DEPROTECTION OF BENZYL AND t-BUTYL PHOSPHATE, PHOSPHITE, AND SULFITE ESTERS BY SILICA CHLORIDE

*Mohanazadeh, Farajollah**
Ranjbar, Yousef
Department of Chemistry, Faculty of Science, Mazandaran University,
P.O.Box 311, Babolsar, Iran

(Received: Feb. 4th 1996 , Accepted: Apr. 8th, 1996)

ABSTRACT: *Deprotection of phosphate, phosphite, and sulfite esters by silica chloride is described. Silica chloride is a mild, selective, and effective reagent for cleavage of benzyl and t- butyl esters of the above compounds.*

KEY WORDS: *Silica chloride, Deprotection, Phosphate ester, Phosphite ester, Sulfite ester.*

INTRODUCTION

Phosphate and phosphite functional group are important part of biological molecules such as nucleosides, proteins, and phospholipids [1,2]. A common requirement in the synthesis of these molecules is that oxyacids of phosphorus must be masked and transformed into derivatives lacl ing active hydrogen. These reactive groups may be protected in the form of alkyl esters.

There are many methods for deprotection of various phosphates and phosphites such as, hydrogenolysis [3], reduction- [4], treatment with base [5], and acid [6]. The use of trimethylsilyl iodide as a non-hydrolytic reagent is one of the best procedures for removal of alkyl groups from phosphonates [7]. Trimethylsilyl chloride [8] was also used instead of trimethylsilyl iodide. The reaction of trimethylchlorosilane with alkyl esters of phosphonic acids, albeit mild, takes several dayes and the yields are not always satisfactory.

We have recently reported [9] the use of silica chloride, as analogue of trimethylsilyl chloride, for the efficient conversion of sulfoxides into sulfides. This reactive inorganic polymeric agent has been used and reported as substrate in *Grignard* reaction [10] and graft polymerization of methyl methacrylate [11]. In this paper we wish to report a new application

* *To whom correspondence should be addressed.*
1021-9981/96/1/35 3/ $ / 2.30

for this reagent dealing with dealkylation of alkyl phosphates and phosphites.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a *Varian* EM 360A NMR spectrometer using tetramethylsilane as the internal standard. Infrared spectra were taken on a *Perkin-Elmer* 267 spectrophotometer. Thin layer chromatography was performed on silica gel (Maccerey Nagel Co., Plygram Sil G/uv). Comparison of spectral data (IR, NMR) and thin layer chromatography with authentic samples confirmed structure and purity of the reported products.

Preparation of Silica Chloride

Into a flask equipped with a reflux condenser, silica gel (6 g) and thionyl chloride (50 mL) were charged. The reaction mixture was refluxed under stirring with a magnetic stirrer for 18 h, and the unreacted thionyl chloride was removed by distillation. The silica chloride was dried in vacuo at 90°C and the resulting greyish powder was stored in a desiccator under vacuum. The chlorosilyl groups on silica surface (0.9 mmol of Cl/g silica) was determind by suspension of reagent (1 g) in $NaHCO_3$ solution (0.005 M, 100 mL). The resulting chloride ion was titrated with silver nitrate solution (0.01 M, 90 mL) using potassium chromate solution as indicator.

General Procedure for Dealkylation of Phosphate, Phosphite, and Sulfite Esters

Silica chloride (6 g, 5.4 mmol of Cl/g silica) and the ester (0.9 mmol) were mixed together in 20 in CCl_4 (20 mL) at room temperature, under dried atmosphere, for 15-90 min (Table 1). The progress of reaction was monitored by TLC and GC. After completion of the reaction, the mixture was filtered. Removal of the solvent afforded the corresponding pure t- butyl or benzyl halide (high purity, GC and NMR tested). The filter cake was washed with aqueous methanol. The filtrate was evaporated to acquire the pure acid.

RESULTS AND DISCUSSION

When silica chloride [9] is added to a solution of alkyl phosphate or phosphite in chlorinated hydrocarbon solvents (CCl_4, CH_2Cl_2, $CHCl_3$) at room temperature, in the absence of moisture, a facile chlorination reaction occurs which is monitored by TLC and NMR spectroscopy. The corresponding alkyl or Benzyl chloride is isolated in a pure state by simple filtration and evaporation of the solvent. The filter cake was washed with aqueous methanol. The filtrate evaporated to provide phosphoric or phosphorus

Table 1: Dealkylation of phosphate, phosphite, and sulfite esters by silica chloride

