NUCLEOPHILIC SUBSTITUTION OF 2,2-BIS(ARYLTHIO)-4,4,6,6-TETRACHLOROCYCLOTRIPHOSPHAZENE WITH AMMONIA, PHENOXIDE, AND THIOPHENOXIDE

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Abstract – Nucleophilic substitution of hexachlorocyclotriphosphazene (HCCP) with arylthiol gave 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazene. Aminolysis of 2,2,4,4-tetrachloro-6,6-bis(4-methoxyphenylthio)-cyclotriphosphazene with gaseous ammonia gave gem-disubstituted 2,2-diamino-4,4-dichloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene in Et₂O and tetrasubstituted 2,2,4,4-tetraamino-6,6-bis(4-methoxyphenylthio)-cyclotriphosphazene in acetonitrile, respectively. The reaction of 2,2,4,4-tetrachloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene with 4-chlorophenol gave a mixture of gem-disubstituted 2,2-dichloro-4,4-bis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene and tetrasubstituted 2,2,4,4-tetrakis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene, whose ratio depended on the reaction solvent. On the other hand, in reaction of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazene with another arylthiol, ArS-groups were scrambled.

INTRODUCTION

Cyclotriphosphazenes, \( P₃N₃X₆ \), has a six-membered flat ring, in which three nitrogen and three phosphorus atoms are connected alternately, and two substituents \( X \) are placed on the each phosphorus atom upper side and lower side of the ring (Figure 1).
Most of cyclotriphosphazenes have been synthesized by nucleophilic substitution of hexachlorocyclotriphosphazene (HCCP), whose synthesis was firstly reported in 1834 by Liebig from reaction of PCl₅ and ammonia.¹ HCCP and its derivatives were used as frame retardants. From 2001, cyclotriphosphazenes were focused as functional materials² such as hosts for molecular motors,³⁻⁵ gas storage materials,⁶⁻⁸ gas separation materials,⁹ liquid crystals,¹⁰,¹¹ antimicrobials,¹²,¹³ and proliferation materials of human osteoblast cells.¹⁴,¹⁵ In these studies, cyclotriphosphazenes having two or three kinds of nucleophiles have been investigated for multi-functional materials.

Previously, we reported that thiolation of HCCP with thiophenol gave gem-disubstituted 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazenes ³ and tetrasubstituted 2,2,4,4-tetrakis(arylthio)-6,6-dichlorocyclotriphosphazenes ⁴, where product selectivity could be controlled by amounts of thiophenols (Scheme 1),¹⁶ i.e., ³ was obtained with 2 equivalents of ArSH, whereas ⁴ was obtained with 4 equivalents of ArSH.

In this article, we report nucleophilic substitution of ³ with ammonia, phenoxide, and thiophenoxide (Scheme 2).

Scheme 1. Synthesis of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazenes ³ and 2,2,4,4-tetrakis(arylthio)-6,6-dichlorocyclotriphosphazenes ⁴
RESULTS AND DISCUSSION

Synthesis of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazene (Eq. 1)\textsuperscript{16}

A MeCN solution of HCCP (1) was treated with 4-methoxythiophenol (2a, 2 equiv.) and Et\textsubscript{3}N (2 equiv.) at room temperature for 24 h to give gem-disubstituted 2,2,4,4-tetrachloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (3a) in 96% yield. Similarly, the reaction of 1 with 4-chlorothiophenol at 0 °C for 3 h afforded 2,2,4,4-tetrachloro-6,6-bis(4-chlorophenylthio)-cyclotriphosphazene (3b) in 80% yield.
Reaction of 3a with ammonia (Table 1)

Aminolysis of 3a with gaseous ammonia gave gem-disubstituted products, 2,2-diamino-4,4-dichloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (5, reaction solvent: Et₂O) and tetrasubstituted 2,2,4,4-tetraamino-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (6, reaction solvent: MeCN), respectively. We investigated solvent effect to find that this tendency was similar in aminolysis of HCCP. Since solubility of 3a in MeCN was not so high, a CHCl₃/MeCN mixed solvent (1 : 3) was used to give tetraamino product 6 in good yield and neither gem-diamino, non-gem-diamino product and its isomers, nor mono- and tri-substituted products were detected (Table 1, Entries 1,2). In CHCl₃/Et₂O (1 : 3), a mixture of gem-diamino product 5 and tetraamino product 6 (5 : 6 = 1 : 2) was obtained, and 5 was the sole product in Et₂O.

