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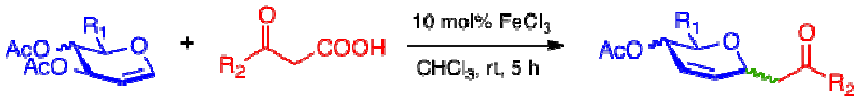
Hong Yee Tan, Shaohua Xiang, Wei Lin Leng and Xue-Wei Liu*



R_1 = H, CH_2OAc, R_2 = phenyl, alkyl *α*-Selective *C*-glycosides

An efficient iron-catalyzed decarboxylative *C*-glycosylation of glycals with *β*-keto acids *via* decarboxylative Ferrier rearrangement reaction has been established. This approach provides a wide range of *β*-keto-functionalized 2,3-unsaturated *C*-glycosides in moderate to good yields. Good selectivities are mainly observed with the use of D-galactals along with bulkier *β*-keto acids bearing phenyl moieties.

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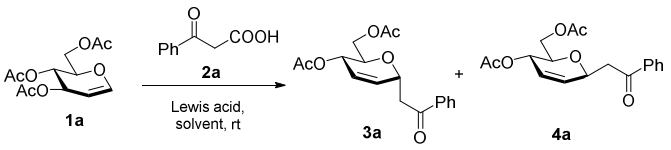
An efficient iron-catalyzed decarboxylative *C*-glycosylation of glycals with *β*-keto acids *via* decarboxylative Ferrier rearrangement reaction has been established. This approach provides a wide range of *β*-keto–functionalized 2,3-unsaturated *C*-glycosides in moderate to good yields. Good selectivities are mainly observed with the use of D-galactal along with bulkier *β*-keto acids bearing phenyl moieties.

Introduction

Ever since Hurd's pioneering work in synthesizing *C*-glycosylate derivatives efficiently dating back to 1945,[1] *C*-glycosides have captured great attention due to their abundant existence in assorted drug molecules with antitumor and antibiotic effects,[2] as demonstrated in several representative natural occurring molecules such as chaetiacandin,[3] showdomycin[4] and aspergillide C.[5] In 2004, Franck successfully demonstrated that the *C*-glycoside analogue of KRN-7000 experienced a prominent boost of activity being approximately a thousand times more potent beyond its natural origin[6] against different cancer cells[7] and diseases.[8] Later, Sieber implemented showdomycin as a useful detecting probe for identifying pathogenesis-associated enzymes in a bacteria.[9] These independent examples have driven us to undergo a further extension of work particularly within the area of *C*-glycosylation.[10]

Notably, the reported viable nucleophiles used for *C*-glycosidations typically consist of the ubiquitous silylated compounds including allyltrimethylsilane,[11] trimethylsilylnitrile[12] and assorted silyl enol ether derivatives.[13] On the other hand, the non-silylated reagents mainly focused on metal derived nucleophiles such as zinc,[14] tin[15] and aluminium reagents.[16] The latter reagents are air and moisture sensitive, thus often face the difficulty in handling. Meanwhile, *β*-keto acids derived from *β*-keto esters have received less consideration, probably due to their low tolerance of elevated temperatures, acids and bases.[17] Amongst various reports, *β*-keto acids have nonetheless proven to be a tantalizing replacement for

Table 1. Optimization of reaction



entry	Lewis acid (10%)	solvent	ratio (α:β)[a]	yield[b]
1	BF_3•Et_2O	CH_2Cl_2	-	-
2	$ZnCl_2$	CH_2Cl_2	-	trace
3	$SnCl_4$	CH_2Cl_2	-	trace
4	$AlCl_3$	CH_2Cl_2	-	-
5	$TiCl_4$	CH_2Cl_2	-	-
6	TMSOTf	CH_2Cl_2	-	-
7	$Fe(acac)_3$	CH_2Cl_2	-	-
8	$FeCl_3$•$6H_2O$	CH_2Cl_2	-	trace
9	Fe_2O_3	CH_2Cl_2	-	-
10	$FeCl_3$	CH_2Cl_2	5:1	34%
11[c]	$FeCl_3$	CH_2Cl_2	-	-
12	$FeCl_3$	$ClCH_2CH_2Cl$	-	-
13	$FeCl_3$	CH_3CN	-	-
14	$FeCl_3$	Et_2O	-	-
15	$FeCl_3$	THF	-	-
16	$FeCl_3$	toluene	-	-
17[d]	$FeCl_3$	$CHCl_3$	5:1	62%
18	$FeCl_3$	$CHCl_3$	5:1	**80%**
19[e]	$FeCl_3$	$CHCl_3$	5:1	81%

[a] Anomeric ratios were determined by ^{1}H NMR. [b] Isolated yields. [c] Reaction was carried out at 0 °C. [d] 5 mol% $FeCl_3$ was used. [e] 15 mol% $FeCl_3$ was used.

ketone derivatives, considering that direct alkylation of the latter endures undesirably poor reactivity as well as regioselectivity. Previous works have demonstrated that *β*-keto acids are capable of reacting with a diverse range of electrophiles, including nitroalkenes,[18] aldehydes,[19] imines,[20] allylic acetates,[21] 1,3-diene monoepoxides[22] and sulfonamides.[23]

