Cis double allylation of cyclopropenes using cyclopropylindium reagents

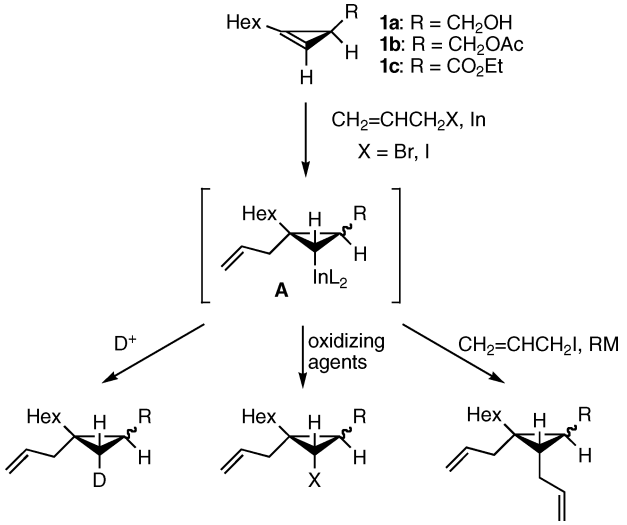
Tsunehisa Hirashita,* Fumio Shiraki, Kenji Onishi, Mamiko Ogura and Shuki Araki

Received 30th April 2007, Accepted 18th May 2007
First published as an Advance Article on the web 5th June 2007
DOI: 10.1039/b706539f

The successive double allylation of cyclopropenes with allylindium sesquiiodide and allyl iodide proceeded with a *cis*-addition mode in the presence of other organometallics (*e.g.* Grignard reagent, cuprate, Et_2Zn and Et_3Al), giving the corresponding *cis*-diallylcyclopropanes in high yields.

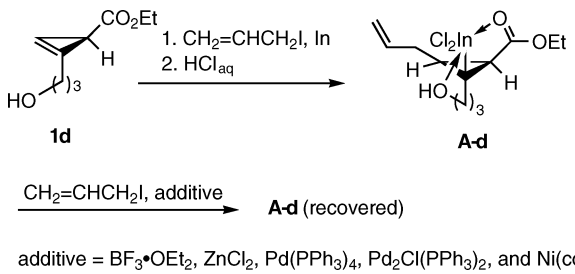
Introduction

Stereoselective synthesis of functionalized cyclopropanes is an attractive chemical process owing to the unique features of the cyclopropane subunit,[1] and carbometallation of cyclopropenes is a powerful and versatile approach to such functionalized cyclopropanes.[2] When the resulting cyclopropylmetal compounds are trapped with electrophiles, two distinct substituents can be introduced into the double bond of cyclopropenes. A variety of organometallic reagents has been used for this transformation.[3] In our continuing studies into carboindation, we found that the stereo-divergent allylindation of cyclopropenes proceeds with high stereoselectivity depending on the nature of the functional group on the cyclopropene ring (Scheme 1).[4,5] When cyclopropene **1a** was employed, the allylindation occurs exclusively from the same direction with respect to the hydroxymethyl group, whereas the allylation of **1b** showed the opposite face-selectivity. As allylindium reagents can be compatible with a broad range of functionalities, including a hydroxy group, the allylindation **1a–c** proceeds smoothly without loss of the allylating agents. Moreover, the cyclopropylindium intermediates **A** stabilized by intramolecular coordination of the hydroxy group were isolated and fully characterized by X-ray crystallographic analysis.[5] Upon the treatment of the cyclopropylindiums **A** with suitable oxidizing agents, the halogenation proceeds with retention of the original stereochemistry, giving stereo-defined allylhalocyclopropanes in high yields.[6] In order to derivatize further the cyclopropylindium intermediates **A**, we next turned our attention to carbon–carbon bond formation using **A**. Here, we report that the addition of organometallic reagents, in particular Et_2Zn and Et_3Al, proves to be effective for activating **A** prior to reaction with allyl iodide, giving functionalized *cis*-diallylcyclopropanes in high yields.[7]



Scheme 1

We first investigated the allylation of an isolable cyclopropylindium **A-d**[5] (Scheme 2). Cyclopropylindium **A-d** derived from **1d** was allowed to react with allyl iodide under various conditions. However, all attempts to use **A-d** for the coupling with allyl iodide in the presence of additives, such as $BF_3{\cdot}OEt_2$, $ZnCl_2$, $Pd(PPh_3)_4$, $Pd_2Cl(PPh_3)_2$ and $Ni(cod)_2$, resulted in no conversion. The low reactivity observed in **A-d** can be rationalized in terms of strong intramolecular coordination of the hydroxy and carbonyl groups to the indium atom.



