# Enantiomerically Pure Allylboronic Esters as Versatile Reagents in the Enantioselective Synthesis of Dihydro-α-pyrone-Containing Natural Products

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**Abstract:** A short and efficient enantio- and diastereoselective synthesis of different representatives from the class of dihydro-α-pyrone natural products, including both enantiomers of goniothalamin, massoia lactone, parasorbic acid, and some derivatives is presented. It is based on the application of enantiopure α-chiral allylboronic esters in allyl additions.

**Key words:** natural products, goniothalamin, allyl addition, boronic ester, dihydro-α-pyrones

Dihydro-α-pyrones, or more precisely 6-substituted 5,6-dihydro-2*H*-pyran-2-ones, represent an interesting group of bioactive natural products that have been isolated from many different plants, in particular from the *Lauraceae*, *Annonaceae*, *Piperaceae*, and *Psilotaceae* families.[1] Some of these have been proven to show cytotoxicity as well as antibacterial, antiviral, or antifungal properties.[2] Dihydro-α-pyrones can be divided into alkyl-, aryl-, and alkenyl-substituted pyrones as three main subcategories.

The naturally occurring styrylpyrone goniothalamin (**1**) was isolated first in 1967 by Hlubucek and Robertson from the bark of *Cryptocarya caloneura*.[1b] Later it was also observed in various other species of the genera *Cryptocarya* (Lauraceae) and *Goniothalamus* (Annonaceae).[1a,c] The cytotoxic and antiproliferative activity of goniothalamin (**1**) and its derivatives against specific cancer cell lines has been verified in several studies, including the development of a structure–activity relationship.[2b,f,g,3] It was concluded that the mechanism of action in human breast cancer involved cell death due to apoptosis.[2d] Moreover some studies have revealed a trypanocidal activity against *Trypanosoma cruzi*, which is known as the cause of South American Chagas disease.[2c] Due to the biological activity of goniothalamin (**1**) and its derivatives, a number of total syntheses (3–12 steps) have been reported in the literature. Most of these are based on a sequence consisting of allylation, esterification, and ring-closing metathesis (RCM), starting from *trans*-cinnamaldehyde or cinnamyl alcohol. The chirality was induced by using chiral allylmetal reagents (Brown, Leighton),[4] asymmetric catalysis (Krische, Maruoka),[3,5] or enzymatic kinetic resolution of racemic allylic alcohols.[6] Other total syntheses have been developed in similar ways, adding some steps for the insertion of the styryl substituent via olefination.[3,7] Another attempt is based on Jacobsen's hydrolytic kinetic resolution of epoxides.[8]

Some naturally occurring alkylpyrones such as parasorbic acid (**2**), isolated from mountain ash berries (*Sorbus aucuparia*), or massoia lactone (**3**) (Figure 1), isolated from the bark oil of *Cryptocarya massoia* and jasmine flowers, either feature bioactivity as well or are used as intermediates in the synthesis of other natural products.[4a] One approach towards the total synthesis of these compounds is identical to the three-step synthesis of goniothalamin (**1**) as described previously by Brown.[4a]

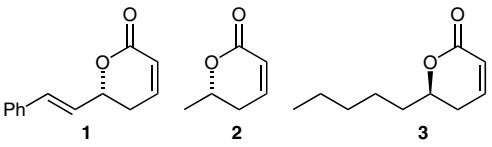


**Figure 1** Structures of goniothalamin (**1**), parasorbic acid (**2**), and massoia lactone (**3**)

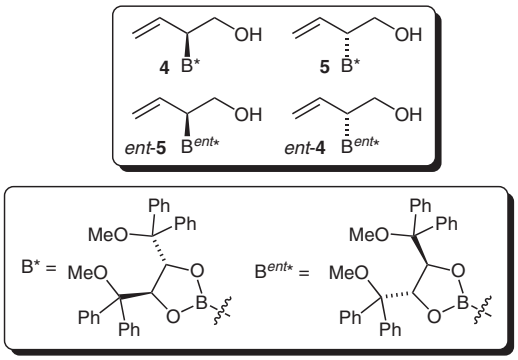


**Figure 2** Allylboronic esters **4** and **5**

As a part of our ongoing project focused on the development of efficient allylboron reagents **4** and **5** for allyl additions to obtain enantioenriched homoallylic alcohols, we have developed a family of new reagents for the stereocontrolled synthesis of ene-1,5-diols **6**–**13** (Figure 2).[9] The ease of access to these reagents, their stability, high stereoselectivity, and the mild conditions of the allyl additions make the use of this method appropriate for multi-

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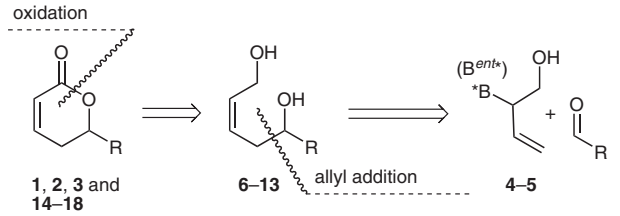
step synthesis. The allylboronic esters have previously been used successfully in the stereoselective total synthesis of rugulactone.[9c]

Herein we wish to demonstrate the scope of the method towards the synthesis of 5,6-dihydro-2*H*-pyran-2-one containing natural products such as goniothalamin (**1**), parasorbic acid (**2**), massoia lactone (**3**), and their derivatives and analogues **14**–**18**. The retrosynthetic approach towards these compounds is highlighted in Scheme 1. Accordingly the major part of the lactone can be installed by a selective oxidation of 2-ene-1,5-diols **6**–**13**. These enantioenriched *Z*-configured diols can be selectively synthesized via the addition of allylboronic esters **4** or **5** to different aldehydes **19**–**26**.

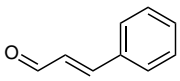
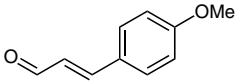
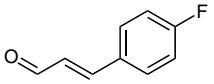
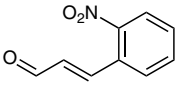
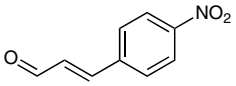



**Scheme 1** Retrosynthetic analysis of 5,6-dihydro-2*H*-pyran-2-ones **1**–**3** and **14**–**18**

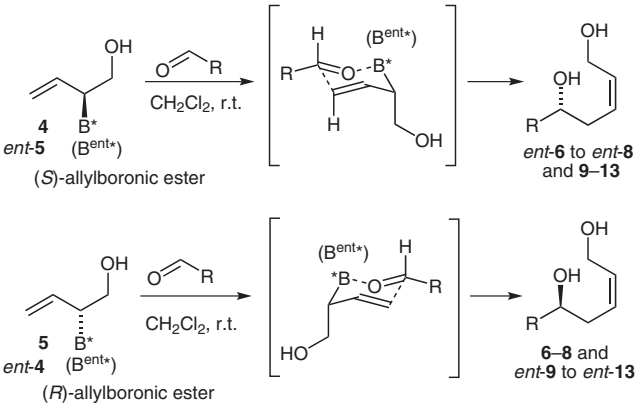
The results of allyl addition of reagents **4**, **5** to various aldehydes **19**–**26** are summarized in Table 1. In all cases the reaction proceeded with excellent diastereoselectivity with respect to the double bond configuration. The diastereomeric ratio was determined by $^1$H NMR analysis of the crude product, and in all cases no *E*-configured byproduct could be detected (dr > 20:1). To ensure full conversion, the reactions were conducted for three days at room temperature. All products were isolated after column chromatography in good (72%, **6**) to excellent (99%, *ent*-**12**) yields. The enantiomeric purities, which were determined by chiral HPLC, were also found to vary from good (91%, **11**) to excellent (99%, **6**) values. In earlier studies it could be shown that the product enantiomeric excess is highly related to the diastereomeric purity of the allylboron reagents **4** and **5**.[9c]

The stereochemical outcome of the allyl addition can be explained by the transition states shown in Scheme 2. It is noteworthy that the allyl addition using allylboronic ester **4** and its diastereomer *ent*-**5** (containing the enantiomeric auxiliary B*ent**) both lead to the same enantiomer of the product **6**–**13**.