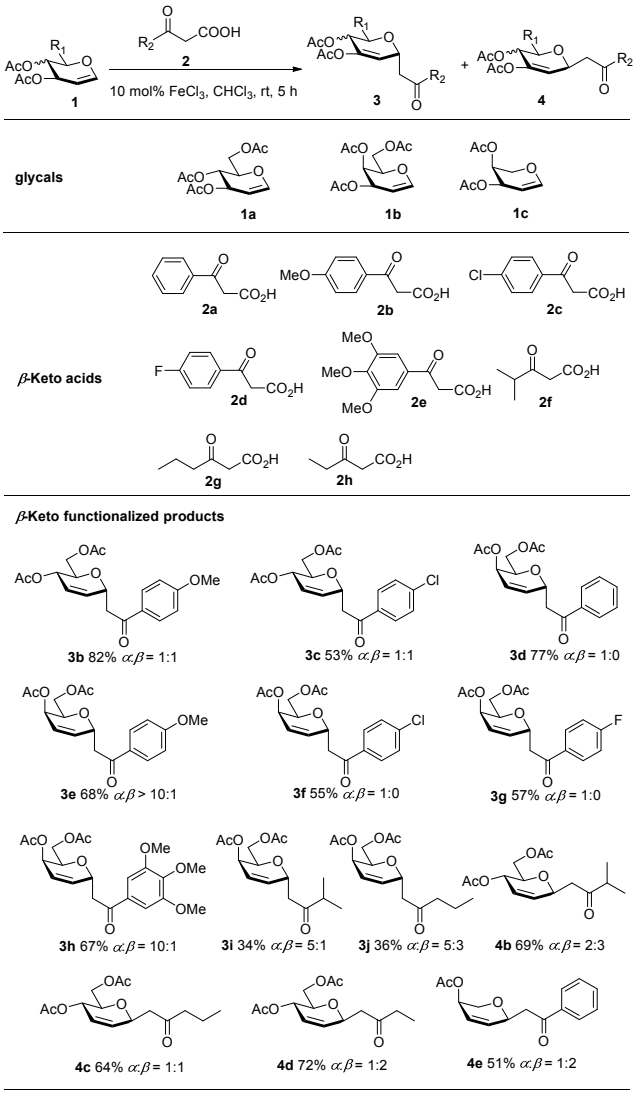
On the other hand, the decarboxylative reaction appears to be one of the more adopted method recently for introducing a carbon-framework formation.[24] In fact, several examples have utilized such strategy as a key-step towards various metal-mediated coupling reactions for the chemical synthesis of glycosides.[25] In particular, the use of iron as an alternative decarboxylative-catalyst source has attracted much attention due to its complementary catalytic efficiencies as related to other transition metal catalysts including palladium and ruthenium.[26] These iron catalysts offer numerous advantages, which include non-hazardousness, environmental benignity, cost effectiveness and availability. Goossen reported that certain Lewis acids, including $FeCl_3$, display remarkable decarboxylative catalytic activity in the esterification of carboxylic acids.[27] Recently, Li demonstrated that iron catalyst catalysts such as $FeSO_4$, $FeBr_2$ and $FeCl_3$ are capable of promoting decarboxylative cross-coupling reactions.[28] Tunge similarly employed iron catalysts as a means to achieve decarboxylative allylic etherification.[29] Encouraged by these successful cases, we anticipated interesting reactivity of *β*-keto acids on peracetylated saccharides with the use of iron reagents. Herein, we wish to disclose a stereo- and regioselective iron-catalyzed decarboxylative *C*-glycosylation *via* Ferrier rearrangement reaction between glycals and *β*-keto acids, to serve as a complementary general approach to achieve *C*-glycosylations.

Results and discussions

We carried out extensive screening of *tri-O*-acetyl-D-glucal and *β*-keto acids with a variety of Lewis acids, such as $BF_3{\bullet}OEt_2$, $ZnCl_2$, $SnCl_4$ and $AlCl_3$. All attempts failed to furnish the desired glycoside, even though several of these catalysts have been previously reported with decarboxylative features (**Table 1**, entries **1-9**).[30] Intriguingly, loading of 10 mol% anhydrous $FeCl_3$ catalyst at room temperature promoted the Ferrier rearrangement along with decarboxylative reaction, which resulted in an unexpected gain of the desired glycoside in 34% yield (**Table 1**, entry **10**). Decreasing the temperature to 0 °C had an adverse effect on the system with no product detected even after 5 h (**Table 1**, entry **11**). In this case, coordinating solvents used such as THF, Et_2O and CH_3CN (**Table 1**, entries **13**, **14** and **15**) were found to be deleterious to the reaction media, conceivably owing to complexation with the iron catalyst,[31] hence the reactions proceeded sluggishly. Upon alteration of the solvents, $CHCl_3$ turned out to be the optimum solvent in our model system with up to 80% isolated yield (**Table 1**, entry **18**). Concomitant conversion of the decarboxylated *β*-keto acids to form acetophenone as a side reaction could be a reason for lower yields in some cases.

In line with the success, additional reactions were carried out with an extensive range of *β*-keto acids, ranging from phenyl containing groups to simple alkyl substituents. The yields for certain phenyl containing carbohydrate adducts were found to be relatively higher (**Figure 1**, compounds **3a** and **3b**). These could be ascribed to the fact that the *β*-keto groups substituted with conjugated aromatics rings might have a stabilizing effect towards the *β*-keto acids, thus these acids were more stable within the reaction system. In particular, electron-withdrawing groups such as 4-chloro phenyl produced

Figure 1. Decarboxylative *C*-Glycosylation of *β*-Keto Acids with Glycals [a,b,c]



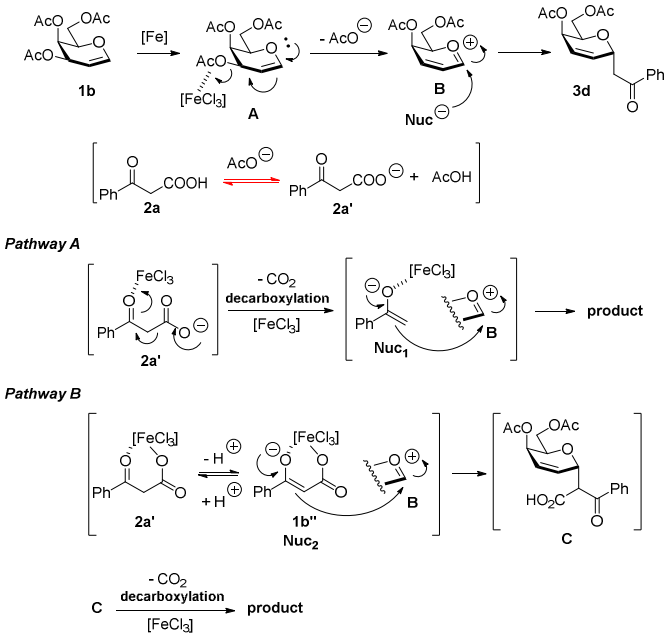
[a] All reactions were carried out with 1 equiv of glycal and 1.2 equiv of *β*-keto acid. [b] Anomeric ratios were determined by ^1H NMR. [c] Isolated yields.

