–1.35 (m, 2H), 1.31–1.24 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.5, 137.0, 135.2, 131.8, 129.0, 125.2, 115.7, 69.0, 36.4, 35.8, 33.0, 32.9, 31.7, 29.2, 28.8, 22.6, 14.1. IR (ATR) ν 2925, 1704, 1397, 1178 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{17}$H$_{29}$NO$_2$ 279.2198, found: 279.2195.

(*Z*)-**7a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.34 (dd, *J* = 14.9, 11.2 Hz, 1H), 5.98 (d, *J* = 11.2 Hz, 1H), 5.84–5.68 (m, 2H), 5.07–5.03 (m, 2H), 4.69 (s, 2H), 2.91–2.86 (m, 8H), 2.08 (q, *J* = 7.1 Hz, 2H), 1.39–1.34 (m, 2H), 1.30–1.26 (m, 7H), 0.87 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.6, 136.5, 135.9, 132.1, 130.3, 125.2, 116.4, 62.8, 39.6, 36.4, 35.9, 32.8, 31.7, 29.2, 28.9, 22.6, 14.0. IR (ATR) ν 2925, 1704, 1397, 1177 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{17}$H$_{29}$NO$_2$ 279.2198; found: 279.2207.

7b *E/Z* = 8:1

According to Procedure D, (**t$_1$**: 30 min, **t$_2$**: 19 h), trienyl ester **4b** (*E/Z* = 8:1, 871 mg, 4.18 mmol) was converted to crude alcohol (708 mg, ca. 99%) by using a 1.03 M solution of DIBAL in *n*-hexane (12.2 mL, 12.5 mmol). A part of crude alcohol (167 mg, ca. 1.00 mmol) was converted to carbamate **7b** (*E/Z* = 8:1, 222 mg, 0.935 mmol, ca. 92%) by using 60% NaH in mineral oil (80.2 mg, 2.01 mmol) and Me$_2$NCOCl (184 μL, 2.00 mmol).

7b (*E/Z* = 8:1): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.32 (dd, *J* = 14.6, 11.1 Hz, 0.11H), 6.20 (dd, *J* = 14.6, 11.1 Hz, 0.89H), 6.10 (d, *J* = 11.1 Hz, 0.89H), 5.98 (d, *J* = 11.1 Hz, 0.11H), 5.84–5.66 (m, 2H), 5.09–5.01 (m, 2H), 4.71 (s, 0.11 × 2H), 4.53 (s, 0.89 × 2H), 2.96–2.91 (m, 8H), 2.40–2.33 (m, 1H), 1.02–0.98 (m, 6H). ^{13}C NMR for (*E*)-**7b** (126 MHz, CDCl$_3$) δ 156.4, 143.8, 135.2, 132.0, 129.1, 122.3, 115.7, 68.9, 36.4 (2C), 35.8 (2C), 33.0, 31.4, 22.3 (2C). IR (ATR) ν 2958, 1703, 1397, 1176 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{14}$H$_{23}$NO$_2$ 237.1729; found: 237.1726.
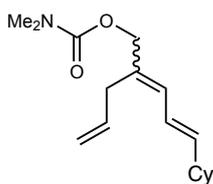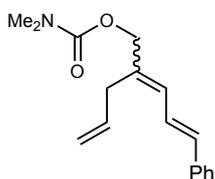

7c *E/Z* = 4:1

According to procedure D (**t$_1$**: 30 min, **t$_2$**: 22 h), trienyl ester **4c** (*E/Z* = 4:1, 63.8 mg, 0.257 mmol) was converted to crude alcohol **5c** by using a 1.02 M solution of DIBAL in *n*-hexane (756 μL, 0.771 mmol). The obtained crude alcohol was converted to carbamate **7c** (*E/Z* = 4:1, 66.5 mg, 0.240 mmol, 93% for 2 steps) by using 55% NaH in paraffin (33.6 mg, 0.771 mmol) and Me$_2$NCOCl (47.3 μL, 0.514 mmol).

7c: colorless oil. ^{1}H NMR (500 MHz, CDCl₃) δ 6.32 (dd, J = 14.8, 10.9 Hz, 0.20H), 6.20 (ddd, J = 14.9, 10.9, 1.1 Hz, 0.80H), 6.09 (d, J = 10.9 Hz, 0.80H), 5.98 (d, J = 10.9 Hz, 0.20H), 5.84–5.64 (m, 2H), 5.08–5.00 (m, 2H), 4.70 (s, 0.20×2H), 4.52 (s, 0.80×2H), 2.95–2.87 (m, 8H), 2.06–2.00 (m, 1H), 1.73–1.59 (m, 5H), 1.31–1.05 (m, 5H). ^{13}C NMR (126 MHz, CDCl₃) δ 156.5, 142.6, 142.2, 135.9, 135.2, 132.3, 132.0, 130.5, 129.3, 122.8, 122.7, 116.4, 115.7, 69.0, 62.9, 41.1, 41.0, 39.6, 36.4, 35.9, 33.0, 32.8, 26.1, 25.9 (Only the detected peaks were recorded). IR (ATR) ν 2923, 1703, 1397, 1176 cm⁻¹. HRMS (FI) m/z [M]⁺ calcd for C₁₇H₂₇NO₂ 277.2042; found: 277.2051.
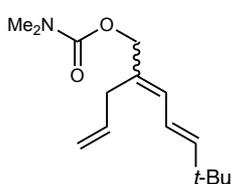
7d E/Z = 2.6:1.0

According to procedure D (**t₁**: 30 min, **t₂**: 20 h), trienyl ester **4d** (E/Z = 2.6:1.0, 162 mg, 0.729 mmol) was converted to crude alcohol **5d** by using a 1.02 M solution of DIBAL in *n*-hexane (2.15 mL, 2.19 mmol). The obtained crude alcohol was converted to carbamate **7d** (E/Z = 2.6:1.0, 172 mg, 0.685 mmol, 94% for 2 steps) by using 60% NaH in mineral oil (87.5 mg, 2.19 mmol) and Me₂NCOCl (134 μL, 1.46 mmol).

7d: colorless oil. ^{1}H NMR (500 MHz, CDCl₃) δ 6.27 (dd, J = 15.2, 10.8 Hz, 0.28H), 6.17 (dd, J = 14.9, 10.6 Hz, 0.72H), 6.10 (d, J = 10.6 Hz, 0.72H), 5.99 (d, J = 10.8 Hz, 0.28H), 5.85–5.73 (m, 2H), 5.09–5.01 (m, 2H), 4.72 (s, 0.28×2H), 4.53 (s, 0.72×2H), 2.96 (d, J = 6.9 Hz, 0.72× 2H), 2.91–2.88 (m, 0.72×6H + 0.28×8H), 1.04 (s, 0.72×9H), 1.03 (s, 0.28×9H). ^{13}C NMR (126 MHz, CDCl₃) δ 156.6, 156.5, 147.7, 147.3, 135.9, 135.2, 132.4, 132.1, 130.5, 129.3, 120.05, 120.01, 116.4, 115.8, 69.0, 63.0, 39.6, 36.4, 35.9, 33.40, 33.37, 33.1, 29.5, 29.4 (Only the detected peaks were recorded). IR (ATR) ν 2957, 1703, 1397, 1177 cm⁻¹. HRMS (FI) m/z [M]⁺ calcd for C₁₅H₂₅NO₂ 251.1885; found: 251.1882.

7e E/Z = 2.6:1.0

According to Procedure D (**t₁**: 30 min, **t₂**: 19 h), trienyl ester **4e** (E/Z = 2.7:1.0, 738 mg, 3.05 mmol) was converted to crude alcohol (635 mg, ca. 99%) by using a 1.03 M solution of DIBAL in *n*-hexane (8.87 mL, 9.14 mmol). A part of crude alcohol (40.1 mg, ca. 0.200 mmol) was converted to carbamate **7e** (E/Z = 2.6:1.0, 46.4 mg, 0.171 mmol, ca. 89%) by using 60% NaH in mineral oil (16.1 mg, 0.403 mmol) and Me₂NCOCl (36.8 μL, 0.400 mmol).

7e (E/Z = 2.6:1.0): colorless oil. ^{1}H NMR (500 MHz, CDCl₃) δ 7.41 (d, J = 7.4 Hz, 2H), 7.33–7.30 (m, 2H), 7.26–7.21 (m, 1H), 7.12 (dd, J = 15.2, 11.4 Hz, 0.28H), 6.99 (dd, J = 15.5, 10.9 Hz, 0.72H), 6.61–6.54 (m, 1H), 6.32 (d, J = 10.9 Hz, 0.72H), 6.20 (d, J = 11.4 Hz, 0.28H), 5.88–5.79 (m, 1H), 5.14–5.05 (m, 2H), 4.82 (s, 0.28 × 2H), 4.61 (s, 0.72 × 2H), 3.07 (d, J = 6.3 Hz, 0.72 ×

2H), 2.97–2.91 (m, 6H + 0.28 × 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.5, 156.4, 137.32, 137.26, 135.5, 135.4, 135.14, 135.05, 133.7, 133.3, 130.2, 128.61, 128.58, 127.61, 127.58, 126.44, 126.40, 124.0, 123.9, 116.8, 116.1, 68.7, 62.8, 39.9, 36.5 (br), 35.9 (br), 33.2 (Only the detected peaks were recorded). IR (ATR) ν 3029, 2932, 1698, 1397, 1176 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{17}$H$_{21}$NO$_2$ 271.1572; found: 271.1585.
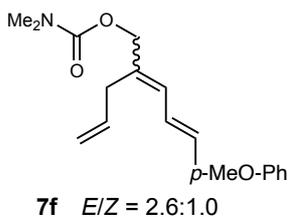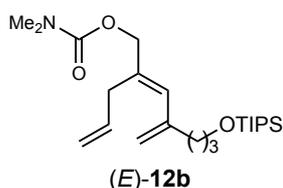
According to procedure D (t_1: 30 min, t_2: 12 h), trienyl ester **4f** (E/Z = 2.6:1.0, 629 mg, 2.31 mmol) was converted to crude alcohol by using a 1.02 M solution of DIBAL in n-hexane (6.79 mL, 6.93 mmol). The obtained crude alcohol was converted to carbamate **7f** (E/Z = 2.6:1.0, 658 mg, 2.18 mmol, 94% for 2 steps) by using 60% NaH in mineral oil (278 mg, 6.95 mmol) and Me$_2$NCOCl (425 µL, 4.62 mmol).

7f (E/Z = 2.6:1.0): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 (dd, J = 8.9, 2.6 Hz, 2H), 6.98 (dd, J = 15.5, 11.2 Hz, 0.28H), 6.88–6.82 (m, 2H + 0.72H), 6.55 (d, J = 15.5 Hz, 0.72H), 6.51 (d, J = 15.5 Hz, 0.28H), 6.29 (d, J = 11.5 Hz, 0.72H), 6.17 (d, J = 11.2 Hz, 0.28H), 5.88–5.79 (m, 1H), 5.13–5.04 (m, 2H), 4.80 (s, 0.28 × 2H), 4.60 (s, 0.72 × 2H), 3.81 (s, 3H), 3.05 (d, J = 6.3 Hz, 0.72 × 2H), 2.96–2.91 (m, 6H + 0.28 × 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 159.3, 159.2, 156.6, 156.4, 135.7, 135.2, 134.1, 133.8, 133.3, 132.9, 130.5, 130.11, 130.05, 129.0, 127.64, 127.60, 122.0, 116.6, 115.9, 114.0, 68.9, 62.8, 55.2, 39.8, 36.4, 35.8, 33.2 (Only the detected peaks were recorded). IR (ATR) ν 2933, 1698, 1508, 1397, 1247, 1172 cm^{-1}. HRMS (FI) calcd for C$_{18}$H$_{23}$NO$_3$ (M$^+$): 301.1678; found: 301.1669.
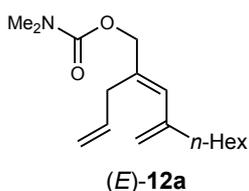
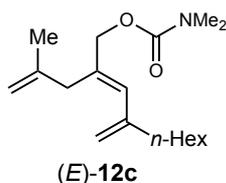According to Procedure D (t_1: 30 min, t_2: 20 h), trienyl ester (E)-**S6a** (169 mg, 0.676 mmol) was converted to crude alcohol (144 mg, ca. 99%) by using a 1.03 M solution of DIBAL in n-hexane (1.97 mL, 2.03 mmol). A part of crude alcohol (41.6 mg, ca. 0.200 mmol) was converted to carbamate (E)-**12a** (48.3 mg, 173 µmol, ca. 89%) by using 60 % NaH in mineral oil (15.5 mg, 0.388 mmol) and Me$_2$NCOCl (36.8 µL, 0.400 mmol).

(E)-**12a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.96 (s, 1H), 5.84–5.76 (m, 1H), 5.08–5.03 (m, 2H), 4.97 (s, 1H), 4.90 (s, 1H), 4.55 (s, 2H), 3.01 (d, J = 6.3 Hz, 2H), 2.93 (s, 6H), 2.08 (t, J = 7.4 Hz, 2H), 1.41–1.35 (m, 2H), 1.31–1.26 (m, 6H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.4, 145.2, 135.9, 134.4, 129.9, 116.0, 113.1, 68.5, 37.2, 36.5 (br), 35.8 (br), 33.6, 31.7, 28.8, 28.1, 22.6, 14.1. IR (ATR) ν 3080, 2927, 2856, 1708, 1397, 1181 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{17}$H$_{29}$NO$_2$ 279.2198; found: 279.2199.
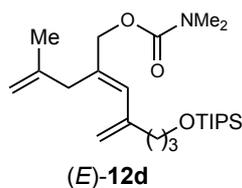
Me₂N group structure

According to Procedure D (**t₁**: 30 min, **t₂**: 17 h), trienyl ester (*E*)-**S6b** (80.6 mg, 0.212 mmol) was converted to crude alcohol by using a 1.03 M solution of DIBAL in *n*-hexane (617 µL, 0.635 mmol). The obtained crude alcohol was converted to carbamate (*E*)-**12b** (84.0 mg, 0.205 mmol, 97% for 2 steps) by using 60% NaH in mineral oil (16.8 mg, 0.420 mmol), and Me₂NCOCl (39.0 µL, 0.424 mmol).

(*E*)-**12b**: colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 5.97 (s, 1H), 5.84–5.76 (m, 1H), 5.07–5.03 (m, 2H), 5.00 (s, 1H), 4.92 (s, 1H), 4.55 (s, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 3.00 (d, *J* = 6.3 Hz, 2H), 2.93 (s, 6H), 2.17 (t, *J* = 7.7 Hz, 2H), 1.67–1.61 (m, 2H), 1.10–1.05 (m, 21H). ¹³C NMR (126 MHz, CDCl₃) δ 156.3, 144.6, 135.8, 134.6, 129.7, 116.0, 113.4, 68.5, 62.7, 36.4 (br), 35.9 (br), 33.7, 33.5, 31.5, 18.0 (6C), 11.9 (3C). IR (ATR) ν 2941, 1709, 1463, 1396, 1179, 1103 cm⁻¹. HRMS (FD) *m/z* [M]⁺ calcd for C₂₃H₄₃NO₃Si 409.3012; found: 409.2999.
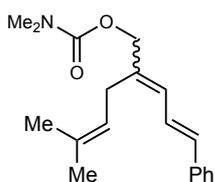
According to Procedure D (**t₁**: 45 min, **t₂**: 17 h), trienyl ester (*E*)-**S6c** (140 mg, 0.529 mmol) was converted to crude alcohol (117 mg, ca. 99%) by using a 1.03 M solution of DIBAL in *n*-hexane (1.54 mL, 1.59 mmol). A part of crude alcohol (66.3 mg, ca. 0.300 mmol) was converted to carbamate (*E*)-**12c** (78.9 mg, 0.269 mmol, ca. 90%) by using 60% NaH in mineral oil (23.7 mg, 0.593 mmol) and Me₂NCOCl (55.1 µL, 0.600 mmol).

(*E*)-**12c**: colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 6.02 (s, 1H), 4.94 (s, 1H), 4.91 (s, 1H), 4.79 (s, 1H), 4.69 (s, 1H), 4.52 (s, 2H), 2.94–2.92 (m, 8H), 2.07 (t, *J* = 7.4 Hz, 2H), 1.71 (s, 3H), 1.41–1.36 (m, 2H), 1.31–1.25 (m, 6H), 0.88 (t, *J* = 6.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 156.4, 145.1, 143.0, 134.2, 130.4, 112.7, 111.4, 68.7, 37.4, 37.3, 36.4 (br), 35.9 (br), 31.7, 28.9, 28.1, 22.9, 22.6, 14.1. IR (ATR) ν 2927, 1707, 1397, 1178 cm⁻¹. HRMS (FD) *m/z* [M]⁺ calcd for C₁₈H₃₁NO₂ 293.2355; found: 293.2357.
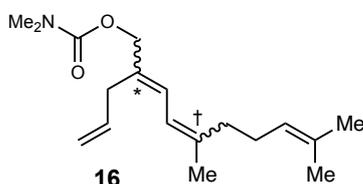
According to Procedure D (**t₁**: 30 min, **t₂**: 17 h), trienyl ester (*E*)-**S6d** (59.7 mg, 0.151 mmol) was converted to crude alcohol by using a 1.03 M solution of DIBAL in *n*-hexane (441 µL, 0.454 mmol). The obtained crude alcohol was converted to carbamate (*E*)-**12d** (62.7 mg, 0.148 mmol, 98% for 2 steps) by using 60% NaH in mineral oil (12.3 mg, 0.308 mmol) and Me₂NCOCl (27.8 µL, 0.302 mmol).

(*E*)-**12d**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.03 (s, 1H), 4.97 (s, 1H), 4.93 (s, 1H), 4.79 (s, 1H), 4.69 (s, 1H), 4.52 (s, 2H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.93–2.90 (m, 8H), 2.17 (t, *J* = 7.7 Hz, 2H), 1.71 (s, 3H), 1.67–1.62 (m, 2H), 1.10–1.04 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.4, 144.6, 143.0, 134.4, 130.1, 113.0, 111.4, 68.6, 62.8, 37.4, 36.4 (br), 35.8 (br), 33.6, 31.5, 22.9, 18.0 (6C), 12.0 (3C). IR (ATR) ν 2865, 1709, 1462, 1396, 1179, 1103, 882 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{24}$H$_{45}$NO$_3$Si 423.3169; found: 423.3186.

14 *E/Z* = 1.2:1.0

According to Procedure D (**t$_1$**: 30 min, **t$_2$**: 1.5 days), trienyl ester **S12** (*E/Z* = 1.2:1.0, 243 mg, 0.900 mmol) was converted to crude alcohol (209 mg, ca. 99%) by using a 1.03 M solution of DIBAL in *n*-hexane (2.62 mL, 2.70 mmol). A part of crude alcohol (45.7 mg, ca. 0.200 mmol) was converted to carbamate **14** (*E/Z* = 1.2:1.0, 39.1 mg, 0.131 mmol, ca. 66%) by using 60% NaH in mineral oil (16.6 mg, 0.415 mmol) and Me$_2$NCOCl (36.8 μL, 0.400 mmol).

14 (*E/Z* = 1.2:1.0): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41–7.40 (m, 2H), 7.33–7.20 (m, 3H), 7.12 (dd, *J* = 15.5, 11.5 Hz, 0.45H), 7.04 (dd, *J* = 15.5, 11.2 Hz, 0.55H), 6.59–6.53 (m, 1H), 6.23 (d, *J* = 11.2 Hz, 0.55H), 6.17 (d, *J* = 11.5 Hz, 0.45H), 5.19 (t, *J* = 7.4 Hz, 0.45H), 5.11 (t, *J* = 7.4 Hz, 0.55H), 4.79 (s, 0.45 × 2H), 4.58 (s, 0.55 × 2H), 3.02 (d, *J* = 7.4 Hz, 0.55 × 2H), 2.94–2.90 (m, 6H + 0.45 × 2H), 1.75 (s, 0.45 × 3H), 1.71 (s, 0.55 × 6H), 1.65 (s, 0.45 × 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.6, 156.4, 137.44, 137.37, 137.3, 136.7, 133.8, 133.2, 132.9, 132.8, 129.2, 128.6, 128.5, 127.5, 127.4, 127.3, 126.4, 126.3, 124.15, 124.12, 121.3, 121.0, 68.7, 63.0, 36.4 (br), 35.8 (br), 34.1, 27.9, 25.8, 25.7, 17.8, 17.7 (Only the detected peaks were recorded). IR (ATR) ν 2926, 1700, 1397, 1176 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{19}$H$_{25}$NO$_2$ 299.1885; found: 299.1875.
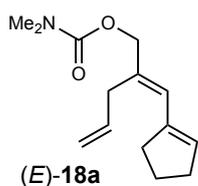

16
E/Z = 10:1, †*E/Z* = 1:1

According to Procedure D (**t$_1$**: 30 min, **t$_2$**: 18 h), trienyl ester **S13** (**E/Z* = 13:1, †*E/Z* = 1:1, 184 mg, 0.701 mmol) was converted to crude alcohol by using a 1.03 M solution of DIBAL in *n*-hexane (2.04 mL, 2.10 mmol). A part of crude alcohol was converted to carbamate **16** (**E/Z* = 10:1, †*E/Z* = 1:1, 136 mg, 0.467 mmol, 67% for 2 steps) by using 60% NaH in mineral oil (56.4 mg, 1.41 mmol) and Me$_2$NCOCl (129 μL, 1.40 mmol).

16 (**E* only, †*E/Z* = 1:1): yellow oil. ^{1}H NMR for **16** (**E* only, †*E/Z* = 1:1) (500 MHz, CDCl$_3$) δ 6.36–6.33 (m, 1H), 6.03 (s, 0.53H), 6.01 (s, 0.47H), 5.82–5.74 (m, 1H), 5.12–5.00 (m, 3H), 4.56–4.55 (d, *J* = 8.0 Hz, 2H), 2.96–2.92 (m, 8H), 2.20–2.06 (m, 4H), 1.82 (s, 0.47 × 3H), 1.77 (s, 0.53

× 3H), 1.68 (s, 0.53 × 6H), 1.61 (s, 0.47 × 6H). ^{13}C NMR for **16** ($^*E$ only, $^{\dagger}E/Z$ = 1:1) (126 MHz, CDCl$_3$) δ 156.5, 141.0, 140.8, 135.31, 135.28, 131.9, 131.70, 131.68, 131.4, 125.1, 124.8, 123.9, 123.8, 120.4, 119.7, 115.58, 115.56, 69.47, 69.46, 40.3, 36.4 (br), 35.8 (br), 32.9, 32.8, 32.4, 26.7, 26.5, 25.6, 24.3, 17.7, 17.6, 16.7 (Only the detected peaks were recorded). IR (ATR) ν 2923, 1703, 1396, 1177 cm^{-1}. HRMS (FD) calcd m/z [M]$^+$ for C$_{18}$H$_{29}$NO$_2$ 291.2198; found: 291.2206.
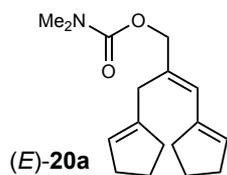
According to Procedure D (t_1: 30 min, t_2: 14 h), trienyl ester **S22a** (179 mg, 0.866 mmol) was converted to crude alcohol by using a 1.02 M solution of DIBAL in n-hexane (2.55 mL, 2.60 mmol). The obtained crude alcohol was converted to carbamate (*E*)-**18a** (182 mg, 0.771 mmol, 89% for 2 steps) by using 60% NaH in mineral oil (105 mg, 2.63 mmol) and Me$_2$NCOCl (159 μL, 1.73 mmol).

(*E*)-**18a**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.21 (s, 1H), 5.85–5.78 (m, 1H), 5.76 (s, 1H), 5.07–5.02 (m, 2H), 4.54 (s, 2H), 3.04 (d, J = 5.7 Hz, 2H), 2.92 (s, 6H), 2.56–2.53 (m, 2H), 2.36 (t, J = 6.0 Hz, 2H), 1.93–1.87 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.5, 140.5, 135.8, 132.7, 132.6, 126.1, 115.7, 69.6, 36.4 (br), 35.9 (br), 34.6, 33.5, 32.3, 23.9. IR (ATR) ν 2842, 1702, 1397, 1177 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{14}$H$_{21}$NO$_2$ 235.1572; found: 235.1581.
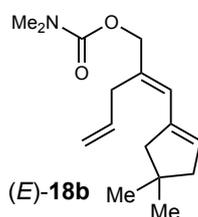
According to Procedure D (t_1: 30 min, t_2: 17 h), trienyl ester **S22b** (109 mg, 0.467 mmol) was converted to crude alcohol by using a 1.02 M solution of DIBAL in n-hexane (1.37 mL, 1.40 mmol). The obtained crude alcohol was converted carbamate (*E*)-**18b** (115 mg, 0.438 mmol, 94% for 2 steps) by using 60% NaH in mineral oil (56.0 mg, 1.40 mmol) and Me$_2$NCOCl (85.8 μL, 0.934 mmol).

(*E*)-**18b**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.15 (s, 1H), 5.85–5.77 (m, 1H), 5.63 (s, 1H), 5.07–5.02 (m, 2H), 4.53 (s, 2H), 3.01 (d, J = 5.7 Hz, 2H), 2.92 (s, 6H), 2.37 (d, J = 1.7 Hz, 2H), 2.18 (s, 2H), 1.09 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.5, 139.2, 135.9, 132.4, 131.5, 126.5, 115.8, 69.6, 49.8, 47.3, 39.0, 36.4 (br), 35.9 (br), 33.5, 29.7 (2C). IR (ATR) ν 2952, 1703, 1397, 1177 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{16}$H$_{25}$NO$_2$ 263.1885; found: 263.1893.

According to Procedure D (t_1: 40 min, t_2: 15 h), trienyl ester **S23a** (398 mg, 1.62 mmol) was converted to crude alcohol by using a 1.02 M solution of DIBAL in n-hexane (4.75 mL, 4.85 mmol). The obtained crude alcohol was converted to carbamate (*E*)-**20a** (434 mg, 1.57 mmol, 97% for 2 steps) by

using 60% NaH in mineral oil (196 mg, 4.91 mmol) and Me_2NCOCl (297 µL, 3.23 mmol).

(*E*)-**20a**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.22 (s, 1H), 5.73 (s, 1H), 5.33 (t, *J* = 1.7 Hz, 1H), 4.52 (s, 2H), 3.00 (s, 2H), 2.93–2.91 (m, 6H), 2.54–2.51 (m, 2H), 2.37–2.34 (m, 2H), 2.31–2.26 (m, 2H), 2.23 (t, *J* = 6.6 Hz, 2H), 1.92–1.83 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.5, 141.9, 140.7, 133.1, 132.4, 125.8, 125.0, 69.9, 36.4 (br), 35.9 (br), 35.5, 34.5, 32.4, 32.2, 31.3, 23.9, 23.4. IR (ATR) ν 2928, 1703, 1396, 1176 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for $C_{17}H_{25}NO_2$ 275.1885; found: 275.1898.
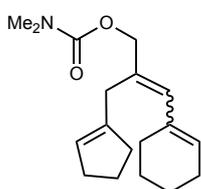

According to Procedure D (CH$_2$Cl$_2$ was used instead of THF in DIBAL reduction. **t$_1$**: 10 min, **t$_2$**: 18 h), trienyl ester **S23b** (*E/Z* = 1.4:1.0, 69.8 mg, 0.268 mmol) was converted to crude alcohol by using a 1.03 M solution of DIBAL in *n*-hexane (781 µL, 0.804 mmol). The obtained crude alcohol was converted to carbamate **20b** (*E/Z* = 1.6:1.0, 70.3 mg, 0.243 mmol, 91% for 2 steps) by using 60% NaH in mineral oil (21.4 mg, 0.535 mmol) and Me_2NCOCl (49.3 µL, 0.536 mmol).

20b *E/Z* = 1.6:1.0

20b: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.92 (s, 0.62H), 5.80 (s, 0.38H), 5.66 (s, 0.62H), 5.53 (s, 0.38H), 5.36 (s, 0.38H), 5.32 (s, 0.62H), 4.66 (s, 0.38 × 2H), 4.48 (s, 0.62 × 2H), 2.97 (s, 0.62 × 2H), 2.90–2.88 (m, 6H + 0.38 × 2H), 2.28 (br, 2H), 2.22–2.17 (m, 2H), 2.08–2.04 (m, 4H), 1.87–1.80 (m, 2H), 1.63–1.53 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 156.7, 156.5, 142.2, 142.1, 134.5, 134.4, 133.9, 132.2, 131.9, 131.7, 127.3, 127.2, 125.8, 125.0, 69.8, 63.7, 37.4, 36.4 (br), 35.8 (br), 35.5, 34.8, 32.5, 32.4, 31.2, 28.9, 28.6, 25.6, 25.5, 23.5, 23.4, 22.8, 22.7, 22.1, 22.0 (Only the detected peaks were recorded). IR (ATR) ν 2926,, 1703, 1395, 1177 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for $C_{18}H_{27}NO_2$ 289.2042; found: 289.2041.

General Procedure for 8π Electrocyclization/β-Elimination Sequence
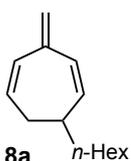
Procedure E
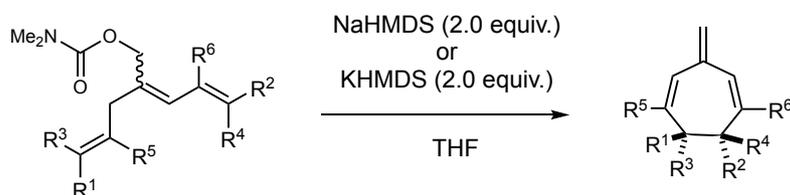
To a 0.1 M solution of carbamate in THF was added a ca. 1 M solution of base in THF (NaHMDS or KHMDS, 2.0 equiv.) at 50 °C. The reaction mixture was stirred at the same temperature until no further changes in TLC spots were observed (15 min–2 h). The reaction mixture was then cooled and 3-*tert*-butyl-4-hydroxyanisole (catalytic amount) was added. The reaction was quenched with brine. The two layers were separated, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$ neutralized by elution of *N,N*-dimethylaniline, *n*-hexane only) afforded 3-methylene-1,4-cycloheptadiene derivatives.

NOTE: 3-Methylene-1,4-cycloheptadiene derivatives are unstable and decomposed within a few days in a freezer. Flash column chromatography was performed as quickly as possible. Also, CDCl$_3$ (A solvent for NMR measurement) was passed through a plug of basic alumina just before using.

Synthesis of 3-Methylene-1,4-cycloheptadiene Derivatives

6-Hexyl-3-methylenecyclohepta-1,4-diene (8a)

0.1 mmol scale: According to Procedure E (reaction time: 1 h), carbamate **7a** (*E/Z* = 4:1, 37.4 mg, 0.134 mmol) was converted to cyclic triene **8a** (16.6 mg, 87.2 μmol, 65%) by using a 1.1 M solution of NaHMDS in THF (243 μL, 0.267 mmol).

1 mmol scale: According to Procedure E (reaction time: 1 h), carbamate **7a** (*E/Z* = 4:1, 351 mg, 1.25 mmol) was converted to cyclic triene **8a** (174 mg, 0.915 mmol, 73%) by using a 1.1 M solution of NaHMDS in THF (2.27 mL, 2.50 mmol).