Table 1. Aminolysis of 3a with gaseous ammonia

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvents</th>
<th>Time (h)</th>
<th>Ratioₐ (%)</th>
<th>5</th>
<th>6</th>
<th>3a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mmol)</td>
<td>(mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.49</td>
<td>CHCl₃/MeCN (0.5/1.5)</td>
<td>24</td>
<td>n.d.ᵇ</td>
<td>77</td>
<td>n.d.ᵇ</td>
</tr>
<tr>
<td>2</td>
<td>0.49</td>
<td>CHCl₃/MeCN (0.5/1.5)</td>
<td>31</td>
<td>n.d.ᵇ</td>
<td>82</td>
<td>n.d.ᵇ</td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>CHCl₃/Et₂O (3.0/10)</td>
<td>71</td>
<td>31</td>
<td>69</td>
<td>n.d.ᵇ</td>
</tr>
<tr>
<td>4</td>
<td>0.49</td>
<td>Et₂O (40)</td>
<td>17</td>
<td>83</td>
<td>n.d.ᵇ</td>
<td>17</td>
</tr>
</tbody>
</table>

ₐ Determined by ³¹P NMR of the reaction mixture. ᵇ Not detected.

Scheme 3. A plausible mechanism of aminolysis of 3a with ammonia
Previously we reported that reaction of HCCP with ammonia gave 2,2-diamino-4,4,6,6-tetrachlorocyclotriphosphazene in Et₂O and 2,2,4,4-tetraamino-6,6-dichlorocyclotriphosphazene in MeCN. Beşli et al. reported that amination of 2,2,4,4-tetrachloro-6,6-bis(phenylthio)cyclotriphosphazene (3e) with sterically hindered secondary amine such as dibenzylamine gave trans-2,4-bis(dibenzylamino)-2,4-dichloro-6,6-bis(phenylthio)cyclotriphosphazene (di-non-gem/trans), whereas aminolysis with less hindered secondary amines such as dimethylamine and piperidine gave a mixture of di-non-gem/trans and cis-2,4-bis(dimethylamino)-(di-non-gem/cis) or 2,4-dipiperidyl-2,4-dichloro-6,6-bis(phenylthio)-cyclotriphosphazene (di-non-gem/cis). In both cases, only non-gem type products were obtained. They explained this selectivity from the view point of steric hindrance. On the other hand, since ammonia is very small and have high nucleophilicity, the second and the fourth ammonia were introduced at geminal position and more quickly than the first and the third ammonia, respectively, in which both S_N1 and S_N2 processes would proceed (Scheme 4).

**Scheme 4. A plausible mechanism of aminolysis of HCCP and 3**

**Reaction of 2a with phenoxide**

Chen-Yang investigated phenoxylation of HCCP, and reported that 1) number of introduced phenoxide depends on the amount of phenoxide: i.e., n equiv. of phenoxide were introduced when n equivalents of
phenoxide were used. When 2 equiv. of phenoxide were used, a mixture of diphenoxylated triphosphazenes N₃P₃Cl₃(OPh)₂ (gem, non-gem-trans, non-gem-cis), were obtained, wherein non-gem-diphenoxylated products was mainly obtained.

