# Allylsamarium Bromide-Mediated Cascade Cyclization of Homoallylic Esters. Synthesis of 2-(2-Hydroxyalkyl)cyclopropanols and 2-(2-Hydroxyethyl)bicyclo[2.1.1]hexan-1-ols

Mengmeng Shen,<sup>†</sup> Yawei Tu,<sup>†</sup> Guanqun Xie,<sup>†</sup> Qingsheng Niu,<sup>†</sup> Hui Mao,<sup>†</sup> Tingting Xie,<sup>†</sup> Robert A. Flowers, II,<sup>‡</sup> Xin Lv,<sup>\*,†</sup> and Xiaoxia Wang<sup>\*,†</sup>

<sup>†</sup>Department of Chemistry, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua 321004, People's Republic of China

<sup>‡</sup>Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015, United States

**S** Supporting Information

**ABSTRACT:** In continuation of our previous study on the intramolecular reductive coupling of simple homoallylic esters promoted by allylSmBr/HMPA/H<sub>2</sub>O, which afforded a facile synthesis of 2-(2-hydroxyalkyl)cyclopropanols, here we report the reductive cascade cyclization of but-3-enyl but-3-enoates mediated by allylSmBr/HMPA/CuCl<sub>2</sub>·2H<sub>2</sub>O, in which the two C=C bonds were successively coupled to allow the construction of the structurally interesting bridged bicyclic tertiary alcohols. Thus, the 2-(2-hydroxyethyl)bicyclo[2.1.1]-



hexan-1-ols were prepared in moderate to good yields with excellent diastereoselectivity.

# INTRODUCTION

1,4-Diols are widely used for the preparation of important heterocycles such as  $\gamma$ -lactones, pyrroles, tetrahydrofurans, and related natural products.<sup>1</sup> While a large number of methods have been published for the synthesis of 1,2-, 1,3-, and 1,5-diols, only a handful of methods are available for the synthesis of 1,4-diols.<sup>2</sup>

2-(2-Hydroxyalkyl)cyclopropanols are 1,4-diols with a cyclopropanol motif, which exists in a number of pharmaceutical phorbol derivatives,<sup>3</sup> and have also been utilized to assemble multisubstituted tetrahydrofurans<sup>4a,b</sup> and in other transformation.<sup>4c</sup> They could be prepared by Kulinkovich hydroxycyclopropanation of alkene with an ester in the presence of  $Ti(O^{i}Pr)_{4}$  and Grignard reagents.<sup>5</sup> On the other hand, 2-(2hydroxyethyl)bicyclo[2.1.1]hexan-1-ols are 1,4-diols with a pentacyclic alcohol motif, which is a component of, or used for, the synthesis of a number of natural products or pharmaceuticals.<sup>6</sup> The assembly of 1,4-diols with the pentacyclic alcohol subunit<sup>7</sup> was achieved via SmI<sub>2</sub>/HMPApromoted intramolecular coupling of unactivated olefinic ketones followed by treatment with carbonyl electrophiles, but no bridged structure was reported in the initial work.

In this paper, we report the allylSmBr-promoted intramolecular reductive coupling of the aliphatic esters of homoallylic alcohols in the presence of appropriate additives. The reaction afforded a facile and diastereoselective synthesis of 2-(2-hydroxyalkyl)cyclopropanols<sup>8</sup> and 2-(2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ols from readily available materials.

Reductive coupling reactions promoted by  $\text{SmI}_2^9$  have played a unique role in C–C bond formation and have been employed as the key step in natural product synthesis.<sup>10</sup> One of the most important SmI<sub>2</sub>-promoted coupling reactions is the coupling of a carbonyl with an alkene that typically proceeds through initial reduction of an aldehyde or ketone.<sup>11</sup> Active carboxylic acid derivatives such as acid chlorides<sup>12</sup> could also be transformed into a ketyl-like intermediate (acyl radical) by treatment with samarium reagent. Activated amides<sup>13a</sup> and thioesters<sup>13b,c</sup> underwent addition to activated alkenes via the acyl-type radical intermediate. Although the reduction of unactivated carboxylic acid derivatives, such as esters and amides, by SmI<sub>2</sub> have been known for some time,<sup>14</sup> reports concerning the reductive coupling of unactivated carboxylic acid derivatives with alkenes have only recently been developed by the Procter group who expanded the work to a number of lactone-alkenes and related coupling reactions with  $SmI_2/H_2O$  as the reducing agent.<sup>15,16</sup> Mechanistic studies by the Procter group have shown that the key for the reduction or reductive coupling of esters is to trap the ketyl radicals that were formed by electron transfer from Sm(II) to the ester carbonyl, findings consistent with a fast reversible first electron transfer.<sup>17</sup> However, the reductive coupling between aliphatic acyclic esters and alkenes promoted by Sm(II) still remains a challenge.

AllylSmBr, known as a C-nucleophilic reagent used for the allylation reaction<sup>18</sup> has been recognized as an effective SET reagent.<sup>19a,b</sup> We found the addition of HMPA could prohibit its nucleophilicity and at the same time enhance the reducing ability significantly.<sup>19c</sup> It is our hypothesis that the application

Received: August 4, 2014

### The Journal of Organic Chemistry

of allylSmBr as a SET reagent is worth further study because it may exhibit unique advantages in comparison to  $SmI_2$  or related reagents.

## RESULTS AND DISCUSSION

During the preliminary studies in our previous work,<sup>8</sup> homoallylic alcohol acetate **1a** was employed as the model substrate in our initial attempt to investigate the reductive coupling between an acyclic ester group and an alkene moiety. Without any additive, the use of 2.2 equiv of allylSmBr afforded 1-phenylbut-3-en-1-ol **2a** in 86% yield (Scheme 1).

Scheme 1. Reaction of 1a with AllylSmBr without or with Additive



When fresh anhydrous HMPA was used as the additive (10 equiv),<sup>20</sup> a complex mixture resulted. Fortunately, the accidental use of undistilled HMPA as the additive afforded the desired product **3a** in 38% yield. We thus deduced that the presence of water should facilitate the reductive ester–alkene coupling reaction despite the strong moisture sensitivity of allylSmBr. By carefully optimizing the conditions, the reaction could afford the desired **3a** in 73% yield with the molar ratio of the reagent allylSmBr/HMPA/H<sub>2</sub>O being 2.2/10.0/1.0 (Scheme 1). A number of variously substituted 2-(2-hydroxyalkyl)cyclopropanols were also prepared (Scheme 2) in this way.<sup>8</sup>





To further expand the scope of the reaction and explore the use of allylSmBr in the preparation of structurally novel compounds that may otherwise be difficult to access, we examined the reductive cascade coupling of alternative substrates with varying the tether length between the ester group and the C==C bond (Scheme 3).

Substrate 1r with the incorporation of an additional allylic C==C bond afforded 3r in good yield and left the allylic C==C bond untact. The reactions of allylic ester 1s and substrate 1t resulted in deprotection of the acetyl by simple reduction.<sup>21</sup> During these investigations, we observed that the use of the homoallylic ester 4a produced bicyclohexanols of the type 5a. The structure of  $5a^{22}$  was confirmed unambiguously by X-ray diffraction analysis, NMR, and HRMS characterization (Figure 1).

To further develop the protocol, a number of conditions were screened to improve the yield of **5a**. We anticipated that

Scheme 3. Reactions of the Substrates with Different Positions of the C=C Bond



Figure 1. X-ray crystal structure of 5a.

identifying appropriate conditions to increase the yield would enable us to develop the reaction into a useful synthetic tool for the construction of a variety of 2-(2-hydroxyethyl)-bicyclo[2.1.1]hexan-1-ols.

Excess Sm powder (4.76 equiv) and allylBr (3.3 equiv) were used to ensure more efficient transformation. Increase of the amount of  $H_2O$  to 1.6 equiv led to improvement of the isolated yield to 46% (Table 1, entry 1), but no reaction occurred with excess  $H_2O$  (entry 2). Room temperature was found suitable (entries 3 and 4). A recent report showed that addition of diethyl phosphate (EtO)<sub>2</sub>P(O)H to allylSmBr could promote reductive deoxygenation.<sup>23</sup> Unfortunately, only a trace amount of **5a** was produced with this additive (entry 5). With both HMPA and (EtO)<sub>2</sub>P(O)H as the additives, the HPLC yield increased to 46% (entry 6). Because HMPA was shown to be required, all subsequent conditions were examined in its presence unless otherwise specified.

Other proton sources such as MeOH and PhOH afforded even lower yields (entries 7 and 8). We then turned to a basic proton source,<sup>14c</sup> but no major improvement was observed with saturated aq NaHCO<sub>3</sub> (entry 9). A literature survey prompted us to attempt ferric salt as the additive.<sup>7</sup> However, neither anhydrous FeCl<sub>3</sub> nor FeCl<sub>3</sub>·6H<sub>2</sub>O afforded good results (entries 10 and 12). LiCl<sup>24</sup> was reported to positively influence the SET ability of Sm(II) and was examined as well. The addition of LiCl or LiCl/H2O both failed to provide any improvement (entry 11 and 13). Fortunately, when 1.6 equiv of CuCl<sub>2</sub>·2H<sub>2</sub>O was used as the additive, a 78% yield of the desired product was obtained (entry 14). For comparison, the reductive cyclization of 4a using SmI<sub>2</sub>/HMPA/H<sub>2</sub>O and SmBr<sub>2</sub>/HMPA/H<sub>2</sub>O were also attempted. However, in both cases, no desired 5a was obtained and 4a was recovered almost quantitatively. Therefore, the use of HMPA (16 equiv) and  $CuCl_2 \cdot 2H_2O$  (1.6 equiv) as the additives was established as the optimal conditions. A number of 2-(2-hydroxyethyl)-

Table 1. Optimization of the Intramolecular Ester–Alkene Coupling Reaction of 4a Mediated by AllylSmBr/Additives



<sup>*a*</sup>Reaction conditions: **4a** (0.5 mmol), allylBr (3.3 equiv), HMPA (16 equiv unless otherwise specified), Sm powder (4.67 equiv), THF (15 mL), N<sub>2</sub>, 10 h. <sup>*b*</sup>HPLC yields with naphthalene as the internal standard unless otherwise specified. <sup>*c*</sup>Isolated yield. <sup>*d*</sup>No reaction. <sup>*e*</sup>No HMPA was used.

bicyclo[2.1.1]hexan-1-ols were prepared in moderate to good yields as listed in Table 2.