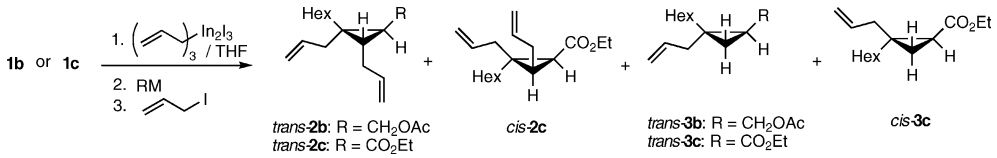
Scheme 2

Next, we used cyclopropylindium **A-b**, prepared by allylindation of **1b**, for reaction with allyl iodide. As **A-b** has no coordinative group, its nucleophilicity is expected to be higher than that of **A-d**. However, no coupling product was observed with the above-mentioned catalysts. We envisioned that the nucleophilicity of **A** should be enhanced by ate-complexation. We have previously found that the use of polar co-solvents promotes the reaction of indates leading to a significant improvement in the yield.[8] Thus, **A-b** prepared by allylindation of **1b** in THF for 4 h was treated with ethylmagnesium bromide and *N*-butylpyrrolidone (NBP), followed by an addition of allyl iodide. To our delight, the desired double-allylated cyclopropane *trans*-**2b** was obtained in 56% yield along with mono-allylated product **3b** (Table 1, entry 1).

The stereochemical purity of the double-allylated cyclopropane **2b** was confirmed by ^{13}C NMR analysis. The stereochemistry (both

Omohi College, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya, 466-8555, Japan. E-mail: hirasita@nitech.ac.jp; Fax: +81 52-735-5206; Tel: +81 52-735-5206

Table 1 Cascade allylation of cyclopropenes **1b** and **1c** with allylindium sesquiiodide and allyl iodide with the aid of Grignard reagent or cuprate[a]



Entry	**1** (mmol)	RM (mol%)	Co-solvent (mL)	Equiv. of allyl iodide	Conditions	Yield of product(s)	
1	**1b** (0.25)	EtMgBr (520)	NBP (2)	14	rt, 15 h	*trans*-**2b**: 56%	*trans*-**3b**: 15%
2	**1c** (0.50)	EtMgBr (480)	NBP (2)	7	rt, 15 h	**2c**: 34% (44 : 56)[b]	**3c**: 26%[c]
3	**1c** (0.50)	EtMgBr (500)	DMF (2)	8	rt, 15 h	**2c**: 24% (41 : 59)[b]	**3c**: 30%[c]
4	**1c** (0.50)	EtMgBr (800)	None	13	rt, 15 h	**2c**: 71% (45 : 55)[b]	—
5	**1b** (0.50)	$Me_2CuCNLi_2$ (240)	None	4	−78 °C, 15 h	—	*trans*-**3b**: 92%
6	**1b** (0.25)	$Me_2CuCNLi_2$ (480)	None	4	0 °C, 15 h	*trans*-**2b**: 48%	*trans*-**3b**: 21%
7	**1c** (0.50)	$Me_2CuCNLi_2$ (240)	None	4	rt, 15 h	**2c**: 71% (44 : 56)[c]	—

[a] Allylindation of **1** was performed with **1**/In/allyl iodide = 1 : 1.2 : 1.8 in THF at room temperature. [b] *Cis*/*trans* ratio. [c] The *cis*/*trans* ratio was not determined.

