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UNUSUAL FORMATION OF 5-HALO-2,2'-BIPYRIDYLS BY TREATMENT OF TRIS(2-PYRIDYL)PHOSPHINE DERIVATIVES WITH HALOGENS

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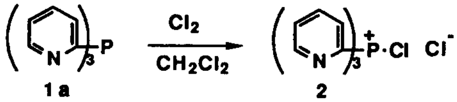
Abstract: Reaction of tris(2-pyridyl)phosphine with chlorine in dichloromethane or acetonitrile gave chlorotris(2-pyridyl)phosphonium chloride which afforded a coupling product, 2,2'-bipyridyl, by treating with dilute HCl. Treatment of tris(2-pyridyl)phosphine or tris(2-pyridyl)phosphine oxide with chlorine or bromine in methanol gave unusual 5-halo-2,2'-bipyridyl as a major coupling product. This is undoubtedly an electrophilic substitution on a pyridyl ring in the pentacovalent phosphorane.

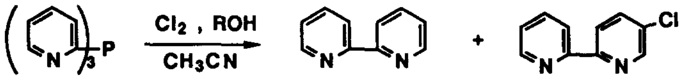
In our previous papers,[1,2] we have reported that phosphine oxides or phosphonium compounds bearing two or three 2-pyridyl groups gave a coupling product, 2,2'-bipyridyls, upon treatment with dilute hydrochloric acid. These reaction were considered to proceed via pentacoordinated phosphorus intermediates by nucleophilic attack of water on the phosphorus atoms. A similar coupling was postulated to occur by the reaction of phosphorus compounds bearing 2-pyridyl groups with a positively charged phosphorus atom with nucleophiles. This paper reports the unusual reaction of halotris(2-pyridyl)phosphonium halides derived from tris(2-pyridyl)phosphines (**1**) with chlorine or bromine.

Treatment of tris(2-pyridyl)phosphine (**1a**) with excess chlorine in dichloromethane or acetonitrile at room temperature and followed by the removal of solvent and excess chlorine gave crystalline adduct, $Py_3P^+Cl\ Cl^-$ (**2**), which was hygroscopic and sensitive to moisture.[3] The adduct was also obtained by treating **1a** in liquid chlorine. The adduct (**2**) afforded tris(2-pyridyl)phosphine oxide upon treatment with aqueous sodium hydroxide in a 49% yield. In contrast, the reaction with dilute hydrochloric acid led to the formation of 2,2'-bipyridyl (**3a**) (51%). These results are similar to that previously reported on the reaction of benzyltris(2-pyridyl)phosphonium bromide, in which benzylbis(2-pyridyl)phosphine oxide and **3a** were formed upon treatment with aqueous sodium hydroxide and dilute hydrochloric acid, respectively.[1,2]



When **1a** was treated with chlorine in acetonitrile and then the resulting adduct was treated with refluxing methanol, the coupling product (**3a**) was obtained in a 68 % yield together with a trace amount of

5-chloro-2,2'-bipyridyl (**4a**). Interestingly, when the chlorination of **1a** was carried out in acetonitrile in the presence of water or alcohols, the yield of **4a** markedly increased. These results are summarized in Table 1.



1a **3a** **4a**

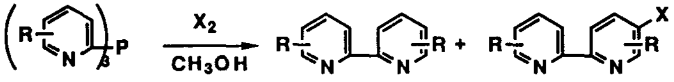
Table 1 Chlorination of **1** in the presence of alcohols or water in acetonitrile

R-OH	R-OH / Py_3P a)	Reaction time	Product Yield (%) b)	
		(h)	**3a**	**4a**
H_2O	10	4	14	73
MeOH	10	4	7	61
EtOH	10	4	11	75
i-PrOH	10	4	5	85
t-BuOH	10	4	2	84

a) Mol ratio. b) Determined by gas chromatography

Chlorination of **1a** in methanol gave **4a** as the major coupling product together with a small amount of **3a**. The reactions of some substituted tris(2-pyridyl)phosphines (**1**) with chlorine in methanol were carried out and found to afford the corresponding 5-chloro-2,2'-bipyridyls (**4**), except in the reaction with tris(6-bromo-2-pyridyl)phosphine (**1f**). The reaction of **1f** with chlorine in methanol afforded no coupling product but tris(6-bromo-2-pyridyl)phosphine oxide in quantitatively.

