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Palladium-Catalyzed Suzuki–Miyaura, Heck and Hydroarylation Reactions on (–)-Levoglucosenone and Application to the Synthesis of Chiral γ-Butyrolactones

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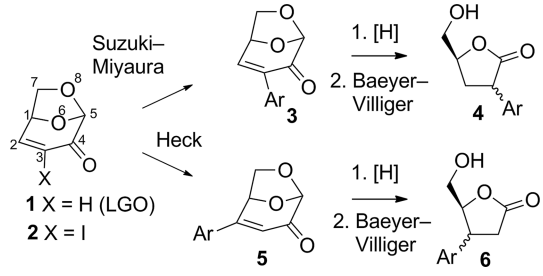
The chiral pool material (–)-levoglucosenone (6,8-dioxabicyclo[3.2.1]oct-2-en-4-one, LGO) has been substituted by using a series of Pd-mediated cross-coupling reactions. Iodination of LGO followed by Suzuki–Miyaura cross-coupling reaction with boronic acids by employing the Buchwald ligand SPhos with $Pd(OAc)_2$ afforded 3-aryl derivatives in excellent yields. Selective Heck arylation reaction at the 2-position was achieved with aryl iodides with K_3PO_4 as base and SPhos ligand with $Pd(OAc)_2$ (1–5 mol-%). A selective hydroarylation reaction (formal conjugate addition) was developed by using the same aryl iodides, benzyldiethylamine, $Pd(OAc)_2$, and P(*o*-tol)$_3$. The products were converted, either directly or after alkene reduction, through a Baeyer–Villiger oxidation into chiral 3- and 4-substituted 5-(hydroxymethyl)-dihydrofuran-2(3*H*)-ones.

Introduction

(–)-Levoglucosenone (6,8-dioxabicyclo[3.2.1]oct-2-en-4-one, **1**, LGO) is obtained from the pyrolysis of acidified cellulose and has attracted interest as a chiral synthon since its characterization by Broido in 1973.[1] The main barrier to LGO use has been the failure to scale up production, and so LGO has historically had a high price despite the ready availability of the starting material cellulose. Reactors have recently been developed to allow large-scale production and have provided new opportunities to use this chiral molecule in synthesis.[2]

The development of new transformations that utilize LGO is crucial to make use of this biorenewable resource. Reactions previously reported for LGO include the reaction of the alkene with electrophiles,[3] cycloaddition reactions,[4] redox chemistry,[1b] and conjugate addition chemistry.[5] First investigated by Shafidazeh et al.,[6] the Baeyer–Villiger reaction of LGO was used extensively by Ebata et al. to generate butyrolactones that include naturally occurring eldanolide and whiskey lactone.[7] In these reports, the LGO scaffold was derivatized with organometallic reagents that used the anhydro bridge to direct conjugate addition reactions, and only a limited set of substitution patterns were produced. More recently, enzyme-catalyzed Baeyer–Villiger-type reactions have been reported on LGO and dihydrolevoglucosenone.[8]

Chiral butyrolactones are found in many flavors, fragrances,[9] and natural products,[10] and LGO could be a useful starting material for their construction if additional methods for derivatization of the bicyclic skeleton were available. Few examples exist of palladium-catalyzed cross-coupling reactions on LGO or its 3-halo derivatives.[11] However, modern metal-catalyzed cross-coupling techniques would provide opportunities to derivatize LGO into arylglycals such as **3** and **5** to access chiral butyrolactones shown by general structures **4** and **6** (Scheme 1). In this current report we describe attempts to derivatize LGO by using Suzuki,[12] Heck[13] and palladium-catalyzed hydroarylation reactions (also referred to as a reductive Heck reaction)[14] and have converted selected products into chiral 5-hydroxymethyl-γ-butyrolactones.



Scheme 1. Palladium-catalyzed cross-coupling reactions of LGO.

Results and Discussion

We have found no reports of Suzuki–Miyaura reactions that use **2** despite this seeming a straightforward way to

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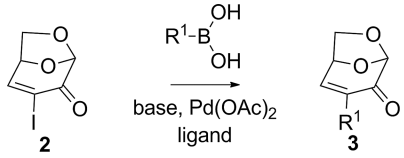
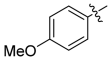
further functionalize LGO. Iodination of LGO with I_2/pyridine afforded 3-iodolevoglucosenone (**2**) in 96% yield.[11a,15] The isolation of **2** required only filtration through a pad of silica gel then evaporation of volatiles and so could be performed on a multi-gram scale. The reaction of phenylboronic acid with **2** and Cs_2CO_3 as base with $Pd(OAc)_2$ (5 mol-%) and triphenylphosphine as ligand provided expected coupled product **3a** in 67% yield (Scheme 2; Table 1, Entry 1). Following this success, we applied these conditions to the series of boronic acids shown in Table 1, which gave the coupled products in moderate to good yield (Table 1, Entries 5, 7, and 12). As yields were somewhat lower than expected with significant byproducts of protodeboronation, we examined alternative ligands and conditions. Superior results were obtained with Buchwald ligand SPhos,[16] which allowed a reduction of the palladium loading to 1.0 mol-% and gave clean reactions with excellent yields (Table 1, Entries 6, 8, and 10). Electron-poor boronic acids, 2-formylphenylboronic acid and 2-fluorophenyl boronic acid, afforded the cross-coupled products, but required Pd (5 mol-%) and SPhos (10 mol-%) for complete reaction (Table 1, Entries 14 and 15).



Scheme 2. Suzuki–Miyaura coupling reactions of iodide **2**.

Table 1. Suzuki–Miyaura coupling reactions of iodide **2**.

Entry[a]	R^1	Solvent	Temperature [°C]	$Pd(OAc)_2$ [mol-%]	Ligand	Time [h]	Product	Yield [%]
1	Ph	toluene	110	5	PPh_3	18	**3a**	67
2	Ph	toluene	110	1	SPhos	18	**3a**	61
3		DMF	100	5	PPh_3	0.5	**3b**	18
4		toluene	110	5	$P(o\text{-tol})_3$	3	**3b**	43
5		toluene	110	5	PPh_3	3	**3b**	76
6		toluene	110	1	SPhos	1.5	**3b**	85
7		toluene	110	5	PPh_3	2	**3c**	64
8		toluene	110	1	SPhos	1.5	**3c**	89
9		DMF	100	5	$P(o\text{-tol})_3$	3	**3d**	49
10		toluene	110	1	SPhos	3	**3d**	74
11[b]	Bn	dioxane	90	5	–	36	**3e**	0
12		toluene	110	5	PPh_3	18	**3f**	25
13		toluene	110	1	SPhos	36	**3f**	27
14		toluene	110	5	SPhos	24	**3f**	53
15		toluene	110	5	SPhos	16	**3g**	88

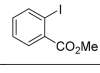
[a] Reactions performed with Cs_2CO_3 (2 equiv.), with a 2:1 Pd/L ratio at a concentration of 50 mg/mL. [b] Benzyl pinacol boronate ester was used with $PdCl_2$(dppf) and CsF (2 equiv.) as base.

The coupling of the unreactive sp^3 benzyl boronate ester was unsuccessful, the literature conditions for this ester failing due to the sensitivity of **2** to water under basic conditions (Table 1, Entry 11).[17]

Heck reactions with LGO as the alkene seemed another exciting and unexplored way to derivatize the 2-position of LGO. We envisaged that hydrogenation of product **5** would occur from the face opposite the anhydro bridge to give derivatives epimeric to those obtained from conjugate addition reactions with organometallic reagents.[18] A compounding factor in these reactions is that the palladium-catalyzed hydroarylation reaction[14] (formal conjugate addition) competes with the Heck reaction of LGO. The central role of base selection to promote either the Heck reaction or hydroarylation in addition reactions to enones was recently identified by de Vries et al. with a Pd^0-NHC complex.[14a] Trialkylamine bases gave rise to hydroarylation products, whereas CsOPiv afforded Heck-type adducts. This work built upon the pioneering reports of Cacchi et al., who first studied the Pd-mediated hydroarylation reactions with trialkylammonium formate, and recent reports that have used formate as a reducing agent.[14b,14c,19]

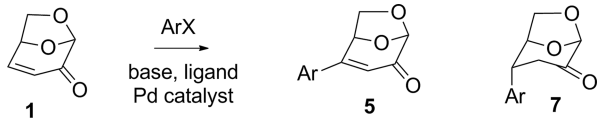
A base and solvent optimization study was conducted on the Heck reaction of LGO with iodobenzene (Table 2, Scheme 3). The reaction catalyzed by 5 mol-% $Pd(OAc)_2$, with $P(o\text{-tol})_3$ with Cs_2CO_3 as the base gave a moderate yield of 2-phenyl adduct **5a** in toluene (Table 2, Entry 1). No products of cross coupling were observed when the reaction was conducted in *N*,*N*-dimethylformamide (DMF) with Cs_2CO_3, which we attributed to the sensitivity of the

Table 2. Heck selective reactions of LGO (**1**), see Scheme 3.