We investigated phenoxylation of 3a to find that gem-disubstituted product 7 and tetrasubstituted product 8 were obtained in the presence of 5 equiv. of 4-chlorophenol/K₂CO₃. When CHCl₃/MeCN mixed solvent was used, disubstituted 7 was obtained as a sole product, whereas a mixture of 7 and tetrasubstituted 8 was obtained (7 : 8 = 87 : 13) in more polar MeCN and/or acetone (Table 2, Entries 1 and 3). The substitution did not occur at all in less polar solvents such as THF, Et₂O, and toluene. In all cases, gem-disubstituted product was obtained as a major product, and monosubstituted, non-gem-disubstituted, and trisubstituted products were not obtained even 5 equiv. of p-chlorophenol was used.

Table 2. Substitution reaction of 3a with p-chlorophenol

<table>
<thead>
<tr>
<th>Entry</th>
<th>4-chlorophenol (equiv)</th>
<th>K₂CO₃ (equiv)</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>7</th>
<th>8</th>
<th>3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.1</td>
<td>5.2</td>
<td>MeCN</td>
<td>reflux</td>
<td>45</td>
<td>87</td>
<td>13</td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>5.2</td>
<td>5.1</td>
<td>CHCl₃/MeCN (1 : 3)</td>
<td>reflux</td>
<td>20</td>
<td>60</td>
<td>n.d.</td>
<td>40</td>
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<tr>
<td>3</td>
<td>5.0</td>
<td>5.0</td>
<td>acetone</td>
<td>reflux</td>
<td>48</td>
<td>87</td>
<td>13</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>5.0</td>
<td>5.0</td>
<td>THF</td>
<td>50</td>
<td>48</td>
<td>no reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5.2</td>
<td>5.2</td>
<td>Et₂O</td>
<td>reflux</td>
<td>15</td>
<td>no reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5.0</td>
<td>5.0</td>
<td>Tol</td>
<td>reflux</td>
<td>15</td>
<td>no reaction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Determined by ³¹P NMR.  bNot detected.

When HCCP was treated with NaOH and phenol (3 equiv.), a mixture of non-gem P₃N₃(OC₆H₅)₃Cl₃ (66%), gem-P₃N₃(OC₆H₅)₃Cl₃ (17%), non-gem P₃N₃(OC₆H₅)₂Cl₄ (10%), and non-gem P₃N₃(OC₆H₅)₄Cl₂ (7%) were obtained (Scheme 5). This means that thiophenoxy-substituted cyclotriphosphazene 3 was less active than HCCP or phenoxy-substituted cyclotriphosphazene.
Scheme 5. Reaction of HCCP with phenol/NaOH

Reaction of 3a with Thiophenol

Firstly, reaction of 3a and 4-methoxythiophenol (2a) was investigated (Scheme 6). When 3a was treated with 2 equiv. of 2a/Et₃N, 2,2,4,4-tetrathiolated product 14 was obtained in 39% yield, and neither gem/non-gem isomers 18 nor trisubstituted product 19 was obtained. When the reaction was carried out at 0 °C, 4 : 1 mixture of 3a and 14 was obtained.

Though this reaction seems as simple second geminal nucleophilic dissubstitution of P-Cl bonds by P-S bond, we found that this reaction proceeded more complicated pathway. When 3a was treated with 4-chlorothiopenol (2b), exchange reaction occurred:
Table 3. Scramble of arylthio group on cyclotriphosphazene ring

3a: ArS = p-MeOC₆H₄S
3b: ArS = p-ClC₆H₄S
2a: Ar'S = p-MeOC₆H₄S
2b: Ar'S = p-ClC₆H₄S

From both 3a and 3b, arylthio groups were scrambled. We investigate this phenomenon in detail by changing bases and solvents (Table 4, 5).