the allyl groups oriented *trans* to the CH_2OAc group) was deduced by the following observations: (1) Allylindation of cyclopropene **2b** occurs with a *cis*-addition mode from the *trans*-face with respect to the CH_2OAc group;[4] (2) The coupling constant (J = 7.4 Hz) of the vicinal protons on the cyclopropane ring supports the *trans* relationship;[9] (3) The reactions of other cyclopropyl-metal ate complexes, exemplified by cuprates, zincates and manganates, proceed with retention of configuration.[10] When **1c** (having an ethoxycarbonyl group) was employed in the presence of NBP or DMF, the corresponding diallylcyclopropane **2c** was produced as a mixture of *cis*- and *trans*-isomers (Table 1, entries 2 and 3). The *cis*/*trans* ratios were close to that observed in the allylindation of **1c**. The use of large amount of EtMgBr and allyl iodide gave **2c** in good yield without the help of polar solvents (entry 4).

The alkylation of organic halides using higher-order cuprates has been recognized as one of the most promising procedures for C–C bond formation.[11] Thus, cyclopropylindium **A** was also activated by transformation into the corresponding cuprate. To a solution of **A-b**, $Me_2CuCNLi_2$ (prepared from CuCN and MeLi) and allyl iodide were successively added. When the reaction was kept cold, the alkylation did not proceed (Table 1, entry 5). By increasing the reaction temperature, **2b** was obtained in 48% yield and the mono-allylated product **3b** in 21% yield (entry 6). The cyclopropylindium **A-c** gave the corresponding double-allylated compound **2c** in 71% yield as a mixture of *cis* and *trans* isomers (44 : 56) (entry 7).

Although the addition of Grignard reagent and cuprate was found to be useful for the allylation of **A**, the need for careful treatment of the highly active organometallic compounds and their lower compatibility toward functional groups are major drawbacks of this process. Recently, it was revealed that the pretreatment with MeLi or Et_2Zn is crucial for the successful protonolysis and iodonolysis of vinylgallium intermediates.[12] This prompted us to treat cyclopropylindium **A** with Et_2Zn before the addition of allyl iodide, and the addition of Et_2Zn was indeed effective for this allylation. The results are summarized in Table 2. The reaction at room temperature afforded **2b** in 18% yield (entry 1). The reaction performed at lower temperature gave better results (entry 2). A dramatic increase in the yield was achieved by the addition of DMF, which gave **2b** in 68% yield as a single isomer (entry 3). TMEDA was not effective for the allylation (entry 4), but HMPA served as a good co-solvent, affording **2b** in moderate yield (entry 5). The amount of Et_2Zn could be reduced to 150 mol% without a reduction in the yield (entry 6); however, 50 mol% Et_2Zn were not enough for this allylation (entry 7). A similar tendency was also observed for **1c**, although a larger amount of Et_2Zn was required to promote the allylation (entries 8–11). The addition of Et_3Al was also tested; pretreatment of **A-b** with Et_3Al gave no cyclopropane products, but instead the ring-opened triene **4** in 36% yield (entry 12). Adding DMF had a large effect on the allylation, the formation of **4** was suppressed and the double-allylated product **2b** was obtained in 72% yield (entry 13).

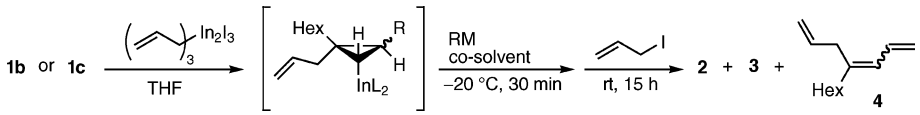
Finally, we examined the reaction of cyclopropene **1a**. However, the corresponding cyclopropylindium resisted allylation, and the coupling product was obtained in very low yield. This low reactivity implies that strong intramolecular chelation of the hydroxyl group operates during the reaction.

It is known that the reaction of allylic halides with organozinc reagents can be achieved by the addition of suitable polar solvents, such as DMF, HMPA and TMEDA, which are considered to serve as good ligands and dissociate diethylzinc.[13] The cyclopropylindiums **A-b** and **A-c** may be activated similarly by the complexes Et_2Zn–DMF and Et_3Al–DMF.

Conclusions

The *cis*-double allylation of cyclopropenes has been achieved by allylindation followed by the reaction of the resulting cyclopropylindium with allyl iodide using standard organometallic compounds. The two allyl groups can be introduced into cyclopropenes on the same side of the molecule. Further applications and investigations into the mechanism for the activation of organoindium compounds by Et_2Zn or Et_3Al are currently in progress.

