Tetrahedron 68 (2012) 5356–5362

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Iron(III) triflate, a new efficient catalyst for Type I Ferrier Rearrangement

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ARTICLE INFO

Article history:
Received 19 March 2012
Received in revised form 23 April 2012
Accepted 28 April 2012
Available online 4 May 2012

Keywords:
Type I Ferrier Rearrangement
Iron(III) triflate
Tri-*O*-acetyl–D-glucal
2,3-Unsaturated-*O*-glycoside

ABSTRACT

By using iron(III) triflate as catalyst, an improved method for the synthesis of 2,3-unsaturated-*O*-glycosides has been established. A series of 2,3-unsaturated-*O*-glucosides were obtained from 2,4,6-tri-*O*-acetyl-D-glucal in good yield and high anomeric selectivity.

1. Introduction

2,3-Unsatureted-*O*-glycosides are useful chiral intermediates in the synthesis of biologically active compounds[1] and functional materials.[2] Type I Ferrier Rearrangement is the most direct and efficient method for preparing 2,3-unsatureted-*O*-glycosides, in which glycals are reacted with nucleophiles under the promotion of various Lewis acid catalysts. This reaction is supposed to proceed through a cyclic allylic oxocarbonium intermediate, which is formed via displacement of the leaving group in the C-3 position of glycal with the promotion of Lewis acid catalyst, followed by the attack of a nucleophile via quasi–equatorial orientation.[3]

Catalysts play a key role in Type I Ferrier Rearrangement. A wide range of Lewis acid catalysts,[4] such as $BF_3 \cdot Et_2O$, $FeCl_3$, $Fe_2(SO_4)_3$, $Fe(NO_3)_3$, $InCl_3$, $BiCl_3$, $CeCl_3$, $ZnCl_2$, $Pd(OAc)_2$, $ZrCl_4$, $K_5CoW_{12}O_{40} \cdot 3H_2O$, $Bi(OTf)_3$, $Er(OTf)_3$, $Yb(OTf)_3$,$TiCl_4$, $AuCl_3$, HBF_4–SiO_2, $ZnCl_2/Al_2O_3$, and other catalysts[5] like I_2, IDCP, NIS, and DDQ have been investigated to promote such glycosidation. However, some of these reaction systems suffered from the disadvantages in terms of large excess of nucleophile, stoichiometric amounts of catalyst, harsh reaction conditions, which lead to extensive work up. Therefore, there still is of interest to find new efficient catalyst for milder and more efficient synthetic process with good anomeric selectivity by using stoichiometric amount of nucleophile under low catalyst load.

Herein, we report our results using iron(III) triflate as a new efficient catalyst for Type I Ferrier Rearrangement.

2. Results and discussion

2.1. Role of the counter-ion in the iron(III) catalysts

Use of iron(III) chloride, iron(III) sulfate, and iron(III) nitrate has been reported in Type I Ferrier Rearrangement as economic and eco-friendly catalyst.[4r–t] For comparison of the catalytic activity of different iron(III) catalysts, we carried out a comparative study by using tri-*O*-acetyl –D-glucal (**1**) and EtOH as the nucleophile in a model system catalyzed by different iron(III) Lewis acid catalysts. Results are shown in Table 1.

Results shown in Table 1 demonstrate the remarkably different catalytic activity of the iron(III) catalysts with various counter-ions in this reaction. Among the observed iron(III) catalysts, iron(III) triflate is the most efficient one in terms of conversion and selectivity. Although all of hydrochloric acid, sulfuric acid, nitric acid, and triflic acid belong to strong acid, triflate acid is the strongest one, causing the iron (III) in $Fe(OTf)_3$ more active in attracting the leaving group to form the intermediate allyloxycarbenium ion (Scheme 1):

2.2. Optimization of solvent

Solvent also has influence on the reaction outcomes. Therefore, optimization has been carried out. Table 2 shows the results.

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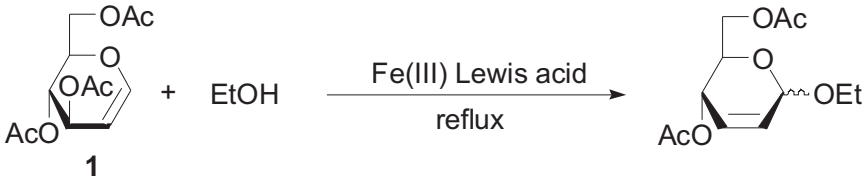
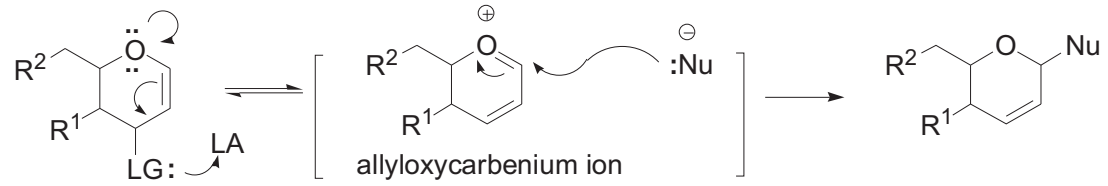
doi:10.1016/j.tet.2012.04.115

