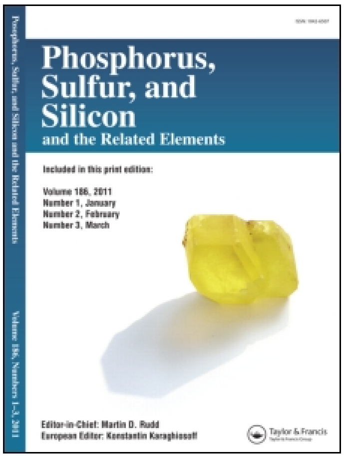

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Competition of Methanol and *Tert*-Butanol in Nucleophilic Substitution at Phosphorus Atom

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*2,3-Oxaphosphabicyclo[2.2.2]octene **1** reacts with alcohols simultaneously according to two competitive mechanisms: bimolecular addition-elimination and unimolecular elimination-addition with the intermediacy of metaphosphonate Ph-PO$_2$ (**2**). In 1,2-dichloroethane at 60°C, cyclic phosphinate **1** reacts with methanol in the bimolecular reaction five times faster than with* tert-*butanol. The reaction of metaphosphonate **2** with alcohols is unselective.*

Keywords Fragmentation; mechanism; metaphosphonate; nucleophilic substitution

INTRODUCTION

The nucleophilic substitution at tetracoordinated phosphorus atom can proceed in accordance with the elimination-addition (EA) mechanism via tricoordinate intermediate, via the addition-elimination (AE) mechanism with formation of pentacoordinated intermediate, or as a synchronous $S_N2(P)$ pathway. 2,3-Oxaphosphabicyclo[2.2.2]octenes were found to be good models in mechanistic studies as a source of metaphosphoric (RO-PO$_2$) or metaphosphonic (R-PO$_2$) acid anhydride.[1] Recently, we have found that aryl-2,3-oxaphosphabicyclo[2.2.2]octenes react with alcohols via both EA and AE mechanisms.[2,3]

In this article, we present the kinetic studies on reaction of *P*-phenyl-2,3-oxaphosphabicyclo[2.2.2]octene **1** with methanol or/and *tert*-butanol (Scheme 1) in order to compare the selectivity of these alcohols towards tri- and tetracoordinated phosphorus atoms.

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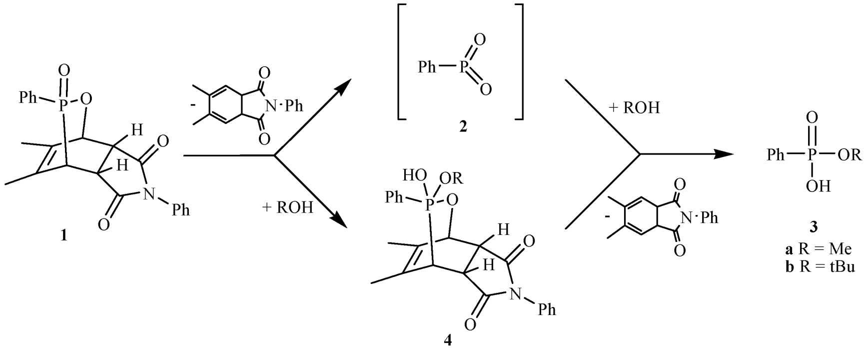

SCHEME 1

RESULTS AND DISCUSSION

Heating of **1** in toluene at 110°C or irradiation at 254 nm in dioxane led to complete decomposition in 15 and 120 min, respectively. In both cases, the Ph-PO_2 polymer was formed. When alcohol was present in the reaction medium, the corresponding phenylphosphonate was formed.[4]

The reaction of bicyclooctene **1** with MeOH or *tert*-BuOH was carried out in 1,2-dichloroethane (1,2-DCE) at 60°C and monitored by means of ^{31}P NMR. The concentration of **1** was 0.025 mol/L and constant in all experiments. The concentration of alcohol was at least 10 times higher than of **1** to avoid the formation of trimer $(PhPO_2)_3$ (δ_P 8.2).[4] The expected signals of phosphonic acid esters **3a** or/and **3b** appeared at δ_P 21.4 and 15.3, respectively.[3] In some experiments, an additional signal appeared at 18.9 ppm (2–4% of total phosphorus content) and was identified as phosphonic acid $PhP(O)_2OH$,[5] the product of the reaction of **2** with traces of water. The alcohol excess is important because eliminates the subsequent reaction of the intermediate Ph-PO_2 with substrate, which may cause the reaction rate increase.[1,6]

