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Enantioselective Baeyer–Villiger Oxidation Catalyzed by Palladium(II) Complexes with Chiral *P,N*-Ligands[||]

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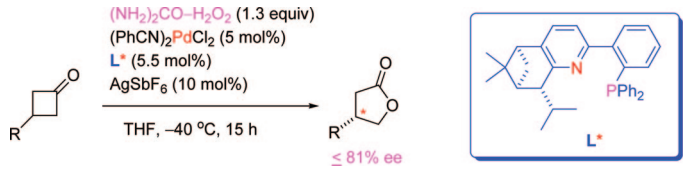
Received January 30, 2008

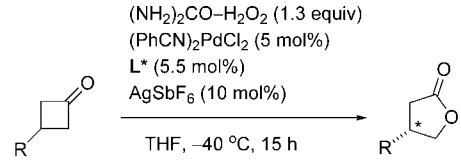


Asymmetric Baeyer–Villiger reaction of symmetrical cyclobutanones **1a**−**j** with urea−hydrogen peroxide (UHP) can be catalyzed by a complex of Pd(II) and the new terpene-derived *P*,*N*-ligand **7**. The resulting lactones **2a**−**j** were obtained in high yields and with good enantioselectivity (≤81% ee).

Introduction

The Baeyer–Villiger conversion of aldehydes and ketones into the corresponding esters by insertion of an oxygen atom into the C−C bond[1] is an established, regioselective, and stereospecific synthetic tool.[2] In the case of symmetrical cyclic ketones, such as 3-substituted cyclobutanones (**1**), 4-substituted cyclohexanones, etc., the Baeyer–Villiger reaction results in the formation of a chiral lactone, e.g., **2** (Scheme 1). Preferential formation of one of its enantiomers requires a chiral reagent or auxiliary. While a successful use of stoichiometric amounts of chiral peroxy acids has not been reported, the application of chiral stoichiometric auxiliaries proved quite effective[3] and particularly high enantioselectivities were attained in specific cases by application of enzymes.[4] Catalytic processes, using atransition metal coordinated to a chiral ligand with a hydroperoxide as the stoichiometric oxidant, represent an attractive

SCHEME 1. Baeyer−Villiger Oxidation of Prochiral Cyclobutanones



1a, R = Ph	**2a**, R = Ph
1b, R = 4-Me-C_6H_4	**2b**, R = 4-Me-C_6H_4
1c, R = 4-F-C_6H_4	**2c**, R = 4-F-C_6H_4
1d, R = 4-Cl-C_6H_4	**2d**, R = 4-Cl-C_6H_4
1e, R = 4-Br-C_6H_4	**2e**, R = 4-Br-C_6H_4
1f, R = 2-Br-C_6H_4	**2f**, R = 2-Br-C_6H_4
1g, R = 2-Naphth	**2g**, R = 2-Naphth
1h, R = 4-MeO-$C_6H_4CH_2$	**2h**, R = 4-MeO-$C_6H_4CH_2$
1i, R = Cyclohexyl	**2i**, R = Cyclohexyl
1j, R = *n*-Octyl	**2j**, R = *n*-Octyl

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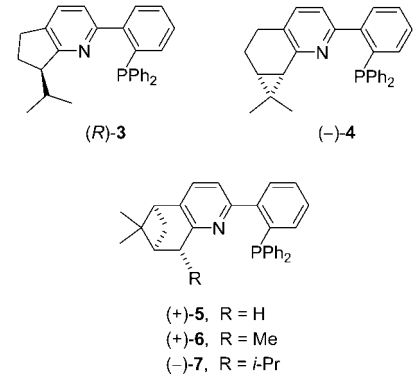
10.1021/jo800246g CCC: $40.75 © 2008 American Chemical Society
Published on Web 05/01/2008

alternative[2] but further development is required as the enantioselectivities do not reach the level attained by enzymatic systems.

Nonenantioselective transition metal-catalyzed Baeyer–Villiger oxidation reactions, which laid the foundations to further development, included Mo,[5] W,[6] Re,[7] Pt,[8] Ni,[9] and Fe[10] as catalysts with H_2O_2[5–8] or the Mukaiyama O_2−aldehyde systems as stoichiometric oxidizing reagents.[9,10]

The first examples of asymmetric transition metal-catalyzed Baeyer–Villiger oxidation were reported by Strukul (≤58% ee)[11] and Bolm (≤69% ee),[12] who utilized this approach for the resolution of racemic α-substituted cyloalkanones. While Strukul employed a Pt−BINAP complex with 2-vaniline as an additional ligand and H_2O_2 as oxidant,[11] Bolm used a Cu−oxazoline complex and the Mukaiyama system (O_2 with a sacrificial aldehyde).[12] Lopp[13] was the first to report on the oxidation of prochiral cyclobutanone **1** (R = CH_2OH) to afford (*R*)-**2** (40% ee) using (*i*-PrO)$_4$Ti, (+)-diethyl tartrate, and *tert*-butyl hydroperoxide, a system originally developed by Sharpless for epoxidation of allylic alcohols. Bolm[14] extended the scope of his Cu(II) catalyst to the oxidation of prochiral cyclobutanones but the enantioselectivity remained moderate (≤47% ee). His new complex of Zr(IV) with BINOL had to be used in stoichiometric amounts and gave 21–31% ee for 3-substituted cyclobutanones and 12–84% ee for 2,3-substituted cyclobutanones.[15] Kotsuki[16] reported on oxidation of cyclobutanones with O_2, using a complex generated from Et_2Zn and a chiral amino alcohol, but the reaction required high catalyst loading and the enantioselectivities remained moderate (≤39% ee). Bolm then improved his BINOL system by replacing Zr(IV) with Mg(II): using cumene hydroperoxide and 50 mol % catalyst loading, he obtained lactones **2** in 52–65% ee.[17] A combination of the Lewis-acidic Me_2AlCl and BINOL or vaulted BINOL (VANOL) as chiral ligands resulted in further improvement in enantioselectivity (37–84% ee) and lowering of the catalyst loading to 20 mol %.[18] A slightly increased level of asymmetric induction for **1** (60–87% ee) was attained by Katsuki, who developed several new salen-type complexes of Co(III), Zr(IV), and Hf(IV), which proved efficient in combination with the urea−H_2O_2 complex (percarbamide) as the stoichiometric oxidant.[19] The Pd(II) complex with the phosphinopyridine ligand **3** (Chart 1) gave lactone **2** in 60–80% ee[20](Table 1, entries 1–3). Herein, we report on the application of the terpene-derived *P*,*N*-ligands **4**−**7** (Chart 1) in the Pd(II)-catalyzed oxidation of **1a**−**j** to produce chiral lactones **2a**−**j**.

CHART 1. *P*,*N*-Ligands



Results and Discussion

Synthesis of Ligands. Being inspired by the Katsuki *P*,*N*-ligand **3**, we have now studied the role of the analogous terpene-derived *P*,*N*-ligands **4**–**7**. The synthesis of (−)-**4** from (+)-Δ^2-carene in five steps was described by us recently in connection with our studies on asymmetric Heck reaction[21] and Pd(0)-catalyzed allylic substitution.[22,23] In the same paper we have also reported on the synthesis of the enantiomeric (−)-**6** from (−)-*β*-pinene or (−)-α-pinene, both in 4 steps.[21] Using an analogous procedure and (+)-α-pinene as starting material, we have now prepared (+)-**5**, (+)-**6**, and (−)-**7** as follows (Scheme 2). (+)-α-Pinene was first converted into (−)-pinocarvone (−)-**8** via an ene reaction with singlet oxygen[21,24] and the latter terpene was submitted to Kröhnke annulation[21,25,26] with the pyridinium salt **9**,[21] derived from *o*-fluoro acetophenone (**9**, $AcONH_4$, AcOH, reflux, 6 h), to afford the pyridine derivative (+)-**10** (67%). Deprotonation of **10** in the "benzylic" position (*n*-BuLi, THF, –40 °C, 1 h),[21,26] followed by alkylation with MeI (−40 °C to rt, overnight), afforded (+)-**11** (59%) in the same highly diastereoselective manner as that reported by us previously[21] for its enantiomer. In analogy, alkylation of (+)-**10** with *i*-PrI afforded the new isopropyl derivative (+)-**12** (67%). Aromatic nucleophilic substitution of the fluorine in **10**−**12** with Ph_2PK (Ph_2PH, *t*-BuOK, 18-crown-6, THF, rt, 48 h)[27] furnished the required phosphines (+)-**5**, (+)-**6**, and (−)-**7** in 42%, 50%, and 52% yields, respectively.[28]

Synthesis of Cyclobutanones. The required cyclobutanones **1a**−**j** were synthesized in two steps via [2 + 2] cycloaddition

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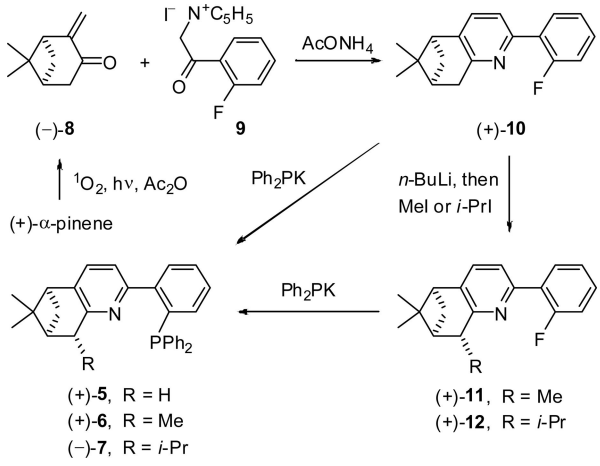
TABLE 1. Baeyer−Villiger Oxidation of Ketones 1a−j with Urea−H_2O_2, Catalyzed by the Pd(II) Complexes with *P,N*-Ligands 3–7[a]

