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Regioselective Sodium Cation-Assisted Synthesis of the First Bis-Transannular Cyclotriphosphazatriene Derivatives of a Chiral Ligand Type

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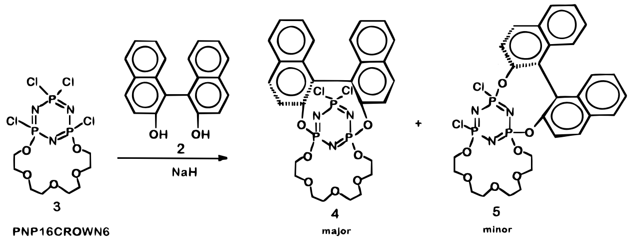
The reactions of hexachlorocyclotriphosphazatriene $N_3P_3Cl_6$ (**1**) with aromatic ortho-dinucleophiles are known to be generally dominated by closure at one phosphorus atom to give the respective spirocyclic derivatives.[1,2] We have previously found that direct reaction of **1** with 2,2′-dihydroxy-1,1′-binaphthyl (**2**) yields exclusively spiro-substituted products,[3] confirming that geminal spiro-cyclosubstitution at the PCl_2 groups is also the thermodynamically favored reaction route for such a sterically hindered diol substrate. In the present communication we demonstrate that the gem−spiro substitution pattern is not universal for all PCl_2-containing cyclophosphazenes and can be radically altered toward nongem ansa-cyclosubstitution, when employing as starting reagents the recently reported cyclophosphazene crown 1,3-$[O(C_2H_4O)_4]P_3N_3Cl_4$ (**3**)[4] and **2** in the form of its disodium derivative as outlined in Scheme 1.

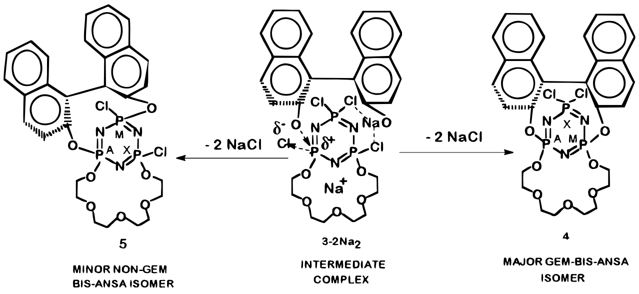
The only hitherto reported cyclophosphazene derivative with a conjugated ansa-dioxybiarylene bridge, 1,3-$[N_3P_3(OCH_2CF_3)_4(O_2C_{12}H_8)]$ (**6**),[2] was obtained by interaction of the nongem tetra(trifluoroethoxy)dichlorocyclotriphosphazene 1,3-$[N_3P_3(OCH_2CF_3)_4Cl_2]$ (**7**) with 2,2′-dihydroxybiphenyl. Substrate **7** contained its only two reactive chloride functions at two different P atoms (P_1 and P_3), therefore making transannular substitution the only possible cyclocondensation pattern.

Although several monoansa derivatives of **1** with nonaromatic bridges have been described,[2] the only known representative of bisansa cyclophosphazenes is the tetrameric nongem “double-transannular” ruthenocenyl derivative, in which each bridging unit cross-links two different P atoms of the N_4P_4 ring.[5] No trimeric cyclophosphazene bis-transannular derivatives have been reported hitherto; in particular there are no data on the synthesis of cyclotriphosphazenes (or any other cyclophosphazenes) in which two different ansa substituents are linked geminally to the same two P atoms, while the third one remains unsubstituted. This communication describes a facile high-yield synthesis of the first representative of this class of cyclophosphazenes (gem-compound **4**), and the respective nongem transannular **5** derivative (asymmetric isomer of **4**), which is formed as the minor product.

Scheme 1



Scheme 2[a]



[a] The P atoms are labeled AMX corresponding to their analysis by ^{31}P NMR (see ref 10).

