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The Preparation and Reaction of Disubstituted Aminophosphonium Bromide. Reaction of Triphenylphosphine Dibromide with Secondary Amines

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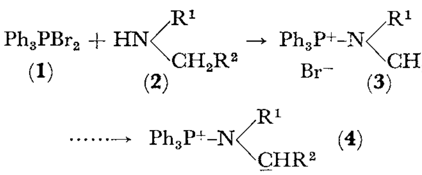
Disubstituted aminotriphenylphosphonium bromides were obtained in excellent yields from the reaction of triphenylphosphine dibromide and the secondary amines using simple procedures. This method has an advantage in the preparation of cyclic aminophosphonium salts, such as those of morpholine or piperidine. The treatment of the disubstituted aminophosphonium salt with bases resulted in dehydrohalogenation, followed by a Hofmann-like decomposition, and gave imine and triphenylphosphine.

Triphenylphosphine dihalide (**1**) has been used as a halogenation reagent, like phosphorus pentachloride, or as a dehydrating reagent.[1] There have also been several reports on the use of this reagent for the activation of compounds like the malonic ester[2] or primary amines[2b,3] in the form of phosphonium salt or ylide.

In this paper, the preparation of the salt by the reaction of triphenylphosphine dibromide with secondary amines will be reported; the activation of the carbon adjacent to the amino group was also attempted by converting the salt to ylide through the elimination of hydrogen bromide (Eq. (1)).



$$\underset{(\mathbf{1})}{Ph_3PBr_2} + \underset{(\mathbf{2})}{HN{<}^{R^1}_{CH_2R^2}} \rightarrow \underset{Br^-\quad(\mathbf{3})}{Ph_3P^+\text{-}N{<}^{R^1}_{CH_2R^2}} \cdots\cdots\rightarrow Ph_3P^+\text{-}N{<}^{R^1}_{\underline{C}HR^2} \quad (\mathbf{4})$$

Eq. (1)

Disubstituted aminophosphonium salt was obtained by Staudinger[4] through the addition of alkyl halide to phosphoimine, and the scope and the limitations of the dialkylaminophosphonium salt were studied by Zimmer.[3] The disubstituted aminophosphonium salt is obtained by the method used in the preparation of monosubstituted aminophosphonium salt, *i.e.*, directly by the reaction of triphenylphosphine dibromide and secondary amine in the presence of triethylamine.

The reaction of triphenylphosphine dibromide with *N*-ethylaniline (**2a**) in acetonitrile in the presence of an equimolar amount of triethylamine gave *N*-ethylanilinotriphenylphosphonium bromide (**3a**) in an 82% yield. On the other hand, the addition of ethyl bromide or ethyl iodide to tetraphenylphosphoimine gave the corresponding salts in 29% and 73% yields respectively, even after refluxing in benzene for 24 hr. When diethylamine (**2b**), *N*-methylbenzylamine (**2c**), piperidine (**2d**), or morpholine (**2e**) was used as the secondary amine, the corresponding salts were obtained almost quantitatively by this method. In the case of *N*-benzylaniline (**2f**), which would exert a rather large steric hindrance in the salt, there was only a 19% yield of salt after 5 hr refluxing.

In sum, except for the case of bulky amines, the preparations of disubstituted aminophosphonium

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[1] R. F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry," Academic Press, London and N. Y. (1965), p. 214.

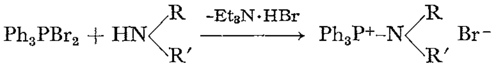
[2] a) L. Horner and H. Oediger, *Chem. Ber.*, **91**, 437 (1958). b) L. Horner and H. Oediger, *ibid.*, **95**, 2526 (1962).

[3] H. Zimmer and G. Singth, *J. Org. Chem.*, **28**, 483 (1963).

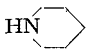
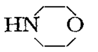
[4] H. Staudinger and E. Hauser, *Helv. Chim. Acta*, **4**, 861 (1921).

