

TRANSESTERIFICATION OF TRIMETHYLPHOSPHATE CATALYZED BY SODIUM ALKOXIDES

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ABSTRACT

The transesterification process of trimethylphosphate with ethanol and isopropanol is examined. It is found that the reaction does not proceed in the absence of base even at temperatures up to 100°C, whereas in the presence of sodium alkoxide as a catalyst it takes place at room temperature leading to a mixture of mono-, bi-, tri-substituted esters as well as the minor by-products resulting from the nucleophilic attack of the alkoxide ion on the alkyl groups of the starting ester. The substitution extent is dependent on the relative concentration of the reactants, the temperature, the solvent, and the amount of the catalyst used.

Keywords: Ttansesterification; trimethylphosphate; sodium alkoxides; mixed trialkylphosphates; ethanol; isopropanol

INTRODUCTION

Since a direct synthesis of phosphate esters from alcohols and appropriate oxychlorides of phosphorus is unsatisfactory or impossible, transesterification of phosphate esters with appropriate alcohols seems to be an alternative way to produce the desired trialkylphosphates. Generally, such reactions are facilitated by increased electrophilic nature of substituents in the initial ester; an opposite effect is caused by similar groups in the alkyl group of the attacking alcohol. In general, it may be assumed that an ion does not displace a more basic group from a phosphoryl group at a measurable rate in a solvolytic medium, and consequently the number of anions which can displace alkoxy groups from esters is very limited.¹

These considerations suggest strongly that only the most basic anions, such as alkoxides, can remove the alkoxy groups from phosphorus esters at an appropriate rate by attack at the phosphorus atom. The reactions of a wide variety of nucleophiles with trimethylphosphate have previously been examined. Small nucleophiles such as hydroxide², alkoxides³⁻⁴, and enolates⁵, yield products arising from nucleophilic attack at phosphorus.

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Table 1. ^{31}P chemical shifts of the initial and the product trialkylphosphates

Compound	Formula	Abbreviation	$^a\delta$
Trimethylphosphate	(MeO) $_3$ PO	TMP	3.58
Dimethyl ethylphosphate	(MeO) $_2$ (EtO)PO	DMEP	2.45
Diethyl methylphosphate	(EtO) $_2$ (MeO)PO	DEMP	1.32
Triethylphosphate	(EtO) $_3$ PO	TEP	0.19
Dimethyl isopropylphosphate	(MeO) $_2$ (i-PrO)PO	DMIP	1.9
Diisopropyl methylphosphate	(i-PrO) $_2$ (MeO)PO	DIMP	0.4
Triisopropylphosphate	(i-PrO) $_3$ PO	TIP	-1.05

^achemical shifts measured relative to external 85% H $_3$ PO $_4$ (T=27°C)

The studies on the transesterification reaction between TMP and selected primary and secondary alcohols (ethanol and isopropanol) revealed that TMP reacted with isopropanol at a considerably lower rate than with ethanol as seen in Table 2 comparing the extent of conversion of TMP to substituted products.

The lower rate at which the reaction takes place in the case of isopropanol can only be explained by the steric effect of the isopropyl group. The increased steric effect, on the other hand, will bring about a lower rate of P-O bond formation and in this manner a lower rate of the transesterification process. As expected the reaction proceeded smoothly with the formation of mono-substituted products. Smaller yields of di-, and tri-substituted products were also obtained as well as the hydrolysis products changing in quantity based on the reaction conditions.

The molar TMP to alcohol ratio is considered as a key factor in controlling the products' composition. Less than one equivalent of alcohol led to production of the mono-substituted ester as the major product while increasing the alcohol to phosphate ratio resulted in faster rate of conversion and production of more substituted phosphates (Table 3).

