JOC The Journal of Organic Chemistry

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Direct Asymmetric Vinylogous Mannich Reaction of 3,4-Dihalofuran-2(5*H*)-one with Aldimine Catalyzed by Quinine

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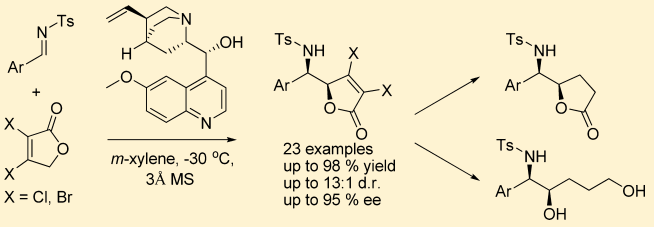
Supporting Information

ABSTRACT: The direct asymmetric vinylogous Mannich reaction of 3,4-dihalofuran-2(5*H*)-one with aldimine catalyzed by quinine was first reported, and γ-butenolides have been obtained in excellent yield (up to 98%) and enantioselectivities (up to 95% ee). The synthetic applications of this protocol are demonstrated in the preparations of γ-substituted amino butyrolactones and vicinal amino alcohols.



Mannich reaction is an important and effective carbon−carbon bond formation reaction for β-amino functional moieties.[1] Particularly, the vinylogous Mannich reaction, a vinyl insertion Mannich reaction, generates a new C−C bond and leads to the formation of δ-amino α,β-unsaturated carbonyl compounds, which are widely found in natural compound skeletons,[2] the donors of which mainly include acyclic silyl dienolate,[3] 2-silyloxyfurans,[4] dicyanoalkylidenes,[5] and γ-butyrolactams.[6] Typically, the utilization of 2-silyloxyfuran as the nucleophile for vinylogous Mannich reaction catalyzed by transition metal catalysts[4a−h] and chiral phosphoric acids[4i,j] has been well documented. However, the direct asymmetric vinylogous Mannich reaction of 2-(5*H*)furanone derivatives has not drawn enough attention until Shibasaki's group reported the first direct asymmetric Mannich-type reactions of γ-butenolides catalyzed by a chiral lanthanumpyridine bisoxazolinecomplex.[7] To the best of our knowledge, the small molecular catalytic direct asymmetric Mannich reaction of furanones has not been reported, partially because of the relative lower activities of furanones. In 2010, Terada[8] reported the first asymmetric direct vinylogous aldol reaction of 3,4-dihalofuran-2(5*H*)-one with aldehydes catalyzed by chiral guanidines, in which 3,4-dihalofuran-2(5*H*)-one showed extremely high reactivity. On the basis of those backgrounds, we envisioned that the asymmetric direct vinylogous Mannich reaction of 3,4-dihalofuran-2(5*H*)-one with imines may be realized by an organocatalyst and afford the chiral 3,4-dihalofuran-2(5*H*)-one motifs with multifunctional groups and can be used as versatile building blocks after successive transformations.[9]

Cinchona alkaloids are widely used chiral organic catalysts for asymmetric synthesis.[10] In our previous work,[11] we have successfully applied their derivatives in some asymmetric catalyses. Inspired by those achievements, we recognized that the tertiary amine group would activate the 3,4-dihalofuran-2(5*H*)-one and the hydroxyl group would activate the imine through hydrogen bondings. Thus the synergistic interactions would ensure high stereoselectivity in this transformation, affording the corresponding optically active products via a postulated transition state (TS) as shown in Figure 1. As a part

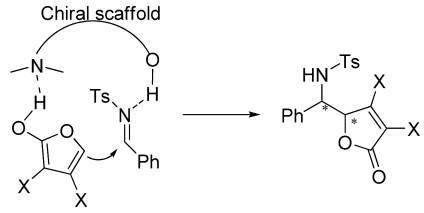


Figure 1. Proposed transition state.

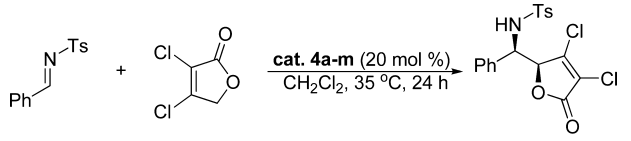
of our continuing interests in asymmetric syntheses,[12] herein, we wish to report the first asymmetric direct vinylogous Mannich reaction of 3,4-dihalofuran-2(5*H*)-one with aldimine catalyzed by quinine.

To devise a model reaction, imine **1a** and 3,4-dichlorofuran-2(5*H*)-one **2a** were selected as reactants to screen the asymmetric reaction conditions, and the results were summarized in Table 1. The reaction was performed smoothly in CH_2Cl_2 with 20 mol % catalyst **4a** at 35 °C and afforded excellent yield and moderate enantioselectivitiy (91% yield, 41% ee; Table 1, entry 1). While other cinchona alkaloids **4b**−**4d** gave relative lower yields and enantioselectivities (76−85% yield, 6−24% ee, Table 1, entries 2−4). To further improve the results, a series of bifunctional tertiary amine-thiourea catalysts **4e**−**m** were also evaluated, and the products were obtained in poor ee values (6−23% ee, Table 1, entries 5−13). On the basis

Received: June 20, 2012
Published: August 17, 2012

dx.doi.org/10.1021/jo301115t | *J. Org. Chem.* 2012, 77, 8338−8343

Table 1. Screenings of Catalyst for the Vinylogous Mannich Reaction of 2a with 1a[a]



1a 2a 3a

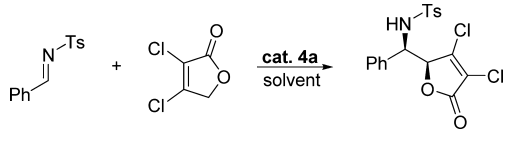
entry	catalyst	yield[b] (%)	dr[c] (%)	ee[d] (%)
1	**4a**	91	1.2:1	41/40
2	**4b**	85	1.2:1	−24/−27
3	**4c**	85	1.5:1	−6/−10
4	**4d**	76	1.2:1	19/24
5	**4e**	77	1.3:1	−9/−2
6	**4f**	71	1.2:1	7/−4
7	**4g**	61	1.2:1	8/−8
8	**4h**	74	1.3:1	−23/−13
9	**4i**	76	1.7:1	−23/−10
10	**4j**	66	1.9:1	−12/−8
11	**4k**	32	2.9:1	−13/−20
12	**4l**	73	1.3:1	−13/−2
13	**4m**	68	1.2:1	−6/−9

[a]Reactions were performed with 0.1 mmol of **1a**, 0.2 mmol of **2a** in 1 mL of dichloromethane at 35 °C for 24 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Enantiomeric excess determined by chiral HPLC.

of the screenings of catalysts (Scheme 1), catalyst **4a**, with 91% yield, 41% ee and a diastereomeric ratio (dr) of 1.2:1, was selected for further optimization (Table 1, entry 1).

