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ARTICLE

Cross dehydrogenative coupling of sugar enol ethers with terminal alkenes in the synthesis of pseudo disaccharides, chiral oxadecalins and conjugated triene

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An efficient strategy for the synthesis of C-2 and C-3 branched sugar dienes via cross dehydrogenative coupling of sugar enol ethers with terminal alkenes was developed. Both pyran and furan based enol ethers coupled smoothly with electron rich as well as deficient alkene sources yielding sugar dienes with complete *E*-stereoselectivity. This coupling reaction was applied successfully for the synthesis of orthogonally protected pseudo-C-saccharides as an alternative to olefin metathesis. Substrate scope was further enhanced by reacting exoglycals with methyl acrylate to generate C-5 branched sugar with moderate diastereoselectivity. These diene subunits were reacted with maleic anhydride under [4+2] cycloaddition condition to generate highly functionalised chiral oxadecalin cores. Finally, utilizing this C-C bond formation, sugar based conjugated triene was synthesized in excellent yield and selectivity.

Introduction

Naturally occurring carbohydrates and their downstream products represent useful chiral pool intermediates for enantioselective synthesis of biologically active natural and non-natural products due to their diversity, multi chiral architecture, well defined stereochemistry, and high degree of oxygenation.[1] During the last few decades glycals, which are inexpensive and readily available carbohydrate vinyl ethers endowed with a plethora of stereo chemical and functional attributes, have served extensively as ''chiral pool'' resources in the total synthesis of a wide range of molecules.[2] However, the scope of glycals as chiral building blocks relies on the development of convenient strategies dedicated to these requirements. For example, glycals can be utilized in the synthesis of both 2-deoxy C-glycosides (using anomeric carbon) and 2-C-branched sugars (using C-2 position).[3a]

C-glycosides, in which two monosaccharide units are linked carbon to carbon instead of an oxygen atom, are highly stable towards enzymatic hydrolysis and hence can act as carbohydrate mimics. Pseudo-C-disaccharides bearing double bond stitching monosaccharide units together are of great synthetic and biochemical prominence as double bond sets the stage for several chemical modifications.[3b] For example reduction of bridging double bond may lead to C-disaccharide having methylene[3b], or ethylene[3c] linkage. Synthetically the major difficulty associated with the synthesis of a pseudo-C-saccharides is the elaborate building block strategies of two coupling monosaccharides units. One way of achieving this type of pseudo-C-disaccharides is via olefin cross metathesis approach which requires multiple steps with very poor overall yield and loss of two carbon units in the coupling step.[3c] Daniel Werz and his co-workers successfully synthesized Pseudo-C-disaccharides containing a diene subunit from glycals via Stille type coupling of 1-stannylglucal and exocyclic bromoolefins.[3b] Till date, synthesis of a C-glycosidic bond from glycal mostly utilizes anomeric carbon atom, whereas C-2/C-3 positions of sugar is yet to be exploited towards this end. Thus, an innovative approach for the synthesis of a variety of different *C*-pseudodisaccharide linkages by utilizing C-2 position of glycals would be of high synthetic value.

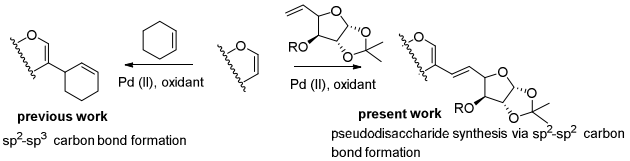

Figure 1. Methods for sugar enol ether based CDC coupling reactions.

Further, 2-C-branched sugars have immense importance in biological systems, besides acting as a precursor for the synthesis of natural products and medicinally important scaffolds.[4] Molinaro and Yu have demonstrated very recently the utilization of 2-C branched sugar based diene in the synthesis of an important inositol-fused monosaccharide called

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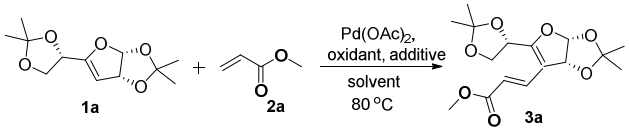
bradyrhizose that is relevant to a Nod-factor-independent nitrogen fixation pathway.[5a,5b] The advantage of 2-C-branched sugars is their propensity to undergo 1,2 annulation which may lead to the synthesis of some biologically important 1-oxadecalin scaffold, which is a key structural unit found in a wide range of biologically active molecules and natural products.[6] Earlier we have reported[7a] synthesis of C-2 sugars via sp^2-sp^3 bond formation (Figure 1). In the present study we wanted to a cross-dehydrogenative coupling (CDC) based strategy (Fig 1) for synthesizing ethylene linked C-2 branched sugars including pseudo-*C*-disaccharides which contain a diene subunit, and further cyclization with suitable dienophiles for the generation of densely substituted optically active oxadecalin and conjugated triene frameworks.

Results and discussion

Our approach for the synthesis of the diene subunit started from sugar enol ethers and a terminal alkene source. The most common approaches for the synthesis of glycal based dienes are the coupling of vinyl iodides with activated alkenes and the application of Wittig reaction on 2-formyl glycals.[7b,7c] These methods require an additional step to preactivate the C-2 position of glycals and have limited substrate scope. Due to these prefunctionalization issues, the use of unactivated C-H bond as a coupling partner for CDC has gained tremendous interest in contemporary organic synthesis.[7d,7e] In the literature there is only two reports one is from our group[7a] with unactivated cycloalkenes and another one by Xue-liu[8a] in which C-2 position of glycals was coupled with activated alkenes, but the latter approach suffers from various drawbacks like requirement of activated alkenes, poor yield and use of stoichiometric amount of Lewis acid which affects acid labile protecting groups. Further, most of the reported research focuses on coupling of C-2 position of pyranose glycals with alkenes under various reaction conditions, but there is no report in which C-3 position of furanose sugar is coupled to generate furanose sugar based dienes. The importance of C-3 linked furanose sugar lies in the fact that this sugar can be easily converted to pyranose form and has immense importance in the synthesis of a wide range of biologically important molecules.[8b] Our experience in glycal chemistry[9] and the drawbacks of the reported procedure prompted us to develop an improved method for the construction of dienes (C-3 and C-2 branched glycosides). For this purpose, initially we examined the reaction of furanoid glycal **1a** with methyl acrylate **2a** in the presence $Pd(OAc)_2$ (10 mol%) along with AgOAc. Taking DMF/DMSO as solvent, we obtained the desired product in excellent yield (Table 1, entry 1). In order to replace silver acetate with a cheaper oxidant, we tested several combinations of copper salts with different palladium catalysts but in all cases the yield of the desired product was not satisfactory. However, when we added pyridine as an additive in place of DMSO along with $Pd(OAc)_2$ and $Cu(OAc)_2.H_2O$ (Table 1, entry 4) we observed some improvement in yield of the desired product. By changing the catalyst loading and oxidant along with solvent, we came to the conclusion that use of 10 mol% of $Pd(OAc)_2$ along with 3 equiv. of $Cu(OAc)_2.H_2O$ and 2 equiv. pyridine as an additive in 2 mL of dioxane (Table 1, entry 5) is the optimum reaction condition. Further when we use 1 equiv. of pyridine, the desired product was obtained in lower yield (Table 1, entry 9). Further, when we changed the Pd source from $Pd(OAc)_2$ to $PdCl_2$ or $Pd(TFA)_2$,the desired product was still obtained (Table 1, entry 7, 8) but in lower yields. In summary, we have developed two reaction conditions (A, B) which are equally efficient for the coupling reaction but we used the more economical condition A for the rest of the study.

After successfully optimizing the reaction condition, we next explored the substrate scope of coupling reaction for C-2 and C-3 branched furanoid and pyranoid glycals taking panel of unactivated and activated terminal alkene sources. In general

Table 1: Optimization of reaction condition for direct sp2-sp2 bond formation[a]



Entry	Catalyst (mol %)	Oxidant (equiv.)	Additive (equiv.)	Solvent[a]	Yield[b] %
1	**$Pd(OAc)_2$ (10)**	**AgOAc (2)**	**DMSO (3)**	**DMF**	**86**
2	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$ (3)	DMSO (3)	DMF	30
3	$Pd(OAc)_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	DMSO (3)	DMF	45
4	$Pd(OAc)_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	Pyridine (2)	DMF	65
5	**$Pd(OAc)_2$ (10)**	**$Cu(OAc)_2.H_2O$ (3)**	**Pyridine (2)**	**Dioxane**	**91**
6	$Pd(OAc)_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	----------	Dioxane	Traces
7	$PdCl_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	Pyridine (2)	Dioxane	30
8	$Pd(TFA)_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	Pyridine (2)	Dioxane	60
9	$Pd(OAc)_2$ (10)	$Cu(OAc)_2.H_2O$ (3)	Pyridine (1)	Dioxane	67

[a]**Reaction conditions**: **1a** (1 equiv.) and **2a** (1.5 equiv.) were taken in 2 mL of solvent at 80 °C for 24 h. [b]isolated yields after column chromatography.

