Association of Halogen Bonding and Hydrogen Bonding in Metal Acetate-Catalyzed Asymmetric Halolactonization
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SUMMARY

Cooperative activation using halogen bonding and hydrogen bonding works in metal-catalyzed asymmetric halolactonization. The Zn3(OAc)4-3,3'-bis(aminomino)binaphthoxide (tri-Zn) complex catalyzes both asymmetric iodolactonization and bromolactonization. Carboxylic acid substrates are converted to zinc carboxylates on the tri-Zn complex, and the N-halosuccinimide (N-bromosuccinimide [NBS] or N-iodosuccinimide [NIS]) is activated by hydrogen bonding with the diamine unit of chiral ligand. Halolactonization is significantly enhanced by the addition of catalytic I2. Density functional theory calculations revealed that a catalytic amount of I2 mediates the alkene portion of the substrates and NIS to realize highly enantioselective iodolactonization. The tri-Zn catalyst activates both sides of the carboxylic acid and alkene moieties, so that asymmetric five-membered iodolactonization of prochiral diallyl acetic acids proceeded to afford the chiral γ-butyrolactones. In the total description of the catalytic cycle, iodolactonization using the NIS-I2 complex proceeds with the regeneration of I2, which enables the catalytic use of I2. The actual iodination reagent is I2 and not NIS.

INTRODUCTION

Electrostatic forces are fundamental forces that work in a wide range of molecular interactions. In catalysis, various metal cations act as the center of catalytic activity to enhance the reactivity of substrates (Figure 1A) (Yamamoto, 2001). Hydrogen bonding is the other representative electrostatic interaction observed between hydrogen (H) atoms with electronegative functionality (Figure 1B) (Pihko, 2009). Although these interactions have been widely utilized in the design and development of a wide range of catalysts, abundantly observed metal coordination and hydrogen bonding networks sometimes make the specific activation of substrates difficult. As a different type of noncovalent electrostatic interaction, halogen bonding has received much attention in organic chemistry. The origin of halogen bonding comes from the Lewis acidity of sigma holes that emerge on the opposite side of halogen-R sigma bonds, so that halogen bonding can effectively facilitate the direction of molecular recognition and can thus realize functional group selectivity (Figure 1C) (Cavallo et al., 2016).

Although the halogen bonding has recently been examined in several solution-phase catalyses, successful application in asymmetric reactions is limited (Beale et al., 2013; Bruckmann et al., 2008; Builfield and Huber, 2016; Chan and Yeung, 2018; Coulembier et al., 2010; Dreger et al., 2018; Farina et al., 1999; Gliese et al., 2017; Haraguchi et al., 2018; He et al., 2014; Heiden et al., 2017; Heinen et al., 2018; Jungbauer et al., 2014; Jungbauer and Huber, 2015; Kaasik et al., 2017; Kazi et al., 2017; Kniep et al., 2013; Kuwano et al., 2018; Lim et al., 2016; Lindsay and Charette, 2012; Matsuzaki et al., 2018; Saito et al., 2017; Takeda et al., 2015; Zong et al., 2014). Here, halogen bonding and hydrogen bonding are merged with the metal-catalyzed asymmetric halolactonization (Castellanos and Fletcher, 2011; Chen and Ma, 2010; Cheng et al., 2014; Denmark et al., 2012; Hennecke, 2012; Tan et al., 2011a, 2011b, 2014).

RESULTS AND DISCUSSION

Structure-Activity Relationship of Zn3(OAc)4-3,3'-bis(aminomino)binaphthoxide-Catalyzed Asymmetric Iodolactonization

Among the wide range of halogen chemistry, halolactonization has been well utilized in the stereoselective synthesis of versatile natural products, biologically significant pharmaceutical compounds, and agricultural chemicals. For the catalytic asymmetric version of iodolactonization, Gao reported a unique system of a
chiral salen-Co complex, in which I2 was used as an I+ source and the catalyst activity was enhanced by the addition of N-chlorosuccinimide (Ning et al., 2009). Jacobsen pioneered a tertiary amine-catalyzed asymmetric iodolactonization using N-iodo-4-fluorophthalimide as the I+ source and I2 as an additive (Veitch and Jacobsen, 2010). In the subsequently developed metal-catalyzed and organocatalyzed asymmetric iodolactonization reactions, the combined use of an I+ source (e.g., N-iodosuccinimide [NIS]) with I2 is often effective to improve the results (Araki et al., 2014, 2015a, 2015b; Brindle et al., 2013; Dobish and Johnston, 2012; Fang et al., 2012; Filippova et al., 2014; Kwon et al., 2018; Lu et al., 2018; Mizar et al., 2014; Murai et al., 2014a, 2014b; Nakatsuji et al., 2014; Toda et al., 2014; Tuppen and Mukherjee, 2013; Tuppen et al., 2012; Sakakura et al., 2007; Suresh et al., 2018; Wang et al., 2012). In 2014, we also reported a highly efficient catalytic asymmetric iodolactonization using a 3,3′-bis(aminomino)binaphthol ligand (L1) and Zn(OAc)2. Only 1 mol% of trinuclear Zn3(OAc)4-3,3′-bis(aminomino)binaphthoxide (tri-Zn) was required to catalyze the asymmetric iodolactonization using NIS with the catalytic assistance of I2 to afford the products at up to over 99% enantiomeric excess (ee) (Figure 2) (Araki et al., 2014, 2015a, 2015b).

The structure-activity relationship of the aminoiminophenol ligands for Zn-catalyzed asymmetric iodolactonization is summarized in Table 1. The best ligand (L1) is prepared from (R, R)-diphenylethylenediamine and (R)-3,3′-diformylbinaphthol. The diastereomeric ligand (L2) prepared from (S, S)-diphenylethylenediamine and (R)-3,3′-diformylbinaphthol reduced asymmetric induction with 68% ee. Interestingly, a simple bis(aminomino)binaphthol (L3) prepared using an achiral amine also provided an efficient chiral zinc catalyst to afford chiral 2a with 98% ee. Thus the use of expensive chiral diamine is not essential for asymmetric induction. The catalyst prepared using (R, R)-diphenylethylenediamine-derived bis(aminomino)binaphenol (L4) gave (R)-enriched 2a in 75% yield with 72% ee. From density functional theory (DFT) calculations of the L4-Zn(OAc)2 complex, the conformation with the (R)-axis L4-Zn3 complex is more stable by 6.0 kcal/mol than the (S)-axis configuration (Figure S1). The (R)-enriched formation of iodolactone 2a from entry 1 to 4 shows the importance of axial chirality for the construction of an efficient asymmetric reaction sphere. 3-Aminoiminobinaphthol (L6) for the dinuclear Zn complex and aminoiminophenol (L7) for the mononuclear Zn complex resulted in low catalyst activity. Overall, high catalytic activity for asymmetric iodolactonization is obtained when the trinuclear zinc acetates are precisely arranged on the axially chiral bis(aminomino)binaphenol ligands (Shibasaki and Yamamoto, 2004).

Questions on Catalytic Asymmetric Halolactonization

Despite the success with a series of efficient catalysts for asymmetric iodolactonization, there are still unsolved problems in the catalyst behavior, especially with respect to the activation mode of the alkene moiety. Conventional catalysts for asymmetric iodolactonization generally result in low asymmetric...
induction for other halolactonization (bromo-, chloro-, and fluorolactonization) reactions. The substrate scope is limited, and it is difficult to apply to rather complex molecules. For example, the catalyst developed for five-membered lactone formation tends to be unsuitable for the six-membered lactone system. The positive role of I$_2$ in asymmetric catalysis is also unclear. Without the addition of catalytic I$_2$, the tri-Zn catalyst gave 2a in only 7% yield with 97% ee. The answer to the actual role of I$_2$ would provide realization of a true transition state, which would enable the appropriate selection of reaction substrates for the catalyst and the rational design of next-generation asymmetric catalysis.

**Asymmetric Bromolactonization Using Tri-Zn Catalyst**

The catalytic performance of the tri-Zn complex prepared using the best ligand (L1) was examined for asymmetric bromolactonization (Aursnes et al., 2016; Jiang et al., 2012, 2018; Murai et al., 2010; Tan et al., 2011a, 2011b; Zhou et al., 2010). When the reaction was conducted using N-bromosuccinimide (NBS) at −78 °C, 5 mol% tri-Zn complex catalyzed the bromolactonization to give the bromolactone 3a in 38% yield with 92% ee (entry 1, Table 2). Similar to the previously studied iodolactonization, the addition of I$_2$ or Br$_2$ enhanced the catalytic activity to give the bromolactone in higher chemical yields while maintaining the ees. However, interestingly, when 0.2 equiv. of I$_2$ was added to the bromolactonization of 1a, 36% iodolactone 2a (98% ee) was coproduced with 58% bromolactone 3a (93% ee) shown in entry 2.
| Entry | Ligand | X (mol %) | Time (h) | Yield of 2a (%) | ee of 2a (%) |
|-------|--------|-----------|----------|----------------|-------------|
| 1     | L1     | 3         | 24       | 99             | 99.6 (R)    |
| 2     | L2     | 3         | 24       | 99             | 68 (R)      |
| 3     | L3     | 3         | 18       | 99             | 98 (R)      |
| 4     | L4     | 3         | 24       | 75             | 72 (R)      |
| 5     | L5     | 3         | 18       | 79             | 68 (R)      |
| 6     | L6     | 2         | 24       | 34             | 89 (R)      |
| 7     | L7     | 1         | 24       | Trace          | –           |

Table 1. Structure-Activity Relationship of the Aminooiminophenol Ligands for Zn-Catalyzed Asymmetric Iodolactonization
As a result of optimization for the bromolactonization, the reaction at \(-40°C\) without additive was selected to afford \(3a\) in quantitative yield with 94% ee. At this stage, it seems likely that the addition of \(I_2\) (or \(Br_2\)) mainly contributes to accelerate the reaction and is not essential for asymmetric induction.

The scopes of both iodolactonization and bromolactonization were similar, and a comparison of bromolactonization and iodolactonization is summarized in Table S1.

### DFT Calculation of the Transition State for Iodolactonization

DFT calculations were conducted to fully clarify the stereocontrol mechanism, the ligand structure-activity relationship, and the role of \(I_2\) for Zn-catalyzed asymmetric iodolactonization. The addition of \(I_2\) had a significant impact on the acceleration of the reaction, but no effect on stereochemical control. Therefore the transition state (TS)-A model for alkene activation by NIS was studied first (Figure 3A).

Negligible non-linear effect suggests the iodolactonization conducted on the unimolecular catalyst. In addition, a Job plot analysis suggests a 1:1 interaction between tri-Zn complex and 1a (Figure S3). This is consistent with the rational TS-A model for the tri-Zn-catalyzed asymmetric iodolactonization supposed by the previous experimental data and preliminary computational studies (Figures S6 and S7) (Arai et al., 2014). The TS-A model for the tri-Zn-catalyzed asymmetric iodolactonization involved the zinc carboxylate of 1a replaced by the outer acetoxy anion on the tri-Zn complex. In TSmajor-A, to produce the preferentially obtained \((R)-2a\), bidentate and strong electrostatic interaction between the Zn atom and acetoxy anion of 1a is formed to locate the bulky substituent (e.g., Ph group of 1a) in the empty space of tri-Zn. The anti-addition to the alkene portion of 1a locates NIS close to the aminoimino moiety of L1 and forms a hydrogen bond with the imino-proton. The cooperative electrostatic or hydrogen bonding interactions stabilize TSmajor-A. In contrast, different structural features regarding these two interactions were found in TSmajor-A to give the minor enantiomer (S)-2a. The bidentate Zn-carboxylate interaction is broken by the steric repulsion between the Ph group of 1a and the naphthyl moiety of L1. The axial chirality plays a key role in the asymmetric induction rather than the terminal \((R, R)\)-diphenylenediamine part of L1. These computational results are consistent with the experimentally observed structure-activity relationship (entries 1 and 3 in Table 1, Figure S2). In addition, NIS stays away from tri-Zn to lose the hydrogen bond. The changes in the attractive non-covalent interactions between 1a, NIS, and tri-Zn are thus major factors in directing the stereochemical outcome. In addition, TSminor-A is 5.1 kcal/mol less stable than TSmajor-A.

