

Iron Perchlorate on Silica Gel as Multi-purpose Reagent for Catalysis of Closure and Rupture of Carbon–Oxygen Bond in Epoxides, Alcohols, and Esters

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Received September 4, 2002

Abstract—Aliphatic alcohols and water in the presence of catalytic amounts of Fe³⁺ ion introduced as iron(III) perchlorate on silica gel carrier perform efficient regiospecific opening of an epoxy ring. Carbon acids esterification with various type alcohols was carried out using the system Fe(ClO₄)₃-silica gel in dichloromethane under conditions excluding solvolysis. Acetylation and formylation of alcohols was performed by efficient transesterification with ethyl acetate and ethyl formate.

Olefin epoxidation followed by regioselective opening of the epoxy ring is an efficient preparation method of compounds with versatile functional groups [1, 2]. β-Alkoxyalcohols constitute an important class of organic compounds for this type of functionality frequently appears in natural substances and also because their oxidation is the easiest way of preparation of α-alkoxycarboxylic acids [3]. The most general procedure for epoxides alcoholysis consists in treating them with an appropriate alcohol in acidic medium where the same alcohol serves as solvent [4, 5]. However this method not always ensures sufficient yield, and in some cases a mixture of regioisomers is obtained.

The simplest method of esters synthesis is direct reaction between alcohols and carboxylic acids. Nowadays the esterification is often carried out under catalysis of transition metal salts [6–12], and in most published procedures an excess of alcohol or acid is applied. However this method is inapplicable when both reagents are solids or if they are expensive. Therefore the task of developing new esterification procedures in the presence of an inert solvent is urgent.

Another classical method of esters preparation is transesterification [13], and in some cases it is more desirable. The conversion of one ester into another is especially valuable when the initial carboxylic acids are labile and difficult to isolate. This is true in respect to formates synthesis that is carried out at stringent conditions: The alcohol is heated in 85%

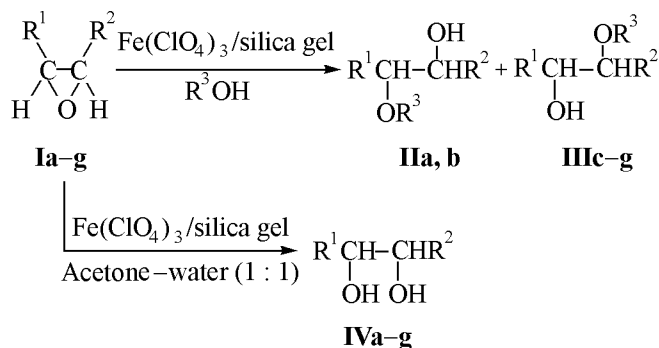
formic acid [14] or in *N,N*-dimethylformamide [15]. Since the formic anhydride and the formyl chloride are unstable compounds the development of alcohol formylation methods under mild conditions is very important. Recently a number of acidic reagents was used in esterification procedures (see, e.g., [16, 17].

The iron(III) perchlorate is a versatile reagent. One of its disadvantages is hygroscopicity that limits the scope of its laboratory applications. However on applying Fe(ClO₄)₃ on silica gel a stable nonhygroscopic reagent is obtained that can be used without special precautions [18].

In extension of our studies on application of iron(III) perchlorate for catalysis of closure and rupture of carbon–oxygen bonds in organic compounds [19, 20] and in order to show the possibilities provided by this versatile reagent we report here on efficient regioselective epoxy ring opening with aliphatic alcohols and water, and also on the synthesis of esters by esterification and transesterification in the presence of catalytic amounts of iron(III) perchlorate on silica gel carrier.

We studied reactions of epoxides with primary, secondary, and tertiary alcohols in the presence of 0.05–0.15 mol-equiv of Fe³⁺ ion, and β-alkoxyalcohols were obtained in good and even excellent yields, with high regioselectivity.