**Table 1** Allyl Additions of Allylboron Reagents **4** and **5** to Different Aldehydes **19**–**26**

| Entry | RCHO | Aldehyde | Allylboronate | (*R*)-Product | | | Allylboronate | (*S*)-Product | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Yield[a] (%) | ee (%) | | | Yield[a] (%) | ee (%) |
| 1 | Me | **19** | **5** | **6** | 72 | 99 | **4** | *ent*-**6** | 85 | 98 |
| 2 | PrCHO | **20** | **5** | **7** | 91 | 99 | **4** | *ent*-**7** | 85 | 93 |
| 3 | $Me(CH_2)_4CHO$ | **21** | **5** | **8** | 91 | 95 | **4** | *ent*-**8** | 85 | 94 |
| 4 |  | **22** | *ent*-**5** | **9** | 70 | 94 | *ent*-**4** | *ent*-**9** | 88 | 94 |
| 5 |  | **23** | *ent*-**5** | **10** | 78 | 95 | *ent*-**4** | *ent*-**10** | 92 | 93 |
| 6 |  | **24** | *ent*-**5** | **11** | 85 | 91 | *ent*-**4** | *ent*-**11** | 95 | 97 |
| 7 |  | **25** | **4** | **12** | 93 | 97 | **5** | *ent*-**12** | 99 | 95 |
| 8 |  | **26** | **4** | **13** | 90 | 97 | **5** | *ent*-**13** | 91 | 95 |

[a] Isolated yield after flash column chromatography.




**Scheme 2** Proposed transition states for the allyl addition

With the 2-ene-1,5-diols **6**–**13** in hand we turned our attention towards the synthesis of the 5,6-dihydro-2*H*-pyran-2-one containing natural products **1**–**3** and their derivatives **14**–**18** by means of oxidative ring closure. Therefore 2-ene-1,5-diols **6**–**13** were directly oxidized to the corresponding lactones **1**–**3** and **14**–**21** using an excess of (diacetoxyiodo)benzene and catalytic amounts of 2,2,6,6-tetramethylpyrrolidin-1-oxyl (TEMPO). The results of this reaction, which are summarized in Table 2, vary from moderate (30%, *ent*-**2**) to excellent (98%, *ent*-**3**) yields.

In conclusion we have reported the enantioselective synthesis of both enantiomers of goniothalamin (**1** and *ent*-**1**) and a number of derivatives employing highly stereoselective allyl additions of allylboronic esters **4** and **5** as the source of chirality. The synthesis was short (two steps starting from cinnamaldehyde), efficient [51% for (*R*)-goniothalamin (**1**) and 64% for (*S*)-goniothalamin (*ent*-**1**) overall yield], and highly selective (94% ee for both enantiomers **1** and *ent*-**1**). The success of this total synthesis shows the versatility and viability of the family of α-substituted allylboronic esters. Further applications of these reagents in natural product synthesis are currently under investigation in our laboratories.

Unless otherwise specified the reactions were carried out using standard Schlenk techniques under dry $N_2$ with magnetic stirring. Glassware was oven dried at 120 °C overnight. Solvents were dried and purified by conventional methods prior to use. All reagents were used as purchased from commercial suppliers without further purification. Common solvents for chromatography [petroleum ether (PE) bp 40–60 °C, EtOAc] were distilled prior to use. Flash column chromatography was performed on silica gel 60, 0.040–0.063 mm (230–400 mesh). TLC (monitoring the course of the reaction) was performed on pre-coated plastic sheets with detection by UV (254 nm) and/or by coloration with cerium molybdenum soln [phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), concd $H_2SO_4$ (60 mL), $H_2O$ (940 mL)]. $^1H$ and $^{13}C$ NMR spectra were recorded at r.t. in $CDCl_3$ on a spectrometer at 600 and 151 MHz respectively, relative to internal standard TMS ($^1H$: $\delta_{TMS} = 0.00$) or relative to the resonance of the solvent [$^{13}C$: $\delta(CDCl_3) = 77.0$]. Higher order δ and *J* values are not corrected. $^{13}C$ signals were assigned by means of C, H, COSY and HSQC, or HMBC spectroscopy. Enantiomeric excesses were determined by HPLC analysis using Dionex (UltiMate® 3000) equipped with a Chiralpak IC, 250 × 4.6 mm, Daicel column. Optical rotations were measured using a quartz cell with 1-mL capacity and a 10-cm path length. Melting points are uncorrected. Synthesis of allylboronic esters **4**, **5**, *ent*-**4**, and *ent*-**5** was accomplished according to literature procedures.[9b]

**Addition of Allylboronic Esters 4 and 5 to Aldehydes 19–26; General Procedure A**

Aldehyde **19**–**26** (5.00 equiv) was added to a precooled soln (0 °C) of the allylboronic ester **4**, **5**, *ent*-**4**, or *ent*-**5** (1.00 equiv) in anhyd $CH_2Cl_2$ (0.5 mL/mmol allylboronic ester) before warming to r.t.. The mixture was stirred until full conversion as determined by TLC. The solvent was removed under reduced pressure and the products were purified by column chromatography to afford the allylic alcohols **6**–**13**.

**Oxidation of Allylic Alcohols 6–13 to Lactones 1–3 and 14–18; General Procedure B**

To a soln of alcohols **6**–**13** in $CH_2Cl_2$ were added $PhI(OAc)_2$ (4–6 equiv) and TEMPO (0.2 equiv). The soln was stirred at r.t. until full conversion was determined, and the reaction was quenched with a mixture of sat. aq $NaHCO_3$ (5 mL) and aq 10% $Na_2S_2O_3$ (5 mL). The layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated in vacuo, and purified by column chromatography to afford the lactones **1**–**3** and **14**–**18**.

**(2*Z*,5*R*,6*E*)-7-Phenylhepta-2,6-diene-1,5-diol (9)**

According to general procedure A using allylboronic ester *ent*-**5** (350 mg, 0.65 mmol) and cinnamaldehyde (**21**, 0.25 mL, 1.97 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 99:1) gave **9** (94 mg, 70%) as a colorless oil; 94% ee [HPLC (flow rate 0.5 mL/min, 20% *i*-PrOH–heptane): $t_R$ = 14.7 (**9**), 17.9 min (*ent*-**9**)]; $R_f$ = 0.2 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +83.4 (*c* 0.21, $CHCl_3$).

FT-IR (film): 3332, 3023, 2871, 1494, 1029, 966, 749, 697 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 1.96 (br, 1 H, OH), 2.05 (br, 1 H, OH), 2.45 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 7.4 Hz, $^3J$ = 4.7 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_b$), 2.50 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 8.7 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_a$), 4.15 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_b$), 4.22 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_a$), 4.37 (mc, 1 H, H5), 5.69 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.4 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.1 Hz, $^4J$ = 1.1 Hz, 1 H, H3), 5.91 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.0 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.3 Hz, $^4J$ = 1.3 Hz, 1 H, H2), 6.26 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.4 Hz, 1 H, H6), 6.62 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H7), 7.25 (t, $^3J$ = 7.4 Hz, 1 H, H11), 7.32 (dd, $^3J$ = 7.4 Hz, $^3J$ = 7.4 Hz, 2 H, H10), 7.38 (d, $^3J$ = 7.4 Hz, 2 H, H9).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 35.3 (C4), 57.9 (C1), 71.6 (C5), 126.5 (C9), 127.8 (C11), 128.6 (C3), 128.6 (C10), 130.7 (C7), 131.4 (C6), 131.8 (C2), 136.4 (C8).

MS (EI, 70 eV): *m*/*z* (%) = 186 (9, [(M – $H_2O$)$^+$]), 131 (100, [$C_9H_7O^+$]), 104 (77, [$C_8H_8^+$]), 91 (10, [$C_7H_7^+$]), 77 (13, [$C_6H_5^+$]).

FT-ICR-MS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{16}O_2Na$: 227.1048; found: 227.1043.

