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Reinvestigation of the reaction between sodium diethyl phosphite and diethyl phosphorochloridate. Evidence for a SET process in the formation of a direct P(IV)–P(IV) bond†

Ryszard W. Kinas, Andrzej Okruszek* and Wojciech J. Stec

Department of Bioorganic Chemistry, Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Sienkiewicza 112, 90-363 Łódź, Poland

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Abstract—Alkali metal salts of diethyl phosphites act as nucleophiles or electron donors in reactions with diethyl phosphorochloridate. Evidence is provided that formation of the direct P(IV)–P(IV) bond proceeds via a single electron transfer process (SET) from phosphite anion to phosphorochloridate.

Base-activated reactions of dialkyl phosphites with dialkyl phosphorochloridates show great variation in product formation depending on the nature of base (sodium salt or amine promoted condensation), solvent and other parameters.[1–3] Tetraalkyl hypophosphates were found to be formed in moderate yields when one molar equivalent of dialkyl phosphorochloridate was added dropwise into benzene solution/suspension of 1.5 molar equivalent of sodium dialkyl phosphite. As the side products accompanying the formation of tetraalkyl hypophosphate, some organophosphorus anhydrides, including tetraalkyl pyrophosphite, tetraalkyl phosphorous–phosphoric anhydride, and tetraalkyl pyrophosphate, were reported to be present in a fraction of the reaction mixture isolated by distillation in vacuo.[1,3] The reaction between dialkyl phosphite and dialkyl phosphorochloridate performed in the presence of tertiary amines, afforded the mixture of aforementioned anhydrides, with no formation of hypophosphate.[4] Taking advantage of the possibilities offered by ^{31}P NMR spectroscopy for the qualitative and quantitative control of the reaction progress, the reaction between sodium diethyl phosphite **1** and diethyl phosphorochloridate **2** was reinvestigated.[5] The relative intensities of ^{31}P NMR signals of phosphorus containing compounds formed in the reaction between **1** and **2** (added in a portionwise manner) are shown in Fig. 1.

After addition of ca. 30% of molar equivalent of **2**, ^{31}P NMR analysis revealed the presence of tetraethyl pyrophosphite **4**, diethyl phosphate **7** and unreacted sodium diethyl phosphite **1** in the ratio 20:32:35, respectively. This observation can be rationalized by assuming that phosphorochloridate **2** was subject to nucleophilic attack by ambident diethyl phosphite oxyanion **1** with a formation of pentacoordinate intermediate **8a**, with attacking phosphite residue and one of ethoxy groups in apical positions. This intermediate can

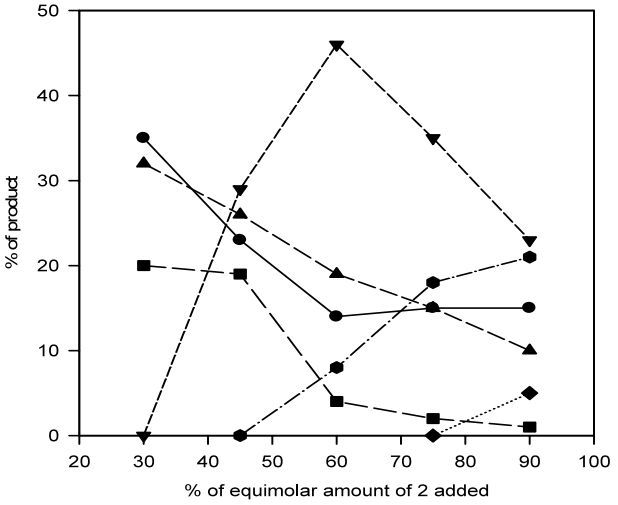

Figure 1. The course of products formation in the reaction of **1** with **2**: -▼- tetraethyl hypophosphate (**3**); -●- sodium diethyl phosphite (**1**); -▲- diethyl phosphate (**7**); -■- tetraethyl pyrophosphite (**4**); -◆- tetraethyl phosphorous–phosphoric anhydride (**5**); -⬢- tetraethyl pyrophosphate (**6**).

