Doubly Diastereocontrolled Cyclization Based on Intramolecular Conjugate Addition Reactions Involving an Allylic Radical and an Anion

Takashi Tokoroyama*,† and Takehiko Aoto‡

Department of Material Science, Faculty of Science, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka 558, Japan

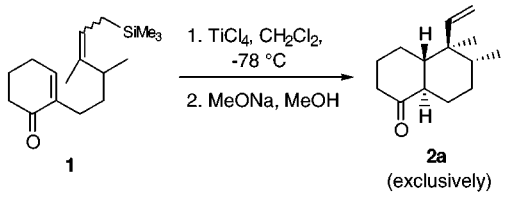
Received February 3, 1998

Maximization of efficiency is nowadays a pivotal problem for synthetic organic chemists. Stereoselective cyclizations represented by a variety of cycloaddition reactions are a means to meet this demand. Previously, we reported a doubly stereocontrolled cyclization based on the intramolecular Hosomi−Sakurai reaction (Scheme 1),[1] application of which led to the efficient stereoselective total synthesis of a *cis*-clerodane diterpenoid.[2] One of the involved stereoselectivities (diastereoface selection) has been generalized in terms of folding strain stereocontrol,[1,3,4] and the potentiality of the ring-closure reactions based on this concept as an additional stereochemical strategy has been pointed out.[5] With the aim of developing the scope of their utility, we carried out an examination of diastereoselectivity in radical and anionic versions of the cyclization reaction **1** → **2a**. Comparison of the diastereoselectivity in regard to the TS characteristics associated with the reaction types[6] would be intriguing, and in particular, the stereoselectivity in radical reactions is an issue of current interest.[7]

Results

2-[(*E*)-6-Bromo-3,4-dimethyl-4-hexenyl]-2-cyclohexenone (**11a**), the substrate for the radical cyclization, was prepared stereoselectively as shown in Scheme 2 by the use of Claisen rearrangement under Johnson's condition[8] and Smith's coupling procedure[9] as the key steps. When the conversion of allyl alcohol **10** to the corresponding bromide was conducted by way of a mesylate, the product

Scheme 1



1 **2a** (exclusively)

was obtained as a mixture of (*E*) and (*Z*) isomers (**11a**/**11b** = 1:1). Cyclization of the (*E*) isomer **11a** was performed by refluxing of the benzene solution with tri-*n*-butyltin hydride in the presence of AIBN. The reaction, after equilibration of the product with sodium methoxide in methanol, afforded a mixture of *trans*-fused decalone derivatives in 95% yield. Analysis of the mixture with ^{1}H NMR revealed that it was composed of three diastereomers **2a**, **2b**, and **2c** in a 77:21:2 ratio (Scheme 3). The diastereomeric products ratio should be invariant as regards the double-bond geometry of the cyclization precursor **11**, since reaction of the 1:1 *E*/*Z* mixture was found to give a mixture of decalones **2a**−**c** in exactly the same ratio. An attempt to conduct the cyclization at lower temperature using triethylborane/oxygen as radical initiator[10] resulted in the recovery of the starting material. The stereochemistry of the major product **2a** was identified by comparison of spectral data with those of an authentic sample.[1,2] Configurational assignment of the other two products **2b** and **2c** was secured by reference of the ^{1}H NMR to that of the authentic mixture **2a**−**d** derived from Birch reduction of the previously obtained octalone mixture **12a**−**d** (Scheme 4).[11]

As the substrate for the anionic cyclization, we designed allylic phosphine oxide **13** and allylic sulfone **14**.[12] Compounds **13**, both in (*E*) and (*Z*) forms, and **14** with (*E*) configuration were synthesized stereoselectively as shown in Scheme 5. First, (*E*) and (*Z*) side chain synthons **8a** and **8b** were prepared according to the previously reported method for the stereodivergent synthesis of trisubstituted olefines.[13] This time, in the alkylation of enol phosphates **18**, the reaction condition was improved in such a way that the reagent and the catalyst were used in fairly less amounts than those reported before. For the (*E*) series, the stereoselectivity was >99% in both phosphorylation and alkylation steps, while in the case of the (*Z*) series isomerization of a minor degree occurred in the latter reaction to afford the product **19b** with a purity ratio of 96:4. The iodides **8** were attached to the cyclohexenone moiety as before, and after chlorination of the hydroxyl terminals, the intro-

* To whom correspondence should be addressed.

† Present address: 3-25-1 Makizuka-dai, Sakai-shi, Osaka, Japan 590-0114.

‡ Present address: Japan Tobacco Inc., Central Pharmaceutical Research Institute, 1-1 Murasaki-cho, Takatsuki-shi, Osaka, Japan 569-1125.

(1) Tokoroyama, T.; Tsukamoto, M.; Iio, H. *Tetrahedron Lett.* **1984**, *25*, 5067−5070.

(2) Tokoroyama, T.; Tsukamoto, M.; Asada, T.; Iio, H. *Tetrahedron Lett.* **1987**, *28*, 6645−6648.

(3) Tokoroyama, T.; Okada, K.; Iio, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1572−1573.

(4) Tokoroyama, T.; Kusaka, H. *Can. J. Chem.* **1996**, *74*, 2487−2502.

(5) For review, see: Tokoroyama, T. *J. Synth. Org. Chem. Jpn.* **1996**, *54*, 586−595.

(6) Paddon-Row, M. N.; Rondon, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162−7166.

(7) For review, see: (a) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*: *Concepts, Guidelines, and Synthetic Applications*; VCH: Weinheim, 1996. (b) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon: New York, 1991; Vol. 4, pp 778−831. (c) Jasperse, C. P.; Curran, D. P. Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237−1286. (d) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon: New York, 1986. (e) Giese, B.; Kopping, B.; Gobel, T.; Dickhaut, J.; Thomas, G.; Kulicke, K. J.; Trach, F. In *Organic Reactions*; John Wiley & Sons Inc.: New York, 1996; Vol. 48, Chapter 2.

(8) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.-T.; Faukner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741−743.

(9) Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B., III. *Tetrahedron Lett.* **1978**, 4661−4664.

(10) (a) Nozaki, K.; Oshima, K.; Utimoto, K.*Tetrahedron Lett.* **1988**, 29, 6125−6126. (b) Nozaki, K.; Ohshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547−2549.

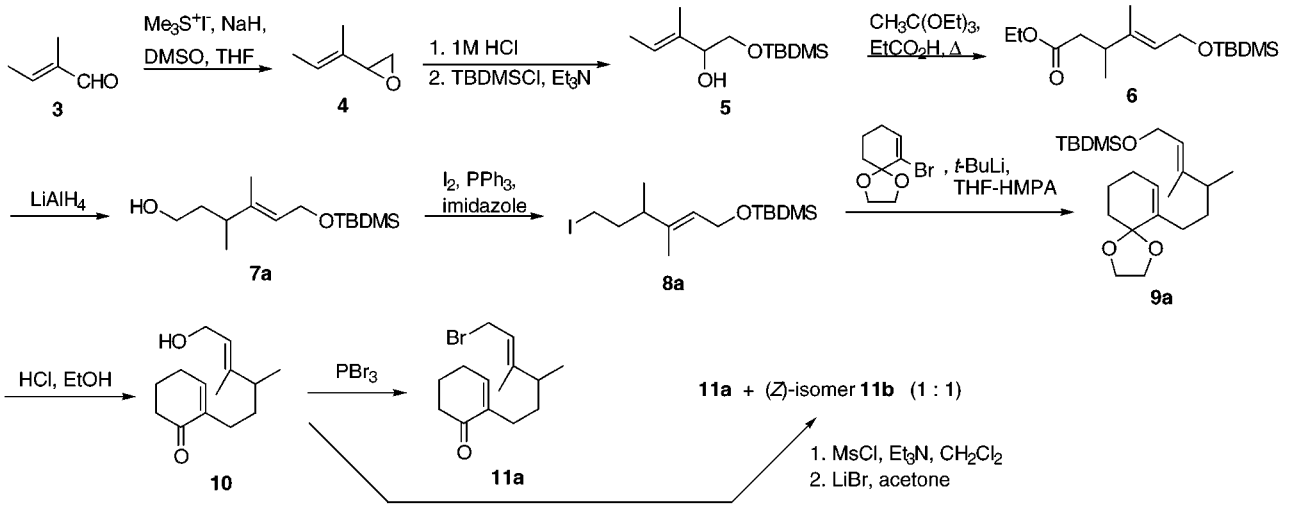
(11) Tokoroyama, T.; Kato, M.; Aoto, T.; Hattori, T.; Iio, H.; Odagaki, Y. *Tetrahedron Lett.* **1994**, *35*, 8247−8250.

