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Synthesis and structural studies of two pyridine-armed reinforced cyclen chelators and their transition metal complexes

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ABSTRACT

Two novel pyridine pendant-armed macrocycles structurally reinforced by an ethyl bridge, either between adjacent nitrogens (for side-bridged) or non-adjacent nitrogens (for cross-bridged), have been synthesized and complexed with a range of transition metal ions (Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}). X-ray crystal structures of selected cross-bridged complexes were obtained which showed the characteristic cis-V configuration with potential labile cis binding sites. The complexes have been characterized by their electronic spectra and magnetic moments, which show the expected high spin divalent metal complex in most cases. Exceptions are the nickel side-bridged complex, which shows a mixture of high-spin and low spin, and the cobalt cross-bridged complex which has oxidized to cobalt(III). Cyclic voltammetry in acetonitrile was carried out to assess the potential future use of these complexes in oxidation catalysis. Selected complexes offer significant catalytic potential enhanced by the addition of the pyridyl arm to a reinforced cyclen backbone.

1. Introduction

Tetraazamacrocycles form complexes of high thermodynamic and kinetic stability with transition metals [1]. Depending on the chelated metal, tetraazamacrocyclic complexes have found use in a range of applications, including medical imaging [2–5], protein binding agents [6,7], and as anti-malarial drugs [8,9]. Recently we have been interested in the use of this complex type as oxidation catalysts [10–12]. A recent papers by Que and co-workers, has shown that addition of a pyridyl pendant arm to a tetraazamacrocycle can result in new and improved oxidation catalysis [13]. The literature contains numerous other pyridyl pendant armed tetraazamacrocycles, indicating a general interest in the community and known synthetic techniques for adding pendant pyridyl donors [14–24].

Our specific exploration is aimed at forming catalysts which can perform under a range of aqueous conditions. Transition metal complexes of tetraazamacrocycles reinforced with additional ethylene bridges have produced oxidation catalysts with high kinetic stability under such harsh conditions [25–29]. Transition metal complexes of macrocycles of this type are known to be stable to a range of pH's and temperatures. A cross-bridged cyclen ligand with two pyridyl pendant arms (CB-Py_2Cyclen, Fig. 1) has been reported [30], but its hexadentate nature coordinatively saturates its complexed metal ions, while we wished to leave at least one coordination site available for interaction with oxidant and/or substrate. Our first communications regarding complexes incorporating a single pyridyl labile coordinating group have described reinforced cyclam derivatives with modified steric and electronic properties to cause improved properties as oxidation catalysts [10,12], see Fig. 1. Herein, we report the synthesis and characterization of analogous smaller cyclen derivatives as potential future oxidation catalysts. Comparisons between our cyclam and cyclen derivatives, as well as with other closely related cyclen-pyridyl ligands (Fig. 1) will be presented.

2. Results and discussion

2.1. Synthesis

We have recently demonstrated that alkylation of tetraazamacrocycle-glyoxal condensates using typical acetonitrile conditions described by Weisman et al. [32–34] and Handel and co-workers [35] are not ideal when using pyridyl derived alkyl halides and nonpolar chlorinated solvents are preferred [10,12].

