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First rhenium complexes based on cyclotriphosphazene scaffolds with exocyclic pyrazolyl substituents†

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Functionalized cyclotriphosphazenes with two or six pyrazolyl substituents have been employed for the preparation of rhenium carbonyl complexes; depending on the nature of the ligand system rhenium complexes with either *gem*-N_2, *gem*-N_3 or *non-gem*-N_3 coordination modes can be prepared.

The immobilization of ^{99m}Tc or $^{186/188}$Re utilizing dendritic or soluble polymer supports has broad implications for the development of novel radiopharmaceuticals.[1] Among the numerous families of possible inorganic and organic polymeric backbones, polyphosphazenes are superior frameworks to simultaneously introduce water-soluble entities, metal binding sites and receptor-targeting vectors *via* sequential substitution reactions. The derivatization of cyclotriphosphazenes can often be accomplished in analogy to the methods developed for the high molecular weight polymeric materials, and the resulting N/P-heterocycles are valuable models to understand the modes of metal complexation on functionalized polyphosphazenes.[2] This method provides vital information to evaluate the efficiency of the related macromolecular metal binding prior to more complex studies of the polymer. Although multiple reports address the preparation of metallacyclophosphazenes with rhenium,[3] to the best of our knowledge no studies have examined the use of functionalized phosphazenes for the binding of heavier group 7 metals. In our initial study we therefore investigated the utility of hexakis(3,5-dimethylpyrazolyl)cyclotriphosphazene $P_3N_3(3,5\text{-}Me_2Pz)_6$[4] and novel 2:1 site-differentiated dipyrazolyl substituted *spiro*-cyclotriphosphazenes towards the complexation of Re(I).

Reaction of $P_3N_3(3,5\text{-}Me_2Pz)_6$ with three equivalents of $[ReCl(CO)_5]$ in refluxing toluene for 5 h does not yield multinuclear rhenium species but instead leads to the formation of the cationic *non-gem*-N_3 mononuclear tricarbonyl complex *fac*-$[Re(CO)_3\{P_3N_3(3,5\text{-}Me_2Pz)_6\}]^+$ (**1a**) with $[Re_2Cl_3(CO)_6]^-$ as the counter anion (Fig. 1). The formation of the dinuclear anion may be attributed to the increased tendency of $[ReCl(CO)_5]$ to undergo dimerisation in aromatic solvents such as C_6Me_6 which usually results in the formation of complex salts of the type $[Re(CO)_3Ar]^+[Re_2Cl_3(CO)_6]^-$.[5]

As shown in Fig. 1, the distorted octahedrally coordinated Re(1) center is surrounded in a *fac*-fashion by three carbonyl carbons [Re(1)–C, av. 1.91(3) Å], two pyrazole nitrogens [Re(1)–N, 2.20(1) Å] and one phosphazene core nitrogen [Re(1)–N(1) 2.247(12) Å] and is displaced 0.70 Å away from the mean plane defined by the cyclophosphazene backbone.‡ The coordination of the Re center by the core nitrogen slightly affects the structural parameters within the phosphazene ring. The coordinating nitrogen is displaced 0.17 Å from the phosphazene plane‡ and displays increased bond lengths to surrounding phosphorus atoms [1.62(1) *vs*. 1.58(1) Å]; consistent with decreased π-bond character.[6] This coordination environment remains intact and static in solution as witnessed by the ^1H NMR spectrum (CD_3CN) showing the signal pattern of four (2:2:1:1) inequivalent pyrazole units. Compound **1a** as its hexafluoroantimonate salt can also be prepared by reacting $[Re(CH_3CN)_3(CO)_3]^+SbF_6^-$ [7] with $P_3N_3(3,5\text{-}Me_2Pz)_6$.

