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Rhodium-catalyzed addition reaction of diphosphine disulfide to aldehydes and ketones

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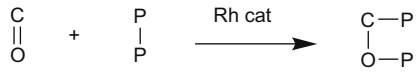
ABSTRACT

In the presence of $RhH(PPh_3)_4$ and 1,2-bis(diphenylphosphino)ethane, tetramethyldiphosphine disulfide and aldehydes were added producing [1-(dimethylthiophosphinoyloxy)alkyl]dimethylphosphine sulfides in high yields. Acetophenones with electron-withdrawing *p*-groups also yielded 1,2-adducts.

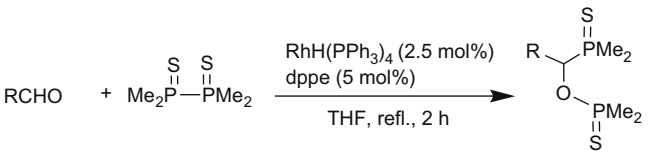
Geminal-phosphorus-phosphorusoxy compounds, the formal adducts of P–P and C=O compounds, are a group of organophosphorus compounds, that have attracted interest in regard to their biological activity.[1] Several methods of synthesis have been reported: (1) phosphorylation of α-hydroxyphosphorus compounds[2], (2) hydrophosphorylation of acylphosphorus compounds[1,3], and (3) phosphorylation of acid chlorides and derivatives.[4,5] It is often observed in these methods that the initially formed 1-hydroxy-1,1-diphosphorus compounds are rearranged to form *geminal*-phosphorus-phosphorusoxy compounds under basic conditions. It appeared, however, to us that the addition reaction of P–P compounds to aldehydes and ketones may be a straightforward method, because the organic substrates are readily available (Scheme 1). Unfortunately, such reaction has very few precedents, and noncatalyzed addition reaction of $(CF_3)_2PP(CF_3)_2$ and acetone has been recently reported.[6,7]

During the course of our study on the development of transition-metal-catalyzed methods for the synthesis of organophosphorus compounds,[8] the metathesis and addition reactions with concomitant P–P bond cleavage have become important. We reported the rhodium-catalyzed reaction of 1-alkynes and tetraphenydiphosphine in the presence of a nitrobenzene yielding 1-phosphinoyl-1-alkynes.[9] This reaction proceeded via the metal-catalyzed addition of the P–P bond with the nitrobenzene followed by the C–H substitution of 1-alkynes. A single-bond metathesis reaction of the diphosphine disulfide P–P bond and the disulfide S–S bond giving thiophosphinates was also developed.[10] Recently, the rhodium-catalyzed C–P bond-forming reaction of 1,2-alkadienes with diphosphine disulfide has been reported,[11] which involved P–P bond cleavage and the transfer of the phosphorus group to the unsaturated compounds. Thus, rhodium complexes were found to be excellent catalysts for the synthesis of organophosphorus compounds via P–P bond cleavage. In this Letter, we describe a novel and fundamental rhodium-catalyzed carbonyl addition reaction of a P–P compound: The addition reaction of tetramethyldiphosphine disulfide[12] to aldehydes and ketones giving [1-(dimethylthiophosphinoyloxy)alkyl]dimethylphosphine sulfide (Table 1). Such diphosphine disulfide adducts with aldehydes and ketones were not known before. This is a convenient method for the synthesis of polyphosphorus compounds from simple aldehydes and ketones. It should also be noted that transition metal catalysis can be used for such carbonyl addition reaction of P–P compounds.



Scheme 1.

Table 1
Rhodium-catalyzed addition reaction of tetramethyldiphosphine disulfide and aldehydes



Entry	R	Yield (%)
1	Ph	99
2	*p*-$MeOC_6H_4$	98
3	*p*-BrC_6H_4	94
4	*n*-C_6H_{13}	92
5	$Ph(CH_2)_2$	97
6	*cyclo*-C_6H_{11}	81

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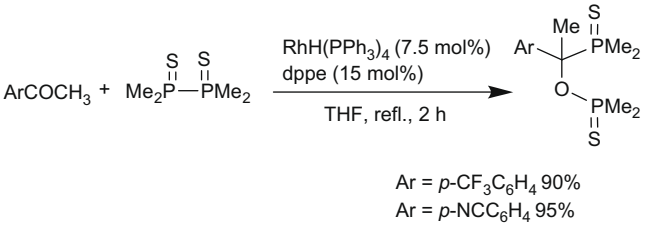

Scheme 2.

