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Tetrahedron Letters 46 (2005) 2923–2926
Tetrahedron Letters

Pillared salicylaldehyde derivatives as building blocks for the design of cofacial salen-type ligands

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Received 9 February 2005; revised 15 February 2005; accepted 16 February 2005

Abstract—The syntheses of pillared salicylaldehyde derivatives on a naphthalene block are reported. These compounds can be considered as building blocks for the elaboration of cofacial salen-typed ligands. The X-ray structure of a dinuclear manganese(III) complex is described, supporting our strategy to build topologically controlled multinuclear metal complexes.

1. Introduction

Often nature makes use of di- or polynuclear metallic centres at their active sites for the proper functioning of enzymes. For instance, the active site of catalase,[1] enzyme responsible for the dismutation of H_2O_2, consists of two Mn ions held in close proximity by the polypeptide skeleton. In PSII, four Mn ions are present in the oxygen evolving complex (OEC).[2] The actual X-ray data for this enzyme indicates a cubane-type structure for these ions.[3] In the field of bioinorganic chemistry, chemists devote a particular effort in the preparation of simple low-molecular-weight models for the active di(poly)nuclear sites of enzymes. The transfer of the first coordination spheres, disposition and topologies of the metal centres within the active sites into synthetic low-molecular-weight models are the main parameters that the chemist must take into account in the design of the ligand. The aim is to reproduce as close as possible the 3D structure and the electronic behaviour of the active sites.[4]

At the forefront of this research, is the design of specific ligands that can hold metallic ions into a predefined disposition and in a given environment. The pioneering work of Collman group in the modelization of C*c*O is an excellent example.[5] Different families of ligand have also been elaborated in the aim to gain a synergistic effect between the two metal centres. He and Lippard[6] have designed biscompartmental ligands based on the 1,8-naphtyridine skeleton as bridging unit. These ligands have been used to devise Hemerytrin models[7] among others. The originality of these ligands is to maintain two metal centres in a given disposition without any common shared intraligand atom. Whereas ligands developed by Gavrilova and Bosnich[8] to study chemical cooperativity between two metal ions contain common coordinating atoms, oxygen atom of phenol group. In these systems, the coordinating environment of the two metal ions are not similar. One site is composed of a hexadentate coordinating environment and the other site is 4- or 5-coordinated. The unsaturation for the coordination sphere of the second metal centre is the privilege site for activation of small molecules such as dioxygen and the second metal centre acting as a redox relay.

These examples illustrate the fact that ligand design remain the tour de force in the modelization of dinuclear enzymatic sites.

2. Discussion

In our laboratory, polydentate ligands containing amine, pyridine and phenol groups have been extensively used in the study of redox active manganese[9] and iron[10] chemistry. In many cases, starting with a mononuclear compound, resulted in the formation of

Keywords: Suzuki coupling; Duff reaction; Cofacial salen-type ligand; Dinuclear manganese(III) complex.
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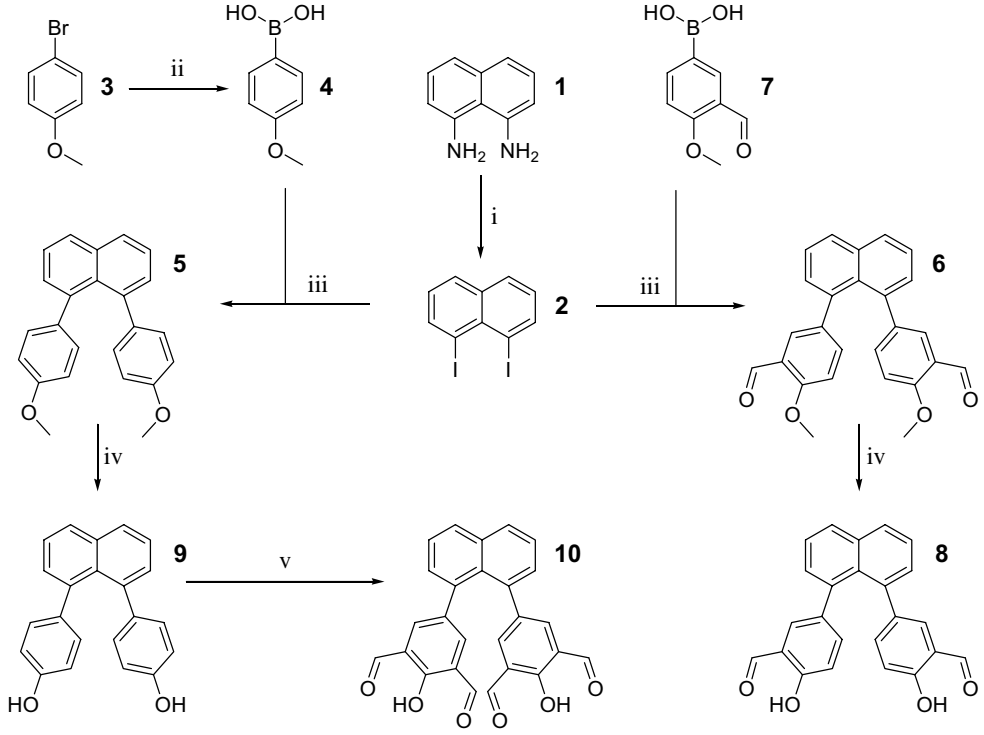
doi:10.1016/j.tetlet.2005.02.092

