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Reactions of Aldonitrones with Phenylphosphonothioic Dichloride and Related Compounds. Formation of 2-Arylbenzothiazoles from α,*N*-Diarylnitrones

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Reactions of α-aryl-*N*-methylnitrones with phenylphosphonothioic dichloride (**1**), diphenylphosphinothioic chloride (**6**), or thiophosphoryl trichloride (**7**) gave *N*-methylbenzamide and *N*-methylthiobenzamide derivatives, and the latter became major in the presence of tertiary amine. α,*N*-Diarylnitrones (**4**) reacted with **1** to give 2-arylbenzothiazoles (**5**) at room temperature in moderate yields. Reaction of **4** with **6** (at room temperature) or **7** (in refluxing THF) gave **5** in a low yield, whereas a similar reaction of **4** with **7** at 0 °C afforded *N*-benzylidene-2-chloroaniline in a high yield. A mechanism for the formation of **5** has been discussed briefly.

During the course of investigations on phosphinothioylidenes (R–$\ddot{\text{P}}$=S),[1] we tried reaction of *N*-methyl-α-phenylnitrone with phenylphosphonothioic dichloride (**1**) in the presence of magnesium in an attempt to prepare phosphorus-containing heterocycles such as 1,3,5,2-oxathiazaphospholidine, but the products were *N*-methylbenzamide (**2**) and *N*-methylthiobenzamide (**3**).

$$\underset{\mathbf{1}}{\text{PhP(S)Cl}_2} + \text{PhCH=N(O)Me} \longrightarrow$$

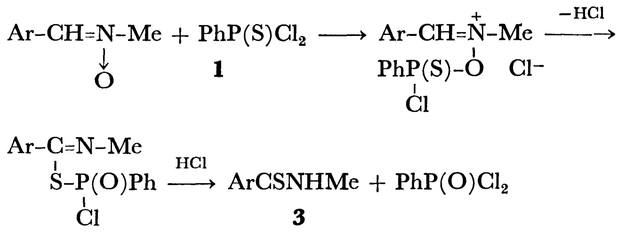
$$\underset{\mathbf{2}}{\text{PhCONHMe}} + \underset{\mathbf{3}}{\text{PhCSNHMe}}$$

Even without magnesium, however, a similar result was obtained. Therefore, reactions of nitrones with **1** and related compounds were investigated and it was found that α,*N*-diarylnitrones gave 6-substituted 2-arylbenzothiazoles.[2] This paper describes these results.

Reactions of N-*Methylaldonitrones.* Reaction of *N*-methyl-α-phenylnitrone with **1** gave **2** (43%) and **3** (41%), together with the nitrone hydrochloride (17%). A similar reaction with diphenylphosphinothioic chloride gave also **2** (61%) and **3** (6%), and that with thiophosphoryl trichloride gave only **3** (60%). However, *N*-methyl-α-phenylnitrone did not react with triphenylphosphine sulfide even at 140 °C.

In order to remove hydrogen chloride evolved during the reaction, a base such as triethylamine and pyridine was added. As shown in Table 1, in the presence of base, formation of **3** was remarkably suppressed. Similarly, reaction of α-(p-methoxyphenyl)-*N*-methylnitrone with **1** gave the corresponding amide (8%) and thioamide (28%), along with the nitrone hydrochloride (17%).

It has been reported that the nitrones rearrange to give the corresponding amide by acid chlorides and anhydrides such as phosphoryl trichloride, phosphorus trichloride, thionyl chloride, benzoyl chloride, benzenesulfonyl chloride, and acetic anhydride.[3] Analogously to these rearrangements,[3c,3f] the formation of thioamide (**3**) is explained as follows:



$$\underset{\underset{\displaystyle\text{O}}{\downarrow}}{\text{Ar-CH=N-Me}} + \underset{\mathbf{1}}{\text{PhP(S)Cl}_2} \longrightarrow \begin{array}{l}\text{Ar-CH=}\overset{+}{\text{N}}\text{-Me}\\ \text{PhP(S)-}\overset{|}{\text{O}}\ \ \text{Cl}^-\\ \quad\ \ \overset{|}{\text{Cl}}\end{array} \xrightarrow{-\text{HCl}}$$

$$\begin{array}{l}\text{Ar-C=N-Me}\\ \ \ \overset{|}{\text{S}}\text{-P(O)Ph}\\ \qquad\ \overset{|}{\text{Cl}}\end{array} \xrightarrow{\text{HCl}} \underset{\mathbf{3}}{\text{ArCSNHMe}} + \text{PhP(O)Cl}_2$$

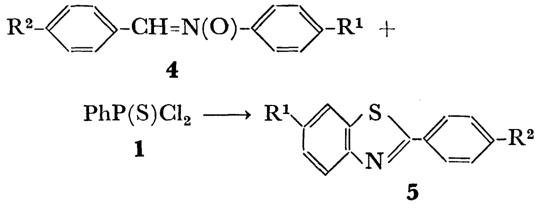
Table 1. Effect of base on formation of **2** and **3**

Base	**2**(%)	**3**(%)
None	43	41[a)]
Et_3N	9	35[a)]
Et_3N	0	60[b)]
C_5H_5N	20	41[b)]

a) A solution of **1** was added dropwise. b) A solution of nitrone was added dropwise.