slightly lower yield (**Figure 1**, compound **3c**) whereas alkyl containing moieties provided moderate to good yields (**Figure 1**, compounds **4b**, **4c**, and **4d**). Notably, when *tri-O*-acetyl-D-galactal (**Figure 1**, compound **1b**) was employed instead of *tri-O*-acetyl-D-glucal (**Figure 1**, compound **1a**), the stereoselectivity was improved, although the overall chemical yield was lower. The *α/β* selectivity ratio was determined by the empirical rule described by Isobe, in which the chemical shift for H_5 is generally located between 4.07–4.09 ppm for the *α*-glycoside, whereas it is between 3.74–3.77 ppm for *β*-glycoside.[32] Alternatively, the former can also be further confirmed by the chemical shift of C_5, which is found lower than 75 ppm.[33] These empirical rules do not match exactly for each and every compound. However, the general trend is that the H_5 proton for the *α*-glycoside is more deshielded than the corresponding one for the *β*-glycoside. Interestingly, the presence of a halide group as well as non-substituted phenyl *β*-keto acid coupled onto the galactal

were capable of giving glycosides with up to exclusive α-isomer formation only (**Figure 1**, compounds **3d**, **3f** and **3g**). β-Keto acids with saturated alkyl moieties provided lower yields and poorer selectivities (**Figure 1**, compounds **3i** and **3j**). Based on the anomeric ratio, the reaction mechanism is probably sensitive to steric repulsion, hence, the system inclines to single-face reaction with minimal steric interference. 3,4-Di-*O*-acetyl-L-arabinal (**Figure 1**, compound **1c**) was used as a standard probe to examine the actual trigger involved in such observation. Experiments revealed that without the presence of a C_5 substituent on the glycal, the stereoselectivity deteriorated to an anomeric ratio of 1:2, with the β-isomer being the major product formed (**Figure 1**, compound **4e**).

With regards to the mechanism, we hypothesize that initial phase of the reaction pathway proceeds through the formation of an active glycosyl intermediate via Ferrier rearrangement reaction when subjected to the iron catalyst. There are two plausible pathways in this system. In pathway A, formation of CO_2 acts as a driving force to undergo decarboxylative reaction to generate an enolate anion intermediate. The stability of enolate is enhanced by the delocalization of the charge over the carbonyl group as well as the iron catalyst. Hence, the enolate is stable enough to act as a reasonably good source of nucleophile towards attacking the electron deficient anomeric position of the glycosyl donor (intermediate **B**, **Scheme 1**). On the contrary, for pathway B, removal of the acetyl group located on the C3 position (intermediate **A**, **Scheme 1**) is followed by the attack of β-keto acid onto the electrophilic oxonium ion (intermediate **B**, **Scheme 1**) generated previously. Each of the β-keto acid in the reaction system possesses two α-hydrogen atoms which are highly acidic, as they are located adjacent to two electron withdrawing carbonyl groups. Deprotonation of these acidic protons *via* keto-enol tautomerism will result in the formation of carbanion, and this anion is capable of existing in the form of enolate anion intermediate through resonance (intermediates **1b'** and **1b"**, **Scheme 1**). The alkylation occurs to form a sugar carboxylic acid derivative (intermediate **C**, **Scheme 1**) and this intermediate further undergoes decarboxylative reaction with the exposure of iron catalyst to generate the final product (compound **3d**, **Scheme 1**).[23]

Scheme 1. Proposed mechanisms for the iron-catalyzed decarboxylative C-glycosylation



Conclusions

In summary, we have achieved the first example of intermolecular regio- and stereo- selective *C*-glycosylation of glycals with a range of easily prepared β-keto acids to form structurally diverse ketone functionalized *C*-glycosides with moderate to good yields. The coupling process could be made feasible *via* a milder, economical and greener approach by incorporating an iron-catalyzed decarboxylative Ferrier rearrangement reaction strategy. Furthermore, the 2,3-unsaturated glycosides possess remarkable synthetic versatility due to the presence of the olefin group, which could be utilized to undergo further manipulations for creating molecular diversity, as well as providing rapid access to various natural and unnatural saccharides. Development of a more selective variant and application to total synthesis of numerous therapeutic *C*-glycosides is ongoing.

Experimental

All reactions were performed under nitrogen atmosphere. Unless specified, all reagents and starting materials were purchased from commercial sources and used as received. Solvents were purified following standard literature procedures. Analytical thin layer chromatography (TLC) was performed using pre-coated silica gel plate. Visualization was achieved by UV light (254 nm) and/or $KMNO_4$ stain. Flash chromatography was performed using silica gel and a gradient solvent system (EtOAc-hexane as eluent). NMR spectra were recorded at room temperature on Bruker 400 spectrometer. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as: s (singlet), d (doublet), t (triplet), dd (doublet of doublets) or m (multiplet).The number of protons (*n*) for a given resonance is indicated by *n*H and coupling constants are reported in Hz. Solid samples were examined as a thin film between NaCl salt plates. High resolution mass spectra (HRMS) were recorded on Waters Q-Tof premier™ mass spectrometer.

General procedure for the preparation of β-keto acids[22]

The β-keto ester (10 mmol) was treated with aqueous sodium hydroxide solution (2 M, 10 mL) and stirred vigorously at room temperature for 12 h. The resulting mixture was extracted with diethyl ether (3 x 30 mL) to remove unreacted starting material. The aqueous layer was cooled, acidified with aqueous HCl (1 M), and extracted with diethyl ether (3 x 30 mL). The organic layers were combined, dried over anhydrous sodium sulfate, concentrated under reduced pressure at a temperature below 30 °C. The residue was dried in vacuum and used directly for the reaction.

