Versatile Palladium-catalyzed intramolecular cyclization to access new luminescent azaphosphaphenalene motifs

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Abstract: *Using a straightforward sequence of diphosphonylation and a Pd-catalysed concerted-metalation-deprotonation (CMD), a synthetic strategy towards polyaromatic phosphorus containing heterocycles was developed. Herein, we report the synthesis and characterization of new azaphosphaphenalenes, using easily accessible palladium catalysts and starting materials. The key tetrahydroquinoline intermediates of the reaction were synthesised via a fast and effective procedure and could be isolated as such, or further reacted towards the target polyaromatic structures. The obtained products showed interesting luminescent properties and their emission, excitation and quantum yields were evaluated.*

Introduction

Organophosphorus compounds play important roles in organic chemistry as they can serve as valuable ligands in transition metal catalysis and as functional materials. A still somewhat underrepresented category in this class of compounds are the phosphacycles.[1] In general, large π-conjugated molecules have found applications in several fields such as bioimaging,[2] organic photovoltaic cells (OPVs),[3] light-emitting diodes (OLEDs),[4] among others, due to their capacity to absorb and emit light through efficient electron delocalization. Researchers are therefore actively searching for molecules with tuneable photo-electronic properties suited for these specific applications.

The presence of different heteroatoms within the polyaromatic moiety brings new structural features and properties for these systems. Phosphorus atoms are an attractive and versatile addition as they further lower the optical band gap and can appear in their reversible trivalent or pentavalent form as well as a cationic quaternized centre. By altering the phosphorus centre, the properties of the entire π -system can be engineered, tailoring properties such as the energy level of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), aromaticity, redox potential, etc… Additionally, phosphorus possesses a non-planar geometry, and out-of-plane substituents could disturb the intermolecular stacking, giving rise to unique intermolecular interactions.[5] The presence of phosphorus also opens up the door to its rich synthetic toolbox, enabling further functionalization with main group elements (S, Se, O, N, B) or transition metals (Au, Fe, Ru, Cu, etc).[6,1a]

One of these polyaromatic, phosphorus containing motifs are the so called phosphaphenalenes. These stable six-membered phosphorus heterocycles were originally envisioned and synthesized by the group of Prof. Romero-Nieto.[7a] Since then, they have established a rich body of work related to these compounds,[7] evaluating both their application in material sciences[6,8] and as ligands in promising anticancer complexes.[9] The original synthesis consisted of a non-catalysed cyclisation reaction which occurred upon treatment of a lithiated naphthalene derivative with an equimolar amount of dichlorophenylphosphane (Figure 1a). To obtain air stable compounds, H_2O_2 was added to the mixture containing the phosphaphenalene, which yielded the pentavalent phosphorus heterocycle.[7a] Later, Mathey et al. proposed the use of diarylphosphine oxides as substrates for a Ag-catalysed cycloaddition reaction towards the desired six-membered phosphacycles. This protocol, which proceeds through a phosphorus radical-directed arylation, showed more flexibility towards the position of the phosphoryl group (Figure 1b).[10] In early 2022, Duan et al. reported an intramolecular phosphination of alkynes. Their chemo- and regioselective protocol could lead towards the 5-exo-dig or 6-endo-dig phosphacycle, by opting for the addition of LiBr or H_2O, respectively. Depending on the chosen route, this method could give access to both 1-phosphaacenaphthenes or phosphaphenalenes (Figure 1c). [11]

Inspired by these interesting new structures and building further on a rich experience in the phosphonylation of heterocyclic compounds within our group,[12] we envisioned that a closely related, nitrogen containing, phosphaphenalene motif could easily be constructed starting from a quinoline core. Apart from its presence in many naturally occurring alkaloids, the nitrogen provides also an extra potential functionalization point compared to the otherwise carbon-based skeleton of naphtalenes. Since its isolation from the bark of the Cinchona tree in 1820, the quinoline moiety has found a way into countless bioactive substances currently available on the market, including antimalaria, anticancer, antibacterial, antifungal, antiviral, anti-inflammatory and many others.[13]