The reactions between the phosphines and bromine in methanol gave corresponding 5-bromo-2,2'-bipyridyls and 2,2'-bipyridyls (**5**). These results are summarized in Table 2.[4]



1 **3**

4; X = Cl
5; X = Br

We have also examined halogenation of tris(2-pyridyl)phosphine oxide (**6**) in methanol and found that the chlorination or bromination smoothly took place to give **3a** and **4a** or **3a** and **5a**, respectively, as shown in Table 2. It is known that triphenylphosphine dihalide reacts with alcohol to afford the corresponding haloalkane and triphenylphosphine oxide.[5] The ^{1}H-NMR spectra of the reaction mixture of **2** with methanol in $CDCl_3$ showed a signal of chloromethane at 3.01 ppm, but the signal was not strong. These results suggest that some of **6** are formed and then undergo chlorination to give **4a**. When **6** was treated with chlorine in dichloromethane and then alkali solution, the starting material was recovered, but no chlorine

Table 2 Halogenation of phosphines (**1**) or phosphine oxide (**6**) in methanol

	R	X_2	Product Yield (%) a)			
1a	H	Cl_2	**3a**	3	**4a**	77
6	H	Cl_2	**3a**	8	**4a**	62
1b	3-Me	Cl_2	**3b**	2	**4b**	11
1c	4-Me	Cl_2	**3c**	6	**4c**	63
1d	6-Me	Cl_2	**3d**	2	**4d**	73
1e	6-Ph	Cl_2	**3e**	19 c)	**4e**	3 c)
1f	6-Br	Cl_2	**3f**	0	**4f**	0
1a	H	Br_2 b)	**3a**	14	**5a**	76
6	H	Br_2 b)	**3a**	15	**5a**	74
1c	4-Me	Br_2 b)	**3c**	36	**5c**	48
1d	6-Me	Br_2 b)	**3d**	22	**5d**	69

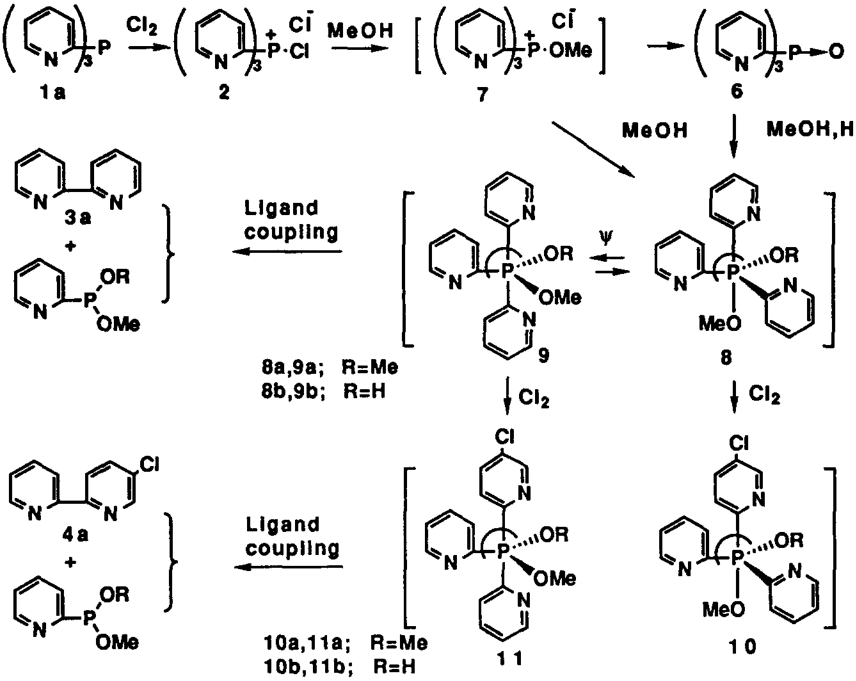
a) Determined by gas chromatography. b) Three equivalents of bromine were used. c) Isolated yield.

substituted phosphine oxide, 2-(5-chloropyridyl)bis(2-pyridyl)phosphine oxide. The result ruled out the mechanism of the formation of **4a** in which the ligand coupling of the chlorine substituted phosphine oxide to **4a**, is involved.

