

Synthesis of a Monophosphorus Analog of Hexamethylenetetramine

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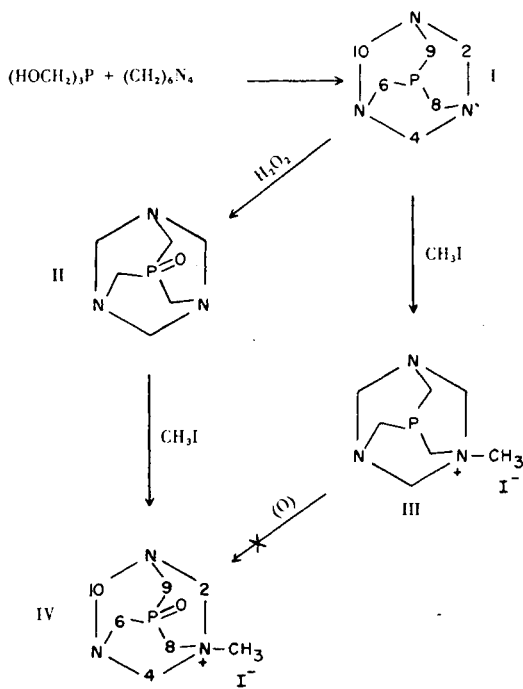
The reaction of sodium hydroxide neutralized tetrakis-(hydroxymethyl)phosphonium chloride (THPC) solutions with ammonia forms a polymeric product which is the basis for one of the commercial methods of flameproofing cotton (2). It has been shown that sodium hydroxide neutralized THPC solution, referred to as "tetrakis(hydroxymethyl)phosphonium hydroxide" (THPOH), is a mixture of products, principally tris(hydroxymethyl)phosphine (THP) and formaldehyde (3,4). Formaldehyde was also found to be the key to polymerization between THP and aqueous ammonia; a Mannich type mechanism has been proposed for this reaction (5).

While working with solutions containing excess formaldehyde, THP and ammonium hydroxide, we found that a 4:1 molar excess of formaldehyde to THP in solution with one mole of hexamethylenetetramine or the equivalent formaldehyde-ammonium hydroxide solution prevented polymerization. After evaporation of the solution a white crystalline compound was isolated. This solid was shown to be 1,3,5-triaza-7-phosphaadamantane (I) by elemental analysis, ir, and nmr spectra. The nmr spectrum of I was simple. The singlet

at δ 4.43 was assigned to the methylene protons at C-2, C-4, and C-10. That these methylene protons were all equivalent was unexpected since axial and equatorial differences would normally be predicted. The doublet centered at δ 3.9 ($J=9\text{Hz}$) was assigned to the methylene protons at C-6, C-8, and C-9. The integrated ratio of these bands was 1:1. The product was obtained in 40% yield based on THP. The use of methyl or ethyl alcohol as part of the solvent system produced a polymeric product whether excess formaldehyde was present or not. Although some formaldehyde is needed for polymer formation it is not known at this time why the excess of formaldehyde prevents polymerization.

The oxide (II), prepared as an additional proof of structure, gave excellent elemental analyses and molecular weight. Their spectrum showed the strong peak at 8.62 microns characteristic of the P=O stretch. The nmr spectrum of II also was simple. The singlet at δ 4.28 was assigned to the methylene protons at C-2, C-4, and C-10 and the doublet centered at δ 4.0 ($J=11\text{ Hz}$) was assigned to the methylene protons at C-6, C-8 and C-9. The larger coupling constant of these latter protons was caused by the deshielding effect of the phosphoryl group.