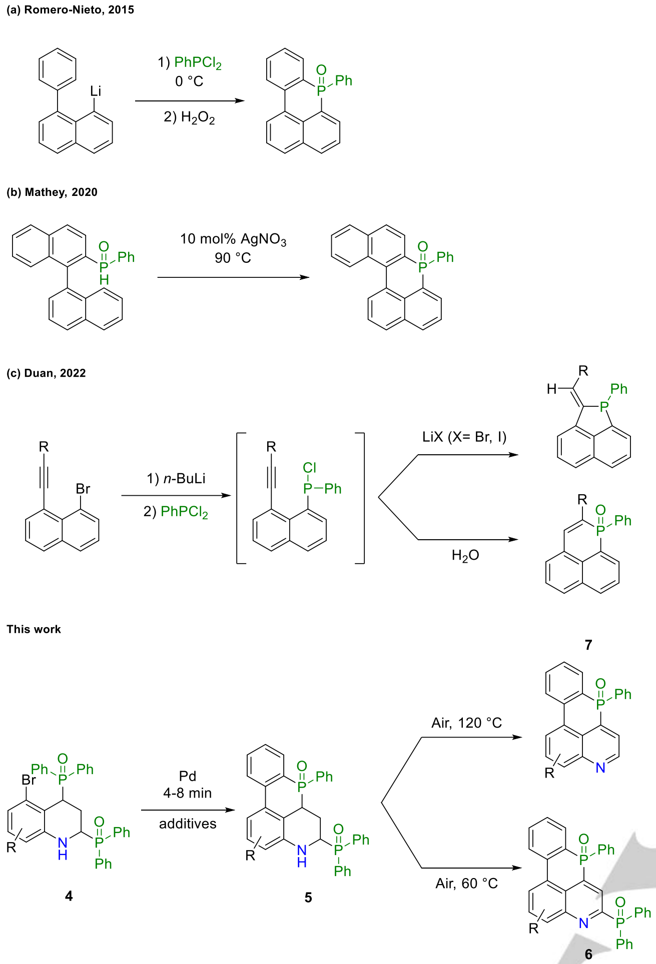


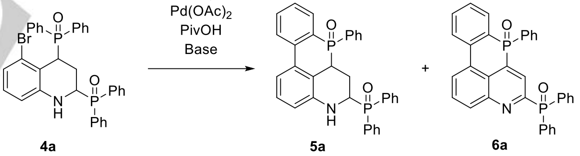
Figure 1. Comparison between the previous methods for the synthesis of phosphaphenalenes

In this work we describe the synthesis of a new azaphosphaphenalene core structure, obtained using a straightforward diphosphonylation of several 5-bromoquinoline cores, followed by a Pd-catalysed intramolecular arylation. The cyclisation step proceeds very quickly, and the resulting tetrahydroquinoline intermediates **5** can be isolated or readily oxidized in a one-pot fashion towards luminescent, polyaromatic end products. Further, the emission, excitation and quantum yields of these compounds were analysed and compared.

Results and discussion

Using a slightly adapted protocol,[14] we were able to produce the model substrate **4** from commercially available 5-bromoquinoline and diphenylphosphine oxide. Using this easily accessibly starting material, we envisioned that an intramolecular arylation should be possible, to reach our target phosphacycle.[15] Duan et al. previously described a palladium catalysed intramolecular CMD reaction using 0.3 equivalents of pivalic acid, 3 equivalents of K_2CO_3 and 10 mol% $Pd(OAc)_2$ in DMAc at 60 °C. Employing these initial reaction conditions on our substrate, we achieved hopeful, however improvable results (Table 1, entry **1**). Maintaining a higher temperature (130 °C) for 20 hours, only led towards the debromination of the starting product (entry **3**). Next, several bases were evaluated to try and improve upon the conversion, eventually finding the combination of 3 eq. Cs_2CO_3 and DMF as a solvent to be optimal. Using these conditions we soon achieved a respectable 98% conversion of the starting material (entry **9**). Further increasing the amount of base to 5 equivalents did not push the reaction towards completion (entry **13**). However, apart from the desired intramolecular cyclization reaction, it was clear from the mass obtained in the LC-MS data, that for an increasing fraction of the product **5a**, aromatization readily occurred over time forming azaphosphaphenalene **6a**. The presence of oxygen and Pd most likely promoted this spontaneous dehydrogenation of the tetrahydroquinoline structures.[16] The initial optimization experiments entries **1-7 & 9-13** were indeed all conducted in an open vial and always yielded a mixture of the aromatized **6a** and non-aromatized **5a** products. Even though our original target compound was the fully aromatic azaphosphaphenalene, we were interested to explore whether these intermediates could be isolated selectively. Indeed, when the reaction was performed in a closed vial and the mixture was first purged with argon, the resulting mixture contained much more of the non-aromatized tetrahydroquinoline motif (entry **14**). With this information in mind, we sought to quickly and selectively produce **5a** using a short reaction time at elevated temperatures. In case the temperature was raised too high, dehalogenation of the starting material occurred even in a closed vial. But if the reaction was stirred for a longer time, increasing amounts of the aromatized product formed, again yielding a mixture. Eventually, the conditions (110 °C for 4 min) presented in entry **15** proved successful at completely and selectively converting the starting material into **5a**. This cyclisation also includes the formation of an additional stereo centre, however as ^{31}P NMR analysis showed us, the transformation was quite selective, forming only small amounts of other diastereomers (ratio 86:10:4 for **5a**).

Table 1. Optimization of the synthetic protocol.



Entry	Temp (˚C)	Time (h)	Base	Solvent	Conv. (%)[a]
1	60	20	K_2CO_3	DMAc	50
2	60	72	K_2CO_3	DMAc	80
3	130	20	K_2CO_3	DMAc	0[b]
4	60	20	K_3PO_4	DMAc	62
5	60	20	K_2CO_3	DMF	75
6	60	20	Et_3N	DMF	0
7	60	20	KOAc	DMF	40
8	110	1	K_2CO_3	DMF	trace[c]
9	60	20	Cs_2CO_3	DMF	98
10	60	20	CsOAc	DMF	85
11	50	20	Cs_2CO_3	DMF	85
12	rt	72	Cs_2CO_3	DMF	trace
13	60	20	Cs_2CO_3[d]	DMF	70

14	60	20	Cs_2CO_3	DMF	95[e]
15	110	4 min	Cs_2CO_3	DMF	**100**[e]

Conditions: 0.5 mmol **4a**, 10 mol% $Pd(OAc)_2$, 0.3 eq. PivOH, 3 eq. Base, 2 mL DMF

[a] Determined by integrating HPLC-UV-MS measurement at 254 nm, sum of both **5a** & **6a**.

[b] Debromination of the starting product occurred.

[c] 10 mol% $Pd(PPh_3)_4$ as added as catalyst, capped under nitrogen atmosphere.