The nucleophile attack on the sterically more hindered carbon of styrene oxide (**Ia**) indicates that the reaction is controlled by electronic effect. The



$\text{R}^1 = \text{Ph}, \text{R}^2 = \text{H}$ (a); $\text{R}^1 + \text{R}^2 = -(\text{CH}_2)_4-$ (b);
 $\text{R}^1 = \text{Bu}, \text{R}^2 = \text{H}$ (c); $\text{R}^1 = \text{ClCH}_2, \text{R}^2 = \text{H}$ (d);
 $\text{R}^1 = \text{BuOCH}_2, \text{R}^2 = \text{H}$ (e); $\text{R}^1 = \text{PhOCH}_2, \text{R}^2 = \text{H}$ (f);
 $\text{R}^1 = \text{CH}_2=\text{CHOCH}_2, \text{R}^2 = \text{H}$ (g); $\text{R}^3 = \text{Me}, \text{Et}, \text{Pr}, i\text{-Pr}, t\text{-Bu}$.

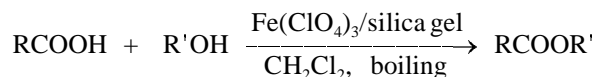
methanolysis of the optically active styrene oxide (-)(**Ia**) in the presence of $\text{Fe}(\text{ClO}_4)_3/\text{silica gel}$ afforded the corresponding (-)- β -methoxyalcohol (**IIa**) with nearly totally reversed configuration (optical yield 94%). This fact evidences that the nucleophile attack and the opening of epoxide ring occur simultaneously. Similar behavior was observed also for cyclohexene oxide (**Ib**) which gave rise only to isomers of vicinal alkoxyalcohols (**IIb**, $\text{R}^3 = \text{Me}, \text{Et}, \text{Pr}, i\text{-Pr}, t\text{-Bu}$) in 85–95% yield.

With 1,2-epoxyhexene (**Ic**) the prevailing site of nucleophile attack is the less hindered carbon atom; it means that here the reaction direction depends on the sterical factor, and compounds **IIIc** form as a result (**IIIc**, $\text{R}^3 = \text{Me}, i\text{-Pr}, t\text{-Bu}$). In compounds **Id-g** containing electron-withdrawing groups attached to the epoxide ring the steric and electronic effects direct the nucleophile attack in a similar way, and it occurs at the less shielded carbon atom providing compounds **IIIId-g**. These reactions are chemoselective leaving intact the other carbon-oxygen bonds in ethers and also the carbon-halogen and double carbon-carbon bonds.

We also investigated hydrolysis of epoxides in the presence of catalytic amounts of iron(III) perchlorate on silica gel. The reaction was carried out in a mixture of equal volumes of acetone and water, and it gave rise to vicinal diols **IVa-g** in excellent yields. For instance, from cyclohexane oxide (**Ib**) *trans*-cyclohexane-1,2-diol (**IVb**) was obtained in 90% yield.

The direct esterification with various acids and alcohols we performed in dichloromethane. Reactions of acetic and butyric acids with saturated, cyclic, benzyl, and allyl alcohols were successfully run in the presence of 0.1–0.4 mol-equiv of Fe^{3+} in di-

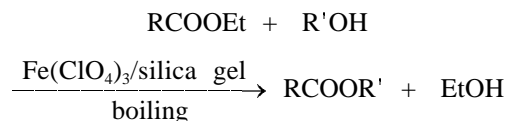
chloromethane within 5–19 h. Similar reactions were also carried out with benzoic and cinnamic acids to obtain the corresponding esters in good or excellent yields (70–92%).



$\text{R} = \text{Me}, \text{Pr}, \text{Ph}, \text{PhCH}=\text{CH}$; $\text{R}' = \text{CH}_3(\text{CH}_2)_7, \text{CH}_3(\text{CH}_2)_4\text{CH}(\text{CH}_3), \text{cycloheptyl}, \text{PhCH}=\text{CHCH}_2, \text{Bn}, 4\text{-ClC}_6\text{H}_4\text{CH}_2$.

One of the most important drawbacks of the solvolytic esterification is impossibility to perform a process between two solid substances. However our method makes possible such reactions in the presence of an inert solvent. As examples may be cited the reactions of benzoic and cinnamic acids with 4-chlorobenzyl alcohol which furnished the corresponding esters in 91 and 84% yields respectively.

The system $\text{Fe}(\text{ClO}_4)_3$ -silica gel can be useful as a catalyst for acetylating and formylating alcohols of various structure with ethyl acetate and ethyl formate.



$\text{R} = \text{Me}, \text{H}$; $\text{R}' = \text{CH}_3(\text{CH}_2)_7, \text{CH}_3(\text{CH}_2)_4\text{CH}(\text{CH}_3), \text{cyclooctyl}, \text{cycloheptyl}, 4\text{-ClC}_6\text{H}_4\text{CH}_2, 4\text{-BrC}_6\text{H}_4\text{CH}_2, \text{Bn}, \text{C}_6\text{H}_5\text{CH}=\text{CHCH}_2$.