(12) For diastereoselectivity in intermolecular conjugate addition of the carbanions derived from phosphine oxides and sulfones, see: (a) Binns, M. R.; Haynes, R. K.; Katsifis, A. G.; Schober, P. A.; Vonwiller, S. C. *J. Am. Chem. Soc.* **1988**, *110*, 5411−5423 and references therein. (b) Haynes, R. K.; Katsifis, A. G.; P. A.; Vonwiller, S. C.; Hambley, T. W. *J. Am. Chem. Soc.* **1988**, *110*, 5423−5433. (c) Haynes, R. K.; Vonwiller, S. C.; Hambley, T. W. *J. Org. Chem.* **1989**, *54*, 5162−5170.

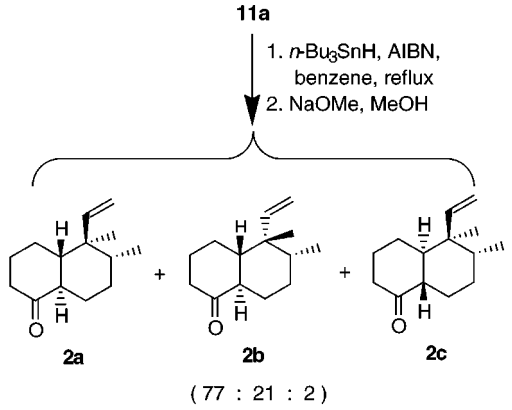
(13) Asao, K.; Iio, H.; Tokoroyama, T. *Synthesis* **1990**, 382−386.

S0022-3263(98)00188-1 CCC: $15.00
Published on Web 05/27/1998

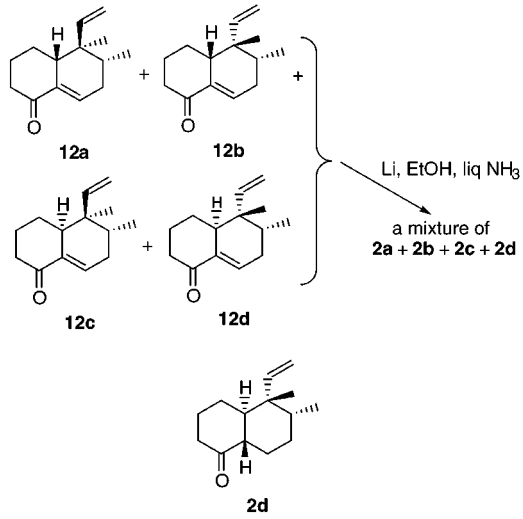
Scheme 2



Scheme 3



Scheme 4



duction of phosphine oxide and sulfone groups was performed to give the desired products **13a**, **13b**, and **14**. No appreciable isomerization was observed through conversion of **19** to **13** or **14**.

The cyclization was first examined for the allylic sulfone **14**. However, it showed no sign of the reaction on treatment with LDA at −78 °C to room temperature, being recovered unchanged. Then the preliminary experiments on (*E*) allylic phosphine oxide **13a** indicated that treatment with LDA afforded two kinds of cyclization products, a hydroxyoctaline **23** and a decalone **24** (Scheme 6) and that the formation ratio was altered depending on the presence of additives such as lithium bromide or HMPA and the reaction temperature. The results in these regards are summarized in Table 1. Whereas addition of lithium bromide and lower reaction temperature favored the formation of **23**, the reaction in the presence of HMPA and at higher temperature gave **24** preferentially. Thus exclusive formation of **23** and **24** was observed in the reactions, respectively, with lithium bromide at −78 °C (entry 1) and with HMPA at −40 °C (entry 5). Reaction of (*Z*) substrate **13b** under the latter conditions afforded **24** selectively similar to that of (*E*) substrate **12a** but at somewhat slower rate (entry 6). The reaction at temperatures higher than −40 °C resulted in the contamination of diastereomers of **24**. Close spectroscopic analyses of both products revealed that the former compound **23** represented the product of 1,2-intramolecular addition and that the latter compound **24** represented the product of intramolecular 1,4-conjugate addition. Although the rigid stereochemical assignment for **23** was not achieved (see Discussion), **24** was determined to have the same configuration as **2a** by a direct chemical correlation as shown in Scheme 7.

Table 1. 1,4- vs 1,2-Addition in Anionic Cyclization of Phophine Oxides 13

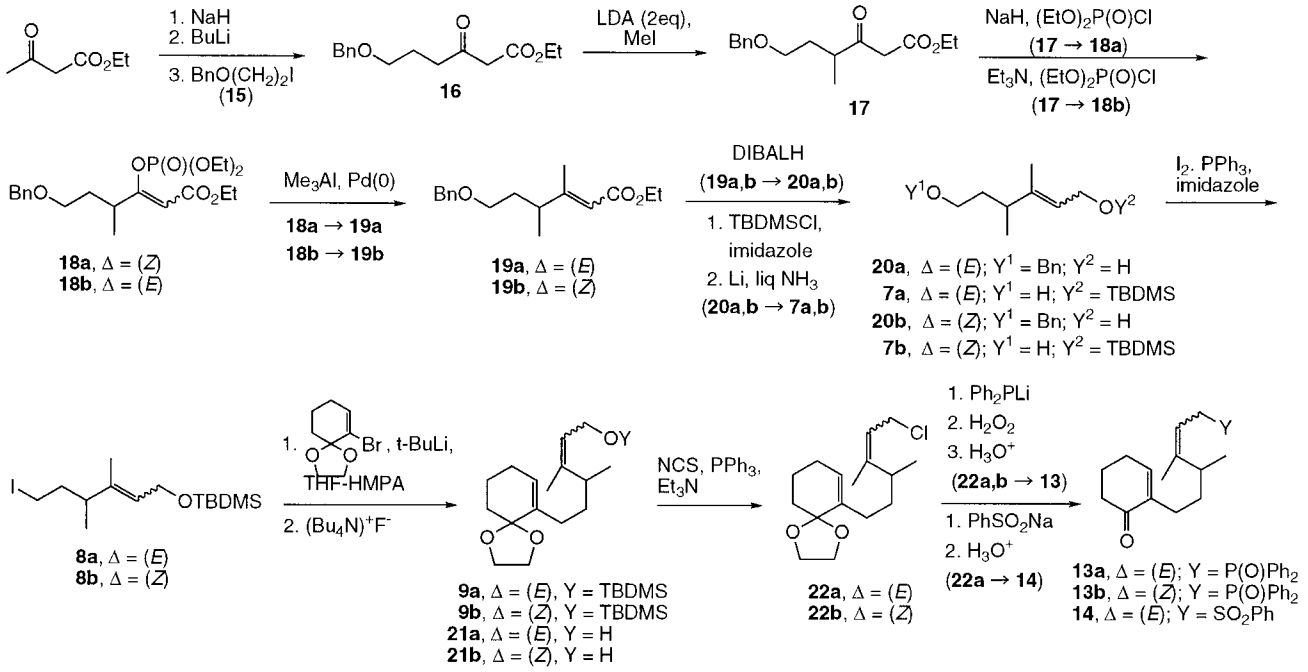
entry	substrate	additive	temp (°C)	time (h)	yield (%)	product ratio (**23**:**24**)
1	**13a**	LiBr[a]	−78	1.5	44	100:0
2	**13a**	LiBr[a]	−40	1.5	38	1:3
3	**13a**	LiBr[a]	−20	1.5	64	0:100[c]
4	**13a**	HMPA[b]	−78	1.5	41	1:3
5	**13a**	HMPA[b]	−40	1.5	71	0:100
6	**13b**	HMPA[b]	−40	3.0	30	0:100

[a] 1.1 equiv. [b] 23%. [c] Contaminated with a small amount of diastereomers.

Since the decalone derivative **24** has the same stereochemistry as that of clerodane diterpenoids at three consecutive stereogenic centers (8, 9, and 10 in clerodane numbering),[14] we investigated further on the utilization of the anionic cyclization method for their synthesis, to

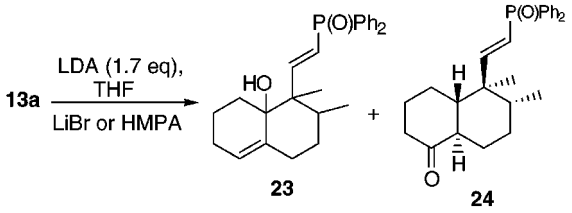
(14) Meritt, A.; Ley, S. V. *Nat. Prod. Rep.* **1992**, 243−287.
(15) (a) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1987**, *65*, 1859−1866. (b) Reference 7a, pp 77−81.

