JOC The Journal of Organic Chemistry
Cite This: J. Org. Chem. XXXX, XXX, XXX−XXX
Note
pubs.acs.org/joc

Use of XtalFluor-E as an Alternative to $POCl_3$ in the Vilsmeier−Haack Formylation of *C*-2-Glycals

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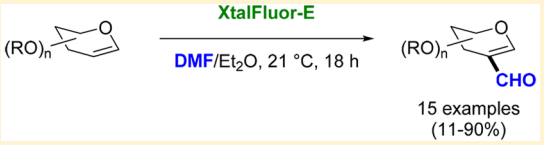
Supporting Information

ABSTRACT: We report the use of XtalFluor-E ($[Et_2NSF_2]BF_4$) as an alternative to $POCl_3$ in the Vilsmeier−Haack formylation reaction of *C*-2-glycals. Employing a XtalFluor-E/DMF combination allowed the desired *C*-2-formyl glycals to be isolated in 11−90% yield. This method was extended to the synthesis of a *C*-2-formylated disaccharide glycal.

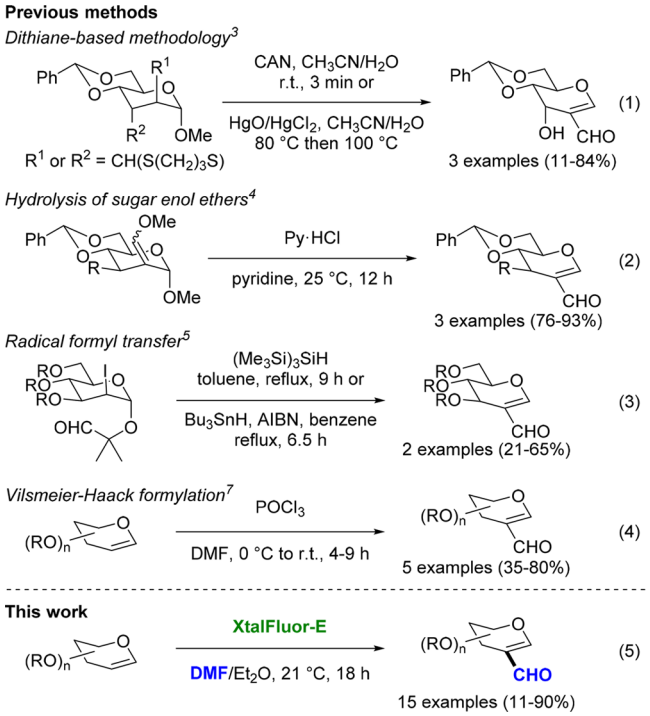


INTRODUCTION

C-2-Formyl-glycals, a class of carbohydrates incorporating an α,β-unsaturated aldehyde, have been the subject of increased attention as they afford valuable chiral building blocks. The presence of a conjugated enal group, their built-in chirality, and their synthetic versatility make them attractive intermediates in synthetic organic chemistry.[1] Apart from their synthetic interest, *C*-2-formyl glycals have found applications in medicinal, biological, supramolecular, and material chemistry.[2] A number of methods have been reported for the preparation of *C*-2-formylated glycals (Scheme 1, eqs 1−3),[3−5] but the Vilsmeier−Haack reaction[6] remains the most employed technique as it offers a direct access to introduce the formyl group at the *C*-2-position from readily accessible precursors (eq 4).[7] However, this reaction employs $POCl_3$, a highly toxic and corrosive reagent that reacts violently with water. Herein, we report alternative conditions for the Vilsmeier−Haack formylation where $POCl_3$ is replaced by XtalFluor-E ($[Et_2NSF_2]BF_4$),[8−11] a less toxic and more hydrolytically stable reagent, for the synthesis of *C*-2-formyl glycals possessing diverse functional groups (eq 5).

Initial Vilsmeier−Haack formylation reaction on tri-OBn glycal **1a** was realized using 3 equiv of XtalFluor-E in DMF (1 M) during 18 h at 21 °C and showed promise with the isolation of the corresponding formylated glucal **2a** in 59% yield (Table 1, entry 1). However, the reaction did not go to completion and starting material was recovered. Leaving the reaction longer (2 days) did not improve the conversion, and **2a** was obtained in slightly lower yield (entry 2). Conducting the reaction at higher temperatures resulted in lower yields and led to the degradation of the starting material **1a** (entry 3).[12] Diluting the reaction did not furnish better results, and concentrating the reaction led to solubility issues (entries 4 and 5). Various additives (pivalic acid, citric acid, DBU, and DIPEA), in both catalytic and stoichiometric amounts, were also tested, but no improvements were noticed (data not shown). We next investigated the use of various cosolvents in a 1:1 mixture with DMF, and selected results are shown (entries 6−12).[13] Gratifyingly, the formylated glucal was isolated in 80% yield when Et_2O was used (entry 12). Increasing the amount of Et_2O in the mixture resulted in lower yield due the insolubility of XtalFluor-E. Reducing the amount of XtalFluor-E resulted in a much slower reaction (entries 12−14), probably because it lowered the concentration of the formylating agent (vide infra). Overall, the conditions shown in Table 1, entry 12, proved to be optimal.[14]

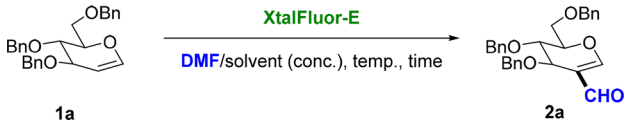
Scheme 1. Previous Methods and Current Approach



Received: April 20, 2018

DOI: 10.1021/acs.joc.8b01006
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 1. Key Optimization Results for Formylation of 1a Using XtalFluor-E



1a 2a

entry	XtalFluor-E (equiv)	cosolvent (ratio)	conc (M)	temp (°C)	time (h)	yield (%)[a]
1	3		1	21	18	59
2	3		1	21	42	45
3	3		1	50	18	30
4	3		0.1	21	18	12
5	3		2	21	18	20
6	3	CH_3CN (1:1)	1	21	18	73
7	3	EtOAc (1:1)	1	21	18	72
8	3	$CHCl_3$ (1:1)	1	21	18	73
9	3	toluene (1:1)	1	21	18	73
10	3	THF (1:1)	1	21	18	65
11	3	DCE (1:1)	1	21	18	67
12	3	Et_2O (1:1)	1	21	18	80
13	2	Et_2O (1:1)	1	21	18	18
14	1	Et_2O (1:1)	1	21	18	8

[a]Isolated yield of **2a** after purification on silica gel.