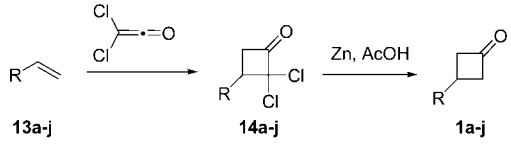
entry	ligand	ketone	R	temp (°C)	solvent	yield (%)[b]	**2**[c] (% ee)
1	**3**	**1a**	Ph	rt	THF	92	59 (*R*)[d]
2	**3**	**1a**	Ph	−40	THF	100	78 (*R*)[d]
3	**3**	**1j**	*n*-octyl	−60	THF	65	60 (*R*)[d]
4	**4**	**1a**	Ph	rt	THF	≥99	22 (*S*)[e]
5	**5**	**1a**	Ph	rt	THF	≥99	4 (*S*)[e]
6	**6**	**1a**	Ph	rt	THF	≥99	17 (*S*)[e]
7	**7**	**1a**	Ph	rt	THF	≥99	64 (*S*)[e]
8	**7**	**1a**	Ph	rt	MeCN	98	46 (*S*)[e]
9	**7**	**1a**	Ph	rt	CH_2Cl_2	≥99	36 (*S*)[e]
10	**7**	**1a**	Ph	−40	THF	97	81 (*S*)[e]
11	**7**	**1b**	4-Me-C_6H_4	−40	THF	93	75 (*S*)[e]
12	**7**	**1c**	4-F-C_6H_4	−40	THF	96	72 (+)[e]
13	**7**	**1d**	4-Cl-C_6H_4	−40	THF	94	73 (*S*)[e]
14	**7**	**1e**	4-Br-C_6H_4	−40	THF	95	76 (+)[f]
15	**7**	**1f**	2-Br-C_6H_4	−40	THF	92	70 (+)[f]
16	**7**	**1g**	2-Naphth	−40	THF	83	71 (+)[f]
17	**7**	**1h**	4-MeO-$C_6H_4CH_2$	−40	THF	91	58 (*R*)[g,h]
18	**7**	**1i**	cyclohexyl	−40	THF	89	65 (−)[f]
19	**7**	**1j**	*n*-octyl	−40	THF	83	55 (*R*)[f]

[a] The reaction was carried out at 0.5 mmol scale with 1.3 equiv of urea−H_2O_2 and 5 mol % of the Pd(II) catalysts overnight, unless stated otherwise. [b] Isolated yield. [c] The absolute configuration was established from the optical rotation (measured in $CHCl_3$) by comparison with the literature data (see the Experimental Section). Lactones **2a**, **2b**, and **2d** were (*S*)-configured; the configuration of **2c** and **2e−g** is assumed to be (*S*) in analogy with the rest of the series. [d] Reference 20. [e] Determined by chiral GC. [f] Determined by chiral HPLC (Chiralpak IB) after conversion into the corresponding hydroxy benzylamide derivative.[32] [g] Determined by optical rotation.[33] [h] Note the change in the substituent priorities in the Cahn-Ingold-Prelog system.

SCHEME 2. Synthesis of *P,N*-ligands from α-pinene; $N^+C_5H_5$ = pyridinium



SCHEME 3. Synthesis of 3-Substituted Cyclobutanones (for a−j, See Scheme 1)



of dichloro ketene (generated in situ from trichloroacetyl chloride, Zn−Cu couple, and $POCl_3$) to the vinyl derivative **13a−j**, followed by reduction of the resulting dichloro ketones **14a−j** with zinc in AcOH (Scheme 3).[29,30]

Asymmetric Baeyer–Villiger Oxidation. The precatalysts for the oxidation were generated in situ from $(PhCN)_2PdCl_2$ and the respective ligand (**4−7**) in THF at room temperature. Each of the resulting complexes was then treated with $AgSbF_6$, the insoluble AgCl was removed by filtration, and the solution of the catalyst thus generated, i.e., (Ligand)$Pd(SbF_6)_2$, was used in the individual oxidation reactions.

The oxidation of the respective cyclobutanone derivatives **1a−j** was carried out with the urea−H_2O_2 complex as the stoichiometric oxidant, either at room temperature or at −40 °C, in the presence of a catalytic amount of (Ligand)$Pd(SbF_6)_2$ (5 mol %),[31] where Ligand = **4**, **5**, **6**, and **7**, respectively (Scheme 1 and Table 1). Oxidation of 3-phenylcyclobutanone (**1a**), catalyzed by the **4**/Pd complex, afforded lactone **2a** in quantitative yield but with only 22% ee (entry 4). Similarly inferior results were obtained with ligands **5** and **6** (entries 5 and 6). On the other hand, ligand **7** (FredPhos) turned out to be substantially more effective, with 64% ee at room temperature (entry 7). Variation of the solvent proved detrimental to enantioselectivity (entries 8 and 9) but lowering the temperature to −40 °C resulted in an increase to 81% ee (entry 10). Since

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the reaction at even lower temperatures proved to be impractically slow, the latter conditions (entry 10) were accepted as optimized.

Variation of the substitution pattern in the 4-position of the cyclobutanone (**1b**−**j**) showed reduction in enantioselectivity to 70–75% ee for the aromatics with electron-withdrawing or neutral groups **1b**−**g** (entries 11–16) and to 58% ee for the *p*-methoxybenzyl derivative **1h** (entry 17). The asymmetric induction observed for the cyclohexyl derivative **1i** was in the middle between the two groups (entry 18), whereas *n*-octylcyclobutanone **1j** leaned toward the lower end of the spectrum (entry 19).

Conclusion

We have developed a series of new terpene-derived pyridine−phosphine ligands **4**–**7**, whose complexes with Pd(II) proved to catalyze Baeyer–Villiger oxidation of prochiral cyclobutanones **1a**−**j** with the urea−H_2O_2 complex as the stoichiometric oxidant. Low temperature (−40 °C), THF as the solvent, and 5 mol % catalyst loading[31] were identified as optimal conditions. Ligand **7** (FredPhos) exhibited the highest enantioselectivities (≤81% ee; Table 1, entry 10), which brings it into the same category as the most successful ligand reported to date (**3** with 78% ee;[20] entry 2).

Experimental Section

(8*S*,10*S*)-(+)-2-(2′-Fluorophenyl)-11,11-dimethyl-1-azatricyclo-[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-10. A solution of pinocarvone (−)-**8**[21,24] (1.05 g, 7.0 mmol), with the Kröhnke salt **9**[21] (2.41 g, 7.0 mmol) and ammonium acetate (9.25 g) in acetic acid (12 mL) was refluxed for 6 h. The mixture was then diluted with water (25 mL), made neutral by addition of an aqueous solution of sodium hydroxide (2 M), and extracted with ethyl acetate (3 × 50 mL). The organic phase was washed successively with water (3 × 50 mL) and brine (50 mL) and dried over $MgSO_4$. The solvent was removed under vacuum to afford pure (+)-**10** (1.25 g, 67%) as a red oil: $[\alpha]^{19}_D$ +68.8 (*c* 1.0, $CHCl_3$) [the enantiomer[21] had $[\alpha]_D$ –75.2 (*c* 0.8, $CHCl_3$)]; IR (NaCl) ν 2939 (s, C−H), 1588 (s, Ar), 1595 (s, Ar), 1440 (s, Ar), 1225 (m, C−H methyl), 1108 (s, C−F), 752 (m, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.69 (s, 3H, CH_3), 1.32 (d, J = 9.6 Hz, 1H, 9-H), 1.41 (s, 3H, CH_3), 2.39 (tt, J = 5.8, 2.9 Hz, 1H, 8-H), 2.71 (dt, J = 9.6, 5.8 Hz, 1H, 9-H′), 2.79 (t, J = 5.8 Hz, 1H, 10-H), 3.18 (d, J = 2.9 Hz, 2H, 7-H), 7.12 (ddd, J = 11.3, 8.1, 1.2 Hz, 1H, 3′-H), 7.23 (td, J = 7.9, 1.3 Hz, 1H, 5′-H), 7.25 (d, J = 7.8 Hz, 1H, 4-H), 7.31 (m, 1H, 4′-H), 7.46 (dd, J = 7.8, 2.4 Hz, 1H, 3-H), 7.96 (td, J = 7.9, 1.9 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3 (CH_3), 26.0 (CH_3), 31.9 (CH_2-9), 36.7 (CH_2-7), 39.5 (C-11), 40.2 (CH-8), 46.3 (CH-10), 116.0 (d, J = 23 Hz, CH-3′), 121.1 (d, J = 9 Hz, CH-3), 124.4 (d, J = 4 Hz, CH-5′), 127.9 (d, J = 12 Hz, C-1′), 129.6 (d, J = 8 Hz, CH-4′), 130.9 (d, J = 3 Hz, CH-6′), 133.1 (CH-4), 140.7 (C-5), 150.3 (d, J = 2 Hz, C-2), 156.9 (C-6), 160.3 (d, J = 249 Hz, C-2′); ^{19}F NMR (376 MHz, $CDCl_3$) δ –117.4 (s); MS (EI) *m*/*z* (%) 267 ($M^{\bullet+}$, 68), 252 ($M^{\bullet+}$ − CH_3, 52), 224 (100), 83 (38); HRMS (EI) 267.1427 ($C_{18}H_{18}FN$ requires 267.1423).

