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A novel stereoselective synthesis of (*E*)-2-arylvinylphosphonates in $InCl_3$–$NaBH_4$–MeCN system

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Abstract

Hydroindation of arylalkynylphosphonates gives a intermediate which can be hydrolyzed to (*E*)-2-arylvinylphosphonates in $InCl_3$–$NaBH_4$–MeCN system, the stereoselectivity and yield are rather high, but under the same conditions 2-alkylalkynylphosphonates do not react very well.

Keywords: $InCl_3$–$NaBH_4$–MeCN system; Hydroindation; (*E*)-2-Arylvinylphosphonates; Stereoselectivity; Alkynylphosphonates

1. Introduction

Vinylphosphonates have been widely used as synthetic intermediates in organic chemistry [1] and investigated as biologically active compounds [2], especially in stereoselective synthesis of trisubstituted olefins [3] and heterocycle compounds [4]. Up to now, the synthesis of vinylphosphonates has been explored extensively. However the synthesis methods include a variety of non-catalytic reactions [5] and palladium-catalytic cross-coupling reactions [6], these methods are limited by the requirement of highly active functional groups in the substrates. For example, 2-arylvinylphosphonates can be also prepared by the palladium-catalyzed arylation of diethyl vinylphosphonate with aryl bromides [7], but this synthetic route gives a mixture of (*E*)-vinylphosphonates and (*Z*)-vinylphosphonates. Palladium-catalyzed phosphonylation of (*E*)-α-haloolefins could give (*E*)-2-arylvinylphosphonates, in which the starting material is not easily available [8]. In addition, vinylphosphonates could also be prepared by olefin cross-metathesis. (*Z*)-Vinylphosphonates could be prepared by addition of ''zirconocene'' to alkynylphosphonates and hydrolysis [9]. Recently it has been reported that Palladium-catalytic coupling reactions of bromoalkenylphosphonates with aryl boronic acids and alkenyl borates or using vinylboronates both gave vinylphosphonates [10]. Even now, a new and high stereoselective synthetic method for vinylphosphonates would be valuable. In this paper, we would present a synthetic method of (*E*)-2-arylvinylphosphonates.

Since dichloroindium hydride (Cl_2InH) was prepared firstly and applied in organic synthesis, it has received more and more attention [11]. Recently, dichloroindium hydride (Cl_2InH) generated in situ from the combination of sodium borohydride and a catalytic amount of indium trichloride has been demonstrated to be a benign alternative to $InCl_3$/*n*-Bu_3SnH system [12]. $InCl_3$–$NaBH_4$–MeCN system is easy to handle and has low toxicity compared to the latter. So it has been applied in organic synthesis widely, such as the dehalogenation of alkyl halides and other radical cyclizations [13], the cross-coupling reaction of terminal alkynes with iodides [14], dimerization of terminal

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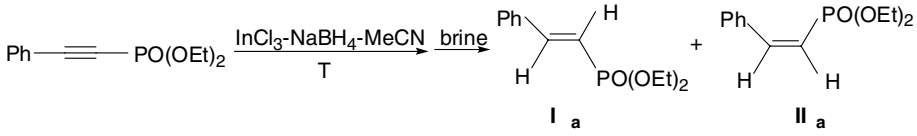
alkynes [15]. Now, this paper wants to present a stereoselective synthesis of (*E*)-2-arylvinylphosphonates by hydroindation of 2-arylalkynylphosphonates in $InCl_3$–$NaBH_4$–MeCN system.

2. Results and discussion

Initially, we optimized the reaction conditions involving the reaction temperature and equivalence of $NaBH_4$. Phenylalkynylphosphonate was employed as model in these reactions (Scheme 1). The reactions were monitored by TLC. The products were purified by silica gel column chromatography. The conversion and the ratio of (*E*)-phenylvinylphosphonates ($\mathbf{I_a}$) and (*Z*)-phenylvinylphosphonates ($\mathbf{II_a}$) were detected by ^1H NMR and HPLC-MS. The stereostructure was determined by the coupling constant between two *trans* vinyl protons ($J = 17.59$ Hz) of (*E*)-phenylvinylphosphonates ($\mathbf{I_a}$), which was consistent with the literature reported in the references cited [6]. As shown in Table 1, the entries **1** and **2** suggested that $InCl_3$ could play a catalytic role in this reaction. However, the yields were very low. So the equivalent mole of $InCl_3$ with the substrate was selected. Entries **3**, **6** and **9** optimized the mole ratio of $NaBH_4$ with the substrate. At the same time the best conversion was observed when the reaction was performed at −15 °C to r.t. Excess of $NaBH_4$ gave higher stereoselectivity and conversion. To our surprise, when 1 mmol iodobenzene was added, the main product was (*Z*)-phenylvinylphosphonates ($\mathbf{II_a}$). Because of the propensity of the lower valent group 13 metals to form complexes with aryl rings benzene and toluene were added to the reaction mixture respectively. But the stereoselectivity and conversion have no change compared to entry **9**. When 1 mmol iodine was added, no expectant compound was obtained. The rational explanation is not clear so far. The results were listed in Table 1.

