



Mn^{III}-catalyzed phosphorylation of vinyl azides: The synthesis of β -keto phosphine oxides



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ABSTRACT

Mn^{III}-catalyzed functionalization of vinyl azides via phosphorylation was developed to synthesize various β -keto phosphine oxides in high yields. The transformation is operated in mild conditions and tolerant of a range of functional groups. Control reaction indicates that the reaction mechanism might proceed via the generation of a phosphonated iminyl radical intermediate.

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Introduction

Organophosphorus compounds play vital role in organic chemistry, pharmaceuticals and material science.¹ Among them, β -keto phosphine oxides are highly valuable and interesting intermediates that facilitate the α,β -unsaturated carbonyl compounds via the Horner-Wadsworth-Emmons (HWE) reactions,² diversified construction of heterocycles³ or the synthesis of chiral β -hydroxy phosphonic acids.⁴ In recent years, strategies between organophosphorus radicals⁵ and radical acceptor have been well developed for affording organophosphorus compounds, especially for the formation of β -keto phosphine oxides.^{5a-f} (Scheme 1a–f) However, reported works required O₂ assistance, co-catalyst system or stoichiometric amount of catalyst.

Vinyl azides as attractive and challenging three-atom synthons have drawn much attention for their application for diverse heterocycles construction.⁶ The unique properties of the azide group adjacent to an alkene moiety facilitate to tune this functional group into interesting building blocks. Moreover, vinyl azides have been employed as a potential radical acceptor in organic synthesis.⁷ For example, formation of pyridines via radical reactions of vinyl azides with cyclopropanols,^{7b} trifluoromethylation^{7c} or perfluoroalkylation^{7d} of vinyl azides through iminyl radicals. Recently, our group has reported an efficient synthesis of 5-thiocyano-2-aminothiazoles via Fe-catalyzed radical cyclization

of vinyl azides.^{6f} Thus, in the continue interest in functionalization of vinyl azides, the development of interesting radicals with vinyl azides is still attracting.

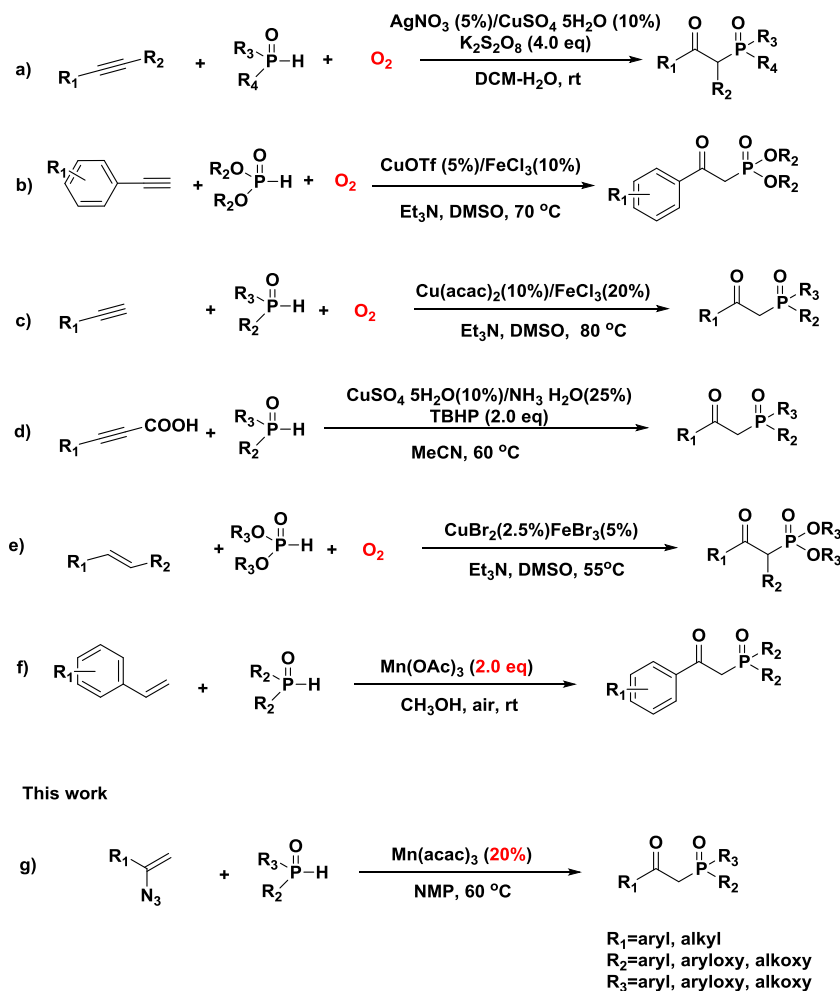
Here, we disclose a Mn^{III}-catalyzed phosphorylation of vinyl azides with phosphine oxides to afford iminyl radicals. Subsequent conversion of the transient radicals for the β -ketophosphine oxides. (Scheme 1-g) Preliminary mechanistic investigation revealed that the phosphine oxides radical is likely involved in the phosphorylation process.