Entry[a]	ArX	Solvent	Temperature [°C]	Base	$Pd(OAc)_2$ [mol-%]	Ligand	Time [h]	Products	Yield (**5**/**7**) [%]
1	PhI	toluene	110	Cs_2CO_3	5	$P(o\text{-tol})_3$	18	**5a/7a**	34 (n.d.)
2	PhI	dioxane	100	K_3PO_4	5	PPh_3	18	**5a/7a**	37 (19:1)
3	PhI	dioxane	100	K_3PO_4	1	SPhos	5	**5a/7a**	65 (10:1)
4	PhI	toluene	110	K_3PO_4	2.5	SPhos	48	**5a/7a**	60 (>20:1)
5	PhBr	NMP	130	NaOAc[b]	0.005	–	18	**5a/7a**	24 (8:1)
6		toluene	110	K_3PO_4	2.5	SPhos	12	**5b/7b**	62 (>20:1)
7		toluene	110	K_3PO_4	2.5	SPhos	10	**5c/7c**	59 (>20:1)
8		toluene	110	K_3PO_4	2.5	SPhos	10	**5h/7h**	57 (>20:1)
9		toluene	110	K_3PO_4	2.5	SPhos	48	**5i/7i**	35 (>20:1)

[a] Reactions performed at an LGO concentration of 50 mg/mL with a Pd/L ratio of 1:2 with base (2 equiv.). [b] NaOAc (1.05 equiv.) was used.

substrate to amines generated by the base (not shown). The substrate LGO is also sensitive to water in the presence of strong bases, and we found that yields were variable with Cs_2CO_3 (0–34%), so alternatives were examined. Attempted Heck–Matsuda coupling reactions with phenyldiazonium tetrafluoroborate in methanol as reported by Sotiropoulos et al.[20] for reactions of methyl acrylate gave only products from methanol conjugate addition (not shown), and other polar aprotic solvents were not examined. We also found that de Vries' ligand-free Pd nanoparticle conditions[21] gave low yields, which we attributed to slow decomposition of LGO (TLC) in *N*-methyl-2-pyrrolidone (NMP) at 130 °C (Table 2, Entry 5).



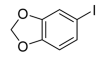
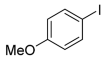
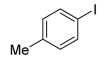
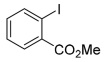
Scheme 3. Heck and hydroarylation reactions of LGO.

We achieved complete selectivity for the Heck reaction of LGO at the expense of the hydroarylation with iodobenzene, SPhos, and K_3PO_4 in toluene (Table 2, Entry 4). The Heck reactions of electron-rich aromatics proceeded more quickly than the electron-poor aromatics and in better yield (Table 2, Entries 6–8 and 9). In all reactions, 0–3% of 3-substituted product **3a**–**3h** was also observed. The Heck reaction product was confirmed for **5h** by single-crystal X-ray diffraction (see Supporting Information, Figure S4).

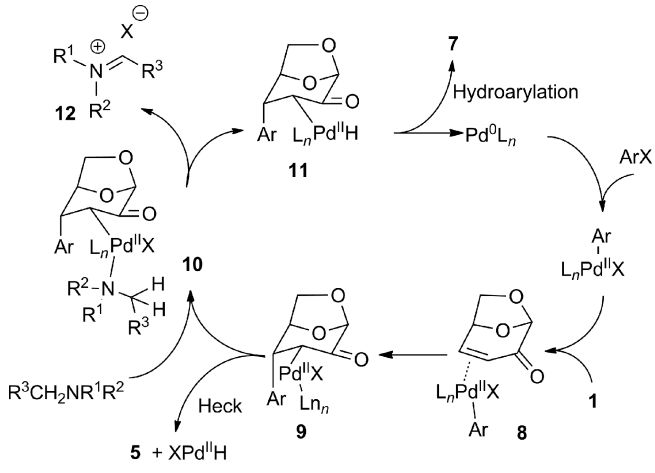
The reactions performed to optimize the hydroarylation on LGO are shown in Table 3, and the proposed mechanism for the reaction that gives the hydroarylation reaction is shown in Scheme 4.[14a,14e] The reaction initially proceeds as per the Heck reaction and transfer of the aryl group to the enone gives **9**. The facial selectivity in the transfer of the aryl group results from the selective coordination of the palladium atom to the face of LGO opposite the anhydro bridge. The *syn*-dehydropalladation that usually occurs in the Heck reaction is not possible due to restricted rotation, and instead coordinated amine complex **10** transfers a hydride from the carbon atom attached to the nitrogen atom to the palladium center. Reductive elimination from palladium hydride intermediate **11** gives observed hydroarylation product **7**, and the process also affords iminium byproduct **12**. Evidence for this mechanism has previously been found in the observation of products from the cross coupling of the imine byproduct and aryl iodide.[14b]

We began our investigation into the hydroarylation reaction with PhI, triethylamine with the ligand P(*o*-tol)$_3$, and we obtained only moderate selectivity for diastereomerically pure hydroarylation product **7a** (Table 3, Entry 1). It occurred to us that by reducing the C–H bond strength by the use of a benzylic amine could improve selectivity towards the hydroarylation reaction as long as coordination to the palladium center was not affected. This hypothesis was tested by using tribenzylamine, which gave excellent selectivity for the hydroarylation product; however, this resulted in a moderately complex mixture and poor yield of product

Table 3. Hydroarylation selective reactions of LGO (**1**), see Scheme 3.

Entry[a]	ArX	Temperature [°C]	Base	Pd(OAc)$_2$ [mol-%]	Ligand	Time [h]	Products	Yield (**5**/**7**) [%]
1	PhI	90	NEt_3	5	P(*o*-tol)$_3$	4	**5a**/**7a**	83 (1:4)
2	PhI	90	NEt_3	5	PPh_3	4	**5a**/**7a**	69 (1:4)
3	PhI	110	DABCO	5	PPh_3	18	**5a**/**7a**	73 (1:1)
4	PhI	110	DIPEA	5	P(*o*-tol)$_3$	18	**5a**/**7a**	32 (1:1.75)
5	PhI	90	NEt_3	5	SPhos	3	**5a**/**7a**	72 (1:3)
6	PhI	110	$BnNEt_2$	1	P(*o*-tol)$_3$	2	**5a**/**7a**	71 (1:5.5)
7	PhI	110	Bn_3N	5	P(*o*-tol)$_3$	18	**5a**/**7a**	25 (1:34)
8	PhI	110	NBu_3	5	P(*o*-tol)$_3$	4	**5a**/**7a**	55 (1:4)
9[b,c]	PhI	80	NBu_3	3	–	2	**5a**/**7a**	56 (1:7.7)
10[b,c]	PhI	80	$BnNEt_2$	3	–	24	**5a**/**7a**	51 (1:7)
11[b,d]	PhI	80	$BnNEt_2$	3	–	18	**5a**/**7a**	50 (1:9.8)
12[e]		110	$BnNEt_2$	1	P(*o*-tol)$_3$	12	**5b**/**7b**	90 (1:4)
13		90	NEt_3	5	P(*o*-tol)$_3$	10	**5c**/**7c**	71 (1:2.2)
14[d]		110	$BnNEt_2$	1	P(*o*-tol)$_3$	2	**5c**/**7c**	69 (1:4)
15		90	NEt_3	5	P(*o*-tol)$_3$	10	**5h**/**7h**	60 (1:2.5)
16[e]		110	$BnNEt_2$	1	P(*o*-tol)$_3$	4	**5h**/**7h**	70 (1:4)
17		90	NEt_3	5	P(*o*-tol)$_3$	4	**5i**/**7i**	40 (1:>20)
18[e]		110	$BnNEt_2$	1	P(*o*-tol)$_3$	10	**5i**/**7i**	53 (1:>20)

[a] Reactions performed at a concentration of 20 mL/g LGO with a Pd/L ratio of 1:2 with base (4.5 equiv.) and aryl iodide (1.2 equiv.). Reactions performed with 1.0 mmol of **1** unless indicated. [b] 0.50 mmol scale. [c] [{Pd(*i*Pr)(NQ)}$_2$] was used in place of Pd(OAc)$_2$. [d] [{Pd(Mes)(NQ)}$_2$] was used in place of Pd(OAc)$_2$. [e] 4.0 mmol scale.



Scheme 4. Mechanism for the hydroarylation of LGO.

(Table 3, Entry 7). The crude reaction mixture showed the presence of dibenzylamine as well as the Schiff base *N*-benzylidenebenzylamine by GC–MS (data not shown). The Schiff base was formed from the transfer of a second

hydride from the byproduct dibenzylamine, and the presence of both adducts are consistent with the proposed mechanism. We thought it likely that the imine formed from the base was reacting with one of the palladated intermediates to give the complex reaction outcome. By reducing the number of benzyl groups by using benzyldiethylamine improved the selectivity over the trialkylamines and gave good selectivity for the hydroarylation products (Table 3, Entries 1, 6 and 8). When the cross-coupling reaction of **1** with PhI with $BnNEt_2$ was performed in a sealed tube to trap volatile components and followed by GC–MS, an 8:1 ratio, corrected by using authentic standards, of the byproduct *N*-benzyl-*N*-ethylamine/diethylamine was observed. This indicated that greater hydride transfer occurred from the *N*-alkyl groups rather than the benzylic position, and the role of the benzyl group in improving selectivity is therefore not clear.

The hindered base *N*,*N*-diisopropylethylamine (DIPEA) showed poor selectivity, probably as a result of decreased coordination to the palladium center (Table 3, Entry 4), although this base has been used with excellent results in the reductive Heck reactions reported recently by Zhou et al.[22] The bicyclic base 1,4-diazabicyclo[2.2.2]octane (DABCO) also showed poor selectivity, which we attributed to slow hydride transfer to the palladium atom (Table 3, Entry 3).

The optimized conditions were then applied to a range of aryl iodides to give hydroarylation products **7b**, **7c**, **7h**, and **7i** in improved yield and selectivity relative to the reactions with trialkylamines (Table 3, Entries 13–18). In the case of **7i** (Table 3, Entry 17) the stereochemistry of the C2 position of the hydroarylation product was confirmed as (*R*) by single-crystal X-ray crystallography (see Supporting Information, Figure S5), consistent with the coupling constants around the bicyclic ring, which were conserved in the series.