Table 4. Reaction of 3b with 2a

<table>
<thead>
<tr>
<th>Entry</th>
<th>3b (mmol)</th>
<th>2a (mmol)</th>
<th>Base (mmol)</th>
<th>Solvents (mL)</th>
<th>Temp. (℃)</th>
<th>Time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.29</td>
<td>0.57</td>
<td>Et₃N (0.57)</td>
<td>MeCN (5.0)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>0.20</td>
<td>0.39</td>
<td>K₂CO₃ (0.39)</td>
<td>MeCN (4.0)</td>
<td>-18</td>
<td>16</td>
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<tr>
<td>3</td>
<td>0.20</td>
<td>0.40</td>
<td>K₂CO₃ (0.39)</td>
<td>MeCN (5.0)</td>
<td>rt.</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>1.0</td>
<td>Et₃N (1.0)</td>
<td>CHCl₃/MeCN (1.0/3.0)</td>
<td>rt.</td>
<td>15</td>
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</tbody>
</table>
In the reaction of \textbf{3b} with \textbf{2a}, when Et\textsubscript{3}N was used as a base, tetrasubstituted products 11 and 14 were obtained as a major products (Entry 1), whereas K\textsubscript{2}CO\textsubscript{3} as a base gave disubstituted products 7, 8, and 9 (Entry 3). At low temperature (-18 °C), no reaction occurred (Entry 2). In CHCl\textsubscript{3}/MeOH, a complex mixture of di- and tetrasubstituted products was obtained (Entry 4).

<table>
<thead>
<tr>
<th>Entry</th>
<th>(7)</th>
<th>(8)</th>
<th>(9) ((3b))</th>
<th>(10)</th>
<th>(11)</th>
<th>(12)</th>
<th>(13)</th>
<th>(14)</th>
<th>(15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>trace</td>
<td>56</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>43</td>
<td>n.d.\textsuperscript{b}</td>
</tr>
<tr>
<td>2</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>100</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>18</td>
<td>35</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
<td>n.d.\textsuperscript{b}</td>
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<td>n.d.\textsuperscript{b}</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>21</td>
<td>n.d.\textsuperscript{b}</td>
<td>12</td>
<td>7</td>
<td>21</td>
<td>13</td>
<td>n.d.\textsuperscript{b}</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 5. Reaction of \textbf{3a} with \textbf{2b}

<table>
<thead>
<tr>
<th>Entry</th>
<th>(3a) ((\text{mmol}))</th>
<th>(2b) ((\text{mmol}))</th>
<th>Base ((\text{mmol}))</th>
<th>Solvents ((\text{mL}))</th>
<th>Time. ((\text{h}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.49</td>
<td>0.99</td>
<td>K\textsubscript{2}CO\textsubscript{3} (0.99)</td>
<td>MeCN (6.0)</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>0.50</td>
<td>0.99</td>
<td>Et\textsubscript{3}N (1.0)</td>
<td>MeCN (6.0)</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>0.50</td>
<td>1.0</td>
<td>Et\textsubscript{3}N (1.0)</td>
<td>CHCl\textsubscript{3}/MeCN (0.5/1.5)</td>
<td>15</td>
</tr>
</tbody>
</table>

In the reaction of \textbf{3a} and \textbf{2b}, Et\textsubscript{3}N gave tetrasubstituted products, whereas K\textsubscript{2}CO\textsubscript{3} gave di- and tetrasubstituted products (Table 5).

In all cases, the scramble occurred, and a mixture of \textit{gem}-dithiosubstituted and \textit{gem}-tetrathiosubstituted products was obtained: trithiosubstituted, non-\textit{gem}-dithiosubstituted, pentathiosubstituted, and hexathiosubstituted products were not detected. This phenomenon would occur because thiophenol is soft nucleophile. As ammonia and phenoxide are hard nucleophile, they would attack chlorinated phosphorous (PCl\textsubscript{2}) atom. Therefore, exchange of ArS- group with these nucleophile would not occur.
On the other hand, soft thiophenoxide (ArS’) would attack thio-substituted phosphorous atom (P(SAr)₂), and as a result, exchange of SAr with SAr’ would occur and SAr would be released in the reaction media (Scheme 7). Some thiophenoxide would attack PCl₂ to give tetrathiosubstituted products.

