

# Radical Alkylphosphanylation of Olefins with Stannylated or Silylated Phosphanes and Alkyl Iodides

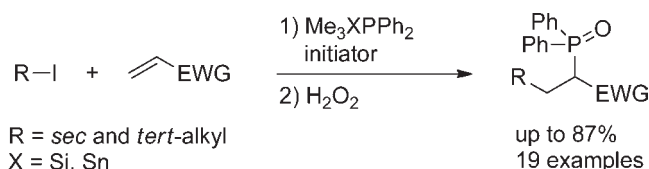
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## ABSTRACT



Intermolecular conjugate radical addition reactions of secondary and tertiary alkyl radicals derived from the corresponding alkyl iodides to activated olefins such as  $\alpha,\beta$ -unsaturated esters, amides, imides, nitriles, and sulfones are described. The adduct radicals are trapped by either diphenyl(trimethylstannyl)phosphane or the commercially available diphenyl(trimethylsilyl)phosphane as chain transfer reagents to give the corresponding phosphanylated products in moderate to good yields. The overall process comprises a C–C followed by a C–P bond formation.

Reductive radical addition of alkyl iodides or bromides to olefins known as the Giese reaction has been intensively used in synthetic radical chemistry.<sup>1</sup> In these reactions the adduct radical is reduced by an H-donor providing the corresponding reduced product (Scheme 1). In most cases tin hydrides have been used as reagents. However, synthetically more valuable is a functionalization of the adduct radical via reaction with an X-donor forming a C–X bond along with the initial C–C bond. This can be achieved by applying a halogen atom transfer method where R–X is added to an olefin with ideal atom economy.<sup>2</sup> Such halogen transfer processes can be catalyzed by various transition metals.<sup>3</sup> Recently, we embarked on a program of

radical phosphanylation.<sup>4,5</sup> In our eyes, C–P bond formation using the radical approach has a lot of potential, however it has not been intensively investigated to date.<sup>6</sup> We showed that homolytic substitution at phosphorus with alkyl and aryl radicals at P in  $\text{Me}_3\text{SnPPH}_2$  and  $\text{Me}_3\text{SiPPH}_2$ <sup>7</sup> occurs with rate constants similar to those for the corresponding reductions of C-radicals with  $\text{Bu}_3\text{SnH}$ .<sup>5</sup> Based on these kinetics, we assumed that unprecedented alkylative radical phosphanylation of olefins using alkyl iodides in combination with  $\text{Me}_3\text{SiPPH}_2$  (**1a**) or  $\text{Me}_3\text{SnPPH}_2$  (**1b**) as trapping and chain transfer reagents should be feasible (Scheme 1). Herein we present the first results along this line.

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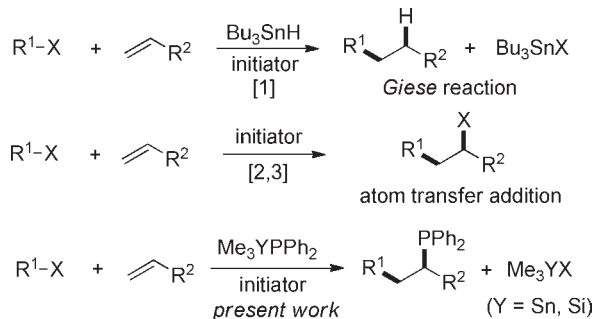
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**Scheme 1.** Reductive Radical Addition of Alkyl Halides to Olefins and Olefin Functionalization via C–C and C–X Bond Formation (X = Halogen)



Initial studies were performed using the readily prepared  $\text{Me}_3\text{SiPPh}_2$  (**1a**), which is also commercially available.<sup>8,9</sup> As a model reaction we investigated addition of cyclohexyl iodide to *tert*-butyl acrylate using various initiators under different conditions (80 °C, 24 h, Table 1). The crude reaction mixture was treated with  $\text{H}_2\text{O}_2$  to give phosphine oxide **2a**, which was readily isolated. Pleasingly, reacting cyclohexyl iodide, *tert*-butyl acrylate (1.1 equiv), and the silane **1a** (1.1 equiv) in the presence of 1,1'-azobis(cyclohexane-1-carbonitrile) (V-40, 0.25 equiv) as an initiator in *n*-heptane afforded after oxidation phosphine oxide **2a** in 56% isolated yield (Table 1, entry 1). Increasing the amount of silane and acrylate provided a better yield (entry 2), and the best result was achieved with 1.3 equiv of these reagents (72%, entry 3). Further increasing the amount of **1a** and acrylate afforded lower yields (entries 4–6), and 0.25 equiv of V-40 was observed to be optimal for our alkylative radical phosphanylation (entries 7–9). Other initiators delivered worse results (entries 10–13). The reaction was also efficient using the stannylated phosphane **1b** (entry 14). Since stannyl radicals tolerate benzene as a solvent, the reaction was also conducted in the aromatic solvent, and under these conditions the highest yield was achieved (84%, entry 15). It is important to note that the reaction worked well with only a little excess of the olefin with respect to the iodide. Surprisingly, cyclohexyl bromide did not work as a radical precursor in this particular process (entry 16) and also the corresponding xanthate delivered a lower yield (entry 17).