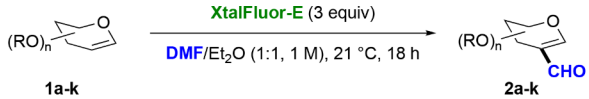
We next evaluated the reactivity of different glycals possessing diverse functional groups under the optimized conditions. The results are summarized in Table 2 with the corresponding yields of the formyl glycals reported so far in the literature. Under our conditions, we obtained moderate to excellent yields of the formylated ether protected products **2a**–**f**,**m**. These yields are comparable to the ones reported in the literature or even better for some examples. The yields for MOM protected products **2g** and **2h** are particularly low due to their instability on silica gel. Acetyl and benzylidene (acid-labile groups) are compatible. Hence, **2i**, **2j**, **2k**, and **2l** were isolated in 19%, 36%, 46%, and 27% yield, respectively. In those cases, conversion was not complete under those conditions. In general, the yields were found to be lower for the formylation in the glucal series than in the galactal series. This can be explained by electronic and steric effects of the 4-protected group in the pseudoequatorial position that is closer to the incoming Vilsmeier–Haack reagent and that decreases the electron density of the double bond.[15]

Lellouche and co-workers reported the particular sensitivity of silyl ether glucals toward Vilsmeier–Haack conditions.[19] When these glucals were treated with the Vilsmeier–Haack reagent, selective silyl deprotection of the *C*-6 primary alcohol occurred followed by its *O*-formylation to afford the corresponding *O*-6-formate. However, in the presence of an excess of reagent neither subsequent *O*-formylation to di- or triformates nor *C*-2 formylation was observed. In that context, we were curious to try our conditions on 3,4-di-OBn-6-OTBS glucal **1n**. Interestingly, we did not isolate the expected product from the *C*-6 formylation, but we isolated formyl formate glucal **4** (obtained from the bis formylation at the *O*-6- and *C*-2- positions) along with the formate glucal **3** (product of the *O*-6-formylation) (Scheme 2, eq 1). In a similar way, when subjected to our Vilsmeier–Haack conditions, 3,4-di-OPMB-6-OTr glucal **1o** provided 12% of the desired formyl glucal **2o** along with 10% of the formate glucal **5** and 22% yield of the formyl formate glucal **6** (eq 2).

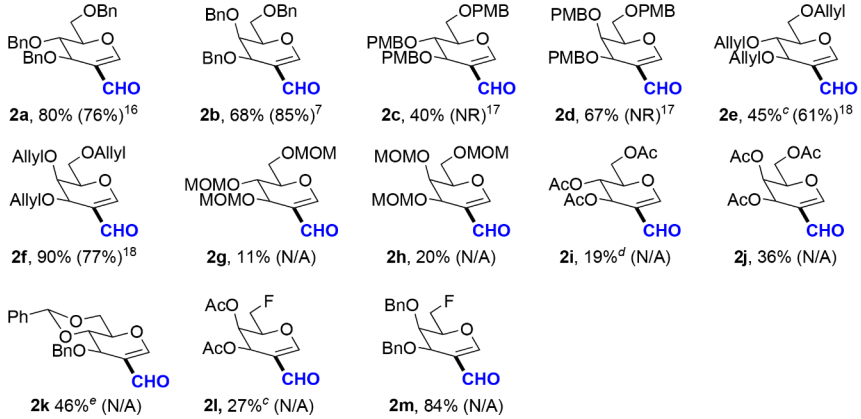
Finally, our methodology was extended to disaccharide glycal, in the form of hexa-OBn lactal **7**. The corresponding formyl lactal **8** was obtained in 56% yield, whereas a 37% yield was obtained using classical Vilsmeier–Haack conditions (Scheme 3).[20]

With respect to the reaction mechanism, we propose one similar to the classical $POCl_3$-promoted Vilsmeier–Haack formylation but with a structurally different formylating agent (Scheme 4).[15,19a] In the present case, nucleophilic attack of the amide carbonyl group of DMF at the electrophilic sulfur of $[Et_2NSF_2]BF_4$ would generate intermediate **9**.[8a] As the

Table 2. Scope of the Formylation of *C*-2-Glycals Using XtalFluor-E[a,b]



1a-k 2a-k



[a]Isolated yield of **2** after column chromatography. [b]Literature isolated yield using a $POCl_3$-mediated Vilsmeier–Haack protocol is provided in parentheses, when available, with the appropriate reference.[16−18] NR = not reported. N/A = not available. [c]The reaction was performed in 1 M DMF. [d]The reaction was carried out with 0.1 equiv of DIPEA. [e]The reaction was conducted at 0.5 M.

DOI: 10.1021/acs.joc.8b01006
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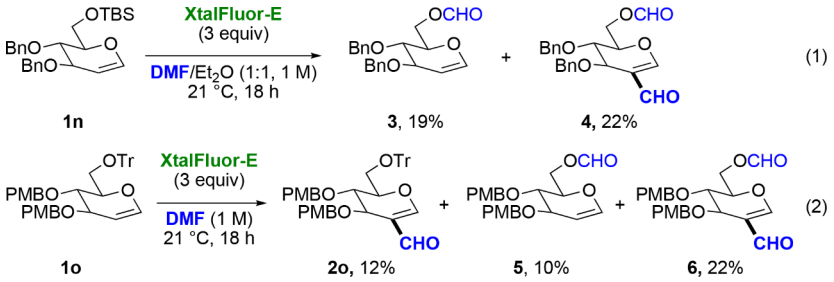
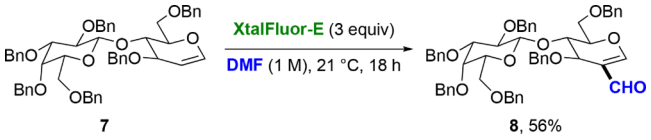
Scheme 2. Unexpected Formylation Outcomes



Scheme 3. Formylation of a Disaccharide Glycal



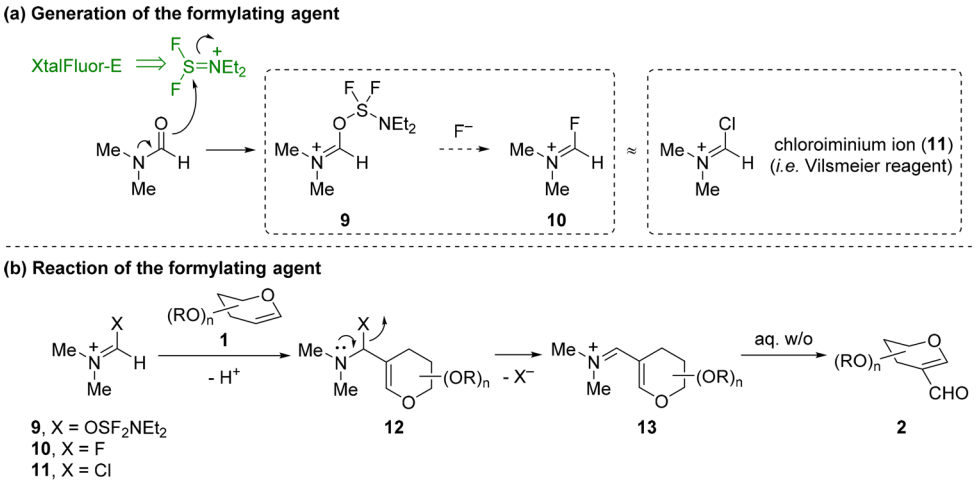
formylation reaction proceeds and fluoride ions are released into the reaction mixture (vide infra), **9** could potentially be converted to **10**,[21] the fluoride equivalent of the Vilsmeier reagent (Scheme 4a). We hypothesize that intermediate **9** or **10** could react similarly to the classical Vilsmeier reagent (**11**) in promoting the formylation reaction of *C*-2-glycals (Scheme 4b). Here, the formylating agent (**9** or **10**) would react with a *C*-2-glycal (**1**) to generate intermediate **12**. Nitrogen-assisted expulsion of the X group would produce the iminium **13** that would, upon an aqueous workup, release the *C*-2-formyl glycal (**2**). In the case of **9**, the (diethylamino)difluoro-λ^4-sulfanolate expelled would decompose to diethylsulfuramidous fluoride and fluoride, the latter being required for the potential conversion of **9** to **10** (Scheme 4a).

In conclusion, we have reported the use of a XtalFluor-E/DMF combination for the Vilsmeier–Haack formylation reaction of *C*-2-glycals. The *C*-2-formyl-glycals were obtained in yields similar to or even better than those reported in the literature using the classical $POCl_3$/DMF mixture. Additionally, we showed that the formylation of a disaccharide glycal was possible. Notably, this transformation showcases the potential of using a XtalFluor-E/DMF combination for the formylation of other nucleophilic organic molecules.

