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Phosphonation of Arenes with Dialkyl Phosphites Catalyzed by Mn(II)/Co(II)/O$_2$ Redox Couple

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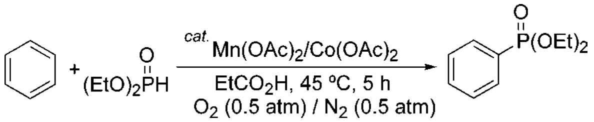
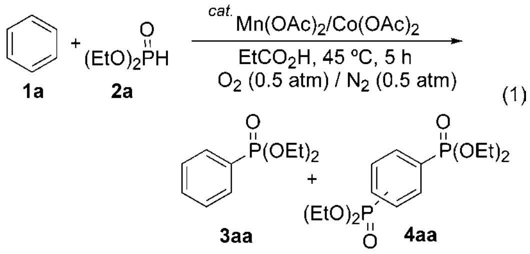
ABSTRACT



Arylphosphonates were first synthesized through a catalytic phosphonation of various arenes with dialkyl phosphites under the influence of an Mn(OAc)$_2$/Co(OAc)$_2$/O$_2$ redox couple. For instance, the reaction of benzene with diethyl phosphite in the presence of Mn(OAc)$_2$ (5 mol %) and Co(OAc)$_2$ (1 mol %) under a mixed gas of O$_2$ (0.5 atm) and N$_2$ (0.5 atm) at 45 °C led to diethyl phenylphosphonate in 81% selectivity at 62% conversion. This is the first successful phosphonation of benzene with dialkyl phosphites through a catalytic radical process.

Dialkyl arylphosphonates are important intermediates in the synthesis of pesticides and biologically active compounds.[1] There have been several methods for the synthesis of dialkyl arylphosphonates. Among them, the Michaelis−Arbuzov reaction is frequently used for this purpose.[2] The photolysis of iodobenzenes in the presence of trialkyl phosphates is reported to lead to arylphosphonates in good yields.[3] Jason reported free-radical phosphonation of naphthalene with diethyl phosphate using *tert*-butyl peroxide as a radical initiator.[4] Masui reported the formation of dialkyl arylphosphonates by anodic oxidation.[5] Chemical phosphonation of arenes with diethyl phosphite has been made under the influence of $(NH_4)_2[Ce(NO_3)_6]$[6] or $Na_2S_2O_8$ and $AgNO_3$.[7] In recent years, we have developed a novel catalytic method for the addition of diethyl phosphite to alkenes by using Mn(II)/Co(II)/O$_2$ redox system.[8] In this reaction, it is thought that diethyl phosphate undergoes one-electron oxidation by Mn(III) generated in situ from Mn(II) by the action of Co(II) and O$_2$ to form phosphonyl radicals which then add to alkenes leading to diethyl alkyphosphonates.

In continuation of this study, we have now developed a catalytic phosphonation of benzenes with dialkyl phosphites such as HP(O)(OEt)$_2$ by an Mn(II)/Co(II)/O$_2$ redox system under mild conditions (eq 1).



(1)

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To confirm an optimum reaction condition for the phosphonation of arenes with phosphites, the reaction of benzene (**1a**) with diethyl phosphite (**2a**) was carried out under various conditions (Table 1).

Table 1. Phosphonation of Benzene (**1a**) with Diethyl Phosphite (**2a**) by $Mn(OAc)_2/Co(OAc)_2/O_2$ System under Various Conditions[a]

	metal (mmol)				conv (%)		selectivity[b] (%)	
run	$Mn(OAc)_2$	$Co(OAc)_2$	*T* (°C)	time (h)	**1a**	**2a**	**3aa**	**4aa**
1	0.1	0.02	45	5	62	59	81	9
2	0.1	-	45	5	18	48	62	n.d.
3	-	0.1	45	5	7	7	n.d.	n.d.
4[c]	0.1	0.02	45	5	1	9	trace	n.d.
5[d]	0.1	0.02	45	5	38	33	89	trace
6[e]	0.1	0.02	45	5	80	79	41	6
7	0.1	0.02	60	5	69	74	80	8
8	0.1	0.02	25	5	6	22	33	n.d.
9[f]	0.01	0.002	45	5	55	46	85	5
10[f]	0.01	0.002	25	5	25	25	92	n.d.
11[g]	0.1	0.02	45	5	NR			
12[h]	0.1	0.02	45	15	68	66	87	8
13[i]	0.1	0.02	45	15	30	61	83	n.d.

