CARBOMETALATION OF CYCLOPROPENES. STEREOSELECTIVE SYNTHESIS OF DIVINYL KETONES *VIA* 1,5-HYDROGEN MIGRATION REACTION OF VINYLCYCLOPROPANES†

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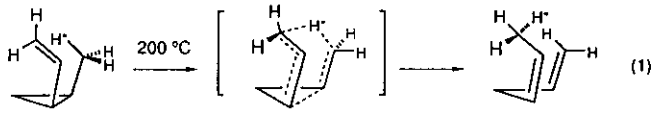
†*Dedicated to the memory of Prof. Yoshio Ban who contributed immensely to the promotion of chemistry in our country*

Abstract——Stereoselective addition of a vinyl cuprate reagent to a cyclopropenone acetal (**2**) followed by in situ electrophilic trapping with an alkylating agent affords a *cis*-1-alkyl-2-vinylcyclopropanone acetal (**3**), which then undergoes thermal 1,5-hydrogen migration reaction to give the acetal of a *Z,E*-dienone (**4**) in 70-90% overall yield. Hydrolysis under mild acidic conditions affords the corresponding dienone or trienone (**5**) in high yield.

Conversion of a *cis*-1-alkyl-2-vinylcyclopropane to a 1,4-diene through 1,5-sigmatropic hydrogen migration has long attracted attention of organic chemists owing to its mechanistic significance (eq. 1).[1,2] Synthetically, however, this reaction may be considered strategically unattractive, since efficient synthetic routes to the starting *cis*-substituted cyclopropane are rather scarce.



(1)

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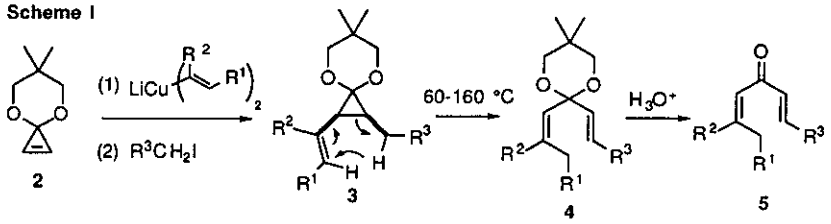
We report in this article that stereospecific addition of a vinyl cuprate to a cyclopropene (**2**) provides a highly effective synthetic entry to the required *cis*-1-alkyl-2-vinylcyclopropane (**3**): the necessary *cis*-stereochemistry is secured through the mechanism of the carbocupration as well as the stereo retentive electrophilic trapping of the intermediate cyclopropyl copper species,[3,4] and mild thermolysis of the cyclopropropane (**3**) produces the desired diene (**4**) in two steps from **2** with overall yield of 70-90% (Scheme I). The stereo electronic and steric control in the transition state of the 1,5-hydrogen migration realized excellent stereoselectivity with respect to *both* of the two newly formed double bonds in **4**. only

the olefin originated from the vinyl side chain being controlled through a stereoelectronically favored Not *endo* transition state (**1**), but the other derived from the alkyl side chain is also rigorously stereocontrolled.

Scheme I

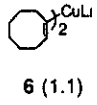
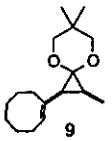
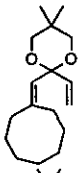
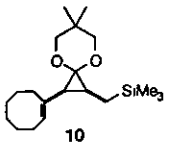
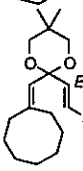
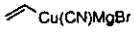
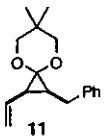
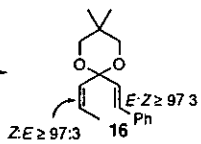
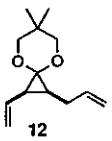
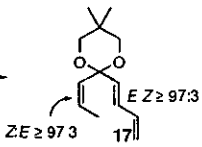
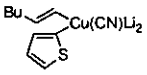
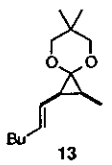
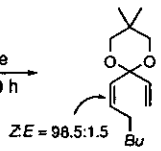


Results and Discussion

The cyclopropene (**2**) is a stable compound and is available in two steps from 1,3-dichloroacetone on a multi-gram scale.[5] The use of **2** as the cyclopropene substrate is of particular synthetic benefit,[6] since the product represents the acetal of a cross conjugated dienyl ketone (**5**) –a useful substrate for Nazarov synthesis of cyclopentenes.[7] Efficiency of the vinylcupration/alkyl trapping sequence (**2** to **3**) was examined first and the results are shown in Table I. The reaction was found to tolerate a variety of cuprate structures used in nearly equimolar quantity to the cyclopropene. Both vinyl lithium (cf. **6** and **8**) and vinyl magnesium bromide (cf. **7**) can be employed as a cuprate precursor. In addition to homocuprate (entries 1 and 2), heterocuprate (entries 3 and 4) and higher order cuprate with dummy ligands (entry 5) serve as a vinyl donor, transferring selectively the vinyl group to the cyclopropene. The use of a dummy ligand thus allowed the use of nearly stoichiometric amounts of the vinylmetal precursor and the electrophilic trapping agent (cf. entry 3): for convenience, however, the reactions were routinely carried out with an excess of the latter reagent. The overall yield of the carbocupration and trapping may average 80%.

1,5-Hydrogen migration reaction of the vinylcyclopropanes (**3**) was found to proceed under relatively mild conditions between 60-160 °C in a 0.2-0.6 M solution in an aromatic solvent, and gave the desired rearranged products in quantitative isolated yield (Table I). Some dienone acetals (**4**), were however found to undergo stereochemical isomerization of the olefinic bond during the thermolysis. A reasonable rationale for such isomerization involves acid-base interaction between the glassware surface and the acetal, causing the formation of a pentadienyl cation through C-O bond cleavage. In consonance with this analysis, when the thermolysis was carried out in the presence of *N,O*-bis(trimethylsilyl)acetamide (BSA) (entries 3 and 4), the olefin isomerization was almost completely suppressed. The rearrangement reaction made accessible a variety of dienones as well as trienone as shown in Table I. There was found a marked difference in the rate of the rearrangement. The 1-hexenyl compound (**13**) reacted much slower than the structurally related 1-cyclooctenyl one (**9**), which in turn reacted much slower than the silyl compound (**10**). The rearrangement of the last compound proceeded slowly even at room temperature, and completed in *ca.* 2 days at 60 °C. The benzyl (**11**) and allyl compounds (**12**) rearranged smoothly at 100 °C. Such observed effects of the alkyl substitutent on the alkyl side chain are in accord with the trend (Me_3Si > phenyl) reported for 1,5-hydrogen migration reaction of vinylcyclopropanes.[8] The rate difference caused by the 1-octenyl and the 1-hexenyl groups may be, in part, related to the difference in the conformation of these compounds. In order to investigate this hypothesis, two model compounds (**A**) and (**B**) were examined with the MMX force field[9] for the conformational energy with respect to the rotation of the

