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Bismuth-Mediated Diastereoselective Allylation Reaction of Carbonyl Compounds with Cyclic Allylic Halides or Cinnamyl Halide

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Abstract. An efficient diastereoselective allylation of various carbonyl compounds with cyclic allylic halides by using commercially available bismuth powder in the presence of LiI was developed. Among all the metals screened, bismuth was found to be the best mediator for the transformation. The reactions involving various cyclic allylic halides proceeded smoothly at room temperature to produce the desired homoallylic alcohols in good to excellent yields with high diastereoselectivities (>99:1 dr). Reversed

Introduction

Metal-mediated additions of allylic halides to carbonyl compounds serve as an efficient method for the synthesis of synthetically versatile homoallylic alcohols which important are intermediates in organic synthesis.^[1,2] When ysubstituted allylic halides were used as substrates, normally the reactions proceeded via an S_N2'-type pathway to generate a mixture of two diastereomers, having the potential to predominantly produce only one diastereomer, depending on the substrates used. For typical examples, Knochel and co-workers have demonstrated that pre-prepared cyclic allylic aluminium^[3a] or zinc^[3b] reagents, derived from the insertion of metal into cyclic allylic halides, could efficiently react with carbonyl compounds to afford the corresponding homoallylic alcohols with excellent diastereoselectivity. However, in their cases, the reactions need to be performed under strictly anhydrous conditions with the use of preformed cyclic allylic metallic reagents. Although indium could be used as reaction mediator for the analogous allylation reactions as well. somewhat erosion of product diastereoselectivity (mostly 90:10 dr) was observed.^[3c] Thus, the development of a one-pot,

diastereoselectivity was obtained when carbonyl substrate (e.g., 2-pyridinecarboxaldehyde, glyoxylic acid) containing I chelating substituent was used in the allylation reaction. In addition, the reactions involving acyclic (E)-cinnamyl bromide as substrate worked equally well with high diastereocontrol.

Keywords: Bismuth; Cyclic Allylic Halide; Allylation; Homoallylic alcohol; Diastereoselectivity

operationally simple, and highly diastereoselective allylation of carbony compounds by using cyclic allylic halides as substrates in the presence of a metal mediator is still highly desirable, especially under relatively loose conditions without the preclusion of air and moisture.

In recent decades, the use of bismuth(0 or III) in organic synthesis has aroused considerable attention from synthetic community because of its mild reactivity, low toxicity, relatively cheap cost, and good functional group compatibility.^[4] However, compared with other metals^[5] (such as Mg, Zn, Al, Sn, In, etc.), the use of bismuth(0) as reaction mediator in organic synthesis has been rarely studied. In this context, metallic bismuth, especially commercial but unactivated bismuth powder, has not been widely employed in allylation reaction due to its poor reactivity and the existence of an oxide layer on the metal surface which needs to be removed by preactivation.^[6,7,8] In continuation of our efforts to develop metal-mediated organic transformations,^[9] herein we describe an efficient and highly diastereoselective allylation reaction of various carbonyl compounds with cyclic allylic halides or cinnamyl bromide by using commercially available bismuth powder as reaction mediator in the presence

of LiI as reaction additive in DMF. The reactions proceeded smoothly at room temperature to produce the desired homoallylic alcohols in good to excellent yields with high diastereoselectivities (>99:1 dr). Remarkably, reversed diastereoselectivity was obtained when carbonyl substrate (e.g., 2pyridinecarboxaldehyde, glyoxylic acid) containing chelating substituent was used in the allylation reaction.

Results and Discussion

Table 1. Optimization of reaction conditions.[a]

| CI | + Br | Bi additive or catalyst conditions | |
|----|------|--|----|
| 1a | 2a | | 3a |

