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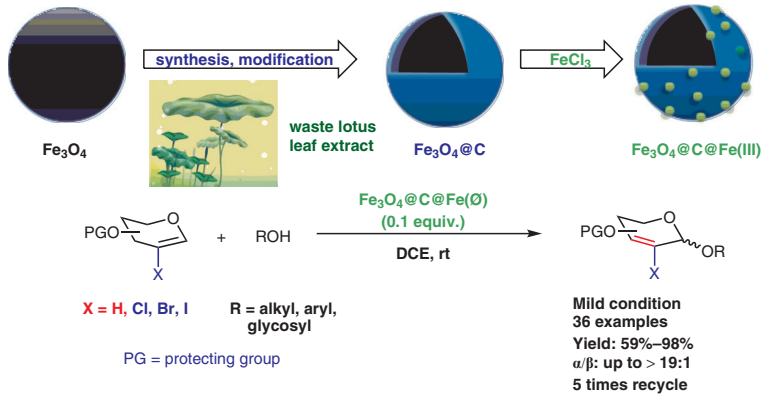
A Highly Efficient Magnetic Iron(III) Nanocatalyst for Ferrier Rearrangements

Youxian Dong
Zekun Ding
Hong Guo
Le Zhou
Nan Jiang
Heshan Chen
Saifeng Qiu
Xiaoxia Xu
Jianbo Zhang*

School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, P. R. of China
jbzhang@chem.ecnu.edu.cn



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Abstract A novel and highly efficient magnetic Fe_3O_4@C@Fe(III) core–shell catalyst, in which the carbon shell was prepared from lotus leaf, was fabricated. This nanocatalyst was successfully applied in the synthesis of a series of 2,3-unsaturated *O*-glycosides in excellent yields and with high selectivity, especially in the case of 2-halo *O*-glycosides, which differ in reactivity from nonsubstituted *O*-glycosides, but which have scarcely been explored before. Moreover, the catalyst could be easily separated from the reaction by the application of an external magnetic force and reused a minimum of five times without any significant decrease in the yields of the products. In addition, the reaction proceeded readily on a gram scale, which provides a bright prospect for future applications.

Key words nanocatalyst, Ferrier rearrangement, haloglucals, iron catalysis, catalyst recycling, magnetic catalyst

Glycoconjugates are involved in many biological processes such as cell–cell communication, cell development, viral infection, inflammation, and the immune response. Consequently, they have become a focus theme in biochemistry and synthetic targets for pharmaceutical studies.[1–9] Among the various reactions available for the synthesis of glycoconjugates, the Ferrier rearrangement is an important reaction for the synthesis of 2,3-unsaturated glycosides.[10] The products of this transformation are versatile chiral intermediates for the synthesis of a variety of important biologically active compounds and natural products.[11–19] For instance, the 2,3-unsaturated sugar derivatives of 5-(hydroxymethyl)furfural showed excellent antitumor activities in our previous research, highlighting the significance of exploring more-efficient method for the synthesis of 2,3-unsaturated glycosides.[20] A wide range of reagents have been used to promote this reaction, including Bronsted acids, Lewis acids, oxidants, etc.[14,21–27] Although many methods for performing Ferrier rearrangements have been described in recent decades, most have involved Lewis acids as catalysts; these are difficult to use in mass production because they contain rare and expensive elements or are not easily prepared. Consequently, the development of a green and efficient strategy for the synthesis of 2,3-unsaturated glycosides remains as a challenge.

Compared with common catalysts, most ferric salts are harmless and inexpensive. In particular, ferric chloride has been widely used in a variety of organic reactions because of its superior and unique catalytic properties under extremely mild conditions; however, its characteristic moisture absorption limits its further application.[28–34] In recent years, our group has introduced immobilized ferric catalysts such as $FeCl_3{\cdot}6H_2O$/C and $FeCl_3$/C into glycosylation reactions, thereby reducing the catalyst cost and overcoming the problem of moisture absorption.[24–27,35] However, the posttreatment separation and recycling performance of solid-acid catalysts require further improvements. For this reason, we recently reported a magnetic core–shell nanomaterial, Fe_3O_4@C@SO_3H, as novel Bronsted acid catalyst, and we successfully employed it in a Ferrier rearrangement, thereby solving the problems of isolation and recycling.[28,36] Nevertheless, there is still scope for improving the Fe_3O_4@C@SO_3H catalyst, because it requires a reaction temperature of 80 °C, which may be incompatible with some heat-sensitive acceptors or donors. In our continuing search for greener and more widely applicable catalysts for the Ferrier rearrangement, we decided to fabricate a magnetic Fe_3O_4@C@Fe(III) catalyst, the immobilized ferric ion of

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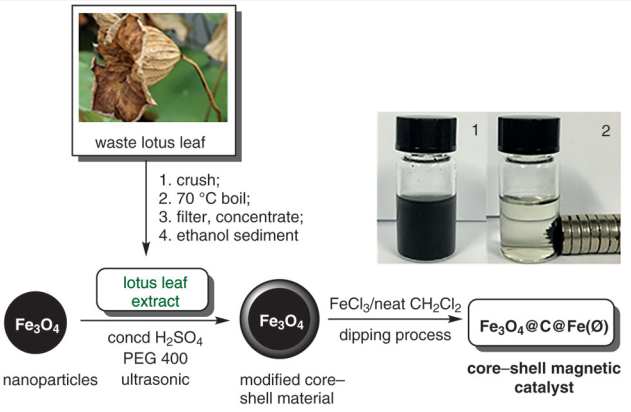
which should readily catalyze the Ferrier reaction under mild conditions. However, previous work on the immobilization of metal Lewis acids on core–shell materials is relatively scarce because difficulties in binding metal ions firmly to a carbon shell can lead to poor recycling performance of such composite when used as catalysts.[37–45] After modification, common carbon resources such as simple monosaccharides or oligosaccharides can contain surfactant groups (–COOH, $–SO_3H$, –OH, etc.). To fabricate Fe_3O_4@C@Fe(III) nanoparticles by surface modification of core–shell Fe_3O_4@C with subsequent immobilization of the metal ions, we focused on exploiting a biomass material containing many polysaccharides.

Although lotus leaves are rich in polysaccharides, flavones, and proteins,[46–49] they are generally discarded in the autumn. To use them as a sustainable source of carbon and to improve the efficiency of its preparation, we proposed the novel catalyst-preparation route shown in Scheme 1.



