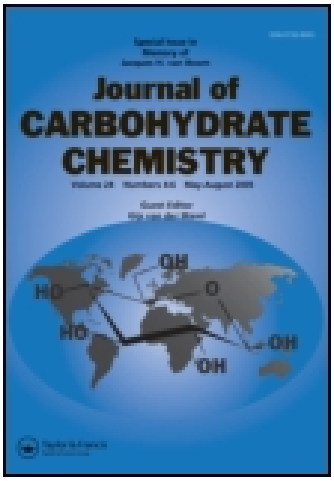

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$FeCl_3 \cdot 6H_2O/C$: An Efficient and Recyclable Catalyst for the Synthesis of 2,3-Unsaturated O- and S-Glycosides

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DOI: 10.1080/07328303.2014.941995

$FeCl_3 \cdot 6H_2O$/C: An Efficient and Recyclable Catalyst for the Synthesis of 2,3-Unsaturated *O*- and *S*-Glycosides

Jiafen Zhou,[1] Heshan Chen,[1] Junjie Shan,[2] Juan Li,[1] Guofang Yang,[1] Xuan Chen,[1] Kunyun Xin,[1] Jianbo Zhang,[1] and Jie Tang[1]

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A novel method for synthesizing 2,3-unsaturated glycosides has been developed using a handy and eco-friendly immobilized catalyst, $FeCl_3 \cdot 6H_2O$/C. A series of 2,3-unsaturated *O*- and *S*-glycosides were obtained for bioassay from corresponding 3,4,6-tri-*O*-acetyl-*D*-glucal and *D*-galactal in good to excellent yields (56%–99%) and high anomeric selectivity ($\alpha/\beta = 7{:}1$ to $>19{:}1$). Furthermore, the catalyst was efficient on gram-scale reactions and recyclable for at least three times.

Keywords $FeCl_3 \cdot 6H_2O$/C; Tri-*O*-acetyl-*D*-glycals; 2,3-Unsaturated glycosides; Ferrier-rearrangement; Recyclable

INTRODUCTION

2,3-Unsaturated glycosides as chiral intermediates have played an important role in the synthesis of bioactive compounds, such as oligosaccharides,[1] glycopeptide building blocks,[2] modified carbohydrates,[3] nucleosides,[4] and antibiotics.[5] Besides, the unsaturated part of the sugar ring allows many straightforward modifications such as hydroxylation, oxidation, epoxidation, and hydrogenation, which contributes to their diversity and complexity.[6–11] As we know, the most valuable method for preparing 2,3-unsaturated glycosides is Lewis acid–catalyzed allelic rearrangement of glycals, which is well known as the Ferrier rearrangement reaction.[12,13] Up to now, a wide range of Lewis acids and oxidizing agents, such as $BF_3 \cdot OEt_2$,[12] IDCP,[14]

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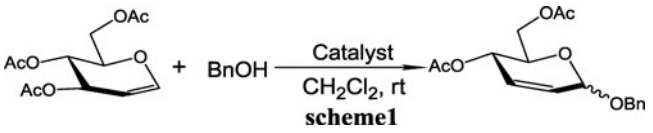
Table 1: Optimization of reaction conditions for the synthesis of 2,3-unsaturated glucosides



scheme1

Entry	Conditions	Yield (%)
1	$FeCl_3.6H_2O$/C (0.01eq), 240min	45
2	$FeCl_3.6H_2O$/C (0.02eq), 40min	95
3	$FeCl_3.6H_2O$/C (0.05eq), 10min	99
4	$FeCl_3.6H_2O$/C (0.05eq), 10min	98
5	$FeCl_3.6H_2O/SiO_2$ (0.05eq), 120min	80
6	$FeCl_3.6H_2O$/4 ÅMS (0.05eq), 120min	traces

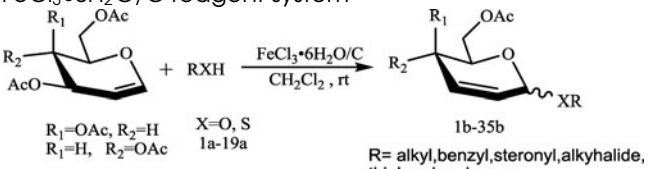
TMSOTf,[15] I_2,[16] $Sc(OTf)_3$,[17] $InCl_3$,[18] $Yb(OTf)_3$,[19] $BiCl_3$,[20] $Dy(OTf)_3$ immobilized in ionic liquids,[21] $ZnCl_2$,[22] $HClO_4$-SiO_2,[23] $NiCl_5$,[224] $Er(OTf)_3$,[25] $ZnCl_2/Al_2O_3$,[26] H_2SO_4-SiO_2,[27] $NaHSO_4$-SiO_2,[28] and CF_3SO_3H-SiO_2,[29] have been employed for this transformation. However, the present methods for the synthesis of 2,3-unsaturated glycosides possess some drawbacks, such as use of expensive and toxic reagents and/or stoichiometric amount of catalyst, low efficiency, and complicated operation.

