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REACTIONS OF NITRONES WITH SOME THIOPHOSPHORYL COMPOUNDS. FORMATIONS OF THIAZOLES AND OXAZOLES

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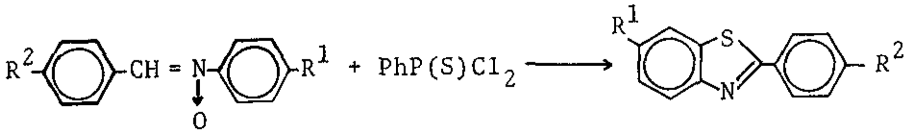
α,N-Diarylnitrones reacted with phenylphosphonothioic dichloride to give 2-arylbenzothiazoles in fairly good yield, while the reactions of nitrones with O-methyl diphenylphosphinothioate gave benzoxazoles. Reactions of nitrones with some other thiophosphoryl compounds are also described.

Nitrones have been widely used as 1,3-dipolar reagents to form heterocyclic compounds.[1] In an attempt to prepare new phosphorus-containing heterocycles, we found that nitrones reacted with some thiophosphoryl compounds to give benzothiazoles and benzoxazoles. We wish to report the preliminary results.

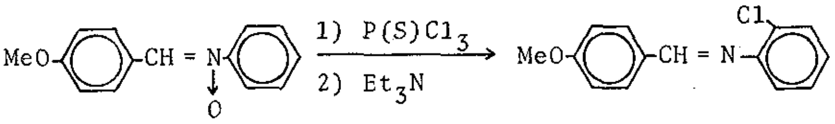
α,N-Diarylnitrones were allowed to react with phenylphosphonothioic dichloride in THF at room temperature to give 6-substituted 2-arylbenzothiazoles.



(1)

The typical procedure is as follows. A mixture of α-p-methoxyphenyl-N-phenylnitrone (2.12 g, 9.34 mmol) and phenylphosphonothioic dichloride (1.96 g, 9.29 mmol) in THF (25 ml) was stirred at room temperature overnight. The nitrone hydrochloride precipitated (340 mg, 1.29 mmol, 14 %) was filtered off and the filtrate was concentrated. The residue was chromatographed on silica gel to give 2-p-methoxyphenylbenzothiazole ($R^1 = H$, $R^2 = MeO$)(1.04 g, 4.32 mmol, 54 %), mp 123-125°C (from ethanol) (lit.,[2] 121.5-122°C) Other results were as follows: $R^1 = R^2 = H$, 32 %; $R^1 = H$, $R^2 = Cl$, 39 %; $R^1 = Me$, $R^2 = H$, 33 %; $R^1 = R^2 = Me$, 34 %; $R^1 = Me$, $R^2 = Cl$, 39 %. The structure of the nitrone hydrochloride was confirmed by recovery of the starting nitrone after treatment with triethylamine.

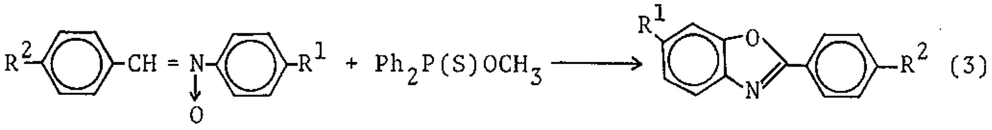
A similar reaction of the nitrone with thiophosphoryl trichloride at 0°C gave 4'-methoxybenzylidene-2-chloroaniline in 78 % yield after treatment with triethylamine.



(2)

No p-chloro derivative was detected. The method appears generally useful for the selective synthesis of chlorinated imines and anilines (after hydrolysis). Similar results have been reported in the reactions of N-arylnitrones with thionyl chlroide and phosgene.[3]

Unexpectedly the reactions of α,N-diarylnitrones with O-methyl diphenylphosphinothioate at 150°C gave 2-arylbenzoxazoles.



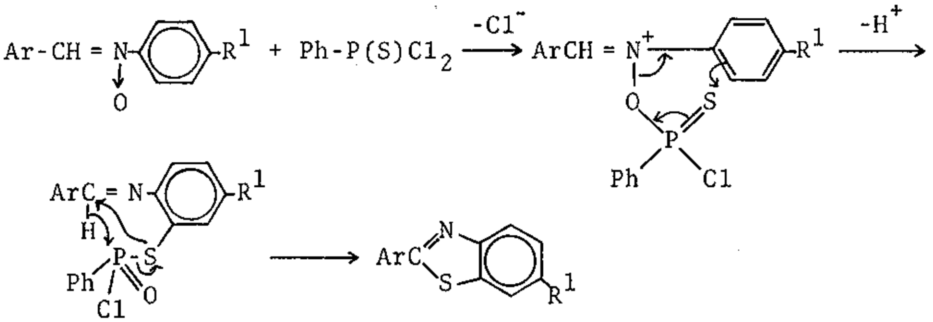
(3)

The typical procedure is as follows. A mixture of α-p-methoxyphenyl-N-phenylnitrone (252 mg, 1.11 mmol) and O-methyl diphenylphosphinothioate (288 mg, 1.16 mmol) was allowed to react in o-dichlorobenzene (15 ml) at 150°C for 2 days. Usual work-up gave 2-p-methoxyphenylbenzoxazole (152 mg, 0.68 mmol, 61 %), mp 100 - 101°C (lit.,[4] 101°C). Other results were as follows: $R^1 = H$, $R^2 = Me$, 40 %; $R^1 = H$, $R^2 = Cl$, 50 %; $R^1 = Me$, $R^2 = MeO$, 56 %. O-Methyl diphenylphosphinothioate was recovered in 53 % yield in the case of $R^1 = H$, $R^2 = Me$.

Attempts to prepare 2-phenylbenzoxazole by this method were unsuccessful. These reactions without the phosphinothioate gave only a trace amount of benzoxazoles.

α-Aryl-N-methylnitrones reacted with phenylphosphonothioic dichloride or diphenylphosphinothioic chloride to give N-methylbenzamides (8 - 61 %) and N-methylthiobenzamides (6 - 41 %). N-Methyl-α-phenylnitrone reacted with thiophosphoryl trichloride to give N-methylthiobenzamide in 60 % yield. The reaction with triphenylphosphine sulfide did not proceed under similar conditions. It has been reported that nitrones gave amide by the reactions with $POCl_3$, PCl_3, or $SOCl_2$.[5]

Since thiobenzamide did not give benzothiazole with phenylphosphonothioic dichloride under similar conditions, the formation of benzothiazoles is considered as follows.



However, the formation mechanism of benzoxazoles is obscure at present. Further studies are in process.

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