However, there still remains a question with respect to the tri-Zn-catalyzed iodolactonization regarding the role of \(I_2\). For the full description of the transition state, extensive studies with DFT calculations were conducted for the TS-B model involving the tri-Zn complex, 1a, NIS, and \(I_2\) in Figure 3B. The relative arrangement and electrostatic interaction between the tri-Zn complex and 1a are well stored in the

### Table S1

| Entry | Additive | Additive | Temp (°C) | Yield (%) | ee (%) |
|-------|----------|----------|-----------|-----------|--------|
| 1     | –        | –        | -78       | 38        | 92     |
| 2     | \(I_2\)  | \(I_2\)  | -78       | 58 (36)   | 93 (98) |
| 3     | \(Br_2\) | \(Br_2\) | -78       | 89        | 91     |
| 4     | –        | –        | -40       | 99        | 94     |

Table 2. Catalytic Asymmetric Bromolactonization Using Zn3(OAc)4-3,3’-bis(amoimino)binaphthoxide (tri-Zn) Catalyst

*Values in parentheses are yield or ee of iodolactone.
Importantly, an I₂ molecule inserts between NIS and the alkene moiety of 1a by forming a bent configuration. The bent interaction of I₂ with NIS is well explained by the halogen bonding observed in the I₃⁺ species (Cavallo et al., 2016; Nakatsuji et al., 2014; Lu et al., 2018). The 1:1 interaction of the tri-Zn with the NIS-I₂ species was suggested by ultraviolet-visible analysis (Figure S4). One obvious difference from the TS-A model is the lack of hydrogen bonding interaction between NIS and the imine-proton. Owing to the insertion of I₂, NIS moves to the right side and forms a new hydrogen bonding interaction with two methine protons of the diphenylethylenediamine framework and one proton on the benzene ring of diphenylethylenediamine. This plural hydrogen bonding scenario is well supported by the structure-activity relationship examined in Table 1 (entries 1, 3, and 5). The tri-Zn complex prepared from the simple ethanediamine-derived bis( aminoimino)binaphthol (L3)-tri-Zn catalyst gave 2a with 98% ee, although the catalyst prepared from tetramethyl-substituted ethanediamine-derived bis( aminoimino)binaphthol (L5), which lacked the hydrogen-bonding-donating methine protons, gave 2a with only 68% ee. In TSmajor-B, the interaction energy analysis (Figure S9) clearly indicates that the electrostatic interaction (Zn carboxylate, 102 kcal/mol)
is associated with hydrogen bonding (NIS-tri-Zn, 6 kcal/mol) and halogen bonding interactions (I2-NIS, 18 kcal/mol). Overall, in the tri-Zn-catalyzed asymmetric iodolactonization, three types of attractive non-covalent interactions cooperatively stabilize the transition state to achieve high catalytic activity and almost perfect enantioselectivity.

**Design of Asymmetric Five-Membered Iodolactonization Based on DFT Simulation**

The five-membered lactone system was also computationally addressed (Figure 4) based on the rational TS model for formation of the six-membered lactone (Figure 3B).

There is no difference in the steric environment around the prochiral hydrogen atoms bonded to the \(\alpha\)-carbon of the carboxyl group in the six-membered TS model (dotted circles around \(\text{H}_a\) and \(\text{H}_b\) in the left-hand side figure). On the five-membered TS model, the dotted circles around \(\text{H}_a\) and \(\text{H}_b\) in the right-hand side figure are differentiated in each space due to ring flipping. The introduction of a substituent at the prochiral hydrogen \(\text{H}_a\) would induce a repulsive interaction with the isoindoline moiety to increase the energy difference of the \(\text{H}_a\)- and \(\text{H}_b\)-substituted diastereomeric transition states and lead to high stereo-discrimination. Such transition state models predicted facilitation of the nucleophilic attack by the carboxylate anion to one side of the alkene moiety of the meso-substrate in the five-membered lactone system to yield the (3S, 5R)-product preferentially. These computational results prompted us to design the catalytic asymmetric iodolactonization of prochiral diallyl acetic acids as shown in Figure 5 (Ikeuchi et al., 2012; Jiang et al., 2018; Klosowski and Martin, 2018; Knowe et al., 2018; Murai et al., 2014a, 2014b; Wilking et al., 2013, 2016).

To accomplish the asymmetric reaction shown in Figure 5, the catalyst must recognize each side of the alkene moiety in an enantioselective manner. At the same time, the catalyst must allow incorporation of the bulky branched substrate into the asymmetric reaction sphere. This requirement can be satisfied with tri-Zn catalysis because the bulky substituent of the substrate remains in the empty space, as presented in Figure 4. The tri-Zn catalyst controlled the asymmetric iodolactonization efficiently to give the five-membered iodolactone 5 in a highly diastereo- and enantioselective manner. In agreement with the computational prediction, the absolute structure of chiral \(\gamma\)-butyrolactone 5a was determined by X-ray crystallographic analysis to be (3S,5R)-5-(iodomethyl)-5-phenyl-3-(2-phenylallyl)dihydrofuran-2(3H)-one (see Supplemental Information, Data S1 for details.).

The synthetic utilities of the five-membered iodolactone 5 are demonstrated in Scheme 1. From 94% ee of 5a, epoxyster 6a and furan 7a were obtained, which maintain the exo-olefine functionality. A radical cyclization of 5a provided 7-oxabicyclo[4.2.1]nonan-8-one 8a.

**Discussion of the Catalytic Cycle of Asymmetric Iodolactonization**

Based on the realization of the transition state in Figure 3B, the catalytic cycle of tri-Zn-catalyzed asymmetric iodolactonization can be described as shown in Figure 6A. The tri-Zn (A) would react with the
Figure 5. Catalytic Asymmetric Five-Membered Iodolactonization Using Zn$_3$(OAc)$_4$·3,3’-bis(aminooimino)binaphthoxide (tri-Zn) Catalyst

R$ightarrow$O$ightarrow$R

L1 (5 mol %)
Zn(OAc)$_2$ (15 mol %)
NIS (1.1 eq), I$_2$ (0.2 eq)
toluene/CHCl$_3$=3/1, -78 °C, time

5a (20 h) 94% yield 
dr = 99/1 
94% ee

5b (23 h) 95% yield 
dr = 99/1 
99% ee

5c (24 h) 96% yield 
dr = 96/4 
79% ee

5d (21 h) 93% yield 
dr = 99/1 
98% ee

5e (24 h) 99% yield 
dr = 99/1 
96% ee

5f (24 h) 99% yield 
dr = 99/1 
93% ee

5g (24 h) 80% yield 
dr = 99/1 
92% ee
alkenoic acid substrate (1) to generate the Zn carboxylate (B). With the Zn carboxylate (B), the complex of NIS with I₂ (C) would activate the alkene moiety to give the model transition state (e.g., TS-B model). When the origin of the I-source is carefully considered (as marked by purple and green), the alkene moiety is activated by I₂, and not by NIS. However, by following the relay of arrows, the iodolactonization to yield product 2 would proceed with the co-production of N-succinimide and regeneration of I₂. From this mechanistic hypothesis, the tri-Zn-catalyzed reaction pathways with and without I₂ were compared (Figure 6B; black: with I₂, gray: without I₂). Ligand exchange process between tri-Zn and 1 readily proceeds without significant energy loss to generate the Zn carboxylate (B). Although additional I₂ entropically destabilizes the complex of NIS with I₂ (C) when compared with the complex of NIS without I₂ (C'), the TS-B model is -12.6 kcal/mol more stable than the TS-A model. By receiving the insertion of I₂, TS is significantly stabilized to accelerate the iodolactonization.

The halogen-incorporated reaction mechanism described in Figure 6A is strongly supported by the experimental results of entry 2 in Table 2, in which 36% yield of iodolactone is produced using 0.2 equiv. of I₂ for the NBS-promoted bromolactonization. This clearly indicates that both iodine atoms of I₂ are rapidly introduced to the product. The phenomenon is also well explained by the DFT simulation for the second catalytic cycle (Figure 7). In the first catalytic cycle based on the halogen-incorporated reaction mechanism, I-Br should be generated. When the I-Br is incorporated into the TS, the reaction should proceed from TS-I described on the left-hand side of Figure 7 to give the iodolactone.

Limitations of Study
This study is limited to catalytic asymmetric iodolactonization and bromolactonization. The method based on the current approach would be potentially applicable to other chlorolactonization or fluorolactonization.

Conclusions
Excellent catalytic activity of the tri-Zn catalyst to achieve highly enantioselective asymmetric halolactonization was realized. Both activation of the metal-carboxylate and hydrogen bonding activation of NIS
Figure 6. Reaction Mechanism of Asymmetric Iodolactonization
(A) Plausible catalytic cycle of tri-Zn-promoted asymmetric iodolactonization.
(B) Energy profile of plausible reaction pathways with I₂ (black) and without I₂ (gray).
are harmonized by the halogen bonding with I$_2$ to enable highly asymmetric iodolactonization. In the tri-Zn-catalyzed iodolactonization, the actual iodination reagent was identified for the first time; it is I$_2$, and not NIS.

**METHODS**

All methods can be found in the accompanying Transparent Methods supplemental file.

**SUPPLEMENTAL INFORMATION**

Supplemental Information includes Transparent Methods, 99 figures, 8 schemes, 1 table, and 2 data files and can be found with this article online at https://doi.org/10.1016/j.isci.2019.01.029.

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**AUTHOR CONTRIBUTIONS**

T.A. designed the experiments and wrote the paper; K.H., O.W., J.K., N.S., and H.M. conducted the experiments; Y.K., S.Y., and M.Y. performed all computational work.

**DECLARATION OF INTERESTS**

The authors declare no competing interests.
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Supplemental Information

Association of Halogen Bonding and Hydrogen Bonding in Metal Acetate-Catalyzed Asymmetric Halolactonization

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Transparent Methods

1. General

Dry solvents were purchased from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230-400 mesh silica gel containing a fluorescent indicator (Merck, #1.05715.0009). Silica-gel column chromatography was performed on Kanto silica gel 60 (spherical, 100-210 μm). IR spectra were recorded on JASCO FT/IR-4100 using ATR. 1H-NMR spectra were recorded on JEOL ECS-400 (400MHz), ECA-500 (500MHz), ECX-400 (400MHz) spectrometers. Chemical shifts of 1H-NMR spectra were reported relative to tetramethyl silane (δ 0). 13C-NMR spectra were recorded on JEOL ECS-400 (100MHz), ECA-500 (125MHz), ECX-400 (100MHz) spectrometers. Chemical shifts of 13C-NMR spectra were reported relative to CDCl3 (δ 77.0). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

2. Synthesis and analytical data of aminomine ligands

(R)-3,3'-bis((E)-(((1R,2R)-2-(isoindolin-2-yl)-1,2-diphenylethyl)imino)methyl)-[1,1'-binaphthylene]-2,2'-dil (L1) (Arai et al., 2014)

Scheme S1. Synthesis of L1, related to Figure 2.

