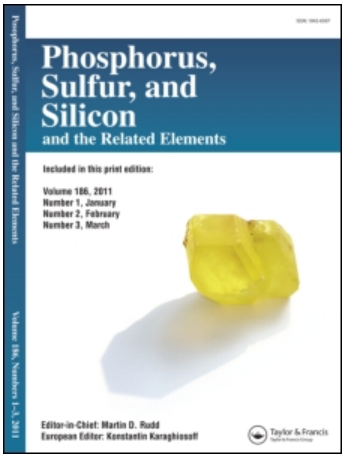

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Mualla, Maher and Macomber, Roger S.(1990) 'REACTIONS OF 1,2-OXAPHOSPHOLENE-2- OXIDES 5.[1] CONSEQUENCES OF REDUCTION', Phosphorus, Sulfur, and Silicon and the Related Elements, 47: 1, 15 — 20
To link to this Article: DOI: 10.1080/10426509008046840
URL: http://dx.doi.org/10.1080/10426509008046840

Phosphorus, Sulfur, and Silicon, 1990, Vol. 47, pp. 15–20
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REACTIONS OF 1,2-OXAPHOSPHOLENE-2-OXIDES 5.[1] CONSEQUENCES OF REDUCTION

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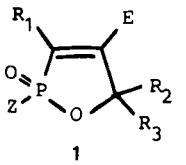
(Received April 5, 1989)

The reactions of 5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-oxide (**1a**) with a variety of reducing agents have been studied. Catalytic hydrogenation of **1a** (Pd/C) resulted in reduction of the C=C bond, giving 5,5-dimethyl-2-phenyl-1,2-oxaphospholane 2-oxide (**6**). By contrast, hydroboration with excess BH_3-THF left the double bond intact, and reduced the P=O group. The product, 5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene (**7**), is itself unstable, but it can be isolated as the novel borano complex **8**. The P=O group in **1a** can also be reduced by trichlorosilane. In this case the unstable **7** was isolated as the corresponding tungsten pentacarbonyl complex **10**. Conversion of **1a** to the corresponding P-sulfide **9** was readily accomplished, but **9** could not be selectively reduced with metallic sodium. Lithium aluminum hydride reduced both the C=C bond and the P=O group, but the presumed product 5,5-dimethyl-2-phenyl-1,2-oxaphospholane (**5**) was unstable and underwent ring opening to a compound tentatively identified as (3-hydroxy-3-methylbutyl) phenylphosphinic acid (**3**), which is in equilibrium with its phosphine oxide tautomer **4**.

Key words: 1,2-Oxaphospholene-2-oxides; cyclic phosphinate; reduction; phosphoryl-borane complex; trichlorosilane; hydrogenation.

INTRODUCTION

Over the past fifteen years our attention has been directed toward a general synthetic route to 1,2-oxaphosphol-3-ene-2-oxides (**1**) starting from propargyl alcohols.[3] Because this heterocyclic system had received no systematic attention



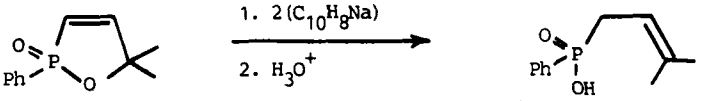
1

a: $R_1 = E = H$, $R_2 = R_3 = CH_3$, Z = Ph

prior to our work, we have also devoted considerable effort to studying the properties and reactivity patterns of **1**.[1,4] Being a cyclic phosphonate (if Z = OR) or phosphinate (if Z = e.g. Ph) with a polar and electron-poor carbon-carbon double bond[1,3,4a] and an allylic hydrogen (if R_2 or R_3 = H), heterocycle **1** incorporates considerable functionality into a small molecule, thereby promising a rich and varied chemistry. It also constitutes the phosphorus analog of a butenolide, suggesting the possibility of significant pharmacological properties.

