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Synthesis of Glycosides Bearing Chalcone Derivatives *via* Ferrier Rearrangement

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Abstract : A series of glycoside derivatives bearing chalcones moieties has been synthesized. A convenient synthetic method was performed from the reaction of 3,4,6-tri-O-acetyl-D-glucal with *(E)*-1-(4-alkyloxyphenyl)-3-(4-hydroxy-phenyl)prop-2-en-1-one **(2a-2c)** employing O→C rearrangement to afford *C*-glycoside **4a-c** over prolonged reaction times, in the presence of $BF_3.OEt_2$ as a catalyst. The compounds differ in the length of alkyl groups, $C_nH_{2n+1,}$ where n= 7, 8 and 9.

Keywords: glycosylation, chalcones, glycosides, O→C rearrangement

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Introduction

Glycosides are found abundantly in nature and serve many important roles in living organisms.[1,2] Plants usually store chemicals in the form of inactive glycosides which are activated by enzyme hydrolysis. Naturally occurring glycosides commonly show high potential as antibiotics. There are a wide range of glycoside antibiotics isolated from natural products.[3]. For many years, numerous research have been devoted to the total synthesis of *C*- and *O*-glycoside antibiotics, such as erythromycin A, amphotericin B, olivomycin A, urdamycinone B, vancomycin and digitoxin.[4] Besides, glycosides are also increasingly utilized in the synthesis of non-carbohydrate compounds and carbohydrate mimetics.[5] Glycosides have also been synthesized for liquid crystalline materials. Over the past years, tremendous attention has been dedicated to research on the synthesis of glycoside derivatives and studies on the application for liquid crystal properties.[6-8]

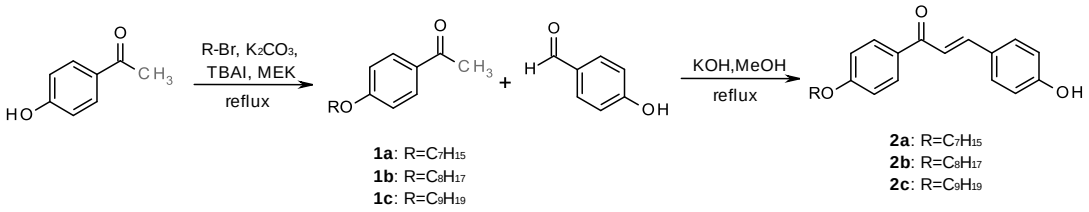
Ferrier rearrangement, on the other hand, is an attractive methodology for the synthesis of glycoside derivatives with various alcohols. It is an efficient reaction for the substitution at the anomeric position with allylic rearrangement.[9,10] The Ferrier rearrangement involves the addition of nucleophile onto the intermediate allylic oxycarbenium ion, preferentially in a quasi-axial orientation.[9] This rearrangement leads to the formation of alkyl and aryl 2,3-unsaturated-*O*-glycosides, which are versatile chiral intermediates in the synthesis of several biologically active natural products.[9,10] 2,3-unsaturated-*O*-glycosides are also important building blocks in the synthesis of some antibiotics.[9]

Recently, we reported on the preparation of Lewis acid-promoted allylic rearrangement of 3,4,6-tri-O-acetyl-D-glucal with 4-hydroxybenzaldehyde and aliphatic alcohols with different type of catalysts in different solvents.[11] This prompted us to study the reaction of glycoside bearing chalcone derivatives *via* Claisen-Schmidt condensation of aldehyde and acetophenone. Chalcone derivatives were reported to have outstanding non linear optic properties for optical electronics and communications[12], liquid crystal displays[13,14] and alignment film[15]. Chalcones were also reported to promote excellent blue light transmittance and good crystallability,[16,17] high photosensitivity and thermal stability for various crystalline electro-optical devices.

We herein report the synthesis of new glycosides bearing hydroxylated chalcone **(2a-c)** which differ in the length of the alkyl groups ranging from C7 to C9. This study could be used as a reaction model for potential liquid crystals compounds.

Results and Discussion

The series of chalcone derivatives (*E)*-1-[4-(alkyloxy)phenyl]-3-[4-hydroxyphenyl] prop-2-en-1-one **(2a-2c)** were prepared *via* Claisen-Schmidt condensation of **1a-1c** and 4-hydroxybenzaldehyde by the route depicted in Scheme 1.



