A Novel Palladium-Catalyzed Asymmetric Cyclocarbonylation of Allylic Alcohols to γ-Butyrolactones

Wing-Yiu Yu, Corinne Bensimon, and Howard Alper*

Abstract: A catalyst system based on $[Pd_2(dba)_3]\cdot CHCl_3$/(−)-BPPM has been found to effect asymmetric cyclocarbonylation of certain prochiral allylic alcohols to produce good yields of optically enriched γ-butyrolactones. The reaction was performed under an atmosphere of H_2 (400 psi) and CO (400 psi) at 100 °C in methylene chloride for 48 hours. Asymmetric cyclocarbonylation of allylic alcohols with aliphatic substituents proceeded with moderate enantioselectivities (*ee* = 25–43%). However, enantiomeric excesses of up to 83% were obtained for substrates containing aromatic substituents, in which case the *ee* was found to be more sensitive to steric, rather than to electronic factors. Recrystallization of the lactones containing an aromatic group from a mixture of CH_2Cl_2/Et_2O/hexanes (0.5/1.0/8.5), by slow evaporation of the solvent or at low temperature, improved the enantiopurities to >98% *ee* on a reproducible basis. The asymmetric center of the aromatic lactones was assigned the (*S*)-configuration based on the X-ray crystal structure analysis of enantiopure (*S*)-(+)-3,3-dimethyl-2-(2′-methylphenyl)-γ-butyrolactone (**2k**). A hydridopalladium intermediate is believed to play a key role in this reaction. Enantioselectivity is thought to be brought about by the preferential formation of **6b**. The carbon skeleton of **6b** fits into the chiral scaffold of (−)-BPPM.

Keywords
asymmetric synthesis · butyrolactones · carbonylations · catalyst system · palladium

Introduction

The transition metal catalyzed carbonylation of organic substrates represents one of the most efficient ways of homologation.[1] Since chiral transition metal catalysts are known to produce a large quantity of optically active molecules from minute amounts of chiral materials (chirality amplification[2]), there has been intensive research on the potential application of asymmetric hydroformylation or hydrocarboxylation of prochiral olefinic substrates for the manufacture of useful pharmaceuticals such as (*S*)-naproxen. Whilst the transition metal catalyzed cyclocarbonylation of unsaturated alcohols is well documented in the literature,[3, 4] there are, to our knowledge, few examples[4c] demonstrating the application of this reaction to asymmetric lactonization using chiral transition metal complexes. Since the OH group is close to the C=C bond, coordination of the OH unit to the chiral metal center may lead to a more organized transition state, and thus enhance enantiodiscrimination. The preparation of optically active γ-butyrolactones has attracted substantial interest, primarily because of their synthetic usefulness for the construction of biologically active molecules.[5]

We have previously reported the cyclocarbonylation of allylic alcohols to γ-butyrolactones in the presence of catalytic amounts of $[Pd_2(dba)_3]\cdot CHCl_3$ (dba = *trans,trans*-dibenzylideneacetone) and 1,4-bis(diphenylphosphino)butane (dppb) in DME at 190 °C.[4d] In order to develop an efficient asymmetric catalytic reaction, it is essential to find a suitable ligand for asymmetric induction as well as carbonylation. For efficient chirality transfer from the chiral diphosphine ligand to the prochiral substrate, the chiral ligand should possess a rigid carbon skeleton; paradoxically, however, a flexible metal–ligand chelate framework is necessary for efficient carbonylation. It has already been demonstrated that the yield of the γ-lactones obtained from the above-mentioned reaction decreased in the order dppb > dppp ≫ dppe (where dppp = 1,3-bis(diphenylphosphino)propane, dppe = 1,2-bis(diphenylphosphino)ethane), which corresponds to the flexibility of the metal-chelate ring. This agrees with the rate of carbon monoxide insertion into the methyl–palladium bond for complexes containing diphosphine ligands, which was found to decrease in the same order.[6]

Phosphinopyrrolidine-rhodium catalysts have proven to be useful for the asymmetric hydrogenation of dehydroamino acids with enantiomeric excesses exceeding 90%.[7] Stille and co-workers have found that the platinum catalyst containing (−)-BPPM (Figure 1)—$[((-)\text{-bppm})PtCl_2]/SnCl_2$ and its polymer-supported analogue[8]—are useful for the asymmetric hydroformylation of a variety of prochiral olefins. Because the phosphine units of (−)-BPPM are structurally very similar to

[*] Prof. H. Alper, Dr. W.-Y. Yu, Dr. C. Bensimon[+]
Department of Chemistry, University of Ottawa
10 Marie Curie, Ottawa, Ontario, K1N 6N5 (Canada)
Fax: Int. code +(613) 562-5871

[+] X-Ray analysis.

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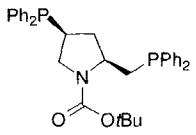
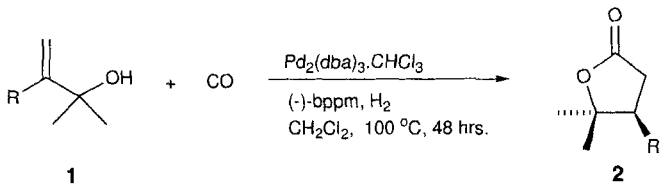


Figure 1. (−)-BPPM.

those of dppb, which was used as a ligand for our palladium-catalyzed intramolecular cyclocarbonylation reactions, we anticipated that (−)-BPPM would exhibit significant chiral discrimination in the palladium-catalyzed synthesis of lactones. We now report the catalytic asymmetric cyclocarbonylation of allylic alcohols to give optically active γ-butyrolactones using $[Pd_2(dba)_3]\cdot CHCl_3$/(−)-BPPM as the catalyst.

Results and Discussion

The allylic alcohols (**1a**–**p**, Scheme 1) employed in this study were generally prepared by electrophilic quenching of vinyllithium reagents with the appropriate carbonyl compound. The vinyllithium compounds leading to **1b**, **1c**, and **1d** were generated by a halogen–metal exchange reaction with *tert*-butyllithium from the corresponding vinyl bromide in THF at −98 °C; **1g** and **3** were prepared by a Grignard reaction; the remainder were obtained by means of the Shapiro reaction.



1

a, R = Me
b, R = *n*Bu
c, R = *n*Hex
d, R = nC_8H_{17}
e, R = *c*Hex
f, R = 1-adamantyl
g, R = Ph
h, R = *p*-$MeOC_6H_4$
i, R = *m*-$MeOC_6H_4$
j, R = *p*-MeC_6H_4
k, R = *o*-MeC_6H_4
l, R = *o*-FC_6H_4
m, R = *p*-ClC_6H_4
n, R = *o*-ClC_6H_4
o, R = 2-naphthyl
p, R = 1-naphthyl

2

Scheme 1. Palladium-catalyzed asymmetric cyclocarbonylation of allylic alcohols.

By treatment of the allylic alcohols **1** with carbon monoxide (400 psi) and dihydrogen (400 psi) together with $[Pd_2(dba)_3]\cdot CHCl_3$ and (−)-BPPM in dichloromethane, cyclocarbonylation could be brought about at 100 °C to afford the γ-lactones **2**, usually in excellent yield. The results for the cyclocarbonylation of certain aliphatic and aromatic alcohols catalyzed by $[Pd_2(dba)_3]\cdot CHCl_3$ and (−)-BPPM (Scheme 1) are given in Table 1.