| Entry | Additive or Catalyst | Conditions | Yield [%] ^[b] |
|-------|----------------------------------|------------------------------|-------------------------------|
| 1 | | DMF, 120 °C, 12 h | 23 |
| 2 | InCl ₃ (0.1 equiv) | DMF, 120 °C, 12 h | 32 |
| 3 | PbCl ₂ (0.1 equiv) | DMF, 120 °C, 12 h | 24 |
| 4 | Yb(OTf) ₃ (0.1 equiv) | DMF, 120 °C, 12 h | 50 |
| 5 | CuCl (2 equiv) | DMF, 120 °C, 12 h | 4 |
| 6 | I ₂ (2 equiv) | DMF, 120 °C, 12 h | 29 |
| 7 | NaI (2 equiv) | DMF, 120 °C, 12 h | 65 |
| 8 | LiCl (2 equiv) | DMF, 120 °C, 12 h | 70 |
| 9 | LiI (2 equiv) | DMF, 120 °C, 12 h | 79 |
| 10 | LiI (2 equiv) | DMF, 120 °C, 24 h | 72 |
| 11 | LiI (2 equiv) | DMF, 120 °C, 48 h | 69 |
| 12 | LiI (2 equiv) | DMF, 60 °C, 12 h | 82 |
| 13 | LiI (2 equiv) | DMF, rt, 12 h | 98 (96) ^[c] |
| 14 | LiI (2 equiv) | THF, rt, 12 h | 97 |
| 15 | LiI (2 equiv) | CH ₃ CN, rt, 12 h | 83 |
| 16 | LiI (2 equiv) | DME, rt, 12 h | 63 |
| 17 | LiI (2 equiv) | Et ₂ O, rt, 12 h | 4 |
| 18 | LiI (2 equiv) | DMSO, rt, 12 h | 98 |

^[a] The reactions were performed at room temperature to 120
^oC for 12-48 h by using 4-chlorobenzaldehyde (1a, 1 mmol),
3-bromocyclohexene (2a, 3 mmol), Bi (3 mmol), and additive (0.1-2 equiv) in organic solvent (2 mL).
^[b] Yields were determined by NMR analysis of crude reaction mixture after work-up by using 1,4-dimethoxybenzene as an internal standard.
^[c] Isolated yield.

Initial studies were focused on optimization of reaction conditions by using 4-chlorobenzaldehyde (1a) and 3-bromocyclohexene (2a) as model substrates in the presence of bismuth powder (preactivated by 1,2-dibromoethane and TMSCI) and different additives/catalysts in DMF at 120 °C for 12 h. As shown in Table 1, poor yield was obtained

when the reaction was performed in the absence of any additive or catalyst (entry 1). Among the different additives/catalysts (e.g., $InCl_3, [1b,2j,10,11]$ PbCl₂, [10,12] CuCl, [13] LiCl, [3b,10,14] LiI[15]) screened (entries 2-9), LiI was found to be the optimum additive for the allylation, giving rise to the desired product 3a in 79% NMR yield with >99:1 dr (entry 9). In addition, it was found that the product yield gradually diminished when the reaction time was prolonged from 12 h to 48 h (entries 9-11), indicating that the product 3a might not be very stable at 120 °C. Moreover, decreasing the reaction temperature from 120 °C to room temperature led to overall enhancement of reaction performance (96% isolated yields; entries 12-13), a reflection of the relative stability of the generated product at room temperature. Further screening of reaction solvents (entries 14-18) revealed that comparably high reaction efficiency could also be achieved by performing the model reaction either in THF (97% NMR yield, entry 14) or in DMSO (98% NMR yield, entry 18).

A further study of the equivalents of substrate **2a** and bismuth powder showed that similarly high product yield (96% NMR yield) could also be obtained by decreasing the amount of bismuth powder from 3 equiv to 2 equiv (Table 2, entry 2). However, decreasing the amount of substrate **2a** from 3 equiv to 2 equiv led to remarkably decreased product yield (Table 2, entry 3).

Table 2. Optimization of reaction conditions by usingdifferent equivalents of 2a and bismuth powder.

| CI- | CHO la | 2a (X equiv.) Bi (Y equiv.) LiI (2 equiv.) DMF, rt, 12 h | | OH |
|--------------------------------------|-----------|--|-------|--------------------------|
| Entry | 2a | | Bi | Yield [%] ^[a] |
| 1 | 3 equiv | 3 | equiv | 98 |
| 2 | 3 equiv | 2 | equiv | 96 |
| 3 | 2 equiv | 3 | equiv | 78 |
| [a] $\mathbf{V}_{i+1}\mathbf{J}_{i}$ | | | | |

^[a] Yields were determined by NMR analysis of crude reaction mixture after work-up by using 1,4dimethoxybenzene as an internal standard.