Phenylphosphonic dichloride produced during the reaction can similarly react with the nitrones to give amide (**2**). Therefore, in the presence of a base, hydrogen chloride eliminated during the reaction is trapped by the base, and decomposition of the second intermediate by hydrogen chloride is prevented before work-up. Thus the formation of amide (**2**) is strongly retarded.

Reactions of α,N-*Diarylnitrones.* α,*N*-Diarylnitrones (**4**) reacted with an equimolar amount of **1** in tetrahydrofuran (THF) at room temperature to give 6-substituted 2-arylbenzothiazoles (**5**) unexpectedly, along with the nitrone hydrochloride. The results are summarized in Table 2.



a: $R^1=R^2=H$; **b**: $R^1=H$, $R^2=OMe$; **c**: $R^1=H$, $R^2=Cl$; **d**: $R^1=Me$, $R^2=H$; **e**: $R^1=Me$, $R^2=OMe$; **f**: $R^1=Me$, $R^2=Cl$; **g**: $R^1=H$, $R^2=Me$; **h**: $R^1=H$, $R^2=NMe_2$

The nitrones **4g** and **4h** did not give **5g** and **5h**, respectively. The reason is obscure.

In order to suppress the formation of nitrone hydrochloride, a scavenger of hydrogen chloride such as pyridine and methyloxirane was added. Reaction of **4a** in the presence of pyridine gave thiobenzanilide

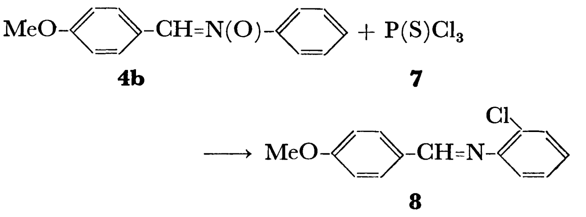
Table 2. Yield of 2-arylbenzothiazole (5) from 4

	4		
	R^1	R^2	5(%)
4a	H	H	32
4b	H	OMe	54
4c	H	Cl	39
4d	Me	H	33
4e	Me	OMe	34
4f	Me	Cl	39

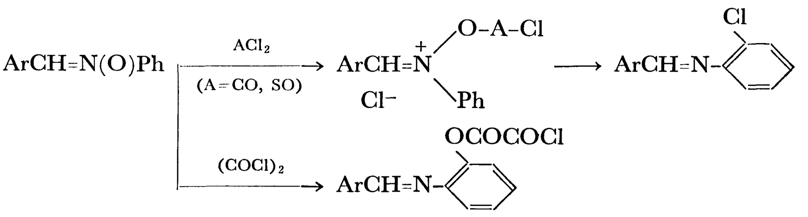
(36%) instead of **5a**, but that of **4b** in the presence of methyloxirane gave **5b** (57%), indicating no improvement of the yields.

Next, diphenylphosphinothioic chloride (**6**) analogous to **1** was used in order to examine the effect on the yield of **5**. Reaction of **4b** with **6** in the absence or the presence of methyloxirane gave N-(4-methoxybenzylidene)-2-chloroaniline (**8**) instead of **5b** in 4 or 18% yield, respectively.

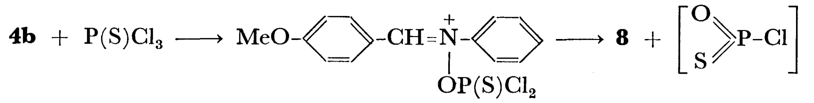
Furthermore, reaction of **4b** with thiophosphoryl trichloride (**7**) also gave **5b** in refluxing THF, but the yield was low (22%). On the other hand, reaction of **4b** with **7** at 0 °C gave **8** in 78% yield, which gave o-chloroaniline after hydrolysis. No p-chloro derivative was detected.



