



# A general enantioselective route to the chamigrene natural product family

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## ABSTRACT

Described in this report is an enantioselective route toward the chamigrene natural product family. The key disconnections in our synthetic approach include sequential enantioselective decarboxylative allylation and ring-closing olefin metathesis to form the all-carbon quaternary stereocenter and spirocyclic core present in all members of this class of compounds. The generality of this strategy is demonstrated by the first total syntheses of elatol and the proposed structure of laurencenone B, as well as the first enantioselective total syntheses of laurencenone C and  $\alpha$ -chamigrene. A brief exploration of the substrate scope of the enantioselective decarboxylative allylation/ring-closing metathesis sequence with fully substituted vinyl chlorides is also presented.

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## 1. Introduction

The chamigrene subclass of sesquiterpenes is an abundant and continually expanding family of natural products, with over one hundred members discovered to date (Fig. 1).<sup>1,2</sup> Isolated from

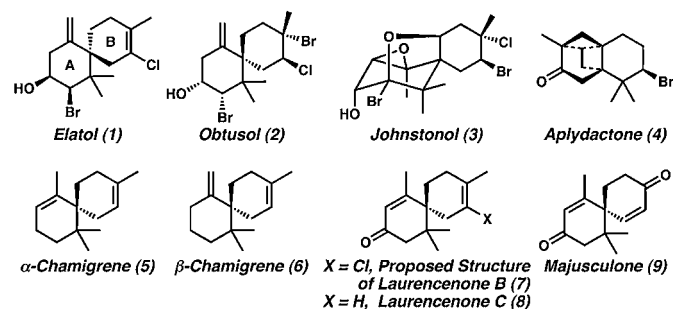


Figure 1. Examples of chamigrene natural products.

a variety of sources including terrestrial and marine plants, these compounds have demonstrated a diverse array of biological activity and have been suggested to play a chemical defense role in the marine alga genus *Laurencia*.<sup>3</sup> For example, elatol (**1**), originally isolated from *Laurencia eletata*,<sup>2a</sup> has displayed antifeedant activity,<sup>3a</sup> antifouling activity,<sup>4a</sup> antibacterial activity (including human pathogenic bacteria),<sup>3b–c,4b</sup> antifungal activity,<sup>3d</sup> and cytotoxicity against HeLa and Hep-2 human carcinoma cell lines.<sup>4c</sup> As

a consequence, significant effort has been devoted to the total synthesis of several members of this class;<sup>5</sup> nevertheless, no general strategy for their preparation has yet been developed. Inspired by both this lack of a common approach and the overall synthetic challenge posed by these molecules, we sought to generate a new route toward the chamigrene family that would allow ready access to a wide range of its constituents in enantioenriched form. Herein we report in full our efforts toward this goal, culminating in the first enantioselective total syntheses of elatol (**1**),  $\alpha$ -chamigrene (**5**), laurencenone C (**8**), and the proposed structure of laurencenone B (**7**).<sup>6</sup>

Structurally, chamigrenes are characterized by a spiro[5.5]undecane core bearing an all-carbon quaternary stereocenter at the spirocycle junction. Moreover, this stereocenter is found to occur in both enantiomeric series in nature. The moderately-to-densely functionalized A ring also contains a second, non-stereogenic quaternary carbon, that is vicinal to the spirocycle junction, while the B ring often possesses a tri- or tetrasubstituted olefin, or functionality readily derived from such an alkene. We envisioned a strategy toward these challenging motifs based on methodological advances recently reported by our laboratories. Specifically, enantioselective decarboxylative allylation<sup>7</sup> could be used to generate either enantiomer of the all-carbon quaternary stereocenter, while ring-closing metathesis (RCM)<sup>8</sup> could be employed to concomitantly provide the B-ring tri- or tetrasubstituted olefin and the spirocyclic core of **10** (Eq. 1). Through proper functionalization,



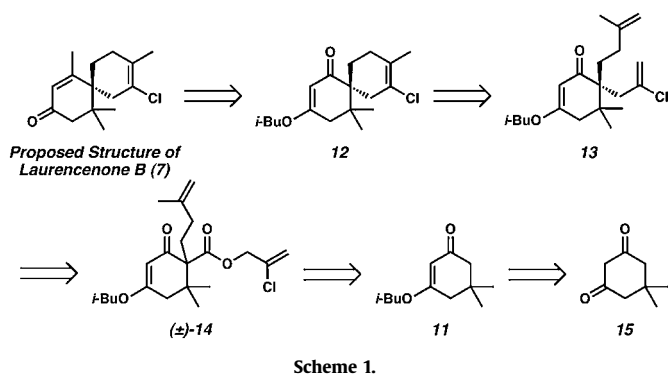
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we anticipated that intermediate **11** could thus serve as a common precursor to a variety of chamigrene natural products.

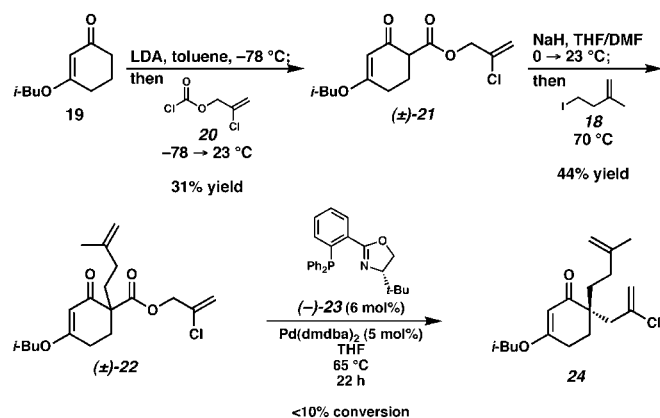
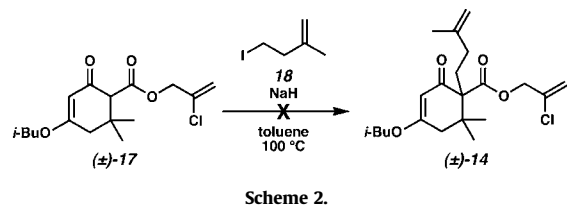
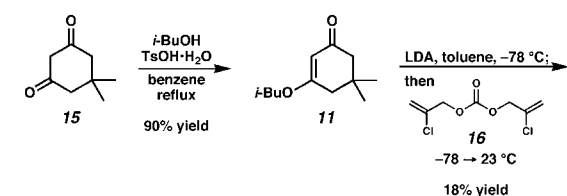
## 2. Results and discussion

### 2.1. Synthesis of the proposed structure of laurencenone B (**7**)

From the outset, we set as the final goal of our studies the preparation of elatol (**1**), one of the more biologically interesting and synthetically demanding chamigrenes. Initially, however, we chose to focus on a simpler target in order to validate our synthetic approach. The proposed structure of laurencenone B (**7**) possesses features identical to those of elatol (**1**) with respect to our key disconnections, namely the all-carbon quaternary stereocenter and B-ring tetrasubstituted olefin, but contains a less elaborately functionalized A ring. Also like **1**,<sup>9</sup> no total synthesis of **7** had yet been reported.<sup>10</sup> Scheme 1 outlines our retrosynthetic analysis.<sup>11</sup> Laurencenone B (**7**) could ultimately arise from spirocycle **12** through Stork–Danheiser alkylation using an appropriate methyl anion source. Compound **12** in turn could be obtained by RCM of  $\alpha,\omega$ -diene **13**. Although unprecedented in the literature,<sup>12,13</sup> we anticipated formation of a fully substituted chlorinated olefin could be achieved with the enhanced reactivity of catalyst **49** (vide infra).<sup>8</sup>  $\alpha,\omega$ -Diene **13** itself could be the product of an enantioselective decarboxylative allylation of racemic  $\beta$ -ketoester ( $\pm$ )-**14** using the Pd(0) complex of a phosphinoxazoline (PHOX) ligand.<sup>14,15</sup> Finally, intermediate **14** could be prepared from commercially available dimedone (**15**) via vinylogous ester **11**.<sup>16</sup>

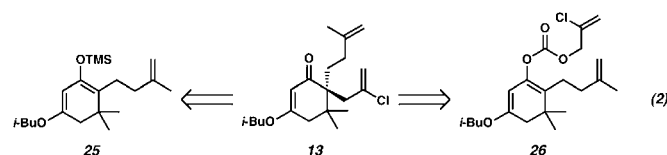


We began our synthetic efforts with the condensation of dimedone (**15**) and isobutyl alcohol to afford known vinylogous ester **11** as shown in Scheme 2.<sup>16</sup> Acylation of **11** with carbonate **16** then provided racemic  $\beta$ -ketoester ( $\pm$ )-**17**, albeit in low yield. Unfortunately, direct alkylation of **17** with 4-iodo-2-methyl-1-butene (**18**)<sup>17</sup> did not yield any of the desired product ( $\pm$ )-**14** even under forcing conditions. Alternative routes to ( $\pm$ )-**14** were briefly examined; however, concurrent model studies indicated that the proposed  $\beta$ -ketoester ( $\pm$ )-**14** would likely not be a viable substrate in the enantioselective decarboxylative allylation step. Racemic  $\beta$ -ketoester analog ( $\pm$ )-**22**, readily prepared due to the absence of  $\beta$ -dimethyl substitution, surprisingly provided less than 10% conversion to allylated product **24** under our standard reaction conditions at 65 °C after 22 h (Scheme 3). Although a rigorous explanation of this unexpectedly low reactivity awaits further study, we speculated that the presence of the tethered olefin substituent at the  $\alpha$ -position may interact with the Pd(0)/PHOX complex, thus interfering with oxidative addition to the allyl ester moiety. Similar retardation of reaction rates has been observed with analogous substrates in our laboratories.<sup>18</sup>

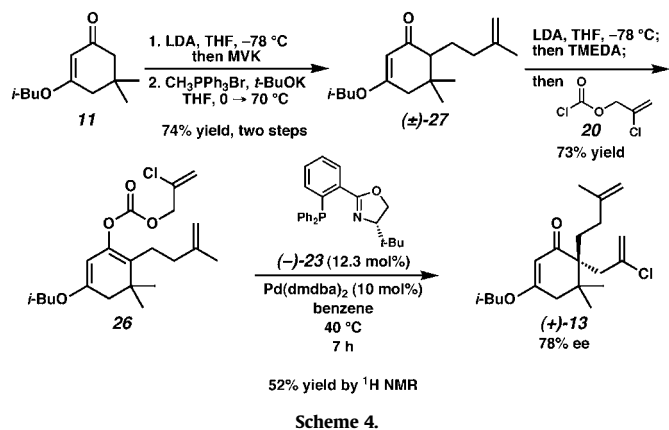


Scheme 3. dmdba=bis(3,5-dimethoxybenzylidene)acetone.

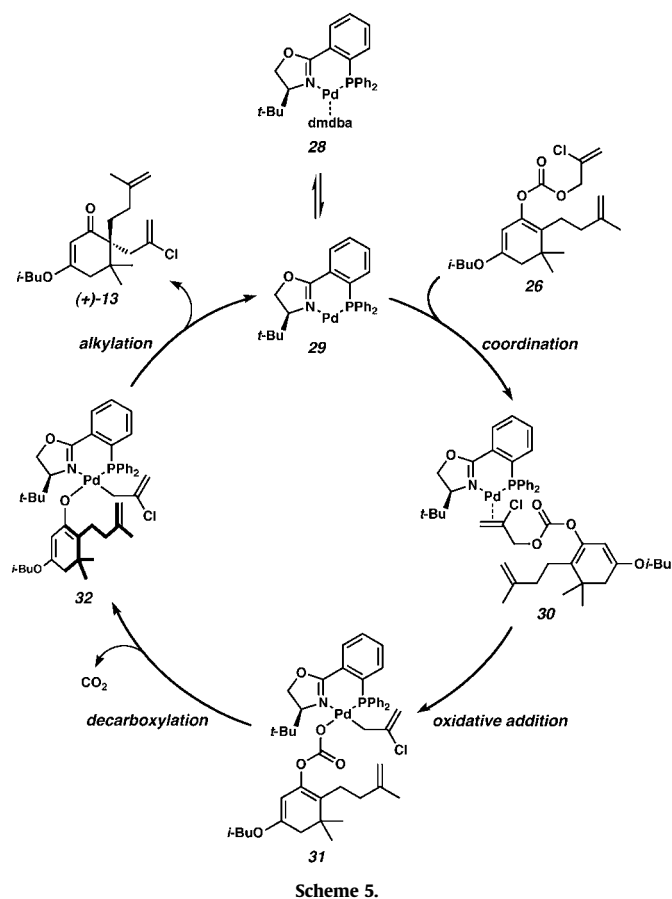
To circumvent the anticipated poor performance of proposed  $\beta$ -ketoester ( $\pm$ )-**14** in the enantioselective decarboxylative allylation, we attempted to take advantage of the ability to effect this transformation through one of two other structurally discreet substrates: namely a trimethylsilyl enol ether (**25**) or enol



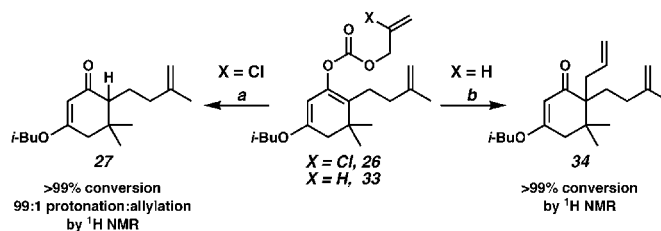
carbonate (**26**) (Eq. 2). Not only would this approach provide the necessary reactivity to produce  $\alpha,\omega$ -diene **13**, it would also alleviate the need to perform vicinal quaternary carbon centers, allowing such functionality to be installed in the allylation step. To this end, we prepared vinylogous ester ( $\pm$ )-**27**, the immediate precursor to both **25** and **26** (Scheme 4). Direct conversion of **11** to ( $\pm$ )-**27** by alkylation with 4-iodo-2-methyl-1-butene (**18**) proceeded in only low conversion;<sup>19</sup> alternatively, 1,4-addition to methyl vinyl ketone (MVK)<sup>20</sup> followed by Wittig methylenation of the crude product mixture led to ( $\pm$ )-**27** in good yield over two steps. While an attempt to capture the corresponding lithium enolate of ( $\pm$ )-**27** with trimethylsilyl chloride did not generate an isolatable product,<sup>21</sup> treatment of the same enolate with TMEDA and chloroformate **20** afforded stable enol carbonate **26** in 73% yield. Gratifyingly, exposure of **26** to our standard allylation conditions<sup>22</sup> at 40 °C now provided  $\alpha,\omega$ -diene (+)-**13** in 52% yield by <sup>1</sup>H NMR and 78% ee. Slightly higher enantioselectivity (81% ee) could be obtained by reaction at 24 °C,<sup>23</sup> but at a significant expense of yield (28% by <sup>1</sup>H NMR, 23% isolated).



Having achieved base reactivity using enol carbonate **26**, we sought to further optimize the enantioselective decarboxylative allylation in order to generate a synthetically viable reaction. Based on the temperature dependence of enantioselectivity in our initial screening, we reasoned that increasing catalyst reactivity should allow access to lower reaction temperatures and thus improved ee. Careful scrutiny of the proposed catalytic pathway<sup>24</sup> (Scheme 5) led



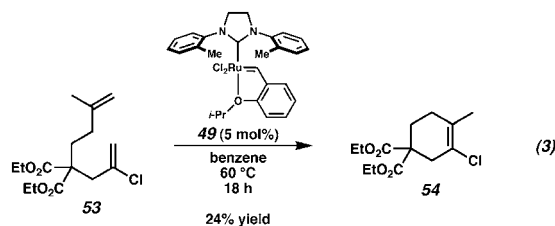
us to hypothesize that the low reactivity of **26** was likely derived from one of three scenarios: (1) slow oxidative addition of Pd(0)-PHOX complex **29** to allyl enol carbonate **26**; (2) slow decarboxylation of Pd(II)-enol carbonate **31** to provide Pd(II)-enolate **32**; or (3), slow alkylation of **32** to yield the desired product (+)-**13**. To differentiate between these possibilities, we conducted the set of control reactions depicted in Scheme 6. Subjection of enol



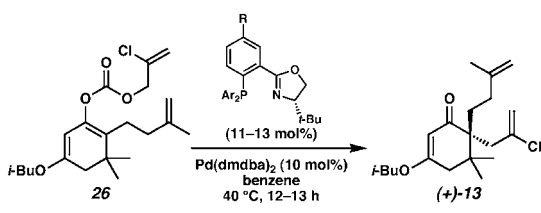
carbonate **26** to conditions developed in our laboratories for enantioselective decarboxylative protonation<sup>25</sup> readily afforded olefin **27**,<sup>26</sup> demonstrating that oxidative addition and decarboxylation proceed as desired. Furthermore, less sterically-hindered deschloro analog **33** underwent facile decarboxylative allylation to yield bis(olefin) **34**. From these studies, slow alkylation was determined to be the problematic step in this transformation.

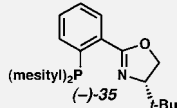
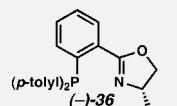
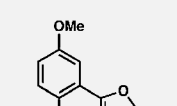
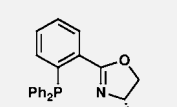
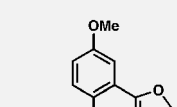
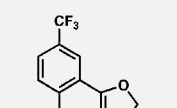
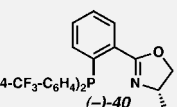
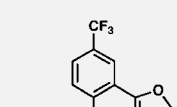
In order to enhance the sluggish rate of alkylation identified above, we attempted to increase the electrophilicity of the π-allyl Pd(II) intermediate by incorporating electron-withdrawing substituents into the PHOX ligand framework.<sup>27</sup> As shown in Table 1, moving from electron-rich to electron-deficient ligands resulted in a dramatic improvement in conversion from <20% to >99%, with good selectivity for the desired allylation product (+)-**13** over the undesired protonation byproduct **27**. A solvent screen employing one of the most active PHOX analogs, ligand (–)-**40**, revealed higher enantioselectivity with aromatic solvents compared to ethereal solvents (Table 2), while a temperature screen using the two most active ligands, (–)-**40** and (–)-**41**, demonstrated the latter to exhibit the sharpest dependence of enantioselectivity on temperature (Table 3). Ultimately, the best compromise between reactivity and selectivity was provided by ligand (–)-**41** in benzene at 13 °C (Table 3, entry 5), affording bis(olefin) (+)-**13** in 90% isolated yield and 87% ee (Table 4, entry 2). A brief examination of closely related analogs of enol carbonate **26** gave similarly good yields and enantioselectivities for the corresponding α,ω-dienes (Table 4, entries 1, 3–4).

We next turned our attention to the completion of the chami-grene spirocyclic core via RCM of bis(olefin) (+)-**13**. In a limited survey of catalysts, second generation complex **47** provided moderate conversion to the desired tetrasubstituted olefinic product (–)-**12** and minor unidentified byproducts, while complex **48** yielded comparable reactivity and substantial unknown impurities (Table 5, entries 1 and 2). Catalyst **49**, however, afforded rapid and clean conversion under our standard conditions (Table 5, entry 3), furnishing spirocycle (–)-**12** in 97% isolated yield (Table 6, entry 2). Interestingly, this catalytic system proved ineffective when applied to the RCM of the α,ω-diene analogs synthesized above. Removal of the dimethyl substitution vicinal to the spirocycle junction led to significantly diminished conversion (Table 6, entry 4), while extension or contraction of the homoallyl chain by a single methylene unit resulted in complete loss of reactivity (Table 6, entries 1 and 3). Similarly, a simplified acyclic substrate (**53**) produced little of the ring-closed product using catalyst **49** (Eq. 3). This seemingly unique



**Table 1**  
Effect of ligand electronics on enantioselective decarboxylative allylation



Entry	Ligand	Conversion <sup>a</sup> (%)	Allylation <sup>a,b</sup> (%)	ee <sup>c,d</sup> (%)
1		11	6	n.d.
2		18	14	n.d.
3		12	6	n.d.
4 <sup>e</sup>		59	52	78
5		75	60	76
6		98	87	83
7		>99	92	75
8		>99	>99	78

<sup>a</sup> Determined by <sup>1</sup>H NMR spectroscopic analysis of the crude product mixture.