When  $R^1$  is an aryl with  $R^2$ ,  $R^3$ , and  $R^4$  being H, the reaction of but-3-envl but-3-enoates 4 proceeded smoothly under the optimized conditions and afforded the corresponding 2-(2hydroxyethyl)bicyclo[2.1.1]hexan-1-ols 5 in good to excellent yields (Table 2, entries 1-10). When a heteroaryl such as 2furyl was introduced, the desired product was obtained in 25% yield accompanied by a complex mixture (entry 11). When both R<sup>3</sup> and R<sup>4</sup> are methyl instead of H, the reaction afforded the desired product in a moderate yield (45%, entry 12). The same result was obtained for the reaction of 4s (52% yield, entry 19), where  $R^2$  is a methyl rather than H. In the cases where R<sup>1</sup> is an alkenyl or alkyl, good yields were usually obtained (entries 13-18) except for 4t (entries 20, 18%). These results showed that the reductive double cyclization was not substantially affected by electronic effects, but steric hindrance did exert a greater influence on the efficiency. It is noteworthy that the cascade double cyclization reaction afforded only one diastereomer as determined by both HPLC and NMR, showing excellent diastereoselectivity.

The role of CuCl<sub>2</sub>·2H<sub>2</sub>O was also investigated. Because the addition of chloride did not enhance the yields (Table 1, entries 10–13), several studies were conducted to gain further insight into the role of the salt. First, CuCl<sub>2</sub>·2H<sub>2</sub>O alone was treated by the allylSmBr/HMPA system to ascertain if the reduction of Cu(II) occurred. XPS results showed that Cu(II) was reduced into low-valent copper (Figure 3). The XPS of CuCl/ allylSmBr/HMPA/H<sub>2</sub>O system and Cu standard sample was also detected for comparison.

As shown in Figure 2, it is apparent that no satellite peaks (ca. 943 eV) appear for both samples a and b, which indicates that Cu(II) was absent. The Cu(II) in sample a should have been reduced into low-valent copper<sup>25</sup> by the allylSmBr/

HMPA/THF system during the reaction. Recent work by Flowers<sup>26</sup> has shown that Ni(0) is the likely reactive species in  $SmI_2/Ni(II)$  coupling of halides with ketones. Unfortunately, it is difficult in this case to determine whether the low valent copper is Cu(0) or Cu(I). The Cu 2p photoelectron spectra of samples a, b, and c were very similar and also the overlap of Sm MNN (Auger electron spectra) on that of Cu species interferes with the characterization.

Nevertheless, subsequent experiments demonstrated that neither Cu(0) nor Cu(I) in combination with allylSmBr/ HMPA/H<sub>2</sub>O was more effective. The use of CuCl (1.6 equiv) afforded 46% yield of 5a, while Cu(0) afforded a comparable vield (58%) to that obtained from the allvlSmBr/HMPA/H<sub>2</sub>O system (62%). Therefore, it is probable that the coordinated water in CuCl<sub>2</sub>·2H<sub>2</sub>O plays the main role in improving the efficiency for the cascade reaction of substrates 5. Although water is a good proton source for many Sm(II)-promoted reactions,<sup>9</sup> the water released in situ during the reduction of CuCl<sub>2</sub>·2H<sub>2</sub>O into low-valent copper appears to match well with the requirement of a proton source for this reaction. It was fortunate that in our initial attempts, we used excess Sm powder (4.76 equiv) to ensure the complete reductive coupling and there still remained sufficient reducing reagent for the ester-coupling reactions despite the consumption of electrons by 1.6 equiv of Cu(II). It is also worth mentioning that when more than 1.6 equiv of CuCl<sub>2</sub>·2H<sub>2</sub>O was used, the efficiency of the reaction decreased (the loading of  $CuCl_2 \cdot 2H_2O$  was optimized, see Table 3 and Figure 3). The consumption of more electrons by Cu(II) and the supply of excess water are both detrimental to the cascade coupling reaction.

More comprehensive studies may be required to clarify the role of the respective additives. Meanwhile, a probable single electron transfer (SET) mechanism for the allylSmBr-promoted cascade intramolecular cyclization for the generation of **3** and **5** was proposed in Schemes 4 and 5.

As shown in Scheme 4, ester 1 accepts an electron (e) from allylSmBr to form ketyl I, which undertakes a radical addition to the C=C bond and affords radical II in high stereoselectivity. The stereochemistry of II can be rationalized via the chairlike transition state T-1 according to the model proposed by Beckwith for the 5-hexenyl radical cyclization.<sup>27a</sup> The more bulkyl substituent such as OSmL (L represents all the ligands around Sm, including HMPA, THF, and Br) and  $R^1$  ( $R^1$  = aryl or alkyl while  $R^2 = H$ ) adopt pseudoequatorial orientation in T-1, and such a conformer will lead to the formation of II, where  $R^1$ , OSmL, and the newly formed methylene radical are all cis. Subsequent protonation by H<sub>2</sub>O<sup>15e</sup> transforms II into hemiketal III, which then undergoes ring-opening to afford ketone IV. A second electron transfer generates carbanion intermediate V. Intramolecular nucleophilic addition<sup>7,27b</sup> to the ketone carbonyl of V provides both 1,2-trans and 1,2-cis diastereomers depending upon whether the chelation of Sm(III) is available. Therefore, the employment of racemic substrate 1 would finally afford products 3 in two diastereomers. The chelation of Sm(III) does not seem to dominate as much as that of Ti(IV)as in the Kulinkovich reaction,<sup>5d</sup> and the diastereoselectivity of the trans: cis isomers for 3 is only moderate.

When substrate 4 is applied, intermediate VII is first generated and stereoselectively affords key intermediate VIII via T-2 (Scheme 5). Protonation transforms VIII into hemiketals IX and ketones X. Instead of undergoing a further SET process as described in Scheme 3 (from IV to V), X preferably undergoes a second radical cyclization to give new

Table 2. Preparation of 2-(2-Hydroxyethyl)bicyclo[2.1.1]hexan-1-ols Mediated by AllylSmBr/HMPA/CuCl<sub>2</sub>·2H<sub>2</sub>O



"Reaction conditions: allylBr (3.3 equiv), Sm powder (4.67 equiv), HMPA (16 equiv), CuCl<sub>2</sub>·2H<sub>2</sub>O (1.6 equiv), THF (15 mL), N<sub>2</sub>, 10 h. <sup>b</sup>Isolated yield.

radical XI, which then abstracts an electron from Sm(II) to transform into carbanion XII. Finally, intramolecular nucleophilic addition<sup>7,27b</sup> onto the carbonyl followed by protonation affords product 5. The highly stereoselective radical cyclization process (from VII to VIII) rationalizes the excellent diastereoselectivity for the formation of 5.

## CONCLUSIONS

We have achieved the intramolecular unactivated ester–alkene radical cyclization promoted by allylSmBr/HMPA/H<sub>2</sub>O or allylSmBr/HMPA/CuCl<sub>2</sub>·2H<sub>2</sub>O at ambient temperature. The cascade coupling provides a facile synthesis of *cis*-2-(2-hydroxyalkyl)cyclopropanols or 2-(2-hydroxyethyl)-

bicyclo[2.1.1]hexan-1-ols depending upon the structures of the homoallylic esters. With but-3-envl but-3-enoates as the substrates, the two C=C bonds were successively coupled, allowing the construction of the structurally interesting bridged bicyclic tertiary alcohols. The mild reaction conditions, readily available starting materials, good yields, and excellent diastereoselectivity make the reaction attractive for the preparation of the corresponding 1,4-diols.

# EXPERIMENTAL SECTION

**General Information.** Unless otherwise noted, all the cascade reactions were carried out under a nitrogen atmosphere in oven-dried flasks. THF was distilled from sodium/benzophenone. The homoallyl alcohols and their esters were prepared according to literature



Figure 2. Cu 2p photoelectron spectra: (a) CuCl<sub>2</sub>·2H<sub>2</sub>O/allylSmBr/HMPA/THF system; (b) CuCl/allylSmBr/HMPA/H<sub>2</sub>O/THF system; (c) Cu standard sample.

Table 3. Yields of 5a by Using Different Loadings of  $CuCl_2$ ·  $2H_2O$  as the Additive

HPLC yield of <b>5a</b> $(\%)^a$
39
45
53
65
78
48

 $^a\mathrm{HPLC}$  yields were determined using naphthalene as the internal standard.



