



*A Reliable and Innovative Partner
to Speed up Your Success*

Expertise

Super-Chelating Agents

Table of Contents

About Granlen	2
Lariat and Butterfly-Shaped Macrocyclic Polyethers	3
Cryptands Macrobicyclic Polyethers	3
N-Containing Polyazacyclophanes	4
Intercalator-Conjugated Polyazacyclophanes	5
Suitcase-Shaped and Bridged Macrocyclic Polyethers	5
Super-chelating agent-metal complexes	6
Summary	6

For quotes or additional information contact Dr. Haoyun (Harry) An: han@granlen.com or Dr. William Stevens: wstevens@granlen.com or info@granlen.com



About Granlen

Granlen is a preclinical contract research organization that specializes in the “*more difficult*” chemistries of nucleosides, peptides, and phosphorous chemistry. Our research facility is located in Zhengzhou, China and we offer project management and business development support from San Diego. We can offer made-to-order compound libraries, hit-to-lead optimization, medicinal chemistry, and a wide range of chemistry services including custom synthesis, intermediates, references compounds, metabolites and impurities, route scouting, process development, and scale-up. We can provide super-chelating agents, nucleosides, peptide conjugates, disaccharides, haptens, antigens, and bioreagents. Heterocyclic chemistry is easy and always a welcome change. Teams at Granlen are also specialized in macrocyclic compounds used as super-chelating and MRI contrast agents.

Apart from our expertise in chemistry, as a preclinical CRO we offer an integrated development platform in order to speed projects toward clinical trials. We have developed relationships with some specialized facilities that may be able to assist with your preclinical and clinical development.



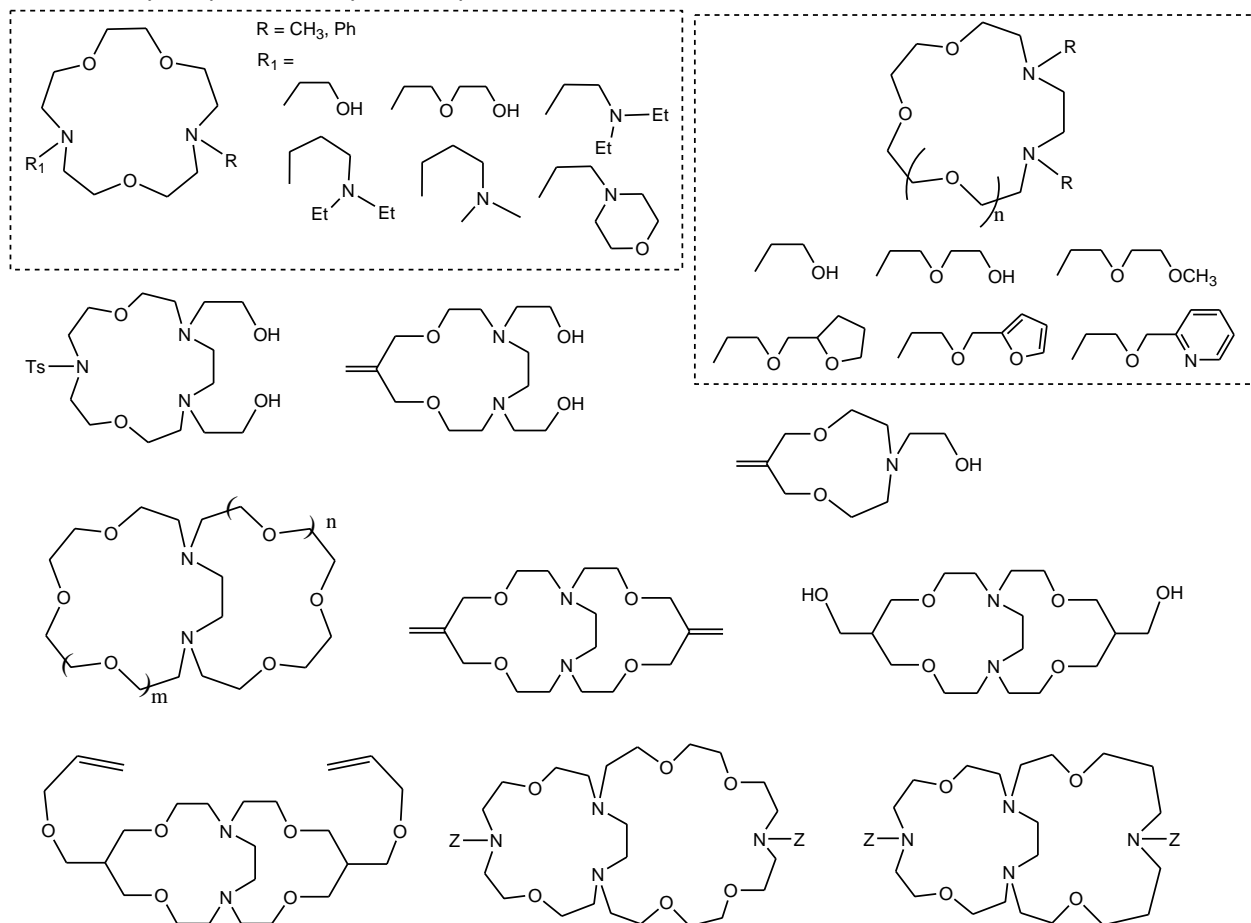
Our management team has led several compounds into clinical trials and we have expertise in every step toward Phase I. In conjunction with our drug discovery services we provide expertise in:

