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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-teterachloro-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 Et_2O and tetrasubstituted 2,2,4,4-tetraamino-6,6-bis(4-methoxyphenylthio)-cyclotriphosphazene in acetonitrile, respectively. The reaction of 2,2,4,4-teterachloro-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.

INTRODUCTIOIN

Cyclotriphosphazenes, $P_3N_3X_6$, 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).

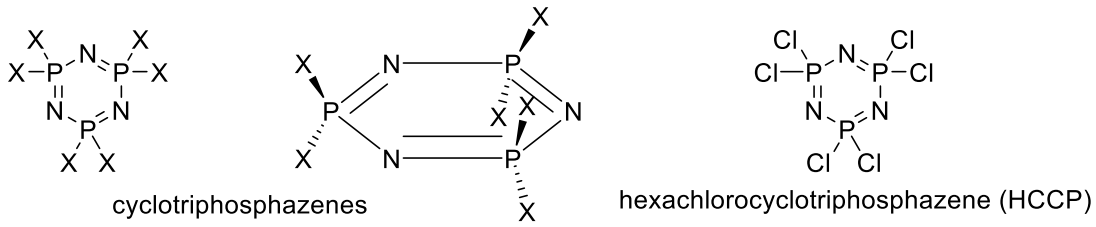
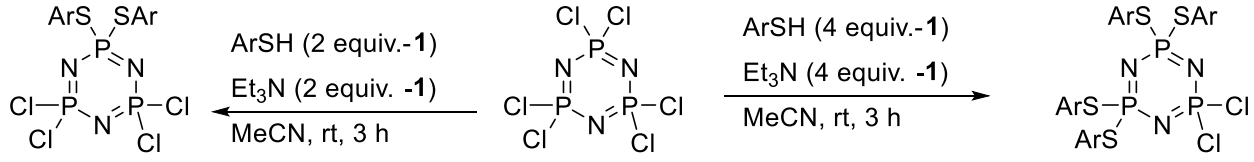


Figure 1. Cyclotriphosphazenes

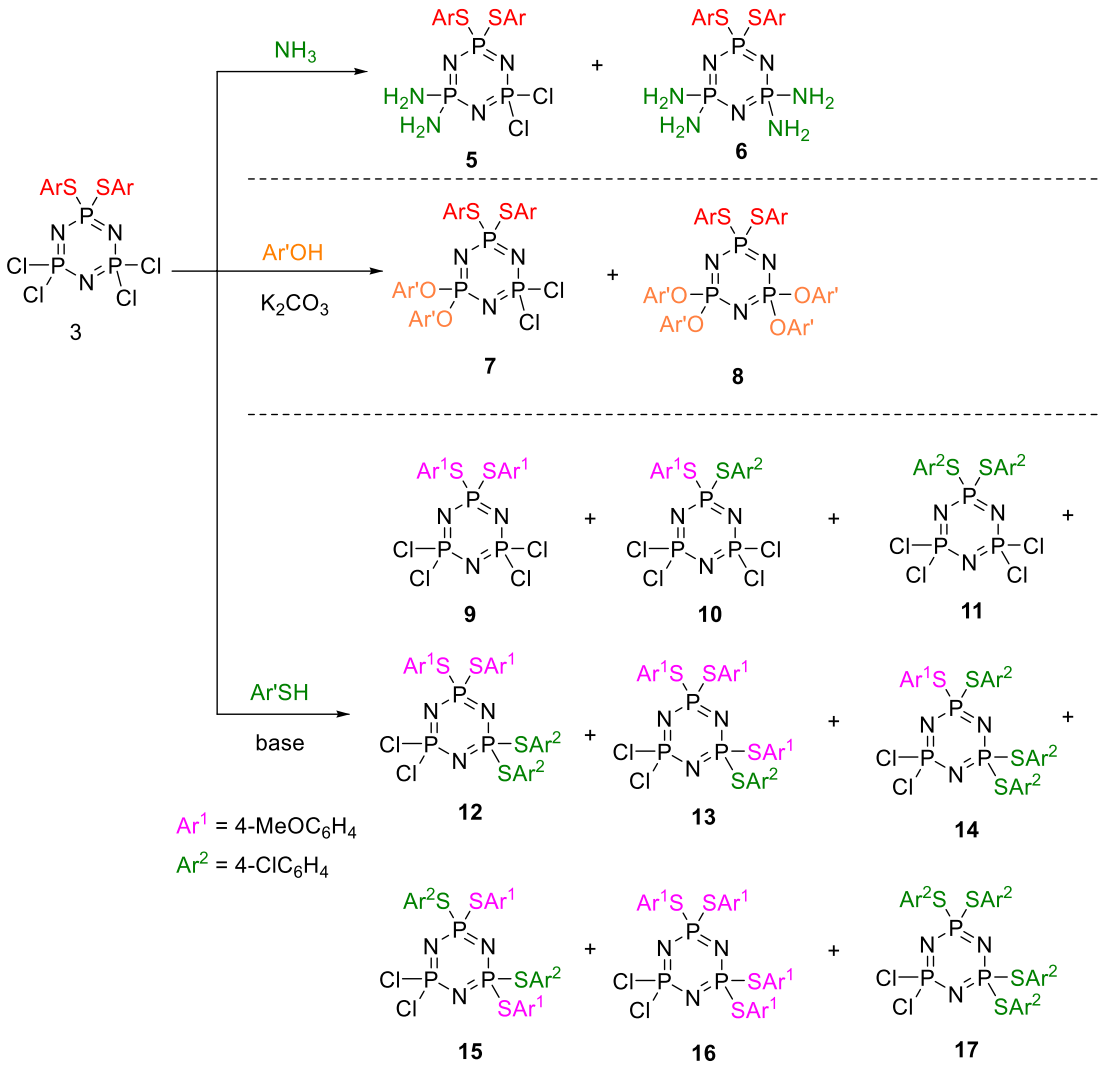
Most of cyclotriphosphazenes have been synthesized by nucleophilic substitution of hexachlorocyclotriphosphazene (HCCP), whose synthesis was firstly reported in 1834 by Liebig from reaction of PCl_5 and ammonia.[1] HCCP and its derivatives were used as frame retardants. From 2001, cyclotriphosphazenes were focused as functional materials[2] 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 thiophenols 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).