Compound	Products	Time (min)	Yield[a] (%)
$(PhCH_2O)_2POH$	$PhCH_2Cl+H_3PO_3$	40	90
$(Ph_2CHO)_2POH$	$Ph_2CHCl+H_3PO_3$	15	85
$(PhCH_2O)_3PO$	$PhCH_2Cl+H_3PO_4$	45	80
$(PhCH_2O)_2POCH_2OH$	$PhCH_2Cl+HOCH_2PO_3H_2$	40	90
$(t\text{-}BuO)_3P$	$t\text{-}BuCl+H_3PO_3$	30	90
$(iso\text{-}PrO)_3P$	–	90	0
$(PhO_3)_3P$	–	90	0
$(PhCH_2O)_2SO$	$PhCH_2Cl+H_2SO_3$	40	90
$(Ph_2CHO)_2SO$	$Ph_2CHCl+H_2SO_3$	25	85

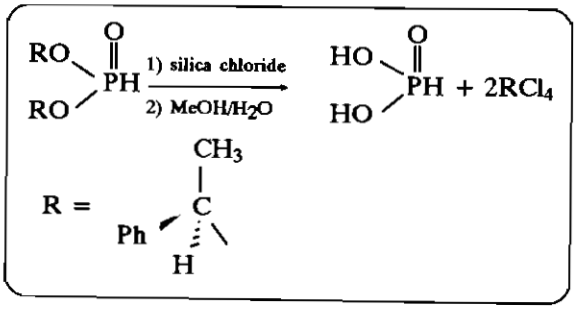
a: Isolated halides.

acid with high purity.

From the data (Table 1), it is obvious that, this reactive polymer is a useful reagent for mild cleavage of benzyl and t-butyl phosphates and phosphites. The present procedure is a mild and an effective method for this purpose by using an inexpensive reagent, and thus offering significant advantages.

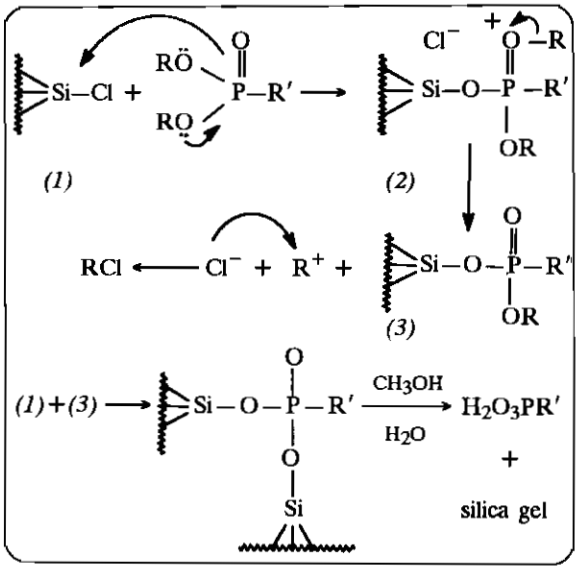
Deprotection of benzyl phosphate by dry HCl in CCl_4 was unsuccesful. This reaction was tried with silica gel in presence of dry HCl in CCl_4. The reaction proceeds very slowly which shows that HCl itself isnot a good reagent for this purpose.

The reaction proceeds predominantly with racemization of configuration, eg; S-bis-1-phenylethyl phosphite was treated with silica chloride, a racemic mixture of 1-phenylethyl chloride was obtained in 85% yield (Scheme 1).



(Scheme 1)

This offers the generation of carbocations in the mixture, for which the mechanism shown in Scheme 2 is suggested. Dibenzyl sulfite and bis (diphenyl methyl) sulfite are also cleaved by this reagent under similar conditions. Di-n-propyl and di-i- propyl sulfite are stable towards reaction with this reagent under similar conditions (Table 1).



(Scheme 2)

REFERENCES

[1] Huryn, D. M., Okabe, M., *Chem. Rev.*, **92**, 1745 (1992).

[2] Slotin, L. A., *Synthesis*, 737 (1977).

[3] Jones, G. H., Moffatt, J. G., *J. Am. Chem. Soc.*, **90**, 5337 (1968).

[4] Eckstein, F., Rizk, I., *Chem. Ber.*, **102**, 2362 (1969).

[5] Reese, C. B., Saffbill, R., *J. Chem. Soc. Chem. Commun.*, 767 (1968).

[6] Dfeiffer, F. R., Mier, J. D., *J. Med. Chem.*, **17**, 112 (1974).

[7] Zygmunt, J., Kafarski, P., Mastalerz, P., *Synthesis*, 609 (1978).

[8] Machida, Y., Nomoto, S., Satio, I., *Syn. Commun.*, **9**, 97 (1979).

[9] Mohanazadeh, F., Momeni, A. R., Ranjbar, Y., *Tetrahedron Lett.*, **35**, 6127 (1994).

[10] Saunders, D. H., Barford, R. A., Magidman, P., Olszewski, L. T., Rothbart, H. L., *Anal. Chem.*, **46**, 834 (1974).

[11] Tsubokawa, N., Ishida, H., *J. Poly. Sci. Part A: Poly Chem.*, **30**, 2241 (1992).