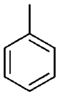
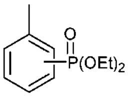
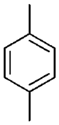
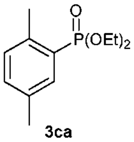
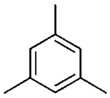
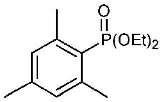
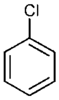
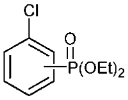
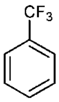
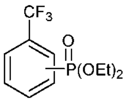
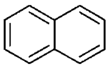
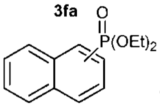
[a] **1a** (2 mmol) was reacted with **2a** (6 mmol) in the presence of $Mn(OAc)_2$ and $Co(OAc)_2$ in $EtCO_2H$ (1 mL) under O_2 (0.5 atm)/N_2 (0.5 atm) at 25 or 45 °C for 5 h. [b] Based on **1a** reacted. [c] Under Ar (1 atm). [d] Under air (1 atm). [e] Under O_2 (1 atm). [f] AcOK (1 mmol) was added. [g] 2,6-Di-*tert*-butyl-4-methylphenol (BHT) (0.1 mmol) was added. [h] $HP(O)(MeO)_2$ (**2b**) was used, and **3ab** and **4ab** were obtained. [i] $HP(O)(^{i}PrO)_2$ (**2c**) was used, and **3ac** was obtained.

The reaction of **1a** (2 mmol) with **2a** (6 mmol) in the presence of $Mn(OAc)_2$ (5 mol %) and $Co(OAc)_2$ (1 mol %) under O_2 (0.5 atm) and N_2 (0.5 atm) in propionic acid at 45 °C for 5 h gave diethyl phenylphosphonate (**3aa**) in 81% selectivity and a small amount of disubstituted product **4aa** (9%), which was formed by the further reaction of the resulting **3aa** with **2a** at 62% conversion of **1a** (run 1). The yield of **3aa** was considerably decreased when $Co(OAc)_2$ was removed from the catalytic system (run 2), while no phosphonation took place in the absence of $Mn(OAc)_2$ (run 3). The same reaction under Ar (1 atm) resulted in recovery of the starting **1a** (run 4). Under air (1 atm), however, **3aa** was obtained in high selectivity (89%), although the conversion of **1a** was low (38%) (run 5). On the other hand, under pure oxygen (1 atm), the selectivity of the reaction was considerably lowered (run 6). The selectivity of the reaction at 60 °C was almost the same as that at 45 °C (run 7). The reaction did not proceed appreciably at 25 °C (run 8). In a previous paper, we showed that the addition of activated methylene compounds such as ethyl cyanoacetate to alkenes was markedly accelerated by adding AcOK to the $Mn(OAc)_2/Co(Ac)_2/O_2$ redox system.[10]

In the present reaction, we observed a similar acceleration effect of AcOK on the phosphonation of **1a** with **2a**. Thus, when AcOK was added to the reaction system, the amounts of $Mn(OAc)_2$ and $Co(OAc)_2$ could be reduced to 0.5 and 0.1 mol %, respectively (runs 9 and 10). Surprisingly, the reaction was found to be induced even at room temperature by adding AcOK to this system to give **3aa** in 92% selectivity, although the conversion was low (25%) (run 10). When 2,6-di-*tert*-butyl-4-methylphenol (BHT) (0.1 mmol, 5 mol %) was added to the reaction system, no reaction took place at all (run 11). This fact indicates that the present phosphonation proceeds through a radical process. Like **2a**, dimethyl phosphite (**2b**) reacted also with **1a** to form dimethyl phenylphosphonate (**3ab**) in 87% selectivity at 68% conversion of **1a**, but diisopropyl phosphite (**2c**) was less reactive than **2a** to give diisopropyl phenylphosphonate (**3ac**) in 83% selectivity at 30% conversion of **1a** (runs 12 and 13).

On the basis of these results, a variety of substituted benzenes were allowed to react with **2a** under these conditions (Table 2).