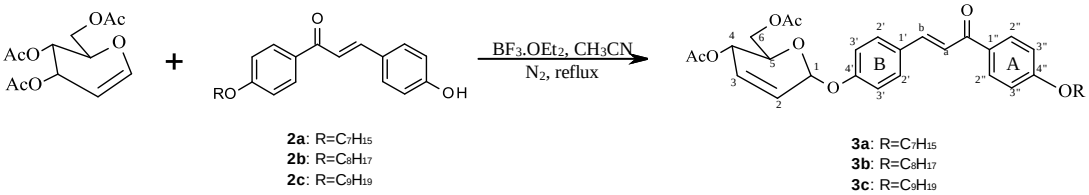
Scheme 1 : Synthesis of hydroxylated chalcones **2a-c**

The IR spectra of the hydroxylated chalcones **2a-2c** showed the presence of bands at 2921 -2852 cm^{-1} which were attributed to the introduction of aliphatic carbon chains via etherification of 4-hydroxyacetophenone and vOH at 3100-3400 cm^{-1}. The presence of a new C=O stretching frequency at 1651 cm^{-1} substantiated to the formation of the title compound. The chemical structures of **2a-2c** were found to be consistent with ^{1}H NMR and ^{13}C NMR spectroscopic data and showed the peaks corresponded to the structures. In ^{1}H-NMR spectra, the coupling constant, J_{ab} 15.0-16.0 Hz indicated all chalcones obtained were in *trans* configuration. The relatively low yield of **2a-2c** (24-64%) was attributed to the trace amount of side products of Cannizaro reaction or ketone auto condensation.[18,19]

The synthetic route for the glycosylation of the commercially available tri-*O*-acetyl-D-glucal with chalcones **2a-2c** is illustrated in Scheme **2**. The reaction was performed in the presence of $BF_3.OEt_2$ as a catalyst and monitored by TLC.[11]

ring B as doublets at 6.89 and 7.02 ppm. Olefinic protons which appeared as doublets at 7.40 and 7.64 ppm with coupling constant, J_{ab} = 15.5 Hz, indicated *trans* configuration of the chalcones moiety. The signals of aromatic ring A were resonated as doublet at 7.48 and 7.94 ppm to indicate that the formation of *O*-glycoside occurred *via* the hydroxyl group to form C-O-C bond. Methyl groups of acetates were resonated as two singlets which indicated that the acetates were stable to the reaction condition. The ^{13}C NMR spectra showed the appearance of four signals attributed to four symmetrical peaks of aromatic carbons. The *trans* vinylic alkene C_a and C_b appeared at 119.8 and 141.2 ppm. C-2 and C-3 appeared at 127.5 and 129.6 ppm respectively.[20]

The other compound with R_f 0.90 was also subjected to spectroscopic analysis. The appearance of a broad band at 3373 cm^{-1} indicated the presence of hydroxyl group in the compound structure. The stretching vibration of paraffinic