In addition, a spectrum of metals (pre-activated by 1,2-dibromoethane and TMSCl), including In, Cr, Sm, Zn, Fe, Mg, Al, Mn, and Pb were also investigate. (Table 3). However, under the above optimized reaction conditions, bismuth was found to be the best mediator for the present allylation reaction, in terms of both product yield and diastereoselectivity (98% NMR yield, >99:1 dr, entry 1). It should be noted that, without the pre-activation of bismuth powder by 1,2-dibromoethane and TMSCl, a decreaded yield of the product 3a was obtained (82% NMR yield, entry 1). In comparison, except indium metal which mediated the reaction in 79% NMR yield with relatively good diastereoselectivity (entry 2), the use of other metals mostly led to poor product yields (entries 3-10).

Although Knochel and co-workers have reported that pre-prepared cyclic allylic aluminium^[3a] or zinc^[3b] reagents could efficiently react with carbonyl compounds to afford the corresponding homoallylic alcohols with excellent diastereoselectivity, Al and Zn powder almost failed to promote the allylation reaction under optimized reaction conditions. Encouraged by the above results, subsequently we continued our task to explore the substrate scope of the reactions by using various aldehydes and cyclic allylic halides as substrates.

Table 3. Optimization of reaction conditions by using different metals.^[a]

| Cl la | 2a (3 equiv.) metal (2 equiv.) LiI (2 equiv.) DMF, rt, 12 h | |
|----------------|--|--------------------------|
| Entry | Metal ^[b] | Yield [%] ^[c] |
| 1 | Bi | 98 (82) ^[d] |
| 2 | In | 79 ^[e] |
| 3 | Cr | 0 |
| 4 | Sm | 0 |
| 5 | Zn | <10 |
| 6 | Fe | 0 |
| 7 | Mg | 35 ^[f] |
| 8 | Al | <10 |
| 9 | Mn | 0 |
| 10 | Pb | <5 |
| [a] 771 | | 0 1 |

^[a] The reactions were performed at room temperature for 12 h in DMF by using aldehyde 1a (1 mmol), 3-bromocyclohexene (2a, 3 mmol), metal (2 mmol), and LiI (2 mmol) in DMF (2 mL).
^[b] Unless otherwise noted, the metal was preactivated by 1,2-dibromoethane and TMSC1
^[c] Yields were determined by NMR analysis of crude reaction mixture after work-up by using 1,4-dimethoxybenzene as an internal standard.

^[d] Bismuth powder was not pre-activated by 1,2-dibromoethane and TMSCl.

^[e] 93:7 dr.

^[f] 52:48 dr.

As listed in Table 4, under the optimized reaction conditions, the bismuth-mediated allylation reaction involving a wide array of aldehydes took place with high efficiency to give the anticipated homoallylic alcohols in moderate to good yields with excellent diastereoselectivity (>99:1 dr). In addition to the high performance observed with aryl aldehydes, heteroaryl aldehydes (entries 9-10) and alkyl aldehydes (entries 12-14) were also proven to be suitable substrates for the reaction. Moreover, the allylation reaction occurred selectively at the formyl group of α , β unsaturated aldehyde **11**, rather than proceeding at the C-C double bond via a Michael-type reaction pathway (entry 11). Furthermore, the reaction could also be applied to the use of ferrocenyl aldehyde as starting





^[a] The reactions were performed at room temperature for 12 h by using aldehyde **1b-p** (1 mmol), 3bromocyclohexene (**2a**, 3 mmol), Bi (2 mmol), LiI (2 mmol) in DMF (2 mL). ^[b] Isolated yields.

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material (entry 15). Besides, the reactions employing bismuth as mild reaction mediator also allowed the use of aryl aldehydes bearing functional groups, such as nitro, cyano, and carbonyl group (entries 1-3).

