Lack of co-crystal formation with cyclotriphosphazenes: a cautionary tale

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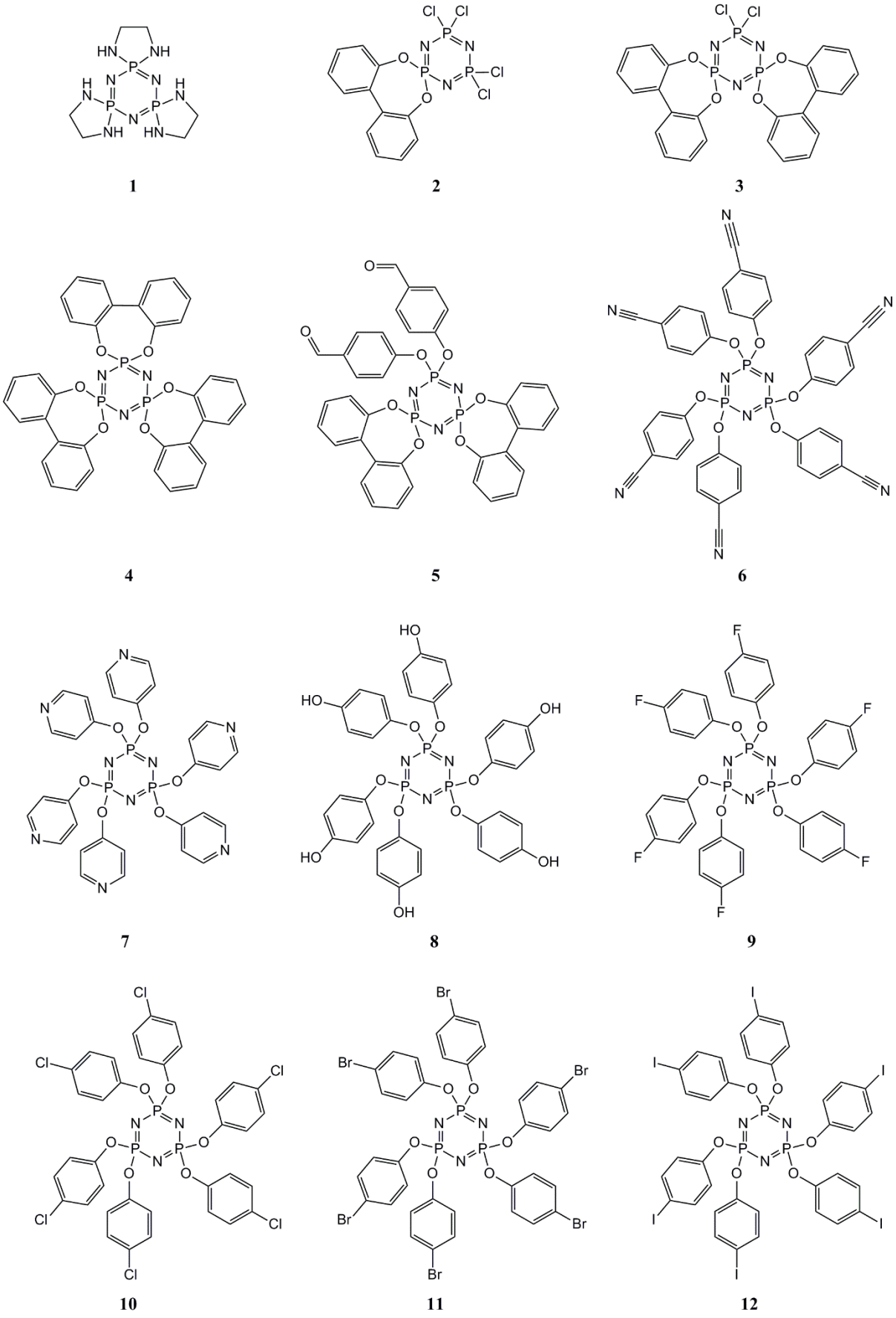
Supporting Information



Scheme S1 The cyclotriphosphazenes investigated in this work.

Co-crystallisation experiments

The components of each crystallisation experiment (see Tables S1, S2, S4, S6, S8-14) were dissolved in the appropriate solvent with gentle heat and stirring. In cases where there were still undissolved particles, the solution was filtered through a non-sterile 33 mm Millex-HV syringe filter unit into a glass vial. All solutions were left to stand at room temperature and crystals were formed either *via* slow evaporation of the solvent, vapour diffusion of one solvent into another or solutions were layered with a second solvent to induce crystal formation at the interface of the two solutions.

Table S1 Co-crystallisation experiments carried out with **1**. All crystallisations were carried out *via* slow evaporation. Crystals obtained were that of the known hydrate of **1** (CSD-COPVAE) or no product was obtained.

Co-former	**Quantity (1; co-former) /mg**	**Mole ratio (1:co-former)**	**Solvent system**	**Product**
isophthalic acid	29; 14	1:1	methanol	none
terephthalic acid	15; 15	1:2	methanol	terephthalic acid
trimesic acid	29; 20	1:1	methanol	none
succinic acid	14; 15	1:3	methanol	none
maleic acid	13; 13	1:3	methanol/THF	none
tartaric acid	13; 12	1:3	methanol	none
2,6-naphthalene dicarboxylic acid	29:18	1:1	methanol	2,6-naphthalene dicarboxylic acid
solvent	-	-	THF	none
solvent	-	-	hexane/THF	known COPVAE
solvent	-	-	DCM	none
solvent	-	-	DMSO	none
solvent	-	-	acetonitrile	known COPVAE
solvent	-	-	methanol	none
solvent	-	-	ethanol	none
solvent	-	-	DMF	none
solvent	-	-	NMP	none
solvent	-	-	chloroform	none

Table S2 Co-crystallisation experiments carried out with **2**. All crystallisations were carried out *via* slow evaporation. In some cases crystals of the starting materials were obtained, otherwise no crystals were obtained.

Co-former	Quantity (2; co-former) /mg	Mole ratio (2:co-former)	Solvent system	Product
DCM	50	As solvent	-	none
benzene	45	As solvent	-	none
toluene	46	As solvent	-	none
chloroform	54	As solvent	-	none
acetonitrile	49	As solvent	-	none
pyridine	48	As solvent	-	none
1,4-dioxane	55	As solvent	-	none
NMP	51	As solvent	-	none
THF	74	As solvent	-	none
DMF	68	As solvent	-	none
isophthalic acid	53; 41	1:2	DCM/THF	none
imidazole	55; 25	1:3	DCM/THF	none
benzimidazole	59; 33	1:3	DCM/THF	benzimidazole hydrate
4,4'-bipyridine	52; 35	1:2	DCM/THF	none
benzonitrile	54	As solvent	-	none
3,4-lutidine	62; 35	1:3	DCM	none

Table S3 Mechanochemical experiments carried out with **2**. Samples were ground by hand in a mortar and pestle for approximately 5 minutes, yielding homogenous powders.

Co-former	Quantity (2; co-former) /mg	Mole ratio (2: co-former)
4,4'-bipyridine	28; 32	1:2
imidazole	56; 24	1:2
benzimidazole	51; 28	1:2
4,4'-bipyridine	62; 21	1:1
imidazole	61; 10	1:1
benzimidazole	64; 15	1:1
piperazine	61; 12	1:1
4,4'-trimethylene dipyridine	65; 30	1:1

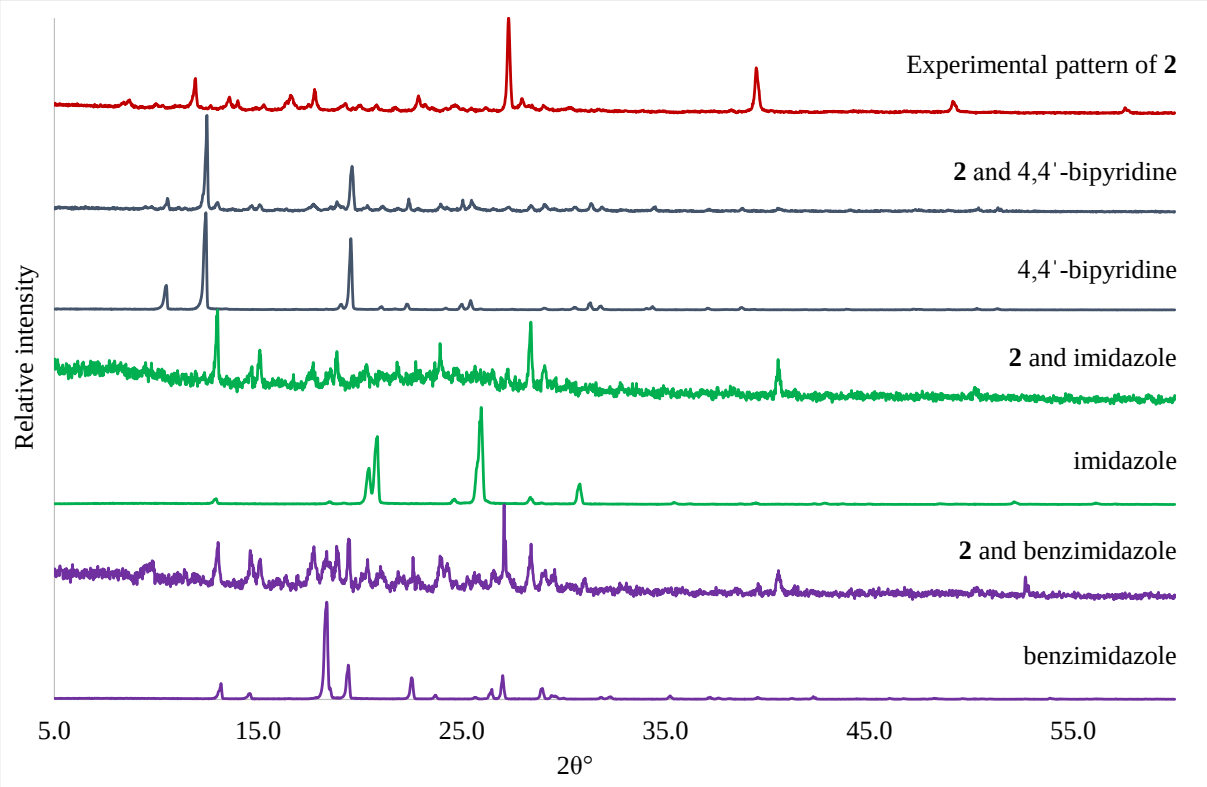


Figure S1 PXRD results of the grinding experiments with **2**. The powder patterns of the products either correspond to that of **2** or the co-crystal former.