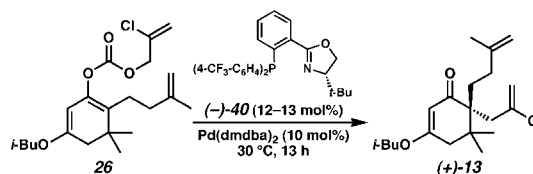
<sup>b</sup> The remaining mass balance was comprised of protonation byproduct **27**.

<sup>c</sup> Determined by chiral HPLC analysis.

<sup>d</sup> n.d.=not determined.

<sup>e</sup> 7 h reaction time.

**Table 2**  
Effect of solvent on enantioselective decarboxylative allylation with ligand (–)-**40**



Entry	Solvent	Conversion <sup>a</sup> (%)	Allylation <sup>a,b</sup> (%)	ee <sup>c,d</sup> (%)
1	TEA	7	3	n.d.
2	Et <sub>2</sub> O	>99	88	67
3	THF	>99	90	71
4	1,4-Dioxane	>99	87	72
5	toluene	>99	90	76
6	benzene	>99	93	77

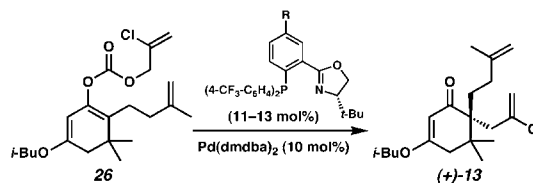
<sup>a</sup> Determined by <sup>1</sup>H NMR spectroscopic analysis of the crude product mixture.

<sup>b</sup> The remaining mass balance was comprised of protonation byproduct **27**.

<sup>c</sup> Determined by chiral HPLC analysis.

<sup>d</sup> n.d.=not determined.

**Table 3**  
Effect of temperature on enantioselective decarboxylative allylation with ligands (–)-**40** and (–)-**41**



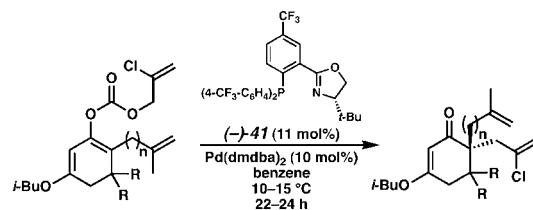
Entry	Ligand	Solvent	T (°C)	t (h)	Conversion <sup>a</sup> (%)	Allylation <sup>a,b</sup> (%)	ee <sup>c</sup> (%)
1	(–)- <b>40</b>	Benzene	40	13	>99	92	75
2	(–)- <b>40</b>	Benzene	30	13	>99	93	77
3	(–)- <b>41</b>	Benzene	40	13	>99	>99	78
4	(–)- <b>41</b>	Benzene	30	15	>99	97	83
5	(–)- <b>41</b>	<b>Benzene 13</b>	<b>24</b>	<b>&gt;99</b>	<b>95</b>	<b>87</b>	
6	(–)- <b>41</b>	Toluene	0	17	72	63	89

<sup>a</sup> Determined by <sup>1</sup>H NMR spectroscopic analysis of the crude product mixture.

<sup>b</sup> The remaining mass balance was comprised of protonation byproduct **27**.

<sup>c</sup> Determined by chiral HPLC analysis.

**Table 4**  
Scope of enantioselective decarboxylative allylation with ligand (–)-**41**

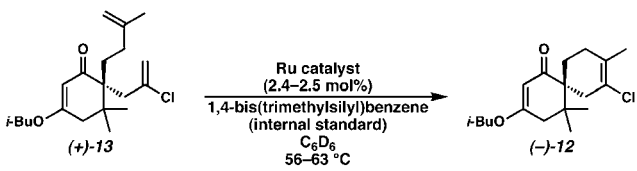


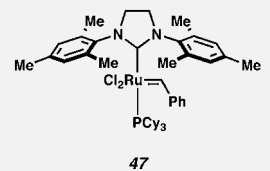
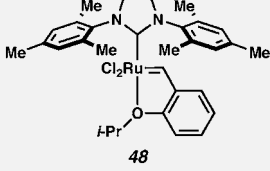
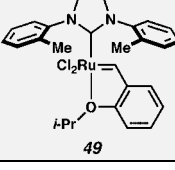
Entry	Enol carbonate	R	n	α,ω-diene	Yield <sup>a</sup> (%)	ee <sup>b</sup> (%)
1	<b>42</b>	Me	1	(+)- <b>45</b>	92	91
2	<b>26</b>	Me	2	(+)- <b>13</b>	90	87
3	<b>43</b>	Me	3	(–)- <b>46</b>	91	90
4	<b>44</b>	H	2	(+)- <b>24</b>	80	94

<sup>a</sup> Isolated yield.

<sup>b</sup> Determined by chiral HPLC analysis.

**Table 5**  
Catalyst comparison in RCM of  $\alpha,\omega$ -diene (+)-**13**

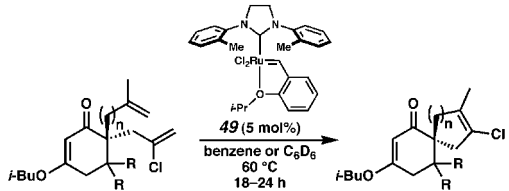


Entry	Ru catalyst	t (h)	Conversion <sup>a</sup> (%)
1	 47	1	43
		5	78
		24	85
2 <sup>b</sup>	 48	1	29
		5	83
		24	91
3	 49	1	63
		5	>99

<sup>a</sup> Determined by <sup>1</sup>H NMR spectroscopic analysis using 1,4-bis(trimethylsilyl)benzene as an internal standard.

<sup>b</sup> Conversion values are approximate due to overlapping of significant amounts of unknown impurities with (+)-**13** in the <sup>1</sup>H NMR spectrum.

**Table 6**  
Scope of RCM with catalyst **49**



Entry	$\alpha,\omega$ -diene	R	n	Spirocycle	Result
1 <sup>a</sup>	(+)- <b>45</b>	Me	1	<b>50</b>	no conversion <sup>c</sup>
2 <sup>b</sup>	(+)- <b>13</b>	Me	2	(-)- <b>12</b>	97% yield <sup>d</sup>
3 <sup>a</sup>	(-)- <b>46</b>	Me	3	<b>51</b>	no conversion <sup>c</sup>
4 <sup>b</sup>	(+)- <b>24</b>	H	2	<b>52</b>	19% conversion <sup>c,e</sup>

<sup>a</sup> C<sub>6</sub>D<sub>6</sub>.

<sup>b</sup> Benzene.

<sup>c</sup> Determined by <sup>1</sup>H NMR spectroscopic analysis of the crude product mixture.

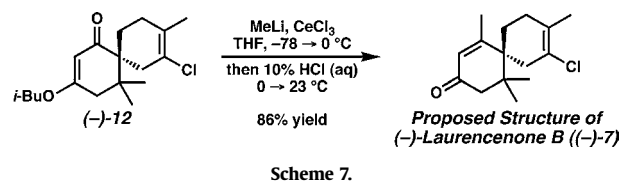
<sup>d</sup> Isolated yield.

<sup>e</sup> Did not determine optical rotation.

reactivity of intermediate (+)-**13** was unanticipated, and efforts to understand the basis of these effects are ongoing.

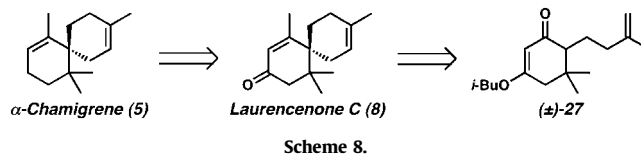
With spirocycle (–)-**12** in hand, all that remained to complete Laurencenone B (**7**) was Stork–Danheiser alkylation using methyl anion. While methyl lithium alone added only very slowly to vinylogous ester (–)-**12**,<sup>28</sup> inclusion of CeCl<sub>3</sub><sup>29</sup> provided a significant increase in reaction rate,<sup>30</sup> generating (–)-Laurencenone B ((–)-**7**) in 86% isolated yield after acid-mediated hydrolysis and elimination (Scheme 7). Overall, the first total synthesis of the proposed structure of (–)-Laurencenone B ((–)-**7**) was carried out in seven steps and 37% yield from dimedone (**15**). Unfortunately, discrepancies existed between the published <sup>1</sup>H NMR data for the

natural product<sup>2g</sup> and that of the synthetic material, although the single IR peak reported did match. Furthermore, no <sup>13</sup>C NMR data or natural sample was available for comparison. <sup>1</sup>H NMR, <sup>13</sup>C NMR, and IR data for semisynthetic (+)-laurencenone B ((+)-**7**)<sup>10</sup> did however match that of the synthetic material, while the opposite sign of optical rotation was obtained.<sup>31</sup> Based on these observations,<sup>32</sup> we conclude that the structure of the natural product designated as laurencenone B (**7**) has been incorrectly assigned.



## 2.2. Syntheses of laurencenone C (**8**) and $\alpha$ -chamigrene (**5**)

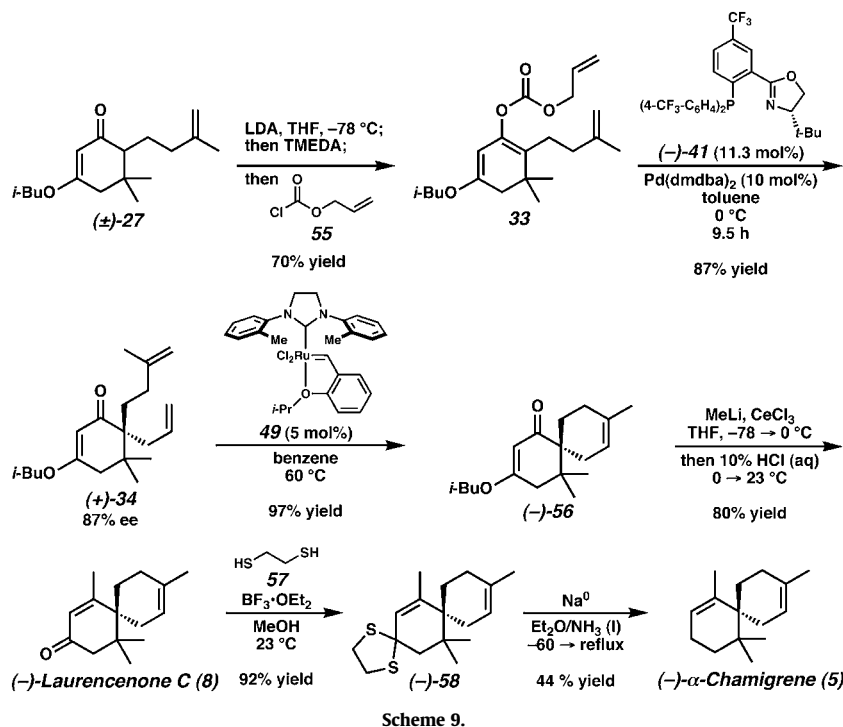
Having established a viable synthetic route to the chamigrene natural product family, we chose to demonstrate the generality of this strategy by preparing the related compounds laurencenone C (**8**)<sup>2g–h</sup> and  $\alpha$ -chamigrene (**5**).<sup>2e</sup> Although four racemic total syntheses of (±)-laurencenone C ((±)-**8**)<sup>5a–c,e</sup> and ten of (±)- $\alpha$ -chamigrene ((±)-**5**)<sup>5a–c,33</sup> have been previously reported, no enantioselective approaches have yet been devised.<sup>34,35</sup> Conversion of (±)-**8** to (±)-**5** has been described by both Takeshita<sup>5a</sup> and Chen,<sup>5b</sup> and retrosynthetically we planned the same final two-step sequence to access  $\alpha$ -chamigrene (**5**) (Scheme 8). Laurencenone C (**8**) could then be traced back to vinylogous ester (±)-**27**, the same intermediate used for (–)-Laurencenone B ((–)-**7**), through an analogous set of transformations. In the forward direction, acylation of compound (±)-**27** with allyl chloroformate (**55**) proceeded smoothly to provide enol carbonate **33** in 70% yield (Scheme 9). Now in the absence of a 2-chloro substituent on the allyl moiety (cf. Table 3, entry 6), enol carbonate **33** displayed excellent reactivity at 0 °C in the enantioselective decarboxylative allylation, affording  $\alpha,\omega$ -diene (+)-**34** in 87% yield and 87% ee. RCM, followed by methyl cerium addition<sup>29,30</sup> and acid-mediated hydrolysis/elimination, then yielded (–)-laurencenone C (**8**) in seven steps and 31% overall yield from dimedone (**15**).<sup>36</sup> Following a modified variant of the reported procedures,<sup>37</sup> (–)-**8** was subsequently condensed with ethanedithiol (**57**) to afford dithiolane (–)-**58** in 92% yield. Finally, reduction with Na<sup>0</sup> <sup>5b</sup> provided (–)- $\alpha$ -chamigrene (**5**) in nine steps and 13% overall yield from **15**,<sup>38</sup> completing the first enantioselective total syntheses of both (–)- $\alpha$ -chamigrene (**5**) and (–)-laurencenone C (**8**).



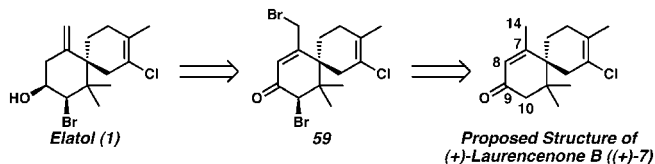
## 2.3. Synthesis of elatol (**1**)

Following the completion of the syntheses of three simpler chamigrenes, we returned to the preparation of elatol (**1**) in order to demonstrate the ability of our approach to access a more complex member of this natural product class. Comparison of **1** to

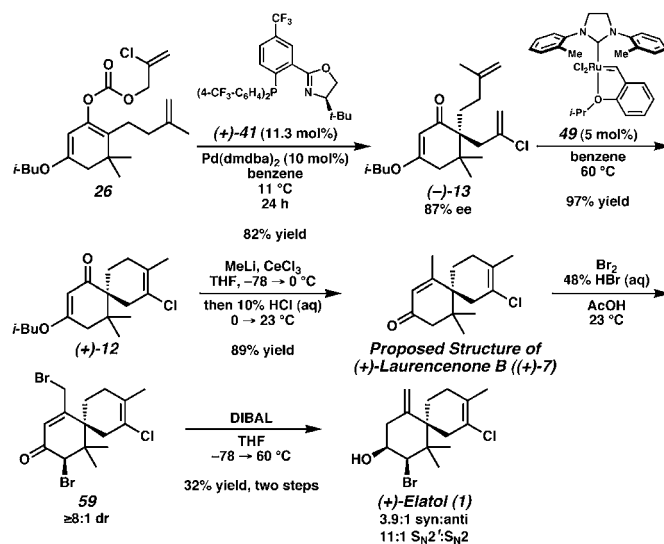




the proposed structure of (+)-laurencenone B ((+)-7) revealed the two molecules to be separated by three formal chemical reactions: (1) diastereoselective introduction of the 10-bromide; (2) diastereoselective reduction of the 9-ketone; and (3) transposition of the 7,8-olefin to the 7,14-position. We envisioned a simple two-step procedure to effect these transformations as shown in Scheme 10. Elatol (1) could ultimately be derived from sequential directed reductive olefin transposition and diastereoselective reduction of 10,14-dibromolaurencenone B (59) in a single pot.<sup>39</sup> Dibromide 59 in turn could be the product of concomitant allylic and  $\alpha'$ -bromination of (+)-laurencenone B ((+)-7).<sup>40</sup> Substitution of PHOX ligand (+)-41 for (-)-41 in the initial synthesis of (-)-laurencenone B ((-)-7) would then provide the necessary starting material (+)-7.



Repetition of the (-)-laurencenone B ((-)-7) synthesis in the opposite enantiomeric series afforded (+)-7 in comparable yield and 87% ee as expected (Scheme 11). After surveying several electrophilic bromine sources<sup>41</sup> and reaction conditions, conversion of (+)-7 to 10,14-dibromolaurencenone B (59) was effected in  $\geq 8:1$  dr<sup>42</sup> using Br<sub>2</sub> in the presence of HBr (aq)/AcOH,<sup>40c</sup> presumably under thermodynamic control. Double reduction of  $\alpha$ -bromo-ketone 59 with DIBAL<sup>39b</sup> then provided (+)-elatol (1) in 32% isolated yield over two steps (3.9:1 *syn/anti*,<sup>43</sup> 11:1 *S<sub>N</sub>2':S<sub>N</sub>2*).<sup>44</sup> In comparison, reduction with LAH<sup>45</sup> or Red-Al<sup>46</sup> provided  $\leq 2:1$  *S<sub>N</sub>2':S<sub>N</sub>2* for the reductive olefin transposition. The first total synthesis of (+)-elatol (1) was thus completed in only nine steps and 11% overall yield from dimedone (15).



### 3. Conclusion

We have successfully developed a concise and general enantioselective route to the chamigrene natural product family, resulting in the first total syntheses of (+)-elatol (1) and the proposed structure of laurencenone B (7), the first asymmetric total syntheses of (-)- $\alpha$ -chamigrene (5) and (-)-laurencenone C (8), and the first preparation of a fully substituted chlorinated olefin via RCM. Moreover, we have demonstrated the ability of our enantioselective decarboxylative allylation reaction to readily access enantioenriched vinylogous esters bearing vicinal quaternary carbon centers. Efforts to expand the scope of both the enantioselective decarboxylative allylation with vinylogous esters and the RCM with vinyl halides are the focus of ongoing studies.

## 4. Experimental

### 4.1. General

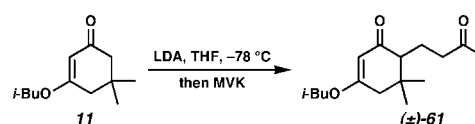
Unless stated otherwise, reactions were conducted under an ambient atmosphere. Anhydrous solvents were prepared by passing the solvents through activated alumina columns. Commercially obtained reagents were used as received, unless specified otherwise. Anhydrous diisopropylamine, triethylamine, *N,N,N',N'*-tetramethylethylenediamine, and *N,N'*-dimethylethylenediamine (**79**) were obtained from distillation over CaH<sub>2</sub>. Methyl vinyl ketone, boron trifluoride diethyl etherate, and hexamethylphosphoramide were distilled prior to use. 4-Iodo-2-methyl-1-butene (**18**) was prepared according to the method of Hiersemann.<sup>17</sup> Phosphinooxazoline ligands (–)-**23** and (–)-**35–41** were prepared according to the previously published method.<sup>27</sup> Anhydrous CeCl<sub>3</sub> was prepared according to the method of Imamoto.<sup>47</sup> 5-Iodo-2-methyl-1-pentene (**67**) was prepared according to the method of Boyer.<sup>48</sup> Olefin **70** was prepared according to the previously published method.<sup>49</sup> Salt **75** was prepared according to the method of Drauz.<sup>50</sup> Phosphine **78**<sup>51</sup> was prepared according to the method of Bussaca.<sup>52</sup> Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F<sub>254</sub> pre-coated plates [0.25 mm (analytical) or 0.5 mm (preparative)] and visualized using a combination of UV light (254 nm), *p*-anisaldehyde staining, and potassium permanganate staining. TLC data include *R<sub>f</sub>* and eluent (% by volume). ICN silica gel (particle size 0.032–0.063 mm), SiliCycle® SiliaFlash® P60 Academic Silica Gel (particle size 40–63 μm; pore diameter 60 Å), or Florisil® (100–200 mesh) were used for flash column chromatography. All flash column chromatographic purification steps are reported as follows: size of immobile phase column (length×diameter) and eluent (% by volume). Analytical chiral HPLC analyses were performed with an Agilent 1100 Series HPLC instrument. Preparative HPLC purifications were performed with a Beckman System Gold® or an Agilent 1200 Series HPLC instrument. <sup>1</sup>H NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz) or a Varian Inova 500 (at 500 MHz) instrument and are reported relative to the residual solvent peak ( $\delta$  7.26 for CDCl<sub>3</sub>, 7.16 for C<sub>6</sub>D<sub>6</sub>, and  $\delta$  2.05 for acetone-*d*<sub>6</sub>) or Me<sub>4</sub>Si ( $\delta$  0.00) in the case of CCl<sub>4</sub>. Data for <sup>1</sup>H NMR spectra are reported as follows: chemical shift ( $\delta$  ppm), multiplicity, coupling constant (Hz), and integration. <sup>13</sup>C NMR spectra were recorded on a Varian Mercury 300 (at 75 MHz), or a Varian Inova 500 (at 126 MHz) instrument and are reported relative to the residual solvent peak ( $\delta$  77.0 for CDCl<sub>3</sub> and 128.06 for C<sub>6</sub>D<sub>6</sub>). Data for <sup>13</sup>C NMR spectra are reported in terms of chemical shift ( $\delta$  ppm), as well as multiplicity and coupling constant (Hz) where applicable. <sup>19</sup>F NMR spectra were recorded on a Varian Inova 500 (at 470 MHz) instrument and are reported in terms of chemical shift ( $\delta$  ppm) without the use of a reference peak. IR spectra were recorded on a Perkin–Elmer Spectrum BXII spectrometer and are reported in frequency of absorption (cm<sup>-1</sup>). Optical rotations were measured with a Jasco P-1010 polarimeter, using a 100 mm path-length cell. High-resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility.