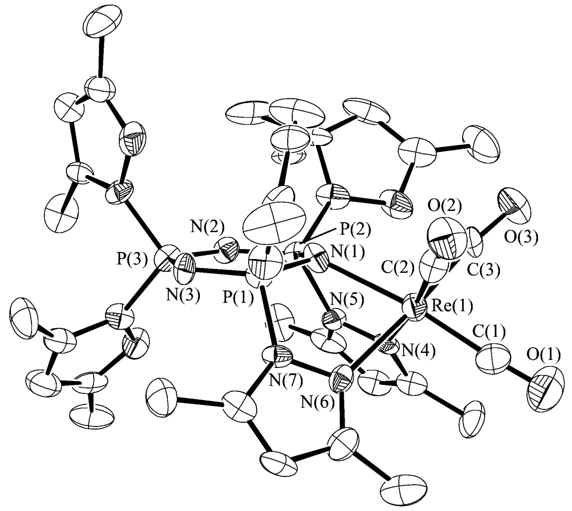
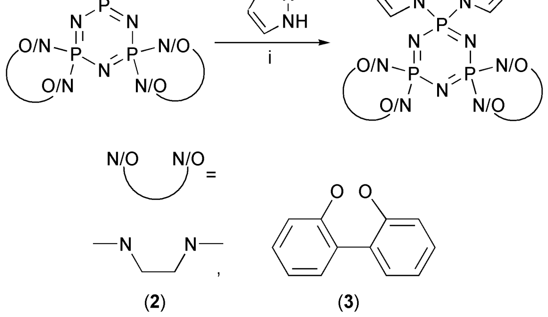


Fig. 1 ORTEP diagram of the complex cation $[Re(CO)_3\{P_3N_3(3,5\text{-}Me_2Pz)_6\}]^+$ (**1a**) (ellipsoids at 50% probability level). Selected bond lengths (Å): Re(1)–N(1) 2.247(12), Re(1)–N(4) 2.216(11), Re(1)–N(6) 2.183(11), Re(1)–C(1) 1.879(18), Re(1)–C(2) 1.918(17), Re(1)–C(3) 1.941(18), P(1)–N(1) 1.596(11), P(2)–N(1) 1.634(12), P(2)–N(2) 1.555(12), P(3)–N(2) 1.592(11), P(1)–N(3) 1.573(12), P(3)–N(3) 1.583(12).

To reduce possible coordination sites and examine other potential coordination modes, we targeted the use of cyclotriphosphazenes with only two pyrazole substituents. Although bispyrazolyl substituted cyclotriphosphazenes have been prepared,[8] current synthetic pathways to these materials require multiple reaction steps or prolonged reaction times. We found that these materials can be conveniently prepared in good yields by a solvent free reaction of readily available *spiro*-tricyclic 2,2-dichlorocyclophosphazenes[9]§ in molten pyrazole (Scheme 1).

Depending on the cyclophosphazene derivative, reaction times vary between 2 and 3 h. Excess pyrazole can be removed



Scheme 1 Synthesis of the bispyrazolyl *spiro*-tricyclic cyclotriphosphazenes **2** and **3**. *Reagents and conditions*: i, solvent free, excess pyrazole, 186 °C, 2–3 h.Yield: 76% (**2**), 82% (**3**).

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† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b2/b203254f/

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by washing the crude product with hot cyclohexane and can be reused after sublimation. Purification has been typically achieved by dissolving the crude product in CH_2Cl_2 and washing the organic phase repeatedly with water. Subsequent drying with Na_2SO_4 and removing the solvent *in vacuo* yielded **2** and **3** as white crystalline solids which can be further purified by recrystallization from hot toluene (**3**) or a methanol/diethyl ether mixture (**2**).¶‖

Reaction of $P_3N_3(MeNC_2H_4NMe)_2Pz_2$ (**2**) with one mol equivalent of $[Re(CH_3CN)_3(CO)_3]^+SbF_6^-$ in refluxing THF again yields a cationic complex of the type *fac*-$[Re(CO)_3L]^+$ (**2a**, Fig. 2). The bispyrazolyl ligand **2** acts as a tridentate ligand and coordinates facially to the Re(I) center. In contrast to **1a**, now the coordinating nitrogen atoms from two geminal pyrazolyl groups are both occupying *cis* positions and together with the core nitrogen constitute two five-membered chelate rings. These chelate rings deviate significantly from planarity as indicated by the torsion angles of 51.3° [(N(7)–P(1)–N(1)–Re(1)] and 52.4° [N(5)–P(1)–N(1)–Re(1)] respectively. The distortion from the ideal octahedral geometry is also visible in the small N–Re(1)–N angles, which vary between 76.8(3)° for N(1)–Re(1)–Ne(4) to 82.4(3)° for N(4)–Re(1)–N(6). The Re(1)–N and Re(1)–C bond lengths are comparable to those in $[Re(CO)_3\{P_3N_3(3,5\text{-}Me_2Pz)_6\}]^+$ but other than observed for **1a**, the P–N bond lengths within in the phosphazene scaffold vary throughout the ring which is mainly due to the different binding situations at the respective phosphorus atoms.