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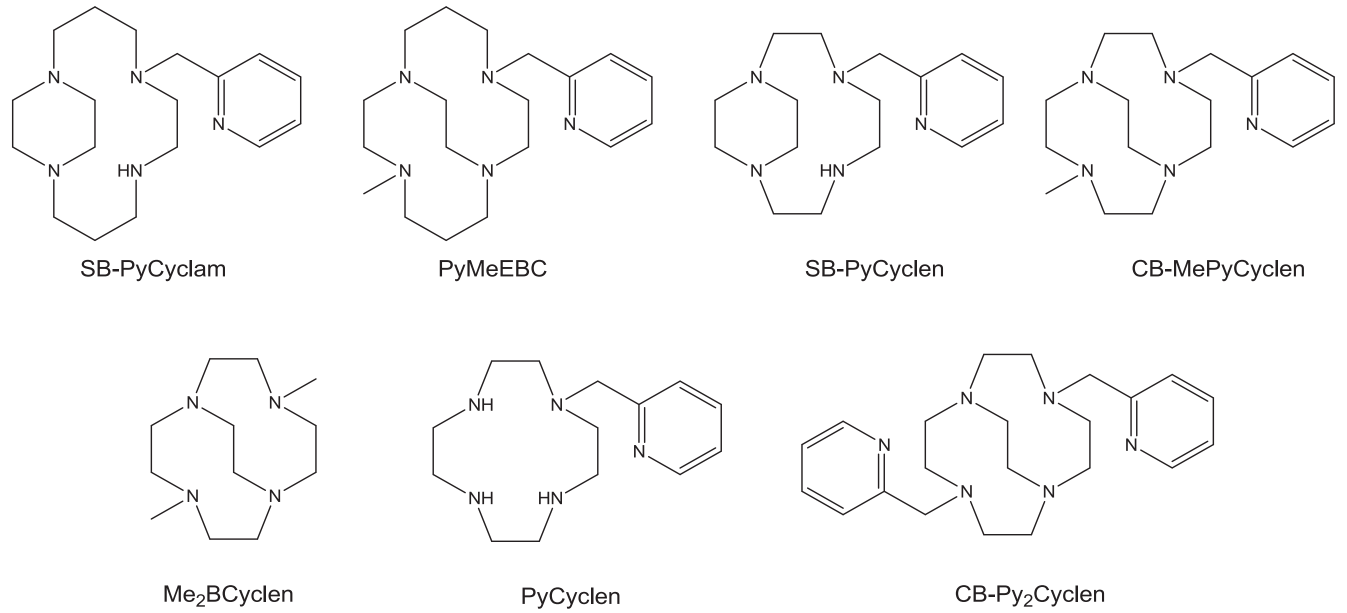
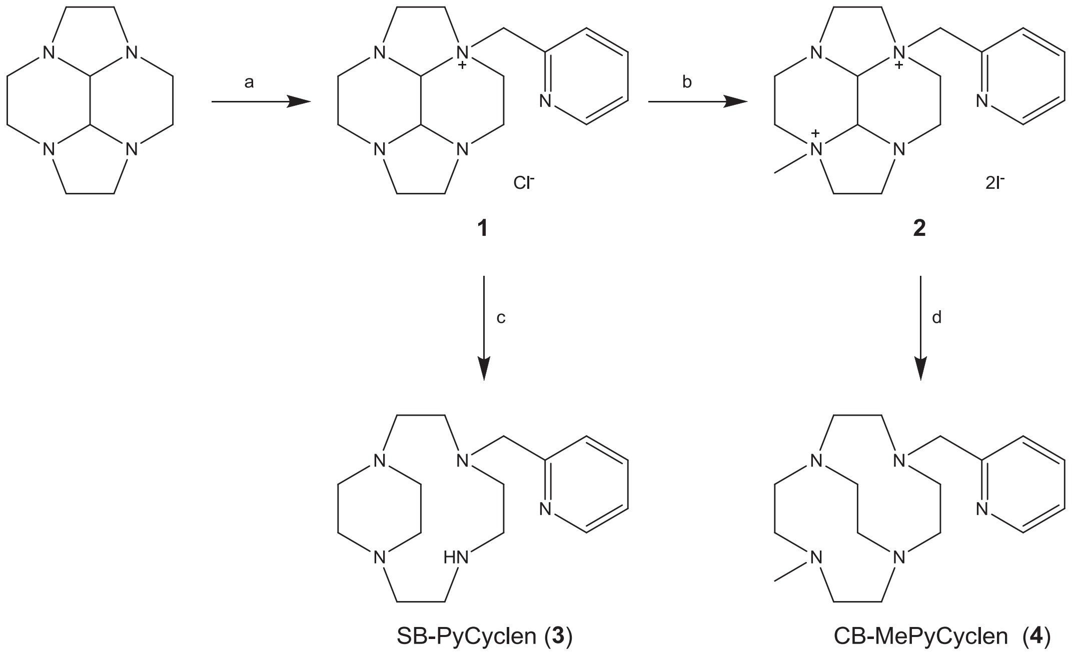


Fig. 1. Ligands discussed within this work; SB-PyCyclam [10] PyMeEBC [12] $Me_2BCyclen$ [31], PyCyclen [21,22] $CB-Py_2Cyclen$ [30]; alongside SB-PyCyclen and CB-MePyCyclen first described in this study.

Analogous conditions were used for the formation of 1. Using dichloromethane gave the desired product in relatively high yields (~80%), see Scheme 1. Methylation of the non-adjacent nitrogen atom with methyl iodide gives a bis-quaternary ammonium salt **2** by what are now routine methods for cyclam [12,36], although this is the first reported use of methylation to form unsymmetrical ethyl bridged cyclen derivatives. Reduction of mono (**1**) and bis (**2**) quaternary ammonium salts is carried out with sodium borohydride to form ethyl side-bridged (SB-PyCyclen) **3** and cross-bridged (CB-MePyCyclen) **4** derivatives respectively using well described analogous reactions [32–34].

Metal complexes have been formed with both SB **3** and CB **4** ligands with a range of divalent transition metals (Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}). Due to the proton sponge nature of cross-bridged tetraazamacrocyclic ligands, complexation reactions were carried out in an inert atmosphere glovebox using anhydrous metal salts in acetonitrile (with additional DMF for acetonitrile-insoluble $NiCl_2$). In a similar manner to our cyclam analogs [10,12], the reactions did not require heating and the complexes did not precipitate from the reaction solution. After drying the crude solutions the complexes were purified by changing the counter ion from chloride to hexafluorophosphate in methanol, with the conversion



Scheme 1. Ligand synthesis. (a) (i) CH_2Cl_2, 2-picolyl chloride hydrochloride, $NaHCO_3$ (ii) Decahydro-2a,4a,6a,8a-tetraazacyclopenta[fg]acenaphthylene, KI. (b) MeCN, CH_3I. (c) EtOH, $NaBH_4$. (d) EtOH, $NaBH_4$.