EXPERIMENTAL SECTION

General Information. All commercial compounds were used as received. Solvents were used as purchased unless stated as dry. Et_2O, THF, CH_3CN, DCM, and toluene were purified using a Vacuum Atmospheres Inc. solvent purification system. All air and water sensitive reactions were carried out under an argon atmosphere. Reactions were monitored by TLC on precoated plates (Silicycle silica gel 60 Å F254), and products were visualized under 254 nm UV light followed by staining with $KMnO_4$ or DNPH when appropriate. Purification was carried out using a Biotage Isolera one flash chromatography system using Biotage KPSIL SNAP or Silicycle SiliaSep silica gel cartridges. NMR spectra were recorded on an Agilent DD2 500 spectrometer in the indicated solvent at 298 K. Chemical shifts for ^1H and ^{13}C spectra are reported on the delta scale in ppm and were referenced to residual solvent references or internal TMS reference. Resonances are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sxt = sextet, m = multiplet, or a combination of the above), coupling constant (Hz), integration, and attribution. H and C signals were assigned using 2D correlations (HSQC and COSY) and DEPT experiments, and hydrogen/carbon assignations refer to the standard sugar nomenclature.[22] High-resolution mass (HRMS) spectra were recorded on a LC/MS-TOF Agilent 6210 using electrospray ionization in positive mode (ESI+) at 100 °C. Infrared spectra (IR) were recorded on an ABB MB 3000 FT-IR spectrometer and on a Thermo Scientific Nicolet 380 FT-IR spectrometer. Absorptions are described as s (strong), m (medium), w (weak), and br (broad) and reported in cm^{-1}. Melting points were measured on a Stanford Research System OptiMelt MPA100 automated melting

Scheme 4. Potential Nature of the Formylating Reagent[a]



[a]The BF_4^- counterion of XtalFluor-E has been omitted for clarity.

DOI: 10.1021/acs.joc.8b01006
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point apparatus and are uncorrected. Optical rotations were recorded on a Jasco DIP-360 digital polarimeter at 589 nm. Tri-OAc glucal **1i** and tri-OAc galactal **1j**,[23] tri-OBn glucal **1a** and tri-OBn galactal **1b**,[23,24] tri-OPMB glucal **1c** and tri-OPMB galactal **1d**,[23,25] tri-Oallyl glucal **1e** and tri-Oallyl galactal **1f**,[23,18] tri-OMOM glucal **1g** and tri-OMOM galactal **1h**,[23,26] 3-OBn-4,6-benzylidene glucal **1k**,[27] 6-F-3,4-di-OAc galactal **1l** and 6-F-3,4-di-OBn galactal **1m**,[28] 3,4-di-OBn-6-OTBS glucal **1n**,[23,19b] 3,4-di-OPMB-6-OTr glucal **1o**,[23,29] and hexa-OBn lactal **7**[30] were prepared according to the methods in the literature.

General Procedure for the Formylation of *C*-2 Glycals. To a solution of glycal (50 mg) in dry DMF/Et_2O (1:1, 1 M) was added XtalFluor-E (3 equiv). After 18 h at rt, saturated brine (10 mL) and EtOAc (10 mL) were added and the aqueous phase was separated and extracted with EtOAc (2 × 10 mL). The organic phases were combined, dried over $MgSO_4$, filtered, concentrated in vacuo, and purified on silica gel using an automated flash purification system (AFP).

(2R,3S,4R)-3,4-Bis(benzyloxy)-2-((benzyloxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2a)***. According to the general procedure on a 0.12 mmol scale, formyl glucal **2a** was isolated as a yellow oil (42.5 mg, 80%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). Data are in accordance with the one described in the literature.[24]

(2R,3R,4R)-3,4-Bis(benzyloxy)-2-((benzyloxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2b)***. According to the general procedure on a 0.12 mmol scale, formyl galactal **2b** was isolated as a yellow oil (36.2 mg, 68%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). Data are in accordance with the one described in the literature.[31]

((2R,3S,4R)-3,4-Bis((4-methoxybenzyl)oxy)-2-(((4-methoxybenzyl)oxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2c)***. According to the general procedure on a 0.10 mmol scale, formyl glucal **2c** was isolated as a yellow oil (21.3 mg, 40%) after purification by AFP (15−60% EtOAc/hexanes, 3-15-3 CV). FT-IR (ν/cm^{-1}): 3001 (w), 2953 (w), 2932 (w), 2910 (w), 2862 (w), 2835 (w), 1672 (m), 1612 (m), 1512 (s), 1464 (m), 1302 (m), 1244 (s), 1173 (m), 1074 (s), 1032 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.39 (s, 1H, C**H**O), 7.37 (s, 1H, $\mathbf{H_1}$), 7.22−7.12 (m, 6H, 6 × Ar**H**), 6.90−6.80 (m, 6H, 6 × Ar**H**), 4.70−4.62 (m, 1H, $\mathbf{H_5}$), 4.58 (d, J = 11.1 Hz, 1H, C**H**HOPh), 4.50 (d, J = 11.2 Hz, 1H, CH**H**OPh), 4.47 (d, J = 11.7 Hz, 1H, C**H**HOPh), 4.45 (d, J = 11.5 Hz, 1H, C**H**HOPh), 4.39 (d, J = 11.8 Hz, 1H, CH**H**OPh), 4.38 (d, J = 11.1 Hz, 1H, CH**H**OPh), 4.39−4.34 (m, 1H, $\mathbf{H_3}$), 3.81 (s, 3H, OC$\mathbf{H_3}$), 3.801 (s, 3H, OC$\mathbf{H_3}$), 3.800 (s, 3H, OC$\mathbf{H_3}$), 3.79−3.70 (m, 2H, C$\mathbf{H}H_6$ + $\mathbf{H_4}$), 3.56 (dd, J = 10.9, 4.5 Hz, 1H, CH$\mathbf{H}_6$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.4 (**C**HO, C_7), 164.3 (**C**H, C_1), 159.5 (**C**, C_{Ar}), 159.32 (**C**, C_{Ar}), 159.25 (**C**, C_{Ar}), 130.3 (**C**, C_{Ar}), 129.7 (**C**, C_{Ar}), 129.5 (**C**H, CH_{Ar}), 129.42 (**C**H, CH_{Ar}), 129.41 (**C**H, CH_{Ar}), 129.3 (**C**, CH_{Ar}), 117.8 (**C**, C_2), 113.9 (**C**H, CH_{Ar}), 113.8 (**C**H, CH_{Ar}), 113.7 (**C**H, CH_{Ar}), 79.5 (**C**H, C_5), 73.0 (**C**H_2, CH_2OPh), 72.1 (**C**H_2, CH_2OPh), 71.2 (**C**H_2, CH_2OPh), 70.9 (**C**H, C_4), 68.2 (**C**H_2, C_6), 65.1 (**C**H, C_3), 55.28 (2 × **C**H_3, 2 × OCH_3), 55.27 (**C**H_3, OCH_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{31}H_{35}O_8$, 535.2326; found, 535.2315. $[\alpha]_D^{22.8}$ −2.99 (c = 0.94, MeOH).