Palladium complexes such as $[Pd(PhCN)_2Cl_2]$, $[Pd(PPh_3)_2Cl_2]$ and $[(Pd(MeCN)_4)(BF_4)_2]$ were completely inactive, whereas the $[\{Pd(\eta^3\text{-2-methallyl})Cl\}_2]$ dimer produced results identical (in both chemical yield and enantioselectivity) to those obtained with $[Pd_2(dba)_3]\cdot CHCl_3$. In the case of $[Pd(OAc)_2]$, an excess of (−)-BPPM (2 equiv relative to Pd) is required in order to effect any reaction with comparable yield and *ee*. The presence of a hydrogen atmosphere is essential in order to obtain lactones in good yield. In the presence of carbon monoxide alone, 90% of the allylic alcohol was recovered, and the yield of the lactone was less than 8%. In addition to H_2, dimethylphenylsilane was also found to be equally effective for this transformation; the silane was fully recovered after the reaction.

Table 1. Palladium-catalyzed asymmetric cyclocarbonylation using (−)-BPPM as the ligand.

Entry	Alcohol	Lactone	Yield (%) [a,b]	*ee* (%) [c,f]
1	**1a**	**2a**	96	27
2	**1b**	**2b**	90	45
3	**1c**	**2c**	87	41
4	**1d**	**2d**	84 [e]	38
5	**1e**	**2e**	85	39
6	**1f**	**2f**	84 [e]	25
7	**1g**	**2g** [d]	86	81
8	**1h**	**2h**	85	65
9	**1i**	**2i**	82	71
10	**1j**	**2j**	84	69
11	**1k**	**2k** [d]	82	84
12	**1l**	**2l**	56	67
13	**1m**	**2m** [d]	75	80
14	**1n**	**2n**	64	83
15	**1o**	**2o**	83	69
16	**1p**	**2p**	86	79

[a] Isolated yield. [b] All products gave satisfactory elemental analyses, and ^1H NMR, ^{13}C NMR, and IR spectra. [c] The optical purity of the products was determined by ^1H NMR spectroscopy with the use of the chiral shift reagent, Eu(hfc)$_3$. [d] *ee* > 98% for **2g**, **2k**, and **2m** after recrystallization, whereas *ee* = 87% for **8b**. [e] These substrates required a prolonged reation time of 7 days for complete conversion. [f] Lactones **2g**–**2p** have a positive sign of rotation and the (*S*) configuration was assigned; **2a**–**2f** gave a negative sign of rotation and the configuration was not determined.

Whilst allylic alcohols bearing aliphatic substituents (**1a**–**1f**) produced lactones with modest enantiomeric excesses (25–45%, entries 1–6), we were pleased to discover that alcohols containing an aromatic substituent gave lactones in up to 84% *ee*. For example, carbonylation of **1g** (R = Ph) in the presence of the Pd/(−)-BPPM catalyst system afforded **2g** in 81% *ee*. Importantly, recrystallization of the lactones **2g**, **2k**, and **2m** from CH_2Cl_2/Et_2O/hexanes (0.5/1.0/8.5), by slow evaporation of the solvent, or at low temperature (−20 °C), improved the enantiopurity to >98% on a *reproducible* basis.[9] Other chiral diphosphine ligands, for example, (+)-DIOP, (+)-BINAP, and (−)-*p*-tol-BINAP, showed poorer enantioselectivity with **1g** as the substrate (see Table 2). No carbonylation occurred—i.e., the starting material was recovered—when the palladium-catalyzed reaction was performed in the presence of (−)-CHIRAPHOS, (+)-PROPHOS, or (−)-Me-DUPHOS.

Table 2. Palladium-catalyzed asymmetric cyclocarbonylation of **1g** to give **2g**.

Entry	Ligand	Yield (%)	*ee* (%)
1	(+)-BINAP	91	31
2	(−)-*p-tol*-BINAP	86	15
3	(−)-BPPM	86	81
4	(+)-DIOP	79	45
5	(−)-CHIRAPHOS	–	–
6	(−)-Me-DUPHOS	–	–
7	(+)-PROPHOS	–	–

In the reactions catalyzed by $[Pd_2(dba)_3]$/(−)-BPPM, conversion of the substrate was lower in solvents such as THF and benzene, although enantioselectivity was unimpaired; the reaction was completely inhibited in DMF. The reactivity of the allylic alcohols was enhanced by the presence of an allylic substituent (at least one substituent is required for successful lactonization; the *gem*-dialkyl effect).[10] A primary alcohol, such as 2-phenyl-2-propen-1-ol, did not afford any lactone under

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typical carbonylation conditions, and the substrate was fully recovered.

For aromatic substrates, the *ee* was quite insensitive to the electronic substituent effect. However, substituents at the *ortho* position (e.g. **2k**, **2n**) gave a slightly higher *ee* than *para* substituents (c.f. *ee* of **2h**, **2j**, **2m**), probably for steric reasons. Among the aliphatic allylic alcohols (**1a–f**), the aliphatic alcohol bearing the *n*Bu group, **1b**, appears to be the optimum substrate for the Pd/(−)-BPPM catalyzed asymmetric carbonylation as far as the *ee* is concerned. Alcohols containing sterically more demanding R groups reacted with much lower enantioselectivities (see entries 2–6). Indeed, alcohols **1d** (R = n-C_8H_{17}) and **1f** (R = 1-adamantyl), required 7 days for complete reaction. In the aromatic lactones **2g–p** the same enantiomer predominates, according to the changes in their ^{1}H NMR spectra on exposure to the shift reagent Eu(hfc)$_3$ and to their rotation of plane-polarized light. The asymmetric center was assigned the (*S*) configuration on the basis of a single crystal X-ray diffraction study of **2k** (R = *o*-tolyl) (Figure 2).[11] The pertinent crystallographic data are given in Table 3.

When racemic **3** was subjected to carbonylation with the Pd/(−)-BPPM catalyst, a 1:1 mixture of *syn* and *anti* lactones[12] was formed without diastereomeric bias (Scheme 2). Gas chromatographic analysis of the lactones on a chiral capillary β-cyclodextrin column revealed that the *anti* and *syn* diastereoisomers of **4** were formed in 81 and 69% *ee*, respectively. The *ee* of

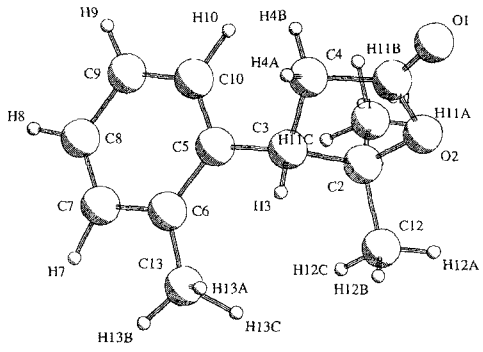
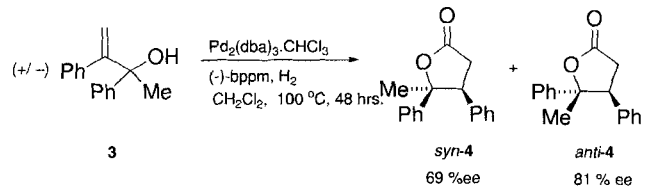


Figure 2. Structure of (*S*)-(+)-**2k**, showing atomic labeling scheme. Selected bond distances (Å): O1–C1, 1.206(3); O2–C1, 1.357(3); O2–C2, 1.469(3); C2–C3, 1.550(3), C3–C4, 1.531(3); C1–C4, 1.479(4); C3–C5, 1.504(4). Selected bond angles (°): O1-C1-O1, 110.20(19); O1-C1-C4, 129.5(3); C1-O2-C2, 110.20(19); O2-C2-C3, 103.76(19); C2-C3-C4, 101.42(20); C1-C3-C4, 104.98(21); C4-C3-C5, 116.95(21); O2-C1-C4, 110.31(22); C5-C3-H3, 106.2(11); C4-C3-H3, 107.0(10).

