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Palladium-Catalyzed One-Pot Stereospecific Synthesis of 2-Deoxy Aryl *C*-Glycosides from Glycals and Anilines in the Presence of *tert*-Butyl Nitrite

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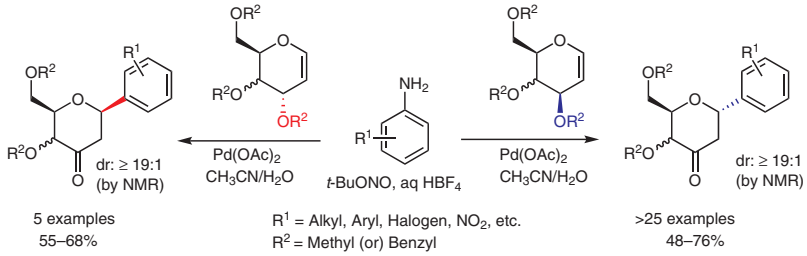

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Abstract The palladium-catalyzed one-pot synthesis of 2,3-deoxy-3-keto aryl *C*-glycosides is achieved from glycals and anilines in the presence of *tert*-butyl nitrite and aqueous HBF_4 under mild conditions. This one-pot method stereospecifically provides α- and β-aryl glycosides (≥19:1 by NMR) in good yields at room temperature. The configuration at the *C*-3 position in the glycal determines the anomeric selectivity (i.e., α or β) of the desired products.

Key words palladium, *C*-glycosylation, aryldiazonium salts, stereospecific, *tert*-butyl nitrite, anilines

Aryl *C*-glycosides are an important class of compounds that display various biological activities.[1] Among the different types, 2-deoxy aryl *C*-glycoside motifs are found in various bioactive molecules and natural products.[1] For instance, natural products such as the pluramycins, angucyclines and benzoisochromanequinones consist of 2-deoxy aryl *C*-glycoside units (Figure 1).[2] There are a few different routes that have been developed for the preparation of 2-deoxy aryl glycosides.[1,3,4] Among them, the direct coupling of aryl donors such as aryl halides, arylboronic acids, arylhydrazines, aryl carboxylic acids, arylsulfonyl halides, etc. with glycals has received considerable attention in carbohydrate synthesis.[4] Notably, all these methods provide 2-deoxy α-aryl *C*-glycosides, while most of the naturally occurring aryl *C*-glycosides exist with β-configuration at the anomeric center.

Aryldiazonium salts are highly useful synthetic intermediates that have been explored in many organic reactions.[5] In particular, palladium-catalyzed Heck couplings of allyl alcohols, allyl ethers and vinyl ethers with aryldiazonium salts have received considerable attention in the past few decades because such reactions take place at room temperature in the absence of any ligand.[6] In this context, the Correia and Schmidt research groups independently explored the palladium-catalyzed arylations of different cyclic enol ethers using aryldiazonium salts.[6c–n]

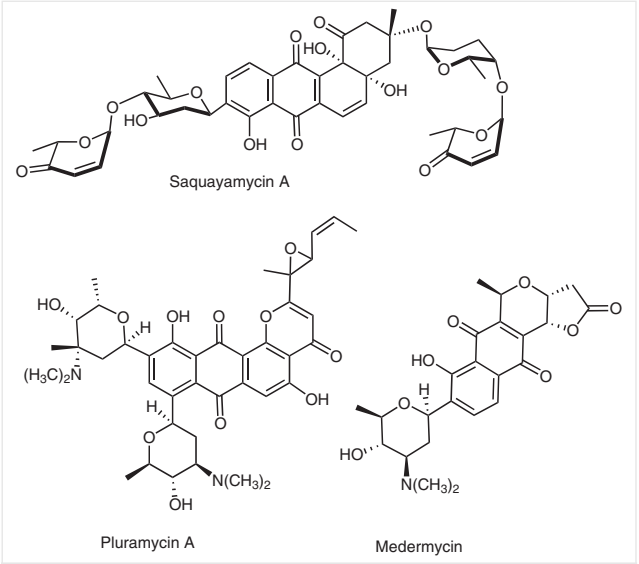

Figure 1 Natural products containing 2-deoxy aryl *C*-glycosides

Recently, we demonstrated a stereocontrolled synthesis of 2,3-deoxy 3-keto α-aryl *C*-glycosides from glycals and aryldiazonium salts in the presence of palladium acetate at room temperature.[7] In addition, Ye et al. reported a palladium-catalyzed one-pot synthesis of 2-deoxy aryl *C*-glycosides from glycals and anilines using nitrosonium tetrafluoroborate as the nitrosating reagent.[8] The important advantage of this one-pot method is that isolation of the unstable aryldiazonium salt intermediate is not required. However, the use of nitrosonium tetrafluoroborate ($NOBF_4$) as a nitro-

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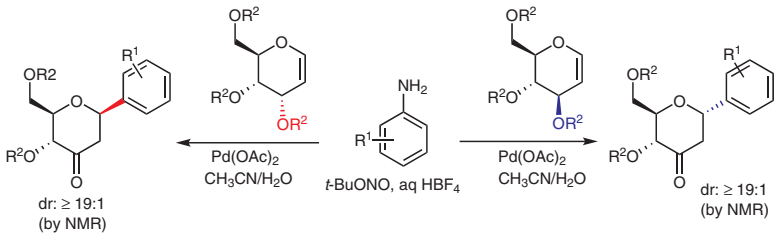
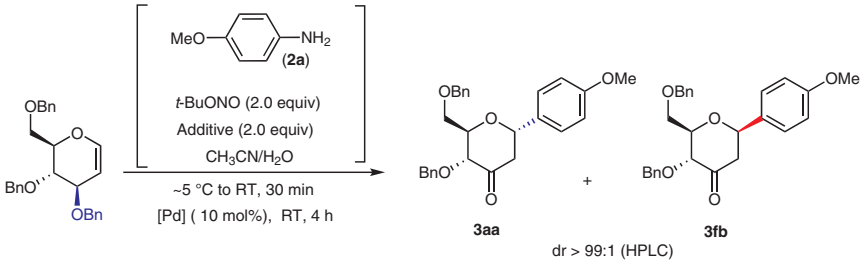


Scheme 1 Palladium-catalyzed stereoselective synthesis of 2-deoxy aryl *C*-glycosides

sating agent has some disadvantages. For instance, $NOBF_4$ is an expensive reagent and is highly reactive, which necessitates a low temperature (i.e., –40 °C) and moisture-free conditions for the diazotization process.[8] Therefore, we believe that the development of an alternative one-pot procedure using an inexpensive, stable and easily accessible nitrosating agent would provide a simple access to 2-deoxy aryl *C*-glycosides from glycals and anilines under mild conditions.

tert-Butyl nitrite (TBN) is an efficient nitrosating reagent that has been explored in many organic transformations.[9] The diazotization of anilines has been successfully achieved using *tert*-butyl nitrite under mild conditions.[10] Moreover, TBN-mediated diazotizations followed by cross-coupling reactions have also been successfully demonstrated in organic synthesis.[9c,d] Other advantages of TBN are its low cost and commercially availability, and the fact that it is economic and easy to store and handle. We have recently demonstrated different applications of *tert*-butyl nitrite in organic synthesis, including *N*-nitrosation of secondary amines,[11] oxidative dimerization of thioamides,[12] conversion of *o*-phenylenediamines into triazoles,[13] nitration of *N*-alkyl anilines[14] and one-pot transamidation of secondary amides.[15] In continuation of this work, we herein report the palladium-catalyzed one-pot synthesis of 2,3-deoxy 3-keto aryl *C*-glycosides from glycals and anilines in the presence of *tert*-butyl nitrite under mild conditions (Scheme 1).

Table 1 Optimization of the Reaction Conditions[a]



Entry	Additive	Catalyst	Yield of **3aa** (%)[b]
1	HBF_4 (aq 48%)	$Pd(OAc)_2$	76
2	$BF_3{\cdot}OEt_2$ (48%)	$Pd(OAc)_2$	56
3	HPF_6 (aq 55%)	$Pd(OAc)_2$	72
4	$CSA{\cdot}H_2O$	$Pd(OAc)_2$	10
5	$PTSA{\cdot}H_2O$	$Pd(OAc)_2$	7
6	AcOH	$Pd(OAc)_2$	5
7	HCl (aq 31%)	$Pd(OAc)_2$	<5
8	HBF_4 (aq 48%)	$PdCl_2$	55
9	HBF_4 (aq 48%)	$Pd(TFA)_2$	70
10	HBF_4 (aq 48%)	$Pd(dba)_2$	67
11	HBF_4 (aq 48%)	$Pd_2(dba)_3$	69
12	HBF_4 (aq 48%)	$Pd(PPh_3)_4$	52

[a] *Reaction conditions*: glucal **1a** (52 mg, 0.125 mmol) and the catalyst (0.012 mmol, 10 mol%) were added to a solution of the aryldiazonium compound generated in situ from aniline **2a** (30 mg, 0.25 mmol, 2.0 equiv) and *tert*-butyl nitrite (0.029 mL, 0.25 mmol, 2.0 equiv) in the appropriate solvent (4 mL).
[b] Yield of isolated product.

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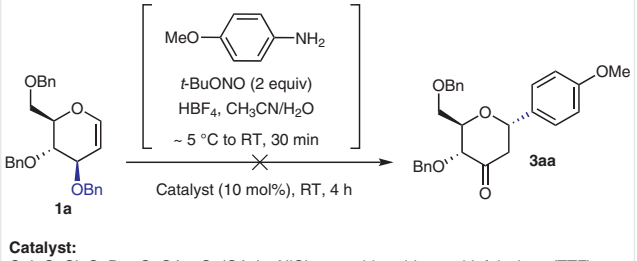
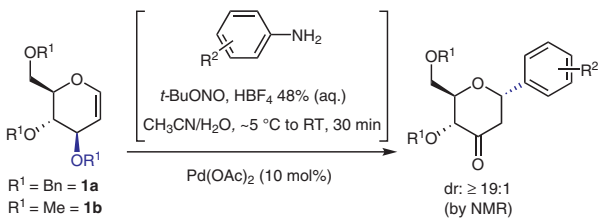
At the outset, optimization of the reaction conditions was performed using tri-*O*-benzyl glucal (**1a**) and 4-methoxyaniline (**2a**) in the presence of TBN and $Pd(OAc)_2$. Initially, 4-methoxyaniline was treated with 2 equivalents of TBN at ~5 °C (in an ice bath) in different solvents including acetonitrile/water, THF and methanol, and then subjected to the coupling reaction with glucal **1a** in the presence of 10 mol% of $Pd(OAc)_2$ or $Pd(dba)_2$ at room temperature (Table 1) (see also the Supporting Information). However, the desired coupling product was not obtained. Hence, the reaction was performed using different acid additives including HBF_4, $BF_3{\cdot}OEt_2$, HPF_6, CSA, PTSA, AcOH and HCl in acetonitrile/water mixture (Table 1, entries 1–7). To our delight, the desired coupling product **3aa** was obtained as a single isomer (i.e., the α-anomer) with most of these acid additives. Among these additives, HBF_4 was found to be the most efficient and provided the desired product in 76% yield (dr > 99:1) (Table 1, entry 1). It is also interesting to note that the corresponding β-anomer **3fb** was not observed by TLC or HPLC analysis (see the Supporting Information). It is noteworthy that Mabit et al. recently demonstrated a palladium-catalyzed stereospecific synthesis of α- and β-aryl 2-deoxy glycosides from glycals and haloarenes.[4i] In their report, the authors showed that the stereochemistry at the pseudo-anomeric position was controlled by the stereocenter at the C-3 position in glycals. In fact, a similar mechanistic aspect has been previously proposed by Schmidt et al. in the preparation of diarylheptanoids using diazonium salts.[6j]

Further, the reaction was optimized with different solvents in the presence of HBF_4 (Table 1) (see also the Supporting Information). Among them, acetonitrile/water mixture proved to be the best solvent for the coupling reaction. Under all these conditions, only the α-isomer **3aa** was obtained, while the β-anomer **3fb** was not detected by TLC. Further, different palladium catalysts including $PdCl_2$, $Pd(TFA)_2$, $Pd(dba)_2$, $Pd_2(dba)_3$ and $Pd(PPh_3)_4$ were screened in the presence of TBN and HBF_4 (Table 1, entries 8–12). The catalysts $Pd(TFA)_2$, $Pd(dba)_2$ and $Pd_2(dba)_3$ showed similar reactivity to that of palladium acetate in the coupling reaction. Furthermore, optimization of the reaction conditions was investigated with different metal and non-metal catalysts (those known for the activation of aryldiazonium salts), including CuI, CuCl, $CuBr_2$, CuOAc, $Cu(OAc)_2$, $NiCl_2$, ascorbic acid and tetrathiafulvalene (Scheme 2).[5] Unfortunately, none of these catalysts yielded the desired product.



