Phosphanes

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Highly Selective Phosphinylphosphination of Alkenes with Tetraphenyldiphosphine Monoxide

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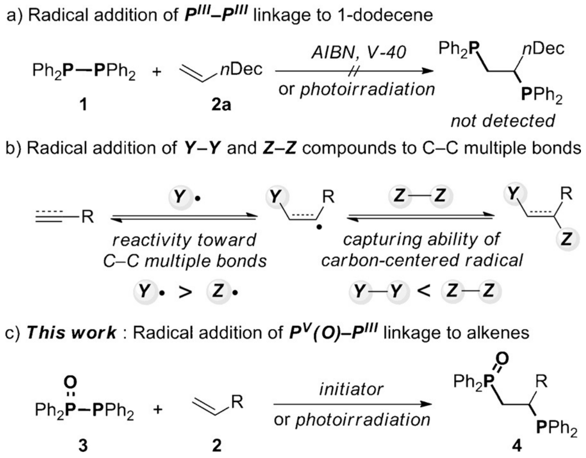
Abstract: *In sharp contrast to tetraphenyldiphosphine, which does not add to carbon–carbon double bonds efficiently, its monoxide, [$Ph_2P(O)PPh_2$] can engage in a radical addition to various alkenes, thus affording the corresponding 1-phosphinyl-2-phosphinoalkanes regioselectively, and they can be converted into their sulfides by treatment with elemental sulfur. The phosphinylphosphination proceeds by the homolytic cleavage of the $P^V(O)-P^{III}$ single bond of $Ph_2P(O)PPh_2$, followed by selective attack of the phosphinyl radical at the terminal position of the alkenes, and selective trapping of the resulting carbon radical by the phosphino group. Furthermore, the phosphinylphosphination product could be converted directly into its platinum complex with a hemilabile P,O chelation.*

Organophosphorus compounds play a vital role in organic synthesis, catalysis, materials chemistry, medicinal chemistry, and coordination chemistry.[1] Therefore, the development of new synthetic methods to create organophosphorus species is of great importance. For the selective introduction of phosphorus moieties onto organic molecules, the addition reaction to carbon–carbon multiple bonds is one of the most useful and atom-economical methods.[2] In particular, the 1,2-addition of phosphorus compounds, bearing a P–P single bond, to carbon–carbon multiple bonds is the most straightforward method for the preparation of vicinal bis(phosphine)s,[3] which are useful bidentate ligands in transition metal catalyzed reactions.[4] Although several attractive examples of the addition of phosphorus compounds to alkynes have been reported,[5] to the best of our knowledge, the corresponding addition to alkenes has not been achieved, with the exception of the addition of specified diphosphines, such as tetramethyldiphosphine [$(Me_2P)_2$],[6] tetrachlorodiphosphine [$(Cl_2P)_2$],[7] tetrafluorodiphosphine [$(F_2P)_2$],[8] and 1,1-diaminodiphosphine,[9] to only very a few alkenes.

We initiated our study by investigating the addition of tetraphenyldiphosphine (**1**) to 1-dodecene (**2a**) in either the presence of a radical initiator [AIBN or V-40 (1,1′-azobis-(cyclohexane-1-carbonitrile)] or under photoirradiation (Scheme 1a). The addition reaction did not proceed at all, and **1** was recovered quantitatively. We previously reported that the regioselective thioselenation of alkenes proceeds smoothly using a disulfide–diselenide mixed system,[10] although the addition to alkenes did not proceed efficiently using either a disulfide or diselenide species alone. In such heteroatom-mixed systems, two different heteroatom-centered radicals ($Y^\bullet$, $Z^\bullet$) can be generated and two heteroatom-containing compounds (*Y-Y*, *Z-Z*) with different radical capturing abilities exist. The more reactive radical attacks carbon–carbon multiple bonds and the generated carbon radical is captured by the heteroatom-containing compound with the better capturing ability (Scheme 1b).



Scheme 1. Radical addition of the diphosphine **1** ($P^{III}-P^{III}$) and diphosphine monoxide **3** [$P^V(O)-P^{III}$] to alkenes.

