

## Hydrophosphorylation of Alkenes with Dialkyl Phosphites Catalyzed by Mn(III) under Air

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**Abstract:** A facile method for the synthesis of organophosphonates from alkenes and dialkyl phosphites was developed by the use of Mn(II) under air. Thus, the reaction of 1-octene with diethyl phosphite in the presence of Mn(OAc)<sub>2</sub> (5 mol %) under air at 90 °C led to diethyl octylphosphonate (78%) and diethyl (2-hexyl)decylphosphonate (6%). Internal alkenes such as *cis*-2-octene gave a regioisomeric mixture of the corresponding hydrophosphorylation products in 84% yields.

Organophosphonates are an important class of intermediates in the synthesis of biologically active compounds and are generally prepared by the Arbuzov reaction.<sup>1</sup> Recently, Tanaka et al. have reported Pd-catalyzed hydrophosphorylation of alkynes via oxidative addition of HP(O)(OR)<sub>2</sub> leading to alkenyl- and alkylphosphonates.<sup>2</sup> In addition, the Pd-catalyzed hydrophosphorylation of alkenes with a five-membered cyclic hydrogen phosphonate is successfully achieved by them.<sup>3</sup> Montchamp et al. reported the Pd-catalyzed hydrophosphinylation of alkenes and alkynes with H<sub>2</sub>P(O)OR.<sup>4</sup> Quite recently, Rh complexes are reported to catalyze the regio- and stereoselective addition of diphenylphosphine oxide to alkynes<sup>5</sup> and the regioselective olefin hydrophosphorylation.<sup>6</sup>

On the other hand, the radical addition of HP(O)(OR)<sub>2</sub> to alkenes is well-known.<sup>7</sup> For example, peroxide (or light)- or triethylborane-initiated radical addition of hypophosphites to olefins is reported.<sup>8</sup> In recent years, we have developed a new catalytic radical addition of ketones to alkenes by the Mn(II)/Co(II)/O<sub>2</sub> redox system.<sup>9</sup> In this reaction, Mn(III) generated in situ from Mn(II)

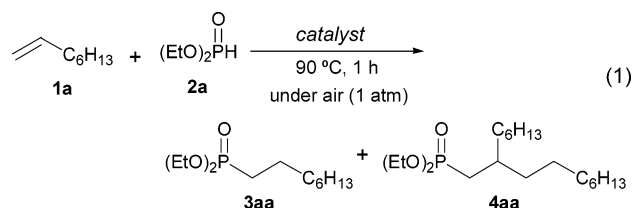
**TABLE 1.** Hydrophosphorylation of 1-Octene (**1a**) with Dialkyl Phosphite Catalyzed by Mn(OAc)<sub>2</sub> under Air<sup>a</sup>

run	Co(II) (mol %)	Mn(II) (mol %)	yield <sup>b</sup> (%)	
			<b>3aa</b>	<b>4aa</b>
1	2	5	82	6
2	0	5	78 (61)	6
3	2	0	nd	nd
4 <sup>c</sup>	0	5	79	6
5 <sup>d</sup>	0	5	nd	nd
6 <sup>c,d</sup>	0	5	15	3
7 <sup>e</sup>	0	1	21	2
8 <sup>f</sup>	1	1	69	5
9 <sup>g</sup>	0	5	<b>3ab</b> (81)	<b>4ab</b> (7)
10 <sup>h</sup>	0	5	<b>3ac</b> (73)	<b>4ac</b> (6)

<sup>a</sup> **1a** (3 mmol) was allowed to react with **2a** (9 mmol) catalyzed by Mn(OAc)<sub>2</sub> (5 mol %) in the presence or absence of Co(OAc)<sub>2</sub> (2 mol %) under air at 90 °C for 1 h. <sup>b</sup> Based on **1a** used. The number in parentheses shows the isolated yield. <sup>c</sup> Mn(OAc)<sub>3</sub> was used in place of Mn(OAc)<sub>2</sub>. <sup>d</sup> Under Ar. <sup>e</sup> 8 h. <sup>f</sup> 6 h. <sup>g</sup> HP(O)(<sup>*n*</sup>BuO)<sub>2</sub> (**2b**) was used at 100 °C. <sup>h</sup> HP(O)(MeO)<sub>2</sub> (**2c**) was used at 110 °C.

by the action of Co(II) and oxygen oxidizes ketones to give α-keto radicals which then add to alkenes leading to alkylated ketones. Thus, these results prompted us to investigate the generation of phosphorus radicals through one-electron oxidation by Mn(III) ions, and we found that Mn(OAc)<sub>2</sub> efficiently catalyzes the addition of dialkyl phosphites, HP(O)(OR)<sub>2</sub>, to alkenes through a radical process under air. In this paper, we disclose the Mn-catalyzed hydrophosphorylation of a variety of alkenes with HP(O)(OR)<sub>2</sub>.

