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Photoinduced highly selective thiophosphination of alkynes using a $(PhS)_2/(Ph_2P)_2$ binary system

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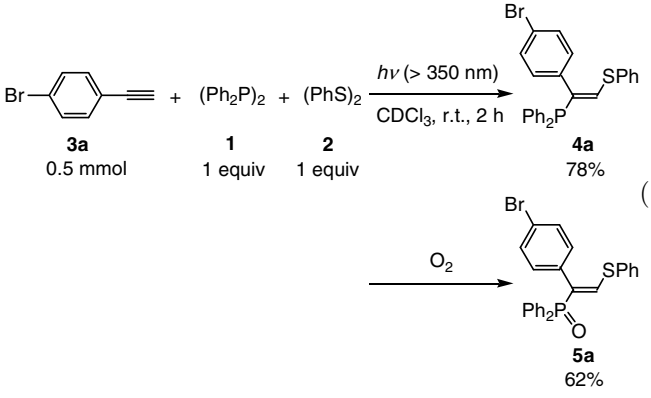
Abstract

Development of highly selective method for simultaneous introduction of different heteroatom functions into carbon–carbon unsaturated bonds is of special interest. When a mixture of tetraphenyldiphosphine $(Ph_2P)_2$, diphenyl disulfide $(PhS)_2$, and phenylacetylene in $CDCl_3$ was irradiated with a xenon lamp through Pyrex at ambient temperature, a highly regioselective addition of phosphino and thio groups into carbon–carbon triple bond took place simultaneously to give the corresponding thiophosphination product in high yield.

Radical addition of heteroatom compounds to carbon–carbon unsaturated bonds based on the photoinduced homolytic cleavage of heteroatom–heteroatom linkage is one of the most useful and highly atom-economical methods for the selective introduction of heteroatom functions into organic molecules.[1] In particular, the development of a highly selective method for simultaneous introduction of different heteroatom functions into carbon–carbon unsaturated bonds is of special interest.[2,3]

Herein we report a highly regioselective photoinduced thiophosphination of alkynes using a novel diphosphine-disulfide binary system (Eq. 1).[4,5] It has become apparent for this methodology that the present thiophosphination proceeds smoothly at room temperature using commercially available $(Ph_2P)_2$ and $(PhS)_2$ as the starting reagents with excellent *E*-selectivity and can be applied to internal alkynes.

When a mixture of tetraphenyldiphosphine (1 mmol), diphenyl disulfide (1 mmol), and 1-bromo-4-ethynyl-benzene (0.5 mmol) in $CDCl_3$ (0.6 mL) was irradiated with a xenon lamp through Pyrex for 2 h at ambient temperature, a novel highly regioselective thiophosphination took place



to give the corresponding thiophosphination product (**4a**). The present thiophosphination proceeded smoothly without a decrease in the yield of **4a**, even when stoichiometric (or slightly excess) amounts of $(Ph_2P)_2$ (0.6 mmol) and $(PhS)_2$ (0.6 mmol) were employed. A consequent air-oxidation of **4a** afforded the corresponding oxide (**5a**) in high isolated yield.[6,7] Interestingly, in this thiophosphination using a $(PhS)_2/(Ph_2P)_2$ binary system, neither bisphosphination product nor bisthiolation product was

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formed. When the reaction was conducted in the dark, thiophosphination did not proceed.

Compound **5a** was recrystallized from EtOH to obtain a single crystal suitable for X-ray analysis. The regio- and stereochemistries of the major product ((***E***)-**5a**) were fully determined by the X-ray crystallographic analysis (Fig. 1).[7]

A possible reaction pathway for the thiophosphination is as follows (Scheme 1). Figure 2 indicates UV–visible spectra of $(Ph_2P)_2$, $(PhS)_2$, and thiophoshine (**6**) (Fig. 2). The absorption based on the n-σ^* transition of $(Ph_2P)_2$, $(PhS)_2$, and thiophoshine (**6**) reaches 330 nm, 375 nm, and 370 nm, respectively.[8] Therefore, irradiation with the light of wavelength over 350 nm induces preferential cleavage of S–S single bond, generating PhS**.**, which adds to alkynes to form vinylic radical (**7**) (Scheme 1). PhS**.** also attacks $(Ph_2P)_2$ to give thiophosphine (**6**)[9] and Ph_2P**.**, the former of which captures the vinylic radical (**7**) to afford the thiophosphinated product (**4**) regioselectively.[10]

