Novel Heterocycles. 10. Reactions of 1,3,2-Benzodiazaphosphorin-4(1*H*)-one 2-Oxides

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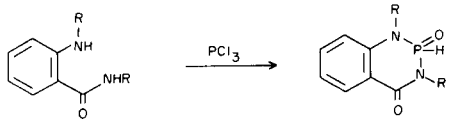
Reactions of 1,3-disubstituted-2,3-dihydro-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-oxides (**1**) with various electrophiles were investigated. The treatment of **1** with aldehydes in the absence of a basic catalyst directly afforded alcohols **7a-h** in good yield. The product from the reaction of **1** with chloral, on treatment with sodium hydride, resulted in the formation of a dichloroepoxide (**8**). When **1** was allowed to react with isocyanates or isothiocyanates in the presence of triethylamine, amides **10a-e** and thioamide **11** were produced in good yields. Compounds **1a** and **1b** were readily halogenated on their phosphorus atom by treatment with either carbon tetrachloride or carbon tetrabromide and triethylamine. The *P*-chloro compound **12a** reacted with ethanol to furnish the *P*-ethoxy derivative **13** and, in an attempt to react **12a** with bis(2-chloroethyl)-amine, anhydride **14** was formed in high yield. Spectral data for the majority of the products are also discussed.

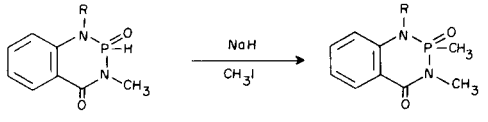
J. Heterocyclic Chem., **20**, 331 (1983).

In a previous report (2), the reaction between *N*-substituted anthranilamides and phosphorus trichloride to produce 1,3,2-benzodiazaphosphorins (**1**) was described.



1

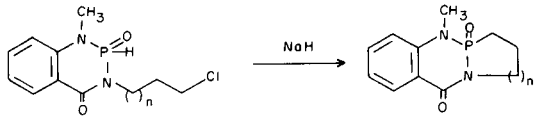
The following paper (3) began to explore the chemistry of this interesting ring system, where the reactivity of the posphorus atom as a nucleophile in alkylation reactions was investigated. When compounds **1a** and **1b** were treated with sodium hydride and methyl iodide, the corresponding *P*-methylated products **2a** and **2b** were isolated.



1a, R = CH_3
1b, R = C_6H_5

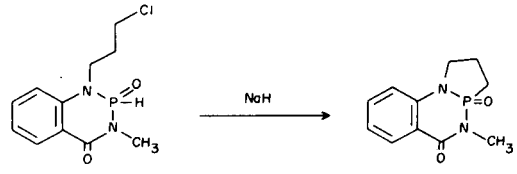
2a, R = CH_3
2b, R = C_6H_5

The scope of the reaction was expanded to include the intramolecular alkylation of **3a, 3b** and **5** which afforded the novel tricyclic phosphorus heterocycles **4a, 4b** and **6**.



3a, n = 1
3b, n = 2

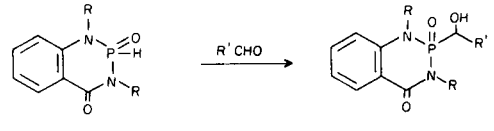
4a, n = 1
4b, n = 2



5 **6**

The purpose of this paper is to describe additional chemistry associated with the phosphorus atom in compounds of type **1** and to show the variety of products available from these transformations.

The initial reaction chosen for investigation was that with aldehydes due to their desired electrophilic character. When compounds of type **1** are allowed to react with a variety of aldehydes, alcohols **7a-h** (Table 1) are isolated in good yields. The reaction proceeds smoothly without catalyst and the reaction mixtures are usually clean, only requiring a short column of silica gel to remove any polar material.



1 **7a-h**

Initially, the reaction of **1a** with benzaldehyde in dioxane was performed at room temperature and after 18 hours, approximately 40% conversion to **7a** took place. Additional reaction time does not appreciably change the ratio of product and starting materials. However, when heated at 50-55° the condensation is complete within 48 hours.