Scheme 1 Fabrication of magnetic Fe_3O_4@C@Fe(III) core–shell catalyst from waste lotus leaves

Compared with reported methods, our method successfully simplified the two-step process of carbonization and sulfonation by performing it in one pot with concentrated sulfuric acid as both a carbonization and sulfonation agent.[42]

The morphology and structure of the resulting nanocomposites were analyzed by transmission electron microscopy (TEM). As shown in Figures 1(a) and 1(b), the nanocomposites had a cubic shape with an average size of 50–60 nm. The dark/light contrast shown in Figure 1(b) suggest a composition consisting of different phases and confirmed the formation of Fe_3O_4@C core–shell nanostructures. It was clearly shown that the Fe_3O_4 nanoparticles were completely coated with carbon shells, and that the diameter of the Fe_3O_4 cores encapsulated within the carbon shells was about 50–60 nm. The high-resolution TEM (HRTEM) image shown in Figure 1(c) provides detailed structural information about the Fe_3O_4@C nanoparticles. The lattice fringe, as calculated from the HRTEM image, is 0.48 nm, which fits well with the (111) planes of a cubic Fe_3O_4 structure. Furthermore, the elemental composition of the Fe_3O_4@C samples was determined by energy-dispersive X-ray (EDX) analysis [Figure 1(d)], which revealed that the as-prepared products contained abundant Fe and C, and also confirmed the nanocomposite structure of Fe_3O_4@C@Fe(III). In view of the invisible external structure of the core–shell material, the external Fe^{3+} content of the catalyst was determined by complexometric titration.[50,51] The load capacity of external ferric ion was 1.25×10^{-3} mmol/mg, which fits well with the results of our previous work.[28]

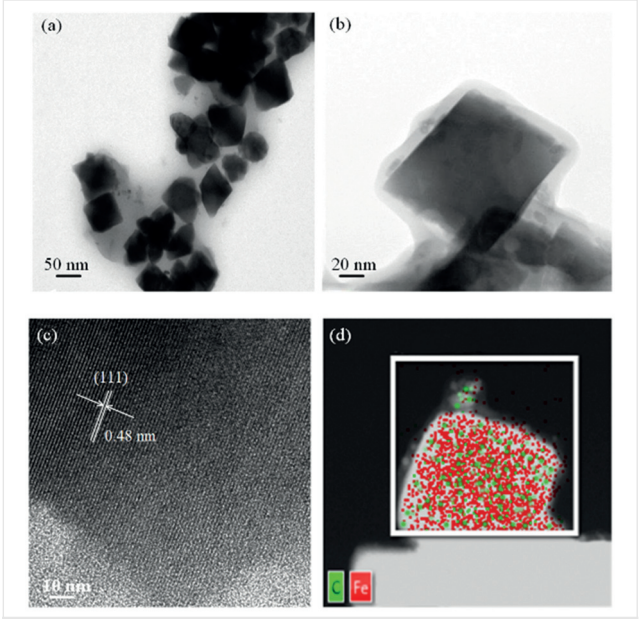


Figure 1 (a) and (b) TEM images of Fe_3O_4@C@Fe(III); (c) HRTEM image of Fe_3O_4@C@Fe(III); (d) EDX analysis.

The results described above showed that the prepared core–shell Fe_3O_4@C@Fe(III) particles are of nanometer-level sizes and therefore might be expected to show better performance as solid-acid catalysts. To examine their catalytic activity, a Ferrier rearrangement reaction was conducted with D-glucal triacetate and benzyl alcohol (Table 1). First, we examine whether the newly prepared nanoFe_3O_4-modified core–shell Fe_3O_4@C material with -COOH, $-SO_3H$, -OH, and other groups, after sulfonation with H_2SO_4 as a Bronsted acid, contained an abundance of surface groups and would combine firmly with ferric ions (Table 1, entries 1–4). The presence of a Fe_3O_4 coating on the carbon shell was shown to be essential for catalytic performance (entries 1–4), a result that is consistent with our previous work.[28] Compared with $FeCl_3$/C, the core–shell microspheres produced a superior reaction rate due their smaller particle size (entries 5 and 6). These results encouraged us to further study and optimize the conditions for the Ferrier reaction. On increasing the reaction temperature, the yield fell due to the increased production of byproducts (entries 6–

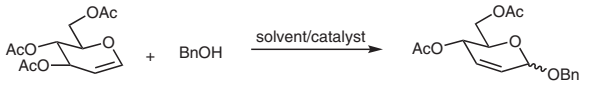
8). Next, we examined various solvents commonly used in Ferrier reactions (DCE, CH_2Cl_2, MeCN, Et_2O, and 1,4-dioxane) (entries 6 and 9–12). The reaction rate at room temperature was slow in solvents other than DCE or CH_2Cl_2, and therefore DCE was identified as the optimal solvent in terms of the reaction time and yield. Next, the loading of the Fe_3O_4@C@Fe(III) catalyst in this system was explored (entries 6 and 13–15). When the number of equivalents was reduced from 0.3 to 0.1 equivalents, the glucal triacetate was completely consumed in ten minutes and the yield reached 93% (entry 13). However, when 0.5 equivalents of catalyst were used, the yield fell slightly and the reaction time was extended to 15 minutes (entry 14). Therefore, the optimal reaction conditions were room temperature with 0.1 equivalents of catalyst in DCE.

Encouraged by these results, we explored the substrate scope of the rearrangement reaction with a range of alcohols, phenols, and saccharides **2a–r** as glycosyl acceptors (Scheme 2). Various alcohols, including primary, secondary, benzylic, allylic, propargylic, and halogenated alcohols showed good anomeric selectivities in producing products **3a–i** in high yields. It is noteworthy that when *tert*-butanol was used as the nucleophile, the expected product **3e** was obtained in high yield despite its high degree of steric hindrance. The reaction of the significant platform compound 5-(hydroxymethyl)furural (HMF; **2j**) with our catalytic system gave a higher yield of the corresponding product **3j** than that produced with $FeCl_3$/C in our previous work. This result shows the advantages of Fe_3O_4@C@Fe(III) in exploring more-bioactive HMF derivatives. The complex biomolecules cholesterol (**2l**) and menthol (**2m**) also reacted reacted in excellent yields and with high selectivities. Moreover, various disaccharides were obtained smoothly when monosaccharides were used as the acceptors, and the desired 2,3-unsaturated glycoside products **3n** and **3o** were obtained in high yields and with moderate selectivities. With phenolic acceptors, the Ferrier rearrangement proceeded with in the presence of 0.01 equivalents of catalyst, due to the acidity of the phenols. Phenol (**2p**), 4-methoxyphenol (**2q**), and 4-bromophenol (**2r**) provided the corresponding Ferrier products in yields that reflected the substituent effect to some extent. Both 3,4,6-tri-*O*-acetyl-D-glucal and 3,4-di-*O*-acetyl-L-rhamnal were studied as representative glycosyl donors. The latter reacted with HMF and 4-methoxyphenol as representative alcoholic and phenolic acceptors, respectively, giving the corresponding products **4a** and **4b** in yields of 82% and 60% with higher stereoselectivities.