Primary and secondary aliphatic alcohols as well as alicyclic hydroxy derivatives within 3–5 h were converted into the corresponding esters in good yield. Also benzyl and allyl alcohols were acetylated and formylated in one stage with fair yields within 4–5 h.

These new methods have the following outstanding characteristics: catalytic character, high regio- and chemoselectivity, stability of the reagent, and high product yield. They also possess the chemical and economical advantages inherent to the application of reagents fixed on solid carriers, in particular, the simple work-up of the reaction mixtures. The reaction products were characterized by comparison of their IR and ^1H NMR spectra and physical properties with the published data.

EXPERIMENTAL

IR spectra were run on spectrometer Shimadzu 470. The ^1H NMR spectra were registered on Bruker Avance instrument at operating frequency 200 MHz. Optical rotation was measured on a potentiometer

Perkin Elmer 240 Mc. The purity of compounds was checked and the reaction progress was monitored by GLC on a gas chromatograph Shimadzu GC 8A equipped with a flame-ionization detector, or by TLC on silica gel plates (SIL G/UV 254, Merck).

Iron(III) perchlorate on silica gel. A solution of 1 g of $\text{Fe}(\text{ClO}_4)_3$ in 10 ml of ethanol was added to a suspension of 10 g of silica gel (Merck, Kieselgel 40, 70–230 mesh) in 30 ml of ethanol. The mixture was stirred for 30 min and evaporated in a vacuum. The brown powder obtained was further dried in a vacuum drying cabinet at 60°C and reduced pressure (20 mm Hg).

Epoxides alcoholysis. Iron(III) perchlorate on silica gel (0.08–1.16 g) containing 0.02–0.3 mmol of Fe^{3+} ion was added to a solution of epoxide (2 mmol) in 7 ml of alcohol. The mixture was stirred at room temperature for the required time (from 1 min to 8 h). The reaction was monitored by GLC. Then the mixture was passed through a short column packed with silica gel and backwashed with ethyl ether (50 ml). The ether solution was dried on CaCl_2 and evaporated in a vacuum to obtain the corresponding β -alkoxy-alcohol of high purity in 75–96% yield.

Hydrolysis of epoxides. To a solution of 2 mmol of epoxide in 7 ml of acetone–water mixture (1:1 by volume) was added iron(III) perchlorate on silica gel (0.08–0.78 g) containing 0.02–0.2 mmol of Fe^{3+} ion, and the reaction mixture was stirred at room temperature or at reflux. On completion of the reaction the mixture was passed through a short column packed with silica gel and backwashed with ethyl ether (50 ml). The ether solution was dried on CaCl_2 and evaporated in a vacuum to obtain the corresponding vicinal diols in 75–95% yield.

Esterification of carboxylic acids with alcohols in the presence of iron(III) perchlorate on silica gel in dichloromethane. To a solution of alcohol (2 mmol) and acid (6 mmol) in 7 ml of dichloromethane was added iron(III) perchlorate on silica gel (0.2–1.0 mmol of Fe^{3+}), and the mixture was stirred at reflux till the completion of the reaction. Then 50 ml of ether was added and the mixture was filtered. The filtrate was twice washed with 10% water solution of NaHCO_3 and with water. The organic layer was separated and dried on MgSO_4 . The solvent was evaporated, the residue was submitted to chromatography on a short column packed with silica gel using as eluent hexane–ether mixture. Yields of reaction products were 70–90%.

Acetylation and formylation of alcohols with ethyl acetate and ethyl formate. A mixture of an

alcohol (2 mmol) and iron(III) perchlorate on silica gel (2.34–3.9 g corresponding to 0.6–1.0 mmol of Fe^{3+}) was stirred at reflux in 6 ml of ethyl acetate or ethyl formate for a period required for completion of the reaction (TLC monitoring). The solvent was removed in a vacuum, to the residue was added ethyl ether (50 ml). The mixture was filtered, and the filtrate was dried on Na_2SO_4 . Then it was evaporated and passed through a short column packed with silica gel. Esters were obtained in 65–92% yield.

The authors are grateful to the Scientific Council of the Razi University for financial support.

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