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Synthesis of Dimeric 1,3,2λ^5-Benzoxazaphospholes from Phosphinic Acid Derivatives by Silylation/Desiloxylation

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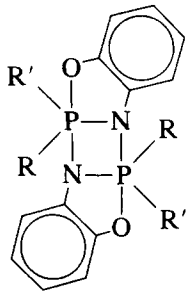
ABSTRACT

The reaction of N,N,O-*tris*(*trimethylsilyl*)-o-*aminophenol with two equivalents of phosphinic chloride yielded dimeric 2,2-disubstituted 1,3,2λ^5-benzoxazaphospholes and trimethylsilyl phosphinate. The chlorides having the bulk substituents* (o-*chlorophenyl or tert-butyl*) *at phosphorus or containing P—N and P—O bonds* (*instead of a P—C bond*) *either didn't react at all or reacted to retain the phosphoryl group. Being stable in solution at 20°C, the individual diastereoisomers of dimeric 1,3,2-benzoxazaphospholes were converted upon warming to an equilibrium mixture of isomers. When reacted with another dimer each gave a mixed dimeric compound having two different phosphorus atoms in the molecule.*

Dimeric 2,2-dialkyl(or diaryl)-1,3,2-benzoxazaphospholes (**1**) were synthesized by different routes; for example, by reaction of *o*-azidophenol with chlorophosphines [2], by dealkoxylation of 2-alkoxy-2,3-dihydro-2,2-diphenyl-1,3,2-benzoxazaphosphole (**2**) [3], or by reaction of *o*-aminophenol with trichloro- or trifluorophosphoranes followed by treatment with base [2, 4, 5]. The reaction of 2-alkyl-2,3-dihydro-1,3,2-benzoxazaphosphole with acrylonitrile [6] or bis(diethylamino)methane [7] could serve as a more specific method for preparing the dimers **1** containing P—C bonds.



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Phosphoryl compounds were not employed as precursors of dimers **1**, though it is known that 1,3,2-benzoxazaphosphole-containing phosphoranes, for example, may be prepared from *o*-aminophenol and phenyl dichlorophosphate [8]. On the other hand, the conversion of catechol-containing phosphates into the corresponding phosphoranes may be facilitated by silylation of the oxygen on phosphorus [9]. Having taken these facts into account, we attempted to prepare the dimer **1a** (R = Ph) via the hypothetical phosphorane **2**. However, the silylation of *o*-aminophenyl diphenylphosphinate **3** with subsequent heating to 200°C did not lead to dimer **1a**. Instead, the reaction mixture contained only silyl derivatives **4** and **5** in a 4:5 ratio, as revealed by ^{31}P NMR spectroscopy, from which amide 6 was isolated in 52% yield after hydrolysis. Thus, the result of the reaction is a reversible migration of the diphenylphosphinoyl group from oxygen to nitrogen. Interestingly, the isomerization of **6** into **3**, for which severe conditions (~200°C) are described by Cadogan [3], proceeded upon refluxing in xylene.

