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Fe(III) chloride catalyzed conversion of epoxides to acetonides

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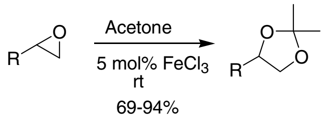
ABSTRACT

A mild and efficient method for the preparation of acetonides from epoxides catalyzed by iron(III) chlorides has been developed.

Acetonides constitute important synthetic intermediates during the synthesis of complex organic molecules, more specially, in the field of carbohydrate and steroid chemistry.[1] Traditionally, acetone, 2,2-dimethoxypropane or 2-methoxypropene undergo condensation under acidic conditions with a diol, prepared via either hydrolysis of epoxides or osmium-catalyzed dihydroxylation of alkenes, to produce acetonides.[2]

Epoxides are attractive intermediates in organic synthesis due to their wide range of chemo-, regio- and stereo-selective transformations with concomitant ring opening.[3] Epoxides can be converted to acetonides directly catalyzed by a Lewis acid. Several procedures are reported in the literature for the preparation of acetonides from epoxides using Lewis acid catalysts such as $BF_3{\cdot}Et_2O$,[4] $SnCl_4$,[5] $SnCl_2$,[6] anhydrous $CuSO_4$,[7] 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TABCO),[8] tetracyanoethylene,[9] $Er(OTf)_3$,[10] $Cu(OTf)_2$,[11] $LiBF_4$,[12] Zeolite,[13] $K_5CoW_{12}O_{40}{\cdot}3H_2O$,[14] Sn(IV)(tpp)-$(OTf)_2$,[15] Bi(III)-salt,[16] $Fe(OTf)_3$,[17] $RuCl_3$,[18] $TiCl_4$,[19] $TiO(TFA)_2$,[20] K10-Montmorillonite,[21] CH_3ReO_3,[22] heteropolyacids[23]electro-generated acids,[24] and by other methods.[25] Table 1 shows a comparison between different reported procedures. However, there is still scope for further improvement in this field since most of the reported methods suffer from long reaction times, elevated temperatures, functional group intolerance and the use of expensive and toxic catalysts. Herein, we disclose a mild and efficient method for the direct conversion of epoxides to acetonides using inexpensive anhydrous Fe(III) chloride as the catalyst at room temperature in acetone as substrate and solvent (Scheme 1). In a preliminary



Scheme 1.

Table 1
A comparison of different reported procedures for the conversion of epoxides to acetonides

Ref.	Reagent used	Reaction conditions[a]	Yield[b] (%)
4	$BF_3{\cdot}Et_2O$	rt, 15–120 min	0–95
5	$SnCl_4$	40–50 °C, 80 min	22–35
6	$SnCl_2$	Reflux, 1–7 h	48–87
7	Anhyd $CuSO_4$	rt-reflux, 2–24 h	0–100
8	TABCO	reflux, 2.5–24 h	22–95
9	Tetracyanoethylene	rt-reflux, 0.5–48 h	0–87
10	$Er(OTf)_3$	rt, 0.5–48 h	30–99
11	$Cu(OTf)_2$	rt, 4 h	62–87
12	$LiBF_4$	Reflux, 15–120 min	90–96
13	Zeolite	Reflux, 1.5 h	11–56
14	$K_5CoW_{12}O_{40}{\cdot}3H_2O$	rt-reflux, 5–420 min	25–95
15	Sn(IV)(tpp)$(OTf)_2$	rt-reflux, 0.4–4 h	88–98
16	Bi(III)-salt	Reflux, 0.25–2.5 h	87–99
17	$Fe(OTf)_3$	Reflux, 2–5 h	85–92
18	$RuCl_3$	Reflux, 1.5–5 h	86–91
19	$TiCl_4$	−78 °C, 6 h	63–94
20	$TiO(TFA)_2$	rt, 10 min	92–98
21	K10-Montmorillonite	rt, 8 h	50–80
22	CH_3ReO_3	rt, 2–5 d	<5–39
23	Heteropolyacid	rt, 5 min	19–91
24	Electro-generated acid	rt, few min	30–97

[a] In most cases reflux in acetone.
[b] Range of yields refers to products derived from the different substrated.

