

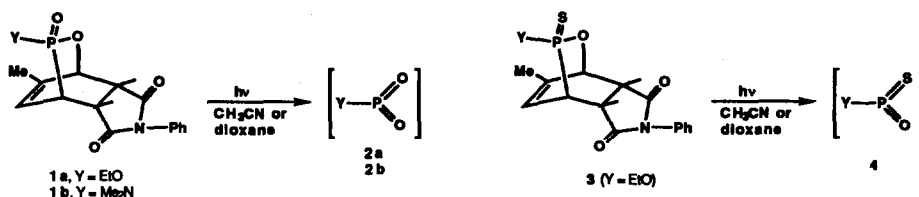
DIRECT DETECTION OF TWO METAPHOSPHORAMIDATES IN -75° THF SOLUTIONS BY ³¹P NMR SPECTROSCOPY

Louis D. Quin,* Catherine Bourdieu, and Gyöngyi S. Quin

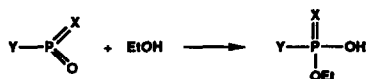
Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003, U.S.A.

Abstract: 2,3-Oxaphosphabicyclo[2.2.2]-oct-5-ene 3-oxide derivatives with Et₂N- or Mesityl NH groups on phosphorus undergo fragmentation readily when irradiated at -75 °C in tetrahydrofuran. The solutions give ³¹P NMR signals at δ +12 and +9, respectively, which are attributed to solvated metaphosphoramidates (RR'N-PO₂). These are rapidly converted to phosphoramidates (EtO-P(O)(OH)(NRR')) on addition of ethanol.

In 1988, we announced the discovery of a simple method for the generation of metaphosphoric acid derivatives (2a, 2b) at room temperature in non-protic solvents.¹ This consists of the irradiation at 254 nm of an ester (1a) or amide (1b) derivative of the 2,3-oxaphosphabicyclo[2.2.2]octene system, which causes fragmentation with release of the bridging P-O unit. We later showed² that an alkyl metathiophosphate (4) can be generated in the same way from the sulfide (3) corresponding to 1a.

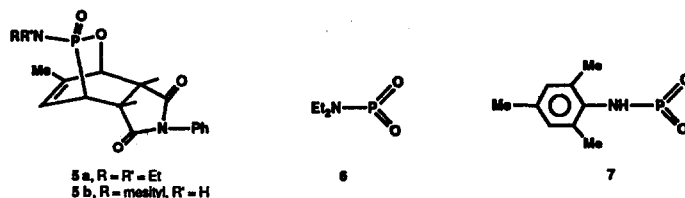


These low-coordination species are highly reactive, and immediately condense to P-O-P derivatives unless trapped, e.g., by alcohols to form phosphates.

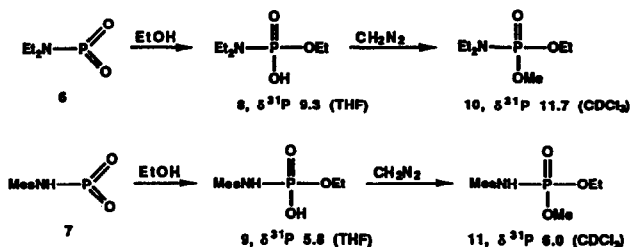


Our photolytic procedure has the potential of being useful for the generation of special metaphosphoric acid esters and amides with lifetimes of sufficient length to allow their direct spectral and chemical observation, an accomplishment not yet found in the literature (some pertinent reports of others are mentioned at the end of this paper) but potentially of great significance to the further development of this area of phosphorus chemistry. By designing structures with large RO or RN substituents on P to provide kinetic stabilization, and more importantly, by performing the photolysis at low temperatures to increase further the lifetime of the species, it was felt that photochemically generated ester and amide derivatives of metaphosphoric acid could be observed in solution by appropriate NMR methods. Use of a nucleophilic solvent might also be expected to assist in the stabilization through donation of an electron pair to the highly electrophilic 3-coordinate phosphorus. We now report on successful experiments along these lines that have resulted in the first NMR and chemical proof that a metaphosphoramidate can have a finite existence in solution.

The metaphosphoramidates 6 and 7 were generated by photolysis of the bicyclic derivatives 5a and 5b, respectively (the synthesis of these compounds was based on a general method,³ details will be reported elsewhere⁴).