Similar conditions can be employed with several acetylenes (**3b**–**g**) (Table 1). In the case of aromatic acetylenes

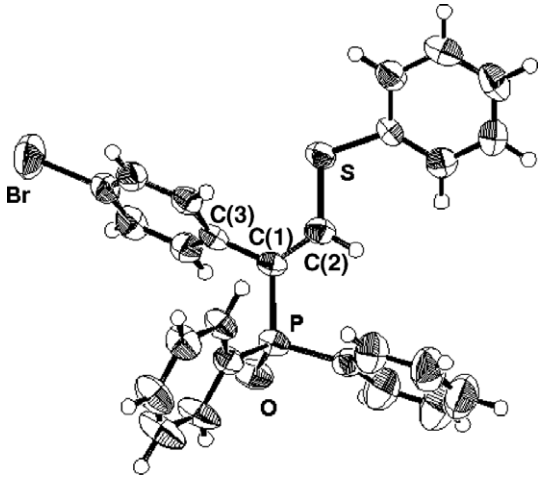
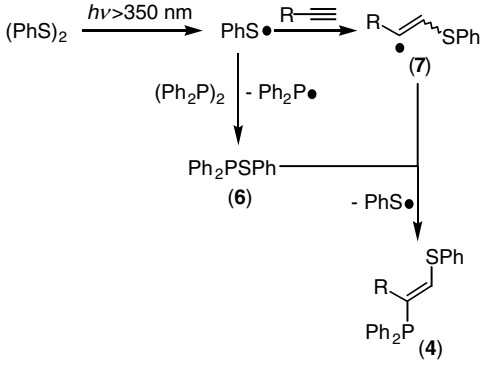


Fig. 1. Molecular structure of (***E***)-**5a** by X-ray crystallographic studies. Space group: C2/*c* (#15), $Z = 8$, $R = 0.0665$, $Rw = 0.0729$, GOF = 1.075, Selected bond lengths (Å) and angles (°): C(1)–C(2) = 1.331(7), P–C(1) = 1.796(4), S–C(2) = 1.736(4), C(1)–C(3) = 1.480(6), P–C(1)–C(2) = 121.7(3), S–C(2)–C(1) = 122.4(3).



Scheme 1. A possible pathway for thiophosphination.

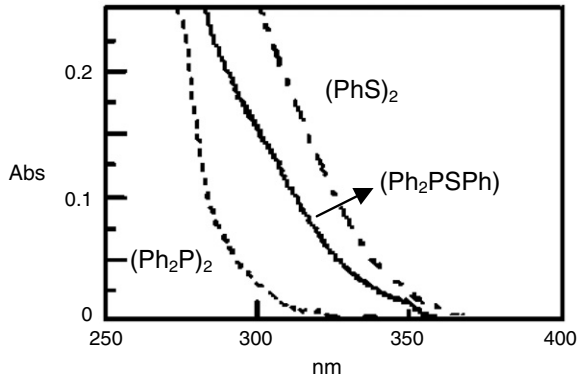
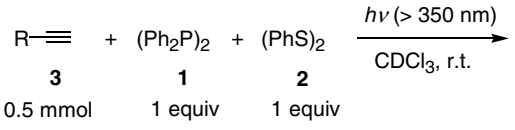
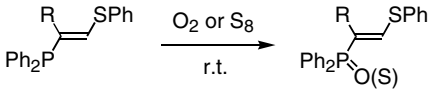


Fig. 2. UV–visible spectra of $(Ph_2P)_2$ (- - -), $(PhS)_2$ (– • –) and Ph_2PSPh (—).