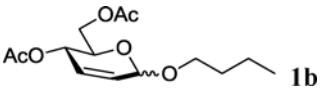
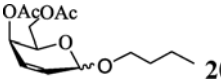
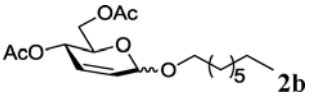
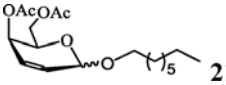
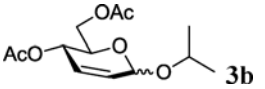
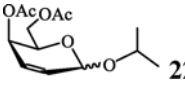
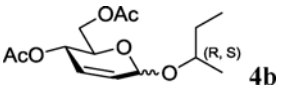
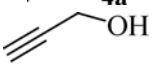
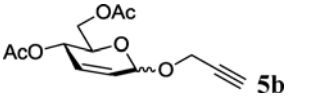
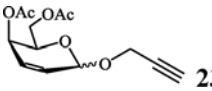
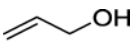
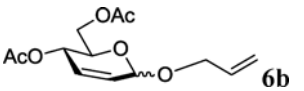
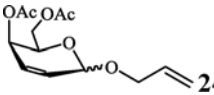
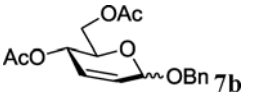
Recently, iron (III) catalysts have been widely used in organic synthesis,[30,31] and some of these types of catalysts, such as $FeCl_3$,[32] $Fe_2(SO_4)_3.xH_2O$,[33] $FeCl_3$ immobilized in ionic liquids,[34] and $Fe(OTf)_3$,[35] have been successfully utilized for the Ferrier rearrangement. In our previous research for diverse syntheses of glycosides, we have successfully used immobilized catalysts for Ferrier rearrangement.[27,36] The present work aimed at developing a new and reusable immobilized iron (III) catalyst for Ferrier rearrangement.

Initially, we screened different carriers, including carbon, SiO_2, and molecular sieves, to immobilize iron (III) chloride hexahydrate ($FeCl_3{\cdot}6H_2O$) according to the literature method.[37,38] We found that $FeCl_3{\cdot}6H_2O$/C was the most promising for catalyzing the reaction between 3,4,6-tri-*O*-acetyl-D-glucal and benzyl alcohol, because other immobilized iron (III) catalysts, including $FeCl_3{\cdot}6H_2O/SiO_2$ and $FeCl_3{\cdot}6H_2O$/4 ÅMS, could only give the desired product either in longer time or poorer yield (Table 1). Therefore, $FeCl_3{\cdot}6H_2O$/C was explored in detail to establish the proper reaction conditions. We found that 0.05 equiv $FeCl_3{\cdot}6H_2O$/C was sufficient to promote the reaction and gave an excellent yield (99%) in 10 min at rt using CH_2Cl_2 as solvent. When a smaller amount of catalyst was used, the reaction preceded much slower, while the reaction rate and yield were not improved with a larger amount of catalyst.

With the optimal conditions established, we next investigated the reaction scope using a variety of acceptors. As shown in Table 2, glycosidation of

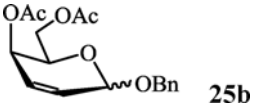
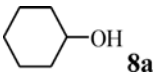
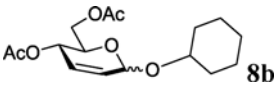
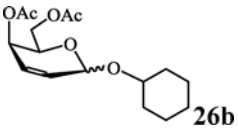
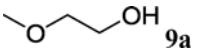
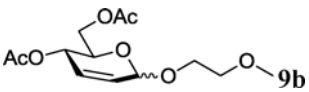
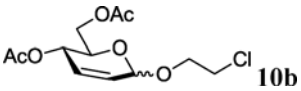
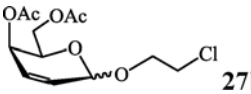
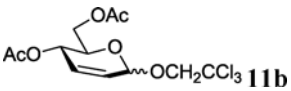
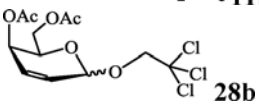
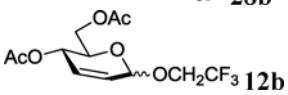
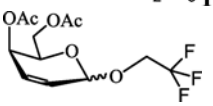
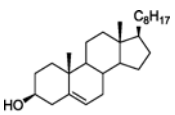
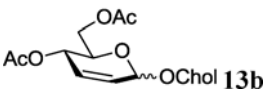
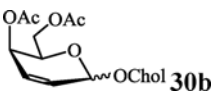
Table 2: Ferrier reaction of 3, 4, 6-tri-*O*-acetyl-*D*-glycal with acceptors in the presence of the $FeCl_3{\bullet}6H_2O/C$ reagent system



Entry	Acceptors	Products	Time (h)	Yield (%)[a]	α/β ratios[b]
1	$CH_3(CH_2)CH_2OH_2$ **1a**	 **1b**	1.5	93[36]	7.5:1
2		 **20b**	1.5	93[40]	>19:1
3	$CH_3(CH_2)_6CH_2OH$ **2a**	 **2b**	1.5	97[25]	7:1
4		 **21b**	2.5	85[25]	>19:1
5	$(CH_3)_2CHOH$ **3a**	 **3b**	1	90[36]	9:1
6		 **22b**	2	82[24]	>19:1
7	 **4a**	 **4b**	2	88[36]	15:1
8	 **5a**	 **5b**	1.5	86[36]	7:1
9		 **23b**	2	89[24]	>19:1
10	 **6a**	 **6b**	5.5	75[36]	7:1
11		 **24b**	4	87[2]	>19:1
12	$PhCH_2OH$ **7a**	 **7b**	10 min	99[36]	8:1