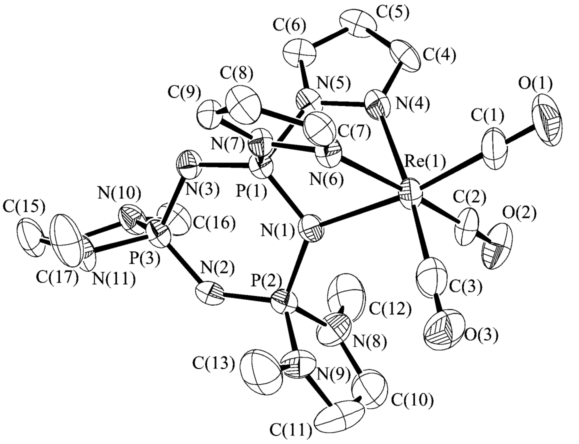
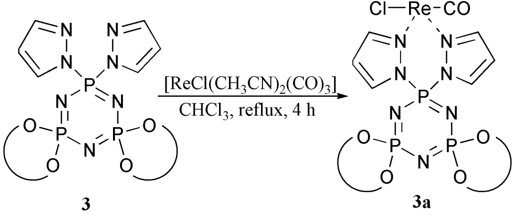


Fig. 2 ORTEP diagram of the complex cation $[Re(CO)_3\{P_3N_3(MeNC_2H_4NMe)_2Pz_2\}]^+$ (**2a**) (ellipsoids drawn at 50% probability level). Selected bond lengths (Å): Re(1)–N(1) 2.239(6), Re(1)–N(4) 2.206(7), Re(1)–N(6) 2.193(7), Re(1)–C(1) 1.919(10), Re(1)–C(2) 1.908(10), Re(1)–C(3) 1.922(12), P(1)–N(1) 1.574(7), P(2)–N(1) 1.660(7), P(2)–N(2) 1.578(8), P(3)–N(2) 1.596(8), P(1)–N(3) 1.542(7), P(3)–N(3) 1.640(7).

Interestingly, if $P_3N_3(O_2C_{12}H_8)_2Pz_2$ (**3**) is allowed to react with $[ReCl(CH_3CN)_2(CO)_3]$[10] in refluxing chloroform, a white crystalline material precipitates that has been identified and structurally characterized§‖ as the neutral species $[ReCl(CO)_3\{P_3N_3(O_2C_{12}H_8)_2Pz_2\}]$ (**3a**) (Scheme 2). This compound is remarkably air stable and has been recrystallized under aerobic conditions from neat DMF/diethyl ether.



Scheme 2

3a is one of the very few examples of a mononuclear (*gem*-N_2) pyrazolylcycltriphosphazene based metal complex with no evidence of an interaction between the core nitrogen and the central metal ion. This highlights again the flexibility of the given ligand system in supporting different coordination modes which may also facilitate the stabilization of rhenium complexes in higher oxidation states.

In conclusion we have successfully demonstrated the utility of pyrazole substituted cyclotriphosphazenes for the preparation of Re(I) carbonyl complexes. In conjunction with the broad library of possible cosubstituents at the phosphazene backbone, these materials may be modified accordingly to impart water solubility and allow for the complexation of technetium. Studies addressing these issues are currently under way.

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Notes and references

‡ Mean plane defined by P(1), P(2), P(3).

