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FORMATION OF 2,2'-BIPYRIDYL BY LIGAND COUPLING ON THE PHOSPHORUS ATOM

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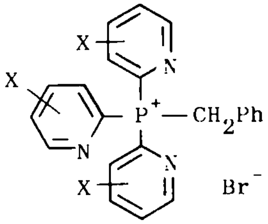
Abstract: Phosphonium salts and phosphine oxides, bearing at least two 2-pyridyl or substituted 2-pyridyl groups gave the corresponding 2,2'-bipyridyls and pyridines upon treatment with acid or neutral solvents such as water and alcohols, in substantial yields.

Earlier, Newkome and Haeger reported the formation of 2,2'-bipyridyl derivatives by treatment of bis(6-substituted 2-pyridyl)phenyl phosphine oxides with sodium ethoxide.1) A similar coupling reaction has been found to take place in the reaction of some phosphine oxides with Grignard reagents.2) The reaction has been considered to proceed *via* formation of a pentacoordinated intermediate in which an axial group couples with an equatorial one.3) In continuation of our works on ligand coupling within the pentacoordinated phosphorus intermediates, we have studied on the reactions of some phosphonium salts and phosphine oxides, bearing at least two 2-pyridyl or substituted 2-pyridyl groups, with nucleophiles. Although there are many reports for the reactions of phosphonium salts and phosphine oxides with bases such as alkali hydroxides, alkoxides, and organometallic reagents, only a few studies have been carried out on the reactions of these phosphorus compounds with acids.4) In this paper, we report the ligand coupling reactions on the phosphorus atom which take place during the reactions of phosphonium salts and phosphine oxides with nucleophiles under neutral or even acidic conditions, giving 2,2'-bipyridyl derivatives.

Benzyltri(2-pyridyl)phosphonium bromide (**1a**) underwent rapid alkaline hydrolysis at room temperature to give benzyldi(2-pyridyl)phosphine oxide (**2a**) and pyridine in good yields. However, when the phosphonium salt was dissolved in water, a slow decomposition was found to take place at room temperature, giving a ligand coupling product, *i.e.*, 2,2'-bipyridyl (**3**, X=H) and benzyl(2-pyridyl)phosphine oxide (5), in addition to **2a** and pyridine. The reaction was accelerated in dil HCl and completed within 30 min at room temperature, affording preferentially the ligand coupling products, **3** and **5**.



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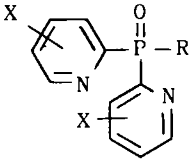

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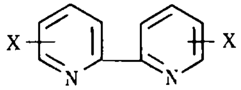

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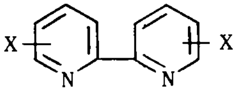
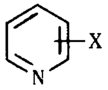
Table 1. Ligand Coupling Reaction of Phosphonium Salts **1**

Phosphonium salt		Reaction conditions			Product Yield (%)$^{a,b)}$	
	X					
1a	H	H_2O	60 °C,	2.5h	47	64
		H_2O/HCl$^{c)}$	r.t.,	0.5h	64	17
		H_2O/HCl$^{c)}$	reflux,	10h	73	80
		CH_3OH	r.t.,	72h	26	20
1b	4-Me	H_2O	60 °C,	2.5h	42	31
		H_2O/HCl$^{c)}$	r.t.,	0.5h	84	17
1c	6-Me	H_2O	60 °C,	2.5h	39	64
		H_2O/HCl$^{c)}$	r.t.,	0.5h	73	20
		H_2O/HCl$^{c)}$	reflux,	10h	87	68

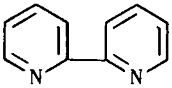
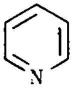
a) Determined by GC analysis. b) Based on **1** used. c) 0.2 M/1.

Similarly, benzyltri[2-(4-methylpyridyl)]phosphonium bromide (**1b**) and benzyltri[2-(6-methylpyridyl)]phosphonium bromide (**1c**) gave the corresponding substituted 2,2'-bipyridyls in good yields by treating with dil HCl. These results are summarized in Table 1.

A typical procedure for the treatment of **1** with dil HCl is as follows: After keeping **1a** (2 mmol) in dil HCl (0.2 M/1, 20 ml) for 30 min, the whole mixture was made slightly alkaline with NaOH, and then extracted with CH_2Cl_2 (30 ml). The organic layer was dried over Na_2SO_4 and subjected to GC analysis, using biphenyl (200 mg) as an internal standard.

It is known that 2,2'-bipyridyl is formed by the reaction of tri(2-pyridyl)phosphine oxide (**2b**) with alkoxide.[1] We have examined whether the coupling product is formed from phosphine oxides in acidic conditions. When **2a** was allowed to stand overnight in water or dil HBr (0.05 M/l), no detectable decomposition was found to occur at room temperature. However, when the phosphine oxide was refluxed for 20 h in dil HCl, 2,2'-bipyridyl was formed in 39% yield, together with pyridine. Meanwhile, refluxing **2b** with dil HCl produced the coupling product in a good yield. Moreover, we found that the coupling reaction took place by heating the phosphine oxides in acetic acid and even in water or ethylene glycol under neutral conditions. The results are shown in Table 2.

