A one-pot synthesis of a branched tertiary phosphine oxide from red phosphorus and 1-(*tert*-butyl)-4-vinylbenzene in KOH–DMSO: an unusually facile addition of P-centered nucleophiles to a weakly electrophilic double bond

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Abstract

Red phosphorus reacts with 1-(*tert*-butyl)-4-vinylbenzene in a superbase media (KOH–DMSO, 90–100 °C, 3 h) to give tris[4-(*tert*-butyl)phenethyl]phosphine oxide in 77% yield. Microwave activation of the reaction affords the phosphine oxide in 82% yield in 6 min.
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The easy addition of phosphorus-centered nucleophiles, generated in situ from red phosphorus (P_n) in a superbasic KOH–DMSO system, to styrenes 1^1 yielding secondary **2** and tertiary **3** phosphine oxides (Scheme 1) remains fascinating from a mechanistic point of view.[2] Indeed, styrenes are unusual electrophiles. To the best of our knowledge, there are no explicit examples of nucleophilic addition to their double bond except for the reaction of the CH-acid, 2-methylpropanoic acid, with styrene under special forced superbasic conditions (sodium naphthalenide–TMEDA–THF).[3] Meanwhile the nucleophilic character of the above reaction is strongly supported by the fact that it does not proceed without alkali metal hydroxides and in the presence of radical initiators, being also unaffected by typical inhibitors of radical processes.[1b,2]

Until now, tris(phenethyl)phosphine oxide **3** is still the only representative of the family of tris(arylethyl)phosphine oxides.
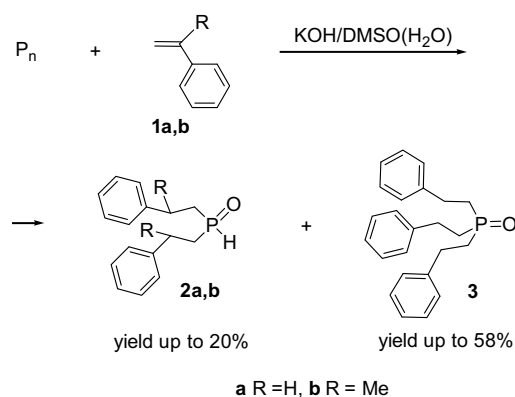
Scheme 1.

Tertiary phosphine oxides are used widely as Wittig–Horner building blocks or for tertiary phosphine generation,[4] ligands for metal complexes (particularly those phosphine oxides having bulky and branched substituents[5]), intermediates for the design of nano-electronic materials,[6]

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extractants of noble, rare-earth and transuranic elements,[7] and flame retardants.[8]

Therefore, evaluation of the generality of the above synthesis (Scheme 1) is timely. Since electron-donating substituents on the benzene ring should slow down the nucleophilic addition to the double bond of vinylbenzene, we chose 'a difficult' case: 1-(tert-butyl)-4-vinylbenzene, as a substrate. Our purpose was threefold. Firstly, if the reaction occurs with good preparative results, other alkyl substituted vinyl benzenes should also undergo the addition. Secondly, the syntheses of strongly branched bulky triarylethylphosphine oxides would probably be realized. Thirdly, valuable information concerning the substituent effect on the nucleophilic addition would be obtained allowing better understanding of the mechanism.

We have found that red phosphorus reacts with tert-butylstyrene **4** in a KOH–DMSO suspension (including ~1.1 mass% H_2O as a proton transfer agent and ~0.1 mass% of hydroquinone as a radical inhibitor) under an argon blanket at 90–100 °C for 3 h to give tris[4-(tert-butyl)phenethyl]phosphine oxide **5** and 4-(tert-butyl)phenethylphosphinic acid **6** in 77% and 17% yields, respectively (Scheme 2).[9] The corresponding secondary phosphine oxide **7** (traces) was also detected (^{31}P NMR) in the reaction mixture.[9]