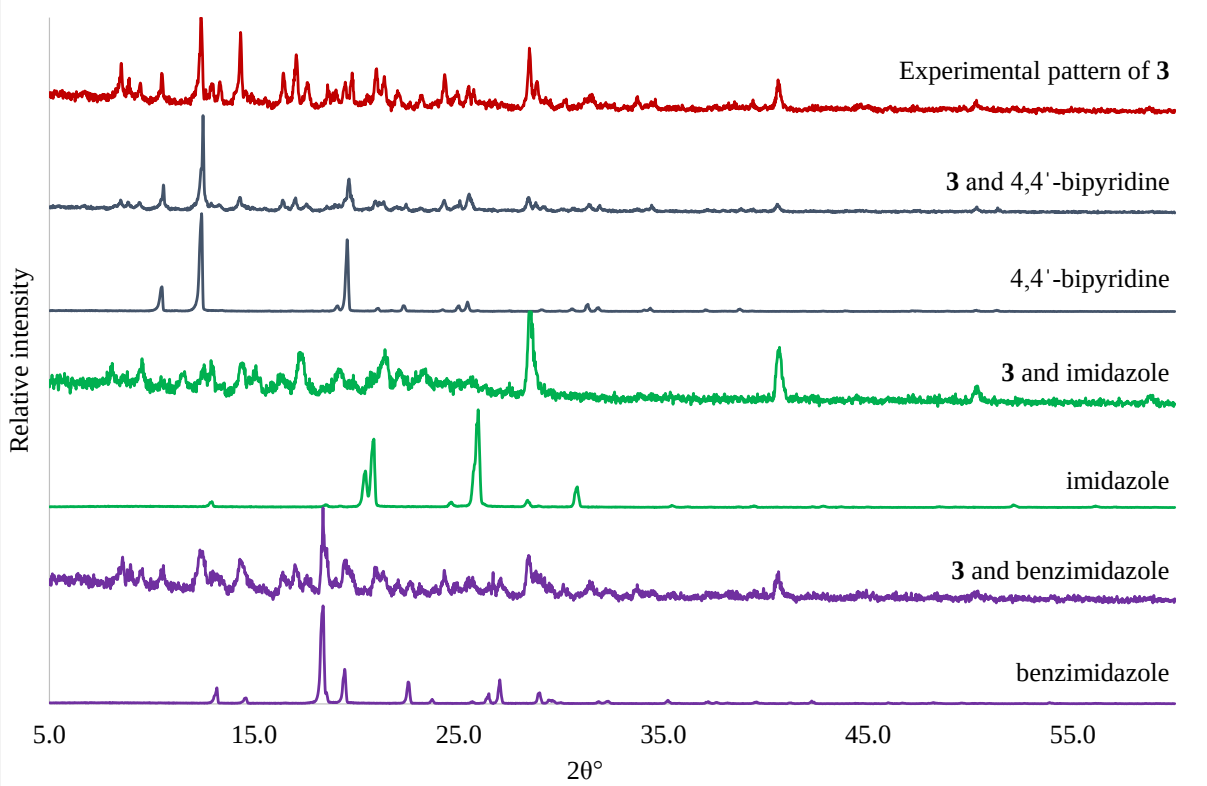


Figure S2 The PXRD results of the mechanochemical experiments between **3** and 4,4'-bipyridine, imidazole and benzimidazole. In most cases there appears to be an agreement between the patterns of the product and 4,4'-bipyridine, imidazole and benzimidazole.

Table S4 Co-crystallisation experiments carried out with **3**. All crystallisations were carried out *via* slow evaporation. In most cases no crystals were obtained, and in a few cases crystals of the starting materials were obtained.

Co-former	Quantity (3; co-former) /mg	Mole ratio (3: co-crystal former)	Solvent system	Product
4,4'-bipyridine	108; 111	1:3	DCM	none
imidazole	107; 65	1:3	DCM	none
benzimidazole	103; 83	1:3	DCM	benzimidazole hydrate
m-xylene	100	excess	*m*-xylene	none
benzene	59	As solvent	-	none
toluene	60	As solvent	-	Known **3**
DCM	60	As solvent	-	none
chloroform	57	As solvent	-	none
acetonitrile	53	As solvent	-	none
pyridine	52	As solvent	-	none
1,4-dioxane	57	As solvent	-	none
NMP	63	As solvent	-	none
THF	62	As solvent	-	none
DMF	67	As solvent	-	none
isophthalic acid	62; 35	1:2	DCM/THF	none
imidazole	69; 15	1:2	DCM/THF	none
benzimidazole	63; 31	1:2	DCM/THF	none
4,4'-bipyridine	63; 33	1:2	DCM/THF	none

Table S5 Mechanochemical experiments carried out with **3**. Samples were ground by hand in a mortar and pestle for approximately 5 minutes, yielding homogenous powders.

Co-former	Quantity (3; co-former) /mg	Mole ratio (3: co-former)
4,4'-bipyridine	62; 33	1:2
imidazole	61; 14	1:2
benzimidazole	60; 13	1:2

Table S6 Summary of crystallisation experiments with **4** in a range of solvents and with a series of potential co-crystal formers. All crystallisations were carried out *via* slow evaporation. Only one crystal of **4** was obtained.

Co-former	**Quantity (4; co-former) /mg**	**Mole ratio (4: co-former)**	**Solvent system**	**Product**
benzene	58	-	-	none
toluene	61	-	-	none
DCM	60	-	-	known **4**
chloroform	58	-	-	none
pyridine	60	Excess	-	none
acetonitrile	62	-	-	none
dioxane	60	-	-	none
NMP	59	-	-	none
THF	61	-	-	none
DMF	60	-	-	none
m-xylene	60	-	-	none
isophthalic acid	60; 51	1:3	THF	none
imidazole	61; 21	1:3	THF	none
benzimidazole	63; 36	1:3	THF	none
4,4'-bipyridine	62; 48	1:3	THF	none

Table S7 Mechanochemical experiments carried out with **4**. Samples were ground by hand in a mortar and pestle for approximately 5 minutes, yielding homogenous powders.

Co-former	**Quantity (4; co-former) /mg**	**Mole ratio (4: co-former)**
4,4'-bipyridine	61; 20	1:1
imidazole	61; 9	1:1
benzimidazole	64; 14	1:1
piperazine	63; 9	1:1
4,4'-trimethylene dipyridine	63; 28	1:1

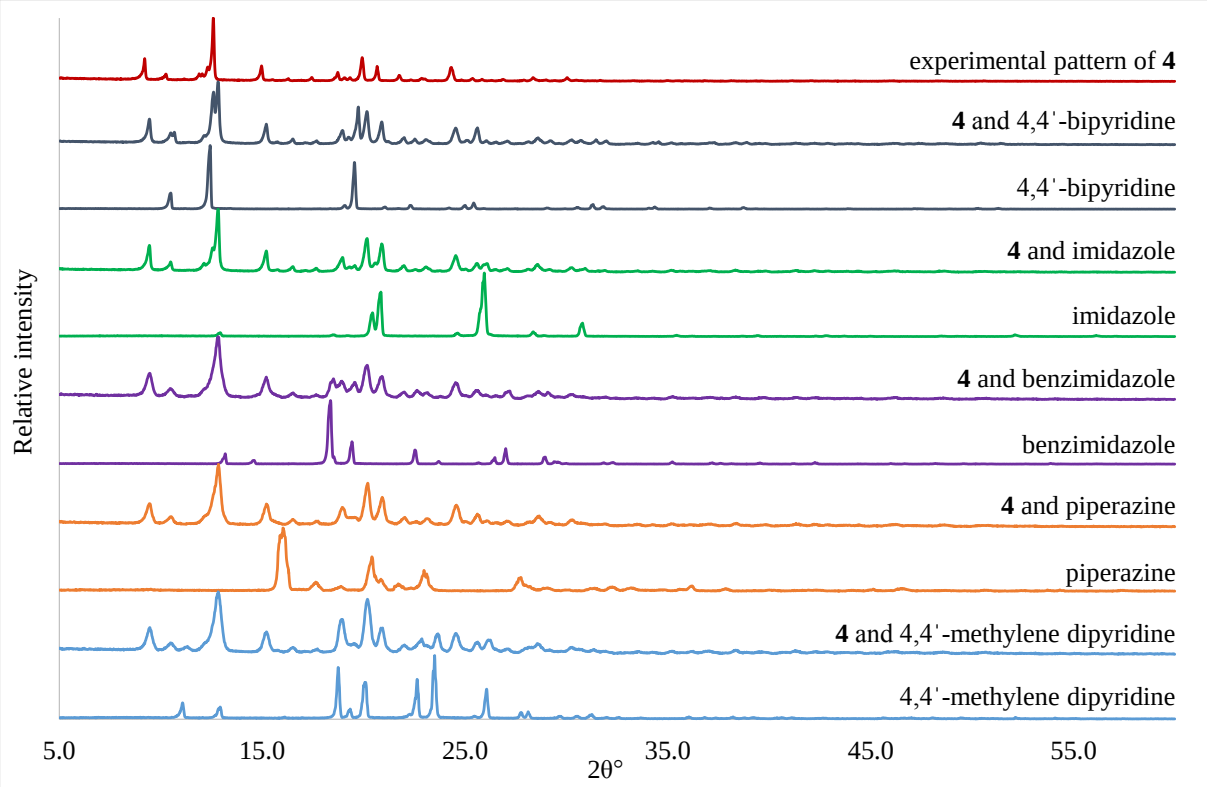


Figure S3 The PXRD results of mechanochemical experiments with **4**. In all cases the product of the grinding experiment corresponds to the powder pattern of **4**, indicating that no co-crystals were formed.