### 4.2. Procedures for the synthesis of the proposed structure of (+)-laurencenone B ((+)-**7**)

**4.2.1. Vinylogous ester **11**<sup>16</sup>.** To a 500 mL round-bottomed flask equipped with a magnetic stir bar, a Dean/Stark trap, and a condenser was added dimedone (**15**) (10.0 g, 71.3 mmol), *p*-toluenesulfonic acid monohydrate (269 mg, 1.41 mmol), anhydrous benzene (120 mL), and isobutanol (33.0 mL, 358 mmol). The resulting solution was then heated to reflux in an oil bath and

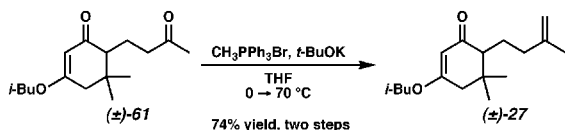
stirred for 21 h. After cooling to 23 °C, the reaction was washed with saturated NaHCO<sub>3</sub> (aq) (100 mL), and the aqueous layer was extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine (2×100 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure, and the crude product mixture was azeotroped with toluene (4×) to remove excess isobutyl alcohol. The product was then distilled at 109–110 °C and 1.3 Torr to provide vinylogous ester **11**<sup>16</sup> (12.561 g, 90%) as a slightly yellow liquid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  5.33 (br s, 1H), 3.60 (d, *J*=6.6 Hz, 2H), 2.28 (s, 2H), 2.21 (s, 2H), 2.03 (app. septet, *J*=6.7 Hz, 1H), 1.07 (s, 6H), 0.97 (d, *J*=6.7 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  199.6, 176.4, 101.4, 74.7, 50.7, 42.8, 32.4, 28.3, 27.7, 19.0; IR (neat film, NaCl)  $\nu$  2961, 2876, 1660, 1608, 1471, 1404, 1382, 1367, 1320, 1221, 1162, 1145, 1014, 992, 822 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>12</sub>H<sub>20</sub>O<sub>2</sub> [M]<sup>+</sup>: 196.1463, found 196.1463.

### 4.2.2. Olefin (±)-**27**. 4.2.2.1. Part 1: Alkylation<sup>20</sup>.

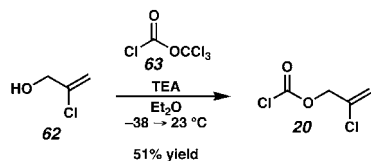


A 250 mL two-neck round-bottomed flask equipped with a 25 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (95 mL) and anhydrous diisopropylamine (2.0 mL, 14.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.6 M in hexanes, 5.4 mL, 14.0 mmol) was added dropwise via syringe and the solution stirred at 0 °C for 1 h. The resulting LDA solution was then cooled to –78 °C over 16 min. Vinylogous ester **11** (2.50 g, 12.7 mmol) in anhydrous THF (10 mL) was then added dropwise over 16 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at –78 °C for 1 h, methyl vinyl ketone (1.05 mL, 12.9 mmol) was added dropwise quickly via syringe. A slight exotherm was observed. The reaction was stirred for an additional 3 h at –78 °C, whereupon H<sub>2</sub>O (20 mL) was added. The mixture was warmed to 23 °C, at which time the organic layer was separated. The aqueous layer was extracted with Et<sub>2</sub>O (2×100 mL) and EtOAc (2×100 mL), at which point it was completely incorporated into the organic layers. The combined organic layers were washed with saturated NaHCO<sub>3</sub> (aq) (300 mL) and brine (2×300 mL), respectively, and then dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure to provide 3.469 g of ketone (±)-**61** as a reddish-orange liquid containing 12.9% by mass starting vinylogous ester **11**, 4.1% by mass EtOAc, and 1% by mass Et<sub>2</sub>O as determined by <sup>1</sup>H NMR spectroscopy. The crude yield corrected for impurities was 84%. The crude material was carried directly to Part 2. An aliquot from a separate run was purified by preparative thin-layer chromatography (0.25 mm thickness, eluted twice with 30% EtOAc/hexanes eluent). *R<sub>f</sub>* 0.40 (eluting twice with 30% EtOAc/hexanes eluent); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.20 (s, 1H), 3.57 (dd, *J*=9.4, 6.7 Hz, 1H), 3.54 (dd, *J*=9.5, 6.6 Hz, 1H), 2.64 (ddd, *J*=18.2, 9.0, 5.2 Hz, 1H), 2.51 (ddd, *J*=18.3, 9.0, 6.6 Hz, 1H), 2.36 (d, *J*=17.8, 1H), 2.19 (d, *J*=17.6 Hz, 1H), 2.13 (s, 3H), 2.01 (app. septet, *J*=6.7 Hz, 1H), 1.82–1.92 (m, 2H), 1.53–1.64 (m, 1H), 1.08 (s, 3H), 1.00 (s, 3H), 0.96 (d, *J*=6.6 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  209.1, 202.6, 175.0, 100.4, 74.6, 55.9, 42.2, 41.3, 35.0, 30.2, 28.5, 27.7, 24.6, 20.0, 19.1; IR (neat film, NaCl)  $\nu$  2962, 2934, 2897, 2876, 1716, 1652, 1611, 1471, 1424, 1406, 1382, 1366, 1324, 1298, 1276, 1221, 1199, 1179, 1155, 1131, 1067, 1056, 1008, 994, 968, 952, 912, 904, 851, 831, 745, 710, 693, 627 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>16</sub>H<sub>26</sub>O<sub>3</sub> [M]<sup>+</sup>: 266.1882, found 266.1928.

## 4.2.2.2. Part 2: Wittig olefination.



To a flame-dried 500 mL round-bottomed flask equipped with a magnetic stir bar was added methyltriphenylphosphonium bromide (8.00 g, 22.4 mmol). After attaching an oven-dried condenser and sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous THF (255 mL) was added via syringe, and the mixture was cooled to 0 °C in an ice bath. Potassium *tert*-butoxide (2.39 g, 21.5 mmol) was added under positive Ar pressure to give a yellow mixture, and the system was flushed with Ar while being allowed to warm to 23 °C over 25 min. The crude ketone (**±**)-**61** from Part 1 (3.461 g, 82% pure by mass, 10.7 mmol) in anhydrous THF (5 mL) was then added via syringe, washing the original flask with THF (5 mL). The reaction was placed in a 70 °C oil bath and stirred for 2 h. After cooling to 23 °C, the reaction mixture was filtered through a pad of silica gel (2.5 × 10 cm), eluting with THF (1 L). Solvent was removed under reduced pressure. Flash chromatography over silica gel (9 × 5 cm, 20% Et<sub>2</sub>O/pentane eluent) then provided olefin (**±**)-**27** (2.489 g, 74% over two steps) as a slightly yellow liquid. The isolated yield for Part 2 corrected for impurities in crude ketone (**±**)-**61** was 88%. *R<sub>f</sub>* 0.33 (20% Et<sub>2</sub>O/pentane eluent); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.23 (s, 1H), 4.69–4.73 (m, 1H), 4.66–4.69 (m, 1H), 3.57 (d, *J*=6.4 Hz, 2H), 2.33 (d, *J*=17.6 Hz, 1H), 2.20 (d, *J*=17.6 Hz, 1H), 2.08–2.19 (m, 1H), 1.960–2.07 (m, 2H), 1.90–1.96 (m, 1H), 1.72 (s, 3H), 1.55–1.69 (m, 2H), 1.07 (s, 3H), 0.98 (s, 3H), 0.96 (d, *J*=6.8 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 202.3, 174.3, 145.9, 109.9, 100.6, 74.6, 56.3, 41.7, 36.6, 35.1, 28.6, 27.7, 24.6, 24.1, 22.6, 19.1; IR (neat film, NaCl) ν 2961, 2933, 2875, 1656, 1613, 1471, 1424, 1404, 1382, 1365, 1297, 1220, 1191, 1153, 1007, 885, 832 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>17</sub>H<sub>28</sub>O<sub>2</sub> [M]<sup>+</sup>: 264.2089, found 264.2081.

4.2.3. Chloroformate **20**<sup>53</sup>.

A 500 mL three-neck round-bottomed flask equipped with a 250 mL addition funnel, a stir bar, and three septa was flame dried under vacuum. After refilling with Ar, anhydrous Et<sub>2</sub>O (30 mL) was added via syringe, and the system was cooled to approx. -10 °C. Diphosgene (**63**) (7.7 mL, 63.8 mmol) was added dropwise via syringe and the solution was cooled to approx. -20 °C. 2-Chloroallyl alcohol (**62**) (5.0 mL, 62.8 mmol) in anhydrous Et<sub>2</sub>O (75 mL) was added dropwise via the addition funnel, and the solution was stirred at approx. -20 °C for an additional 15 min. The reaction was cooled to approx. -30 °C, and anhydrous triethylamine (8.8 mL, 63.1 mmol) in anhydrous Et<sub>2</sub>O (75 mL) was added dropwise via the addition funnel, generating a white precipitate. The reaction was then cooled to approx. -38 °C and stirred for 3 h, at which time it was allowed to warm to 23 °C while stirring for an additional 15 h. During this time, the reaction mixture became very thick, and Et<sub>2</sub>O (50 mL) was added to obtain a stirable suspension. Ar was bubbled through the suspension for 2 h to remove excess phosgene, employing a saturated NaHCO<sub>3</sub> (aq)/triethylamine trap. The reaction mixture was filtered via vacuum filtration through a fritted funnel, and the filtrate was concentrated by rotary

evaporation under reduced pressure. The product was then distilled at 50 °C and 20 Torr to provide chloroformate **20** (4.987 g, 51%) as a colorless liquid containing a minor unidentified impurity (1% by area) by <sup>1</sup>H NMR spectroscopy; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.58 (dt, *J*=1.0, 2.0 Hz, 1H), 5.53 (d, *J*=2.2 Hz, 1H), 4.84 (d, *J*=0.7 Hz, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 150.4, 133.5, 117.4, 72.2; IR (CHCl<sub>3</sub>, KBr) ν 1775 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>4</sub>H<sub>4</sub>Cl<sub>2</sub>O<sub>2</sub> [M]<sup>+</sup>: 153.9588, found 153.9593.

4.2.4. Enol carbonate **26**. A 250 mL two-neck round-bottomed flask equipped with a 50 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (55 mL) and anhydrous diisopropylamine (1.45 mL, 10.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.5 M in hexanes, 3.8 mL, 9.5 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 30 min. The resulting LDA solution was then cooled to -78 °C over 15 min. Olefin (**±**)-**27** (2.282 g, 8.63 mmol) in anhydrous THF (10 mL) was then added dropwise over 26 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at -78 °C for 1 h, anhydrous *N,N,N',N'*-tetramethylethylenediamine (1.55 mL, 10.3 mmol) was added dropwise over 2 min via syringe. After stirring at -78 °C for an additional 1 h, chloroformate **20** (1.471 g, 9.49 mmol) in anhydrous THF (10 mL) was then added dropwise over 22 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. A visible exotherm was observed, and the solution changed from yellow to brownish-red in color. The reaction was stirred for an additional 3 h at -78 °C, whereupon saturated NaHCO<sub>3</sub> (aq) (35 mL) and H<sub>2</sub>O (35 mL) were added. The mixture was allowed to warm to 23 °C, at which time the organic layer was immediately separated. The aqueous layer was extracted with Et<sub>2</sub>O (2 × 200 mL), and the combined organic layers were washed with brine (2 × 200 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (12 × 5 cm, 2.5% Et<sub>2</sub>O/petroleum ether eluent) then provided enol carbonate **26** (2.412 g, 73%) as a colorless liquid containing minor unidentified impurities (2% by area) by <sup>1</sup>H NMR spectroscopy. *R<sub>f</sub>* 0.17 (2.5% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.52–5.56 (m, 1H), 5.43–5.46 (m, 1H), 4.76 (s, 1H), 4.71–4.74 (m, 2H), 4.66–4.72 (br m, 2H), 3.48 (d, *J*=6.6 Hz, 2H), 2.19 (s, 2H), 2.01–2.19 (m, 4H), 1.97 (app. septet, *J*=6.7 Hz, 1H), 1.74 (br s, 3H), 1.09, (s, 6H), 0.94 (d, *J*=6.7 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 157.7, 153.0, 145.9, 142.0, 135.2, 123.3, 115.2, 109.8, 91.1, 73.9, 69.1, 43.4, 37.9, 35.4, 27.9, 26.0, 24.2, 22.4, 19.2; IR (neat film, NaCl) ν 3074, 2960, 2873, 1762, 1662, 1622, 1470, 1382, 1365, 1329, 1276, 1240, 1183, 1160, 1100, 1046, 1024, 972, 952, 922, 888, 782, 639 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>21</sub>H<sub>31</sub>ClO<sub>4</sub> [M]<sup>+</sup>: 382.1911, found 382.1912.

4.2.5.  $\alpha,\omega$ -Diene (–)-**13**. To a flame-dried 500 mL round-bottomed flask equipped with a magnetic stir bar was added phosphinooxazoline ligand (+)-**41** (0.36 g, 0.61 mmol) and bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (0.44 g, 0.54 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (150 mL, deoxygenated prior to use by sparging with N<sub>2</sub> in a flame-dried flask for 1.9 h) was added via syringe, and the resulting solution was stirred for 30 min at 23 °C during which time it turned dark yellow-brown. The solution was then cooled in an ice bath until solution just begins to freeze (7 min) and transferred to an 11 °C cooling bath. Concurrently, a second flame-dried round-bottomed flask was charged with enol carbonate **26** (2.056 g, 5.37 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Deoxygenated anhydrous benzene (6.5 mL) was added via syringe, and the resulting solution was cooled in an ice



bath, becoming very viscous at this time. The enol carbonate solution was then transferred via syringe to the catalyst solution at 11 °C, washing the original flask with deoxygenated anhydrous benzene (6.5 mL, allowed to cool briefly before transferring). The reaction, which turned green, was then stirred at 11 °C for 24 h. Solvent was removed under reduced pressure. The residue was suspended in Et<sub>2</sub>O and filtered through filter paper to remove precipitated Pd. The filtrate was then concentrated under reduced pressure. The residue was suspended in 5% Et<sub>2</sub>O/petroleum ether (some solid precipitates) and applied to a silica gel column (12×5 cm). Flash chromatography (5% Et<sub>2</sub>O/petroleum ether eluent) then provided  $\alpha,\omega$ -diene (–)-**13** (1.488 g, 82%) as a highly viscous, slightly yellow oil. Observed 87% ee as determined by chiral HPLC analysis (Chiralpak<sup>®</sup> AD, 1% EtOH/hexanes, 1 mL/min, 254 nm, *t<sub>R</sub>* (minor)=6.1 min; *t<sub>R</sub>* (major)=6.7 min). *R<sub>f</sub>* 0.06 (5% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>24</sup> –10.55 (c 0.995, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.30 (br s, 1H), 5.28 (s, 1H), 5.23 (s, 1H), 4.67–4.71 (m, 1H), 4.64–4.68 (m, 1H), 3.59 (dd, *J*=9.5, 6.6 Hz, 1H), 3.54 (dd, *J*=9.3, 6.8 Hz, 1H), 2.94–3.18 (br m, 1H), 2.46–2.83 (br m, 1H), 2.57 (br d, *J*=15.6 Hz, 1H), 2.12–2.38 (br m, 1H), 2.12–2.26 (m, 1H), 1.88–2.12 (br m, 1H), 2.01 (app. septet, *J*=6.7 Hz, 1H), 1.71 (s, 3H), 1.50–1.82 (br m, 2H), 1.21 (br s, 3H), 1.11 (s, 3H), 0.97 (d, *J*=6.8 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  202.6, 172.9, 146.2, 141.7 (br), 116.7, 109.5, 100.2 (br), 74.5, 54.6, 43.1, 38.9, 37.4 (br), 32.9, 28.3, 27.7, 24.8, 24.6, 22.8, 19.0; IR (neat film, NaCl)  $\nu$  3073, 2963, 2939, 2877, 1651, 1622, 1471, 1449, 1431, 1406, 1383, 1367, 1298, 1222, 1206, 1172, 1157, 1134, 1069, 1009, 967, 956, 884, 845, 767, 752, 692, 656, 624 cm<sup>–1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>20</sub>H<sub>31</sub>ClO<sub>2</sub> [M]<sup>+</sup>: 338.2013, found 338.2009.

**4.2.6. Chloroalkene (+)-12.** To a flame-dried 100 mL round-bottomed flask equipped with a magnetic stir bar was added catalyst **49** (124.9 mg, 0.219 mmol). After attaching an oven-dried condenser and sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (26 mL, deoxygenated prior to use by sparging with N<sub>2</sub> in a flame-dried flask for  $\geq$ 1 h) was added via syringe. To the resulting solution was added  $\alpha,\omega$ -diene (–)-**13** (1.483 g, 4.38 mmol) in deoxygenated anhydrous benzene (6 mL) via syringe, washing the original flask with deoxygenated anhydrous benzene (2×6 mL). The reaction was placed in a 60 °C oil bath and stirred for 18 h. After cooling to 23 °C, solvent was removed under reduced pressure. Flash chromatography over silica gel (12×5 cm, 20% Et<sub>2</sub>O/petroleum ether eluent until product begins to elute, then 30% Et<sub>2</sub>O/petroleum ether eluent) then provided chloroalkene (+)-**12** (1.313 g, 97%) as an off-white waxy powder. *R<sub>f</sub>* 0.38 (20% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>24</sup> +99.27 (c 1.005, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.19–5.23 (m, 1H), 3.59 (dd, *J*=9.3, 6.3 Hz, 1H), 3.52 (dd, *J*=9.5, 6.6 Hz, 1H), 2.50–2.70 (br m, 1H), 2.47 (br d, *J*=17.1 Hz, 1H), 2.19–2.33 (br m, 1H), 1.61–2.14 (br m, 5H), 2.01 (app. septet, *J*=6.7 Hz, 1H), 1.76 (br s, 3H), 1.06 (s, 3H), 0.97 (d, *J*=6.8 Hz, 6H), 0.95 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  202.3, 172.5, 127.3, 125.5 (br), 99.7, 74.5, 52.6, 41.5, 37.5, 34.4 (br), 29.5, 27.7, 25.7 (br), 24.1, 23.8, 19.7, 19.1; IR (neat film, NaCl)  $\nu$  2961, 2931, 2876, 2838, 1657, 1618, 1470, 1434, 1404, 1383, 1365, 1344, 1297, 1220, 1169, 1137, 1045, 1008, 965, 908, 858, 830, 817, 742, 685, 621 cm<sup>–1</sup>; HRMS (FAB<sup>+</sup>) *m/z* calcd for C<sub>18</sub>H<sub>28</sub>ClO<sub>2</sub> [M+H]<sup>+</sup>: 311.1778, found 311.1789.