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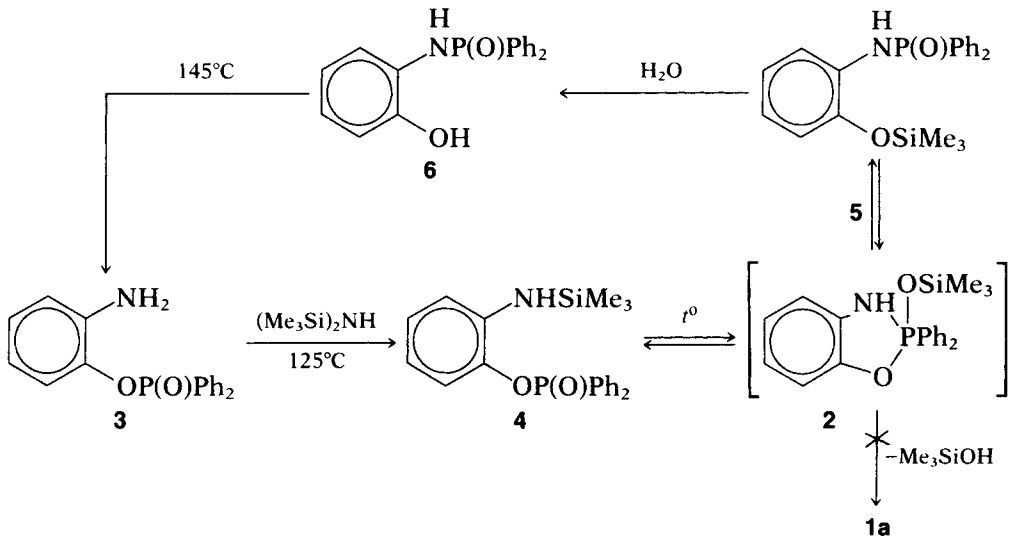
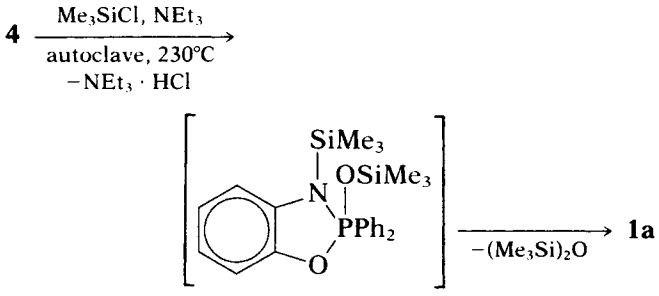
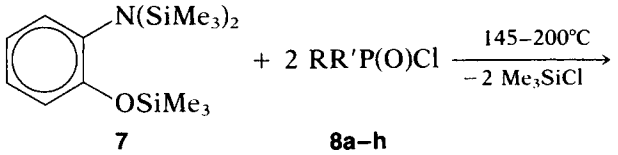


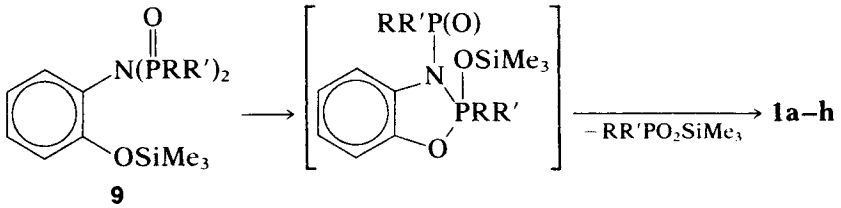
By silylation of the supposed intermediate phosphorane **2** with trimethylchlorosilane under more severe conditions (autoclave 230°C × 6 h), we prepared the dimer **1a** in 41% yield (from ester **3**):



Because of the experimental inconvenience of the autoclave method, we also prepared dimer **1a** and related ones (Table 1) by a simplified method. In this case, the mixture of *N,N,O*-tris(trimethylsilyl)-*o*-aminophenol (**7**) and chloride **8** (1:2 ratio) was refluxed in xylene to give (after removal of Me_3SiCl) the dimers **1a–h** and trimethylsilyl phosphinate as a byproduct:



7 **8a–h**



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R = R′ = Ph(a), Et(b), Oct(c), R = Me,
R′ = Et(d), Bu(e), Ph(f).
R + R′ = *o*-$CH_2OC_6H_4$(g), *o*-$(CH_2O)_2C_6H_4$(h).

With an equimolar ratio of 7 and 8, the hydrolysis of the reaction mixture, after removal of dimer **1**, gave its *o*-hydroxyphenylammonium salt as demonstrated for dimers **1g,h**, not the phosphinic acid (from $RR'PO_2SiMe_3$). The compounds **1b–e** had already been formed at 110°C (under refluxing in toluene), whereas heating to 200°C was necessary to complete the conversion of **9a** to **1a**. The dimers **1d–g** (R ≠ R′) were obtained as a mixture of two diastereoisomers. In this case, the formation of the intermediate imidodiphosphinate **9** was confirmed by the observation of pairs of equal signals at $\delta^{31}P = +52.17, 52.29$ and $+50.72, 50.84$, corresponding to diastereomers **9d,e** in the ^{31}P NMR spectra of reaction mixtures of **1d,e** (formed after refluxing for 1–3 h in toluene).

