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Manganese amido-imine bisphenol Hangman complexes

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ABSTRACT

A modular ligand macrocycle is composed from two phenolic groups linked to a cyclohexane bridge through an amide bond and an imine bond. The stability of the asymmetric linkers to metathesis permits a macrocyclic platform to be assembled from the condensation of two different phenolic groups in a single-step, high yield, reaction. The primary coordination sphere may be tuned with functional groups on one phenolic group. The other phenolic group may be modified with a scaffold possessing a proton transfer group. In this way, control over the secondary coordination sphere of the macrocycle is achieved. Manganese complexes of the amido-imine linked macrocycle catalytically epoxidizes 1,2-dihydronapthalene using sodium hypochlorite as the oxidant. The amido-imine macrocycles represent a new metal active site capable of supporting high oxidation states and attendant atom transfer chemistry while at the same time permitting control over the primary and secondary sphere of the metal center.

Manganese Schiff-base Hangman complexes shown in Chart 1[1–3] activate O–O bonds by mechanisms involving proton-coupled electron transfer (PCET).[4–8] The Hangman ligand architecture comprises a macrocyclic ligand platform appended to a scaffold possessing a proton transfer group, PTG (HSX in Chart 1). The PTG is poised over the macrocyclic ligand so the redox activation of substrate bound to the metal center can be mediated by proton transfer. The O–O bond heterolysis is promoted within the Hangman cleft by the same 'pull effect' that is common to oxidation conversions promoted at heme cofactors.[9] The original HSX design appended the PTG to the bridge of the salen platform. In this configuration, the redox potential is easily tuned by modifying the functionalities para to the phenolic oxygens.[1] However, this point of attachment obviates the incorporation of the chiral functionality that is a mainstay of reactivity for this ligand class.[10] Alternatively, the scaffold may be moved to the position para to the phenolic oxygens so that the chiral functionality, such as the cyclohexanediamine bridge of HSX*, may be retained at the salen platform.[2,3] However, owing to facile hydrolysis of the imine bond even under very mild conditions (vide infra),[11] an asymmetric Hangman platform with a single scaffold is difficult to prepare. Hence, only the double bridge Hangman complex shown in Chart 1 is available. This double-scaffold design has two drawbacks with regard to elaborating PCET activation chemistry. (1) The easiest position (para position to the phenolic oxygen) at which to tune the redox properties of the macrocyclic platform is unavailable because it is occupied by the scaffold and (2) protons from the convergent interfaces may interact; in the case of PTG = benzoic acid, a dicarboxylic acid dimer is obtained.[2] Hence the proton needed for PCET reactivity is engaged in the dimer and unavailable for interaction with bound substrate.

We attempted to synthesize ligand A, shown in Chart 1, where one of the xanthenes is removed to open a site where electron-donating and withdrawing functionalities, –X, can be installed to tune the redox properties. However, isolated salen ligands that are asymmetric across their diamine bridge are rare (i.e., composed of two unique salicylaldehydes),[12–15] and when prepared are often contaminated by the symmetric impurity owing to the facility at which imine hydrolysis occurs.[12,13] This hydrolysis problem has been overcome by the incorporation of an ethylene diether backbone to bridge the functionalized phenolic arms of the ligand. The equilibrium constant for the formation of the oxime is larger than that of the imine by several orders of magnitude.[11] Thus, the oxime-type ligand is able to resist metathesis of the C=N bonds. In this Letter, we propose an alternative modification of the basic salen framework in which one of the imine bonds is replaced by an amido bond (B in Chart 1), which is less prone to hydrolysis. The synthesis of macrocyclic 'half-units' are targeted where a cyclohexanediamine is singly condensed to form an amido bond, leaving the other amine available to form an imine bond. In stabilizing the macrocycle in this way, Hangman salen-based platforms may be derivatized by a single Hangman platform so that the electronic properties of the salen platform may be tuned and the stereogenic centers of the salen scaffold may be unperturbed.

The step-wise synthesis of scaffold **B** is outlined in Scheme 1 for a 3-*tert*-butyl salicylaldehyde functionalized with *tert*-butyl (**5**), methoxy (**8**), bromo (**9**), and nitro (**10**) in the 5 position. 3,5-di-*tert*-butyl salicylaldehyde and 3-*tert*-butyl salicylaldehyde were obtained commercially. The methoxy,[16] bromo,[17] and nitro[18] analogues can all be prepared in one step.

