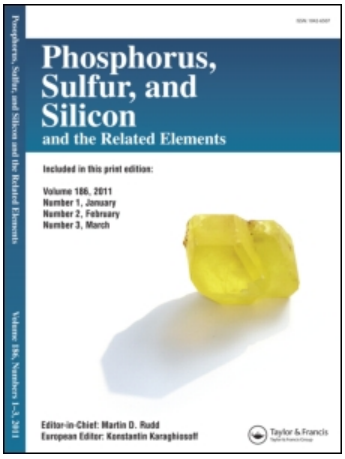


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# Reaction of Red Phosphorus with 4-Methoxystyrene in KOH-DMSO System: One-Pot Synthesis of Tris[2-(4-methoxyphenyl)ethyl]phosphane Oxide

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# REACTION OF RED PHOSPHORUS WITH 4-METHOXYSTYRENE IN KOH-DMSO SYSTEM: ONE-POT SYNTHESIS OF TRIS[2-(4-METHOXYPHENYL) ETHYL]PHOSPHANE OXIDE

**Nina K. Gusarova, Svetlana F. Malysheva, Natal'ya A. Belogorlova, Alexander V. Artem'ev, Vladimir A. Kuimov, and Boris A. Trofimov**

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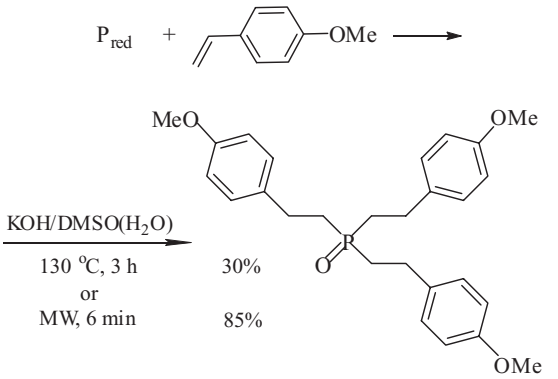
## GRAPHICAL ABSTRACT




**Abstract** *Red phosphorus reacts with 4-methoxystyrene in the KOH-DMSO superbase system (130 °C, 3 h, Ar) in the presence of a small quantity of $H_2O$ to give tris[2-(4-methoxyphenyl)ethyl]phosphane oxide as the main product in 30% yield. Microwave activation of the reaction (600 W, 6 min) affords basically a mixture of the phosphane oxide and tris[2-(4-methoxyphenyl)ethyl]phosphane (in a ratio of 1:1). When the mixture is exposed to air (r.t., 24 h), the phosphane oxide is formed in 85% yield.*

**Keywords** 4-Methoxystyrene; microwave irradiation; phosphane oxide; red phosphorus; superbase system

## INTRODUCTION

One-pot phosphorylation of available electrophiles (e.g., aryl- and hetarylalkenes, acetylenes, organic halides, alkene oxides) with red phosphorus in combination with

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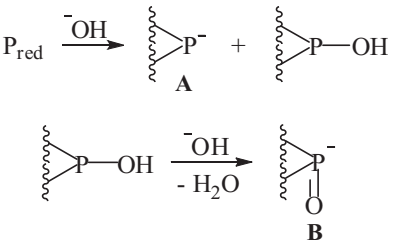
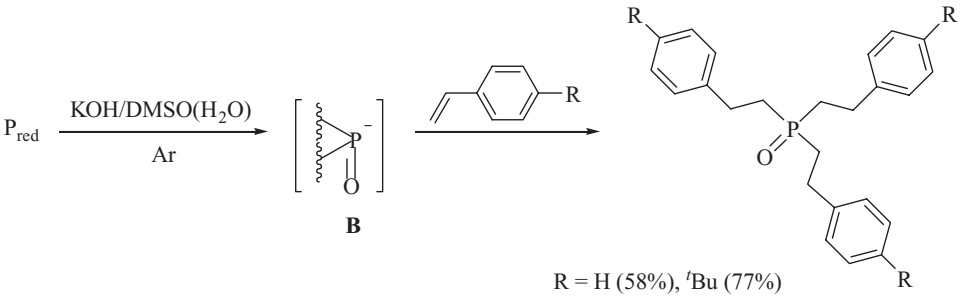
superbase systems such as KOH–nonhydroxylic polar solvent (DMSO, HMPA)–$H_2O$ represents one of the most convenient and promising approaches to the C—P bond formation and synthesis of fundamental organophosphorus compounds, in particular, phosphanes, phosphane oxides, and phosphinic acids.[1] The key steps of these phosphorylations include likely the cleavage of P—P bonds in the macromolecule of red phosphorus (probably occurring in phosphorus nanoparticles) by hydroxide anions to form highly active P-centered nucleophiles such as polyphosphide **A** and polyphosphinite **B** anions and their further interaction with an electrophile[1c] (Scheme 1).