Previously, we reported on the mechanism of nucleophilic substitution at phosphorus (resulting in both exo- and endocyclic cleavage),[4b–d] and the response

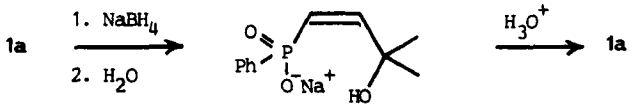
of the carbon-carbon double bond in model system **1a** toward electrophiles, oxidizing agents, nucleophiles, and 1,3-dienes.[1] As part of these studies we noted that **1a** reacted with one electron reducing agents such as sodium naphthalenide to give phosphinic acid **2**, the product of net reduction at both C_3 and C_5.[1] We now wish to describe our studies on the reaction of **1a** with a variety of other reducing agents.



1a **2**

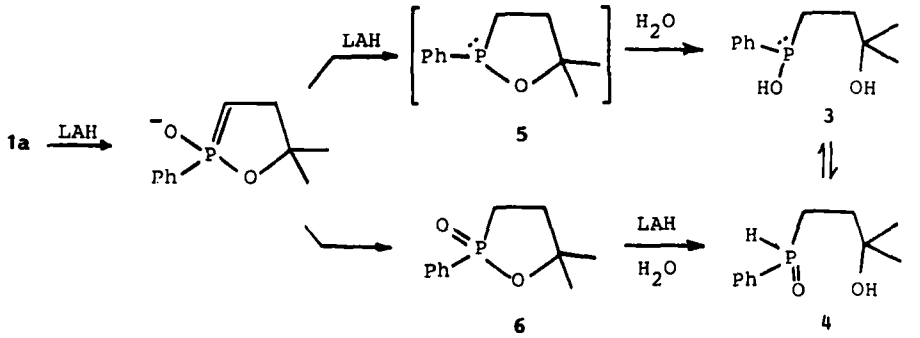
RESULTS AND DISCUSSION

Structure 1 presents two obvious sites for reduction, the phosphoryl group and the carbon-carbon double bond. Our initial intent was to determine which reducing agents could selectively reduce just one of the two functional groups, and which would reduce both. Because of the electron-poor nature of the C=C bond in **1**, we first examined nucleophilic hydride donors. Sodium borohydride (in ethanol) reduced neither functional group in **1a**, though the hydroxide ion generated during workup led to reversible hydrolytic ring opening of the type we have reported before.[4b,c] By contrast, the reaction of **1a** with lithium aluminum hydride gave a product tentatively identified as phosphinous acid **3** (in equilibrium with its tautomer **4**),[5] the product of reduction at both the P=O group



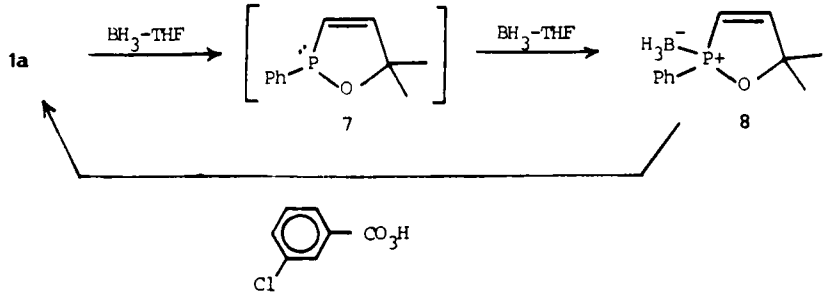
and the C=C bond. It is reasonable to suspect that the polar double bond was reduced first, but we were not able to isolate any partially reduced products such as **5** or **6** (*vide infra*).

The C=C bond in **1a** is sterically protected above and below the plane of the ring by the phosphorus substituents (oxygen and phenyl) and the *gem*-dimethyl



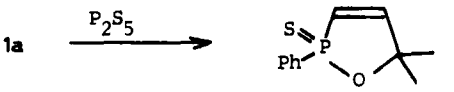
groups at C_5. It was, therefore, somewhat surprising that **1a** underwent catalytic hydrogenation (Pd/C) to give heterocyclic phosphinate **6** as the only isolable product. The fact that **6**, with its phosphoryl group intact, survived extended periods in ethanol demonstrates that it is reasonably stable with respect to solvolytic ring opening.