furanose sugar enol ethers coupled well with various terminal alkenes and were compatible under the standard reaction condition, giving the corresponding dienes with complete *E* stereochemistry (Scheme 1,**3a-3c**). E-Stereochemistry of newly formed olefinic protons of **3a** was confirmed by coupling constant values 7.77 (d, *J* = 15.7 Hz, 1H), 5.98 (d, *J* = 15.7 Hz, 1H) which are characteristics of E-olefins. In order to check whether this condition work well with pyranoid glucals, we selected styrene or substituted styrenes for coupling with glucals as this is otherwise not possible with existing methods. Gratifyingly, we obtained satisfactory results when various styrenes were checked; obtaining desired products in

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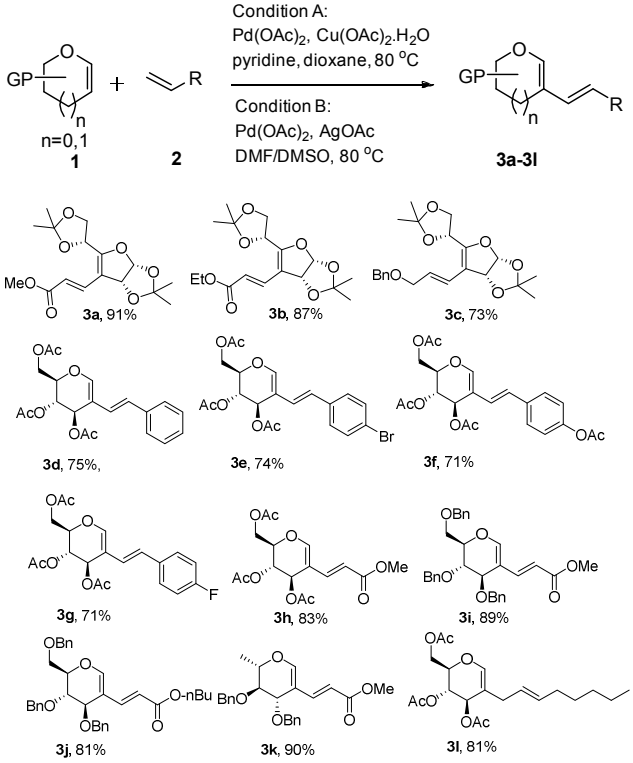
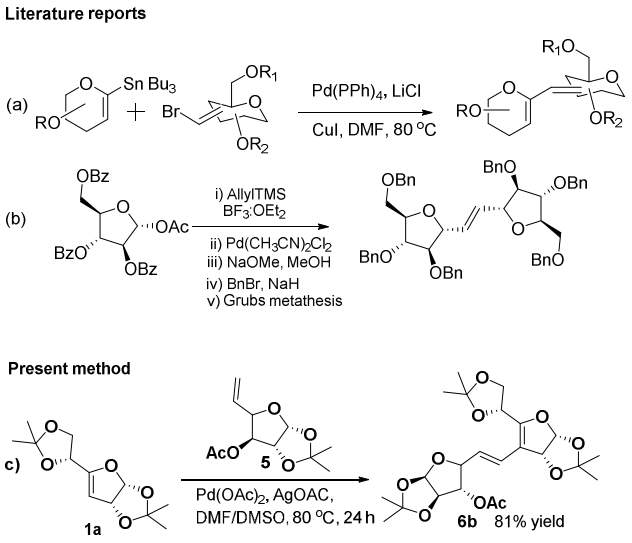
moderate to good yield (Scheme 1, **3d-3g**). Activated alkenes like acrylates gave the desired product in excellent yield with exclusive *E*-selectivity (Scheme 1, **3h**). Ether protected D-glucals react with equal ease under similar set of reaction condition (Scheme 1, **3i-j**). In order to check the feasibility of the method, reactions of glycals other than D-glucal were tested. A substrate derived from L-rhamnose protected with benzyl group also afforded the desired product with good yield (Scheme 1, **3k**). It was observed that terminal unactivated alkene like 1-octene also underwent the coupling reaction only to afford allylated product (Scheme 1, **3l**).



Scheme 1: Csp2-Csp2 coupling of sugar enol ethers with terminal alkenes. **Reaction conditions:** Condition A: **1** (1 equiv.), **2** (1.2 equiv.), $Pd(OAc)_2$ (0.1 equiv.), $Cu(OAc)_2.H_2O$ (3 equiv.), pyridine (2 equiv.), in Dioxane at 80 °C for 24 h Condition B : **1** (1 equiv.), **2** (1.2 equiv.), $Pd(OAc)_2$ (0.1 equiv.), AgOAc (2.5 equiv.) in DMF/DMSO at 80 °C, for 24 h. All the yields were isolated yields after column chromatography. Both the reaction condition works equally well for any substrate listed in scheme 1 and takes 20-24 h to complete.

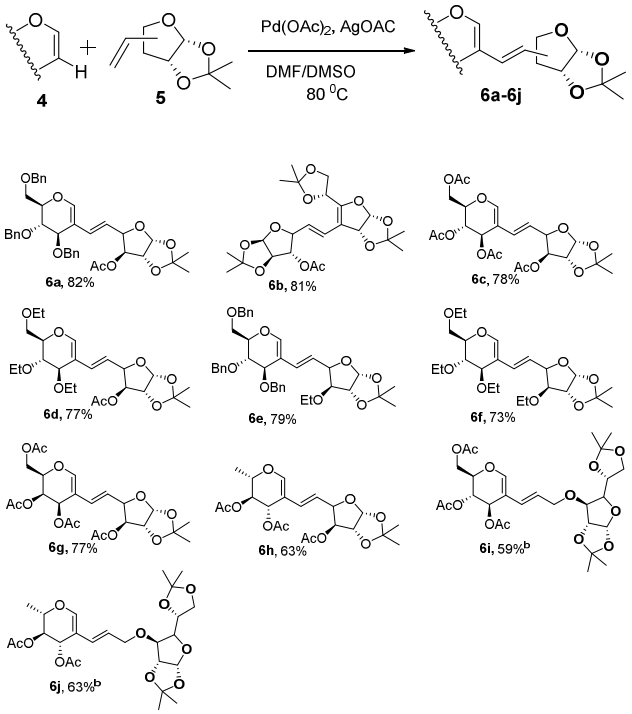
With this efficient tool for the synthesis of sugar based dienes, we were curious to see whether this method can be applied for the synthesis of ethylene linked C-disaccharides. According to the literature there is only two ways of getting this type of pseudo C-disaccharides one is via Stille type coupling of 1-stannylglucal and exocyclic bromoolefins (Scheme 2, a) [3b] and other is olefin cross metathesis approach (Scheme 2, b)[3c] which requires multiple steps with very poor overall yield and loss of two carbon units in the coupling step. We were keen to apply our CDC condition for the synthesis of theses C-linkedglycoconjugates in single step with complete atomic economy.

Towards this endeavor we performed areaction between a



Scheme 2: Comparison between literature and current methods for the synthesis of ethylene linked disaccharides

benzyl protected glucal and a furanose based terminal alkene. Gratifyingly, we obtained the required alkenyl linked pseudo C-disaccharide with excellent (up to 82%) yield (Scheme 3, **6a**).



Scheme 3: Single step synthesis of ethylene-linked disaccharides using Pd-catalysis**. Reaction conditions** - **4** (1 equiv.), **5** (1.2 equiv) $Pd(OAc)_2$ (0.1 equiv.) AgOAc (2.5 equiv.) in 2 mL of DMF: DMSO (20:1) at 80 °C; Yields refer to products isolated after column chromatography. [b] 0.2 equiv. of PPh_3 was used and takes 30 h to complete.

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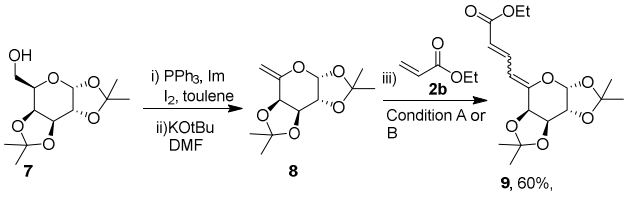
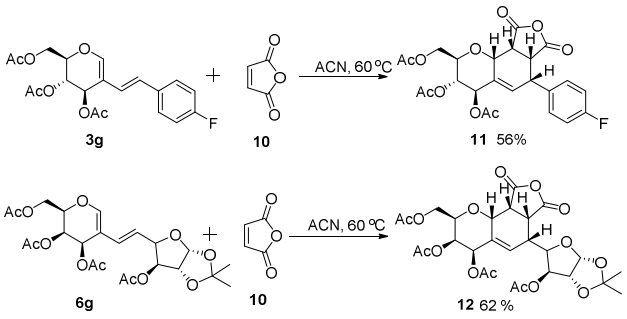
Synthesis of pseudodisaccharides were successful with different coupling partners such as furanoid glycals and glucals protected with different protecting groups (Scheme 3, **6b-6f**). Glycals such as acetyl protected D-galactal and L-rhamnal generated the ethylene linked pseudo C-disaccharides with excellent yield and complete *E*-selectivity (Scheme 3, **6g-6h**). We further utilized C-3-*O*-allylated furanose sugar as a terminal alkene partner and obtained four atom linked disaccharides (Scheme 3, **6i-6j**).