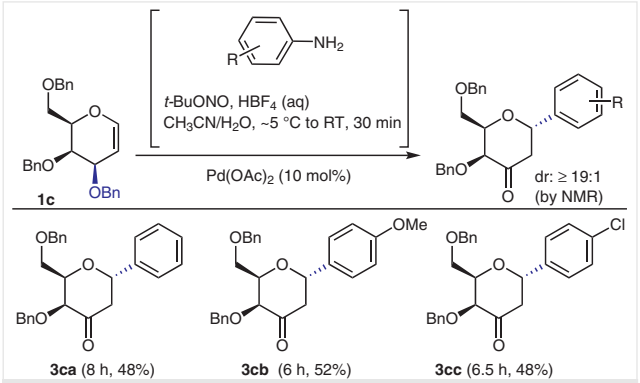
Scheme 2 Arylation of tri-*O*-benzyl glucal (**1a**) with 4-methoxyaniline (**2a**) with different metal and non-metal catalysts

Table 2 Reactions of Protected Glucals with Different Anilines[a]



Entry	R^1	R^2 (**2**)	Time (h)	Product	Yield (%)[b]
1	Bn	H (**2b**)	5.5	**3ab**	60
2	Bn	4-Me (**2c**)	4.0	**3ac**	79
3	Bn	4-Br (**2d**)	3.5	**3ad**	75
4	Bn	4-Cl (**2e**)	4.0	**3ae**	65
5	Bn	4-F (**2f**)	4.0	**3af**	72
6	Bn	4-Ac (**2g**)	4.5	**3ag**	63
7	Bn	4-CN (**2h**)	6.0	**3ah**	60
8	Bn	4-COOMe (**2i**)	5.5	**3ai**	64
9	Bn	4-F_3C (**2j**)	4.0	**3aj**	61
10	Bn	4-O_2N (**2k**)	5.5	**3ak**	61
11	Bn	3-Cl (**2l**)	3.5	**3al**	70
12	Bn	3-O_2N (**2m**)	6.0	**3am**	59
13	Bn	2-Cl (**2n**)	3.5	**3an**	65
14	Bn	2,4-Me (**2o**)	4.0	**3ao**	65
15	Me	H (**2b**)	4.5	**3ba**	72
16	Me	4-MeO (**2a**)	3.5	**3bb**	76
17	Me	4-O_2N (**2k**)	5.5	**3bc**	64

[a] *Reaction conditions*: see the general procedure.
[b] Yield of isolated product.



Scheme 3 Reactions of tri-*O*-benzyl galactal (**1c**) with different anilines. See the general procedure for the reaction conditions

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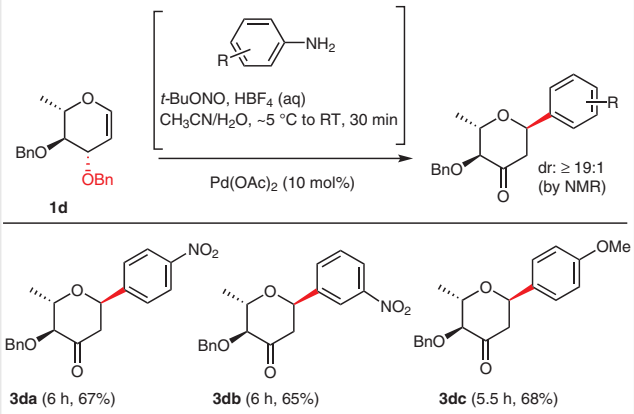
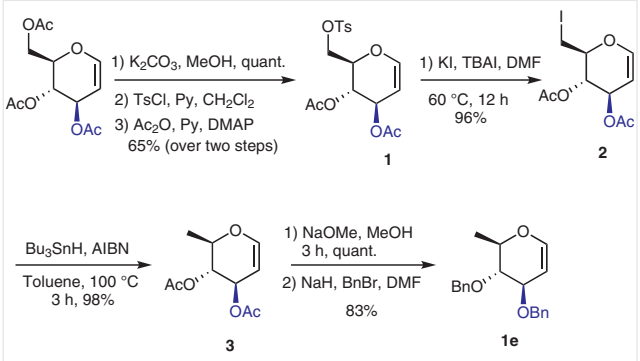


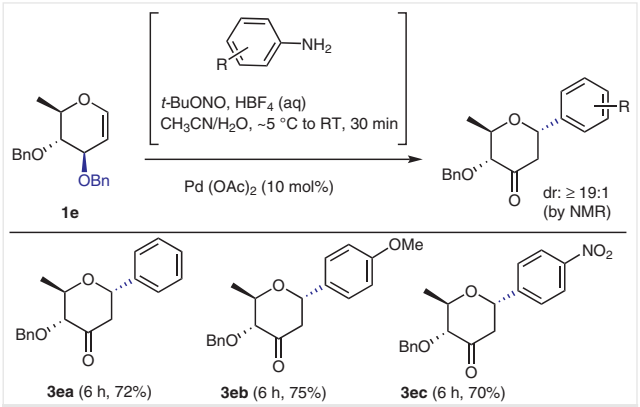
Scheme 4 Reactions of di-*O*-benzyl L-rhamnal (**1d**) with different anilines. See the general procedure for the reaction conditions

With optimized conditions in hand, different functionalized anilines were subjected to the diazotization followed by the coupling reaction with protected glucals in the presence of TBN, aqueous HBF_4 and palladium acetate (Table 2). Alkyl-, halo-, cyano-, nitro- and carbonyl-functionalized anilines underwent coupling reactions with perbenzylated and permethylated glucals **1a** and **1b** to provide the desired products **3ab–bc** as single diastereomers (α) in 59–79% yields (Table 2, entries 1–17). It is noteworthy that sterically hindered *ortho*-substituted anilines (Table 2, entries 13 and 14) also led to the coupling products with similar efficiency to those obtained with *para*- and *meta*-substituted anilines. In general, anilines functionalized with electron-withdrawing groups (e.g., CN, NO_2, CF_3) required slightly longer reaction times compared to anilines functionalized with electron-donating groups. Further, tri-*O*-benzyl galactal (**1c**) was subjected to the one-pot *C*-arylation with different anilines under the optimized conditions to afford the desired products **3ca–cc** in 48–52% yields (Scheme 3).

Having studied the scope of different diazonium salts with D-glucal and D-galactal, the developed one-pot methodology was further evaluated with di-*O*-benzyl L-rhamnal (**1d**) under the optimized conditions (Scheme 4). To our delight, 2-deoxy *C*-arylated L-rhamnose derivatives **3da–dc** were obtained as single diastereomers (i.e., α anomers) in 65–68% yields.

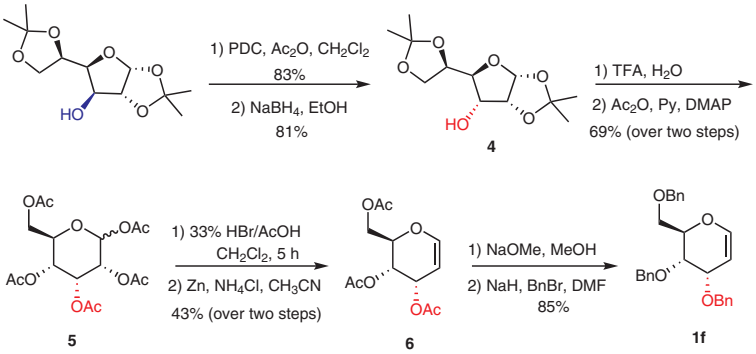


Scheme 5 Synthesis of di-*O*-benzylD-rhamnal from tri-*O*-acetyl glucal



Scheme 6 Reaction of benzyl-protected D-rhamnal with different anilines. See the general procedure for the reaction conditions

Among the different *C*-aryl glycosides, 2-deoxy *C*-aryl D-rhamnose motifs are found in many natural products and bioactive molecules.[1,2] Hence, di-*O*-benzyl D-rhamnal (**1e**) was synthesized from tri-*O*-acetyl glucal (Scheme 5) and subjected to the *C*-arylation with different anilines under



Scheme 7 Synthesis of tri-*O*-benzylD-altral from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose

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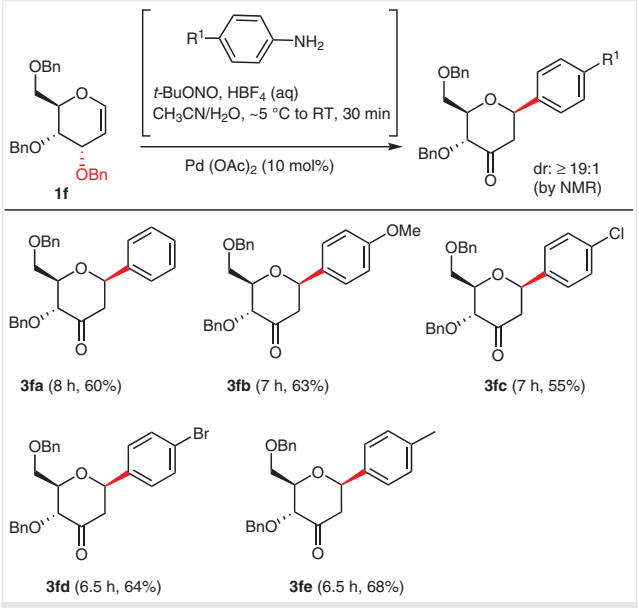
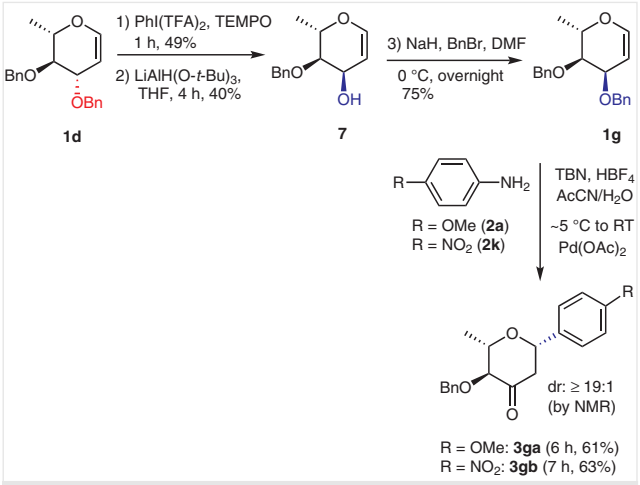
the optimized conditions (Scheme 6). The *C*-arylation reactions proceeded smoothly and gave the desired products in 70–75% yields.

To understand the stereospecificity of the reaction, we have synthesized tri-*O*-benzyl D-altral (**1f**), (i.e., *C*-3 inverted glucal) from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (Scheme 7) and subjected it to the coupling reaction with different anilines under the optimized conditions. To our delight, the reactions proceeded smoothly and provided β-aryl glycosides **3fa–fg** in good yields at room temperature (Scheme 8). Likewise, di-*O*-benzyl 6-deoxy-L-allal (**1g**) (i.e., *C*-3 inverted L-rhamnal), prepared from di-*O*-benzyl L-rhamnal, was subjected to the coupling reaction with 4-methoxyaniline (**2a**) and 4-nitroaniline (**2k**) under the optimized conditions (Scheme 9). As expected, the reactions gave only the 2-deoxy β-*C*-aryl glycosides **3ga** and **3gb** in 61% and 63% yields, respectively.