Scheme 5

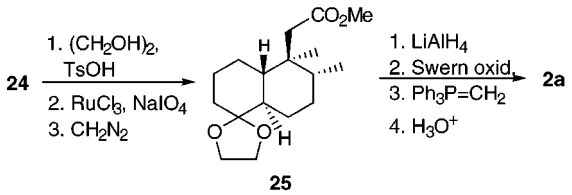


which stereoselective introduction of an angular substituent at C-5 position turned out to be a requisite task. One approach to this end is delineated in Scheme 8. The enolate intermediate formed on the anionic cyclization of **13a** was trapped with allyl bromide to afford an allyl enol ether, Claisen rearrangement of which gave product **26** as a single diastereomer. In the ^{1}H NOESY NMR spectrum, correlations were observed between 9-methyl protons and respective axial protons at C-3 and C-7. Thus, compound **26** was deduced to have a *cis*-steroidal conformation.

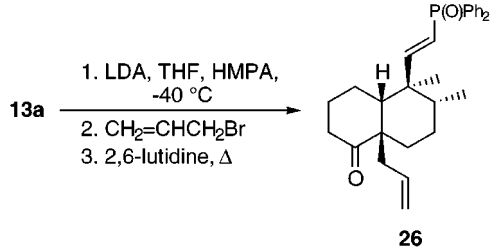
Scheme 6



Scheme 7



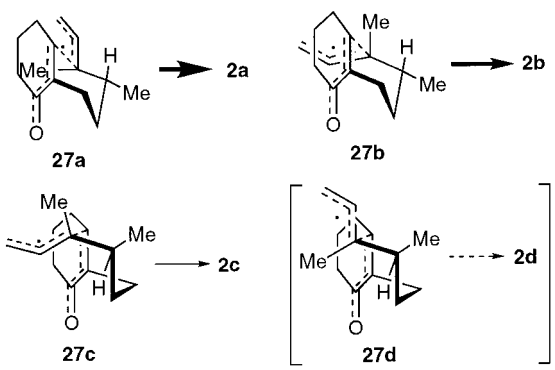
Scheme 8



Discussion

The cyclization of **11a** under radical conditions proved to proceed smoothly, but the diastereoselectivity was lower in comparison with the case of an analogous reaction involving the allylsilane substrate **1**, although the temperature effect on stereoselectivity has to be taken into account. The cyclization involves two types of diastereoselection—one is simple diastereoselection as regards mutual orientation of the two sp^2 carbon atoms which participate in bond formation and the other is diastereoface selection with respect to the stereogenic center (3′-C) present in the side chain of substrate **11a**. These diastereoselections would be rationalized in a manner similar to that of the previous case respectively in terms of orientation stereocontrol[1] and folding strain stereocontrol.[1,3,4] Namely, by the orientation stereocontrol the preference of antiperiplanar TS **27a** over synclinal TS **27b** (or TS **27d** over TS **27c**, Scheme 9) is assumed from steric[15] and stereoelectronic reasons, and the folding strain stereocontrol predicts the prepondrance of TS **27a** over TS **27d** (TS **27b** over TS **27c**) due to the presence of stronger A^{1,3}-strain and additional gauche effects[4,5] in TS **27d** and TS **27c**. Thus, the order of preference in the diastereomeric TS's is **27a** > **27b** > **27c**; hence that in the favored formation of diastereomers, **2a** > **2b** > **2c**, is

Scheme 9

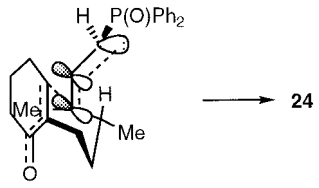


explained, though the reason for preference of TS **27c** over **27d** is not clear. The diastereoface selection involved (**27a** > **27d** or **27b** > **27c**) is also accommodated by Beckwith's model[7,16] for the stereoselective 6-*exo* radical cyclization, which predicts the preference of TS with an equatorial-like substituent. When the contribution to the observed diastereomer ratio is compared to the orientation and the folding strain stereocontrols, the selectivity (normal versus reversed) is 77:23 (**27a**:**27b** + **27c**) and 98:2 (**27a** + **27b**:**27c**) respectively—namely the folding strain stereocontrol is effective enough also in the present radical reaction, whereas the orientation stereocontrol decreases considerably. It is noteworthy that the folding strain stereocontrol is relatively unaffected by the TS position in the reaction coordinate, but this is not unexpected from the nature of major strain factors concerned with the chain folding.[6,17] The lowering of the orientation control in the radical reaction would be associated, partly at least, with the relatively less constrained TS conformation due to its early nature,[7] which should decrease the strain energy difference between antiperiplanar and synclinal orientations of the interacting two π-orbitals.

For the anionic cyclization of the substrate **13**, two selectivity problems are to be discussed—one is the selectivity of 1,4- versus 1,2-intramolecular addition reactions and the other is diastereoselectivity. Exclusive formation of the 1,2-addition product **23** for the reaction in the presence of lithium bromide at −78 °C (Table 1, entry 1) indicates that it assists the carbonyl addition reaction through the enhancement of charge separation by the complexation of the lithium cation rather than the suppression of α-proton transfer, which contrasts to the situation in a reported[12a] intermolecular case. The reaction at higher temperature (entry 2) turned out to form a larger amount of the intramolecular 1,4-addition product **24**, until the reaction at −20 °C afforded **24**, mixed with a small amount of diastereomers, without the formation of 1,2-product **23** (entry 3). These results are anticipated from the reversible nature of conjugate additions involving π-stabilized carbanions,[18] as demonstrated in many examples. The suppressing effect of HMPA, a polar and highly coordinating solvent, on carbonyl addition is also well documented,[18,19] and in line with this, the addition of HMPA resulted in the preferred formation of **24**, the exclusive production of which was achieved in the reaction at −40 °C (entry 5). Thus, the anionic cyclization of **13** is shown to proceed under the effective orientation and folding strain stereocontrols in a way similar to that in the case of the conversion **1** → **2a** based on the Hosomi−Sakurai reaction. Different from intermolecular reactions,[12] (*E*) and (*Z*) substrates **13a** and **13b** exhibited the same stereoselectivity on cyclization. The reaction of **13b**, slower than that of **13a**, might reflect the stronger $A^{1,3}$ repulsion present in TS **28** derived from the former (Scheme 10).

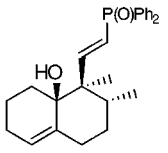
An additional advantage of the anionic cyclization **13** → **24** is the enolate trapping exemplified by the conversion **13a** → **26**. This fact would widen synthetic utility of the anionic cyclization method, the product **26** having functionalities such as the 4-keto group and the phosphine oxide group which would serve for further manipulation of the molecule. Thus, compound **26** could be a useful intermediate for the synthesis of *cis*-clerodane diterpenoids.[2,20,21]

Scheme 10

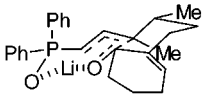


28

Finally, the probable steric configuration for 1,2-addition product **23** remains to be mentioned. Provided that the reaction would proceed under the normal orientation and folding strain stereocontrols as experienced in conversions, **1** → **2a** or **13** → **24**, the stereostructure **23a** for the product is readily rationalized. The assumption of *trans*-decalyl TS **29** involving chelation of the lithium cation by a carbonyl group, similar to the one postulated in the intermolecular case,[12] might also explain the simple diastereoselection in the same direction (orientation control). Spectroscopic evidence corroborating the assignment of stereoformula **23a** is provided from the comparison of chemical shift data in the ^{1}H NMR spectrum of **23** with those of 1,4-addition product **24**. The product **23** exhibits the signals due to the β-proton of the vinyl phosphine oxide group at δ 6.91, a considerably deshielded position relative to that of **24** (δ 6.52), whereas the signals due to secondary methyl protons appear at similar positions in both products (δ 0.70 and δ 0.73 respectively). This fact indicates that the β-proton rather than the secondary methyl protons in **23** is influenced by the deshielding anisotropy effect of the hydroxyl oxygen atom, being in conformity with the assignment of the formula **23a**.



23a



29

Conclusion

Radical and anionic cyclizations analogous to the dually diastereoselective cyclization reaction **1** → **2a** have been investigated, aiming to see the relevance of the stereoselectivity to the type of reaction. Lowering of the diastereoselectivity in the radical cyclization of **11** to give a mixture of diastereomers (**2a**/**2b**/**2c** = 77:21:2) was found to connect mainly with the orientation stereocontrol, and thus the folding strain stereocontrol remained effective at a ratio as high as 98:2, which is notable in view of early TS nature of the reaction. The anionic cyclization of (*E*)- and (*Z*)-phosphine oxides **13a** and **13b**, both prepared stereoselectively, was achieved without the formation of 1,2-addition product **23** by treatment with

(16) (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073−3100. (b) Beckwith, A. L.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925−3941 and references therein.