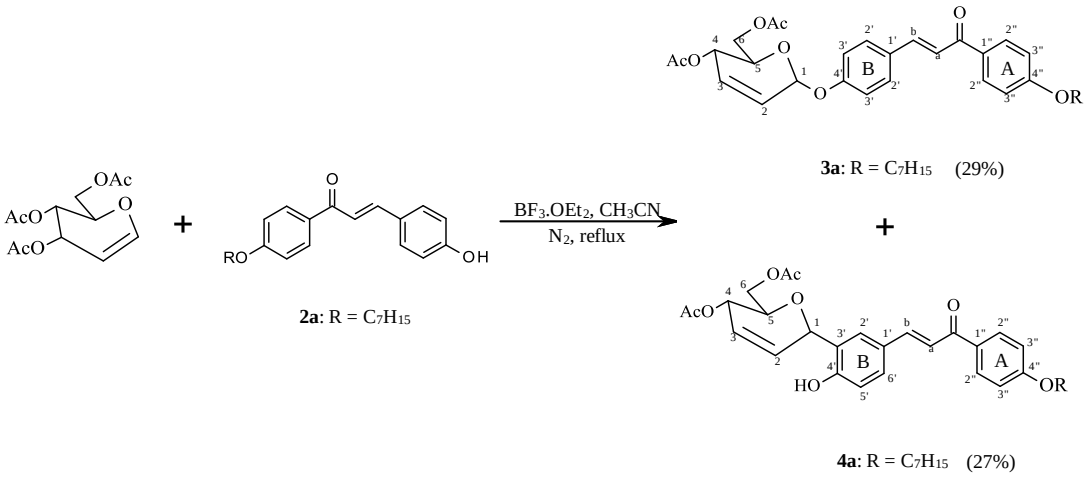


Scheme 2 : Proposed synthesis of glycosides **3**

Two products were observed at R_f 0.22 and 0.90 after 4 h reaction. Both compounds were characterized separately using IR, ^{1}H and ^{13}C NMR spectroscopy. The IR spectra of compound with R_f 0.22 showed the presence of long paraffinic chain at 2925 and 2855 cm^{-1}. The conjugated C=O stretching frequency was observed at 1680 cm^{-1} and non-conjugated C=O stretching frequency at 1723 cm^{-1}. The υ_{COC} stretching frequency of acetates appeared at 1357 – 1171 cm^{-1}. The ^{1}H NMR spectra showed characteristic signals of aromatic chain was observed at 2923 and 2853 cm^{-1} while υ_{COC} of acetates appeared at 1257 – 1166 cm^{-1}. The ^{1}H NMR spectrum showed the presence of two signals as doublets attributed to H-5' and H-6' of aromatic ring B at 6.85 and 6.95 ppm respectively while characteristic resonance corresponded to H-2' as singlet was observed at 7.43 ppm, which indicate the formation of *C*-glycoside. Resonances appeared as doublets assigned at 7.37 and 7.52 ppm with J_{ab} = 15.5 Hz, indicated the aglycone was in *trans* configuration. The formation of *C*-glycoside

is also supported by the presence of -OH which resonated as a singlet at 9.86 ppm. The lower in resonance of -OH might be due to the formation of hydrogen bonding with the nearby hydrogen moieties. ^{13}C NMR verified the formation of the proposed *C*-glycoside**.** ^{13}C NMR showed the presence of five signals attributed to five different carbons of ring B, while two symmetrical peaks attributed to C-3" and C-2" of ring A were observed at 130.9 and 131.1 ppm. The peaks present at 119.8 and 143.8 ppm were corresponded to *trans* vinylic alkene. The presence of COH also appeared in ^{13}C NMR with the signal at 161.7 ppm.[21] The formation of *C*-glycoside via Ferier rearrangement is depicted in Scheme 3.

Upon prolonging the reaction times (6 h), only one product appeared with R_f 0.90 which corresponded to *C*-glycoside, and the disappearance of R_f 0.22 corresponded to *O*-glycosides.[22] ^{1}H and ^{13}C NMR showed good agreement to the formation of *C*-glycoside. It was envisaged that compound **3** (*O*-glycoside) was rearranged to form compound **4** (*C*-glycoside) *via* O→C glycoside rearrangement[23], in correspond to the reaction times. The overall reaction is shown in Scheme 4.

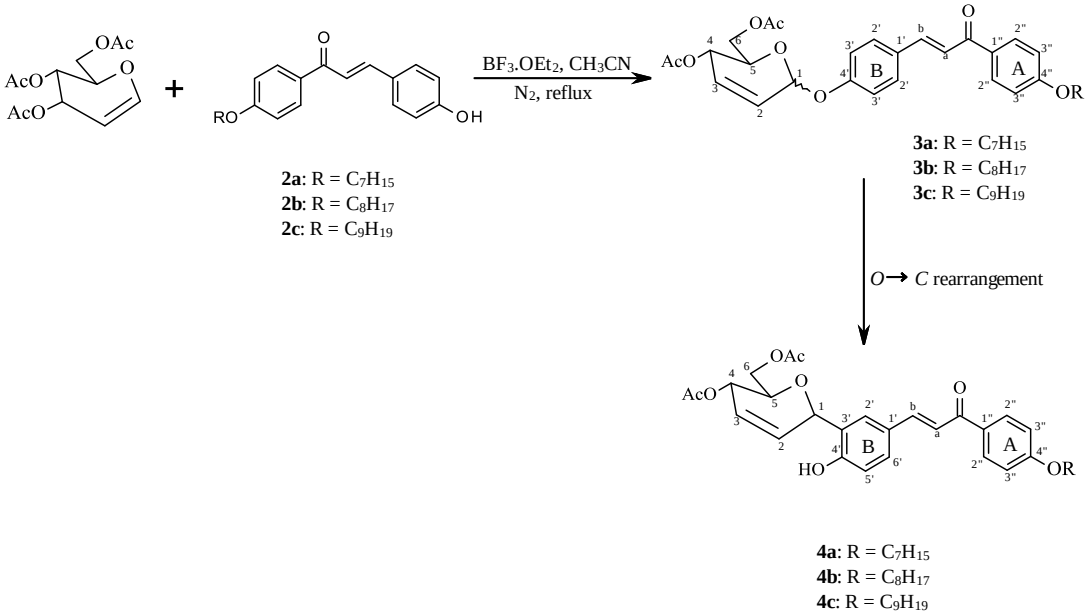


2a: R = C_7H_{15}

3a: R = C_7H_{15} (29%)