Table 5. Substrate scope study by employing different cyclic allylic bromides.^[a]

| (| | $Y^X \underline{B}$ | i (2 equiv.) |
|-------|----------|---------------------|-------------------------------------|
| R | H H 1 21 | Li n Dif | iI (2 equiv.) WF, rt, 12 h 3 |
| | Cl I | C1 | Br Br |
| | \frown | | |
| | | \sim | |
| Entry | Aldehyde | Allylic bromide | Product (Yield ^[b] ; dr) |
| | | oronnae | ОН |
| | | | |
| 1 | 1c | 2b | 3c (98%; >99:1) |
| | | | |
| | | | |
| 2 | 1d | 2b | 3d (99%; >99:1) |
| | | | |
| | | | |
| 3 | 1d | 2c | $MeO_2C' > 3d (94\%; >99:1)$ |
| | | | OH A L A |
| | | | |
| | | | NC' 🖉 📈 |
| 4 | 1c | 2d | 3q (93%; >99:1) OH |
| | | | |
| _ | _ | | NC |
| 5 | 1c | 2e | 3r (71%; >99:1) OH |
| | | | |
| 6 | 14 |)f | MeO_2C |
| 0 | IU | 21 | OH |
| | | | |
| 7 | 1. | 26 | |
| / | 18 | 21 | st (80%; >99:1) |

^[a] The reactions were performed at room temperature for 12 h by using aldehyde **1** (1 mmol), cyclic allylic halides **2b-f** (3 mmol), Bi (2 mmol), and LiI (2 mmol) in DMF (2 mL).

^[b] Isolated yields.

Next, substrate scope of the present protocol was further surveyed by using various cyclic allylic halides as starting materials. As outlined in Table 5, the reactions employing 3-chlorocyclohexene and 3iodocyclohexene as substrates worked equally well under the optimum reaction conditions to give the expected products with both excellent yields and excellent diastereoselectivities (entries 1-3). Sixmembered allylic chloride **2d** bearing two methyl groups reacted with equal success under the optimal reaction conditions (entry 4). Moreover, both sevenmembered and eight-membered allylic bromides were demonstrated to be appropriate candidates for the present organic transformations and reacted in an analogous manner to afford the corresponding homoallylic alcohols **3r-t** in 71%-99% yields, with the exclusive formation of the *syn*-diastereomer (entries 5-7).

In comparison, the same reaction using less reactive acetophenone as substrate proceeded sluggishly under the optimized reaction conditions to give the desired product in negligible amount. This mildness of the present protocol allowed the selective allylation of aldehyde in the co-existence of ketone. For instance, when biphenyl **1q** containing both formyl and acetyl substituents were treated with cyclic allylic bromide 2a in the presence of bismuth and LiI under the well-established reaction conditions, the reaction took place regioselectively at the formyl group, leading to the expected product **3u** in 96% yield with >99:1 dr (Scheme 1). The reluctancy of acetyl group to participate in the allylation reaction clearly indicated that the in situ formed allylic bismuth reagent was a mild organometallic reagent. when compared to its allylic aluminium^[3a] or zinc^[3l] counterparts which might react with both aldehyde and ketone without regioselectivity.



Scheme 1. Selective allylation of formyl group of substrate **1q** in the presence of acetyl group.





Scheme 2 Bismuth-mediated highly diastereoselective allylation reaction using isatin (1r or 1s) as substrate; X-ray crystal structure of product 3w (CCDC 1858982; only one of the two enantiomers is shown here).

In contrast with acetophenone which was not susceptible to the present allylation, ketones 1r and 1s containing electron-withdrawing groups at their α -position reacted efficiently with 3-bromocyclohexene (2a) to deliver the target products 3v and 3w in good yields with excellent diastereoselectivities (Scheme 2). The stereochemistry of the homoallylic alcohol 3w was fully characterized by single crystal X-ray diffraction analysis.^[16]

It was reported that tin-mediated allylation of 2pyridinecarboxaldehyde with acyclic allylic halide might lead to the generation of homoallylic alcohol with the reversal of product stereochemistry.^[2d] To test whether the same principle could also be applied to the present transformation using cyclic allylic halide as substrate, we also examined the reaction of 2-pyridinecarboxaldehyde (1t and 1u) with six-, seven-, and eight-membered cyclic allylic bromides (2a and 2e-f). As expected, the reactions proceeded efficiently under the optimum reaction conditions to provide the products 4a-e in good yields with exclusive inversion of stereochemistry, with the antidiastereomer being the exclusive diastereomer (Scheme 3). The stereochemistry of product 4a was unambiguously determined with the aid of X-ray crystal diffraction analysis.^[16]



Scheme 3. Bismuth-mediated highly diastereoselective allylation using 2-pyridinecarboxaldehyde (**1t** and **1u**) as substrate with inversion of stereochemistry; X-ray crystal structure of product **4a** (CCDC 1858983; only one of the two enantiomers is shown here).

