NEW SYNTHETIC ROUTE TO 3-FURYLPHOSPHONATES

Chi-Wan Lee and Dong Young Oh*

Department of Chemistry, Korea Advanced Institute of Science and Technology, 373-1, Kusung-Dong, Yusung-Gu, Taejon, 305-701, Korea

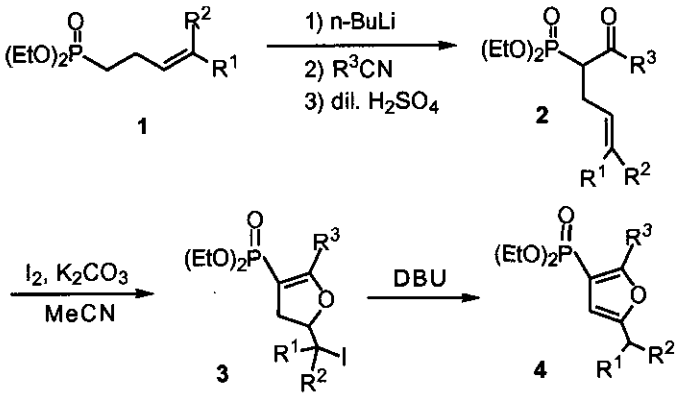
Abstract - A method for the preparation of 3-furylphosphonates has been developed starting with the addition of homoallylic phosphonates to nitrile, followed by a sequence consisting of acidic hydrolysis, iodine-mediated cyclization and dehydroiodination by DBU.

In contrast to the significant number of preparations of arylphosphonates,[1] only a few reports are found in the literature for the preparation of furylphosphonates.[2] A literature survey on the preparation of 2-furylphosphonates showed that some of the methods reported involve the photoinitiated arylation of trialkyl phosphites,[2a] and the reaction of 2-furyllithium with diethyl chlorophosphate.[2c] But there is only one literature about the method for the preparation of 3-furylphosphonate to our knowledge.[3] Therein, 3-furylphosphonates were obtained through halophilic attack of a phosphite anion, but halophilic attack occurs only when the bromomethyl group in furan is conjugated with the ethoxycarbonyl group.

Recently, we have developed method for the synthesis of 2,4-disubstituted furans,[4] and β-diethoxyphosphinyl-β,γ-unsaturated ketones *via* iodocyclization.[5] As an extension of thesemethods we investigated a new route to 3-furylphosphonates *via* iodocyclization. The

method is depicted in **Scheme 1**.

Scheme 1



Treatment of lithiated homoallylic phosphonates (**1**) with nitriles followed by hydrolysis with 5N H_2SO_4 gave the 2-oxophosphonate derivatives (**2**).[6] The reaction of 2-oxophosphonates (**2**) with 1.5 equiv. of K_2CO_3 and 2 equiv. of iodine in dry acetonitrile at room temperature afforded dihydrofurans (**3**). The conversion of **2** to **3** could be reasonably explained by assuming the formation of a iodonium ion, which allow an intramolecular attack by enolic -OH,[7] leading to the cyclization product (**3**). And the dehydroiodination of dihydrofurans (**3**) by DBU in anhydrous THF and subsequent basic isomerization gave 3-furylphosphonates (**4**) in good overall yields from **1** (**Table 1**).

Table 1. Synthesis of 3-Furylphosphonates *via* Iodocyclization

3-Furylphosphonate	R^1	R^2	R^3	Yield (%)
4a	H	H	Ph	80
4b	H	H	*p*-Cl-Ph	83
4c	H	H	*p*-CH_3O-Ph	80
4d	Me	H	*p*-Cl-Ph	66
4e	Me	Me	*p*-Cl-Ph	63
4f	Ph	H	*p*-Cl-Ph	57

When the reaction was carried out with aliphatic nitriles, we have found none of the desired 2-

oxophosphonate derivatives (**2**). In the case of synthesis of **4f** (R^1=Ph, R^2=H), **2f** could be prepared as in the literature[8] not by the above method, because the acylation step of homoallylic phosphonate (**1f**) afforded 2-oxophosphonate (**2f**) in low yield.

When *t*-BuOK was used in place of DBU, the desired prodct could not be obtained.

In summary, we have developed a new alternative and mild route to 3-furylphosphonates. Although this procedure involved the well-known halocyclization, the reaction pathway proved to be of a significant value since it is the first approach to the synthesis of 3-furylphosphonates *via* iodocyclization.

Representative Procedure.

To a solution of diethyl 3-butenylphosphonate (**1**) (1 mmol) in 5 ml of THF was added dropwise a solution of 1.6 M *n*-BuLi (0.69 ml, 1.1 mmol) in hexane at -78 °C. After stirring for 1 h at this temperature, a solution of benzonitrile (1.1 mmol) in 5 ml of THF was added dropwise and the reaction mixture was stirred at room temperature for 30 min under N_2, followed by addition of 5N H_2SO_4 (2 ml). After usual work-up, to the reaction mixture in dry acetonitrile (30 ml) was added iodine (558.4 g, 2.2 mmol) and K_2CO_3(207.3 g, 1.5 mmol). The mixture was stirred for 2 h at room temperature. To the resultant solution was added saturated aq. sodium thiosulfate and the mixture was extracted with CH_2Cl_2. Then the combined organic extracts were concentrated and treated with DBU (380.6 g, 2.5 mmol) in 5 ml of THF at room temperature. After 3 h, the mixture was quenched and extracted with CH_2Cl_2. The combined organic extracts were dried with $MgSO_4$, and concentrated *in vacuo*. The mixture was purified by silica gel chromatography.

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