With 20 mol % **4a** as the catalyst, solvents, temperature and additives were screened, and the results were listed in Table 2. Solvents dramatically affected the ee values (Table 2, entries 1−7). Aprotic solvents, such as toluene, mesitylene, *m*-xylene and tetrahydrofuran resulted in higher enantioselectivities than protonic solvent (Table 2, entries 1−6 vs entry 7). Relative strong polar solvents led to lower ee values (Table 2, entries 4−7). In the presence of 3 Å MS, *m*-xylene afforded 63% ee (Table 2, entry 10). Lowering the temperature to −30 °C resulted in an increase of enantioselectivity (77% ee, Table 2, entry 14). When 10 mol % of **4a** used, the ee value slightly raised to 81% in 95% yield (Table 2, entry 16). The concentration of the substrates was also screened, and **3a** was obtained in 85% ee and 85% yield in 2 mL of *m*-xylene (Table 2, entry 19). On the basis of the above results, 0.1 mmol **1a** and 0.2 mmol **2a** in 2 mL of *m*-xylene with 10 mol % catalyst **4a** at −30 °C were established as optimal reaction conditions.

Table 2. Screening of Optimal Reaction Conditions for the Vinylogous Mannich Reaction of 1a with 2a[a]



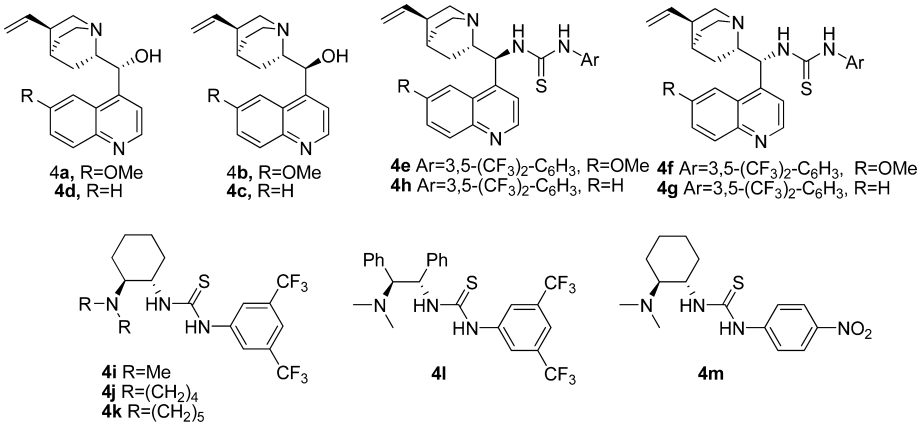
1a 2a 3a

entry	solvent	*t* (h)	*T* (°C)	yield[b] (%)	dr[c] (%)	ee[d] (%)
1	toluene	24	35	71	1.2:1	47
2	mesitylene	24	35	75	1:1	44
3	*m*-xylene	24	35	67	1.2:1	44
4	1,2-dichloroethane	24	35	71	1.3:1	33
5	tetrahydrofuran	24	35	76	1.4:1	27
6	acetonitrile	24	35	73	2.2:1	11
7	methanol	24	35	91	3:1	2
8[e]	toluene	24	35	99	1.2:1	53
9[e]	mesitylene	24	35	82	1.8:1	54
10[e]	*m*-xylene	24	35	72	1.3:1	63
11[e]	*m*-xylene	69	0	99	2.2:1	64
12[e]	*m*-xylene	52	−10	99	2.3:1	68
13[e]	*m*-xylene	71	−20	98	2.4:1	74
14[e]	*m*-xylene	76	−30	99	2.0:1	77
15[e,f]	*m*-xylene	71	−30	94	1.9:1	82
16[e,g]	*m*-xylene	71	−30	95	3.2:1	81
17[e,h]	*m*-xylene	71	−30	71	4.9:1	84
18[e,g,i]	*m*-xylene	144	−30	88	6.0:1	84
19[e,g,j]	*m*-xylene	168	−30	85	6.5:1	85

[a]Reactions were performed with 0.1 mmol of **1a**, 0.2 mmol of **2a**, 20 mol % **4a** in 1 mL of solvent. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Enantiomeric excess of the major diastereoisomer determined by chiral HPLC. [e]30 mg of 3 Å MS was added. [f]With 15 mol % **4a**. [g]With 10 mol % **4a**. [h]With 5 mol % **4a**. [i]The reaction was carried out in 1.5 mL of *m*-xylene. [j]The reaction was carried out in 2.0 mL of *m*-xylene.