Similarly, glyoxylic acid might also react in a same manner to produce the anticipated homoallylic alcohol with the inversion of product diastereoselectivity.^[2d] As shown in Scheme 4, the reactions involving cyclic allylic bromides (**2a** and **2f**) and glyoxylic acid (1v) or phenylglyoxylic acid (1w) worked with the same high performance, delivering the expected products **4f-h** with both excellent yields and diastereoselectivities, with the *anti*-diastereomer being the exclusive product. The stereochemistry of the homoallylic alcohol **4g** was unambiguously determined by X-ray diffraction analysis.^[16]



Scheme 4. Bismuth-mediated highly diastereoselective allylation using glyoxylic acid (1v) or phenylglyoxylic acid (1w) as substrate; X-ray crystal structure of product 4g (CCDC 1858981; only one of the two enantiomers is shown here).

Aside from cyclic allylic halides, exceptionally high performance could also be accomplished by employing acyclic allylic halides of (*E*)-cinnamyl bromide as substrate. As outlined in Scheme 5, (*E*)cinnamyl bromide (**2g**) efficiently participated in allylation reaction with aromatic aldehydes **1c-e** to furnish the corresponding homoallylic alcohols **4i-k** with both excellent yield and diastereoselectivity (exclusive generation of *anti*-diastereomer). In addition, the mild reaction conditions also allowed the tolerance of cyano and carbonyl groups.



Scheme 5. Bismuth-mediated highly diastereoselective allylation using (E)-cinnamyl bromide (2g) as substrate.

In comparison, when (E)-4-bromobut-2-enoate (2h) containing sterically less hindered methoxycarbonyl group was employed as substrate, the allylation

reaction worked with equal success (Scheme 6), but with slightly reduced diastereoselectivity (90:10 dr).



Scheme 6. Bismuth-mediated diastereoselective allylation using (E)-4-bromobut-2-enoate (2h) as substrate.

Mechanistically, the exclusive formation of the syn-diastereomer by using cyclic allylic halide as substrate (Tables 4 and 5) could be explained a Zimmerman-Traxler^[17] six-membered ring transition state A where the C-C double bond of the in situ generated cyclic allylic bismuth reagents always possesses a Z configuration and is not susceptible to Z/E-isomerization (Figure 1). ^[3] In cases where 2-pyridinecarboxaldehyde (1t)was used as substrate, the adoption of a Cramtransition state **B** involving chelated the coordination of the nitrogen atom and carbonyl group to the allylbismuth species forces the 2pyridinyl substituent to possess an axial position in the six-membered ring transition state, which leads to the inversion of the stereochemistry of the final product of homoallylic alcohol. A similar Cram-chelated transition state C can also be applied to the use of glyoxylic acid (1v) or phenylglyoxylic acid (1w) as substrates, where the COOH group resides in the axial position of the six-membered ring and coordinates with bismuth atom.^[18] When (E)-cinnamyl bromide was used as substrate, the C-C double bond possessed an E-configuration and sterically hindered phenyl substituent adopted an equatorial position in the Zimmerman-Traxler six-membered ring transition state **D**, thus leading to preferential formation of the anti-diastereomer.



Figure 1. Zimmerman-Traxler six-membered ring transition state accounted for the high diastereoselectivity obtained.

To determine whether cyclic allylic bismuth reagent was formed in the present allylation reaction, we treated 3-bromocyclohexene (2a) with bismuth powder in the presence of LiI in DMF (Scheme 7). After stirring at room temperature for 6 h, the upper clear solution was separated from the bottom precipitate and transferred to another flask followed by the addition of aldehyde **1d**. After reacting at room temperature for another 6 h, the desired product **3d** could be isolated in 62% yield with >99:1 dr. Thus, we believed that cyclic allylic bismuth reagent must have formed in the transformation, otherwise the allylation reaction would not take place.



Scheme 7. Pre-formation of cyclic allylic bismuth reagent from substrate 2a and ensuing allylation reaction with aldehyde 1d.