**Scheme 1**



The essence of these reactions is a competition between the polyphosphide and polyphosphinite anions for the electrophile. For example, red phosphorus reacts with weak electrophilic alkenes such as styrene[2] and 4-(*tert*-butyl)styrene[3] in the KOH-DMSO system under an argon blanket to deliver tris(2-phenylethyl)- and tris[4-(*tert*-butylphenyl)ethyl]phosphane oxides (but not the corresponding phosphanes). Therefore, in these processes, polyphosphinite anions **B** win the competition over polyphosphide anions **A** (Scheme 2).




**Scheme 2**

In these cases, DMSO does not act as an oxidizer, since under the conditions studied, phosphane, which is easily generated from red phosphorus in KOH/$H_2O$/toluene (or dioxane) medium,[4,5] is added to styrene[4,6] and 4-(*tert*-butyl)styrene[5] in a KOH/DMSO system to give the corresponding secondary or tertiary phosphanes.

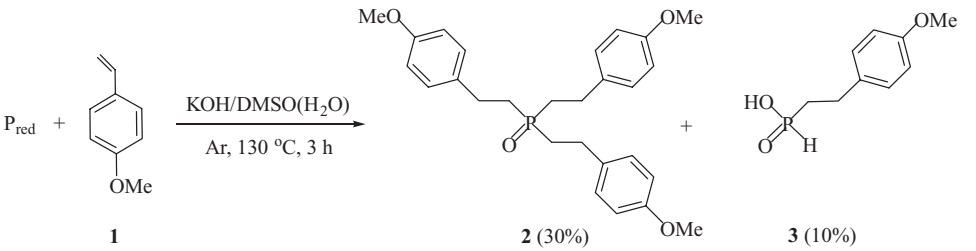
At the same time, the literature is lacking data on the interaction of phosphorus-centered nucleophiles with alkoxyvinylarenes. The realization of such reactions is problematic, because the presence of an electron-donating methoxy group in the 2- or 4-positions of the benzene ring of alkoxyvinylbenzenes decreases electrophilicity of the double bond

of these alkenes and, therefore, their reactivity towards nucleophiles. For example, 4-methoxystyrene reacts with such nucleophiles as BuLi, *tert*-BuLi,[7] or $PhCH_2NH_2$[8] and $Me_2CHCN$[9] in the presence of superbase systems more slowly and under harsher conditions than styrene.

In this article, based on the example of 4-methoxystyrene, we report for the first time the addition of phosphorus-centered nucleophiles generated from red phosphorus in the superbase system to the double bond of alkoxyvinylarenes.

## RESULTS AND DISCUSSION

We have found that 4-methoxystyrene (**1**) reacts with red phosphorus in the KOH-DMSO suspension in the presence of small quantity of $H_2O$ (as a proton donor) and hydroquinone as a radical process inhibitor at 130 °C for 3 h under an argon blanket to give tris[2-(4-methoxyphenyl)ethyl]phosphane oxide (**2**) and 2-(4-methoxyphenyl)ethylphosphinic acid (**3**) in 30% and 10% yields, respectively (Scheme 3).




**Scheme 3**

Styrene turns out to be more reactive in this reaction. The phosphorylation of styrene with red phosphorus in the system KOH-DMSO($H_2O$) proceeds at 120°C for 3 h to furnish tris(2-phenylethyl)phosphane oxide, bis(2-phenylethyl)phosphinic, and 2-phenylethylphosphinic acids in up to 64% total yield. The yield of the main product, tris(2-phenylethyl)phosphane oxide, is 59%.