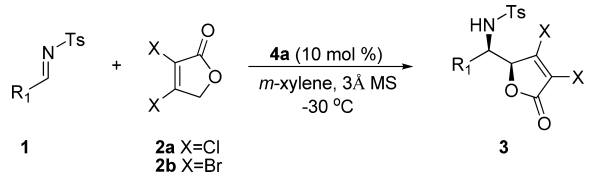
Under the optimized reaction conditions, the substrate scope of the reaction was further explored to test the generality of this protocol (Table 3). A series of aldimines derived from aromatic aldehydes bearing electron-withdrawing and electron-donating

Scheme 1. Catalysts 4a−m Investigated



dx.doi.org/10.1021/jo301115t | J. Org. Chem. 2012, 77, 8338−8343

Table 3. Direct Catalytic Asymmetric Vinylogous Mannich Reactions of Imines 1 and γ-Dihalobutenolides 2[a]



1 **2a** X=Cl **2b** X=Br **3**

entry	R_1	1	2	3	t (days)	yield[b] (%)	dr	ee[e] (%)
1	Ph	**1a**	**2a**	**3aa**	7	85	6.5:1[c]	85
2	4-MeO-Ph	**1b**	**2a**	**3ba**	7	54	4:1[c]	95
3	4-Me-Ph	**1c**	**2a**	**3ca**	7	89	4:1[d]	80
4	4-Br-Ph	**1d**	**2a**	**3da**	7	66	6:1[d]	86
5	4-Cl-Ph	**1e**	**2a**	**3ea**	7	81	7:1[d]	84
6	4-F-Ph	**1f**	**2a**	**3fa**	11	60	13:1[d]	86
7	4-NO_2-Ph	**1g**	**2a**	**3ga**	7	37	7:1[c]	88
8	2-F-Ph	**1h**	**2a**	**3ha**	10	86	5:1[d]	90
9	2-Cl-Ph	**1i**	**2a**	**3ia**	8	86	8:1[d]	91
10	2-Br-Ph	**1j**	**2a**	**3ja**	7	98	12:1[d]	92
11	2-naphthyl	**1k**	**2a**	**3ka**	7	95	10:1[d]	84
12	3-Me-Ph	**1l**	**2a**	**3la**	7	95	4:1[d]	85
13	3-Cl-Ph	**1m**	**2a**	**3ma**	7	nd		
14	Ph	**1a**	**2b**	**3ab**	11	80	3:1[d]	89
15	4-MeO-Ph	**1b**	**2b**	**3bb**	13	44	6:1[c]	90
16	4-Me-Ph	**1c**	**2b**	**3cb**	11	55	5:1[d]	86
17	4-Br-Ph	**1d**	**2b**	**3db**	10	41	3:1[d]	88
18	4-Cl-Ph	**1e**	**2b**	**3eb**	10	41	7:1[d]	88
19	4-F-Ph	**1f**	**2b**	**3fb**	10	51	4:1[d]	94
20	2-F-Ph	**1g**	**2b**	**3gb**	8	90	4:1[d]	91
21	2-Cl-Ph	**1h**	**2b**	**3hb**	7	90	4:1[d]	94
22	2-Br-Ph	**1i**	**2b**	**3ib**	8	94	10:1[d]	93
23	2-naphthyl	**1j**	**2b**	**3jb**	11	95	11:1[d]	88
24	3-Me-Ph	**1k**	**2b**	**3kb**	11	76	4:1[d]	84

[a]Reactions performed with 0.1 mmol of **1**, 0.2 mmol of **2**, **4a** (10 mol %), 3 Å MS (30 mg) in 2.0 mL of *m*-xylene at −30 °C for 7−13 days. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Determined by isolated yield of two diastereoisomers. [e]Enantiomeric excess of the major diastereoisomer determined by chiral HPLC.

groups were selected and gave the adducts in moderate to high yields (37−98%), moderate diastereoselectivities (3:1−13:1), and excellent ee (up to 95% ee). Aldimines with ortho-substitutents afforded slightly higher enantioselectivities than their para-substituted counterparts (Table 3, entries 4−6 vs 8−10). When meta-chloride substituted aldimine used, no product was detected (Table 3, entry 13). 4-OMe aromatic aldimine gave moderate yield and the highest enantioselectivity (54% yield, 95% ee; Table 3, entry 2). The optimized protocol was also expanded to 3,4-dibromofuran-2(5*H*)-one **2b**, and moderate to good yields and excellent enantioselectivities were obtained (41−95% yield, 84−94% ee, Table 3, entries 14−24).

Vinylogous Mannich products **3**, with multiple functional groups and potential chiral centers, may be easily transformed to γ-butyrolactones,[13] which were the core structure of sapinofuranones.[14] Importantly, γ-butyrolactone derivatives could be readily converted to vicinal amino alcohols,[15] important pharmaceutical skeletons widely existing in protease inhibitors such as ritonavir[16a] and swainsonine.[16b] Typically as shown in Scheme 2, reduction and dehalogation of **3ja** afforded the chiral γ-butyrolactone **5**. After further reduction of **5** with $LiBH_4$ at room temperature, vicinal amino alcohol **6** was obtained in almost unchanged ee value (Scheme 2). The absolute configuration was determined by an X-ray analysis of the single crystal of **6**, which was assigned as (C7R, C8R) (see the Supporting Information).

In summary, we have developed a direct vinylogous Mannich reaction of aldimines with 3,4-dihalofuran-2(5*H*)-one catalyzed by quinine. A series of γ-butenolides derivatives were obtained in good yields (up to 98% yield) and enantioselectivities (up to 95% ee), which were easily transformed to some chiral pharmaceutical intermediates γ-butyrolactones and vicinal amino alcohols.

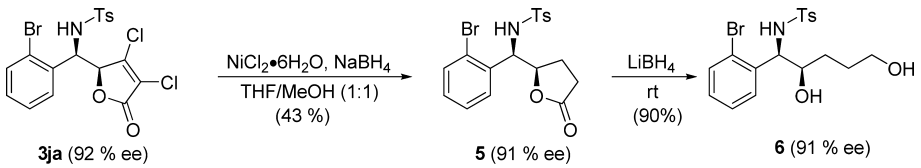
EXPERIMENTAL SECTION

General Procedure for Vinylogous Mannich Reaction. Catalyst **4a** (10 mol %), 3 Å MS (30 mg) and imine **1** (0.1 mmol) were dissolved in 2 mL of *m*-xylene at −30 °C for 0.5 h. Substrate **2** (0.2 mmol) was added to the solution and stirred for 7−13 days. The reaction was monitored by TLC analysis. The reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate) to furnish the corresponding products **3**.