Next, we attempted to employ our catalyst to promote more-challenging reactions with other glucal donors. Among the various substituted glycals, 2-haloglycals have recently become recognized as new entries to 2C-functionalized glycals, and are widely used as important synthons in organic chemistry.[52–54] Thus, 2-iodo- and 2-bromoglycals and the corresponding 2,3-unsaturated 2-haloglycosides have been used in the synthesis of 2C-arylglycosides, the oxadecalin core of phomactin A, and biologically active scaffolds such as chromans and isochromans.[55–57]

Substitution at C-2 position has a marked influence on the reactivity of glycals, especially in the case of halogen substituents, which have both an electron-donating inductive effect and an electron-withdrawing conjugation effect. However, previous research on 2-haloglycals and the corresponding reaction activity is inadequate. Our interest was intrigued by the activity of 2-haloglycals and the efficiency of the core–shell metal Lewis acid catalyst. Based on our previous preparation of 2-haloglycals, we employed tri-*O*-acetyl-2-iodoglucal (**5a**) to explore the optimal condition for Ferrier rearrangement reactions with ethanol in the presence of Fe_3O_4@C@Fe(III) catalyst. First, we used 1.0 equivalent of catalyst to promote the reaction at 25 °C, but no product was detected (Table 2, entry 1). When the temperature was increased to 40 °C, the reaction rate improved and product **7a** was obtained in 70% yield in 60 minutes (entry 2). At 60 °C, we obtained the product in 95% yield after 20 min (entry 3) and 80 °C, it was formed in 88% yield after 10 min. However, at these higher temperatures the formation of byproducts also increased and, therefore, the

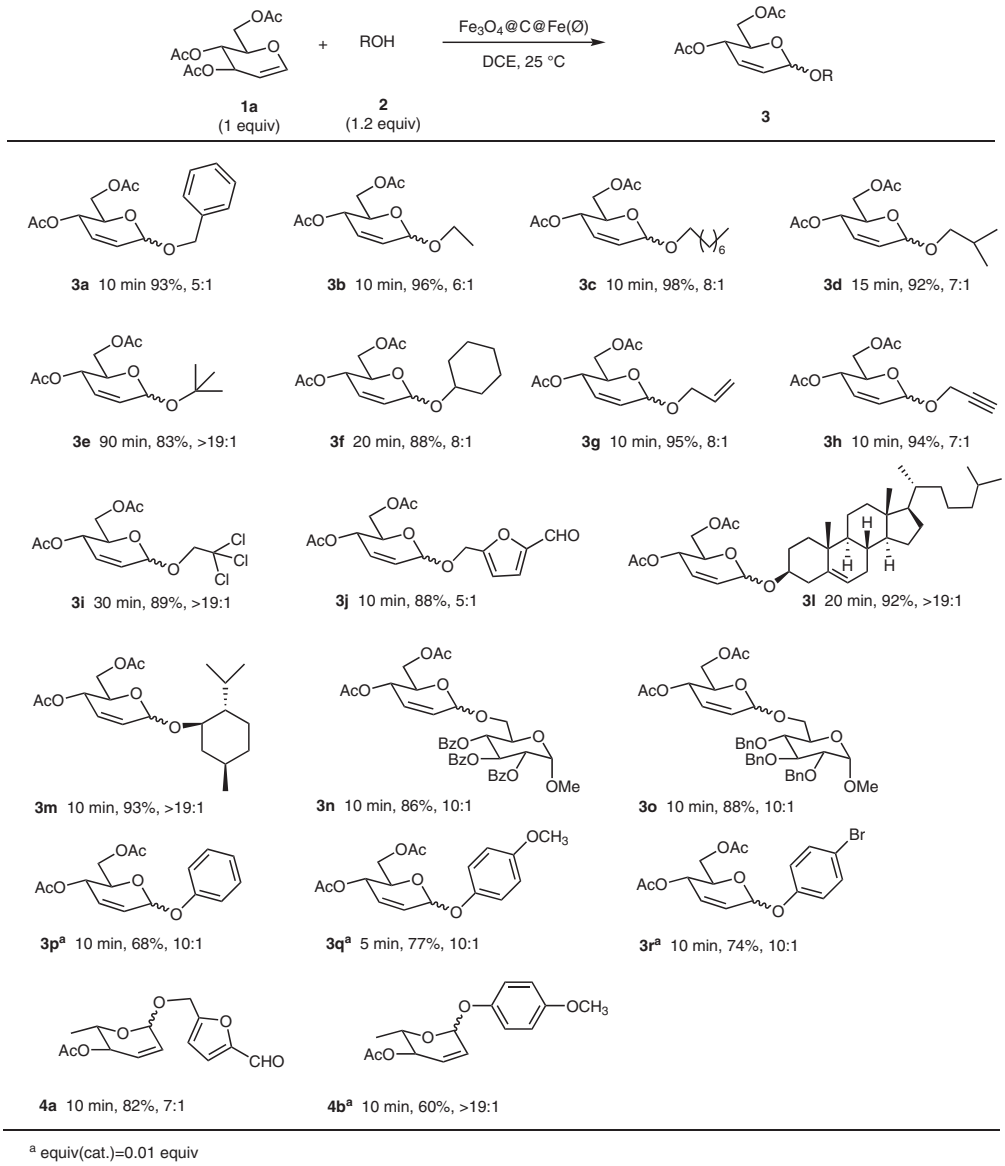
Table 1 Optimizing the Conditions for the Ferrier Rearrangement of D-Glucal Triacetate with Benzyl Alcohol