[d] 5 eq. of Cs_2CO_3

[e] Capped under argon atmosphere, 92% **5a**, 8% **6a**

The presented reaction occurs through a Pd-catalysed concerted metalation deprotonation (CMD) reaction (Figure **2**), creating a new carbon-carbon bond in the process. Omission of $Pd(OAc)_2$, pivalic acid or the base from the mixture, inhibited the transformation. The use of ancillary ligands such as triphenylphosphine (PPh_3) proved to be unnecessary and no change in conversion was observed when using this additive. This however means the Pd(0) species has to be generated in situ from $Pd(OAc)_2$ by oxidation of another reagent present in the mixture. This reduction is probably linked to the aromatization of the starting material. Initially, a small amount of starting material gets oxidized to activate the catalytic cycle. Then at the end of the cyclization, when the vial is opened, the Pd(0) species get oxidized by air to Pd(II), which subsequently get reduced again with aromatization of the nitrogen ring. This observation is supported by the fact that the cyclization reaction did not work when using the already aromatised starting product 5-bromo-4-diphenylphosphorylquinoline with the optimized conditions from entry **15**. The aromatization of tetrahydroquinolines towards quinolines in the presence of palladium has been previously described in literature.[17]

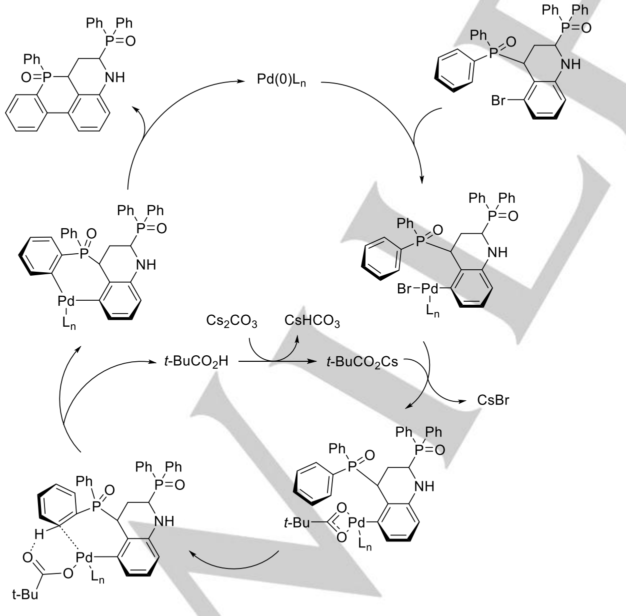
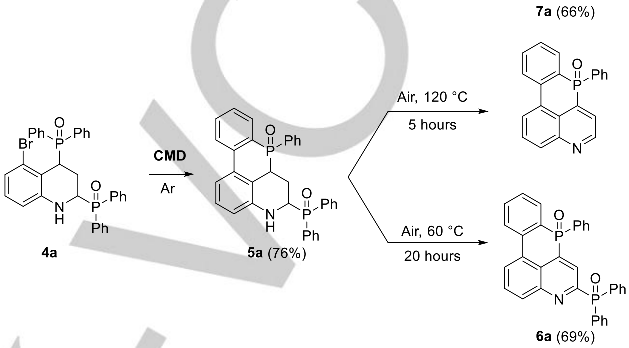


Figure 2. Proposed reaction mechanism based on a Pd-catalysed concerted-metalation-deprotonation pathway.

The oxidation of product **5a** in a one-pot fashion could lead to two possible outcomes as depicted in Table 2. If the vial is opened after completion of the cyclization step and stirred at 120 °C for 5 hours, product **7a** (entry **18**, 66%) can be obtained as the oxidation at high temperature leads to cooccurring elimination of the phosphorus group adjacent to the nitrogen. On the other hand, if the vial is first cooled and subsequently stirred at 60 °C for 20 hours, product **6a** was obtained (entry **17**, 69%). A similar type of backward aromatization product has been previously described in literature and is known to occur at elevated temperatures or in the presence of acids or copper halides.[18] The expelled phosphorus group shows up on the LCMS-UV analysis of the crude mixture and is removed during the purification.

Table 2. Selective one-pot synthesis of the desired products.



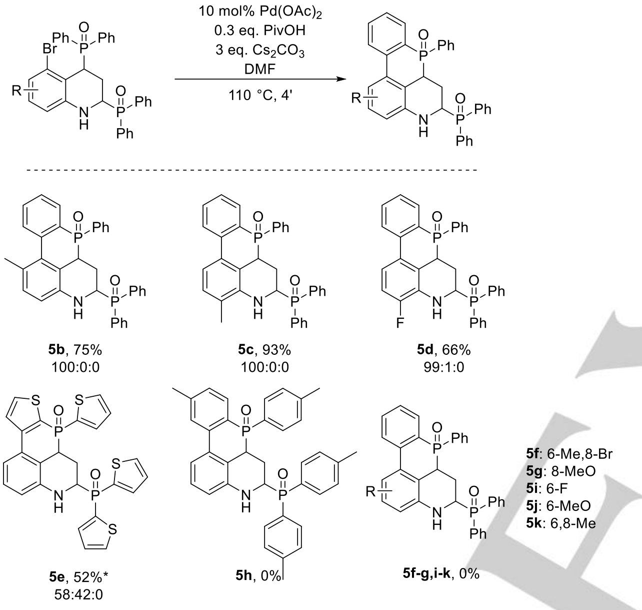
	Step 1:	**Argon**	**Step 2:**	**Air**	
No.	**Temp (˚C)**	**Time (min)**	**Temp (°C)**	**Time (h)**	**Yield (%)***
16	110	4	/	/	76 **5a****
17	110	4	60	20	69 **6a**
18	110	4	120	5	66 **7a**

*Pure isolated yield after reverse phase chromatography.