Table 1. Preparation of triphenylphosphine dibromide

All the reactions were carried out in acetonitrile.



$$Ph_3PBr_2 + HN{<}^{R}_{R'} \xrightarrow{-Et_3N\cdot HBr} Ph_3P^{+}{-}N{<}^{R}_{R'}\ Br^-$$

No.	R	R'	Temp.	Time (hr)	Yield	Mp °C	Elemental anal. (%) (Found/Calcd)		
							C	H	N
a.	C_2H_5	Ph	25°	8	82%	242—242.5	67.38	5.67	2.94
							67.53	5.41	3.16
b.	C_2H_5	C_2H_5	25°	8	68%	136.5—137	62.14*	6.30	3.16
							63.77	6.04	3.38
c.	CH_3	CH_2Ph	25°	24	81%	222	67.60	5.16	3.19
							67.53	5.14	3.03
d.			25°	8	68%	226.5—229	64.96	6.13	3.33
							64.79	5.86	3.28
e.			25°	24	42%	245—247	61.43	5.09	2.98
							61.69	5.38	3.27
f.	Ph	CH_2Ph	82°	5	19%	221	71.49	5.34	2.54
							70.99	5.16	2.67

* This compound seems to be contaminated with triethylamine salt, and the purification from the triethylamine salt was extremely difficult because of the solubility of both the salts in water.

salts by the reaction of triphenylphosphine dibromide (**1**) with secondary amines (**2**) quantitatively proceed readily and under mild conditions. The cyclic aminophosphonium salts can be also obtained by this procedure. The results are summarized in Table 1.

In an attempt to obtain *β*-phosphonium ylide (**4**), *N*-methyl-*N*-benzylaminotriphenylphosphonium bromide (**3c**) was treated with sodium methoxide in methanol. However, the products were triphenylphosphine oxide and dimethylamine; this was similar to the case of the hydrolysis of disubstituted aminophosphonium salt with sodium hydroxide.3) *N*-Methylbenzylamine was also obtained; it is probably a hydrolysis product.

When *N*-methyl-*N*-benzylaminotriphenylphosphonium bromide (**3c**) was treated with an equimolar amount of butyllithium in THF, triphenylphosphine (**6**; 40%), benzylidenemethylamine (**7**; 25%), an unidentified amine, and two hydrolysis products, triphenylphosphine oxide (**5**; 14%) and *N*-methyl-*N*-benzylamine (**2c**; 41%), were obtained. Thirteen per cent of the unreacted phosphonium salt was recovered.

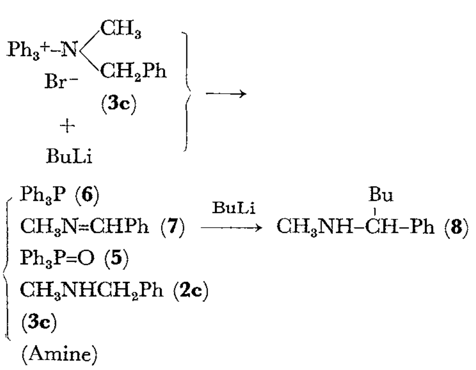


Fig. 1

The unidentified amine is probably the reaction product from benzylidene-methylamine (**7**) and butyllithium, because the treatment of *N*-methyl-*N*-benzylaminotriphenylphosphonium bromide (**3c**) with two mole equivalents of butyllithium gave *N*-methyl-*N*-(1-phenylpentyl)amine (**8**).

These results indicate that the following processes take place in the reaction:

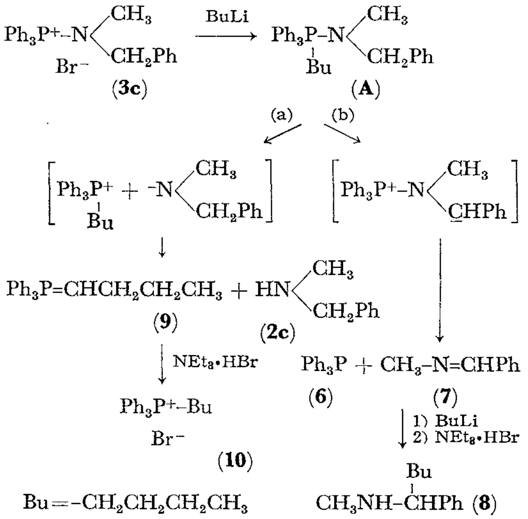


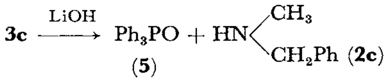
Fig. 2

In the first step, an intermediate, **A**, is formed from the reaction of *N*-methyl-*N*-benzylaminotriphenylphosphonium bromide (**3c**) and butyllithium.