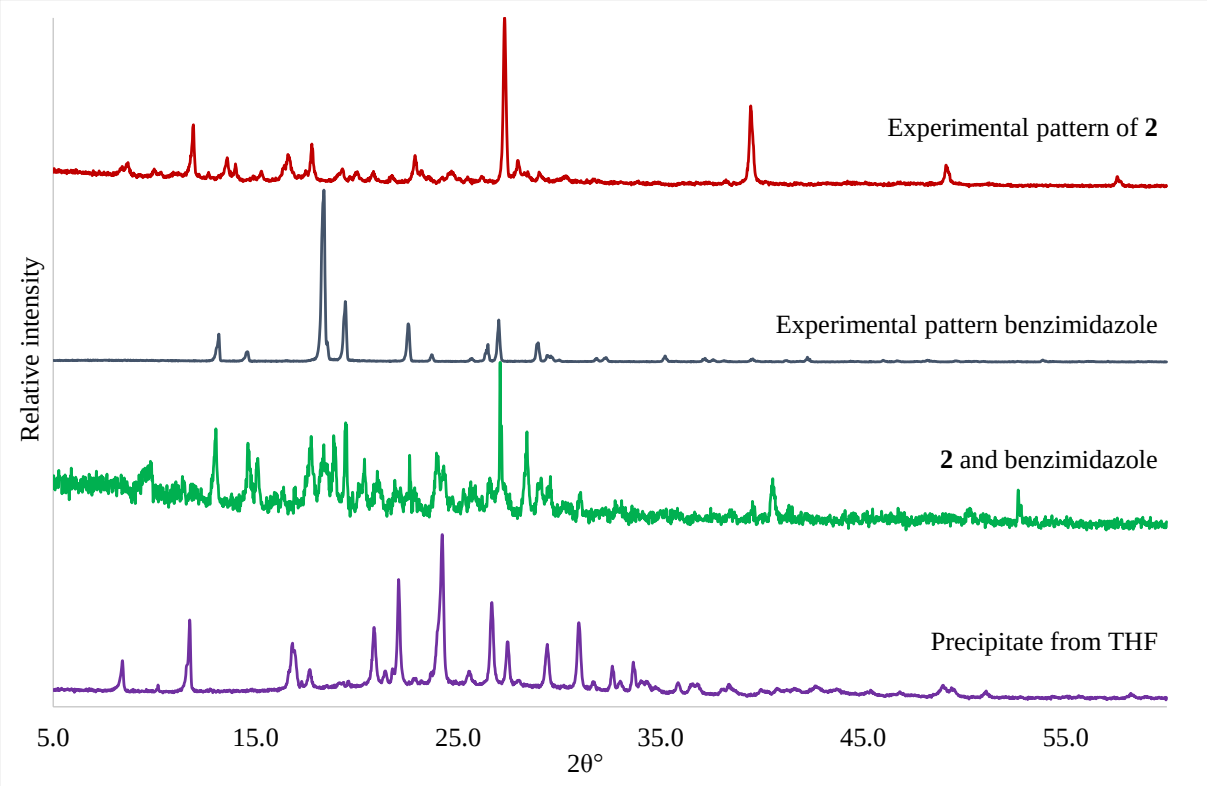


Figure S4 The PXRD results of the precipitate formed when the product of mechanochemical synthesis between **2** and benzimidazole is dissolved in THF.

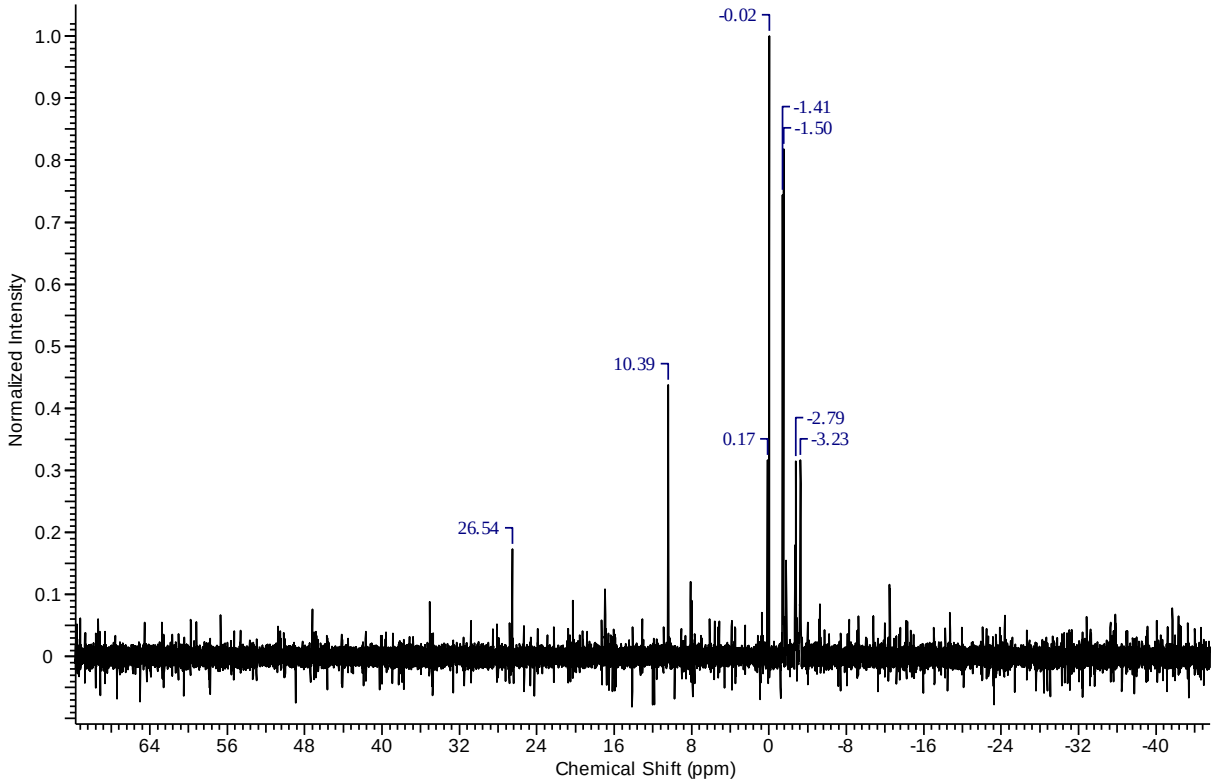


Figure S5 The ^{31}P NMR spectrum of the precipitate formed when the product of mechanochemical synthesis between **2** and benzimidazole is dissolved in THF. Multiple peaks for phosphorous indicates that ring cleavage could have occurred.

Table S8 Summary of crystallisation experiments with **5** from a range of solvents. Approximately 60 mg of **5** was used in each crystallisation.

Solvent system	**Co-crystal former**	**Crystallisation technique**	**Result**
benzene	none	slow evaporation	crystals of **5**
toluene	none	slow evaporation	no crystalline product
methanol	none	slow evaporation	no crystalline product
NMP	none	slow evaporation	no crystalline product
DMSO	none	slow evaporation	no crystalline product
chloroform	none	slow evaporation	no crystalline product
acetone	none	slow evaporation	crystals of **5**

Table S9 Co-crystallisation experiments carried out with **5**.

Co-former	Quantity (5; co-former) /mg	Mole ratio (5: co-former)	Solvent system	Crystallisation technique	Product
pamoic acid	44; 21	1:1	THF	slow evaporation	none
piperazine	40; 6	1:1	THF	slow evaporation	none
2,6-diaminopyridine	41; 7	1:1	THF	slow evaporation,	none
trimesic acid	46; 12	1:1	THF/hexane	layering	trimesic acid and hexane
isophthalic acid	41; 10	1:1	THF/hexane	layering	none
benzonitrile	42; excess	-	THF	slow evaporation	none
2,6-diaminopyridine	40; 12	1:2	THF/diethyl ether	vapour diffusion	none
1,2-diaminoethane	42; 20	1:6	THF/diethyl ether	vapour diffusion	none
1,3-diaminopropane	43; 21	1:6	THF/diethyl ether	vapour diffusion	none
1,4-diaminobutane	42; 15	1:3	THF/diethyl ether	vapour diffusion	none none
1,5-diaminopentane	42; 18	1:3	THF/diethyl ether	vapour diffusion	none
1,6-diaminohexane	41; 15	1:3	THF/diethyl ether	vapour diffusion	none
piperazine	40; 12	1:2	THF/diethyl ether	vapour diffusion	none
p-aminobenzoic acid	40; 15	1:2	DCM/diethyl ether	vapour diffusion	none
p-aminobenzoic acid	40; 17	1:2	DMF/diethyl ether	vapour diffusion	none
2-aminoterephthalic acid	41; 21	1:2	THF/diethyl ether	vapour diffusion	crystals of **5**
2-aminoterephthalic acid	43; 21	1:2	DMF/diethyl ether	vapour diffusion	none
2,6-dipicolinic acid	42; 21	1:2	THF/DCM	vapour diffusion	none
2,6-dipicolinic acid	43; 19	1:2	DMF/ether	vapour diffusion	crystals of **5**
3,5-dinitrobenzoic acid	40; 30	1:2	THF/diethyl ether	vapour diffusion	3,5-dinitrobenzoic acid
3,5-dinitrobenzoic acid	43; 25	1:2	DMF/diethyl ether	vapour diffusion	none
1,6-dihydroxynaphthalene	42; 19	1:2	THF/diethyl ether	vapour diffusion	crystals of **5**
1,6-dihydroxynaphthalene	45; 19	1:2	DMF/diethyl ether	vapour diffusion	crystals of **5**
o-phenylenediamine	48; 15	1:2	THF/diethyl ether	vapour diffusion	none
o-phenylenediamine	40; 16	1:2	DMF/diethyl ether	vapour diffusion	none
phenol	41; 15	1:2	THF/diethyl ether	vapour diffusion	crystals of **5**
phenol	40; 11	1:2	DMF/diethyl ether	vapour diffusion	crystals of **5**
thiourea	100; 23	1:2	THF	Slow evaporation	none
triphenylphosphine oxide (TPPO)	64; 59	1:2	THF	Slow evaporation	none
4-hydroxybenzaldehyde	63; 22	1:2	THF	Slow evaporation	none

Table S10 Summary of co-crystallisation experiments with **6**.

Co-crystal former	Quantity (6; co-former) /mg	Mole ratio (6: co-former)	Solvent system	Crystallisation technique	Product
iodopentafluorobenzene	52; 41	1:3	DCM	Slow evaporation	none
bromopentafluorobenzene	53; 34	1:3	DMSO	Slow evaporation	crystals of **6**
hexakis(4-iodophenoxy)-cyclotriphosphazene	29; 59	1:1	DMSO/chloroform	Layered	none
hexakis(4-bromophenoxy)-cyclotriphosphazene	36; 54	1:1	DMSO/chloroform	Layered	crystals of **11**
none	50	-	DMSO	Slow evaporation	crystals of **6**

Table S11 Summary of co-crystallisation experiments with **7**. The first four crystallisations in the table were carried out *via* slow evaporation, and the rest listed in the table were carried out by layering two solutions.