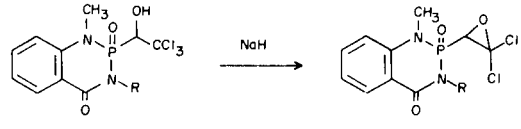
When chloral, a much more reactive aldehyde, is used instead of benzaldehyde the reaction is complete within 3 hours at room temperature and **7f** is isolated in 68% yield.

The times of formation of **7g** and **7h** are equally as short as **7f**, however the reactions were allowed to continue for 18 hours.

The spectral characteristics of compounds **7** are as follows: in the infrared spectrum (chloroform), the OH absorption appears between 3340 and 3220 cm^{-1}. The frequency for the amide absorption falls within the range of 1690-1660 cm^{-1} while a moderately intense band characteristic for the P=O stretching vibration is observed between 1350 and 1330 cm^{-1}.

In the nmr spectra, the proton in position 5 of the benzodiazophosphorin system (peri to the amide carbonyl) is observed as a multiplet between δ 8.15-8.0 (deuteriochloroform) or δ 7.9 (DMSO-d_6). The *N*-methyl groups of the parent system (*e.g.* **1a**, deuteriochloroform) exhibit pronounced PNCH couplings (2). Both methyl groups appear as doublets nearly superimposable on one another at δ 3.25, however the methyl at position 1 has a coupling constant of 9 Hz while the 3-methyl has a J value of 8 Hz. In compounds **7**, the methyl groups fall in approximately the same position but are usually seen as broadened doublets, multiplets (actually several sets of overlapping doublets) or a combination of both (10). In the case of **7c**, where DMSO-d_6 is used as the solvent, one methyl group is observed as a multiplet centered at δ 3.3 while the other (a slightly broadened doublet, J = 7 Hz) is shifted upfield to δ 2.85. The asymmetric nature of the phosphorus atom plus the newly formed adjacent asymmetric carbon possessing the hydroxyl function results in a molecule with two chiral centers and it is the resulting mixture of diastereomers which is responsible for the additional complexity of the nmr spectra. The methinyl proton adjacent to the hydroxyl group appears either as a multiplet or two overlapping doublets generally between δ 5.4-5.1. In the case of **7a**, deuterium exchange exposes the PCH coupling and the resulting signal is seen as a slightly broadened doublet with a coupling constant of 9 Hz.

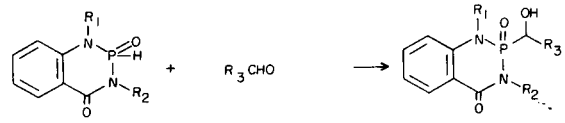
Compounds **7f-7h** represent interesting intermediates with the possibility of further transformations. It has been reported that the trichloromethylcarbinol function, when treated with base, forms a dichloro epoxide (11,12). The general instability of this epoxide functionality usually requires its formation *in situ*, however in certain instances isolation and characterization have been achieved (13).



7f, R = CH_3 **8a**, R = CH_3
7h, R = CH_2CH_2Cl **8b**, R = CH_2CH_2Cl

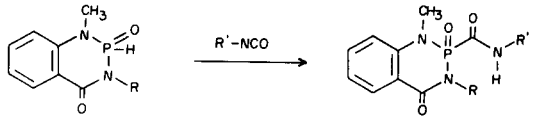
When a solution of **7f** in dioxane is treated with sodium hydride for 18 hours at room temperature, a new product forms, and after column chromatography the stable dichloro epoxide **8a** is isolated in 56% yield. Its infrared spectrum exhibits the characteristic epoxide C-H stretching vibration (14) at 3090 cm^{-1} while the amide and P=O frequencies absorb at 1690 and 1350 cm^{-1}, respectively. In the nmr spectrum, the N-CH_3 (position 1) ap-