General Procedure for the Alkylation of (+)-10. A solution of *n*-butyllithium in hexane (2.5 M; 0.6 mL, 1.5 mmol, 1 equiv) was added dropwise to a solution of (+)-**10** (400 mg, 1.5 mmol, 1 equiv) in anhydrous THF (2 mL) under argon at –40 °C. The solution was stirred at that temperature for 1 h, then the respective electrophile, iodomethane (0.1 mL, 1.5 mmol, 1 equiv) or 2-iodopropane (0.15 mL, 1.5 mmol, 1 equiv), was added dropwise at –40 °C. The solution was then gradually warmed to room temperature and stirred overnight. The reaction was quenched by addition of water (15 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on a column of silica gel (15 g) with a mixture of petroleum ether and AcOEt (97:3) to give respectively pure (+)-**11** (246 mg, 59%) as a colorless oil or pure (+)-**12** (309 mg, 67%).

(7*R*,8*S*,10*S*)-(+)-2-(2′-Fluorophenyl)-7,11,11-trimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-11. $[\alpha]^{20}_D$ +38.4 (*c* 1.0, $CHCl_3$) [the enantiomer[21] had $[\alpha]_D$ –39.5 (*c* 1.3, $CHCl_3$)]; IR (NaCl) ν 2945 (s, C−H), 1586 (m, Ar), 1488 (m, Ar), 1437 (m, Ar), 1206 (m, CH_3), 1031 (s, C−F), 754 (m, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (s, 3H, CH_3), 1.31 (d, J = 9.8 Hz, 1H, 9-H), 1.38 (s, 3H, CH_3), 1.44 (d, J = 7.1 Hz, 3H, CH_3C(7)), 2.13 (td, J = 5.8, 2.5 Hz, 1H, 8-H), 2.53 (dt, J = 9.8, 5.8 Hz, 1H, 9-H′), 2.74 (t, J = 5.8 Hz, 1H, 10-H), 3.24 (qd, J = 7.1, 2.5 Hz, 1H, 7-H), 7.09 (ddd, J = 11.5, 8.1, 1.3 Hz, 1H, 3′-H), 7.18 (d, J = 7.8 Hz, 1H, 4-H), 7.20 (td, J = 7.6, 1.3 Hz, 1H, 5′-H), 7.24–7.29 (m, 1H, 4′-H), 7.48 (dd, J = 7.8, 2.0 Hz, 1H, 3-H), 7.96 (td, J = 7.9, 1.9 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2 (CH_3C(7)), 20.8 (CH_3), 26.2 (CH_3), 28.5 (CH_2-9), 38.8 (CH-7), 41.3 (C-11), 46.7 (CH-8), 46.9 (CH-10), 115.9 (d, J = 23 Hz, CH-3′), 121.0 (d, J = 9 Hz, CH-3), 124.2 (d, J = 4 Hz, CH-5′), 127.8 (d, J = 12 Hz, C-1′), 129.5 (d, J = 9 Hz, CH-4′), 130.9 (d, J = 4 Hz, CH-6′), 132.8 (CH-4), 140.4 (C-5), 149.9 (d, J = 3 Hz, C-2), 160.4 (d, J = 249 Hz, C-2′), 160.6 (C-6); ^{19}F NMR (376 MHz, $CDCl_3$) δ –116.9 (s); MS (EI) *m*/*z* (%) 281 ($M^{\bullet+}$, 19), 266 ($M^{\bullet+}$ − CH_3, 50), 238 (62), 224 (12), 83 (100); HRMS (EI) 281.1583 ($C_{19}H_{20}FN$ requires 281.1580).

(7*R*,8*S*,10*S*)-(+)-2-(2′-Fluorophenyl)-7-isopropyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-12. $[\alpha]^{25}_D$ +15.8 (*c* 1.0, $CHCl_3$); IR (NaCl) ν 2942 (s, C−H), 1587 (m, Ar), 1483 (m, Ar), 1432 (m, Ar), 1213 (m, C−H methyl), 1056 (s, C−F), 752 (m, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.59 (s, 3H, CH_3), 0.81 (d, J = 7.0 Hz, 3H, CH_3CH), 1.17 (d, J = 7.0 Hz, 3H, CH_3'CH)), 1.35 (d, J = 9.7 Hz, 1H, 9-H), 1.36 (s, 3H, CH_3), 2.32 (td, J = 5.7, 2.0 Hz, 1H, 8-H), 2.52 (dt, J = 9.7, 5.7 Hz, 1H, 9-H′), 2.68 (t, J = 5.7 Hz, 1H, 10-H), 2.83 (spd, J = 7.0, 4.7 Hz, 1H, $(CH_3)_2CH$), 2.93 (dd, J = 4.7, 2.0 Hz, 1H, 7-H), 7.06 (ddd, J = 11.5, 8.1, 1.3 Hz, 1H, 3′-H), 7.17 (d, J = 7.8 Hz, 1H, 4-H), 7.18 (td, J = 7.5, 1.4 Hz, 1H, 5′-H), 7.22–7.27 (m, 1H, 4′-H), 7.47 (dd, J = 7.8, 2.0 Hz, 1H, 3-H), 8.04 (td, J = 7.9, 2.0 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0 (CH_3CH), 21.0 (CH_3), 22.2

(27) For the method, see, e.g.: Kündig, E. P.; Meier, P. *Helv. Chim. Acta* **1999**, *82*, 1360.

(28) While the synthesis of **5** was straightforward, the preparation of **6** and **7** was complicated by the difficulties associated with the isolation of the pure product from the crude mixture. Since phosphines **6** and **7** could not be fully separated from the unreacted, respective fluorides **11** and **12** and traces of Ph_2PH, the crude mixture was oxidized (H_2O_2, Me_2CO, rt, 10 min) to convert the phosphines into the corresponding phosphine oxides, which were then readily separated from the fluorides **11** and **12** by column chromatography. However, the phosphine oxides were still contaminated by $Ph_2P(O)H$, generated from Ph_2PH. Therefore, the mixture was treated with KOH in EtOH (reflux, 4 h), which generated the water-soluble Ph_2PO_2K (presumably via air oxidation), whose separation from the respective phosphine oxides was carried out by partitioning between the aqueous and organnic phase (for the method, see: Tsvetkov, E. N.; Bondarenko, N. A.; Malakhova, I. G.; Kabachnik, M. I. *Synthesis* **1986**, 198). The pure phosphine oxides were then reduced [Cl_3SiH, Et_3N, toluene, reflux, 24 h; for the method, see: (a) Kurz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Wars, T. *Tetrahedron Lett.* **1990**, *31*, 6321. (b) Vyskočil, Š.; Smrčina, M.; Hanuš, V.; Polášek, M.; Kočovský, P. *J. Org. Chem.* **1998**, *63*, 7738.] to afford the respective phosphines (+)-**6** and (−)-**7**. The yields (50% and 52%, respectively) correspond to the overall procedure.

(29) For the method, see the following: (a) Krepski, L. R.; Hassner, A. *J. Org. Chem.* **1978**, *43*, 2879. (b) Hassner, A.; Dillon, J. L. *J. Org. Chem.* **1983**, *48*, 3382.

(30) Most of the cyclobutanones **1a**−**j** were obtained in good yields. However, we failed to prepare *p*-methoxyphenylcyclobutanone due to the polymerization of the starting *p*-methoxystyrene under the reaction conditions.

(31) Lower catalyst loading was not explored.

(32) (a) Uchida, T.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 6911. (b) Uchida, T.; Katsuki, T. *Helv. Chim. Acta* **2002**, *85*, 3078.

(33) Koul, S.; Singh, B.; Taneja, S. C.; Qazi, G. N. *Tetrahedron* **2003**, *59*, 3487.

(*C*'H_3CH), 26.3 (CH_3), 29.4 (CH_2-9), 30.3 (CH_3*C*HCH_3), 41.2 (CH-8), 41.9 (C-11), 46.5 (CH-10), 49.1 (CH-7), 116.0 (d, J = 23 Hz, CH-3′), 121.0 (d, J = 10 Hz, CH-3), 124.3 (d, J = 4 Hz, CH-5′), 127.9 (d, J = 12 Hz, C-1′), 129.5 (d, J = 9 Hz, CH-4′), 130.9 (d, J = 3 Hz, CH-6′), 132.9 (CH-4), 141.1 (C-5), 149.6 (d, J = 3 Hz, C-2), 159.2 (C-6), 160.5 (d, J = 249 Hz, C-2′); ^{19}F NMR (376 MHz, $CDCl_3$) δ –116.9 (s); MS (EI) m/z (%) 309 ($M^{\bullet+}$, 17), 294 ($M^{\bullet+} - CH_3$, 15), 266 ($M^{\bullet+} - CH(CH_3)_2$, 84), 224 (100), 83 (78); HRMS (EI) 309.1897 ($C_{21}H_{24}FN$ requires 309.1893).

