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A New Zincate-Mediated Rearrangement Reaction of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanol

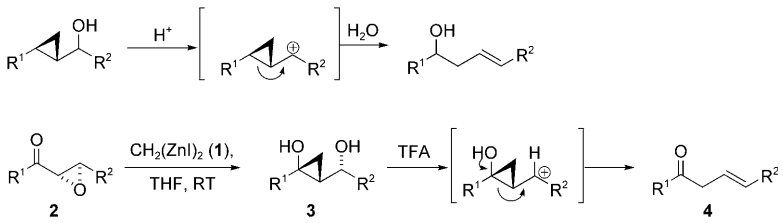
Kenichi Nomura and Seijiro Matsubara*[a]

Abstract: A novel rearrangement of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol has been found. It proceeds in the presence of a catalytic amount of organozinc ate complex to give *vic*-diols. The rearrangement can be applied to various types of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol, which can be easily prepared from the corresponding α,β-epoxyketones and bis(iodozincio)methane. When bicyclo[13.1.0]-pentadecane-1,15-diol was treated with the organozinc ate complex, the corresponding 14-membered cyclic *vic*-diol was obtained. Thus, this rearrangement is also useful for changing the ring size of cyclic substrates.

Keywords: cyclopropanol · homogeneous catalysis · organozinc ate complexes · rearrangement · zinc

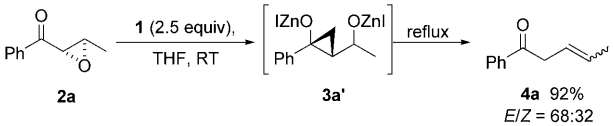
Introduction

Cyclopropanes have been recognized as variants of C-3 open-chain units in organic synthesis,[1] and a large number of cyclopropane ring-opening reactions have been reported.[2] Triggered by the formation of a cation or a radical at a carbon adjacent to the cyclopropane ring, most of the reactions proceed to release the strain of the three-membered ring.[3] In 1960, Julia et al. reported an acid-catalyzed ring-opening isomerization of cyclopropyl alkyl carbinol (Scheme 1, top).[4] The reaction affords an (*E*)-homoallylic alcohol via the formation of a carbocation on the cyclopropyl-substituted carbon. We have reported a preparation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3** from α,β-epoxyketone **2** and bis(iodozincio)-methane **1**.[5] When the Julia-type reaction was applied to 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, the carbocation-mediated ring-opening reaction with trifluoroacetic acid (TFA) gives the corresponding β,γ-unsaturated ketone **4**, as shown in Scheme 1, bottom.[6,7]



Scheme 1. Julia-type transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropane and 2-(1-hydroxyalkyl)-1-alkylcyclopropanol.

We also tried to convert the zinc alkoxide of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3a′**) directly into the corresponding β,γ-unsaturated ketone by making use of the Lewis acidity of the zinc species in the reaction mixture.[8] α,β-Epoxyketone **2a** (0.5 mmol) was treated with an excess amount of bis(iodozincio)methane (**1**, 1.25 mmol) at 25 °C, then the reaction mixture was heated at reflux for 2 h to give desired β,γ-unsaturated ketone **4a** in good yield (Scheme 2). However, treatment of **2a** with 1.1 equivalents of **1** gave 2,3-dihydroxy-3-phenyl-4-pentene (**5a**) as the



Scheme 2. Tandem transformation of **2a** into **4a** by a [2+1] cycloaddition of bis(iodozincio)methane (**1**).