interdinuclear compounds, which can be considered as thermodynamic products. In the aim to prevent the uncontrolled formation of these stable dimers and to expect a cooperative effect between metal ions, we have launched a project for the synthesis of multidentate dinucleating ligands whereby after metallation, the metal centres will be settled in a face to face fashion separated by a well defined distance. As, already proposed in the literature, such synthetic approach requires the use of a rigid molecular brick to hold the coordinating cavities in a given topology.

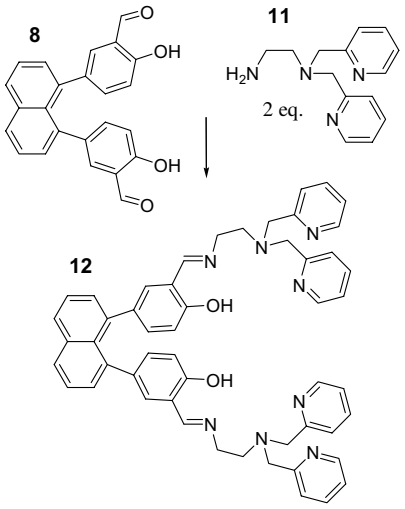
We report herein the synthesis and characterization of pillared salicylaldehyde derivatives, which can be considered as the building block in the elaboration of cofacial salen-type ligands. In this study, naphthalene was chosen as the rigid molecular basement to hold the salicylaldehyde motifs.

A similar synthetic strategy was developed precedently by McAuliffe and co-workers.[11] However, the poor yield reported has lead us to conceive different reaction pathways leading to the target compounds with more convenient yields. The synthetic route leading to the salicylaldehyde derivatives is shown in Scheme 1.[12] 1,8-Diiodonaphthalene **2** has been synthesized as described by House et al.[13] Although the starting diamino **1** compound was purified by distillation under reduced pressure, in our hands, the yield of this reaction has never exceeded 35–40% when the reaction was carried on a 50 g scale. Contrary to what has been previously described, where compound **2** was converted to the 1,8-naphthalene diboronic acid to undergo a Suzuki cross coupling reaction, we have preferred to realise the coupling reaction on **2** using a monoboronic derivative **4** and **7** leading to the formation of **5** and **6**, respectively. The 4-methoxyphenyl boronic acid **4** was synthesized starting from **3** following literature procedure,[14] while compound **7** is commercially available. Typical Suzuki cross coupling reaction was performed[15–17] with compounds **2** and **4** in a mixture of toluene/ethanol/water (2/2/1) using Na_2CO_3 as base and $Pd(PPh_3)_4$ (10 mol %) as catalyst. The reaction mixture was first degassed and put under an argon atmosphere before heating to reflux for 18 h. The bis(4-methoxyphenyl)-1,8-naphthalene **5** was obtained after purification by column chromatography (CH_2Cl_2/hexane 1/1, silica gel) in good yield (65%). While compound **6** was isolated after purification by column chromatography (CH_2Cl_2/MeOH 98/2, silica gel) in a 60% yield. Deprotection of the phenol groups upon treatment with BBr_3[18] gave compound **8** quantitatively. Hence, following this synthetic sequence, we have found that the crucial step, that is, Suzuki cross coupling reaction, works best.