4a: R = C_7H_{15} (27%)

Scheme 3 : Preparation of *O*-glycoside **3a** and *C*-glycoside **4a**



2a: R = C_7H_{15}
2b: R = C_8H_{17}
2c: R = C_9H_{19}

3a: R = C_7H_{15}
3b: R = C_8H_{17}
3c: R = C_9H_{19}

4a: R = C_7H_{15}
4b: R = C_8H_{17}
4c: R = C_9H_{19}

Scheme 4 : Synthesis of **4a-4c** via O→C rearrangement

Experimental

General

4-Hydroxybenzaldehyde, 4-hydroxyacetophenone and 1-bromoalkanes were obtained from Merck and used without further purification. Acetonitrile was distilled from $KMnO_4$ and $MgSO_4$. All other reagents and solvents were used as received. Melting points were determined in open capillaries and uncorrected. Infrared spectra were recorded on (FT-IR) 1605 Shimadzu Spectrometer using neat liquid film and KBr pellets. ^{1}H-NMR spectra were recorded on a 500 MHz Jeol Delta 2-NMR and ^{13}C NMR spectra were recorded on a 125.7 MHz using TMS as the internal standard.

Synthesis of *alkyloxyphenyl-ethanone* (1a–1c)

General procedure[24]

Bromoalkane (72 mmol), 4-hydroxyacetophenone (72 mmol), potassium carbonate (K_2CO_3) (72 mmol), Tetrabutylammonium iodide **(**TBAI) (6 mmol) in Methyl Ethyl Ketone (200 mL) were heated at reflux for 10 h. The mixture was filtered and cooled at room temperature. Water (30 mL) was added to the filtrate and the layers separated. The aqueous layer was extracted with dichloromethane (2 x 30 mL). The combined layers were washed with water (2 x 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude was recrystallized from ethanol to give **1a-1c.** The same general procedure gave compounds **1b–c**, with the scale (mmol, mL [**1b–c**]) and yields given below.

1-(4-heptyloxyphenyl)-ethanone (1a)

Bromoheptane (5.66 mL, 36.0 mmol), 4-hydroxyacetophenone (4.08 g, 30.0 mmol), gave colourles crystals **1a** (4.57 g, 65%), m.p. 40.0 ^{o}C; R_f 0.93 (hexane:ethyl acetate, 3:1); The FTIR and NMR data were consistent with the reported literature.[25] The same general procedure gave compounds **1b–c**, with the scale (mL, mmol, [bromoalkane]) and yields given below.

1-(4-octyloxyphenyl)-ethanone (1b)

Bromooctane (6.26 mL, 36.0 mmol), 4-hydroxyacetophenone (4.08 g, 30.0 mmol), gave colourless crystals **1b** (3.88 g, 52%), m.p. 44.4 ^{o}C; R_f 0.93 (hexane:ethyl acetate, 3:1); FTIR and NMR data were consistent with the reported literature.[25]

1-(4-nonyloxyphenyl)-ethanone (1c)

Bromononane (6.78 mL, 36.0 mmol), 4-hydroxyacetophenone (4.08 g, 30.0 mmol), gave colourless crystals **1c** (6.45 g, 87%), m.p. 46.0 ^{o}C; R_f 0.95 (hexane:ethyl acetate, 3:1); FTIR and NMR data were consistent with the reported literature.[25]

Synthesis of (alkyloxy)phenyl-hydroxyphenyl]prop-2-en-1-one (2a–2)

General procedure[26]

A mixture of *p*-hydroxybenzaldehydes (12.5 mmol), **1a-c** (12.5 mmol) in 35 mL of methanol was added under stirring to a solution of KOH (2.52 g) in methanol (10 mL). The mixture was heated at reflux for 10 h. The reaction was cooled to room temperature and acidified with cold diluted HCl (2N). The resulting precipitate was filtered, washed and dried. The crude product was recrystallized from hexane:ethanol (7:1) to give **(2a–2c**). The same general procedure gave compounds **2b–c**, with the scale (mL, mmol, [bromoalkane]) and yields given below.