[a] K. Nomura, Prof. S. Matsubara
Department of Material Chemistry
Graduate School of Engineering, Kyoto University
Kyoutodaigaku-katsura
Nishikyo-ku, Kyoto 615-8510 (Japan)
Fax: (+81) 75-383-2463
E-mail: matsubar@orgrxn.mbox.media.kyoto-u.ac.jp

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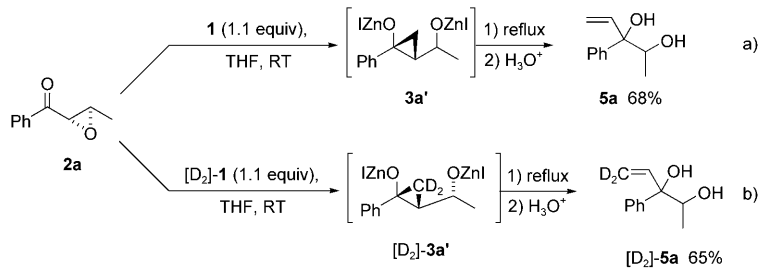
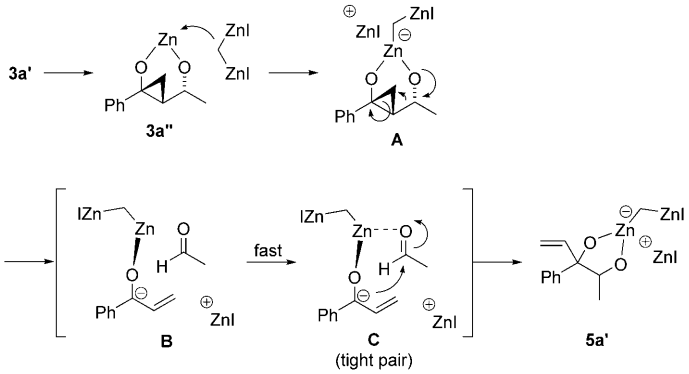


Scheme 3. A novel rearrangement reaction of **3a′** or [D_2]-**3a′**.

major product instead of β,γ-unsaturated ketone **4a** (Scheme 3a).[9,10] When the latter reaction was examined by using the labeled reagent $CD_2(ZnI)_2$ ([D_2]-**1**), 5,5-dideuterio-3-phenylpent-4-ene-2,3-diol ([D_2]-**5a**) was obtained (Scheme 3b). We investigated the details of this novel rearrangement.

Results and Discussion

We speculated that the reaction proceeded via a zincate intermediate. The working hypothesis of this rearrangement is shown in Scheme 4. Zinc alkoxide **3a″**, which was formed

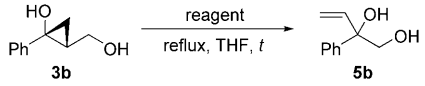


Scheme 4. A working hypothesis of the rearrangement.

from **3a′** under heating, would coordinate with the remaining **1**. Zincate **A** may fragment into aldehyde and carbanion fragments (**B**) due to the strong electron-donating effect of the zincate. The aldehyde and carbanion fragments then form a tight pair through zinc (**C**) and give **5a′** through nucleophilic addition.[11]

In considering the role of the zincate complex, we optimized the rearrangement of 2-hydroxymethyl-1-phenylcyclopropanol (**3b**; Table 1). Treatment of **3b** with two equivalents of dimethylzinc (Table 1, entry 2) or three equivalents of butyllithium (Table 1, entry 3) resulted in complete recovery of the starting material. One equivalent of zinc(II) chloride and three equivalents of butyllithium, however, gave the desired product in 88% yield (Table 1, entry 4). The combination was expected to form a zincate complex with alkoxy and butyl groups. The reaction became sluggish if the proportion of butyllithium to zinc(II) chloride was decreased (Table 1, entries 5 and 6) because the conditions would not allow formation of a zincate complex, such as $(RO)_2BuZnLi$. A stoichiometric amount of zincate (tBu_3ZnLi),[12,13] which can be

Table 1. The rearrangement of **3b** into **5b**.