8a: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.08 (d, J = 11.6 Hz, 1H), 6.03 (d, J = 11.9 Hz, 1H), 5.77 (dt, J = 11.9, 6.0 Hz, 1H), 5.71 (dd, J = 11.6, 4.9 Hz, 1H), 5.05 (s, 1H), 5.04 (s, 1H), 2.41 (br, 1H), 2.35–2.30 (m, 1H), 2.25–2.17 (m, 1H), 1.45–1.27 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0, 137.1, 130.8, 130.1, 129.4, 120.6, 38.6, 36.1, 33.7, 31.8, 29.4, 27.2, 22.7, 14.1. IR (ATR) ν 2924, 1567, 1458, 881, 786 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{14}$H$_{22}$ 190.1722; found: 190.1716.

**Synthesis of 6-Alkylated-3-methylene-1,4-cycloheptadienes (Scheme 6)**

6-Isopropyl-3-methylenecyclohepta-1,4-diene (8b)
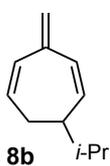
According to Procedure E (reaction time: 1 h, eluent for flash column chromatography: *n*-pentane only), carbamate **7b** (*E/Z* = 8:1, 48.0 mg, 0.202 mmol) was converted to cyclic triene **8b** (22.1 mg, 0.149 mmol, 74%) by using a 1.1 M solution of NaHMDS in THF (364 μL, 0.400 mmol).

8b: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.08 (d, J = 12.0 Hz, 2H), 5.83–5.76 (m, 2H), 5.05 (d, J = 6.6 Hz, 2H), 2.30–2.23 (m, 3H), 1.79–1.72 (m, 1H), 0.91 (dd, J = 8.6, 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.1, 135.9, 130.8, 130.3, 129.8, 120.5, 44.9, 32.7, 31.0, 19.8, 19.6. IR (ATR) ν 2956, 1567, 1463, 880, 785 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{11}$H$_{16}$ 148.1252; found: 148.1245.

6-Cyclohexyl-3-methylenecyclohepta-1,4-diene (8c)
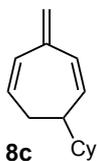
According to Procedure E (reaction time: 1.5 h), carbamate **7c** (*E/Z* = 4:1, 55.3 mg, 0.199 mmol) was converted to cyclic triene **8c** (25.0 mg, 0.133 mmol, 67%) by using a 1.1 M solution of NaHMDS in THF (364 μL, 0.400 mmol).

8c: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.07 (t, J = 10.0 Hz, 2H), 5.81–5.77 (m, 2H), 5.04 (d, J = 6.3 Hz, 2H), 2.34–2.25 (m, 3H), 1.74–1.63 (m, 5H), 1.44–1.37 (m, 1H), 1.30–0.95 (m, 5H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.1, 136.4, 130.8, 130.3, 129.6, 120.4, 44.4, 42.7, 30.7, 30.3, 30.1, 26.60, 26.58, 26.56. IR (ATR) ν 2921, 1566, 1446, 879 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{14}$H$_{20}$ 188.1565; found: 188.1561.

## 6-(*tert*-Butyl)-3-methylenecyclohepta-1,4-diene (8d)
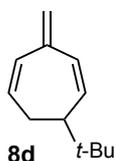
According to procedure E (reaction time: 1.5 h), carbamate **7d** (*E/Z* = 2.6:1.0, 49.7 mg, 0.198 mmol) was converted to cyclic triene **8d** (15.3 mg, 94.3 µmol, 48%) by using a 1.1 M solution of NaHMDS in THF (364 µL, 0.400 mmol).

8d: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.11 (d, *J* = 11.5 Hz, 1H), 6.06 (d, *J* = 11.5 Hz, 1H), 5.88–5.83 (m, 2H), 5.04 (s, 2H), 2.39 (q, *J* = 8.0 Hz, 1H), 2.25–2.23 (m, 1H), 2.18–2.12 (m, 1H), 0.93 (s, 9H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0, 134.8, 131.4, 130.5, 129.9, 120.1, 49.1, 33.3, 29.5, 27.5. IR (ATR) ν 2959, 1567, 1366, 879 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{12}$H$_{18}$ 162.1409; found: 162.1405.

## Synthesis of 6-Arylated-3-methylene-1,4-cycloheptadienes (Scheme 7)

3-Methylene-6-phenylcyclohepta-1,4-diene (8e)
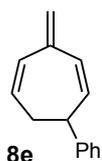
According to Procedure E (reaction time: 30 min), carbamate **7e** (*E/Z* = 2.6:1.0, 27.0 mg, 99.5 µmol) was converted to cyclic triene **8e** (12.0 mg, 65.8 µmol, 66%) by using a 1.1 M solution of NaHMDS in THF (182 µL, 0.200 mmol).

8e: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (t, *J* = 7.4 Hz, 2H), 7.22–7.20 (m, 3H), 6.17 (t, *J* = 10.9 Hz, 2H), 5.87 (dd, *J* = 11.7, 4.3 Hz, 1H), 5.78–5.73 (m, 1H), 5.17 (s, 1H), 5.15 (s, 1H), 3.78 (br 1H), 2.66–2.60 (m, 1H), 2.56–2.51 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.9, 143.6, 135.3, 131.3, 130.4, 129.7, 128.5 (2C), 127.5 (2C), 126.2, 121.9, 45.4, 37.0. IR (ATR) ν 3022, 1492, 884, 787, 758, 698 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{14}$H$_{14}$ 182.1096; found: 182.1093.

## 6-(4-Methoxyphenyl)-3-methylenecyclohepta-1,4-diene (8f)
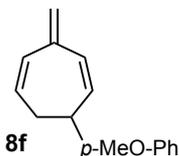
According to procedure E (reaction time: 30 min), carbamate **7f** (*E/Z* = 2.6:1.0, 60.8 mg, 0.202 mmol) was converted to cyclic triene **8f** (20.7 mg, 97.5 µmol, 48%) by using a 1.1 M solution of NaHMDS in THF (364 µL, 0.400 mmol).

8f: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.13 (d, *J* = 9.2 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 2H), 6.18–6.15 (m, 2H), 5.85 (dd, *J* = 12.0, 4.6 Hz, 1H), 5.76–5.72 (m, 1H), 5.15 (d, *J* = 12.6 Hz, 2H), 3.79 (s, 3H), 3.73 (br, 1H), 2.62–2.49 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 158.0, 143.7, 138.0, 135.7, 131.2, 130.2, 129.7, 128.4, 121.7, 113.8, 55.2, 44.6, 37.1. IR (ATR) ν 3017, 1509, 1245,

1176, 1036 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{15}$H$_{16}$O 212.1201; found: 212.1211.

Synthesis of 1-Substituted- and 1,5-Disubstituted-3-methylene-1,4-cycloheptadienes (Scheme 8)

1-Hexyl-3-methylenecyclohepta-1,4-diene (13a)

13a
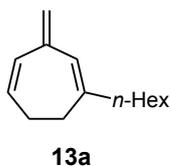
According to Procedure E (reaction time: 1 h), carbamate **12a** (27.3 mg, 97.7 μmol) was converted to cyclic triene **13a** (10.3 mg, 54.1 μmol, 55%) by using a 1.0 M solution of KHMDS in THF (200 μL, 0.200 mmol).

13a: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.05 (d, *J* = 11.5 Hz, 1H), 5.93 (s, 1H), 5.83–5.80 (m, 1H), 4.96 (d, *J* = 4.6 Hz, 2H), 2.30 (d, *J* = 2.9 Hz, 4H), 2.07 (t, *J* = 7.4 Hz, 2H), 1.44–1.40 (m, 2H), 1.32–1.25 (m, 6H), 0.88 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.6, 143.9, 131.5, 130.9, 125.8, 119.1, 41.5, 32.2, 31.8, 29.1, 27.9 (2C), 22.6, 14.1. IR (ATR) ν 2925, 1567, 1457, 1435, 876 cm^{-1}. HRMS (FI) *m/z* [M]$^+$ calcd for C$_{14}$H$_{22}$ 190.1722; found: 190.1723.

Triisopropyl(3-(3-methylenecyclohepta-1,4-dien-1-yl)propoxy)silane (13b)

13b
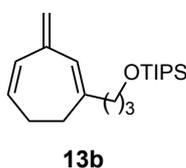
According to Procedure E (reaction time: 1 h), carbamate **12b** (40.7 mg, 99.3 μmol) was converted to cyclic triene **13b** (18.8 mg, 58.6 μmol, 59%) by using a 1.0 M solution of KHMDS in THF (200 μL, 0.200 mmol).

13b: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.05 (d, *J* = 11.5 Hz, 1H), 5.95 (s, 1H), 5.81 (br, 1H), 4.96 (s, 2H), 3.69 (t, *J* = 6.3 Hz, 2H), 2.31 (s, 4H), 2.16 (t, *J* = 7.4 Hz, 2H), 1.71–1.65 (m, 2H), 1.11–1.05 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0, 143.8, 131.5, 130.9, 126.0, 119.3, 62.9, 37.7, 32.3, 31.3, 27.9, 18.0 (6C), 12.0 (3C). IR (ATR) ν 2941, 1463, 1103, 880 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{20}$H$_{36}$OSi 320.2535; found: 320.2547.

### 1-Hexyl-5-methyl-3-methylenecyclohepta-1,4-diene (13c)

13c
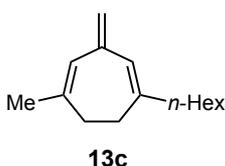
According to Procedure E (reaction time: 1.5 h), carbamate **12c** (29.1 mg, 99.2 μmol) was converted to cyclic triene **13c** (11.3 mg, 55.3 μmol, 56%) by using a 1.0 M solution of KHMDS in THF (200 μL, 0.200 mmol).

13c: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.92 (s, 1H), 5.89 (s, 1H), 4.85 (s, 2H), 2.26 (s,

4H), 2.05 (t, $J = 7.4$ Hz, 2H), 1.82 (s, 3H), 1.43–1.39 (m, 2H), 1.30–1.28 (m, 6H), 0.88 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.2, 143.5, 140.3, 126.1, 125.7, 117.2, 41.3, 33.1, 31.8, 31.3, 29.1, 27.9, 27.4, 22.6, 14.1. IR (ATR) ν 2924, 1566, 1433, 876 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{15}$H$_{24}$ 204.1878; found: 204.1884.

**Triisopropyl(3-(5-methyl-3-methylenecyclohepta-1,4-dien-1-yl)propoxy)silane (13d)**
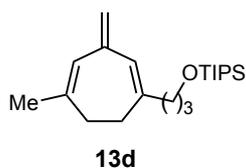
According to Procedure E (reaction time: 2 h), carbamate **12d** (20.8 mg, 49.1 μmol) was converted to cyclic triene **13d** (6.8 mg, 20 μmol, 41%) by using a 1.0 M solution of KHMDS in THF (100 μL, 0.100 mmol).

13d: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.92 (s, 2H), 4.85 (s, 2H), 3.68 (t, $J = 6.6$ Hz, 2H), 2.29–2.22 (m, 4H), 2.14 (t, $J = 7.7$ Hz, 2H), 1.82 (s, 3H), 1.70–1.64 (m, 2H), 1.10–1.05 (m, 21H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.6, 143.4, 140.3, 126.1, 125.9, 117.4, 62.9, 37.5, 33.1, 31.4, 31.3, 27.4, 18.0 (6C), 12.0 (3C). IR (ATR) ν 2941, 1567, 1463, 1102, 880 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{21}$H$_{38}$OSi 334.2692; found: 334.2688.

**Construction of a Quaternary Carbon Center (Scheme 9)**

6,6-Dimethyl-3-methylene-7-phenylcyclohepta-1,4-diene (15)
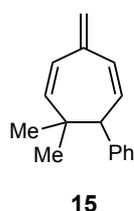
According to Procedure E (reaction time: 15 min, under diluted condition [0.01 M]), carbamate **14** ($E/Z = 1.2:1.0$, 22.2 mg, 74.1 μmol) was converted to cyclic triene **15** (7.9 mg, 38 μmol, 51%) by using a 1.0 M solution of KHMDS in THF (77.9 μL, 77.9 μmol).

15: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.24–7.18 (m, 5H), 6.19 (d, $J = 12.0$ Hz, 1H), 6.07 (dd, $J = 12.0, 1.1$ Hz, 1H), 5.83 (dd, $J = 12.0, 7.0$ Hz, 1H), 5.44 (d, $J = 12.0$ Hz, 1H), 5.19 (d, $J = 3.4$ Hz, 2H), 3.44 (d, $J = 7.0$ Hz, 1H), 1.16 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.3, 142.5, 140.2, 132.7, 130.0, 129.6, 128.3, 127.7 (2C), 126.4 (2C), 122.0, 57.2, 40.1, 31.5, 29.0. IR (ATR) ν 2956, 1566, 1452, 885, 699 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{16}$H$_{18}$ 210.1409; found: 210.1402.

6-Methyl-3-methylene-6-(4-methylpent-3-en-1-yl)cyclohepta-1,4-diene (17)
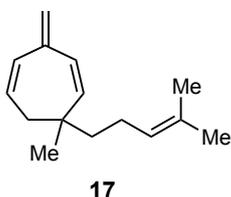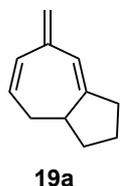
According to Procedure E (reaction time: 1.5 h), carbamate **16** ($^*E/Z$ = 10:1, $^†E/Z$ = 1:1, 58.9 mg, 0.202 mmol) was converted to cyclic triene **17** (23.0 mg, 0.114 mmol, 56%) by using a 1.1 M solution of NaHMDS in THF (364 μL, 0.400 mmol).

17: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.12 (d, J = 11.5 Hz, 1H), 5.95 (d, J = 12.0 Hz, 1H), 5.71–5.67 (m, 1H), 5.58 (d, J = 12.0 Hz, 1H), 5.10–5.03 (m, 3H), 2.30 (dd, J = 15.9, 6.6 Hz, 1H), 2.19 (dd, J = 15.9, 5.7 Hz, 1H), 1.98–1.93 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.42–1.39 (m, 2H), 1.05 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.6, 141.0, 131.2, 131.0, 128.6, 127.9, 124.8, 120.9, 42.4, 39.4, 39.3, 27.8, 25.7, 23.0, 17.6. IR (ATR) ν 2966, 1566, 1454, 1375, 882 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{15}$H$_{22}$ 202.1722; found: 202.1718.

**Synthesis of Bicyclic and Tricyclic Compounds (Scheme 10)**

7-Methylene-1,2,3,3a,4,7-hexahydroazulene (19a)

According to Procedure E (reaction time: 2 h, Eluent for flash column chromatography: *n*-pentane only), carbamate **18a** (46.7 mg, 0.198 mmol) was converted to cyclic triene **19a** (19.9 mg, 0.136 mmol, 69%) by using a 1.1 M solution of NaHMDS in THF (364 μL, 0.400 mmol).

19a: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.06–6.04 (m, 2H), 5.79–5.74 (m, 1H), 4.94 (s, 1H), 4.93 (s, 1H), 2.73–2.67 (m, 1H), 2.46–2.43 (m, 2H), 2.35 (qd, J = 8.2, 2.9 Hz, 1H), 2.23–2.17 (m, 1H), 1.99–1.94 (m, 1H), 1.76–1.70 (m, 1H), 1.58–1.49 (m, 1H), 1.35–1.25 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 150.9, 143.4, 131.0, 130.0, 121.4, 118.6, 43.4, 35.8, 35.4, 33.9, 25.1. IR (ATR) ν 2950, 1566, 1448, 876 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{11}$H$_{14}$ 146.1096; found: 146.1089.
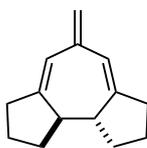
2,2-Dimethyl-7-methylene-1,2,3,3a,4,7-hexahydroazulene (19b)
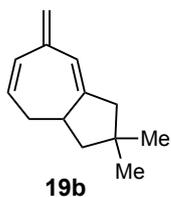
According to Procedure E (reaction time: 2 h), carbamate **18b** (28.3 mg, 0.107 mmol) was converted to cyclic triene **19b** (11.8 mg, 67.7 μmol, 63%) by using a 1.1 M solution of NaHMDS in THF (195 μL, 0.215 mmol).

19b: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.04 (d, J = 11.5 Hz, 1H), 6.01 (s, 1H), 5.78–5.74 (m, 1H), 4.94 (s, 2H), 2.94–2.88 (m, 1H), 2.34–2.27 (m, 2H), 2.23–2.18 (m, 2H), 1.72–1.67 (m, 1H), 1.24 (t, J = 11.2 Hz, 1H), 1.06 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 151.0, 143.4, 131.0, 130.1, 122.1, 118.7, 50.0, 48.8, 42.3, 37.6, 34.2, 28.8, 27.2. IR (ATR) ν 2951, 2925, 1566, 874 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{13}$H$_{18}$ 174.1409; found: 174.1402.

Anti-5-methylene-2,3,5,7,8,9,9a,9b-octahydro-1_H_-cyclopenta[_e_]azulene (21a)
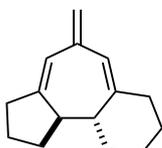

According to Procedure E (reaction time: 1.5 h), carbamate **20a** (216 mg, 0.785 mmol) was converted to cyclic triene **21a** (70.1 mg, 0.376 mmol, 48%) by using a 1.0 M solution of KHMDS in THF (1.57 mL, 1.57 mmol).

21a

21a: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.05 (s, 2H), 4.81 (s, 2H), 2.45–2.42 (m, 6H), 2.02–1.98 (m, 2H), 1.77–1.71 (m, 2H), 1.54–1.43 (m, 2H), 1.37–1.29 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 149.1, 142.3 (2C), 121.9 (2C), 116.2, 48.2 (2C), 35.6 (2C), 34.1 (2C), 24.9 (2C). IR (ATR) ν 2951, 1565, 1446, 1429, 874 cm^{-1}. HRMS (FI) m/z [M]$^+$ calcd for C$_{14}$H$_{18}$ 186.1409; found: 186.1417.

**_Anti_-5-methylene-1,2,3,5,7,8,9,10,10a,10b-decahydrobenzo[_e_]azulene (21b)**

According to Procedure E (reaction time: 2 h), carbamate **20b** (E/Z = 1.6:1.0, 57.8 mg, 0.200 mmol) was converted to cyclic triene **21b** (15.8 mg, 78.9 μmol, 39%) by using a 1.0 M solution of KHMDS in THF (400 μL, 0.400 mmol).

21b

21b: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.10 (s, 1H), 5.94 (s, 1H), 4.90 (s, 1H), 4.87 (s, 1H), 2.55–2.50 (m, 1H), 2.39–2.36 (m, 2H), 2.29 (d, J = 14.3 Hz, 1H), 2.14–2.05 (m, 3H), 1.94–1.91 (m, 1H), 1.76–1.69 (m, 3H), 1.47–1.25 (m, 4H), 1.12–1.03 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 149.3, 144.0, 143.2, 125.2, 122.7, 117.2, 47.4, 44.9, 38.3, 36.0, 34.3, 32.3, 26.1, 25.2, 24.9. IR (ATR) ν 2927, 1566, 1445, 876 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{15}$H$_{20}$ 200.1565; found: 200.1561.

Determination of *trans*-configuration of 21a after cyclopropanation (Scheme 11)
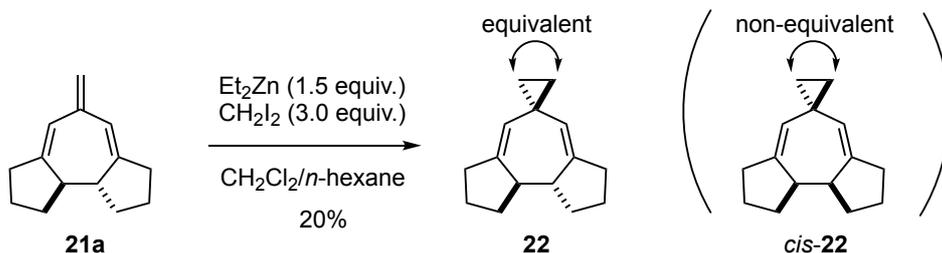
To a solution of cyclized product **21a** (18.2 mg, 97.7 µmol) in CH$_2$Cl$_2$ (0.50 mL) was added a 1.0 M solution of Et$_2$Zn in *n*-hexane (150 µL, 0.150 mmol) at 0 °C. To the mixture was added CH$_2$I$_2$ (24.1 µL, 0.300 mmol) dropwise, and the reaction mixture was stirred for 1 h at the same temperature. The reaction was quenched with saturated aqueous NH$_4$Cl (0.5 mL). The two layers were separated, and the aqueous layer was extracted with *n*-hexane (3 × 0.5 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by PTLC (*n*-hexane only) afforded cyclopropane *trans*-**22** (along with several impurities, 4.0 mg, 20 µmol, ca. 20%).

22: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.67 (s, 2H), 2.44 (t, *J* = 5.7 Hz, 2H), 2.33 (q, *J* = 4.8 Hz, 4H), 2.01–1.95 (m, 2H), 1.70–1.64 (m, 2H), 1.51–1.42 (m, 2H), 1.37–1.28 (m, 2H), 0.78–0.72 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.8 (2C), 125.7 (2C), 47.8 (2C), 35.4 (2C), 34.2 (2C), 25.0 (2C), 21.2, 18.1 (2C). IR (ATR) ν 2947, 1446, 971, 870 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{15}$H$_{20}$ 200.1565; found: 200.1566.

Transformation of Cross-Conjugated Cyclic Triene into Tropylium Salt (Scheme 12)
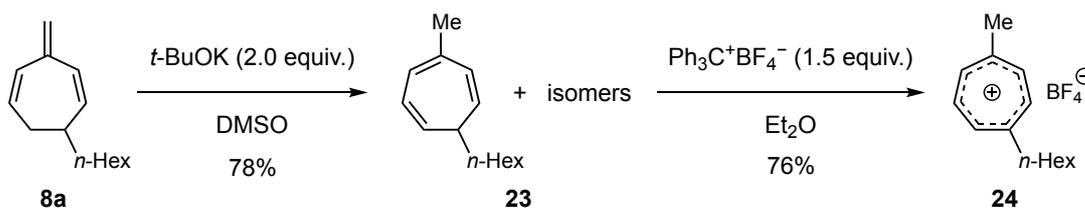
To a solution of cycloheptatriene **8a** (24.1 mg, 0.127 mmol) in DMSO (1.27 mL) was added *t*-BuOK (28.1 mg, 0.250 mmol) at room temperature. After stirring for 15 min, the reaction was quenched with saturated aqueous NH$_4$Cl (1 mL), and the mixture was extracted with Et$_2$O (5 × 1 mL). The combined organic layer was washed with brine (1 mL), dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification through a short pad of silica gel (*n*-hexane only) afforded linear-conjugated cyclic trienes **23** (18.7 mg, 98.3 µmol, 78%) as a mixture of regioisomers.

To a solution of **23** and isomers (13.5 mg, ca. 70.9 µmol) in Et$_2$O (0.14 mL) was added tritylium

tetrafluoroborate (35.1 mg, 0.106 mmol) and the reaction mixture was stirred for 17 h at room temperature. The solvent was then removed under reduced pressure. The resulting residue was washed with Et$_2$O (3 × 2 mL) and concentrated under reduced pressure to afford tropylium salt **24** (14.9 mg, 54.0 μmol, 76%).

24: dark purple oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.94–8.87 (m, 3H), 8.84–8.82 (m, 2H), 3.22 (t, J = 8.0 Hz, 2H), 3.10 (s, 3H), 1.85–1.79 (m, 2H), 1.46–1.40 (m, 2H), 1.35–1.27 (m, 4H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 174.2, 170.3, 154.1, 153.4, 153.0, 152.5, 151.4, 42.3, 32.4, 31.4, 29.0, 28.6, 22.4, 14.0. IR (ATR) ν 3566 (br), 2928, 1494, 1052 cm^{-1}. HRMS (FD) m/z [M]$^+$ calcd for C$_{14}$H$_{21}$ 189.1643; found: 189.1639.

2.6 References for Experimental Section

(1) (a) Ando, K.; Yamada, K. *Green Chem.* **2011**, *13*, 1143–1146. (b) Yanai, H.; Takahashi, A.; Taguchi, T. *Chem. Commun.* **2010**, *46*, 8728–8730.

(2) Kim, D. D.; Lee, S. J.; Beak, P. *J. Org. Chem.* **2005**, *70*, 5376–5386.

(3) McCourt, R. O.; Dénès, F.; Sanchez-Sanz, G.; Scanlan, E. M. *Org. Lett.* **2018**, 20, 2948–2951.

(4) (a) Liu, Q.; Ferreira, E. M.; Stoltz, B. M. *J. Org. Chem.* **2007**, *72*, 7352–7358. (b) Huang, S.-H.; Tian, X.; Mi, X.; Wang, Y.; Hong, R. *Tetrahedron Lett.* **2015**, *56*, 6656–6658.

(5) Yoshimura, F.; Saito, H.; Abe, T.; Tanino, K. *Synlett* **2017**, *28*, 1816–1820.

(6) Lo, J. C.; Yabe, Y; Baran, P. S. *J. Am. Chem. Soc.* **2014**, *136*, 1304–1307.

(7) Erkkilä, A.; Pihko, P. M. *J. Org. Chem.* **2006**, *71*, 2538–2541.

(8) Crimmins, M. T.; Vanier, G. S. *Org. Lett.* **2006**, *8*, 2887–2890.

(9) Ozeki, M.; Egawa, H.; Kuse, A.; Takano, T.; Yasuda, N.; Mizutani, H.; Izumiya, S.; Nakashima, D.; Arimitsu, K.; Miura, T.; Kajimoto, T.; Hosoi, S.; Iwasaki, H.; Kojima, N.; Node, M.; Yamashita, M. *Synthesis* **2015**, *47*, 3392–3402.

CHAPTER 2
Electrocyclization of Heptatrienyl Anion
with an Electron-Withdrawing Group

3.1 Introduction

The successful results described in Chapter 1 inspired the author to explore the scope of the anionic 8π electrocyclization. Consequently, 1,3,6-heptatrienes having an electron-withdrawing group (W = -CO$_2$Et, -CN, -P(=O)(OEt)$_2$) were designed as new substrates (Scheme 1). Upon treatment with a base, triene substrate **i-1** would undergo deprotonation at the doubly allylic position followed by 8π electrocyclization to afford seven-membered anion **i-3**, which would be reacted with an electrophile (El$^+$), giving rise to **i-4**. The reaction with an electrophile probably would proceed at the α-position of an electron-withdrawing group, where the coefficient of the HOMO orbital would be biggest.[1] Moreover, the electron-withdrawing group seems advantageous, because (i) the cyclization precursor would be prepared in short steps (*vide infra*), (ii) generation of heptatrienyl anion **i-2** would be facilitated by its inductive effect, (iii) stabilization of the seven-membered anion **i-3** would prevent the reverse cyclization to reproduce **i-2**.[2]
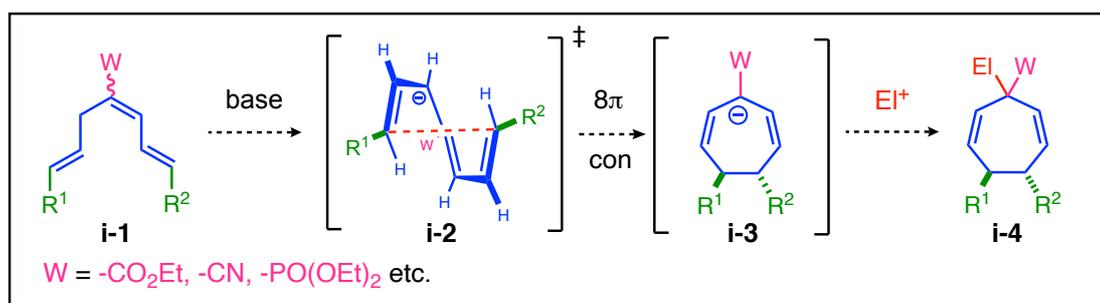

Scheme 1. Reaction design of a new 8π electrocyclization

3.2 Results and Discussion

Ester, cyano, and phosphoryl groups were chosen as the electron-withdrawing groups of the new substrates. First, the reaction of each substrate bearing phenyl groups at each terminus were examined. The ester substrate (*E*)-**1** was synthesized stereoselectively according to a reported single-step protocol using ethyl (triphenylphosphoranylidene)acetate, *trans*-cinnamyl alcohol, and *trans*-cinnamaldehyde in the presence of barium and palladium catalysts (Scheme 2, top).[3] Upon treatment with 1.1 equiv of KHMDS, (*E*)-**1** underwent the desired cyclization reaction to afford seven-membered ester **2** in moderate yield (Scheme 2, bottom).
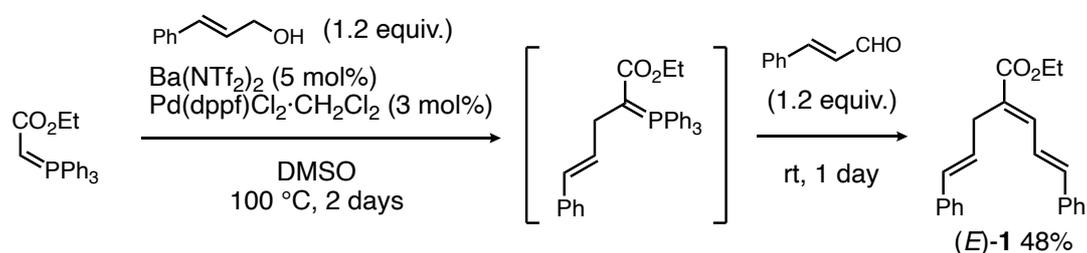

ref.) Xie, P.; Loh, T.-P. *et al. Org. Lett.* **2019**, *21*, 7055.
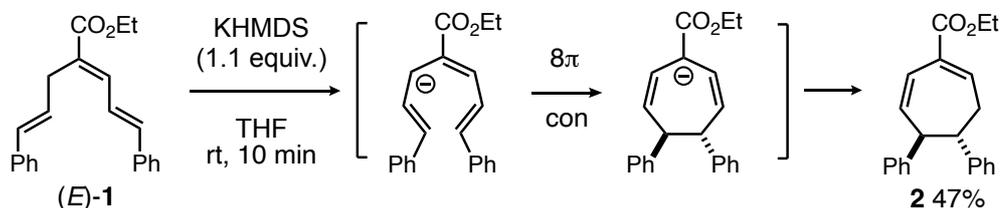
Scheme 2. 8π electrocyclization of ester derivative

Dr. Domon, a former member of the author's laboratory, independently reported in his doctoral thesis that malononitrile derivative **3** underwent 8π electrocyclization upon treatment with 2.0 equiv of lithium diethylamide (LiNEt$_2$) (Scheme 3).[4] The reaction was expected to be initiated with deprotonation at the allylic position followed by β-elimination of a cyano group to afford cyano triene **4**. The reaction further proceeds from **4** via deprotonation and 8π electrocyclization to give seven-membered nitrile **5** in 76% yield.
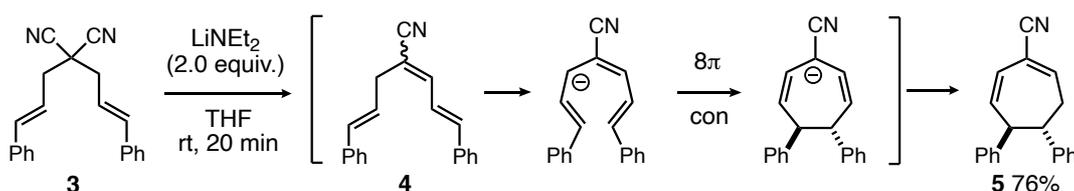

Scheme 3. Preceded work described in a doctoral thesis written by Domon

Nitrile substrate (*E*)-**7** can be directly synthesized in 2 steps from acetonitrile (Scheme 4). The organocopper species generated from acetonitrile was reacted with cinnamyl bromide to afford nitrile **6** in high yield. Introduction of another side chain was conducted by a one-pot HWE reaction,[5] in which **6** was successively treated with 2.1 equiv of LDA, 1.05 equiv of diethyl chlorophosphate, and 1.05 equiv of *trans*-cinnamaldehyde. The resulting isomeric mixture of **7** (*E*/*Z* = 2.5:1.0) was purified by silica gel column chromatography, giving rise to (*E*)-**7** in 60% yield. Upon treatment with 1.1 equiv of KHMDS, (*E*)-**7** underwent 8π electrocyclization to give **5** as a 19:1 inseparable mixture with *cis*-**5**.
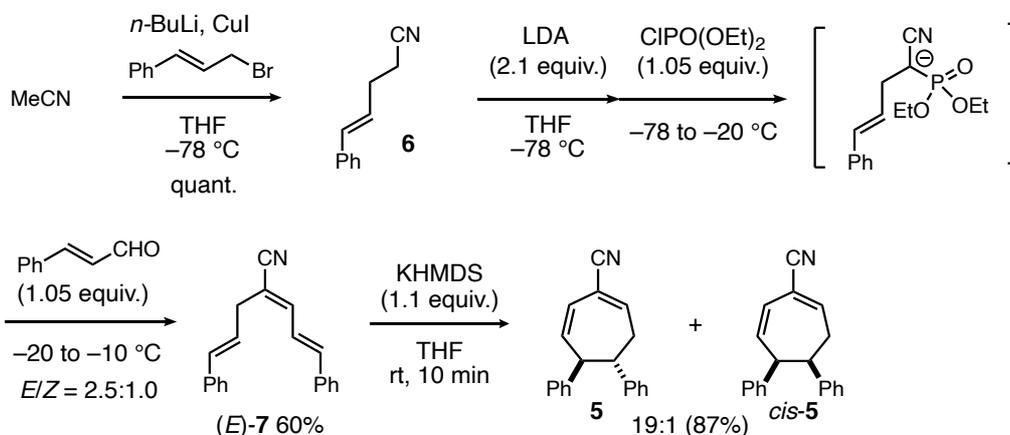

Scheme 4. 8π electrocyclization of nitrile derivative

Next, triene substrate having a phosphonate moiety was synthesized as shown in Scheme 5. Diethyl methylphosphonate was reacted with *n*-butyllithium (*n*-BuLi) followed by cinnamyl bromide to afford phosphonate **8**. The introduction of another side chain was achieved by a method similar to that for nitrile substrate **7**.[5] The product obtained as a mixture of *E/Z* isomers was purified following the silica gel column chromatography, affording (*E*)-**9** (50%) and (*Z*)-**9** (43%), respectively. The stereochemistry of the C3-C4 double bond was assigned by comparing the values of the H-P coupling constants (between the phosphonate moiety and the β-vinyl proton) obtained using the proton NMR spectroscopy.[5]
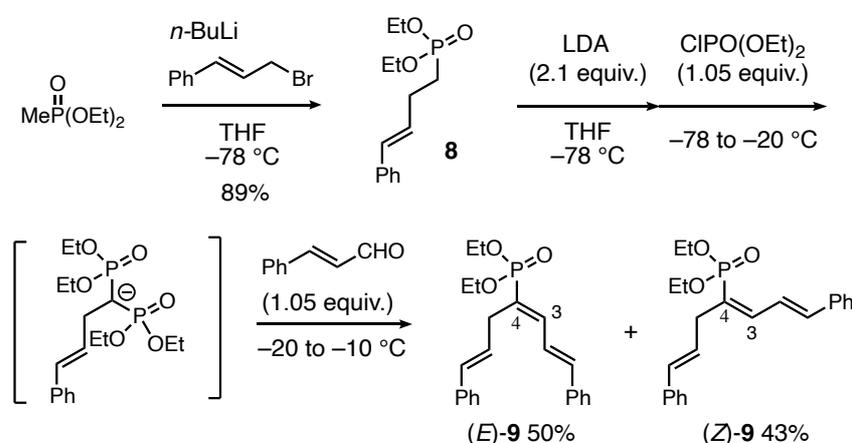
Scheme 5. Preparation of cyclization precursor with a phosphonate moiety.