§ 2,2-Dichloro-4,4,6,6-bis[*spiro*(2′2″-dioxy-1′1″-biphenyl)]cyclotriphosphazene and 2,2,-dichloro-4,4,6,6-bis[*spiro*-N,N′-dimethylethylenediamino)cyclotriphosphazene can be isolated as the sole isomer in 79 and 80% yield, respectively, by reaction of commercially available $P_3N_3Cl_6$ with 2,2′-biphenol or *N,N′*-dimethylethylenediamine, see ref. 9.

¶ For experimental (**2**, **3**, **1a**–**3a**) and structural details of **1a** and **2a** see ESI. The structure of **3a** was found to be severely disordered but connectivities have been clearely resolved.

‖ *Crystal data*: for **1a**: $C_{43}H_{52}Cl_3N_{15}O_{10}P_3Re_3$, monoclinic, space group, $P2_1/c$, a = 10.987(3), b = 24.360(6), c = 21.664(5) Å, β = 101.356(4)°, V = 5685(2) Å^3, T = 203 K, Z = 4, D_c = 1.983 g cm^{-3}, μ(Mo-Kα) = 6.664 mm^{-1}, 9845 reflections collected, 9845 unique, of which 6469 with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using full-matrix least squares refinement on F^2 and difference Fourier synthesis. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were included at calculated positions. R_1 = 0.0732 [$I > 2\sigma(I)$], wR_2 = 0.1458, GOF = 1.084 for 649 parameters.

For **2a**: $C_{17}H_{26}N_{11}O_3F_6P_3SbRe$, triclinic, space group, $P1$, a = 8.838.(3), b = 13.475(5), c = 13.819(5) Å, α = 97.523(5), β = 108.543(5), γ = 91.604(6)°, V = 1542.8(9) Å^3, T = 203 K, Z = 2, D_c = 2.039 g cm^{-3}, μ(Mo-Kα) = 5.028 mm^{-1}, 7230 reflections collected, 4123 unique, of which 3614 with $I > 2\sigma(I)$ were used in the refinement. Refinement and solution as above. R_1 = 0.0418 [$I > 2\sigma(I)$], wR_2 = 0.1007, GOF = 1.085 for 379 parameters.

CCDC reference numbers 183233 and 183234. See http://www.rsc.org/suppdata/cc/b2/b203254f/ for crystallographic data in CIF or other electronic format.

1 S.-E. Stiriba, H. Frey and R. Haag, *Angew. Chem., Int. Ed.*, 2002, **41**, 1329.
2 V. Chandrasekhar and S. Nagendran, *Chem. Soc. Rev.*, 2001, **30**, 193; V. Chandrasekhar and K. R. J. Thomas, *J. Appl. Organomet. Chem.*, 1993, **7**, 1; H. R. Allcock, J. L. Desorcie and G. H. Riding, *Polyhedron*, 1987, **6**, 119 and references therein.
3 M. Witt and H. W. Roesky, *Chem. Rev.*, 1994, **94**, 1163.
4 K. D. Gallicano, N. L. Paddock, S. J. Rettig and J. Trotter, *Inorg. Nucl. Chem. Lett.*, 1979, **15**, 417.
5 R. L. Davis and N. C. Baenziger, *Inorg. Nucl. Chem. Lett.*, 1977, **13**, 475; B. J. Brisdon, D. A. Edwards and J. W. White, *J. Organomet. Chem.*, 1978, **161**, 233.
6 D. P. Craig and K. A. R. Mitchell, *J. Chem. Soc.*, 1965, 4682.
7 D. A. Edwards and J. Marshalsea, *J. Organomet. Chem.*, 1977, **131**, 73.
8 A. Chandrasekaran, S. S. Krishnamurthy and M. Nethaji, *J. Chem. Soc., Dalton Trans.*, 1994, 63; A. Chandrasekaran, S. S. Krishnamurthy and M. Nethaji, *Inorg. Chem.*, 1993, **32**, 6102; K. D. Gallicano and N. L. Paddock, *Can. J. Chem.*, 1982, **60**, 521.
9 I. Dez and R. De Jaeger, *Phosphorus, Sulfur Silicon*, 1997, **130**, 1; T. Chivers and R. Hedgeland, *Can. J. Chem.*, 1972, **50**, 1017.
10 M. F. Farona and K. F. Kraus, *Inorg. Chem.*, 1970, **9**, 1700.