**4.2.7. Proposed structure of (+)-laurencenone B ((+)-7)<sup>29</sup>.** In a glovebox, anhydrous CeCl<sub>3</sub> (3.973 g, 16.1 mmol) was added to a flame-dried 250 mL round-bottomed flask equipped with a magnetic stir bar. The flask was sealed with a septum and removed from the glovebox. The flask was placed under high vacuum and refilled with Ar. Anhydrous THF (39 mL) was added via syringe, and the suspension was stirred for 3 h at 23 °C. The suspension was cooled to –78 °C over 15 min, and MeLi (1.37 M in Et<sub>2</sub>O, 9.0 mL,

12.3 mmol) was added dropwise over 10 min via syringe. An exotherm was observed, and the liquid phase turned yellow. After stirring for 35 min at –78 °C, chloroalkene (+)-**12** (1.286 g, 4.14 mmol) in anhydrous THF (5 mL) was added dropwise over 3 min via syringe, washing the original flask with THF (2×4 mL). The reaction was stirred for 30 min at –78 °C and then placed in an ice bath. After stirring an additional 68 min at 0 °C, 10 wt % HCl (aq) (52 mL) was added, during which time a significant exotherm was observed. The mixture was then allowed to warm to 23 °C as it was stirred for 66 min. The reaction mixture was extracted with Et<sub>2</sub>O (3×150 mL), and the combined organic layers were washed with brine (2×250 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over silica gel (10×4 cm, 15% Et<sub>2</sub>O/pentane eluent until product begins to elute, then 30% Et<sub>2</sub>O/pentane eluent) then provided (+)-laurencenone B ((+)-7) (929 mg, 89%) as a white powder. Discrepancies existed between the published <sup>1</sup>H NMR data reported in the original isolation paper<sup>28</sup> and that of the synthetic material. IR data matched that reported for the natural product. No <sup>13</sup>C NMR or optical rotation data were reported. <sup>1</sup>H NMR, <sup>13</sup>C NMR, and IR data matched that reported for semisynthetic material obtained from the degradation of elatol.<sup>10</sup> The optical rotation matched in sign, but not in magnitude. These comparisons are outlined in the [Supplementary data](#). *R<sub>f</sub>* 0.26 (30% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>24</sup> +47.08 (c 0.36, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.89 (s, 1H), 2.50–2.69 (br m, 2H), 2.26 (br d, *J*=18.3 Hz, 1H), 2.13–2.23 (br m, 1H), 1.99–2.14 (br m, 2H), 1.98 (d, *J*=0.98 Hz, 3H), 1.93 (ddd, *J*=12.3, 12.3, 5.4 Hz, 1H), 1.81 (br s, 3H), 1.72–1.80 (m, 1H), 1.06 (s, 3H), 0.97 (s, 3H); <sup>1</sup>H NMR (500 MHz, acetone-*d*<sub>6</sub>)  $\delta$  5.80 (s, 1H), 2.52–2.69 (br m, 2H), 2.31 (dd, *J*=18.1, 0.98 Hz, 1H), 2.19–2.27 (br m, 1H), 2.02–2.16 (br m, 1H), 1.88–2.02 (m, 2H), 1.98 (d, *J*=1.2 Hz, 3H), 1.76–1.88 (br m, 1H), 1.80 (br s, 3H), 1.09 (s, 3H), 0.96 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  198.2, 168.6, 129.6, 127.5, 126.2 (br), 48.8, 46.3, 40.4, 36.3, 30.4 (br), 30.1, 24.8, 23.9 (two overlapping CH<sub>3</sub> peaks as determined by gHSQC and DEPT NMR spectroscopy; second peak appears as an upfield shoulder), 19.7; IR (neat film, NaCl)  $\nu$  3025, 2963, 2933, 2855, 1667, 1612, 1462, 1439, 1417, 1392, 1375, 1350, 1331, 1319, 1306, 1282, 1257, 1207, 1192, 1171, 1150, 1137, 1125, 1106, 1070, 1048, 1023, 1010, 988, 972, 954, 930, 913, 869, 834, 818, 684 cm<sup>–1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>15</sub>H<sub>21</sub>ClO [M]<sup>+</sup>: 252.1281, found 252.1270.

### 4.3. Procedures for the synthesis of the proposed structure of (–)-laurencenone B ((–)-7)

**4.3.1.  $\alpha,\omega$ -Diene (+)-13.** Following a similar procedure to that for the preparation of  $\alpha,\omega$ -diene (–)-**13**, enol carbonate **26** (299.9 mg, 0.783 mmol) was converted to  $\alpha,\omega$ -diene (+)-**13** (240.2 mg, 90%) using phosphinooxazoline ligand (–)-**41** (52.3 mg, 0.0884 mmol), bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (63.7 mg, 0.0781 mmol), and deoxygenated anhydrous benzene (24 mL total) at 12 °C. Observed 87% ee as determined by chiral HPLC analysis (Chiralpak<sup>®</sup> AD, 1% EtOH/hexanes, 1 mL/min, 254 nm, *t<sub>R</sub>* (major)=6.0 min; *t<sub>R</sub>* (minor)=6.6 min). <sup>1</sup>H NMR data matched that of  $\alpha,\omega$ -diene (–)-**13**. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +10.46 (c 1.005, CHCl<sub>3</sub>).

**4.3.2. Chloroalkene (–)-12.** Following a similar procedure to that for the preparation of chloroalkene (+)-**12**,  $\alpha,\omega$ -diene (+)-**13** (229.7 mg, 0.678 mmol) was converted to chloroalkene (–)-**12** (204.7 mg, 97%) using catalyst **49** (19.3 mg, 0.0338 mmol) and deoxygenated anhydrous benzene (7 mL total). <sup>1</sup>H NMR data matched that of chloroalkene (+)-**12**. [ $\alpha$ ]<sub>D</sub><sup>26</sup> –101.03 (c 1.0, CHCl<sub>3</sub>).

**4.3.3. Proposed structure of (–)-laurencenone B ((–)-7).** Following a similar procedure to that for the preparation of the proposed structure of (+)-laurencenone B ((+)-7), chloroalkene (–)-**12** (99.9 mg, 0.321 mmol) was converted to the proposed structure of

(–)-laurencenone B ((–)-**7**) (69.6 mg, 86%) using anhydrous CeCl<sub>3</sub> (312 mg, 1.27 mmol), MeLi (1.3 M in Et<sub>2</sub>O, 0.74 mL, 0.962 mmol), anhydrous THF (4 mL total), and 10 wt % HCl (aq) (4 mL). A minor unidentified impurity was observed by <sup>1</sup>H NMR spectroscopy (≤3 mol % as determined by DEPT NMR spectroscopy). <sup>1</sup>H NMR data matched that of (+)-laurencenone B ((+)-**7**). [ $\alpha$ ]<sub>D</sub><sup>25</sup> –42.01 (c 0.357, CHCl<sub>3</sub>).

#### 4.4. Procedures for the synthesis of (–)-laurencenone C (**8**)

**4.4.1. Enol carbonate 33.** A 250 mL two-neck round-bottomed flask equipped with a 50 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (40 mL) and anhydrous diisopropylamine (1.45 mL, 10.3 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.51 M in hexanes, 3.8 mL, 9.54 mmol) was added dropwise via the addition funnel over 22 min, washing the funnel sequentially with anhydrous hexanes (5 mL) and anhydrous THF (5 mL) upon complete addition. The reaction was then stirred at 0 °C for 30 min. The resulting LDA solution was cooled to –78 °C over 30 min. Olefin ( $\pm$ )-**27** (2.285 g, 8.64 mmol) in anhydrous THF (10 mL) was then added dropwise over 11 min via the addition funnel, washing the funnel with anhydrous THF (5 mL) upon complete addition. A yellow solution was obtained. After stirring at –78 °C for 66 min, anhydrous *N,N,N',N'*-tetramethylethylenediamine (1.55 mL, 10.3 mmol) was added dropwise over 2 min via syringe. After stirring at –78 °C for an additional 69 min, allyl chloroformate (**55**) (1.0 mL, 9.41 mmol) in anhydrous THF (10 mL) was then added dropwise over 21 min via the addition funnel, washing the funnel with THF (5 mL) upon complete addition. The reaction was stirred for an additional 3 h at –78 °C, at which time saturated NaHCO<sub>3</sub> (aq) (35 mL) and H<sub>2</sub>O (35 mL) were added. The mixture was allowed to warm to 23 °C with the aid of a 23 °C water bath, at which time the organic layer was immediately separated. The aqueous layer was extracted with Et<sub>2</sub>O (2×200 mL), and the combined organic layers were washed with brine (2×200 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (12.5×5 cm, 2.5% Et<sub>2</sub>O/petroleum ether eluent) then provided enol carbonate **33** (2.101 g, 70%) as a slightly pale yellow liquid containing residual Et<sub>2</sub>O (<1% by mass) and minor unidentified impurities (5% by area) by <sup>1</sup>H NMR spectroscopy. *R*<sub>f</sub> 0.21 (2.5% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.96 (ddt, *J*=17.1, 10.5, 5.7 Hz, 1H), 5.39 (ddt, *J*=7.1, 1.5, 1.5 Hz, 1H), 5.28 (ddt, *J*=10.5, 1.2, 1.2 Hz, 1H), 4.76 (s, 1H), 4.66–4.71 (m, 2H), 4.66 (ddd, *J*=5.7, 1.4, 1.4 Hz, 2H), 3.47 (d, *J*=6.6 Hz, 2H), 2.19 (s, 2H), 2.09–2.17 (m, 2H), 2.01–2.09 (m, 2H), 1.97 (app. septet, *J*=6.7 Hz, 1H), 1.74 (br s, 3H), 1.08 (s, 6H), 0.94 (d, *J*=6.8 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  157.5, 153.5, 146.0, 141.9, 131.5, 123.1, 119.0, 109.7, 91.3, 73.8, 68.6, 43.4, 37.9, 35.4, 27.8, 26.0, 24.1, 22.4, 19.2; IR (neat film, NaCl)  $\nu$  2960, 2874, 1758, 1662, 1622, 1470, 1422, 1382, 1363, 1330, 1292, 1241, 1160, 1146, 1109, 1041, 1024, 994, 970, 952, 887, 784 cm<sup>–1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>21</sub>H<sub>32</sub>O<sub>4</sub> [M]<sup>+</sup>: 348.2301, found 348.2307.

**4.4.2.  $\alpha,\omega$ -Diene (+)-34.** To a flame-dried 250 mL round-bottomed flask equipped with a magnetic stir bar was added phosphino-oxazolone ligand (–)-**41** (192 mg, 0.325 mmol) and bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (234 mg, 0.287 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous toluene (77 mL) was added via syringe, and the resulting solution was stirred for 31 min at 23 °C. The solution was then cooled to 0 °C over 15 min in an ice bath. Concurrently, a second flame-dried round-bottomed flask was charged with enol carbonate **33** (1.003 g, 2.88 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous toluene (5 mL) was added via syringe,

and the resulting solution was cooled to 0 °C in an ice bath. The enol carbonate solution was then transferred via cannula under positive N<sub>2</sub> pressure to the catalyst solution, washing the original flask with anhydrous toluene (5 mL, allowed to cool briefly before transferring). The reaction was then stirred at 0 °C for 9.5 h, at which point solvent was removed under reduced pressure. Flash chromatography over silica gel (12.5×5 cm, 5% Et<sub>2</sub>O/petroleum ether eluent) then provided  $\alpha,\omega$ -diene (+)-**34** (760 mg, 87%) as a yellow liquid. Observed 87% ee as determined by chiral HPLC analysis (Chiralcel® OD-H, 0.25% EtOH/hexanes, 1 mL/min, 254 nm, *t*<sub>R</sub> (minor)=9.0 min; *t*<sub>R</sub> (major)=10.3 min). *R*<sub>f</sub> 0.07 (5% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>24</sup> +25.52 (c 0.995, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.85–6.04 (br m, 1H), 5.24 (d, *J*=0.97 Hz, 1H), 5.03–5.10 (m, 1H), 4.96–5.01 (m, 1H), 4.65–4.69 (m, 1H), 4.64 (br s, 1H), 3.58 (dd, *J*=9.5, 6.6 Hz, 1H), 3.54 (dd, *J*=9.3, 6.8 Hz, 1H), 2.35–2.90 (br m, 2H), 2.28 (dd, *J*=15.4, 8.1 Hz, 1H), 1.94–2.10 (br m, 2H), 2.01 (app. septet, *J*=6.7 Hz, 1H), 1.62–1.89 (br m, 3H), 1.69 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H), 0.96 (d, *J*=6.8, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  203.2, 173.0, 146.5, 137.1 (br), 116.1, 109.3, 100.7, 74.5, 53.5, 42.7, 38.7, 33.7 (br), 32.8, 28.7, 27.7, 25.5, 25.3, 22.8, 19.1; IR (neat film, NaCl)  $\nu$  3072, 2961, 2937, 2876, 1653, 1621, 1471, 1449, 1405, 1383, 1366, 1297, 1221, 1207, 1172, 1149, 1009, 995, 967, 955, 907, 885, 846, 833, 768, 755, 654 cm<sup>–1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>20</sub>H<sub>32</sub>O<sub>2</sub> [M]<sup>+</sup>: 304.2402, found 304.2388.

**4.4.3. Olefin (–)-56.** To a flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar was added catalyst **49** (70.6 mg, 0.124 mmol). After attaching an oven-dried condenser and sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (20 mL, deoxygenated prior to use by sparging with N<sub>2</sub> in a flame-dried flask for 1 h) was added via syringe. To the resulting solution was added  $\alpha,\omega$ -diene (+)-**34** (750 mg, 2.46 mmol) in deoxygenated anhydrous benzene (3 mL) via syringe, washing the original flask with deoxygenated anhydrous benzene (2×1 mL). The reaction was placed in a 60 °C oil bath and stirred for 11.5 h. After cooling to 23 °C, solvent was removed under reduced pressure. Flash chromatography over silica gel (9×3 cm, 20% Et<sub>2</sub>O/petroleum ether eluent until product begins to elute, then 30% Et<sub>2</sub>O/petroleum ether eluent) then provided olefin (–)-**56** (663 mg, 97%) as a white powder. *R*<sub>f</sub> 0.23 (20% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>25</sup> –91.53 (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.38–5.50 (br m, 1H), 5.17–5.24 (m, 1H), 3.58 (dd, *J*=9.3, 6.8 Hz, 1H), 3.52 (dd, *J*=9.5, 6.6 Hz, 1H), 2.40–2.82 (br m, 1H), 2.13–2.23 (br m, 1H), 1.87–2.13 (br m, 2H), 2.00 (app. septet, *J*=6.7 Hz, 1H), 1.58–1.87 (br m, 4H), 1.64 (d, *J*=1.5 Hz, 3H), 1.03 (s, 3H), 0.96 (d, *J*=6.3 Hz, 6H), 0.94 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, overlapping of resonances was observed)  $\delta$  203.7, 172.3, 132.1 (br), 120.4 (br), 99.9, 74.4, 49.9, 41.5, 37.6, 27.72, 27.68, 26.1 (br), 24.2, 23.9, 23.4, 19.1; IR (neat film, NaCl)  $\nu$  3066, 3017, 2960, 2923, 2901, 2876, 2835, 1657, 1620, 1470, 1445, 1403, 1383, 1364, 1294, 1262, 1218, 1201, 1169, 1133, 1077, 1033, 1009, 968, 944, 906, 860, 830, 797, 765, 730, 714, 656 cm<sup>–1</sup>; HRMS (FAB<sup>+</sup>) *m/z* calcd for C<sub>18</sub>H<sub>29</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 277.2168, found 277.2155.

**4.4.4. (–)-Laurencenone C (**8**)<sup>29</sup>.** In a glovebox, anhydrous CeCl<sub>3</sub> (689 mg, 2.80 mmol) was added to a flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar. The flask was sealed with a septum and removed from the glovebox. The flask was placed under high vacuum and refilled with Ar. Anhydrous THF (7 mL) was added via syringe, and the suspension was stirred for 2 h at 23 °C. The suspension was cooled to –78 °C over 15 min, and MeLi (1.30 M in Et<sub>2</sub>O, 1.7 mL, 2.21 mmol) was added dropwise over 5 min via syringe. An exotherm was observed, and the liquid phase turned yellow. After stirring for 30 min at –78 °C, olefin (–)-**56** (200.3 mg, 0.725 mmol) in anhydrous THF (1 mL) was added dropwise over 7 min via syringe, washing the original flask with

THF (1 mL). The reaction was stirred for 35 min at  $-78\text{ }^{\circ}\text{C}$  and then placed in an ice bath. After stirring an additional 65 min at  $0\text{ }^{\circ}\text{C}$ , 10 wt % HCl (aq) (9 mL) was added, during which time a significant exotherm was observed. The mixture was then allowed to warm to  $23\text{ }^{\circ}\text{C}$  as it was stirred for 1.5 h. The reaction mixture was extracted with  $\text{Et}_2\text{O}$  ( $3\times 50\text{ mL}$ ), and the combined organic layers were washed with brine ( $2\times 150\text{ mL}$ ) and dried over  $\text{MgSO}_4$ . Solvent was removed under reduced pressure. Flash chromatography over silica gel ( $10\times 3\text{ cm}$ , 10%  $\text{Et}_2\text{O}$ /pentane eluent until product begins to elute, then 30%  $\text{Et}_2\text{O}$ /pentane eluent) then provided (–)-laurencenone C (**8**) (127 mg, 80%) as a colorless oil containing a minor unidentified impurity (2% by area) by  $^1\text{H}$  NMR spectroscopy. Discrepancies existed between the published  $^1\text{H}$  NMR data reported in the original isolation paper<sup>2g</sup> and that of the synthetic material. IR data matched that reported for the natural product. No  $^{13}\text{C}$  NMR or optical rotation data were reported.  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, and IR data matched that reported for isolation of the natural product from a second source,<sup>2h</sup> with the exception of one  $^{13}\text{C}$  NMR resonance. The optical rotation matched in sign, but not in magnitude. These comparisons are outlined in the **Supplementary data**.  $R_f$  0.28 (30%  $\text{Et}_2\text{O}$ /petroleum ether eluent);  $[\alpha]_D^{26} -87.98$  ( $c$  1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.87 (br s, 1H), 5.47–5.53 (br m, 1H), 2.48–2.76 (br m, 1H), 2.19–2.28 (br m, 1H), 1.82–2.14 (br m, 5H), 1.97 (d,  $J=1.5\text{ Hz}$ , 3H), 1.71–1.82 (br m, 1H), 1.68 (br s, 3H), 1.03 (s, 3H), 0.95 (s, 3H);  $^1\text{H}$  NMR (500 MHz, acetone- $d_6$ )  $\delta$  5.76 (br s, 1H), 5.49–5.55 (br m, 1H), 2.46–2.73 (br m, 1H), 2.21–2.31 (br m, 1H), 1.74–2.12 (br m, 6H), 1.97 (d,  $J=1.5\text{ Hz}$ , 3H), 1.65–1.69 (br m, 3H), 1.03 (s, 3H), 0.93 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  198.6, 170.4, 134.1, 127.0, 121.6, 48.9, 43.4, 40.4, 30.6 (br), 28.2, 27.9, 24.8, 24.2, 23.9 (br), 23.3; IR (neat film, NaCl)  $\nu$  3016, 2963, 2928, 2907, 2879, 2853, 1667, 1610, 1447, 1437, 1418, 1390, 1376, 1332, 1320, 1282, 1257, 1209, 1190, 1170, 1146, 1122, 1074, 1036, 1022, 977, 944, 912, 870, 834, 818, 800, 767  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{O}$  [ $\text{M}]^+$ : 218.1671, found 218.1673.