((2R,3R,4R)-3,4-Bis((4-methoxybenzyl)oxy)-2-(((4-methoxybenzyl)oxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2d)***. According to the general procedure on a 0.10 mmol scale, formyl galatal **2d** was isolated as a yellow oil (35.5 mg, 67%) after purification by AFP (15−60% EtOAc/hexanes, 3-15-3 CV). FT-IR (ν/cm^{-1}): 2955 (w), 2935 (w), 2910 (w), 2864 (w), 2837 (w), 2253 (w), 1672 (m), 1612 (s), 1512 (s), 1464 (m), 1302 (m), 1246 (s), 1198 (m), 1173 (s), 1086 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.35 (s, 1H, C**H**O), 7.27−7.20 (m, 7H, 6 × Ar**H** + $\mathbf{H_1}$), 6.90−6.84 (m, 6H, 6 × Ar**H**), 4.70 (d, J = 10.9 Hz, 1H, C**H**HOPh), 4.66 (d, J = 11.0 Hz, 1H, CH**H**OPh), 4.65−4.60 (m, 2H, $\mathbf{H_5}$ + C**H**HOPh), 4.57 (dd, J = 3.5, 1.4 Hz, 1H, $\mathbf{H_3}$), 4.50 (d, J = 11.6 Hz, 1H, C**H**HOPh), 4.47 (d, J = 12.3 Hz, 1H, CH**H**OPh), 4.41 (d, J = 11.5 Hz, 1H, CH**H**OPh), 3.96−3.88 (m, 2H, 2 × $\mathbf{H_6}$), 3.820 (s, 3H, OC$\mathbf{H_3}$), 3.816 (s, 6H, 2 × OC$\mathbf{H_3}$), 3.81−3.77 (m, 1H, $\mathbf{H_4}$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 189.5 (**C**HO, C_7), 164.4 (**C**H, C_1), 159.5 (**C**, C_{Ar}), 159.3 (**C**, C_{Ar}), 159.2 (**C**, C_{Ar}), 131.1 (**C**, C_{Ar}), 130.1 (**C**, C_{Ar}), 129.7 (**C**H, CH_{Ar}), 129.6 (**C**, C_{Ar}), 129.5 (**C**H, CH_{Ar}), 129.4 (**C**H, CH_{Ar}), 119.5 (**C**, C_2), 114.0 (**C**H, CH_{Ar}), 113.9 (**C**H, CH_{Ar}), 113.7 (**C**H, CH_{Ar}), 79.0 (**C**H, C_5), 73.5 (**C**H_2, CH_2OPh), 73.2 (**C**H_2, CH_2OPh), 72.8 (**C**H, C_4), 71.3 (**C**H_2, CH_2OPh), 68.2 (**C**H_2, C_6), 64.7 (**C**H, C_3), 55.40 (**C**H_3, OCH_3), 55.37 (**C**H_3, 2 × OCH_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{31}H_{35}O_8$, 535.2326; found, 535.2315. $[\alpha]_D^{22.8}$ −0.79 (c = 1.64, MeOH).

(2R,3S,4R)-3,4-Bis(allyloxy)-2-((allyloxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2e)***. According to the general procedure on a 0.19 mmol scale using DMF (1 M) as the solvent instead, formyl glucal **2e** was isolated as a yellow oil (10.9 mg, 45%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). FT-IR (ν/cm^{-1}): 2920 (w), 2858 (w), 1672 (s), 1622 (s), 1456 (w), 1421 (m), 1294 (m), 1265 (w), 1198 (s), 1070 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.38 (s, 1H, C**H**O), 7.38 (s, 1H, $\mathbf{H_1}$), 5.96−5.81 (m, 3H, 3 × C**H**=CH$_2$), 5.32−5.13 (m, 6H, 3 × OC$\mathbf{H_2}$CH), 4.70 (app ddt, J = 7.9, 4.5, 2.0 Hz, 1H, $\mathbf{H_5}$), 4.29 (dd, J = 2.7, 2.0 Hz, 1H, $\mathbf{H_3}$), 4.20−3.95 (m, 6H, 3 × C**H**H=CH + 3 × CH**H**=CH), 3.84 (app t, J = 2.3 Hz, 1H, $\mathbf{H_4}$), 3.76 (dd, J = 10.9, 7.9 Hz, 1H, C$\mathbf{H}H_6$), 3.62 (dd, J = 10.9, 4.5 Hz, 1H, CH$\mathbf{H}_6$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.3 (**C**HO, C_7), 164.3 (**C**H, C_1), 134.7 (**C**H, CH=CH_2), 134.2 (**C**H, CH=CH_2), 134.0 (**C**H, CH=CH_2), 118.0 (**C**H_2, OCH_2CH), 117.59 (**C**, C_2), 117.56 (**C**H_2, OCH_2CH), 116.8 (**C**H_2, OCH_2CH), 79.5 (**C**H, C_5), 72.3 (**C**H_2, CH_2=CH), 71.2 (**C**H, C_4), 71.0 (**C**H_2, CH_2=CH), 70.8 (**C**H_2, CH_2=CH), 68.4 (**C**H_2, C_6), 64.8 (**C**H, C_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{16}H_{23}O_5$, 295.1540; found, 295.1512. $[\alpha]_D^{22.8}$ +35.6 (c = 1.22, MeOH).

(2R,3R,4R)-3,4-Bis(allyloxy)-2-((allyloxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2f)***. According to the general procedure on a 0.19 mmol scale, formyl galactal **2f** was isolated as a yellow oil (50.5 mg, 90%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). FT-IR (ν/cm^{-1}): 2955 (w), 2924 (m), 2854 (m), 1676 (m), 1620 (s), 1460 (w), 1408 (w), 1333 (w), 1263 (m), 1198 (s), 1090 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.34 (s, 1H, C**H**O), 7.26 (s, 1H, $\mathbf{H_1}$), 5.96−5.86 (m, 3H, 3 × C**H**=CH$_2$), 5.33−5.10 (m, 6H, 3 × OC$\mathbf{H_2}$CH), 4.64 (dddd, J = 8.8, 5.4, 2.1, 1.4 Hz, 1H, $\mathbf{H_5}$), 4.47 (dd, J = 3.6, 1.4 Hz, 1H, $\mathbf{H_3}$), 4.22−4.16 (m, 3H, 3 × C**H**H=CH), 4.12−4.01 (m, 3H, 3 × CH**H**=CH), 3.91 (dd, J = 11.8, 8.8 Hz, 1H, C$\mathbf{H}H_6$), 3.85 (dd, J = 11.9, 2.1 Hz, 1H, CH$\mathbf{H}_6$), 3.76 (dd, J = 5.4, 3.6 Hz, 1H, $\mathbf{H_4}$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 189.3 (**C**HO, C_7), 164.3 (**C**H, C_1), 135.1 (**C**H, CH=CH_2), 134.4 (**C**H, CH=CH_2), 134.0 (**C**H, CH=CH_2), 119.2 (**C**, C_2), 117.8 (**C**H_2, OCH_2CH), 117.5 (**C**H_2, OCH_2CH), 116.3 (**C**H_2, OCH_2CH), 78.7 (**C**H, C_5), 73.1 (**C**H, C_4), 72.4 (**C**H_2, CH_2=CH), 72.3 (**C**H_2, CH_2=CH), 70.8 (**C**H_2, CH_2=CH), 68.3 (**C**H_2, C_6), 64.2 (**C**H, C_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{16}H_{23}O_5$, 295.1540; found, 295.1519. $[\alpha]_D^{22.8}$ +24.2 (c = 0.74, MeOH).