The photolyses were first performed at room temperature on 0.08 mmol samples in 2 mL of solvent, using a sealed 5 or 10 mm quartz NMR tube as the reactor. These were attached to the outer wall of an Ace Glass low-temperature quartz immersion well. A Hanovia 450 watt medium pressure lamp was used. Tetrahydrofuran was employed as the electron-donating solvent; it is not totally unreactive during the usual irradiation period and it gives rise to several gas-chromatographable minor products. By using a Hewlett-Packard Atomic Emission Detector set at the frequency for phosphorus (186 nm), it was possible to prove that none of these minor products contained phosphorus. Both 5a and 5b were completely consumed after 2-3 hours, and all phosphorus appeared in the expected polymeric forms based on P-O-P units, as evidenced in each case by ³¹P NMR⁵ signals in the regions -10 to -12 (terminal phosphate) and -22 to -25 (internal and cyclic phosphate). When ethanol was included in the photolysis medium, the self-condensation products were avoided and the major species detected by NMR were the expected O-ethyl phosphoramidates 8 and 9. These compounds are not very stable, and extensive to complete loss of the amino groups occurred during isolation attempts. The expedient was therefore taken of stabilizing the species by methylation with diazomethane; these products (10 and 11) were quite stable and sufficiently volatile to allow further characterization by GC-MS (details will be published elsewhere⁶).

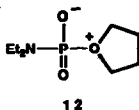


In both cases the major peak so identified was analyzed by mass spectrometry (Hewlett-Packard Mass Selective Detector) and found to give a spectrum consistent with the expected structure (for 10, M^+ 195, 10.1%, base peak m/z 152; for 11, M^+ 257, 33.4%, base peak m/z 134).

The photolyses were then conducted at about -75° by immersing the photolysis unit with the attached NMR tubes in a Dry Ice-pentane bath. When ethanol was present as a trap, the same products (8 from 5a, 9 from 5b) were obtained as when the photolyses were conducted at room temperature, based on direct ³¹P NMR and then examination of the methylation products by ³¹P NMR and GC-MS analysis. There was usually no residual starting material after 3 hrs of photolysis; the major phosphorus products were the expected 10 and 11, although usually minor signals indicated the presence of hydrolysis products of the metaphosphoramidates as well as of displacement of the amino groups.

These minor products, which were detectable (after methylation) by GC-MS, usually constituted only about 1-10% of the total phosphorus product. This experiment therefore demonstrated that the fragmentations to the desired metaphosphates occurred readily at -75°C .

In the next experiments, the photolyses were conducted at -75° in the *absence* of a trapping agent. The NMR tubes were maintained in the cold bath until they could be directly inserted in the probe of the NMR spectrometer pre-set at -75° . The ^{31}P NMR spectra were recorded at -75° , and then at temperatures elevated by 20-30° increments. The final spectrum was recorded after overnight standing at room temperature. The spectrum at -75° from the photolysis of 5a contained no P-O-P material as evidenced by the absence of signals in the δ -10 and δ -20 regions. These signals did appear on warming, and the solution after overnight standing contained phosphorus primarily in P-O-P form. This indicates that the metaphosphoramidate 6 had been preserved in the medium at -75° . Furthermore, at that temperature the only ^{31}P NMR signal was found at δ +12, and we attribute this signal to the species giving rise to the P-O-P final product. This signal diminished as the temperature was raised and was absent in the solution after overnight standing at room temperature. We assign this signal to *N,N*-diethylaminometaphosphoramidate (6), probably as a strongly solvated form represented in the extreme by 12. Powerful electrophiles such as SO_3 are well known to form such Lewis salts with cyclic ethers, and complexation of metaphosphates with dioxane, acetonitrile, etc., has long been suspected and represented by structures analogous to 12.⁷

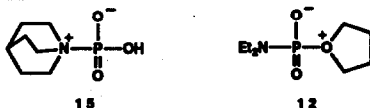


The photolysis of the mesitylamino derivative 5b at -75° gave very similar results. The only ^{31}P NMR signal observed at that temperature was found at δ +8.5 (weak, broad). This signal sharpened as the temperature rose, but diminished and finally was replaced by the typical P-O-P signals found in the room temperature photolyses at δ -10 to -12 and δ -22 to -25. An additional signal, presently unassigned, was occasionally seen at δ -5 in the final product.⁸