With this information in mind, we selected tetraphenyldiphosphine monoxide (**3**), bearing a $P^V(O)-P^{III}$ single bond, as an initial phosphorus compound for the radical addition to alkenes. This choice was because the homolytic cleavage of the $P^V(O)-P^{III}$ bond can afford two different phosphorus-centered radicals and **3** has pentavalent and trivalent phosphorus atoms, which might have different radical capturing abilities. The 1,2-addition of **3** to alkenes proceeded regioselectively to afford the 1-phosphinyl-2-phosphinoalkanes **4** (Scheme 1c). Recently, organophosphines with vicinal soft (P^{III}) and hard [$P^V(O)$] Lewis-base centers[11] were used as hemilabile ligands in transition metal catalyzed reactions.[12] Furthermore, the reduction of **4** readily affords bidentate bis(phosphine) ligands. Therefore, we set out to investigate

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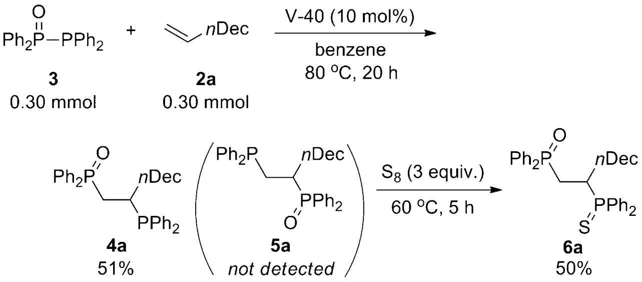
the novel phosphinylphosphination of alkenes with diphosphine monoxides.

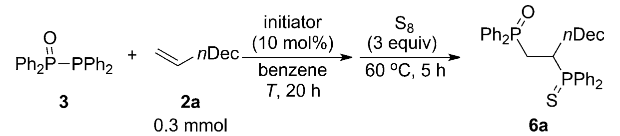
When a mixture of **3** (0.3 mmol), **2a** (0.3 mmol), and V-40 (0.03 mmol, 10 mol %) was dissolved in benzene and refluxed for 20 hours, the complete consumption of **2a** and the formation of the phosphinylphosphination product **4a**, which has a diphenylphosphinyl group at the terminal carbon atom, were confirmed by ^{1}H and ^{31}P NMR spectroscopy (Scheme 2). The regioisomer **5a** was not detected, and **4a** was converted into the bis(phosphino)alkane 1-*P*-oxide 2-*P*-sulfide (BPOS) **6a** upon treatment with elemental sulfur.



Scheme 2. Phosphinylphosphination of **2a** with **3**.

Since a small amount of the self-polymerization product of **2a** was observed, the ratio of **3** to **2a**, initiator, and temperature were screened (Table 1) to identify the optimal reaction conditions. When the reaction was conducted at low temperatures, such as 30 and 60 °C, the self-polymerization of **2a** preferentially occurred (entries 2 and 3). In contrast, at high temperature (80 °C) and with the use of excess **3** suppressed the polymerization effectively and thus improved the yield of **6a** (entry 4). The phosphinylphosphination did not take place without a radical initiator (entry 5). Photoirradiation with a xenon lamp (500 W) through a sealed Pyrex NMR tube afforded **6a** in a good yield, although a prolonged reaction time was required (entry 6).

Table 1: Optimization of the phosphinylphosphination of alkene **2a** with **3**.[a]