At least for the dimers **1b–e**, the conversion of **9** into **1** became reversible at high temperature (>170°C) and possibly at high concentration. It was demonstrated that after heating (200°C, 5 h) the mixture of $Ph_2PO_2SiMe_3$ and **1b** or **1e** in nitrobenzene gave ^{31}P NMR spectra with the signals at δ =

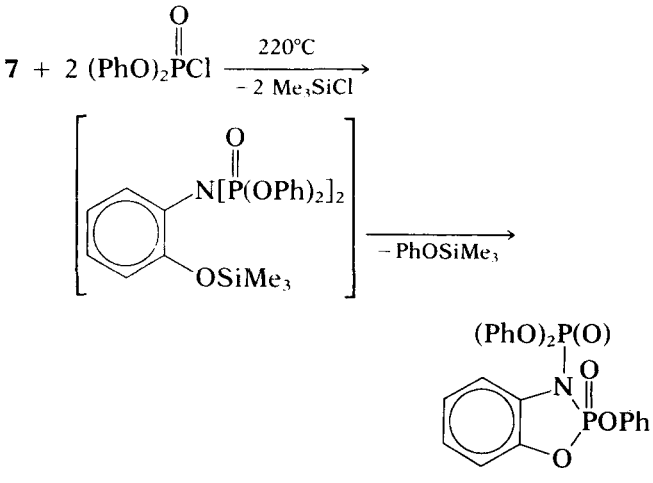
TABLE 1 Selected Data of Dimeric 1,3,2-Benzoxazaphospholes **1a–h**

Compd.	R, R′	Yield,[a] %	Mp, °C (solvent)	$^{31}P\{^1H\}$[b] (nitrobenzene)	Mass Spectrum, m/z, M^+ and 1/2 M^+ (rel. intensity)
1a	Ph_2	69	226–227[c] dec.	−50.9[d]	582(8), 291(100)
1b	Et_2	77	157–160[e] (toluene)	−33.8[f]	390(12), 195(100)
1c	$Octyl_2$	59	82–85 (hexane)[g]	−36.2[f]	726(2), 363(50)
1d	Me, Et	64	175–177[h] (benzene)	−39.4, −38.7[i]	362(7), 181(100)
1e	Me, Bu	74	144–148[h] (diethyl ether)	−40.5, −40.1[i]	418(34), 209(100)
1f	Me, Ph	73	165–185[j]	−49.1, −47.9	458(4), 229(100)
1g	o-$CH_2OC_6H_4$	33[k]	230–250[j] dec.	−36.9, −35.5[l]	486(0), 243(60)
1f	o-$(CH_2O)_2C_6H_4$	41[k]	225–230 dec.	−42.4	546(8), 273(100)

[a] Based on **7**; for **1b–e** after column chromatography.
[b] Downfield signals (δ +20–45) of possible monomers in nitrobenzene are not indicated.
[c] 210–220 [3].
[d] In all cases the signal at δ −41.6 also was registered.
[e] 169–170 [2].
[f] $CDCl_3$.
[g] Recrystallized at −10°C.
[h] Less soluble isomer.
[i] Minor (more soluble) and major (less soluble) isomers in C_6D_6.
[j] Mixture of isomers.
[k] At 1:1 ratio of **7** and **8**.
[l] In all cases the signals at δ −45.3, and −45.0 also were registered.

+49 or +45 corresponding to $Et_2PO_2SiMe_3$ and $BuMePO_2SiMe_3$. In both cases, the insoluble precipitate of **1a** was also obtained.