Borane-tetrahydrofuran complex, which is known to reduce a variety of carbon-carbon multiple bonds, failed to react with the C=C bond in **1a**. But a reaction *did* occur, and we were able to isolate a new compound whose ^1H nmr spectrum was very similar to that of the starting material.[6] However, its infrared spectrum was quite different, showing no P=O absorption, but instead a strong band at 2380 cm^{-1} attributable to B–H stretch.[7] The mass spectrum of the compound exhibited a molecular ion at m/z 192 (**7**, $C_{11}H_{13}OP$), but elemental analysis indicated a molecular formula of $C_{11}H_{16}BOP$. We therefore assign to this compound structure **8**, the borano derivative of **7**.[8] Thus, BH_3-THF is capable of reducing the phosphoryl group, leaving the C=C bond intact.



Although stable complexes of borane with various trivalent organo-phosphorus compounds are well known,[8,9,10] we have found no reports in the literature describing borane complexes of phosphinous esters. Therefore, we performed several preliminary experiments to determine the properties and hydroborating capacity of **8**. The mass spectrum (vide supra) indicated that the borane was readily lost in the gas phase. We also found that **8** regenerated **1a** when treated with m-chloroperbenzoic acid. For comparison, the borane complex of triphenylphosphine is inert toward hydrogen peroxide.[10] More significantly, **8** was found to mimic BH_3-THF in its ability to serve as a hydroborating agent. Both compounds react with phenylacetylene to give (after oxidative workup) a mixture of several products, the major ones being acetophenone and phenylacetaldehyde.[11]

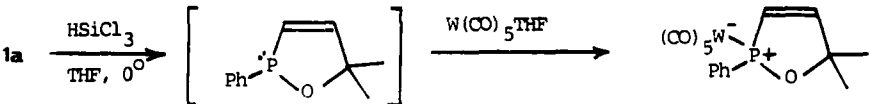
As part of our search for a direct route to deoxygenated product **7**, we noticed a report in the Russian literature[12] that the phosphoryl group of a 1,2-oxaphosphol-4-ene 2-oxide could be reduced by first converting the P=O to P=S, then reducing the sulfide with metallic sodium. The C=C bond (in the δ^4 position) survived these conditions. We were able to convert **1a** to the corresponding sulfide **9** with P_2S_5. But attempts to reduce **9** with sodium proved futile. Temperatures high enough to bring about any reaction provided intractable mixtures from which no **7** could be detected. It is likely that the δ^3 double bond in **9** is subject to the same type of one electron reduction as seen with **1a**.[1]



9

Finally, we explored the reaction of **1a** with trichlorosilane. This compound is known to be an effective reducing agent for phosphine oxides,[13] though in one instance the C=C bond of a phosphol-3-ene oxide was reduced in preference to the P=O group.[14] With considerable effort we were able to effect the reduction of **1a** to **7**, which was trapped as its tungsten pentacarbonyl adduct **10**.[15] Attempts to isolate **7** itself were unsuccessful owing to its instability.

To summarize, cyclic phosphinate **1a** can be reduced at either the P=O group or the C=C bond, or both, by a variety of reducing agents. The C=C bond can be readily hydrogenated (Pd/C), without reducing the P=O group. The P=O group can be reduced, leaving the C=C bond intact, by either BH_3-THF or



7 10

trichlorosilane. In either case, the product (**7**) is quite unstable and must be trapped as either the BH_3 adduct, or the tungsten pentacarbonyl complex. Lithium aluminum hydride reduced both the C=C bond and the P=O group, but the resulting intermediate (**5**?), like **7**, is unstable and undergoes ring opening. Attempted reduction of the sulfide analog of **1a** (**9**) with metallic sodium gave only intractable mixtures.

EXPERIMENTAL SECTION

General. The following instruments were used in this work: ir spectra, Perkin-Elmer Models 700 and 599; ^{1}H nmr spectra, IBM NR-80 and Nicolet NT-300 (deuteriochloroform solution); mass spectra, Hewlett-Packard HP-5995C GC/MS (low resolution) and Kratos MS-80/D555 (high resolution). Melting points were determined using an oil bath and are uncorrected. Column chromatography was performed with Merck silica gel 60. THF was dried by distillation from potassium. Elemental analyses were performed by Galbraith Laboratories.

