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Synthesis of Chiral Tetrahydrofurans via Catalytic Asymmetric [3 + 2] Cycloaddition of Heterosubstituted Alkenes with Oxiranes

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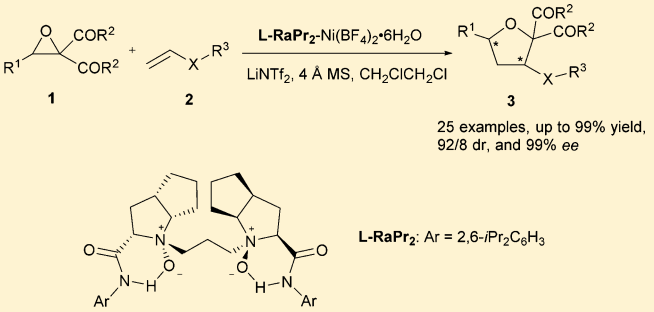
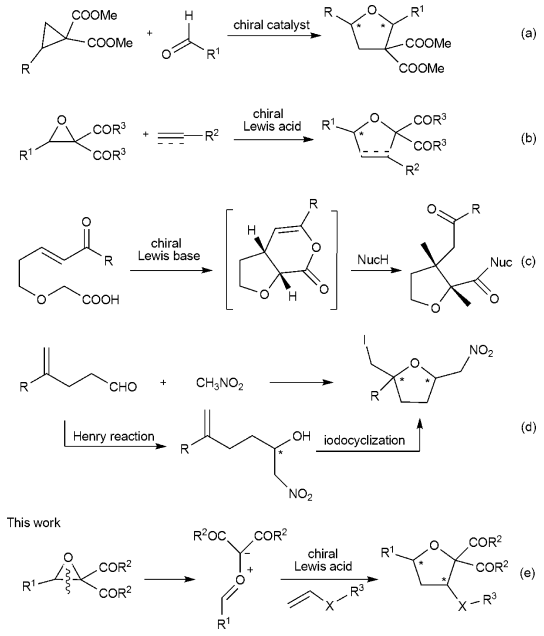
Supporting Information

ABSTRACT: An efficient diastereo- and enantioselective [3 + 2] cycloaddition of heterosubstituted alkenes with oxiranes via selective C−C bond cleavage of epoxides has been developed. The reaction was catalyzed by a chiral *N*,*N*′-dioxide/Ni(II) catalyst, and a variety of chiral highly substituted tetrahydrofurans were obtained in up to 99% yield, 92/8 dr, and 99% *ee*.



Tetrahydrofurans (THFs) represent a class of common heterocyclic scaffolds and are found in myriads of natural products and biologically active molecules.[1] Thus, considerable efforts have been devoted to developing efficient methodologies for their synthesis.[2] For the synthesis of chiral tetrahydrofurans, asymmetric [3 + 2] cycloadditions (Scheme 1a, b),[3−5] cyclization of alcohols,[6] oxidative cyclization of olefins,[7] intramolecular Michael addition/lactonization[8] (Scheme 1c), and sequential Henry reaction/iodocyclization[9] (Scheme 1d) have been developed. Though great progress has been achieved, other efficient methods are still desirable. Oxiranes have obviously become interesting reagents for the past few years. Particularly, their selective C−C bond cleavage has been proved to be an atom-economical approach to generate carbonyl ylides.[10] Up to now, chemoselective [4 + 3] cycloadditions of oxiranes with nitrones,[11] tandem heterocyclization/[4 + 1] cycloaddition of oxiranes,[12] ring-opening/Friedel−Crafts alkylation,[13] and a range of [3 + 2] cycloaddition of oxiranes[14] have been achieved. Recently, we demonstrated that our chiral *N*,*N*′-dioxide/metal complexes[15] could realize the asymmetric cycloaddition of oxiranes with aldehydes,[16] alkynes,[4] and indoles[5] for the first time. Therefore, it is reasonable to predict that chiral *N*,*N*′-dioxide/metal complexes would be workable for the catalytic asymmetric [3 + 2] cycloaddition of oxiranes with heterosubstituted alkenes, which would offer a facile way to construct chiral furan derivatives. Herein, we described our efforts in developing an efficient chiral *N*,*N*′-dioxide−Ni(II) catalyst system for the asymmetric [3 + 2] cycloaddition of heterosubstituted alkenes with oxiranes. A variety of chiral substituted tetrahydrofurans were obtained in up to 99% yield, 92/8 dr, and 99% *ee*.

Scheme 1. Methods for Catalytic Asymmetric Synthesis of Highly Substituted Tetrahydrofurans



In our initial work, the [3 + 2] cycloaddition of oxirane **1a** and heterosubstituted alkene **2a** was employed as the model reaction to optimize the reaction conditions. We first examined various *N*,*N*′-dioxides derived from L-ramipril (**Ra**) by complexing with $Ni(BF_4)_2·6H_2O$. As shown in Table 1, the steric hindrance at the *ortho* positions of the aniline of *N*,*N*′-

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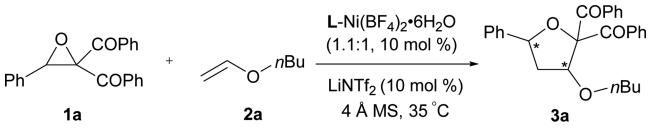
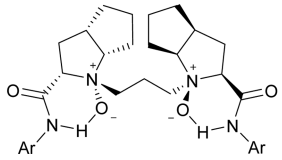
Table 1. Optimization of the Reaction Conditions





L-RaPh: Ar = C_6H_5
L-RaMe$_2$: Ar = 2,6-$Me_2C_6H_3$
L-RaEt$_2$: Ar = 2,6-$Et_2C_6H_3$
L-RaPr$_2$: Ar = 2,6-*i*$Pr_2C_6H_3$

entry[a]	ligand	solvent	yield (%)[b]	*dr*[c] *cis*/*trans*	*ee* (%)[c] *cis*-**3a**[e]
1	**L-RaPh**	CH_2Cl_2	trace	56/44	−11[d]
2	**L-RaMe$_2$**	CH_2Cl_2	99	72/28	−17[d]
3	**L-RaEt$_2$**	CH_2Cl_2	99	80/20	23
4	**L-RaPr$_2$**	CH_2Cl_2	99	92/8	87
5	**L-RaPr$_2$**	$CHCl_3$	99	90/10	89
6	**L-RaPr$_2$**	CH_2ClCH_2Cl	99	90/10	91

[a]Unless otherwise noted, all reactions were carried out with ligand−metal (1.1:1, 10 mol %), **1a** (0.10 mmol), **2a** (0.12 mmol, 1.2 equiv), $LiNTf_2$ (10 mol %) and 20 mg of 4 Å MS in solvent (0.5 mL) under N_2 at 35 °C for 24 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]"−" represents that the optical rotation is opposite to the others. [e]Determined by NOESY.