Table 1



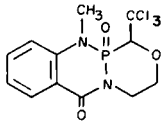
Compound No.	R_1	R_2	R_3	Reaction Time (hr)	Mp °C	Yield %	Molecular Formula	Analysis Calcd. (Found) C	H	N
7a	Methyl	Methyl	Phenyl	48	196-198	81	$C_{16}H_{17}N_2O_3P$	60.8	5.4	8.9
								(61.2	5.4	8.8)
7b	Methyl	2-Chloro-ethyl	Phenyl	48	145-160	92	$C_{17}H_{18}ClN_2O_3P$	56.0	5.0	7.7
								(55.9	5.1	7.6)
7c	Methyl	Methyl	3-Trifluoro-methylphenyl	48	175-195	58	$C_{17}H_{16}F_3N_2O_3P$	53.1	4.2	7.3
								(52.8	4.5	7.3)
7d	Methyl	Methyl	2-Furyl	48	131-134	67	$C_{14}H_{15}N_2O_4P$	54.9	4.9	9.1
								(55.1	5.0	9.1)
7e	Methyl	Methyl	2-Thienyl	120	120-124	49	$C_{14}H_{15}N_2O_3PS$	52.2	4.7	8.7
								(51.9	4.6	8.7)
7f	Methyl	Methyl	Trichloro-methyl	3	186-189 dec	68	$C_{11}H_{12}Cl_3N_2O_3P$	36.9	3.4	7.8
								(37.0	3.5	7.7)
7g	Benzyl	Methyl	Trichloro-methyl	18	180-183	73	$C_{17}H_{16}Cl_3N_2O_3P$	47.1	3.7	6.5
								(46.7	3.9	6.3)
7h	Methyl	2-Chloro-ethyl	Trichloro-methyl	18	185-187	60	$C_{12}H_{13}Cl_4N_2O_3P$	35.5	3.7	6.9
								(35.9	3.4	7.0)

Table 2



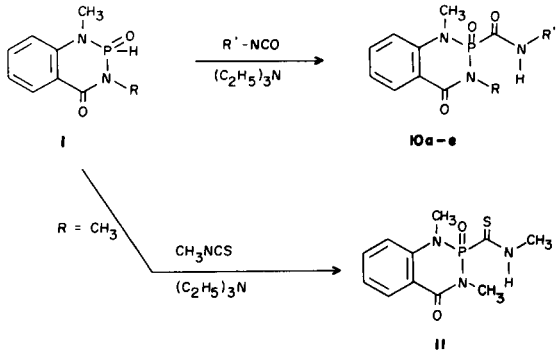
Compound No.	R	R'	Mp °C	Yield %	Crystallization Solvent	Molecular Formula	Analysis Calcd. (Found) C	H	N	Cl
10a	Methyl	Phenyl	208-209	71	Methylene chloride/ ethanol	$C_{16}H_{16}N_3O_3P$	58.3 (58.5	4.9 4.8	12.8 12.9)	
10b	Methyl	2-Trifluoro-methylphenyl	135-138	73	Methylene chloride/ ether	$C_{17}H_{15}F_3N_3O_3P$	51.4 (51.3	3.8 4.0	10.6 10.4)	
10c	Methyl	Methyl	178-180	87	Methylene chloride/ ethyl acetate	$C_{11}H_{14}N_3O_3P$	49.4 (49.3	5.3 5.5	15.7 15.7)	
10d	2-Chloro-ethyl	methyl	183-186	70	Methylene chloride/ ethyl acetate	$C_{12}H_{15}ClN_3O_3P$	45.6 (45.3	4.8 4.9	13.3 12.9	11.2 11.4)
10e	Methyl	Carbethoxy-methyl	132-135	53	Methylene chloride/ ether	$C_{14}H_{18}N_3O_5P$	49.6 (49.2	5.4 5.6	12.4 12.3)	

pears as a doublet at δ 3.35 with a coupling of 9 Hz, while the methyl at position 3 is also seen as a double at δ 3.3 with a slightly smaller coupling of 8 Hz.