It has been reported that α-aryl-N-phenylnitrones gave N-benzylidene-2-chloroanilines in the reactions with thionyl or carbonyl chloride and gave N-benzylidene-2-(chlorooxalyloxy)anilines in the reactions with oxalyl chloride.[4]

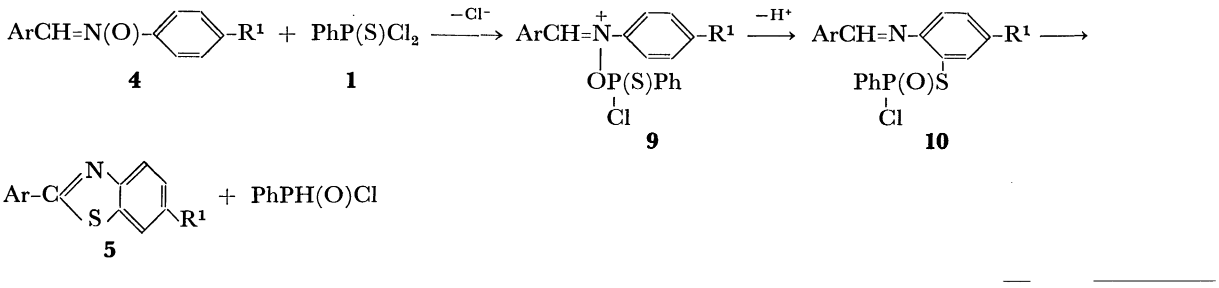


Therefore, the formation of **8** is analogously explained as follows:



Analogously to reactions of N-methylaldonitrones with **1**, it is possible that thiobenzanilide is first formed by reaction of **4** with **1** and then thiobenzanilide may cyclize to **5**. However, thiobenzanilide did not give 2-phenylbenzothiazole with **1** under similar conditions.

Thus, a mechanism for formation of **5** is considered as follows, in connection with the formation of **8**.



An intermediate (**9**) formed by a nucleophilic attack of **4** towards **1** rearranges to second intermediate (**10**) through [3,3] sigmatropic rearrangement containing P=S bond, and then **10** is converted into benzothiazole (**5**).

This new reactions might be used as a preparation method of 2-arylbenzothiazoles under mild conditions.

Experimental

All the melting points are uncorrected. The IR spectra were taken with a Hitachi EPI-G2 spectrophotometer, and the NMR spectra were measured with a Hitachi R-24 or R-20B spectrometer using TMS as an internal standard.

Materials. The following compounds were prepared by reported methods; phenylphosphonothioic dichloride (**1**),[5] diphenylphosphinothioic chloride (**6**),[6] and N-methyl-α-phenyl-,[7] N-methyl-α-(4-methoxyphenyl)-,[8] α,N-diphenyl- (**4a**),[7] α-(4-methoxyphenyl)-N-phenyl- (**4b**),[7] α-(4-chlorophenyl)-N-phenyl- (**4c**),[9] α-phenyl-N-(p-tolyl)- (**4d**),[10] α-(4-methoxyphenyl)-N-(p-tolyl)- (**4e**),[10] α-(p-chlorophenyl)-N-(p-tolyl)- (**4f**),[11] N-phenyl-α-(p-tolyl)- (**4g**),[3e] and α-(p-dimethylaminophenyl)-N-phenyl-nitrones (**4h**).[12]

Reaction of N-*Methyl-α-phenylnitrone with* **1**. *Reaction in the Absence of Base:* To a THF solution (25 ml) of the nitrone (1.29 g, 9.6 mmol) was added **1** (2.0 g, 9.5 mmol) with stirring under nitrogen. After the mixture was slightly heated, an exothermic reaction took place and white precipitates were formed. After the reaction mixture was allowed to stand overnight, the precipitates (278 mg) were collected and washed with THF. The filtrate and the washings were evaporated to give a red residue. Since the precipitates contained halogen (by Beilstein test), a mixture of the precipitates and triethylamine in benzene was stirred overnight at room temperature to give the starting nitrone. Thus, the precipitates were identified with the nitrone hydrochloride (17% yield). The red residue was subjected to dry column chromatography (DCC; SiO_2, CH_2Cl_2) to give recovered **1** (48 mg, 2.3%), **3** (497 mg, 41%), mp 79.5—81 °C (from CCl_4) (lit,[13] mp 79 °C); IR (KBr): 1520, 1340, and 1240 cm^{-1}, and **2** (459 mg, 43%), mp 78—81 °C (from EtOH) (lit,[14] mp 78—80 °C); IR (KBr): 1630, 1540, 1400, and 1300 cm^{-1}. The yields of the amides are based on the nitrone consumed.

Reaction in the Presence of Base: Only typical procedure is described.

To a THF solution (5 ml) of **1** (928 mg, 4.42 mmol) and triethylamine (1.5 ml) was added a THF solution (15 ml) of the nitrone (506 mg, 3.75 mmol) dropwise and the mixture was stirred at room temperature for 1 h. After addition of water, the mixture was extracted with ether, the ethereal extract was dried ($MgSO_4$), and evaporated. The residue was subjected to DCC (SiO_2, CH_2Cl_2) to give **3** (317 mg, 60%) (by IR). The other results were shown in Table 1.