**(2*Z*,5*S*,6*E*)-7-Phenylhepta-2,6-diene-1,5-diol (*ent*-9)**

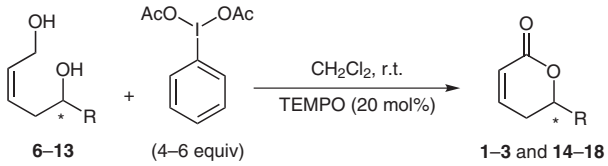
According to general procedure A using allylboronic ester *ent*-**4** (350 mg, 0.65 mmol) and cinnamaldehyde (**21**, 0.25 mL, 1.97 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 99:1) gave *ent*-**9** (118 mg, 88%) as a colorless oil; $[\alpha]_D^{20}$ –85.9 (*c* 0.20, $CHCl_3$), 94% ee. The spectroscopic data are identical with those of diol **9**.

**(2*Z*,5*R*,6*E*)-7-(4-Methoxyphenyl)hepta-2,6-diene-1,5-diol (10)**

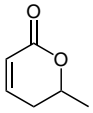
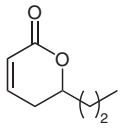
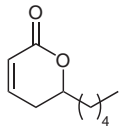
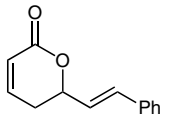
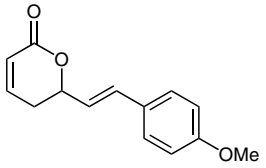
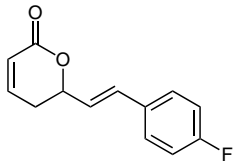
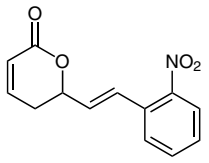
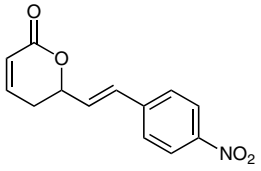
According to general procedure A using allylboronic ester *ent*-**5** (350 mg, 0.65 mmol) and 4-methoxycinnamaldehyde (**22**, 327 mg, 1.97 mmol); after 8 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave **10** (120 mg, 78%) as

**Table 2** Oxidation towards 5,6-Dihydro-2*H*-pyran-2-one Containing Natural Products [(*S*)-Products from Diols *ent*-**6** through *ent*-**13**]




**6–13** (4–6 equiv) **1–3** and **14–18**

| Entry | 1,5-Diol | Product | (*R*)-Product | Yield[a] (%) | (*S*)-Product | Yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 | **6** |  | *ent*-**2** | 30 | **2** | 39 |
| 2 | **7** |  | **14** | 50 | *ent*-**14** | 50 |
| 3 | **8** |  | **3** | 82 | *ent*-**3** | 98 |
| 4 | **9** |  | **1** | 73 | *ent*-**1** | 73 |
| 5 | **10** |  | **15** | 52 | *ent*-**15** | 52 |
| 6 | **11** |  | **16** | 77 | *ent*-**16** | 77 |
| 7 | **12** |  | **17** | 78 | *ent*-**17** | 59 |
| 8 | **13** |  | **18** | 80 | *ent*-**18** | 77 |

[a] Isolated yield after column chromatography.

a colorless solid; mp 58 °C; 95% ee [HPLC (flow rate 0.5 mL/min, 20% *i*-PrOH–heptane): $t_R$ = 22.6 (**10**), 27.6 min (*ent*-**10**)]; $R_f$ = 0.1 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +77.6 (*c* 0.48, $CHCl_3$).

FT-IR (film): 3334, 3013, 2935, 2835, 1607, 1512, 1250, 1175, 1032, 969, 816 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 1.99 (br, 2 H, OH), 2.43 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 7.4 Hz, $^3J$ = 4.7 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_b$), 2.50 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 8.7 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_a$), 3.81 (s, 3 H, $OCH_3$), 4.14 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_b$), 4.22 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_a$), 4.34 (mc, 1 H, H5), 5.69 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.4 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.1 Hz, $^4J$ = 1.1 Hz,

1 H, H3), 5.91 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.0 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.3 Hz, $^4J$ = 1.3 Hz, 1 H, H2), 6.12 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.8 Hz, 1 H, H6), 6.55 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H7), 6.86 (d, $^3J$ = 6.6 Hz, 2 H, H10), 7.32 (d, $^3J$ = 6.6 Hz, 2 H, H9).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 35.3 (C4), 55.3 ($OCH_3$), 57.9 (C1), 71.8 (C5), 114.1 (C10), 127.7 (C9), 128.7 (C3), 129.2 (C6), 129.2 (C8), 130.3 (C7), 131.7 (C2), 159.4 (C11).

MS (EI, 70 eV): *m*/*z* (%) = 216 (10, [(M – $H_2O$)$^+$]), 163 (100, [$C_{10}H_{11}O_2^+$]), 145 (16, [$C_{10}H_9O^+$]), 91 (12, [$C_7H_7^+$]), 77 (8, [$C_6H_5^+$]).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.60; H, 7.66.

**(2*Z*,5*S*,6*E*)-7-(4-Methoxyphenyl)hepta-2,6-diene-1,5-diol (*ent*-10)**

According to general procedure A, allylboronic ester *ent*-**4** (350 mg, 0.65 mmol) and 4-methoxycinnamaldehyde (**22**, 327 mg, 1.97 mmol); after 8 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave *ent*-**10** (142 mg, 92%) as a colorless oil; $[\alpha]_D^{20}$ –84.5 (*c* 0.49, $CHCl_3$); 93% ee. The spectroscopic data are identical with those of diol **10**.

**(2*Z*,5*R*,6*E*)-7-(4-Fluorophenyl)hepta-2,6-diene-1,5-diol (11)**

According to general procedure A using allylboronic ester *ent*-**5** (497 mg, 0.93 mmol) and 4-fluorocinnamaldehyde (**23**, 0.37 mL, 2.80 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave **11** (176 mg, 85%) as a colorless oil; 91% ee [HPLC (flow rate 0.5 mL/min, 10% *i*-PrOH–heptane): $t_R$ = 26.6 (**11**), 29.0 min (*ent*-**11**)]; $R_f$ = 0.1 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +75.0 (*c* 0.52, $CHCl_3$).

FT-IR (film): 3338, 3018, 2932, 2876, 1602, 1509, 1228, 968, 816 cm$^{-1}$.

$^1$H NMR (600 MHz, $CDCl_3$): δ = 1.92 (br, 1 H, OH), 2.08 (br, 1 H, OH), 2.44 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 7.4 Hz, $^3J$ = 4.7 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_b$), 2.49 (dddd, $^2J$ = 14.2 Hz, $^3J$ = 8.7 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.3 Hz, 1 H, $H4_a$), 4.15 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_b$), 4.22 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_a$), 4.35 (mc, 1 H, H5), 5.69 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.4 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.1 Hz, $^4J$ = 1.1 Hz, 1 H, H3), 5.91 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.0 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.3 Hz, $^4J$ = 1.3 Hz, 1 H, H2), 6.17 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.4 Hz, 1 H, H6), 6.58 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H7), 7.01 (dd, $^3J$ = 8.7 Hz, $^3J$ = 8.7 Hz, 2 H, H10), 7.35 (dd, $^3J$ = 8.7 Hz, $^4J$ = 5.3 Hz, 2 H, H9).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 35.3 (C4), 57.9 (C1), 71.5 (C5), 115.6 (d, $^2J_{10,F}$ = 21.4 Hz, C10), 128.0 (d, $^3J_{9,F}$ = 8.2 Hz, C9), 128.6 (C3), 129.5 (C7), 131.1 (C6), 131.9 (C2), 132.6 (d, $^4J_{8,F}$ = 3.3 Hz, C8), 162.4 (d, $^1J_{11,F}$ = 247.0 Hz, C11).

MS (EI, 70 eV): *m*/*z* (%) = 204 (9, [(M – $H_2O$)$^+$]), 151 (100 [$C_9H_8FO^+$]), 149 (30, [$C_9H_6FO^+$]), 133 (48, [$C_9H_6F^+$]), 77 (13 [$C_6H_5^+$]).

Anal. Calcd for $C_{13}H_{15}FO_2$: C, 70.25; H, 6.80. Found: C, 70.28; H, 6.83.

