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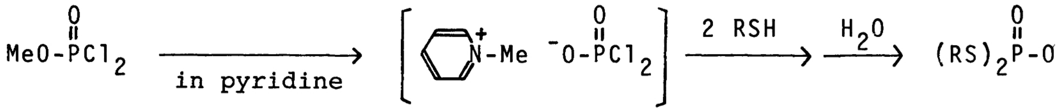
A CONVENIENT METHOD FOR THE PREPARATION OF S,S-DIARYL PHOSPHORODITHIOATES

Tsujiaki HATA, Kazuo YAMAGUCHI, Shinkichi HONDA, and Iwao NAKAGAWA
Department of Life Chemistry, Tokyo Institute of Technology
Nagatsuta, Midoriku, Yokohama 227

N-Methylpyridinium dichlorophosphate formed from the reaction of methyl phosphorodichloridate with pyridine was treated with aromatic thiols in the presence of triethylamine to give the corresponding S,S-diaryl phosphorodithioates in good yields.

Protected phosphoric acids, especially diester derivatives, are of importance as a synthetic component of the terminal phosphate in oligonucleotide synthesis via phosphotriester approach.[1] One of the diesters, S,S-diaryl phosphorodithioate has been promised as a useful synthetic intermediate. To date there are no methods available in pure material for the preparation of S,S-diaryl phosphorodithioates. Recently, we have established a method for the preparation of S,S-diaryl phosphorodithioates by the reaction of bis(trimethylsilyl) hypophosphite[2] with diaryl disulfides.[3] However, a novel preparative method for S,S-diarylphosphorodithioates has been desired by the reactions employing easily available starting materials. N-Methylpyridinium dichlorophosphate reported by Smrt[4] and Rubinstein[5] seemed to be applicable to the synthesis of S,S-diaryl phosphorodithioates since the dichlorophosphate has two active chlorine atoms.

In this communication, we wish to report a convenient and practical method for the preparation of S,S-diarylphosphorodithioates by the reaction of N-methylpyridinium dichlorophosphate with aryl thiols.



A typical procedure is described as follows: Methyl phosphorodichloridate (1.5 ml, 15 mmol) was added dropwise to dry pyridine (22.5 ml) at -20° and the mixture was kept for 5 min until N-methylpyridinium dichlorophosphate precipitated, and then benzenethiol (3.3 g, 30 mmol) and triethylamine (4.2 ml, 30 mmol) were added. It was further stirred at -20° for 3 h and the mixture was poured into ice-water (150 ml). The aqueous solution was extracted with two portions of chloroform (2 x 150 ml) and the chloroform layer was dried over sodium sulfate. After removal of sodium sulfate, the chloroform was evaporated to dryness. The oily residue was further dissolved in chloroform (30 ml) and cyclohexylamine (6.5 ml, 15 mmol) was added. After evaporation of chloroform, ether (200 ml) was added. Precipitates appeared and were collected by filtration. It was washed with ether. Monocyclohexylammonium salt of S,S-diphenyl phosphorodithioate (mp. 178-179°, 5.7 g) was obtained in 92% yield.

Alkanethiols were also reacted with N-methyl dichlorophosphate. But the yields are lower than those in the cases of substituted benzenethiols even when the reaction was carried out at 110° for 4 h.

The results are summarized in Table 1.

It is concluded that the yield depends on pKa value of the thiol.

Table 1. Preparation of S,S-Diaryl phosphorodithioates

R	pKa value[6] of RSH	temp (°C)	time (h)	yield (%)
p-ClC_6H_4	6.96	-20	3	92
C_6H_5	7.76	-20	3	92
p-$CH_3OC_6H_4$	7.99	-20	3	86
p-$CH_3C_6H_4$	8.03	-20	4	85
$C_6H_5CH_2$	9.43	110	4	30
C_2H_5	10.6	110	4	37

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