As shown by X-ray crystallography,[4] the tetrachlorocyclophosphazene **3** used in this work contains one PCl_2 group and two nongeminal chlorine atoms adjacent to the *cis* ansa-macrocyclic polyether substituent, thus providing the possibility for both spiro (geminal) and ansa (nongeminal) cyclosubstitution. From the point of view of macrocyclic chemistry the cyclophosphazene substrate **3** represents a 16-membered diphosphaza-crown ether, 16-crown-6, well-fitted for complexing sodium cations within the macrocyclic cavity.[4] The disodium derivative of **2** exists in the form of ion pairs: $Na^+[^-OArO^-]Na^+$, in which the active nucleophile is the 2,2′-dioxy-1,1′-binaphthylene dianion. Due to the coordinating ability of the crown−cyclophosphazene substrate **3** the sodium counterion can be “trapped” inside the macrocyclic cavity in the first step of the process, thus sterically favoring nucleophilic substitution of the nongeminal chlorine atoms adjacent to the macrocycle (→**4**) over reaction with the more distant PCl_2 site, which might otherwise have been expected.[1,2] However in the case of reaction of **3** with **2**-Na_2 the alternative nongem ansa bridging (→**5**) is also observed. A hypothetical intermediate supramolecular complex, formed by the S_N2 substitution of **3** with **2**-Na_2, which can further react toward either **4** (major) or **5** (minor), respectively, is shown in Scheme 2.

The molecular structures of both isomers, **4** and **5**, have been confirmed by X-ray structure determination (Figures 1 and 2).[6] The nongeminal isomer **5** is also the first example of its kind with two different ansa substituents spanning three phosphorus atoms. The X-ray proven *trans*-configuration of its oxy(tetraethylenoxy) ansa bridge (Figure 2) provides crystallographic evidence of the Walden inversion[7] in the respective S_N2 reaction (Scheme 2). In the conversion of **3** to the geminal isomer **4**, inversion of both phosphorus centers gives rise to a net retention of *cis*-configuration (Figure 1).

The supramolecular control of the sodium-assisted phenolysis of **3**, occurring via the coordinative interaction between the polyether crown substituent of **3** and the sodium cation-paired nucleophile **2**, seems to be the driving force for the regioselective substitution of the chlorine atoms adjacent to the macrocycle “capturing” the Na counterions.[8] Some examples of metal-

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(1) Allcock, H. R.; Kugel, R. L. *Inorg. Chem.* **1966**, *5*, 1016−1020.

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(6) Detailed discussion of the structural parameters of **4** and **5** will be published elsewhere.

(7) Walden, B. *Ber.* **1893**, *26*, 210; **1896**, *29*, 133; **1899**, *32*, 1855.

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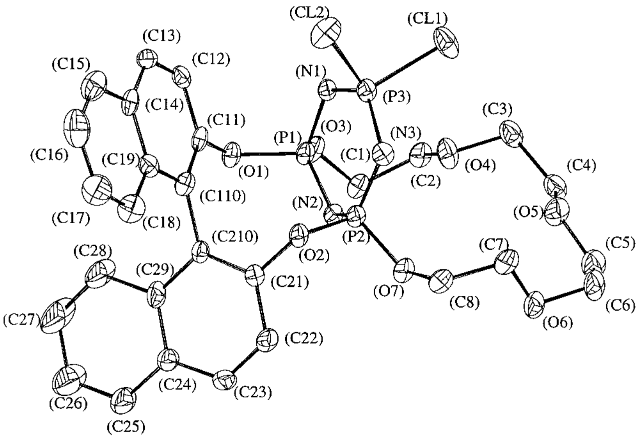

Figure 1. The molecular structure of gem bisansa {1,3-(oxytetraethylenoxy)[1,3-(2,2′-dioxybinaphthyl-1,1′)]}cyclotriphosphazatriene (**4**).

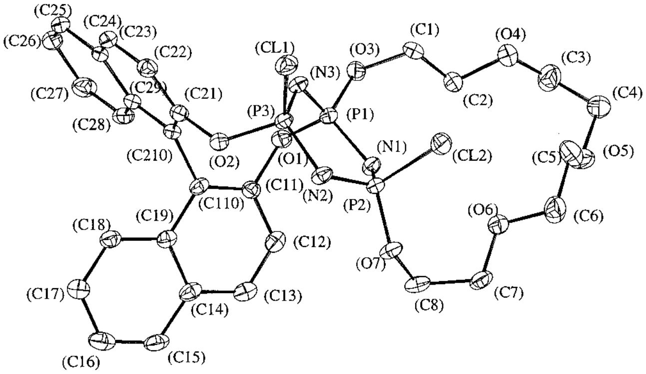

Figure 2. The molecular structure of nongem bisansa {1,3-(oxytetraethylenoxy)[1,5-(2,2′-dioxybinaphthyl-1,1′)]}cyclotriphosphazatriene (**5**).