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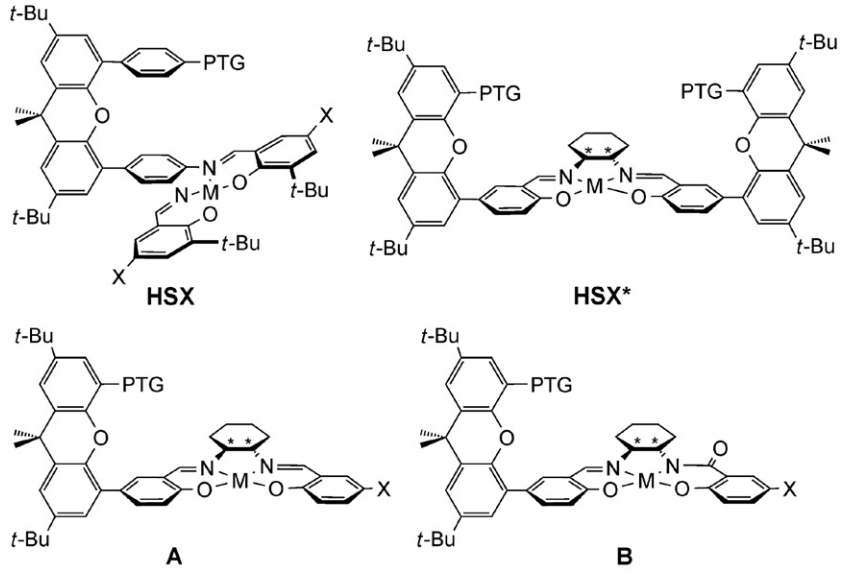
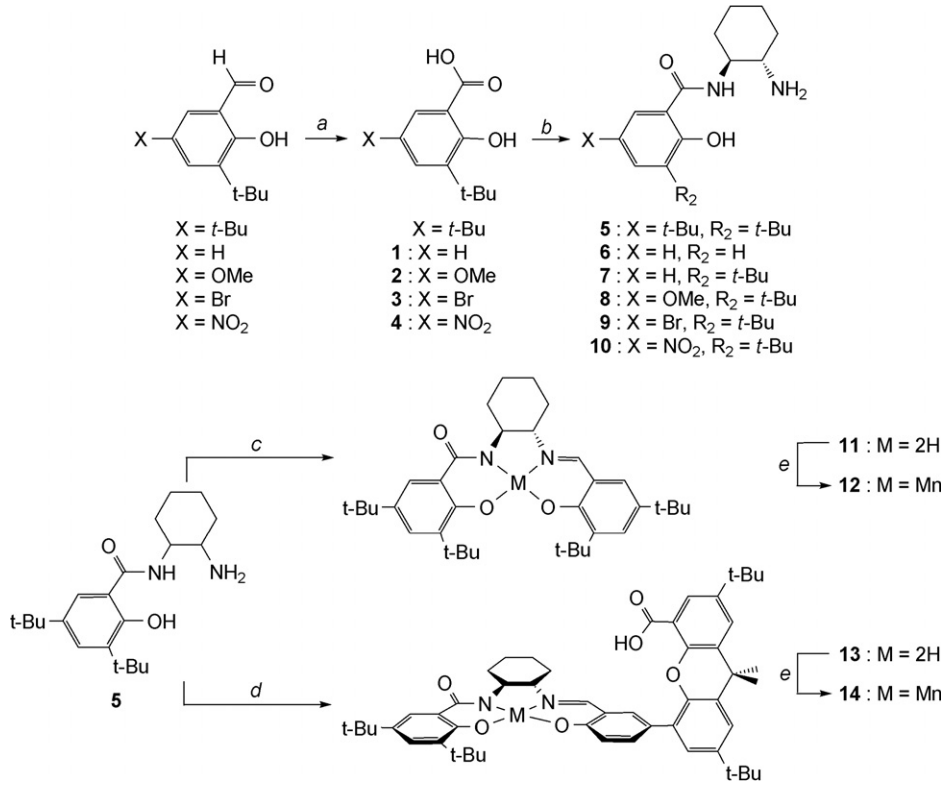


Chart 1.



