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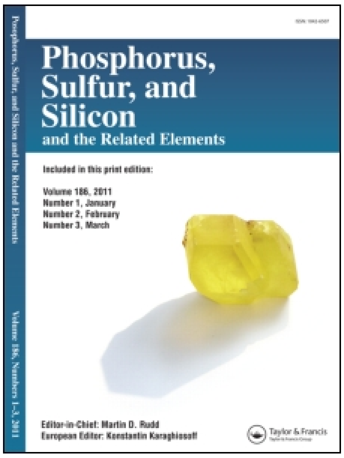

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Synthesis of Mixed Alkylphosphites and Alkylphosphates

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SYNTHESIS OF MIXED ALKYLPHOSPHITES AND ALKYLPHOSPHATES

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Some mixed phosphites having two different alkyl chain were obtained as forerunners for mixed phosphates Mixed dialkyl phosphates were obtained in good yields (40–80%) by phase transfer catalysis in liquid-liquid sistem, starting from different dialkyl phosphites and aliphatic alcohols. The reaction conditions were optimized in order to obtain good yields in phosphites and phosphates respectively. Compounds were analyzed by IR, P^{31}-NMR.

Keywords: Mixed phosphates; mixed phosphites; phase transfer catalysis

The reaction of phosphorus chlorine derivatives with alcohols is well known and is used for obtaining a wide range of phosphorus esters,[1] but the yields were low. For the synthesis of mixed phosphates Steinberg,[2] then Kenner and Williams[3] proposed the system dialkylphosphite/carbontetrachloride/triethylammine and alcohol. This system has a few major disadvantages: it needs an equivalent mol of amine; reaction products are impure and contain ammonium chlorohydrate; reaction times a very long (more than 12 h); only moderate yields.

Zwierzak[4] showed that alcohols can react with dialkyphosphites in a biphasic system, carbon trachloride-aqueous sodium hydroxide (Scheme 1). The studies were limited to a few aliphatic alcohols. We found that this method can be applied to series of aliphatic alcohols[5] and aliphatic phosphite. This article presents the obtained results in optimal conditions.

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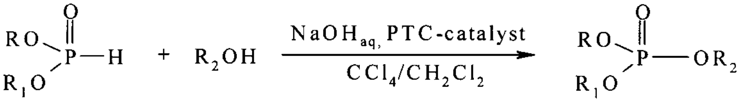
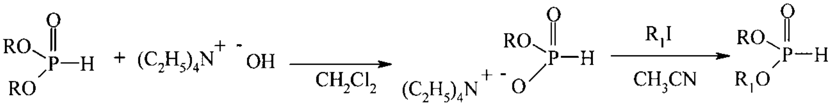


SCHEME 1

Also, a new method was found for the synthesis of mixed dialkyl phosphites[6] used in the synthesis of mixed phosphates having three different alkyl groups (Scheme 2).



2 3

SCHEME 2

RESULT AND DISCUSSION

In the phase transfer catalysis reactions are involved a lot of factors which influence the development of the process as: stirring speed, the catalyst, reaction time, mass transfer, and the shape of the flask.

Stirring speed was one of the studied factors because it has a major influence on the mass transfer processes and reaction speed. As is known[7] phase transfer catalysis reactions took place by putting in contact two immiscible phases when the reagent is transferred from one phase to another by a catalyst where it reacts with the substrate.

The speed of the reaction increases when the contact between the two phases is intimate. The studies were performed in a 250 ml flask and with a teflon stirrer having a semicircle shape and a diameter of 20 mm (Figure 1).

Even when the mixture is not stirred the reaction takes place but the yields are low. Increasing the speed increases the yield to a maximum then it decreases again. The best results were obtained at 700–800 rpm. Furthermore the influence of the reaction time on the yield was studied (Figure 2).

The yields are optimal when the reagents were kept in contact for about 3 h, then decrease due to saponification reactions in contact with aqueous sodium hydroxide; saponification could lead to phosphoric acid. This process depends on the pH, nature of the radical, temperature, concentration, and so on.

The influence of phase transfer catalyst was studied (Table I). The best results were obtained with tetrabutylammonium salts.

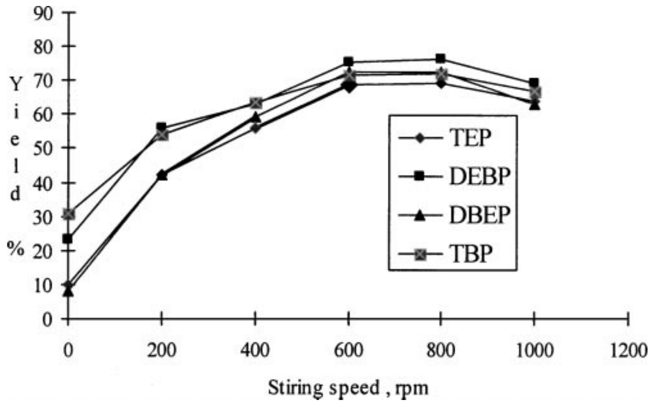
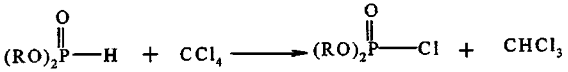


FIGURE 1 The influence of stirring speed on the yield of phosphates.