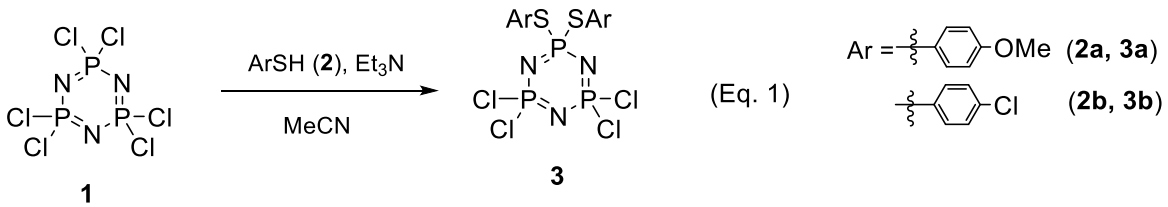
Scheme 1. Synthesis of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazenes **3** and 2,2,4,4-tetrakis(arylthio)-6,6-dichlorocyclotriphosphazenes **4**



Scheme 2. Nucleophilic substitution of **3** with NH_3, Ar'OH, and Ar'SH

RESULTS AND DISCUSSION

Synthesis of 2,2-bis(arylthio)-4,4,6,6-tetrachlorocyclotriphosphazene (Eq. 1)[16]

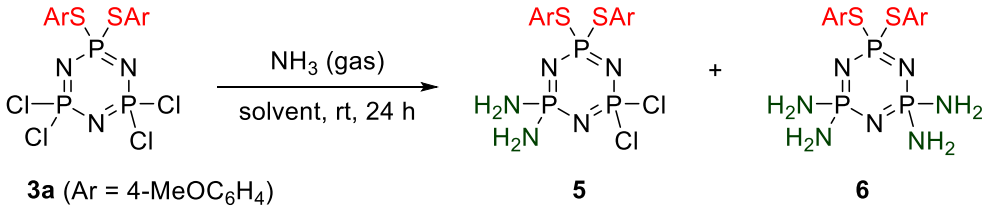


A MeCN solution of HCCP (**1**) was treated with 4-methoxythiophenol (**2a**, 2 equiv.) and Et_3N (2 equiv.) at room temperature for 24 h to give *gem*-disubstituted 2,2,4,4-tetrachloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (**3a**) in 96% yield. Similarly, the reaction of **1** with 4-chlorothiophenol at 0 ºC 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)