Co-crystal former	Mole ratio (7: co-former)	Quantity (7: co-former) /mg	Solvent	Product
iodopentafluorobenzene	1:2	52:51	chloroform	none
bromopentafluorobenzene	1:2	51:34	chloroform	none
hexakis(4-iodophenoxy)-cyclotriphosphazene	1:1	28:50	chloroform	crystals of **12**
hexakis(4-bromophenoxy)-cyclotriphosphazene	1:1	31:54	chloroform	none
trimesic acid	1:2	52:32	chloroform/THF	none
terephthalic acid	1:2	51:27	chloroform/DMF	co-crystal **7**
fumaric acid	1:3	31:21	THF/DMF	none
pamoic acid	1:3	32:51	THF/DMF	none
boric acid	1:3	33:13	THF/DMF	none
2-aminopyridine	1:3	32:15	THF/DMF	none
urea	1:3	30:12	THF/acetonitrile	urea
adipic acid	1:3	31:14	chloroform/DMF	none
tartaric acid	1:3	30:17	chloroform/DMF	none
maleic acid	1:3	32:10	chloroform/DMF	Fumaric acid /1,4'-bipyridin-1-ium-4-olate co-crystal
citric acid	1:3	33:17	chloroform/DMF	none
succinic acid	1:3	32:13	chloroform/DMF	succinic acid/4,4'-bipyridyl-1-oxide co-crystal
trimesic acid	1:3	33:24	chloroform/DMF	none

Table S11 (continued)

Co-crystal former	Mole ratio (7: co-former)	Quantity (7: co-former) /mg	Solvent	Product
malic acid	1:3	31:15	chloroform/DMF	none
pamoic acid	1:3	31:33	chloroform/DMF	known SIQCIF
fumaric acid	1:3	34:12	chloroform/DMF	none
isophthalic acid	1:3	37:16	chloroform/DMF	none

Table S12 Summary of crystallisation experiments with **8** in a range of solvents and with a series of potential co-crystal formers.

Co-crystal former	Quantity (8; co-former) /mg	Mole ratio (8: co-former)	Solvent system	Crystallisation technique	Product
p-aminobenzoic acid	45; 43	1:6	THF	slow evaporation	none
2-aminoterephthalic acid	50; 56	1:6	THF	slow evaporation	none
3,5-dinitrobenzoic acid	44; 64	1:6	THF	slow evaporation	3,5-dinitrobenzoic acid
phenol	45; 34	1:6	THF	slow evaporation	none
o-phenylene diamine	59; 34	1:6	THF	slow evaporation	none
2,6-dipicolinic acid	46; 52	1:6	DMF	slow evaporation	none
pyridine	46	excess	THF	slow evaporation	none
4,4'-bipyridine	45; 51	1:6	THF	slow evaporation	4,4-bipyridine hydrate
4,4'-trimethylene dipyridine	42; 64	1:6	THF	slow evaporation	none
3,4-lutidine	51; 42	1:6	THF	slow evaporation	none
3,5-lutidine	55; 41	1:6	THF	slow evaporation	none
2,3-lutidine	48; 45	1:6	THF	slow evaporation	none
2,5-lutidine	44; 36	1:6	THF	Slow evaporation	none
2,4-lutidine	44; 38	1:6	THF	slow evaporation	none
2,6-lutidine	44; 35	1:6	THF	Slow evaporation	none
2-picoline	42; 29	1:6	THF	slow evaporation	none
3-picoline	49; 28	1:6	THF	Slow evaporation	none
4-picoline	43; 31	1:6	THF	Slow evaporation	none
3,4-lutidine	54; 47	1:6	Methanol/ hexane	Layering	none

Table S12 (continued)

Co-crystal former	Quantity (8; co-former) /mg	Mole ratio (8: co-former)	Solvent system	Crystallisation technique	Product
3,5-lutidine	55; 45	1:6	Methanol/ hexane	Layering	none
2,4-lutidine	54; 45	1:6	Methanol/ hexane	Layering	none
2,6-lutidine	52; 45	1:6	Methanol/ hexane	layering	none
3,4-lutidine	50; 44	1:6	DMF	Slow evaporation	none
3,5-lutidine	55; excess	-	DMF	Slow evaporation	none
2,3-lutidine	58; excess	-	-	Slow evaporation	none
2,4-lutidine	68; 55	1:6	DMF	Slow evaporation	none
2,6-lutidine	53; 41	1:6	DMF	Slow evaporation	none
2-picoline	neat	-	-	Slow evaporation	none
3-picoline	neat	-	-	Slow evaporation	none
4-picoline	neat	-	-	Slow evaporation	none
pyridine	neat	-	-	Slow evaporation	none
2,6-diaminopyridine	53; 41	1:6	DMF	slow evaporation	none
piperazine	71; 50	1:6	THF	slow evaporation	none
2,3-lutidine	52; 42	1:6	DMF	Slow evaporation	none
2,5-lutidine	58; 46	1:6	DMF	Slow evaporation	none
3,5-lutidine	52; 42	1:6	DMF	Slow evaporation	none
2-picoline	50; 38	1:6	DMF	Slow evaporation	none
3-picoline	54; 34	1:6	DMF	Slow evaporation	none
4-picoline	50; 46	1:6	DMF	Slow evaporation	none
pyridine	56; 35	1:6	DMF	Slow evaporation	none
4,4'-bipyridine	58; 60	1:6	DMF	Slow evaporation	none
4,4'-trimethylene dipyridine	50; 90	1:6	DMF	Slow evaporation	none
piperazine	57; 39	1:6	DMF	Slow evaporation	none
2,6-diaminopyridine	65; 50	1:6	THF	Slow evaporation	none
thiourea	101; 58	1:6	THF	Slow evaporation	none

Table S13 Summary of crystallisation experiments with **9** in a range of solvents and with a series of potential co-crystal formers.

Co-former	Quantity (9; co-former) /mg	Mole ratio (9: co-former)	Solvent system	Crystallisation technique	Product
imidazole	100; 25	1:3	THF	Inert (under N_2)	none
benzimidazole	109; 46	1:3	THF	Inert (under N_2)	none
4,4'-bipyridine	118; 57	1:3	THF	Inert (under N_2)	none
2-aminopyridine	106; 35	1:3	THF	Inert (under N_2)	none
urea	98; 22	1:3	THF/acetonitrile	Inert (under N_2)	none
pyridine	118; 34	1:3	THF	Inert (under N_2)	none
3,4-lutidine	118; 40	1:3	THF	Inert (under N_2)	none
4-picoline	99; 32	1:3	THF	Inert (under N_2)	none
2,6-diaminopyridine	120; 41	1:3	THF	Inert (under N_2)	none
benzonitrile	161	As solvent	-	Inert (under N_2)	none
2-cyanopyridine	135; 56	1:3	THF	Inert (under N_2)	crystals of **9α**
3-cyanopyridine	109; 55	1:3	THF	Inert (under N_2)	none
4-cyanopyridine	140; 44	1:3	THF	Inert (under N_2)	none
fluorophenol	50; 37	1:3	Acetonitrile/DCM	Slow evaporation	none
1,4-difluorobenzene	48; 22	1:3	acetonitrile	Slow evaporation	none
1,3-dibromobenzene	48; 48	1:3	acetonitrile	Slow evaporation	none
4-bromobenzonitrile	54; 35	1:3	Acetonitrile/DCM	Slow evaporation	crystals of **9β**
4-chlorotoluene	51; 28	1:3	acetonitrile	Slow evaporation	none
4-iodoaniline	53; 44	1:3	Acetonitrile/DCM	Slow evaporation	none
3-bromopyridine	52; 36	1:3	acetonitrile	Slow evaporation	none
3-bromoanisol	50; 19	1:1	acetonitrile	Slow evaporation	none
α-dibromo-*p*-xylene	51; 23	1:1	Acetonitrile/DCM	Slow evaporation	crystals of **9β**
α-dibromo-*m*-xylene	52; 21	1:1	Acetonitrile/DCM	Slow evaporation	none
α-dibromo-*o*-xylene	51; 18	1:1	Acetonitrile/DCM	Slow evaporation	crystals of **9β**
3-bromobenzotrifluoride	52; 20	1:1	acetonitrile	Slow evaporation	none
1,2-dichlorobenzene	52; 18	1:1	acetonitrile	Slow evaporation	none
imidazole	61; 10	1:3	THF	Slow evaporation	crystals of **9β**
benzimidazole	60; 19	1:3	THF	Slow evaporation	none
4,4'-bipyridine	60; 23	1:3	THF	Slow evaporation	none

Table S13 (continued)

Co-former	Quantity (9; co-former) /mg	Mole ratio (9: co-former)	Solvent system	Crystallisation technique	Product
4,4'-trimethylene dipyridine	64; 35	1:3	THF	Slow evaporation	none
2-aminopyrimidine	61; 17	1:3	THF	Slow evaporation	none
pyridine	62; 19	1:3	THF	Slow evaporation	crystals of **9α**
3,4-lutidine	61; 17	1:3	THF	Slow evaporation	crystals of **9α**
4-picoline	61; 16	1:3	THF	Slow evaporation	crystals of **9α**
benzonitrile	62; 18	1:3	THF	Slow evaporation	none
2-cyanopyridine	62; 22	1:3	THF	Slow evaporation	none
3-cyanopyridine	61; 17	1:3	THF	Slow evaporation	none
4-cyanopyridine	65; 20	1:3	THF	Slow evaporation	none
cobalt(II)acetate	60; 20	1:1	THF/MeOH	Layered	crystals of **9β**
copper(II)acetate	62; 34	1:1	THF/MeOH	Layered	crystals of **9β**

Table S14 Summary of crystallisation experiments with **10** in a range of solvents and with a series of potential co-crystal formers.