**(2*Z*,5*S*,6*E*)-7-(4-Fluorophenyl)hepta-2,6-diene-1,5-diol (*ent*-11)**

According to general procedure A using allylboronic ester *ent*-**4** (345 mg, 0.65 mmol) and 4-fluorocinnamaldehyde (**23**, 0.26 mL, 1.97 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave *ent*-**11** (136 mg, 95%) as a colorless oil; $[\alpha]_D^{20}$ –79.0 (*c* 0.48, $CHCl_3$); 97% ee. The spectroscopic data are identical with those of diol **11**.

**(2*Z*,5*R*,6*E*)-7-(2-Nitrophenyl)hepta-2,6-diene-1,5-diol (12)**

According to general procedure A using allylboronic ester **4** (320 mg, 0.60 mmol) and 2-nitrocinnamaldehyde (**24**, 318 mg, 1.80 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave **12** (139 mg, 93%) as a colorless oil; 97% ee [HPLC (flow rate 0.5 mL/min, 20% *i*-PrOH–heptane): $t_R$ = 44.4 (**12**), 47.7 min (*ent*-**12**)]; $R_f$ = 0.3 ($CH_2Cl_2$–MeOH, 97:3); $[\alpha]_D^{20}$ +56.7 (*c* 0.93, $CHCl_3$).

FT-IR (film): 3342, 1521, 1345, 967, 742 cm$^{-1}$.

$^1$H NMR (600 MHz, $CDCl_3$): δ = 2.21 (br, 1 H, OH), 2.60 (br, 1 H, OH), 2.45–2.55 (m, 2 H, $H4_a$, $H4_b$), 4.16 (ddd, $^2J$ = 12.4 Hz, $^3J$ = 6.9 Hz, $^4J$ = 0.9 Hz, 1 H, $H1_a$), 4.22 (ddd, $^2J$ = 12.4 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.0 Hz, 1 H, $H1_b$), 4.42 (dddd, $^3J$ = 7.0 Hz, $^3J$ = 6.2 Hz, $^3J$ = 4.6 Hz, $^4J$ = 1.5 Hz, 1 H, H5), 5.69 (ddd, $^3J$ = 11.0 Hz, $^3J$ = 8.0 Hz, $^3J$ = 7.6 Hz, $^4J$ = 1.0 Hz, $^4J$ = 0.9 Hz, 1 H, H3), 5.89–5.95 (m, 1 H, H2), 6.23 (dd, $^3J$ = 15.8 Hz, $^3J$ = 6.2 Hz, 1 H, H6), 7.08 (dd, $^3J$ = 15.8 Hz, $^4J$ = 1.5 Hz, 1 H, H7), 7.40 (ddd, $^3J$ = 8.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.8 Hz, 1 H, H11), 7.55–7.60 (m, 2 H, H12, H13), 7.92 (dd, $^3J$ = 8.3 Hz, $^4J$ = 0.9 Hz, 1 H, H10).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 35.0 (C4), 57.8 (C1), 71.1 (C5), 124.6 (C10), 125.8 (C7), 128.2 (C3), 128.2 (C11), 128.8 and 133.1 (C12, C13), 131.9 (C2), 137.0 (C8), 147.9 (C9).

MS (EI, 70 eV): *m*/*z* (%) = 178 (55, [(M – $C_4H_7O$)$^+$]), 176 (57, [$C_9H_{10}NO_3^+$]), 132 (74, [$C_9H_8O^+$]), 77 (70, [$C_6H_5^+$]).

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07. Found: C, 62.36; H, 6.07.

**(2*Z*,5*S*,6*E*)-7-(2-Nitrophenyl)hepta-2,6-diene-1,5-diol (*ent*-12)**

According to general procedure A using allylboronic ester **5** (320 mg, 0.60 mmol) and 2-nitrocinnamaldehyde (**24**, 318 mg, 1.80 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave *ent*-**12** (148 mg, 99%) as a colorless oil; $[\alpha]_D^{20}$ –56.3 (*c* 0.94, $CHCl_3$); 95% ee. The spectroscopic data are identical with those of diol **12**.

**(2*Z*,5*R*,6*E*)-7-(4-Nitrophenyl)hepta-2,6-diene-1,5-diol (13)**

According to general procedure A using allylboronic ester **4** (377 mg, 0.71 mmol) and 4-nitrocinnamaldehyde (**25**, 375 mg, 2.12 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave **13** (159 mg, 90%) as a yellow solid; mp 85 °C; 97% ee [HPLC (flow rate 0.5 mL/min, 20% *i*-PrOH–heptane): $t_R$ = 34.9 (**13**), 30.8 min (*ent*-**13**)]; $R_f$ = 0.3 ($CH_2Cl_2$–MeOH, 97:3); $[\alpha]_D^{20}$ +129.3 (*c* 0.99, $CHCl_3$).

FT-IR (film): 3329, 2871, 1594, 1509, 1338, 1108, 971, 747 cm$^{-1}$.

$^1$H NMR (600 MHz, $CDCl_3$): δ = 2.16 (br, 1 H, OH), 2.63 (br, 1 H, OH), 2.46–2.54 (m, 2 H, $H4_a$, $H4_b$), 4.16 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 6.9 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_a$), 4.23 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.1 Hz, $^4J$ = 1.3 Hz, 1 H, $H1_b$), 4.43 (dddd, $^3J$ = 5.4 Hz, $^3J$ = 5.4 Hz, $^3J$ = 5.4 Hz, $^4J$ = 1.7 Hz, 1 H, H5), 5.69 (ddddd, $^3J$ = 10.9 Hz, $^3J$ = 7.8 Hz, $^3J$ = 6.6 Hz, $^4J$ = 1.1 Hz, 1 H, H3), 5.93 (ddddd, $^2J$ = 10.9 Hz, $^3J$ = 7.1 Hz, $^3J$ = 6.9 Hz, $^4J$ = 1.5 Hz, $^4J$ = 1.3 Hz, 1 H, H2), 6.45 (dd, $^3J$ = 15.9 Hz, $^3J$ = 5.4 Hz, 1 H, H6), 6.71 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.7 Hz, 1 H, H7), 7.50 (d, $^3J$ = 8.8 Hz, 2 H, H9), 8.20 (d, $^3J$ = 8.8 Hz, 2 H, H10).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 35.2 (C4), 57.1 (C1), 70.8 (C5), 124.1 (C10), 127.0 (C9), 128.1 (C7), 128.4 (C2), 132.0 (C3), 136.5 (C6), 143.1 (C8), 147.0 (C11).

MS (EI, 70 eV): *m*/*z* (%) = 231 (10, [M – $H_2O$]$^+$), 178 (55, [(M – $C_4H_7O$)$^+$]), 132 (68, [$C_9H_8O^+$]), 77 (70, [$C_6H_5^+$]).

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07. Found: C, 62.53; H, 6.09.

**(2*Z*,5*S*,6*E*)-7-(4-Nitrophenyl)hepta-2,6-diene-1,5-diol (*ent*-13)**

According to general procedure A using allylboronic ester **5** (320 mg, 0.60 mmol) and 4-nitrocinnamaldehyde (**25**, 318 mg, 1.80 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 98:2) gave *ent*-**13** (136 mg, 91%) as a colorless oil; $[\alpha]_D^{20}$ –114.7 (*c* 1.00, $CHCl_3$); 95% ee. The spectroscopic data are identical with those of diol **13**.



**(2*Z*,5*R*)-Hex-2-ene-1,5-diol (6)**
According to general procedure A using allylboronic ester **5** (343 mg, 0.64 mmol) and acetaldehyde (**19**, 0.12 mL, 3.32 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave **6** (54 mg, 72%) as colorless oil; 99% ee [HPLC (flow rate 0.5 mL/min, 5% *i*-PrOH–heptane): $t_R$ = 47.2 (*ent*-**6**), 44.5 min (**6**)]; $R_f$ = 0.3 ($CH_2Cl_2$–MeOH, 95:5); $[\alpha]_D^{20}$ –15.0 (*c* 0.20, $CHCl_3$).