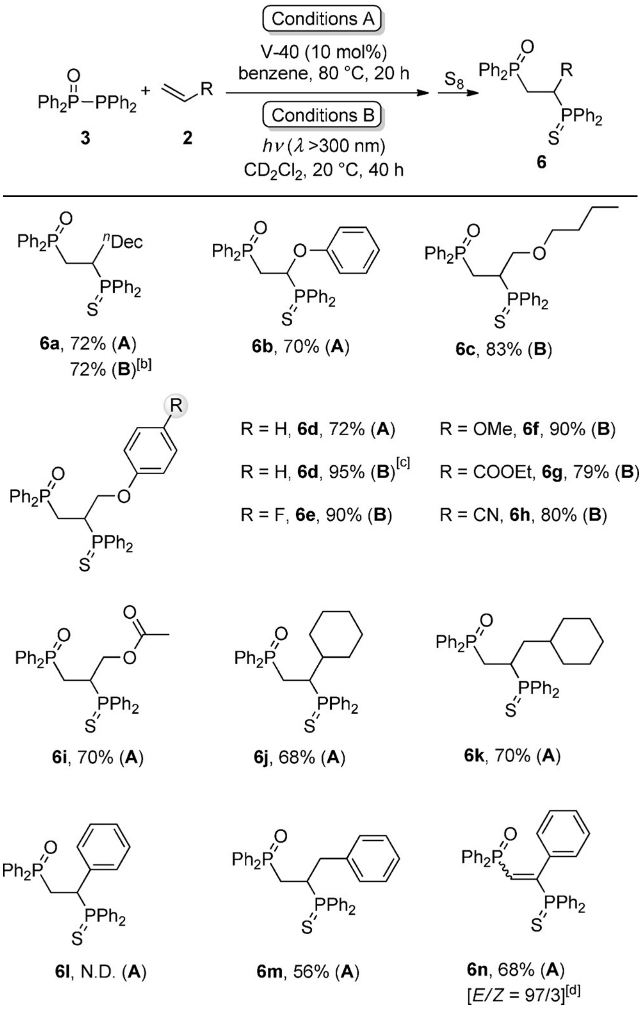


Entry	**3** (mmol)	Initiator	*T* [°C]	Yield [%][b]
1	0.30	V-40	80	50
2	0.30	AIBN	60	23
3[c]	0.30	V-70	30	14
4	0.45	V-40	80	79 (72)
5	0.45	–	80	0
6[c,d]	0.90	xenon lamp	20	78 (72)

[a] Reaction conditions: **2a** (0.3 mmol), benzene (0.6 mL). [b] Determined by ^{1}H NMR spectroscopy. Isolated yields are shown within parentheses. [c] The substrates were dissolved in CH_2Cl_2. [d] The mixture was irradiated with a xenon lamp (500 W) through a sealed Pyrex NMR tube for 55 h at room temperature. V-40 = 1,1′-azobis(cyclohexane-1-carbonitrile), V-70 = 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile), AIBN = 2,2′-azobis(isobutyronitrile).

The phosphinylphosphination of various alkenes with **3** was conducted in the presence of either a catalytic amount of V-40 (Conditions A) or under photoirradiation (Conditions B; Table 2). The vinyl ether **2b** reacted with **3** efficiently. After the mixture was treated with S_8 (0.9 mmol) at 60 °C for 5 hours, the BPOS **6b** was obtained in a good yield. Allyl ethers afforded the corresponding 1,2-adducts **6c–h** in excellent yields under photoirradiation. The reaction was tolerant of various functional groups such as fluoro (**2e**), methoxy (**2f**), ester (**2g**), and nitrile (**2h**) groups. The use of the allyl ester **2i** also gave the corresponding 1,2-adduct **6i** in a good yield. Cyclohexane-containing species (**2j** and **2k**) gave the corresponding BPOSs in good yields. Styrene (**2l**) did not undergo the phosphinylphosphination at all, because

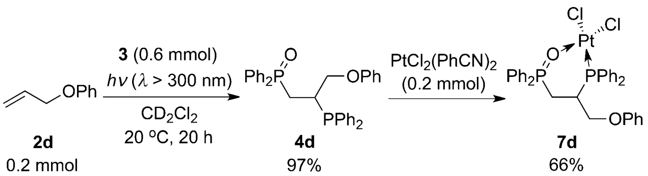
Table 2: Phosphinylphosphination of several alkenes **2** with diphosphine monoxide **3**.[a]



[a] Reaction conditions A: **3** (0.45 mmol), **2** (0.3 mmol), V-40 (0.03 mmol), benzene (0.6 mL), 80 °C, and 20 h. After the reaction, the resulting mixture was treated with S_8 (0.9 mmol) at 60 °C for 5 h. Reaction conditions B: **3** (0.6 mmol), **2** (0.2 mmol), CD_2Cl_2 (0.4 mL), xenon lamp (500 W), 40 h, room temperature, and subsequent treatment with S_8. [b] The mixture was irradiated for 55 h. [c] The mixture was irradiated for 20 h. [d] Phenylacetylene (0.3 mmol) was added.