After getting successful results in the preparation of various dienes with endoglycals, we pursued our efforts to extend this methodology to exoglycals. Towards this, we prepared the exoglycal **8** starting from diacetone-D-galactose **7** and coupled it with ethyl acrylate under optimized reaction conditions to obtain the desired diene **9** (Scheme 4) in good yield (60%) as a mixture of *trans,anti,cis* and *trans,anti,trans (E,anti,Z:E,anti,E).* as determined from matching the *J* value of similar conjugated compounds in the literature.[9j,9k]



Scheme 4: Coupling of exoglycals with ethyl acrylate. **Reaction condition**: I) **7** (1 equiv.), PPh_3 (4 equiv.), Im (4 equiv.), I_2 (3.5 equiv.), in toluene at 60 °C for 3h II) KOtBu (2 equiv.) in DMF rt 1 h III) **Condition A**: **8** (1 equiv.), ethyl acrylate (1.2 equiv.), $Pd(OAc)_2$ (0.1 equiv.), $Cu(OAc)_2.H_2O$ (3 equiv.), pyridine (2 equiv.), PPh_3 (0.2 equiv.), in Dioxane at 100 °C for 24 h **Condition B** : **8** (1 equiv.), ethyl acrylate (1.2 equiv.) $Pd(OAc)_2$ (0.1 equiv.), AgOAc (2.5 equiv.), PPh_3 (0.2 equiv.), in DMF/DMSO at 100 °C, for 24 h. Im : Imidazole

Fused medium sized rings are privileged structures and attractive targets for synthesis. There are several notable contributions for the synthesis of oxadecalin cores from monosaccharides involving ring-closing metathesis,[10] Robinson annulation,[11]intramolecular aldol condensation,[12] radical cyclization,[13] and Diels–Alder cycloaddition[14] for the construction 6,6 and 5,6 bicyclic ring systems. Another approach for the construction 1-oxabicyclic core is stereo selective 6-*endo-tet* cyclization of homoallylic alcohols as reported from our group[15].



Scheme 5: Synthesis of oxadecalin cores via Diels-Alder cycloaddition. Reaction condition: **3g, 6g** (1 equiv.), **10** (2 equiv.), 2 mL of ACN in a sealed tube at 60 °C for 6 h. ACN: Acetonitrile

For the present study; we selected Diels Alder approach for the generation of oxadecalin core from already synthesized sugar based dienes. We obtained satisfactory yield when we reacted these dienes with maleic anhydride in sealed tube at 60 °C (Scheme 5, **11**, and **12**). The basic skeleton of Diels-Alder adduct **12** was confirmed through ^{1}HNMR and ^{13}CNMR. In the ^{1}HNMR of **12,** there is a shift in the anomeric proton with respect to diene **6g** from □ 6.58 to □ 4.64, appearance of new peak at □ 5.72 (d, *J* = 2.0 Hz, 1H) of olefinic protons at the cost of two diene (**6g**) olefinic protons at □ 6.16, 5.23 and new peak at □ 2.69 – 2.52 (m, 1H) of allylic proton clearly indicated the formation of Diels- Alder adduct **12**. Further ^{13}CNMR also indicated six carbonyl carbon peaks at δ 171.19, 170.06, 169.69, 169.36, 169.20, and 167.27 which confirmed the attachment of maleic anhydride with the pseudo disaccharides. Finally, stereochemistry of newly formed chiral centres of **12** (Figure 2) was determined by 2D NMR. In NOESY spectrum of compound **12,** cross peak between H_1 and βH_{6a} confirmed β stereochemistry at anomeric proton and strong cross peaks between $\beta H_1/H_8$ explained cofaciality of the protons.(See SI for detailed analysis).

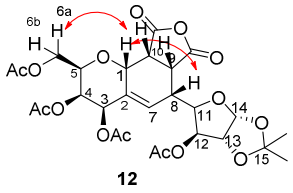
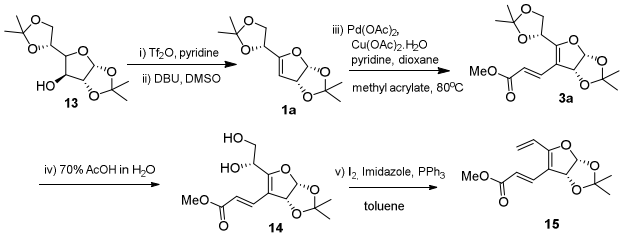


Figure 2: Stereo chemical assignment of compound **12** based on NOE

A furanose sugar based triene **15** (Scheme 6) was also synthesized in four steps by taking diacetone-D-glucose **13** (Scheme 6). The importance of this triene lies in the fact that this type conjugated system present in wide range of natural products and can be utilized further for the synthesis of medium to large fused rings attached with sugar moiety.[15a,b] Thus diacetone-D-glucose **13** was converted into furanoid glycal **1a** and coupled with methyl acrylate to yield diene **3a** with *E*- selectivity. Selective deprotection of 5,6-diacetonide and dehydration yielded the desired triene **15** with 68% overall yield.



Scheme 6: Synthesis of a sugar based conjugated triene. Reaction conditions: i) **13** (3.84 mmol) in DCM, pyridine (15.38 mmol) at 0 °C, triflic anhydride (5.76 mmol) for 2h. 75% ii) DBU (5.10 mmol) in DMSO overnight at rt. (quantitative) iii) **1a** (2.54mmol), $Pd(OAc)_2$ (0.25 mmol) and $Cu(OAc)_2.H_2O$ (7.64 mmol) in 6mL of dioxane, methyl acrylate (3.05 mmol) and pyridine (5.09 mmol) at 80 °C, 24 h, 78% iv) **3a** (2.69 mmol) in 70% ACOH:H_2O (10 mL) overnight rt. 87% V) **14** (1.74 mmol) in dry toluene, Im

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(6.99mmol), PPh_3 (6.99 mmol) and iodine (6.99 mmol) 60 °C for 3 h. 68%.Im: Imidazole

Conclusions

The present study describes an efficient method based upon cross dehydrogenative coupling for the synthesis of C-2 branched sugars having diene subunits from furanoid and pyranoid glycals under CDC condition. Pseudodisaccharides were prepared in a single step by utilizing furanose based terminal alkene as coupling partner.Tolerance of various protecting groups of sugar enol ethers and the applicability of a wide array of activated and unactivated alkenes establishes the mildness of conditions and generality of the method. Sugar based dienes could be used for the generation of oxadecalin cores via Diels Alder cyclization.

EXPERIMENTAL SECTION

General information

^1H and ^{13}C NMR spectra were recorded using 400 and 500 MHz spectrometers with TMS as internal standard. Chemical shifts are expressed in parts per million (δ ppm). Silica gel coated aluminium plates were used for TLC. The products were purified by column chromatography on silica gel (60-120 mesh) using petroleum ether–ethyl acetate as the eluent to obtain the pure products. Exact masses of all products were derived by using HRMS having QTOF analyzer. Reagents used were mostly purchased from Sigma Aldrich.

(A) General procedure for the synthesis of compound 3a-3l, 6a-6h

Method A: with **3a** as the example: To a solution furanose glycal (0.41 mmol, 100 mg), palladium(II)acetate (0.041 mmol, 9.18 mg) and $Cu(OAc)_2.H_2O$ (1.23 mmol, 247.5 mg) in 3 mL of dioxane at 80 °C under open air condition, methyl acrylate (0.49 mmol, 0.44 mL) and pyridine (0.82 mmol, 0.66 mL) were added. The mixture was allowed to stir at 80 °C for 24 h. After completion the mixture was diluted with ethyl acetate (2 mL), filtered, washed with water (5 mL) and finally with brine (5 mL). The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc, 9:1) to afford the product as white solid (123 mg 91% yield).

Method B: with **3a** as the example: To a solution of furanose glycal (0.41 mmol, 100 mg), in 2mL (10:1) mixture DMF and DMSO, palladium(II)acetate (0.041 mmol, 9.18 mg), silver acetate (1.03 mmol, 171 mg) and methyl acrylate (0.49 mmol, 0.44 mL) were added at 80 °C under open air condition for 24 h. After completion the mixture was diluted with ethyl acetate (2 mL), filtered, washed with water (5 mL) and finally with brine (5 mL). The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc 9:1) to afford the product as white solid (116 mg 80% yield).

B) General procedure for the preparation of compound 6i and 6j.