Table 3. Crystallographic Data for (*S*)-(+)-**2k**.

formula	$C_{13}H_{16}O_2$
M_r	204.27
crystal shape	cube
crystal dimensions, mm	0.2 × 0.2 × 0.2
crystal system	orthorhombic
a, Å	9.319(4)
b, Å	14.8122(15)
c, Å	8.1273(22)
space group	$P2_12_12_1$
Z	4
V, Å^3	1121.8(5)
ρ_{calcd}, g cm^{-3}	1.209
T, K	163
radiation (λ, Å)	$Mo_{K\alpha}$ (1.5405)
μ, mm^{-1}	0.61
R (R_w), %	5.4 (5.3)

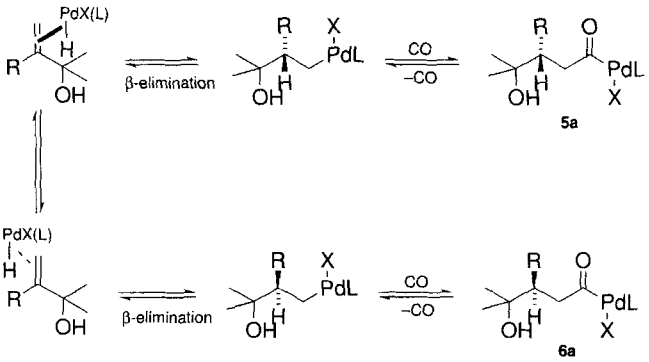


Scheme 2.

the *anti* diastereoisomer is identical to that of **2g**, which does not have a phenyl substituent at the allylic carbon, whereas the *ee*'s of *syn*-**4** and **2o** are very similar. The chirality of the allylic carbon atom does not influence the stereochemical outcome of the reaction. Assuming a hydridopalladium intermediate, the similarities in *ee* between *anti*-**4** and **2g**, and between *syn*-**4** and **2o**, suggest that the Pd/(−)-BPPM catalyst only recognizes the particular face of the allylic alcohol at which hydropalladation occurs.

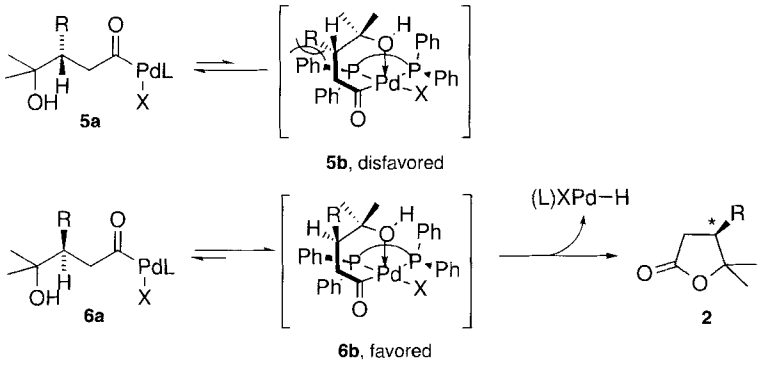
The mechanism of this reaction is unclear, and a hydridopalladium complex is assumed to be the active species, since the presence of a H_2 atmosphere (or a silane as an alternative hydride source) is crucial for this transformation. Only a few of the reported hydridopalladium complexes formed between Pd^0 and dihydrogen have been unequivocally characterized; Schunn proposed that a dimeric bis-μ_2-hydridopalladium complex was formed when [Pd{P(C_2H_5)$_3$}$_3$] was pressurized with 150 psi of hydrogen in toluene in an NMR tube.[13] Fryzuk and co-workers have published an X-ray characterization of a binuclear bis-μ_2-hydridopalladium(I) complex; it was, however, prepared from the reaction of [(dippp)PdCl$_2$] (dippp = bis(diisopropylphosphino)propane) with LiBEt$_3$H at −40 °C, and the reactivity of this type of complex is not well known.[14]

It is conceivable that an acylpalladium complex is generated by addition of a palladium hydride species, which first coordinated to the allylic alcohol, followed by insertion of CO (Scheme 3). In the presence of *p*-toluenesulfonic acid (10 mol%),



Scheme 3. Proposed mechanism for the hydrocarbonylation of allylic alcohol via a hydridopalladium intermediate (L = (−)-BPPM).

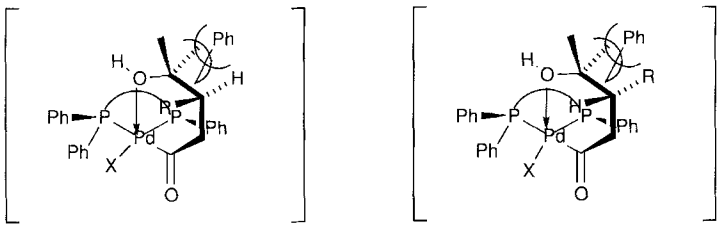
Pd/(−)-BPPM catalyzes the hydroesterification (CO/H_2, methanol) of α-methylstyrene to form *racemic* methyl 3-phenylbutanoate quantitatively. Based on this result, we believe that the hydrocarbonylation of an allylic alcohol to give its corresponding acylpalladium complex by means of a palladium hydride may not take place enantioselectively, and the two diastereomers **5a** and **6a** should always be present in equal amounts.



Scheme 4. Enantioselection results from the preferential formation of **6b**; here, the carbon skeleton fits into the chiral scaffold during cyclization (L = (−)-BPPM).

The cyclization involving coordination of the OH group to the Pd center may therefore be responsible for the enantioselection. The chirality of the diphosphine ligand governs the disposition of the phenyl rings on the phosphorus atoms, which is the major element of the steric interaction between the chiral diphosphine and the substrate (Scheme 4). The formation of **5b** from **5a** is expected to be disfavored because of the steric interactions between the R group and the phenyl rings, which are not present in the cyclization of **6a** to **6b**, and **6b** can react further to form the lactone **(*S*)-2** (if R = Ar).

An alternative mode of cyclization of **5a** and **6a** could also lead to **5c** and **6c**, respectively. These two arrangements are disfavored because of steric congestion between the geminal methyl group and the axial phenyl ring of (−)-BPPM.



Scheme 5. Conformation **5c** and **6c** are disfavored due to steric crowding among the geminal methyl groups and the axial phenyl ring of the (−)-BPPM ligand.

Irrespective of the mechanistic details, the cyclocarbonylation of allylic alcohols by means of a chiral palladium complex generated in situ by mixing $[Pd_2(dba)_3]\cdot CHCl_3$ and (−)-BPPM yields γ-butyrolactones of high optical purity and represents a simple and viable method. This methodology has a genuine potential in organic synthesis, particularly for the preparation of chiral γ-butyrolactones.

Experimental Section

General Procedures: All ^1H and ^{13}C NMR spectra were recorded at room temperature on a Gemini 200 spectrometer or a VXR-500 spectrometer as indicated. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane as the internal standard and referenced to the proton signal of the residual solvent ($CDCl_3$, $\delta = 7.24$ for ^1H and $\delta = 77.0$ for ^{13}C). Mass spectra were obtained on a VG 7070 E mass spectrometer. Gas chromatography was performed on the Hewlett Packard 5890 series II gas chromatograph containing a OV-17 column, and the chromatograms were obtained using a Hewlett Packard HP 3396 series II integrator. Chiral chromatographic analyses were performed on a Varian 3300 gas chromatograph installed with a Supelco β-Dex 120 column (30 m) permethylated β-cyclodextrin fused silica capillary column 0.25 mm i.d. × 0.25 μm d_f using helium as the carrier gas. Elemental analyses were performed by MHW Laboratories (Phoenix, AZ) or by the elemental analysis service of the Department of Chemistry at the University of Ottawa, Canada.