dioxide ligands affected the reaction greatly (Table 1, entries 1−4). When **L-RaPh** was employed, only a trace amount of the desired product was obtained and the *ee* value was only 11% (Table 1, entry 1). In the presence of **L-RaMe$_2$** bearing methyl groups, the yield was improved to 99% and the dr was improved to 72/28, albeit with still a low *ee* value (Table 1, entry 2). When it came to **L-RaEt$_2$** with ethyl groups, the dr value was further improved to 80/20 and the configuration of the product was reversed (23% *ee*, Table 1, entry 3). Gratifyingly, **L-RaPr$_2$** bearing *i*-propyl groups increased sharply the *ee* to 87% and the dr to 92/8 (Table 1, entry 4). Further optimization of reaction conditions revealed that solvents affected the reaction to a great extent. When the reaction was performed in $CHCl_3$, the *ee* increased slightly to 89%, but the dr decreased a little (90/10) (Table 1, entry 5). When the reaction was performed in CH_2ClCH_2Cl, the *ee* further increased to 91% with the yield and dr maintained (Table 1, entry 6). Finally, the optimal reaction conditions were established as follows: **1a**:**2a** = 1:1.2, **L-RaPr$_2$**:$Ni(BF_4)_2{\cdot}6H_2O$ = 1.1:1 (10 mol %), $LiNTf_2$ (10 mol %) and 20 mg of 4 Å MS in CH_2ClCH_2Cl (0.5 mL) under N_2 at 35 °C for 24 h.

With the optimized conditions in hand, we investigated the scope of the reaction. With respect to oxiranes (Table 2), aromatic (R^1) substituted epoxides with either electron-withdrawing or electron-donating substitutes at the *para* position on the phenyl ring transformed to the corresponding products in good to excellent yields (85−98%) with high dr (>90/10) and *ee* values (91−93%) (Table 2, entries 2−6). Meanwhile, when an electron-donating group was at the *meta* or *ortho* position, excellent outcomes also can be obtained (Table 2, entries 7−10). Unfortunately, the aromatic oxiranes with electron-withdrawing groups at the *meta* or *ortho* position (**1r**, **1s**) exhibited much lower reactivity. We got only 71% and 66% yields even if we added 2 equiv of **2a** and prolonged the reaction time to 48 h (Table 2, entries 18−19). What's more, the desired products were very difficult to separate from the starting materials.[17] These problems may be due to the electronic effects of the aryl group substituents. In addition, ring-fused epoxides **1k**, **1l** and heteroaromatic epoxides **1m**, **1n** were also well tolerated, delivering the corresponding products in 87−99% yields with 83/17 to 91/9 dr and 88−91% *ee* (Table 2, entries 11−14). Remarkably, unsaturated oxirane **1o** could also undergo this reaction smoothly, affording product **3o** in 98% yield with 92/8 dr and 90% *ee* (Table 2, entry 15). Moreover, we also varied the substituent R^2 on the acyl group; **1p**, **1q** were transformed to **3p**, **3q** in quantitative yields with 90/10 dr and 88−92% *ee* (Table 2, entries 16−17).

Subsequently, we explored the scope of heterosubstituted alkenes (Figure 1). It was found that large steric hindrance on

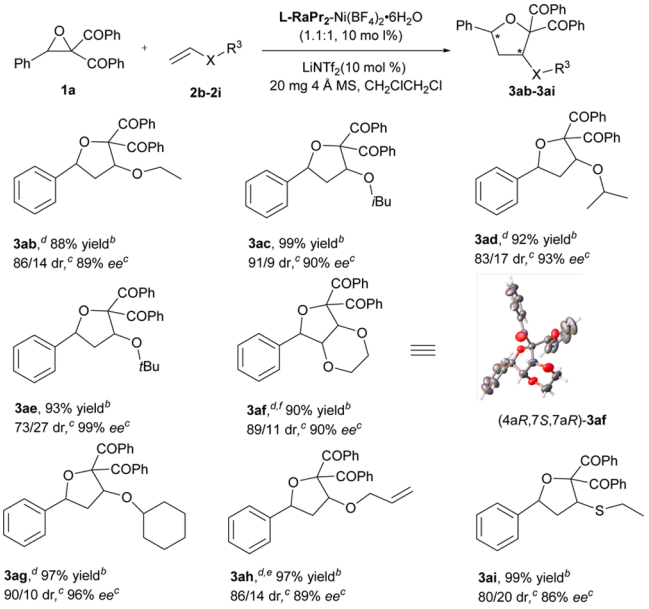


Figure 1. Substrate scope of heterosubstituted alkenes. Unless otherwise noted, all reactions were carried out with **L-RaPr$_2$**−metal (1.1:1, 10 mol %), **1a** (0.10 mmol), **2a** (0.12 mmol, 1.2 equiv), $LiNTf_2$ (10 mol %), and 20 mg of 4 Å MS in CH_2ClCH_2Cl (0.5 mL) under N_2 at 35 °C for 24 h. (b) Isolated yield. (c) Determined by HPLC analysis. (d) 2 equiv of **2a** was added. (e) The reaction time was prolonged to 48 h. (f) The absolute configuration was determined to be (4a*R*,7*S*,7a*R*) by X-ray crystallographic analysis.

vinyl ether was beneficial for the enantioselectivity, but not for diastereoselectivity. From **2b** to **2e**, enantioselectivity increased little by little as the steric hindrance on heterosubstituted alkenes became larger. When **2e** was employed, 99% *ee* of **3ae** was obtained while the dr decreased sharply to 73/27. Besides, cyclohexyl vinyl ether **2g** also proceeded in the reaction well, giving **3ag** in 97% yield with 90/10 dr and 96% *ee*. Cyclic vinyl ether 1,4-dioxene **2f** was also tested, generating **3af** with three stereogenic centers in 90% yield, 89/11 dr, and 90% *ee*. Furthermore, the absolute configuration of **3af** was determined to be (4a*R*,7*S*,7a*R*) by X-ray analysis.[18] Finally, allyl vinyl ether **2h** and vinyl sulfide **2i** were examined, generating **3ah** in 97% yield, 86/14 dr, 89% *ee* and **3ai** in 99% yield, 80/20 dr, 86% *ee*.

To show the prospect of the methodology, a gram-scale synthesis of **3a** was carried out. As shown in Scheme 2, 3.0 mmol of oxirane **1a** reacted smoothly with 3.6 mmol of heterosubstituted alkenes **2a**, affording 1.28 g of the corresponding product **3a** (99% yield) with 90/10 dr and 90% *ee*.