Reduction of 5,5-Dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-Oxide (**1a**) *with LAH.* A suspension of 100 mg (2.63 mmol) lithium aluminum hydride and 500 mg (2.40 mmol) **1a**[1] in 20 mL anhydrous THF was stirred for 3 h at 0°C. During this period the suspension took on a drab green color. Water (2 mL) was added and the mixture filtered. The filtrate was dried ($MgSO_4$) and rotary evaporated to give an oil with a strong phosphine-like odor. Column chromatography (8 g silica gel, eluting with ethyl acetate) gave 340 mg (62%) of a colorless oil which was homogeneous by tlc. This material is tentatively identified as (3-hydroxy-3-methylbutyl) phenylphosphinic acid (**3**);[5] ir: 3330, 2960, 1150 cm^{-1}; ^{1}H nmr: δ1.22 and 1.23 (singlets, total 6H), 1.80 and 2.16 (AA'BB' multiplets, total 4H), 3.71 (s, 2H),[16] 7.56 and 7.75 (multiplets, total 5H); ms: m/z 212.0967 ($M^{\cdot+}$), calc'd for $C_{11}H_{17}O_2P$, 212.0963.

Catalytic Hydrogenation of **1a**. A solution of 500 mg (2.40 mmol) **1a** in 70 mL absolute ethanol containing 70 mg of palladium on charcoal was subjected to 30 psi hydrogen at room temperature for 18 h. The suspension was filtered, rotary evaporated, and chromatographed (18 g of silica gel, eluting with chloroform). This resulted in 340 mg (68%) of 5,5-dimethyl-2-phenyl-1,2-oxaphospholane

2-oxide (**6**) as a colorless solid with mp 55–58°; ir: 3045, 2960, 1430, 1370, 1220 cm^{-1}; ^1H nmr: δ 1.53 (s, 3H), 1.65 (s, 3H), 2.2 (m, 4H), 7.5 and 7.8 (multiplets totalling 5H); ms: m/z 210.0810 ($M^{\cdot+}$, calc'd for $C_{11}H_{15}O_2P$ 210.0797), 195, 182, 167, 142, 124, 91, 77.

Anal. Calc'd: C, 62.85% H, 7.19%
Found: C, 62.79%; H, 7.27%

Reaction of **1a** *with Borane-Tetrahydrofuran Complex.* To a solution of 1.00 g (4.81 mmol) **1a** in 20 mL dry THF was added 11.0 mL (11.0 mmol) 1 M BH_3-THF complex (Aldrich). After 5 h at room temperature, the mixture was rotary evaporated and chromatographed (20 g of silica gel, eluting with 3/7 cyclohexane/chloroform). This provided 740 mg (74%) of 2-borano-5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene (**8**) as a stable white solid with mp 56–58°; ir: 3045, 2980, 2380, 1590, 1050 cm^{-1}; ^1H nmr: δ 1.51 (s, 3H), 1.59 (s, 3H), 6.25 (dd, J = 37.5 and 7.9 Hz, 1H), 6.89 (dd, J = 31.8 and 7.9 Hz, 1H), 7.5 and 7.75 (multiplets totalling 5H); ms: m/z 192 ($M^{\cdot+}$ —BH_3), 177, 129, 109, 99, 77.

Anal. Calcd for $C_{11}H_{16}BOP$: C, 64.12%; H, 7.82%; B, 5.25%.
Found: C, 63.82%; H, 7.71%, B, 5.95%.