General procedure for the synthesis of β-keto functionalized glycals

To a mixture of glycal **1a** (0.40 mmol) in chloroform (3.0 mL) at room temperature were added β-keto acid **2a** (0.48 mmol) and anhydrous $FeCl_3$ (6.4 mg, 10 mol%). The resulting mixture was stirred at ambient temperature and monitored by thin layer chromatography (TLC). After completion, the resulting mixture was purified by column chromatography on silica gel, eluting with hexane/ethyl acetate (4:1), to give product **3a**.

1-((4,6-Di-acetyl)-2,3-dideoxy-α-D-erythro-hex-2-enopyrano-xyl)-1-phenylethanone (3a) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal

1a (150 mg, 0.55 mmol) with *β*-keto acid **2a** (108 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3a** as a separable mixture of *α*/*β* = 5:1 with a combined yield of 146 mg (80%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ +32.2 (*c* 2.2, $CHCl_3$); IR (neat): ν_{max} 3059, 3022, 2954, 1736, 1684, 1597, 1510, 1448, 1369, 1230, 1217, 1126, 1047, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.98-7.95 (m, 2H), 7.61-7.57 (m, 1H), 7.50-7.47 (m, 2H), 6.08 (ddd, J_1 = 10.4 Hz, J_2 = 2.4 Hz, J_3 = 1.6 Hz, 1H), 5.85 (ddd, J_1 = 10.4 Hz, J_2 = 2.8 Hz, J_3 = 2.0 Hz, 1H), 5.17-5.13 (m, 1H), 4.96-4.92 (m, 1H), 4.25 (dd, J_1 = 12.0 Hz, J_2 = 6.8 Hz, 1H), 4.13 (dd, J_1 = 12.0 Hz, J_2 = 3.6 Hz, 1H), 3.99 (td, J_1 = 6.4 Hz, J_2 = 3.6 Hz, 1H), 2.09 (s, 3H), 2.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.3, 170.8, 170.4, 136.8, 133.4, 132.8, 128.7, 128.2, 124.0, 70.3, 68.4, 64.8, 62.7, 42.1, 21.1, 20.7 ppm; HRMS (ESI) calcd. for $C_{15}H_{16}O_4Na$ $[M+Na]^+$: 355.1158; found: 355.1160.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-erythro-hex-2-enopyrano-xyl)-1-(4-methoxyphenyl)-ethanone (3b) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (150 mg, 0.55 mmol) with *β*-keto acid **2b** (128 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3b** as a separable mixture of *α*/*β* = 1:1 with a combined yield of 159 mg (82%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ +19.3 (*c* 3.3, $CHCl_3$); IR (neat): ν_{max} 2957, 1739, 1674, 1599, 1510, 1369, 1259, 1232, 1170, 1047, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.95-7.93 (m, 2H), 6.95-6.93 (m, 2H), 6.07 (ddd, J_1 = 10.4 Hz, J_2 = 2.5 Hz, J_3 = 1.6 Hz, 1H), 5.83 (ddd, J_1 = 10.4 Hz, J_2 = 2.9 Hz, J_3 = 2.1 Hz, 1H), 5.15-5.13 (m, 1H), 4.91-4.90 (m, 1H), 4.24 (dd, J_1 = 11.9 Hz, J_2 = 6.5 Hz, 1H), 4.12 (dd, J_1 = 11.9 Hz, J_2 = 3.7 Hz), 3.98 (dt, J_1 = 6.3 Hz, J_2 = 3.7 Hz, 1H), 3.87 (s, 3H), 3.41 (dd, J_1 = 16.1 Hz, J_2 = 7.0 Hz, 1H), 3.09 (dd, J_1 = 16.1 Hz, J_2 = 6.7 Hz), 2.08 (s, 3H), 2.02 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.5, 170.8, 170.4, 163.7, 132.9, 130.5, 129.9, 123.8, 113.8, 70.3, 68.6, 64.8, 62.7, 55.5, 41.8, 21.1, 20.7 ppm; HRMS (ESI) calcd. for $C_{19}H_{22}O_7Na$ $[M+Na]^+$: 385.1263; found: 385.1266.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-erythro-hex-2-enopyrano-xyl)-1-(4-chlorophenyl)-ethanone (3c) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (150 mg, 0.55 mmol) with *β*-keto acid **2c** (131 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3c** as a separable mixture of *α*/*β* = 1:1 with a combined yield of 107 mg (53%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ +27.8 (*c* 3.4, $CHCl_3$); IR (neat): ν_{max} 2954, 1741, 1683, 1589, 1489, 1435, 1400, 1369, 1232, 1126, 1092, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.91-7.89 (m, 2H), 7.46-7.43 (m, 2H), 6.07-6.04 (m, 1H), 5.85 (dt, J_1 = 10.4 Hz, J_2 = 2.4 Hz, 1H), 5.13-5.12 (m, 1H), 4.93-4.89 (m, 1H), 4.24 (dd, J_1 = 11.8 Hz, J_2 = 6.6 Hz, 1H), 4.12 (dd, J_1 = 11.8 Hz, J_2 = 3.8 Hz, 1H), 4.00-3.96 (m, 1H), 3.42 (dd, J_1 = 16.2 Hz, J_2 = 7.0 Hz, 1H), 3.10 (dd, J_1 = 16.2 Hz, J_2 = 6.2 Hz, 1H), 2.08 (s, 3H), 2.03 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.8, 170.8, 170.3, 139.9, 135.08, 132.6, 129.6, 129.0, 124.0, 70.4, 68.2, 64.7, 62.6, 42.2, 21.0, 20.7 ppm; HRMS (ESI) calcd. for $C_{18}H_{19}O_6{}^{35}ClNa$ $[M+Na]^+$: 389.0768; found: 389.0768.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyrano-xyl)-1-phenyl-ethanone (3d) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1b** (150 mg, 0.55 mol) with *β*-keto acid **2a** (108 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3d** (141 mg, 77%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ −167.7 (*c* 4.7, $CHCl_3$); IR (neat): ν_{max} 3020, 2960, 1738, 1681, 1597, 1448, 1371, 1232, 1089, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.91-7.89 (m, 2H), 7.55-7.51 (m, 1H), 7.44-7.41 (m, 2H), 6.13 (dd, J_1 = 10.4 Hz, J_2 = 2.8 Hz, 1H), 5.97 (ddd, J_1 = 10.2 Hz, J_2 = 5.2 Hz, J_3 = 2.2 Hz, 1H), 5.05 (d, J = 5.2 Hz, 1H), 5.00-4.95 (m, 1H), 4.11 (s, 3H), 3.40 (dd, J_1 = 16.2 Hz, J_2 = 7.4 Hz, 1H), 3.06 (dd, J_1 = 16.2 Hz, J_2 = 6.2 Hz, 1H), 2.02 (s, 3H), 1.91 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.8, 170.5, 170.3, 136.6, 134.3, 133.2, 128.5, 128, 122.2, 69.3, 68.3, 63.4, 62.5, 40.7, 20.7, 20.5 ppm; HRMS (ESI) calcd. for $C_{18}H_{20}O_6Na$ $[M+Na]^+$: 355.1157; found: 355.1157.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl) -1-(4-methoxy-phenyl)-ethanone (3e) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (150 mg, 0.55 mmol) with *β*-keto acid **2b** (128 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3c** as a separable mixture of *α*/*β* > 10:1 with a combined yield of 136 mg (68%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ −170.4 (*c* 5.0, $CHCl_3$); IR (neat): ν_{max} 3018, 1732, 1674, 1598, 1510, 1371, 1259, 1232, 1170, 1089, 1049, 1029, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 400MHz): δ 7.92 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 6.16 (dd, J_1 = 10.4 Hz, J_2 = 3.2 Hz, 1H), 6.00 (dd, J_1 = 10.4 Hz, J_2 = 5.2 Hz, 1H), 5.09 (d, J = 5.2 Hz, 1H), 5.01-4.98 (m, 1H), 4.15 (s, 3H), 3.86 (s, 3H), 3.38 (dd, J_1 = 16.0 Hz, J_2 = 7.2 Hz, 1H), 3.04 (dd, J_1 = 16.0 Hz, J_2 = 6.4 Hz, 1H), 2.06 (s, 3H), 1.96 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.4, 170.7, 170.5, 163.7, 134.6, 130.4, 129.8, 122.2, 113.8, 69.5, 68.4, 63.6, 62.7, 55.5, 40.6, 20.8, 20.7 ppm; HRMS (ESI) calcd. for $C_{19}H_{22}O_7Na$ $[M+Na]^+$: 385.1263; found: 385.1260.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl) -1-(4-chlorophenyl)-ethanone (3f) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (150 mg, 0.55 mmol) with *β*-keto acid **2c** (131 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3f** (111 mg, 55%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ −158.4 (*c* 5.1, $CHCl_3$); IR (neat): ν_{max} 3020, 2960, 2939, 1740, 1681, 1589, 1487, 1402, 1371, 1232, 1091, 1049, 1029,1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.89 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 6.15 (dd, J_1 = 10.2 Hz, J_2 = 3.0 Hz, 1H), 6.02 (ddd, J_1 = 10.4 Hz, J_2 = 5.2 Hz, J_3 = 2.0 Hz, 1H), 5.10 (dd, J_1 = 5.0 Hz, J_2 = 1.4 Hz, 1H), 5.02-4.97 (m, 1H), 4.15 (s, 3H), 3.40 (dd, J_1 = 16.0 Hz, J_2 = 7.2 Hz, 1H), 3.06 (dd, J_1 = 16.4 Hz, J_2 = 6.4 Hz, 1H), 2.07 (s, 3H), 1.98 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.8, 170.7, 170.5, 139.9, 135.0, 134.2, 129.6, 129.0, 122.6, 69.3, 68.5, 63.5, 62.6, 41.0, 20.9, 20.7 ppm; HRMS (ESI) calcd. for $C_{18}H_{19}O_6{}^{35}ClNa$ $[M+Na]^+$: 389.0768; found: 389.0767.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl) -1-(4-fluorophenyl)-ethanone (3g) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (150 mg, 0.55 mmol) with *β*-keto acid **2d** (120 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3g** (110 mg, 57%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 4:1). $[\alpha]_D^{23}$ −159.8 (*c* 1.2, $CHCl_3$); IR (neat): ν_{max} 1734, 1678, 1635, 1598, 1506, 1371, 1228, 1157, 1087, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.00-7.97 (m, 1H), 7.17 (t, J = 8.6 Hz, 1H), 6.16 (dd, J = 10.4, 2.8 Hz, 1H), 6.03 (ddd, J = 10.0, 5.2, 1.6 Hz, 1H), 5.12-5.11 (m, 1H), 5.02-4.99 (m, 1H), 4.17 (s, 3H), 3.41 (dd, J = 16.0, 7.2 Hz,