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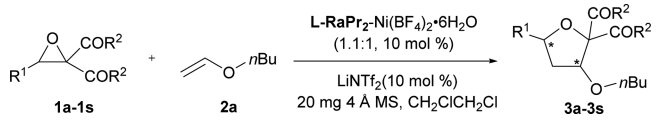
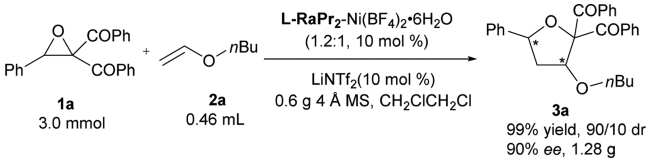
Table 2. Substrate Scope of Oxiranes



Entry[a]	R^1	R^2	1	Yield (%)[b]	*dr*[c] *cis/trans*	*ee* (%)[c] *cis*
1	C_6H_5	C_6H_5	**1a**	99 (**3a**)	90/10	91
2	4-FC_6H_4	C_6H_5	**1b**	93 (**3b**)	91/9	93
3	4-ClC_6H_4	C_6H_5	**1c**	93 (**3c**)	90/10	91
4[e,f]	4-BrC_6H_4	C_6H_5	**1d**	85 (**3d**)	90/10	91
5	4-MeC_6H_4	C_6H_5	**1e**	98 (**3e**)	92/8	93
6	4-$MeOC_6H_4$	C_6H_5	**1f**	97 (**3f**)	91/9	93
7	3-MeC_6H_4	C_6H_5	**1g**	99 (**3g**)	90/10	90
8	3-$MeOC_6H_4$	C_6H_5	**1h**	98 (**3h**)	90/10	88
9	3-$PhOC_6H_4$	C_6H_5	**1i**	99 (**3i**)	91/9	90
10	2-$MeOC_6H_4$	C_6H_5	**1j**	93 (**3j**)	89/11	89
11	1-Naphthyl	C_6H_5	**1k**	99 (**3k**)	83/17	88
12	2-Naphthyl	C_6H_5	**1l**	98 (**3l**)	91/9	90
13	3-Furyl	C_6H_5	**1m**	87 (**3m**)	91/9	91
14	3-Thienyl	C_6H_5	**1n**	96 (**3n**)	91/9	91
15		C_6H_5	**1o**	98 (**3o**)	92/8	90
16[e,f]	C_6H_5	4-MeC_6H_4	**1p**	99 (**3p**)	90/10	92
17	C_6H_5	4-BrC_6H_4	**1q**	99 (**3q**)	90/10	88
18[e,f]	3-FC_6H_4	C_6H_5	**1r**	71 (**3r**)[d]	88/12	86
19[e,f]	2-FC_6H_4	C_6H_5	**1s**	66 (**3s**)[d]	88/12	88

[a]Unless otherwise noted, all reactions were carried out with **L-RaPr$_2$**-Ni$(BF_4)_2$·$6H_2O$ (10 mol %, 1.1:1), **1a** (0.10 mmol), **2a** (0.12 mmol, 1.2 equiv), $LiNTf_2$ (10 mol %), and 20 mg of 4 Å MS in CH_2ClCH_2Cl (0.5 mL) under N_2 at 35 °C for 24 h. [b]Isolated yield. [c]Determined by chiral HPLC analysis. [d]Determined by ^1H NMR (CH_2Br_2 as a standard). [e]2 equiv of **2a** was added. [f]The reaction time was prolonged to 48 h.

Scheme 2. Gram-Scale Synthesis of 3a



On the basis of our previous study[15] and the absolute configuration of **3af** by X-ray analysis,[18] a possible transition state was proposed in Figure 2. The prepared catalyst coordinates with the two carbonyl groups of oxirane in a bidentate fashion, which leads to the formation of the carbonyl ylide, forming a rigid octahedral complex. The 2,6-diisopropylaniline group underneath the ligand shields the *Si* face of the carbonyl ylide. Therefore, heterosubstituted alkene attacks the *Re* face of the carbonyl ylide, giving (4a*R*,7*S*,7a*R*)-configured **3af**.

In summary, we have demonstrated a catalytic asymmetric [3 + 2] cycloaddition of heterosubstituted alkenes with oxiranes via C−C bond cleavage of epoxides in the presence of a chiral *N*,*N*′-dioxide−Ni(II) complex. A variety of chiral highly substituted tetrahydrofurans were furnished in good to excellent yields (up to 99%) with good to excellent enantioselectivities and diastereoselectivities (up to 92/8 dr and 99% *ee*) under mild reaction conditions.

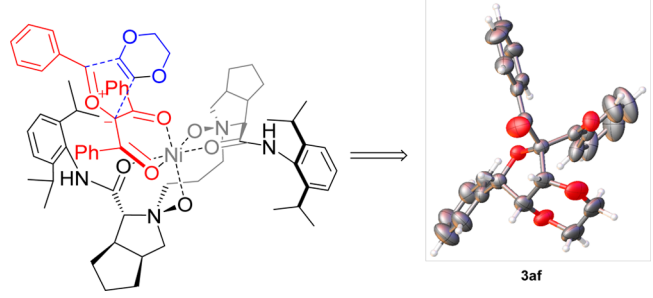


Figure 2. Proposed transition-state model and the absolute configuration of **3af**.

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EXPERIMENTAL SECTION

General Remarks. ^{1}H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR spectra were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). The enantiomeric excesses (*ee*) were determined by HPLC analysis on commercial chiral columns. Optical rotations were reported as follows: $[\alpha]_D^T$ (*c* = g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (ESI Source). All reagents and solvents were obtained from commercial suppliers and used without further purification except as indicated below. All catalytic reactions were run in dried glassware. Solvent was distilled over CaH_2.

General Procedure for Substrates. AcOH (10 mol %) and piperidine (10 mol %) were added to the solution of 1,3-diphenyl-1,3-propanedione (5.6 g) and benzaldehyde (2.5 mL) in toluene (25 mL). After addition, the mixture was heated to reflux for 4 h (separate the produced water from reaction system). Then, the solvent was removed under reduced pressure. The resulting residue was purified by silica gel column chromatography eluting with PE/EA = 10:1. The white solid, crude unsaturated diketone, was obtained in 86% yield. To a well-stirred solution of unsaturated diketone (22 mmol) in 1,2-dichloroethane (DCE, 15 mL) which was cooled in an ice bath were added *t*-BuOOH (in DCE, 21 mL) and DBU (4 mL). Commercial *t*-BuOOH (70% in H_2O, 13 mL) should be extracted with DCE (20 mL). The reaction mixture was further stirred for 40 min. After removing the solvent DCE, the crude product **1** was purified by silica gel column chromatography eluting with PE/EA = 10:1 and recrystallized in ethyl acetate. After it was washed with petroleum ether and dried under vacuum, the pure product was obtained. Substrate **2** was obtained from commercial suppliers.

General Procedure for Chiral *N,N′*-Dioxide Preparation. The *N,N′*-dioxides were prepared according to the methods reported in the literature.[19]

General Procedure for the Catalytic [3 + 2] Cycloaddition. A dry reaction tube was charged with **L-RaPr$_2$** (11 mol %), $Ni(BF_4)_2\cdot 6H_2O$ (10 mol %), $LiNTf_2$ (10 mol %), and 20 mg of 4 Å MS. CH_2ClCH_2Cl (0.5 mL) was added, and the mixture was stirred at 35 °C for 0.5 h until $Ni(BF_4)_2\cdot 6H_2O$ is solved entirely. Then, the heterosubstituted alkenes **2** (1.2 or 2.0 equiv) and oxiranes **1** (0.1 mmol) were added to the reaction mixture. After being stirred at 35 °C for 24 or 48 h, the crude reaction mixture was purified by flash chromatography on silica gel (PE/EA = 10/1) to afford the desired product.