Figure 3. Yields of 5a vs the loading of  $CuCl_2 \cdot 2H_2O$ .

reports.<sup>28</sup> The synthesis of substrates 1a, 1d, 1g, and 1n have been reported.<sup>28a</sup> Compounds 1b, 1c, 1f, and 1h are known compounds as reported in the literature.<sup>28b</sup> Compound 1j is also known.<sup>28c</sup> All other reagents were received from commercial sources and utilized without further purification, if not stated otherwise. All melting points are uncorrected. The NMR spectra were recorded in CDCl<sub>3</sub> on a 400 MHz or 600 MHz instrument with TMS as internal standard. Chemical shifts ( $\delta$ ) are reported in parts per million (ppm) downfield from TMS. Data are represented as follows: chemical shift, mutiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b =broad), coupling constant (J, Hz), and integration. Thin layer chromatography (TLC) was performed with 0.2 mm thick silica gel plates (GF 254). Visualization was accomplished by UV light. The columns were hand packed with silica gel 60 (160-200 mesh). Unknown products were additionally confirmed by high-resolution mass spectra (HRMS) using a TOF-MS instrument with an ESI Scheme 4. Proposed Mechanism for the Formation of 3



Scheme 5. Proposed Mechanism for the Formation of 5

![](_page_4_Figure_13.jpeg)

source. HPLC yields of 4a were detected by using naphthalene as internal standard. HPLC conditions: C18 column; CH<sub>3</sub>CN/H<sub>2</sub>O = 40:60; flow rate = 0.8 mL/min; retention time 6.8 min). X-ray photoelectron spectra (XPS) detection of Cu 2p spectra were recorded by using an electron spectrometer. An X-ray source of 250 W power and Al K<sub>a</sub> radiation ( $\hbar\nu$  = 1486.6 eV) were used. All spectra were calibrated by using the C 1s line at 284.6 eV as a reference.

General Procedure for the Synthesis of the But-3-enyl But-3-enoates.<sup>28e-g</sup> To a solution of the homoallyl alcohol (10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) were added Ac<sub>2</sub>O (30 mmol) and pyridine (50 mmol) sequentially. The reaction mixture was stirred at 34–37 °C until the reaction was complete (monitored by TLC). The reaction was quenched by the addition of aq HCl (10%). The organic phase was washed with brine (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (300–400 mesh) using petroleum/EtOAc (15/1, v:v) as the eluent to afford compounds 1.

1-(3,4-Dimethoxyphenyl)but-3-en-1-yl Acetate (1e). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.83–6.72 (m, 3H), 5.68–5.59 (m, 2H), 5.01– 4.94 (m, 2H), 3.79 (s, 3H), 3.75 (s, 3H), 2.60–2.43 (m, 2H), 1.95 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.1, 148.8, 148.7, 133.4, 132.5, 119.1, 117.8, 110.8, 109.8, 75.0, 55.8, 55.7, 40.5, 21.1. HRMS (ESI) *m*/ *z*: calcd for C<sub>14</sub>H<sub>18</sub>O<sub>4</sub>Na [M + Na]<sup>+</sup>: 273.1097; found: 273.1099.

*Hept-1-en-4-yl Acetate (1i).* Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.77–5.66 (m, 1H), 5.05–5.00 (m, 2H), 4.91–4.86 (m, 1H), 2.27–

2.24 (m, 2H), 1.99 (s, 3H), 1.53–1.46 (m, 2H), 1.36–1.25 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.7, 133.8, 117.5, 73.0, 38.6, 35.7, 21.1, 18.5, 13.8. HRMS (ESI) *m/z*: calcd for C<sub>9</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 179.1043; found: 179.1048.

1-Cyclopropylbut-3-en-1-yl Acetate (1k). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.80–5.70 (m, 1H), 5.06–4.98 (m, 2H), 4.27–4.21 (m, 1H), 2.43–2.33 (m, 2H), 2.00 (s, 3H), 0.98–0.92 (m, 1H), 0.54–0.40 (m, 2H), 0.38–0.19 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.6, 133.8, 117.3, 77.7, 39.2, 21.2, 14.8, 3.2, 3.1. HRMS (ESI) *m*/*z*: calcd for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 177.0886; found: 177.0882.

1-Allylcyclohexyl Acetate (1). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.77–5.67 (m, 1H), 5.04–5.00 (m, 2H), 2.62–2.61 (m, 2H), 2.17– 2.13 (m, 2H), 1.97–1.96 (m, 3H), 1.57–1.43 (m, 5H), 1.37–1.30 (m, 2H), 1.27–1.16 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.3, 133.0, 118.0, 83.2, 41.9, 34.4, 25.5, 22.2, 21.8, 21.7. HRMS (ESI) *m/z*: calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 205.1199; found: 205.1206.

2,2-Dimethyl-1-phenylbut-3-en-1-yl Acetate (1m). Oil. <sup>1</sup>HNMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.35–7.29 (m, 5H), 5.98–5.93 (m, 1H), 5.66 (s, 1H), 5.09–4.99 (m, 2H), 2.10 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.0, 144.0, 138.0, 128.0, 127.7, 127.6, 113.1, 81.7, 41.1, 24.1, 22.6, 21.1. HRMS (ESI) *m*/*z*: calcd for C<sub>14</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 241.1199; found: 241.1192.

1-Phenylbut-3-en-1-yl Propionate (10). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.42–7.31 (m, 5H), 5.92–5.90 (m, 1H), 5.81–5.74 (m, 1H), 5.16–5.10 (m, 2H), 2.74–2.61 (m, 2H), 2.44–2.36 (m, 2H), 1.19 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  173.5, 140.4, 133.5, 128.5, 127.9, 126.5, 118.0, 74.9, 40.9, 27.8, 9.1. HRMS (ESI) *m*/*z*: calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 227.1043; found: 227.1046.

1-(*p*-Tolyl)but-3-en-1-yl lsobutyrate (**1***p*). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.30–7.20 (m, 4H), 5.87–5.84 (m, 1H), 5.82–5.75 (m, 1H), 5.16–5.10 (m, 2H), 2.73–2.68 (m, 1H), 2.65–2.59 (m, 2H), 2.39 (s, 3H), 1.23 (dd, *J* = 20.7, 7.0 Hz, 6H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 176.1, 137.5, 137.4, 133.6, 129.1, 126.4, 117.9, 74.6, 41.0, 34.2, 21.2, 19.1, 18.9. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 255.1356; found: 255.1358.

2-Phenylpent-4-en-2-yl Acetate (1q). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.38–7.25 (m, 5H), 5.69–5.58 (m, 1H), 5.09–5.05 (m, 2H), 2.88–2.73 (m, 2H), 2.07 (s, 3H), 1.82 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 144.7, 132.9, 128.2, 127.0, 124.6, 118.7, 83.1, 46.4, 25.0, 22.2. HRMS (ESI) *m*/*z*: calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 227.1043; found: 227.1039.

(*E*)-*Hepta*-1,5-*dien*-4-*yl* Acetate (1*r*). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.76–5.69 (m, 2H), 5.45–5.41 (m, 1H), 5.27–5.23 (m, 1H), 5.09–5.05 (m, 2H), 2.39–2.33 (m, 2H), 2.03 (s, 3H), 1.69 (d, *J* = 6.5 Hz, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.2, 133.4, 129.3, 129.0, 117.6, 73.9, 39.0, 21.2, 17.7. HRMS (ESI) *m*/*z*: calcd for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 177.0886; found: 177.0889.

General Procedure for the Cascade Synthesis of Diol  $3.^{29}$  To a two-necked flask containing samarium powder (2.5 mmol) were added THF (18 mL) and allyl bromide (2.2 mmol) under nitrogen. The mixture was stirred at rt for 1 h (the color would turn purple). HMPA (2 mL) and H<sub>2</sub>O (1 mmol) were then added in sequence via a syringe. A solution of substrate 1 (1 mmol) in THF (5 mL) was subsequently added. The color would fade in 3 h (monitored by TLC). The reaction mixture was quenched with aq sodium—potassium tartrate and extracted with diethyl ether (3 × 20 mL). The organic phase was washed with brine (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (300–400 mesh) using petroleum/ EtOAc (5/1, v:v) as the eluent to afford the corresponding products 3.

General Procedure for the Synthesis of the But-3-enyl But-3-enoates.<sup>30</sup> To a solution of homoallylic alcohol (7.9 mmol) in Et<sub>3</sub>N (2.4 g, 23.6 mmol) at 0 °C was added crotonyl chloride (1.57g, 15 mmol). When a yellow precipitate appeared, the reaction mixture was allowed to warm to room temperature and stirred for 3 h before being quenched with 6 N HCl solution (150 mL) and extracted with ether. The organic layer was washed with water, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was purified by chromatography on silica gel (150–200 mesh) using petroleum/EtOAc (15/1, v:v) as the eluent to afford the corresponding esters 4. 1-Phenylbut-3-en-1-yl But-3-enoate (4a). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.38–7.31 (m, SH), 6.02–5.86 (m, 2H), 5.79–5.69 (m, 1H), 5.22–5.08 (m, 4H), 3.17–3.15 (m, 2H), 2.74–2.58 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.7, 140.0, 133.3, 130.2, 128.5, 128.0, 126.5, 118.6, 118.2, 75.4, 40.8, 39.3. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 239.1043; found: 239.1045.

1-(2-Methoxyphenyl)but-3-en-1-yl But-3-enoate (**4b**). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34–7.24 (m, 2H), 6.98–6.87 (m, 2H), 6.30–6.27 (m, 1H), 6.02–5.73 (m, 2H), 5.21–5.03 (m, 4H), 3.85 (s, 3H), 3.16–3.14 (m, 2H), 2.65–2.54 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.5, 156.1, 133.8, 130.4, 128.7, 128.6, 126.3, 120.5, 118.4, 117.5, 110.6, 69.9, 55.5, 39.7, 39.4. HRMS (ESI) m/z: calcd for C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 269.1148; found: 269.1147.

1-(4-Methoxyphenyl)but-3-en-1-yl But-3-enoate (4c). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.34–7.29 (m, 2H), 6.92–6.90 (m, 2H), 5.98–5.91 (m, 1H), 5.86–5.81 (m, 1H), 5.76–5.69 (m, 1H), 5.19–5.16 (m, 2H), 5.13–5.07 (m, 2H), 3.82 (s, 3H), 3.14–3.12 (m, 2H), 2.72–2.67 (m, 1H), 2.61–2.56 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 170.7, 159.3, 133.4, 132.1, 130.3, 128.0, 118.5, 118.0, 113.8, 75.1, 55.2, 40.6, 39.4. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 269.1148; found: 269.1147.