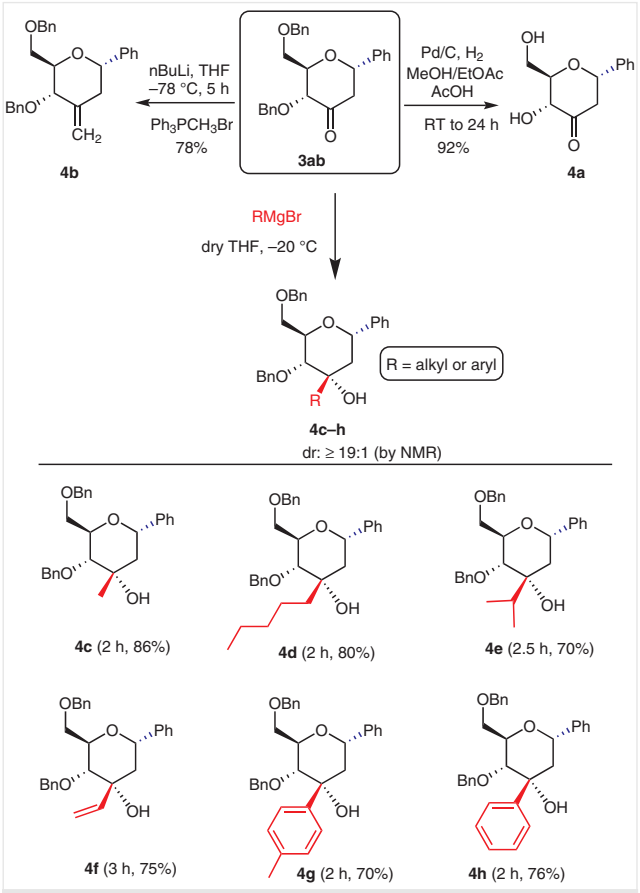


Scheme 8 Reaction of tri-*O*-benzylD-altral with different anilines. See the general procedure for the reaction conditions

Having established a simple one-pot procedure, different transformations of the synthesized 2,3-deoxy 3-keto aryl *C*-glycoside **3ab** were investigated (Scheme 10). The reduction of **3ab** with Pd/C in the presence of H_2 provided the debenzylated product **4a** in 92% yield. Wittig reaction of **3ab** with methyltriphenylphosphonium bromide in the presence of *n*-BuLi furnished the corresponding alkene **4b** in 80% yield. Treatment of **3ab** with methylmagnesium bromide gave 3-methyl-3-hydroxy *C*-glycoside **4c** as a single diastereomer in 86% yield. This reaction was extended to other Grignard reagents to give the corresponding products **4d–h** in yields ranging from 70–80% yield.



Scheme 9 Synthesis and reactions of di-*O*-benzyl 6-deoxy-L-allal with 4-methoxyaniline and 4-nitroaniline



Scheme 10 Different transformations of 2,3-deoxy 3-keto aryl *C*-glycoside **3ab**

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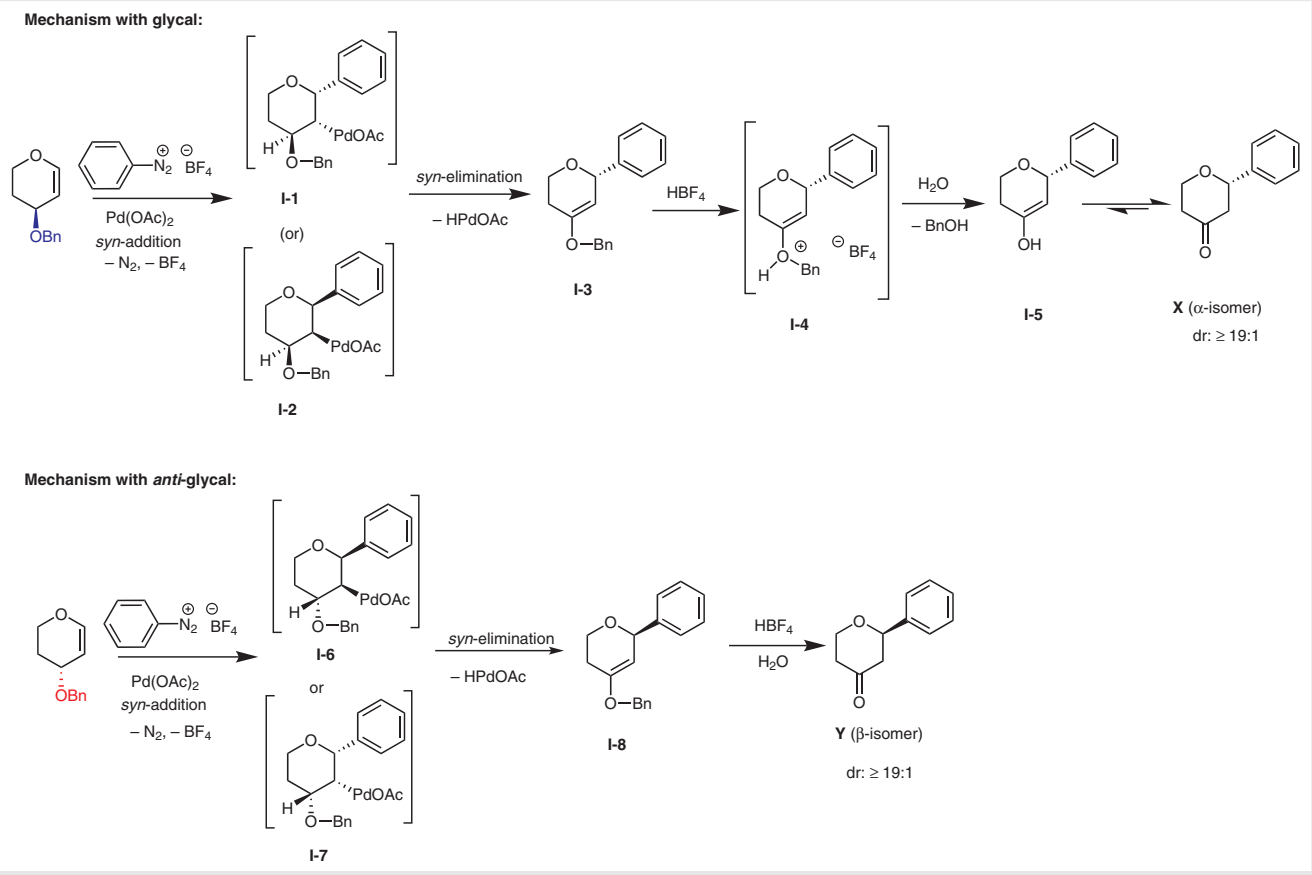

Scheme 11 Plausible mechanisms for the palladium-catalyzed *C*-arylation of glycals and *anti*-glycals

A plausible mechanism for the palladium-catalyzed stereospecific *C*-arylation of glycals is shown in Scheme 11. *Mechanism with glycals*: The oxidative *syn*-addition of palladium to the aryldiazonium salt in the presence of the glycal would provide intermediates **I-1** or **I-2**. In the next step, intermediate **I-1** or **I-2** undergoes *syn*-β-elimination to form enol ether **I-3**. However, in the case of intermediate **I-2**, there is no possibility for the *syn*-β-elimination due to the lack of a *syn*-β-hydrogen. Therefore, we believe that only intermediate **I-1** is formed during the reaction. In the presence of HBF_4/water, enol ether **I-3** undergoes hydrolysis via intermediate **I-4** to give enol **I-5**, which leads to the desired product **X** [i.e., α-*C*-aryl glycosides, (dr ≥ 19:1)]. *Mechanism with anti-glycals*: the reaction of *C*-3 inverted glycals (i.e., *anti*-glycals) with the aryldiazonium salt and palladium acetate would similarly provide intermediates **I-6** or **I-7**. Due to the lack of a *syn*-β-hydrogen in **I-7**, only intermediate **I-6** is formed. This intermediate undergoes *syn*-β-elimination to provide the β-*C*-aryl glycosides (dr ≥ 19:1) stereospecifically as shown in the mechanism.

In summary, an efficient one-pot procedure for the stereospecific synthesis of α- and β-aryl *C*-glycosides using glycals and anilines in the presence of palladium acetate and *tert*-butyl nitrite has been demonstrated. All the reactions proceeded at room temperature and provided the desired aryl *C*-glycosides in good yields. The configuration at the *C*-3 position in the glycals dictates the anomeric selectivity (i.e., either α or β).

All reactions were carried out in oven-dried glassware. Starting materials **1a–d** were prepared using literature procedures.[7] Starting materials **1e–g** have been prepared using modified procedures as described in the experimental section. Anilines were purchased from Aldrich and Alfa Aesar chemicals. Thin-layer chromatography was performed using pre-coated plates obtained from E. Merck (TLC silica gel 60 F254). TLC plates were visualized by exposure to ultraviolet light (UV), then further analyzed by staining (5% H_2SO_4 in MeOH) and charring. Column chromatography was performed on Sigma-Aldrich silica gel (100–200 mesh) using mixtures of ethyl acetate and hexane as eluents. Melting points were obtained using a Kruss Optronic KSP1D Automatic melting point apparatus. Optical rotations were recorded using a Jasco P-2000 polarimeter. IR spectra for new compounds were recorded using a PerkinElmer spectrometer. NMR spectra were recorded on a Bruker Avance 500 MHz NMR spectrometer. The ^1H and ^{13}C NMR spectra are reported as chemical shifts (δ) in parts per million (ppm), with TMS (0.00 ppm) or residual undeuterated $CDCl_3$ (7.26 ppm) (for ^1H NMR spectra) and the $CDCl_3$ signal at 77.0 ppm (for ^{13}C NMR spectra) used as references. High-resolution mass spectrometry (HRMS) was performed using a Waters Quattro Micro V

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4.1 spectrometer. HPLC analysis was performed on an Agilent LC/192168254.11 instrument. A C-8 reverse-phase column was used for the analysis with acetonitrile/water (70:30) as the solvent. The flow rate was maintained at 1 mL/min. A 10 µL sample was injected for each analysis.

3,4-Di-*O*-acetyl-6-*O*-tosyl-D-glucal (1)[16]

Potassium carbonate (0.5 g, 3.6 mmol, 0.1 equiv) was added to a solution of tri-*O*-acetyl-D-glucal (10.0 g, 36.7 mmol, 1.0 equiv) in MeOH (70 mL) and the mixture was stirred at room temperature for 4 h. After completion, the mixture was filtered through Celite and concentrated on a rotary evaporator to give D-glucal as a viscous oil in quantitative yield (~5.3 g). The obtained crude product (5.3 g, 36.4 mmol) was dissolved in a mixture of dry CH_2Cl_2 (73 mL) and dry pyridine (73 mL), cooled to 0 °C, and treated with *p*-toluenesulfonyl chloride (10.4 g, 54.6 mmol, 1.5 equiv). The resulting mixture was stirred for 8 h at room temperature and then cooled to 0 °C. Water (30 mL) was added and the mixture stirred for 30 min at 0 °C. The reaction mixture was diluted with CH_2Cl_2 and the organic layer was separated, washed with water and brine, and then dried over Na_2SO_4 and concentrated to afford the desired 6-*O*-tosylate which was directly used in the next step without further purification. The crude tosylate was stirred in pyridine (50 mL) and then Ac_2O (50 mL, 439 mmol) was added slowly at room temperature followed by DMAP (0.44 g, 3.6 mmol). The mixture was allowed to stir for 24 h at room temperature and then diluted with ethyl acetate, washed with water and brine, and dried over anhydrous Na_2SO_4. The organic layer was evaporated and the residue purified by silica gel chromatography (petroleum ether/EtOAc, 80:20) to give compound **1**.

Yield: 9.1 g (65%); white solid; mp 104 °C (Lit.[17] 106–107 °C); $[\alpha]_D^{27}$ +28.9 (*c* 1.0, CHCl3) {Lit.[18] $[\alpha]_D^{25}$ +7.1 (*c* 0.51, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.5 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 6.28 (dd, *J* = 6.0, 1.0 Hz, 1 H), 5.20 (t, *J* = 4.0 Hz, 1 H), 5.07–5.05 (m, 1 H), 4.75 (dd, *J* = 6.5, 3.5 Hz, 1 H), 4.21–4.16 (m, 2 H), 4.16–4.11 (m, 1 H), 2.38 (s, 3 H), 1.97 (s, 3 H), 1.96 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 169.4, 145.2, 145.1, 132.5, 129.8, 128.0, 98.9, 73.1, 66.9, 66.5, 66.3, 21.6, 20.9, 20.7.