Co-former	Quantity (10; co-former) /mg	Mole ratio (10: co-former)	Solvent system	Crystallisation technique	Product
imidazole	56; 12	1:3	THF	Slow evaporation	crystals of **10**
benzimidazole	50; 13	1:3	THF	Slow evaporation	crystals of **10**
α-dibromo-*p*-xylene	51; 30	1:3	THF/DCM	Slow evaporation	none
α-dibromo-*o*-xylene	53; 34	1:3	THF/DCM	Slow evaporation	crystals of **10**
4-bromobenzonitrile	50; 21	1:3	THF/DCM	Slow evaporation	none
3,4-lutidine	53; 14	1:3	DCM	Slow evaporation	none
pyridine	51; 14	1:3	THF	Slow evaporation	none
cobalt(II)acetate	48; 15	1:1	THF/MeOH	Layered	none
copper(II)acetate	54; 12	1:1	THF/MeOH	Layered	none
hexakis(4-fluorophenoxy)cyclo-triphosphazene	28; 24	1:1	THF	Slow evaporation	none
hexakis(4-bromophenoxy)cyclo-triphosphazene	26; 33	1:1	THF	Slow evaporation	none
phosphonitrilic chloride trimer	51; 19	1:1	THF	Slow evaporation	none
4-chlorophenol	57; 16	1:3	THF	Slow evaporation	crystals of **10**
iodopentafluoroben-zene	52; 18	1:1	Chloroform/aceto-nitrile	Vapour diffusion (AcCN)	crystals of **10**
bromopentafluoroben-zene	50;24	1:1	Chloroform/aceto-nitrile	Vapour diffusion (AcCN)	crystals of **10**

Table S15 Summary of crystallisation experiments with **11** in a range of solvents and with a series of potential co-crystal formers.

Co-former	**Amount (11; co-former) in mg**	**Ratio (11: co-former)**	**Solvent system**	**Crystallisation technique**	**Product**
hexakis(4-fluorophenoxy)cyclo-triphosphazene	63; 41	1:1	THF	Slow evaporation	crystals of **11**
hexakis(4-iodophenoxy)-cyclotriphosphazene	65; 78	1:1	THF	Slow evaporation	none
imidazole	62; 10	1:3	THF	Slow evaporation	crystals of **11**
α-dibromo-*p*-xylene	63; 30	1:3	THF/DCM	Slow evaporation	α-dibromo-*p*-xylene
α-dibromo-*o*-xylene	64; 36	1:3	THF/DCM	Slow evaporation	none
4-bromobenzonitrile	63; 29	1:3	THF/DCM	Slow evaporation	crystals of **11**
cobalt(II)acetate	60; 18	1:2	THF/MeOH	Layered	crystals of **11**
copper(II)acetate	60; 12	1:2	THF/MeOH	Layered	crystals of **11**
3,4-lutidine	61; 14	1:3	THF	Slow evaporation	crystals of **11**
pyridine	62; 17	1:3	THF	Slow evaporation	crystals of **11**
5	68; 39	1:1	THF	Slow evaporation	crystals of **11**
phosphonitrilic chloride trimer	65; 18	1:1	THF	Slow evaporation	crystals of **11**
bromopentafluoroben-zene	54; 18	1:1	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **11**
iodopentafluorobenzene	52; 14	1:1	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **11**
bromopentafluorobenzene	51; 52	1:4	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **11**

Table S16 Summary of crystallisation experiments with **12** in a range of solvents and with a series of potential co-crystal formers.

Co-former	Quantity (12; co-former) /mg	Mole ratio (12: co-former)	Solvent system*	Crystallisation technique	Product
4-iodoaniline	61; 32	1:3	DCM	Slow evaporation	crystals of **12**
acetonitrile	59	excess	DCM/ acetonitrile	Slow evaporation	none
4-bromobenzonitrile	62; 26	1:3	DCM	Slow evaporation	crystals of **12**
1,3-dicyanobenzene	62; 19	1:3	DCM	Slow evaporation	crystals of **12**
2-cyanopyridine	59; 16	1:3	DCM	Slow evaporation	none
3-cyanopyridine	61; 16	1:3	DCM	Slow evaporation	none
4-cyanopyridine	65; 22	1:3	DCM	Slow evaporation	crystals of **12**
4-iodobenzonitrile	64; 31	1:3	DCM	Slow evaporation	none
benzonitrile	63; 16	1:3	DCM	Slow evaporation	crystals of **12**
nitrobenzene	66; 26	1:3	DCM	Slow evaporation	none
o-tolunitrile	65; 21	1:3	DCM	Slow evaporation	none
m-tolunitrile	61; 22	1:3	DCM	Slow evaporation	none
p-tolunitrile	61; 19	1:3	DCM	Slow evaporation	none
iodophenol	60; 32	1:3	DCM/THF	Slow evaporation	crystals of **12**
1,2-bis(2-pyridyl)ethylene	65; 25	1:3	DCM/THF	Slow evaporation	crystals of **12**
4,4'-diiodobiphenyl	67; 51	1:3	DCM	Slow evaporation	none
1,4-diiodobenzene	64; 46	1:3	DCM	Slow evaporation	none
2-iodopropane	62; 24	1:3	DCM	Slow evaporation	none
propionitrile	64; 13	1:3	DCM	Slow evaporation	none
terephthalonitrile	64; 19	1:3	DCM/ acetonitrile	Slow evaporation	crystals of **12**
4-(4-fluorophenyl)benzonitrile	62; 26	1:3	DCM	Slow evaporation	none
hexakis(4-fluorophenoxy)cyclotri-phosphazene	66; 38	1:1	Chloroform	Slow evaporation	crystals of **12** and **9**
iodopentafluorobenzene	51; 11	1:1	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **12**
iodopentafluorobenzene	51; 50	1:4	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **12**
bromopentafluorobenzene	50; 24	1:1	Chloroform/ acetonitrile	Vapour diffusion (AcCN)	crystals of **12**

*These crystallisations were also repeated in chloroform

Table S17 Crystallisations from the melt with **9**, **10**, **11** and **12** in a 1:1 mole ratio

Compound 1	**Compound 2**	**Amount (cmp 1; cmp 2) /mg**	**Method**
hexakis(4-fluorophenoxy)-cyclotriphosphazene	hexakis(4-chlorophenoxy)-cyclotriphosphazene	46; 52	Ground together & melted
hexakis(4-fluorophenoxy)-cyclotriphosphazene	hexakis(4-bromophenoxy)-cyclotriphosphazene	45; 68	Ground together & melted
hexakis(4-fluorophenoxy)-cyclotriphosphazene	hexakis(4-iodophenoxy)-cyclotriphosphazene	42; 82	Ground together & melted
hexakis(4-chlorophenoxy)-cyclotriphosphazene	hexakis(4-bromophenoxy)-cyclotriphosphazene	39; 53	Ground together & melted
hexakis(4-chlorophenoxy)-cyclotriphosphazene	hexakis(4-iodophenoxy)-cyclotriphosphazene	41; 66	Ground together & melted
hexakis(4-iodophenoxy)-cyclotriphosphazene	hexakis(4-bromophenoxy)-cyclotriphosphazen	51; 41	Ground together & melted

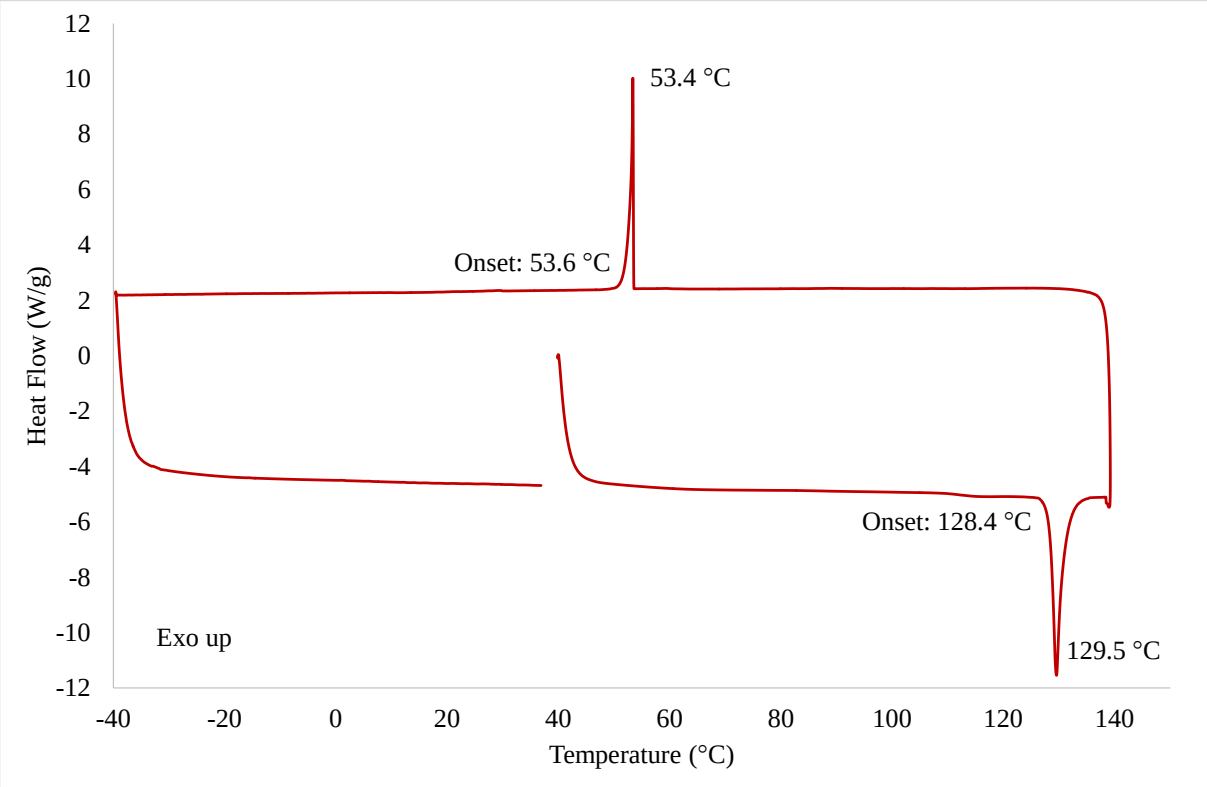


Figure S6 DSC analysis of the monoclinic form of hexakis(4-fluorophenoxy)cyclotriphosphazene (**9**), with a melt at 128.4 °C and a recrystallization event upon cooling at 53.6 °C. This structure undergoes single-crystal to single-crystal polymorphic transitions where **9α** (the monoclinic *P* form) converts to **9γ** between 115 and 125 °C before melting.