Scheme 7. A plausible mechanism of exchange of thiophenoxide

When 4-trifluoromethylthiophenol was used as the second thiophenols, only a complex mixture of unidentified products was obtained.

CONCLUSION

Hexachlorocyclotriphosphazene was allowed to react with thiophenols to give 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazenes. To introduce the second nucleophile, we tried to introduce ammonia, phenoxides, and thiophenoxides. Nucleophilic substitution of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazenes with ammonia and phenoxides occurred at P-Cl phosphorous atom to give diamino-, tetraamino-, diphenoxy-, and tetraphenoxy-substituted products, depends on the reaction conditions. On the other hand, in the reaction with thiophenoxides, exchange reaction (reaction at P-S phosphorous atom) mainly occurred. Though the reaction mechanism was not clear, we proposed a plausible mechanism.

EXPERIMENTAL

Synthesis of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazene¹⁶

![Chemical structure diagram]
To a solution of hexachlorocyclotriphosphazene (1, 5.08 mmol, 1.73 g) in MeCN (67 mL) were added 4-methoxythiophenol (2a, 10 mmol, 1.21 g) and Et$_3$N (10 mmol, 1.4 mL), and the mixture was stirred at room temperature for 24 h under an argon atmosphere. The reaction mixture was diluted with AcOEt (30 mL), and washed with a saturated aqueous NH$_4$Cl solution (60 mL). The organic phase was dried with sodium sulfate and concentrated under reduced pressure. The residue was analyzed by $^1$H and $^{31}$P NMR, to confirm that 3a (2.52 g, 4.80 mmol, 96%) was obtained.

2,2,4,4-Tetrachloro-6,6-bis(4-methoxybenzenethio)cyclotriphosphazene (3a): colorless solids; $R_f$ = 0.53 (hexane/AcOEt = 7/2); $^{31}$P NMR (162 MHz, CDCl$_3$) δ 48.90 (t, $J = 11.1$ Hz, 1P), 19.90 (d, $J = 10.8$ Hz, 2P); $^1$H NMR (400 MHz, CDCl$_3$) δ 3.79-3.99 (m, 6H), 6.90 (d, $J = 8.7$ Hz, 4H), 7.48-7.51 (m, 4H).

Similarly, treatment of HCCP (1, 341.7 mg, 0.99 mmol) with 4-chlorothiophenol (2b, 256.7 mg, 1.8 mmol) and Et$_3$N (0.30 mL, 2.2 mmol) in MeCN (8 mL) at 0 °C for 3 h afforded 2,2,4,4-tetrachloro-6,6-bis(4-chlorophenylthio)cyclotriphosphazene (3b, 443.6 mg, 0.79 mmol, 80%): colorless solids; $R_f$ = 0.40 (hexane/toluene = 3/1); $^{31}$P NMR (162 MHz, CDCl$_3$) δ 20.23 (2P), 46.92 (1P) (Coupling constant was too small to measure.); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.39 (d, $J = 8.4$ Hz, 4H), 7.52 (d, $J = 8.4$ Hz, 4H).

**Reaction of 3a with ammonia**

\[
\begin{align*}
\text{ArS} & \quad \text{SAr} \\
\text{Cl} & \quad \text{P} \quad \text{P} \quad \text{Cl} \quad \text{Cl} \\
\text{Cl} & \quad \text{N} \\
\text{N} & \quad \text{P} \quad \text{Cl} \\
\text{N} & \quad \text{P} \quad \text{Cl} \\
\text{3a (Ar} & = 4-\text{MeOCH}_2\text{H}_4) \\
\end{align*}
\]

A suspension of 3a (274.3 mg, 0.49 mmol) in a mixed solvent of CHCl$_3$ (0.5 mL) and MeCN (1.5 mL) was stirred at room temperature for 24 h under ammonia atmosphere (balloon). The residue was analyzed by $^{31}$P NMR to find that tetraamino product 6 was obtained in good yield. On the other hand, the aminolysis in Et$_2$O gave gem-diamino product 5 selectively.