A mixture of (R)-2,2'-dihydroxy-[1,1'-binaphthyl]-3,3'-dicarbaldehyde (Belkon et al., 2006) (61.0 mg, 0.195 mmol) and (1R,2R)-2-(isoindolin-2-yl)-1,2-diphenylethanamine (0.41 mmol) (Arai et al., 2007) in ethanol (30 mL) was heated to reflux. After being stirred for 24 hours, the solvent was removed under reduced pressure and the resulting residue was washed with cold ethanol to give bis(aminomino)binaphthol as a yellow brown solid. 1H NMR (500 MHz, CDCl3) δ 8.78 (s, 2H), 7.96 (s, 2H), 7.88 (d, J=7.73 Hz, 2H), 7.37-7.30 (m, 6H), 7.14-7.00 (m, 30 H), 4.95 (d, J=7.45 Hz, 2H), 4.25 (d, J=7.45 Hz, 2H), 4.05 (d, J=11.46 Hz, 4H), 3.98 (d, J=11.46 Hz, 4H); 13C NMR (125MHz,CDCl3)δ164.97, 154.57, 139.89, 139.48, 138.02, 135.27, 133.92, 129.54, 128.89, 128.26, 128.11, 127.93, 127.74, 127.62, 127.22, 127.06, 126.58, 124.94, 123.35, 122.12, 121.09, 116.59, 78.70, 77.54, 58.32;HRMS calced for C50H35O2N4 (M+H)+: 935.4320, found: m/z 935.4314; [α]D20.0° +30.6 (c=0.115, CHCl3); IR (neat) 3696, 3028, 2870, 2783, 1628, 1494, 1464, 1451, 1384, 1341, 1316, 1299, 1263, 1176, 1149, 1119, 1073, 1053, 1028, 934 cm⁻¹.
3,3’-bis((E)-((1R,2R)-2-(isoindolin-2-yl)-1,2-diphenylethylimino)methyl)-[1,1’-biphenyl]-2,2’-dihydroxy-[1,1’-biphenyl]-3,3’-dicarbaldehyde (L4)

Scheme S2. Synthesis of L4, related to Table 1.

A mixture of 2,2’-dihydroxy-[1,1’-biphenyl]-3,3’-dicarbaldehyde (Wünnemann et al., 2008) (0.195 mmol) and (1R,2R)-2-(isoindolin-2-yl)-1,2-diphenylethanamine (0.41 mmol) (Arai et al., 2007) in ethanol (30 mL) was stirred for 24 hours at 80 °C. Then the solvent was removed under reduced pressure and the resulting residue was washed with cold ethanol to give bis(aminoimino)biphenol L4 as a brown solid.

TLC Rf = 0.50 (Hexane/ethyl acetate = 4/1); ¹H NMR (400 MHz, CDCl₃) δ 8.55 (s, 2H), 7.51 (dd, J = 7.52, 1.57 Hz, 2H), 7.27 (dd, J = 7.63, 1.57 Hz, 2H), 7.13-7.04 (m, 28H), 6.98 (dd, J = 7.63, 7.52 Hz, 2H), 4.89 (d, J = 6.96 Hz, 2H), 4.17 (d, J = 6.96 Hz, 2H), 3.97 (d, J = 11.67 Hz, 4H), 3.92 (d, J = 11.67 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 165.1, 158.7, 140.4, 139.5, 138.4, 134.5, 131.2, 129.4, 127.9, 127.8, 127.7, 127.1, 126.9, 126.5, 125.6, 122.2, 119.1, 118.2, 78.1, 75.6, 58.3; HRMS calced for C₅₈H₅₁N₄O₂ (M+H)⁺: 835.4007, found: m/z 835.4014; [α]D19.0 = + 95.67 (c = 0.1, CHCl₃); IR (neat) 3029, 2784, 1626, 1452, 1127, 908, 748, 704 cm⁻¹.

2-(isoindolin-2-yl)ethan-1-amine

Scheme S3. Synthesis of 2-(isoindolin-2-yl)ethan-1-amine, related to Table 1.

A mixture of tert-butyl (2-aminoethyl)carbamate (Hoffmann and Kazmaier, 2014) (3 mmol) and DIPEA (6.6 mmol) in DMF (15 mL) were heated to 40 °C. o-xylene dibromide (3.3 mmol) was added to the solution and stirred for 24h at the same temperature. Then, the reaction mixture was quenched by water, and extracted with ethyl acetate in three times. The corrected organic layer was washed with brine, and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/1) to afford the tert-butyl (2-(isoindolin-2-yl)ethyl)carbamate. TLC Rf = 0.2 (Hexane/ethyl acetate = 2/1); ¹H NMR (400 MHz, CDCl₃) δ 7.20 (s, 4H), 5.15 (br, 1H), 3.94 (s, 4H), 3.31 (dt, J = 5.61, 5.39 Hz, 2H), 2.86 (t, J = 5.39 Hz, 2H), 1.44 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 156.0, 139.7, 126.7, 122.1, 121.8, 78.9, 58.6, 54.6, 38.9, 28.3; HRMS calced for C₁₅H₁₃N₂O₂ (M+H)⁺: 263.1754, found: m/z 263.1750; IR (neat) 3431, 2975, 1706, 1489, 1158, 1051, 748 cm⁻¹.
To a solution of the tert-butyl (2-(isoindolin-2-yl)ethyl)carbamate (1.8 mmol) in chloroform (12 mL) was added TFA (36 mmol). The resulting mixture was stirred overnight, then quenched by saturated K$_2$CO$_3$ aq. The organic layer was extracted with chloroform and collected organic layer was dried over Na$_2$SO$_4$. The solvent was removed in vacuo to give 2-(isoindolin-2-yl)ethan-1-amine.

TLC Rf = 0.1 (Chloroform/methanol = 10/1) $^1$H NMR (400 MHz, CDCl$_3$) δ 7.20 (s, 4H), 3.95 (s, 4H), 2.88-2.81 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ; 139.9, 126.6, 122.1, 59.0, 58.9, 40.8; HRMS calcd for C$_{10}$H$_{15}$N$_2$ (M+H)$^+$: 163.1230, found: m/z 163.1228; IR (neat) 2933, 2774, 1467, 1353, 1148, 1094, 931, 870, 744 cm$^{-1}$.

### Scheme S4

Synthesis of 3-(isoindolin-2-yl)-2,3-dimethylbutan-2-amine, related to Table 1.

To a mixture of 2,3-Dimethyl-2,3-butanediamine dihydrochloride (2.4 mmol) and Et$_3$N (4.8 mmol) in dichloromethane (20 mL), Boc$_2$O (2 mmol) in dichloromethane (20 mL) was slowly added over 3h at room temperature. After concentration and addition of Na$_2$CO$_3$ solution (20%, 3 mL), the mixture was extracted with dichloromethane and dried over Na$_2$SO$_4$ affording tert-butyl (3-amino-2,3-dimethylbutan-2-yl)carbamate.

TLC Rf = 0.1 (chloroform/methanol = 20/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 5.69 (br, 1H), 1.67 (br, 2H), 1.43 (s, 9H), 1.33 (s, 6H), 1.15 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 155.5, 78.2, 57.3, 54.9, 28.4, 26.4, 21.8; HRMS calcd for C$_{11}$H$_{25}$N$_2$O$_2$ (M+H)$^+$: 217.1911, found: m/z 217.1906; IR (neat) 2993, 2806, 1705, 1555, 1354, 1165, 839 cm$^{-1}$.

A mixture of tert-butyl (3-amino-2,3-dimethylbutan-2-yl)carbamate (0.2 mmol) and DIPEA (0.44 mmol) in DMF (1 mL) were heated to 40 °C. o-xylylenedibromide (0.22 mmol) was added to the solution and stirred for 24h at the same temperature. Then, the reaction mixture was quenched by water, and extracted with ethyl acetate in three times. The corrected organic layer was washed with brine, and dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 4/1) to afford the tert-butyl (3-(isoindolin-2-yl)-2,3-dimethylbutan-2-yl)carbamate.

TLC Rf = 0.5 (Hexane/ethyl acetate = 2/1); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.22 (s, 4H), 6.34 (br, 1H), 4.14 (s, 4H), 1.45 (s, 6H), 1.41 (s, 9H), 1.15 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 155.2, 139.3, 126.6, 122.2, 78.1, 61.2, 57.0, 54.3, 28.6, 24.7, 18.7; HRMS calcd for C$_{19}$H$_{31}$N$_2$O$_2$ (M+H)$^+$: 319.2380, found: m/z 319.2387; IR (neat) 3436, 2978, 1709, 1492, 1162, 1049, 742 cm$^{-1}$.
To a solution of the tert-butyl (3-(isoindolin-2-yl)-2,3-dimethylbutan-2-yl)carbamate (0.17 mmol) in chloroform (1.2 mL) was added TFA (3.4 mmol). The resulting mixture was stirred overnight, and then quenched by saturated K₂CO₃ aq. The organic layer was extracted with chloroform and collected organic layer was dried over Na₂SO₄. The solvent was removed in vacuo to give 3-(isoindolin-2-yl)-2,3-dimethylbutan-2-amine.

TLC Rf = 0.1 (Chloroform/methanol = 20/1) ¹H NMR (400 MHz, CDCl₃) δ 7.19 (s, 4H), 4.21 (s, 2H), 2.03 (br, 2H), 1.22 (s, 6H), 1.21 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 139.9, 126.4, 122.0, 60.7, 57.1, 54.6, 28.0, 20.0; HRMS calcd for C₁₂H₂₁N₂ (M+H)⁺: 219.1856, found: m/z 219.1854; IR (neat) 2984, 2806, 1555, 1353, 1162, 742 cm⁻¹.

3. Procedures of structure-activity relationship study on the catalytic asymmetric iodolactonization (Fig. 2B)

[For entry 1]

A mixture of 3,3′-bis(aminomino)binaphthol L₁ (0.001 mmol) and Zn(OAc)₂ (0.003 mmol) was stirred for 0.5 hour in anhydrous dichloromethane (1.0 ml) at rt. Then added (R)-bisformylbinaphthol for L₂, (R)-monoformylbinaphthol for L₆ and salicylaldehyde for L₇ (0.001 mmol) and 2-(isoindolin-2-yl)-1,2-diphenylethan-1-amine (0.002 mmol of (1S,2S)-configuration for L₂, 0.001mmol (1R,2R)-configuration for L₆ and L₇) was stirred for 2 hours in anhydrous dichloromethane (1.0 ml) at rt. Then added Zn(OAc)₂ (0.003 mmol for L₂, 0.002 mmol for L₆ and 0.001mmol for L₇) and stirred for 0.5 hour in the same temperature to afford Zn complex solution.

To a solution of in situ prepared Zn-complex as describe above, 5-phenylhex-5-enoic acid (0.1 mmol) in toluene (3.0 ml) was added and stirred for 0.5 hour at -78 °C. Then, N-iodosuccinimide (NIS) (0.11 mmol) and I₂ (5.0 mg, 0.02 mmol) were added to the reaction mixture. After being stirred for appropriate time, the reaction mixture was quenched with saturated Na₂SO₄ aq and 1N NaOH aq, and then the products were extracted with dichloromethane in 3 times. The collected organic layer was dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 5/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column.

[For entries 6, 7]

A mixture of corresponding aldehydes ((R)-bisformylbinaphthol for L₂, (R)-monoformylbinaphthol for L₆ and salicylaldehyde for L₇) (0.001 mmol) and 2-(isoindolin-2-yl)-1,2-diphenylethan-1-amine (0.002 mmol of (1S,2S)-configuration for L₂, 0.001mmol (1R,2R)-configuration for L₆ and L₇) was stirred for 2 hours in anhydrous dichloromethane (1.0 ml) at rt. Then added Zn(OAc)₂ (0.003 mmol for L₂, 0.002 mmol for L₆ and 0.001mmol for L₇) and stirred for 0.5 hour in the same temperature to afford Zn complex solution.

To a solution of in situ prepared Zn-complex as describe above, 5-phenylhex-5-enoic acid (0.1 mmol) in toluene (3.0 ml) was added and stirred for 0.5 hour at -78 °C. Then, N-iodosuccinimide (NIS) (0.11 mmol) and I₂ (0.02 mmol) were added to the reaction mixture. After being stirred for 24 h, the reaction mixture was quenched with saturated Na₂SO₄ aq and then the products were extracted with dichloromethane in three times. The collected organic layer was dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=5/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column.

[For entries 3, 5]

A mixture of (R)-bisformylbinaphthol and corresponding diamine (0.005 mmol) was stirred for 2 hours in anhydrous dichloromethane (1.0 ml) at rt. Then added Zn(OAc)₂ (0.015 mmol) and stirred for 0.5 hour in same temperature to afford Zn complex solution. 5-phenylhex-5-enoic acid (0.1 mmol) in toluene (3.0 ml) was added and stirred for 0.5 hour at -78°C. Then, N-iodosuccinimide (NIS) (0.11 mmol) and I₂ (0.02 mmol) were added to the...
reaction mixture. After being stirred for 24h, the reaction mixture was quenched with saturated Na₂SO₃ aq and then the products were extracted with dichloromethane in three times. The collected organic layer was dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=5/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column.

