

Polymer-Supported Ferric Chloride as a Heterogeneous Catalyst for Chemoselective Deprotection of Acetonides

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Abstract: Acetonides undergo chemoselective deprotection to afford the corresponding 1,2-diols in excellent yields using polymer (PVP)-supported ferric chloride as a heterogeneous catalyst in acetonitrile–dichloromethane at room temperature.

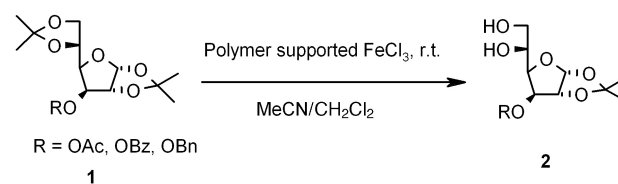
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Polyhydroxy compounds are extremely useful in organic synthesis, especially in the field of carbohydrate and nucleoside chemistry, and due to selective reactions on a hydroxy group they can act as protective groups.¹ Acetonides are the most frequently used protecting groups for 1,2-diols in carbohydrate synthesis. In the field of drugs and pharmaceuticals, the selective deprotection of acetonide groups is an important transformation. They have also been used as chiral auxiliaries.² Many reagents have been used in this transformation, such as aqueous HCl,³ aqueous HBr,⁴ aqueous HOAc,⁵ H₂SO₄ in MeOH,⁶ and other Lewis acid base reagents such as CuCl₂·2H₂O in ethanol,⁷ Zn(NO₃)₂,⁸ CeCl₃,⁹ and bismuth(III) chloride¹⁰ have also been used in deprotection of acetonide. Due to their wide range of applications, these compounds have received a great deal of attention in connection with their synthesis. However many of these methodologies are associated with several shortcomings, such as strong oxidizing conditions, high acidity, longer reaction times, expensive reagents, harsh conditions, low product yields, low chemoselectivity, high amounts of reagent or catalyst, occurrence of several side products, difficulty in recovery and reusability of the catalysts. Due to these problems, development of an efficient and versatile method for chemoselective deprotection of acetonides is an important aspect, and which is an active ongoing research area, and there is a scope for the further improvement towards mild reaction conditions and improved yields.

In recent years the organic reactions on solid supported reagents^{11–14} has received considerable importance in organic synthesis because of their ease of handling, enhanced reaction rates, greater selectivity, simple workup, and recoverability of catalysts. Among the various heterogeneous catalysts, particularly, polymer supported reagents have advantages of low cost, ease of preparation,

and catalyst recycling. Since the reaction is heterogeneous in nature, the catalyst can conveniently be separated by simple filtration.

We wish to report a facile conversion of acetonides to corresponding 1,2-diols by using polymer supported FeCl₃ as a heterogeneous catalyst (Scheme 1).



Scheme 1

FeCl₃ is an inexpensive and powerful oxidant used for the transformation of a wide range of functional groups. A wide range of structurally varied acetonides has been subjected to cleavage with FeCl₃ supported on polymer to provide the corresponding carbonyl compounds. It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over-oxidation of ensuing aldehydes is not observed under the reaction conditions. Acetonides were prepared by known literature procedure. All resulting 1,2-diols are identified by comparison of their physical data, and IR and NMR spectra with those of authentic samples. Polymer supported FeCl₃ was prepared by using a known procedure.¹⁵

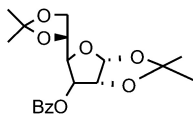
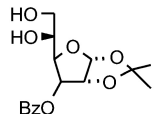
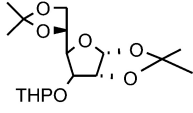
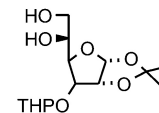
We wish to report polymer (PVP)-supported ferric chloride as a heterogeneous catalyst for efficient, chemoselective deprotection of acetonide. The selective cleavage of acetonide in the presence of other acid-labile protective groups such as *tert*-butyldimethylsilyl (TBDMS) ether and tetrahydropyranyl ether (THP) proceeded smoothly.

In view of the current thrust on catalytic processes there is a merit in developing a truly catalytic deprotection of acetonide using inexpensive and non-polluting reagents. Herein, we wish to report PVP-supported, FeCl₃-catalyzed acetonide deprotection. The reaction proceeds efficiently at room temperature and the products are obtained in excellent yields without by-products. Furthermore, other functionalities such as OMe, OBn, OBz, NHBoc, TBDMS, THP and OAc were compatible under the reaction conditions. The deprotection of acetonide for other substrates proceeded smoothly (Table 1).

