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Fluoride-catalyzed three-component coupling reaction of a silylphosphine, activated alkenes and aldehydes

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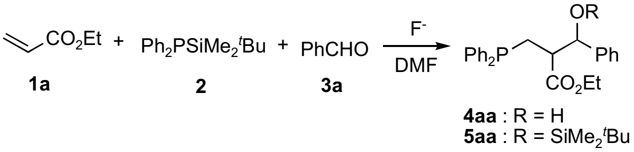
Abstract—A novel CsF-catalyzed three-component coupling reaction of a silylphosphine, activated alkenes and aldehydes is described. Multi-functional phosphines were obtained by forming both carbon–phosphorus and carbon–carbon bonds in good yields under mild conditions.

A mild and convenient procedure for obtaining a variety of new multi-functional organophosphorus compounds have received great attention due to the wide use of these functional phosphines as ligands in catalysis.[1] Formation of a carbon–phosphorus bond through the phosphination of carbon–carbon unsaturated bonds is of interest in recent times.[2,3] In addition, a three-component coupling reaction including both carbon–phosphorus and carbon–carbon bond formation is a quite promising method to produce a variety of multi-functional phosphines. We have recently reported a novel phosphination of alkenes and alkynes by use of a fluoride-activated silylphosphine, and a stoichiometric three-component coupling reaction with an aldehyde giving multi-functional phosphines.[4] In this study, we report a novel catalytic version of the three-component coupling reaction.

We first surveyed the reactivity of several kinds of fluoride source toward silylphosphine in the presence of ethyl acrylate and benzaldehyde as an alkene and an additional electrophile, respectively (Table 1). As already reported, stoichiometric reaction using TASF in DMF proceeded well (entry 1).[4] The CsF-mediated reaction in DMF also proceeded smoothly, whereas KF did not work probably because of its low solubility. Other solvents, such as CH_2Cl_2, CH_3CN and THF, gave poor results due to low reactivity of the intermediate phosphide in these solvents, as seen in the previous Michael addition.[4]

Table 1. Fluoride-promoted three-component coupling reaction[a]



Entry	Fluoride	Equiv	Time (h)	**4aa**[b]	**5aa**[b]
1	TASF	1.2	3	95	—[c]
2		0.1	4	—[c]	—[c]
3	KF	1.2	1	—[c]	—[c]
4	CsF	1.2	2	55	5
5		0.1	3	9	68
6		0.05	4	8	67

[a] The reactions were conducted at rt.
[b] Isolated yields.
[c] Not observed.

When the reaction was performed with CsF, a small amount of the silyl ether **5aa** was isolated (entry 4). This result clearly showed that a part of the initially formed alkoxide of the adduct **4aa** attacked the silylphosphine and reproduced the nucleophilic phosphide.[5] Therefore, we next examined the catalytic reactivity of those fluorides, and found that only CsF promoted the reaction in a catalytic way to afford the silyl ether **5aa** as a main product together with the parent alcohol **4aa** in totally good yield (entries 5 and 6).

Keywords: Silylphosphine; Phosphination; Michael addition; Three-component coupling.

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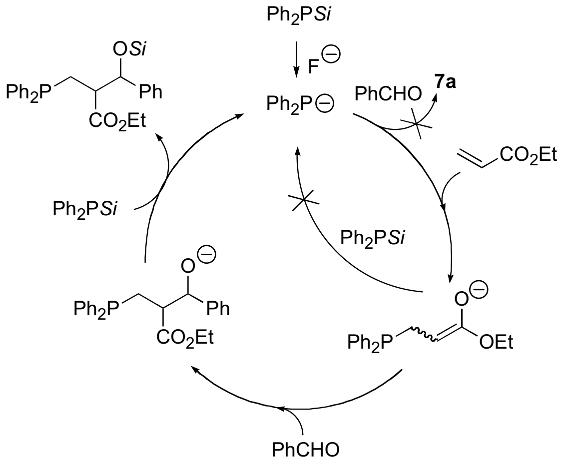


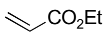
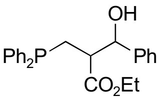
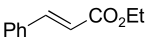
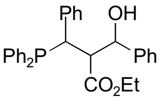
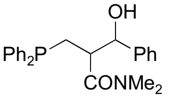
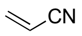
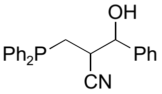
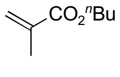
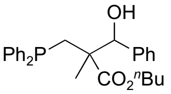
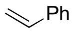
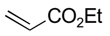
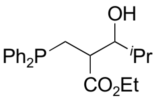
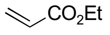
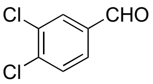
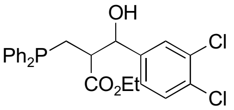
Scheme 1.

The present catalytic reaction proceeded selectively in one pot because of low reactivity of **2** toward aldehydes and sufficient nucleophilicity of the phosphide derived from **2** toward Michael acceptors, although some silylphosphines easily reacted with aldehydes.[6] When the reaction was attempted in the absence of aldehyde, CsF did not catalyze the addition; only a trace of the corresponding adduct **6a** was formed instead. Noteworthy was that the enolate formed after Michael addition did not give the silyl enolate, whereas the alkoxide of the aldol-type adduct smoothly attacked the silylphosphine to promote the catalytic cycle (Scheme 1). It is in contrast to the formation of the silyl enolate in the reaction of trimethylsilyldiphenylphosphine and acrolein.[7] An alkoxide, such as sodium methoxide, reacted with the silylphosphine to produce the corresponding phosphide, and it indeed catalyzed the three-component coupling reaction. However, the results of alkoxide-catalyzed reactions were not satisfactory compared with the present CsF-catalyzed reaction.

The results of the CsF-catalyzed coupling of several alkenes and carbonyl compounds are shown in Table 2.[8,9]

Since the reaction started with Michael-type phosphination, the alkenes having electron-withdrawing group, such as typical Michael acceptors like α,β-unsaturated carbonyl compounds, reacted smoothly to give the corre-

Table 2. CsF-catalyzed three-component coupling reaction[a]

Entry	Acceptor		Electrophile		Products		Yields[b] (%)	dr[c]
1		**1a**	PhCHO	**3a**		**4aa**	88	1:1.5
2		**1b**	PhCHO	**3a**		**4ba**	72[d]	—[e]
3		**1c**	PhCHO	**3a**		**4ca**	85	1:1.2
4		**1d**	PhCHO	**3a**		**4da**	80	1:1.3
5		**1e**	PhCHO	**3a**		**4ea**	72	1:1.3
6		**1f**	PhCHO	**3a**	—[f]		—[f]	—
7		**1a**	*i*PrCHO	**3b**		**4ab**	76[g]	1:1.2
8		**1a**		**3c**		**4ac**	67	1:2

[a] Unless otherwise noted, the reaction was conducted in DMF at rt for 4 h by using 5 mol% of CsF, an alkene (1.1 equiv) and **2** (1.1 equiv).

[b] Yields of the alcohol products isolated after hydrolysis of the initially formed silyl ethers.

[c] Diastereomer ratios were determined by ^{1}H and ^{31}P NMR.

[d] The adduct was isolated as its oxide because the initially formed adduct **4ba** readily oxidized in air. The ratio of diastereomers was determined by ^{31}P NMR.

[e] Not determined.

[f] No adduct was formed after 4 h. Extended reaction time resulted in the formation of aldehyde adduct **7a**.

[g] The reaction was continued for 6 h.