Scheme 1. Reagents: (a) Ag_2O, 3 M $NaOH_{aq}$; (b) (1*R*,2*R*)-(−)-1,2-diaminocyclohexane, *N*-methylmorpholine, 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimine·HCl, CH_2Cl_2; or (i) $SOCl_2$, (ii) (1*R*,2*R*)-(−)-1,2-diaminocyclohexane, Et_3N, CH_2Cl_2; (c) 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde, EtOH; (d) 2,7-di-*tert*-butyl-5-(3-formyl-4-hydroxy-phenyl)-9,9-dimethyl-9*H*-xanthene-4-carboxylic acid, EtOH; (e) $Mn(OAc)_2(H_2O)_4$, EtOH.

The aldehydes are oxidized to the corresponding carboxylic acid to give the salicylic acid derivatives by heating with silver(I) oxide in basic solution. Coupling proceeds with one equivalent of (1*R*,2*R*)-(−)-1,2-diaminocyclohexane by either of two methods to form the amide bond: **5** and **6** were synthesized in good yields by allowing the acid and diamine to react with 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimine·HCl and *N*-methylmorpholine; **7**–**10** were synthesized by allowing the acid to react with thionyl chloride to form the acetyl chloride in situ, followed by addition of the diamine. Both methods give small amounts of the symmetric diamide ligand impurity despite dilute reaction conditions. The symmetric diamido bisphenolate ligand can be separated from products **5**–**10** by column chromatography. Macrocycle formation is completed by condensation in refluxing ethanol of the free amine with the appropriately functionalized salicylaldehyde to form the imine bond, thus furnishing the amido-imine macro-

cycles. NMR spectra of **11** and **13** show no evidence for functional group redistribution. The NMR peaks of the phenolic groups of the singly functionalized platform are maintained in the NMR spectrum (see Figs. S1 and S2). Manganese(III) ion insertion into **11** and **13** to give **12** and **14**, respectively, proceeds smoothly upon refluxing manganese(II) acetate tetrahydrate in ethanol in air. The amido nitrogen is deprotonated during metalation to afford the neutral complex.[19] The molecular weights of the ions (sodium adduct) obtained by high resolution mass spectrometry are consistent with this formulation for the complex. Unique amide (C=O) and imine (C=N) stretches are present in the infrared spectra. The C=O stretch is observed at 1628 cm^{-1} in **11** and 1638 cm^{-1} in **13**. In the manganese complexes, the stretching frequency shifts to 1624 cm^{-1} in **12** and 1626 cm^{-1} in **14**. The shift upon metalation is more dramatic for the imine bond; the stretching frequency at 1587 cm^{-1} in **11** and 1588 cm^{-1} in **13** shifts to 1535 cm^{-1} and 1531 cm^{-1} in their respective manganese complexes.

We were interested in ascertaining how our substitution of an amido group for an imine in Hangman platform would affect the PCET reactivity. Accordingly, the epoxidation activity of **12** and **14** was examined using 1,2-dihydronapthalene as the substrate. Sodium hypochlorite was used as the external oxidant, under the same conditions previously used to study the double-scaffold Hangman salen complexes.[2,3] **12** and **14** support the catalytic oxidation of 1,2-dihydronapthalene to the corresponding epoxide with 32% and 28% yield, respectively. We note however, despite the presence of the (1*R*,2*R*)-(−)-1,2-diaminocyclohexane backbone, the epoxide product isolated is a racemic mixture. The lack of asymmetric induction by these ligands may be due to the greater flexibility afforded by an amido linker. In salens, the geometry of the macrocycle in the Mn(V) oxo species is proposed to be roughly planar.[20] However, the analogous diamido macrocycles are known to be more structurally flexible and they can deviate from a non-planar coordination.[21] If such conformational changes perturb substrate approaches toward the oxidizing intermediate, then communication with the chiral cyclohexane bridge may be prevented.

In summary, the trianionic amido-amine ligands permit a salen-like ligand to be modified with a single Hangman scaffold. The oxygen atom transfer chemistry performed by the manganese complexes suggest they are capable of supporting a high-valent metal oxo intermediate, consistent with the ability of diamido diphenolic ligands ability to stabilize metals in high oxidation states.[22,23] The synthetic method to construct these ligands is modular, thus allowing the electronic and redox properties of the scaffold to be tuned with facility.