(17) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982; pp 86−88.

(18) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon: New York, 1992; pp 7−9.

(19) Lee, V. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon: New York, 1991; Vol. 4, pp 71−72.

(20) Tokoroyama, T. *J. Synth. Org. Chem. Jpn.* **1993**, *51*, 1164−1177.

(21) For a recent approach, see: Liu, H.-J.; Shia, K.-S.; Han, Y.; Sun, D.; Wand, Yu. *Can. J. Chem.* **1997**, *75*, 646−655.

LDA at −40 °C using HMPA as additives to afford decalone derivative **24** as a single diastereomer, being highly stereoselective as in the conversion **1** → **2a**. The stereoselective introduction of a *cis*-angular substituent to **24** was performed via enolate trapping to give **26**, which could be a useful intermediate for the synthesis of *cis*-clerodane diterpenoids.

Experimental Section

NMR specta were recorded in $CDCl_3$ solutions at either 90 or 400 MHz for ^1H and at 100 MHz for ^{13}C NMR. MS spectra were obtained using EI ionization. Merck Art 5715 (0.25 mm thickness) and 5744 (0.5 mm thickness) silica gel plates (60-F_{254}) were used for analytical and preparative TLC, respectively. Flash chromatography was performed using either Fuji−Davison BW-820MH or BW-300MH silica gel. Gas chromatographic analyses were performed on an instrument equipped with an OV-1 column. For use in reactions at anhydrous conditions, THF, diethyl ether, and benzene were distilled from sodium−benzophenone ketyl. DMF, diisopropylamine, HMPA (highly toxic cancer suspect agent), and DMSO were distilled from CaH_2, and dichloromethane, carbon tetrachloride, acetonitrile, and 1,2-dichloroethane were distilled over P_2O_5. Usual workup was carried out as follows: the quenched reaction mixture was extracted three times with Et_2O and the combined organic layers were washed successively with pertinent aqueous wash solution and saturated brine and then dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation. The standard procedure was employed for handling air-sensitive reagents, and all reactions were carried out under Ar.

2-[(*E*)-6-*tert*-Butyldimethylsilyloxy-3,4-dimethyl-4-hexenyl]-2-cyclohexenespiro-2′,5′-dioxacyclopentane (9a). A 1.68 M hexane solution of *tert*-butyllithium (16 mL, 26.9 mmol) was added dropwise to a solution of 2-bromo-2-cyclohexenespiro-2′,5′-dioxacyclopentane (3.7 g, 16.9 mmol) in anhydrous THF (30 mL) cooled to −78 °C and the mixture was stirred for 1 h, before a solution of (*E*) iodide **8a** (2.1 g, 5.7 mmol) in a mixture of HMPA (9 mL) and THF (6 mL) was added dropwise. After removal of the cooling bath, the reaction mixture was stirred for 2 h and was quenched by the addition of water and then extracted with Et_2O. The extract solution was dried with anhydrous K_2CO_3, and the crude product thus obtained was purified by silica gel chromatography (hexane/Et_2O 19/1) to furnish the title ketal **9a** (1.78 g, 82% yield) as a colorless oil: ^1H NMR (400 MHz) δ 0.06 (6H, s), 0.90 (9H, s), 0.99 (3H, d, J = 7.0 Hz), 1.41 (1H, m), 1.53 (3H, s), 1.67−1.73 (4H, m), 1.89−2.11 (5H, m), 3.97 (4H, s), 4.20 (2H, d, J = 6.1 Hz), 5.30 (1H, t, J = 6.1 Hz), 5.68 (1H, t, J = 3.7 Hz); ^{13}C NMR (100 MHz) δ −5.0, 12.8, 15.3, 19.5, 20.8, 25.3, 26.0, 27.5, 34.0, 34.2, 42.8, 60.4, 65.0, 107.9, 124.2, 128.4, 138.4, 140.6; MS (*m*/*z*) 380 (M^+, 5), 75 (100); HRMS calcd for $C_{22}H_{40}O_3Si$ 380.2747, found 380.2733.

2-[(*Z*)-6-*tert*-Butyldimethylsilyloxy-3,4-dimethyl-4-hexenyl]-2-cyclohexenespiro-2′,5′-dioxacyclopentane (9b). The coupling reaction of 2-lithio-2-cyclohexene-spiro-2′,5′-dioxacyclopentane with (*Z*) iodide **8b** in the same way as above gave title product **9b** in 75% yield: ^1H NMR (400 MHz) δ 0.06 (6H, s), 0.90 (9H, s), 0.98 (3H, d, J = 7.0 Hz), 1.45 (2H, m), 1.60 (3H, d, J = 1.2 Hz), 1.67−1.75 (4H, m), 1.90 (2H, m), 2.20 (2H, m), 2.55 (1H, sextet, J = 7.0 Hz), 3.97 (4H, m), 4.14 (1H, ddq, J_d = 12.2, J_d' = 6.1, J_{tq} = 1.2 Hz), 4.23 (1H, ddq, J_d = 12.2, J_d' = 7.3, J_{tq} = 1.2 Hz), 5.29 (1H, dd, J = 7.3, 6.1, Hz), 5.68 (1H, t, J = 3.7 Hz); ^{13}C NMR (100 MHz) δ −5.1, 17.9, 18.4, 19.2, 20.8, 25.3, 26.1, 27.5, 34.0 (×2), 34.7, 59.6, 65.0, 107.9, 125.5, 128.4, 138.2, 141.0; MS (*m*/*z*) 380 (M^+, 28.5), 225 (100); HRMS calcd for $C_{22}H_{40}O_3Si$ 380.2747, found 380.2735.

2-[(*E*)-3,4-Dimethyl-6-hydroxy-4-hexenyl]-2-cyclohexenone (10). (*E*)-Ethylene ketal **9a** (648 mg, 1.70 mmol) was hydrolyzed by treatment with a 1% mixture of concentrated HCl and EtOH (12 mL) at room temperature for 7 h under stirring. After neutralization by addition of $NaHCO_3$, most of the EtOH was evaporated and the product was extracted. Purification on a silica gel column (CH_2Cl_2/MeOH 98/2) afforded the title compound **10** (322 mg, 85% yield) as a colorless oil: IR (neat) 3425 (br), 1670 cm^{-1}; ^1H NMR (400 MHz) δ 1.00 (3H, d, J = 7.0 Hz), 1.34−1.54 (2H, m), 1.60 (3H, s), 1.97 (2H, tt, J = 7.0, 6.1 Hz), 2.15−2.06 (3H, m), 2.34 (2H, td, J_t = 6.1, J_d = 4.3 Hz), 2.40 (2H, t, J = 7.0 Hz), 4.16 (2H, d, J = 7.0 Hz), 5.41 (1H, d, J = 7.0 Hz), 6.70 (1H, t, J = 4.3 Hz); ^{13}C NMR (100 MHz) δ 12.6, 19.5, 23.2, 26.1, 27.7, 33.8, 38.6, 42.5, 59.4, 123.4, 140.0, 143.4, 144.9, 199.5,, MS (*m*/*z*) 222 (M^+, 0.7), 95 (100); HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1638.

2-[(*E*)-6-Bromo-3,4-dimethyl-4-hexenyl]-2-cyclohexenone (11a). Phosphorus tribromide (0.12 mL, 1.26 mmol) was added to a solution of **10** (520 mg, 2.34 mmol) in hexane (2 mL) at 0 °C and the mixture was stirred for 10 min, before it was quenched by the addition of MeOH. A saturated $NaHCO_3$ solution was added, and product was extracted with Et_2O. Crude product was purified by chromatography on a silica gel column (hexane/Et_2O 29/1) to afford the title bromide **11a** (334 mg, 50%) without admixture of (*Z*) isomer. **11a**: IR (neat) 1680 cm^{-1}; ^1H NMR (400 MHz) δ 1.00 (3H, d, J = 7.0 Hz), 1.38−1.49 (2H, m), 1.66 (3H, s), 1.97 (2H, tt, J = 7.0, 6.1 Hz), 2.07 (2H, br t, J = 7.9 Hz), 2.14 (1H, sextet, J = 7.0 Hz), 2.34 (2H, td, J_t = 6.1, J_d = 4.3 Hz), 2.41 (2H, t, J = 7,0 Hz), 4.05 (2H, d, J = 7.9 Hz), 5.55 (1H, t, J = 7.8 Hz), 6.70 (1H, t, J = 4.3 Hz); ^{13}C NMR (100 MHz) δ 12.3, 19.3, 23.2, 26.1, 27.9, 29.6, 33.8, 38.7, 42.5, 120.4, 139.8, 145.2, 147.6, 199.4; MS (*m*/*z*) 204 (M^+ − HBr, 31), 95 (100); HRMS calcd for $C_{14}H_{20}O$ (M^+ − HBr) 204.1514, found 204.1542.