Entry	Reagent	t [h]	Yield[a] [%]
1	$CH_2(ZnI)_2$ (1 equiv)	3	18
2	Me_2Zn (2 equiv)	3	0[b]
3	BuLi (3 equiv)	3	0[b]
4	BuLi (3 equiv)/$ZnCl_2$ (1 equiv)	3	88
5	BuLi (3 equiv)/$ZnCl_2$ (2 equiv)	3	53
6	BuLi (2 equiv)/$ZnCl_2$ (1 equiv)	3	0[c]
7	tBu_3ZnLi (1 equiv)	3	70
8	tBu_3ZnLi (0.2 equiv)/BuLi (2 equiv)	6	88
9	tBu_3ZnLi (0.1 equiv)/BuLi (2 equiv)	12	65

[a] The yield was determined by using ^1H NMR spectroscopy with bromoform as the internal standard. [b] The starting material was recovered completely. [c] A complex mixture was obtained.

prepared easily from $ZnCl_2$ and tBuLi, was also effective in this rearrangement (Table 1, entry 7). Treatment of the prepared lithium alkoxide of **3b** with a catalytic amount of tBu_3ZnLi also gave **5b** (Table 1, entries 8 and 9).

We traced the rearrangement of **3b** with reactIR (Figure 1).[14] The reaction proceeded gradually, and was almost complete after 4.5 h.

To determine the generality of the rearrangement, we treated various lithium alkoxides of 2-(1-hydoxyalkyl)-1-alkylcyclopropanol **3** with the zincate complex as a catalyst (Table 2). Substrates **3c** and **3d** gave the corresponding 1,2-diols in good yields (Table 2, entries 1 and 2). Cyclopropyl alkyl carbinols were also converted into the corresponding 1,2-diols in good yields with a low diastereoselectivity

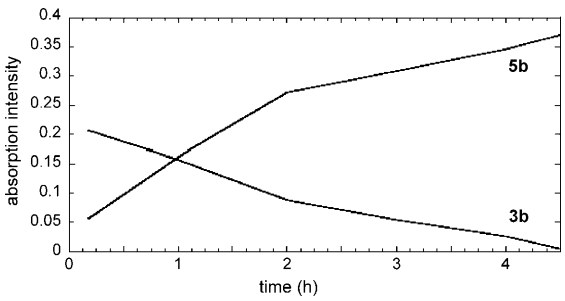
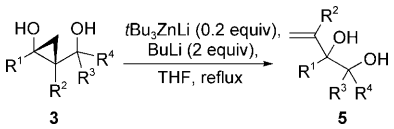
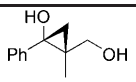
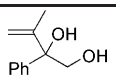
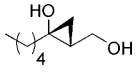
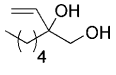
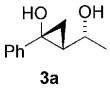
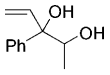
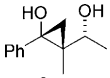
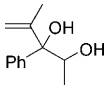
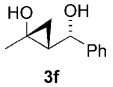
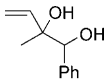
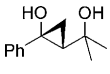
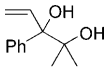
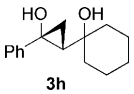
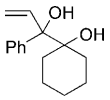


Figure 1. ReactIR results for the conversion of **3b** into **5b**.

Table 2. Examples of the rearrangement of **3** into **5**.



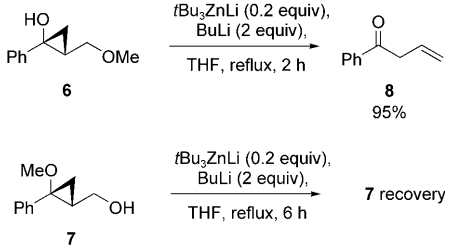
3 **5**

Entry	Substrate	Product	*t* [h]	Yield[a] [%]
1	 **3c**	 **5c**	24	89
2	 **3d**	 **5d**	24	89
3	 **3a**	 **5a**	24	78 d.r. (3:2)[b,c]
4	 **3e**	 **5e**	24	98 d.r. (2:1)[b,d]
5	 **3f**	 **5f**	24	86 d.r. (3:1)[b,e]
6[f]	 **3g**	 **5g**	1	57[g]
7[h]	 **3h**	 **5h**	1	n.d.[i]

[a] Isolated yields. [b] The diastereomeric ratios were determined by using 1H NMR spectroscopy. [c] The stereochemistry of the major product was (2*S**,3*R**). [d] The stereochemistry of major product was (2*S**,3*S**). [e] The stereochemistry of the major product was (2*S**,3*R**). [f] The reaction was carried out at 47 °C. [g] Propiophenone was also obtained in 30% yield. [h] The reaction was carried out at 60 °C. [i] Propiophenone and cyclohexanone were obtained in 68 and 52% yield, respectively.