***N*-((*R*)-((*S*)-3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)-(phenyl)methyl)-4-methylbenzenesulfonamide (3aa).** White solid: mp 148−149 °C; $[\alpha]_D^{20}$= −85 (*c* 0.1, CH_2Cl_2), yield 85%; 6.5:1 dr, enantiomeric excess 85%, determined by HPLC (Chiralcel AY-H column, hexane/ethanol/TFA = 55/45/0.1%, flow rate 0.7 mL/min, UV detection at 220 nm), t_R (major) = 14.1 min, t_R (minor) = 24.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.24−7.15 (m, 5H), 7.10 (d, *J* = 8.0 Hz, 2H), 5.54 (d, *J* = 10.0 Hz, 1H), 5.09 (d, *J* = 1.6 Hz, 1H), 4.97 (dd, *J* = 10.0 Hz, 1.5 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 149.8, 143.6, 136.9, 135.9, 129.5, 129.4, 128.9, 128.6, 126.9, 122.8, 84.4, 56.6, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{15}Cl_2NNaO_4S$ $[M + Na]^+$ 433.9985, found 433.9991; IR (KBr) ν_{max}/cm^{-1} 3295, 2923, 1769, 1627, 1337, 1239, 1162, 701.

***N*-((*R*)-((*S*)-3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (3ba).** White solid: $[\alpha]_D^{20}$= −76 (*c* 0.1, CH_2Cl_2), yield 54%; 4:1 dr, enantiomeric excess 95%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 26.1 min, t_R (major) = 39.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.11−7.07 (m, 4H), 6.73 (d, *J* = 8.7 Hz, 2H), 5.59 (d, *J* = 9.8 Hz, 1H), 5.08 (d, *J* = 1.7 Hz, 1H), 4.91 (dd, *J* = 9.7 Hz, 1.3 Hz, 1H), 3.75 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 160.7, 150.8,

Scheme 2. Preparation of Chiral γ-Substituted Butyrolactone 5 and Vicinal Amino Alcohol 6



3ja (92 % ee) **5** (91 % ee) **6** (91 % ee)

dx.doi.org/10.1021/jo301115t | J. Org. Chem. 2012, 77, 8338−8343

149.6, 144.5, 138.0, 130.5, 129.3, 128.0, 124.3, 115.2, 85.5, 57.2, 56.2, 22.4; HRMS (EI) Calcd. for $C_{19}H_{17}NO_5SCl_2$ $[M]^+$ 441.0205, found 441.0247; IR (KBr) ν_{max}/cm^{-1} 3296, 2936, 1778, 1629, 1334, 1257, 1161, 734.

***N*-((*R*)-((*S*)-3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(*p*-tolyl)methyl)-4-methylbenzenesulfonamide (3ca).** White solid: mp 163−164 °C; $[\alpha]_D^{20}$= −160 (*c* 0.2, CH_2Cl_2), yield 89%; 4:1 dr, enantiomeric excess 80%, determined by HPLC (Chiralcel AY-H column, hexane/ethanol/TFA = 55/45/0.1%, flow rate 0.7 mL/min, UV detection at 220 nm), t_R (minor) = 20.5 min, t_R (major) = 14.7 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.06−7.00 (m, 4H), 5.47 (d, *J* = 9.7 Hz, 1H), 5.08 (d, *J* = 1.7 Hz, 1H), 4.92 (d, *J* = 10.0 Hz), 2.34 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 149.8, 143.5, 138.6, 136.9, 132.7, 129.5, 129.4, 127.0, 126.8, 122.7, 84.4, 56.4, 21.4; HRMS (EI) Calcd. for $C_{19}H_{17}NO_4SCl_2$ $[M]^+$ 425.0255, found 425.0246; IR (KBr) ν_{max}/cm^{-1} 3316, 2967, 1770, 1622, 1324, 1247, 1160, 706.

***N*-((*R*)-(4-Bromophenyl)((*S*)-3.4-dichloro-5-oxo-2,5-dihydrofuran-2-yl)methyl)-4-methylbenzenesulfonamide (3da).** White solid: mp 186−187 °C; $[\alpha]_D^{20}$= −98 (*c* 0.1, CH_2Cl_2), yield 66%; 6:1 dr, enantiomeric excess 86%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 11.0 min, t_R (major) = 21.2 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.12−7.03 (m, 4H), 6.82 (d, *J* = 10.3 Hz, 1H), 5.04 (d, *J* = 1.1 Hz, 1H), 4.94 (d, *J* = 10.3 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 149.7, 143.8, 136.7, 134.6, 131.9, 129.7, 129.5, 128.7, 126.9, 122.7, 84.3, 56.1, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{18}BrCl_2N_2O_4S$ $[M + NH_4]^+$ 506.9542, found 506.9539; IR (KBr) ν_{max}/cm^{-1} 3316, 2968, 1770, 1621, 1326, 1247, 1163, 722.

***N*-((*R*)-(4-Chlorophenyl)((*S*)-3,4-dichloro-5-oxo-2,5-dihydrofuran-2-yl)methyl)-4-methylbenzenesulfonamide (3ea).** White solid: mp 182−183 °C; $[\alpha]_D^{20}$= −105 (*c* 0.1, CH_2Cl_2), yield 81%; 7:1 dr, enantiomeric excess 84%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 80/20, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 10.3 min, t_R (major) = 19.8 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.2 Hz, 2H), 7.18−7.07 (m, 6H), 5.87 (d, *J* = 10.2 Hz, 1H), 5.04 (d, *J* = 1.4 Hz, 1H) 4.95 (d, *J* = 10.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 149.6, 143.7, 136.8, 134.6, 134.1, 129.4, 128.9, 128.4, 126.8, 122.8, 84.3, 56.0, 21.3; HRMS (EI) Calcd. for $C_{18}H_{14}NO_4SCl_3$ $[M]^+$ 444.9709, found 444.9721; IR (KBr) ν_{max}/cm^{-1} 3265, 2924, 1760, 1628, 1340, 1243, 1159, 742.