A mixture of **11a** with (*Z*) isomer **11b** (1:1) was obtained in 34% yield, when **8** was first mesylated by treatment of mesyl chloride and Et_3N in CH_2Cl_2 at 0 °C for 3 h and the mesylated product was heated with LiBr in acetone under reflux for 1 h. **11b**: ^1H NMR (400 MHz) δ 1.01 (3H, d, J = 7.0 Hz), 1.38−1.49 (2H, m), 1.66 (3H, s), 1.97 (2H, tt, J = 7.0, 6.1 Hz), 2.07 (2H, brt, J = 7.9 Hz), 2.14 (1H, sextet, J = 7.0 Hz), 2.33 (2H, td, J_t = 6.1, J_d = 4.3 Hz), 2.41 (2H, t, J = 7.0 Hz), 4.10 (2H, d, J = 7.9 Hz), 5.46 (1H, t, J = 7.9 Hz), 6.70 (1H, t, J = 4.3 Hz); ^{13}C NMR (100 MHz) δ 12.4, 19.4, 23.2, 26.1, 27.9, 29.6, 33.7, 38.7, 42.3, 120.2, 139.9, 145.1, 146.6, 199.4.

Cyclization of 11a at Radical Conditions. To a solution of the bromide **11a** (49 mg, 0.173 mmol) in anhydrous benzene (30 mL) were added tributyltin hydride (0.06 mL, 0.2 mmol) and AIBN (3.4 mg, 0.02 mmol), and the mixture was refluxed for 2 h. After addition of water, the product was extracted with Et_2O and Et_2O layers were washed successively with a saturated KF solution and brine. The obtained crude product dissolved in anhydrous MeOH (2 mL) was treated with sodium methoxide (10 mg) overnight under stirring. After the reaction was quenched by the addition of a 1 M HCl solution, the reaction miture was worked up as usual. Purification by silica gel chromatography (hexane/Et_2O 29/1) gave a diastereomeric mixture of cyclization products **2**, 34 mg (95% yield), as a colorless oil: MS (*m*/*z*) 206 (M^+, 25); HRMS calcd for $C_{14}H_{22}O$ 206.16, found 206.1696. The following ^1H (400 MHz) and ^{13}C (100 MHz) NMR signals were readable with reference to the authentic mixture.[11] ^1H NMR: **(4a*S**,5*S**,6*R**,8a*R**)-3,4,4a,5,6,7,8,8a-octahydro-5,6-dimethyl-5-vinyl-1(2*H*)-naphthalenone (2a)**, δ 0.73 (3H, d, J = 6.7 Hz), 0.89 (3H, s), 1.14−1.59 (7H, m), 1.79 (1H, dt, J_d = 12.8, J_t = 2.4 Hz), 1.87−2.08 (2H, m), 2.16−2.39 (3H, m), 4.95 (1H, dd, J = 17.7, 1.2 Hz), 5.47 (1H, dd, J = 17.7, 11.0 Hz); **(4a*S**,5*R**,6*R* *,8a*R**)-3,4,4a,5,6,7,8,8a-octahydro-5,6-dimethyl-5-vinyl-1(2*H*)-naphthalenone, (2b)**, δ 0.77 (3H, d, J = 6.1 Hz), 5.02 (1H, dd, J = 11.0, 1.8 Hz), 5.25 (1H, dd, J = 11.0, 1.8 Hz), 5.98 (1H, dd, J = 17.7, 11.0 Hz); **(4a*S**,5*R**,6*S**,8a*R**)-3,4,4a,5,6,7,8,8a-octahydro-5,6-dimethyl-5-vinyl-1(2*H*)-naphthalenone (2c)**, δ 6.38 (1H, dd, J = 17.7, 11.0 Hz). ^{13}C NMR: **2a**, δ 8.9, 16.6, 25.5, 26.1, 26.4, 28.7, 39.8, 41.9, 44.2, 49.4, 51.8, 113.2, 147.9, 213.4; **2b**, δ 16.8, 22.0, 25.7, 26.0, 26.1, 29.5, 41.3, 41.6, 43.6, 50.1, 53.2, 116.4, 137.7, 213.4.

Ethyl (*Z*)-6-Benzyloxy-3-diethylphosphoryloxy-4-methyl-2-hexanoate (18a). To a suspension of NaH (60% oil dispersion, 1.0 g, 25 mmol, washed with hexane before use) in Et_2O (100 mL), cooled to 0 °C, was added a solution of β-keto ester **17** (5.95 g, 21.4 mmol) in Et_2O (20 mL), and after stirring of the mixture for 20 min, diethyl chlorophosphate was added. After removal of the ice bath, the stirring was continued for 4 h and then the reaction was quenched by the addition of a saturated NH_4Cl solution. The crude product was chromatographed on a column of silica gel (hexane/Et_2O 1/1) to provide the title compound **18a** (8.33 g, 94% yield) as a colorless oil. As

shown in the 400 MHz NMR, the product was stereochemically >99% pure. **18a**: IR (neat) 1730, 1660, 1280, 1030 cm^{-1}; ^1H NMR (400 MHz) δ 1.18 (3H, J = 7.0 Hz), 1.28 (3H, t, J = 7.0 Hz), 1.32 (3H, t, J = 7.0 Hz), 1.34 (3H, t, J = 7.0 Hz), 1.66 (1H, dq, J_d = 14.0, J_q = 7.0 Hz), 2.01 (1H, dq, J_d = 14.0, J_q = 7.0 Hz), 2.77 (1H, sextet, J = 7.0 Hz), 3.54 (2H, t, J = 7.0 Hz), 4.16 (2H, q, J = 7.0 Hz), 4.23 (2H, q, J = 7.0 Hz), 4.24 (2H, q, J = 7.0 Hz), 4.46 (1H, d, J = 11.6 Hz), 4.51 (1H, d, J = 11.6 Hz), 5.41 (1H, s), 7.28−7.34 (5H, m); ^{13}C NMR (100 MHz) δ 14.2, 16.0, 16.1, 18.0, 34.1, 36.5, 60.0, 64.7, 67.7, 73.0, 104.9, 127.5, 127.7, 128.3, 138.5, 164.0, 165.3, 165.4; MS (*m*/*z*) 415 (MH^+ 0.9), 91 (100); HRMS calcd for $C_{20}H_{32}O_7P$ (MH^+) 415.1886, found 415.1909.

Ethyl (*E*)-6-Benzyloxy-3-diethylphosphoryloxy-4-methyl-2-hexanoate (18b). A solution of β-keto ester **15** (10.5 g, 37.7 mmol) in HMPA (100 mL) cooled at 0 °C was mixed with Et_3N (7.0 mL, 50.2 mmol) and DMAP (200 mg), and after stirring of the mixture for 1 h, diethyl chlorophosphate (7.3 mL, 50.5 mmol) was added dropwise. The cooling bath was removed, and the reaction mixture was allowed to react overnight at room temperature, before it was quenched by the addition of a saturated NH_4Cl solution. The Et_2O extract solution was washed with a saturated $NaHCO_3$ solution and brine. Purification of the crude product with silica gel flash chromatography (hexane/Et_2O 1/1) furnished the title phosphate **18b** (12.5 g, 80% yield) as a colorless oil. From analysis of the ^1H NMR spectrum (400 MHz), the product was found to be stereochemically pure (>99%): IR (neat) 1720, 1650, 1280, 1040 cm^{-1}; ^1H NMR (400 MHz) δ 1.14 (3H, d, J = 7.0 Hz), 1.25 (3H, t, J = 7.0 Hz), 1.35 (3H, t, J = 7.0 Hz), 1.36 (3H, t, J = 7.0 Hz), 1.72 (1H, m), 1.88 (1H, m), 3.49 (2H, t, J = 7.0 Hz), 4.03 (1H, m), 4.13 (2H, q, J = 7.0 Hz), 4.17 (2H, q, J = 7.0 Hz), 4.18 (2H, q, J = 7.0 Hz), 4.45 (1H, d, J = 12.2 Hz), 4.49 (1H, d, J = 12.2 Hz), 5.89 (1H, d, J = 1.2 Hz), 7.23−733 (5H, m); ^{13}C NMR (100 MHz) δ 14.2, 16.05, 16.1, 17.8, 31.7, 33.5, 60.1, 64.8, 68.4, 73.0, 104.2, 127.5, 127.6, 128.3, 138.6, 166.0, 168.6, 168.7; MS (*m*/*z*) 415 (MH^+, 0.2), 155 (100); HRMS calcd for $C_{20}H_{32}O_7P$ (MH^+) 415.1886, found 415.1904.