The isolation of hydroarylation products **7a**–**7h** free of Heck adducts was challenging. In cases for which it was not possible to remove all traces of the Heck adduct by chromatography, the reaction mixture was treated with potassium permanganate (1.0 M) in water/dioxane or water/ethyl acetate, which oxidized the remaining alkene in the Heck adducts without affecting the hydroarylation products. Flash chromatography then provided analytically pure material.

With a series of substituted glycals in hand we turned our attention to their conversion to the corresponding γ-butyrolactones. Attempts to convert cross-coupled product **3a** into the butenolide by using *meta*-chloroperoxybenzoic acid catalyzed by *p*-toluenesulfonic acid (*p*-TSA) gave only unreacted starting material. We also attempted hydrogenation of **3a** (ethyl acetate, Pd/C or $PdCl_2$, 45 psi, 48 h); however, the starting material was recovered unchanged. These results may be explained by the preferred conformation of the phenyl ring, which twists to avoid unfavorable steric interactions. Together with the anhydro bridge in **3**, this reduces the accessibility of the alkene to the catalyst or the carbonyl group to the oxidant. The single-crystal X-ray crystal structure of trifluorophenyl adduct **3d** (Figure 1) shows a C4–C3–C10–C11 torsion angle of 54° consistent with these results. The X-ray crystal structure of benzodioxole substituted **3b** exhibits a 31° torsion angle between the aryl ring and the C3–C4 bond. The X-ray structure of **3a** is more complex and has three distinct conformations present in the unit cell, two of which have the aryl ring twisted relative to the enone, whereas one is planar, likely a result of solid-state packing effects (see Supporting information, Figures S1 and S2).

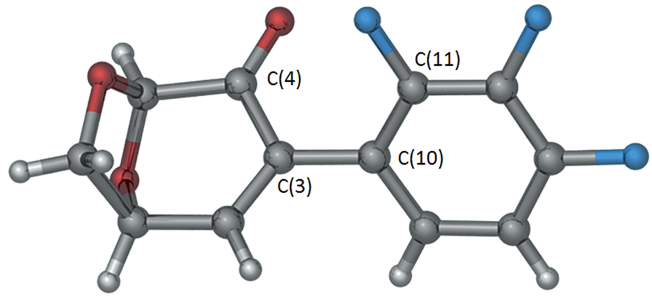


Figure 1. Perspective view of the single-crystal X-ray structure of enone **3d** with the 54° C4–C3–C10–C11 torsion angle atoms labeled.

The reduction of enone **3a** with a mixture of Red-Al/CuBr, which generates a CuH species in situ,[23] afforded reduced product **13a** in good yield. The stereochemistry of **13a** is opposite to that expected from hydrogenation and presumably results from protonation on the face *syn* to the anhydro bridge that gives the sterically less crowded equatorial phenyl group. The structural assignments are based on a *trans*-diaxial H2-H3 coupling and are supported by a single-crystal X-ray structure of **13a** that shows the equatorial reaction product (Figure 2). These same conditions were then applied to **3b** and **3c**, which afforded reduced dioxabicyclo[3.2.1]octanes **13b** and **13c**, respectively. Baeyer–Villiger reactions of 3-aryl ketones **13a** and **13c** with peracetic acid afforded expected γ-butyrolactones **14a** and **14c**, respectively, in good yields. The benzodioxole group in **13b** led to slower oxidation, and there was only 40% consumption of the ketone after 1 week. Oxidations of the Heck and hydroarylation-type products were straightforward and also afforded substituted butyrolactones **15**, **16a**, **16b**, **16h**, and **16i** in good yields (Scheme 5). In all Baeyer–Villiger oxidation reactions, a mixture of alcohol and formate ester was

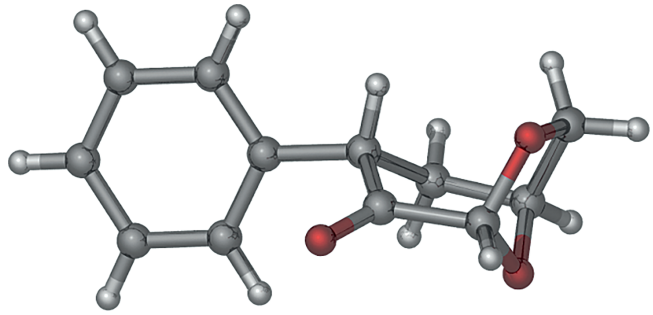
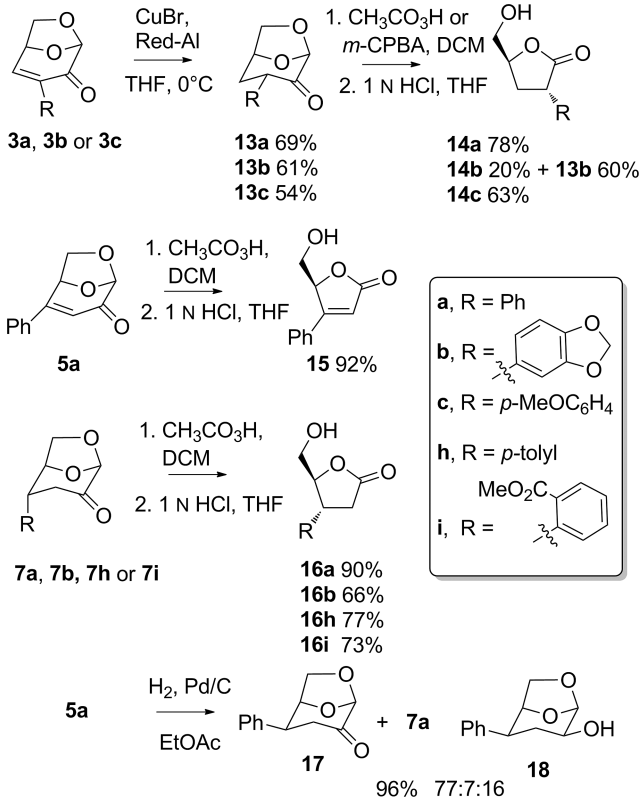


Figure 2. Perspective view of the single-crystal X-ray structure of **13a** that shows the equatorial phenyl substituent.

formed, and a second hydrolysis step with HCl (1 N) in water/tetrahydrofuran (THF) was required to convert all products into the alcohols.[7a,8]



Scheme 5. Preparation of butyrolactones.

To demonstrate the versatility of this chemistry, the hydrogenation of Heck adduct **5a** was also examined (Scheme 5). The unoptimized reduction afforded equatorial product **17**, overreduced alcohol **18**, and small amounts of axial product **7a**. The greater than 10:1 selectivity for the equatorial reduction product, which is epimeric to products of hydroarylation, further demonstrates the flexibility of these cross-coupling approaches for the derivatization of LGO.

Conclusions

We have reported a series of reactions that can be used to derivatize LGO to afford chiral 2-aryl- and 3-aryl-substituted 6,8-dioxabicylo[3.2.1]octan-4-ones, which can be converted into γ-butyrolactones by means of a Baeyer–Villiger oxidation reaction. These substituted butyrolactones, which can be used as synthons for the construction of more complex molecules, can now be accessed from the chiral pool material LGO without the use of air-sensitive organometallic reagents and low temperatures. Further applications of these chiral butyrolactones will be reported in due course. We have also described new conditions for a diastereoselective hydroarylation of LGO optimized with $BnNEt_2$, which may have applications in the addition of aryl iodides to other cycloalkenones. We envisage that this work will inspire new uses for the interesting chiral synthon LGO, which is currently available in kilogram quantities and may soon be available in bulk.

Experimental Section

General Experimental: Solvents were dried in accordance with literature procedures. Cs_2CO_3 and K_3PO_4 were dried at 100 °C under vacuum and were used immediately. All other reagents are commercially available and were used as received. ^1H NMR spectra recorded in $CDCl_3$ are referenced to tetramethylsilane (δ = 0 ppm) and ^{13}C NMR spectra are referenced to the residual solvent. HRMS data were recorded in positive ESI V mode (source temperature 80 °C, desolvation temperature 150 °C, capillary 2.5 kV). MS (EI) data were recorded with an Agilent GC–MS 5975C mass spectrum detector. [{Pd(Mes)(NQ)}$_2$] {[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](1,4-naphthoquinone)palladium(0) dimer (649736-75-4)} and [{Pd(Mes)(NQ)}$_2$] [(1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene)(1,4-naphthoquinone)palladium(0) dimer (467220-49-1)] were obtained from Sigma–Aldrich, St. Louis, USA.

(1*S*,5*R*)-3-Iodo-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (2):[11a,15] To a solution of **1** (1.5 g, 11.9 mmol) in 1,2-dichloroethane (20 mL) was added I_2 (4.2 g, 16.5 mmol), then pyridine (1.08 mL, 13.4 mmol), and the reaction mixture was stirred for 15 min. Toluene (20 mL) was added and the resulting suspension poured onto a 5 cm plug of silica and the product eluted with toluene. Concentration of the filtrate gave a yellow crystalline solid (2.86 g, 96%). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.97 (d, J = 4.9 Hz, 1 H), 5.57 (s, 1 H), 4.94 (dd, J = 4.9, 4.5 Hz, 1 H), 3.88 (dd, J = 7.0, 4.5 Hz, 1 H), 3.82 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 183.1, 155.7, 100.7, 99.7, 74.2, 66.5 ppm. FTIR: $\tilde{\nu}$ = 3067, 2975, 2902, 1697 cm^{-1}. MS (EI): m/z (%) = 251.9 (trace) $[M]^+$, 224.0 (100), 179.0 (16), 126.9 (15), 97.1 (31), 53.1 (14), 41.1 (13), 39.1 (19).

