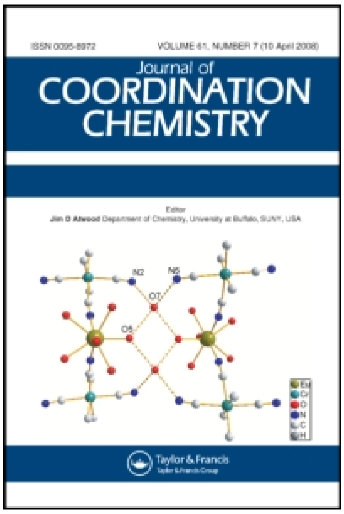
This article was downloaded by:
On: *23 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Coordination Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

From Ring Structures to Helices

J. Libman[a]; Y. Tor[a]; A. Shanzer[a]
[a] Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

To cite this Article Libman, J. , Tor, Y. and Shanzer, A.(1988) 'From Ring Structures to Helices', Journal of Coordination Chemistry, 18: 1, 241 — 244
To link to this Article: DOI: 10.1080/00958978808080720
URL: http://dx.doi.org/10.1080/00958978808080720

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

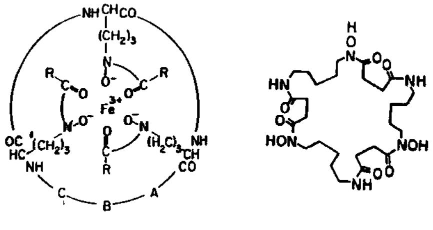
J. Coord. Chem. 1988, Vol. 18, pp. 241–244
Reprints available directly from the publisher
Photocopying permitted by license only

FROM RING STRUCTURES TO HELICES

J. Libman, Y. Tor, and **A. Shanzer**, Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel.

(Received April 18, 1988)

Siderophores[1] are natural Fe^{3+} carriers of microbial origin that are responsible for Fe^{3+} uptake from the medium through the membrane into the cells interior. Although all these molecules bind Fe^{3+} by embedding it in an octahedral ion binding cavity, they do so by making use of different structural solutions such as macrocyclic, tripodal and linear ones.



Ferrichrome

Nocardamine

FIGURE 1

Nocardamine[2] (see Figure 1) is an example for a macrocyclic binder, which forms an octahedral ion binding cavity by folding of its ring skeleton to a C_3-symmetric structure in such a way, that the three hydroxamate binding groups become equally distributed along the tilted segments of the loops. The ferrichromes[3] are examples for tripode-like binders, where the ring merely serves as common platform to direct and tilt the three ligating side arms (possessing each a bidentate hydroxamate group), towards the same type of ion binding arrangement.

We recently synthesized artificial tripode-like ion carriers that simulate the structures, ion-binding configurations and biological activity of some of the natural siderophores.[4,5] Elongation of such binders by a second ion binding cavity was anticipated to provide structures that host a second metal ion in a cooperative manner, provided, the ion binding cavity would be properly spaced. In this article we wish to describe a double ion binder which has been designed according to a topological "Gedanken-Experiment"[6] that makes use of the similarities between the macrocyclic and tripodal natural siderophores. According to this "Gedanken-Experiment" macrocyclic Fe^{3+}-nocardamin complexes are aligned one on the top of the other in such a way that their ion binding backbones collapse to the chains of a tripodal structure (see Figure 2). Part of the methylene bridges of genuine nocardamine become thereby obsolete and are therefore deleted, as schematically represented below.

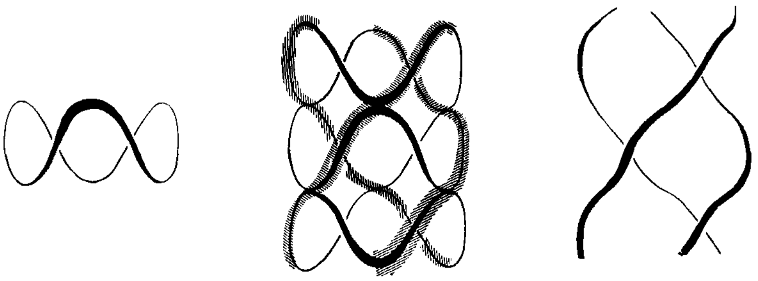
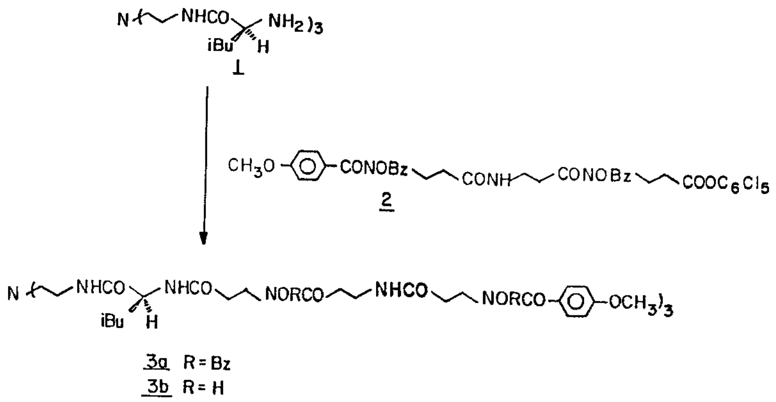


