Tetrahedron 72 (2016) 3084–3091

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Silver-catalyzed direct regioselective phosphonation of β-aryl-α,β-unsaturated carbonyl compounds with *H*-phosphites under microwave irradiation

Jin-Wei Yuan [a,*], Yuan-Zhe Li [a], Wen-Peng Mai [b], Liang-Ru Yang [a], Ling-Bo Qu [a,*]

[a] School of Chemistry & Chemical Engineering, Henan University of Technology, Academician Workstation for Natural Medicinal Chemistry of Henan Province, Zhengzhou 450001, PR China
[b] School of Materials and Chemical Engineering, Henan Institute of Engineering, Zhengzhou 451191, PR China

ARTICLE INFO

Article history:
Received 28 February 2016
Received in revised form 10 April 2016
Accepted 12 April 2016
Available online 13 April 2016

Keywords:
Silver-catalyzed
β-Aryl-α,β-unsaturated carbonyl compound
Alkenylphosphonate
Radical reaction
Phosphonation

ABSTRACT

An efficient protocol for silver-catalyzed direct radical phosphonation of β-aryl-α,β-unsaturated carbonyl compounds with *H*-phosphites to afford *trans*-substituted alkenylphosphonates under microwave irradiation is described. Some notable features of this method are high efficiency, good yield, broad functional groups tolerance, commercially available and cheap catalyst.

1. Introduction

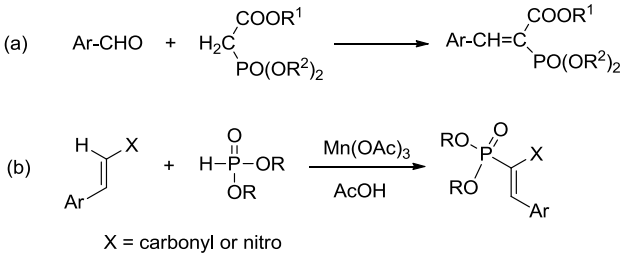
Alkenylphosphonates are especially useful small organic molecules.[1] In addition to their extensive use in polymer science as copolymers, they are routinely used as building blocks for the introduction of remote phosphonate functional groups or to prepare biologically active molecules.[2] Quite recently, the alkenylphosponate scaffold itself has been used as a promising pharmacophore. They have also been shown over the years to be key starting materials for an impressive range of chemical transformations.[3] Not surprisingly, numerous reports on the synthesis of alkenylphosphonates have appeared in the presence of $Mn(OAc)_3$ during the past decade.[4] Moreover, the synthesis of arylalkene phosphonates have also been reported. A stereoselective procedure for the preparation of alkenylphosphonates by copper-mediated cross-coupling between 1,1-dibromo-1-alkenes and dialkyl phosphites was reported by Evano and co-workers group, and $Mn(OAc)_3$-mediated tandem phosphonyl radical addition to β-nitrostyrenes followed by denitration to produce 2-alkenyl phosphonates was described by Pan's group.[5] Wu group reported a silver-catalyzed synthesis of 3-phosphorated coumarins via radical cyclization of alkynonates and dialkyl phosphites.[6] However, similar reactions of the corresponding β-aryl-α,β-unsaturated carbonyl compounds with *H*-phosphites have remained underexplored.

The same reaction was once employed by the coupling of β-aryl-α,β-unsaturated carbonyl compounds with *H*-phosphites. There maybe be two challenges: (1) how to control the reaction position of α,β-unsaturated carbonyl compounds, and (2) how to control the regio- and stereochemistry of the newly formed alkenylphosphonates. A significant amount of efforts have been spent on the coupling reaction of α,β-unsaturated carbonyl compounds with *H*-phosphites. However, the literature search indicated that only few examples described the reaction of β-aryl-α,β-unsaturated carbonyl compounds and *H*-phosphites. Reetz's and Robinson's groups reported a synthetic procedure of triethyl benzylidene phosphonoacetate by Knoevenagel condensation reaction of triethyl phosphonoacetate with benzaldehyde (Scheme 1a).[7] Zou's group described an oxidant coupling reaction of β-aryl-α,β-unsaturated carbonyl compounds and *H*-phosphites in AcOH solvent using $Mn(OAc)_3$ as an oxidant (Scheme 1b).[8] Despite these methods having various levels of success, there still exist some problems, such as: requirement of complicated starting materials, a narrow

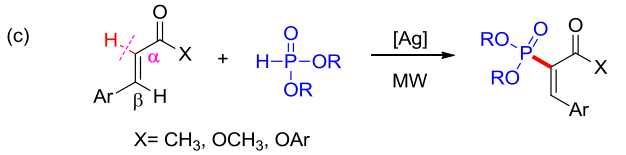
* Corresponding authors. E-mail addresses: yuanjinweigs@126.com (J.-W. Yuan), qulingbo@haut.edu.cn (L.-B. Qu).

http://dx.doi.org/10.1016/j.tet.2016.04.034
0040-4020/

Previous works:



This work:



Scheme 1. Synthesis of phosphonates of β-aryl-α,β-unsaturated carbonyl compounds.