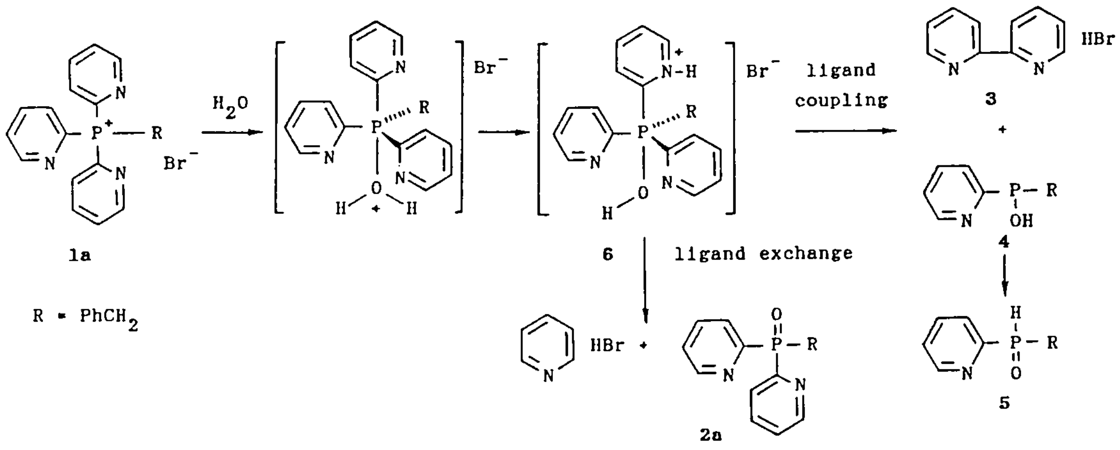
Table 2. Ligand Coupling Reaction of Phosphine Oxides

Phosphine oxide			Reaction conditions		Product Yield %[a,b]	
	X	R				
2a	H	$PhCH_2$	H_2O/HCl[c]	reflux, 20h	39	49
2b	H	2-Pyridyl	H_2O/HCl[c]	reflux, 20h	80	46
			AcOH	reflux, 20h	35	d)
			H_2O	reflux, 20h	50	30
			$HOCH_2CH_2OH$	reflux, 20h	78	85
2c	H	Ph	H_2O/HCl[c]	reflux, 20h	39	49
			H_2O	reflux, 20h	20	trace
2d	H	p-$CH_3C_6H_4$	H_2O/HCl[c]	reflux, 5h	44	26
2e	H	p-$CH_3C_6H_4CH_2$	H_2O/HCl[c]	reflux, 20h	39	48

a) Determined by GC analysis. b) Based on **2** used. c) Phosphine oxides **2** (2 mmol) was refluxed in dil HCl (20 ml, 0.2M/l). d) Not determined.

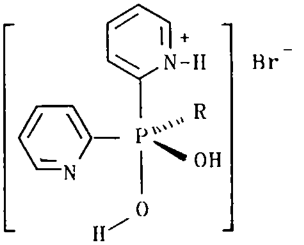
Similarly, refluxing phenyldi(2-pyridyl)phosphine oxide (**2c**), di(2-pyridyl)*p*-tolylphosphine oxide (**2d**), and *p*-methylbenzyldi(2-pyridyl)phosphine oxide (**2e**) in dil HCl or water also gave 2,2'-bipyridyl in moderate yields. The results are summarized in Table 2.

The plausible mechanism for the reaction of **1a** with water under acidic conditions is shown in Scheme 1, which involves the formation of pentacoordinated intermediate (**6**) by nucleophilic attack of water on the phosphorus atom. Within the intermediate, an equatorial 2-pyridyl group would couple with an axial 2-pyridinium group to afford **3** and **4**. The latter compound would isomerize to **5**. Pyridine and **2a** would be formed by ligand exchange *via* the intermediate (**6**). Nucleophilic attack of water on the phosphorus atom of the phosphine oxides as in the case of the



Scheme 1

phosphonium salt would also lead to the formation of pentacoordinated intermediate (7). In the reaction of phenyldi(2-pyridyl)phosphine oxide with dil HCl, phenylphosphinic acid, a tautomer of phenyl phosphonous acid, was isolated as the phosphorus portion.



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Recently, we have reported that pyridyl group easily couples with benzyl group on the ligand coupling reaction of sulfoxides or phosphine oxides with organometallic reagents.[2,3] Unlike those reactions, however, no formation of 2-benzylpyridine has been observed in the reaction of the phosphonium salts or phosphine oxides in the aqueous media. This seems to suggest that in the aqueous media the benzyl group has no chance to come at the axial position in the intermediates, and ligand coupling and exchange would take place immediately upon nucleophilic attack of water on the phosphorus atom.

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