Under optimized conditions, *tert*-butyl iodide and 1-adamantyl iodide were reacted with *tert*-butyl acrylate to give after oxidation the corresponding phosphine oxides **2b** and **2c** in moderate to good yields (entries 18–23). Unfortunately, we were not able to run that alkylative phosphanylation using a primary alkyl iodide (entries 24 and 25). The product was identified by mass spectrometric analysis in trace amounts. The major products observed were *n*-pentyldiphenylphosphine oxide deriving from direct phosphanylation of the primary alkyl radical and  $\text{Ph}_2\text{P}(\text{O})\text{CH}_2\text{CH}_2\text{CO}_2t\text{Bu}$  deriving from background ionic 1,4-phosphanylation. An attempted reaction using phenyl iodide, **1b**, and *tert*-butyl acrylate under similar conditions delivered  $\text{Ph}_2\text{P}(\text{O})\text{CH}_2\text{CH}_2\text{CO}_2t\text{Bu}$  in 87% yield along

with 26% of  $\text{Ph}_3\text{PO}$ . Hence, if the radical reaction is inefficient, the ionic background process takes over.

**Table 1.** Reaction of Alkyl Iodides with *tert*-Butyl Acrylate and **1a/1b** under Different Conditions (0.1 M, 24 h)

$$\text{R-I} + \text{CH}_2=\text{CHCO}_2t\text{Bu} \xrightarrow[\text{2) H}_2\text{O}_2]{\text{1) 1a or 1b, initiator, n-heptane, 80 °C}} \text{R-CH}_2\text{-CH}(\text{P}(\text{O})(\text{Ph})_2)\text{-CO}_2t\text{Bu} \quad \text{2a-d}$$

entry	<b>1x</b> (equiv)	R	initiator (equiv)	acrylate (equiv)	yield (%) <sup>a</sup>
1	<b>1a</b> (1.1)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.1	56 ( <b>2a</b> )
2	<b>1a</b> (1.2)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.2	65 ( <b>2a</b> )
3	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.3	72 ( <b>2a</b> )
4	<b>1a</b> (1.5)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.5	68 ( <b>2a</b> )
5	<b>1a</b> (2.0)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.50)	2.0	63 ( <b>2a</b> )
6	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.5	62 ( <b>2a</b> )
7	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.10)	1.3	48 ( <b>2a</b> )
8	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.20)	1.3	56 ( <b>2a</b> )
9	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.50)	1.3	59 ( <b>2a</b> )
10	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	Et <sub>3</sub> B/O <sub>2</sub> (0.25)	1.3	<2 ( <b>2a</b> )
11	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	AIBN (0.25)	1.3	35 ( <b>2a</b> )
12	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	<i>t</i> BuOO <i>t</i> Bu (0.25) <sup>b</sup>	1.3	<2 ( <b>2a</b> )
13	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	<i>t</i> BuON=NO <i>t</i> Bu (0.25)	1.3	32 ( <b>2a</b> )
14	<b>1b</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.3	64 ( <b>2a</b> )
15 <sup>c</sup>	<b>1b</b> (1.3)	C <sub>6</sub> H <sub>11</sub>	V-40 (0.25)	1.3	84 ( <b>2a</b> )
16	<b>1a</b> (1.3)	C <sub>6</sub> H <sub>11</sub> <sup>d</sup>	V-40 (0.25)	1.3	<2 ( <b>2a</b> )
17	<b>1b</b> (1.3)	C <sub>6</sub> H <sub>11</sub> <sup>e</sup>	V-40 (0.25)	1.3	39 ( <b>2a</b> )
18	<b>1a</b> (1.3)	<i>t</i> Bu	V-40 (0.25)	1.3	76 ( <b>2b</b> )
19	<b>1b</b> (1.3)	<i>t</i> Bu	V-40 (0.25)	1.3	69 ( <b>2b</b> )
20 <sup>c</sup>	<b>1b</b> (1.3)	<i>t</i> Bu	V-40 (0.25)	1.3	50 ( <b>2b</b> )
21	<b>1a</b> (1.3)	1-ada	V-40 (0.25)	1.3	32 ( <b>2c</b> )
22	<b>1b</b> (1.3)	1-ada	V-40 (0.25)	1.3	74 ( <b>2c</b> )
23 <sup>c</sup>	<b>1b</b> (1.3)	1-ada	V-40 (0.25)	1.3	55 ( <b>2c</b> )
24	<b>1a</b> (1.3)	C <sub>5</sub> H <sub>11</sub>	V-40 (0.25)	1.3	<5 ( <b>2d</b> )
25	<b>1b</b> (1.3)	C <sub>5</sub> H <sub>11</sub>	V-40 (0.25)	1.3	<5 ( <b>2d</b> )