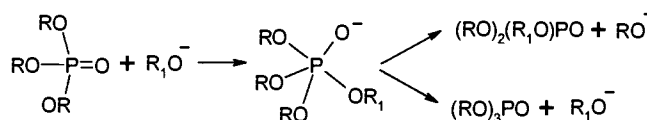
The results of the transesterification reaction of TMP with ethanol and isopropanol at different temperatures (Table 4) showed that in higher temperatures the risk of by-product formation notably increases.

To elucidate the effect of alkoxide concentration on the reaction, a series of experiments were performed (Table 5). It was found that, in general, the transesterification reaction of TMP was not started by heating at 100°C for extended periods of time in neutral alcohol solutions and in the absence of the alkoxides. It was noted that the amount of sodium alkoxide catalyst used to catalyze the reaction has an effect on the composition of the mixed ester and particularly the amount of TMP that remains in the final product. The rates of transesterification reactions were proportional to the concentrations of the catalyst, the rates being higher, the higher the concentration.

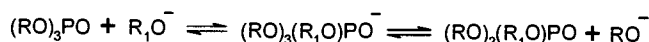
A considerable difference in reaction rate and in product distribution was observed when

polar aprotic solvents such as dioxane and THF were added to alcohol/phosphate ester mixtures. To make a direct comparison between the data obtained in presence and absence of dioxane, the data reflecting the effect of solvent are shown in Table 6. The difference may be attributed to the proton affinity of the solvent.

The reaction mechanism may be assumed to involve alternating addition of alkoxide ion to the phosphorus atom resulting in a pentacoordinate ionic intermediate formation followed by elimination of the alkoxide ion from the intermediate to form either the original or a different trialkylphosphate :



The primary step in the reaction is necessary but insufficient to achieve transesterification of the Phosphate. As shown above, the intermediate can break down in two ways. An equilibrium is established in the alcoholysis of any phosphate with any alcohol :



Transesterification will take place if the equilibrium is displaced to the right, i.e. if an alkoxy of the original phosphate, not the alkoxy of the alcohol taken for the transesterification, splits off from the intermediate. Thus the second step in the reaction, cleavage of the intermediate, plays the decisive part in the process of transesterification, and probably determines not only the direction but also the rate of the reaction.

Which alcohol will be eliminated from the intermediate depends directly on the electrophilic character of the alkoxy groups involved. It is obvious that the more electrophilic an alkoxy the more preferentially will it be eliminated. The slower reaction in case of secondary and tertiary alcohols may be attributed to the negative effect of the bulky groups in formation of the pentavalent intermediates.

Table 2. Relative reactivities of ethanol and isopropanol in transesterification reaction with TMP

Exp. No.	ROH	Ratio TMP/ROH	Na (mol%)	Solvent	t (min)	T (°C)	Product Yields (mol%)				
							TMP	mono-substituted	di-substituted	tri-substituted	by-products
1	EtOH	1:1	15	-	300	14	48.73	32.89	3.65	-	14.73
2	i-PrOH	"	"	-	"	"	89.21	2.59	-	-	8.20
3	EtOH	1:20	"	-	30	100	16.30	26.03	57.67	-	-
4	i-PrOH	"	"	-	"	"	45.39	32.86	17.84	-	3.90

جدول

Table 3. The effect of the reactants' molar ratio on the transesterification reaction

Exp. No.	ROH	Ratio TMP/ROH	Na (mol%)	Solvent	t (min)	T (°C)	Product Yields (mol%)				
							TMP	mono-substituted	di-substituted	tri-substituted	by-products
5	EtOH	1:0.5	15	-	300	100	73.58	22.52	1.25	-	2.65
6	"	1:0.7	"	-	"	"	67.89	26.61	1.97	-	3.52
7	"	1:2	"	-	"	"	15.08	32.70	11.44	0.6	40.15
8	i-PrOH	1:1	7	-	"	40	92.60	1.80	-	-	5.60
9	"	1:3	"	-	"	"	92.34	5.45	-	-	2.21

Table 4. The temperature dependence of the product distribution in transesterification reaction of TMP