- Super-chelating agents and MRI contrast agents – macrocyclic polyethers
- Nucleosides, nucleotides, nucleic acids, and libraries
- Di-nucleotides, aminoacylated dinucleotides, triphosphates, methylene-phosphonates, and other organophosphorus derivatives
- Novel amino acids, dipeptides, and glycopeptides
- Bio-reagents, bio-materials, immunogens



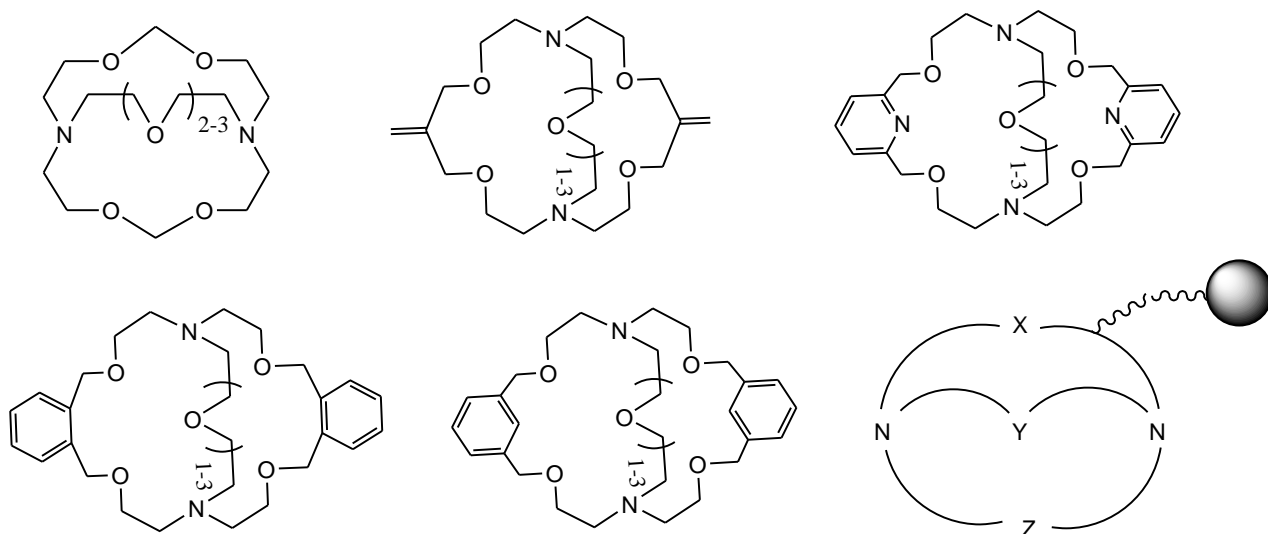
Lariat and Butterfly-Shaped Macrocyclic Polyethers

In addition to heterocyclic and small molecule drug discovery Granlen has a long history of accomplishment in the areas of super-chelating agents, macrocyclic chemistry, and coordination chemistry. Our team has extensive experience in the synthesis of various classes of super-chelating agents for coordinating, concentrating, and/or extracting specific metal cations, as well as for biological applications. As a recognized global expert, our president published *Chem. Rev.* 94, 939–991 (1994) and *Chem. Rev.* 92, 543–572 (1992) as the featured articles in this field. Below are some representative lariat and butterfly-shaped macrocyclic compounds.