(E)-1-(4-heptyloxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (2a)

4-hydroxybenzaldehyde (1.22 g, 10.0 mmol), **1a** (3.38 g, 10.0 mmol) gave yellow crystals **2a** (0.81 g, 24%), m.p. 100.0 ^{o}C; R_f 0.67 (hexane:THF, 3:2); FTIR and NMR data were consistent with the reported literature.[25]

(E)-1-(4-octyloxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (2b)

4-hydroxybenzaldehyde (1.22 g, 10.0 mmol), **1b** (3.52 g, 10.0 mmol), gave yellow crystals **2b** (1.80 g, 51%), m.p. 105.0 ^{o}C; R_f 0.65 (hexane:THF, 3:2); FTIR and NMR data were consistent with the reported literature.[25]

(E)-1-(4-nonyloxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (2c)

4-hydroxybenzaldehyde (1.22 g, 10.0 mmol), **1c** (3.66 g, 10.0 mmol) gave yellow crystals **2c** (2.34 g, 64%), m.p. 115.0 ^{o}C; R_f 0.64 (hexane:THF, 3:2); FTIR and NMR data were consistent with the reported literature.[25]

Synthesis of chalcone glycosides (3a, 4a-4c)

General procedure

Chalcone **2a-2c** was added into tri-*O*-acetyl-D-glucal in dry acetonitrile under nitrogen atmosphere. $BF_3.OEt_2$ was added and the mixture was heated at reflux. The mixture was cooled to room temperature, quenched with saturated sodium hydrogen carbonate and extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated. The product was purified by column chromatography on silica gel 60 (70-230 mesh ASTM).

[2-(acetoxymethyl)-6-[4-[3-(4-heptoxyphenyl)-3-oxo-prop-1-enyl]phenoxy]-3,6-dihydro-2H-pyran-3-yl] acetate (3a)

Tri-*O*-acetyl-D-glucal (0.272 g, 1.0 mmol) was dissolved in a solution of **2a** (0.338 g, 1.0 mmol) in dry acetonitrile (10 mL) under nitrogen atmosphere. $BF_3.OEt_2$ (0.258 mL, 2.0 mmol) was added and the mixture was heated at reflux for 4 h. The reaction was cooled to room temperature and worked up according to general procedure. The crude was purified by column chromatography on silica gel (hexane:ethyl acetate, 5:1 and 10:1) to give **3a** (0.16 g, 29%) as yellow waxy liquid with R_f 0.22 (hexane:ethyl acetate, 3:1); Anal. calcd. (%) $C_{32}H_{38}O_8$ C, 69.84; H, 6.91; Found (%):C, 69.78; H, 6.88. υ_{max} (thin films/cm^{-1}); 2925, 2855 (CH_2CH_3), 1723 (C=O, CH_3CO), 1680 (C=O, conjugated), 1601, 1575, 1510, 1467 (C=C), 1420, 1377 (bending CH_3), 1357, 1305, 1255, 1217, 1171 (COC, CH_3CO), 1114, 1021 (COC, ether), 954 (*trans* vinylic C=C), 828 (*para* disubstituted benzene), 723 (*cis* C=C); ^{1}H NMR ($CDCl_3$): 7.94 (d, *J* = 9.2 Hz, 2H, 2 x ArH), 7.64 (d, *J* = 15.5 Hz, 1H, olefinic H), 7.48 (d, *J* = 8.6 Hz, 2H, 2 x ArH), 7.40 (d, *J* = 15.5 Hz, 1H, olefinic H), 7.02 (d, *J* = 8.0 Hz, 2H, 2 x ArH), 6.89 (d, *J* = 8.6 Hz, 2H, 2 x ArH), 5.63 (m, 1H, H-3), 5.49 (m, 1H, H-2), 4.74 (d, *J* = 9.6 Hz, 1H, H-1), 4.51 (m, 1H, H-4), 4.37 (t, *J* = 4.6 Hz, 2H, H_2-1"), 3.97-3.40 (m, 3H, H-5, H-6_a, H-6_b), 2.10 (s, 3H, CH_3CO-C6), 2.09 (s, 3H, CH_3CO-C4), 1.76 (q, 2H, H_2-2"), 1.49-1.19 (m, 8H, 4 x CH_2), 0.81 (t, *J* = 6.9 Hz, 3H, H_3-7"); ^{13}C NMR ($CDCl_3$): 189.4 (C=O), 173.2 (C=O, CH_3CO-C4), 170.0 (C=O, CH_3CO-C6), 161.3 (COC), 141.2 (*trans* vinylic C=C), 131.9 (C-1"), 130.9 (C-2"), 129.6 (C-3), 128.2 (C-3"), 127.5 (C-2), 123.8 (C-1'), 119.8 (*trans* vinylic C=C), 115.4 (C-2'), 114.4 (C-3'), 90.7 (C-1), 70.7 (C-4), 68.0 (C-1"), 64.0 (C-6), 60.2 (C-5), 37.8 (C-2"), 29.6, 29.3, 26.0, 22.6 (4 x CH_2), 21.3 (CH_3, CH_3CO-C6), 20.7 (CH_3, CH_3CO-C4), 14.0 (C-7").