Table 1
A comparative study of the catalytic effect of different iron(III) Lewis acid catalysts in the Ferrier Rearrangement of glucal **1**[a]



Entry	Lewis acid catalyst	Reaction time	Conversion(%)[b]	α:β[c]
1	$FeCl_3$	120 min	31	5:1
2	$Fe_2(SO_4)_3$	120 min	Trace	/
3	$Fe(NO_3)_3$	120 min	41	9:1
4	**Fe(OTf)$_3$**	**30 min**	**88**	**10:1**

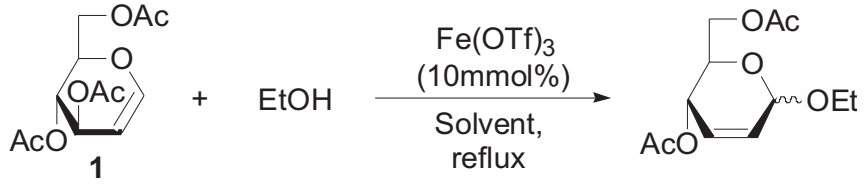
[a] Reaction conditions: tri-*O*-acetyl–D-glucal (**1**) (150 mg, 0.56 mmol), EtOH(5 mL), catalyst(10 mol %), reflux.
[b] Determined by analysis of the ^{1}H NMR spectra of the reaction mixture.
[c] The anomeric ratio was determined by integration of the anomeric hydrogen in the ^{1}H NMR spectra.



LG = leaving group
LA = Lewis acid catalyst

Scheme 1. Mechanism of Type I Ferrier Rearrangement proposed by R. J. Ferrier.[6]

Table 2
Optimization of solvent[a]



Entry	Solvent	Reaction time	Conversion(%)[b]	α:β[c]
1	Acetone	1 h	23	10:1
2	Acetonitrile	1 h	52	10:3
3	**DCM**	**30 min**	**88**	**10:1**
4	THF	1 h	45	5:2
5	Diethyl ether	1 h	NR	/
6	Toluene	1 h	Decomposed	/

[a] Reaction conditions: tri-*O*-acetyl–D-glucal (**1**) (150 mg, 0.56 mmol), EtOH(1.2 equiv), $Fe(OTf)_3$ (10 mol %), solvent (20 mL), reflux.
[b] Determined by analysis of the ^{1}H NMR spectra of the reaction mixture.
[c] The anomeric ratio was determined by integration of the anomeric hydrogen in the ^{1}H NMR spectra.

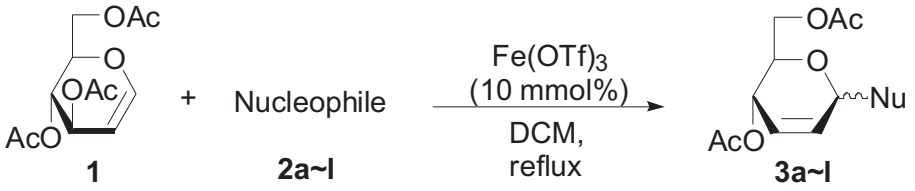
By comparison of the results in entry 3 with the others in Table 2, DCM appeared to be the most proper solvent. Decomposition of substrate might be caused by solvents with high boiling point, such as toluene(entry 6, Table 2). The solvent with high hydrophilic character, such as acetone, MeCN or THF gave lower conversion (entry 1,2, and 4, Table 2).

2.3. Type I Ferrier Rearrangement under the optimized conditions

After the optimization, we have established our reaction conditions: with iron(III) triflate (10 mol %) as the catalyst and DCM as the solvent, Ferrier Rearrangement was performed between tri-*O*-acetyl–D-glucal(**1**) (1 equiv) and various nucleophiles (1.2 equiv) at about 50 °C. Results were summarized in Table 3. The structure and stereochemistry of all the glycosidation products were characterized by ^{1}H NMR, ^{13}C NMR, IR, and MS data.

