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An Intramolecular Arbuzov Rearrangement Initiated by Anodic Oxidation

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Abstract: Dialkyl phenylphosphonite $PhP(OR)_2$ (R = Et, Me) undergoes an intramolecular Arbuzov rearrangement upon electrolysis at an anode in acetonitrile under an oxygen atmosphere to yield alkyl alkylphenylphosphinate PhRP(=O)(OR). The results here suggest that the rearrangement takes place through a radical-chain mechanism initiated by anodic oxidation of the phosphonite to the corresponding cation radical.

Syntheses of a huge number of phosphorus compounds, especially compounds related to naturally occurring ones, are now goals for many chemists. A key step in these syntheses is formation of a phosphorus-carbon covalent bond, and quite often the Arbuzov rearrangement is successfully used in such a step.[1] The Arbuzov rearrangement, however, has a potential disadvantage in such use because it proceeds *inter*molecularly under thermal conditions.[2] The disadvantage is apparent, for example, when a phosphonate with a secondary alkyl on its phosphorus is aimed to synthesize through the Arbuzov reaction between a phosphite and a secondary alkyl halide.[3] The process produces an alkyl halide along with the target phosphonate, and if the resulting alkyl halide is a primary one, formation of an undesired phosphonate that has the primary alkyl on the phosphorus is inevitable.[4] A way to overcome the disadvantage is to develop an *intra*molecular Arbuzov rearrangement. Thus, an *intra*molecular photo-Arbuzov rearrangement has been developed, by which phosphonate analogues of acyclic nucleoside antivirals have been successfully synthesized.[4,5] However, another problem is that photochemical reactions require, in principle, a chromophore attached to the phosphorus compounds.

We found that electrolysis of a certain trivalent-phosphorus compound at an anode results in its *intra*molecular Arbuzov rearrangement. Electrochemical reactions are feasible also for substrates without a chromophore, and, in addition, work-up procedures of these reactions are usually very easy. The electrochemical reaction presented here, therefore, could be a prototype method for making a P-C covalent bond.

Diethyl phenylphosphonite (**1a**) was dissolved in acetonitrile containing tetraethylammonium fluoroborate in an anode room of a divided cell equipped with platinum electrodes, and oxygen gas was bubbled through the cell with magnetic stirring. The potentiostatic electrolysis (2.0 V) was carried out at room temperature for 50 min. The reaction mixture was then analyzed on GC, which showed that ethyl ethylphenylphosphinate (**2a**), the Arbuzov product from **1a**, was formed in a significant amount along with a smaller amount of diethyl phenylphosphonate (**3a**) (Scheme 1). A shorter duration of the electrolysis improved the yield of **2** appreciably. Thus, when a solution of **1a** or dimethyl phenylphosphonite (**1b**) was electrolyzed for 3 min and allowed

Scheme 1

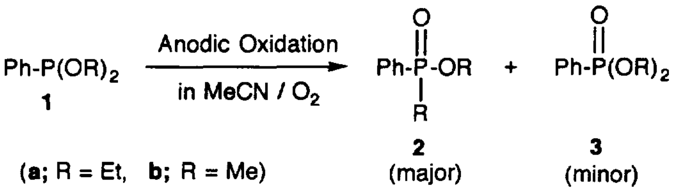


Table 1. Electrolysis of Dialkyl Phenylphosphonite (1).[a]

Phosphonite[b]	Solvent	Atmosphere	E Time[c], min	T Time[d], min	Yield, %[e] 1[f]	2	3
1a	MeCN	O_2	50	0	0	59	20
1a	MeCN	O_2	3	240	0	83	6
1b	MeCN	O_2	3	240	0	75	6
1a	MeCN	Ar	3	300	94	<1	3
1a[g]	MeCN	O_2	3	240	68	7	8
1a[h]	MeCN	O_2	0	60	100	0	0
1b	MeOH	O_2	180	0	0	0	92

[a] At room temperature. At 2.0 V. Tetraethylammonium fluoroborate (1.0×10^{-1} M) was used as a supporting electrolyte. [b] Initial concentration of **1**; 4.0×10^{-2} M. [c] Time for electrolysis. [d] Time for thermal reaction after electrolysis. [e] Determined on GC. Based on **1** used. [f] Recovered. [g] *N-tert*-Butyl-α-phenylnitrone (0.2 eq.) was added after electrolysis. [h] Control without electrolysis.

to react without electrolysis for 4 hr under otherwise identical conditions, **2a** or methyl methylphenylphosphinate (**2b**), respectively, was obtained in a remarkably higher yield. Results are summarized in Table 1. That the rearrangement is intramolecular was confirmed by a cross experiment under these experimental conditions, in which a mixture of **1a** and **1b** yielded a mixture of **2a** and **2b** giving no cross products. Importantly, the time-course of the reaction showed that **1a** and **1b** disappear in a nearly identical rate with simultaneous formation of **2a** and **2b** (Fig. 1). The reaction under an argon atmosphere resulted in nearly quantitative recovery of the starting material even after a prolonged reaction. A radical scavenger exhibited an inhibitory effect on the formation of **2**. No reaction took place without electrolysis.