9

An analogous reaction of **7h** with sodium hydride was performed to investigate whether a competitive cyclization of the 3-(2-chloroethyl) group would produce tricycle **9**. The reaction was allowed to proceed for three hours and after work-up, the only new product that was isolated was the epoxide **8b**, formed in 44% yield. Apparently none of compound **9** was produced, the remainder of the reaction mixture being a small amount of unreacted starting material and polar decomposition products. The infrared spectrum of **8b** exhibits the epoxide C-H frequency at 3095 cm^{-1} and in the nmr spectrum, the methyl signal is seen as a doublet (J = 9 Hz) at δ 3.35.



I **10a-e** **II**

Having observed the encouraging results with aldehydes, the isocyanate and isothiocyanate groups appeared to be the next logical electrophilic species to study in reactions with **1**. Since the condensation of **1** with aldehydes required no catalysts to produce the alcohols **7**, the initial attempt at reactions of **1** with isocyanates was performed also without benefit of catalyst. Stirring a solution of equimolar amounts of **1a** and phenylisocyanate in dry tetrahydrofuran at room temperature surprisingly does not result in any appreciable reaction even after 24 hours. Attempts to force the condensation thermally by refluxing the mixture only results in extensive decomposition of the reactants. However, when the reaction is performed with the addition of one equivalent of triethylamine, after 3 hours at 50-55°, complete reaction is observed. Work-up consists simply of removing the solvent and recrystallization to furnish analytically pure **10a** in 71% yield. The reaction appears to be general and the results of the reaction of **1** with a variety of isocyanates are listed in Table 2 (yields range from 53-87%).

The infrared spectra of compounds of type **10** (taken in chloroform) exhibit an N-H band between 3480-3400 cm^{-1}. The amide carbonyl absorptions fall between 1680-1660 cm^{-1} and in all cases the P=O vibration is seen at 1330 cm^{-1}. In the case of **10e**, the ester carbonyl absorbs at 1740 cm^{-1}. The nmr data pertaining to the shifts and coupling constants for the *N*-methyl groups and the H-5 aromatic proton in compounds **10a-10e** are listed in Table 3. Again, the methyl group with the larger J value resides in position 1 and is further downfield. In compounds **10c** and **10d** the signal for the *N*-methyl of the amide function is seen as a multiplet at δ 2.95 and 2.90, respectively. In compound **10e** the methylene adjacent to the nitrogen and the ester CH_2 fall as overlapping signals and are observed as a

multiplet between δ 4.5-3.9 while the methyl associated with the ester group is seen as a triplet at δ 1.15.

Table 3

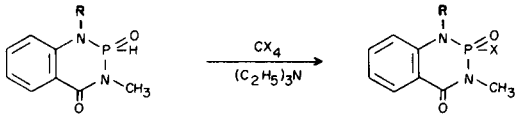
NMR Data for Compounds **10a-10e** (a)

	5-H δ (multiplicity)	N-CH3 (position 1) δ (J, Hz)	N-CH3 (position 3) δ (J, Hz)
10a	8.15 (dd)	3.20 (9)	3.15 (8)
10b	8.25 (m)	3.24 (9)	3.23 (7)
10c	8.25 (dd)	3.15 (9)	3.14 (7)
10d	8.20 (dd)	3.25 (9)	—
10e	8.20 (dd)	3.27 (10)	3.26 (9)

(a) All spectra above were taken in deuteriochloroform. In the case of **10a**, a small amount of DMSO-d_6 was added for solubility reasons. The signals quoted for the *N*-methyl groups represent doublets.

The reaction of **1** with methylisothiocyanate in the presence of one equivalent of triethylamine proceeds analogous to that of **10c** and the thioamide **11** is isolated in 63% yield. Compound **10d** possesses the capability of possible cyclization between the amido functionality and the chloroethyl group, however when treated with lithium diisopropylamide in tetrahydrofuran at -10°, no reaction occurs while at room temperature, extensive decomposition results. Under more forcing conditions (sodium hydride in dioxane), no reaction is observed even at 60° for 24 hours.