$RhH(PPh_3)_4$ (2.5 mol %) and 1,2-bis(diphenylphosphino)ethane (dppe, 5 mol %) were treated in THF for 1 min at room temperature, to which an equimolar mixture of benzaldehyde and tetramethyldiphosphine disulfide in THF was added. After refluxing in THF for 2 h, [1-(dimethylthiophosphinoyloxy)benzyl]dimethylphosphine sulfide was obtained in 99% yield (Table 1, entry 1). ^{31}P NMR spectroscopy indicated the presence of two peaks at δ 43.7 and 99.8 with $J = 25$ Hz. The P–H coupling constants $J = 15.6$ and 6.0 Hz were observed at the benzylic proton by ^1H NMR spectroscopy. ^{13}C NMR absorption of the benzylic carbon exhibited the P–C coupling constants $J = 64.5$ and 6.9 Hz. The rhodium complex and dppe were both essential for the reaction, and no reaction occurred in the absence of either substance. Other metal complexes in the presence of dppe exhibiting similar activity including $RhH(CO)(PPh_3)_3$ and $Rh(NO)(PPh_3)_4$, whereas $Rh(acac)(CH_2{=}CH_2)$, $RhCl(PPh_3)_3$, $[Rh(cod)(NH_3)_2]PF_6$, $[Rh(OAc)_2]_2$, $Pd_2(dba)_3$, and $PdCl_2(PPh_3)_2$ were ineffective.

The initial treatment of the rhodium complex and dppe was essential for obtaining reproducible results. This probably reflects the importance of the Rh–dppe complex formation in a sufficient amount. The effect of the phosphine ligand was critical, and bidentate ligands with diphenylphosphino groups attached by two carbon atoms exhibited catalytic activity, such as *cis*-1,2-bis(diphenylphosphino)ethylene (dppv) and 1,2-bis(diphenylphosphino)benzene (dppBz). Other bidentate ligands, dppm, dppp, dppb, and dppf, as well as monodentate ligands, $(p\text{-}MeOC_6H_4)_3P$ and $(p\text{-}ClC_6H_4)_3P$, were not effective.

The reaction proceeded with several aldehydes as summarized in Table 1 giving the 1,2-adducts in high yields. The electronic effect of the *p*-substituent of benzaldehydes was relatively small (entries 1–3). Aliphatic aldehydes also underwent a smooth addition reaction (entries 4–6).

This reaction was generally inert to ketones, and acetophenone did not give the adduct under the metal-catalyzed conditions. However, it was observed that acetophenones possessing electron-withdrawing cyano and trifluoromethyl groups at the *p*-position reacted with diphosphine disulfide, giving the 1,2-adducts in high yields, provided that the catalyst loading was sufficiently high (Scheme 2).

As for the mechanisms, the involvement of the rearrangement reaction from 1-hydroxy-1,1-diphosphorus compounds to the products is unlikely under the metal-catalyzed conditions. Stepwise addition and concerted carbonyl addition mechanism are conceivable. In either case, it is notable that the rhodium complex can participate in the bond formation of phosphorus and oxygen atoms as well as phosphorus and carbon atoms.

In summary, a rhodium complex catalyzed the addition reaction of tetramethyldiphosphine disulfide to aldehydes and ketones giving [1-(dimethylthiophosphinoyloxy)alkyl]dimethylphosphine sulfides in high yields. The rhodium catalyst is involved in the P–P bond cleavage and carbonyl addition of two phosphorus groups.

Synthesis of [1-(dimethylthiophosphinoyloxy)heptyl]dimethylphosphine sulfide. Into a two-necked flask were placed $RhH(PPh_3)_4$ (2.5 mol %, 7.2 mg) and dppe (5 mol %, 5.0 mg) in distilled THF (1 mL) under an argon atmosphere, and the solution was stirred at room temperature for 1 min. Then, tetramethyldiphosphine disulfide (0.25 mmol, 46.6 mg) and heptanal (0.25 mmol, 34.9 μl) were added, and the solution was heated at reflux for 2 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel giving the product (69.1 mg, 92%) as a colorless solid. Mp 43.5–44.0 °C (hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, $J = 6.8$ Hz), 1.27–1.32 (4H, m), 1.33–1.52 (4H, m), 1.72 (3H, d, $J = 12.4$ Hz), 1.77 (3H, d, $J = 12.4$ Hz), 1.92 (6H, d, $J = 13.2$ Hz), 1.83–1.98 (1H, m), 2.02–2.13 (1H, m), 5.04 (1H, dddd, $J = 16.0$, 8.8, 4.4, 2.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 17.7 (d, $J = 53.0$ Hz), 19.3 (d, $J = 53.8$ Hz), 22.5, 24.7 (d, $J = 76.6$ Hz), 25.5 (d, $J = 69.7$ Hz), 26.1 (d, $J = 9.9$ Hz), 29.0, 29.8, 31.5, 75.3 (d, $J = 65.2$, 8.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 42.8 (d, $J = 14.7$ Hz), 97.4 (d, $J = 14.9$ Hz). IR (KBr) 2927, 2857, 1417, 1289, 947, 910 cm^{-1}. MS (EI) *m*/*z* 300 ($\mathbf{M^+}$, 55%), 207 ($\mathbf{M^+}-PSMe_2$, 75%), 93 ($\mathbf{M^+}-207$, 100%). HRMS Calcd for $C_{11}H_{26}OP_2S_2$: 300.0901. Found: 300.0908.

Acknowledgments

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