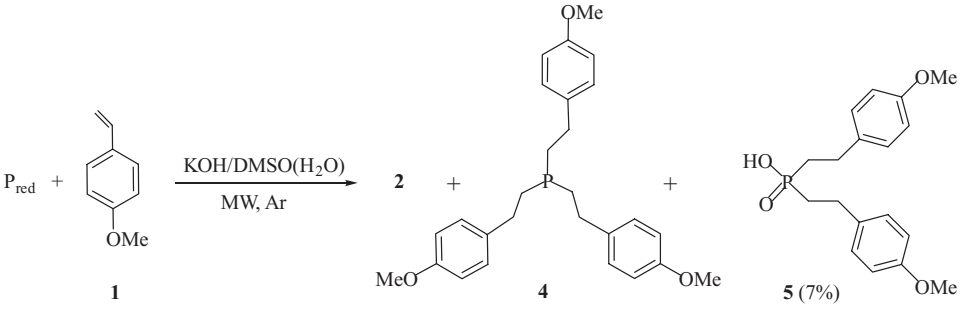
Microwave-assisted reaction of red phosphorus with 4-methoxystyrene not only shortens the process duration (by approx. 20 times), but noticeably affects on its chemoselectivity. Thus, a microwave irradiation (600 W, 6 min) promoted version of the reaction (with the same reactants ratio) delivers, along with the anticipated phosphane oxide **2**, the corresponding tertiary phosphane **4** in 88% total yield, the ratio of the products being 1:1 ($^{31}P$ NMR). In addition, the reaction gives bis[2-(4-methoxyphenyl)ethyl]phosphinic acid (**5**) in small yield (7%) (Scheme 4).

The mixture of compounds **2** and **4** was exposed to air (r.t., 24 h) to afford phosphane oxide **2** in 85% isolated yield.

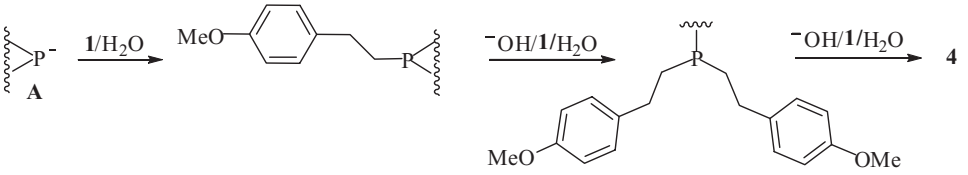
The formation of phosphane **4** in the phosphorylation of styrene **1** with red phosphorus in the KOH-DMSO system likely occurs via polyphosphide anions (**A**) (Scheme 5).

Accordingly, phosphane oxide **2** and phosphinic acids **3** and **5** in the reactions studied are formed apparently with the participation of polyphosphinite anions (**B**) (Scheme 6).

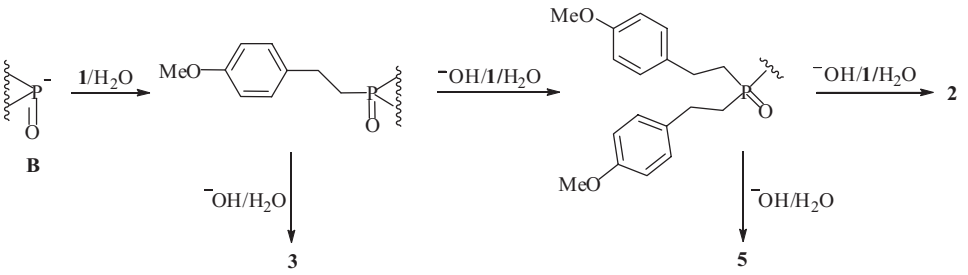
In conclusion, the results obtained contribute fundamentally to phosphorus and arylalkenes chemistry, as well as allow the novel tertiary phosphane oxide **2** to be synthesized in up to 85% yield. Microwave-assisted reaction of red phosphorus with 4-methoxystyrene




**Scheme 4**




**Scheme 5**




**Scheme 6**

affects the chemoselectivity of the process and increases its rate. This approach opens a straightforward route to phosphane oxide, and hence, the corresponding phosphane bears electron-rich alkoxyaryl substituents. Such types of phosphorus compounds are of special importance and are used as ligands for the design of new catalytic systems for cross-coupling reactions,[10] the C—H bond activation reactions,[11] ester hydrogenation,[12] addition of arylboronic acids to aldehydes,[13] cyanosilylation and cyanocarbonation of carbonyl compounds,[14] and aminocarbonylation of alkyl iodides.[15]