Generally, the reaction afforded 2,3-unsaturated *O*-glycosides in high yield with good anomeric selectivity. The simple aliphatic alcohols (entries 1, 2, 4, 8, Table 3) as the nucleophile gave the products with lower selectivity on the anomeric center, while those with higher steric hindrance (entries 3, 5, 6, and 7, Table 3) gave the products, which are good both in yield and in anomeric selectivity. In the series of benzylic alcohols (entries 9～13, Table 3), most of the nucleophiles gave satisfactory reaction outcomes, even the relatively weak nucleophile α-trifluoromethyl benzylic alcohol

Table 3
Glycosidation of 3,4,6-tri-*O*-acetyl-D-glucal **1** catalyzed by $Fe(OTf)_3$[a]



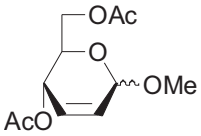
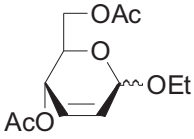
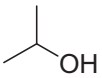
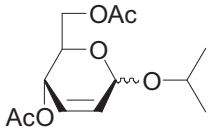
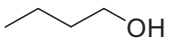
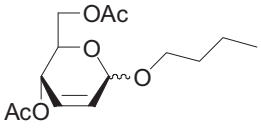
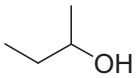
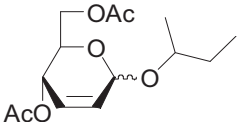
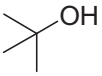
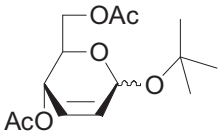
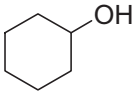
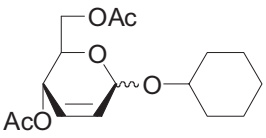
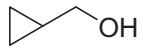
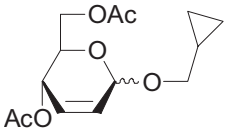
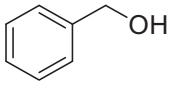
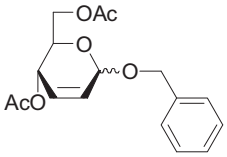
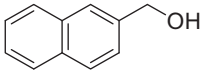
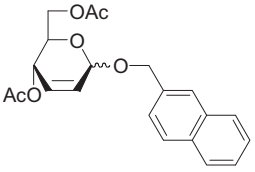
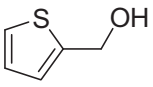
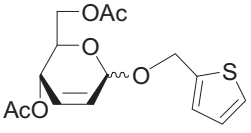
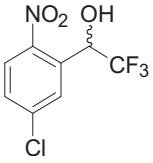
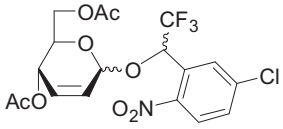
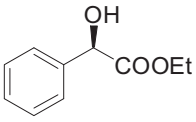
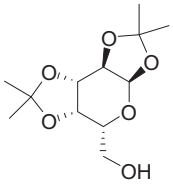
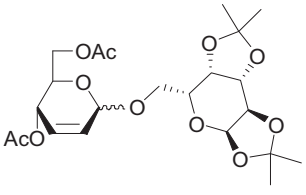
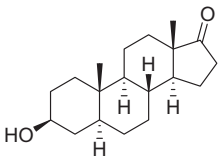
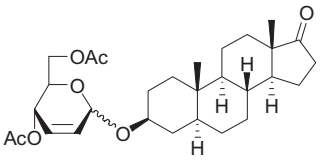
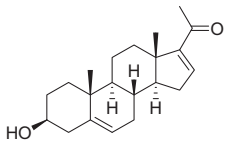
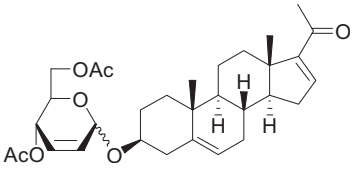
Entry	Nucleophile	Reaction time	Product	Yield(%)[b]	(α:β)[c]
1	MeOH **2a**	25 min	 **3a**	87	10:3
2	EtOH **2b**	30 min	 **3b**	88	10:1
3	 **2c**	30 min	 **3c**	83	α only
4	 **2d**	35 min	 **3d**	78	10:1
5	 **2e**	30 min	 **3e**	83	10:1
6	 **2f**	3 h	 **3f**	80	α only
7	 **2g**	30 min	 **3g**	85	20:1

Table 3 (*continued*)