General Procedure for Suzuki Reactions with 2: To a stirred solution of **2** (250 mg, 0.99 mmol) in toluene (5 mL) under N_2 were added arylboronic acid (1.5 equiv.), phosphine (2–10 mol-%), anhydrous Cs_2CO_3 (2.0 equiv.), and $Pd(OAc)_2$ (1–5 mol-%), and the reaction mixture was heated to 90–110 °C until complete by TLC (3:7, ethyl acetate/hexanes). The resulting mixture was washed with H_2O (10 mL) and the aqueous phase extracted with CH_2Cl_2 (20 mL), then the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Products **3a**–**3d**, **3f**, and **3g** were purified by flash chromatography and then further purified as specified.

(1*S*,5*R*)-3-Phenyl-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3a): The general procedure performed with **2** (2.10 g, 8.33 mmol) afforded a product that was crystallized from CH_2Cl_2/hexanes to give **3a** as off-white crystals (1.12 g, 67%). M.p. 82–85 °C. $[\alpha]_D^{23}$ = –301 (c = 1.53, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.48–7.30 (m, 5 H), 7.24 (d, J = 4.9 Hz, 1 H), 5.49 (s, 1 H), 5.12 (dd, J = 4.9, 4.5 Hz, 1 H), 3.91 (dd, J = 7.0, 4.5 Hz, 1 H), 3.81 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 187.9, 143.1, 137.8, 133.1, 128.6, 128.2, 128.1, 101.6, 72.4, 66.5 ppm. FTIR (neat): $\tilde{\nu}$ = 3047, 2968, 2897, 1686 cm^{-1}. MS (ESI): m/z = 203.0 $[M + H]^+$, 225.0 $[M + Na]^+$. $C_{12}H_{10}O_3$ (202.21): calcd. C 71.28, H 4.98; found C 71.53, H 4.95.

(1*S*,5*R*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3b): The general procedure performed with **2** (250 mg, 0.99 mmol) afforded a product that crystallized upon standing to

give **3b** as yellow crystals (208 mg, 85%). M.p. 129–131 °C. $[\alpha]_D^{26}$ = –260 (c = 1.43, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.17 (d, J = 5.1 Hz, 1 H), 6.93–6.86 (m, 2 H), 6.85–6.74 (m, 1 H), 5.95 (s, 2 H), 5.46 (s, 1 H), 5.12 (dd, J = 5.1, 4.5 Hz, 1 H), 3.92 (dd, J = 6.8, 4.5 Hz, 1 H), 3.81 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 188.1, 148.1, 147.6, 142.0, 136.5, 127.1, 122.1, 108.7, 108.3, 101.7,101.3, 72.6, 66.7 ppm. FTIR (neat): $\tilde{\nu}$ = 3012, 2974, 2924, 1695 cm^{-1}. MS (EI): m/z (%) = 246.1 (44) $[M]^+$, 215 (35), 173 (100), 131 (48), 116 (32), 115 (62), 103 (32). $C_{13}H_{10}O_5$ (246.22): calcd. C 63.42, H 4.09; found C 63.30, H 4.05.

(1*S*,5*R*)-3-(4-Methoxyphenyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3c): The general procedure performed with **2** (250 mg, 0.99 mmol) afforded a product that was crystallized from hot iPr$_2$O to give **3c** as colorless crystals (205 mg, 89%). M.p. 101–102 °C. $[\alpha]_D^{22}$ = –264 (c = 0.96, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.43–7.31 (m, 2 H), 7.18 (d, J = 4.9 Hz, 1 H), 6.96–6.82 (m, 2 H), 5.47 (s, 1 H), 5.11 (dd, J = 4.9, 4.6 Hz, 1 H), 3.91 (dd, J = 6.8, 4.6 Hz, 1 H), 3.81 (d, J = 6.8 Hz, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 188.3, 160.0, 141.5, 136.2, 129.4, 125.6, 113.8, 101.7, 72.6, 66.6, 55.2 ppm. FTIR (neat): $\tilde{\nu}$ = 3027, 3007, 2967, 2889, 2840, 1688, 1602 cm^{-1}. MS (ESI): m/z = 233 $[M + H]^+$, 255 $[M + Na]^+$. $C_{13}H_{12}O_4$ (232.24): calcd. C 67.23, H 5.21; found C 67.26, H 5.26.

(1*S*,5*R*)-3-(2,3,4-Trifluorophenyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3d): The general procedure performed with iodide **2** (250 mg, 0.99 mmol) afforded a product that was crystallized from hot iPr$_2$O to give **3d** as colorless crystals (187 mg, 74%). M.p. 91–92 °C. $[\alpha]_D^{25}$ = –247 (c = 1.10, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.35 (d, J = 4.9 Hz, 1 H), 7.07–6.92 (m, 2 H), 5.49 (br. s, 1 H), 5.17 (dd, J = 4.9, 4.7 Hz, 1 H), 3.97 (dd, J = 6.9, 4.5 Hz, 1 H), 3.89 (br. d, J = 6.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 186.3, 151.2 (ddd, J_{CF} = 251.6, 9.9, 2.4 Hz), 149.1 (ddd, J_{CF} = 252.4, 10.7, 3.2 Hz), 146.8, 140.0 (ddd, J_{CF} = 252.2, 15.2, 15.2 Hz), 131.2, 124.6 (ddd, J_{CF} = 7.6, 4.5, 4.5 Hz), 118.5 (dd, J_{CF} = 12.0, 4.2 Hz), 111.9 (dd, J_{CF} = 17.6, 3.6 Hz), 101.4, 72.2, 66.6 ppm. FTIR (neat): $\tilde{\nu}$ = 3101, 2996, 2961, 1704, 1507, 1469 cm^{-1}. ^{13}C NMR (125 MHz, $CDCl_3$, 125 MHz): δ = 186.3, 151.2 (ddd, J_{CF} = 251.6, 9.9, 2.4 Hz), 149.1 (ddd, J_{CF} = 252.4, 10.7, 3.2 Hz), 146.8, 140.0 (ddd, J_{CF} = 252.2, 15.2, 15.2 Hz), 131.2, 124.6 (ddd, J_{CF} = 7.6, 4.5, 4.5 Hz), 118.5 (dd, J_{CF} = 12.0, 4.2 Hz), 111.9 (dd, J_{CF} = 17.6, 3.6 Hz), 101.4, 72.2, 66.6 ppm. MS (EI): m/z (%) = 228.1 (50) [M – CO], 207.1 (40), 183.1 (100), 182.1 (65), 169 (43), 156 (47), 151 (45). $C_{12}H_7F_3O_3$ (256.18): calcd. C 56.26, H 2.75; found C 56.35, H 2.66.

(1*S*,5*R*)-3-(2-Formylphenyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3f): The general procedure performed with **2** (250 mg, 0.99 mmol) afforded a product that was crystallized from hot iPr$_2$O to give **3f** as bright orange crystals (120 mg, 53%). M.p. 150–151 °C. $[\alpha]_D^{20}$ = –306 (c = 2.67, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.86 (s, 1 H), 7.90 (dd, J = 7.5, 1.5 Hz, 1 H), 7.60 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H), 7.53 (ddd, J = 7.5, 7.5, 1.1 Hz, 1 H), 7.24–7.14 (m, 2 H), 5.52 (s, 1 H), 5.18 (dd, J = 4.7, 4.7 Hz, 1 H), 4.00 (dd, J = 6.8, 4.7 Hz, 1 H), 3.94 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 190.9, 187.1, 144.8, 137.2, 135.1, 134.7, 133.8, 130.7, 130.2, 129.2, 101.4, 72.3, 66.8 ppm. FTIR (neat): $\tilde{\nu}$ = 3010, 2974, 2844, 2761, 1692 (br.), 1601, 1591 cm^{-1}. MS (ESI): m/z = 231 $[M + H]^+$, 253 $[M + Na]^+$. $C_{13}H_{10}O_4$ (230.22): calcd. C 67.82, H 4.38; found C 67.65, H 4.38.

(1*S*,5*R*)-3-(2-Fluorophenyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (3g): The general procedure performed with **2** (250 mg, 0.99 mmol) afforded a product that was crystallized from hot iPr$_2$O to give **3g** as a colorless crystalline solid (191 mg, 88%). M.p. 96–97 °C. $[\alpha]_D^{16}$ = –300 (c = 0.20, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.38–7.27 (m, 3 H), 7.19–7.07 (m, 2 H), 5.53 (s, 1 H), 5.17 (dd, J = 4.7, 4.7 Hz, 1 H), 3.98 (dd, J = 6.7, 4.7 Hz, 1 H), 3.91 (d, J = 6.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 186.8, 160.0 (d, J_{CF} = 248.9 Hz), 146.0 (d, J_{CF} = 3.6 Hz), 132.6, 131.0 (d, J_{CF} = 3.6 Hz), 130.4 (d, J_{CF} = 8.2 Hz), 123.9 (d, J_{CF} = 3.6 Hz), 120.9 (d, J_{CF} = 14.5 Hz), 115.8 (d, J_{CF} = 22.7 Hz), 101.7, 72.3, 66.7 ppm. FTIR (neat): $\tilde{\nu}$ = 1698, 1485, 1214, 1108, 980, 884, 819, 765 cm^{-1}. MS (ESI): m/z = 221.0 $[M + H]^+$. $C_{12}H_9FO_3$ (220.20): calcd. C 65.45, H 4.12; found C 65.21, H 4.04.

General Procedure for Heck Reactions of 1: Aryl iodide (2.4 mmol), SPhos (16 mg, 0.04 mmol), anhydrous K_3PO_4 (4.0 mmol), and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol) were added to a stirred solution of (–)-LGO (**1**; 252 mg, 2.0 mmol) under N_2 in toluene (5 mL), and the reaction mixture was heated at reflux to 110 °C until the reaction was complete according to TLC (3:7, ethyl acetate/hexanes). The resulting mixture was washed with H_2O (10 mL) and the aqueous phase extracted with CH_2Cl_2 (20 mL), then the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The products **5a**–**5c**, **5h**, and **5i** were purified by flash chromatography (1:3, ethyl acetate/hexanes) and then further purified as specified.