***N*-((*R*)-((*S*)-3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(4-fluorophenyl)methyl)-4-methylbenzenesulfonamide (3fa).** White solid: mp 138−139 °C; $[\alpha]_D^{20}$= −84 (*c* 0.1, CH_2Cl_2), yield 60%; 13:1 dr, enantiomeric excess 86%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 85/15, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 13.0 min, t_R (major) = 23.2 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.2 Hz, 2H), 7.19−7.14(m, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.91−6.86 (m, 2H), 5.87 (d, *J* = 10.2 Hz, 1H), 5.05 (d, *J* = 1.6 Hz, 1H), 4.97 (d, *J* = 10.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 160.9 (J_{C-F} = 247.0 Hz), 149.8, 136.9, 131.7, 129.4, 129.0 (J_{C-F} = 8.3 Hz), 128.8, 126.9, 122.7, 115.9 (J_{C-F} = 21.6 Hz), 84.5, 56.0, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{14}Cl_2FNNaO_4S$ $[M + Na]^+$ 451.9897, found 451.9902; IR (KBr) ν_{max}/cm^{-1} 3298, 2959, 1766, 1631, 1338, 1230, 1158, 686.

***N*-((*R*)-((*S*)-3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(4-nitrophenyl)methyl)-4-methylbenzenesulfonamide (3ga).** Light yellow solid: yield 37%; 7:1 dr, enantiomeric excess 88%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 80/20, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 25.4 min, t_R (major) = 58.9 min; ^{1}H NMR (300 MHz, DMSO) δ 8.95 (d, *J* = 10.1 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.47 (m, 2H), 7.13 (m, 1H), 5.60 (d, *J* = 2.4 Hz, 1H), 5.19 (dd, *J* = 10.2 Hz, 2.1 Hz, 1H), 5.09 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 164.4, 147.0, 143.7, 142.6, 141.4, 137.7, 129.2, 126.3, 125.5, 122.8, 84.0, 57.1, 20.8; HRMS (ESI) Calcd. for $C_{18}H_{14}Cl_2N_2NaO_6S$ $[M + Na]^+$ 478.9842, found 478.9837; IR (KBr) ν_{max}/cm^{-1} 3404, 2859, 1789, 1635, 1336, 1233, 1159, 756.

***N*-((3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(2-fluorophenyl)methyl)-4-methylbenzenesulfonamide (3ha).** White solid: mp 150−151 °C; $[\alpha]_D^{20}$= −96 (*c* 0.1, CH_2Cl_2), yield 86%; 5:1 dr, enantiomeric excess 90%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 85/15, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 13.2 min, t_R (major) = 14.1 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 2H), 7.22−7.18 (m, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.98−6.90 (m, 2H), 5.96 (brs, 1H), 5.38 (d, *J* = 10.7 Hz, 1H), 5.04 (d, *J* = 1.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 157.6 (J_{C-F} = 244.5 Hz), 149.8, 143.6, 136.7, 130.3 (J_{C-F} = 8.3 Hz), 129.4, 128.3, 126.9, 126.4, 124.7, 122.9, 115.6 (J_{C-F} = 21.5 Hz), 84.0, 50.3, 21.3; HRMS (ESI) Calcd. for $C_{18}H_{14}Cl_2FNNaO_4S$ $[M + Na]^+$ 451.9897, found 451.9897; IR (KBr) ν_{max}/cm^{-1} 3295, 2925, 1782, 1631, 1343, 1242, 1165, 740.

***N*-((2-Chlorophenyl)(3,4-dichloro-5-oxo-2,5-dihydrofuran-2-yl)methyl)-4-methylbenzenesulfonamide (3ia).** White solid: mp 170−171 °C; $[\alpha]_D^{20}$= −96 (*c* 0.1, CH_2Cl_2), yield 86%; 8:1 dr, enantiomeric excess 91%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 17.6 min, t_R (major) = 20.6 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.29−7.28 (m, 1H), 7.21−7.15 (m, 2H), 7.10−7.02 (m, 3H), 6.22 (d, *J* = 10.9 Hz, 1H), 5.62 (d, *J* = 11.0 Hz, 1H), 5.06 (d, *J* = 1.5 Hz, 1H), 2.28 (s, 3H); ^{13} C NMR (75 MHz, $CDCl_3$) δ 165.4, 150.1, 143.5, 136.7, 133.1, 131.9, 129.5, 129.4, 129.3, 128.3, 127.4, 126.8, 122.5, 83.5, 52.8, 21.3; HRMS (EI) Calcd. for $C_{18}H_{14}NO_4SCl_3$ $[M]^+$ 444.9709, found 444.9697; IR (KBr) ν_{max}/cm^{-1} 3283, 2948, 1785, 1630, 1243, 1163, 736, 709.

***N*-((2-Bromophenyl)(3,4-dichloro-5-oxo-dihydrofuran-2-yl)-methyl)-4-methylbenzenesulfonamide (3ja).** White solid: mp 178−179 °C; $[\alpha]_D^{20}$= −38 (*c* 0.1, CH_2Cl_2), yield 98%; 12:1 dr, enantiomeric excess 92%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 10.5 min, t_R (major) = 14.7 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.46−7.43 (m, 1H), 7.20−7.18 (m, 1H), 7.10−7.00 (m, 4H), 6.35 (d, *J* = 10.9 Hz, 1H), 5.84 (d, *J* = 11.0 Hz, 1H), 5.07 (d, *J* = 1.2 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 150.3, 143.3, 136.6, 134.4, 132.6, 129.7, 129.3, 128.6, 128.0, 126.8, 126.4, 122.2, 83.5, 55.2, 21.3; HRMS (EI) Calcd. for $C_{18}H_{14}NO_4SCl_2Br$ $[M]^+$ 488.9204, found 488.9219; IR (KBr) ν_{max}/cm^{-1} 3286, 2946, 1785, 1630, 1348, 1243, 1163, 658.

***N*-((3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(naphthalene-2-yl)methyl)-4-methylbenzenesulfonamide (3ka).** White solid: mp 168−169 °C; $[\alpha]_D^{20}$= −12 (*c* 0.1, CH_2Cl_2), yield 95%; 10:1 dr, enantiomeric excess 84%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 22.6 min, t_R (major) = 58.2 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.60−7.50 (m, 2H), 7.42−7.34 (m, 3H), 7.28−7.23 (m, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.43 (d, *J* = 10.5 Hz, 1H), 5.98 (d, *J* = 10.7 Hz, 1H), 5.14 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 150.0, 143.2, 136.8, 133.6, 130.9, 129.5, 129.3, 129.1, 128.9, 127.1, 126.7, 125.9, 125.3, 125.0, 122.6, 121.0, 84.0, 51.6, 21.2; HRMS (EI) Calcd. for $C_{22}H_{17}NO_4SCl_2$ $[M]^+$ 461.0255, found 461.0256; IR (KBr) ν_{max}/cm^{-1} 3298, 2920, 1785, 1634, 1339, 1241, 1163, 735.