*(3-Butoxy-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3a**).* Yield 42.7 mg, 99%; green viscous liquid; 91% *ee*, 90/10 dr; $[\alpha]_D^{13}$ = −137.9 (*c* = 0.75 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.26 min, t_2 = 8.18 min, t_3 = 10.03 min, t_4 = 11.42 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.7 Hz, 2H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.54−7.47 (m, 3H), 7.46−7.34 (m, 5H), 7.33−7.26 (m, 3H), 5.33 (dd, *J* = 6.4, 3.4 Hz, 1H), 4.88 (t, *J* = 8.0 Hz, 1H), 3.48−3.40 (m, 1H), 3.33−3.23 (m, 1H), 2.89−2.77 (m, 1H), 2.28−2.18 (m, 1H), 1.32−1.24 (m, 2H), 1.09−0.98 (m, 2H), 0.69 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.3, 194.8, 141.1, 136.7, 134.0, 133.3, 132.7, 130.2, 129.9, 128.5, 128.4, 128.0, 127.9, 126.7, 98.8, 83.7, 81.2, 69.9, 40.7, 31.5, 19.0, 13.7. HRMS (ESI-TOF): calcd for $C_{28}H_{28}NaO_4^+$ ([M + Na$^+$]) 451.1880, found 451.1881.

*(3-Butoxy-5-(4-fluorophenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3b**).* Yield 41.8 mg, 93%; green viscous liquid; 93% *ee*, 91/9 dr; $[\alpha]_D^{13}$ = −129.5 (*c* = 0.70 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.98 min, t_2 = 7.82 min, t_3 = 8.66 min, t_4 = 11.51 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.00 (m, 4H), 7.53−7.45 (m, 3H), 7.45−7.41 (m, 1H), 7.41−7.35 (m, 2H), 7.33−7.27 (m, 2H), 7.12−7.01 (m, 2H), 5.32 (dd, *J* = 6.0, 3.2 Hz, 1H), 4.90 (t, *J* = 7.6 Hz, 1H), 3.46−3.40 (m, 1H), 3.28−3.21 (m, 1H), 2.86−2.77 (m, 1H), 2.22−2.15 (m, 1H), 1.30−1.22 (m, 2H), 1.08−0.96 (m, 2H), 0.69 (t, *J* = 7.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.9, 194.7, 162.4 (d, *J* = 244 Hz), 137.1 (d, *J* = 3 Hz), 136.5, 134.0, 133.4, 132.8, 130.2, 129.7, 128.5 (d, *J* = 8 Hz), 128.4, 128.1, 115.3 (d, *J* = 22 Hz), 98.8, 83.6, 80.7, 69.9, 40.5, 31.4, 19.0, 13.6. HRMS (ESI-TOF): calcd for $C_{28}H_{27}FNaO_4^+$ ([M + Na$^+$]) 469.1786, found 469.1799.

*(3-Butoxy-5-(4-chlorophenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3c**).* Yield 43.1 mg, 93%; green viscous liquid; 91% *ee*, 90/10 dr; $[\alpha]_D^{13}$ = −112.4 (*c* = 0.86 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.79 min, t_2 = 7.91 min, t_3 = 10.12 min, t_4 = 13.24 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−7.96 (m, 4H), 7.53−7.43 (m, 4H), 7.41−7.35 (m, 2H), 7.35−7.28 (m, 4H), 5.31 (dd, *J* = 6.0, 2.8 Hz, 1H), 4.91 (t, *J* = 7.6 Hz, 1H), 3.44−3.88 (m, 1H), 3.26−3.20 (m, 1H), 2.86−2.77 (m, 1H), 2.21−2.14 (m, 1H), 1.28−1.21 (m, 2H), 1.04−0.97 (m, 2H), 0.68 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.7, 194.6, 140.0, 136.5, 134.0, 133.5, 133.5, 132.8, 130.2, 129.7, 128.6, 128.4, 128.1, 128.1, 98.9, 83.6, 80.6, 69.8, 40.4, 31.4, 19.0, 13.6. HRMS (ESI-TOF): calcd for $C_{28}H_{27}{}^{34.9689}ClNaO_4^+$ ([M + Na$^+$]) 485.1491, found 485.1493, $C_{28}H_{27}{}^{36.9659}ClNaO_4^+$ ([M + Na$^+$]) 487.1461, found 487.1491.

*(5-(4-Bromophenyl)-3-butoxytetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3d**).* Yield 42.9 mg, 85%; green viscous liquid; 91% *ee*, 90/10 dr; $[\alpha]_D^{13}$ = −94.5 (*c* = 0.86 in CH_2Cl_2); HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.87 min, t_2 = 8.19 min, t_3 = 10.27 min, t_4 = 13.28 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.88 (m, 4H), 7.44−7.38 (m, 3H), 7.37−7.27 (m, 5H), 7.25−7.20 (m, 2H), 5.23 (dd, *J* = 6.4, 3.2 Hz, 1H), 4.81 (t, *J* = 7.8 Hz, 1H), 3.37−3.28 (m, 1H), 3.20−3.11 (m, 1H), 2.79−2.67 (m, 1H), 2.14−2.04 (m, 1H), 1.20−1.12 (m, 2H), 0.97−0.86 (m, 2H), 0.60 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.7, 193.6, 139.5, 135.5, 133.0, 132.4, 131.7, 130.5, 129.2, 129.1, 128.6, 127.4, 127.4, 127.0, 120.6, 97.9, 82.6, 79.6, 68.8, 39.3, 30.4, 18.0, 12.6. HRMS (ESI-TOF): calcd for $C_{28}H_{27}{}^{78.9183}BrNaO_4^+$ ([M + Na$^+$]) 529.0985, found 529.0989, $C_{28}H_{27}{}^{80.9163}BrNaO_4^+$ ([M + Na$^+$]) 531.0965, found 531.0980.

*(3-Butoxy-5-(p-tolyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3e**).* Yield 43.6 mg, 98%; green viscous liquid; 93% *ee*, 92/8 dr; $[\alpha]_D^{13}$ = −122.9 (*c* = 0.83 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.57 min, t_2 = 8.64 min, t_3 = 9.94 min, t_4 = 12.37 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13−8.07 (m, 2H), 8.04−7.99 (m, 2H), 7.54−7.48 (m, 1H), 7.47−7.42 (m, 1H), 7.42−7.36 (m, 4H), 7.33−7.27 (m, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.32 (dd, *J* = 6.4, 3.6 Hz, 1H), 4.83 (t, *J* = 8.0 Hz, 1H), 3.49−3.42 (m, 1H), 3.32−3.25 (m, 1H), 2.86−2.77 (m, 1H), 2.36 (s, 3H), 2.24−2.17 (m, 1H), 1.33−1.24 (m, 2H), 1.10−1.00 (m, 2H), 0.71 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.8, 137.9, 137.7, 136.7, 134.0, 133.3, 132.7, 130.2, 130.0, 129.1, 128.4, 128.0, 126.8, 98.6, 83.7, 81.2, 69.9, 40.7, 31.5, 21.2, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{29}H_{30}NaO_4^+$ ([M + Na$^+$]) 465.2036, found 465.2041.