(1*S*,5*R*)-2-Phenyl-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (5a): The general procedure for the Heck reaction of **1** (500 mg, 3.97 mmol) gave a product that was crystallized from CH_2Cl_2/hexanes to give **5a** as off-white crystals (483 mg, 60%). M.p. 98–100 °C. $[\alpha]_D^{19}$ = –384 (c = 0.25, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.54–7.41 (m, 5 H), 6.31 (d, J = 1.5 Hz, 1 H), 5.51 (d, J = 5.0 Hz, 1 H), 5.41 (d, J = 1.5 Hz, 1 H), 4.04 (dd, J = 6.8, 5.0 Hz, 1 H), 3.80 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 189.4, 159.1, 133.8, 131.1, 129.4, 126.4, 120.5, 101.2, 74.0, 67.6 ppm. FTIR (neat): $\tilde{\nu}$ = 3030, 2961, 2922, 2886, 2852, 1683, 1258, 1110 cm^{-1}. MS (EI): m/z (%) = 173 (20) [M – HCO], 157 (25), 129 (100), 128 (28), 115 (32), 101.8 (15). $C_{12}H_{10}O_3$ (202.21): calcd. C 71.28, H 4.98; found C 71.49, H 4.78.

(1*S*,5*R*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (5b): The general procedure for the Heck reaction of **1** (504 mg, 4.0 mmol) gave a product that was further crystallized from hot iPr$_2$O to give **5b** as a yellow crystalline solid (612 mg, 62%). M.p. 147–149 °C. $[\alpha]_D^{20}$ = –412 (c = 0.50, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.03 (dd, J = 8.2, 1.5 Hz, 1 H), 6.98 (d, J = 1.5 Hz, 1 H), 6.89 (d, J = 8.2 Hz, 1 H), 6.22 (br. d, J = 1.0 Hz, 1 H), 6.05 (s, 2 H), 5.47 (d, J = 5.0 Hz, 1 H), 5.40 (s, 1 H), 4.03 (dd, J = 6.6, 5.0 Hz, 1 H), 3.77 (d, J = 6.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz,$CDCl_3$, 25 °C): δ = 189.5, 158.5, 150.4, 148.8, 127.7, 121.3, 118.8, 108.9, 106.2, 101.9, 101.1, 73.8, 67.6 ppm. FTIR (neat): $\tilde{\nu}$ = 2985, 2901, 1668, 1504, 1490, 1254, 866 cm^{-1}. MS (ESI): m/z = 247.0 $[M + H]^+$, 269.0 $[M + Na]^+$. $C_{13}H_{10}O_5$ (246.22): calcd. C 63.42, H 4.09; found C 63.69, H 3.94.

(1*S*,5*R*)-2-(4-Methoxyphenyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (5c): The general procedure for the Heck reaction of **1** (250 mg, 1.98 mmol) gave a product that was recrystallized from hot iPr$_2$O to give **5c** as colorless crystals (269 mg, 59%). M.p. 108–110 °C. $[\alpha]_D^{17}$ = –432 (c = 0.44, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.57–7.35 (m, 2 H), 7.07–6.89 (m, 2 H), 6.24 (br. dd, J = 1.3, 0.6 Hz, 1 H), 5.51 (br. d, J = 5.0 Hz, 1 H), 5.39 (d, J = 1.3 Hz, 1 H), 4.01 (dd, J = 6.6, 5.0 Hz, 1 H), 3.84 (s, 3 H), 3.75 (d, J = 6.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 189.6, 162.1, 158.6, 128.0, 125.8, 118.2, 114.8, 101.2, 73.6, 67.5, 55.4 ppm. FTIR (neat): $\tilde{\nu}$ = 3054, 2992, 2981, 2844, 1669, 1587, 1109 cm^{-1}. MS (ESI): m/z = 233.1 $[M + H]^+$, 255.1 $[M + Na]^+$. $C_{13}H_{12}O_4$ (232.24): calcd. C 67.23, H 5.21; found C 67.63, H 5.33.

(1*S*,5*R*)-2-(*p*-Tolyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (5h): The general procedure for the Heck reaction of **1** (250 mg, 1.98 mmol) gave **5h** as colorless crystals (243 mg, 57%). M.p. 99–100 °C. $[\alpha]_D^{20}$ = –410 (*c* = 1.24, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.43–7.33 (m, 2 H), 7.29–7.20 (m, 2 H), 6.27 (br. d, *J* = 1.5 Hz, 1 H), 5.50 (d, *J* = 5.0 Hz, 1 H), 5.38 (d, *J* = 1.5 Hz, 1 H), 4.01 (dd, *J* = 6.6, 5.0 Hz, 1 H), 3.76 (d, *J* = 6.6 Hz, 1 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 189.5, 158.9, 141.8, 130.7, 129.9, 126.2, 119.2, 101.1, 73.7. 67.4, 21.3 ppm. FTIR (neat): ṽ = 3043, 2996, 2904, 1683, 1596, 1107 cm^{-1}. MS (ESI): *m*/*z* = 217.1 $[M + H]^+$, 239.1 $[M + Na]^+$. $C_{13}H_{12}O_3$ (216.24): calcd. C 72.21, H 5.59; found C 72.47, H 5.46.

Methyl 2-[(1*S*,5*R*)-4-Oxo-6,8-dioxabicyclo[3.2.1]oct-2-en-2yl]benzoate (5i): The general procedure for the Heck reaction of **1** (250 mg, 1.98 mmol) gave a product that was further crystallized from hot *i*Pr_2O to give **5i** as colorless crystals (181 mg, 35%). M.p. 149–150 °C. $[\alpha]_D^{21}$ = –447 (*c* = 1.09, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.06 (ddd, *J* = 7.5, 1.5, 1.5 Hz, 1 H), 7.57 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1 H), 7.51 (ddd, *J* = 7.5, 1.5, 1.5 Hz, 1 H), 7.18 (dd, *J* = 7.5, 1.5 Hz, 1 H), 5.90 (dd, *J* = 1.3, 0.6 Hz, 1 H), 5.36 (d, *J* = 1.3 Hz, 1 H), 5.04 (dd, *J* = 4.0, 0.6 Hz, 1 H), 3.89 (s, 3 H), 3.84–3.73 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 188.9, 166.5, 163.9, 136.9, 133.0, 131.3, 130.1, 129.9, 128.7, 122.4, 101.1, 76.6, 66.6, 52.7 ppm. FTIR (neat): ṽ = 3010, 2957, 2922, 2851, 1707, 1693, 1265 cm^{-1}. MS (ESI): *m*/*z* = 261.1 $[M + H]^+$, 283.1 $[M + Na]^+$. $C_{14}H_{12}O_5$ (260.25): calcd. C 64.61, H 4.65; found C 64.26, H 4.62.

General Procedure for Hydroarylation Reactions of 1: Aryl iodide (1.2 equiv.), tri-*o*-tolylphosphine (2.0 mol-%), benzyldiethylamine (4.5 equiv.) and $Pd(OAc)_2$ (1.0 mol-%) were added to a stirred solution of (–)-LGO (**1**; 250 mg, 1.98 mmol) under N_2 in DMF (5 mL), and the reaction mixture was heated at reflux (80–110 °C) until the reaction was complete according to TLC (1:3, ethyl acetate/hexanes). The resulting mixture was washed with H_2O (10 mL) and the aqueous phase extracted with CH_2Cl_2 (20 mL), then the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The products **7a**–**7c**, **7h**, and **7i** were purified by flash chromatography (1:19, ethyl acetate/toluene) and then further purified as specified.

(1*S*,2*R*,5*R*)-2-Phenyl-6,8-dioxabicyclo[3.2.1]octan-4-one (7a): The general procedure for hydroarylation of **1** (1.0 g, 7.92 mmol) gave a mixture of **5a/7a**, 1:5.5 (1.11 g, 69%). A portion of the mixture (**5a/7a**, 2:5, 0.50 g) was dissolved in ethyl acetate (5 mL) and stirred with $KMnO_4$ (1.0 M, 5 mL) for 3 h. The biphasic mixture was filtered through silica, the filtrate concentrated under reduced pressure and crystallized from *i*Pr_2O to give colorless crystals of **7a** (330 mg, 92% recovery). M.p. 104 °C (ref.[24] 68 °C). $[\alpha]_D^{19}$ = –342 (*c* = 0.33, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.48–7.13 (m, 5 H), 5.21 (s, 1 H), 4.68 (br. d, *J* = 5.3 Hz, 1 H), 4.18 (dd, *J* = 7.5, 1.0 Hz, 1 H), 4.06 (dd, *J* = 7.5, 5.3 Hz, 1 H), 3.44 (d, *J* = 8.7 Hz, 1 H), 3.09 (dd, *J* = 16.8, 8.7 Hz, 1 H), 2.60 (ddd, *J* = 16.8. 1.0, 1.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 200.3, 142.0, 128.8, 127.5, 127.3, 101.5, 78.1, 68.3, 46.6, 37.0 ppm. FTIR (neat): ṽ = 3028, 2951, 1741, 1716, 1110 cm^{-1}. MS (EI): *m*/*z* (%) = 204.1 (trace) $[M]^+$, 130.1 (100), 129.1 (74), 117.1 (86), 115.1 (81), 104.1 (29), 91.1 (37), 77.1 (28). $C_{12}H_{12}O_3$ (204.23): calcd. C 70.57, H 5.92; found C 70.35, H 5.80.