6-Iodo-3,4-di-*O*-acetyl-D-glucal (2)[16]

To a solution of **1** (9.1 g, 23.6 mmol, 1.0 equiv) in DMF (118 mL) was added tetrabutylammonium iodide (TBAI) (8.72 g, 23.6 mmol, 1.0 equiv) and KI (11.7 g, 71 mmol, 3.0 equiv). The solution was stirred at 60 °C for 12 h and then cooled to room temperature, diluted with water and extracted using EtOAc. The combined organic layer was washed with saturated aqueous $Na_2S_2O_3$ and brine, and then dried over anhydrous Na_2SO_4. The organic layer was evaporated and the residue was purified by silica gel chromatography (petroleum ether/EtOAc, 90:10) to give **2**.

Yield: 7.7 g (96%); viscous oil; $[\alpha]_D^{27}$ –33.7 (*c* 1.0, $CHCl_3$) {Lit.[18] $[\alpha]_D^{25}$ –35.2 (*c* 1.02, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.46–6.42 (m, 1 H), 5.27–5.18 (m, 2 H), 4.84–4.79 (m, 1 H), 4.08–4.02 (m, 1 H), 3.41–3.27 (m, 2 H), 2.07–1.99 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 169.4, 145.3, 98.8, 74.7, 69.7, 66.5, 20.9, 20.8, 1.9.

3,4-Di-*O*-acetyl-D-rhamnal (3)[18]

To a solution of 6-iodo-3,4-di-*O*-acetyl-D-glucal (**2**) (2.42 g, 7.12 mmol, 1.0 equiv) in dry toluene (50 mL) was added Bu_3SnH (3.12 g, 2.88 mL, 10.7 mmol, 1.5 equiv) and 2,2′-azobis(isobutyronitrile) (AIBN) (117 mg, 712 µmol, 0.1 equiv). The resulting mixture was refluxed at 100 °C for 3 h and then cooled to room temperature. The solvent was removed under reduced pressure and the residue dissolved in ethyl acetate and washed with water. The organic layer was evaporated and the residue was purified by silica gel chromatography (petroleum ether/EtOAc, 80:20) to afford 6-deoxy glucal **3**.

Yield: 1.49 g (98%); colorless liquid; $[\alpha]_D^{27}$ –56.1 (*c* 1.0, $CHCl_3$) {Lit.[18] $[\alpha]_D^{25}$ –54.5 (*c* 0.98, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.42 (dd, *J* = 6.0, 1.5 Hz, 1 H), 5.34–5.32 (m, 1 H), 5.01 (dd, *J* = 8.5, 6.5 Hz, 1 H), 4.76 (dd, *J* = 6.5, 3.0 Hz, 1 H), 4.12–4.07 (m, 1 H), 2.07 (s, 3 H), 2.03 (s, 3 H), 1.30 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 169.8, 145.9, 98.7, 72.4, 71.8, 68.2, 21.0, 20.8, 16.5.

3,4-Di-*O*-benzyl-D-rhamnal (1e)[7]

Compound **3** (1 g, 4.67 mmol) was stirred in MeOH (30 mL) at 0 °C and then NaOMe (22 mg, 0.46 mmol) was added. The resulting mixture was stirred for 3 h and the solvent was evaporated to dryness. Dry DMF (15 mL) was added to the residue and the mixture was cooled to 0 °C. Subsequently, NaH (447 mg, 60% in mineral oil, 18 mmol) was added portionwise followed by stirring of the mixture for 20 min at the same temperature. Benzyl bromide (1.66 mL, 14 mmol) was then slowly added dropwise and the resulting mixture stirred overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl (6 mL) and diluted with ethyl acetate (25 mL). The organic phase was washed with water and brine, and then dried over anhydrous Na_2SO_4. The organic layer was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (hexane/ethyl acetate, 90:10) to afford **1e**.

Yield: 1.2 g (83%); colorless oil; $[\alpha]_D^{27}$ –30.1 (*c* 1.0, $CHCl_3$) {Lit.[19] $[\alpha]_D^{20}$ –33 (*c* 1.0, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 10 H), 6.35 (d, *J* = 6.0 Hz, 1 H), 4.89–4.84 (m, 2 H), 4.70 (d, *J* = 11.5 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 4.57 (d, *J* = 11.0 Hz, 1 H), 4.20 (d, *J* = 6.5 Hz, 1 H), 3.97–3.92 (m, 1 H), 3.48 (dd, *J* = 8.5, 6.5 Hz, 1 H), 1.37 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.7, 138.4, 138.2, 128.38, 128.37, 127.93, 127.75, 127.72, 127.60, 100.1, 79.5, 76.4, 74.0, 73.9, 72.0, 70.5, 17.4.

1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose (4)[20,21]

A mixture of pyridinium dichromate (10.8 g, 28.7 mmol) and acetic anhydride (11 mL, 116 mmol) was stirred in dichloromethane (100 mL) and then a solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (10.0 g, 3.84 mmol) in dichloromethane (30 mL) was added. The resulting mixture was refluxed for 2 h at 40 °C and cooled to room temperature. The solvent was evaporated, diluted with ethyl acetate (100 mL) and filtered through Celite. The filtrate was concentrated under reduced pressure to give the corresponding ketone as a viscous oil (8.20 g, 83%) which was used in the next step without further purification.

To a solution of the ketone (8.0 g, 31.0 mmol) dissolved in 56% aq EtOH (43 mL) and cooled to 0 °C was added sodium borohydride (1.29 g, 34.0 mmol) portionwise. The reaction mixture was brought to room temperature and stirred for 3 h. After completion, the reaction mixture was diluted with dichloromethane (50 mL) and washed with water. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column chromatography (hexane/ethyl acetate, 75:25) to provide 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**4**).

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Yield: 6.5 g (81%); white solid; mp 74 °C (Lit.[22] 73 °C); $[\alpha]_D^{27}$ +54 (*c* 0.1, $CHCl_3$) {Lit.[22] $[\alpha]_D^{25}$ +39.8 (*c* 0.42, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.81 (d, *J* = 3.5 Hz, 1 H), 4.63–4.61 (m, 1 H), 4.33–4.29 (m, 1 H), 4.10–4.00 (m, 3 H), 3.84–3.81 (m, 1 H), 1.58 (s, 3 H), 1.47 (s, 3 H), 1.38 (d, *J* = 6.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 112.8, 109.8, 103.8, 79.6, 78.9, 75.5, 72.4, 65.8, 26.5, 26.4, 26.2, 25.2.

D-Allopyranose Pentaacetate (5)[21]

1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose (**4**) (6.00 g, 23.05 mmol) was dissolved in a mixture of trifluoroacetic acid/water (1:1, 24 mL) and stirred at room temperature for 24 h. After completion, the solvent was removed on a rotary evaporator and co-evaporated with toluene. The resulting yellow syrup was dissolved in acetic anhydride/pyridine mixture (1:1, 80 mL) and stirred at room temperature overnight. The mixture was concentrated in vacuo and co-evaporated with toluene. The resulting white solid was dissolved in ethyl acetate and washed with 1 M hydrochloric acid, saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over anhydrous Na_2SO_4, concentrated and purified by silica gel column chromatography (hexane/ethyl acetate, 80:20) to afford D-allopyranose pentaacetate as a mixture of α/β anomers **5**.

Yield: 6.2 g (69%); colorless syrup.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.11–5.94 (m, 1 H), 5.65–5.44 (m, 1 H), 5.27–4.92 (m, 2 H), 4.36–4.00 (m, 3 H), 2.11 (s, 3 H), 2.07 (s, 3 H), 2.03 (s, 3 H), 1.96–1.95 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (α/β anomers) = 170.4, 170.2, 169.6, 169.5, 169.1, 169.0, 168.9, 168.8, 168.7, 98.1, 89.8, 79.8, 77.2, 74.1, 70.85, 70.81, 67.99, 67.90, 65.4, 61.9, 61.6, 20.75, 20.70, 20.58, 20.52, 20.4, 20.3, 20.25, 20.25.

3,4,6-Tri-*O*-acetyl-D-altral (6)[23]

D-Allopyranose pentaacetate (**5**) (4.00 g, 10.25 mmol) was dissolved in CH_2Cl_2 (20 mL) and HBr solution (33 wt% in acetic acid, 22.60 mL, 92.00 mmol) was added at 0 °C. The resulting solution was stirred for 5 h at room temperature. After completion, the reaction mixture was diluted with CH_2Cl_2 (25 mL) and washed successively with a saturated solution of sodium bicarbonate and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The crude allopyranosyl bromide was dissolved in CH_3CN (25 mL) and zinc dust (5.0 g, 76.80 mmol) and ammonium chloride (4.10 g, 76.80 mmol) were added. The resulting mixture was stirred at 50 °C for 2.5 h. After completion, the reaction mixture was filtered and the filtrate was concentrated and purified by silica gel column chromatography (hexane/ethyl acetate, 85:15) to afford 3,4,6-tri-*O*-acetyl-D-altral (**6**).

Yield: 1.2 g (43%); colorless oil; $[\alpha]_D^{27}$ = +58.1 (*c* 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.47 (d, *J* = 6.0 Hz, 1 H), 5.38 (dd, *J* = 6.0, 4.0 Hz, 1 H), 5.07 (dd, *J* = 11.0, 4.0 Hz, 1 H), 4.86 (t, *J* = 6.0 Hz, 1 H), 4.31–4.19 (m, 3 H), 2.02 (s, 6 H), 1.97 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 170.2, 169.3, 147.7, 97.4, 70.4, 66.3, 62.5, 61.8, 20.9, 20.6, 20.5.

3,4,6-Tri-*O*-benzyl-D-altral (1f)[23]

3,4,6-Tri-*O*-acetyl-D-altral (**6**) (1.0 g, 3.6 mmol) was stirred in MeOH (20 mL) at 0 °C and NaOMe (19.0 mg, 0.37 mmol) was added. The resulting mixture was stirred for 3 h and then the solvent was evaporated to dryness. Dry DMF (15 mL) was added and the solution was cooled to 0 °C and NaH (528 mg, 60% in mineral oil, 22.0 mmol) was added portionwise. The resulting mixture was stirred for 20 min at the same temperature and then benzyl bromide (1.74 mL, 15 mmol) was slowly added dropwise. The mixture was stirred overnight and then quenched with saturated aqueous NH_4Cl (8 mL) and diluted with ethyl acetate (50 mL). The organic phase was washed with H_2O and brine and then dried over anhydrous Na_2SO_4. The organic layer was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography (hexane/ethyl acetate, 90:10) to afford 3,4,6-tri-*O*-benzyl-D-altral (**1f**).

Yield: 1.3 g (85%); colorless oil; $[\alpha]_D^{27}$ +71.1 (*c* 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.15 (m, 15 H), 6.38 (dd, *J* = 6.0, 2.5 Hz, 1 H), 4.82–4.79 (m, 1 H), 4.63 (d, *J* = 12.0 Hz, 1 H), 4.57–4.53 (m, 3 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 11.5 Hz, 1 H), 4.23–4.21 (m, 1 H), 3.89–3.86 (m, 1 H), 3.768–3.763 (m, 2 H), 3.72–3.69 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.6, 138.6, 138.0, 137.8, 128.3, 127.9, 127.8, 127.7, 127.67, 127.56, 127.53, 98.0, 73.8, 73.5, 73.0, 71.2, 70.3, 68.8, 65.4.

Di-*O*-Benzyl-6-deoxy-L-allal (1g)[24]

3,4-Di-*O*-benzyl-L-rhamnal (**1d**) (1.50 g, 4.83 mmol) was stirred in CH_2Cl_2 (35 mL) then $PhI(TFA)_2$ (4.16 g, 9.67 mmol), 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) (151 mg, 0.96 mmol) and water (87 μL, 4.83 mmol) were added at 0 °C under an argon atmosphere. The resulting mixture was stirred for 30 min at the same temperature. After completion (monitored by TLC), the reaction mixture was quenched with a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2 (twice). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The organic layer was evaporated and the residue was purified by silica gel column chromatography (hexane/ethyl acetate, 85:15) to give 3-keto L-rhamnal (0.52 g, 49%). To a solution of 3-keto L-rhamnal (0.50 g, 2.29 mmol) in dry THF (10 mL) at 0 °C under an argon atmosphere was added a solution of lithium tri(*tert*-butoxy)aluminum hydride (0.73 g, 2.98 mmol) in THF. The resulting mixture was brought to room temperature and stirred for 4 h. After completion, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate (twice). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The organic layer was evaporated and the residue purified by silica gel column chromatography (hexane/ethyl acetate, 85:15) to afford 4-*O*-benzyl 6-deoxy-L-allal (**7**) (0.204 g, 40%). Compound **7** (200 mg, 0.908 mmol) was stirred in dry DMF (8 mL) at 0 °C and NaH (60% suspension in paraffin oil, 43.00 mg, 1.82 mmol) was added followed by benzyl bromide (161.0 μL, 1.36 mmol). The reaction mixture was then stirred at room temperature for 10 h. After completion, the reaction mixture was quenched with ice water and extracted with ethyl acetate. The combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was purified by silica gel column chromatography (hexane/ethyl acetate, 90:10) to provide **1g**.