Phosphonate (*E*)-**9** readily underwent a cyclization reaction at room temperature under the influence of 1.1 equiv of KHMDS (Scheme 6). The reaction was quenched with an aqueous solution of ammonium chloride to afford a 10:1 mixture of regioisomers of cycloheptadienyl phosphonates **10a** and **10b** in 88% yield. As these experiments revealed phosphonate derivatives are the most suitable substrates for 8π electrocyclization, the author decided to further investigate the reactions of phosphonates.
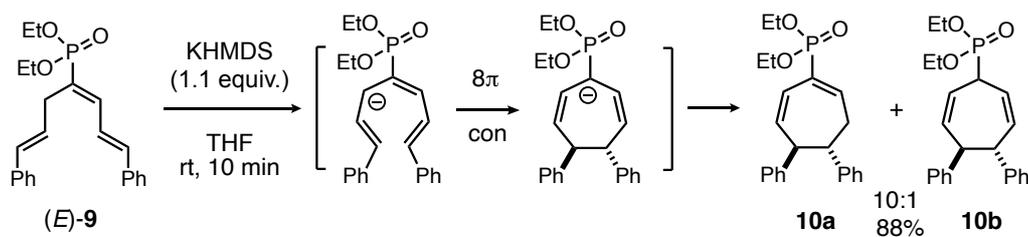
Scheme 6. 8π electrocyclization of phosphonate derivative

The author focused on the anionic species **11** which would participate in the Horner–Wadsworth–Emmons (HWE) reaction[6] in the presence of an aldehyde (Scheme 7). The process would result in the formation of 3-alkylidene-1,4-cycloheptadiene derivative **12**.
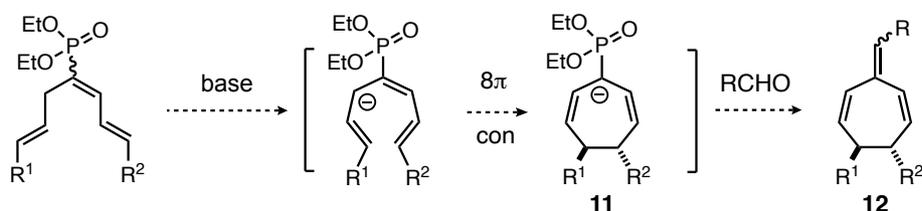
Scheme 7. 8π electrocyclization and subsequent HWE reaction of phosphonate derivative

Indeed, (*E*)-**9** afforded a cross-conjugated triene **13** as a single isomer by the successive treatment with KHMDS and benzaldehyde in 88% yield (Scheme 8). The *trans* orientation of the neighboring phenyl groups was confirmed by the X-ray crystallography of **15d** (*vide infra*). The reaction was conducted on a larger scale (1 mmol), without a decrease in the yield. To the author's delight, the reactivities of (*Z*)-**9** and (*E*)-**9** were almost equal, and the same triene **13** was formed following the one-pot cyclization/HWE sequence. These results suggest that a common heptatrienyl anion is generated from both (*Z*)-**9** and (*E*)-**9**, regardless of the stereochemistry at the C3=C4 bond.
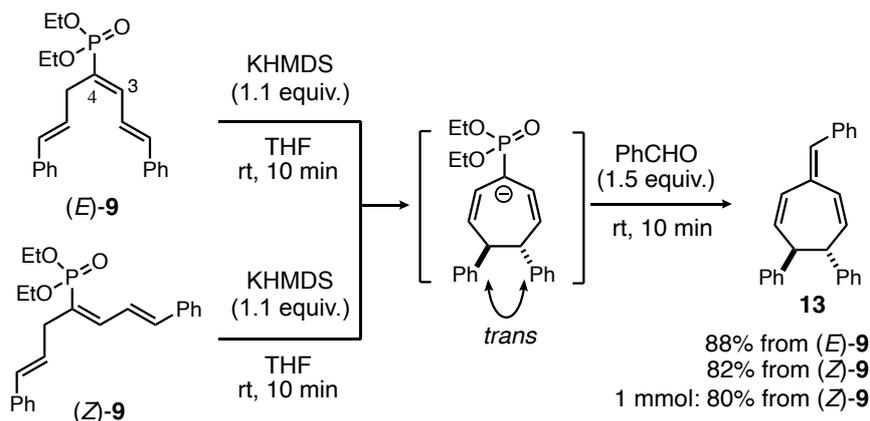

Scheme 8. 8π electrocyclization and subsequent HWE reaction of phosphonate derivative

It is noteworthy that there was a serious limitation in the cyclization reaction of carbamate substrates in Chapter 1 (Scheme B, top). Thus, the (*Z*)-isomer afforded linear conjugated triene as a major product through proton exchange between the anionic species and the substrate. On the other hand, there is no such limitation depending on the *E/Z* stereochemistry of phosphonate substrate **9** (Scheme B, bottom). The different behavior between the (*Z*)-isomers of carbamate and phosphonate would be attributed to difference in the reaction rates of deprotonation. Thus, (*Z*)-**9** would rapidly undergo complete deprotonation to anionic species **A**, that prevents the side reaction through proton exchange between the anionic species and the substrate.
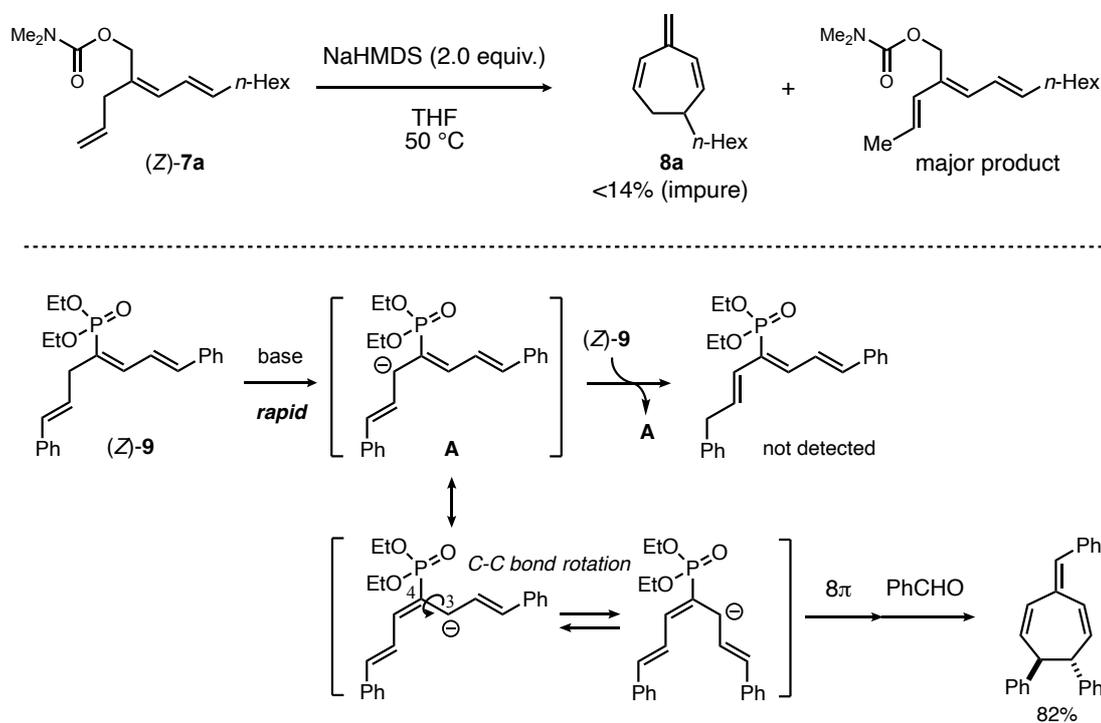

Scheme B. The reaction of carbamate (*Z*)-**7a** in Chapter 1 (top), The reaction mechanism of the electrocyclization of (*Z*)-**9** (bottom)

75

Next, substrates (1*Z*,3*E*)-**9** and (1*Z*,3*Z*)-**9** were synthesized as shown in Scheme 9 from *cis*-cinnamaldehyde as a 1.0:1.4 mixture in 85% yield. It was expected that the stereochemistry of the substrate would be reflected to that of the product of the anionic 8π electrocyclic reaction.
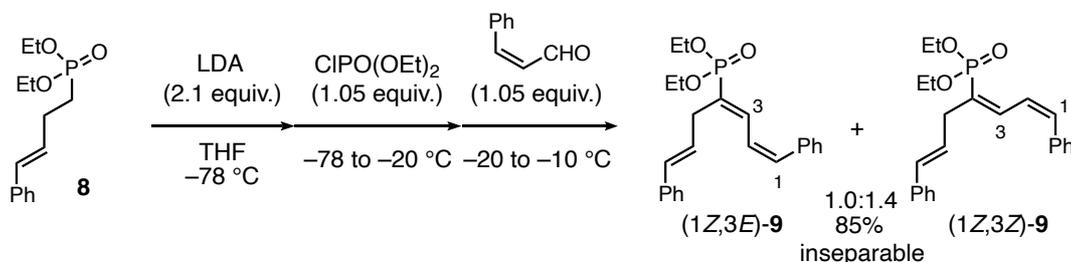
Scheme 9. Preparation of phosphonate derivative having Z-alkene moiety at C1 position

Indeed, the stereochemistry of the substrates at the C1=C2 bond influenced the configuration of the newly formed sp^3 stereogenic centers (Scheme 10). Treatment of a 1.0:1.4 mixture of (1*Z*,3*E*)-**9** and (1*Z*,3*Z*)-**9** with KHMDS was followed by the reaction with benzaldehyde, resulting in formation of a complex mixture. On the other hand, the quenching of the reaction with an aqueous solution of NH₄Cl afforded the cyclic phosphonates **14a** and **14b** in quantitative combined yield. The configuration of **14a**, in which the neighboring phenyl groups are *cis* to each other, was determined by conducting NOE experiments. The formation of the *cis* isomer **14** from (1*Z*)-**9** and the corresponding *trans* isomer **13** from (1*E*)-**9** validated that these reactions proceeded via the 8π electrocyclization in a conrotatory fashion.
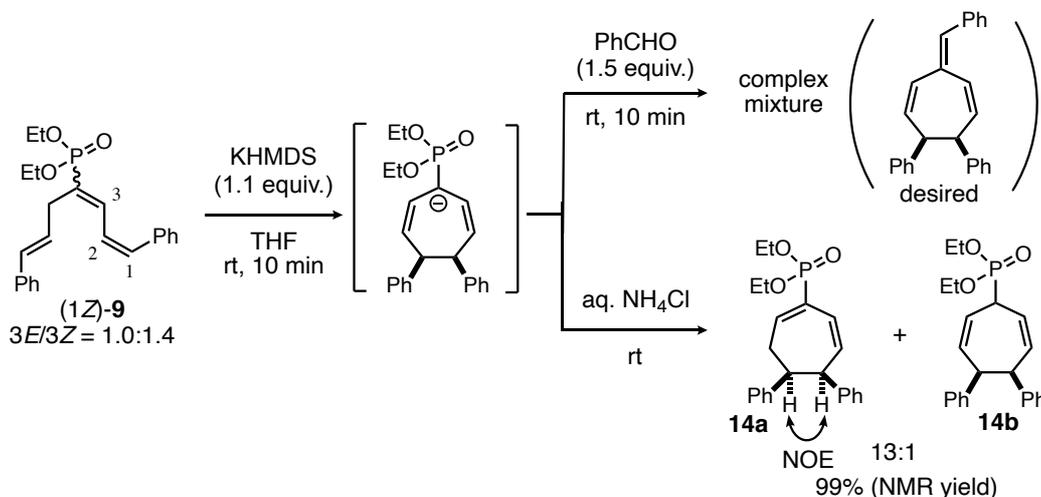
Scheme 10. The reaction of phosphonate having Z-alkene moiety at C1 position

The unsuccessful cyclization/HWE reaction of (1*Z*)-**9** gave a small amount of a seven-membered tetraene (Scheme C, top), suggesting that the desired product *cis*-**13** underwent deprotonation followed by an addition reaction with benzaldehyde. The different behavior between *trans*-**13** and *cis*-**13** would be attributable to the difference in hindrance around the benzylic position. While the benzylic protons of *trans*-**13** are kinetically protected by the neighboring phenyl groups, the corresponding protons of *cis*-**13** would easily be abstracted by a base (Scheme C, bottom).
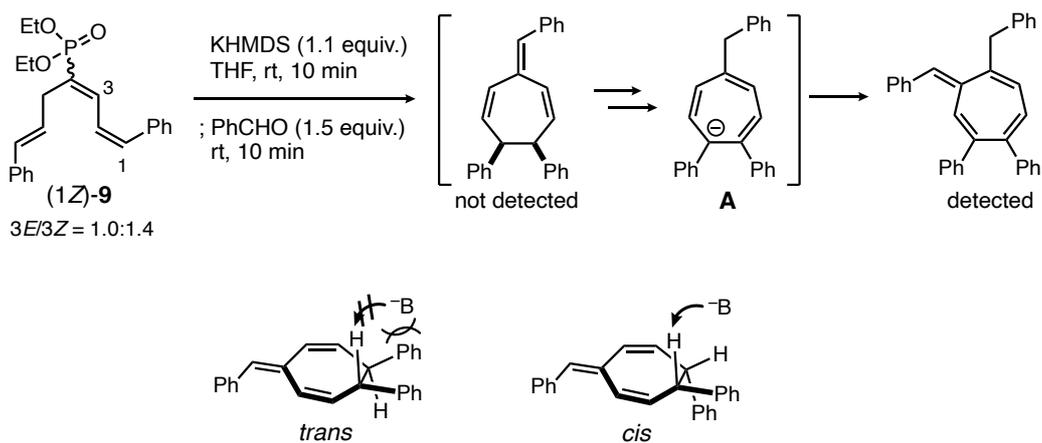
Scheme C. Side reaction in the reaction of (1*Z*)-**9**

The scope of aldehydes in the one-pot HWE reactions were investigated with (1*E*,3*E*)-**9** and (1*E*,3*Z*)-**9** as the substrates (Table 1). Aromatic aldehydes possessing an electron-donating or electron-withdrawing group at the *p*-position yielded the corresponding trienes **15a**, **15b**, and **15c** in good to excellent yields. Triene **15d** was obtained as a crystalline solid from 2-bromobenzaldehyde, which enabled the author to determine the configuration of the product using X-ray crystallography. The ORTEP diagram representing **15d** reveals the *trans* relationship between the two phenyl groups present on the seven-membered ring. Aliphatic aldehydes were also used to conduct this reaction (Table 1). Trienes **15e** and **15f** were obtained in moderate yields. This decrease in the yield could be attributed to the partial enolization of the aldehydes under basic conditions.

Table 1. Scope of aldehydes in one-pot HWE reactions

ORTEP of **15d**
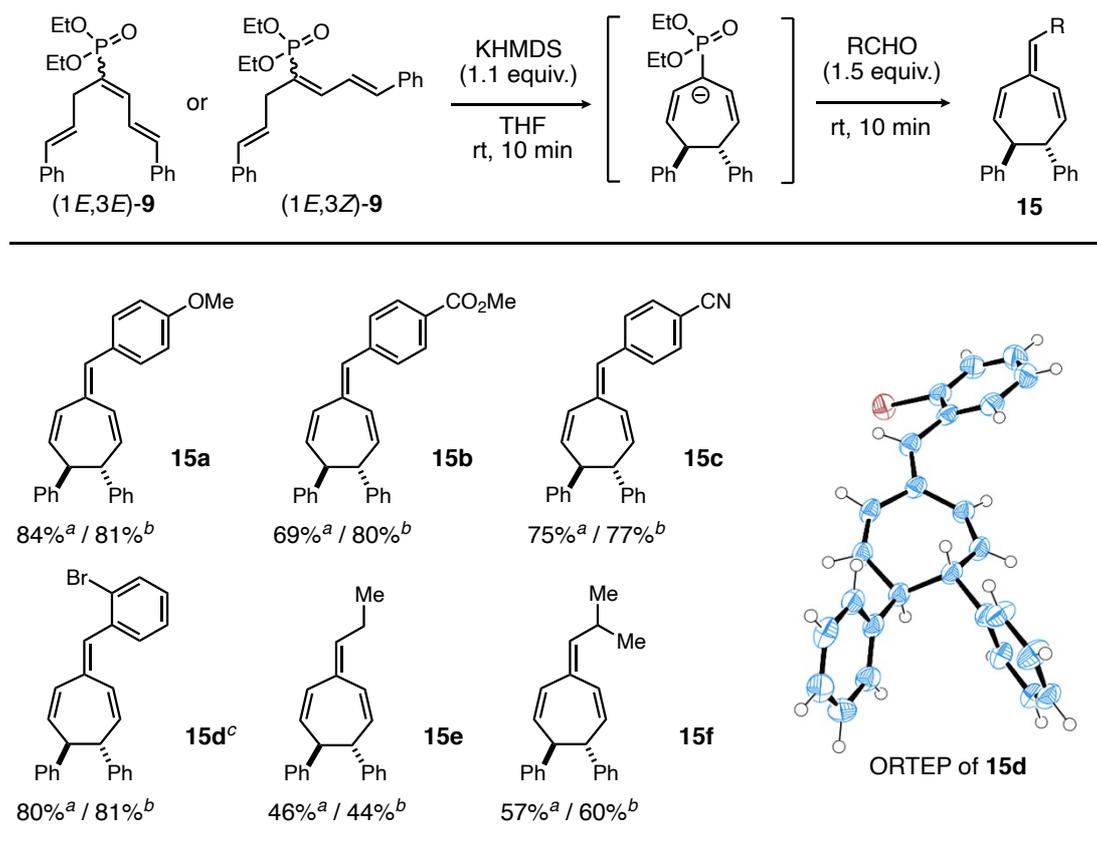
[a]isolated yield from (1*E*,3*E*)-**9**. [b]isolated yield from (1*E*,3*Z*)-**9**.
[c]1.1 equiv of 2-bromobenzaldehyde was used.

Next, the scope of the 8π electrocyclization/HWE reaction was examined using several phosphonate substrates, prepared following a similar sequence to that presented in Scheme 5. It is noteworthy that substrates **16a**, **16d**, **16e**, and **16f**, bearing an alkyl group at the C6 position, were primarily obtained as the (3*Z*)-isomer (see Experimental Section).

Substrates with an alkyl group at the C6 or C7 position afforded the desired trienes **17a** and **17b**, respectively, in moderate to high yields (Scheme 11, top). Triene **17c**, bearing a quaternary carbon atom, was obtained from a substrate bearing a dimethyl group at the C7 position (Scheme 11, bottom).
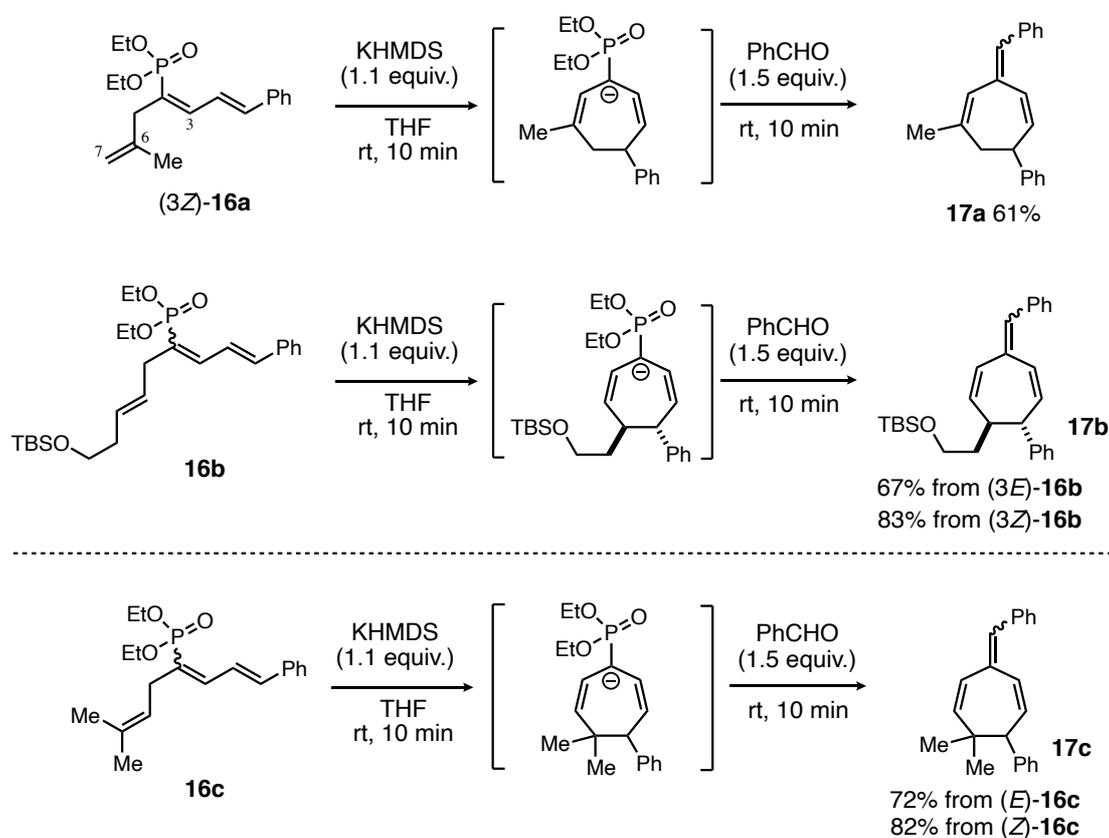
Scheme 11. Reactions of substrates with an alkyl group at the C6 or C7 position (top) and Reactions of substrates with a dimethyl group at the C7 position (bottom)

The cyclization/HWE reaction could also be used to synthesize bicyclic compounds (Scheme 12). Compounds **17d**, **17e**, and **17f** were obtained in high yields from the corresponding substrates bearing cycloalkene moieties. A single diastereomer of the products **17b**, **17d**, **17e**, and **17f**, bearing two neighboring stereogenic centers, was obtained. The conrotatory mode followed for the 8π electrocyclization reaction dictates the configurations of these compounds.
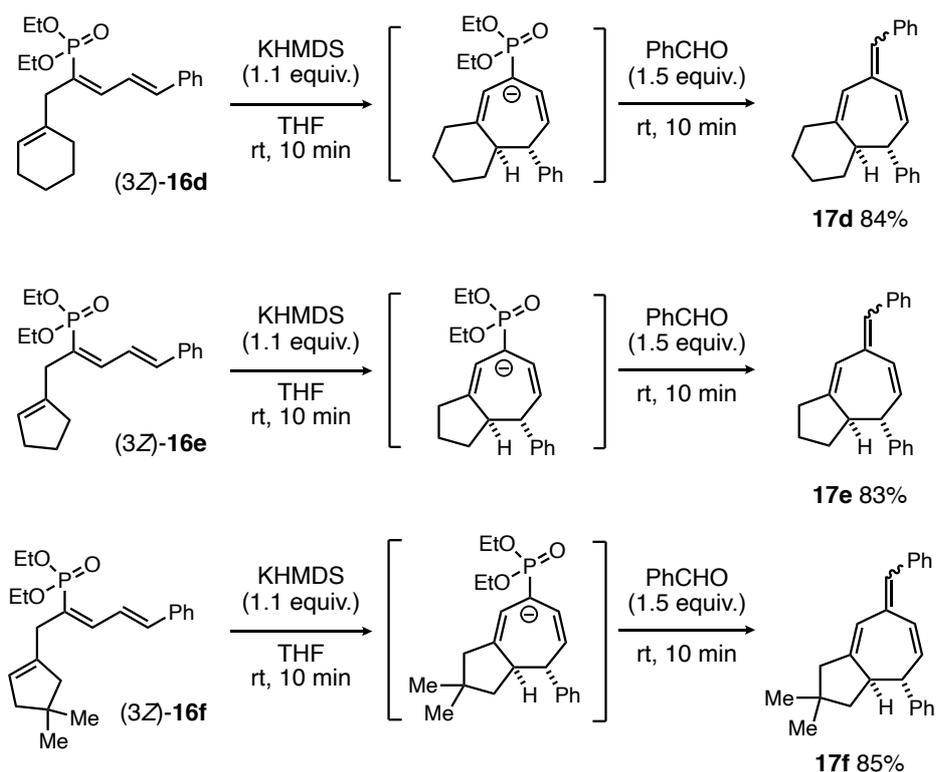
Scheme 12. Reactions of substrates with an alkyl group at the C6 or C7 position

It was inferred that the terminal phenyl groups present in substrates **9** and **16** were not necessary for inducing the 8π electrocyclic reaction (Table 3). Reactions with substrates (3*E*)-**18a** and (3*Z*)-**18a**, bearing two cyclohexyl groups instead of two phenyl groups, afforded the desired triene **19a** in good yield. Replacement of the C1 cyclohexyl group with an *n*-propyl group or a methyl group resulted in a decrease in the yield of the desired compounds **19b** and **19c**.

Table 3. Reactions of trienes with alkyl groups at each terminus
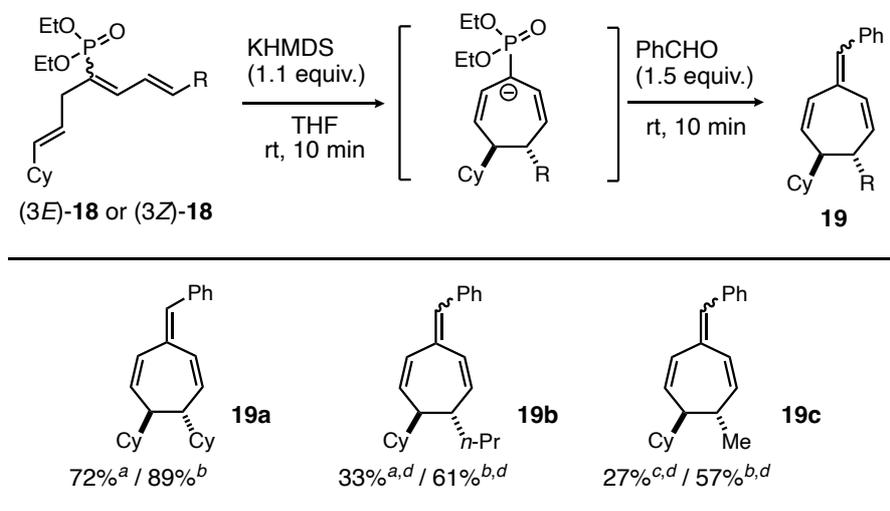
^{a}isolated yield from (3*E*)-**18**. ^{b}isolated yield from (3*Z*)-**18**. ^{c}isolated yield from (3*E*)-**18c** (two steps after the treatment with *N*-phenyl maleimide (scheme 13)). ^{d} *E*/*Z* = ca.1:1.