To obtain the information on the hydrophosphorylation of alkenes with phosphites, the reaction of 1-octene (**1a**) with diethyl phosphite (**2a**) was carried out under various conditions (eq 1, Table 1).



The reaction of **1a** with 3 equiv of **2a** in the presence of Mn(OAc)<sub>2</sub> (5 mol %) and Co(OAc)<sub>2</sub> (2 mol %) under air at 90 °C for 1 h gave diethyl octylphosphonate (**3aa**) (82%) and diethyl (2-hexyl)decylphosphonate (**4aa**) (6%) (run 1). It was found that almost the same results were obtained even in the absence of Co(OAc)<sub>2</sub> from the catalytic system (run 2).<sup>10</sup> However, no reaction took place by removing Mn(OAc)<sub>2</sub> from the catalytic system under these conditions (run 3). It is interesting that the same results were obtained when Mn(OAc)<sub>3</sub> was employed in place of Mn(OAc)<sub>2</sub> (run 4). In the absence of air, Mn(OAc)<sub>2</sub> did not catalyze the hydrophosphorylation of **1a** with **2a**, although Mn(OAc)<sub>3</sub> promoted slightly the

(9) Iwahama, T.; Sakaguchi, S.; Ishii, Y. *Chem. Commun.* **2000**, 2317.

(10) A typical reaction was carried out as follows: To a solution of Mn(OAc)<sub>2</sub> (0.15 mmol) and **2a** (9 mmol) was added **1a** (3 mmol). The mixture was stirred at 90 °C for 1 h under air (1 atm).

(1) (a) *Organic Phosphorus Compounds*; Kosolapoff, G. M., Maier, L., Ed.; Wiley-Interscience: New York, 1972. (b) Corbridge, D. E. C. *Phosphorus: An Outline of Its Chemistry, Biochemistry and Uses*, 5th ed.; Elsevier: Amsterdam, 1995.

(2) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 1571.

(3) Han, L.-B.; Mirzaei, F.; Zhao, C.-Q.; Tanaka, M. *J. Am. Chem. Soc.* **2000**, *122*, 5407.

(4) Deprele, S.; Montchamp, J.-L. *J. Am. Chem. Soc.* **2002**, *124*, 9386.

(5) Han, L.-B.; Zhao, C.-Q.; Tanaka, M. *J. Org. Chem.* **2000**, *66*, 5929.

(6) Reichwein, J. F.; Patel, M. C.; Pagenkopf, B. L. *Org. Lett.* **2001**, *3*, 4303.

(7) (a) Walling, C.; Peason, M. S. *Top. Phosphorus Chem.* **1966**, *3*, 1. (b) Benstrude, W. G. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; Wiley: New York, 1990; Vol. 1, Chapter 14. (c) *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, Chapter 22.

(8) (a) Stiles, A. R.; Vaughan, W. E.; Rust, F. F. *J. Am. Chem. Soc.* **1958**, *80*, 714. (b) Deprele, S.; Montchamp, J.-L. *J. Org. Chem.* **2001**, *66*, 6745.

**TABLE 2. Hydrophosphorylation of Various Alkenes with Diethyl Phosphite (2a) Catalyzed by Mn(OAc)<sub>2</sub> under Air<sup>a</sup>**

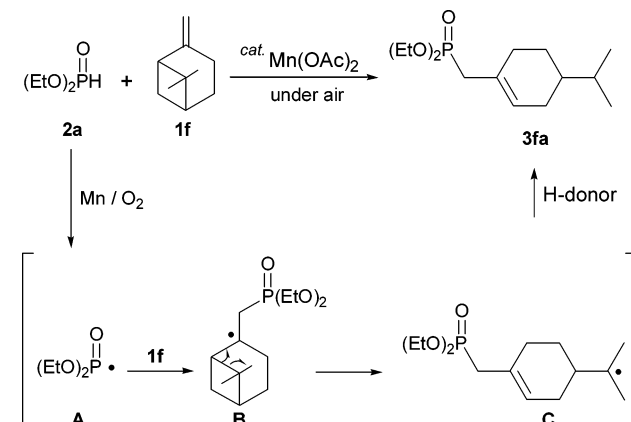
Run	Substrate	Temp./Time (°C/h)	Product (Yield / %)
1		110/2	(49) and  (35)
2		100/1	(80) [78] <sup>b</sup>
3 <sup>c</sup>		100/1	(82)
4 <sup>d</sup>		110/3	(62)
5		110/4	(32)
6		90/2	(35) and  (16)

<sup>a</sup> The reaction was run under the same conditions as Table 1, run 2. <sup>b</sup> The isolated yield. <sup>c</sup> **1d** (2 mmol) and **2a** (12 mmol) were used. <sup>d</sup> **1e** (2 mmol) and **2a** (14 mmol) were used.