A microwave irradiation promoted version of the reaction (with the same reactants ratio) delivered (in 6 min) phosphine oxide **5** as the only product in 82% yield (neither phosphine oxide **7** nor acid **6** was detected in the reaction mixture). Thus, the reaction was more effective, as well as chemospecific and rapid (30 times faster).[10]

In spite of the branched structure and reduced electrophilicity of the starting tert-butylstyrene **4**, the reaction did not stop during the initial steps of the intermediate primary and secondary adduct formation. This proves that the rate-determining steps include the cleavage of the elemental phosphorus P–P bond (probably occurring in phosphorus nanoparticles) by hydroxide anions to form highly active P-centered nucleophiles and their further addition to the tert-butylstyrene **4** double bond affording the mono-adducts. As far as the reaction proceeds under oxygen-free conditions, it is obvious that the initial nucleophiles are polyphosphinite type anions **8** (Scheme 3).

In this case, DMSO does not act as an oxidant since under the conditions studied, phosphine (PH_3) adds to
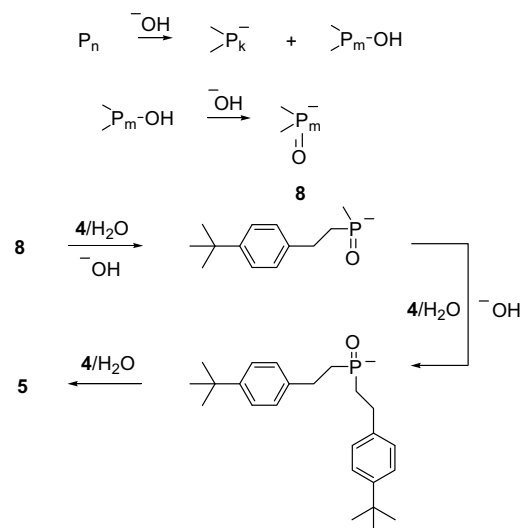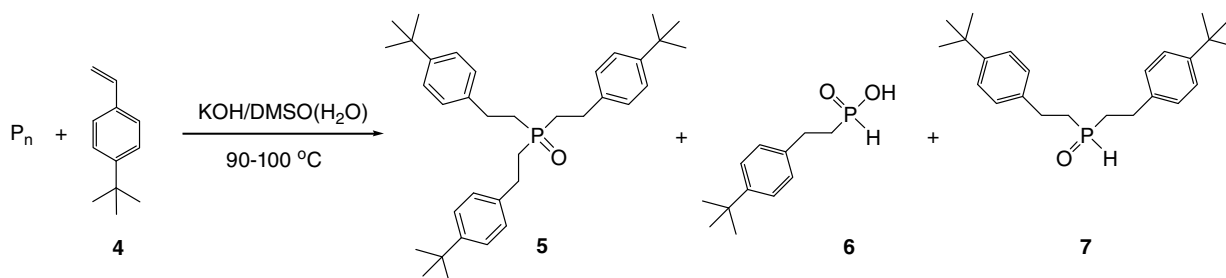
Scheme 3.

styrene to give the corresponding secondary[11a] or tertiary[11b] phosphines (but not phosphine oxides).

Apparently, the polyphosphinite anion clusters **8** thus formed (Scheme 3) possess much higher nucleophilicity compared to simple phosphinite anions ($O=P^-$). This inference is experimentally supported by the fact that the model reaction of tert-butylstyrene **4** with KH_2PO_2 (the latter and PH_3 are the products of the redox reaction of red phosphorus with KOH)[2a] under the same conditions gave only traces of the organophosphorus compounds (^{31}P NMR).

Despite the comparable preparative yields of the corresponding tertiary phosphine oxides from styrene[12] and tert-butylstyrene **4**, a competitive reaction[13] (Fig. 1) indicates that **4** is, as expected, much lower in reactivity than unsubstituted styrene. Indeed, the conversions of styrenes **1a** and **4** (equimolar ratio) in the phosphorylation with red phosphorus were 89% and 40%, respectively (Fig. 1).