Materials: Benzene, THF, 1,2-dimethoxyethane and diethyl ether were dried and distilled from sodium/benzophenone ketyl under nitrogen before use. Dichloromethane for the cyclocarbonylation reaction was freshly distilled from CaH_2 under nitrogen. All other common solvents were used without purification. All chemicals were used as received. The TMEDA and hexanes, for the Shapiro reaction, were predried by distillation over CaH_2, and the acetone for quenching was distilled from anhydrous K_2CO_3 prior to use. The vinyl bromides leading to alcohols **1b**, **1c**, and **1d** were prepared from the reaction of the corresponding alkylacetylene with B-Br-9-BBN according to literature procedures.[15] The preparation of the 2,4,6-triisopropylbenzenesulphonylhydrazones followed a literature procedure[16] using methanol as the solvent, except for the hydrazones leading to alcohols **1f**, **1o**, and **1p**, in which cases acetonitrile was used as the solvent. $[Pd_2(dba)_3]\cdot CHCl_3$[18] and (−)-BPPM[7] were prepared according to literature procedures.

General Procedure for the Preparation of 1b–d:[17] To a THF solution (10 mL) of vinyl bromide (2 mmol) was added 1.5 to 2.0 equiv of *tert*-butyllithium (1.7 M in pentane) at −98 °C. The solution was stirred at this temperature for 15 min, then warmed to −78 °C. The vinyllithium species so formed was quenched with anhydrous acetone (ca. 0.18 mL). The mixture was stirred for a further 20 min, and slowly warmed to room temperature, water (5 mL) was then added, and the organic product extracted with diethyl ether and dried over anhydrous $MgSO_4$. The alcohols were purified by flash column chromatography using hexane/diethyl ether (3:1) as the eluant, and additionally distilled under vacuum before use.

3-Methylene-2-methyl-2-heptanol (1b): ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.85$–0.97 (m, 3H), 1.1–1.75 (m with a singlet at $\delta = 1.4$, 11H), 2.02–2.15 (m, 2H), 4.78 (brs, 1H), 5.11 (brs, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 14.0$, 22.7, 29.2, 30.8, 31.0, 73.4, 106.5, 156.2; HRMS (70 eV, EI): calcd for $C_9H_{18}O$ 142.135765, found 142.13446.

3-Methylene-2-methyl-2-nonanol (1c): ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.7$–1 (m, 3H), 1.1–1.7 (m with a singlet at $\delta = 1.4$, 14H), 2.0–2.15 (m, 2H), 4.75 (brs, 1H), 5.11 (brs, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 14.1$, 22.6, 28.8, 29.2, 31.1, 31.8, 73.5, 106.5, 156.3; HRMS (70 eV, EI): calcd for $C_{11}H_{22}O$ 170.167065, found 170.16624.

3-Methylene-2-methyl-2-undecanol (1d): ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.8$–0.93 (m, 3H), 1.17–1.58 (m with a singlet at $\delta = 1.35$, 18H), 2.0–2.25 (m, 2H), 4.75 (brs, 1H, $h_{1/2} = 3$ Hz), 5.11 (brs, 1H, $h_{1/2} = 3$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 14.1$, 18.6, 22.7, 28.7, 29.2, 29.6, 31.1, 31.8, 31.9, 73.5, 106.5, 156.3; HRMS (70 eV, EI): calcd for $C_{13}H_{26}O$ 198.198365, found 198.19514.

General Procedure for the Preparation of 1g and 3: 1-Phenylvinylmagnesium bromide was prepared from the reaction of α-bromostyrene (1.89 g, 10 mmol) with Mg (0.24 g, 10 mmol) in anhydrous diethyl ether. The reaction mixture was refluxed for 2 h, and then quenched with acetone (8 mmol) to **1g**, or acetophenone (8 mmol) to **3** at 0 °C. The mixture was refluxed gently for 1 h. After cooling to room temperature, saturated aqueous NH_4Cl solution was added, and the organic product was extracted three times with diethyl ether. The combined organic extract was dried ($MgSO_4$), and the solvent removed by rotary evaporation. The residue was loaded on a silica gel column, which was first eluted with hexanes to remove styrene, followed by diethyl ether. The crude alcohol was obtained by evaporation of diethyl ether, and subsequent distillation under vacuum gave purified alcohol **1g** in 45%, and **3** in 37% yield.

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2-Methyl-3-phenyl-3-buten-2-ol (1g): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.40 (s, 6H), 4.95 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.41 (d, 1H, ^2J(H,H) = 1.4 Hz), 7.28 (brs, 5H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.6, 73.0, 112.5, 126.9, 127.7, 128.2, 128.8, 141.5, 157.0; HRMS (70 eV, EI): calcd for $C_{11}H_{14}O$ 162.104465, found 162.10441.

Racemic 2,3-diphenyl-3-buten-2-ol (3): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.73 (s, 3H), 5.29 (d, 1H, ^2J(H,H) = 1.2 Hz), 5.55 (d, 1H, ^2J(H,H) = 1.2 Hz), 6.95–7.19 (m, 2H), 7.25–7.40 (m, 6H), 7.50–7.60 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 30.1, 76.9, 114.5, 125.5, 127.0, 127.3, 127.9, 128.2, 128.4, 140.1, 146.3, 154.8; HRMS (70 eV, EI): calcd for $C_{16}H_{16}O$ 224.120115, found 224.12050.

General Procedure for the Preparation of Alcohols 1e–p, except 1g (Shapiro Reaction):[16] To 2,4,6-triisopropylbenzenesulphonylhydrazone (3 mmol) in 7.5 mL of 10% TMEDA/hexanes at −78 °C was added 2.0–2.2 equiv of *n*-butyllithium (2.5 M in hexanes). After stirring at that temperature for 15 min, the mixture was warmed to 0 °C by immersing in an ice/water bath. Evolution of nitrogen ceased within 5 min leaving a red-brown or deep blue solution depending on the nature of the substrate. The resulting solution was cooled to −78 °C and diluted with anhydrous THF (10 mL). After 2–5 min of stirring, the solution was then quenched with acetone (0.4 mL). The clear yellow solution was stirred for 80 min, water (2 mL) was then added, and the organic layer separated. The remaining aqueous layer was extracted three times with diethyl ether. The combined organic extract was dried ($MgSO_4$), the solvent removed by rotary evaporation, and the alcohol isolated by flash column chromatography. For **1e** and **1f**, hexanes/diethyl ether (3:1) was used as the eluant, whereas aromatic alcohols **1h–1p** were eluted with hexanes/diethyl ether (1:1). All the alcohols were purified by vacuum distillation before being subjected to carbonylation.

3-Cyclohexyl-2-methyl-3-buten-2-ol (1e): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.9–2.33 (m with a singlet at δ = 1.3, 17H), 4.82 (brs, 1H), 5.11 (brs, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 26.2, 27.1, 28.3, 28.8, 35.5, 35.8, 50.7, 76.6, 105.8, 162.2; HRMS (70 eV, EI): calcd for $C_{11}H_{20}O$ 168.151415, found 168.15064.