(1*S*,2*R*,5*R*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-6,8-dioxabicyclo[3.2.1]-octan-4-one (7b): The general procedure for hydroarylation of **1** (0.50 g, 7.92 mmol) gave a mixture of **5b/7b**, 1:4 (0.80 g, 93%). An analytical sample of **7b** was purified by careful flash chromatography (1:19, ethyl acetate/toluene) to give colorless crystals. M.p. 128 °C (*i*Pr_2O). $[\alpha]_D^{20}$ = –309 (*c* = 0.51, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.80–6.71 (m, 2 H), 6.67 (dd, *J* = 7.9, 0.9 Hz, 1 H), 5.94 (s, 2 H), 5.19 (s, 1 H), 4.64 (d, *J* = 5.3 Hz, 1 H), 4.15 (d, *J* = 7.4 Hz, 1 H), 4.05 (dd, *J* = 7.4, 5.3 Hz, 1 H), 3.37 (br. d, *J* = 8.5 Hz, 1 H), 3.06 (dd, *J* = 16.8, 8.5 Hz, 1 H), 2.52 (br. d, *J* = 16.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 200.2, 148.0, 146.8, 135.9, 120.6, 108.4, 108.0, 101.5, 101.1, 78.2, 68.3, 46.4, 37.4 ppm. FTIR (neat): ṽ = 2992, 2909, 2796, 1731, 1499, 1250, 906, 1109, 643 cm^{-1}. MS (ESI): *m*/*z* = 271.1 $[M + Na]^+$. $C_{13}H_{12}O_5$ (248.23): calcd. C 62.90, H 4.87; found C 62.97, H 4.90.

(1*S*,2*R*,5*R*)-2-(4-Methoxyphenyl)-6,8-dioxabicyclo[3.2.1]octan-4-one (7c): The general procedure for hydroarylation of **1** (1.0 g, 7.92 mmol) gave a mixture of **5c/7c**, 1:4 (1.29 g, 70%). The reaction mixture was dissolved in dioxane (10 mL) and stirred with $KMnO_4$ (1.0 M, 10 mL) for 30 min. The reaction mixture was filtered through silica, eluted with ethyl acetate, the filtrate concentrated and the product purified by flash chromatography to give **7c** as a crystalline solid (1.03 g, 56%). M.p. 119–120 °C. $[\alpha]_D^{21}$ = –320 (*c* = 0.51, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.21–7.08 (m, 2 H), 6.92–6.81 (m, 2 H), 5.19 (s, 1 H), 4.63 (br. d, *J* = 5.2 Hz, 1 H), 4.16 (d, *J* = 7.6 Hz, 1 H), 4.04 (dd, *J* = 7.6, 5.2 Hz, 1 H), 3.78 (s, 3 H), 3.40 (d, *J* = 8.6 Hz, 1 H), 3.07 (dd, *J* = 16.8, 8.6 Hz, 1 H), 2.54 (dd, *J* = 16.8, 0.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 200.5, 158.7, 134.1, 128.5, 114.1, 101.5, 78.2, 68.2, 55.3, 45.9, 37.3 ppm. FTIR (neat): ṽ = 3061, 2983, 2836, 1753, 1730, 1697, 1510, 1244, 1109 cm^{-1}. MS (ESI): *m*/*z* = 257.1 $[M + Na]^+$. $C_{13}H_{14}O_4$ (234.25): calcd. C 66.66, H 6.02; found C 66.40, H 6.19.

(1*S*,2*R*,5*R*)-2-(*p*-Tolyl)-6,8-dioxabicyclo[3.2.1]octan-4-one (7h): The general procedure for hydroarylation of **1** (1.0 g, 7.92 mmol) gave a mixture of **5h/7h**, 1:3 (1.21 g, 70%). The reaction mixture was dissolved in dioxane (10 mL) and stirred with $KMnO_4$ (1.0 M, 10 mL) for 30 min. The biphasic mixture was filtered through silica, eluted with ethyl acetate, and the product was purified by flash chromatography (1:3, ethyl acetate/hexanes) to give colorless crystals of **7h** (940 mg, 54%). M.p. 91–93 °C. $[\alpha]_D^{23}$ = –340 (*c* = 0.15, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.19–7.05 (m, 4 H), 5.19 (s, 1 H), 4.65 (br. d, *J* = 5.2 Hz, 1 H), 4.16 (dd, *J* = 7.7, 1.0 Hz, 1 H), 4.04 (dd, *J* = 7.7, 5.2 Hz, 1 H), 3.40 (d, *J* = 8.7 Hz, 1 H), 3.06 (dd, *J* = 16.8, 8.7 Hz, 1 H), 2.56 (ddd, *J* = 16.8, 1.0, 1.0 Hz, 1 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 200.5, 139.0, 136.9, 129.4, 127.3, 101.5, 78.2, 68.2, 46.2, 37.1, 20.9 ppm. FTIR (neat): ṽ = 3047, 3000, 2954, 2924, 1737, 1721, 1111 cm^{-1}. MS (EI): *m*/*z* (%) = 218.1 (8) $[M]^+$, 144.1 (53), 131.1 (85), 130.1 (22), 129.1 (100), 117.1 (24), 116.1 (20), 115.1 (38), 91.1 (37). $C_{13}H_{14}O_3$ (218.25): calcd. C 71.54, H 6.47; found C 71.33, H 6.26.

Methyl 2-[(1*S*,2*R*,5*R*)-4-Oxo-6,8-dioxabicyclo[3.2.1]octan-2-yl]-benzoate (7i): The general procedure for hydroarylation of **1** (1.0 g, 7.92 mmol) and purification by flash chromatography gave colorless crystals of **7i** (1.11 g, 53%). M.p. 113–116 °C. $[\alpha]_D^{25}$ = –277 (*c* = 0.57, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.94 (dd, *J* = 8.3, 1.5 Hz, 1 H), 7.50 (ddd, *J* = 8.3, 7.0, 1.5 Hz, 1 H), 7.38–7.28 (m, 2 H), 5.18 (s, 1 H), 4.80 (br. d, *J* = 5.2 Hz, 1 H), 4.42 (d, *J* = 8.8 Hz, 1 H), 4.22 (dd, *J* = 7.7, 0.9 Hz, 1 H), 4.07 (dd, *J* = 7.7, 5.2 Hz, 1 H), 3.87 (s, 3 H), 3.07 (dd, *J* = 17.2, 8.8 Hz, 1 H), 2.49 (ddd, *J* = 17.2, 0.9, 0.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 201.1, 167.7, 143.8, 132.6, 130.9, 128.8, 128.3, 127.0, 101.5, 77.7, 68.6, 52.1, 42.6, 37.0 ppm. FTIR (neat): ṽ = 3000, 2953, 2913, 1739, 1714, 1266, 1253, 1072 cm^{-1}. MS (ESI): *m*/*z* = 263.1 $[M + H]^+$, 285.1 $[M + Na]^+$. $C_{14}H_{14}O_5$ (262.26): calcd. C 64.12, H 5.38; found C 64.38, H 5.30.

General Procedure for the Conjugate Reduction of 3a, 3b, and 3c: To a suspension of CuBr (4 equiv.) in dry THF (20 mL) under N_2 cooled to –5 °C was added a solution of sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al; 4 equiv., 60%, w/w), and the reaction mixture was stirred for 10 min. The reaction mixture was cooled to –65 °C, and enone **3a**, **3c**, or **3d** (1 equiv.) was added and the mixture stirred at this temperature for 10 min, then carefully quenched with methanol. The resulting mixture was filtered through a plug of silica and eluted with ethyl acetate. The filtrate was then concentrated under reduced pressure, and the resulting mixture was taken up in CH_2Cl_2 (20 mL) and filtered through Celite. The volatiles were removed under reduced pressure, and the residue was purified by column chromatography (1:3, ethyl acetate/hexanes) to give **13a**, **13b**, or **13c**.

(1*S*,3*S*,4*R*)-3-Phenyl-6,8-dioxabicyclo[3.2.1]octan-4-one (13a): Treatment of **3a** (106 mg, 0.52 mmol) as per the general method gave **13a** as a white crystalline solid (74 mg, 69%). M.p. 138–145 °C (CH_2Cl_2/hexanes). $[a]_D^{33}$ = –174 (*c* = 1.08, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.23 (m, 3 H), 7.20–7.10 (m, 2 H), 5.29 (s, 1 H), 4.85–4.73 (m, 1 H), 4.20 (br. d, *J* = 7.2 Hz, 1 H), 4.02 (ddd, *J* = 7.2, 5.4, 1.5 Hz, 1 H), 3.96 (dd, *J* = 11.9, 7.9 Hz, 1 H), 2.48 (dddd, *J* = 13.9, 11.9, 3.6, 1.5 Hz, 1 H), 2.35 (dddd, *J* = 13.9, 7.9, 1.5, 0.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 199.8, 136.8, 128.9, 128.7, 127.5, 102.0, 73.5, 67.7, 47.8, 39.7 ppm. FTIR (neat): $\tilde{\nu}$ = 3028, 2952, 2920, 1731 cm^{-1}. MS (ESI): *m*/*z* = 205.0 [M + H]$^+$, 227.0 [M + Na]$^+$. HRMS: calcd. for $C_{12}H_{12}O_3Na$ [M + Na]$^+$ 227.0679; found: 227.0680.