Notably, the reaction of (3*E*)-**18c** afforded an inseparable mixture of **19c** and acyclic tetraene **20** (Scheme 13). Heating with *N*-phenyl maleimide effected selective conversion of **20** to a highly polar compound, probably by a Diels–Alder reaction, which enabled the author to isolate **19c**, albeit in low yield. The formation of **20** indicates that the low yield of **19c** (and **19b**) is attributed to the deprotonation at the C1 alkyl group.
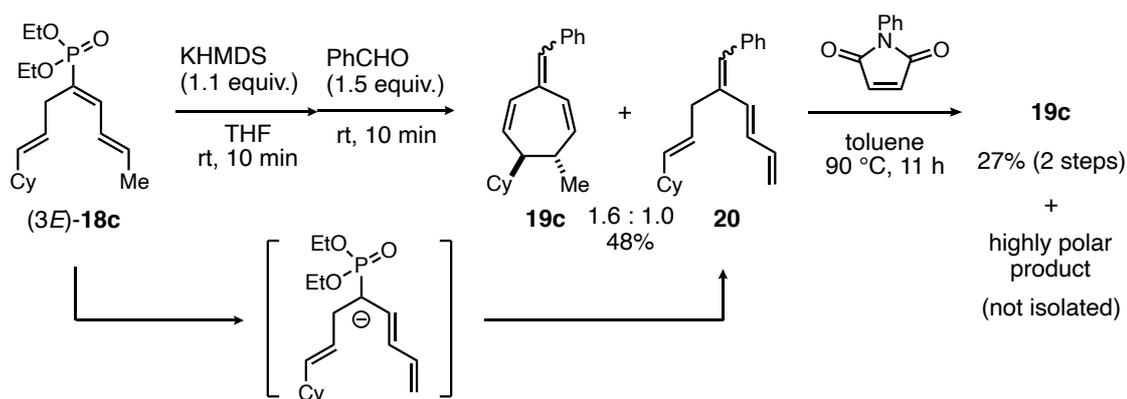
Scheme 13. Reactions of (3*E*)-**18c** and an observed side reaction

Indeed, compound **19d** was obtained in higher yield when the reaction is carried out with (3*E*)-**18d** (the cyclohexyl and the *n*-propyl groups in (3*E*)-**18b** are exchanged with each other) (Scheme 14). The result can be attributed to the difficulty in abstracting the methine proton from the cyclohexyl group.
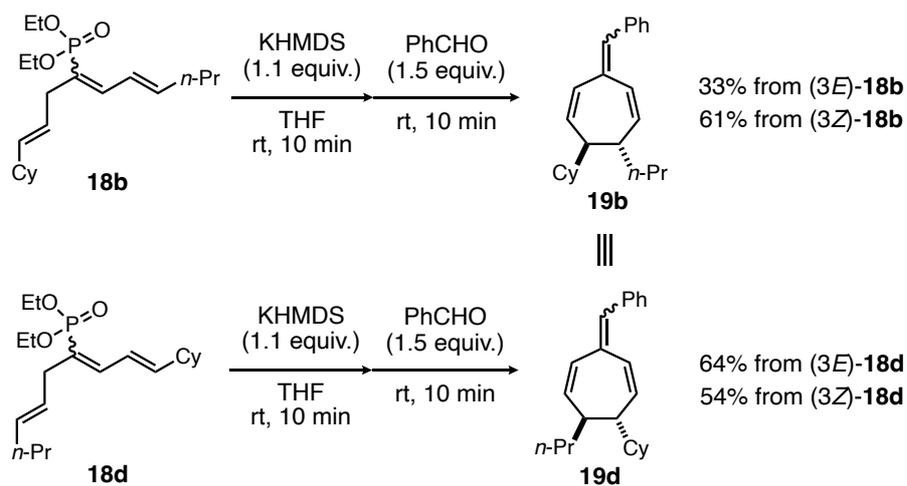
Scheme 14. Exchange of terminal groups in the reaction of (3*E*)-**18b**

Also, 3-methylene-1,4-cycloheptadiene derivatives could be prepared by employing *N*-(hydroxymethyl)phthalimide as a formaldehyde equivalent which is easier to handle than formaldehyde itself (Scheme 15).[7] The reactions of (1*E*)-**9** and nopol-derived **16g** afforded desired **21** and **22** in moderate yields. This protocol gave 3-methylene-1,4-cycloheptadiene derivatives in shorter steps than that described in Chapter 1.
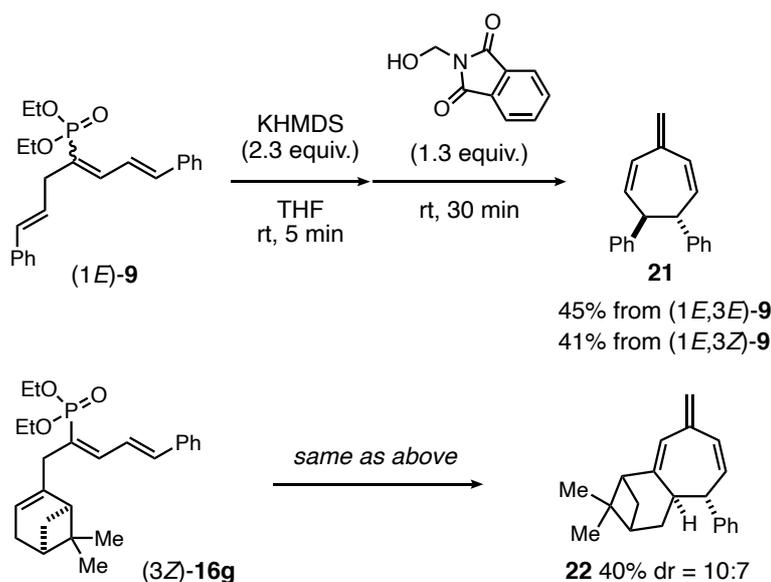
Scheme 15. Synthesis of exo-methylene products

Next, a seven-membered triene bearing an additional functional group was synthesized (Scheme 16). The anion generated from phosphonate **8** was reacted with *trans*-cinnamaldehyde, and the resulting alcohol **23** was oxidized with Dess–Martin periodinane (DMP) to yield keto phosphonate **24**. Silyl enol ether **25** was prepared from ketone **24** in one-pot prior to the cyclization reaction. Thus, **24** was reacted with KHMDS and triisopropylsilyl chloride (TIPSCl) to give a solution of **25** which was then treated with KHMDS followed by benzaldehyde. The desired product **26** was obtained in 72% yield, whose benzylidene moiety was determined to have an (*E*)-configuration by an NOE experiment. The one-pot silylation/cyclization/HWE reaction can be potentially used for the preparation of multifunctional seven-membered compounds.

Scheme 16. Synthesis and reaction of a substrate with an oxygenated functionality

Finally, transformation of the cyclized products was briefly examined (Scheme 17). Alkene isomerization reaction of **17c** smoothly proceeded to give a linear conjugated seven-membered triene **27** in 89% yield. Also, silyl enol ether **26** was efficiently converted to ketone **28** upon treatment with aqueous hydrochloric acid in 70% yield. These transformations revealed the synthetic utility of this cyclized products produced by the author's method.

Scheme 17. Transformations of 3-alkylidene-1,4-cycloheptadiene derivatives

3.3 Conclusion

In summary, the author developed an anionic 8π electrocyclic reaction using 1,3,6-heptatriene derivatives with an ester group, a cyano group, or a phosphoryl group as cyclization precursors (Scheme 18). Upon treatment with KHMDS, these substrates underwent deprotonation at the doubly allylic position followed by 8π electrocyclization to give seven-membered carbocycles in moderate to high yields upon an aqueous quench. By quenching phosphonate anion with an aldehyde, a one-pot HWE reaction proceeded to afford the 3-alkylidene-1,4-cycloheptadiene derivative. The electrocyclic reaction proceeds in a stereospecific manner, that helps achieve stereocontrol in the newly formed neighboring stereogenic centers. As the substrates can be prepared over two steps, the method presented herein can be followed for the total synthesis of natural products.
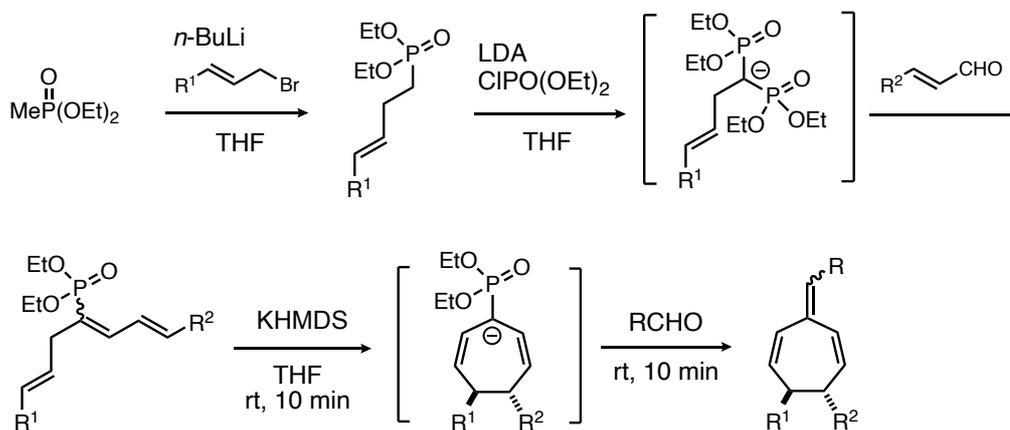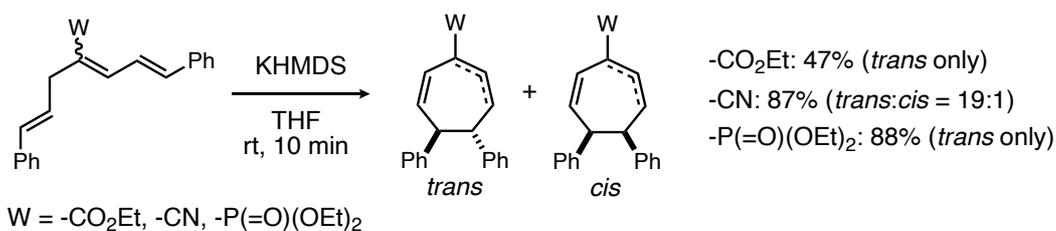
Scheme 18. Electrocyclization of heptatrienyl anion with an electron-withdrawing group

3.4 References

(1)   For the examples of alkylation of a conjugated anion, see: [Cyclopentadienyl anion]: Fujioka, H.; Sawama, Y.; Kotoku, N.; Ohnaka, T.; Okitsu, T.; Murata, N.; Kubo, O.; Li, R.; Kita, Y. *Chem. Eur. J.* **2007**, *13*, 10225–10238.; [Unsaturated ester carbanion]: (a) Herrmann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, *14*, 2433–2436. (b) Peters, B. K.; Liu, J.; Margarita, C.; Andersson, P. G. *Chem. Eur. J.* **2015**, *21*, 7292–7296. [Unsaturated nitrile carbanion]: (a) Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React.* **1984**, *31*, 1. (b) Yoshimura, F.; Abe, T.; Ishioka, Y.; Tanino, K. *J. Antibiot.* **2019**, *72*, 384–388. [Unsaturated phosphonate carbanion]: Nagase, T.; Kawashima, T.; Inamoto, N. *Chem. Lett.* **1984**, *13*, 1997–2000.

(2)   It was reported that conjugated cycloheptadienyl anions without any stabilizing group underwent ring-opening reactions to form heptatrienyl anions, suggesting that the 8π electrocyclization reaction is reversible in certain cases: Williams, D. R.; Reeves, J. T.; Nag, P. P.; Pitcock, W. H. Jr.; Baik, M-H. *J. Am. Chem. Soc.* **2006**, *128*, 12339–12348.

(3)   Xie, P.; Fu, W.; Cai, X.; Sun, Z.; Wu, Y.; Li, S.; Gao, C.; Yang, X.; Loh, P.-T. *Org. Lett.* **2019**, *21*, 7055-7059.

(4)   Domon, D. Doctoral thesis, **2019**, Hokkaido University.

(5)   Teulade, M.-P.; Savignac, P.; Aboujaoude, E. E.; Liétge, S.; Collignon, N. *J. Organomet. Chem.* **1986**, *304*, 283–300.

(6)   For the reviews of Horner–Wadsworth–Emmons reaction see; (a) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87–99. (b) Wadsworth, W. S. Jr. *Org. React.* **1977**, *25*, 73–254. (c) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863–927.

(7)   Deguest, G.; Bischoff, L.; Fruit, C.; Marsais, F. *Org. Lett.* **2007**, *9*, 1165-1167.

3.5 Experimental Section

General Information

The reactions were performed using flame-dried glasswares under a positive pressure of argon. Oil bath was used when reactions required heating. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Anhydrous dichloromethane and toluene were purchased from Kanto Chemical Co. Other anhydrous solvents were purchased from chemical companies. Diisopropylamine was distilled from CaH_2 under argon and stored in the presence of NaOH (pellets). (*E*)-**1**[1], 1-(bromomethyl)cyclohex-1-ene[2], (*E*)-(3-bromoprop-1-en-1-yl)cyclohexane[3], (*E*)-6-iodohex-3-en-1-ol *tert*-butyldimethylsilyl ether[4], (*E*)-3-cyclohexylpropenal[3a,5], and homoallyl iodide **S9**[6] were prepared by the known procedures. All other reagents were used as received from commercial sources without further purification.

Analytical thin layer chromatography (TLC) was performed using 0.25 mm Silica gel (60F-254) plates purchased from Merck Millipore. Reaction components were visualized by illumination with ultraviolet light (254 nm) and by staining with 8% ethanolic phosphomolybdic acid, ceric ammonium molybdate in 10% sulfuric acid, or basic potassium permanganate solution. Flash column chromatography was performed with Silica Gel 60N (neutral, particle size 40–50 μm) purchased from Kanto Chemical Co., Inc. Preparative thin layer chromatography (PTLC) was performed using PLC Silica Gel 60 F254 purchased from Merck Millipore.

The melting points were determined using an AS ONE ATM-02 apparatus and uncorrected. ^{1}H (500 MHz), ^{13}C (126 Hz), and ^{31}P (202 MHz) NMR spectra were measured using a JEOL ECA-500. Chemical shifts are reported in parts per million (ppm) with internal $CDCl_3$ (^{1}H NMR, δ_H 7.26. ^{13}C NMR, δ_c 77.0) or external phosphoric acid (^{31}P NMR, δ_P 0.00). Signals are expressed as broad (br), singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), septet (sept), and multiplet (m). Coupling constants are reported in Hz. IR spectra were recorded on JASCO FT/IR-4100 and the major absorbance bands are all reported in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-T100GCV (GC-TOFMS). X-ray crystallographic analysis was conducted using a Rigaku XtaLAB Synergy-S.

Experimental and Characterization Details

### 8π Electrocyclization of Ester Derivative (Scheme 2)
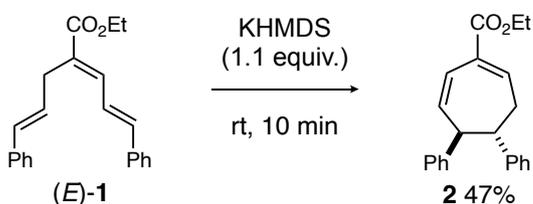
To a solution of (*E*)-**1**[1] (30.3 mg, 95.2 μmol) in THF (1.0 mL) at room temperature was added a 1.0 M solution of KHMDS in THF (104 μL, 0.104 mmol). After stirring for 10 min at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (1 mL). After EtOAc (1 mL) was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 1 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 1:0 to 9:1) afforded cyclic ester (14.2 mg, 44.6 μmol, 47%).

2: yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 7.4, 6.9 Hz, 1H), 7.17–7.07 (m, 6H), 6.94–6.89 (m, 4H), 6.54 (br d, *J* = 12.6 Hz, 1H), 6.11 (dd, *J* = 12.1, 4.6 Hz, 1H), 4.31–4.24 (m, 2H), 3.83 (ddd, *J* = 10.3, 4.6, 1.7 Hz, 1H), 3.31 (ddd, *J* = 10.3, 7.5, 2.9 Hz, 1H), 2.83 (ddd, *J* = 15.5, 7.5, 6.9 Hz, 1H), 2.69 (ddd, *J* =15.5, 7.4, 2.9 Hz, 1H), 1.35 (dd, *J* = 6.9, 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 145.6, 143.6, 143.3, 137.7, 130.7, 128.4 (2C), 128.12 (2C), 128.09 (2C), 127.2 (2C), 126.3, 126.2, 123.2, 60.9, 56.2, 53.8, 35.0, 14.3. IR (ATR) ν 3027, 2359, 1713, 1245, 699 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for $C_{22}H_{22}O_2$ 318.1620; found: 318.1613.

8π Electrocyclization of Nitrile Derivative (Scheme 4)
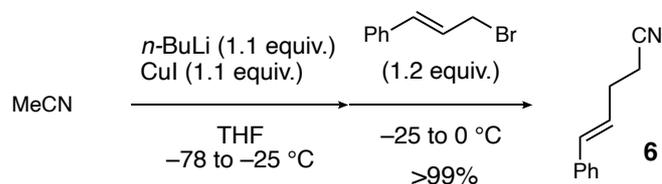
To a solution of acetonitrile (300 μL, 5.70 mmol) in THF (29 mL) at –78 °C was slowly added a 2.64 M solution of *n*-BuLi in *n*-hexane (2.38 mL, 6.27 mmol). After 20 min, the mixture was warmed to –25 °C and then CuI (1.19 g, 6.27 mmol) was added. After stirring for 15 min at –25 °C, cinnamyl bromide (1.35 g, 6.84 mmol) was added in one portion, and then the resulting
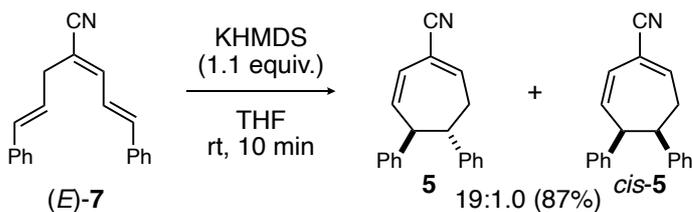
mixture was warmed to 0 °C. After stirring at 0 °C for 1 h, the reaction was quenched with saturated aqueous NH$_4$Cl. EtOAc was added, and the two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 19:1) afforded 5-phenylpent-4-enenitrile (**6**) (1.01 g, ca. 6.27 mmol, >99%).

6: pale yellow oil. ^{1}H NMR spectral property was identical to that reported.[7]
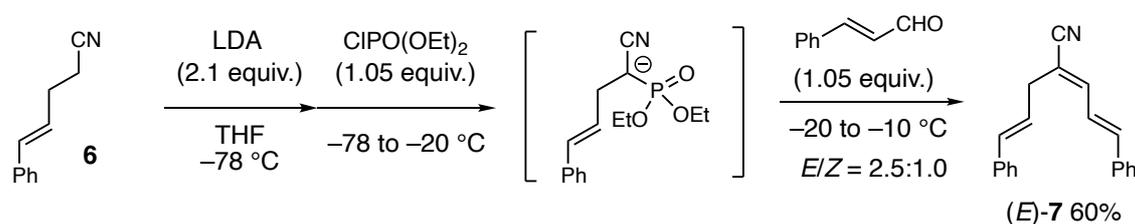
To a solution of diisopropylamine (300 μL, 2.13 mmol) in THF (3 mL) at 0 °C was slowly added a 2.64 M solution of n-BuLi in n-hexane (806 μL, 2.13 mmol). After stirring for 20 min, the mixture was cooled to –78 °C, and a solution of (*E*)-5-phenylpent-4-enenitrile (**6**, 160 mg, 1.02 mmol) in THF (2 mL) was added via cannula. After stirring for 15 min at –78 °C, diethyl chlorophosphate (154 μL, 1.07 mmol) was added dropwise. The mixture was warmed to –20 °C, and then *trans*-cinnamaldehyde (134 μL, 1.07 mmol) was added. When the bath temperature reached –10 °C under ambient atmosphere, the reaction was quenched with saturated aqueous NH$_4$Cl. After EtOAc was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 98:2 to 19:1) afforded trienyl nitrile (*E*)-**7** (276 mg, 1.02 mmol, >99%).
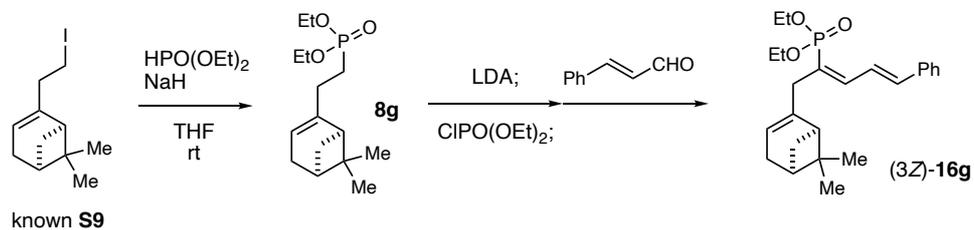
(*E*)-**7**: white crystal. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 (d, J = 7.4 Hz, 2H), 7.42–7.30 (m, 7H), 7.27–7.24 (m, 1H), 7.19 (dd, J = 15.5, 11.5 Hz, 1H), 6.87–6.81 (m, 2H), 6.55 (d, J = 15.5 Hz, 1H), 6.20 (dt, J = 15.5, 6.9 Hz, 1H), 3.22 (d, J = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.6, 139.5, 136.6, 135.7, 133.6, 129.2, 128.8 (2C), 128.6 (2C), 127.7, 127.3 (2C), 126.3 (2C), 124.4, 124.0, 118.0, 111.3, 37.3. IR (ATR) ν 3028, 2206, 1622, 1448, 964 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{20}$H$_{17}$N 371.1361; found: 371.1356.

To a solution of (*E*)-**7** (28.6 mg, 0.105 mmol) in THF (1.0 mL) at room temperature was added a 1.0 M solution of KHMDS in THF (116 μL, 0.116 mmol). After stirring for 10 min at room temperature, the reaction was quenched with saturated aqueous NH$_4$Cl (1 mL). After EtOAc (1 mL) was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 1 mL). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 98:2 to 19:1) afforded cyclic nitrile (24.9 mg, 91.8 μmol, 87%) as a 19:1.0 inseparable mixture with *cis*-**5**.
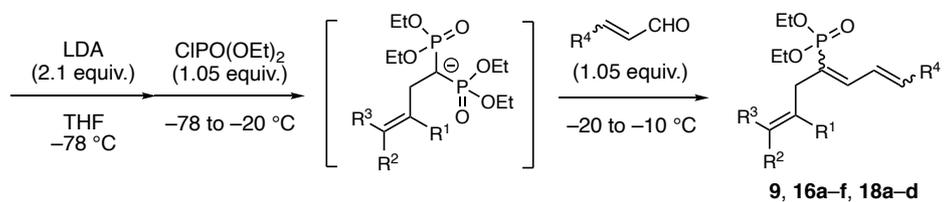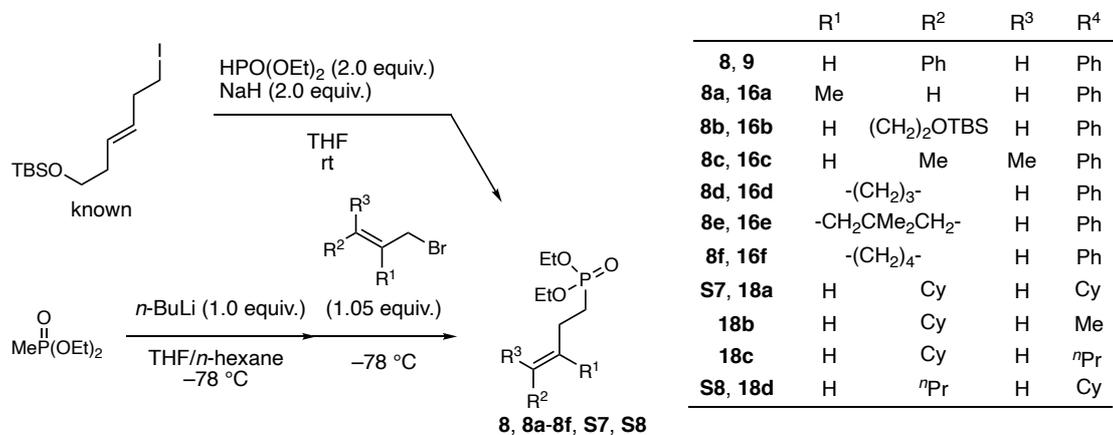
5: yellow crystal. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22–7.12 (m, 6H), 6.95–6.88 (m, 5H), 6.18 (dd, *J* = 12.0, 4.6 Hz, 1H), 6.04 (d, *J* = 12.0 Hz, 1H), 3.94–3.89 (m, 1H), 3.28–3.21 (m, 1H), 2.86 (ddd, *J* = 16.1, 7.8, 7.8 Hz, 1H), 2.70 (ddd, *J* = 16.1, 7.5, 2.9 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 148.4, 144.5, 142.4, 140.1, 128.33 (2C), 128.30 (2C), 128.28 (2C), 127.0 (2C), 126.7, 126.5, 122.2, 119.6, 113.4, 55.8, 51.7, 35.3 IR (ATR) ν 3027, 2221, 1601, 1492, 1452, 697 cm^{-1}. HRMS (FD) *m/z*: [M]$^{+}$ calcd for C$_{20}$H$_{17}$N 271.1361; found: 271.1357.

Outline for preparations of cyclization precursors

	R¹	R²	R³	R⁴
8, **9**	H	Ph	H	Ph
8a, **16a**	Me	H	H	Ph
8b, **16b**	H	(CH$_2$)$_2$OTBS	H	Ph
8c, **16c**	H	Me	Me	Ph
8d, **16d**	-(CH$_2$)$_3$-		H	Ph
8e, **16e**	-CH$_2$CMe$_2$CH$_2$-		H	Ph
8f, **16f**	-(CH$_2$)$_4$-		H	Ph
S7, **18a**	H	Cy	H	Cy
18b	H	Cy	H	Me
18c	H	Cy	H	^{n}Pr
S8, **18d**	H	^{n}Pr	H	Cy

Synthesis of Allyl Bromides

**1-(bromomethyl)-4,4-dimethylcyclopent-1-ene (S4)**
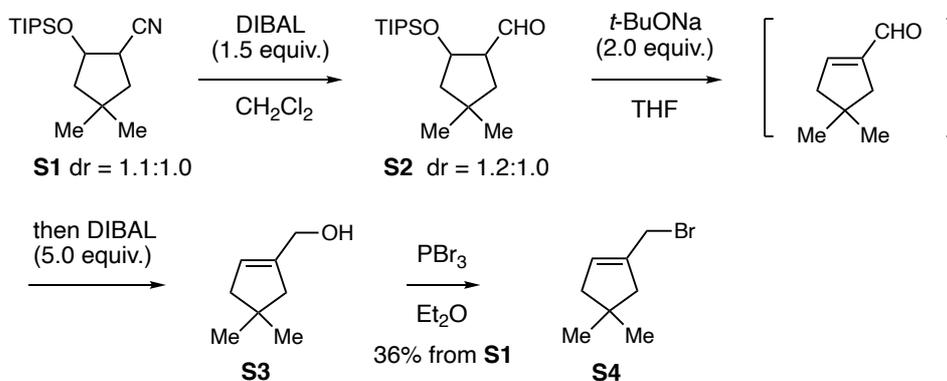
To a solution of 4,4-Dimethyl-2-((triisopropylsilyl)oxy)cyclopentane-1-carbonitrile (**S1**, 1.16 g, 3.93 mmol, dr = 1.1:1.0) prepared to the procedure described in Experimental Section of Chapter 1 in CH$_2$Cl$_2$ (20 mL) at 0 °C was added a 1.03 M solution of DIBAL in *n*-hexane (5.72 mL, 5.89 mmol) over 1 min. After stirring for 1 h, 10% aqueous tartaric acid (20 mL) was added and then the mixture was vigorously stirred for 2.5 h at room temperature. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO$_4$, filtered, and concentrated under reduced pressure to afford crude β–siloxy aldehyde **S2** as a 1.2:1.0 mixture of diastereomers.

The crude **S2** was dissolved in THF (20 mL) and *t*-BuONa (755 mg, 7.86 mmol) was added at 0 °C. The mixture was then allowed to warm to room temperature and stirred for 1 h. Then, the mixture was cooled to –78 °C, and a 1.03 M solution of DIBAL in *n*-hexane (19.1 mL, 19.7 mmol) was added over 2 min. After stirring for 25 min, 10% aqueous tartaric acid (20 mL) was added, and then the mixture was vigorously stirred for 18 h at room temperature. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 20 mL). The combined organic layers were washed with brine (20 mL) dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, Et$_2$O/pentane = 1:5 to 1:3) afforded **S3** accompanied with some impurities.

The obtained **S3** was dissolved in Et$_2$O (6.0 mL) and PBr$_3$ (133 μL, 1.40 mmol) was added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 0.5 h. Then, the mixture was cooled to 0 °C, and saturated aqueous NaHCO$_3$ (3 mL) was added. The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 3 mL). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification through a short pad of silica gel (pentane only) afforded **S4** (267 mg, 1.41 mmol, 36% from **S1**).

S4: colorless oil. ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[8]


(*E*)-1-Bromohex-2-ene (S5)
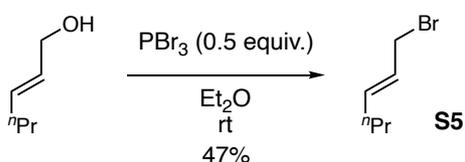
To a solution of (*E*)-2-hexene-1-ol (590 μL, 5.00 mmol) in Et$_2$O (10 mL) was slowly added PBr$_3$ (237 μL, 2.50 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 50 min. Then, to the mixture was added saturated aqueous NaHCO$_3$ (10 mL). The two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 5 mL). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification through a short pad of silica gel (*n*-hexane only) afforded **S5** (380 mg, 2.33 mmol, 47%).

S5: colorless oil. ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[9]

Synthesis of *cis*-Cinnamaldehyde (S6)
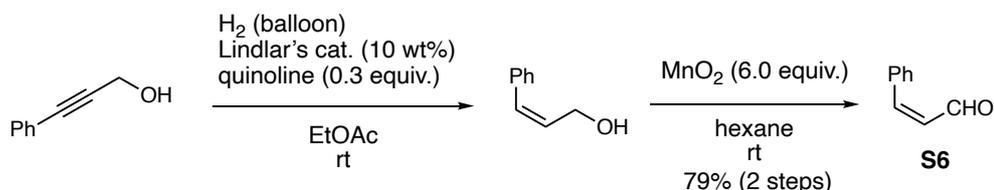
To a solution of 3-phenyl-2-propyn-1-ol (374 μL, 3.00 mmol) in EtOAc (7.5 mL) were added quinoline (107 μL, 0.90 mmol) and Lindlar's catalyst (38 mg, 10 wt%, Kawaken Fine Chemical Co., Ltd.). A balloon filled with hydrogen gas was attached to the reaction vessel, and the reaction atmosphere was replaced with hydrogen gas. The reaction mixture was stirred at room temperature for 1 h. Then, the mixture was filtered through a pad of Celite®, and the filter cake was washed with EtOAc (2 mL). The filtrate was washed with 1M aqueous HCl (3 × 2 mL). The organic layer was dried over MgSO$_4$ and concentrated under reduced pressure to give a crude alcohol.

To a solution of the crude alcohol in *n*-hexane (60 mL) was added MnO$_2$ (1.56 g, 17.9 mmol). After stirring for 14.5 h in dark, the reaction mixture was filtered through a pad of Celite®, and the filter cake was washed with *n*-hexane. The filtrate was concentrated under reduced pressure.

Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 50:1) afforded **S6** (315 mg, 2.38 mmol, 79% for 2 steps).

