

Phosphaadamantanes. Synthesis of 2-Thia-1,3,5-triaza-7-phosphaadamantane
2,2-Dioxide and Derivatives

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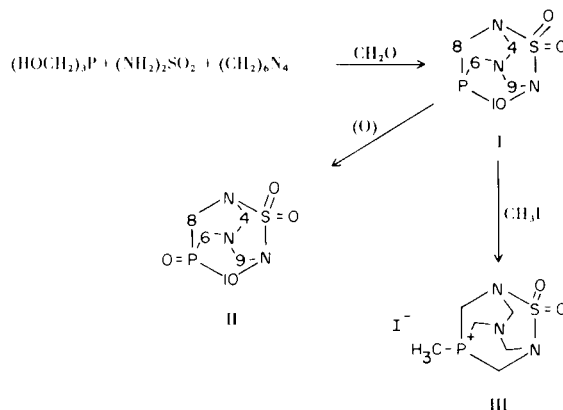
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Tris(hydroxymethyl)phosphine (THP) in the presence of excess formaldehyde, reacted with hexamethylenetetramine gives a phosphorus analog of hexamethylenetetramine, 1,3,5-triaza-7-phosphaadamantane (2). The product is the same if sodium hydroxide-neutralized tetrakis(hydroxymethyl)phosphonium chloride (Thpc) is substituted for THP and/or freshly prepared ammonia-formaldehyde mixtures for hexamethylenetetramine (3).

Paquin (4) had studied the reaction of sulfamide with formaldehyde and amines (ammonia) in preparing a sulfur containing hexamethylenetetramine, 2-thia-1,3,5,7-tetraazaadamantane 2,2-dioxide. Because Paquin used excess formaldehyde to promote precipitation of this compound, it was thought that the reaction of THP with sulfamide and ammonia in excess formaldehyde should proceed with little or no polymerization. However, at room temperature, an amorphous powder precipitated immediately and only a 29% yield of 2-thia-1,3,5-triaza-7-phosphaadamantane 2,2-dioxide (I) was extracted from this powder with hot ethanol. The ethanol insoluble residue melted over a wide range (130-230°) and its infrared spectrum indicated that it was polymeric. With hexamethylenetetramine as the source of ammonia the yield of I was raised to 66%. The small amount of polymer or amorphous powder which also precipitated amounted to only 0.2 g. per 3.3 g. of I.

The oxide (II) and methyl iodide (III) derivatives were prepared by the usual procedures. The oxide, however, melted at a lower temperature than the corresponding phosphine. The nmr spectrum of II was less complex than those of I and III. The singlet at δ 4.8 was assigned to the methylene protons at C-4 and C-9. This assignment was made on the basis that in the compound 1,3,5-triaza-7-phosphaadamantane 7-oxide this type of methylene protons, NCH₂N, showed a singlet at δ 4.28. The methylene protons at C-4 and C-9 appeared at a lower field in II doublet centered at δ 4.38 ($J = 10$ Hz) was assigned to the methylene protons at C-8 and C-10. This type of proton, PCH₂N, in the compound 7-phosphaadamantane 7-oxide showed a singlet at δ 4.0 but in II the deshielding effect of the sulfuranyl group caused the protons to appear at a lower field.

The doublet centered at δ 4.21 ($J = 10$ Hz) was assigned to the methylene protons at C-6. These protons were also affected by the deshielding effect, but not as much as the other protons because their adjunct nitrogen is an amine type and not an amide type. These doublets overlapped and the three resulting bands δ 4.47, δ 4.3, and δ 4.13 had an integrated ratio of 2:3:1, respectively.



EXPERIMENTAL

2-Thia-1,3,5-triaza-7-phosphaadamantane 2,2-Dioxide (I).

THP (3.9 g., 80%, 0.025 mole) was dissolved in formalin (20 ml., 40% 0.267 mole) and water (20 ml.). Sulfamide (2.4 g., 0.025 mole) and hexamethylenetetramine (3.5 g., 0.025 mole) were added together and dissolved in the solution at room temperature. The solution heated up slightly and over the next 24 hours a precipitate formed. Filtration, dissolution of the solid in 4 successive 30 ml. acetone washes and evaporation of the acetone yielded 3.42 g. of crude I (66% yield) [m.p. 274-275° (water)].

The infrared spectrum (potassium bromide) (Perkin-Elmer Model 137B Intracord) exhibited bands at 3.35 (w), 6.85 (w), 6.92 (w), 7.1 (w), 7.29 (m), 7.4 (m), 7.5 (m), 7.8 (m), 7.85 (m), 7.91 (m), 8.0 (m), 8.45 (s), 8.58 (s), 9.08 (m), 9.52 (m), 9.79 (m), 9.92 (m), 10.32 (m), 10.8 (m), 11.05 (m), 11.4 (w), 11.7 (w), 12.08 (s), 13.03 (m), 13.18 (m), and 13.8 μ (s). The nmr spectrum (Varian A-60A spectrometer) of a deuterated dimethyl sulfoxide solution of I at 60 MHz exhibited the following peaks relative to an internal standard (tetramethylsilane): a doublet centered at δ 3.9 with a coupling constant of 10 Hz (proton on C-6), and a series of five uneven peaks centered at 4.87 in the ratio of 2:3, respectively.

