Diastereoselective Aldol Reactions of Furaldehyde Using a Chiral Boronate as Auxiliary: Application to the Synthesis of Enantiomerically Pure and Highly Functionalized 2,3-Disubstituted Furanyl Alcohols

Kin-Fai Chan[a][‡] and Henry N. C. Wong*[a]

Dedicated to Professor Zhi-Tang Huang on the occasion of his 75th birthday

Keywords: Diastereoselectivity / Aldol reaction / Rearrangement / Cross-coupling

The aldol reactions of various ketene silyl acetals or lithium enolates with furaldehyde **2**, which bears a chiral boronate group at the furan C-3 position, as auxiliary have been studied. It was found that (*R*) diastereoselectivity was more favorable than (*S*) diastereoselectivity and moderate diastereoselectivity was achieved. Some of the resulting aldol diastereomers were chromatographically separable by simple flash column chromatography on silica gel, leading to optically pure aldol adducts. The absolute stereochemistry of the aldol adducts were determined by X-ray crystallographic analysis. Further transformation of the carbon–boron bond to a carbon–carbon bond was achieved in a Suzuki coupling reaction to furnish highly functionalized and enantiomerically pure 2,3-disubstituted furyl alcohols. One of the furyl alcohols was allowed to rearrange to hydroxypyranone in order to demonstrate the usefulness of this methodology.

Introduction

6-Hydroxy-2*H*-pyran-3(6*H*)-one (**1**) is a very useful synthetic intermediate in the quest for biologically active natural products. Owning to its wide capability of accommodating other functional groups, its derivatives have become important building blocks for the synthesis of oxygenated natural products (Figure 1).[1] Many methods have therefore been developed in order to realize these compounds.[2] To access these compounds through an oxidative rearrangement of furanyl alcohols, a variety of reagents have been reported. For example, *m*-chloroperbenzoic acid (*m*CPBA),[3] peracetic acid,[4] pyridinium chlorochromate (PCC),[5] iodobenzenediacetate (IBDA)[6] and *N*-bromosuccinimide (NBS)[7] were all employed as oxidants. The use of bromine in methanol,[8] bromine in water[9] and anodic oxidation[10] has also been reported.

Conventional routes developed for the synthesis of chiral furyl alcohols include Sharpless asymmetric dihydroxylation of vinylfuran,[11] asymmetric catalytic hydrogenation of furyl ketone,[12] kinetic[13] and enzymatic[14] resolution of racemic furyl alcohols, asymmetric catalytic allylation of furaldehyde[15] and asymmetric catalytic Mukaiyama aldol reaction of furaldehyde.[16] Despite this, the synthesis of structurally more elaborate chiral 2,3-disubstituted furyl alcohols still awaits investigation. Arai[17] reported that chiral 3-sulfinyl-2-furaldehyde reacted with ketene silyl acetals in the presence of a lanthanide triflate as Lewis acid catalyst to furnish aldol products with high diastereoselectivities and in high yields. In line with this notion, we are interested in synthesizing chiral 2,3-disubstituted furyl alcohols employing a chiral boronate as auxiliary, which could facilitate further functionalization of the carbon−boron bond to a carbon−carbon bond by a Suzuki coupling reaction. In this paper we wish to report the

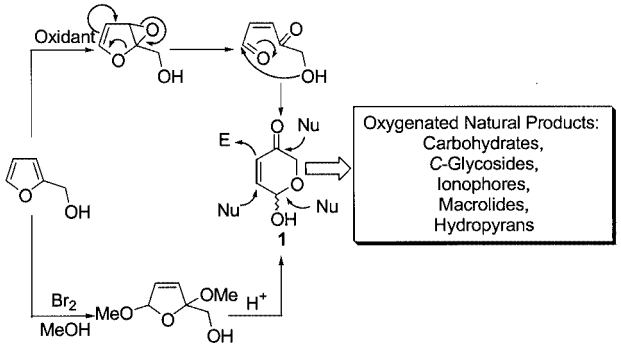

Figure 1. Mechanism for furyl alcohol rearrangement to hydroxypyranone

[‡] Present address: Department of Applied Biology and Chemical Technology, Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR, China
[a] Department of Chemistry and Central Laboratory of the Institute of Molecular Technology for Drug Discovery and Synthesis, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China
Fax: (internat.) + 852/2603-5057
E-mail: hncwong@cuhk.edu.hk

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aldol reactions of various ketene silyl acetals or lithium enolates with optically active furaldehyde **2** bearing a chiral boronate auxiliary at the furan C-3 position.

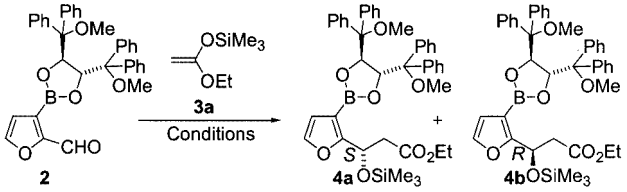
Results and Discussion

The required chiral furaldehyde **2** is available in three steps from the commercially available 3-bromofuran.[18] With this compound in hand we next studied its behavior in the reaction with various ketene silyl acetals.

Reactions with Ketene Silyl Acetals

We first studied the Mukaiyama aldol reactions of furaldehyde **2** with ketene silyl acetal **3a** (Table 1). In most cases, the reactions proceeded smoothly to furnish silyl ethers **4** in good yields with low diastereoselectivities. Both diastereomers were chromatographically separable, leading to pure diastereomers. The newly created chiral center of **4b** was substantiated by an X-ray crystallographic analysis and confirmed to be of (*R*) configuration (Figure 2).[19] The best result for this reaction was then achieved by the use of La(OTf)$_3$ as catalyst at room temperature, which led to silyl

Table 1. Mukaiyama aldol reactions of aldehyde **2** with ketene silyl acetal **3a**



Entry	Catalyst	Conditions Solvent	Temp.	Time	Yield	*de*[a]	Configuration
1	La(OTf)$_3$	DME	room temp.	0.5 h	92%	50%	(*R*)
2	La(OTf)$_3$	DME	−78 °C	4 h	89%	0%	(−)
3	La(OTf)$_3$	DME	0 °C	3 h	70%	7%	(*R*)
4	Yb(OTf)$_3$	DME	room temp.	12 h	52%	26%	(*R*)
5	Yb(OTf)$_3$	Et_2O	room temp.	12 h	81%	15%	(*R*)
6	Yb(OTf)$_3$	THF	0 °C	24 h	79%	0%	(−)
7	$ZnCl_2$	Et_2O	room temp.	1 h	72%	0%	(−)
8	$ZnCl_2$	Et_2O	−78 °C	10 h	35%	39%	(*R*)
9	$CeCl_3$	DME	room temp.	12 h	84%	19%	(*R*)
10	Y(OTf)$_3$	DME	room temp.	12 h	45%	27%	(*R*)

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture. The major diastereomer is indicated in the parentheses. All reactions were performed once only and the *de* values are approximate.

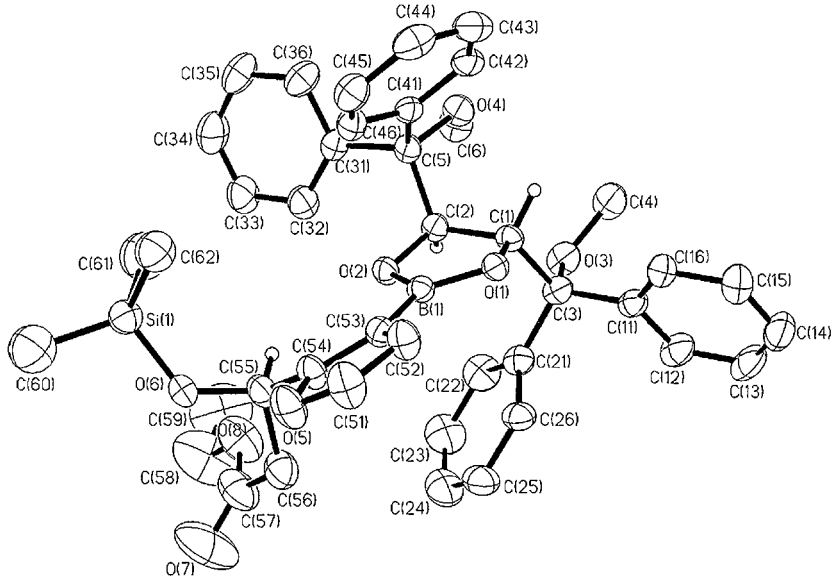
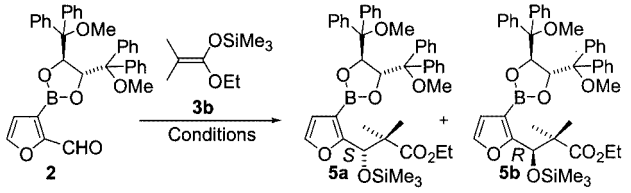