FIGURE 2

The emerging structure is a triple stranded helix, where the sequence of its chains can be read off directly as consisting of alternating hydroxamate and amide groups bridged by $-(CH_2-)_2-$ moieties. This "Gedanken-Experiment" can not however help in selecting an anchor or in predicting the preferred handedness of the helix formed. On the basis of our earlier studies[7] we selected C_3-symmetric molecules that are flanked by chiral amino acids as anchors for the synthesis of these binders. Such tripode-like molecules have been found to adopt propeller-type arrangements of defined handednes by virtue of their chiral centers and inter-strand H-bonds[7], and were therefore anticipated to cause the extended molecules to adopt preferentially either a right or left handed helical structure. In the following, the synthesis of a double ion binder will be described and its helical structure demonstrated by showing that the metals adopt a sequential arrangement, and that the absolute configuration around each metal ion is identical.

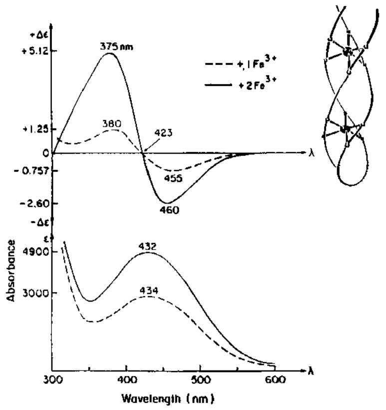
The chiral double ion binder 3 was prepared by condensation of the protected dihydroxamate chain 2 with the chiral anchor 1 and subsequent hydrogenolytic removal of the protecting groups.



SCHEME

Compound 3 was found to bind two Fe^{3+} ions according to titration experiments monitored by the absorption of the Fe^{3+}-hydroxamate chromophore around 430nm. The iron uptake proved to proceed in a stepwise fashion: the double-Fe^{3+}-complex was only obtained after addition of two equivalents of metal ions, while the single Fe^{3+}-complex was the only product observed after addition of one equivalent (established by TLC). In line with this observation, release of Fe^{3+} from the double Fe^{3+} complex occured also stepwise: addition of EDTA to the double-Fe^{3+}-hydroxamate complex caused a decrease of the Fe^{3+}-hydroxamate absorption indicating removal of Fe^{3+} by EDTA. This process followed second order kinetics and showed two distinct rate constants for the removal of each ion with a delay between the release of the first ($k_1 = 6.9\ M^{-1}.sec^{-1}$) and the second one ($k_2 = 2.0\ M^{-1}.sec^{-1}$).

These observations demonstrate that this binder posseses two non-identical ion binding cavities that are loaded and unloaded sequentially. In order to examine if the sequentially aligned metal ions create a helical arrangement, the absolute configuration around each metal ion was determined by CD measurements. The absolute signs of the Cotton effects for the Fe^{3+}-hydroxamate chromophores were found to be identical for the single and double Fe^{3+}-complex (Figure 3). This demonstrates identical configuration, namely delta-cis, around each metal ion and thereby a helical



CD and UV Spectra (0.16 mM, $CDCl_3$)

FIGURE 3

arrangement.[1]

The formation of helical complexes from 3 is not limited to Fe^{3+}. Other metal ions such as Al^{3+}, Ga^{3+} and In^{3+} also formed helical arrangements. The use of such binders to study both, homonuclear and heteronuclear metal-metal interactions, is in progress as is the possibility to tune metal-metal distances by subtle chemical modifications.

REFERENCES

1. Neilands, J.B. Structure and Bonding **1984**, 58, 1-24 Raymond, K.N.; Mueller, G.; Matzanke, B.F. Top. Current Chem. **1984**, 123, 49-102, and references therein. Hider, R.C. Structure and Bonding **1984**, 58, 25-87.
2. Keller-Schierlein, W.; and Prelog, V.; Helv. Chim. Acta. **1961**, 44, 1981-1985.
3. Emery, T., Advan. Enzymol. Relat. Areas Mol. Biol. **1971**, 35, 135-185.
4. Tor, Y.; Libman, J.; Shanzer, A.; Lifson, S.; J. Amer. Chem. Soc. **1987**, 109, in press.
5. Tor, Y.; Libman, J.; Shanzer, A.; J. Amer. Chem. Soc. **1987**, 109, in press
6. 'Gedanken-Experiment', german, 'thinking-experiment'
7. Tor, Y.; Libman, J.; Shanzer, A.; Felder, C.E.; Lifson, S. J. Chem. Soc., Chem. Commun. **1987**, 749.