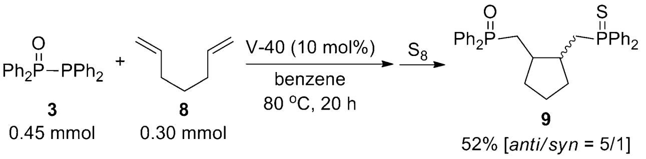
of preference for the self-polymerization. In contrast, the reaction of allylbenzene (**2m**) proceeded to afford BPOS **6m** in a moderate yield. Furthermore, the terminal alkyne **2n** also served as a viable substrate to give the 1,2-adduct **6n** in a good yield with excellent stereoselectivity.

The present reaction is a novel and straightforward method to synthesize 1-phosphinyl-2-phosphinoalkanes, which can be used as ligands for transition metal catalyzed reactions.[12] Therefore, we set out to create a **4d**/transition metal complex using the present method (Scheme 3). When a mixture of **3** (0.6 mmol) and **2d** (0.2 mmol) was photoirradiated, the 1-phosphinyl-2-phosphinoalkane **4d** was obtained in a high yield. Subsequently, $PtCl_2(PhCN)_2$ (0.2 mmol) was added to the resulting reaction mixture, and the platinum complex **7d** was successfully isolated in 66% yield.



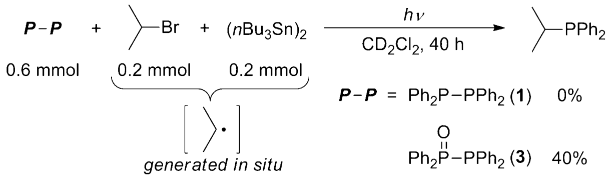
Scheme 3. The facile preparation of platinum(II)/bis(phosphine) monoxide complex **7d**.

To shed light on the reaction pathway, the diene **8** was mixed with **3** in the presence of a catalytic amount of V-40 (Scheme 4). As a result, the cyclized product **9** (*anti*/*syn* = 5/1) was obtained and the noncyclized 1,2-adducts were not detected at all. This result strongly indicates that the phosphinylphosphination proceeds by a radical pathway. In addition, the rate of carbon radical capture by **3** was estimated to be $5\times10^3\ s^{-1}M^{-1}$ at most, because the rate for the 5-*exo* cyclization of 5-hexenyl radical is $4\times10^5\ s^{-1}$.[13] The carbon radical capture rate of **3** is very slow considering the rate constant for the radical attack of diphenylphosphinyl radical on isoprene $[k=(1.4\pm0.3)\times10^7\ s^{-1}M^{-1}]$[14] and phenyl vinyl ether $[k=(2.6\pm0.2)\times10^6\ s^{-1}M^{-1}]$.[15] Therefore, the key step of the phosphinylphosphination is the carbon radical capture by **3**.



Scheme 4. Phosphinylphosphination of diene **8** with **3**.

To clarify the difference in reactivity between **1** and **3**, we conducted the reaction between 2-bromopropane (0.2 mmol) and either **1** or **3** (0.6 mmol) with hexabutylditin (0.2 mmol) under photoirradiation (Scheme 5). In this system, an isopropyl radical was generated in situ by the abstraction of bromine from 2-bromopropane, and it was caused by the Sn–Sn bond cleavage of hexabutylditin upon near-UV irradiation. In sharp contrast to **1**, which did not react with the generated isopropyl radical, **3** caused homolytic substitution at the trivalent phosphorus atom[16] to generate isopropyl(diphenyl)phosphine in 40% yield. This result strongly indicates that the π-type alkyl radical capturing ability of **3**, such as isopropyl radicals, is much higher than that of **1**. So the phosphinylphosphination of various alkenes with **3** successfully proceeded.