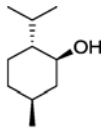
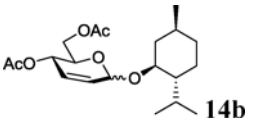
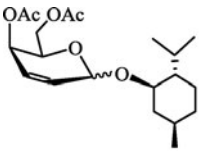
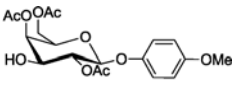
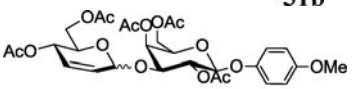
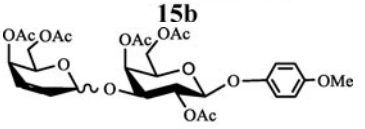
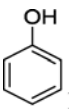
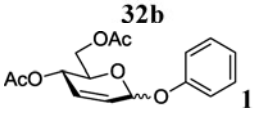
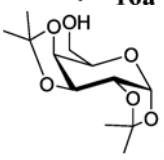
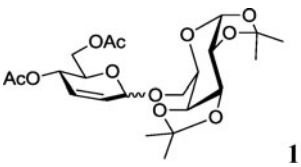
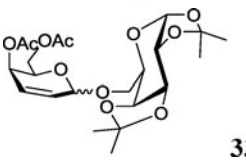
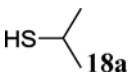
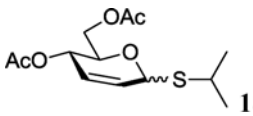
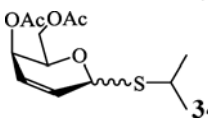
(Continued on next page)

Table 2: Ferrier reaction of 3, 4, 6-tri-*O*-acetyl-*D*-glycal with acceptors in the presence of the $FeCl_3 \bullet 6H_2O$/C reagent system *(Continued)*

Entry	Acceptors	Products	Time (h)	Yield (%)[a]	α/β ratios[b]
13		 **25b**	40 min	92[(2)]	>19:1
14	 **8a**	 **8b**	5.5	88[(36)]	10:1
15		 **26b**	2.5	82[(41)]	>19:1
16	 **9a**	 **9b**	4.5	85[(36)]	8:1
17	$HOCH_2CH_2Cl$ **10a**	 **10b**	1.5	94[(36)]	7.5:1
18		 **27b**	0.5	85[(42)]	>19:1
19	Cl_3CCH_2OH **11a**	 **11b**	1	76[(36)]	9:1
20		 **28b**	1.5	80	>19:1
21	F_3CCH_2OH **12a**	 **12b**	1	69	7:1
22		 **29b**	1	61	>19:1
23	 **13a**	 **13b**	2.5	87[(36)]	18:1
24		 **30b**	1.5	68	>19:1

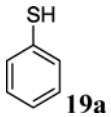
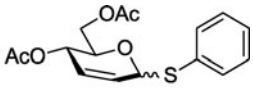
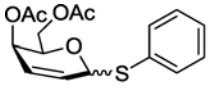
(Continued on next page)

Table 2: Ferrier reaction of 3, 4, 6-tri-*O*-acetyl-*D*-glycal with acceptors in the presence of the $FeCl_3{\bullet}6H_2O/C$ reagent system *(Continued)*

Entry	Acceptors	Products	Time (h)	Yield (%)[a]	α/β ratios[b]
25	 **14a**	 **14b**	1	84[40]	>19:1
26		 **31b**	1.5	67	>19:1
27	 **15a**	 **15b**	1	74	>19:1
28		 **32b**	1.5	57	>19:1
29	 **16a**	 **16b**	0.5	56[c][21]	7:1
30	 **17a**	 **17b**	3.5	82[43]	7:1
31		 **33b**	3	66[43]	>19:1
32	 **18a**	 **18b**	0.5	91[44]	9:1
33		 **34b**	0.5	75[44]	>19:1

(Continued on next page)

Table 2: Ferrier reaction of 3, 4, 6-tri-*O*-acetyl-*D*-glycal with acceptors in the presence of the $FeCl_3 \bullet 6H_2O$/C reagent system *(Continued)*

Entry	Acceptors	Products	Time (h)	Yield (%)[a]	α/β ratios[b]
34	 **19a**	 **19b**	40 min	88(44)	7:1
35		 **35b**	0.5	86(24)	>19:1

[a] Isolated yields.
[b] α/β ratios were determined by ^{1}H NMR.
[c] The dosage of $FeCl_3.6H_2O$/C is 0.001 eq.