Demethylation of compound **5** following the same procedure as above gave the bisphenol derivative **9**. This compound was then formylated at the *ortho* positions following a modified Duff reaction[19,20] to give the tetraformyl derivative **10**. To the best of our knowledge, this is the first time that such a face to face diformylated phenol compound is described. This compound thus opens the way to prepare biscompartmental ligands arranged in a cofacial manner. Indeed, tetranucleating ligands can be easily prepared by Schiff-base condensation reaction of **10** with primary amine derivatives.



Scheme 1. Reagents and conditions: (i) $NaNO_2$/KI at −20 °C in H_2SO_4; (ii) *n*-BuLi/$B(OMe)_3$ at −78 °C; (iii) $NaCO_3$, $Pd(PPh_3)_4$ (5 mol %) in toluene/EtOH/H_2O (2/2/1) reflux 24 h; (iv) BBr_3 in CH_2Cl_2 at −10 °C; (v) HMTA in TFA 5 days.



Scheme 2. Condensation of primary amine **11** in MeOH for 24 h.

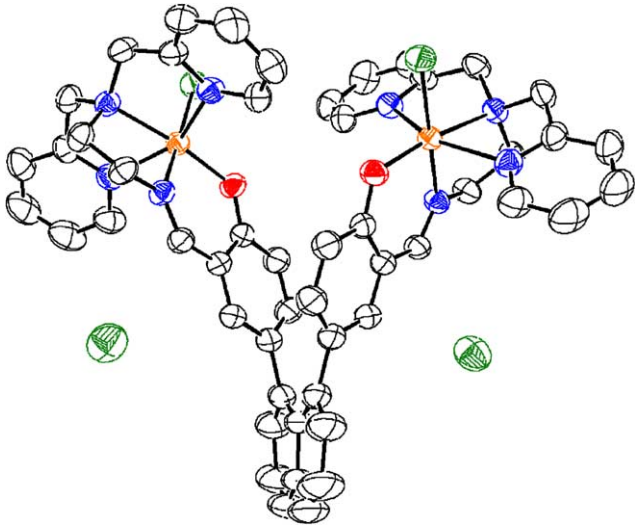


Figure 1. Ortep view of complex **13** (ellipsoid 50%).

Hereby, we report an example on the propensity to prepare dinucleating ligands from **8**. As shown in Scheme 2, treatment of **8** with 2 equiv of amine **11** gave **12**, which was isolated as a yellow solid. The dinuclear manganese(III) complexes has been prepared upon metallation of **12** with 2 equiv of $Mn^{II}(H_2O)_4Cl_2$ to give compound **13**. Oxidation of Mn(II) to Mn(III) occurs upon reaction in air. Slow evaporation of a methanolic solution gives suitable monocrystal for X-ray analysis. The X-ray structure of the dinuclear manganese(III) complex is represented in Figure 1. The hydrogen atoms have been omitted for clarity. Each pentadentate ligand (N_4O coordinating cavity) wraps a manganese ion and its coordination sphere is completed with a bound chloride ion. Two other chloride ions are outside the coordination spheres for electroneurality. The intrametallic distance between two manganese ions is 6.4 Å. It is worth noticing that there is no bridging atom between the two manganese ions.[21]

3. Summary and conclusions

As benchworks in our laboratory we are studying the spectroelectrochemical properties of the dinuclear manganese complex. Also, the tetraformyl derivative described hereby is now being used to prepare tetranucleating ligands.

Acknowledgements

This work was supported by the CNRS (Programme Energie, PRI4), the CEA for the LRC project (LRC-CEA no. 33V) and the European Commission (NEST STRP SOLAR-H contract 516510). The authors wish to thank Professor J.-J. Girerd for fruitful discussions.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.02.092.

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21. Crystal data of the compound **13**: chemical formula $C_{52}H_{46}Cl_4Mn_2N_8O_{14}$, $M = 1258.65$, monoclinic, $a = 29.29(1)$, $b = 13.68(1)$, $c = 17.83(1)$ Å, $\beta = 120.21(1)°$, $V = 6174(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.354$ g cm^{-3}, μ (MoKα) = 0.647 mm^{-1}, $F(000) = 2576$, $T = 293$ K, space group *C*2/*c*. See also supplementary material. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary number CCDC 261270. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].