***N*-((3,4-Dichloro-5-oxo-2,5-dihydrofuran-2-yl)(*m*-tolyl)-methyl)-4-methylbenzenesulfonamide (3la).** White solid: mp 75−76 °C; $[\alpha]_D^{20}$= −95 (*c* 0.1, CH_2Cl_2), yield 95%; 4:1 dr, enantiomeric excess 85%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 95/5, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 16.5 min, t_R (major) = 25.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.15−7.10 (m, 3H), 7.09−6.99 (m, 2H), 6.88 (s, 1H), 5.50 (brs, 1H), 5.09 (d, *J* = 1.4 Hz, 1H), 4.93 (dd, *J* = 10.0 Hz, 1.1 Hz, 1H), 2.35 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 149.9, 143.4, 138.6, 136.9, 135.6, 129.4, 129.3, 128.8, 127.6, 126.9, 123.9, 122.7, 84.5, 56.5, 21.3, 21.1; HRMS (EI) Calcd. for $C_{19}H_{17}NO_4SCl_2$ $[M]^+$ 425.0255, found 425.0276; IR (KBr) ν_{max}/cm^{-1} 3281, 2923, 1785, 1631, 1339, 1234, 1162, 713.

dx.doi.org/10.1021/jo301115t | *J. Org. Chem.* 2012, 77, 8338−8343

***N*-((3,4-Dibromo-5-oxo-2,5-dihydrofuran-2-yl)(phenyl)-methyl)-4-methylbenzenesulfonamide (3ab).** White solid: mp 116−117 °C; $[\alpha]_D^{20}$= −86 (*c* 0.1, CH_2Cl_2), yield 80%; 3:1 dr, enantiomeric excess 89%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 85/15, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 14.9 min, t_R (major) = 19.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.24−7.11 (m, 5H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.36 (d, *J* = 10.1 Hz, 1H), 5.09 (d, *J* = 1.6 Hz, 1H), 5.02 (dd, *J* = 10.1 Hz, 1.5 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 145.4, 143.5, 137.1, 136.0, 130.8, 129.4, 128.9, 128.6, 127.0, 116.5, 87.0, 56.9, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{15}Br_2NNaO_4S$ $[M + Na]^+$ 521.8981, found 521.8993; IR (KBr) ν_{max}/cm^{-1} 3293, 2919, 1758, 1605, 1336, 1214, 1161, 702.

***N*-((3,4-Dibromo-5-oxo-2,5-dihydrofuran-2-yl)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (3bb).** White solid: yield 44%; 6:1 dr, enantiomeric excess 90%, determined by HPLC (Chiralcel AY-H column, hexane/ethanol/TFA= 55/45/0.1%, flow rate 0.6 mL/min, UV detection at 220 nm), t_R (minor) = 22.9 min, t_R (major) = 47.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55−7.50 (m, 4H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 5.09 (d, *J* = 1.7 Hz, 1H), 4.97−4.91 (m, 2H), 3.72 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 145.5, 143.5, 137.1, 129.5, 128.3, 126.9, 123.4, 116.6, 114.2, 87.1, 58.1, 55.3, 21.4; HRMS (ESI) Calcd. for $C_{19}H_{17}Br_2NNaO_5S$ $[M + Na]^+$ 551.9086, found 551.9090; IR (KBr) ν_{max}/cm^{-1} 3294, 2935, 1755, 1607, 1334, 1257, 1159, 733.

***N*-((*R*)-((*S*)-3,4-Dibromo-5-oxo-2,5-dihydrofuran-2-yl)(*p*-tolyl)methyl)-4-methylbenzenesulfonamide (3cb).** White solid: mp 166−167 °C; $[\alpha]_D^{20}$= −92 (*c* 0.1, CH_2Cl_2), yield 55%; 5:1 dr, enantiomeric excess 86%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 15.4 min, t_R (major) = 24.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.09−6.99 (m, 6H), 5.60 (d, *J* = 10.0 Hz, 1H), 5.06 (d, *J* = 1.5 Hz, 1H), 4.97 (d, *J* = 10.1 Hz, 1H), 2.33 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 145.5, 143.3, 138.4, 137.0, 132.9, 129.4, 129.3, 127.0, 126.8, 116.3, 87.2, 56.7, 21.4, 21.0; HRMS (EI) Calcd. for $C_{19}H_{17}NO_4SBr_2$ $[M]^+$ 512.9245, found 512.9232; IR (KBr) ν_{max}/cm^{-1} 3315, 2960, 1763, 1600, 1323, 1224, 1162, 680.

***N*-((*R*)-(4-Bromophenyl)(*S*)-3,4-dibromo-5-oxo-2,5-dihydrofuran-2-yl)methyl)-4-methylbenzenesulfonamide (3db).** White solid: mp 201−202 °C; $[\alpha]_D^{20}$= −74 (*c* 0.1, CH_2Cl_2), yield 41%; 3:1 dr, enantiomeric excess 88%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 20.2 min, t_R (major) = 38.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45(d, *J* = 8.3 Hz, 2H), 7.33−7.30 (m, 2H), 7.09−7.04 (m, 4H), 5.85 (d, *J* = 10.3 Hz, 1H), 5.03 (d, *J* = 1.6 Hz, 1H), 4.98 (dd, *J* = 10.4 Hz, 1.4 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 145.3, 143.7, 136.8, 134.8, 131.9, 129.4, 128.8, 127.0, 122.7, 116.4, 87.0, 56.5, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{14}Br_3NNaO_4S$ $[M + Na]^+$ 599.8086, found 599.8096; IR (KBr) ν_{max}/cm^{-1} 3279, 2933, 1778, 1609, 1339, 1213, 1160, 723.