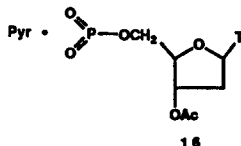
The critical experiment was then performed of adding the ethanol trapping agent (pre-chilled to -75°) to the -75° solutions from both starting materials 5a and 5b *after* the photolysis, so as to provide chemical proof that the metaphosphoramidate indeed existed in the medium. The addition of ethanol gave rise to the same major ^{31}P NMR signals for each as were obtained when the photolyses were done in its presence. As further proof, the methylation products gave the same ^{31}P NMR and GC-MS spectra for the major phosphorus product as were obtained with ethanol initially present. These results confirm that the two species preserved in solutions at -75° have the same chemical characteristics as the species of very high reactivity generated at room temperature, and are consistent with the presence of (solvated) metaphosphoramidates in the low-temperature media. The species can be preserved in the Dry Ice bath overnight, and perhaps longer, with no measurable decomposition, although they must be carefully protected from moisture.

There are no precedents in the literature for the ^{31}P spectra of free metaphosphoric acid derivatives. We are aware of two reports where ^{31}P NMR signals of short lifetime at or near room temperature were attributed to amine-stabilized metaphosphoric acid derivatives. Ramirez and Marecek⁹ observed a transient signal at δ +10.2 when 2,4-dinitrophenyl phosphate and quinuclidine were allowed to react in CH_2Cl_2 at 35°C ; they attributed this signal to the species 15, a Lewis salt of metaphosphoric acid. The similarity in shifts of this suspected species and those we have

observed for metaphosphoramidates 6 and 7 in THF is striking, but explicable in terms of structural similarity if the THF is fully coordinated as in structure 12.



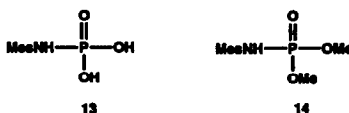
A signal at δ -5.1 was observed¹⁰ in a pyridine solution used for the reaction of 3'-O-acetylthymidine-5'-phosphate with tri-*iso*-propylbenzenesulfonyl chloride, and attributed to a pyridine-solvated metaphosphate (16). The signal vanished on addition of nucleophiles.



Important relevant observations have also been made by Meisel, who has obtained stable solid pyridine complexes of the P-chloro derivatives Cl-PO₂, Cl-P(S)O, and Cl-PS₂. The ³¹P NMR signal for the species PyrP(S)OCl appeared at δ +35¹¹; an X-ray analysis¹² of the ClPS₂ adduct shows the structure to be a donor-acceptor complex and not a betaine.

Acknowledgements. The support of this work by the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. Professor Peter C. Uden, Mr. Dwight Tshudy, and Mr. Thomas Dowling are thanked for the GC-MS determinations.

1. L. D. Quin, B. Pete, J. Szewczyk, and A. N. Hughes, *Tetrahedron Lett.* **29**, 2627 (1988).
2. L. D. Quin, N. D. Sadanani, and X.-P. Wu, *J. Am. Chem. Soc.* **111**, 6852 (1989).
3. L. D. Quin, J. Szewczyk, K. M. Szewczyk, and A. T. McPhail, *J. Org. Chem.* **51**, 3341 (1986).
4. L. D. Quin, C. Bourdieu, and G. S. Quin, to be published.
5. ³¹P NMR measurements were made on a Varian XL-300 spectrometer; signals are referenced to external 85% H₃PO₄ and are positive if downfield. For THF solutions, an insert of THF-d₈ was used as lock.
6. P. C. Uden, T. Dowling, and D. Tshudy, to be published.
7. F. H. Westheimer, *Chem. Rev.* **81**, 313 (1981).
8. This experiment is especially prone to complications by traces of water in the medium, which leads to 13 as a minor product (confirmed by methylation to 14 and GC-MS). We have also observed some displacement of the amino group under our experimental conditions, and this gives rise to methylated phosphate signals around δ ³¹P -1.



9. F. Ramirez and J. F. Marecek, *Tetrahedron* **35**, 1581 (1979).
10. D. G. Knorre, A. V. Lebedev, A. S. Levina, A. I. Rezvukhin, and V. F. Zarytova, *Tetrahedron* **30**, 3073 (1974).
11. M. Meisel and H. Grunze, *Z. anorg. allg. Chem.* **360**, 277 (1968).
12. M. T. Averbuch-Pouchot and M. Meisel, *Acta Cryst.* **C45**, 1937 (1989).

(Received in USA 2 August 1990)