In the previous papers,[1,2] we proposed the mechanism for the formation of 2,2'-bipyridyl in the reaction of tris(2-pyridyl)phosphine oxide or benzyltris(2-pyridyl)phosphonium bromide with nucleophiles, which involves pentacoordinated phosphorus intermediates. For the formation of **4a**, however, the mechanism involving ligand coupling of **1a** and followed by chlorination of the coupling product to give **4a** was ruled out, since **3a** did not give **4a** by treating with chlorine under the same reaction conditions.

For the formation of 5-chloro-2,2-bipyridyls, the postulated mechanism in the chlorination of **1a** and **6** in methanol is shown in Scheme 1. In the chlorination, phosphine (**1a**) reacts with chlorine to form chlorotris(2-pyridyl)phosphonium salt (**2a**) which converts to methoxytris(2-pyridyl)phosphonium salt (**7**) in the presence of methanol. Some of the alkoxyphosphonium salt would undergo the Arbuzov reaction to afford tris(2-pyridyl)phosphine oxide (**6**). The alkoxyphosphonium salt or the phosphine oxide further reacts with methanol to yield pentacoordinated intermediates (**8a**,**9a**) or (**8b**,**9b**), respectively.

For the phosphorus(V) compounds, three molecular orbitals are formed primarily from p-orbitals in a description of axial bonding leading to three-center four-electron bonding in the Rundle's model.[6] The phosphorus groups of **8** and **9** would behave as a strong electron-donating group to the axial pyridine rings because of the electron-rich axial bond. Consequently, the axial pyridine rings of **8** and **9** would readily undergo electrophilic substitution at the 5 position to yield chlorinated intermediates (**10**) and (**11**), respectively. As the corollary to this, other electrophilic reactions such as diazo coupling and deuteration were found to occur very readily, which are the subjects of other papers. Within the intermediates, the chlorinated axial pyridine ring couples with an equatorial pyridyl ligand to form **4a**. On the other hand, **3a** would be formed by ligand coupling within the both intermediates (**8**) or (**9**), before chlorination, and **11**.



Scheme 1

References and Notes

1 Uchida, Y.; Kozawa, H.; Oae, S. *Tetrahedron Lett.*, **1989**, *30*, 6365.

2 Uchida, Y.; Onoue, K.; Tada, N.; Nagao, F.; Kozawa, H.; Oae, S. *Heteratom Chem.*, **1990**, *1*, 295.

3 The values of elementary analysis of **2** differed widely from calculated values, because **2** is hygroscopic and sensitive to moisture. Found: C, 52.97; H, 4.11; N, 12.06%. Calcd for $C_{15}H_{12}N_3PCl_2$: C, 53.60; H, 3.60; N, 12.50%.

4 A typical procedure for the chlorination of **1** in methanol follows: To a solution of **1a** (1 mmol) in methanol (10 ml) was bubbled chlorine gas at room temperature until the solution became yellow. After the solution was kept for 4h, the solvent and chlorine were removed under reduced pressure. The residue was made slightly alkaline with NaOH solution and *m*-dinitrobenzene (100 mg) was added as an internal standard, and then the whole mixter was extracted with dichloromethane (30ml). The organic layer was dried over Na_2SO_4 and subjected to GC analysis.

5 Horner, L.; Oediger, H.; Hoffmann, H. *Ann*, **1959**, *626*, 26.

6 Rundle, R. E. *J. Am. Chem. Soc.*, **1963**, *85*, 112.

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