Figure 2. X-ray crystal structure of **4b**

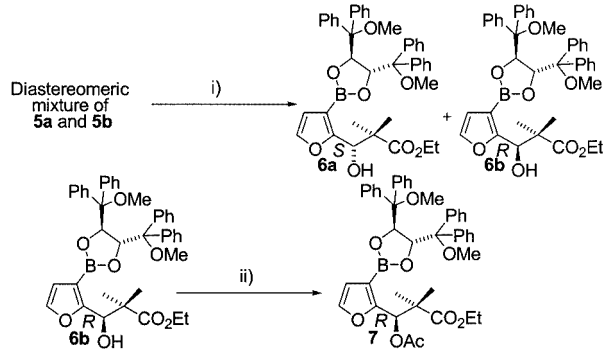
Table 2. Mukaiyama aldol reactions of aldehyde **2** with ketene silyl acetal **3b**



Entry	Conditions				Yield	*de*[a]
	Catalyst	Solvent	Temp.	Time		
1	$La(OTf)_3$	DME	reflux	3 h	76%	46% (*R*)
2	$ZnCl_2$	Et_2O	room temp.	12 h	89%	57% (*R*)
3	$FeCl_3$	DME	reflux	48 h	47%	13% (*R*)
4	$Yb(OTf)_3$	DME	reflux	48 h	79%	56% (*R*)
5	$ZnCl_2$	Et_2O	0 °C	48 h	88%	67% (*R*)
6	$ZnCl_2$	Et_2O	−40 °C	96 h	32%	60% (*R*)
7	$Zn(OTf)_2$	DME	reflux	4 h	86%	43% (*R*)
8	$ZnCl_2$	DME	0 °C	48 h	59%	72% (*R*)
9	$Ti(OiPr)_4$	CH_2Cl_2	reflux	48 h	59%	48% (*R*)
10	$ZnCl_2$	THF	reflux	4 h	32%	54% (*R*)
11	$ZnCl_2$	iPr_2O	0 °C	12 h	80%	69% (*R*)
12	$ZnCl_2$	PhMe	0 °C	3 h	91%	67% (*R*)
13	$ZnCl_2$	CH_2Cl_2	room temp.	48 h	46%	58% (*R*)
14	$ZnCl_2$	dioxane	room temp.	12 h	95%	63% (*R*)
15	$ZnCl_2$	DME	room temp.	2 h	87%	65% (*R*)
16	$ZnCl_2$	THF	−78 °C to room temp.	16 h	98%	58% (*R*)
17	$ZnCl_2$	hexane	room temp.	14 h	75%	61% (*R*)
18	$ZnCl_2$	benzene	room temp.	14 h	99%	63% (*R*)

[a] Determined by ^1H NMR analysis of the crude reaction mixture. The major diastereomer is indicated in the parentheses. All reactions were performed once only and the *de* values are approximate.

ethers **4** in 92% yield with 50% *de*. However, when the reaction was conducted at −78 °C, the diastereoselectivity decreased dramatically to 0% *de*. Change of the Lewis acid



Scheme 1. i) 1 M HCl, THF, room temp., 15 min, 98%; ii) Ac_2O, pyridine, reflux, 2 h, 82%

to other lanthanide triflates [$Yb(OTf)_3$] and employment of other solvents also showed no improved diastereoselectivity.

The following characteristic features of this reaction could be noted: (1) only a catalytic amount of Lewis acid catalyst (20 mol%) was added in each case; (2) in most cases, the reactions proceeded smoothly under extremely mild conditions to give products in high yield. However, there was still no improvement in the diastereoselectivity.

We then carried out the Mukaiyama aldol reactions of furaldehyde **2** with another ketene silyl acetal **3b** (Table 2). All reactions proceeded smoothly to furnish silyl ethers **5** in good yields and improved diastereoselectivities. However, the use of $ZnCl_2$ as a catalyst in Et_2O as a solvent at room temperature furnished silyl ethers **5** in 89% yield and over 57% *de*. Decreasing the reaction temperature to 0 °C gave slightly better diastereoselectivity (67% *de*). By comparing Entries 5, 8, 11 and 12 of Table 2, it was found that DME was the best solvent for this reaction in affording silyl ethers **5** in 72% *de*. In all cases in which the reaction was conducted at room temperature using $ZnCl_2$ as a catalyst in a

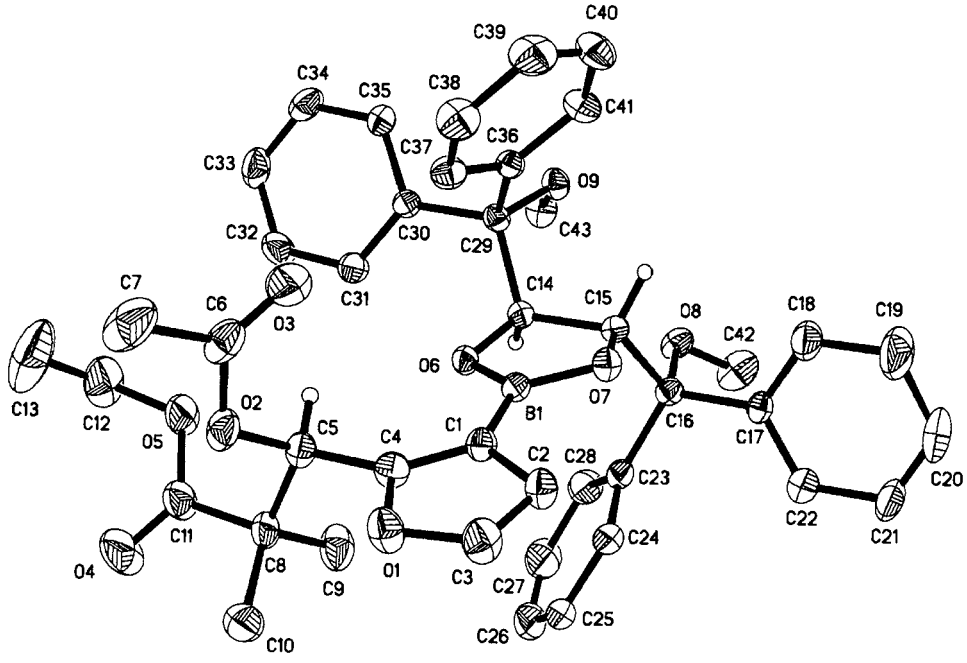
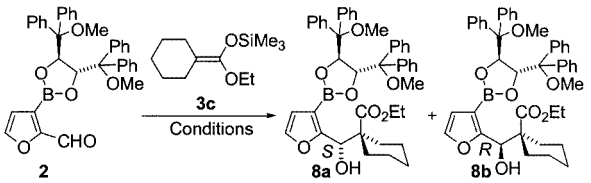


Figure 3. X-ray crystal structure of **7**

variety of solvents, silyl ethers **5** were furnished in good yield and over 50% diastereoselectivity.

It is worthwhile to note that diastereomers **5a**−**b** were chromatographically not separable. However, upon deprotection of the trimethylsilyl groups of both diastereomers with 1 M HCl (Scheme 1), furyl alcohols **6a**−**b** were chromatographically separable, allowing isolation of the diastereomerically pure diastereomers. Our attempts to crystallize both diastereomers **6a** and **6b** were unsuccessful and thus X-ray crystallographic analysis could not be used to determine the absolute stereochemistry of **6a** nor **6b**. Fortunately, protection of the hydroxy group of **6b** with an acetate group furnished compound **7** as a crystalline material. Subsequent X-ray crystallographic analysis of **7** showed the chiral center resulting from the aldol reaction to be of (*R*) configuration (Figure 3).[19]

Table 3. Mukaiyama aldol reactions of aldehyde **2** with ketene silyl acetal **3c**



Entry	Conditions				Yield	*de*[a]
	Catalyst	Solvent	Temp.	Time		
1	$ZnCl_2$	DME	0 °C	12 h	80%	46% (*R*)
2	$ZnCl_2$	iPr_2O	room temp.	12 h	65%	33% (*R*)
3	$ZnCl_2$	THF	0 °C	12 h	90%	43% (*R*)
4	$Yb(OTf)_3$	PhMe	reflux	24 h	72%	24% (*R*)

[a] Determined by ^1H NMR analysis of the crude reaction mixture. The major diastereomer is indicated in the parentheses. All reactions were performed once only and the *de* values are approximate.

Comparing ketene silyl acetals **3a** and **3b**, ketene silyl acetal **3b** is structurally more hindered. For this reason, its reaction with furaldehyde **2** should in principle give better diastereoselectivities than those of ketene silyl acetal **3a**. We then postulated that increasing the bulkiness of the ketene silyl acetal would possibly lead to higher diastereoselectivity. Aldol reactions of aldehyde **2** with ketene silyl acetal **3c** were then carried out (Table 3). However, there was no improvement in the observed diastereoselectivity. Aldol reactions between aldehyde **2** and ketene silyl acetal **3c** afforded furyl alcohols **8** in good yield with only moderate diastereoselectivities. X-ray crystallographic analysis of the less-polar diastereomer **8a** confirmed that the newly created chiral center was of (*S*) configuration (Figure 4).[19]

The mechanism proposed for Mukaiyama aldol reaction has been discussed in detail.[20] It was believed that a three-component reaction intermediate, i.e., Lewis acid, ketene silyl acetal and carbonyl group was involved.[21] In this reaction, a Lewis acid coordinates with and activates the carbonyl functional group. Due to the steric effect exerted by the bulky group, the ketene silyl acetal may then attack on the less hindered *Re*-face of the furaldehyde **2** to give rise to the (*R*) diastereomer because the nearest diphenylcarbinol group in the boronate moiety shields the carbonyl *Si*-face (Figure 5). Thus, (*R*) diastereoselectivity was more favorable over (*S*) diastereoselectivity.