3-(1′-Adamantyl)-2-methyl-3-buten-2-ol (1f): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.46 (s, 6H), 1.65–1.8 (m, 6H), 1.9–2.1 (m, 9H), 4.89 (brs, 1H), 4.97 (brs, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 28.4, 29.0, 34.3, 37.3, 37.0, 39.3, 41.8, 42.2, 76.3, 108.5, 164.4; HRMS (70 eV, EI): calcd for $C_{15}H_{24}O$ 220.182715, found 220.18435.

3-(4′-Methoxyphenyl)-2-methyl-3-buten-2-ol (1h): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.40 (s, 6H), 3.80 (s, 3H), 4.95 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.38 (d, 1H, ^2J(H,H) = 1.4 Hz), 6.82–6.86 (m, 2H), 7.22–7.26 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.6, 55.1, 73.0, 112.3, 113.1, 129.8, 133.8, 156.4, 158.6; MS (70 eV, EI): 192 [M^+].

3-(3′-Methoxyphenyl)-2-methyl-3-buten-2-ol (1i): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.41 (s, 6H), 3.8 (s, 3H), 4.97 (d, 1H, ^2J(H,H) = 1.5 Hz), 5.41 (d, 1H, ^2J(H,H) = 1.5 Hz), 6.75–6.95 (m, 3H), 7.15–7.31 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.6, 55.1, 72.8, 112.2, 112.4, 114.7, 121.2, 128.6, 142.8, 156.7, 158.8; HRMS (70 eV, EI): calcd for $C_{12}H_{16}O_2$ 192.11503, found 192.11320.

3-(4′-Methylphenyl)-2-methyl-3-buten-2-ol (1j): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.40 (s, 6H), 2.35 (s, 3H), 4.94 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.39 (d, 1H, ^2J(H,H) = 1.4 Hz), 7.13–7.17 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.1, 29.6, 73.0, 112.3, 128.4, 128.7, 136.6, 138.6, 156.9; HRMS (70 eV, EI): calcd for $C_{12}H_{16}O$ 176.12012, found 176.12132.

3-(2′-Methylphenyl)-2-methyl-3-buten-2-ol (1k): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.40 (s, 6H), 2.29 (s, 3H), 4.86 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.48 (d, 1H, ^2J(H,H) = 1.4 Hz), 7.11–7.20 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 20.4, 29.6, 73.4, 112.8, 124.8, 127.0, 129.4, 130.1, 136.3, 140.3, 155.5; HRMS (70 eV, EI): calcd for $C_{11}H_{13}O$ ($M^+ - CH_3$) 161.09664, found 161.09434.

3-(2′-Fluorophenyl)-2-methyl-3-buten-2-ol (1l): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.40 (s, 6H), 4.96 (d, 1H, ^2J(H,H) = 1.2 Hz), 5.42 (d, 1H, ^2J(H,H) = 1.2 Hz), 7.05–7.19 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.2, 73.1, 114.5, 115.1, 115.5, 123.4, 128.8, 131.6, 151.3, 157.2; HRMS (70 eV, EI): calcd for $C_{11}H_{13}OF$ 180.095045, found 180.09577.

3-(4′-Chlorophenyl)-2-methyl-3-buten-2-ol (1m): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.39 (s, 6H), 4.96 (d, 1H, ^2J(H,H) = 1.2 Hz), 5.42 (d, 1H, ^2J(H,H) = 1.2 Hz), 7.26 (s, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.5, 72.8, 113.1, 127.9, 130.1, 133.0, 139.9, 155.7; HRMS (70 eV, EI): calcd for $C_{11}H_{13}OCl$ 196.065494, found 196.06342.

3-(2′-Chlorophenyl)-2-methyl-3-buten-2-ol (1n): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.43 (s, 6H), 4.97 (d, 1H, ^2J(H,H) = 1.2 Hz), 5.58 (d, 1H, ^2J(H,H) = 1.2 Hz), 7.18-7.30 (m, 3H), 7.33–7.48 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.4, 73.5, 114.7, 126.0, 128.3, 129.5, 131.0, 133.2, 140.0, 153.8; HRMS (70 eV, EI): calcd for $C_{11}H_{13}OCl$ 196.065494, found 196.06586.

3-(2′-Naphthyl)-2-methyl-3-buten-2-ol (1o): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.44 (s, 6H), 5.05 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.48 (d, 1H, ^2J(H,H) = 1.4 Hz), 7.35–7.55 (m, 3H), 7.61–7.89 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.7, 73.1, 113.0, 125.7, 126.0, 126.7, 127.1, 127.3, 127.9, 132.3, 132.9, 139.1, 156.9; MS (70 eV, EI): 212 [M^+]; Anal. calcd for $C_{15}H_{16}O$: C 84.91, H 7.55; found: C 84.89, H 7.75.

3-(1′-Naphthyl)-2-methyl-3-buten-2-ol (1p): ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.47 (brs, 6H), 5.05 (d, 1H, ^2J(H,H) = 1.4 Hz), 5.75 (d, 1H, ^2J(H,H) = 1.4 Hz), 7.21–7.57 (m, 4H), 7.62–7.91 (m, 2H), 7.93–8.11 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): δ = 29.7, 73.6, 114.6, 124.8, 125.6, 125.8, 126.5, 126.7, 127.5, 128.1, 132.4, 133.1, 139.1, 156.9; HRMS (70 eV, EI): calcd for $C_{15}H_{16}O$ 212.12012, found 212.12275.

General Procedure for the Asymmetric Cyclocarbonylation of Prochiral Allylic Alcohols: The allylic alcohol (1.0 mmol), $[Pd_2(dba)_3]\cdot CHCl_3$ complex (0.04 mmol), (−)-BPPM (0.08 mmol) and dichloromethane (10 mL) were placed in a 20 mL autoclave. The reactor was flushed three times with CO and pressurized to 400 psi of CO. The delivery line connecting the reactor and the hydrogen tank was purged three times with hydrogen and the reactor was charged with hydrogen to a total pressure of 800 psi. The reaction mixture was allowed to stand at room temperature for 20 min and then stirred at 104–106 °C (oil bath temperature) for 48 h. The pressure was released after the reactor had cooled to room temperature. The consumption of the reactant alcohols was monitored by gas chromatography. The solvent was removed by rotary evaporation. The product lactones were isolated by silica-gel column chromatography (eluents: 1) hexanes, 2) hexanes/ethyl acetate 1/1). The lactones were further purified by vacuum distillation.

Procedure for the Determination of the Optical Purity of the Lactones: The enantiomeric excess was generally determined by 200 MHz ^{1}H NMR spectroscopy in $CDCl_3$ in the presence of the chiral shift reagent, Eu(hfc)$_3$. Not more than 6 mg of lactone was dissolved in $CDCl_3$, and the chiral shift reagent then added. All the peaks in the ^{1}H NMR spectrum underwent a down-field shift. The addition of Eu(hfc)$_3$ was continued until the methyl-singlet absorption at the lower field shift resolved into two singlet peaks. A baseline resolution was usually achieved in the region of 2.2–2.8 ppm. The *ee* was evaluated from the ratio of integration of the resolved peaks. The optical purities of lactones *anti*- and *syn*-**4** were analyzed by a gas chromatograph equipped with a chiral β-cyclodextrin column using helium as the carrier gas (flow rate = 15 mL min^{-1}, 180 °C isothermal), *syn*-**4** was eluted as two resolved peaks with a retention time of 93.21 and 95.16 min, and *anti*-**4** was eluted as two resolved peaks at 120.62 and 126.24 min. When the optical purity was greater than 95% *ee*, then it was determined by chiral gas chromatography. The absolute configuration of the aromatic lactones were determined on the basis of the single crystal X-ray diffraction study of **2k** (the absolute configurations of **2a–f** were not determined).