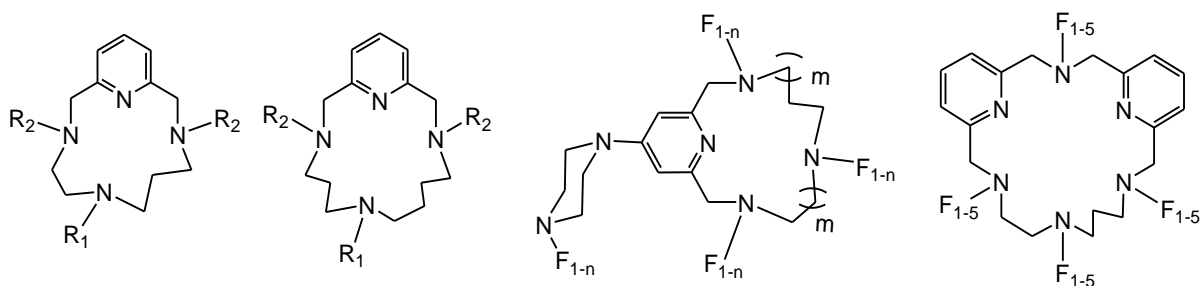
Cryptands and Macrobicyclic Polyethers

Cryptands represent a class of bicyclic polyethers having better chelating properties when compared to monocyclic polyether compounds. The figure below details a series of cryptands that were designed and synthesized for coordination property investigations. Some of these cryptand derivatives were attached onto supporting materials for the concentration of metal cations and removing radioactive metals from nuclear waste.

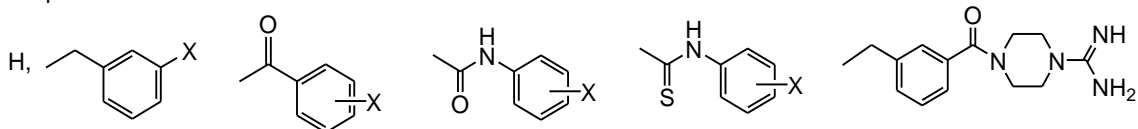


N-Containing Polyazacyclophanes

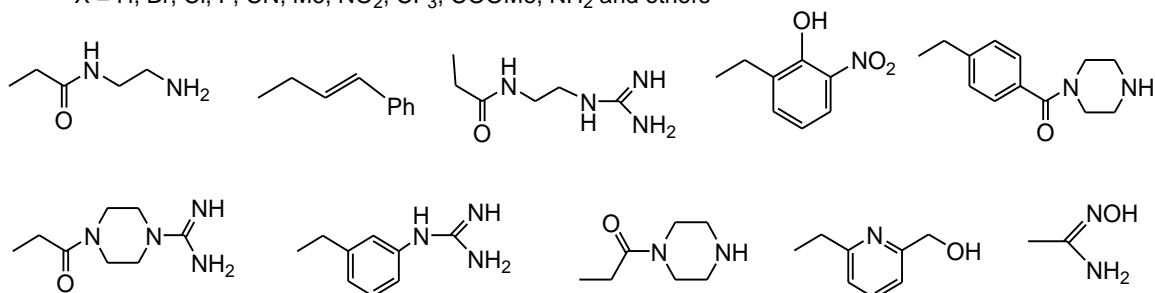
Several thousands of N-containing macrocyclic compounds have been synthesized for drug discovery, RNA interaction, and other application studies.