hydrophosphorylation (runs 5 and 6). These results show that Mn(II) is oxidized to Mn(III) under these conditions, and the resulting Mn(III) ion seems to catalyze the hydrophosphorylation of **1a** with **2a**. When the amount of Mn(OAc)<sub>2</sub> was reduced to 1 mol %, the yield of **3aa** decreased to 21% even for 8 h (run 7). However, the addition of Co(OAc)<sub>2</sub> to this catalytic solution led to **3aa** in 69% yield (run 8). Since the Co(II) ions under air are well-known to generate Co(III)-oxygen complexes such as Co(III)-OO•, it seems to be reasonable to assume Mn(II) is readily oxidized by the Co(III)-oxygen complexes to Mn(III) which promotes smoothly the present hydrophosphorylation. Dibutyl phosphite (**2b**) and dimethyl phosphite (**2c**) added to **1a** to form the corresponding adducts, **3ab** and **3ac**, in good yields (runs 9 and 10).

To extend the present reaction to various alkenes, we tried the reaction between alkenes and **2a** in the presence of Mn(OAc)<sub>2</sub> (5 mol %) under air at 90–110 °C for 1–4 h (Table 2).

*cis*-2-Octene (**1b**) was reacted with **2a** at 110 °C under these conditions to give a regioisomeric mixture of 2- and 3-hydrophosphorylated products, **3ba** and **3ba'**, in a ratio of 49% to 35% (run 1). The reaction was achieved for cyclic alkenes such as cyclooctene (**1c**), giving **3ca** in good yield (80%) (run 2). Ethyl allylmalonate (**1d**) and allylbenzene (**1e**) reacted with **2a** to give the corresponding

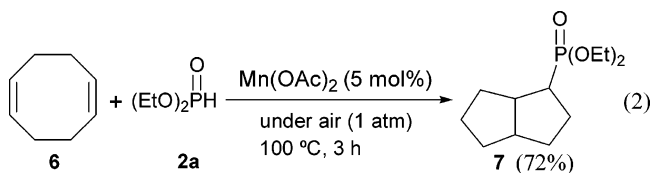
**SCHEME 1**

adducts, **3da** and **3ea**, in 82% and 62% yields, respectively (runs 3 and 4).

The reaction of  $\beta$ -pinene (**1f**) was found to proceed through ring opening of its cyclobutane moiety affording cleaved product **3fa** (32%) (run 5), and the formation of **3fa** can be rationally explained by Scheme 1. The phosphonyl radical (**A**) formed added to **1f** followed by ring opening of the cyclobutane ring giving an alkyl radical **C**, which subsequently abstracts hydrogen from hydrogen donor like **2a** afford the corresponding adduct **3fa**.

When the alkyne instead of alkene was used as a substrate, a similar coupling reaction was found to take place. 1-Octyne (**4**) was allowed to react with **2a** under the influence of Mn(OAc)<sub>2</sub> and air (1 atm) without solvent to form a stereoisomeric mixture of adducts, *cis*- and *trans*-**5** whose ratio was approximately 2:1 (run 6).

It is interesting that the reaction of 1,5-cyclooctadiene (**6**) with **2a** in the presence of Mn(OAc)<sub>2</sub> (5 mol %) under air without solvent at 100 °C for 3 h produced *cis*-fused product **7** in 72% yield (eq 2). In a previous paper, we showed that the dimethyl malonate radical generated by its one-electron oxidation of Mn(OAc)<sub>2</sub>/Co(OAc)<sub>2</sub>/O<sub>2</sub> system adds to **6** in a way similar to that described above to give the corresponding *cis*-fused adduct.<sup>11</sup>



In conclusion, we developed an efficient methodology for the hydrophosphorylation of alkenes and alkynes with dialkyl phosphites assisted by Mn salt under air (1 atm) through radical process. Further application of this catalytic system to many other key transformations are now in progress.

## Experimental Section

All starting materials were commercially available and used without any purification. GLC analysis was performed with a flame ionization detector using a 0.2 mm × 25 m capillary

(11) Hirase, K.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2002**, *67*, 970.

column (OV-1).  $^1\text{H}$  and  $^{13}\text{C}$  NMR were measured at 270 and 67.5 MHz, respectively, in  $\text{CDCl}_3$  with  $\text{Me}_4\text{Si}$  as the internal standard.

A typical reaction procedure of the reaction of **1a** with **2a** is as follows: To a solution of  $\text{Mn}(\text{OAc})_2$  (0.15 mmol) and **2a** (9 mmol) was added **1a** (3 mmol). The mixture was stirred at 90 °C for 1 h under air (1 atm). The product was isolated by column chromatography (230–400 mesh silica gel, *n*-hexane/ethyl acetate = 1:1). The conversions and yields of products were estimated from the peak areas based on the internal standard technique using GLC.

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