With **6i** as an example: Palladium(II)acetate (0.036 mmol, 8.19 mg), PPh_3 (0.073 mmol, 19 mg) silver acetate (0.91 mmol, 152 mg) and 3-*O*-allyl 1,2-5,6-diisopropylidene glucofuranose (0.44 mmol, 132 mg) were added to a stirred solution of Tri-*O*-acetyl-D-glucal (0.36 mmol, 100 mg) in mixture of DMF and DMSO (2mL, 10:1) at 80 °C under open air condition. After 24h the mixture was diluted with ethyl acetate (10 mL), filtered, and washed successively with water (10 mL) and brine (5 mL). The organic layer was dried and concentrated under reduced pressure. The residue was purified by flash column chromatography (Hexane/EtOAc 7:3) to afford the product as colorless oil (130 mg 59% yield).

C) Procedure for the synthesis of compound 8 and 9:

To a stirred solution of compound **7** (0.76 mmol, 200 mg) in dry toluene (5 mL) were added imidazole (3.07 mmol, 209 mg) and triphenylphosphine (3.07 mmol, 806 mg) at 60 °C. After 30 minutes, Iodine (3.07 mmol, 778 mg) was added in portions maintaining the reaction temperature in between 56-62 °C and resulting reaction mixture was allowed to stir for further 3h under reflux. After completion the reaction mixture was cooled to rt and diluted with 10 mL ethyl acetate, and washed with water (5 mL) and $Na_2S_2O_3$. The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc 9:1) to afford the product 6-deoxy-6-iodo-1, 2:3,4-di-*O*-isopropylidene-α-D-galacto-1,5-pyranose (200 mg, 70% gummy oil). To a solution of the purified iodinated product in 5 mL of DMF was added slowly KOtBu (1.08 mmol, 121 mg) and the mixture was kept under stirring at rt for 1h. After completion the reaction mixture was diluted with ethyl acetate (10 mL), filtered, and washed with water (5 mL). The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc 9:1) to afford the product **8** as oily liquid (100 mg, 76% yield). $Pd(OAc)_2$ (0.02 mmol, 9.2 mg), PPh_3 (0.2 equiv), AgOAc (1.03 mmol, 171 mg), and ethyl acrylate (0.49 mmol, 53 µL) were added to a stirred solution of Compound **8** (0.41 mmol, 50 mg) in mixture of 2 mL DMF/DMSO (20:1) at 80 °C for 24 h. After completion the mixture was diluted with ethyl acetate (2 mL), filtered, and washed successively with water (5 mL) and brine (5 mL). The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc, 9:1) to afford the product **9** as oily liquid (80 mg, 60% yield).

D) Procedure for the synthesis of compound 11, 12

By taking **11** as the example: Sugar based diene **3g** (0.12 mmol, 50 mg) and maleic anhydride **10** (0.25 mmol, 24 mg) in ACN were taken in a sealed tube and heated for 6h.The mixture was allowed to cool at room temperature, diluted with ethyl acetate (5 mL), washed with water (5 mL) and finally with brine (5 mL). The organic layer was dried, evaporated, and the residue was purified by flash

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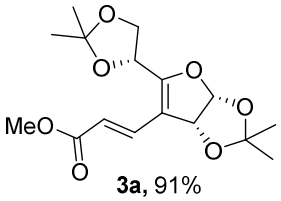
column chromatography (Hexane/EtOAc 7:1) to afford the product **11** as colourless oil (56% yield, 35mg).

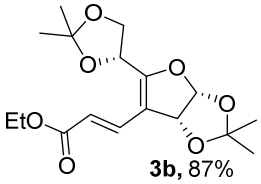
E) Procedure for the synthesis of compound 15 from 13.

To a stirred solution of Compound **13** (3.84 mmol, 1g) in 10 mL DCM was added pyridine (15.38 mmol, 1.24 mL) at 0 ^{o}C. After 5 minutes triflic anhydride (5.76 mmol, 970 µL) was added and the reaction mixture was further stirred for 2h. After completion, the mixture was diluted with DCM (5 mL), washed with water (5 mL) and brine (5 mL). The organic layer was dried, evaporated, and the residue was dried over Na_2SO_4. After super drying the compound over vacuum pump, the crude compound was used as such for next step without purification. 3-trifluromethanesulphonate-1,2:3,4-di-*O*-isopropylidene-α-D-glucofuranose (2.55 mmol, 1g) was dissolved in DMSO and DBU (5.10 mmol, 761µL) was added. The reaction mixture was stirred overnight at rt. The reaction mixture was diluted with ethyl acetate (50 mL), and washed with brine (50 mL). The organic layer was concentrated, evaporated, and the residue was dried over Na_2SO_4 and purified by flash column chromatography (Hexane/EtOAc 9:1) to get compound **1a** as white solid in quantitative yield (617mg). To a solution of furanose glycal **1a** (2.54 mmol, 617 mg) in 6 mL of dioxane were added palladium(II)acetate (0.25 mmol, 56.85 mg) and $Cu(OAc)_2.H_2O$ (7.64 mmol, 1.5 g) methyl acrylate (3.05 mmol, 275 µL) and pyridine (5.09 mmol, 411 µL) at 80 °C under open air condition for 24 h. After completion the reaction mixture was diluted with ethyl acetate (10 mL), filtered, washed with water (10 mL) and brine (10 mL). The organic layer was dried, evaporated, and the residue was purified by flash column chromatography (Hexane/EtOAc, 9:1) to afford the product **3a** as white solid (653 mg, 78% yield). The compound **14** was prepared by dissolving compound **3a** (2.69 mmol, 653 mg) in 70% AcOH:H_2O (10 mL) and stirring overnight at rt. After complete conversion of starting material monitored by TLC, solvent was evaporated and dried over high vacuum pump to obtain compound **14** (500 mg, 87%) as gummy liquid. This compound (1.74mmol, 500mg) was dissolved in dry toluene and warmed to 60 ^{o}C. After 5 minutes imidazole (6.99 mmol, 475 mg), PPh_3 (6.99 mmol, 1.83 g) were added and stirred for 30 minutes at same temperature. Iodine (6.99 mmol, 1.76 g) was added slowly in slots maintaining the reaction temperature 56-62^{o}C. After complete addition, the reaction mixture was stirred for further 3h under reflux. After complete consumption of starting material, the reaction mixture was cooled to rt, diluted with ethyl acetate (50mL), filtered, washed with water (20 mL) and sodium thiosulphate (20 mL). The organic layer was evaporated and the residue was purified by flash column chromatography (Hexane/EtOAc 9:1) to afford the desired triene **15** gummy liquid (300 mg, 68% yield).



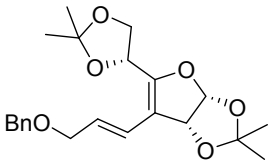
3a, 91%

Following the general procedure (A) **3a** was obtained as white solid (123 mg 91% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.77 (d, *J* = 15.7 Hz, 1H, -C=CH), 6.10 (d, *J* = 5.3 Hz, 1H, H-1), 5.98 (d, *J* = 15.7 Hz, 1H, -C=CH), 5.38 (d, *J* = 5.3 Hz, 1H, H-2), 4.93 (t, *J* = 6.5 Hz, 1H, H-5), 4.18 (dd, *J* = 8.4, 6.9 Hz, 1H, H6a), 4.04 (dd, *J* = 8.5, 6.1 Hz, 1H, H-6b), 3.75 (s, 3H, OMe), 1.49 (s, 3H), 1.47 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.1 (-CO), 161.1 (C-4), 136.3 (-CH=CH), 117.3 (C-3), 115.2 (-CH=CH), 115.0, 112.4, 107.3 (C-1), 84.1, 68.3, 52.9, 29.2, 29.2, 27.1, 26.9. **HRMS (ESI^{+})**: m/z calcd. For $C_{16}H_{23}O_7$ $(M+H)^{+}$327.1444, found 327.1437.



3b, 87%

Following the general procedure (A) **3b** was obtained as white solid (122 mg 87% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (d, *J* = 15.7 Hz, 1H, C=CH), 6.12 (d, *J* = 5.3 Hz, 1H, H-1), 6.00 (d, *J* = 15.7 Hz, 1H, C=CH), 5.39 (d, *J* = 5.3 Hz, 1H, H-2), 4.94 (t, *J* = 6.6 Hz, 1H, H-5), 4.28 – 4.17 (m, 3H, -OCH_2, H-6a), 4.05 (dd, *J* = 8.4, 6.3 Hz, 1H, H-6b), 1.51 (s, 3H), 1.49 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2 (-CO), 161.7 (C-4), 134.6 (-CH=CH), 116.4 (C-3), 113.6(-CH=CH), 111.0, 106.0 (C-1), 82.7, 70.2, 66.9, 60.2, 27.8, 25.7, 25.5, 14.3. **HRMS (ESI^{+})**: m/z calcd. For $C_{17}H_{25}O_7$ $(M+H)^{+}$341.1600, found 341.1609.



