

# Green synthesis of methyl trifluoropyruvate catalyzed by solid acids

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## Abstract

Solid acids –  $\text{NiSO}_4/\text{Al}_2\text{O}_3$ ,  $\text{Fe}_2(\text{SO}_4)_3/\text{Al}_2\text{O}_3$  and  $\text{TiO}_2/\text{SO}_4^{2-}$  – appeared to be effective catalysts for the acid catalyzed synthesis of methyl ester of trifluoropyruvic acid. They are active at 150–180 °C.

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## 1. Introduction

The methyl ester of trifluoropyruvic acid ( $\text{CF}_3\text{COCOOME}$ , MTFP) is a valuable  $\text{C}_3$  fluorinated synthon for organofluorine chemistry [1,2]. As a rule, MTFP is synthesized *via* a two-step procedure starting from hexafluoropropylene oxide [1,3] (Scheme 1).

The key step of this transformation is a decomposition of 2-alkoxytetrafluoropropionic acid ester (**A**) catalyzed by concentrated sulfuric acid (reactions of this type are widely used in organofluorine chemistry [4]). This step is usually performed at elevated temperature (150–170 °C) and very large amount of the acid catalyst (up to 3.8 moles of  $\text{H}_2\text{SO}_4$  for 1 mole of the starting ester) is used. To minimize the amount of acid wastes from this reaction we paid attention to a novel class of solid acids – nickel (II) and iron (III) sulfates supported on  $\text{Al}_2\text{O}_3$ ,  $\text{TiO}_2$  and  $\text{ZrO}_2$  [5–9] and sulfated titania [10] –  $\text{TiO}_2/\text{SO}_4^{2-}$ . These acids are stronger than 100%  $\text{H}_2\text{SO}_4$  [11], and, hence, they are considered to possess superacidic properties [12]. Their catalytic properties for the purposes of organic synthesis are practically not investigated—ethylene dimerization [5–8], cumene dealkylation, 2-propanol dehydration [9] and some condensations [10] are described in a literature.

## 2. Results and discussion

In order to investigate the possible catalytic properties of these solid acids in the reaction in Scheme 1, we have prepared a number of catalyst samples with varied amount of the inorganic sulfate on supporting  $\text{Al}_2\text{O}_3$ . A heterogeneous mixture of the ester **A** and a catalyst was heated in a steel bomb and products were investigated by  $^{19}\text{F}$  NMR. The results are summarized in Table 1.

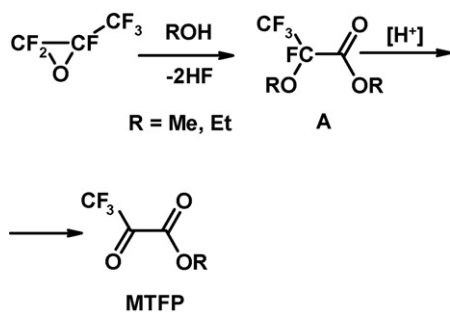
The acid  $\text{TiO}_2/\text{SO}_4^{2-}$  had the highest activity of all catalysts investigated (entry 5). Aluminium oxide sulfated by the same procedure as  $\text{TiO}_2/\text{SO}_4^{2-}$  was significantly less active (entry 6). It is seen from Table 1 that there exists an optimal concentration of the sulfate salt in the catalyst—10% for  $\text{NiSO}_4$  and 2–5% for  $\text{Fe}_2(\text{SO}_4)_3$ , the latter being more active. Pure  $\text{Al}_2\text{O}_3$  was absolutely inactive (entry 1). At 180 °C the reaction yield was much higher than at 150 °C (entries 8, 9). Regenerated catalyst was a little bit less active than a freshly prepared one (entries 8, 12).

The mechanism of the sulfuric acid catalyzed decomposition of **A** has been recently investigated thoroughly [1]. The authors have found that the reaction begins with a protonation of an ether oxygen, followed by methyl sulfate formation as a primary  $\text{CH}_3$ -containing by-product. Gaseous reaction products were supposed to consist mainly of carbon oxide CO, though no evidence of its formation was given.

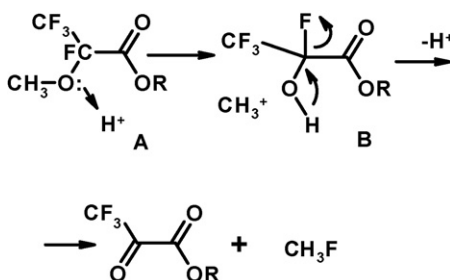
We have investigated the gaseous products of our reaction and have found that they contained a significant amount of methyl fluoride  $\text{CH}_3\text{F}$  together with traces of the starting ester

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Scheme 1.



Scheme 2.

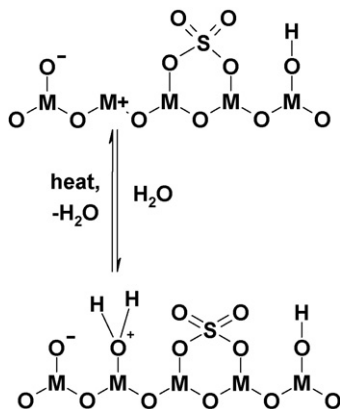
A, MTFP and unidentified CF<sub>3</sub>-containing compound, probably CF<sub>3</sub>COOMe.

In a special experiment we have analyzed the gas phase from an H<sub>2</sub>SO<sub>4</sub>-catalyzed reaction (like in [1]) and have found no traces of methyl fluoride.

The obtained data show that the mechanism and products distribution can vary depending on the catalyst used. In a case of sulfated metal oxides an immobilized sulfate cannot serve as a nucleophile and, hence, a methyl group “finds” another nucleophile (fluoride) to form CH<sub>3</sub>F.

