

Received: February 9, 1988; accepted: February 24, 1988

PRELIMINARY NOTE

Reaction of Fluorinated Ketones with Dialkyl Phosphites: An Efficient and Selective Transformation of Aryl F-Alkyl Ketones into Dialkyl Aryl(F-alkyl)methyl Phosphates

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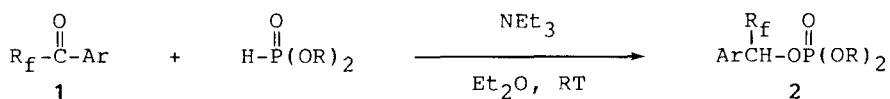
SUMMARY

Aryl F-alkyl ketones smoothly reacted with a variety of dialkyl phosphites in the presence (or absence) of a tertiary amine to give the corresponding dialkyl aryl(F-alkyl)methyl phosphates in high yields. The reaction of methyl F-phenyl ketone with the sodium salt of diethyl phosphite afforded a good yield of diethyl 1-(F-phenyl)ethyl phosphate. This reaction offers a new supplemental route to various polyfluorinated esters of phosphoric acid. A possible mechanism for the reaction is also described briefly.

In recent years, we have been investigating the reactions and synthetic applications of F-alkyl-containing carbonyl compounds such as carboxylic acids and ketones in order to expand their chemistry [1-11]. Quite recently, we reported the reaction of chlorodifluoromethyl ketones with di- or triethyl phosphite, together with some evidence elucidating successfully the Perkow reaction of α -halo ketones [11].

During the course of our studies on the reaction between F-alkyl ketones and nucleophilic trivalent phosphorus compounds, we have found that various aryl F-alkyl ketones (1)

are readily converted to the corresponding aryl(F-alkyl)methyl phosphates (2) in high yields on treatment with dialkyl phosphite in the presence of a tertiary amine at room temperature. This unique type of reaction is regarded as a formal reduction of 1 to their alcoholic derivatives and can serve as a simple and efficient alternative to the method for preparing F-alkyl-substituted esters of phosphoric acid (Scheme 1).



Scheme 1

To a solution of phenyl trifluoromethyl ketone (1) and triethylamine (1.2 equiv.) in diethyl ether was added dropwise diethyl phosphite (1.2 equiv.) at room temperature under an argon atmosphere. After stirring for 3.5 h at the same temperature, the mixture was diluted with ether, washed with 5% sodium hydrogen carbonate solution, dried over sodium sulfate, and was concentrated under reduced pressure. The residue was chromatographed on silica gel to give pure diethyl phenyl(trifluoromethyl)methyl phosphate (2)[†] in an 88% yield (Entry 1). The results of the reaction are summarized in Table 1.

This reaction occurred even by the use of a small amount (0.1 equiv.) of triethylamine, though the reaction time became long (Entry 2). The reaction conducted without triethylamine required the refluxing of benzene (Entry 3). Various aryl F-alkyl ketones 1 and F-phenyl methyl ketone (Entry 11) were converted under the similar conditions to the corresponding phosphates 2 in good yields. Diisopropyl (Entry 4), dibutyl (Entries 5 and 9), and diphenyl phosphite (Entry 6) were also applicable to the reaction, instead of diethyl phosphite.

Noteworthy is that the present reaction leading to 2 is a characteristic reaction of aryl F-alkyl ketones (1) [12,13]: The similar treatment of an alkyl F-alkyl ketone with diethyl phosphite in the presence of triethylamine did not produce the

[†] The spectral and analytical data pertaining to all isolated compounds were consistent with the assigned structures.

TABLE 1

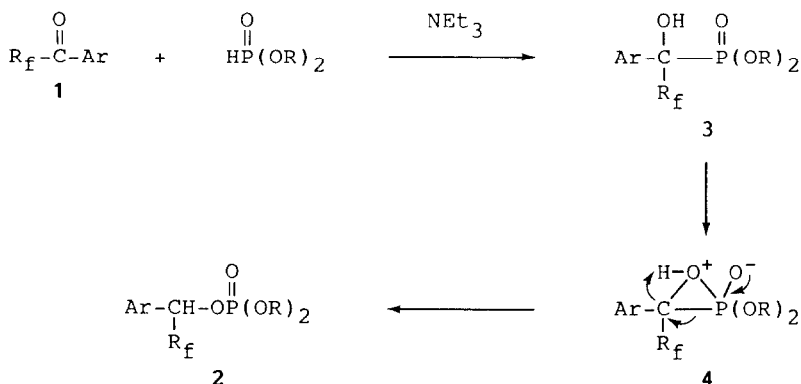
Conversion of fluorinated ketones **1** into the phosphates **2**^a