Exp. No.	ROH	Ratio TMP/ROH	Na (mol%)	Solvent	T (min)	T (°C)	Product Yields (mol%)				
							TMP	mono-substituted	di-substituted	tri-substituted	by-products
10	EtOH	1:2	15	-	300	40	24.42	39.14	9.27	-	27.16
7	"	"	"	-	"	100	15.08	32.70	11.44	0.6	40.15
11	"	"	"	-	1440	40	24.12	39.29	10.05	0.47	26.05
12	"	"	"	-	"	100	10.22	28.79	12.55	0.8	47.63

Table 5. The effect of the alkoxide concentration on transesterification reaction of TMP

Exp. No.	ROH	Ratio TMP/ROH	Na (mol%)	Solvent	t (min)	T (°C)	Product Yields (mol%)				
							TMP	mono-substituted	di-substituted	tri-substituted	by-products
13	EtOH	1:2	5	-	1440	100	85.06	10.22	-	-	4.72
12	"	"	15	-	"	"	10.22	28.79	12.55	0.8	47.63
8	i-PrOH	1:1	5	-	300	40	92.60	1.80	-	-	5.60
14	"	"	14	-	"	"	86.20	6.29	-	-	7.50

Table 6. The solvent effect on transesterification reaction of TMP

Exp. No.	ROH	Ratio TMP/ROH	Na (mol%)	Solvent	t (min)	T (°C)	Product Yields (mol%)				
							TMP	mono- substituted	di- substituted	tri- substituted	by- products
15	EtOH	1:20	20	-	30	40	7.06	15.57	46.47	-	30.9
16	"	"	"	dioxane	"	"	4.05	17.39	58.75	-	19.70
17	i-PrOH	"	"	-	"	100	47.24	34.20	18.56	-	-
18	"	"	"	dioxane	"	"	16.14	36.78	44.58	2.5	-
19	"	"	"	-	180	"	29.24	47.94	22.82	-	-
20	"	"	"	dioxane	"	"	4.22	37.94	57.84	-	-
21	"	"	"	-	1440	"	-	17.63	82.37	-	-
22	"	"	"	dioxane	"	"	-	17.15	82.85	-	-

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EXPERIMENTAL

Analytical grade reagents were used throughout except where otherwise specified. Trimethylphosphate (Aldrich, >99%), dioxane (Aldrich, AR) and dimethyl sulfoxide (Aldrich, AR) were dried over 4A molecular sieves prior to use. Sodium alkoxides were freshly generated by desolving sodium metal in the corresponding alcohols. $^{31}\text{P}\{\text{H}\}$ NMR spectra were recorded using a Bruker 250 MHz fourier transform spectrometer. ^{31}P chemical shifts are reported relative to external 85% H_3PO_4 . Peak heights for each species observed were assumed to be proportional to concentration. The fraction of the substrate unreacted and the products was then calculated from their contribution to the total concentration of ^{31}P containing compounds in solution.

Transesterification of trimethylphosphate. General Procedure.

Predetermined amounts of an appropriate alcohol and trimethylphosphate were placed into a three neck round-bottom flask previously flushed with dry nitrogen, and equipped with an efficient stirrer, N_2 inlet, and a reflux condenser. The reaction temperature was controlled by a silicon oil bath within 0.5°C . 2ml samples of the reaction mixture were collected at the given time intervals,

quenched by diluted HCl solution, dissolved in dimethyl sulfoxide, and finally analyzed by ^{31}P MNR spectroscopy to determine the composition of the reaction mixture.

Transesterification of TMP with ethanol and isopropanol

The transesterification reactions of trimethylphosphate with ethanol and isopropanol were carried out by the general procedure mentioned above using different compositions of the reactants, in absence and presence of different concentrations of the alkoxides (sodium ethoxide and sodium isopropoxide), in absence and presence of dioxane as a selected dipolar aprotic solvent, and at different temperature ranging from 14 up to 100°C . All the experiments were carried out in 0.05 molar scales.

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