1H), 3.08 (dd, J = 16.0, 6.4 Hz, 1H), 2.08 (s, 3H), 1.99 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.3, 170.6, 170.4, 165.8 (d, J_{CF} = 254.0 Hz), 134.2, 133.1 (d, J_{CF} = 3.0 Hz), 130.7 (d, J_{CF} = 9.0 Hz), 122.5, 115.8 (d, J_{CF} = 22.0 Hz), 69.3, 68.4, 63.5, 62.5, 40.9, 20.8, 20.6 ppm; HRMS (ESI) calcd. for $C_{18}H_{19}O_6Na$ $[M+Na]^+$: 373.1063; found: 373.1063.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl)-1-(3,4,5-tri-methoxyphenyl)-ethanone (3h) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (150 mg, 0.55 mmol) with *β*-keto acid **2e** (168 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3h** as a separable mixture of *α*/*β* = 10:1 with a combined yield of 156 mg (67%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 1:1). $[\alpha]_D^{23}$ −128.1 (*c* 7.4, $CHCl_3$); IR (neat): ν_{max} 3016, 2941, 1739, 1676, 1585, 1504, 1456, 1413, 1369, 1325, 1232, 1157, 1128, 1093, 1049, 1026, 1001, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.16 (s, 2H), 6.12 (dd, J_1 = 10.2 Hz, J_2 = 3.0 Hz, 1H), 5.97 (ddd, J_1 = 10.4 Hz, J_2 = 5.2 Hz, J_3 = 2.0 Hz, 1H), 5.07 (d, J = 4.8 Hz, 1H), 4.13 (s, 3H), 3.87 (s, 6H), 3.86 (s, 3H), 3.37 (dd, J_1 = 16.2 Hz, J_2 = 7.4 Hz, 1H), 3.01 (dd, J_1 = 16.0 Hz, J_2 = 6.4 Hz, 1H), 2.04 (s, 3H), 1.92 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.6, 170.6, 170.4, 153.0, 142.8, 134.2, 131.9, 122.3, 105.6, 69.3, 68.4, 63.4, 62.4, 60.8, 56.2, 40.6, 20.7, 20.5 ppm; HRMS (ESI) calcd. for $C_{21}H_{26}O_9Na$ $[M+Na]^+$: 445.1475; found: 445.1474.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl)-2-(2-methyl)-butanone (3i) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (300 mg, 1.10 mmol) with *β*-keto acid **2f** (171 mg, 1.32 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3i** as a separable mixture of *α*/*β* = 5:1 with a combined yield of 112 mg (34%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 2:1). $[\alpha]_D^{23}$ −146.7 (*c* 3.3, $CHCl_3$); IR (neat): ν_{max} 2970, 1745, 1737, 1732, 1714, 1643, 1469, 1371, 1222, 1062, 1099, 1051, 1028, 771 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.07 (dd, J_1 = 10.2 Hz, J_2 = 3.0 Hz, 1H), 6.00 (ddd, J_1 = 10.2 Hz, J_2 = 5.0 Hz, J_3 = 2.0 Hz, 1H), 5.07 (dd, J_1 = 5.0 Hz, J_2 = 2.6 Hz, 1H), 4.89-4.84 (m, 1H), 4.17 (dd, J_1 = 6.2 Hz, J_2 = 1.4 Hz, 2H), 4.07 (td, J_1 = 6.0 Hz, J_2 = 2.7 Hz, 1H), 2.91 (dd, J_1 = 16.4 Hz, J_2 = 8.0 Hz, 1H), 2.65 (septet, J = 7.0 Hz, 1H), 2.56 (dd, J_1 = 16.2 Hz, J_2 = 5.8 Hz, 1H), 2.08 (s, 3H), 2.06 (s, 3H), 1.12 (d, J = 3.6 Hz, 3H), 1.11 (d, J = 3.6 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 211.3, 170.8, 170.5, 134.4, 122.2, 69.2, 68.3, 63.6, 62.9, 42.5, 41.2, 20.8, 20.7, 17.9, 17.8 ppm; HRMS (ESI) calcd. for $C_{15}H_{22}O_6Na$ $[M+Na]^+$: 321.1314; found: 321.1314.