Under the same conditions [$InCl_3$ (1 mmol), $NaBH_4$ (2 mmol), MeCN (10 ml), −15 °C to r.t., 15 h], we examined a variety of alkynylphosphonates (Scheme 2). It was found that when R was Ph or cyclohexenyl, the yield and the stereoselectivity were both satisfactory. When the hydrogen atom of benzene ring was substituted by methyl group (**d**, **f**), the stereoselectivity decreased slightly, while hydrogen atom of benzene ring was substituted at the *para* position by fluorine atom (**g**) the yield and the selectivity were rather high. When R was aliphatic such as *n*-C_4H_9 or *c*-C_3H_5 the yield decreased greatly. Even if the equivalent ratio of $InCl_3$ and alkynylphosphonates was increased to 1.5:1, the yield and stereoselectivity of reactions **b** or **c** were not improved (Table 2). The spectra data of the known products were consistent with the references cited [16].

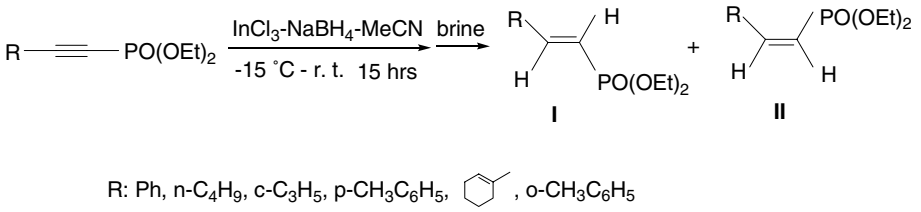


Scheme 1.

Table 1
Studying of the system in reduction of 2-phenylalkynylphosphonates

Entry	*T*	$InCl_3$:$NaBH_4$:alkyne	$\mathbf{I_a}/\mathbf{II_a}$[a,b]	Yield (%)[b]
1	−15 to r.t.	1:10:10	100/0	53
2	−15 to r.t.	1:10:5	100/0	52
3	−15 to r.t.	1:10:1	>98/2	99
4	r. t.	1:10:1	–	–
5	0 to r.t.	1:10:1	>98/2	94
6	−15 to r.t.	1:5:1	98/2	93
7	0 to r.t	1:5:1	98/2	93
8[c]	0 to r.t	1:5:1	42/58	95
9	−15 to r.t.	1:2:1	100/0	95
10	0 to r.t	1:2:1	89/11	88
11[d]	−15 to r.t.	1:2:1	–	–
12[e]	−15 to r.t.	1:2:1	>99/1	96
13[f]	−15 to r.t.	1:2:1	>99/1	96

[a] Determined by ^1H NMR (500 MHz).
[b] Determined by HPLC-MS.
[c] 1 mmol iodobenzene was added.
[d] 1 mmol iodine was added.
[e] 1 mmol benzene was added.
[f] 1 mmol toluene was added.



Scheme 2.

Table 2
Synthesis of vinylphosphonates in $InCl_3$–$NaBH_4$–MeCN system

Entry	R	I/II[a,c]	Total yield (%)[a,c]
a	Ph	100/0	95
b	*n*-C_4H_9	15/1	10
c	*c*-C_3H_5	11/2	38
b[b]	*n*-C_4H_9	7/1	22
c[b]	*c*-C_3H_5	14/1	46
d	*p*-$CH_3C_6H_5$	89/11	99
e		99/1	97
f	*o*-$CH_3C_6H_5$	92/8	96
g	*p*-FC_6H_5	100/0	100

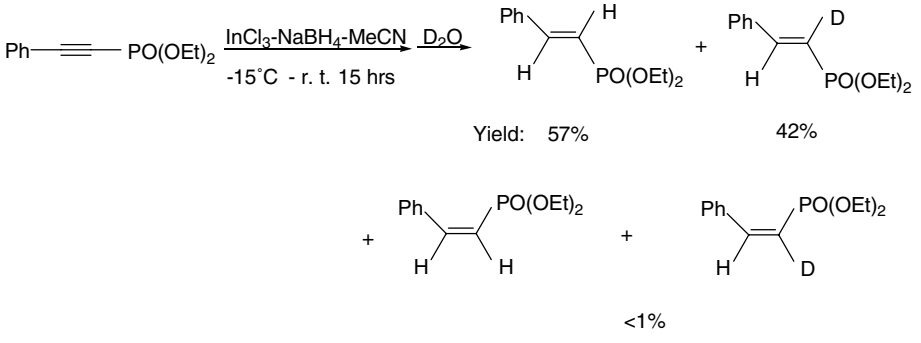
Reaction conditions: $InCl_3$ (1 mmol), $NaBH_4$ (2 mmol), MeCN (10 ml), arylalkynylphosphonates (1 mmol), −15 °C to r.t., 15 h, brine (5 ml).
[a] Determined by ^1H NMR (500 MHz).
[b] $InCl_3$ (1.5 mmol), $NaBH_4$ (3 mmol), MeCN (10 ml), arylalkynylphosphonates (1 mmol).
[c] Determined by HPLC-MS and GC-MS.