***N*-((*R*)-(4-Chlorophenyl)(*S*)-3,4-dibromo-5-oxo-2,5-dihydrofuran-2-yl)methyl)-4-methylbenzenesulfonamide (3eb).** White solid: mp 191−192 °C; $[\alpha]_D^{20}$= −98 (*c* 0.1, CH_2Cl_2), yield 41%; 7:1 dr, enantiomeric excess 88%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 18.6 min, t_R (major) = 35.7 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.19−7.07 (m, 6H), 5.75 (d, *J* = 10.3 Hz, 1H), 5.03 (d, *J* = 1.5 Hz, 1H), 5.00 (d, *J* = 10.4 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 145.3, 143.7, 136.8, 134.6, 129.4, 129.0, 128.5, 127.0, 126.4, 116.5, 87.0, 56.4, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{14}Br_2ClNNaO_4S$ $[M + Na]^+$ 555.8591, found 555.8588; IR (KBr) ν_{max}/cm^{-1} 3296, 2921, 1759, 1602, 1338, 1217, 1158, 739.

***N*-((*R*)-((*S*)-3,4-Dibromo-5-oxo-2,5dihydrofuran-2-yl)(4-fluorophenyl)methyl)-4-methylbenzenesulfonamide (3fb).** White solid: mp 151−152 °C; $[\alpha]_D^{20}$= −85 (*c* 0.1, CH_2Cl_2), yield 51%; 4:1 dr, enantiomeric excess 94%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 18.0 min, t_R (major) = 31.7 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8. 2 Hz, 2H), 7.22−7.17 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.94−6.88 (m, 2H), 5.73 (d, *J* = 10.2 Hz, 1H), 5.06 (d, *J* = 1.6 Hz, 1H), 5.03 (d, *J* = 10.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 160.9 (J_{C-F} = 246.9 Hz), 145.4, 143.6, 137.0, 131.9 (J_{C-F} = 3.3 Hz), 129.4, 129.0 (J_{C-F} = 8. 3 Hz), 127.0, 116.4, 115.9 (J_{C-F} = 21.6 Hz), 87.2, 56.4, 21.4; HRMS (EI) Calcd. for $C_{18}H_{14}NO_4FSBr_2$ $[M]^+$ 516.8994, found 516.8965; IR (KBr) ν_{max}/cm^{-1} 3298, 2922, 1754, 1604, 1337, 1229, 1159, 728.

***N*-((*R*)-((*S*)-3,4-Dibromo-5-oxo-2,5dihydrofuran-2-yl)(2-fluorophenyl)methyl)-4-methylbenzenesulfonamide (3gb).** White solid: mp 168−169 °C; $[\alpha]_D^{20}$= −88 (*c* 0.1, CH_2Cl_2), yield 90%; 4:1 dr, enantiomeric excess 91%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 97/3, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 39.2 min, t_R (major) = 50.2 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.3 Hz, 2H), 7.22−7.16 (m, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 7.01−6.90 (m, 2H), 5.73 (d, *J* = 10.9 Hz, 1H), 5.41 (d, *J* = 10.9 Hz, 1H), 5.03 (d, *J* = 1.7 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 157.6 (J_{C-F} = 244.4 Hz), 145.3, 143.6, 136.7, 130.2 (J_{C-F} = 8.4 Hz), 129.4, 128.3, 126.9, 124.7, 123.3, 116.4, 115.6 (J_{C-F} =21.6 Hz), 86.6, 50.7, 21.4; HRMS (ESI) Calcd. for $C_{18}H_{14}Br_2FNNaO_4S$ $[M + Na]^+$ 539.8887, found 539.8897; IR (KBr) ν_{max}/cm^{-1} 3290, 2946, 1778, 1611, 1348, 1213, 1163, 675.

***N*-((*R*)-(2-Chlorophenyl)((*S*)-3,4-dibromo-5-oxo-2,5-dihydrofuran-2-yl)-4-methylbenzenesulfonamide (3hb).** White solid: mp 179−180 °C; $[\alpha]_D^{20}$= −57 (*c* 0.1, CH_2Cl_2), yield 90%; 4:1 dr, enantiomeric excess 94%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 97/3, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 35.8 min, t_R (major) = 49.2 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.32−7.28 (m, 1H), 7.22−7.08 (m, 2H), 7.04−7.01 (m, 3H), 6.30 (brs, 1H), 5.66 (d, *J* = 11.5 Hz, 1H), 5.06 (d, *J* = 1.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 145.8, 143.4, 136.8, 133.3, 131.9, 129.4, 129.3, 128.4, 127.4, 126.9, 126.5, 116.1, 86.1, 53.2, 21.3; HRMS (ESI) Calcd. for $C_{18}H_{18}Br_2ClN_2O_4S$ $[M + NH_4]^+$ 550.9037, found 550.9049; IR (KBr) ν_{max}/cm^{-1} 3282, 2946, 1778, 1610, 1347, 1213, 1162, 675.

***N*-((*R*)-(2-Bromophenyl)((*S*)-3,4-dibromo-5-oxo-2,5-dihydrofuran-2-yl)-4-methylbenzenesulfonamide (3ib).** White solid: mp 186−187 °C; $[\alpha]_D^{20}$= −28 (*c* 0.1, CH_2Cl_2), yield 94%; 10:1 dr, enantiomeric excess 93%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 15.2 min, t_R (major) = 21.6 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.46−7.43 (m, 1H), 7.11−7.10 (m, 1H), 7.08−7.01 (m, 4H), 6.19 (d, *J* = 11.1 Hz, 1H), 5.64 (d, *J* = 11.0 Hz, 1H), 5.07 (d, *J* = 1.3 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 145.8, 143.4, 136.7, 134.7, 132.7, 129.7, 129.3, 128.6, 128.0, 126.9, 122.4, 116.1, 86.0, 55.6, 21.3; HRMS (EI) Calcd. for $C_{18}H_{14}NO_4SBr_3$ $[M]^+$ 576.8194, found 576.8134; IR (KBr) ν_{max}/cm^{-1} 3291, 2945, 1778, 1610, 1347, 1212, 1163, 655.