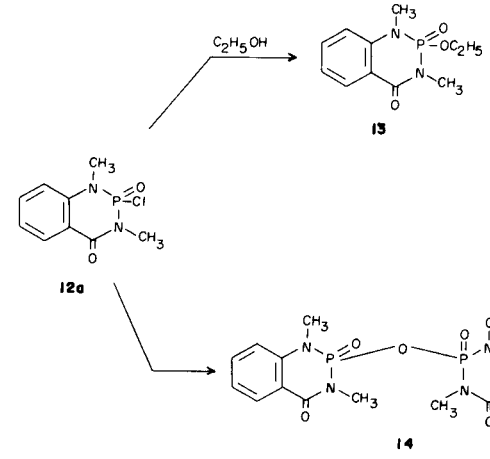
The phosphorus atom in **1a** and **1b** is readily chlorinated by treatment with two equivalents of triethylamine in carbon tetrachloride. The reaction is complete within 30 minutes at room temperature and the resulting 2-chlorobenzodiazaphosphorins(**12a** and **12b**) are isolated in high yields. The analogous 2-bromobenzodiazaphosphorin (**12c**) can be prepared in somewhat lower yield by an analogous reaction with carbon tetrabromide. In contrast with the former reaction where carbon tetrachloride is used as the solvent, the amount of carbon tetrabromide is limited to only two equivalents due to the fact that is a solid. The reaction, therefore, is performed in tetrahydrofuran.



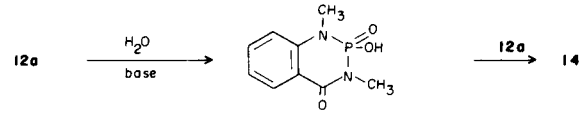
1a, R = CH_3
1b, R = C_6H_5

12a, R = CH_3 X = Cl
12b, R = C_6H_5 X = Cl
12c, R = CH_3 X = Br

Compound **12a** reacts readily with ethanol at 50° to furnish the 2-ethoxybenzodiazaphosphorin (**13**) in quantitative yield. In an attempt to produce a phosphoramide, **12a** was allowed to react with two equivalents of bis(2-chloroethyl)amine in tetrahydrofuran. Heating at 55° for three days is required for the complete consumption of **12a**, however none of the desired 2-bis(2-chloroethyl)aminobenzodiazaphosphorin is formed.



Inspection of the infrared spectrum of the product reveals that the amide (1685 cm^{-1}) and P=O (1350 cm^{-1}) absorptions are still intact, however an intense absorption at 900 cm^{-1} is also present. Vibrations at these wavenumbers are characteristic of a P-O-P linkage (15,16). In addition, its mass spectrum exhibits a molecular ion at 434. Data such as this strongly suggest the anhydride structure **14**. Presumably, compound **14** is formed by the base catalyzed hydration of **12a** (the necessary water may be introduced into the reaction in association with the bis(2-chloroethyl)amine) and subsequent reaction of the resulting 2-hydroxybenzodiazaphosphorin with another molecule of unreacted **12a**. The reaction is very efficient with **14** being isolated in 86% yield. It is curious to note, however, that when **12a** is intentionally treated with two equivalents of triethylamine in moist tetrahydrofuran, no detectable amount of **14** is formed even when refluxed for three days.



EXPERIMENTAL

Melting points were determined on a Thomas-Hoover unimelt apparatus and are uncorrected. The infrared spectra were recorded on a Perkin-Elmer Model 257 and 457 spectrophotometers. Absorption frequencies are quoted in reciprocal centimeters. Nuclear magnetic resonance spectra were determined on a Varian T-60 and EM 360 spectrometers using tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The mass spectra were determined on an LKB 9000 spectrometer.

Unless otherwise stated, all solutions of organic compounds were washed with saturated sodium chloride and dried over sodium sulfate. No attempt has been made to optimize the yields of the described reactions.

General Procedure for the Preparation of Alcohols **7a-7h** (Table 1).