(Table 2, entries 3–5). In the case of cyclopropyl dimethyl carbinol **3g**, the corresponding diol was obtained in 57% yield (Table 2, entry 6). It is worth noting in this case that propiophenone was also obtained in 30% yield. Moreover, when substrate **3h** was treated under these conditions at 60 °C, 1-phenyl-1-propanone and cyclohexanone were obtained (Table 2, entry 7). In this case, the rearranged product was not obtained. The ketones may come from the reaction intermediate (**B** in Scheme 4).[11]

As shown in Scheme 5, we attempted the rearrangement with the mono-protected form



6 **7**

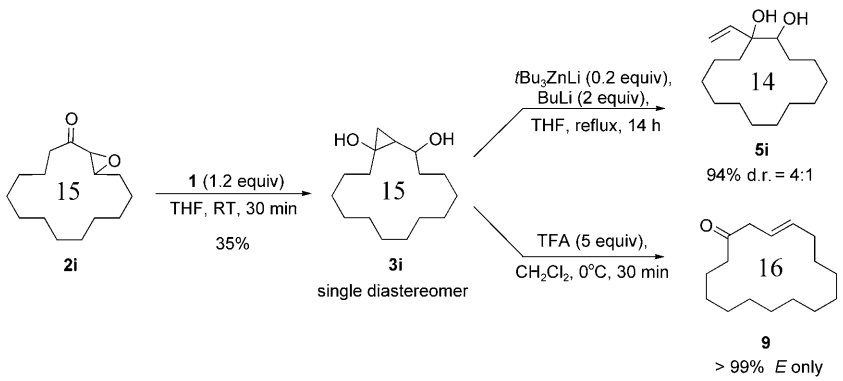
Scheme 5. The reaction of a mono-protected substrate under the rearrangement conditions.

of the diols. The rearrangement did not proceed with substrates **6** or **7**, which have ether groups. In the case of **6**, the corresponding β,γ-unsaturated ketone **8** was obtained quantitatively via cyclopropane ring-opening followed by elimination of methoxy group. Treatment of **7** resulted in complete recovery of the starting material. These results demonstrate the importance of zinc dialkoxide formation (**3a″** in Scheme 4) in the rearrangement.

When the rearrangement is applied to the lithium alkoxide of a bicyclic compound, a ring-contracting reaction occurs. In the case of bicyclo[13.1.0]hexadecane-1,14-diol (**3i**),[15] the zincate-catalyzed reaction gave 14-membered diol **5i** (1-vinylcyclotetradecan-1,2-diol; Scheme 6). The stereochemistry of the major product is (1*R**,2*S**). With the same substrate, the Julia-type reaction with trifluoroacetic acid gave the corresponding ring-expanded product **9**. Meanwhile, treatment of the lithium alkoxide of spirocyclic diol **3j** with *t*Bu$_3$ZnLi gave the corresponding ring-expanded product **5j** in good yield (Scheme 7).

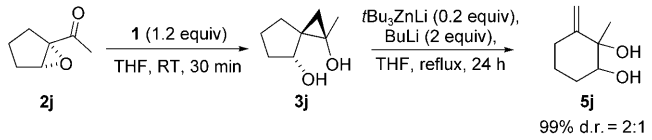
The substrate, 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, is prepared from α,β-epoxyketone **2** and dizinc **1**.[5] We applied this method to α,β-aziridinylketone **10** and obtained 2-(1-aminoalkyl)-1-alkylcyclopropanol **11**. Product **11** was also available as a substrate of the rearrangement and, in this case, the corresponding *vic*-amino alcohol **12** was obtained as a single isomer (Scheme 8).