(−)-2,3,3-Trimethyl-γ-butyrolactone (2a): Colorless oil; *ee* = 27%; $[\alpha]_D^{23} = -6.97$ (*c* = 1.65, $CHCl_3$). The compound shows identical spectral characteristics to those reported in the literature (Ref.: Nikishin et al., *Izu. Akad. Nauk. SSSR, Ser. Khim.* **1976**, 7, 1664.)

(−)-2-*n*-Butyl-3,3-dimethyl-γ-butyrolactone (2b): Colorless oil; IR (neat): $\tilde{\nu}$ = 1772 cm^{-1}; *ee* = 45%; $[\alpha]_D^{23} = -22.4$ (*c* = 1.23, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.85–1.05 (m, 3H), 1.15–1.65 (m with

two singlets at $\delta = 1.25$ and 1.44, 12H), 2.11–2.38 (m, 2H), 2.50–2.79 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.9$, 21.8, 22.7, 27.5, 29.3, 30.5, 35.0, 45.8, 86.8, 175.8; HRMS (70 eV, EI): calcd for $C_9H_{15}O_2$ ($M^+ - CH_3$) 155.107205, found 155.10635.

(−)-3,3-Dimethyl-2-n-hexyl-γ-butyrolactone (2c): Colorless oil; IR (neat): $\tilde{\nu} = 1773\ cm^{-1}$; *ee* = 41%; $[\alpha]_D^{23} = -19.0$ ($c = 1.68$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.86–0.92$ (m, 3H), 1.25–1.47 (m, 16H), 2.22–2.35 (m, 2H), 2.51–2.72 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 13.8$, 21.6, 22.4, 27.3, 28.2, 29.1, 29.5, 31.5, 34.9, 45.6, 86.6, 175.6; HRMS (70 eV, EI): calcd for $C_{11}H_{19}O_2$ ($M^+ - CH_3$) 183.138505, found 183.13851.

(−)-3,3-Dimethyl-2-*n*-octyl-γ-butyrolactone (2d): Colorless oil; IR (neat): $\tilde{\nu} = 1774\ cm^{-1}$; *ee* = 38%; $[\alpha]_D^{23} = -15.2$ ($c = 1.28$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.85–1.46$ (m with two singlets at $\delta = 1.44$ and 1.25, 23H), 2.22–2.34 (m, 2H), 2.60-2.65 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 14.0$, 21.7, 22.5, 27.3, 27.4, 28.4, 29.1, 29.3, 31.7, 35.0, 45.7, 86.7, 175.7; HRMS (70 eV, EI): calcd for $C_{13}H_{23}O_2$ ($M^+ - CH_3$) 211.169805, found 211.16883.

(−)-2-Cyclohexyl-3,3-dimethyl-γ-butyrolactone (2e): Colorless oil; IR (neat): $\tilde{\nu} = 1771\ cm^{-1}$; *ee* = 39%; $[\alpha]_D^{23} = -12.9$ ($c = 3.71$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.8–1.42$ (m with a singlet at $\delta = 1.31$, 8H), 1.50 (s, 3H), 1.56–1.85 (m, 5H), 2.01 (ddd, 1H, ^3J(H,H) = 12, ^3J(H,H) = 9.5, ^3J(H,H) = 8.3 Hz), 2.32 (dd, 1H, ^2J(H,H) = 17.3, ^3J(H,H) = 12 Hz), 2.60 (dd, 1H, ^2J(H,H) = 17.3, ^3J(H,H) = 8.3 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 21.6$, 25.8, 25.9, 29.5, 31.9, 32.1, 34.5, 38.5, 51.4, 87.1, 175.5; HRMS (70 eV, EI): calcd for $C_{11}H_{17}O_2$ ($M^+ - CH_3$) 181.122855, found 181.12402.

(−)-2-(1′-Adamantyl)-3,3-dimethyl-γ-butyrolactone (2f): Waxy solid; m.p. = 93–94 °C; IR (neat): $\tilde{\nu} = 1771\ cm^{-1}$; *ee* = 25%; $[\alpha]_D^{23} = -5.1$ ($c = 1.73$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.40–2.10$ (m with two singlets at $\delta = 1.40$ and 1.53, 20H), 2.40–2.50 (m, 2H), 2.60–2.70 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 24.1$, 27.7, 28.2, 28.5, 29.9, 30.2, 33.8, 36.7, 38.6, 40.8, 41.9, 42.1, 57.1, 88.1, 175.8; HRMS (70 eV, EI): calcd for $C_{13}H_{18}O$ [$M^+ - (CH_3)_2CO$] 190.135765, found 190.13514.

(*S*)-(+)-3,3-Dimethyl-2-phenyl-γ-butyrolactone (2g): Colorless plates; m.p. = 92–93 °C; IR (KBr): $\tilde{\nu} = 1766\ cm^{-1}$; *ee* > 98% (46% yield) after recrystallization; $[\alpha]_D^{23} = +87.6$ ($c = 2.1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.05$ (s, 3H), 1.56 (s, 3H), 2.88 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 8.6 Hz), 3.03 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 10 Hz), 3.53 (dd, 1H, ^3J(H,H) = 10, ^3J(H,H) = 8.6 Hz), 7.15–7.30 (m, 2H), 7.30–7.50 (m, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.2$, 27.7, 34.5, 51.2, 87.2, 127.8, 128.7, 136.7, 175.4; MS (70 eV, EI): 190 [M^+]; Anal. calcd for $C_{12}H_{14}O_2$: C 75.79,H 7.37; found: C 76.11, H 7.46.

(*S*)-(+)-3,3-Dimethyl-2-(4′-methoxyphenyl)-γ-butyrolactone (2h): Colorless plates; m.p. = 120–121 °C; IR (KBr): $\tilde{\nu} = 1768\ cm^{-1}$; *ee* = 87% (52% yield) after recrystallization; $[\alpha]_D^{23} = +68.1$ ($c = 1.57$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.04$ (s, 3H), 1.53 (s, 3H), 2.86 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 8.2 Hz), 2.97 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 9.4 Hz), 3.47 (dd, 1H, ^3J(H,H) = 9.4, ^3J(H,H) = 8.2 Hz), 3.81 (s, 3H), 6.87–6.91 (m, 2H), 7.11–7.26 (m, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.1$, 27.6, 34.7, 50.5, 55.3, 87.4, 114.0, 128.6, 128.8, 159.1, 175.4; MS (70 eV, EI): 220 [M^+]; Anal. calcd for $C_{13}H_{16}O_3$: C 70.91, H 7.27; found: C 70.98, H 7.08.