Table 1
Photoinduced thiophosphination of alkynes



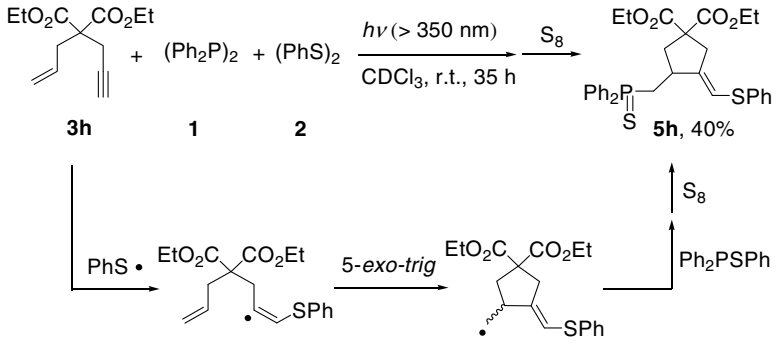


Entry	Alkyne	Time (h)	Yield (%) (*E*/*Z*)	
			4[a]	5[b]
1	MeO– ≡ (**3b**)	1	91 [91/9]	61
2	^{n}C$_5$H$_{11}$– ≡ (**3c**)	1	90 [91/9]	60
3	≡ (**3d**)	2	87 [90/10]	73
4[c]	^{n}C$_6$H$_{13}$– ≡ (**3e**)	27	77 [94/6]	57
5[c]	Ph– ≡ (**3f**)	20	61 [93/7]	41
6[c]	≡ (**3g**)	48	80 [75/25]	67 [71/29][d]

[a] ^{1}H NMR yield.
[b] Isolated yield of *E*-isomer.
[c] Sulfurization with S_8 instead of air-oxidation.
[d] Obtained as a mixture of *E*- and *Z*-isomers.

(entries **1** and **2**), the thiophosphination proceeded smoothly and *E* isomers (**5b** and **5c**) were obtained as the major product. The thiophosphination of enyne (**3d**) proceeded on the triple bond selectively (entry 3). Aliphatic alkynes also underwent regioselective thiophosphination, although a prolonged irradiation was required (entries 4 and 5).[11] Noteworthy is that the thiophosphination of 1-phenyl-1-pentyne (**3g**) as an internal alkyne also proceeded regioselectively in good yields (entry 6).[12]

As an extention of the current $(Ph_2P)_2$–$(PhS)_2$ binary system, the thiophosphination reaction of an enyne via



Scheme 2. Photoinduced thiophosphination of enyne.

5-*exo* radical cyclization[13] was demonstrated (Scheme 2). The photoirradiated reaction of diethyl allylpropargylmalonate (**3h**) with $(Ph_2P)_2$ and $(PhS)_2$ successfully afforded the corresponding five-membered cyclic product (**5h**) bearing phenylthio and diphenylphosphino groups at both the terminal positions regioselectively.[14,15]

In conclusion, we have developed a new method for the simultaneous introduction of phosphino and thio groups into carbon–carbon triple bonds with excellent regio- and stereoselectivities by using a $(Ph_2P)_2/(PhS)_2$ binary system via photoirradiation under mild reaction conditions. We are currently investigating its detailed mechanism and its further application to other substrates.

Acknowledgments

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5. Our preliminary results of this photoinduced thiophosphination and relating works were presented at the 87th Annual Meeting of Chemical Society of Japan (March 26, 2007, Suita, Osaka, Japan) and the 34th Symposium on Main Group Element Chemistry (December 15, 2007, Osaka, Japan).
6. The isolation of **4a** was difficult, due to the sensitivity of **4a** toward air-oxidation.
7. *Compound* **(*E*)-5a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, $J = 7.3$ Hz, 2H), 7.27–7.34 (m, 5H), 7.39–7.45 (m, 6 H), 7.50–7.53 (m, 2H), 7.56 (d, $J_{H-P} = 16.9$ Hz, 1H), 7.64–7.68 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 122.42 (d, $J = 1.9$ Hz), 128.02 (d, $J = 4.7$, 1.9 Hz), 128.44 (dd, $J_{C-P} = 12.7$, $J = 1.9$ Hz), 129.35 (d, $J = 1.9$ Hz), 129.83 (d, $J_{C-P} = 96.9$ Hz), 130.45 (d, $J = 1.9$ Hz), 131.09 (d, $J_{C-P} = 104.6$ Hz), 131.26 (dd, $J = 5.7$, 3.8 Hz), 131.81 (d, $J = 6.7$ Hz), 132.04, 132.08 (d, $J_{C-P} = 10.5$ Hz), 133.63, 134.01 (d, $J_{C-P} = 8.6$ Hz), 146.67 (dd, $J_{C-P} = 14.4$, $J = 5.7$ Hz); ^{31}P NMR (200 MHz, $CDCl_3$) δ 26.66; HRMS calcd for $C_{26}H_{20}BrOPS$: 490.0156, found: 490.0156. Anal. Calcd for $C_{26}H_{20}BrOPS$: C, 63.55; H, 4.10. Found: C, 63.56; H, 4.10.
8. *The UV spectra of diphenyl disulfide and tetraphenyl diphosphine are as follows*: $(PhS)_2$: $\lambda_{max} = 250$ nm, $\varepsilon_{max} = 500$; Schmidt, U.; Miiller, A.; Markau, K. *Chem. Ber.* **1964**, *97*, 405; $(Ph_2P)_2$: $\lambda_{max} = 260$ nm,