[For entry 4]

A mixture of 3,3’-bis(aminooimino)biphenol L₄ (0.005 mmol) and Zn(OAc)₂ (0.015 mmol) was stirred for 0.5 hour in anhydrous dichloromethane (1.0 ml) at rt. After cooling the mixture to -78 °C, 5-phenylhex-5-enoic acid (0.1 mmol) in toluene (3.0 ml) was slowly added to the resulting yellow solution and stirred for 0.5 hour at the same temperature. Then, N-iodosuccinimide (NIS) (24.6 mg, 0.11 mmol) and I₂ (5.0 mg, 0.02 mmol) were added to the reaction mixture. After being stirred for appropriate time, the reaction mixture was quenched with saturated Na₂SO₃ aq and 1N NaOH aq, and then the products were extracted with dichloromethane in 3 times. The collected organic layer was dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 5/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column.

4. DFT calculations of the L₄-Zn(OAc)₂ complex (Figure S1)

In the DFT calculation of L₄-Zn(OAc)₂ complex, the conformation having (R)-axis L₄-Zn₃ complex is stable in 6.0 kcal/mol to the (S)-axis configuration (Fig. S1). Details of computational method are described in the section 11.

![Figure S1](image-url)

**Figure S1.** Gibbs free energy difference (kcal/mol) between (R)-axis L₄-Zn and (S)-axis L₄-Zn, related to Table 1.
5. Enantioselective iodolactonization and bromolactonization

(1) Enantioselective iodolactonization

A mixture of 3,3'-bis(aminoimino)binaphthol (0.001 mmol) and Zn(OAc)$_2$ (0.003 mmol) was stirred for 0.5 hour in anhydrous dichloromethane (1.0 ml) at rt. After cooling the mixture to -78 °C, carboxylic acid (0.1 mmol) in toluene (3.0 ml) was slowly added to the resulting yellow solution and stirred for 0.5 hour at the same temperature. Then, N-iodosuccinimide (NIS) (24.6 mg, 0.11 mmol) and I$_2$ (5.0 mg, 0.02 mmol) were added to the reaction mixture. After being stirred for appropriate time, the reaction mixture was quenched with saturated Na$_2$SO$_3$ aq and 1N NaOH aq, and then the products were extracted with dichloromethane in 3 times. The collected organic layer was dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/acetone=8/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H and Chiralpak AD-H column.

(2) Enantioselective bromolactonization

A mixture of 3,3'-bis(aminoimino)binaphthol (0.005 mmol) and Zn(OAc)$_2$ (0.015 mmol) was stirred for 0.5 hour in anhydrous dichloromethane (1.0 ml) at rt. After cooling the mixture to -40 °C, carboxylic acid (0.1 mmol) in toluene (3.0 ml) was slowly added to the resulting yellow solution and stirred for 0.5 hour at the same temperature. Then, N-bromosuccinimide (NBS) (19.6 mg, 0.11 mmol) was added to the reaction mixture. After being stirred for appropriate time, the reaction mixture was quenched with saturated Na$_2$SO$_3$ aq and 1N NaOH aq, and then the products were extracted with dichloromethane in 3 times. The collected organic layer was dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/acetone=8/1) to afford the bromolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H and Chiralpak AD-H column.
Table S1. Catalytic asymmetric halolactonization using Zn$_3$(OAc)$_4$-3,3'-bis(aminooimino)binaphthoxide (tri-Zn) catalyst, related to Table 2. For 2, X= 1 at -78 °C with 0.2 equiv of I$_2$. For 3, X= 5 at -40 °C.

|   |   |   |
|---|---|---|
| 2a: >99% yield, 99.5% ee | 2b: >99% yield, 99.8% ee | 2c: >99% yield, 99.8% ee |
| 3a: 99% yield, 94% ee | 3b: 99% yield, 92% ee | 3c: 91% yield, 95% ee |
| 2d: >99% yield, 94% ee | 2e: >99% yield, 99.9% ee | 2f: >99% yield, 99.7% ee |
| 3d: 90% yield, 90% ee | 3e: 92% yield, 99% ee | 3f: 99% yield, 92% ee |
| 2g: >99% yield, 82% ee | 2h: 74% yield, 99% ee | 2i: 93% yield, 45% ee |
| 3g: 89% yield, 95% ee | 3h: 88% yield, 87% ee | 3i: 56% yield, 72% ee |
6. Non-linear effect on the catalytic asymmetric iodolactonization

![Graph showing non-linear effect](image)

| ee(%) | ligand | 0 | 28 | 51 | 78 | 99 |
|-------|--------|---|----|----|----|----|
|       | product| 0 | 35 | 55 | 74 | 99 |

**Figure S2.** Non-linear effect on asymmetric iodolactonization, related to Figure 3.
7. Job plot analysis on the interaction between tri-Zn catalyst and carboxylic acid (1a)

The $^1$H-NMR spectra were collected at $-40 \, ^\circ\mathrm{C}$ in toluene-$d_8$. The analysis was conducted using the chemical shift of the imine proton of the tri-Zn catalyst.

![Job Plot](image)

| sample number | 0  | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  |
|---------------|----|----|----|----|----|----|----|----|----|----|
| [cat]/([cat]+[SM]) | 1  | 0.9| 0.8| 0.7| 0.6| 0.5| 0.4| 0.3| 0.2| 0.1|
| $\Delta \delta^* [\text{cat}]/([\text{cat}]+[\text{SM}])$ | 0  | 0.0144 | 0.0232 | 0.028 | 0.0306 | 0.0315 | 0.0288 | 0.024 | 0.0174 | 0.0116 |
| $\Delta \delta$ | 0  | 0.016 | 0.029 | 0.04 | 0.051 | 0.063 | 0.072 | 0.08 | 0.087 | 0.116 |
| peak(imine) | 8.528 | 8.544 | 8.557 | 8.568 | 8.579 | 8.591 | 8.6 | 8.608 | 8.615 | 8.644 |

Figure S3. Job plot analysis on the interaction between tri-Zn catalyst and carboxylic acid (1a), related to Figure 3.
8. UV-Vis analysis on the interaction between tri-Zn catalyst and NIS-I₂ complex

In this analysis, tri-Zn catalyst prepared from L₄ was used for avoiding a fluorescence effects caused by the tri-Zn catalyst prepared from L₁.

The UV-Vis spectra were collected at room temperature in dehydrated CH₂Cl₂, and concentration of tri-Zn catalyst was constant at 5.0*10⁻⁵ M.

**Figure S4.** UV-Vis analysis on the interaction between tri-Zn catalyst and NIS-I₂ complex, related to Figure 3.
9. Analytical data for product of iodolactonization and bromolactonization

(R)-6-(iodomethyl)-6-phenyltetrahydro-2H-pyran-2-one (2a)

TLC Rf = 0.40 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.44-7.33 (m, 5H), 3.57 (dd, J=11.3, 11.1 Hz, 2H), 2.55-2.30 (m, 4H), 1.87-1.79 (m, 1H), 1.63-1.56 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 170.4, 140.1, 129.0, 128.4, 125.1, 84.4, 32.0, 28.9, 17.7, 16.5; HRMS calced for C12H14O2I (M+H)+: 317.0033, found: m/z 317.0031; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 14.5 min, major enantiomer tR = 16.3 min; 99.5% ee; [α]D19.0 = -31.6 (c=1.0, CHCl3, 99.5% ee); IR (neat) 2956, 2933, 2863, 1734, 1682, 1575, 1388, 1276, 1130, 879 cm⁻¹

(R)-6-(bromomethyl)-6-phenyltetrahydro-2H-pyran-2-one (3a)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.45-7.33 (m, 5H), 3.66 (dd, J=19.7 Hz, 11.1 Hz, 2H), 2.55-2.33 (m, 4H), 1.88-1.80 (m, 1H), 1.65-1.53 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.4, 140.2, 129.0, 128.5, 125.3, 85.1, 41.5, 30.0, 29.6, 29.0, 16.2; HRMS calced for C12H13O2BrNa (M+Na)+: 290.9991, found: m/z 290.9990; Enantiomeric excess was determined by HPLC with a Chiralecel OD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm); minor enantiomer tR = 13.2 min, major enantiomer tR = 17.5 min; 94% ee; [α]D19.0 = -15.2 (c=1.0, CHCl3, 94% ee); IR (neat) 2361, 1736, 1447, 1261, 1231, 1180, 1011, 1045, 932, 766, 702 cm⁻¹

(R)-6-(bromomethyl)-6-(p-bromophenyl)tetrahydro-2H-pyran-2-one (3b)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.54 (d, J=8.30 Hz, 2H), 7.28 (d, J=8.53 Hz, 2H), 3.68-3.59 (m, 2H), 2.56-2.31 (m, 4H), 1.92-1.82 (m, 1H), 1.68-1.55 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.0, 139.3, 132.1, 127.2, 122.8, 84.8, 41.0, 30.0, 29.0, 16.2; HRMS calced for C12H13O2BrNa (M+Na)+: 368.9096, found: m/z 368.9092; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm); minor enantiomer tR = 12.6 min, major enantiomer tR = 15.7 min; 92% ee; [α]D19.0 = -13.4 (c=1.0, CHCl3, 92% ee); IR (neat) 2963, 2251, 1744, 1732, 1489, 1231, 1180, 1045, 1009 cm⁻¹

(R)-6-(bromomethyl)-6-(4-chlorophenyl)tetrahydro-2H-pyran-2-one (3c)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.42-7.32 (m, 4H), 3.65 (d, J=11.2 Hz, 1H), 3.60 (d, J=11.2 Hz, 1H), 2.56-2.31 (m, 4H), 1.91-1.82 (m, 1H), 1.65-1.52 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.0, 138.8, 134.6, 129.2, 126.9, 84.8, 41.1, 30.0, 29.1, 16.2; HRMS calced for C12H13O2BrClNa (M+Na)+: 324.9601, found: m/z 324.9595; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 14.8 min, major enantiomer tR = 18.8 min; 90% ee; [α]D18.7 = -5.0 (c=1.0, CHCl3, 90% ee); IR (neat) 2987, 1725, 1491, 1444, 1232, 1043, 886, 821, 664 cm⁻¹

S12
(R)-6-(bromomethyl)-6-(p-fluorophenyl)tetrahydro-2H-pyran-2-one (3d)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.41-7.36 (m, 2H), 7.13-7.07 (m, 2H), 3.63 (dd, J=23.3, 11.2 Hz, 2H), 2.57-2.32 (m, 4H), 1.91-1.77 (m, 1H), 1.68-1.54 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.1, 161.3, 136.1, 127.4, 127.3, 116.1, 115.8, 84.8, 41.4, 30.0, 29.1, 16.2; HRMS calced for C12H12O2BrNa (M+Na)+: 308.9897, found: m/z 308.9897; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm); minor enantiomer tR = 11.6 min, major enantiomer tR = 13.9 min; 94% ee; [α]D^19.0= -12.2 (c=1.0, CHCl3, 94% ee); IR (neat) 2963, 1730, 1603, 1510, 1300, 1261, 1234, 1044, 932, 833 cm⁻¹

(R)-6-(bromomethyl)-6-(p-(trifluoromethyl)phenyl)tetrahydro-2H-pyran-2-one (3e)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.70 (d, J=8.30 Hz, 2H), 7.56 (d, J=8.30 Hz, 2H), 3.70-3.64 (m, 2H), 2.60-2.38 (m, 4H), 1.96-1.86 (m, 1H), 1.64-1.54 (m, 1H); 13C NMR (100MHz, CDCl3) δ 169.7, 144.3, 131.0, 130.6, 126.0, 125.9, 125.1, 122.3, 84.8, 40.8, 30.3, 29.1, 16.2; HRMS calced for C12H12O2BrF3Na (M+Na)+: 358.9865, found: m/z 358.9864; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm); minor enantiomer tR = 10.7 min, major enantiomer tR = 14.0 min; 99.9% ee; [α]D^19.0= -7.2 (c=1.0, CHCl3, 99.9% ee); IR (neat) 2963, 1744, 1410, 1327, 1263, 1231, 1071, 1045, 1017, 934, 837 cm⁻¹

