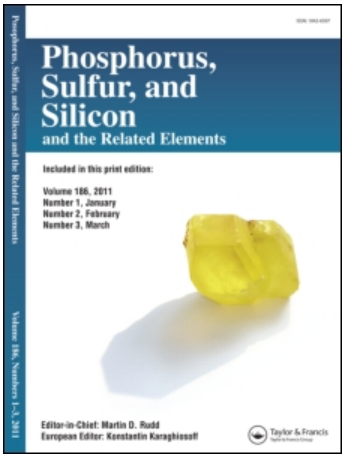

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REACTIVITY OF THE ACIDS OF TRIVALENT PHOSPHORUS AND THEIR DERIVATIVES. PART V. INVESTIGATION OF THE MECHANISM OF THE REACTION OF THE >P-O⁻ NUCLEOPHILES WITH THE C-Br BOND.

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Abstract. The anions of the type >P-O⁻ are of special interest; they are nucleophilic ambident reagents, strong bases and single electron donors. The mechanism of the reductive debromination in the course of the reaction of the P-O⁻ ions with activated alkyl bromides has been investigated. The results of the carried out experiments suggest that the X-philic substitution is the first step in this reaction. The SET process is also being discussed.

Key Words: C-Br bond, dialkyl phosphite ions, Michaelis - Becker reaction, X-philic substitution, SET.

The Michaelis - Becker Reaction has been known for quite some time. The mechanism of this reaction, often assumed to be S_N2 involving the nucleophilic phosphorus atom, is not established with certainty. In the literature one can find some examples of an *unusual* course of this reaction. An analysis of the literature leads to several important observations. Dialkyl phosphite anions give only with primary alkyl halides a satisfactory yield of the Michaelis - Becker reaction. The reaction between bromotriphenylmethane and sodium diethyl phosphite was claimed to be a free radical process. For the synthesis of α-phosphonocarboxylates the Michaelis- Arbuzov reaction is the method of choice. We have shown recently [1] that the anions of the type >P-O⁻ as well as >P-S⁻ undergo reaction with α -bromocarboxylates and - phosphonates yielding debrominated products. We found also that generally for this reductive debromination the electron-withdrawing group bound to the carbon bearing the bromine atom is indispensable.

X: O; S
Y: COOR, $P(O)OR)_2$; $CONH_2$; CN

The results of our investigations show that in the case of the carbon bromine bond also the bromine atom can be a target for a nucleophilic attack by the phosphorus reagent of the type >P-O⁻ as well as >P-S⁻ with the release of the carbon anion as a nucleofuge, stabilised by an electron-withdrawing group (neighbouring group participation). We have to consider that the so-called *positive* bromine can also develop through SET; the radical chain mechanism or cage process. In order to provide evidence for the SET mechanism operating in reductive debromination we designed a set of experiments. We did not find any light influence on the course of the reaction in focus. In the reaction of a bromocyclopropyl system with the >P-O⁻ ions we never observed any cyclopropyl radical - allyl radical rearrangement products, which was the case in the reaction of methyl 1-bromocyclopropylcarboxylate with tributyltin hydride.

The reaction of methyl α-bromocarboxylates with the >P-O⁻ nucleophiles in methanol-O-d produces: methyl α-deuteriocarboxylates and methyl phosphates.
Finally we isolated the bromothiophosphate from the reaction mixture of methyl 1-bromocyclopropanecarboxylate and >P-S⁻ nucleophile .

The absence of a significant effect of light as well as of dicyclohexylphosphine on the rates of the reaction under investigation as well as the deuterium incorporation into the product permits the exclusion of a chain mechanism of the $S_{RN}1$ type for these substrates.

Benzylphosphonates, on the other hand, with a wide range of substituents in the benzyl ring as well as phosphonomethyl pyridines are available in the Michaelis - Becker reaction. The exceptions are nitro derivatives; there is a reported failure of an attempted direct preparation of p-nitrobenzylphosphonate from p-nitrobenzyl bromide and trialkyl phosphites as well as the salts of dialkyl phosphites [2]. It was showed also that tetraphenylethane was isolated from the reaction mixture of bromodiphenyl-methane and sodium diethyl phosphite. [3]

Additionally, G. A. Russell [4] reported that dialkyl phosphite or thiophosphite anions react with p-nitrobenzyl chloride, and α,α-dimethyl-p-nitrobenzyl chloride to form p-nitrobenzylphosphonates or thiophosphonates. He claimed that this reaction proceeds at least partially by the $S_{RN}1$ scheme.

Recently we have shown [5] that the treatment of 1 equiv of p-nitrobenzyl bromide with 1 equiv of the >P-O⁻ produces one major product; namely 1,2-di(p-nitrophenyl)ethane.

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br \xrightarrow[\text{THF or i-PrOH}]{>P\text{-}O^-} p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p$$

The ion of the type >P-O⁻ could a priori react with p-nitrobenzyl bromide either by an attack on the bromine atom, X-philic substitution (pathway A) or through SET; the radical chain mechanism or cage process with the >P-O⁻ ion as a single electron donor (pathway B) or the p-nitrobenzyl anion as a single electron donor (pathway C).

