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The Quest for Free Metaphosphate in Solution: Racemization at Phosphorus in the Transfer of the Phospho Group from Phenyl Phosphate to *tert*-Butyl Alcohol in Acetonitrile

Jonathan M. Friedman and Jeremy R. Knowles*

Department of Chemistry, Harvard University Cambridge, Massachusetts 02138

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Since 1955,[1,2] much evidence has been accumulated to suggest that many nucleophilic displacement reactions of phosphoric monoesters follow a dissociative pathway involving monomeric metaphosphate as an intermediate.[3] Yet recently, when we investigated the stereochemical course of the methanolysis of phenyl [^{16}O,^{17}O,^{18}O]phosphate monoanion and of 2,4-dinitrophenyl [^{16}O,^{17}O,^{18}O]phosphate dianion in aqueous methanol, the product methyl phosphate showed complete *inversion* at phosphorus.[4] Even the methanolysis of an *N*-phosphoguanidine, which is among "the most reactive precursors of metaphosphate",[5] was found to proceed with inversion.[4] To reconcile these findings with the earlier mechanistic results, we suggested that phospho group transfers in protic media occur either by a preassociative pathway[6] in which the metaphosphate-like species is never free or by an "exploded" associative transition state.[4] We have carried the search for free metaphosphate further, and *we report here the first case of racemization at phosphorus during the solvolysis of a phosphoric monoester.*

All the experimental results from studies of nucleophilic reactions of labile phosphoric monoesters indicate almost complete bond breaking between the phospho moiety and the leaving group at the transition state, yet the consistent observation of stereochemical inversion at phosphorus demands that these reactions are either preassociative stepwise (involving a metaphosphate intermediate of extremely short lifetime) or concerted (with a loose S_N2-like transition state).[4] Even when a Conant-Swan fragmentation is used to generate a metaphosphate-like species in protic media, stereochemical inversion is the outcome.[7] For reactions of alcohols in *aprotic* solvents, however, Ramirez and his collaborators have observed phospho group transfer from aryl phosphate monoesters to hindered acceptors such as *tert*-butyl alcohol[8] and have suggested that the formation of *tert*-butyl phosphate is a criterion for the intermediacy of monomeric metaphosphate.[8] We have evaluated the stereochemical course of such a reaction, by studying the phospho group transfer from the dianion of phenyl (*R*)-[^{16}O,^{17}O,^{18}O]phosphate[9] to *tert*-butyl alcohol in acetonitrile.[10] The *tert*-butyl phosphate was isolated,[11]