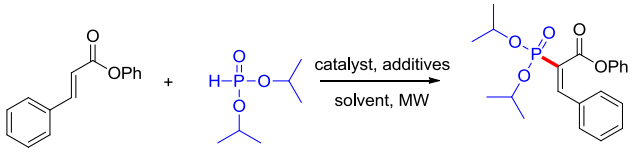
scope of substrates, high temperature, a toxic catalyst or an acid environment. Therefore, developing a general and applicable strategy for the synthesis of phosphonate derivatives of β-aryl-α,β-unsaturated carbonyl compounds is still desirable.

Transition metal-catalyzed dehydrogenative coupling reaction is a fundamental method for the construction of new chemical bonds. By employing this method, two substrates can be coupled without any prefunctionalization. The preparation of phosphonate derivatives via this dehydrocoupling method has recently attracted great attention using $Pd(OAc)_2/AgBF_4$, $Ni(OAc)_2$, $Pd(OAc)_2/Mn(OAc)_3$, $AgNO_3/K_2S_2O_8$, $AgNO_3$, or DTBP as the catalysts.[9] Microwave irradiation is used as an alternative thermal energy source to conventional heating in organic synthesis. The use of microwave irradiation has been applied to a wide range of reaction types. Many of these reactions have been demonstrated to result in higher yield and/or selectivity under microwave irradiation.[10] Herein, we disclose an efficient silver-catalyzed direct dehydrogenative coupling of β-aryl-α,β-unsaturated carbonyl compounds with *H*-phosphites to selectively produce the valuable *E*-isomer, alkenylphosphonates (α-phosphonato-α,β-unsaturated carbonyl compounds) in high yields under microwave irradiation, which opens a new route for the modification at α-phosphonation of β-aryl-α,β-unsaturated carbonyl compounds (Scheme 1c).

2. Results and discussion

Our previous study showed that the phosphonyl radicals could be easily generated from *H*-phosphites with a catalytic amount of silver salts, and the phosphonation of coumarins has been developed with this procedure.[9b] Based on this achievement, the model reaction of phenyl cinnamate (**1a**) and diisopropyl *H*-phosphite (**2a**) was carried out in the presence of $AgNO_3$ (10 mol%) without any the additive in CH_3CN at 90 °C under microwave irradiation for 20 min. Fortunately, the product was detected, and the isolated yield was 20% (Table 1, entry 1). Spectroscopic data were in agreement with the assigned structure of compound **3a**. High-resolution mass spectrometry shows a clear molecular ion peak at *m/z* 389.1514 $[M+H]^+$, which shows that only one proton atom was substituted. ^{31}P NMR indicated a single peak at δ=10.9 ppm. The α carbon atom at δ_C=133.8 ppm appears as a doublet with a coupling constant, $^1J_{P-C}$=19.5 Hz. The carbon atoms of carbonyl group and β position also appear as a doublet with a smaller

Table 1
Optimization of reaction conditions[a]



1a **2a** **3a**

Entry	Catalyst (mol%)	Additive (equiv)	Solvent	Temp (°C)	Time (min)	Yield[b] (%)
1	$AgNO_3$ (10)	—	CH_3CN	90	20	20
2	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (1.0)	CH_3CN	90	20	70
3	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	CH_3CN	90	20	82
4	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.3)	CH_3CN	90	20	79
5	$AgNO_3$ (10)	$Cu(NO_3)_2$ (0.5)	CH_3CN	90	20	<5
6	$AgNO_3$ (10)	$NaNO_3$ (0.5)	CH_3CN	90	20	22
7	$AgNO_3$ (10)	HNO_3[c] (0.5)	CH_3CN	90	20	41
8	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	20	88
9	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	EtOAc	82	20	78
10	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	MeOH	90	20	<5
11	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	H_2O	90	20	nr[d]
12	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	Dioxane	90	20	75
13	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	DCE	90	20	70
14	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	30	20	25
15	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	40	20	52
16	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	50	20	63
17	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	60	20	72
18	Ag_2CO_3 (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	20	80
19	AgOTf (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	20	75
20[e]	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	20	45
21[f]	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	20	80
22	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	1	50
23	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	3	75
24	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	5	80
25	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	10	90
26[g]	$AgNO_3$ (10)	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	6 h	80
27	—	$Mg(NO_3)_2·6H_2O$ (0.5)	THF	70	10	nr

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.5 mmol), catalyst, and additive in solvent (2 mL) was stirred for 20 min under microwave irradiation. The given equivalents (equiv) and mol% are related to **1a**.
[b] Isolated yield.
[c] HNO_3 is 65% concentrated nitric acid.
[d] nr=no reaction.
[e] 1.0 equiv **2a** was used.
[f] 3.0 equiv **2a** was used.
[g] No microwave irradiation.