Yield: 210 mg (75%); colorless syrup; $[\alpha]_D^{27}$ –250 (*c* 1.0, $CHCl_3$) {Lit.[25] $[\alpha]_D^{20}$ –259.4 (*c* 1.1, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 10 H), 6.35 (dd, *J* = 6.0, 1.5 Hz, 1 H), 4.88–4.84 (m, 2 H), 4.69 (d, *J* = 11.0 Hz, 1 H), 4.65 (d, *J* = 11.5 Hz, 1 H), 4.56 (d, *J* = 11.5 Hz, 1 H), 4.21–4.19 (m, 1 H), 3.97–3.91 (m, 1 H), 3.48 (dd, *J* = 9.0, 6.5 Hz, 1 H), 1.38 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.7, 138.3, 138.2, 128.36, 128.35, 127.9, 127.7, 127.5, 100.0, 79.4, 76.4, 74.0, 73.9, 70.4, 17.4.

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C-Glycosides 3; General Procedure

Aniline **2a–k** (0.25 mmol, 2.0 equiv) was dissolved in a mixture of acetonitrile/water (3:1, 4 mL) and stirred at ~5 °C (ice bath). Next, 48% aq HBF_4 (2.0 equiv) was added. After 5 min, *t*-BuONO (0.25 mmol, 2.0 equiv) was added and the resulting mixture was allowed to attain room temperature. After 30 min, glycal **1a–g** (0.125 mmol) and palladium acetate (2.80 mg, 10 mol%) were added at room temperature and the mixture was stirred for the appropriate amount of time. After completion, the reaction mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over Na_2SO_4, concentrated and purified by column chromatography on silica gel.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-methoxyphenyl)dihydro-2*H*-pyran-4(3*H*)-one (3aa)[7]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 41 mg (76%); white foam; R_f = 0.40 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +126 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{21}$ +120.8 (*c* 1.4, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26–7.18 (m, 12 H), 6.79–6.76 (m, 2 H), 5.36 (dd, *J* = 6.5, 2.5 Hz, 1 H), 4.77 (d, *J* = 11.0 Hz, 1 H), 4.51 (d, *J* = 12.5 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.35 (d, *J* = 11.0 Hz, 1 H), 4.16 (d, *J* = 8.5 Hz, 1 H), 3.70 (s, 3 H), 3.63–3.54 (m, 3 H), 3.01 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.97–2.93 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.7, 159.4, 137.9, 137.4, 130.6, 128.8, 128.37, 128.35, 128.1, 127.89, 127.83, 127.71, 114.0, 79.7, 74.8, 74.2, 73.5, 73.4, 69.1, 55.2, 44.0.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (3ab)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 30 mg (60%); white foam; R_f = 0.62 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +140 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{19}$ = +85.3 (*c* 0.2, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.30 (m, 2 H), 7.27–7.19 (m, 13 H), 5.41 (dd, *J* = 6.5, 2.5 Hz, 1 H), 4.76 (d, *J* = 11.0 Hz, 1 H), 4.52 (d, *J* = 12.2 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.0 Hz, 1 H), 4.17 (d, *J* = 8.5 Hz, 1 H), 3.66–3.56 (m, 3 H), 3.05 (dd, *J* = 14.5, 3.0 Hz, 1 H), 2.99–2.95 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.4, 138.5, 137.8, 137.3, 128.7, 128.37, 128.35, 128.2, 128.1, 127.9, 127.8, 127.7, 127.3, 79.5, 75.1, 74.5, 73.5, 73.4, 69.0, 43.8.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(*p*-tolyl)dihydro-2*H*-pyran-4(3*H*)-one (3ac)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 41 mg (79%); white foam; R_f = 0.60 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +60.0 (*c* 0.05, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26–7.18 (m, 12 H), 7.06–7.05 (m, 2 H), 5.37 (dd, *J* = 6.5, 2.5 Hz, 1 H), 4.77 (d, *J* = 11.5 Hz, 1 H), 4.51 (d, *J* = 12.5 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.35 (d, *J* = 11.0 Hz, 1 H), 4.15 (d, *J* = 9.0 Hz, 1 H), 3.65–3.55 (m, 3 H), 3.02 (dd, *J* = 14.5, 3.0 Hz, 1 H), 2.97–2.92 (m, 1 H), 2.23 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.5, 137.9, 137.9, 137.4, 135.5, 129.3, 128.37, 128.34, 128.1, 127.88, 127.83, 127.7, 127.4, 79.6, 75.0, 74.4, 73.5, 73.4, 69.1, 44.0, 21.0.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-bromophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3ad)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 45 mg (75%); white foam; R_f = 0.56 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +57 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{19}$ +104.5 (*c* 0.2, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.36 (m, 2 H), 7.26–7.16 (m, 12 H), 5.33 (dd, *J* = 6.0, 3.5 Hz, 1 H), 4.75 (d, *J* = 11.0 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.5 Hz, 1 H), 4.34 (d, *J* = 11.0 Hz, 1 H), 4.14 (d, *J* = 8.5 Hz, 1 H), 3.65–3.56 (m, 3 H), 2.99–2.91 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.9, 137.74, 137.71, 137.2, 131.8, 129.0, 128.39, 128.36, 128.1, 127.9, 127.8, 127.7, 122.3, 79.4, 75.0, 74.6, 73.5, 73.3, 69.1, 43.9.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-chlorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3ae)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 35 mg (65%); white foam; R_f = 0.56 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +112 (*c* 0.1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 14 H), 5.43 (dd, *J* = 6.5, 3.5 Hz, 1 H), 4.82 (d, *J* = 11.5 Hz, 1 H), 4.57 (d, *J* = 12.0 Hz, 1 H), 4.47 (d, *J* = 12.0 Hz, 1 H), 4.41 (d, *J* = 11.0 Hz, 1 H), 4.22 (d, *J* = 9.0 Hz, 1 H), 3.71–3.63 (m, 3 H), 3.08–2.99 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.0, 137.7, 137.2, 137.1, 134.1, 128.8, 128.7, 128.38, 128.35, 128.1, 127.9, 127.79, 127.75, 79.4, 77.2, 74.8, 74.5, 73.5, 73.3, 69.0, 43.9.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-fluorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3af)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 38 mg (72%); white foam; R_f = 0.56 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +144 (*c* 0.1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.17 (m, 12 H), 6.95–6.92 (m, 2 H), 5.36 (dd, *J* = 6.0, 3.0 Hz, 1 H), 4.75 (d, *J* = 11.0 Hz, 1 H), 4.50 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.35 (d, *J* = 11.5 Hz, 1 H), 4.15 (d, *J* = 9.0 Hz, 1 H), 3.64–3.56 (m, 3 H), 3.01–2.92 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.1, 162.4 (d, *J* = 245 Hz), 137.7, 137.2, 134.4, 129.25 (d, *J* = 8 Hz), 128.38, 128.36, 128.1, 127.88 (d, *J* = 24 Hz), 127.8, 115.6, 115.4, 79.5, 74.7, 74.6, 73.5, 73.3, 69.1, 44.0.

(2*R*,3*R*,6*S*)-6-(4-Acetylphenyl)-3-(benzyloxy)-2-[(benzyloxy)methyl]dihydro-2*H*-pyran-4(3*H*)-one (3ag)

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 35 mg (63%); white foam; R_f = 0.50 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +89 (*c* 0.1, $CHCl_3$).

IR (neat): 2811–2971, 1721, 1680, 1130, 881 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.5 Hz, 2 H), 7.41 (d, *J* = 8.5 Hz, 2 H), 7.27–7.18 (m, 10 H), 5.43 (dd, *J* = 6.5, 4.0 Hz, 1 H), 4.75 (d, *J* = 11.0 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.5 Hz, 1 H), 4.16 (d, *J* = 8.0 Hz, 1 H), 3.66–3.63 (m, 1 H), 3.614–3.611 (m, 2 H), 3.04 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.98 (dd, *J* = 14.5, 6.5 Hz, 1 H), 2.50 (s, 3 H).

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^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.7, 197.5, 143.8, 137.6, 137.1, 136.7, 128.7, 128.4, 128.3, 128.1, 127.9, 127.8, 127.4, 79.3, 75.3, 74.8, 73.5, 73.3, 69.1, 43.9, 26.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{29}O_5$: 445.2015; found: 445.2021.

4-{(2*S*,5*R*,6*R*)-5-(Benzyloxy)-6-[(benzyloxy)methyl]-4-oxotetrahydro-2*H*-pyran-2-yl}benzonitrile (3ah)[7]

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 32 mg (60%); white foam; R_f = 0.25 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +97 (*c* 0.1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56–7.54 (m, 2 H), 7.42 (d, *J* = 8.5 Hz, 2 H), 7.27–7.19 (m, 10 H), 5.39 (t, *J* = 5.5 Hz, 1 H), 4.72 (d, *J* = 11.5 Hz, 1 H), 4.49 (d, *J* = 12.5 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.0 Hz, 1 H), 4.12 (d, *J* = 8.5 Hz, 1 H), 3.69–3.67 (m, 1 H), 3.61–3.60 (m, 2 H), 3.00–2.91 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1, 144.1, 137.5, 137.0, 132.4, 128.42, 128.39, 128.1, 128.0, 127.8, 127.7, 118.3, 112.0, 79.1, 75.8, 74.5, 73.5, 73.2, 69.2, 43.9.

Methyl 4-{(2*S*,5*R*,6*R*)-5-(Benzyloxy)-6-[(benzyloxy)methyl]-4-oxotetrahydro-2*H*-pyran-2-yl}benzoate (3ai)[7]

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 37 mg (64%); white foam; R_f = 0.40 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +62 (*c* 0.1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94–7.91 (m, 2 H), 7.39 (d, *J* = 8.5 Hz, 2 H), 7.27–7.17 (m, 10 H), 5.42 (dd, *J* = 6.5, 4.0 Hz, 1 H), 4.74 (d, *J* = 11.5 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.5 Hz, 1 H), 4.15 (d, *J* = 8.5 Hz, 1 H), 3.83 (s, 3 H), 3.68–3.65 (m, 1 H), 3.63–3.58 (m, 2 H), 3.04 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.98–2.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.7, 166.5, 143.7, 137.6, 137.1, 129.96, 129.90, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.1, 79.3, 75.2, 74.8, 73.5, 73.2, 69.1, 52.1, 43.9.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-[4-(trifluoromethyl)phenyl]dihydro-2*H*-pyran-4(3*H*)-one (3aj)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 36 mg (61%); white foam; R_f = 0.52 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +87.0 (*c* 0.1, $CHCl_3$).

IR (neat): 2911, 2791, 1718, 1130, 881 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52–7.51 (m, 2 H), 7.44–7.42 (m, 2 H), 7.27–7.17 (m, 10 H), 5.43–5.41 (m, 1 H), 4.74 (d, *J* = 11.0 Hz, 1 H), 4.50 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.0 Hz, 1 H), 4.15 (d, *J* = 8.5 Hz, 1 H), 3.66–3.58 (m, 3 H), 3.04–2.94 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.6, 142.6, 137.6, 137.1, 130.33 (q, *J* = 32.5 Hz), 128.4, 128.3, 128.2, 128.0, 127.8, 127.5, 125.67 (q, *J* = 3.75 Hz), 125.66, 125.63, 123.87 (q, *J* = 270.5 Hz), 79.2, 75.3, 74.6, 73.5, 73.3, 69.1, 43.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{26}F_3O_4$: 471.1783; found: 471.1784.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3ak)[8]

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 34 mg (61%); white foam; cc: 20% EtOAc/hexane; R_f = 0.45 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +39 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{23}$ +74.1 (*c* 2.3, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12–8.10 (m, 2 H), 7.49–7.48 (m, 2 H), 7.27–7.17 (m, 10 H), 5.44 (t, *J* = 5.5 Hz, 1 H), 4.72 (d, *J* = 11.5 Hz, 1 H), 4.49 (d, *J* = 12.5 Hz, 1 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.5 Hz, 1 H), 4.13 (d, *J* = 8.0 Hz, 1 H), 3.72–3.69 (m, 1 H), 3.62–3.61 (m, 2 H), 3.02–2.93 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.0, 147.5, 146.1, 137.5, 136.9, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 123.8, 79.0, 75.9, 74.3, 73.5, 73.1, 69.2, 44.0.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(3-chlorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3al)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 37 mg (70%); colorless oil; R_f = 0.64 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +67 (*c* 0.1, $CHCl_3$).