A mixture of 0.02 moles of the benzodiazaphosphorin **1** (2,3) and 0.025 moles of the aldehyde in 100 ml of dioxane was stirred at 50-55° for the amount of time indicated in the table. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using 2% methanol/chloroform to elute the product which was crystallized from methylene chloride/ether.

2-(3,3-Dichloro-2-oxiranyl)-2,3-dihydro-1,3-dimethyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**8a**).

To a solution of 3.0 g of **7f** in 100 ml of dioxane in an ice bath was added 0.4 g of sodium hydride (50% in mineral oil, pentane washed) in portions. The mixture was allowed to warm to room temperature and was stirred there for 18 hours. The insoluble material was filtered from the mixture and the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel using chloroform to elute the product, 1.5 g (56%) of **8a**. An analytical sample was crystallized from pentane, mp 89-91°; ir (chloroform): 3090, 1690, 1615, 1485, 1350 cm^{-1}; nmr (deuteriochloroform): δ 8.2 (dd, 1), 7.8-6.8 (m, 4), 3.35 (d, J = 9 Hz, 3), 3.3 (d, J = 8 Hz, 3); ms (70 eV) m/e 320 (M^+] containing two chlorines.

Anal. Calcd. for $C_{11}H_{11}Cl_2N_2O_3P$: C, 41.1; H, 3.5; N, 8.7. Found: C, 41.5; H, 3.7; N, 8.9.

3-(2-Chloroethyl)-2-(3,3-dichloro-2-oxiranyl)-2,3-dihydro-1-methyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**8b**).

To a solution of 0.5 g of **7h** in 20 ml of dioxane in an ice bath was added 0.06 g of sodium hydride (50% in mineral oil, pentane washed). The mixture was allowed to warm to room temperature and was stirred there for 3 hours. The solvent was removed under reduced pressure and methylene chloride was added to the residue. The insoluble material was filtered and the solvent was removed from the filtrate under reduced pressure. The resulting oil was chromatographed on a column of silica gel using chloroform to elute the product, 0.2 g (44%) of **8b**. An analytical sample was crystallized from pentane, mp 59-62°; ir (chloroform): 3095, 1690, 1615, 1485, 1345 cm^{-1}; nmr (deuteriochloroform): δ 8.2 (dd, 1), 7.85-7.0 (m, 3), 6.9 (d, J = 6 Hz, 1), 4.6-3.6 (m, 4), 3.35 (d, J = 9 Hz, 3).

Anal. Calcd. for $C_{12}H_{12}Cl_3N_2O_3P$: C, 39.0; H, 3.3; N, 7.6. Found: C, 39.0; H, 3.6; N, 7.7.

General Procedure for the Preparation of 1-Methyl-3-substituted-1,2,3,4-tetrahydro-4-oxo-1,3,2-benzodiazaphosphorin-2-carboxamide 2-Oxides **10a-10e** (Table 2).

A mixture of 0.01 moles of **1a** (2) or 3-(2-chloroethyl)-2,3-dihydro-1-methyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (3), 0.011 mole of the isocyanate, and 0.01 mole of triethylamine in 30 ml of dry tetrahydrofuran was heated at 50-55° for 3 hours. The solvent was removed under reduced pressure and the product was crystallized from the solvent indicated in Table 2. Mass spectra (70 eV) of all the amides in Table 2 exhibit a molecular ion corresponding to their molecular weight.

1,3-Dimethyl-1,2,3,4-tetrahydro-*N*-methyl-4-oxo-1,3,2-benzodiazaphosphorin-2-thiocarboxamide 2-Oxide (**11**).