FT-IR (film): 3313, 3017, 2968, 2921, 2875, 1737, 1653, 1374, 1125, 1075, 1044, 1006, 939, 843 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 1.24 (d, $^3J$ = 6.2 Hz, 3 H, H6), 1.97 (br, 2 H, OH), 2.25 (dddd, $^2J$ = 14.0 Hz, $^3J$ = 8.7 Hz, $^3J$ = 7.6 Hz, $^4J$ = 1.4 Hz, 1 H, $H4_a$), 2.31 (dddd, $^2J$ = 14.0 Hz, $^3J$ = 7.3 Hz, $^3J$ = 4.3 Hz, $^4J$ = 1.4 Hz, 1 H, $H4_b$), 3.87 (dqd, $^3J$ = 7.6 Hz, $^3J$ = 6.2 Hz, $^3J$ = 4.3 Hz, 1 H, H5), 4.13 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.3 Hz, 1 H, $H1_a$), 4.21 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.3 Hz, 1 H, $H1_b$), 5.65 (dddd, $^3J$ = 11.0 Hz, $^3J$ = 8.7 Hz, $^3J$ = 7.3 Hz, $^4J$ = 1.3 Hz, 1 H, H3), 5.88 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.0 Hz, $^3J$ = 7.0 Hz, $^4J$ = 1.4 Hz, $^3J$ = 1.4 Hz, 1 H, H2).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 23.2 (C6), 36.8 (C4), 57.9 (C1), 66.6 (C5), 129.3 (C3), 131.5 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 98 (6, $[M - H_2O]^+$), 83 (10, $[(M - CH_3O)^+]$), 69 (6, $[(M - C_2H_7O)^+]$), 57 (12, $[(M - C_3H_7O)^+]$), 54 (100, $[(M - C_2H_6O)_2^+]$).

FT-ICR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_6H_{12}O_2Na$: 138.0735; found: 138.0730.

**(2*Z*,5*S*)-Hex-2-ene-1,5-diol (*ent*-6)**
According to general procedure A using allylboronic ester **4** (342 mg, 0.64 mmol) and acetaldehyde (**19**, 0.12 mL, 2.14 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 99:1) gave *ent*-**6** (63 mg, 85%) as a colorless oil; $[\alpha]_D^{20}$ +19.0 (*c* 0.19, $CHCl_3$); 98% ee. The spectroscopic data are identical with those of diol **6**.

**(2*Z*,5*R*)-Oct-2-ene-1,5-diol (7)**
According to general procedure A using allylboronic ester **5** (233 mg, 0.44 mmol) and butanal (**20**, 0.17 mL, 1.89 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave **7** (57 mg, 91%) as a colorless oil; 99% ee [HPLC (flow rate 0.5 mL/min, 5% *i*-PrOH–heptane): $t_R$ = 37.0 (**7**), 38.5 min (*ent*-**7**)]; $R_f$ = 0.3 ($CH_2Cl_2$–MeOH, 95:5); $[\alpha]_D^{20}$ –3.0 (*c* 2.19, $CHCl_3$).

FT-IR (film): 3335, 3017, 2958, 2926, 2870, 1738, 1366, 1217, 1010 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 0.94 (t, $^3J$ = 7.2 Hz, 3 H, H8), 1.32–1.52 (m, 4 H, H6, H7), 2.06 (br, 2 H, OH), 2.28 (m, 2 H, H4), 3.65–3.69 (m, 1 H, H5), 4.12 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 6.9 Hz, $^4J$ = 1.1 Hz, 1 H, $H1_a$), 4.20 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.1 Hz, $^4J$ = 1.3 Hz, 1 H, $H1_b$), 5.66 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 8.6 Hz, $^3J$ = 7.5 Hz, $^4J$ = 1.3 Hz, $^4J$ = 1.1 Hz, 1 H, H3), 5.89 (ddddd, $^3J$ = 11.0 Hz, $^3J$ = 7.1 Hz, $^3J$ = 6.9 Hz, $^4J$ = 1.4 Hz, $^4J$ = 1.4 Hz, 1 H, H2).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 14.0 (C8), 18.9 (C7), 35.0 (C4), 39.3 (C6), 57.8 (C1), 70.4 (C5), 129.5 (C3), 131.5 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 99 (27, $[C_5H_7O_2^+]$), 83 (20, $[C_5H_7O^+]$), 71 (34, $[C_5H_{11}^+]$), 54 (100, $[C_4H_6^+]$).

FT-ICR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_8H_{16}O_2Na$: 167.1048; found: 167.1043.

**(2*Z*,5*S*)-Oct-2-ene-1,5-diol (*ent*-7)**
According to general procedure A using allylboronic ester **4** (354 mg, 0.66 mmol) and butanal (**20**, 0.25 mL, 2.77 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave *ent*-**7** (63 mg, 85%) as a colorless oil; $[\alpha]_D^{20}$ +1.0 (*c* 3.73, $CHCl_3$); 93% ee. The spectroscopic data are identical with those of diol **7**.

**(2*Z*,5*R*)-Dec-2-ene-1,5-diol (8)**
According to general procedure A using allylboronic ester **5** (300 mg, 0.56 mmol) and hexanal (**21**, 0.20 mL, 1.68 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave **8** (88 mg, 91%) as a colorless oil; 95% ee [HPLC (flow rate 0.5 mL/min, 20% *i*-PrOH–heptane): $t_R$ = 13.5 (**8**), 14.3 min (*ent*-**8**)]; $R_f$ = 0.3 ($CH_2Cl_2$–MeOH, 95:5); $[\alpha]_D^{20}$ –3.0 (*c* 0.82, $CHCl_3$).

FT-IR (film): 3329, 2926, 2926, 2859, 1458, 1018 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, $^3J$ = 7.0 Hz, 3 H, H10), 1.25–1.33 (m, 6 H, H7, H8, H9), 1.41–1.50 (m, 2 H, H6), 2.23–2.33 (m, 2 H, H4), 2.80 (br, 2 H, OH), 3.62–3.66 (m, 1 H, H5), 4.09 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 6.8 Hz, $^4J$ = 1.3 Hz, 1 H, $H1_a$), 4.19 (ddd, $^2J$ = 12.3 Hz, $^3J$ = 7.4 Hz, $^4J$ = 1.5 Hz, 1 H, $H1_b$), 5.64 (ddddd, $^3J$ = 11.1 Hz, $^3J$ = 8.6 Hz, $^3J$ = 7.3 Hz, $^4J$ = 1.3 Hz, $^4J$ = 1.3 Hz, 1 H, H3), 5.87 (ddddd, $^3J$ = 11.1 Hz, $^3J$ = 7.4 Hz, $^3J$ = 6.8 Hz, $^4J$ = 1.5 Hz, $^4J$ = 1.5 Hz, 1 H, H2).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 14.0 (C10), 22.6 (C7), 25.4 (C8), 31.8 (C9), 35.0 (C4), 37.1 (C6), 57.6 (C1), 70.7 (C5), 129.6 (C3), 131.3 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 83 (14, $[(M - C_3H_9O)^+]$), 73 (8, $[(M - C_4H_7O)^+]$), 71 (34 $[(M - C_4H_9O)^+]$), 54 (100 $[(M - C_4H_{10}O_2)^+]$).

FT-ICR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{10}H_{20}O_2Na$: 195.1361; found: 195.1356.

**(2*Z*,5*S*)-Dec-2-ene-1,5-diol (*ent*-8)**
According to general procedure A using allylboronic ester **4** (354 mg, 0.66 mmol) and butanal (**21**, 0.25 mL, 2.77 mmol); after 3 d, workup of the reaction followed by column chromatography ($CH_2Cl_2$–MeOH, 95:5) gave *ent*-**8** (63 mg, 85%) as a colorless oil; $[\alpha]_D^{20}$ +1.4 (*c* 1.04, $CHCl_3$); 94% ee. The spectroscopic data are identical with those of diol **8**.