When quenched with D_2O the reaction mixture obtained from Phenylalkynylphosphonate with $InCl_3$–$NaBH_4$ system (the same condition with **a**) yielded (*E*)-phenylvinylphosphonates in 57% yield, 1-D-(*E*)-phenylvinylphosphonates in 42%, together with trace (*Z*)-phenylvinylphosphonates and 1-D-(*Z*)-phenylvinylphosphonates (the total yield was less than 1%) (Scheme 3). According to all this results, the radical mechanism of hydroindation process was proposed (Scheme 4). The intermediate **A** is more stable than **B**. The radical intermediate in which aryl ring bears the electron-withdrawing group is more stable than the intermediate bearing the electron-releasing group.

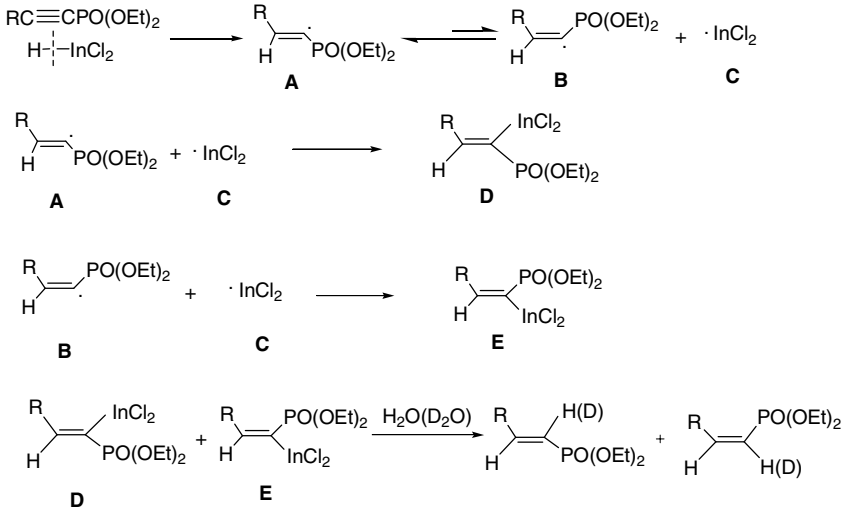
In summary, a new and simple approach to (*E*)-2-arylvinylphosphonates from (*E*)-2-arylalkynylphosphonates has been developed, in which the $InCl_3$–$NaBH_4$–MeCN system was firstly employed in reduction of alkynylphosphonates successfully. The efficiency and operational simplicity of the presented method make it useful and attractive for the synthesis of (*E*)-2-arylvinylphosphonates.

3. Experimental

^1H NMR spectra were obtained with a Bruker AVANCE DMX-500 NMR spectrometer in $CDCl_3$ as a solvent, with TMS as an internal standard. The ESI-MS spectra were taken on a Bruker Esquire 3000 ^{plus} spectrometer. HPLC was performed on Aligent 1100. Precoated thin-layer plates of silica gel 60 GF_{254} (Qingdao Haiyang Chemical Co. Ltd., Qingdao, China.) were



Scheme 3.



Scheme 4.

used for analytical purposed. GC-MS data were recorded by TRACE 2000 GC/ MS(USA TRACE company). Acetonitrile was freshly distilled from phosphorus pentoxide before use. Alkynylphosphonates were prepared according to the literature [17].

$InCl_3$ (1 mmol), dry MeCN (10 ml) and $NaBH_4$ (2 mmol) were mixed at −15 °C under nitrogen. After the mixture was stirred for 30 min, alkynylphosphonates (1 mmol) was added by syringe. The cooling bath was removed. The reaction mixture was warmed to the room temperature, stirred for 15 h. The reaction was monitored by TLC. In order to destroy the excessive $NaBH_4$ brine (5 ml) was added to the reaction mixture. The reaction mixture was stirred for 10 min, filtered. The filtrate was extracted by ether (20 ml × 3). The combined organic layer was dried over $MgSO_4$ and concentrated in vacuum. Purification by silica gel column (100–200 mesh), using petroleum ether / ethyl acetate (3:1) as eluent could afford the corresponding products.

^{1}H NMR (500 MHz, $CDCl_3$) data for **Ic**: δ_H = 0.93 (m, 4H), 1.35 (t, 6H, J = 7.0 Hz), 1.58 (m, 1H), 4.13 (quin, 4H, J = 7.0 Hz), 6.21 (m, 1H); MS (ESI): 204.7 $[M + H]^+$, 226.7 $[M + Na]^+$, 242.8 $[M + K]^+$.

^{1}H NMR (500 MHz, $CDCl_3$) data for **Ie**: δ_H = 1.37 (t, 6H, J = 7.0 Hz), 1.65 (m, 6H), 2.16 (m, 4H), 4.16 (m, 4H), 5.52 (t, 1H, J = 18.0 Hz), 6.12 (s, 1H), 7.09 (m, 1H); MS (ESI): 244.9 $[M + H]^+$, 266.9 $[M + Na]^+$, 282.9 $[M + K]^+$.

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