A mixture of 2.0 g of **1a** (2), 0.7 g of methylisothiocyanate and 0.95 g of triethylamine in 30 ml of dry tetrahydrofuran was stirred at 50° for 1.5 hours. The solvent was removed under reduced pressure and the resulting solid was crystallized from methylene chloride/ethyl acetate to give 1.7 g (63%) of **11**, mp 233-235°; ir (chloroform): 3360, 3220, 1675, 1600, 1475, 1350, 1330 cm^{-1} (17); nmr (deuteriochloroform): δ 9.9 (m, 1, exchangeable), 8.25 (dd, 1), 7.75-6.85 (m, 3), 3.2 (m, 3), 3.12 (d, J = 10 Hz, 3), 3.11 (d, J = 9 Hz, 3); ms (70 eV) m/e 283 [M^+].

Anal. Calcd. for $C_{11}H_{14}N_3O_2PS$: C, 46.6; H, 5.0; N, 14.8. Found: C, 46.9; H, 5.3; N, 14.9.

2-Chloro-2,3-dihydro-1,3-dimethyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**12a**).

To a suspension of 10.0 g of **1a** (2) in 200 ml of carbon tetrachloride (cooled in an ice bath) was added 10.0 g of triethylamine. The mixture was allowed to warm to room temperature and was stirred there for 30 minutes. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 10.7 g (93%) of **12a**. An analytical sample was crystallized from ether/pentane, mp 106-108°; ir (chloroform): 1690, 1610, 1480, 1335 cm^{-1}; nmr (deuteriochloroform): δ 8.25 (dd, 1), 7.9-7.0 (m, 3), 3.4 (d, J = 12 Hz, 3), 3.33 (d, J = 10 Hz, 3); ms (70 eV) m/e 244 (M^+] containing one chlorine.

Anal. Calcd. for $C_9H_{10}ClN_2O_2P$: C, 44.2; H, 4.1; N, 11.5; Cl, 14.5. Found: C, 44.6; H, 4.2; N, 11.5; Cl, 14.5.

2-Chloro-2,3-dihydro-3-methyl-1-phenyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**12b**).

To a solution of 2.0 g of **1b** (2) in 35 ml of carbon tetrachloride was added 1.5 g of triethylamine and the mixture was stirred at room temperature for 30 minutes. The solvent was removed under reduced pessure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 1.8 g (80%) of **12b**. An analytical sample was crystallized from ether/pentane, mp 154-156°; ir (chloroform): 1680, 1600, 1460, 1325 cm^{-1}; nmr (deuteriochloroform): δ 8.28 (dd, 1), 7.7-7.0 (m, 7), 6.55 (m, 1), 3.37 (d, J = 10 Hz, 3).

Anal. Calcd. for $C_{14}H_{12}ClN_2O_2P$: C, 54.8; H, 4.0; N, 9.1; Cl, 11.6. Found: C, 54.9; H, 4.3; N, 9.3; Cl, 12.0.

2-Bromo-2,3-dihydro-1,3-dimethyl-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**12c**).

To a suspension of 0.5 g of **1a** (2) and 1.6 g of carbon tetrabromide in 10 ml of dry tetrahydrofuran was added 0.5 g of triethylamine and the mixture was stirred at room temperature for 45 minutes. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 0.3 g (44%) of **12c**. An analytical sample was crystallized from ether/pentane, mp 131-134°; ir (chloroform): 1690, 1615, 1380, 1340 cm^{-1}; nmr (deuteriochloroform): δ 8.2 (dd, 1), 7.85-6.95 (m, 3), 3.31 (d, J = 13 Hz, 3), 3.30 (d, J = 9.5 Hz, 3).

Anal. Calcd. for $C_9H_{10}BrN_2O_2P$: C, 37.4; H, 3.5; N, 9.7; Br, 27.6. Found: C, 37.3; H, 3.7; N, 9.4; Br, 27.2.

2,3-Dihydro-1,3-dimethyl-2-ethoxy-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2-Oxide (**13**).

A solution of 1.7 g of **12a** in 30 ml of ethanol was heated at 50° for 8 hours. The solvent was removed under reduced pressure and the residue was chromatographed on a column of silica gel using chloroform to elute the product, 1.8 g (100%) of **13** as an oil which crystallized on standing, mp 73-76°; ir (chloroform): 1670, 1615, 1350, 1280 cm^{-1}; nmr (deuteriochloroform): δ 8.25 (dd, 1), 7.8-6.95 (m, 3), 4.05 (m, 2), 3.35 (d, J = 9 Hz, 3), 3.31 (d, J = 8 Hz, 3), 1.3 (t, 3).