In all cases the reaction probably begins with a proton attack on an ether oxygen followed by CH<sub>3</sub>-O bond splitting. Then in our case HF releases from the intermediate  $\alpha$ -fluoroalcohol B forming methyl fluoride (Scheme 2).

The difference in a catalytic activity of titanium, iron and nickel sulfates can be explained by the different chemical nature of their acidity. Solid superacids, namely sulfated metal oxides, usually contain both Lewis (M<sup>+</sup>) and Brønsted (H<sup>+</sup>) acid



Scheme 3.

Table 1  
Solid acids catalyzed synthesis of methyl trifluoropyruvate

Entry	Catalyst <sup>a,b</sup>	MTFP content (%) <sup>c</sup>
1	Al <sub>2</sub> O <sub>3</sub>	0
2	5% NiSO <sub>4</sub> /Al <sub>2</sub> O <sub>3</sub>	18
3	10% NiSO <sub>4</sub> /Al <sub>2</sub> O <sub>3</sub>	29
4	20% NiSO <sub>4</sub> /Al <sub>2</sub> O <sub>3</sub>	16
5	(NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub> /TiO <sub>2</sub>	88
6	(NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub> /Al <sub>2</sub> O <sub>3</sub>	28
7	2% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub>	63
8	5% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub>	58
9	5% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub>	95
10	10% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub>	35
11	20% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub>	46
12	5% Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> /Al <sub>2</sub> O <sub>3</sub> regenerated	54

<sup>a</sup> All samples were calcined at 500 °C during 7 h before a reaction.

<sup>b</sup> Reaction time was 7 h in all cases. Reaction temperature was 150 °C except for entry 9 (180 °C).

<sup>c</sup> Determined by <sup>19</sup>F NMR (see Section 4).

centers [12] (Scheme 3), whereas NiSO<sub>4</sub>/Al<sub>2</sub>O<sub>3</sub> is considered to have mainly Lewis acid centers on the surface [13].

As a consequence a hindered ether oxygen is much easier reached by a small proton than by a Lewis metal atom on the surface.

### 3. Conclusion

This method of methyl trifluoropyruvate synthesis significantly reduces the amount of acid wastes during the preparation procedure. For example, only  $9.3 \times 10^{-5}$  moles of a sulfate salt is used for  $5.3 \times 10^{-3}$  moles of the starting ester A (in the case of 5% Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>), compared with  $2 \times 10^{-2}$  moles of concentrated H<sub>2</sub>SO<sub>4</sub> in a literature procedure.

### 4. Experimental

#### 4.1. General experimental procedure

<sup>1</sup>H and <sup>19</sup>F NMR spectra were recorded using Bruker DPX-200 spectrometer with TMS and CFC<sub>3</sub> as external standards respectively. Methyl ester of 2-methoxytetrafluoropropionic acid A and MTFP were synthesized by a literature procedure [3], their <sup>1</sup>H and <sup>19</sup>F NMR spectra coincided with those described in [1]. NiSO<sub>4</sub>·7H<sub>2</sub>O, Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>·5H<sub>2</sub>O (Acros) and  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (Engelhardt E-800, 200 m<sup>2</sup>/g) were used as purchased.

#### 4.2. Catalyst preparation

A known amount of a metal sulfate was dissolved in water, Al<sub>2</sub>O<sub>3</sub> (small sticks) was added to this solution and the solvent was removed using a rotary evaporator till dryness. The prepared catalyst was then dried in an oven at 120 °C during 1 h. TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup> was prepared by a procedure described in [10].

### 4.3. Catalytic experiment

The catalyst (2 g) was calcined in a quartz tube reactor under conditions shown in Table 1. A reactor was periodically flushed by a stream of dry air for removing of water vapor. A catalyst sample was cooled to 200–250 °C and then was quickly transferred to a stainless steel bomb, which was then sealed to let a catalyst cool under water-protected conditions. A bomb was opened; a sample of the ester **A** (2.7 g,  $1.42 \times 10^{-2}$  mole) was added to a catalyst, a bomb was sealed again and heated as shown in Table 1 with periodical shaking. After cooling the gas from a bomb was passed through  $\text{CDCl}_3$ , a bomb was opened and a reaction mixture was analyzed by  $^{19}\text{F}$  NMR (188 MHz;  $\text{CDCl}_3$ ). The content of MTFP in reaction mixtures was determined by comparison of the ester **A**.  $-80.5$  (3F, d,  $\text{CF}_3$ ,  $^3J_{\text{F-F}} = 3$  Hz),  $-133.5$  (1F, m, CF) and MTFP.  $-74.0$  (s,  $\text{CF}_3$ ) signals. A  $^{19}\text{F}$  NMR spectrum of a gas phase contained a signal of methyl fluoride ( $-266.5$ , q,  $^2J_{\text{F-H}} = 46.4$  Hz [14]) as a main product and signals of the ester **A**, MTFP and  $-82.0$  ppm, probably  $\text{CF}_3\text{COOMe}$ .

In a preparative experiment 13.5 g ( $7.1 \times 10^{-2}$  mole) of the ester **A**, 5 g of sulfated titania (calcined at 600 °C during 2 h) were heated in autoclave at 150 °C during 7 h with periodical shaking. After cooling a liquid part of the reaction mixture was

separated from the catalyst by centrifugation and distilled using a high, vacuum jacketed column. Methyl trifluoropyruvate, MTFP, was obtained in a 50% yield (5.5 g,  $3.5 \times 10^{-2}$  mole). b.p. 85–87 °C.  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ): 4.0 (s).

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