IR (neat): 2931, 2797, 1724, 1488, 1120, 754 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (s, 1 H), 7.29–7.17 (m, 13 H), 5.35 (dd, *J* = 6.0, 3.5 Hz, 1 H), 4.75 (d, *J* = 11.0 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.34 (d, *J* = 11.0 Hz, 1 H), 4.15 (d, *J* = 8.5 Hz, 1 H), 3.69–3.66 (m, 1 H), 3.64–3.58 (m, 2 H), 3.00 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.95–2.91 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.7, 140.7, 137.6, 137.1, 134.8, 129.9, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.4, 125.2, 79.3, 75.1, 74.5, 73.5, 73.3, 69.1, 43.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}ClO_4$: 437.1520; found: 437.1511.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(3-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3am)

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 33 mg (59%); yellow oil; R_f = 0.42 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +89 (*c* 0.1, $CHCl_3$).

IR (neat): 2911, 2747, 1724, 1537, 1358, 1120 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.214–8.211 (m, 1 H), 8.08–8.06 (m, 1 H), 7.64–7.62 (m, 1 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.27–7.19 (m, 10 H), 5.45 (t, *J* = 5.5 Hz, 1 H), 4.73 (d, *J* = 11.5 Hz, 1 H), 4.51 (d, *J* = 12.5 Hz, 1 H), 4.41 (d, *J* = 12.0 Hz, 1 H), 4.35 (d, *J* = 11.5 Hz, 1 H), 4.15 (dd, *J* = 8.0, 0.5 Hz, 1 H), 3.75–3.72 (m, 1 H), 3.64–3.63 (m, 2 H), 3.03 (dd, *J* = 15.0, 5.0 Hz, 1 H), 2.98–2.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.0, 148.5, 141.2, 137.5, 136.9, 132.7, 129.7, 128.44, 128.41, 128.2, 128.0, 127.86, 127.80, 123.0, 122.2, 79.0, 75.9, 74.3, 73.6, 73.1, 69.2, 44.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}NO_6$: 448.1760; found: 448.1764.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(2-chlorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3an)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

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Yield: 35 mg (65%); colorless viscous oil; R_f = 0.60 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +97 (*c* 0.1, $CHCl_3$).

IR (neat): 2922, 2790, 1718, 1488, 1120, 745 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.42 (m, 1 H), 7.30–7.15 (m, 13 H), 5.70 (t, *J* = 6.0 Hz, 1 H), 4.74 (d, *J* = 11.0 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.41–4.38 (m, 2 H), 4.14–4.03 (m, 1 H), 3.90–3.87 (m, 1 H), 3.628–3.622 (m, 2 H), 2.93–2.89 (m, 1 H), 2.78 (dd, *J* = 15.0, 6.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.3, 137.7, 137.3, 137.2, 133.1, 129.8, 129.3, 128.4, 128.3, 128.1, 127.9, 127.69, 127.67, 126.9, 79.2, 75.9, 73.5, 72.9, 71.9, 69.7, 44.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}ClO_4$: 437.1520; found: 437.1527.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(2,4-dimethylphenyl)dihydro-2*H*-pyran-4(3*H*)-one (3ao)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 35 mg (65%); colorless viscous oil; R_f = 0.60 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +59 (*c* 0.1, $CHCl_3$).

IR (neat): 2820–2977, 1714, 1512, 1118, 1041 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.24–7.18 (m, 10 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 6.91 (s, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 5.50 (t, *J* = 5.0 Hz, 1 H), 4.81 (d, *J* = 11.5 Hz, 1 H), 4.48 (d, *J* = 12.0 Hz, 1 H), 4.38 (d, *J* = 11.5 Hz, 2 H), 4.16 (d, *J* = 8.5 Hz, 1 H), 3.59–3.56 (m, 1 H), 3.53–3.47 (m, 2 H), 2.97–2.96 (m, 2 H), 2.30 (s, 3 H), 2.19 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.5, 138.2, 137.8, 137.5, 137.4, 133.5, 131.9, 128.34, 128.33, 128.1, 127.8, 127.7, 127.6, 127.5, 126.3, 79.7, 73.7, 73.5, 73.4, 72.8, 69.1, 44.3, 20.9, 19.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_4$: 431.2222; found: 431.2227.

(2*R*,3*R*,6*S*)-3-Methoxy-2-(methoxymethyl)-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (3ba)[7]

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 23 mg (72%); white foam; R_f = 0.50 (35% EtOAc/hexane); $[\alpha]_D^{27}$ +53 (*c* 0.05, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.19 (m, 5 H), 5.39 (dd, *J* = 7.0, 2.5 Hz, 1 H), 3.89 (d, *J* = 7.5 Hz, 1 H), 3.53–3.51 (m, 3 H), 3.42 (s, 3 H), 3.35 (s, 3 H), 3.05–3.01 (m, 1 H), 2.98–2.93 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.5, 138.3, 128.6, 128.1, 127.3, 81.6, 75.1, 74.3, 71.5, 59.4, 59.3, 43.6.

(2*R*,3*R*,6*S*)-3-Methoxy-2-(methoxymethyl)-6-(4-methoxyphenyl)dihydro-2*H*-pyran-4(3*H*)-one (3bb)[7]

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 27 mg (76%); white foam; R_f = 0.28 (35% EtOAc/hexane); $[\alpha]_D^{27}$ +167 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{17}$ +128.8 (*c* 0.4, $CHCl_3$)}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.5 Hz, 2 H), 6.78 (d, *J* = 9.0 Hz, 2 H), 5.34 (dd, *J* = 6.5, 2.5 Hz, 1 H), 3.87 (d, *J* = 8.5 Hz, 1 H), 3.71 (s, 3 H), 3.53–3.46 (m, 3 H), 3.43 (s, 3 H), 3.34 (s, 3 H), 2.99 (dd, *J* = 14.5, 3.0 Hz, 1 H), 2.96–2.92 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.7, 159.4, 130.5, 128.8, 114.0, 81.8, 74.8, 73.9, 71.5, 59.5, 59.3, 55.2, 43.8.

(2*R*,3*R*,6*S*)-3-Methoxy-2-(methoxymethyl)-6-(4-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3bc)[7]

The product was purified by column chromatography on silica gel (25% EtOAc/hexane).

Yield: 24 mg (64%); white foam; R_f = 0.25 (35% EtOAc/hexane); $[\alpha]_D^{26}$ +104 (*c* 0.1, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 9.0 Hz, 2 H), 7.51 (d, *J* = 8.5 Hz, 2 H), 5.43 (t, *J* = 5.5 Hz, 1 H), 3.87 (d, *J* = 8.0 Hz, 1 H), 3.62–3.60 (m, 1 H), 3.57–3.56 (m, 2 H), 3.41 (s, 3 H), 3.35 (s, 3 H), 3.02–2.94 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1, 147.6, 146.0, 127.9, 123.8, 81.4, 75.8, 74.4, 71.8, 59.4, 59.2, 43.8.

(2*R*,3*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (3ca)[7]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 24 mg (48%); white foam; R_f = 0.62 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +112 (*c* 0.1, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.18 (m, 15 H), 5.25 (dd, *J* = 10.0, 3.5 Hz, 1 H), 4.86 (d, *J* = 12.0 Hz, 1 H), 4.50 (d, *J* = 4.5 Hz, 1 H), 4.48 (d, *J* = 5.0 Hz, 1 H), 4.42 (d, *J* = 12.5 Hz, 1 H), 4.38–4.35 (m, 1 H), 4.09 (dd, *J* = 6.5, 1.0 Hz, 1 H), 3.78–3.71 (m, 2 H), 2.73 (dd, *J* = 14.5, 4.0 Hz, 1 H), 2.59–2.54 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.1, 140.5, 137.9, 137.4, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.6, 127.5, 125.9, 79.2, 76.4, 74.7, 73.5, 72.6, 68.4, 47.9.

(2*R*,3*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-methoxyphenyl)dihydro-2*H*-pyran-4(3*H*)-one (3cb)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 28 mg (52%); white foam; R_f = 0.45 (20% EtOAc/hexane); $[\alpha]_D^{27}$ = +124 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{19}$ +39.5 (*c* 0.3, $CHCl_3$)}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.17 (m, 12 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 5.20 (dd, *J* = 9.5, 4.0 Hz, 1 H), 4.85 (d, *J* = 12.0 Hz, 1 H), 4.50–4.49 (m, 2 H), 4.42 (d, *J* = 12.5 Hz, 1 H), 4.34–4.31 (m, 1 H), 4.07 (dd, *J* = 6.5, 1.0 Hz, 1 H), 3.77–3.70 (m, 5 H), 2.73 (dd, *J* = 14.5, 4.0 Hz, 1 H), 2.61–2.56 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.4, 159.4, 137.9, 137.4, 132.5, 128.4, 128.3, 127.9, 127.8, 127.66, 127.60, 127.4, 113.9, 79.3, 76.2, 74.5, 73.5, 72.6, 68.4, 55.3, 47.6.

(2*R*,3*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-chlorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3cc)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 26 mg (48%); white foam; R_f = 0.64 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +97 (*c* 0.1, $CHCl_3$).

IR (neat): 2945, 2861, 1727, 1487, 1128, 734 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.19 (m, 14 H), 5.22 (dd, *J* = 10.0, 3.5 Hz, 1 H), 4.87 (d, *J* = 12.0 Hz, 1 H), 4.51–4.47 (m, 2 H), 4.42 (d, *J* = 12.5 Hz, 1 H), 4.36–4.33 (m, 1 H), 4.07 (dd, *J* = 6.5, 1.5 Hz, 1 H), 3.78–3.70 (m, 2 H), 2.71 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.52–2.47 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.8, 139.1, 137.8, 137.3, 133.7, 128.7, 128.5, 128.3, 128.0, 127.8, 127.6, 127.3, 79.0, 76.5, 74.1, 73.6, 72.7, 68.4, 47.9.

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HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}ClO_4$: 437.1520; found: 437.1521.

(2*S*,3*S*,6*R*)-3-(Benzyloxy)-2-methyl-6-(4-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3da)[7]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 29 mg (67%); white foam; R_f = 0.25 (20% EtOAc/hexane); $[\alpha]_D^{27}$ –49 (*c* 0.1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.14–8.11 (m, 2 H), 7.50 (d, *J* = 8.5 Hz, 2 H), 7.27–7.22 (m, 5 H), 5.24 (t, *J* = 5.5 Hz, 1 H), 4.73 (d, *J* = 11.5 Hz, 1 H), 4.40 (d, *J* = 11.5 Hz, 1 H), 3.81 (quin, *J* = 6.5 Hz, 1 H), 3.61 (d, *J* = 7.0 Hz, 1 H), 3.06 (dd, *J* = 14.5, 5.0 Hz, 1 H), 2.89–2.85 (m, 1 H), 1.24 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.5, 147.5, 146.4, 136.9, 128.4, 128.18, 128.10, 127.7, 123.8, 84.1, 73.6, 73.2, 72.8, 44.4, 17.5.