Table I. *Synthesis of vinylcyclopropanes (3) and 1,5-hydrogen migration reaction*

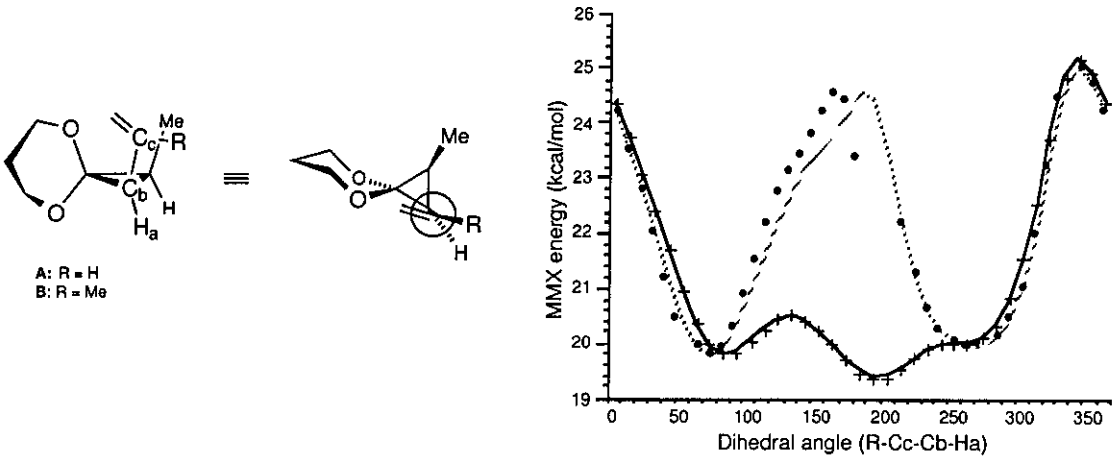
entry	cuprate (equiv.)	R^3CH_2X (equiv.)	3	%yield		4	%yield
1	 **6** (1.1)	MeI (5)	 **9**	79	mesitylene 120 °C, 11 h	 **14**	100
2		Me_3SiCH_2I (5)	 **10**	84	benzene 60 °C, 54 h	 *E Z* ≥ 98.5:1.5 **15**	94
3	 **7** (1.1)	 (1.1)	 **11**	90	toluene BSA 100 °C, 60 h	 *Z*:*E* ≥ 97:3 **16** *E*:*Z* ≥ 97 3	97
4		 (2)	 **12**	68	toluene BSA 100 °C, 29 h	 *Z*:*E* ≥ 97 3 **17** *E Z* ≥ 97:3	96
5	 **8** (1.2)	MeI (2)	 **13**	87	mesitylene 160 °C, 70 h	 *Z*:*E* = 98.5:1.5 **18**	92

a) The *cis* stereoselectivity of the addition/trapping sequence was complete. b) The ratio refers to *E*/*Z* ratio.

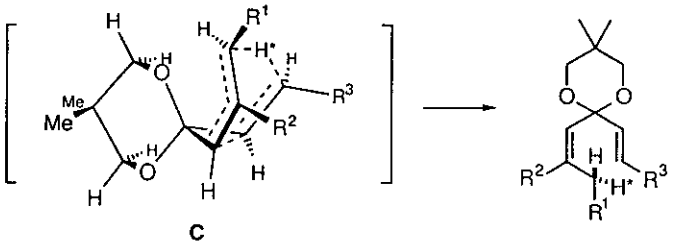
vinylic side chain for the variation of the dihedralangle R-Cc-Cb-Ca from 0 to 360 ° with a 10 ° increment using the dihedral angle driver option in PCModel (with optimization for each dihedral angle). **A** serves as a model for the 1-cyclooctenyl, and **B** for the 1-hexenyl substrates. For **B**, such calculations indicated two minima (Figure 1, dotted line): the one with the dihedral angle of *ca.* 70 °, which goes smoothly to the (preferred) endo transition state (cf. **1**), and the other with *ca.* 270 ° angle, which would lead to the (kinetically disfavored) exo transition state and thus is a non-productive conformer. On the other hand, the vinyl compound (**A**) (Figure 1, solid line) was found to be a very flexible molecule, with its olefinic side chain most of the time pointing toward the exo direction (the dihedral angle between 60-280 °). The highly restricted rotation in B undoubtedly arises from interaction of R (= Me) with the *cis*-methyl and the acetal groups (for the dihedral angle of *ca.* 180 °) as well as the $A^{1,2}$-interaction between the R and H_a (for the 0 ° dihedral angle). However, such conformational effects would still account for only a small fraction of the difference of the activation energies between the cyclooctenyl and hexenyl compounds, and the major difference appears to arise from other effects such as electronic effects (i.e., olefin substitution). Details of the latter effects await further studies.

Stereochemistry is of at most concern in olefin synthesis. Of the two olefins produced by the

Figure 1. MMX energy dependence on the dihedral angle R-C_c-C_b-C_a for cyclopropanes (**A**) (solid line) and (**B**) (dotted line).

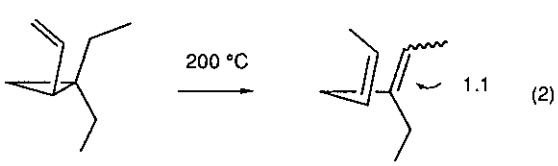


rearrangement, the one originated from the vinyl group has been found to be *cis*, and the other from the alkyl group to be *trans*. The selectivities for both olefins were at least 98.5%. Thus, for instance, the rearrangement of 2-(1- hexenyl)cyclopropane (**13**) gave the *cis*-dienone acetal (**18**) in 92% yield with >98.5 % selectivity. This stereochemistry translates to the *endo* orientation of the vinyl group in the transition state (cf. **1**). The *endo* preference is strong enough to override the steric effects of the neighboring acetal oxygen, which is in good agreement with the several kcal/mol energy preference of the *endo* over the *exo* transition state generally recorded this type of rearrangement.[1] It may be useful to note that the hydrogen (H*) to be transferred from the alkyl group (cf. **C**) would be placed face-selectively to the olefinic carbon connected to R^1 to create a potential stereogenic center. Given the high facial selectivity of such hydrogen transfer reported earlier,[1] and the ready availability of chiral counterparts of the acetal (**3**),[3a] the present sequence would provide a unique approach to optically active molecules.