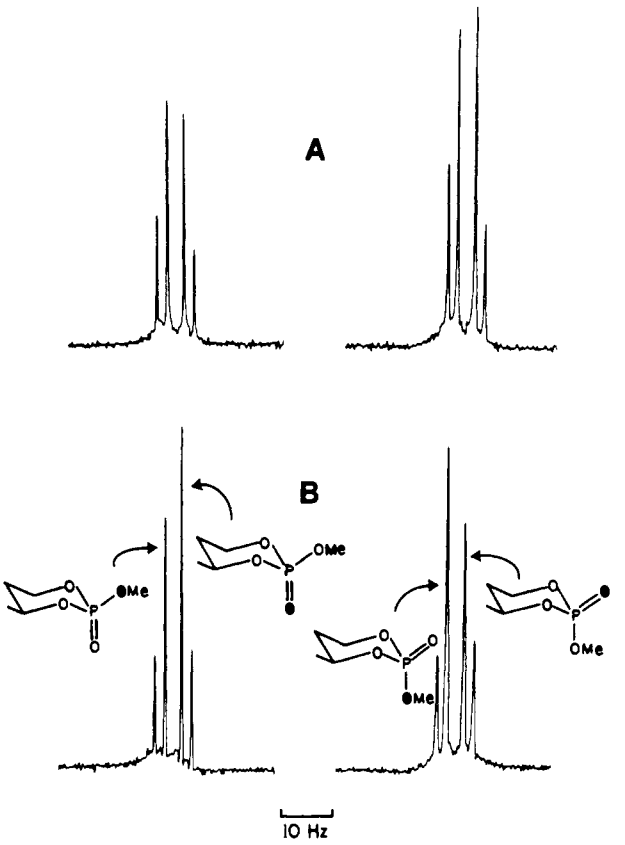

Figure 1. ^{31}P NMR spectra of the products from the "in-line" ring closure and methylation[4] of (A) 3-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-butane-1,3-diol obtained by phospho group transfer by wheat germ acid phosphatase from the sample of *tert*-butyl phosphate deriving from the *tert*-butanolysis of phenyl (*S*)-[^{16}O,^{17}O,^{18}O]phosphate and (B) 1-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-butane-1,3-diol obtained by phospho group transfer by *E. coli* alkaline phosphatase from the reisolated reactant, phenyl (*S*)-[^{16}O,^{17}O,^{18}O]phosphate. The spectra were taken on a Bruker WM-300 WB instrument at 121.5 MHz. Gaussian multiplication with Gaussian broadening, 0.12 Hz, and line broadening, -0.30 Hz. The natural line width at half-height is 0.9 ± 0.05 Hz. The downfield multiplet (syn isomers) is centered around -4.85 ppm and the upfield multiplet (anti isomers) around -5.85 ppm. The isotopically labeled species that provide stereochemical information are illustrated. The downfield signal in each quartet is from the *un*labeled triester, and the upfield signal in each quartet is from the $^{18}O_2$ triester.

Table I. Predicted and Observed ^{31}P Signal Intensities[a]

	predicted[b]			
	if inversion	if retention	if racemization	obsd[c]
peak 2[d]	39	61	50	51
peak 3[d]	61	39	50	49

[a] For the sample of 3-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-butane-1,3-diol derived from the *tert*-butanolysis of phenyl (*S*)-[^{16}O,^{17}O,^{18}O]phosphate in acetonitrile. Peak heights for the stereochemically informative resonances (the middle pair of each quartet) are normalized to 100%. A least-squares curve-fitting program gave results within 1% of those obtained by direct measurement. [b] On the basis of the known isotopic composition of the recovered phenyl [^{16}O,^{17}O,^{18}O]phosphate substrate. [c] See Figure 1A. [d] For the downfield quartet. Peaks are numbered from downfield up.

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(9) The bis(triethylammonium) salt of phenyl (*R*)-[^{16}O,^{17}O,^{18}O]phosphate[4] was converted into the bis(tetra-*n*-butylammonium) salt according to ref 8.
(10) Phenyl (*R*)-[^{16}O,^{17}O,^{18}O]phosphate (4.99 mmol, 0.5 M) in acetonitrile-d_3 containing *tert*-butyl alcohol (1 M), 70 °C, 6 h.
(11) By anion exchange chromatography on AG1-X8 (HCO_3^- form, from BioRad).

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and the absolute configuration at phosphorus was determined as follows.

Since *tert*-butyl phosphate is a poor substrate for alkaline phosphatase from *E. coli* and for human prostatic acid phosphatase (the stereochemical course of each of which is known[12,13]), we used wheat germ acid phosphatase to catalyze the stereospecific transfer of the phospho group to (*S*)-butane-1,3-diol,[4] and the configuration at phosphorus was then determined by analysis[4,14] of the purified 3-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-butane-1,3-diol product. The resulting ^{31}P NMR spectrum (Figure 1A) demonstrated that *the phospho group had largely racemized*. That is, the stereochemically informative resonances (the middle two peaks of each quartet) are almost equal in intensity (see Table I). Control experiments showed that (a) the substrate phenyl phosphate was indeed chiral and had not racemized significantly during the course of the reaction (Figure 1B),[15] (b) the product *tert*-butyl phosphate did not racemize under the reaction conditions,[16] and (c) the wheat germ phosphatase catalyzes the phospho group transer with complete retention at phosphorus.[16] It is therefore clear that the phospho group racemizes in the course of its transfer from phenyl phosphate to *tert*-butyl alcohol.[18]

At first sight, this result provides the most direct confirmation of the proposal of Ramirez that the formation of *tert*-butyl phosphate is diagnostic of the intermediacy of free monomeric metaphosphate. That is, the phenyl phosphate decomposes dissociatively to yield the free monomeric metaphosphate ion, PO_3^-, which, in the absence of an unhindered nucleophile, has a long enough half-life to lose all stereochemical memory before capture by *tert*-butyl alcohol. It is possible, however, that the phospho group is transferred to solvent acetonitrile and that a sequence of rapid phospho group transfers among acetonitrile molecules is only terminated by the irreversible capture by *tert*-butyl alcohol. This interpretation, involving the generation of a highly reactive metaphosphate–acetonitrile adduct, follows the suggestion of Satterthwaite and Westheimer[19] that metaphosphate might form a complex with (or at least be specifically solvated by) such solvents as dioxane and acetonitrile. While it may prove possible to distinguish between the above possibilities by the use of hydrocarbon solvent and to evaluate the reality of truly liberated monomeric metaphosphate, the present experiments provide the first stereochemical evidence for a metaphosphate species (either free or solvent-associated) as an intermediate in the solution reactions of phosphoric monoesters.