1a (1 equiv.) **2a** (1.2 equiv.) **3a**

Entry	Catalyst	Temp (°C)	Equiv of Catalyst[a]	Solvent	Time (min)	Yield[b] (%)
1	Fe_3O_4	25	0.3	DCE	>720	NR[c]
2	Fe_3O_4	80	0.3	DCE	>720	NR
3	Fe_3O_4@C@SO_3H[d]	25	0.3	DCE	>720	NR
4	Fe_3O_4@C@SO_3H[d]	80	0.3	DCE	10	76
5	$FeCl_3$/C	25	0.3	DCE	10	85
6	Fe_3O_4@C@Fe(III)	25	0.3	DCE	10	89
7	Fe_3O_4@C@Fe(III)	40	0.3	DCE	10	84
8	Fe_3O_4@C@Fe(III)	80	0.3	DCE	10	82
9	Fe_3O_4@C@Fe(III)	25	0.3	CH_2Cl_2	30	80
10	Fe_3O_4@C@Fe(III)	25	0.3	MeCN	240	60
11	Fe_3O_4@C@Fe(III)	25	0.3	Et_2O	360	63
12	Fe_3O_4@C@Fe(III)	25	0.3	1,4-dioxane	>720	NR
13	Fe_3O_4@C@Fe(III)	25	0.1	DCE	10	93
14	Fe_3O_4@C@Fe(III)	25	0.5	DCE	15	88
15	Fe_3O_4@C@Fe(III)	25	0.05	DCE	10	91

[a] Fe^{3+} content of the catalyst as determined by complexometric titration.[50]
[b] Isolated yield.
[c] NR = no reaction.
[d] Core–shell microparticles of Fe_3O_4@C modified with –SO_3H and –COOH groups.[28]

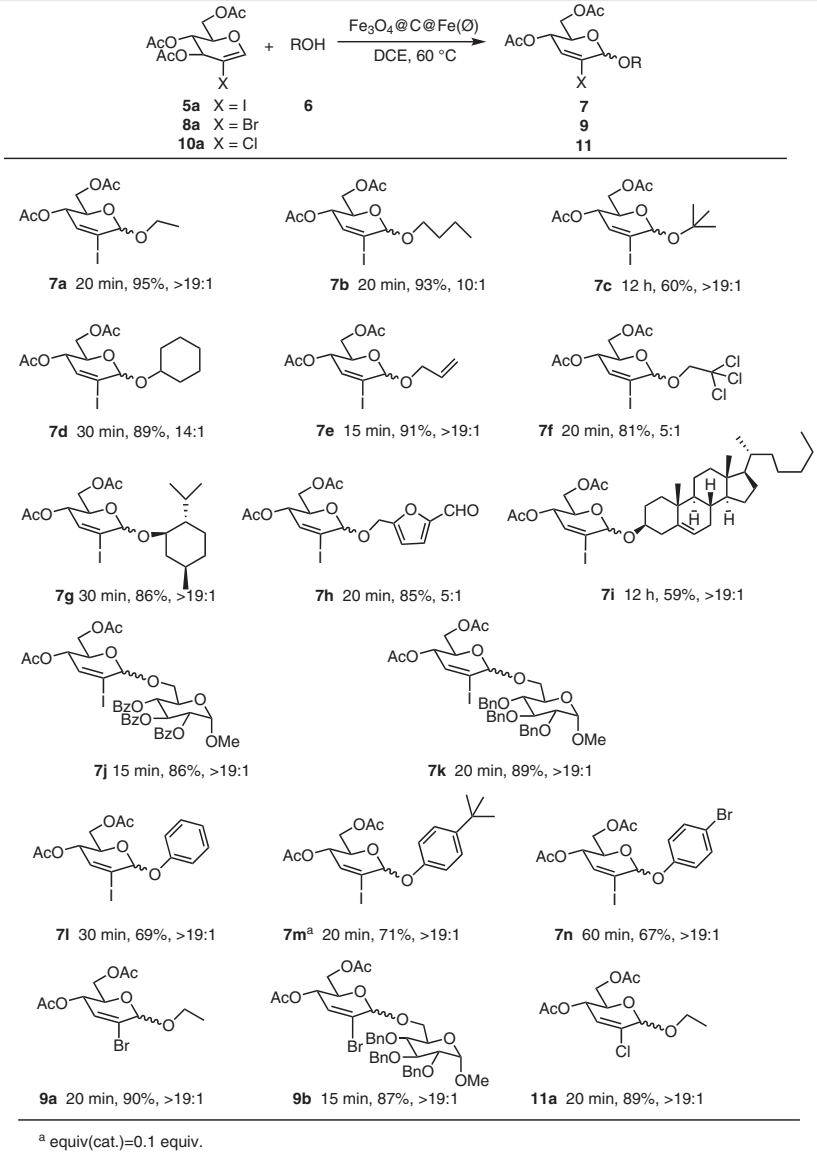


Scheme 2 Scope of the Ferrier rearrangement under the optimized conditions

optimal temperature was 60 °C. Next, we tried different solvent (entries 5–8) apart from DCE, the optimal solvent for the Ferrier reaction of 2-unsubstituted glucals, and we found that DCE remained the best choice. To reduce the use of catalyst, gradient dosages from 1.0 to 0.1 equivalents were tested (entries 3 and 9–11), and we found that 1.0 equivalents of catalyst rapidly and efficiently promoted this reaction. Therefore, the optimal reaction conditions are 60 °C with 1.0 equivalent of catalyst in DCE.

Having established the optimal reaction conditions, we turned our attention to exploring the substrate scope of the Ferrier rearrangement reaction of **5a** and **8a** with a series of O-nucleophiles **6a–n** (Scheme 3). In all cases, the reaction proceeded smoothly and with good to excellent yields and α-selectivity, demonstrating that our catalyst can be used in the presence of not only common or complex bioactive alcohols, phenols, and glycosyl acceptors, but also with 2-iodo-, 2-bromo, and 2-chloroglucal donors.