3c, 73%

Following the general procedure (A) **3c** was obtained as white solid (117 mg 73% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 – 7.25 (m, 5H) , 6.53 (d, *J* = 15.7 Hz, 1H, -C=CH), 5.96 (d, *J* = 5.4 Hz, 1H, H-1), 5.83 (dt, *J* = 15.7, 6.0 Hz, 1H, C=CH), 5.31 (d, *J* = 5.4 Hz, 1H, H-2), 4.79 (t, *J* = 6.6 Hz, 1H, H-5), 4.08 – 4.02 (m, 3H, -CH_2, H-6a), 3.96 (dd, *J* = 8.3, 6.5 Hz, 1H, H-6b), 1.40 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.8 (C-4), 139.7 (C-Olefin), 129.8, 129.2, 129.0, 126.5, 123.6, 116.0 (C-3), 114.3 (C-olefin), 111.9, 106.4 (C-1),

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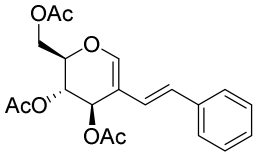
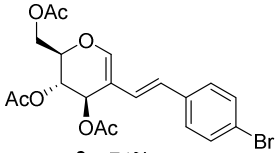
85.1, 73.6, 72.2, 71.3, 68.1, 31.2, 29.3, 29.3, 27.3, 27.1. **HRMS (ESI$^+$)**: m/z calcd. For $C_{22}H_{28}NaO_6$ $(M+Na)^+$411.1784, found 411.1778.



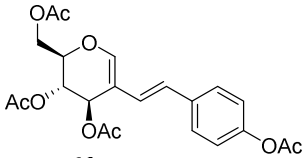
3d, 71%

Following the general procedure (A) **3d** was obtained as colorless oil (98 mg 71% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** 7.31 (m, 4H) 7.21 (m, 1H) 6.81 (s, 1H, H-1) 6.57 (d, *J* = 16.4 Hz, 1H, -C=CH) 6.27 (d, *J* = 16.4 Hz, 1H, -C=CH) 5.77 (d, *J* = 3.0 Hz, 1H, H-3) 5.19 (t, *J* = 3.5 Hz, 1H) 4.52 – 4.42 (m, 2H) 4.27 – 4.17 (m, 1H) 2.13 – 2.08 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.5, 170.2, 169.6, 146.4 (C-1), 137.3, 128.6 (–C=CH-), 127.1, 125.9, 124.9, 123.9 (–C=CH-), 110.7 (C-2), 73.7, 67.0, 63.5, 61.3, 20.9, 20.8. **HRMS (ESI$^+$)**: m/z calcd. for $C_{20}H_{22}NaO_7$ $(M+Na)^+$397.1258, found 397.1234.



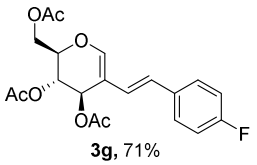
3e, 74%

Following the general procedure (A) **3e** was obtained as colorless oil (125 mg 74% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.44 – 7.34 (m, 2H) 7.26 – 7.15 (m, 2H) 6.82 (s, 1H, H-1) 6.55 (d, *J* = 16.4 Hz, 1H, -C=CH) 6.18 (d, *J* = 16.3 Hz, 1H, -C=CH) 5.74 (d, *J* = 3.1 Hz, 1H) 5.17 (t, *J* = 3.4 Hz, 1H) 4.54 – 4.45 (m, 2H), 4.23 – 4.11 (m, 1H) 2.10 (s, 3H), 2.10 (s, 3H), 2.09 – 2.07 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** 170.5, 170.2, 169.5, 146.9 (C-1), 136.3, 131.7(-C=CH), 127.4, 124.8, 123.5, 120.7 (–C=CH), 110.5 (C-2), 73.8, 66.9, 63.3, 61.2, 20.9, 20.8, 20.8. **HRMS (ESI$^+$)**: m/z calcd. For $C_{20}H_{21}BrNaO_7$ $(M+Na)^+$; 475.0368, found 475.0365.



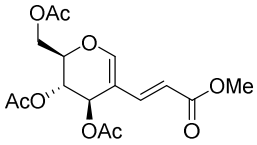
3f, 71%

Following the general procedure (A) **3f** was obtained as colorless oil (113 mg 71% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.34 (m, 2H) 7.04 – 6.95 (m, 2H) 6.81 (s, 1H, H-1) 6.51 (d, *J* = 16.2 Hz, 1H, -C=CH) 6.23 (d, *J* = 16.3 Hz, 1H, -C=CH) 5.75 (d, *J* = 2.9 Hz, 1H), 5.18 (t, *J* = 3.6 Hz, 1H) 4.50 – 4.43 (m, 2H), 4.21 (m, 1H), 2.29 (s, 3H), 2.11 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.9, 171.6, 171.0, 171.0, 151.0, 148.0 (C-1), 144.6, 136.6, 128.2 (-C=CH), 125.6, 125.3, 123.1 (-C=CH) 112.0 (C-2), 75.2, 68.4, 64.9, 62.7, 22.5, 22.3, 22.3, 22.2. **HRMS (ESI$^+$)**: m/z calcd. For $C_{22}H_{24}NaO_9$ (M+Na) $^+$455.1318, found 455.1324.



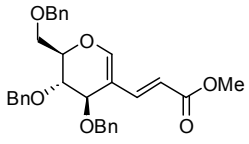
3g, 71%

Following the general procedure (A) **3g** was obtained as colorless oil (103 mg 71% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.34 – 7.27 (m, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.80 (s, 1H, H-1), 6.47 (d, *J* = 16.4 Hz, 1H, -C=CH), 6.22 (d, *J* = 16.4 Hz, 1H, -C=CH), 5.74 (d, *J* = 3.0 Hz, 1H, H-3), 5.18 (t, *J* = 3.5 Hz, 1H), 4.48 (dd, *J* = 15.7, 5.1 Hz, 2H), 4.21 (dd, *J* = 6.8, 3.9 Hz, 1H), 2.11 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 170.2, 169.5, 163.2, 160.8, 146.4(C-1), 133.57, 127.4 (-C=CH), 127.3, 123.8, 123.7, 115.6, 115.4, 110.6 (C-2), 99.0, 73.8, 67.0, 63.6, 61.3, 20.8, 20.7.**HRMS (ESI$^+$)**: m/z calcd. For $C_{20}H_{21}FNaO_7$ $(M+Na)^+$ 415.1169, found 415.1165.



3h, 83%

Following the general procedure (A) **3h** was obtained as colorless oil (108 mg 83% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.14 (d, *J* = 15.9 Hz, 1H), 6.92 (s, 1H), 5.57 (d, *J* = 15.8 Hz, 1H), 5.53 (d, *J* = 2.2 Hz, 1H), 5.10 (t, *J* = 3.4 Hz, 1H), 4.46 – 4.34 (m, 2H), 4.12 (dd, *J* = 11.6, 3.9 Hz, 1H), 3.66 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 2.02 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.3, 169.9, 169.3, 167.4, 152.2, 141.0, 113.8, 109.3, 74.4, 66.3, 62.7, 61.0, 51.5, 29.6, 20.8, 20.7, 20.7. **HRMS (ESI$^+$)**: m/z calcd. For $C_{16}H_{20}NaO_9$ $(M+Na)^+$ 379.1005, found 379.1012.



3i, 89%

Following the general procedure (A) **3i** was obtained as gummy solid (107 mg 89% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.15 (m, 16H, (15HOBn, 1H, -C=CH)), 6.94 (s, 1H, H-1), 5.70 (d, *J* = 15.7 Hz, 1H, -C=CH), 4.65 (m, 2H), 4.59 – 4.52 (m, 1H), 4.51 – 4.43 (m, 4H), 4.22 – 4.15 (m, 1H), 4.01 (t, *J* = 3.1 Hz, 1H), 3.78 (dd, *J* = 10.4, 6.9 Hz, 1H), 3.73 (s, 3H, OMe), 3.66 (dd, *J* = 10.4, 5.2 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 167.9 (-CO), 152.2 (C-1), 143.2 (-C=CH), 137.7, 137.4, 137.2, 128.6, 128.5, 128.5, 128.2, 128.1, 128.1, 127.1, 127.8, 127.8, 112.7 (-C=CH), 111.0

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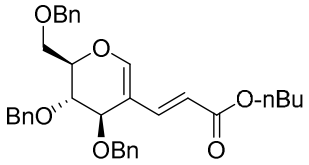
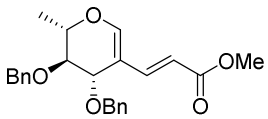
(C-2), 76.5, 73.4, 71.9, 70.8, 69.9, 69.9, 51.4, 31.6, 22.7, 14.2. **HRMS (ESI$^+$)**: m/z calcd. For $C_{31}H_{32}NaO_6$ (M+Na) $^+$; 523.2097, found 523.2090.