**Obtained as a mixture of diastereomers 90/10

With these optimized conditions in hand, a small library of products was prepared, based on readily available or synthesisable starting materials. (Figure **3**). The presence of a methyl or fluorine substituent on the 8-position was well tolerated (**5c** & **5d**). Surprisingly, when a fluorine was added to the 6-position next to the active site of the ring closure, the reaction no longer proceeded (**5i**). However, considering the reaction was successful for the methyl substituent (**5b**), it seems that sterical hindrance alone is not the crucial factor here. Reactions using methoxy- or methyl-substituted tetrahydroquinolines **5g** and **5j** also markedly hindered the reaction. The added electron density is most likely unfavourable for the oxidative addition step of the catalytic cycle. Attempts to push the reaction forward by increasing temperature or reaction time showed either no effect or led to the dehalogenation of the starting material. As would be expected, the presence of a second bromine on the 8-position (**5f**) leads to a complex mixture, considering the obvious interaction it has with the palladium catalyst.

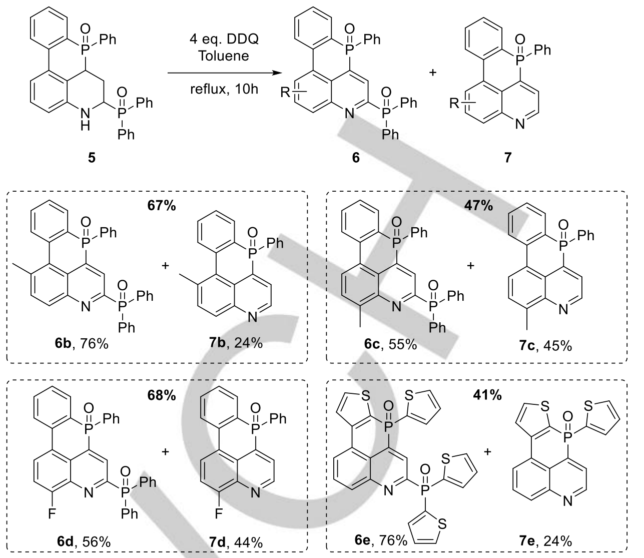
Next, we were curious to see if the aryl groups on the phosphine oxide moiety could be changed, as this would open more possibilities for the tunability of the resulting azaphosphaphenalenes. After some optimization, it was found that the 2-thienyl scaffold (**5e,** 52%) could be made, but only by using a different catalyst, [Pd(IPr)Cl(η^3-cinnamyl)]. It had been reported previously that these NHC bearing catalysts can perform the direct arylation of heterocycles under similar conditions.[19] The catalyst itself could easily be made from commercially available reagents and under mild conditions using a continuous flow procedure developed by our group.[20] To obtain full conversion of the starting material, this NHC (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) catalyst alone was not enough however, and complete conversion towards the desired product was only achieved upon addition of SiO_2. The exact role of this additive on the reaction remains debatable. Other examples of enhanced catalysis based on silica-supported metal complexes have recently been subject to review and the interactions mentioned in this work, between the silica surface and the metal, could potentially help explain the success of the reaction.[21] The intermediate products **5** were all formed with excellent stereoselectivity apart from compound **5e** which presented itself in a 58/42 mixture of diastereomers as observed by ^{31}P NMR.



*use of 5 mol% [Pd(IPr)Cl(η^3-cinnamyl)], 1 eq. SiO_2 instead of $Pd(OAc)_2$.

Figure 3. Evaluating the scope of the cyclisation reaction.

When oxidizing these derivatives further under air, the desired azaphosphaphenalenes were formed. However, for the methyl **5b** and fluorine **5d** containing compounds, the mixtures proved to be more complex as observed by LC-MS and NMR. A number of undesired by-products were present, most likely caused by oxidation of the methyl group or S_NAr substitution of the fluorine by the detached phosphine oxide group as described by Sawamura et al.[22] In order to obtain purifiable mixtures in decent yields, we opted for the intermediate purification of **5** and subsequent oxidation with DDQ to achieve products **6** and **7** simultaneously in the same reaction mixture. Through reverse phase chromatography, it was then possible to separate the two desired products for each substrate (Figure **4**).



*Combined yields are depicted in bold with the % of each compound underneath.

Figure 4. Separate oxidation step towards azaphosphaphenalenes.

For compounds **6e** & **7e** yields proved to be better with the previous one pot procedure, as no significant issue with by-products was observed with this substrate and therefore separating the steps is unnecessary (Figure **5**).

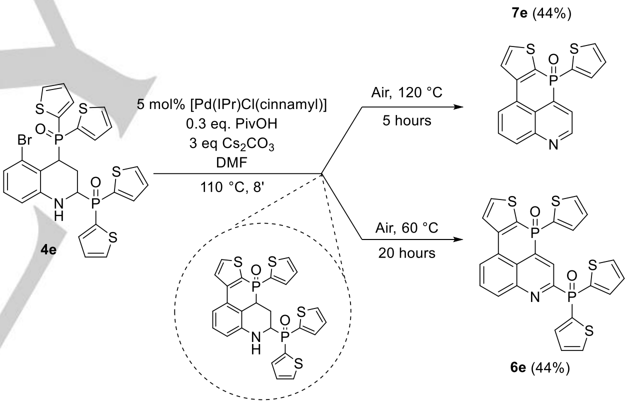


Figure 5. One-pot synthesis of thionyl derivatives.