Entry	Nucleophile	Reaction time	Product	Yield(%)[b]	(α:β)[c]
8	 **2h**	35 min	 **3h**	87	α only
9	 **2i**	45 min	 **3i**	87	α only
10	 **2j**	3.5 h	 **3j**	89	α only
11	 **2k**	6 h	 **3k**	86	α only
12	 **2l**	50 min	 **3l**	76	α only
13	 **2m**	2 h	No reaction	/	/
14	 **2n**	24 h	 **3n**	73	8:1
15	 **2o**	60 min	 **3o**	78	9:1

(*continued on next page*)

Table 3 (*continued*)

Entry	Nucleophile	Reaction time	Product	Yield(%)[b]	(α:β)[c]
16	 **2p**	75 min	 **3p**	75	α only

[a] Reaction conditions: tri-*O*-acetyl–D-glucal (**1**) (150 mg, 0.56 mmol), nucleophile (1.2 equiv), $Fe(OTf)_3$ (10 mol %), DCM (5 mL), reflux.
[b] Isolated yield.
[c] The anomeric ratio was determined by integration of the anomeric hydrogen in the ^1H NMR spectra.

(entry 12, Table 3) could also give the corresponding 2,3-unsaturated *O*-glycoside in high yield and good anomeric selectivity. However, no reaction occurred when ethyl mandelic acid ester was used as the nucleophile. This might be attributed to that a five-membered ring chelation structure was formed between iron(III) ion and the carbonyl group and the hydroxyl group in ethyl mandelic acid ester (Fig. 1), which led to inactivation of the catalyst.

Formation of a disaccharide (Entry 14, Table 3) and two steroid glycosides (Entry 15 and 16, Table 3) in high yield and good selectivety demonstrated the catalytic capability of iron(III) triflate in the synthesis of natural product analogs of biological interest by the Ferrier Rearrangement.

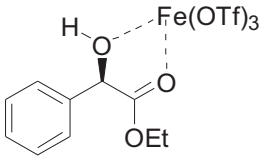


Fig. 1. The proposed chelation between iron(III) triflate and ethyl mandelic acid ester.

3. Conclusion

We have demonstrated that iron(III) triflate was a new efficient catalyst for Type I Ferrier Rearrangement. By use of this catalyst, a series of alcohols was reacted with glucal donor affording 2,3-unsaturated *O*-glycosides in high yield and good anomeric selectivity under mild conditions.

4. Experimental

4.1. Method and materials

^1H and ^{13}C NMR spectra were recorded on a Bruker AV-400 (400 MHz) spectrometer with Me_4Si as an internal standard. ^{19}F NMR spectra were obtained on a Bruker AM-300(282 MHz) spectrometer using $CFCl_3$ as an external standard.; downfield shifts being designated as positive, all chemical shifts (δ) were expressed in parts per million and coupling constants (J) are in Hertz. Mass spectra were recorded on a Finnigan MAT 8430 instrument using EI ionization at 70 eV. High-Resolution mass spectral (ESI) analyses were performed on a Finnigan MAT 8430 spectrometer. IR spectra were recorded on a Nicolet 380 spectrometer. Optical rotations were measured by WZZ-2 polarimeter. Melting points were measured on a WRS-2A melting point apparatus. Glucal was purchased from Energy-Chemical Company. 1-Trifluoromethyl-1-(2-nitro-5-chlorobenzyl) alcohol was given by Lei Yu in courtesy. Other reagents were used as purchased from commercial suppliers without further purification. All the solvents used in the reaction were purified by re-distillation.

4.2. General procedure for preparation of 2,3-unsaturated *O*-glycosides

To a stirred solution of tri-*O*-acetyl-D-glucal (136 mg, 0.5 mmol) in DCM (5 mL) were added the corresponding alcohol (1.2 equiv) and iron(III) triflate (10 mol %) at ambient temperature. The reaction mixture was refluxed and the extent of the reaction was monitored by TLC analysis. The reaction mixture was diluted with cooled sodium bicarbonate (satd, 20 mL) and extracted with DCM (3×10 mL). The combined organics were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum. All the products were purified by silica gel column chromatography (hexane/EtOAc=6/1).

*4.2.1. Methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3a**).* Colorless oil; $[\alpha]_D^{25}$=+135 (*c* 0.72, $CHCl_3$, α:β=10:3) {lit.:[5e] $[\alpha]_D^{31.7}$=+124 (*c* 1.2, MeOH α:β=7:3)}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.07(s, 3H), 2.09(s, 3H), 3.44(s, 3H), 4.03–4.08(m, 1H), 4.19–4.27(m, 2H), 4.92(s, 1H), 5.03 (d, J=1.4 Hz, 0.3H, β-anomer), 5.29–5.32(dd, J=9.7, 1.4 Hz, 1H, α-anomer),5.80–5.96(m, 2H) ppm; IR (film, cm^{-1}):3053, 2954, 2908, 1743, 1440, 1371, 1232, 1189, 1105, 1046; MS(ESI) *m*/*z*: 511.1 ($[2M+Na]^+$, 10), 267.1($[M+Na]^+$, 100), 213.1(23), 153.1(10).