(2R,3S,4R)-3,4-Bis(methoxymethoxy)-2-((methoxymethoxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2g)***. According to the general procedure on a 0.18 mmol scale, formyl glucal **2g** was isolated as a yellow oil (6.1 mg, 11%) after purification by AFP (20−70% EtOAc/hexanes, 3-15-3 CV). ***Caution!*** This compound is particularly unstable and prone to decomposition during purification by flash column chromatography. FT-IR (ν/cm^{-1}): 2935 (w), 2893 (w), 2845 (w), 2826 (w), 1726 (w), 1672 (m), 1626 (s), 1443 (w), 1416 (w), 1292 (m), 1198 (s), 1149 (s), 1097 (s), 1024 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.38 (s, 1H, C**H**O), 7.41 (s, 1H, $\mathbf{H_1}$), 4.88 (d, J = 6.7 Hz, 1H, C**H**HOCH$_3$), 4.77−4.75 (m, 1H, $\mathbf{H_5}$), 4.74 (d, J = 7.0 Hz, 1H, C**H**HOCH$_3$), 4.69 (d, J = 7.1 Hz, 1H, CH**H**OCH$_3$), 4.67 (d, J = 6.7 Hz, 1H, C**H**HOCH$_3$), 4.66 (d, J = 6.7 Hz, 1H, CH**H**OCH$_3$), 4.66 (d, J = 6.7 Hz, 1H, CH**H**OCH$_3$), 4.45 (app t, J = 2.2 Hz, 1H, $\mathbf{H_4}$), 4.10 (app t, J = 1.9 Hz, 1H, $\mathbf{H_3}$), 3.89 (dd, J = 11.4, 8.7 Hz, 1H, C$\mathbf{H}H_6$), 3.73 (dd, J = 11.4, 4.2 Hz, 1H, CH$\mathbf{H}_6$), 3.41 (s, 3H, OC$\mathbf{H_3}$), 3.39 (s, 3H, OC$\mathbf{H_3}$), 3.38 (s, 3H, OC$\mathbf{H_3}$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.2 (**C**HO, C_7), 163.7 (**C**H, C_1), 117.8 (**C**, C_2), 96.9 (**C**H_2, CH_2OCH$_3$), 96.8 (**C**H_2, CH_2OCH$_3$), 95.7 (**C**H_2, CH_2OCH$_3$), 79.8 (**C**H, C_5), 70.1 (**C**H, C_4), 66.1 (**C**H_2, C_6), 63.7 (**C**H, C_3), 56.2 (**C**H_3, OCH_3), 56.0 (**C**H_3, OCH_3), 55.6

DOI: 10.1021/acs.joc.8b01006
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(CH_3, OCH_3). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{13}H_{23}O_8$, 307.1387; found, 307.1399. $[\alpha]_D^{22.8}$ +8.56 (c = 0.90, MeOH).

(2R,3R,4R)-3,4-Bis(methoxymethoxy)-2-((methoxymethoxy)-methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2h).*** According to the general procedure on a 0.18 mmol scale, formyl galactal **2h** was isolated as a yellow oil (10.9 mg, 20%) after purification by AFP (20−70% EtOAc/hexanes, 3-15-3 CV). ***Caution!*** This compound is particularly unstable and prone to decomposition during purification by flash column chromatography. FT-IR (ν/cm^{-1}): 2924 (w), 2849 (w), 2826 (w), 2361 (w), 2341 (w), 1728 (w), 1676 (m), 1622 (s), 1443 (w), 1379 (w), 1273 (w), 1198 (m), 1149 (s), 1111 (s), 1020 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.35 (s, 1H, C**H**O), 7.28 (s, 1H, $\mathbf{H_1}$), 4.90 (d, J = 6.6 Hz, 1H, C**H**HOCH$_3$), 4.86 (d, J = 6.9 Hz, 1H, C**H**HOCH$_3$), 4.73 (d, J = 6.6 Hz, 1H, CH**H**OCH$_3$), 4.71 (d, J = 6.9 Hz, 1H, CH**H**OCH$_3$), 4.70 (d, J = 6.5 Hz, 1H, C**H**HOCH$_3$), 4.69 (d, J = 6.7 Hz, 1H, CH**H**OCH$_3$), 4.69−4.67 (m, 1H, $\mathbf{H_3}$), 4.68−4.60 (m, 1H, $\mathbf{H_5}$), 4.06 (dd, J = 5.3, 3.7 Hz, 1H, $\mathbf{H_4}$), 4.03 (dd, J = 12.2, 8.9 Hz, 1H, C**H**H$_6$), 3.97 (dd, J = 12.1, 2.2 Hz, 1H, CH**H**$_6$), 3.44 (s, 3H, OC**H**$_3$), 3.41 (s, 3H, OC**H**$_3$), 3.40 (s, 3H, OC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 189.0 (**C**HO, C$_7$), 163.8 (**C**H, C$_1$), 119.3 (**C**, C$_2$), 97.2 (**C**H$_2$, CH$_2$OCH$_3$), 96.7 (**C**H$_2$, CH$_2$OCH$_3$), 95.8 (**C**H$_2$, CH$_2$OCH$_3$), 78.9 (**C**H, C$_5$), 70.8 (**C**H, C$_4$), 65.9 (**C**H$_2$, C$_6$), 63.4 (**C**H, C$_3$), 56.01 (**C**H$_3$, OCH$_3$), 56.96 (**C**H$_3$, OCH$_3$), 55.4 (**C**H$_3$, OCH$_3$). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{13}H_{23}O_8$, 307.1387; found, 307.1406. $[\alpha]_D^{22.8}$ +4.73 (c = 0.55, MeOH).

(2R,3S,4R)-2-(Acetoxymethyl)-5-formyl-3,4-dihydro-2H-pyran-3,4-diyl Diacetate ***(2i).*** According to the general procedure on a 0.36 mmol scale using DIPEA (0.1 equiv) as an additive, formyl glucal **2i** was isolated as a yellow oil (20.4 mg, 19%) after purification by biotage (50−100% Et_2O/hexanes, 3-10-3 CV). Data are in accordance with the one described in the literature.[5b]

(2R,3R,4R)-2-(Acetoxymethyl)-5-formyl-3,4-dihydro-2H-pyran-3,4-diyl Diacetate ***(2j).*** According to the general procedure on a 0.36 mmol scale using DIPEA (0.1 equiv) as an additive, formyl galactal **2j** was isolated as a yellow oil (38.6 mg, 36%) after purification by AFP (50−100% Et_2O/hexanes, 3-10-3 CV). FT-IR (ν/cm^{-1}): 2962 (w), 2930 (w), 2851 (w), 2745 (w), 1740 (s), 1660 (m), 1626 (s), 1433 (w), 1371 (m), 1271 (s), 1194 (s), 1121 (w), 1043 (m), 1020 (m). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.32 (s, 1H, C**H**O), 7.38 (s, 1H, $\mathbf{H_1}$), 6.00 (app d, J = 4.4 Hz, 1H, $\mathbf{H_3}$), 5.42 (app t, J = 3.8 Hz, 1H, $\mathbf{H_4}$), 4.57−4.50 (m, 1H, $\mathbf{H_5}$), 4.43 (dd, J = 12.2, 8.3 Hz, 1H, C**H**H$_6$), 4.28 (dd, J = 12.2, 4.0 Hz, 1H, CH**H**$_6$), 2.10 (s, 3H, OCOC**H**$_3$), 2.09 (s, 3H, OCOC**H**$_3$), 2.04 (s, 3H, OCOC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 187.4 (**C**HO, C$_7$), 170.5 (**C**, C═O), 169.8 (**C**, C═O), 169.5 (**C**, C═O), 163.6 (**C**H, C$_1$), 116.6 (**C**, C$_2$), 75.3 (**C**H, C$_5$), 64.0 (**C**H, C$_4$), 61.3 (**C**H$_2$, C$_6$), 59.9 (**C**H, C$_3$), 20.7 (**C**H$_3$, COCH$_3$), 20.5 (**C**H$_3$, 2 × COCH$_3$). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{13}H_{17}O_8$, 301.0918; found, 301.0934. $[\alpha]_D^{22.0}$ +104.3 (c = 1.61, MeOH).