We then examined the differences in the reactivities of 2-unsubstituted and 2-halogenated tri-*O*-acetylglucals under the same mild conditions. We chose tri-*O*-acetylglucal (**1a**),tri-*O*-acetyl-2-iodoglucal (**5a**), 2-bromo-tri-*O*-acetylglucal (**8a**), and 2-chloro-tri-*O*-acetylglucal (**10a**) as donors and ethanol as the acceptor with 0.3 equivalents of the catalyst. A comparison of the reaction time, conversion rate, and yield for the various reactions showed that tri-*O*-



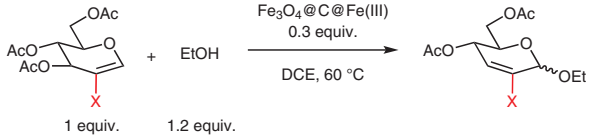
Scheme 3 Scope of the Ferrier rearrangement reaction under the optimized conditions

acetylglucal (**1a**) has the highest reactivity and that the activities of the tri-*O*-acetyl-2-haloglucals decrease with decreasing atomic number of the halogen (Table 3).

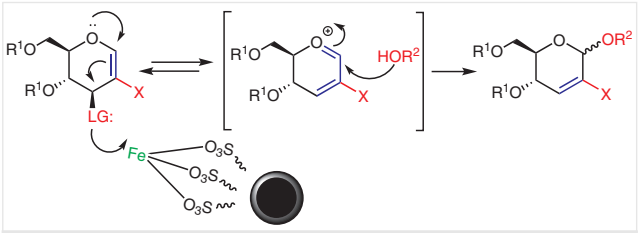
On the basis of reports in the literature,[58–60] we concluded that the substituent at C-2 position has a remarkable effect, and that electron-withdrawing groups reduce the electron density of the oxocarbenium intermediate (Scheme 4).

Recycling of the Fe_3O_4@C@Fe(III) catalyst was studied for the model reaction of tri-O-acetyl-D-glucal with benzyl alcohol. After reaction, the Fe_3O_4@C@Fe(III) catalyst was dispersed in the reaction system but could be easily collected by using an external magnet. The liquid was then removed from the mixture to leave the catalyst, which was washed with CH_2Cl_2 to remove any adsorbed products, dried under vacuum, and reused in a subsequent reaction. As shown in in Scheme 5, in a test over five reaction cycles there was only a slight decrease in the activity of the catalyst. Because the crude extract of lotus leaf is rich in polysaccharides, we suspect that these polysaccharides play a significant role in the carbonization and immobilization process. We therefore examined lotus-leaf polysaccharides obtained by alcohol sedimentation as a shell carbon resource to determine whether the polysaccharides alone could provide enough active groups for immobilization of ferric ions.[43,48,49] However, the catalyst with the polysaccharide-derived carbon shell gave inferior results.

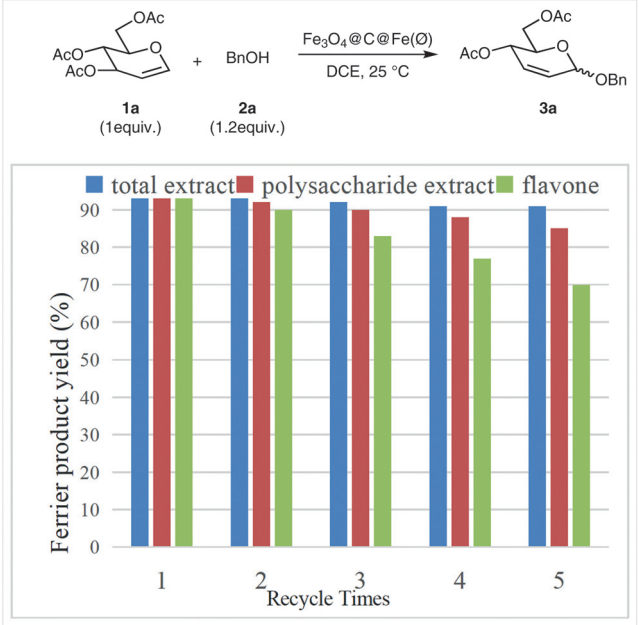
Table 3 Reactivities of Tri-*O*-acetylglucal and 2-Halo-tri-O-acetylglucals



Entry	X	Time (min)	Conversion (%)	Yield (%)
1	H	10	100	92
2	I	90	100	83
3	Br	90	91	79
4	Cl	90	85	72



Scheme 4 Plausible mechanism

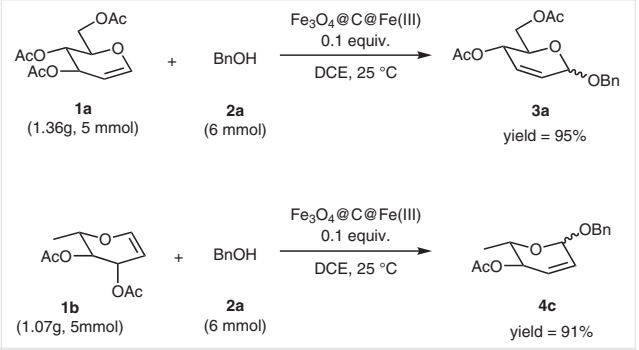


Scheme 5 Recycling experiments of Fe_3O_4@C@Fe(III). *Reaction conditions*: **1a** (0.2 mmol, 54.4 mg), BnOH (0.224 mmol, 24 μL), Fe_3O_4@C@Fe(III) (16 mg), DCE (2 mL), 10 min, rt.

Next, and as a comparison, another important extractive component, flavonoids, were tested as a carbon resource,[48] but, as shown in Scheme 5, the total crude extract as a carbon resource was superior to lotus-leaf polysaccharides or flavonoids individually. We postulate that after carbonization, polysaccharides provide sufficient carbon resources and incomplete carbonization of flavonoid residues results in improved binding of ferric ions, thereby improving the ability of the material to immobilize ferric ions.[48,49]

Because the Ferrier reaction of 2-haloglucals proceeds at 60 °C, which is a fairly high temperature for Ferrier rearrangements in general, we tested the recycling performance of the catalyst by using reaction of tri-*O*-acetyl-2-iodoglucal (**5a**) with ethanol as a model reaction to examine whether the ferric ion remained tightly bound to the core–shell Fe_3O_4@C under heated conditions. The product was still obtained in 86% yield, even after the catalyst had been cycled five times, demonstrating that our catalyst is suitable for use under harsh conditions, thereby significantly broadening its the range applications under recycling conditions.