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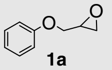
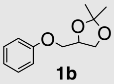
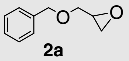
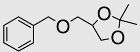
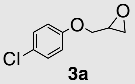
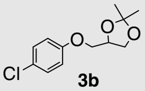
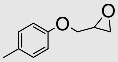
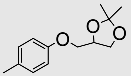
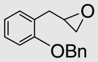
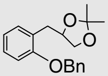
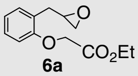
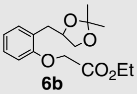
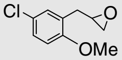
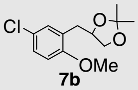
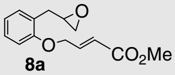
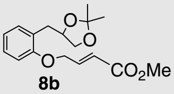
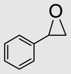
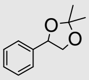
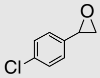
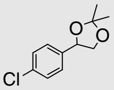
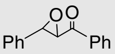
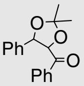
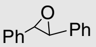
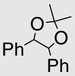
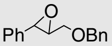
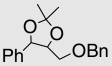
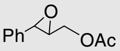
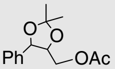
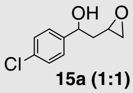
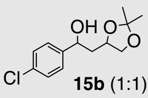
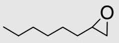
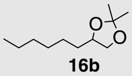
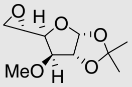
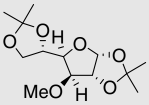
Table 2
Iron(III) chloride catalyzed synthesis of acetonides

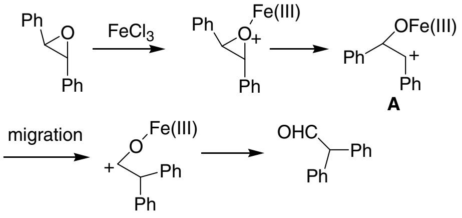
Entry	Epoxide	Product[a]	Time	Yield[b] (%)	Ref.
1	 **1a**	 **1b**	4.5 h	82	8,10
2	 **2a**	 **2b**	5 h	76	10
3	 **3a**	 **3b**	5 h	78	25
4	 **4a**	 **4b**	5 h	85	—
5	 **5a**	 **5b**	2.5 h	83	—
6	 **6a**	 **6b**	2 h	87	—
7	 **7a**	 **7b**	5 h	79	—
8	 **8a**	 **8b**	4 h	76	—
9	 **9a**	 **9b**	12 min	92	8,10
10	 **10a**	 **10b**	10 min	94	—
11	 **11a**	 **11b** (1:0.6)[c]	8 min	70	25b
12	 **12a**	 **12b** (1:0.5)[c]	6 min	69	11
13	 **13a**	 **13b** (1:1)[c]	15 min	84	—
14	 **14a**	 **14b** (1:1)[c]	18 min	76	25c
15	 **15a (1:1)**	 **15b** (1:1)[c]	3 h	73	—
16	 **16a**	 **16b**	4 h	89	6,9
17	 **17a**	 **17b**	8 h	74	28

[a] All products were characterized by IR, NMR and HRMS.
[b] Yield refer to pure isolated products.
[c] Isomeric ratios were determined from ^{1}H NMR spectra.

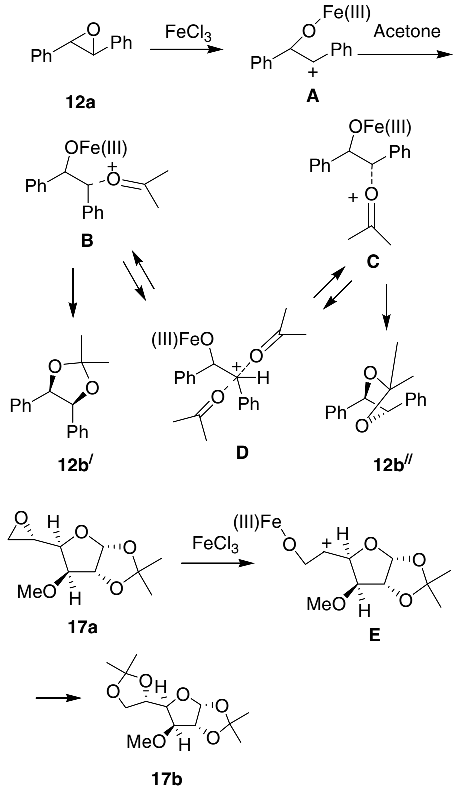
experiment, epoxide **1a** was stirred in the presence of 5 mol % anhydrous $FeCl_3$ and acetone at room temperature for 4.5 h to produce the acetonide **1b** in 82% yield.[26] It was observed that a minimum of 5 mol % of catalyst was required to obtain the optimum yield of the product. Thus, a series of epoxides were subjected to the reaction conditions, and the results are summarized in Table 2. The reaction proceeds smoothly with aliphatic, styrene and α-keto epoxides to yield the corresponding acetonides in excellent yields. All the products gave satisfactory spectral data and were compared with reported values. In all cases, the acetonide exhibited two separate singlets between δ 1.2 and 1.7 for the methyl groups in the ^{1}H NMR spectra and two signals between δ 25 and 27 in the ^{13}C NMR spectra.