C

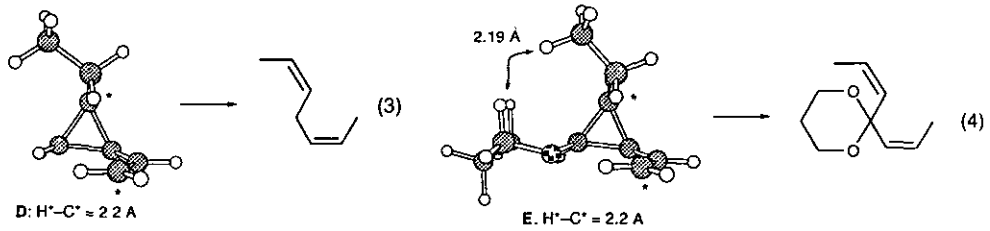
The literature examples indicate that the stereochemistry of the olefin originating from the alkyl group is much more difficult to control. For instance, the rearrangement of 1,1-diethyl-2-vinylcyclopropane gives a 1:1 *trans/cis* mixture with respect to the olefin in question (eq. 2).



(2)

In the present case, the rearrangement exhibited uniformly high *trans*-selectivity (Table I). The crucial factor appeared to be the presence of the acetal moiety as described in the next paragraph.

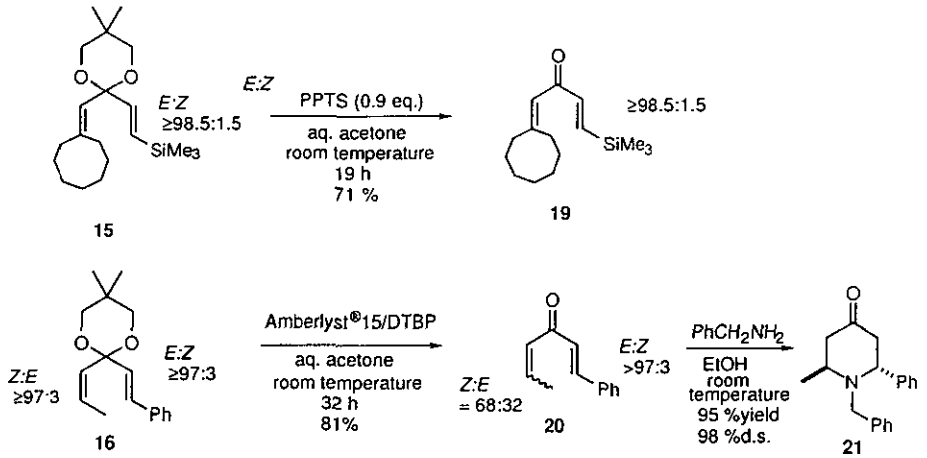
In order to evaluate the steric effects of the acetal group, conformations of 1-ethyl-2-vinylcyclopropane (**D**) and a model cyclopropanone acetal (**E**) was investigated. A "reactive conformation"[10] of **D** that would smoothly goes to the (preferred) *endo* transition state of the 1,5-hydrogen shift, and then further to a Z,Z product is shown in eq. 3. The structure has been minimized with a constraint that the transferred hydrogen (marked with an asterisk) and the reacting vinylic carbon (with an asterisk) is placed at 2.2 Å distance from each other.[11] As would be intuitively expected, this conformation has a steric energy essentially identical with that of an alternative ethyl rotamer leading to the trans product (not shown, cf. **C**). On the other hand, the *endo* "reactive conformer" leading to the *cis* isomer, which has a quite short H-H distance of 2.19 Å between the ethyl group and the acetal moiety, is about 1 kcal/mol higher in energy than the alternative rotamer going to the *trans* product (eq. 4). Thus, ground state analysis of the "reactive conformers" qualitatively reproduces the observed stereoselectivity.



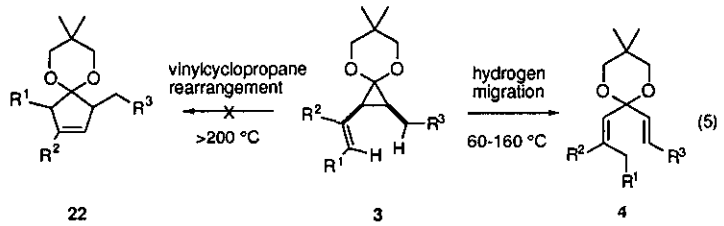
Hydrolysis of the dienone acetals proceeded very smoothly under mild conditions. Thus, treatment of the acetals with either pyridinium *p*-toluenesulfonate (PPTS) or Amberlyst® 15 treated previously with 2,6-di-*tert*-butylpyridine (Amberlyst/DTBP)[5] in an aqueous acetone gave the desired dienones in high yield (Scheme II). However, as also observed during the rearrangement studies (*vide supra*), the acid-catalyzed isomerization of the olefin caused partial isomerization of a *E*,*Z*-isomer to the corresponding *E*,*E*-isomer even under the mild conditions employed here.

The synthetic utility of the dienones may be illustrated by stereoselective synthesis of 4-ketopiperidine (**20**) by the reaction with an amine.[12] The overall three-step reaction provides a strategically novel heteroannulation sequence with high *trans* stereoselectivity (Scheme II).

Scheme II



Finally, an issue of potential competition between the 1,5-hydrogen migration reaction and vinylcyclopropane rearrangement (eq. 5) may be pointed out. An acetal functionality in **3** greatly enhances thermal cleavage of the strained ring.[13] We found however that the 1,5-hydrogen migration reaction of **3** takes place much faster than the vinylcyclopropane rearrangement. Thus, in all of the reactions studied, the dienone **(4)** was the only product, and none of the cyclopentene **(22)** was found in the reaction mixture.



22 3 4

In summary, we have established a short, efficient, and stereoselective synthesis of cross conjugated dienones and their acetals by taking advantage of the rich chemistry of cyclopropenone acetals. The stereochemistry of the carbocupration, electrophilic trapping, and the rearrangement are rigorously controlled by each reaction mechanism, rendering the overall sequence highly efficient despite the fact that two stereogenic centers are destroyed during the reaction course. The *trans*-stereoselectivity with respect to the olefin derived from the alkyl side chain has been achieved by beneficial use of the steric effects of the spiro acetal grouping. The present method represents a strategically novel three-component coupling scheme, wherein the cyclopropene ring serves as a highly reactive conjunctive reagent.

EXPERIMENTAL SECTION

General: All the reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under nitrogen. Routine chromatographic purification was achieved with Merck Kieselgel 60 (230-400 mesh) with hexane/AcOEt as eluent. ^{1}H nmr (200, 270, and 500 MHz) and ^{13}C nmr spectra were measured for a $CDCl_3$ solution on JEOL FX-200, GSX-270 and GSX-500 instruments. The ^{1}H nmr spectra are reported in a parts per million from internal tetramethylsilane, and the ^{13}C nmr spectra from (77.0 ppm). Ir spectra were recorded on a JASCO IR-800; absorptions are reported in cm^{-1}. Gas chromatographic (gc) analysis was performed on a Shimadzu 8A or 14A machine equipped with glass capillary columns.