(*S*)-(+)-3,3-Dimethyl-2-(3′-methoxyphenyl)-γ-butyrolactone (2i): Colorless oil; IR (neat): $\tilde{\nu} = 1767\ cm^{-1}$; *ee* = 71%; $[\alpha]_D^{23} = +55.7$ ($c = 1.32$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.06$ (s, 3H), 1.55 (s, 3H), 2.85 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 8.8 Hz), 3.00 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 10 Hz), 3.49 (dd, 1H, ^3J(H,H) = 10, ^3J(H,H) = 8.8 Hz), 3.81 (s, 3H), 6.74–6.86 (m, 3H), 7.25–7.32 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.1$, 27.7, 34.4, 51.1, 55.1, 87.2, 112.3, 114.2, 120.0, 129.6, 138.3, 159.7, 175.3; HRMS (70 eV, EI): calcd for $C_{13}H_{16}O_3$: 220.109945, found 220.10892

(*S*)-(+)-3,3-Dimethyl-2-(4′-methylphenyl)-γ-butyrolactone (2j): Colorless oil; IR (neat): $\tilde{\nu} = 1766\ cm^{-1}$; *ee* = 69%; $[\alpha]_D^{23} = +57.0$ ($c = 1.13$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.04$ (s, 3H), 1.54 (s, 3H), 2.35 (s, 3H), 2.85 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 8.7 Hz), 3.00 (dd, 1H, ^2J(H,H) = 17.5, ^3J(H,H) = 10.2 Hz), 3.48 (dd, 1H, ^3J(H,H) = 10.2, ^3J(H,H) = 8.7 Hz), 7.07–7.19 (m, 4H), 7.11–7.26 (m, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 21.0$, 23.2, 27.7, 50.8, 87.3, 127.7, 129.3, 133.6, 137.5, 175.8; HRMS (70 eV, EI): calcd for $C_{13}H_{16}O$ 204.115.03, found 204.11329.

(*S*)-(+)-3,3-Dimethyl-2-(2′-methylphenyl)-γ-butyrolactone (2k): Colorless crystals; m.p. = 117–118 °C; IR (KBr): $\tilde{\nu} = 1761\ cm^{-1}$; *ee* > 98% (49% yield) after recrystallization; $[\alpha]_D^{23} = +133.4$ ($c = 1.10$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.09$ (s, 3H), 1.56 (s, 3H), 2.36 (s, 3H) 2.86 (dd, 1H, ^2J(H,H) = 17.9, ^3J(H,H) = 6.9 Hz), 3.05 (dd, 1H, ^2J(H,H) = 17.9, ^3J(H,H) = 8.7 Hz), 3.80 (dd, 1H, ^3J(H,H) = 8.7, ^3J(H,H) = 6.9 Hz), 7.20 (br s, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 20.2$, 23.8, 28.9, 36.5, 45.2, 87.6, 126.4, 126.5, 127.3, 130.8, 136.1, 136.7, 176.0; MS (70 eV, EI): 204 [M^+]; Anal. calcd for $C_{13}H_{16}O_2$: C 76.47, H 7.84; found C 76.67, H 7.85.

(*S*)-(+)-3,3-Dimethyl-2-(2′-fluorophenyl)-γ-butyrolactone (2l): Colorless plates; m.p. = 85–86 °C; IR (KBr): $\tilde{\nu} = 1769\ cm^{-1}$; *ee* = 67%; $[\alpha]_D^{23} = +73.1$ ($c = 1.24$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.10$ (s, 3H), 1.56 (s, 3H), 2.96 (dd, 1H, ^2J(H,H) = 18.1, ^3J(H,H) = 8.9 Hz), 3.03 (dd, 1H, ^2J(H,H) = 18.1, ^3J(H,H) = 8.3 Hz), 3.85 (dd, 1H, ^3J(H,H) = 8.9, ^3J(H,H) = 8.3 Hz), 7.14–7.27 (m, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.4$, 28.1, 34.4, 43.6, 87.1, 115.6, 116.1, 124.4, 128.6, 129.2, 129.4, 175.3; MS (70 eV, EI): 208 [M^+]; Anal. calcd for $C_{12}H_{13}FO_2$: C 69.23, H 6.25; found C 69.23, H 6.43.

(*S*)-(+)-2-(4′-Chlorophenyl)-3,3-dimethyl-γ-butyrolactone (2m): Colorless plates; m.p. = 135–136 °C; IR (KBr): $\tilde{\nu} = 1749\ cm^{-1}$; *ee* > 98% (46% yield) after recrystallization; $[\alpha]_D^{23} = +70.6$ ($c = 0.588$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.04$ (s, 3H), 1.55 (s, 3H), 2.88 (dd, 1H, ^2J(H,H) = 17.8, ^3J(H,H) = 9.2 Hz), 2.98 (dd, 1H, ^2J(H,H) = 17.8, ^3J(H,H) = 9.3 Hz), 3.50 (dd, 1H, ^3J(H,H) = 9.3, ^3J(H,H) = 9.2 Hz), 7.14–7.19 (m, 2H), 7.31–7.37 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.2$, 27.7, 34.6, 50.6, 86.9, 128.9, 129.1, 133.7, 135.3, 174.9; HRMS (70 eV, EI): calcd for $C_{12}H_{13}O_2Cl$ 224.060409, found 224.06133.

(*S*)-(+)-2-(2′-Chlorophenyl)-3,3-dimethyl-γ-butyrolactone (2n): Colorless oil; IR (neat): $\tilde{\nu} = 1762\ cm^{-1}$; *ee* = 83%; $[\alpha]_D^{23} = +121.8$ ($c = 1.31$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.09$ (s, 3H), 1.60 (s, 3H), 2.82 (dd, 1H, ^2J(H,H) = 18.1, ^3J(H,H) = 5.7 Hz), 3.12 (dd, 1H, ^2J(H,H) = 18.1, ^3J(H,H) = 9.0 Hz), 4.15 (dd, 1H, ^3J(H,H) = 9.0, ^3J(H,H) = 5.7 Hz), 7.121–7.28 (m, 3H), 7.40–7.44 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.8$, 28.8, 36.0, 45.4, 87.5, 127.3, 127.9, 128.8, 130.0, 136.5, 175.7; HRMS (70 eV, EI): calcd for $C_{12}H_{13}O_2Cl$ 224.060409, found 224.05903.

(*S*)-(+)-3,3-Dimethyl-2-(2′-naphthyl)-γ-butyrolactone (2o): Colorless plates; m.p. = 156–157 °C; IR (KBr): $\tilde{\nu} = 1757\ cm^{-1}$; *ee* = 69%; $[\alpha]_D^{23} = +79.3$ ($c = 1.11$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.07$ (s, 3H), 1.61 (s, 3H), 2.97 (dd, 1H, ^2J(H,H) = 17.6, ^3J(H,H) = 8.6 Hz), 3.14 (dd, 1H, ^2J(H,H) = 17.6, ^3J(H,H) = 9.8 Hz), 3.69 (dd, 1H, ^3J(H,H) = 9.8, ^3J(H,H) = 8.6 Hz), 7.31–7.36 (m, 1H), 7.48–7.53 (m, 2H), 7.66 (br s, 1H), 7.81–7.87 (m, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.4$, 28.0, 34.7, 51.3, 87.4, 125.6, 126.2, 126.5, 126.7, 127.6, 127.7, 128.5, 132.7, 133.2, 134.3, 175.4; MS (70 eV, EI): 240 [M^+]; Anal. calcd for $C_{16}H_{16}O_2$: C 80.00, H 6.67; found C 79.93, H 6.43.

(*S*)-(+)-3,3-Dimethyl-2-(1′-naphthyl)-γ-butyrolactone (2p): Light yellow crystals; m.p. = 122–124 °C; IR (KBr): $\tilde{\nu} = 1773\ cm^{-1}$; *ee* = 79%; $[\alpha]_D^{23} = +123.6$ ($c = 2.28$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$ 25 °C, TMS): $\delta = 1.01$ (s, 3H), 1.65 (s, 3H), 3.06 (dd, 1H, ^2J(H,H) = 17.9, ^3J(H,H) = 7.7 Hz), 3.16 (dd, 1H, ^2J(H,H) = 17.9, ^3J(H,H) = 8.1 Hz), 4.46 (dd, 1H, J^3(H,H) = 8.1, ^3J(H,H) = 7.7 Hz), 7.38–7.58 (m, 4H), 7.80–7.92 (m, 2H), 8.02–8.07 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 23.8$, 28.8, 36.2, 44.2, 87.7, 122.9, 124.3, 125.3, 125.8, 126.5, 128.2, 129.2, 132.1, 133.9, 134.1, 175.9; MS (70 eV, EI): 240 [M^+]; Anal. calcd for $C_{16}H_{16}O_2$ C 80.00, H 6.67; found: C 80.15, H 6.82.