Table 2 Cascade allylation of cyclopropenes **1b** and **1c** with allylindium sesquiiodide and allyl iodide with the aid of Et_2Zn or Et_3Zn[a]



Entry	**1** (mmol)	RM (mol%)	Co-solvent	Yield of product(s)	
1[b]	**1b** (0.50)	Et_2Zn (360)	None	*trans*-**2b**: 18% [5%][c]	*trans*-**3b**: 0% [6%][c]
2	**1b** (0.50)	Et_2Zn (360)	None	*trans*-**2b**: 37%	—
3	**1b** (0.50)	Et_2Zn (360)	DMF	*trans*-**2b**: 68% [20%][c]	—
4	**1b** (0.25)	Et_2Zn (360)	TMEDA	—	*trans*-**3b**: 57% [19%][c]
5	**1b** (0.25)	Et_2Zn (360)	HMPA	*trans*-**2b**: 34% [19%][c]	*trans*-**3b**: 10% [10%][c]
6	**1b** (0.50)	Et_2Zn (180)	DMF	*trans*-**2b**: 77% [10%][c]	*trans*-**3b**: 0% [2%][c]
7	**1b** (0.25)	Et_2Zn (60)	DMF	—	*trans*-**3b**: 66%
8	**1c** (0.50)	Et_2Zn (360)	None	—	**3c**: 44%[e]
9[d]	**1c** (0.50)	Et_2Zn (360)	None	**2c**: 54%[e]	**3c**: 14%[e]
10	**1c** (0.50)	Et_2Zn (360)	DMF	**2c**: 66% (44 : 56)[f]	—
11	**1c** (0.50)	Et_2Zn (180)	DMF	**2c**: 22% (41 : 59)[f]	**3c**: 30% (40 : 60)[f]
12[g]	**1b** (0.25)	Et_3Al (480)	None	**4**: 36%	—
13[g]	**1b** (0.25)	Et_3Al (480)	DMF	*trans*-**2b**: 72%	—

[a] After the allylindation of **1** was performed with **1**/In/allyl iodide = 1/1.2/1.8 in THF at room temperature for 4 h, Et_2Zn or Et_3 Al and co-solvent (2 mL) were added at −20 °C, followed by the addition of allyl iodide (400 mol%). [b] Et_2Zn was added at room temperature. [c] Figures in square brackets show the yield of the corresponding deacetylated product. [d] The reaction with allyl iodide was performed under reflux conditions. [e] The *cis*/*trans* ratio was not determined. [f] *Cis*/*trans* ratio. [g] Allyl iodide (800 mol%) was used.

Experimental

General

IR spectra were recorded on a JASCO IRA-102 spectrophotometer. ^{1}H NMR spectra were obtained for solutions in $CDCl_3$ on a Varian Gemini 200 spectrometer (200 MHz) with Me_4Si as internal standard, *J*-values are given in Hz. ^{13}C NMR spectra were measured for solutions in $CDCl_3$ with a Varian Gemini 200 spectrometer (50 MHz). Mass spectra were measured on a Hitachi M-2000 spectrometer at 70 eV. Elemental analyses were performed with a Perkin Elmer 2400II instrument. All reactions were carried out under argon. Indium powder (99.99%) was obtained from Aldrich and used as received. THF was dried with $LiAlH_4$ before use.

Synthesis of cyclopropenes

Ethyl 2-hexyl-2-cyclopropene-1-carboxylate (**1c**) was prepared by the rhodium-catalyzed reaction of 1-hexyne with ethyl diazoacetate.[14] Reduction with DIBAL followed by acetylation gave 3-acetoxy-1-hexylcyclopropene (**1b**).[4]