***cis*-2-(1-Cyclooctenyl)-3-methylcyclopropanone 1,3-(2,2-Dimethyl)propanediyl Acetal (9).** To a solution of 1-bromocyclooctene (0.63 ml, 4.4 mmol) in THF (13 ml) was added a 1.53 M *t*-BuLi in pentane (5.8 ml, 8.8 mmol) at -70 °C. After stirring for 3 min, the vinyl lithium solution was added via a cannula to a suspension of CuBr·Me_2S (0.451 g, 2.2 mmol) in ether (3 ml). The mixture was stirred at -40 °C for 20 min, and then cooled to -70 °C. Cyclopropenone acetal (1) (0.281 ml, 2.0 mmol) in ether (1.5 ml) was added to the cuprate solution over 1 min, and the mixture was stirred for 5 min. An Et_2O solution of iodomethane (0.62 ml, 10 mmol) and HMPA (0.38 ml, 2.2 mmol) were added to the solution, and the mixture was slowly warmed to 0 °C over 3 h, and then stirred for 1 h at 0 °C. The solution was poured into sat. NH_4Cl (15 ml), and the water layer was extracted with Et_2O. The combine solution was filtered through a short pad of silica gel, and the filtrate was concentrated in vacuo. The residual oil was chromatographed on silica gel (2% EtOAc in hexane) to obtain the title compound as a colorless oil (0.423 g, 79%): Ir (neat) ν 2950, 2920, 2850, 1470, 1450, 1395, 1260, 1155, 1105, 1070, 1025, 915 cm^{-1}; ^{1}H nmr (200 MHz, $CDCl_3$) δ 0.89 (s, 3 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.12 (s, 3 H), 1.33 (dq, J = 9.7, 6.8 Hz, 1 H), 1.45-1.60 (m, 8 H), 1.69 (dd, J =

9.7, 1.5 Hz, 1 H), 2.06-2.18 (m, 4 H), 2.20-2.36 (m, 4 H), 3.45-3.65 (m, 4 H), 5.63 (dt, J = 1.9, 9.0 Hz, 1 H); ^{13}C nmr (125 MHz, $CDCl_3$) δ 7.8, 22.3, 22.5, 26.3, 26.7, 26.7, 28.5, 30.2, 30.7, 30.8, 31.6, 75.4, 76.1, 91.9, 127.1, 133.4. Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.29; H, 10.69.

***cis*-2-(1-Cyclooctenyl)-3-[(trimethylsilyl)methyl]cyclopropanone 1,3-(2,2-Dimethyl)propanediyl Acetal (10).** To a solution of 1-bromocyclooctene (1.25 ml, 5.6 mmol) in THF (26 ml) was added a 1.52 M *t*-BuLi in pentane (11.5 ml, 17 mmol) at -70 °C. After stirring for 10 min, the vinyl lithium solution was added via a cannula to a suspension of CuBr·Me_2S (1.0 g, 4.9 mmol) in ether (6 ml). The mixture was stirred at -40 °C for 10 min, and then cooled again to -70 °C. Cyclopropenone acetal (1) (0.56 ml, 4.0 mmol) in ether (3 ml) was added to the cuprate solution over 5 min, and the mixture was stirred for 1 min. HMPA (1.05 ml, 6.1 mmol) and (trimethylsilyl)methyl iodide (2.3 ml, 19 mmol) were added to the solution, and the mixture was stirred for 45 min. The mixture was warmed to 0 °C, and warmed slowly to room temperature over 3 h. Water (0.2 ml) was added to the solution. The mixture was stirred for 5 min, and diluted with hexane (40 ml). The combine solution was filtered through a short pad of silica gel, and the filtrate was concentrated in vacuo. The residual oil was chromatographed on silica gel (2% EtOAc in hexane) to obtain the title compound as a colorless oil (1.14 g, 84%): Ir (neat) ν 2960, 2940, 2860, 2700, 1740, 1650, 1480, 1450, 1400, 1250, 1100, 870, 845 cm^{-1}; ^{1}H nmr (270 MHz, $CDCl_3$) δ 0.05 (s, 9 H), 0.47 (dd, J = 5.0, 15.0 Hz, 1 H), 0.67 (dd, J = 9.0, 15.0 Hz, 1 H), 0.88 (s, 3 H), 1.37 (ddd, J = 5.0, 9.0, 13.0 Hz, 1 H), 1.41-1.60 (m, 8 H), 1.52 (d, J =13.0 Hz, 1 H), 2.12-2.31 (m, 4 H), 3.38-3.56 (m, 4 H), 5.46 (t, J = 8.0 Hz, 1 H).

***cis*-2-Vinyl-3-benzylcyclopanone 1,3-(2,2-Dimethyl)propanediyl Acetal (11).** To a suspension of CuCN (1.88 g, 21 mmol) in THF (22 ml) was added a 0.713 M vinylmagnesium bromide in THF (30 ml, 21 m mol) at -70 °C over 3 min, and the mixture was stirred for 20 min. The mixture was warmed to 0 °C, stirred for 10 min, and then cooled to -70 °C. Cyclopropenone acetal (1) (2.8 ml, 20 mmol) in THF (20 ml) was added to the cuprate solution over 5 min. After stirring for 30 min, HMPA (12 ml, 30 mmol) and benzyl bromide (2.60 ml, 22 mmol) were added. The mixture was stirred for 3 h, warmed to 0 °C and stirred for 3 h, the mixture was further warmed to room temperature and stirred for 72 h. Water (0.50 ml, 28 mmol) was added, and the mixture was filtered through a short pad of silica gel, and the filtrate was concentrated in vacuo. The residual oil was chromatographed on silica gel (3% EtOAc in hexane) to obtain the title compound as a colorless oil (4.67 g, 90%): Ir (neat) ν 3075, 3025, 2950, 2850, 1635, 1600, 1493, 1450; 1100 cm^{-1}; ^{1}H nmr (270 MHz, $CDCl_3$) δ 0.84 (s, 3 H),1.20 (s, 3 H), 1.67 (ddd, J = 10.2, 7.0, 8.0 Hz, 1 H), 2.02 (dd, J = 10.2, 10.4 Hz, 1 H), 2.75 (dd, J = 15.0, 7.0 Hz, 1 H), 2.92 (dd, J = 15.0, 8.0 Hz, 1 H), 3.44-3.62 (m, 4 H), 5.10 (dd, J = 10.5, 2.0 Hz, 1 H), 5.26 (dd, J = 17.0, 2.0 Hz, 1 H), 5.69 (ddd, J = 17.0, 10.5, 10.4 Hz, 1 H), 7.30-7.60 (m, 5 H); ^{13}H nmr (126 MHz, $CDCl_3$) δ 21.9, 22.7, 28.7, 30.7, 30.8, 31.7, 75.6, 76.0, 91.4, 115.9, 125.8, 128.3 (2 C), 128.4 (2 C), 132.9, 141.1. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.33; H, 8.34.