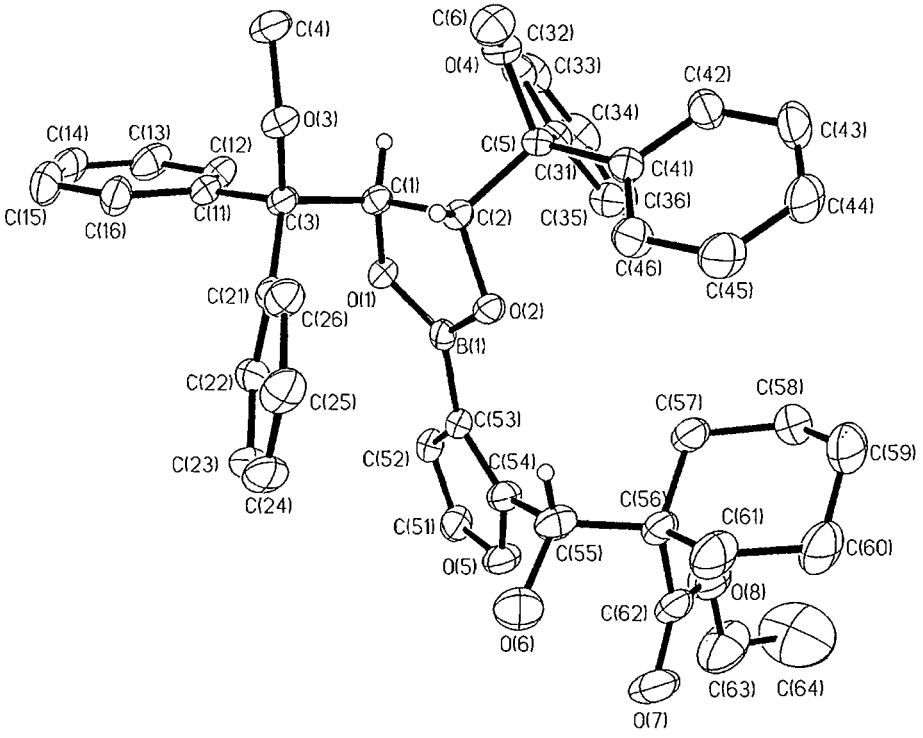


Figure 4. X-ray crystal structure of **8a**

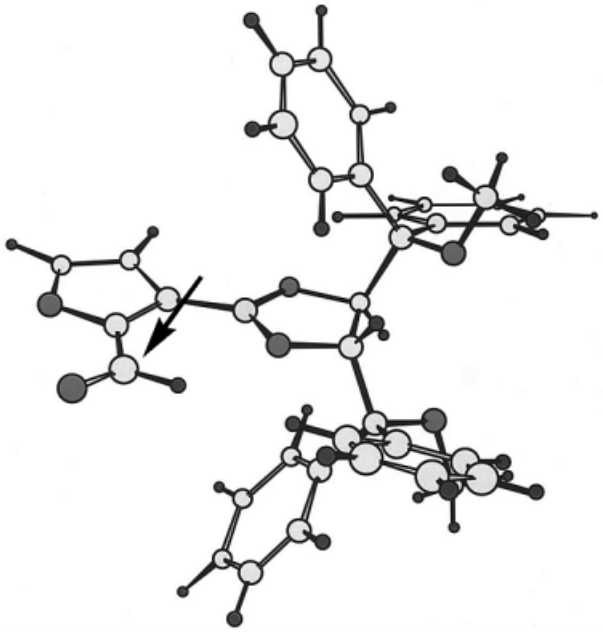
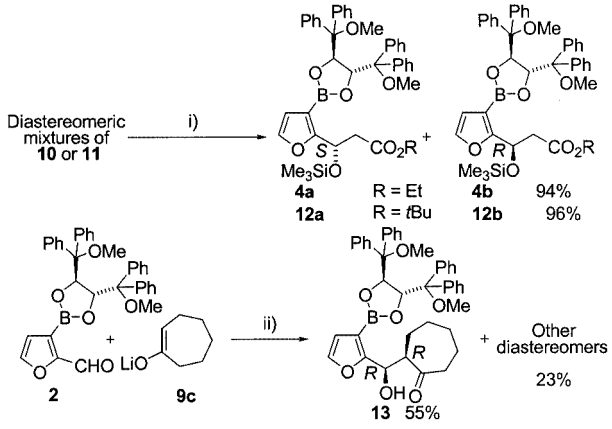


Figure 5. The arrow indicats the more favorable *Re*-face attack of aldehyde **2**

Reactions with Lithium Enolates

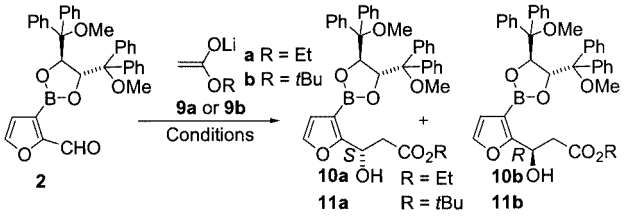
We also investigated the aldol reactions of furaldehyde **2** with a simple lithium enolate **9a** (Table 4). Furyl alcohols **10a**−**b** were isolated in 68% yield with over 50% *de*. However, increasing the bulkiness of the nucleophile by the employment of another lithium enolate **9b** resulted in lower diastereoselectivity. The use of THF as solvent, the addition of tetramethylethylenediamine (TMEDA) or the inverse addition all did not improve the observed diastereoselectivity.

Diastereomers **10a**−**b** and **11a**−**b** were chromatographically also not separable. However, their diastereomeric ratio could be determined directly from a crude diastereomeric mixture through ^{1}H NMR analysis. For compounds **10a**−**b**, their conversion into the known silyl ethers **4** proceeded smoothly and the chiral center could be confirmed (Scheme 2). For compounds **11a**−**b**, their conversion into silyl ethers **12** proceeded smoothly to furnish **12a** and **12b**, which were chromatographically still not separable. Fortunately, the major diastereomer **12b** could be selectively crystallized from a diastereomeric mixture. The newly created chiral center of the major diastereomer **12b** was then studied by X-ray crystallographic analysis and confirmed to be of (*R*) configuration (Figure 6).[19] In this way, the diastereoselectivities were indirectly determined by ^{1}H NMR spectroscopy. Moreover, the reaction of the cyclic lithium enolate **9c**, which was generated from cycloheptanone and LDA in anhydrous Et_2O at low temperature, furnished pure compound **13** in 55% yield and other unidentified diastereomers in 23% yield. The two newly created chiral centers of **13** were confirmed by X-ray crystallographic analysis (Figure 7).[19] It is noteworthy that the (*R*)



Scheme 2. i) Me_3SiCl, imidazole, THF, room temp., 3 h; ii) Et_2O, −78 °C to room temp., 14 h

Table 4. Aldol reactions of aldehyde **2** with lithium enolates **9**



Entry	**9**	Conditions			Time	Products	Yield	*de*[a]
		Additive	Solvent	Temp.				
1	**9a**	None	THF	−78 °C to room temp.	12 h	**10a**−**b**	68%	56% (*R*)
2	**9b**	None	DME	−60 °C to room temp.	12 h	**11a**−**b**	72%	23% (*R*)
3[b]	**9b**	None	THF	−78 °C to room temp.	12 h	**11a**−**b**	85%	20% (*R*)
4	**9b**	TMEDA	THF	−78 °C to room temp.	12 h	**11a**−**b**	94%	16% (*R*)
5[c]	**9b**	None	THF	−78 °C to room temp.	12 h	**11a**−**b**	78%	22% (*R*)

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture. The major diastereomer is indicated in the parentheses. All reactions were performed once only and the *de* values are approximate. [b] Enolate **9b** was added to aldehyde **2**. [c] Aldehyde **2** was added to enolate **9b**.