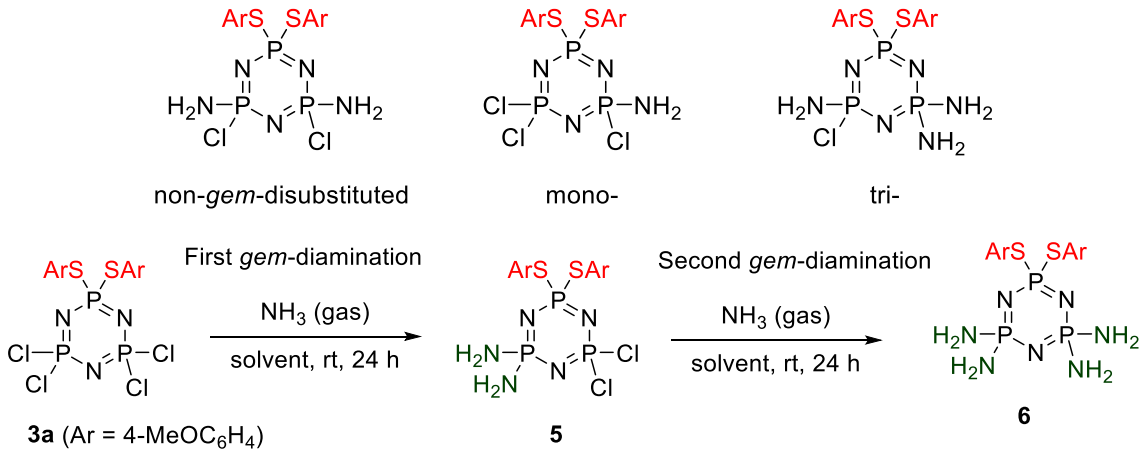
Aminolysis of **3a** with gaseous ammonia gave *gem*-disubstituted products, 2,2-diamino-4,4-dichloro-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (**5**, reaction solvent: Et_2O) and tetrasubstituted 2,2,4,4-tetraamino-6,6-bis(4-methoxyphenylthio)cyclotriphosphazene (**6**, reaction solvent: MeCN), 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 $CHCl_3$/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 $CHCl_3/Et_2O$ (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 Et_2O.

Table 1. Aminolysis of **3a** with gaseous ammonia



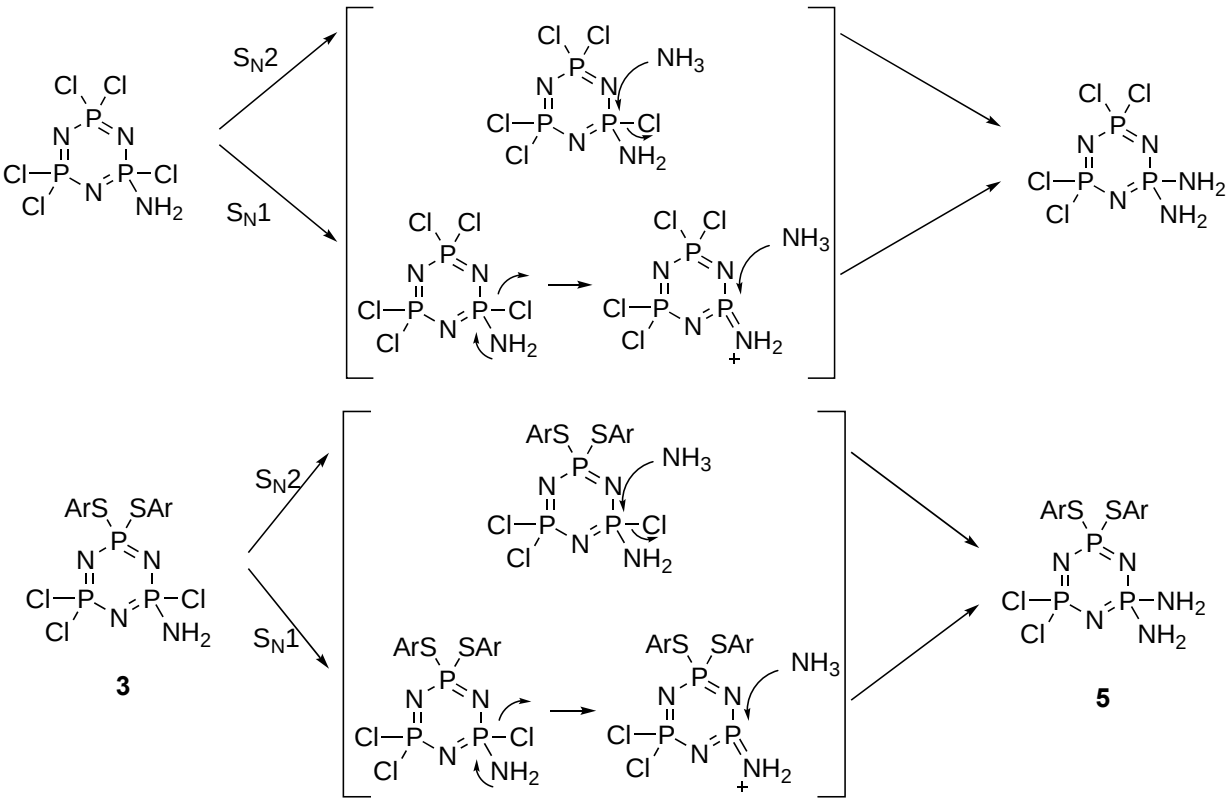
Entry	**3a** (mmol)	Solvents (mL)	Time (h)	Ratio[a] (%) **5**	**6**	**3a**
1	0.49	$CHCl_3$/MeCN (0.5/1.5)	24	n.d.[b]	77	n.d.[b]
2	0.49	$CHCl_3$/MeCN (0.5/1.5)	31	n.d.[b]	82	n.d.[b]
3	1.5	$CHCl_3/Et_2O$ (3.0/10)	71	31	69	n.d.[b]
4	0.49	Et_2O (40)	17	83	n.d.[b]	17