The methyl iodide derivative (III) of I also gave a good elemental analyses. Compound III, 1-methyl-1-azonia-3,5-diaza-7-phosphaadamantane iodide, was assigned this structure on the basis of the nmr spectrum. Although the nmr spectrum of III in dimethyl sulfoxide- d_6 had a complex of peaks from δ 5.1 to δ 3.78, the methyl protons were a singlet at δ 2.71. A doublet with a large coupling constant would be expected if the methyl group was bonded to the phosphorus atom (6). The ratio of the peaks were 4:1. Because tertiary phosphines have been shown to quaternize preferentially in competition with tertiary amines (7,8), the product III was unexpected. To help explain the results, the methyl iodide derivative of II was prepared. This derivative (IV) gave a good elemental analysis and the ir spectrum showed the strong peak at 8.42 microns characteristic of the P=O stretch. The nmr spectrum of IV showed a broad singlet at δ 5.0 assigned to the methylene protons C-2 and C-4, a complex of peaks centered at δ 4.32 assigned to the methylene protons C-6, C-8, C-9, and C-10, and a doublet ($J=3\text{ Hz}$) at δ 3.08 assigned to the methyl protons in the ratio of 4:8:3, respectively. The deshielding effect of the phosphoryl group had two effects: the chemical shift of the methylene protons C-2 and C-4 was



changed more than the chemical shift of the other methylene protons so that a clear separation of bands was possible; and the methyl protons were split into a doublet. Verkade *et al.* (9,10) have shown that this long range, four band phosphorus-proton coupling is expected. On this basis the structures of III and IV were assigned as shown.

The conversion of III to IV by chemical means was attempted using tertiary butylhydroperoxide and hydrogen peroxide under a variety of mild conditions. The only products of these reactions were brown, intractable residues. Efforts are being made to show by other chemical means that the quaternary salt formed is an ammonium salt rather than a phosphonium salt.

EXPERIMENTAL

1,3,5-Triaza-7-phosphaadamantane (I).

Tris(hydroxymethyl)phosphine (3.9 g., 80%, 0.024 moles) and formalin (8 g., 40%, 0.1 mole) were diluted with 70 ml. of water and cooled (0-5°). Hexamethylenetetramine (3.5 g., 0.1 mole) was added to the cold solution and the solution left at room temperature for about 15 hours. Evaporation at room temperature and recrystallization from ethanol led to 1.5 g. of I (40% yield).

Similar results were obtained when a freshly prepared solution of ammonia and formaldehyde was used in place of the hexamethylenetetramine. The infrared spectrum (potassium bromide) (Perkin-Elmer Model 137B Infracord) exhibited peaks at 3.52(m), 6.92(w), 7.02(w), 7.15(w), 7.4(w), 7.79(m), 8.12(s), 8.5(w), 9.12(m), 9.67(w), 9.9(s), 10.0(s), 10.32(s), 10.57(m), 11.27(w), 12.37(m), 12.6(m), 13.51(m), 14.5 μ (w). The nmr spectrum (Varian A-60A spectrometer) of a deuterium oxide solution of I at 60 MHz exhibited the following bands relative to an internal standard of sodium-3-trimethylsilyl-1-propane sulfonate: a singlet at δ 4.43 (NCH₂N) and a doublet (J=9 Hz) centered at δ 3.9 (PCH₂N) in the ratio of 1:1. Because I and hexamethylenetetramine share many of the same characteristics including high melting point (decomposition > 260) and low solubility in organic solvents, the best means of isolating I was by recrystallization from ethanol and monitoring the purity by use of proton nuclear magnetic resonance.

Anal. Calcd. for C₆H₁₂N₃P: C, 45.86; H, 7.70; N, 26.75; P, 19.71; mol. wt., 157. Found: C, 45.63; H, 7.70; N, 26.52; P, 19.83; mol. wt., 158. (boiling point elevation, water)

1,3,5-Triaza-7-phosphaadamantane 7-Oxide (II).