Enantioenriched **3** can be easily obtained from optically active **2**, which can be prepared by a Katsuki–Sharpless asymmetric epoxidation followed by a Swern oxidation. If the rearrangement proceeds in a stereospecific manner, this

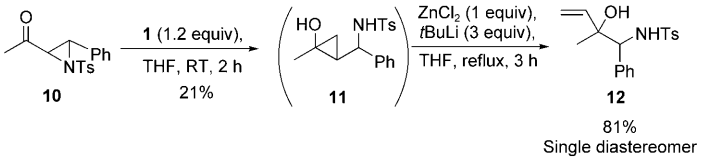


2i **3i** single diastereomer

Scheme 6. The rearrangement of **3i** to **5i**.



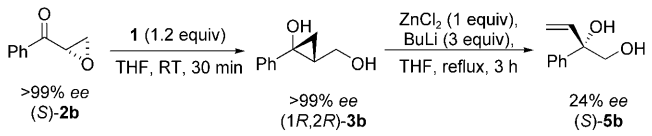
Scheme 7. The rearrangement of **3j** to **5j**.



Scheme 8. The transformation of **10** to **12** by a [2+1] cyclization with bis(iodozincio)methane.

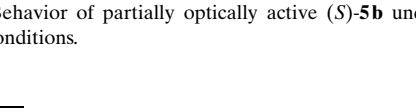
can be a useful method for constructing enantioenriched *vic*-diols. Therefore, we studied the stereochemistry of the rearrangement in detail.

The reaction with optically pure (1*R*,2*R*)-**3b** gave (*S*)-**5b**[16] with a loss of enantiomeric purity (Scheme 9). To explain the loss of enantiomeric purity during the reaction, we propose three possibilities: 1) A racemization of the product proceeds under the reaction condition; 2) the rearrangement is not stereospecific; or 3) a racemization of the substrate proceeds under the reaction condition. To clarify the cause of the loss of enantiomeric purity, we conducted the following experiment.



Scheme 9. The rearrangement of optically active **3b**.

If the obtained optically active product, (*S*)-**5b** (59% *ee*), was treated under the same conditions as in the rearrangement, no significant loss of enantiomeric purity was detected (Scheme 10). We also tracked the enantiomeric purity of substrate (1*R*,2*R*)-**3b** and product (*S*)-**5b** during the reaction. The result is shown in Figure 2. A decrease in the enantiomeric purity of **3b** was observed, and that of **5b** also was gradually lost at the same time. The result in Figure 2 implies that the enantiomeric purity of product **5b** depends on that of starting material **3b**. The rearrangement may proceed in a stereospecific manner, but the racemization of the substrate may determine the enantiomeric purity of the product.



Scheme 10. Behavior of partially optically active (*S*)-**5b** under the rearrangement conditions.

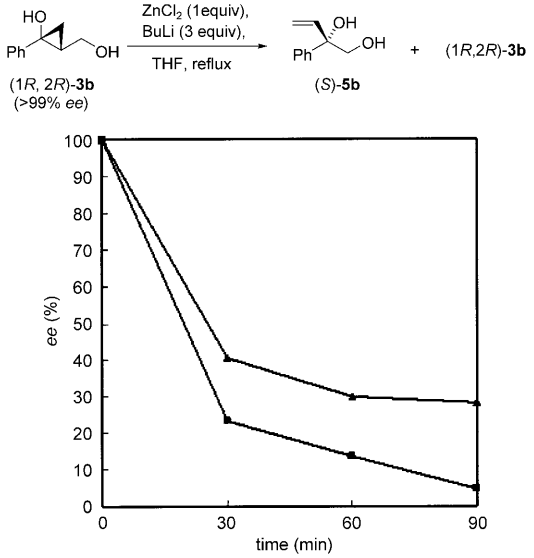
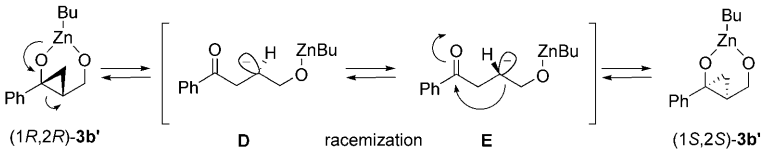


Figure 2. Measurement of the *ee* of (1*R*,2*R*)-**3b** (■) and (*S*)-**5b** (▲) during the reaction.