#### 4.5. Procedures for the synthesis of (–)- $\alpha$ -chamigrene (**5**)

**4.5.1. Dithiolane (–)-58<sup>37</sup>.** To a flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was added laurencenone C (**8**) (88.3 mg, 0.404 mmol). The flask was placed under high vacuum and refilled with Ar. Anhydrous MeOH (3 mL) followed by ethanedithiol (**57**) (60  $\mu\text{L}$ , 0.715 mmol) were added via syringe. Boron trifluoride diethyl etherate (60  $\mu\text{L}$ , 0.486 mmol) was then added via syringe in two portions (41 and 19  $\mu\text{L}$ , respectively) 20 min apart, and the reaction was stirred for a total of 27 h at  $23\text{ }^{\circ}\text{C}$ . During this time, a fine dark precipitate was observed. MeOH was removed under reduced pressure, and the residue was dissolved in EtOAc (50 mL). The solution was washed sequentially with saturated  $\text{NaHCO}_3$  (aq) ( $2\times 25\text{ mL}$ ),  $\text{H}_2\text{O}$  ( $2\times 25\text{ mL}$ ), and brine ( $2\times 25\text{ mL}$ ) and then dried over  $\text{MgSO}_4$ . Solvent was removed under reduced pressure. Flash chromatography over silica gel ( $7.5\times 2\text{ cm}$ , 2.5%  $\text{Et}_2\text{O}$ /pentane eluent) then provided dithiolane (–)-**58** (109.6 mg, 92%) as a colorless oil containing minor unidentified impurities (3% by area by  $^1\text{H}$  NMR spectroscopy), which were present in the starting ethanedithiol.  $^1\text{H}$  NMR data matched that of the reported racemic compound.<sup>5a–b</sup>  $R_f$  0.29 (2.5%  $\text{Et}_2\text{O}$ /petroleum ether eluent);  $[\alpha]_D^{25} -51.47$  ( $c$  1.015,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.53–5.56 (m, 1H), 5.42–5.46 (m, 1H), 3.26–3.44 (m, 4H), 2.63 (d,  $J=14.7\text{ Hz}$ , 1H), 2.06–2.16 (m, 2H), 1.81–1.95 (m, 3H), 1.60–1.71 (m, 2H), 1.69 (d,  $J=0.98\text{ Hz}$ , 3H), 1.64 (br s, 3H), 0.97 (s, 3H), 0.91 (s, 3H).

**4.5.2. (–)- $\alpha$ -Chamigrene (**5**)<sup>5b</sup>.** A 100 ml three-neck round-bottomed flask equipped with a cold finger, a stir bar, and three septa was flame-dried under vacuum. After refilling with Ar, the flask was placed in a dry ice/ $\text{CHCl}_3$  bath, which was used to maintain

a reaction temperature between  $-60$  and  $-45\text{ }^{\circ}\text{C}$ , while the cold finger was maintained at  $-78\text{ }^{\circ}\text{C}$  with dry ice and acetone.  $\text{NH}_3$  (g) was condensed within the flask to give a solvent volume of approx. 10 mL. A solution of dithiolane (–)-**58** (110 mg, 0.373 mmol) in anhydrous  $\text{Et}_2\text{O}$  (14 mL) cooled to  $-60\text{ }^{\circ}\text{C}$  was then added via cannula under positive  $\text{N}_2$  pressure, washing the original flask with anhydrous  $\text{Et}_2\text{O}$  (6 mL, allowed to cool briefly before transferring).  $\text{Na}^0$  (approx. 146 mg, 6.35 mmol) was added portion-wise under positive Ar pressure in small pieces, during which time the solution turned a persistent purple color. After complete addition, the reaction was stirred for 15 min, and the cold bath was then removed giving a gentle reflux while stirring for an additional 55 min. MeOH (1.5 mL) was added portion-wise via syringe to minimize any exotherm, and a mixture of a colorless solution and a white precipitate was obtained. The cold finger was then allowed to warm to  $23\text{ }^{\circ}\text{C}$  while the  $\text{NH}_3$  (l) and  $\text{Et}_2\text{O}$  evaporated overnight.  $\text{H}_2\text{O}$  (40 mL) was added to dissolve most solids, and the reaction was extracted with  $\text{Et}_2\text{O}$  ( $3\times 50\text{ mL}$ ). The organic layer was washed with brine ( $2\times 150\text{ mL}$ ) and dried over  $\text{MgSO}_4$ . Solvent was removed under reduced pressure. The crude product was then split into two approximately equal portions, each of which was subjected to preparative thin-layer chromatography (0.5 mm thickness, 100% hexanes eluent). The product was extracted from the silica with hexanes, and solvent was removed under reduced pressure to provide a combined yield of 33.6 mg (44%) of (–)- $\alpha$ -chamigrene (**5**) as a colorless oil.  $^1\text{H}$  NMR and IR data matched that reported in the original isolation paper,<sup>2e</sup> and these comparisons are outlined in the **Supplementary data**.  $R_f$  0.80 (100% hexanes eluent);  $[\alpha]_D^{25} -64.60$  ( $c$  0.21,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.44–5.48 (m, 1H), 5.31–5.35 (br m, 1H) 2.12 (dddd,  $J=18.1, 5.1, 2.4, 2.4\text{ Hz}$ , 1H), 1.80–2.01 (br m, 5H), 1.60–1.79 (m, 9H), 1.19 (ddd,  $J=13.7, 6.1, 4.39\text{ Hz}$ , 1H), 0.89 (s, 3H), 0.83 (s, 3H);  $^1\text{H}$  NMR (300 MHz,  $\text{CCl}_4$ )  $\delta$  5.36–5.43 (m, 1H), 5.23–5.29 (m, 1H), 2.09 (dddd,  $J=18.1, 4.9, 2.4, 2.4\text{ Hz}$ , 1H), 1.55–2.02 (m, 14H), 1.17 (ddd,  $J=13.3, 4.9, 4.9\text{ Hz}$ , 1H), 0.89 (s, 3H), 0.82 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.3, 133.8, 122.8, 122.5, 40.5, 35.9, 32.8, 30.7, 29.1, 28.9, 25.1, 23.47, 23.46, 23.3 (br), 23.0; IR (neat film, NaCl)  $\nu$  3055, 3015, 2958, 2923, 2841, 2729, 2675, 1683, 1655, 1640, 1473, 1463, 1448, 1436, 1386, 1380, 1366, 1342, 1320, 1312, 1280, 1258, 1248, 1220, 1188, 1163, 1148, 1129, 1088, 1072, 1029, 1020, 1006, 978, 954, 943, 901, 832, 810, 800, 760, 688, 661, 605  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{24}$  [ $\text{M}]^+$ : 204.1878, found 204.1883.

#### 4.6. Procedures for the synthesis of (+)-elatol (**1**)

**4.6.1. (+)-Elatol (**1**).** **4.6.1.1. Part 1: Bromination<sup>40c</sup>.** A half-dram screw-cap vial equipped with a stir bar and a septum-bearing cap was charged with (+)-laurencenone B ((+)-**7**) (9.9 mg, 0.0392 mmol). A solution of 48% HBr (aq) in glacial acetic acid [250:1 v/v AcOH:48% HBr (aq), 0.2 mL] was then added. To the resulting solution was added in one portion a stock solution of bromine in 250:1 v/v AcOH:48% HBr (aq) (0.501 M, 157.5  $\mu\text{L}$ , 0.0789 mmol), resulting in a deep red color. After stirring for approx. 10 min, the reaction turned an orange-red color. After stirring for a total of 31 min, the solution was added to ice water (5 mL). The resulting mixture was extracted with  $\text{Et}_2\text{O}$  ( $4\times 10\text{ mL}$ ), and the combined organic layers were washed with saturated  $\text{NaHCO}_3$  (aq) ( $2\times 20\text{ mL}$ ) and brine ( $2\times 20\text{ mL}$ ). After drying over  $\text{MgSO}_4$ , solvent was removed under reduced pressure, ultimately isolating the crude dibromide **59** in a 1 dram screw-cap vial. The crude material was carried directly to Part 2. A scalemic mixture from additional runs was partially purified (approx. 93% pure by area by  $^1\text{H}$  NMR spectroscopy) by preparative HPLC (Phenomenex<sup>®</sup> Gemini<sup>™</sup>, 25  $\rightarrow$  100%  $\text{CH}_3\text{CN}/0.1\%$  TFA (aq), 8 mL/min, 250 nm,  $t_R=70\text{--}72\text{ min}$ ).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  6.05 (s, 1H), 4.55 (s, 1H), 3.67 (d,  $J=10.7\text{ Hz}$ , 1H), 3.36–3.41 (m, 1H), 2.56–2.67 (m, 1H), 2.22–2.32 (br



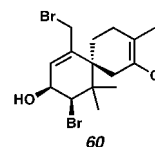
m, 1H), 1.52–1.56 (br m, 3H), 1.35–1.44 (br m, 1H), 1.14–1.25 (br m, 1H), 1.08 (ddd,  $J=12.5, 12.5, 5.1$  Hz, 1H), 0.80 (s, 3H), 0.68–0.76 (br m, 1H), 0.74 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  190.1, 164.1, 129.9, 129.8, 126.1, 65.7, 49.1, 47.1, 36.5, 30.9, 30.3, 29.7, 24.3, 19.8, 18.7; IR (neat film, NaCl)  $\nu$  2979, 2932, 1678, 1438, 1396, 1376, 1284, 1251, 1216, 1170, 1133, 1007, 911, 868, 818, 760, 733  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{19}\text{ClOBr}^{81}\text{Br}$  [ $\text{M}]^+$ : 409.9471, found 409.9482. A minor diastereomer was not isolated. The dr was determined to be  $\geq 8:1$  by  $^1\text{H}$  NMR spectroscopic analysis of the crude product of a third run. This minimal value was based upon resonances that could not be ruled out as corresponding to a minor diastereomer based on the preparative HPLC separation above.

**4.6.1.2. Part 2: Reduction<sup>39b</sup>.** The 1 dram screw-cap vial containing the crude dibromide **59** from Part 1 was equipped with a stir bar and a septum-bearing cap and placed under high vacuum. After refilling with Ar, anhydrous THF (0.3 mL) was added via syringe, and the solution was cooled to  $-78^\circ\text{C}$ . Concurrently, a second 1 dram screw-cap vial equipped with a septum-bearing cap was flame-dried under high vacuum and refilled with Ar. A stock solution of diisobutylaluminum hydride in anhydrous THF (1.59 M, 0.15 mL, 0.239 mmol) was added via syringe, and the solution was cooled to  $-78^\circ\text{C}$ . The precooled stock solution was then added to the crude dibromide **59** solution at  $-78^\circ\text{C}$  in one portion via cannula under positive  $\text{N}_2$  pressure, whereupon gas evolution was observed. The colorless solution was stirred for 2 h at  $-78^\circ\text{C}$ , at which point the reaction was placed in a  $60^\circ\text{C}$  heating block, and the Ar inlet was removed. After stirring for an additional 2 h at  $60^\circ\text{C}$ , the reaction was cooled to  $23^\circ\text{C}$  with the aid of a  $23^\circ\text{C}$  water bath.  $\text{Et}_2\text{O}$  (0.5 mL) was added, and the reaction was quenched with a saturated solution of potassium sodium tartrate (aq) (0.5 mL), whereupon gas evolution was observed. After stirring vigorously for 1 h, the opaque biphasic mixture was transferred to a 25 mL round-bottomed flask with  $\text{Et}_2\text{O}$  (5 mL) and a saturated solution of potassium sodium tartrate (aq) (5 mL). The mixture was then stirred vigorously until both layers were transparent. The organic layer was separated, and the aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $2 \times 10$  mL). The combined organic layers were washed with brine ( $2 \times 20$  mL) and dried over  $\text{MgSO}_4$ . Solvent was removed under reduced pressure. The ratio of  $\text{S}_{\text{N}}2'$ : $\text{S}_{\text{N}}2$  reduction was determined to be 11:1 by  $^1\text{H}$  NMR spectroscopic analysis of the crude reaction mixture. The crude product was azeotroped with hexanes ( $4 \times$ ) and then subjected to preparative thin-layer chromatography (0.5 mm thickness, eluted four times with 15%  $\text{Et}_2\text{O}$ /petroleum ether eluent, then once with 15%  $\text{EtOAc}$ /hexanes eluent). The product was extracted from the silica with  $\text{EtOAc}$  and azeotroped with hexanes ( $3 \times$ ). Finally, flash chromatography over silica gel ( $5.3 \times 0.5$  cm, 5%  $\text{EtOAc}$ /hexanes eluent until product begins to elute, then 30%  $\text{EtOAc}$ /hexanes eluent) then provided (+)-elatol (**1**) (4.4 mg) as a colorless oil containing 6% of the undesired  $\text{S}_{\text{N}}2$  reduction product by  $^1\text{H}$  NMR spectroscopy. The corrected yield was 32% over two steps. The dr of the initial ketone reduction was determined to be 3.9:1 *syn/anti* (relative to the bromide) by  $^1\text{H}$  NMR spectroscopic analysis of the crude product of separate run quenched at  $-78^\circ\text{C}$  after 2 h.  $^1\text{H}$  NMR data matched that reported in the original isolation paper,<sup>2a</sup> and this comparison is outlined in the Supplementary data.  $R_f$  0.64 (eluted four times with 15%  $\text{Et}_2\text{O}$ /petroleum ether eluent, then once with 15%  $\text{EtOAc}$ /hexanes eluent);  $[\alpha]_D^{23} +92.09$  (c 0.22,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.13 (s, 1H), 4.80 (s, 1H), 4.61 (d,  $J=2.9$  Hz, 1H), 4.13–4.17 (m, 1H), 2.55–2.66 (br m, 2H), 2.51 (dd,  $J=14.6, 2.7$  Hz, 1H), 2.33–2.41 (br m, 1H), 2.16–2.20 (m, 1H), 1.92–2.00 (br m, 1H), 1.75–1.86 (br m, 2H), 1.70 (br s, 3H), 1.58–1.67 (m, 1H), 1.08 (s, 3H), 1.07 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  140.7, 128.1, 124.1, 115.9, 72.2, 70.9, 49.1, 43.1, 38.6, 37.9, 29.3, 25.6, 24.2, 20.8, 19.4; IR (neat film, NaCl)  $\nu$  3564, 3475, 3086, 2975, 2949, 2913, 2831, 1808, 1724, 1681, 1643, 1470, 1453, 1430, 1394, 1372, 1354, 1340,

1319, 1292, 1254, 1225, 1207, 1188, 1165, 1141, 1130, 1106, 1086, 1073, 1031, 1014, 982, 956, 943, 897, 879, 826, 811, 761, 737, 685, 706, 667, 642, 615  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{BrClO}$  [ $\text{M}]^+$ : 332.0543, found 332.0546.

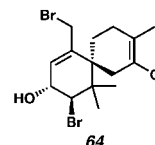
**4.6.2. Analysis of a natural sample of (+)-elatol (**1**).** A natural sample of (+)-elatol (**1**) provided by Prof. Mercedes Cueto was identical in all respects to the synthetic material except for its optical rotation:  $[\alpha]_D^{25} +109.78$  (c 0.045,  $\text{CHCl}_3$ ).

**4.6.3. Characterization data for diastereomers from the initial ketone reduction of crude dibromide **59**.** **4.6.3.1. cis-Bromohydrin **60**.**



$R_f$  0.54 (30%  $\text{EtOAc}$ /hexanes eluent);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.14 (d,  $J=3.9$  Hz, 1H), 4.79 (d,  $J=5.1$  Hz, 1H), 4.22–4.27 (br m, 1H), 4.04–4.11 (m, 2H), 2.73–2.81 (br m, 1H), 2.50–2.59 (br m, 1H), 2.38 (d,  $J=3.4$  Hz, 1H), 2.10–2.18 (br m, 1H), 1.92–2.03 (br m, 1H), 1.76–1.85 (m, 4H), 1.53–1.60 (m, 1H), 1.14 (s, 3H), 1.07 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 130.9, 129.6, 127.0, 68.6, 65.9, 47.7, 41.1, 36.9, 33.5, 30.2, 29.8, 24.3, 19.8, 19.0; IR (neat film, NaCl)  $\nu$  3541, 3455, 2976, 2932, 1678, 1438, 1219, 731  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{ClOBr}^{81}\text{Br}$  [ $\text{M}]^+$ : 411.9627, found 411.9620. The relative stereochemistry of the bromohydrin functionality was established by NOESY1D NMR spectroscopy and subsequent conversion to elatol (**1**).

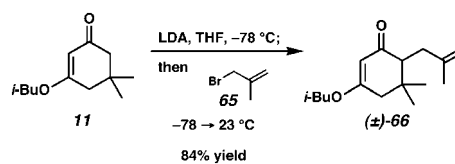
**4.6.3.2. trans-Bromohydrin **64**.**



$R_f$  0.44 (30%  $\text{EtOAc}$ /hexanes eluent);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.00 (d,  $J=3.4$  Hz, 1H), 4.48 (d,  $J=9.0$  Hz, 1H), 4.35–4.41 (br m, 1H), 4.03–4.11 (m, 2H), 2.77–2.84 (br m, 1H), 2.54–2.63 (br m, 1H), 2.43 (d,  $J=3.7$  Hz, 1H), 2.10–2.19 (br m, 1H), 1.89–2.00 (br m, 1H), 1.87 (ddd,  $J=12.2, 12.2, 5.0$  Hz, 1H), 1.80–1.84 (br m, 3H), 1.62–1.69 (m, 1H), 1.16 (s, 3H), 1.05 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.6, 131.6, 129.6, 126.9, 73.3, 70.5, 47.4, 44.3, 36.3, 33.8, 31.4, 29.7, 24.6, 19.8, 17.6; IR (neat film, NaCl)  $\nu$  3383, 2977, 2932, 1677, 1438, 1039, 733  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{ClOBr}^{81}\text{Br}$  [ $\text{M}]^+$ : 411.9627, found 411.9621.

## 4.7. Procedures for the syntheses of enantioselective decarboxylative allylation products (+)-**45**, (+)-**46**, and (+)-**24**

### 4.7.1. Olefin ( $\pm$ )-**66**

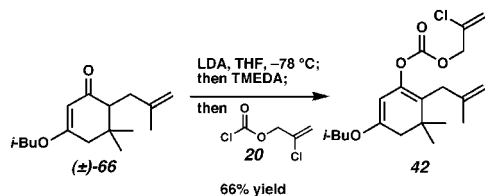


A 250 mL round-bottomed flask equipped with a stir bar and a septum was flame dried under vacuum. After refilling with Ar, anhydrous THF (42 mL) and anhydrous diisopropylamine (1.6 mL, 11.4 mmol) were added via syringe, and the solution was cooled to



0 °C in an ice bath. *n*-BuLi (2.57 M in hexanes, 4.1 mL, 10.5 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 33 min. The resulting LDA solution was then cooled to –78 °C over 15 min. Vinylogous ester **11** (2.0 g, 10.2 mmol) in anhydrous THF (2 mL) was then added dropwise over 2 min via syringe, washing the original flask with anhydrous THF (2×2 mL). The reaction was then stirred for 1 h at –78 °C to provide a yellow solution. Methallyl bromide (**65**) (1.0 mL, 9.92 mmol) was added dropwise over 2 min via syringe. The cold bath was removed, and the reaction was allowed to warm to 23 °C as it was stirred for 26.6 h. Saturated NH<sub>4</sub>Cl (aq) (40 mL) was added, and the organic layer was separated. The aqueous layer was extracted with Et<sub>2</sub>O (2×150 mL), and the combined organic layers were washed with brine (2×200 mL). After drying over MgSO<sub>4</sub>, solvent was removed under reduced pressure. Flash chromatography over silica gel (15.5×5 cm, 15% Et<sub>2</sub>O/petroleum ether eluent) then provided olefin (±)-**66** (2.135 g, 84%) as a slightly yellow liquid. *R*<sub>f</sub> 0.10 (15% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.24 (br s, 1H), 4.71–4.76 (br m, 1H), 4.64–4.69 (br m, 1H), 3.57 (d, *J*=6.4 Hz, 2H), 2.12–2.40 (m, 5H), 2.02 (app. septet, *J*=6.7 Hz, 1H), 1.78 (br s, 3H), 1.09 (s, 3H), 0.99 (s, 3H), 0.97 (d, *J*=6.6 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 201.4, 174.1, 144.6, 111.4, 100.5, 74.5, 41.6, 35.1, 34.7, 28.6, 27.7, 24.5, 22.3, 19.07, 19.06; IR (neat film, NaCl) ν 3074, 2962, 2933, 2875, 1661, 1615, 1471, 1425, 1404, 1382, 1364, 1315, 1299, 1278, 1222, 1192, 1178, 1152, 1131, 1008, 968, 954, 885, 834, 815, 686, 626 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>16</sub>H<sub>26</sub>O<sub>2</sub> [M]<sup>+</sup>: 250.1933, found 250.1945.