As for the role of LiI,^[15] we believed that Li⁺ should help to facilitate the insertion of bismuth powder into cyclic allylic halides for the generation of the corresponding cyclic allylic bismuth reagent, typical of the positive effects observed in LiCl-enhanced insertion of other metals into organohalides which were reported by Knochel and others.^[10,14] In addition, I⁻ should facilitate the conversion of relatively less reactive allyl chlorides or bromides to more reactive allyl iodides via a Felkinstein-type reaction pathway so that the latter might more readily undergo bismuth insertion to *in situ* generate the corresponding allylbismuth reagent.

Conclusion

In conclusion, we have developed an efficient bismuth-mediated highly diastereoselective allylation reaction of carbonyl compounds with cyclic allylic halides by using commercially available bismuth powder as reaction mediator in the presence of LiI in DMF. The reactions proceeded smoothly at room temperature to produce the desired homoallylic alcohols in good to excellent yields with high diastereoselectivities (>99:1 dr). Among all the metals screened, bismuth was found to be the best mediator for the reaction. A plethora of functional groups, such as nitro, cyano, ester, and acetyl group, could be well tolerated in the reaction. Remarkably, reversed diastereoselectivity was obtained when carbonyl substrate (e.g., 2-pyridinecarboxaldehyde, glyoxylic acid) containing chelating substituent was used in the allylation. In addition, the reactions involving acyclic (E)-cinnamyl bromide as substrate worked equally well, giving rise to the corresponding products with both excellent yields and diastereoselectivities. In contrast with the documented methods where preprepared cyclic allylic aluminium^[3a] or zinc^[3b] reagents were used, the present allylation reaction using bismuth as reaction mediator, in which cyclic

allylic bismuth species might be *in situ* formed, proceeded effectively in a simple one-pot fashion with no exclusion of air and moisture. Further applications of the methodology in organic synthesis are currently underway in our laboratories.

Experimental Section

Typical procedures for the preparation of homoallylic alcohols by the addition of allyl halides to carbonyl compounds:

To a 10 mL Schlenk flask was sequentially added bismuth powder (418.0 mg, 2 mmol) and DMF (2 mL). Then bismuth was activated by the addition of 1,2dibromoethane (18.8 mg, 5 mol%) and TMSCl (10.9 mg, 5 mol%). After stirring for 5 min, LiI (267.7 mg, 2 mmol), allyl halides (3 mmol), and aldehyde or ketone (1 mmol) was sequentially added to the reaction mixture. The suspension was vigorously stirred at room temperature for 12 h before quenching with sat. NH₄Cl solution (30 mL) and extracting with ethyl acetate (20 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The residue obtained was purified by silica gel column chromatography using ethyl acetate/petroleum ether as eluent to give the pure products.

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References

- For selected reviews regarding allylation reactions, see:
 a) Z.-L. Shen, S.-Y. Wang, Y.-K. Chok, Y.-H. Xu, T.-P. Loh, *Chem. Rev.* 2013, *113*, 271; b) T.-P. Loh, G.-L. Chua, *Chem. Commun.* 2006, 2739; c) U. K. Roy, S. Roy, *Chem. Rev.* 2010, *110*, 2472; d) M. Yus, J. C. Gonzalez-Gomez, F. Foubelo, *Chem. Rev.* 2011, *111*, 7774; e) S. E. Denmark, J. Fu, *Chem. Rev.* 2003, *103*, 2763; f) D. Kumar, S. R. Vemula, N. Balasubramanian, G. R. Cook, *Acc. Chem. Res.* 2016, *49*, 2169; g) H. Lachance, D. G. Hall, *Org. React.* 2008, *73*, 1; h) B. W. Gung, *Org. React.* 2004, *64*, 1.
- [2] For selected examples, see: a) S. Araki, H. Ito, Y. Butsugan, J. Org. Chem. 1988, 53, 1831; b) C.-J. Li, D.-L. Chen, Y.-Q. Lu, J. X. Haberman, J. T. Mague, J. Am. Chem. Soc. 1996, 118, 4216. c) L. A. Paquette, T. M. Mitzel, J. Am. Chem. Soc. 1996, 118, 1931; d) T. P. Loh, X. R. Li, Angew. Chem., Int. Ed. 1997, 36, 980; e) T.-P. Loh, K.-T. Tan, S.-S. Chng, H.-S. Cheng, J. Am. Chem. Soc. 1999, 121, 3228. g) S. A. Babu, M. Yasuda, A. Baba, J. Org. Chem. 2007, 72, 10264. h) K. Lee, H. Kim, T. Miura, K. Kiyota, H. Kusama, S. Kim, N. Iwasawa, P. H. Lee, J. Am. Chem. Soc. 2003, 125, 9682. i) L. A. Paquette, P. C. Lobben, J. Am. Chem. Soc.