*(3-Butoxy-5-(4-methoxyphenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3f**).* Yield 44.7 mg, 97%; green viscous liquid; 93% *ee*, 91/9 dr; $[\alpha]_D^{13}$ = −113.0 (*c* = 0.72 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 10.20 min, t_2 = 12.57 min, t_3 = 13.77 min, t_4 = 18.25 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.2 Hz, 2H), 8.00 (t, *J* = 7.6 Hz, 2H), 7.53−7.50 (m, 1H), 7.46−7.35 (m, 5H), 7.33−7.26 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 5.31 (dd, *J* = 6.4, 3.6 Hz, 1H), 4.83 (t, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.50−3.41 (m, 1H), 3.32−3.25 (m, 1H), 2.85−2.74 (m, 1H), 2.25−2.15 (m, 1H), 1.34−1.25 (m, 2H), 1.11−1.00 (m, 2H), 0.71 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.8, 159.4, 136.7, 134.0, 133.3, 133.0, 132.7, 130.2, 130.0, 128.4, 128.3, 128.0, 113.8, 98.6, 83.7, 81.1, 69.9, 55.3, 40.6, 31.5, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{29}H_{30}NaO_5^+$ ([M + Na$^+$]) 481.1985, found 481.1988.

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*(3-Butoxy-5-(m-tolyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3g**).* Yield 44.7 mg, 99%; green viscous liquid; 90% *ee*, 90/10 dr; $[\alpha]_D^{16} = -100.3$ (c = 0.89 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.99 min, t_2 = 8.24 min, t_3 = 9.14 min, t_4 = 11.31 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 2H), 7.94 (d, J = 7.6 Hz, 2H), 7.47−7.40 (m, 1H), 7.39−7.27 (m, 3H), 7.27−7.14 (m, 5H), 7.06−6.97 (m, 1H), 5.24 (dd, J = 6.4, 3.2 Hz, 1H), 4.75 (t, J = 8.0 Hz, 1H), 3.42−3.32 (m, 1H), 3.26−3.16 (m, 1H), 2.79−2.68 (m, 1H), 2.28 (s, 3H), 2.17−2.09 (m, 1H), 1.25−1.16 (m, 2H), 1.04−0.92 (m, 2H), 0.62 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.8, 140.9, 138.1, 136.8, 134.0, 133.3, 132.7, 130.2, 130.0, 128.7, 128.4, 128.4, 127.9, 127.5, 123.8, 98.8, 83.7, 81.3, 69.9, 40.7, 31.5, 21.5, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{29}H_{30}NaO_4^+$ ([M + Na^+]) 465.2036, found 465.2046.

*(3-Butoxy-5-(3-methoxyphenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3h**).* Yield 45.1 mg, 98%; green viscous liquid; 88% *ee*, 90/10 dr; $[\alpha]_D^{15} = -116.4$ (c = 0.67 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 8.57 min, t_2 = 9.70 min, t_3 = 11.72 min, t_4 = 15.26 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 2H), 8.02 (d, J = 7.6 Hz, 2H), 7.54−7.48 (m, 1H), 7.47−7.37 (m, 3H), 7.34−7.27 (m, 2H), 7.27−7.23 (m, 1H), 7.15 (s, 1H), 7.03 (d, J = 7.6 Hz, 1H), 6.84 (dd, J = 8.0, 2.4 Hz, 1H), 5.31 (dd, J = 6.4, 3.2 Hz, 1H), 4.87 (t, J = 7.8 Hz, 1H), 3.81 (s, 3H), 3.47−3.39 (m, 1H), 3.30−3.22 (m, 1H), 2.88−2.77 (m, 1H), 2.27−2.16 (m, 1H), 1.31−1.23 (m, 2H), 1.08−0.98 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.3, 194.7, 159.8, 142.8, 136.7, 134.0, 133.3, 132.7, 130.2, 129.9, 129.4, 128.4, 128.0, 119.0, 113.8, 111.8, 98.9, 83.7, 81.3, 69.9, 55.2, 40.6, 31.5, 19.0, 13.6. HRMS (ESI-TOF): calcd for $C_{29}H_{30}NaO_5^+$ ([M + Na^+]) 481.1985, found 481.1993.

*(3-Butoxy-5-(3-phenoxyphenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3i**).* Yield 53.3 mg, 99%; green viscous liquid; 90% *ee*, 91/9 dr; $[\alpha]_D^{13} = -92.4$ (c = 1.07 in CH_2Cl_2); HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 8.16 min, t_2 = 9.50 min, t_3 = 13.59 min, t_4 = 24.14 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.03 (m, 2H), 8.03−7.98 (m, 2H), 7.54−7.38 (m, 3H), 7.37−7.29 (m, 7H), 7.22−7.18 (m, 1H), 7.15−7.05 (m, 1H), 7.05−6.99 (m, 2H), 6.96−6.91 (m, 1H), 5.29 (dd, J = 6.4, 3.2 Hz, 1H), 4.86 (t, J = 7.8 Hz, 1H), 3.44−3.37 (m, 1H), 3.30−3.20 (m, 1H), 2.87−2.77 (m, 1H), 2.24−2.17 (m, 1H), 1.27−1.19 (m, 2H), 1.06−0.95 (m, 2H), 0.68 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.2, 194.7, 157.3, 157.2, 143.3, 136.6, 133.9, 133.4, 132.7, 130.2, 129.9, 129.8, 129.8, 128.4, 128.0, 123.3, 121.6, 118.9, 118.8, 118.2, 117.2, 98.9, 83.6, 80.9, 69.9, 40.5, 31.4, 19.0, 13.7. HRMS (ESI-TOF): calcd for $C_{34}H_{32}NaO_5^+$ ([M + Na^+]) 543.2142, found 543.2141.

*(3-Butoxy-5-(2-methoxyphenyl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3j**).* Yield 42.7 mg, 93%; green viscous liquid; 89% *ee*, 89/11 dr; $[\alpha]_D^{15} = -141.5$ (c = 0.85 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.89 min, t_2 = 9.86 min, t_3 = 12.26 min, t_4 = 13.10 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (m, 4H), 7.85 (d, J = 7.2 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.47−7.37 (m, 3H), 7.36−7.20 (m, 3H), 7.05−6.96 (m, 1H), 6.85−6.76 (m, 1H), 5.37 (dd, J = 6.4, 3.6 Hz, 1H), 5.12 (t, J = 8.0 Hz, 1H), 3.74 (s, 3H), 3.44−3.34 (m, 1H), 3.28−3.19 (m, 1H), 3.00−2.86 (m, 1H), 2.11−1.99 (m, 1H),1.29−1.18 (m, 2H), 1.05−0.92 (m, 2H), 0.66 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.7, 195.0, 155.8, 136.7, 134.1, 133.2, 132.6, 130.3, 130.0, 129.9, 128.3, 128.0, 126.5, 120.7, 109.9, 98.3, 83.7, 76.0, 69.8, 55.2, 39.8, 31.5, 19.0, 13.6. HRMS (ESI-TOF): calcd for $C_{29}H_{30}NaO_5^+$ ([M + Na^+]) 481.1985, found 481.1991.