(2R,4aR,8R,8aS)-8-(Benzyloxy)-2-phenyl-4,4a,8,8a-tetrahydropyrano[3,2-d][1,3]dioxine-7-carbaldehyde ***(2k).*** According to the general procedure on a 0.15 mmol scale using DMF/Et_2O (1:1, 0.5 M) as the solvent instead, formyl glucal **2k** was isolated as a yellow solid (24.3 mg, 46%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). Data are in accordance with the one partially described in the literature.[32] Mp: 105.8−110.0 °C. FT-IR (ν/cm^{-1}): 3067 (w), 3032 (w), 2959 (w), 2924 (m), 2854 (m), 1726 (w), 1684 (s), 1622 (s), 1497 (w), 1452 (m), 1367 (m), 1273 (s), 1225 (m), 1186 (s), 1155 (m), 1094 (s), 1068 (s), 1005 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.42 (s, 1H, C**H**O), 7.52−7.28 (m, 11H, 10 × Ar**H** + $\mathbf{H_1}$), 5.65 (s, 1H, OC**H**O), 5.01 (d, J = 10.7 Hz, 1H, C**H**HOPh), 4.89 (d, J = 10.8 Hz, 1H, CH**H**OPh), 4.65 (dd, J = 7.3, 0.9 Hz, 1H, $\mathbf{H_3}$), 4.49 (dd, J = 10.4, 5.0 Hz, 1H, C**H**H$_6$), 4.11 (dd, J = 10.3, 7.4 Hz, 1H, $\mathbf{H_5}$), 4.01 (app tdd, J = 10.4, 4.9, 0.6 Hz, 1H, $\mathbf{H_4}$), 3.93 (app t, J = 10.3 Hz, 1H, CH**H**$_6$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 188.6 (**C**HO, C$_7$), 162.5 (**C**H, C$_1$), 138.2 (**C**, C$_{Ar}$), 136.7 (**C**, C$_{Ar}$), 129.2 (**C**H, CH$_{Ar}$), 128.34 (**C**H, CH$_{Ar}$), 128.32 (**C**H, CH$_{Ar}$), 128.29 (**C**H, CH$_{Ar}$), 127.7 (**C**H, CH$_{Ar}$), 126.0 (**C**H, CH$_{Ar}$), 120.9 (**C**, C$_2$), 101.5 (**C**H, OCHO), 80.0 (**C**H, C$_5$), 75.1 (**C**H$_2$, CH$_2$OPh), 72.4 (**C**H, C$_4$), 70.5 (**C**H, C$_3$), 67.8 (**C**H$_2$, C$_6$). HRMS (ESI-TOF), m/z: $[M + Na]^+$ calcd for $C_{21}H_{20}NaO_5$, 375.1203; found, 375.1212. $[\alpha]_D^{22.5}$ +0.68 (c = 0.44, $CHCl_3$).

(2S,3R)-2-(Fluoromethyl)-5-formyl-3,4-dihydro-2H-pyran-3,4-diyl Diacetate ***(2l).*** According to the general procedure on a 0.22 mmol scale using DMF (1 M) as the solvent instead, formyl galactal **2l** was isolated as a white solid (15.4 mg, 27%) after purification by AFP (40−100% Et_2O/hexanes, 3-15-3 CV). Mp: 119.5−122.7 °C. FT-IR (ν/cm^{-1}): 2958 (w), 1751 (s), 1683 (m), 1629 (m), 1506 (m), 1375 (w), 1238 (s), 1206 (s), 1043 (m), 1023 (m). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.35 (s, 1H, C**H**O), 7.44 (s, 1H, $\mathbf{H_1}$), 6.02 (app d, J = 4.2 Hz, 1H, $\mathbf{H_3}$), 5.44 (app td, J = 4.1, 1.3 Hz, 1H, $\mathbf{H_4}$), 4.77 (ddd, J = 49.3, 11.3, 8.8 Hz, 1H, C**H**H$_6$), 4.69−4.61 (m, 1H, $\mathbf{H_5}$), 4.57 (ddd, J = 45.1, 10.5, 2.7 Hz, 1H, CH**H**$_6$), 2.10 (s, 3H, OCOC**H**$_3$), 2.05 (s, 3H, OCOC**H**$_3$). ^{19}F NMR (470 MHz, $CDCl_3$) (δ_F/ppm): −227.1 (app br, s, 1F, CH$_2$**F**). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 187.3 (**C**HO, C$_7$) 169.6 (**C**, C═O), 169.3 (**C**, C═O), 163.6 (**C**H, C$_1$), 116.6 (**C**, C$_2$), 80.5 (d, J = 171.8 Hz, **C**H$_2$, C$_6$), 76.1 (d, J = 21.7 Hz, **C**H, C$_5$), 64.1 (d, J = 7.1 Hz, **C**H$_2$, C$_4$), 59.5 (**C**H, C$_3$), 20.5 (**C**H$_3$, 2 × COCH$_3$). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{11}H_{14}FO_6$, 261.0769; found, 261.0777. $[\alpha]_D^{25.1}$ +51.9 (c = 0.48, MeOH).

(2S,3R)-3,4-Bis(benzyloxy)-2-(fluoromethyl)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(2m).*** According to the general procedure on a 0.15 mmol scale, formyl galactal **2m** was isolated as a yellow oil (45.0 mg, 84%) after purification by AFP (10−40% EtOAc/hexanes, 3-15-3 CV). FT-IR (ν/cm^{-1}): 2875 (w), 1676 (m), 1624 (s), 1455 (w), 1267 (m), 1200 (s), 1062 (s), 1045 (w). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.40 (s, 1H, C**H**O), 7.41−7.26 (m, 11H, 10 × ArH + $\mathbf{H_1}$), 4.90 (ddd, J = 50.5, 11.4, 8.2 Hz, 1H, C**H**H$_6$), 4.82 (ddd, J = 46.8, 11.5, 2.0 Hz, 1H, CH**H**$_6$), 4.81−4.75 (m, 1H, $\mathbf{H_5}$), 4.73 (s, 2H, C**H**$_2$OPh), 4.71 (d, J = 11.9 Hz, 1H, C**H**HOPh), 4.64 (td, J = 3.1, 1.3 Hz, 1H, $\mathbf{H_3}$), 4.55 (d, J = 11.9 Hz, 1H, CH**H**OPh), 3.87 (ddd, J = 5.7, 3.4, 2.2 Hz, 1H, $\mathbf{H_4}$). ^{19}F NMR (470 MHz, $CDCl_3$) (δ_F/ppm): −221.2 (app dt, J = 49.6, 48.9 Hz, 1F, CH$_2$**F**). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 189.2 (**C**HO, C$_7$), 164.0 (**C**H, C$_1$), 138.4 (**C**, C$_{Ar}$), 137.0 (**C**, C$_{Ar}$), 128.7 (**C**H, CH$_{Ar}$), 128.3 (**C**H, CH$_{Ar}$), 128.2 (**C**H, CH$_{Ar}$), 127.72 (**C**H, CH$_{Ar}$), 127.66 (**C**H, CH$_{Ar}$), 127.59 (**C**H, CH$_{Ar}$), 119.4 (**C**, C$_2$), 82.0 (d, J = 166.6 Hz, **C**H$_2$, C$_6$), 78.1 (d, J = 20.0 Hz, **C**H, C$_5$), 73.6 (**C**H$_2$, CH$_2$OPh), 72.9 (d, J = 8.1 Hz, **C**H, C$_4$), 71.4 (**C**H$_2$, CH$_2$OPh), 63.7 (**C**H, C$_3$). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{21}H_{22}FO_4$, 357.1497; found,: 357.1519. $[\alpha]_D^{25.1}$ −90.8 (c = 0.46, MeOH).