Results and discussion

We envisioned utilizing H-phosphonate (**2a**) as a source of radical. Interesting, a diethyl (2-oxo-2-phenylethyl) phosphonate (**3a**) was isolated in 18% yield by the reaction with vinyl azide (**1a**) using a 50 mol% amount of Mn(OAc)₃·2H₂O (Table 1, entry 1). Increasing the amount of Mn(OAc)₃·2H₂O to 80 mol% or 100 mol% lead to a slight increase in the yields (25%, Table 1, entries 2–3). While 68% of the product (**3a**) was observed when the reaction was performed with 2.5 equivalents of Mn(OAc)₃·2H₂O (Table 1, entry 4). The combined of catalytic amount of Mn (III) and other oxidant such as DDQ resulted in a lower yield (12%, Table 1, entry 5). Other manganese salts such as Mn(OAc)₂·4H₂O and Mn(acac)₃ were also investigated (Table 1, entries 6–7). Utilization of Mn (III) acetylacetonate [Mn(acac)₃] was found to be essential in rendering this reaction with an excellent yield of 70%. Reducing the catalyst loading to 20 mol% could still initiate this reaction with a slightly decreased yield of 60% (Table 1, entry 8). The reaction

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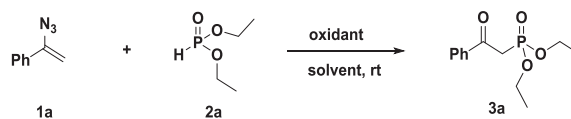
Scheme 1. The formation of β -keto phosphine oxides via a P-centered radical.

yields can be improved by elevating the reaction temperature (Table 1, entries 9–10). Next, we intended to explore the relationship of the solvent systems in this reaction. Conducting the reaction in DMSO, DMF and DCE gave the product **3a** in moderate yields (Table 1, entries 11–13), while the reaction conducted in NMP gave **3a** in 92%. Therefore, the best yield of **3a** (92%) was obtained by employing 20 mol% Mn(acac)₃ in *N*-methyl-2-pyrrolidone (NMP) at 60 °C for 6 h.

Following the established reaction conditions for the construction of **3a**, the generality of this β -ketophosphonate **3** synthesis was examined using a series of vinyl azides **1**. α -Aryl-substituted vinyl azides were facile to give the corresponding products **3** in good yields (Table 2, **3a–3i**). The addition of the phosphonate radical to vinyl azides bearing electron-withdrawing groups (Table 2, **3e–3i**) or electron-rich aryl groups (Table 2, **3b–3d**) proceeded smoothly to give the corresponding β -keto phosphonate in good yields. α -Alkyl-substituted vinyl azide was also capable of coupling with the phosphine oxide radical efficiently (Table 2, **3j**). While trisubstituted vinyl azides having an aryl group at the β -position failed to be employed in this synthesis, probably due to steric hindrance (Table 2, **3k**).

Next, the generality of phosphine oxides was also examined using α -azidostyrene and 1-(1-azidovinyl)-3-nitrobenzene as shown in Table 3. Not only dialkyl and diaryl H-phosphonates (**4a–4c**) but also diarylphosphine oxide (**4d**) and benzyloxyphosphine oxides (**4e–4f**) were successfully converted into the

Table 1
Optimization of the reaction conditions.^a



Entry	Additive (equiv.)	Solvent	Yield (%) ^b
1	Mn(OAc) ₃ ·2H ₂ O(0.5)	NMP	18
2	Mn(OAc) ₃ ·2H ₂ O(0.8)	NMP	25
3	Mn(OAc) ₃ ·2H ₂ O(1.0)	NMP	25
4	Mn(OAc) ₃ ·2H ₂ O(2.5)	NMP	68
5	Mn(OAc) ₃ ·2H ₂ O(0.5)+DDQ(2.0)	NMP	12
6	Mn(OAc) ₂ ·4H ₂ O(0.5)	NMP	5
7	Mn(acac) ₃ (0.5)	NMP	70
8	Mn(acac) ₃ (0.2)	NMP	60
9 ^c	Mn(acac) ₃ (0.2)	NMP	71
10 ^d	Mn(acac) ₃ (0.2)	NMP	92
11 ^d	Mn(acac) ₃ (0.2)	DMSO	78
12 ^d	Mn(acac) ₃ (0.2)	DMF	70
13 ^d	Mn(acac) ₃ (0.2)	DCM	73

^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), additive in solvent (1.0 mL) containing 18 μ L of H₂O) stirring at 25 °C for 6 h.

^b Yield of the isolated product.

^c Performed at 40 °C.

^d Performed at 60 °C

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