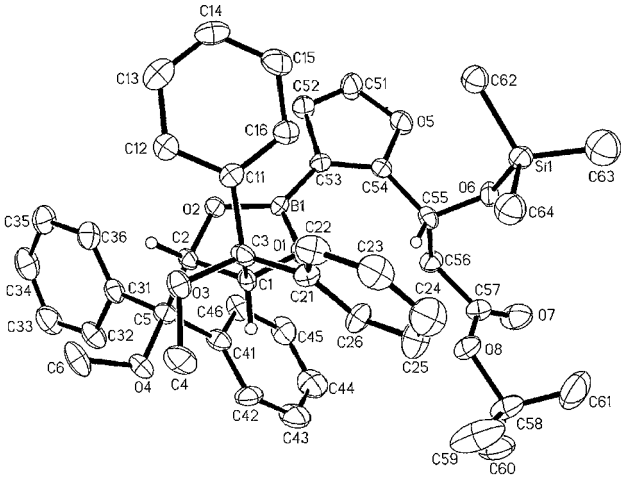


Figure 6. X-ray crystal structure of **12b**

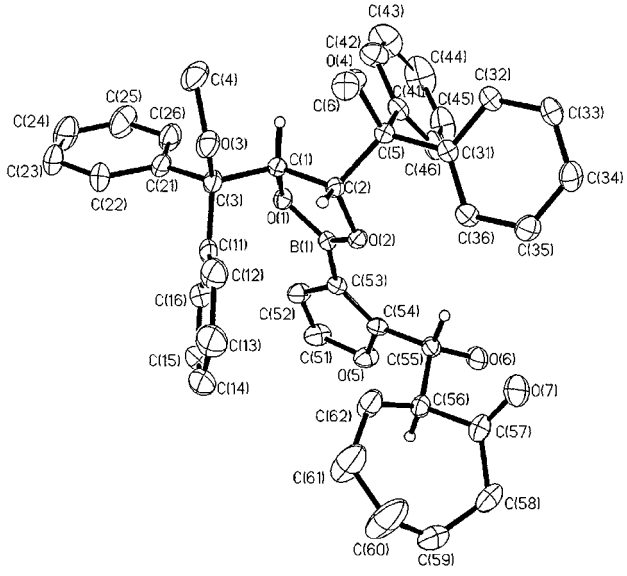
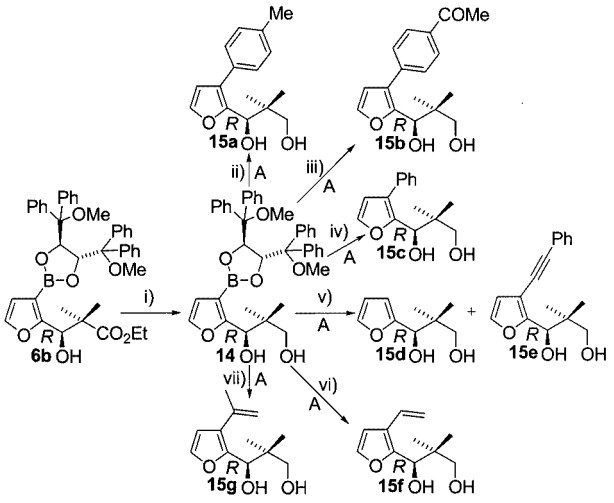


Figure 7. X-ray crystal structure of **13**

diastereoselectivity was more favorable than the (*S*) diastereoselectivity.

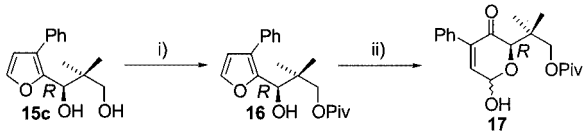
Functionalization of the C−B bond and Rearrangement of Furyl Alcohols

For fural alcohol **6b**, a direct cross coupling with an aryl iodide under the standard Suzuki coupling condition was not successful to give the optically pure 2,3-disubstituted furyl alcohol. The employment of stronger bases such as $Ba(OH)_2$ also did not give the desired product. However, when the ester group of compound **6b** was reduced by diisobutylaluminum hydride (DIBAL-H) to afford diol **14** (Scheme 3), a direct cross coupling with halides under standard Suzuki coupling conditions was now successful to furnish optically pure 2,3-disubstituted furyl alcohols with various functionalities.[22] Suzuki coupling with aryl iodides generally afforded furyl diols **15a**−**c** in high yields. Cross coupling with vinyl bromides afforded furyl diols **15f**−**g** in reasonable yields. However, Suzuki coupling with an iodoalkyne afforded furyl diol **15e** in low yield due to the side reaction leading to diol **15d**.



Scheme 3. i) DIBAL-H, THF, 0 °C, 2 h, 94%; ii) iodotoluene, 84%; iii) 4-iodoacetophenone, 95%; iv) iodobenzene, 89%; v) 1-iodo-3-phenylacetylene, **15d**, 42%, **15e**, 38%; vi) vinyl bromide, 75%; vii) 2-bromopropene, 70%; A: $Pd(PPh_3)_4$, $Ba(OH)_2$, DME/H_2O (4:1), reflux, 1 h

Chiral 2,3-disubstituted furyl alcohols are able to serve as important precursors for hydroxypyranones. Thus, for furyl diol **15c**, a selective protection of the primary alcohol in the presence of a secondary alcohol with pivaloyl chloride (PivCl) was achieved to afford furyl alcohol **16** in high yield. Subsequent treatment of furyl alcohol **16** with NBS in refluxing ethyl acetate afforded hydroxypyranone **17** in 82% yield (Scheme 4).



Scheme 4. i) PivCl, pyridine, room temp., 1 h, 89%; ii) NBS, EtOAc, reflux, 4 h, 82%

Conclusion

In conclusion, diastereoselective aldol reactions of various ketene silyl acetals or lithium enolates with furaldehyde **2**, which has a chiral boronate group at the furan C-3 position as auxiliary, were discussed. In all cases, (*R*) diastereoselectivity was more favorable than (*S*) diastereoselectivity, which can be rationalized by the steric effect on the chiral auxiliary. Some of the resulting aldol adducts were found to be chromatographically separable leading to pure diastereomers. The transformation of a carbon−boron bond of chiral furyl alcohols into a carbon−carbon bond was achieved by employing palladium-catalyzed Suzuki coupling with various halides to afford optically active 2,3-disubstituted furyl alcohols. Further investigations on conversion of furyl aldehyde **2** to imine derivatives and their reactions are currently underway.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker MHz DPX spectrometer at 300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C. All NMR measurements were carried out at room temperature and the chemical shifts are reported as ppm on the delta scale downfield from tetramethylsilane (TMS: δ = 0.00 ppm) or relative to the resonance of $CDCl_3$ (δ = 7.26 ppm in the ^{1}H, δ = 77.0 ppm for the central line of the triplet in the ^{13}C modes, respectively). Coupling constants (*J*) are reported in Hz. Low-resolution mass spectra were obtained with an HP 5989B mass spectrometer by electron ionization mode at an ionizing voltage of 70 eV or API 2000 LC/MS/MS system and the relevant data were tabulated as *m*/*z*. Optical rotation measurements were recorded with a Perkin−Elmer 341 Polarimeter. Melting points were measured using an Electrothermal IA9100 digital melting point apparatus and are uncorrected. Elemental analyses were performed at the Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, China or at MEDAC Ltd, Department of Chemistry, Brunel University, Uxbridge, U.K. X-ray crystallographic analyses were obtained by SHELXTL PLUS (PC version) with a P4 X-ray four-circle diffractometer or a Bruker CCD Area Detector. The plates used for thin-layer chromatography (TLC) were E. Merck silica gel 60F_{254} (0.25-mm thickness) precoated on an aluminum plate and they were visualized under both long (365-nm) and short (254-nm) UV light. Compounds on TLC plates were visualized with a spray of 5% (w/v) dodecamolybdophosphoric acid in ethanol, or with acidified potassium permanganate solution, and with subsequent heating. Chromatography purifications were carried out using E. Merck silica gel 60 (230−400 mesh) or Qingdao Haiyang silica gel (300−400 mesh). All reactions involving moisture-sensitive compounds were performed in flame-dried apparatus under nitrogen introduced by alternately evacuating and filling the reaction vessel 3 times with dried nitrogen.

General Procedure 1 for the Lewis Acid Catalyzed Mukaiyama Aldol Reaction of Furaldehyde 2 with Various Ketene Silyl Acetals: A Lewis acid catalyst was added to a well-stirred solution of aldehyde **2** and ketene silyl acetal in a specified solvent at a specified temperature. The mixture was then stirred until all the starting material was consumed. If $ZnCl_2$ was employed as the Lewis acid, saturated $NaHCO_3$ was then added to quench the reaction. If another Lewis acid was employed, H_2O was added. The mixture was then extracted with CH_2Cl_2 (15 mL × 3). The combined extracts were dried with $MgSO_4$. Filtration and evaporation of the solvent gave the crude residue, which was then purified by column chromatography on silica gel to afford the desired compound.

