MANAGING TIGHT-BINDING RECEPTORS FOR NEW SEPARATION

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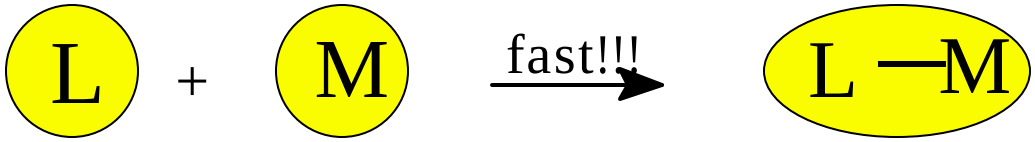
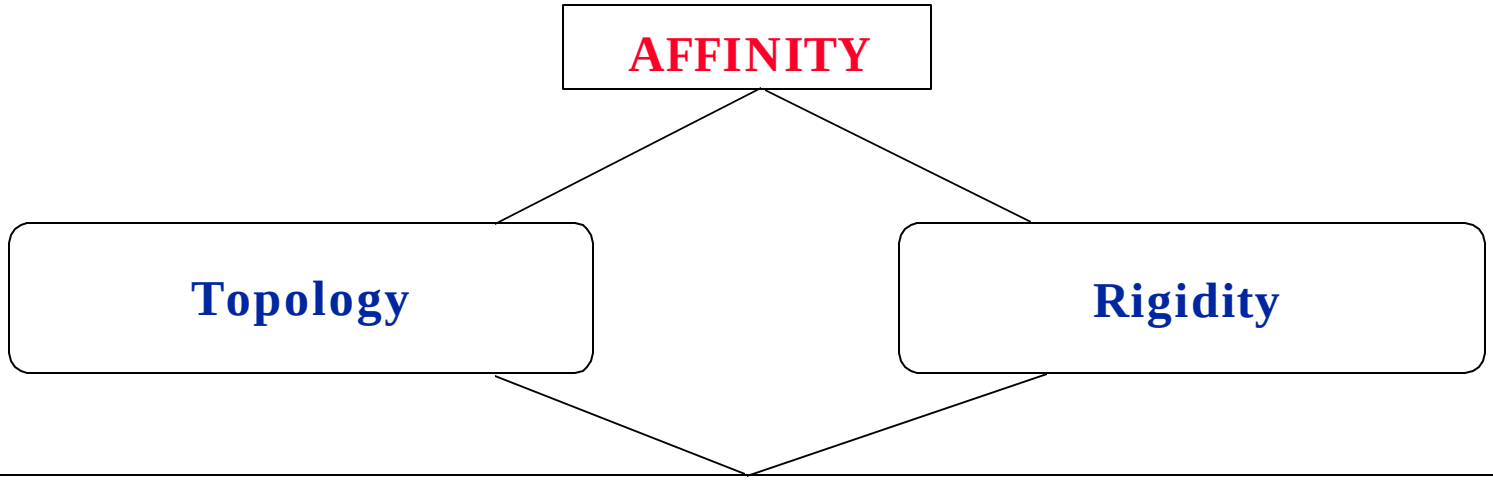
Traditional separation methods like ion exchange and solvent extraction require *rapid* interaction between ligands and metal ions:



However, the most tight-binding receptors invariably bind *slowly* due to their affinity for appropriate metal ions:



Slow Kinetic Processes Result:

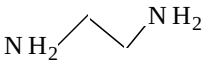
- **Constraints imposed by topology and rigidity restrict motion during binding**
- **Rigidity and topology even more drastically inhibit dissociation**

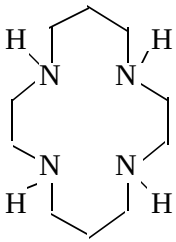
THE INFLUENCE OF VARIABLE TOPOLOGY IN THE FORMATION OF COMPLEXES

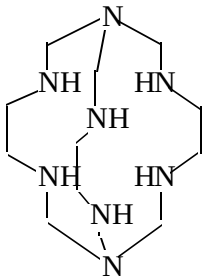
Stability of Complexes

	monodentate	<	chelate	<	macrocycle	<	cryptate
Relative Thermodynamic Stabilities:	1		10^3 -10^4		10^6 -10^8		10^{10} -10^{13}