Entry	Ketone 1	Time h	Product 2	Yield ^b %
1	CF ₃ COPh	3.5	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{OEt})_2$	88
2	CF ₃ COPh	28	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{OEt})_2$	88 ^c
3	CF ₃ COPh	16	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{OEt})_2$	88 ^d
4	CF ₃ COPh	48	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{OPr-}i)_2$	68
5	CF ₃ COPh	6.5	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{O}Bu)_2$	95
6	CF ₃ COPh	0.5	$\text{CF}_3\text{CH}(\text{Ph})\text{-OP}(\text{OPh})_2$	94
7	CF ₃ COC ₆ H ₄ -Me- <u>p</u>	18	$\text{CF}_3\text{CH}(\text{p-MeC}_6\text{H}_4)\text{-OP}(\text{OEt})_2$	83
8	CF ₃ (CF ₂) ₂ COPh	12	$\text{CF}_3(\text{CF}_2)_2\text{CH}(\text{Ph})\text{-OP}(\text{OEt})_2$	99
9	CF ₃ (CF ₂) ₂ COPh	15	$\text{CF}_3(\text{CF}_2)_2\text{CH}(\text{Ph})\text{-OP}(\text{O}Bu)_2$	78
10	CF ₃ (CF ₂) ₆ COPh	15	$\text{CF}_3(\text{CF}_2)_6\text{CH}(\text{Ph})\text{-OP}(\text{OEt})_2$	87
11	C ₆ F ₅ COMe	3	$\text{C}_6\text{F}_5\text{CH}(\text{Me})\text{-OP}(\text{OEt})_2$	60 ^e

^a All the reactions were performed under the conditions described in the text, unless otherwise cited. ^b The yields are of pure isolated products. ^c A catalytic amount (0.1 equiv.) of triethylamine was used. ^d The reaction was performed without triethylamine in refluxing benzene. ^e Obtained by the reaction of **1** with sodium diethyl phosphite, generated from sodium hydride and diethyl phosphite, at 0 °C.

corresponding phosphate, 1-(F-alkyl)-1-hydroxyalkylphosphonate which corresponds to **3** in Scheme 2 being formed in an equilibrium with the starting ketone and not isolable in a pure form. Furthermore, a fluorine-free ketone such as acetophenone failed to react at all with diethyl phosphite under the same reaction conditions [14].

On monitoring the reaction of phenyl trifluoromethyl ketone **1** with dibutyl phosphite (Entry 5) by ^{31}P NMR,* the spectra showed three kinds of signals due to the resonances of dibutyl phosphite, 1-hydroxyalkylphosphonate **3**, and the final product **2**. The signal (δ 7.5, singlet) due to the phosphite gradually decreased, whereas the signal (δ -1.8, singlet) due to **2** increased as the reaction proceeded. The other signal (δ 14.0, quartet, $J_{\text{P-F}} = 3$ Hz) due to **3**, which increased at the beginning of the reaction, completely disappeared at the end of the reaction. The similar circumstances were observed in other reactions (Entries 2, 4, and 7).



Scheme 2

These observations allow us to derive a possible mechanism, shown in Scheme 2, for explaining the formation of **2** in this reaction. Thus, the carbonyl carbon of **1** is attacked by

* The spectra were determined under proton noise decoupling conditions on a JEOL FX-90Q spectrometer and the phosphorus chemical shifts downfield from the external standard of phosphoric acid are expressed in ppm with positive values.

the phosphorus of dialkyl phosphite to lead to 1-hydroxyalkylphosphonate **3**, which subsequently undergoes rapid rearrangement through **4** in a synchronous or stepwise fashion, giving rise to the product **2**. Probably, the stabilizing effect of aryl and F-alkyl groups on a partial negative charge in **4** plays an important role in causing the rearrangement.

In connection with the present reaction, studies on the reactions of polyfluorinated carbonyl compounds with halophilic or nucleophilic reagents and their mechanisms are now in progress.

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