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THE REACTION OF O-ALKYL S,S-DIARYL PHOSPHORODITHIOATES WITH ALKYLOXYSTANNANES

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The reaction of O-alkyl S,S-diaryl phosphorodithioates with alkyloxytrialkylstannanes afforded the corresponding O,O-dialkyl S-aryl phosphorothioates in good yields.

Recently, we have reported that the reaction of 2-alkyloxybenzoxazoles with diphenyl hydrogen phosphate affords the corresponding alkyl diphenyl phosphates in good yields.[1)] These phosphates can be easily derived to mono-alkyl esters by catalytic removal of two phenoxy groups.[2)] Our attention has been now focused on developing an efficient method for the synthesis of phosphoric diesters via "Phosphotriester approach"[3)] employing arylthio groups as protecting groups. These groups were recently shown to be effective for the protection of phosphates in the oligonucleotide synthesis.[4)]

In this communication, we describe preliminarily a method for the preparation of O,O-dialkyl S-aryl phosphorothioate from O-alkyl S,S-diaryl phosphorodithioate by the action of alkyloxytrialkylstannane.[5)]

The following is a typical example for the present procedure: A mixture of S,S-di(p-chlorophenyl) O-ethyl phosphorodithioate (0.5 mmol) and triethyltetrahydrofurfuryloxystannane (0.625 mmol) in N,N-dimethylformamide (1 ml) was stirred at room temperature for 17 h under an argon atmosphere. After the addition of ether to the reaction mixture the solution was washed three times with water and dried over anhydrous sodium sulfate and then evaporated in vacuo. The residue was chromatographed on a column of silica gel with chloroform eluant to give S-p-chlorophenyl O-ethyl O-tetrahydrofurfuryl phosphorothioate (80%).

In a similar manner, various O,O-dialkyl S-aryl phosphorothioates were obtained in good yields.

Arylthio groups in the above reactions play an important role as so-called activatable protecting groups[8)] which involve simultaneous occurrences of deprotection and phosphorylation of alcohol. The feature enables the one-step synthesis of O,O-dialkyl S-aryl phosphorothioate from O-alkyl phosphorodithioate, while the conventional method requires deprotection and subsequent condensation steps. Consequently, the present reaction is applied to the preparation of mixed diesters of phosphoric acid, since phosphorothioic O,O,S-esters can be converted to phosphoric diesters by the known methods.[4)]

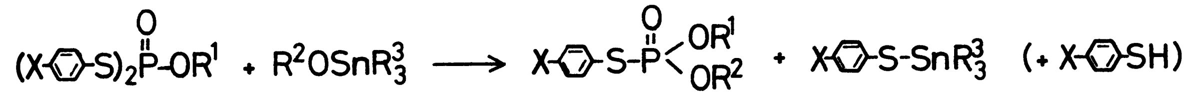
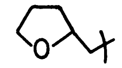
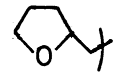
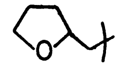
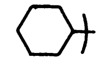
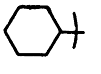
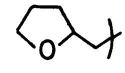


Table. The Synthesis of O,O-dialkyl S-aryl Phosphorothioates

R^1	R^2	X	R^3	Solv.$^{a)}$	Reaction conditions	Yield(%)
Et	Me	Cl	Bu	B	r.t., 4h	84
$Ph(CH_2)_2$	Me	Cl	Et	B	r.t., 4h	88
$Ph(CH_2)_2$	Me	Me	Bu	B	r.t., 5h	75
$Ph(CH_2)_2$	$CH_3(CH_2)_7$	Cl	Et	D	r.t., 21h	69
$Ph(CH_2)_2$	$CH_3(CH_2)_7$	Me	Et	D	r.t., 24h	72
$Ph(CH_2)_2$		Cl	Et	D	r.t., 15h	67
$Ph(CH_2)_2$		Me	Et	D	r.t., 40h	67
Et		Cl	Et	D	r.t., 17h	80
Et	$CH_3(CH_2)_7$	Cl	Et	D	r.t., 24h	80
Et		Cl	Et	D	65°C, 20h	63
		Cl	Et	D	60°C, 17h	74

a) B=benzene, D=N,N-dimethylformamide.

References and Notes

1) Y. Watanabe and T. Mukaiyama, Chem. Lett., 1978, 349.

2) For example see: T. Posternak, J. Am. Chem. Soc., 72, 4824 (1950).

3) For recent reviews see: C. B. Reese, Tetrahedron, 34, 3143 (1978); J. H. van Boom, Heterocycles, 7, 1197 (1977).

4) M. Sekine and T. Hata, Tetrahedron Lett., 1975, 1711; and also see: Y. Ishido and T. Hata in "Kagaku Sosetsu No. 19", Ed. by the Chemical Society of Japan, Japan Scientific Societies Press, Tokyo 113 (1978), P. 207.

5) Alkyloxytrialkylstannanes were prepared from trialkylmethoxystannanes and alcohols essentially as described by Gaur et al. (ref. 6) except for the use of an apparatus with a trap of the Dean and Stark type (ref. 7) containing calcium chloride for the removal of methanol.

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