The attempts to prepare dimers from bis(*o*-chlorophenyl)- or di-*tert*-butylphosphinoyl chloride as well as tetraethylphosphorodiamidic chloride were unsuccessful. Under the same conditions, diphenyl chlorophosphate gave 2-oxo-2-phenoxy-3-diphenoxyphosphoryl-1,3,2-benzoxazaphosphole (**10**) in 90% yield:



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The less soluble major diastereomers **1d,e** were isolated from the mixture of isomers by crystallization. X-ray analysis of the isomer **1e** [10] demonstrated the trans orientation of butyl (or methyl) substituents relative to the diazadiphosphetidine ring. Having compared the ^{31}P NMR spectra of **1d,e**, we assigned a trans configuration to the major isomer **1d**.

Being stable in solution at 20°C, the isomers **1d,e** were converted into an equilibrium mixture (1:3) of cis- and trans-dimers upon warming in benzene (75°C, 2–3 h) as revealed by ^{31}P NMR spectroscopy. In this connection, the recrystallization of the major isomer **1d** from benzene sometimes resulted in its partial isomerization. The reaction between two different dimers proceeded as easily as their isomerization. For example, the mixed dimer **1be** (from **1b** and **1e**) was obtained in benzene after heating (75°C, 3 h) and appeared in the ^{31}P NMR spectrum as a pair of doublets ($^2J_{pp}$ 18 Hz). The ^{31}P NMR data of **1be** and other mixed dimers obtained in solution are listed in Table 2.

EXPERIMENTAL

NMR spectra (chemical shifts from internal Me_4Si for ^1H and from external H_3PO_4 for $^{31}P\{^1H\}$; positive for downfield shifts) were recorded on a Bruker CXP-200 spectrometer at 200 and 81 MHz, respectively.

TABLE 2 $^{31}P\{^1H\}$ NMR Spectra of Mixed Dimeric 1,3,2-benzoxazaphospholes Prepared by Heating of Mixture of Dimers **1a,b,d** and **1e–h** in Solution

Compd.	R^1, R^2 *at* P^1	R^3, R^4 *at* P^2	δP^1	δP^2	$^2J_{PP}$, Hz
1be[a]	Et_2	Me, Bu	−33.95	−40.28	18
1ag[b]	Ph_2	o-$CH_2OC_6H_4$	−51.34	−37.98	29
1de[a]	Me, Et	Me, Bu	−40.56	−39.44	20
1gh[c]	o-$(CH_2O)_2C_6H_4$	o-$CH_2OC_6H_4$	−42.74	−37.31	29
1df[b]	Me, Et	Me, Ph	−38.30	−48.90	20

[a] C_6D_6.
[b] Nitrobenzene.
[c] Benzonitrile.

Mass spectra were obtained on a Finnigan 4021 chromatomass spectrometer. All reactions involving silyl derivatives were carried out under argon. Chromatographic separations were performed on silica gel (eluent: benzene). All new compounds exhibited acceptable elemental analysis data.

o-*Aminophenyl Diphenylphosphinate* (**3**)

To a stirred solution of 5.7 g (52 mmol) of *o*-aminophenol and 5.3 g (52 mmol) of NEt_3 in 30 mL of dry dioxane, 12.4 g (52 mmol) of diphenylphosphinoyl chloride was added dropwise. The mixture then was heated for 30 min at 50°C. After removal of a precipitate, the solution was concentrated to dryness *in vacuo*, and the residue was crystallized from benzene to afford 13.1 g (81%) of **3**, mp 114–116°C; ^{31}P NMR ($CDCl_3$), δ 32.9; ^1H NMR ($CDCl_3$), δ 4.49 (s, NH_2), 6.57, and 6.91 (m, 1 + 3H, C_6H_4), 7.50, and 7.94 (m, 6 + 4H, C_6H_5).