*4.2.2. Ethyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3b**).* Colorless oil; $[\alpha]_D^{25}$=+142 (*c* 0.52, CHCl3, α:β=10:1) {lit.:[4k] $[\alpha]_D^{31.7}$=+113.1 (*c* 1.0, CHCl3 α:β=9:1)}; ^1H NMR (400 MHz, CDCl3): δ1.25 (t, J=7.1 Hz, 3H), 2.07(s,3H), 2.09(s,3H), 3.54–3.61(m,1H), 3.81–3.85(m,1H), 4.12 (d, J=8.5 Hz, 1H), 4.16–4.27 (m, 2H), 5.04 (s,1H), 5.31 (d, J=9.6 Hz, 1H), 5.82–5.94(m, 2H) ppm; IR (film, cm^{-1}):3043, 2974, 2847, 1743, 1442, 1370, 1229, 1107, 1048; MS(EI 70 eV) *m*/*z*: 257(M^+-1), 213(8), 156(17), 153(10), 114(100), 111(21), 86(10), 43(29).

*4.2.3. Isopropyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3c**).* Colorless oil; $[\alpha]_D^{25}$=+158 (*c* 0.64, CHCl3, α:β=20:3) {lit.:[4k] $[\alpha]_D^{31.7}$=+115.3 (*c* 1.0, CHCl3 α:β=7:3)}; ^1H NMR (400 MHz, CDCl3) : δ 1.19(d, J=6.2 Hz, 3H), 1.26(d, J=6.2 Hz, 3H), 2.09(s,3H), 2.10(s,3H), 3.95–4.03(m,1H), 4.14–4.22(m,3H), 5.14(s,1H), 5.31(dd, J=9.6, 1.5 Hz, 1H), 5.79–5.89(m,2H) ppm; IR (film, cm^{-1}):3043, 2971, 2921, 1744, 1449, 1376, 1317, 1238, 1119, 1035, 732, 609, 418; MS(EI 70 eV) *m*/*z*: 271(M^+-1), 213(9), 170(20), 153(16), 128(85), 111(42), 86(72), 81(9), 57(10), 43(100), 41(8).

*4.2.4. n-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3d**).* Colorless oil; $[\alpha]_D^{25}$=+153 (*c* 0.63, CHCl3,

α:β=100:9) {lit.:[4k] $[\alpha]_D^{31.7}$=+115.3 (*c* 1.0, CHCl3, α:β=7:3)}; ^{1}H NMR (400 MHz, CDCl3) : δ 0.96(t, *J*=7.3 Hz, 3H), 1.38–1.44(m, 2H), 1.57–1.62(m, 2H), 2.09(s, 3H), 2.11(s, 3H), 3.50–3.56(m, 1H), 3.77–3.88(m, 1H), 4.10–4.14(m,1H), 4.17–4.28(m,2H), 5.04(s,1H), 5.32(d, *J*=9.6.1H), 5.83–5.96(m,2H) ppm; IR (film, cm^{-1}):3043, 2974, 2847, 1743, 1442, 1370, 1229, 1107, 1048, 980, 906, 726, 596, 489; MS(ESI) *m/z*: 595.2 ([2M+Na]$^+$,10), 309.1 ([M+Na]$^+$,100), 213.1(23),153.1(8).

*4.2.5. sec-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3e**).* Colorless oil; $[\alpha]_D^{25}$=+134 (*c* 0.63, CHCl3, α:β=10:1) {lit.:[7e] (α:β=11:1)}; ^{1}H NMR (400 MHz, CDCl3) : δ 0.93(dt, *J*=18.9, 7.4 Hz, 3H), 1.15(d, *J*=6.2 Hz, 2H), 1.25(d, *J*=6.3 Hz, 1H), 1.47–1.59(m,2H), 2.09(s, 3H), 2.10(s, 3H), 3.70–3.80(m, 1H), 4.16–4.23(m, 3H), 5.13(dd,*J*=4.0,2.9 Hz, 1H), 5.30(dd, *J*=9.6,1.4 Hz, 1H), 5.78–5.86(m, 2H) ppm; IR (film, cm^{-1}):3053, 2956, 2880, 1745, 1452, 1373, 1233, 1102, 1042, 901, 730; MS(ESI) *m/z*: 595.2([2M+Na]$^+$, 8), 309.1([M+Na]$^+$, 100), 213.1(20), 153.1(10).