* Corresponding author. Tel.: (+48 42) 681 69 70; fax: (+48 42) 681 54 83; e-mail: okruszek@bio.cbmm.lodz.pl

† This paper is dedicated to Professor Andrzej Zwierzak on the occasion of his 70th birthday.

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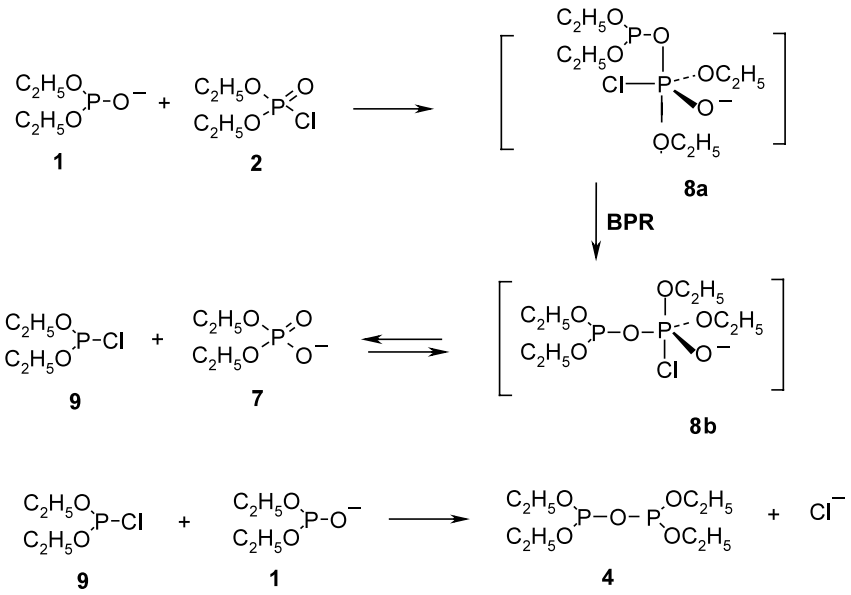
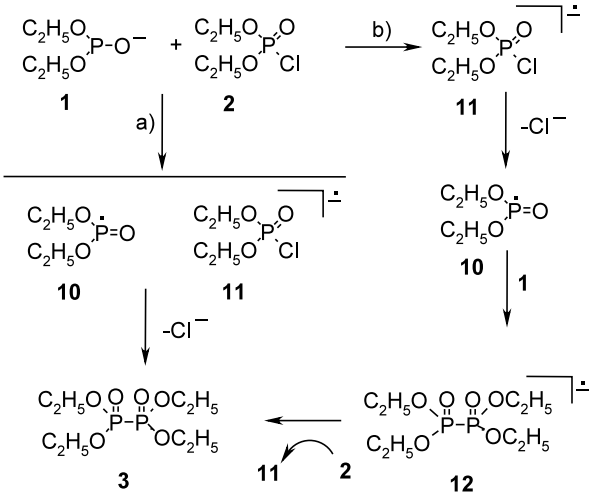


Scheme 1.

undergo Berry Pseudorotation (BPR) to give isomeric bypyramide **8b**, possessing chlorine atom, a potential leaving group, in apical position. Its collapse, which can proceed by departure of chloride anion and its instantaneous (inside a solvent cage) attack at the trivalent phosphorus, leads to the diethyl phosphate **7** and diethyl phosphorochloridite **9**.[4] The latter compound could not be observed in ^{31}P NMR spectrum because of its instantaneous reaction with an excess of **1** giving rise to the formation of tetraethyl pyrophosphite **4** (Scheme 1). Further addition of **2** caused a decrease of concentration of the anhydride **4** and initiated the formation of tetraethyl hypophosphate **3**. The content of **3** reached its highest value (46% of relative intensity) after addition of ca. 60% of molar equivalent of **2**. In addition, some amounts of tetraethyl pyrophosphate **6** and tetraethyl phosphorous–phosphoric anhydride **5** were also identified in the reaction mixture. The formation of these two products can be rationalized in terms of subsequent reactions of **7** with **2**, **4** or **9**.[4]