***N*-((*R*)-((*S*)-3,4-Dibromo-5-oxo-2,5dihydrofuran-2-yl)-(naphthalene-2-yl)methyl)-4-methylbenzenesulfonamide (3jb).** White solid: mp 105−106 °C; $[\alpha]_D^{20}$= −28 (*c* 0.1, CH_2Cl_2), yield 94%; 10:1 dr, enantiomeric excess 93%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 15.2 min, t_R (major) =21.6 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.63−7.51 (m, 2H), 7.39−7.36 (m, 3H), 7.30−7.28 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.01 (d, *J* = 10.4 Hz, 1H), 5.86 (d, *J* = 10.4 Hz, 1H), 5.13 (d. *J* = 1.2 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 145.6, 143.2, 136.8, 133.6, 131.1, 129.5, 129.2, 129.1, 128.9, 127.1, 126.7, 125.9, 125.2, 124.8, 121.0, 116.2, 86.4, 51.9, 21.2; HRMS (EI) Calcd. for $C_{22}H_{17}NO_4SBr_2$ $[M]^+$ 548.9245, found 548.9240; IR (KBr) ν_{max}/cm^{-1} 3278, 3062, 1778, 1610, 1336, 1207, 1160, 666.

***N*-((*R*)-((*S*)-3,4-Dibromo-5-oxo-2,5dihydrofuran-2-yl)(*m*-tolyl)methyl)-4-methylbenzenesulfonamide (3kb).** White solid: mp 83−84 °C; $[\alpha]_D^{20}$= −88 (*c* 0.1, CH_2Cl_2), yield 76%; 4:1 dr, enantiomeric excess 84%, determined by HPLC (Chiralcel OD-H column, hexane/*i*-propanol = 85/15, flow rate 1 mL/min, UV

dx.doi.org/10.1021/jo301115t | *J. Org. Chem.* 2012, 77, 8338−8343

detection at 220 nm), t_R (minor) = 11.7 min, t_R (major) = 15.6 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.48 (m, 2H), 7.14−7.08 (m, 3H), 6.88 (s, 1H), 5.36 (d, J = 9.8 Hz, 1H), 5.07 (d, J = 1.5 Hz, 1H), 4.96 (dd, J = 10.1 Hz, 1.2 Hz, 1H), 2.33 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 145.5, 143.4, 138.6, 137.0, 135.8, 129.4, 129.2, 128.8, 127.6, 127.0, 123.9, 116.3, 87.1, 56.9, 21.4, 21.1; HRMS (EI) Calcd. for $C_{19}H_{17}NO_4SBr_2$ $[M]^+$ 512.9245, found 512.9227; IR (KBr) ν_{max}/cm^{-1} 3284, 2920, 1766, 1608, 1339, 1215, 1159, 705.

***N*-((2-Bromophenyl)(5-oxotetradrofuran-2-yl)methyl)-4-methylbenzenesulfonamide 5.** To a solution of **3ja** (129 mg, 0.26 mmol, 92% ee) in 1:1 THF/MeOH (2 mL) at 0 °C were added $NiCl_2{\cdot}6H_2O$ (187 mg, 0.79 mmol) and $NaBH_4$ (100 mg, 2.6 mmol). The reaction was quenched with the addition of saturated NH_4Cl until starting material disappeared. The mixture was then filtered, the filtrate was concentrated, and the residue was extracted with ethyl acetate several times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (hexane/EtOAc = 5/1 as eluent) to give **5** (47 mg, 43%) as a white solid: mp 129−130 °C; $[\alpha]_D^{20}$= −55 (c 0.1, CH_2Cl_2), yield 43%; enantiomeric excess 91%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 92/8, flow rate 1 mL/min, UV detection at 220 nm), t_R (minor) = 17.8 min, t_R (major) = 18.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 2H), 7.38−7.35 (m, 1H), 7.18−7.15 (m, 1H), 7.01−6.95 (m, 4H), 6.34 (brs, 1H), 5.03 (dd, J = 9.8 Hz, 2.1 Hz, 1H), 4.66−4.62 (m, 1H), 2.57−2.31 (m, 4H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2, 143.1, 136.7, 136.2, 132.4, 129.2, 129.0, 128.7, 127.5, 126.8, 122.5, 81.8, 58.8, 28.3, 24.3, 21.3; HRMS (ESI) Calcd. for $C_{18}H_{18}BrNNaO_4S$ $[M + Na]^+$ 446.0032, found 446.0040; IR (KBr) ν_{max}/cm^{-1} 3234, 2959, 1769, 1337, 1197, 1161, 690.

***N*-((1*R*,2*R*)-1-(2-Bromophenyl)-2,5-dihydroxypentyl)-4-methylbenzenesulfonamide 6.** To a solution of **5** (31 mg, 0.73 mmol) in dry THF (1 mL) at 0 °C was added $LiBH_4$ (33 mg, 1.46 mmol), and the resulting mixture was stirred at 0 °C until starting material disappeared. Saturated aqueous NH_4Cl solution was added to quench the reaction. The solvent was extracted with ethyl acetate several times. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by column chromatography (hexane/EtOAc = 5/1 as eluent) afforded **6** (28 mg, 90%) as a white solid: yield 90%; enantiomeric excess 91%, determined by HPLC (Chiralcel OD-H column, hexane/ethanol = 90/10, flow rate 1 mL/min, UV detection at 220 nm), t_R (major) = 16.8 min, t_R (minor) = 19.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 7.05−6.93 (m, 4H), 6.26 (d, J = 8.2 Hz, 1H), 4.80 (dd, J = 8.1 Hz, 3.4 Hz, 1H), 3.74 (d, J = 3.4 Hz, 1H), 3.64 (d, J = 10.3 Hz, 1H), 3.55 (d, J = 10.3 Hz, 1H), 3.15 (brs, 1H), 2.28 (s, 3H), 1.64−1.58 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 137.9, 136.9, 132.5, 129.1, 128.8, 128.6, 127.2, 126.9, 122.8, 73.5, 62.5, 60.2, 31.0, 28.7, 21.3; HRMS (ESI) Calcd. for $C_{18}H_{23}NO_4SBr$ $[M + H]^+$ 428.0531, found 428.0534.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectra and HPLC analysis spectra of all compounds, X-ray structural data (CIF) of compound **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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