2,2-Diamino-4,4-dichloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (5); $^{31}$P NMR (162 MHz, CDCl$_3$) δ 12.23 (dd, $J = 6.8, 43.3$ Hz, 1P), 21.17 (d, $J = 43.3$ Hz, 1P), 46.65 (d, $J = 6.8$ Hz, 1P).

2,2,4,4-Tetraamino-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (6); $^{31}$P NMR (162 MHz, CDCl$_3$) δ 15.43 (d, $J = 13.6$ Hz, 2P), 46.07 (m, 1P).
Reaction of $3\text{a}$ with phenoxide

To a solution of $3\text{a}$ (271.3 mg, 0.49 mmol) in MeCN (5.0 mL) were added 4-chlorophenol (216.2 mg, 1.99 mmol) and K$_2$CO$_3$ (348.5 mg, 2.54 mmol). The mixture was heated to reflux for 19 h under an argon atmosphere. After usual work-up, the reaction mixture was analyzed by $^{31}$P NMR to find that a mixture of 2,2-dichloro-4,4-bis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene $7$ and 2,2,4,4-tetrakis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene $8$ was obtained, whose ratio was also determined to 87 : 13 (Table 1, Entry 1). The residue was purified by silica gel column chromatography to give an inseparable mixture of $7$ and $8$. The ratio of $7$ to $8$ was determined by $^{31}$P NMR.

2,2-Dichloro-4,4-bis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene ($7$): $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ 51.12 (dd, $J = 21.7$, 15.5 Hz, 1P), 19.49 (dd, $J = 66.9$, 15.5 Hz, 1P), 4.44 (dd, $J = 67.5$, 21.7 Hz, 1P).

2,2,4,4-Tetrakis(4-chlorophenoxy)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene ($8$): $^{31}$P NMR (162 MHz, CDCl$_3$) $\delta$ 51.94 (t, $J = 25.4$ Hz, 1P), 6.67 (d, $J = 25.4$ Hz, 2P).

Reaction of $3\text{a}$ with 4-methoxythiophenol ($2\text{a}$)

To a mixture of $3\text{a}$ (274.3 mg, 0.49 mmol), 4-methoxythiophenol ($2\text{a}$, 139.8 mg, 0.99 mmol) and MeCN (6 mL) was added Et$_3$N (0.14 mL, 1.0 mmol) dropwise under argon atmosphere at room temperature. The mixture was stirred at room temperature for 3 h. AcOEt (6.0 mL) and sat. aq. NH$_4$Cl (12 mL) were added to the reaction mixture, and the resulting mixture was separated. The aqueous layer was extracted with AcOEt (10 mL x 3). The extracted organic layers were combined and washed with H$_2$O and sat. aq. NaCl, successively. The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. This residue was purified by column chromatography (SiO$_2$, hexane/toluene =
3/1) to afford the raw material 3a (122.4 mg, 0.22 mmol, 44%) and 2,2-dichloro-4,4,6,6-tetrakis(4-methoxyphenylthio)cyclotriphosphazene (14, 443.6 mg, 0.79 mmol, 39%).

2,2-Dichloro-4,4,6,6-tetrakis(4-methoxyphenylthio)cyclotriphosphazene (14): colorless solids; mp 112.0-113.5 °C; Rf = 0.30 (hexane/AcOEt = 7/2); 31P NMR (162 MHz, CDCl3) δ 18.40 (t, J = 5.7 Hz, 1P), 46.80 (d, J = 5.7 Hz, 2P); 1H NMR (400 MHz, CDCl3) δ 3.80 (s, 12H), 6.88 (d, J = 8.8 Hz, 8H), 7.44 (d, J = 8.8 Hz, 8H).