S6: pale yellow oil. ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[10]

General Procedure for Synthesis of γ,δ-Unsaturated Phosphonate

Procedure A (via allyl bromide)
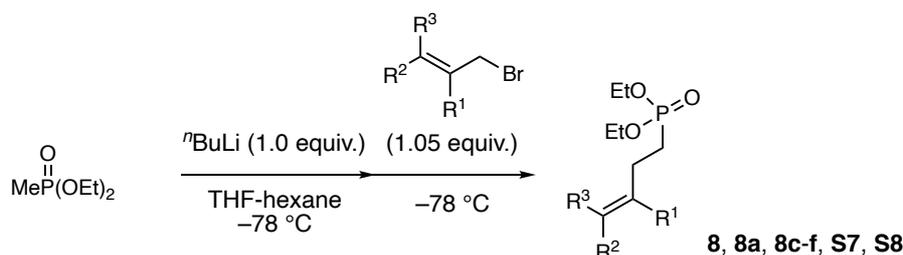
To a solution of diethyl methylphosphonate (1.00 equiv.) in THF (0.2 M) at –78 °C was slowly added a solution of *n*-BuLi in *n*-hexane (1.00 equiv.). After 20 min, allyl bromide (1.05 equiv.) was quickly added, and resulting mixture was stirred for 0.5 ~ 1.5 h at –78 °C. Then, the reaction was quenched with saturated aqueous NH$_4$Cl. EtOAc was added, and the two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by silica gel flash column chromatography (EtOAc only) afforded γ,δ-unsaturated phosphonate.

**Procedure B** (via homoallyl halide)
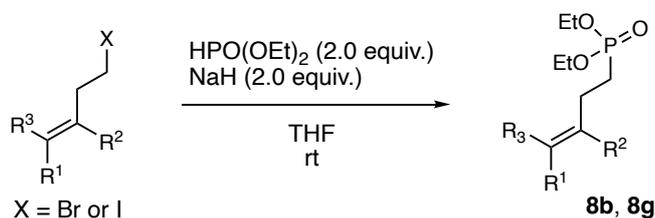
55% NaH in paraffin (2.0 equiv.) placed in a flask was washed with *n*-hexane under argon atmosphere, and then THF was added. To the resulting suspension cooled in an ice bath was slowly added diethyl phosphite (2.0 equiv.) and then the mixture was warmed to room temperature. After stirring for 1 h, a solution of homoallyl halide in THF (1 M to diethyl phosphite at this time) was slowly added at room temperature. After stirring for 15–20.5 h at room temperature, the

mixture was cooled in an ice bath and saturated aqueous NH₄Cl was added. EtOAc was added, and the two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by silica gel flash column chromatography afforded γ,δ-unsaturated phosphonate.

**Synthesis of γ,δ-Unsaturated Phosphonates**

Diethyl (*E*)-(4-phenylbut-3-en-1-yl)phosphonate (8)
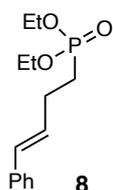
Phosphonate **8** (1.19 g, 4.44 mmol, 89%) was obtained from diethyl methylphosphonate (722 μL, 5.00 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (1.87 mL, 5.00 mmol), and cinnamyl bromide (1.03 g, 5.25 mmol) according to Procedure A (reaction time: 50 min).

8: colorless oil. ^{1}H NMR (500 MHz, CDCl₃) δ 7.36–7.27 (m, 4H), 7.21 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.43 (d, *J* = 16.1 Hz, 1H), 6.22 (dt, *J* = 15.5, 6.9 Hz, 1H), 4.17–4.06 (m, 4H), 2.57–2.46 (m, 2H), 1.96–1.86 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl₃) δ 137.2, 130.6, 128.9 (d, J_{C-P} = 16.8 Hz), 128.5 (2C), 127.2, 126.0 (2C), 61.5 (d, J_{C-P} = 6.0 Hz, 2C), 26.0 (d, J_{C-P} = 3.6 Hz), 25.5 (d, J_{C-P} = 139 Hz), 16.5 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl₃) δ 31.9. IR (ATR) ν 2981, 1240, 1163, 1024, 958 cm^{-1}. HRMS (FD) *m/z*: [M]$^{+}$ calcd for C₁₄H₂₁O₃P 268.1228; found: 268.1218.

Diethyl (3-methylbut-3-en-1-yl)phosphonate (8a)
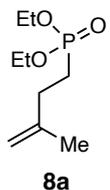
Phosphonate **8a** (372 mg, 1.80 mmol, 90%) was obtained from diethyl methylphosphonate (289 μL, 2.00 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (0.75 mL, 2.0 mmol), and 3-bromo-2-methylpropene (215 μL, 2.10 mmol) according to Procedure A (reaction time: 1.5 h).

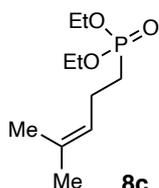**8a**: colorless oil. ^{1}H NMR spectral property in CDCl₃ was identical to that reported.[11]

Diethyl (*E*)-(6-(((*tert*-butyldimethylsilyl)oxy)hex-3-en-1-yl)phosphonate (8b)
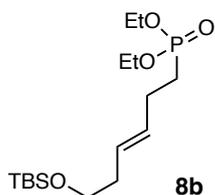
Phosphonate **8b** (258 mg, 0.735 mmol, 74%) was obtained from diethylphosphite (252 μL, 2.00 mmol), 55% NaH in paraffin (87.3 mg, 2.00 mmol) and (*E*)-6-iodohex-3-en-1-ol *tert*-butyldimethylsilyl ether [4] (340 mg, 1.00 mmol) according to Procedure B (reaction time: 15 h).

8b: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.53–5.43 (m, 2H), 4.14–4.04 (m, 4H), 3.61 (t, *J* = 6.9 Hz, 2H), 2.33–2.25 (m, 2H), 2.21 (dt, *J* = 6.3, 6.3 Hz, 2H), 1.84–1.74 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 6H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 130.6 (d, J_{C-P} = 18.0 Hz), 127.5, 62.9, 61.3 (d, J_{C-P} = 6.0 Hz, 2C), 36.0, 25.8 (3C), 25.6 (d, J_{C-P} = 140 Hz), 25.4 (d, J_{C-P} = 4.8 Hz), 18.2, 16.3 (d, J_{C-P} = 6.0 Hz, 2C), –5.4 (2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 32.3. IR (ATR) ν 2929, 1248, 1028, 833, 774 cm^{-1}. HRMS (FD) *m/z*: [M + H]$^+$ calcd for C$_{16}$H$_{36}$O$_4$PSi 351.2121; found: 351.2120.

## Diethyl (4-methylpent-3-en-1-yl)phosphonate (8c)

Phosphonate **8c** (391 mg, 1.78 mmol, 89%) was obtained from diethyl methylphosphonate (289 μL, 2.00 mmol), a 2.64 M solution of *n*-BuLi in *n*-hexane (758 μL, 2.00 mmol), and 1-bromo-3-methyl-2-butene (243 μL, 2.10 mmol) according to Procedure A (reaction time: 50 min).

8c: colorless oil. ^{1}H NMR spectral property in CDCl$_3$ was identical to that reported.[11]
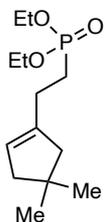
Diethyl (2-(cyclopent-1-en-1-yl)ethyl)phosphonate (8d)
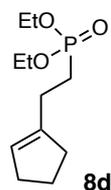
Phosphonate **8d** (316 mg, 1.36 mmol, 68%) was obtained from diethyl methylphosphonate (287 μL, 1.99 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (740 μL, 1.99 mmol), and 1-(bromomethyl)cyclopent-1-ene (336 mg, 2.09 mmol) according to Procedure A (reaction time: 30 min).

8d: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.36 (s, 1H), 4.15–4.04 (m, 4H), 2.39–2.26 (m, 4H), 2.24 (br t, *J* = 6.6 Hz, 2H), 1.94–1.83 (m, 4H), 1.32 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.3 (d, J_{C-P} = 18.0 Hz), 123.8, 61.4 (d, J_{C-P} = 7.2 Hz, 2C), 34.8, 32.3, 24.2 (d, J_{C-P} = 140 Hz), 23.9 (d, J_{C-P} = 4.8 Hz), 23.3, 16.4 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 32.7. IR (ATR) ν 2979, 1242, 1056, 1025, 956 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{11}$H$_{21}$O$_3$P

232.1228; found: 232.1222.

Diethyl (2-(4,4-dimethylcyclopent-1-en-1-yl)ethyl)phosphonate (8e)

Phosphonate **8e** (323 mg, 1.24 mmol, 93%) was obtained from diethyl methylphosphonate (192 μL, 1.33 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (498 μL, 1.33 mmol), and 1-(bromomethyl)-4,4-dimethylcyclopent-1-ene (264 mg, 1.40 mmol) according to Procedure A (reaction time: 30 min).

8e: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.23 (s, 1H), 4.16–4.04 (m, 4H), 2.29 (br ddd, J = 8.3, 8.3, 8.3 Hz, 2H), 2.11 (dd, J = 4.0, 2.3 Hz, 2H), 2.05 (s, 2H), 1.91–1.83 (m, 2H), 1.33 (t, J = 7.2 Hz, 6H), 1.06 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 141.6 (d, J_{C-P} = 18.0 Hz), 122.3, 61.2 (d, J_{C-P} = 7.2 Hz, 2C), 49.8, 47.4, 38.3, 29.7 (2C), 24.0 (d, J_{C-P} = 4.8 Hz), 23.9 (d, J_{C-P} = 140 Hz), 16.3 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 32.8. IR (ATR) ν 2952, 1244, 1056, 1027, 960 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{13}$H$_{25}$O$_3$P 260.1541; found: 260.1543.
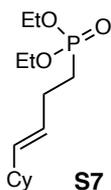
Diethyl (2-(cyclohex-1-en-1-yl)ethyl)phosphonate (8f)
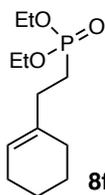
Phosphonate **8f** (198 mg, 0.804 mmol, 87%) was obtained from diethyl methylphosphonate (133 mL, 0.919 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (344 mL, 0.919 mmol), and 1-(bromomethyl)cyclohex-1-ene[2] (169 mg, 0.965 mmol) according to Procedure A (reaction time: 70 min).

8f: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.44 (s, 1H), 4.15–4.03 (m, 4H), 2.20 (br ddd, J = 8.6, 8.6, 8.6 Hz, 2H), 2.01–1.95 (m, 2H), 1.91 (br, 2H), 1.87–1.79 (m, 2H), 1.65–1.51 (m, 4H), 1.32 (t, J = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 136.2 (d, J_{C-P} = 16.8 Hz), 121.1, 61.2 (d, J_{C-P} = 7.2 Hz, 2C), 30.1 (d, J_{C-P} = 3.6 Hz), 27.8, 24.9, 23.9 (d, J_{C-P} = 139 Hz), 22.6, 22.2, 16.2 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 33.1. IR (ATR) ν 2926, 1245, 1027, 961 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{12}$H$_{23}$O$_3$P 246.1385; found: 246.1379.

Diethyl (*E*)-(4-cyclohexylbut-3-en-1-yl)phosphonate (S7)

Phosphonate **S7** (405 mg, 1.48 mmol, 70%) was obtained from diethyl methylphosphonate (289 μL, 2.00 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (743 μL, 2.00 mmol), and (*E*)-(3-bromoprop-1-en-1-yl)cyclohexane[3] (427 mg, 2.10 mmol) according to Procedure A (reaction time: 1 h).

S7: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.44–5.34 (m, 2H), 4.14–4.04 (m, 4H), 2.31–2.23 (m, 2H), 1.93–1.84 (m, 1H), 1.82–1.74 (m, 2H), 1.73–1.64 (m, 4H), 1.32 (t, J = 6.9 Hz, 6H), 1.29–1.19 (m, 3H), 1.14 (tt, J = 12.3, 2.9 Hz, 1H), 1.08–0.98 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 137.2, 125.9 (d, J_{C-P} = 18.0 Hz), 61.3 (d, J_{C-P} = 7.2 Hz, 2C), 40.4, 32.9, 26.3, 26.1, 25.9, 25.41, 25.37, 25.2, 16.4 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 32.5. IR (ATR) ν 2923, 1240, 1025, 961 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{14}$H$_{27}$O$_3$P 274.1698; found: 274.1700.

Diethyl (*E*)-(hept-3-en-1-yl)phosphonate (S8)
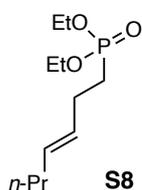
Phosphonate **S8** (438 mg, 1.87 mmol, 84%) was obtained from diethyl methylphosphonate (320 µL, 2.22 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (825 µL, 2.22 mmol), and (*E*)-1-bromo-2-hexene (380 mg, 2.33 mmol) according to Procedure A (reaction time: 1 h).

S8: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.50–5.38 (m, 2H), 4.14–4.04 (m, 4H), 2.32–2.24 (m, 2H), 1.96 (q, J = 6.9 Hz, 2H), 1.84–1.74 (m, 2H), 1.39–1.30 (m, 8H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 131.1, 128.7 (d, J_{C-P} = 18.0 Hz), 61.3 (d, J_{C-P} = 7.2 Hz, 2C), 34.4, 25.7 (d, J_{C-P} = 140 Hz), 25.4 (d, J_{C-P} = 3.6 Hz), 22.4, 16.3 (d, J_{C-P} = 6.0 Hz, 2C), 13.5. ^{31}P NMR (202 MHz, CDCl$_3$) δ 32.4. IR (ATR) ν 2958, 1244, 956, 791 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{11}$H$_{23}$O$_3$P 234.1385; found: 234.1389.

Nopol-derived phosphonate 8g
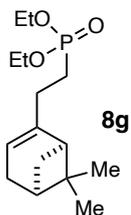
Phosphonate **8g** (1.17 g, 4.09 mmol, 82%) was obtained from the corresponding homoallyl iodide **S9**[6] (1.38 g, 5.00 mmol), diethylphosphite (1.29 mL, 10.0 mmol) and 55% NaH in paraffin (436 mg, 10.0 mmol) according to Procedure B (reaction time: 20.5 h).

8g: colorless oil. [α]$^{26}_D$ –29.7 (c 1.01, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.23 (s, 1H), 4.14–4.05 (m, 4H), 2.36 (dt, J = 8.0, 5.2 Hz, 1H), 2.28–2.14 (m, 4H), 2.08 (br, 1H), 1.99 (t, J = 5.2 Hz, 1H), 1.82–1.72 (m, 2H), 1.33 (t, J = 6.8 Hz, 6H), 1.27 (s, 3H), 1.14 (d, J = 8.0 Hz, 1H), 0.81 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 146.9 (d, J_{C-P} = 19.2 Hz), 116.2, 61.4 (d, J_{C-P} = 6.0 Hz), 45.5, 40.7, 37.9, 31.5, 31.1, 29.2 (d, J_{C-P} = 3.6 Hz), 26.1, 23.6 (d, J_{C-P} = 140 Hz), 21.1, 16.4 (d, J_{C-P} = 6.0 Hz). ^{31}P NMR (202 MHz, CDCl$_3$) δ 33.0. IR (ATR) ν 2913, 1244, 1027, 956 cm^{-1}; HRMS

(FD) calcd for $C_{15}H_{27}O_3P$ (M^+): 286.1698, found: 286.1693.

General Procedure for Preparations of Trienyl Phosphonates[12]

Procedure C
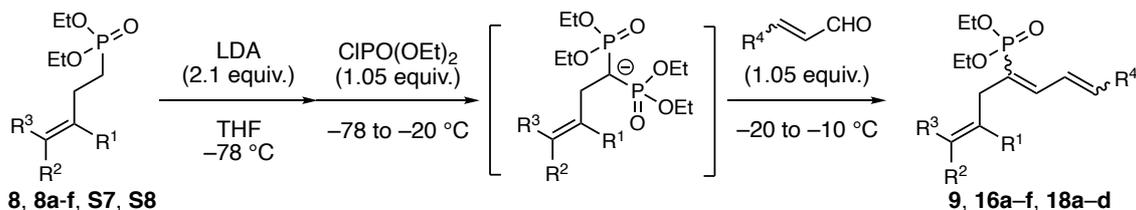
To a solution of diisopropylamine (2.10 equiv.) in THF at 0 °C was slowly added a solution of *n*-BuLi in *n*-hexane (2.10 equiv.). After stirring for 20 ~ 30 min, the mixture was cooled to –78 °C, and a solution of γ,δ-unsaturated phosphonate in THF was added via cannula (at this time 0.2 M to γ,δ-unsaturated phosphonate). After stirring for 15 min at –78 °C, diethyl chlorophosphate (1.05 equiv.) was added dropwise. The mixture was warmed to –20 °C over ca. 0.5 h, and then α,β-unsaturated aldehyde (1.05 equiv.) was added. When the bath temperature reached –10 °C under ambient atmosphere, the reaction was quenched with saturated aqueous NH₄Cl. After EtOAc was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by silica gel flash column chromatography afforded cyclization precursor.

Synthesis of Trienyl Phosphonates
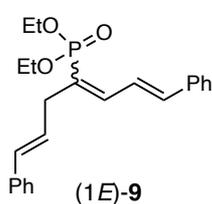
According to Procedure C, an isomeric mixture of crude phosphonate (1*E*)-**9** (3*E*/3*Z* = 1.2:1.0) was obtained from **8** (1.34 g, 5.00 mmol), diisopropylamine (1.48 mL, 10.5 mmol), a 2.64 M solution of *n*-BuLi in *n*-hexane (3.98 mL, 10.5 mmol), diethyl chlorophosphate (755 μL, 5.25 mmol) and *trans*-cinnamaldehyde (661 μL, 5.25 mmol). Purification by flash column chromatography (SiO₂, *n*-hexane/EtOAc = 4:1 to 1:1) afforded (1*E*,3*E*)-**9** (961 mg, 2.51 mmol, 50%) and (1*E*,3*Z*)-**9** (828 mg, 2.17 mmol, 43%).

(1*E*,3*E*)-**9**: pale orange oil. ¹H NMR (500 MHz, CDCl₃) δ 7.46 (d, *J* = 7.5 Hz, 2H), 7.37–7.23 (m, 8H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.10 (ddd, *J* = 15.5, 11.5, 2.3 Hz, 1H), 6.88 (d, *J* = 15.5 Hz, 1H),

6.49 (d, J = 15.5 Hz, 1H), 6.22 (dt, J = 15.5, 6.6 Hz, 1H), 4.16–4.00 (m, 4H), 3.34 (dd, J = 18.3, 6.9 Hz, 2H), 1.31 (t, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.8 (d, J_{C-P} = 12.0 Hz) 139.9, 137.2, 136.2, 131.2, 128.9, 128.7, 128.5 (2C), 127.2 (2C), 127.1 (2C), 126.9 (d, J_{C-P} = 2.4 Hz), 126.3 (d, J_{C-P} = 181 Hz), 126.0 (2C), 122.6 (d, J_{C-P} = 22.8 Hz), 61.7 (d, J_{C-P} = 4.8 Hz, 2C), 30.9 (d, J_{C-P} = 9.6 Hz), 16.3 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 22.2. IR (ATR) ν 2980, 1240, 1019, 961, 748 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{27}$O$_3$P 382.1698, found; 382.1715.

(1E,3Z)-**9**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.92 (ddd, J = 15.5, 11.5, 1.2 Hz, 1H), 7.49 (d, J = 7.5 Hz, 2H), 7.40 (dd, J = 8.6, 1.7 Hz, 2H), 7.36–7.31 (m, 4H), 7.29–7.23 (m, 2H), 6.87 (dd, J = 47.0, 10.3 Hz, 1H), 6.69 (d, J = 15.5 Hz, 1H), 6.50 (d, J = 15.5 Hz, 1H), 6.27 (dt, J = 16.1, 7.2 Hz, 1H), 4.21–4.06 (m, 4H), 3.24 (dd, J = 12.6, 6.9 Hz, 2H), 1.36 (t, J = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.3 (d, J_{C-P} = 10.8 Hz), 138.5 (d, J_{C-P} = 2.4 Hz), 137.2, 136.6, 132.2, 128.6 (2C), 128.5, 128.4, 127.3 (2C), 127.20, 127.17 (2C), 127.0 (d, J_{C-P} = 173 Hz), 126.1 (2C), 125.7 (d, J_{C-P} = 8.4 Hz), 61.6 (d, J_{C-P} = 6.0 Hz, 2C), 37.9 (d, J_{C-P} = 12.0 Hz), 16.4 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.1. IR (ATR) ν 2981, 1235, 1047, 1017, 963, 749 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{27}$O$_3$P 382.1698; found: 382.1682.
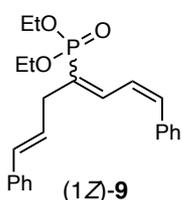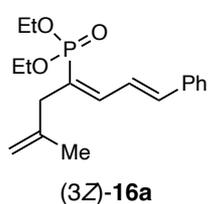

According to Procedure C, purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 2:1) afforded an isomeric mixture of phosphonate (1Z)-**9** (326 mg, 0.852 mmol, 85%, 3E/3Z = 1.0:1.4) by using **8** (268 mg, 1.00 mmol), diisopropylamine (296 μL, 2.10 mmol), a 2.64 M solution of n-BuLi in n-hexane (795 μL, 2.10 mmol), diethyl chlorophosphate (151 μL, 1.05 mmol) and

cis-cinnamaldehyde (133 μL, 1.05 mmol).

(1Z,3E)-**9** and (1Z,3Z)-**9** were partially separated by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 2:1) to give analytically pure samples.

(1Z,3E)-**9**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (dd, J = 22.9, 12.0 Hz, 1H), 7.40–7.32 (m, 6H), 7.32–7.18 (m, 3H), 7.21 (t, J = 7.5 Hz, 1H), 6.81 (dd, J = 11.5, 3.5 Hz, 1H), 6.57 (ddd, J = 12.0, 11.5, 3.5 Hz, 1H), 6.48 (d, J = 15.5 Hz, 1H), 6.22 (dt, J = 15.5, 6.3 Hz, 1H), 4.13–4.00 (m, 4H), 3.34 (dd, J = 18.4, 6.3 Hz, 2H), 1.28 (t, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 138.9 (d, J_{C-P} = 12.0 Hz), 137.3, 136.8, 136.2, 131.2, 129.3 (2C), 128.7 (d, J_{C-P} = 181 Hz), 128.5 (2C), 128.4, 128.0, 127.2 (2C), 126.6 (d, J_{C-P} = 2.4 Hz), 126.1 (2C), 123.6 (d, J_{C-P} = 22.8 Hz), 61.7 (d, J_{C-P} = 6.0 Hz, 2C), 30.8 (d, J_{C-P} = 10.8 Hz), 16.3 (d, J_{C-P} = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 21.7. IR (ATR) ν 2980, 1241, 1020, 961, 745, 695 cm^{-1}. HRMS (FD)

m/z: [M]$^+$ calcd for C$_{23}$H$_{27}$O$_3$P 382.1698; found: 382.1699.

(1*Z*,3*Z*)-**9**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34–7.28 (m, 4H), 7.28–7.15 (m, 8H), 6.74 (d, *J* = 11.5 Hz, 1H), 6.43 (d, *J* = 15.5 Hz, 1H), 6.19 (dt, *J* = 15.5, 7.2 Hz, 1H), 4.19–4.05 (m, 4H), 3.19 (dd, *J* = 12.6, 6.9 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 140.9 (d, *J*$_{C-P}$ = 10.8 Hz), 137.2, 136.4, 135.2, 132.2, 129.3 (2C), 129.1 (d, *J*$_{C-P}$ = 173 Hz), 128.4, 128.2 (2C), 127.6, 127.2 (2C), 127.1 (2C), 126.2 (d, *J*$_{C-P}$ = 8.4 Hz), 126.1, 61.6 (d, *J*$_{C-P}$ = 6.0 Hz, 2C), 38.0 (d, *J*$_{C-P}$ = 12.0 Hz), 16.3 (d, *J*$_{C-P}$ = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 18.7. IR (ATR) ν 2980, 1234, 1019, 958, 745, 694 cm^{-1}. HRMS (FD) calcd for C$_{23}$H$_{27}$O$_3$P [M]$^+$: 382.1698, found: 382.1695.

(3*Z*)-**16a**

According to Procedure C, an isomeric mixture of crude phosphonate **16a** (3*E*/3*Z* = 1:7) was obtained from **8a** (206 mg, 1.00 mmol), diisopropylamine (296 μL, 2.10 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (0.79 mL, 2.10 mmol), diethyl chlorophosphate (151 μL, 1.05 mmol) and *trans*-cinnamaldehyde (132 μL, 1.05 mmol). Purification by flash column chromatography (SiO$_2$, h *n*-hexane/EtOAc = 4:1 to 2:1) afforded (3*Z*)-**16a** (211 mg, 0.659 mmol, 66%).

(3*Z*)-**16a**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (dd, *J* = 15.5, 11.5 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.32 (dd, *J* = 7.4, 7.2 Hz, 2H), 7.28–7.23 (m, 1H), 6.79 (dd, *J* = 48.1, 11.5 Hz, 1H), 6.68 (d, *J* = 15.5 Hz, 1H), 4.91 (s, 1H), 4.83 (s, 1H), 4.17–4.02 (m, 4H), 3.01 (d, *J* = 12.6 Hz, 2H), 1.74 (s, 3H), 1.33 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.4 (d, *J*$_{C-P}$ = 10.8 Hz), 142.9 (d, *J*$_{C-P}$ = 4.8 Hz), 138.3 (d, *J*$_{C-P}$ = 2.4 Hz), 136.6, 128.6 (2C), 128.4, 127.1 (2C), 126.2 (d, *J*$_{C-P}$ = 174 Hz), 125.8 (d, *J*$_{C-P}$ = 8.4 Hz), 113.4, 61.5 (d, *J*$_{C-P}$ = 4.8 Hz, 2C), 42.3 (d, *J*$_{C-P}$ = 10.8 Hz), 22.1, 16.3 (d, *J*$_{C-P}$ = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.4. IR (ATR) ν 2980, 1235, 1019, 957, 750 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{18}$H$_{25}$O$_3$P 320.1541; found: 320.1539.

16b
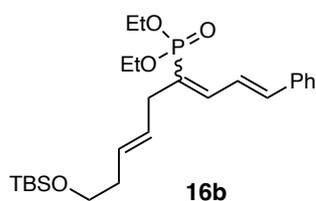
According to Procudure C, an isomeric mixture of crude phosphonate **16b** (3*E*/3*Z* = 1.0:1.0) was obtained from **8b** (185 mg, 0.528 mmol), diisopropylamine (157 μL, 1.11 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (416 μL, 1.11 mmol), diethyl chlorophosphate (79.7 μL, 0.554 mmol) and *trans*-cinnamaldehyde (69.7 μL, 0.554 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1 to 1:1) afforded (3*E*)-**16b** (88.7 mg, 0.191 mmol, 36%) and (3*Z*)-**16b** (87.7 mg, 0.189 mmol, 36%).

(3*E*)-**16b**: yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.45 (d, *J* = 7.4 Hz, 2H), 7.35 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.19 (dd, *J* = 21.8, 10.9 Hz, 1H), 7.04 (ddd, *J* = 15.5, 10.9, 1.7 Hz, 1H), 6.83 (d, *J* = 15.5 Hz, 1H), 5.60–5.46 (m, 2H), 4.15–3.98 (m, 4H), 3.60 (t, *J* = 6.9 Hz, 2H), 3.13 (dd, *J* = 20.2, 5.8 Hz, 2H), 2.23 (dt, *J* = 6.9, 6.9 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 6H), 0.87 (s, 9H), 0.02 (s, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 143.3 (d, J_{C-P} = 12.0 Hz), 139.4, 136.4, 128.74, 128.71 (2C), 128.68 (d, J_{C-P} = 2.4 Hz), 128.2, 127.1 (2C), 126.9 (d, J_{C-P} = 181 Hz), 122.9 (d, J_{C-P} = 22.8 Hz), 63.0, 61.6 (d, J_{C-P} = 4.8 Hz, 2C), 36.1, 30.7 (d, J_{C-P} = 9.6 Hz), 25.9 (3C), 18.3, 16.3 (d, J_{C-P} = 6.0 Hz, 2C), –5.3 (2C). ³¹P NMR (202 MHz, CDCl₃) δ 22.2. IR (ATR) ν 2928, 1247, 1023, 963, 834, 774 cm⁻¹. HRMS (FD) *m*/*z*: [M]⁺ calcd for C₂₅H₄₁O₄PSi 464.2512; found: 464.2514.

(3*Z*)-**16b**: yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.88 (dd, *J* = 15.5, 10.9 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.32 (dd, *J* = 7.5, 7.2 Hz, 2H), 7.28–7.23 (m, 1H), 6.79 (dd, *J* = 48.7, 10.9 Hz, 1H), 6.66 (d, *J* = 15.5 Hz, 1H), 5.55–5.52 (m, 2H), 4.17–2.02 (m, 4H), 3.65 (t, *J* = 6.9 Hz, 2H), 3.01 (dd, *J* = 12.1, 3.5 Hz, 2H), 2.28 (dt, *J* = 6.9, 6.9 Hz, 2H), 1.33 (t, *J* = 6.9 Hz, 6H), 0.90 (s, 9H), 0.06 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 144.8 (d, J_{C-P} = 12.0 Hz), 138.1 (d, J_{C-P} = 2.4 Hz), 136.7, 129.5, 128.9 (d, J_{C-P} = 6.0 Hz), 128.6 (2C), 128.3, 127.6 (d, J_{C-P} = 173 Hz), 127.1 (2C), 125.8 (d, J_{C-P} = 8.4 Hz), 63.1, 61.4 (d, J_{C-P} = 6.0 Hz, 2C), 37.5 (d, J_{C-P} = 10.8 Hz), 36.2, 25.9 (3C), 18.3, 16.3 (d, J_{C-P} = 6.0 Hz, 2C), –5.3 (2C). ³¹P NMR (202 MHz, CDCl₃) δ 19.1. IR (ATR) ν 2928, 1238, 1022, 834, 774 cm⁻¹. HRMS (FD) *m*/*z*: [M]⁺ calcd for C₂₅H₄₁O₃PSi 464.2512; found: 464.2526.
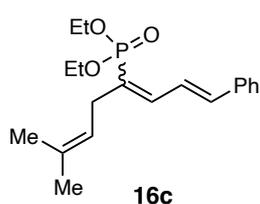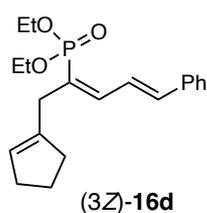

According to Procedure C, an isomeric mixture of crude phosphonate **16c** (3*E*/3*Z* = 1.4:1.0) was obtained from **8c** (220 mg, 1.00 mmol), diisopropylamine (296 μL, 2.10 mmol), a 2.64 M solution of *n*-BuLi in *n*-hexane (795 μL, 2.10 mmol), diethyl chlorophosphate (151 μL, 1.05 mmol) and *trans*-cinnamaldehyde (132 μL, 1.05 mmol). Purification by flash column chromatography (SiO₂, *n*-hexane/EtOAc = 4:1 to 1:1) afforded (3*E*)-**16c** (152 mg, 0.455 mmol, 46%) and (3*Z*)-**16c** (104 mg, 0.311 mmol, 31%).

(3*E*)-**16c**: yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.45 (d, *J* = 7.5 Hz, 2H), 7.35 (dd, *J* = 7.5, 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.16 (dd, *J* = 21.8, 10.9 Hz, 1H), 7.04 (ddd, *J* = 15.5, 10.9, 2.3 Hz, 1H), 6.83 (d, *J* = 15.5 Hz, 1H), 5.10 (br t, *J* = 6.9 Hz, 1H), 4.14–3.98 (m, 4H), 3.12 (dd, *J* = 18.4, 7.5 Hz, 2H), 1.76 (s, 3H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.32 (t, *J* = 6.9 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 142.7 (d, J_{C-P} = 12.0 Hz), 139.0, 136.4, 132.3, 128.7 (2C), 128.6, 128.0 (d,

J_{C-P} = 179 Hz), 127.0 (2C), 122.9 (d, J_{C-P} = 24.0 Hz), 121.7 (d, J_{C-P} = 4.4 Hz), 61.5 (d, J_{C-P} = 4.8 Hz, 2C), 26.6 (d, J_{C-P} = 9.6 Hz), 25.6, 17.9, 16.2 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 22.5. IR (ATR) ν 2979, 1243, 1021, 957, 750 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{19}$H$_{27}$O$_3$P 334.1698; found: 334.1681.