 $1\-(3,4\-Dimethoxyphenyl)but\-3\-en-1\-yl$ But\-3\-enoate (4d). Oil.  $^1\mathrm{H}$ NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  6.91–6.82 (m, 3H), 5.95–5.66 (m, 3H), 5.16–5.03 (m, 4H), 3.88 (s, 3H), 3.85 (s, 3H), 3.14–3.06 (m, 2H), 2.68–2.53 (m, 2H).  $^{13}\mathrm{C}$ NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.6, 148.9, 148.8, 133.4, 132.5, 130.3, 119.1, 118.5, 118.0, 110.9, 109.9, 75.2, 55.9, 55.8, 40.6, 39.3. HRMS (ESI) m/z: calcd for  $\mathrm{C_{16}H_{20}O_4Na}\[\mathrm{M}\+\mathrm{Na}\]^+$ : 299.1254; found: 299.1263.

1-(m-Tolyl)but-3-en-1-yl But-3-enoate (4e). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.31–7.29 (m, 1H), 7.25–7.22 (m, 2H), 7.17–7.15 (m, 1H), 6.04–5.98 (m, 1H), 5.96–5.89 (m, 1H), 5.83–5.76 (m, 1H), 5.26–5.21 (m, 2H), 5.18–5.12 (m, 2H), 3.22–3.15 (m, 2H), 2.78–2.71 (m, 1H), 2.68–2.62 (m, 1H), 2.42 (s, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 170.6, 140.1, 138.0, 133.5, 130.4, 128.8, 128.4, 127.3, 123.6, 118.5, 118.0, 75.4, 40.9, 39.3, 21.5. HRMS (ESI) *m/z*: calcd for  $C_{15}H_{18}O_2Na$  [M + Na]<sup>+</sup>: 253.1199; found: 253.1200.

1-(4-Chlorophenyl)but-3-en-1-yl But-3-enoate (4f). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.33–7.26 (m, 4H), 5.96–5.63 (m, 3H), 5.19– 5.05 (m, 4H), 3.13–3.11 (m, 2H), 2.66–2.52 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.6, 138.5, 133.8, 132.8, 130.0, 128.6, 128.0, 118.7, 118.5, 74.7, 40.6, 39.3. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>15</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 273.0653; found: 273.0657.

1-(3-Chlorophenyl)but-3-en-1-yl But-3-enoate (**4g**). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.35–7.22 (m, 4H), 5.98–5.91 (m, 1H), 5.82–5.80 (m, 1H), 5.74–5.67 (m, 1H), 5.21–5.09 (m, 4H), 3.19–3.12 (m, 2H), 2.68–2.55 (m, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.5, 142.1, 134.4, 132.7, 130.0, 129.8, 128.2, 126.6, 124.7, 118.8, 118.6, 74.6, 40.7, 39.2. HRMS (ESI) *m*/*z*: calcd for C<sub>14</sub>H<sub>15</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 273.0653; found: 273.0656.

*1*-(2-Chlorophenyl)but-3-en-1-yl But-3-enoate (4h). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.44–7.43(m, 1H), 7.37–7.35 (m, 1H), 7.30– 7.27 (m, 1H), 7.24–7.21 (m, 1H), 6.30–6.28 (m, 1H), 6.01–5.94 (m, 1H), 5.84–5.77 (m, 1H), 5.22–5.19 (m, 2H), 5.14–5.09 (m, 2H), 3.19–3.17 (m, 2H), 2.70–2.58 (m, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 170.2, 138.0, 132.9, 132.1, 130.1, 129.6, 128.9, 127.1, 127.0, 118.7, 118.3, 71.9, 39.6, 39.2. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>15</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 273.0653; found: 273.0657.

1-(4-Fluorophenyl)but-3-en-1-yl But-3-enoate (4i). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.36–7.32 (m, 2H), 7.06–7.03 (m, 2H), 5.97– 5.91 (m, 1H), 5.87–5.82 (m, 1H), 5.74–5.67 (m, 1H), 5.19–5.16 (m, 2H), 5.11–5.07 (m, 2H), 3.15–3.12 (m, 2H), 2.70–2.65 (m, 1H), 2.60–2.54 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 170.6, 162.4 (d, J = 244.9 Hz), 135.8 (d, J = 3.2 Hz), 133.0, 130.1, 128.4 (d, J = 8.1 Hz), 118.6, 118.4, 115.3 (d, J = 21.4 Hz), 74.7, 40.7, 39.3. HRMS (ESI) *m*/ *z*: calcd for C<sub>14</sub>H<sub>15</sub>FO<sub>2</sub>Na [M + Na]<sup>+</sup>: 257.0948; found: 257.0946.

1-([1,1'-Biphenyl]-4-yl)but-3-en-1-yl But-3-enoate (4j). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.67–7.65 (m, 4H), 7.53–7.49 (m, 4H), 7.44–7.40 (m, 1H), 6.09–5.97 (m, 2H), 5.88–5.78 (m, 1H), 5.28–5.16 (m, 4H), 3.24–3.21 (m, 2H), 2.81–2.70 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.8, 141.0, 140.8, 139.0, 133.3, 130.3, 128.9,

127.5, 127.3, 127.2, 127.1, 118.7, 118.3, 75.3, 40.8, 39.4. HRMS (ESI) m/z: calcd for C<sub>20</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 315.1356; found: 315.1360.

1-(Furan-2-yl)but-3-en-1-yl But-3-enoate (**4k**). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.40–7.39 (m, 1H), 6.35–6.34 (m, 2H), 5.95–5.90 (m, 2H), 5.74–5.69 (m, 1H), 5.18–5.12 (m, 3H), 5.09–5.07 (m, 1H), 3.12–3.10 (m, 2H), 2.77–2.72 (m, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 170.6, 152.0, 142.6, 132.7, 130.1, 118.6, 118.3, 110.2, 108.8, 68.0, 39.1, 36.9. HRMS (ESI) *m*/*z*: calcd for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 229.0835; found: 229.0834.

2,2-Dimethyl-1-phenylbut-3-en-1-yl But-3-enoate (**4**). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.35–7.29 (m, 5H), 6.03–5.93 (m, 2H), 5.72–5.68 (m, 1H), 5.23–5.21 (m, 2H), 5.10–5.00 (m, 2H), 3.22–3.15 (m, 2H), 1.13–1.09 (m, 6H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.3, 143.9, 137.8, 130.3, 128.0, 127.6, 120.8, 118.6, 113.2, 81.9, 41.2, 39.5, 24.1, 22.6. HRMS (ESI) *m*/*z*: calcd for C<sub>16</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 267.1356; found: 267.1356.

1-Cyclopropylbut-3-en-1-yl But-3-enoate (4m). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 5.96–5.89 (m, 1H), 5.82–5.75 (m, 1H), 5.18–5.15 (m, 2H), 5.10–5.04 (m, 2H), 4.33–4.29 (m, 1H), 3.12–3.05 (m, 2H), 2.48–2.38 (m, 2H), 1.03–0.97 (m, 1H), 0.58–0.53 (m, 1H), 0.50–0.46 (m, 1H), 0.42–0.38 (m, 1H), 0.28–0.24 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 171.1, 133.7, 130.5, 118.3, 117.5, 76.9, 39.4, 39.2, 14.8, 3.3, 3.1. HRMS (ESI) *m*/*z*: calcd for C<sub>11</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 203.1043; found: 203.1044.

*Hept-1-en-4-yl But-3-enoate (4n).* Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.91–5.84 (m, 1H), 5.73–5.66 (m, 1H), 5.12–5.09 (m, 2H), 5.03–4.99 (m, 2H), 4.94–4.89 (m, 1H), 3.03–3.01 (m, 2H), 2.30–2.22 (m, 2H), 1.54–1.44 (m, 2H), 1.35–1.23 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 133.6, 130.5, 118.2, 117.5, 73.2, 39.3, 38.6, 35.7, 18.5, 13.8. HRMS (ESI) *m/z*: calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 205.1199; found: 205.1198.

2-Methylhex-5-en-3-yl But-3-enoate (40). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.98–5.87 (m, 1H), 5.79–5.69 (m, 1H), 5.19–5.14 (m, 2H), 5.09–5.02 (m, 2H), 4.82–4.77 (m, 1H), 3.09–3.08 (m, 2H), 2.37–2.26 (m, 2H), 1.89–1.85 (m, 1H), 0.92 (s, 3H), 0.90 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  171.4, 134.1, 130.5, 118.3, 117.4, 76.7, 39.4, 36.0, 31.0, 18.6, 17.5. HRMS (ESI) *m*/*z*: calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 205.1199; found: 205.1197.

1-Cyclohexylbut-3-en-1-yl But-3-enoate (**4***p*). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 5.96–5.89 (m, 1H), 5.77–5.70 (m, 1H), 5.18–5.15 (m, 2H), 5.08–5.02 (m, 2H), 4.81–4.78 (m, 1H), 3.12–3.04 (m, 2H), 2.38–2.34 (m, 1H), 2.30–2.25 (m, 1H), 1.75–1.73 (m, 3H), 1.68–1.65 (m, 2H), 1.55–1.49 (m, 1H), 1.26–1.11 (m, 3H), 1.05–0.98 (m, 2H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 171.2, 134.1, 130.6, 118.3, 117.4, 77.1, 40.7, 39.4, 35.9, 29.0, 28.0, 26.3, 26.0, 25.9. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 245.1512; found: 245.1511.

1-Phenylpent-4-en-2-yl But-3-enoate (4q). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.34–7.31 (m, 2H), 7.27–7.23 (m, 3H), 5.92–5.87 (m, 1H), 5.86–5.80 (m, 1H), 5.22–5.20 (m, 1H), 5.19–5.17 (m, 2H), 5.15–5.12 (m, 2H), 3.10–3.03 (m, 2H), 2.96–2.88 (m, 2H), 2.43–2.39 (m, 1H), 2.37–2.33 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 137.4, 133.5, 130.3, 129.5, 128.4, 126.6, 118.5, 118.1, 74.1, 39.9, 39.4, 37.9. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 253.1199; found: 253.1197.