**(*R*)-Goniothalamin (1)**
According to general procedure B using alcohol **9** (80 mg, 0.39 mmol), $PhI(OAc)_2$ (650 mg, 1.98 mmol), and TEMPO (13 mg, 0.08 mmol) in $CH_2Cl_2$ (1.6 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **1** (63 mg, 73%) as colorless solid; mp 83 °C; $R_f$ = 0.2 (PE–EtOAc, 85:15); $[\alpha]_D^{20}$ +167.1 (*c* 0.21, $CHCl_3$) [Lit.[7] $[\alpha]_D^{20}$ +169.8 (*c* 1.45, $CHCl_3$)].

FT-IR (film): 3028, 1722, 1494, 1383, 1245, 1058, 1021, 968, 814, 750, 695 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 2.53–2.56 (m, 2 H, H5), 5.11 (dddd, $^3J$ = 9.1 Hz, $^3J$ = 6.2 Hz, $^3J$ = 6.2 Hz, $^4J$ = 1.3 Hz, 1 H, H6), 6.10 (ddd, $^3J$ = 9.8 Hz, $^4J$ = 1.9 Hz, $^4J$ = 1.9 Hz, 1 H, H3), 6.28 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.2 Hz, 1 H, H7), 6.73 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H8), 6.93 (ddd, $^3J$ = 9.8 Hz, $^3J$ = 4.9 Hz, $^3J$ = 3.6 Hz, 1 H, H4), 7.28 (t, $^3J$ = 7.4 Hz, 1 H, H12), 7.34 (dd, $^3J$ = 7.4 Hz, $^3J$ = 7.4 Hz, 2 H, H11), 7.40 (d, $^3J$ = 7.4 Hz, 2 H, H10).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 29.9 (C5), 78.0 (C6), 121.7 (C3), 125.7 (C7), 126.7 (C10), 128.4 (C12), 128.7 (C11), 133.2 (C8), 135.8 (C9), 144.6 (C4), 163.9 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 200 (61, $[M^+]$), 172 (27, $[(M - CO)^+]$), 131 (28, $[C_9H_7O^+]$), 115 (26), 104 (100, $[C_8H_8^+]$), 91 (42, $[C_7H_7^+]$), 77 (31, $[C_6H_5^+]$), 68 (93).

The analytical data are in full agreement with the reported data.[7,13]

**(*S*)-Goniothalamin (*ent*-1)**
According to general procedure B using alcohol *ent*-**9** (100 mg, 0.49 mmol), $PhI(OAc)_2$ (807 mg, 2.46 mmol), TEMPO (16 mg, 0.10 mmol) in $CH_2Cl_2$ (1.6 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**1**

(71 mg, 73%) as a colorless solid; $[\alpha]_D^{20}$ –166.4 (*c* 0.19, $CHCl_3$). The spectroscopic data are identical with those of enantiomer **1**.

**(*R*)-6-[(*E*)-2-(4-Methoxyphenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (15)**

According to general procedure B using alcohol **10** (100 mg, 0.43 mmol), $PhI(OAc)_2$ (702 mg, 2.14 mmol), and TEMPO (14 mg, 0.09 mmol) in $CH_2Cl_2$ (1.8 mL); after 3 d, workup of the reaction followed by column chromatography (PE–EtOAc, 75:25) gave **15** (51 mg, 52%) as a colorless solid; mp 102 °C; $R_f$ = 0.4 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +140.5 (*c* 0.51, $CHCl_3$).

FT-IR (film): 2935, 1708, 1607, 1515, 1260, 1027, 969, 848, 812 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 2.52–2.55 (m, 2 H, H5), 3.82 (s, 3 H, $OCH_3$), 5.08 (dddd, $^3J$ = 9.1 Hz, $^3J$ = 6.6 Hz, $^3J$ = 6.6 Hz, $^4J$ = 1.3 Hz, 1 H, H6), 6.09 (ddd, $^3J$ = 9.8 Hz, $^4J$ = 1.9 Hz, $^4J$ = 1.9 Hz, 1 H, H3), 6.14 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.6 Hz, 1 H, H7), 6.67 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H8), 6.87 (d, $^3J$ = 8.7 Hz, 2 H, H11), 6.92 (ddd, $^3J$ = 9.8 Hz, $^3J$ = 4.5 Hz, $^3J$ = 4.0 Hz, 1 H, H4), 7.34 (d, $^3J$ = 8.7 Hz, 2 H, H10).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 30.0 (C5), 55.3 ($OCH_3$), 78.3 (C6), 114.1 (C11), 121.7 (C3), 123.4 (C7), 128.0 (C10), 128.5 (C9), 132.9 (C8), 144.6 (C4), 159.8 (C12), 164.0 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 230 (73, $[M^+]$), 202 (5, $[(M - CO)^+]$), 185 (21, $[(M - CHO_2)^+]$), 162 (42), 161 (41, $[C_{10}H_9O_2^+]$), 134 (100, $[C_9H_{10}O^+]$), 121 (41, $[C_8H_9O^+]$), 91 (18, $[C_7H_7^+]$).

The analytical data are in full agreement with the reported data.[2f,g]

**(*S*)-6-[(*E*)-2-(4-Methoxyphenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (*ent*-15)**

According to general procedure B using alcohol *ent*-**10** (100 mg, 0.43 mmol), $PhI(OAc)_2$ (702 mg, 2.14 mmol), and TEMPO (14 mg, 0.09 mmol) in $CH_2Cl_2$ (1.8 mL); after 3 d, workup of the reaction followed by column chromatography (PE–EtOAc, 75:25) gave *ent*-**15** (51 mg, 52%) as a colorless solid; $[\alpha]_D^{20}$ –141.7 (*c* 0.35, $CHCl_3$) [Lit.[2f] $[\alpha]_D^{25}$ –133.7 (*c* 1.02, $CHCl_3$)]. The spectroscopic data are identical with those of enantiomer **15**.

**(*R*)-6-[(*E*)-2-(4-Fluorophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (16)**

According to general procedure B using alcohol **11** (100 mg, 0.45 mmol), $PhI(OAc)_2$ (740 mg, 2.25 mmol), and TEMPO (15 mg, 0.09 mmol) in $CH_2Cl_2$ (1.9 mL); after 3 d, workup of the reaction followed by column chromatography (PE–EtOAc, 75:25) gave **16** (75 mg, 77%) as a colorless solid; mp 128 °C; $R_f$ = 0.4 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +156.8 (*c* 0.49, $CHCl_3$).

FT-IR (film): 3043, 2916, 1713, 1600, 1508, 1417, 1380, 1246, 1228, 1053, 1014, 972, 849, 821 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 2.53–2.65 (m, 2 H, H5), 5.09 (dddd, $^3J$ = 9.3 Hz, $^3J$ = 6.3 Hz, $^3J$ = 6.3 Hz, $^4J$ = 1.3 Hz, 1 H, H6), 6.10 (ddd, $^3J$ = 9.8 Hz, $^4J$ = 2.3 Hz, $^4J$ = 1.5 Hz, 1 H, H3), 6.19 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.3 Hz, 1 H, H7), 6.70 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H8), 6.93 (ddd, $^3J$ = 9.8 Hz, $^3J$ = 4.9 Hz, $^3J$ = 3.6 Hz, 1 H, H4), 7.03 (dd, $^3J$ = 8.7 Hz, $^3J$ = 8.7 Hz, 2 H, H11), 7.37 (d, $^3J$ = 8.7 Hz, $^4J$ = 5.3 Hz, 2 H, H10).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 29.9 (C5), 77.8 (C6), 115.7 (d, $^2J_{11,F}$ = 21.7 Hz, C11), 121.7 (C3), 125.4 (C7), 128.3 (d, $^3J_{10,F}$ = 8.2 Hz, C10), 132.0 (d, $^4J_{9,F}$ = 3.4 Hz, C9), 132.0 (C8), 144.6 (C4), 162.7 (d, $^1J_{12,F}$ = 247.9 Hz, C12), 163.8 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 218 (51 $[M^+]$), 190 (31, $[(M - CO)^+]$), 149 (24, $[C_9H_6FO^+]$), 122 (100, $[C_8H_7F^+]$), 68 (91, $C_4H_2F^+$).

Anal. Calcd for $C_{13}H_{11}FO_2$: C, 71.55; H, 5.08. Found: C, 71.38; H, 5.15.