The molecular structures of compounds **6a**, **7a**, **6e** and **7e** were unambiguously determined by means of single-crystal X-ray diffraction analysis (Figure **6**). The respective intermediate tetrahydroquinolines (**5a** & **5e**) could not successfully be crystallized after numerous attempts. From the analysis it is clear that **6a** has one molecule in the asymmetric unit and appears without disorder of the phenyl rings. **6e** also contains one molecule in the asymmetric unit and all free thiophene rings are disordered over two possible positions. Structure **7a** contains three molecules in the asymmetric unit, which each present themselves in one of the three different configurations. Finally, compound **7e** has one molecule in the asymmetric unit with the thiophene ring being disordered over 2 positions (ratio 87/13). More technical information and detailed figures regarding this analysis can be found in the supporting material.

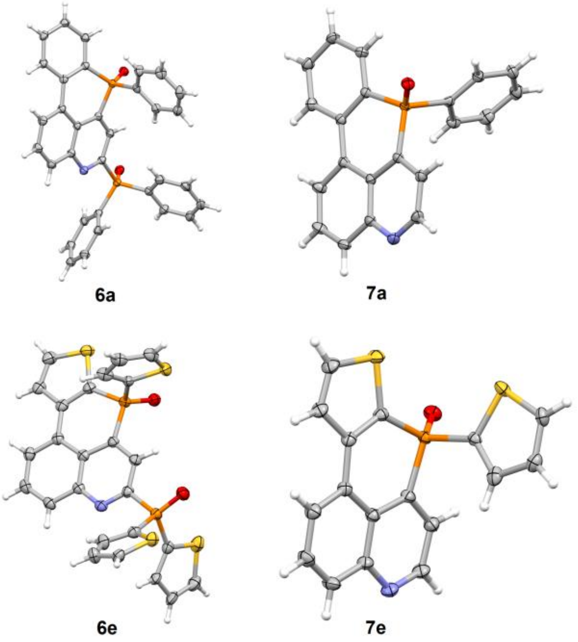


Figure 6. Molecular structures of **6a**, **7a**, **6e** and **7e**, as confirmed by single-crystal X-ray analysis. For **7a**, only one out of three molecules in the asymmetric unit is shown. Disorder of the thiophene rings is omitted for clarity.

The obtained polyaromatic products exhibited luminescent properties (Figure **7**), in their solid state as well as in solution when placed under a 365 nm UV lamp. The compounds with two phosphorus groups appeared noticeably brighter in the solid form. Given the interesting applications possible for such compounds based on their luminescent properties, a full evaluation of their emission, excitation and quantum yields was performed (in the solid state).

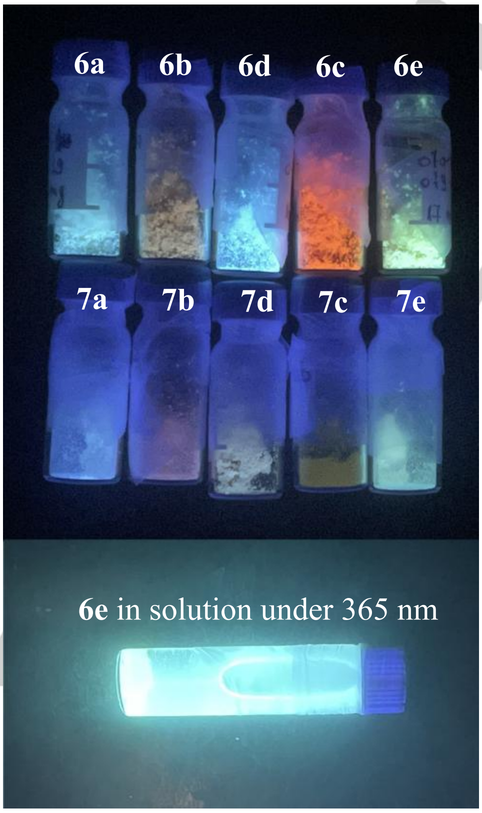
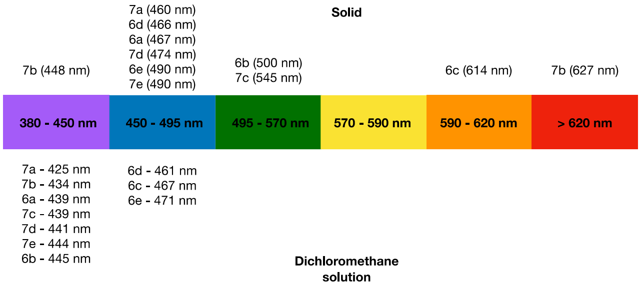


Figure 7. Photos of the prepared samples showing luminescence when placed under a 365 nm UV lamp. The top images are for samples in solid form. The bottom image is an example of a sample in solution (in acetonitrile).

The excitation and emission spectra of all samples were recorded in the solid state as well as after dissolving in dichloromethane. Dichloromethane was chosen based on the very good solubility of all the compounds in this solvent, which allowed preparing 5 μmol/L solutions. In the solid state the excitation maximum varied from 354 nm (**7c**) to 396 nm (**7a**). The emission spectra were recorded upon exciting into the excitation peak maximum. All samples, with the exception of **7b**, showed one broad band in the emission spectrum. For sample **7b** two emission bands were observed covering the electromagnetic spectrum from 400 – 750 nm. The emission maxima for all samples have been overviewed in Figure 8. For samples **6b**, **6c**, **7b** and **7c** a clear red shift of the emission band(s) is observed compared to the other samples. The combined excitation-emission spectra of the samples have been presented in Figure 9 and in the supporting materials. When dissolved in dicholoromethane significant changes to both the excitation and emission spectra are observed (see Figure **8**, Figure **9** and SI). The excitation spectra extend to the much lower UV range then for the solid-state samples. More than one peak is visible in the excitation spectra of these samples. The emission spectra were recorded after exciting into the excitation peak maximum located in the 300–400 nm range to keep a similar excitation wavelength to the samples in solid state. For all samples the emission spectrum consists of one broad band with a maximum located in the 425–471 nm range. The emission bands of the samples in dichloromethane are much more blue-shifted compared to the emission spectra recorded in solid state.