Anal. Calcd. for $C_{11}H_{15}N_2O_3P$: C, 52.0; H, 6.0; N, 11.0. Found: C, 52.3; H, 6.4; N, 10.8.

2,2'-Oxybis(2,3-dihydro-1,3-dimethyl)-1,3,2-benzodiazaphosphorin-4(1*H*)-one 2,2'-Dioxide (**14**).

A mixture of 1.3 g of **12a** and 1.5 g of bis(2-chloroethyl)amine in 15 ml of tetrahydrofuran was stirred at 50° for 3 days. Methylene chloride was added and any insoluble material was filtered off. The solvent from the filtrate was removed under reduced pressure and the residue was chromatographed on a column of silica gel using a mixture of 1% methanol/chloroform to elute the product, 1.0 g (86%)l of **14**. An analytical sample was crystallized from methylene chloride ether, mp 184-187°; ir (chloroform): 1685, 1615, 1485, 1350, 1340, 900 cm^{-1}; nmr (deuteriochloroform): δ 8.15 (m, 2), 7.8-6.9 (m, 6), 3.45-2.9 (m, 12); ms (70 eV) m/e 434 [M^+].

Anal. Calcd. for $C_{18}H_{20}N_4O_5P_2$: C, 49.8; H, 4.7; N, 12.9. Found: C, 49.6; H, 4.8; N, 12.7.

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REFERENCES AND NOTES

(1) Part 1: G. M. Coppola, *J. Heterocyclic Chem.*, **15**, 645 (1978).

(2) Part 2: G. M. Coppola and R. I. Mansukhani, *ibid*, **15**, 1169 (1978).

(3) Part 3: G. M. Coppola, *ibid.*, **16**, 897 (1979).

(4) Part 4: G. M. Coppola and G. E. Hardtmann, *ibid.*, **16**, 1361 (1979).

(5) Part 5: G. M. Coppola and M. J. Shapiro, *ibid.*, **17**, 1163 (1980).

(6) Part 6: G. M. Coppola and R. E. Damon *ibid.*, **17**, 1729 (1980).

(7) Part 7: G. M. Coppola and M. J. Shapiro, *ibid.*, **18**, 495 (1981).

(8) Part 8: G. M. Coppola, *ibid.*, **18**, 767 (1981).

(9) Part 9: G. M. Coppola, *ibid.*, **18**, 845 (1981).

(10) Two instances where the methyl groups remain as fairly distinct doublets are **7g**(δ 3.35, J = 6.5 Hz) and **7h** (δ 3.3, J = 8 Hz). The size of the coupling constants are in accord with prior observations (2) with the J value for the methyl in position 1 being larger than that for the methyl in position 3.

(11) W. Reeve and W. R. Coley III, *Can. J. Chem.*, **57**, 444 (1979).

(12) W. Reeve, J. R. McKee, R. Brown, S. Lakshmanan and G. A. McKee, *ibid.*, **58**, 485 (1980).

(13) O. Neunhoeffer and A. Spange, *Ann. Chem.*, **632**, 22 (1960).

(14) A. D. Cross, "Practical Infra-red Spectroscopy", 2nd Ed, Butterworth and Co., Washington, D. C., 1964, p 66.

(15) L. J. Bellamy, "Infrared Spectra of Complex Molecules", John Wiley and Sons, New York, NY, 1966, p 311.

(16) R. C. Elder, L. R. Florian, E. R. Kennedy and R. S. Macomber, *J. Org. Chem.*, **38**, 4177 (1973).

(17) The absorption at 3360 cm^{-1} is probably due to a hydrogen bonded species. When a spectrum is taken in the solid phase (potassium bromide), this peak is not seen while the absorption at 3220 cm^{-1} remains intact.