#### 4.7.2. Enol carbonate **42**.

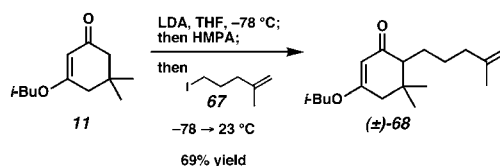


A 250 mL two-neck round-bottomed flask equipped with a 10 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (25 mL) and anhydrous diisopropylamine (0.67 mL, 4.78 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.57 M in hexanes, 1.7 mL, 4.37 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 33 min. The resulting LDA solution was then cooled to –78 °C over 18 min. Olefin (±)-**66** (1.0 g, 3.99 mmol) in anhydrous THF (5 mL) was then added dropwise over 8 min via the addition funnel, washing the funnel with THF (2.5 mL) upon complete addition. After stirring at –78 °C for 1 h, anhydrous *N,N,N',N'*-tetramethylethylenediamine (0.72 mL, 4.80 mmol) was added dropwise over 2 min via syringe. After stirring at –78 °C for an additional 1 h, chloroformate **20** (0.68 g, 4.39 mmol) in anhydrous THF (5 mL) was then added dropwise over 19 min via the addition funnel, washing the funnel with THF (2.5 mL) upon complete addition. The reaction was stirred for an additional 3 h at –78 °C, whereupon saturated NaHCO<sub>3</sub> (aq) (17 mL) and H<sub>2</sub>O (17 mL) were added. The mixture was allowed to warm to 23 °C with the aid of a 23 °C water bath, at which time the organic layer was immediately separated. The aqueous layer was extracted with Et<sub>2</sub>O (2×100 mL), and the combined organic layers were washed with brine (2×100 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (100–200 mesh, 13.5×5 cm, 1% Et<sub>2</sub>O/petroleum ether eluent until product begins to elute, then 2.5% Et<sub>2</sub>O/petroleum ether eluent) then provided enol carbonate **42** (973 mg, 66%) as a somewhat viscous colorless liquid containing residual Et<sub>2</sub>O (<1% by mass) and a minor unidentified impurity (4% by area) by <sup>1</sup>H NMR spectroscopy. *R*<sub>f</sub> 0.27 (2.5% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (500 MHz,

CDCl<sub>3</sub>) δ 5.50–5.54 (m, 1H), 5.42–5.46 (m, 1H), 4.80 (s, 1H), 4.76–4.80 (br m, 1H), 4.72–4.76 (br m, 1H), 4.68–4.72 (m, 2H), 3.49 (d, *J*=6.6 Hz, 2H), 2.76 (s, 2H), 2.19 (s, 2H), 1.98 (app. septet, *J*=6.7 Hz, 1H), 1.71 (br s, 3H), 1.04 (s, 6H), 0.95 (d, *J*=6.8 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 158.1, 152.7, 144.0, 142.6, 135.0, 120.5, 115.3, 111.3, 91.0, 73.8, 69.1, 43.4, 35.5, 33.4, 27.8, 25.6, 22.5, 19.2; IR (neat film, NaCl) ν 3077, 2960, 2932, 2913, 2874, 1763, 1663, 1648, 1638, 1620, 1470, 1465, 1444, 1421, 1382, 1367, 1363, 1331, 1276, 1242, 1217, 1174, 1150, 1099, 1040, 1023, 997, 969, 890, 782 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>20</sub>H<sub>29</sub>ClO<sub>4</sub> [M]<sup>+</sup>: 368.1754, found 368.1738.

4.7.3.  $\alpha,\omega$ -Diene (+)-**45**. To a flame-dried 100 mL round-bottomed flask equipped with a magnetic stir bar was added phosphinooxazoline ligand (–)-**41** (54.4 mg, 0.0920 mmol) and bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (66.2 mg, 0.0812 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (22.5 mL, deoxygenated prior to use by sparging with N<sub>2</sub> in a flame-dried flask for 2 h) was added via syringe, and the resulting solution was stirred for 30 min at 23 °C, during which time it turned dark yellow-brown. The solution was then cooled to 11 °C over 13 min. Concurrently, a flame-dried 1 dram screw-cap vial was charged with enol carbonate **42** (300.1 mg, 0.814 mmol). After sealing with a septum-bearing cap, the vial was placed under high vacuum and refilled with Ar. Deoxygenated anhydrous benzene (1 mL) was added via syringe, and the resulting solution was cooled to 11 °C. The enol carbonate solution was then transferred via cannula under positive N<sub>2</sub> pressure to the catalyst solution, washing the original flask with deoxygenated anhydrous benzene (1 mL, allowed to cool briefly before transferring). The reaction, which turned green, was then stirred at 12 °C for 21.5 h. Solvent was removed under reduced pressure. The residue was suspended in Et<sub>2</sub>O and filtered through a plug of cotton to remove precipitated Pd. The filtrate was then concentrated under reduced pressure. The residue was suspended in 10% Et<sub>2</sub>O/pentane and applied to a silica gel column (11×2.5 cm). Flash chromatography (10% Et<sub>2</sub>O/pentane eluent) then provided  $\alpha,\omega$ -diene (+)-**45** (242.9 mg, 92%) as an off-white solid. Observed 91% ee as determined by chiral HPLC analysis (Chiralpak® AD, 0.5% EtOH/hexanes, 1 mL/min, 254 nm, *t*<sub>R</sub> (major)=10.4 min; *t*<sub>R</sub> (minor)=12.6 min). *R*<sub>f</sub> 0.16 (10% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>24</sup> +7.15 (c 1.015, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.10–5.52 (br m, 1H), 5.28 (s, 1H), 5.27 (d, *J*=0.97 Hz, 1H), 4.87 (br s, 1H), 4.85 (br s, 1H), 3.51–3.63 (m, 2H), 1.85–3.10 (br m, 6H), 2.02 (app. septet, *J*=6.7 Hz, 1H), 1.72 (br s, 3H), 1.22 (br s, 3H), 1.16 (s, 3H), 0.97 (d, *J*=6.8 Hz, 6H); <sup>13</sup>C NMR (126 MHz, C<sub>6</sub>D<sub>6</sub>, overlapping of resonances was observed) δ 200.4 (br), 171.4, 142.6 (br), 117.5, 116.5 (br), 101.7, 74.2, 55.9, 43.6, 39.9 (br), 39.1, 27.9, 24.9 (br), 24.5 (br), 19.0; IR (neat film, NaCl) ν 3073, 2962, 2935, 2877, 1655, 1622, 1471, 1445, 1429, 1406, 1383, 1366, 1341, 1298, 1280, 1222, 1199, 1172, 1151, 1134, 1053, 1010, 968, 892, 856, 832, 789, 691, 653, 622 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>19</sub>H<sub>29</sub>ClO<sub>2</sub> [M]<sup>+</sup>: 324.1856, found 324.1865.

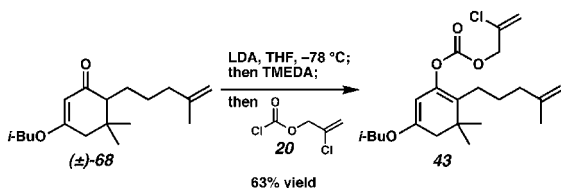
#### 4.7.4. Olefin (±)-**68**.



A 100 mL round-bottomed flask equipped with a stir bar and a septum was flame dried under vacuum. After refilling with Ar, anhydrous THF (26 mL) and anhydrous diisopropylamine (1.0 mL, 7.14 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.57 M in hexanes, 2.65 mL, 6.81 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C

for 30 min. The resulting LDA solution was then cooled to  $-78\text{ }^{\circ}\text{C}$  over 20 min. Vinylogous ester **11** (1.29 g, 6.57 mmol) in anhydrous THF (1 mL) was then added dropwise over 1 min via syringe, washing the original flask with anhydrous THF ( $2\times 1\text{ mL}$ ). The reaction was then stirred for 1 h at  $-78\text{ }^{\circ}\text{C}$  to provide a yellow solution. Anhydrous hexamethylphosphoramide (1.25 mL, 7.18 mmol) was added in one portion via syringe over 1 min, and the reaction was stirred for 1 h at  $-78\text{ }^{\circ}\text{C}$ . 5-Iodo-2-methyl-1-pentene (**67**)<sup>48</sup> (1.67 g, 82.6% pure by mass [contained 15.8% pentane and 1.6% benzene by mass], 6.57 mmol) was added in one portion via syringe, washing the original flask with anhydrous THF ( $2\times 2\text{ mL}$ ). The cold bath was removed, and the reaction was allowed to warm to  $23\text{ }^{\circ}\text{C}$  as it was stirred for 45 h. Saturated  $\text{NH}_4\text{Cl}$  (aq) (40 mL) was added to give a colorless biphasic mixture, and the organic layer was separated. The aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $2\times 150\text{ mL}$ ), and the combined organic layers were washed with brine ( $2\times 200\text{ mL}$ ). After drying over  $\text{MgSO}_4$ , solvent was removed under reduced pressure. Flash chromatography over silica gel (15.5 $\times$ 5 cm silica, 10%  $\text{Et}_2\text{O}$ /petroleum ether eluent until product begins to elute, then 20%  $\text{Et}_2\text{O}$ /petroleum ether eluent) then provided olefin ( $\pm$ )-**68** (1.261 g, 69%) as a very slightly yellow liquid.  $R_f$  0.11 (10%  $\text{Et}_2\text{O}$ /petroleum ether eluent);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.22 (s, 1H), 4.66–4.70 (m, 1H), 4.64–4.68 (m, 1H), 3.53–3.60 (m, 2H), 2.35 (d,  $J=17.6\text{ Hz}$ , 1H), 2.16 (d,  $J=17.8\text{ Hz}$ , 1H), 1.95–2.08 (m, 3H), 1.92 (dd,  $J=6.5\text{ Hz}$ , 1H), 1.70 (s, 3H), 1.51–1.62 (m, 1H), 1.35–1.51 (m, 3H), 1.06 (s, 3H), 0.97 (s, 3H), 0.96 (d,  $J=6.6\text{ Hz}$ , 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  202.7, 174.4, 145.7, 109.9, 100.4, 74.5, 57.0, 41.2, 37.8, 34.9, 28.6, 27.7, 26.5, 25.8, 24.9, 22.3, 19.1; IR (neat film, NaCl)  $\nu$  3072, 2960, 2933, 2873, 1654, 1612, 1471, 1424, 1403, 1382, 1364, 1317, 1297, 1218, 1189, 1179, 1153, 1130, 1008, 968, 884, 842, 826  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{18}\text{H}_{30}\text{O}_2$  [ $\text{M}]^+$ : 278.2246, found 278.2250.

#### 4.7.5. Enol carbonate **43**.



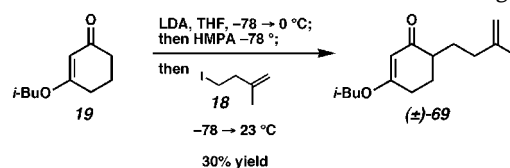
A 250 mL two-neck round-bottomed flask equipped with a 10 mL addition funnel, a stir bar, and two septa was flame dried under vacuum. After refilling with Ar, anhydrous THF (28 mL) and anhydrous diisopropylamine (0.72 mL, 5.14 mmol) were added via syringe, and the solution was cooled to  $0\text{ }^{\circ}\text{C}$  in an ice bath.  $n\text{-BuLi}$  (2.57 M in hexanes, 1.85 mL, 4.75 mmol) was added dropwise via syringe, and the solution was stirred at  $0\text{ }^{\circ}\text{C}$  for 41 min. The resulting LDA solution was then cooled to  $-78\text{ }^{\circ}\text{C}$  over 20 min. Olefin ( $\pm$ )-**68** (1.20 g, 4.31 mmol) in anhydrous THF (5 mL) was then added dropwise over 6 min via the addition funnel, washing the funnel with THF (2.5 mL) upon complete addition. After stirring at  $-78\text{ }^{\circ}\text{C}$  for 1 h, anhydrous  $N,N,N',N'$ -tetramethylethylenediamine (0.78 mL, 5.20 mmol) was added dropwise over 1 min via syringe. After stirring at  $-78\text{ }^{\circ}\text{C}$  for an additional 1 h, chloroformate **20** (737 mg, 4.76 mmol) in anhydrous THF (5 mL) was then added dropwise over 15 min via the addition funnel, washing the funnel with THF (2.5 mL) upon complete addition. The reaction was stirred for an additional 3 h at  $-78\text{ }^{\circ}\text{C}$ , whereupon saturated  $\text{NaHCO}_3$  (aq) (17 mL) and  $\text{H}_2\text{O}$  (17 mL) were added. The mixture was allowed to warm to  $23\text{ }^{\circ}\text{C}$  with the aid of a  $23\text{ }^{\circ}\text{C}$  water bath, at which time the organic layer was immediately separated. The aqueous layer was extracted with  $\text{Et}_2\text{O}$  ( $2\times 100\text{ mL}$ ), and the combined organic layers were washed with brine ( $2\times 100\text{ mL}$ ) and dried over  $\text{MgSO}_4$ . Solvent was removed under reduced pressure. Flash chromatography over Florisil<sup>®</sup> (100–200 mesh, 12 $\times$ 5 cm, 2.5%  $\text{Et}_2\text{O}$ /petroleum ether

eluent) then provided enol carbonate **43** (1.074 g, 63%) as a colorless liquid containing residual  $\text{Et}_2\text{O}$  (<1% by mass) and a minor unidentified impurity (4% by area) by  $^1\text{H NMR}$  spectroscopy.  $R_f$  0.21 (2.5%  $\text{Et}_2\text{O}$ /petroleum ether eluent);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.53–5.56 (m, 1H), 5.43–5.47 (m, 1H), 4.75 (s, 1H), 4.71–4.74 (m, 2H), 4.68–4.71 (br m, 1H), 4.65–4.68 (br m, 1H), 3.47 (d,  $J=6.6\text{ Hz}$ , 2H), 2.18 (s, 2H), 1.92–2.05 (m, 5H), 1.71 (s, 3H), 1.47–1.55 (m, 2H), 1.07 (s, 6H), 0.94 (d,  $J=6.6\text{ Hz}$ , 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  157.6, 153.0, 145.6, 141.8, 135.1, 123.5, 115.4, 110.0, 91.0, 73.8, 69.1, 43.4, 38.0, 35.3, 27.8, 27.5, 26.0, 25.0, 22.3, 19.2; IR (neat film, NaCl)  $\nu$  3073, 2958, 2913, 2873, 2823, 1762, 1661, 1648, 1639, 1621, 1470, 1420, 1382, 1367, 1362, 1329, 1280, 1240, 1183, 1157, 1109, 1054, 1023, 1003, 965, 922, 887, 782  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{22}\text{H}_{33}\text{ClO}_4$  [ $\text{M}]^+$ : 396.2067, found 396.2083.

4.7.6.  $\alpha,\omega$ -Diene (–)-**46**. To a flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar was added phosphinooxazoline ligand (–)-**41** (50.8 mg, 0.0859 mmol) and bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (61.5 mg, 0.0754 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (21 mL, deoxygenated prior to use by sparging with  $\text{N}_2$  in a flame-dried flask for >1 h) was added via syringe, and the resulting solution was stirred for 30 min at  $23\text{ }^{\circ}\text{C}$ , during which time it turned dark yellow-brown. The solution was then cooled to  $10\text{ }^{\circ}\text{C}$  over 15 min. Concurrently, a flame-dried 1 dram screw-cap vial with a magnetic stir bar was charged with enol carbonate **43** (299.6 mg, 0.755 mmol). After sealing with a septum-bearing cap, the vial was placed under high vacuum and refilled with Ar. Deoxygenated anhydrous benzene (1 mL) was added via syringe, and the resulting solution was cooled to  $10\text{ }^{\circ}\text{C}$ . The enol carbonate solution was then transferred via cannula under positive  $\text{N}_2$  pressure to the catalyst solution, washing the original flask with deoxygenated anhydrous benzene (1 mL, allowed to cool briefly before transferring). The reaction, which turned green, was then stirred at  $14\text{ }^{\circ}\text{C}$  for 23.3 h. Solvent was removed under reduced pressure. The residue was suspended in  $\text{Et}_2\text{O}$  and filtered through a plug of cotton to remove precipitated Pd. The filtrate was then concentrated under reduced pressure. The residue was suspended in 10%  $\text{Et}_2\text{O}$ /pentane and applied to a silica gel column (11 $\times$ 2.5 cm). Flash chromatography (10%  $\text{Et}_2\text{O}$ /pentane eluent) then provided  $\alpha,\omega$ -diene (–)-**46** (242.3 mg, 91%) as a viscous yellow liquid. Observed 90% ee as determined by chiral HPLC analysis (Chiralcel<sup>®</sup> OD-H, 0.5%  $\text{EtOH}$ /hexanes, 1 mL/min, 254 nm,  $t_R$  (minor)=6.8 min;  $t_R$  (major)=8.9 min).  $R_f$  0.18 (10%  $\text{Et}_2\text{O}$ /petroleum ether eluent);  $[\alpha]_D^{24}$   $-10.19$  (c 0.515, benzene);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  5.31–5.34 (m, 1H), 5.19 (br s, 2H), 4.81 (br s, 1H), 4.79 (br s, 1H), 3.10–3.50 (br m, 1H), 3.01–3.12 (m, 2H), 2.67 (br d,  $J=15.6\text{ Hz}$ , 1H), 2.30–2.70 (br m, 1H), 1.54–2.20 (br m, 6H), 1.67 (app. septet,  $J=6.7\text{ Hz}$ , 1H), 1.64 (s, 3H), 1.38–1.54 (br m, 1H), 1.04 (br s, 3H), 0.95 (br s, 3H), 0.71 (d,  $J=6.6\text{ Hz}$ , 6H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{C}_6\text{D}_6$ , overlapping of resonances was observed)  $\delta$  200.9, 171.7, 145.6, 142.5 (br), 116.9, 110.5, 100.8 (br), 74.2, 55.1, 43.2, 38.8, 38.2 (br), 30.1, 27.9, 24.8, 24.6, 23.6 (br), 22.4, 18.9; IR (neat film, NaCl)  $\nu$  3072, 2961, 2937, 2876, 1652, 1622, 1471, 1456, 1430, 1405, 1383, 1366, 1339, 1297, 1279, 1220, 1205, 1170, 1133, 1080, 1009, 968, 885, 847, 825, 736, 692, 655, 623  $\text{cm}^{-1}$ ; HRMS ( $\text{EI}^+$ )  $m/z$  calcd for  $\text{C}_{21}\text{H}_{33}\text{ClO}_2$  [ $\text{M}]^+$ : 352.2169, found 352.2175.