Reaction of N-*Methyl-α-phenylnitrone with Other Phosphorus Chlorides.* Reaction with diphenylphosphinothioyl chloride is described as a typical procedure.

A THF solution (25 ml) of the nitrone (1.30 g, 9.6 mmol) and the phosphinothioyl chloride (2.47 g, 9.8 mmol) was stirred at room temperature overnight. After usual workup, the recovered chloride (1.70 g, 69%), and **3** (90 mg, 6%), and **2** (786 mg, 61%) were isolated by DCC (SiO_2, CH_2Cl_2).

*Reaction of α-(*p*-Methoxyphenyl)-*N*-methylnitrone with **1**.* A THF solution (25 ml) of the nitrone (1.41 g, 8.52 mmol) and **1** (1.82 g, 8.64 mmol) was stirred at room temperature overnight. After precipitates (296 mg, 17%) (the nitrone hydrochloride) were removed by filtration, the residue from the filtrate was subjected to DCC (SiO_2, CH_2Cl_2) to give *N*-methyl-*p*-methoxythiobenzamide (365 mg, 28%), mp 118—119 °C (from C_6H_6–hexane (1:1)) (lit,[15] 110—111 °C) and *N*-methyl-*p*-methoxybenzamide (89 mg, 8%), mp 122.5—124 °C (from C_6H_6) (lit,[16] 119.5—120.5 °C).

*Reactions of α,*N*-Diarylnitrones with **1**.* Reaction of α-(*p*-methoxyphenyl)-*N*-phenylnitrone (**4b**) is described as a typical procedure.

A mixture of **4b** (2.12 g, 9.33 mmol) and **1** (1.96 g, 9.27 mmol) in THF (25 ml) was stirred at room temperature overnight under nitrogen and precipitates thus obtained were filtered off. The precipitates were the nitrone hydrochloride (340 mg, 14%). The residue (3.27 g) from the filtrate was subjected to DCC (SiO_2, $CHCl_3$) to give **5b** (1.04 g, 54%), mp 123—125 °C (from EtOH) (lit,[17] 121.5—122 °C).

Reactions of other nitrones were carried out similarly. **4a** gave the nitrone hydrochloride (4%) and **5a** (32%), mp 108—113 °C (from EtOH) (lit,[18] 112—114 °C) by DCC (SiO_2, C_6H_6). **4c** gave **5c** (39%), mp 119—120 °C (from EtOH) (lit,[17] 120—121 °C) by DCC (SiO_2, CH_2Cl_2–CCl_4 (1:1)). **4d** gave **5d** (33%), mp 125.5—127 °C (from EtOH) (lit,[19] 125—125.5 °C) by DCC (SiO_2, CH_2Cl_2–CCl_4 (1:2)). **4e** gave **5e** (34%), mp 176—177 °C (from EtOH) (lit,[19] 174 °C) by DCC (SiO_2, CH_2Cl_2). **4f** gave **5f** (39%), mp 160—161 °C (from EtOH) (lit,[20] 160 °C) by DCC (SiO_2, CH_2Cl_2–CCl_4 (1:1)).

*Reaction of **4a** with **1** in the Presence of Pyridine.* To a mixture of **1** (1.14 g, 5.43 mmol) and pyridine (1 ml) in THF (5 ml) was added a solution of **4a** (990 mg, 5.03 mmol) in THF (15 ml) and then the mixture was stirred at room temperature overnight. After addition of water, the reaction mixture was extracted with ether, the ethereal extract was dried with $MgSO_4$, and evaporated. The residue was subjected to DCC (SiO_2, CH_2Cl_2–CCl_4 (1:1)) to give thiobenzanilide (387 mg, 36%), mp 100—101 °C (lit,[13] 97 °C).

*Reaction of **4b** with at 0 °C.* A mixture of **4b** (351 mg, 1.5 mmol) and **7** (275 mg, 1.63 mmol) in THF (10 ml) was stirred at 0 °C under nitrogen overnight. After addition of hexane (50 ml), the precipitates thus produced were collected by filtration and washed twice with hexane. The precipitates were suspended in benzene (10 ml) and stirred in the presence of triethylamine (0.3 ml). After precipitates were filtered off, the filtrate was evaporated to give **8** (282 mg, 78%); NMR ($CDCl_3$): δ 3.9 (s, 3H), 6.95—7.6 (m, 6H), 7.86 (d, $J=10$, 2H), and 8.3 (s, 1H). The NMR spectrum was the same as that of an authentic sample prepared from *p*-methoxybenzaldehyde and *o*-chloroaniline.

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