NH_3







Complexation Kinetics

	monodentate	≥	chelate	>>	macrocycle	>>	cryptate
Relative Rates of Complexation (k_f, M^{-1} s^{-1})	1		1		10^{-1} -10^{-2}		10^{-2} -10^{-5}
Relative Rates of Dissociation(k_d, M^{-1} s^{-1})	1		10^{-3}		10^{-7} -10^{-10}		10^{-12}-10^{-18}

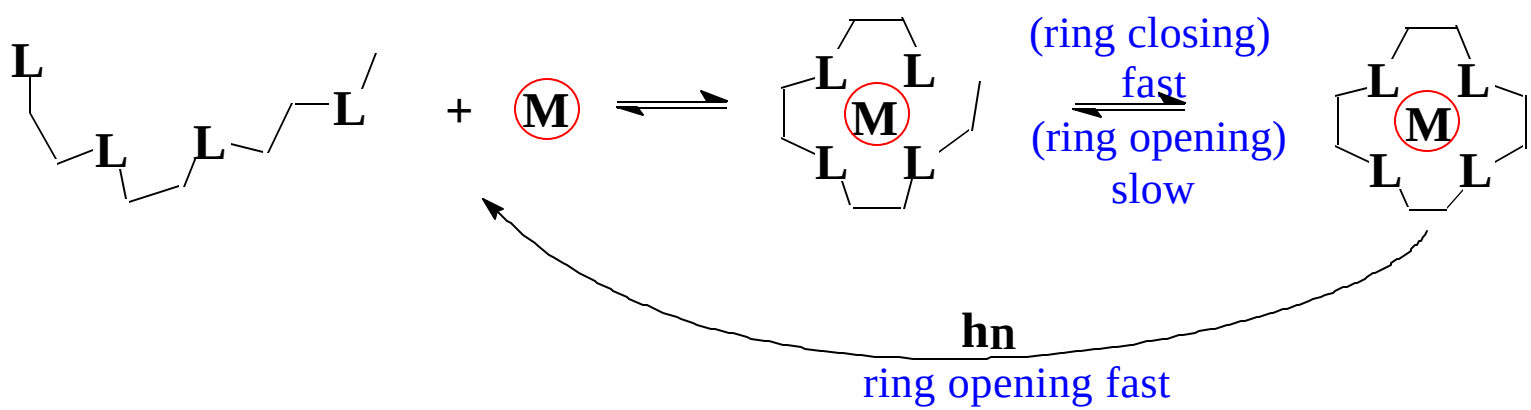
NEEDED: Rate processes with the velocity of simple chelation giving a product with the stability of a macrocycle

PROPOSED: For Formation

Design linear molecules capable of undergoing *template macrocyclization* in the process of complex formation

For Dissociation

Design a macrocyclic ligand in a complex that can be converted into a linear chelating ligand following cleavage via a ligand reaction