$\varepsilon_{max} = 40$; Troy, D.; Turpin, R.; Voigt, D. *Bull. Soc. Chim. Fr.* **1979**, 241.

9. The formation of thiophsophine (**6**) (δ 33.0) was confirmed by ^{31}P NMR spectrum.
10. In this thiophosphination, recombination of heteroatom-centered radicals such as PhS**.** and Ph_2P**.** to form $(PhS)_2$, $(Ph_2P)_2$, and/or $PhSPPh_2$ is conceivably a very fast process. Accordingly, the present thiophosphination of alkynes requires continuous photoirradiation during the reaction.
11. In the cases of aliphatic acetylene, prolonged reaction time was required. This is because α-aryl-substituted vinylic radicals are assumed to be π-radicals and more stable than alkyl-substituted vinylic σ-radicals. See: Singer, L. A.; Chen, J. *Tetrahedron Lett.* **1969**, *10*, 4849.
12. *Compound* **(*E*)-5g**: ^1H NMR (500 MHz, $CDCl_3$) δ 0.35 (t, $J = 7.3$ Hz, 3H), 1.32–1.40 (m, 2H), 2.51 (t, $J = 7.3$ Hz, 2H), 6.99–7.06 (m, 5 H), 7.23–7.36 (m, 11 H), 7.78–7.82 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.47, 21.35, 35.77 (d, $J_{C-P} = 7.6$ Hz), 127.00, 127.79, 127.85 (d, $J_{C-P} = 12.4$ Hz), 128.12, 128.81, 129.88, 130.80, 131.92 (d, $J = 8.6$ Hz), 132.25 (d, $J_{C-P} = 75.8$ Hz), 132.89 (d, $J = 110.3$ Hz), 133.89, 138.60 (d, $J_{C-P} = 9.5$ Hz), 157.69 (d, $J_{C-P} = 13.4$ Hz); ^{31}P NMR (200 MHz, $CDCl_3$) δ 40.23; HRMS calcd for $C_{29}H_{27}PS_2$: 470.1292, found: 470.1299.
13. Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reaction*; VCH: Weinheim, 1996.
14. *Compound* **5h**: ^1H NMR (500 MHz, $CDCl_3$) δ 1.09–1.13 (m, 6 H), 1.65 (dd, $J = 12.3$, 9.6 Hz, 1H), 2.36–2.40 (m, 1 H), 2.55 (dt, $J = 14.6$, 9.6 Hz, 1H), 1.65 (dt, $J = 13.3$, 3.6 Hz, 1H), 2.84 (dt, $J = 17.8$, 2.3 Hz, 1H), 3.01 (d, $J = 17.9$ Hz, 1 H), 3.16–3.23 (m, 1 H), 4.03–4.08 (m, 4H), 5.98 (s, 1 H), 7.18–7.20 (m, 2 H), 7.33–7.41 (m, 8 H), 7.73–7.82 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.90, 13.95, 37.22 (d, $J_{C-P} = 54.6$ Hz), 38.24, 40.55, 58.63, 59.35, 61.54, 115.21, 126.24, 128.48, 128.93, 130.81 (d, $J_{C-P} = 10.5$ Hz), 131.22 (d, $J_{C-P} = 9.5$ Hz), 131.48, 132.21 (d, $J_{C-P} = 73.8$ Hz), 132.58 (d, $J_{C-P} = 71.0$ Hz), 135.95, 146.23 (d, $J_{C-P} = 12.54$ Hz), 170.88, 171.31; ^{31}P NMR (200 MHz, $CDCl_3$) δ 41.03; HRMS calcd for $C_{31}H_{33}O_4PS_2$: 564.1558, found: 564.1631. Anal. Calcd for $C_{31}H_{33}O_4PS_2$: C, 65.93; H, 5.89. Found: C, 65.90; H, 5.92.
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