A Novel Generation of Perfluoroalkylated Enolates by the Reaction of PhMgBr with Fluorinated β-Ketophosphonium Salts

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A novel one-pot generation of perfluoroalkylated enolates by the reaction of PhMgBr with fluorinated β-ketophosphonium salts and its application to the synthesis of perfluoroalkylated vinyl ethers, β-hydroxy ketones, ketones and vinyl ethers are described.

In view of the central position of enolate chemistry in synthetic organic chemistry, fluorinated enolate chemistry should, in principle, occupy an equally important position in organofluorine chemistry.[1] However, only a few reports have appeared in the literature concerning the generation and utilization of enolates bearing a perfluoroalkyl group.[1,2] Thus, it is of much value to develop a convenient method for the generation of perfluoroalkylated enolates.

Recently we found that carbon nucleophiles could attack fluorinated β-ketophosphonium salts leading to the formation of tetrasubstituted fluoroalkenes[3] and fluoroenynes.[4] However, in our continuing investigation to exploit the synthetic utility of fluorinated β-ketophosphonium salts in organic synthesis, we found that PhMgBr could react with fluorinated β-ketophosphonium salts to give fluorinated enolates which could be applied to the synthesis of perfluoroalkylated vinyl esters, β-hydroxy ketones, ketones and vinyl ethers.

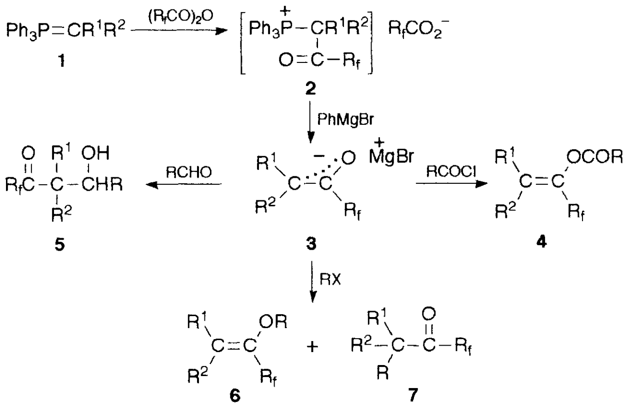
The fluorinated enolate **3** generated from the reaction of PhMgBr with fluorinated β-ketophosphonium salt **2** exhibits the normal enolate reactivity in relation to its O- and C-nucleophilicity. Compound **3** reacts with acyl chlorides and aldehydes to give unique fluorinated vinyl esters or β-hydroxy ketones, respectively. Reaction with benzyl bromide gives fluorinated vinyl ether **6** and ketone **7** (Scheme 1). The results are shown in Table 1.

In a typical procedure, n-butyllithium (4 mmol in 4 ml of n-hexane) was added dropwise with stirring to a suspension of cyclopentyltriphenylphosphonium bromide **1a** (1.64 g, 4 mmol) in absolute tetrahydrofuran (THF) (40 ml) under

Table 1 Preparation of compounds **4**, **5**, **6** and **7**

Product	R^1	R^2	R_f	Electrophile[c]	B.p./°C at 2 mmHg	Yield (%)[a]
4a	$-(CH_2)_4-$		CF_3	PhCOCl	88	90
4b	$-(CH_2)_4-$		CF_3	*p*-ClPhCOCl	92	94
4c	$-(CH_2)_4-$		CF_3	MeCOCl	56	80
4d	$-(CH_2)_4-$		n-C_3F_7	PhCOCl	94	69
4e	$-(CH_2)_5-$		CF_3	PhCOCl	92	73
4f	Me	Me	CF_3	PhCOCl	76	74
4g	Me	Me	CF_3	*p*-ClPhCOCl	85	79
5a	$-(CH_2)_4-$		CF_3	EtCHO	82	51
5b	$-(CH_2)_4-$		CF_3	Pr^nCHO	88	43
6a	Me	Me	CF_3	$PhCH_2Br$	115	36[b]
7a	Me	Me	CF_3	$PhCH_2Br$	115	29[b]

[a] Isolated yields. [b] **6a** and **7a** are two products isolated from one reaction. [c] RCOCl, RCHO or RX.



Scheme 1

nitrogen. The reaction mixture was stirred at −20 °C for 30 min and trifluoroacetic anhydride (0.63 g, 3 mmol) was added slowly at −78 °C until the characteristic ylidic colour disappeared. After stirring at −78 °C for 15 min, PhMgBr (4 mmol in 4 ml Et_2O) was added slowly for 15 min and the mixture was stirred for another 30 min. Then benzoyl chloride (0.56 g, 4 mmol) was added at −78 °C for 30 min and the mixture warmed to 20 °C for another 3 h (in the case of aldehydes and benzyl bromide, the solution was stirred at 20 °C for 10 h). The product **4a** was isolated by column chromatography.

It is noteworthy that other types of Grignard reagents such as Bu^nMgBr, PhC≡CMgBr and $PhCH_2MgCl$ only give the tetrasubstituted fluoroalkenes when they react with fluorinated β-ketophosphonium salt **2a**. They act as nucleophiles like organolithium compounds[3,4] and the detailed mechanism of the reaction of Grignard reagents with fluorinated β-ketophosphonium salts is being pursued.

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