(R)-6-(bromomethyl)-6-(m-tolyl)tetrahydro-2H-pyran-2-one (3f)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.33-7.27 (m, 1H), 7.24-7.15 (m, 3H), 3.65 (dd, J=11.0, 18.3 Hz, 2H), 2.57-2.18 (m, 7H), 1.91-1.72 (m, 1H), 1.66-1.53 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.6, 140.2, 138.8, 129.2, 128.8, 126.0, 122.4, 85.1, 41.6, 30.0, 29.1, 21.6, 16.2; HRMS calced for C13H16O2Br (M+H)+: 283.0328, found: m/z 283.0327; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 13.3 min, major enantiomer tR = 14.3 min; 94% ee; [α]D^19.5= -8.5 (c=1.0, CHCl3, 94% ee); IR (neat) 2988, 1743, 1264, 1234, 1183, 1106, 1046, 931, 789, 711 cm⁻¹

(R)-6-(bromomethyl)-6-(4-methoxyphenyl)tetrahydro-2H-pyran-2-one (3g)

TLC Rf = 0.41 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.37-7.27 (m, 2H), 6.94-6.93 (m, 2H), 3.82 (s, 3H), 3.67 (d, J=11.0 Hz, 1H), 3.60 (d, J=11.2 Hz, 1H), 2.57-2.31 (m, 4H), 1.88-1.80 (m, 1H), 1.75-1.56 (m, 1H); 13C NMR (100MHz, CDCl3) δ 170.6, 159.5, 132.0, 126.7, 114.2, 84.9, 55.3, 41.7, 29.7, 29.0, 16.2; HRMS calced for C13H16O2BrNa (M+Na)+: 321.0097, found: m/z 321.0091; Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm);
minor enantiomer $t_r = 20.4$ min, major enantiomer $t_r = 22.5$ min; 97% ee; $[\alpha]_D^{18.1} = -9.0$ ($c=1.0$, CHCl$_3$, 97% ee)

IR (neat) 2988, 2957, 1742, 1610, 1512, 1461, 1306, 1253, 1181, 1045, 931, 833, 734 cm$^{-1}$

$97\%$ ee; $[\alpha]_D^{18.1} = -9.0$ ($c=1.0$, CHCl$_3$, 97% ee)

$13\%$ ee; $[\alpha]_D^{18.0} = -23.1$ ($c=1.0$, CHCl$_3$, 87% ee)

IR (neat) 2961, 1746, 1447, 1265, 1244, 1211, 1175, 1146, 1053, 764, 704 cm$^{-1}$

Enantiomeric excess was determined by HPLC with a Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm); minor enantiomer $t_r = 7.4$ min, major enantiomer $t_r = 8.3$ min; 87% ee; $[\alpha]_D^{18.0} = -23.1$ ($c=1.0$, CHCl$_3$, 87% ee)

IR (neat) 2956, 1738 cm$^{-1}$

Enantiomeric excess was determined by HPLC with a Chiralpack OD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer $t_r = 13.6$ min, major enantiomer $t_r = 15.1$ min; 45% ee; $[\alpha]_D^{27.0} = -29.0$ ($c=1.0$, CHCl$_3$, 45% ee)

IR (neat) 2956, 1738 cm$^{-1}$

Enantiomeric excess was determined by HPLC with a Chiralpack OD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer $t_r = 12.8$ min, major enantiomer $t_r = 15.9$ min; 78% ee; $[\alpha]_D^{18.6} = -2.3$ ($c=1.0$, CHCl$_3$, 78% ee)

IR (neat) 2988, 1747, 1444, 1351, 1329, 1267, 1178, 1037, 709 cm$^{-1}$
10. Substrate preparation for desymmetric asymmetric iodolactonization

a. General procedure for preparation of diolefinic acid 4

Scheme S5. Synthetic routes of diolefinic acid 4, related to Figure 5.

Diolefinic acid 4 was prepared from α-methylstyrene derivatives and dimethyl malonate according to the procedure (Pratch and Overmann, 2015; Tay et al. 2014).

b. Analytical data for substrate 4

4-phenyl-2-(2-phenylallyl)pent-4-enoic acid (4a)

\[
\text{TLC } R_f = 0.32 \text{ (hexane : ethyl acetate = 2:1), } \delta \text{ NMR } (400 \text{ MHz, CDCl}_3) \delta 7.30-7.24 \text{ (m, 10H), 5.33 (s, 2H), 5.11 (s, 2H), 2.90-2.83 (m, 2H), 2.74-2.67 (m, 3H) The NMR spectra was identical to those previously reported (Niu et al. 2015).}
\]

4-(m-tolyl)-2-(2-(m-tolyl)allyl)pent-4-enoic acid (4b)

\[
\text{TLC } R_f = 0.42 \text{ (hexane : ethyl acetate = 2:1), } \delta \text{ NMR } (400 \text{ MHz, CDCl}_3) \delta 7.16-7.04 \text{ (m, 8H), 5.31 (d, J=0.8 Hz, 2H), 5.09 (s, 2H), 2.87-2.80 (m, 2H), 2.74-2.67 (m, 3H); } \delta \text{ C NMR } (100 \text{ MHz, CDCl}_3) \delta 181.4, 145.3, 139.9, 137.8, 128.4, 128.2, 126.8, 123.2, 114.6, 42.7, 37.4, 21.5; \text{ HRMS calced for } \text{C}_{22}\text{H}_{23}\text{O}_{2} (\text{M-H})^{-}: 319.1704, \text{ found: } m/z 319.1711; \text{ IR (neat) 2925, 1708, 1446, 1240, 897, 795, 713 cm}^{-1}\]

S15
4-(o-tolyl)-2-(2-(o-tolyl)allyl)pent-4-enoic acid (4c)

TLC Rf = 0.48 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl₃) δ 7.17-7.13 (m, 4H), 7.11-7.04 (m, 2H), 6.95 (d, J=7.6 Hz), 5.18 (s, 1H), 4.91 (d, J=1.6 Hz, 2H), 2.75-2.68 (m, 2H), 2.58-2.50 (m, 3H), 2.24 (s, 6H); 13C NMR (100 MHz, CDCl₃) δ 181.8, 146.6, 141.6, 134.8, 130.1, 128.5, 127.1, 125.4, 116.3, 42.2, 39.7, 19.7; HRMS calced for C₂₂H₂₃O₂ (M-H) : 319.1704, found: m/z 319.1707; IR (neat) 2945, 1708, 1444, 1240, 942, 725 cm⁻¹

4-(3-(trifluoromethyl)phenyl)-2-(2-(3-(trifluoromethyl)phenyl)allyl)pent-4-enoic acid (4d)

TLC Rf = 0.27 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl₃) δ 7.56 (s, 2H), 7.50 (d, J=7.6 Hz, 2H), 7.43-7.35 (m, 4H), 5.38 (s, 2H), 5.20 (d, J=0.8 Hz, 2H), 2.89 (dd, J=14.4 Hz, 8.4 Hz, 2H), 2.73 (dd, J=14.2 Hz, 5.6 Hz, 2H), 2.62-2.54 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ 181.1, 144.1, 140.8, 130.8 (q, J_CF=31.9 Hz), 129.3, 128.9, 124.4 (q, J_CF=3.8 Hz), 124.0 (q, J_CF=276.6 Hz), 122.9 (q, J_CF=3.8 Hz), 116.6, 42.8, 37.2; HRMS calced for C₂₂H₁₇O₂F₆ (M-H) : 427.1138, found: m/z 427.1143; IR (neat) 3005, 1709, 1333, 1165, 1120, 1073, 902, 696 cm⁻¹

4-(3-methoxyphenyl)-2-(2-(3-methoxyphenyl)allyl)pent-4-enoic acid (4e)

TLC Rf = 0.31 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl₃) δ 7.18-7.14 (m, 2H), 6.86-6.84 (m, 4H), 6.79-6.76 (m, 2H), 5.32 (d, J=1.2 Hz, 2H), 5.09 (s, 2H), 3.77 (s, 6H), 2.83 (dd, J=14.4 Hz, 8.0 Hz, 2H), 2.68-2.54 (m, 3H); 13C NMR (100 MHz, CDCl₃) δ 181.3, 159.5, 145.2, 141.6, 129.3, 118.6, 115.0, 113.0, 112.0, 55.1, 42.8, 37.5; HRMS calced for C₂₂H₂₃O₄ (M-H) : 351.1602, found: m/z 351.1610; IR (neat) 2948, 1706, 1576, 1241, 903, 835 cm⁻¹

4-(4-chlorophenyl)-2-(2-(4-chlorophenyl)allyl)pent-4-enoic acid (4f)

TLC Rf = 0.32 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl₃) δ 7.26-7.22 (m, 4H), 7.20-7.17 (m, 4H), 5.30 (s, 2H), 5.11 (s, 2H), 2.83 (dd, J=14.4 Hz, 8.0 Hz, 2H), 2.68-2.54 (m, 3H); 13C NMR (100 MHz, CDCl₃) δ 181.2, 144.1, 138.3, 133.5, 128.5, 127.4, 115.5, 42.6, 37.1; HRMS calced for C₂₀H₁₇O₂Cl₂ (M-H) : 359.0611, found: m/z 359.0623; IR (neat) 2968, 1698, 1494, 1241, 903, 835 cm⁻¹

4-(naphthalen-2-yl)-2-(2-(naphthalen-2-yl)allyl)pent-4-enoic acid (4g)

TLC Rf = 0.30 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl₃) δ 7.75 (d, J=8.0 Hz, 2H), 7.67-7.65 (m, 4H), 7.53 (d, J=8.0 Hz, 2H), 7.46-7.35 (m, 6H), 5.49 (d, J=0.8 Hz, 2H), 5.24 (s, 2H), 3.00 (dd, J=13.8 Hz, 8.0 Hz, 2H), 2.90-2.78 (m, 3H);
11. General procedure of catalytic desymmetric asymmetric iodolactonization

A mixture of 3,3′-bis(aminomino)binaphthol (4.7 mg, 0.005 mmol) and Zn(OAc)$_2$ (2.8 mg, 0.015 mmol) was stirred for 1 hour in anhydrous CHCl$_3$ (1.0 ml) at rt, the reaction mixture was added carboxylic acid (0.1 mmol) and toluene (3.0 ml). After cooling the mixture to -78 °C, the reaction mixture was stirred for 0.5 hour at the same temperature. Then, N-iodosuccinimide (NIS) (24.7 mg, 0.11 mmol) and I$_2$ (5.1 mg, 0.02 mmol) were added to the reaction mixture. After being stirred for appropriate time, the reaction mixture was quenched with saturated Na$_2$SO$_3$aq and then the products were extracted with CH$_2$Cl$_2$ in 3 times. The collected organic layer was dried over Na$_2$SO$_4$. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexane/ethyl acetate=20/1 ~ 10/1) to afford the iodolactone. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H and Chiralpak AD-H and AS-H and Chiralpak IC-3 column.