*4.2.6. tert-Butyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3f**).* Colorless oil; $[\alpha]_D^{25}$=+126 (*c* 0.72, CHCl3, α only) {lit.:[7c] $[\alpha]_D^{25}$=+100.69(*c* 0.75, CHCl3)}; ^{1}H NMR (400 MHz, CDCl3) : δ 1.28(s, 9H), 2.06(s, 3H), 2.07(s, 3H), 4.12–4.24(m,3H), 5.25 (dd,*J*=9.0, 1.3 Hz, 1H), 5.31 (d, *J*=2.1 Hz, 1H), 5.71–5.84(m, 2H) ppm; IR (film, cm^{-1}):3051, 2975, 2722, 1746, 1436, 1369, 1195, 1099, 1043, 982, 892, 774; MS(ESI) *m/z*: 595.2([2M+Na]$^+$,8),309.1 ([M+Na]$^+$,100), 213.1(30), 153.1(15).

*4.2.7. Cyclohexyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3g**).* Colorless oil; $[\alpha]_D^{25}$=+162 (*c* 0.58, $CHCl_3$, α:β=20:1) {lit.:[4k] $[\alpha]_D^{31.7}$=+110.7 (*c* 1.0, $CHCl_3$ α:β=9:1)}; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 1.11–1.20(m, 5H), 1.46–1.49(m, 1H), 1.67–1.71(m, 2H), 1.81–1.90(m, 2H), 2.01(s, 3H), 2.02(s, 3H), 3.54–3.60(m, 1H), 4.11–4.18(m, 3H), 5.10(s, 1H), 5.21(dd, *J*=9.2, 1.5 Hz, 1H), 5.73–5.81(m, 2H) ppm; IR (film, cm^{-1}):3055, 2934, 2857, 1744, 1450, 1371, 1233, 1101, 1036, 742, 606; MS(EI 70 eV) *m/z*: 313(M$^+$+1), 213(24), 210(16), 168(23), 153(36), 128(27), 111(73), 86(58), 55(28), 43(100), 41(15).

*4.2.8. Cyclopropylmethyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3h**).* Colorless oil; $[\alpha]_D^{25}$=+144 (*c* 0.67, CHCl3, α:β=5:1) {lit.:[7a] $[\alpha]_D^{25}$=+105.6 (*c* 1.45, CHCl3 α:β=7:1)}; ^{1}H NMR (400 MHz, CDCl3) : δ 0.28–0.15 (m, 2H), 0.53–0.57(m, 2H), 1.07–1.12(m, 1H), 2.08(s, 6H), 3.41–3.53(m, 2H), 4.11–4.18(m, 3H), 5.07(s, 1H), 5.30 (d, *J*=9.6 Hz, 1H), 5.83–5.96(m, 2H) ppm; IR (film, cm^{-1}):3078, 2945, 1744, 1437, 1374, 1230, 1094, 1040, 967, 906, 830, 730, 677; MS(ESI) *m/z* :307.1([M+Na]$^+$,100) 213.1(20), 153.1(8).

*4.2.9. Benzyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3i**).* Colorless oil; $[\alpha]_D^{25}$=+96 (*c* 0.56, $CHCl_3$, α only) {lit.:[4k] $[\alpha]_D^{31.7}$=+56.34 (*c* 1.0, $CHCl_3$ α:β=9:1)}; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 2.10(s, 3H), 2.11(s, 3H), 4.12–4.32(m, 3H), 4.62 (d, *J*=11.7 Hz, 1H). 4.83 (d, *J*=11.7 Hz, 1H), 5.16 (s, 1H), 5.36 (d, *J*=9.3 Hz, 1H), 6.03–5.85 (m, 2H), 7.35–7.40(m, 5H) ppm; IR (film, cm^{-1}): 3062, 2903, 1746, 1606, 1496, 1453, 1371, 1235, 1186, 1101, 1040, 735, 535, 478; MS(EI 70 eV) *m/z*: 319(M$^+$−1), 213(7), 187(8), 176(9), 153(8), 111(26), 109(8), 94(19), 91(100), 81(8), 65(7), 43(69).