It should be noted that the diastereomer of **3b** was not observed during the reaction, even though the enantiomeric purity was gradually lost. The substrate recovered at each point had a *cis* configuration. We suppose that the racemization of **3b** proceeds as shown in Scheme 11.[17] Zinc alkoxide (1*R*,2*R*)-**3b′** is converted into β-carbanion **D** by cyclopropane ring-opening with an electron-donating effect from the electron-rich zinc atom. Racemization of carbanion **D** may proceed under the THF reflux conditions and give **E**. Formation of a cyclopropane ring from **E** gives the opposite enantiomer of the substrate, (1*S*,2*S*)-**3b′**.[18]



Scheme 11. Proposed mechanism for the isomerization of **3b′** under the reaction conditions.

Based on all these results, we attributed the loss of enantiomeric purity of the product to the racemization of the substrate.

Conclusions

We found some novel rearrangements of lithium alkoxides of 2-(hydroxyalkyl)-1-alkylcyclopropanols that were mediated by a zincate complex. Various types of substrates are available and the reaction can be applied for fascinating transformations of molecular skeleton. And at the same time, we have proposed the ability of the zincate complex to donate electrons.[19] This electron-pushing effect may apply to other reactions.

Experimental Section

General procedure for the rearrangement: tBu$_3$ZnLi was prepared according the procedure reported in reference [13g]. tBuLi (1.6 M in pentane, 3 mmol) was added to a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3**, 1 mmol) in THF (8 mL) at 0 °C and stirred for 10 min. The prepared tBu$_3$ZnLi (THF solution, 0.2 mmol) was added to the solution at 0 °C and the mixture was heated to reflux. Then saturated aqueous NH_4Cl was added to quench the reaction and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by using silica gel column chromatography to give the corresponding *vic*-diol.

Acknowledgements

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[1] For recent examples, see: a) S. K. Jackson, A. Karadeolian, A. B. Driega, M. A. Kerr, *J. Am. Chem. Soc.* **2008**, *130*, 4196; b) T. Ok, A. Jeon, J. Lee, J. H. Lim, C. S. Hong, H.-S. Lee, *J. Org. Chem.* **2007**, *72*, 7390; c) M. Tanaka, M. Ubukata, T. Matsuo, K, Yasue, K. Matsumoto, Y. Kajimoto, T. Ogo, T. Inaba, *Org. Lett.* **2007**, *9*, 3331; d) T. Tada, Y. Ishida, K. Saigo, *Org. Lett.* **2007**, *9*, 2083; e) A. Srikrishna, R. R. Babu, P. C. Ravikumar, *Synlett* **2007**, 0655; f) H. Fujii, Y. Osa, M. Ishihara, S. Hanamura, T. Nemoto, M. Nakajima, K. Hasebe, H. Mochizuki, H. Nagase, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4978; g) N. T. Tzvetkov, T. Arndt, J. Mattay, *Tetrahedron* **2007**, *63*, 10497.

[2] For representative examples, see: a) D. H. Gibson, C. H. DePuy, *Chem. Rev.* **1974**, *74*, 605; b) O. G. Kulinkovich, *Chem. Rev.* **2003**, *103*, 2597; c) R. I. Khusnutdinov, U. M. Dzhemilev, *J. Organomet. Chem.* **1994**, *471*, 1–18; d) S. C. Wang, D. J. Tantillo, *J. Organomet. Chem.* **2006**, *691*, 4386; e) M. Rubin, M. Runina, V. Gevorgyan, *Chem. Rev.* **2007**, *107*, 3117; f) J. E. Baldwin, *Chem. Rev.* **2003**, *103*, 1197; g) H.-U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151; h) M. Yu, B. L. Pagenkoph, *Tetrahedron* **2005**, *61*, 321.