***cis*-2-Vinyl-3- allylcyclopropanone 1,3-(2,2-Dimethyl)propanediyl Acetal (12).** To a suspension of CuCN (2.03 g, 22 mmol) in THF (22 ml) was added a 1.0 M solution of vinyl magnesium bromide in THF (22 ml, 22 m mol) at -70 °C over 3 min, and the mixture was stirred for 20 min. The mixture was warmed to 0 °C, stirred for 20 min, and then cooled to -70 °C. Cyclopropenone acetal (1) (2.8 ml, 20 mmol) in THF (20 ml) was added to the cuprate solution over 5 min. After stirring for 15 min, HMPA (12 ml, 30 mmol) and allyl bromide (3.5 ml, 40 mmol) were added, and the mixture was stirred for 4.5 h. Water (0.45 ml, 25 mmol) was added, and the mixture was filtered through a short pad of silica gel, and the filtrate was concentrated in vacuo. The residual oil was chromatographed on silica gel (5% EtOAc in hexane) to obtain the title compound as a colorless oil (2.84 g, 68%): Ir (neat) ν 3080, 2960, 2870, 1642, 1476, 1105 cm^{-1}; ^{1}H nmr (200 MHz, $CDCl_3$) δ 0.87 (s, 3 H), 1.12 (s, 3 H), 1.44 (dt, J = 10.5, 7.6 Hz, 1 H), 1.95 (dd, J = 10.2, 10.2 Hz, 1 H), 2.23 (dddd, J = 1.3, 1.3, 6.3, 7.6 Hz, 2 H), 3.46 (d, J = 11.4 Hz, 2 H), 3.52 (d, J = 11.4 Hz, 2 H), 4.96 (ddt, J = 1.4, 10.3, 1.3 Hz, 1 H), 5.07 (dd, J = 2.5, 10.0 Hz, 1 H), 5.09 (ddt, J = 1.4, 17.7, 1.3 Hz, 1 H), 5.22 (dd, J = 2.5, 17.1 Hz, 1 H), 5.88 (dt, J = 17.1, 10.0 Hz, 1 H), 5.89 (ddt, J = 17.7, 10.3, 6.1 Hz, 1 H); ^{13}C nmr

(67.5 MHz, $CDCl_3$) δ 22.1, 22.6, 26.8, 28.9, 30.8, 31.2, 75.6, 76.0, 91.3, 114.9, 115.8, 132.6, 137.0. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.70. Found: C, 75.10; H, 9.91.

***cis*-2-(1-Hexenyl)-3-methylcyclopropanone 1,3-(2,2-Dmethyl)propanediyl Acetal (13).** To a solution of 1-bromohexene (0.56 ml, 3.9 mmol) in ether (6 ml) was added a 1.56 M *t*-BuLi in pentane (4.90 ml, 7.65 mmol) at -70 °C over 1 min, and the mixture was stirred for 2 h. To the solution was added a 0.25 M solution of lithium 2-thienycyanocuprate in THF (18 ml, 4.5 mmol). 1-Cyclopropenone acetal (**1**) (0.42 ml, 3.0 mmol) in THF (3 ml) was added to the cuprate solution over 1 min. After stirring for 30 min, HMPA (2.6 ml, 15 mmol) and methyl iodide (0.93 ml, 15 mmol) in THF (3 ml) were added. The mixture was stirred for 3 h, warmed to 0 °C and stirred for 3 h, then warmed to room temperature. Water was added, and the mixture was filtered through a short path of silica gel, and the filtrate was concentrated in vacuo. The residual oil was chromatographed on silica gel (1% EtOAc in hexane) to obtain the title compound as a colorless oil (0.622 g, 87%): Ir (neat) ν 3020, 2930, 2870, 1740, 1470, 1460, 1070, 1095, 1030 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ 0.89 (s, 3 H), 1.07 (d, *J* = 6.9 Hz, 3 H), 1.11 (s, 3 H), 1.25-1.40 (m, 4 H), 1.86 (dd, *J* = 10.1, 9.7 Hz, 1 H),2.00-2.11 (m, 2 H), 3.43-3.61 (m, 4 H), 5.16 (ddt, *J* = 15.6, 9.7, 1.3 Hz, 1 H), 5.61 (dt, *J* = 15.6, 9.5 Hz, 1 H); ^{13}C nmr (67.5 MHz, $CDCl_3$) δ 7.2, 13.9, 22.1, 22.2, 22.7, 23.6, 29.9, 30.9, 31.8, 32.6, 75.5, 76.0, 91.5, 123.5, 132.5.

1-Cyclooctylidene-3-buten-2-one 1,3-(2,2-Dimethyl)propanediyl Acetal (14). A solution of *cis*-2-(1-octenyl)-3-methylcyclopropanone acetal (**9**) (0.804 g, 2.76 mmol) in mesitylene (10 ml) was heated at 120 °C for 11 h. The mixture was chromatographed on silica gel (1% EtOAc in hexane) to obtain the title compound as a colorless oil (0.804 g, 100%): Ir (neat) ν 2860, 2825, 1640, 1470, 1450, 1405, 1395, 1112, 1096, 922 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ 0.80 (s, 3 H), 1.12 (s, 3 H), 1.36 -1.75 (m, 10 H), 2.21 (t, *J* = 7.0 Hz, 2 H), 2.33 (t, *J* = 5.9 Hz, 2 H), 3.41 (dd, *J* = 10.0, 1.1 Hz, 2 H), 3.62 (dd, *J* = 10.0, 1.1 Hz, 2 H), 5.18 (dd, *J* = 1.7, 10.5 Hz, 1 H), 5.23 (s, 1 H), 5.43 (dd, *J* = 1.7, 17.3 Hz, 1 H), 5.89 (dd, *J* = 10.5, 17.3 Hz, 1 H); ^{13}C nmr(125 MHz, $CDCl_3$) δ 22.3, 22.7, 23.6, 25.6, 25.9, 28.2, 30.0, 30.1, 30.8, 35.4, 71.4 (2 C), 98.9, 114.9, 124.2, 138.2, 149.0. Anal. Calcd for $C_{17}H_{28}O_2$ C, 77.21, H, 10.69. Found: C, 77.47; H, 10.84.