(3*Z*)-**16c**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.90 (dd, *J* = 15.5, 11.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.32 (dd, *J* = 7.5, 7.4 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 6.77 (dd, *J* = 48.7, 11.5 Hz, 1H), 6.65 (d, *J* = 15.5 Hz, 1H), 5.20 (t, *J* = 7.2 Hz, 1H), 4.16–4.02 (m, 4H), 3.00 (dd, *J* = 10.9, 7.5 Hz, 2H), 1.77 (s, 3H), 1.66 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0 (d, J_{C-P} = 12.0 Hz), 137.8 (d, J_{C-P} = 2.4 Hz), 136.7, 134.1, 128.5 (2C), 128.2, 127.0 (2C), 126.5 (d, J_{C-P} = 169 Hz), 125.8, 120.9 (d, J_{C-P} = 7.2 Hz), 61.3 (d, J_{C-P} = 4.8 Hz, 2C), 32.8 (d, J_{C-P} = 10.8 Hz), 25.7, 17.7, 16.3 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.5. IR (ATR) ν 2980, 1237, 1022, 959, 751 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{19}$H$_{27}$O$_3$P 334.1698; found: 334.1699.
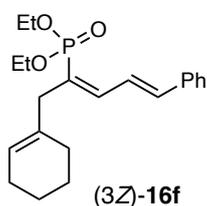

(3*Z*)-**16d**

According to Procedure C, an isomeric mixture of crude phosphonate **16d** (3*E*/3*Z* = 1:6) was obtained from **8d** (103 mg, 0.443 mmol), diisopropylamine (131 μL, 0.930 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (348 μL, 0.930 mmol), diethyl chlorophosphate (66.9 μL, 0.465 mmol) and *trans*-cinnamaldehyde (58.5 μL, 0.465 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 2:1) afforded phosphonate (3*Z*)-**16d** (106 mg, 0.306 mmol, 69%).

(3*Z*)-**16d**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.88 (dd, *J* = 15.5, 11.5 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.32 (dd, *J* = 7.4, 7.2 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 6.76 (dd, *J* = 48.7, 12.1 Hz, 1H), 6.66 (d, *J* = 16.1 Hz, 1H), 5.49 (s, 1H), 4.15–4.00 (m, 4H), 3.08 (d, *J* = 13.2 Hz, 2H), 2.38–2.30 (m, 2H), 2.25 (br t, *J* = 6.6 Hz, 2H), 1.89 (tt, *J* = 7.4, 7.4 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.2 (d, J_{C-P} = 12.0 Hz), 141.6 (d, J_{C-P} = 4.8 Hz), 138.0 (d, J_{C-P} = 2.4 Hz), 136.7, 128.6 (2C), 128.3, 127.1 (2C), 127.0, 126.5 (d, J_{C-P} = 174 Hz), 125.8 (d, J_{C-P} = 8.4 Hz), 61.4 (d, J_{C-P} = 4.8 Hz, 2C), 35.9 (d, J_{C-P} = 12.0 Hz), 34.6, 32.5, 23.5, 16.3 (d, J_{C-P} = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.5. IR (ATR) ν 2980, 1235, 1020, 956, 750 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{20}$H$_{27}$O$_3$P 346.1698; found: 346.1689.
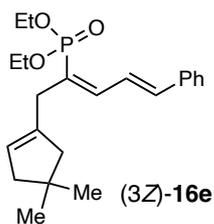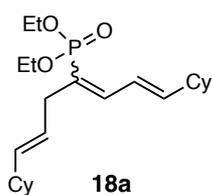
According to Procedure C, an isomeric mixture of crude phosphonate **16e** (3*E*/3*Z* = 2:11) was obtained from **8e** (130 mg, 0.500 mmol), diisopropylamine (148 μL, 1.05 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (393 μL, 1.05 mmol), diethyl chlorophosphate (75.5 μL, 0.525 mmol) and *trans*-cinnamaldehyde (66.1 μL, 0.525 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1) afforded phosphonate (3*Z*)-**16e** (136 mg, 0.363 mmol, 73%).

(3*Z*)-**16e**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.88 (dd, *J* = 15.5, 11.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.32 (dd, *J* = 7.5, 7.3 Hz, 2H), 7.28–7.23 (m, 1H), 6.74 (dd, *J* = 48.1, 11.5 Hz, 1H), 6.65 (d, *J* = 15.5 Hz, 1H), 5.36 (br s, 1H), 4.16–4.00 (m, 4H), 3.03 (d, *J* = 12.6 Hz, 2H), 2.16 (d, *J* = 1.8 Hz, 2H), 2.07 (s, 2H), 1.33 (t, *J* = 7.2 Hz, 6H), 1.09 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.2 (d, $J_{C\text{-}P}$ = 10.8 Hz), 140.0 (d, $J_{C\text{-}P}$ = 4.8 Hz), 138.0 (d, $J_{C\text{-}P}$ = 2.4 Hz), 136.7, 128.6 (2C), 128.3, 127.1 (2C), 126.4 (d, $J_{C\text{-}P}$ = 173 Hz), 125.9 (d, $J_{C\text{-}P}$ = 8.4 Hz), 125.8, 61.4 (d, $J_{C\text{-}P}$ = 4.8 Hz, 2C), 49.8, 47.8, 38.6, 36.0 (d, $J_{C\text{-}P}$ = 10.8 Hz), 30.0 (2C), 16.4 (d, $J_{C\text{-}P}$ = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.2. IR (ATR) ν 2951, 1236, 1021, 957, 750 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{22}$H$_{31}$O$_3$P 374.2011; found: 374.2003.

According to Procedure C, an isomeric mixture of crude phosphonate **16f** (3*E*/3*Z* = 1:11) was obtained from **8f** (198 mg, 0.804 mmol), diisopropylamine (239 μL, 1.69 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (633 μL, 1.69 mmol), diethyl chlorophosphate (121 μL, 0.844 mmol) and *trans*-cinnamaldehyde (109 μL, 0.844 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1) afforded phosphonate (3*Z*)-**16f** (188 mg, 0.522 mmol, 65%).

(3*Z*)-**16f**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.89 (dd, *J* = 15.5, 11.5 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.32 (dd, *J* = 7.5, 7.4 Hz, 2H), 7.25 (t, *J* = 7.5 Hz , 1H), 6.73 (dd, *J* = 48.1, 11.5 Hz, 1H), 6.66 (d, *J* = 15.5 Hz, 1H), 5.55 (br s, 1H), 4.15–4.00 (m, 4H), 2.93 (d, *J* = 13.2 Hz, 2H), 2.04 (br s, 2H), 1.92 (br s, 2H), 1.66–1.54 (m, 4H), 1.33 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.0 (d, $J_{C\text{-}P}$ = 10.8 Hz), 137.9 (d, $J_{C\text{-}P}$ = 2.4 Hz), 136.7, 134.8 (d, $J_{C\text{-}P}$ = 6.0 Hz), 128.6 (2C), 128.3, 127.1 (2C), 126.6 (d, $J_{C\text{-}P}$ = 173 Hz), 125.9 (d, $J_{C\text{-}P}$ = 8.4 Hz), 124.6, 61.4 (d, $J_{C\text{-}P}$ = 6.0 Hz, 2C), 42.6 (d, $J_{C\text{-}P}$ = 10.8 Hz), 27.9, 25.4, 22.9, 22.3, 16.3 (d, $J_{C\text{-}P}$ = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.7. IR (ATR) ν 2925, 1235, 1020, 955, 749 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{21}$H$_{29}$O$_3$P 360.1854; found: 360.1839.
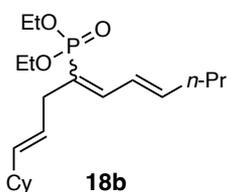
According to Procedure C, an isomeric mixture of crude phosphonate **18a** (3*E*/3*Z* = 1.4:1.0) was obtained from **S7** (176 mg, 0.645 mmol), diisopropylamine (191 μL, 1.35 mmol), a 2.67 M solution of *n*-BuLi in *n*-hexane (506 μL, 1.35 mmol), diethyl chlorophosphate (97.3 μL, 0.677 mmol) and (*E*)-3-cyclohexylpropenal[3a,5] (93.6 mg, 0.677 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 6:1 to 2:1) afforded (3*E*)-**18a** (104 mg, 0.264 mmol, 41%) and (3*Z*)-**18a** (77.4 mg, 0.196 mmol, 30%).

(3*E*)-**18a**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.98 (dd, *J* = 22.4, 10.9 Hz, 1H), 6.28 (br dd, *J* = 14.9, 10.9 Hz, 1H), 5.99 (dd, *J* = 14.9, 6.9 Hz, 1H), 5.42 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.32 (dt, *J* = 15.5, 6.3 Hz, 1H), 4.10–3.94 (m, 4H), 2.98 (dd, *J* = 18.3, 6.3 Hz, 2H), 2.13–2.03 (m, 1H), 1.95–1.86 (m, 1H), 1.77–1.63 (m, 10H), 1.32–0.98 (m, 16H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 148.8, 144.3 (d, J_{C-P} = 12.0 Hz), 137.7, 124.3 (d, J_{C-P} = 180 Hz), 123.9 (d, J_{C-P} = 3.6 Hz), 122.5 (d, J_{C-P} = 22.8 Hz), 61.3 (d, J_{C-P} = 4.8 Hz, 2C), 41.1, 40.6, 32.9 (2C), 32.3 (2C), 30.4 (d, J_{C-P} = 9.6 Hz), 26.1, 26.0, 25.9 (2C), 25.8 (2C), 16.3 (d, J_{C-P} = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 23.4. IR (ATR) ν 2922, 1637, 1447, 1247, 1023, 963 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{23}$H$_{39}$O$_3$P 394.2637; found: 394.2620.

(3*Z*)-**18a**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.01 (dd, *J* = 15.5, 11.5 Hz, 1H), 6.58 (dd, *J* = 48.7, 11.5 Hz, 1H), 5.80 (dd, *J* = 15.5, 7.5 Hz, 1H), 5.44 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.35 (dt, *J* = 15.5, 6.3 Hz, 1H), 4.12–3.97 (m, 4H), 2.98 (dd, *J* = 12.1, 6.3 Hz, 2H), 2.15–2.05 (m, 1H), 1.99–1.90 (m, 1H), 1.78–1.68 (m, 8H), 1.68–1.61 (m, 2H), 1.34–1.20 (m, 10H), 1.20–1.00 (m, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 147.5, 145.5 (d, J_{C-P} = 10.8 Hz), 139.0, 125.2 (d, J_{C-P} = 7.2 Hz), 125.0 (d, J_{C-P} = 173 Hz), 124.4 (d, J_{C-P} = 6.0 Hz), 61.2 (d, J_{C-P} = 4.8 Hz, 2C), 41.0, 40.6, 37.3 (d, J_{C-P} = 12.0 Hz), 33.0 (2C), 32.5 (2C), 26.1, 26.0 (overlapped, 2C + 1C), 25.8 (2C), 16.3 (d, J_{C-P} = 7.2 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.9. IR (ATR) ν 2922, 2850, 1636, 1447, 1241, 963 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{23}$H$_{39}$O$_3$P 394.2637; found: 394.2646.
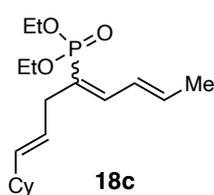

According to Procedure C, an isomeric mixture of crude phosphonate **18b** (3*E*/3*Z* = 1.3:1.0) was obtained from **S7** (137 mg, 0.500 mmol), diisopropylamine (148 μL, 1.05 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (390 μL, 1.05 mmol), diethyl chlorophosphate (75.5 μL, 0.525 mmol) and (*E*)-2-hexenal (60.9 μL, 0.525 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1 to 2:1) afforded phosphonate (3*E*)-**18b** (74.5 mg, 0.210 mmol, 42%) and (3*Z*)-**18b** (56.2 mg, 0.159 mmol, 32%).

(3*E*)-**18b**: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.99 (dd, *J* = 22.4, 10.9 Hz, 1H), 6.33 (br dd, *J* = 14.3, 10.9 Hz, 1H), 6.04 (dt, *J* = 14.3, 7.2 Hz, 1H), 5.42 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.32 (dt, *J* = 15.5, 5.7 Hz, 1H), 4.10–3.94 (m, 4H), 2.98 (dd, *J* = 17.8, 5.7 Hz, 2H), 2.15 (td, *J* = 7.3, 7.2 Hz, 2H), 1.95–1.86 (m, 1H), 1.73–1.62 (m, 5H), 1.45 (tq, *J* = 7.3, 7.2 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 6H), 1.26–1.18 (m, 2H), 1.14 (br dd, *J* = 12.3, 12.3 Hz, 1H), 1.07–0.98 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0 (d, J_{C-P} = 12.0 Hz), 143.1, 137.7, 125.2 (d, J_{C-P} = 22.8 Hz), 124.2 (d, J_{C-P} = 180 Hz), 123.9 (d, J_{C-P} = 2.4 Hz), 61.3 (d, J_{C-P} = 6.0 Hz, 2C), 40.5, 35.0 (d, J_{C-P} = 2.4 Hz), 32.9 (2C), 30.4 (d, J_{C-P} = 9.6 Hz), 26.1, 25.9 (2C), 21.9, 16.3 (d, J_{C-P} = 6.0 Hz, 2C), 13.6. ^{31}P NMR (202 MHz, CDCl$_3$) δ 23.4. IR (ATR) ν 2924, 1639, 1447, 1245, 1023, 963 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{20}$H$_{35}$O$_3$P 354.2324; found: 354.2333.

(3*Z*)-**18b**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.03 (dd, *J* = 14.6, 11.5 Hz, 1H), 6.59 (dd, *J* = 48.7, 11.5 Hz, 1H), 5.87 (dt, *J* = 14.6, 7.3 Hz, 1H), 5.44 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.35 (dt, *J* = 15.5, 6.3 Hz, 1H), 4.10–3.98 (m, 4H), 2.91 (dd, *J* = 12.1, 6.3 Hz, 2H), 2.14 (td, *J* = 7.4, 7.3 Hz, 2H), 1.99-1.90 (m, 1H), 1.74–1.61 (m, 5H), 1.44 (tq, *J* = 7.4, 7.4 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 6H), 1.29–1.20 (m, 2H), 1.15 (br dd, *J* = 12.3, 12.3 Hz, 1H), 1.10–1.02 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.2 (d, J_{C-P} = 12.0 Hz), 141.8, 139.0, 127.7 (d, J_{C-P} = 7.2 Hz), 124.9 (d, J_{C-P} = 173 Hz), 124.4 (d, J_{C-P} = 6.0 Hz), 61.2 (d, J_{C-P} = 6.0 Hz, 2C), 40.6, 37.2 (d, J_{C-P} = 10.8 Hz), 34.8, 33.0 (2C), 26.1, 26.0 (2C), 22.1, 16.3 (d, J_{C-P} = 7.2 Hz, 2C), 13.7. ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.9. IR (ATR) ν 2924, 1638, 1447, 1241, 1022, 962 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{20}$H$_{35}$O$_3$P 354.2324; found: 354.2313.
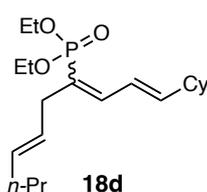

According to Procedure C, an isomeric mixture of crude phosphonate **18c** (3*E*/3*Z* = 1.2:1.0) was obtained from **S7** (134 mg, 0.488 mmol), diisopropylamine (145 μL, 1.03 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (381 μL, 1.03 mmol), diethyl chlorophosphate (73.8 μL, 0.513 mmol) and crotonaldehyde (42.5 μL, 0.513 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 2:1 to 1:1) afforded phosphonate (3*E*)-**18c** (72.0 mg, 0.221 mmol, 45%) and (3*Z*)-**18c** (62.5 mg, 0.191 mmol, 39%).

(3*E*)-**18c**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.99 (dd, *J* = 22.9, 11.5 Hz, 1H), 6.35 (br dd, *J* = 14.5, 11.5 Hz, 1H), 6.04 (dq, *J* = 14.5, 6.9 Hz, 1H), 5.43 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.32 (dt, *J* = 15.5, 6.3 Hz, 1H), 4.13–3.94 (m, 4H), 2.98 (dd, *J* = 17.8, 6.3 Hz, 2H), 1.96–1.87 (m, 1H), 1.85 (d, *J* = 6.9 Hz, 3H), 1.74–1.60 (m, 5H), 1.36–1.19 (m, 8H), 1.14 (tt, *J* = 12.3, 2.3 Hz, 1H), 1.08–0.98 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.8 (d, J_{C-P} = 10.8 Hz), 137.9, 137.7, 126.5 (d, J_{C-P} = 22.8 Hz), 124.1 (d, J_{C-P} = 180 Hz), 123.9 (d, J_{C-P} = 2.4 Hz), 61.4 (d, J_{C-P} = 4.8 Hz, 2C),

40.5, 32.9 (2C), 30.4 (d, $J_{C\text{-}P}$ = 9.6 Hz), 26.1, 26.0 (2C), 18.7, 16.2 (d, $J_{C\text{-}P}$ = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 23.4. IR (ATR) ν 2923, 1644, 1446, 1246, 1022, 962 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{18}$H$_{31}$O$_3$P 326.2011; found: 326.2003.

(3*Z*)-**18c**: colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.07 (br dd, *J* = 14.0, 10.9 Hz, 1H), 6.59 (dd, *J* = 48.7, 10.9 Hz, 1H), 5.89 (dq, *J* = 14.0, 6.9 Hz, 1H), 5.44 (dd, *J* = 15.5, 6.3 Hz, 1H), 5.35 (dt, *J* = 15.5, 6.9 Hz, 1H), 4.12–3.98 (m, 4H), 2.90 (dd, *J* = 12.0, 6.3 Hz, 2H), 1.98–1.89 (m, 1H), 1.83 (d, *J* = 6.9 Hz, 3H), 1.74–1.67 (m, 4H), 1.67–1.60 (m, 1H), 1.31 (t, *J* = 6.9 Hz, 6H), 1.28–1.20 (m, 2H), 1.15 (tt, *J* = 12.6, 2.9 Hz, 1H), 1.11-1.01 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.2 (d, $J_{C\text{-}P}$ = 12.0 Hz), 138.9, 136.6, 128.9 (d, $J_{C\text{-}P}$ = 8.4 Hz), 124.6 (d, $J_{C\text{-}P}$ = 173 Hz), 124.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 61.2 (d, $J_{C\text{-}P}$ = 4.8 Hz, 2C), 40.6, 37.1 (d, $J_{C\text{-}P}$ = 10.8 Hz), 33.0 (2C), 26.1, 26.0 (2C), 18.4, 16.3 (d, $J_{C\text{-}P}$ = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.8. IR (ATR) ν 2923, 1642, 1446, 1239, 1022, 958 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{18}$H$_{31}$O$_3$P 326.2011; found: 326.2005.


According to Procedure C, an isomeric mixture of crude phosphonate **18d** (3*E*/3*Z* = 1.5:1.0) was obtained from **S8** (117 mg, 0.500 mmol), diisopropylamine (148 μL, 1.05 mmol), a 2.69 M solution of *n*-BuLi in *n*-hexane (390 μL, 1.05 mmol), diethyl chlorophosphate (75.5 μL, 0.525 mmol) and (*E*)-3-cyclohexylpropenal[3a,5] (72.6 mg, 0.525 mmol). Purification by flash column chromatography (SiO$_2$, *n*-hexane/EtOAc = 4:1 to 1:1) afforded phosphonate (3*E*)-**18d** (89.8 mg, 0.253 mmol, 51%) and (3*Z*)-**18d** (62.3 mg, 0.176 mmol, 35%).

(3*E*)-**18d**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.99 (dd, *J* = 22.4, 10.9 Hz, 1H), 6.29 (br dd, *J* = 14.9, 10.9 Hz, 1H), 5.99 (dd, *J* = 14.9, 6.9 Hz, 1H), 5.47 (dt, *J* = 15.5, 6.9 Hz, 1H), 5.38 (dt, *J* = 15.5, 6.3 Hz, 1H), 4.10–3.94 (m, 4H), 2.99 (dd, *J* = 17.8, 6.3 Hz, 2H), 2.14–2.03 (m, 1H), 1.96 (td, *J* = 7.3, 6.9 Hz, 2H), 1.78–1.70 (m, 4H), 1.67–1.55 (m, 2H), 1.40–1.23 (m, 10H), 1.22–1.08 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 148.9, 144.3 (d, $J_{C\text{-}P}$ = 12.0 Hz), 131.6, 126.6 (d, $J_{C\text{-}P}$ = 2.4 Hz), 124.3 (d, $J_{C\text{-}P}$ = 181 Hz), 122.5 (d, $J_{C\text{-}P}$ = 22.8 Hz), 61.4 (d, $J_{C\text{-}P}$ = 6.0 Hz, 2C), 41.1, 34.5, 32.3 (2C), 30.4 (d, $J_{C\text{-}P}$ = 10.8 Hz), 26.0, 25.8, 22.5 (2C), 16.3 (d, $J_{C\text{-}P}$ = 7.2 Hz, 2C), 13.6. ^{31}P NMR (202 MHz, CDCl$_3$) δ 23.1. IR (ATR) ν 2925, 1637, 1248, 1024, 960 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{20}$H$_{35}$O$_3$P 354.2324; found: 354.2311.

(3*Z*)-**18d**: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.01 (dd, *J* = 14.9, 10.9 Hz, 1H), 6.59 (dd, *J* = 48.1, 10.9 Hz, 1H), 5.80 (dt, *J* = 14.9, 7.5 Hz, 1H), 5.48 (dt, *J* = 15.5, 6.3 Hz, 1H), 5.40 (dt, *J* = 14.9, 6.9 Hz, 1H), 4.12–3.98 (m, 4H), 2.92 (dd, *J* = 11.5, 6.3 Hz, 2H), 2.14–2.05 (m, 1H),

1.99 (td, J = 7.3, 6.9 Hz, 2H), 1.77–1.68 (m, 4H), 1.67–1.61 (m, 1H), 1.39 (qt, J = 7.5, 7.3 Hz, 2H), 1.32–1.20 (m, 8H), 1.20–1.06 (m, 3H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 147.5, 145.5 (d, J_{C-P} = 12.0 Hz), 132.9, 127.1 (d, J_{C-P} = 6.0 Hz), 125.2 (d, J_{C-P} = 7.2 Hz), 124.9 (d, J_{C-P} = 173 Hz), 61.2 (d, J_{C-P} = 4.8 Hz, 2C), 41.0, 37.3 (d, J_{C-P} = 10.8 Hz), 34.6, 32.5 (2C), 26.0, 25.8, 22.5 (2C), 16.3 (d, J_{C-P} = 6.0 Hz, 2C), 13.7. ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.9. IR (ATR) ν 2925, 1637, 1242, 1023, 962 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{20}$H$_{35}$O$_3$P 354.2324; found: 354.2312.
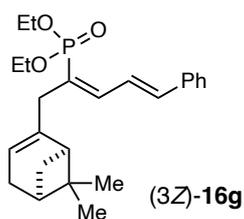
According to Pocedure C, phosphonate (3Z)-**16g** was obtained with a trace amount of (3E)-**16g** from **8g** (573 mg, 2.00 mmol), diisopropylamine (593 µL, 4.20 mmol), a 2.67 M solution of n-BuLi in n-hexane (1.57 mL, 4.20 mmol), diethyl chlorophosphate (302 µL, 2.10 mmol) and *trans*-cinnamaldehyde (264 µL, 2.10 mmol). Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 4:1 to 2:1) afforded phosphonate (3Z)-**16g** (521 mg, 1.30 mmol, 65%).

(3Z)-**16g**: yellow oil. [α]$^{26}_D$ –35.3 (c 1.01, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.86 (dd, J = 16.6, 12.6 Hz, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.32 (dd, J = 7.4, 7.4 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 6.76 (dd, J = 48.7, 11.5 Hz, 1H), 6.64 (d, J = 15.5 Hz, 1H), 5.35 (s, 1H), 4.16–4.02 (m, 4H), 3.03 (dd, J = 16.7, 10.9 Hz, 1H), 2.92 (dd, J = 14.6, 14.6 Hz, 1H), 2.40 (dt, J = 8.6, 5.7 Hz, 1H), 2.32 (d, J = 17.8 Hz, 1H), 2.24 (d, J = 17.8 Hz, 1H), 2.10 (br, 1H), 2.01 (t, J = 4.9 Hz, 1H), 1.33 (t, J = 7.2 Hz, 6H), 1.26 (s, 3H), 1.22 (d, J = 8.6 Hz, 1H), 0.86 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.6, 145.5, 145.3, 145.2, 137.87, 137.85, 136.6, 128.5, 128.2, 127.0, 126.7, 125.83, 125.76, 125.3, 119.4, 61.4, 61.32, 61.28, 45.5, 41.1 (d, J_{C-P} = 10.8 Hz), 40.5, 37.9, 31.7, 31.4, 26.2, 21.0, 16.3 (d, J_{C-P} = 6.0 Hz, 2C) (C-P coupling could not be fully assigned). ^{31}P NMR (202 MHz, CDCl$_3$) δ 19.7. IR (ATR) ν 2981, 1622, 1236, 1021, 956 cm^{-1}; HRMS (FD) m/z [M]$^+$ calcd for C$_{24}$H$_{33}$O$_3$P 400.2167; found: 400.2167.
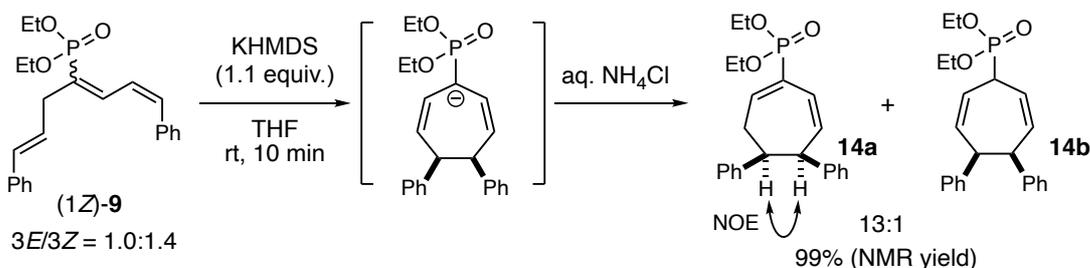
8π Electrocyclization of Phosphonate Derivative (Scheme 6)
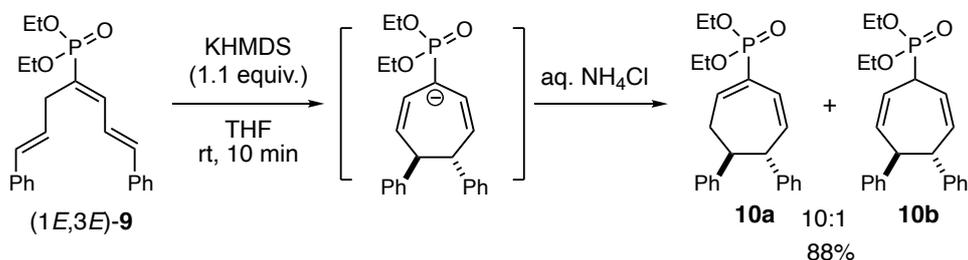
To a solution of (1E,3E)-**9** (38.2 mg, 0.100 mmol) in THF (1.0 mL) at room temperature was added a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol). After stirring for 10 min at room temperature, the reaction was quenched with saturated aqueous NH$_4$Cl (1 mL). After EtOAc (1 mL) was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 1 mL). The combined organic layers were dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 2:1 to 1:1) afforded *trans*-cyclic phosphonate (33.6 mg, 87.9 μmol, 88%) as a mixture of regioisomers (**10a**:**10b** = 10:1) regarding double bonds.

10a (major isomer): pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.16–7.05 (m, 7H), 6.94–6.89 (m, 4H), 6.20–6.09 (m, 2H), 4.15–3.94 (m, 4H), 3.87 (dd, J = 8.6, 4.0 Hz, 1H), 3.31–3.24 (m, 1H), 2.84 (ddd, J = 15.5, 8.0, 8.0 Hz, 1H), 2.70 (ddd, J = 15.5, 6.9, 2.9 Hz, 1H), 1.38 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 147.8 (d, J_{C-P} = 8.4 Hz), 145.1, 143.4, 138.4 (d, J_{C-P} = 16.8 Hz), 128.42 (2C), 128.36 (d, J_{C-P} = 180 Hz), 128.2 (2C), 128.1 (2C), 127.2 (2C), 126.4, 126.2, 123.0 (d, J_{C-P} = 10.8 Hz), 61.9–61.7 (m, 2C), 55.5, 53.3 (d, J_{C-P} = 9.6 Hz), 35.3 (d, J_{C-P} = 20.4 Hz), 16.5–16.3 (m, 2C). ^{31}P NMR (202 MHz, CDCl$_3$) δ 20.1. IR (ATR) ν 2980, 1248, 1023, 961, 700 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{27}$O$_3$P 382.1698; found: 382.1682.

The Reaction of Phosphonate Having Z-Alkene Moiety at C1-C2 Positions (Scheme 10)
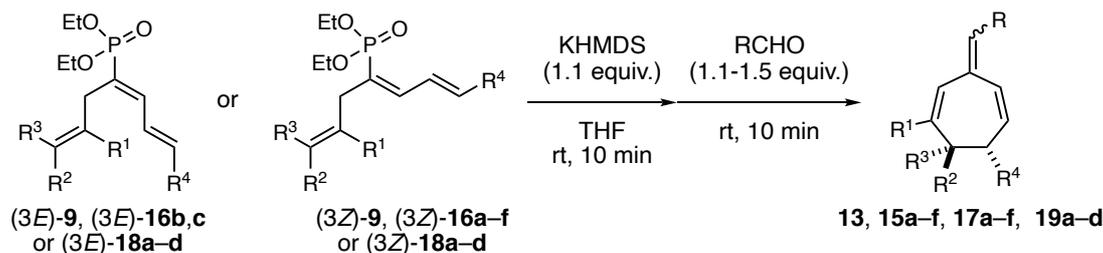

To a solution of isomeric mixture of (1Z)-**9** (3E/3Z = 1.0:1.4, 38.2 mg, 0.100 mmol) in THF (1.0

mL) at room temperature was added a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol). After stirring for 10 min at room temperature, the mixture was cooled to 0 °C and saturated aqueous NH₄Cl (1 mL) was added immediately. After EtOAc (1 mL) was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 1 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. NMR measurement with internal pyrazine (10.0 mg) elucidated an obtained crude oil to contain *cis*-cyclic phosphonate (**14a** + **14b**) (99% NMR yield) as a mixture of regioisomers (**14a**:**14b** = 13:1) regarding double bonds.