Double allylation of cyclopropenes 1b using EtMgBr

(Table 1, entry 1): A mixture of indium powder (35 mg, 0.30 mmol) and allyl iodide (47 μL, 0.45 mmol) was stirred in THF (0.5 mL) at room temperature for 1 h. Cyclopropene **1b** (49 mg, 0.25 mmol) in THF (0.5 mL) was added and the mixture was stirred at room temperature for 4 h. EtMgBr (0.89 M in THF, 1.5 mL, 1.3 mmol) and NBP (2 mL) were added to the reaction mixture at −20 °C and the resulting mixture was kept at this temperature for 30 min. Allyl iodide (319 μL, 3.5 mmol) was added to the solution, the mixture allowed to rise to room temperature, and stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 80) to give a mixture of *trans*-**2b** and *trans*-**3b**[2] (48 mg, **2b**: 56% and **3b**: 15%). The ratio was determined by ^{1}H NMR analysis.

trans-**2b**: ^{1}H NMR δ_H (200 MHz, $CDCl_3$): 0.59 (dt, J = 7.4 and 6.9 Hz, 1H, cyclopropyl-H), 0.75 (ddd, J = 8.4, 7.4 and 7.1 Hz, 1H, cyclopropyl-H), 0.88 (t, J = 6.5 Hz, 3H, CH_3), 1.10–1.42 (m, 10H, CH_2), 2.05 (s, 3H, OCH_3), 1.89–2.27 (m, 4H, allyl-CH_2), 3.98 (dd, J = 11.7 and 8.4 Hz, 1H, OCH_2), 4.21 (dd, J = 11.7 and 7.1 Hz, 1H, OCH_2), 4.92–5.12 (m, 4H, =CH_2), 5.68–5.94 (m, 2H, =CH–); ^{13}C NMR δ_C (50 MHz, $CDCl_3$): 14.1, 21.1, 22.6, 26.4, 28.3, 28.5, 28.7, 29.6, 31.9, 32.2, 32.9, 36.2, 65.1, 114.5, 116.0, 136.6, 138.0, 171.2; IR (neat, cm^{-1}): 2940, 2875, 1740, 1640, 1448, 1364, 1232, 1028, 912; CIMS: 219 (100%, MH^+ − HOAc), 177 (14%, MH^+ − HOAc − C_3H_6), 135 (20%, MH^+ − HOAc − $2C_3H_6$); Anal. Calcd for $C_{18}H_{30}O_2C$, 77.59; H, 10.86. Found C, 77.33; H, 11.07.

Double allylation of cyclopropenes 1c using EtMgBr

The following reaction of **1c** (Table 1, entry 4) represents the general procedure for the double allylation of **1b** and **1c** using EtMgBr. A mixture of indium powder (69 mg, 0.60 mmol) and allyl iodide (82 μL, 0.90 mmol) was stirred in THF (1.0 mL) at room temperature for 1 h. Cyclopropene **1c** (98 mg, 0.50 mmol) in THF (0.5 mL) was added and the mixture was stirred under reflux for 4 h. EtMgBr (0.89 M in THF, 4.5 mL, 4.0 mmol) was added to the reaction mixture at −20 °C and the resulting mixture was kept at this temperature for 30 min. Allyl iodide (586 μL, 6.4 mmol) was added to the solution, the mixture allowed to rise to room temperature, and stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 80)

to give **2c** (*cis*/*trans* = 45 : 55, 99 mg, 71%). Pure *cis*- and *trans*-**2c** were obtained by repeating the chromatography.

2c: ^{1}H NMR δ_H (200 MHz, $CDCl_3$) *trans*: 0.83–0.90 (m, 3H, CH_3), 1.16–1.30 (m, 14H, CH_2, ester-CH_3 and cyclopropyl-H), 1.48 (d, J = 5.9 Hz, 1H, cyclopropyl-H), 2.10–2.28 (m, 4H, allyl-CH_2), 4.11 (q, J = 7.0 Hz, 2H, OCH_2), 4.95–5.17 (m, 4H, =CH_2), 5.68–5.96 (m, 2H, =CH–); IR (neat, cm^{-1}): 2945, 2865, 1720, 1438, 1160, 910; *cis*: ^{1}H NMR δ_H (200 MHz, $CDCl_3$) 0.87 (t, J = 6.0 Hz, 3H, CH_3), 1.16–1.30 (m, 14H, CH_2, ester-CH_3 and cyclopropyl-H), 1.48 (d, J = 8.8 Hz, 1H, cyclopropyl-H), 2.42–2.52 (m, 4H, allyl-CH_2), 4.09 (q, J = 7.0 Hz, 2H, OCH_2), 4.92–5.13 (m, 4H, =CH_2), 5.68–5.96 (m, 2H, =CH–); IR (neat, cm^{-1}): 2965, 2900, 1730, 1380, 1168, 918. Anal. Calcd. for $C_{18}H_{30}O_2$ (mixture of *cis* and *trans*) C, 77.59; H, 10.86. Found C, 77.71; H, 11.14.