<sup>a</sup> Isolated yield after  $\text{SiO}_2$  chromatography. <sup>b</sup> Conducted in a sealed tube at 140 °C. <sup>c</sup> Conducted in benzene. <sup>d</sup> Conducted with cyclohexyl bromide. <sup>e</sup> Conducted with cyclohexyl-*S*-methyl xanthate.

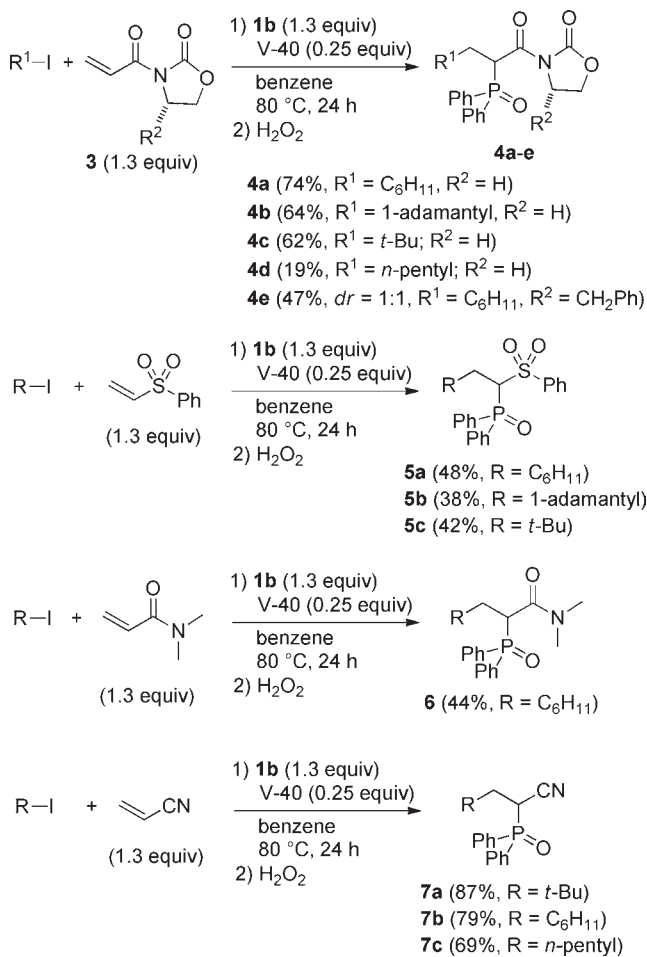
To study the scope of our reaction further we tested other typical radical acceptors in the alkylative phosphanylation. Oxazolidinone **3** (R = H) was observed to be an efficient acceptor in the reaction using the stannylated phosphane **1b** as a chain transfer/trapping reagent. Reactions were conducted in benzene under the optimized conditions discussed in Table 1. Cyclohexyl iodide reacted with **1b** to give after oxidation phosphine oxide **4a** in 74% yield (Scheme 2). 1-Iodoadamantane and *tert*-butyl iodide provided products **4b** and **4c** in a 64% and 62% yield, respectively. Again, reaction with *n*-pentyl iodide was not

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efficient and the targeted product **4d** was isolated in low yield even by using 3.2 equiv of acceptor **3** ( $R = H$ ).

**Scheme 2.** Variation of the Radical Acceptor



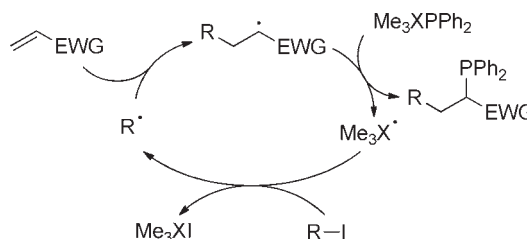
We also tested whether stereoselective phosphanylation can be achieved. To this end, we reacted Evans' oxazolidinone<sup>10</sup> derived acceptor **3** ( $R^2 = \text{benzyl}$ ) with cyclohexyl iodide under optimized conditions with **1b**. After oxidation, product **4e** was isolated as a 1:1 mixture of diastereoisomers. Reactions with the silane **1a** using oxazolidinone **3** ( $R^2 = H$ ) did not work. As a product we identified the product of phosphanylation at the  $\beta$ -position without any C–C bond formation. This product derives from an ionic  $\beta$ -C–P bond formation which is known to occur in propiolates.<sup>11</sup> Most of the subsequent studies with Lewis basic radical acceptors were therefore conducted only with the stannylated phosphane **1b**.