tri-*O*-acetyl-*D*-glucal with primary, secondary, benzyl, allyl, propargyl, and halogenated alcohols; thioalcohol; and thiophenol proceeded smoothly under the specified conditions. The reaction afforded 2,3-unsaturated glucosides in good to excellent yields (69%–99%) with good anomeric selectivity ($\alpha/\beta > 7{:}1$). Comparing the results among entry 17, entry 19, and entry 21, it is clear that the reaction rate became slower and the yield was decreased with the reduction in the nucleophilicity of acceptors. Additionally, complex alcohols such as cholesterol also produced a high yield of product (87%, entry 23). Moreover, we could obtain disaccharide smoothly while using sugar-derived alcohols as the acceptor (entries 27 and 30). When the dosage of $FeCl_3 \cdot 6H_2O$/C reduced to 0.001 equiv, we successfully obtained the phenol glycoside in 56% yield (entry 29), which is hardly synthesized with other catalyst systems.[32,33]

However, the reaction between tri-*O*-acetyl-D-galactal and benzyl alcohol needed harsher conditions. We found that 0.5 equiv $FeCl_3 \cdot 6H_2O$/C was required to promote the glycosylation with 92% yield and only α anomeric selectivity. Likewise, a number of 2,3-unsaturated galactosides were obtained successfully from primary, secondary, benzyl, allyl, propargyl, and halogenated alcohols; thioalcohol; thiophenol; cholesterol; and sugar-derived alcohols, with sole α anomeric selectivity, which probably resulted from the steric and anomeric effects.

The structure and stereochemistry of all glycosidation products were determined through spectroscopic analysis and also by comparison with the reported data.[39–44] In vitro antitumor activity of some of the compounds was evaluated against the human k562 cancer cell line by the standard MTT assay.[45] They were proven to possess moderate antitumor activity as shown in Table 3.

More significantly, this synthetic methodology was shown to be reliable on a 2 g scale of tri-*O*-acetyl-D-glucal in the presence of benzyl alcohol to give

Table 3: Inhibition of resistant K562 cell proliferation by some glycosidation products

Compound	Sample concentration (μg/mL)	Inhibition rate (%)
DDP	10	60.1
9b	100	23.2
13b	100	11.5
22b	100	24.0
31b	100	23.1

DDP: *cis*-dichlorodiamminoplatinum-II.

an excellent yield (95%), and the catalyst could be easily recovered by simple filtration and drying at 120°C for 3 h. Furthermore, over three cycles, the catalyst did not show any significant loss in activity. [32,39]

In summary, we have developed a mild and environmentally friendly iron (III)–catalyzed glycosylation method for synthesizing 2,3-unsaturated glucosides and 2,3-unsaturated galactosides in high anomeric selectivity. This method was applied to a wide range of acceptors, including primary, secondary, benzyl, allyl, propargyl, and halogenated alcohols; thioalcohol; thiophenol; cholesterol; and sugar derivatives. Furthermore, the efficient applicability of this methodology to gram scales of synthesis and the recyclability of the catalyst make this approach highly practical.

EXPERIMENTAL

General Experimental Methods

^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker DRX-500 MHz spectrometer using tetramethylsilane as internal standard and $CDCl_3$ as solvent. Mass spectra were determined on LTQ-XL (Thermo Scientific, USA) with an (ESI) ion trap mass spectrometer. Silica gel (10–40 μm, Yantai, China) was used for column chromatography. TLC plates (10–40 μm, Yantai, China) were applied to monitor the reactions. All the reagents were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and were used as received without further purification. The supported ferric catalysts were prepared according to the reported methods.[37,38]

Preparation of $FeCl_3 \cdot 6H_2O/C$ Catalyst

The preparation of $FeCl_3 \cdot 6H_2O/C$ followed the literature method.[38] In brief, 1 g of iron (III) chloride hexahydrate, 1 g of activated carbon, and 4.0 mL of absolute ethanol were added to a round-bottom flask. Then, the mixture was

refluxed for 30 min. Finally, the solvent was evaporated under reduced pressure and the resulting catalyst was baked in an oven at 120°C for 2 h.[46]

General Experimental Procedure for the Synthesis of 2,3-Unsaturated Glucosides

To a stirred solution of tri-*O*-acetyl-*D*-glucal (100 mg, 0.37 mmol) in DCM (1 mL) were added the corresponding alcohol (0.41 mmol, 1.1 equiv) and $FeCl_3{\cdot}6H_2O$/C (5 mol%) at ambient temperature. After the reaction was completed (monitored by TLC), the reaction mixture was filtered and the catalyst was washed with dichloromethane. After evaporation of the solvent under vacuum, the crude products were purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1).

General Experimental Procedure for the Synthesis of 2,3-Unsaturated Galactosides

To a stirred solution of tri-*O*-acetyl-D-galactal (50 mg, 0.185 mmol) in DCM (1 mL) were added the corresponding alcohol (0.204 mmol, 1.1 equiv) and $FeCl_3{\cdot}6H_2O$/C (50 mol%) at ambient temperature. After the reaction was completed (monitored by TLC), the reaction mixture was filtered and the catalyst was washed with dichloromethane. After evaporation of the solvent under vacuum, the crude products were purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1).