Groups:



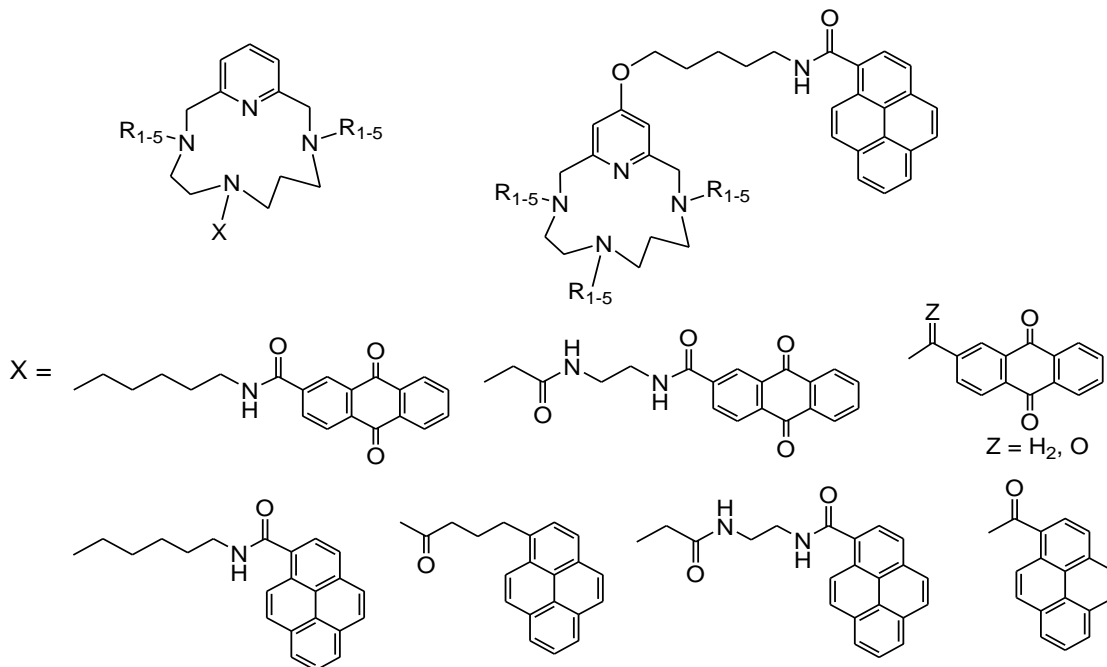
X = H, Br, Cl, F, CN, Me, NO₂, CF₃, COOMe, NH₂ and others





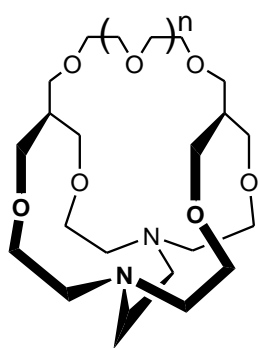
Intercalator-Conjugated Polyazacyclophanes

These macrocyclic compounds, conjugated with various intercalators, were designed and synthesized for RNA interaction and coordination studies (R_{1-5} are various functional groups).

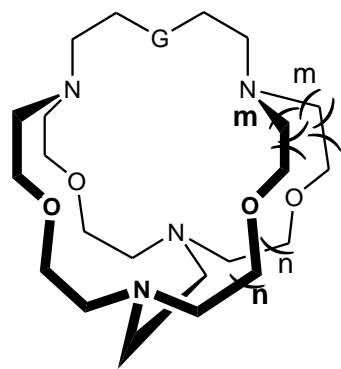


Suitcase-Shaped and Bridged Macrocyclic Polyethers

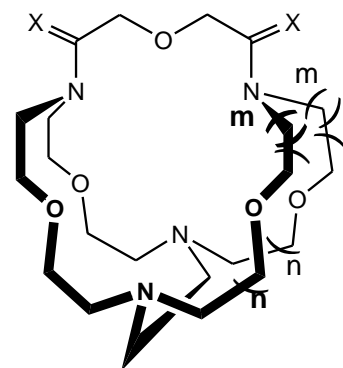
Several series of suitcase-shaped polycyclic macrocyclic polyethers were designed and synthesized to maximize their chelating properties. The bis-phenyl bridged polycyclic compounds were constructed with special synthetic skills.