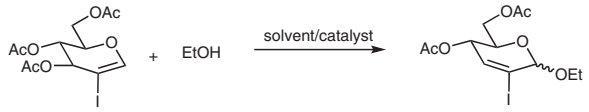
As shown by the above experiments, our catalyst has outstanding catalytic activity and recycling performance. To further demonstrate the mass production of glycosides, we tested the catalyst in large-scale Ferrier rearrangement reactions (Scheme 6). When 5 mmol of tri-*O*-acetyl-D-glucal (**1a**) or di-*O*-acetyl-L-rhamnal (**1b**) was treated with benzyl alcohol (**2a**) under the optimal conditions (0.1 equiv catalyst, DCE, rt), the corresponding products **3a** and **4c** were obtained in excellent yields in 10 minutes through simple magnetic separation and column chromatography.



Scheme 6 Ferrier rearrangement reactions on a large scale

In summary, we have developed a green synthesis of magnetic Fe_3O_4@C@Fe(III) core–shell microspheres from lotus leaf as a carbon resource; this is the first report of the immobilization of Fe(III) on a carbon shell as a Lewis acid catalyst. Our Fe_3O_4@C@Fe(III) catalyst was successfully applied in Ferrier rearrangement reactions, including those of 2-haloglycals.[61] This core–shell magnetic catalyst is not only superior to Fe_3O_4@C-SO_3H in terms of the reaction conditions and the substrate scope, but also overcomes the problems of reuse and moisture absorption associated with $FeCl_3$. Compared with recently developed Lewis acid cata-

Table 2 Optimization of the Conditions for the Ferrier Rearrangement Tri-O-acetyl-2-iodoglucal with Ethanol



5a (1 equiv.) **6a** (1.2 equiv.) **7a**

Entry	Catalyst	Temp (°C)	Equiv catalyst[a]	Solvent	Time (min)	Yield[b] (%)
1	Fe_3O_4@C@Fe(III)	25	1.0	DCE	>720	trace
2	Fe_3O_4@C@Fe(III)	40	1.0	DCE	60	70
3	Fe_3O_4@C@Fe(III)	60	1.0	DCE	20	95
4	Fe_3O_4@C@Fe(III)	80	1.0	DCE	10	88
5	Fe_3O_4@C@Fe(III)	60	1.0	CH_2Cl_2	30	79
6	Fe_3O_4@C@Fe(III)	60	1.0	MeCN	>720	NR[c]
7	Fe_3O_4@C@Fe(III)	60	1.0	Et_2O	>720	NR
8	Fe_3O_4@C@Fe(III)	60	1.0	THF	>720	NR
9	Fe_3O_4@C@Fe(III)	60	0.5	DCE	90	85
10	Fe_3O_4@C@Fe(III)	60	0.3	DCE	90	83
11	Fe_3O_4@C@Fe(III)	60	0.1	DCE	>720	71

[a] Fe^{3+} content of the catalyst as determined by complexometric titration.[50]
[b] Isolated yield.
[c] NR = no reaction.

lysts, the solid Lewis acid Fe_3O_4@C@Fe(III) has advantages in terms of catalytic efficiency and substrate range, paving the way for use of this green and low-cost Lewis acid in organic reactions other than the Ferrier rearrangement reaction. Gram-scale production revealed the advantages of this catalyst in environmental and economic terms. Therefore, our magnetic core–shell nanoparticle system holds great promise as a novel ferric-based catalyst system for various catalytic Ferrier reactions. Additionally, the design concept for the green preparation method can be extended to the fabrication of other Lewis acid metal systems with integrated and enhanced properties for various advanced applications.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611855.

References and Notes

(1) Park, Y.; Harper, K.; Kuhl, N.; Kwan, E.; Liu, R. Y.; Jacobsen, E. N. *Science* **2017**, *355*, 162.
(2) Jung, H. J.; Pamer, E. G. *Nature* **2017**, *546*, 479.
(3) Thomas, T. S.; Wang, W. H.; Sita, L. R. *Angew. Chem. Int. Ed.* **2016**, *55*, 4683.
(4) Wang, Z.; Chinoy, Z. S.; Ambre, S. G.; Peng, W.; McBride, R.; De Vries, R. P.; Glushka, J.; Paulson, J. C.; Boons, G.-J. *Science* **2013**, *341*, 379.
(5) Gloster, T. M.; Vocadlo, D. J. *Nat. Chem. Biol.* **2012**, *8*, 683.
(6) Gu, Z.-y.; Zhang, X.-t.; Zhang, J.-x.; Xing, G.-w. *Org. Biomol. Chem.* **2013**, *11*, 5017.
(7) Lowary, T. L. *Acc. Chem. Res.* **2016**, *49*, 1379.
(8) Yang, Q.; An, Y.; Wang, L. X. *ACS Chem. Biol.* **2017**, *12*, 1665.
(9) Shao, L.; Zhang, H.; Li, Y.; Gu, G.; Cai, F.; Guo, Z.; Gao, J. *J. Org. Chem.* **2018**, *83*, 5920.
(10) Zhang, J. In *Glycoscience: Chemistry and Chemical Biology I–III (2nd ed)*; Fraser-Reid, B. O.; Tatsuta, K.; Thiem, J., Ed.; Springer: Berlin, **2008**, 375.
(11) Li, J. In *Name Reactions: A Collection of Detailed Reaction Mechanisms (3rd ed)*; Young, D. G. J., Ed.; Springer: Berlin, **2006**, 227.
(12) Ferrier, R. J. *Top. Curr. Chem.* **2001**, *215*, 153.
(13) Ferrier, R. J.; Zubkov, O. A. In *Organic Reactions*; Wiley: Weinheim, **2004**, DOI:10.1002/0471264180.or062.04.
(14) Gómez, A. M.; Lobo, F.; Uriel, C.; López, J. C. *Eur. J. Org. Chem.* **2013**, 7221.
(15) Ram, R. N.; Kumar, N.; Gupta, D. K. *Adv. Synth. Catal.* **2017**, *359*, 432.
(16) Saquib, M.; Husain, I.; Sharma, S.; Yadav, G.; Singh, V. P.; Sharma, S. K.; Shah, P.; Siddiq, M. I.; Kumar, B.; Lal, J.; Jain, G. K.; Srivastava, B. H.; Shaw, A. K. *Eur. J. Med. Chem.* **2011**, *46*, 2217.
(17) Kusumi, S.; Wang, S.; Watanabe, T.; Sasaki, K.; Takahashi, D.; Toshima, K. *Org. Biomol. Chem.* **2011**, *8*, 988.
(18) Kusumi, S.; Sasaki, K.; Wang, S.; Watanabe, T.; Takahashi, D.; Toshima, K. *Org. Biomol. Chem.* **2010**, *8*, 3164.
(19) Di Bussolo, V.; Kim, Y.-J.; Gin, D. Y. *J. Am. Chem. Soc.* **1998**, *120*, 13515.
(20) Ding, Z.; Luo, X.; Ma, Y.; Chen, H.; Qiu, S.; Sun, G.; Zhang, W.; Wu, Z.; Zhang, J. *J. Carbohydr. Chem.* **2018**, *37*, 81.
(21) Sau, A.; Galan, M. C. *Org. Lett.* **2017**, *19*, 2857.
(22) Chen, P.; Su, J. *Tetrahedron* **2016**, *72*, 84.
(23) Roy, R.; Rajasekaran, P.; Mallick, A.; Vankar, Y. D. *Eur. J. Org. Chem.* **2014**, *2014*, 5564.
(24) Zhou, J.; Chen, H.; Shan, J.; Yang, G.; Chen, X.; Xin, K.; Zhang, J.; Tang, J. *J. Carbohydr. Chem.* **2014**, *33*, 313.
(25) Zhang, J.; Zhang, B.; Zhou, J.; Chen, H.; Li, J.; Yang, G.; Wang, Z.; Tang, J. *J. Carbohydr. Chem.* **2013**, *32*, 380.
(26) Zhou, J.; Zhang, B.; Yang, G.; Chen, X.; Wang, Q.; Wang, Z.; Zhang, J.; Tang, J. *Synlett* **2010**, 893.