[3] For examples, see: a) H. Rinderhagen, P. A. Waske, J. Mattay, *Tetrahedron* **2006**, *62*, 6589; b) T. Irshaidat, *Tetrahedron Lett.* **2008**, *49*, 5894; c) A. E. Nadany, J. E. Mckendrick, *Tetrahedron Lett.* **2007**, *48*, 4071; d) A. D. Allen, M. F. Fenwick, H. H. Riyad, T. T. Tidwell, *J. Org. Chem.* **2001**, *66*, 5759; e) A. L. J. Beckwith, V. W. Bowry, *J. Org. Chem.* **1989**, *54*, 2681; f) A. L. J. Beckwith, V. W. Bowry, *J. Am. Chem. Soc.* **1994**, *116*, 2710; g) B. S. J. Blagg, M. B. Jarstfer, D. H. Rogers, C. D. Poulter, *J. Am. Chem. Soc.* **2002**, *124*, 8846; h) K. B. Wiberg, G. Szeimies, *J. Am. Chem. Soc.* **1968**, *90*, 4195.

[4] a) M. Julia, S. Julia, R. Guegan, *Bull. Soc. Chim. Fr.* **1960**, 1072; b) M. Julia, S. Julia, S.-Y. Tchen, *Bull. Soc. Chim. Fr.* **1961**, 1849; c) K. Sakaguchi, M. Fujita, Y. Ohfune, *Tetrahedron Lett.* **1998**, *39*, 4313; d) K. Sakaguchi, M. Higashino, Y. Ohfune, *Tetrahedron* **2003**, *59*, 6647; e) M. Honda, Y. Yamamoto, H. Tsuchida, M. Segi, T. Nakajima, *Tetrahedron Lett.* **2005**, *46*, 6465; f) M. Honda, T. Mita, T. Nishizawa, T. Sano, M. Segi, T. Nakajima, *Tetrahedron Lett.* **2006**, *47*, 5751; g) S. R. Wilson, A. E. Davey, M. E. Guazzaroni, *J. Org. Chem.* **1992**, *57*, 2007; h) C. Singh, S. Pandey, G. Saxena, N. Srivastava, M. Sharma, *J. Org. Chem.* **2006**, *71*, 9057.

[5] K. Nomura, K. Oshima, S. Matsubara, *Angew. Chem.* **2005**, *117*, 6010; *Angew. Chem. Int. Ed.* **2005**, *44*, 5860.

[6] K. Nomura, S. Matsubara, *Synlett* **2008**, 1412.

[7] a) T. Sato, T. Kikuchi, N. Sootome, E. Murayama, *Tetrahedron Lett.* **1985**, *26*, 2205; b) T. Sato, T. Kikuchi, H. Tsujita, A. Kaetsu, N. Sootome, K. Nishida, K. Tachibana, E. Murayama, *Tetrahedron* **1991**, *47*, 3281; c) C. Brükner, H. Reissig, *J. Org. Chem.* **1988**, *53*, 2440; d) C. Toratsu, T. Fujii, T. Suzuki, K. Takai, *Angew. Chem.* **2000**, *112*, 2837; *Angew. Chem. Int. Ed.* **2000**, *39*, 2725.

[8] Preparation of bis(iodozincio)methane was accompanied by formation of zinc(II) iodide. The Lewis acidity of zinc(II) iodide seems to be sufficient for β,γ-unsaturated ketone formation. See: S. Matsubara, H. Yoshino, Y. Yamamoto, K. Oshima, H. Matsuoka, K. Matsumoto, K. Ishikawa, E. Matsubara, *J. Organomet. Chem.* **2005**, *690*, 4859.

[9] K. Nomura, S. Matsubara, *Chem. Commun.* **2009**, 2212.

