

# Chelate Cooperativity in Supramolecular Systems

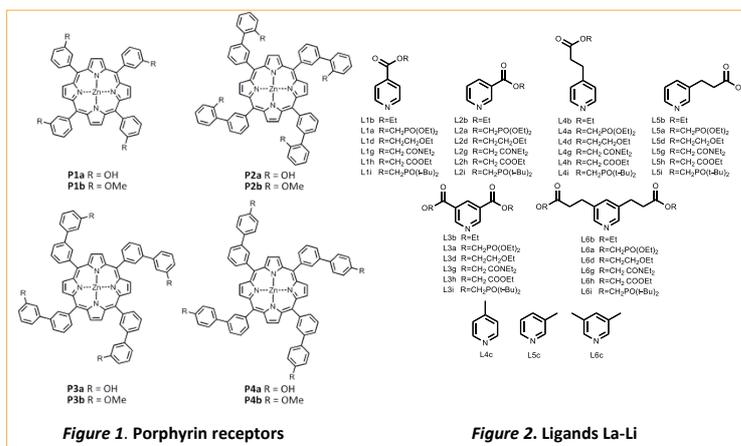
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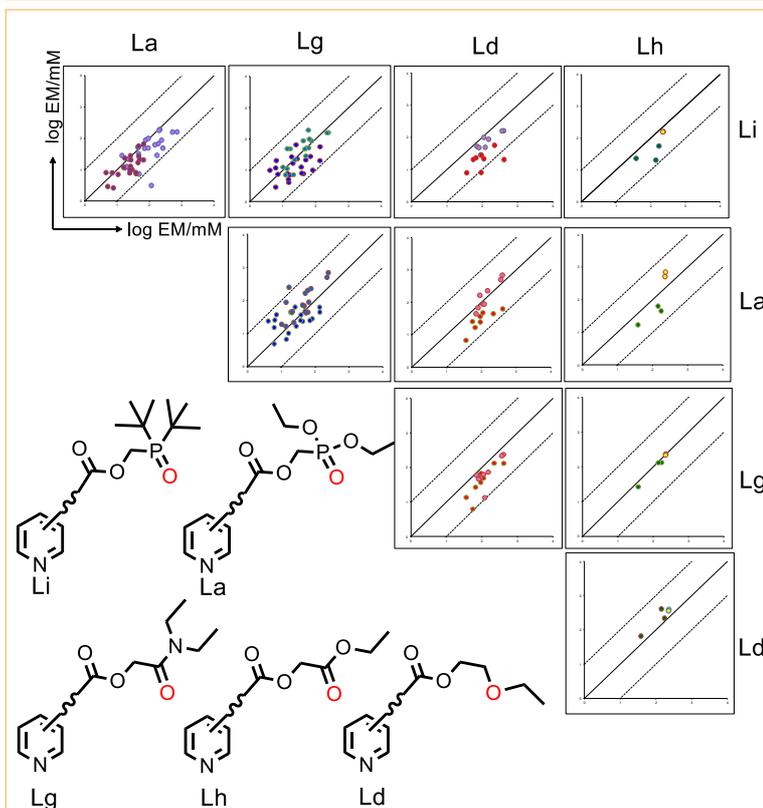
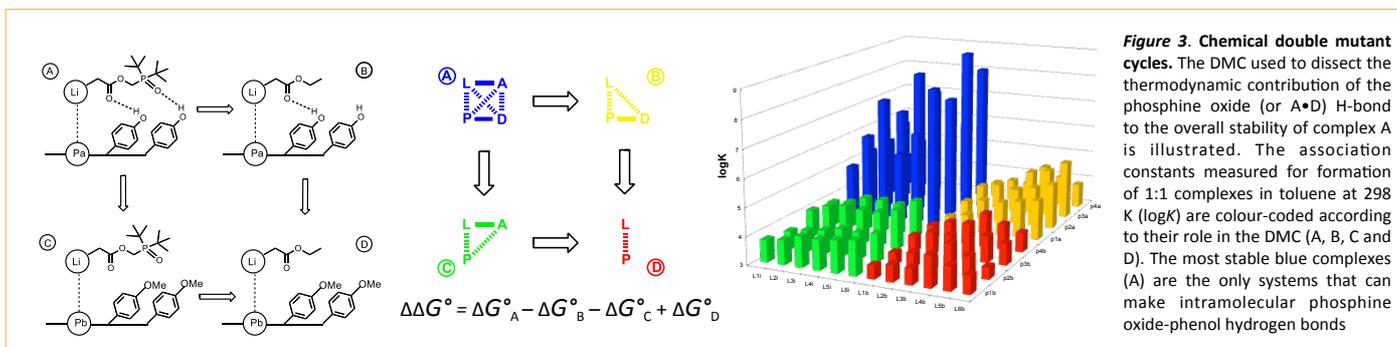
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## INTRODUCTION

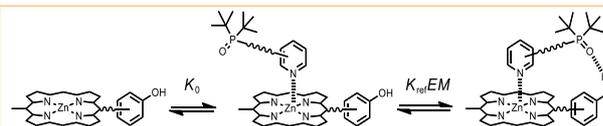
The phenomenon of **cooperativity** pervades supramolecular chemistry and biology.<sup>1</sup> However, the quantification and prediction of the magnitude of cooperative effects in multivalent systems remains a challenge.<sup>2</sup> The contribution of individual functional group interactions to the stability of a complex can be dissected using the **chemical double mutant cycle (DMC)** methodology developed in our laboratory.<sup>3</sup> Through pairwise comparisons, the effect of all secondary interactions can be removed, and we have used this approach to measure the free energy contributions of a series of specific intramolecular hydrogen bonds in zinc porphyrin-pyridine complexes.<sup>4</sup> **Effective molarity (EM)** is used as the key parameter to quantify chelate cooperativity in these systems. This poster compares effective molarities for intramolecular hydrogen bond interactions made with five different functional groups located at the same positions in the supramolecular architecture. The influence of functional group and intrinsic hydrogen bond strength on chelate cooperativity has been quantified by systematically comparing a large body of data on closely related systems.



## Double mutant cycle methodology



## Effective molarity analysis



where  $\sigma_i$  are statistical factors that account for the degeneracies of the partially bound states.

## CONCLUSIONS

For all five types of functional group, the values of EM range from 3 to 700 mM. There is no solvent effect, and the variation in EM with geometric complementarity is also surprisingly small. For systems sharing the same supramolecular framework, the values of EM are the same within an order of magnitude. Trends in EM values are more similar for ligands with similar functional groups. For example, the agreement between the results for ester ligands (Lh) and amide ligands (Lg) is excellent. The data for phosphine oxide ligands (Li) and phosphonate diester ligands (La) are less well correlated, but this is a consequence of the fact that for these very polar functional groups, the intramolecular hydrogen bonds are strong enough to form even in systems with a significant geometric mismatch, which give rise to small EM values that are subject to a large error.

## REFERENCES

- (1) Whitty, A. *Nat Chem Biol.* 2008, 4, 435.
- (2) Hunter, C. A.; Anderson, H. L. *Angew Chem. Int. Ed.* 2009, 48, 7488.
- (3) Cockroft, S. L.; Hunter, C. A. *Chem. Soc. Rev.* 2007, 36, 172.
- (4) Hunter, C. A.; Misuraca, M. C.; Turega, S. M. *J. Am. Chem. Soc.* 2011, 133, 582.