1-((4,6-Di-acetyl)-2,3-dideoxy-*α*-D-threo-hex-2-enopyranoxyl)-2-pentanone (3j) Glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal **1b** (300 mg, 1.10 mmol) with *β*-keto acid **2g** (172 mg, 1.32 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **3j** as a separable mixture of *α*/*β* = 5:3 with a combined yield of 118 mg (36%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 2:1). $[\alpha]_D^{23}$ −155.1 (*c* 1.9, $CHCl_3$); IR (neat): ν_{max} 3018, 1732, 1716, 1371, 1215, 1051, 769, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.04 (dd, J_1 = 10.4 Hz, J_2 = 2.8 Hz, 1H), 5.97 (ddd, J_1 = 10.0, J_2 = 4.8, J_3 = 1.6 Hz, 1H), 5.07-5.05 (m, 1H), 4.83-4.80 (m, 1H), 4.16 (d, J = 6.4 Hz, 2H), 4.06 (td, J_1 = 6.2 Hz, J_2 = 2.4 Hz, 1H), 2.82 (dd, J_1 = 15.6, J_2 = 8.4 Hz, 1H), 2.51 (dd, J_1 = 16.0, J_2 = 5.6 Hz, 1H), 2.44 (t, J = 7.2 Hz, 2H), 2.06 (s, 1H), 2.05 (s, 1H), 1.60 (h, J = 7.2 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 207.8, 170.7, 170.4, 134.2, 122.3, 69.2, 68.3, 63.6, 62.8, 45.3, 44.8, 20.8, 20.7, 16.9, 13.6 ppm; HRMS (ESI) calcd. for $C_{15}H_{22}O_6Na$ $[M+Na]^+$: 321.1314; found: 321.1315.

1-((4,6-Di-acetyl)-2,3-dideoxy-*β*-D-erythro-hex-2-enopyrano-xyl-2-(2-methyl)-butanone (4b) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (150 mg, 0.55 mmol) with *β*-keto acid **2f** (86 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **4b** as a separable mixture of *α*/*β* = 2:3 with a combined yield of 113 mg (69%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 2:1). $[\alpha]_D^{23}$ +68.3 (*c* 1.2, $CHCl_3$); IR (neat): ν_{max} 2970, 2936, 2876, 1742, 1713, 1653, 1467, 1369, 1231, 1124, 1094, 1049, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.85 (dt, J_1 = 10.4 Hz, J_2 = 1.6 Hz, 1H), 5.72 (dt, J_1 = 10.0, J_2 = 2.0 Hz, 1H), 5.26-5.22 (m, 1H), 4.67-4.62 (m, 1H), 4.16-4.14 (m, 1H), 3.73-3.69 (m, 1H), 2.82 (dd, J_1 = 16.6 Hz, J_2 = 7.0 Hz, 1H), 2.63-2.58 (m, 1H), 2.53 (dd, J_1 = 16.4 Hz, J_2 = 6.8 Hz, 1H), 2.07 (s, 6H), 1.09 (d, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 211.9, 170.9, 170.3, 132.2, 125.4, 74.3, 71.6, 65.3, 63.5, 45.3, 41.6, 21.0, 20.8, 17.8, 17.8 ppm; HRMS (ESI) calcd. for $C_{15}H_{22}O_6Na$ $[M+Na]^+$: 321.1314; found: 321.1315.