Vinyl phenyl sulfone was also successfully converted in the presence of **1b** to the corresponding products **5a–c** resulting from the addition of cyclohexyl, 1-adamantyl, and *tert*-butyl radicals, followed by phosphanylation and oxidation. Amides are also substrates for the alkylative phosphanylation as documented by the reaction of *N,N*-dimethylacrylamide with cyclohexyl iodide and phosphane **1b** ( $\rightarrow$  **6**). The more Lewis basic

acceptors (sulfone and the dimethyl amide) showed lower yields. This is probably due to competing ionic reactions initiated by the Lewis basic O-atom (see below). We found that the radical alkylative phosphanylation works very well with acrylonitrile as a radical acceptor. Using *t*-BuI the product **7a** was isolated in 87% yield and the reaction with cyclohexyl iodide delivered **7b** in 79% yield. We were very pleased to find that acrylonitrile also allowed successful alkylative phosphanylation with a primary alkyl radical. *n*-Pentyl iodide reacted under optimized conditions in good yield to produce **7c** (69%).

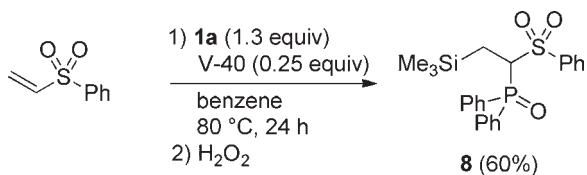
The alkylative phosphanylations proceed via initial radical addition onto the radical acceptor to give the adduct radical that is trapped by the phosphane **1a,b** via homolytic substitution at phosphorus to provide the product along with the stannyl or silyl radical (Scheme 3). Iodine abstraction by the Si or Sn radical, liberating radical R, sustains the chain. H<sub>2</sub>O<sub>2</sub> oxidation eventually provides the isolated product.

**Scheme 3.** Radical Chain (EWG = Electron-Withdrawing Group)



Based on the mechanism it should be possible by leaving out the alkyl halide to add  $Me_3XPPH_2$  to the olefin giving the corresponding 1,2-addition product. Using the stannylated phosphane **1b** this was not successful since stannyl radical addition is reversible and the ionic reaction competed. Hence, reaction of **1b** with *tert*-butyl acrylate under radical conditions provided only the product of the ionic addition ( $Ph_2P(O)CH_2CH_2CO_2tBu$ ) in 38% yield. Switching to  $Me_3SiPPh_2$  (**1a**) provided basically the same result (40% of  $Ph_2P(O)CH_2CH_2CO_2tBu$ ). However, efficient radical silylphosphanylation was achieved with phenylvinylsulfone (PVS) as an acceptor. Reaction of **1a** with PVS in *n*-heptane at 80 °C in the presence of V-40 for 24 h delivered adduct **8** in 60% yield (Scheme 4). None of the ionic product was identified. With the oxazolidinone acceptor **3** ( $R = H$ ) the reaction had to be conducted in benzene, and the radical silylphosphanylation product was not identified. The product of the ionic  $\beta$ -phosphanylation was isolated in 79% yield (see Supporting Information). It seems that for acceptors bearing Lewis basic carbonyl functional groups radical chemistry cannot compete with the ionic process under the tested conditions. Likely, the silylphosphane is activated for ionic addition with the Lewis base via O–Si interaction.

**Scheme 4.** Radical Silylphosphanylation



In summary, we presented the first radical alkylphosphanylations of various activated olefins using Me<sub>3</sub>SnPPh<sub>2</sub> and Me<sub>3</sub>SiPPh<sub>2</sub> (commercially available) as radical trapping/chain transfer reagents. Their reactions comprise a C–C and C–P bond formation, and the trapping process

occurs via homolytic substitution at phosphorus. Reactions work with secondary and tertiary alkyl iodides. Moreover, in the absence of an alkyl iodide, Me<sub>3</sub>SiPPh<sub>2</sub> can undergo a transition-metal-free silylphosphanylation under radical conditions.

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**Supporting Information Available.** Experimental details, characterization data for the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.