*(3-Butoxy-5-(naphthalen-1-yl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3k**).* Yield 49.7 mg, 99%; green viscous liquid; 88% *ee*, 83/17 dr; $[\alpha]_D^{13} = -116.4$ (c = 0.99 in CH_2Cl_2); HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.47 min, t_2 = 8.82 min, t_3 = 9.89 min, t_4 = 14.88 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13−8.07 (m, 4H), 8.06−8.02 (m, 1H), 7.87−7.77 (m, 3H), 7.54−7.49 (m, 2H), 7.48−7.42 (m, 3H), 7.41−7.36 (m, 2H), 7.35−7.29 (m, 2H), 5.54 (t, J = 8.0 Hz, 1H), 5.47 (dd, J = 6.8, 3.6 Hz, 1H), 3.39−3.32 (m, 1H), 3.27−3.18 (m, 1H), 3.11−3.01 (m, 1H), 2.38−2.29 (m, 1H), 1.26−1.18 (m, 2H), 1.01−0.92 (m, 2H), 0.64 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.8, 195.1, 136.6, 136.6, 134.1, 133.6, 133.5, 132.8, 130.3, 129.8, 128.8, 128.4, 128.1, 128.1, 126.0, 125.7, 125.5, 123.4, 123.3, 98.7, 83.7, 78.2, 69.8, 39.8, 31.4, 19.0, 13.6. HRMS (ESI-TOF): calcd for $C_{32}H_{30}NaO_4^+$ ([M + Na^+]) 501.2037, found 501.2046.

*(3-Butoxy-5-(naphthalen-2-yl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3l**).* Yield 47.1 mg, 98%; green viscous liquid; 90% *ee*, 91/9 dr; $[\alpha]_D^{16} = -89.0$ (c = 0.94 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 8.86 min, t_2 = 10.38 min, t_3 = 11.72 min, t_4 = 15.65 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 7.2 Hz, 2H), 8.06 (d, J = 7.6 Hz, 2H), 7.88 (s, 1H), 7.87−7.78 (m, 2H), 7.72−7.64 (m, 1H), 7.54−7.45 (m, 3H), 7.44−7.35 (m, 3H), 7.30 (t, J = 7.8 Hz, 2H), 5.36 (dd, J = 6.3, 3.0 Hz, 1H), 5.06 (t, J = 7.8 Hz, 1H), 3.51−3.39 (m, 1H), 3.36−3.22 (m, 1H), 2.97−2.82 (m, 1H), 2.38−2.23 (m, 1H), 1.33−1.23 (m, 2H), 1.11−0.98 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.3, 194.8, 138.5, 136.7, 134.0, 133.4, 133.2, 133.1, 132.8, 130.2, 130.0, 128.4, 128.1, 128.0, 127.7, 126.2, 126.1, 125.7, 124.7, 99.0, 83.8, 81.5, 69.9, 40.6, 31.5, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{32}H_{30}NaO_4^+$ ([M + Na^+]) 501.2036, found 501.2042.

*(3-Butoxy-5-(furan-3-yl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3m**).* Yield 36.5 mg, 87%; green viscous liquid; 91% *ee*, 91/9 dr; $[\alpha]_D^{15} = -181.0$ (c = 0.73 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.84 min, t_2 = 8.79 min, t_3 = 10.94 min, t_4 = 12.11 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6 Hz, 2H), 7.98 (d, J = 7.6 Hz, 2H), 7.53−7.48 (m, 1H), 7.48−7.41 (m, 3H), 7.40−7.35 (m, 2H), 7.33−7.28 (m, 2H), 6.60 (s, 1H), 5.26 (dd, J = 6.0, 2.8 Hz, 1H), 4.95 (t, J = 7.6 Hz, 1H), 3.53−3.45 (m, 1H), 3.33−3.25 (m, 1H), 2.77−2.68 (m, 1H), 2.27−2.18 (m, 1H), 1.34−1.25 (m, 2H), 1.11−1.00 (m, 2H), 0.71 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.6, 143.5, 140.3, 136.6, 133.9, 133.3, 132.7, 130.1, 130.0, 128.4, 127.9, 125.8, 109.5, 98.7, 83.9, 74.1, 70.0, 39.1, 31.5, 19.0, 13.7. HRMS (ESI-TOF): calcd for $C_{26}H_{26}NaO_5^+$ ([M + Na^+]) 441.1672, found 441.1673.

*(3-Butoxy-5-(thiophen-3-yl)tetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3n**).* Yield 41.9 mg, 96%; green viscous liquid; 91% *ee*, 91/9 dr; $[\alpha]_D^{15} = -179.0$ (c = 0.61 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.91 min, t_2 = 8.95 min, t_3 = 11.76 min, t_4 = 12.81 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.6 Hz, 2H), 8.00 (d, J = 8.0 Hz, 2H), 7.53−7.41 (m, 2H), 7.41−7.35 (m, 2H), 7.35−7.22 (m, 5H), 5.29 (dd, J = 6.4, 3.2 Hz, 1H), 5.02 (t, J = 7.6 Hz, 1H), 3.51−3.41 (m, 1H), 3.33−3.22 (m, 1H), 2.84−2.71 (m, 1H), 2.33−2.20 (m, 1H), 1.32−1.24 (m, 2H), 1.11−0.97 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.4, 194.7, 142.3, 136.6, 133.9, 133.3, 132.7, 130.2, 130.0, 128.4, 128.0, 126.5, 126.2, 122.5, 98.7, 83.8, 77.6, 70.0, 39.7, 31.5, 19.0, 13.7. HRMS (ESI-TOF): calcd for $C_{26}H_{26}NaO_4S^+$ ([M + Na^+]) 457.1444, found 457.1447.

*(E)-(3-Butoxy-5-styryltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3o**).* Yield 44.7 mg, 98%; green viscous liquid; 90% *ee*, 92/8 dr; $[\alpha]_D^{15} = -105.0$ (c = 0.89 in CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 8.09 min, t_2 = 9.48 min, t_3 = 10.31 min, t_4 = 14.04 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.6 Hz, 2H), 8.00 (d, J = 7.6 Hz, 2H), 7.53−7.48 (m, 1H), 7.47−7.36 (m, 5H), 7.36−7.28 (m, 4H), 7.28−7.21 (m, 1H), 6.59−6.46 (m, 2H), 5.26 (dd, J = 5.8, 2.4 Hz, 1H), 4.67 (dd, J = 13.2, 6.8 Hz, 1H), 3.52−3.42 (m, 1H), 3.31−3.23 (m, 1H), 2.66−2.52 (m, 1H), 2.19−2.07 (m, 1H), 1.34−1.24 (m, 2H), 1.13−1.01 (m, 2H), 0.71 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.5, 136.6, 136.4, 134.0, 133.3, 132.7, 132.1, 130.2, 129.8, 129.5, 128.6, 128.4, 128.0, 127.9, 126.7, 98.8, 84.0, 81.7, 69.9, 38.4, 31.5, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{30}H_{30}NaO_4^+$ ([M + Na^+]) 477.2036, found 477.2036.