	380 - 450 nm	450 - 495 nm	495 - 570 nm	570 - 590 nm	590 - 620 nm	> 620 nm
Solid	7b (448 nm)	7a (460 nm) 6d (466 nm) 6a (467 nm) 7d (474 nm) 6e (490 nm) 7e (490 nm)	6b (500 nm) 7c (545 nm)		6c (614 nm)	7b (627 nm)
Dichloromethane solution	7a - 425 nm 7b - 434 nm 6a - 439 nm 7c - 439 nm 7d - 441 nm 7e - 444 nm 6b - 445 nm	6d - 461 nm 6c - 467 nm 6e - 471 nm				

Figure 8. Color chart showing the emission maxima of samples investigated in this study. The top values are for samples recorded in solid form. The bottom values are for samples recorded in dichloromethane. Sample **7b** (in solid form) showed 2 emission peaks and is mentioned twice in the scheme.

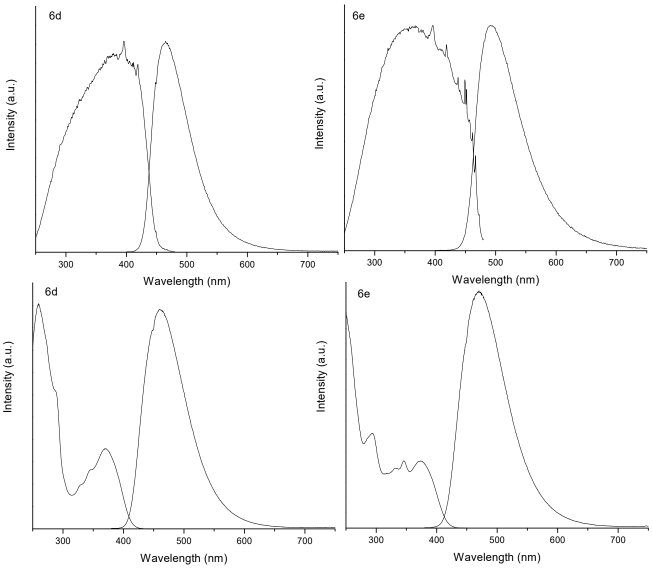


Figure 9. Selected combined excitation-emission spectra (left: sample **6d**, right: sample **6e**). Top row present measurements carried out in the solid state; bottom row measurements carried out after dissolving the samples in dichloromethane (5 µmol/L).

Absolute quantum yields of the solid and liquid samples were determined using an integrating sphere. Quantum yields (QY) were calculated using equation (1):

$$\eta = \frac{\int L_{emission}}{\int E_{blank} - \int E_{sample}} \qquad (1)$$

Where $L_{emission}$ is the integrated area under the emission spectrum, E_{blank} is the integrated area under the “excitation” band of the blank, and E_{sample} is the integrated area under the excitation band of the sample (as the sample absorbs part of the light, this area will be smaller than E_{blank}). The QY values have been presented in Table 3. Much higher QY values were obtained upon dissolving the samples in dichloromethane compared to measurements carried out in the solid state. In solid state, the highest values were obtained for samples **6d** (17%), **6e** (12.5%), and **6c** (9%). It is also clear that these samples showed visibly stronger emission intensities under a 365 nm UV lamp (see Figure 7). In dichloromethane, the highest QY values were obtained for samples **6c** (72%), **6d** (99%), and **7d** (72.6%). Some similar trends are observed for the samples recorded in solid-state and solvent as visualized in Figure **10**. A higher quantum yield for fluorine and thiophene containing structures is observed. Next to the presence of a push-pull system in these molecules, these heteroatoms can have a significant influence on the electronic properties of organic molecules. The inductively withdrawing and mesomerically donating properties of the fluorine atom result in a decrease of the band gap, it is the element with the strongest electronegativity and its presence instils a stability towards photo-oxidation.[23] The sulfur atom of the thiophene ring has a high polarizability, which facilitate its electron donating properties and make it available for nonbonding interactions.[24]

To summarize the photoluminescence investigation, the solid-state emission of all studied compounds is red shifted compared to studies carried out in a polar solvent like dichloromethane. These samples show very good QY values in solution and much lower QY values in solid state. The phenomenon of fluorescent molecules experiencing loss of their emission in the solid state is known as Aggregation Caused Quenching (ACQ) and is known in literature for other compounds.[25]

Table 3. Overview of absolute QY values.

Sample nr.	QY [%] solid	QY [%] CH_2Cl_2 solution
6a	3.6	26.2
6b	3	49.4
6c	9	72
6d	17	99
6e	12.5	49.7
7a	5	41.5
7b	1	20.3
7c	0.5	54.3
7d	2	72.6
7e	1	19.3

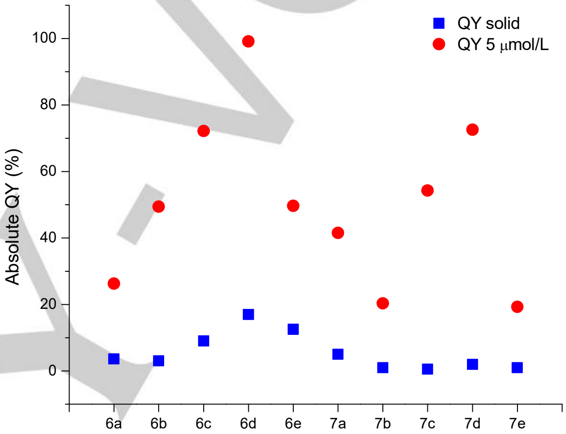


Figure 10. Absolute QY values for the samples recorded both in solid-state and in CH_2Cl_2 solution (5 µmol/L). The QY values for samples in solution are much higher, however both solid samples and CH_2Cl_2 solutions follow some similar trends within the series of samples.