General Procedure for the Reaction of Fluoro Derivatives 10–12 with Ph_2PK. Diphenylphosphine (0.32 mL, 1.86 mmol, 2 equiv) was added to a suspension of potassium *tert*-butoxide (210 mg, 1.86 mmol, 2 equiv) and 18-crown-6 (490 mg, 1.86 mmol) in THF (10 mL) at 0 °C and the resulting deep red solution was stirred at this temperature for 1 h. A solution of the respective fluoro derivative **10** (250 mg, 0.93 mmol, 1 equiv), **11** (262 mg, 0.93 mmol, 1 equiv), and **12** (287 mg, 0.93 mmol) in THF (2 mL) was then added dropwise and the mixture was stirred at room temperature for 48 h. Methanol (2 mL) was then added and the solvent was removed in vacuo to afford an oil that was purified via flash chromatography on silica gel (25 g) with use of petroleum ether followed by a 9:1 mixture of petroleum ether and ethyl acetate to give pure (+)-**5** (167 mg, 42%) as a white solid. In the case of (+)-**6** and (−)-**7**,[28] after evaporation of the solvent, the residue was dissolved in acetone (20 mL) and a 30% aqueous solution of hydrogen peroxide (3 mL) was then added. The resulting mixture was stirred at room temperature for 10 min and then partitioned between water and CH_2Cl_2. The layers were separated, the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with water (20 mL) and brine (20 mL), dried over $MgSO_4$, and concentrated under vacuum. The crude mixture was then purified via flash chromatography on silica gel (17 g) with a 1:1 mixture of petroleum ether and ethyl acetate, followed by pure methanol. The methanolic fraction was concentrated in vacuo and the residue was dissolved in ethanol (1.5 mL). Potassium hydroxide (1.3 mmol, 56.1 mg, 1.3 equiv) was added to the ethanolic solution and the reaction mixture was refluxed for 4 h. The latter mixture was then cooled to room temperature and diluted with water (20 mL). The aqueous phase was extracted with ethyl acetate (3 × 20 mL) and the combined organic extracts were then washed with a saturated aqueous solution of $NaHCO_3$ (3 × 20 mL), dried over $MgSO_4$, and concentrated under vacuum. Finally, the residue was dissolved in toluene (10 mL), triethylamine (2.1 mL, 15 mmol, 15 equiv) and trichlorosilane (1 mL, 10 mmol, 10 equiv) were added, and the resulting reaction mixture was refluxed for 24 h. The mixture was then diluted with an aqueous solution of sodium hydroxide (2 M, 10 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with water (20 mL) and brine (20 mL) and dried over $MgSO_4$ and concentrated under vacuum to afford pure (+)-**6** (208 mg, 50%) and (−)-**7** (230 mg, 52%), respectively.

(8*S*,10*S*)-(+)-2-[2′-(Diphenylphosphino)phenyl]-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-5. $[\alpha]^{19}_D$ +58.5 (*c* 1.0, $CHCl_3$); IR (KBr) ν 2936 (m, C−H), 1576 (m, Ar), 1445 (m, Ar), 1432 (m, Ar), 1213 (m), 757 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.46 (s, 3H, CH_3), 1.13 (d, J = 9.4 Hz, 1H, 9-H), 1.27 (s, 3H, CH_3), 2.18 (tt, J = 5.7, 2.9 Hz, 1H, 8-H), 2.52 (dt, J = 9.4, 5.7 Hz, 1H, 9-H′), 2.60 (t, J = 5.7 Hz, 1H, 10-H), 2.75 (d, J = 2.9 Hz, 2H, 7-H), 6.92 (ddd, J = 7.7, 4.1, 1.1 Hz, 1H, 3′-H), 7.02 (d, J = 7.7 Hz, 1H, 4-H), 7.08 (d, J = 7.7 Hz, 1H, 5-H), 7.12–7.22 (m, 11H, aromH), 7.31 (td, J = 7.6, 1.3 Hz, 1H, 5′-H), 7.51 (ddd, J = 7.6, 4.2, 1.2 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3 (CH_3), 26.0 (CH_3), 31.7 (CH_2-9), 36.0 (CH_2-7), 39.4 (C-11), 40.1 (CH-8), 46.2 (CH-10), 120.14 (d, J = 3.7 Hz, CH-3), 127.7, (CH-4′), 128.0–128.2 (6 × aromCH), 128.5 (CH-5′), 129.3 (d, J = 4 Hz, CH-6′), 132.6 (CH-4), 133.9 (d, J = 6.4 Hz, 2 × aromCH), 134.1 (d, J = 6.4 Hz, 2 × aromCH), 134.2 (d, J = 30.5 Hz, CH-3′), 136.6 (d, J = 18 Hz, C-1′), 138.6 (d, J = 11 Hz, *C*PAr_2), 138.7 (d, J = 11 Hz, *C*'PAr_2), 139.7 (C-5), 145.9 (d, J = 24 Hz, C-2′), 155.6 (C-6), 155.8 (d, J = 2 Hz, C-2); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ −9.3 (s); MS (EI) m/z (%) 433 ($M^{\bullet+}$, 10), 356 ($M^{\bullet+} - C_6H_5$, 100), 248 ($M^{\bullet+} - PPh_2$, 5), 91 (12), 44 (76); HRMS (EI) 433.1953 ($C_{30}H_{28}NP$ requires 433.1959).

(7*R*,8*S*,10*S*)-(+)-2-[2′-(Diphenylphosphino)phenyl]-7,11,11-trimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (+)-6. $[\alpha]^{26}_D$ +3.4 (*c* 1.0, $CHCl_3$) [the enantiomer[21] had $[\alpha]_D$ −10.1 (*c* 2.00, $CHCl_3$)]; IR (KBr) ν 2942 (m, C−H), 1573 (m, Ar), 1452 (m, Ar), 1431 (m, Ar), 1217 (m), 755 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.51 (s, 3H, CH_3), 0.90 (d, J = 7.0 Hz, 3H, C*H*$_3$C(7)), 1.17 (d, J = 9.9 Hz, 1H, 9-H), 1.31 (s, 3H, CH_3), 1.97 (td, J = 5.7, 2.4 Hz, 1H, 8-H), 2.41 (dt, J = 9.9, 5.7 Hz, 1H, 9-H′), 2.63 (t, J = 5.7 Hz, 1H, 10-H), 2.90 (qd, J = 7.0, 2.4 Hz, 1H, 7-H), 6.96 (dd, J = 7.5, 3.8 Hz, 1H, 3′-H), 7.06 (d, J = 7.7 Hz, 1H, 4-H), 7.11 (d, J = 7.7 Hz, 1H, 3-H), 7.15–7.25 (m, 11H, aromH), 7.34 (td, J = 7.5, 1.0 Hz, 1H, 5′-H), 7.55 (ddd, J = 7.5, 4.3, 1.1 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (*C*H_3C(7)), 20.9 (CH_3), 26.2 (CH_3), 28.5 (CH_2-9), 38.7 (CH-7), 41.3 (C-11), 46.8 (CH-8), 46.9 (CH-10), 120.2 (d, J = 3.0 Hz, CH-3), 127.7, (CH-4′), 128.0–128.2 (6 × aromCH), 128.4 (CH-5′), 129.4 (d, J = 4.2 Hz, CH-6′), 132.5 (CH-4), 133.7 (d, J = 15.1 Hz, 2 × aromCH), 134.9 (d, J = 14.8 Hz, 2 × aromCH), 134.4 (d, J = 21.4 Hz, CH-3′), 136.1 (d, J = 18 Hz, C-1′), 139.0 (d, J = 11 Hz, *C*PAr_2), 139.2 (d, J = 11 Hz, *C*'PAr_2), 139.5 (C-5), 146.4 (d, J = 23 Hz, C-2′), 156.0 (d, J = 2 Hz, C-2), 159.6 (C-6); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ −9.9 (s); MS (EI) m/z (%) 447 ($M^{\bullet+}$, 14), 370 ($M^{\bullet+} - C_6H_5$, 100); HRMS (EI) 447.2118 ($C_{31}H_{30}NP$ requires 447.2116).

(7*R*,8*S*,10*S*)-(−)-2-[2′-(Diphenylphosphino)phenyl]-7-isopropyl-11,11-dimethyl-1-azatricyclo[7.1.1.0^{5,6}]undeca-2,4,6-triene (−)-7. $[\alpha]^{26}_D$ −15.0 (*c* 1.0, $CHCl_3$); IR (KBr) ν 2951 (m, C−H), 1571 (m, Ar), 1449 (m, Ar), 1433 (m, Ar), 1215 (m), 752 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.49 (s, 3H, CH_3), 0.53 (d, J = 7.0 Hz, 3H, C*H*$_3$CH), 0.73 (d, J = 7.0 Hz, 3H, C*H*$_3$'CH), 1.30 (d, J = 9.9 Hz, 1H, 9-H), 1.31 (s, 3H, CH_3), 2.15–2.25 (m, 2H, 8-H, CH_3C*H*CH_3), 2.44 (dt, J = 9.9, 5.6 Hz, 1H, 9-H′), 2.60 (t, J = 5.6 Hz, 1H, 10-H), 2.63–2.67 (m, 1H, 7-H), 6.99 (dd, J = 7.2, 3.8 Hz, 1H, 3′-H), 7.09 (d, J = 7.7 Hz, 1H, 4-H), 7.12 (d, J = 7.7 Hz, 1H, 3-H), 7.14–7.26 (m, 11H, aromH), 7.33 (t, J = 7.2 Hz, 1H, 5′-H), 7.54 (dd, J = 7.2, 4.4 Hz, 1H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7 (*C*H_3CH), 21.1 (CH_3), 22.0 (*C*'H_3CH), 26.3 (CH_3), 29.1 (*C*H(CH_3)$_2$), 29.5 (CH_2-9), 40.4 (CH-8), 41.9 (C-11), 46.6 (CH-10), 48.9 (CH-7), 120.4 (d, J = 3.1 Hz, CH-3), 127.7–128.2 (7 × aromCH), 128.6 (CH-5′), 129.6 (d, J = 5.0 Hz, CH-6′), 132.5 (CH-4), 133.6 (d, J = 18.8 Hz, 2 × aromCH), 133.8 (d, J = 18.8 Hz, 2 × aromCH), 135.2 (d, J = 22.2 Hz, CH-3′), 135.8 (d, J = 18 Hz, C-1′), 139.0 (d, J = 12.8 Hz, *C*PAr_2), 139.3 (d, J = 12.6 Hz, *C*'PAr_2), 140.3 (C-5), 147.4 (d, J = 25.7 Hz, C-2′), 156.2 (d, J = 2.7 Hz, C-2), 158.2 (C-6); ^{31}P NMR (162.0 MHz, $CDCl_3$) δ −11.2 (s); MS (EI) m/z (%) 475 ($M^{\bullet+}$, 39), 398 ($M^{\bullet+} - C_6H_5$, 100), 355 ($M^{\bullet+} - C_6H_5 - (CH_3)_2CH$, 32), 194 (60); HRMS (EI) 475.2428 ($C_{33}H_{34}NP$ requires 475.2429).