[a] Determined by ^{31}P 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 Et_2O and 2,2,4,4-tetraamino-6,6-dichlorocyclotriphospazene in MeCN.[18,19] Beşli *et al.*[17] reported that amination of 2,2,4,4-tetrachloro- 6,6-bis(phenylthio)cyclotriphosphazene (**3c**) 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.[16,17] 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**

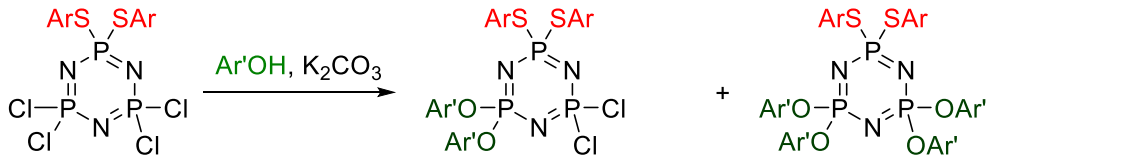
Reaction of 2a with phenoxide

Chen-Yang investigated phenoxylation of HCCP,[20] 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. 2) when 2 equiv. of phenoxide were used, a mixture of diphenoxylated triphosphazenes $N_3P_3Cl_4(OPh)_2$ (*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/K_2CO_3. When $CHCl_3$/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, Et_2O, 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

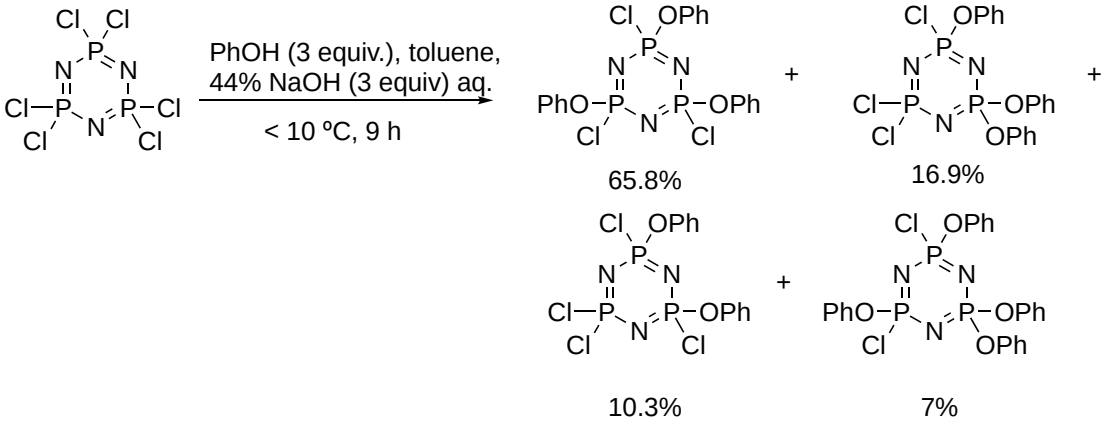


3a (Ar = 4-$MeOC_6H_4$) **7** **8** (Ar' = 4-ClC_6H_4)

Entry	4-chlorophenol (equiv)	K_2CO_3 (equiv)	Solvent	Temp (°C)	Time (h)	Ratio[a] **7**	**8**	**3a**
1	4.1	5.2	MeCN	reflux	45	87	13	n.d.[b]
2	5.2	5.1	$CHCl_3$/MeCN (1 : 3)	reflux	20	60	n.d.[b]	40
3	5.0	5.0	acetone	reflux	48	87	13	n.d.[b]
4	5.0	5.0	THF	50	48	no reaction		
5	5.2	5.2	Et_2O	reflux	15	no reaction		
6	5.0	5.0	Tol	reflux	15	no reaction		

[a]Determined by ^{31}P NMR. [b]Not detected.