Spectral Data for New Compounds

*Trifluoroethyl 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranoside (12b)*

Viscous oil; α/β = 7:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 2.06–2.09 (m, 6 H), 3.95–4.09 (m, 3 H), 4.18–4.20 (m, 1H), 5.09 (s, 1 H), 5.31 (dd, 1 H, J = 1.4, 9.8 Hz), 5.82–5.94 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 20.60, 20.82, 62.51, 64.78, 64.85, 65.06, 67.39, 94.47, 126.19, 130.34, 170.15, 170.63. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{12}H_{15}F_3O_6Na$ 335.07, found 335.17. ESI-HRMS: Calcd for $C_{12}H_{15}F_3O_6Na$ ($M+Na^+$) 335.0713, found 335.0731.

*2,4,6-tri-*O*-acetyl mequinol galactosyl-4,6-di-*O*-acetyl-2, 3-dideoxy-α-D-erythro-hex-2-enopyranoside (15b)*

Viscous oil; $[\alpha]_D^{20}$ = +108 (c 0.23, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 2.05–2.18 (m, 15H), 3.78 (s, 3H), 3.92–3.95 (m, 2H), 4.10–4.21 (m, 3 H), 4.24–4.28 (m, 2H), 4.83–4.85 (d, 1H), 5.24 (s, 1H), 5.32–5.39 (m, 1H), 5.44–5.45 (d, 1 H, J = 2.9 Hz), 5.63–5.66 (m, 1H), 5.85–5.87 (m, 1H), 6.81–6.83

(dd, J = 2.2, 6.9 Hz), 6.94–6.96 (dd, J = 2.2, 6.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 14.09, 20.65, 20.78, 20.80, 20.92, 22.67, 29.34, 29.68, 31.91, 55.65, 61.55, 62.51, 64.96, 65.30, 67.29, 69.67, 70.81, 73.30, 91.05, 101.09, 114.55, 118.58, 127.04, 129.34, 151.11, 155.71, 169.16, 170.14, 170.37, 170.65. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{29}H_{36}O_{15}Na$ 647.20, found 647.33. ESI-HRMS: Calcd for $C_{29}H_{36}O_{15}Na$ ($M+Na^+$) 647.1946, found 647.1990.

*Trichloroethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-derythro-hex-2-enopyranoside (28b)*

Yellow oil; $[\alpha]_D{}^{20}$ = –130 (c 0.16, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.20 (1H, dd, J = 10.0, 5.5 Hz), 6.12 (1H, dd, J = 10.0, 3.0 Hz), 5.30 (1H, d, J = 2.5 Hz), 5.05 (1H, dd, J = 5.0, 2.0 Hz), 4.45–4.42 (1H, m), 4.33–4.31 (1H, m), 4.23–4.17 (3H, m), 2.07 (3H, s), 2.06 (3H, s); 13C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.5, 170.2, 129.2, 126.2, 96.4, 94.1, 79.3, 67.5, 62.6, 62.5, 20.7 (2C). MS (ESI): m/z calculated for $[M+Na]^+$ $C_{12}H_{15}Cl_3O_6Na$ 382.98, found 383.08. ESI-HRMS: Calcd for $C_{12}H_{15}Cl_3O_6Na$ ($M+Na^+$) 382.9826, found 382.9858.

*Trifluoroethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-derythro-hex-2-enopyranoside (29b)*

Viscous liquid; $[\alpha]_D{}^{20}$ = –104 (c 0.14, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.21 (1H, dd, J = 10.0, 5.5 Hz), 6.07 (1H, dd, J = 10.0, 3.0 Hz), 5.16 (1H, d, J = 2.5 Hz), 5.05 (1H, dd, J = 5.5, 2.0 Hz), 4.34–4.33 (1H, m), 4.28–4.21 (2H, m), 4.20–3.96 (2H, m), 2.09 (3H, s), 2.08 (3H, s); ^{13}C NMR (125MHz, $CDCl_3$) δ (ppm): 170.5, 170.2, 129.1, 126.2, 94.0, 67.4, 64.6, 64.4, 62.6, 62.4, 20.7, 20.6. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{12}H_{15}F_3O_6Na$ 335.07, found 335.17. ESI-HRMS: Calcd for $C_{12}H_{15}F_3O_6Na$ ($M+Na^+$) 335.0713, found 335.0727.

*Cholesteryl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-enopyranoside (30b)*

White solid; $[\alpha]_D{}^{20}$ = –45 (c 0.08, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.09 (1H, dd, J = 10.0, 5.4 Hz), 6.01 (1H, dd, J = 10.0, 3.0 Hz), 5.34 (1H, d, J = 4.9 Hz), 5.20 (1H, d, J = 2.6 Hz), 5.00 (1H, dd, J = 5.2, 2.5 Hz), 4.40–4.39 (1H, m), 4.22–4.20 (2H, m), 3.54–3.59 (1H, m), 2.43–2.39 (1H, m), 2.34–2.29 (1H, m), 2.06 (3H, s), 2.05 (3H, s), 2.01–0.66 (41H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.6, 170.3, 130.7, 124.7, 95.6, 80.7, 66.6, 63.2, 63.0, 48.9, 43.2, 34.3, 31.7, 25.6, 23.1, 22.4, 21.1, 20.8 (2C), 16.1. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{37}H_{58}O_6Na$ 621.43, found 621.50. ESI-HRMS: Calcd for $C_{37}H_{58}O_6Na$ ($M+Na^+$) 621.4126, found 621.4141.

*Methyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (31b)*

White solid; $[\alpha]_D^{20} = -159$ (c 0.16, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.09 (1H, dd, J = 10.1, 5.2 Hz), 6.04 (1H, dd, J = 10.1, 2.9 Hz), 5.13 (1H, d, J = 2.6 Hz), 5.00 (1H, dd, J = 5.2, 2.5 Hz), 4.41–4.38 (1H, m), 4.22–4.19 (2H, m), 3.45–3.40 (1H, m), 2.19 (1H, m), 2.07 (3H, s), 2.06 (3H, s), 1.65–0.65 (17H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.6, 170.3, 130.7, 124.7, 95.6, 80.7, 66.6, 63.2, 63.0, 48.9, 43.2, 34.3, 31.7, 25.6, 23.1, 22.4, 21.1, 20.8(2C), 16.1. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{20}H_{32}O_6Na$ 391.21, found 391.33. ESI-HRMS: Calcd for $C_{20}H_{32}O_6Na$ ($M+Na^+$) 391.2091, found 391.2100.

*2,4,6-tri-*O*-acetyl mequinol galactosyl-4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (33b)*

Viscous liquid; $[\alpha]_D^{20} = -47$ (c 0.33, CH_2Cl_2); α only; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.95–6.94 (2H, d, J = 9.0 Hz), 6.95–6.94 (2H, d, J = 9.1 Hz), 6.10–6.07 (1H, m), 5.86–5.83 (1H, dd, J = 10.1, 3.0 Hz), 5.47–5.46 (1H, d, J = 3.1 Hz), 5.38–5.34 (1H, m), 5.03–5.01 (1H, dd, J = 5.7, 1.9 Hz), 4.85–4.83 (1H, d), 4.28–4.22 (2H, m), 4.20–4.17 (2H, m), 4.14–4.11 (2H, m), 3.97–3.96 (1H, m), 3.99–3.97 (1H, m), 3.78 (3H, s), 2.18–2.05 (15H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.65, 170.38, 170.30, 170.26, 169.26, 155.68, 151.10, 129.92, 125.28, 118.55, 114.53, 101.09, 90.44, 72.78, 70.82, 69.60, 67.16, 65.21, 62.26, 62.23, 61.61, 60.36, 55.62, 29.66, 20.75, 20.73, 20.63, 14.16. MS (ESI): m/z calculated for $[M+Na]^+$ $C_{29}H_{36}O_{15}Na$ 647.20, found 647.33. ESI-HRMS: Calcd for $C_{29}H_{36}O_{15}Na$ ($M+Na^+$) 647.1946, found 649.1974.

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REFERENCES

1. Bussolo, V.D.; Kim, Y.J.; Gin, D.Y. Direct oxidative glycosylations with glycal donors. *J. Am. Chem. Soc.* **1998**, *120*, 13515–13516.

2. Schmidt, R.R.; Angerbauer, R. A convenient preparation of 2,3-unsaturated N-galactosyl derivatives. *Carbohydr. Res.* **1979**, *72*, 272–275.

3. Schmidt, R.R.; Angerbauer, R. Simple *de-novo* synthesis of reactive pseudoglycals (hex-2-enopyranosides)—stereospecific α-glycoside coupling. *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 783–784.

4. Bracherro, M.M.; Cabrera, F.E.; Gomez, M.G.; Maria, D.P. Synthesis of 4-(4, 6-di-*O*-benzyl-2, 3-dideoxy-β-D-erythro-hex-2-enopyranosyl)pyrazoles from 3,4,6-tri-*O*-acetyl-D-glucal. *Carbohydr. Res.* **1998**, *308*, 181–190.

5. Kartika, R.; Frein, J.D.; Taylor, R.E. Electrophile-induced ether transfer: stereoselective synthesis of 2,6-disubstituted-3,4-dihydropyrans. *J. Org. Chem.* **2008**, *73*, 5592–5594.

6. Isobe, M.; Ichikawa, Y.; Funabashi, Y.; Mio, S.; Goto, T. Acyclic stereocontrol by heteroconjugate addition—4: anti-diastereoselection by a β-chelation effect. *Tetrahedron* **1986**, *42*, 2863–2866.

7. Neyts, J.; Clercq, E.D.; Singha, R. Structure-activity relationship of new anti-hepatitis C virus agents: heterobicycle-coumarin conjugates. *J. Med. Chem.* **2009**, *52*, 1486–1490.

8. Fernandes, A.; DellOlmo, M.A. Dramatic effect of PSE clamping on the behavior of D-glucal under Ferrier I conditions. *Tetrahedron Lett.* **2008**, *49*, 3484–3488.

9. Gordon, D.M.; Danishefskys, S.J. Ritter-like reactions of 1,2-anhydropyranose derivatives. *J. Org. Chem.* **1991**, *56*, 3713–3715.