Double allylation of cyclopropenes 1c using cuprate

The following reaction of **1c** (Table 1, entry 7) represents the general procedure for the double allylation of **1b** and **1c** using cuprate. A mixture of indium powder (70 mg, 0.60 mmol) and allyl iodide (82 μL, 0.90 mmol) was stirred in THF (1.0 mL) at room temperature for 1 h. Cyclopropene **1c** (98 mg, 0.50 mmol) in THF (0.5 mL) was added and the mixture was stirred under reflux for 4 h. $Me_2CuCNLi$, prepared by the reaction of MeLi (1.14 M in Et_2O, 2.1 mL, 2.4 mmol) and CuCN (108 mg, 1.2 mmol) in THF (2 mL), was added to the cyclopropylindium compound at −40 °C and the mixture kept at room temperature for 10 min. Allyl iodide (184 μL, 2.0 mmol) was added to the mixture, the mixture allowed to rise to room temperature, and stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 80) to give **2c** (*cis*/*trans* = 44 : 56, 99 mg, 71%).

Double allylation of cyclopropenes using Et_2Zn

The following reaction of **1b** (Table 2, entry 6) represents the general procedure for the double allylation of **1b** and **1c** using Et_2Zn. A mixture of indium powder (70 mg, 0.60 mmol) and allyl iodide (82 μL, 0.90 mmol) was stirred in THF (1.5 mL) in THF (0.5 mL) at room temperature for 1 h. Cyclopropene **1b** (98 mg, 0.50 mmol) was added and the mixture was stirred at room temperature for 4 h. DMF (2 mL) and Et_2Zn (1.0 M in hexane, 0.90 mL, 0.90 mmol) were added to the reaction mixture at −20 °C and the resulting mixture was kept at this temperature for 30 min. To the solution, allyl iodide (181 μL, 2.0 mmol) was added and the temperature was allowed to be raised to room temperature and the mixture was stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 30) to give *trans*-**2b** (107 mg, 77%) and a deacetylated mixture of *trans*-**2b** and *trans*-**3b** (14 mg) with a ratio of 83 : 17. The yields were determined by ^{1}H NMR to be 10% and 2%, respectively.

Deacetylated *trans*-**2b**: ^{1}H NMR δ_H (200 MHz, $CDCl_3$): 0.55 (dt, J = 7.4 and 5.8 Hz, 1H, cyclopropyl-H), 0.71 (dt, J = 7.4 and 6.0 Hz, 1H, cyclopropyl-H), 0.88 (t, J = 6.4 Hz, 3H, CH_3), 1.11–1.55 (m, 10H, CH_2), 1.86–2.27 (m, 4H, allyl-CH_2), 3.53–3.73 (m, 2H, CH_2O), 4.95–5.11 (m, 4H, =CH_2) and 5.71–5.96 (m, 2H, =CH–); ^{13}C NMR δ_C (50 MHz, $CDCl_3$): 14.0, 22.6, 26.5, 28.4, 28.6, 29.6, 31.8, 31.9, 32.5, 33.0, 36.3, 63.1, 114.6, 116.1, 136.8, 138.2. IR (neat, cm^{-1}): 3350, 3085, 2935, 2855, 1638, 1436, 1020, 992, 908; CIMS: 220 (33%, MH − OH), 219 (100%, MH − H_2O).

Double allylation of cyclopropenes using Et_3Al

(Table 2, entry 12): A mixture of indium powder (47 mg, 0.40 mmol) and allyl iodide (55 μL, 0.60 mmol) was stirred in THF (0.5 mL) at room temperature for 1 h. Cyclopropene **1b** (49 mg, 0.25 mmol) in THF (0.5 mL) was added and the mixture was stirred at room temperature for 4 h. Et_3Al (0.92 M in hexane, 1.3 mL, 1.2 mmol) was added to the reaction mixture at −20 °C and the resulting mixture was kept at this temperature for 30 min. Allyl iodide (181 μL, 2.0 mmol) was added to the solution, the mixture allowed to rise to room temperature, and stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 30) to give **4** (16 mg, 36%).