*(3-Butoxy-5-phenyltetrahydrofuran-2,2-diyl)bis(p-tolylmethanone) (**3p**).* Yield 48.7 mg, 99%; green viscous liquid; 92% *ee*, 90/10

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dr; $[\alpha]_D^{16} = -114.7$ (c = 0.97 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 10.90 min, t_2 = 11.43 min, t_3 = 15.38 min, t_4 = 16.34 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 7.2 Hz, 2H), 7.41−7.33 (m, 2H), 7.32−7.26 (m, 1H), 7.20−7.16 (m, 2H), 7.12−7.06 (m, 2H), 5.31 (dd, J = 6.4, 3.2 Hz, 1H), 4.86 (t, J = 7.8 Hz, 1H), 3.47−3.37 (m, 1H), 3.31−3.20 (m, 1H), 2.89−2.75 (m, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 2.24−2.15 (m, 1H), 1.31−1.22 (m, 2H), 1.10−0.98 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.6, 194.6, 144.2, 143.4, 141.3, 134.1, 131.5, 130.4, 130.0, 129.08, 128.7, 128.4, 127.8, 126.7, 98.8, 83.6, 81.0, 69.8, 40.7, 31.5, 21.7, 21.7, 19.0, 13.7. HRMS (ESI-TOF): calcd for $C_{30}H_{32}NaO_4^+$ ([M + Na$^+$]) 479.2193, found 479.2206.

(3-Butoxy-5-phenyltetrahydrofuran-2,2-diyl)bis((4-bromophenyl)methanone) (**3q**). Yield 59.7 mg, 99%; green viscous liquid; 88% *ee*, 90/10 dr; $[\alpha]_D^{16} = -108.2$ (c = 1.19 in CH_2Cl_2); HPLC (Daicel chiralcel ID, n-hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.85 min, t_2 = 7.54 min, t_3 = 9.78 min, t_4 = 10.50 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 2H), 7.91−7.82 (m, 2H), 7.60−7.51 (m, 2H), 7.50−7.43 (m, 4H), 7.42−7.36 (m, 2H), 7.35−7.29 (m, 1H), 5.27 (dd, J = 6.4, 3.2 Hz, 1H), 4.86 (t, J = 8.0 Hz, 1H), 3.50−3.41 (m, 1H), 3.33−3.25 (m, 1H), 2.87−2.77 (m, 1H), 2.29−2.17 (m, 1H), 1.34−1.24 (m, 2H), 1.11−1.00 (m, 2H), 0.73 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.5, 193.6, 140.5, 135.1, 132.6, 131.8, 131.7, 131.6, 131.6, 131.4, 128.9, 128.6, 128.3, 128.1, 126.7, 98.6, 83.6, 81.6, 70.0, 40.3, 31.5, 19.1, 13.7. HRMS (ESI-TOF): calcd for $C_{28}H_{26}{}^{78.9183}Br_2NaO_4^+$ ([M + Na$^+$]) 607.0090, found 607.0096, $C_{28}H_{26}{}^{78.9183}Br^{80.9163}BrNaO_4^+$ ([M + Na$^+$]) 609.0070, found 609.0075.

(3-Ethoxy-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ab**). Yield 35.2 mg, 88%; green viscous liquid; 89% *ee*, 86/14 dr; $[\alpha]_D^{28} = -181.6$ (c = 0.83 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 8.18 min, t_2 = 9.20 min, t_3 = 11.73 min, t_4 = 12.10 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10−8.05 (m, 2H), 8.04−8.00 (m, 2H), 7.53−7.47 (m, 3H), 7.46−7.40 (m, 2H), 7.39−7.34 (m, 3H), 7.33−7.27 (m, 3H), 5.36 (dd, J = 6.8, 4.0 Hz, 1H), 4.86 (t, J = 8.0 Hz, 1H), 3.57−3.46 (m, 1H), 3.40−3.30 (m, 1H), 2.90−2.80 (m, 1H), 2.27−2.17 (m, 1H), 0.93 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.7, 194.8, 140.9, 136.8, 134.0, 133.3, 132.7, 130.2, 129.9, 128.5, 128.4, 128.4, 128.0, 127.9, 126.7, 98.7, 83.4, 81.2, 65.8, 40.9, 14.9. HRMS (ESI-TOF): calcd for $C_{26}H_{24}NaO_4^+$ ([M + Na$^+$]) 423.1567, found 423.1572.

(3-Isobutoxy-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ac**). Yield 45.2 mg, 99%; green viscous liquid; 90% *ee*, 91/9 dr; $[\alpha]_D^{16} = -162.9$ (c = 0.50 in CH_2Cl_2); HPLC (Daicel chiralcel ID, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 6.50 min, t_2 = 7.81 min, t_3 = 8.88 min, t_4 = 13.21 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.09 (m, 2H), 8.04−8.00 (m, 2H), 7.54−7.47 (m, 3H), 7.47−7.40 (m, 2H), 7.39−7.35 (m, 3H), 7.33−7.27 (m, 3H), 5.32 (dd, J = 6.4, 3.2 Hz, 1H), 4.89 (t, J = 7.8 Hz, 1H), 3.26−3.19 (m, 1H), 3.09−2.99 (m, 1H), 2.88−2.76 (m, 1H), 2.28−2.17 (m, 1H), 1.61−1.53 (m, 1H), 0.61 (dd, J = 12.8, 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.1, 194.7, 141.1, 136.6, 134.0, 133.3, 132.8, 130.2, 130.0, 128.5, 128.4, 128.0, 128.0, 126.7, 98.9, 83.9, 81.3, 77.0, 40.4, 28.4, 19.2, 19.1. HRMS (ESI-TOF): calcd for $C_{28}H_{28}NaO_4^+$ ([M + Na$^+$]) 451.1880, found 451.1884.

(3-Isopropoxy-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ad**). Yield 38.3 mg, 92%; green viscous liquid; 93% *ee*, 83/17 dr; $[\alpha]_D^{28} = -125.1$ (c = 0.77 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.56 min, t_2 = 8.45 min, t_3 = 10.30 min, t_4 = 11.25 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.07 (m, 2H), 8.06−7.97 (m, 2H), 7.54−7.48 (m, 3H), 7.46−7.40 (m, 2H), 7.40−7.33 (m, 3H), 7.33−7.27 (m, 3H), 5.44 (dd, J = 6.4, 3.6 Hz, 1H), 4.84 (t, J = 8.0 Hz, 1H), 3.65−3.55 (m, 1H), 2.92−2.81 (m, 1H), 2.24−2.16 (m, 1H), 1.03 (d, J = 6.2 Hz, 3H), 0.81 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.7, 193.9, 139.9, 135.7, 133.0, 132.2, 131.6, 129.2, 129.1, 129.0, 127.4, 127.3, 127.1, 126.9, 126.8, 125.7, 124.7, 97.7, 80.2, 80.1, 41.0, 21.4, 20.4. HRMS (ESI-TOF): calcd for $C_{27}H_{26}NaO_4^+$ ([M + Na$^+$]) 437.1723, found 437.1730.