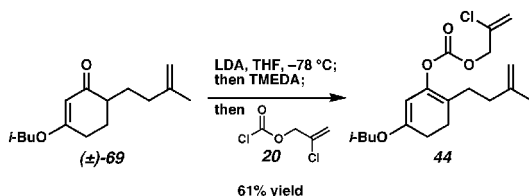
#### 4.7.7. Olefin ( $\pm$ )-**69**.

A 250 mL round-bottomed flask equipped with a stir bar and a septum was flame dried under vacuum. After refilling with Ar,



anhydrous THF (42 mL) and anhydrous diisopropylamine (1.65 mL, 11.8 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.52 M in hexanes, 4.5 mL, 11.3 mmol) was added dropwise via syringe, and the solution was stirred at 0 °C for 47 min. The resulting LDA solution was then cooled to –78 °C over 52 min. 3-Isobutoxy-2-cyclohexen-1-one (**19**) (1.811 g, 10.8 mmol) in anhydrous THF (3 mL) was then added dropwise over 2 min via syringe, washing the original flask with anhydrous THF (3 mL). The reaction was then placed in an ice bath and stirred at 0 °C for 1.25 h. A yellow solution was obtained, which was subsequently cooled to –78 °C over 15 min. Anhydrous hexamethylphosphoramide (2.0 mL, 11.5 mmol) was added in one portion via syringe, and the reaction was stirred for 30 min at –78 °C. 4-Iodo-2-methyl-1-butene (**18**)<sup>17</sup> (2.110 g, 10.8 mmol) in anhydrous THF (3 mL) was added via syringe, washing the original flask with anhydrous THF (3 mL). The cold bath was removed, and the reaction was allowed to warm to 23 °C as it was stirred for 24 h. Saturated NH<sub>4</sub>Cl (aq) (40 mL) was added, and the organic layer was separated. The aqueous layer was extracted with Et<sub>2</sub>O (2×150 mL), and the combined organic layers were washed with brine (2×200 mL). After drying over MgSO<sub>4</sub>, solvent was removed under reduced pressure. Flash chromatography over silica gel (10% Et<sub>2</sub>O/petroleum ether eluent until product begins to elute, then 25% Et<sub>2</sub>O/petroleum ether eluent) then provided olefin (±)-**69** (751 mg, 30%) as a yellow liquid. *R*<sub>f</sub> 0.04 (10% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.30 (s, 1H), 4.69–4.73 (br m, 2H), 3.58 (dd, *J*=9.5, 6.6 Hz, 1H), 3.56 (dd, *J*=9.4, 6.5 Hz, 1H), 2.40–2.46 (m, 2H), 2.14–2.22 (m, 1H), 1.96–2.14 (m, 5H), 1.68–1.77 (m, 1H), 1.73 (br s, 3H), 1.39–1.49 (m, 1H), 0.967 (d, *J*=6.59 Hz, 3H), 0.966 (d, *J*=6.59 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 201.6, 176.9, 145.6, 110.1, 102.2, 74.7, 44.5, 35.1, 27.9, 27.7, 27.3, 26.1, 22.4, 19.07, 19.06; IR (neat film, NaCl) ν 3072, 2960, 2935, 2874, 1655, 1609, 1470, 1452, 1428, 1404, 1384, 1368, 1299, 1239, 1218, 1194, 1177, 1103, 1084, 1044, 990, 968, 952, 885, 833 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>15</sub>H<sub>24</sub>O<sub>2</sub> [M]<sup>+</sup>: 236.1776, found 236.1783.

#### 4.7.8. Enol carbonate **44**.



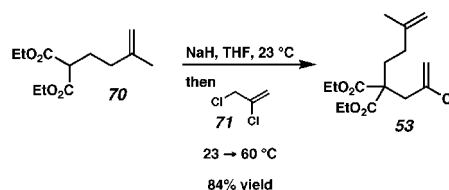
A 100 mL round-bottomed flask equipped with a stir bar and a septum was flame dried under vacuum. After refilling with Ar, anhydrous THF (18 mL) and anhydrous diisopropylamine (0.51 mL, 3.64 mmol) were added via syringe, and the solution was cooled to 0 °C in an ice bath. *n*-BuLi (2.52 M in hexanes, 1.3 mL, 3.28 mmol) was added dropwise via syringe, and the solution was stirred for 30 min. The resulting LDA solution was cooled to –78 °C over 10 min. Olefin (±)-**69** (714 mg, 3.02 mmol) in anhydrous THF (3 mL) was then added dropwise over 3 min via syringe, washing the original flask with anhydrous THF (3 mL). After stirring at –78 °C for 1 h, anhydrous *N,N,N',N'*-tetramethylethylenediamine (0.54 mL, 3.6 mmol) was added over 1 min via syringe. After stirring at –78 °C for an additional 1.3 h, chloroformate **20** (517 mg, 3.34 mmol) in anhydrous THF (3 mL) was then added dropwise over 2 min via syringe, washing the original flask with anhydrous THF (3 mL). The reaction was stirred for an additional 2.7 h at –78 °C, at which time saturated NaHCO<sub>3</sub> (aq) (13 mL) and H<sub>2</sub>O (13 mL) were added. The mixture was allowed to warm to 23 °C, at which time the mixture was extracted with Et<sub>2</sub>O (2×100 mL). The combined organic layers were washed with brine (2×100 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over Florisil® (100–200 mesh, 13×2.5 cm, 5% Et<sub>2</sub>O/petroleum ether eluent) then

provided enol carbonate **44** (658 mg, 61%) as a colorless liquid containing a minor unidentified impurity (3% by area) by <sup>1</sup>H NMR spectroscopy. *R*<sub>f</sub> 0.15 (5% Et<sub>2</sub>O/petroleum ether eluent); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.52–5.56 (m, 1H), 5.43–5.47 (m, 1H), 4.72–4.76 (m, 3H), 4.69–4.72 (m, 1H), 4.66–4.69 (m, 1H), 3.46 (d, *J*=6.7 Hz, 2H), 2.23–2.40 (m, 4H), 2.13–2.23 (m, 2H), 2.02–2.13 (m, 2H), 1.96 (app. septet, *J*=6.6 Hz, 1H), 1.70–1.74 (m, 3H), 0.94 (d, *J*=6.7 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 158.5, 152.9, 145.4, 140.8, 135.1, 115.4, 115.1, 110.1, 91.4, 73.9, 69.2, 35.7, 27.9, 27.6, 27.1, 26.0, 22.3, 19.2; IR (neat film, NaCl) ν 3076, 2958, 2934, 2915, 2875, 2833, 1763, 1676, 1625, 1471, 1451, 1439, 1426, 1400, 1383, 1369, 1242, 1183, 1151, 1105, 1052, 1017, 1004, 988, 970, 950, 919, 888, 842, 781, 728, 712, 701, 644 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>19</sub>H<sub>27</sub>ClO<sub>4</sub> [M]<sup>+</sup>: 354.1598, found 354.1596.

4.7.9.  $\alpha,\omega$ -Diene (+)-**24**. To a flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar was added phosphinooxazoline ligand (–)-**41** (56.2 mg, 0.0950 mmol) and bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (68.7 mg, 0.0843 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (24 mL, deoxygenated prior to use by sparging with N<sub>2</sub> in a flame-dried flask for 1 h) was added via syringe, and the resulting solution was stirred for 32 min at 23 °C. The solution was then cooled to 12 °C over 15 min. Concurrently, a flame-dried 1 dram screw-cap vial was charged with enol carbonate **44** (299.5 mg, 0.844 mmol). After sealing with a septum-bearing cap, the vial was placed under high vacuum and refilled with Ar. Deoxygenated anhydrous benzene (1 mL) was added via syringe, and the resulting solution was cooled to 12 °C. The enol carbonate solution was then transferred via cannula to the catalyst solution at 12 °C, washing the original flask with deoxygenated anhydrous benzene (1 mL, allowed to cool briefly before transferring). The reaction was then stirred at 12 °C for 24.4 h, at which time it was filtered while still cold through a silica gel plug (4.5×1.5 cm), eluting with Et<sub>2</sub>O (200 mL). Solvent was removed under reduced pressure. The residue was suspended in Et<sub>2</sub>O and filtered through a plug of cotton to remove precipitated Pd. The filtrate was then concentrated under reduced pressure. The residue was suspended in 10% Et<sub>2</sub>O/pentane and applied to a silica gel column (12×2.5 cm). Flash chromatography (10% Et<sub>2</sub>O/pentane eluent) then provided  $\alpha,\omega$ -diene (+)-**24** (210.7 mg, 80%) as a viscous colorless oil. Observed 94% ee as determined by chiral HPLC analysis (Chiralcel® OD-H, 1% EtOH/hexanes, 1 mL/min, 254 nm, *t*<sub>R</sub> (minor)=6.6 min; *t*<sub>R</sub> (major)=7.2 min). *R*<sub>f</sub> 0.17 (10% Et<sub>2</sub>O/petroleum ether eluent); [ $\alpha$ ]<sub>D</sub><sup>25</sup> +9.23 (c 1.04, CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.28 (br s, 2H), 5.17 (br s, 1H), 4.64–4.71 (m, 2H), 3.58 (d, *J*=6.4 Hz, 2H), 2.93 (dd, *J*=14.5, 0.67 Hz, 1H), 2.38–2.60 (m, 3H), 1.82–2.18 (m, 5H), 1.58–1.82 (m, 2H), 1.71 (br s, 3H), 0.97 (d, *J*=6.9 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 201.3, 175.9, 145.7, 139.0, 116.6, 109.7, 101.7, 74.7, 46.6, 43.2, 33.2, 32.0, 28.9, 27.7, 25.8, 22.7, 19.1; IR (neat film, NaCl) ν 3073, 2961, 2935, 2875, 1651, 1628, 1611, 1471, 1449, 1431, 1405, 1384, 1370, 1360, 1338, 1310, 1300, 1284, 1242, 1192, 1178, 1157, 1123, 1115, 1088, 1023, 993, 968, 952, 930, 886, 839, 800, 765, 752, 691, 644 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>18</sub>H<sub>27</sub>ClO<sub>2</sub> [M]<sup>+</sup>: 310.1700, found 310.1708.

#### 4.8. Procedures for the synthesis of RCM product **54**

##### 4.8.1. $\alpha,\omega$ -Diene **53**.



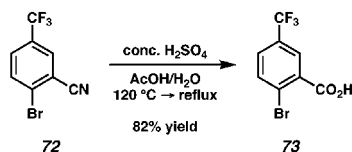
To an oven-dried 50 mL 2-neck round-bottomed flask equipped with a magnetic stir bar was added sodium hydride (100 mg,

4.17 mmol) and THF (10 mL) in a N<sub>2</sub>-filled glovebox. The flask was sealed with a septum and a hose adapter, and removed from the glovebox. Under a positive pressure of Ar, a reflux condenser was attached, and olefin **70**<sup>49</sup> (1.0 g, 4.38 mmol) was added via syringe. The suspension was stirred for 30 min, or until gas evolution ceased. 2,3-Dichloropropene (**71**) (0.40 mL, 4.34 mmol) was then added via syringe. The suspension was heated to 60 °C in an oil bath and stirred for 18 h. After cooling to 23 °C, H<sub>2</sub>O (2 mL) was added, and the mixture was diluted with Et<sub>2</sub>O (50 mL). The organic layer was separated, washed with brine (2×100 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over silica gel (10×2 cm, 10% EtOAc/hexane eluent) the provided  $\alpha,\omega$ -diene **53** (1.11 g, 84%) as a colorless liquid. *R*<sub>f</sub> 0.47 (15% Et<sub>2</sub>O/pentane); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  5.29 (br s, 1H), 5.20 (br s, 1H), 4.70 (br s, 1H), 4.68 (br s, 1H), 4.19 (m, 4H), 3.06 (s, 2H), 2.12 (m, 2H), 1.88 (m, 2H), 1.71 (s, 3H), 1.25 (t, *J*=4.2 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  170.7, 144.8, 137.6, 117.1, 110.7, 61.7, 56.7, 41.2, 32.4, 29.9, 22.6, 14.2; IR (neat film, NaCl)  $\nu$  2981, 1734, 1631, 1449, 1367, 1278, 1238, 1183, 1155, 1088, 1030, 890, 860 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) *m/z* calcd for C<sub>15</sub>H<sub>24</sub>ClO<sub>4</sub> [M+H]<sup>+</sup>: 303.1363, found 302.1355.

**4.8.2. Chloroalkene 54.** To a flame-dried 10 mL 2-neck round-bottomed flask equipped with a magnetic stir bar and a condenser was added catalyst **49** (4.7 mg, 0.008 mmol). Anhydrous benzene (1.6 mL) was added via syringe. To the resulting solution was added  $\alpha,\omega$ -diene **53** (50 mg, 0.16 mmol) via syringe. The solution was placed in a 60 °C oil bath and stirred for 18 h. After cooling to 23 °C, solvent was removed under reduced pressure. Flash chromatography over silica gel (10×1 cm, 2.5% Et<sub>2</sub>O/pentane eluent until product begins to elute, then 30% Et<sub>2</sub>O/pentane eluent) then provided chloroalkene **54** (11 mg, 24%) as a colorless oil. *R*<sub>f</sub> 0.43 (15% Et<sub>2</sub>O/pentane); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  4.19 (q, *J*=7.8 Hz, 4H), 2.84 (br s, 2H), 2.13 (app. s, 4H), 1.75 (app. t, *J*=2.1 Hz, 3H), 1.24 (t, *J*=7.5 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  170.5, 128.3, 122.7, 61.6, 54.6, 37.9, 28.9, 27.5, 19.6, 14.0; IR (neat film, NaCl)  $\nu$  2981, 1735, 1446, 1367, 1252, 1179, 1091, 1029 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>13</sub>H<sub>19</sub>ClO<sub>4</sub> [M]<sup>+</sup>: 274.0972, found 274.0968.

## 4.9. Procedures for the synthesis of phosphinooxazoline ligand (+)-**41**

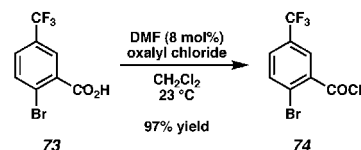
### 4.9.1. 2-Bromo-5-(trifluoromethyl)-benzoic acid (**73**)<sup>54</sup>.



A 250 mL round-bottomed flask equipped with a stir bar and a condenser was charged with 2-bromo-5-(trifluoromethyl)-benzonitrile (**72**) (5.0 g, 20 mmol) and AcOH (22 mL, 384 mmol) to give a homogeneous solution. H<sub>2</sub>O (22 mL) was added and the benzonitrile oiled out to provide a biphasic mixture. Conc. H<sub>2</sub>SO<sub>4</sub> (22 mL, 396 mmol) was added, and the mixture was stirred at 120 °C for 1 h and then at reflux for an additional 5 h. The mixture was cooled to 23 °C, and the pH was adjusted to 14 with KOH (aq) followed by NaOH (s). A significant exotherm was observed during this process, and an ice bath was employed to control temperature. H<sub>2</sub>O was added to dissolve all solids, and the aqueous solution was washed with EtOAc (3×200 mL). The pH of the aqueous solution was then adjusted to 1 with concd HCl (aq), and the resulting biphasic mixture was extracted with EtOAc (3×200 mL). The combined organic layers were washed with brine (3×200 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure,

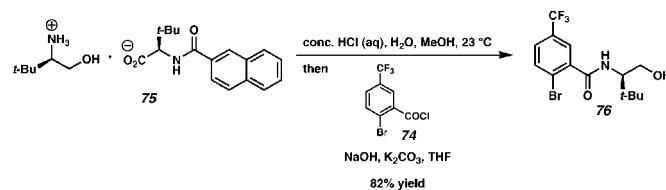
and the residue was azeotroped with heptane (4×) to remove any remaining AcOH. Residual solvent was then removed under high vacuum to provide 2-bromo-5-(trifluoromethyl)-benzoic acid (**73**)<sup>55</sup> (4.42 g, 82%) as a white powder. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.25 (d, *J*=2.0 Hz, 1H), 7.87 (d, *J*=8.8 Hz, 1H), 7.64 (dd, *J*=8.1, 2.7 Hz, 1H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  169.6, 135.7, 131.0, 130.1 (q, *J*<sub>F</sub>=33.9 Hz), 129.9 (q, *J*<sub>F</sub>=3.5 Hz), 129.4 (q, *J*<sub>F</sub>=3.8 Hz), 126.7 (q, *J*<sub>F</sub>=1.4 Hz), 123.2 (q, *J*<sub>F</sub>=272.5 Hz); <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>)  $\delta$  -63.3; IR (neat film, NaCl)  $\nu$  3454, 2957, 2925, 2872, 2853, 1664, 1618, 1586, 1513, 1464, 1444, 1419, 1376, 1365, 1342, 1301, 1248, 1220, 1171, 1138, 1092, 1072, 1039, 1018, 1010, 961, 908, 874, 861, 819, 745, 686, 666 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>8</sub>H<sub>4</sub>F<sub>3</sub>BrO<sub>2</sub> [M]<sup>+</sup>: 267.9347, found 267.9334.

### 4.9.2. 2-Bromo-5-(trifluoromethyl)-benzoyl chloride (**74**).



A 50 mL round-bottomed flask equipped with a stir bar was charged with 2-bromo-5-(trifluoromethyl)-benzoic acid (**73**) (1.719 g, 6.39 mmol), CH<sub>2</sub>Cl<sub>2</sub> (13 mL), oxalyl chloride (1.1 mL, 13.0 mmol), and anhydrous DMF (40  $\mu$ L, 0.517 mmol). A drying tube was attached to the flask, and the reaction was stirred for 12.7 h at 23 °C. Solvent was removed under reduced pressure, and the residue was suspended in hexanes and filtered through a plug of cotton to remove a precipitate. Solvent was removed under reduced pressure. The crude product was then distilled under high vacuum to provide 2-bromo-5-(trifluoromethyl)-benzoyl chloride (**74**) as a colorless liquid (1.787 g, 97%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.27 (d, *J*=2.0 Hz, 1H), 7.88 (d, *J*=8.3 Hz, 1H), 7.65–7.70 (m, 1H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  165.1, 135.8, 135.7, 130.5 (q, *J*<sub>F</sub>=3.4 Hz), 130.4 (q, *J*<sub>F</sub>=34.1 Hz), 129.7 (q, *J*<sub>F</sub>=3.8 Hz), 125.3 (q, *J*<sub>F</sub>=1.2 Hz), 122.9 (q, *J*<sub>F</sub>=272.8 Hz); <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>)  $\delta$  -63.4; IR (CHCl<sub>3</sub>, KBr)  $\nu$  1775, 1607, 1572, 1469, 1401, 1330 cm<sup>-1</sup>; HRMS (EI<sup>+</sup>) *m/z* calcd for C<sub>8</sub>H<sub>3</sub>BrClF<sub>3</sub>O [M]<sup>+</sup>: 285.9008, found 285.9002.

### 4.9.3. Amide **76**<sup>27</sup>.

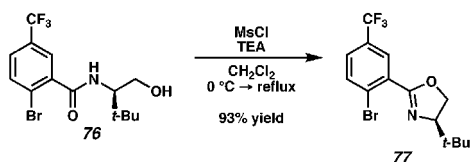


Salt **75**<sup>50</sup> (99% ee, 4.94 g, 12.3 mmol) was suspended in H<sub>2</sub>O (32 mL) and MeOH (16 mL). Conc HCl (aq) (5.5 mL) was added, and the mixture was stirred for several minutes. The mixture was then filtered through a Büchner funnel into a round-bottomed flask equipped with a stir bar, washing with H<sub>2</sub>O (45 mL). The pH of the filtrate solution was adjusted to 10 with NaOH (s). K<sub>2</sub>CO<sub>3</sub> (1.87 g, 13.5 mmol) and THF (30 mL) were then added. 2-Bromo-5-(trifluoromethyl)-benzoyl chloride (**74**) (3.991 g, 88.3% pure by mass [contained 11.7% benzene by mass], 12.3 mmol) was added, washing the original flask with THF (2×3 mL). The reaction mixture turned opaque, and an exotherm was observed. The mixture was stirred for 19 h at 23 °C, at which point it was extracted with Et<sub>2</sub>O (3×100 mL). The combined organic layers were washed with 10% HCl (aq) (100 mL) and brine (2×150 mL). After drying over MgSO<sub>4</sub>, solvent was removed under reduced pressure. The crude product was then recrystallized from EtOAc (17 mL)/hexanes (86.5 mL) at reflux to provide amide **76** (3.68 g, 82%) as fine white needles.