12. Analytical data for product of desymmetric iodolactonization

(3S,5R)-5-(iodomethyl)-5-phenyl-3-(2-phenylallyl)dihydrofuran-2(3H)-one (5a)

TLC Rf= 0.74 (hexane : ethyl acetate = 2:1), $^1$H NMR (400 MHz, CDCl$_3$) δ 7.38-7.24 (m, 10H), 5.34 (s, 1H), 5.15 (s, 1H), 3.61 (d, $J$=11.2 Hz, 1H), 3.55 (d, $J$=11.2 Hz, 1H), 3.38-3.27 (m, 1H), 2.71-2.57 (m, 3H), 2.41-2.30 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 176.8, 145.1, 139.7, 139.4, 128.8, 128.5, 127.9, 126.0, 124.8, 114.7, 84.0, 40.1, 39.0, 36.2, 16.9; HRMS calced for C$_{20}$H$_{19}$O$_2$(M+Na)$^+$: 441.0322, found: m/z 441.0313; Enantiomeric excess was determined by HPLC with a Chiralpack AS-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer $t_r=16.5$ min, major enantiomer $t_r=9.6$ min; 94% ee; [$\alpha$]$_D^{253}=-12.5$ (c=1.0, CHCl$_3$), 99/1 diastereomixture, 94% ee); IR (neat) 3060, 3940, 1772, 1440, 1143, 908, 701 cm$^{-1}$

(3S,5R)-5-(iodomethyl)-5-(m-toly)-3-(2-(m-tolyl)allyl)dihydrofuran-2(3H)-one (5b)

TLC Rf= 0.75 (hexane : ethyl acetate = 2:1), $^1$H NMR (400 MHz, CDCl$_3$) δ 7.25-7.07 (m, 8H), 5.33 (d, $J$=0.4 Hz, 1H), 5.13 (s, 1H), 3.61 (d, $J$=11.2 Hz, 1H), 3.55 (d, $J$=11.2 Hz, 1H), 3.33-3.30 (m, 1H), 2.70-2.55 (m, 3H), 2.38-2.34 (m, 1H), 2.32 (s, 3H), 2.31 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.1, 145.2, 139.7, 139.5, 138.6, 138.1, 129.3, 128.7, 128.6, 128.4, 126.7, 125.5, 123.2, 121.9, 114.5, 84.0, 40.1, 38.9, 36.3, 21.49, 21.46, 17.2; HRMS calced for C$_{22}$H$_{27}$O$_2$NI (M+NH$_4$)$^+$: 464.1081, found: m/z 464.1072; Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer $t_r=16.9$ min, major enantiomer $t_r=8.8$ min; 99% ee; [$\alpha$]$_D^{261}=-12.6$ (c=1.0, CHCl$_3$), 99/1 diastereomixture, 99% ee); IR (neat) 3033, 2925, 1776, 1604, 1452, 1146, 903, 787, 724, 705 cm$^{-1}$
(3S,5R,5’-iodomethyl)-5’-tolyl)-3-(2’-tolylallyl)dihydrofuran-2(3H)-one (5c)

TLC Rf = 0.74 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.39 (d, J=8.0 Hz, 1H), 7.26-7.09 (m, 6H), 7.02 (d, J=7.2 Hz, 1H), 5.30 (d, J=1.2 Hz, 1H), 4.99 (d, J=0.8 Hz, 1H), 3.75 (d, J=11.6 Hz, 1H), 3.69 (d, J=11.6 Hz, 1H), 3.15-3.11 (m, 1H), 2.77 (dd, J=13.2 Hz, 9.6 Hz, 1H), 2.66-2.48 (m, 2H), 2.38 (s, 3H), 2.35-2.26 (m, 4H); 13C NMR (100 MHz, CDCl3) δ 176.8, 146.6, 140.8, 137.5, 134.9, 133.8, 132.8, 130.4, 128.6, 128.3, 127.4, 126.3, 125.58, 125.5, 116.5, 84.7, 39.5, 38.6, 38.5, 21.3, 19.8, 16.0; HRMS calced for C22H27O2NI (M+NH4)+; 464.1081, found: m/z 464.1072; Enantiomeric excess was determined by HPLC with a Chiralpack AS-H column (99:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 46.9 min, major enantiomer tR = 19.3 min; 79% ee; [α]D26.9 = +19.8 (c=1.0, CHCl3, 96/4 diastereomixture, 79% ee); IR (neat) 3060, 2929, 1774, 1487, 1314, 1218, 1165, 1148, 1140, 1148, 908, 728 cm−1

(3S,5R,5’-iodomethyl)-5’-(3-(trifluoromethyl)phenyl)-3’-(2’-(3’-(trifluoromethyl)phenyl)allyl)dihydrofuran-2(3H)-one (5d)

TLC Rf = 0.70 (hexane : ethyl acetate = 2:1), 1H NMR (500 MHz, CDCl3) δ 7.62-7.44 (m, 8H), 5.43 (s, 1H), 5.27 (s, 1H), 3.62 (d, J=11.0 Hz, 1H), 3.56 (d, J=11.0 Hz, 1H), 3.33 (d, J=12.5 Hz, 1H), 2.73-2.58 (m, 3H), 2.45-2.37 (m, 1H); 13C NMR (100 MHz, CDCl3) δ 176.0, 143.8, 140.8, 140.4, 131.4 (q, JCF=32.5 Hz), 121.0 (q, JCF=32.4 Hz), 129.5, 129.3, 129.2, 128.3, 125.7 (q, JCF=3.0 Hz), 124.7 (q, JCF=3.9 Hz), 123.9 (q, JCF=276.6 Hz), 123.6 (q, JCF=276.8 Hz), 122.9 (q, JCF=3.8 Hz), 121.8 (q, JCF=3.8 Hz), 116.5, 83.6, 40.0, 38.8, 35.9, 16.0; HRMS calced for C22H17O2F6Na (M+Na)+; 577.0070, found: m/z 577.0055; Enantiomeric excess was determined by HPLC with two Chiralcel OD-H columns (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 18.8 min, major enantiomer tR = 26.6 min; 98% ee; [α]D26.9 = -7.2 (c=1.0, CHCl3, 99/1 diastereomixture, 98% ee); IR (neat) 1779, 1332, 1165, 1119, 1073, 805, 701 cm−1

(3S,5R,5’-iodomethyl)-5’-(3-methoxyphenyl)-3’-(2’-(3’-methoxyphenyl)allyl)dihydrofuran-2(3H)-one (5e)

TLC Rf = 0.63 (hexane : ethyl acetate = 2:1), 1H NMR (400 MHz, CDCl3) δ 7.27-7.20 (m, 2H), 6.97-6.95 (m, 1H), 6.91-6.90 (m, 1H), 6.87-6.81 (m, 4H), 5.35 (s, 1H), 5.16 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.62 (d, J=11.2 Hz, 1H), 3.56 (d, J=11.6 Hz, 1H), 3.33-3.29 (m, 1H), 2.72-2.56 (m, 3H), 2.35 (dd, J=12.6 Hz, 11.2 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 176.8, 159.8, 159.6, 145.0, 141.3, 141.2, 129.9, 129.5, 118.5, 117.0, 114.9, 113.7, 113.1, 112.1, 110.9, 83.9, 55.3, 55.2, 40.1, 38.9, 36.2, 16.8; HRMS calced for C22H27O4Na (M+Na)+; 496.0979, found: m/z 496.0967; Enantiomeric excess was determined by HPLC with a Chiralpack IC-3 column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer tR = 22.9 min, major enantiomer tR = 24.1 min; 96% ee; [α]D26.9 = -18.1 (c=1.0,
CHCl₃, 99/1 diastereomixture, 96% ee; IR (neat) 1774, 1578, 1487, 1290, 1229, 1145, 908, 728 cm⁻¹

\( \text{CHCl}_3, 99/1 \text{ diastereomixture, 96\% ee) ; I} \text{R (neat) 1774, 1578, 1487, 1290, 1229, 1145, 908, 728 cm}^{-1} \)

\( (3S,5R)-5-(4\text{-chlorophenyl})-3-(2-(4\text{-chlorophenyl})\text{allyl})-5-(\text{iodomethyl})\text{dihydrofuran-2(3H)}\text{-one (5f)} \)

TLC Rf = 0.72 (hexane : ethyl acetate = 2:1), \( ^1\text{H} \text{NMR (400 MHz, CDCl}_3 \))
\( \delta 7.34-7.24 \text{ (m, 8H), 5.35 (s, 1H), 5.17 (s, 1H), 3.59 (d, J=11.2 Hz, 1H), 3.53 (d, J=11.2 Hz, 1H), 3.32-3.24 \text{ (m, 1H), 2.61-2.53 \text{ (m, 3H), 2.61-2.53 \text{ (m, 1H) ; } ^1\text{C} \text{NMR (100 MHz, CDCl}_3 \)) \delta 176.4, 144.0, 138.3, 137.9, 134.8, 134.0, 129.2, 128.9, 127.5, 126.5, 115.5, 83.7, 40.3, 39.0, 36.2, 16.4; HRMS calced for C\text{20}H\text{21}O\text{2NCl}_2I (M+NH}_4^+) : 503.9989, found: m/z 503.9978; Enantiomeric excess was determined by HPLC with a Chiralpack AS-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer \( t_r = 21.5 \text{ min, major enantiomer } t_r = 12.4 \text{ min; 93\% ee; } [\alpha]_D^{25.8} = -25.5 \text{ (c=1.0, CHCl}_3, 99/1 \text{ diastereomixture, 93\% ee)}; \text{IR (neat) 3087, 2950, 1775, 1491, 1139, 1011, 831, 727 cm}^{-1} \)

\( (3S,5R)-5-(\text{iodomethyl})-5-(\text{naphthalen-2-yl})-3-(2-(\text{naphthalen-2-yl})\text{allyl})\text{dihydrofuran-2(3H)}\text{-one (5g)} \)

TLC Rf = 0.72 (hexane : ethyl acetate = 2:1), \( ^1\text{H} \text{NMR (400 MHz, CDCl}_3 \))
\( \delta 7.80-7.69 \text{ (m, 8H), 7.52 (dd, J=8.6 Hz, 1.6 Hz, 1H), 7.46-7.42 \text{ (m, 4H), 7.29 (dd, J=8.8 Hz, 1.6 Hz, 1H), 5.50 (s, 1H), 5.27 (s, 1H), 3.70 (d, J=11.2 Hz, 1H), 3.66 (d, J=11.2 Hz, 1H), 3.53-3.45 \text{ (m, 1H), 2.79-2.68 \text{ (m, 3H), 2.49-2.42 \text{ (m, 1H); } ^1\text{C} \text{NMR (100 MHz, CDCl}_3 \)) \delta 177.0, 144.8, 136.7, 136.5, 133.2, 132.9, 132.8, 132.7, 128.9, 128.25, 128.20, 128.1, 127.5, 126.7, 126.3, 126.1, 124.7, 124.2, 124.1, 122.2, 115.3, 84.2, 40.1, 39.1, 36.1. 16.6; HRMS calced for C\text{28}H\text{27}O\text{2NI (M+NH}_4^+) : 536.1081, found: m/z 536.1070; Enantiomeric excess was determined by HPLC with a Chiralpack AS-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer \( t_r = 22.6 \text{ min, major enantiomer } t_r = 17.0 \text{ min; 92\% ee; } [\alpha]_D^{25.7} = -42.7 \text{ (c=0.25, CHCl}_3, 99/1 \text{ diastereomixture, 92\% ee)}; \text{IR (neat) 3057, 2930, 1773, 1167, 1134, 905, 819, 750, 730 cm}^{-1} \)
13. Transformation of iodolactone 5a

13-1. Transformation to epoxyester 6a

![Scheme S6. Transformation to epoxyester 6a, related to Scheme 1.](image)

A mixture of iodolactone 5a (41.8 mg, 0.1 mmol, 99/1 diastereomixture, 94% ee) and K$_2$CO$_3$ (27.6 mg, 0.2 mmol) in MeOH (1 ml) was stirred for 30 min at rt. After the completion of the reaction, the reaction mixture was partitioned H$_2$O and Et$_2$O. The organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 8/1) to afford the epoxyester 6a (94% yield, 96/4 diastereomixture, 90% ee).