(2*S*,3*S*,6*R*)-3-(Benzyloxy)-2-methyl-6-(3-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3db)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 28 mg (65%); white foam; R_f = 0.25 (20% EtOAc/hexane); $[\alpha]_D^{27}$ –84 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{19}$ –87.3 (*c* 0.3, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (s, 1 H), 8.08–8.07 (m, 1 H), 7.64 (d, *J* = 7.5 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 1 H), 7.27–7.22 (m, 5 H), 5.24 (t, *J* = 5.5 Hz, 1 H), 4.74 (d, *J* = 11.5 Hz, 1 H), 4.41 (d, *J* = 11.5 Hz, 1 H), 3.83 (quin, *J* = 6.5 Hz, 1 H), 3.62 (d, *J* = 7.0 Hz, 1 H), 3.09 (dd, *J* = 14.5, 5.5 Hz, 1 H), 2.88 (dd, *J* = 14.0, 6.0 Hz, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.5, 148.5, 141.5, 136.9, 132.6, 129.7, 128.4, 128.2, 128.1, 123.0, 122.0, 84.1, 73.5, 73.1, 72.8, 44.5, 17.5.

(2*S*,3*S*,6*R*)-3-(Benzyloxy)-6-(4-methoxyphenyl)-2-methyldihydro-2*H*-pyran-4(3*H*)-one (3dc)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 28 mg (68%); white foam; R_f = 0.30 (20% EtOAc/hexane); $[\alpha]_D^{27}$ –64 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{27}$ = –141.2 (*c* 1.1, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 7 H), 6.86 (d, *J* = 9.0 Hz, 2 H), 5.27 (dd, *J* = 7.0, 3.0 Hz, 1 H), 4.87 (d, *J* = 11.5 Hz, 1 H), 4.49 (d, *J* = 11.5 Hz, 1 H), 3.82–3.73 (m, 4 H), 3.66 (d, *J* = 8.0 Hz, 1 H), 3.11 (dd, *J* = 14.5, 3.0 Hz, 1 H), 2.95–2.91 (m, 1 H), 1.28 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.6, 159.2, 137.2, 131.0, 128.6, 128.3, 128.2, 127.9, 113.9, 84.8, 74.3, 73.0, 71.4, 55.2, 44.5, 18.2.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-methyl-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (3ea)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 27 mg (72%); white foam; R_f = 0.45 (10% EtOAc/hexane); $[\alpha]_D^{27}$ +153 (*c* 0.1, $CHCl_3$).

IR (neat): 2949, 2877, 1730, 1514, 1166 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 10 H), 5.28 (dd, *J* = 6.5, 4.0 Hz, 1 H), 4.84 (d, *J* = 11.5 Hz, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 3.81 (quin, *J* = 6.5 Hz, 1 H), 3.66 (d, *J* = 7.5 Hz, 1 H), 3.14 (dd, *J* = 14.0, 3.5 Hz, 1 H), 2.93–2.89 (m, 1 H), 1.28 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.3, 139.0, 137.2, 128.6, 128.3, 128.1, 128.0, 127.9, 127.0, 84.6, 74.5, 72.9, 71.8, 44.4, 18.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{21}O_3$: 297.1491; found: 297.1497.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-6-(4-methoxyphenyl)-2-methyldihydro-2*H*-pyran-4(3*H*)-one (3eb)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 30 mg (75%); white foam; R_f = 0.25 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +150 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{19}$ +102.8 (*c* 0.4, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 7 H), 6.87–6.85 (m, 2 H), 5.27 (dd, *J* = 6.5, 3.0 Hz, 1 H), 4.87 (d, *J* = 11.5 Hz, 1 H), 4.49 (d, *J* = 11.5 Hz, 1 H), 3.82–3.73 (m, 4 H), 3.66 (d, *J* = 8.0 Hz, 1 H), 3.12 (dd, *J* = 14.5, 3.0 Hz, 1 H), 2.94 (dd, *J* = 14.0, 6.5 Hz, 1 H), 1.28 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.6, 159.2, 137.2, 131.0, 128.6, 128.3, 128.2, 127.9, 113.9, 84.8, 74.3, 73.0, 71.4, 55.2, 44.5, 18.2.

(2*R*,3*R*,6*S*)-3-(Benzyloxy)-2-methyl-6-(4-nitrophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3ec)

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 30 mg (70%); white foam; R_f = 0.35 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +87 (*c* 0.1, $CHCl_3$).

IR (neat): 2949, 2877, 1724, 1531, 1356 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.21–8.19 (m, 2 H), 7.57 (d, *J* = 8.5 Hz, 2 H), 7.36–7.28 (m, 5 H), 5.31 (t, *J* = 5.5 Hz, 1 H), 4.80 (d, *J* = 11.5 Hz, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 3.89 (quin, *J* = 6.5 Hz, 1 H), 3.70 (dd, *J* = 7.0, 0.5 Hz, 1 H), 3.13 (dd, *J* = 14.5, 5.0 Hz, 1 H), 2.96–2.92 (m, 1 H), 1.32 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.5, 147.5, 146.4, 136.9, 128.4, 128.1, 128.0, 127.7, 123.8, 84.1, 73.6, 73.2, 72.8, 44.5, 17.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{20}NO_5$: 342.1341; found: 342.1344.

(2*R*,3*R*,6*R*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (3fa)[8]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 30 mg (60%); white foam; R_f = 0.63 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +65 (*c* 0.05, $CHCl_3$) {Lit.[12] $[\alpha]_D^{20}$ +84.8 (*c* 0.2, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.19 (m, 15 H), 4.86 (d, *J* = 11.0 Hz, 1 H), 4.61–4.57 (m, 1 H), 4.61 (t, *J* = 7.2 Hz, 1 H), 4.50 (d, *J* = 12.5 Hz, 1 H), 4.42 (d, *J* = 11.5 Hz, 1 H), 4.20–4.18 (m, 1 H), 3.77–3.75 (m, 3 H), 2.69–2.67 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.7, 139.9, 138.1, 137.3, 128.5, 128.38, 128.36, 128.2, 128.1, 127.9, 127.69, 127.63, 125.6, 80.8, 79.6, 79.3, 73.5, 69.1, 49.9.

(2*R*,3*R*,6*R*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-methoxyphenyl)dihydro-2*H*-pyran-4(3*H*)-one (3fb)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 34 mg (63%); white foam; R_f = 0.42 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +106 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{16}$ +105.0 (*c* 0.1, $CHCl_3$)}.

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^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.29 (m, 12 H), 6.89 (d, *J* = 8.5 Hz, 2 H), 4.93 (d, *J* = 11.5 Hz, 1 H), 4.65–4.63 (m, 1 H), 4.57 (dd, *J* = 10.5, 3.0 Hz, 1 H), 4.56 (d, *J* = 12.5 Hz, 1 H), 4.49 (d, *J* = 11.0 Hz, 1 H), 4.26 (d, *J* = 9.0 Hz, 1 H), 3.82–3.79 (m, 6 H), 2.78–2.69 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.9, 159.4, 138.1, 137.4, 132.1, 128.38, 128.35, 128.2, 127.9, 127.7, 127.6, 127.0, 113.9, 80.7, 79.6, 79.1, 73.52, 73.50, 69.1, 55.3, 49.9.

(2*R*,3*R*,6*R*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-chlorophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3fc)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 30 mg (55%); white foam; R_f = 0.58 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +53 (*c* 0.05, $CHCl_3$).

IR (neat): 2949, 2870, 1727, 1514, 1166, 742 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.26 (m, 14 H), 4.93 (d, *J* = 11.0 Hz, 1 H), 4.66–4.62 (m, 1 H), 4.58 (dd, *J* = 10.4, 3.2 Hz, 1 H), 4.56 (d, *J* = 12.5 Hz, 1 H), 4.48 (d, *J* = 11.0 Hz, 1 H), 4.26–4.24 (m, 1 H), 3.84–3.80 (m, 3 H), 2.74–2.66 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.2, 138.5, 138.0, 137.3, 133.8, 128.7, 128.38, 128.35, 128.2, 127.9, 127.6, 127.0, 80.7, 79.5, 78.5, 73.51, 73.50, 69.0, 49.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}ClO_4$: 437.1520; found: 437.1525.

(2*R*,3*R*,6*R*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(4-bromophenyl)dihydro-2*H*-pyran-4(3*H*)-one (3fd)[8]

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 38 mg (64%); white foam; R_f = 0.58 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +69 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{20}$ +133.6 (*c* 0.2, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.5 Hz, 2 H), 7.26–7.18 (m, 12 H), 4.86 (d, *J* = 11.0 Hz, 1 H), 4.56–4.55 (m, 1 H), 4.57 (dd, *J* = 10.5, 3.0 Hz, 1 H), 4.49 (d, *J* = 12.5 Hz, 1 H), 4.42 (d, *J* = 11.0 Hz, 1 H), 4.19–4.17 (m, 1 H), 3.76–3.73 (m, 3 H), 2.68–2.59 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.2, 139.0, 138.0, 137.3, 131.7, 128.4, 128.3, 128.2, 128.0, 127.7, 127.3, 122.0, 80.7, 79.5, 78.6, 73.55, 73.53, 69.0, 49.8.

(2*R*,3*R*,6*R*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-(*p*-tolyl)dihydro-2*H*-pyran-4(3*H*)-one (3fe)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 35 mg (68%); white foam; R_f = 0.62 (20% EtOAc/hexane); $[\alpha]_D^{27}$ +74 (*c* 0.1, $CHCl_3$).

IR (neat): 2952, 2894, 1729, 1515, 1248, 833 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.39 (m, 1 H), 7.36–7.30 (m, 11 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 4.96 (d, *J* = 11.0 Hz, 1 H), 4.72–4.67 (m, 1 H), 4.67 (dd, *J* = 10.8, 2.9 Hz, 1 H), 4.59 (d, *J* = 12.5 Hz, 1 H), 4.52 (d, *J* = 11.0 Hz, 1 H), 4.30 (d, *J* = 9.0 Hz, 1 H), 3.86–3.83 (m, 3 H), 2.82–2.73 (m, 2 H), 2.37 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.9, 138.1, 137.9, 137.4, 137.0, 129.2, 128.5, 128.38, 128.35, 128.2, 127.9, 127.7, 127.6, 126.9, 125.6, 80.8, 79.6, 79.3, 73.51, 73.50, 69.1, 49.9, 21.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_4$: 417.2066; found: 417.2061.

(2*S*,3*S*,6*S*)-3-(Benzyloxy)-6-(4-methoxyphenyl)-2-methyldihydro-2*H*-pyran-4(3*H*)-one (3ga)[8]

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 25 mg (61%); white foam; R_f = 0.35 (20% EtOAc/hexane); $[\alpha]_D^{27}$ –109 (*c* 0.1, $CHCl_3$) {Lit.[12] $[\alpha]_D^{22}$ –224.9 (*c* 0.7, $CHCl_3$)}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.35 (m, 4 H), 7.32 (d, *J* = 7.0 Hz, 1 H), 7.28 (d, *J* = 9.0 Hz, 2 H), 6.90–6.88 (m, 2 H), 4.99 (d, *J* = 11.5 Hz, 1 H), 4.62 (dd, *J* = 11.0, 3.0 Hz, 1 H), 4.54 (d, *J* = 11.5 Hz, 1 H), 3.80 (s, 3 H), 3.77–3.76 (m, 2 H), 2.78–2.68 (m, 2 H), 1.45 (d, *J* = 5.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.6, 159.4, 137.4, 132.2, 128.4, 128.2, 128.0, 127.0, 114.0, 84.8, 78.9, 77.6, 77.2, 73.2, 55.3, 49.9, 19.3.

(2*S*,3*S*,6*S*)-3-(Benzyloxy)-6-(4-nitrophenyl)-2-methyldihydro-2*H*-pyran-4(3*H*)-one (3gb)

The product was purified by column chromatography on silica gel (20% EtOAc/hexane).

Yield: 27 mg (63%); white foam; R_f = 0.30 (20% EtOAc/hexane); $[\alpha]_D^{27}$ –106 (*c* 0.1, $CHCl_3$).

IR (neat): 2911, 2821, 1734, 1514, 1358, 841 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 9.0 Hz, 2 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.41–7.30 (m, 5 H), 5.99 (d, *J* = 11.5 Hz, 1 H), 4.78 (dd, *J* = 12.0, 2.5 Hz, 1 H), 4.55 (d, *J* = 11.5 Hz, 1 H), 3.85–3.76 (m, 2 H), 2.81–2.77 (m, 1 H), 2.67–2.61 (m, 1 H), 1.48 (d, *J* = 5.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.2, 147.6, 147.2, 137.2, 128.5, 128.3, 128.1, 126.3, 123.9, 84.5, 77.86, 77.80, 73.4, 49.7, 19.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{20}NO_5$: 342.1341; found: 342.1338.