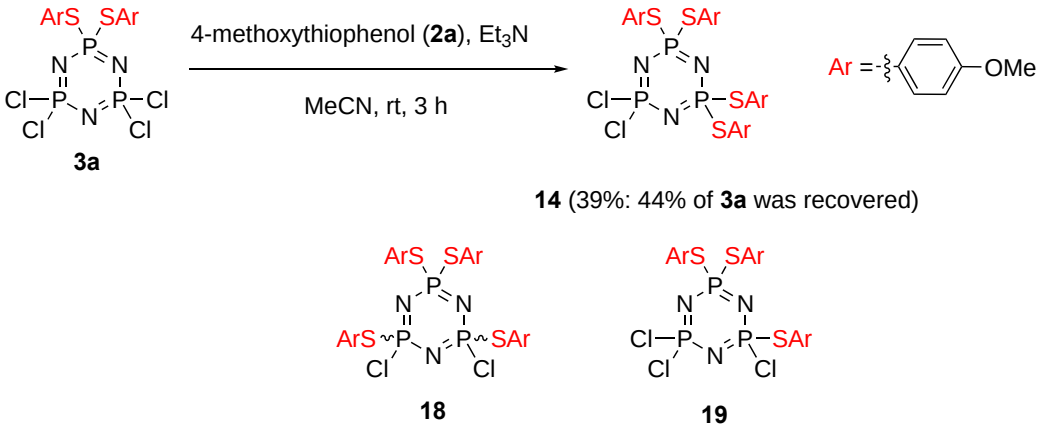
When HCCP was treated with NaOH and phenol (3 equiv.), a mixture of non-*gem* $P_3N_3(OC_6H_5)_3Cl_3$ (66%), *gem*-$P_3N_3(OC_6H_5)_3Cl_3$ (17%), non-*gem* $P_3N_3(OC_6H_5)_2Cl_4$ (10%), and non-*gem* $P_3N_3(OC_6H_5)_4Cl_2$ (7%) were obtained (Scheme 5).[22] This means that thiophenoxy-substituted cyclotriphosphazene **3** was less active than HCCP or phenoxy-substituted cyclotriphosphazene.



Scheme 5. Reaction of HCCP with phenol/NaOH

Reaction of 3a with Thiophenol

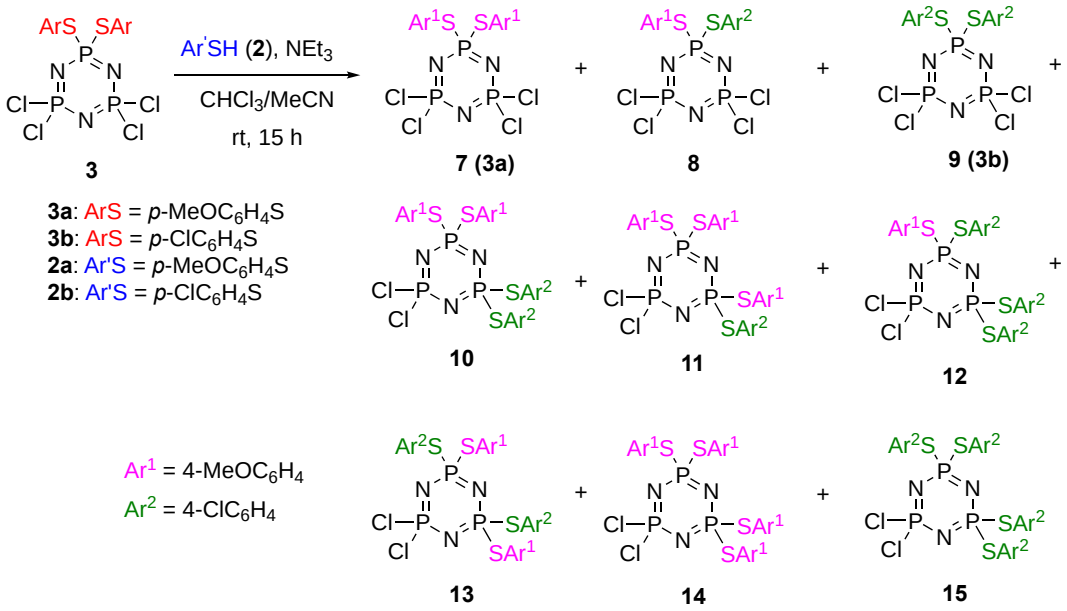
Firstly, reaction of **3a** and 4-methoxythiophenol (**2a**) was investigated (Scheme 6). When **3a** was treated with 2 equiv. of **2a**/Et_3N, 2,2,4,4-tetrathiolated product **14** was obtained in 39% yield, and neither *gem*/non-*gem* isomers **18** nor trisubstituted product **19** was obtained. When the reaction was carried out at 0 ºC, 4 : 1 mixture of **3a** and **14** was obtained.



Scheme 6. Reaction of **3a** with **2a**

Though this reaction seems as simple second geminal nucleophilic disubstitution 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



3	2	Product Ratio[a,b]						
		7 (3a)	**8**	**10**	**11**	**12**	**13**	**15**
3a	**2b**	20	13	12	21	7	13	8
3b	**2a**	24	10	trace	12	8	13	trace

[a]Ar^1 = 4-$MeOC_6H_4$, Ar^2 = 4-ClC_6H_4. [b]The ratio was determined by ^{31}P NMR.