Consequently, according to ^{31}P NMR monitoring (Fig. 2), the rates of formation of the adducts **2a** and **3** in the case of styrene are considerably higher than those of adduct **7** formed from tert-butylstyrene **4**. The mixed secondary phosphine oxide **9** (^{31}P NMR: 32.04 ppm, $^1J_{P,H}$ 452 Hz) was also detected in the reaction mixture (Fig. 2).[13]

In conclusion, a one-pot chemoselective synthesis of novel tertiary phosphine oxide **5** in up to 82% yield directly
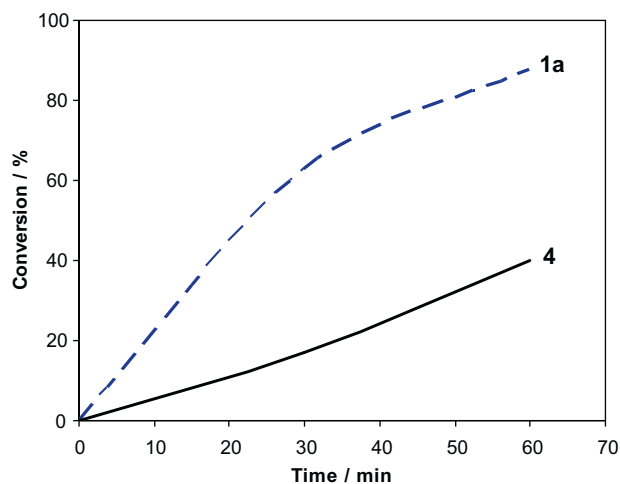
Scheme 2.

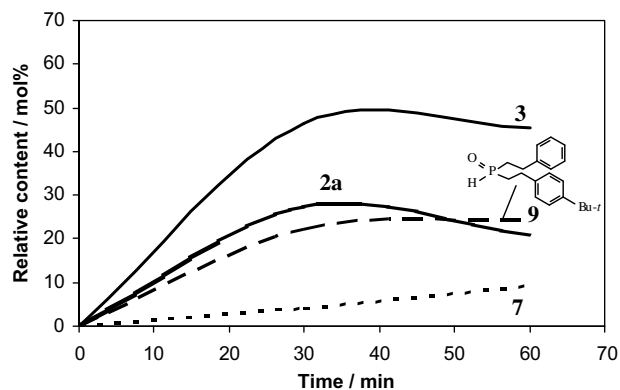Fig. 1. Change in the conversion of styrenes **1a** and **4** during phosphorylation with red phosphorus.[13]

Fig. 2. Dynamics of phosphine oxides **2a**, **3**, **7**, and **9** formation.[13]

from red phosphorus and *tert*-butylstyrene **4** in the system KOH–DMSO has been developed thus implying the validity of the reaction for diverse alkylvinylbenzenes. It has also been shown that this approach opens a straightforward route to highly branched, previously inaccessible phosphine oxides and hence, the corresponding phosphines. Evidence for the generation of highly nucleophilic polyphosphinite anion clusters as key intermediate species complementary to weakly electrophilic vinylbenzenes has been obtained.

Acknowledgment

References and notes

1. (a) Gusarova, N. K.; Trofimov, B. A.; Rakhmatulina, T. N.; Malysheva, S. F.; Arbuzova, S. N.; Shaikhudinova, S. I.; Albanov, A. I. *Russ. Chem. Bull.* **1994**, *43*, 1591; (b) Arbuzova, S. N.; Gusarova, N. K.; Malysheva, S. F.; Brandsma, L.; Albanov, A. I.; Trofimov, B. A. *Russ. J. Gen. Chem.* **1996**, *66*, 56.

2. (a) Trofimov, B. A.; Rakhmatulina, T. N.; Gusarova, N. K.; Malysheva, S. F. *Russ. Chem. Rev.* **1991**, *60*, 1360; (b) Trofimov, B. A.; Gusarova, N. K.; Brandsma, L. *Main Group Chem. News* **1996**, *4*, 18; (c) Gusarova, N. K.; Brandsma, L.; Malysheva, S. F.; Arbuzova, S. N.; Trofimov, B. A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1996**, *111*, 174; (d) Malysheva, S. F.; Arbuzova, S. N. In *Sovremennyi organicheskii sintez (Modern Organic Synthesis)*; Rakhmankulov, D. L., Ed.; Khimiya: Moscow, Russia, 2003; pp 160–187 (in Russian).