(*E*)-*Hepta*-1,5-*dien*-4-yl But-3-enoate (4r). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.85–5.79 (m, 1H), 5.67–5.60 (m, 2H), 5.37–5.33 (m, 1H), 5.21–5.17 (m, 1H), 5.07–5.04 (m, 2H), 5.00–4.96 (m, 2H), 2.98–2.97 (m, 2H), 2.30–2.26 (m, 2H), 1.61–1.60 (m, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  170.3, 133.3, 130.4, 129.2, 128.9, 118.1, 117.6, 73.9, 39.2, 39.0, 17.5. HRMS (ESI) *m*/*z*: calcd for C<sub>11</sub>H<sub>16</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 203.1043; found: 203.1044.

2-Phenylpent-4-en-2-yl But-3-enoate (4s). Oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.39–7.36 (m, 4H), 7.31–7.28 (m, 1H), 6.01–5.90 (m, 1H), 5.69–5.62 (m, 1H), 5.23–5.21 (m, 2H), 5.11–5.09 (m, 2H), 3.15–3.14 (m, 2H), 2.90–2.87 (m, 1H), 2.83–2.79 (m, 1H), 1.87 (s, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  169.9, 144.6, 132.8, 130.6, 128.3, 127.1, 124.6, 118.7, 118.4, 83.5, 46.4, 40.3, 25.0. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 253.1199; found: 253.1204.

1-Allylcyclohexyl But-3-enoate (4t). Oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.92–5.63 (m, 2H), 5.12–4.97 (m, 4H), 2.99–2.97 (m,

2H), 2.61–2.59 (m, 2H), 2.17–2.14 (m, 2H), 1.56–1.52 (m, 1H), 1.47–1.41 (m, 4H), 1.34–1.27 (m, 2H), 1.23–1.17 (m, 1H).  $^{13}$ C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.4, 132.8, 130.9, 118.0, 117.9, 83.5, 42.0, 40.4, 34.4, 25.4, 21.7. HRMS (ESI) *m*/*z*: calcd for C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 231.1356; found: 231.1345.

General Procedure for the Reductive Cascade Double Cyclization of But-3-enyl But-3-enoates 4 To Synthesize the Bridged Bicyclic Tertiary Alcohols 5. To a two-necked flask containing samarium powder (0.7 g, 4.67 mmol) were added THF (30 mL) and allyl bromide (0.4 g, 3.3 mmol) under nitrogen. A small crystal of I<sub>2</sub> was added to trigger the reaction. The mixture was stirred at rt for 1 h (the color would turn deep purple). HMPA (3 mL, 16 mmol) and CuCl<sub>2</sub>·2H<sub>2</sub>O (0.27 g, 1.6 mmol) were then added in sequence. A solution of but-3-envl but-3-enoate 4 (1 mmol) in THF (5 mL) was subsequently added. The mixture was stirred at rt for 10 h. The reaction mixture was guenched with ag sodium-potassium tartrate and extracted with diethyl ether  $(3 \times 20 \text{ mL})$ . The organic phase was washed with brine (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (150-200 mesh) using petroleum/ EtOAc (8/1, v:v) as the eluent to afford the corresponding alcohols 5.

2-(2-Hydroxy-2-phenylethyl)bicyclo[2.1.1]hexan-1-ol (**5a**). White solid (135 mg, 62% yield), mp 103–105 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.37–7.31 (m, 4H), 7.27–7.24 (m, 1H), 5.77 (b, s, 1H), 4.73–4.70 (m, 1H), 4.24 (b, s, 1H), 2.09–2.00 (m, 3H), 1.95–1.86 (m, 1H), 1.77–1.72 (m, 1H), 1.59–1.51 (m, 2H), 1.50–1.44 (m, 1H), 1.41 (s, 1H), 1.12–1.10 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  145.2, 128.4, 127.4, 125.7, 80.3, 75.3, 46.4, 43.6, 40.9, 40.0, 38.2, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 241.1199; found: 241.1203.

2-(2-Hydroxy-2-(2-methoxyphenyl)ethyl)bicyclo[2.1.1]hexan-1-ol (**5b**). White solid (228 mg, 92% yield), mp 97–98 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.43–7.41 (m, 1H), 7.29–7.26 (m, 1H), 7.00–6.98 (m, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 5.84 (b, s, 1H), 5.06 (dd, *J* = 10.2, 1.7 Hz, 1H), 3.88 (s, 3H), 2.14–2.06 (m, 3H), 1.96–1.83 (m, 3H), 1.69–1.67 (m, 1H), 1.59–1.56 (m, 1H), 1.53–1.51 (m, 1H), 1.47–1.46 (s, 1H), 1.18–1.16 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  156.1, 132.6, 128.4, 126.3, 120.9, 110.4, 80.5, 70.9, 55.4, 46.4, 41.0, 40.9, 40.1, 38.3, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 271.1305; found: 271.1310.

2-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)bicyclo[2.1.1]hexan-1-ol (**5c**). White solid (219 mg, 88% yield), mp 103–105 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.30 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.74 (b, s, 1H), 4.72 (dd, *J* = 10.4, 1.7 Hz, 1H), 3.89 (b, s, 1H), 3.82 (s, 3H), 2.12–2.05 (m, 3H), 1.97–1.91 (m, 1H), 1.75–1.73 (m, 1H), 1.64–1.62 (m, 1H), 1.58–1.56 (m, 1H), 1.51–1.49 (m, 1H), 1.45–1.44 (m, 1H), 1.14–1.12 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  159.0, 137.3, 126.9, 113.8, 80.4, 75.1, 55.3, 46.4, 43.5, 41.0, 40.0, 38.3, 27.9. HRMS (ESI) *m*/*z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 271.1305; found: 271.1301.

2-(2-(3,4-Dimethoxyphenyl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (5d). White solid (195 mg, 70% yield), mp 98–100 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.88 (s, 1H), 6.84–6.81 (m, 1H), 6.78–6.76 (m, 1H), 4.63–4.61 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.03–1.97 (m, 3H), 1.91–1.82 (m, 1H), 1.72–1.68 (m, 1H), 1.55–1.50 (m, 2H), 1.45–1.41 (m, 1H), 1.37 (s, 1H), 1.10–1.07 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  148.9, 148.2, 138.0, 117.8, 110.9, 108.8, 80.2, 75.0, 55.92, 55.86, 46.4, 43.7, 40.9, 40.1, 38.1, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>Na [M + Na]<sup>+</sup>: 301.1410; found: 301.1408.

2-(2-Hydroxy-2-(m-tolyl)ethyl)bicyclo[2.1.1]hexan-1-ol (**5e**). White solid (184 mg, 79% yield), mp 78–80 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.27–7.24 (m, 1H), 7.22 (s, 1H), 7.19–7.18 (m, 1H), 7.12–7.11 (m, 1H), 5.45 (b, s, 1H), 4.77–4.75 (m, 1H), 3.56 (b, s, 1H), 2.38 (s, 3H), 2.14–2.06 (m, 3H), 1.99–1.93 (m, 1H), 1.80–1.77 (m, 1H), 1.68–1.66 (m, 1H), 1.60–1.57 (m, 1H), 1.54–1.52 (m, 1H), 1.47–1.46 (m, 1H), 1.17–1.15 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  145.0, 138.2, 128.4,128.3, 126.3, 122.7, 80.5, 75.7, 46.5, 43.5, 41.1, 40.1, 38.4, 27.8, 21.5. HRMS (ESI) *m*/*z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 255.1356; found: 255.1365.

2-(2-(4-Chlorophenyl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (**5f**). White solid (179 mg, 71% yield), mp 98–100 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.32–7.28 (m, 4H), 4.72–4.70 (m, 1H), 2.10–2.03 (m, 3H), 1.91–1.85 (m, 1H), 1.75–1.72 (m, 1H), 1.61–1.59 (m, 1H), 1.58–1.49 (m, 2H), 1.43–1.42 (m, 1H), 1.14–1.13 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  143.6, 133.0, 128.5, 127.0, 80.3, 74.6, 46.5, 43.7, 41.0, 39.9, 38.2, 27.9. HRMS (ESI) *m*/*z*: calcd for C<sub>14</sub>H<sub>17</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 275.0809; found: 275.0814.

2-(2-(3- $\tilde{C}$ hlorophenyl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (**5g**). White solid (152 mg, 60% yield), mp 91–93 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.39–7.34 (m, 3H), 7.30–7.26 (m, 1H), 5.76 (b, s, 1H), 4.76 (dd, *J* = 10.5, 1.8 Hz, 1H), 4.18 (b, s, 1H), 2.14–2.11 (m, 1H), 2.09–2.04 (m, 2H), 1.97–1.91 (m, 1H), 1.79–1.76 (m, 1H), 1.63–1.61 (m, 1H), 1.58–1.55 (m, 1H), 1.51–1.49 (m, 1H), 1.44–1.43 (m, 1H), 1.15–1.13 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  145.1, 128.5, 127.5, 125.7, 80.4, 75.5, 46.4, 43.6, 41.0, 40.1, 38.3, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>17</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 275.0809; found: 275.0816.

2-(2-(2-Chlorophenyl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (**5h**). White solid (167 mg, 66% yield), mp 120–121 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.59–7.57(m, 1H), 7.28–7.23 (m, 2H), 7.17–7.14 (m, 1H), 5.95 (b, s, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 4.98 (b, s, 1H), 2.14–2.11 (m, 1H), 2.05–2.02 (m, 2H), 1.85–1.82 (m, 1H), 1.71–1.65 (m, 1H), 1.53–1.49 (m, 2H), 1.46–1.44 (m, 1H), 1.36–1.35 (m, 1H), 1.13–1.12 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  142.5, 131.4, 129.2, 128.2, 127.1, 126.8, 80.2, 71.4, 46.3, 41.7, 40.9, 39.9, 37.9, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>17</sub>ClO<sub>2</sub>Na [M + Na]<sup>+</sup>: 275.0809; found: 275.0810.