Ethyl (*E*)-6-Benzyloxy-3,4-dimethyl-2-hexenoate (19a). A suspension of *trans*-bis(triphenylphosphine)palladium(II) chloride (100 mg, 0.14 mmol) in THF 5 mL) was reduced with a 2 M DIBALH toluene solution (0.15 mL, 0.3 mmol) at 0 °C for 10 min, and the so-formed zerovalent palladium solution was diluted with anhydrous 1,2-dichloroethane (25 mL). To this mixture was added a solution of (*Z*)-enol phosphate **18a** (5.73 g, 13.8 mmol) in 1,2-dichloroethane (10 mL), followed by the dropwise addition of a 1.4 M trimethylaluminum solution in hexane (15 mL, 21 mmol). The ice bath was removed, and the mixture was allowed to react for 72 h at room temperature. After having been cooled to 0 °C, it was quenched by the addition of 1 M HCl. The crude product, isolated by Et_2O extraction, was purified by silica gel chromatography (hexane/Et_2O 8/1) to afford (*E*)-conjugated ester **19a** (3.56 g, 94% yield) as a colorless oil. **19a**: IR (neat) 1710, 1640 cm^{-1}; ^1H NMR (400 MHz) δ 1.06 (3H, d, J = 7.0 Hz), 1.28 (3H, t, J = 7.0 Hz), 1.65 (1H, m), 1.77 (1H, m), 2.10 (3H, s), 2.44 (1H, sextet, J = 7.0 Hz), 3.39 (1H, dt, J_d = 9.2, J_t = 7.0 Hz), 3.44 (1H, dt, J_d = 9.2, J_t = 7.0 Hz), 4.14 (2H, q, J = 7.0 Hz), 4.46 (2H, s), 5.69 (1H, s), 7.25−7.36 (5H, m); ^{13}C NMR (100 MHz) δ 14.3, 15.4, 19.2, 34.6, 40.7, 59.5, 68.3, 73.1, 115.4, 127.6, 127.7, 128.4, 138.5, 163.5, 167.0; MS (*m*/*z*) 276 (M^+, 1.1), 91 (100); HRMS calcd for $C_{17}H_{24}O_3$ 276.1725, found 276.1697.

Ethyl (*Z*)-6-Benzyloxy-3,4-dimethyl-2-hexenoate (19b). Starting from (*E*)-enol phosphate **18a**, preparation of the title (*Z*)-conjugated ester **19b** was carried out in the same way as that of (*E*) isomer **19a**. Analysis of 400 MHz ^1H NMR revealed that the product obtained in 93% yield was contaminated by (*E*) isomer **19a** in a 96:4 ratio (comparison of vinyl methyl signals at δ 1.78 and δ 2.10, respectively). **19b**: IR (neat) 1720, 1650 cm^{-1}; ^1H NMR (400 MHz) δ 1.05 (3H, d, J = 7.0 Hz), 1.25 (3H, t, J = 7.0 Hz), 1.73 (2H, m), 1.78 (3H, d, J = 1.2 Hz), 3.44 (2H, m), 4.00 (1H, sextet, J = 7.0 Hz), 4.12 (2H, q, J = 7.0 Hz), 4.45 (1H, d, J = 11.6 Hz), 4.48 (1H, d, J = 11.6 Hz), 5.63 (1H, q, J = 1.2 Hz), 7.23−7.35 (5H, m); ^{13}C NMR (100 MHz) δ 14.3, 19.0, 19.2, 31.6, 34.6, 59.5, 69.1, 73.0, 116.7, 127.4, 127.6, 128.3, 138.7, 163.1, 166.2; MS (*m*/*z*) 276 (M^+, 3.8), 91 (100); HRMS calcd for $C_{17}H_{24}O_3$ 276.1725, found 276.1728.

2-[(*E*)-6-Hydroxy-3,4-dimethyl-4-hexenyl]-2-cyclohexenespiro-2′,5′-dioxa-cyclopentane (21a). A solution of (*E*)-ethylene ketal **9a** (1.08 g, 2.84 mmol) in THF cooled to 0 °C was mixed with a 1 M $Bu_4N^+F^-$ solution in THF (6 mL), and after removal of the cooling bath, the mixture was stirred at ambient temperature for 1 h. Water was added, the product was extracted with Et_2O, and the combined organic layers were washed successively with a saturated $NaHCO_3$ solution and brine and then dried with anhydrous K_2CO_3. Purification of the crude product with flash chromatography (hexane/Et_2O 1/2) furnished the title alcohol **21a** (746 mg, 99% yield) as a colorless oil: IR (neat) 3700−3100 (br) cm^{-1}; ^1H NMR (400 MHz) δ 1.00 (3H, d, J = 7.0 Hz), 1.39−1.48 (1H, m), 1.49−1.57 (1H, m), 1.59 (3H, s), 1.68−1.73 (4H, m), 1.91 (2H, br t, J = 7.0 Hz), 2.02 (2H, br s), 2.13 (1H, t, J = 7.0 Hz), 3.97 (4H, brs), 4.14 (2H, br s), 5.41 (1H, t, J = 7.0 Hz), 5.69 (1H, t, J = 3.7 Hz); ^{13}C NMR (100 MHz) δ 12.7, 19.5, 20.8, 25.3, 27.2, 33.9, 34.0, 42.6, 59.4, 65.0, 107.9, 123.1, 128.4, 138.1, 143.7; MS (*m*/*z*) 266 (M^+, 16), 99 (100); HRMS calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1865.

2-[(*Z*)-6-Hydroxy-3,4-dimethyl-4-hexenyl]-2-cyclohexenespiro-2′,5′-dioxa-cyclopentane (21b). Title alcohol **21b** was obtained in 99% yield from **9b** by the same procedure as above: IR (neat) 3700−3100 (br) cm^{-1}; ^1H NMR (400 MHz) δ 0.99 (3H, d, J = 7.0 Hz), 1.50 (2H, q, J = 7.0 Hz), 1.62 (3H, s), 1.65−1.78 (4H, m), 1.92 (2H, m), 2.04 (2H, m), 2.74 (1H, sextet, J = 7.0 Hz), 3.98 (4H, m), 3.98 (1H, J = 12.2, 6.7 Hz), 4.15 (1H, dd, J = 12.2, 7.9 Hz), 5.42 (1H, ddd, J = 7.9, 6.7, 1.2 Hz), 5.71 (1H, m); ^{13}C NMR (100 MHz) δ 17.9, 19.5, 20.7, 25.3, 26.5, 32.5, 33.1, 33.9 (2), 58.4, 64.9, 65.0, 107.9, 125.0, 128.4, 137.2, 143.1; MS (*m*/*z*) 266 (M^+, 3.1), 99 (100); HRMS calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1865.

2-[(*E*)-6-Chloro-3,4-dimethyl-4-hexenyl]-2-cyclohexene-2′,5′-dioxacyclo-pentane (22a). A solution of NCS (3 g, 22.5 mmol) in THF (280 mL) was mixed with triphenylphosphine (6 g, 22.9 mmol), and the mixture was stirred at room temperature for 1 h, before a solution of alcohol **21a** (3.05 g, 11.4 mmol) in THF (20 mL) was added. Stirring of the reaction mixture was continued overnight. After addition of water, most of the solvent was evaporated, the product was extracted with hexane, and the organic layers were washed with brine and dried with anhydrous K_2CO_3. Crude product was purified by chromatography on alumina (Activity II, hexane/Et_2O 8/1) to provide the title chloride **22a** (2.90 g, 90% yield) as a colorless oil: ^1H NMR (400 MHz) δ 1.01 (3H, d, J = 7.0 Hz), 1.44 (1H, m), 1.55 (1H, m), 1.65 (3H, d, J = 1.2 Hz), 1.68−1.74 (4H, m), 1.91 (2H, td, J_t = 7.0, J_d = 1.8 Hz), 2.02 (2H, br t, J = 1.8 Hz), 2.15 (1H, sextet, J = 7.0 Hz), 3.98 (4H, s), 4.10 (2H, dd, J = 7.9, 3.7 Hz), 5.46 (1H, t, J = 7.9 Hz), 5.69 (1H, t, J = 3.7 Hz); ^{13}C NMR (100 MHz) δ 12.5, 19.4, 20.8, 25.3, 27.3, 34.0, 41.1, 42.8, 65.0, 107.9, 120.0, 128.5, 138.2, 147.0.