(3*E*)-1-Cyclooctylidene-4-trimethylsilyl-3-buten-2-one 1,3-(2,2-Dimethyl)propanediyl Acetal (15). A 9:1 mixture of *cis*-2-(1-octenyl)-3-[(trimethylsilyl)methyl]cyclopropanone acetal (**10**) and the rearranged product (**15**) (0.515 g, 1.53 mmol) which formed on standing was heated for 60 h at 60 °C in toluene (2.7 ml). The mixture was chromatographed on silica gel (5% EtOAc in hexane) to obtain the title compound as a colorless oil (0.486 g, 94%): Ir (neat) ν 2940, 2920, 2850, 1635, 1463, 1390, 1360, 1240, 1170, 860, 840 cm^{-1}; ^1H nmr (270 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 0.77 (s, 3 H), 1.14 (s, 3 H), 1.40-1.70 (m, 10 H), 2.21 (t, *J* = 7.2 Hz, 2 H), 2.30 (t, *J*= 7.2 Hz, 2 H), 3.40 (d, *J* = 10.6 Hz, 2 H), 3.63 (d, *J* = 10.6 Hz, 2 H), 5.22 (s, 1 H), 6.00 (d, *J* = 19.0 Hz, 1 H), 6.09 (d, *J* = 19.0 Hz, 1 H); ^{13}C nmr (125 MHz, $CDCl_3$) δ -1.4 (3 C), 22.2, 22.8, 23.1, 25.4, 25.8, 28.3, 30.1 (2 C), 31.1, 35.2, 67.8 (2 C), 99.3, 124.0. 129.1, 144.5, 149.1. Anal. Calcd for $C_{20}H_{36}O_2Si$: C, 71.35; H, 10.80. Found: C, 71.06; H, 10.83.

We observed signals at δ 6.24, 6.30 of the vinylsilane moiety of the minor isomer in the ^1H nmr, and capillary gc analyses (HR-1, 0.25 mm I.D. X 25 m, 180 °C) showed a 98.5:1.5 ratio of (*E*)- and (*Z*)-isomer (retention times; 6.39 and 7.32 min.).

(1*E*,4*Z*)-1-Phenyl-1,4-hexadien-3-one 1,3-(2,2-Dimethyl)propanediyl Acetal (16). A mixture of *cis*-2-vinyl-3-benzylcyclopanone 1,3-(2,2-dimethyl)propanediyl acetal (**11**) (95.8 mg, 0.38 mmol) and *N,O*-bis(trimethylsilyl)acetamide (0.1 ml) in toluene (2.0 ml) was heated for 60 h at 100 °C. The mixture was concentrated in vacuo, and the residual oil was chromatographed on silica gel (5% EtOAc in hexane) to obtain the title compound as a colorless oil (92.5 mg, 97%): Ir (neat) ν 3020, 2950, 2850, 1650, 1490, 1465, 1445, 1390, 1360, 1180, 1120, 1080, 980, 960, 740, 690 cm^{-1}; ^1H nmr (270 MHz, $CDCl_3$) δ 0.83 (s, 3 H), 1.15 (s, 3 H), 1.78 (dd, *J* = 1.6, 7.0 Hz, 3 H), 3.48 (d, *J* = 11.0 Hz, 2 H), 3.68 (d, *J* = 11.0 Hz, 2 H), 5.47 (dq, *J* = 11.6, 1.6 Hz, 1 H), 5.83 (dq, *J* = 11.6, 7.0 Hz, 1 H), 6.24 (d, *J* = 16.0 Hz, 1 H), 6.77 (d, *J* = 16.0 Hz, 1 H), 7.15-7.35 (m, 3 H),

7.35-7.45 (m, 2 H), ^{13}C nmr (125 MHz, $CDCl_3$) δ 17.6, 22.4, 22.6, 30.3, 71.7 (2 C), 98.6, 126.7 (2 C), 127.9, 128.6 (2 C), 128.8, 129.4, 131.7, 132.2, 136.4. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.30; H, 8.74.

In the ^{1}H nmr analysis, we observed a signal (δ 6.12, J = 12.8 Hz) of the styryl moiety of the minor isomer, and that analysis indicated a 99.5:0.5 ratio of (1*E*,4*Z*)- and (1*E*,4*E*)-isomer.

(3*E*,6*Z*)-1,3,6-Octatrien-5-one 1,3-(2,2-Dimethyl)propanediyl Acetal (17). A mixture of *cis*-2-vinyl-3-allylcyclopropanone acetal (**12**) (1.13 g, 5.4 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (1.35 ml) in toluene (10 ml) was heated for 29 h at 100 °C. The mixture was concentrated in vacuo, and the residual oil was chromatographed on silica gel (5% EtOAc in hexane) to obtain the title compound as a colorless oil (1.09 g, 96%): Ir (neat) ν 3080, 3025, 2955, 2870, 1650, 1610, 1470, 1400, 1365, 1200, 1190, 1170, 1120, 1090 cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$) δ 0.79 (s, 3 H), 1.14 (s, 3 H), 1.74 (dd, J = 1.9, 7.4 Hz, 3 H), 3.43 (d, J = 11.1 Hz, 2 H), 3.63 (d, J = 11.1 Hz, 2 H), 5.14 (dd, J = 10.4, 1.9 Hz, 1 H), 5.26 (dd, J = 16.7, 1.9 Hz, 1 H), 5.39 (dd, J = 11.9, 1.9 Hz, 1 H), 5.73 (d, J = 14.8 Hz, 1 H), 5.79 (dd, J = 11 9, 7.4 Hz, 1 H), 6.35 (ddd, J = 16.7, 10.4, 10 4 Hz, 1 H), 6.41 (dd, J = 14.8, 10.4 Hz, 1 H); ^{13}C nmr (67.5 MHz, $CDCl_3$) δ 13.6, 22.1, 22.7, 30.0, 71.4 (2 C), 98.8, 118.5, 129.2, 130.7, 130.9, 133.3, 136.3. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.70. Found: C, 75.10; H, 9.94.

The ratio of the diastereomers was determined by ^{13}C nmr. There were found low intensity small peaks, whose height were 1.2-2.4% of corresponding one, nearby most peaks of major isomer.

(4*Z*)-1,4-Decadien-3-one 1,3-(2,2-Dimethyl)propanediyl Acetal (18). A solution of *cis*-2-(1-hexenyl)-3-methylcyclopropanone acetal (**13**) (38.3 mg, 0.16 mmol) in mesitylene (0.79 ml) was heated at 160 °C for 70 h. The mixture was chromatographed on silica gel (5% EtOAc in hexane) to obtain the title compound as a colorless oil (35.1 mg, 92%): Ir (neat) ν 3015, 2950, 2925, 2850, 1470, 1400, 1200, 1180, 1120, 1100, 930 cm^{-1}; ^{1}H nmr (270 MHz, $CDCl_3$) δ 0.79 (s, 3 H), 0.90 (t, J = 7.2 Hz, 3 H), 1.13 (s, 3 H), 1.22-1.40 (m, 6 H), 2.15-2.35 (m, 2 H), 3.42 (d, J = 10.4 Hz, 2 H), 3.64 (d, J = 10.4 Hz, 2 H), 5.19 (d, J = 11.0 Hz, 1 H), 5.34 (d, J = 12.0 Hz, 1 H), 5.44 (d, J = 17.4 Hz, 1 H), 5.69 (dt, J = 12.0, 9.0 Hz, 1H), 5.90 (dd, J = 17.4, 11.0 Hz, 1 H); ^{13}C nmr (67.5 MHz, $CDCl_3$) δ 14.0, 22.2, 22.5, 22.7, 28.9, 30.1, 31.6, 71.5 (2 C), 99.1, 115.5, 127.7, 137.1, 138.3. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.56; H, 11.01. Found: C, 75.30; H, 11.31.