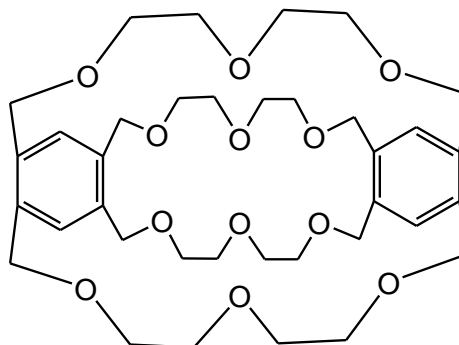
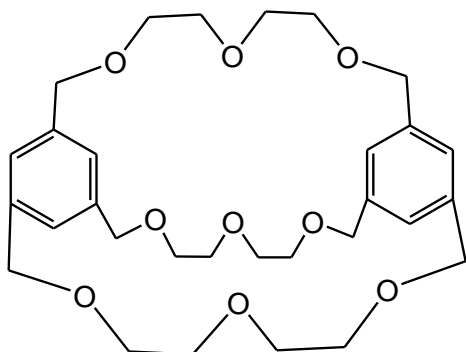
1, $n = 1$
2, $n = 2$



3, $G = \text{OC}(=\text{CH}_2)\text{CH}_2\text{O}$, $n = 2, m = 1$
4, $G = \text{OCH}_2\text{CH}_2\text{O}$, $n = 2, m = 1$
5, $G = \text{OCH}_2(=\text{CH}_2)\text{CH}_2\text{O}$, $n = 1, m = 2$
6, $G = \text{OCH}_2\text{CH}_2\text{O}$, $n = 1, m = 2$

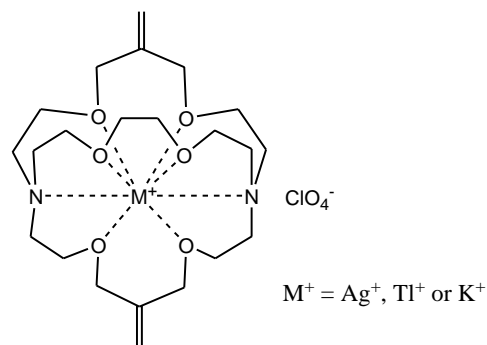
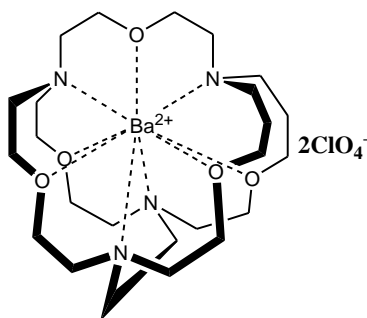
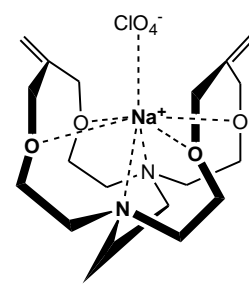
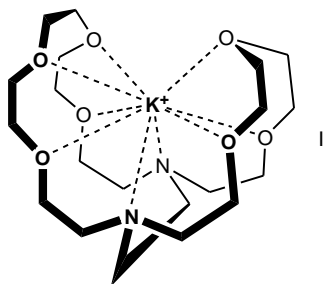
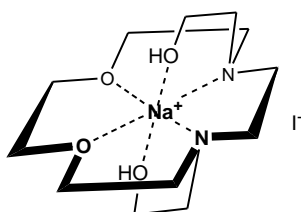


7, $X = \text{O}$, $n = 2, m = 1$
8, $X = \text{H}_2$, $n = 2, m = 1$
9, $X = \text{O}$, $n = 1, m = 2$
10, $X = \text{H}_2$, $n = 1, m = 2$



Super-Chelating Agent-Metal Complexes

The super-chelating property of some compounds toward metal cations was verified by X-ray crystallographic studies. Below are some of the examples that our team obtained.



Summary

The management and employees of Granlen have significant expertise in the areas of super-chelating agents, ribofuranoses, modified nucleosides, nucleotides, and related phosphorus compounds. In a bulleted fashion, the team at Granlen can assist with:

- Super-chelating agents – macrocyclic polyethers and coordination chemistry
- Modified ribofuranoses, Nucleosides, nucleotides, nucleic acids, Novel nucleoside libraries
- H-Phosphonates, C-phosphonates, C-phosphoramidites, phosphoramidites
- Triphosphates, C-triphosphonates, Dinucleotides, and other organophosphorus derivatives