3. Fujita, T.; Watanabe, S.; Suga, K.; Nakayama, H. *Synthesis* **1979**, 310.

4. (a) Gusarova, N. K.; Arbuzova, S. N.; Shaikhudinova, S. I.; Kazantseva, T. I.; Reutskaya, A. M.; Ivanova, N. I.; Papernaya, L. K.; Trofimov, B. A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2001**, *175*, 163; (b) Ivanova, N. I.; Gusarova, N. K.; Reutskaya, A. M.; Shaikhudinova, S. I.; Arbuzova, S. N.; Trofimov, B. A. *Russ. J. Gen. Chem.* **2003**, *73*, 877; (c) Nassar, R.; Noll, B. C.; Henderson, K. W. *Polyhedron* **2004**, *23*, 2499; (d) Silveira, C. C.; Cella, R.; Braga, A. L.; Jacob, R. G.; Lenardão, E. J.; Perin, G. *Tetrahedron* **2005**, *61*, 7712; (e) Lenardão, E. J.; Cella, R.; Jacob, R. G.; Silva, T. B.; Perin, G. *J. Braz. Chem. Soc.* **2006**, *17*, 1031; (f) Abdou, W. M.; Ganoub, N. A.; Fahmy, A. F.; Shaddy, A. A. *Monatsh. Chem.* **2006**, *137*, 105.

5. (a) Liu, W.; Malinoski, J. M.; Brookhart, M. *Organometallics* **2002**, *21*, 2836; (b) Canepa, G.; Brandt, C. D.; Werner, H. *Organometallics* **2004**, *23*, 1140; (c) Ishikawa, S.; Manabe, K. *Chem. Lett.* **2007**, *36*, 1302; (d) Lerebours, R.; Wolf, Ch. *Org. Lett.* **2007**, *9*, 2737.

6. (a) *The Chemistry of Nanomaterials*; Rao, C. N. R., Müller, A., Cheetham, A. K., Eds.; Wiley-VCH: New York, 2004; Vol. 2; (b) Sashchiuk, A.; Amirav, L.; Bashouti, M.; Krueger, M.; Sivan, U.; Lifshitz, E. *Nano Lett.* **2004**, *4*, 159; (c) Gubin, S. P.; Kataeva, N. A.; Khomutov, G. B. *Russ. Chem. Bull.* **2005**, *54*, 827; (d) Halpert, J. E.; Porter, V. J.; Zimmer, J. P.; Bawendi, M. G. *J. Am. Chem. Soc.* **2006**, *128*, 12590; (e) Latham, A. H.; Wilson, M. J.; Schiffer, P.; Williams, M. E. *J. Am. Chem. Soc.* **2006**, *128*, 12632.

7. (a) Alguacil, F. J.; Alonso, M. *Hydrometallurgy* **2004**, *74*, 157; (b) Chan, Z.; Yan-zhao, Y.; Tao, Z.; Jian, H.; Chang-Hong, L. *J. Radioanal. Nucl. Chem.* **2005**, *265*, 419; (c) Menshikov, V. I.; Voronova, I. Yu.; Malysheva, S. F.; Sukhov, B. G.; Proydakova, O. A.; Belogorlova, N. A. *International Congress on Analytical Sciences ICAS-2006.* Moscow, 2006, Vol. 1, p 12.

8. (a) Raskulova, T. V.; Malysheva, S. F.; Sukhov, B. G.; Khaliullin, A. K. *Russ. Polym. Sci., Ser. A.* **2002**, *44*, 919; (b) Marklund, A.; Andersson, B.; Haglund, P. *Environ. Sci. Technol.* **2005**, *39*, 3555; (c) Faghihi, K.; Zamani, K. *J. Appl. Polym. Sci.* **2006**, *101*, 4263; (d) Ribera, G.; Mercado, L. A.; Galia, M.; Cadiz, V. *J. Appl. Polym. Sci.* **2006**, *99*, 1367.