 $\overline{2}$ -(2-(4-Fluorophenyl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (5i). White solid (180 mg, 76% yield), mp 94–96 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.32–7.28 (m, 2H), 7.02–6.98 (m, 2H), 5.65 (b, s, 1H), 4.71–4.68 (m, 1H), 4.60 (b, s, 1H), 2.10–2.00 (m, 3H), 1.91–1.83 (m, 1H), 1.73–1.69 (m, 1H), 1.57–1.52 (m, 2H), 1.48–1.44 (m, 1H), 1.40 (s, 1H), 1.12–1.10 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 162.1 (d,  $J_{C-F} = 243.4$  Hz, 1C), 141.0 (d,  $J_{C-F} = 3.1$  Hz, 1C), 127.2 (d,  $J_{C-F} = 8.0$  Hz, 1C), 115.1 (d,  $J_{C-F} = 21.2$  Hz, 1C), 80.3, 74.6, 46.5, 43.7, 41.0, 39.9, 38.1, 27.9. HRMS (ESI) *m*/*z*: calcd for C<sub>14</sub>H<sub>17</sub>FO<sub>2</sub>Na [M + Na]<sup>+</sup>: 259.1105; found: 259.1108.

2-(2-([1,1'-Biphenyl]-3-yl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1ol (5j). White solid (200 mg, 68% yield), mp 99–102 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.61–7.58 (m, 4H), 7.47–7.45 (m, 4H), 7.39– 7.36 (m, 1H), 5.49 (b, s, 1H), 4.83 (dd, J = 10.4, 1.6 Hz, 1H), 4.02 (b, s, 1H), 2.19–2.16 (m, 1H), 2.11–2.07 (m, 2H), 2.03–1.97 (m, 1H), 1.85–1.82 (m, 1H), 1.68–1.66 (m, 1H), 1.62–1.59 (m, 1H), 1.56– 1.53 (m, 1H), 1.49–1.48 (m, 1H), 1.19–1.17 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 144.1, 140.8, 140.5, 128.8, 127.3, 127.2, 127.1, 126.1, 80.5, 75.3, 46.5, 43.6, 41.1, 40.1, 38.3, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>20</sub>H<sub>22</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 317.1512; found: 317.1515.

2-(2-(Furan-2-yl)-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (5k). White solid (52 mg, 25% yield), mp 75–78 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.37–7.36 (m, 1H), 6.34–6.33 (m, 1H), 6.25–6.24 (m, 1H), 4.79–4.77 (m, 1H), 2.12–2.10 (m, 1H), 2.08–2.02 (m, 3H), 1.97–1.93 (m, 1H), 1.64–1.58 (m, 2H), 1.52–1.49 (m, 1H), 1.46–1.45 (m, 1H), 1.20–1.18 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  156.9, 141.7, 110.2, 105.3, 80.3, 68.4, 46.4, 40.9, 39.4, 39.2, 37.8, 28.0. HRMS (ESI) *m*/*z*: calcd for C<sub>12</sub>H<sub>16</sub>O<sub>3</sub>Na [M + Na]<sup>+</sup>: 231.0992; found: 231.0998.

2-(1-Hydroxy-2-methyl-1-phenylpropan-2-yl)bicyclo[2.1.1]hexan-1-ol (5l). White solid (111 mg, 45% yield), mp 115–117 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.29–7.28 (m, 4H), 7.26–7.24 (m, 1H), 4.49 (s, 1H), 2.01 (s, 1H), 1.96–1.94 (m, 1H), 1.84–1.80 (m, 1H), 1.74–1.72 (m, 1H), 1.53–1.50 (m, 1H), 1.46–1.44 (m, 2H), 1.27 (s, 1H), 0.92 (s, 3H), 0.54 (s, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 142.2, 128.3, 127.6, 127.4, 83.9, 80.4, 51.3, 48.7, 41.6, 41.1, 33.7, 26.5, 25.9, 14.6. HRMS (ESI) *m*/*z*: calcd for C<sub>16</sub>H<sub>22</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 269.1512; found: 269.1516.

2-(2-Cyclopropyl-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (5m). White solid (129 mg, 71% yield), mp 97–100 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.86 (b, s, 1H), 3.66 (b, s, 1H), 2.94–2.90 (m, 1H), 2.06–1.98 (m, 2H), 1.92–1.88 (m, 1H), 1.77–1.69 (m, 2H), 1.63–

1.61 (m, 1H), 1.56–1.52 (m, 1H), 1.46–1.42 (m, 2H), 1.15–1.12 (m, 1H), 0.96–0.90 (m, 1H), 0.52–0.49 (m, 2H), 0.33–0.28 (m, 1H), 0.21–0.19 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  80.3, 78.0, 46.4, 40.8, 40.4, 39.7, 38.2, 27.9, 18.5, 3.3, 2.7. HRMS (ESI) *m/z*: calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 205.1199; found: 205.1199.

2-(2-Hydroxypentyl)bicyclo[2.1.1]hexan-1-ol (**5n**). White solid (140 mg, 76% yield), mp 76–78 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  3.70–3.66 (m, 1H), 2.08–2.07 (m, 1H), 2.03–1.99 (m, 1H), 1.97–1.94 (m, 1H), 1.64–1.62 (m, 1H), 1.60–1.59 (m, 1H), 1.57–1.53 (m, 2H), 1.51–1.46 (m, 2H), 1.45–1.41 (m, 3H), 1.39–1.34 (m, 1H), 1.14–1.12 (m, 1H), 0.95–0.93 (m, 3H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  80.3, 72.5, 46.5, 40.8, 40.7, 40.5, 39.7, 38.1, 27.9, 18.9, 14.1. HRMS (ESI) *m*/*z*: calcd for C<sub>11</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 207.1356; found: 207.1351.

2-(2-Hydroxy-3-methylbutyl)bicyclo[2.1.1]hexan-1-ol (**5o**). White solid (153 mg, 83% yield), mp 77–79 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.86 (s, 1H), 3.64 (b, s, 1H), 3.49–3.44 (m, 1H), 2.07–1.98 (m, 2H), 1.96–1.90 (m, 1H), 1.70–1.66 (m, 1H), 1.63–1.60 (m, 1H), 1.56–1.51 (m, 3H), 1.48–1.44 (m, 1H), 1.42–1.41 (m, 1H), 1.14–1.12 (m, 1H), 0.93–0.91 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 80.4, 77.7, 46.4, 40.9, 39.8, 38.2, 36.9, 34.4, 27.9, 18.5, 17.6. HRMS (ESI) *m/z*: calcd for C<sub>11</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 207.1355; found: 207.1358.

2-(2-Cyclohexyl-2-hydroxyethyl)bicyclo[2.1.1]hexan-1-ol (**5p**). White solid (153 mg, 68% yield), mp 87–90 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.72 (b, s, 1H), 3.50–3.46 (m, 1H), 3.21 (b, s, 1H), 2.08–2.01 (m, 2H), 1.96–1.90 (m, 1H), 1.80–1.67 (m, 5H), 1.66–1.58 (m, 3H), 1.57–1.52 (m, 1H), 1.50–1.46 (m, 1H), 1.44–1.43 (m, 1H), 1.38–1.32 (m, 1H), 1.27–1.19 (m, 2H), 1.16–1.13 (m, 2H), 1.11–0.99 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  80.4, 46.4, 44.6, 41.0, 39.9, 38.3, 37.3, 29.1, 28.0, 27.8, 26.5, 26.3, 26.2. HRMS (ESI) *m/z*: calcd for C<sub>14</sub>H<sub>24</sub>O<sub>2</sub><sup>+</sup>Na [M + Na]<sup>+</sup>: 247.1669; found: 247.1662.

2-(2-Hydroxy-3-phenylpropyl)bicyclo[2.1.1]hexan-1-ol (5q). White solid (174 mg, 75% yield), mp 98–101 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.36–7.33 (m, 2H), 7.29–7.23 (m, 3H), 5.50 (s, 1H), 3.94–3.91 (m, 1H), 3.19 (s, 1H), 2.86–2.83 (m, 1H), 2.77–2.73 (m, 1H), 2.09 (s, 1H), 2.05–1.96 (m, 2H), 1.75–1.67 (m, 2H), 1.65–1.63 (m, 1H), 1.58–1.55 (m, 1H), 1.49–1.47 (m, 1H), 1.44 (s, 1H), 1.16–1.14 (m, 1H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  138.2, 129.4, 128.7, 126.7, 80.4, 73.8, 46.4, 44.8, 40.9, 40.2, 39.6, 38.3, 27.9. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub><sup>+</sup>Na [M + Na]<sup>+</sup>: 255.1356; found: 255.1362.

(E)-2-(2-Hydroxypent-3-en-1-yl)bicyclo[2.1.1]hexan-1-ol (5r). White solid (109 mg, 60% yield), mp 80–82 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.71–5.62 (m, 1H), 5.56–5.50 (m, 1H), 4.15–4.11 (m, 1H), 2.07–1.98 (m, 3H), 1.69–1.66 (m, 4H), 1.63–1.58 (m, 2H), 1.54–1.51 (m, 1H), 1.48–1.44 (m, 1H), 1.43–1.41 (m, 1H), 1.14–1.12 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  134.4, 126.1, 80.3, 73.7, 46.4, 41.1, 40.9, 39.6, 38.2, 27.9, 17.6. HRMS (ESI) *m/z*: calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 205.1199; found: 205.1198.