Preliminary studies alowed a few observations: a) In order to obtain good yields it needs 50% aqueous sodium hydroxide; b) it needs an excess of dialkylphosphite due to saponification reactions; c) the order of reagent addition is important; and d) the solvent is important.

Based on these observation it can be concluded that, in the phosphorylation reaction of alcohols by the phase transfer catalysis method, the phosphite is oxidized to dialkylchlorophosphate which reacts with alcohols by nucleophilic substitution, and mixed phosphates are obtained (Scheme 3).



$$(RO)_2\overset{\text{O}}{\overset{\|}{\text{P}}}\text{—H} + CCl_4 \longrightarrow (RO)_2\overset{\text{O}}{\overset{\|}{\text{P}}}\text{—Cl} + CHCl_3$$

SCHEME 3

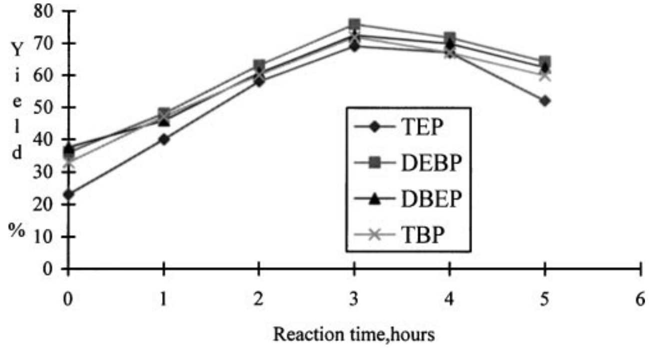


FIGURE 2 The influence of the reaction time on the yields of phosphates.

TABLE I The Influence of the Catalyst on the Yield

Synthesis	Catalyst	Yields (%)
0	1	2
TEP	TEAC	50,1
DEBP	TEAC	58,2
DBEP	TEAC	54,1
TBP	TEAC	56
TEP	TEAB	55,2
DEBP	TEAB	63,3
DBEP	TEAB	59,8
TBP	TEAB	60,2
TEP	TBAC	63,3
DEBP	TBAC	71,4
DBEP	TBAC	68,7
TBP	TBAC	69,8
TEP	TBAB	68,9
DEBP	TBAB	75
DBEP	TBAB	72,3
TBP	TBAB	71

TEAC(B) = tetraetylammonium chloride (bromide).
TBAC(B) = tetrabutylammonium chloride (bromide).

Side reactions, with formation of dihalocarbene, apear when 50% aqueous sodium hydroxide is used (Scheme 4). Dihalocarbene can reacts also with alkohols.

$$CHCl_3 + NaOH \rightleftharpoons Cl_3C^{-+}Na + OH_2 \rightleftharpoons NaCl + :CCl_2 + OH_2$$

SCHEME 4

In accordance with the general procedure, the reactions were performed with different alcohols and diethylphosphite, dipropylphosphite and dibutylphosphite by the phase transfer catalysis method in liquid-liquid system (Table II, Table III, and Table IV).

In all syntheses, the reaction temperature was kept at 15°C and the reaction time was 3 h. Decreasing the reaction temperature below 15°C did increase the reaction time and side reactions and the yields did decrease. Mixed phosphates obtained from C1–C4 were chromatographically pure. The obtained products were analyzed also by IR. In the IR spectra, the disappearance of the band at 2430–2440 cm^{-1}(P—H) was used for the reaction control.

Also mixed phosphites were obtained, by direct hydrolysis of dialkyl phosphites with 20% aqueous tetraethylammonium hydroxide followed

TABLE II Experimental Results in the Synthesis of Some Phosphates Starting from Diethylphosphite (Catalyst-Tetrabutylammonium Bromide 0.5 mmol %)

Synthesis	R_2OH	Yield (%)	Yield from lit (%)	b.p. Lit., °C/mm Hg	b.p. °C/mm Hg	^{31}P NMR (ppm)
0	1	5	6	7	8	9
DEMF	Methanol	72	—	100.2/20*	109/30	1.04
TEP	Ethanol	68.9	—	116/30*	123/40	1.00
DEPP	*n*-Propanol	70.5	67**	50/0.2**	116/35	0.97
DEBP	*n*-Butanol	75	71**	123/15**	138/25	1.10
DEPnP	*n*-Pentanol	69	—	—	150/25	1.25
DEHP	*n*-Hexanol	41	—	—	162/25	1.03
DEHPP	*n*-Heptanol	47	—	—	173/26	1.20
DEOP	*n*-Octanol	45	—	—	!79/25	1.13

* = [4]; ** = [8].