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**

Entry	**3b** (mmol)	**2a** (mmol)	Base (mmol)	Solvents (mL)	Temp. (°C)	Time. (h)
1	0.29	0.57	Et_3N (0.57)	MeCN (5.0)	0	3
2	0.20	0.39	K_2CO_3 (0.39)	MeCN (4.0)	-18	16
3	0.20	0.40	K_2CO_3 (0.39)	MeCN (5.0)	rt.	3
4	0.5	1.0	Et_3N (1.0)	$CHCl_3$/MeCN (1.0/3.0)	rt.	15

Entry	**7**	**8**	**9 (3b)**	**10**	**11**	**12**	**13**	**14**	**15**
1	n.d.[b]	n.d.[b]	n.d.[b]	trace	56	n.d.[b]	n.d.[b]	43	n.d.[b]
2	n.d.[b]	n.d.[b]	100	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]
3	26	18	35	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]	n.d.[b]
4	13	21	n.d.[b]	12	7	21	13	n.d.[b]	8

In the reaction of **3b** with **2a**, when Et_3N was used as a base, tetrasubstituted products **11** and **14** were obtained as a major products (Entry 1), whereas K_2CO_3 as a base gave disubdtituted products **7**, **8**, and **9** (Entry 3). At low temperature (-18 ºC), no reaction occurred (Entry 2). In $CHCl_3$/MeOH, a complex mixture of di- and tetrasubstituted products was obtained (Entry 4).

Table 5. Reaction of **3a** with **2b**

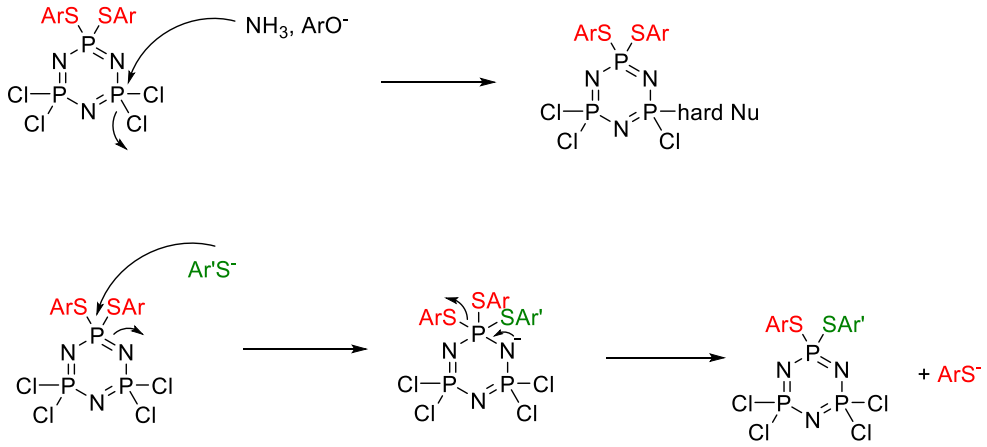
Entry	**3a** (mmol)	**2b** (mmol)	Base (mmol)	Solvents (mL)	Time. (h)
1	0.49	0.99	K_2CO_3 (0.99)	MeCN (6.0)	3
2	0.50	0.99	Et_3N (1.0)	MeCN (6.0)	3
3	0.50	1.0	Et_3N (1.0)	$CHCl_3$/MeCN (0.5/1.5)	15

Entry	**7 (3a)**	**8**	**10**	**11**	**12**	**13**	**15**
1	11	7	10	n.d.[b]	9	17	n.d.[b]
2	trace	trace	21	27	21	31	n.d.[b]
3	3	trace	22	23	23	21	4

In the reaction of **3a** and **2b**, Et_3N gave tetrasubstituted products, whereas K_2CO_3 gave di- and tetrasubstituted products (Table 5).

In all cases, the scramble occurred, and a mixture of *gem*-dithiosubstituted and *gem*-tetrathiosubstituted products was obtained: trithiosubstituted, non-*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 (**P**Cl_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 **P**Cl_2 to give tetrathiosubstituted products.



Scheme 7. A plausible mechanism of exchange of thiophenoxide

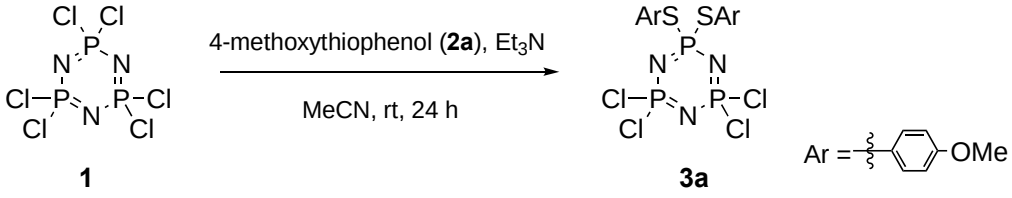
When 4-trifluoromethylthiophenol was used as the second thiophenols, only a complex mixture of unidentified products was obtained.