*4.2.10. (2-Naphthyl)-methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3j**).* Colorless solid; Mp 73 °C, $[\alpha]_D^{25}$=+97.5 (*c* 1.6, $CHCl_3$, α only) {lit.:[7b] mp 72 °C,$[\alpha]_D^{23}$=+12(*c* 1.0, $CHCl_3$ α:β=9:1)}; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 2.11(s, 3H), 2.12(s, 3H), 4.17–4.31(m, 3H), 4.79 (d, *J*=11.8 Hz, 1H), 4.99 (d, *J*=11.8 Hz, 1H), 5.21(s, 1H), 5.37 (dd,*J*=9.3, 1.3 Hz, 1H), 5.90–5.95(m, 2H), 7.44–7.58 (m, 3H), 7.84–7.87(m, 4H) ppm; IR (film, cm^{-1}): 3054, 2933, 2876, 1737, 1375, 1236, 1046, 1021, 859, 821, 752; MS(EI 70 eV) *m/z*: 370(M$^+$,3), 237(3), 213(5), 157(3), 143(12), 142(100), 141(84), 140(8), 127(6), 115(15), 111(18), 81(6), 43(41).

*4.2.11. (2-Thienyl)-methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3k**).* Colorless oil; $[\alpha]_D^{25}$=+82 (*c* 0.62, $CHCl_3$, α only); ^{1}H NMR (400 MHz, $CDCl_3$) : δ 2.09 (s, 3H), 2.13 (s, 3H), 4.07–4.35 (m, 3H), 4.82 (d, *J*=12.4 Hz, 1H), 4.93 (d, *J*=12.4 Hz, 1H), 5.17 (s, 1H), 5.35 (d, *J*=9.3 Hz, 1H), 5.87 (dd, *J*=30.4, 10.2 Hz, 2H), 6.94–7.10 (m, 2H), 7.32 (d, *J*=5.0 Hz, 1H) ppm; IR (film, cm^{-1}):3063, 2937, 2358, 1740, 1531, 1446, 1364, 1323, 1228, 1180, 1135, 1094, 1024, 972, 898, 845, 706, 600. ^{13}C NMR (101 MHz, $CDCl_3$) : δ 20.82, 20.96, 53.40, 62.92, 64.35, 66.28, 67.20, 93.07, 126.22, 126.79, 127.03, 127.60, 129.45, 170.25, 170.77 ppm. MS(ESI) *m/z*: 349.0 ([M+Na]$^+$,100), 283.3(34), 213.3 (14); HR-ESI $C_{15}H_{18}O_6SNa$ [M+Na]$^+$ Calcd: 349.0716, Found 349.0719.

*4.2.12. 1-Trifluoromethyl-1-(2-nitro-5-chlorophenyl)-methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3l**).* Pale yellow solid; Mp 52 °C; $[\alpha]_D^{25}$=+115 (*c* 0.41, CHCl3, α only); ^{1}H NMR (400 MHz, CDCl3: δ 2.15(s, 3H), 2.18(s, 3H), 3.57–3.74 (m, 1H), 3.99–4.03(m, 1H), 4.24–4.27(m, 1H), 4.99(s, 1H), 5.33 (dd, *J*=13.1, 4.7 Hz, 1H), 5.82–6.12 (m, 2H), 6.43 (q, *J*=6.1 Hz, 1H), 7.60 (ddd, *J*=8.8, 4.2, 2.3 Hz, 1H), 7.89 (dd, *J*=21.3, 1.9 Hz, 1H), 8.10 (dd, *J*=8.8, 1.6 Hz, 1H) ppm; IR (film, cm^{-1}): 2923, 2851, 2361, 1745, 1575, 1531, 1462, 1370, 1231, 1183, 1140, 1090, 1046, 977, 902, 853, 698; ^{13}C NMR (101 MHz, CDCl3) : δ 20.68, 20.98, 30.99, 62.04, 62.59, 64.74, 64.99, 67.89, 92.50, 125.80, 126.63, 126.95, 129.87, 130.36, 131.21, 140.68, 170.26, 170.93 ppm; ^{19}F NMR(282 MHz, CDCl3): δ: −75.54(d, *J*=6.5 Hz), −75.89(d, *J*=6.3 Hz) ppm; MS(ESI) *m/z*: 490.0([M+Na]$^+$, 100), 213.1(13), 153.1(8); HR-ESI C18H17ClF3NO8Na [M+Na]$^+$ Calcd 490.0493, Found 490.0497.