Two different reaction paths from **A** may be considered:

a) The decomposition of **A** produces the amine (**2c**) and butylidenetriphenylphosphorane (**9**), which then, yield phosphonium salt (**10**) after treatment with triethylamine hydrobromide. In this case, the most stable anion, the *N*-methylbenzylamide anion, would leave from the five ligands around the phosphorus atom in **A**.[5]

b) The *β*-deprotonation of **A** by the butyl anion, followed by a Hofmann-like decomposition gives benzylidenemethylamine (**7**). A similar decomposition of phosphonium salt has been reported by Trippett and[6] Bestmann.[7] The last compound (**7**) was converted to amine (**8**) by the excess butyllithium. If a trace of water is present in the reaction mixture, a portion of the butyllithium will be changed to lithium hydroxide, which will then hydrolyze the phosphonium salt (**3c**) to triphenylphosphine oxide (**5**) and *N*-methylbenzylamine (**2c**).



$$\mathbf{3c} \xrightarrow{\text{LiOH}} \underset{(\mathbf{5})}{Ph_3PO} + HN\begin{matrix} CH_3 \\ CH_2Ph \end{matrix} \ (\mathbf{2c})$$

The expected ylide from the elimination of the hydrogen halide of disubstituted aminophosphonium salt was found to be very unstable; as a result, the activation of the carbon adjacent to the amino group as an anion was unsuccessful. However, the results indicate the possibility of the use of this reaction in the preparation of imines and in the reduction of triphenylphosphine dihalide to triphenylphosphine.

In fact, the treatment of *N*-methyl-*N*-benzylaminotriphenylphosphonium bromide with sodium hydride in acetonitrile at room temperature gave triphenylphosphine (**6**; 42%) and benzylidenemethylamine (**7**; 25%). Sodium hydride was used in place of butyllithium to avoid the side reaction of the reagent with the imines.

Experimental

Preparation of Disubstituted Aminophosphonium Salts. *a) From Triphenylphosphine Dibromide (***1***) and Secondary Amines.* Into a solution of triphenylphosphine (2.62 g, 10 mmol) in acetonitrile (50 m*l*), a solution of bromine (1.60 g, 10 mmol) in the same solvent (15 m*l*) was stirred, drop by drop, at room temperature. A solution of *N*-ethylaniline (**2a**) (1.21 g, 10 mmol) in acetonitrile (15 m*l*) and a solution of triethylamine (1.01 g, 10 mmol) in 15 m*l* of the same solvent were then added to the mixture from a dropping funnel. After stirring at room temperature for 8 hr the solvent was removed under reduced pressure at 40—50°C. The concentrated residue was triturated with benzene, and the precipitates were collected by filtration. The precipitates were dissolved in 50 m*l* of water, and the insoluble solids were filtered off. *N*-Ethylanilinotriphenylphosphonium bromide (**3a**) was obtained in an 82% (3.8 g) yield. The crude product was recrystallized from chloroform - ethyl acetate and gave white crystals, mp 242—242.5°C.

The reactions of **1** with all the other secondary amines were carried out by a similar procedure under the reaction conditions shown in Table 1. The solvent for the recrystallization of the crude products was chloroform-ethyl acetate, except for the case of *N*-benzylanilinotriphenylphosphonium salt (**3f**), where water was used as the solvent. The results of elementary analysis and the melting points are listed in Table 1.

b) From the Addition Reaction of Alkyl Halide to Tetraphenylphosphoimine. A solution of tetraphenylphosphoimine[2] (3.53 g) and ethyl bromide (15 m*l*) in benzene (30 m*l*) was refluxed for 24 hr, and then the precipitated crystals were collected at room temperature. **3a** was obtained in a 29% (1.3 g) yield. The crude product was recrystallized from a chloroform - ethyl acetate mixture. The melting point was 242—242.5°C, and there was no depression shown in a mixed-melting point determination with the product from a). Unreacted tetraphenylphosphoimine (2.2 g; 62%) was recovered from the concentrated benzene solution by the addition of isopropyl alcohol.

In a similar fashion, the reaction of ethyl iodide or benzyl chloride with tetraphenylphosphoimine was carried out. The resulting salts were recrystallized from water. The melting points and the results of elementary analysis are as follows: *N*-Ethylanilinotriphenylphosphonium iodide, mp 221—221.5°C. *N*-Benzylanilinotriphenylphosphonium chloride, mp 205—206°C. Found: C, 77.07; H, 5.88; N, 2.92%. Calcd for $C_{31}H_{27}ClNP$: C, 77.60; H, 5.84; N, 2.92%.

Reaction of *N*-Methyl-*N*-benzylaminophosphonium Bromide (3c) with Sodium Methoxide. To a methanol (50 m*l*) solution of sodium (0.5 g), **3c** (9.46 g) in methanol (50 m*l*) was added under cooling. After standing at room temperature for one day, the mixture was refluxed for 3 hr and then concentrated under reduced pressure. Benzene and water were added to the residue. The benzene layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed to give an oily product, which was then dissolved in *n*-hexane. The insoluble solids were filtered off. Triphenylphosphine oxide was thus obtained in a 97% (5.4 g) yield. The *n*-hexane solution was concentrated and subsequently distilled. A distillate with a bp 80—83°C/26 mmHg was analyzed by gas-liquid chromatography, using an Apiezon Grease M column (10%, 3 mm×2 m); column temperature, 100°C, carrier gas, He. It gave two peaks, whose relative retention times were equal to those of authentic dimethylamine and *N*-methylbenzylamine (**2c**).