The formation of **2** may be rationalized by a chain-mechanism depicted in Scheme 2. A chain-character of the present reaction has indeed been witnessed by the observation that a very short duration of the electrolysis brings about almost complete rearrangement of **1** to **2**. Clearly, anodic oxidation of **1** to the cation radical $1^{+\bullet}$ initiates the reaction. Evidence for the initial generation of $1^{+\bullet}$ is that the electrolysis of **1b** in methanol gives **3b** (instead of **2b**) in a nearly quantitative yield; a trivalent-phosphorus cation radical once formed is facilely

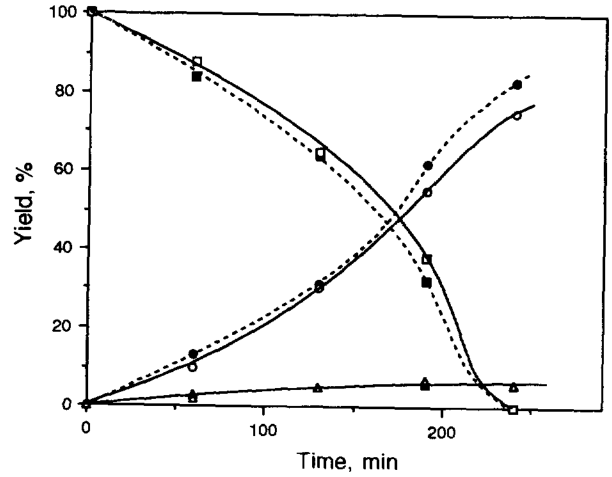
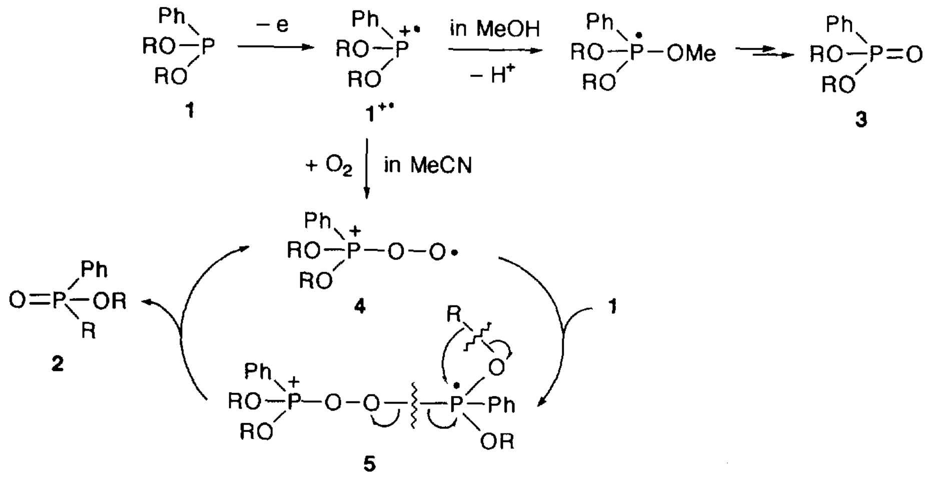


Fig. 1. Progress of the reaction after a 3-minute electrolysis of the mixture of the phosphonites **1a** and **1b** in acetonitrile under an oxygen atmosphere. Symbols, ■, ●, ▲, □, ○, and △, denote the yields of **1a**, **2a**, **3a**, **1b**, **2b**, and **3b**, respectively. Lines are drawn arbitrarily.

Scheme 2



trapped by a nucleophile such as an alcohol, with which the corresponding four-coordinate pentavalent compound such as **3** is eventually produced.[6,7] Since there is no nucleophile available in the reaction in acetonitrile, $\mathbf{1}^{+\bullet}$ undergoes a radical reaction with an oxygen molecule to give a peroxy cation radical **4**.[8] It has been reported that phosphoranyl radicals similarly react with an oxygen molecule to give peroxy radicals.[9] It seems likely that **4** thus formed reacts with another molecule of **1** since a free-radical attacks the phosphorus atom of a trivalent-phosphorus compound exothermically.[10] In fact, higher yield of **2** has been achieved with a shorter duration of the electrolysis, suggesting that another molecule of **1** is necessary for the rearrangement to take place. This reaction of **4** produces a dimeric cation radical **5**, which affords **2** with reproduction of **4**.

The proposed mechanism should be examined more carefully. In particular, 1,2-migration of the alkyl group from the oxygen atom to the phosphorus atom within the dimer **5** should be elucidated by other evidence. It is also uncertain at the present why **5** undergoes cleavage of the P-O bond even though it is stronger than the O-O bond. It is nevertheless important that we have developed an electrochemical *intra*molecular Arbuzov rearrangement, which would be applicable to synthesis of phosphorus compounds that have a secondary alkyl on the phosphorus atom. An attempt to synthesize these compounds using this method is now in progress.

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