2-[(*Z*)-6-Chloro-3,4-dimethyl-4-hexenyl]-2-cyclohexene-2′,5′-dioxacyclo-pentane (22b). Treatment of (*Z*)-alcohol **21b** with NCS and triphenylphosphine in the same way as above gave the title (*Z*)-chloride **22b** in 59% yield: ^1H NMR (100 MHz) δ 1.02 (3H, d, J = 7.0 Hz), 1.51 (2H, m), 1.66 (3H, s), 1.68−1.72 (4H, m), 1.92 (2H, m), 2.03 (2H, m), 2.70 (1H, sextet, J = 7.0 Hz), 3.98 (4H, s), 4.08 (1H, dd, J = 11.6, 7.9 Hz), 4.11 (1H, dd, J = 11.6, 7.9 Hz), 5.43 (1H, td, J_t = 7.9, J_d = 1.2 Hz), 5.69 (1H, m); ^{13}C NMR (100 MHz) δ 18.1, 19.3, 20.8, 25.3, 27.5, 33.7, 34.0, 34.2, 40.4, 65.0, 107.8, 211.0, 128.5, 138.0, 146.9.

2-[(*E*)-6-Diphenylphosphoryl-4-hexenyl]-3,4-dimethyl-2-cyclohexenone (13a). To a solution of diphenylphosphine (0.8 mL, 4.6 mmol) in THF (10 mL), cooled to 0 °C, was added a 1.6 M *n*-butyllithium solution in hexane (3.0 mL, 4.8 mmol), and the mixture was stirred for 30 min. The solution, thus prepared, was added dropwise to a solution of chloride **22a** (662 mg, 2.32 mmol) in THF (10 mL) at −78 °C until an orange color persisted in the solution, which was stirred further for 30 min. The reaction mixture was queched by the addition of water, and the solvent was evaporated. The residue, dissolved in CH_2Cl_2 (40 mL), was treated with a 30% H_2O_2 solution (5 mL) for 5 min under stirring. The organic layer was separated, and after being washed with a saturated Na_2SO_3 solution, the solvent was evaporated. The residue was dissolved in EtOH (20 mL) containing a 1% concd hydrochloric acid solution, and the solution was stirred for 1 h. After evaporation of most of the EtOH, the product was extracted with CH_2Cl_2 and the organic

layers were washed with saturated $NaHCO_3$ and brine. Purification of the crude product by silica gel chromatography (CH_2Cl_2/MeOH 99/1) afforded (*E*)-phosphine oxide **13a** (893 mg, 95% yield) as a viscous oil: IR (CH_2Cl_2) 1660 cm^{-1}; ^1H NMR (400 MHz) δ 0.85 (3H, d, J = 7.0 Hz), 1.19−1.35 (2H, m), 1.37 (3H, d, J = 1.8 Hz), 1.87−1.97 (4H, m), 2.07 (1H, sextet, J = 7.0 Hz), 2.29 (2H, td, J_t = 6.1, J_d = 3.7 Hz), 2.38 (2H, t, J = 7.0 Hz), 3.08 (1H, ddd, J = 14.6, 14.6, 7.3 Hz), 3.11 (1H, ddd, J = 14.6, 14.6, 7.3 Hz), 5.27 (1H, brt, J = 7.3 Hz), 6.58 (1H, t, J = 3.7 Hz), 7.29−7.59 (6H, m), 7.61−7.81 (4H, m); ^{13}C NMR (100 MHz) δ 12.5, 19.6, 23.2, 26.0, 27.8, 30.6, 33.6, 38.6, 42.7, 112.2 (d, J = 4 Hz), 128.4, 128.5, 131.0 (d, J = 4 Hz), 131.1 (d, J = 3 Hz), 131.6 (2), 132.6, 133.5, 139.8, 144.9 (d, J = 12 Hz), 145.1, 199.3; MS (*m*/*z*) 406 (M^+, 28), 202 (100); HRMS calcd for $C_{26}H_{31}O_2P$ 406.2062, found 406.2043.

2-[(*Z*)-6-Diphenylphosphoryl-4-hexenyl]-3,4-dimethyl-2-cyclohexenone (13b). Conversion of (*Z*)-chloride **22b** in manner similar to that above provided (*Z*)-phosphine oxide **13b** in 87% yield: ^1H NMR (400 MHz) δ 0.75 (3H, d, J = 7.0 Hz), 1.31 (2H, m), 1.57 (3H, d, J = 3.7 Hz), 1.90−2.02 (4H, m), 2.31 (2H, td, J_t = 6.1, J_d = 4.3 Hz), 2.39 (2H, t, J = 6.7 Hz), 2.49 (1H, sextet, J = 7.0 Hz), 3.05 (1H, ddd, J = 15.9, 14.7, 6.7 Hz), 3.18 (1H, ddd, J = 14.7, 14.0, 8.5 Hz), 5.27 (1H, ddd, J = 8.5, 6.7, 6.7 Hz), 6.64 (1H, t, J = 4.3 Hz), 7.44−7.53 (6H, m), 7.69−7.76 (4H, m); ^{13}C NMR (100 MHz) δ 18.2, 18.6, 23.2, 26.1, 27.9, 30.1 (d, J = 70 Hz), 33.8, 34.4, 38.6, 112.7, 128.5 (d, J = 4 Hz), 128.6 (d, J = 3 Hz), 131.0 (d, J = 4 Hz), 131.6 (×2), 132.5, 133.5, 139.9, 144.6 (d, J = 12 Hz), 144.9, 199.4.

2-[(*E*)-6-Phenylsulfonyl-4-hexenyl]-3,4-dimethyl-2-cyclohexenone (14). To a solution of chloride **22a** (500 mg, 1.76 mmol) in anhydrous DMF (10 mL) was added sodium phenylsulfinate (300 mg, 1.83 mmol), and the mixture was stirred overnight at ambient temperature, before a 1 M HCl solution was added. After being stirred for 20 min, the mixture was made basic by the addition of a saturated $NaHCO_3$ solution and was worked up. Purification of the crude product by flash chromatography on silica gel (hexane/Et_2O 1/1) provided the title sulfone **14** (573 mg, 93% yield) as a colorless oil: IR (neat) 1680, 1310, 1150 cm^{-1}; ^1H NMR (400 MHz) δ 0.91 (3H, d, J = 7.0 Hz), 1.26 (3H, s), 1.25−1.43 (2H, m), 1.94−2.04 (4H, m), 2.11 (1H, sextet, J = 7.0 Hz), 2.34 (2H, td, J_t = 6.1, J_d = 3.7 Hz), 2.40 (2H, t, J = 7.0 Hz), 3.83 (2H, d, J = 7.9 Hz), 5.20 (1H, t, J = 7.9 Hz), 6.67 (1H, t, J = 3.7 Hz), 7.51−7.55 (2H, m), 7.60−7.64 (1H, m), 7.85−7.88 (2H, m); ^{13}C NMR (100 MHz) δ 12.5, 19.3, 23.1, 26.1, 27.8, 33.6, 38.6, 42.9, 56.0, 110.2, 128.5, 128.9, 133.5, 138.8, 139.7, 145.0, 150.3, 199.3; MS (*m*/*z*) 346 (M^+, 15), 205 (100); HRMS calcd for $C_{20}H_{26}O_3S$ 346.1603, found 346.1617.