Reaction of 3c with Equimolar Butyllithium. To a suspension of **3c** (6.95 g) in THF (50 m*l*) cooled by ice, a *n*-hexane solution of butyllithium (10.5 m*l*) was added, drop by drop, under a nitrogen atmosphere. The mixture was then stirred at room temperature for one day. The precipitated crystals were collected. **3c** (0.9 g, 13%) was recovered. The filtrate was concentrated to give an oily residue. The residue was dissolved in methanol,

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[5] A. W. Johnson, "Ylid Chemistry," Academic Press, N. Y. and London (1966), pp 59—61.

[6] S. Trippett, *Proc. Chem. Soc.*, **1963**, 19.

[7] H. J. Bestmann and R. Zimmerman, *Chem. Ber.*, **101**, 2185 (1968).

and the insoluble products were filtered off. By repeating these procedures twice, triphenylphosphine was obtained in a 40% (1.65 g) yield. The filtrate was concentrated and distilled. Benzylidenemethylamine (**7**) was thus obtained in a 40% (0.6 g) yield. The IR spectrum of **7** was equal to that of an authentic sample. The residue of the distillation was dissolved in *n*-hexane. Insoluble solids were thus collected. Triphenylphosphine oxide (**5**) was obtained in a 14% (0.6 g) yield.

Reaction of 3c with 2 Molar Equivalents of Butyllithium. To a suspension of **3c** (23.1 g) in THF (100 m*l*) cooled by a dry ice-acetone mixture, a *n*-hexane solution of butyllithium (68 m*l*) was added, drop by drop, under a nitrogen atmosphere. After keeping the mixture under 0°C for 8 hr, triethylammonium bromide (9 g) and then 50 m*l* of ethanol was added. The crystals were filtered off after 2 hr and washed with water. Butyltriphenylphosphonium bromide (**10**) (8 g, 40%) was thus obtained. The product was recrystallized from water; mp 238°C. Found: C, 65.82; H, 5.99%. Calcd for $C_{22}H_{24}BrP$: C, 66.1; H, 6.01%.

The filtrate was then concentrated and distilled. *N*-Methylbenzylamine (**2c**) (bp 87°C/20 mmHg, 2.5 g, 41%) was thus obtained. Benzene and water was added to the residue of distillation. The precipitated crystals were **10** (2.15 g, 10%). The separated benzene solution was washed with water and dried over anhydrous sodium sulfate. The benzene solution was concentrated and distilled. The distillate with a bp 107—142°C/17 mmHg was identified as *N*-methyl-*N*-(1-phenylpentyl)amine (**8**) (0.55 g, 7%) by IR, bp, and elemental analysis. Found: C, 81.31; H, 10.55; N, 7.91%. Calcd for $C_{12}H_{19}N$: C, 81.3; H, 10.72; N, 7.91%.

Reaction of 3c with Sodium Hydride. To a mixture of **3c** (9.24 g) and sodium hydride (1.0 g), acetonitrile (50 m*l*) was added. A violent gas evolution was observed. The mixture was stirred at room temperature for 8 hr, and then triethylammonium bromide (3.64 g) was added and the mixture was stirred for 2 more hours. After the precipitate had been removed the filtrate was concentrated. To the residue, 2 *N*-hydrochloric acid (10 m*l*), water (20 m*l*), and benzene (30 m*l*) were added, and the two layers were separated. The aqueous solution was neutralized with a sodium bicarbonate solution and was made alkaline by sodium hydroxide. The precipitates were extracted with benzene, washed with water, and dried over anhydrous sodium sulfate. HCl gas was passed through the solution, and the precipitated crystals were collected. The crystals (0.75 g, 24%) showed an IR spectrum identical with that of *N*-methylbenzylammonium chloride prepared from **2c** and hydrogen chloride. The benzene filtrate was washed with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. *n*-Hexane (30 m*l*) was added to the residue, and the precipitated crystals were collected. **5** (2.2 g, 40%) was thus obtained. The *n*-hexane solution was concentrated under reduced pressure, the residue was triturated with isopropyl alcohol, and the precipitated crystals were collected by filtration. By repeating these procedures twice, 2.2 g (42%) of triphenylphosphine (**6**) were obtained.