TABLE III Experimental Results in the Synthesis of Some Phosphates Starting from Dipropylphosphite (Catalyst-Tetrabutylammonium Bromide 0.5 mmol %)

Synthesis	R_2OH	Yield (%)	b.p. °C/mm Hg	^{31}P NMR (ppm)
DPMP	Methanol	63	113/15	0.72
DPEP	Ethanol	71	126/14	1.07
TPP	*n*-Propanol	70	130/15	0.76
DPBP	*n*-Butanol	73.5	138/14	1.00
DPPnP	*n*-Pentanol	73	147/12	0.97
DPHP	*n*-Hexanol	54.5	153/12	0.98
DPHpP	*n*-Heptanol	55	169/11	1.02
DPOP	*n*-Octanol	52	179/10	1.09

TABLE IV Experimental Results in the Synthesis of Some Phosphates Starting from Dibutylphosphite (Catalyst-Tetrabutylammonium Bromide 0.5 mmol %)

Synthesis	R_2OH	Yield (%)	Yield lit (%)	b.p. Literat. °C/mm Hg	b.p. °C/mm Hg	^{31}P NMR (ppm)
DBMP	Methanol	65	—	—	95/10	0.65
DBEP	Ethanol	72	71*	60–1/0,1*	103/15	1.00
DBPP	*n*-Propanol	68	—	—	121/20	1.09
TBP	*n*-Butanol	71.6	—	180-3/25**	190/30	0.97
DBPnP	*n*-Pentanol	78	—	—	186/15	1.03
DBHP	*n*-Hexanol	69	—	—	175/10	1.10
DBHpP	*n*-Heptanol	62	—	—	182/10	1.09
DBOP	*n*-Octanol	60	—	—	198/10	1.12

* = [4]; ** = [8].

TABLE V Preparation of Tetraethylammonium Hydrogenphosphites (2), Mixed Phosphites (3), and Phosphates

Product	R	R1	R2	31P NMR (ppm)	Yield (%)
2a	C_2H_5	—	—	—	75
2b	n-C_4H_9	—	—	—	80
3a	C_2H_5	CH_3	—	−4.3	61
3b	C2H5	n-C_4H_9	—	−6.6	73
3b	n-C_4H_9	C2H5	—	−6.6	72
EMPP	C_2H_5	CH_3	n-C_3H_7	0.89	67
BEMP	C_2H_5	n-C_4H_9	n-C_3H_7	1.0	76
BEMP	n-C_4H_9	C_2H_5	n-C_3H_7	1.0	75

by reaction with alkyl iodides in acetonitrile. They are the forerunners for mixed phosphates having three different alkyl chains (Table V).

The yields were good in all syntheses. Mixed phosphites were used for obtaining phosphates with three different alkyl radicals.

EXPERIMENTAL

General Procedure for the Synthesis of Mixed Phosphates

To a stirred solution of 50% aqueous sodium hydroxide (60 ml), alkyl alcohol (0.2 mmol), carbon tetrachloride (50 ml), methylene chloride (50 ml) and a phase transfer catalyst, was added dropwise a solution of a phosphite (0.25 moles) in carbon tetrachloride (60 ml). The temperature was kept at 15°C. Then the mixture was kept under stirring 3 h at 15°C. The mixture is diluted with methylene chloride (50 ml), filtered, separated, and the organic layer washed with 2% aqueous hydrogen chloride (25 ml), and water (2 × 25 ml), and dried with anhydrous sodium sulfate and the solvents distilled under reduced pressure.

General Procedure for the Synthesis of Mixed Phosphites

A 20% aqueous solution of tetrabutylammonium hydroxide (0.2 mmol) is added to stirred phosphite (0.2 mmol) at 5–10°C and the mixture is kept at this temperature for 2 h. The salt is extracted with methylene chloride, the solvent is distilled and the crude intermediate mixed with 50 ml acetonitrile and the appropriate alkyl iodide and heated for 6 h at 60°C. The solvent is distilled and the product is purified by distillation under reduced pressure.

CONCLUSIONS

Mixed phosphites were obtained with good yields. Mixed phosphates starting from diethyl-, dipropyl-, dibutyl phosphite and mixed phosphites, respectively, were synthesized using a liquid-liquid system. The best results were obtained when 50% $NaOH_{aq}$ was used, the reaction temperature was 15°C, and the reaction time 3 h and the molar ratio phosphite : alcohol = 1.25:1. P^{31}-NMR spectra, performed with a Bruker Avance DRX 400 spectrometer, showed chemical shift values of $\delta = 0.6$–1.25 ppm (ref. $H_3PO_4 85\%$). Mixed phosphates obtained from C_1—C_4 were chromatographically pure.

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