Conclusion

In summary, an easy and versatile synthetic route towards azaphosphaphenalene ring systems was developed. This method gives simple access to various six-membered polyaromatic phosphacycles, using readily available starting materials and reagents. The structures of some of these newly constructed motifs were confirmed by X-ray analyses and their photoluminescent properties were evaluated and compared. Research into further structural modifications is currently ongoing in our laboratory to expand the emission spectrum and/or improve quantum yields. The potential application of the trivalent phosphine variants of these molecules as ligands is also being evaluated in our group.

Experimental details

Di(thiophen-2-yl)phosphine oxide (1): A flame dried flask is filled with a suspension of 720 mg (30 mmol) magnesium turnings in 20 ml dry THF. To this suspension is then added 0.4 ml (4 mmol) 2-bromothiophene. When the reaction mixture starts to heat up and the Grignard reagent is forming, the remaining 2.5 ml (26 mmol) 2-bromothiophene in 10 ml THF is added. After stirring this mixture for 2 hours at room temperature, the flask is cooled to -20°C using a cooling bath with a NaCl:ice mixture of 1:3 mass ratio. When the contents are sufficiently cooled, 1.28 ml (10 mmol) diethyl phosphite in 10 ml THF is added dropwise to the mixture. Next, the cooling bath is removed and the reaction is stirred at room temperature for another 2 hours. To quench the reaction, 30 ml of 0.5 M HCl solution is added dropwise to the mixture, after which the contents are transferred to a separatory funnel. The product is extracted using EtOAc (2 x 30 mL), and the organic phase is subsequently washed with brine. After drying the combined organic fractions with MgSO4 and filtering off the solids, the desired product is obtained as a yellow oil (89% yield). The resulting product is pure enough for further use. Adapted from and spectral data in accordance with [26].

Skraup quinoline synthesis (2): 1.2 eq. of glycerine was added to a solution of a substituted aniline (1 g), NaI (0.02 eq.) and 80% H2SO4 (4 ml) at 140 °C. The reaction mixture was stirred at the this temperature for 6 h. Afterwards the mixture was poured onto ice and neutralized with 25% aq. NaOH solution to increase the pH to 10. The basic mixture is then extracted with toluene (3 x 30 mL). The organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure. The crude products were purified using column chromatography on silica gel (1:4 mixture of ethyl acetate : hexane). Adapted from and spectral data in accordance with [27].

Bromination of 6-substituted quinolines (3a, 3b & 3f): 1 eq. of NBS (or 2 eq. in case of **b**) was added to a solution of 1 g of 6-substituted quinoline in 120 mL of 93% sulfuric acid, and the mixture was maintained for 3 h at room temperature. It is then poured into 900 ml of ice water, and the aqueous mixture was made alkaline with 45% KOH solution. The precipitated salts are removed by filtration and extracted with chloroform (3 x 25 mL). The extract was dried with magnesium sulfate, the solvent was evaporated, and the crude product was purified using column chromatography (1:4 mixture of acetone : chloroform). Adapted from and spectral data in accordance with [28].

5-bromo-6-methoxyquinoline (3c): To a solution of 6-methoxyquinoline (1.19 g, 5 mmol) in DCM (5 mL) at room temperature was added NBS (1.0 g, 5.63 mmol) in one portion and the resulting mixture was stirred at for 20 hours. the reaction mixture was quenched with 1 M HCl. After being extracted with dichloromethane and washed with water twice, the combined organic layer is dried with $MgSO_4$, concentrated in vacuo. A short silica gel column filtration of the crude mixture afforded pure 5-bromo-6-methoxyquinoline (1.43 g, 80%).

5-bromo-6-fluoroquinoline (3d): 1 eq. of NBS was added to a solution of 1g of 6-fluoroquinoline in 120 mL of 93% sulfuric acid, and the mixture was stirred at 50 °C for 5 h. It is then poured into 900 ml of ice water, and the aqueous mixture was made alkaline with 45% KOH solution. The precipitated salts are removed by filtration and extracted with chloroform (3 x 25 mL). The extract was dried with magnesium sulfate and the solution is passed through a silica pad. Finally, the solvent was evaporated and the crude product was purified using reverse phase column chromatography (C18, 30% to 100% gradient acetonitrile in water) to obtain white crystals (21%).

Diphosphorylation of 5-bromoquinolines (4): To a solution of 500 mg of a 5-bromoquinoline derivative is added 2 eq. phosphine oxide or di(thiophen-2-yl)phosphine oxide. The mixture is stirred at 75°C for 20h. The mixture solidifies upon formation of the desired product, when this happens and stirring becomes impossible, add a small amount of acetonitrile and let the suspension stir open to the air until the solvent evaporates and stirring stops once again. Next, the flask is taken out of the heating bath and acetone is added. Some breaking of the solid product with a spatula might be needed in order to free the stirring bar. The target product does not dissolve in the solvent and after being given some time to precipitate, it can be filtered off using a glassinterfilter. Wash the white powder with some acetone to obtain pure product free of starting material. Chloroform can be used to dissolve the phosphorylated tetrahydroquinolines, when evaporating this solvent a white crystalline powder is obtained instead of the aforementioned powder. Adapted from [14].