(1*S*,3*S*,5*R*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-6,8-dioxabicyclo[3.2.1]-octan-4-one (13b): Treatment of **3b** (500 mg, 2.15 mmol) as per the general method gave **13b** as a colorless crystalline solid (306 mg, 61%). M.p. 122–126 °C (*i*Pr_2O). $[a]_D^{21}$ = –140 (*c* = 0.35, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.78 (d, *J* = 7.9 Hz, 1 H), 6.63 (d, *J* = 1.8 Hz, 1 H), 6.60 (dd, *J* = 7.9, 1.8 Hz, 1 H), 5.95 (s, 2 H), 5.27 (br. s, 1 H), 4.80 (dddd, *J* = 4.4, 3.4, 1.8, 0.8 Hz, 1 H), 4.19 (dd, *J* = 7.5, 0.9 Hz, 1 H), 4.03 (ddd, *J* = 7.5, 4.4, 1.4 Hz, 1 H), 3.89 (dd, *J* = 11.8, 7.9 Hz, 1 H), 2.43 (dddd, *J* = 13.7, 11.8, 3,4, 1.4 Hz, 1 H), 2.34 (dddd, *J* = 13.7, 7.9, 1.8, 0.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 200.0, 148.0, 147.0, 130.4, 122.2, 109.1, 108.5, 101.9, 101.1, 73.5, 67.7, 47.6, 40.0 ppm. FTIR (neat): $\tilde{\nu}$ = 2974, 2931, 2891, 1731, 1614, 1231, 1100 cm^{-1}. MS (ESI): *m*/*z* 249.1 [M + H]$^+$. $C_{13}H_{12}O_5$ (248.23): calcd. C 62.90, H 4.87; found C 63.06, H 4.65.

(1*S*,3*S*,5*R*)-3-(4-Methoxyphenyl)-6,8-dioxabicyclo[3.2.1]octan-4-one (13c): Treatment of **3c** (260 mg, 1.06 mmol) as per the general method gave **13c** as a colorless crystalline solid (134 mg, 54%). M.p. 99–102 °C (*i*Pr_2O). $[a]_D^{22}$ = –152 (*c* = 0.29, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.10–7.00 (m, 2 H), 6.93–6.81 (m, 2 H), 5.26 (s, 1 H), 4.86–4.68 (m, 1 H), 4.18 (br. d, *J* = 7.2 Hz, 1 H), 4.00 (ddd, *J* = 7.2, 5.8, 1.3 Hz, 1 H), 3.91 (dd, *J* = 11.7, 7.9 Hz, 1 H), 3.78 (s, 3 H), 2.43 (dddd, *J* = 13.5, 11.7, 3.4, 1.3 Hz, 1 H), 2.32 (dddd, *J* = 13.5, 7.9, 0.9, 0.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 200.3, 158.8, 129.8, 128.7, 114.1, 101.8, 73.5, 67.6, 55.1, 46.9, 39.8 ppm. FTIR (neat): $\tilde{\nu}$ = 3036, 2985, 2952, 2931, 2840, 1731 1511, 1260, 1240, 1099 cm^{-1}. MS (ESI): *m*/*z* = 235.1 [M + H]$^+$. $C_{13}H_{14}O_4$ (234.25): calcd. C 66.66, H 6.02; found C 66.70, H 6.10.

General Procedure for the Baeyer–Villiger Oxidation of 5a, 7a, 7c, 7h, 13a, 13b, and 13c: Peracetic acid (32%, 600 μL, 2.78 mmol) was added to a stirred solution of bicyclo[3.2.1]octane derivative (1 mmol) dissolved in CH_2Cl_2 (3 mL), and the reaction mixture was stirred overnight. The reaction was quenched with Pd/C (10%, 15 mg) and the mixture stirred for 20 min or until the evolution of O_2 had ceased and a negative test for peroxides was obtained (starch/iodide). The mixture was then filtered through Celite, concentrated under reduced pressure and taken up in 1:1, THF/HCl (1 M; 12 mL) and stirred for 3 h. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (1:1–7:3, ethyl acetate/hexanes).

(3*S*,5*S*)-5-(Hydroxymethyl)-3-phenyldihydrofuran-2(3*H*)-one (14a): Treatment of **13a** (75 mg, 0.37 mmol) in accordance with the general procedure gave a colorless oil that crystallized upon standing (55 mg, 78%). M.p. 97–99 °C. $[a]_D^{20}$ = +57.1 (*c* = 0.98, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.47–7.16 (m, 5 H), 4.77–4.67 (m, 1 H), 4.04 (dd, *J* = 10.0, 8.2 Hz, 1 H), 3.94 (br. d, *J* = 11.9 Hz, 1 H), 3.69 (dd, *J* = 11.9, 2.8 Hz, 1 H), 3.17 (br. s, 1 H), 2.66 (ddd, *J* = 13.2, 10.0, 4.5 Hz, 1 H), 2.43 (ddd, *J* = 13.2, 8.2, 8.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 178.3, 137.5, 128.9, 127.7, 127.5, 78.9, 64.1, 46.0, 32.6 ppm. FTIR (neat): $\tilde{\nu}$ = 3458, 3033, 2968, 1749, 1184, 1056, 1027 cm^{-1}. MS (ESI): *m*/*z* = 193.1 [M + H]$^+$, 215.1 [M + Na]$^+$. $C_{11}H_{12}O_3$ (192.21): calcd. C 68.74, H 6.29; found C 68.53, H 6.46.

(3*S*,5*S*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (14b): To a solution of **13b** (91 mg, 0.37 mmol) in CH_2Cl_2 (1 mL) was added *m*-chloroperbenzoic acid (70%, 99 mg, 0.40 mmol), then *p*-TSA (30 mg, 0.17 mmol), and the reaction mixture was stirred for 10 d. The ^{1}H NMR spectrum of an aliquot of the reaction mixture showed 40% conversion of starting material to desired lactone **14b** and its formate ester derivative. The reaction was quenched by pouring the mixture onto iron filings, and the mixture was stirred for 5 min until the evolution of O_2 had ceased and a negative test for peroxides was obtained (starch/iodide). The mixture was then filtered through Celite, concentrated under reduced pressure and taken up in 1:1, THF/HCl (1 M; 2 mL) and stirred for 3 h. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (7:3, ethyl acetate/hexanes) to give **14b** as a colorless syrup (17 mg, 50% based on conversion of starting material). $[a]_D^{15}$ = +45 (*c* = 0.80, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.95–6.60 (m, 3 H), 5.96 (s, 2 H), 4.74 (dddd, *J* = 8.2, 4.6, 4.1, 3.1 Hz, 1 H), 4.06–3.89 (m, 2 H), 3.74 (dd, *J* = 12.4, 4.1 Hz, 1 H), 2.66 (ddd, *J* = 13.1, 9.8, 4.6 Hz, 1 H), 2.43 (ddd, *J* = 13.1, 8.2, 8.2 Hz, 1 H), 2.12 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 177.6, 148.2, 147.1, 131.0, 121.0, 108.6, 108.1, 101.2, 78.4, 64.5, 45.0, 32.7 ppm. FTIR (neat): $\tilde{\nu}$ = 3450, 2950, 2922, 2852, 1765, 1736, 1233, 1034 cm^{-1}. MS (ESI): *m*/*z* = 259.1 [M + Na]$^+$. HRMS: calcd. for $C_{12}H_{12}O_5Na$ [M + Na]$^+$ 259.0577; found 259.0573.

(3*S*,5*S*)-5-(Hydroxymethyl)-3-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (14c): Treatment of **13c** (115 mg, 0.49 mmol) in accordance with the general procedure gave **14c** as a white crystalline solid (69 mg, 63%). M.p. 90–93 °C (toluene). $[a]_D^{18}$ = +42.4 (*c* = 0.33, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.23–7.14 (m, 2 H), 6.95–6.82 (m, 2 H), 4.73 (dddd, *J* = 8.0, 5.0, 4.7, 2.7 Hz, 1 H), 4.06–3.93 (m, 2 H), 3.80 (s, 3 H), 3.74 (ddd, *J* = 12.2, 6.3, 5.0 Hz, 1 H), 2.65 (ddd, *J* = 13.2, 9.8, 4.7 Hz, 1 H), 2.43 (ddd, *J* = 13.2, 8.0, 8.0 Hz, 1 H), 2.07 (dd, *J* = 6.3, 6.3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 177.8, 159.0, 129.4, 128.7, 114.4, 78.4, 64.5, 55.3, 45.1, 32.7 ppm. FTIR (neat): $\tilde{\nu}$ = 3499, 3421, 3032, 3008, 2954, 2831, 1762, 1746, 1249, 1030 cm^{-1}. MS (ESI): *m*/*z* = 223.1 [M + H]$^+$, 245.0 [M + Na]$^+$. $C_{12}H_{14}O_4$ (222.24): calcd. C 64.85, H 6.35; found C 64.81, H 6.40.

(S)-5-(Hydroxymethyl)-4-phenylfuran-2(5*H*)-one (15a): Treatment of **5a** (100 mg, 0.50 mmol) in accordance with the general procedure gave **15a** as a white crystalline solid (78 mg, 92%). M.p. 135 °C (MeOH/Et_2O). $[a]_D^{17}$ = –172 (*c* = 0.25, CH_2Cl_2). ^{1}H NMR

(500 MHz, CD_3OD, 25 °C): δ = 6.25–6.01 (m, 2 H), 5.99–5.86 (m, 3 H), 4.94 (s, 1 H), 4.19 (br. dd, *J* = 3.8, 2.6 Hz, 1 H), 2.51 (dd, *J* = 12.7, 2.6 Hz, 1 H), 2.21 (dd, *J* = 12.7, 3.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, CD_3OD, 25 °C): δ = 175.7, 167.4, 132.6, 131.6, 130.4, 128.8, 116.3, 85.3, 62.8 ppm. FTIR (neat): ṽ = 3393, 3110, 2932, 1723, 1707, 1614, 1513 cm^{-1}. MS (ESI): *m*/*z* = 191.1 [M + H]$^+$, 213.1 [M + Na]$^+$. $C_{11}H_{10}O_3$ (190.20): calcd. C 69.46, H 5.30; found C 69.35, H 5.24.