9. *Experimental procedure*: All the reaction steps were carried out under an inert atmosphere (argon). A solution of **4** (4.7 g, 29.3 mmol) in DMSO (10 mL) was added dropwise over 40 min to a heated (90–95 °C) suspension of red phosphorus (1 g, 32.3 mmol), KOH (2.5 g, 44.6 mmol), water (0.38 mL), DMSO (15 mL), and hydroquinone (0.03 g) with stirring. The reaction mixture was stirred for 2 h 20 min at 99–100 °C, then diluted with water and extracted with benzene (3 × 25 mL). The benzene extract was washed with a 10% aq solution of KCl (3 × 20 mL), dried over K_2CO_3, and the benzene removed. The residue was dried under vacuum to give 4.38 g of mixed product, containing (^{31}D NMR) **5** (47.61 ppm) and **7** (32.08 ppm, $^1J_{P,H}$ 452 Hz) in the ratio 10:1. The latter was removed as (4-*t*-$BuC_6H_4CH_2CH_2)_2P(O)OK$ by consecutive treatment of the product with 35% aq H_2O_2 and aq KOH.[12] This procedure gave 4 g (77%) of **5**. The aqueous layer was acidified with a 35% aq solution of HCl up to pH 4, and extracted with benzene[14] (2× 20 mL). The benzene extract was washed with water (2 × 10 mL), dried over $CaCl_2$, the solvent removed, and the residue dried under vacuum to give 1.15 g (17%) of **6** as a colorless powder, mp 106–108 °C (benzene). ^{1}H NMR (400.13 MHz, $CDCl_3$, ppm) δ: 1.28 (s, 9H, CH_3), 2.08 (m, 2H, CH_2P), 2.87 (m, 2H, $CH_2C_6H_4$), 7.10 (d, 1H, $^1J_{P,H}$ = 544.0 Hz, PH),

7.11–7.30 (m, 4H, C$_6$H$_4$),11.74 (s, 1H, OH); ^{13}C NMR (100.62 MHz, CDCl$_3$, ppm) δ: 26.35 (*C*H$_2$C$_6$H$_4$), 31.27 (d, $^1J_{P,C}$ = 91.7 Hz, *C*H$_2$P), 31.34 (*C*H$_3$), 34.37 (*C*CH$_3$), 125.51 (C-*o*), 127.75 (C-*m*, C$_6$H$_4$), 137.28 (d, $^1J_{P,C}$ = 15.9 Hz, C-*i*), 149.28 (C-*p*); ^{31}P NMR (161.98 MHz, CDCl$_3$, ppm) δ: 36.73 (d, $^1J_{P,H}$ = 544 Hz). IR (KBr, cm^{-1}): 3030, 3022 (*v*, =CH of phenyl rings); 2950, 2900, 2860 (*v*, CH); 2630 (*v*, OH); 2370 (*v*, PH); 2150, 1680 (*v*, OH); 1506,1450 (*v*, C=C of phenyl rings); 1463, 1430, 1390 (δ, CH$_2$); 1360, 1350, 1260, 1203 (δ, CH); 1190, 1170 (*v*, P=O); 1098 (δ, CH of phenyl rings); 950 (δ, OH); 816, 800 (δ, CH of phenyl rings); 550 (*v*, P–C). Anal. Calcd for C$_{12}$H$_{19}$O$_2$P: C, 63.70; H, 8.46; P, 13.69. Found: C, 63.75; H, 8.57; P, 13.47.