(1′*S*,4*R*,5*R*)-4a and (1′*R*,4*R*,5*R*)-4b: Table 1, Entry 1. This reaction was performed from aldehyde **2** (100 mg, 0.18 mmol), ketene silyl acetal **3a** (115 mg, 0.72 mmol), La(OTf)$_3$ (21 mg) and DME (15 mL) at room temp. according to the General Procedure 1 described above. Purification by column chromatography on silica gel (40 g, 5% EtOAc in hexane) afforded compounds **4** (118 mg) in 92% yield with 50% *de* (*R*). Further purification by flash column chromatography on silica gel (40 g, 3% EtOAc in hexane) afforded diastereomerically pure **4a** first and then **4b**. Compound **4a** was isolated as a white foam. **4a:** Softening range: 70−76 °C. $[\alpha]_D^{20}$ = −51 (*c* = 1.23, acetone). ^{1}H NMR ($CDCl_3$): δ = −0.18 (s, 9 H), 1.02 (t, *J* = 7.2 Hz, 3 H), 2.78 (dd, *J* = 10.5, 10.8 Hz, 1 H), 3.04 (s, 6 H), 3.90 (q, *J* = 7.2 Hz, 2 H), 5.16 (dd, *J* = 3.0, 10.6 Hz, 1 H), 5.49 (s, 2 H), 6.17 (d, *J* = 1.8 Hz, 1 H), 7.16−7.22 (m, 8 H), 7.28−7.41 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = −0.4, 14.2, 42.8, 51.9, 60.0, 64.2, 77.6, 83.4, 114.0, 127.2, 127.4, 127.5, 127.8, 128.4, 129.7, 141.1, 141.4, 141.6, 162.6, 169.9 ppm. MS: *m*/*z* (%) = 741 (100) [M + Na]$^+$. Compound **4b** was isolated as a white foam.**4b:** Softening range: 140−146 °C. $[\alpha]_D^{20}$ = −71 (*c* = 0.89, acetone). ^{1}H NMR ($CDCl_3$): δ = −0.24 (s, 9 H), 1.33 (t, *J* = 7.2 Hz, 3 H), 2.52 (dd, *J* = 10.5, 10.5 Hz, 1 H), 3.02 (s, 6 H), 4.19 (m, 2 H), 5.12 (dd, *J* = 2.7, 10.5 Hz, 1 H), 5.45 (s, 2 H), 6.12 (d, *J* = 1.8 Hz, 1 H), 7.16−7.21 (m, 8 H), 7.27−7.40 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = −0.7, 14.4, 43.2, 51.8, 60.1, 64.7, 77.8, 83.3, 113.7, 127.2, 127.5, 127.9, 128.4, 129.7, 141.2, 163.4, 170.3 ppm. MS: *m*/*z* (%) = 741 (100) [M + Na]$^+$. Crystallization of **4b** from 3% EtOAc in hexane at room temperature gave colorless crystals, which were suitable for X-ray crystallographic analysis. Elemental analysis was carried out on a mixture of both diastereomers. $C_{42}H_{47}BO_8Si$ (718.71): calcd. C 70.19, H 6.59; found C 70.06, H 6.73.

(1′*S*,4*R*,5*R*)-5a and (1′*R*,4*R*,5*R*)-5b: Table 2, Entry 1. These compounds were prepared from aldehyde **2** (78 mg, 0.14 mmol), ketene silyl acetal **3b** (105 mg, 0.56 mmol), La(OTf)$_3$ (16 mg) and DME (15 mL) at refluxing temperature according to the General Procedure 1 described above. Purification by column chromatography on silica gel (30 g, 5% EtOAc in hexane) afforded the diastereomeric mixture of **5a** and **5b** (79 mg) in 76% yield with 46% *de* as a white foam. ^{1}H NMR ($CDCl_3$): δ = −0.33 (s, 9 H), 0.47 (s, 3 H), 0.97 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 2.99 (s, 6 H), 4.05−4.21 (m, 2 H), 5.02 (s, 1 H), 5.43 (s, 2 H), 6.26 (d, *J* = 1.8 Hz, 1 H), 7.18−7.20 (m, 6 H), 7.25−7.39 (m, 15 H) ppm. ^{13}C NMR ($CDCl_3$): δ = −0.9, 14.4, 18.5, 23.7, 48.9, 51.9, 60.2, 72.5, 78.1, 83.4, 114.1, 127.3, 127.4, 127.8, 128.5, 129.7, 141.3, 141.4, 141.6, 161.1, 176.3 ppm. MS: *m*/*z* (%) = 769 (100) [M + Na]$^+$. $C_{44}H_{51}BO_8Si$ (746.77): calcd. C 70.77, H 6.88; found C 70.56, H 7.01.

(1′*S*,4*R*,5*R*)-6a and (1′*R*,4*R*,5*R*)-6b: 1 M HCl (10 mL) was added dropwise to a well-stirred solution of a diastereomeric mixture of **5a** and **5b** (150 mg, 0.20 mmol) in THF (20 mL) at room temp. The resulting mixture was stirred for 15 min at that temperature and was quenched by addition of saturated $NaHCO_3$ (30 mL). Extraction with CH_2Cl_2 (15 mL × 3), drying with $MgSO_4$, filtration and evaporation of the solvent under reduced pressure gave the crude reaction mixture. Purification by flash column chromatography on silica gel (60 g, 10% EtOAc in hexane) afforded the diastereomeric mixture of **6a** and **6b** (93 mg, 98%). Further purification by flash column chromatography on silica gel (60 g, 5% EtOAc in hexane) afforded diastereomerically pure **6a** first and then **6b**. Compound **6a** was isolated as a white foam. **6a:** Softening range: 62−68 °C. $[\alpha]_D^{20}$ = −67 (*c* = 1.15, acetone). ^{1}H NMR ($CDCl_3$): δ = 0.82 (s, 3 H), 0.85 (s, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 3.00 (s, 6 H), 3.58 (d, *J* = 10.2 Hz, 1 H), 4.11−4.16 (m, 2 H), 4.67 (d, *J* = 9.9 Hz, 1 H), 5.45 (s, 2 H), 6.17 (d, *J* = 1.5 Hz, 1 H), 7.16−7.35 (m, 21 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.8, 22.2, 47.4, 51.9, 60.6, 73.3, 78.2, 83.4, 114.0, 127.4, 127.7, 127.9, 128.4, 129.6, 140.8, 140.9, 141.0, 162.5, 176.5 ppm. MS: *m*/*z* (%) = 697 (100) [M + Na]$^+$. Compound **6b** was also isolated as a white foam. **6b:** Softening range: 53−58 °C. $[\alpha]_D^{20}$ = −64 (*c* = 3.67, acetone). ^{1}H NMR ($CDCl_3$): δ = 0.79 (s, 3 H), 1.00 (s, 3 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 3.03 (s, 6 H), 3.68 (d, *J* = 9.0 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.66 (d, *J* = 9.0 Hz, 1 H), 5.46 (s, 2 H), 6.19 (d, *J* = 1.8 Hz, 1 H), 7.18−7.38 (m, 21 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 20.7, 23.8, 46.3, 51.8, 60.8, 72.5, 77.7, 83.3, 113.5, 127.3, 127.6, 127.8, 128.4, 129.6, 141.1, 141.3, 161.8, 177.1 ppm. MS: *m*/*z* (%) = 697 (100) [M + Na]$^+$. Elemental analysis was carried out on a mixture of both diastereomers. $C_{41}H_{43}BO_8$ (674.59): calcd. C 73.00, H 6.42; found C 72.90, H 6.50.

(1′*R*,4*R*,5*R*)-7: Acetic anhydride (0.1 mL, 1.1 mmol) was added to a well-stirred solution of **6b** (95 mg, 0.14 mmol) in pyridine (5 mL). The mixture was heated to reflux for 2 h. When TLC showed consumption of all starting material, the reaction was quenched by adding 3 M HCl (20 mL). Extraction with CH_2Cl_2 (10 mL × 3), washing with saturated $NaHCO_3$, drying with $MgSO_4$, filtration and evaporation of the solvent under reduced pressure gave the crude reaction mixture. Purification by flash column chromatography on silica gel (50 g, 5% EtOAc in hexane) afforded the desired compound **7** (83 mg, 82%) as a white solid. M.p. 164−165 °C. $[\alpha]_D^{20} = -49$ (*c* = 1.40, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 0.56 (s, 3 H), 1.02 (s, 3 H), 1.08 (t, *J* = 7.2 Hz, 3 H), 1.91 (s, 3 H), 3.04 (s, 6 H), 3.92−4.00 (m, 1 H), 4.14−4.25 (m, 1 H), 5.46 (s, 2 H), 5.90 (s, 1 H), 6.23 (d, *J* = 1.8 Hz, 1 H), 7.17−7.22 (m, 7 H), 7.26−7.43 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1, 19.5, 20.6, 23.3, 29.7, 46.8, 51.8, 60.4, 72.9, 77.8, 83.3, 114.2, 127.2, 127.3, 127.4, 127.8, 128.5, 129.7, 141.0, 141.5, 141.7, 157.0, 168.6, 175.3 ppm. MS: *m*/*z* (%) = 686 (34) $[MH - Et]^+$, 740 (6) $[MH + Na]^+$. $C_{43}H_{45}BO_9$ (716.62): calcd. C 72.07, H 6.33; found C 72.14, H 6.57. Crystallization of **7** from 5% EtOAc in hexane at room temperature gave colorless crystals, which were sufficient for X-ray crystallographic analysis.