((2R,3S,4R)-3,4-Bis(benzyloxy)-3,4-dihydro-2H-pyran-2-yl)methyl Formate ***(3)*** *and ((2R,3S,4R)-3,4-bis(benzyloxy)-5-formyl-3,4-dihydro-2H-pyran-2-yl)methyl Formate* ***(4).*** According to the general procedure on a 0.11 mmol scale, formate glucal **3** was first isolated as a yellow oil (7.3 mg, 19%) followed by formyl formate glucal **4** as a yellow oil (9.1 mg, 22%) after purification by AFP (5−60% EtOAc/hexanes, 3-15-3 CV). Data for **3** are in accordance with the one described in the literature.[19b] Data for **4** follow. FT-IR (ν/cm^{-1}): 2953 (m), 2924 (s), 2854 (m), 1724 (s), 1672 (m), 1626 (m), 1456 (m), 1379 (w), 1163 (s), 1090 (m), 1074 (m). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.45 (s, 1H, C**H**O), 8.07 (q, J = 0.7 Hz, 1H, COC**H**O), 7.39 (s, 1H, $\mathbf{H_1}$), 7.37−7.29 (m, 9H, 9 × Ar**H**), 7.25−7.22 (m, 1H, 1 × Ar**H**), 4.75−4.68 (m, 1H, $\mathbf{H_5}$), 4.70 (d, J = 11.6 Hz, 1H, C**H**HOPh), 4.60 (ddd, J = 12.5, 9.0, 0.7 Hz, 1H, C**H**H$_6$), 4.60 (d, J = 11.6 Hz, 1H, CH**H**OPh), 4.55 (d, J = 12.0 Hz, 1H, C**H**HOPh), 4.46 (d, J = 11.6 Hz, 1H, CH**H**OPh), 4.45 (dd, J = 4.8, 2.1 Hz, 1H, $\mathbf{H_3}$), 4.26 (ddd, J = 12.4, 3.2, 0.7 Hz 1H, CH**H**$_6$), 3.77 (app t, J = 2.2 Hz, 1H, $\mathbf{H_4}$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.3 (**C**HO, C$_7$), 163.6 (**C**H, C$_1$), 160.3 (**C**H, C$_8$), 137.9 (**C**, C$_{Ar}$), 136.9 (**C**, C$_{Ar}$), 128.6 (**C**H, CH$_{Ar}$), 128.5 (**C**H, CH$_{Ar}$), 128.2 (**C**H, CH$_{Ar}$), 128.0 (**C**H, CH$_{Ar}$), 127.9 (**C**H, CH$_{Ar}$), 127.8 (**C**H, CH$_{Ar}$), 118.0 (**C**, C$_2$), 77.8 (**C**H, C$_5$), 72.6 (**C**H$_2$, CH$_2$OPh), 71.8 (**C**H$_2$, CH$_2$OPh), 71.3 (**C**H, C$_4$), 64.5 (**C**H, C$_3$), 62.0 (**C**H$_2$, C$_6$). HRMS (ESI-TOF), m/z: $[M + H]^+$ calcd for $C_{22}H_{23}O_6$, 383.1489; found, 383.1490. $[\alpha]_D^{22.8}$ +2.00 (c = 0.35, MeOH).

DOI: 10.1021/acs.joc.8b01006
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((2R,3S)-3,4-Bis((4-methoxybenzyl)oxy)-3,4-dihydro-2H-pyran-2-yl)methyl Formate ***(5)****, (2R,3S,4R)-3,4-bis((4-methoxybenzyl)oxy)-2-((trityloxy)methyl)-3,4-dihydro-2H-pyran-5-carbaldehyde* ***(2o)****, and (2R,3S,4R)-2-(hydroxymethyl)-3,4-bis((4-methoxybenzyl)oxy)-3,4-dihydro-2H-pyran-5-carbaldehyde* ***(6)****.* According to the general procedure on a 0.16 mmol scale using DMF (1 M) as solvent instead, formate glucal **5** was first isolated as a yellow oil (6.5 mg, 10%) followed by formyl glucal **2o** (13.1 mg, 12%) as a yellow oil and formyl formate glycal **6** as a yellow oil (15.6 mg, 22%) after purification by AFP (50−100% Et_2O/hexanes, 3-10-3 CV). Data for **5** follow. FT-IR (ν/cm^{-1}): 2934 (w), 2837 (w), 1724 (s), 1647 (w), 1612 (m), 1512 (s), 1464 (w), 1302 (w), 1248 (s), 1175 (m), 1094 (m), 1034 (m). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 8.05 (app q, J = 0.8 Hz, 1H, COC**H**O), 7.30−7.27 (m, 2H, 2 × Ar**H**), 7.25−7.21 (m, 2H, 2 × Ar**H**), 6.94−6.84 (m, 4H, 4 × Ar**H**), 6.38 (dd, J = 6.2, 1.4 Hz, 1H, $\mathbf{H}_1$), 4.91 (dd, J = 6.2, 2.7 Hz, 1H, $\mathbf{H}_2$), 4.78 (d, J = 11.0 Hz, 1H, C**H**HOPh), 4.61 (d, J = 11.4 Hz, 1H, CH**H**OPh), 4.60 (d, J = 11.0 Hz, 1H, CH**H**OPh), 4.50 (d, J = 11.3 Hz, 1H, CH**H**OPh), 4.46 (ddd, J = 12.1, 2.9, 0.7 Hz, 1H, C**H**H_6), 4.42 (ddd, J = 11.9, 5.3, 0.7 Hz, 1H, CH**H**$_6$), 4.19 (dddd, J = 6.1, 2.7, 1.4, 0.5 Hz, 1H, $\mathbf{H}_3$), 4.09 (ddd, J = 8.4, 5.2, 3.1 Hz, 1H, $\mathbf{H}_5$), 3.82 (s, 3H, OC**H**$_3$), 3.81 (s, 3H, OC**H**$_3$), 3.74 (dd, J = 8.6, 6.1 Hz, 1H, $\mathbf{H}_4$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 160.6 (**C**H, C_7), 159.4 (**C**, C_{Ar}), 159.3 (**C**, C_{Ar}), 144.1 (**C**H, C_1), 130.2 (**C**, C_{Ar}), 129.83 (**C**, C_{Ar}), 129.80 (**C**H, CH_{Ar}), 129.43 (**C**H, CH_{Ar}), 113.90 (**C**H, CH_{Ar}), 113.89 (**C**H, CH_{Ar}), 100.4 (**C**, C_2), 75.1 (**C**H, C_3), 74.8 (**C**H, C_5), 73.29 (**C**H, C_4), 73.28 (CH_2, CH_2OPh), 70.2 (CH_2, CH_2OPh), 62.2 (CH_2, C_6), 55.31 (CH_3, OCH_3), 55.30 (CH_3, OCH_3). HRMS (ESI-TOF), m/z: [M + NH_4]$^+$ calcd for $C_{23}H_{30}NO_7$, 432.2017; found, 432.2028. $[\alpha]_D^{22.2}$ +0.04 (c = 0.22, $CHCl_3$). Data for **2o** are in accordance with the one described in the literature.[29] Data for **6** follow. FT-IR (ν/cm^{-1}): 2959 (m), 2924 (s), 2854 (m), 1724 (m), 1672 (m), 1626 (m), 1512 (s), 1464 (m), 1379 (w), 1302 (m), 1248 (s), 1171 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.44 (s, 1H, C**H**O), 8.07 (app d, J = 0.6 Hz, 1H, COC**H**O), 7.37 (s, 1H, $\mathbf{H}_1$), 7.26−7.23 (m, 2H, 2 × Ar**H**), 7.17−7.12 (m, 2H, 2 × Ar**H**), 6.90−6.85 (m, 4H, 4 × Ar**H**), 4.66 (app ddt, J = 9.1, 3.4, 1.9 Hz, 1H, $\mathbf{H}_5$), 4.62 (d, J = 11.3 Hz, 1H, C**H**HOPh), 4.58 (ddd, J = 12.5, 9.0, 0.7 Hz, 1H, C**H**H$_6$), 4.53 (d, J = 11.3 Hz, 1H, CH**H**OPh), 4.48 (d, J = 11.7 Hz, 1H, C**H**HOPh), 4.41 (dd, J = 2.7, 1.8 Hz, 1H, $\mathbf{H}_3$), 4.38 (d, J = 11.7 Hz, 1H, CH**H**OPh), 4.23 (ddd, J = 12.5, 3.1, 0.9 Hz 1H, CH**H**$_6$), 3.82 (s, 3H, OC**H**$_3$), 3.81 (s, 3H, OC**H**$_3$), 3.72−3.70 (m, 1H, $\mathbf{H}_4$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.3 (**C**HO, C_7), 163.5 (**C**H, C_1), 160.3 (**C**H, C_8), 159.6 (**C**, C_{Ar}), 159.3 (**C**, C_{Ar}), 130.1 (**C**, C_{Ar}), 129.6 (**C**H, CH_{Ar}), 129.5 (**C**H, CH_{Ar}), 128.9 (**C**, C_{Ar}), 118.1 (**C**, C_2), 114.0 (**C**H, CH_{Ar}), 113.8 (**C**H, CH_{Ar}), 77.9 (**C**H, C_5), 72.2 (CH_2, CH_2OPh), 71.3 (CH_2, CH_2OPh), 70.8 (**C**H, C_4), 64.2 (**C**H, C_3), 62.0 (CH_2, C_6), 55.29 (CH_3, OCH_3), 55.27 (CH_3, OCH_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{24}H_{27}O_8$, 443.1700; found, 443.1708. $[\alpha]_D^{22.8}$ −18.9 (c = 0.46, MeOH).