8a: pale yellow oil. ^{1}H NMR (500 MHz, CDCl₃) δ 7.20–7.05 (m, 7H), 6.79–6.76 (m, 2H), 6.62 (d, J = 6.9 Hz, 2H), 6.28 (dd, J = 11.5, 11.2 Hz, 1H), 6.18 (ddd, J = 11.5, 6.9, 2.9 Hz, 1H), 4.24–4.09 (m, 4H), 3.87–3.82 (m, 1H), 3.48 (ddd, J = 9.2, 2.6, 2.3 Hz, 1H), 2.83–2.72 (m, 1H), 2.62 (ddd, J = 18.4, 8.1, 2.3 Hz, 1H), 1.42–1.35 (m, 6H). ^{13}C NMR (126 MHz, CDCl₃) δ 146.8 (d, $J_{C\text{-}P}$ = 8.4 Hz), 143.2, 139.5, 136.8 (d, $J_{C\text{-}P}$ = 18.0 Hz), 130.4 (2C), 128.1 (2C), 127.8 (2C), 127.7, 127.5 (2C), 126.8, 126.3, 122.4 (d, $J_{C\text{-}P}$ = 10.8 Hz), 61.9–61.8 (m, 2C), 54.4, 46.0, 33.2 (d, $J_{C\text{-}P}$ = 21.6 Hz), 16.4 (d, $J_{C\text{-}P}$ = 6.0 Hz, 2C). ^{31}P NMR (202 MHz, CDCl₃) δ 21.7. IR (ATR) ν 2980, 1247, 1024, 961, 701 cm^{-1}. HRMS (FD) *m/z*: [M]$^{+}$ calcd for C₂₃H₂₇O₃P 382.1698; found: 382.1694.

General Procedure for 8π Electrocyclization/HWE Reaction Sequence

Procedure D

(3*E*)-**9**, (3*E*)-**16b,c**
or (3*E*)-**18a–d**

(3*Z*)-**9**, (3*Z*)-**16a–f**
or (3*Z*)-**18a–d**

KHMDS
(1.1 equiv.)

RCHO
(1.1-1.5 equiv.)

THF
rt, 10 min

rt, 10 min

13, **15a–f**, **17a–f**, **19a–d**

To a 0.1 M solution of cyclization precursor in THF at room temperature was added a 1.0 M solution of KHMDS in THF (1.1 equiv.). After stirring for 10 min at room temperature, aldehyde (1.5 equiv.) was added, and the resulting mixture was stirred for another 10 min at room temperature. Then, the reaction was quenched with saturated aqueous NH₄Cl. After EtOAc was added, the two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, *n*-hexane/EtOAc = 1:0 to 30:1)

afforded the corresponding cycloheptatriene. When cycloheptatriene was obtained as a mixture with benzaldehyde, benzaldehyde was azeotropically removed together with toluene (3 times).

Scope of Aldehydes in One-pot HWE Reactions (Table 1)

**3-Benzylidene-6,7-*anti*-diphenyl-1,4-cycloheptadiene (13)**
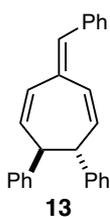
According to Procedure D, phosphonate (1*E*,3*E*)-**9** (76.5 mg, 0.200 mmol) was converted to cycloheptatriene **13** (58.8 mg, 0.176 mmol, 88%) by using a 1.0 M solution of KHMDS in THF (220 μL, 0.220 mmol) and PhCHO (30.6 μL, 0.300 mmol). Also, (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **13** (54.7 mg, 0.164 mmol, 82%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and PhCHO (15.3 μL, 0.150 mmol).

The reaction was also conducted at 1 mmol scale. (1*E*,3*Z*)-**9** (382 mg, 1.00 mmol) was converted to **13** (269 mg, 0.804 mmol, 80%) by using a 1.0 M solution of KHMDS in THF (1.10 mL, 1.10 mmol) and PhCHO (153 μL, 1.50 mmol).

13: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41 (d, J = 7.5 Hz, 2H), 7.37 (dd, J = 7.5, 7.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 1H), 7.22–7.08 (m, 10H), 6.70 (s, 1H), 6.68 (d, J = 12.1 Hz, 1H), 6.35 (d, J = 12.1 Hz, 1H), 5.94 (dd, J = 12.1, 5.7 Hz, 1H), 5.78 (dd, J = 12.1, 5.2 Hz, 1H), 4.02 (dd, J = 6.6, 5.7 Hz, 1H), 3.96 (dd, J = 6.6, 5.2 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.12, 144.05, 137.1, 135.9, 135.4 134.6, 132.6, 132.5, 129.9 (2C), 128.5 (2C), 128.3 (2C), 128.14 (overlapped, 2C + 2C), 128.09 (2C), 128.0, 127.6, 127.3, 126.1, 52.9, 52.6. IR (ATR) ν 3019, 1597, 1489, 1449 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{26}$H$_{22}$ 334.1722; found: 334.1720.

3-(4-Methoxybenzylidene)-6,7-*anti*-diphenyl-1,4-cycloheptadiene (15a)
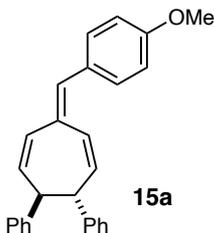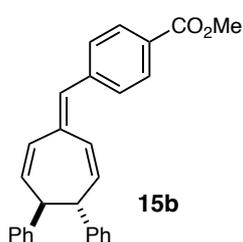

According to Procedure D, phosphonate (1*E*,3*E*)-**9** (38.2 mg, 0.100 mmol) was converted to cycloheptatriene **15a** (30.6 mg, 84.0 μmol, 84%). Also, (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **15a** (29.6 mg, 81.2 μmol, 81%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol, and *p*-anisaldehyde (18.2 μL, 0.150 mmol).

15a: pale yellow solid. Mp 87–91 °C (*n*-hexane/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, J = 9.2 Hz, 2H), 7.20–7.06 (m, 10H), 6.91 (d, J = 8.6 Hz, 2H), 6.69–6.63 (m, 2H), 6.35 (d, J =

12.0 Hz, 1H), 5.93 (dd, J = 11.5, 5.7 Hz, 1H), 5.73 (dd, J = 12.0, 5.2 Hz, 1H), 4.00 (dd, J = 6.6, 5.7 Hz, 1H), 3.95 (dd, J = 6.6, 5.2 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 159.0, 144.3, 144.2, 135.1, 134.5, 134.2, 132.7, 131.8, 131.3 (2C), 129.8, 128.5 (2C), 128.3 (2C), 128.1 (2C), 128.0 (2C), 127.8, 126.0, 113.6 (2C), 55.3, 52.9, 52.6 (One signal could not be judged due to overlap to the signals among 126.0–135.1 ppm.). IR (ATR) ν 3025, 1601, 1505, 1302, 1249, 1176, 1028 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{27}$H$_{24}$O 364.1827; found: 364.1845.

3-(4-methoxycarbonylbenzylidene)-6,7-*anti*-diphenyl-1,4-cycloheptadiene (15b)

According to Procedure D, phosphonate (1*E*,3*E*)-**9** (42.3mg, 0.111 mmol) was converted to cycloheptatriene **15b** (30.2 mg, 76.9 μmol, 69%) by using a 1.0 M solution of KHMDS in THF (122 μL, 0.122 mmol) and methyl-4-formylbenzate (20.0 mg, 0.166 mmol). Also, (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **15b** (31.3 mg, 79.7 μmol, 80%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and methyl 4-formylbenzate (24.6 mg, 0.150 mmol).

15b: pale yellow crystal. Mp 134–136 °C (*n*-hexane/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.21–7.07 (m, 10H), 6.69 (s, 1H), 6.63 (d, J = 12.0 Hz, 1H), 6.35 (d, J = 12.6 Hz, 1H), 6.00 (dd, J = 12.0, 6.3 Hz, 1H), 5.84 (dd, J = 12.6, 5.2 Hz, 1H), 4.03 (dd, J = 6.9, 6.3 Hz, 1H), 3.96 (dd, J = 6.9, 5.2 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.8, 143.81, 143.76, 141.7, 137.6, 135.9, 134.0, 133.7, 132.3, 129.8 (2C), 129.4 (overlapped, 2C), 128.6, 128.4 (2C), 128.3 (2C), 128.13 (2C), 128.06 (2C), 127.1 (2C), 126.1, 52.8, 52.4, 52.1. IR (ATR) ν 3025, 1709, 1599, 1276, 1182, 1104 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{28}$H$_{24}$O$_2$ 392.1777; found: 392.1772.

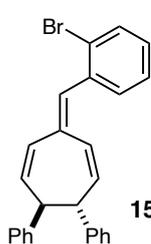### 3-(4-Cyanobenzylidene)-6,7-*anti*-diphenyl-1,4-cycloheptadiene (15c)
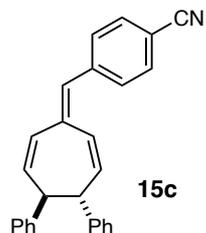
According to Procedure D, phosphonate (1*E*,3*E*)-**9** (38.2 mg, 0.100 mmol) was converted to cycloheptatriene **15c** (26.8 mg, 74.6 μmol, 75%), and (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) to **15c** (27.7 mg, 77.1 μmol, 77%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and 4-formylbenzonitrile (19.7 mg, 0.150 mmol).

15c: colorless crystal. Mp 145–147 °C (*n*-hexane/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.21–7.15 (m, 4H), 7.14–7.07 (m, 6H), 6.64 (s, 1H),

6.56 (d, J = 11.5 Hz, 1H), 6.34 (d, J = 12.6 Hz, 1H), 6.04 (dd, J = 12.0, 6.3 Hz, 1H), 5.87 (dd, J = 12.0, 4.6 Hz, 1H), 4.03 (dd, J = 6.6, 6.3 Hz, 1H), 3.97 (dd, J = 6.6, 4.6 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.6, 143.5, 141.8, 138.5, 136.8 (overlapped, 2C), 134.6, 132.8, 131.93, 131.88 (2C), 130.3, 128.4 (2C), 128.23 (2C), 128.17 (2C), 128.1 (2C), 126.7, 126.2 (2C), 118.9, 110.4, 52.7, 52.3. IR (ATR) ν 2888, 2225, 1725, 1598, 1489, 1448, 1180, 1072 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{27}$H$_{21}$N 359.1674; found: 359.1658.

### 3-(2-Bromobenzylidene)-6,7-*anti*-diphenyl-1,4-cycloheptadiene (15d)

For the synthesis of **15d**, a crude material was purified by Brindle's aldehyde-removal method[13]. After separation operation and removal of solvent, obtained crude residue was dissolved in MeOH (1 mL), and saturated aqueous NaHSO$_3$ (1 mL) was added. After stirring for a few minutes, MeOH was removed under reduced pressure. The resulting residue was added H$_2$O (2~3 mL) and extracted with CH$_2$Cl$_2$. The combined organic layer was dried over MgSO$_4$, filtered and concentrated. The resulting residue was purified through a short pad of silica gel (*n*-hexane/EtOAc = 30:1) to afford **15d**.

According to the modified Procedure D described above, phosphonate (1*E*,3*E*)-**9** (38.2 mg, 0.100 mmol) was converted to **15d** (33.0 mg, 79.8 μmol, 80%), and (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) to **15d** (33.3 mg, 80.6 μmol, 81%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and 2-bromobenzaldehyde (12.8 μL, 0.110 mmol).

15d: pale yellow crystal. Mp 138–140 °C (*n*-hexane/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.62 (d, J = 8.1 Hz, 1H), 7.43 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.24–7.08 (m, 11H), 6.72 (s, 1H), 6.46 (d, J = 12.1 Hz, 1H), 6.43 (d, J = 12.1 Hz, 1H), 5.91 (dd, J = 11.5, 5.8 Hz, 1H), 5.83 (dd, J = 12.0, 5.2 Hz, 1H), 4.00 (dd, J = 6.9, 5.8 Hz, 1H), 3.97 (dd, J = 6.9, 5.2 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.9, 137.0, 136.9, 135.0, 134.5, 133.0, 132.7, 132.4, 132.1, 128.8, 128.5 (2C), 128.3 (2C), 128.11 (2C), 128.07 (2C), 127.1, 126.8, 126.1 (overlapped, 2C), 124.7, 53.0, 52.7 (One signal could not be judged due to overlap to the signals among 126.8–135.0 ppm.). IR (ATR) ν 3060, 1490, 1452, 1022, 697 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{26}$H$_{21}$Br 412.0827; found: 412.0808.

The ORTEP drawing of **15d** (Ellipsoids are drawn at 50% probability.)
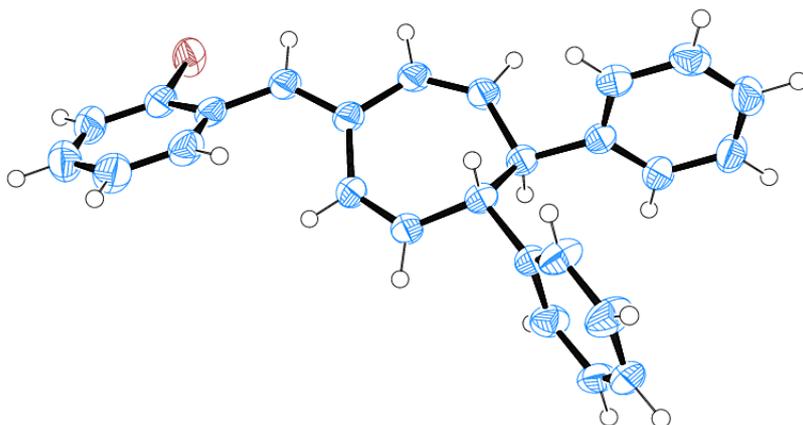
Crystal Data for **15d** (CCDC No. 2121233), $C_{26}H_{21}Br$ (M = 413.34 g/mol), size 0.745 × 0.485 × 0.081 mm^3, triclinic, space group P-1 (no. 2), a = 8.4129(5) Å, b = 9.1770(5) Å, c = 14.5231(4) Å, α = 94.903(4)°, β = 102.152(4)°, γ = 113.531(6)°, V = 986.85(9) Å^3, Z = 2, T = 150 K, μ(Cu Kα) = 0.700 mm^{-1}, $Dcalc$ = 1.391 g/cm^3, 11150 reflections measured (6.340° ≤ 2θ ≤ 155.430°), 4013 unique (R_{int} = 0.0450, R_{sigma} = 0.0405) which were used in all calculations. The final R_1 was 0.0604 (I > 2σ(I)) and wR_2 was 0.1717 (all data).
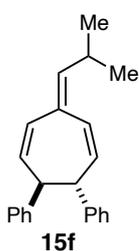
Anti-6,7-diphenyl-3-propylidene-1,4-cycloheptadiene (15e)
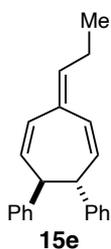
According to Procedure D, phosphonate (1*E*,3*E*)-**9** (38.2 mg, 0.100 mmol) was converted to cycloheptatriene **15e** (13.3 mg, 46.4 μmol, 46%), and (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **15e** (12.5 mg, 43.6 μmol, 44%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and EtCHO (10.8 μmol, 0.150 mmol).

15e: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22–7.16 (m, 4H), 7.15–7.08 (m, 6H), 6.54 (d, J = 12.1 Hz, 1H), 6.17 (d, J = 12.0 Hz, 1H), 5.80 (dd, J = 12.1, 5.8 Hz, 1H), 5.72 (t, J = 7.7 Hz, 1H), 5.59 (dd, J = 12.0, 5.7 Hz, 1H), 3.93 (dd, J = 6.3, 5.8 Hz, 1H), 3.88 (dd, J = 6.3, 5.7 Hz, 1H), 2.34 (qd, J = 7.8, 7.7 Hz, 2H), 1.10 (t, J = 7.8 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.5, 144.3, 140.9, 134.7, 133.1, 132.3, 129.4, 128.5 (2C), 128.4 (2C), 128.02 (2C), 127.99 (2C), 126.00, 125.98 125.6, 53.5, 52.9, 21.5, 14.1. IR (ATR) ν 3025, 1600, 1491, 1452, 696 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for $C_{22}H_{22}$ 286.1722; found: 286.1735.

### *Anti*-3-(2-methylpropylidene)-6,7-diphenyl-1,4-cycloheptadiene (15f)

According to Procedure D, phosphonate (1*E*,3*E*)-**9** (53.1 mg, 0.139 mmol) was converted to cycloheptatriene **15f** (24.0 mg, 79.9 μmol, 57%) by using a 1.0 M solution of KHMDS in THF (153 μL, 0.153 mmol) and ^{i}PrCHO (19.0 μL, 0.208 mmol). Also, (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **15f** (17.9 mg, 59.6 μmol, 60%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and ^{i}PrCHO (13.7 μL, 0.150 mmol).

15f: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.21–7.15 (m, 4H), 7.15–7.07 (m, 6H), 6.55 (d, *J* = 12.6 Hz, 1H), 6.13 (d, *J* = 12.1 Hz, 1H), 5.80 (dd, *J* = 12.6, 5.7 Hz, 1H), 5.59 (dd, *J* = 12.1, 5.2 Hz, 1H), 5.54 (d, *J* = 9.2 Hz, 1H), 3.92 (dd, *J* = 6.3, 5.7 Hz, 1H), 3.87 (dd, *J* = 6.3, 5.2 Hz, 1H), 2.86 (dqq, *J* = 9.2, 6.3, 5.8 Hz, 1H), 1.09 (d, *J* = 5.8 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 146.5, 144.6, 144.4, 133.1, 132.5, 129.7, 128.5 (2C), 128.4 (overlapped, 2C + 1C), 128.00 (2C), 127.97 (2C), 125.97, 125.95, 125.8, 53.4, 52.9, 27.2, 22.98, 22.96. IR (ATR) ν 2958, 1599, 1491, 1452, 696 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{23}$H$_{24}$ 300.1878; found: 300.1883.

Reactions of substrates with an alkyl group at the C6 or C7 position, and Reactions of substrates with a dimethyl group at the C7 position (Scheme 11)

### 3-Benzylidene-1-methyl-6-phenyl-1,4-cycloheptadiene (17a)
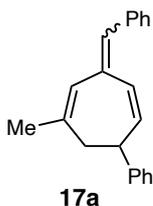
According to Procedure D, phosphonate (3*Z*)-**16a** (64.1 mg, 0.200 mmol) was converted to cycloheptatriene **17a** (33.1 mg, 0.122 mmol, 61%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (220 μL, 0.220 mmol) and PhCHO (61.2 μL, 0.300 mmol).

17a (1.0:1.0 isomeric mixture): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39–7.20 (m, 10H), 6.53–6.48 (m, 0.50×3H), 6.29 (s, 0.50H), 6.25 (d, *J* = 11.5 Hz, 0.50H), 6.10 (s, 0.50H), 5.97 (dd, *J* = 11.5, 4.6 Hz, 0.50H), 5.82 (dd, *J* = 11.5, 4.6 Hz, 0.50H), 3.90–3.84 (m, 0.50H), 3.80–3.74 (m, 0.50H), 2.72–2.64 (m, 0.50×2H), 2.60 (dd, *J* = 14.3, 2.3 Hz, 0.50H), 2.46 (dd, *J* = 15.5, 2.3 Hz, 0.50H), 1.80 (s, 0.50×3H), 1.70 (s, 0.50×3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 145.7, 145.0, 139.9, 138.1, 137.6, 136.6, 136.0, 135.8, 133.9, 133.0, 132.8, 132.6, 129.82, 129.75, 129.5, 128.5, 128.34, 128.27, 128.02, 128.00, 127.7, 127.4, 126.9, 126.8, 126.6, 126.3, 126.2, 123.6, 44.7, 44.0, 41.7, 41.6, 27.8, 27.3 (Only the detected signals were recorded.). IR (ATR) ν 2925, 1719, 1598,

1491, 1450, 1272, 1028, 695 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{21}$H$_{20}$ 272.1565; found: 272.1568.

(2-(4-Benzylidene-7-phenylcyclohepta-2,5-dien-1-yl)ethoxy)(*tert*-butyl)dimethylsilane(17b)
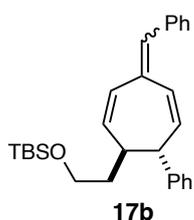
According to Procedure D, phosphonate (3*E*)-**16b** (85.0 mg, 0.183 mmol) was converted to cycloheptatriene **17b** (57.5 mg, 0.138 mmol, 75%, isomeric ratio =1.0:1.2) by using a 1.0 M solution of KHMDS in THF (201 μL, 0.201 mmol) and PhCHO (28.0 μL, 0.274 mmol). Also, (3*Z*)-**16b** (92.8 mg, 0.200 mmol) was converted to **17b** (71.5 mg, 0.172 mmol, 86%, isomeric ratio = 1.0:1.2 in random order) by using a 1.0 M solution of KHMDS in THF (220 μL, 0.220 mmol) and PhCHO (30.6 μL, 0.300 mmol).

17b (1.0:1.2 isomeric mixture): yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38–7.16 (m, 10H), 6.69 (d, *J* = 12.1 Hz, 0.46H), 6.60 (s, 0.54H), 6.58 (s, 0.46H), 6.47 (d, *J* = 12.1 Hz, 0.54H), 6.32 (d, *J* = 12.1 Hz, 0.54H), 6.17 (d, *J* = 12.1 Hz, 0.46H), 5.89 (dd, *J* = 12.1, 6.9 Hz, 0.46H), 5.78–5.70 (m, 0.54×2H), 5.63 (dd, *J* = 12.1, 6.9 Hz, 0.46H), 3.78–3.65 (m, 3H), 2.88–2.80 (m, 1H), 1.89–1.80 (m, 2H), 0.90–0.88 (m, 9H), 0.05–0.02 (m, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.0, 143.9, 137.3, 136.54, 136.50, 135.1, 134.7, 134.6, 133.3, 133.0, 132.6, 130.8, 130.0, 129.8, 128.6, 128.4, 128.2, 128.12, 128.10, 128.0, 127.5, 127.2, 127.1, 127.0, 126.2, 61.3, 61.1, 50.0, 49.7, 42.12, 42.05, 38.8, 38.4, 26.0, 18.3, –5.26, –5.28, –5.32 (Only the detected signals were recorded.). IR (ATR) ν 2952, 1598, 1491, 1254, 1096, 833, 696 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{28}$H$_{36}$OSi 416.2535; found: 416.2523.

## 3-Benzylidene-6,6-dimethyl-7-phenyl-1,4-cycloheptadiene (17c)
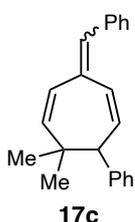
According to Procedure D, phosphonate (3*E*)-**16c** (147 mg, 0.440 mmol) was converted to cycloheptatriene **17c** (90.1 mg, 0.315 mmol, 72%, isomeric ratio = 1.0:1.1) by using a 1.0 M solution of KHMDS in THF (484 μL, 0.484 mmol) and PhCHO (67.3 μL, 0.659 mmol). Also, (3*Z*)-**16c** (102 mg, 0.305 mmol) was converted to **17c** (71.5 mg, 0.250 mmol, 82%, isomeric ratio = 1.0:1.2) by using a 1.0 M solution of KHMDS in THF (336 μL, 0.336 mmol) and PhCHO (46.7 μL, 0.458 mmol).

17c (1.0:1.1 isomeric mixture): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40–7.18 (m, 10H), 6.62–6.56 (m, 0.47H + 0.53×2H), 6.44 (d, *J* = 12.0 Hz, 0.47H), 6.24 (d, *J* = 12.0 Hz, 0.47H), 6.10 (d, *J* = 12.0 Hz, 0.53H), 5.97 (ddd, *J* = 12.0, 6.9, 1.2 Hz, 0.53H), 5.81 (dd, *J* = 12.0, 6.9 Hz,

0.47H), 5.58 (d, J = 12.0 Hz, 0.47H), 5.51 (d, J = 6.9 Hz, 0.53H), 3.65 (d, J = 6.9 Hz, 0.53H), 3.48 (d, J = 6.9 Hz, 0.47H), 1.27 (s, 0.47×3H), 1.08 (s, 0.53×3H), 1.02 (s, 0.53×3H), 0.99 (s, 0.47×3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 142.7, 142.4, 141.8, 140.6, 137.3, 137.2, 136.1, 135.8, 135.0, 134.5, 132.0, 131.1, 130.1, 130.0, 129.9, 129.80, 129.79, 128.1, 128.0, 127.8, 127.6, 127.2, 127.1, 126.37, 126.35, 126.0, 125.2, 56.9, 56.4, 39.8, 39.4, 31.3, 30.7, 28.8, 27.0 (Only the detected signals were recorded.). IR (ATR) ν 2956, 1597, 1490, 1451, 695 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{22}$H$_{22}$ 286.1722; found: 286.1720.

Reactions of Substrates with an Alkyl Group at the C6 or C7 Position (Scheme 12)

7-Benzylidene-4-phenyl-1,2,3,3a,4,7-hexahydroazulene (17d)
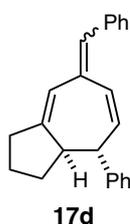
According to Procedure D, phosphonate (3Z)-**16d** (34.6 mg, 0.100 mmol) was converted to cycloheptatriene **17d** (24.7 mg, 82.8 μmol, 83%, isomeric ratio = 1.0:1.3) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and PhCHO (15.3 μL, 0.150 mmol).

17d (1.0:1.3 isomeric mixture): colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.28–7.07 (m, 10H), 6.45–6.35 (m, 2H), 6.10 (s, 0.44H), 6.04 (br d, J = 12.1 Hz, 0.56H), 5.77 (ddd, J = 12.1, 3.5, 1.2 Hz, 0.44H), 5.61 (dd, J = 12.1, 2.9 Hz, 0.56H), 3.41 (ddd, J = 10.9, 3.5, 3.5 Hz, 0.44H), 3.31 (ddd, J = 10.3, 3.5, 2.9 Hz, 0.56H), 2.99–2.91 (m, 0.56H), 2.86–2.78 (m, 0.44H), 2.49–2.45 (m, 0.44× 2H), 2.44–2.35 (m, 0.56×2H), 1.60–1.52 (m, 1H), 1.40–1.25 (m, 2H), 1.18–1.02 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 150.99, 150.95, 149.0, 145.8, 145.7, 137.74, 137.65, 137.6, 135.4, 135.2, 135.1, 132.7, 132.4, 131.8, 129.71, 129.69, 128.5, 128.04, 128.01, 127.9, 126.7, 126.2, 125.8, 124.2, 118.1, 50.6, 50.4, 49.3, 48.7, 36.5, 36.1, 34.6, 34.4, 24.9, 24.2 (Only the detected signals were recorded.). IR (ATR) ν 2953, 1596, 1491, 1450, 696 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{22}$ 298.1722; found: 298.1711.

7-Benzylidene-2,2-dimethyl-4-phenyl-1,2,3,3a,4,7-hexahydroazulene (17e)
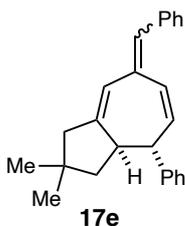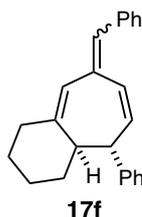

According to Procedure D, phosphonate (3Z)-**16e** (136 mg, 0.363 mmol) was converted to cycloheptatriene **17e** (101 mg, 0.309 mmol, 85%, isomeric ratio = 1.0:1.3) by using a 1.0 M solution of KHMDS in THF (399 μL, 0.399 mmol) and PhCHO (55.6 μL, 0.545 mmol).

17e (1.0:1.3 isomeric mixture): pale yellow viscous oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.37–7.30

(m, 6H), 7.25–7.17 (m, 4H), 6.52–6.46 (m, 2H), 6.18–6.11 (m, 1H), 5.84 (dd, J = 13.8, 3.5 Hz , 0.44H), 5.69 (dd, J = 14.9, 2.9 Hz, 0.56H), 3.50 (ddd, J = 10.9, 3.5, 2.9 Hz, 0.44H), 3.41 (ddd, J = 10.3, 2.9, 2.6 Hz, 0.56H), 3.29–3.15 (m, 1H), 2.47–2.38 (m, 1H), 2.30 (d, J = 16.0 Hz, 0.44H), 2.22 (d, J = 16.1 Hz, 0.56H), 1.17 (d, J = 9.2 Hz, 0.56×2H), 1.14 (d, J = 9.7 Hz, 0.44×2H), 1.00 (s, 0.56×3H), 1.00 (s, 0.44×3H), 0.92 (s, 0.56×3H), 0.91 (s, 0.44×3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 150.9, 149.0, 145.6, 137.8, 137.7, 137.6, 135.3, 135.2, 132.8, 132.6, 131.7, 129.73, 129.69, 128.5, 128.4, 128.1, 128.03, 127.98, 126.8, 126.7, 126.2, 125.4, 124.9, 119.1, 50.9, 50.7, 50.6, 48.03, 47.97, 47.9, 47.5, 37.1, 36.6, 28.9, 28.6, 27.1, 26.6 (Only the detected signals were recorded.) IR (ATR) ν 2951, 1598, 1492, 1453, 699 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{25}$H$_{26}$ 326.2035; found: 326.2042.

## 8-Benzylidene-5-phenyl-2,3,4,4a,5,8-hexahydro-1H-benzo[7]annulene (17f)

According to Procedure D, phosphonate (3Z)-**16f** (72.1 mg, 0.200 mmol) was converted to **17f** (52.2 mg, 0.167 mmol, 84%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (220 μL, 0.220 mmol) and PhCHO (30.6 μL, 0.300 mmol).

17f (1.0:1.0 isomeric mixture): pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.42–7.39 (m, 1H), 7.38–7.33 (m, 2H), 7.33–7.29 (m, 2H), 7.29–7.19 (m, 5H), 6.51 (s, 0.50H), 6.44 (s, 0.50H), 6.41 (d, J = 12.1 Hz, 0.50H), 6.33–6.27 (m, 1H), 6.14 (s, 0.50H), 5.95 (ddd, J = 12.1, 6.3, 1.2 Hz, 0.50H), 5.78 (dd, J = 11.5, 5.2 Hz, 0.50H), 3.64 (ddd, J = 10.9, 6.3, 1.2 Hz , 0.50H), 3.57 (ddd, J = 10.9, 5.2, 1.2 Hz, 0.50H), 2.70–2.63 (m, 0.50H), 2.55–2.47 (m, 0.50H), 2.37–2.27 (m, 1H), 2.18–2.09 (m, 1H), 1.81–1.71 (m, 1H), 1.71–1.63 (m, 1H), 1.49–1.24 (m, 3H), 1.20 (dddd, J = 11.5, 11.5, 11.5, 3.5 Hz, 0.50H), 1.08 (dddd, J = 11.5, 11.5, 11.5, 3.5 Hz, 0.50H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 146.9, 145.20, 145.16, 144.9, 137.6, 137.5, 136.10, 136.07, 136.0, 134.3, 133.8, 132.4, 131.8, 129.8, 129.7, 129.6, 128.5, 128.4, 128.2, 128.14, 128.07, 128.0, 126.9, 126.2, 126.1, 125.7, 120.8, 50.7, 50.0, 47.8, 46.3, 40.2, 38.4, 34.6, 33.5, 28.2, 27.4, 26.1, 25.0 (Only the detected signals were recorded.). IR (ATR) ν 2925, 1596, 1491, 1444, 694 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{24}$H$_{24}$ 312.1878; found: 312.1876.

Reactions of Trienes with Two Alkyl Groups at Each Terminus (Table 3) and **Exchange of Terminal Groups in the Reaction of (3E)-18b (Scheme 14)**

3-Benzylidene-6,7-*anti*-dicyclohexyl-1,4-cycloheptadiene (19a)
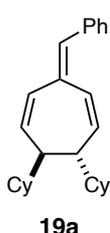
According to Procedure D, phosphonate (3*E*)-**18a** (39.5 mg, 0.100 mmol) was converted to cycloheptatriene **19a** (25.1 mg, 72.4 μmol, 72%), and (3*Z*)-**18a** (39.5 mg, 0.100 mmol) was converted to **19a** (30.8 mg, 88.9 μmol, 89%) by using a 1.0 M solution of KHMDS in THF (110 μL, 0.110 mmol) and PhCHO (15.3 μL, 0.150 mmol).

