

# Diphosponium fluorosulfonate reagent as a dehydrating agent in organic synthesis

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## Abstract

A facile, one-pot dehydration of organic substrates is afforded by the 'diphosponium fluorosulfonate' reagent,  $\text{Ph}_3\text{P}^+\text{OP}^+\text{Ph}_3 \cdot 2\text{SO}_3\text{F}^-$ . This reagent has been used to convert acids to anhydrides, acid and alcohols to esters, acids and amines to amides and in double dehydrations to form heterocycles.

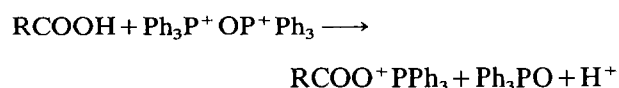
## Introduction

Hendrickson and Hussoin [1, 2] have reported that the trifluoromethanesulfonate derivative  $\text{Ph}_3\text{P}^+\text{OP}^+\text{Ph}_3 \cdot 2\text{SO}_3\text{CF}_3^-$  is a good reagent for the activation of oxygen to effect its removal in an isohypsic manner from organic molecules. Thus, it was found to convert carboxylic acids to anhydrides, esters, amides, amidines, benzimidazoles and cyclic aryl ketones in good yield. We have reported earlier [3] the synthesis and characterization of the fluorosulfonate analogue,  $\text{Ph}_3\text{P}^+\text{OP}^+\text{Ph}_3 \cdot 2\text{SO}_3\text{F}^-$ . In this communication, we report its use as a reagent to extract oxygen from organic moieties, causing a net loss of water molecules and thus showing promise as an 'ideal dehydrating agent'. No application of this nature in fluorosulfonate chemistry has been reported previously in the literature to the best of our knowledge.

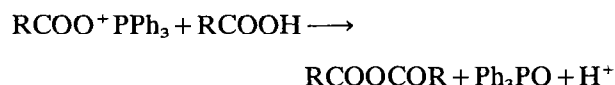
## Results and discussion

The reactions were carried out with the 'diphosponium fluorosulfonate' reagent generated *in situ*. A detailed mechanism describing the dehydration reactions involving the 'trifluoromethanesulfonate' derivative has been described by Hendrickson and Hussoin [2]. Probably, a similar mechanism is operative in the case of the 'fluorosulfonate' analogue.

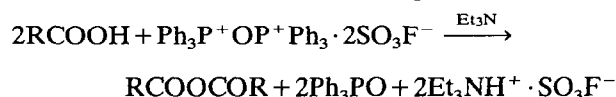
The carboxylic acid was activated as expressed in the following equation:



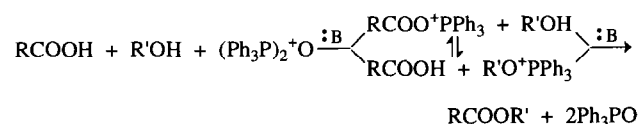
In such a situation, either elimination can occur at the  $\alpha$ -CH giving a ketene, or else there can be substitution by a nucleophile, e.g. another carboxylic acid, alcohol or amine, to form the corresponding anhydride, ester or amide in the presence of a base. Anhydride formation is illustrated below:



The overall reaction may be represented as:



With reactions involving an alcohol and an acid, oxygen activation by the 'phosponium' anhydride may occur at either oxygen. If the carboxylate is activated first, the ester should form via acylation of the alcohol. If the alcohol is activated first, the carboxylate may still displace the  $\text{ROPR}_3^+$  group to create an ester by O-alkylation. If, however, there is a fast exchange of phosponium between the activated acid and alcohol, either mode of ester formation may proceed. These three paths are summarized below:



A similar pathway is followed when using a mixture of acid and amine to form the amide.