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Supplementary data

Full experimental details and characterization data for all new compounds, including copies of ^{1}H NMR spectra for **11** and **12**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.05.111.

References and notes

1. Liu, S.-Y.; Nocera, D. G. *J. Am. Chem. Soc.* **2005**, *127*, 5278–5279.
2. Yang, J. Y.; Bachmann, J.; Nocera, D. G. *J. Org. Chem.* **2006**, *71*, 8706–8714.
3. Yang, J. Y.; Nocera, D. G. *J. Am. Chem. Soc.* **2007**, *129*, 8192–8198.
4. Chang, C. J.; Chang, M. C. Y.; Damrauer, N. H.; Nocera, D. G. *Biophys. Biochim. Acta* **2004**, *1655*, 13–28.
5. Stubbe, J.; Nocera, D. G.; Ye, C. S.; Chang, M. C. Y. *Chem. Rev.* **2003**, *103*, 2167–2202.
6. Cukier, R. I.; Nocera, D. G. *Annu. Rev. Phys. Chem.* **1998**, *49*, 337–369.
7. Dempsey, J. L.; Esswein, A. J.; Manke, D. R.; Rosenthal, J.; Soper, J. D.; Nocera, D. G. *Inorg. Chem.* **2005**, *44*, 6879–6892.
8. Rosenthal, J.; Hodgkiss, J. M.; Young, E. R.; Nocera, D. G. *J. Am. Chem. Soc.* **2006**, *128*, 10474.
9. Soper, J. D.; Kryatov, S. V.; Rybak-Akimova, E. V.; Nocera, D. G. *J. Am. Chem. Soc.* **2007**, *129*, 5069–5075.
10. Jacobsen, E. N. *Adv. Synth. Catal.* **2004**, *346*, 109.
11. Akine, S.; Taniguchi, T.; Dong, W.; Masubuchi, S.; Nabeshima, T. *J. Org. Chem.* **2005**, *70*, 1704–1711.
12. Sasaki, I.; Pujol, D.; Gaudemer, A. *Inorg. Chim. Acta* **1987**, *134*, 53–57.
13. Daly, A. M.; Dalton, C. T.; Renehan, M. F.; Gilheany, D. G. *Tetrahedron Lett.* **1999**, *40*, 3617–3620.
14. Lopez, J.; Liang, S.; Bu, X. R. *Tetrahedron Lett.* **1998**, *39*, 4199–4202.
15. Campbell, E. J.; Nguyen, S.-B. T. *Tetrahedron Lett.* **2001**, *42*, 1221–1225.
16. Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.* **1994**, *59*, 1939–1942.
17. Cavazzini, M.; Manfredi, A.; Montanari, F.; Quici, S.; Pozzi, G. *Eur. J. Org. Chem.* **2001**, 4639–4649.
18. Braud, M.; Fleischer, R.; Mai, B.; Schneider, M.-A.; Lachenicht, S. *Adv. Synth. Catal.* **2004**, *346*, 474–482.
19. Costes, J.-P.; Daha, F.; Donnadieu, B.; Douton, M.-J. R.; Garcia, M.-I. F.; Bousseksou, A.; Tuchagues, J.-P. *Inorg. Chem.* **2004**, *43*, 2736–2744.
20. Jacobsen, E. N.; Wu, M. H. Epoxidation of Alkenes other than Allylic Alcohols. In *Comprehensive Asymmetric Catalysis*; Pfaltz, A., Jacobsen, E. N., Yamamoto, H., Eds.; Springer: Berlin, Heidelberg, New York, 1999; Vol. 2,. Chapter 18.2 and references cited therein.
21. Collins, T. J.; Keech, J. T. *J. Am. Chem. Soc.* **1988**, *110*, 1162–1167.
22. Anson, F. C.; Collins, T. J.; Richmond, T. G.; Santarsiero, B. D.; Toth, J. E.; Treco, B. G. R. T. *J. Am. Chem. Soc.* **1987**, *109*, 2974–2979.
23. Koola, J. D.; Kochi, J. K. *J. Org. Chem.* **1987**, *52*, 4545–4553.