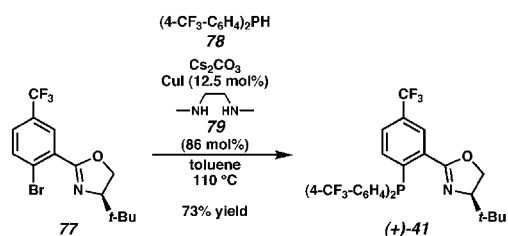


Observed >99% ee as determined by chiral HPLC analysis (Chiralpak<sup>®</sup> AD, 5% *i*-PrOH/hexanes, 1 mL/min, 220 nm,  $t_R$  (major) = 8.8 min; the minor enantiomer was not observed). A scalemic mixture afforded retention times of 6.6 and 8.9 min for the two enantiomers.  $[\alpha]_D^{26}$  –11.78 (99.5% ee material, *c* 0.495, MeOH); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.82 (d, *J* = 2.2 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.52–7.56 (m, 1H), 6.19 (br d, *J* = 8.6 Hz, 1H), 4.09 (ddd, *J* = 9.4, 7.3, 3.5 Hz, 1H), 3.98 (ddd, *J* = 11.2, 5.9, 3.5 Hz, 1H), 3.73 (ddd, *J* = 11.5, 7.3, 5.5 Hz, 1H), 1.99 (dd, *J* = 5.7, 5.7 Hz, 1H), 1.06 (s, 9H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  167.2, 138.7, 134.0, 130.3 (q, *J*<sub>F</sub> = 33.6 Hz), 127.8 (q, *J*<sub>F</sub> = 3.5 Hz), 126.7 (q, *J*<sub>F</sub> = 3.8 Hz), 123.0 (q, *J*<sub>F</sub> = 1.6 Hz), 123.3 (q, *J*<sub>F</sub> = 272.5 Hz), 62.7, 60.2, 33.9, 27.1; <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>)  $\delta$  –63.2; IR (neat film, NaCl)  $\nu$  3410, 3278, 3076, 2965, 2910, 2874, 1644, 1608, 1581, 1548, 1472, 1401, 1368, 1349, 1330, 1300, 1277, 1262, 1173, 1131, 1080, 1050, 1034, 1021, 999, 946, 908, 828, 796, 772, 733, 703, 668, 648 cm<sup>–1</sup>; HRMS (FAB<sup>+</sup>) *m/z* calcd for C<sub>14</sub>H<sub>18</sub>BrNO<sub>2</sub>F<sub>3</sub> [M+H]<sup>+</sup>: 368.0473, found 368.0487.

#### 4.9.4. Oxazoline 77<sup>27</sup>.



To a flame-dried 250 mL round-bottomed flask equipped with a magnetic stir bar and an oven-dried condenser was added amide **76** (3.67 g, 9.97 mmol). After sealing with a septum, the flask was placed under high vacuum and refilled with Ar. Anhydrous CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and anhydrous triethylamine (4.2 mL, 30.1 mmol) were added via syringe, and the reaction was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.85 mL, 11.0 mmol) was added via syringe, and the reaction was stirred at 0 °C for 5 min. The reaction was then heated at reflux for 6 h, at which point additional CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added to maintain the appropriate solvent volume. After stirring an additional 18 h at reflux, the reaction was cooled to 23 °C. The reaction was washed with H<sub>2</sub>O (50 mL), and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 50 mL). The combined organic layers were washed with brine (150 mL) and dried over MgSO<sub>4</sub>. Solvent was removed under reduced pressure. Flash chromatography over silica gel (10 × 5 cm, 7.5% Et<sub>2</sub>O/petroleum ether eluent) then provided oxazoline **77**<sup>27</sup> (3.244 g, 93%) as a colorless viscous liquid. *R*<sub>f</sub> 0.37 (7.5% Et<sub>2</sub>O/petroleum ether eluent);  $[\alpha]_D^{24}$  +68.01 (*c* 1.035, CHCl<sub>3</sub>); lit.<sup>27</sup>  $[\alpha]_D^{25}$  –64.7 (*c* 1.26, CHCl<sub>3</sub>, *S* enantiomer); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.93 (d, *J* = 2.2 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.49–7.54 (m, 1H), 4.41 (dd, *J* = 10.3, 8.8 Hz, 1H), 4.28 (dd, *J* = 8.4, 8.4 Hz, 1H), 4.14 (dd, *J* = 10.3, 8.1 Hz, 1H), 1.01 (s, 9H).



#### 4.9.5. Phosphinooxazoline ligand (+)-41<sup>27</sup>.

To a flame-dried 250 mL round-bottomed Schlenk flask equipped with a magnetic stir bar and a septum was added copper (I) iodide (64.4 mg, 0.338 mmol). After sealing with a septum, the flask was wrapped in aluminum foil, placed under high vacuum, and refilled with Ar. Anhydrous toluene (11 mL), anhydrous *N,N*-dimethylethylenediamine (**79**) (0.25 mL, 2.32 mmol), and

phosphine **78**<sup>51,52</sup> (1.35 g, 4.19 mmol) were added sequentially via syringe, and the reaction was stirred at 23 °C for 30 min. Oxazoline **77** (944 mg, 2.70 mmol) in anhydrous toluene (3 mL) was then added via syringe, washing the original flask with anhydrous toluene (2 × 4 mL). The flask was opened under positive Ar pressure, and Cs<sub>2</sub>CO<sub>3</sub> (3.29 g, 10.1 mmol) was added. The flask was flushed with Ar and sealed with the stopcock, and the reaction was heated to 110 °C for 16.3 h. After cooling to 23 °C, the reaction was filtered through a pad of silica gel, eluting with CH<sub>2</sub>Cl<sub>2</sub>. Solvent was removed under reduced pressure. Flash chromatography over silica gel (18 × 2.5 cm, 1% Et<sub>2</sub>O/pentane eluent) then provided phosphinooxazoline (+)-**41**<sup>27</sup> (1.17 g, 73%) as a white powder. *R*<sub>f</sub> 0.087 (1% Et<sub>2</sub>O/petroleum ether eluent);  $[\alpha]_D^{24}$  +15.04 (*c* 0.495, CHCl<sub>3</sub>); lit.<sup>27</sup>  $[\alpha]_D^{24}$  –16.0 (*c* 2.56, CHCl<sub>3</sub>, *S* enantiomer); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.23–8.27 (m, 1H), 7.54–7.62 (m, 5H), 7.27–7.37 (m, 4H), 6.95 (dd, *J* = 8.2, 3.3 Hz, 1H), 4.24 (dd, *J* = 10.3, 8.6 Hz, 1H), 4.09 (dd, *J* = 8.5, 8.5 Hz, 1H), 3.94 (dd, *J* = 10.1, 8.7 Hz, 1H), 0.68 (s, 9H).

#### 4.10. Procedures for optimization studies for the enantioselective decarboxylative allylation and RCM

**4.10.1. General procedure for enantioselective decarboxylative allylation screening (from Scheme 6, reaction b)<sup>7a</sup>.** To a flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was added bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) (4.0 mg, 0.00491 mmol) and phosphinooxazoline ligand (–)-**23** (2.5 mg, 0.00645 mmol). After sealing with the septum cap, the vial was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the resulting solution was stirred for 29 min at 23 °C. Concurrently, a second flame-dried 1 dram screw-cap vial equipped with a septum-bearing cap was charged with enol carbonate **33** (17.5 mg, 99.5% pure by mass [contained 0.5% Et<sub>2</sub>O by mass], 0.050 mmol), and the flask was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the resulting solution was transferred to the catalyst solution via syringe. The reaction was transferred to a 40 °C heating block and stirred for 68 min. After cooling to 23 °C, the reaction was filtered through a plug of silica gel in a pipette, eluting with Et<sub>2</sub>O. Solvent was removed under reduced pressure. <sup>1</sup>H NMR spectroscopic analysis of the crude reaction mixture revealed >99% conversion and ≥99%  $\alpha,\omega$ -diene **34**.

For runs in which the ee was determined, the crude product was subjected to purification by preparative thin-layer chromatography (0.25 mm thickness, 15% EtOAc/hexanes eluent) prior to chiral HPLC analysis.

For runs below 23 °C, the catalyst and substrate solutions were pre-cooled for 5–7 min after metal-ligand complexation and prior to addition.

Scheme 4, reaction **26** → (+)-**13** (24 °C conditions), Table 2, entries 2–3 and 5–6, and Table 3, entries 2 and 4 were conducted in an N<sub>2</sub>-filled glovebox.

For Table 3, entry 6, the anhydrous toluene was deoxygenated prior to use by freeze-pump-thawing under high vacuum in a flame-dried 1 dram screw-cap vial equipped with a septum-bearing cap for a total of four cycles.

**4.10.2. Decarboxylative protonation of enol carbonate 26 (from Scheme 6, reaction a)<sup>25</sup>.** A flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was charged with powdered activated 4 Å molecular sieves (119 mg). The vial was placed under high vacuum, the sieves were flame-dried, and the vial was refilled with Ar. This was repeated for a total of three cycles. After cooling to 23 °C, Pd(OAc)<sub>2</sub> (1.1 mg, 0.0049 mmol) and phosphinooxazoline ligand (–)-**23** (2.4 mg, 0.0062 mmol) were added, and the flask was placed under high vacuum and refilled

with Ar. Anhydrous benzene (0.75 mL) was added via syringe, and the reaction was placed in 40 °C heating block and stirred for 31 min. Concurrently, a second oven-dried 1 dram screw-cap vial equipped with a septum-bearing cap was charged with enol carbonate **26** (19.0 mg, 0.0496 mmol), and the vial was placed under high vacuum and refilled with Ar. Anhydrous benzene (0.75 mL) was added via syringe. To the catalyst solution at 40 °C was then added formic acid (19  $\mu$ L, 0.504 mmol) followed by the enol carbonate **26** solution via syringe. The reaction was stirred at 40 °C for 3.1 h. After cooling to 23 °C, the reaction was filtered through a plug of silica gel in a pipette, eluting with Et<sub>2</sub>O. Solvent was removed under reduced pressure. <sup>1</sup>H NMR spectroscopic analysis of the crude reaction mixture revealed >99% conversion and 99:1 olefin **27**: $\alpha,\omega$ -diene **13**.

**4.10.3. General procedure for RCM catalyst comparison (from Table 5, entry 3)<sup>8a</sup>.** To a flame-dried 1 dram screw-cap vial equipped with a stir bar and a septum-bearing cap was added  $\alpha,\omega$ -diene (+)-**13** (16.8 mg, 99.6% pure by mass [contained 0.4% Et<sub>2</sub>O by mass], 0.0494 mmol) and 1,4-bis(trimethylsilyl)benzene (5.7 mg, 0.0256 mmol). The vial was brought into a N<sub>2</sub>-filled glovebox, and a solution of catalyst **49** in anhydrous C<sub>6</sub>D<sub>6</sub> (0.00118 M, 1 mL, 0.00118 mmol) was added via syringe. The reaction solution was transferred to a screw-cap NMR tube equipped a septum-bearing cap, and the NMR tube was removed from the glovebox and placed in a 56–63 °C oil bath. Conversion was monitored by <sup>1</sup>H NMR spectroscopy. The reaction was allowed to cool to 23 °C prior to <sup>1</sup>H NMR analysis for each time point. The total time at 23 °C for each time point measurement was 45 min. Reaction times are given for the time the reaction spent at 60 °C only; time spent at 23 °C was not included.

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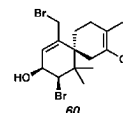
## Supplementary data

Comparisons of published characterization data for natural and semisynthetic material with that of synthetic material for **1**, **5**, (+)-**7**, and **8**; copies of <sup>1</sup>H NMR, <sup>13</sup>C NMR, and IR spectra for synthetic **1**, **5**, (+)-**7**, and **8**; a copy of the <sup>1</sup>H NMR spectrum for a natural sample of **1**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.04.128.

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31.  $[\alpha]_D^{25} -42.01$  (c 0.357,  $\text{CHCl}_3$ , synthetic),  $[\alpha]_D^{25} +58.3$  (c 0.36,  $\text{CHCl}_3$ , semisynthetic, Ref. 10).
32. See the Supplementary data for a detailed comparison.
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35. For the preparation of ( $-$ )- $\alpha$ -chamigrene (**5**) from ( $-$ )-thujopsene, see: (a) Daeniker, H. U.; Hochstetler, A. R.; Kaiser, K.; Kitchens, G. C. *J. Org. Chem.* **1972**, *37*, 1–5; (b) Dauben, W. G.; Aoyagi, E. I. *J. Org. Chem.* **1972**, *37*, 251–259; The stereochemistry of  $\alpha$ -chamigrene (**5**) was not determined; (c) Kitchens, G.C.; Hochstetler, A.R.; Kaiser, K. Acid Isomerization of Chamigrenes. U.S. Patent 3,678,119, July 18, 1972. The stereochemistry of  $\alpha$ -chamigrene (**5**) was not determined; (d) Kitchens, G.C.; Hochstetler, A.R.; Kaiser, K. Acid Isomerization of Thujopsene and Novel Tricyclic Olerinic C15 H24 Hydrocarbons Formed Thereby. U.S. Patent 3,681,470, August 1, 1972. The stereochemistry of  $\alpha$ -chamigrene (**5**) was not determined; (e) Yarovaya, O. I.; Polovinka, M. P.; Korzhagina, D. V.; Gatilov, Yu. V.; Bagryanskaya, I. Yu.; Shcherbukhin, V. V.; Shal'ko, A. A.; Zenkovets, G. A.; Barkhash, V. A. *Russ. J. Org. Chem.* **2001**, *37*, 362–374; *Zhurnal Organicheskoi Khimii* **2001**, *37*, 389–400; For the preparation of ( $-$ )- $\alpha$ -chamigrene (**5**) from ( $-$ )-glanduliferol, see: (f) Suzuki, M.; Furusaki, A.; Kurosawa, E. *Tetrahedron* **1979**, *35*, 823–831. For the preparation of ( $+$ )- $\alpha$ -chamigrene (( $+$ )-**5**) from a ( $+$ )-bromo- $\alpha$ -chamigrene, see: (g) Guella, G.; Öztunç, A.; Mancini, I.; Pietra, F. *Tetrahedron Lett.* **1997**, *38*, 8261–8264. For the preparation of ( $+$ )- $\alpha$ -chamigrene (( $+$ )-**5**) from a ( $-$ )- $\alpha$ -chamipinene, see: (h) Cool, L. G. *Phytochemistry* **2005**, *66*, 249–260.
36. Synthetic ( $-$ )-laurencenone C (**8**) was identical in all respects to the  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, IR, and  $[\alpha]_D$  data reported for the natural product in Ref. 2h except for a single  $^{13}\text{C}$  NMR resonance and the magnitude of its optical rotation:  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  134.1 ppm (synthetic),  $^{13}\text{C}$  NMR (22.5 or 100 MHz,  $\text{CDCl}_3$ )  $\delta$  131.4 ppm (natural);  $[\alpha]_D^{25} -87.98$  (c 1.00,  $\text{CHCl}_3$ , synthetic),  $[\alpha]_D -43$  (c 1.0,  $\text{CHCl}_3$ , natural). We believe the reported  $^{13}\text{C}$  NMR peak to be a typographical error. Discrepancies between the published  $^1\text{H}$  NMR data for the natural product in Ref. 2g and that of the synthetic material exist. No  $^{13}\text{C}$  NMR data was available for comparison from Ref. 2g. No natural sample was available for comparison. Based on these observations, we conclude that the structure of the compound designated as laurencenone C (**8**) in Ref. 2g has been incorrectly assigned. See the Supplementary data for a detailed comparison.
37. Williams, J. R.; Sarkisian, G. M. *Synthesis* **1974**, 32–33.
38. Synthetic ( $-$ )- $\alpha$ -chamigrene (**5**) was identical in all respects to the  $^1\text{H}$  NMR, IR, and  $[\alpha]_D$  data reported for the natural product in Ref. 2e except for the magnitude of its optical rotation:  $[\alpha]_D^{25} -64.60$  (c 0.21,  $\text{CHCl}_3$ , synthetic),  $[\alpha]_D -14.5$  (c 0.21,  $\text{CHCl}_3$ , natural). No  $^{13}\text{C}$  NMR data was reported. No natural sample was available for comparison. See the Supplementary data for a detailed comparison.
39. For an example of a sequential ketone reduction and directed reductive olefin transposition of a  $\gamma$ -halo- $\alpha,\beta$ -unsaturated ketone, see: (a) Pattison, V. A. *J. Org. Chem.* **1970**, *35*, 2096–2099; For an example of a sequential ester reduction and directed reductive olefin transposition of a  $\gamma$ -halo- $\alpha,\beta$ -unsaturated ester, see: (b) Nakamura, Y.; Okada, M.; Horikawa, H.; Taguchi, T. *J. Fluorine Chem.* **2002**, *117*, 143–148; For an example of a directed reductive olefin transposition of a  $\gamma$ -benzyloxy-allylic alcohol, see: (c) Hatakeyama, S.; Satoh, K.; Takano, S. *Tetrahedron Lett.* **1993**, *34*, 7425–7428.
40. For examples of concomitant allylic and  $\alpha'$ -bromination of enones, see: (a) Djerassi, C.; Rosenkranz, G.; Romo, J.; Kaufmann, S.; Pataki, J. *J. Am. Chem. Soc.* **1950**, *72*, 4534–4540; (b) Brown, F. J.; Djerassi, C. *J. Org. Chem.* **1981**, *46*, 954–963; (c) Kurzer, F.; Patel, J. N. *Monatsh. Chem.* **1987**, *118*, 793–812; (d) Oda, T.; Hashimoto, H.; Sato, Y. *Chem. Pharm. Bull.* **1990**, *38*, 525–528; (e) Shimizu, T.; Tobari, A.; Koyanagi, J.; Kawase, M.; Saito, S. *Chem. Pharm. Bull.* **2001**, *49*, 23–28; (f) Ma, D.; Tang, G.; Kozikowski, A. P. *Org. Lett.* **2002**, *4*, 2377–2380; (g) Yick, C.-Y.; Tsang, T.-K.; Wong, H. N. C. *Tetrahedron* **2003**, *59*, 325–333.
41. Other electrophilic bromine sources examined consisted of  $\text{CuBr}_2$ , pyridinium bromide perbromide, and *N*-bromosuccinimide.
42. Purification of  $\alpha$ -bromoketone **59** was hampered by its poor stability to silica gel and reverse phase HPLC.
43. Determined by quenching the reaction at  $-78^{\circ}\text{C}$  in a separate run, resulting in the isolation a 3.9:1 mixture of alcohol diastereomers favoring **60**.



44. Synthetic ( $+$ )-elatol (**1**) was identical in all respects to a natural sample provided by Prof. Karen L. Erickson except for the magnitude of its optical rotation:  $[\alpha]_D^{25} +92.09$  (c 0.22,  $\text{CHCl}_3$ , synthetic),  $[\alpha]_D^{25} +109.78$  (c 0.045,  $\text{CHCl}_3$ , natural). Based on 87% ee, the expected  $[\alpha]_D$  value for the synthetic material would be  $+95.5^{\circ}$ , which differed from the observed value by 3.6%. The  $^1\text{H}$  NMR data also matched that reported for the natural product in Ref. 2a. No  $^{13}\text{C}$  NMR or IR data was reported. See the Supplementary data for a detailed comparison.
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