10. Ernst, C.; Klaffke, W. Chemical synthesis of uridine diphospho-D-xylose and UDP-L-arabinose. *J. Org. Chem.* **2003**, *68*, 5780–5783.

11. Tanmaya, P. Vinyl sulfone-modified carbohydrates: an inconspicuous group of chiral building blocks. *Tetrahedron* **2008**, *64*, 3605–3628.

12. Ferrier, R.J.; Prasad, N. Unsaturated carbohydrates. IX. Synthesis of 2, 3-dideoxy-α-D-erythro-hex-2-enopyranosides from tri-*O*-acetyl-D-glucal. *J. Chem. Soc. C.* **1969**, 570–575.

13. Gõmez, A.M.; Lobo, F.; Uriel, C.; Lõpez, J.C. Recent developments in the Ferrier rearrangement. *Eur. J. Org. Chem.* **2013**, *32*, 7221–7262.

14. Lopez, J.C. *n*-Pentenyl esters facilitate an oxidative alternative to the Ferrier rearrangement. An expeditious route to sucrose. *J. Chem. Soc. Chem. Commun.* **1992**, *2*, 94–96.

15. Toshima, K.; Ishizuka, T.; Matsuo, G., Nakana, M. Allyl C-glycosidations of totally unprotected glycals and allyltrimethylsilane with trimethylsilyl trifluoromethanesulfoante (TMSOTf). *Tetrahedron Lett*. **1994**, *35*, 5673–5676.

16. Koreeda, M.; Shull, T.A.; Lemke, E.B.K.; Tuinman, R.J. Iodine-catalyzed Ferrier reaction. 1. A mild and highly versatile glycosidation of hydroxyl and phenolic groups. *Synlett* **1995**, *1*, 90–92.

17. Yadav, J.S.; Reddy, B.; Subba, V.; Murthy, C.V.S.R.; Kumar, G.M. Scandium triflate catalyzed Ferrier rearrangement: an efficient synthesis of 2,3-unsaturated glycopyranosides. *Synlett* **2000**, *10*, 1450–1451.

18. Babu, B.S.; Balsubramanian, K.K. Indium trichloride-catalyzed glycosylation. An expeditious synthesis of 2,3-unsaturated glycopyranosides. *Tetrahedron Lett.* **2000**, *41*, 1271–1274.

19. Takhi, M.; Abdel Rahman, A.A.H.; Schmidt, R.R. Yb(OTf)3-catalyzed C-glycosylation: highly stereoselective synthesis of C-pseudoglycals. *Tetrahedron Lett.* **2001**, *42*, 4053–4056.

20. Swamy, N.R.; Venkateswarlu, Y. An efficient method for the synthesis of 2,3-unsaturated glycopyranosides catalyzed by bismuth trichloride in Ferrier rearrangement. *Synthesis* **2002**, 598–600.

21. Yadav, J.S.; Reddy, B.V.; Reddy, J.S. Dy(OTf)3-immobilized in ionic liquids: a novel and recyclable reaction media for the synthesis of 2,3-unsaturated glycopyranosides. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 2390–2394.

22. Bettadaiah, B.K.; Srinnivas, P. ZnCl2-catalyzed Ferrier reaction; synthesis of 2,3-unsaturated-*O*-glucopyranosides of allylic, benzylic and tertiary alcohols. *Tetrahedron Lett.* **2003**, *44*, 7257–7259.

23. Agarwal, A.; Rani, S.; Vankar, Y.D. Protic acid ($HClO_4$ supported on silica gel)-mediated synthesis of 2,3-unsaturated-O-glucosides and a chiral furan diol from 2,3-glycals. *J. Org. Chem.* **2004**, *69*, 6137–6140.

24. Hotha, S.; Tripathi, A. Niobium(V) chloride catalyzed microwave assisted synthesis of 2,3-unsaturated *O*-glycosides by the Ferrier reaction. *Tetrahedron Lett.* **2005**, *46*, 4555–4558.

25. Procopio, A.; Dalpozzo, R.; Nino, A.D.; Maiuolo, L.; Nardi, M.; Oliverio, M.; Russo, B. A facile $Er(OTf)_3$-catalyzed synthesis of 2,3-unsaturated O- and S-glycosides. *Carbohydr Res.* **2007**, *342*, 2125–2131.

26. Pasunooti, K.K.; Leow, M.L.; Vedachalam, S.; Gorityala, B.K.; Liu, X.W. A general and mild copper-catalyzed three-component synthesis of protected homoallyl amines. *Tetrahedron Lett.* **2009**, *50*, 2979–2981.

27. Zhou, J.F.; Chen, X.; Wang, Q.B.; Zhang, B.; Zhang, J.B. H_2SO_4-SiO_2: highly efficient and novel catalyst for the Ferrier-type glycosylation. *Chin. Chem. Lett.* **2010**, *21*, 922–926.

28. Kinfe, H.H.; Mebrahtu, F.M.; Sithole, K. NaHSO4 supported on silica gel: an alternative catalyst for Ferrier rearrangement of glycals. *Carbohydr. Res.* **2011**, *346*, 2528–2532.