(27) Zhou, J.; Chen, X.; Wang, Q. B.; Zhang, B.; Zhang, L. Y.; Yusulf, A.; Wang, Z. F.; Zhang, J. B.; Tang, J. *Chin. Chem. Lett.* **2010**, *21*, 922.
(28) Sun, G.; Wu, Y.; Liu, A.; Qiu, S.; Zhang, W.; Wang, Z.; Zhang, J. *Synlett* **2018**, *29*, 668.
(29) Qiu, S.; Sun, G.; Ding, Z.; Chen, H.; Zhang, J. *Synlett* **2017**, *28*, 2024.
(30) Kumar, K.; Ramulu, M.; Rajesham, B.; Kumar, N.; Voora, V.; Kancha, R. K. *Org. Biomol. Chem.* **2017**, *15*, 4468.
(31) Qiu, S.; Zhang, W.; Sun, G.; Wang, Z.; Zhang, J. *ChemistrySelect* **2016**, *1*, 4840.
(32) Li, J.; Zhang, X.; Zhang, M.; Xiu, H.; He, H. *Carbohydr. Polym.* **2015**, *117*, 917.
(33) Zhang, L.; Yu, H.; Wang, P.; Li, Y. *Bioresour. Technol.* **2014**, *151*, 355.
(34) Cornil, J.; Guérinot, A.; Reymond, S.; Cossy, J. *J. Org. Chem.* **2013**, *78*, 10273.
(35) Guo H., Si W., Li J., Yang G., Tang T., Wang Z., Tang J., Zhang. J.; *Synthesis*; DOI: 10.1055/s-0037-1611801.
(36) Thombal, R. S.; Jadhav, V. H. *RSC Adv.* **2016**, *6*, 30846.
(37) Ma, J.-f.; Xing, J.-x.; Wang, K.; Yang, H.-y.; Fei, B.-h.; Liu, X.-e. *Carbohydr. Polym.* **2017**, *164*, 127.
(38) Jin, Z.; Dong, Y.; Dong, N.; Yang, Z.; Wang, Q.; Lei, Z.; Su, B. *Mater. Lett.* **2017**, *186*, 322.
(39) Zhang, Y.; Xue, Z.; Wang, J.; Zhao, X.; Deng, Y.; Zhao, W.; Mu, T. *RSC Adv.* **2016**, *6*, 51229.
(40) Wu, S.; Huang, J.; Zhuo, C.; Zhang, F.; Sheng, W.; Zhu, M. *J. Inorg. Organomet. Polym.* **2016**, *26*, 632.
(41) Wang, D.; Zhou, J.; Chen, R.; Shi, R.; Xia, G.; Zhou, S.; Liu, Z.; Zhang, N.; Wang, H.; Guo, Z.; Chen, Q. *Biomaterials* **2016**, *107*, 88.
(42) Fang, X.; Wang, S.; Li, Y.; Liu, X.; Li, X.; Lin, S.; Cui, Z.-K.; Zhuang, Q. *RSC Adv.* **2016**, *6*, 107533.
(43) Chen, Z.; Geng, Z.; Zhang, Z.; Ren, L.; Tao, T.; Yang, R.; Guo, Z. *Eur. J. Inorg. Chem.* **2014**, 3172.
(44) Deng, Y.; Cai, Y.; Sun, Z.; Liu, J.; Liu, C.; Wei, J.; Li, W.; Liu, C.; Wang, Y.; Zhao, D. *J. Am. Chem. Soc.* **2010**, *132*, 8466.
(45) Toda, M.; Takagaki, A.; Okamura, M.; Kondo, J. N.; Hayashi, S.; Domen, K.; Hara, M. *Nature* **2005**, *438*, 178.
(46) Fan, J.-P.; Zheng, B.; Qin, Y.; Yang, D.; Liao, D.-D.; Xu, X.-K.; Zhang, X.-H.; Zhu, J.-H. *Appl. Surf. Sci.* **2016**, *364*, 332.
(47) Kung, H. H.; Kung, M. C. *Catal. Lett.* **2014**, *144*, 1643.
(48) Zhao, X.; Shen, J.; Kim, S. H. *J. Agric. Food Chem.* **2014**, *62*, 6227.
(49) Huang, C. F.; Chen, Y. W.; Yang, C. Y.; Ling, H. Y.; Way, T. D.; Chiang, W.; Liu, S. H. *J. Agric. Food Chem.* **2011**, *59*, 1087.
(50) Li, Z.; Chen, W.; Xu, H. *Guangdong Huagong* **2015**, *42*, 220.
(51) Xu, J.; Koopal, L.; Fang, L.; Xiong, J.; Tan, W. *Environ. Sci. Technol.* **2018**, *52*, 4099.
(52) Cobo, I.; Matheu, M. I.; Castillón, S.; Boutureira, O.; Davis, B. G. *Org. Lett.* **2012**, *14*, 1728.
(53) Dharuman, S.; Vankar, Y. D. *Org. Lett.* **2014**, *16*, 1172.
(54) Shamim, A.; Vasconcelos, S.; Ali, B.; Madureira, L. S.; Zukerman-Schpector, J.; Stefani, H. A. *Tetrahedron Lett.* **2015**, *56*, 5836.
(55) Leibeling, M.; Milde, B.; Kratzert, D.; Werz, D. B. *Chem. Eur. J.* **2011**, *17*, 9888.
(56) Leibeling, M.; Koester, D. C.; Pawliczek, M.; Dittrich, B.; Werz, D. B. *Bioorg. Med. Chem.* **2010**, *18*, 3656.
(57) Leibeling, M.; Koester, D. C.; Pawliczek, M.; Schild, D. C.; Werz, D. B. *Nat. Chem. Biol.* **2010**, *6*, 199.
(58) Michigami, K.; Hayashi, M. *Tetrahedron* **2012**, *68*, 1092.
(59) Chen, P.; Lin, L. *Tetrahedron* **2013**, *69*, 10045.