Compound I (0.5 g., 0.0032 mole) was dissolved in 20 ml. of methanol. Hydrogen peroxide (0.5 g., 30%, 0.0044 mole), diluted with 20 ml. of ethanol, was added slowly over 10 minutes and the total solution was left to stir for twenty minutes. Evaporation at room temperature and recrystallization from ethanol yielded 0.44 g. (80% yield) of II. The infrared spectrum (potassium bromide) showed peaks at 3.55(w), 7.0(m), 7.15(m), 7.25(w), 7.35(w), 7.6(w), 7.85(s), 8.15(m), 8.62(s), 9.16(m), 9.65(w), 10.0(s), 10.3(s), 10.6(w), 11.08(s), 12.4(s), 12.82(w), 13.5(w), 13.7 μ (w). The nmr spectrum of II in deuterium oxide exhibited a singlet at δ 4.28 and doublet (J=11 Hz) centered at δ 4.0 in the ratio of 1:1.

Anal. Calcd. for C₆H₁₂N₃OP: C, 41.62; H, 6.99; N, 24.27; P, 17.87; mol. wt. 173. Found: C, 41.75; H, 7.02; N, 24.15; P, 17.99; mol. wt. 169. (boiling point elevation, water)

1-Methyl-1-azonia-3,5-diaza-7-phosphaadamantane Iodide (III).

Compound I (0.5 g., 0.0032 mole) and methyl iodide (0.46 g., 0.0032 mole) were refluxed in 40 ml. of acetone for 1 hour. The solution was filtered to yield 0.91 g. of crude III (96% yield) [m.p. 203-204° (methanol-ethyl acetate)]. The infrared spectrum (potassium bromide) exhibited peaks at 3.5(m), 3.55(w), 6.97(s), 7.23(m), 7.3(w), 7.5(w), 7.65(s), 7.85(m), 7.95(m), 8.05(m), 8.17(m), 8.33(w), 8.8(m), 9.04(s), 9.25(s), 9.35(m), 9.57(w), 9.67(w), 9.38(s), 10.1(w), 10.26(s), 10.3(w), 10.51(w), 10.65(w), 10.96(s), 11.2(m), 11.7(w), 11.85(w), 12.23(m), 12.35(s), 12.9(w), 13.1(s), 13.65(m), 13.75(m), 14.65 μ (w). The nmr spectrum of II in dimethyl sulfoxide-d₆ had a complex of peaks from δ 5.1 to δ 3.78 and a singlet at δ 2.71 in the ratio of 4:1, respectively.

Anal. Calcd. for C₇H₁₅IN₃P: C, 28.11; H, 5.06; N, 14.05; P, 10.36; I, 42.43. Found: C, 28.06; H, 5.06; N, 14.26; P, 10.37; I, 42.43.

1-Methyl-1-azonia-3,5-diaza-7-phosphaadamantane 7-Oxide Iodide (IV).

Compound II (0.2 g., 0.00115 mole) and methyl iodide (0.2 g., 0.00141 mole) were refluxed in 20 ml. of methanol-20 ml. of ethanol solution. Evaporation down to one-third volume and addition of 20 ml. of ethyl acetate and filtration yielded 0.32 g. of crude IV (88% yield) [m.p. 213-214° (methanol-ethyl acetate)]. The infrared spectrum (potassium bromide) showed peaks at 3.45(w), 3.55(w), 6.92(m), 7.0(m), 7.12(w), 7.28(w), 7.5(w), 7.8(s), 7.91(m), 7.98(w), 8.11(m), 8.42(s), 9.11(m), 9.23(m), 9.3(w), 9.45(w), 9.88(m), 9.98(m), 10.25(s), 10.78(s), 11.05(m), 11.15(m), 11.48(w), 12.3(s), 12.68(w), 13.23(m), 13.38 μ (m). The nmr spectrum of a deuterium oxide solution of IV had a broad singlet at δ 5.0, a complex of peaks centered at δ 4.32, and a doublet centered at δ 3.08 with a coupling constant of 3 Hz (J_{PCNCH}) in the ratio of 4:8:3, respectively.

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