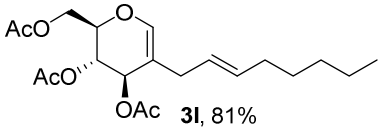
3j, 81%

Following the general procedure (A) **3j** was obtained as gummy solid (106 mg 81% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.38 – 7.26 (m, 14H, 13H-OBN, 1H -C=CH), 7.25 – 7.20 (m, 2H), 6.94 (s, 1H, H-1), 5.68 (d, *J* = 15.7 Hz, 1H, -C=CH) 4.66 (d, *J* = 5.8 Hz, 2H), 4.57 – 4.44 (m, 5H), 4.19 (s, 1H), 4.15 (m, 2H), 4.02 (t, *J* = 3.1 Hz, 1H), 3.78 (dd, *J* = 10.4, 6.9 Hz, 1H), 3.67 (dd, *J* = 10.4, 5.2 Hz, 1H), 1.65 (m, 2H), 1.43 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 167.5, 152.0 (C-1), 142.8 (-C=CH), 137.8, 137.5, 137.3, 128.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 113.3 (-C=CH), 111.1 (C-2), 76.5, 73.4, 71.9, 70.7, 70.1, 70.0, 68.1, 63.9, 30.9, 19.2, 13.6.**HRMS (ESI$^+$)**: m/z calcd. For $C_{34}H_{38}NaO_6$ (M+Na) $^+$565.2566, found 565.2571.



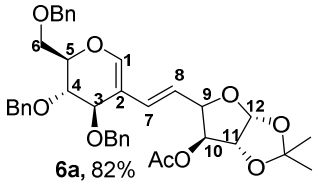
3k, 90%

Following the general procedure (A) **3k** was obtained as gummy white solid (115 mg 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.15 (m, 11H, 10H–OBn, 1H-C=CH), 6.82 (s, 1H, H-1) 5.66 (d, *J* = 15.7 Hz, 1H, -C=CH), 4.58 (s, 2H), 4.42 (s, 2H), 4.33 (m, 1H), 4.16 (d, *J* = 1.5 Hz, H), 3.63 (s, 3H, OMe), 1.31 (d, *J* = 6.9 Hz, 3H, CH_3). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.0, 152.5 (C-1), 143.4 (-C=CH), 137.6, 128.6, 128.5, 128.1, 127.9, 127.9, 112.5 (-C=CH), 110.1 (C-2), 74.1, 72.0, 71.2, 70.4, 51.3, 16.7. **HRMS (ESI$^+$)**: m/z calcd. For $C_{24}H_{26}NaO_5$ (M+Na) $^+$417.1678, found 417.1674.



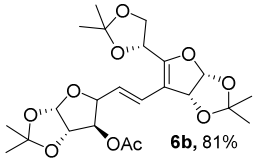
3l, 81%

Following the general procedure (A) **3l** was obtained as colorless oil (114 mg 81% yield). **1H NMR (400 MHz, CDCl$_3$)** δ 6.30 (s, 1H, C-1), 5.46 (d, J = 5.5 Hz, 1H), 5.42 (m, 1H), 5.29 (m, 1H), 5.17 (dd, J = 7.4, 5.4 Hz, 1H), 4.38 (dd, J = 12.0, 5.8 Hz, 1H), 4.23 – 4.14 (m, 2H), 2.58 (d, J = 6.6 Hz, 2H), 2.09 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.97 (m, 2H), 1.36 – 1.26 (m, 6H), 0.88 (t, J = 7.0 Hz, 3H). **13C NMR (126 MHz, CDCl$_3$):** δ 170.6, 170.5, 169.7, 141.6, 133.3, 126.0, 109.8, 73.5, 68.3, 68.1, 61.5, 32.4, 31.6, 31.4, 22.5, 20.8, 20.7, 14.0. **HRMS (ESI+)**: m/z calcd. for$C_{20}H_{30}NaO_7$ (M+Na)$^+$ 405.1889, found 405.1893.



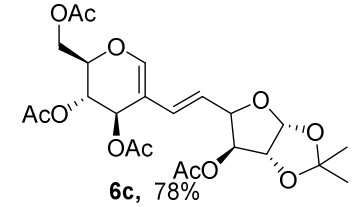
6a, 82%

Following the general procedure (A) **6a** was obtained as gummy solid (131 mg 82% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.32 (m, 8H), 7.27 (m, 7H), 6.67 (s, 1H, H-1), 6.26 (d, *J* = 15.9 Hz, 1H, H-7), 5.94 (d, *J* = 3.8 Hz, 1H, H-12), 5.51 (dd, *J* = 15.8, 6.7 Hz, 1H, H-8), 5.16 (d, *J* = 3.0 Hz, 1H, H-11), 4.80 (dd, *J* = 6.6, 2.5 Hz, 1H), 4.66 (d, *J* = 1.5 Hz, 1H), 4.54 (d, *J* = 3.8 Hz, 1H), 4.49 (d, *J* = 6.3 Hz, 2H), 4.44 (s, 2H), 4.38 – 4.33 (m, 1H), 4.22 (d, *J* = 2.9 Hz, 1H), 4.00 – 3.95 (m, 1H), 3.78 (dd, *J* = 10.5, 6.5 Hz, 1H), 3.65 (dd, *J* = 10.6, 4.4 Hz, 1H), 1.93 (s, 3H), 1.54 (s, 3H), 1.33 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 169.8, 146.7 (C-1), 137.9, 137.8, 131.2 (C-7), 128.5, 128.4, 128.4, 127.1, 127.9, 127.7, 127.7, 116.8 (C-8), 111.9 (C-2), 111.4, 104.4 (C-12), 83.6, 80.3, 77.7, 76.2, 73.4, 72.1, 71.8, 71.1, 69.8, 68.24, 26.7, 26.3, 20.7.**HRMS (ESI+)** :(m/z) calcd. for$C_{38}H_{42}NaO_9$ (M+Na)$^+$ 665.2727, found 665.2732.



6b, 81%

Following the general procedure (A) **6b** was obtained as gummy white solid (165 mg 81% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 6.69 (d, *J* = 15.7 Hz, 1H, H-7), 6.01 (d, *J* = 5.4 Hz, 1H, H-1), 5.96 (d, *J* = 3.8 Hz, 1H, H-9), 5.66 (dd, *J* = 15.8, 6.4 Hz, 1H, H-8), 5.31 (d, *J* = 5.4 Hz, 1H, H-2), 5.22 (d, *J* = 3.0 Hz, 1H), 4.85 (m, 2H), 4.57 (d, *J* = 3.8 Hz, 1H), 4.11 (dd, *J* = 8.3, 6.8 Hz, 1H), 4.01 (dd, *J* = 8.3, 6.5 Hz, 1H), 2.05 (s, 3H), 1.53 (s, 3H), 1.46 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 1.39 (s, 3H) 1.33 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 169.6, 153.3 (C-4), 123.6 (C-7), 120.5 (C-3), 114.3 (C-8), 112.9, 112.0, 110.5, 104.1 (C-1), 104.5 (C-9), 83.6, 80.1, 77.5, 69.8, 66.6, 27.9, 27.8, 26.7, 26.2, 25.8, 25.7, 20.7.
HRMS (ESI$^+$): m/z calcd. for$C_{23}H_{32}NaO_{10}$ (M+Na)$^+$491.1823, found 491.1818.



6c, 78%

Following the general procedure (A) **6c** was obtained as gummy solid (150 mg 78% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 6.68 (s, 1H, H-1), 6.20 (d, *J* = 16.0 Hz, 1H, H-7), 5.92 (d, *J* = 3.8 Hz, 1H, H-12), 5.55 (d, *J* = 3.1 Hz, 1H, H-11), 5.22 (dd, *J* = 16.0, 6.3 Hz, 1H, H-8), 5.16 (d, *J* = 2.8 Hz, 1H, H-3), 5.10 (t, *J* = 3.7 Hz, 1H), 4.74 (dd, *J* = 6.2, 2.4 Hz, 1H), 4.55 (d, *J* = 3.8 Hz, 1H), 4.45 –

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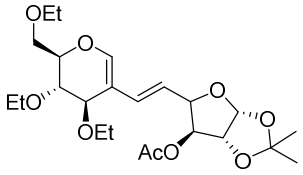
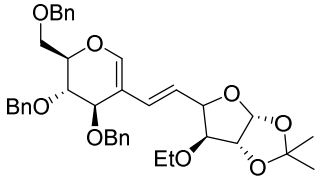
4.36 (m, 2H), 4.19 – 4.06 (m, 1H), 2.09 – 2.07 (s, 9H), 2.04 (s, 3H), 1.51 (s, 3H), 1.31 (s, 5H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.4, 170.3, 169.6, 169.5, 146.9 (C-1), 129.1 (C-7), 117.6 (C-8), 111.1, 109.8 (C-2), 104.4 (C-12), 83.5, 79.8, 73.8, 67.1, 63.6, 61.1, 29.7, 26.7, 26.2, 20.8, 20.7, 20.6. **HRMS (ESI$^+$)**: m/z calcd. For $C_{23}H_{30}NaO_{12}$ $(M+Na)^+$521.1635, found 521.1639.