10. *Tris[4-(tert-butyl)phenethyl]phosphine oxide* (**5**). Under microwave irradiation: a mixture of red phosphorus (1 g, 32.3 mmol), **4** (4.7 g, 29.3 mmol), hydroquinone (0.03 g), KOH (2.5 g, 44.6 mmol), water (0.38 mL), and DMSO (25 mL) was irradiated (600 W) for 6 min (Microwave oven, model: Samsung M181DNR, maximum power level 850 W). The reaction mixture was cooled, diluted with water, and extracted with benzene (3 × 25 mL). The benzene extract was washed with a 10% aq solution of KCl (3 × 10 mL) and dried over K$_2$CO$_3$. The benzene and unreacted 4-*tert*-butylstyrene (0.84 g, 82% conversion) were removed under vacuum, and the residue was washed with hexane and dried under vacuum to give 4.26 g (82%) of phosphine oxide **5** as a colorless powder, mp 145–146 °C (benzene). ^{1}H NMR (400.13 MHz, CDCl$_3$, ppm) δ: 1.31 (s, 27H, CH$_3$), 2.03–2.04 (m, 6H, CH$_2$P), 2.89–2.91 (m, 6H, CH$_2$C$_6$H$_4$), 7.11–7.34 (m, 12H, C$_6$H$_4$); ^{13}C NMR (100.62 MHz, CDCl$_3$, ppm) δ: 27.31 (*C*H$_2$C$_6$H$_4$), 30.15 (d, $^1J_{P,C}$ = 62.3 Hz, *C*H$_2$P), 31.40 (*C*H$_3$), 34.46 (*C*CH$_3$), 125.66 (C-*o*), 127.80 (C-*m*), 137.86 (d, $^3J_{P,C}$ = 12.7 Hz, C-*i*), 149.48 (C-*p*); ^{31}P NMR (161.98 MHz, CDCl$_3$, ppm) δ: 47.21. IR (KBr, cm^{-1}): 3090, 3050, 3012 (*v*, =CH of phenyl rings); 2949, 2900, 2855 (*v*, CH); 1510 (*v*, C=C of phenyl rings); 1463, 1390 (δ, CH$_2$); 1360, 1270, 1220 (δ, CH); 1150 (*v*, P=O); 1100, 1010, 990, 930, 910 (δ, CH of phenyl rings); 835, 817, 800 (δ, CH$_2$), 770, 726, 559 (*v*, P–C). Anal. Calcd for C$_{36}$H$_{51}$OP: C, 81.46; H, 9.69; P, 5.84. Found: C, 81.57; H, 9.73; P, 5.81.

11. (a) Trofimov, B. A.; Brandsma, L.; Arbuzova, S. N.; Malysheva, S. F.; Gusarova, N. K. *Tetrahedron Lett.* **1994**, *35*, 7647; (b) Trofimov, B. A.; Gusarova, N. K.; Brandsma, L. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1996**, *109–110*, 601; (c) Trofimov, B. A.; Brandsma, L.; Arbuzova, S. N.; Malysheva, S. F.; Belogorlova, N. A.; Gusarova, N. K. *Russ. J. Gen. Chem.* **1997**, *67*, 650.

12. Malysheva, S. F.; Gusarova, N. K.; Kuimov, V. A.; Sukhov, B. G.; Kudryavtsev, A. A.; Sinyashin, O. G.; Budnikova, Yu. H.; Pai, Z. P.; Tolstikov, A. G.; Trofimov, B. A. *Russ. J. Gen. Chem.* **2007**, *77*, 415.

13. *Reaction conditions*: 70–75 °C, 1 h; red phosphorus (1 g, 32.3 mmol), KOH (3.3 g, 59.5 mmol), water (1.4 mL), **1a** (1.3 g, 12.5 mmol) and **4** (2 g, 12.5 mmol), hydroquinone (0.03 g), toluene (1 g) (as standard), and DMSO (25 mL). Conversion of styrenes **1a** and **4** was determined by GLC. The relative content of secondary **2a**, **7**, and **9** and tertiary **3** phosphine oxides in the reaction mixture was determined by ^{31}P NMR using standard samples of **2a**,[1a] **7**, and **3**.[1b,12]

14. Toluene, CHCl$_3$, and CH$_2$Cl$_2$ can be used as extractants instead of benzene.