4: ^{1}H NMR δ_H (200 MHz, $CDCl_3$): 0.88 (t, J = 6.5 Hz, 3H, CH_3), 1.23–1.48 (m, 8H, CH_2), 2.05 (d, J = 7.3 Hz, 2H, allyl-CH_2), 2.80 (t, J = 6.4 Hz, 2H, allyl-CH_2, *E* isomer), 2.91 (t, J = 6.4 Hz, 2H, allyl-CH_2, *Z* isomer), 4.97–5.17 (m, 4H, =CH_2), 5.79 (ddt, J = 17.1 Hz, 10.1 Hz, 6.4 Hz, 1H, =CH–), 5.91 (d, J = 10.6 Hz, 1H, =CH–), 6.58 (dt, J = 16.6 Hz, 10.6 Hz, 1H, =CH–); ^{13}C NMR δ_C (50 MHz, $CDCl_3$): 14.1, 22.6, 27.9, 29.1, 31.8, 35.3, 37.2, 115.2, 115.4, 126.2, 133.1, 136.0, 141.3; IR (neat, cm^{-1}): 3090, 2930, 2860, 1638, 1454, 1416, 1378, 1260, 984, 898, 804, 734, 660; Anal. Calcd. for $C_{13}H_{22}C$, 87.56; H, 12.44. Found C, 87.80; H, 12.18.

Double allylation of cyclopropenes using Et_3Al

(Table 2, entry 13): A mixture of indium powder (47 mg, 0.40 mmol) and allyl iodide (55 μL, 0.60 mmol) was stirred in THF (0.5 mL) at room temperature for 1 h. Cyclopropene **1b** (49 mg, 0.25 mmol) in THF (0.5 mL) was added and the mixture was stirred at room temperature for 4 h. DMF (2 mL) and Et_3Al (0.92 M in hexane, 1.3 mL, 1.2 mmol) were added to the reaction mixture at −20 °C and the resulting mixture was kept at this temperature for 30 min. Allyl iodide (181 μL, 2.0 mmol) was added to the solution, the mixture allowed to rise to room temperature, and stirred for 15 h. The reaction was quenched with 1 M HCl and the products were extracted with diethyl ether. The extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was separated by chromatography on silica gel (EtOAc–hexane = 1 : 30) to give *trans*-**2b** (50 mg, 72%).

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research (No. 14340195) from the Ministry of Education, Science, Sport and Culture, Japan.

References

1 (*a*) S. Patai and Z. Rappoport, *The Chemistry of the Cyclopropyl Group*, Wiley & Sons, New York, 1987; (*b*) *Small Ring Compounds in Organic Synthsis VI*, ed. A. de Meijere, Springer, Berlin, Germany, 2000, vol. 207; (*c*) *Houblen–Weyl Methods of Organic Chemistry*, Thieme, Stuttgart, 1997, vol. E17c; (*d*) H. Lebel, J.-F. Marcoux, C. Molinaro and A. B. Charette, *Chem. Rev.*, 2003, **103**, 977–1050.

2 For reviews of carbometallation of cyclopropenes, see: (*a*) J. M. Fox and N. Yan, *Curr. Org. Chem.*, 2005, **9**, 719–732; (*b*) M. Rubin, M. Rubina and V. Gevorgyan, *Synthesis*, 2006, 1221–1245. For recent carbometallations of cyclopropenes, see: (*c*) Z. Yang, X. Xie and J. M. Fox, *Angew. Chem., Int. Ed.*, 2006, **45**, 3960–3962; (*d*) X. Liu and J. M. Fox, *J. Am. Chem. Soc.*, 2006, **128**, 5600–5601; (*e*) M. A. Smith and H. G. Richey, Jr., *Organometallics*, 2007, **26**, 609–616.