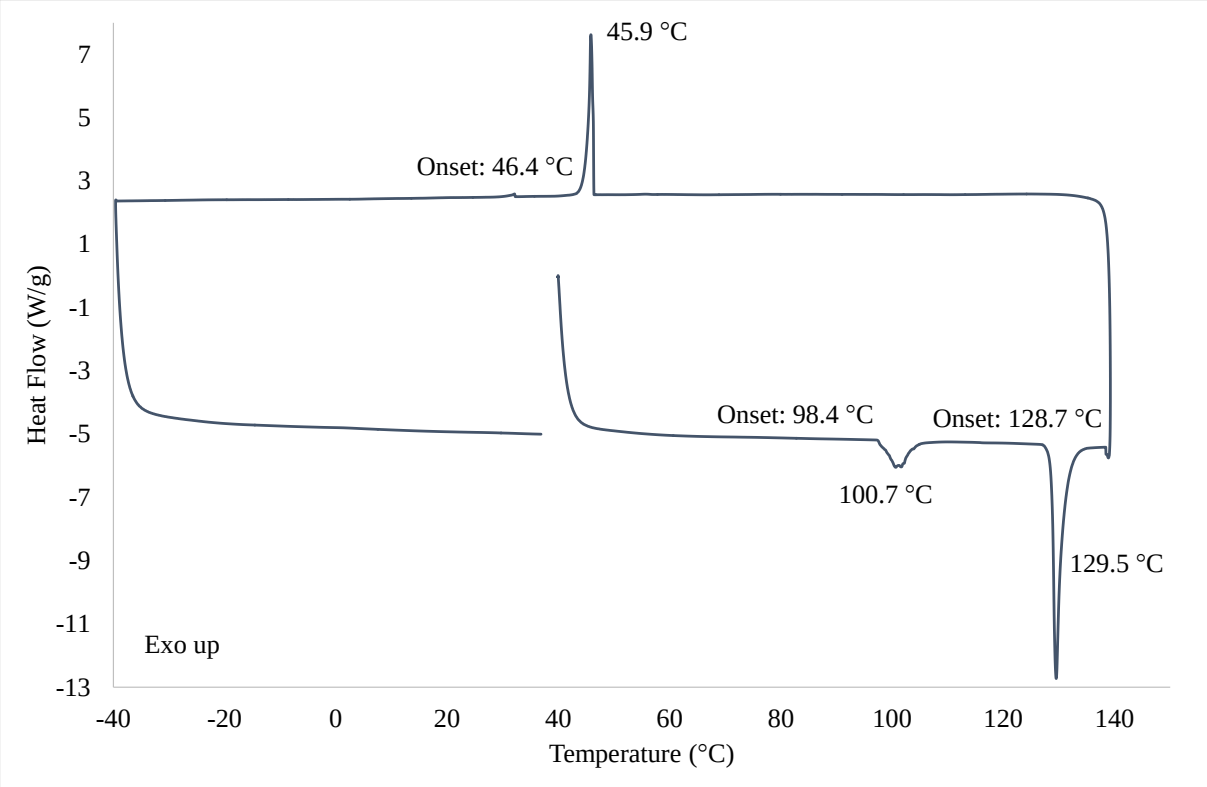


Figure S7 DSC analysis of the triclinic form of hexakis(4-fluorphenoxy)cyclotriphosphazene (**9**). The triclinic form (**9β**) converts to **9γ** around 100 °C before the melt at 129.5 °C.

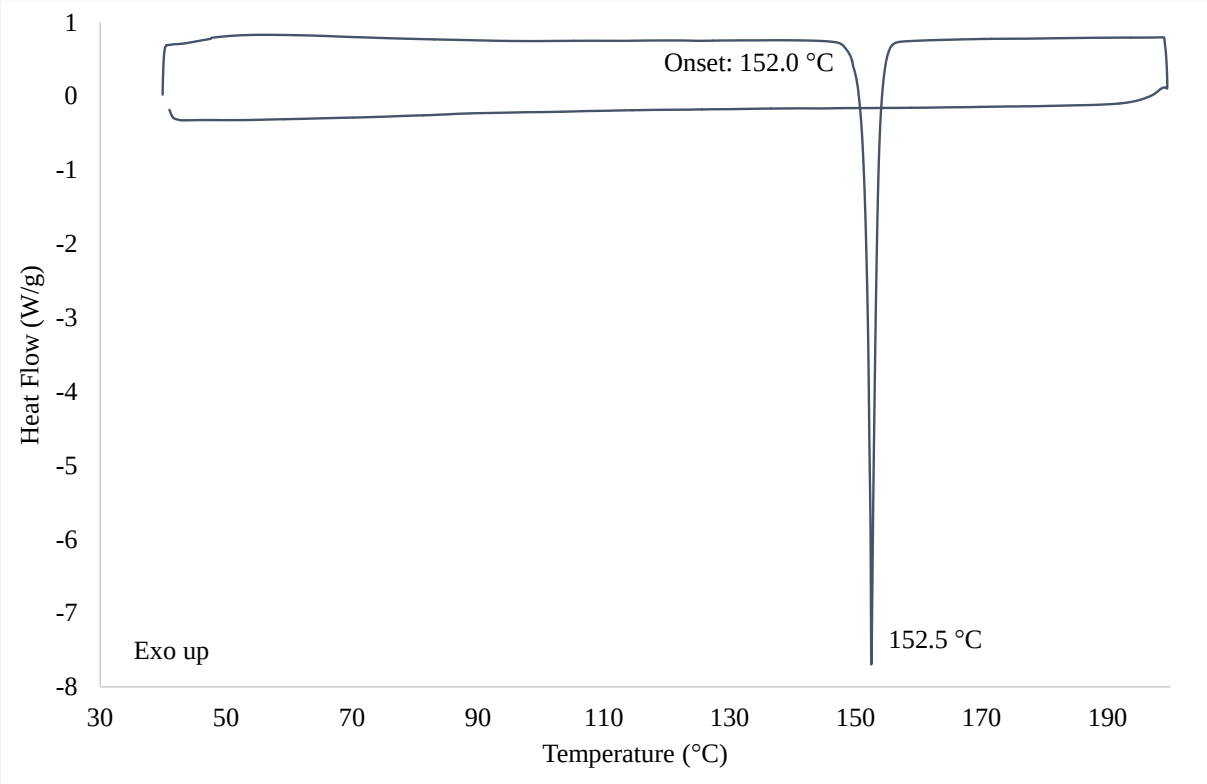


Figure S8 DSC analysis of hexakis(4-chlorophenyl)cyclotriphosphazene (**10**), with a melt occurring at 152.0 °C.

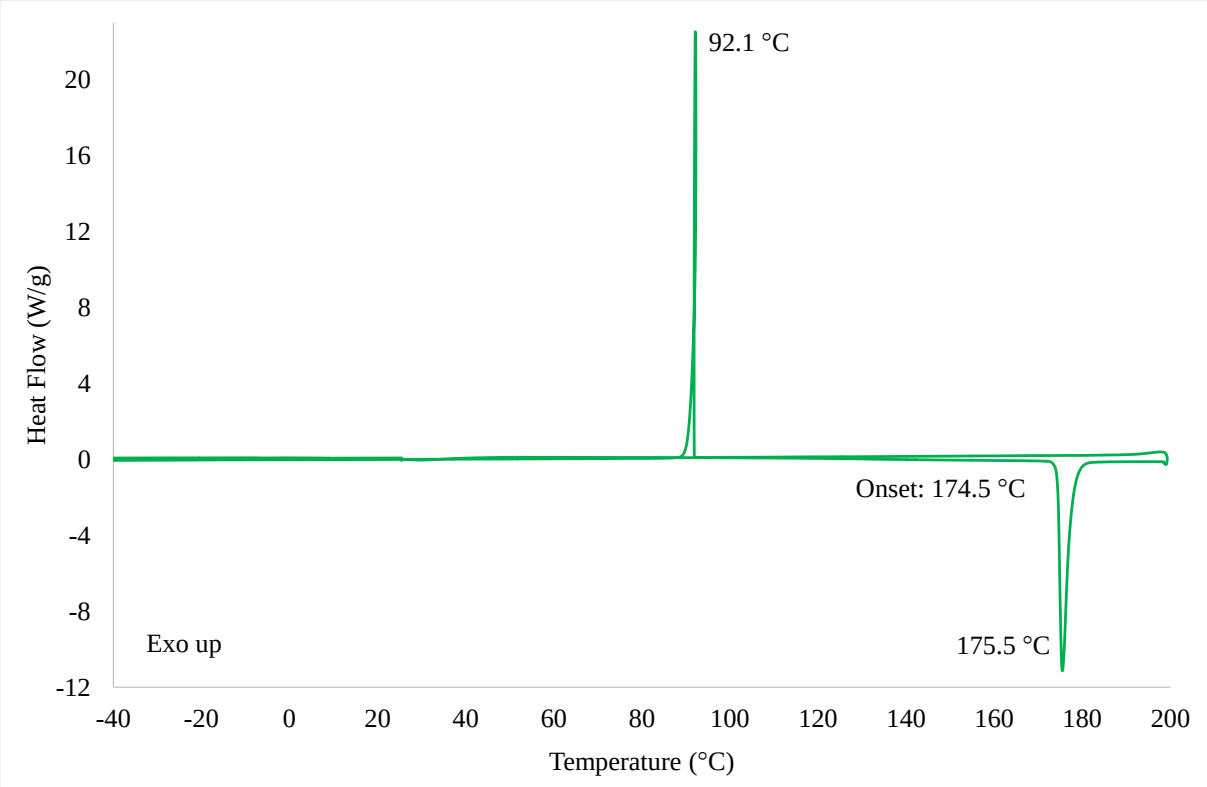


Figure S9 DSC analysis of hexakis(4-bromophenyl)cyclotriphosphazene (**11**), with a melt occurring at 174.5 °C and a recrystallization event upon cooling at 92.1 °C.