Zinc−Copper Couple Preparation. A solution of copper sulfate ($CuSO_4 \cdot 5H_2O$, 0.76 g) in water (5 mL) was added in two portions at 30-s intervals to a stirred mixture of zinc dust (6.5 g, 0.1 mol) in water (10 mL). After 1 min the mixture was filtered through a sintered-glass Büchner funnel and the zinc−copper couple was washed with water (2 × 5 mL), acetone (2 × 5 mL), and ether (5 mL). The resulting dark-gray powder was dried at 100 °C under vacuum for 6 h and then stored under argon.

General Procedure for the Formation of 2,2-Dichlorocyclobutanones 14a−j. A solution of trichloroacetyl chloride (1.12 mL, 10.0 mmol, 2.0 equiv) and phosphorus oxychloride (0.51 mL, 5.5 mmol, 1.1 equiv) in ether (5 mL) was added dropwise to a solution of the vinyl derivative **13a−j** (5.0 mmol, 1.0 equiv) and zinc−copper couple (0.98 g, 15.0 mmol, 3.0 equiv) in ether (10 mL). The resulting solution was heated at 40 °C for 2 h and then stirred at room temperature overnight. The resulting mixture was filtered over Celite and the Celite was washed with ether (12 mL). Hexane (40 mL) was added to the filtrate, which was then gently

stirred to help zinc dichloride to precipitate. The supernatant solution was successively washed with water (20 mL), a saturated aqueous solution of $NaHCO_3$ (20 mL), and brine (20 mL) and dried over Na_2SO_4, then concentrated under vacuum to afford pure **14a**−**j**, which were used directly in the next step (i.e., conversion into **1a–j**) without further purification.

2,2-Dichloro-3-phenylcyclobutanone (14a). Yield 1.042 g, 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (dd, J = 17.6, 10.3 Hz, 1H, 4-H), 3.73 (dd, J = 17.6, 10.3 Hz, 1H, 4-H′), 4.26 (t, J = 10.3 Hz, 1H, 3-H), 7.33 (d, J = 7.2 Hz, 2H, 2′-H, 6′-H), 7.40 (t, J = 7.2 Hz, 1H, 4′-H), 7.45 (t, J = 7.2 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.7 (CH_2-4), 50.5 (CH-3), 89.5 (C-2), 128.0 (2 × CH-2′,6′), 128.3 (CH-4′), 128.6 (2 × CH-3′,5′), 134.4 (C-1′), 191.9 (C=O) in agreement with the literature data.[29]

2,2-Dichloro-3-(4′-toluyl)cyclobutanone (14b). Yield 1.040 g, 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H, CH_3), 3.41 (dd, J = 17.7, 10.3 Hz, 1H, 4-H), 3.59 (dd, J = 17.7, 10.3 Hz, 1H, 4-H′), 4.13 (t, J = 10.3 Hz, 1H, 3-H), 7.14 (d, J = 8.2 Hz, 2H, 3′-H, 5′-H), 7.18 (dd, J = 8.2 Hz, 2H, 2′-H, 6′-H).

2,2-Dichloro-3-(4′-fluorophenyl)cyclobutanone (14c). Yield 1.092 g, 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (dd, J = 17.7, 10.3 Hz, 1H, 4-H), 3.55 (dd, J = 17.7, 10.3 Hz, 1H, 4-H′), 4.10 (t, J = 10.3 Hz, 1H, 3-H), 6.97 (t, J = 8.7 Hz, 2H, 3′-H, 5′-H), 7.17 (dd, J = 8.7, 5.2 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.8 (CH_2-4), 49.8 (CH-3), 89.4 (C-2), 115.5 (d, J = 21.6 Hz, 2 × CH-3′,5′), 129.7 (d, J = 8.2 Hz, 2 × CH-2′,6′), 130.2 (d, J = 3.3 Hz, C-1′), 162.4 (d, J = 247.4 Hz, CF-4′), 191.5 (C=O); ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.2 (s).

2,2-Dichloro-3-(4′-chlorophenyl)cyclobutanone (14d). Yield 1.121 g, 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49 (dd, J = 17.7, 10.3 Hz, 1H, 4-H), 3.61 (dd, J = 17.7, 10.3 Hz, 1H, 4-H′), 4.14 (t, J = 10.3 Hz, 1H, 3-H), 7.18 (d, J = 8.9 Hz, 2H, 3′-H, 5′-H), 7.34 (dd, J = 8.9 Hz, 2H, 2′-H, 6′-H).

2,2-Dichloro-3-(4′-bromophenyl)cyclobutanone (14e). Yield 1.352 g, 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (dd, J = 17.6, 10.3 Hz, 1H, 4-H), 3.67 (dd, J = 17.6, 10.3 Hz, 1H, 4-H′), 4.19 (t, J = 10.3 Hz, 1H, 3-H), 7.19 (d, J = 8.5 Hz, 2H, 3′-H, 5′-H), 7.56 (dd, J = 8.5 Hz, 2H, 2′-H, 6′-H).

2,2-Dichloro-3-(2′-bromophenyl)cyclobutanone (14f). Yield 1.314 g, 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (d, J = 9.8 Hz, 2H, 4H), 4.67 (t, J = 9.8 Hz, 1H, 3-H), 7.13 (td, J = 7.7, 1,5 Hz, 1H, 4′-H), 7.17 (dd, J = 7.7, 1,5 Hz, 1H, 6′-H), 7.28 (td, J = 7.7, 1.1 Hz, 1H, 5′-H), 7.58 (dd, J = 7.7, 1.1 Hz, 1H, 3′-H).

2,2-Dichloro-3-(2′-naphthyl)cyclobutanone (14g). Yield 547 mg, 41%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.35 (dd, J = 17.7, 10.3 Hz, 1H, 4-H), 3.63 (dd, J = 17.7, 10.3 Hz, 1H, 4-H′), 4.17 (t, J = 10.3 Hz, 1H, 3-H), 7.33 (dd, J = 8.5, 1.8 Hz, 1H, 3′-H), 7.37–7.45 (m, 2H, 6′-H, 7′-H), 7.63–7.67 (m, 1H, 1′-H), 7.72–7.80 (m, 3H, 4′-H, 8′-H, 5′-H).

2,2-Dichloro-3-(4′-methoxybenzyl)cyclobutanone (14 h). Yield 1.287 g, 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (dd, J = 14.0, 8.7 Hz, 1H, 4-H), 3.03 (dd, J = 16.7, 8.0 Hz, 1H, 4-H′), 3.10–3.30 (m, 3H, CH_2CH), 3.77 (s, 3H, CH_3O), 6.86 (d, J = 8.7 Hz, 2H, 3′-H, 5′-H), 7.15 (dd, J = 8.7, 2H, 2′-H, 6′-H).

2,2-Dichloro-3-(cyclohexyl)cyclobutanone (14i). Yield 1.062 g, 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92–1.35 (m, 5H), 1.51–1.79 (m, 5H), 2.00–2.12 (m, 1H, 1′-H), 2.54 (q, J = 10.3 Hz, 1H, 3-H), 3.03 (dd, J = 17.4, 10.3 Hz, 1H, 4-H), 3.13 (dd, J = 17.4, 10.3 Hz, 1H, 4-H′).

2,2-Dichloro-3-octylcyclobutanone (14j). Yield 1.062 g, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 6.8 Hz, 3H, CH_3CH$_2$), 1.16–1.46 (m, 12H, 6 × CH_2), 1.50–1.62 (m, 1H, CH_2CH_2CH), 1.80–1.90 (m, 1H, CH_2CH_2'CH), 2.78–2.87 (m, 1H, 3-H), 2.91 (dd, J = 17.1, 9.2 Hz, 1H, 4-H), 3.30 (dd, J = 17.1, 9.2 Hz, 1H, 4-H′).

General Procedure for the Formation of Cyclobutanones 1a−j. A mixture of dichloro ketone **14a**−**j** (1 equiv) and zinc dust (4 equiv) in acetic acid (15 mL) was stirred at room temperature for 2 h and then refluxed for 5 h. The resulting mixture was diluted with water (20 mL) and extracted with ether (2 × 30 mL). The organic phase was washed successively with a saturated solution of aqueous $NaHCO_3$ (3 × 20 mL), water (30 mL), and brine (30 mL), then dried over $MgSO_4$ and concentrated under vacuum. The crude material was then purified by flash chromatography on silica gel (20 g) with a mixture of petroleum ether and ethyl acetate (5:1) to afford **1a**−**j** as colorless oils.