N-(*2-Hydroxyphenyl*)-*diphenylphosphinic Amide* (**6**)

A mixture of 1.3 g (4.2 mmol) of the ester **3**, 0.01 g of $(NH_4)_2SO_4$ as a catalyst, and 6 mL of $(Me_3Si)_2NH$ was refluxed until the solution became transparent (2 h). To the resulting solution, which gave a ^{31}P NMR spectrum with two signals: δ 30.6 and 15.7 (11:1 ratio), 10 drops of dry pyridine were added. The mixture then was heated for 1 h to 170–200°C with simultaneous distillation of solvent. The ^{31}P NMR spectrum of the residue obtained showed a 4:5 ratio of the same signals (δ 34.0 and 19.0 in $CDCl_3$). The residue was dissolved in 15 mL of acetone and allowed to stand for 20 h. The resultant precipitate was collected and crystallized from 2-butanone–ethanol to afford 0.7 g (52%) of **6**, mp 224–227°C (228–231°C [3], 219–222°C [5]), ^{31}P NMR (DMSO), δ 19.74; ^1H NMR (DMSO-D_6), δ 6.58, 6.80, and 7.04 (m, 1 + 2 + 1H, C_6H_4), 6.92 (d, $^2J_{HP}$ 11 Hz, NH), 7.56, and 7.84 (m, 6 + 4H, C_6H_5), 9.86 (s, OH).

Conversion of Amide **6** *into Ester* **3**

A mixture of 0.8 g (2.6 mmol) of amide **6** and 30 mL of xylene was refluxed for 15 h in a Dean-Stark apparatus. The resultant solution was concentrated by rotary evaporation, and the residue was crystallized from ether to yield 0.7 g (84%) of ester **3**.

Preparation of Dimer **1a** *from Ester* **3** *by Silylation in an Autoclave*

A mixture of 5.5 g (18 mmol) of ester **3**, 0.01 g of $(NH_4)_2SO_4$, and 8 mL of $(Me_3Si)_2NH$ was refluxed for 2 h to form a transparent solution and was then concentrated *in vacuo*. The resultant oil was dissolved in 15 mL of toluene (or acetonitrile) and heated with 2.9 g (27 mmol) of Me_3SiCl and 3.6 g (35 mmol) of NEt_3 in a sealed autoclave tube (230°C, 6 h). After having been cooled to 20°C, the resultant solid was collected and washed with benzene (20 mL) and ethanol (3 × 20 mL) to afford 2.2 g (41%) of **1a**.

N,N,O-*tris*(*Trimethylsilyl*)-o-*aminophenol* (**7**)

A mixture of 38.0 g (350 mmol) of *o*-aminophenol, 0.05 g of $(NH_4)_2SO_4$ and 150 mL of $(Me_3Si)_2NH$ was refluxed for 10 h. The resulting solution was cooled to 20°C, and then 13.0 g (120 mmol) of Me_3SiCl and 12.0 g (120 mmol) of NEt_3 were added. After 2 days the mixture was filtered under argon and the filtrate was distilled to afford 88.0 g (~100%) of *N,O*-bis(trimethylsilyl)-*o*-aminophenol, bp 120–121°C (10 mm Hg).

To a stirred solution of 37.0 g (146 mmol) of *N,O*-bis(trimethylsilyl)-*o*-aminophenol in 20 mL of anhydrous ether was added dropwise to a solution of phenyllithium prepared from 2.4 g (350 mg-at) of Li and 30.6 g (195 mmol) of bromobenzene in 150 mL of ether. To the resultant mixture, which was cooled to 0°C, was added 21.2 g (195 mmol) of Me_3SiCl. This solution was stirred 2 h at 20°C and filtered. The filtrate was distilled to give 43.0 g (91%) of **7**, bp 102–103°C (2 mm Hg), n_D^{20} 1.4812. ^1H NMR spectrum matched that of Narkon [11].

[*1,3,2*λ^5,*4*λ^5]*Diazadiphospheto*[*2,1-b*:*4,3-b'*]-*bis*[*1,3,2*]*benzoxazaphospholes* (**1a-h**): *Typical Procedure*