1-((4,6-Di-acetyl)-2,3-dideoxy-*β*-D-erythro-hex-2-enopyrano-xyl)-2-pentanone (4c) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (150 mg, 0.55 mmol) with *β*-keto acid **2g** (86 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **4c** as a separable mixture of *α*/*β* = 1:1 with a combined yield of 105 mg (64%) as a light yellow oil. The product was purified by column chromatography (hexane/ethyl acetate = 2:1). $[\alpha]_D^{23}$ +90.7 (*c* 1.8, $CHCl_3$); IR (neat): ν_{max} 2962, 2936, 2876, 1740, 1715, 1665, 1653, 1458, 1437, 1410, 1371, 1231, 1123, 1096, 1049 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.84 (dt, J_1 = 10.3 Hz, J_2 = 1.6 Hz, 1H), 5.73 (dt, J_1 = 10.3 Hz, J_2 = 2.1 Hz, 1H), 5.26-5.23 (m, 1H), 4.65-4.62 (m, 1H), 4.19-4.15 (m,1H), 3.74-3.70 (m, 1H), 2.75 (dd, J_1 = 16.1 Hz, J_2 = 7.1 Hz, 1H), 2.50 (dd, J_1 = 16.2 Hz, J_2 = 6.3 Hz, 1H), 2.43 (t, J = 7.3 Hz, 1H), 2.42 (t, J = 7.3 Hz, 1H), 2.07 (s, 6H), 1.63-1.57 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 208.4, 170.9, 170.3, 132.1, 125.5, 74.3, 71.5, 65.3, 63.5, 47.6, 45.8, 21.0, 20.8, 16.9, 13.6 ppm; HRMS (ESI) calcd. for $C_{15}H_{22}O_6Na$ $[M+Na]^+$: 321.1314; found: 321.1316.

1-((4,6-Di-acetyl)-2,3-dideoxy-*β*-D-erythro-hex-2-enopyrano-xyl)-2-butanone (4d) Glycosylation of 3,4,6-tri-*O*-acetyl-D-glucal **1a** (150 mg, 0.55 mmol) with *β*-keto acid **2h** (77 mg, 0.66 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **4d** as a separable mixture of *α*/*β* = 1:2 with a combined yield of 116 mg (74%) as a light yellow oil. $[\alpha]_D^{23}$ +97.3 (*c* 1.6, $CHCl_3$); IR (neat): ν_{max} 3018, 2939, 1737, 1668, 1456, 1435, 1411, 1371, 1230, 1112, 1089, 1049 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.83 (dt, J_1 = 10.4 Hz, J_2 = 1.6 Hz, 1H), 5.72 (dt, J_1 = 10.4 Hz, J_2 = 2.2 Hz, 1H), 5.25-5.22 (m, 1H), 4.65-4.60 (m, 1H), 4.15-4.14 (m, 1H), 3.73-3.68 (m, 1H), 2.74 (dd, J_1 = 16.0 Hz, J_2 = 7.2 Hz, 1H), 2.50 (dd, J_1 = 16.2 Hz, J_2 = 6.2 Hz, 1H), 2.46 (q, J = 7.2 Hz, 1H), 2.45 (q, J = 7.2 Hz, 1H), 2.06 (s, 6H), 1.04 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 208.7, 170.8, 170.3, 132.1, 125.4, 74.3, 71.5, 65.3, 63.4, 47.3, 37.1, 21.0, 20.8, 7.5 ppm; HRMS (ESI) calcd. for $C_{14}H_{20}O_6Na$ $[M+Na]^+$: 307.1158; found: 307.1159.

(2*R*-*cis*)-1-(5-Acetoxy-5,6-dihydro-2H-pyran-2-yl)-acetophe-none (4e) Glycosylation of 3,4-di-*O*-acetyl-L-arabinal **1c** (150 mg, 0.75

mmol) with *β*-keto acid **2a** (148 mg, 0.90 mmol) at room temperature *via* general procedure for the synthesis of *β*-keto functionalized glycals for 5 hours afforded compound **4e** as a separable mixture of *α*/*β* = 1:2 with a combined yield of 100 mg (51%) as a light yellow oil. $[\alpha]_D^{23}$ −101.7 (*c* 4.5, $CHCl_3$); IR (neat): ν_{max} 3059, 2936, 2862, 1732, 1682, 1597, 1448, 1371, 1238, 1124, 1095, 1036 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.96-7.94 (m, 2H), 7.59-7.55 (m, 1H), 7.49-7.45 (m, 2H), 6.04 (dt, J_1 = 10.4 Hz, J_2 = 1.8 Hz, 1H), 5.88 (dt, J_1 = 10.4 Hz, J_2 = 2.4 Hz, 1H), 5.28-5.24 (m, 1H), 4.85-4.81 (m, 1H), 4.10 (dd, J_1 = 11.5 Hz, J_2 = 5.0 Hz, 1H), 3.59 (dd, J_1 = 11.4 Hz, J_2 = 6.7 Hz, 1H), 3.37 (dd, J_1 = 16.5 Hz, J_2 = 7.0 Hz, 1H), 3.05 (dd, J_1 = 16.5 Hz, J_2 = 6.4 Hz, 1H), 2.07 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.3, 170.6, 136.7, 133.1, 128.6, 128.4, 128.1, 124.7, 70.1, 65.1, 64.6, 42.7, 21.0 ppm; HRMS (ESI) calcd. for $C_{15}H_{16}O_4Na$ $[M+Na]^+$: 283.0946; found: 283.0952.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization of new compounds are detailed. See DOI: 10.1039/c000000x/