[2-(acetoxymethyl)-6-[2-hydroxy-5-[3-(4-heptoxyphenyl)-3-oxo-prop-1-enyl]phenyl]-3,6-dihydro-2H-pyran-3-yl] acetate (4a)

Tri-*O*-acetyl-D-glucal (0.272 g, 1.0 mmol) was added to a solution of **2a** (0.338 g, 1.0 mmol) in dry acetonitrile (10 mL) under nitrogen atmosphere. $BF_3.OEt_2$ (0.258 mL, 2.0 mmol) was added and the mixture was heated at reflux for 6 h. The reaction was cooled to room temperature and worked up according to general procedure. The mixture was purified by column chromatography on silica gel (hexane:ethyl acetate, 10:1) to afford **4a** (0.13 g, 24%) as yellow waxy liquid. R_f 0.90 (hexane: ethyl acetate, 3:1). Anal. calcd. (%) $C_{32}H_{38}O_8$: C, 69.84; H, 6.91; Found (%): C, 69.73; H, 6.78. υ_{max} (thin films/cm^{-1}); 3373 (OH), 2923, 2853 (CH_2CH_3), 1738 (C=O, CH_3CO), 1660 (C=O, conjugated), 1601, 1581, 1513, 1463, 1456 (C=C), 1422, 1377 (bending CH_3), 1257, 1225, 1166 (COC, CH_3CO), 1116, 1080, 1027 (COC, ether), 972 (*trans* vinylic C=C), 826 (*para* disubstituted benzene), 722 (*cis* C=C); ^{1}H NMR ($CDCl_3$): 9.86 (s, 1H, OH), 8.02 (d, *J* = 7.5 Hz, 1H, ArH), 7.78 (d, *J* = 8.6 Hz, 1H, ArH), 7.52 (d, *J* = 14.9 Hz, 1H, olefinic H), 7.43 (s, 1H, H-2'), 7.37 (d, *J* = 15.5 Hz, 1H, olefinic H), 6.95 (d, *J* = 8.0 Hz, 2H, 2 x ArH), 6.85 (d, *J* = 9.2 Hz, 2H, 2 x ArH), 6.00 (m, 1H, H-3), 5.78 (m, 1H, H-2), 5.07 (s, 1H, H-1), 4.92 (d, *J* = 9.7 Hz, 1H, H-4), 4.49 (d, *J* = 4.6 Hz, 2H, H_2-1"), 4.29-3.98 (m, 3H, H-5, H-6_a, H-6_b), 2.04 (s, 3H, CH_3CO-C6), 2.03 (s, 3H, CH_3CO-C4), 1.77 (q, 2H, H_2-2"), 1.42-1.22 (m, 8H, 4 x CH_2), 0.87 (t, *J* = 6.9 Hz, 3H, H_3-9"); ^{13}C NMR ($CDCl_3$): 191.6 (C=O), 173.9 (C=O, CH_3CO-C4), 171.5 (C=O, CH_3CO-C6), 161.7 (C-4), 160.4 (C-4"), 143.8 (*trans* vinylic C=C, CH), 132.3 (C-1"), 131.1 (C-2", CH), 130.8 (C-3", CH), 129.6 (C-3, CH), 129.0 (C-1'), 128.3 (C-2', CH), 126.6 (C-2, CH), 124.7 (C-6', CH), 119.8 (*trans* vinylic C=C, CH), 115.9 (C-5', CH), 114.5 (C-3', CH), 89.5 (C-1, CH), 69.2 (C-4, CH), 68.1 (C-1'", CH_2), 64.0 (C-6, CH_2), 59.4 (C-5, CH), 38.7 (aliphatic, CH_2), 29.6, 29.5, 26.4, 23.2 (4 x CH_2), 22.6 (CH_3CO-C6, CH_3), 22.3 (CH_3CO-C4, CH_3,), 14.0 (aliphatic , CH_3).