Conversion of styrene epoxides **9a**–**14a** to the corresponding 1,3-dioxolanes was much faster than the conversion of aliphatic epoxides. This can be rationalized by the stability of the benzylic carbonium ion formed during epoxide cleavage. Epoxides **11a** and **12a** were also converted to the corresponding acetonides but a small amount of aldehyde was observed as a side product due to rearrangement of the oxiranes to carbonyl compounds.[11] Formation of the aldehyde proceeds via coordination of Fe(III) to the oxygen atom of the epoxide followed by C–O bond cleavage to form an electron-deficient carbon centre. Then, the aryl substituent migrates to the adjacent carbon centre with simultaneous formation of a carbonyl compound (Scheme 2).

It is noteworthy that *trans*-epoxides **11a**–**14a** resulted in diastereomeric mixtures of acetonides in different ratios, which were determined from the ^{1}H NMR spectra of the crude reaction products. On the other hand, a 1:1 mixture of the epoxide **15a** furnished acetonide **15b** as a mixture of isomers in the same ratio. In contrast, the enantiopure epoxide **17a** (entry 17)[27] furnished solely 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**17b**) where the stereochemistry is retained in the product.[28] The stereoselectivity of the products can be rationalized by analogy with Hanzlik.[7] The loss of stereochemistry from the epoxides **11a**–**14a** must be due to the formation of a common symmetrical intermediate, such as **D** for example, from which both products could be formed (Scheme 3). Thus, because of the greater stability of the benzylic carbonium ion **A** generated from **11a** to **14a**, formation of complexes **B** and **C**



Scheme 2.



Scheme 3.

requires relatively little nucleophilic assistance or solvation from acetone and is inter-convertible through the common intermediate **D**. As a result, the epoxide **12a** gave acetonide **12b** as a mixture of two isomers **12b′** and **12b″**. In contrast, opening of epoxide **17a** probably requires much more assistance from the acetone carbonyl due to the reduced stability of the non-benzylic carbonium ion **E**, and thus acetonide formation is completely stereospecific leading to **17b** as the sole product. There may be other factors which control the approach of the acetone molecule to furnish **17b** exclusively. Sensitive functional groups such as chloride, methyl and benzyl ethers, esters and hydroxyl remained unaffected under the reaction conditions.

In conclusion, we have developed a mild and efficient method for the conversion of epoxides to acetonides using cheap and commercially available Fe(III) chloride as the catalyst. This reaction worked smoothly for a wide range of epoxides.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.07.147.

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26. *Typical procedure*: To a well-stirred solution of **1a** (150 mg, 1.0 mmol) in acetone (10 mL), anhydrous $FeCl_3$ (8 mg, 0.05 mmol) was added at room temperature. After completion of the reaction (monitored by TLC) it was quenched with saturated aqueous sodium bicarbonate solution, and the volatiles were removed under reduced pressure. The residue obtained was extracted with ether (2×50 mL). The combined ether extract was washed successively with water (20 mL), brine (20 mL) and finally dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue obtained was purified by column chromatography over silica gel (5% ethyl acetate in petroleum ether) to obtain pure acetonide **1b** (170 mg, 82%) as a crystalline solid, mp 65–67 °C. IR (neat): 2977, 1602, 1456, 1255 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (s, 3H), 1.47 (s, 3H), 3.88–3.97 (m, 2H), 4.07 (dd, $J = 5.4, 9.5$ Hz, 1H), 4.17 (dd, $J = 6.6, 8.4$ Hz, 1H), 4.45–4.52 (m, 1H), 6.91–6.99 (m, 3H), 7.29 (appeared as a triplet, $J = 8.2$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.5, 26.9, 67.0, 68.8, 74.1, 109.8, 114.6 (2C), 121.2, 129.6 (2C), 158.7; HRMS: calcd for $C_{12}H_{16}O_3Na$ 231.0997 $[M+Na]^+$, found 231.0995.
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