(60) Chen, H.; Luo, X.; Qiu, S.; Sun, G.; Zhang, J. *Glycoconj. J.* **2017**, *34*, 13.
(61) **Benzyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (3a); Typical Procedure**
Fe_3O_4@C@Fe(III) catalyst (8 mg, 0.01 mmol) was added to a mixture of 3,4,6-tri-*O*-acetyl-D-glucal (**1a**, 0.1 mmol, 27.2 mg) and BnOH (**2a**; 1.2 mmol, 12.5 ul) in CH_2Cl_2 (1.0 mL) and the mixture was stirred at rt (25 °C) under N_2. On consumption of the glucal (TLC), the mixture and catalyst were separated magnetically. The solution was then evaporated to give a crude product that was purified by column chromatography [silica gel, PE–EtOAc (6:1)] to give a colorless oil; yield 29.8 mg. (93%).
Benzyl 4,6-Di-*O*-diacetyl-2,3-dideoxyalpha-D-*erythro*-2-hexenopyranoside (3a)
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 4.9 Hz, 5 H), 5.90 (d, *J* = 10.4 Hz, 1 H), 5.87–5.83 (m, 1 H), 5.33 (dd, *J* = 9.4, 1.3 Hz, 1 H), 5.14 (s, 1 H), 4.81 (d, *J* = 11.7 Hz, 1 H), 4.60 (d, *J* = 11.7 Hz, 1 H), 4.25 (dd, *J* = 11.6, 5.0 Hz, 1 H), 4.18–4.14 (m, 1 H), 4.14–4.11 (m, 1 H), 2.10 (s, 3 H), 2.08 (s, 3 H). LRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{20}NaO_6$: 343.12; found: 343.15
(5-Formyl-2-furyl)methyl 4,6-Di-*O*-acetyl-2,3-dideoxy-2-iodo-α-D-*erythro*-hex-2-enopyranoside (7h)
Yellow oil; yield: 39.4 mg (85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.63 (s, 1 H), 7.23 (d, *J* = 3.1 Hz, 1 H), 6.63 (d, *J* = 2.9 Hz, 1 H), 6.50 (s, 1 H), 5.31 (d, *J* = 8.6 Hz, 1 H), 5.10 (s, 1 H), 4.75 (ddd, *J* = 19.2, 13.5, 7.4 Hz, 2 H), 4.20 (ddd, *J* = 30.1, 16.3, 5.3 Hz, 3 H), 2.09 (d, *J* = 6.9 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.85, 170.79, 170.11, 157.15, 152.98, 138.61, 121.97, 112.01, 99.17, 73.08, 67.21, 66.84, 62.93, 62.55, 20.99, 20.92. HRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{16}H_{17}INaO_6$: 486.9866; found: 486.9860.
Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(4,6-di-*O*-acetyl-2-bromo-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-α-D-glucopyranoside (9b)
Yellow oil; yield: 65.6 mg (87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 15 H), 6.19 (s, 1 H), 5.32 (d, *J* = 8.7 Hz, 1 H), 5.15 (s, 1 H), 4.97 (d, *J* = 10.8 Hz, 1 H), 4.92 (d, *J* = 11.1 Hz, 1 H), 4.84–4.77 (m, 2 H), 4.66 (dd, *J* = 11.2, 8.5 Hz, 2 H), 4.59 (d, *J* = 3.0 Hz, 1 H), 4.19 (dd, *J* = 12.3, 5.1 Hz, 1 H), 4.13 (d, *J* = 10.9 Hz, 2 H), 4.01 (t, *J* = 9.2 Hz, 1 H), 3.89–3.81 (m, 2 H), 3.76 (d, *J* = 10.6 Hz, 1 H), 3.66 (t, *J* = 9.4 Hz, 1 H), 3.53 (dd, *J* = 9.7, 2.9 Hz, 1 H), 3.37 (s, 3 H), 2.08 (s, 3 H), 2.04 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.81, 170.17, 138.87, 138.47, 138.24, 129.74, 128.60, 128.57, 128.54, 128.30, 128.19, 128.08, 127.88, 127.77, 122.54, 98.17, 97.80, 82.06, 80.01, 77.75, 75.93, 75.17, 73.54, 70.92, 66.93, 66.85, 66.57, 62.53, 55.37, 53.57, 21.00, 20.87. HRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{38}H_{43}BrNaO_{11}$: 777.1887; found: 777.1881.
Ethyl 4,6-Di-*O*-acetyl-2-chloro-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (11a)
Yellow oil; yield: 26.0 mg (89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.98 (s, 1 H), 5.35 (d, *J* = 9.3 Hz, 1 H), 4.91 (s, 1 H), 4.25–4.14 (m, 3 H), 3.84 (dq, *J* = 14.3, 7.1 Hz, 1 H), 3.70–3.61 (m, 1 H), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.80, 170.22, 132.85, 125.48, 96.65, 66.82, 66.25, 65.25, 62.62, 20.99, 20.86, 15.26. HRMS (ESI$^+$): *m/z* [M + Na]$^+$ calcd for $C_{12}H_{17}ClNaO_6$: 315.0612; found: 315.0606.