[2-(acetoxymethyl)-6-[2-hydroxy-5-[3-(4-octoxyphenyl)-3-oxo-prop-1-enyl]phenyl]-3,6-dihydro-2H-pyran-3-yl] acetate (4b)

Tri-*O*-acetyl-D-glucal (0.272 g, 1.0 mmol) was added to a solution of **2b** (0.353 g, 1.0 mmol) in dry acetonitrile (10 mL) under nitrogen atmosphere. $BF_3.OEt_2$ (0.258 mL, 2.0 mmol) was added and the mixture was heated at reflux for 6 h. The reaction was cooled to room temperature and worked up according to general procedure. The mixture was purified by column chromatography on silica gel (hexane:ethyl acetate, 10:1) to afford **4b** (0.16 g, 29%) as yellow waxy liquid. R_f 0.91 (hexane: ethyl acetate, 3:1). Anal. calcd. (%) $C_{33}H_{40}O_8$: C, 70.24; H, 7.09; Found (%): C, 70.10; H, 7.01. υ_{max} (thin films/cm^{-1}); 3290 (OH), 2924, 2854 (CH_2CH_3), 1739 (C=O, CH_3CO), 1654 (C=O, conjugated), 1601, 1583, 1512, 1466, 1455 (C=C), 1442, 1364 (bending CH_3), 1298, 1246, 1167 (COC, CH_3CO), 1111, 1072, 1025 (COC, ether), 990 (*trans* vinylic C=C), 831 (para disubstituted benzene), 737 (*cis* C=C); ^{1}H NMR ($CDCl_3$): 9.86 (s, 1H, OH), 8.01 (d, *J* = 7.5 Hz, 1H, ArH), 7.80 (d, *J* = 8.6 Hz, 1H, ArH), 7.52 (d, *J* = 14.9 Hz, 1H, olefinic H), 7.46 (s, 1H, ArH), 7.37 (d, *J* = 15.5 Hz, 1H, olefinic H), 6.97 (d, *J* = 8.6 Hz, 2H, 2 x ArH), 6.89 (d, *J* = 9.2 Hz, 2H, 2 x ArH), 5.79 (m, 1H, H-3), 5.61 (m, 1H, H-2), 5.00 (s, 1H, H-1), 4.90 (d, *J* = 10.3 Hz, 1H, H-4), 4.49 (t, *J* = 4.6 Hz, 2H, H_2-aliphatic), 4.32-3.99 (m, 3H, H-5, H-6_a, H-6_b), 2.03 (s, 3H, CH_3CO-C6), 2.02 (s, 3H, CH_3CO-C4), 1.80 (q, 2H, H_2-aliphatic), 1.45-1.24 (m, 10H, 5 x CH_2), 0.87 (t, *J* =

6.7 Hz, 3H, H_3- aliphatic); ^{13}C NMR ($CDCl_3$): 190.1 (C=O), 173.9 (C=O, CH_3CO-C4), 171.4 (C=O, CH_3CO-C6), 163.0 (C-4), 159.1 (C-4"), 144.1 (*trans* vinylic C=C, CH), 132.9 (C-1"), 131.8 (C-2", CH), 130.4 (C-3", CH), 130.0 (C-3, CH), 128.8 (C-1'), 128.5 (C-2', CH), 127.0 (C-2), 123.9 (C-6', CH), 118.9 (*trans* vinylic C=C, CH), 115.7 (C-5', CH), 115.2 (C-3', CH), 89.9 (C-1, CH), 69.9 (C-4, CH), 68.0 (aliphatic, CH_2), 64.1 (C-6, CH_2), 59.2 (C-5, CH), 37.0 (aliphatic, CH_2), 30.1, 30.0, 29.2, 25.8, 23.3 (5 x CH_2), 22.6 (CH_3CO-C6, CH_3), 22.1 (CH_3CO-C4, CH_3), 14.1 (aliphatic, CH_3).