When there are two functional centres in a substrate at which the 'diphosponium' reagent can attack, it seems reasonable that an acid nucleophile will allow

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TABLE 1. Reaction conditions and products obtained using 'diphosphonium fluorosulfonate' reagent

Starting materials		Conditions/work-up	Product <sup>d</sup>	Yield (%) (m.p. °C)
Acid	Nucleophile			
<i>p</i> -Toluic acid <sup>a</sup>	<i>p</i> -Toluic acid	a	<i>p</i> -Toluic anhydride	89 (92–93)
Phenylacetic acid	Phenylacetic acid	a	Phenylacetic anhydride	90 (Oil)
<i>p</i> -Toluic acid	Methanol	b	Methyl <i>p</i> -toluate	72 (Oil)
<i>p</i> -Toluic acid	Ethanol	b	Ethyl <i>p</i> -toluate	82 (Oil)
<i>p</i> -Toluic acid	Aniline	b	<i>N</i> -Phenyl- <i>p</i> -toluamide	89 (149)
<i>p</i> -Toluic acid	<i>p</i> -Toluidine	b	<i>N-p</i> -Tolyl- <i>p</i> -toluamide	78 (158–160)
Benzoic acid	<i>o</i> -Phenylenediamine	c	<i>o</i> -Phenylenebenzimidazole	83 (287)
<i>p</i> -Toluic acid	<i>o</i> -Aminophenol	c	2- <i>p</i> -Tolyl-benzoxazole	80 (84)

<sup>a</sup>Stirring (15 min) and solution passed through a short column of silica (4:1 hexane/ethyl acetate).

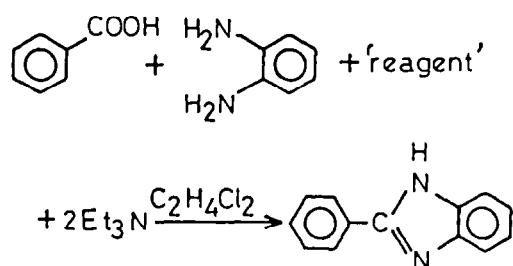
<sup>b</sup>Stirring (15 min) after which contents washed (3x) with 5% aqueous sodium bicarbonate, water and brine, dried over sodium sulfate, evaporated and the residual oil passed through a short column of silica (6:1 hexane/ethyl acetate).

<sup>c</sup>Stirring (30 min) and the remaining procedure as in b.

<sup>d</sup>Products identified by IR/NMR spectroscopy.

<sup>e</sup>This reaction was carried out with direct addition of the 'reagent' as well as generating the 'reagent' *in situ*. The products and yields in both cases were identical. Other reaction conditions remained the same.

a double dehydration to take place. For instance, benzoic acid and *o*-phenylenediamine in the presence of 2 mol of the reagent and a base generate 2-benzyl-benzimidazole in 83% yield. This simple procedure contrasts sharply with the traditional procedure [4] which requires more stringent conditions.



Other conversions are listed in Table 1.

## Experimental

In a typical experiment, fluorosulfonic anhydride,  $S_2O_5F_2$  (0.46 g, 2.5 mmol) [5], was condensed on to a solution of triphenylphosphine oxide (1.39 g, 5 mmol) in 15 ml of ethylene dichloride,  $C_2H_4Cl_2$ . Precipitates appeared after the contents were allowed to come to room temperature, when a solution of *p*-toluic acid (0.68 g, 5 mmol) in 10 ml of ethylene dichloride was added followed by 0.57 ml of anhydrous triethylamine. The contents were stirred for 15 min. When all had dissolved and a clear solution obtained, this was passed

through a short column of silica (4:1 hexane/ethyl acetate) to remove triphenylphosphine oxide. Evaporation of the solvent gave 0.565 g (89%) of *p*-toluic anhydride (m.p. 92–93 °C).

The IR spectra of the compounds were recorded on a Perkin-Elmer PE 1430 ratio recording spectrophotometer as neat liquids/Nujol mulls between AgCl plates. The  $^1H$  NMR spectra in  $CDCl_3$  were recorded on a Varian EM-390 spectrometer at 90 MHz. The observed IR frequencies and NMR chemical shift values agreed well with the reported data [2].

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