(4*R*,5*S*)-5-(Hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (16a):[25] Treatment of **7a** (330 mg, 1.62 mmol) in accordance with the general procedure afforded **16a** as a straw-colored oil that crystallized upon standing (279 mg, 90%). M.p. 89–91 °C (*i*Pr_2O). $[\alpha]_D^{19}$ = +41.6 (*c* = 0.89, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.44–7.12 (m, 5 H), 4.61–4.43 (m, 1 H), 3.95 (d, *J* = 12.8 Hz, 1 H), 3.80–3.55 (m, 2 H), 3.03 (dd, *J* = 17.7. 9.0 Hz, 1 H), 2.78 (dd, *J* = 17.7, 9.6 Hz, 1 H), 2.35 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 176.1, 139.1, 129.1, 127.7, 127.2, 87.0, 61.9, 42.0, 37.2 ppm. FTIR (neat): ṽ = 3479, 3065, 3036, 2949, 2926, 1762, 1743 cm^{-1}. MS (ESI): *m*/*z* = 193.1 [M + H]$^+$, 215.1 [M + Na]$^+$.

(4*R*,5*S*)-5-(Hydroxymethyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (16c): Treatment of **7c** (184 mg, 0.79 mmol) in accordance with the general procedure afforded **16c** as a colorless oil that crystallized upon standing (116 mg, 66%). M.p. 92–93 °C (*i*PrOH/Et_2O). $[\alpha]_D^{20}$ = +22.7 (*c* = 0.75, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.22–7.14 (m, 2 H), 6.98–6.83 (m, 2 H), 4.50 (ddd, *J* = 8.2, 3.7, 2.4 Hz, 1 H), 3.95 (dd, *J* = 12.8, 2.4 Hz, 1 H), 3.81 (s, 3 H), 3.71–3.59 (m, 2 H), 3.00 (dd, *J* = 17.7, 9.2 Hz, 1 H), 2.76 (dd, *J* = 17.7 Hz, 10.1 1 H), 2.09 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 175.8, 159.2, 130.7, 128.3, 114.6, 87.0, 61.9, 55.3, 41.4, 37.3 ppm. FTIR (neat): ṽ = 3441, 2963, 2910, 2840, 1757, 1733, 1610, 1029 cm^{-1}. MS (ESI): *m*/*z* = 245.1 [M + Na]$^+$. $C_{12}H_{14}O_4$ (222.24): calcd. C 64.85, H 6.35; found C 64.58, H 6.22.

(4*R*,5*S*)-5-(Hydroxymethyl)-4-(*p*-tolyl)dihydrofuran-2(3*H*)-one (16h): Treatment of **7h** (152 mg, 0.70 mmol) in accordance with the general procedure afforded **16h** as a colorless syrup (110 mg, 77%). $[\alpha]_D^{21}$ = +29.2 (*c* = 0.24, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.24–6.93 (m, 4 H), 4.44 (ddd, *J* = 7.9, 4.0, 2.4 Hz, 1 H), 3.86 (dd, *J* = 12.8, 2.4 Hz, 1 H), 3.66–3.50 (m, 2 H), 2.92 (dd, *J* = 17.7, 9.0 Hz, 1 H), 2.68 (dd, *J* = 17.7, 9.8 Hz, 1 H), 2.56 (br. s, 1 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 176.1, 137.5, 136.0, 129.8, 127.0, 87.1, 61.9, 41.6, 37.2, 20.9 ppm. FTIR (neat): ṽ = 3417, 3025, 2923, 2869. 1769, 1755, 1516 cm^{-1}. MS (ESI): *m*/*z* = 207.1 [M + H]$^+$, 229.1 [M + Na]$^+$. HRMS: calcd. for $C_{12}H_{14}O_3Na$ [M + Na]$^+$ 229.0835; found 229.0840.

Methyl 2-[(2*S*,3*R*)-2-(Hydroxymethyl)-5-oxotetrahydrofuran-3-yl]-benzoate (16i): Treatment of **7i** (152 mg, 0.58 mmol) in accordance with the general procedure afforded **16i** as a colorless syrup (106 mg, 73%). $[\alpha]_D^{17}$ = +21.2 (*c* = 0.33, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.90 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.57 (ddd, *J* = 7.9, 7.7, 1.2 Hz, 1 H), 7.44 (dd, *J* = 7.9, 0.9 Hz, 1 H), 7.37 (ddd, *J* = 7.9, 7.7, 0.9 Hz, 1 H), 4.59 (ddd, *J* = 6.9, 3.7, 2.7 Hz, 1 H), 4.51 (ddd, *J* = 9.5, 7.3, 6.9 Hz, 1 H), 4.00–3.87 (m, 1 H), 3.93 (s, 3 H), 3.82 (ddd, *J* = 12.1, 6.1, 4.8 Hz, 1 H), 3.12 (dd, *J* = 18.0, 9.5 Hz, 1 H), 2.94 (dd, *J* = 6.1, 6.1 Hz, 1 H), 2.72 (dd, *J* = 18.0, 7.3 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 176.2, 168.2, 141.5, 132.9, 130.9, 129.9, 127.4, 127.3, 87.0, 62.8, 52.5, 38.1, 37.4 ppm. FTIR (neat): ṽ = 3439, 2952, 1771, 1713, 1601, 1577 cm^{-1}. MS (ESI): *m*/*z* = 251.1 [M + H]$^+$, 273.1 [M + Na]$^+$. HRMS: calcd. for $C_{13}H_{14}O_5Na$ [M + Na]$^+$ 273.0733; found 273.0734.

(1*S*,2*S*,5*R*)-2-Phenyl-6,8-dioxabicyclo[3.2.1]octan-4-one (17): To a solution of **5a** (202 mg, 1.0 mmol) in ethyl acetate (3 mL) was added Pd/C (10%; 20 mg), and the reaction mixture was stirred under H_2 overnight. The reaction mixture was filtered through Celite and concentrated under reduced pressure to give a residue that was then purified by column chromatography (1:3–1:1, ethyl acetate/hexanes) to give a 10:1 mixture of isomers **17**/**7a** (166 mg, 81%) and alcohol **18** (30 mg, 15%). An analytical sample of **17** was obtained by careful chromatography. **17:** Crystalline solid. M.p. 83–86 °C. $[\alpha]_D^{14}$ = –77.9 (*c* = 1.72, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.36 (m, 2 H), 7.35–7.29 (m, 1 H), 7.28–7.21 (m, 2 H), 5.18 (br. s, 1 H), 4.79–4.72 (m, 1 H), 4.14 (dd, *J* = 8.1, 1.1 Hz, 1 H), 3.82 (br. ddd, *J* = 12.5, 5.9, 3.7 Hz, 1 H), 3.78 (dddd, *J* = 8.1, 5.5, 0.9, 0.9 Hz, 1 H), 3.03 (dd, *J* = 15.6, 12.5 Hz, 1 H), 2.63 (dddd, *J* = 15.6, 5.9, 0.9, 0.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.1, 136.9, 129.1, 127.8, 127.4, 100.9, 78.0, 64.2, 46.0, 35.9 ppm. FTIR (neat): ṽ = 2989, 2917, 2852, 1735, 1599 cm^{-1}. MS (ESI): *m*/*z* = 227 [M + Na]$^+$. HRMS: calcd. for $C_{12}H_{12}O_3Na$ [M + Na]$^+$ 227.0679; found 227.0677.

(1S,2S,4S,5R)-2-Phenyl-6,8-dioxabicyclo[3.2.1]octan-4-ol (18): Colorless syrup. $[\alpha]_D^{18}$ = –50.4 (*c* = 1.17, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.32 (m, 2 H), 7.32–7.21 (m, 3 H), 5.43 (br. s, 1 H), 4.78–4.47 (m, 1 H), 3.95 (dd, *J* = 7.6, 0.6 Hz, 1 H), 3.85 (dddd, *J* = 10.0, 10.0, 5.8, 1.7 Hz, 1 H), 3.68 (dd, *J* = 7.6, 5.2 Hz, 1 H), 3.38 (ddd, *J* = 12.8, 4.0. 4.0 Hz, 1 H), 2.32 (ddddd, *J* = 12.8, 5.8, 4.0, 1.4, 1.4 Hz, 1 H), 1.90 (ddd, *J* = 12.8, 10.0 Hz, 10.0 1 H), 1.78 (d, *J* = 10 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.6, 128.8, 127.5, 127.2, 102.5, 77.6, 69.5, 65.2, 42.7, 30.7 ppm. FTIR (neat): ṽ = 3481, 3090, 2981, 2932, 2949, 2866, 1602 cm^{-1}. MS (ESI): *m*/*z* = 229 [M + Na]$^+$. HRMS: calcd. for $C_{12}H_{14}O_3Na$ [M + Na]$^+$ 229.0835; found 229.0835.

Single-Crystal X-ray Crystallography: Single crystals were mounted in paratone-N oil on a plastic loop. X-ray diffraction data were collected at 150(2) K with an Oxford X-calibur single-crystal diffractometer by using Mo-K_α radiation.[26] Data sets were corrected for absorption by using a multi-scan method, and structures were solved by direct methods by using SHELXS-2014 and refined by full-matrix least squares on F^2 by SHELXL-2014,[27] interfaced through the program X-Seed.[28] In general, all non-hydrogen atoms were refined anisotropically and hydrogen atoms were included as invariants at geometrically estimated positions, unless specified otherwise in additional details below. Table S1 lists the X-ray experimental data and refinement parameters for the crystal structures. CCDC-1412235, -1412236, -1412237, -1412238, -1412239, and -1412240 (for **3a**, **3b**, **3d**, **5h**, **7i**, and **13a**, respectively) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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