Reaction of 3b with 2a
A mixture of 4-methoxythiophenol (2a, 55.5 mg, 0.40 mmol), K2CO3 (54.4 mg, 0.39 mmol), and MeCN (5.0 mL) was stirred at room temperature for 10 min under argon atmosphere. To the reaction mixture was added 3b (111.6 mg, 0.2 mmol), and stirred at room temperature for 3 h. The reaction mixture was poured into a mixture of AcOEt (10 mL) and sat. aq. NH4Cl (20 mL). The mixture was extracted with AcOEt (10 mL x 3). The combined organic layer was washed with H2O (10 mL) and sat. aq. NaCl, successively, dried over anhydrous Na2SO4, and filtered. The filtrate was concentrated under reduced pressure. The residue was confirmed by 31P NMR, to find a mixture of 3b, 2,2,4,4-tetrachloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (7) and 2,2,4,4-tetrachloro-6-(4-chlorophenylthio)-6-(4-methoxyphenylthio)cyclotriphosphazene (8), where Ar1S and Ar2S were exchanged, was obtained. The ratio of these compounds was determined by 31P NMR.

2,2,4,4-Tetrachloro-6-(4-chlorophenylthio)-6-(4-methoxyphenylthio)cyclotriphosphazene (8): 31P NMR (162 MHz, CDCl3) δ 20.12 (2P), 47.70 (1P) (Coupling constant was too small to measure.).

Reaction of 3a with 2b
A mixture of 4-chlorothiophenol (2b, 142.9 mg, 0.99 mmol), K2CO3 (136.4 mg, 0.99 mmol) and MeCN (6.0 mL) was stirred at room temperature for 10 min under argon atmosphere. To the reaction mixture was added 3a (271.6 mg, 0.49 mmol), and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was poured into a mixture of AcOEt (10 mL) and sat. aq. NH4Cl (20 mL). The mixture was extracted with AcOEt (10 mL x 3). The organic layers were combined and washed with H2O (10 mL) and sat. aq. NaCl, successively, dried over Na2SO4, and filtered. The filtrate was concentrated under reduced pressure. The residue was confirmed by 31P NMR to find an inseparable mixture of 3a, 2,2-dichloro-4,4-bis(4-chlorophenylthio)-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (10), 2,2-dichloro-4,4,6-tris(4-chlorophenylthio)-6-(4-methoxyphenylthio)cyclotriphosphazene (12), and 2,2-dichloro-4,6-bis(4-chlorobenzenethio)-4,6-bis(4-methoxybenzenethio)cyclotriphosphazene (13) was
obtained. The ratio of these compounds was determined by \(^{31}\text{P} \mathrm{NMR}\).

2,2-Dichloro-4-(4-chlorobenzothiophen-4-yl)-6,6-tris(4-methoxybenzenethio)cyclotriphosphazene (11): \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.47 \ (d, J = 2.5 \text{ Hz}, \text{1P}), 45.80 \ (d, J = 35.3 \text{ Hz}, \text{1P}), 46.99 \ (dd, J = 5.0, 35.3 \text{ Hz}, \text{1P}).

2,2-Dichloro-4,6-bis(4-chlorobenzothiophen-4-yl)-6,6-bis(4-methoxybenzenethio)cyclotriphosphazene (13): \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.50 \ (d, J = 5.0 \text{ Hz}, \text{1P}), 46.02 \ (s, 2P).

2,2-Dichloro-4,4,6,6-tetrakis(4-methoxybenzenethio)cyclotriphosphazene (14): colorless solids; \(R_f = 3.0\) (hexane/acetone = 7/2); \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.40 \ (t, J = 5.7 \text{ Hz}, \text{1P}), 46.80 \ (d, J = 5.7 \text{ Hz}, 2 \text{P}); \(^{1}\text{H} \mathrm{NMR} \ (400 \text{ MHz, } \text{CDCl}_3) \delta 3.80 \ (s, 12 \text{H}), 6.88 \ (d, J = 8.8 \text{ Hz}, 8 \text{H}), 7.44 \ (d, J = 8.8 \text{ Hz}, 8 \text{H}).