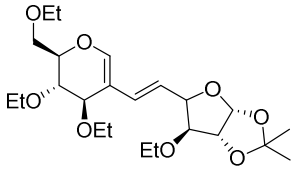
6d,77%

Following the general procedure (A) **6d** was obtained as gummy liquid (161 mg 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.56 (s, 1H, H-1), 6.20 (d, *J* = 15.8 Hz, 1H, H-7), 5.92 (d, *J* = 3.8 Hz, 1H, H-12), 5.51 (dd, *J* = 15.8, 6.7 Hz, 1H, H-8), 5.15 (d, *J* = 2.9 Hz, 1H, H-11), 4.77 (dd, *J* = 6.6, 2.7 Hz, 1H), 4.53 (d, *J* = 3.8 Hz, 1H), 4.19 (d, *J* = 5.3 Hz, 1H), 4.01 (d, *J* = 3.8 Hz, 1H), 3.75 – 3.48 (m, 9H), 2.04 (s, 3H), 1.51 (s, 3H), 1.30 (s, 3H), 1.20 (m, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.7, 146.4 (C-1), 131.3 (C-7), 116.6 (C-8), 111.8 (C-2), 111.8, 104.4 (C-12), 83.6, 80.3, 77.7, 76.5, 72.4, 72.0, 68.5, 66.8, 66.0, 62.9, 26.7, 26.2, 20.6, 15.5, 15.5, 15.1. **HRMS (ESI$^+$)**: m/z calcd. for$C_{23}H_{36}NaO_9$ $(M+Na)^+$479.2257, found 479.2251.



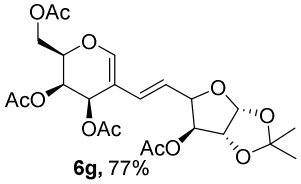
6e, 79%

Following the general procedure (A) **6e** was obtained as gummy solid (124 mg 79% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 – 7.28 (m, 10H), 7.26 (dd, *J* = 7.2, 2.2 Hz, 5H), 6.66 (s, 1H, H-1), 6.25 (d, *J* = 15.9 Hz, 1H, H-7), 5.92 (d, *J* = 3.8 Hz, 1H, H-12), 5.73 (dd, *J* = 15.9, 7.6 Hz, 1H, H-8), 4.65 (m, 2H), 4.54 (m, 2H), 4.48 (m, 3H), 4.36 (dd, *J* = 6.4, 4.2 Hz, 1H), 4.27 (d, *J* = 2.8 Hz, 1H), 3.96 (t, *J* = 4.0 Hz, 1H), 3.80 – 3.64 (m, 4H), 3.57 (dd, *J* = 9.4, 7.0 Hz, 1H), 3.50 – 3.42 (m, 1H), 1.52 (s, 3H), 1.33 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 146.2 (C-1), 138.1, 138.0, 137.9, 130.6 (C-7), 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 118.8 (C-8), 111.7, 111.3 (C-2), 104.7 (C-12), 84.4, 83.3, 81.8, 76.2, 73.4, 72.1, 71.1, 71.4, 70.2, 68.4, 66.2, 26.9, 26.3, 15.2. **HRMS (ESI$^+$)**: m/z calcd. for $C_{38}H_{44}NaO_8$ $(M+Na)^+$651.2934, found 651.2939.



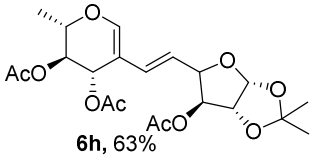
6f, 73%

Following the general procedure (A) **6f** was obtained as gummy liquid (149 mg 73% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.58 (s, 1H, H-1), 6.20 (d, *J* = 15.9 Hz, 1H, H-7), 5.91 (d, *J* = 3.8 Hz, 1H, H-12), 5.71 (dd, *J* = 15.9, 7.6 Hz, 1H,H-8), 4.62 (dd, *J* = 7.6, 2.9 Hz, 1H), 4.55 (d, *J* = 3.9 Hz, 1H), 4.24 – 4.15 (m, 1H), 4.06 (d, *J* = 3.7 Hz, 1H), 3.74 (m, 1H), 3.70 (m, 3H), 3.68 – 3.59 (m, 4H), 3.58 – 3.49 (m, 4H), 1.50 (s, 3H), 1.32 (s, 3H), 1.24 – 1.16 (m, 12H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 145.1 (C-1), 130.8 (C-7), 118.6 (C-8), 111.1, 111.3 (C-2), 104.7 (C-1), 84.5, 83.2, 81.9, 72.4, 72.3, 68.7, 66.8, 66.2, 65.1, 63.2, 26.8, 26.3, 15.6, 15.5, 15.2, 15.1. **HRMS (ESI$^+$)**: m/z calcd. for $C_{23}H_{38}NaO_8$ $(M+Na)^+$ 465.2464, found 465.2466.



6g, 77%

Following the general procedure (A) **6g** was obtained as gummy liquid (149 mg 77% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.58 (s, 1H, H-1), 6.16 (d, *J* = 15.9 Hz, 1H, H-7), 5.90 (d, *J* = 3.8 Hz, 1H, H-12), 5.80 (d, *J* = 4.3 Hz, 1H, H-3), 5.37 (t, *J* = 4.2 Hz, 1H), 5.23 (dd, *J* = 16.0, 6.4 Hz, 1H, H-8), 5.14 (d, *J* = 2.9 Hz, 1H, H-11), 4.72 (dd, *J* = 6.4, 2.4 Hz, 1H), 4.53 (d, *J* = 3.8 Hz, 1H), 4.42 (m, 1H), 4.38 – 4.32 (m, 1H), 4.24 (m, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.49 (s, 3H), 1.29 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.6, 170.6, 169.5, 169.5, 146.5 (C-1), 128.5 (C-7), 117.9 (C-8), 111.1, 110.5 (C-2), 104.4 (C-12), 83.5, 72.1, 65.4, 61.8, 61.4, 26.7, 26.2, 20.8, 20.6, 20.6, 20.5. **HRMS (ESI$^+$)**: m/z calcd. for $C_{23}H_{30}NaO_{12}$ $(M+Na)^+$ 521.1635, found 521.1643



6h, 63%

Following the general procedure (A) **6h** was obtained as gummy liquid (140 mg 63% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.68 (s, 1H, H-1), 6.24 (d, *J* = 15.9 Hz, 1H, H-7), 5.90 (d, *J* = 3.8 Hz, 1H, H-12), 5.61 (d, *J* = 2.8 Hz, 1H, H-3), 5.30 (dd, *J* = 15.9, 8.0 Hz, 1H, H-8), 5.14 (d, *J* = 2.8 Hz, 1H, H-11), 4.92 (t, *J* = 3.7 Hz, 1H), 4.70 (dd, *J* = 8.0, 2.7 Hz, 1H), 4.52 (d, *J* = 3.8 Hz, 1H), 4.28 (m, 1H), 2.08 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.52 (s, 3H), 1.35 (d, *J* = 6.9 Hz, 3H), 1.30 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.1, 169.7, 169.7, 147.1 (C-1), 132.2 (C-7), 115.9 (C-8), 111.9, 109.1 (C-2), 104.3 (C-12), 83.7, 80.4, 72.4, 70.9, 63.9,

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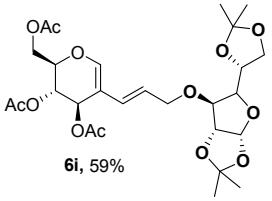
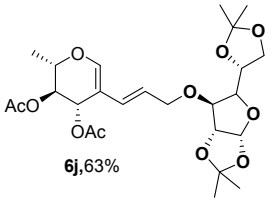
26.7, 26.2, 20.9, 20.8, 20.6, 16.2. **HRMS (ESI$^+$)**: m/z calcd. for $C_{21}H_{28}NaO_{10}$ $(M+Na)^+$ 463.1580, found 463.1573



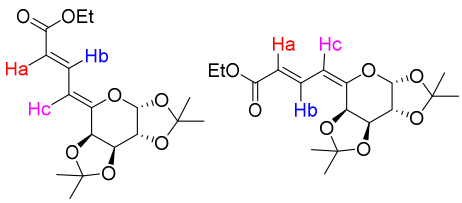
6i, 59%

Following the general procedure (B) **6i** was obtained as colorless liquid (125 mg 59% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 6.67 (s, 1H, H-1), 6.09 (d, *J* = 16.1 Hz, 1H, H-7), 5.86 (d, *J* = 3.7 Hz, 1H, H-12), 5.60 (d, *J* = 3.2 Hz, 1H, H-3), 5.42 (dt, *J* = 15.9, 5.8 Hz, 1H, H-8), 5.13 (t, *J* = 3.6 Hz, 1H), 4.52 (d, *J* = 3.7 Hz, 1H), 4.47 – 4.38 (m, 2H), 4.35 – 4.26 (m, 1H), 4.17 (dd, *J* = 11.1, 3.4 Hz, 1H), 4.15 – 4.09 (m, 3H), 4.09 – 4.05 (m, 1H), 3.99 (dd, *J* = 8.6, 5.7 Hz, 1H), 3.92 (d, *J* = 2.9 Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 1.49 (s, 4H), 1.42 (s, 4H), 1.35 (s, 4H), 1.31 (s, 4H).**^{13}C NMR (101 MHz, CDCl$_3$)** δ 170.4, 170.1, 169.5, 146.4 (C-1), 127.9 (C-7), 121.3 (C-8), 111.8, 109.7 (C-2), 109.0, 105.2 (C-12), 82.8, 81.3, 81.2, 73.7, 72.5, 70.9, 67.3, 67.1, 63.9, 61.2, 26.8, 26.3, 25.5, 25.4 20.8, 20.7, 20.7. **HRMS (ESI$^+$)**: m/z calcd. for $C_{27}H_{38}NaO_{13}$ $(M+Na)^+$ 593.2210, found 593.2219