Anal. Calcd. for C₅H₁₀O₂PS: C, 28.98; H, 4.86; N, 20.28;

P, 14.95; S, 15.48; mol. wt. 207.2. Found: C, 28.85; H, 4.82; N, 20.26; P, 15.14; S, 15.62; ml. wt. 210.

2-Thia-1,3,5-triaza-7-phosphaadamantane 2,2,7-Trioxide (II).

Compound I (0.5 g., 0.0024 mole) and *t*-butyl hydroperoxide (70% solution, 0.3 g., 0.0024 mole) were stirred in a 25 ml. acetone-25 ml. ethanol solution for 1 hour at room temperature. The solution was filtered to yield 0.5 g. of crude II (92% yield) [m.p. 245-246° (propanol)].

The infrared spectrum (potassium bromide) showed bands at 3.31 (w), 6.81 (w), 6.92 (m), 7.05 (w), 7.29 (m), 7.4 (m), 7.62 (m), 7.73 (m), 7.85 (m), 7.93 (m), 8.05 (m), 8.38 (s), 8.5 (s), 8.6 (s), 9.14 (m), 9.55 (w), 9.77 (m), 9.9 (m), 10.2 (m), 11.1 (m), 11.8 (s), 12.7 (m), 12.8 (m), 13.13 (m), and 13.9 μ (s). The nmr spectrum of a deuterated dimethylsulfoxide solution of II showed a pair of overlapping doublets centered at δ 4.3 and a singlet at δ 4.8 (protons on C-4 and C-9) in the ratio of 6:4, respectively. One doublet was centered at δ 4.38 ($J = 10$ Hz; protons on C-8 and C-10) and the other doublet was centered at δ 4.21 ($J = 10$ Hz; protons on C-6); The result of the overlapping doublet was three peaks, δ 4.47, δ 4.3, and δ 4.13 which had an integrated ratio of 2:3:1, respectively.

Anal. Calcd. for $C_5H_{10}N_3O_3PS$: C, 26.90; H, 4.52; N, 18.83; P, 13.87; S, 14.37; mol. wt. 223.2. Found: C, 27.11; H, 4.55; N, 18.98; P, 14.10; S, 14.20; mol. wt. 227.

1-Thia-2,4,6-triaza-8-methyl-8-phosphoniaadamantane 1,1-Dioxide Iodide (III).

Compound I (0.35 g., 0.0017 mole) and methyl iodide (0.3 g., 0.002 mole) were refluxed for 24 hours in a 5 ml. chloroform-40 ml. ethyl acetate solution. The solution was filtered to yield 0.45 g. of crude III (76% yield) [m.p. 202-203° (methanol-ethyl acetate)].

The infrared spectrum (potassium bromide) showed bands at 3.35 (m), 3.4 (w), 6.84 (w), 6.92 (w), 7.05 (w), 7.2 (s), 7.4 (m), 7.63 (w), 7.85 (m), 8.02 (m), 8.3 (w), 8.41 (s), 8.55 (s), 8.92 (w), 9.18 (w), 9.45 (w), 9.54 (w), 9.72 (w), 9.82 (m), 10.21 (m), 10.45 (m), 10.63 (w), 10.7 (w), 10.93 (m), 11.1 (m), 11.38 (w), 11.7 (w), 12.05 (s), 12.4 (m), 12.65 (m), 12.9 (m), 13.25 (m), 13.5 (broad) (w), and 14.05 μ (s). The nmr spectrum of a deuterated dimethylsulfoxide solution of III showed a doublet centered δ 2.03 with a coupling constant of 17 Hz ($P-CH_3$) and a complex of peaks centered at δ 4.93 in the ratio 3:10, respectively.

Anal. Calcd. for $C_6H_{13}N_3O_2PSI$: C, 20.64; H, 3.75; N, 12.04; P, 8.87; S, 9.19; I, 36.35. Found: C, 20.82; H, 3.75; N, 12.14; P, 8.90; S, 9.34; I, 36.52.

REFERENCES

- (1) One of the facilities of the Southern Region, Agricultural Research Service, U.S. Department of Agriculture.
- (2) D. J. Daigle, A. B. Pepperman, Jr., and S. L. Vail, Jr., *J. Heterocyclic Chem.*, **11**, 407 (1974).
- (3) D. J. Daigle and A. B. Pepperman, Jr., in review.
- (4) A. M. Paquin, *Angew. Chem.*, **A60**, 3.6 (1948).