3-Phenylcyclobutanone (1a). Yield 612 mg, 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18 (ddt, J = 19.9, 8.2, 3.7 Hz, 2H, 2-H, 4-H), 3.42 (ddt, J = 19.9, 8.2, 3.7 Hz, 2H, 2-H′, 4-H′), 3.57 (pent, J = 8.2 Hz, 1H, 3-H), 7.16 (t, J = 7.1 Hz, 1H, 4′-H), 7.20 (d, J = 7.1 Hz, 2H, 2′-H, 6′-H), 7.26 (t, J = 7.1 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3 (CH-3), 54.6 (2 × CH_2-2,4), 126.4 (2 × CH-2′,6′), 126.5 (CH-4′), 128.6 (2 × CH-3′,5′), 143.5 (C-1′), 206.5 (C=O) in agreement with the literature data.[29]

3-(4′-Toluyl)cyclobutanone (1b). Yield 232 mg, 32%; IR (NaCl) ν 2922 (w, C−H), 1783 (s, C=O), 1608 (m, Ar), 1570 (m, Ar), 1515 (m, Ar), 1161 (m), 1019 (m), 813 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H, CH_3), 3.17 (ddt, J = 20.0, 8.6, 3.1 Hz, 2H, 2-H, 4-H), 3.42 (ddt, J = 20.0, 8.6, 3.1 Hz, 2H, 2-H′, 4-H′), 3.54 (pent, J = 8.6 Hz, 1H, 3-H), 7.09 (d, J = 8.4 Hz, 2H, 3′-H, 5′-H), 7.12 (dd, J = 8.4 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7 (CH_3), 27.7 (CH-3), 54.4 (2 × CH_2-2,4), 126.1 (2 × CH-2′,6′), 129.0 (2 × CH-3′,5′), 135.8 (C-4′), 140.3 (C-1′), 206.5 (C=O); MS (EI) m/z (%) 160 (M$^{\bullet+}$, 12), 118 (M$^{\bullet+}$ − CH_2C=O, 100), 91 (M$^{\bullet+}$ − C_3H_5C=O, 26), 83 (32); HRMS (EI) 160.0889 ($C_{11}H_{12}O$ requires 160.0888).

3-(4′-Fluorophenyl)cyclobutanone (1c). Yield 409 mg, 56%; IR (NaCl) ν 2977 (w, C−H), 1785 (s, C=O), 1604 (m, Ar), 1511 (m, Ar), 1431 (m, Ar), 1226 (s), 1103 (m, C−F), 829 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (ddt, J = 20.0, 8.3, 3.0 Hz, 2H, 2-H, 4-H), 3.40 (ddt, J = 20.0, 8.3, 3.0 Hz, 2H, 2-H′, 4-H′), 3.58 (pent, J = 8.3 Hz, 1H, 3-H), 6.95 (t, J = 8.6 Hz, 2H, 3′-H, 5′-H), 7.19 (dd, J = 8.6, 5.4 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5 (CH-3), 54.5 (2 × CH_2-2,4), 115.2 (d, J = 21.3 Hz, 2 × CH-3′,5′), 127.8 (d, J = 8.0 Hz, 2 × CH-2′,6′), 139.1 (d, J = 3.1 Hz, C-1′), 161.3 (d, J = 244.7 Hz, CF-4′), 206.0 (C=O);^{19}F NMR (376 MHz, $CDCl_3$) δ –116.3 (s); MS (EI) m/z (%) 164 (M$^{\bullet+}$, 4), 122 (M$^{\bullet+}$ − CH_2C=O, 100), 84 (61), 49 (86); HRMS (EI) 164.0638 ($C_{10}H_9FO$ requires 164.0637).

3-(4′-Chlorophenyl)cyclobutanone (1d). Yield 371 mg, 46%; IR (NaCl) ν 2974 (w, C−H), 1786 (s, C=O), 1593 (m, Ar), 1493 (m, Ar), 1092 (s, C−Cl), 1013 (m), 821 (s, Ar) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (ddt, J = 20.2, 8.3, 3.1 Hz, 2H, 2-H, 4-H), 3.47 (ddt, J = 20.2, 8.3, 3.1 Hz, 2H, 2-H′, 4-H′), 3.63 (pent, J = 8.3 Hz, 1H, 3-H), 7.21 (d, J = 8.4 Hz, 2H, 2′-H, 6′-H), 7.29 (d, J = 8.4 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.7 (CH-3), 54.5 (2 × CH_2-2,4), 127.7 (2 × CH-3′,5′), 128.5 (2 × CH-2′,6′), 132.1 (C-4′), 141.9 (C-1), 205.8 (C=O) in agreement with the literature data.[34]

3-(4′-Bromophenyl)cyclobutanone (1e). Yield 459 mg, 51%; IR (NaCl) ν 2976 (w, C−H), 1786 (s, C=O), 1589 (m, Ar), 1489 (m, Ar), 1073 (s), 1009 (m), 817 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.20 (ddt, J = 20.1, 8.3, 3.7 Hz, 2H, 2-H, 4-H), 3.50 (ddt, J = 20.1, 8.3, 3.7 Hz, 2H, 2-H′, 4-H′), 3.64 (pent, J = 8.4 Hz, 1H, 3-H), 7.17 (d, J = 8.3 Hz, 2H, 2′-H, 6′-H), 7.47 (d, J = 8.3 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0 (CH-3), 54.6 (2 × CH_2-2,4), 120.4 (C-4′), 128.2 (2 × CH-2′,6′), 131.7 (2 × CH-3′,5′), 142.5 (C-1′), 206.0 (C=O); MS (EI) m/z (%) 225 (d, M$^{\bullet+}$, 7), 183 (d, M$^{\bullet+}$ − CH_2C=O, 100), 115 (17), 103 (M$^{\bullet+}$ − CH_2C=O−Br, 60), 77 (42); HRMS (EI) 223.9835 ($C_{10}H_9$-BrO requires 223.9837).

3-(2′-Bromophenyl)cyclobutanone (1f). Yield 468 mg, 52%; IR (NaCl) ν 2981 (w, C−H), 1786 (s, C=O), 1590 (m, Ar), 1566 (m, Ar), 1472 (m, Ar), 1102 (s), 1026 (s), 754 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.23 (ddt, J = 20.2, 8.3, 3.2 Hz, 2H, 2-H, 4-H), 3.53 (ddt, J = 20.2, 8.3, 3.2 Hz, 2H, 2-H′, 4-H′), 3.95

(34) Resende, P.; Almeida, W. P.; Coelho, F. *Tetrahedron: Asymmetry* **1999**, *10*, 2113.

(pent, J = 8.3 Hz, 1H, 3-H), 7.14 (ddd, J = 8.4, 6.1, 3.0 Hz, 1H, 4′-H), 7.32–7.38 (m, 2H, 5′-H, 6′-H), 7.61 (d, J = 8.4 Hz, 1H, 3′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9 (CH-3), 52.9 (2 × CH_2-2,4), 124.7 (C-2′), 126.4 (CH-5′), 127.5 (CH-4′), 128.2 (CH-6′), 133.0 (CH-3′), 141.5 (C-1′), 205.9 (C=O); MS (EI) m/z (%) 225 ($M^{\bullet+}$, 100), 183 ($M^{\bullet+}$ − CH_2C=O, 30), 147 (28), 103 ($M^{\bullet+}$ − CH_2C=O−Br, 25); HRMS (CI-isobutane) 224.9912 ($C_{10}H_{10}BrO$ (MH^+) requires 224.9915).

3-(2′-Naphthyl)cyclobutanone (1g). Yield 60.8 mg, 15%; IR (NaCl) ν 3050 (w, Car−H), 1781 (s, C=O), 1623 (m, Ar), 1511 (m, Ar), 1430 (m, Ar), 1226 (s), 817 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.26 (ddt, J = 20.0, 8.3, 3.4 Hz, 2H, 2a-H, 4a-H), 3.47 (ddt, J = 20.0, 8.3, 3.4 Hz, 2H, 2-H′, 4-H′), 3.74 (pent, J = 8.3 Hz, 1H, 3-H), 7.33 (dd, J = 8.5, 1.8 Hz, 1H, 3′-H), 7.37–7.45 (m, 2H, 6′-H, 7′-H), 7.64 (br s, 1H, 1′-H), 7.72–7.80 (m, 3H, 4′-H, 8′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5 (CH-3), 54.5 (2 × CH_2-2,4), 124.7 (CH-1′), 124.8 (CH-3′), 125.7 (CH-6′), 126.3 (CH-7′), 127.48 (CH-4′), 127.54 (CH-8′), 128.5 (CH-5′), 132.1 (C-8a′), 133.2 (C-4a′), 140.7 (C-2′), 206.6 (C=O); MS (CI-isobutane) m/z (%) 197 ($MH^{\bullet+}$, 95), 154 ($M^{\bullet+}$ − CH_2C=O, 12), 85 (72), 69 (100); HRMS (CI-isobutane) 197.0967 ($C_{14}H_{13}O$ (MH^+) requires 197.0966).

3-(4′-Methoxybenzyl)cyclobutanone (1h). Yield 400 mg, 43%; IR (NaCl) ν 2957 (w, Car−H), 1777 (s, C=O), 1612 (m, Ar), 1590 (m, Ar), 1512 (m, Ar), 1247 (s, C−O), 836 (s, Ar−H) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51–2.61 (m, 1H, 3-H), 2.6 (ddt, J = 20.3, 7.1, 2.7 Hz, 2H, 2-H, 4-H), 2.75 (d, J = 7.5 Hz, 2H, CH_2CH), 2.99 (ddt, J = 20.3, 7.1, 2.7 Hz, 2H, 2-H′, 4-H′), 3.70 (s, 3H, CH_3O), 6.80 (d, J = 8.6 Hz, 2H, 3′-H, 5′-H), 7.05 (d, J = 8.6 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7 (CH-3), 40.4 (CH_2CH), 51.6 (2 × CH_2-2,4), 54.7 (CH_3), 113.5 (2 × CH-3′,5′), 129.0 (2 × CH-2′,6′), 131.6 (C-1′), 157.7 (C-4′), 207.1 (C=O); MS (EI) m/z (%) 190 ($M^{\bullet+}$, 56), 148 ($M^{\bullet+}$ − CH_2C=O, 96), 121 ($M^{\bullet+}$ − C_3H_5C=O, 100), 77 (32); HRMS (EI) 190.0997 ($C_{12}H_{14}O_2$ requires 190.0994).