(1′*S*,4*R*,5*R*)-8a and (1′*R*,4*R*,5*R*)-8b: Table 3, Entry 1. These compounds were prepared from aldehyde **2** (91 mg, 0.16 mmol), ketene silyl acetal **3c** (149 mg, 0.65 mmol), $ZnCl_2$ (5 mg) and DME (15 mL) at 0 °C according to the General Procedure 1 described above. Purification by column chromatography on silica gel (30 g, 10% EtOAc in hexane) afforded compounds **8a** and **8b** (93 mg) in 80% yield with 46% *de* (*R*). Further purification by column chromatography on silica gel (30 g, 5% EtOAc in hexane) afforded diastereomerically pure **8a** first and then **8b**. Compound **8a** was isolated as a white solid. **8a:** M.p. 172−173 °C. $[\alpha]_D^{20} = -71$ (*c* = 1.40, acetone). ^1H NMR ($CDCl_3$): δ = 0.75−1.08 (m, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H), 1.27−1.32 (m, 3 H), 1.49−1.52 (m, 2 H), 1.61−1.66 (m, 1 H), 1.87−1.91 (m, 1 H), 3.00 (s, 6 H), 3.56 (d, *J* = 11.1 Hz, 1 H), 4.07−4.17 (m, 2 H), 4.39 (d, *J* = 11.1 Hz, 1 H), 5.44 (s, 2 H), 6.17 (d, *J* = 1.8 Hz, 1 H), 7.14 (d, *J* = 1.5 Hz, 1 H), 7.18−7.25 (m, 6 H), 7.28−7.36 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1, 22.8, 23.2, 25.6, 26.9, 29.1, 30.8, 51.9, 52.4, 60.5, 74.6, 78.3, 83.4, 114.1, 127.4, 127.6, 127.9, 128.4, 129.6, 140.8, 141.1, 162.2, 174.8 ppm. MS: *m*/*z* (%) = 197 (100) $[Ph_2COMe^+]$, 697 (< 1) $[M - OH]^+$. Crystallization of **8a** from 5% EtOAc in hexane at room temperature gave colorless crystals, which were sufficient for X-ray crystallographic analysis. Compound **8b** was isolated as a white foam. **8b:** Softening range: 72−81 °C. $[\alpha]_D^{20} = -27$ (*c* = 1.20, acetone). ^1H NMR ($CDCl_3$): δ = 0.70−0.77 (m, 1 H), 1.12−1.43 (m, 6 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 1.52−1.54 (m, 2 H), 2.01−2.04 (m, 1 H), 3.03 (s, 6 H), 3.52 (d, *J* = 10.5 Hz, 1 H), 4.12−4.23 (m, 2 H), 4.55 (d, *J* = 10.5 Hz, 1 H), 5.45 (s, 2 H), 6.17 (d, *J* = 1.8 Hz, 1 H), 7.13 (d, *J* = 1.8 Hz, 1 H), 7.18−7.20 (m, 5 H), 7.29−7.40 (m, 15 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.1, 22.8, 25.9, 26.9, 29.3, 32.7, 50.5, 51.8, 60.7, 72.1, 77.6, 83.3, 113.6, 127.3, 127.6, 127.8, 128.4, 129.6, 140.9, 141.2, 141.3, 161.7, 175.8 ppm. MS: *m*/*z* (%) = 197 (100) $[Ph_2COMe^+]$, 697 (< 1) $[M - OH]^+$. Elemental analysis was carried out on a mixture of both diastereomers. $C_{44}H_{47}BO_6$ (714.65): calcd. C 73.95, H 6.63; found C 73.83, H 6.89.

(1′*S*,4*R*,5*R*)-10a and (1′*R*,4*R*,5*R*)-10b: Table 4, Entry 1. Freshly prepared enolate **9a** (0.5 M in THF, 1.5 mL, 0.75 mmol) was added to a well-stirred solution of **2** (102 mg, 0.18 mmol) in anhydrous THF (10 mL) at −78 °C under N_2. The mixture was then stirred for 12 h from −78 °C to room temp. and the reaction was quenched by addition of saturated NH_4Cl (30 mL). The resulting mixture was extracted with CH_2Cl_2 (10 mL × 3), dried with $MgSO_4$, and filtered to give a crude mixture. Purification by flash column chromatography on silica gel (50 g, 15% EtOAc in hexane) afforded the inseparable diastereomeric mixture of **10a** and **10b** (80 mg, 68%) as a white foam with 56% *de* (*R*). ^1H NMR ($CDCl_3$, major diastereomer **10b**): δ = 1.28 (t, *J* = 6.9 Hz, 3 H), 2.37−2.44 (m, 1 H), 2.55−2.67 (m, 1 H), 3.00 (s, 6 H), 3.08 (d, *J* = 5.7 Hz, 1 H), 4.09−4.21 (m, 2 H), 4.90−4.97 (m, 1 H), 5.45 (s, 2 H), 6.17 (d, *J* = 1.5 Hz, 1 H), 7.16−7.38 (m, 21 H) ppm; (minor diastereomer **10a**): δ = 1.21 (t, *J* = 7.2 Hz, 3 H), 2.37−2.44 (m, 1 H), 2.55−2.67 (m, 1 H), 2.95 (d, *J* = 7.2 Hz, 1 H), 3.01 (s, 6 H), 4.09−4.21 (m, 2 H), 4.90−4.97 (m, 1 H), 5.48 (s, 2 H), 6.17 (d, *J* = 1.5 Hz, 1 H), 7.16−7.38 (m, 21 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.1, 14.2, 40.2, 41.0, 44.9, 51.9, 60.5, 64.1, 64.6, 78.1, 83.4, 114.0, 127.4, 127.6, 127.9, 128.4, 129.5, 140.9, 141.0, 141.0, 163.3, 171.4 ppm. MS: *m*/*z* (%) = 669 (100) $[M + Na]^+$. $C_{39}H_{39}BO_8$ (646.53): calcd. C 72.45, H 6.08; found C 72.46, H 5.94.

(1′*S*,4*R*,5*R*)-11a and (1′*R*,4*R*,5*R*)-11b: Table 4, Entry 2. This reaction was carried out with **2** (200 mg, 0.36 mmol), enolate **9b** (0.5 M in DME, 2.9 mL, 1.45 mmol) and anhydrous DME (20 mL) according to the procedure described above for the preparation of compounds **10**. Purification by flash column chromatography on silica gel (80 g, 15% EtOAc in hexane) afforded the diastereomeric mixture of **11a** and **11b** (175 mg, 72%) with 23% *de* (*R*). The diastereomeric mixture of **11a** and **11b** was isolated as a white foam. ^1H NMR ($CDCl_3$, major diastereomer **11b**): δ = 1.45 (d, *J* = 3.3 Hz, 1 H), 1.48 (s, 9 H), 2.28−2.34 (m, 1 H), 2.47−2.55 (m, 1 H), 3.01 (s, 6 H), 4.86−4.93 (m, 1 H), 5.45 (s, 2 H), 6.17 (d, *J* = 1.5 Hz, 1 H), 7.16−7.38 (m, 21 H) ppm; (minor diastereomer **11a**): δ = 1.41 (s, 9 H), 1.45 (d, *J* = 3.3 Hz, 1 H), 2.28−2.34 (m, 1 H), 2.47−2.55 (m, 1 H), 3.02 (s, 6 H), 4.86−4.93 (m, 1 H), 5.49 (s, 2 H), 6.17 (d, *J* = 1.5 Hz, 1 H), 7.16−7.38 (m, 21 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.0, 28.1, 41.2, 42.3, 51.9, 64.2, 64.8, 78.1, 80.6, 80.8, 83.4, 113.9, 114.1, 127.4, 127.4, 127.6, 127.7, 127.8, 127.9, 127.9, 128.2, 128.4, 129.5, 140.7, 140.8, 140.9, 141.1, 163.5, 164.6, 170.1, 170.8 ppm. MS: *m*/*z* (%) = 197 (34) $[Ph_2COMe^+]$, 697 (59) $[M + Na]^+$. $C_{41}H_{43}BO_8$ (674.59): calcd. C 73.00, H 6.42; found C 72.91, H 6.50.

(1′*S*,4*R*,5*R*)-4a and (1′*R*,4*R*,5*R*)-4b: Me_3SiCl (0.1 mL, 0.80 mmol) was added to a well-stirred solution of **10** (70 mg, 0.11 mmol), imidazole (29 mg, 0.43 mmol) in THF (10 mL) at room temp. The reaction mixture turned milky immediately. The mixture was stirred for a further 3 h. Saturated $NaHCO_3$ solution (20 mL) was added to quench the reaction. Extraction with CH_2Cl_2 (10 mL × 3), drying with $MgSO_4$, and filtration gave crude colorless oil. Purification by flash column chromatography on silica gel (50 g, 5% EtOAc in hexane) afforded a diastereomeric mixture of **4a** and **4b** (73 mg, 94%), whose physical and spectrometric data are identical with those reported previously.