19a: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35–7.29 (m, 4H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.47 (s, 1H), 6.46 (d, *J* = 11.5 Hz, 1H), 6.08 (d, *J* = 11.5 Hz, 1H), 5.97 (dd, *J* = 11.5, 8.1 Hz, 1H), 5.82 (dd, *J* = 11.5, 8.6 Hz, 1H), 2.17–2.12 (m, 2H), 1.97–1.88 (m, 2H), 1.82–1.76 (m, 2H), 1.71–1.64 (m, 4H), 1.64–1.57 (m, 3H), 1.48–1.39 (m, 1H), 1.23–1.08 (m, 6H), 1.02–0.91 (m, 2H), 0.87–0.76 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 137.6, 137.5, 135.6, 133.5, 133.1, 131.4, 129.8 (2C), 128.0, 126.8, 125.5 (2C), 45.9, 45.8, 42.4, 41.4, 32.3, 32.1, 31.03, 30.97, 26.74, 26.70, 26.43, 26.35, 26.2 (overlapped, 2C). IR (ATR) ν 2918, 1446, 694 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{26}$H$_{34}$ 346.2661; found: 346.2672.

3-Benzilidene-1,4-cycloheptadiene 19b (= 19d)
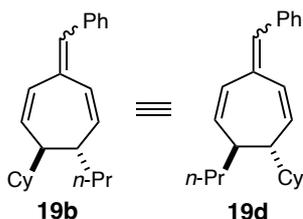
According to Procedure D, phosphonate (3*E*)-**18b** (73.2 mg, 0.207 mmol) was converted to cycloheptatriene **19b** (20.9 mg, 68.2 μmol, 33%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (227 μL, 0.227 mmol) and PhCHO (31.6 μL, 0.310 mmol) Also, (3*Z*)-**18b** (54.3 mg, 0.153 mmol) was converted to **19b** (28.8 mg, 94.0 μmol, 61%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (169 μL, 0.169 mmol) and PhCHO (23.5 μL, 0.230 mmol). Moreover, phosphonate (3*E*)-**18d** (85.8 mg, 0.242 mmol) was converted to cycloheptatriene **19d** (47.6 mg, 0.155 mmol, 64%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (266 μL, 0.266 mmol) and PhCHO (37.0 μL, 0.363 mmol) Also, (3*Z*)-**18d** (58.1 mg, 0.164 mmol) was converted to **19d** (27.1 mg, 88.4 μmol, 54%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (180 μL, 0.180 mmol) and PhCHO (25.1 μL, 0.246 mmol).

19b (**19d**) (1.0:1.0 isomeric mixture): pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35–7.28

(m, 4H), 7.24–7.20 (m, 1H), 6.47–6.41 (m, 2H), 6.10 (d, J = 12.0 Hz, 0.50H), 6.06 (d, J = 12.0 Hz, 0.50H), 5.98–5.90 (m, 1H), 5.82–5.75 (m, 1H), 2.53–2.46 (m, 1H), 2.08–2.00 (m, 1H), 1.97–1.87 (m, 1H), 1.74–1.65 (m, 1H), 1.74–1.64 (m, 2H), 1.62–1.58 (m, 2H), 1.52–0.84 (m, 12H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 137.63, 137.61, 137.4, 137.3, 135.62, 135.58, 133.55, 133.4, 133.2, 133.0, 131.4, 131.3, 129.8, 128.0, 126.83, 126.81, 125.65, 125.61, 49.2, 48.9, 42.5, 41.5, 39.40, 39.36, 38.2, 37.5, 32.2, 31.9, 31.19, 31.17, 26.73, 26.69, 26.5, 26.3, 21.0, 20.8, 14.30, 14.29 (Only the detected signals were recorded.) IR (ATR) ν 2921, 1446, 694 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{30}$ 306.2348; found: 306.2362.

3-Benzilidene-1,4-cycloheptadiene 19c
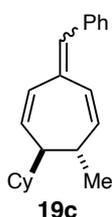
According to Procedure D, phosphonate (3Z)-**18c** (65.3 mg, 0.200 mmol) was converted to cycloheptatriene **19c** (32.0 mg, 0.115 mmol, 57%, isomeric ratio = 1.0:1.0) by using a 1.0 M solution of KHMDS in THF (210 μL, 0.210 mmol). (NOTE: As same as the reaction of (3E)-**18c**, the generation of tetraene **20** was also detected in another trial of the reaction of (3Z)-**18c**, while the yield of the **19c** was constant. That fact implied **20** decomposed partially or completely under the reaction conditions.)

19c (1.0:1.0 isomeric mixture): pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36–7.29 (m, 4H), 7.25–7.20 (m, 1H), 6.49–6.44 (m, 0.50×3H), 6.41 (d, J = 11.5 Hz, 0.50H), 6.13 (d, J = 12.0 Hz, 0.50H), 6.04 (d, J = 12.0 Hz, 0.50H), 5.95 (dd, J = 12.0, 8.0 Hz, 0.50H), 5.89 (dd, J = 11.5, 7.5 Hz, 0.50H), 5.79 (dd, J = 12.0, 7.5 Hz, 0.50H), 5.73 (dd, J = 12.0, 6.9 Hz, 0.50H), 2.68–2.58 (m, 1H), 2.04–1.96 (m, 1H), 1.95–1.84 (m, 1H), 1.82–1.58 (m, 4H), 1.51–1.41 (m, 0.50H), 1.30–1.09 (0.50×5H), 1.07 (d, J = 5.9 Hz, 0.50×3H), 1.04–0.86 (0.50×5H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 137.59, 137.56, 137.2, 137.1, 136.6, 135.4, 134.3, 133.5, 133.3, 132.8, 131.5, 131.0, 129.79, 129.76, 128.0, 126.9, 126.8, 125.9, 125.3, 51.0, 50.9, 42.4, 41.5, 34.24, 34.21, 31.5, 31.3, 31.23, 31.18, 26.72, 26.68, 26.52, 26.46, 26.4, 21.0, 20.5 (Only the detected signals were recorded.). IR (ATR) ν 2921, 1446, 694 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{21}$H$_{26}$ 278.2035; found: 278.2023.

Reactions of (3*E*)-18c and an Observed Side Reaction (Scheme 13)
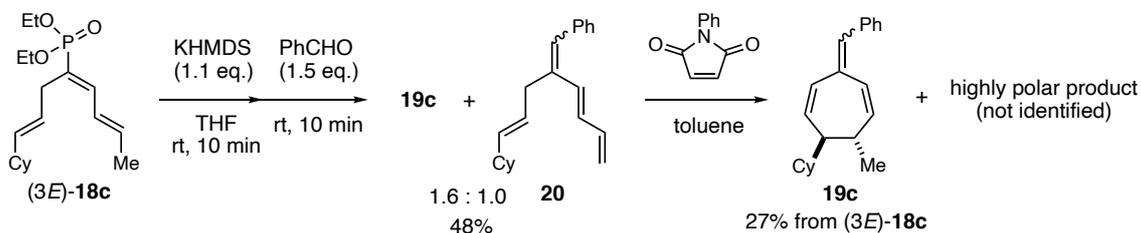
According to Procedure D, a mixture of cycloheptatriene **19c** and tetraene **20** (27.0 mg, 97.0 μmol, 48%, **19c**:**20** = 1.6:1.0) was obtained from (3*E*)-**18c** (65.3 mg, 0.200 mmol), a 1.0 M solution of KHMDS in THF (210 μL, 0.220 mmol) and PhCHO (30.6 μL, 0.300 mmol).

The mixture of **19c** and **20** was dissolved in toluene (0.20 mL), and *N*-phenyl maleimide (19.4 mg, 0.112 mmol) was added at room temperature. The mixture was heated to 90 °C and stirred for 11 h. Then, the mixture was cooled to room temperature, and the solvent was removed under reduced pressure. Purification through a short pad of silica gel (*n*-hexane/EtOAc = 30:1) afforded cycloheptatriene **19c** (14.9 mg, 53.5 μmol, 27% from (3*E*)-**18c**) as a 1.0:1.1 mixture of isomers about the benzylidene moiety.

Analytically pure tetraene **20** was partially separated by PTLC (*n*-hexane only) as a 1.0:1.1 isomeric mixture.

20 (1.0:1.1 isomeric mixture): pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36–7.30 (m, 3H), 7.28–7.20 (m, 2H), 6.70 (d, *J* = 15.5 Hz, 0.53H), 6.60 (s, 0.47H), 6.49–6.33 (m, 3H), 5.52–5.47 (m, 2H), 5.26 (dd, *J* = 5.2, 1.2 Hz, 0.53H), 5.23 (d, *J* = 5.2 Hz, 0.47H), 5.11 (br s, 0.53H), 5.09 (br s, 0.47H), 3.16 (d, *J* = 4.6 Hz, 0.47 × 2H), 3.06 (d, *J* = 4.0 Hz, 0.53 × 2H), 2.02–1.92 (m, 1H), 1.76–1.67 (m, 4H), 1.67–1.60 (m, 1H), 1.32–1.02 (m, 5H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 138.7, 138.3, 138.2, 137.8, 137.7, 137.60, 137.58, 137.3, 132.7, 131.4, 130.8, 130.2, 129.9, 129.8, 129.4, 128.9, 128.14, 128.07, 126.8, 126.6, 125.1, 124.5, 117.3, 116.8, 40.8, 40.7, 37.4, 33.1, 33.0, 31.6, 30.8, 26.2, 26.1, 26.0. IR (ATR) ν 2922, 1447, 906, 732, 697 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{21}$H$_{26}$ 278.2035; found: 278.2044.

## General Procedure for Preparations of 3-Methylene-1,4-cycloheptadine Derivatives

Procedure E
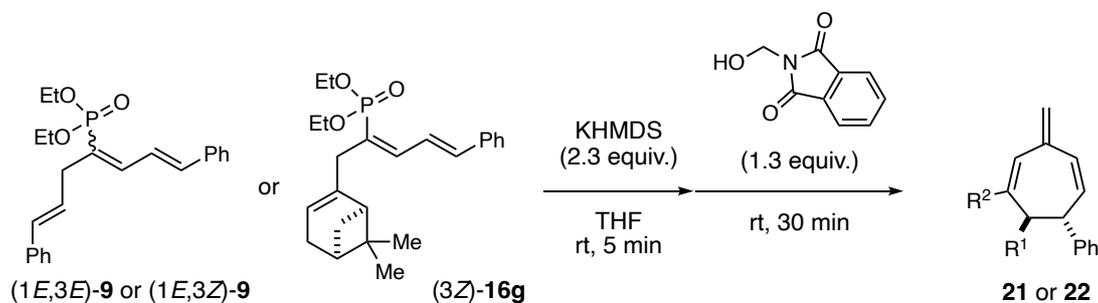
To a solution of cyclization precursor in THF (0.1 M), was added a 1.0 M solution of KHMDS in THF (2.3 equiv.) at rt. After 5 min at rt, *N*-(hydroxymethyl) phthalimide (1.3 equiv.) was added, and the mixture was stirred for another 30 min at rt. Then, the mixture was added saturated aq. NH₄Cl. EtOAc was added. The two layers were separated, and the aqueous layer was extracted with EtOAc (2 times). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Purification through a short pad of silica gel afforded desired cycloheptatriene.

## Synthesis of 3-Methylene-1,4-cycloheptadiene Derivatives (Scheme 15)

3-Methylene-6,7-*anti*-diphenylcyclohepta-1,4-diene (21)
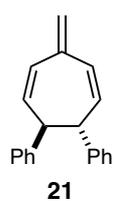
According to Procedure E (Eluent for silica gel short pad: hexane/EtOAc = 30:1), phosphonate (1*E*,3*E*)-**9** (38.2 mg, 0.100 mmol) was converted to cycloheptatriene **21** (11.7 mg, 45 μmol, 45%). Also, (1*E*,3*Z*)-**9** (38.2 mg, 0.100 mmol) was converted to **21** (10.5 mg, 41 μmol, 41%) by using a 1.0 M solution of KHMDS in THF (230 μL, 0.230 mmol) and *N*-(hydroxymethyl)phthalimide (23.0 mg, 0.130 mmol)

21: yellowish oil. ^{1}H NMR (500 MHz, CDCl₃) δ 7.28-7.12 (10H, m), 6.34 (2H, d, J = 12.1 Hz), 5.74 (2H, dd, J = 10.9, 5.2 Hz), 5.31 (2H, s), 3.94 (2H, dd, J = 4.1, 1.8 Hz); ^{13}C NMR (126 MHz, CDCl₃) δ 143.9, 143.6, 131.8, 131.4, 128.5, 128.1, 126.2, 123.1, 53.4. IR (ATR) ν 3023, 1567, 1490, 1030, 889 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C₂₀H₁₈ 258.1409; found: 258.1415.

Nopol-derived cycloheptatriene 22

22
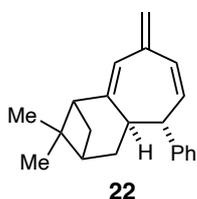
According to Procedure E (Eluent for a short pad of silica gel: *n*-hexane/EtOAc/Et₃N = 30:1:0.1), phosphonate (3*Z*)-**16g** (80.1 mg, 0.200 mmol) was converted to cycloheptatriene **22** (22.0 mg, 80 μmol, 40%, dr = 10:7) using a 1.0 M solution of KHMDS in THF (460 μL, 0.460 mmol) and *N*-(hydroxymethyl)phthalimide (46.1 mg, 0.260 mmol).

22 (dr =10:7): yellowish oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38–7.31 (2H, m), 7.26–7.12 (3H, m), 6.13 (br d, *J* = 11.5 Hz, 0.59H), 6.08 (br d, *J* = 12.1 Hz, 0.41H), 5.96–5.93 (m, 1H), 5.76–5.68 (m, 1H), 5.10–5.05 (m, 0.59H + 0.41 × 2H), 5.02 (br, 0.59H), 3.71 (br ddd, *J* = 10.9, 2.9, 2.9 Hz, 0.59H), 3.54 (br d, *J* = 10.4 Hz, 0.41H), 3.27–3.21 (m, 0.41H), 3.21–3.13 (m, 0.59H), 3.18–2.41 (m, 1H), 2.42–2.35 (m, 0.41H), 2.29–2.23 (m, 0.59H), 1.89–1.84 (m, 1H), 1.66 (m, 0.41H), 1.46–1.18 (m, 0.59H × 6H + 0.41 × 5H), 0.82–0.80 (m, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 149.1, 148.7, 146.1, 146.0, 142.6, 142.6, 137.1, 136.7, 129.8, 128.9, 128.4, 128.3, 126.19, 126.17 124.9, 124.5, 119.5, 119.4, 55.9, 54.7, 54.1, 50.6, 41.1, 40.9, 40.3, 40.1, 38.5, 37.4, 32.3, 31.7, 29.4, 27.0, 26.0, 25.8, 22.21, 22.15 (Only the detected peaks are recorded). IR (ATR) ν 2915, 1453, 758, 701 cm^{-1}. HRMS (FD) *m/z* [M]$^+$ calcd for C$_{21}$H$_{24}$ 276.1878; found: 276.1866.

Synthesis and Reaction of a Substrate with an Oxygenated Functionality (Scheme 16)
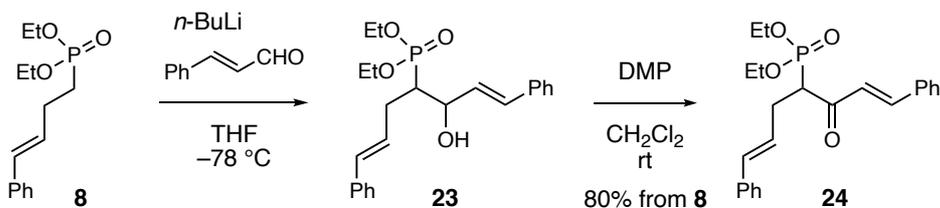

To a solution of phosphonate **8** (268 mg, 1.00 mmol) in THF (5.0 mL) at –78 °C was slowly added a 2.69 M solution of *n*-BuLi in *n*-hexane (372 μL, 1.00 mmol). After stirring at –78 °C for 0.5 h, *trans*-cinnamaldehyde (132 μL, 1.05 mmol) was added, and the mixture was further stirred for 10 min at –78 °C. Then, the reaction was quenched by adding saturated aqueous NH₄Cl. EtOAc (5 mL) was added to the mixture and the two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layer was dried over MgSO₄, filtered, and concentrated to give crude **23** as a 3:2 mixture of diastereomers.

The obtained crude product was dissolved in CH₂Cl₂ (5.0 mL) and added Dess-Martin periodinane (DMP) (467 mg, 1.10 mmol) at room temperature, and the resulting mixture was

stirred for 15 min. Then the mixture was added saturated aqueous NH$_4$Cl (5 mL) and solid Na$_2$S$_2$O$_3$. After stirring vigorously for several hours, the two layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 5 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/EtOAc = 1:1) afforded β–ketophosphonate **24** (317 mg, 0.796 mmol, 80% from **8**).

24: yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.64 (d, J = 15.5 Hz, 1H), 7.60–7.54 (m, 2H), 7.41–7.36 (m, 3H), 7.30–7.23 (m, 4H), 7.18 (t, J = 7.2 Hz, 1H), 7.00 (d, J = 16.0 Hz, 1H), 6.46 (d, J = 15.5 Hz, 1H), 6.13 (dt, J = 15.5, 7.2 Hz, 1H), 4.20–4.16 (m, 4H), 3.56 (ddd, J = 20.4, 10.3, 4.0 Hz, 1H), 3.09–2.99 (m, 1H), 2.84–2.74 (m, 1H), 1.34 (t, J = 6.9 Hz, 3H), 1.32 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.6, 143.5, 136.9, 134.2, 132.2, 130.7, 128.8 (2C), 128.5 (2C), 128.4 (2C), 127.2, 126.5 (d, J_{C-P} = 15.6 Hz), 126.1 (2C), 125.5, 62.69 (d, J_{C-P} = 7.2 Hz), 62.67 (d, J_{C-P} = 6.0 Hz), 51.8 (d, J_{C-P} = 125 Hz), 29.9 (d, J_{C-P} = 4.8 Hz), 16.4 (d, J_{C-P} = 6.0 Hz), 16.3 (d, J_{C-P} = 6.0 Hz). ^{31}P NMR (202 MHz, CDCl$_3$) δ 22.5. IR (ATR) ν 2979, 1607, 1247, 1019, 961 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{23}$H$_{27}$O$_4$P 398.1647; found: 398.1637.
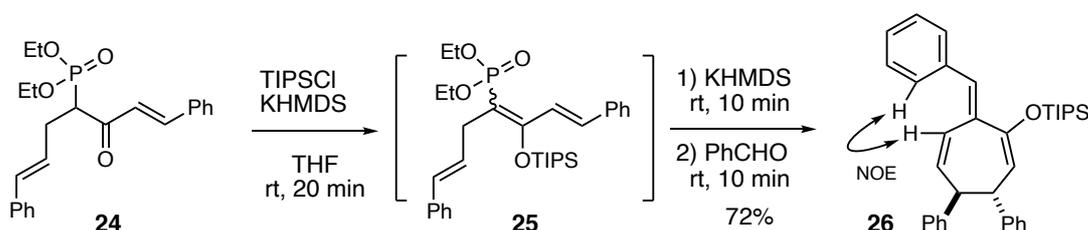

To a solution of **24** (79.7 mg, 0.200 mmol) in THF (2.0 mL) at room temperature was added a 1.0 M solution of KHMDS (210 µL, 210 mmol), and after 4 min, TIPSCl (44.5 µL, 0.210 mmol) was added. After stirring for 25 min at room temperature, a 1.0 M solution of KHMDS (210 µL, 210 mmol) was added. The mixture was further stirred for 10 min, and then added PhCHO (30.6 µL, 0.300 mmol). After stirring for 10 min, the reaction was quenched by addition of saturated aqueous NaHCO$_3$ (2 mL), and the mixture was diluted with EtOAc (2 mL). The two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 2 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO$_2$, n-hexane/Et$_2$O = 50:1) afforded cyclic triene **26** (73.2 mg, 0.144 mmol, 72%).

26: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 (d, J = 7.5 Hz, 2H), 7.38 (dd, J = 7.7, 7.7 Hz, 2H), 7.34 (s, 1H),7.28 (t, J = 7.5 Hz, 1H), 7.16–7.10 (m, 4H), 7.08–7.03 (m, 6H), 6.56 (d, J

= 11.5 Hz, 1H), 5.84 (ddd, J = 11.5, 4.6, 1.2 Hz, 1H), 5.28 (d, J = 5.8 Hz, 1H), 3.93 (dd, J = 8.6, 5.2 Hz, 1H), 3.90–3.85 (m, 1H), 1.22 (sept, J = 7.5 Hz, 3H), 1.12 (d, J = 7.5 Hz, 9H), 1.10 (d, J = 7.5 Hz, 9H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 150.5, 144.7, 143.8, 137.0, 134.4, 134.1, 132.3, 130.2 (2C), 128.4 (2C), 128.2 (2C), 128.1 (2C), 127.94 (2C), 127.92 (2C), 127.4, 125.9, 125.83, 125.77, 112.8, 52.5, 49.5, 18.1 (6C), 12.7 (3C). IR (ATR) ν 2943, 1196, 1126, 881, 695 cm^{-1}. HRMS (FD) m/z: [M]$^+$ calcd for C$_{35}$H$_{42}$OSi 506.3005; found: 506.2996.

Transformation of 3-Alkylidene-1,4-cycloheptatriene Derivatives (Scheme 17)
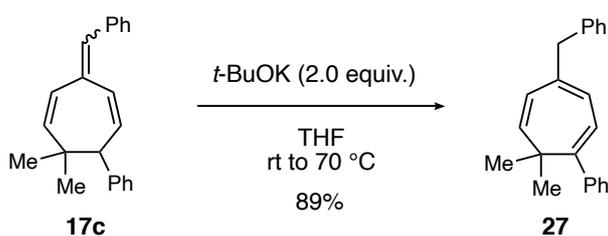
To a solution of **17c** (25.7 mg, 89.7 μmol) in THF (0.45 mL) was added a 1.0 M solution of *t*-BuOK in THF (180 μL, 0.180 mmol) at room temperature. Then, the mixture was heated to 70 °C. After stirring for 45 min, the mixture was cooled to room temperature. The reaction vessel was placed in an ice bath, and saturated aqueous NH$_4$Cl (0.5 mL) was added. EtOAc (0.5 mL) was added, and the two layers were separated. The aqueous layer was extracted with EtOAc (2 × 0.5 mL). The combined organic layer was dried over MgSO$_4$, filtered, and concentrated under reduced pressure. Purification through a short pad of silica gel (*n*-hexane/EtOAc = 30:1) linear-conjugated cycloheptatriene **27** (23.0 mg, 80.3 μmol, 89%).

27: pale yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32–7.18 (m, 8H), 7.14 (d, J = 8.0 Hz, 2H), 6.39 (d, J = 7.5 Hz, 1H), 6.05 (d, J = 7.5 Hz, 1H), 6.03 (d, J = 10.4 Hz, 1H), 5.19 (d, J = 10.4 Hz, 1H), 3.69 (s, 2H), 0.93 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 143.2, 143.1, 140.5, 140.4, 132.9, 129.4 (2C), 128.9 (2C), 128.3 (2C), 127.4, 127.3 (2C), 126.8, 126.4, 126.1, 124.4, 44.5, 37.3, 26.1 (2C). IR (ATR) ν 2961, 1597, 1492, 699 cm^{-1}.
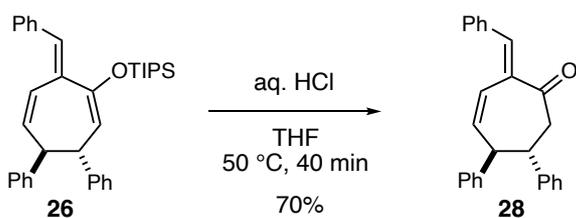
To a solution of silyl enol ether **26** (31.7 mg, 62.5 μmol) in THF (0.47 mL) at room temperature was added 1 M aq. HCl (0.13 mL). The mixture was warmed to 50 °C and stirred for 40 min. Then, the mixture was cooled to room temperature, and diluted with EtOAc (0.5 mL). The two layers were separated, and the aqueous layer was extracted with EtOAc (2 × 0.5 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, *n*-hexane/EtOAc = 20:1) and removal of TIPSOH by heating to 90 °C under high vacuum afforded ketone **28** (15.4 mg, 43.9 μmol, 70%).

28: white solid. Mp 116–118 °C (*n*-hexane/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.69 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.47–7.36 (m, 3H), 7.19–7.07 (m, 6H), 6.96 (d, *J* = 6.3 Hz, 2H), 6.91 (d, *J* = 6.9 Hz, 2H), 6.60 (d, *J* = 12.6 Hz, 1H), 6.07 (dd, *J* = 12.6, 4.0 Hz, 1H), 3.82 (dd, *J* = 10.9, 4.0 Hz, 1H), 3.38 (ddd, *J* = 10.9, 8.6, 2.3 Hz, 1H), 3.29 (dd, *J* = 13.8, 8.6, 1H), 3.12 (d, *J* = 13.8, 2.3 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 200.7, 143.9, 142.2, 138.7, 135.7, 135.4, 134.5, 130.9 (2C), 129.3, 128.5 (2C), 128.3 (2C), 128.25 (2C), 128.18 (2C), 127.5 (2C), 126.6, 126.4, 124.0, 56.4, 48.2, 47.4. IR (ATR) ν 3027, 1682, 1563, 1491, 695 cm^{-1}. HRMS (FD) *m/z*: [M]$^+$ calcd for C$_{26}$H$_{22}$O 350.1671; found: 350.1680.

3.6 References for Experimental Section

(1)   Xie, P.; Fu, W.; Cai, X.; Sun, Z.; Wu, Y.; Li, S.; Gao, C.; Yang, X.; Loh, P.-T. *Org. Lett.* **2019**, *21*, 7055-7059.

(2)   (a) Sato, K.; Tanino, K. *Synlett* **2021**, *32*, 674–678. (b) Hazelden, I. R.; Ma, X.; Langer, T.; Bower, J. F. *Angew. Chem., Int. Ed.* **2016**, *55*, 11198–11202.

(3)   (a) Ando, K.; Yamada, K. *Green Chem.* **2011**, *13*, 1143–1146. (b) Xiong, W.; Xu, G.; Tang, W. *Organometallics* **2019**, *38*, 4003–4013.

(4)   Triantafyllakis, M.; Tofi, M.; Montagnon, T.; Kouridaki, A.; Vassilikogiannakis, G. *Org. Lett.* **2014**, *16*, 3150–3153.

(5)   Yanai, H.; Takahashi, A.; Taguchi, T. *Chem. Commun.* **2010**, *46*, 8728–8730.

(6)   Hazra, A.; Chen, J.; Lalic, G. *J. Am. Chem. Soc* **2019**, *141*, 12464-12469.

(7)   Sharma, R.; Bulger, P. G.; McNevin, M.; Dormer, P. G.; Ball, R. G.; Streckfuss, E.; Cuff, J. F.; Yin, J.; Chen, C. *Org. Lett.* **2009** *11*, 3194-3197.

(8)   Kueh, J. S. H.; Mellor, M.; Pattenden G. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1052–1057.

(9)   Mancini, I.; Guella, G.; Pietra, F. *Helv. Chim. Acta* **1991**, *74*, 941–950.

(10)   Pachali, S.; Hofmann, C.; Rapp, G.; Schobert, R.; Baro, A.; Frey, W.; Laschat, S. *Eur. J. Org. Chem.* **2009**, 2828–2835.

(11)   Zgani, I.; Menut, C.; Seman, M.; Gallois, V.; Laffont, V.; Liautard, J.; Liautard, J.-P.; Criton, M.; Montero J.-L. *J. Med. Chem.* **2004**, *47*, 4600–4612.

(12)   Teulade, M.-P.; Savignac, P.; Aboujaoude, E. E.; Liétge, S.; Collignon, N. *J. Organomet. Chem.* **1986**, *304*, 283–300.

(13)   Boucher, M. M.; Furigay, M. H.; Quach, P. K.; Brindle, C. S. *Org. Process Res. Dev.* **2017**, *21*, 1394–1403.

CONCLUSION

In conclusion, the author developed new efficient 8π electrocyclization reactions for the construction of seven-membered carbocycles. In chapter 1, the cyclization reactions of 1,3,6-heptatrienes bearing a leaving group were explored, and the substrates having a carbamate moiety were found to afford 3-methylene-1,4-cycloheptadiene derivatives. The cyclization reaction can be applied to the synthesis of various seven-membered compounds including bicyclic and tricyclic ones. In chapter 2, a new triene substrate bearing a phosphonate moiety was designed to expand the substrate scope of the reaction. The cyclization reaction under basic conditions was followed by the Horner–Wadsworth–Emmons reaction with an aldehyde in one-pot, giving rise to various 3-alkylidene-1,4-cycloheptadiene derivatives. The stereospecificity of the 8π electrocyclization was confirmed by using each E/Z isomer of a substrate. The stereocontrolled formation of seven-membered carbocycles with contiguous stereogenic centers makes the present method advantageous to conventional methods. These results have opened a door for development of new reactions of trienes with various electron-withdrawing groups and applications in total synthesis of natural products having seven-membered carbocycles.
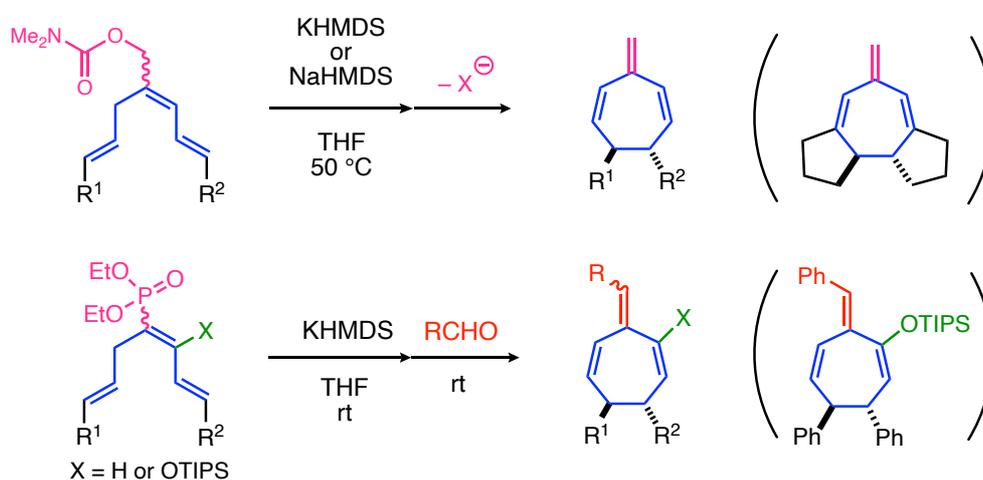
LIST OF PUBLICATIONS

CHAPTER 1

(1)   Kato, R.; <u>Saito, H.</u>; Uda, S.; Domon, D.; Ikeuchi, K.; Suzuki, T.; Tanino, K. Synthesis of Seven-Membered Cross-Conjugated Cyclic Trienes by 8π Electrocyclic Reaction. *Org. Lett.* **2021**, *23*, 8878–8882.

CHAPTER 2

(2)   <u>Saito, H.</u>; Kato, R.; Ikeuchi, K.; Suzuki, T.; Tanino, K. 8π Electrocyclic Reaction of Phosphonate Derivatives: Access to Seven-Membered Cross-Conjugated Cyclic Trienes. *Org. Lett.* **2021**, *23*, 9606–9610.

ACKNOWLEDGEMENT