1996, *118*, 1917. j) G. Hilt, K. I. Smolko, *Angew. Chem., Int. Ed.* **2001**, *40*, 3399. k) J.-M. Huang, X.-X. Wang, Y. Dong, *Angew. Chem., Int. Ed.* **2011**, *50*, 924.

- [3] a) Z. Peng, T. D. Blumke, P. Mayer, P. Knochel, Angew. Chem., Int. Ed. 2010, 49, 8516; b) H. Ren, G. Dunet, P. Mayer, P. Knochel, J. Am. Chem. Soc. 2007, 129, 5376; c) F. A. Khan, B. Prabhudas, Tetrahedron 2000, 56, 7595.
- [4] For a selected review, see: a) Bismuth-mediated organic reactions, ed. T. Ollevier, Springer, Berlin, Heidelberg, 2012. b) A. Gagnon, J. Dansereau, A. Le Roch, Synthesis 2017, 49, 1707. For selected typical examples of bismuth chemistry (usually Bi³⁺ salt functions as Lewis acid catalysis) developed in the field of organic synthesis, see: c) P. A. Evans, J. Cui, S. J. Gharpure, R. J. Hinkle, J. Am. Chem. Soc. 2003, 125, 11456; d) S. Shimada, O. Yamazaki, T. Tanaka, M. L. N. Rao, Y. Suzuki, M. Tanaka, Angew. Chem., Int. Ed. 2003, 42, 184; e) T. Huang, Y. Meng, S. Venkatraman, D. Wang, C.-J. Li, J. Am. Chem. Soc. 2001, 123, 7451; f) P. K. Koech, M. J. Krische, J. Am. Chem. Soc. 2004, 126, 5350; g) Y. Matano, Chem. Commun. 2000, 2233.
- [5] For selected reviews, see: a) Handbook of Functionalized Organometallics, ed. P. Knochel, Wiley-VCH, Weinheim, Germany, 2005. b) Comprehensive Organometallic Chemistry III, ed. R. H. Crabtree, D. M. P. Mingos, Elsevier, Oxford, U.K., 2007.
- [6] For allylation reactions using bismuth powder as reaction mediators, see: a) M. Wada, K.-y. Akiba, *Tetrahedron Lett.* 1985, 26, 4211; b) P. J. Bhuyan, D. Prajapati, J. S. Sandhu, *Tetrahedron Lett.* 1993, 34, 7975; c) K. Smith, S. Lock, G. A. El-Hiti, M. Wada, N. Miyoshi, *Org. Biomol. Chem.* 2004, 4, 935. d) M. Wada, H. Ohki, K.-y. Akiba, *Bull. Chem. Soc. Jpn.* 1990, 63, 1738.
- [7] For allylation reaction using *in situ* generated more reactive bismuth as reaction mediators from the reduction of BiX₃ by reducing agent (e.g., Zn, Al, NaBH₄), see: a) S. Donnelly, E. J. Thomasa, M. Fielding, *Tetrahedron Lett.* 2004, 45, 6779; b) M. Wada, T. Fukuma, M. Morioka, T. Takahashi, N. Miyoshi, *Tetrahedron Lett.* 1997, 38, 8045; c) T. Fukuma, M. Morioka, T. Takahashi, N. Miyoshi, *Tetrahedron Lett.* 1997, 38, 8045; c) T. Fukuma, M. Morioka, T. Takahashi, N. Miyoshi, *Tetrahedron Lett.* 1993, 34, 7975; d) M. Wada, M. Honna, Y. Kuramoto, N. Miyoshi, *Bull. Chem. Soc. Jpn.* 1997, 70, 2265; e) P.-D. Ren, S.-F. Pan, T.-W. Dong, S.-H. Wu, *Synth. Commun.* 1997, 27, 2569; f) X. Xu, Z. Zha, Q. Miao, Z. Wang, *Synlett* 2004, 1171.
- [8] For two examples of allylation reaction using allylbismuth reagent prepared from the transmetalation of allylmagnesium with BiX₃, see: a) T. Basile, A. Bocoum, D. Savoia, A. Umani-Ronchi, *J. Org. Chem.* **1994**, *59*, 7766; b) C. Lichtenberg, F. Pan, T. P. Spaniol, U. Englert, J. Okuda, *Angew. Chem. Int. Ed.* **2012**, *51*, 13011.
- [9] For selected examples of metal-mediated organic reactions developed in our group, see: a) Y. S. Yang, Z. L. Shen, T. P. Loh, *Org. Lett.* 2009, *11*, 1209; b) M. J.