For the formation of the direct P(IV)–P(IV) bond in the reaction of **1** with **2**, two feasible pathways can be considered. One route, as was assumed previously,[1,3] involves an ionic process of nucleophilic substitution of the S_N2P type at the phosphorus atom of phosphorochloridate **2**, with the dialkyl phosphite anion acting as an ambident nucleophile. Inspection of Fig. 1 leads to a conclusion that the process of direct P(IV)–P(IV) bond formation leading to **3** is initiated after partial (ca. 30%) addition of the phosphorochloridate **2**. An alternative to the aforementioned nucleophilic substitution reaction leading to the hypophosphate **3**, so far not considered, is a *single electron transfer* process (SET). It is now assumed that tetraethyl pyrophosphite **4**, formed at the first stage of the process, interacts with **1** by binding the sodium cation, thus causing the initiation of the SET pathway. The phosphite anion and phosphorochloridate **2** form an electron donor–electron acceptor complex, in which a single electron is transferred from the anion **1** to **2**, giving rise to the formation of the radical–radical anion pair **10**/**11**, a typical electron donor–electron acceptor complex (EDA). The formation of tetraethyl hypophosphate **3** may result either from the coupling of the radical **10** with radical anion **11** within EDA complex in a solvent cage (Scheme 2, path *a*), or from free radical chain process outside the solvent cage, with the participation of radical **10** and hypophosphate radical anion **12** (path *b*).

The participation of free radicals accompanying reactions of dialkyl phosphites and their salts has been well documented in the literature. Free radicals were detected in reaction mixtures during photochemical decomposition of dialkyl (trichloromethyl)phosphonates,[6] electrochemical oxidation of dialkyl phosphites[7] and photolysis of acetone in the presence of dialkyl phosphites.[8] The functioning of dialkyl phosphite anions as single electron donors was observed in their reactions with alkyl halides or aryl halides, otherwise



Scheme 2.

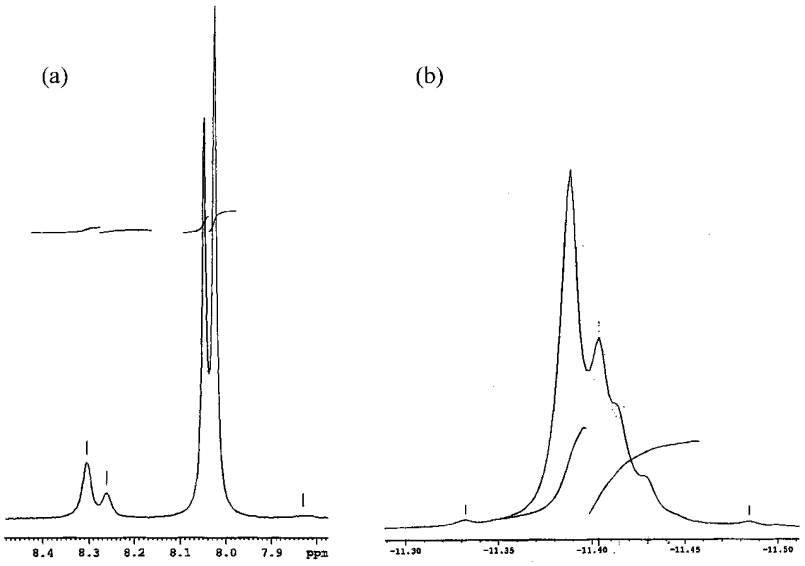


Figure 2. ^{31}P NMR spectrum of (a) hypophosphate **3** and (b) pyrophosphate **6** derived from the reaction of sodium diethyl ^{18}O-phosphite **1** with diethyl phosphorochloridate **2**. Minor resonances at 8.304 and 8.261 (spectrum a) correspond to labeled diethyl phosphite formed by partial hydrolysis of labeled hypophosphate **3** during its isolation.

known to be very efficient electron acceptors.[9–11] Dialkyl phosphorochloridate radical anion **11**, proposed as the key component of reactive EDA complex **10**/**11** leading to hypophosphate **3** (Scheme 2), was recently suggested as an intermediate in the reductive cleavage of halogen–phosphorus bond.[12]