The analytical data are in full agreement with the reported data.[2f]

**(*S*)-6-[(*E*)-2-(4-Fluorophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (*ent*-16)**

According to general procedure B using alcohol *ent*-**11** (100 mg, 0.45 mmol), $PhI(OAc)_2$ (740 mg, 2.25 mmol), and TEMPO (15 mg, 0.09 mmol) in $CH_2Cl_2$ (1.8 mL); after 3 d, workup of the reaction followed by column chromatography (PE–EtOAc, 75:25) gave *ent*-**16** (76 mg, 77%) as a colorless solid; $[\alpha]_D^{20}$ –160.1 (*c* 0.51, $CHCl_3$) [Lit.[2f] $[\alpha]_D^{25}$ –158.0 (*c* 1.00, $CHCl_3$)]. The spectroscopic data are identical with those of enantiomer **16**.

**(*R*)-6-[(*E*)-2-(2-Nitrophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (17)**

According to general procedure B using alcohol **12** (111 mg, 0.45 mmol), $PhI(OAc)_2$ (732 mg, 2.25 mmol), and TEMPO (14 mg, 0.09 mmol) in $CH_2Cl_2$ (1.9 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **17** (85 mg, 78%) as a yellow solid; mp 78 °C; $R_f$ = 0.3 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +134.4 (*c* 1.01, $CHCl_3$).

FT-IR (film): 3027, 2338, 1721, 1520, 1344, 1243, 1059, 1023, 964, 812 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 2.55–2.65 (m, 2 H, H5), 5.16 (dddd, $^3J$ = 10.2 Hz, $^3J$ = 6.4 Hz, $^3J$ = 5.1 Hz, $^4J$ = 1.3 Hz, 1 H, H6), 6.11 (ddd, $^3J$ = 9.9 Hz, $^4J$ = 1.5 Hz, $^4J$ = 1.3 Hz, 1 H, H3), 6.26 (dd, $^3J$ = 15.9 Hz, $^3J$ = 6.4 Hz, 1 H, H7), 6.95 (ddd, $^3J$ = 9.9 Hz, $^3J$ = 5.4 Hz, $^3J$ = 3.0 Hz, 1 H, H4), 7.20 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.3 Hz, 1 H, H8), 7.46 (ddd, $^3J$ = 8.2 Hz, $^3J$ = 8.2 Hz, $^4J$ = 1.7 Hz, 1 H, H12), 7.59–7.63 (m, 2 H, H13, H14), 7.99 (dd, $^3J$ = 8.2 Hz, $^4J$ = 1.7 Hz, 1 H, H11).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 25.9 (C5), 77.5 (C6), 121.6 (C3), 124.7 (C11), 128.8 (C8), 128.9 (C12), 130.0 and 133.4 (C13, C14), 131.0 (C7), 131.8 (C9), 144.5 (C4), 147.8 (C10), 163.5 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 97 (64, $[C_5H_5O_2^+]$), 68 (100, $C_4H_4O^+$).

Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52. Found: C, 63.59; H, 4.56.

The analytical data are in full agreement with the reported data.[10]

**(*S*)-6-[(*E*)-2-(2-Nitrophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (*ent*-17)**

According to general procedure B using alcohol *ent*-**12** (120 mg, 0.48 mmol), $PhI(OAc)_2$ (792 mg, 2.41 mmol), and TEMPO (16 mg, 0.10 mmol) in $CH_2Cl_2$ (2.0 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**17** (70 mg, 59%) as a colorless solid; $[\alpha]_D^{20}$ –128.6 (*c* 1.03, $CHCl_3$). The spectroscopic data are identical with those of enantiomer **17**.

**(*R*)-6-[(*E*)-2-(4-Nitrophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (18)**

According to general procedure B using alcohol **13** (95 mg, 0.38 mmol), $PhI(OAc)_2$ (627 mg, 1.91 mmol), and TEMPO (12 mg, 0.08 mmol) in $CH_2Cl_2$ (1.6 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **18** (74 mg, 80%) as a yellow solid; mp 125 °C; $R_f$ = 0.3 (PE–EtOAc, 60:40); $[\alpha]_D^{20}$ +196.2 (*c* 1.03, $CHCl_3$).

FT-IR (film): 3032, 1721, 1594, 1509, 1340, 1246, 1107, 1089, 979, 822 $cm^{-1}$.

$^1H$ NMR (600 MHz, $CDCl_3$): δ = 2.55 (dddd, $^2J$ = 18.3 Hz, $^3J$ = 10.7 Hz, $^3J$ = 2.8 Hz, $^4J$ = 2.5 Hz, 1 H, $H5_a$), 2.62 (dddd, $^2J$ = 18.3 Hz, $^3J$ = 5.7 Hz, $^3J$ = 4.5 Hz, $^4J$ = 1.2 Hz, 1 H, $H5_b$), 5.17 (dddd, $^3J$ = 10.7 Hz, $^3J$ = 5.7 Hz, $^3J$ = 4.5 Hz, $^4J$ = 1.5 Hz, 1 H, H6), 6.12 (ddd, $^3J$ = 9.7 Hz, $^4J$ = 2.5 Hz, $^4J$ = 1.2 Hz, 1 H, H3), 6.45 (dd, $^3J$ = 15.9 Hz, $^3J$ = 5.7 Hz, 1 H, H7), 6.84 (dd, $^3J$ = 15.9 Hz, $^4J$ = 1.5 Hz, 1 H, H8), 6.96 (ddd, $^3J$ = 9.7 Hz, $^3J$ = 5.7 Hz, $^3J$ = 2.8 Hz, 1 H, H4), 7.50 (d, $^3J$ = 9.0 Hz, 2 H, H10), 8.20 (d, $^3J$ = 9.0 Hz, 2 H, H11).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ = 29.6 (C5), 77.0 (C6), 121.7 (C3), 124.1 (C11), 127.3 (C10), 130.2 (C7), 130.5 (C8), 142.4 (C9), 144.4 (C4), 147.4 (C12).

MS (EI, 70 eV): *m*/*z* (%) = 245 (35 [$M^+$]), 217 (31, [(M – CO)$^+$]), 149 (24, [$C_8H_7NO_2^+$]), 68 (100, $C_4H_4O^+$).

Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52. Found: C, 63.59; H, 4.56.

The analytical data are in full agreement with the reported data.[2f]

**(*S*)-6-[(*E*)-2-(4-Nitrophenyl)ethenyl]-5,6-dihydro-2*H*-pyran-2-one (*ent*-18)**

According to general procedure B using alcohol *ent*-**13** (100 mg, 0.40 mmol), $PhI(OAc)_2$ (656 mg, 2.00 mmol), and TEMPO (13 mg, 0.08 mmol) in $CH_2Cl_2$ (1.7 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**18** (76 mg, 77%) as a colorless solid; $[\alpha]_D^{20}$ –191.6 (*c* 1.04, $CHCl_3$) [Lit.[2f] $[\alpha]_D^{25}$ –205.0 (*c* 1.0, $CHCl_3$)]. The spectroscopic data are identical with those of enantiomer **18**.

**(*S*)-Parasorbic Acid [(*S*)-6-Methyl-5,6-dihydro-2*H*-pyran-2-one] (2)**

According to general procedure B using alcohol *ent*-**6** (58 mg, 0.50 mmol), $PhI(OAc)_2$ (823 mg, 2.50 mmol), and TEMPO (16 mg, 0.10 mmol) in $CH_2Cl_2$ (2.2 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **2** (17 mg, 30%) as a colorless oil; $[\alpha]_D^{20}$ +156.8 (*c* 0.49, $CHCl_3$); $R_f$ = 0.3 (PE–EtOAc, 70:30).