## EXPERIMENTAL

IR spectra were measured with a Bruker IFS 25 instrument in microlayer or KBr ($cm^{-1}$). $^{1}H$, $^{13}C$, and $^{31}P$ NMR spectra were recorded on a Bruker DPX-400 spectrometer (at 400.13, 100.61, and 161.98 MHz, respectively) in $CDCl_3$ solutions and referenced to internal HMDS ($^{1}H$), $CHCl_3$ ($^{13}C$) and external 85% $H_3PO_4$ ($^{31}P$). Two-dimensional homo- and heteronuclear NMR correlation experiments (NOESY, HSQC) were used to assign the signals in $^{1}H$ and $^{13}C$ NMR spectra. Microwave irradiation was performed in multimode,

modified microwave oven, Samsung M181DNR (max. power level 850 W) equipped with a reflux condenser. We used an open vessel microwave technology (atmospheric pressure). The reaction of red phosphorus with styrene was performed in a round bottom flask (Pyrex). A 500 mL one-necked flask was placed into the multimode reactor [impulse magnetron OM75P(31), power 1.25 MW/2.45 GHz] and was equipped with a reflux condenser, which was brought out via a special hole. Red phosphorus from KSAN "SIA" was employed. 4-Methoxystyrene was synthesized according to the literature.[16] All reactions were conducted under an argon atmosphere.

### Synthesis of Tertiary Phosphine Oxide 2

A mixture of red phosphorus (11 mmol), styrene **1** (13.3 mmol), $KOH{\cdot}0.5H_2O$ (13 mmol), water (0.07 mL), DMSO (15 mL), and hydroquinone (0.01 g) was stirred for 3 h at 130 °C, diluted with water (25 mL), and extracted with $CHCl_3$ (3 × 20 mL). The chloroform extract was washed with a 20% aq solution of KCl (3 × 15 mL) and dried over $K_2CO_3$. The solvent and unreacted 4-methoxystyrene (1.02 g, 43% conversion) were removed under reduced pressure. The residue was washed with hexane (3 mL) and dried in vacuum to furnish 0.27 g (30%) phosphane oxide **2**. The aqueous layer was acidified with a 35% aq HCl up to pH 4–5 (to neutralize $4\text{-}MeOC_6H_4CH_2CH_2PH(O)OK$) and extracted with chloroform (3 × 20 mL). The chloroform extract was washed with water (3 × 15 mL) and dried over $CaCl_2$. Then the solvent was removed, and the residue was dried in vacuum to give 0.11 g (10%) of phosphinic acid **3**.

**Tris[2-(4-methoxyphenyl)ethyl]phosphane oxide 2.** Colorless powder, 1.04 g (85%) yield, mp 129–131°C (hexane). $^1$H NMR ($CDCl_3$), $\delta$ (ppm), $J$ (Hz): 1.92–2.00 (m, 6H, $CH_2P$), 2.79–2.86 (m, 6H, $C\underline{H}_2C_6H_4$), 3.76 (m, 9H, OMe), 6.86–7.06, and 7.06–7.08 (m, 12H, $C_6H_4$); $^{13}$C NMR ($CDCl_3$), $\delta$ (ppm), $J$ (Hz): 26.91 ($\underline{C}H_2C_6H_4$), 31.40 (d, $^1J_{PC}$ = 61.5 Hz, $\underline{C}H_2P$), 55.28 (Me), 114.10 (C-o$C_6H_4$), 129.02 (C-m$C_6H_4$), 132.75 (d, $^3J_{PC}$ = 12.4 Hz, $\overline{C}$-i$C_6H_4$), 158.56 (C-p$C_6H_4$); $^{31}$P NMR ($CDCl_3$), $\delta$ (ppm): 47.01. IR (KBr), $\nu$, $cm^{-1}$: 3058, 3016, 2955, 2932, 2908, 2870, 2836, 1610, 1583, 1512, 1461, 1440, 1301, 1273, 1180, 1161, 1129, 1099, 1033, 948, 851, 832, 817, 788, 751, 722, 661, 637, 541, 525, 469. Anal. Calcd for $C_{27}H_{33}O_4P$: C, 71.66; H, 7.35; P, 6.84. Found: C, 71.57; H, 7.33; P, 6.70.