Pd-catalysed intramolecular CMD reaction (5a, 5b, 5c, 5d): 0.5 mmol of a diphosphorylated tetrahydroquinoline derivative was added to a glass SPME vial together with 3 eq. (1.5 mmol) Cs_2CO_3, 0.3 eq. (0.17 mmol) pivalic acid, 0.1 eq. (0.05 mmol) $Pd(OAc)_2$ and 2 mL dry DMF. After capping the vial, a long needle is put through the cap to bubble argon gas through the solution for 15 minutes. The mixture is stirred and heated in a preheated oil bath at 110°C for exactly 4 minutes, after which the vial is immediately put in an ice bath. When the mixture is sufficiently cooled the vial can be opened and the contents are diluted with acetone and filtered through a pad of silica. After evaporation of the solvent the product is obtained in a purity of higher than 90%, with a small amount of aromatized product also present. To isolate the pure intermediate structures, reverse phase chromatography can be used (C18, 30% to 100% gradient acetonitrile in water). Dissolving the pure product in chloroform and subsequently evaporating this solvent, yields the product in a yellow crystalline powder. Depending on the derivative, different diastereomeric ratios were obtained.

Pd-catalysed intramolecular CMD reaction (5e): 0.5 mmol of **4e** was added to a glass SPME vial together with 3 eq. (1.5 mmol) Cs_2CO_3, 0.3 eq. (0.17 mmol) pivalic acid, 0.05 eq. (0.025 mmol) [Pd(IPr)(cin)Cl], 1 eq (0.5 mmol) of SiO_2 and 2 mL dry DMF. After capping the vial, a long needle is put through the cap to bubble argon gas through the solution for 15 minutes. The mixture is stirred and heated in a preheated oil bath at 110°C for exactly 8 minutes, after which the vial is immediately put in an ice bath. When the mixture is sufficiently cooled the vial can be opened and the contents are diluted with acetone and filtered through a pad of silica. After evaporation of the solvent the product is obtained in a purity of higher than 90%, with a small amount of aromatized product also present. To isolate the pure intermediate structures, reverse phase chromatography can be used (C18, 30% to 100% gradient acetonitrile in water). Dissolving the pure product in chloroform and subsequently evaporating this solvent, yields the product in a yellow crystalline structure with a diastereomeric ratio of 57/43.

Aromatization towards aza-phosphaphenalenes (6a, 6e, 7a, 7e): When performing the Pd-catalysed cyclisation, after the initial 4 or 8 minutes of stirring at 110 °C, the aromatisation can be performed by removing the cap and continuing stirring in open air. There are two options for this aromatisation: Either towards **6a** & **6e** or towards **7a** & **7e**. In order to produce the former, the vial is briefly cooled before being opened and then stirred at 60 °C for 20 hours. To produce the latter compounds the vial is simply opened and stirred at 120 °C for 5 hours. The subsequent work up remains the same and the pure product can be obtained either by reverse phase chromatography (C18, 30% to 100% gradient acetonitrile in water) or normal phase chromatography (SiO_2, 25% acetone in chloroform) with indistinguishable differences in yield.

Aromatization towards aza-phosphaphenalenes (6b, 6c, 6d, 7b, 7c, 7d): To a solution of 0.15 mmol of **5b**, **5c** or **5d** in 10 ml toluene is added 4 eq. DDQ (0.6 mmol). The mixture is stirred at reflux for 10 hours. The mixture is extracted with DCM (3 x 10 mL), washed with $NHCO_3$ solution several times until the orange/red colour turns yellow and finally with brine. Dry the organic phase with $MgSO_4$ and evaporate the solvent to obtain the crude mixtures of **6b** & **7b**, **6c** & **7c** or **6d** & **7d**. These could then be separated into their respective pure compounds by means of reverse phase chromatography (C18, 30% to 100% gradient acetonitrile in water). Finally the isolated products were redissolved in chloroform and presented themselves as yellow or orange crystalline powders after evaporation of the solvent.

[Pd(IPr)Cl(η3-cinnamyl)]: Made with flow chemistry procedure previously published by our group. [20]

Supporting information

Additional details regarding the setup as well as the analytical spectra of new compounds can be found in the supporting information file.[26, 29-36]

Deposition Number(s) <url href="https://www.ccdc.cam.ac.uk/services/structures?id=doi:10.1002/chem.202303072"> 2296137 (for **6a**), 2296138 (for **6e**), 2296139 (for **7a**), 2296140 (for **7e**)</url> contain(s) the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe <url href="http://www.ccdc.cam.ac.uk/structures">Access Structures service</url>.

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Keywords: Phosphorus • Phosphine oxides • Pd-catalysis • Luminescence • Cross coupling reaction • Polyaromatic

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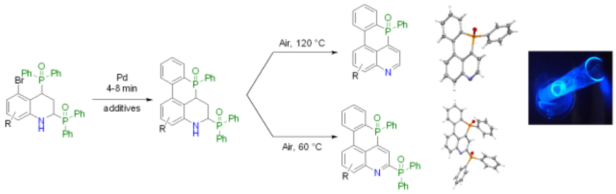

Herein a swift and versatile palladium cyclization is presented using readily accessible catalysts and starting materials to produce new azaphosphaphenalene motifs. The luminescent properties of these products were evaluated and some of the key compounds had their structure unambiguously confirmed by X-ray analysis. The phosphorus atom offers interesting possibilities for post functionalization.