3-(Cyclohexyl)cyclobutanone (1i). Yield 371 mg, 51%; IR (NaCl) ν 2923 (s, C−H), 2851 (s, C−H), 1786 (s, C=O), 1448 (m, CH_2), 1108 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78–0.92 (m, 2H), 1.02–1.22 (m, 4H), 1.54–1.74 (m, 5H), 1.90–2.03 (m, 1H, 3-H), 2.60–2.70 (m, 2H, 2-H, 4-H), 2.89–3.00 (m, 2H, 2-H′, 4-H′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7 (2 × CH_2), 25.9 (CH_2-4′), 29.6 (CH-3), 30.6 (2 × CH_2), 43.4 (CH-1′), 50.5 (2 × CH_2-2,4), 207.9 (C=O); MS (CI-isobutane) m/z (%) 153 ($MH^{\bullet+}$, 100), 135 ($MH^{\bullet+}$ − O, 15), 71 (10); HRMS (CI-isobutane) 153.1281 ($C_{10}H_{17}O$ (MH^+) requires 153.1279).

3-Octylcyclobutanone (1j). Yield 354 mg, 46%; IR (NaCl) ν 2923 (s, C−H), 2854 (m, C−H), 1785 (s, C=O), 1461 (w), 1380 (w), 1095 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 6.8 Hz, 3H, CH_3CH$_2$), 1.16–1.31 (m, 12H, 6 × CH_2), 1.48–1.56 (m, 2H, CH_2CH), 2.29 (pent, J = 7.5, 1.2 Hz, 1H, 3-H), 2.59 (ddt, J = 20.4, 7.5, 3.2 Hz, 2H, 2-H, 4-H), 3.06 (ddt, J = 20.4, 7.5, 3.2 Hz, 2H, 2-H′, 4-H′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3CH_2), 22.5 (CH_2), 23.7 (CH-3), 28.1 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 31.7 (CH_2), 36.2 (CH_2CH), 52.3 (2 × CH_2-2,4), 208.1 (C=O); MS (CI-isobutane) m/z (%) 183 ($MH^{\bullet+}$, 100), 165 ($MH^{\bullet+}$ − H_2O, 9), 71 (18); HRMS (CI-isobutane) 183.1747 ($C_{12}H_{23}O$ (MH^+) requires 183.1749).

General Procedure for the Formation of γ-Butyrolactones 2a−j via the Baeyer–Villiger Reaction. A mixture of dichlorobis(benzonitrile)palladium(II) (9.5 mg, 0.025 mmol, 5.0 mol%) and ligand (−)-**7** (13 mg, 0.0275 mmol, 5.5 mol%) in THF (2 mL) was stirred at room temperature for 1 h. Silver hexafluoroantimonate (17 mg, 0.05 mmol, 10 mol %) was then added and the reaction mixture was stirred for an additional 1 h. The mixture was then filtered over a Celite pad, cyclobutanone **1a−j** (0.5 mmol, 1 equiv) was then added to the filtrate, and the solution was cooled to –40 °C. Urea−hydrogen peroxide (61 mg, 0.65 mmol, 1.3 equiv) was then added and the mixture was then stirred at –40 °C overnight. Concentration in vacuo, followed by flash chromatography on silica gel (15 g), using a mixture of petroleum ether and ethyl acetate (9:1), afforded pure γ-butyrolactones **2a−j**.

(*S*)-(+)-3-Phenyl-γ-butyrolactone ((*S*)-(+)-(2a). Yield 78.6 mg, 97%; $[\alpha]^{24}_D$ +38.4 (*c* 1.0, $CHCl_3$, 81% ee), [lit.[35] gives $[\alpha]_D$ +46.0 (*c* 0.95, $CHCl_3$, 96% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (dd, J = 17.5, 8.9 Hz, 1H, 2-H), 2.83 (dd, J = 17.5, 8.9 Hz, 1H, 2-H′), 3.70 (pent, J = 8.9 Hz, 1H, 3-H), 4.18 (dd, J = 8.9, 8.1 Hz, 1H, 4-H), 4.57 (dd, J = 8.9, 8.1 Hz, 1H, 4-H′), 7.14 (d, J = 7.3 Hz, 2H, 2′-H, 6′-H), 7.21 (t, J = 7.3 Hz, 1H, 4′-H), 7.28 (t, J = 7.3 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6 (CH_2-2), 41.0 (CH-3), 74.0 (CH_2-4), 126.6 (2 × CH-2′,6′), 127.6 (CH-4′), 129.1 (2 × CH-3′,5′), 139.3 (C-1′), 176.3 (C=O) in agreement with the literature data;[36] Chiral GC (Supelco α-DEX), carrier gas He (flow 2 mL·min^{-1}), injection temp 200 °C, initial column temp 110 °C for 3 min, rate 1 deg·min^{-1}, final temp 220 °C, t_R = 56.11 min, t_S = 56.58 min.

(*S*)-(+)-3-(4′-Toluyl)-γ-butyrolactone (*S*)-(+)-(2b). Yield 81.9 mg, 93%; $[\alpha]^{24}_D$ +36.9 (*c* 1.0, $CHCl_3$, 75% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H, CH_3), 2.65 (dd, J = 17.5, 8.9 Hz, 1H, 2-H), 2.90 (dd, J = 17.5, 8.9 Hz, 1H, 2-H′), 3.75 (pent, J = 8.9 Hz, 1H, 3-H), 4.23 (dd, J = 8.9, 8.0 Hz, 1H, 4-H), 4.64 (dd, J = 8.9, 8.0 Hz, 1H, 4-H′), 7.11 (d, J = 8.1 Hz, 2H, 3′-H, 5′-H), 7.17 (dd, J = 8.1 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (CH_3), 35.7 (CH_2-2), 40.8 (CH-3), 74.1 (CH_2-4), 126.5 (2 × CH-3′,5′), 129.7 (2 × CH-2′,6′), 136.3 (C-1′), 137.4 (C-4′), 176.4 (C=O) in agreement with the literature data;[37] Chiral GC (Supelco α-DEX), carrier gas, He (flow 2 mL·min^{-1}), injection temp 200 °C, initial column temp 110 °C for 3 min, rate 1 deg·min^{-1}, final temp 220 °C, t_R = 66.18 min, t_S = 66.67 min.

(+)-3-(4′-Fluorophenyl)-γ-butyrolactone (+)-(2c). Yield 86.5 mg, 96%; $[\alpha]^{24}_D$ +29.8 (*c* 1.0, $CHCl_3$, 72% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (dd, J = 17.5, 8.9 Hz, 1H, 2-H), 2.90 (dd, J = 17.5, 8.9 Hz, 1H, 2-H), 3.77 (pent, J = 8.9 Hz, 1H, 3-H), 4.21 (t, J = 8.9 Hz, 1H, 4-H′), 4.64 (t, J = 8.9 Hz, 1H, 4-H′), 7.04 (t, J = 8.6 Hz, 2H, 3′-H, 5′-H), 7.20 (dd, J = 8.6, 5.2 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6 (CH_2-2), 40.2 (CH-3), 73.8 (CH_2-4), 115.9 (d, J = 21.5 Hz, 2 × CH-3′,5′), 128.2 (d, J = 8.1 Hz, 2 × CH-2′,6′), 135.1 (d, J = 3.2 Hz, C-1′), 161.9 (d, J = 246.4 Hz, C-4′), 176.1 (C=O); ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.5 (s) in agreement with the literature data;[36] Chiral GC (Supelco α-DEX), carrier gas, He (flow 2 mL·min^{-1}), injection temp 200 °C, initial column temp 110 °C for 3 min, rate 1 deg·min^{-1}, final temp 220 °C, t_{minor} = 58.06 min, t_{major} = 58.64 min.

(*S*)-(+)-3-(4′-Chlorophenyl)-γ-butyrolactone (*S*)-(+)-(2d). Yield 92.6 mg, 94%; $[\alpha]_D{}^{24}$ +36.5 (*c* 1.0, $CHCl_3$, 73% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (dd, J = 17.5, 8.8 Hz, 1H, 2-H), 2.93 (dd, J = 17.5, 8.8 Hz, 1H, 2-H′), 3.77 (pent, J = 8.8 Hz, 1H, 3-H), 4.23 (dd, J = 8.8, 7.8 Hz, 1H, 4-H), 4.65 (dd, J = 8.8, 7.8 Hz, 1H, 4-H′), 7.17 (d, J = 8.3 Hz, 2H, 2′-H, 6′-H), 7.34 (d, J = 8.3 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6 (CH_2-2), 40.5 (CH-3), 73.7 (CH_2-4), 128.0 (2 × CH-2′,6′), 129.2 (2 × CH-3′,5′), 133.5 (C-4′), 137.9 (C-1′), 175.8 (*C*=O); in agreement with the literature data;[36] Chiral GC (Supelco α-DEX), carrier gas, He (flow 2 mL.min^{-1}), injection temp 200 °C, initial column temp 110 °C for 3 min, rate 1 °C.min^{-1}, final temp 220 °C, t_{minor} = 81.43 min, t_{major} = 81.90 min.