**2-(4-Methoxyphenyl)ethylphosphinic acid 3.** Colorless crystalline powder, 0.11 g (10%) yield, mp 229–232°C (ethanol). $^1$H NMR ($D_2O$), $\delta$ (ppm), $J$ (Hz): 1.80–1.88 (m, 2H, $CH_2P$), 2.75–2.82 (m, 2H, $C\underline{H}_2C_6H_4$), 3.83 (s, 3H, OMe), 6.94 (d, 1H, $^1J_{PH}$ = 505.7 Hz, PH), 6.94 and 7.48 (m, 4H, $\overline{C}_6H_4$), 8.02 (br. s, 1H, OH); $^{13}$C NMR ($CDCl_3$), $\delta$ (ppm), $J$ (Hz): 25.94 ($\underline{C}H_2C_6H_4$), 32.72 (d, $^1J_{PC}$ = 94.2 Hz, $CH_2P$), 54.95 (OMe), 113.80 (C-o$C_6H_4$), 129.01 (C-m$C_6H_4$), 134.27 (C-i$C_6H_4$), 147.61 (C-p$C_6H_4$); $^{31}$P NMR ($D_2O$), $\delta$ (ppm), $J$ (Hz): 30.18 (d, $^1J_{PH}$ = 505.8 Hz); IR (KBr), $\nu$, $cm^{-1}$: 3436, 2956, 2935, 2837, 2295, 2100, 2600, 1629, 1613, 1585, 1514, 1465, 1443, 1421, 1302, 1250, 1210, 1176, 1129, 1057, 1036, 938, 919, 903, 847, 817, 783, 736, 637, 620, 581, 549, 520, 490, 474, 442. Anal. Calcd for $C_9H_{13}O_3P$: C, 54.00; H, 6.55; P, 15.47. Found: C, 54.27; H, 6.73; P, 15.76.

### Phosphorylation of 4-Methoxystyrene with Red Phosphorus Under Microwave Irradiation

A mixture of red phosphorus (11 mmol), styrene **1** (13.3 mmol), hydroquinone (0.01 g), $KOH{\cdot}0.5H_2O$ (13 mmol), water (0.07 mL), and DMSO (15 mL) was irradiated in

microwave oven (600 W) at 180°C for 6 min (real time of magnetron action was 3 min). The reaction mixture was cooled and analyzed by $^{31}P$ NMR. The mixture contained phosphine oxide **2** (47.01 ppm) and phosphine **4** (–28.13 ppm) in the ratio of 1:1. The mixture was exposed to air for 24 h, diluted with water (25 mL). Unreacted phosphorus was filtered off and washed with water (30 mL) up to neutral pH, and dried on air to recover 0.104 g of red phosphorus (conversion 69%). The filtrate was extracted with $CHCl_3$ (3 × 25 mL), then the chloroform extract was washed with a 20% aq solution of KCl (3 × 10 mL) and dried over $K_2CO_3$. The solvent and unreacted 4-methoxystyrene (0.82 g, 64% conversion) were removed under reduced pressure. The residue (1.1 g) was precipitated from $CHCl_3$ (5 mL) with hexane (40 mL), and the precipitate was dried in vacuum to give 1.04 g (85%) of phosphine oxide **2**. The aqueous layer was acidified with a 35% aq HCl up to pH 4–5 (to neutralize (4-$MeOC_6H_4CH_2CH_2)_2P(O)OK$) and extracted with chloroform (3 × 20 mL). The chloroform extract was washed with water (3 × 15 mL) and dried over $CaCl_2$. Then the solvent was removed, and the residue was dried in vacuum to give 0.1 g (7%) of phosphinic acid **5**.

**Bis[2-(4-methoxyphenyl)ethyl]phosphinic acid 5.** Colorless crystalline powder, 0.1 g (7%) yield, mp 237–241°C (ethanol). $^1H$ NMR ($D_2O$), $\delta$ (ppm), $J$ (Hz): 1.50–1.70 (m, 4H, $CH_2P$), 2.50–2.72 (m, 4H, $C\underline{H}_2C_6H_4$), 3.69 (s, 6H, OMe), 6.83 and 7.08 (m, 8H, $C_6H_4$), 7.87 (br. s, OH); $^{13}C$ NMR ($D_2O$), $\delta$ (ppm), $J$ (Hz): 27.64 ($\underline{C}H_2C_6H_4$), 31.68 (d, $^1J_{PC} = 80.1$ Hz, $CH_2P$), 55.43 (OMe), 114.02 (C-$oC_6H_4$), 129.36 (C-$mC_6H_4$), 135.34 (d, $^3J_{PC} = 14$ Hz, C-$iC_6H_4$), 157.15 (C-$pC_6H_4$); $^{31}P$ NMR ($D_2O$), $\delta$ (ppm), $J$ (Hz): $\delta$ 44.73; IR (KBr), $\nu$, $cm^{-1}$: 3440, 2956, 2937, 2856, 2838, 2600, 2200, 1632, 1614, 1585, 1556, 1514, 1465, 1454, 1417, 1405, 1335, 1303, 1249, 1215, 1178, 1135, 1120, 1099, 1035, 938, 872, 853, 824, 785, 753, 699, 667, 636, 618, 558, 444. Anal. Calcd for $C_{18}H_{23}O_4P$: C, 64.66; H, 6.93; P, 9.26. Found C, 64.57; H, 6.85; P, 9.47.



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