In order to provide evidence for the reaction mechanism outlined in Scheme 2, involving the intermediacy of radical **10** and radical anion **11**, condensation experiments were carried out with ^{18}O-labeled **1**, or in the presence of radical scavengers. The reaction of ^{18}O-labeled **1** with **2**, performed by addition of 0.66 mol. equiv. of **2** into a suspension of 1 mol. equiv. of **1** in toluene yielded, after chromatographic separation from unreacted **1**, a mixture of **3** and **6**.[13] Hypophosphate **3** showed in the proton-decoupled ^{31}P NMR spectrum (Fig. 2a) two distinguishable signals at δ 8.047 (42%) and δ 8.025 (58%). The presence of ^{18}O isotope induced a small upfield shift ($\Delta\delta$ 0.022 ppm) in the ^{31}P NMR frequency of hypophosphate **3**, the magnitude of which is characteristic to a P=^{18}O double bond.[14] Isotope enrichment of the hypophosphate **3**, as determined by ^{31}P NMR (58%) and GC MS (55%) was, within experimental error, the same as isotope enrichment of the substrate **1** (56%, GC MS). No resonance with $\Delta\delta$ ca. 0.044 ppm and no M+4 ion, corresponding to ^{18}O-double labeled hypophosphate **3**, the hypothetical product of recombination of two ^{18}O-phosphite radicals **10**, was observed. As anticipated, the hypophosphate **3** was built up from fragments of one molecule of the phosphorochloridate **2** and one molecule of the ^{18}O-phosphite **1**. Another important conclusion can be drawn from ^{31}P NMR spectrum of the pyrophosphate **6** obtained from ^{18}O-labeled **1**[13] (Fig. 2b) which showed a resonance at −11.388 ppm due to the unlabeled **6**, and three upfield shifted resonances corresponding to oxygen-labeled pyrophosphate. The lines at −11.403 and −11.429 ppm can be assigned to compounds containing ^{18}O-isotope in the bridging site, and in both bridging and non-bridging positions of the labeled pyrophosphate **6**, respectively. The isotopomer containing ^{18}O in non-bridging position shows an extreme AB system,[15,16] with weak outer lines at −11.330 and −11.484 ppm and resolved inner lines at −11.403 and −11.413 ppm (the downfield line overlaps with the resonance of the symmetrically labeled **6**, $^2J_{PP}=14.6$ Hz). The observed $\Delta\delta$ values 0.015, 0.025 and 0.041 ppm are in reasonable agreement with previously described magnitude of upfield shift induced by ^{18}O isotope in single (P–^{18}O) and double (P=^{18}O) bond. The calculated total isotope enrichment of the pyrophosphate **6** (53%) was found to be only slightly lower than that of phosphite **1** (56%), indicating that one of the oxygen atoms of pyrophosphate molecule originates from starting phosphite. Since the most probable source of pyrophosphate **6** is the side reaction of **2** (unlabeled) with phosphate **7**, the presence of oxygen label in **6** confirms the postulated mechanism of the first step of process, in which oxygen atom migrates from **1** to **7** with the participation of pentacoordinate intermediate **8** (Scheme 1).

The results of further experiments, involving the reaction of diethyl phosphorochloridate **2** with sodium diethyl phosphite **1** and its analogs containing other cations (Li^+, K^+), under various experimental conditions, are listed in Table 1. Using free radical scavenger–galvinoxyl (Table 1, entry 2) or radical anion scavenger–*p*-dinitrobenzene (PDB, Table 1, entry 3) added to the reaction mixture, a marked lowering of the yield of the hypophosphate **3** was observed, from 74% (no scavenger added) to 44 or 28%, respectively. Partial inhibition by radical scavengers confirms our assumption that the formation of hypophosphate **3** in

Table 1. Reactions of alkali metal salts of diethyl phosphite **1** with diethyl phosphorochloridate **2**