***anti*-2,3-Diphenyl-3-methyl-γ-butyrolactone (*anti*-4)**: Colorless plates; m.p. = 136–137 °C; IR (KBr): $\tilde{\nu} = 1770\ cm^{-1}$; *ee* > 98% (21% yield) after recrystallization; $[\alpha]_D^{23} = +6.9$ ($c = 1.08$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$

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25 °C, TMS): $\delta = 1.37$ (s, 3H), 2.87 (dd, 1H, $^2J(H,H) = 17.7$, $^3J(H,H) = 8.2$ Hz), 2.91 (dd, 1H, $^2J(H,H) = 17.7$, $^3J(H,H) = 7.4$ Hz), 3.75 (dd, 1H, $^3J(H,H) = 8.2$, $^3J(H,H) = 7.4$ Hz), 7.12–7.17 (m, 2H), 7.33–7.50 (m, 8H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 24.0$, 35.2, 52.8, 89.5, 124.4, 127.8, 127.9, 128.1, 128.5, 128.7, 137.2, 144.2, 175.9; MS (70 eV, EI): 252 [M^+]; Anal. calcd for $C_{17}H_{16}O_2$ C 80.95, H 6.35; found C 80.53, H 6.28.

***syn*-2,3-Diphenyl-3-methyl-γ-butyrolactone** (*syn*-**4**): Colorless crystals; m.p. = 81–83 °C; IR (KBr): $\tilde{\nu} = 1771$ cm^{-1}; 87% of mixture of *syn* and *anti* isomers; ^{1}H NMR (500 MHz, $CDCl_3$ 25 °C, TMS): $\delta = 1.89$ (s, 3H), 2.83 (dd, 1H, $^2J(H,H) = 17.9$, $^3J(H,H) = 10.7$ Hz), 2.92 (dd, 1H, $^2J(H,H) = 17.9$, $^3J(H,H) = 8.6$ Hz), 3.85 (dd, 1H, $^3J(H,H) = 10.7$, $^3J(H,H) = 8.6$ Hz), 6.75–6.82 (m, 4H), 7.09–7.16 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 27.9$, 34.7, 53.4, 89.8, 124.4, 125.5, 127.4, 127.6, 127.8, 127.9, 128.1, 128.8, 128.5, 128.7, 135.9, 139.4, 175.9; MS (70 eV, EI): 252 [M^+]; Anal. calcd for $C_{17}H_{16}O_2$ C 80.95, H 6.35; found C 81.35, H 6.40.

X-ray Analysis of (*S*)-(+)-3,3-Dimethyl-2-(2′-methylphenyl)-γ-butyrolactone (2k): A plate crystal of $C_{13}H_{16}O_2$ with approximate dimensions $0.2 \times 0.2 \times 0.2$ mm was mounted on a glass capillary. All the measurements were made on a Rigaku diffractometer with $Cu_{K\alpha}$ radiation. Cell constants, and the orientation matrix for data collection, were obtained from a least-square refinement using setting angles of 25 reflections in the range $80 < 2\theta < 100°$, which corresponded to an orthorombic cell with dimensions: $a = 9.319(4)$, $b = 14.8122(15)$, $c = 8.1272(22)$ Å. For $Z = 4$ and $M_r = 204.27$, $\rho_{calcd} = 1.209$ g cm^{-3}. The space group was determined to be $P2_12_12_1$ from the systemic absences. Data was collected at $T = -110$ °C using the ω–2θ scan technique to a maximum 2θ value of 99.9°. A total of 3642 reflections were collected. The unique set contained only 1154 reflections. The standards were measured after every 150 reflections. No crystal decay was observed. Corrections were made for Lorentz and polarization effects,[19] however, no absorption correction was made.

The structure was solved by direct methods. All atoms, except hydrogen, were refined anisotropically. The hydrogen atoms were found by differences Fourier map. The final cycle of full-matrix least-square refinement was based on 1141 observed reflections ($I > 2.5\sigma(I)$) and 201 variable parameters. Weights based on counting statistics were used. The maximum and minimum peaks on the final differences Fourier map corresponded to 0.190 and -0.140 e Å^{-3}, respectively. The absolute structure was determined by the approach developed by Lepage, Gabe, and Gainsford[20] and applied as follows: the structure solution allowed the 200 most sensitive Bijvoet pairs to be found by the utility Bijvoet; 120 individual indications for the hand pointed one way and 80 the other way, giving a strong possibility of 2×10^{-3} of having a wrong hand. The procedure was repeated with a new crystal. The crystal was oriented with the same orientation matrix and the 200 most sensitive pairs were collected giving 3×10^{-3}. If we cumulate the statistics, the probability of being wrong is 6×10^{-6}. All the calculations were performed using the NRCVAX crystallographic software package.[21]

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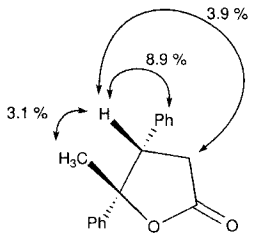
[9] 46% of **2g** were recovered after recrystallization, and >98% enantiopurity was confirmed by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$. A further crop of **2g**, obtained from the remaining solution, was found to have only 27% *ee*.

[10] The *gem*-dialkyl effect was found in intramolecular reactions, where *gem*-dialkyl substitution on a chain connecting reacting functional groups was particularly effective in enhancing ring-closure or retarding ring-opening reations. a) R. M. Beesley, C. K. Ingold, J. F. Thorpe, *J. Chem. Soc.* **1915**, *107*, 1080; b) C. K. Ingold, E. W. Lanfear, J. F. Thorpe, *ibid*, **1923**, *123*, 3140; c) T. C. Bruice, F. C. Lightstone, *J. Am. Chem. Soc.* **1994**, *116*, 10789 and references therein.

[11] **2k** was recrystallized from CH_2Cl_2/Et_2O/hexanes (0.5:1.0:8.5) by slow evaporation of the solvent. Enantiopurity of >99% *ee* of **2k** was confirmed by ^{1}H NMR using Eu(hfc)$_3$ as the shift reagent as well as by chiral gas chromatographic analysis.

[12] The sample was recrystallized from CH_2Cl_2/Et_2O/hexanes at -20 °C. *anti*-**4** crystallized first, and the crystallization of *syn*-**4** followed upon further standing in the cold. The purities of *anti*-**4** and *syn*-**4** were 95 and 87%, respectively (based on the integration ratio of the methyl protons in the ^{1}H NMR spectrum of *anti*- and *syn*-**4** (at $\delta = 1.87$ for *syn* and 1.36 for *anti*). *syn*-**4** was unambiguously characterized by ^{1}H NMR spectroscopy. Irradiation of the methine proton caused an NOE enhancement of 3.1% at the methyl protons, 3.9% at the methylene protons, and 8.9% at the protons on the phenyl ring at the β-position (Scheme 6). No NOE enhancement was observed for *anti*-**4**.



Scheme 6. *syn*-**4**.

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