To a solution of 3 mmol of **7** in 5 mL of dry xylene was added 6 mmol of phosphinic chloride **8**. This

mixture was refluxed for 4–5 h or, in the case of **8a**, heated to 200°C with simultaneous distillation of volatile products. Then the mixture was cooled to 20°C, diluted with dry benzene (10 mL), and either filtered to yield the precipitate of **1a,f–h** (after washing with benzene and dry DMSO) or chromatographed to afford **1b–e**. At a 1:1 ratio of **7** and **8g,h**, the corresponding *o*-hydroxyphenylammonium phosphinates were isolated from the mother liquor obtained after hydrolysis: 3-hydroxy-3-oxo-2H-1,3-benzoxaphosphole, *o*-hydroxyphenylammonium salt ($C_7H_7O_3P{\cdot}C_6H_7NO$, mp 206–210°C dec. (wet ethanol)) and 3-hydroxy-3-oxo-2H, 4H-1,3,5-benzodioxaphosphepin, *o*-hydroxyphenylammonium salt ($C_8H_9O_4P{\cdot}C_6H_7NO$, mp 175°C (dioxane-ethanol)). At a 1:2 ratio of **7** and **8a**, diphenylphosphinic acid (mp 192–195°C) was isolated in 58% yield after removal of dimer **1a** and subsequent hydrolysis. For **1b** ^{1}H NMR ($CDCl_3$), δ 1.22 (dt, $^3J_{HH}$ 7 Hz, $^3J_{HP}$ 22 Hz, 12H, CH_3), 2.25 (quintet, 8H, CH_2), 6.60 and 6.72 (m, 2 + 6H, C_6H_4). For **1c** ^{1}H NMR ($CDCl_3$), δ 0.87 (t, 12H, CH_3), 1.25 (m, 4OH, $(CH_2)_5Me$), 1.63 (m, 8H, PC—CH_2), 2.19 (m, 8H, PCH_2), 6.58 and 6.73 (m, 2 + 6H, C_6H_4). For **1d** (*trans*) ^{1}H NMR (C_6D_6), δ 0.85 (dt, $^3J_{HH}$ 7 Hz, $^3J_{HP}$ 24 Hz, 6H, C—CH_3), 1.62 (d, $^2J_{HP}$ 13 Hz, 6H, PCH_3), 1.94 (m, 4H, PCH_2—C), 6.37, 6.78, and 6.94 (m, 2 + 4 + 2H, C_6H_4). For **1e** (*trans*) ^{1}H NMR ($CDCl_3$), δ 0.85 (t, 6H, C—CH_3), 1.32 and 1.55 (m, 4H + 4H, C—$(CH_2)_2$—C), 1.99 (d, $^2J_{HP}$ 13 Hz, 6H, PCH_3), 2.23 (m, 4H, PCH_2—C), 6.64 and 6.72 (m, 2 + 6H, C_6H_4). Mp's, ^{31}P NMR and mass spectra of **1a–h** are in Table 1.

2-Oxo-2-phenoxy-3-diphenoxyphosphoryl-1,3,2-benzoxazaphosphole (**10**)

A solution of 4.4 g (16 mmol) of $(PhO)_2P(O)Cl$ and 2.7 g (8 mmol) of **7** in 10 mL of dry xylene was heated for 5 h at 220°C with simultaneous distillation of volatile products. Then the reaction mixture was concentrated *in vacuo* at 150°C to yield 3.5 g (90%) of **10** as a viscous oil, which was induced to crystallize from ether. Recrystallization from toluene gave the compound **10** as a very hygroscopic solid, mp 98–100°C, ^{31}P NMR ($CDCl_3$), δ −14.6 d, +6.8 d ($^2J_{PP}$ 24.4 Hz); ^{1}H NMR ($CDCl_3$), δ 7.25 (m, 14H), 7.34 (m, 4H), 7.45 (m, 1H).

Reaction of **1b,e** *with Trimethylsilyl Diphenylphosphinate: Typical Procedure*

A solution of 0.6 mmol of trimethylsilyl diphenylphosphinate (prepared by refluxing of Ph_2PO_2H in $(Me_3Si)_2NH$) and 0.6 mmol of **1b,e** in 1.5 mL of nitrobenzene was heated in a sealed NMR tube for 5 h at 200°C. The substantial signals of $Et_2PO_2SiMe_3$ (δ +49.0) or $BuMePO_2SiMe_3$ (δ +45.0) were detected and matched the ^{31}P NMR spectra of separately prepared silyl esters. In both cases the insoluble precipitate of **1a** was formed.

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