Scheme 5. Photoinduced homolytic substitution of **1** and **3** with isopropyl radical.

A plausible reaction pathway for the present reaction is illustrated in Figure 1. The $P^V(O)$–P^{III} bond cleavage of **3** is induced by the radical initiator or near-UV light to generate the diphenylphosphinyl radical $[Ph_2P(O)^\bullet]$.[17] The generated radical reacts with **2** at the terminal carbon atom to generate the alkyl radical **10**. The alkyl radical **10** is captured by **3** to give **4** by an S_H2-type mechanism.

Preliminary density functional theory (DFT) calculations (B3LYP/6-31G(d)) were performed to explain the observed regioselectivity of the reaction. Regarding the addition of **3** to **2o** ($R=CH_3$ in Figure 1a), the single occupied molecular orbital (SOMO) level of **10o** (−4.85 eV) was similar to the highest occupied molecular orbital (HOMO) level of **3** (−5.74 eV), which is localized on the trivalent phosphorus

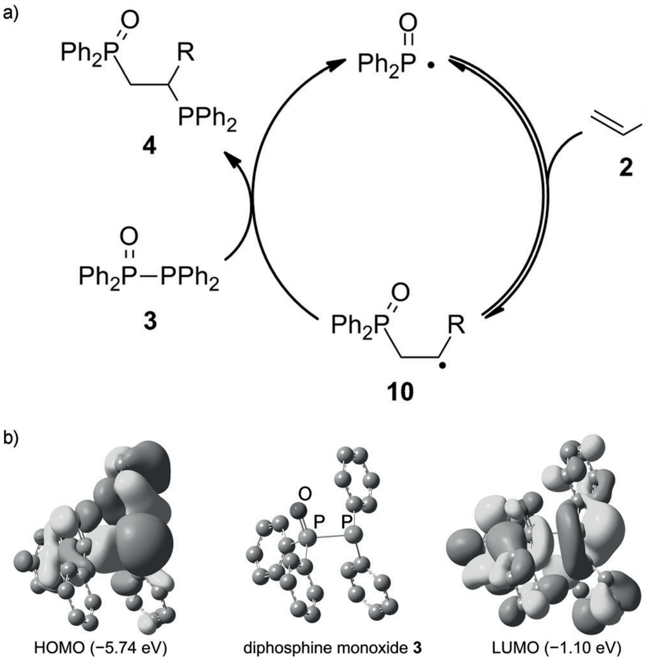


Figure 1. a) A plausible reaction pathway for the highly regioselective phosphinylphosphination of **3** to alkenes. b) Kohn–Sham molecular orbitals (HOMO and LUMO) of **3** calculated at the B3LYP/6-31G(d) level of theory.

atom. The lowest unoccupied molecular orbital (LUMO) level of **3** was −1.10 eV. This result indicates that the reactive site of **3** to **10 o** is at the trivalent phosphorus atom. Therefore, the radical-chain reaction, involving both the radical attack of $Ph_2P(O)^\bullet$ to alkenes and the radical capture of **10** by **3**, proceeds to afford **4**, selectively.[18]

In summary, we have developed a protocol for the highly regioselective addition of tetraphenyldiphosphine monoxides to a variety of alkenes. This approach enables the regioselective introduction of diphenylphosphino and diphenylphosphinyl groups on various aliphatic alkenes and phenylacetylene. A plausible reaction pathway involving a regioselective radical capturing process was proposed. We believe this method will facilitate significant opportunities in the synthesis of bis(phosphine) monoxide ligands.

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[17] The diphenylphosphino radical ($Ph_2P^\bullet$) is also generated by near-UV light. However, $Ph_2P(O)^\bullet$ is more reactive with alkenes than $Ph_2P^\bullet$ and initiates the radical-chain reaction. In this reaction, the $P^V(O)-P^{III}$ bond cleavage, induced by near-UV light, is much slower than the radical chain reaction.
[18] 1,2-Bisphosphinoalkane was obtained in < 1 % yield.

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