CONCLUSION

Hexachlorocyclotriphosphazene was allowed to react with thiophenols to give 2,2-bis(arylthio)-4,4,6,6-tetrachlocyclotriphosphazenes. To introduce the second nucleophile, we tried to introduce ammonia, phenoxides, and thiophenoxides. Nucleophilic substitution of 2,2-bis(arylthio)-4,4,6,6-tetrachlocyclotriphosphazenes 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-tetrachlorocyclotriphosphazene[16]



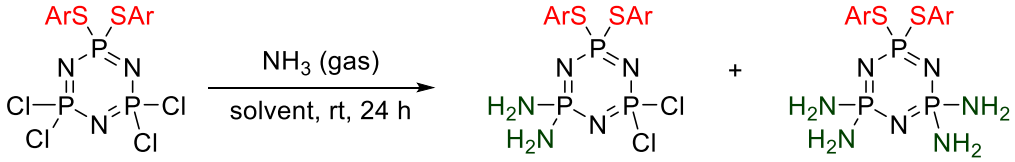
1 **3a**

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_3N (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_4Cl solution (60 mL). The organic phase was dried with sodium sulfate and concentrated under reduced pressure. The residue was analyzed by ^1H 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); ^1H 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_3N (0.30 mL, 2.2 mmol) in MeCN (8 mL) at 0 ºC 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.); ^1H 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



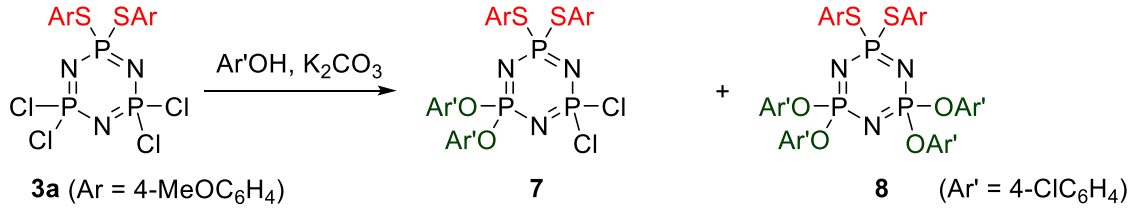
3a (Ar = 4-$MeOC_6H_4$) **5** **6**

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_2O 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-Ttetraamino-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 3a with phenoxide

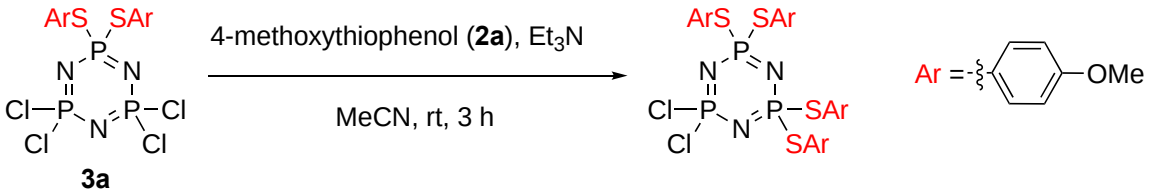


To a solution of **3a** (271.3 mg, 0.49 mmol) in MeCN (5.0 mL) were added 4-chlorophenol (216.2 mg, 1.99 mmol) and K_2CO_3 (348.5 mg, 2.54 mmol). The mixture was heated to reflux for 19 h under an argon atmosphere. After usual work-up, the reaction mixture was analyzed by ^{31}P NMR to find that a mixture 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, $CDCl_3$) δ 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, $CDCl_3$) δ 51.94 (t, *J* = 25.4 Hz, 1P), 6.67 (d, *J* = 25.4 Hz, 2P).

Reaction of 3a with 4-methoxythiophenol (2a)



14 (39%: 44% of **3a** was recovered)

To a mixture of **3a** (274.3 mg, 0.49 mmol), 4-methoxythiophenol (**2a**, 139.8 mg, 0.99 mmol) and MeCN (6 mL) was added Et_3N (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_4Cl (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_2O and sat. aq. NaCl, successively. The organic layer was dried over anhydrous Na_2SO_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 ℃; R_f = 0.30 (hexane/AcOEt = 7/2); ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.40 (t, *J* = 5.7 Hz, 1P), 46.80 (d, *J* = 5.7 Hz, 2P); ^{1}H NMR (400 MHz, $CDCl_3$) 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), K_2CO_3 (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. NH_4Cl (20 mL). The mixture was extracted with AcOEt (10 mL x 3). The combined organic layer was washed with H_2O (10 mL) and sat. aq. NaCl, successively, dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure. The residue was confirmed by ^{31}P NMR, to find tha 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 Ar^1S and Ar^2S were exchanged, was obtained. The ratio of these compounds was determined by ^{31}P NMR.

2,2,4,4-Tetrachloro-6-(4-chlorophenylthio)-6-(4-methoxyphenylthio)cyclotriphosphazene (**8**): ^{31}P NMR (162 MHz, $CDCl_3$) 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), K_2CO_3 (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. NH_4Cl (20 mL). The mixture was extracted with AcOEt (10 mL x 3). The organic layers were combined and washed with H_2O (10 mL) and sat. aq. NaCl, successively, dried over Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure. The residue was confirmed by ^{31}P 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}P NMR.