1 C. D. Hurd and W. A. Bonner, *J. Am. Chem. Soc.*, 1945, **67**, 1664.
2 (a) D, E. Levy, C. Tang, *The Chemistry of C-Glycosides*; Elservier Science: Tarrytown, New York, 1995. (b) M. H. D. Postema, *Tetrahedron*, 1992, **48**, 8545. (c) J. S. Thorson, *Nat. Prod. Rep.* 2005, **22**, 742. (d) P. G. Hultin, *Curr. Top. Med. Chem.*, 2005, **5**, 1299. (e) W. Zou, *Curr. Top. Med. Chem.*, 2005, **5**, 1363.
3 T. Komori, M. Yamashita, Y. Tsurumi and M. Kohsaka, *J. Antibiot.*, 1985, **38**, 455.
4 H. Nishimura, N. Shimaoka, Y. Tanaka, Y. Komatsu, H. Kato and M. Mayama, *J. Antibiot.*, 1964, **17**, 148.
5 K. Kito, R. Ookura, S. Yoshida, M. Namikoshi, T. Ooi and T. Kusumi, *Org. Lett.*, 2008, **10**, 225.
6 G. L. Yang, J. Schmieg, M. Tsuji, and R. W. Franck, *Angew. Chem. Int. Ed.*, 2004, **43**, 3818.
7 (a) R. Nakagawa, K. Motoki, H. Ueno, R. Iijima, H. Nakamura, E. Kobayashi, A. Shimosaka and Y. Koezuka, *Cancer Res.*, 1998, **58**, 1202. (b) G. Matsumoto, S. Nagai, M. Muta, K. Tsuruta, A. Okamoto and M. Toi, *Oncol. Rep.*, 2003, **10**, 1201. (c) G. Gonzalez-Aseguinolaza, C. de Oliveira, M. Tomaska, S. Hong, O. Bruna-Romero, T. Nakayama, M. Taniguchi, A. Bendelac, L. Van Kaer, Y. Koezuka and M. Tsuji, *Proc. Natl. Acad. Sci., USA* 2000, **97**, 8461.
8 (a) K. Kakimi, L. G. Guidotti, Y. Koezuka and F. V. Chisari, *J. Exp. Med.*, 2000, **192**, 921. (b) S. Sharif, G. A. Arreaza, P. Zucker, Q. S. Mi, J. Sondhi, O. V. Naidenko, M. Kronenberg, Y. Koezuka, T. L. Delovitch, J. M. Gombert, M. Leite-De-Moraes, C. Gouarin, R. Zhu, A. Hameg, T. Nakayama, M. Taniguchi, F. Lepault, A. Lehuen, J. F. Bach and A. Herbelin, *Nat. Med.*, 2001, **7**, 1057.
9 T. Bottcher and S. A. Sieber, *J. Am. Chem. Soc.*, 2010, **132**, 6964.
10 (a) S. Vedachalam, S. M. Tan, H. P. Teo, S. T. Cai and X.-W. Liu, *Org. Lett.*, 2012, **14**, 174. (b) Y. G. Bai, M. Leow, J. Zeng and X.-W. Liu, *Org. Lett.*, 2011, **13**, 5648.
11 (a) M. D. Lewis, J. K. Cha and Y. Kishi, *J. Am. Chem. Soc.*, 1982, **104**, 4976. (b) R. Nakamura, K. Tanino and M. Miyashita, *Org. Lett.*, 2003, **5**, 3579.
12 G. Grynkiewicz and J. N. Bemiller, *Carbohydr. Res.*, 1982, **108**, 229.
13 (a) D. B. Tulshian and B. Fraserreid, *J. Org. Chem.*, 1984, **49**, 518. (b) W. H. Pearson and J. M. Schkeryantz, *J. Org. Chem.*, 1992, **57**, 2986.
14 H. G. Gong, R. Sinisi and M. R. Gagne, *J. Am. Chem. Soc.*, 2007, **129**, 1908.
15 D. G. Zhai, W. X. Zhai and R. M. Williams, *J. Am. Chem. Soc.*, 1988, **110**, 2501.
16 K. C. Nicolaou, C. K. Hwang and M. E. Duggan, *J. Chem. Soc., Chem.Commun.*, 1986, 925.
17 T. Kourouli, P. Kefalas, N. Ragoussis and V. Ragoussis, *J. Org. Chem.*, 2002, **67**, 4615.
18 D. A. Evans, S. Mito and D. Seidel, *J. Am. Chem. Soc.*, 2007, **129**, 11583.
19 K. Rohr and R. Mahrwald, *Org. Lett.*, 2011, **13**, 1878.
20 G. Baxter, J. C. Melville and D. J. Robins, *Synlett*, 1991, 359.
21 T. Tsuda, M. Okada, S. Nishi and T. Saegusa, *J. Org. Chem.*, 1986, **51**, 421.
22 T. Tsuda, M. Tokai, T. Ishida and T. Saegusa, *J. Org. Chem.*, 1986, **51**, 5216.
23 C. F. Yang, J. Y. Wang and S. K. Tian, *Chem. Commun.*, 2011, **47**, 8343.
24 N. Rodriguez and L. J. Goossen, *Chem. Soc. Rev.*, 2011, **40**, 5030.
25 S. H. Xiang, S. T. Cai, J. Zeng and X.-W. Liu, *Org. Lett.*, 2011, **13**, 4608.
26 C. Bolm, J. Legros, J. Le Paih and L. Zani, *Chem. Rev.*, 2004, **104**, 6217.
27 L. Goossen and A. Dohring, *Adv. Synth. Catal.*, 2003, **345**, 943.
28 H. P. Bi, W. W. Chen, Y. M. Liang and C. J. Li, *Org. Lett.*, 2009, **11**, 3246.
29 R. Trivedi and J. A. Tunge, *Org. Lett.*, 2009, **11**, 5650.
30 S. Enthaler, K. Junge and M. Beller, *Angew. Chem. Int. Ed.*, 2008, **47**, 3317.
31 C. Masson, J. Soto and M. Bessodes, *Synlett*, 2000, 1281.
32 M. Isobe, W. Phoosaha, R. Saeeng, K. Kira and C. Yenjai, *Org. Lett.*, 2003, **5**, 4883.
33 S. Price, S. Edwards, T. Wu and T. Minehan, *Tetrahedron Lett.*, 2004, **45**, 5197.