(1′*R*,4*R*,5*R*)-12b: This compound was prepared from a diastereomeric mixture of **11** (150 mg, 0.22 mmol), imidazole (60 mg, 0.88 mmol), Me_3SiCl (0.2 mL, 1.59 mmol) and THF (20 mL) according to the procedure described above for the synthesis of **4**. Purification by flash column chromatography on silica gel (70 g, 5% EtOAc in hexane) afforded the diastereomeric mixture of **12a** and **12b** (159 mg, 96%). The major diastereomer **12b** (28 mg) was crystallized from 3% EtOAc in hexane and was isolated as colorless crystals. **12b:** M.p. 207−208 °C. $[\alpha]_D^{20} = -69$ (*c* = 0.55, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = −0.25 (s, 9 H), 1.52 (s, 9 H), 1.82 (dd, *J* = 2.7, 14.9 Hz, 1 H), 2.44 (dd, *J* = 10.5, 14.9 Hz, 1 H), 3.02 (s, 6 H), 5.05 (dd, *J* = 2.7, 10.6 Hz, 1 H), 5.45 (s, 2 H), 6.09 (d, *J* = 1.8 Hz, 1 H), 7.16−7.21 (m, 7 H), 7.25−7.40 (m, 14 H) ppm. ^{13}C NMR

($CDCl_3$): δ = −0.6, 28.2, 44.3, 51.8, 64.9, 79.8, 83.3, 113.7, 127.2, 127.5, 127.9, 128.4, 129.7, 141.2, 163.5, 169.5 ppm. MS: *m*/*z* (%) = 197 (25) [Ph_2COMe^+], 769 (64) [M + Na]$^+$. $C_{44}H_{51}BO_8Si$ (746.77): calcd. C 70.77, H 6.88; found C 71.07, H 7.12.

(1′*R*,1′′*R*,4*R*,5*R*)-13: This compound was prepared from **2** (100 mg, 0.18 mmol), enolate **9c** (0.38 m in Et_2O, 1.9 mL, 0.72 mmol) and anhydrous Et_2O (20 mL) according to the procedure described above for synthesis of compounds **10**. Purification by flash column chromatography on silica gel (60 g, 15% EtOAc in hexane) afforded diastereomerically pure **13** (66 mg, 55%) and other diastereomers (28 mg, 23%). Compound **13** was isolated as a white foam. M.p. 151−152 °C. $[\alpha]_D^{20}$ = −67 (*c* = 0.75, acetone). ^{1}H NMR ($CDCl_3$): δ = 0.78−0.90 (m, 1 H), 0.98−1.05 (m, 1 H), 1.14−1.32 (m, 2 H), 1.47−1.68 (m, 2 H), 1.76−1.84 (m, 2 H), 2.38−2.42 (m, 2 H), 2.86 (dt, *J* = 3.9, 9.6 Hz, 1 H), 3.03 (s, 6 H), 4.86 (dd, *J* = 6.0, 9.0 Hz, 1 H), 5.46 (s, 2 H), 6.20 (d, *J* = 1.8 Hz, 1 H), 7.17−7.20 (m, 6 H), 7.23 (d, *J* = 1.8 Hz, 1 H), 7.31−7.40 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.0, 27.3, 28.0, 28.9, 43.2, 51.8, 56.5, 68.0, 77.8, 83.3, 107.6, 113.6, 127.2, 127.3, 127.6, 127.9, 128.4, 129.6, 141.0, 141.2, 141.6, 162.3, 215.7 ppm. MS: *m*/*z* (%) = 197 (19) [Ph_2COMe^+], 693 (100) [M + Na]$^+$. $C_{42}H_{43}BO_7$ (670.60): calcd. C 75.22, H 6.46; found C 75.20, H 6.53. Crystallization of **13** from 5% EtOAc in hexane at room temperature gave colorless crystals, which were sufficient for X-ray crystallographic analysis.

(1′*R*,4*R*,5*R*)-14: Diisobutylaluminum hydride (DIBAL-H, 1 M in PhMe, 1.2 mL, 1.20 mmol) was added dropwise to a well-stirred solution of **6b** (190 mg, 0.28 mmol) in anhydrous THF (20 mL) at 0 °C under N_2. The mixture was then stirred for 2 h at 0 °C; Et_2O (60 mL) was then added to the reaction mixture. Saturated aq. NH_4Cl (2 mL) and H_2O (1 mL) were added until a heavy white precipitate was formed. The precipitate was removed by filtration and the filtrate was dried with $MgSO_4$. The crude reaction mixture was then subjected to column chromatography on silica gel (60 g, 25% EtOAc in hexane) to give diol **14** (167 mg, 94%) as a white foam. Softening range: 75−88 °C. $[\alpha]_D^{20}$ = −53 (*c* = 1.17, acetone). ^{1}H NMR ($CDCl_3$): δ = 0.64 (s, 3 H), 0.73 (s, 3 H), 2.28 (br, 1 H), 2.67 (d, *J* = 6.9 Hz, 1 H), 3.02 (s, 6 H), 3.11 (dd, *J* = 4.5, 11.4 Hz, 1 H), 3.31 (dd, *J* = 6.9, 11.1 Hz, 1 H), 4.58 (d, *J* = 6.6 Hz, 1 H), 5.46 (s, 2 H), 6.22 (d, *J* = 1.8 Hz, 1 H), 7.17−7.20 (m, 6 H), 7.24 (d, *J* = 1.8 Hz, 1 H), 7.31−7.39 (m, 14 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.3, 21.2, 40.1, 51.9, 71.4, 73.8, 77.8, 83.3, 113.6, 127.3, 127.7, 127.9, 128.3, 129.6, 140.9, 141.2, 141.5, 162.6 ppm. MS: *m*/*z* (%) = 197 (100) [Ph_2COMe^+], 655 (34) [M + Na]$^+$. $C_{39}H_{41}BO_7$ (632.55): calcd. C 74.05, H 6.53; found C 74.03, H 6.77.

General Procedure 2 for the Palladium-Catalyzed Suzuki Coupling Reaction of Chiral Furylboronate with Various Halides: A base was added at once to a well-stirred solution containing chiral furylboronate, $Pd(PPh_3)_4$ and halide in the solvent mentioned, under nitrogen at room temp. The resulting mixture was heated to reflux for 2 h and was poured into cold water. The mixture was then extracted with Et_2O (10 mL × 3). The combined extracts were dried with $MgSO_4$. Filtration and evaporation of the solvent gave the crude residue, which was then purified by column chromatography on silica gel to afford the desired compound. As chiral furyl alcohols are very sensitive to acidic conditions, Et_3N (1% v/v) must be added to the eluent used for chromatography in order to minimize racemization.

(*R*)-2,2-Dimethyl-1-[3-(4-methylphenyl)-2-furyl]propane-1,3-diol (15a): This compound was prepared from **14** (40 mg, 0.06 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), *p*-iodotoluene (55 mg, 0.25 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (10 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15a** (14 mg, 84%) as a white solid: M.p. 121−123 °C. $[\alpha]_D^{20}$ = −23 (*c* = 0.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.80 (s, 3 H), 0.90 (s, 3 H), 2.31 (s, 3 H), 3.37 (d, *J* = 10.8 Hz, 1 H), 3.63 (d, *J* = 10.8 Hz, 1 H), 4.74 (s, 1 H), 6.39 (d, *J* = 1.8 Hz, 1 H), 7.13 (d, *J* = 8.1 Hz, 2 H), 7.22 (d, *J* = 8.1 Hz, 2 H), 7.36 (d, *J* = 1.8 Hz, 1 H) (signals of two OH groups were not observed) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.2, 20.1, 21.4, 39.3, 71.2, 72.2, 110.9, 123.8, 127.3, 128.4, 129.5, 135.8, 140.5, 148.5 ppm. HRMS: calcd. for $C_{16}H_{20}O_3$ 260.1412; found 260.1401.

(*R*)-1-[3-(4-Methoxyphenyl)-2-furyl]-2,2-dimethylpropane-1,3-diol (15b): This compound was prepared from **14** (32 mg, 0.05 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), *p*-iodoacetophenone (50 mg, 0.20 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (10 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15b** (14 mg, 95%) as a white solid: M.p. 132−135 °C. $[\alpha]_D^{20}$ = −28 (*c* = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.84 (s, 3 H), 0.95 (s, 3 H), 2.51 (br, 1 H), 2.61 (s, 3 H), 3.44 (d, *J* = 10.5 Hz, 1 H), 3.55 (d, *J* = 5.4 Hz, 1 H), 3.72 (d, *J* = 10.8 Hz, 1 H), 4.82 (d, *J* = 5.4 Hz, 1 H), 6.51 (d, *J* = 1.8 Hz, 1 H), 7.47 (d, *J* = 1.8 Hz, 1 H), 7.51 (d, *J* = 8.4 Hz, 2 H), 7.98 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.0, 22.4, 26.6, 40.3, 72.1, 73.2, 111.4, 123.9, 128.5, 128.8, 135.6, 138.6, 141.9, 150.7, 197.8 ppm. HRMS: calcd. for $C_{17}H_{20}O_4$288.1362; found 288.1357.