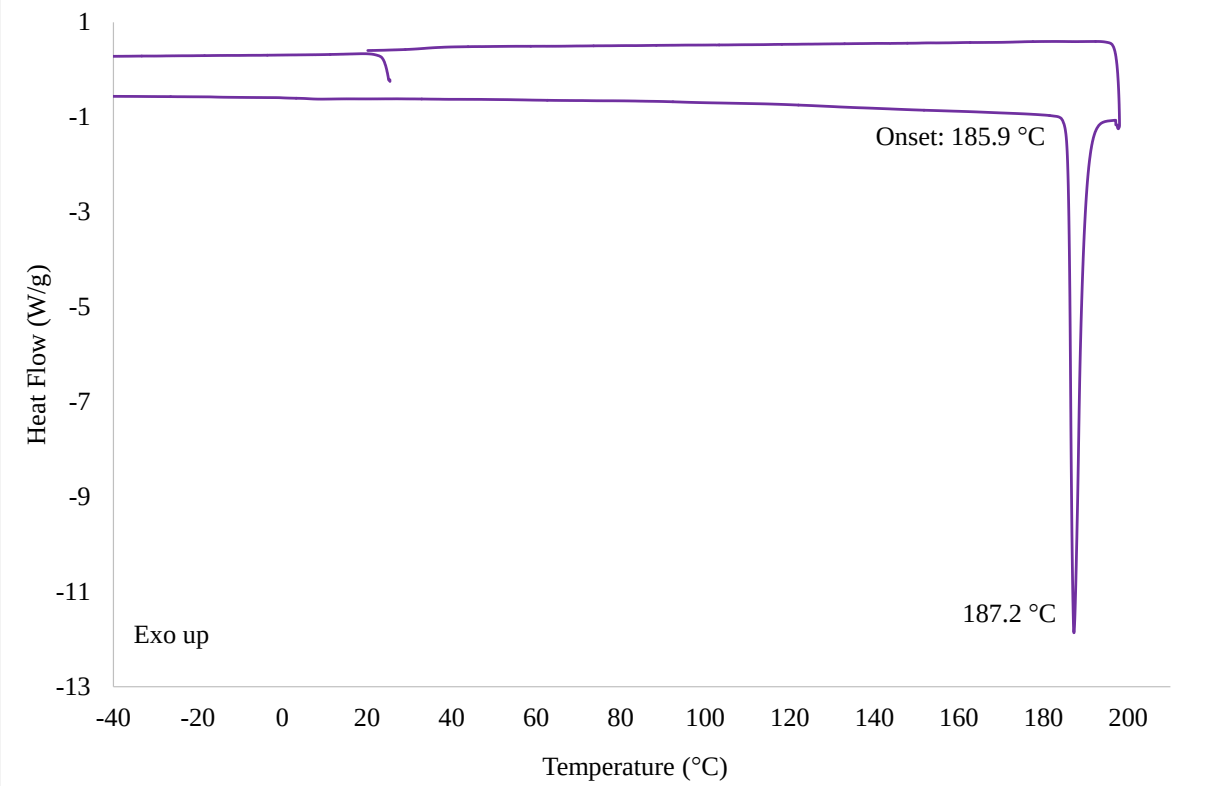


Figure S10 DSC analysis of hexakis(4-iodophenyl)cyclotriphosphazene (**12**), with a melt at 185.9 °C.

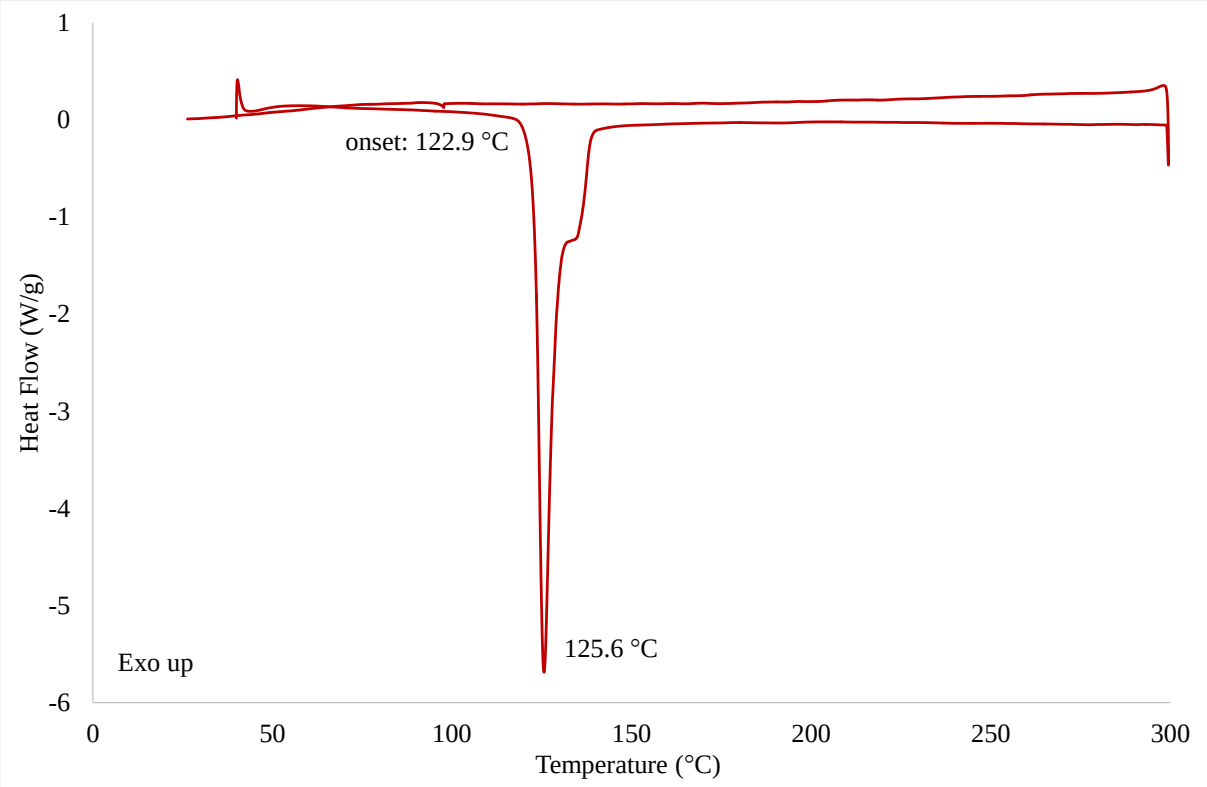


Figure S11 DSC analysis of the melt product (**9/10**) of the fluoro and chloro derivatives. Melting occurs before the melting point of the fluorophenoxy derivative (129 °C).

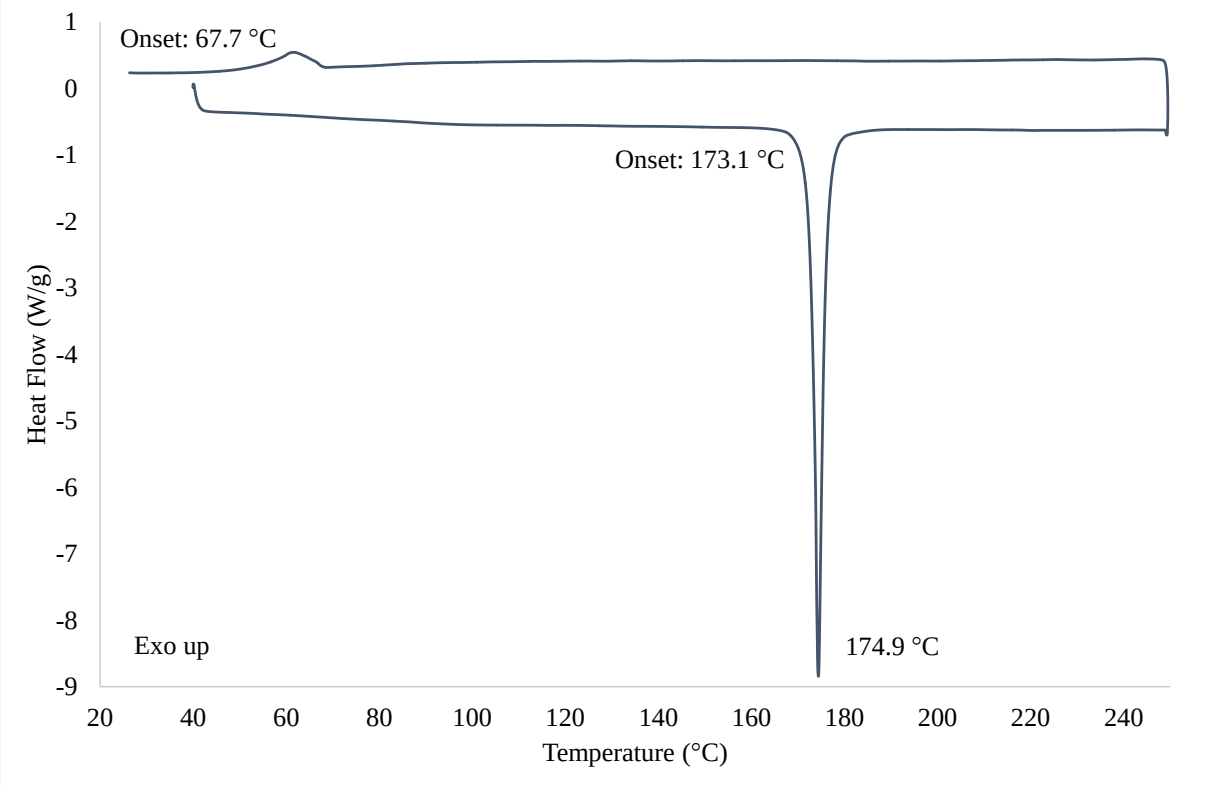


Figure S12 DSC analysis of the product of **11** and **12**. The melting point of **11**/**12** is lower than that of both the reagents.

Synthesis of 1-12

All chemicals were purchased from Sigma-Aldrich and used without further purification. THF, diethylether and toluene were distilled over sodium sand or wire with benzophenone as indicator, under an atmosphere of dry nitrogen. DCM and acetonitrile were distilled over dried calcium hydride under an atmosphere of dry nitrogen. Acetone and *n*-hexane were distilled over dried calcium chloride under nitrogen.

^{1}H and ^{31}P NMR spectra were obtained using a 300 MHz Varian VNMRS or a 400 MHz Varian Unity Inova. Chemical shift values are in ppm and were referenced to either chloroform-*d* or DMSO-d_6. Data for ^{1}H spectra are reported as chemical shift (δ ppm) (integration, multiplicity, coupling constant (Hz)). H_3PO_4 was used as an external standard for ^{31}P NMR.

All reactions were performed under an atmosphere of dry nitrogen unless otherwise stated.

Tris(1,3-diaminopropane)cyclotriphosphazene (1)[1]

$N_3P_3Cl_6$ (0.5 g,1.44 mmol) was dissolved in 50 ml of a 7:3 mixture of *n*-hexane:DCM. To this mixture, 0.8 ml (8.64 mmol) 1,3-diaminopropane was added. The reaction mixture was refluxed for 4 hours, after which the solution was cooled and filtered and the solvent removed under reduced pressure. The resultant white powder was further purified by recrystallisation from methanol. Yield: 62% (0.313 g, 0.89 mmol).

^{1}H NMR (DMSO-d_6, 400 MHz): δ ppm 1.53 (2H, m), 3.04 (4H, m), 3.48 (2H, s), ^{31}P NMR (DMSO-d_6, 400 MHz, H_3PO_4): δ ppm 13.86 (d), 20.45 (t).