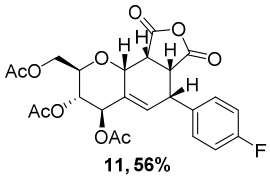
6j,63%

Following the general procedure (B) **6j** was obtained as colorless liquid (154 mg 63% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 6.66 (s, 1H, H-1), 6.07 (d, J = 16.0 Hz, 1H, H-7), 5.93 (d, J = 3.6 Hz, 1H, H-3), 5.86 (d, J = 3.6 Hz, 1H, H-11), 5.58 (d, J = 3.3 Hz, 1H), 5.36 (dt, J = 15.9, 6.0 Hz, 1H), 4.96 (t, J = 4.0 Hz, 1H), 4.51 (dd, J = 8.5, 3.7 Hz, 1H), 4.33 – 4.25 (m, 2H), 4.18 – 4.12 (m, 1H), 4.11 – 4.03 (m, 2H), 4.01 – 3.95 (m, 1H), 3.93 (d, J = 3.0 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.48 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.30 (d, J = 4.3 Hz, 3H).**^{13}C NMR (101 MHz, CDCl$_3$)** δ 170.3, 169.8, 147.0 (C-1), 128.7 (C-7), 120.7 (C-8), 111.8, 111.8, 109.6 (C-2), 109.2, 108.1, 105.3, 105.3 (C-12), 85.1, 82.9, 81.3, 81.2, 80.1, 75.2, 73.5, 72.5, 72.3, 71.3, 71.2, 67.7, 67.3, 64.9, 26.3, 26.2, 25.4, 25.2, 20.9, 20.8, 16.2. **HRMS (ESI$^+$)**: m/z calcd. for $C_{25}H_{36}NaO_{11}$ $(M+Na)^+$ 535.2155, found 535.2147



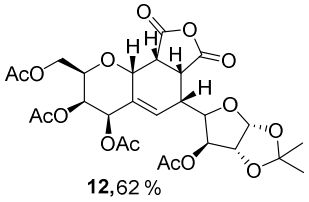
9 *E,Z*: *E,E* 1:0.7 (60%)
Inseparable mixture

Following the general procedure (C) **9** was obtained as oily liquid (80 mg 60% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.69 (dd, *J* = 15.6, 11.3 Hz, 1H, Hb, *E,E*), 7.57 (dd, *J* = 15.1, 12.2 Hz, 1H, Hb, *E,Z*), 6.02 (d, *J* = 12.2 Hz, 1H, Hc, *E,Z*), 5.87 (dd, *J* = 15.4, 11.9 Hz, 2H, Ha, *E,E*), Hc (*E,E*), 5.76 – 5.71 (m, 2H, Ha, *E,E*)), 5.66 (d, *J* = 3.7 Hz, 1H), 5.12 (d, *J* = 7.3 Hz, 1H), 4.63 (ddd, *J* = 11.3, 7.2, 2.2 Hz, 2H), 4.56 (d, *J* = 7.1 Hz, 1H), 4.34 (dd, *J* = 3.6, 2.5 Hz, 1H), 4.28 (dd, *J* = 3.3, 2.1 Hz, 1H), 4.24 – 4.16 (m, 4H), 1.47 (s, 6H), 1.42 (s, 3H), 1.40 (s, 3H), 1.38 (s, 3H), 1.35 (m, 5H), 1.30 – 1.27 (m, 5H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 167.0 (CO), 167.0 (CO), 154.1, 152.1, 138.1, 137.5, 120.7, 120.6, 115.2, 112.9, 111.0, 110.9, 110.5, 110.2, 97.6, 97.6, 73.5, 72.70, 72.1, 70.9, 70.5, 66.9, 60.3, 60.2, 26.9, 26.7, 26.5, 26.4, 25.6, 24.6, 24.5, 14.3. **HRMS (ESI$^+$)**: m/z calcd. for $C_{17}H_{25}O_7$ $(M+H)^+$ 341.1600, found 341.1595



11, 56%

Following the general procedure (D) **11** was obtained as oily liquid (35 mg 56% yield). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.27 (m, 2H), 7.08 (m, 2H), 6.34 (s, 1H), 5.54 (d, *J* = 4.9 = 4. Hz, 1H), 4.92 (m, 1H), 4.89 – 4.84 (m, 1H), 4.25 – 4.17 (m, 1H), 4.04 (m, 1H), 3.75 (m, 1H), 3.58 (m, 1H), 2.13 (s, 3H), 2.12 (s, 6H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 171.1, 169.7, 169.3, 168.6, 167.4, 132.6, 130.5, 130.4, 130.4, 115.7, 115.5, 74.5, 71.1, 69.1, 63.4, 60.3, 45.1, 44.7, 38.5, 29.7, 20.1, 20.8, 20.8. **HRMS (ESI$^+$)**: m/z calcd. for $C_{24}H_{23}FNaO_{10}$ $(M+Na)^+$ 513.1173, found 513.1168.



12,62 %

Following the general procedure (D) **12** was obtained as white gummy solid (37 mg 62% yield). **1H NMR (400 MHz, CDCl3)** δ 5.90 (d, *J* = 3.6 Hz, 1H), 5.72 (d, *J* = 2.0 Hz, 1H), 5.54 (s, 1H), 5.44 (dd, *J* = 5.4, 3.0 Hz, 1H), 5.40 (d, *J* = 2.7 Hz, 1H), 5.06 (dd, *J* = 11.1, 2.7 Hz, 1H), 4.74 (dd, *J* = 11.9, 9.0 Hz, 1H), 4.62 (dd, *J* = 8.1, 1.6 Hz, 1H), 4.56 (d, *J* = 3.6 Hz, 1H), 4.45 – 4.39 (m, 1H), 3.91 (dd, *J* = 12.0, 4.9 Hz, 1H), 3.74 – 3.64 (m, 2H), 2.69 – 2.52 (m, 1H), 2.09 (s, 3H), 2.04 (s, 6H), 2.01 (s, 3H), 1.58 (s, 3H), 1.33 (s, 6H).**^{13}C NMR (101 MHz, CDCl$_3$)** δ 171.2, 170.1, 169.7, 169.4, 169.2, 167.3, 134.4, 123.2, 113.1, 104.5, 83.5, 75.5, 73.1, 69.5, 67.6, 64.2, 59.2, 44.6, 40.7, 33.3, 31.9, 26.8, 26.7, 20.8, 20.8, 20.6, 20.5. **HRMS (ESI$^+$)**: m/z calcd. for $C_{27}H_{32}NaO_{15}$ $(M+Na)^+$ 619.1639, found 619.1647.

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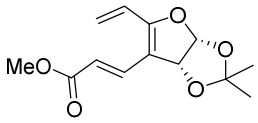

15, (68% overall yield in 4 steps)

Following the general procedure (E) **15** was obtained as oily liquid (300 mg 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 (dd, *J* = 15.5, 0.6 Hz, 1H), 6.59 (dd, *J* = 17.1, 11.0 Hz, 1H), 6.14 (d, *J* = 5.3 Hz, 1H), 6.01 (d, *J* = 15.5 Hz, 1H), 5.94 (dd, *J* = 17.1, 1.4 Hz, 1H), 5.59 (dd, *J* = 11.0, 1.4 Hz, 1H), 5.42 (d, *J* = 5.2 Hz, 1H), 3.76 (s, 3H), 1.47 (s, 3H), 1.34 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.7, 158.0, 134.3, 122.8, 121.1, 115.6, 113.6, 113.4, 105.3, 82.5, 51.4, 27.8, 27.5. **HRMS (ESI$^+$)**: m/z calcd. for $C_{13}H_{16}NaO_5$ $(M+Na)^+$ 275.0895, found 275.0890.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

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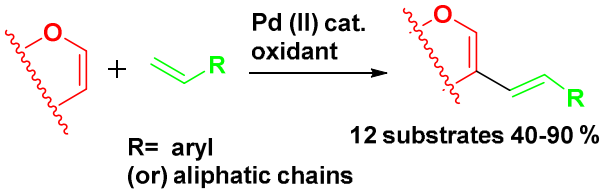

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