Reaction of **8** *with m-Chloroperbenzoic Acid.* A mixture of 10 mg (0.05 mmol) **8** and 40 mg (0.24 mmol) m-chloroperbenzoic acid in 10 mL chloroform was refluxed for 3 h. The solution was washed with 1 × 15 mL 5% aqueous sodium bicarbonate, dried ($MgSO_4$), and rotary evaporated. Chromatography on 6 g of silica gel (eluting with chloroform) gave 8 mg (80%) of **1a**.[1]

Reaction of **8** *with Phenylacetylene.* A mixture of 50 mg (0.23 mmol) **8** and 25 mg (0.23 mmol) phenylacetylene in 10 mL anhydrous THF was heated to reflux for 10 h. After the mixture cooled, 10 mL of 3 N sodium hydroxide was added, followed by 3 mL 30% hydrogen peroxide. The resulting mixture was stirred for 2 h, and then extracted with 3 × 20 mL ether. The combined extracts were filtered through silica gel, and evaporated to give 15 mg of a mixture of five components (by tlc). The two major ones were identical (tlc) with authentic acetophenone and phenylactaldehyde.[11]

Reaction of **1a** *with Diphosphorus Pentsulfide.* A mixture of 300 mg (1.44 mmol) **1a** and 64.0 mg (0.144 mmol) P_2S_5 was heated to 150° for 90 m. Kugelrohr distillation at 2 mm and 160° afforded 236 mg (73%) of 5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene 2-sulfide (**9**) as a yellow oil; ir: 3045, 2961, 2905, 1730, 1585, 1430, 1350, 1305, 1165, 950, 905, 845, 805, 750 (P═S), 670 cm^{-1}; ^1H nmr: δ 1.59 (s, 3H), 1.68 (s, 3H), 6.19 (dd, J = 34.3 and 8.0 Hz, 1H), 6.90 (dd, J = 35.4 and 8.0 Hz, 1H), 7.3–8.2 (m, 5H); ms: m/z 224.0419 (calc'd for $C_{11}H_{13}OPS$: 224.0426).

Attempted Reduction of **9** *with Sodium Metal.* A mixture of 68 mg (2.95 mg-atom) of sodium and 200 mg (0.89 mmol) **9** in 20 mL dry toluene was heated to 110° for 2 h. Sodium sulfide was removed by filtration, and the filtrate was rotary evaporated. Tlc of the residue indicated the presence of at least four products. By contrast, **9** could be recovered unchanged after 24 h at 25°C in the presence of freshly cut sodium metal.

Reaction of **1a** *with Trichlorosilane.* To a solution at 0°C of 200 mg (0.96 mmol) **1a** in 15 mL anhydrous THF was added 1.0 mL (6.72 mmol) trichlorosilane. The solution was stirred for 20 m, then it was added to a second solution of $W(CO)_5$-THF [prepared by irradiating 2.80 g (3.84 mmol) $W(CO)_6$ in 50 mL dry THF through quartz with uv light from a 450 W medium pressure Hanovia lamp for 40 m.[17]] The reaction mixture was stirred for 6 h at 0°C, after which it was rotary evaporated and chromatographed (15 g silica gel, eluting with 3/7 cyclohexane/chloroform). This afforded 258 mg (52%) of 5,5-dimethyl-2-phenyl-1,2-oxaphosphol-3-ene tungsten pentacarbonyl as an unstable colorless solid with mp 99–105°; ir: 3050, 2980, 1910, 1590, 1050 cm^{-1}; ^1H nmr: δ 1.34 (*s*, 3H), 1.59 (s, 3H), 6.53 (dd, 29.3 and 2.2 Hz, 1H), 7.02 (dd, J = 34.1 and 2.2 Hz, 1H), 7.4–7.7 (m, 5H); ms: m/z 515.9987 (calc'd for $C_{16}H_{13}O_6P^{184}W$: 515.9960), 488, 432, 374, 296, 129.

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5. The ir spectrum of **3** exhibits weak broad bands for the P=O group (1190 cm^{-1}) and P—H (2300–2400 cm^{-1}). In addition, there is a weak doublet in the ^1H spectrum at δ 7.54 (J = 510 Hz). This indicates that **3** exists in tautomeric equilibrium with **4**. The relative amounts of these tautomers is nearly equal, judging from the intensities of their gem-dimethyl singlets.
6. For comparison, the ^1H nmr spectrum of **1a** shows the following signals: δ 1.58 (s, 3H), 1.67 (s, 3H), 6.18 (dd, J = 33.5 and 8.2 Hz, 1H), 7.08 (dd, J = 40.1 and 8.2 Hz, 1H), 7.4–8.0 (m, 5H).[1]
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