Crystals of **1** were also grown from a THF/hexane solution. This proved to be the known hydrate.[1a]

4,4,6,6-Tetrachloro-2,2-(biphenyl-2,2'-dioxy)cyclotriphosphazene (2)[2]

A mixture of $N_3P_3Cl_6$ (1.018 g, 2.88 mmol), 2,2'-biphenol (0.543 g, 2.88 mmol) and K_2CO_3 (2.013 g, 14.4 mmol) were stirred together in 40 ml acetone at room temperature for 30 minutes. The volatiles were evaporated *in vacuo* and the residue extracted with 4 x 15 ml DCM. The solvent was evaporated to give a white solid, which was recrystallised from DCM/petroleum ether. Yield: 80% (1.071 g, 2.32 mmol). Mp.: 181 – 189 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.57 (2H, d, *J* = 7.62 Hz), 7.49 (2H, t, *J* = 7.42 Hz), 7.41 (2H, t, *J* = 7.62 Hz), 7.33 (2H, d, 8.01 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 21.87 (d, Cl_2), 9.74 (t, $C_{12}O_2H_8$).

2,2-Dichloro-4,4,6,6-bis[spiro(2',2''-dioxy-1',1''-biphenylyl]cyclotriphosphazene (3)[3]

$N_3P_3Cl_6$ (2 g, 5.75 mmol), biphenyl-2,2'-diol (2.14 g, 11.51 mmol) and K_2CO_3 (3.98 g, 28.77 mmol) were mixed in 20 ml acetone at 0 °C. The reaction mixture was stirred at room temperature for 24 hours, and then the solvent was removed *in vacuo*. The product was extracted by washing with 15 ml of DCM four times, filtering each time with a cannula filter. The solvent was then removed under vacuum, yielding a white powder. Yield: 86% (2.847 g, 4.96 mmol). Mp.: 268 – 275 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ ppm 7.55 (4H, d, *J* = 7.63 Hz), 7.46 (4H, d, *J* = 7.63 Hz), 7.36 (8H, m), ^{31}P NMR ($CDCl_3$, 300 MHz, H_3PO_4): δ ppm 19.79 (d, $C_{12}O_2H_8$), 29.19 (dd, Cl_2).

Tris(2,2'-dioxybiphenyl)cyclotriphosphazene (4)[4]

$N_3P_3Cl_6$ (1.003 g, 2.88 mmol), 2,2'-biphenol (1.815 g, 9.66 mmol) and K_2CO_3 (3.010 g, 21.8 mmol) were refluxed for 7 hours in 140 ml acetone. The solvent was evaporated *in vacuo* and the residue washed with 100 ml water, 100 ml aqueous NaOH (0.5 M), 2 x 50 ml water, 50 ml ethanol and 50 ml ether. The white product was dried under vacuum. Yield: 75% (1.278 g, 1.86 mmol). Mp.: >350 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.52 (2H, d, J = 7.62 Hz), 7.41 (4H, m), 7.33 (2H, t, J = 7.642 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 26.27 (s).

2,2-Bis(4-formylphenoxy)-4,4,6,6-bis[spiro(2',2''-dioxy-1',1''-biphenylyl]cyclotriphosphazene (5)[3]

Compound **3** (2 g, 3.48 mmol), 4-hydroxybenzaldehyde (0.854 g, 6.96 mmol) and K_2CO_3 (2.663 g, 19.28 mmol) were added to 20 ml THF at 0 °C. The mixture was refluxed for 5 hours and the solvent removed under vacuum. The resulting solid was extracted with DCM (4 x 10 ml), and the solvent subsequently removed under vacuum. The product was recrystallised from acetone. Yield: 72% (1.881 g, 2.52 mmol). Mp.: 220 – 224 °C

^{1}H NMR ($CDCl_3$, 300 MHz): δ ppm 7.07 (2H, d, J = 7.80 Hz), 7.31 – 7.41 (4H, m), 7.54 (4H, t, J = 8.58 Hz), 7.96 (2H, d, 8.19 Hz), 10.01 (1H, s) ^{31}P NMR ($CDCl_3$, 300 MHz, H_3PO_4): δ ppm 9.62 – 11.69 (tt), 25.59 – 26.71 (dt).

Hexakis(4-cyanophenoxy)cyclotriphosphazene (6)[5]

A mixture of 4-cyanophenol (2.071 g, 17.28 mmol) and K_2CO_3 (4.804 g, 34.56 mmol) was prepared in 80 ml THF. $N_3P_3Cl_6$ (1.030 g, 2.88 mmol) in 15 ml THF was added dropwise to this mixture. The reaction mixture was refluxed for 6 hours with vigorous stirring. The solvent was removed *in vacuo* and the residue dispersed in 100 ml water. The resultant white solid was separated by filtration and allowed to dry. Yield: 94 % (2.284 g, 2.707 mmol). Mp.: 263 – 265 °C.

^{1}H NMR (DMSO-d_6, 400 MHz): δ ppm 7.16 (2H, d, 8.79 Hz), 7.82 (2H, d, 8.79 Hz), ^{31}P NMR (DMSO-d_6, 400 MHz, H_3PO_4): δ ppm 8.51 (s).

Hexakis(4-pyridyloxy)cyclotriphosphazene (7)[6]

4-hydroxypyridine (0.826 g, 8.64 mmol) and K_2CO_3 (1.818 g, 12.96 mmol) were added to 50 ml THF. $N_3P_3Cl_6$ (0.503 g, 1.44 mmol) was added to this mixture, which was then stirred for two and a half days at room temperature, after which it was refluxed for approximately 6 hours. The solvent was removed under vacuum and the residue washed with 100 ml water. The product was isolated by filtration and dried *in vacuo* to yield a light yellow product. Yield: 89% (0.897 g, 1.28 mmol). Mp.: 163 – 165 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 6.93 (2H, d, 6.44 Hz), 8.50 (2H, d, 6.25 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 7.30 (s).

Hexakis(4-hydroxyphenoxy)cyclotriphosphazene (8)[7]

Hexakis(4-methoxyphenoxy)cyclotriphosphazene

A suspension of sodium 4-methoxyphenoxide was prepared in 20 ml dry THF by allowing 4-methoxyphenol (4.274 g, 34.5 mmol) to react with NaH (1.385 g as a 60 % dispersion in mineral oil; equivalent to 0.828 g, 34.5 mmol pure NaH). The NaH was washed with dry petroleum ether to remove the mineral oil prior to use. A solution of $N_3P_3Cl_6$ (2 g, 5.75 mmol) in 20 ml THF was added dropwise to this suspension. On complete addition of the phosphonitrilic chloride trimer, the reaction mixture was refluxed for 24 hours with stirring. The reaction mixture was cooled and washed with 100 ml water in order to precipitate the product as a white powder. Yield: 82% (4.136 g, 4.733 mmol). Mp.: 105 – 106 °C

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 3.72 (3H, s), 6.77 (4H, s)

Hexakis(4-hydroxyphenoxy)cyclotriphosphazene (**8**)

Hexakis(4-methoxyphenoxy)-cyclotriphosphazene (3 g, 3.43 mmol) was dissolved in 30 ml DCM. A solution of BBr_3 (2 ml, 20.6 mmol) in 30 ml DCM was added dropwise to the solution of cyclotriphosphazene. The solution was allowed to stir for 3 hours, after which it was poured carefully into 100 ml of water to precipitate the product. The white precipitate was filtered off, washed with water and dried. Yield: 85% (2.303 g, 2.92 mmol).

^{1}H NMR (DMSO-d_6, 400 MHz): δ ppm 6.59 (2H, s), 6.61 (2H, s), ^{31}P NMR (DMSO-d_6, 400 MHz, H_3PO_4): δ ppm 22.32 (s).

Hexakis(4-fluorophenyl)cyclotriphosphazene (9)[8,9]

This synthetic procedure was not performed under inert conditions.

4-fluorophenol (1.94 g, 17.28 mmol) and $N_3P_3Cl_6$ (0.998 g, 2.88 mmol) were dissolved in 60 ml acetone. K_2CO_3 (4.797 g, 120.96 mmol) was added to this mixture, and the reaction mixture was refluxed for 12 hours. The precipitate was filtered off, washed with DCM and combined with the filtrate. The solvent was then removed *in vacuo*. The white powder thus obtained was recrystallised from methanol. Yield: 65% (3.131 g, 3.91 mmol). Mp. 129 °C

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 6.88 (2H, s), 6.9 (2H, s), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 9.86 (s).

Hexakis(4-chlorophenyl)cyclotriphosphazene (10)[8]

4-chlorophenol (2.240 g, 17.28 mmol) and K_2CO_3 (4.793 g, 34.56 mmol) were stirred together in 50 ml acetone. $N_3P_3Cl_6$ (1.004 g, 2.88 mmol) dissolved in 10 ml acetone was added to the mixture, which was then refluxed for 1 day. The solvent was removed under vacuum and the product extracted with DCM. The product was further purified by recrystallisation from acetonitrile. Yield: 76 % (1.982 g, 2.2 mmol). Mp. 152 °C

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 6.68 (2H, d, 8.20 Hz), 7.17 (2H, d, 8.40 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 9.59 (s).

Hexakis(4-bromophenyl)cyclotriphosphazene (11)[8]

4-bromophenol (3.030 g, 17.28 mmol) and K_2CO_3 (4.779 g, 34.56 mmol) were added to 50 ml acetone. $N_3P_3Cl_6$ (1.011 g, 2.88 mmol) in 10 ml acetone was added to the mixture, which was then refluxed for 2 days. The solvent was removed under vacuum and the product purified by recrystallisation from acetonitrile. Yield: 79 % (2.684 g, 2.3 mmol). Mp. 176.8 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 6.75 (2H, d, 8.79 Hz), 7.33 (2H, d, 8.89 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 9.29 (s).

Hexakis(4-iodophenyl)cyclotriphosphazene (12)[8]

4-iodophenol (3.844 g, 17.28 mmol) and $N_3P_3Cl_6$ (1.007 g, 2.88 mmol) were dissolved in 75 ml acetone. K_2CO_3 (4.821 g, 34.56 mmol) was added to this mixture, which was refluxed for 2 days. The solvent was evaporated under vacuum and the product was extracted with 3 x 20 ml DCM. The product was further purified by recrystallisation from acetonitrile. Yield: 65% (2.702 g, 1.86 mmol). Mp. 187.6 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 6.62 (2H, d, J = 8.79 Hz), 7.52 (2H, d, 8.79 Hz), ^{31}P NMR ($CDCl_3$, 400 MHz, H_3PO_4): δ ppm 9.27 (s).

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