2-(2-Hydroxy-2-phenylpropyl)bicyclo[2.1.1]hexan-1-ol (**5s**). White solid (121 mg, 52% yield), mp 111–113 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.52–7.51 (m, 2H), 7.39–7.36 (m, 2H), 7.29–7.27 (m, 1H), 4.97 (b, s, 1H), 3.18 (b, s, 1H), 2.29–2.26 (m, 1H), 2.11–2.10 (m, 1H), 2.09–2.01(m, 2H), 1.84–1.81 (m, 1H), 1.70 (s, 3H), 1.68 (s, 1H), 1.59–1.53 (m, 2H), 1.44–1.43 (m, 1H), 1.18–1.16 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ 149. 7, 128.3, 126.8, 124.5, 80.5, 75.0, 47.8, 46.5, 40.9, 38.6, 35.9, 28.0, 27.7. HRMS (ESI) *m/z*: calcd for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup>: 255.1356; found: 255.1359.

2-((1-Hydroxycyclohexyl)methyl)bicyclo[2.1.1]hexan-1-ol (5t). White solid (38 mg, 18% yield), mp 113–115 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.42 (s, 1H), 2.62 (s, 1H), 2.17–2.16 (m, 1H), 2.10–2.09 (m, 1H), 2.05–2.02 (m, 1H), 1.77–1.72 (m, 2H), 1.69–1.68 (m, 2H), 1.67–1.65 (m, 1H), 1.60–1.57 (m, 2H), 1.56–1.54 (m, 4H), 1.52–1.49 (m, 3H), 1.42–1.41 (m, 1H), 1.34–1.28 (s, 1H), 1.15–1.14 (m, 1H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  80.5, 72.2, 46.4, 40.7, 40.3, 38.6, 35.4, 34. 6, 28.0, 25.7, 22.6, 22.2. HRMS (ESI) *m/z*: calcd for C<sub>13</sub>H<sub>2</sub>O<sub>2</sub> Na [M + Na]<sup>+</sup>: 233.1512; found: 233.1518.

**Preparation of the CuCl<sub>2</sub>·2H<sub>2</sub>O/allyISmBr/HMPA/THF System.** To a two-necked flask containing samarium powder (0.7 g, 4.67 mmol) were added THF (30 mL) and allyl bromide (0.4 g, 3.3 mmol)

under nitrogen. A small crystal of I<sub>2</sub> was added to trigger the reaction. The mixture was stirred at rt for 1 h (the color would turn into deep purple). HMPA (3 mL, 16 mmol) and CuCl<sub>2</sub>·2H<sub>2</sub>O (0.27g, 1.6 equiv) were then added in sequence. The mixture was stirred at rt for 10 h. Rapid filtration of the mixture afforded deep green powder, which was washed by THF (3 × 3 mL) and then Et<sub>2</sub>O (3 × 3 mL). The powder was dried under vacuum before submission to the XPS detection.

**Preparation of the CuCl/allyISmBr/H<sub>2</sub>O/HMPA/THF System.** To a two-necked flask containing samarium powder (0.7 g, 4.67 mmol) were added THF (30 mL) and allyl bromide (0.4 g, 3.3 mmol) under nitrogen. A small crystal of I<sub>2</sub> was added to trigger the reaction. The mixture was stirred at rt for 1 h (the color would turn into deep purple). HMPA (3 mL, 16 mmol) and H<sub>2</sub>O (30  $\mu$ L, 1.6 mmol) were then added in sequence via a syringe. CuCl (0.16 g, 1.6 equiv) was then added, and the mixture was stirred at rt for 10 h. Rapid filtration of the mixture afforded deep green powder, which was washed by THF (3 × 3 mL) and then Et<sub>2</sub>O (3 × 3 mL). The powder was dried under vacuum before submission to the XPS detection.

# ASSOCIATED CONTENT

#### **Supporting Information**

Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra for the new compounds and the crystallographic data of **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

# AUTHOR INFORMATION

#### Corresponding Authors

\*E-mail: wangxiaoxia@zjnu.cn.

\*E-mail: lvxin@zjnu.cn.

#### Notes

The authors declare no competing financial interest.

# ACKNOWLEDGMENTS

This work was supported by Natural Science Foundation of Zhejiang Province (LY14B020001) and by National Natural Science Foundation of China (no. 21202152). R.A.F. thanks the National Science Foundation (CHE 1266333) for support of the work at Lehigh University.

#### REFERENCES

(1) (a) Corey, E. J.; Cheng, X. M. The Logic of Chemical Synthesis; John Wiley and Sons: New York, 1989. (b) Lindberg, T. Strategies and Tactics in Organic Synthesis; Academic Press: San Diego, 1994; Vol. 1. (c) Ho, T. L. Tactics of Organic Synthesis; John Wiley and Sons: New York, 1994. (d) Comprehensive Organic Functional Group Transformations, Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W., Eds.; Pergamon Press: Oxford, 1995; Vol. 6. (e) Robinson, A.; Aggarwal, V. K. Angew. Chem., Int. Ed. 2010, 49, 6673.

(2) For recent examples for the synthesis of 1,4-diols, see: (a) Ghavtadze, N.; Melkonyan, F. S.; Gulevich, A. V.; Huang, C.; Gevorgyan, V. Nat. Chem. **2014**, *6*, 122. (b) Hashimoto, T.; Hirose, D.; Taniguchi, T. Angew. Chem., Int. Ed. **2014**, *53*, 2730 and the literatures cited therein..

(3) For selected examples, see: (a) Han, Z. T.; Chen, H.-F. U.S. Pat. Appl. US 20140017196 A1 20140116, 2014. (b) Han, Z. T.; Chen, H.-F. U.S. Pat. Appl. US 20140011873 A1 20140109, 2014. (c) Chang, R. L.; Han, Z. T. PCT Int. Appl. WO 2013110006 A2 20130725, 2013. (d) Pagani, A.; Navarrete, C.; Fiebich, B. L.; Munoz, E.; Appendino, G. *J. Nat. Prod.* **2010**, 73, 447. (e) Klausen, T. K.; Pagani, A.; Minassi, A.; Ech-Chahad, A.; Prenen, J.; Owsianik, G.; Hoffmann, E. K.; Pedersen, S. F.; Appendino, G.; Nilius, B. *J. .Med. Chem.* **2009**, *52*, 2933. (f) Bertolini, T. M.; Giorgione, J.; Harvey, D. F.; Newton, A. C. J. Org. *Chem.* **2003**, *68*, 5028.

(4) (a) Lee, H. G.; Lysenko, I. L.; Cha, J. K. Angew. Chem., Int. Ed. 2007, 46, 3326. (b) Parida, B. B.; Lysenko, I. L.; Cha, J. K. Org. Lett.

**2012**, *14*, 6258. (c) Shklyaruck, D. G.; Fedarkevich, A. N.; Kozyrkov, Y. Yu. *Synlett* **2014**, *25*, 1855.

(5) (a) Astashko, D.; Cha, J. K.; Rao, N. N.; Parida, B. B. *Eur. J. Org. Chem.* **2014**, 181. (b) Lee, H. G.; Lysenko, I. L.; Cha, J. K. *ARKIVOC (Gainesville, FL, U. S.)* **2008**, 133. (c) Quan, L. G.; Kim, S.-H.; Lee, J. C.; Cha, J. K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2160. (d) Kasatkin, A.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 6079.

(6) For selected most recent publications: (a) Ding, C.; Zhang, Y.; Chen, H.; Yang, Z.; Wild, C.; Ye, N.; Ester, C. D.; Xiong, A.; White, M. A.; Shen, Q.; Zhou, J. J. Med. Chem. **2013**, 56, 8814. (b) Zubrytski, D. M.; Kananovich, D. G.; Kulinkovich, O. G. Tetrahedron **2014**, 70, 2944. (c) Mukai, K.; Urabe, D.; Kasuya, S.; Aoki, N.; Inoue, M. Angew. Chem., Int. Ed. **2013**, 52, 5300. (d) Fazakerley, N. J.; Helm, M. D.; Procter, D. J. Chem.—Eur. J. **2013**, 19, 6718.

(7) Molander, G. A.; McKie, J. A. J. Org. Chem. 1992, 57, 3132.

(8) Tu, Y.; Zhou, L.; Yin, R.; Lv, X.; Flowers, R. A.; Choquette, K. A.; Liu, H.; Niu, Q.; Wang, X. *Chem. Commun.* **2012**, *4*8, 11026.

(9) For selected reviews of  $SmI_2$ -mediated reactions, see: (a) Choquette, K. A.; Flowers, R. A. Sm and Yb Reagents. In Comprehensive Organic Synthesis, 2nd ed.; Molander, G. A., Knochel, P., Eds.; Elsevier: Oxford, 2014; Vol. 1, p 279. (b) Szostak, M.; Fazakerley, N. J.; Parmar, D.; Procter, D. J. Chem. Rev. 2014, 114, 5959. (c) Szostak, M.; Spain, M.; Procter, D. J. Chem. Soc. Rev. 2013, 42, 9155. (d) Beemelmanns, C.; Reißig, H.-U. Chem. Soc. Rev. . 2011, 40, 2199. (e) Procter, D. J.; Flowers, R. A.; Skrydstrup, T. Organic Synthesis Using Samarium Diiodide: A Practical Guide; Royal Society of Chemistry: London, 2010. (f) Gopalaiah, K.; Kagan, H. B. New J. Chem. 2008, 32, 607. (g) Edmonds, D. J.; Johnston, D.; Procter, D. J. Chem. Rev. 2004, 104, 3371. (h) Kagan, H. B. Tetrahedron 2003, 59, 10351. (i) Steel, P. G. J. Chem. Soc., Perkin Trans. 1 2001, 2727. (j) Krief, A.; Laval, A.-M. Chem. Rev. 1999, 99, 745. (k) Molander, G. A.; Harris, C. R. Tetrahedron 1998, 54, 3321. (1) Molander, G. A.; Harris, C. R. Chem. Rev. 1996, 96, 307.