Capillary gc analysis (HR-1, 0.25 mm I.D. x 25 m, 120 °C) showed a 98.5:1.5 ratio of (*Z*)- and (*E*)-isomer (retention times; 13.46 and 14.27 min.).

(3*E*)-1-Octylidene-4-trimethylsilyl-4-buten-3-one (19). To a solution of acetal (**15**) (57.1 mg, 0.17 mmol) in acetone (1.5 ml) was added water (1.5 ml). The mixture was stirred for 19 h at room temperature. The reaction mixture was washed with an aq. sat. $NaHCO_3$, was dried over anhydrous Na_2SO_4. The filtrate was concentrated in vacuo, and residual oil was chromatographed on silica gel (1.5% EtOAc and 0.05% triethylamine in hexane) to obtain the title compounds as a yellow oil (30.2 mg, 71%): Ir (neat) ν 2930, 2860, 1670, 1660, 1610, 1250, 1220, 870, 845 cm^{-1}; ^{1}H nmr (200 MHz, $CDCl_3$) δ 0.16 (s, 9 H), 1.40-1.57 (m, 6 H), 1.71-1.86 (m, 4 H), 2.36 (t, J = 5.7 Hz, 2 H), 2.64 (t, J = 6.2 Hz, 2 H), 6.37 (s, 1 H), 6.54 (d, J = 19.0 Hz, 1 H), 7.03 (d, J = 19.0 Hz, 1 H).

(1*E*,4*Z*)-and (1*E*,4*E*)-1-Phenyl-1,4-hexadien-3-ones (20). To a solution of acetal (**16**) (33.3 mg, 0.12 mmol) in acetone (3.6 ml) was added Amberlyst®15 (8.4 mg).which was previously treated with 2,6-di-*t*-butylpyridine.[5] Water (1.2 ml) was added to the solution, and the mixture was stirred for 32 h at room temperature. The reaction mixture was washed with an aq. sat. $NaHCO_3$, was dried over anhydrous Na_2SO_4. The filtrate was concentrated in vacuo, and residual oil was chromatographed on silica gel (1.5% EtOAc and 0.05% triethylamine in hexane) to obtain the title compound as a yellow oil (16.8 mg, 81%) of a 68:32 mixture of *cis* - and *trans* -isomers.

(1*E*,4*Z*)-1-Phenyl-1,4-hexadien-3-one. Ir (neat) ν 3080, 3070, 3030, 2925, 2850, 1680, 1660, 1630, 1600, 1450, 1440, 1200, 1100, 1090 cm^{-1}; ^{1}H nmr (270 MHz, $CDCl_3$) δ 2.18 (dd, J = 1.4, 7.0 Hz, 3 H), 6.34 (dq, J = 11.0, 7.0 Hz, 1 H), 6.46 (dd, J =

11.0 1.4 Hz, 1 H), 6.81 (d, J = 16.0 Hz, 1 H), 7.36-7.42 (m, 3 H), 7.54 -7.58 (m, 2 H), 7.57 (d, J = 16.0 Hz, 1 H); ^{13}C nmr (125 MHz, $CDCl_3$) δ 17.6, 22.4, 22.6, 30.3, 71.7 (2 C), 98.6, 126.7 (2 C), 127.9, 128.6 (2 C), 128.8, 129.4, 131.7, 132.2, 136.4. Anal. Calcd for $C_{12}H_{12}O$: C, 83.67; H, 7.04. Found: C, 83.37; H, 7.34.

(1*E*,4*E*)-1-Phenyl-1,4-hexadien-3-one. Ir (neat) ν 3070, 3030, 2960, 2855, 1665, 1637, 1602, 1580, 1450, 1340, 1200 cm^{-1}; ^{1}H nmr (200 MHz, $CDCl_3$) δ 1.93 (dd, J = 7.0, 1.7 Hz, 3 H), 6.44 (dd, J = 15.7, 1.7 Hz, 1 H), 6.94 (d, J = 16.3 Hz, 1 H), 7.00 (dq, J = 15.7, 7.0 Hz, 1 H), 7.35-7.39 (m, 3 H), 7.50-7.57 (m, 2 H), 7.58 (d, J = 16.2 Hz, 1 H).

The ratio of the (1*E*,4*Z*)-and (1*E*,4*E*)-isomers was determined by Capillary gc analysis (HR-1, 0.25 mm I.D. x 25 m, 150 °C) of the crude product. Retention time of the (1*E*,4*Z*)-isomer was 5.71 min, and that of the (1*E*,4*E*)-isomer was 6.76 min. Two isomers were separated by chromatographic purification on silica gel (5% EtOAc in hexane).

***trans*-2-Aza-1-phenyl-2-benzyl-3-methyl-5-cyclohexanone (21).** To an ethanol solution of (1*E*,4*Z*)-1-phenyl-1,4-hexadien-3-one (**20**) (68.8 mg, 0.40 mmol) was added benzylamine (44 μL, 0.40 mmol) and the mixture was stirred for 1 h at room temperature. The solution was combined in vacuo, and the residual oil was chromatographed on silica gel (10% EtOAc in hexane) to obtain the title compound as a yellow solid (103 mg, 95%) of a 98:2 mixture of *trans*- and *cis*-isomers: Ir (neat) ν 3075, 3500, 3020, 2950, 2925, 2825, 1950, 1880, 1810, 1740, 1490, 1450, 1380, 1360, 1310, 1235, 1205, 1175, 1115, 1060, 1020, 770, 750, 725, 700 cm^{-1}; ^{1}H nmr (200MHz, $CDCl_3$) δ 1.07 (d, J = 6.9 Hz, 3 H), 2.23 (ddd, J = 2.3, 3.4, 13.5 Hz, 1 H), 2.56 (ddd, J = 2.3, 4.8, 14.7 Hz, 1 H), 2.69 (ddd, J = 1.0, 9.5, 14.7 Hz, 1 H), 2.80 (dd, J = 6.7, 13.5 Hz, 1 H), 3.33 (d, J = 13.9 Hz, 1 H), 3.38 (ddq, J = 3.4, 6.7, 6.9 Hz, 1 H), 3.68 (d, J = 13.9 Hz, 1 H), 4.08 (dd, J = 4.8, 9.5 Hz, 1 H), 7.23-7.47 ppm (m, 10 H). Anal. Calcd for $C_{19}H_{21}NO$: C, 81.67; H, 7.59; N, 5.01. Found: C, 81.44; H, 7.74; N, 5.09.