catalyzed reactions of crown ether substrates occurring in close proximity to the crown structure have been recently reported, the regioselectivity of substitution being interpreted on the basis of a transition state, where the complexed cation assists the departure of the leaving group ("electrophilic catalysis").[9] Plausibly a similar type of transition state (Scheme 2, intermediate complex **3**-Na_2) results in the formation of two unusual bisansa-cyclosubstituted derivatives **4** and **5**. The gem-isomer **4**, containing two transannular bridges (oxytetraethylenoxy and oxybinapthylenoxy) at the same two P atoms, was obtained as the major product (~70% in the crude reaction mixture), whereas the nongem **5** formed more reluctantly (yield ~30%).[10] Quite suprisingly, the thermodynamically most favored spiro-substitution at the third PCl_2 atom was found not to occur at all in the sodium cation-assisted reaction of **3** with **2**.[8,11] The structural assignments for **4** and **5** (as well as for their respective spiro[binaphthylenedioxy] isomer[11]) have been supported by MS and ^{31}P NMR data, details of which, together with synthetic procedures, will be published elsewhere.

Of particular interest is the significant enhancement of reactivity of the dianion **2** due to its counterion complexation, which can be explained in terms of the *naked anion phenomenon*.[12] Whereas the syntheses described by Allcock (comprising the formation of the transannular derivative **6** in the reaction of **7** with 2,2′-biphenol) required prolonged heating of the substrates,[2] substitution of **3** with **2** proceeds rapidly at room temperature, resulting in the complete conversion of **3** to the respective transannular derivatives **4** and **5**.

The bis-transannular isomers **4** and **5** represent heterotopic (i.e. containing two different complexing units) phosphorus bridgehead ligands with chiral 1,1′-binaphthylene-2,2′-dioxy units and thus offer promise as molecular receptors for enantiomeric recognition via host−guest interactions, as reported for some other crowns with chiral units,[13] in particular Cram's 1,1′-binaphthyl-containing chiral crown ethers.[14] Studies of their optical resolution as well as on the syntheses of **4** and **5** starting from **1** and optically active isomers of **2** are currently under way.

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Supporting Information Available: Tables of crystal data and structure refinement, anisotropic displacement parameters, bond lengths and angles, selected torsion angles, and least square planes for compounds **4** and **5** (59 pages); tables of observed and calculated structure factors for compounds **4** and **5** (20 pages); This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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[8] No substitution products (neither transannular **4**, **5** nor their respective 5,5-spiro(2,2-dioxy-1,1′-binaphthtyl)-substituted isomer) have been found to be formed in the reaction of **3** with **2** when carried out in the presence of triethylamine or pyridine as hydrogen chloride acceptors (TLC and ^{31}P NMR evidence) under the same reaction conditions as those employed for the synthesis of **4** and **5** (1−2 h of stirring the equimolar mixture of **3** and **2** in dry THF at room temperature, at concentrations of **3** and **2** equal to 0.01 mol/L).

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[10] (a) The relative yields of isomers **4** and **5** were estimated on the basis of the ^{31}P NMR spectrum of the crude reaction mixture, when compared with those of the chromatographically isolated individuals (**4**: $R_f = 0.42$ (in hexane−THF = 2:3), mp = 192 °C, $M^+ = 681$. ^{31}P NMR-AMX spin system: $\delta P_A = 11.5$, $\delta_{PM} = 14.5$, $\delta_{PX} = 29.3$. **5**: $R_f = 0.33$, mp = 270 °C, $M^+ = 681$. ^{31}P NMR-AMX spin system: $\delta_{PA} = 10.3$, $\delta_{PM} = 30.0$, $\delta_{PX} = 26.4$). (b) Detailed discussion of the NMR and MS spectra, together with synthetic procedures, will be published elsewhere.

[11] Spiro isomer was obtained by reversing the order of addition of dinucleophiles to **1**, i.e. by reacting **1** first with **2**-Na_2 (→ spiro(2,2′-dioxy-1,1′-binaphthyl)tetrachlorocyclotriphosphazene[3]) and then with tetraoxyethylene glycol (→ spiro[1,1(2,2′-dioxy-1,1′-binaphthyl)]ansa[3,5(oxytetraethylenoxy)]-3,5-dichlorocyclotriphosphazene: $M^+ = 681$. ^{31}P NMR-A_2B spin system: $\delta_{PA} = 24.6$, $\delta_{PB} = 22.3$.[10b]

[12] For a definition of the *naked anion phenomenom* see, for example: Lindoy, L. F. *The Chemistry of Macrocyclic Ligand Complexes*; Cambridge University Press: New York, 1989; pp 107−108. Gokel, G. *Crown Ethers & Cryptands*; The Royal Society of Chemistry: Cambridge, 1991; pp 141−142.

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