(10) For recent examples of SmI<sub>2</sub>-promoted organic reactions in natural products synthesis, see: (a) Pinho, V. D.; Procter, D. J.; Burtoloso, A. C. B. Org. Lett. 2013, 15, 2434. (b) Li, J.; Liu, G.-L.; Zhao, X.-H.; Du, J.-Y.; Qu, H.; Chu, W.-D.; Ding, M.; Jin, C.-Y.; Wei, M.-X.; Fan, C.-A. Chem.-Asian J. 2013, 8, 1105. (c) Huang, J.; Yang, J. R; Zhang, J.; Yang, J. J. Am. Chem. Soc. 2012, 134, 8806. (d) Gilles, P.; Py, S. Org. Lett. 2012, 14, 1042. (e) Szostak, M.; Procter, D. J. Angew. Chem., Int. Ed. 2011, 50, 7737. (f) Ito, Y.; Takahashi, K.; Nagase, H.; Honda, T. Org. Lett. 2011, 13, 4640. (g) Xu, T.; Li, C.-C.; Yang, Z. Org. Lett. 2011, 13, 2630. (h) Nicolaou, K. C.; Li, A.; Edmonds, D. J.; Tria, G. S.; Ellery, S. P. J. Am. Chem. Soc. 2009, 131, 16905. (i) Nicolaou, K. C.; Ding, H.; Richard, J.-A.; Chen, D. Y.-K. J. Am. Chem. Soc. 2010, 132, 3815. See also a review: (j) Nicolaou, K. C.; Ellery, S. P.; Chen, J. S. Angew. Chem., Int. Ed. 2009, 48, 7140.

(11) For selected SmI<sub>2</sub>-promoted carbonyl-alkene reactions, see:
(a) Molander, G. A.; Czakó, B.; Rheam, M. J. Org. Chem. 2007, 72, 1755.
(b) Inui, M.; Nakazaki, A.; Kobayashi, S. Org. Lett. 2007, 9, 469.
(c) Saadi, J.; Lentz, D.; Reissig, H.-U. Org. Lett. 2009, 11, 3334.
(d) Reissig, H.-U.; Khan, F. A.; Czerwonka, R.; Dinesh, C. U.; Shaikh, A. L.; Zimmer, R. Eur. J. Org. Chem. 2006, 4419. (e) Molander, G. A.; McKie, J. A. J. Org. Chem. 1994, 59, 3186. See also a review: (f) Harb, H. Y.; Procter, D. J. Synlett 2012, 6.

(12) (a) Liu, Y. J.; Zhang, Y. M. Tetrahedron Lett. 2004, 45, 1295.
(b) Liu, Y. J.; Zhang, Y. M. Tetrahedron 2003, 59, 8429.

(13) (a) Jensen, C. M.; Lindsay, K. B.; Taaning, R. H.; Karaffa, J.; Hansen, A. M.; Skrydstrup, T. J. Am. Chem. Soc. 2005, 127, 6544.
(b) Hansen, A. M.; Lindsay, K. B.; Antharjanam, P. K. S.; Karaffa, J.; Daasbjerg, K.; Flowers, R. A., II; Skrydstrup, T. J. Am. Chem. Soc. 2006, 128, 9616. (c) Blakskjær, P.; Høj, B.; Riber, D.; Skrydstrup, T. J. Am. Chem. Soc. 2003, 125, 4030.

(14) (a) Kamochi, Y.; Kudo, T. Chem. Lett. **1991**, 893. (b) Kamochi, Y.; Kudo, T. Bull. Chem. Soc. Jpn. **1992**, 65, 3049. (c) Kamochi, Y.; Kudo, T. Chem. Lett. **1993**, 1495.

(15) (a) Parmar, D.; Duffy, L. A.; Sadasivam, D. V.; Matsubara, H.; Bradley, P. A.; Flowers, R. A., II; Procter, D. J. *J. Am. Chem. Soc.* **2009**, 131, 15467. (b) Collins, K. D.; Oliveira, J. M.; Guazzelli, G.; Sautier, B.; De Grazia, S.; Matsubara, H.; Helliwell, M.; Procter, D. J. Chem.— Eur. J. 2010, 16, 10240. (c) Parmar, D.; Price, K.; Spain, M.; Matsubara, H.; Bradley, P. A.; Procter, D. J. J. Am. Chem. Soc. 2011, 133, 2418. (d) Sautier, B.; Lyons, S. E.; Webb, M. R.; Procter, D. J. Org. Lett. 2012, 14, 146. (e) Parmar, D.; Matsubara, H.; Price, K.; Spain, M.; Procter, D. J. J. Am. Chem. Soc. 2012, 134, 12751.

(16) Szostak, M.; Sautier, B.; Spain, M.; Behlendorf, M.; Procter, D. J. Angew. Chem., Int. Ed. 2013, 52, 12559.

(17) Mechanistic study of ester reductions: (a) Szostak, M.; Spain, M.; Eberhart, A. J.; Procter, D. J. J. Am. Chem. Soc. 2014, 136, 2268.
(b) Szostak, M.; Spain, M.; Procter, D. J. Chem.-Eur. J. 2014, 20, 4222. (c) Szostak, M.; Spain, M.; Procter, D. J. J. Am. Chem. Soc. 2014, 136, 8459.

(18) For selected examples, see: (a) Fan, X.; Zhang, Y. Tetrahedron Lett. 2002, 43, 5475. (b) Li, Z.; Cao, X.; Lai, G.; Liu, J.; Ni, Y.; Wu, J.; Qiu, H. J. Organomet. Chem. 2006, 691, 4740. (c) Yu, M.; Zhang, Y. Chem. J. Chin. Univ. 2003, 1618. (d) Zhang, S.; Di, J. Synlett 2008, 1491. (e) Gao, X.; Wang, X.; Cai, R.; Wei, J.; Wu, S. Acta Chim. Sin. 1993, 1139.

(19) (a) Hu, Y.; Zhao, T.; Zhang, S. Chem.—Eur. J. 2010, 16, 1697.
(b) Zhong, Z.; Hong, R.; Wang, X. Tetrahedron Lett. 2010, 51, 6763.
(c) Yin, R.; Zhou, L.; Liu, H.; Mao, H.; Lü, X.; Wang, X. Chin. J. Chem. 2013, 31, 143.

(20) (a) Shabangi, M.; Flowers, R. A., II. Tetrahedron Lett. 1997, 38, 1137. (b) Shotwell, J. B.; Sealy, J. M.; Flowers, R. A., II. J. Org. Chem. 1999, 64, 5251. (c) Prasad, E.; Flowers, R. A., II J. Am. Chem. Soc. 2002, 124, 6895. (d) Prasad, E.; Knettle, B. W.; Flowers, R. A., II. J. Am. Chem. Soc. 2004, 126, 6891. (e) Sadasivam, D. V.; Antharjanam, P. K. S.; Flowers, R. A., II. J. Am. Chem. Soc. 2008, 130, 7228. (f) Choquette, K. A.; Sadasivam, D. V.; Flowers, R. A., II. J. Am. Chem. Soc. 2010, 132, 17396.

(21) For the recent report concerning the reduction of esters to the corresponding alcohols by SmI<sub>2</sub>, see: (a) Lam, K.; Markó, I. E. Org. Lett. **2009**, *11*, 2752. (b) Szostak, M.; Spain, M.; Procter, D. J. Chem. Commun. **2011**, 47, 10254.

(22) The crystal data of **5a** have been deposited at Cambridge Crystallographic Data Center, UK, and the CCDC reference number is 1011576.

(23) Li, Y.; Hu, Y. Y.; Zhang, S. L. Chem. Commun. 2013, 49, 10635.
(24) (a) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A., II. J. Am. Chem. Soc. 2000, 122, 7718.
(b) Fuchs, J. R.; Mitchell, M. L.; Shabangi, M.; Flowers, R. A., II. Tetrahedron Lett. 1997, 38, 8157.

(25) CuCl<sub>2</sub> by XPS: (a) Vasquez, R. P. Surf. Sci. Spectra **1993**, 2, 160. CuCl by XPS: (b) Vasquez, R. P. Surf. Sci. Spectra **1993**, 2, 138.

(26) Choquette, K. A.; Sadasivam, D. V.; Flowers, R. A., II. J. Am. Chem. Soc. 2011, 133, 10655.

(27) (a) Serelis, A. K. Aust. J. Chem. 2011, 64, 358. and references cited therein. (b) Curran, D. P.; Totleben, M. J. J. Am. Chem. Soc. 1992, 114, 6050.

(28) (a) Du, Z.; Li, Y.; Wang, F.; Zhou, W.; Wang, J. Tetrahedron 2010, 51, 1745. (b) Warner, M. C.; Shevchenko, G. A.; Jouda, S.; Bogár, K.; Bäckvall, J.-E. Chem.—Eur. J. 2013, 19, 13859. (c) Fraunhoffer, K. J.; Bachovchin, D. A.; White, M. C. Org. Lett. 2005, 7, 223. (d) Wilson, S. R.; Guazzaroni, M. E. J. Org. Chem. 1989, 54, 3087. (e) Khan, F. A.; Krishnakumar, K. S.; Sudheer, C. Synthesis 2007, 1054. (f) Singh, S.; Das, G.; Singh, O. V.; Han, H. Tetrahedron Lett. 2007, 48, 1983. (g) Chen, P.; Xiang, P. Tetrahedron Lett. 2011, 52, 5758.

(29) The spectra data of products 3 are available in the Supporting Information of ref 8.

(30) (a) Cook, C.; Guinchard, X.; Liron, F.; Roulland, E. Org. Lett. **2010**, *12*, 744. (b) Roulland, E.; Ermolenko, M. S. Org. Lett. **2005**, *7*, 2225.