(3*R,4*S**,4a*R**)-1,2,3,4,4a,5,6,7-Octahydro-4-[(*E*)-2-(diphenylphosphoryl)ethenyl]-3,4-dimethyl-4a-naphthalenol (23).** To a solution of *i*-Pr_2NH (0.35 mL, 2.50 mmol), cooled to 0 °C, was added a 1.65 M BuLi solution in hexane (1.5 mL, 2.48 mmol), and the mixture was stirred for 30 min. An LDA solution, thus prepared, was added dropwise to a solution of (*E*)-phosphine oxide **13a** (600 mg, 1.47 mmol), mixed with LiBr (130 mg, 1.50 mmol), and cooled to −78 °C, and the mixture was stirred for 30 min. The reaction was quenched by the addition of a saturated NH_4Cl solution, and the product was extracted with CH_2Cl_2. The combined organic layers were washed in succession with a saturated $NaHCO_3$ solution and brine. The crude product purified by flash chromatography on silica gel (CH_2Cl_2/MeOH 98/2) gave the cyclized product **23** (440 mg, 74% yield) as a colorless oil: IR (CCl_4) 3275 (br), 1610, 1180, 1125 cm^{-1}; ^1H NMR (400 MHz) δ 0.70 (3H, d, J = 7.0 Hz), 0.91 (3H, s), 1.28 (1H, qd, J_q = 13.4, J_d = 4.8 Hz), 1.41−1.59 (4H, m), 1.68 (1H, td, J_t = 14.1, J_d = 3.7 Hz), 1.84 (1H, m), 1.92 (1H, m), 2.04 (1H, m), 2.37 (1H, m), 2.49 (1H, m), 5.61 (1H, brs), 6.21 (1H, dd, J = 23.8, 17.7 Hz), 6.91 (1H, dd, J = 21.4, 17.7 Hz), 7.44−7.53 (6H, m), 7.68−7.73 (4H, m); ^{13}C NMR (100 MHz) δ 12.7, 16.9, 19.3, 25.5, 29.9, 31.0, 32.9, 33.4, 50.1 (d, J = 13 Hz), 74.2, 121.9 (d, J = 103 Hz), 125.6, 128.5 (d, J = 12 Hz), 131.4 (d, J = 6 Hz), 131.6, 133.5 (d, J = 110 Hz), 137.4, 158.2; MS (*m*/*z*) 406 (M^+, 57), 283 (100); HRMS calcd for $C_{26}H_{31}O_2P$ 406.2062, found 406.2038.

(4a*S,5*R**,6*R**,8a*R**)-3,4,4a,5,6,7,8,8a-Octahydro-5-[(*E*)-2-(diphenylphosphoryl)ethenyl]-5,6-dimethyl-1(2*H*)-naphthalenone (24).** An LDA solution, prepared from *i*-$PrNH_2$ (0.25 mL, 1.7 mmol) in THF (10 mL) and a 1.65 M BuLi solution in hexane (1.1 mL, 1.76 mmol), was added dropwise to a solution of phosphine oxide **13a** (400 mg, 0.98 mmol), cooled at −78 °C, and the mixture was allowed to react for 30 min under stirring. After quenching, it was worked up as above to yield the crude product, which was purified by flash chromatography on a silica gel column (CH_2Cl_2/MeOH 98/2). **24**: colorless oil (283 mg, 71% yield); IR (CH_2Cl_2) 1700, 1605, 1180, 1120 cm^{-1}; ^1H NMR (400 MHz) δ 0.73 (3H, d, J = 7.0 Hz), 1.02 (3H, s), 1.17−1.27 (1H, m), 1.32−1.56 (4H, m), 1.57−1.66 (2H, m), 1.93−2.00 (2H, m), 2.14−2.27 (2H, m), 2.36 (1H, m), 6.19 (1H, dd, J = 25.0, 17.7 Hz), 6.52 (1H, dd, J = 20.8, 17.7 Hz), 7.43−7.56 (6H, m), 7.64−7.22 (4H, m); ^{13}C NMR (100 MHz) δ 9.5, 16.8, 25.3, 25.7, 26.7, 28.5, 39.4, 41.8, 46.0, 120.9 (d, J = 101 Hz), 128.5, 128.6, 131.1, 131.2, 131.7, 133.4 (d, J = 104 Hz), 160.8, 212.4; MS (*m*/*z*) 406 (M^+, 55), 202 (100); HRMS calcd for $C_{26}H_{31}O_2P$ 406.2062, found 406.2041.

(4a*S,5*R**,6*R**,8a*R**)-3,4,4a,5,6,7,8,8a-Octahydro-8a-allyl-5-[(*E*)-2-(diphenylphosphoryl)ethenyl]-5,6-dimethyl-1(2*H*)-naphthalenone (26).** To a solution of LDA, prepared from *i*-Pr_2NH (0.06 mL, 0.43 mmol) in THF (5 mL) and a 1.65 M BuLi solution in hexane (0.26 mL, 0.43 mmol) and cooled at −40 °C, was added dropwise a solution of phosphine oxide **13a** (100 mg, 0.25 mmol) in a mixture of HMPA (5 mL) and THF (15 mL), and mixture was stirred for 30 min, before allyl bromide (0.05 mL, 0.58 mmol) was added. After the reaction mixture was stirred for 1 h, it was quenched by the addition of water and then extracted with CH_2Cl_2. The organic layers were washed with brine and were dried with anhydrous K_2CO_3. The crude product was purified by silica gel chromatography (hexane/Et_2O) to give **(3*R**,4*S**,4a*R**)-1,2,3,4,4a,5,6,7-octahydro-8-allyloxy-4-[(*E*)-2-(diphenylphosphorylethenyl]-3,4-dimethylnaphthalene** (59 mg, 52% yield) as a colorless oil: ^1H NMR (400 MHz) δ 0.72 (3H, d, J = 6.7 Hz), 0.85 (3H, s), 1.21 (2H, m), 1.30−1.71 (6H, m), 2.01 (2H, brs), 2.14 (1H, t, J = 6.7 Hz), 3.02 (1H, dd, J = 14.3, 2.7 Hz), 4.14 (1H, ddt, J_d = 12.8, J_d' = 5.5, J_t = 1.2 Hz), 4.20 (1H, ddt, J_d = 12.8, J_d' = 5.5, J_t = 1.2 Hz), 5.17 (1H, dd, J = 10.4, 1.8 Hz), 5.29 (1H, dd, J = 17.1, 1.8 Hz), 5.94 (1H, ddt, J_d = 17.1, J_d' = 10.4, J_t = 5.5 Hz), 6.13 (1H, dd, J = 25.0, 17.7 Hz), 6.56 (1H, dd, J = 20.8, 17.7 Hz), 7.44−7.57 (6H, m), 7.64−7.72 (4H, m); ^{13}C NMR (100 MHz) δ 10.2, 17.0, 22.3, 24.7, 25.3, 25.9, 29.6, 30.3, 40.0, 47.2 (d, J = 13 Hz), 69.4, 116.7, 117.0, 120.1 (d, J = 103 Hz), 128.4, 128.7, 131.1 (2), 131.6, 133.1 (d, J = 6 Hz), 134.2 (d, J = 6 Hz), 134.9, 148.0, 161.7.

A solution of this allyl enol ether (25 mg, 0.06 mmol) in anhydrous 2,6-lutidine (1 mL) was heated under reflux for 1 h. The residue, left after evaporation in vacuo of the solvent, was chromatographed on silica gel column (CH_2Cl_2/MeOH 99/1) to afford the title product **26** (25 mg, 100% yield) as a colorless oil: IR (CH_2Cl_2) 1700, 1640, 1180, 1120 cm^{-1}; ^1H NMR (400 MHz) δ 0.68 (3H, d, J = 6.1 Hz), 0.94 (3H, s), 0.97 (1H, m), 1.30−1.43 (3H, m), 1.54 (1H, m), 1.93−2.12 (4H, m), 2.15 (dd, J = 14.0, 7.3 Hz), 2.25 (1H, m), 2.40 (1H, m), 2.58 (1H, m), 2.77 (1H, dd, J = 14.0, 7.3 Hz), 5.06 (2H, m), 5.56 (1H, ddt, J_d = 17.1, J_d' = 9.8, J_t = 7.3 Hz), 6.15 (1H, dd, J = 25.0, 17.4 Hz), 6.48 (1H, dd, J = 20.8, 17.4 Hz), 7.43−7.56 (6H, m), 7.64−7.72 (4H, m); ^{13}C NMR (100 MHz) δ 13.0, 16.9, 20.7, 23.9, 26.6, 31.2, 36.6, 40.3, 46.3, 47.5 (d, J = 13 Hz), 50.5, 51.5, 118.6, 120.8 (d, J = 101 Hz), 128.5 (d, J = 3 Hz), 128.7 (d, J = 3 Hz), 131.1, 131.2, 131.3, 131.7, 132.1, 133.0 (d, J = 13 Hz), 134.0 (d, J = 13 Hz), 162.1, 215.0.

Acknowledgment. We thank Drs. Hideo Iio and Yoshinosuke Usuki for their helpful discussion and support of this work.

Supporting Information Available: Complete syntheses of **4**−**8a**, **15**−**17**, **19a**−**8a**, and **19b**−**8b** along with experimental and characterization data for all intermediates, and ^1H NMR spectra for **2a**, **2a**−**c** (mixture in 77:21:2 ratio), **5**, **7a**,**b**−**9a**,**b**, **10a**, **11a**, **13a**,**b**, **14**−**17**, **18a**,**b**−**22a**,**b**, and **23**−**26** (39 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO980188T