*4.2.13. 6-O-(4,6-Di-O-acetyl-2,3-dideoxy-α-D-erythreo-hex-2-enopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**3n**).* White solid; Mp 132–134 °C; $[\alpha]_D^{25}$=+9 (*c* 0.75, $CHCl_3$, α:β=8:1), {lit:[7d] mp 137 °C $[\alpha]_D^{25}$=+16.8(*c* 1.0, $CHCl_3$ α:β=5:1)}; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 1.34 (s, 3H), 1.36(s, 3H), 1.45 (s, 3H), 1.54 (s, 3H), 2.09 (s, 3H) 2.12 (s, 3H), 3.73–3.79 (m, 1H), 3.86–3.91 (m, 1H), 4.00–4.04(m, 1H), 4.12–4.18(m, 2H), 4.23–4.34(m, 3H), 4.63 (d, *J*=7.8 Hz, 1H), 5.10(s, 1H), 5.33 (d, *J*=9.8 Hz, 1H), 5.54 (d, *J*=4.9 Hz, 1H), 5.84–5.91 (m, 2H) ppm. IR (film, cm^{-1}): 2998, 2930, 2365, 1742, 1580, 1456, 1377, 1227, 1049, 1003, 967, 892, 677; MS(ESI) *m/z*: 495.0 ([M+Na]$^+$,100); 256.0(10).

*4.2.14. Epiandrosteronyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3o**).* White solid; Mp 124–126 °C; $[\alpha]_D^{25}$=+105 (*c* 0.53, $CHCl_3$, α:β=9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.69 (dd, *J*=16.3, 6.0 Hz, 1H), 0.84(s, 3H), 0.87(s, 3H), 0.94–1.92 (m, 20H), 2.09 (s, 3H), 5.21(s, 1H), 2.11 (s, 3H), 2.45 (dd, *J*=19.2, 8.8 Hz, 1H), 3.83–3.51 (m, 1H), 4.31–4.10 (m, 3H), 5.18 (s, 1H), 5.32 (d, *J*=9.6 Hz, 1H), 5.98–5.73 (m, 2H) ppm; IR (film, cm^{-1}): 2934, 2855, 1743, 1635, 1454, 1374, 1232, 1035, 910, 829, 744, 653; ^{13}C NMR (101 MHz, $CDCl_3$): δ 12.23, 13.82, 20.48, 20.83, 20.99, 21.78, 28.09, 28.55, 30.91, 30.94, 31.55, 35.05, 35.75, 35.85, 36.26, 36.92, 45.11, 47.80, 51.40, 54.45, 63.19, 65.35, 66.77, 77.77, 93.07, 128.42, 128.86, 170.33, 170.81 ppm; MS(ESI) *m/z*: 525.1 ([M+Na]$^+$,100), 212.9(10); HR-ESI $C_{29}H_{42}O_7Na$ [M+Na]$^+$ Calcd 525.2828, found 525.2823.

*4.2.15. 16-Dehydropregnenolonyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3p**).* White solid; Mp 70–72 °C; $[\alpha]_D^{25}$=+174 (*c* 0.6, CHCl3, α only); ^{1}H NMR (400 MHz, CDCl3) : δ 0.92 (s, 3H), 0.99–1.08(m, 5H), 1.24–2.06(m, 12H), 2.08 (s, 3H), 2.10 (s, 3H), 2.26 (s, 3H), 2.37 (dd, *J*=25.4, 11.5 Hz, 3H), 3.56 (dd, *J*=13.5, 8.6 Hz, 1H), 4.18–4.27(m, 3H), 5.18(s, 1H), 5.30 (d, *J*=9.3 Hz, 1H), 5.37 (s, 1H), 5.85 (dd, *J*=23.2, 10.4 Hz, 2H), 6.71 (s, 1H) ppm; IR (film, cm^{-1}): 3043,2939, 2859, 1745, 1666, 1576, 1442, 1372, 1232,

1037, 963, 906, 747, 661; ^{13}C NMR (400 MHz, CDCl3): δ: 15.71, 19.23, 20.82, 27.12, 28.22, 30.18, 30.89, 31.56, 32.23, 34.63, 36.87, 37.02, 40.44, 46.09, 50.51, 56.41, 63.19, 65.40, 66.84, 78.14, 92.87, 121.19, 128.42, 128.40, 128.88, 141.39, 144.34, 155.38, 170.30, 170.79, 196.77 ppm. MS(ESI) *m*/*z*: 549.1 ([M+Na]$^+$,100), 212.9(10). HR-ESI C31H42O7Na [M+Na]$^+$ Calcd 549.2828, found 549.2823.

Acknowledgements

This work is financially supported by a grant of The Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, CAS and The Fundamental Research Funds for the Central Universities (11D10508).

Supplementary data

Supplementary data include **^{1}H NMR**, **^{19}F NMR** spectra, of all the products; **^{13}C NMR**, **HRMS** of the new compounds. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2012.04.115.

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