Entry	Counter-ion of **1**	Solvent and molar concentration of **1**	Additives or reaction conditions	Yield of **3**[a] (%)
1	Na^+ [(c)]	Toluene, 1.2	None	74
2	Na^+ [(c)]	Toluene, 1.2	Galvinoxyl[b]	44
3	Na^+ [(c)]	Toluene, 1.2	PDB[b]	28
4	Na^+ [(c)]	Toluene, 1.2	Reaction in the dark	73
5	Li^+ [(d)]	THF, 2.4	None	0
6	Na^+ [(c)]	THF, 2.4	None	2
7	K^+ [(e)]	THF, 2.4	None	17
8	Na^+ [(f)]	Acetonitrile, 1.2	None	29

[a] Yields were determined by integration of ^{31}P NMR spectra and calculated as a percentage of conversion of **2** to **3**.
[b] 0.132 molar equiv. of galvinoxyl or PDB was added into suspension of **1**.
Elemental sodium[(c)], butyllithium[(d)], potassium *tert*-butoxide[(e)] and sodium hydride[(f)] were used for diethyl phosphite salt generation prior to its reaction with **2**.

the reaction of sodium diethyl phosphite **1** with diethyl phosphorochloridate **2** could be an example of a single electron transfer process. The electron transfer nature of this reaction should then be a function of the oxygenation potential of diethyl phosphite salt and the solvent. Indeed, while sodium and potassium phosphites **1** gave observable yields of tetraethyl hypophosphate **3** when the reaction was performed in THF solution (Table 1, entries 6 and 7), under identical experimental conditions formation of **3** was not observed with lithium salt (entry 5), otherwise known to undergo electrochemical oxidation at higher anodic potential than sodium salt.[17] No influence on the yield of hypophosphate formation was observed when reaction was carried out in the dark in toluene solution (entry 4).

Higher yields of the hypophosphate **3** were obtained in aprotic nonpolar solvents (benzene, toluene) than in aprotic polar ones (acetonitrile, THF). The absence of doubly labeled ^{18}O-hypophosphate **3** in experiments with oxygen labeled **1**, its nearly the same isotope enrichment as that of the substrate **1**, as well as the lack of photostimulation and lowering of the yield of the hypophosphate **3** in the presence of free radical scavengers suggest, that non-chain process occurs inside the solvent cage, and no radical intermediates are left free in solution. On the basis of product analysis, ^{18}O isotope scrambling, and the results of trapping experiments, one can postulate that two parallel processes occur in the reaction of diethyl phosphorochloridate **2** with sodium diethyl phosphite **1**. One is ionic nucleophilic substitution with diethyl phosphite anion acting as a nucleophile, which leads to the formation of diethyl phosphorochloridite **9** and diethyl phosphate **7** as primary products, and formation, in subsequent reactions, anhydrides **4**, **5** and **6**. Another one is a single electron transfer pathway, which may be induced by ion-complexing properties of tetraethyl pyrophosphite **4** formed in the aforementioned ionic reaction. The SET pathway, with diethyl phosphorochloridate **2** and diethyl phosphite anion **1** acting as electron acceptor and electron donor, respectively, involves the formation of radical–radical ion EDA-type complex **10**/**11**, which undergoes recombination within the solvent cage (Scheme 2, path *a*) to form the final product—tetraethyl hypophosphate **3**.

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13. Samples for ^{31}P NMR and GC MS analysis of ^{18}O labeled compounds obtained in reaction of **1** (1 mmol) with **2** (0.66 mmol), were purified before use. Reaction mixture was filtered and purified by column chromatography on silica gel using 19:1 toluene/ethanol as the developing system. Fractions containing a mixture of hypophosphate **3** and pyrophosphate **6** were isolated (partial decomposition of hypophosphate **3** was observed during purification). The ^{31}P NMR analysis of ^{18}O-labeled **3** and **6** were performed in C_6D_6 and $CDCl_3$ on a Bruker DRX 500 spectrometer. GC MS analysis were performed on a Trace GC 2000 gas chromatograph fitted with DB-1 (30 m) capillary column and coupled with Automass III mass spectrometer. The peak at RT 18,58 min after MS analysis gave the fragments characteristic to **3** [m/z 275 (64.1), 277 (79.6)] and **6** [m/z 291 (100), 293 (65.7), 295 (14.6)].
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