***cis*-2-Aza-1-phenyl-2-benzyl-3-methyl-5-cyclohexanone (21).** Ir (neat) ν 3050, 3025, 3000, 2930, 2880, 1940, 1860, 1800, 1700, 1480, 1440, 1370, 1320, 1290, 1150, 1050, 1010, 740, 710, 680 cm^{-1}; ^{1}H nmr (200MHz, $CDCl_3$) δ 1.11 (d, J = 6.3 Hz, 1 H), 2.40-2.53 (m, 3 H), 2.71 (dd, J = 11.4, 15.2 Hz, 1 H), 2.94-3.09 (m, 1 H), 3.51 (d, J = 15.2 Hz, 1 H), 3.84 (dd, J = 3.4, 11.8 Hz, 1 H), 3.88 (d, J = 15.2 Hz, 1 H), 7.17-7.46 (m, 10 H). Anal. Calcd for $C_{19}H_{21}NO$: C, 81.67; H, 7.59, N, 5.01. Found: C, 81.37; H, 7.33; N, 4.77.

ACKNOWLEDGEMENT

We thank the Ministry of Education, Science and Culture, and the Asahi Glass Foundation for financial support. K.K. thank the Japan Society of Promotion for predoctoral fellowship.

REFERENCE AND NOTE

1. R. J. Ellis and H. M. Frey, *J. Chem. Soc. Supple 1*, 1964, 5578; R. J. Ellis and H. M. Frey, *Proc. Chem. Soc., London*, 1964, 221; W. R. Roth and J. Konig, *Liebigs Ann. Chem.*, 1965, **688**, 28; D. S. Glass, R. S. Boikess, and S. Winstein, *Tetrahedron Lett.*, 1966, 999; J. A. Berson, *Acc. Chem. Res.*, 1991, **24**, 215; P. A. Parziale and J. A. Berson, *J. Am. Chem. Soc.*, 1990, **112**, 1650; S. J. Getty and J. A. Berson, *J. Am. Chem. Soc.*, 1991, **113**, 4607; C. W. Spangler, *Chem. Rev.*, 1976, **76**, 187; G. Ohloff, *Tetrahedron Lett.*, 1965, **42**, 3795; E. J. Corey and D. K. Herron, *Tetrahedron Lett.*, 1971, **20**, 1641; E. J. Corey, H. Yamamoto, D. K. Herron, and K. J. Achiwa, *J. Am. Chem. Soc.*, 1970, **92**, 6635; B. M. Trost and P. L. Ornstein, *J. Org. Chem.*, 1982, **47**, 748.
2. J. P. Daub and J. A. Berson, *Tetrahedron Lett.*, 1984, **25**, 4463. The ab initio calculations at HF/3-21G level would still give us only a qualitative estimate of energetics in this 1,5-hydrogen shift reaction: R. J. Loncharich and K. N. Houk, *J. Am. Chem. Soc.*, 1988, **110**, 2089.

3. (a) M. Isaka and E. Nakamura, *J. Am. Chem. Soc.*, 1990, **112**, 7428. (b) E. Nakamura, M. Isaka, and S. Matsuzawa, *J. Am. Chem. Soc.*, 1988, **110**, 1297. Cf. K. Kubota, M. Isaka, M. Nakamura, and E. Nakamura, *J. Am. Chem. Soc.*, 1993, **115**, 5867; M. Nakamura, M. Arai, and E. Nakamura, *J. Am. Chem. Soc.*, 1995, **117**, 1179; E. Nakamura, *J. Syn. Org. Chem., Jpn.*, 1993, **51**, 985. Theoretical study of carbometalation of cyclopropene: E. Nakamura, M. Nakamura, Y. Miyachi, N. Koga, and K. Morokuma, *J. Am. Chem. Soc., 1993*, **115**, *1789*; Nakamura, E. Nakamura, N. Koga, and K. Morokuma, *J. Chem. Soc. Faraday Trans.*, 1994, **90**, 1789.

4. Preliminary. E. Nakamura, K. Kubota, and M. Isaka, *J. Org. Chem.*, 1992, **57**, 5809.

5. M. Isaka, S. Matsuzawa, S. Yamago, S. Ejiri, Y, Miyachi, and E. Nakamura, *J. Org. Chem.*, 1989, **54**, 4727; M. Isaka, R. Ando, Y. Morinaka, and E. Nakamura, *Tetrahedron Lett.*, 1991, **32**, 1339; M. Isaka, S. Ejiri, and E. Nakamura, *Tetrahedron Symposium-in-Print*, 1992, **48**, 2045.

6. However, the present sequence may also be applicable to simple cyclopropenes, which serve as an acceptor in carbometalation reaction. Cf. E. Nakamura and M. Isaka, *Organometallic News*, 1990, 194; A. M. Moiseenkov, B, A. Czeskis, and A. V. Semenovsky, *J. Chem. Soc., Chem. Commun.*, 1982, 109; M. Y. Lukina, T. Y. Rudashevskaya, and O. A. Nesmeyanova, *Dokl. Akad. Nauk SSSR.*, 1970, **190**, 1109; H. Lehmkuhl and K. Mehler, *Liebigs Ann. Chem.*, 1982, 2244; A. T. Stoll and E.-i. Negishi, *Tetrahedron Lett.*, 1985, **26**, 5671. We have found that spiro[2,5]oct-1-ene, an all carbon congener of **2**, also serves as a good acceptor of dialkylcuprates: unpublished results.

7. C. Santelli-Rouvier and M. Santelli, *Synthesis*, 1983, 429.

8. E. Piers and A. R. Maxwell, *Can. J. Chem.*, 1984, **62**, 2392.

9. The MMX force field implemented in PCModel software: Serena Software, Bloomington, Indiana.

10. Cf. Y. Horiguchi, E. Nakamura, and I. Kuwajima, *J. Am. Chem. Soc.*, 1989, **111**, 6257.

11. Upon removal of this constraint (2.2 Å, with 5 m dyne/Å) the structure relaxes to a local minimum ca. 4 kcal/mol lower in energy. Thus, this structure represents a very early stage toward the transition state.

12. Starting with a pure *Z*, *E*-isomer.

13. Cf. E. Nakamura, S. Yamago, S. Ejiri, A. E. Dorigo, and K. Morokuma, *J. Am. Chem. Soc.*, 1991, **113**, 3183; H. Tokuyama, M. Isaka, and E. Nakamura, *J. Am. Chem. Soc.*, 1992, **114**, 5523; T. Fujimura, S. Aoki, and E. Nakamura, *J. Org. Chem.*, 1991, **56**, 2809.

Received, 9th March, 1995