(+)-3-(4′-Bromophenyl)-γ-butyrolactone (+)-(2e). Yield 114.5 mg, 95%; mp 61 °C (hexane); $[\alpha]^{25}_D$ +28.6 (*c* 1.0, $CHCl_3$, 76% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (dd, J = 17.5, 8.8 Hz, 1H, 2-H), 2.92 (dd, J = 17.5, 8.8 Hz, 1H, 2-H′), 3.75 (pent, J = 8.8 Hz, 1H, 3-H), 4.22 (dd, J = 8.8, 7.7 Hz, 1H, 4-H), 4.65 (dd, J = 8.8, 7.7 Hz, 1H, 4-H′), 7.11 (d, J = 8.3 Hz, 2H, 2′-H, 6′-H), 7.48 (d, J = 8.3 Hz, 2H, 3′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$)

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δ 35.5 (CH_2-2), 40.5 (CH-3), 73.6 (CH_2-4), 121.5 (C-4′), 128.3 (2 × CH-2′,6′), 132.1 (2 × CH-3′,5′), 138.4 (C-1′), 175.8 (C═O); MS (EI) *m*/*z* (%) 241 ($M^{\bullet+}$, 31), 183 ($M^{\bullet+} - CH_2CO_2$, 100), 103 ($M^{\bullet+} - CH_2CO_2$−Br, 40); HRMS (EI) 239.9792 ($C_{10}H_9BrO_2$ requires 239.9786); Chiral HPLC (Chiracel IB, 0.75 mL·min^{-1}, hexane/2-propanol, 92:8) t_{major} = 33.4 min, t_{minor} = 39.1 min after derivatization into the hydroxyl benzylamide derivative.[32]

(+)-3-(2′-Bromophenyl)-γ-butyrolactone (+)-(2f). Yield 110.9 mg, 92%; mp 42 °C (hexane); $[\alpha]^{25}_D$ +26.6 (*c* 1.0, $CHCl_3$, 70% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (dd, *J* = 17.6, 8.7 Hz, 1H, 2-H), 2.98 (dd, *J* = 17.6, 8.7 Hz, 1H, 2-H′), 4.23 (pent, *J* = 8.7 Hz, 1H, 3-H), 4.31 (dd, *J* = 8.7, 6.7 Hz, 1H, 4-H), 4.71 (dd, *J* = 8.7, 6.7 Hz, 1H, 4-H′), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H, 4′-H), 7.28 (dd, *J* = 7.7, 1.7 Hz, 1H, 6′-H), 7.35 (td, *J* = 7.7, 1.2 Hz, 1H, 5′-H), 7.61 (dd, *J* = 7.7, 1.2 Hz, 1H, 3′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.6 (CH_2-2), 40.0 (CH-3), 72.8 (CH_2-4), 124.3 (C-2′), 126.6 (CH-6′), 128.2 (CH-5′), 129.1 (CH-4′), 133.4 (CH-3′), 138.6 (C-1′), 176.0 (C═O); MS (EI) *m*/*z* (%) 241 ($M^{\bullet+}$, 29), 183 ($M^{\bullet+} - CH_2CO_2$, 100), 103 ($M^{\bullet+} - CH_2CO_2$−Br, 67); HRMS (EI) 239.9787 ($C_{10}H_9BrO_2$ requires 239.9786); Chiral HPLC (Chiracel OJ-H, 0.75 mL·min^{-1}, hexane/2-propanol, 75:25) t_{minor} = 9.1 min, t_{major} = 10.4 min after derivatization into the hydroxyl benzylamide derivative.[32]

(+)-3-(2′-Naphthyl)-γ-butyrolactone (+)-(2g). Yield 88.1 mg, 83%; $[\alpha]^{24}_D$ +43.6 (*c* 1.0, $CHCl_3$, 71% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79 (dd, *J* = 17.5, 8.9 Hz, 1H, 2-H), 3.00 (dd, *J* = 17.5, 8.9 Hz, 1H, 2-H), 3.95 (pent, *J* = 8.9 Hz, 1H, 3-H), 4.37 (dd, *J* = 8.9, 7.9 Hz, 1H, 4-H′), 4.74 (dd, *J* = 8.9, 7.9 Hz, 1H, 4-H′), 7.34 (dd, *J* = 8.5, 1.8 Hz, 1H, 3′-H), 7.47–7.55 (m, 2H, 7′-H, 6′-H), 7.67 (br s, 1H, 1′-H), 7.80–7.90 (m, 3H, 4′-H, 8′-H, 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6 (CH_2-2), 41.1 (CH-3), 73.9 (CH_2-4), 124.4 (CH-3′), 125.4 (CH-1′), 126.2 (CH-6′), 126.6 (CH-7′), 127.60 (CH-4′), 127.63 (CH-8′), 129.0 (CH-5′), 132.6 (C-8a′), 133.3 (C-4a′), 136.6 (C-2′), 176.4 (C═O) in agreement with the literature data;[36] Chiral HPLC (Chiracel IB, 0.75 mL·min^{-1}, hexane/2-propanol, 90:10) t_{major} = 31.5 min, t_{minor} = 34.7 min after derivatization into the hydroxyl benzylamide derivative.[32]

(*R*)-(+)-3-(4′-Methoxybenzyl)-γ-butyrolactone (*R*)-(+)-(2h). Yield 93.8 mg, 91%; $[\alpha]^{23}_D$ +3.2 (*c* 0.5, $CHCl_3$, 58% ee), [lit.[33] gives $[\alpha]_D$ +5.4 (*c* 6.8, $CHCl_3$, 98% ee)]; ^{1}H NMR (400 MHz, $CDCl_3$) 2.56 (dd, *J* = 17.5, 8.0 Hz, 1H, 2-H), 2.57 (dd, *J* = 17.5, 8.0 Hz, 1H, 2-H′), 2.70 (dd, *J* = 7.6, 3.3 Hz, 2H, C*H*$_2$CH), 2.72–2.86 (m, 1H, 3-H), 3.78 (s, 3H, CH_3O), 4.00 (dd, *J* = 9.1, 6.5 Hz, 1H, 4-H), 4.30 (dd, *J* = 9.1, 6.5 Hz, 1H, 4-H′), 6.84 (d, *J* = 8.6 Hz, 2H, 3′-H, 5′-H), 7.06 (d, *J* = 8.6 Hz, 2H, 2′-H, 6′-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.1 (CH_2-2), 37.2 (CH-3), 37.9 (*C*H_2CH), 55.2 (CH_3), 72.5 (CH_2-4), 114.0 (2 × CH-3′,5′), 129.5 (2 × CH-2′,6′), 130.1 (C-1′), 158.3 (C-4′), 176.8 (C═O) in agreement with the literature data.[33]

(−)-3-Cyclohexyl-γ-butyrolactone (−)-(2i). Yield 74.8 mg, 89%; $[\alpha]^{24}_D$ −6.8 (*c* 0.5, $CHCl_3$, 65% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89–1.02 (m, 2H), 1.09–1.35 (m, 4H), 1.56–1.77 (m, 5H), 2.20 (dd, *J* = 16.6, 8.0 Hz, 1H, 2-H), 2.30 (pent, *J* = 9.8 Hz, 1H, 3-H), 2.53 (dd, *J* = 16.6, 8.0 Hz, 1H, 2-H′), 3.96 (dd, *J* = 8.9, 8.0 Hz, 1H, 4-H), 4.39 (dd, *J* = 8.9, 8.0 Hz, 1H, 4-H′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7 (CH_2), 25.8 (CH_2), 26.1 (CH_2), 30.4 (CH_2), 31.1 (CH_2), 32.7 (CH_2-2), 41.3 (CH-1′), 41.6 (CH-3), 72.1 (CH_2-4), 177.3 (C═O); MS (EI) *m*/*z* (%) 168 ($M^{\bullet+}$, 49), 150 (21), 137 (66), 86 (100), 83 (95); HRMS (EI) 168.1153 ($C_{10}H_{16}O_2$ requires 168.1150); Chiral HPLC (Chiracel IB, 0.75 mL·min^{-1}, hexane/2-propanol, 90:10) t_{major} = 14.0 min, t_{minor} = 17.5 min after derivatization into the hydroxyl benzylamide derivative.[32]

(*R*)-(+)-3-Octyl-γ-butyrolactone (*R*)-(+)-(2j). Yield 82.5 mg, 83%; $[\alpha]^{24}_D$ +0.6 (*c* 1.0, $CHCl_3$, 55% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 6.9 Hz, 3H, C*H*$_3$CH$_2$), 1.19–1.30 (m, 12H, 6 × CH_2), 1.40–1.48 (m, 2H, C*H*$_2$CH), 2.14 (dd, *J* = 16.7, 7.7 Hz, 1H, 2-H), 2.46–2.56 (m, 1H, 3-H), 2.58 (dd, *J* = 16.7, 8.3 Hz, 1H, 2-H′), 3.89 (dd, *J* = 8.9, 7.1 Hz, 1H, 4-H), 4.38 (dd, *J* = 8.9, 7.4 Hz, 1H, 4-H′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (*C*H$_3$CH$_2$), 22.5 (CH_2), 27.2 (CH_2), 29.0 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 32.9 (*C*H$_2$CH), 34.4 (CH_2-2), 35.5 (CH-3), 73.3 (CH_2-4), 177.2 (C═O) in agreement with the literature data;[36] Chiral HPLC (Chiracel IB, hexane/2-propanol 95:5, 0.75 mL·min^{-1}) t_R = 30.12 min, t_S = 33.66 min after derivatization into hydroxyl the hydroxyl benzylamide derivative.[32]

Acknowledgment. We thank the GSK and EPSRC for an industrial CASE award to F.F.

Supporting Information Available: Additional experimental procedures, ^{1}H and ^{13}C NMR spectra of key compounds, and chiral GC and HPLC traces for lactones **2a**−**j**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800246G