Pathway A:

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br + {}^-O\text{-}P< \longrightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^- + Br\text{-}\overset{O}{\overset{\|}{P}}<$$

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^- + Br\text{-}CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p \longrightarrow p\text{-}NO_2\text{-}C_6H_4CH_2CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p$$

Pathway B:

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br + {}^{-}O\text{-}P< \longrightarrow [\,p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br\,]^{\cdot-} + O{=}\dot{P}<$$

$$[\,p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br\,]^{\cdot-} \longrightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{\bullet} + Br^{-}$$

$$2\ p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{\bullet} \longrightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p$$

Pathway C:

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br + {}^{-}O\text{-}P< \longrightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{-} + Br\text{-}\overset{O}{\overset{\|}{P}}<$$

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{-} + p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br$$

$$\Big|\ \text{SET}$$

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{\bullet} + [\,p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br\,]^{\cdot-}$$

$$[\,p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}Br\,]^{\cdot-} \longrightarrow p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{\bullet} + Br^{-}$$

$$p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2^{\bullet} + {}^{-}CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p \longrightarrow [\,p\text{-}NO_2\text{-}C_6H_4CH_2CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p\,]^{\cdot-}$$

$$\xrightarrow{-\,1e} p\text{-}NO_2\text{-}C_6H_4\text{-}CH_2CH_2\text{-}C_6H_4\text{-}NO_2\text{-}p$$

The major difference between these three pathways is that in pathway A and C the p-nitrobenzyl anion as an intermediate is proposed, whereas in pathway B the p-nitrobenzyl radical; and additionally in pathway B >P-O$^-$ acts as a single electron donor.

We decided to run the reaction in THF with 1 equiv of o-, m-, and p-nitrobenzyl bromides and sodium diisopropylphosphite under a variety of conditions; in darkness, day light and irradiation with 500 W bulb. From the reaction mixture in the case of o-, and p-nitrobenzyl bromide in this set of experiments we isolated mainly a dimer as a major product and the starting material. In the case of m-nitrobenzyl bromide we isolated from the reaction mixture diisopropyl m-nitrobenzylphosphonate, a dimer and a small amount of m-nitrotoluene.

We found a substantial influence of light on the yield of the isolated dimer. The yield of diisopropyl m-nitrobenzylphosphonate was not affected by the illumination of the reaction mixture by light.

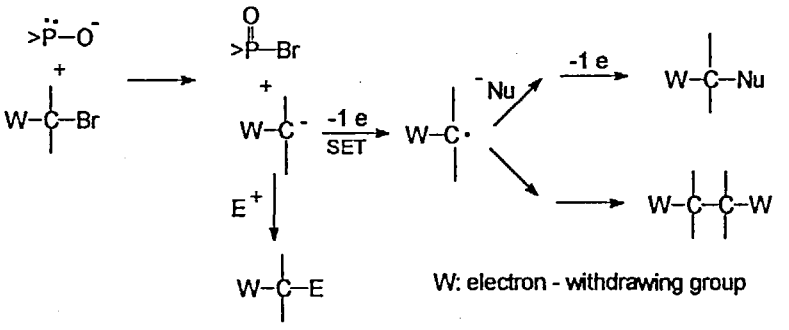
The results of these experiments strongly suggest that the SET process operates in the case of the dimer formation. On the other hand the UV investigation as well as the isolation of nitrotoluene from the reaction mixture carried out in alcohol as solvent speak for the nitrobenzyl anion as an intermediate in the investigated reaction.

Dialkyl phosphite ions are known to be radical traps [6]. We decided to run the set of experiments with the different ratio of p-nitrobenzyl bromide to sodium diisopropylphosphite. We found that increasing the amount of the dialkyl phosphite ion in the reaction mixture causes a higher yield of the benzylphosphonate production. From the reaction mixture of 10 equivs of sodium diisopropylphosphite and 1 equiv of p-nitrobenzyl bromide we isolated diisopropyl p-nitrobenzylphosphonate as a major product.

The deuterium incorporation into the methyl group of p-nitrotoluene [5] as well as the UV experiment speak strongly for the carbanion and against the free radical as an intermediate in the reaction in focus. Additionally, the isolation of methyl dibenzylphosphinate from the reaction mixture of p-nitrobenzyl bromide and dibenzylphosphine oxide in methanol [5] is in agreement with the X-philic substitution. On the other hand on the basis of the results of the crossover experiment as well as on the basis of the light influence on the dimer formation, pathway A can be excluded and the SET mechanism (pathway C) is the most plausible one.

In order to check our postulate of this mechanism as well as to check the scope and limitations of this type of reactivity of >P-O$^-$ ions, we decided to study other benzyl systems possessing electron withdrawing groups in the phenyl ring with a different redox potential. We were able to show that the dimer or reduction product formation depends on the redox potential of the bromoderivatives.

The results of our study explain a failure of an attempted direct preparation of phosphonates as well as phosphine oxides from bromoderivatives possessing electron-withdrawing groups as starting materials in the Michaelis - Becker reaction. Moreover, we are able to present a much more complete picture of the >P-O$^-$ ion reactivity towards the C-Br bond.



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