(2*R*,3*R*,6*S*)-3-Hydroxy-2-(hydroxymethyl)-6-phenyldihydro-2*H*-pyran-4(3*H*)-one (4a)

To a solution of **3ab** (100 mg, 0.25 mmol) in methanol/EtOAc/AcOH (1:1:.2) was added 10% Pd/C (25 mg) and the resulting suspension was stirred for 24 h at room temperature in the presence of H_2 gas (balloon). The Pd/C was removed from the reaction by filtration through Celite and the filtrate was concentrated. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate, 50:50) to afford the pure product **4a**.

Yield: 52 mg (92%); colorless oil; $[\alpha]_D^{26}$ = +57 (*c* 0.1, $CHCl_3$).

IR (neat): 3353, 1721, 831 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.21 (m, 5 H), 5.48 (d, *J* = 7.5 Hz, 1 H), 4.25 (d, *J* = 10.0 Hz, 1 H), 3.79–3.72 (m, 2 H), 3.57 (s, 1 H), 3.27–3.23 (m, 1 H), 3.17–3.14 (m, 1 H), 3.10–3.06 (m, 1 H), 2.24 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.8, 137.8, 128.8, 128.3, 127.4, 76.2, 75.4, 73.6, 62.5, 41.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}O_4$: 223.0970; found: 223.0957.

(2*R*,3*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-4-methylene-6-phenyltetrahydro-2*H*-pyran (4b)

A solution of *n*-BuLi (0.6 mL, 1.6 M in *n*-hexane, 1.0 mmol) was added to a stirred suspension of methyltriphenylphosphonium bromide (355 mg, 1.0 mmol) in dry THF (10 mL) at –20 °C. The reaction mixture was stirred at the same temperature for 1 h and then treated with a solution of compound **3ab** (200 mg, 0.5 mmol) in dry THF (5 mL). Following the addition, the mixture was allowed to stir at room temperature for 5 h. After completion, the reaction mixture was

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poured into ice water and then extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The crude residue was purified by silica gel column chromatography (hexane/ethyl acetate, 90:10) to afford the pure alkene **4b**.

Yield: 155 mg (78%); colorless viscous oil; $[\alpha]_D^{27}$ +17 (*c* 0.1, $CHCl_3$).

IR (neat): 2842, 1615, 1248, 814 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 7.5 Hz, 2 H), 7.25–7.15 (m, 13 H), 5.03 (s, 1 H), 4.91 (s, 1 H), 4.59 (dd, *J* = 9.5, 3.5 Hz, 1 H), 4.54 (d, *J* = 11.5 Hz, 1 H), 4.44 (s, 2 H), 4.30 (d, *J* = 12.0 Hz, 1 H), 4.17–4.14 (m, 1 H), 3.80 (d, *J* = 3.0 Hz, 1 H), 3.60 (dd, *J* = 10.0, 6.0 Hz, 1 H), 3.53 (dd, *J* = 10.0, 7.0 Hz, 1 H), 2.67 (dd, *J* = 13.5, 10.0 Hz, 1 H), 2.33 (dd, *J* = 13.5, 3.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.5, 141.0, 138.2, 138.0, 128.32, 128.30, 128.2, 127.7, 127.67, 127.60, 127.4, 126.2, 113.8, 76.8, 76.1, 74.4, 73.0, 70.0, 67.7, 37.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_3$: 401.2117; found: 401.2113.

Grignard Reaction; General Procedure

To a stirred solution of compound **3ab** (100 mg, 0.25 mmol) in dry THF (10 mL) at –20 °C was added dropwise a solution of the corresponding Grignard reagent (RMgBr) in THF or Et_2O (0.35 mmol) via a syringe. The resulting mixture was stirred at this temperature for 30 min and then at room temperature for another 2–3 h. After completion, the reaction mixture was diluted with ice-cold water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford the product **4c–h**.

(2*R*,3*R*,4*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-4-methyl-6-phenyltetrahydro-2*H*-pyran-4-ol (4c)

The product was purified by column chromatography on silica gel (15% EtOAc/hexane).

Yield: 89 mg (86%); yellowish viscous oil; R_f = 0.70 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +26 (*c* 0.1, $CHCl_3$).

IR (neat): 3460, 2914, 2894, 1515, 1248, 798 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 7.5 Hz, 2 H), 7.31–7.11 (m, 13 H), 4.94 (dd, *J* = 6.0, 4.0 Hz, 1 H), 4.61 (d, *J* = 12.0 Hz, 1 H), 4.54–4.47 (m, 3 H), 3.88–3.85 (m, 1 H), 3.68 (d, *J* = 3.5 Hz, 2 H), 3.48 (d, *J* = 8.0 Hz, 1 H), 2.43 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.01 (dd, *J* = 14.5, 6.5 Hz, 2 H), 1.23 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.2, 137.9, 137.7, 128.36, 128.33, 128.02, 128.01, 127.77, 127.70, 127.6, 126.6, 126.0, 79.0, 74.5, 73.5, 72.3, 70.28, 70.24, 69.3, 38.8, 27.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{31}O_4$: 419.2222; found: 419.2217.

(2*R*,3*R*,4*S*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-4-pentyl-6-phenyltetrahydro-2*H*-pyran-4-ol (4d)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 94 mg (80%); yellowish viscous oil; R_f = 0.70 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +26 (*c* 0.1, $CHCl_3$).

IR (neat): 3252, 2894, 1500, 1244, 811 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.45 (m, 2 H), 7.39–7.36 (m, 2 H), 7.34–7.26 (m, 8 H), 7.22–7.16 (m, 3 H), 5.03 (dd, *J* = 6.0, 4.5 Hz, 1 H), 4.69 (d, *J* = 12.0 Hz, 1 H), 4.59–4.53 (m, 3 H), 4.94–3.92 (m, 1 H), 3.75 (d, *J* = 3.5 Hz, 2 H), 3.60 (d, *J* = 8.5 Hz, 1 H), 2.45 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.06 (dd, *J* = 14.5, 6.5 Hz, 1 H), 1.65–1.59 (m, 1 H), 1.51–1.43 (m, 2 H), 1.35–1.24 (m, 5 H), 0.90 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.5, 137.9, 137.8, 128.9, 128.5, 128.4, 128.35, 128.32, 128.0, 127.7, 127.67, 127.64, 126.6, 126.0, 77.8, 74.4, 73.5, 72.4, 72.3, 70.2, 69.6, 40.0, 35.9, 32.4, 22.9, 22.6, 14.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{39}O_4$: 475.2848; found: 475.2845.

(2*R*,3*R*,4*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-4-isopropyl-6-phenyltetrahydro-2*H*-pyran-4-ol (4e)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 77 mg (70%); colorless viscous oil; R_f = 0.68 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +17 (*c* 0.05, $CHCl_3$).

IR (neat): 3311, 2886, 1522, 1212, 836 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.46 (m, 2 H), 7.39–7.26 (m, 10 H), 7.23–7.21 (m, 1 H), 7.14 (dd, *J* = 7.5, 2.0 Hz, 2 H), 5.09 (dd, *J* = 6.5, 3.5 Hz, 1 H), 4.71 (d, *J* = 12.0 Hz, 1 H), 4.57–4.54 (m, 3 H), 3.93–3.87 (m, 2 H), 3.78–3.72 (m, 2 H), 2.34 (dd, *J* = 14.5, 3.5 Hz, 1 H), 2.10–2.04 (m, 1 H), 2.00–1.94 (m, 1 H), 1.04 (d, *J* = 7.0 Hz, 3 H), 1.01 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.7, 138.0, 137.9, 128.37, 128.33, 128.0, 127.9, 127.7, 127.6, 127.4, 126.5, 126.1, 77.2, 74.9, 74.8, 74.0, 73.6, 72.4, 70.1, 69.8, 34.0, 18.1, 16.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{35}O_4$: 447.2535; found: 447.2531.

(2*R*,3*R*,4*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-phenyl-4-vinyltetrahydro-2*H*-pyran-4-ol (4f)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 80 mg (75%); yellowish viscous oil; R_f = 0.65 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +59 (*c* 0.1, $CHCl_3$).

IR (neat): 3261, 2869, 1519, 1248, 825 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.48 (m, 2 H), 7.38–7.24 (m, 10 H), 7.21–7.20 (m, 1 H), 7.10–7.09 (m, 2 H), 5.98 (dd, *J* = 17.0, 10.5 Hz, 1 H), 5.46 (d, *J* = 17.0 Hz, 1 H), 5.20 (d, *J* = 10.5 Hz, 1 H), 5.09 (d, *J* = 5.5 Hz, 1 H), 4.69 (d, *J* = 12.0 Hz, 1 H), 4.55 (dd, *J* = 10.5, 3.5 Hz, 2 H), 4.44 (d, *J* = 10.5 Hz, 1 H), 3.92–3.89 (m, 1 H), 3.74 (d, *J* = 3.5 Hz, 2 H), 3.70 (d, *J* = 9.0 Hz, 1 H), 2.49 (dd, *J* = 14.5, 2.0 Hz, 1 H), 2.24 (dd, *J* = 15.0, 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.4, 140.9, 138.0, 137.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.74, 127.67, 127.64, 126.5, 126.2, 125.9, 114.4, 77.4, 74.4, 73.6, 72.7, 72.0, 69.3, 69.2, 36.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_4$: 431.2222; found: 431.2228.

(2*R*,3*R*,4*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-6-phenyl-4-(*p*-tolyl)tetrahydro-2*H*-pyran-4-ol (4g)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 86 mg (70%); colorless viscous oil; R_f = 0.70 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +27 (*c* 0.1, $CHCl_3$).

IR (neat): 3221, 2886, 1511, 1236, 789 cm^{-1}.

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^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 4 H), 7.39–7.37 (m, 2 H), 7.35–7.27 (m, 6 H), 7.20–7.12 (m, 5 H), 6.77 (dd, *J* = 7.5, 1.5 Hz, 2 H), 5.21 (d, *J* = 6.5 Hz, 1 H), 4.71 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.11–4.06 (m, 2 H), 3.99–3.96 (m, 1 H), 3.75–3.72 (m, 4 H), 2.71–2.68 (m, 1 H), 2.58 (dd, *J* = 15.5, 7.5 Hz, 1 H), 2.36 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.3, 141.0, 138.0, 137.4, 136.6, 128.9, 128.3, 128.06, 128.05, 127.9, 127.7, 127.6, 127.5, 126.4, 126.2, 125.2, 78.8, 74.2, 74.1, 73.6, 72.5, 69.5, 69.4, 67.9, 39.2, 20.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{35}O_4$: 495.2535; found: 495.2539.

(2*R*,3*R*,4*R*,6*S*)-3-(Benzyloxy)-2-[(benzyloxy)methyl]-4,6-diphenyltetrahydro-2*H*-pyran-4-ol (4h)

The product was purified by column chromatography on silica gel (10% EtOAc/hexane).

Yield: 91 mg (76%); colorless viscous oil; R_f = 0.68 (20% EtOAc/hexane); $[\alpha]_D^{26}$ +29 (*c* 0.1, $CHCl_3$).

IR (neat): 3251, 2785, 1541, 833 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62–7.60 (m, 2 H), 7.54–7.52 (m, 2 H), 7.40–7.21 (m, 11 H), 7.15–7.10 (m, 3 H), 6.74–6.72 (m, 2 H), 5.22 (d, *J* = 6.5 Hz, 1 H), 4.71 (d, *J* = 12.5 Hz, 1 H), 4.56 (d, *J* = 12.5 Hz, 1 H), 4.12 (d, *J* = 9.5 Hz, 1 H), 4.07 (d, *J* = 10.5 Hz, 1 H), 4.00–3.97 (m, 1 H), 3.78–3.73 (m, 2 H), 3.68 (d, *J* = 10.5 Hz, 1 H), 2.72 (dd, *J* = 15.0, 1.5 Hz, 1 H), 2.60 (dd, *J* = 15.0, 6.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.2, 140.9, 138.0, 137.3, 128.3, 128.2, 128.08, 128.06, 127.9, 127.66, 127.59, 127.5, 127.0, 126.4, 126.1, 125.3, 78.8, 77.2, 74.3, 74.2, 73.6, 72.5, 69.5, 69.4, 39.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{33}O_4$: 481.2379; found: 481.2384.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611916.

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