[2-(acetoxymethyl)-6-[2-hydroxy-5-[3-(4-nonoxyphenyl)-3-oxo-prop-1-enyl]phenyl]-3,6-dihydro-2H-pyran-3-yl] acetate (4c)

Tri-*O*-acetyl-D-glucal (0.272 g, 1.0 mmol) was added to a solution of **2c** (0.367 g, 1.0 mmol) in dry acetonitrile (10 mL) under nitrogen atmosphere. $BF_3.OEt_2$ (0.258 mL, 2.0 mmol) was added and the mixture was refluxed for 6 h. The reaction was cooled to room temperature and worked up according to general procedure. The mixture was purified by column chromatography on silica gel (hexane:ethyl acetate, 10:1) to afford **4c** (0.26 g, 45%) as yellow waxy liquid. R_f 0.94 (hexane: ethyl acetate, 3:1). Anal. calcd. (%) $C_{34}H_{42}O_8$: C, 70.61; H, 7.26; Found (%): C, 70.46; H, 7.14. υ_{max} (thin films/cm^{-1}); 3408 (OH), 2923, 2853 (CH_2CH_3), 1739 (C=O, CH_3CO), 1689 (C=O, conjugated), 1606, 1579, 1513, 1494, 1469, 1463, 1434 (C=C), 1397, 1377 (bending CH_3), 1258, 1208, 1169 (COC, CH_3CO), 1127, 1080, 1065, 1015 (COC, ether), 963 (*cis* C=C), 846 (*para* disubstituted benzene), 742 (*cis* C=C); ^1H NMR ($CDCl_3$): 9.83 (s, 1H, OH), 8.00 (d, *J* = 7.5 Hz, 1H, ArH), 7.75 (d, *J* = 8.6 Hz, 1H, ArH), 7.51 (d, *J* = 14.9 Hz, 1H, olefinic H), 7.45 (s, 1H, ArH), 7.36 (d, *J* = 15.5 Hz, 1H, olefinic H), 6.94 (d, *J* = 8.6 Hz, 2H, 2 x ArH), 6.87 (d, *J* = 7.5 Hz, 2H, 2 x ArH), 6.00 (m, 1H, H-3), 5.78 (m, 1H, H-2), 5.06 (s, 1H, H-1), 4.89 (d, *J* = 9.2 Hz, 1H, H-4), 4.48 (t, *J* = 4.6 Hz, 2H, H_2-aliphatic), 4.38-4.04 (m, 3H, H-5, H-6_a, H-6_b), 2.06 (s, 3H, CH_3CO-C6), 2.03 (s, 3H, CH_3CO-C4), 1.76 (q, 2H, H_2- aliphatic), 1.45-1.23 (m, 12H, 6 x CH_2), 0.84 (t, *J* = 7.5 Hz, 3H, H_3- aliphatic); ^{13}C NMR ($CDCl_3$, DEPT): 190.2 (C=O), 174.0 (C=O, CH_3CO-C4), 170.6 (C=O, CH_3CO-C6), 162.8 (C-4), 158.8 (C-4"), 144.0 (*trans* vinylic C=C, CH), 133.6 (C-1"), 132.4 (C-2", CH), 130.9 (C-3", CH), 129.4 (C-3), 128.7 (C-1'), 128.2 (C-2', CH), 126.8 (C-2), 123.9 (C-6', CH), 119.7 (*trans* vinylic C=C, CH), 115.4 (C-5', CH), 114.6 (C-3', CH), 90.2 (C-1, CH), 70.9 (C-4, CH), 68.0 (aliphatic, CH_2), 63.5 (C-6, CH_2), 58.9 (C-5, CH), 37.3 (aliphatic, CH_2), 31.7, 29.6, 29.3, 29.2, 26.0, 23.5 (6 x CH_2), 22.6 (CH_3CO-C6, CH_3), 22.0 (CH_3CO-C4, CH_3), 14.0 (aliphatic, CH_3).

Conclusion

We have successfully synthesized chalcone glycosides **3a** and **4a**-**4c** by incorporation of chalcone derivatives onto 3,4,6-tri-O-acetyl-D-glucal. Over prolonged reaction times resulted in the formation of *C*-glycosides **4a**-**4c** via O→C rearrangements. Overall, synthetic approaches towards chalcone glycosides were developed during this study. This study has provided a better understanding towards the glycosylation reactions involving aromatic compounds.

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