**methyl (S)-4-phenyl-2-(((R)-2-phenyloxiran-2-yl)methyl)pent-4-enoate (6a)**

TLC R$_f$ = 0.63 (hexane : ethyl acetate = 2:1), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31-7.17 (m, 10H), 5.30 (s, 1H), 5.06 (s, 1H), 3.58 (s, 3H), 2.89-2.82 (m, 2H), 2.65-2.55 (m, 3H), 2.44 (dd, $J=15.0$ Hz, 3.6 Hz, 1H), 2.12-2.05 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 175.9, 145.5, 140.2, 139.3, 128.5, 128.4, 127.8, 127.6, 126.3, 125.9, 115.1, 59.2, 55.6, 51.7, 40.3, 38.6, 37.2; HRMS calced for C$_{21}$H$_{22}$O$_3$Na (M+Na)$^+$: 345.1461, found: m/z 345.1456; Enantiomeric excess was determined by HPLC with a Chiralpack IC-3 column (70:30 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer $t_r$ = 5.6 min, major enantiomer $t_r$ = 6.4 min; 90% ee; $[\alpha]_{D}^{22.4}$ = -23.4 (c=1.0, CHCl$_3$, 96/4 diastereomixture, 90% ee); IR (neat) 1732, 1435, 1223, 1193, 1166, 899, 779, 760, 736, 698 cm$^{-1}$

13-2. Transformation to furan 7a

![Scheme S7. Transformation to furan 7a, related to Scheme 1.](image)

A solution of iodolactone 5a (41.8 mg, 0.1 mmol, 99/1 diastereomixture, 94% ee) in THF/MeOH (2/1, 0.9 ml) was added LiBH$_4$ (12.1 mg, 0.5 mmol) at 0°C and the reaction mixture was stirred for 5 h at rt. The reaction mixture was quenched by 1 M NaOH aq. and extracted with CH$_2$Cl$_2$. The organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo. To the solution of crude epoxyalcohol in CH$_2$Cl$_2$ (1 ml) was added PPTS (2.5 mg, 0.01 mmol) and stirred for 1 h at rt. The reaction mixture was quenched by sat. NaHCO$_3$ aq. and extracted with CH$_2$Cl$_2$. The organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 4/1) to afford the furan 7a (67% yield, 96/4 diastereomixture, 94% ee).
((2S,4S)-2-phenyl-4-(2-phenylallyl)tetrahydrofuran-2-yl)methanol (7a)

TLC R_f = 0.48 (hexane : ethyl acetate = 2:1); 1H NMR (400 MHz, CDCl_3) δ 7.37-7.25 (m, 10H), 5.21 (s, 1H), 4.92 (s, 1H), 4.05 (dd, J=8.6 Hz, 6.8 Hz, 1H), 3.60-3.49 (m, 3H), 2.55-2.39 (m, 4H), 2.02 (dd, J=8.0 Hz, 6.0 Hz, 1H), 1.87 (m, 1H); 13C NMR (100 MHz, CDCl_3) δ 147.1, 145.0, 140.8, 128.48, 128.45, 127.7, 127.1, 126.2, 125.3, 113.7, 87.5, 73.4, 70.1, 41.1, 39.3, 38.9; HRMS calced for C_{20}H_{26}O_2N (M+NH_4)^+: 312.1958, found: m/z 312.1955;

Enantiomeric excess was determined by HPLC with a Chiralpack OJ-H column (90:10 hexane:2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 12.0 min, major enantiomer t_r = 14.4 min; 90% ee; [α]_D^{22}\text{D} = +18.1 (c=0.5, CHCl_3, 96/4 diastereomixture, 90% ee); IR (neat) 3439, 3056, 2936, 2863, 1493, 1445, 1044, 1028, 896, 778, 699 cm^{-1}

13-3. Transformation to bicyclic lactone 8a

![Scheme 8](image)

To the solution of iodolactone 5a (41.8 mg, 0.1 mmol, 99/1 diastereomixture, 90% ee) in toluene (2.5 ml) was added AIBN (3.3 mg, 0.02 mmol) and Bu_3SnH (0.15 ml, 0.15 mmol) at 0 °C. The reaction mixture was stirred for 6 h at 80 °C. After cooling to rt, the reaction mixture was concentrated in vacuo and purified by silica-gel column chromatography (hexane/ethyl acetate = 8/1) to afford the bicyclic lactone 8a (80% yield, 93/7 diastereomixture, 94% ee).

(1S,6R)-3,6-diphenyl-7-oxabicyclo[4.2.1]nonan-8-one (8a)

TLC R_f = 0.45 (hexane : ethyl acetate = 4:1); 1H NMR (400 MHz, CDCl_3) δ 7.45-7.17 (m, 10H), 3.05-2.99 (m, 1H), 2.96-2.88 (m, 1H), 2.82 (d, J=13.2 Hz, 1H), 2.57 (dd, J=13.2 Hz, 9.0 Hz, 1H), 2.38-2.11 (m, 4H), 2.07-1.99 (m, 1H), 1.89 (dt, J=2.8 Hz, 13.3 Hz, 1H); 13C NMR (100 MHz, CDCl_3) δ 178.3, 147.0, 146.1, 128.8, 128.6, 127.5, 126.6, 126.5, 123.9, 90.3, 41.7, 41.62, 41.55, 40.7, 37.9, 33.3; HRMS calced for C_{20}H_{21}O_2 (M+H)^+: 293.1536, found: m/z 293.1534; Enantiomeric excess was determined by HPLC with a Chiralpack IC-3 column (90:10 hexane:2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 24.2 min, major enantiomer t_r = 21.9 min; 94% ee; [α]_D^{22}\text{D} = +45.5 (c=1.0, CHCl_3, 93/7 diastereomixture, 94% ee); IR (neat) 1766, 1266, 1239, 1186, 1101, 971, 956, 755, 733, 698 cm^{-1}
14. Details of DFT calculations

All calculations were performed with the Gaussian 09 package (Frisch et al. 2013). The promising TS model was explored first using the simplified chemical model. Based on the rationale TS model, the origin of high enantioselectivity and the role of I₂ were clarified using the realistic chemical model. All geometries were optimized by B3LYP/LANL2DZ for Zn, LANL2DZdp for I, 6-31G* for the rest. Frequency analyses were also carried out to identify the stationary points (TS: one imaginary frequency) and to estimate thermodynamic properties and Gibbs free energies at 298.15 K and 1atm. To evaluate more reliable non-bonding attractive interaction energies (especially halogen bond), TSmajor-B was also optimized by M06/SDD for Zn, aug-cc-pVTZ and SDB pseudopotential for I, 6-31G* for the rest. (Zhao and Truhlar, 2008; Kee and Wong, 2016) The molecular structures were depicted by using the CYLview v1.0.561 β. (Legault, 2009)

![Figure S5. Realistic chemical model and simplified chemical model, related to Figure 3.](image)

As a preliminary study, possible diastereomeric TS structures corresponding to facial-selectivity (major: TSr, minor: TSs), coordination position/nucleophilic oxygen atom in carboxylate anion (terminal: TS_a1, TS_a2, central: TS_b1, TS_b2), and six-membered ring structures in char-like TS (olefin in axial site: TS-1, equatorial site: TS-2) were compared using simplified chemical models (Fig. S6). In agreement with our previously reported experimental result, in which the terminal acetate anion was replaced by the carboxylate anion of 1a, TS_a series were found to be energetically more stable than TS_b series. To clarify the ligand structure-activity relationship, the rationale TS_a series were expanded to the corresponding realistic chemical models (brackets in Fig. S6).TSr_a1_2 (= TSmajor-A) is energetically most stable in consistent with the experimentally observed major enantiomer. Relative Gibbs free energies showed a similar tendency in both simplified and realistic chemical models. This indicates that the chiral diamine framework at 3,3’-positions are not essential for asymmetric induction as observed in the experimentally observed ligand structure-activity relationship.
Figure S6. Schematic diastereomeric TS structures and relative Gibbs free energies (kcal/mol) of simplified chemical models (realistic chemical models in brackets), related to Figure 3.

To identify the rationale TS model involving I₂, various coordination modes of I₂ were explored based on the most stable TSₐ₁ (Fig. S7). Detailed screening of various TS models allowed us to find two possible functions of additional I₂: iodine source for iodination (TS_IN) and Lewis acid activation (TS_NI). The computational results of energetically more favored TS_IN than TS_NI indicate that additional I₂ act as the
iodine source for iodination. Therefore, further screening of TS_IN model was conducted for TSr_a1 series and TSs_a series located within 1 kcal/mol. TSr_a1_2_IN1 (= TSmajor-B) is 3.3-kcal/mol more stable than TSs_a1_2_IN2 (= TSminor-B). Both stable TSs have similar gross structures of TS-A models with slightly different hydrogen bonding network of NIS-tri-Zn. Steric repulsion between the Ph group of 1a and the naphthyl moiety of L1 significantly destabilizes TSs_a1_2_IN2, albeit with the presence of halogen bonding and hydrogen bonding interactions with NIS (Fig. S8).

**Figure S7.** Relative Gibbs free energies (kcal/mol) of TS models involving I₂, related to Figure 3.

**Figure S8.** The most stable diastereomeric TS models of I₂/NIS in the tri-Zn-catalyzed iodolactonization. Bond lengths are in angstroms, related to Figure 3.
The details of three types of attractive non-covalent interactions in \( \text{TS}_{\text{major-B}} \), each interaction energy \( (E_{\text{int}}) \) was estimated using the counterpoise method at the same level as geometry optimization. \( \text{TS}_{\text{major-B}} \) was dissected into three fragments (\( 1a-I_2 \), NIS, and tri-Zn), of which single-point energies were compared with those of partial components (\( \text{tri-Zn}/1a-I_2 \), tri-Zn/NIS, \( 1a-I_2/NIS \)), estimating each interaction energy (Fig. S9A). Electrostastic interaction (101.5 kcal/mol) was found to be a major factor in attractive non-covalent interactions in \( \text{TS}_{\text{major-B}} \). Both hydrogen bond (5.8 kcal/mol) and halogen bond (17.9 kcal/mol) act cooperatively in stabilizing \( \text{TS}_{\text{major-B}} \). To evaluate more reliable non-bonding attractive interaction energies (especially halogen bond), \( \text{TS}_{\text{major-B}} \) was also optimized by M06/SDD for Zn, aug-cc-pVTZ and SDB pseudopotential for I, 6-31G* for the rest (Fig. S9B). TS structure optimized by the M06 method has almost the same gross structure as that by the B3LYP method. Contribution of three types of interaction energies (electrostatic interaction: 12.8 kcal/mol, hydrogen bond: 18.4 kcal/mol, halogen bond: 22.2 kcal/mol) is not fundamentally changed by the M06 method, albeit with the slightly different hydrogen bonding network in the NIS moiety.

![Figure S9](image-url)

**Figure S9.** (A) Interaction energy analysis and (B) \( \text{TS}_{\text{major-B}} \) optimized by M06/SDD for Zn, aug-cc-pVTZ and SDB pseudopotential for I, 6-31G* for the rest, related to Figure 3.
Figure S10 DFT simulations on the second catalytic cycle of Tri-Zn-catalyzed bromocyclization using NBS and I₂ (entry 2 in Table 2), related to Figure 7.

In the first catalytic cycle based on the halogen-incorporated reaction mechanism (Figure 6a), I-Br should be generated after the first catalytic cycle of the Tri-Zn-catalyzed bromocyclization using NBS and I₂ (entry 2 in Table 2). When the I-Br is incorporated into the TS for the second catalytic cycle, the reaction should proceed from TS-I described in the left side of the Figure S10 to give the iodolactone.
15. $^1$H-NMR and $^{13}$C-NMR spectra

Figure S11. $^1$H-NMR of L1, related to Figure 2.

Figure S12. $^{13}$C-NMR of L1, related to Figure 2.
Figure S13. $^1$H-NMR of L4, related to Table 1.

Figure S14. $^{13}$C-NMR of L4, related to Table 1.
Figure S15. $^1$H-NMR of tert-butyl (2-(isoindolin-2-yl)ethyl)carbamate, related to Table 1.

Figure S16. $^{13}$C-NMR of tert-butyl (2-(isoindolin-2-yl)ethyl)carbamate, related to Table 1.
Figure S17. $^1$H-NMR of 2-(isoindolin-2-yl)ethan-1-amine, related to Table 1.

Figure S18. $^{13}$C-NMR of 2-(isoindolin-2-yl)ethan-1-amine, related to Table 1.
Figure S19. $^1$H-NMR of tert-butyl (3-amino-2,3-dimethylbutan-2-yl)carbamate, related to Table 1.