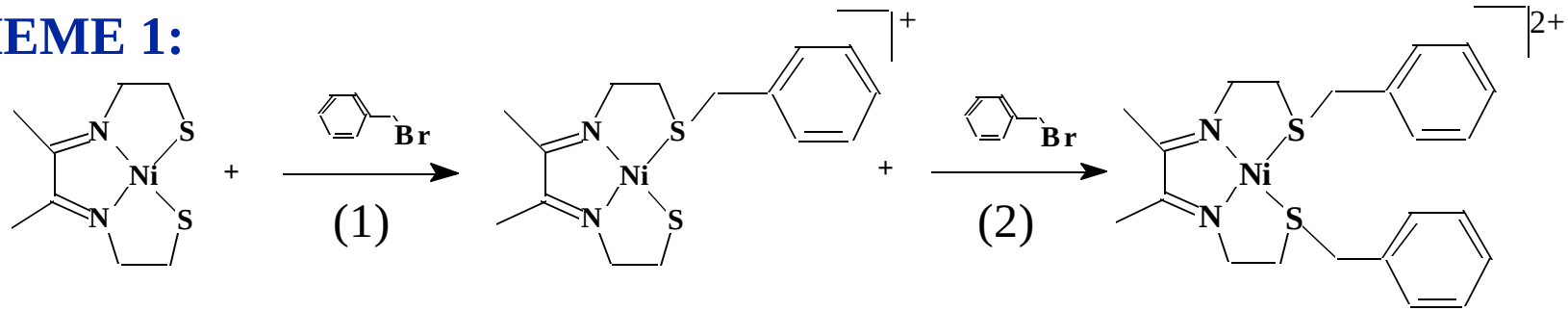


TEMPLATE MACROCYCLIZATION AS A MEANS TO ACCELERATE BINDING

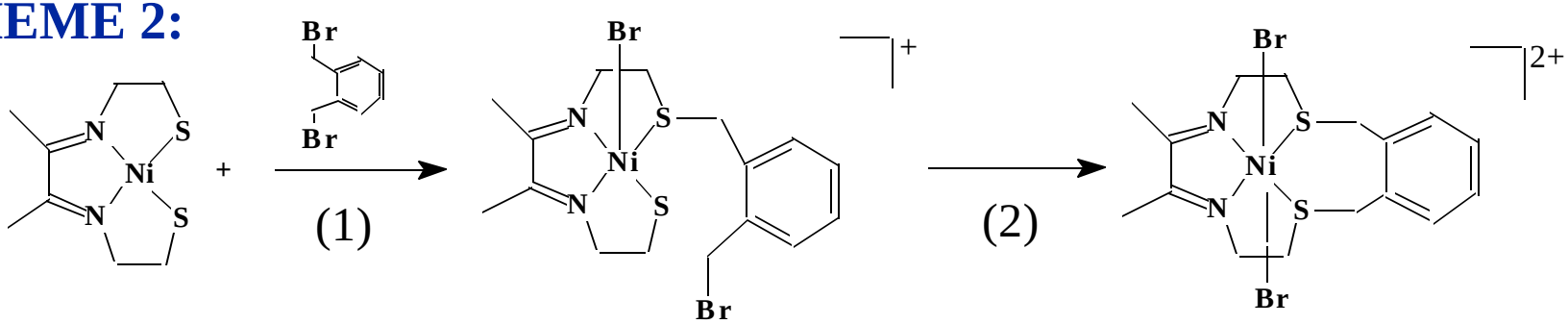
Linear Chelate ⇨ Macrocycle

Supporting Evidence: Blinn, E. L. and Busch, D. H. *Inorg. Chem.*, **7**, 820 (1968).

SCHEME 1:



SCHEME 2:

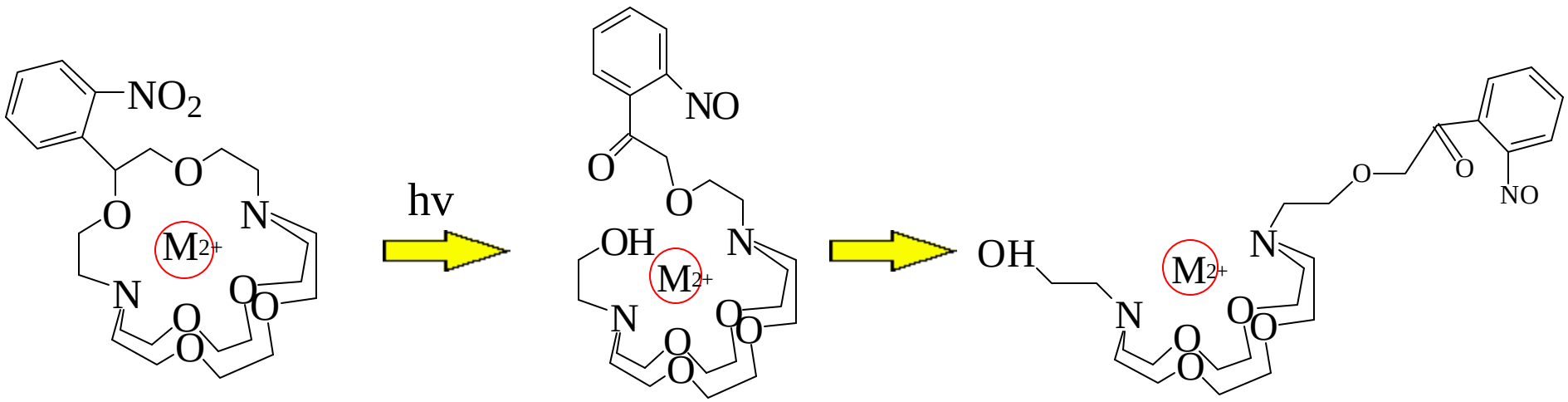


The relative rates of the consecutive steps (1) and (2) change minimally by a factor of 350 between Scheme 1 (monomer) and Scheme 2 (chelate)