Lin, T. P. Loh, J. Am. Chem. Soc. 2003, 125, 13042; c) Y. S. Yang, Z. L. Shen, T. P. Loh, Org. Lett. 2009, 11, 2213; d) Z.-L. Shen, T.-P. Loh, Org. Lett. 2007, 9, 5413; e) Z. L. Shen, H. L. Cheong, T. P. Loh, Chem.-Eur. J. 2008, 14, 1875; f) Z. L. Shen, Y. L. Yeo, T. P. Loh, J. Org. Chem. 2008, 73, 3922; g) Z.-L. Shen, K. K. K. Goh, H.-L. Cheong, C. H. A. Wong, Y.-C. Lai, Y.-S. Yang, T.-P. Loh, J. Am. Chem. Soc. 2010, 132, 15852.

- [10] T. D. Blümke, Y.-H. Chen, Z. Peng, P. Knochel, *Nat. Chem.* 2010, 2, 313.
- [11] a) T. D. Blümke, T. Klatt, K. Koszinowski, P. Knochel, Angew. Chem., Int. Ed. 2012, 51, 9926. b) K. Takai, Y. Ikawa, Org. Lett. 2002, 4, 1727.
- [12] K. Takai, T. Kakiuchi, K. Utimoto, J. Org. Chem. 1994, 59, 2671.
- [13] a) Z.-L. Shen, K. K. K. Goh, Y.-S. Yang, Y.-C. Lai, C. H. A. Wong, H.-L. Cheong, T.-P. Loh, *Angew. Chem., Int. Ed.* 2011, *50*, 511. b) Z.-L. Shen, K. K. Goh, C. H. A. Wong, Y.-S. Yang, Y.-C. Lai, H.-L. Cheong, T.-P. Loh, *Chem. Commun.* 2011, *47*, 4778. c) S. Kim, C.-E. Kim, B. Seo, P. H. Lee, *Org. Lett.* 2014, *16*, 5552.
- [14] For representative LiCl-mediated metal insertions into organic halides, see: a) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel, Angew. Chem., Int. Ed. 2008, 47, 6802; b) A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, Angew. Chem. Int. Ed. 2006, 45, 6040; c) N. Boudet, S. Sase, P. Sinha, C.-Y. Liu, A. Krasovskiy, P. Knochel, J. Am. Chem. Soc. 2007, 129, 12358; d) Y.-H. Chen, P. Knochel, Angew. Chem., Int. Ed. 2008, 47, 7648; e) Z.-L. Shen, P. Knochel, ACS Catal. 2015, 5, 2324; f) P. H. Lee, K. Lee, Y. Kang, J. Am. Chem. Soc. 2006, 128, 1139. g) P. H. Lee, K. Lee, Angew. Chem., Int. Ed. 2005, 44, 3253. h) K. Lee, D. Seomoon, P. H. Lee, Angew. Chem., Int. Ed. 2002, 41, 3901.
- [15] B.-Z. Chen, M.-L. Zhi, C.-X. Wang, X.-Q. Chu, Z.-L. Shen, T.-P. Loh, Org. Lett. 2018, 20, 1902.
- [16] CCDC 1858982, 1858983, and 1858981 contain the crystallographic data for compounds 3w, 4a, and 4g. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/ data_request/cif.
- [17] a) H. E. Zimmerman, M. D. Traxler, J. Am. Chem. Soc. 1957, 79, 1920; b) C. H. Heathcock, Science 1981, 214, 395.
- [18] For a chelation controlled addition of ethyl pyruvate to cyclic allylic stannane, see: I. W. Muderawan, R. C. Bott, D. J. Young, *Synthesis* **1998**, 1640.

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Bismuth-Mediated Diastereoselective Allylation Reaction of Carbonyl Compounds with Cyclic Allylic Halides or Cinnamyl Halide

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