3 Magnesium: (*a*) O. A. Nesmeyanova, T. Y. Rudashevskaya, A. I. Dyachenko, S. F. Savilova and O. M. Nefedov, *Synthesis*, **1982**, 296–297; (*b*) L. Liao and J. M. Fox, *J. Am. Chem. Soc.*, 2002, **124**, 14322–14323. Zinc: (*c*) M. Nakamura, A. Hirai and E. Nakamura, *J. Am. Chem. Soc.*, 2000, **122**, 978–979. Copper: (*d*) M. Nakamura, H. Isobe and E. Nakamura, *Chem. Rev.*, 2003, **103**, 1295–1326; (*e*) E. Nakamura, M. Isaka and S. Matsuzawa, *J. Am. Chem. Soc.*, 1988, **110**, 1297–1298; (*f*) E. Nakamura, K. Kubota and M. Isaka, *J. Org. Chem.*, 1992, **57**, 5809–5810; (*g*) M. Isaka and E. Nakamura, *J. Am. Chem. Soc.*, 1990, **112**, 7428–7430.

4 S. Araki, H. Nakano, K. Subburaj, T. Hirashita, K. Shibutani, H. Yamamura, M. Kawai and Y. Butsugan, *Tetrahedron Lett.*, 1998, **39**, 6327–6330.

5 S. Araki, F. Shiraki, T. Tanaka, H. Nakano, K. Subburaj, T. Hirashita, H. Yamamura and M. Kawai, *Chem.–Eur. J.*, 2001, **7**, 2784–2790.

6 S. Araki, O. Kenji, F. Shiraki and T. Hirashita, *Tetrahedron Lett.*, 2002, **43**, 8033–8035.

7 For cascade reactions using allylindium reagents, see: (*a*) T. Hirashita, H. Yamamura, M. Kawai and S. Araki, *Chem. Commun.*, 2001, 387–388; (*b*) T. Hirashita, Y. Hayashi, K. Mitsui and S. Araki, *J. Org. Chem.*, 2003, **68**, 1309–1313; (*c*) T. Hirashita, S. Kambe, H. Tsuji and S. Araki, *Chem. Commun.*, 2006, 2595–2597; (*d*) T. Hirashita, K. Akutagawa, T. Kamei and S. Araki, *Chem. Commun.*, 2006, 2598–2600.

8 T. Hirashita, Y. Hayashi, K. Mitsui and S. Araki, *Tetrahedron Lett.*, 2004, **45**, 3225–3228.

9 K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, 1963, **85**, 2788–2790.

10 Cuprates: K. Kitatani, T. Hiyama and H. Nozaki, *J. Am. Chem. Soc.*, 1976, **98**, 2362–2364; K. Kitatani, T. Hiyama and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 1600–1607; K. Kitatani, T. Hiyama and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 3288–3294; K. Kitatani, H. Yamamoto, T. Hiyama and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 2158–2160. Zincates:; T. Harada, K. Hattori, T. Katsuhira and A. Oku, *Tetrahedron Lett.*, 1989, **30**, 6035-6038—6039-6040; T. Harada, T. Katsuhira, K. Hattori and A. Oku, *J. Org. Chem.*, 1993, **58**, 2958–2965. Manganates:; R. Inoue, H. Shimokubo and K. Oshima, *Tetrahedron Lett.*, 1996, **37**, 5377–5380; H. Kakiya, R. Inoue, H. Shimokubo and K. Oshima, *Tetrahedron*, 2000, **56**, 2131–2137.

11 B. H. Lipshutz, R. S. Wilhelm and D. M. Floyd, *J. Am. Chem. Soc.*, 1981, **103**, 7672–7674.

12 Y. Kido, S. Yoshimura, M. Yamaguchi and T. Uchimaru, *Bull. Chem. Soc. Jpn.*, 1999, **72**, 1445–1458.

13 M. Arai, T. Kawasuji and E. Nakamura, *Chem. Lett.*, 1993, 357–360.

14 (*a*) P. Müller, N. Pautex, M. P. Doyle and V. Bagheri, *Helv. Chim. Acta*, 1990, **73**, 1233–1241; (*b*) N. Petiniot, A. J. Anciaux, A. F. Noels, A. J. Hubert and Ph. Teyssié, *Tetrahedron Lett.*, 1978, **19**, 1239–1242.