PHOTOLYSIS ACCELERATES METAL ION RELEASE BY DECREASING TOPOLOGICAL CONSTRAINTS:

Macrocycle → Linear Chelate

Supporting Evidence: Grell, E. and Warmuth, R. *Pure & Appl. Chem.*, **65**, 373 (1993).
Lehn, J.-M. *et al*. *Helv. Chim. Acta*, **74**, 671 (1991).

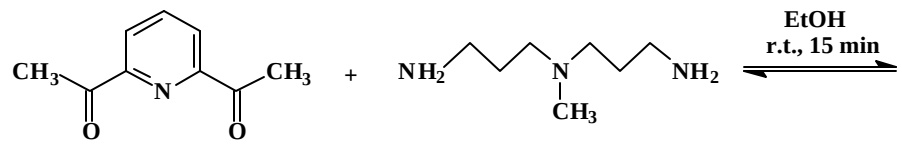


- Developed in research to facilitate concentration jumps
- Ca^{2+} and Mg^{2+} were released in such systems
- Using photolysis, a macrocyclic ligand in a complex can be converted to the corresponding linear ligand, concomitantly releasing the metal ion

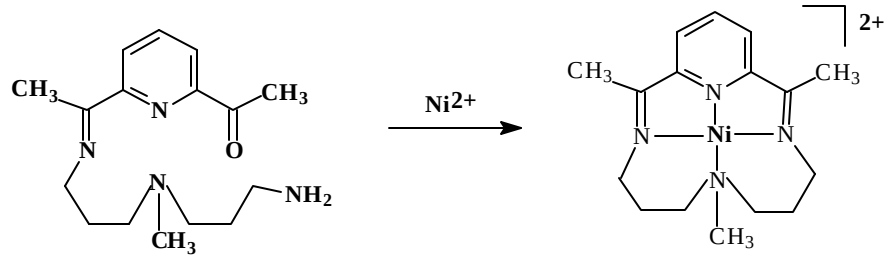
VALIDATION OF CONCEPT

METAL TEMPLATED RING CLOSING STUDIES ON A TERNARY COMPONENT SYSTEM

Pre-equilibration of Ligand Components:



Metal Ion Complexation

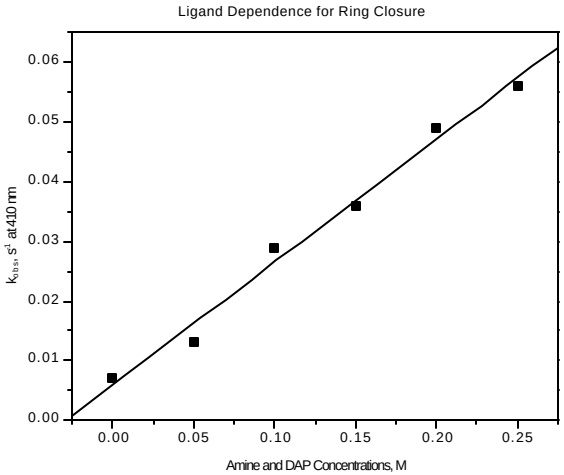


^{1}H NMR, ^{13}C NMR, and IR confirm linear tetradentate generated in situ

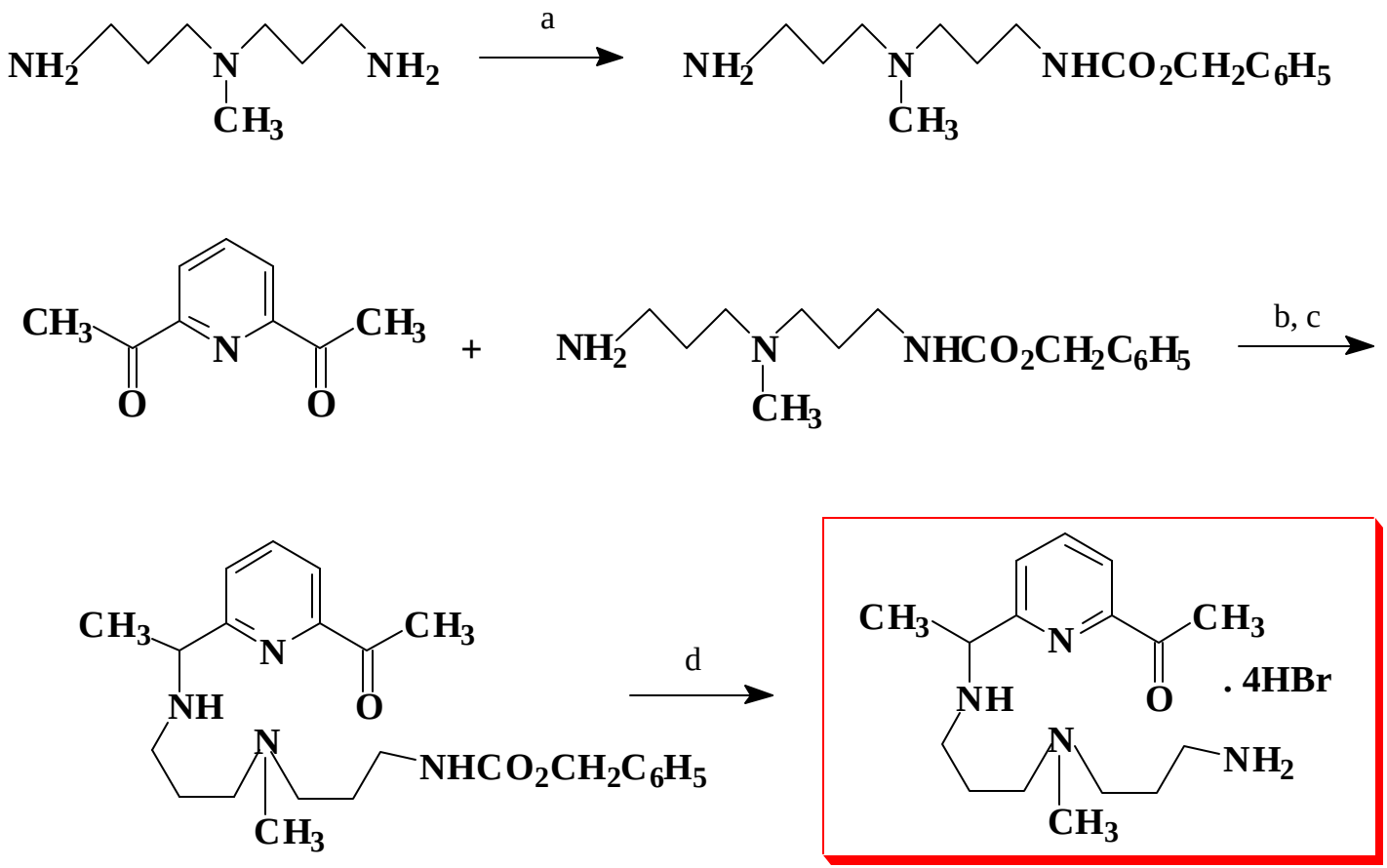
UV/VIS, IR, and MS confirm formation of macrocyclic complex

Kinetic Studies

- Single wavelength UV/VIS scans used to monitor complexation of Ni^{2+} with monocondensed species and subsequent ring closure into complete macrocycle.
- Linear dependence on ligand concentration noted and k, the rate constant of ligand complexation to the metal ion, was found to be 0.21 s^{-1}.
- The rate of consequent ring closure was unobservable, validating the notion that open chain ligands are capable of binding rapidly to form very stable macrocycles.



FIRST GENERATION LIGAND



Structure determined by NMR, IR, MS, and EA.
Overall yield: 60%

a) Benzylchloroformate, EtOH/H_2O, r.t., 8 h b) EtOH, reflux, 24 h, N_2 c) $NaBH_4$, r.t., 24 h, N_2

d) HBr/HOAc, r.t., 12 h, N_2