$^1$H NMR (600 MHz, $CDCl_3$): δ = 1.44 (d, $^3J$ = 6.4 Hz, 3 H, H7), 2.30 (dddd, $^2J$ = 18.3 Hz, $^3J$ = 11.3 Hz, $^4J$ = 2.6 Hz, $^3J$ = 2.6 Hz, 1 H, $H5_a$), 2.37 (dddd, $^2J$ = 18.3 Hz, $^4J$ = 5.9 Hz, $^3J$ = 4.2 Hz, $^3J$ = 1.1 Hz, 1 H, $H5_b$), 4.57 (dqd, $^3J$ = 11.3 Hz, $^3J$ = 6.4 Hz, $^3J$ = 4.2 Hz, 1 H, H6), 6.03 (ddd, $^3J$ = 9.7 Hz, $^3J$ = 2.6 Hz, $^3J$ = 1.1 Hz, 1 H, H4), 6.87 (ddd, $^3J$ = 9.7 Hz, $^4J$ = 5.9 Hz, $^4J$ = 2.6 Hz, 1 H, H3).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 20.8 (C7), 31.0 (C5), 74.4 (C6), 121.4 (C3), 144.9 (C4), 164.6 (C2).

The analytical data are in full agreement with the reported data.[4a,11]

**(*R*)-6-Methyl-5,6-dihydro-2*H*-pyran-2-one (*ent*-2)**

According to general procedure B using alcohol **6** (41 mg, 0.29 mmol), $PhI(OAc)_2$ (397 mg, 1.21 mmol), and TEMPO (8 mg, 0.05 mmol) in $CH_2Cl_2$ (1.1 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**2** (16 mg, 39%) as a colorless oil; $[\alpha]_D^{20}$ –160.1 (*c* 0.51, $CHCl_3$). The spectroscopic data are identical with those of enantiomer **2**.

**(*R*)-6-Propyl-5,6-dihydro-2*H*-pyran-2-one (14)**

According to general procedure B using alcohol *ent*-**7** (71 mg, 0.49 mmol), $PhI(OAc)_2$ (678 mg, 2.06 mmol), and TEMPO (14 mg, 0.17 mmol) in $CH_2Cl_2$ (1.8 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **14** (35 mg, 50%) as a colorless solid; $R_f$ = 0.5 (PE–EtOAc, 70:30); $[\alpha]_D^{20}$ –109.1 (*c* 0.63, $CHCl_3$).

FT-IR (film): 2960, 2931, 2875, 2298, 1716, 1467, 1421, 1386, 1245, 1158, 1114, 1069, 1028, 960, 920, 814, 743, 662 cm$^{-1}$.

$^1$H NMR (600 MHz, $CDCl_3$): δ = 0.96 (t, $^3J$ = 7.3 Hz, 3 H, H9), 1.45 (ddqd, $^2J$ = 14.5 Hz, $^3J$ = 10.2 Hz, $^3J$ = 7.3 Hz, $^3J$ = 5.8 Hz, 1 H, $H8_a$), 1.55 (ddqd, $^2J$ = 14.5 Hz, $^3J$ = 10.0 Hz, $^3J$ = 7.3 Hz, $^3J$ = 5.2 Hz, 1 H, $H8_b$), 1.62 (dddd, $^2J$ = 13.7 Hz, $^3J$ = 10.0 Hz, $^3J$ = 5.8 Hz, $^3J$ = 5.3 Hz, 1 H, $H7_a$), 1.80 (dddd, $^2J$ = 13.7 Hz, $^3J$ = 10.2 Hz, $^3J$ = 7.5 Hz, $^3J$ = 5.2 Hz, 1 H, $H7_b$), 2.28–2.38 (m, 2 H, H5), 4.44 (dddd, $^3J$ = 10.3 Hz, $^3J$ = 7.5 Hz, $^3J$ = 5.3 Hz, $^3J$ = 5.1 Hz, 1 H, H6), 6.02 (ddd, $^3J$ = 9.7 Hz, $^4J$ = 2.5 Hz, $^4J$ = 1.3 Hz, 1 H, H3), 6.88 (ddd, $^3J$ = 9.7 Hz, $^3J$ = 5.5 Hz, $^3J$ = 2.8 Hz, 1 H, H4).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 13.8 (C9), 18.1 (C8), 29.4 (C5), 36.9 (C7), 77.7 (C6), 121.5 (C3), 145.0 (C4), 164.6 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 97 (100, [(M – $C_3H_7$)$^+$]), 68 (73, [(M – $C_4H_8O$)$^+$]).

The analytical data are in full agreement with the reported data.[11b]

**(*S*)-6-Propyl-5,6-dihydro-2*H*-pyran-2-one (*ent*-14)**

According to general procedure B using alcohol **8** (71 mg, 0.49 mmol), $PhI(OAc)_2$ (678 mg, 2.06 mmol), and TEMPO (14 mg, 0.17 mmol) in $CH_2Cl_2$ (1.8 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**14** (35 mg, 50%) as a colorless solid; $[\alpha]_D^{20}$ +135.1 (*c* 1.66, $CHCl_3$) [Lit.[11b] $[\alpha]_D^{22}$ +130.0 (*c* 1.20, $CHCl_3$)]. The spectroscopic data are identical with those of enantiomer **14**.

**Massoia Lactone [(*R*)-6-Pentyl-5,6-dihydro-2*H*-pyran-2-one] (3)**

According to general procedure B using alcohol **8** (50 mg, 0.29 mmol), $PhI(OAc)_2$ (636 mg, 1.94 mmol), and TEMPO (10 mg, 0.06 mmol) in $CH_2Cl_2$ (1.7 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave **3** (40 mg, 82%) as a colorless solid; $R_f$ = 0.5 (PE–EtOAc, 70:30) $[\alpha]_D^{20}$ –112.5 (*c* 0.65, $CHCl_3$) [Lit.[12] $[\alpha]_D^{25}$ –115.6 (*c* 1.00, $CHCl_3$)].

FT-IR (film): 2931, 2861, 1712, 1467, 1386, 1248, 1037, 813 cm$^{-1}$.

$^1$H NMR (600 MHz, $CDCl_3$): δ = 0.90 (t, $^3J$ = 6.9 Hz, 3 H, H11), 1.28–1.35 (m, 4 H, H9, H10), 1.37–1.44 (m, 1 H, $H8_a$), 1.49–1.55 (m, 1 H, $H8_b$), 1.64 (dddd, $^2J$ = 13.9 Hz, $^3J$ = 10.4 Hz, $^3J$ = 5.4 Hz, $^3J$ = 5.2 Hz, 1 H, $H7_a$), 1.80 (dddd, $^2J$ = 13.9 Hz, $^3J$ = 10.4 Hz, $^3J$ = 7.4 Hz, $^3J$ = 5.2 Hz, 1 H, $H7_b$), 2.28–2.38 (m, 2 H, H5), 4.42 (dddd, $^3J$ = 10.4 Hz, $^3J$ = 7.4 Hz, $^3J$ = 5.4 Hz, $^3J$ = 5.2 Hz, 1 H, H6), 6.02 (ddd, $^3J$ = 9.8 Hz, $^4J$ = 2.5 Hz, $^4J$ = 1.3 Hz, 1 H, H3), 6.88 (ddd, $^3J$ = 9.8 Hz, $^3J$ = 5.5 Hz, $^3J$ = 3.0 Hz, 1 H, H4).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ = 14.0 (C11), 22.5 (C10), 24.5 (C8), 29.4 (C5), 31.6 (C9), 34.8 (C7), 78.0 (C6), 121.5 (C3), 145.0 (C4), 164.6 (C2).

MS (EI, 70 eV): *m*/*z* (%) = 97 (100, [(M – $C_5H_{11}$)$^+$]), 68 (90, [(M – $C_6H_{12}O$)$^+$]).

The analytical data are in full agreement with the reported data.[12]

**(*S*)-6-Pentyl-5,6-dihydro-2*H*-pyran-2-one (*ent*-3)**

According to general procedure B using alcohol *ent*-**8** (46 mg, 0.27 mmol), $PhI(OAc)_2$ (581 mg, 1.77 mmol), and TEMPO (10 mg, 0.06 mmol) in $CH_2Cl_2$ (1.7 mL); after 1 d, workup of the reaction and column chromatography (PE–EtOAc, 75:25) gave *ent*-**3** (44 mg, 98%) as a colorless oil; $[\alpha]_D^{20}$ +113.1 (*c* 0.65, $CHCl_3$). The spectroscopic data are identical with those of enantiomer **3**.

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