29. Chen, P.R.; Wang, S.S. CF_3SO_3H-SiO_2 as catalyst for Ferrier rearrangement: an efficient procedure for the synthesis of pseudoglycosides. *Tetrahedron* **2013**, *69*, 583–586.

30. Enthaler, S.; Junge, K.; Beller, M. Sustainable metal catalysis with iron: from rust to a rising star? *Angew. Chem. Int. Ed.* **2008**, *47*, 3317–3321.

31. Jose, C.A.; Antonio, L.P.; Avelino, C. Iron-catalyzed Markovnikov hydrothiolation of styrenes. *Adv. Synth. Catal.* **2012**, *354*, 678–687.

32. Masson, C.; Soto, J.; Bessodes, M. Ferric chloride: a new and very efficient catalyst for the Ferrier glycosylation reaction *Synlett*. **2000**, *9*, 1281–1282.

33. Zhang, G.S.; Liu, Q.F.; Shi, L.; Wang, J. Ferric sulfate hydrate-catalyzed O-glycosylation using glycals with or without microwave irradiation. *Tetrahedron* **2008**, *64*, 339–342.

34. Tilve, R.D.; Alexander, M.V.; Khandekar, A.C. Synthesis of 2,3-unsaturated glycopyranosides by Ferrier rearrangement in $FeCl_3$ based ionic liquid. *J. Mol. Catal. A: Chem.* **2004**, *223*, 237–240.

35. Chen, P.R.; Wang, S.S. Iron(III) triflate, a new efficient catalyst for type I Ferrier rearrangement. *Tetrahedron* **2012**, *68*, 5356–5362.

36. Zhou, J.; Zhang, B.; Yang, G.; Chen, X.; Wang, Q.; Wang, Z.; Zhang, J. A facile H_2SO_4/4 Å molecular sieves catalyzed synthesis of 2, 3-unsaturated *O*-glycosides via Ferrier-type rearrangement. *Synlett* **2010**, *6*, 893–896.

37. Calleja, G.; Melero, J.A.; Martinez, F.; Molina, R. Activity and resistance of iron containing amorphous, zeolitic and mesostructured materials for wet peroxide oxidation of phenol. *Water Res.* **2005**, *39*, 1741–1750.

38. (a). Ramirez, J.H.; Maldonado-Hodar, F.J.; Perez-Cadenas, A.F. Azo-dye orange II degradation by heterogeneous Fenton-like reaction using carbon–Fe catalysts. *Appl. Catal. B: Environ.* **2007**, *75*, 312–323. (b) . Rodríguez, A.; Ovejero, G.; Sotelo, J.L.; Mestanza, M.; Garcí, J. Heterogeneous Fenton catalyst supports screening for mono azo dye degradation in contaminated wastewaters. *Ind. Eng. Chem. Res.* **2010**, *49*, 498–505. (c) Fontecha-Cámara, M.A.; Álvarez-Merino, M.A.; Carrasco-Marín, F.; López-Ramón, M.V.; Moreno-Castilla, C. Heterogeneous and homogeneous Fenton processes using activated carbon for the removal of the herbicide amitrole from water. *Appl. Catal. B: Environ.* **2011**, *101*, 425–430. (d) He, L.; Du, G.; Gao, J.; Wang, X. Synthesis of tributyl citrate catalyzed by active carbon supported solid acid. *Chem. Res. Appli.* **2013**, *25*, 1628–1631.

39. See the Supporting Information for the details.

40. Balamurugan, R.; Koppolu, S.R. Scope of $AuCl_3$ in the activation of per-*O*-acetylglycals. *Tetrahedron* **2009**, *65*, 8139–8142.

41. Shanmugsundaram, B.; Bose, A.K.; Balasubramanian, K.K. Microwave-induced, montmorillonite K10-catalyzed Ferrier rearrangement of tri-*O*-acetyl-D-galactal: mild, eco-friendly, rapid glycosidation with allylic rearrangement. *Tetrahedron Lett*. **2002**, *43*, 6795–6798.

42. Du, W.; Hu, Y. Microwave-enhanced Ferrier reaction: a facile synthesis of 2,3-unsaturated-*O*-glycosides under solvent-free conditions. *Synth. Commun.* **2006**, *36*, 2035–2046.

43. Misra, A.K.; Tiwari, P.; Agnihotri, G. Ferrier rearrangement catalyzed by $HClO_4$-SiO_2: synthesis of 2, 3-unsaturated glycopyranosides. *Synthesis* **2005**, 260–266.

44. Erich, K.R.; Masata, K. PCT. *Int. Appl.* WO9301821, **1993**.

45. Kuroda, M.; Mimaki, Y.; Sashida, Y.; Hirano, T.; Oka, K.; Dobashi, A.; Li, H.; Harada, N. Novel cholestane glycosides from the bulbs of *Ornithogalum saundersiae* and their cytostatic activity on leukemia HL-60 and MOLT-4 cells. *Tetrahedron* **1997**, *53*, 11549–11562.

46. XRD experiments were attempted to characterize our catalyst but failed with the low dosage of Ferric ion in the catalyst. The baking operation was used to remove the ethanol residue in the catalyst; otherwise, it might affect the reaction as a glycosyl acceptor.