(2R,3S,4R)-4-(Benzyloxy)-2-((benzyloxy)methyl)-3-(((2S,3R,4S,5S,6R)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)-tetrahydro-2H-pyran-2-yl)oxy)-3,4-dihydro-2H-pyran-5-carbaldehyde ***(8)****.* According to the general procedure on a 0.06 mmol scale using DMF (1 M) instead as the solvent, formyl lactal **6** was isolated as a yellow oil (28.9 mg, 56%) after purification by AFP (5−40% EtOAc/hexanes, 3-15-3 CV). Data are in accordance with the one partially described in the literature.[20] FT-IR (ν/cm^{-1}): 3030 (w), 2959 (w), 2924 (m), 2854 (m), 1676 (m), 1626 (s), 1497 (w), 1452 (m), 1364 (w), 1292 (w), 1198 (m), 1070 (s). ^{1}H NMR (500 MHz, $CDCl_3$) (δ_H/ppm): 9.39 (s, 1H, C**H**O), 7.40−7.22 (m, 31H, 30 × Ar**H** + $\mathbf{H}_1$), 4.93 (d, J = 11.6 Hz, 1H, C**H**HOPh), 4.83−4.77 (m, 1H, $\mathbf{H}_5$), 4.77 (d, J = 10.8 Hz, 1H, C**H**HOPh), 4.74 (d, J = 11.9 Hz, 1H, C**H**HOPh), 4.70 (d, J = 12.0 Hz, 1H, CH**H**OPh), 4.69 (d, J = 11.6 Hz, 1H, C**H**HOPh), 4.69 (d, J = 10.7 Hz, 1H, CH**H**OPh), 4.63 (d, J = 11.5 Hz, 1H, CH**H**OPh), 4.62 (d, J = 11.7 Hz, 1H, CH**H**OPh), 4.56 (app t, J = 2.3 Hz, 1H, $\mathbf{H}_3$), 4.52 (d, J = 12.0 Hz, 1H, C**H**HOPh), 4.45 (d, J = 12.1 Hz, 2H, CH**H**OPh + C**H**HOPh), 4.40 (d, J = 11.8 Hz, 1H, CH**H**OPh), 4.38 (d, J = 7.7 Hz, 1H, $\mathbf{H}_I$), 4.18 (app t, J = 2.0 Hz, 1H, $\mathbf{H}_4$), 3.88 (dd, J = 3.1, 1.0 Hz, 1H, $\mathbf{H}_{IV}$), 3.81 (dd, J = 10.8, 8.0 Hz, 1H, C**H**H$_6$), 3.75 (dd, J = 9.8, 7.6 Hz, 1H, $\mathbf{H}_{II}$), 3.61 (dd, J = 10.9, 4.5 Hz, 1H, CH**H**$_6$), 3.57−3.52 (m, 2H, C**H**$\mathbf{H}_{VI}$ + CH$\mathbf{H}_{VI}$), 3.52−3.44 (m, 2H, $\mathbf{H}_{III}$ + $\mathbf{H}_V$). ^{13}C NMR (125 MHz, $CDCl_3$) (δ_C/ppm): 190.1 (**C**HO, C_7), 163.8 (**C**H, C_1), 138.46 (**C**, C_{Ar}), 138.45 (**C**, C_{Ar}), 138.37 (**C**, C_{Ar}), 138.36 (**C**, C_{Ar}), 137.78 (**C**, C_{Ar}), 137.62 (**C**, C_{Ar}), 128.5 (**C**H, CH_{Ar}), 128.43 (**C**H, CH_{Ar}), 128.38 (2 × **C**H, 2 × CH_{Ar}), 128.35 (**C**H, CH_{Ar}), 128.3 (**C**H, CH_{Ar}), 128.24 (**C**H, CH_{Ar}), 128.18 (**C**H, CH_{Ar}), 127.9 (**C**H, CH_{Ar}), 127.83 (2 × **C**H, 2 × CH_{Ar}), 128.81 (**C**H, CH_{Ar}), 127.80 (**C**H, CH_{Ar}), 127.7 (**C**H, CH_{Ar}), 127.64 (**C**H, CH_{Ar}), 127.61 (**C**H, CH_{Ar}), 127.57 (**C**H, CH_{Ar}), 127.5 (**C**H, CH_{Ar}), 117.8 (**C**, C_2), 103.0 (**C**H, C_I), 82.0 (**C**H, C_{III}), 79.0 (**C**H, C_{II}), 78.8 (**C**H, C_5), 75.3 (CH_2, CH_2OPh), 74.6 (CH_2, CH_2OPh), 73.62 (**C**H, C_V), 73.58 (CH_2, CH_2OPh), 73.3 (CH_2 + **C**H, CH_2OPh + C_{IV}), 73.1 (CH_2, CH_2OPh), 72.5 (CH_2, CH_2OPh), 71.8 (**C**H, C_4), 68.7 (CH_2, C_{VI}), 68.2 (CH_2, C_6), 66.6 (**C**H, C_3). HRMS (ESI-TOF), m/z: [M + H]$^+$ calcd for $C_{55}H_{57}O_{10}$, 877.3946; found, 877.3953. $[\alpha]_D^{22.8}$ −1.98 (c = 1.22, MeOH).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b01006.

NMR spectra for the known (^{1}H) and new compounds (^{1}H, ^{13}C, ^{19}F) prepared (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Natural Sciences and Engineering Research Council of Canada, OmegaChem, and Université Laval.

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