Table 2. Phosphonation of Substituted Benzenes with Diethyl Phosphate (2a) by $Mn(OAc)_2/Co(OAc)_2/O_2$[a]

run	substrate	solvent (mL)	time /h	conv.[b] /%	product	select[b] /%
1	 **1b**	AcOH (1)	3	56	 **3ba**	90 (*o, m, p* 59/24/17)
2	 **1c**	AcOH (1)	3	58	 **3ca**	90
3	 **1d**	$EtCO_2H$ (1)	5	59	 **3da**	82
4[c]	 **1e**	$EtCO_2H$ (2)	15	69	 **3ea**	80
5[c]	 **1f**	AcOH (2)	15	71	 **3fa**	89
6[c]	 **1g**	AcOH (9)	15	56	 **3ga**	89 (α/β=87/13)

[a] Substituted benzene (2 mmol) was reacted with **2a** (6 mmol) in the presence of $Mn(OAc)_2$ (0.1 mmol) and $Co(OAc)_2$ (0.02 mmol) under O_2 (0.5 atm)/N_2 (0.5 atm) at 45 °C for 3−15 h. [b] Based on substituted benzene reacted. The selectivity (%) stands for the yield (%) of **3** based on **1** consumed. [c] AcOK (1 mmol) was added.

The reaction of *p*-xylene (**1c**) with **2a** afforded diethyl 2,5-dimethylphenylphophonate (**3ca**) in good selectivity (90%)

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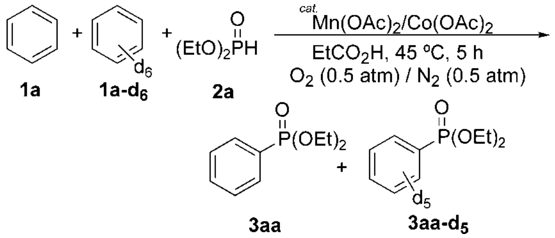
(run 2). Similarly, mesitylene (**1d**) reacted with **2a** to give diethyl mesitylphosphonate (**3da**) in 82% selectivity at 59% conversion (run 3). In the reaction of chlorobenzene (**1e**) and trifluoromethylbenzene (**1f**) bearing an electron-withdrawing group with **2a**, longer reaction time was needed to obtain diethyl phophonates, **3ea** and **3fa**, in satisfactory conversions and selectivities, although it was difficult to determine the ratio of ortho, meta, and para isomers (runs 4 and 5). Naphthalene (**1g**) underwent phophonation with **2a** to form a regioisomeric mixture of diethyl naphthylphosphonate (**3ga**) ($\alpha/\beta = 87/13$) (Run 6).

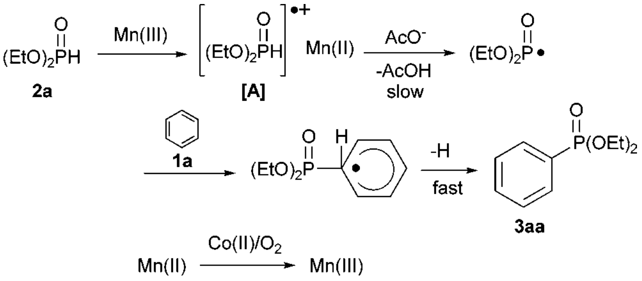
To obtain the information on the reaction pathway in the present phosphonation, a 1:1 mixture of benzene **1a** and deutrated benzene (**1a-*d*$_6$**) was reacted with **2a** under the same conditions as run 1 in Table 1 (eq 2). The ratio of the resulting phophonated product **3aa** to the deutrated product **3aa-*d*$_5$** was found to consist of an almost 1:1 mixture of **3aa** and **3aa-*d*$_5$** (eq 2). No isotope effect was observed in the present reaction. This shows that the loss of hydrogen atom or proton from benzene is not involved in the rate-determining step.



(2)

As shown in Table 1 (run 8), the fact that the reaction was markedly accelerated by the addition of a weak base like AcOK indicates that the abstraction of proton by the AcO$^-$ in the sequential reaction setps may be involved. Therefore, it is reasonable to assume the following reaction path involving the abstraction of the H$^+$ by AcO$^-$ from the diethyl phosphonate cation radical (**A**) generated by the one-electron oxidation by Mn(III) of **2a** (Scheme 1).

Scheme 1. Plausible Reaction Path for Phosphonation of **1a** with **2a**



In conclusion, we have successfully achieved the catalytic phosphonation of arenes with dialkyl phosphites through a radical process by using a Mn(II)/Co(II)/O_2 redox couple. This method provides a simple route to arylphosphonates which are difficult to prepare so far.

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Supporting Information Available: Experimental procedures and copies of ^{1}H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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