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(15) Stereochemical analysis[4,14] of the unreacted phenyl [^{16}O,^{17}O,^{18}O]-phosphate recovered from the reaction mixture showed the configuration was 81 ± 6% *R*.
(16) *tert*-Butyl (*S*)-[^{16}O,^{17}O,^{18}O]phosphate was synthesized by a modification of our general route.[17] This chiral sample was then subjected to the conditions of the solvolysis reaction[10] and reisolated, and the phospho group was transferred to (*S*)-butane-1,3-diol using the wheat germ phosphatase. Stereochemical analysis[4,14] of the configuration at phosphorus in the 3-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-butane-1,3-diol product showed the configuration was 84 ± 6% *S*. We may note in passing that, as expected, the wheat germ acid phosphatase proceeds with overall retention at phosphorus.
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(18) Inspection of Figure 1A and Table I suggests a small degree of *retention* at phosphorus. If real, this could arise from the transfer of the phospho group to acetonitrile, followed by its occasional immediate capture by *tert*-butyl alcohol, each of these steps, predictably,[4] going with inversion. Just as with S_N reactions at carbon centers in solution, incomplete racemization does not eliminate carbonium ion mechanisms. The necessary distinction can, however, be made by the use of solvents that have no solvating lone pairs.
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Synthesis and Properties of Doped μ-Oxo(tetrabenzoporphyrinato)germanium(IV)†

Michael Hanack* and Tilman Zipplies

Institut für Organische Chemie, Lehrstuhl für Organische Chemie II der Universität Tübingen Auf der Morgenstelle 18 D-7400 Tübingen, West Germany

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During the past several years great progress has been made in the field of conducting organic materials based on polymeric cofacially assembled bridged macrocycles. Thus, compounds of the type $[PcML]_n$ (Pc = phthalocyaninato) with M = Si, Ge, Al, Ga and L =, e.g., O, F, S, NCN,[1-5] as well as M = transition metals like Fe, Ru, Co, Rh, Cr, Mn and L = organic bridging ligands capable of conjugation, e.g., pyrazine (pyz), tetrazine (tz), diisocyanobenzene (dib) or the cyanide ion, have been prepared.[6-14] All of them show comparatively high conductivities up to 1 Ω^{-1} cm^{-1} after doping with electron acceptors. Several of the polymeric macrocyclic metal compounds containing a transition metal exhibit similarly high conductivities, even without external doping. With regard to the electronic transport properties, the conductivities observed reach a broad spectrum, ranging from "synthetic metals" to wide gap semiconductors.

We have recently reported[15,16] on the use of tetrabenzoporphyrine ($TBPH_2$), structurally related to phthalocyanine, in polymers of the type $[TBPML]_n$, with M = Fe, L = pyz, dib, M = Co, L = CN^-. These have similar electrical conductivities as the corresponding $[PcML]_n$ compounds.

To our knowledge, the polymers $[TBPMO]_n$ (M = Si, Ge), which should be similar to the well-studied $[PcMO]_n$ (M = Si, Ge) polymers, have not yet been described. We report here on the synthesis and the electrical conductivities of doped and undoped $[TBPGeO]_n$. According to SCF calculations,[17] the TBP radical cation generated by oxidative doping has a larger bandwidth for the free electron, i.e., a greater electron mobility in comparison to phthalocyanine. On the other hand, the conclusion was drawn that Pc and TBP should behave analogously with regard to their charge carrier properties, since the MO mainly responsible for the conduction band possesses nodes at the four aza-bridged positions in phthalocyanine.[18]

$[TBPGeO]_n$ (**5**) was synthesized as shown in scheme I: The tetrabenzoporphyrinato system was prepared as the best available zinc derivative TBPZn (**1**).[19] Demetalation of TBPZn (**1**) to

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