The reaction of **1** with alcohols followed the first-order kinetics for at least 2 half-lives and the rate constants were found to be alcohol concentration dependent (Table I and II). This observation is consistent with the possibility that the reaction of **1** with alcohols follows simultaneously EA and AE reaction pathways (Scheme 1). In the case of monomolecular fragmentation via metaphosphonate **2** (k_{EA}) the rate constant should be independent of the alcohol concentration. When reaction runs in accordance with the bimolecular formation of pentacoordinate intermediate **4** (k_{AE}), the rate of reaction should be depended on both concentrations of **1** and alcohol. Thus, the overall rate of reaction

TABLE I Kinetics of Reaction of Bicyclooctene 1 with Methanol in 1,2-DCE at 60°C

	Rate constant × 10^4		
MeOH, mol/L	$^1k_{exp}$, s^{-1}	k_{EA}, s^{-1}	$^{Me}k_{AE}$, M^{-1} s^{-1}
0.25	5.67 ± 0.29	4.01 ± 0.24	5.25 ± 0.35
	5.17 ± 0.33		
0.30	5.80 ± 0.24		
	6.04 ± 0.23		
0.38	6.03 ± 0.26		
	6.28 ± 0.20		
0.50	7.00 ± 0.28		
	7.08 ± 0.21		
0.76	8.81 ± 0.23		
0.81	8.93 ± 0.32		

depends on alcohol concentration according to the following equation:

$$v = {}^1k_{exp}\, c_P = k_{EA}c_P + k_{AE}c_Pc_{ROH} \tag{1}$$

and the first-order constant $^1k_{exp}$ is a function of the alcohol concentration:

$$^1k_{exp} = k_{EA} + k_{AE}c_{ROH} \tag{2}$$

According to Equation (2) the rate constants were calculated from the data collected in Tables I and II. The first-order rate constant k_{EA} is independent of the alcohol used in the experiment and its mean value is equal to (3.94 ± 0.27) × 10^{-4} s^{-1}. The second-order rate constant of

TABLE II Kinetics of Reaction of Bicyclooctene 1 with *tert*-Butanol in 1,2-DCE at 60°C

	Rate constant × 10^4		
tert-BuOH, mol/L	$^1k_{exp}$, s^{-1}	k_{EA}, s^{-1}	$^{tBu}k_{AE}$, M^{-1} s^{-1}
0.25	3.96 ± 0.29	3.87 ± 0.21	1.07 ± 0.48
	4.13 ± 0.22		
	4.15 ± 0.20		
0.30	4.19 ± 0.23		
0.38	4.09 ± 0.24		
	4.24 ± 0.26		
0.50	4.41 ± 0.18		
0.60	4.98 ± 0.18		
0.83	4.90 ± 0.21		

the bimolecular reaction between **1** and methanol $^{Me}k_{AE}$ is about five times larger than the rate constant $^{tBu}k_{AE}$ of the reaction with *tert*-butanol. This is the first quantitative comparison of alcohols reactivity towards 2,3-oxaphosphabicyclo[2.2.2]octene. From the previous kinetic measurements of the thermal fragmentation of *P*-ethoxy and *P*-NEt$_2$ analogues of **1** in the presence of alcohols the retrocycloaddition mechanism was documented and the bimolecular process was precluded.[6,7]

When methanol and *tert*-butanol are used in the same experiment, the product ratio [**3a**]/[**3b**] depends on the selectivity of both the bicyclic substrate **1** and the intermediate metaphosphonate **2**. The rate expresssions of **3a** and **3b** formation are:

$$d[\mathbf{3a}]/dt = {}^{Me}k_{AE}[\mathbf{1}][MeOH] + k_{Me6}[\mathbf{2}][MeOH] \tag{3}$$

$$d[\mathbf{3b}]/dt = {}^{tBu}k_{AE}[\mathbf{1}][tBuOH] + k_{tBu}[\mathbf{2}][tBuOH] \tag{4}$$

where k_{Me} and k_{tBu} are the rate constants for the reaction of metaphosphonate **2** with methanol and *tert*-butanol, respectively. Rate constants k_{Me} and k_{tBu} cannot be measured directly, but their ratio can be determined on the basis of concentrations of products and alcohols. Assuming the steady-state approximation for the concentration of metaphosphonate **2**, its concentration is equal to:

$$[\mathbf{2}] = k_{EA}[\mathbf{1}]/(k_{Me}[MeOH] + k_{tBu}[tBuOH]) \tag{5}$$

If concentrations of alcohols are high enough to neglect their changes during the reaction, the ratio of rate constants $^{Me}k/^{tBu}k$ can be calculated from the equation:

$$k_{Me}/k_{tBu} = (Ak_{EA} + A\,{}^{tBu}k_{AE} - {}^{Me}k_{AE}[tBuOH])/(k_{EA} + {}^{Me}k_{AE}[MeOH] - A\,{}^{tBu}k_{AE}[MeOH]) \tag{6}$$

where

$$A = ([\mathbf{3a}]/[\mathbf{3b}])/([tBuOH]/[MeOH]). \tag{7}$$

The ratio k_{Me}/k_{tBu} is equal to A if bimolecular reactions are negligible.