2,2-Dichloro-4,4-bis(4-chlorobenzothiophen-6-yl)-6,6-bis(4-methoxybenzenethio)cyclotriphosphazene (10): \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.50 \ (d, J = 5.0 \text{ Hz}, \text{1P}), 44.78 \ (d, J = 34.1 \text{ Hz}, \text{1P}), 47.19 \ (dd, J = 5.6, 34.1 \text{ Hz}, \text{2P}).

2,2-Dichloro-4,4,6,6-tris(4-chlorobenzothiophen-4-yl)-6-(4-methoxybenzenethio)cyclotriphosphazene (12): \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.64 \ (s, 1 \text{P}), 44.91 \ (d, J = 32.8 \text{ Hz}, \text{1P}), 46.18 \ (d, J = 32.2 \text{ Hz}, \text{1P}).

2,2-Dichloro-4,4,6,6-tetrakis(4-chlorobenzothiophen-6-yl)cyclotriphosphazene (15): colorless solids; \(R_f = 0.27\) (hexane/toluene = 3/1); \(^{31}\text{P} \mathrm{NMR} \ (162 \text{ MHz, } \text{CDCl}_3) \delta 18.75 \ (1 \text{P}), 46.36 \ (2 \text{P}) \ (\text{Coupling constant was too small to measure}); \(^{1}\text{H} \mathrm{NMR} \ (400 \text{ MHz, } \text{CDCl}_3) \delta 7.34 \ (d, J = 7.6 \text{ Hz}, 8 \text{H}), 7.42 \ (d, J = 7.6 \text{ Hz}, 8 \text{H}).

**Reaction of 3b with 4-trifluoromethylthiophenol (2c)**

\[
\begin{array}{ccc}
ArS \ P \ N \ P \ N \ P \ SAr & \xrightarrow{\text{4-trifluoromethylthiophenol (2c), Et}_3N} & ArS \ P \ N \ P \ N \ P \ SAr' \\
\text{Cl} \ P \ P \ Cl & \xrightarrow{\text{CHCl}_3/\text{MeCN (1/3), rt.}} & \text{Cl} \ P \ P \ \text{Cl}
\end{array}
\]

Into a two-necked reaction vessel were placed 3a (280.1 mg, 0.5 mmol), 4-trifluoromethylthiophenol (2c, 177.4 mg, 1.0 mmol), CHCl\textsubscript{3} (1.0 mL), and MeCN (3.0 mL). To the reaction mixture was added Et\textsubscript{3}N (0.14 mL, 1.0 mmol) dropwise, and the resulting mixture was stirred at room temperature for 15 h under argon atmosphere. The reaction mixture was diluted with AcOEt (6 mL) and sat. aq. NH\textsubscript{4}Cl (12 mL), and extracted with AcOEt (10 mL x 3). The combined organic layer was washed with H\textsubscript{2}O and sat. aq. NaCl, successively. The organic layer was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. The residue was analyzed by \(^{31}\text{P} \mathrm{NMR} \) to find a complex mixture of unidentified products was obtained.
Into a two-necked reaction vessel were placed 14 (388.3 mg, 0.51 mmol), 2c (175.3 mg, 0.98 mmol), CHCl₃ (1.0 mL), and MeCN (3.0 mL). To the reaction mixture was added Et₃N (0.14 mL, 1.0 mmol) dropwise, and the resulting mixture was stirred at 40 ºC for 23 h under argon atmosphere. To the resulting mixture was added AcOEt (6 mL) and sat. aq. NH₄Cl (12 mL), and extracted with AcOEt (10 mL × 3). The combined organic layer was washed with H₂O and sat. aq. NaCl successively. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was analyzed by 3¹P NMR to find a complex mixture of unidentified products was obtained.

REFERENCES