(*R*)-1-[3-(1,1′-Biphenyl-4-yl)-2-furyl]-2,2-dimethylpropane-1,3-diol (15c): This compound was prepared from **14** (52 mg, 0.08 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), iodobenzene (67 mg, 0.33 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (15 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15c** (18 mg, 89%) as a white solid: mp: 111−113 °C. $[\alpha]_D^{20}$ = −16 (*c* = 2.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.87 (s, 3 H), 0.97 (s, 3 H), 2.37 (dd, *J* = 4.8, 5.1 Hz, 1 H), 3.17 (d, *J* = 5.7 Hz, 1 H), 3.45 (dd, *J* = 3.6, 10.8 Hz, 1 H), 3.71 (dd, *J* = 5.1, 10.5 Hz, 1 H), 4.81 (d, *J* = 5.4 Hz, 1 H), 6.48 (d, *J* = 1.8 Hz, 1 H), 7.29−7.41 (m, 5 H), 7.44 (d, *J* = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.1, 22.4, 40.3, 72.2, 73.2, 111.8, 124.9, 127.1, 128.5, 128.7, 133.5, 141.6, 149.8 ppm. HRMS: calcd. for $C_{15}H_{18}O_3$ 246.1256; found 246.1227.

(*R*)-1-(2-Furyl)-2,2-dimethylpropane-1,3-diol (15d) and (*R*)-2,2-Dimethyl-1-{3-[4-(phenylethynyl)phenyl]-2-furyl}propane-1,3-diol (15e): This compound was prepared from **14** (62 mg, 0.10 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), 1-iodo-3-phenylacetylene (89 mg, 0.41 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (10 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15e** (10 mg, 38%) first and then **15d** (7 mg, 42%). Compound **15e** was isolated as a colorless oil. **15e:** $[\alpha]_D^{20}$ = −25 (*c* = 0.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 1.00 (s, 3 H), 1.02 (s, 3 H), 2.45 (br, 1 H), 3.24 (d, *J* = 5.4 Hz, 1 H), 3.52 (d, *J* = 11.1 Hz, 1 H), 3.69 (d, *J* = 10.8 Hz, 1 H), 4.92 (d, *J* = 4.8 Hz, 1 H), 6.48 (d, *J* = 2.1 Hz, 1 H), 7.32−7.35 (m, 3 H), 7.37 (d, *J* = 1.8 Hz, 1 H), 7.46−7.49 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.0, 22.0, 40.6, 71.6, 74.5, 80.6, 93.1, 105.6, 112.7, 123.0, 128.3, 128.4, 131.3, 141.7, 157.5 ppm. HRMS: calcd. for $C_{17}H_{18}O_3$ 270.1256; found 270.1238. Compound **15d** was also isolated as a colorless oil. **15d:** $[\alpha]_D^{20}$ = +20 (*c* = 0.80, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.93 (s, 6 H), 2.44 (br, 1 H), 3.02 (d, *J* = 4.2 Hz, 1

H), 3.49 (d, J = 10.8 Hz, 1 H), 3.63 (d, J = 10.8 Hz, 1 H), 4.65 (d, J = 3.3 Hz, 1 H), 6.27 (d, J = 3.0 Hz, 1 H), 6.36 (dd, J = 1.8, 3.3 Hz, 1 H), 7.38 (dd, J = 0.9, 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.5, 22.1, 39.5, 71.7, 75.8, 107.5, 110.1, 141.7, 155.1 ppm. HRMS: calcd. for $C_9H_{14}O_3$ 170.0943; found 170.0925.

(*R*)-2,2-Dimethyl-1-(3-vinyl-2-furyl)propane-1,3-diol (15f): This compound was prepared from **14** (39 mg, 0.06 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), vinyl bromide (42 mg, 0.39 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (10 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15f** (9 mg, 75%) as a colorless oil: $[\alpha]_D^{20}$ = −24 (c = 0.35, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.92 (s, 3 H), 0.95 (s, 3 H), 2.36 (br, 1 H), 3.01 (d, J = 4.8 Hz, 1 H), 3.49 (d, J = 12.0 Hz, 1 H), 3.67 (d, J = 10.8 Hz, 1 H), 4.77 (d, J = 4.5 Hz, 1 H), 5.16 (dd, J = 1.5, 10.8 Hz, 1 H), 5.45 (dd, J = 1.5, 17.4 Hz, 1 H), 6.54 (d, J = 2.1 Hz, 1 H), 6.65 (dd, J = 10.8, 17.4 Hz, 1 H), 7.33 (d, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.9, 22.1, 40.4, 71.8, 73.7, 107.6, 111.8, 113.8, 126.4, 141.9, 150.6 ppm. HRMS: calcd. for $C_{11}H_{16}O_3$ 196.1099; found 196.1087.

(*R*)-1-(3-Isopropenyl-2-furyl)-2,2-dimethylpropane-1,3-diol (15g): This compound was prepared from **14** (39 mg, 0.06 mmol), $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), 2-bromopropene (37 mg, 0.31 mmol), $Ba(OH)_2$ (0.5 g) and 20% H_2O in DME as solvent (10 mL) according to the General Procedure 2 described above. Purification by flash column chromatography on silica gel (30 g, 20% EtOAc in hexane) afforded **15g** (9 mg, 70%) as a colorless oil: $[\alpha]_D^{20}$ = −10 (c = 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.93 (s, 3 H), 0.98 (s, 3 H), 2.02 (dd, J = 0.9, 1.2 Hz, 3 H), 2.45 (br, 1 H), 2.98 (d, J = 5.7 Hz, 1 H), 3.48 (d, J = 10.5 Hz, 1 H), 3.72 (d, J = 10.8 Hz, 1 H), 4.86 (d, J = 5.1 Hz, 1 H), 5.06 (dd, J = 0.9, 2.4 Hz, 1 H), 5.08 (dd, J = 1.5, 3.3 Hz, 1 H), 6.34 (d, J = 1.8 Hz, 1 H), 7.34 (d, J = 2.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.1, 22.5, 23.7, 40.2, 72.1, 73.0, 110.5, 114.6, 125.7, 136.6, 141.2, 149.3 ppm. HRMS: calcd. for $C_{12}H_{18}O_3$ 210.1256; found 210.1227.

(*R*)-3-Hydroxy-2,2-dimethyl-3-(3-phenyl-2-furyl)propyl Pivalate (16): Pivaloyl chloride (0.05 mL, 0.41 mmol) was added to a well-stirred solution of diol **15c** (20 mg, 0.08 mmol) in anhydrous pyridine (3 mL) at room temp. under N_2. The mixture was then stirred for 1 h. The reaction was then quenched by adding 1 M HCl (20 mL). Extraction with CH_2Cl_2 (5 mL × 3), washing with $NaHCO_3$, drying with $MgSO_4$ and filtration furnished a crude reaction mixture, which was subjected to column chromatography on silica gel (20 g, 20% EtOAc in hexane) to give compound **16** (24 mg, 89%) as a colorless oil. $[\alpha]_D^{20}$ = −13 (c = 0.20, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.83 (s, 3 H), 1.08 (s, 3 H), 1.09 (s, 9 H), 2.64 (br, 1 H), 3.74 (d, J = 10.8 Hz, 1 H), 4.19 (d, J = 11.1 Hz, 1 H), 4.75 (s, 1 H), 6.48 (d, J = 1.8 Hz, 1 H), 7.26−7.39 (m, 5 H), 7.42 (d, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.9, 21.7, 27.1, 38.8, 40.1, 69.3, 70.2, 111.6, 125.0, 127.0, 128.4, 128.6, 133.5, 141.6, 149.4, 178.6 ppm. HRMS: calcd. for $C_{20}H_{26}O_4$ 330.1831; found 330.1821.

3-[6-Hydroxy-3-oxo-4-phenyl-3,6-dihydro-2*H*-pyran-2-yl]-3-methylbutyl Pivalate (17): *N*-Bromosuccinimide (NBS, 35 mg, 0.20 mmol) was added at once to a well-stirred solution of **16** (22 mg, 0.07 mmol) in EtOAc (10 mL) at room temp. The mixture was heated to reflux for 4 h until complete consumption of the starting material. After cooling the reaction mixture to room temp., 20% aq. KI solution (20 mL) was added. Washing with saturated aq. $Na_2S_2O_3$ solution, extraction with CH_2Cl_2 (10 mL × 3), drying with $MgSO_4$ and filtration furnished a crude reaction mixture, which was subjected to column chromatography on silica gel (30 g, 15% EtOAc in hexane) to give compound **17** (19 mg, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.85 (s, 3 H), 1.08 (s, 3 H), 1.10 (s, 9 H), 2.61 (d, J = 6.9 Hz, 1 H), 3.71 (d, J = 11.1 Hz, 1 H), 4.18 (d, J = 11.1 Hz, 1 H), 4.65 (d, J = 6.9 Hz, 1 H), 6.40 (s, 1 H), 7.30−7.38 (m, 5 H) (signals of OH groups were not observed) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.8, 21.7, 27.1, 38.8, 40.0, 69.2, 70.2, 113.1, 121.6, 127.6, 127.7, 128.3, 128.7, 132.3, 151.5, 178.6 ppm. HRMS: calcd. for $C_{20}H_{26}O_5$ 346.1780; found 346.1765.

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