Kinetic runs for the reaction of **1** with two alcohols were performed as in previous experiments. If previous assumptions of two parallel processes (EA and AE) were correct, the rate constant in the presence of MeOH and tBuOH should be equal to the rate constant calculated from the equation:

$$k_{exp} = k_{EA} + {}^{Me}k_{AE}[MeOH] + {}^{tBu}k_{AE}[tBuOH] \tag{8}$$

The experimental and calculated first-order rate constants are equal within the experimental error (Table III). The average rate constants

TABLE III Kinetics of Reaction of Bicyclooctene 1 with Methanol and *tert*-Butanol in 1,2-DCE at 60°C

Alcohol conc., mol L^{-1}		Rate constant × 10^4 s^{-1}			
MeOH	*tert*-BuOH	exp.	calc.[a]	A[b]	k_{MeOH}/k_{tBuOH}
0.60	0.42	6.76 ± 0.15	7.46 ± 0.68	1.85	1.00
0.36	0.39	6.22 ± 0.18	6.20 ± 0.58	1.79	1.12
0.29	0.51	5.75 ± 0.0.23	5.98 ± 0.61	1.78	1.09
0.51	0.26	5.93 ± 0.28	6.80 ± 0.58	1.95	1.24
0.40	1.20	7.28 ± 0.19	7.32 ± 0.99	2.25	1.08

[a] Calculated using the Equation 8.

[b] Calculated according to the Equation 7.

ratio k_{Me}/k_{tBu} is equal to 1.10 ± 0.10, thus metaphosphonate **2** reacts with methanol and *tert*-butanol practically nonselectively.

The lack of selectivity means that metaphosphonate **2** reacts faster than it can diffuse and is more reactive in comparison with EtO-P(O)S, which reacts 2.1 times faster with ethanol than with *tert*-butanol in chloroform at 100°C.[6] The higher selectivity was observed for reaction of monomeric metaphosphate anion PO_3^- in aprotic solvents.[8] As sources of metaphosphate 2,4-dinitrophenylphosphate or *erythro*-1-phenyl-1,2-dibromopropylphosphonic acid in the presence of diisopropylamine were used. Methyl phosphate predominated over *tert*-butyl phosphate 3–7 times, but no selectivity was found between ethanol and *tert*-butanol. The observed selectivity of metaphosphate anion in reaction with alcohols was discussed in terms of the self-association of alcohols and preferential salvation of substrates. However, the hypothesis of the preferential solvation leading, at least partially, to the change of the rate-limiting step from the unimolecular to the bimolecular process was not verified and this question is still opened.

EXPERIMENTAL

^{31}P NMR spectra were recorded on Bruker Avance DPX 250 spectrometer at 101.2 MHz, using 85% H_3PO_4 as external standard, applying pulse 90° and repetition time 3 s.

1,2-Dichloroethane (P. O. Ch., Poland, analytical grade) was carefully dried by distillation over P_2O_5.

Synthesis of 5,6-dimethyl-3-phenyl-2,3-oxaphosphabicyclo[2.2.2]oct-5-ene-*N*-phenyl-7,8-dicarboximide-3-oxide (**1**) was carried out according to the known procedure.[4]

By-product Ph-P(O)(OH)$_2^8$ was identified by adding the excess of diazomethane in diethylether at room temperature to the reaction mixture. ^{31}P NMR signals at 21.4 ppm (**3a**) and 18.9 (Ph-P(O)(OH)$_2$) merged into one signal at 22.3 ppm, corresponding to Ph-P(O)(OMe)$_2$.[5]

Kinetic Measurements

A solution (0.7 mL) of **1** and alcohol or mixture of alcohols in dry 1,2-DCE were placed in 5 mm NMR tubes together with capillary containing Ph$_3$PO in 1,2-DCE (external standard) and sealed under argon. Samples were placed in thermostat at 60°C, and the reaction was monitored by ^{31}P NMR. The reaction was followed for at least one half-life and the rate constants were calculated on the basis of integration of the substrate and the internal standard peaks.

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