A Novel One-Pot Synthesis of 6,6″-Dibromo-2,2′:6′2″-terpyridine

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This paper is dedicated to Professor Manfred Regitz on the occasion of his 60th birthday.

Dibromo-2,2′:6′2″-terpyridine was obtained in a moderate yield by lithiation of four molar amounts of 2,6-dibromopyridine with butyllithium followed by treatment with phosphorus trichloride in diethyl ether.

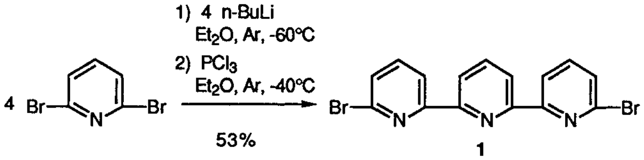
The reactions of three molar amounts of organometallic reagents with phosphorus trichloride have been used widely to prepare tertiary alkyl or aryl phosphines. However, we have recently found that some heteroaryllithium compounds such as 2-benzothiazyllithium or substituted 2-pyridyllithium give a coupling compound as the major product together with a small amount of the corresponding phosphine upon treatment with phosphorus trichloride.[1-3] A similar coupling of the lithium compound was found to take place in its reaction with phosphorus oxychloride or thionyl chloride to afford the corresponding biaryl in good yield.[3]

In the course of our study of the reaction of the heteroaryllithium compounds with phosphorus trichloride, we also found that 6,6″-dibromo-2,2′:6′2″-terpyridine (**1**) was formed together with 6,6′-dibromobipyridyl and tris[2-(6-bromopyridyl)]phosphine in the reaction of four molar amounts of 6-bromopyrid-2-yllithium with phosphorus trichloride.[3]

2,2′:6′2″-Terpyridine derivatives have attracted considerable attention in transition metal chemistry as tridendate chelating ligands. The terpyridine **1** was used as starting material for a variety of macrocycles incorporating a 2,2′:6′2″-terpyridyl moiety.[4,5] Recently, the preparative methods for **1** were reported by the Newkome[4] and Constable groups[5] which involve multiple steps. The final steps were the reaction of 1,5-bis(6-bromo-2-pyridyl)-1,5-dioxopentane with ammonium acetate[4] and the reaction of [2′-(6″-bromo-2″-pyridyl)-2′-oxoethyl]pyridinium iodide with 2-bromo-6-(3′-dimethylammonio-1′-oxopropyl)pyridine chloride in the presence of ammonium acetate,[5] respectively. Therefore, we have reinvestigated the reaction of 6-bromopyrid-2-yllithium with phosphorus trichloride to apply the reaction to the synthesis of **1**. In this paper we report on a novel one-pot synthesis of **1**.

2,6-Dibromopyridine was converted into 6-bromopyrid-2-yllithium by treatment with an equimolar amount of butyllithium at −60 °C in diethyl ether under argon atmosphere. When three molar amounts of the lithium compound were added to phosphorus trichloride in diethyl ether and allowed to react for 4 hours at −40 °C, tris[2-(6′-pyridyl)]phosphine was obtained in 52 % yield, together with a small amount of 6,6″-dibromo-2,2′-dipyridyl. However, addition of phosphorus trichloride to four molar amounts of the lithium compound gave a mixture of tris[2-(6′-pyridyl)]phosphine, 6,6″-dibromo-2,2′-dipyridyl, and **1** in 9, 16, and 36 % yields, respectively, based on phosphorus trichloride.[3]

The most satisfactory results were obtained by the slow addition of phosphorus trichloride to the lithium reagent in diethyl ether with prolonged reaction time. When the reaction was carried out for 20 hours at −40 °C after the addition of phosphorus trichloride and allowed to warm to room temperature, **1** was obtained in 53 % yield, and 6,6′-dibromo-2,2′-pyridyl and the phosphine were absent in the reaction mixture. Therefore, the required product was easily separated from the other side products by passing a hot toluene solution of the reaction products through a short silica gel column.



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Aside from the simple one-pot procedure, an additional advantage of our method is that the starting material, i.e., 2,6-dibromopyridine, is commercially available. Furthermore, by replacing phosphorus trichloride with phosphorus oxychloride, or thionyl chloride, 6,6″-dibromo-2,2′-dipyridyl can also be prepared from the lithium reagent in good yield.[3] Our synthesis is based on the ligand coupling on the phosphorus atom. The intermediate is tris[2-(6′-pyridyl)phosphine. Although a possible mechanism for the formation of **1** has been reported in a previous paper,[3] further studies are under way.

6,6″-Dibromo-2,2′:6′2″-terpyridine (1):

A solution of 2,6-dibromopyridine (11.85 g, 50 mmol) in Et_2O (50 mL) was cooled to −60 °C with a dry ice-acetone bath under an Ar atmosphere, and a solution of BuLi (50 mmol) in hexane was added with stirring. After stirring the mixture for 2 h at −40 °C, a solution of PCl_3 (1.72 g, 12.5 mmol) in Et_2O (50 mL) was added dropwise over a period of 2 h, and the mixture was stirred for 20 h at −40 °C. The mixture was allowed to warm up to r.t., and then poured into H_2O (100 mL). The crystalline product was collected by filtration and washed with H_2O and dried. The crystals were dissolved in hot toluene (400 mL) and the product was filtered. The hot toluene solution was passed through a short silica gel column. Toluene was removed by distillation under reduced pressure and the residue was washed with Et_2O to give **1** (2.48 g). The Et_2O layer was washed with H_2O and dried. The Et_2O was evaporated and the residue was separated by column chromatography on silica gel using toluene as eluent. An additional 0.09 g of **1** was obtained. The total yield of **1** was 2.57 g (53 % based on PCl_3, or 39 % from 2,6-dibromopyridine). Crystallization from toluene gave colorless needles; mp 263–264 °C (Lit.[4] mp 262–263 °C).

MS: *m/z* (rel intensity, %) = 392 ($M^+ + 3$, 52), 390 ($M^+ + 1$, 100), 388 ($M^+ - 1$, 53), 312 (14), 311 (77), 309 (80), 230 (30), 203 (13), 153 (21), 126 (14), 115 (16), 102 (14), 76 (16).

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