[10] Treatment of an α,β-unsaturated ketone with an aldehyde in the presence of chromium(II) gives 2-(1-hydroxyalkyl)-1-alkylcyclopropanol. Meanwhile, the same reaction with the addition of chlorotrimethylsilane affords cross-pinacol coupling product. See: a) K. Takai, R. Morita, C. Toratsu, *Angew. Chem.* **2001**, *113*, 1150; *Angew. Chem. Int. Ed.* **2001**, *40*, 1116; b) K. Takai, R. Morita, H. Matsushita, C. Toratsu, *Chirality* **2003**, *15*, 17.

[11] Still and Macdonald have reported that α-alkoxyallyl carbanions undergo preferential protonation and alkylation at the unsubstituted terminus and react with carbonyl compounds at the alkoxy-substituted terminus. See, W. C. Still, T. L. Macdonald, *J. Org. Chem.* **1976**, *41*, 3620.

[12] M. Isobe, S. Kondo, N. Nagasawa, T. Goto, *Chem. Lett.* **1977**, 679.

[13] For representative examples, see: a) T. Harada, T. Katsuhira, D. Hara, Y. Kotani, K. Maejima, R. Kaji, A. Oku, *J. Org. Chem.* **1993**, *58*, 4897; b) T. Harada, T. Katsuhira, K. Hattori, A. Oku, *Tetrahedron* **1994**, *50*, 7987; c) Y. Kondo, M. Fujinami, M. Uchiyama, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **1997**, 799; d) T. Harada, T. Kaneko, T. Fujiwara, A. Oku, *J. Org. Chem.* **1997**, *62*, 8966; e) T. Harada, T. Kaneko, T. Fujiwara, A. Oku, *Tetrahedron* **1998**, *54*, 9317; f) Y. Kondo, T. Komine, M. Fujinami, M. Uchiyama, T. Sakamoto, *J. Comb. Chem.* **1999**, *1*, 123; g) M. Uchiyama, T. Furuyama, M. Kobayashi, Y. Matsumoto, K. Tanaka, *J. Am. Chem. Soc.* **2006**, *128*, 8404.

[14] The reactIR measurement was conducted every 30 s. Figure 1 shows the absorption intensity of **3b** and **5b** plotted every 30 min to simplify the figure. See the Supporting Information for more details.

[15] Although **3i** was used as a single diastereomer form, we could not determine the relative stereochemistry of **3i**.

[16] Compared with the result of specific rotation in the literature, it was found that **5b** has (*S*)-configuration. See: M. E. Vargas-Diaz, L. Chacon-Garcia, P. Valezquez, J. Tamariz, P. Joseph-Nathan, L. G. Zepeda, *Tetrahedron: Asymmetry* **2003**, *14*, 3225.

[17] a) D. Seyferth, L. G. Vaughan, *J. Am. Chem. Soc.* **1964**, *86*, 883; b) Y. D. Wu, K. N. Houk, J. A. Marshall, *J. Org. Chem.* **1990**, *55*, 1421; c) E. J. Verner, T. Cohen, *J. Am. Chem. Soc.* **1992**, *114*, 375; d) K. Tomooka, T. Igarashi, M. Watanabe, T. Nakai, *Tetrahedron Lett.* **1992**, *33*, 5795; e) R. Hoffmann, T. Rückert, R. Brückner, *Tetrahedron Lett.* **1993**, *34*, 297; f) K. Tomooka, T. Igarashi, T. Nakai, *Tetrahedron Lett.* **1993**, *34*, 8139; g) R. Gawley, *Tetrahedron Lett.* **1999**, *40*, 4297.

[18] Although we attempted to trap **D** and **E** with allyl bromide and methyl iodide, the corresponding β-allylated ketone or β-methylated ketone was not obtained.
[19] Kondo and Uchiyama have reported the directed *ortho* metalation of aromatic compounds, such as ethyl benzoate, with di-*tert*-butyl-TMP zincate (LiZn(tmp)tBu$_2$). The reaction directly affords *o*-zincated aromatic compounds. This reactivity is in contrast to the low basicity found for conventional zinc reagents. Because the ligand on the zinc atom of the zincate has stronger basicity than that on conventional zinc reagents, we are expecting that a ligand of zincate complex, such as an alkoxy group, has an ability as electron donor. See: Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539.

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