Table 1 Polymer-Supported FeCl₃-Catalyzed Acetonide Deprotection

Entry	Substrate (1)	Product (2)	Time (min)	Yield (%)
a			25	90
b			30	92
c			30	90
d			32	92
e			34	88
f			34	87
g			33	90
h			32	94
i			34	93
j			35	92
k			30	90
l			34	90
m			30	91

Table 1 Polymer-Supported FeCl₃-Catalyzed Acetonide Deprotection (continued)

Entry	Substrate (1)	Product (2)	Time (min)	Yield (%)
n			30	94
o			25	94

In conclusion, we have developed a simple, convenient and effective method for the synthesis of 1,2-diols, which has the advantages of mild reaction conditions, high chemoselectivity, reduced reaction time, inexpensive catalyst, high yields of products and simple experimental work-up procedure. Polymer (PVP)-supported, ferric chloride-catalyzed acetonide deprotection has been developed to produce 1,2-diols, which will be an important addition to the present existing procedures. To our knowledge, this is first time report of an efficient general method for the synthesis of 1,2-diols by using a simple catalyst.

1,2-Diols from Acetonides; General Procedure

A solution of the acetonide (1 mmol) in MeCN (10 mL) was treated with polymer supported FeCl₃ (5 mol%) and H₂O (2 drops) and stirred for an appropriate time (Table 1) at r.t. After completion of the reaction, NaHCO₃ was added and solvent was removed under reduced pressure, H₂O was added the mixture extracted into EtOAc, washed with brine, dried (Na₂SO₄) and concentrated to give the crude product, which was purified (silica gel column) to provide the pure 1,2-diols in high yields.

Catalyst Preparation

Powdered poly(4-vinylpyridine) (1 g) was dissolved in a standard solution of FeCl₃ in H₂O (0.1 M, 10 mL). FeCl₃ (1 mmol, 161 mg) was added. After the solution had been stirred for 30 min at 30 °C, the solid PVP-Fe(III) was filtered off. The excessive ferric ions in the complex were washed off with deionized H₂O. The solid powder was dried under vacuum at 65 °C for 24 h. The absorbed amounts of the ferric ions in the complex were obtained using UV spectrophotometry. The catalyst was washed with solvents and dried then reused for subsequent reactions. In the polymer-supported FeCl₃, the polymer strongly binds to the catalyst, so the catalyst can be recovered without loss of any FeCl₃.

Spectral Data for Selected Compounds

3-O-Tetrahydropyranyl-1,2-isopropylidene- α -D-glucofuranose (2i)

¹H NMR (CDCl₃, 200 MHz): δ = 1.35 (s, 3 H), 1.48 (s, 3 H), 1.54–1.62 (m, 2 H), 1.77–1.90 (m, 2 H), 3.47–3.62 (m, 2 H), 3.64–3.79 (m, 2 H), 3.73–3.81 (m, 1 H), 4.01 (m, 3 H), 4.22–4.32 (m, 1 H), 4.0–4.51 (m, 1 H), 4.6–4.69 (m, 1 H), 5.91 (d, J = 7.5 Hz, 1 H).

3-O-(*tert*-Butyldimethylsilyl)-1,2-O-isopropylidene- α -D-glucofuranose (2j)

IR: 1250 cm⁻¹.

¹H NMR (CDCl₃, 200 MHz): δ = 0.16 (s, 6 H), 0.83 (s, 9 H), 1.32 (s, 3 H), 1.50 (s, 3 H), 2.0 (br s, 1 H), 2.51 (br s, 1 H), 3.75–4.40 (m, 6 H), 5.93 (d, J = 3.7 Hz, 1 H).

¹³C NMR (CDCl₃, 50 MHz): δ = -5.14, -4.86, 17.94, 25.63, 26.23, 64.43, 68.71, 75.72, 80.85, 85.28, 104.93, 111.74.

MS (FAB): m/z = 318 (M + 1).

Anal. Calcd for C₁₅H₃₀O₆Si: C, 53.86; H, 9.04. Found: C, 53.80; H, 8.97.

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