(3-(tert-Butoxy)-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ae**). Yield 40.6 mg, 93%; green viscous liquid; 99% *ee*, 73/27 dr; $[\alpha]_D^{17} = -101.6$ (c = 1.54 in CH_2Cl_2); HPLC (Daicel chiralcel ADH, n-hexane/i-PrOH = 99/1, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 15.34 min, t_2 = 17.65 min, t_3 = 25.06 min, t_4 = 30.01 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.11 (m, 2H), 8.00−7.94 (m, 2H), 7.55−7.48 (m, 3H), 7.47−7.40 (m, 3H), 7.40−7.34 (m, 2H), 7.32−7.29 (m, 2H), 7.19−7.15 (m, 1H), 5.61 (dd, J = 7.20, 4.00 Hz, 1H), 4.75 (t, J = 8.00 Hz, 1H), 2.94−2.83 (m, 1H), 2.24−2.15 (m, 1H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.7, 193.9, 140.0, 135.7, 133.0, 132.2, 131.6, 129.1, 129.1, 127.4, 127.3, 126.9, 126.8, 125.7, 97.8, 80.3, 80.1, 41.0, 31.5, 30.1, 24.5, 22.5, 22.4. HRMS (ESI-TOF): calcd for $C_{28}H_{28}NaO_4^+$ ([M + Na$^+$]) 451.1880, found 451.1885.

(7-Phenylhexahydrofuro[3,4-b][1,4]dioxine-5,5-diyl)bis(phenylmethanone) (**3af**). Yield 37.2 mg, 90%; a white amorphous solid, mp 154−156 °C; 90% *ee*, 89/11 dr; $[\alpha]_D^{28} = -54.7$ (c = 0.74 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 26.05 min, t_2 = 28.01 min, t_3 = 46.86 min, t_4 = 50.86 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.2 Hz, 2H), 8.04−7.98 (m, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.56−7.51 (m, 1H), 7.46−7.37 (m, 5H), 7.35−7.26 (m, 3H), 5.62 (d, J = 4.8 Hz, 1H), 5.02 (d, J = 5.6 Hz, 1H), 4.54 (m, 1H), 3.59−3.50 (m, 1H), 3.48−3.40 (m, 1H), 3.35 (t, J = 5.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 193.8, 136.1, 135.9, 134.0, 133.5, 133.3, 130.3, 129.9, 128.5, 128.5, 128.4, 128.3, 128.1, 127.9, 127.2, 125.6, 95.9, 82.3, 78.2, 75.0, 62.4, 62.0. HRMS (ESI-TOF): calcd for $C_{26}H_{22}NaO_5^+$ ([M + Na$^+$]) 437.1359, found 437.1367.

(3-(Cyclohexyloxy)-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ag**). Yield 44.2 mg, 97%; green viscous liquid; 96% *ee*, 90/10 dr; $[\alpha]_D^{22} = -74.5$ (c = 0.88 in CH_2Cl_2); HPLC (Daicel chiralcel ID, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.36 min, t_2 = 8.51 min, t_3 = 11.04 min, t_4 = 14.26 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.09 (m, 2H), 8.07−7.97 (m, 2H), 7.54−7.48 (m, 3H), 7.46−7.40 (m, 2H), 7.39−7.33 (m, 3H), 7.32−7.26 (m, 3H), 5.47 (dd, J = 6.6, 3.2 Hz, 1H), 4.85 (t, J = 8.0 Hz, 1H), 3.36−3.28 (m, 1H), 2.91−2.79 (m, 1H), 2.25−2.18 (m, 1H), 1.74−1.71 (m, 1H), 1.53−1.41 (m, 3H), 1.29−1.16 (m, 4H), 1.11−1.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.8, 195.0, 141.1, 136.8, 134.1, 133.3, 132.6, 130.2, 130.1, 128.4, 128.4, 128.4, 127.9, 127.9, 126.8, 98.9, 81.3, 81.2, 77.3, 42.0, 32.5, 31.2, 25.6, 23.5, 23.4. HRMS (ESI-TOF): calcd for $C_{30}H_{30}NaO_4^+$ ([M + Na$^+$]) 477.2036, found 477.2042.

(3-(Allyloxy)-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ah**). Yield 40.0 mg, 97%; green viscous liquid; 89% *ee*, 86/14 dr; $[\alpha]_D^{22} = -132.0$ (c = 0.80 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 9.02 min, t_2 = 10.71 min, t_3 = 13.81 min, t_4 = 15.34 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13−8.08 (m, 2H), 8.05−7.98 (m, 2H), 7.54−7.47 (m, 3H), 7.47−7.43 (m, 1H), 7.43−7.41 (m, 1H), 7.41−7.36 (m, 3H), 7.33−7.27 (m, 3H), 5.68−5.57 (m, 1H), 5.43 (dd, J = 6.8, 4.0 Hz, 1H), 5.09−4.98 (m, 2H), 4.86 (t, J = 8.0 Hz, 1H), 4.03−3.93 (m, 1H), 3.92−3.80 (m, 1H), 2.92−2.79 (m, 1H), 2.30−2.19 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 194.7, 140.7, 136.6, 133.9, 133.8, 133.4, 132.8, 130.2, 130.0, 128.5, 128.4, 128.1, 128.0, 126.7, 117.0, 98.6, 83.0, 81.1, 71.0, 40.9. HRMS (ESI-TOF): $C_{27}H_{24}NaO_4^+$ ([M + Na$^+$]) 435.1567, found 435.1579.

(3-(Ethylthio)-5-phenyltetrahydrofuran-2,2-diyl)bis(phenylmethanone) (**3ai**). Yield 41.7 mg, 99%; green viscous liquid; 86% *ee*, 80/20 dr; $[\alpha]_D^{28} = -52.2$ (c = 0.90 in CH_2Cl_2); HPLC (Daicel chiralcel IE, n-hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm) retention time: t_1 = 7.05 min, t_2 = 7.97 min, t_3 = 9.25 min, t_4 = 15.37 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−8.01 (m, 2H), 7.98−7.91 (m, 2H), 7.49−7.43 (m, 1H), 7.38−7.31 (m, 5H), 7.30−7.20 (m, 5H), 4.80−4.69 (m, 2H), 2.96−2.86 (m, 1H), 2.60−2.50 (m, 1H), 2.44−2.33 (m, 1H), 2.18−2.08 (m, 1H), 1.13 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.1, 194.0, 138.2, 135.5, 132.8, 132.1, 131.9, 129.4, 129.2, 128.6, 127.5, 127.4, 127.3, 127.1, 127.0, 125.2, 124.7,

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J. Org. Chem. 2016, 81, 1237−1243

97.2, 80.1, 45.4, 41.7, 26.2, 13.3. HRMS (ESI-TOF): calcd for $C_{26}H_{24}NaO_3S^+$ ([M + Na^+]) 439.1338, found 439.1349.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02524.

Optimization details, X-ray data for compound **3af**, HPLC data, and ^1H and ^{13}C NMR spectra (PDF)
Crystallographic data for **3af** (CIF)

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Notes

The authors declare no competing financial interest.

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