2,2-Dichloro-4-(4-chlorobenzenethio)-4,6,6-tris(4-methoxybenzenethio)cyclotriphosphazene (**11**): ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.47 (d, *J* = 2.5 Hz, 1P), 45.80 (d, *J* = 35.3 Hz, 1P), 46.99 (dd, *J* = 5.0, 35.3 Hz, 1P).

2,2-Dichloro-4,6-bis(4-chlorobenzenethio)-4,6-bis(4-methoxybenzenethio)cyclotriphosphazene (**13**): ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.50 (d, *J* = 5.0 Hz, 1P), 46.02 (s, 2P).

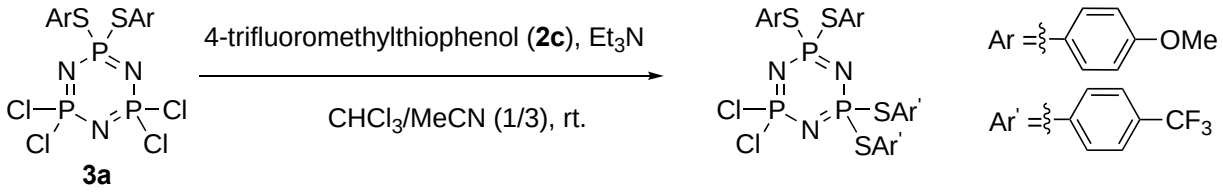
2,2-Dichloro-4,4,6,6-tetrakis(4-methoxybenzenethio)cyclotriphosphazene (**14**): colorless solids; R_f = 3.0 (hexane/AcOEt = 7/2); ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.40 (t, *J* = 5.7 Hz, 1P), 46.80 (d, *J* = 5.7 Hz, 2P); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 12H), 6.88 (d, *J* = 8.8 Hz, 8H), 7.44 (d, *J* = 8.8 Hz, 8H).

2,2-Dichloro-4,4-bis(4-chlorobenzenethio)-6,6-bis(4-methoxybenzenethio)cyclotriphosphazene (**10**):^{31}P NMR (162 MHz, $CDCl_3$) δ 18.50 (d, *J* = 5.0 Hz, 1P), 44.78 (d, *J* = 34.1 Hz, 1P), 47.19 (dd, *J* = 5.6, 34.1 Hz, 1P).

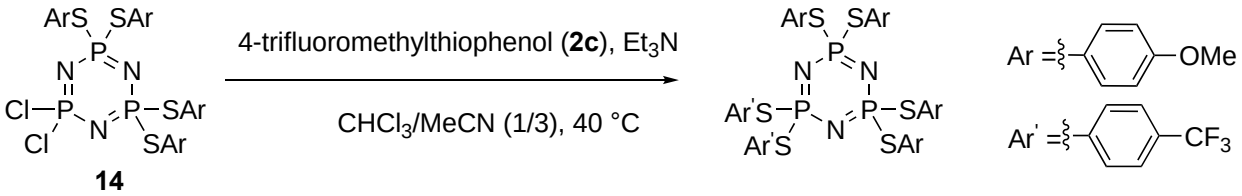
2,2-Dichloro-4,4,6-tris(4-chlorobenzenethio)-6-(4-methoxybenzenethio)cyclotriphosphazene (**12**): ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.64 (s, 1P), 44.91 (d, *J* = 32.8 Hz, 1P), 46.18 (d, *J* = 32.2 Hz, 1P).

2,2-Dichloro-4,4,6,6-tetrakis(4-chlorobenzenethio)cyclotriphosphazene (**15**): colorless solids; R_f = 0.27 (hexane/toluene = 3/1); ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.75 (1P), 46.36 (2P) (Coupling constant was too small to measure.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.6 Hz, 8H), 7.42 (d, *J* = 7.6 Hz, 8H).

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



Into a two-necked reaction vessel were placed **3a** (280.1 mg, 0.5 mmol), 4-trifluoromethylthiophenol (**2c**, 177.4 mg, 1.0 mmol), $CHCl_3$ (1.0 mL), and MeCN (3.0 mL). To the reaction mixture was added Et_3N (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_4Cl (12 mL), and extracted with AcOEt (10 mL x 3). The combined organic layer was washed with H_2O and sat. aq. NaCl, successively. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was analyzed by ^{31}P 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), $CHCl_3$ (1.0 mL), and MeCN (3.0 mL). To the reaction mixture was added Et_3N (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. NH_4Cl (12 mL), and extracted with AcOEt (10 mL x 3). The combined organic layer was washed with H_2O and sat. aq. NaCl successively. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was analyzed by ^{31}P NMR to find a complex mixture of unidentified products was obtained.

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