Figure S20. $^{13}$C-NMR of tert-butyl (3-amino-2,3-dimethylbutan-2-yl)carbamate, related to Table 1.

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Figure S21. $^1$H-NMR of tert-butyl (3-(isoindolin-2-yl)-2,3-dimethylbutan-2-yl)carbamate, related to Table 1.

Figure S22. $^{13}$C-NMR of tert-butyl (3-(isoindolin-2-yl)-2,3-dimethylbutan-2-yl)carbamate, related to Table 1.
Figure S23. $^1$H-NMR of 3-(isoindolin-2-yl)-2,3-dimethylbutan-2-amine, related to Table 1.

Figure S24. $^{13}$C-NMR of 3-(isoindolin-2-yl)-2,3-dimethylbutan-2-amine, related to Table 1.
Figure S25. $^1$H-NMR of (R)-2a, related to Table 1.

Figure S26. $^{13}$C-NMR of (R)-2a, related to Table 1.
Figure S27. $^1$H-NMR of (R)-3a, related to Table 2.

Figure S28. $^{13}$C-NMR of (R)-3a, related to Table 2.
Figure S29. $^1$H-NMR of (R)-3b, related to Table S2.

Figure S30. $^{13}$C-NMR of (R)-3b, related to Table S2.
Figure S31. $^1$H-NMR of (R)-3c, related to Table S2.

Figure S32. $^{13}$C-NMR of (R)-3c, related to Table S2.
Figure S33. $^1$H-NMR of (R)-3d, related to Table S2.

Figure S34. $^{13}$C-NMR of (R)-3d, related to Table S2.
Figure S35. $^1$H-NMR of (R)-3e, related to Table S2.

Figure S36. $^{13}$C-NMR of (R)-3e, related to Table S2.
Figure S37. $^1$H-NMR of (R)-3f, related to Table S2.

Figure S38. $^{13}$C-NMR of (R)-3f related to Table S2.
Figure S39. $^1$H-NMR of (R)-3g, related to Table S2.

Figure S40. $^{13}$C-NMR of (R)-3g, related to Table S2.
Figure S41. $^1$H-NMR of (R)-3h, related to Table S2.

Figure S42. $^{13}$C-NMR of (R)-3h, related to Table S2.
Figure S43. $^1$H-NMR of (R)-2i, related to Table S2.

Figure S44. $^{13}$C-NMR of (R)-2i, related to Table S2.
Figure S45. $^1$H-NMR of (R)-3i, related to Table S2.

Figure S46. $^{13}$C-NMR of (R)-3i, related to Table S2.
Figure S47. $^1$H-NMR of 4b, related to Figure 5.

Figure S48. $^{13}$C-NMR of 4b, related to Figure 5.
Figure S49. $^1$H-NMR of 4c, related to Figure 5.

Figure S50. $^{13}$C-NMR of 4c, related to Figure 5.
Figure S51. $^1$H-NMR of 4d, related to Figure 5.

Figure S52. $^{13}$C-NMR of 4d, related to Figure 5.
Figure S53. $^1$H-NMR of 4e, related to Figure 5.

Figure S54. $^{13}$C-NMR of 4e, related to Figure 5.
Figure S55. $^1$H-NMR of 4f, related to Figure 5.

Figure S56. $^{13}$C-NMR of 4f, related to Figure 5.
Figure S57. $^1$H-NMR of 4g, related to Figure 5.

Figure S58. $^{13}$C-NMR of 4g, related to Figure 5.
Figure S59. $^1$H-NMR of (3S,5R)-5a, related to Figure 5.

Figure S60. $^{13}$C-NMR of (3S,5R)-5a, related to Figure 5.
Figure S61. $^1$H-NMR of (3S,5R)-5b, related to Figure 5.

Figure S62. $^{13}$C-NMR of (3S,5R)-5b, related to Figure 5.
Figure S63. $^1$H-NMR of (3S,5R)-5c, related to Figure 5.

Figure S64. $^{13}$C-NMR of (3S,5R)-5c, related to Figure 5.
Figure S65. $^1$H-NMR of (3S,5R)-5d, related to Figure 5.

Figure S66. $^{13}$C-NMR of (3S,5R)-5d, related to Figure 5.
Figure S67. $^1$H-NMR of (3S,5R)-5e, related to Figure 5.

Figure S68. $^{13}$C-NMR of (3S,5R)-5e, related to Figure 5.
Figure S69. $^1$H-NMR of (3S,5R)-5f, related to Figure 5.

Figure S70. $^{13}$C-NMR of (3S,5R)-5f, related to Figure 5.
Figure S71. $^1$H-NMR of (3S,5R)-5g, related to Figure 5.

Figure S72. $^{13}$C-NMR of (3S,5R)-5g, related to Figure 5.
Figure S73. $^1$H-NMR of 6a, related to Scheme 1.

Figure S74. $^{13}$C-NMR of 6a, related to Scheme 1.
Figure S75. $^1$H-NMR of 7a, related to Scheme 1.

Figure S76. $^{13}$C-NMR of 7a, related to Scheme 1.
Figure S77. $^1$H-NMR of 8a, related to Scheme 1.

Figure S78. $^{13}$C-NMR of 8a, related to Scheme 1.
16. HPLC spectra

Chiralpack AD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S79. HPLC of 2a, related to Table 1.
Figure S80. HPLC of 3a, related to Table 2.

Chiralcel OD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm)
Figure S81. HPLC of 3b, related to Table S2.
Figure S82. HPLC of 3c, related to Table S2.
Figure S83. HPLC of 3d, related to Table S2.

Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm)
Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm)

**Figure S84.** HPLC of 3e, related to Table S2.
Figure S85. HPLC of 3f, related to Table S2.
Figure S86. HPLC of 3g, related to Table S2.
Chiralpack AD-H column (92:8 hexane: 2-propanol, 1.0 mL/min, 210 nm)

**Figure S87.** HPLC of 3h, related to Table S2.
Figure S88. HPLC of 2i, related to Table S2.
Figure S89. HPLC of 3i, related to Table S2.
Chiralpack AD-3 column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S90. HPLC of 5a, related to Figure 5.
Chiralpack AS-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S91. HPLC of 5b, related to Figure 5.
Figure S92. HPLC of 5c, related to Figure 5.
Two Chiralcel OD-H columns (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S93. HPLC of 5d, related to Figure 5.
Chiralpack IC-3 column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S94. HPLC of 5e, related to Figure 5.
Figure S95. HPLC of 5f, related to Figure 5.
Chiralpack AS-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S96. HPLC of 5g, related to Figure 5.
Chiralpack IC-3 column (70:30 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S97. HPLC of 6a, related to Table 1.
Chiralpack OJ-H column (90:10 hexane:2-propanol, 1.0 mL/min, 254 nm)

Figure S98. HPLC of 7a, related to Scheme 1.
Chiralpack IC-3 column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Figure S99. HPLC of 8a, related to Scheme 1.
17. X-Ray Crystallographic Data for γ-butyrolactone 5a (dataS1 related to Figure 5)

| Parameter                          | Value                      |
|------------------------------------|----------------------------|
| Identification code                | CCDC 1825566               |
| Chemical formula moiety            | 'C20 H19 I O2'             |
| Chemical formula weight            | 418.25                     |
| Chemical absolute configuration    | ad                         |
| Space group crystal system         | 'orthorhombic'             |
| Space group IT number              | 19                         |
| Space group name H-M alt           | 'P 2 1 2 1'                |
| Space group name Hall              | 'P 2ac 2ab'                |
| Cell length a                       | 5.9572(11)                 |
| Cell length b                       | 12.269(2)                  |
| Cell length c                       | 23.607(5)                  |
| Cell angle alpha                   | 90                         |
| Cell angle beta                    | 90                         |
| Cell angle gamma                   | 90                         |
| Cell volume                         | 1725.4(6)                  |
| Cell formula units Z               | 4                          |
| Cell measurement reflns used       | 3082                       |
| Cell measurement temperature       | 173                        |
| Cell measurement theta max         | 24.4412                    |
| Cell measurement theta min         | 2.3944                     |
| Shelx estimated absorpt T max      | 0.913                      |
| Shelx estimated absorpt T min      | 0.707                      |
| Exptl absorpt coefficient mu       | 1.863                      |
| Exptl absorpt correction T max     | 0.91                       |
| Exptl absorpt correction T min     | 0.84                       |
| Exptl absorpt correction type      | empirical                  |
| Exptl absorpt process details      | 'SADABS (Sheldrick 1996)'  |
| Exptl crystal colour               | colourless                 |
| Exptl crystal density diffrn       | 1.610                      |
| Exptl crystal description          | plate                      |
| Exptl crystal F 000                | 832                        |
| Exptl crystal size max             | 0.2                        |
| Exptl crystal size mid             | 0.05                       |
| Exptl crystal size min             | 0.05                       |
| Exptl special details             | 'SADABS (Sheldrick 1996)'  |
| Diffn reflns av R equivalents     | 0.0356                     |
| Diffn reflns av unetl/nnetl        | 0.0505                     |
| Diffn reflns Laue measured fraction full | 0.998                  |
| Diffn reflns Laue measured fraction max | 0.932                |
| Diffn reflns limit h max           | 7                          |
| Diffn reflns limit h min           | -8                         |
| Diffn reflns limit k max           | 14                         |
| Diffn reflns limit k min           | -16                        |
| Diffn reflns limit l max           | 30                         |
| Diffn reflns limit l min           | -25                        |
| Property                                      | Value                          |
|----------------------------------------------|--------------------------------|
| diffrn_reflns_number                        | 10190                          |
| diffrn_reflns_point_group_measured_fraction_full | 0.995                          |
| diffrn_reflns_point_group_measured_fraction_max | 0.900                          |
| diffrn_reflns_theta_full                     | 25.242                         |
| diffrn_reflns_theta_max                      | 28.771                         |
| diffrn_reflns_theta_min                      | 2.394                          |
| diffrn_detector_area_resol_mean              | 8.3333                         |
| diffrn_measured_fraction_theta_full          | 0.998                          |
| diffrn_measured_fraction_theta_max           | 0.932                          |
| diffrn_measurement_device_type               | 'Bruker APEXII CCD area detector' |
| diffrn_measurement_method                    | 'Phi and Omega scans'          |
| diffrn_radiation_type                        | MoKα                           |
| diffrn_radiation_wavelength                  | 0.71073                        |
| reflns_Friedel_coverage                      | 0.672                          |
| reflns_Friedel_fraction_full                 | 0.991                          |
| reflns_Friedel_fraction_max                  | 0.856                          |
| reflns_number_gt                             | 3601                           |
| reflns_number_total                          | 4033                           |
| reflns_threshold_expression                  | 'I > 2σ(I)'                    |
| refine_diff_density_max                      | 0.413                          |
| refine_diff_density_min                      | -0.347                         |
| refine_diff_density_rms                      | 0.082                          |
| refine_is_abs_structure_Flack               | -0.017(16)                     |
| refine_is_goodness_of_fit_ref                | 1.036                          |
| refine_is_hydrogen_treatment                 | constr                         |
| refine_is_matrix_type                        | full                           |
| refine_is_number_parameters                  | 208                            |
| refine_is_number_reflns                      | 4033                           |
| refine_is_number_restraints                  | 0                              |
| refine_is_R_factor_all                       | 0.0379                         |
| refine_is_R_factor_gt                        | 0.0304                         |
| refine_is_restrained_S_all                   | 1.036                          |
| refine_is_shift/su_max                       | 0.000                          |
| refine_is_shift/su_mean                      | 0.000                          |
| refine_is_structure_factor_coef              | Fsqd                           |
| refine_is_weighting_details                  | 'w=1/[σ(I)^2+(0.0111P)^2+0.0059P] where P=(Fo^2+2Fc^2)/3' |
| refine_is_weighting_scheme                   | calc                           |
| refine_is_wR_factor_gt                       | 0.0502                         |
| refine_is_wR_factor_ref                      | 0.0532                         |
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